3-Substituted chromones as convenient building blocks for the design and synthesis of functionalized 2-hydroxybenzophenones, 6*H*-benzo[*c*]chromenes, benzo[*c*]coumarins, fused pyridine derivatives, 2-salicyloylfurans and 2-benzoyl-8*H*-thieno[2,3-*b*]indoles

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Declaration

Hereby I declare that this thesis has been written without any assistance from third parties. Furthermore, I confirm that no sources have been used in the preparation of this thesis other than those indicated in the thesis itself.

Erklärung

Hiermit erkläre ich, dass ich die vorliegende Arbeit selbstständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

Iryna Savych

Dezember 2014, Rostock

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"And now these three remain: faith, hope and love. But the greatest of these is love. "

Bible, 1. Corinthians 13

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Iryna Savych, December 2014, Rostock

Abstract

The present thesis is dedicated to the design and synthesis of novel biologically relevant carbo- and heterocycles and describes the synthetic potential of different 3-substituted chromones, namely 3-acyl- and 3-halochromones, illustrated by the domino reactions with different binucleophiles. The reactions of 3-acylchromones with dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone afforded a variety of functionalized 2-hydroxybenzophenones, 6*H*-benzo[*c*]chromenes and benzo[*c*]coumarins, while reactions with heterocyclic ketene aminals proceeded to the formation of various fused pyridine-related heterocycles. An efficient and convenient method for the synthesis of functionalized 2-salicyloylfurans and 2-benzoyl-8*H*-thieno[2,3-*b*]indoles was developed by the cyclization reactions of 3-halochromones with *β*-ketoamides and 1,3-dihydroindole-2-thiones, respectively. Electronic and steric effects play an important role in these reactions with regard to the product distribution. Synthesized compounds are of pharmacological relevance due to their structural similarity to bioactive natural products and synthetic drugs. Various fluorine-containing products were synthesized using 3-perfluoroacylchromones. Some synthesized compounds show promising photophysical properties.

Kurzbeschreibung

Die vorliegende Arbeit ist dem Design und der Synthese von neuartigen biologisch relevanten Carbo- und Heterocyclen gewidmet und beschreibt das synthetische Potential von 3-Substituierten Chromonen, nämlich 3-Acyl- und 3-Halogenchromonen, durch Dominoreaktionen mit verschiedenen Dinukleophilien. Die Reaktionen von 3-Acylchromonen mit Dimethyl 1,3-Acetondicarboxylat und 1,3-Diphenylaceton lieferten funktionalisierte 2-Hydroxybenzophenone, 6*H*-Benzo[*c*]chromene und Benzo[*c*]coumarine, während die Reaktionen mit heterocyclischen Ketenaminalen verschiedene kondensierte Pyridin Derivate lieferten. Eine effiziente und günstige Methode für die Synthese von funktionalisierten 2-Salicyloylfuranen und 2-Benzoyl-8*H*-thieno[2,3-*b*]indolen wurde durch die Zyklisierungsreaktionen von 3-Halogenchromonen mit *β*-Ketoamiden und 1,3-Dihydroindol-2-thionen entwickelt. Elektronische und sterische Effekte spielen eine entscheidende Rolle in diesen Reaktionen. Synthetisierte Verbindungen sind pharmakologisch relevant wegen ihrer Strukturähnlichkeit zu biologisch aktiven natürlichen und synthetischen Produkten. Verschiedene fluorierte Produkte wurden durch den Gebrauch von 3-Fluoroacylchromonen hergestellt. Einige synthetisierte Substanzen zeigen vielversprechende Absorption- und Fluoreszenzeigenschaften.

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Chapter 1

Preface

1.1 Task and Motivation

Organic chemistry plays a great role in modern society. This fact can be well illustrated by the synthesis of drugs, new materials for technology, polymers and petrochemical industry.

In 1763, Edward Stone isolated the active ingredient of aspirin.[1] In 1853, acetylsalicylic acid was first prepared by Charles Gerhardt.[2] By the late 1920s, only a few compounds were used as medicals, *e.g.* aspirin, codeine, morphine, nitroglycerin and insulin. In the 1930s, antibiotics including penicillin were discovered.[3, 4] Since then, the development of new drugs increased with a huge speed.

One of the main focuses of modern organic chemistry is the discovery of new biologically active compounds and drugs. An important method for the development of new pharmacologically valuable scaffolds is based on the diversity oriented synthesis of compound libraries, which are inspired by natural products.[5, 6] This method is coupled with high-throughput biological screening. Therefore, development of simple, efficient and convenient methods for the synthesis of target compound collections is an important task for organic chemists nowadays.

Among the various synthetic approaches, those that utilize cascade (domino) reactions of readily accessible starting materials are highly attractive owing to their simplicity and atom economy.[7] Cascade reactions can be a powerful tool to construct diverse combinatorial compound libraries. In this context, 3-substituted chromones can be very good synthetic platforms due to the presence of several reactive centres. The multiplicity of electrophilic centres of 3-substituted chromones allows cascades of elemental steps, which can lead to the selective formation of elaborated molecular architectures.[8-11]

On the other hand, many organofluorine compounds have found their use as pharmaceuticals and agrochemicals.[12] Fluorine-containing compounds often show interesting biological activities, because of the unique properties of the fluorine atom, which is the most electronegative element. Thus, the carbon-fluorine bond is one of the strongest single bond in organic chemistry. As a result, organofluorine compounds are metabolically stable. Moreover,

fluorine acts as a bioisostere of the hydrogen atom due to its small size. In view of these facts, 3-perfluoroacylchromones were suggested as fluorinated building blocks for the synthesis of a variety of perfluoroalkyl-substituted heterocycles.

1.2 3-Substituted chromones as bielectrophiles for domino cyclization reactions

Chromones (4*H*-chromen-4-ones) are an important class of oxygen-containing heterocyclic compounds, which represent a part of the flavonoid family (Figure 1.1).[13] Many natural and synthetic chromone derivatives show a wide range of valuable biological activities, for example, anti-bacterial, anti-fungal, anti-cancer, anti-oxidant, anti-HIV, anti-ulcers, immunostimulators, biocidal, wound healing, anti-inflammatory and immune-stimulatory.[13-16] Chromones have occupied an important place in drug research and nowadays are so-called privileged drug scaffolds.[6, 17] Very recently, Keri *et al.*[14] and Gaspar *et al.*[15] have published excellent reviews related to biological properties of chromones. Some examples of chromone-based compounds, which have found their use as pharmaceutical agents, are shown in Figure 1.2.

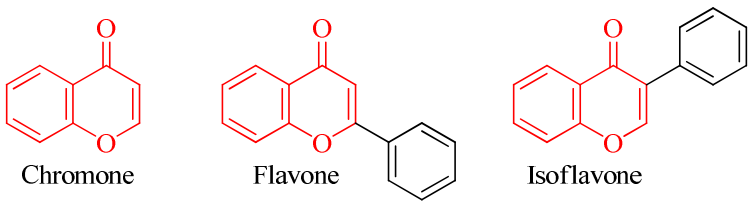


Figure 1.1 Chromone scaffold and flavonoids.

Furthermore, the biological and industrial importance of chromones has led to a considerable amount of synthetic works in the field of these compounds. Nowadays, they are important building blocks in organic chemistry and are used as valuable synthetic intermediates in the preparation of new biologically relevant carbo- and heterocyclic systems.[18-22]

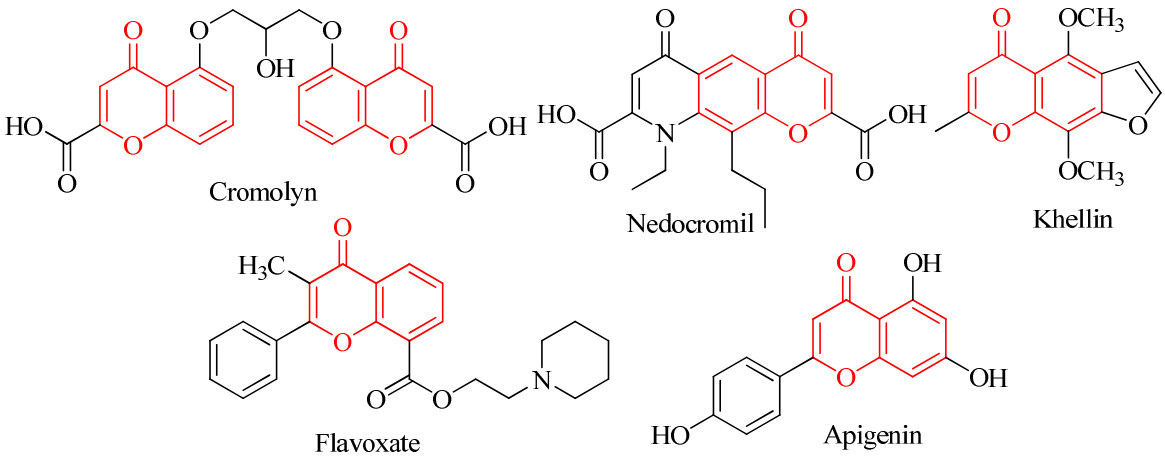


Figure 1.2 Chromone-based compounds used as pharmaceutical agents.

3-Substituted chromones, for instance, 3-halo-,[11] 3-cyano-,[23-25] 3-nitro-,[19, 20] and 3-acylchromones,[28-32] especially 3-formylchromones,[33-43] have received much attention in last decades. One of the reasons behind the interest in 3-substituted chromones as building blocks is the presence of several reactive centres, which allows different domino reactions and formation of more complex molecules.

3-Acylchromones are highly reactive molecules, which possess three electrophilic centres, namely C-2 and C-4 carbon atoms of the chromone system and carbonyl carbon atom of the acyl group (3-COR^2), see Figure 1.3. Because of that, they can react with different nucleophiles. The 2-position of 3-acylchromones is the most electrophilic centre, because of electron-withdrawing effects of the oxygen atom O1 and two adjacent carbonyl groups. Hence, the reactions of 3-acylchromones usually proceed *via* initial nucleophilic conjugate addition at the 2-position of chromone. Nevertheless, because of electronic and steric effects, induced by the R^2-substituent and the nature of the nucleophile, the initial attack can also be directed to the carbonyl group COR^2.

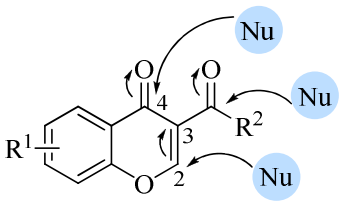
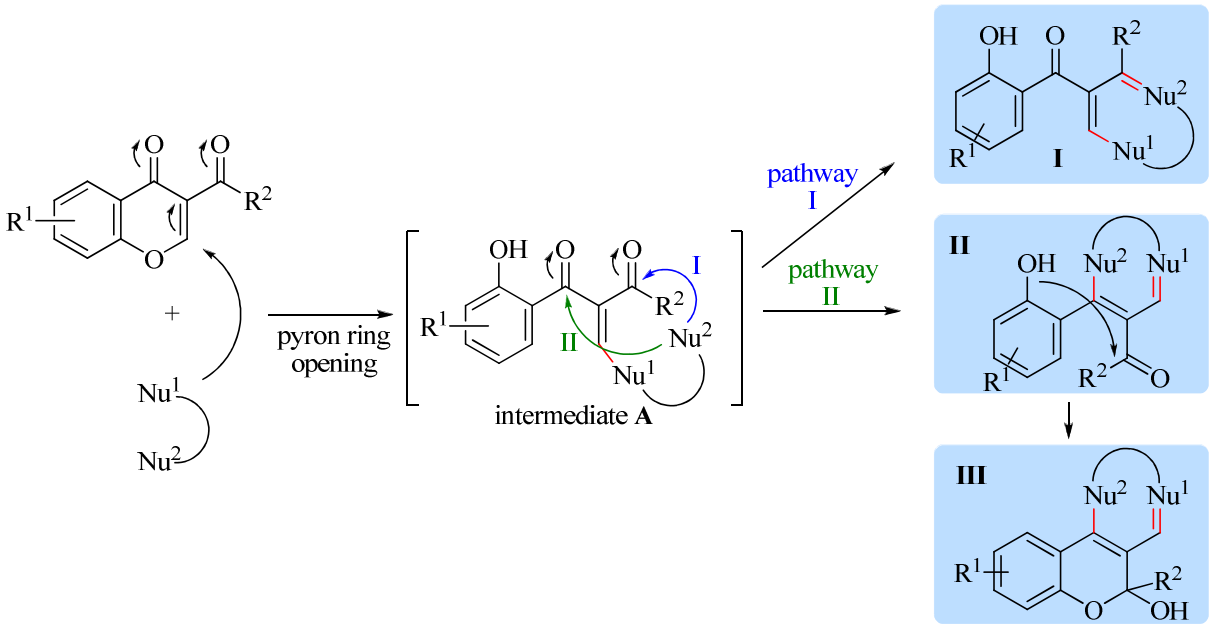


Figure 1.3 Reactive centres of 3-acylchromones.

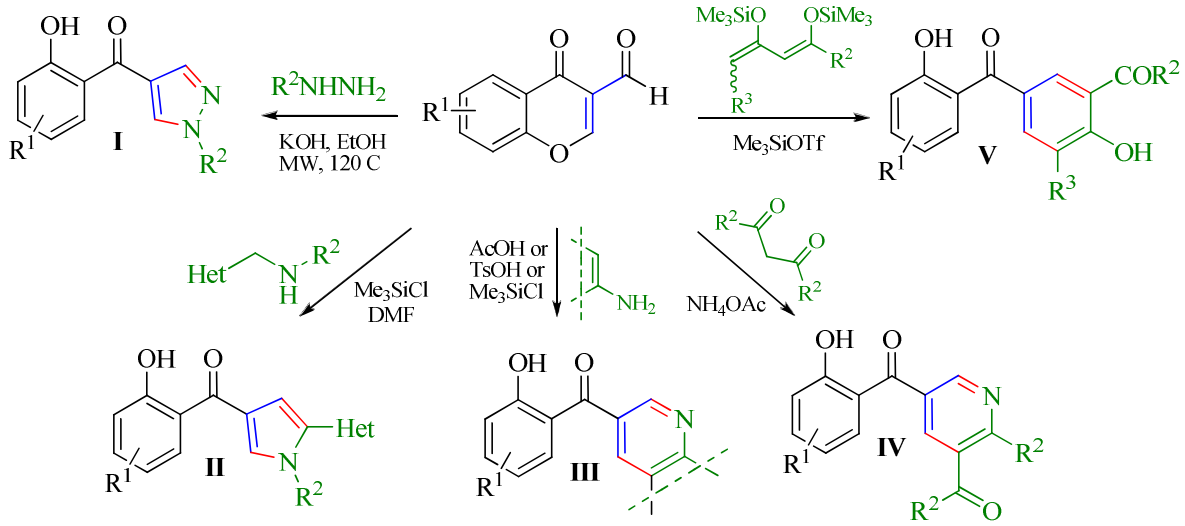
According to the literature, the opening of the γ-pyrone ring of the chromone moiety, which leads to the formation of *β*-dicarbonyl intermediate **A**, is characteristic for the reactions of 3-acylchromones with binucleophiles (Scheme 1.1).[10] Ergo, 3-acylchromones can be considered as 1,3-dicarbonyl compounds with a masked salicyloyl fragment. *β*-Dicarbonyl intermediate **A** is capable of different intramolecular cyclizations. Two main general directions of the reaction are possible in this step, see Scheme 1.1. The second nucleophilic attack can be directed to the acyl carbonyl group COR^2 (pathway I) or to the carbonyl carbon atom of the formed salicyloyl moiety (pathway II). Pathway II is often accompanied by additional cyclization of the phenolic hydroxyl group with remaining acyl carbonyl group. Nonetheless, other additional cyclizations can take place as well. In summary, different functionalized salicyloyl derivatives (structure I) or fused heterocycles (structure III) can be synthesized (Scheme 1.1).[8-10] In the next chapters, based on the general Scheme 1.1, I will discuss possible mechanisms of the reactions of 3-acylchromones, which are studied in this work.



Scheme 1.1 General possible pathways of the reactions of 3-acylchromones with binucleophiles.

3-Formylchromone is the simplest representative of 3-acylchromones and was first synthesized in the early 1970s. This chromone is well investigated and widely used in the synthesis of heterocycles. Excellent reviews, related to the chemical behaviour of 3-formylchromones towards various nucleophiles, were published by Ghosh *et al.*,[8] Ali *et al.*[9] and Plaskon *et al.*[10] It was shown that 3-formylchromones can react with simple nucleophiles,

specifically with amines or methylene active compounds, as ordinary aromatic aldehydes, where only formyl group is participating in the reaction.[10] But, these reactions are less typical for 3-formylchromones, because of the presence of several active centres, which can take part in the reaction. In most common cases, 3-formylchromones react as 1,3-bielectrophiles *via* C-2 carbon atom and aldehyde moiety, because of the higher reactivity of these centres compared to the C-4 carbon atom. Though, it should be noticed that it is difficult to determine which part of 3-formylchromone reacts at first: C-2 carbon atom or aldehyde group. Such reactions usually proceed with γ-pyrone ring opening accompanied by further recyclization (pathway I, Scheme 1.1). This direction of chemical behaviour of 3-formylchromones can be illustrated by numerous reactions.[10] The most well-known and studied of them are presented in the Scheme 1.2.



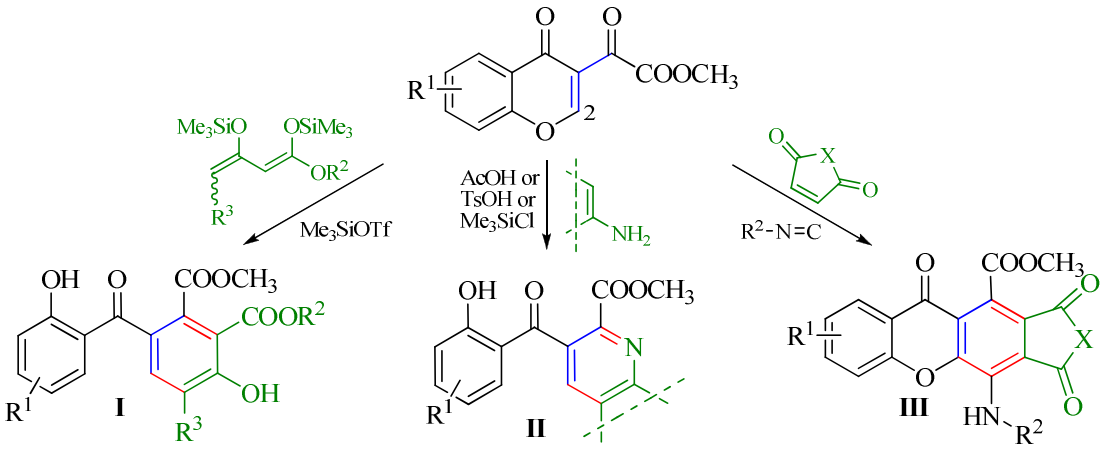
Scheme 1.2 Reactivity of 3-formylchromones towards different binucleophiles.

In this way, different heterocycles, such as pyrazoles (structure I), pyrroles (structure II) and hetero-fused pyridine (structure III) derivatives, were synthesized *via* reactions of 3-formylchromones with aryl hydrazines, hetarylmethylamines and aminoheterocycles, respectively (Scheme 1.2).[10] Besides, three-component reactions of 3-formylchromones with active methylene compounds in the presence of ammonia source have attracted much attention and led to the formation of pyridine derivatives (structure IV).[10] In the group of Prof. Langer, 3-formylchromones, as well as 3-acetylchromones, have received much attention in domino "Michael-retro-Michael-aldol" reactions with 1,3-bis-silyl enol ethers, which proceeded to the formation of different 2-hydroxybenzophenones (structure V).[38, 44-47] In summary, reactions of 3-formylchromones with different binucleophiles are a valuable approach to the synthesis of

various salicyloyl derivatives containing carbo- or heterocycles. Also, after the initial attack to the C-2 atom of 3-formylchromone, the second nucleophilic attack can occur at the C-4 atom (pathway II) followed by additional cyclization (structure III, Scheme 1.1). Thus, reactions of 3-formylchromones with amidines, guanidines and urea under alkaline gave 5-hydroxybenzopyrano[4,3-*d*]pyrimidine derivatives.[10] However, other examples of such reactions are rare. Finally, 3-formylchromones, as well as 3-acetylchromones, can take part in heterodiene cycloaddition or other ring annulation reactions.[10, 48-52]

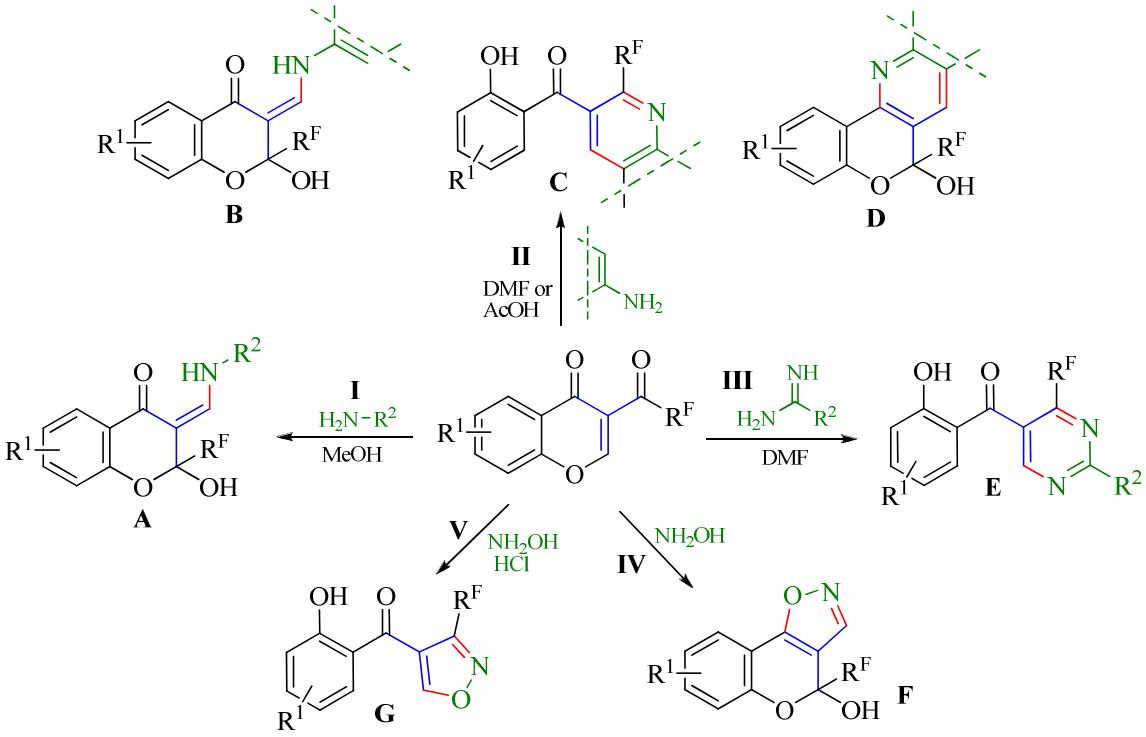
It was proposed that the introduction of electron-withdrawing groups, like methoxalyl, polyfluoroacyl or aroyl (which also contain electron-withdrawing groups, for example, nitro-group), into the 3-position of chromone can increase its reactivity towards nucleophiles and provide new synthetic applications of this important oxygen-containing heterocyclic system.

3-Methoxalylchromone containing an additional ester group was first synthesized by the group of Prof. Langer in 2010.[31] Its reactions with 1,3-bis-silyl enol ethers (1,3-*C*,*C*-binucleophiles) and electron-excessive aminoheterocycles (1,3-*C*,*N*-binucleophiles) proceeded to the formation of functionalized 2-hydroxybenzophenones (structure I)[28] or 2-salicyloylpyridines (structure II),[29, 31] respectively (Scheme 1.3). Very recently, Bornadiego *et al.* reported the synthesis of polysubstituted 4-aminoxanthones (structure III) *via* multicomponent reactions using 3-methoxalylchromone.[53] Noteworthy, in all these mentioned reactions, 3-methoxalylchromone reacted *via* C-2 carbon atom and carbonyl carbon atom $\underline{C}OCOOCH_3$ with a very good regioselectivity. Although there are only few reports dedicated to the reactivity of 3-methoxalylchromones, these chromones have already proven themselves as promising building blocks for the synthesis of new carbo- and heterocycles.



Scheme 1.3 Reactivity of 3-methoxalylchromones in reactions with binucleophiles.

Other useful examples of 3-substituted chromones, namely 3-polyfluoroacylchromones, were first synthesized by the group of Prof. Yokoe in the early 1990s.[32] Since then, they have attracted much attention as fluorinated building blocks for the synthesis of a wide variety of polyfluoroalkylated heterocycles. Sosnovskikh *et al.* reported a significant number of articles, related to the reactivity of 3-polyfluoroacylchromones towards *N*,*N*-, *C*,*N*- and *N*,*O*-binucleophiles, *e.g.* primary amines (reaction I),[54, 55] diamines,[56] heterocyclic amines and anilines (reaction II),[57, 58] hydroxylamine (reaction IV), hydroxylamine hydrochloride (reaction V),[59, 60] amidines (reaction III)[61] and hydrazines[62] (Scheme 1.4).



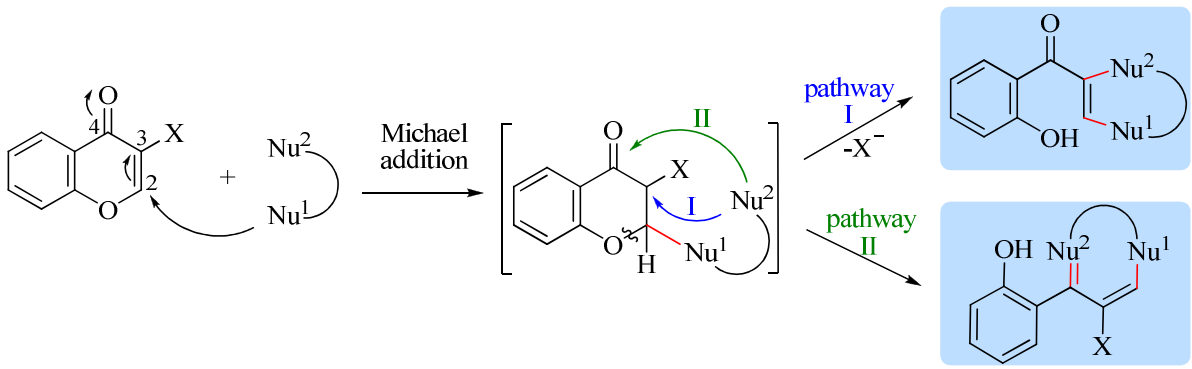
Scheme 1.4 Reactivity of 3-polyfluoroacylchromones towards different binucleophiles.

It is interesting to notice that the formation of a stable cyclic semiketal forms containing the polyfluoroalkyl group is typical for reactions of 3-polyfluoroacylchromones (structures A, B, D, F). However, in some reactions of 3-polyfluoroacylchromones, mixtures of regioisomers due to competing pathways I and II (Scheme 1.1) were obtained. The structures of obtained products are often dependent on the reaction conditions. For instance, in the reaction with heterocyclic amines and anilines, different products (structures B, C, D) were obtained depending on the type of heterocycle and reaction conditions (reaction II, Scheme 1.4).[57, 58] Another example is the reaction with hydroxylamine hydrochloride ($NH_2OH \cdot HCl$, MeOH, reflux), which gave 4-

salicyloylisoxazoles (structure G), while reaction with hydroxylamine ($NH_2OH \cdot HCl$, KOH, MeOH, r. t.) proceeded to the formation of 4*H*-chromeno[3,4-*d*]isoxazol-4-ols (structure F).[59, 60] Examples of the participation of 3-polyfluoroacylchromones in the reactions with active methylene compounds or other C-nucleophiles are very scarce. Only three-component reactions of 3-polyfluoroacylchromones with acetoacetamide, ethyl acetoacetate and dimedone in the presence of ammonium acetate have been reported.[63, 64]

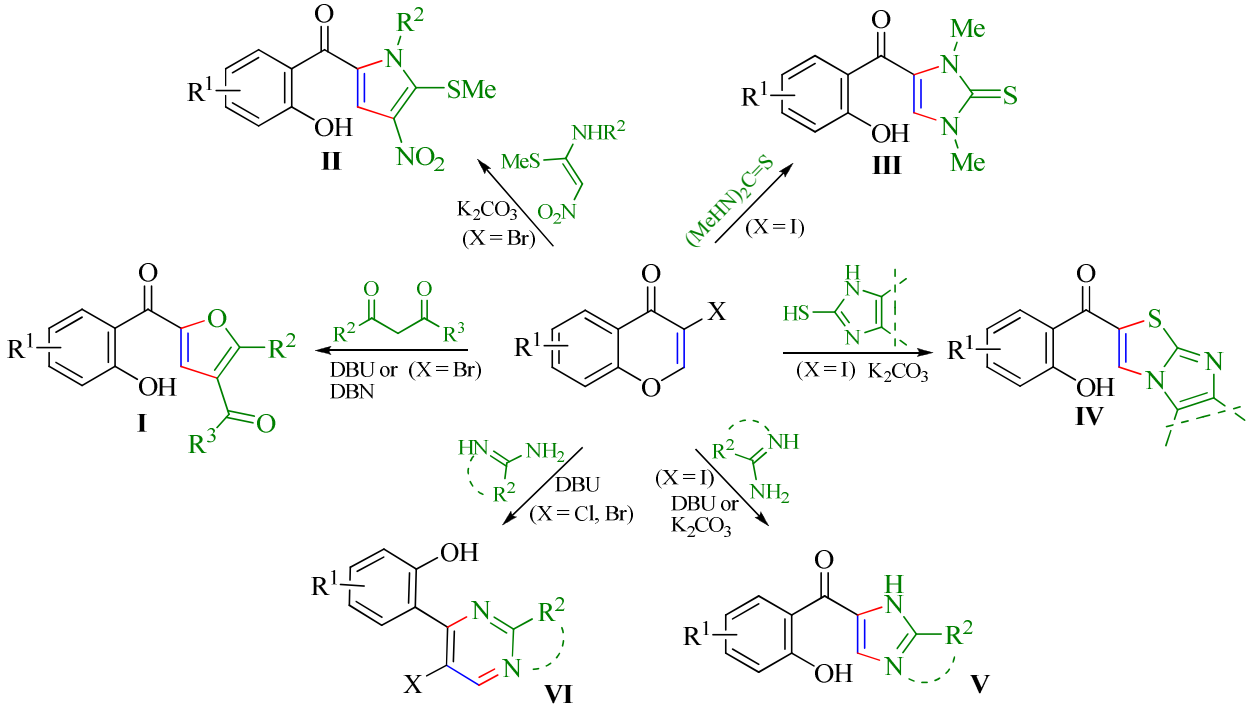
Additionally, due to steric and electronic factors, 3-aroylchromones are less active than 3-methoxalyl- and 3-polyfluoroacylchromones. For this reason, these chromones have not received much attention. Only a few reports, which describe reactions of 3-benzoylchromone with binucleophiles, have been reported.[50, 65-70] In this work, it was proposed to synthesize new 3-aroylchromones, which will be activated by electron-withdrawing substituents located at the aryl moiety, specifically nitro-group or fluorine atom.

3-Halochromones are another class of 3-substituted chromones. They are highly functionalized molecules, which contain an *α,β*-unsaturated carbonyl moiety and a halogen atom as a good leaving group,[71] and are used for the synthesis of various heterocycles.[11, 52, 72-74] Sosnovskikh *et al*. reported a very informative review related to the synthesis and reactivity of 3-halochromones towards different substrates.[11] It was shown that different reactions of 3-halochromones with simple nucleophiles can proceed to the syntheses of 3-substituted chromones,[11, 75] 2,3-methanochromanones,[76] 2-substituted chromones[77] and benzofuranone derivatives.[11] In contrast, it should be noted that data on the reactions of 3-halochromones with binucleophiles are scarce. The reported transformations of 3-halochromones with binucleophiles show that, in general, there are two characteristic pathways of these reactions (Scheme 1.5).



Scheme 1.5 Possible pathways of 3-halochromones in reactions with binucleophiles.

In this way, similar to other 3-substituted chromones, the first attack of binucleophile usually takes place at the carbon atom in the 2-position of 3-halochromones. The second nucleophilic attack can be directed to the carbon atom attached to the halogen (pathway I) or to the carbonyl group (pathway II). As a result, new synthetic ways can be developed for the synthesis of different salicyloyl derivatives (pathway I) or highly functionalized phenols (pathway II). The most attention have attracted the reactions of 3-halochromones with 1,3-binucleophiles (Scheme 1.6). Commonly, they proceeded *via* pathway I giving different five-membered heterocycles, for example, furan (structure I), pyrrole (structure II), imidazole-2-thione (structre III) and imidazo[2,1-*b*]thiazole (structure IV)[73] derivatives.[11] Besides, it is known that 3-bromo- and 3-chlorochromones reacted with amidines *via* pathway II and gave 2-(5-chloropyrimidin-4-yl)phenols (structure VI),[78] while the reaction of 3-iodochromones proceeded to the formation of imidazole derivatives (structure V).[79] It might be explained by the fact that iodine atom is a better leaving group than chlorine atom. Even so, it is necessary to mention that examples of formation of six-membered heterocycles are very rare.[80] All these data illustrate the effectiveness of 3-halochromones as building blocks for the synthesis of different salicyloyl derivatives containing five-membered heterocycles.



Scheme 1.6 Reactivity of 3-halochromones towards different 1,3-binucleophiles.

In conclusion, all these above discussed facts show that transformations of 3-substituted chromones, such as 3-acylchromones and 3-halochromones, with binucleophiles demonstrate the broad synthetic potential of these compounds. Their high reactivity ensures the existence of several pathways of reaction. On the one hand, this diversity of properties complicates prediction of the structures of the final products, but, on the other hand, this fact makes 3-acyl- and 3-halochromones attractive objects for further studies from the point of their chemo- and regioselectivity.

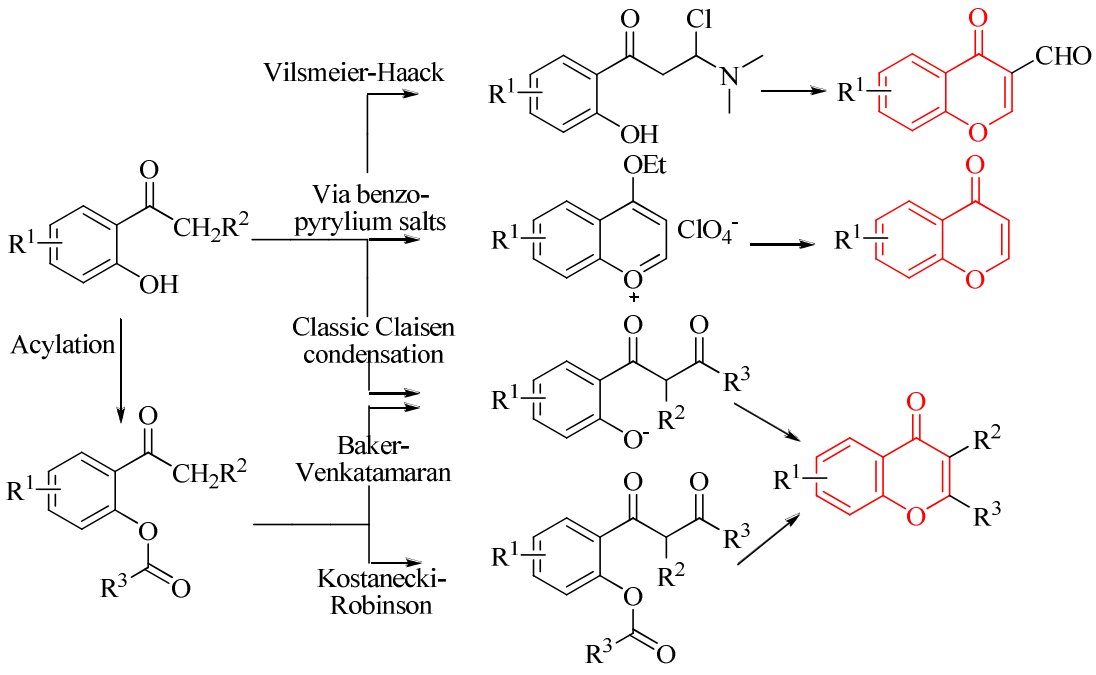
In view of the various unique biological properties and a great synthetic potential of different chromones as building blocks, this thesis is dedicated to the design and synthesis of novel biologically relevant carbo- and heterocycles based on the domino reactions of 3-substituted chromones, namely 3-acylchromones (3-methoxalyl-, 3-polyhaloacyl-, 3-aroylchromones) and 3-halochromones, with various substrates, like 1,3-*C*,*C*-, 1,3-*C*,*N*-, 1,3-*C*,*O*- and 1,3-*C*,*S*- binucleophiles.

Chapter 2

Synthesis of starting materials: 3-substituted chromones

2.1 Introduction

The widespread usefulness of chromones in life sciences has stimulated the development of numerous methodologies for their synthesis. For this reason, a range of well-established classical methods for the synthesis of chromones is available and has been well documented in reviews reported by Ellis *et al.*[81] and Gaspar *et al.*[15] In general, the synthesis of chromones can be attained using phenols (for example, *via* Simonis or Ruhemann reactions), *ortho*-hydroxyarylalkylketones or salicylic acids.[15] One of the most common and widely used routes for the synthesis of chromones involves *ortho*-hydroxyarylalkylketones as starting materials. These methods include Vilsmeier-Haack reaction, Claisen condensation (classic Claisen condensation, Baker-Venkatamaran or Kostanecki-Robinson reactions), as well as reactions *via* benzopyrylium salts (Scheme 2.1).[15]



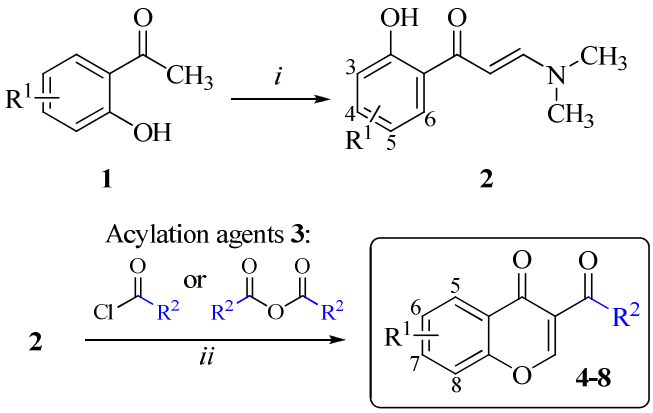
Scheme 2.1 Classic methods of synthesis of chromones using *ortho*-hydroxyarylalkylketones.[15]

Over the years, a big number of modifications of these reactions has been reported. In 1973, the Vilsmeier-Haack reaction using formylating agent (DMF, $POCl_3$) was applied for the first time for the synthesis of 3-formylchromones.[82] Since then, this methodology is widely used for the synthesis of different 3-substituted chromones.[30-32, 54, 83, 84] In this work, a simple and convenient method, based on the modification of the Vilsmeier-Haack reaction, was chosen for the synthesis of different 3-acylchromones and 3-halochromones.

2.2 Results and discussions

As it was mentioned above, this work describes the reactivity of 3-substituted chromones towards different 1,3-binucleophiles. According to this task, various chromones containing different substituents R^1 in the aryl moiety and different groups at the 3-position, namely acyl groups, containing a variety of substituents R^2, or halogen atoms X, were synthesized (Schemes 2.2 and 2.3).

My initial point was the synthesis of a series of 3-acylchromones **4-8** by a modified Vilsmeier-Haack reaction using procedures reported already in the literature (Scheme 2.2, Table 2.1).[30-32, 54, 83, 84]



Scheme 2.2 Synthesis of 3-acylchromones **4-8**.

Reaction conditions: (*i*) **1** (1.0 equiv.), DMF-DMA (1.5 equiv.), 90 ºC, ≈ 2h;

(*ii*) **2** (1.0 equiv.), **3** (1.1 equiv.), pyridine (3.3 equiv.), DCM or MeCN.

At first, commercially available 2-hydroxyacetophenones **1**, which allowed the variation of substituents R^1, were converted into 3-dimethylamino-1-(2-hydroxyaryl)prop-2-en-1-ones **2** using DMF-DMA. Then, the acylation in the presence of electrophiles **3**, which introduced the functional groups R^2, has resulted in the formation of 3-acylchromones **4-8**. In this way, different 3-methoxalyl-, 3-perfluoroacyl-, 3-aroylchromones and also chromones **7** and **8** were synthesized in good to excellent yields (Table 2.1 (a-c)). Almost in all cases, corresponding acyl chlorides were used as acylation agents **3**. Only for the synthesis of 3-trifluoroacetyl- and 3-pentafluoropropanoylchromones, trifluoroacetyl and pentafluoropropanoyl anhydrides were used, respectively. In addition, the procedure for the synthesis of chromones **5-7** was improved in the acylation step by using MeCN instead of DCM.

Table 2.1 (*a*) Synthesis of 3-methoxalylchromones **4**.

2	**3**	**4**	**R^1**	**R^2**	**Yield,[a] %**
a	**a**	**a***	H	$COOCH_3$	82
b		**b***	6-CH_3	$COOCH_3$	93
c		**c**	7-OCH_3	$COOCH_3$	83
d		**d**	6-Cl	$COOCH_3$	90
e		**e**	6-Cl, 7-CH_3	$COOCH_3$	83
f		**f***	6-Br	$COOCH_3$	95
g		**g**	7,8-benzo	$COOCH_3$	77

* Compounds have already been reported.

[a] Yields of isolated products.

It is necessary to note that 3-perfluoroacylchromones **5** were obtained as a mixture of hydrated and non-hydrated forms (Table 2.1 (*b*)). It was proved according to ^1H and ^{19}F NMR spectral data, which showed two sets of signals. Nevertheless, this fact did not hinder the use of 3-perfluoroacylchromones **5** in further investigations. They were used as intermediates and are not described in this work.

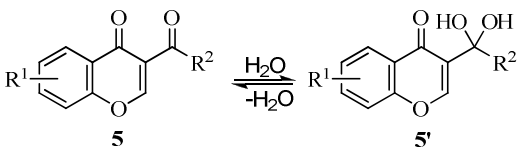
Table 2.1 (*b*) Synthesis of 3-perfluoroacylchromones **5**.

2	3	5[b]	R^1	$R^2 = R^F$	Yield,[a] %
a		**a**[c,*]	H	CF_3	60
c		**b**	7-OCH_3	CF_3	75
d	**b**	**c**	6-Cl	CF_3	84
f		**d**	6-Br	CF_3	80
g		**e**	7,8-benzo	CF_3	99
a		**f**[*]	H	C_2F_5	96
b		**g**[*]	6-CH_3	C_2F_5	92
h		**h**[*]	7-CH_3	C_2F_5	88
i		**i**	6-OCH_3	C_2F_5	91
c		**j**[*]	7-OCH_3	C_2F_5	95
j	**c**	**k**	6,7-$(OCH_3)_2$	C_2F_5	67
d		**l**	6-Cl	C_2F_5	99
e		**m**	6-Cl, 7-CH_3	C_2F_5	93
f		**n**	6-Br	C_2F_5	80
k		**o**	7-F	C_2F_5	58
g		**p**	7,8-benzo	C_2F_5	91
a		**q**	H	C_3F_7	76
b		**r**	6-CH_3	C_3F_7	45
c		**s**	7-OCH_3	C_3F_7	36
d	**d**	**t**	6-Cl	C_3F_7	85
e		**u**	6-Cl, 7-CH_3	C_3F_7	86
f		**v**	6-Br	C_3F_7	95
g		**w**	7,8-benzo	C_3F_7	87

[*] Compounds have already been reported.

[a] Yields of isolated products.

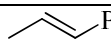
[b] A mixture of hydrated and non-hydrated forms:



5 **5'**

[c] Compound was purified by sublimation and used in non-hydrated form.

Table 2.1 (*c*) Synthesis of 3-aroylchromones **6** and chromones **7**, **8**.

2	3	6	R^1	R^2	Yield,[a] %
a	**e**	**a***	H	Ph	80
a	**f**	**b**	H	2-FC_6H_4	86
a	**g**	**c**	H	2-C_4H_3S	81
a	**h**	**d**	H	2-$NO_2C_6H_4$	70
b	**i**	**e**	6-CH_3	2-$NO_2C_6H_4$	81
c	**j**	**f**	7-OCH_3	2-$NO_2C_6H_4$	79
a	**k**	**g**	H	3-$NO_2C_6H_4$	81
b	**l**	**h**	6-CH_3	3-$NO_2C_6H_4$	85
a	**m**	**i**	H	4-$NO_2C_6H_4$	83
a	**n**	**j**	H	3,5-$(NO_2)_2C_6H_3$	58
a	**o**	**7***	H		68
a	**p**	**8***	H	$CHCl_2$	75

[*] Compounds have already been reported.

[a] Yields of isolated products.

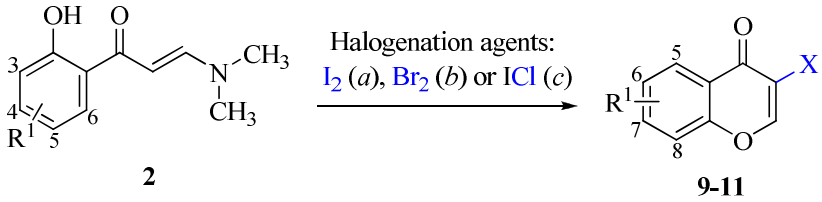
3-Aroylchromones are less reactive than 3-methoxalyl- and 3-perfluoroacylchromones. Therefore, electron-withdrawing groups, for example, nitro-group or a fluorine atom, were introduced into their aroyl moiety to increase their reactivity. In this way, the described protocol was first applied for the synthesis of a series of new 3-aroylchromones **6** (Table 2.1 (*c*)).

Additionally, 3-[(2*E*)-3-phenylprop-2-enoyl]chromone **7** (3-cinnamoylchromone) was prepared. The synthesis of chromone **7** and some other its derivatives has already been reported. However, other synthetic approaches were used.[85, 86] It should be emphasised that almost no data on the chemical properties of this molecule was reported. At the same time, it was found that some chromones, which contain hydrophobic side chain, possess antioxidant and acetylcholinesterase inhibitor activities.[87] In the context of this work, it was assumed that the presence of a double bond as an additional reactive centre can allow alternative selectivity in the domino cyclization reactions apart from usual pathways reported for 3-substituted chromones.

Finally, 3-(2,2-dichloroacetyl)chromone **8**, which is a polydentate electrophilic agent utilized for the synthesis of dichloromethylated compounds, was first synthesized and studied by

my colleague Dr. Satenik Mkrtchyan.[30] This chromone was also used for some experiments in the present work.

As a second goal, the series of 3-halochromones **9-11** were prepared starting from already obtained 3-dimethylamino-1-(2-hydroxyaryl)prop-2-en-1-ones **2** by further halogenation using iodine, bromine or iodine monochloride, respectively (Scheme 2.3, Table 2.2).[11, 32, 83] All obtained 3-halochromones **9-11** have already been reported and described. Nonetheless, the synthesis of 3-iodochromones **11** was optimized by using iodine in the presence of pyridine. Almost all obtained 3-halochromones **9-11** were purified by recrystallization from heptane/isopropanol. Only compounds **10a** and **10d** were purified using column chromatography in order to remove a dibrominated by-product. The yields of these compounds were lower.



Scheme 2.3 Synthesis of 3-halochromones **9-11**.

Reaction conditions: (*a*) **2** (1.0 equiv.), I_2 (1.5 equiv.), pyridine (2.0 equiv.), $CHCl_3$; (*b*) **2** (1.0 equiv.), Br_2 (1.1 equiv.), MeCN; (*c*) **2** (1.0 equiv.), ICl (1.3 equiv.), MeCN.

Table 2.2 Synthesis of 3-halochromones **9-11**.

3-Halochromone*	X	R^1	Yield,[a] %
9a	I	H	80
9b	I	7,8-benzo	86
10a	Br	H	49
10b	Br	6-CH_3	74
10c	Br	6-Cl, 7-CH_3	81
10d	Br	7,8-benzo	58
11a	Cl	H	82
11b	Cl	7-OCH_3	86
11c	Cl	7,8-benzo	76

* Compounds have already been reported

[a] Yields of isolated products.

2.3 Conclusions

The scope of the already known protocol of the modified Vilsmeier-Haack reaction was significantly expanded by the synthesis of various new 3-substituted chromones. In the following chapters, the use of synthesized 1,3-bielectrophiles **4-11** in cyclization reactions with different binucleophiles will be considered.

Chapter 3

Reactions of 3-acylchromones with active methylene compounds: Synthesis of 2-hydroxybenzophenones, 6*H*-benzo[*c*]chromenes and benzo[*c*]coumarins

3.1 Introduction

Benzophenones represent a class of natural compounds, which consists of about 300 members and exhibits a great structural diversity and various biological activities, like antifungal, anti-HIV, antimicrobial, antioxidant, antiviral and cytotoxic.[88] Noteworthy, basic skeletons of natural benzophenones contain the structure of 2-hydroxybenzophenone (Figure 3.1). For this reason, 2-hydroxybenzophenone derivatives are attractive targets from the point of their pharmacological properties.[89-94] Furthermore, 2-hydroxybenzophenones are well-known UV-A/B filters widely used in sun-creams and as photostabilizers in cosmetics.[95]

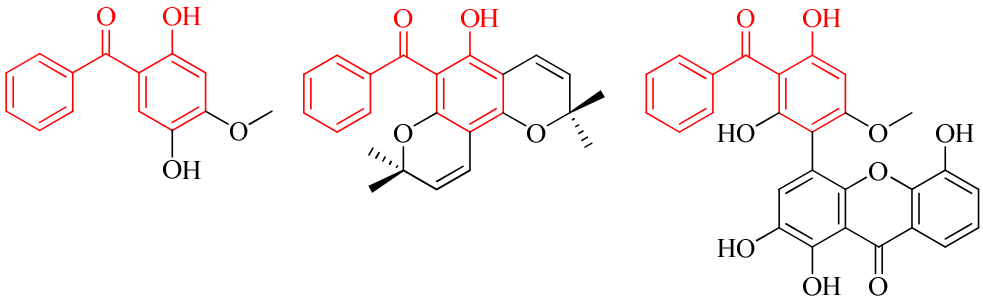


Figure 3.1 Basic skeletons of natural benzophenones.

On the other hand, coumarins are a well-known class of natural products, which are extensively used as biologically active compounds.[96-102] Natural and synthetic coumarins were verified to have antioxidant, antiinflammatory, antibacterial, antifungal,[103] anticoagulating, estrogenic, dermal photosensitizing, vasodilator, analgesic, anticancer,[104, 105] anti-HIV[106] and other activities.[107-109] Also, coumarins are widely used as additives in food, perfumes, cosmetics, also as optical brighteners[110] and fluorescent or laser dyes.[111] Some of the coumarins are of

economic importance. For instance, 3,4-dihydrocoumarin is used in the perfume industry, while 7-hydroxycoumarin found its applications in sun-screens and fluorescent brighteners.[111]

In addition, 6*H*-benzo[*c*]chromen-6-ones occur in a number of pharmacologically active natural products, *e.g.* autumnariol,[99] autumnariniol,[112] alternariol[113] and altenuisol,[102] and are specific inhibitors of the growth of endothelic cells[114] and estrogen receptors.[115, 116] Moreover, dibenzo[*c,h*]chromen-6-ones represent a class of natural antibiotics and antitumor agents, specifically, gilvocarcins, chrymycins and ravidomycins.[117-120] Some of the important biologically active natural 6*H*-benzo[*c*]chromen-6-ones are shown in the Figure 3.2.

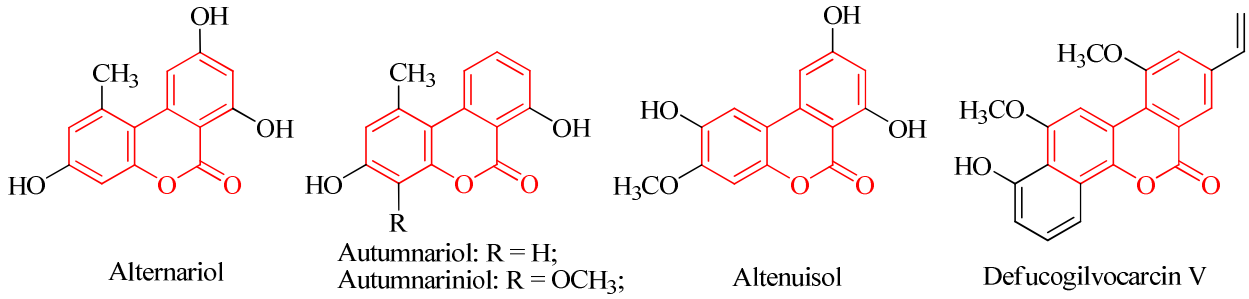


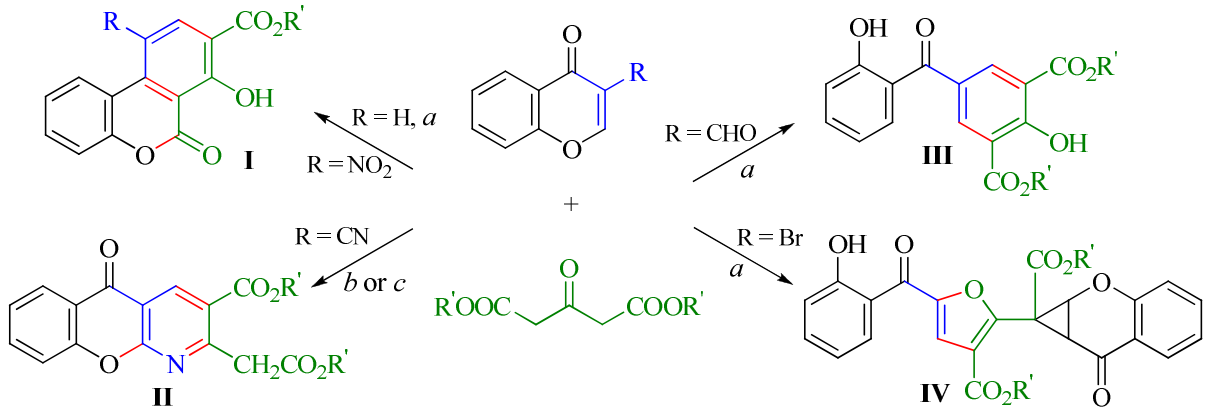
Figure 3.2 Examples of biologically active natural 6*H*-benzo[*c*]chromen-6-ones.

Classical methods for the synthesis of benzophenone derivatives mainly rely on the Friedel-Crafts acylation,[121-124] while coumarins and their derivatives can be synthesized, for example, by Pechmann,[125] Perkin,[126, 127] Knoevenagel,[128] Reformatsky[129] and Wittig[130-133] reactions.[108, 134] Besides, classical methods of the synthesis of 6*H*-benzo[*c*]chromen-6-ones are based on the cyclizations of *o*-bromobenzoic acid with phenols.[135-138] Other modern methods including various metal-catalysed reactions have also been reported.[139-143] Nevertheless, these methods are limited and are often expensive and complex. Therefore, the new routes of synthesis of benzophenones and coumarins are still of great interest due to the wide field of their applications.

As illustrated in Chapter 1, chromones are valuable building blocks in organic chemistry nowadays. The use of the chromone derivatives for the synthesis of 2-hydroxybenzophenones,[144, 145] coumarins[144, 146-152] and 6*H*-benzo[*c*]chromen-6-ones[153-155] has attracted much attention in recent years. Our research group has also reported new routes of the synthesis of functionalized 2-hydroxybenzophenones,[28, 38, 156-160] as well as 6*H*-benzo[*c*]chromen-6-ones,[47, 161-164] by reactions of unsubstituted chromones as well as 3-formyl-, 3-acetyl- and 3-methoxalylchromones. In these cases, 1,3-bis-silyl enol ethers were used as 1,3-*C,C*-

binucleophiles. The examples of the participation of 3-acylchromones in the reactions with other 1,3-*C*,*C*-binucleophiles, which also could proceed to the formation of interesting carbocycles, are very scarce. In this context, dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone were proposed to examine as 1,3-*C*,*C*-binucleophiles in the reactions with 3-acylchromones.

Dialkyl 1,3-acetonedicarboxylates are well-known polyfunctional nucleophiles containing two active methylene components. They have already proven themselves as valuable substrates in the reactions with chromones. In this way, different carbo- and heterocycles were synthesized depending on the substituent in the 3-position of chromone (Scheme 3.1).



Scheme 3.1 Reactions of 3-substituted chromones with dialkyl 1,3-acetonedicarboxylates. *Reaction conditions*: (*a*) DBU, THF; (*b*) DABCO, EtOH, reflux; (*c*) piperidine, MeOH, reflux.

So, the reactions of unsubstituted chromones[165] and 3-nitrochromones[154] with dialkyl 1,3-acetonedicarboxylates proceeded to the formation of benzo[*c*]coumarins (structure I). Interestingly, the nitro-group of 3-nitrochromone did not take part in the reaction. At the same time, 5*H*-chromeno[2,3-*b*]pyridine derivatives were obtained from 3-cyanochromones due to the participation of the CN-group in the domino cyclization reaction (structure II).[166, 167] 3-Formylchromones reacted with dimethyl 1,3-acetonedicarboxylate *via* C-2 carbon atom and formyl group giving functionalized 2-hydroxybenzophenones (structure III), while by the use of 3-halochromone, namely 3-bromochromone, an unexpected compound containing a cyclopropyl ring was obtained as a major product (structure IV).[165] It is necessary to underline that described reactions proceeded under basic reaction conditions in order to activate the methylene components of dialkyl 1,3-acetonedicarboxylate. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) was used for this purpose in almost all cases considered above (reaction conditions (*a*), Scheme 3.1).

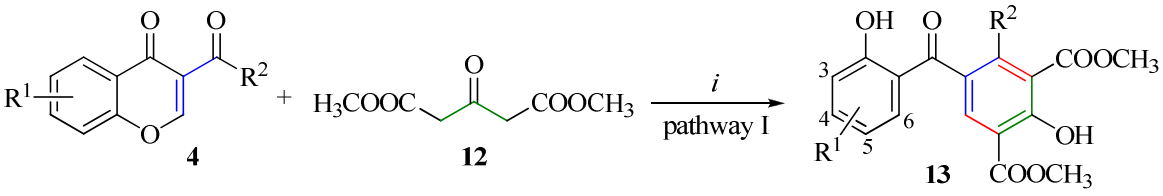
In addition, 1,3-diphenylacetone also contains two methylene carbon atoms. This compound is less reactive than dialkyl 1,3-acetonedicarboxylates due to steric and electronic factors. Nonetheless, 1,3-diphenylacetone is frequently used in aldol condensation reactions with dicarbonyl compounds giving different polyphenyl compounds, which found their use for the synthesis of chromophores[168, 169] and polymers.[170] No data on the reactions of 1,3-diphenylacetone with any chromones was reported before us.

According to the importance of carbocycles, particularly, benzophenones and coumarins, and to the successful results obtained in the chemistry of chromones and dialkyl 1,3-acetonedicarboxylates, I was motivated to study the reactions of different 3-acylchromones, such as 3-methoxalyl-, 3-perfluoroacyl- and 3-aroylchromones, with dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone. One of the main points was the investigation of the influence of the acyl group at 3-position of chromone on the course of the reaction and the structure of obtained products.

3.2 Results and discussions

3.2.1 Reactions of 3-acylchromones with dimethyl 1,3-acetonedicarboxylate

The investigation, related to the reactivity and chemical behaviour of 3-acylchromones **4-6** in the presence of dimethyl 1,3-acetonedicarboxylate **12**, was started by the study of the reactions of 3-methoxalylchromones **4** (R^2 = $COOCH_3$). A test reaction of chromone **4a** with binucleophile **12** was performed under basic reaction conditions using DBU (1.3 equiv), which was well-proven in the reactions of 3-formyl- and other 3-substituted chromones with active methylene compounds,[165] in dioxane at room temperature (Scheme 3.2, Table 3.1). The reaction was carried out approximately 10-12 h until full conversion of the chromone.



Scheme 3.2 Synthesis of compounds **13**.

Reaction conditions: (*i*) **4** (1.0 equiv.), **12** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC.

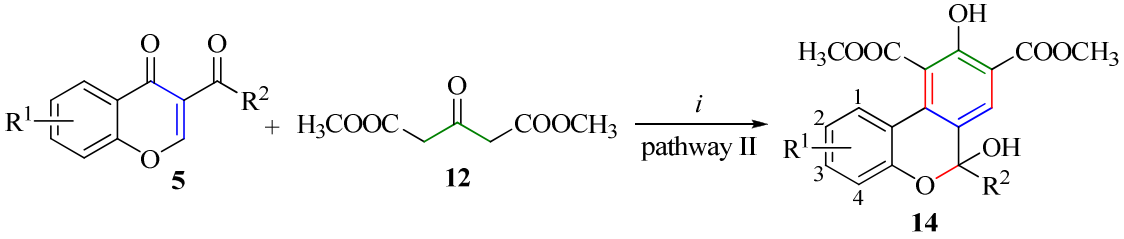
Gratifyingly, the experiment was successful. In spite of the multiplicity of reactive centres of 3-methoxalylchromones, 2-hydroxybenzophenone **13a** was obtained in good yield (74%) with an excellent regioselectivity. Encouraged by the obtained result, the scope and limitation of proposed reaction protocol were next studied. Thus, reactions of 3-methoxalylchromones **4** with dimethyl 1,3-acetonedicarboxylate **12** resulted in the formation of functionalized 2-hydroxybenzophenones **13a-g** with a good regioselectivity in 46-87% yields (Scheme 3.2, Table 3.1). The highest yield (87%) was obtained for compound **13b** (R^1 = 5´-CH_3), while compound **13g** with the largest substituent (R^1 = 3´,4´-benzo) showed the lowest yield of 46%, probably caused by steric effect.

Table 3.1 Synthesis of compounds **13**.

4	R^1	R^2	13	Yield,[a] %
a	H	$COOCH_3$	**a**	74
b	6-CH_3	$COOCH_3$	**b**	87
c	7-OCH_3	$COOCH_3$	**c**	73
d	6-Cl	$COOCH_3$	**d**	72
e	6-Cl, 7-CH_3	$COOCH_3$	**e**	71
f	6-Br	$COOCH_3$	**f**	81
g	7,8-benzo	$COOCH_3$	**g**	46

[a] Yields of isolated products.

Inspired by the obtained results, the reactions of 3-perfluoroacylchromones **5** (R^2 = R^F) with dimethyl 1,3-acetonedicarboxylate **12** under the same reaction conditions were next studied. Surprisingly, the reactions took an entirely different course and gave a series of 6*H*-benzo[*c*]chromenes **14a-u** with good yields in most cases (Scheme 3.3, Table 3.2).



Scheme 3.3 Synthesis of compounds **14**.

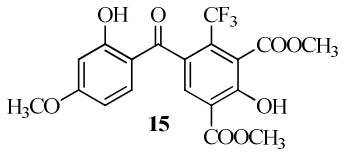
Reaction conditions: (*i*) **5** (1.0 equiv.), **12** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC.

Table 3.2 Synthesis of compounds **14**.

5	R^1	$R^2 = R^F$	14	Yield,[a] %
a	7-OCH_3	CF_3	**a**[*]	21
b	6-Cl	CF_3	**b**	64
c	6-Br	CF_3	**c**	59
d	H	C_2F_5	**d**	65
e	6-CH_3	C_2F_5	**e**	31
f	7-CH_3	C_2F_5	**f**	40
g	6-OCH_3	C_2F_5	**g**[**]	27
h	7-OCH_3	C_2F_5	**h**	65
i	6,7-$(OCH_3)_2$	C_2F_5	**i**	52
j	6-Cl	C_2F_5	**j**	67
k	6-Cl, 7-CH_3	C_2F_5	**k**	57
l	6-Br	C_2F_5	**l**	68
m	7-F	C_2F_5	**m**	33
n	7,8-benzo	C_2F_5	**n**	78
o	H	C_3F_7	**o**	69
p	6-CH_3	C_3F_7	**p**	64
q	7-OCH_3	C_3F_7	**q**	67
r	6-Cl	C_3F_7	**r**	77
s	6-Cl, 7-CH_3	C_3F_7	**s**	71
t	6-Br	C_3F_7	**t**	56
u	7,8-benzo	C_3F_7	**u**	71

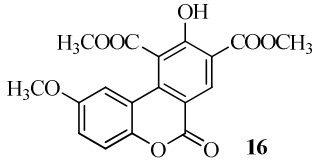
[a] Yields of isolated products.

[*] Besides, compound **15** was isolated in 23% yield (structure see below).



15

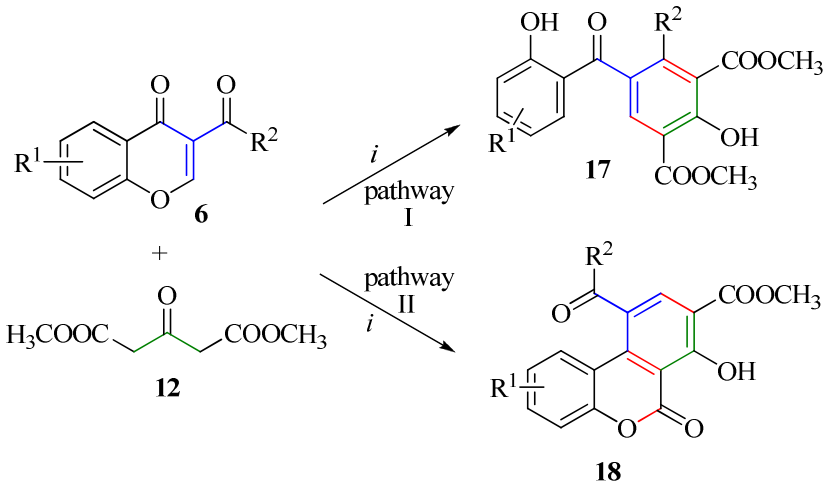
[**] Besides, compound **16** was isolated in 33% yield (structure see below).



16

The study of scope and limitation of the reaction has shown that the present protocol could be applicable to various types of 3-perfluoroacylchromones **5** (R^F = CF_3, C_2F_5, C_3F_7) providing a convenient route for the synthesis of a wide range of the fluorine-containing 6*H*-benzo[*c*]chromenes **14** (Scheme 3.3, Table 3.2). The highest yields were obtained for compounds **14n** and **14u** (R^1 = 3´,4´-benzo). The lowest yields were obtained for the products **14a** and **14g**. The low yield of compound **14a** can be explained by the formation of side-product **15** formed by a competing pathway of the reaction. 2-Hydroxybenzophenone **15** could be isolated in 23% yield, its structure is similar to the obtained 2-hydroxybenzophenones **13** (Scheme 3.2). In contrast, the low yield of **14g** can be explained by the formation of by-product **16** in 33% yield. Apparently, compound **14g** has lost its perfluoroalkyl-group and thereby turned into coumarin **16**. Even so, it should be emphasised that synthesized 6*H*-benzo[*c*]chromenes **14** were stable and could be used for the further investigations. Furthermore, the formation of a stable cyclic semiketal form containing the polyfluoroalkyl group was already observed in reactions of 3-polyfluoroacylchromones (Scheme 1.4).

Motivated by the finding of significant influence of the acyl group of chromone on the course of the reaction, I was next interested to study the reactions of 3-aroylchromones **6** (R^2 = Aryl) with binucleophile **12** using the same reaction conditions (Scheme 3.4, Table 3.3).



Scheme 3.4 Synthesis of compounds **17** and **18**.

Reaction conditions: (*i*) **6** (1.0 equiv.), **12** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC.

It was found that 3-aroylchromones **6a-c** (R^2 = Ph, 2-FC_6H_4, 2-C_4H_3S) in reactions with dimethyl acetonedicarboxylate **12** gave mixtures of 2-hydroxybenzophenones **17** and

benzo[*c*]coumarins **18**. Gratifyingly, compounds **17a-c** and **18a-c** could be isolated by column chromatography in a pure form. At the same time, 3-aroylchromones **6g**, **i**, **j** (Ar = 3-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 3,5-$(NO_2)_2C_6H_3$) containing nitro-group in the reactions with binucleophile **12** delivered 2-hydroxybenzophenones **17d-f** in good yields, 47-83%. Highly interestingly, in contrast, similar reactions of 3-(2-nitrobenzoyl)chromones **6d-f** with substrate **12** proceeded to the formation of benzo[*c*]coumarins **18d-f** with a very good regioselectivity in 72-84% yields. The structures and ratio of obtained products were dependent on the electronic and steric effects of the R^2-substituent of 3-aroylchromones **6**. It will be considered in details by the explanation of a reaction mechanism (see below).

Table 3.3 Synthesis of compounds **17** and **18**.

6	R^1	R^2 = Ar	17	Yield,[a] %	18	Yield,[a] %
a	H	Ph	**a**	49	**a**	27
b	H	2-FC_6H_4	**b**	23	**b**	46
c	H	2-C_4H_3S	**c**	7	**c**	63
d	H	2-$NO_2C_6H_4$	—	—	**d**	72
e	6-CH_3	2-$NO_2C_6H_4$	—	—	**e**	84
f	7-OCH_3	2-$NO_2C_6H_4$	—	—	**f**	73
g	H	3-$NO_2C_6H_4$	**d**	83	—	—
i	H	4-$NO_2C_6H_4$	**e**	47	—	—
j	H	3,5-$(NO_2)_2C_6H_3$	**f**	70	—	—

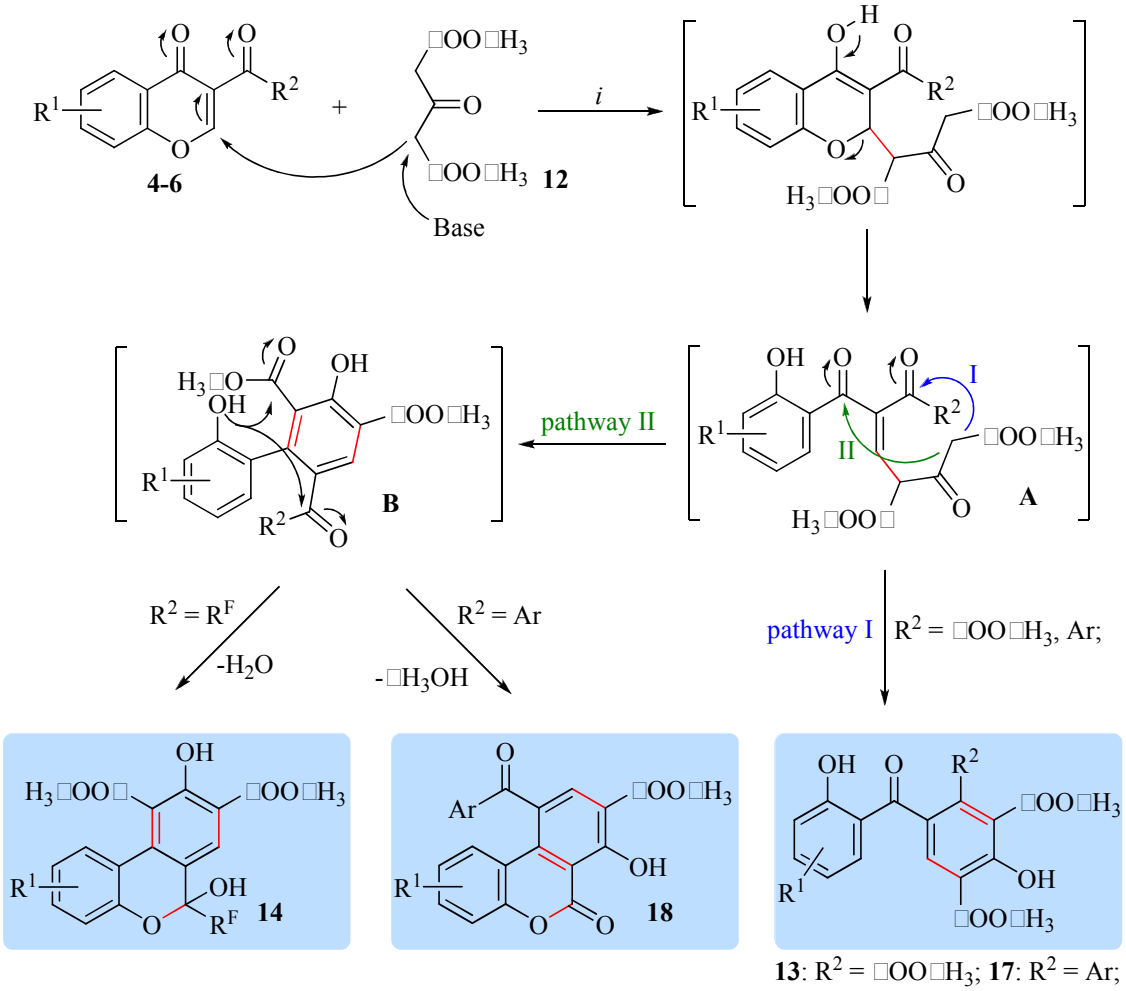
[a] Yields of isolated products.

3.2.1.1 Proposed reaction mechanism

The proposed mechanism of the domino reactions of 3-acylchromones **4**-**6** with 1,3-*C*,*C*-binucleophile, specifically dimethyl 1,3-acetonedicarboxylate **12**, is outlined in the Scheme 3.5.

According to the chemical behaviour of known 3-acylchromones towards binucleophiles, which was described in Chapter 1 (Scheme 1.1), and the structures of synthesized products **13**, **14**, **17** and **18**, it was suggested that all reactions of 3-acylchromones **4**-**6** have started by nucleophilic attack of one of the base-activated CH_2-groups of dimethyl 1,3-

acetonedicarboxylate **12**, directed to the most electrophilic carbon atom C-2 of the chromone. Subsequent opening of the γ-pyrone ring of chromone proceeded to the formation of *β*-dicarbonyl intermediate **A** containing several electrophilic centres (1,4-addition). In general, nucleophilic attack of the second active methylene component (CH_2-group) of binucleophile **12** can be directed to the acyl carbonyl group COR^2 (pathway I) or to the carbonyl carbon atom of the formed salicyloyl moiety (pathway II) (Schemes 1.1 and 3.5).



Scheme 3.5 Proposed reaction mechanism for the formation of compounds **13**, **14**, **17** and **18**. *Reaction conditions*: (*i*) **4-6** (1.0 equiv.), **12** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC.

Ergo, 2-hydroxybenzophenones **13** were formed by reactions of 3-methoxalylchromones **4** *via* the second nucleophilic attack of dimethyl 1,3-acetonedicarboxylate **12**, directed to the acyl carbonyl group COR^2 (pathway I). This trend can be explained by the higher electrophilicity of the carbonyl carbon atom of methoxalyl moiety ($\underline{C}OCOOCH_3$) compared to the salicyloyl

carbonyl group, because of the activating (electron-withdrawing) effect of additional ester group. Noteworthy, the carbonyl group of the ester moiety itself did not take part in the reaction.

In contrast, in the reactions of 3-perfluoroacylchromones **5**, the second nucleophilic attack of binucleophile **12** was directed to the salicyloyl carbonyl group (pathway II). As a result, 6*H*-benzo[*c*]chromenes **14** were formed including further additional intramolecular cyclization of phenolic OH-group with remained-free COR^F-group (see intermediate **B**), delivering cyclic semiketal form (Scheme 3.5). This fact indicates that the perfluoroacyl-group of chromones **5** was less active towards nucleophilic attack of compound **12** than the salicyloyl carbonyl group under the used reaction conditions.

Finally, 2-hydroxybenzophenones **17** (pathway I) and benzo[*c*]coumarins **18** (pathway II) could be synthesized by reactions of 3-aroylchromones **6** with substrate **12**. It should be noticed that coumarins **18** were formed *via* additional intramolecular cyclization of OH-group with carbonyl group of $COOCH_3$ moiety (see intermediate **B**). Further fission of the OCH_3-group led to the formation of the coumarin core (Scheme 3.5).

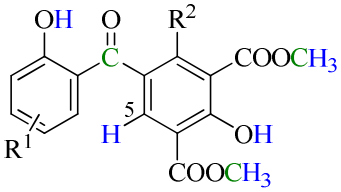
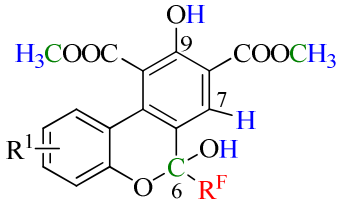
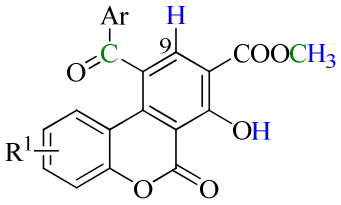
Thus, mixtures of products **17** and **18** were formed by reactions of 3-aroylchromones **6a-c** (R^2 = Ph, 2-FC_6H_4, 2-C_4H_3S) with binucleophile **12**, because of similar electronic and steric properties of aroyl carbonyl COR^2 and salicyloyl carbonyl groups of formed intermediate **A** (Table 3.3, Scheme 3.5). Nevertheless, reaction of chromone **6c** (R^2 = 2-C_4H_3S) proceeded *via* salicyloyl carbonyl group giving compound **18c** as a major product in a good yield (63%), because of the deactivating (electron-donating) effect of thenoyl moiety on the acyl carbonyl group COR^2. At the same time, a slightly activating influence of electron-withdrawing properties of *ortho*-fluorophenylene substituent on the carbonyl COR^2 group caused that the product **17b** was also formed (23%), while product **18b** gave only 46% yield. Obviously, 3-aroylchromones **6g**, **i**, **j** containing electron-withdrawing NO_2-groups, which activate the aroyl moiety COR^2, in reactions with substrate **12** delivered 2-hydroxybenzophenones **17d-f** (pathway I). Formation of coumarins **18d-f** (pathway II) by similar reactions of 3-(2-nitrobenzoyl)chromones **6d-f** can probably be explained by a steric effect of the NO_2-group in *ortho*-position. This phenomenon was also observed for reactions of 3-aroylchromones with electron-rich aminoheterocyles in current study of our group.

In summary, electronic and steric effects of acyl group COR^2 play a great role in the cyclization reactions of 3-acylchromones **4-6** with dimethyl 1,3-acetonedicarboxylate **12** and have a huge influence on the course of the reaction. The structure of obtained products is mainly depend on the intramolecular cyclization step of intermediate **A** (Scheme 3.5).

3.2.1.2 Structure identification

All structures were confirmed by spectroscopic methods, *i.e.* NMR, IR and mass spectrometry, as well as X-ray single crystal analysis. The characteristic signals of compounds **13**, **14**, **17** and **18**, observed from NMR-spectra, are shown in the Table 3.4.

Table 3.4 Observation from NMR analyses for compounds **13**, **14**, **17** and **18**.

Compound	Structure	Characteristic signals in NMR-spectra
13 or **17**		^{1}H NMR: 2 OH: s, δ = 10.5-13.5 ppm; C5-H_{Ar}: s, δ ≈ 8.1 ppm; 3 OCH_3: s, δ = 3.5-4.0 ppm, in the case of **13**; 2 OCH_3: s, δ = 3.5-4.0 ppm, in the case of **17**.
		^{13}C NMR: C=O: s, δ = 192-202 ppm; 3 OCH_3: s, δ = 50-54 ppm, in the case of **13**; 2 OCH_3: s, δ = 50-54 ppm, in the case of **17**.
14		^{1}H NMR: C9-OH: s, δ ≈ 11.0 ppm, C6-OH: d, δ ≈ 9.6 ppm ($^{4}J_{H,F}$ ≈ 4.0 Hz), C7-H_{Ar}: d, δ ≈ 8.1 ppm ($^{5}J_{H,F}$ ≈1.5 Hz); 2 OCH_3: s, δ = 3.5-4.0 ppm.
		^{13}C NMR: if R^F = CF_3: C6: q, δ ≈ 95 ppm ($^{2}J_{C,F}$ ≈ 32.5 Hz), CF_3: q, δ ≈ 122 ppm ($^{1}J_{C,F}$ ≈ 291.0 Hz); if R^F = C_2F_5, C_3F_7: C6: t, δ ≈ 97 ppm ($^{2}J_{C,F}$≈ 27.5 Hz); 2 OCH_3: s, δ = 50-54 ppm.
		^{19}F NMR: if R^F = CF_3: s, δ ≈ -82 ppm; if R^F = C_2F_5: s, δ ≈ -78 ppm, CF_3, two d, δ ≈ -122 and -124 ppm, CF_2, ($^{2}J_{F,F}$ ≈ 279 Hz); if R^F = C_3F_7: s, δ ≈ -80 ppm, CF_3, two dq, δ ≈ -118 and -121 ppm, CF_2, ($^{2}J_{F,F}$ ≈ 285 Hz, $J_{F,F}$ ≈ 8.5 Hz), two d, δ ≈ -123 and -124 ppm, CF_2, ($^{2}J_{F,F}$ ≈ 290 Hz).
18		^{1}H NMR: OH: s, δ = 12.5-13.5 ppm; C9-H_{Ar}: s, δ ≈ 8.1 ppm; OCH_3: s, δ = 3.5-4.0 ppm.
		^{13}C NMR: C=O: s, δ = 188-197 ppm; OCH_3: s, δ = 50-54 ppm.

In the low field of ^{1}H-NMR spectra of 2-hydroxybenzophenones **13** and **17** in DMSO-d_6, two phenolic OH-groups appeared as singlets at δ = 10.5-13.5 ppm. The shift of OH-groups to δ ≈ 11.0 ppm can be explained by hydrogen bond formation involving neighbouring carbonyl group (O-H···O=C). However, the values of chemical shifts of OH-group of the salicyloyl moiety were also dependent on the R^1-substituent. A typical singlet of the aromatic hydrogen atom C5-H_{Ar} could be detected at δ ≈ 8.1 ppm. Expectedly, three and two singlets of OCH_3-groups were observed at δ = 3.5-4.0 ppm for compounds **13** and **17**, respectively. In the ^{13}C-NMR spectra of products **13** and **17**, the salicyloyl carbonyl carbon atom gave a signal in the low field at δ = 192-202 ppm. Additionally, a corresponding number of singlets of OCH_3-groups were observed at δ = 50-54 ppm.

In the low field of ^{1}H-NMR spectra of 6*H*-benzo[*c*]chromenes **14** in DMSO-d_6, three characteristic signals were found, which belong to two OH-groups (δ ≈ 9.6 and 11.00 ppm) and the aromatic hydrogen atom C7-H_{Ar} (δ ≈ 8.1 ppm). The shift of singlet of phenolic C9-OH-group to δ ≈ 11.0 ppm can be caused by the hydrogen bond formation. At the same time, C6-OH-group has not aromatic character (δ ≈ 9.6). It is necessary to note that signals of hydrogen atoms C6-OH and C7-H_{Ar} appeared as doublets, because of the coupling with the fluorine nucleus. In contrast to compounds **13** and **17**, in the low field of ^{13}C-NMR spectra of compounds **14**, no signals of any carbonyl groups were detected. In addition, ^{13}C-NMR analyses gave spectra containing typical quartets at δ ≈ 95 and 122 ppm, caused by the presence of the CF_3-group. In the cases of C_2F_5 and C_3F_7 moieties, it was possible to see only the triplets of the carbon atom C6 at δ ≈ 97 ppm. Other signals of these moieties were too low to be detected due to the multiple C-F couplings. In addition, two singlets of two OCH_3-groups were observed at δ = 3.5-4.0 ppm and δ = 50-54 ppm in the ^{1}H-NMR and ^{13}C-NMR spectra, respectively.

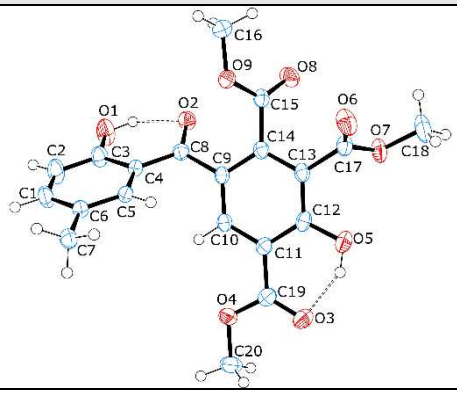
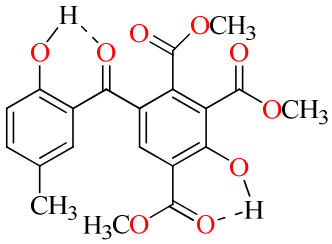
In the ^{1}H-NMR spectra of benzo[*c*]coumarins **18** in DMSO-d_6, the OH-group appeared as a singlet at δ = 12.5-13.5 ppm, indicating the possibility of hydrogen bond formation. A singlet of the aromatic hydrogen atom C9-H_{Ar} could be detected at δ ≈ 8.1 ppm. It is important to mention that, in contrast to the other products **13**, **14** and **17**, in the ^{1}H-NMR spectra of compounds **18**, only one singlet of OCH_3-group was observed (δ = 3.5-4.0 ppm), since the other $COOCH_3$-group, derived from binucleophile **12**, was lost during the cyclization. In the ^{13}C-NMR spectra, aroyl carbonyl group appeared at δ = 188-197 ppm.

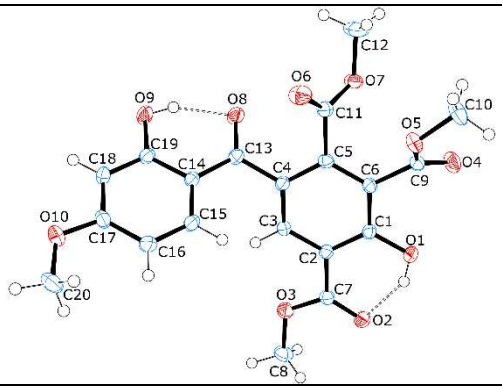
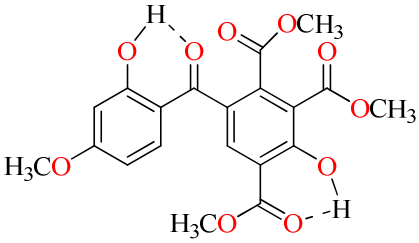
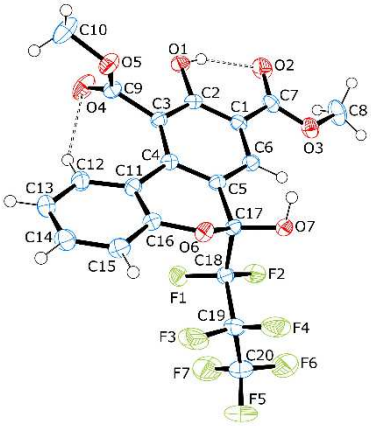
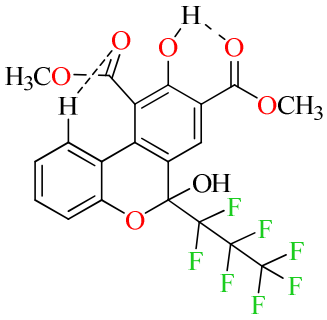
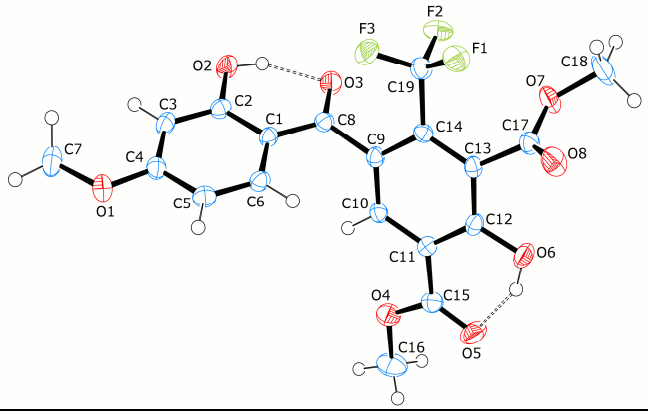
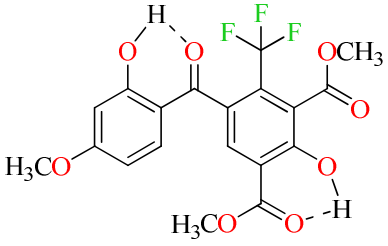
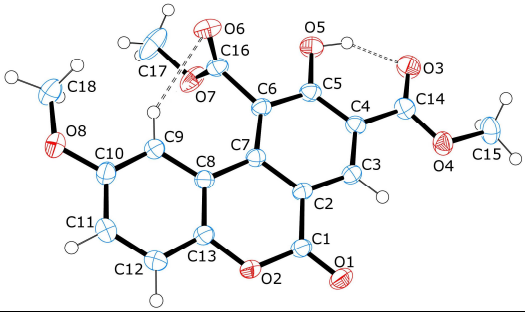
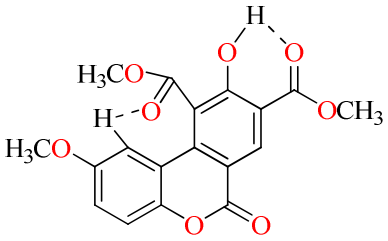
The structures of fluorine-containing compounds **14**, **15**, **17b** and **18b** were also confirmed by ^{19}F-NMR. The CF_3-group appeared as a singlet at δ ≈ -82 ppm. The C_2F_5-group

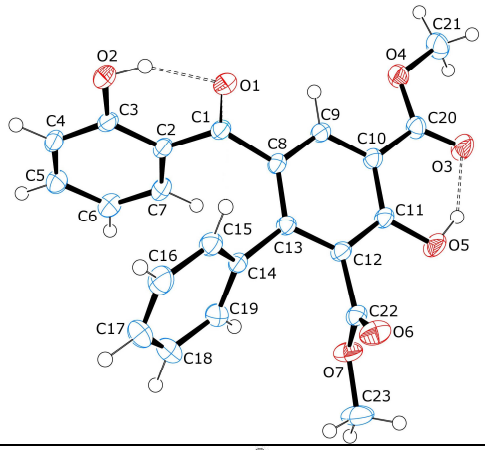
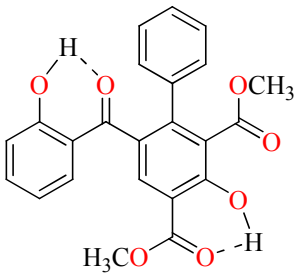
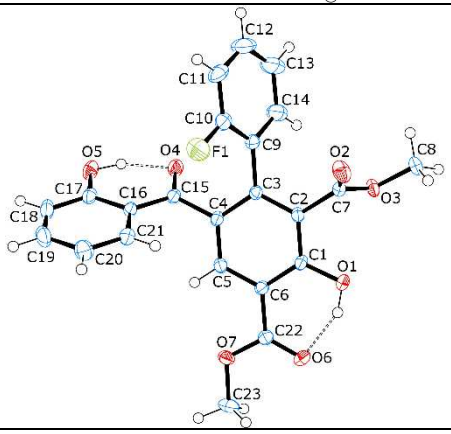
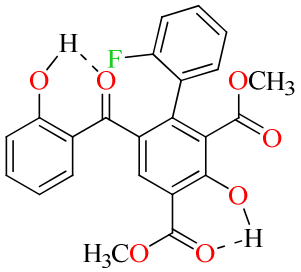
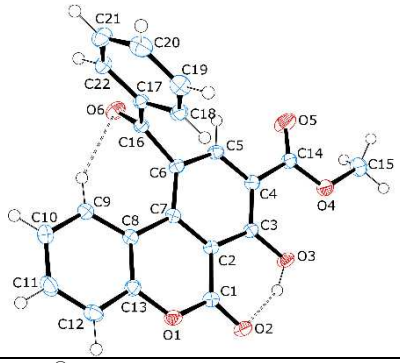
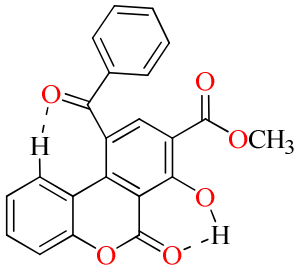
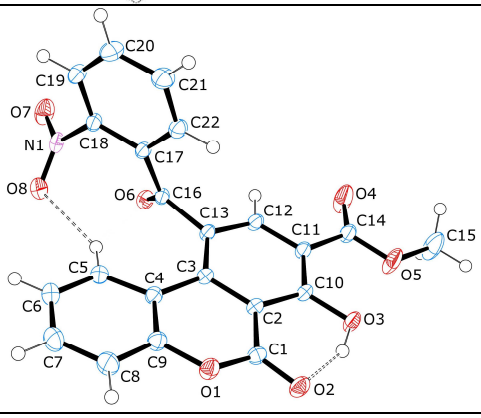
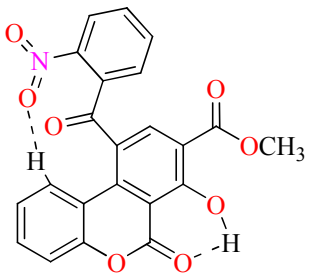
appeared as a singlet at δ ≈ -78 ppm (CF_3-group) and two doublets at δ ≈ -122 and -124 ppm, indicating that two fluorine-atoms of CF_2-group in the C_2F_5 moiety are not equivalent and couple to each other. The C_3F_7-group appeared as a singlet at δ ≈ -80 ppm (CF_3-group), two double quartets at δ ≈ -118 and -121 ppm (CF_2) and two doublets at δ ≈ -123 and -124 ppm (CF_2). The fluorine atoms in aryl moieties of compounds **17b** and **18b** appeared as singlets at δ ≈ -113 and -109 ppm, respectively. Besides, in the ^{13}C-NMR spectra of **17b** and **18b** the corresponding doublets of carbon atoms of the aromatic ring containing a fluorine atom were observed.

Due to the high diversity of potential intramolecular cyclizations of the studied reactions leading to the formation of different regioisomers, X-ray crystal analysis was crucial for initial structure determination. Thus, the structures of compounds **13b, 13c, 14o**, **15**, **16**, **17a**, **17b**, **18a** and **18d** were unambiguously confirmed by X-ray single crystal analyses (Table. 3.5). In addition, X-ray analysis allowed to determine the presence of hydrogen bonds in the crystalline state of compounds due to the values of distances and angles between corresponding groups. A value for such bonds appears by summing the normal bond length of an H-X bond, where X is an electronegative atom, the covalent radius of hydrogen atom and the van der Waals radius of X. The calculated distance of O-H···O is≈ 2.7 Å.[171] Therefore, also in the present work, this value was considered as critical for the determination of plausible hydrogen bond formation.

Table 3.5 Crystal structures of compounds **13b**, **c**, **14o**, **15**, **16**, **17a**, **b** and **18a**, **d**.

Crystal structure	Compound	Structure
	**13b**	

	**13c**	
	**14o**	
	**15**	
	**16**	

	**17a**	
	**17b**	
	**18a**	
	**18d**	

For all 2-hydroxybenzophenones **13b**, **13c, 15**, **17a** and **17b**, X-ray single crystal analyses showed distances of 1.7-1.9 Å between the hydrogen atom of O<u>H</u>-groups and oxygen atom of neighbouring carbonyl groups, indicating the presence of two hydrogen bonds of these groups for each structure. As expected, the molecules of 2-hydroxybenzophenones are not planar. The salicyloyl phenol ring of these compounds is in one plane with the linking carbonyl group twisted out of the plane with a torsion angle of 46-70º to another phenol ring.

6*H*-Benzo[*c*]chromene **14o** and benzo[*c*]coumarin **16** crystallized in a monoclinic system with space groups $P2_1$ and $P2_1/c$, respectively. The space group of the X-ray structure of compound **14o** revealed that the obtained crystal consists of one pure R- or S-enantiomer. The presence of hydrogen bonds (about 1.9 Å) between OH and carbonyl oxygen atom was confirmed by crystal structures of compound **14o** and **16**. Moreover, X-ray structures of described products indicated weak intramolecular non-classical hydrogen bonds, involving aromatic hydrogen atoms[172] (C12-H of **14o**, C9-H of **16**) and the oxygen atoms of carbonyl groups (O4 of **14o**, O6 of **16**) as distances of 2.7 Å and 2.5 Å, respectively.

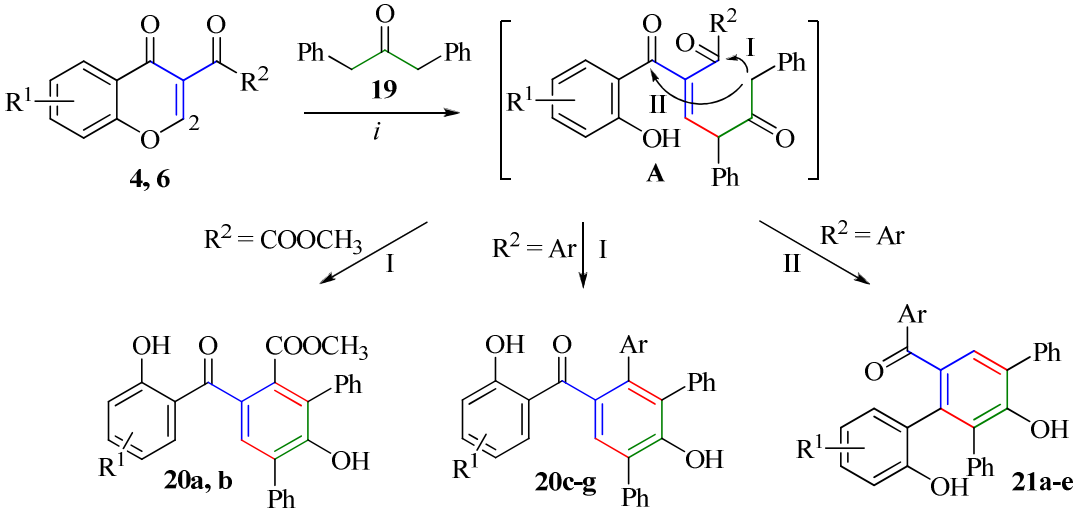
The presence of typical hydrogen bonds, involving an O<u>H</u>-group and the neighbouring C=<u>O</u> group, were indicated also for compounds **18a** and **18d**. In addition, the X-ray structure of **18a** indicated **a** non-classic hydrogen bond (2.6 Å) between the aromatic hydrogen atom C9-H and neighbouring C=O group of aroyl moiety, while crystal structure of **18d** showed similar hydrogen bond (2.4 Å) between the hydrogen atom C5-H and oxygen atom O8 of NO_2-group.

Obviously, the core of benzo[*c*]coumarin moiety of compounds **16**, **18a** and **18d** is planar. In contrast, the structure of 6*H*-benzo[*c*]chromene **14o** is not planar, because of the presence of a quaternary carbon atom C17, whose configuration is near to tetrahedral. The values of angles lie within 104-113º. The theoretic value of a tetrahedral angle is about 109.47º.

3.2.2 Reactions of 3-acylchromones with 1,3-diphenylacetone

Encouraged by the successful results, obtained during the study of the reactions of different 3-acylchromones **4-6** with dimethyl 1,3-acetonedicarboxylate **12**, I was next interested to examine the reaction of 3-acylchromones **4** and **6** with another 1,3-*C*,*C*-binucleophile, such as 1,3-diphenylacetone **19** (Scheme 3.6). The condensations were performed under similar reaction conditions using DBU as a base, but at reflux, because of the less expressed nucleophilic properties of 1,3-diphenylacetone **19** in comparison with substrate **12**.

The reactions of 3-methoxalylchromones **4** with binucleophile **19** proceeded to the formation of 2-hydroxybenzophenones **20a**, **b** in moderate yields (Scheme 3.6, Table 3.6). Similar to the 2-hydroxybenzophenones **13** obtained by reactions of 3-methoxalylchromones **4** with 1,3-*C*,*C*-binucleophile **12**, these products were formed *via* initial 1,4-addition of substrate **19** (CH_2-group) to the C-2 carbon atom of chromone followed by *γ*-pyrone ring opening (intermediate **A**). Subsequent intramolecular nucleophilic attack of the second CH_2-group of **19** was directed to the acyl carbonyl group COR^2 (R^2 = $COOCH_3$), activated by the electron-withdrawing ester group (pathway I, Scheme 3.6, see also Schemes 1.1 and 3.5). Nonetheless, the regioselectivity of these reactions was lower than the regioselectivity of the reactions with substrate **12** (Scheme 3.2, Table 3.1). By-products were observed by TLC. However, it was not possible to isolate them.



Scheme 3.6 Synthesis of compounds **20** and **21**.

Reaction conditions: (*i*) **4**, **6** (1.0 equiv.), **19** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, reflux.

As the next step, I studied reactions of 3-aroylchromones **6** with 1,3-diphenylacetone **19** (Scheme 3.6, Table 3.6). In this way, 2-hydroxybenzophenones **20c-g** (pathway I) and phenols **21a-e** (pathway II) were obtained. It should be emphasised that synthesis of compounds **21** proceeded without additional cyclization involving phenolic OH-group and acyl group COR^2 (R^2 = Aryl), see also Scheme 1.1. As a result, highly functionalized phenols **21** were delivered. Noteworthy, these structures were not obtained by reactions of 3-aroylchromones **6** with substrate **12** due to the presence of active $COOCH_3$-moiety, derived from **12**, which took part in cyclization with phenolic OH-group (Schemes 3.4 and 3.5).

Table 3.6 Synthesis of compounds **20** and **21**.

4 or 6	R^1	R^2	20	Yield, [a] %	21	Yield, [a] %
4a	H	$COOCH_3$	**a**	49	—	—
4f	6-Br	$COOCH_3$	**b**	54	—	—
6a	H	Ph	**c**	32	**a**	25
6c	H	2-C_4H_3S	**d**	29	**b**	18
6d	H	2-$NO_2C_6H_4$	—	—	**c**	59
6e	6-CH_3	2-$NO_2C_6H_4$	—	—	**d**	73
6f	7-OCH_3	2-$NO_2C_6H_4$	—	—	**e**	61
6g	H	3-$NO_2C_6H_4$	**e**	42	—	—
6i	H	4-$NO_2C_6H_4$	**f**	69	—	—
6j	H	3,5-$(NO_2)_2C_6H_3$	**g**	74	—	—

[a] Yields of isolated products.

Specifically, 3-benzoyl- and 3-(2-thenoyl)chromones **6a** and **6c** reacted with 1,3-diphenylacetone **19** to give mixtures of compounds **20c**, **d** (pathway I) and **21a**, **b** (pathway II), which were possible to separate. However, due to the similar physical properties of compounds **20** and **21**, its separation by column chromatography was complicated, causing the losses in yields of isolated products (Table 3.6). The reactions of 3-aroylchromones **6g**, **i**, **j** containing NO_2-groups with binucleophile **19** led to the formation of 2-hydroxybenzophenones **20e-g** with a good regioselectivity in 42-74% yields, because of the activating (electron-withdrawing) effect of the nitro-substituent on the aroyl group COR^2 (pathway I). In contrast, because of the steric effect of the NO_2-group in *ortho*-position of the aroyl moiety COR^2, reactions of 3-(2-nitrobenzoyl)chromones **6d-f** resulted in the synthesis of phenols **21c-e** in 59-73% yields (pathway II).

In summary, all these results are in a good correspondence to the results obtained by the study of reactivity of 3-acylchromones **4** and **6** towards dimethyl 1,3-acetonedicarboxylate **12** considered above. Synthesis of obtained products **20** and **21** can be explained by a similar reaction mechanism *via* β-dicarbonyl intermediate **A** formation, which was described for the reactions of 3-acylchromones **4-6** with binucleophile **12** (Schemes 1.1, 3.5 and 3.6).

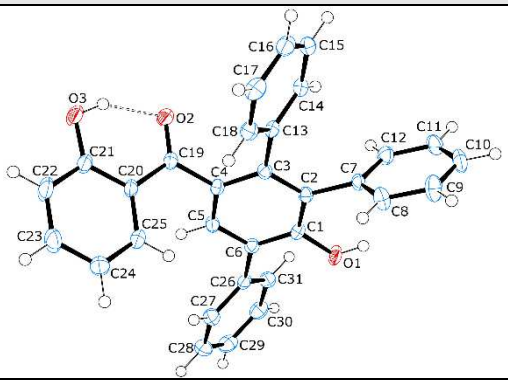
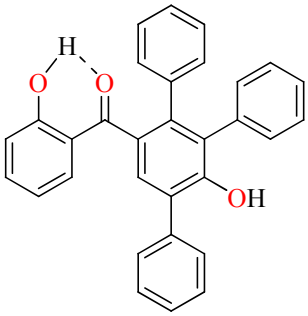
3.2.2.1 Structure identification

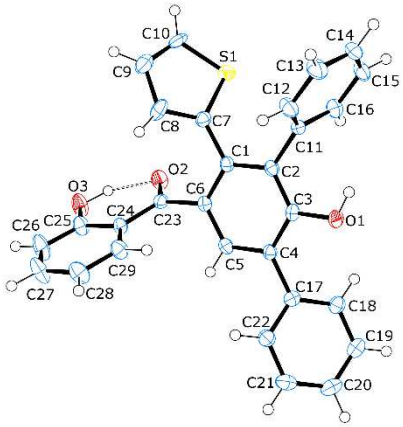
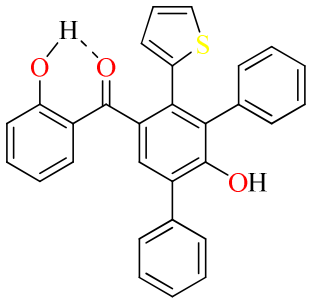
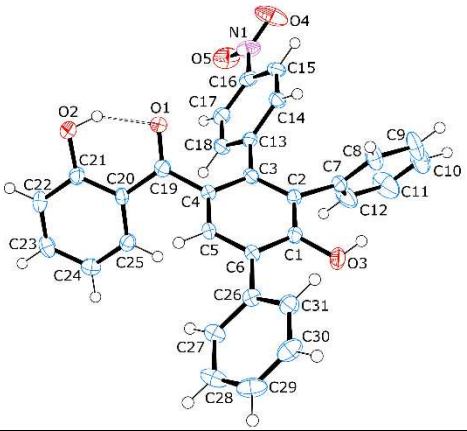
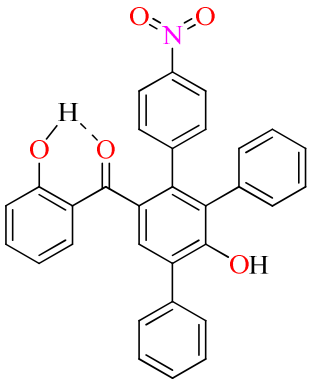
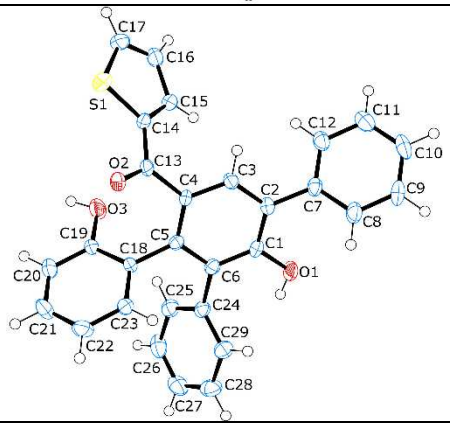
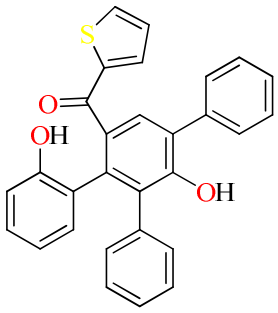
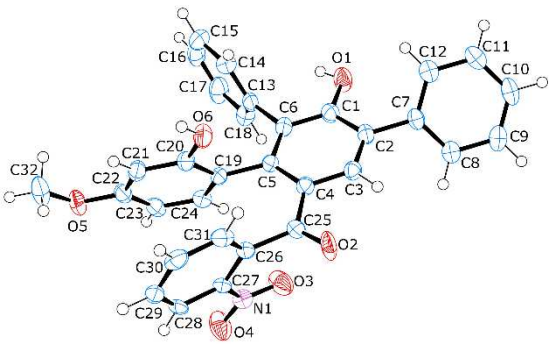
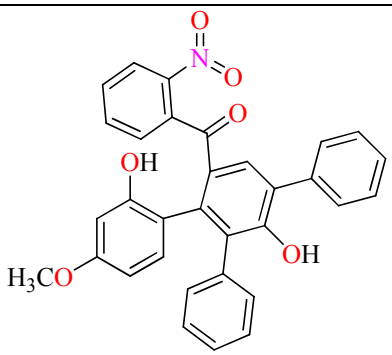
All structures of compounds **20** and **21** were confirmed by NMR, IR and mass spectrometry, as well as X-ray single crystal analysis.

In the ^{1}H-NMR spectra of compounds **20** in DMSO-d_6, two OH-groups appeared as singlets at δ = 8.6-9.3 ppm and 10.5-11.6 ppm. Most probably, the signals shifted to δ ≈ 11 ppm belong to protons of OH-groups of salicyloyl moiety, which could form an intramolecular hydrogen bond with the neighbouring carbonyl group. In contrast, in the ^{1}H-NMR spectra of compounds **21**, two singlets of two OH-groups were observed at δ = 8.4-9.2 ppm. The shift of both signals of OH-groups to δ ≈ 9 ppm can indicate the absence of hydrogen bonds in both cases. In the ^{13}C-NMR spectra, the salicyloyl carbonyl groups of compounds **20** and **21** appeared at δ = 193-202 ppm and δ = 188-193 ppm, respectively. In addition, the O$\underline{C}$H$_3$-group of compounds **20a** and **20b** obtained from 3-methoxalylchromones was observed as a singlet at δ = 3.5-4.0 ppm in the ^{1}H-NMR spectra and at δ = 50-54 ppm in the ^{13}C-NMR spectra.

The exact structures of compounds **20c**, **20d**, **20f**, **21b** and **21e** were established by X-ray single crystal analysis (Table 3.7).

Table 3.7 Crystal structures of compounds **20c**, **d**, **f** and **21b**, **e**.

Crystal structure	Compound	Structure
	**20c**	

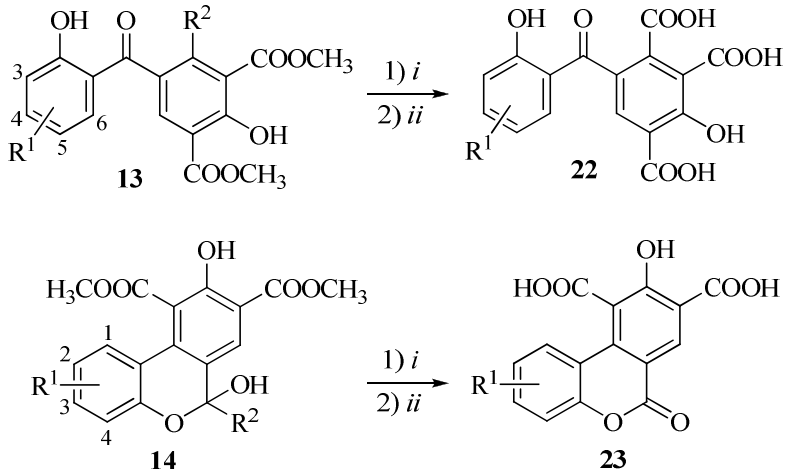
	**20d**	
	**20f**	
	**21b**	
	**21e**	

Expectedly, X-ray analyses of compounds **20** confirmed the existence of an intramolecular hydrogen bond (about 1.8 Å), involving the salicyloyl phenolic OH-group and

neighbouring carbonyl group (C=O). In contrast, in crystal structures of compounds **21**, the distances between the aroyl carbonyl group COR^2 and OH-group of another phenol ring were too long for hydrogen bond formation, because of the significant torsion angle between phenolic rings. These facts correspond to the data obtained by ^{1}H-NMR analyses. The structures of compounds **20** are also not planar. In the analyzed structures of compounds **20**, the plane of salicyloyl moiety made a torsion angle of 57-64º to the adjacent phenol ring.

3.3 Additional investigations

Modification of benzophenones and benzo[*c*]coumarins is of interest, since these scaffolds are important structural fragments of many natural and biologically active substances, as mentioned in the introduction. Furthermore, some benzoylbenzoic acids exhibit attractive biological properties.[173] In view of that, base-mediated hydrolysis of obtained 2-hydroxybenzophenones **13** and 6*H*-benzo[*c*]chromenes **14** was performed. The obtained results are shown in the Scheme 3.7 and Table 3.8.



Scheme 3.7 Synthesis of compounds **22** and **23**.
Reaction conditions: (*i*) **13** or **14** (1.0 equiv.), KOH (8.0 equiv.), methanol, reflux;
(*ii*) aqueous solution of HCl (30%).

Thereby, compounds **13** reacted with potassium hydroxide in methanol at reflux resulting in the formation of tricarboxylic acids **22** with excellent yields of 80-92%. Interestingly,

structurally similar 3-methoxybenzene-1,2,4-tricarboxylic acid was first obtained as the minor product of the oxidation of gladiolic acid.[174] Likewise, 6*H*-benzo[*c*]chromenes **14d** and **14u** reacted with potassium hydroxide to produce products **23a** and **23b** in 70% and 92% yields, respectively. So far, acids, which are structurally similar to compounds **23**, have not been described. All structures of compounds **22** and **23** were confirmed by NMR, IR and mass spectrometry.

Table 3.8 Synthesis of compounds **22** and **23**.

13	**R^1**	**R^2**	**22**	**Yield, [a] %**
a	H	$COOCH_3$	**a**	80
b	5-CH_3	$COOCH_3$	**b**	84
e	5-Cl, 4-CH_3	$COOCH_3$	**c**	92
g	3,4-benzo	$COOCH_3$	**d**	89
14	**R^1**	**R^2**	**23**	**Yield, [a] %**
d	H	C_2F_5	**a**	70
u	3,4-benzo	C_3F_7	**b**	92

[a] Yields of isolated products.

3.4. Photophysical properties

The sunlight ultraviolet radiation (UV) can cause photoallergic and cytotoxic reactions leading to skin cancer, because of the possibility of photochemical reactions of the DNA, for instance, [2+2] cycloadditions of thymine.[95] The most dangerous radiation of sunlight for the human skin lies in the range of UV-A (400-320 nm) and UV-B (320-280 nm) bands, while the UV-light with shorter wavelengths in the range of UV-C (280−200 nm) bands is absorbed by ozone in the upper parts of the atmosphere.[95] Organic compounds, which contain system with certain unsaturated groups (π orbitals) or atoms with unpaired electrons (n orbitals), can absorb UV radiation without decomposition by exciting an electron from its ground state into an excited state. In such way, these compounds can act as UV-filters. In an effort to protect the human skin from negative effects of UV light, a variety of personal care products containing UV filters has been investigated and produced.[175] Optimal sun-protecting compounds should have a broad and

strong absorption of UV-A and UV-B radiation, be photo-, thermo- and chemically stable and have a moderate lipophilicity. Sun-creams can contain UV-A/B broad spectrum filters or a mixture of UV-A and UV-B filters. Many organic compounds, *e.g.* para-amino benzoates, salicylates, dibenzoyl methanes and camphor derivatives, are approved for use in sun-protecting materials.[175] However, they do not possess full UV-light protecting properties. Besides, many of them are thought to be toxic, carcinogenic, aggressive or unstable and need photostabilizers.

Benzophenone derivatives are an important class of organic UV-filters. 2-Hydroxybenzophenones, like so called benzophenone-2, benzophenone-3 and benzophenone-8, are widely used as UV-filters in sun-protecting materials in cosmetics due to their ability to absorb in both the UV-A and UV-B ranges (Figure 3.3).[175, 176] Benzophenone-3 is one of the most widely used UV filters in commercial sunscreens. Nonetheless, this compound is thought to be photocarcinogenic.[177-180] In addition, the highly lipophilic properties of known benzophenones enable them to rapidly cross the dermal tissue, what can cause bioaccumulation in the human body. For these reasons, the development of new UV-A/B filters is still of much interest. The group of Prof. Langer has previously reported the synthesis of a series of new 2-hydroxybenzophenones as novel UV-A/B filters, which have shown intensive absorption properties.[28]

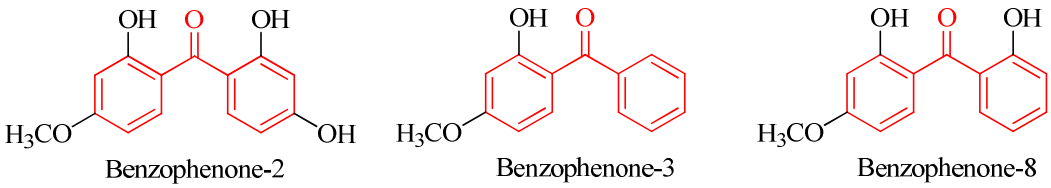
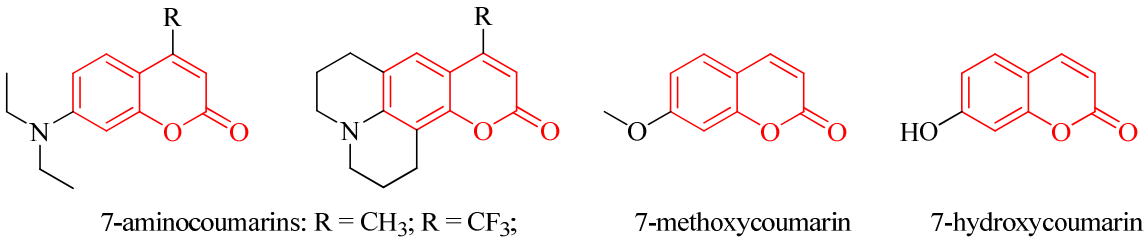


Figure 3.3 2-Hydroxybenzophenones approved as UV-A/B broad spectrum filters.

On the other hand, coumarins are very attractive targets from the point of their absorption and especially emission properties. Coumarin derivatives present a wide range of fluorescence properties.[181-184] They often exhibit high fluorescence quantum yields, large Stokes shifts, very good light stability and low toxicity. Because of that, these compounds have found use as optical brighteners[110] and fluorescent and laser dyes. 7-Substituted coumarins, which contain electron-withdrawing groups participating in the coumarin conjugation system, are the most important subsets, for example, 7-amino, 7-methoxy- and 7-hydroxycoumarins (Figure 3.4).[184, 185] Moreover, benzocoumarins and benzochromenones, which represent π-extended coumarin systems, have also attracted attention due to their interesting fluorescence properties.[186-188]

Additionally, some fluorinated coumarin derivatives have shown intensive fluorescence properties and improved photostability. These factors make them superior fluorescent dyes for use as reporter molecules in biological systems.[189]

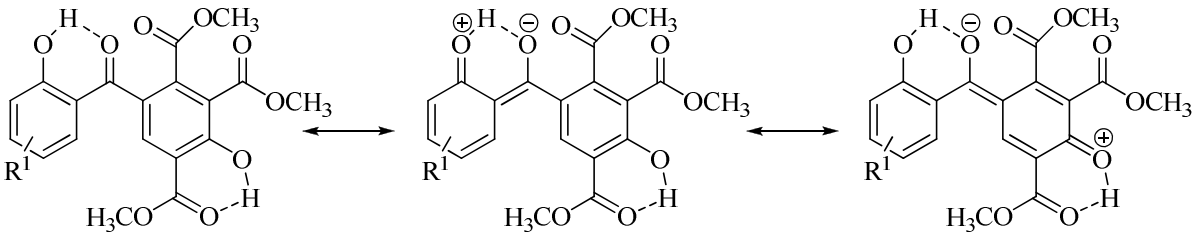


7-aminocoumarins: R = CH_3; R = CF_3; 7-methoxycoumarin 7-hydroxycoumarin

Figure 3.4 Commonly-used coumarin fluorescent probes.

Taking into account the structural similarities of the synthesized carbocycles in this chapter with presently known UV-filter, it was proposed to study the UV-activity of 2-hydroxybenzophenones **13**, 6*H*-benzo[*c*]chromenes **14** and products of their hydrolysis (compounds **22** and **23**). At the same time, one of the attractive features of the synthesized 6*H*-benzo[*c*]chromenes **14** was their intensive fluorescence behaviour. Also, they can be considered as systems related to the coumarins. Therefore, it was proposed to start the investigation of the emission properties of compounds **14** in collaboration with Dr. S. Tschierlei and Prof. S. Lochbrunner (Institute of Physics, University of Rostock).

The structure of benzophenones consists of two phenyl rings (π orbitals) connected through a carbonyl group (n orbitals) forming one conjugated system. Accordingly, benzophenones usually show n → π* and π → π* transitions, which result in two peaks in the UV-A and UV-B ranges, respectively.[190] The low-energy transitions (320-340 nm) of o-hydroxybenzophenone have been attributed to a charge-transfer transition involving the carbonyl and hydroxyl groups.[191] In the structure of synthesized 2-hydroxybenzophenones **13**, two hydroxyl groups form hydrogen bonds with their neighboring carbonyl groups. This fact lowers the energy required for the π → π* and n → π* transitions and increases the wavelength of the UV absorbance. In addition, the presence of a number of carbonyl and hydroxyl substituents in the phenyl rings provides different tautomeric forms. The electron density delocalization in the molecules of benzophenones **13** can be illustrated by resonance structures, which are shown in Scheme 3.8.



Scheme 3.8 Resonance structures of 2-hydroxybenzophenones **13**.

As expected, 2-hydroxybenzophenones **13** have shown intensive absorption resulting usually in three absorption maxima at 230 nm (UV-C), 240-290 nm (UV-C) and 315-380 nm (UV-A/B). The absorption coefficients are about ε = 45000-89000 $cm^{-1}mol^{-1}l$ (Figure 3.5, Table 3.9).

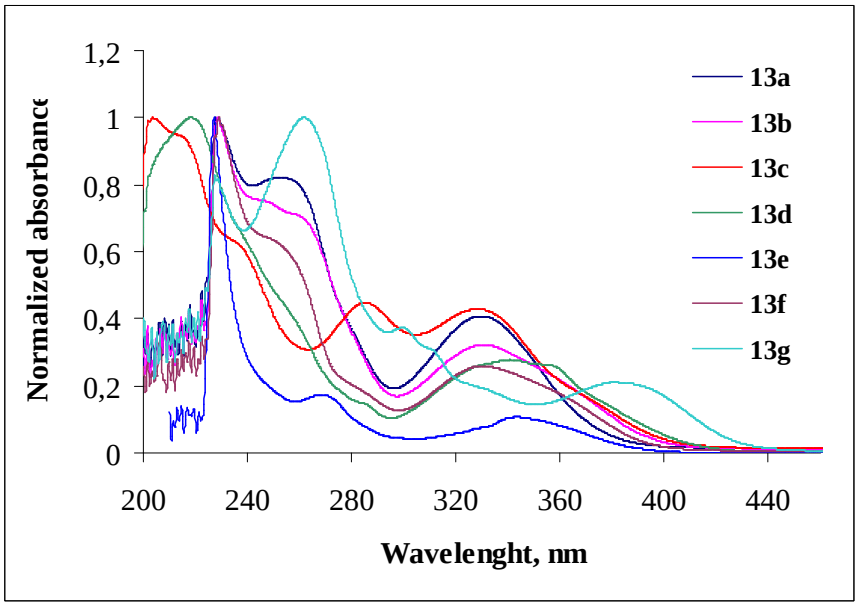


Figure 3.5 UV absorbance spectra of compounds **13**.

Continuing the investigation of absorption properties of the synthesized compounds, 6*H*-benzo[*c*]chromenes **14** were next studied (Figure 3.6, Table 3.10). Compounds **14** have shown high absorption coefficients, which can be explained by the maximal overlapping between the orbitals of two benzene rings, caused by the rigidity of the structure. The absorption coefficients are about ε = 29000-88000 $cm^{-1}mol^{-1}l$. The highest absorption coefficient was measured for compound **14r**, ε = 88200 $cm^{-1}mol^{-1}l$. It is necessary to underline that absorption coefficients obtained in this study for compounds **13** and **14** are significantly higher compared to other known UV-A/B filters.[175]

Table 3.9 The UV properties of compounds **13**.

13[a]	**c·10^{-5}, mol·l^{-1}**	**A**	**λ_{max}, nm**	**ε, cm^{-1}·mol^{-1}·l**	**log ε**
13a	1.45	0.656 0.538 0.268	228 252 330	45248 37127 18460	4.66 4.57 4.27
13b	1.61	0.872 0.281	229 331	54161 17422	4.73 4.24
13c	1.61	0.722 0.324 0.311	204 285 328	44870 20114 19307	4.65 4.30 4.29
13d	2.38	1.289 0.358	218 341	54151 15024	4.73 4.18
13e	0.57	0.507 0.088 0.054	227 269 344	89745 15585 9554	4.95 4.19 3.98
13f	1.70	1.240 0.320	229 331	72935 18834	4.86 4.27
13g	1.14	0.690 0.830 0.175	227 262 381	60491 72811 15388	4.78 4.86 4.19

[a] Compounds were dissolved in DCM.

c – concentration, A – absorption, ε – extinction coefficient.

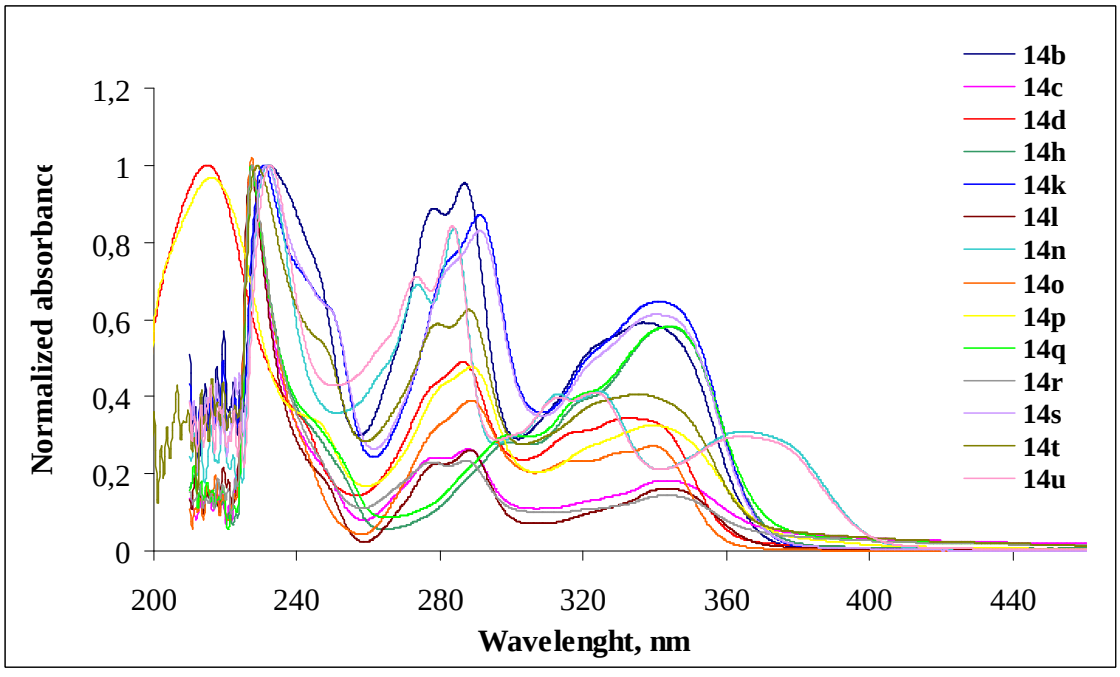


Figure 3.6 UV absorbance spectra of compounds **14**.

Table 3.10 The UV properties of compounds **14**.

14[a]	**c·10^{-5}, mol·l^{-1}**	**A**	**λ_{max}, nm**	**ε, cm^{-1}·mol^{-1}·l**	**log ε**
14b	1.21	0.356 0.340 0.211	232 287 337	29421 28099 17438	4.47 4.45 4.24
14c	131	0.578 0.153 0.105	227 288 344	44122 11679 8015	4.64 4.07 3.90
14d[b]	1.38	0.618 0.302 0.213	215 286 333	44783 21884 15435	4.65 4.34 4.19
14h	1.06	0.641 0.373	228 344	60472 35189	4.78 4.55
14k	1.25	0.445 0.388 0.288	231 291 341	35600 31040 23040	4.55 4.49 4.36
14l	0.69	0.583 0.152 0.094	227 288 344	84249 21965 13584	4.93 4.34 4.13
14n	1.19	0.812 0.679 0.336 0.251	232 284 325 365	68235 57059 28235 21092	4.83 4.76 4.45 4.32
14o	0.96	0.630 0.241 0.168	227 289 339	65831 25183 17555	4.82 4.40 4.24
14p	1.31	0.620 0.305 0.209	216 289 339	47328 23282 15954	4.68 4.37 4.20
14q	1.31	0.633 0.368	227 344	48321 28092	4.68 4.45
14r	0.84	0.740 0.173 0.106	227 287 344	88200 20620 12634	4.95 4.31 4.10
14s	1.09	0.371 0.308 0.227	232 291 341	34037 28257 20826	4.53 4.45 4.32
14t	0.47	0.361 0.225 0.146	229 288 334	76972 47974 31130	4.89 4.68 4.49
14u	1.04	0.535 0.450 0.219 0.159	232 283 323 365	51442 43269 21058 15288	4.71 4.64 4.32 4.18

[a] Compounds were dissolved in DCM; [b] Compounds were dissolved in methanol;

c – concentration, A – absorption, ε – extinction coefficient.

The study of fluorescence properties of 6*H*-benzo[*c*]chromenes **14** was started by the investigation of the influence of different substituents R^F and R^1 and their electronic effects on the emission properties. The comparison of absorption and emission spectra and calculated quantum yields of studied compounds **14** are shown in Figure 3.7 and Table 3.11.

The study of compounds **14a**, **14h** and **14q** which contain the same substituent R^1 but different perfluoroalkyl-groups R^F (CF_3, C_2F_5, C_3F_7), has shown that the R^F group does not have an influence on the absorption as well as the fluorescence spectra of these compounds (Figure 3.7 (a)). With regards to the intensity of the fluorescence, the different substituents R^F have a slight impact on the quantum yields: all 6*H*-benzo[*c*]chromenes **14a**, **14h** and **14q** are very strong emitters in the order 54%, 63% and 73%, respectively (Table 3.11).

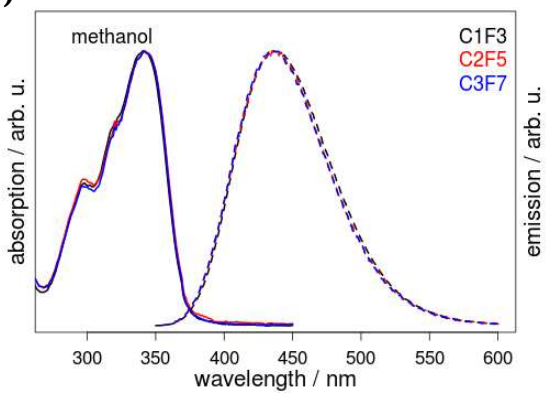
Table 3.11 The quantum yields of studied 6*H*-benzo[*c*]chromenes **14**.

Compound[a]	**R^1**	**R^2**	**Φ**[b]
14a	3-OCH_3	CF_3	0.54
14d	H	C_2F_5	0.06
14e	2-CH_3	C_2F_5	0.14
14f	3-CH_3	C_2F_5	0.21
14h	3-OCH_3	C_2F_5	0.63
14j	2-Cl	C_2F_5	0.08
14k	2-Cl, 3-CH_3	C_2F_5	0.15
14l	2-Br	C_2F_5	0.01
14n	3,4-benzo	C_2F_5	0.19
14q	3-OCH_3	C_3F_7	0.73

[a] Compounds were dissolved in methanol.

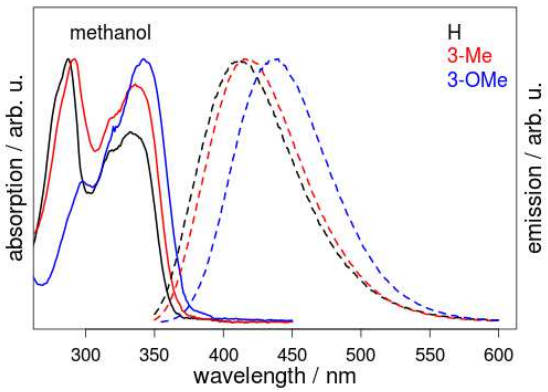
[b] Quantum yields were determined relative to quinine bisulfate in 0.05 M sulfuric acid as quantum yield standard (ϕ = 0.54).

a)



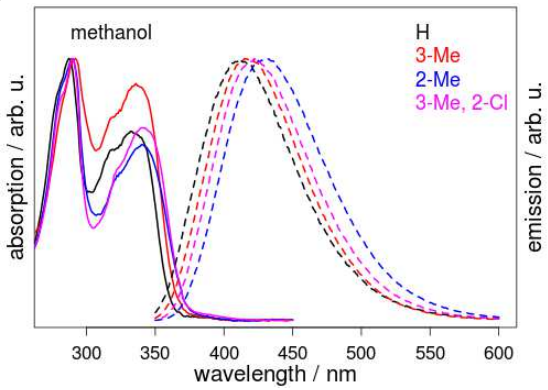
14a (R^1 = 3-OCH_3, R^F = CF_3),
14h (R^1 = 3-OCH_3, R^F = C_2F_5),
14q (R^1 = 3-OCH_3, R^F = C_3F_7);

(b)



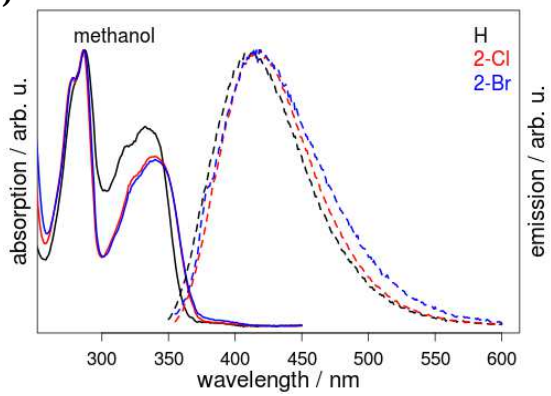
14d (R^1 = H, R^F = C_2F_5),
14f (R^1 = 3-CH_3, R^F = C_2F_5),
14h (R^1 = 3-OCH_3, R^F = C_2F_5);

(c)



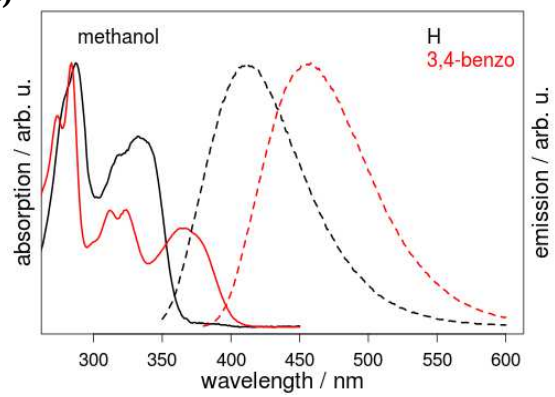
14d (R^1 = H, R^F = C_2F_5),
14f (R^1 = 3-CH_3, R^F = C_2F_5),
14e (R^1 = 2-CH_3, R^F = C_2F_5),
14k (R^1 = 2-Cl, 3-CH_3, R^F = C_2F_5);

(d)



14d (R^1 = H, R^F = C_2F_5),
14j (R^1 = 2-Cl, R^F = C_2F_5),
14l (R^1 = 2-Br, R^F = C_2F_5):

(e)



14d (R^1 = H, R^F = C_2F_5);
14n (R^1 = 3,4-benzo, R^F = C_2F_5);

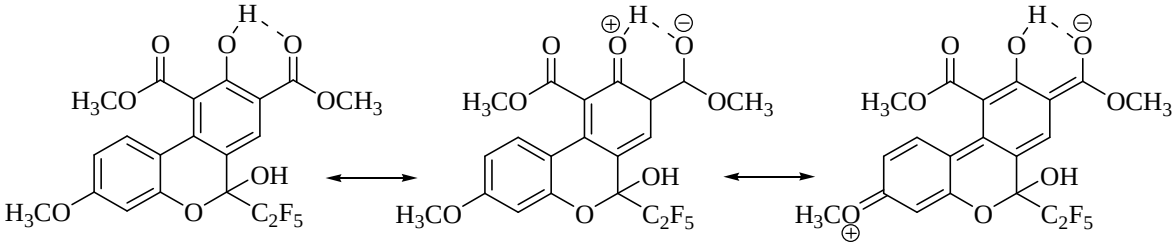
Figure 3.7 Normalized absorption spectra (solid lines) and emission spectra of 6*H*-benzo[*c*]chromenes **14** dissolved in methanol.

As a next step, different 6*H*-benzo[*c*]chromenes **14**, which possess the similar perfluoroalkyl-group R^F (C_2F_5) but different substituents R^1, were studied. As a result, the first absorption maxima as well as the emission maxima of compounds **14d**, **14f** and **14h** were shifted in the order of substituents R^1: H < 3-CH_3 < 3-OCH_3 to higher wavelengths (Figure 3.7 (b)). Hence, the methoxy group at the 3-position has a stronger impact on the electronic properties compared to the methyl group. Similar results were obtained for the quantum yields. The quantum yield of compound **14d** was only 6%. In contrast, the substituted systems **14f** (3-CH_3) and **14h** (3-OCH_3) gave quantum yields of 21% and 63%, respectively (Table 3.11).

If the methyl group was located at the 2-position (**14e**), the emission maximum was shifted to higher wavelengths compared to the maximum obtained for compound **14f** (3-CH_3), (Figure 3.7 (c)). The quantum yields were approximately in the same range of 21% (**14f**) and 14% (**14e**). Compounds **14j**, **14k** and **14l** showed that Cl- or Br-substituents in the 2-position did not have any significant influence on the emission spectra (Figure 3.7 (c) and (d)). The quantum yields of products **14j** and **14l** were very low of 8% and 1%, respectively (Table 3.11).

Finally, 6*H*-benzo[*c*]chromene **14n** containing a 2,3-benzo-substituent has shown the biggest shift of emission maximum to higher wavelengths (Figure 3.7 (e)). Obviously, this result is caused by the extended π-system due to the presence of the additional benzo-substituent. However, the quantum yield was not strongly influenced. The compound emitted only 19% of the incoming photons (Table 3.11).

In summary, substituents in the 3-position of compounds **14**, which can take part in the conjugated π-system of two benzene rings of 6*H*-benzo[*c*]chromene moiety, have the biggest influence on the emission properties of these products. The great results were obtained for compounds **14a**, **14h** and **14q** containing a methoxy group in the 3-position. The electron density delocalization in molecules of 6*H*-benzo[*c*]chromenes exemplified by compound **14h** is shown in Scheme 3.9. The mechanism of photophysical properties of 6*H*-benzo[*c*]chromenes **14** is now under further studies in collaboration with Dr. S. Tschierlei and Prof. S. Lochbrunner.



Scheme 3.9 Examples of possible resonance structures of 6*H*-benzo[*c*]chromene **14h**.

The last goal of photophysical investigations was the study of absorption properties of compounds **22** and **23** (Figure 3.8, Table 3.12). Also for these compounds three absorption maxima were observed at ≈ 220 nm (UV-C), ≈ 260 nm (UV-C) and 310-360 nm (UV-A/B). In general, the absorption coefficients are very high, ε = 66000-99000 $cm^{-1}mol^{-1}l$.

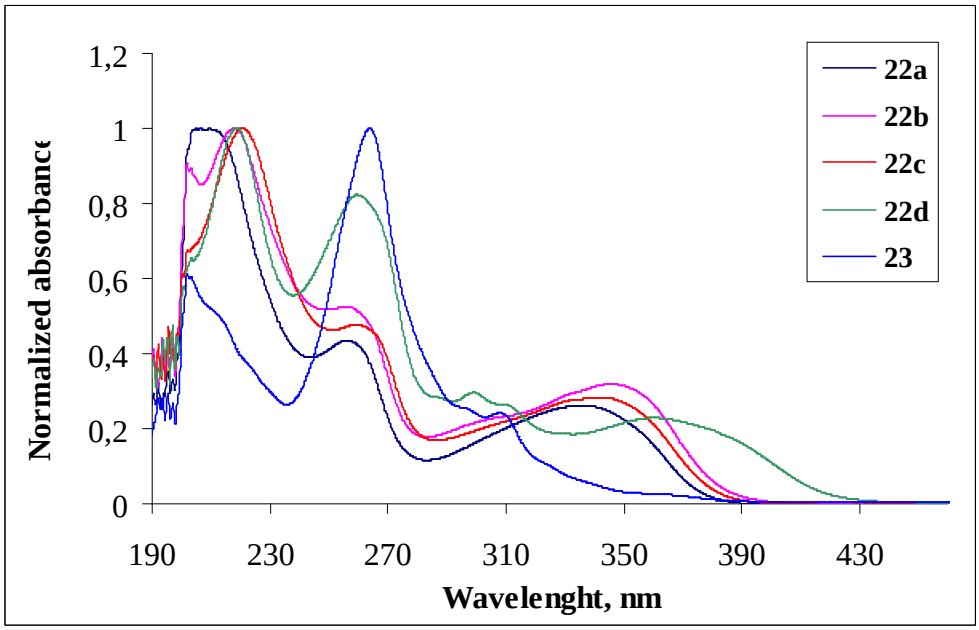


Figure 3.8 UV absorbance spectra of compounds **22** and **23**.

Table 3.12 The UV properties of compounds **22** and **23**.

Compound[a]	c·10^{-5}, mol·l^{-1}	A	λ_{max}, nm	ε, $cm^{-1}\cdot mol^{-1}\cdot l$	log ε
22a	1.30	0.860 0.374 0.224	206 256 335	66154 28769 17231	4.82 4.46 4.24
22b	1.20	0.805 0.422 0.257	218 256 346	67083 35167 21417	4.83 4.55 4.33
22c	1.10	0.831 0.397 0.235	221 259 342	75545 36091 21364	4.88 4.56 4.33
22d	1.32	1.307 1.076 0.387 0.298	219 260 299 360	99015 81515 29318 22576	5.00 4.91 4.47 4.35
23	1.50	1.198 0.289	264 308	79867 19267	4.90 4.28

[a] Compounds were dissolved in methanol;

c – concentration, A – absorption, ε – extinction coefficient.

In summary, due to the intensive UV-absorption properties, investigated compounds **13**, **14**, **22** and **23** might find use in the preparation of sun-protective materials. Moreover, some of 6*H*-benzo[*c*]chromenes **14** have shown promising fluorescence properties with high quantum yields and might be useful as fluorescent dyes.

3.5 Conclusions

The domino reactions of different 3-acylchromones with 1,3-*C*,*C*-binucleophiles, namely dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone, were studied. It was found that electronic and steric effects of the acyl group of 3-acylchromones play an important role and have a huge influence on the course of the reaction.

In this way, a simple and convenient method for the synthesis of functionalized 2-hydroxybenzophenones was developed based on domino reactions of 3-methoxalylchromones and electron-deficient 3-aroylchromones with dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone. At the same time, the domino reactions of 3-perfluoroacylchromones with dimethyl 1,3-acetonedicarboxylate afforded various fluorine-containing 6*H*-benzo[*c*]chromenes. Furthermore, the significant influence of the steric effect of the NO_2-group in *ortho*-position in the aroyl moiety of 3-(2-nitrobenzoyl)chromones was found. Thus, reactions of these 3-aroylchromones with dimethyl 1,3-acetonedicarboxylate proceeded to the formation of benzo[*c*]coumarin derivatives. In addition, their reactions with 1,3-diphenylacetone delivered highly functionalized phenols.

The synthesized compounds might be very attractive objects from the point of their pharmacological properties, because of their structural similarity to bioactive natural and synthetic products. The biological evaluation of all obtained compounds described in this chapter is now in the study. Moreover, the synthesized 2-hydroxybenzophenones **13** and 6*H*-benzo[*c*]chromenes **14** have shown strong UV-absorption properties. Therefore, they may find application in the preparation of the sun-protective materials. Additionally, some 6*H*-benzo[*c*]chromenes **14** exhibit intensive fluorescence properties.

Chapter 4

Reactions of 3-acylchromones with heterocyclic ketene aminals: Synthesis of functionalized fused pyridine derivatives

4.1 Introduction

Heteroannulated pyridines are present in a variety of natural and synthetic molecules exhibited a wide range of important biological activities.[192-198] Pyridine derivatives fused with five- or six-membered nitrogen heterocycles, such as pyrrolopyridines,[199-202] pyrazolopyridines,[203-212] imidazopyridines[213] and pyridopyrimidines,[214, 215] can be considered as purine isosteres. Purines are valuable components in a number of important biomolecules, namely DNA, RNA, ATP, GTP, AMP and NAD.[216] Therefore, purine-related compounds are privileged scaffolds in drug discovery (Figure 4.1).[17] Additionally, purine and pyridine derivatives, which possess an ester group at 2-position of the purine structure, are potent inhibitors of inosine-5′-monophosphate dehydrogenase (IMPDH).[217]

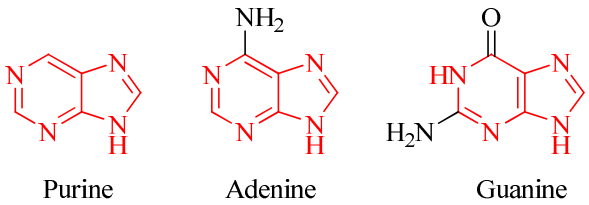


Figure 4.1 Main purine-derived nucleobases.

Chromenopyridines consist of two important moieties, like chromone and pyridine. Its core structure occurs in a number of pharmacologically active products, which show, for example, anticancer, anti-HIV-1, antibacterial and antistress activities.[218-223] Noteworthy, chromenopyridines, specifically amlexanox and nedocromil, are used as medicals nowadays. Nedocromil is used for the treatment of asthma and other breathing problems (Figure 4.2).[14] Amlexanox is a commonly prescribed topical antiulcer and antiallergic agent.[224] Other 5*H*-chromeno[2,3-*b*]pyridin-5-ones (1-azaxanthones) have been reported to show antiallergic,[225] anti-tumor,[226, 227] anticancer[228, 229] and acetylcholinesterase inhibitor[230] activities. Moreover, 1-

azaxanthones have been designed and developed as novel fluorescent[231, 232] and optical probes,[233, 234] as well as effective sensitizers for terbium and europium luminescence.[235-238] In addition, other pyridine derivatives 3-salicyloylpyridines also exhibit interesting biological activities[239-242] and are effective ultraviolet absorbers.[243-246]

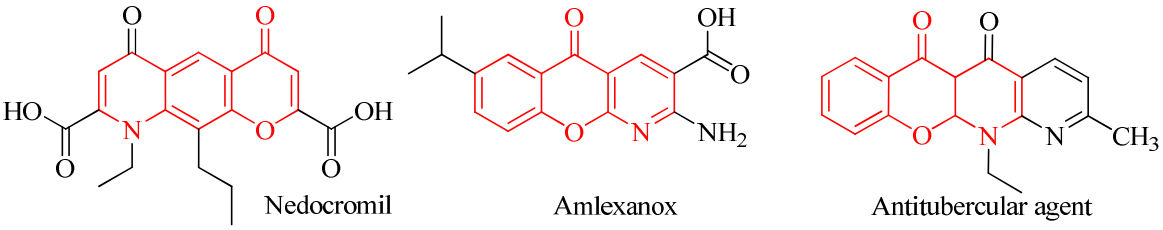
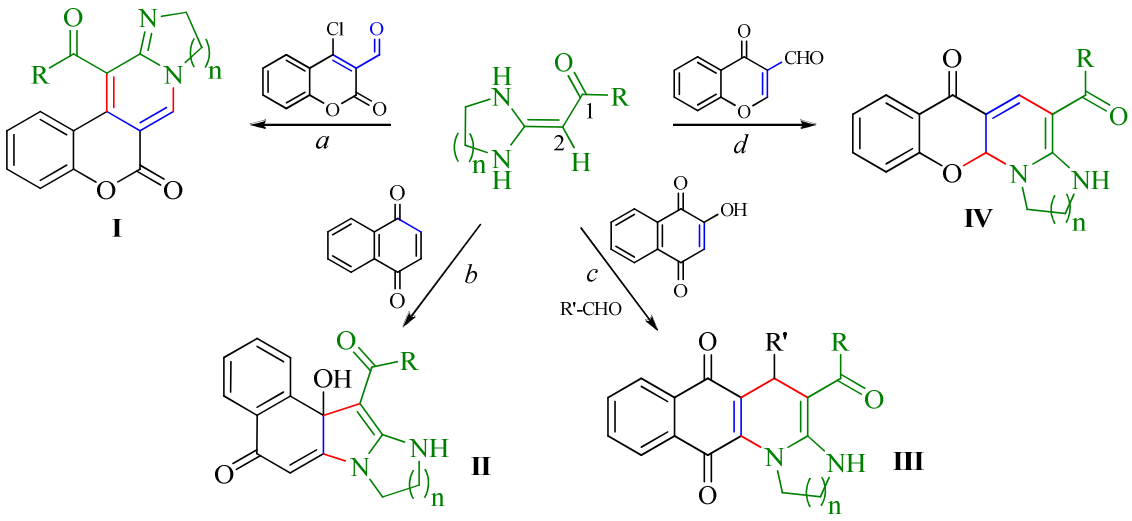


Figure 4.2 Biologically active chromenopyridines.

In a view of unique biological properties of pyridines, the development of new synthetic approaches for their preparation is of much interest for organic chemists.[247] One of the convenient and efficient methods for the synthesis of fused pyridine derivatives is based on the cyclization reactions of enamine-like substrates (N-source) as 1,3-*C*,*N*-binucleophiles with different bielectrophiles.[248-251] In this context, chromones can be proposed as 1,3-*C*,*C*-bielectrophiles. In the last decades, Langer *et al.*,[26, 27, 29-31] Sosnovskikh *et al.*[33, 57, 58, 63] and other groups[39, 252] have studied the cyclization reactions of different 3-substituted chromones, especially 3-acylchromones, with enamine-like binucleophiles (electron-excessive aminoheterocyles and anilines). This methodology was successfully applied for the synthesis of various fused pyridine derivatives. Besides, 3-substituted chromones are also known as building blocks for the synthesis of chromeno[2,3-*b*]pyridines. As mentioned in the introduction of Chapter 3, 5*H*-chromeno[2,3-*b*]pyridine derivatives were synthesized by reactions of 3-cyanochromones with dialkyl 1,3-acetonedicarboxylates (Scheme 3.1).[166, 167] Moreover, different three-component reactions using 3-formylchromones and amines resulted in the synthesis of chromeno[2,3-*b*]pyridines.[253, 254]

Heterocyclic ketene aminals (HKAs) are polyfunctional molecules containing three nucleophilic centres (C-2 carbon and two nitrogen atoms), which can react with various electrophilic agents. HKAs can also be considered as highly active enamines. For these reasons, HKAs are widely used in efficient domino and multi-component[255, 256] reactions for the synthesis of various fused heterocyclic systems containing, for instance, indoles,[257] quinolines, naphthyridines,[258] 1,2,3-triazoles, coumarins,[259] pyridines and pyrimidines.[260] In most these

cases, HKAs react as 1,3-*C*,*N*-binucleophiles. The double bond of HKAs is highly polarized due to the presence of two electron-donating amino groups and the electron-withdrawing carbonyl group. For this reason, the C-2 carbon atom is the most nucleophilic centre. Therefore, the first electrophilic attack is usually directed to the C-2 carbon atom. It is also interesting to note that many reactions of HKAs are catalyst-free[261] or/and solvent-free representing green chemistry. However, the reactions of HKAs with chromone-related compounds have not received much attention so far. In fact, only a few articles related to the reactions of coumarins and naphthoquinones with HKAs have been reported (Scheme 4.1).[257, 262, 263] Thereby, different fused pyridine derivatives were synthesized (structures I, II, IV). Recently, the reaction of 3-formylchromone with HKAs was described to form very attractive tetracyclic fused chromenopyridine derivatives (structure IV), which are structurally similar to some natural alkaloids, particularly, circumdatin D and E.[264] It is necessary to mention that this reaction proceeded under base-free conditions.



Scheme 4.1 Reactions of HKAs with chromone-related compounds and naphthoquinones. *Reaction conditions*: (*a*) Et_3N, EtOH, 20 ºC; (*b*) EtOH, 20 ºC; (*c*) Et_3N, 120 ºC; (*d*) DCM, reflux.

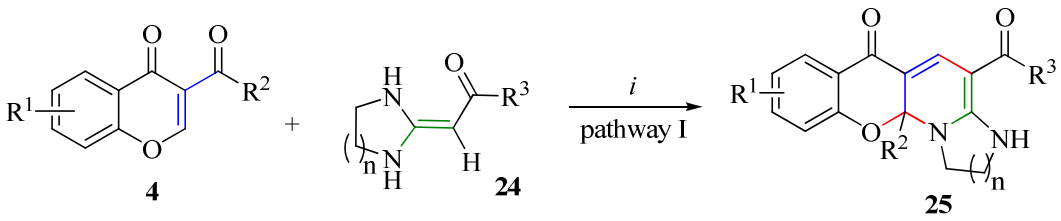
Being inspired by the biological importance of fused pyridine derivatives and the great chemical potential of HKAs for the synthesis of nitrogen heterocycles, and continuing the research program dedicated to the study of reactivity of 3-acylchromones, I was interested to investigate the reactions of 3-acylchromones **4-8** with HKAs in a role of 1,3-*C*,*N*-binucleophiles.

4.2 Results and discussions

4.2.1 Reactions of 3-methoxalyl-, 3-aroyl- and 3-cinnamoylchromones with HKAs

HKAs **24** containing five- or six-membered heterocyclic rings were prepared in collaboration with group colleagues[265] according to reported literature procedures. At first, *a*-oxoketene dithioacetals were synthesized starting from corresponding aryl ketones by reaction with carbon bisulphide in the presence of potassium *tert*-butoxide followed by alkylation with methyliodide.[266] In the second step, obtained *a*-oxoketene dithioacetals were used in the reactions with diamines to give the corresponding HKAs **24**.[267, 268]

The investigation of reactivity of different 3-acylchromones **4-8** towards HKAs was started by the study of the reactions of 3-methoxalylchromones **4** (R^2 = $COOCH_3$). The test reactions of 3-methoxalylchromone **4a** were performed with HKA **24a** (n = 1) and **24b** (n = 2) in 1,4-dioxane at room temperature (Scheme 4.2, Table 4.1). The reactions were carried out approximately two days. As a result, tetracyclic fused chromenopyridine derivatives **25a** and **25d** were obtained with an excellent regioselectivity in yields of 71% and 91%, respectively.



Scheme 4.2 Synthesis of compounds **25**.

Reaction conditions: (*i*) **4** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, 20 ºC.

In an effort to decrease the reaction time, reactions of 3-methoxalylchromone **4a** with HKA **24a** (n = 1) and **24b** were carried out in 1,4-dioxane at reflux, as well as in solvent with higher polarity, namely DCM, at room temperature. Both procedures resulted in an acceleration of the reactions, full conversion of the starting materials took about 3-4 h. However, more side-products were detected by TLC and the regioselectivity of the reaction decreased. In the reaction proceeded in the presence of DBU (1.3 equiv.), in 1,4-dioxane at room temperature, chromenopyridine derivatives were not observed by TLC. In contrast, another product was detected. Most probably, it was a salicyloyl derivative with remained open γ-pyrone ring of the

chromone moiety, without additional cyclization into chromenopyridine derivative. Based on the performed experiments, mild reaction conditions, specifically stirring in 1,4-dioxane at room temperature, was preferred to use for the further investigations. Noteworthy, the reactions of 3-formylchromones with HKAs, which proceeded to the formation of chromenopyridine derivatives, showed the best results without the use of any additives.[264]

Table 4.1 Synthesis of compounds **25**.

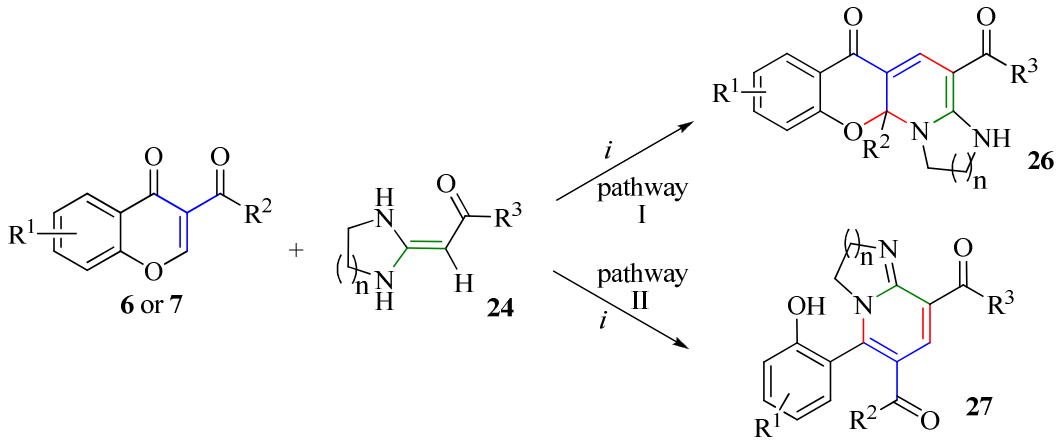
3-Methoxalylchromone			HKA			Product	
4	**R^1**	**R^2**	**24**	**n**	**R^3**	**25**	**Yield, [a] %**
a	H	$COOCH_3$	**a**	**1**	Ph	**a**	71
c	7-OCH_3	$COOCH_3$	**a**	**1**	Ph	**b**	72
g	7,8-benzo	$COOCH_3$	**a**	**1**	Ph	**c**	77
a	H	$COOCH_3$	**b**	**2**	Ph	**d**	91
c	7-OCH_3	$COOCH_3$	**b**	**2**	Ph	**e**	88
d	6-Cl	$COOCH_3$	**b**	**2**	Ph	**f**	77
g	7,8-benzo	$COOCH_3$	**b**	**2**	Ph	**g**	94

[a] Yields of isolated products.

The preparative scope was next studied. Products **25** were obtained with an excellent regioselectivity and in very good yields of 72-94% (Table 4.1). In general, the yields of compounds **25d-g** containing a six-membered heterocyclic ring derived from the HKA were slightly higher than the yields of compounds **25a-c** with a five-membered heterocyclic ring. The difference might be explained by the slight influence of the steric effect of the heterocyclic ring of the HKAs. The highest yield (94%) was obtained for product **25g** containing a benzo-substituent in the case of reaction of HKA **24b** (n = 2). In addition, it is worth mentioning that the obtained tetracyclic fused chromenopyridine derivatives **25** showed intensive fluorescence properties observed under the UV-light.

Following the initial successful results, as a next goal, a set of other 3-acylchromones, such as 3-aroylchromones **6** and 3-cinnamoylchromone **7**, were studied. A test reaction of 3-benzoylchromone **6a** with HKA **24a** using proposed reaction conditions afforded the expected chromenopyridine derivative **26a**, albeit, only in 14% yield (Scheme 4.3, Table 4.2). Surprisingly, 2*H*,3*H*-imidazo[1,2-*a*]pyridine **27a** was isolated as a major product in 76% yield.

Gratifyingly, because of the different physical properties of products **26a** and **27a**, they could be easily separated. Thus, because of low solubility of compound **27a** in 1,4-dioxane, this product was isolated by simple filtration of the precipitate formed in the reaction mixture. Afterwards, product **26a** was isolated from the filtrate using column chromatography (ethyl acetate-heptane). Accordingly, non-polar solvent (1,4-dioxane) was very useful to perform this reaction.



Scheme 4.3 Synthesis of compounds **26** and **27**.

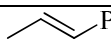
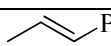
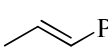
Reaction conditions: (*i*) **6** or **7** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, 20 ºC.

For a deeper understanding of the reaction course, the preparative scope was next studied (Scheme 4.3, Table 4.2). It was found that reactions of 3-acylchromones **6** and 3-cinnamoylchromone **7** with HKA **24a** (n = 1) delivered 2*H*,3*H*-imidazo[1,2-*a*]pyridine derivatives **27a-f**, **h** in moderate to excellent yields (51-96%). In contrast, reactions of the same chromones with HKA **24b** or **24c** (n = 2) resulted in the formation of chromenopyridine derivatives **26d-n** with an excellent regioselectivity and in very good yields (60-98%).

Thereby, obtained results show the huge influence of the size of the heterocyclic moiety of HKAs **24** on the course of the reaction and the structures of formed products. At the same time, talking about 3-acylchromones **6** and **7**, their substituent (R^2 = Aryl or cinnamoyl) in 3-position seems not to have a significant influence on the structure of obtained products. An exception from this trend was observed only in the reaction of 3-(2-nitrobenzoyl)chromone **6d** resulting in the formation of 2*H*,3*H*,4*H*-pyrido[1,2-*a*]pyrimidine **27g** in 92% yield, because of a steric effect of the NO_2-group in *ortho*-position. This fact corresponds to the results obtained during the study of the reactions of 3-(2-nitrobenzoyl)chromones with dimethyl 1,3-acetonedicarboxylate **12** described in Chapter 3 (Scheme 3.4, Table 3.3). It should be noted that

a steric influence of the substituent in *ortho*-position of the aroyl moiety was observed only for the NO_2-group, while the fluorine atom of 3-(2-fluorobenzoyl)chromone **6b** did not show such an effect, obviously, because of its small size. In addition, the electron-withdrawing character of the NO_2-group of chromones **6h** and **6i** also had an influence on the product distribution. This was observed during the synthesis of 2*H*,3*H*-imidazo[1,2-*a*]pyridines **27e** and **27f**, where by-products **26b** and **26c** could be isolated in 42% and 32% yields, respectively.

Table 4.2 Synthesis of compounds **26** and **27**.

3-Aroylchromone			HKA			Product (pathway I)		Product (pathway II)	
6	**R^1**	**R^2 = Ar**	**24**	**n**	**R^3**	**26**	**Yield, [a] %**	**27**	**Yield, [a] %**
a	H	Ph	**a**	1	Ph	**a**	14	**a**	76
b	H	2-FC_6H_4	**a**		Ph	**—**	—	**b**	96
c	H	2-C_4H_3S	**a**		Ph	**—**	—	**c**	62
d	H	2-$NO_2C_6H_4$	**a**		Ph	**—**	—	**d**	78
h	6-CH_3	3-$NO_2C_6H_4$	**a**		Ph	**b**	42	**e**	54
i	H	4-$NO_2C_6H_4$	**a**		Ph	**c**	32	**f**	51
a	H	Ph	**b**	2	Ph	**d**	91	**—**	—
a	H	Ph	**c**		4-ClC_6H_4	**e**	98	**—**	—
b	H	2-FC_6H_4	**b**		Ph	**f**	92	**—**	—
c	H	2-C_4H_3S	**b**		Ph	**g**	63	**—**	—
d	H	2-$NO_2C_6H_4$	**b**		Ph	**—**	—	**g**	92
g	H	3-$NO_2C_6H_4$	**b**		Ph	**h**	75	**—**	—
g	H	3-$NO_2C_6H_4$	**c**		4-ClC_6H_4	**i**	60	**—**	—
i	H	4-$NO_2C_6H_4$	**b**		Ph	**j**	70	**—**	—
i	H	4-$NO_2C_6H_4$	**c**		4-ClC_6H_4	**k**	62	**—**	—
j	H	3,5-$(NO_2)_2C_6H_3$	**b**		Ph	**l**	88	**—**	—
7	H		**a**	1	Ph	**—**	—	**h**	65
7	H		**b**	2	Ph	**m**	84	**—**	—
7	H		**c**	2	4-ClC_6H_4	**n**	87	**—**	—

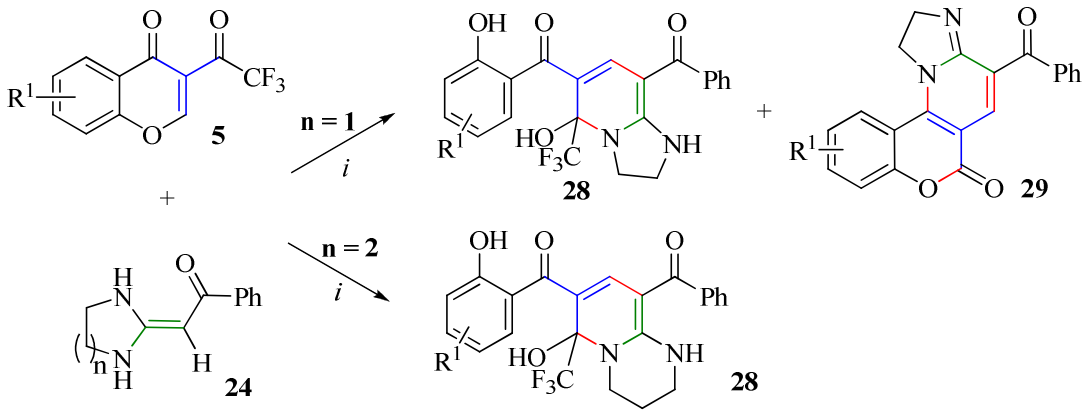
[a] Yields of isolated products.

In summary, by means of the steric effect of the heterocyclic moiety of HKAs **24**, the course of the reactions of 3-aroylchromones **6** and 3-cinnamoylchromone **7** and the structure of obtained products can be controlled. It is necessary to emphasise that 3-formylchromones in the reactions with HKAs proceeded only to the formation of chromenopyridine derivatives; 2*H*,3*H*-imidazo[1,2-*a*]pyridine derivatives were not obtained.[264] In addition, obtained tetracyclic fused chromenopyridine derivatives **26** showed intensive fluorescence properties under the UV-light.

4.2.2 Reactions of 3-polyhaloacylchromones with HKAs

To further explore the potential of proposed methodology, the reactions of 3-perfluoroacylchromones **5** with HKAs **24** were studied. Obtained results are presented in the Schemes 4.4 and 4.5, Tables 4.3 and 4.4.

At first, 3-trifluoroacetylchromones were investigated. Unexpectedly, the reactions of 3-trifluoroacetylchromones **5** with HKA **24a** (n = 1) afforded mixtures of 2-salicyloylpyridines **28** and coumarin derivatives **29** in 34-61% and 29-46% yields, respectively (Schemes 4.4, Tables 4.3).



Scheme 4.4 Synthesis of compounds **28** and **29** starting from 3-trifluoroacetylchromones **5**. *Reaction conditions*: (*i*) **5** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, 20 ºC.

Compounds **28** and **29** were separated by column chromatography using ethyl acetate-heptane for the isolation of products **28** and methanol for the elution of coumarins **29**. However, in case of the reaction of chromone **5c**, only product **28c** could be isolated, because of the formation of a number of other by-products in small amounts. Nonetheless, during the synthesis

of compounds **28d** and **29c**, by-product (chromenopyridine derivative **26o**) was isolated in 18% yield. Noteworthy, in the case of formation of coumarin derivatives **29** the intermediate semi-ketal form containing OH- and CF_3-groups was not stable (Scheme 1.4, Scheme 3.3). Therefore, the reactions proceeded with elimination of the CF_3-group as a leaving group.

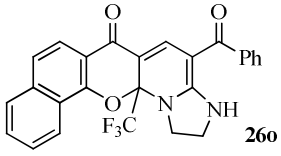
At the same time, reactions of the same 3-trifluoroacetylchromones **5** with HKAs **24b** (n = 2) delivered functionalized 2-salicyloylpyridine derivatives **28e-h** with an excellent regioselectivity and in very good yields (78-95%). Obtained results again display the significant steric influence of the heterocyclic moiety of HKAs **24** on the product distribution.

Table 4.3 Synthesis of compounds **28** and **29** starting from 3-trifluoroacetylchromones **5**.

5	R^1	24	n	28	Yield,[a] %	29	Yield,[a] %
a	H	a	1	**a**	47	**a**	46
b	7-OCH_3			**b**	61	**b**	31
c	6-Cl			**c**	48	—	—
e	7,8-benzo			**d**	34*	**c**	29
a	H	b	2	**e**	88	—	—
b	7-OCH_3			**f**	72	—	—
c	6-Cl			**g**	95	—	—
e	7,8-benzo			**h**	78	—	—

[a] Yields of isolated products.

* Compound **26o** was isolated in 18% yield (structure see below).

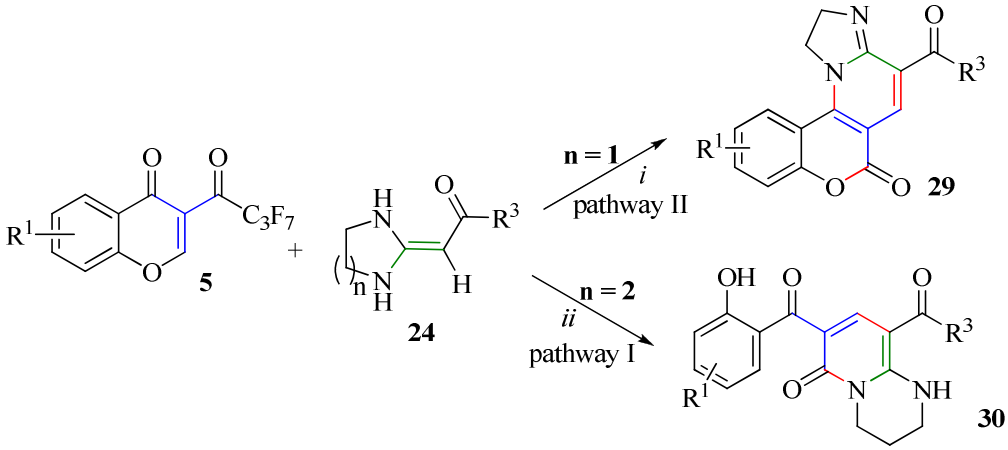


26o

As the second step, 3-heptafluorobutanoylchromones were studied. Coumarin derivatives **29a** and **29c** were obtained by the reactions of 3-heptafluorobutanoylchromones **5q** and **5w** with HKA **24a** (n = 1) with excellent regioselectivity, in yields of 84 and 91%, respectively (Scheme 4.5, Table 4.4). This finding shows the influence of the electronic and steric effects of the perfluoroalkyl-group on the regioselectivity of the reaction and the product distribution. It is worth mentioning that during the attempt to prepare compounds **29a** and **29c** at first mixtures of the fluorinated semi-ketal and product **29** were observed by NMR. The products were not possible to separate, because of the unstable nature of the fluorinated product. For this reason,

the reactions were carried out at reflux until full conversion of the fluorinated semi-ketals into coumarin derivatives **29**.

As could be expected, similar to the reactions of 3-trifluoroacetylchromones, reactions of 3-heptafluorobutanoylchromones **5** with HKAs **24b** and **24c** (n = 2) afforded 2-salicyloylpyridine-related derivatives **30** in good yields of 60-76% (Scheme 4.5, Table 4.4). However, the reactions also involved elimination of the heptafluoropropyl-group. A small amount of fluorinated 2-salicyloylpyridine derivatives could be detected on the TLC. In addition, it should be mentioned that all described reactions of 3-perfluoroacylchromones **5** with HKAs **24** continued approximately 10-12 h.



Scheme 4.5 Synthesis of compounds **29** and **30** using 3-heptafluorobutanoylchromones **5**. *Reaction conditions*: (*i*) **5** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, reflux; (*ii*) **5** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, 20 ºC.

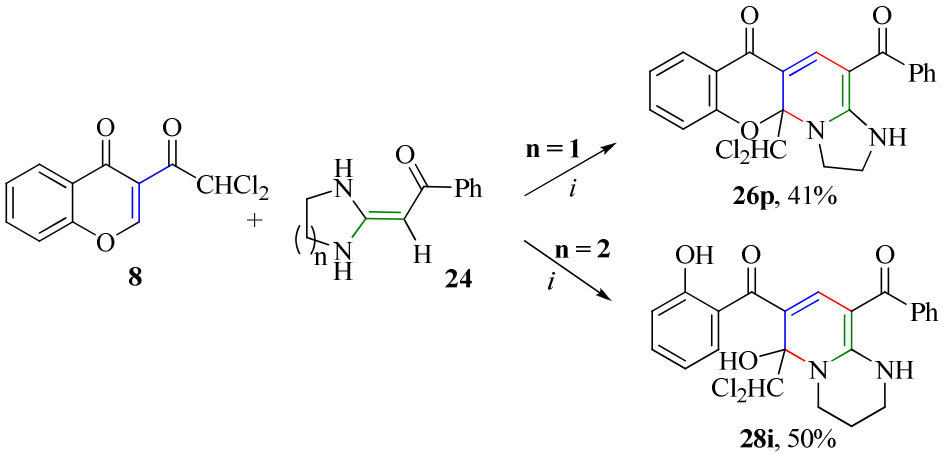
Table 4.4 Synthesis of compounds **29** and **30** using 3-heptafluorobutanoylchromones **5**.

5	**R^1**	**24**	**n**	**R^3**	**30**	**Yield,[a] %**	**29**	**Yield,[a] %**
q	H	a	1	Ph	—	—	**a**	91
w	7,8-benzo	a		Ph	—	—	**c**	84
r	6-CH_3	b	2	Ph	**a**	76	—	—
t	6-Cl	c		4-ClC_6H_4	**b**	60	—	—
v	6-Br	b		Ph	**c**	76	—	—
w	7,8-benzo	b		Ph	**d**	70	—	—

[a] Yields of isolated products.

Unfortunately, the use of 3-pentafluoropropanoylchromones in the reactions with HKAs was unsuccessful, because of the formation of inseparable mixture of products. Most probably, it was a mixture of fluorinated and non-fluorinated 2-salicyloylpyridine and coumarin derivatives.

Additionally, the reactions of 3-(2,2-dichloroacetyl)chromone **8** with HKAs **24** were carried out using the described protocol (Scheme 4.6). The treatment of chromone **8** with HKA **24a** (n = 1) proceeded to the formation of tetracyclic chromenopyridine derivative **26p** in 41% yield, while the reaction of the same chromone with HKA **24b** (n = 2) delivered 2-salicyloylpyridine derivative **28i** in 50% yield. The reaction times were about 10-12 h. Noteworthy, in both cases the reaction proceeded *via* the 2,2-dichloroacetyl carbonyl fragment by the second nucleophilic attack. Nonetheless, product **26p** was formed *via* an additional intramolecular cyclization involving the phenolic OH-group and semi-ketal centre. The moderate yields can be explained by the formation of a number of by-products detected by TLC. Unfortunately, these by-products could not be isolated.



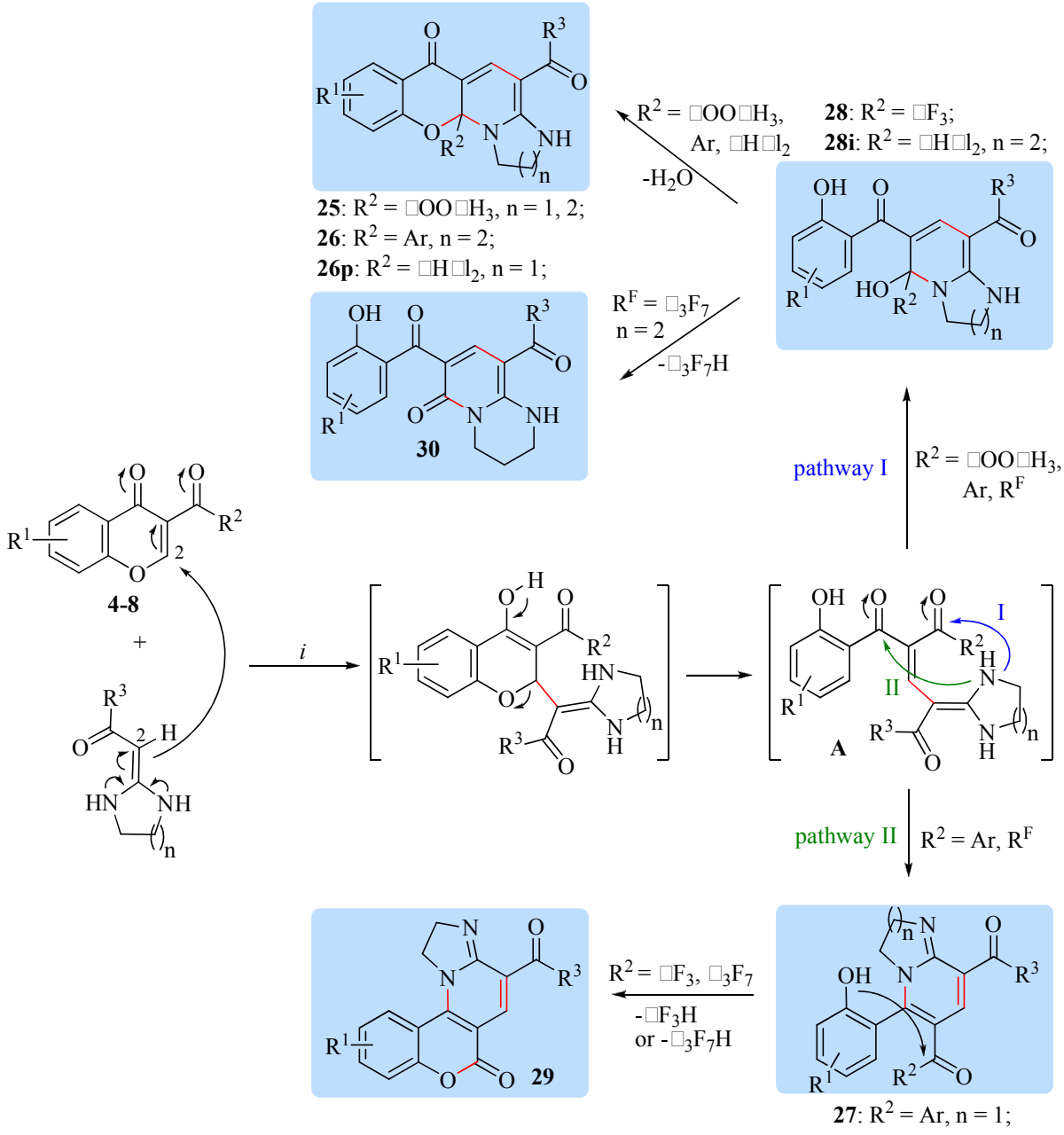
Scheme 4.6 Reaction of 3-(2,2-dichloroacetyl)chromone **8** with HKAs **24**.
Reaction conditions: (*i*) **8** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane, 20 ºC.

4.2.3 Proposed reaction mechanism

The proposed mechanism of the domino reactions of 3-acylchromones **4**-**8** with 1,3-*C*,*N*-binucleophile, namely HKAs **24**, is outlined in the Scheme 4.7.

Based on the chemical behaviour of 3-acylchromones in the reactions with 1,3-binucleophiles described in Chapter 1 and Chapter 3, it was suggested that all studied reactions

of chromones **4-8** with HKAs **24** have started by nucleophilic 1,4-addition, directed to the C-2 atom of the chromone. As usual, the HKAs acted first as C-nucleophile *via* the most nucleophilic C-2 carbon atom. Afterwards, opening of the γ-pyrone ring proceeded to the formation of *β*-dicarbonyl intermediate **A**, which is capable to different intramolecular cyclizations. The second nucleophilic attack of HKAs **24** (amino-group) could be directed to the acyl carbonyl group COR^2 (pathway I) or to the carbonyl group of salicyloyl moiety (pathway II).



Scheme 4.7 Proposed reaction mechanism for the formation of compounds **25-30**.

Reaction conditions: (*i*) **4-8** (1.0 equiv.), **24** (1.1 equiv.), 1,4-dioxane.

In this way, 2-salicyloylpyridine derivatives **28** ($R^2 = CF_3$, n = 1, 2; $R^2 = CHCl_2$, n = 2) and **30** ($R^2 = C_3F_7$), as well as chromenopyridine derivatives **25** ($R^2 = COOCH_3$) and **26** (R^2 = Aryl, n = 2; $R^2 = CHCl_2$, n = 1), were formed *via* pathway I. It is necessary to note that, in case of the synthesis of chromenopyridine derivatives **25** and **26**, an additional cyclization involving the phenolic OH-group and semi-ketal centre, followed by fission of a water molecule, took place. 2-Pyridone-related derivatives **30** were obtained starting from 3-heptafluorobutanoylchromones **5** and HKAs **24b**, **c** (n = 2) including elimination of the heptafluoropropyl-moiety as a leaving group in the last step of the reaction.

Compounds **27 (**R^2 = Aryl, n = 1**)** and fused coumarin derivatives **29** ($R^2 = CF_3, C_3F_7$, n = 1) were formed *via* pathway II. Synthesis of compounds **29** included additional cyclization of the phenolic OH-group with acyl group COR^F eliminating the perfluoroalky-group, resulting in the formation of the fused coumarin core.

In summary, reactions of different 3-acylchromones **4-8** with HKAs **24** led to the formation of various types of products **25-30** due to the electronic and steric effects of the substituent in 3-position of the 3-acylchromones and the ring size of the heterocyclic moiety of the HKAs. The last factor played the most significant role. The intramolecular cyclization of *β*-dicarbonyl intermediate **A** is the most important step determining the structure of formed products.

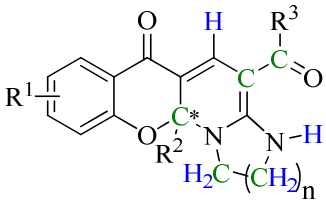
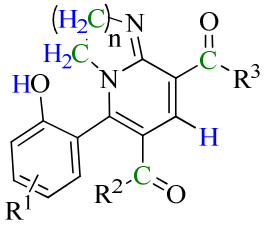
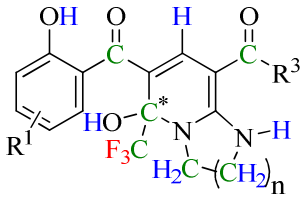
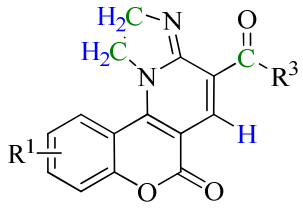
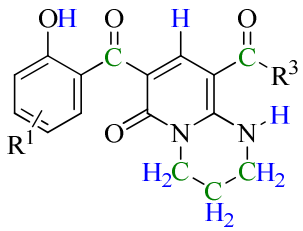
4.2.4 Structure identification

All structures of synthesized compounds **25-30** were confirmed by spectroscopic methods, specifically NMR, IR and mass spectrometry, as well as X-ray crystal analysis. The characteristic signals observed from NMR spectra of compounds **25-30** are shown in Table 4.5.

All obtained compounds **25-30** contain an alkyl-chain of heterocyclic moiety derived from the HKAs ($>$N-CH_2-$(CH_2)_n$-N$<$). The alkyl-chain appeared as multiplets (or bright singlets) of four hydrogen atoms (2^xNC$\underline{H_2}$) in the range of δ ≈ 3.2-4.3 ppm of $\underline{^1H\text{-NMR}}$ spectra and two singlets of carbon atoms (2^xN$\underline{C}H_2$) at δ ≈ 40-44 ppm in the $\underline{^{13}C\text{-NMR}}$ spectra. In case of the alkyl chain derived from the HKAs containing a six-membered heterocyclic ring (n = 2), signals of additional -CH_2-group were detected: two multiplets of two hydrogen atoms at δ ≈ 2.0 ppm and one signal of carbon atom at δ ≈ 19 ppm in the $\underline{^1H\text{-}}$ and $\underline{^{19}C\text{-NMR}}$ spectra, respectively.

Observed multiplets of hydrogen atoms of alkyl-chain showed their non-equivalence. In addition, in most cases, typical singlet of the hydrogen atom of pyridine-related ring of synthesized compounds **25-30** could be seen at δ ≈ 8 ppm in the ^{1}H-NMR spectra.

Table 4.5 Observation from NMR analyses for compounds **25-30**.

Compound	Structure	Characteristic signals in NMR-spectra
25 or **26**		^{1}H NMR: NH: if n = 1: s, δ ≈ 9.6 ppm; if n = 2: s, δ = 11.5-12.5 ppm; H (pyridine-related ring): s, δ ≈ 7.8 ppm; OCH_3: s, δ = 3.5-4.0 ppm, in the case of **25**; ^{13}C NMR: C=O: s, δ = 189-193 ppm; C: s, δ = 90-94 ppm; C*: s, δ = 90-94 ppm; OCH_3: s, δ ≈ 54.0 ppm, in the case of **25**;
27		^{1}H NMR: OH: s, δ ≈ 10.3 ppm; H (pyridine-related ring): s, δ ≈ 7.7 ppm; ^{13}C NMR: 2 C=O: s, δ = 188-195 ppm;
28		^{1}H NMR: 2OH and NH: if n=1: s, δ = 8.78-10.76 ppm, if n=2: s, δ = 9.72-11.46 ppm; H (pyridine-related ring): s, δ ≈ 7.3 ppm; ^{13}C NMR: 2 C=O: s, δ = 188-197 ppm; C*: q, δ ≈ 84 ppm ($^2J_{C,F}$ ~ 32.5 Hz); CF_3: q, δ ≈ 125 ppm ($^1J_{C,F}$ ~ 296.0 Hz); ^{19}F NMR: CF_3: s, δ ≈ -83 ppm;
29		^{1}H NMR: H (pyridine-related ring): s, δ ≈ 7.6 ppm; ^{13}C NMR: C=O: s, δ ≈ 191 ppm;
30		^{1}H NMR: OH and NH: s, δ = 10.2-13.5 ppm; H (pyridine-related ring): s, δ ≈ 7.9 ppm; ^{13}C NMR: 2 C=O: s, δ = 190-197 ppm;

In the low field of ^{1}H-NMR spectra of chromenopyridine derivatives **25** and **26** in DMSO-d_6, the NH-group appeared as a singlet at δ ≈ 9.6 ppm (if n = 1) and δ = 11.5-12.5 ppm (if n = 2). In the low field of ^{13}C-NMR spectra, the carbonyl group COR^3 gave a signal at δ = 189-193 ppm. Besides, two typical signals were found at δ = 90-94 ppm, related to the chiral carbon atom and the carbon atom attached to the COR^3-group (proved by 2D NMR).

Similar to compounds **25** and **26**, in the low field of ^{1}H-NMR spectra of 2*H*,3*H*-imidazo[1,2-*a*]pyridine derivatives **27** in DMSO-d_6, one singlet (OH-group) was observed at δ ≈ 10.3 ppm. At the same time, in contrast to compounds **25** and **26**, in the ^{13}C-NMR spectra of products **27**, two signals stemming from two carbonyl groups were detected at δ = 188-195 ppm and no signals were found in the range of δ = 90-94 ppm. Therefore, compounds **26** and **27**, which were formed in the reactions of 3-aroyl- and 3-cinnamoylchromones, could be distinguished by the ^{13}C-NMR spectra.

In the low field of ^{1}H-NMR spectra of compounds **28**, three characteristic proton signals of two OH- and one NH-groups appeared as a singlets at δ = 8.78-10.76 ppm (if n = 1) and δ = 9.72-11.46 ppm (if n = 2), showing that the γ-pyrone ring of the chromone moiety is opened. In the low field of ^{13}C-NMR spectra, two signals of two carbonyl groups were observed at δ = 188-197 ppm. The presence of CF_3-group in the structures of compounds **28** was confirmed by ^{13}C-NMR analysis, which showed typical quartets at δ ≈ 84 ppm (chiral carbon atom) and δ ≈ 125 ppm (CF_3), and by ^{19}F-NMR spectra, where the CF_3-group appeared as a singlet at δ ≈ -83 ppm.

In contrast to products **27**, for compounds **29** the absence of any signals in the low field of ^{1}H-NMR spectra was typical, indicating that the phenolic OH-group of opened γ-pyrone ring was involved in intramolecular cyclization. In the low field of ^{13}C-NMR spectra, one carbonyl group (COR^3) was detected at δ ≈ 191 ppm, indicating that formed salicyloyl carbonyl group of opened γ-pyrone ring and carbonyl carbon atom COR^2 were involved in the interaction during the reaction.

In contrast to compounds **28**, in the low field of the ^{1}H-NMR spectra of products **30**, only two signals belonging to the OH- and NH-groups were observed at δ = 10.2-13.5 ppm. This confirms the elimination of the perfluoroalkyl-group and the conversion of the OH-group into a keto-group. In the ^{13}C-NMR spectra, two carbonyl groups appeared at δ = 190-197 ppm.

Compounds **29** and **30**, which synthesis proceeded involving the elimination of the perfluoroalkyl-group, did not show any signals in the ^{13}C- and ^{19}F-NMR spectra, which could indicate the presence of fluorine atoms in these molecules. The fluorine atom in the aryl moiety

of compounds **26k** and **27e** appeared in the ^{19}F-NMR spectra as a singlet at δ ≈ -114.16 and -114.40 ppm, respectively. In the ^{13}C-NMR spectra of these products, the corresponding doublets of the carbon atoms of the aromatic ring containing a fluorine atom were detected.

For an additional examining of the obtained structures, HMBC NMR analyses were performed for compounds **26b** and **30b**. The most important correlations are shown in Figure 4.3. In the HMBC spectrum of compound **26b** the cross-peaks between the carbonyl group (δ = 177.0 ppm) and the aromatic hydrogen atoms (δ = 7.19-7.39 ppm) of chromone moiety could be detected through 3 and 4 bonds. Besides, correlations between the hydrogen atom of the formed pyridine-related ring (δ = 7.82 ppm) and two neighbouring carbonyl groups (δ = 177.0 and 189.6 ppm), the chiral carbon atom (δ = 90.5 ppm) and the carbon atom attached to COPh (δ = 91.2 ppm) were observed.

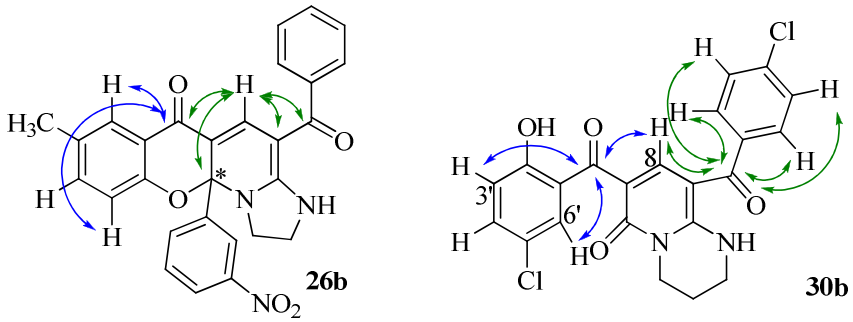


Figure 4.3 Observations from 2D HMBC analyses for compounds **26b** and **30b**.

The HMBC spectrum of **30b** displayed cross-peaks between the salicyloyl carbonyl carbon atom (δ = 190.7 ppm) and the hydrogen atoms: C3′-H, C6′-H (δ = 6.82-7.29 ppm) and C8-H (δ = 7.88 ppm), as well as correlations between another carbonyl group (δ = 192.1 ppm) attached to the carbon atom C9 and the hydrogen atoms of 4-chlorophenylene moiety (δ = 7.45-7.61 ppm) and C8-H (Figure 4.3).

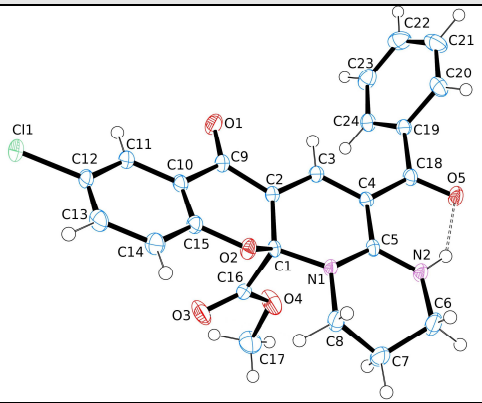
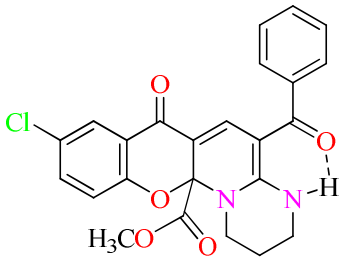
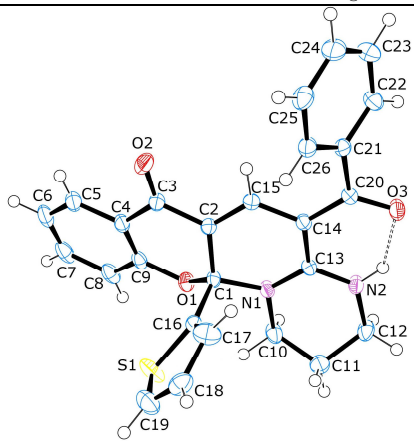
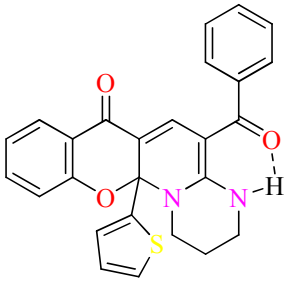
The structures of compounds **25f**, **26g**, **m**, **n**, **o**, **p**, **27b**, **e**, **g**, **28e**, **29b**, **30b** and **31** were unambiguously established by X-ray single crystal analysis (Table. 4.6).

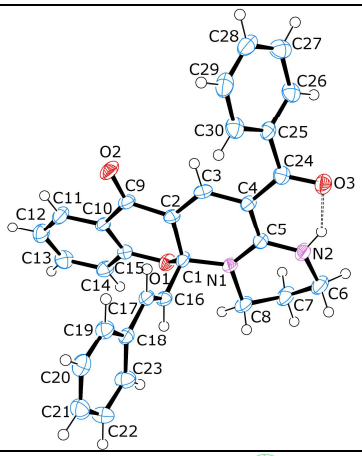
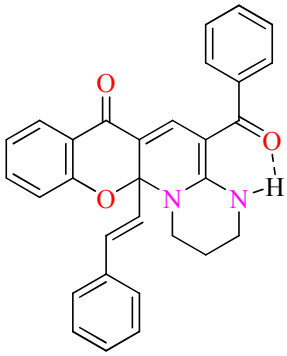
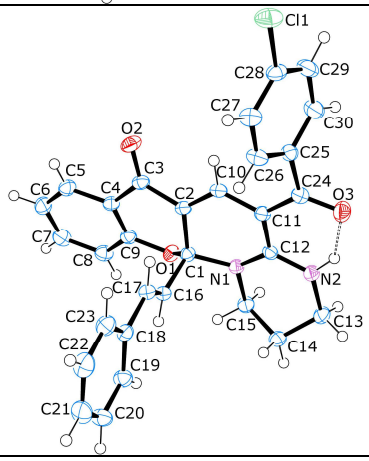
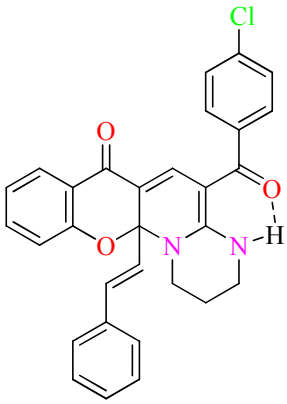
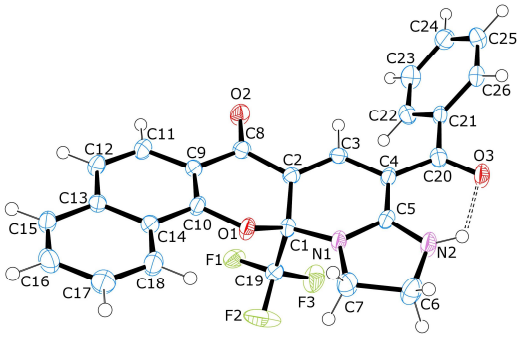
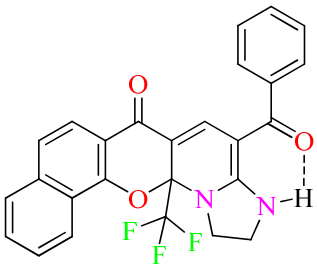
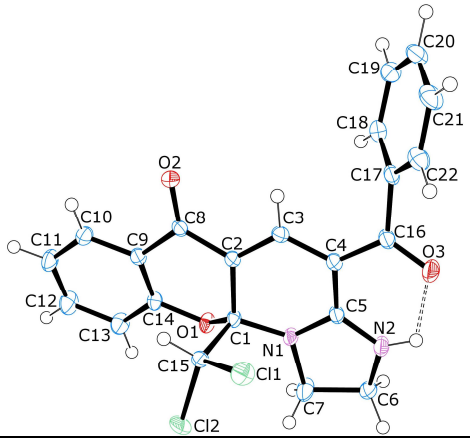
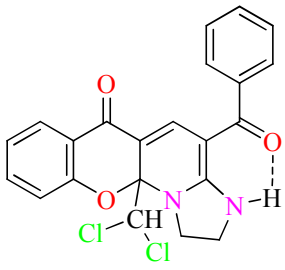
With the aid of the X-ray crystal analysis for chromenopyridine-related derivatives **25f** and **26g**, **m**, **n**, **o**, **p**, the presence of intermolecular hydrogen bonds between the NH-group and the neighbouring carbonyl group C=O was confirmed (if n = 1, ≈ 2.2 Å; if n = 2, 1.8-1.9 Å). Likewise, the X-ray analyses of compounds **28e** and **30b** indicated the hydrogen bonds between OH- and NH-groups and the neighbouring carbonyl groups C=O as distances of 1.7-1.9 Å. In the

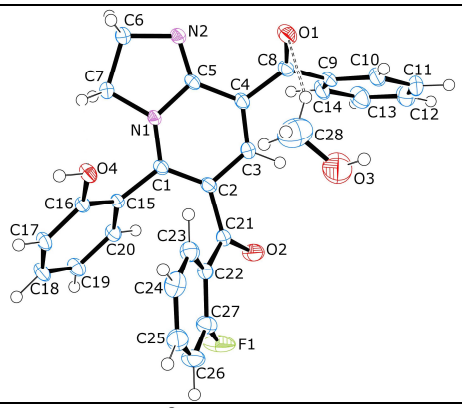
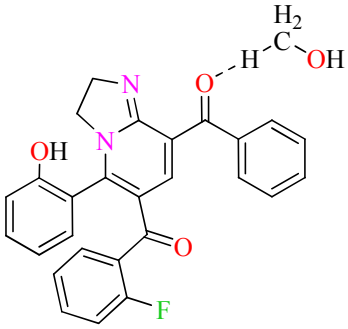
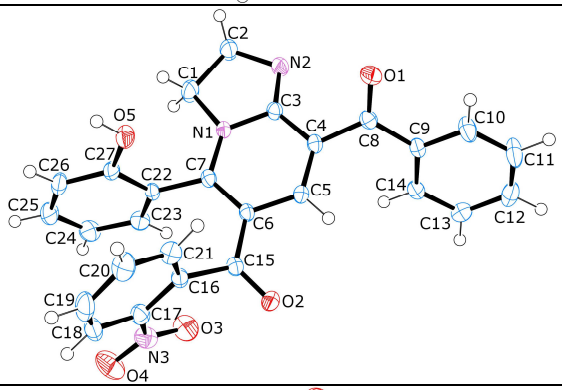
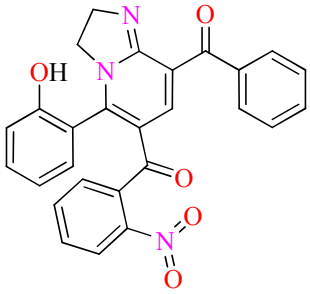
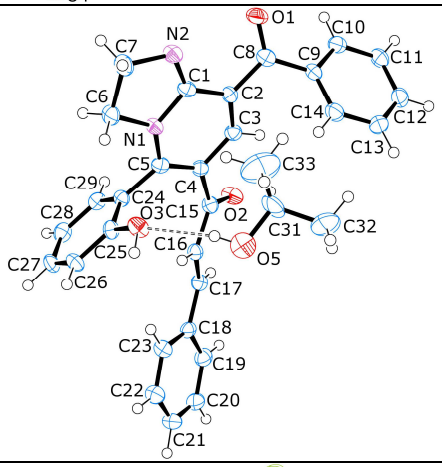
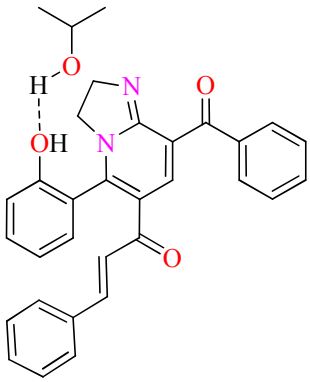
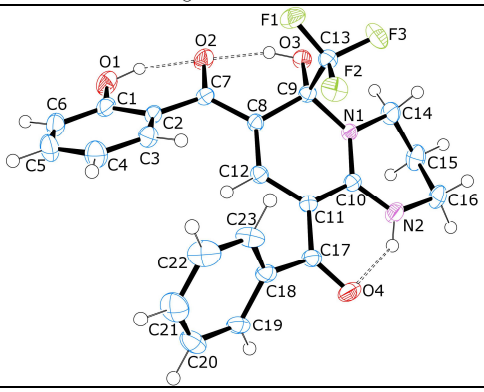
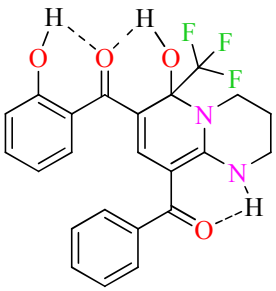
cases of compounds **27e** and **27g**, weak hydrogen bonds with molecules of solvents could be indicated by X-ray structure analysis. The distances are 2.7 and 2.1 Å long, respectively.

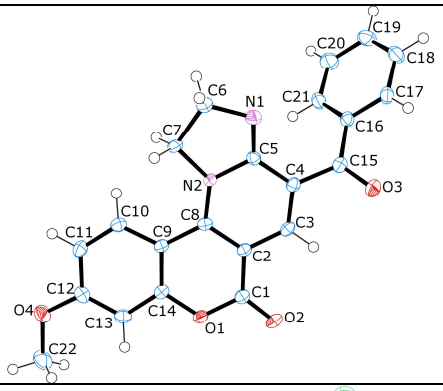
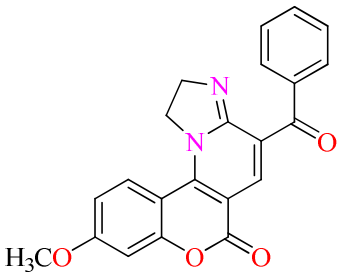
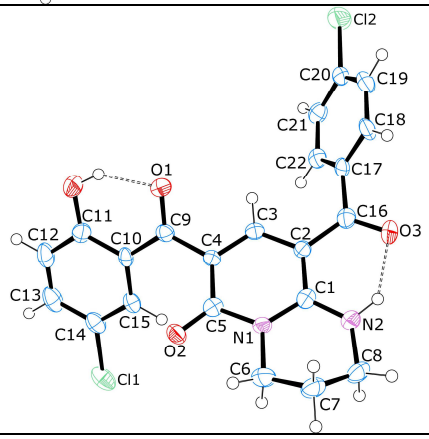
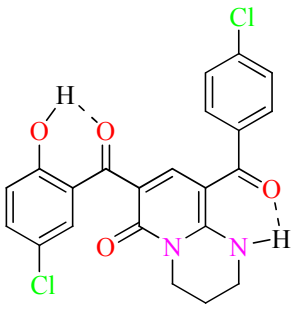
Expectedly, the structures of the fused chromenopyridine derivatives **25f** and **26g**, **m**, **n**, **o**, **p** and the pyridopyrimidine-related system of compound **28e** are not planar, because of the presence of a quaternary carbon atom (chiral centre), which configuration is near to tetrahedral (the values of angles lie within 106-113º). In contrast, the heterocyclic core of the 2*H*,3*H*-imidazo[1,2-*a*]pyridine moiety of compounds **27b**, **e**, **g** and fused coumarin system of compound **29b** is near to planar. Interestingly, in the cases of compounds **27b** and **27e**, the phenolic ring and the phenylene moiety of the aroyl-group (COR^3) approximate to be parallel to each other. Noteworthy, the alkyl chain of the six-membered heterocyclic ring derived from the HKAs is in a half-chair conformation in all crystal structures. The analyzed crystals of chiral compounds **25f**, **26g**, **m**, **n**, **o**, **p** and **28e** consisted of a racemic mixture, in contrast to previously obtained 6*H*-benzo[*c*]chromene **14o**, which crystallized as one enantiomer (see Chapter 3).

Table 4.6 Crystal structures of compounds **25f**, **26g**, **m**, **n**, **o**, **p**, **27b**, **d** , **h**, **28e**, **29b** and **30b**.

Crystal structure	Compound	Structure
	**25f**	
	**26g**	

	**26m**	
	**26n**	
	**26o**	
	**26p**	

	**27b**	
	**27d**	
	**27h**	
	**28e**	

	**29b**	
	**30b**	

4.3 Conclusions

The reactions of different 3-acylchromones, such as 3-methoxalyl-, 3-aroyl-, 3-cinnamoyl and 3-polyhaloacylchromones, with HKAs afforded a variety of different pyridine-related heterocycles. Electronic and steric effects of the acyl group of the 3-acylchromones and the ring size of the heterocyclic moiety of the HKAs play a great role in these reactions with regard to the product distribution.

In this way, an efficient and convenient method was proposed for the synthesis of tetracyclic fused chromenopyridine derivatives *via* domino reactions of 3-methoxalylchromones with HKAs, as well as *via* domino reactions of 3-aroyl- and 3-cinnamoylchromones with HKAs containing six-membered heterocyclic ring. In contrast, functionalized 2*H*,3*H*-imidazo[1,2-*a*]pyridine derivatives were synthesized with excellent regioselectivity by domino reactions of 3-aroyl- and 3-cinnamoylchromones with five-membered HKAs. Fluoroalkylated 2-salicyloylpyridine derivatives were delivered by reactions of 3-trifluoroacetylchromones with HKAs.

The synthesized pyridine-related heterocycles might exhibit useful biological properties. The investigation of biological activity of compounds **25**, **26** and **27** is currently in progress. Furthermore, obtained chromenopyridine derivatives **25** and **26** might be of interest due to their promising fluorescence properties, which are now being studied.

Chapter 5

Reactions of 3-halochromones with β-ketoamides and 1,3-dihydroindole-2-thiones: Synthesis of functionalized 2-salicyloylfurans and 2-benzoyl-8*H*-thieno-[2,3-*b*]indoles

5.1 Introduction

Five-membered heterocycles are immensely important organic compounds, which occur in an enormous number of natural products and demonstrate a wide range of biological activities.[269-271]

Furans, specifically polysubstituted furans, are key structural units in a variety of natural products and pharmaceuticals.[271-274] Among different substituted furans, 2-benzoylfurans have received much attention. For example, the natural product morachalcone C displays cytotoxic activity against HCT-8 and BGC823 human cancer cell lines.[275] 2-Benzoylfurans, such as benziodarone, benzbromarone and amiodarone, are clinically used nowadays (Figure 5.1). Benziodarone possesses vasodilation activity,[276] while benzbromarone is a uricosuric agent used in the treatment of gout, because of its xanthine oxidase inhibitor activity.[277] Amiodarone is applied as an antiarrhythmic agent.[278] Besides, another benzoylfuran, furidarone, is a coronary vasodilator.[279, 280] In addition, benzofuran befunolol exhibits antiglaucoma activity.[17]

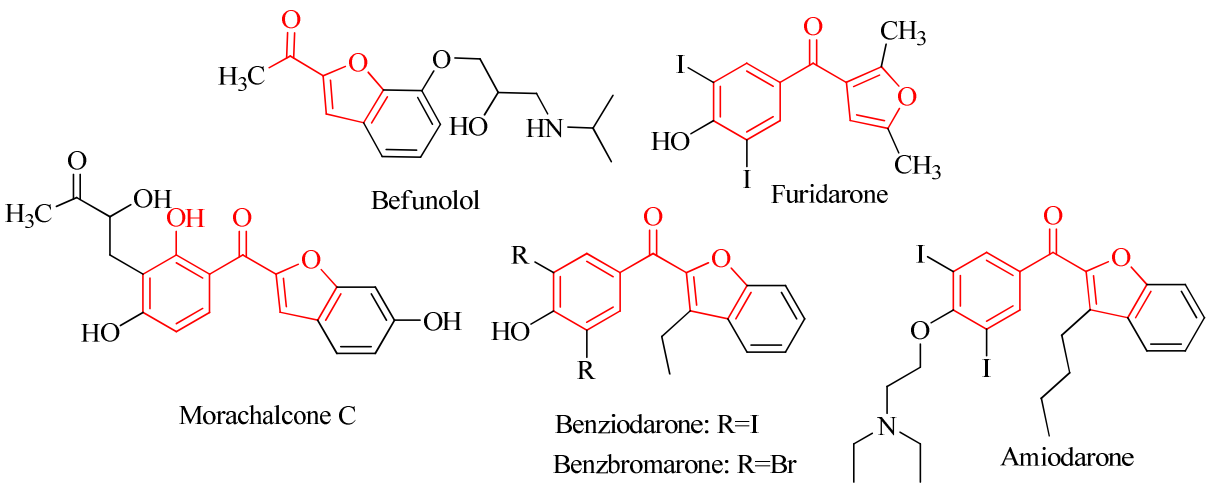


Figure 5.1 Pharmacologically relevant furan and 2-benzoylfuran derivatives.

At the same time, the indole ring system is one of the most important privileged scaffolds in medicinal chemistry.[17] Indoles fused to a sulfur containing ring systems[281-283] have attracted considerable attention due to their presence in natural products, for instance, thienodolin,[284, 285] brassilexin[286-290] and sinalexin[286, 291] (Figure 5.2). Furthermore, synthetic thienoindoles exhibit antifungal,[284, 288] anticancer[292, 293] activities and are used in the treatment of different neurological diseases.[294] In addition, thienoindoles are used in organic electronics as electroluminescence materials[295, 296] and conducting polymers.[297, 298]

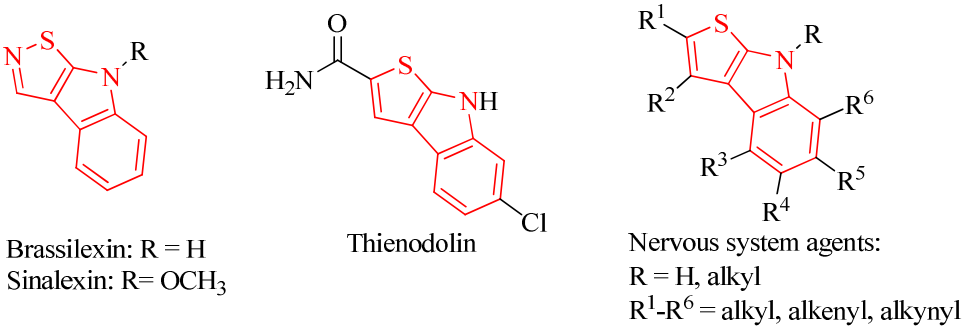


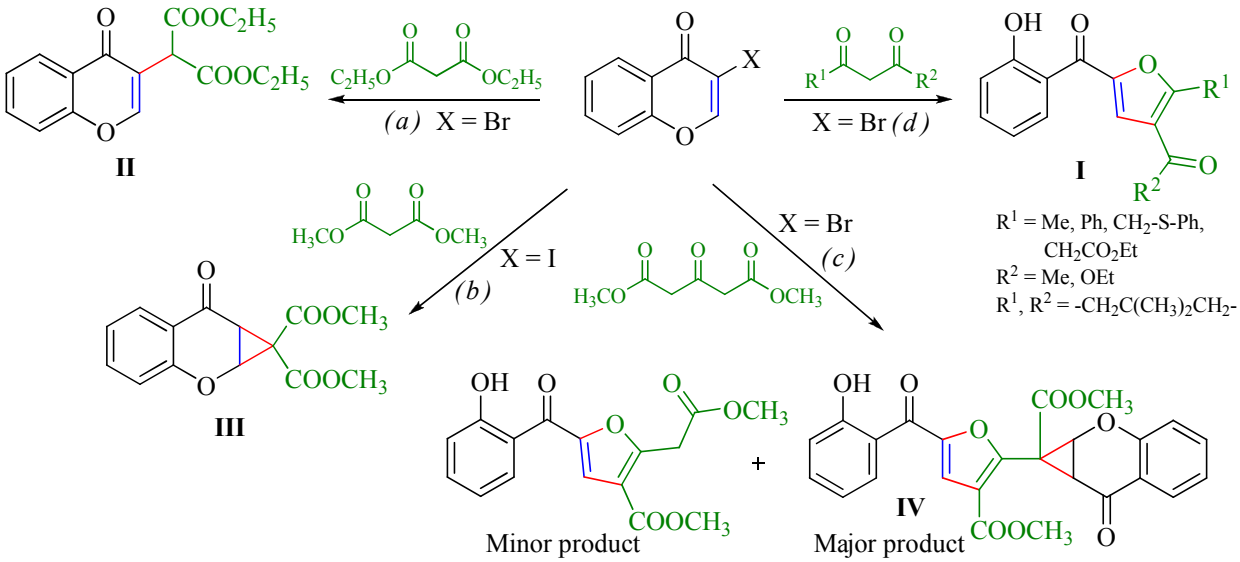
Figure 5.2 Pharmacologically relevant indoles fused with sulfur-containing heterocycles.

A number of approaches for the synthesis of furan derivatives,[299-301] as well as thieno[2,3-*b*]indole derivatives,[302-310] are reported. However, most of these methods suffer from some drawbacks and are limited in scope and generality. Therefore, flexible and efficient general methods for the preparation of new multiply substituted furan and thieno[2,3-*b*]indole derivatives are still desirable.

As already mentioned in Chapter 1, 3-halochromones are other representatives of 3-substituted chromones, which are well-proven bielectrophiles for the synthesis of different five-membered heterocycles (Scheme 1.6). In this context, it was proposed to consider 3-halochromones as potential building blocks for the synthesis of new furan and thiophene-related molecules. A few works related to the synthesis of these derivatives starting from 3-halochromones were already reported.[11, 73, 311-313]

1,3-Dicarbonyl compounds are exceptional synthetic platforms widely used in domino and multicomponent reactions.[314] 3-Halochromones, especially 3-bromochromone, have also attracted attention in the reactions with 1,3-dicarbonyl compounds (Scheme 5.1). Thus, 3-bromochromone reacted with various *β*-diketones and *β*-ketoesters giving highly functionalized furans (structure I).[11, 315] Nevertheless, the addition of diethyl malonate to 3-bromochromone

afforded the 3-substituted chromone (structure II).[316] At the same time, the reaction of 3-iodochromone with dimethyl malonate gave unexpected 2,3-methanochromanone containing a cyclopropyl ring (structure III).[76] Additionally, the reaction of 3-bromochromone with tricarbonyl compounds, specifically dimethyl 1,3-acetonedicarboxylate, was also reported and proceeded to the formation of furan derivative containing cyclopropyl ring (structure IV), due to the additional interaction with a second molecule of chromone.[165] Interestingly, in this case the carbonyl group (C=O) of dimethyl 1,3-acetonedicarboxylate was involved in the interaction, in contrast to the reactions with 3-acylchromones described in Chapter 3, where it played a role of a 1,3-*C*,*C*-binucleophile. Predictably, all described reactions were carried out under basic reaction conditions for the activation of the methylene component of 1,3-dicarbonyl compounds. Noteworthy, similar to reactions of 3-acylchromones with active methylene compounds studied in this work and before (see Chapter 3), most of the mentioned above reactions of 3-halochromones were performed using DBU as a base.



Scheme 5.1 Reactions of 3-halochromones with 1,3-dicarbonyl compounds.

Reaction conditions: (*a*) DBU, MeCN, 20 ºC; (*b*) K_2CO_3, DMF, 20 ºC; (*c*) DBU, THF, 20 ºC; *(d)* DBU or DBN, $CHCl_3$, 20 ºC;

The structure of *β*-ketoamides compared to *β*-diketones contains an additional nucleophilic centre, namely the nitrogen atom of the amide group. These compounds are widely used substrates. They can react as *C*,*O*-,[317-331] *C*,*N*-,[332-338] *N*,*O*-,[339] or *O*,*O*-binucleophiles[340] in different cyclization reactions. By now, the use of *β*-ketoamides in the reactions with chromones

has not been reported. The investigation of the reactions of 3-halochromones with *β*-ketoamides is mechanistically very interesting, because of the presence of a multiplicity of reactive centres in the molecule of these nucleophiles, such as an active methylene component, two oxygen and one nitrogen atoms, which can react by electrophilic attack leading to the synthesis of highly functionalized furan, pyrrole or other derivatives .

On the other hand, powerful 1,3-*C*,*S*-binucleophiles, like 1,3-dihydroindole-2-thiones, are widely used as building blocks in cyclization reactions with diverse bielectrophiles for the synthesis of various sulfur-containing heterocycles.[341-347] Such reactions have also attracted attention in our group.[348, 349] The interaction of *α*-halocarbonyl compounds, which are structurally similar to the 3-halochromones, with 1,3-dihydroindole-2-thione derivatives is reported and led to the synthesis of thieno[2,3-*b*]indoles.[304] The reactions of 3-halochromones with *S*-nucleophiles are very rare. Only reactions of 3-iodochromones with 1-methyl-2-sulfanylimidazole, 1,2,4-triazole derivatives, *N*,*N*′-dimethylthiourea and 2-mercapto-benzimidazoles were reported.[11, 73]

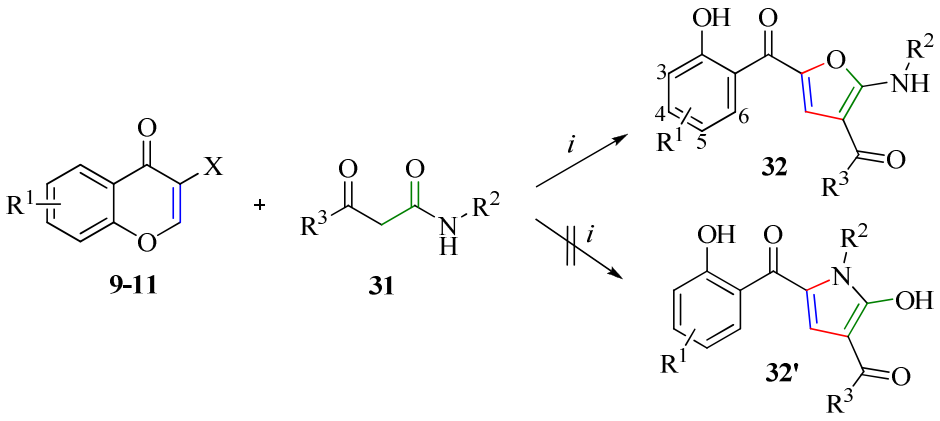
All these facts have inspired me to study the reactions of 3-halochromones with *β*-ketoamides and 1,3-dihydroindole-2-thiones, which have not been studied previously. It is worth mentioning that there are only a few reports, which contain the comparison of the reactivity of different 3-halochromones towards binucleophiles.[78-81] Another aspect of this part of my work was to study the influence of the type of halogen atom on the selectivity of the reactions of 3-halochromones. This project was performed with help from Tim Gläsel during his work on bachelor thesis.

5.2 Results and discussions

5.2.1 Reactions of 3-halochromones with *β*-ketoamides

The investigation was started with a study of reactions of 3-halochromones **9-11** with *β*-ketoamides **31**. It was suggested to perform a test reaction using the well-proven general procedure, described in Chapter 3 during the study of reactivity of 3-acylchromones towards active methylene compounds. The treatment of 3-bromochromone **10a** with *β*-ketoamide **31a** (1.1 eqiuv.) in the presence of DBU (1.3 equiv.) in 1,4-dioxane at room temperature proceeded

in the formation of 2-salicyloylfuran **32a** with an excellent regioselectivity, in 87% yield (Scheme 5.2, Table 5.1). The reaction time was about 10-12 hours. Interestingly, in spite of the high nucleophilicity of a nitrogen atom of the amide group, 2-benzoylpyrrole **32′** was not observed.



Scheme 5.2 Synthesis of compounds **32**.

Reaction conditions: (*i*) **9-11** (1.0 equiv.), **31** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC.

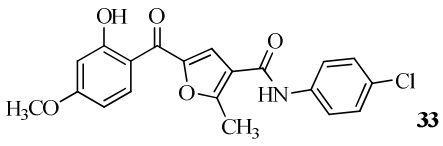
The preparative scope was next studied. The investigation has shown that the present protocol could be applicable to various types of *β*-ketoamides **31** providing a convenient route for the synthesis of a wide range of 2-salicyloylfurans **32** (Scheme 5.2, Table 5.1). 2-Salicyloylfurans **32a-x** were obtained in moderate to excellent yields (46-99%). Gratifyingly, most products could be isolated by simple filtration of the formed precipitate. Otherwise, recrystallization from heptane/isopropanol or column chromatography was used. In the case of the synthesis of compound **32o**, a by-product, isomeric 2-benzoylfuran **33**, could be isolated and identified.

Table 5.1 Synthesis of compounds **32**.

3-Halochromone	X	31	32	R^1	R^2	R^3	Yield,[a] %
10a	Br	**a**	**a**	H	Ph	CH_3	87
10c	Br	**a**	**b**	5-Cl, 4-CH_3	Ph	CH_3	99
11b	Cl	**a**	**c**	4-OCH_3	Ph	CH_3	98
11c	Cl	**a**	**d**	3,4-benzo	Ph	CH_3	53
10a	Br	**b**	**e**	H	2,4-$(CH_3)_2C_6H_3$	CH_3	93
11b	Cl	**b**	**f**	4-OCH_3	2,4-$(CH_3)_2C_6H_3$	CH_3	69
11c	Cl	**b**	**g**	3,4-benzo	2,4-$(CH_3)_2C_6H_3$	CH_3	76
11a	Cl	**c**	**h**	H	2-$CH_3C_6H_4$	CH_3	85
10c	Br	**c**	**i**	5-Cl, 4-CH_3	2-$CH_3C_6H_4$	CH_3	99
11b	Cl	**c**	**j**	4-OCH_3	2-$CH_3C_6H_4$	CH_3	98
11c	Cl	**c**	**k**	3,4-benzo	2-$CH_3C_6H_4$	CH_3	93
9a	I	**d**	**l**	H	4-ClC_6H_4	CH_3	46
10b	Br	**d**	**m**	5-CH_3	4-ClC_6H_4	CH_3	99
10c	Br	**d**	**n**	5-Cl, 4-CH_3	4-ClC_6H_4	CH_3	98
11b	Cl	**d**	**o**	4-OCH_3	4-ClC_6H_4	CH_3	47*
9b	I	**d**	**p**	3,4-benzo	4-ClC_6H_4	CH_3	56
11a	Cl	**e**	**q**	H	H	OCH_3	98
10b	Br	**e**	**r**	5-CH_3	H	OCH_3	90
11b	Cl	**e**	**s**	4-OCH_3	H	OCH_3	79
11c	Cl	**e**	**t**	3,4-benzo	H	OCH_3	88
11a	Cl	**f**	**u**	H	Ph	Ph	81
10c	Br	**f**	**v**	5-Cl, 4-CH_3	Ph	Ph	72
11b	Cl	**f**	**w**	4-OCH_3	Ph	Ph	69
11c	Cl	**f**	**x**	3,4-benzo	Ph	Ph	70

[a] Yields of isolated products.

* Compound **33** was isolated in 7% yield (structure see below).



33

In addition, the influence of the halogen atom of the 3-halochromone **9-11** on the yields of compounds **32** was studied for each type of *β*-ketoamides **31** (see Table 5.2). Thus, 3-chlorochromone **11a** gave the best yields of products **32q** and **32u**, while 3-bromochromone **10a** gave a little bit lower yields. Though, for the synthesis of compound **32a** 3-bromochromone **10a** showed to give the best yield (87%), slightly higher than 3-chlorochromone **11a** (83%). The use of 3-iodochromone **9a** resulted in a dramatic decrease of the yields (45-53%). Besides, the type of halogen had also an influence on the reaction time. The reactions of 3-chlorochromones proceeded approximately 3-4 h, while reactions of 3-bromo and 3-iodochromones required 10-12 h to reach full conversion. In this way, it was shown that the yields of obtained 2-benzoylfurans **32** strongly depend on the type of halogen substituent of the 3-halochromones **9-11**. 3-Bromo- and 3-chlorochromones were the most effective for the synthesis of compounds **32**.

Table 5.2 The influence of the halogen atom of 3-halochromones on the obtained yields.

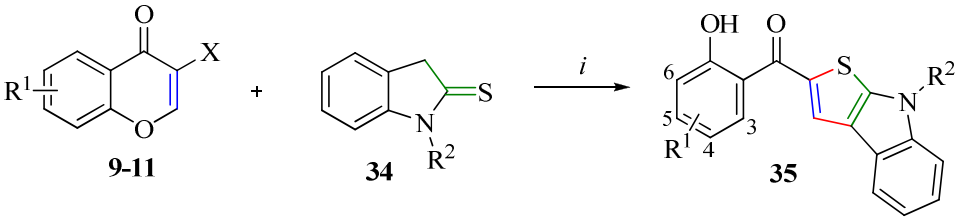
3-Halochromone	X	*β*-Ketoamide	Product	Yield, %[a]
9a	I	**31a**	**32a**	53
10a	Br	**31a**		87
11a	Cl	**31a**		83
9a	I	**31e**	**32q**	49
10a	Br	**31e**		79
11a	Cl	**31e**		98
9a	I	**31f**	**32u**	45
10a	Br	**31f**		63
11a	Cl	**31f**		81

[a] Yields of isolated products.

5.2.2 Reactions of 3-halochromones with 1,3-dihydroindole-2-thiones

The next goal in this investigation was to study the reactions of 3-halochromones **9-11** with 1,3-dihydroindole-2-thiones **34** (Scheme 5.3, Table 5.3). In order to activate the binucleophiles, DBU and potassium carbonate were examined as bases. The reaction of 3-chlorochromone **11a** with 3*H*-indole-2-thione **34a**, in the presence of DBU (1.3 equiv.) in 1,4-

dioxane, afforded 2-{8*H*-thieno[2,3-*b*]indole-2-carbonyl}-phenol **35a** in 57% yield (Method A). The same reaction using K_2CO_3 (4.0 equiv.) in DMF gave product **35a** in an improved yield of 74% (Method B). Further studies of the preparative scope showed that by the use of DBU more by-products were formed (detected by TLC) and the yields of obtained products **35** (35-60%) were lower than using a less strong base, like K_2CO_3 (56-78%), see Table 5.3. Both methods were carried out at room temperature for 3-4 hours (monitored by TLC). The products were isolated by column chromatography.



Scheme 5.3 Synthesis of compounds **35**.

Reaction conditions: (*i*) **9-11** (1.0 equiv.), **34** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 ºC (method A); K_2CO_3 (4.0 equiv.), DMF, 20 ºC (method B).

Table 5.3 Synthesis of compounds **35**.

3-Halochromone	X	34	35	R^1	R^2	Yield, [a] %
11a	Cl	**a**	**a**	H	H	57,[b] 74[c]
9a	I	**a**	**a**	H	H	30[c]
11b	Cl	**a**	**b**	5-OCH_3	H	56[c]
11c	Cl	**a**	**c**	5,6-benzo	H	78[c]
10b	Br	**b**	**d**	4-CH_3	CH_3	43[b]
11b	Cl	**b**	**e**	5-OCH_3	CH_3	46[b]
11c	Cl	**b**	**f**	5,6-benzo	CH_3	55[b]
11a	Cl	**c**	**g**	H	Ph	60[b]
11b	Cl	**c**	**h**	5-OCH_3	Ph	35[b]
11c	Cl	**c**	**i**	5,6-benzo	Ph	58[b]

[a] Yields of isolated products.

[b] Reaction was carried out using method A.

[c] Reaction was carried out using method B.

Expectedly, 3-bromo and 3-chlorochromones showed the highest activity in reactions with 1,3-dihydroindole-2-thiones **34**. The use of 3-iodochromone **9a** instead of 3-chlorochromone **11a** employing method B dramatically decreased the yield of product **35a** to only 30% (Table 5.3). This fact demonstrates the significant influence of the type of halogen atom in the 3-position of chromones **9-11** on the yields of obtained products. This finding corresponds to the results obtained in the reaction with *β*-ketoamides **31**.

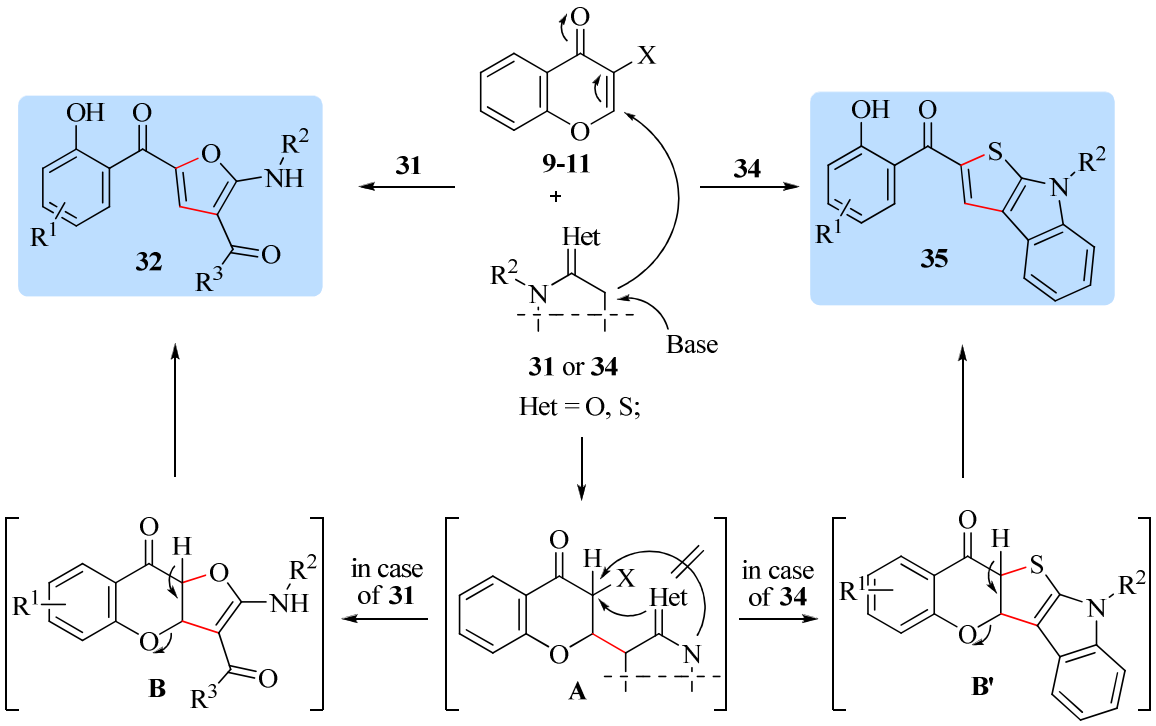
5.2.3 Proposed reaction mechanism

The proposed mechanism of the reactions of 3-halochromones **9-11** with *β*-ketoamides **31** and 1,3-dihydroindole-2-thiones **34** is outlined in Scheme 5.4.

In all described cases, 3-halochromones **9-11** reacted as 1,3-*C,C*-bielectrophiles. The first attack of binucleophiles **31** or **34** took place at the most electrophilic carbon atom at 2-position of 3-halochromones giving intermediate **A** (1,4-addition). The second nucleophilic attack of substrates **31** and **34** was directed to the halogen-substituted carbon atom. Further elimination of the halogen atom led to the formation of intermediates **B** and **B′**, respectively (Scheme 5.4). These intermediates underwent the cleavage of the carbon-oxygen bond to give new compounds **32** and **35** containing five-membered heterocyclic ring (see pathway I, Scheme 1.6, Chapter 1). It should be noted that products containing a six-membered ring, formed *via* a second attack of the nucleophile directed to the carbonyl group of the chromone moiety, were not observed (pathway II, Scheme 1.6, Chapter 1).

Regarding binucleophiles, in the first step, *β*-ketoamides **31** and 1,3-dihydroindole-2-thiones **34** reacted as *C*-nucleophiles *via* their methylene component activated by base. At the second electrophilic attack, two oxygen and nitrogen atoms of *β*-ketoamides **31** could be exposed providing several possible isomers, specifically 2-benzoylfurans **32** and **33**, as well as 2-benzoylpyrroles **32′** mentioned above. Obviously, the amide oxygen atom is more nucleophilic than the other oxygen. It could be expected that the second electrophilic attack would be directed to the most nucleophilic centre, the amide nitrogen atom. Nonetheless, it was mechanistically interesting to discover that the cyclizations proceeded *via* the amide oxygen atom of *β*-ketoamides **31** giving 2-benzoylfurans **32**. Isomeric 2-benzoylpyrroles **32′** were not detected, while isomeric 2-benzoylfuran **33** was isolated in a small amount as a by-product. As for nucleophiles **34**, the cyclization *via* the nitrogen atom by the second electrophilic attack was not

possible due to a steric hindrance. Therefore, the subsequent attack was directed to the sulfur atom, followed by elimination of the halogen atom. The γ-pyrone ring opening resulted in the formation of compounds **35**.



Scheme 5.4 Proposed reaction mechanism for the formation of compounds **32** and **35**.

5.2.4 Structure identification

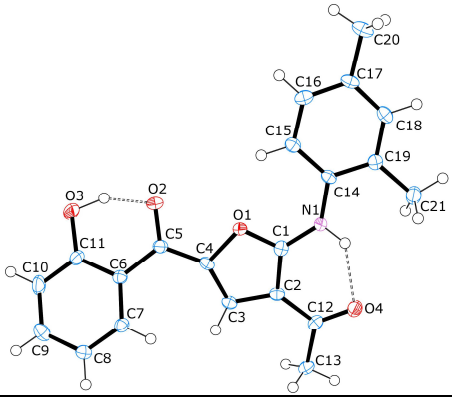
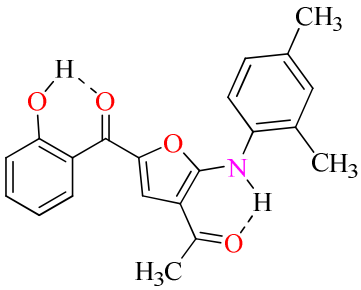
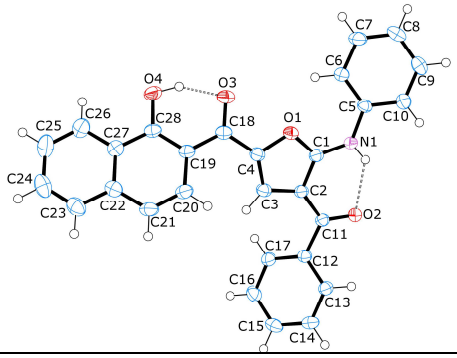
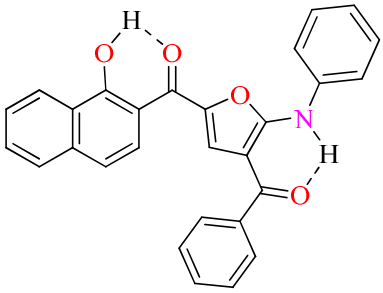
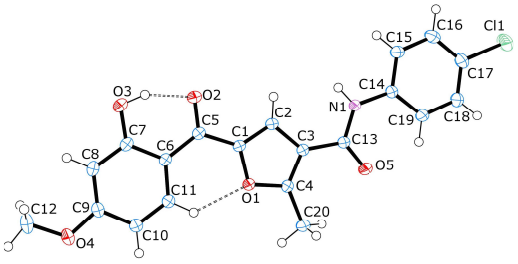
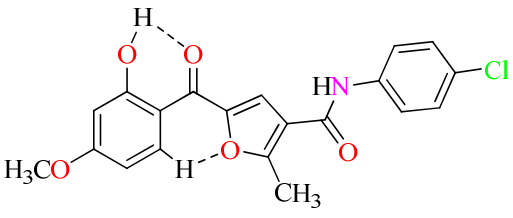
All structures were confirmed by NMR, IR, MS and X-ray single crystal analyses.

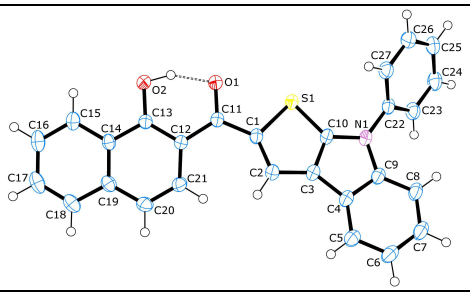
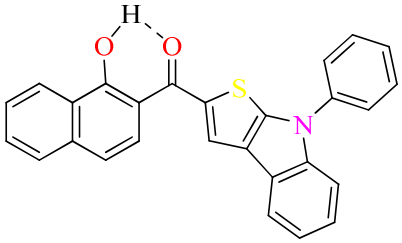
In the low field of ^{1}H-NMR spectra of compounds **32** in DMSO-d_6, two singlets of NH- and OH-groups were observed at δ = 10.2-13.9 ppm. The shift of these groups to δ ≈ 11.0 ppm can be caused by the presence of intramolecular hydrogen bond with the neighbouring carbonyl group. Nevertheless, the values of chemical shifts of OH-group were also dependent on the R^1-substituent in the salicyloyl moiety. In the ^{13}C-NMR spectra, two carbonyl groups appeared at δ ≈ 180 and 190 ppm. Similar observations were seen in the ^{1}H- and ^{13}C-NMR spectra of isomeric 2-benzoylfurans **33**. In the ^{1}H-NMR spectra of compounds **35** in DMSO-d_6, the singlet of phenolic OH-group appeared at δ = 10.6-13.9 ppm indicating also in this case the hydrogen bond formation. For compounds **35a-c**, an additional singlet of the NH-group was detected in the low

field of ^{1}H-NMR spectra (δ ≈ 11 ppm). The signal of the carbonyl group was observed at δ ≈ 190 ppm in the ^{13}C-NMR spectra.

The structures of compounds **32e**, **32x**, **33** and **35i** were independently established by X-ray crystal structure analysis (Table 5.4). Typical hydrogen bonds involving OH- or NH-groups and oxygen atom of neighbouring carbonyl groups (C=O) were confirmed as well (1.5-2.1 Å). Obviously, the structures of products **32e**, **32x** and **35i** are not planar. The torsion angles between the salicyloyl moiety and heterocyclic ring are in the range of 15-22º. A planar core of thieno[2,3-*b*]indole was observed in the molecule of compound **35i**. Interestingly, the structure of product **33** is planar including 2-salicyloylfuran and amide moieties. Most likely, a non-classical hydrogen bond (C11-H···O1, 2.1 Å) plays a significant role in the formation of such planar crystal structure.

Table 5.4 Crystal structures of compounds **32e**, **32x**, **33** and **35i**.

Crystal structure	Compound	Structure
	**32e**	
	**32x**	
	**33**	

	**35i**	

5.3 Additional investigations

Furochromones contain two important fragments, like chromone and furan moieties, and are of much interest, because of their biological properties. For example, phytoestrogen lupinalbin A represents a selective estrogen receptor modulator (Figure 5.3).[350] Broussofluorenones A and B show potent *α*-glucosidase and anticholinesterase inhibitions.[351, 352] Due to continued interest in furochromones as pharmacological agents, it was interesting for me to study the transformation of 2-benzoylfurans **32** to furo[3,2-*b*]chromen-9-ones.

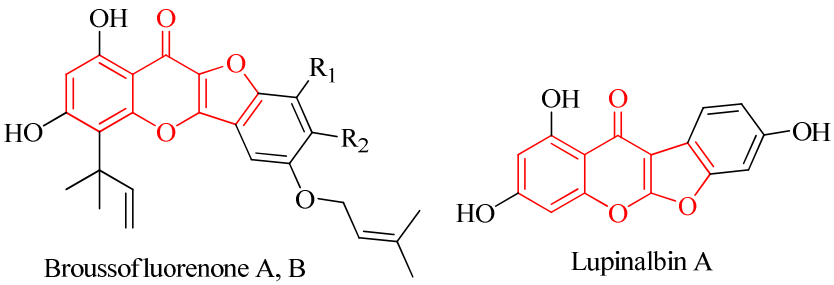
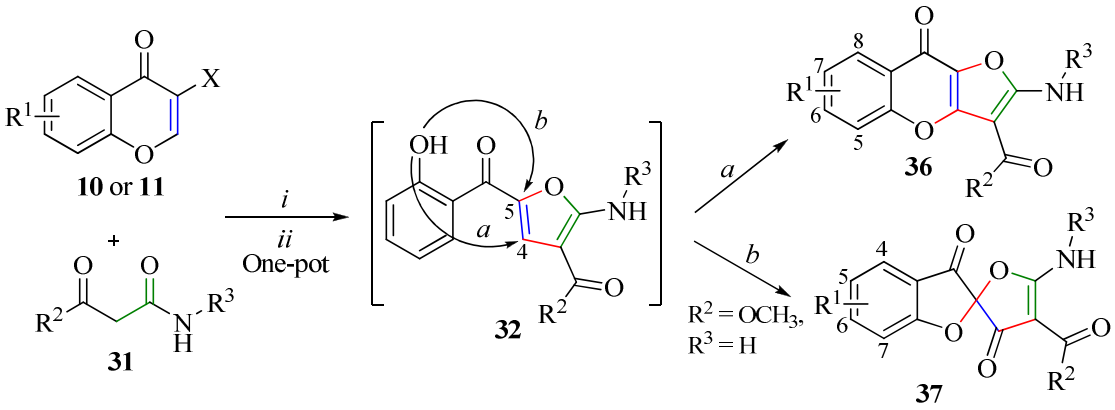


Figure 5.3 Pharmacologically relevant furochromones.

For this purpose, the use of various oxidizing agents (iodine,[73] *o*-chloranil and DDQ[350]), which were applied in similar cyclizations, different bases (DBU and potassium carbonate) and solvents (DCM, MeCN and DMF) were studied. The best yield of the furo[3,2-*b*]chromen-9-one **36a** (up to 32%) was obtained using iodine (2 equiv.) and DBU (3 equiv.) in MeCN (Scheme 5.5, Table 5.5). The rather low yield can be explained by the instability and decomposition of the formed product. A metal-catalyzed reaction using $Cu(OAc)_2$ (catalyst) in the presence of $Zn(OTf)_2$ (additive) was also applied for the synthesis of target structure.[353] However, this method was not successful and no product could be isolated.



Scheme 5.5 Synthesis of compounds **36** and **37**.

Reaction conditions: (*i*) **10** or **11** (1.0 equiv.), **31** (1.1 equiv.), DBU (1.3 equiv.), 1,4-dioxane, 20 °C; (*ii*) I_2 (2.0 equiv.), DBU (3 equiv.), DCM or DMF.

Table 5.5 Synthesis of compounds **36** and **37**.

3-Halochromone	X	*β*-Ketoamide	Product	R^1	R^2	R^3	Yield, [a] %
Starting from **32m**			**36a**	7-CH_3	CH_3	4-ClC_6H_4	32
10a	Br	**31a**	**36b**	H	CH_3	Ph	37
11b	Cl	**31a**	**36c**	6-OCH_3	CH_3	Ph	28
10d	Br	**31a**	**36d**	5,6-benzo	CH_3	Ph	14
11a	Cl	**31f**	**36e**	H	Ph	Ph	42
11b	Cl	**31f**	**36f**	6-OCH_3	Ph	Ph	21
10a	Br	**31e**	**37a**	H	OCH_3	H	30
11b	Cl	**31e**	**37b**	6-OCH_3	OCH_3	H	27

[a] Yields of isolated products.

As a next step, I have studied a one-pot protocol for the direct preparation of furo[3,2-*b*]chromen-9-ones starting from 3-halochromones (Scheme 5.5, Table 5.5). The reaction of chromone **10a** with *β*-ketoamide **31a** in the presence of DBU (1.3 equiv.) in 1,4-dioxane followed by subsequent oxidative cyclization by addition iodine (2 equiv.), DBU (3 equiv.) and DCM gave product **36b** in 37% yield. The obtained yield is slightly higher than the yield in the stepwise process. The main loss in yield took place in the cyclization of 2-benzoylfuran.

In view of the obtained results and operational simplicity, the preparative scope was next studied using the one-pot protocol, starting from 3-bromo- and 3-chlorochromones **10** and **11**, as they proved to give better yields than 3-iodochromones **9** for the synthesis of 2-benzoylfurans.

Accordingly, reactions of chromones **10** and **11** with *β*-ketoamides **31** with subsequent oxidative cyclization gave furo[3,2-*b*]chromen-9-ones **36b-f** in moderate or low yields (Scheme 5.5, Table 5.5). The lowest yield was obtained for the benzo-substituted product **36d** (14%) with, presumably due to a steric hindrance. It is necessary to emphasise that, in the case of reaction of 3-halochromones with methyl 2-carbamoylacetate **31e**, the interesting unexpected spiro-compounds **37** were obtained. The spiro-structure formation can be explained by the nucleophilic attack of phenolic OH-group of formed 2-benzoylfuran **32**, directed to the position 5 (instead of position 4) of the activated double bond, followed by further additional oxidation at 4-position.

All structures of compounds **36** and **37** were confirmed by NMR, mass spectrometry and IR. In contrast to 2-benzoylfurans **32**, in the low field of ^{1}H-NMR spectra of furo[3,2-*b*]chromen-9-ones **36** in DMSO-d_6, only one singlet (NH-group) was detected at δ ≈ 10.6 ppm. At the same time, the ^{1}H-NMR spectra of spiro-compounds **37** showed two singlets of NH_2 group (δ ≈ 9.1 and 10.1 ppm), indicating non-equivalence of these hydrogen atoms. In the low field of the ^{13}C-NMR spectra of products **37**, typical signals of carbon atoms C-3, C3´, C-5´, C-7a and the carbonyl carbon atom of the ester group were observed (δ = 163-192 ppm). In contrast, for compounds **36** only one signal of the carbonyl group was detected in the low field of the ^{13}C-NMR spectra (δ ≈ 190 ppm).

The structure of **37b** was additionally confirmed using 2D NMR analysis (COSY, HMBC). In the HMBC spectrum, cross-peaks between carbon atom C-3 (δ = 189.0 ppm) and the aromatic hydrogen atoms (δ = 6.86-7.67 ppm) of chromone moiety were detected through three and four bonds (see Figure 5.4). Besides, carbon atom C-5′ (δ = 178.0 ppm) gave cross-peak with one of the hydrogen atoms of the amino group (δ = 9.06 ppm). Expectedly, the spiro-carbon (δ = 102.7 ppm) did not show significant cross-peaks with any hydrogen atoms.

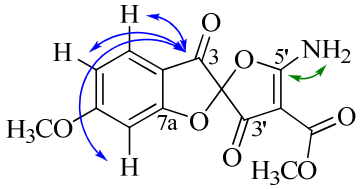
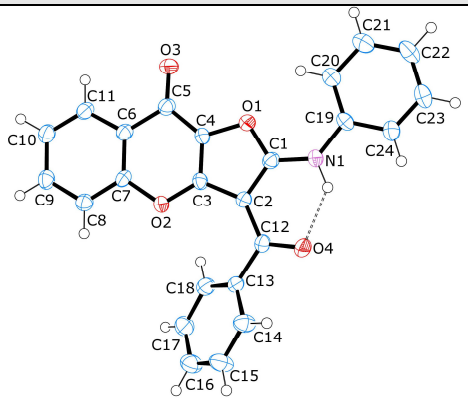
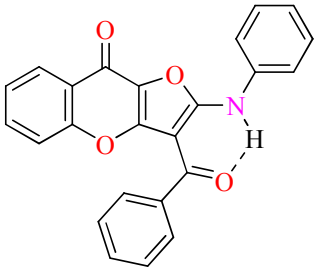


Figure 5.4 Observations from 2D HMBC analysis for compound **37b**.

The structure of **36e** was independently confirmed by X-ray crystal structure analysis (Table 5.6). The hydrogen bond between NH-group and the oxygen atom O4 of the carbonyl group was indicated as a distance of 2.0 Å. Predictably, the furo[3,2-*b*]chromen-9-one moiety is

planar. In addition, based on the X-ray crystal structure analysis of derivative **37b**, the spirocyclic structure of compounds **37a** and **37b** was suggested. This structure is also in accordance with 2D NMR analysis. Nonetheless, due to the relatively low quality of the obtained crystal data, the X-ray structure of **37b** cannot be published.

Table 5.6 Crystal structure of compound **36e**.

Crystal structure	Compound	Structure
	**36e**	

Unfortunately, the attempts to carry out the oxidative cyclizations of obtained 2-benzoyl-8*H*-thieno[2,3-*b*]indoles **35** under the same reaction conditions did not give any results. On the TLC, no conversion of the starting materials was observed.

5.4 Conclusions

A new efficient and convenient method for the synthesis of functionalized 2-salicyloylfurans and 2-benzoyl-8*H*-thieno[2,3-*b*]indoles was developed *via* cyclization reactions of 3-halochromones with *β*-ketoamides and 1,3-dihydroindole-2-thiones, respectively. The influence of the halogen atom of the 3-halochromones on the yields of obtained products was studied. 3-Bromo- and 3-chlorochromones proved to be more active than 3-iodochromones in this type of reactions. In addition, furo[3,2-*b*]chromen-9-ones were synthesized using a one-pot two-step protocol starting from 3-halochromones and *β*-ketoamides followed by subsequent oxidative cyclization of formed 2-salicyloylfurans using iodine. The products obtained during this study might be of pharmacological relevance. The biological properties of compounds **32** and **33** are presently being studied.

Chapter 6

Summary

This thesis was dedicated to the study of the chemical potential of different 3-substituted chromones, namely 3-acylchromones **4-8** and 3-halochromones **9-11**, as building blocks for the synthesis of new interesting carbo- and heterocycles. The overview containing the number of structural classes synthesized *via* domino reactions of 3-substituted chromones with different binucleophiles is shown in Scheme 6.1.

In Chapter 2, an already known protocol of the modified Vilsmeier-Haack reaction was applied for the synthesis of various 3-substituted chromones. New 3-methoxalyl-, 3-perfluoroacyl- and 3-aroylchromones derivatives were prepared.

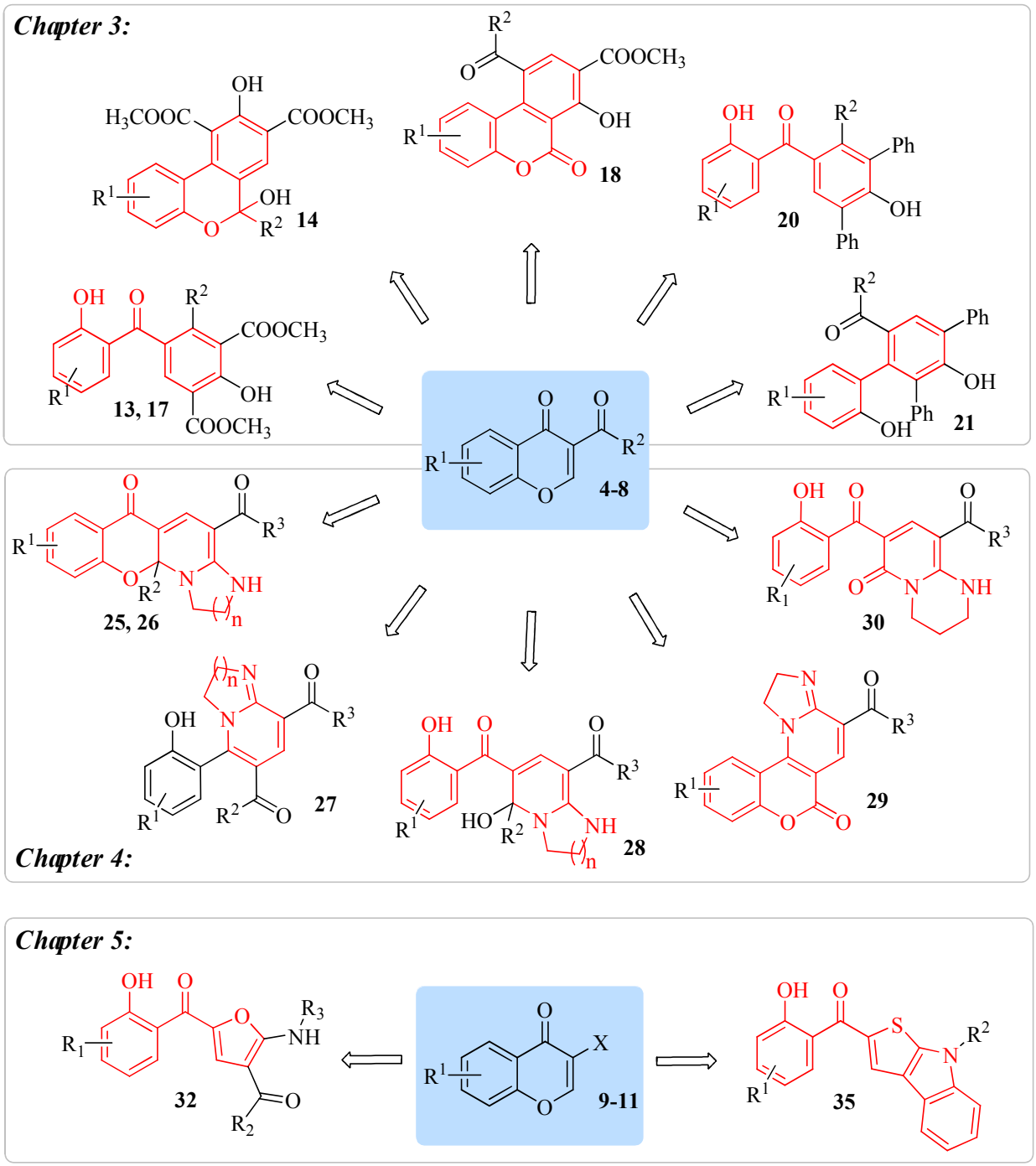
According to Chapter 3, the domino reactions of 3-acylchromones **4-6** with 1,3-*C,C*-binucleophiles, such as dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone, led to the formation of various functionalized 2-hydroxybenzophenones, fluorine-containing 6*H*-benzo[*c*]chromones, benzo[*c*]coumarins and phenols depending on the substituent at the 3-position of chromone and used 1,3-*C,C*-binucleophile. Photophysical properties of synthesized products were studied. It was found that 2-hydroxybenzophenones **13**, 6*H*-benzo[*c*]chromenes **14** and products of their hydrolysis exhibit strong UV-absorption properties. Furthermore, some of 6*H*-benzo[*c*]chromenes **14** demonstrate intensive fluorescence behaviour.

As described in Chapter 4, a simple and efficient method for the synthesis of various pyridine-related heterocycles was developed based on domino reactions of 3-acylchromones **4-8** with heterocyclic ketene aminals (HKAs). It was discovered that the ring size of the heterocyclic moiety of the HKAs, as well as electronic and steric effects of the acyl group of 3-acylchromones, play an important role in these reactions and have a significant influence on the structure of the formed products. Moreover, the synthesized tetracyclic fused chromenopyridine derivatives **25** and **26** show promising fluorescence properties, which are now in the study.

Finally, in Chapter 5, an efficient and convenient method for the synthesis of functionalized 2-salicyloylfurans and 2-benzoyl-8*H*-thieno[2,3-*b*]indoles was proposed *via* cyclization reactions of 3-halochromones with *β*-ketoamides and 1,3-dihydroindole-2-thiones,

respectively. Furo[3,2-*b*]chromen-9-ones were synthesized using a one-pot two steps protocol starting from 3-halochromones and *β*-ketoamides with subsequent oxidative cyclization.

The products obtained in this thesis are not readily available by other methods and might be of pharmacological relevance due to their structural similarity to bioactive natural products and synthetic drugs. The biological evaluation of synthesized compounds is now in progress.



Scheme 6.1 The chemical potential of 3-substituted chromones **4-11**.

Supplement 1

Experimental part

1.1. Analytics

^{1}H-NMR-Spectroscopy:

Bruker AVANCE 250 II (250 MHz), Bruker AVANCE 300 III (300 MHz), Bruker AVANCE 500 (500 MHz). The spectra were calibrated according to the solvent signals: 7.26 ppm for $CDCl_3$, 2.50 ppm for DMSO-d_6.[354] Peak characterization: s = singlet, d = doublet, t = triplet, dd =double of doublets, td = triplet of doublets, dt = doublet of triplets, q = quartet, m = multiplet.

^{13}C-NMR-Spectroscopy:

Bruker AVANCE 250 II (62.9 MHz), Bruker AVANCE 300 III (75.5 MHz), Bruker AVANCE 500 (125 MHz). The spectra were calibrated according to the solvent signals: 77.00 ppm for $CDCl_3$, 39.5 ppm for DMSO-d_6. Peak characterization: t = triplet, q = quartet. DEPT method was used for determining the presence of primary, secondary, tertiary and quaternary carbon atoms.

^{19}F-NMR-Spectroscopy:

Bruker AVANCE 300 III (282 MHz).

All chemical shifts are given in ppm. All coupling constants *J* are indicated in Hz.

Mass spectrometry (MS):

GC 6890N / MSD 5973 (Agilent) or Finnigan MAT 95-XP (Thermo Electron).

High resolution MS (HRMS):

Finnigan MAT 95 XP (Thermo Electron) (electron ionisation EI, 70 eV) or 6210 Time-of-Flight LC/MS (Agilent) (electrospray ionization, ESI). Only the measurements with an average deviation from the theoretical mass of ± 2 μDa were accounted as correct.

Infrared spectroscopy (IR):

Nicolet 380 FT-IR spectrometer with ATR sampling technique for solids as well as liquids. Abbreviations for signal allocations: w = weak, m = medium, s = strong.

X-ray crystallography:

Bruker-Nonius Apex X8 or Bruker Apex Kappa-II diffractometers with CCD-Kamera (Mo-Kα and graphite monochromator, λ = 0.71073 Å).

Absorption spectroscopy:

Lambda 2 (Perkin Elmer) or Specord 50 spectrophotometer. Cuvette length *l* = 1 cm.

Fluorescence spectroscopy:

Spectrafluorometer FluoroMax-4P, Horiba Scientific. The luminescence quantum yields were determined relative to quinine bisulfate (Sigma Aldrich Co.) in 0.05 M sulfuric acid (Titripu, Merck AG) as quantum yield standard (ϕ = 0.54). The optical densities of all solutions were below an absorbance of 0.1.

Melting point determination (mp):

Microscope Laborlux 12 Pol S, Mettler FP90 central Processor, SNT 12 V 100 K. The melting points are uncorrected.

Thin layer chromatography (TLC):

Merck silica gel 60 F_{254}. Detection under UV light at 254 nm and 366 nm without dipping reagent.

Column chromatography:

Chromatography was performed over Merck silica gel 60 (0.063-0.200 mm, 70-230 mesh). All solvents were distilled before use.

All chemicals and solvent (extra dry) for carring out of reactions were purchased from the standard chemical suppliers, such as Sigma-Aldrich®, Arcos®, Merck® and others. All reactions were monitored by TLC using UV light to visualize the course of reaction.

1.2 General synthetic procedures and product characterization

1.2.1 Supplement for Chapter 2

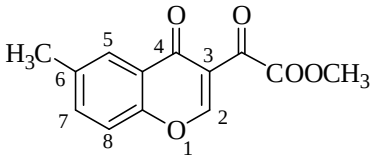
Starting 3-acylchromones **4-8** were prepared according to described procedures.[30-31, 54, 83, 84]

General procedure for the synthesis of 3-methoxalylchromones 4:

To a round-bottom 50 ml flask, fitted with a septum, containing corresponding 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2** (10.0 mmol) dissolved in 25 ml of dry DCM, dry pyridine (3.3 equiv.) was added. The solution was set on stirring on ice bath and acylation agent **3a** (methyl oxalyl chloride) (1,1 equiv.) was added dropwise. The reaction mixture was stirred at the room temperature for 8 hours (approximately) and after was stripped of solvents and liquid residues. The obtained solid was well washed with water to give the corresponding 3-methoxalylchromones **4**.

3-Methoxalylchromone **4a** has already been described and reported by Dr. S. Mkrtchyan in the group of Prof. Langer.[31]

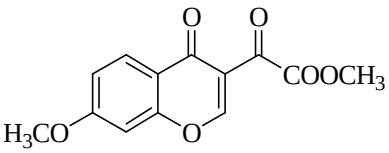
3-Methoxalyl-6-methylchromone (4b):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxy-5-methyl-phenyl)prop-2-en-1-one **2b** (4.105 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4b** was isolated as a yellow solid (4.580 g, 93%), mp = 134-136 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.44 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 7.66-7.74 (m, 2H, 7,8-H_{Ar}), 7.89 (s, 1H, 5-H_{Ar}), 9.08 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.4 (CH_3), 52.7 (OCH_3), 118.4, 118.7, 123.6, 124.5, 136.5, 136.9, 153.9, 164.0, 164.4, 174.1, 184.7; MS (GC, 70 eV) *m/z* (%): 246 ([M]$^+$, 5), 218 (19), 203 (15), 187 (100), 135 (29), 77 (12), 53 (9); HRMS (EI): calcd for $C_{13}H_{10}O_5$ ([M]$^+$) 246.05227, found 246.05262; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2954 (w), 1749 (s), 1715 (w), 1685 (s), 1658 (s), 1596 (s), 1553 (s), 1475 (s), 1430 (s), 1377 (w), 1338 (m), 1295 (s), 1239 (s), 1204 (s), 1135 (m), 1116 (m), 1029 (s), 998 (m), 976 (m), 960 (m), 914 (m), 872 (m), 830 (s), 816 (m), 795 (s), 762 (m), 746 (s), 712 (s), 658 (m), 550 (m).

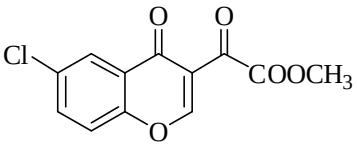
7-Methoxy-3-methoxalylchromone (4c):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one **2c** (4.442 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4c** was isolated as a yellow solid (4.353 g, 83%), mp = 152-154 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.87 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 7.15 (dd, ^{3}J = 8.9 Hz, ^{4}J = 2.3 Hz, 1H, 6-H_{Ar}), 7.28 (d, ^{4}J = 2.3 Hz, 1H, 8-H_{Ar}), 8.00 (d, 1H, ^{3}J = 8.9 Hz, 5-H_{Ar}), 9.04 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.6 (OCH_3), 56.4 (OCH_3), 101.6, 115.9, 117.3, 118.5, 126.7, 157.6, 164.1, 164.2, 164.8, 173.3, 184.8; MS (GC, 70 eV) *m/z* (%): 262 ([M^+], 2), 234 (23), 219 (24), 203 (100), 151 (54), 119 (12), 63 (10), 53 (16); HRMS (ESI): calcd for $C_{13}H_{11}O_6$ ([M+H]$^+$) 263.05501, found 263.05528; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3043 (w), 2967 (w), 2848 (w), 1743 (m), 1683 (m), 1650 (s),1614 (s), 1552 (w), 1504 (m), 1464 (w), 1436 (s), 1393 (m), 1350 (w), 1326 (m), 1276 (s), 1226 (s), 1197 (m), 1179 (m), 1143 (m), 1104 (s), 1030 (m), 1012 (s), 971 (m), 943 (m), 921 (w), 879 (m), 849 (s), 818 (s), 785 (s), 748 (s), 721 (s), 677 (m), 633 (w), 599 (m), 578 (m), 543 (m).

6-Chloro-3-methoxalylchromone (4d):

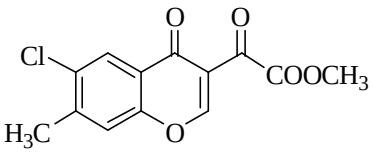


Starting with (2*E*)-1-(5-chloro-2-hydroxyphenyl)-3-(dimethylamino)prop-2-en-1-one **2d** (4.513 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4d** was isolated as a yellow solid (4.799 g, 90%), mp = 137-139 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.88 (s, 3H, OCH_3), 7.84 (d, ^{3}J = 9.0 Hz, 1H, 8-H_{Ar}), 7.93 (dd, ^{3}J = 9.0 Hz, ^{4}J = 2.6 Hz, 1H, 7-H_{Ar}), 8.01 (d, ^{4}J = 2.6 Hz, 1H, 5-H_{Ar}), 9.13 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.8 (OCH_3), 118.5, 121.4, 124.3, 125.2, 131.5, 135.3, 154.3, 163.8, 164.8, 173.2, 184.2; MS (GC, 70 eV) *m/z* (%): 266 ([$M]^+$, 4), 238 (12), 223 (10), 207 (100), 155 (34), 123 (13), 63 (12), 53 (30); HRMS (ESI): calcd for $C_{12}H_8{}^{35}ClO_5$ ([M+H]$^+$) 267.00548, found 267.00586, calcd for $C_{12}H_8{}^{37}ClO_5$ ([M+H]$^+$) 269.00298, found 269.00315; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2956 (w), 1739 (m), 1688 (m), 1651 (s), 1607 (m), 1553 (s), 1482 (w), 1464 (s), 1439 (s), 1391 (w), 1372 (w), 1327 (s), 1297 (s), 1253 (m), 1219 (m), 1191 (m),

1173 (m), 1139 (w), 1121 (m), 1073 (m), 1023 (s), 955 (s), 899 (m), 868 (m), 840 (s), 816 (s), 795 (s), 761 (s), 744 (m), 715 (s), 685 (m), 665 (s), 633 (s), 590 (w), 543 (s).

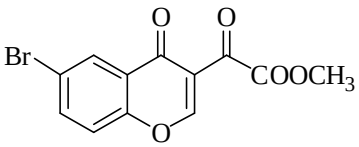
6-Chloro-7-methyl-3-methoxalylchromone (4e):



Starting with (2*E*)-1-(5-chloro-2-hydroxy-4-methyl-phenyl)-3-(dimethylamino)prop-2-en-1-one **2e** (4.794 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4e** was isolated as a white solid (4.659 g, 83%), mp = 184-186 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 7.43 (s, 1H, 8-H_{Ar}), 8.16 (s, 1H, 5-H_{Ar}), 8.60 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.9 (CH_3), 53.0 (OCH_3), 119.7, 120.3, 123.6, 125.9, 133.7, 144.7, 154.2, 162.1, 164.0, 173.4, 184.1; MS (GC, 70 eV) *m/z* (%): 280 ([M]$^+$, 4), 252 (15), 237 (13), 221 (100), 169 (30), 53 (12); HRMS (EI): calcd for $C_{13}H_9{}^{35}ClO_5$ ([M]$^+$) 280.01324, found 280.01330; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2956 (w), 1739 (m), 1683 (m), 1650 (s), 1615 (m), 1588 (m), 1541 (m), 1454 (m), 1436 (m), 1414 (s), 1383 (w), 1367 (w), 1332 (m), 1290 (s), 1247 (m), 1217 (m), 1167 (w), 1128 (m), 1029 (s), 995 (m), 952 (w), 941 (m), 901 (m), 885 (s), 823 (m), 796 (s), 761 (s), 714 (s), 689 (m), 651 (s), 595 (w), 552 (w).

6-Bromo-3-methoxalylchromone (4f):

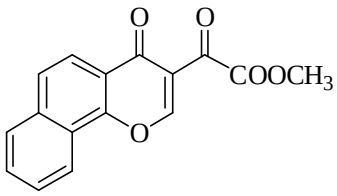


Starting with (2*E*)-1-(5-bromo-2-hydroxy-phenyl)-3-(dimethylamino)prop-2-en-1-one **2f** (5.402 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4f** was isolated as a yellow solid (6.549 g, 95%), mp = 138-140 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.88 (s, 3H, OCH_3), 7.79 (d, ^{3}J = 8.9 Hz, 1H, 8-H_{Ar}), 8.07 (dd, ^{3}J = 8.9 Hz, ^{4}J = 2.5 Hz, 1H, 7-H_{Ar}), 8.17 (d, ^{4}J = 2.5 Hz, 1H, 5-H_{Ar}), 9.14 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.8 (OCH_3), 118.6, 119.5, 121.6, 125.5, 127.4, 138.1, 154.7, 163.8, 164.9, 173.1, 184.2; MS (GC, 70 eV) *m/z* (%): 310 ([M]$^+$, 6), 284 (11), 282 (13), 269 (12), 253 (100), 199 (26), 88 (9), 53 (18); HRMS (EI): calcd for $C_{12}H_7{}^{79}BrO_5$ [M]$^+$ 309.94714, found 309.94763, calcd for $C_{12}H_7{}^{81}BrO_5$ [M]$^+$ 311.94509, found 311.94583; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3078 (w), 2961 (w), 1731 (m), 1691 (m), 1651 (s), 1605 (m), 1552 (m), 1504

(w), 1461 (s), 1435 (s), 1380 (w), 1365 (m), 1326 (s), 1295 (s), 1260 (s), 1223 (m), 1179 (m),1119 (m), 1061 (w), 1021 (s), 949 (m), 886 (m), 862 (m), 829 (s), 812 (s), 795 (s), 770 (s), 744 (m), 705 (s), 674 (m),655 (m), 604 (s), 536 (s).

3-Methoxalylbenzo[*h*]chromone (4g):



Starting with (2*E*)-3-(dimethylamino)-1-(1-hydroxy-naphthalen-2-yl)prop-2-en-1-one **2g** (4.826 g, 20.0 mmol) and methyl 2-chloro-2-oxoacetate **3a** (2.0 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in DCM (25 mL), the product **4g** was isolated as a pale yellow solid (4.347 g, 77%), mp = 112-114 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.02 (s, 3H, OCH_3), 7.68-7.82 (m, 3H, H_{Ar}), 7.92 (d, ^{3}J = 7.3 Hz, 1H, H_{Ar}), 8.08 (d, ^{3}J = 8.8 Hz, 1H, H_{Ar}), 8.42 (d, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 8.74 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 53.0 (OCH_3), 120.2, 120.9, 121.3, 122.0, 123.4, 126.9, 127.9, 128.2, 130.1, 136.2, 153.6, 161.0, 164.1, 174.3, 184.5; MS (GC, 70 eV) *m/z* (%): 282 ($[M]^+$, 7), 254 (22), 239 (29), 223 (100), 171 (49), 139 (33), 114 (16), 53 (21); HRMS (ESI): calcd for $C_{16}H_{11}O_5$ ($[M+H]^+$) 283.06010, found 283.06061; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3078 (w), 2961 (w), 1727 (w), 1690 (w), 1641 (s), 1633 (s), 1601 (m), 1590 (m), 1557 (m), 1509 (m), 1462 (m), 1440 (m), 1410 (m), 1402 (m), 1384 (s), 1360 (m), 1338 (m), 1303 (s), 1259 (m), 1236 (m), 1215 (m), 1176 (m), 1153 (w), 1132 (m), 1064 (m), 1039 (m), 1021 (s), 959 (w), 935 (w), 924 (w), 865 (w), 830 (m), 808 (s), 798 (s), 755 (s), 745 (s), 708 (m), 691 (m), 639 (m), 605 (w), 574 (s), 547 (m).

General procedure for the synthesis of 3-perfluoroacylchromones 5:

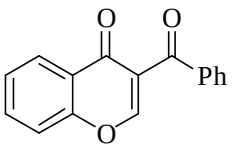
To a stirred reaction mixture of the corresponding 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2** (10.0 mmol) and pyridine (3.3 equiv.) in 25 ml of dry MeCN, the corresponding acylation agent **3** (trifluoroacetyl anhydride **3b**, pentafluoropropanoyl anhydride **3c** or heptafluorobutanoyl chloride **3d**) (2.2 equiv.) was added slowly *via* a syringe at room temperature. The reaction mixture was stirred for one-two hours and after was stripped of solvents and liquid residues. The obtained solid was washed well with water to give the corresponding 3-perfluoroacylchromones **5**.

3-Perfluoroacylchromones **5** were obtained as mixture of hydrated and non-hydrated forms and were used in the further investigations without additional purification. They were used as intermediate products and are not described in this thesis.

General procedure for the synthesis of 3-aroylchromones 6:

To a stirred reaction mixture of the corresponding 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2** (10.0 mmol) and pyridine (3.3 equiv.) in 25 ml of dry MeCN, the corresponding benzoylchloride **3e-k** (1.1 equiv.) was added slowly *via* a syringe at room temperature. The reaction mixture was stirred at reflux for 10-12 hours and after was stripped of solvents and liquid residues. The obtained solid was washed well with water to give the corresponding 3-aroylchromones **6**. In some cases, it was necessary to use column chromatography.

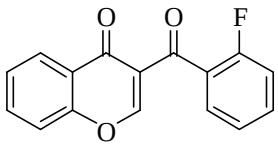
3-Benzoylchromone (6a):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and benzoylchloride **3e** (2.6 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6a** was isolated as a white solid (4.004 g, 80%), mp = 129-131 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.50-7.59 (m, 3H, H_{Ar}), 7.67 (tt, ^{3}J = 7.4 Hz, ^{4}J = 1.3 Hz, 1H, H_{Ar}), 7.75 (dd, ^{3}J = 8.4 Hz, ^{4}J = 0.6 Hz, 1H, H_{Ar}), 7.86-7.92 (m, 3H, H_{Ar}), 8.09 (dd, ^{3}J = 7.9 Hz, ^{4}J = 1.5 Hz, 1H, H_{Ar}), 8.72 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 118.7, 124.2, 124.5, 125.3, 126.1, 128.5, 128.6, 129.4, 129.5, 133.6, 134.8, 136.9, 155.8, 158.8, 174.3, 191.6; MS (GC, 70 eV) *m/z* (%): 250 ($[M]^+$, 27), 249 (43), 221 (100), 194 (13), 173 (22), 121 (28), 105 (20), 77 (47), 63 (11), 51 (18); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 1946 (w), 1823 (w), 1644 (s), 1610 (s), 1563 (s), 1461 (s), 1383 (m), 1340 (m), 1308 (s), 1251 (m), 1210 (m), 1156 (w), 1135 (s), 1031 (w), 999 (w), 968 (m), 920 (m), 862 (s), 808 (w), 787 (m), 758 (s), 717 (s), 688 (s), 632 (s), 558 (w).

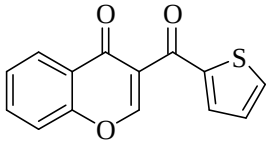
3-(2-Fluorobenzoyl)chromone (6b):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)-prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and 2-fluorobenzoyl chloride **3f** (2.6 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6b** was isolated as a pale yellow solid (4.613 g, 86%), mp 143-144 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04-7.11 (m, 1H, H_{Ar}), 7.27 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 7.44 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 7.50-7.58 (m, 2H, H_{Ar}), 7.69-7.78 (m, 2H, H_{Ar}), 8.22 (dd, ^3J = 8.0 Hz, ^4J = 1.5 Hz, 1H, H_{Ar}), 8.44 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 115.8 (d, $J_{C,F}$ = 22.1 Hz), 118.3, 124.4 (d, $J_{C,F}$ = 3.3 Hz), 124.9, 125.8, 126.1, 126.4, 127.4 (d, $J_{C,F}$ = 12.6 Hz), 130.4 (d, $J_{C,F}$ = 2.2 Hz), 134.3 (d, $J_{C,F}$ = 4.4 Hz), 134.4 (d, $J_{C,F}$ = 4.4 Hz), 156.0, 159.5, 161.2 (d, $^1J_{C,F}$ = 252.7 Hz, $C_{Ar}F$), 174.4 (d, $J_{C,F}$ = 2.0 Hz), 188.7 (C=O); ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = -111.4 (s, F); MS (GC, 70 eV) *m/z* (%): 268 ($[M]^+$, 63), 239 (100), 221 (34), 173 (28), 121 (30), 95 (31), 75 (21), 63 (13), 53 (12); HRMS (EI): calcd for $C_{16}H_9FO_3$ ($[M]^+$) 268.05302, found 268.05295; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 1664 (m), 1644 (s), 1609 (s), 1563 (m), 1477 (w), 1460 (s), 1388 (m), 1339 (m), 1314 (m), 1261 (w), 1240 (m), 1207 (m), 1152 (w), 1136 (m), 1099 (m), 1029 (w), 1002 (w), 973 (m), 933 (w), 864 (s), 817 (w), 758 (s), 706 (m), 679 (w), 665 (m), 629 (s), 565 (w), 538 (m).

3-(2-Thenoyl)chromone (6c):

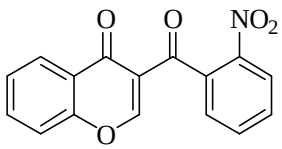


Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and thiophene-2-carbonyl chloride **3g** (2.4 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6c** was isolated as a white solid (4.152 g, 81%), mp 145-147 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.24 (t, ^3J = 4.4 Hz, 1H, H_{Ar}), 7.56 (td, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 7.73 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.84-7.90 (m, 2H, H_{Ar}), 8.10-8.15 (m, 2H, H_{Ar}), 8.76 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 118.6, 124.1, 124.2, 125.4, 126.1, 128.9, 134.8, 136.5, 136.6, 143.5, 155.6, 158.1, 173.9, 182.7; MS (GC, 70 eV) *m/z* (%): 256 ($[M]^+$, 71), 228 (87), 200 (24), 173 (35), 121 (52), 111 (100), 92 (25), 83 (17), 63 (26), 53 (30), 39 (50); HRMS (EI): calcd for $C_{14}H_8O_3S$ ($[M]^+$) 256.01887, found 256.01828; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3097 (w), 1699 (w), 1646 (s), 1606 (s), 1564 (s), 1525 (m), 1460 (s), 1434 (m), 1406 (s), 1381 (s), 1353 (s), 1340 (s), 1308 (s), 1253 (m), 1212 (s), 1168 (m), 1130 (s), 1102 (m), 1084

(m), 1059 (m), 1029 (m), 955 (w), 937 (w), 918 (m), 851 (m), 816 (s), 793 (s), 751 (s), 722 (s), 677 (s), 628 (s), 557 (m), 534 (w).

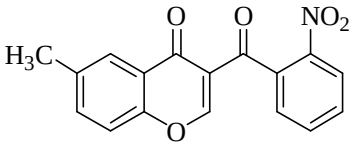
3-(2-Nitrobenzoyl)chromone (6d):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)-prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and 2-nitrobenzoyl chloride **3h** (2.9 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6d** was isolated as pale brown solid (4.132 g, 70%), mp 155-157 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.51-7.57 (m, 2H, H_{Ar}), 7.74-7.80 (m, 2H, H_{Ar}), 7.85-7.91 (m, 2H, H_{Ar}), 7.97 (dd, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 8.26 (d, ^3J = 7.5 Hz, 1H, H_{Ar}), 9.17 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 118.7, 120.5, 123.7, 124.3, 125.4, 126.7, 127.8, 130.7, 134.8, 135.2, 137.4, 145.9, 155.5, 164.0, 173.7, 189.6; MS (EI, 70 eV) *m/z* (%): 249 ([M-NO_2], 100), 173 (6), 121 (10), 57 (5); HRMS (ESI): calcd for $C_{16}H_{10}NO_5$ ([M+H]$^+$) 296.05535, found 296.05606; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3108 (w), 3078 (w), 2861 (w), 1671 (m), 1652 (m), 1611 (m), 1574 (w), 1552 (m), 1517 (s), 1463 (s), 1404 (w), 1388 (m), 1349 (s), 1307 (s), 1205 (m), 1175 (w), 1156 (m), 1141 (m), 1105 (w), 1084 (w), 1028 (w), 996 (w), 957 (m), 888 (w), 869 (m), 850 (s), 808 (w), 792 (m), 764 (s), 745 (m), 734 (s), 705 (s), 658 (m), 638 (m), 575 (m), 535 (s).

6-Methyl-3-(2-nitrobenzoyl)chromone (6e):

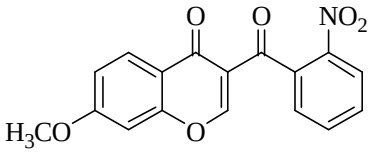


Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxy-5-methyl-phenyl)prop-2-en-1-one **2b** b(4.105 g, 20.0 mmol) and 2-nitrobenzoyl chloride **3h** (2.9 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6e** was isolated as pale brown solid (5.010 g, 81%), mp 168 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.38 (s, 3H, CH_3), 7.54 (dd, ^3J = 7.5 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 7.62–7.69 (m, 2H, H_{Ar}), 7.74–7.79 (m, 2H, H_{Ar}), 7.86 (td, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1H, H_{Ar}), 8.25 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1H, H_{Ar}), 9.12 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.4 (CH_3), 118.5, 120.3, 123.6, 124.0, 124.8, 127.8, 130.7, 134.7, 136.1, 136.5, 137.5, 145.9, 153.8, 163.8, 173.6, 189.7; MS (EI, 70 eV) *m/z* (%): 264 ([M-NO_2+H], 33), 263 (100), 187 (6), 135 (13), 76 (5); HRMS (ESI): calcd for $C_{17}H_{12}NO_5$ ([M+H]$^+$) 310.07100, found 310.07139; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2921 (w), 2859 (w), 1668 (m), 1650 (m), 1615 (m),

1574 (m), 1552 (m), 1517 (s), 1478 (s), 1440 (m), 1348 (s), 1306 (s), 1229 (m), 1186 (w), 1163 (m), 1132 (m), 1082 (w), 1041 (w), 1018 (w), 959 (w), 910 (m), 853 (s), 814 (s), 786 (s), 753 (m), 731 (s), 702 (s), 640 (s), 575 (m), 541 (m).

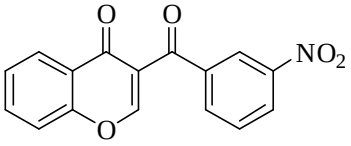
7-Methoxy-3-(2-nitrobenzoyl)chromone (6f):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxy-4-methoxy-phenyl)prop-2-en-1-one **2c** (4.442 g, 20.0 mmol) and 2-nitrobenzoyl chloride **3h** (2.9 mL, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6f** was isolated as pale brown solid (5.139 g, 79%), mp 146-148 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.90 (s, 3H, OCH_3), 7.08 (dd, ^3J = 8.9 Hz, ^4J = 2.3 Hz, 1H, H_{Ar}), 7.24 (d, ^4J = 2.3 Hz, 1H, H_{Ar}), 7.54 (dd, ^3J = 7.5 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 7.75 (td, ^3J = 7.5 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 7.83–7.89 (m, 2H, H_{Ar}), 8.24 (dd, ^3J = 8.1 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 9.08 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 56.3 (OCH_3), 101.3, 115.7, 117.8, 120.4, 123.6, 126.9, 127.8, 130.7, 134.7, 137.6, 145.9, 157.3, 163.6, 164.5, 172.9, 189.8; MS (GC, 70 eV) *m/z* (%): 279 ([M-NO_2], 100), 236 (23), 151 (12), 76 (6), 63 (5); HRMS (ESI): calcd for $C_{17}H_{12}NO_6$ ([M+H]$^+$) 326.06591, found 326.06567; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2952 (w), 2845 (w), 1673 (w), 1621 (s), 1552 (m), 1514 (s), 1435 (s), 1385 (m), 1341 (s), 1302 (s), 1271 (s), 1237 (m), 1207 (m), 1143 (m), 1090 (m), 1035 (w), 1020 (m), 939 (s), 879 (w), 850 (s), 804 (m), 786 (s), 753 (s), 733 (m), 718 (m), 701 (s), 627 (s), 590 (w), 562 (s), 529 (m).

3-(3-Nitrobenzoyl)chromone (6g):

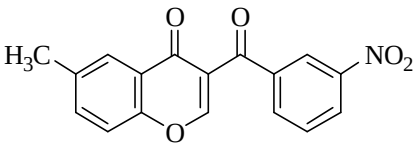


Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)-prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and 3-nitrobenzoyl chloride **3i** (4.082 g, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6g** was isolated as a white solid (4.783 g, 81%), mp = 209-211 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.58 (td, ^3J = 7.5 Hz, ^4J = 1.1 Hz, 1H, H_{Ar}), 7.77-7.84 (m, 2H, H_{Ar}), 7.91 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H, H_{Ar}), 8.08 (dd, ^3J = 7.9 Hz, ^4J = 1.5 Hz, 1H, H_{Ar}), 8.27 (dt, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H, H_{Ar}), 8.48 (dq, ^3J = 8.2 Hz, ^4J = 1.0 Hz, 1H, H_{Ar}), 8.56 (t, ^4J = 1.8 Hz, 1H, H_{Ar}), 8.83 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 118.7, 123.3, 123.4, 124.3, 125.4, 126.4, 127.5, 130.3, 135.0, 135.6, 138.4, 147.9, 155.7, 160.8, 174.2, 190.2; MS (GC, 70 eV) *m/z* (%): 295 ([M]$^+$, 48), 278 (100), 266 (93), 248 (56), 220 (73), 173

(71), 165 (13), 150 (10), 121 (95), 104 (20), 92 (26), 76 (35), 63 (19), 53 (27); HRMS (EI): calcd for $C_{16}H_9NO_5$ ([M]$^+$) 295.04752, found 295.04744; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3087 (w), 1843 (w), 1668 (m), 1634 (s), 1611 (s), 1559 (w), 1533 (s), 1463 (s), 1384 (m), 1345 (s), 1316 (m), 1292 (m), 1210 (w), 1177 (w), 1141 (m), 1100 (w), 1081 (m), 1030 (w), 992 (m), 966 (w), 924 (m), 897 (m), 854 (m), 823 (w), 802 (w), 757 (s), 739 (m), 715 (s), 661 (m), 630 (m), 556 (w).

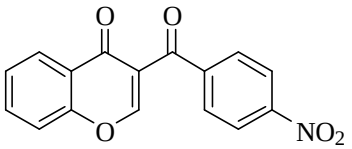
6-Methyl-3-(3-Nitrobenzoyl)chromone (6h):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxy-5-methyl-phenyl)prop-2-en-1-one **2b** (4.105 g, 20.0 mmol) and 3-nitrobenzoyl chloride **3i** (4.082 g, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6h** was isolated as a white solid (5.258 g, 85%), mp 232-234 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.44 (s, 3H, CH_3), 7.65-7.73 (m, 2H, H_{Ar}), 7.78-7.86 (m, 2H, H_{Ar}), 8.25 (d, ^3J = 7.6 Hz, 1H, H_{Ar}), 8,48 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 8.53 (s, 1H, H_{Ar}), 8.80 (s, 1H, 2-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 20.4 (CH_3), 118.5, 123.2, 123.3, 123.9, 124.6, 127.5, 130.3, 135.5, 135.9, 136.1, 138.4, 147.8, 154.0, 160.6, 174.2, 190.3; MS (GC, 70 eV) *m/z* (%): 309 ([M]$^+$, 57), 292 (82), 280 (100), 262 (55), 234 (70), 187 (54), 135 (74), 104 (19), 89 (10), 76 (35), 63 (10), 53 (17); HRMS (EI): calcd for $C_{17}H_{11}NO_5$ ([M]$^+$) 309.06317, found 309.06329; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3088 (w), 3049 (w), 2919 (w), 2864 (w), 1661 (m), 1636 (s), 1614 (s), 1564 (w), 1526 (s), 1478 (w), 1438 (m), 1373 (w), 1339 (s), 1321 (s), 1253 (m), 1234 (m), 1159 (m), 1081 (m), 1024 (w), 991 (w), 954 (m), 923 (m), 879 (m), 845 (m), 816 (s), 796 (s), 710 (s), 662 (s), 638 (m), 561 (w), 539 (m).

3-(4-Nitrobenzoyl)chromone (6i):

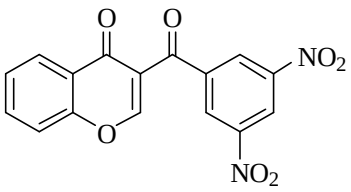


Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)-prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and 4-nitrobenzoyl chloride **3j** (4.082 g, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6i** was isolated as a white solid (4.901 g, 83%), mp 239-240 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.58 (t, ^3J = 7.6 Hz, 1H, H_{Ar}), 7.77 (d, ^3J = 8.4 Hz, 1H, H_{Ar}), 7.90 (td, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 8.06–8.09 (m, 3H, H_{Ar}), 8.30–8.33 (m, 2H, H_{Ar}), 8.83 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 118.8, 123.5, 123.6, 123.7, 124.3, 125.4, 126.4, 130.5, 130.6, 135.1, 142.1, 149.9, 155.8, 160.7, 174.3, 191.1; MS (GC, 70

eV) *m/z* (%): 295 ([M]$^+$, 29), 278 (64), 266 (100), 248 (29), 220 (50), 173 (40), 165 (12), 121 (65), 104 (18), 92 (25), 76 (25), 63 (15), 53 (21); HRMS (EI): calcd for $C_{16}H_9NO_5$ ([M]$^+$) 295.04752, found 295.04745; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3107 (w), 2848 (w), 1949 (w), 1661 (w), 1633 (s), 1604 (m), 1563 (w), 1516 (m), 1461 (m), 1406 (w), 1379 (m), 1318 (m), 1287 (m), 1253 (m), 1215 (m), 1150 (w), 1132 (m), 1028 (w), 962 (w), 926 (m), 868 (s), 842 (m), 798 (m), 775 (m), 755 (s), 709 (s), 687 (s), 634 (s), 596 (w), 549 (m), 534 (w).

3-(3,5-Dinitrobenzoyl)chromone (6j):



Starting with (2*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)-prop-2-en-1-one **2a** (3.825 g, 20.0 mmol) and 3,5-dinitrobenzoyl chloride **3k** (5.072 g, 22.0 mmol) and pyridine (5.3 mL, 66.0 mmol) in MeCN (25 mL), the product **6j** was isolated as a brown solid (3.947 g, 58%), mp 181-183 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.59 (t, ^3J = 7.6 Hz, 1H, H_{Ar}), 7.80 (d, ^3J = 8.5 Hz, 1H, H_{Ar}), 7.89–7.95 (m, 1H, H_{Ar}), 8.08 (d, ^3J = 7.9 Hz, 1H, H_{Ar}), 8.91–8.93 (m, 3H, H_{Ar}), 9.03 (s, 1H, 2-H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 118.7, 122.0, 122.5, 124.4, 125.4, 126.5, 128.8, 128.9, 135.1, 140.1, 148.1, 148.2, 155.7, 162.5, 174.3, 188.6; MS (GC, 70 eV) *m/z* (%): 340 ([M]$^+$, 32), 323 (100), 311 (59), 293 (35), 265 (35), 247 (17), 219 (39), 173 (67), 121 (81), 92 (16), 75 (24), 53 (17); HRMS (EI): calcd for $C_{16}H_8N_2O_7$ ([M]$^+$) 340.03260, found 340.03257; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3100 (w), 1644 (m), 1611 (m), 1538 (m), 1463 (m), 1384 (w), 1341 (m), 1314 (m), 1290 (m), 1211 (w), 1173 (w), 1105 (m), 1031 (w), 1004 (m), 917 (m), 854 (m), 831 (m), 745 (m), 714 (s), 644 (m), 557 (w).

General procedure for the synthesis of 3-[(2*E*)-3-phenylprop-2-enoyl]chromone (7):

To a round-bottom 50 ml flask, fitted with a septum, containing 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one **2a** (10.0 mmol), dissolved in 25 ml of dry MeCN, dry pyridine (3.3 equiv.) was added. The solution was set on stirring on the ice bath, and (2*E*)-3-phenylprop-2-enoyl chloride **3l** (1,1 equiv.) was added slowly. The reaction mixture stirred at the room temperature for 3 days (controlled by TLC). The formed precipitate was filtrated and well washed with water to give the chromone **7**.

3-[(2*E*)-3-phenylprop-2-enoyl]chromone **7** has already been reported and described. However, another synthetic approach was used.[85]

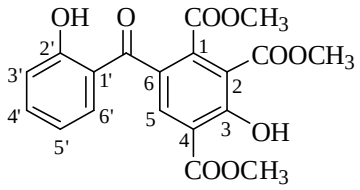
3-Dichloroacetylchromone **8** has been synthesized and reported by the group of Prof. Langer.[28]

1.2.2 Supplement for Chapter 3

General procedure for the synthesis of compounds 13-18:

To a stirred reaction mixture of the corresponding 3-acylchromone **4-6** (1.0 mmol) and dimethyl 1,3-acetonedicarboxylate **12** (1.1 mmol) in 1,4-dioxane (6-7 mL), DBU (1.3 mmol) was added slowly *via* a syringe at room temperature. Stirring at room temperature was continued until chromone was consumed completely (followed by TLC, approximately 10-12 h). The reaction mixture was quenched with an aqueous solution of 10% NH_4Cl, extracted with $CHCl_3$ and dried (Na_2SO_4). The solvent was distilled off under reduced pressure. The resulting residue was subjected to column chromatography on silica gel using heptane-ethylacetate (5:1) as eluent, slowly increasing the polarity up to 3:1 to give the isolated products.

Trimethyl 3-hydroxy-6-(2-hydroxybenzoyl)benzene-1,2,4-tricarboxylate (13a):

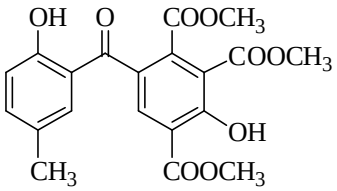


Starting with 3-methoxalylchromone **4a** (0.232 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **13a** was isolated as a pale yellow solid (0.298 g, 74%), mp 138-140 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.63 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 6.85 (ddd, ^3J = 8.0 Hz, ^3J = 7.3 Hz, ^4J = 1.0 Hz, 1H, 5′-H_{Ar}), 7.06 (dd, ^3J = 8.4 Hz, ^4J = 1.0 Hz, 1H, 3′-H_{Ar}), 7.29 (dd, ^3J = 8.0 Hz, ^4J = 1.6 Hz, 1H, 6′-H_{Ar}), 7.51 (ddd, ^3J = 8.4 Hz, ^3J = 7.3 Hz, ^4J = 1.6 Hz, 1H, 4′-H_{Ar}), 8.04 (s, 1H, 5-H_{Ar}), 11.56 (s, 1H, OH), 11.63 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.9 (OCH_3), 53.0 (OCH_3), 53.2 (OCH_3), 114.3, 118.4, 119.1, 119.4, 124.0, 129.3, 131.9, 132.4, 136.4, 136.8, 160.2, 162.7, 165.2, 165.3, 168.8, 199.3 (C=O); MS (GC, 70 eV) *m/z* (%): 388 ([M]$^+$, 7), 356 (40), 297 (92), 265 (100), 238 (10); HRMS (EI): calcd for $C_{19}H_{16}O_9$ ([M]$^+$) 388.07888, found 388.07794; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2951 (w), 1732 (s), 1682 (m), 1631 (m), 1611 (m), 1581 (m), 1514 (w), 1484 (w), 1443 (s), 1415 (w), 1353 (m), 1323 (m), 1295 (s), 1234 (s), 1193 (s), 1140 (s), 1049 (s), 992 (m), 949 (m), 904 (m), 883 (m),

847 (m), 809 (m), 785 (s), 756 (s), 731 (s), 719 (s), 706 (s), 652 (s), 607 (m), 578 (m), 561 (s), 530 (m).

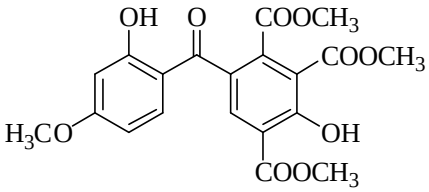
Trimethyl 3-hydroxy-6-(2-hydroxy-5-methylbenzoyl)benzene-1,2,4-tricarboxylate (13b):



Starting with 3-methoxalyl-6-methylchromone **4b** (0.246 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **13b** was isolated as a white solid (0.350 g, 87%), mp 136-138 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 2.22 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.88 (d, ^3J = 8.4 Hz, 1H, 3′-H_{Ar}), 7.21 (s, 1H, 6′-H_{Ar}), 7.31 (dd, ^3J = 8.4 Hz, ^4J = 1.9 Hz, 1H, 4′-H_{Ar}), 7.98 (s, 1H, 5-H_{Ar}), 10.40 (s, 1H, OH), 11.30 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.8 (CH_3), 2^{x}52.8 (OCH_3), 53.2 (OCH_3), 115.5, 117.1, 122.2, 122.8, 128.0, 129.8, 131.1, 133.0, 136.0, 136.3, 156.4, 158.5, 164.8, 165.8, 167.4, 194.9 (C=O); MS (GC, 70 eV) *m/z* (%): 402 ([M]$^+$, 10), 370 (31), 311 (71), 279 (100); HRMS (EI): calcd for $C_{20}H_{18}O_9$ ([M]$^+$) 402.09453, found 402.09435; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 1733 (s), 1682 (w), 1633 (m), 1606 (w), 1582 (m), 1484 (w), 1441 (m), 1408 (w), 1372 (w), 1352 (m), 1320 (w), 1283 (m), 1232 (s), 1206 (s), 1153 (s), 1137 (s), 1048 (m), 1014 (m), 993 (m), 983 (m), 953 (m), 931 (w), 882 (w), 828 (m), 809 (m), 787 (s), 767 (m), 728 (m), 708 (m), 670 (s), 607 (w), 575 (w), 538 (m).

Trimethyl 3-hydroxy-6-(2-hydroxy-4-methoxybenzoyl)benzene-1,2,4-tricarboxylate (13c):

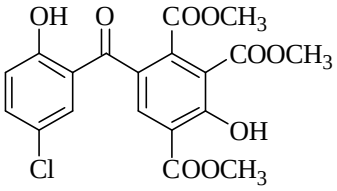


Starting with 7-methoxy-3-methoxalylchromone **4c** (0.262 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **13c** was isolated as a white solid (0.305 g, 73%), mp 137-139 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.61 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.50-6.54 (m, 2H, 3′, 5′-H_{Ar}), 7.36 (d, ^3J = 8.5 Hz, 1H, 6′-H_{Ar}), 7.97 (s, 1H, 5-H_{Ar}), 11.24 (s, 1H, OH), 11.52 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.8 (OCH_3), 53.0 (OCH_3), 53.2 (OCH_3), 55.8 (OCH_3), 101.2, 107.4, 114.3, 115.6, 123.3, 129.6, 132.3, 134.1, 135.7, 158.0, 163.3, 164.8, 165.5, 165.8, 167.4, 195.3 (C=O); MS (GC, 70 eV) *m/z* (%): 418 ([M]$^+$, 16), 386 (14), 359 (12), 327 (92), 295 (100), 151 (11); HRMS (ESI): calcd for

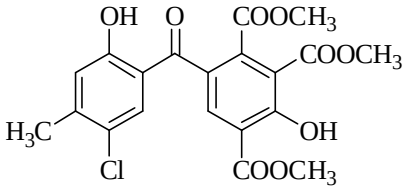
$C_{20}H_{19}O_{10}$ ([M+H]$^+$) 419.09727, found 419.09759; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2960 (w), 1738 (s), 1691 (m), 1639 (m), 1601 (m), 1573 (m), 1505 (w), 1429 (m), 1345 (m), 1299 (s), 1248 (s), 1216 (s), 1195 (s), 1165 (s), 1128 (s), 1053 (m), 1002 (m), 973 (m), 950 (m), 922 (m), 870 (m), 817 (m), 780 (s), 712 (s), 624 (m), 558 (m), 531 (m).

Trimethyl 3-hydroxy-6-(5-chloro-2-hydroxybenzoyl)benzene-1,2,4-tricarboxylate (13d):



Starting with 6-chloro-3-methoxalylchromone **4d** (0.266 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **13d** was isolated as a yellow solid (0.304 g, 72%), mp 172-174 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.61 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.97 (d, ^3J = 8.8 Hz, 1H, 3′-H_{Ar}), 7.40 (d, ^4J = 2.7 Hz, 1H, 6′-H_{Ar}), 7.50 (dd, ^3J = 8.8 Hz, ^4J = 2.7 Hz, 1H, 4′-H_{Ar}), 7.99 (s, 1H, 5-H_{Ar}), 10.65 (s, 1H, OH), 11.33 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 2^{x}52.8 (OCH_3), 53.2 (OCH_3), 115.5, 119.0, 122.7, 122.9, 124.9, 129.4, 129.9, 133.3, 134.1, 136.5, 156.2, 158.8, 164.8, 165.9, 167.3, 192.4 (C=O); MS (GC, 70 eV) *m/z* (%): 422 ([M]$^+$, 5), 392 (12), 391 (15), 390 (30), 333 (22), 332 (12), 331 (65), 301 (36), 300 (22), 299 (100), 272 (8), 155 (8), 99 (8); HRMS (ESI): calcd for $C_{19}H_{15}{}^{35}ClNaO_9$ ([M+Na]$^+$) 445.02968, found 445.03049, calcd for $C_{19}H_{15}{}^{37}ClNaO_9$ ([M+Na]$^+$) 447.02767, found 447.02796; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3019 (w), 2957 (w), 1742 (m), 1730 (w), 1693 (m), 1682 (m), 1667 (m), 1622 (m), 1602 (m), 1564 (w), 1525 (w), 1471 (w), 1434 (m), 1402 (w), 1359 (m), 1338 (m), 1317 (m), 1287 (m), 1269 (s), 1229 (s), 1203 (s), 1154 (s), 1104 (m), 1048 (m), 1008 (w), 978 (m), 944 (m), 915 (w), 869 (w), 842 (m), 823 (m), 810 (s), 798 (s), 778 (m), 749 (s), 730 (s), 691 (s), 647 (m), 622 (m), 601 (s), 559 (m), 530 (m).

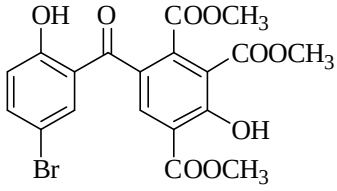
Trimethyl 6-(5-chloro-2-hydroxy-4-methylbenzoyl)-3-hydroxybenzene-1,2,4-tricarboxylate (13e):



Starting with 6-chloro-7-methyl-3-methoxalylchromone **4e** (0.280 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **13e** was isolated as a yellow solid (0.310 g, 71%), mp 175-177 ºC;

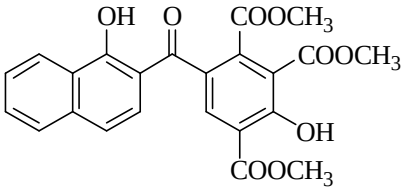
^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.94 (s, 1H, 3′-H_{Ar}), 7.41 (s, 1H, 6′-H_{Ar}), 7.99 (s, 1H, 5-H_{Ar}), 10.65 (s, 1H, OH), 11.30 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.0 (CH_3), 52.8 (OCH_3), 52.9 (OCH_3), 53.2 (OCH_3), 115.5, 119.6, 122.2, 122.8, 123.5, 129.7, 130.5, 133.0, 136.2, 142.9, 156.7, 158.6, 164.8, 165.8, 167.4, 192.7 (C=O); MS (EI, 70 eV) *m/z* (%): 436 ([M]$^+$, 9), 406 (13), 405 (16), 404 (31), 347 (24), 346 (15), 345 (76), 313 (100), 77 (8); HRMS (ESI): calcd for $C_{20}H_{17}{}^{35}ClNaO_9$ ([M+Na]$^+$) 459.04533, found 459.04554, calcd for $C_{20}H_{17}{}^{37}ClNaO_9$ ([M+Na]$^+$) 461.04388, found 461.04340; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2951 (w), 2847 (w), 1731 (s), 1682 (m), 1567 (w), 1482 (w), 1449 (m), 1433 (m), 1360 (w), 1315 (m), 1287 (m), 1252 (s), 1223 (s), 1194 (s), 1179 (s), 1155 (s), 1132 (s), 1058 (m), 1016 (w), 993 (s), 961 (w), 944 (m), 918 (m), 896 (m), 872 (w), 842 (w), 794 (s), 778 (s), 751 (m), 727 (s), 702 (m), 675 (s), 645 (m), 609 (m), 593 (m), 531 (w).

Trimethyl 6-(5-bromo-2-hydroxybenzoyl)-3-hydroxybenzene-1,2,4-tricarboxylate (13f):



Starting with 6-bromo-3-methoxalylchromone **4f** (0.311 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **13f** was isolated as a white solid (0.378 g, 81%), mp 192-194 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 6.97 (d, ^3J = 8.9 Hz, 1H, 3′-H_{Ar}), 7.38 (d, ^4J = 2.4 Hz, 1H, 6′-H_{Ar}), 7.58 (dd, ^3J = 8.9 Hz, ^4J = 2.4 Hz, 1H, 4′-H_{Ar}), 8.00 (s, 1H, 5-H_{Ar}), 11.56 (s, 1H, OH), 11.60 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 53.0 (OCH_3), 53.1 (OCH_3), 53.3 (OCH_3), 110.7, 114.5, 120.5, 120.7, 124.3, 128.7, 131.6, 134.3, 136.2, 139.5, 160.5, 161.7, 165.0, 165.1, 168.7, 198.6 (C=O); MS (EI, 70 eV) *m/z* (%): 466 ([M]$^+$, 7), 437 (16), 436 (46), 435 (167), 434 (44), 378 (12), 377 (89), 376 (14), 375 (88), 346 (19), 345 (100), 344 (19), 343 (98), 201 (10), 69 (8); HRMS (EI): calcd for $C_{19}H_{15}{}^{79}BrO_9$ ([M]$^+$) 465.98940, found 465.98946, calcd for $C_{19}H_{15}{}^{81}BrO_9$ ([M]$^+$) 467.98735, found 467.98749; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 1743 (m), 1730 (m), 1688 (m), 1651 (w), 1623 (m), 1598 (m), 1584 (m), 1531 (w), 1465 (w), 1468 (w), 1440 (m), 1403 (w), 1354 (m), 1318 (m), 1289 (m), 1271 (m), 1257 (m), 1233 (s), 1206 (s), 1164 (s), 1139 (s), 1048 (w), 1006 (w), 984 (m), 943 (m), 904 (w), 878 (w), 838 (m), 812 (m), 789 (m), 761 (m), 728 (m), 686 (s), 632 (w), 616 (m), 562 (m), 546 (w).

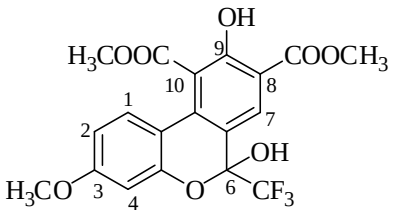
Trimethyl 3-hydroxy-6-(1-hydroxy-2-naphthoyl)benzene-1,2,4-tricarboxylate (13g):



Starting with 3-methoxalylbenzo[*h*]chromone **4g** (0.282 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **13g** was isolated as a yellow solid (0.201 g, 46%), mp 187-188 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.64 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.19-7.25 (m, 2H, H_{Ar}), 7.53-7.59 (m, 1H, H_{Ar}), 7.63-7.68 (m, 1H, H_{Ar}), 7.74-7.76 (m, 1H, H_{Ar}), 8.08 (s, 1H, 5-H_{Ar}), 8.50 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 11.56 (s, 1H, OH), 13.47 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 2^{x}53.0 (OCH_3), 53.2 (OCH_3), 112.8, 114.3, 118.5, 123.9, 124.4, 125.0, 126.0, 126.2, 127.5, 129.5, 130.6, 131.9, 136.4, 137.4, 160.1, 163.4, 165.3, 168.9, 199.0 (C=O); MS (EI, 70 eV) *m/z* (%): 438 ([M]$^+$, 10), 406 (23), 347 (64), 315 (100); HRMS (EI): calcd for $C_{23}H_{18}O_9$ ([M]$^+$) 438.09453, found 438.09494; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3019 (w), 2960 (w), 1753 (m), 1738 (m), 1690 (m), 1628 (w), 1598 (m), 1568 (m), 1503 (w), 1463 (w), 1439 (m), 1418 (w), 1389 (w), 1334 (m), 1297 (s), 1272 (m), 1245 (s), 1217 (s), 1192 (s), 1167 (s), 1128 (s), 1065 (m), 1024 (w), 1009 (w), 988 (s), 949 (m), 930 (w), 890 (w), 868 (w), 832 (w), 808 (s), 795 (s), 765 (s), 730 (s), 709 (s), 667 (w), 640 (w), 615 (m), 593 (m), 574 (m), 560 (m).

8,10-Dimethyl 6,9-dihydroxy-3-methoxy-6-(trifluoromethyl)-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14a):

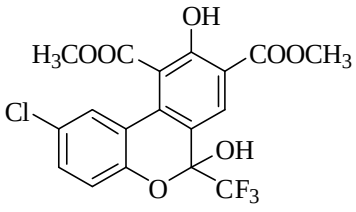


Starting with 7-methoxy-3-(trifluoroacetyl)chromone **5b** (0.272 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14a** was isolated as a white solid (0.090 g, 21%), mp 244-246 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.82 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.73 (d, ^4J = 2.6 Hz, 1H, 4-H_{Ar}), 6.78 (d, ^3J = 8.9 Hz, ^4J = 2.6 Hz, 1H, 2-H_{Ar}), 7.38 (d, ^3J = 8.9 Hz, 1H, 1-H_{Ar}), 8.07 (s, 1H, 7-H_{Ar}), 9.29 (s, 1H, 6-OH), 11.05 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.9 (OCH_3), 53.0 (OCH_3), 55.7 (OCH_3), 95.1 (q, $^2J_{C,F}$ = 32.1 Hz, 6-C), 102.5, 110.1, 110.3, 111.4, 117.9, 119.7, 126.2, 129.5, 133.1, 153.4, 158.5, 162.4, 167.4, 168.0; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -82.5 (s, 3F, CF_3); MS (GC 70 eV) *m/z* (%): 428 ([M]$^+$, 33), 397 (12), 359 (27), 327 (100), 295 (86), 211 (10), 151 (61), 108 (10); HRMS (ESI):

calcd for $C_{19}H_{16}F_3O_8$ ($[M+H]^+$) 429.07918, found 429.07901, calcd for $C_{19}H_{15}F_3NaO_8$ ($[M+Na]^+$) 451.06112, found 451.06158; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3233 (w), 2964 (w), 2941 (w), 2845 (w), 1684 (m), 1611 (m), 1591 (m), 1559 (w), 1514 (w), 1505 (w), 1457 (w), 1440 (m), 1432 (m), 1355 (m), 1336 (w), 1298 (m), 1276 (m), 1253 (m), 1214 (s), 1182 (s), 1162 (s), 1137 (s), 1111 (s), 1070 (m), 1035 (s), 980 (s), 942 (m), 925 (m), 897 (m), 882 (w), 865 (s), 809 (w), 795 (s), 770 (m), 743 (m), 724 (m), 707 (m), 679 (s), 660 (m), 638 (m), 628 (m), 578 (m), 543 (m).

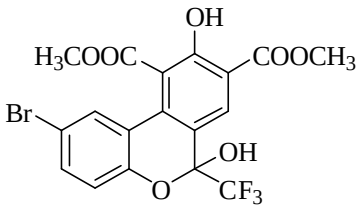
Dimethyl 2-chloro-6,9-dihydroxy-6-(trifluoromethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14b):



Starting with 6-chloro-3-(trifluoroacetyl)chromone **5c** (0.272 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14b** was isolated as a yellow solid (0.276 g, 64%), mp 212-214 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.26 (d, ^3J = 8.7 Hz, 1H, 4-H_{Ar}), 7.42 (d, ^4J = 2.4 Hz, 1H, 1-H_{Ar}), 7.54 (dd, ^3J = 8.7, ^4J = 2.4 Hz, 1H, 3-H_{Ar}), 8.13 (s, 1H, 7-H_{Ar}), 9.49 (s, 1H, 6-OH), 11.09 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.2 (OCH_3), 95.3 (q, $^2J_{C,F}$ = 32.6 Hz, 6-C), 113.8, 119.3, 119.4, 119.9, 120.8, 122.4 (q, $^1J_{C,F}$ = 290.6 Hz, CF_3), 124.3, 126.8, 129.7, 131.1, 131.9, 150.5, 158.4, 167.1, 167.6; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -82.3 (s, 3F, CF_3); MS (GC, 70 eV) *m/z* (%): 402 ([M-OCH_3+H], 15), 400 (45), 369 (22), 333 (33), 332 (17), 331 (91), 301 (34), 300 (16), 299 (100), 264 (10), 231 (13); HRMS (ESI): calcd for $C_{18}H_{13}{}^{35}ClF_3O_7$ ($[M+H]^+$) 433.02964, found 433.03073, calcd for $C_{18}H_{13}{}^{37}ClF_3O_7$ ($[M+H]^+$) 435.02750, found 435.02865; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3425 (w), 2951 (w), 1705 (m), 1687 (m), 1615 (w), 1594 (w), 1563 (w), 1482 (w), 1461 (w), 1445 (m), 1432 (m), 1408 (w), 1340 (m), 1310 (m), 1272 (w), 1246 (m), 1227 (s), 1191 (s), 1176 (s), 1144 (s), 1056 (m), 996 (s), 947 (m), 937 (m), 924 (m), 887 (w), 858 (m), 825 (m), 806 (s), 778 (m), 759 (m), 746 (m), 721 (m), 703 (s), 665 (s), 619 (w), 591 (m), 568 (w), 545 (m).

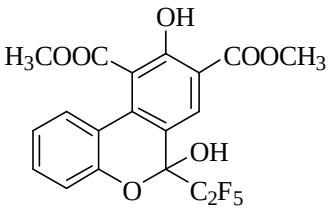
Dimethyl 2-bromo-6,9-dihydroxy-6-(trifluoromethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14c):



Starting with 6-bromo-3-(trifluoroacetyl)chromone **5d** (0.321 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14c** was isolated as a white solid (0.281 g, 59%), mp 204-206 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.19 (d, ^{3}J = 8.7 Hz, 1H, 4-H_{Ar}), 7.56 (d, ^{4}J = 2.3 Hz, 1H, 1-H_{Ar}), 7.65 (dd, ^{3}J = 8.7 Hz, ^{4}J = 2.3 Hz, 1H, 3-H_{Ar}), 8.12 (s, 1H, 7-H_{Ar}), 9.50 (s, 1H, 6-OH), 11.09 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.2 (OCH_3), 95.3 (q, $^{2}J_{C,F}$ = 32.5 Hz, 6-C), 113.8, 114.4, 119.3, 119.8, 120.2, 120.7, 122.4 (q, $^{2}J_{C,F}$ = 291.3 Hz, CF_3), 127.3, 129.7, 131.0, 134.7, 150.9, 158.3, 167.1, 167.6; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -82.3 (s, 3F, CF_3); MS (GC, 70 eV) *m/z* (%): 476 ($[M]^+$, 23), 447 (12), 446 (11), 445 (15), 378 (14), 377 (74), 376 (12), 375 (71), 346 (15), 345 (100), 344 (16), 343 (90), 201 (23), 200 (34), 199 (25), 198 (39), 173 (23), 172 (16); HRMS (ESI): calcd for $C_{18}H_{12}{}^{79}BrF_3O_7$ ($[M+H]^+$) 476.97913, found 476.97958, calcd for $C_{18}H_{12}{}^{81}BrF_3O_7$ ($[M+H]^+$) 478.97733, found 478.97748; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3434 (w), 3076 (w), 2953 (w), 1922 (w), 1717 (s), 1677 (m), 1614 (w), 1593 (w), 1557 (w), 1462 (w), 1446 (m), 1403 (w), 1346 (w), 1312 (m), 1229 (s), 1197 (s), 1174 (s), 1143 (s), 1082 (w), 1051 (m), 995 (s), 933 (w), 921 (w), 878 (w), 853 (w), 835 (m), 806 (s), 788 (w), 750 (m), 699 (m), 662 (m), 587 (m), 569 (w), 536 (w).

Dimethyl 6,9-dihydroxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14d):

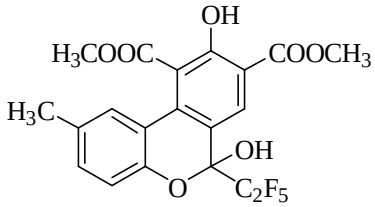


Starting with 3-(pentafluoropropanoyl)chromone **5f** (0.292 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14d** was isolated as a white solid (0.291 g, 65%), mp 221-223 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.10-7.20 (m, 2H, 2,4-H_{Ar}), 7.43-7.50 (m, 2H, 1,3-H_{Ar}), 8.13 (d, $^{5}J_{H,F}$ = 1.6 Hz, 1H, 7-H_{Ar}), 9.46 (d, $^{4}J_{H,F}$ = 3.9 Hz, 1H, 6-OH), 11.08 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.1 (OCH_3), 96.7 (t, $^{2}J_{C,F}$ = 28.2 Hz, 6-C), 112.8, 117.7, 117.9, 119.0, 120.9, 123.3, 124.9, 130.6,

132.4, 133.2, 151.8, 158.6, 167.3, 167.9; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.9 (s, 3F, CF_3), –121.8 (d, ^2J = 279.5 Hz, 1F, C*F*F), –124.0 (d, ^2J = 279.5 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 448 ([M]$^+$, 3), 417 (10), 385 (18), 329 (86), 297 (100), 265 (70), 210 (12), 133 (9); HRMS (ESI): calcd for $C_{19}H_{14}F_5O_7$ ([M+H]$^+$) 449.06542, found 449.06548; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3420 (w), 2959 (w), 1712 (m), 1676 (m), 1608 (w), 1596 (w), 1568 (w), 1494 (w), 1464 (w), 1433 (m), 1393 (w), 1337 (m), 1319 (m), 1298 (w), 1273 (w), 1251 (m), 1222 (s), 1175 (s), 1143 (s), 1072 (s), 1052 (m), 1042 (m), 998 (s), 970 (m), 946 (w), 933 (m), 908 (m), 877 (w), 863 (w), 842 (m), 806 (m), 778 (s), 759 (s), 736 (s), 709 (m), 687 (m), 662 (m), 645 (w), 614 (m), 579 (w), 533 (m).

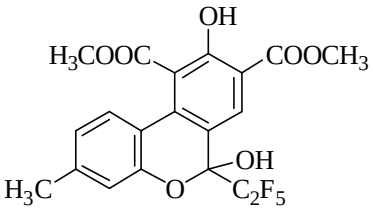
8,10-Dimethyl 6,9-dihydroxy-4-methyl-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14e):



Starting with 6-methyl-3-(pentafluoropropanoyl)chromone **5g** (0.306 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14e** was isolated as a white solid (0.143 g, 31%), mp 239-241 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.29 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.01 (d, ^3J = 8.1 Hz, 1H, 4-H_{Ar}), 7.24-7.28 (m, 2H, 1,3-H_{Ar}), 8.11 (d, $^5J_{H,F}$ = 1.5 Hz, 1H, 7-H_{Ar}), 9.39 (d, $^4J_{H,F}$ = 3.9 Hz, 1H, 6-OH), 11.07 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.5 (CH_3), 52.9 (OCH_3), 53.1 (OCH_3), 96.7 (t, $^2J_{C,F}$ = 27.3 Hz, 6-C), 112.7, 117.5, 117.6, 118.9, 121.0, 125.0, 130.5, 131.9, 133.0, 133.2, 149.7, 158.6, 167.3, 167.9; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.9 (s, 3F, CF_3), –121.7 (d, ^2J = 279.4 Hz, 1F, C*F*F), –123.9 (d, ^2J = 279.4 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 462 ([M]$^+$, 7), 430 (17), 399 (17), 343 (79), 311 (100), 279 (69), 140 (9), 69 (8); HRMS (ESI): calcd for $C_{20}H_{16}F_5O_7$ ([M+H]$^+$) 463.08107, found 463.08170, calcd for $C_{20}H_{15}F_5NaO_7$ ([M+Na]$^+$) 485.06301, found 485.06357; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3412 (w), 3012 (w), 2958 (w), 2932 (w), 1726 (s), 1676 (m), 1616 (w), 1597 (w), 1574 (w), 1490 (w), 1444 (m), 1383 (w), 1371 (w), 1348 (m), 1339 (m), 1315 (w), 1293 (w), 1273 (w), 1255 (m), 1215 (s), 1182 (s), 1155 (m), 1143 (s), 1130 (m), 1075 (s), 1048 (m), 1011 (m), 977 (w), 950 (w), 932 (w), 911 (m), 880 (w), 848 (w), 817 (s), 804 (m), 786 (w), 775 (w), 740 (w), 732 (m), 716 (w), 676 (w), 664 (w), 640 (m), 611 (w), 584 (w), 564 (w), 534 (w).

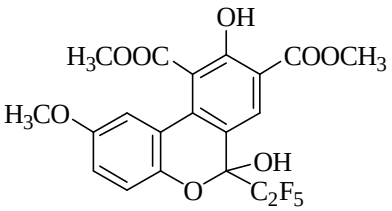
8,10-Dimethyl 6,9-dihydroxy-3-methyl-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14f):



Starting with 7-methyl-3-(pentafluoropropanoyl)chromone **5h** (0.306 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14f** was isolated as a white solid (0.185 g, 40%), mp 225-227 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.33 (s, 3H, CH_3), 3.90, 3.97 (both s, 3H, OCH_3), 6.94-7.00 (m, 2H, 2,4-H_{Ar}), 7.34 (d, ^3J = 8.1 Hz, 1H, 1-H_{Ar}), 8.10 (d, $^5J_{H,F}$ = 1.6 Hz, 1H, 7-H_{Ar}), 9.41 (d, $^4J_{H,F}$ = 4.0 Hz, 1H, 6-OH), 11.06 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 20.8 (CH_3), 52.9 (OCH_3), 53.1 (OCH_3), 96.8 (t, $^2J_{C,F}$ = 27.0 Hz, 6-C), 112.2, 115.1, 117.8, 118.6, 120.5, 124.1, 124.7, 130.6, 133.4, 143.0, 151.8, 158.6, 167.3, 168.0; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.8 (s, 3F, CF_3), –121.8 (d, ^2J = 278.5 Hz, 1F, C*F*F), –124.1 (d, ^2J = 278.5 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 462 ([M]$^+$, 8), 431 (11), 399 (19), 343 (95), 311 (100), 279 (56), 224 (11), 140 (11); HRMS (ESI): calcd for $C_{20}H_{16}F_5O_7$ ([M+H]$^+$) 463.08107, found 463.08133, calcd for $C_{20}H_{15}F_5NaO_7$ ([M+Na]$^+$) 485.06301, found 485.06367; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3324 (w), 3009 (w), 2956 (w), 2853 (w), 1703 (s), 1681 (m), 1614 (m), 1593 (m), 1563 (w), 1512 (w), 1460 (w), 1443 (m), 1435 (m), 1392 (w), 1332 (m), 1276 (w), 1257 (m), 1213 (s), 1182 (s), 1164 (s), 1146 (s), 1137 (s), 1073 (s), 1045 (m), 997 (s), 972 (m), 963 (m), 931 (s), 922 (m), 891 (m), 866 (s), 825 (w), 814 (m), 802 (s), 783 (m), 765 (m), 742 (m), 730 (s), 705 (m), 672 (w), 662 (m), 648 (w), 620 (m), 582 (m), 540 (m).

8,10-Dimethyl 6,9-dihydroxy-4-methoxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14g):

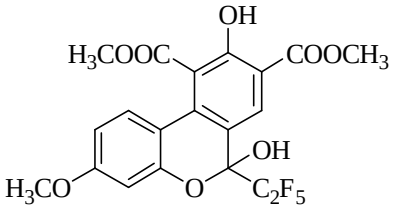


Starting with 6-methoxy-3-(pentafluoropropanoyl)chromone **5i** (0.322 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14g** was isolated as a pale yellow solid (0.116 g, 27%), mp 226-228 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.75 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.01-7.06 (m, 3H, 1,3,4-H_{Ar}), 8.11 (s, 1H, 7-H_{Ar}), 9.36 (d, $^4J_{H,F}$ = 3.8 Hz, 1H, 6-OH), 11.06 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.2 (OCH_3), 55.5

(OCH_3), 97.1 (t, $^2J_{C,F}$ = 27.0 Hz, 6-C), 109.2, 112.9, 118.3, 118.4, 118.6, 119.1, 121.3, 130.5, 133.0, 145.7, 154.5, 158.5, 167.4, 167.8; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –77.8 (s, 3F, CF_3), –121.5 (d, ^2J = 279.6 Hz, 1F, C*F*F), –123.7 (d, ^2J = 279.6 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 478 ([M^+], 45), 447 (19), 446 (38), 415 (23), 359 (100), 327 (92), 295 (91), 268 (22), 240 (15), 148 (19); HRMS (ESI): calcd for $C_{20}H_{16}F_5O_8$ ([M+H]$^+$) 479.07598, found 479.07630, calcd for $C_{20}H_{15}F_5NaO_8$ ([M+Na]$^+$) 501.05793, found 501.05833; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3403 (w), 3004 (w), 2960 (w), 2924 (w), 2850 (w), 1717 (m), 1673 (w), 1615 (w), 1570 (w), 1490 (w), 1470 (w), 1444 (m), 1342 (m), 1314 (m), 1295 (w), 1247 (m), 1207 (s), 1173 (s), 1144 (s), 1109 (m), 1068 (s), 1041 (s), 998 (s), 946 (m), 937 (m), 912 (m), 882 (m), 849 (m), 810 (s), 799 (s), 771 (s), 731 (s), 680 (m), 665 (m), 649 (m), 611 (m), 577 (w), 535 (w).

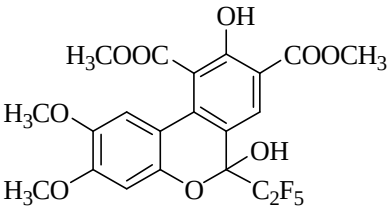
Dimethyl 6,9-dihydroxy-3-methoxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14h):



Starting with 7-methoxy-3-(pentafluoropropanoyl)chromone **5j** (0.322 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14h** was isolated as a pale yellow solid (0.185 g, 65%), mp 217-219 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.81 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.65 (d, ^4J = 2.5 Hz, 1H, 4-H_{Ar}), 6.79 (dd, ^3J = 9.0 Hz, ^4J = 2.6 Hz, 1H, 2-H_{Ar}), 7.38 (d, ^3J = 9.0 Hz, 1H, 1-H_{Ar}), 8.08 (d, $^5J_{H,F}$ = 1.4 Hz, 1H, 7-H_{Ar}), 9.43 (d, 1H, $^4J_{H,F}$ = 3.8 Hz, 6-OH), 11.07 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.9 (OCH_3), 53.0 (OCH_3), 55.7 (OCH_3), 97.0 (t, $^2J_{C,F}$ = 28.1 Hz, 6-C), 102.5, 109.9, 110.5, 111.5, 117.9, 119.7, 126.3, 130.6, 133.5, 153.5, 158.8, 162.4, 167.4, 168.1; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.8 (s, 3F, CF_3), –122.0 (d, ^2J = 279.5 Hz, 1F, C*F*F), –124.4 (d, ^2J = 279.5 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 478 ([M^+, 9), 446 (16), 415 (12), 359 (42), 327 (100), 295 (61), 240 (7), 148 (7); HRMS (ESI): calcd for $C_{20}H_{16}F_5O_8$ ([M+H]$^+$) 479.07598, found 479.07621; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3287 (w), 2960 (w), 2847 (w), 1716 (m), 1668 (w), 1606 (m), 1567 (w), 1512 (w), 1442 (m), 1392 (w), 1361 (w), 1315 (m), 1283 (w), 1236 (s), 1218 (s), 1192 (s), 1168 (s), 1146 (s), 1111 (s), 1070 (s), 1028 (m), 997 (s), 973 (m), 940 (w), 929 (m), 890 (m), 843 (m), 811 (w), 797 (s), 767 (w), 744 (m), 727 (m), 709 (m), 650 (m), 619 (m), 608 (m), 596 (m), 536 (w).

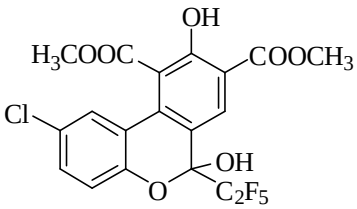
8,10-Dimethyl 6,9-dihydroxy-2,3-dimethoxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14i):



Starting with 6,7-dimethoxy-3-(pentafluoropropanoyl)chromone **5k** (0.352 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14i** was isolated as a yellow solid (0.264 g, 52%), mp 209-211 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.72 (s, 3H, OCH_3), 3,82 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.71 (s, 1H, 4-H_{Ar}), 6.97 (s, 1H, 1-H_{Ar}), 8.06 (s, 1H, 7-H_{Ar}), 9.36 (s, 1H, 6-OH), 11.07 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.9 (OCH_3), 53.1 (OCH_3), 55.9 (OCH_3), 56.0 (OCH_3), 96.9 (t, $^2J_{C,F}$ = 26.7 Hz, 6-C), 101.5, 107.1, 108.9, 111.3, 117.8, 119.9, 130.4, 133.6, 144.4, 147.2, 152.4, 158.7, 167.7, 168.0; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.7 (s, 3F, CF_3), –122.0 (d, ^2J = 277.4 Hz, 1F, C*F*F), –124.2 (d, ^2J = 277.4 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 508 ([M]$^+$, 22), 477 (13), 476 (48), 445 (13), 389 (52), 358 (20), 357 (100), 341 (13), 325 (41), 222 (10); HRMS (EI): calcd for $C_{21}H_{17}F_5O_9$ ([M]$^+$) 508.07872, found 477.07925; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3265 (w), 2956 (w), 2921 (w), 2851 (w), 1712 (m), 1672 (m), 1614 (w), 1595 (w), 1569 (w), 1518 (w), 1465 (w), 1439 (m), 1409 (w), 1348 (m), 1337 (m), 1306 (m), 1284 (w), 1266 (m), 1232 (s), 1199 (s), 1177 (s), 1162 (s), 1145 (s), 1113 (m), 1079 (s), 1048 (m), 1035 (m), 1006 (m), 990 (m), 973 (m), 937 (m), 889 (m), 877 (w), 819 (w), 800 (s), 782 (m), 769 (m), 748 (m), 717 (m), 683 (w), 670 (m), 645 (m), 622 (m), 595 (w), 579 (w), 534 (w).

8,10-Dimethyl 4-chloro-6,9-dihydroxy-3-methyl-6-(pentafluoroethyl)-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14j):

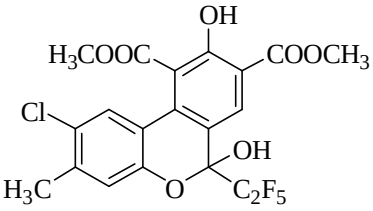


Starting with 6-chloro-3-(pentafluoropropanoyl)chromone **5l** (0.327 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14j** was isolated as a white solid (0.323 g, 67%), mp 236-238 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.18 (d, ^3J = 8.7 Hz, 1H, 4-H_{Ar}), 7.41 (d, ^4J = 2.1 Hz, 1H, 1-H_{Ar}), 7.53 (d, ^3J = 8.7 Hz, ^4J = 2.1 Hz, 1H, 3-H_{Ar}), 8.13 (s, 1H, 7-H_{Ar}), 9.63 (d, $^4J_{H,F}$ = 3.7 Hz, 1H, 6-OH), 11.10 (s, 1H, 9-OH); ^{13}C NMR (62.9

MHz, DMSO-d_6): δ = 53.2 (OCH_3), 53.1 (OCH_3), 97.1 (t, $^2J_{C,F}$ = 27.3 Hz, 6-C), 113.8, 119.2, 119.4, 119.7, 120.7, 124.2, 126.8, 130.7, 131.5, 131.9, 150.6, 158.5, 167.1, 167.6; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.9 (s, 3F, CF_3), –121.7 (d, ^2J = 277.8 Hz, 1F, C*F*F), –123.9 (d, ^2J = 277.8 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 482 ([M]$^+$, 2), 452 (10), 451 (16), 450 (23), 419 (26), 365 (32), 364 (15), 363 (87), 333 (58), 332 (25), 331 (100), 301 (29), 300 (13), 299 (86), 244 (12), 209 (11), 150 (13); HRMS (ESI): calcd for $C_{19}H_{12}{}^{35}ClF_5NaO_7$ ([M+Na]$^+$) 505.00839, found 505.00853; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3416 (w), 2960 (w), 1719 (s), 1674 (m), 1614 (w), 1593 (w), 1562 (w), 1480 (w), 1461 (w), 1443 (m), 1405 (w), 1383 (w), 1343 (m), 1309 (m), 1285 (w), 1253 (m), 1217 (s), 1176 (s), 1162 (m), 1144 (s), 1127 (m), 1093 (w), 1070 (s), 1043 (m), 998 (s), 972 (m), 939 (m), 910 (m), 886 (w), 877 (w), 845 (m), 820 (s), 808 (m), 786 (w), 776 (m), 756 (m), 738 (m), 725 (m), 712 (s), 666 (m), 636 (m), 611 (w), 562 (w).

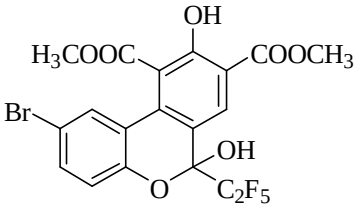
Dimethyl 2-chloro-6,9-dihydroxy-3-methyl-6-(pentafluoroethyl)-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14k):



Starting with 6-chloro-7-methyl-3-(pentafluoropropanoyl)-chromone **5m** (0.341 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14k** was isolated as a white solid (0.283 g, 57%), mp 223-225 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.35 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.18 (s, 1H, 4-H_{Ar}), 7.41 (s, 1H, 1-H_{Ar}), 8.11 (d, $^5J_{H,F}$ = 1.4 Hz, 1H, 7-H_{Ar}), 9.59 (d, $^4J_{H,F}$ = 3.9 Hz, 1H, 6-OH), 11.09 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.6 (CH_3), 53.0 (OCH_3), 53.1 (OCH_3), 97.1 (t, $^2J_{C,F}$ = 28.8 Hz, 6-C), 113.3, 117.0, 118.8, 120.0, 120.4, 124.5, 127.2, 130.8, 131.7, 140.5, 150.5, 158.5, 167.2, 167.7; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.9 (s, 3F, CF_3), –122.8 (d, ^2J = 279.5 Hz, 1F, C*F*F), –124.1 (d, ^2J = 279.5 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 496 ([M]$^+$, 7), 465 (11), 464 (18), 433 (18), 379 (27), 378 (15), 377 (88), 347 (48), 346 (23), 345 (100), 315 (21), 314 (10), 313 (74), 258 (11), 157 (11); HRMS (ESI): calcd for $C_{20}H_{15}{}^{35}ClF_5O_7$ ([M+H]$^+$) 497.04210, found 497.04264, calcd for $C_{20}H_{15}{}^{37}ClF_5O_7$ ([M+H]$^+$) 499.04007, found 499.04068; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3434 (w), 3006 (w), 2953 (w), 1713 (s), 1687 (m), 1613 (m), 1592 (w), 1552 (w), 1497 (w), 1443 (m), 1385 (w), 1336 (s), 1306 (m), 1289 (w), 1261 (m), 1228 (s), 1188 (s), 1171 (s), 1155 (s), 1140 (s), 1080 (s), 1053 (s), 1016 (m), 998 (s), 974 (m), 935 (m), 926 (m), 898 (m), 887 (m), 868 (m), 818 (m), 808 (s), 783 (m),

767 (m), 744 (m), 731 (m), 710 (s), 665 (m), 641 (w), 631 (s), 615 (w), 603 (m), 583 (w), 550 (m), 535 (w).

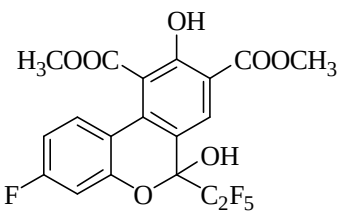
Dimethyl 2-bromo-6,9-dihydroxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14l):



Starting with 6-bromo-3-(pentafluoropropanoyl)chromone **5n** (0.371 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14l** was isolated as a white solid (0.358 g, 68%), mp 225-227 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.93 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.13 (d, ^{3}J = 8.7 Hz, 1H, 4-H_{Ar}), 7.55 (d, ^{4}J = 2.2 Hz, 1H, 1-H_{Ar}), 7.65 (dd, ^{3}J = 8.7 Hz, ^{4}J = 2.2 Hz, 1H, 3-H_{Ar}), 8.12 (d, $^{5}J_{H,F}$ = 1.3 Hz, 1H, 7-H_{Ar}), 9.65 (d, $^{4}J_{H,F}$ = 3.6 Hz, 1H, 6-OH), 11.10 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.2 (OCH_3), 97.1 (t, $^{2}J_{C,F}$ = 28.8 Hz, 6-C), 113.8, 114.4, 119.2, 119.9, 120.1, 120.7, 127.2, 130.8, 131.4, 134.8, 151.0, 158.5, 167.2, 167.6; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –78.0 (s, 3F, CF_3), –121.8 (d, ^{2}J = 279.7 Hz, 1F, C*F*F), –124.0 (d, ^{2}J = 279.7 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 496 ([M-OCH_3+H], 14), 494 (13), 465 (12), 463 (12), 410 (10), 409 (57), 408 (10), 407 (57), 378 (15), 377 (100), 376 (15), 375 (99), 345 (34), 343 (34), 265 (12), 264 (62), 236 (13), 173 (10), 172 (10), 44 (11); HRMS (ESI): calcd for $C_{19}H_{12}{}^{79}BrF_5NaO_7$ ([M+Na]$^+$) 548.95788, found 548.95771, calcd for $C_{19}H_{12}{}^{81}BrF_5NaO_7$ ([M+Na]$^+$) 550.95610, found 550.95591; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3427 (w), 2957 (w), 1722 (s), 1674 (m), 1650 (w), 1613 (w), 1592 (w), 1556 (w), 1480 (w), 1442 (m), 1341 (m), 1308 (m), 1253 (m), 1217 (s), 1177 (s), 1143 (s), 1071 (s), 1043 (m), 997 (s), 937 (m), 908 (m), 877 (m), 843 (m), 819 (s), 775 (m), 748 (s), 708 (s), 664 (m), 628 (s), 561 (w), 542 (m).

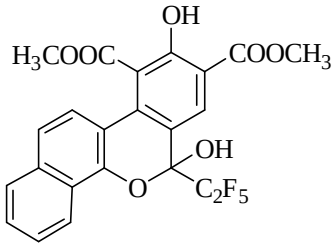
8,10-Dimethyl 3-fluoro-6,9-dihydroxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14m):



Starting with 7-fluoro-3-(pentafluoropropanoyl)chromone **5o** (0.310 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14m** was isolated as a white solid (0.154 g, 33%), mp 213-214 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.05-7.11 (m, 2H, H_{Ar}), 7.48-7.53 (m, 1H, H_{Ar}), 8.11 (d, ^5J = 1.5 Hz, 1H, 7-H_{Ar}), 9.63 (d, $^4J_{H,F}$ = 3.9 Hz, 1H, 6-OH), 11.09 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 53.1 (OCH_3), 53.2 (OCH_3), 97.3 (t, $^2J_{C,F}$ = 27.4 Hz, 6-C), 105.2 (d, $J_{C,F}$ = 25.0 Hz), 110.8 (d, $J_{C,F}$ = 22.4 Hz), 112.8, 114.7 (d, $J_{C,F}$ = 3.6 Hz), 118.8, 120.1, 127.0 (d, $J_{C,F}$ = 10.6 Hz), 130.7 (d, $J_{C,F}$ = 2.2 Hz), 132.4, 153.4 (dd, $J_{C,F}$ = 12.1 Hz, $J_{C,F}$ = 1.2 Hz), 158.7, 163.7 (d, $^1J_{C,F}$ = 250.2 Hz, $C_{Ar}F$), 167.2, 167.8; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.9 (s, 3F, CF_3), –106.9 (s, 1F, F), –121.9 (d, ^2J = 279.5 Hz, 1F, C*F*F), –124.2 (d, ^2J = 279.5 Hz, 1F, CF*F*); MS (GC, 70 eV) *m/z* (%): 434 ([M-OCH_3-H], 18), 403 (21), 316 (14), 315 (77), 284 (16), 283 (100), 215 (24), 144 (11); HRMS (ESI): calcd for $C_{19}H_{11}F_6O_7$ ([M-H]$^-$) 465.04145, found 465.04137; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3424 (w), 3086 (w), 3010 (w), 2959 (w), 2927 (w), 2872 (w), 2857 (w), 1709 (s), 1682 (m), 1616 (m), 1602 (m), 1510 (w), 1458 (w), 1431 (m), 1389 (w), 1360 (w), 1335 (m), 1310 (w), 1280 (m), 1262 (m), 1225 (s), 1209 (s), 1184 (s), 1158 (s), 1142 (s), 1121 (s), 1106 (m), 1073 (s), 1040 (m), 997 (s), 980 (m), 968 (m), 931 (m), 923 (m), 891 (m), 870 (s), 824 (w), 815 (w), 803 (s), 784 (m), 769 (m), 757 (m), 743 (s), 730 (m), 704 (m), 674 (m), 663 (m), 646 (w), 626 (m), 606 (m), 577 (w), 540 (w).

Dimethyl 6,9-dihydroxy-6-(pentafluoroethyl)-6*H*-dibenzo[*c,h*]chromene-8,10-dicarboxylate (14n):

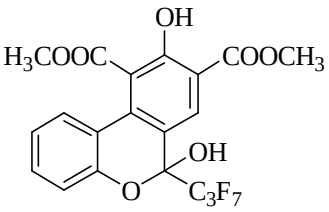


Starting with 3-(pentafluoropropanoyl)benzo[*h*]chromone **5p** (0.342 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14n** was isolated as a pale yellow solid (0.388 g, 78%), mp 233-235 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.94 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 7.53 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 7.64-7.72 (m, 3H, H_{Ar}), 7.93-7.97 (m, 1H, H_{Ar}), 8.17-8.23 (m, 2H, H_{Ar}), 9.74 (d, $^4J_{H,F}$ = 3.8 Hz, 1H, 6-OH), 11.14 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.1 (OCH_3), 97.6 (t, $^2J_{C,F}$ = 28.6 Hz, 6-C), 112.4, 118.9, 120.1, 120.7, 120.9, 121.8, 122.5, 123.8, 127.0, 127.7, 128.6, 130.5, 133.6, 134.6, 147.9, 158.8, 167.3, 167.9; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –77.5 (s, 3F, CF_3), –121.8 (d, ^2J = 277.9 Hz, 1F, C*F*F), –124.6 (d, ^2J = 277.9 Hz, 1F, CF*F*); MS (EI, 70 eV) *m/z* (%): 498 ([M]$^+$, 11), 466 (64), 435 (10), 379 (20), 347 (100), 315 (91), 287 (13), 259 (9), 231 (10), 157 (15), 97 (10), 57 (15); HRMS (ESI): calcd

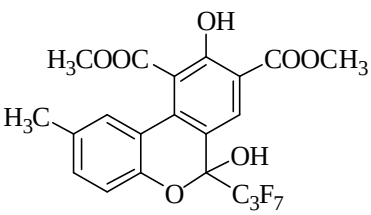
for $C_{23}H_{16}F_5O_7$ ([M+H]$^+$) 499.08107, found 499.08116; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3282 (w), 3107 (w), 2953 (w), 1708 (m), 1679 (m), 1633 (w), 1615 (m), 1603 (w), 1589 (w), 1565 (w), 1479 (w), 1443 (m), 1433 (m), 1403 (w), 1383 (w), 1327 (m), 1306 (w), 1251 (m), 1205 (s), 1174 (s), 1156 (s), 1140 (s), 1087 (s), 1049 (m), 1031 (m), 1016 (m), 984 (m), 964 (m), 949 (w), 926 (m), 907 (m), 876 (m), 827 (w), 812 (m), 794 (s), 780 (m), 761 (w), 751 (m), 712 (s), 660 (m), 627 (w), 608 (m), 687 (w), 572 (m), 555 (w).

Dimethyl 6-(heptafluoropropyl)-6,9-dihydroxy-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14o):



Starting with 3-(heptafluorobutanoyl)chromone **5q** (0.342 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14o** was isolated as a white solid (0.344 g, 69%), mp 211-212 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.09-7.20 (m, 2H, 2,4-H_{Ar}), 7.43-7.50 (m, 2H, 1,3-H_{Ar}), 8.13 (s, 1H, 7-H_{Ar}), 9.51 (d, $^4J_{H,F}$ = 4.1 Hz, 1H, 6-OH), 11.08 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.3 (OCH_3), 53.1 (OCH_3), 97.4 (t, $^2J_{C,F}$ = 29.1 Hz, 6-C), 112.8, 115.2, 117.7, 119.0, 121.0, 123.2, 124.9, 130.7, 132.3, 133.1, 151.7, 158.6, 167.3, 167.9; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.0 (s, 3F, CF_3), –118.3, –120.7 (both dq, ^2J = 284.6 Hz, J = 8.5 Hz, 1F, CF_2), –123.5 (d, ^2J = 289.7 Hz, 1F, CF_2), –124.2 (d, ^2J = 289.4 Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 498 ([M]$^+$, 2), 466 (12), 435 (18), 329 (62), 297 (100), 265 (85), 238 (10), 210 (11), 133 (10); HRMS (ESI): calcd for $C_{20}H_{14}F_7O_7$ ([M+H]$^+$) 499.06223, found 499.06318; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3417 (w), 2960 (w), 1716 (m), 1675 (m), 1607 (w), 1567 (w), 1494 (w), 1454 (w), 1440 (m), 1392 (w), 1336 (m), 1319 (m), 1297 (w), 1213 (s), 1143 (s), 1115 (s), 1058 (m), 997 (s), 927 (m), 903 (w), 882 (m), 837(w), 810 (m), 774 (m), 759 (s) 735 (s), 712 (s), 694 (w), 678 (m), 646 (w), 618 (m), 582 (w), 532 (m).

Dimethyl 6-(heptafluoropropyl)-6,9-dihydroxy-2-methyl-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14p):

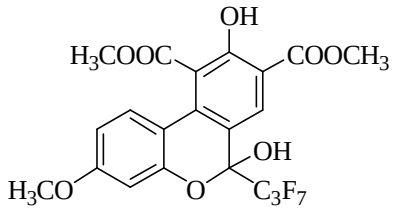


Starting with 3-(heptafluorobutanoyl)-6-methylchromone **5r** (0.356 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14p** was isolated as a white solid (0.328 g,

64%), mp 322-324 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.29 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.00 (d, ^3J = 8.2 Hz, 1H, 4-H_{Ar}), 7.24-7.28 (m, 2H, 1,3-H_{Ar}), 8.11 (d, $^5J_{H,F}$ = 1.6 Hz, 1H, 7-H_{Ar}), 9.44 (d, $^4J_{H,F}$ = 4.3 Hz, 1H, 6-OH), 11.07 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.0 (CH_3), 50.8 (OCH_3), 51.1 (OCH_3), 95.4 (t, $^2J_{C,F}$ = 27.1 Hz, 6-C), 109.7, 115.7, 116.4, 118.6, 123.6, 128.5, 130.2, 130.7, 132.3, 147.5, 158.2, 166.4, 167.4; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.0 (t, J = 8.7 Hz, 3F, CF_3), –118.3 (dq, ^2J = 284.9 Hz, J = 9.1 Hz, 1F, CF_2), –120.7 (dq, ^2J = 284.9 Hz, J = 8.4 Hz, 1F, CF_2), –123.5 (d, ^2J = 290.2 Hz, 1F, CF_2), –124.2 (d, ^2J = 289.0 Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 512 ([M]$^+$, 4), 480 (20), 449 (16), 343 (53), 311 (100), 279 (80), 251 (8), 224 (15), 139 (13); HRMS (ESI): calcd for $C_{21}H_{16}F_7O_7$ ([M+H]$^+$) 513.07788, found 513.07787; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3234 (w), 2958 (w), 2925 (w), 2853 (w), 1709 (m), 1682 (m), 1616 (w), 1596 (w), 1573 (w), 1491 (w), 1439 (m), 1405 (w), 1337 (m), 1317 (w), 1291 (m), 1275 (m), 1223 (s), 1186 (s), 1147 (s), 1116 (s), 1072 (m), 1017 (m), 995 (s), 949 (m), 928 (w), 890 (m), 841 (w), 822 (m), 803 (s), 781 (w), 741 (m), 728 (m), 679 (m), 642 (m), 599 (w), 564 (m), 533 (w).

Dimethyl 6-(heptafluoropropyl)-6,9-dihydroxy-3-methoxy-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14q):

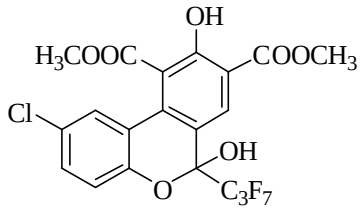


Starting with 3-(heptafluorobutanoyl)-7-methoxy-chromone **5s** (0.372 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14q** was isolated as a white solid (0.354 g, 67%), mp 193-195 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.81 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.62 (d, ^4J = 2.1 Hz, 1H, 4-H_{Ar}), 6.79 (dd, ^3J = 8.9 Hz, ^4J = 2.1 Hz, 1H, 2-H_{Ar}), 7.38 (d, ^3J = 8.9 Hz, 1H, 1-H_{Ar}), 8.09 (s, 1H, 7-H_{Ar}), 9.49 (s, 1H, 6-OH), 11.08 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.9 (OCH_3), 53.1 (OCH_3), 55.7 (OCH_3), 97.7 (t, $^2J_{C,F}$ = 29.0 Hz, 6-C), 102.5, 109.9, 110.4, 111.5, 117.9, 119.7, 126.2, 130.7, 133.5, 153.4, 158.8, 162.4, 167.4, 168.1; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.0 (t, J = 8.7 Hz, 3F, CF_3), –118.5 (dq, ^2J = 284.2 Hz, J = 8.5 Hz, 1F, CF_2), –121.2 (dq, ^2J = 284.2, J = 8.7 Hz, 1F, CF_2), –123.4 (d, ^2J = 290.1 Hz, 1F, CF_2), –124.1 (d, ^2J = 289.4 Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 528 ([M]$^+$, 7), 496 (19), 465 (13), 359 (43), 327 (100), 295 (70), 240 (7), 148 (8), 97 (9), 57 (15); HRMS (ESI):

calcd for $C_{21}H_{16}F_7O_8$ ([M+H]$^+$) 529.07279, found 529.07372; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3271 (w), 2960 (w), 1714 (m), 1673 (m), 1651 (w), 1607 (m), 1537 (w), 1512 (w), 1444 (m), 1352 (m), 1331 (m), 1314 (m), 1291 (w), 1212 (s), 1189 (s), 1141 (s), 1110 (s), 1058 (m), 1028 (m), 994 (s), 958 (m), 920 (s), 882 (m), 861 (m), 836 (m), 816 (w), 797 (s), 764 (m), 739 (m), 713 (m), 672 (m), 618 (s), 579 (m), 548 (m), 535 (m).

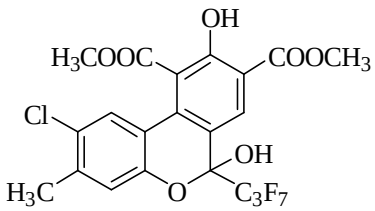
Dimethyl 2-chloro-6-(heptafluoropropyl)-6,9-dihydroxy-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14r):



Starting with 6-chloro-3-(heptafluorobutanoyl)chromone **5t** (0.377 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14r** was isolated as a pale yellow solid (0.410 g, 77%), mp 200-201 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 7.17 (d, ^3J = 8.7 Hz, 1H, 4-H_{Ar}), 7.42 (d, ^4J = 2.4 Hz, 1H, 1-H_{Ar}), 7.53 (dd, ^3J = 8.7, ^4J = 2.4 Hz, 1H, 3-H_{Ar}), 8.13 (d, $^5J_{H,F}$ = 1.7 Hz, 1H, 7-H_{Ar}), 9.69 (d, $^4J_{H,F}$ = 3.8 Hz, 1H, 6-OH), 11.10 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 53.1 (OCH_3), 53.2 (OCH_3), 97.8 (t, $^2J_{C,F}$ = 26.2 Hz, 6-C), 113.8, 119.2, 119.3, 119.7, 120.8, 124.3, 126.8, 130.9, 131.5, 131.9, 150.5, 158.5, 167.2, 167.6; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.1 (t, ^3J = 8.9 Hz, 3F, CF_3), –118.3 (dq, ^2J = 285.2 Hz, J = 9.2 Hz, 1F, CF_2), –120.7 (dq, ^2J = 285.2 Hz, J = 8.6 Hz, 1F, CF_2), –123.5, –124.2 (both d, ^2J = 289. Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 532 ([M]$^+$, 3), 501 (10), 469 (14), 365 (23), 364 (12), 363 (78), 333 (33), 332 (16), 331 (100), 301 (16), 299 (54), 244 (11), 150 (10); HRMS (ESI): calcd for $C_{20}H_{12}{}^{35}ClF_7NaO_7$ ([M+Na]$^+$) 555.00520, found 555.00474, calcd for $C_{20}H_{12}{}^{37}ClF_7NaO_7$ ([M+Na]$^+$) 557.00317, found 557.00270; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3426 (w), 2956 (w), 2850 (w), 1721 (s), 1675 (m), 1643 (w), 1616 (w), 1563 (w), 1484 (w), 1462 (w), 1443 (m), 1407 (w), 1385 (w), 1347 (m), 1310 (m), 1253 (m), 1212 (s), 1193 (s), 1174 (s), 1142 (s), 1120 (s), 1098 (m), 1054 (m), 996 (s), 962 (m), 939 (m), 905 (m), 885 (m), 824 (m), 809 (m), 773 (m), 756 (s), 738 (m), 726 (m), 715 (m), 684 (w), 664 (w), 632 (m), 597 (w), 552 (w), 533 (w).

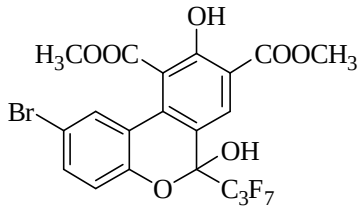
Dimethyl 2-chloro-6-(heptafluoropropyl)-6,9-dihydroxy-3-methyl-6*H*-benzo[*c*]-chromene-8,10-dicarboxylate (14s):



Starting with 6-chloro-3-(heptafluorobutanoyl)-7-methyl-chromone **5u** (0.391 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **14s** was isolated as a pale yellow solid (0.388 g, 71%), mp 207-208 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.35 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.17 (s, 1H, 4-H_{Ar}), 7.41 (s, 1H, 1-H_{Ar}), 8.12 (s, 1H, 7-H_{Ar}), 9.64 (d, $^4J_{H,F}$ = 4.2 Hz, 1H, 6-OH), 11.09 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.6 (CH_3), 53.0 (OCH_3), 53.2 (OCH_3), 97.8 (t, $^2J_{C,F}$ = 29.4 Hz, 6-C), 113.3, 116.9, 118.8, 120.0, 120.4, 124.5, 127.2, 130.9, 131.7, 140.5, 150.4, 158.5, 167.2, 167.7; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.0 (t, ^3J = 8.3 Hz, 3F, CF_3), –118.4 (dq, ^2J = 284.8, J = 9.0 Hz, 1F, CF_2), –120.8 (dq, ^2J = 284.8, J = 8.5 Hz, 1F, CF_2), –123.4 (d, ^2J = 289.8 Hz, 1F, CF_2), –124.2 (d, ^2J = 289.4 Hz, 1F, CF_2); MS (GC, 70 eV) *m/z* (%): 514 ([M-OCH_3-H], 21), 483 (14), 347 (32), 346 (18), 345 (100), 315 (29), 314 (14), 313 (81), 278 (16), 245 (9), 139 (10); HRMS (ESI): calcd for $C_{21}H_{14}{}^{35}ClF_7NaO_7$ ([M+Na]$^+$) 569.02085, found 569.02137, calcd for $C_{21}H_{14}{}^{37}ClF_7NaO_7$ ([M+Na]$^+$) 571.01888, found 571.01913; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3272 (w), 2956 (w), 2853 (w), 1707 (m), 1687 (m), 1652 (w), 1613 (m), 1589 (w), 1549 (w), 1496 (w), 1436 (m), 1395 (w), 1352 (m), 1336 (m), 1295 (m), 1259 (m), 1207 (s), 1169 (s), 1144 (s), 1120 (s), 1075 (m), 1018 (m), 988 (m), 949 (w), 920 (m), 885 (m), 856 (m), 825 (m), 801 (m), 777 (w), 769 (w), 744 (m), 720 (m), 704 (s), 692 (m), 665 (m), 645 (m), 595 (m), 561 (m), 554 (m), 535 (w).

Dimethyl 2-bromo-6-(heptafluoropropyl)-6,9-dihydroxy-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (14t):

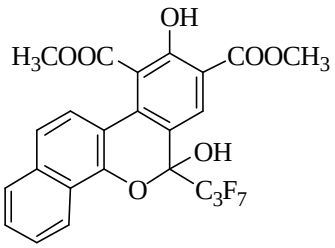


Starting with 6-bromo-3-(heptafluorobutanoyl)chromone **5v** (0.421 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **14t** was isolated as a white solid (0.323 g, 56%), mp 205-207ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.93 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 7.11 (d, ^3J = 8.7 Hz, 1H, 4-H_{Ar}), 7.55 (d, ^4J = 2.3 Hz, 1H, 1-H_{Ar}), 7.65 (dd, ^3J = 8.7, ^4J = 2.3 Hz, 1H, 3-H_{Ar}), 8.12

(d, $^{5}J_{H,F}$ = 1.4 Hz, 1H, 7-H_{Ar}), 9.69 (d, $^{4}J_{H,F}$ = 4.3 Hz, 1H, 6-OH), 11.10 (s, 1H, 9-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 53.0 (OCH_3), 53.2 (OCH_3), 97.6 (t, $^{2}J_{C,F}$ = 29.6 Hz, 6-C), 113.8, 114.4, 119.1, 119.8, 120.0, 120.7, 127.2, 130.9, 131.4, 134.8, 150.9, 158.5, 167.1, 167.5; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.0 (t, ^{3}J = 8.7 Hz, 3F, CF_3), –118.3, –120.7 (both dq, ^{2}J = 285.5 Hz, J = 8.7 Hz, 2F, CF_2), –123.5 (d, ^{2}J = 290.0 Hz, 1F, CF_2), –124.2 (d, ^{2}J = 289.7 Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 546 ([M-OCH_3-H], 15), 544 (14), 515 (10), 513 (10), 409 (42), 407 (42), 378 (14), 377 (100), 376 (15), 375 (99), 345 (28), 343 (28), 265 (10), 264 (61), 236 (9); HRMS (EI): calcd for $C_{20}H_{12}{}^{79}BrF_7O_7$ ([M]$^+$) 575.96491, found 575.96594, calcd for $C_{20}H_{12}{}^{81}BrF_7O_7$ ([M]$^+$) 577.96287, found 577.96435; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3341 (w), 2962 (w), 1715 (w), 1688 (w), 1617 (w), 1595 (w), 1562 (w), 1462 (w), 1440 (w), 1403 (w), 1333 (w), 1290 (w), 1258 (m), 1213 (m), 1191 (m), 1143 (m), 1118 (s), 1089 (s), 1055 (s), 994 (s), 397 (m), 878 (m), 839 (m), 800 (s), 731 (s), 709 (s), 657 (m), 628 (m), 599 (m), 534 (m).

Dimethyl 6-(heptafluoropropyl)-6,9-dihydroxy-6*H*-dibenzo[*c*,*h*]chromene-8,10-dicarboxylate (14u):

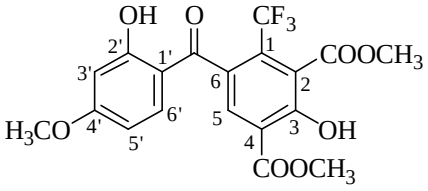


Starting with 3-(heptafluorobutanoyl)benzo[*h*]chromone **5w** (0.392 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **14u** was isolated as a pale yellow solid (0.389 g, 71%), mp 210-211ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.94 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 7.53 (d, ^{3}J = 8.9 Hz, 1H, H_{Ar}), 7.64-7.72 (m, 3H, H_{Ar}), 7.93-7.96 (m, 1H, H_{Ar}), 8.19-8.22 (m, 2H, H_{Ar}), 9.81 (s, 1H, 6-OH), 11.14 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.9 (OCH_3), 53.1 (OCH_3), 98.3 (t, $^{2}J_{C,F}$ = 29.2 Hz, 6-C), 112.3, 112.4, 118.9, 120.2, 120.9, 121.8, 122.5, 123.8, 127.0, 127.7, 128.5, 130.5, 133.6, 134.6, 147.9, 158.9, 167.3, 168.0; ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –80.2 (t, ^{3}J = 9.2 Hz, 3F, CF_3), –118.0 (dq, ^{2}J = 283.1 Hz, J = 8.8 Hz, 1F, CF_2), –121.5 (dq, ^{2}J = 288.1, J = 8.7 Hz, 1F, CF_2), –122.8 (d, ^{2}J = 289.0 Hz, 1F, CF_2), –124.0 (d, ^{2}J = 287.7 Hz, 1F, CF_2); MS (EI, 70 eV) *m/z* (%): 548 ([M]$^+$, 6), 516 (26), 378 (100), 347 (80), 315 (99), 288 (32), 260 (10), 231 (13), 175 (13), 88 (6); HRMS (ESI): calcd for $C_{24}H_{16}F_7O_7$ ([M+H]$^+$) 549.07788, found 549.07701; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3271 (w), 2953 (w), 1738 (w), 1704 (m), 1683 (m), 1634 (w), 1616 (w), 1591 (w), 1565 (w), 1539 (w), 1476 (w), 1444 (m), 1351 (m), 1333 (m), 1315 (w), 1252 (m), 1220 (s), 1152 (m), 1138 (m), 1119 (s), 1059 (w), 1040

(m), 1020 (w), 910 (m), 971 (m), 961 (w), 923 (w), 888 (m), 875 (m), 796 (s), 780 (w), 769 (w), 759 (w), 738 (s), 714 (m), 685 (m), 663 (w), 648 (w), 608 (m), 572 (m), 530 (m).

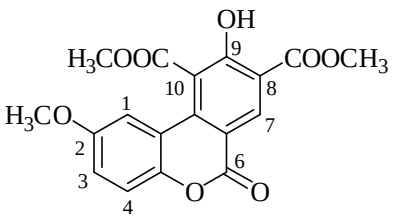
1,3-Dimethyl 2-hydroxy-5-(2-hydroxy-4-methoxybenzoyl)-4-(trifluoromethyl)-benzene-1,3-dicarboxylate (15):



Starting with 7-methoxy-3-(trifluoroacetyl)chromone **5b** (0.272 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **15** was isolated as a white solid (0.098 g, 23%), mp 147-148 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.83 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.49-6.53 (m, 2H, 3′,5′-H_{Ar}), 7.35 (d, ^{3}J = 9.1 Hz, 1H, 6′-H_{Ar}), 7.89 (s, 1H, 5-H_{Ar}), 11.12 (s, 1H, OH), 11.55 (s, 1H, OH); ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 53.1 (OCH_3), 53.2 (OCH_3), 55.9 (OCH_3), 101.1, 107.7, 114.2, 117.5, 122.4 (q, $^{1}J_{C,F}$ = 276.2 Hz, CF_3), 123.6 (m), 127.9 (q, $^{2}J_{C,F}$ = 32.1 Hz, 1-C), 129.4 (m), 130.8, 134.6, 156.6, 163.9, 164.6, 166.4, 166.7, 195.1 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –55.1 (s, 3F, CF_3); MS (GC 70 eV) *m/z* (%): 428 ($[M]^+$, 37), 397 (12), 359 (30), 328 (19), 327 (100), 296 (17), 295 (92), 151 (82), 150 (31); HRMS (EI): calcd for $C_{19}H_{15}F_3O_8$ ($[M]^+$) 428.07135, found 428.07183; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3229 (w), 3057 (w), 2991 (w), 2958 (w), 2852 (w), 1749 (m), 1707 (w), 1685 (m), 1607 (m), 1590 (m), 1508 (w), 1488 (w), 1459 (w), 1437 (m), 1403 (w), 1384 (w), 1360 (m), 1333 (m), 1306 (m), 1289 (m), 1255 (s), 1219 (s), 1194 (s), 1159 (s), 1149 (s), 1120 (s), 1028 (m), 1016 (m), 1000 (m), 962 (m), 947 (m), 941 (m), 922 (m), 899 (w), 874 (w), 835 (m), 820 (m), 806 (s), 793 (m), 779 (m), 751 (m), 719 (m), 709 (m), 690 (m), 681 (m), 651 (w), 609 (s), 598 (m), 564 (m), 533 (w).

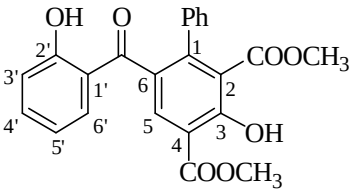
8,10-Dimethyl 9-hydroxy-2-methoxy-6-oxo-6*H*-benzo[*c*]chromene-8,10-dicarboxylate (16):



Starting with 6-methoxy-3-(pentafluoropropanoyl)chromone **5i** (0.322 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **16** was isolated as a white solid (0.118 g, 33%), mp 219-222 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 7.09-7.13 (m, 1H, 4-H_{Ar}), 7.27-7.31 (m, 2H, 1,3-H_{Ar}), 9.03 (s, 1H, 7-H_{Ar}), 11.74 (s, 1H, 9-OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 2^{x}53.2 (OCH_3), 55.8 (OCH_3), 108.7, 113.4, 113.9, 116.3, 118.6, 119.2, 119.5, 135.4, 137.0, 146.5, 156.1, 160.0, 162.8, 167.7, 169.2; MS (GC, 70 eV) *m/z* (%): 358 ([M^+], 100), 327 (18), 326 (51), 298 (10), 296 (10), 295 (57), 268 (28), 267 (14); HRMS (ESI): calcd for $C_{18}H_{13}O_8$ ([M-H]$^-$) 357.06159, found 357.06066; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3402 (w), 3049 (w), 3004 (w), 2959 (w), 2925 (w), 2849 (w), 1717 (s), 1673 (m), 1615 (w), 1570 (w), 1490 (w), 1471 (w), 1443 (m), 1424 (w), 1381 (w), 1342 (m), 1313 (m), 1294 (w), 1247 (m), 1207 (s), 1173 (s), 1144 (s), 1110 (m), 1068 (s), 1041 (s), 997 (s), 978 (m), 945 (m), 937 (m), 912 (s), 882 (m), 849 (m), 810 (s), 799 (s), 771 (s), 750 (m), 738 (m), 731 (s), 716 (m), 680 (m), 665 (m), 649 (m), 611 (m), 590 (w), 577 (w), 567 (w), 535 (w).

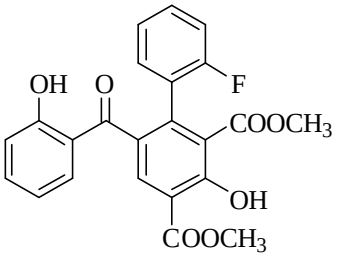
Dimethyl 3-hydroxy-6-(2-hydroxybenzoyl)[1,1'-biphenyl]-2,4-dicarboxylate (17a):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17a** was isolated as a white solid (0.199 g, 49%), mp 178-180 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.52 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.76-6.82 (m, 2H, H_{Ar}), 7.12-7.16 (m, 2H, H_{Ar}), 7.24-7.26 (m, 3H, H_{Ar}), 7.29 (dd, ^{3}J = 7.7 Hz, ^{4}J = 1.5 Hz, 1H, H_{Ar}), 7.37 (td, ^{3}J = 7.7 Hz, ^{4}J = 1.5 Hz, 1H, H_{Ar}), 7.95 (s, 1H, 5-H_{Ar}), 10.78 (s, 1H, OH), 11.11 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.1 (OCH_3), 53.0 (OCH_3), 112.1, 117.1, 119.0, 122.4, 124.8, 2^{x}127.9, 128.2, 2^{x}128.3, 130.7, 131.6, 132.0, 135.5, 136.3, 144.2, 157.5, 159.2, 165.8, 168.1, 197.9 (C=O); MS (GC, 70 eV) *m/z* (%): 406 ([$M]^+$, 38), 374 (67), 342 (13), 314 (27), 297 (100), 286 (16), 265 (28), 223 (14), 196 (17), 171 (13), 139 (13), 121 (52), 65 (10); HRMS (EI): calcd for $C_{23}H_{18}O_7$ ([$M]^+$) 406.10470, found 406.10499; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2923 (w), 2852 (w), 1733 (m), 1679 (w), 1625 (m), 1607 (w), 1582 (w), 1564 (w), 1486 (w), 1433 (m), 1348 (w), 1324 (w), 1293 (m), 1272 (w), 1260 (w), 1238 (m), 1198 (s), 1160 (s), 1147 (m), 1123 (m), 1111 (m), 1075 (w), 1034 (w), 1010 (w), 987 (m), 945 (w), 926 (w), 907 (w), 876 (w), 817 (w), 802 (w), 788 (w), 764 (s), 738 (m), 724 (m), 704 (s), 677 (m), 644 (s), 619 (m), 603 (w), 584 (m), 565 (w), 536 (m).

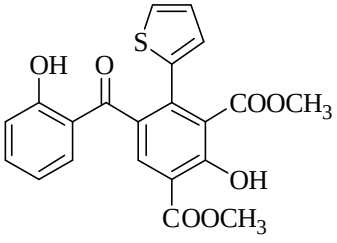
Dimethyl 2'-fluoro-3-hydroxy-6-(2-hydroxybenzoyl)[1,1'-biphenyl]-2,4-dicarboxylate (17b):



Starting with 3-(2-fluorobenzoyl)chromone **6b** (0.268 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17b** was isolated as a white solid (0.098 g, 23%), mp 170-173 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.59 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.76 (t, ^{3}J = 7.6 Hz, 1H, H_{Ar}), 6.89–6.96 (m, 2H, H_{Ar}), 7.06 (t, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 7.18-7.28 (m, 2H, H_{Ar}), 7.34-7.43 (m, 2H, H_{Ar}), 8.02 (s, 1H, 5-H_{Ar}), 11.50 (s, 2H, 2OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 52.4 (OCH_3), 53.0 (OCH_3), 111.8, 115.4 (d, $J_{C,F}$ = 21.5 Hz), 118.1, 118.8, 119.4, 123.9 (d, $J_{C,F}$ = 3.4 Hz), 124.0 (d, $J_{C,F}$ = 15.5 Hz), 125.4, 130.3, 130.7 (d, $J_{C,F}$ = 2.7 Hz), 130.8 (d, $J_{C,F}$ = 7.7 Hz), 131.4, 133.1, 136.6, 140.0, 158.9 (d, $^{1}J_{C,F}$ = 247.5 Hz, C_{Ar}F), 159.9, 162.8, 165.8, 169.4, 200.1 (C=O); ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –113.4 (s, 1F); MS (EI, 70eV) *m/z* (%): 392 (M-OCH_3-H], 100), 359 (50), 332 (16), 297 (19), 265 (37), 237 (18), 180 (12), 123 (53), 95 (13); HRMS (EI): calcd for $C_{23}H_{17}FO_7$ ([M]$^{+}$) 424.09528, found 424.09549; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3000 (w), 2946 (w), 2839 (w), 1711 (m), 1678 (s), 1602 (s), 1503 (w), 1480 (w), 1444 (s), 1351 (w), 1302 (m), 1274 (m), 1238 (s), 1198 (s), 1168 (s), 1115 (m), 1036 (w), 1005 (m), 968 (m), 942 (w), 913 (m), 884 (w), 858 (w), 814 (m), 793 (m), 765 (s), 742 (s), 686 (w), 665 (s), 641 (s), 568 (m).

Dimethyl 2-hydroxy-5-(2-hydroxybenzoyl)-4-(2-thienyl)isophthalate (17c):

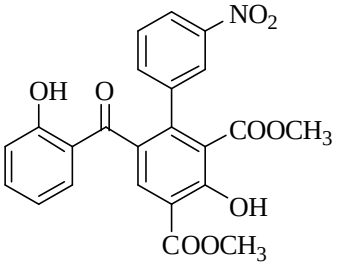


Starting with 3-(2-thenoyl)chromone **17c** (0.256 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17c** was isolated as a white solid (0.029 g, 7%), mp 205-207 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.69 (td, ^{3}J = 7.6 Hz, ^{4}J = 1.1 Hz, 1H, H_{Ar}), 6.84-6.91 (m, 2H, H_{Ar}), 6.97 (dd, ^{3}J = 3.6 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 7.18 (dd, ^{3}J = 8.0 Hz, ^{4}J = 1.6 Hz, 1H, H_{Ar}), 7.22-7.24 (m, 1H, H_{Ar}), 7.37 (td, ^{3}J = 7.8 Hz, ^{4}J = 1.6 Hz, 1H, H_{Ar}), 7.97 (s, 1H, 5-H_{Ar}), 11.38 (s, 1H, OH), 11.70 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 52.7 (OCH_3), 53.0 (OCH_3), 111.9, 118.1, 118.8, 119.8, 127.4, 128.3, 129.2, 129.4, 130.6, 130.8, 133.0, 136.3, 136.7, 137.7, 159.3, 162.6, 166.2, 169.4, 201.2 (C=O); MS (GC, 70 eV) *m/z* (%): 412 ([M]$^{+}$, 100), 380 (37), 362 (14), 348 (63), 330 (12), 320 (68), 292 (54), 260 (48), 229 (19), 202 (29), 174 (26), 145 (15), 121 (48), 93 (17), 65 (23);

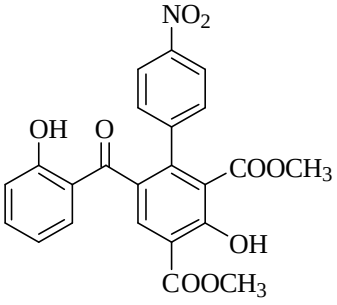
HRMS (EI): calcd for $C_{21}H_{16}O_7S$ ($[M]^+$) 412.06112, found 412.06127; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3110 (w), 2956 (w), 2923 (w), 2853 (w), 1732 (s), 1682 (m), 1622 (s), 1606 (s), 1568 (m), 1527 (w), 1505 (w), 1486 (w), 1433 (s), 1415 (m), 1353 (m), 1323 (m), 1294 (s), 1269 (m), 1237 (s), 1198 (s), 1159 (s), 1122 (m), 1100 (s), 1081 (m), 1045 (m), 1035 (m), 985 (s), 944 (s), 914 (m), 890 (w), 874 (m), 851 (m), 841 (w), 816 (m), 798 (s), 762 (s), 721 (s), 708 (s), 645 (s), 633 (s), 596 (m), 587 (m), 562 (m), 535 (m).

Dimethyl 3'-nitro-3-hydroxy-6-(2-hydroxybenzoyl)[1,1'-biphenyl]-2,4-dicarboxylate (17d):



Starting with 3-(3-nitrobenzoyl)chromone **6g** (0.295 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17d** was isolated as a yellow solid (0.374 g, 83%), mp 214-216 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.54 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.73-6.78 (m, 2H, H_{Ar}), 7.26-7.33 (m, 2H, H_{Ar}), 7.57-7.59 (m, 2H, H_{Ar}), 7.99 (s, 1H, H_{Ar}), 8.00 (s, 1H, H_{Ar}), 8.10-8.14 (m, 1H, H_{Ar}), 10.48 (s, 1H, OH), 11.17 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.3 (OCH_3), 53.1 (OCH_3), 113.2, 116.8, 119.1, 123.0, 123.1, 124.0, 124.9, 129.7, 131.1, 131.6, 131.9, 134.7, 135.1, 137.9, 141.8, 147.0, 157.7, 157.8, 165.6, 167.8, 196.9 (C=O); MS (GC, 70 eV) *m/z* (%): 451 ($[M]^+$, 24), 419 (56), 388 (10), 359 (18), 297 (100), 265 (38), 193 (16), 121 (57), 93 (10), 65 (12); HRMS (EI): calcd for $C_{23}H_{17}NO_9$ ($[M]^+$) 451.08978, found 451.09001; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3045 (w), 2965 (w), 2855 (w), 1726 (m), 1678 (m), 1622 (m), 1602 (m), 1573 (w), 1533 (m), 1487 (w), 1441 (m), 1408 (w), 1344 (m), 1296 (m), 1219 (s), 1164 (s), 1132 (m), 1081 (w), 991 (m), 930 (w), 882 (w), 843 (w), 806 (w), 765 (s), 752 (s), 735 (s), 694 (s), 637 (s), 597 (m), 563 (w), 534 (w).

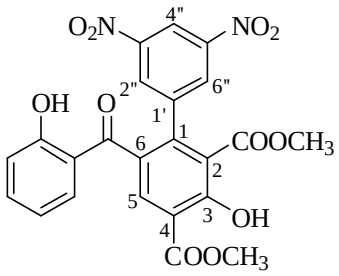
Dimethyl 4'-nitro-3-hydroxy-6-(2-hydroxybenzoyl)[1,1'-biphenyl]-2,4-dicarboxylate (17e):



Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17e** was isolated as a white solid (0.212 g, 47%), mp 185-187 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.54 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.79-6.83 (m, 2H, H_{Ar}), 7.31-7.41 (m, 2H, H_{Ar}), 7.42 (d, ^3J = 8.8 Hz, 2H, H_{Ar}), 7.99 (s, 1H, 5-H_{Ar}), 8.15 (d, ^3J = 8.8 Hz, 2H, H_{Ar}), 10.52 (s, 1H, OH),

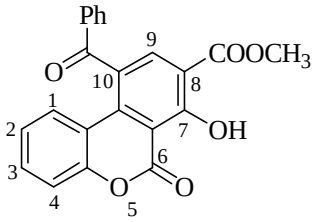
11.19 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.4 (OCH_3), 53.1 (OCH_3), 113.1, 117.0, 119.1, 123.0, 123.1, 123.5, 124.8, 129.9, 130.0, 131.4, 131.5, 131.6, 135.1, 142.3, 143.5, 147.0, 157.7, 158.2, 165.5, 167.8, 196.1 (C=O); MS (EI, 70 eV) *m/z* (%): 451 ([M]$^+$, 25), 419 (77), 388 (10), 359 (21), 297 (100), 265 (25), 241 (9), 121 (52); HRMS (EI): calcd for $C_{23}H_{17}NO_9$ ([M]$^+$) 451.08978, found 451.09051; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3089 (w), 3004 (w), 2950 (w), 2850 (w), 1745 (m), 1690 (m), 1622 (m), 1604 (m), 1572 (m), 1518 (m), 1482 (m), 1438 (m), 1347 (s), 1296 (m), 1266 (m), 1234 (m), 1208 (s), 1159 (s), 1147 (s), 1119 (m), 1106 (m), 1035 (w), 1001 (m), 949 (m), 931 (w), 917 (w), 877 (w), 864 (m), 854 (m), 845 (m), 799 (m), 767 (s), 740 (m), 713 (s), 698 (s), 664 (m), 642 (m), 623 (m), 599 (m), 562 (m), 534 (m).

Dimethyl 3',5'-dinitro-3-hydroxy-6-(2-hydroxybenzoyl)[1,1'-biphenyl]-2,4-dicarboxylate (17f):



Starting with 3-(3,5-dinitrobenzoyl)chromone **6j** (0.340 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **17f** was isolated as a yellow solid (0.347 g, 70%), mp 198-200 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.58 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.69-6.77 (m, 2H, H_{Ar}), 7.23-7.28 (m, 2H, H_{Ar}), 8.09 (s, 1H, 5-H_{Ar}), 8.38 (d, ^4J = 2.1 Hz, 2H, 2″,6″-H_{Ar}), 8.72 (t, ^4J = 2.1 Hz, 1H, 4″-H_{Ar}), 10.35 (s, 1H, OH), 11.27 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.6 (OCH_3), 53.1 (OCH_3), 114.1, 116.6, 118.3, 119.2, 124.9, 125.0, 2^{x}128.8, 130.6, 131.6, 132.4, 134.3, 139.5, 140.0, 2^{x}147.3, 156.8, 158.0, 165.4, 167.6, 194.8 (C=O); MS (GC, 70 eV) *m/z* (%): 496 ([M]$^+$, 28), 464 (65), 433 (11), 404 (22), 297 (100), 265 (48), 216 (13), 120 (66), 93 (11), 65 (12); HRMS (ESI): calcd for $C_{23}H_{17}N_2O_{11}$ ([M+H]$^+$) 497.08270, found 497.08200; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3090 (w), 2958 (w), 1732 (m), 1682 (m), 1651 (w), 1622 (m), 1593 (m), 1568 (m), 1538 (s), 1485 (m), 1442 (s), 1341 (s), 1298 (s), 1256 (m), 1209 (s), 1163 (s), 1116 (m), 1075 (m), 1033 (m), 997 (m), 957 (w), 938 (m), 922 (m), 908 (m), 878 (w), 855 (w), 839 (m), 804 (m), 761 (s), 728 (s), 707 (s), 680 (m), 650 (s), 609 (m), 565 (m), 530 (m).

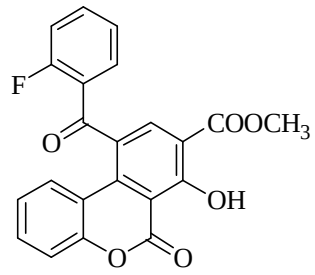
Methyl 10-benzoyl-7-hydroxy-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18a):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **18a** was isolated as a yellow solid (0.101 g, 27%), mp 144-146 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.84 (s, 3H, OCH_3), 7.12-7.18 (m, 1H, H_{Ar}), 7.50-7.59 (m, 5H, H_{Ar}), 7.64-7.70 (m, 1H, H_{Ar}), 7.85 (d, ^{3}J = 7.8 Hz, 2H, H_{Ar}), 8.08 (s, 1H, 9-H_{Ar}), 12.80 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.4 (OCH_3), 108.6, 116.1, 116.7, 117.8, 124.9, 126.4, 127.3, 129.1, 129.2, 129.9, 130.0, 132.3, 134.5, 135.9, 137.0, 137.8, 150.7, 162.4, 164.3, 164.4, 196.4 (C=O); MS (EI, 70 eV) *m/z* (%): 374 ([M]$^+$, 100), 343 (23), 297 (22), 265 (28), 183 (20), 105 (43), 77 (24); HRMS (EI): calcd for $C_{22}H_{14}O_6$ ([M]$^+$) 374.07849, found 374.07772; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2952 (w), 1693 (s), 1651 (m), 1639 (m), 1607 (w), 1593 (m), 1576 (w), 1556 (m), 1538 (w), 1519 (m), 1488 (w), 1441 (s), 1408 (w), 1352 (w), 1311 (m), 1279 (w), 1228 (s), 1178 (s), 1163 (s), 1144 (s), 1082 (m), 1008 (w), 978 (w), 939 (w), 923 (w), 849 (w), 823 (m), 783 (w), 758 (m), 734 (s), 720 (w), 698 (m), 673 (s), 647 (m), 633 (s), 567 (w), 551 (w).

Methyl 7-hydroxy-10-(2-fluorobenzoyl)-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18b):

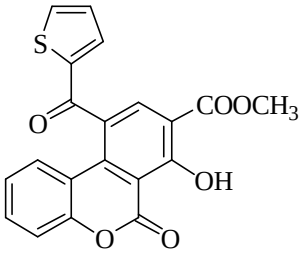


Starting with 3-(2-fluorobenzoyl)chromone **6b** (0.268 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **18b** was isolated as a white solid (0.180 g, 46%), mp 158-160 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.92 (s, 3H, OCH_3), 7.03-7.13 (m, 2H, H_{Ar}), 7.24-7.28 (m, 1H, H_{Ar}), 7.36 (dd, ^{3}J = 8.3 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 7.46 (td, ^{3}J = 7.3 Hz, ^{4}J = 1.3 Hz, 1H, H_{Ar}), 7.52-7.60 (m, 1H, H_{Ar}), 7.67 (dd, ^{3}J = 8.2 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 7.84 (td, ^{3}J = 7.6 Hz, ^{4}J = 1.8 Hz, 1H, H_{Ar}), 8.23 (s, 1H, 9-H_{Ar}), 13.05 (s, 1H, OH); ^{13}C NMR (62.9MHz, DMSO-d_6): δ = 52.6 (OCH_3), 108.2, 116.2, 116.4, 117.1 (d, $J_{C,F}$ = 21.5 Hz), 117.8, 124.8, 125.0 (d, $J_{C,F}$ = 8.8 Hz), 125.1 (d, $J_{C,F}$ = 3.2 Hz), 127.4, 127.9, 132.1, 132.5, 136.4 (d, $J_{C,F}$ = 9.4 Hz), 137.1 (d, $J_{C,F}$ = 1.1 Hz), 137.6, 151.0, 161.2 (d, $^{1}J_{C,F}$ = 257.0Hz, $C_{Ar}F$), 165.5, 164.1, 164.3, 192.7 (d, $^{3}J_{C,F}$ = 1.1 Hz, C=O); ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –109.0 (s, 1F); MS (GC, 70 eV) *m/z* (%): 392 ([M]$^+$, 100), 359 (40), 332 (13), 297 (15), 265 (36), 237 (22), 181 (13), 123 (68), 95 (35), 75 (18); HRMS (ESI): calcd for

$C_{22}H_{14}FO_6$ ([M+H]$^+$) 393.07689, found 393.07703, calcd for $C_{22}H_{13}FNaO_6$ ([M+Na]$^+$) 416.06222, found 416.06204; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3108 (w), 2923 (w), 2851 (w), 1712 (m), 1679 (s), 1602 (s), 1574 (m), 1504 (w), 1480 (w), 1444 (m), 1350 (w), 1302 (m), 1274 (m), 1259 (m), 1238 (s), 1221 (s), 1198 (s), 1185 (s), 1168 (s), 1152 (s), 1134 (m), 1101 (m), 1006 (s), 968 (m), 941 (w), 913 (m), 858 (m), 814 (s), 793 (s), 763 (s), 742 (s), 701 (m), 686 (m), 665 (s), 641 (m), 625 (m), 567 (m), 550 (m).

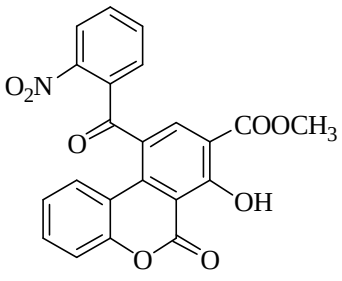
Methyl 7-hydroxy-10-(2-thenoyl)-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18c):



Starting with 3-(2-thenoyl)chromone **6c** (0.256 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **18c** was isolated as a yellow solid (0.239 g, 63%), mp 175-178 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.85 (s, 3H, OCH_3), 7.14-7.26 (m, 2H, H_{Ar}), 7.50-7.67 (m, 4H, H_{Ar}), 8.16-8.19 (m, 2H, H_{Ar}), 12.81 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.4 (OCH_3), 108.7, 116.1, 116.6, 117.8, 125.0, 126.1, 127.0, 129.3, 132.3, 136.7, 137.3, 137.8, 138.0, 143.1, 150.7, 162.4, 164.2, 164.4, 188.6 (C=O); MS (EI, 70 eV) *m/z* (%): 380 ([M]$^+$, 50), 347 (49), 315 (50), 292 (19), 265 (12), 237 (11), 181 (17), 131 (13), 111 (100), 83 (14), 69 (43), 57 (10), 44 (33); HRMS (EI): calcd for $C_{20}H_{12}O_6S$ ([M]$^+$) 380.03491, found 380.03487; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3107 (w), 2945 (w), 1712 (m), 1681 (m), 1651 (m), 1595 (m), 1516 (w), 1431 (m), 1409 (m), 1351 (w), 1308 (m), 1275 (m), 1250 (s), 1185 (s), 1132 (m), 1100 (m), 1056 (m), 991 (w), 971 (w), 944 (w), 920 (w), 889 (w), 852 (m), 815 (m), 794 (w), 761 (s), 738 (s), 671 (m), 649 (s), 627 (s), 564 (m).

Methyl 7-hydroxy-10-(2-nitrobenzoyl)-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18d):

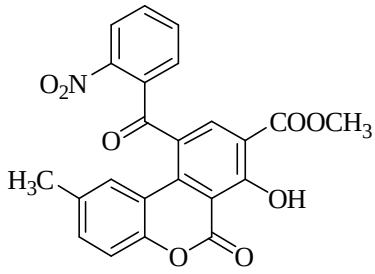


Starting with 3-(2-nitrobenzoyl)chromone **6d** (0.295 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **18d** was isolated as a white solid (0.302 g, 72%), mp 330-332 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3H, OCH_3), 7.23-7.28 (m, 1H, H_{Ar}), 7.41 (d, ^3J = 8.4 Hz, 1H, H_{Ar}), 7.53-7.58 (m, 2H, H_{Ar}), 7.66-7.76 (m, 2H, H_{Ar}), 8.01 (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1H, H_{Ar}), 8.20 (s, 1H, 9-H_{Ar}), 8.28 (dd, ^3J = 8.3 Hz, ^4J = 1.2 Hz, 1H, H_{Ar}), 13.31 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =

52.7 (OCH_3), 116.1, 116.2, 117.6, 124.8, 125.5, 129.5, 131.2, 132.9, 133.0, 133.3, 133.4, 134.9, 140.5, 141.1, 148.8, 151.2, 164.7, 164.9, 165.1, 165.6, 191.9 (C=O); MS (EI, 70 eV) *m/z* (%): 419 ($[M]^+$, 8), 388 (8), 285 (100), 265 (10), 253 (70), 225 (11), 134 (29), 104 (17); HRMS (EI): calcd for $C_{22}H_{13}NO_8$ ($[M]^+$) 419.06357, found 419.06374; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3032 (w), 2949 (w), 2824 (w), 1711 (s), 1678 (s), 1594 (m), 1541 (s), 1434 (m), 1366 (m), 1352 (w), 1307 (m), 1274 (m), 1245 (s), 1198 (s), 1167 (s), 1107 (m), 1006 (w), 973 (m), 950 (w), 914 (w), 852 (w), 815 (s), 775 (s), 743 (s), 711 (m), 669 (m), 638 (m), 584 (w), 569 (w).

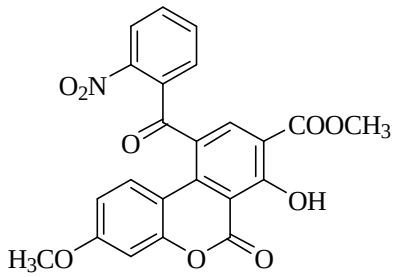
Methyl 7-hydroxy-2-methyl-10-(2-nitrobenzoyl)-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18e):



Starting with 6-methyl-3-(2-nitrobenzoyl)chromone **6e** (0.309 g, 1.0 mmol), dimethyl 1,3-acetonedicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **18e** was isolated as a yellow solid (0.364 g, 84%), mp 326-328 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.18 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 7.37-7.39 (m, 2H, H_{Ar}), 7.48-7.57 (m, 2H, H_{Ar}), 7.63 (s, 1H, 1-H_{Ar}), 7.77 (td, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 8.01 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 8.24 (s, 1H, 9-H_{Ar}), 13.00 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.9 (CH_3), 52.5 (OCH_3), 109.0, 115.6, 116.8, 117.2, 124.0, 124.5, 128.4, 130.5, 131.6, 132.7, 133.6, 134.1, 134.4, 138.9, 140.5, 148.8, 149.0, 163.7, 164.2, 164.4, 191.8 (C=O); MS (EI, 70 eV) *m/z* (%): 433 ($[M]^+$, 17), 402 (11), 299 (100), 267 (87), 239 (15), 134 (29), 104 (15), 44 (11); HRMS (ESI): calcd for $C_{23}H_{16}NO_8$ ($[M+H]^+$) 434.08704, found 434.08618; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 2951 (w), 1707 (m), 1672 (s), 1590 (m), 1550 (s), 1430 (m), 1403 (w), 1368 (m), 1350 (w), 1299 (m), 1273 (w), 1245 (s), 1183 (s), 1137 (m), 1111 (m), 1024 (w), 977 (w), 921 (m), 816 (s), 779 (s), 760 (s), 711 (m), 679 (m), 657 (m), 637 (s), 615 (m), 589 (m), 532 (m).

Methyl 7-hydroxy-3-methoxy-10-(2-nitrobenzoyl)-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (18f):



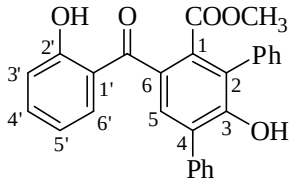
Starting with 7-methoxy-3-(2-nitrobenzoyl)chromone **6f** (0.325 g, 1.0 mmol), dimethyl 1,3-acetone-dicarboxylate **12** (0.16 mL, 1.1 mmol) and DBU (0.20 mL, 1,3 mmol) in 1,4-dioxane (6-7 mL), the product **18f** was isolated as a yellow solid (0.328 g, 73%), mp 370-372 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.81 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.80 (dd, ^3J = 9.1 Hz, ^4J = 2.6 Hz, 1H, H_{Ar}), 7.07 (d, ^4J = 2.5 Hz, 1H, H_{Ar}), 7.62-7.72 (m, 2H, H_{Ar}), 7.81-7.86 (m, 2H, H_{Ar}), 8.06-8.11 (m, 2H, H_{Ar}), 12.95 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 52.3 (OCH_3), 56.1 (OCH_3), 101.3, 108.8, 112.3, 115.1, 123.2, 124.7, 130.0, 131.3, 131.8, 132.0, 133.3, 134.0, 139.9, 140.2, 148.7, 152.6, 162.6, 164.1, 164.3, 164.6, 192.0 (C=O); MS (EI, 70 eV) *m/z* (%): 449 ($[M]^+$, 31), 419 (24), 386(18), 343 (10), 315 (100), 300 (19), 283 (94), 255 (33), 227 (10), 207 (12), 134 (30), 104 (20), 77 (11), 44 (65); HRMS (ESI): calcd for $C_{23}H_{16}NO_9$ ($[M+H]^+$) 450.08196, found 450.08216; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3035 (w), 2944 (w), 1716 (m), 1670 (m), 1593 (m), 1537 (s), 1433 (m), 1362 (m), 1321 (w), 1288 (m), 1241 (s), 1201 (s), 1162 (m), 1111 (m), 1027 (m), 989 (w), 948 (w), 918 (w), 841 (m), 804 (s), 742 (m), 710 (w), 692 (m), 650 (w), 618 (m), 580 (w), 546 (w).

General procedure for the synthesis of compounds 20 and 21:

To a stirred reaction mixture of the corresponding 3-acylchromone **4** or **6** (1.0 mmol) and 1,3-diphenylacetone **19** (1.1 mmol) in 1,4-dioxane (6-7 mL), DBU (1.3 mmol) was added slowly *via* a syringe at room temperature. Stirring at reflux was continued until chromone was consumed completely (followed by TLC, approximately 10-12 h). The reaction mixture was quenched with an aqueous solution of 10% NH_4Cl, extracted with chloroform and dried (Na_2SO_4). The solvent was distilled off under reduced pressure. The resulting residue was subjected to column chromatography on silica gel using heptane-ethylacetate (5:1) as eluent, slowly increasing the polarity up to 3:1 to give the isolated products.

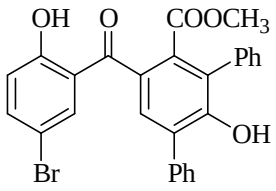
Methyl 3-hydroxy-6-(2-hydroxybenzoyl)-2,4-diphenylbenzoate (20a):



Starting with 3-methoxalylchromone **6a** (0.232 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20a** was isolated as a white solid (0.208 g, 49%), mp 180-182 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.34 (s, 3H, OCH_3), 6.91-7.00 (m, 2H, H_{Ar}), 7.29-7.53 (m, 13H, H_{Ar}), 9.22 (s, 1H, 3-OH), 11.64 (s, 1H, 2′-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 51.6 (OCH_3), 117.0, 119.1, 123.4, 127.6, 127.7, 2^{x}128.0, 2^{x}128.4, 2^{x}129.2, 129.6, 2^{x}130.0, 131.2, 132.8, 132.9, 134.1, 134.2, 134.6, 134.8, 137.1, 154.6, 157.9, 167.9, 196.3 (C=O); MS (GC, 70 eV) *m/z* (%): 424 ([M]$^+$, 10), 392 (100), 375 (18), 363 (36), 347 (13), 315 (54), 274 (7), 215 (19), 121 (11), 65 (7); HRMS (ESI): calcd for $C_{27}H_{21}O_5$ ([M+H]$^+$) 425.13835, found 425.13906; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3432 (w), 2952 (w), 1731 (s), 1628 (m), 1599 (w), 1579 (w), 1568 (w), 1487 (m), 1443 (w), 1430 (w), 1406 (m), 1353 (w), 1332 (w), 1312 (w), 1284 (m), 1268 (s), 1244 (s), 1217 (m), 1193 (m), 1172 (w), 1152 (m), 1132 (s), 1120 (m), 1082 (m), 1030 (m), 998 (m), 967 (m), 921 (w), 899 (w), 868 (w), 840 (m), 821 (w), 801 (w), 790 (w), 774 (m), 763 (s), 745 (s), 708 (m), 696 (s), 672 (m), 663 (m), 638 (w), 608 (m), 596 (m), 567 (m), 545 (m).

Methyl 3-hydroxy-6-(5-bromo-2-hydroxybenzoyl)-2,4-diphenylbenzoate (20b):

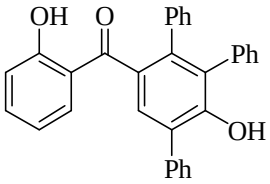


Starting with 6-bromo-3-methoxalylchromone **6f** (0.311 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20b** was isolated as a yellow solid (0.271 g, 54%), mp 256-258 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.37 (s, 3H, OCH_3), 6.93 (d, ^3J = 8.8 Hz, 1H, H_{Ar}), 7.28-7.31 (m, 2H, H_{Ar}), 7.36-7.57 (m, 11H, H_{Ar}), 9.30 (s, 1H, 3-OH), 10.52 (s, 1H, 2′-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 51.6 (OCH_3), 110.1, 119.0, 126.7, 127.1, 127.7, 127.8, 2^{x}128.0, 2^{x}128.5, 2^{x}129.1, 129.4, 129.9, 2^{x}130.0, 132.3, 133.6, 134.6, 134.8, 135.5, 137.1, 155.2, 155.6, 167.9, 193.2 (C=O); MS (EI, 70 eV) *m/z* (%): 502 ([M]$^+$, 7), 473 (28), 472 (100), 471 (43), 470 (96), 469 (13), 444 (11), 443 (25), 441 (15), 395 (18), 393 (19), 391 (15), 215 (24), 69 (17), 41 (10); HRMS (ESI): calcd for $C_{27}H_{20}{}^{79}BrO_5$ ([M+H]$^+$) 503.04886, found 503.04855, calcd for $C_{27}H_{20}{}^{81}BrO_5$ ([M+H]$^+$) 505.04724, found 505.04682; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3397 (w), 3025 (w), 2945 (w), 1743 (s), 1629 (m), 1600 (w), 1580 (w), 1568 (w), 1492 (w), 1464 (m), 1446 (w), 1431 (m), 1409 (m), 1352 (m), 1321 (w), 1288 (m), 1271 (m), 1251 (s), 1201 (s), 1173 (m), 1122

(s), 1089 (m), 1080 (m), 1028 (m), 1010 (m), 972 (m), 959 (w), 909 (m), 889 (w), 847 (w), 829 (m), 821 (m), 800 (m), 779 (m), 755 (m), 740 (m), 699 (s), 657 (m), 646 (w), 609 (s), 594 (m), 552 (m).

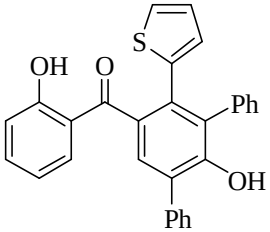
4-(2-Hydroxybenzoyl)-2,3,6-triphenylphenol (20c):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20c** was isolated as a yellow solid (0.141 g, 32%), mp 209-212 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.79-6.98 (m, 7H, H_{Ar}), 7.09-7.23 (m, 5H, H_{Ar}), 7.33-7.48 (m, 6H, H_{Ar}), 7.60-7.63 (m, 2H, H_{Ar}), 8.56 (s, 1H, 3-OH), 11.44 (s, 1H, 2′-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 117.2, 118.9, 126.4, 126.6, 2^{x}127.0, 127.3, 2^{x}127.5, 2^{x}128.3, 129.2, 2^{x}129.3, 2^{x}130.0, 131.1, 2^{x}131.2, 131.3, 133.2, 135.8, 135.9, 137.6, 138.4, 140.0, 152.6, 160.7, 201.9 (C=O); MS (GC, 70 eV) *m/z* (%): 442 ([M]$^{+}$, 63), 365 (50), 322 (100), 302 (14), 215 (12), 121 (19); HRMS (EI): calcd for $C_{31}H_{22}O_3$ ([M]$^{+}$) 442.15635, found 442.15625; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3467 (w), 3429 (w), 3053 (w), 3025 (w), 2918 (w), 2851 (w), 1714 (w), 1622 (m), 1601 (m), 1575 (w), 1557 (w), 1539 (w), 1532 (w), 1520 (w), 1514 (w), 1504 (w), 1495 (w), 1485 (w), 1471 (w), 1456 (w), 1446 (w), 1403 (w), 1342 (m), 1310 (w), 1274 (m), 1234 (m), 1211 (s), 1186 (m), 1155 (s), 1130 (m), 1107 (m), 1075 (m), 1064 (m), 1028 (m), 1001 (m), 966 (m), 924 (w), 897 (m), 866 (w), 852 (w), 835 (m), 820 (m), 801 (m), 783 (w), 748 (s), 697 (s), 669 (m), 638 (m), 630 (m), 618 (m), 594 (m), 568 (m), 541 (m).

4-(2-Hydroxybenzoyl)-2,6-diphenyl-3-(2-thienyl)phenol (20d):

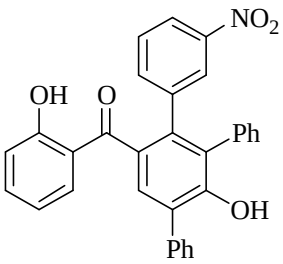


Starting with 3-(2-thenoyl)chromone **6c** (0.256 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20d** was isolated as a yellow solid (0.130 g, 29%), mp 207-210 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.56 (dd, ^{3}J = 3.5 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 6.63-6.66 (m, 1H, H_{Ar}), 6.78-6.87 (m, 2H, H_{Ar}), 7.16-7.21 (m, 3H, H_{Ar}), 7.22-7.30 (m, 3H, H_{Ar}), 7.34 (s, 1H, 5-H_{Ar}), 7.37-7.48 (m, 5H, H_{Ar}), 7.60-7.63 (m, 2H, H_{Ar}), 8.61 (s, 1H, 3-OH), 11.50 (s, 1H, 2′-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 117.2, 118.9, 120.9, 126.1, 127.1, 127.3, 127.4, 2^{x}127.7, 2^{x}128.3, 128.9, 129.0, 2^{x}129.2, 129.3, 2^{x}130.9, 131.7, 132.1, 132.2,

133.0, 135.8, 136.0, 137.4, 138.9, 152.6, 160.7, 201.9 (C=O); MS (GC, 70 eV) *m/z* (%): 448 ([M]$^+$, 100), 413 (14), 353 (16), 328 (96), 295 (15), 121 (18); HRMS (EI): calcd for $C_{29}H_{20}O_3S$ ([M]$^+$) 448.11277, found 448.11285; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3422 (w), 3055 (w), 3029 (w), 2961 (w), 2924 (w), 2853 (w), 1622 (m), 1579 (w), 1531 (w), 1483 (w), 1458 (w), 1445 (w), 1425 (w), 1398 (w), 1343 (m), 1308 (w), 1277 (m), 1266 (m), 1239 (w), 1219 (m), 1210 (m), 1192 (m), 1147 (m), 1101 (w), 1072 (w), 1039 (m), 1028 (w), 976 (w), 962 (w), 921 (w), 903 (w), 878 (w), 868 (w), 849 (w), 839 (w), 819 (w), 793 (w), 778 (w), 755 (s), 726 (m), 709 (m) , 698 (s), 666 (m), 635 (w), 621 (m), 608 (w), 596 (m), 573 (w), 531 (w).

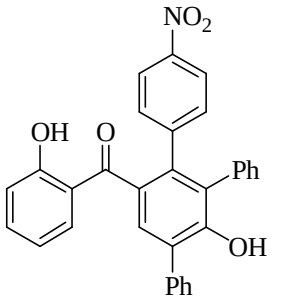
4-(2-Hydroxybenzoyl)-2,6-diphenyl-3-(3-nitrophenyl)phenol (20e):



Starting with 3-(3-nitrobenzoyl)chromone **6g** (0.295 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20e** was isolated as a white solid (0.205 g, 42%), mp 211-213 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.78-6.83 (m, 2H, H_{Ar}), 7.14-7.28 (m, 5H, H_{Ar}), 7.31-7.50 (m, 8H, H_{Ar}), 7.60-7.63 (m, 2H, H_{Ar}), 7.73 (s, 1H, 5-H_{Ar}), 7.82-7.86 (m, 1H, H_{Ar}), 8.81 (s, 1H, 3-OH), 10.92 (s, 1H, 2′-OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 117.0, 118.9, 121.2, 121.3, 122.7, 124.7, 127.0, 127.4, 127.7, 127.8, 128.3, 128.4, 128.6, 129.1, 129.2, 129.3, 130.3, 131.1, 131.2, 131.4, 132.3, 135.2, 135.3, 136.7, 137.4, 138.0, 140.5, 146.4, 153.2, 159.3, 199.9 (C=O); MS (EI, 70 eV) *m/z* (%): 487 ([M]$^+$, 90), 367 (100), 289 (10), 121 (50); HRMS (EI): calcd for $C_{31}H_{21}NO_5$ ([M]$^+$) 487.14142, found 487.14136; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3533 (w), 3502 (w), 1599 (w), 1529 (m), 1483 (m), 1443 (w), 1402 (w), 1348 (m), 1304 (w), 1278 (m), 1239 (m), 1214 (m), 1158 (m), 1129 (m), 1030 (w), 971 (w), 933 (w), 903 (w), 860 (w), 822 (w), 789 (w), 761 (m), 731 (m), 698 (s), 666 (m), 619 (m), 594 (w), 547 (w).531 (w).

4-(2-Hydroxybenzoyl)-2,6-diphenyl-3-(4-nitrophenyl)phenol (20f):

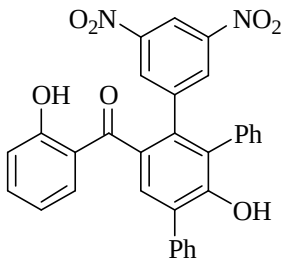


Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20f** was isolated as a yellow solid (0.336 g, 69%), mp 231-235 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.83-6.87 (m, 2H, H_{Ar}), 7.11-7.16 (m, 2H, H_{Ar}), 7.18-7.25 (m, 5H, H_{Ar}), 7.35-7.40 (m, 3H, H_{Ar}), 7.44-7.51

(m, 3H, H_{Ar}), 7.60-7.62 (m, 2H, H_{Ar}), 7.85-7.88 (m, 2H, H_{Ar}), 8.82 (s, 1H, 3-OH), 11.01 (s, 1H, 2′-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 117.2, 119.0, 122.0, 122.1, 122.4, 127.0, 127.4, 127.7, 127.8, 128.2, 128.4, 128.5, 129.0, 129.2, 129.3, 130.4, 131.0, 131.1, 131.2, 131.3, 131.4, 132.5, 135.3, 135.4, 137.4, 138.5, 145.7, 146.4, 153.2, 159.7, 199.9 (C=O); MS (GC, 70 eV) *m/z* (%): 487 ([M]$^+$, 63), 367 (100), 289 (16), 121 (51); HRMS (EI): calcd for $C_{31}H_{21}NO_5$ ([M]$^+$) 487.14142, found 487.14134; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3453 (w), 3077 (w), 2925 (w), 2849 (w), 1623 (w), 1597 (m), 1578 (w), 1515 (s), 1481 (w), 1446 (w), 1394 (w), 1339 (s), 1285 (m), 1240 (m), 1209 (s), 1156 (m), 1128 (m), 1106 (m), 1031 (m), 967 (m), 901 (w), 852 (m), 749 (s), 700 (s), 638 (w), 617 (m), 571 (w), 545 (w).

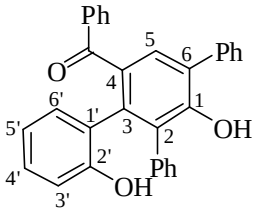
4-(2-Hydroxybenzoyl)-2,6-diphenyl-3-(3,5-dinitrophenyl)phenol (20g):



Starting with 3-(3,5-dinitrobenzoyl)chromone **6j** (0.340 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **20g** was isolated as a yellow solid (0.394 g, 74%), mp 100-102 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.74-6.81 (m, 2H, H_{Ar}), 7.13-7.31 (m, 6H, H_{Ar}), 7.36-7.41 (m, 2H, H_{Ar}), 7.45-7.50 (m, 3H, H_{Ar}), 7.55-7.61 (m, 2H, H_{Ar}), 8.14 (d, ^4J = 2.1 Hz, 2H, H_{Ar}), 8.48 (t, ^4J = 2.1 Hz, 1H, H_{Ar}), 9.04 (s, 1H, 3-OH), 10.53 (s, 1H, 2′-OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 116.4, 116.8, 116.9, 119.0, 119.1, 124.5, 127.3, 127.6, 128.0, 128.1, 128.4, 128.5, 129.2, 129.3, 129.7, 130.3, 130.4, 131.1, 131.2, 131.3, 131.4, 134.3, 134.8, 136.6, 137.3, 142.6, 146.6, 146.7, 153.8, 157.8, 197.9 (C=O); MS (EI, 70 eV) *m/z* (%): 532 ([M]$^+$, 62), 438 (10), 412 (81), 365 (84), 289 (19), 121 (100), 93 (11), 65 (11); HRMS (EI): calcd for $C_{31}H_{20}N_2O_7$ ([M]$^+$) 532.12650, found 532.12681; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3507 (w), 3086 (w), 2921 (w), 1622 (m), 1605 (w), 1579 (w), 1538 (s), 1481 (w), 1446 (w), 1401 (w), 1342 (s), 1313 (m), 1286 (m), 1212 (m), 1170 (m), 1154 (m), 1127 (m), 1075 (w), 1031 (w), 1001 (w), 979 (w), 952 (w), 908 (w), 867 (w), 848 (w), 832 (w), 758 (m), 725 (s), 699 (s), 670 (m), 618 (m), 595 (w), 567 (w), 530 (w).

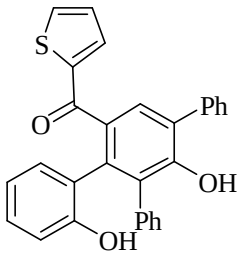
4-Benzoyl-2,6-diphenyl-3-(2-hydroxyphenyl)phenol (21a):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **21a** was isolated as a yellow solid (0.111 g, 25%), mp 145-148 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.35-6.45 (m, 2H, H_{Ar}), 6.67 (d, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 6.75 (td, ^{3}J = 7.2 Hz, ^{4}J = 1.5 Hz, 1H, H_{Ar}), 7.07-7.15 (m, 4H, H_{Ar}), 7.26 (s, 1H, 5-H_{Ar}), 7.34-7.50 (m, 7H, H_{Ar}), 7.60 (d, ^{3}J = 7.2 Hz, 2H, H_{Ar}), 7.70 (d, ^{3}J = 7.1 Hz, 2H, H_{Ar}), 8.39 (s, 1H, OH), 9.07 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 114.3, 117.5, 125.6, 126.4, 127.1, 127.2, 127.4, 127.6, 127.7, 2^{x}127.9, 2^{x}128.3, 128.9, 2^{x}129.2, 2^{x}129.5, 129.7, 130.6, 131.7, 131.8, 132.2, 132.3, 136.4, 137.7, 137.9, 138.0, 152.6, 154.1, 196.1 (C=O); MS (EI, 70 eV) *m/z* (%): 426 ([M-OH+H], 32), 425 (18), 424 (28), 423 (50), 350 (18), 349 (71), 138 (17), 105 (28), 96 (13), 95 (10), 83 (16), 82 (14), 81 (15), 77 (10), 71 (12), 70 (13), 69 (15), 67 (14), 57 (19), 56 (12), 55 (23), 45 (11), 43 (100), 41 (18); HRMS (EI): calcd for $C_{31}H_{22}O_3$ ([M]$^{+}$) 442.15635, found 442.15592; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3518 (w), 3508 (w), 3360 (w), 3057 (w), 3029 (w), 2920 (w), 2851 (w), 1732 (w), 1653 (m), 1634 (w), 1598 (w), 1575 (w), 1557 (w), 1539 (w), 1486 (w), 1462 (w), 1442 (m), 1397 (w), 1343 (w), 1319 (w), 1300 (w), 1286 (w), 1258 (m), 1220 (m), 1153 (m), 1108 (w), 1075 (w), 1049 (w), 1022 (w), 993 (m), 967 (m), 939 (w), 918 (w), 899 (m), 861 (w), 822 (w), 822 (w), 767 (m), 749 (s), 734 (s), 721 (m), 692 (s), 667 (m), 639 (m), 614 (m), 604 (m), 590 (m), 562 (w), 539 (w).

2,6-Diphenyl-3-(2-hydroxyphenyl)-4-(2-thenoyl)phenol (21b):

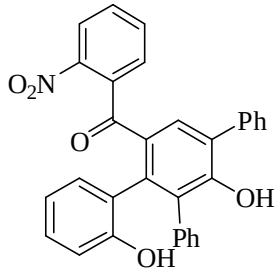


Starting with 3-(2-thenoyl)chromone **6c** (0.256 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **21b** was isolated as a yellow solid (0.081 g, 18%), mp 175-177 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.39-6.50 (m, 2H, H_{Ar}), 6.70 (d, ^{3}J = 7.4 Hz, 1H, H_{Ar}), 6.80 (t, ^{3}J = 7.6 Hz, 1H, H_{Ar}), 7.12-7.14 (m, 6H, H_{Ar}), 7.33-7.49 (m, 4H, H_{Ar}), 7.60-7.65 (m, 3H, H_{Ar}), 7.90 (dd, ^{3}J = 4.9 Hz, ^{4}J = 1.0 Hz, 1H, H_{Ar}), 8.40 (s, 1H, OH), 9.08 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 114.4, 117.6, 125.6, 126.4, 127.1, 127.2, 127.7, 127.8, 128.2, 2^{x}128.3, 2^{x}129.3, 129.5, 130.5, 130.6, 130.7, 131.6, 131.9, 132.0, 134.5, 135.1, 136.4, 137.7, 137.9, 144.4, 152.7, 154.2, 188.0 (C=O); MS (GC, 70 eV) *m/z* (%): 448 ([M]$^{+}$, 31),

111 (100), 39 (6); HRMS (ESI): calcd for $C_{29}H_{21}O_3S$ ($[M+H]^+$) 449.12059, found 449.12008; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3508 (w), 3390 (w), 3055 (w), 2922 (w), 2852 (w), 1622 (m), 1603 (w), 1580 (w), 1557 (w), 1539 (w), 1505 (w), 1495 (w), 1446 (w), 1435 (w), 1408 (m), 1353 (m), 1343 (m), 1318 (w), 1284 (m), 1259 (m), 1228 (m), 1150 (m), 1120 (w), 1099 (w), 1075 (w), 1063 (w), 1046 (w), 1028 (w), 1001 (w), 958 (w), 940 (w), 903 (w), 889 (w), 854 (w), 821 (w), 796 (w), 749 (s), 721 (s), 698 (s), 674 (m), 637 (w), 618 (m), 610 (m), 593 (s), 549 (w).

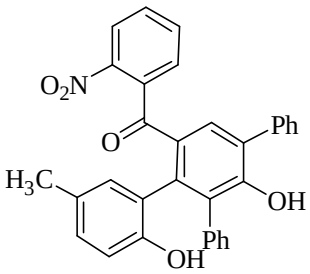
2,6-Diphenyl-3-(2-hydroxyphenyl)-4-(2-nitrobenzoyl)phenol (21c):



Starting with 3-(2-nitrobenzoyl)chromone **6d** (0.295 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **21c** was isolated as a yellow solid (0.287 g, 59%), mp 119-121 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.28-6.32 (m, 2H, H_{Ar}), 6.57 (dd, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1H, H_{Ar}), 6.67 (td, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 7.02-7.18 (m, 5H, H_{Ar}), 7.34-7.51 (m, 4H, H_{Ar}), 7.53-7.62 (m, 5H, H_{Ar}), 7.89 (dd, ^3J = 7.8 Hz, ^4J = 1.3 Hz, 1H, H_{Ar}), 8.72 (s, 1H, OH), 9.15 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 114.2, 117.7, 123.7, 123.8, 125.5, 126.6, 127.3, 127.4, 128.0, 128.2, 128.5, 129.1, 129.2, 129.3, 130.6, 130.7, 130.7, 130.8, 131.9, 132.4, 133.2, 133.3, 136.0, 136.4, 137.6, 139.9, 146.3, 154.1, 155.0, 170.4, 193.1 (C=O); MS (EI, 70 eV) *m/z* (%): 487 ($[M]^+$, 100), 470 (37), 455 (16), 438 (72), 365 (84), 337 (40), 319 (11), 289 (14), 44 (13); HRMS (ESI): calcd for $C_{31}H_{22}NO_5$ ($[M+H]^+$) 488.14925, found 488.15003; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3494 (w), 3058 (w), 1651 (w), 1606 (w), 1575 (w), 1553 (w), 1524 (m), 1445 (w), 1403 (w), 1344 (m), 1281 (m), 1217 (m), 1151 (m), 1123 (w), 1103 (w), 1028 (w), 966 (w), 902 (w), 855 (w), 825 (w), 788 (w), 748 (m), 699 (s), 609 (m), 547 (w).

2,6-Diphenyl-3-(2-hydroxy-5-methylphenyl)-4-(2-nitrobenzoyl)phenol (21d):

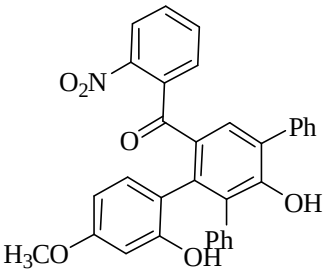


Starting with 6-methyl-3-(2-nitrobenzoyl)chromone **6e** (0.309 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **21d** was isolated as a yellow solid (0.366 g, 73%), mp 211-213 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.86 (s, 3H, CH_3), 6.15 (d, ^3J = 7.5 Hz, 1H, H_{Ar}), 6.33 (s, 1H, 6′-H_{Ar}), 6.44 (d, ^3J = 7.5 Hz, 1H, H_{Ar}), 6.91-7.10 (m, 5H, H_{Ar}), 7.36-7.39 (m, 2H, H_{Ar}), 7.45-7.59 (m, 6H, H_{Ar}), 7.65 (s, 1H, 5-H_{Ar}), 7.86 (d, ^3J = 7.6 Hz, 1H,

H_{Ar}), 8.71 (s, 1H, OH), 8.90 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.8 (CH_3), 114.0, 123.5, 125.0, 125.6, 126.6, 127.2, 127.3, 128.2, 2^{x}128.5, 128.6, 129.1, 2^{x}129.2, 130.3, 131.4, 131.7, 132.3, 133.2, 136.0, 136.5, 137.7, 140.0, 146.0, 151.9, 154.9, 193.3 (C=O); MS (EI, 70 eV) *m/z* (%): 501 ([M]$^+$, 49), 484 (12), 452 (33), 379 (20), 351 (21), 287 (72), 273 (100), 215 (33), 197 (96), 183 (68), 165 (12), 135 (72), 121 (55), 73 (56); HRMS (ESI): calcd for $C_{32}H_{24}NO_5$ ([M+H]$^+$) 502.16490, found 502.16558; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3509 (w), 3350 (w), 2920 (w), 1732 (w), 1651 (m), 1591 (w), 1556 (w), 1529 (s), 1443 (w), 1402 (w), 1341 (m), 1312 (m), 1257 (m), 1223 (s), 1149 (m), 1130 (m), 1061 (w), 1030 (m), 1001 (w), 968 (w), 911 (m), 887 (w), 857 (m), 819 (m), 774 (s), 742 (s), 697 (s), 667 (m), 610 (s), 591 (m), 566 (m).

2,6-Diphenyl-3-(2-hydroxy-4-methoxyphenyl)-4-(2-nitrobenzoyl)phenol (21e):



Starting with 7-methoxy-3-(2-nitrobenzoyl)chromone **6f** (0.325 g, 1.0 mmol), 1,3-diphenylacetone **19** (0.22 mL, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **21e** was isolated as a yellow solid (0.315 g, 61%), mp 198-200 ºC;

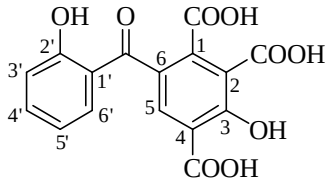
^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.50 (s, 3H, OCH_3), 5.82 (d, ^4J = 2.4 Hz, 1H, H_{Ar}), 5.89 (dd, ^3J = 8.4 Hz, ^4J = 2.4 Hz, 1H, H_{Ar}), 6.44 (d, ^3J = 8.4 Hz, 1H, H_{Ar}), 6.99-7.28 (m, 5H, H_{Ar}), 7.34-7.40 (m, 2H, H_{Ar}), 7.45-7.52 (m, 3H, H_{Ar}), 7.54-7.59 (m, 3H, H_{Ar}), 7.62 (s, 1H, 5-H_{Ar}), 7.88 (dd, ^3J = 7.9 Hz, ^4J = 1.3 Hz, 1H, H_{Ar}), 8.68 (s, 1H, OH), 9.19 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 54.6 (OCH_3), 100.1, 103.5, 118.2, 123.6, 126.5, 127.3, 127.4, 128.2, 128.4, 128.5, 129.1, 129.2, 129.6, 130.2, 130.3, 131.2, 131.3, 132.1, 132.3, 132.4, 133.2, 133.3, 136.2, 136.6, 137.7, 139.7, 146.0, 154.9, 155.0, 159.1, 193.4 (C=O); MS (EI, 70 eV) *m/z* (%): 517 ([M]$^+$, 100), 500 (25), 485 (10), 468 (40), 395 (74), 367 (25), 351 (10), 276 (8), 151 (8); HRMS (ESI): calcd for $C_{32}H_{24}NO_6$ ([M+H]$^+$) 518.15981, found 518.16061; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3480 (w), 2917 (w), 2849 (w), 1711 (w), 1674 (w), 1640 (m), 1615 (m), 1552 (w), 1525 (s), 1464 (w), 1440 (m), 1346 (m), 1292 (m), 1244 (s), 1197 (m), 1149 (s), 1099 (s), 1025 (m), 966 (m), 915 (m), 853 (m), 822 (m), 791 (m), 764 (m), 744 (m), 724 (m), 701 (s), 609 (s), 559 (m), 531 (m).

General procedure for the synthesis of compounds 22 and 23:

To a stirred reaction mixture of the corresponding compound **13** or **14** (1.0 mmol) in methanol (6-7 mL) potassium hydroxide (4.0 mmol) was added. Stirring at reflux was continued until the reagent was consumed completely (followed by TLC, approximately 2 days). The solvent was distilled off in a vacuum, and the resulting residue was quenched with water, then, neutralized with an aqueous solution of HCl (30%). The resulting residue was filtered and dried.

Some of protons in the low field of ^{1}H NMR spectra of compounds **22** and **23** could not be detected due to their fast exchange.

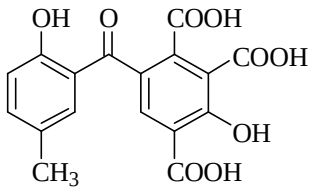
3-Hydroxy-6-(2-hydroxybenzoyl)-1,2,4-benzenetricarboxylic acid (22a):



Starting with trimethyl 3-hydroxy-6-(2-hydroxybenzoyl)-benzene-1,2,4-tricarboxylate **13a** (0.116 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **22a** was isolated as a white solid (0.083 g, 80%), mp 279-281 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.87-6.95 (m, 2H, H_{Ar}), 7.30 (d, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 7.42 (t, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 7.85 (s, 1H, 5-H_{Ar}); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 116.0, 116.4, 117.2, 118.8, 122.3, 124.5, 130.9, 133.7, 136.3, 144.5, 158.1, 167.0, 167.7, 169.6, 170.8, 196.8 (C=O); HRMS (ESI): calcd for $C_{16}H_9O_9$ ($[M-H]^-$) 345.02521, found 345.02546; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3401 (w), 1660 (w), 1643 (w), 1623 (m), 1588 (s), 1537 (w), 1485 (w), 1462 (w), 1446 (m), 1332 (m), 1291 (m), 1224 (s), 1157 (w), 1039 (w), 968 (w), 944 (w), 888 (w), 844 (w), 827 (m), 806 (w), 787 (w), 757 (s), 699 (m), 639 (s), 589 (m), 553 (m), 530 (w).

3-Hydroxy-6-(2-hydroxy-5-methylbenzoyl)-1,2,4-benzenetricarboxylic acid (22b):

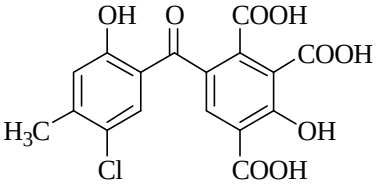


Starting with trimethyl 3-hydroxy-6-(2-hydroxy-5-methylbenzoyl)-benzene-1,2,4-tricarboxylate **13b** (0.121 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **22b** was isolated as a white solid (0.091 g, 84%), mp 298-300 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.21 (s, 3H, CH_3), 6.88 (d, ^{3}J = 8.4 Hz, 1H, 3′-H_{Ar}), 7.11 (s, 1H, 6′-H_{Ar}), 7.28 (dd, ^{3}J = 8.4 Hz, ^{4}J = 2.0 Hz, 1H, 4′-H_{Ar}), 7.93 (s, 1H, 5-H_{Ar}), 10.47 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.9 (CH_3), 115.4, 117.0, 119.1, 123.0, 124.4, 127.8, 131.0, 135.1, 135.6, 140.7, 156.2, 166.1, 167.1, 167.9, 168.5, 196.1 (C=O); MS (EI, 70 eV) *m/z* (%): 343 ([M-OH-H], 76), 342 (71), 297 (21), 280 (23), 279 (100), 270 (13), 252 (21), 224 (12),

135 (14), 134 (21), 77 (11), 44 (22); HRMS (ESI): calcd for $C_{17}H_{11}O_9$ ([M-H]$^-$) 359.04086, found 359.04120; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2858 (w), 1704 (w), 1681 (w), 1651 (w), 1644 (m), 1582 (m), 1519 (w), 1504 (w), 1434 (m), 1384 (w), 1334 (s), 1292 (s), 1222 (s), 1169 (m), 1037 (w), 974 (w), 880 (w), 822 (m), 793 (m), 745 (m), 700 (m), 672 (m), 640 (m), 582 (m), 534 (m).

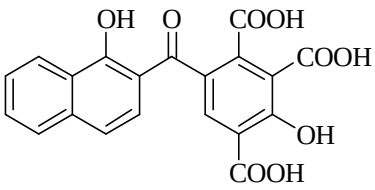
3-Hydroxy-6-(5-chloro-2-hydroxy-4-methylbenzoyl)-1,2,4-benzenetricarboxylic acid (22c):



Starting with trimethyl 6-(5-chloro-2-hydroxy-4-methylbenzoyl)-3-hydroxybenzene-1,2,4-tricarboxylate **13e** (0.131 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **22c** was isolated as a white solid (0.109 g, 92%), mp 362-364 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 6.96 (s, 1H, 3′-H_{Ar}), 7.33 (s, 1H, 6′-H_{Ar}), 7.91 (s, 1H, 5-H_{Ar}), 10.71 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.0 (CH_3), 114.7, 119.6, 122.3, 122.5, 123.3, 127.0, 130.7, 133.4, 138.6, 142.7, 157.1, 162.6, 166.1, 167.3, 169.8, 194.2 (C=O); MS (EI, 70 eV) *m/z* (%): 376 ([M-OH-H], 76), 331 (15), 313 (100), 286 (23), 258 (11), 168 (17), 139 (11), 77 (19); HRMS (ESI): calcd for $C_{17}H_{10}{}^{35}ClO_9$ ([M-H]$^-$) 393.00188, found 393.00275; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3490 (w), 2848 (w), 2521 (w), 1704 (m), 1688 (m), 1622 (m), 1599 (m), 1574 (m), 1476 (w), 1434 (w), 1392 (w), 1374 (w), 1334 (m), 1239 (s), 1212 (s), 1179 (s), 1160 (s), 1052 (m), 1009 (w), 952 (w), 884 (m), 826 (m), 816 (w), 803 (m), 792 (m), 747 (s), 722 (m), 709 (m), 686 (s), 635 (m), 619 (m), 596 (s).

3-Hydroxy-6-(1-hydroxy-2-naphthoyl)benzene-1,2,4-tricarboxylic acid (22d):

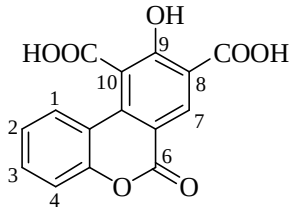


Starting with trimethyl 3-hydroxy-6-(1-hydroxy-2-naphthoyl)benzene-1,2,4-tricarboxylate **13g** (0.131 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **22d** was isolated as a yellow solid (0.106 g, 89%), mp 304-306 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.32-7.42 (m, 2H, H_{Ar}), 7.63 (t, ^3J = 7.2 Hz, 1H, H_{Ar}), 7.74 (t, ^3J = 7.1 Hz, 1H, H_{Ar}), 7.93 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.98 (s, 1H, 5-H_{Ar}), 8.38 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 13.37 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 113.5, 116.4, 117.4, 118.3, 122.1, 123.6, 124.4, 126.4, 127.0, 127.8, 130.4, 135.2, 136.8, 141.7, 161.4, 166.2, 167.6, 168.1, 169.7, 199.3 (C=O); MS (EI, 70 eV) *m/z* (%): 378 ([M-OH-H], 58), 360 (10), 315 (45), 288 (20),

260 (13), 217 (11), 170 (32), 144 (29), 115 (25), 97 (30), 78 (76), 69 (56), 63 (100), 43 (86); HRMS (ESI): calcd for $C_{20}H_{11}O_9$ ([M-H]$^-$) 395.04086, found 395.04184; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3391 (w), 2916 (w), 2590 (w), 1714 (w), 1651 (w), 1627 (w), 1584 (m), 1514 (m), 1504 (m), 1485 (w), 1455 (s), 1413 (m), 1384 (m), 1329 (m), 1271 (s), 1250 (s), 1210 (s), 1151 (m), 1108 (w), 1054 (w), 1023 (w), 991 (w), 946 (w), 876 (w), 829 (w), 778 (s), 742 (m), 717 (m), 685 (w), 660 (w), 640 (w), 612 (m), 601 (m), 575 (w), 557 (m).

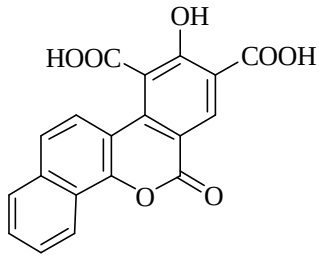
9-Hydroxy-6-oxo-6*H*-benzo[*c*]chromene-8,10-dicarboxylic acid (23a):



Starting with dimethyl 6,9-dihydroxy-6-(pentafluoroethyl)-6*H*-benzo[*c*]chromene-8,10-dicarboxylate **14d** (0.134 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **23a** was isolated as a white solid (0.063 g, 70%), mp 361 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37-7.44 (m, 2H, H_{Ar}), 7.61 (t, ^3J = 7.7 Hz, 1H, H_{Ar}), 8.13 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 8.68 (s, 1H, 7-H_{Ar}); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 109.9, 116.3, 116.9, 117.9, 120.5, 124.4, 125.1, 133.6, 131.7, 133.6, 151.4, 159.6, 166.1, 169.2, 169.6; MS (EI, 70 eV) *m/z* (%): 256 ([M-CO_2], 86), 239 (28), 238 (100), 211 (16), 210 (90), 182 (21), 154 (15), 126 (48), 119 (11), 91 (27), 78 (21), 63 (31), 44 (87); HRMS (ESI): calcd for $C_{15}H_7O_7$ ([M-H]$^-$) 299.01973, found 299.02026; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2849 (w), 1704 (m), 1682 (m), 1651 (m), 1594 (s), 1557 (m), 1495 (w), 1446 (w), 1417 (w), 1318 (m), 1286 (m), 1200 (s), 1148 (s), 1113 (s), 932 (m), 893 (m), 855 (m), 809 (m), 744 (s), 727 (s), 713 (s), 686 (s), 640 (s).

9-Hydroxy-6-oxo-6*H*-dibenzo[*c,h*]chromene-8,10-dicarboxylic acid (23b):



Starting with dimethyl 6-(heptafluoropropyl)-6,9-dihydroxy-6*H*-dibenzo[*c,h*]chromene-8,10-dicarboxylate **14u** (0.164 g, 0.3 mmol) and potassium hydroxide (0.134 g, 2.4 mmol) in methanol (2-3 mL), the product **23b** was isolated as a pale yellow solid (0.097 g, 92%), mp 310-312 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.70-7.73 (m, 2H, H_{Ar}), 7.87 (d, ^3J = 9.2 Hz, 1H, H_{Ar}), 7.99-8.02 (m, 1H, H_{Ar}), 8.12 (d, ^3J = 9.1 Hz, 1H, H_{Ar}), 8.39-8.42 (m, 1H, H_{Ar}), 8.76 (s, 1H, 7-H_{Ar}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 111.2, 112.1, 115.0, 120.5, 120.7, 122.0, 123.0, 124.0, 127.6, 127.7, 129.0, 133.8, 134.1, 135.2, 147.9, 159.2, 163.3, 168.6, 170.3; MS (EI, 70

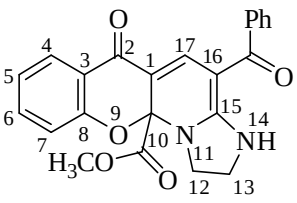
eV) *m/z* (%): 306 ([M-CO_2], 87), 288 (100), 260 (33), 232 (11), 204 (14), 176 (30), 144 (8), 116 (11), 88 (21), 63 (10), 44 (39); HRMS (ESI): calcd for $C_{19}H_9O_7$ ([M-H]$^-$) 349.03538, found 349.03602; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3418 (w), 2872 (w), 2538 (w), 1713 (s), 1699 (s), 1682 (s), 1668 (s), 1633 (m), 1587 (s), 1557 (m), 1505 (w), 1495 (w), 1477 (w), 1446 (s), 1424 (m), 1353 (m), 1336 (m), 1302 (m), 1257 (s), 1216 (s), 1195 (s), 1164 (s), 1145 (s), 1122 (s), 1034 (m), 1013 (m), 964 (m), 939 (m), 895 (m), 870 (w), 800 (s), 773 (s), 736 (s), 680 (s), 666 (s), 634 (s), 622 (s), 609 (s), 563 (s), 537 (m).

1.2.3 Supplement for Chapter 4

General procedure for the synthesis of compounds 25-30:

Reaction mixture of the corresponding 3-acylchromone **4-8** (1.0 mmol) and HKAs **24** (1.1 mmol) in 1,4-dioxane (6-7 mL) was stirred at room temperature. Stirring was continued until chromone was consumed completely (followed by TLC). The reaction time was dependent on solubility and activity of 3-acylchromones: the reaction time of 3-metoxalylchromones was about 2 days, for 3-aroylchromones about 1-7 days and for 3-polyhaloacylchromones about 10-12 h. Compounds **27** and **29** (synthesized starting from 3-heptafluorobutanoylchromones) were formed as a precipitate. They were filtered and washed with a mixture of ethyl acetate and heptane (1:3) to give pure products. The filtrates or reaction mixtures of other syntheses were distilled off under reduced pressure. The resulting residues were purified by column chromatography (silica gel, heptane/ethyl acetate) to isolate compounds **25**, **26**, **28** and **30**. Compounds **29** synthesized from 3-trifluoroacetylchromones were purified by column chromatography using ethyl acetate/methanol. In the case of synthesis of compounds **29a** and **29c** using 3-heptafluorobutanoylchromones, the reactions were carried out under reflux.

Methyl 16-benzoyl-2-oxo-9-oxa-11,14-diazatetracyclo[8.7.0.0^{3,8}.0^{11,15}]heptadeca-1(17),3(8),4,6,15-pentaene-10-carboxylate (25a):

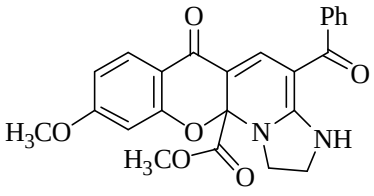


Starting with 3-methoxalylchromone **4a** (0.232 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25a** was isolated as a yellow solid (0.285 g, 71%), mp 207-208 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.65 (s, 3H, OCH_3), 3.82-4.10 (m,

4H, CH), 7.08-7.10 (m, 2H, H_{Ar}), 7.45-7.73 (m, 8H, H_{Ar}), 9.68 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 43.6 (NCH_2), 43.7 (NCH_2), 53.6 (OCH_3), 90.2 and 91.8 (10-C and 16-C), 105.8, 117.3, 121.8, 122.4, 126.4, 2^{x}127.6, 2^{x}128.4, 130.2, 135.4, 138.2, 139.7, 155.5, 158.4, 167.2, 175.8, 189.6 (C=O); MS (EI, 70 eV) *m/z* (%): 402 ([M]$^+$, 3), 401 (6), 345 (55), 344 (92), 343 (100), 342 (12), 341 (29), 315 (12), 314 (10), 313 (15), 265 (17), 171 (13), 105 (20), 77 (26); HRMS (ESI): calcd for $C_{23}H_{19}N_2O_5$ ([M+H]$^+$) 403.12885, found 403.12894, calcd for $C_{23}H_{18}NaN_2O_5$ ([M+Na]$^+$) 425.11079, found 425.11082; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3345 (w), 3308 (w), 3061 (w), 2963 (w), 2902 (w), 1731 (w), 1644 (w), 1604 (w), 1578 (m), 1548 (s), 1476 (m), 1461 (s), 1443 (s), 1376 (w), 1321 (s), 1286 (m), 1244 (m), 1194 (s), 1134 (m), 1101 (m), 1088 (m), 1074 (m), 997 (s), 952 (m), 926 (w), 838 (w), 820 (w), 800 (w), 782 (m), 744 (s), 705 (s), 660 (m), 626 (s), 584 (m), 561 (m), 528 (m).

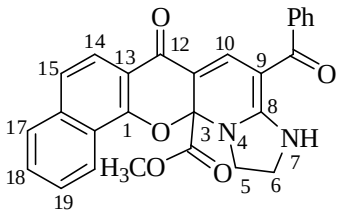
Methyl 16-benzoyl-6-methoxy-2-oxo-9-oxa-11,14-diazatetracyclo[8.7.0.0^{3,8}.0^{11,15}]heptadeca-1(17),3(8),4,6,15-pentaene-10-carboxylate (25b):



Starting with 7-methoxy-3-methoxalylchromone **4c** (0.262 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25b** was isolated as a yellow solid (0.311 g, 72%), mp 240-241 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.89-4.25 (m, 4H, CH), 6.48 (d, ^4J = 2.1 Hz, 1H, H_{Ar}), 6.62 (dd, ^4J = 2.1 Hz, ^3J = 8.8 Hz, 1H, H_{Ar}), 7.42-7.54 (m, 5H, H_{Ar}), 7.85-7.88 (m, 2H, H_{Ar}), 9.50 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 43.3 (NCH_2), 44.0 (NCH_2), 53.4 (OCH_3), 55.6 (OCH_3), 90.6 and 91.9 (10-C and 16-C), 100.8, 107.5, 110.1, 115.9, 2^{x}128.1, 2^{x}128.3, 129.0, 130.4, 137.8, 139.3, 157.7, 160.1, 165.6, 167.3, 176.8, 191.6 (C=O); MS (EI, 70 eV) *m/z* (%): 432 ([M]$^+$, 2), 431 (4), 376 (11), 375 (61), 374 (52), 373 (100), 186 (7); HRMS (ESI): calcd for $C_{24}H_{21}N_2O_6$ ([M+H]$^+$) 433.13941, found 433.13959, calcd for $C_{24}H_{20}NaN_2O_6$ ([M+Na]$^+$) 455.12136, found 455.12152; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3295 (w), 3053 (w), 2949 (w), 2888 (w), 2848 (w), 1741 (m), 1629 (w), 1606 (m), 1575 (m), 1546 (s), 1500 (w), 1482 (m), 1441 (s), 1428 (s), 1381 (m), 1316 (s), 1243 (s), 1212 (s), 1163 (s), 1127 (m), 1106 (s), 1019 (s), 1005 (s), 979 (s), 959 (m), 933 (m), 885 (w), 871 (w), 837 (s), 813 (w), 787 (m). 756 (s), 710 (m), 663 (s), 627 (s), 593 (s), 543 (m).

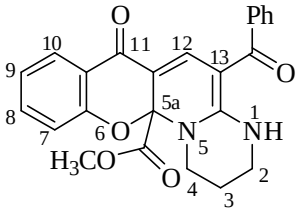
Methyl 9-benzoyl-12-oxo-2-oxa-4,7-diazapentacyclo[11.8.0.0^{3,11}.0^{4,8}.0^{16,21}]henicosa-1(13),8,10,14,16(21),17,19-heptaene-3-carboxylate (25c):



Starting with 3-methoxalylbenzo[*h*]chromone **4g** (0.282 g, 1.0 mmol)and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25c** was isolated as a yellow solid (0.348 g, 77%), mp 244-246 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.63 (s, 3H, OCH_3), 3.70-3.77 (m, 1H, CH), 3.88-4.03 (m, 2H, CH), 4.40-4.42 (m, 1H, CH), 7.48-7.75 (m, 10H, H_{Ar}), 7.95 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 8.37 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 9.73 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 43.6 (NCH_2), 43.7 (NCH_2), 53.7 (OCH_3), 91.0 and 91.6 (3-C and 9-C), 105.8, 116.6, 121.6, 121.9, 123.0, 123.8, 126.7, 2^{x}127.6, 127.9, 2^{x}128.4, 129.5, 130.2, 136.7, 137.7, 139.8, 152.8, 158.3, 166.9, 175.9, 189.6 (C=O); MS (EI, 70 eV) *m/z* (%): 452 ([M]$^+$, 18), 395 (59), 394 (100), 393 (59), 391 (18), 315 (11), 196 (29), 105 (17), 77 (21); HRMS (ESI): calcd for $C_{27}H_{21}N_2O_5$ ([M+H]$^+$) 453.14450, found 453.14454, calcd for $C_{27}H_{20}NaN_2O_5$ ([M+Na]$^+$) 475.12636, found 475.12644; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3578 (w), 3311 (w), 3055 (w), 2955 (w), 2905 (w), 2852 (w), 1738 (m), 1626 (m), 1596 (w), 1572 (w), 1543 (s), 1506 (m), 1482 (m), 1468 (s), 1426 (s), 1378 (m), 1350 (w), 1324 (m), 1288 (w), 1269 (s), 1236 (s), 1221 (s), 1200 (m), 1187 (s), 1133 (s), 1094 (s), 1071 (m), 1036 (m), 1017 (s), 971 (m), 957 (m), 926 (m), 871 (w), 843 (w), 828 (m), 811 (m), 799 (m), 792 (m), 769 (s), 746 (s), 729 (m), 702 (s), 681 (m), 665 (s), 650 (s), 632 (s), 601 (m), 579 (m), 548 (m).

Methyl 13-benzoyl-11-oxo-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphene-5a-carboxylate (25d):

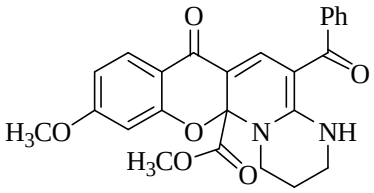


Starting with 3-methoxalylchromone **4a** (0.232 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25d** was isolated as a green-brown solid (0.379 g, 91%), mp 253-255 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.81-1.95 (m, 1H, CH), 2.07-2.16 (m, 1H, CH), 3.41-3.52 (m, 2H, CH), 3.59-3.65 (m, 1H, CH), 3.67 (s, 3H, OCH_3), 3.78-3.87 (m, 1H, CH), 7.07-7.12 (m, 2H, H_{Ar}), 7.39-7.42 (m, 2H, H_{Ar}), 7.46-7.59 (m, 5H, H_{Ar}), 7.70 (dd, ^4J = 1.6 Hz, ^3J = 7.9 Hz, 1H, H_{Ar}), 11.69 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.6 (CH_2), 38.4 (NCH_2), 41.4 (NCH_2), 53.7 (OCH_3), 91.1 and 93.2 (5a-C and 13-C), 104.1, 117.2, 121.6, 122.3, 126.1, 2^{x}127.7, 2^{x}128.3, 129.9, 135.3, 138.3, 140.3, 154.6, 155.6, 167.7, 175.7,

191.1 (C=O); MS (EI, 70 eV) *m/z* (%): 359 ([M-$COOCH_3$+2H], 31), 358 (62), 357 (100), 329 (34), 178 (13), 105 (12), 91 (40), 77 (14); HRMS (ESI): calcd for $C_{24}H_{21}N_2O_5$ ($[M+H]^+$) 417.14450, found 417.14448, calcd for $C_{24}H_{20}NaN_2O_5$ ($[M+Na]^+$) 439.12644, found 439.12618; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3021 (w), 2959 (w), 2940 (w), 1738 (w), 1643 (w), 1607 (m), 1581 (m), 1564 (s), 1480 (m), 1458 (s), 1441 (s), 1382 (w), 1365 (m), 1333 (m), 1304 (w), 1290 (m), 1274 (s), 1243 (s), 1219 (s), 1204 (m), 1173 (m), 1143 (m), 1103 (m), 1081 (m), 1058 (w), 1027 (m), 1004 (m), 951 (w), 920 (w), 887 (w), 873 (w), 829 (w), 801 (w), 777 (m), 752 (s), 742 (s), 698 (m), 682 (m), 675 (m), 629 (s), 601 (m), 575 (w), 554 (w), 528 (w).

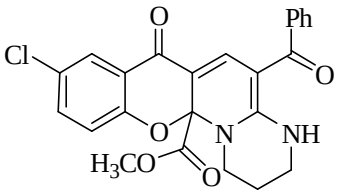
Methyl 13-benzoyl-8-methoxy-11-oxo-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphene-5a-carboxylate (25e):



Starting with 7-methoxy-3-methoxalylchromone **4c** (0.262 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25e** was isolated as a yellow solid (0.392 g, 88%), mp 250-251 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.85-1.98 (m, 1H, CH), 2.06-2.15 (m, 1H, CH), 3.42-3.55 (m, 2H, CH), 3.58-3.65 (m, 1H, CH), 3.68 (s, 3H, OCH_3), 3.78-3.88 (m, 1H, CH), 3.83 (s, 3H, OCH_3), 6.62 (d, ^4J = 2.3 Hz, 1H, H_{Ar}), 6.67 (dd, ^3J = 8.7 Hz, ^4J = 2.4 Hz, 1H, H_{Ar}), 7.37-7.40 (m, 2H, H_{Ar}), 7.45-7.52 (m, 4H, H_{Ar}), 7.62 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 11.73 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 18.7 (CH_2), 38.3 (NCH_2), 41.4 (NCH_2), 53.7 (OCH_3), 55.8 (OCH_3), 91.3 and 92.7 (5a-C and 13-C), 100.9, 104.3, 110.1, 115.2, 2^{x}127.6, 127.9, 2^{x}128.2, 129.8, 137.3, 140.4, 154.6, 157.6, 165.0, 167.6, 175.0, 190.8 (C=O); MS (EI, 70 eV) *m/z* (%): 388 ([M-$COOCH_3$+H], 56), 387 (100), 359 (15), 193 (9), 105 (7), 91 (20); HRMS (EI): calcd for $C_{25}H_{22}N_2O_6$ ($[M]^+$) 446.14724, found 446.14589; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2978 (w), 2946 (w), 1742 (m), 1641 (w), 1605 (s), 1584 (m), 1559 (s), 1498 (w), 1476 (s), 1459 (m), 1426 (s), 1381 (m), 1364 (m), 1347 (m), 1325 (m), 1293 (w), 1283 (w), 1238 (s), 1217 (s), 1196 (m), 1175 (m), 1162 (s), 1140 (s), 1101 (s), 1078 (m), 1058 (m), 1014 (s), 990 (m), 965 (s), 930 (m), 903 (w), 883 (w), 874 (w), 864 (w), 839 (s), 811 (m), 800 (s), 785 (s), 767 (s), 748 (s), 706 (s), 679 (m), 661 (s), 646 (s), 639 (m), 627 (s), 596 (s), 561 (m), 550 (m).

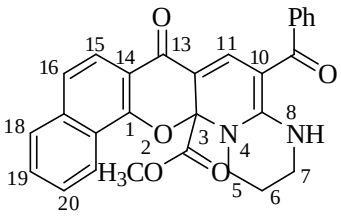
Methyl 13-benzoyl-9-chloro-11-oxo-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphene-5a-carboxylate (25f):



Starting with 6-chloro-3-methoxalylchromone **4d** (0.266 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25f** was isolated as a yellow solid (0.347 g, 77%), mp 254-255 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.85-1.94 (m, 1H, CH), 2.07-2.15 (m, 1H, CH), 3.41-3.54 (m, 2H, CH), 3.62-3.66 (m, 1H, CH), 3.68 (s, 3H, OCH_3), 3.76-3.85 (m, 1H, CH), 7.15 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.38-7.42 (m, 2H, H_{Ar}), 7.46-7.53 (m, 3H, H_{Ar}), 7.57-7.61 (m, 3H, H_{Ar}), 11.64 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.5 (CH_2), 38.4 (NCH_2), 41.6 (NCH_2), 53.8 (OCH_3), 91.4 and 93.7 (5a-C and 13-C), 103.1, 119.5, 122.8, 125.1, 126.4, 2^{x}127.8, 2^{x}128.3, 130.1, 134.7, 139.1, 140.1, 154.3, 154.5, 167.5, 174.3, 191.4 (C=O); MS (EI, 70 eV) *m/z* (%): 391 ([M-$COOCH_3$], 100), 363 (17), 105 (5), 91 (19), 77 (5); HRMS (ESI): calcd for $C_{24}H_{20}{}^{35}ClN_2O_5$ ([M+H]$^+$) 451.10553, found 451.10509, calcd for $C_{24}H_{20}{}^{37}ClN_2O_5$ ([M+H]$^+$) 453.10368, found 453.10405; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 2909 (w), 2847 (w), 2749 (w), 2675 (w), 1740 (w), 1644 (w), 1614 (m), 1600 (m), 1580 (m), 1568 (m), 1557 (m), 1539 (w), 1520 (w), 1505 (w), 1480 (m), 1464 (s), 1442 (s), 1428 (s), 1386 (w), 1364 (m), 1327 (w), 1296 (w), 1249 (s), 1219 (s), 1185 (m), 1145 (m), 1117 (s), 1096 (s), 1078 (m), 1058 (s), 1045 (s), 1008 (s), 976 (m), 955 (m), 913 (w), 901 (w), 886 (w), 872 (s), 825 (m), 800 (m), 772 (m), 749 (w), 733 (m), 700 (m), 684 (w), 661 (w), 629 (s), 609 (s), 572 (w), 541 (w).

Methyl 10-benzoyl-13-oxo-2-oxa-4,8-diazapentacyclo[12.8.0.0^{3,12}.0^{4,9}.0^{17,22}]docosa-1(14),9,11,15,17(22),18,20-heptaene-3-carboxylate (25g):

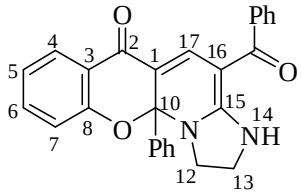


Starting with 3-methoxalylbenzo[*h*]chromone **4g** (0.282 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **25g** was isolated as a yellow-brawn solid (0.438 g, 94%), mp 282-284 ºC;

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.06-2.19 (m, 1H, CH), 2.23-2.32 (m, 1H, CH), 3.45-3.56 (m, 1H, CH), 3.64 (s, 4H, OCH_3, CH), 3.78-3.88 (m, 1H, CH), 3.99-4.10 (m, 1H, CH), 7.40-7.62 (m, 8H, H_{Ar}), 7.80 (d, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.90-7.93 (m, 2H, H_{Ar}), 8.24 (d, ^3J = 7.9 Hz, 1H, H_{Ar}), 12.21 (s, 1H, NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.4 (CH_2), 38.6 (NCH_2), 41.6 (NCH_2), 53.5 (OCH_3), 92.3 and 93.8 (3-C and 10-C), 104.9, 117.0, 122.0, 122.1, 122.7, 124.2, 126.1,

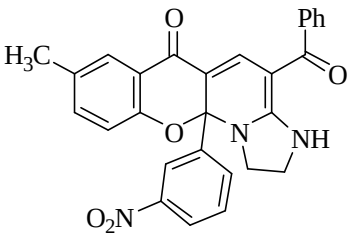
128.0, 128.2, 2x128.3, 128.9, 130.0, 130.1, 137.2, 138.9, 140.1, 153.1, 155.4, 167.8, 177.3, 192.6 (C=O); MS (EI, 70 eV) *m/z* (%): 466 ([M]$^+$, 10), 408 (84), 379 (86), 349 (47), 301 (14), 274 (13), 246 (15), 189 (34), 175 (11), 127 (13), 114 (48), 105 (85), 91 (100), 77 (91), 59 (23), 51 (17); HRMS (EI): calcd for $C_{28}H_{22}N_2O_5$ ([M]$^+$) 466.15232, found 466.15166; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2951 (w), 2922 (w), 2853 (w), 1747 (m), 1641 (w), 1615 (m), 1574 (s), 1557 (s), 1539 (m), 1506 (w), 1489 (m), 1479 (s), 1430 (s), 1417 (m), 1398 (m), 1381 (m), 1368 (m), 1346 (m), 1323 (m), 1297 (m), 1256 (s), 1240 (s), 1230 (s), 1208 (m), 1189 (m), 1175 (m), 1148 (m), 1140 (m), 1111 (m), 1093 (m), 1062 (m), 1045 (m), 1024 (m), 1007 (s), 984 (m), 954 (m), 921 (w), 899 (w), 868 (w), 837 (w), 820 (w), 802 (s), 787 (m), 776 (m), 766 (s), 747 (s), 718 (m), 700 (s), 686 (m), 657 (s), 638 (s), 605 (m), 574 (s).

16-Benzoyl-10-phenyl-9-oxa-11,14-diazatetracyclo[8.7.0.0^{3,8}.0^{11,15}]heptadeca-1(17),3(8),4,6,15-pentaen-2-one (26a):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26a** was isolated as a yellow solid (0.059 g, 14%), mp 284-286 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.23-3.33 (m, 1H, CH), 3.65-3.83 (m, 2H, CH), 4.04-4.16 (m, 1H, CH), 6.88 (td, ^4J = 0.9 Hz, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.00 (d, ^3J = 7.7 Hz, 1H, H_{Ar}), 7.17-7.25 (m, 3H, H_{Ar}), 7.31-7.41 (m, 6H, H_{Ar}), 7.51-7.54 (m, 2H, H_{Ar}), 7.71 (dd, ^4J = 1.6 Hz, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.98 (s, 1H, 17-H), 9.28 (s, 1H, NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 42.5 (NCH_2), 42.7 (NCH_2), 91.4 and 91.7 (10-C and 16-C), 112.6, 117.4, 122.1, 123.2, 2x126.9, 127.5, 2x128.1, 2x128.4, 2x128.6, 129.0, 130.3, 135.2, 136.6, 138.5, 139.6, 155.4, 158.9, 179.4, 191.5 (C=O); MS (EI, 70 eV) *m/z* (%): 420 ([M]$^+$, 76), 391 (56), 343 (100), 315 (32), 77 (10); HRMS (ESI): calcd for $C_{27}H_{21}N_2O_5$ ([M+H]$^+$) 421.15467, found 421.15482; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3272 (w), 3060 (w), 3030 (w), 2982 (w), 2961 (w), 2901 (w), 2888 (w), 1643 (w), 1624 (w), 1601 (w), 1545 (s), 1484 (m), 1472 (m), 1450 (m), 1441 (s), 1406 (w), 1374 (m), 1321 (m), 1311 (m), 1284 (m), 1253 (m), 1217 (m), 1204 (m), 1189 (m), 1172 (m), 1147 (m), 1126 (m), 1097 (w), 1077 (w), 1052 (m), 1023 (m), 1008 (m), 997 (m), 978 (w), 969 (w), 957 (m), 942 (w), 929 (m), 917 (w), 898 (w), 863 (w), 834 (w), 804 (w), 791 (w), 759 (s), 748 (s), 707 (s), 696 (s), 679 (m), 658 (w), 642 (w), 628 (s), 621 (s), 609 (s), 591 (m), 559 (m), 536 (w), 531 (m);

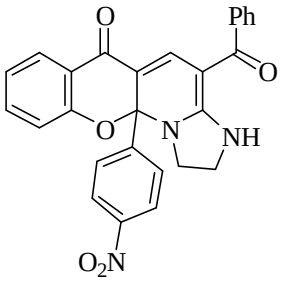
16-Benzoyl-5-methyl-10-(3-nitrophenyl)-9-oxa-11,14-diazatetracyclo-[8.7.0.0^{3,8}.0^{11,15}]-heptadeca-1(17),3(8),4,6,15-pentaen-2-one (26b):



Starting with 6-methyl-3-(3-nitrobenzoyl)chromone **6h** (0.309 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26b** was isolated as a yellow solid (0.201 g, 42%), mp 305-306 ºC;

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.19 (s, 3H, CH_3), 3.21-3.25 (m, 1H, CH), 3.73 (td, ^3J = 4.8 Hz, ^2J = 10.9 Hz, 1H, CH), 3.78-3.82 (m, 1H, CH), 4.15 (td, ^3J = 4.7 Hz, ^2J = 10.0 Hz, 1H, CH), 7.19 (d, ^3J = 9.0 Hz, 1H, H_{Ar}), 7.38-7.39 (m, 2H, H_{Ar}), 7.54-7.59 (m, 5H, H_{Ar}), 7.69 (t, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.82 (s, 1H, 17-H), 7.85 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 8.11 (t, ^4J = 2.0 Hz, 1H, H_{Ar}), 8.17-8.18 (m, 1H, H_{Ar}), 9.50 (s, 1H, NH); ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 19.9 (CH_3), 42.0 (NCH_2), 43.1 (NCH_2), 90.4 and 91.2 (10-C and 16-C), 110.1, 117.8, 120.9, 122.3, 124.1, 126.3, 2^{x}127.7, 2^{x}128.4, 130.2, 130.6, 131.8, 133.2, 136.5, 137.1, 139.9, 140.4, 147.9, 152.6, 157.2, 177.0, 189.6 (C=O); MS (EI, 70 eV) *m/z* (%): 479 ([M]$^+$, 34), 450 (19), 449 (14), 358 (19), 357 (100); HRMS (ESI): calcd for $C_{28}H_{22}N_3O_5$ ([M+H]$^+$) 480.15540, found 480.15591; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3318 (w), 3097 (w), 3076 (w), 3051 (w), 3023 (w), 2958 (w), 2924 (w), 2857 (w), 1731 (w), 1652 (m), 1619 (w), 1611 (w), 1564 (s), 1534 (s), 1478 (s), 1454 (s), 1402 (m), 1377 (m), 1346 (m), 1310 (s), 1277 (s), 1253 (m), 1215 (m), 1198 (m), 1173 (m), 1155 (m), 1133 (m), 1091 (m), 1077 (m), 1053 (m), 1033 (w), 1015 (m), 979 (m), 938 (w), 924 (w), 899 (w), 867 (w), 850 (w), 827 (m), 819 (m), 796 (w), 777 (w), 752 (s), 740 (s), 709 (s), 681 (m), 670 (m), 631 (s), 571 (m), 538 (m).

16-Benzoyl-10-(4-nitrophenyl)-9-oxa-11,14-diazatetracyclo[8.7.0.0^{3,8}.0^{11,15}]heptadeca-1(17),3(8),4,6,15-pentaen-2-one (26c):

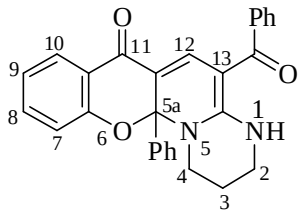


Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26c** was isolated as a orange solid (0.149 g, 32%), mp 278-280 ºC;

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.20-3.24 (m, 1H, CH), 3.75 (td, ^2J = 10.9 Hz, ^3J = 4.9 Hz, 1H, CH), 3.79-3.83 (m, 1H, CH), 4.15 (td, ^2J = 10.2 Hz, ^3J = 4.9 Hz, 1H, CH), 7.02 (t, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.27 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.53-7.60 (m, 7H, H_{Ar}), 7.68 (t, ^3J = 8.9 Hz, 2H, H_{Ar}), 7.81 (s, 1H, 17-H), 8.21 (dt, ^3J = 8.9 Hz, ^4J = 2.0 Hz, 2H, H_{Ar}), 9.53 (s, 1H, NH); ^{13}C NMR (125.8 MHz, DMSO-

d_6): δ = 42.1 (NCH_2), 43.0 (NCH_2), 90.8 and 91.1 (10-C and 16-C), 109.8, 118.0, 122.5, 122.6, 2^x123.9, 126.5, 2^x127.8, 2^x128.2, 2^x128.3, 130.1, 135.7, 137.1, 139.8, 144.8, 147.7, 154.6, 157.1, 177.0, 189.6 (C=O); MS (EI, 70 eV) *m/z* (%): 465 ($[M]^+$, 50), 437 (10), 436 (31), 435 (11), 390 (15), 360 (33), 344 (24), 343 (100), 241 (11), 222 (10), 105 (13), 77 (16), 44 (12), 43 (28), 40 (15); HRMS (ESI): calcd for $C_{27}H_{20}N_3O_5$ ($[M+H]^+$) 466.13975, found 466.13992, calcd for $C_{27}H_{19}NaN_3O_5$ ($[M+Na]^+$) 488.12169, found 488.12142; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3309 (w), 3061 (w), 2984 (w), 2921 (w), 2851 (w), 1728 (w), 1645 (w), 1618 (w), 1603 (w), 1577 (m), 1554 (s), 1519 (w), 1486 (m), 1474 (s), 1460 (s), 1441 (s), 1376 (w), 1343 (m), 1317 (s), 1283 (m), 1232 (m), 1205 (s), 1175 (s), 1129 (m), 1114 (m), 1065 (m), 1046 (m), 1034 (m), 1023 (m), 1008 (m), 977 (m), 953 (m), 922 (m), 896 (w), 851 (m), 792 (w), 748 (s), 724 (s), 702 (s), 672 (m), 649 (m), 631 (s), 589 (m), 561 (m), 530 (m).

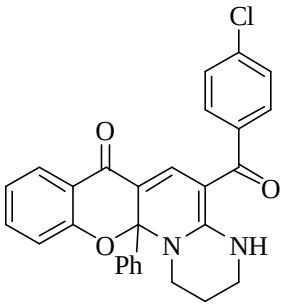
13-Benzoyl-5a-phenyl-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26d):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26d** was isolated as a yellow solid (0.395 g, 91%), mp 287-288 ºC;

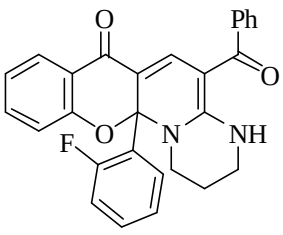
^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.51-1.63 (m, 1H, CH), 1.94-2.07 (m, 1H, CH), 3.29-3.38 (m, 1H, CH), 3.39-3.46 (m, 2H, CH), 3.90-4.00 (m, 1H, CH), 7.01 (t, ^3J = 7.6 Hz, 1H, H_{Ar}), 7.27-7.41 (m, 6H, H_{Ar}), 7.50-7.61 (m, 7H, H_{Ar}), 7.67 (s, 1H, 12-H), 11.66 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.2 (NCH_2), 39.1 (NCH_2), 92.0 and 92.2 (5a-C and 13-C), 110.2, 117.9, 122.3, 122.4, 2^x126.3, 2^x127.8, 2^x128.2, 2^x128.6, 128.9, 2^x129.7, 135.6, 135.9, 139.7, 140.6, 153.8, 155.2, 177.3, 190.7 (C=O); MS (EI, 70 eV) *m/z* (%): 434 ($[M]^+$, 48), 405 (22), 358 (20), 357 (100), 330 (12), 329 (58), 301 (21), 91 (11); HRMS (ESI): calcd for $C_{28}H_{23}N_2O_3$ ($[M+H]^+$) 435.17032, found 435.17090, calcd for $C_{28}H_{22}NaN_2O_3$ ($[M+Na]^+$) 457.15226, found 457.15269; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2944 (w), 2872 (w), 1650 (w), 1576 (m), 1558 (s), 1480 (m), 1461 (s), 1435 (s), 1368 (m), 1328 (m), 1314 (m), 1287 (m), 1269 (w), 1248 (s), 1217 (m), 1203 (m), 1187 (m), 1179 (w), 1167 (w), 1156 (w), 1135 (m), 1104 (w), 1084 (w), 1076 (w), 1063 (m), 1027 (m), 1000 (w), 962 (m), 943 (m), 924 (m), 889 (w), 872 (w), 829 (m), 810 (m), 784 (m), 747 (s), 726 (m), 698 (s), 678 (s), 654 (w), 630 (s), 606 (m), 575 (m), 558 (m), 544 (w).

13-(4-Chlorobenzoyl)-5a-phenyl-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26e):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol) and HKA **24c** (0.237 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26e** was isolated as a yellow solid (0.459 g, 98%), mp 280-282 ºC;
^{1}H NMR (250 MHz, DMSO-d_6): δ = 1.55-159 (m, 1H, CH), 1.97-2.01 (m, 1H, CH), 3.29-3.45 (m, 3H, CH), 3.89-4.00 (m, 1H, CH), 7.01 (t, ^{3}J = 7.3 Hz, 1H, H_{Ar}), 7.30 (m, 6H, H_{Ar}), 7.53-7.62 (m, 7H, H_{Ar}), 11.60 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.3 (NCH_2), 39.1 (NCH_2), 92.0 and 92.1 (5a-C and 13-C), 110.5, 117.9, 122.2, 122.3, 2^{x}126.3, 2^{x}128.3, 2^{x}128.6, 128.7, 128.9, 2^{x}129.7, 134.4, 135.4, 135.6, 139.3, 139.6, 153.8, 155.2, 177.3, 189.1 (C=O); MS (EI, 70 eV) *m/z* (%): 468 ([M]$^{+}$, 70), 439 (32), 391 (100), 363 (11), 329 (75), 301 (29), 149 (21), 71 (14), 57 (21); HRMS (ESI): calcd for $C_{28}H_{22}{}^{35}ClN_2O_3$ ([M+H]$^{+}$) 469.13135, found 469.13210, calcd for $C_{28}H_{22}{}^{37}ClN_2O_3$ ([M+H]$^{+}$) 471.12971, found 471.13006; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2923 (w), 2854 (w), 1658 (w), 1606 (m), 1580 (s), 1574 (s), 1557 (m), 1538 (w), 1504 (w), 1480 (m), 1471 (m), 1457 (m), 1435 (m), 1417 (w), 1395 (w), 1368 (m), 1330 (m), 1292 (m), 1274 (m), 1246 (m), 1216 (m), 1191 (m), 1181 (m), 1172 (w), 1141 (m), 1104 (m), 1087 (m), 1067 (m), 1038 (m), 1029 (m), 1013 (m), 972 (m), 953 (m), 939 (m), 882 (w), 842 (w), 825 (m), 792 (s), 781 (m), 752 (s), 734 (m), 719 (w), 694 (s), 666 (m), 644 (m), 636 (m), 606 (w), 579 (m), 558 (w), 544 (m), 530 (m).

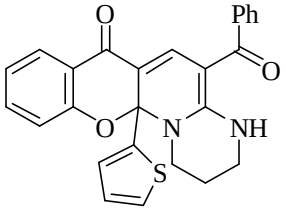
13-Benzoyl-5a-(2-fluorophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26f):



Starting with 3-(2-fluorobenzoyl)chromone **6b** (0.268 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26f** was isolated as a yellow solid (0.416 g, 92%), mp 278-280 ºC;
^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.51-1.63 (s, 1H, CH), 1.94-2.06 (s, 1H, CH), 3.20-3.29 (m, 2H, CH), 3.39-3.46 (m, 1H, CH), 3.86-3.94 (m, 1H, CH), 7.03-7.13 (m, 2H, H_{Ar}), 7.20-7.41 (m, 4H, H_{Ar}), 7.43-7.52 (m, 5H, H_{Ar}), 7.54 (s, 1H, 12-H), 7.58-7.64 (m, 2H, H_{Ar}), 11.69 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.3 (NCH_2), 39.8 (NCH_2), 91.2 (d, $J_{C,F}$ = 1.4 Hz, 5a-C or 13-C), 92.7 (d, $J_{C,F}$ = 2.7 Hz, 5a-C or 13-C), 108.1, 117.2 (d, $J_{C,F}$ = 22.3 Hz), 117.5, 122.1, 122.3, 124.0 (d, $J_{C,F}$ = 2.8 Hz), 126.2 (d, $J_{C,F}$ = 10.5 Hz), 126.3, 2^{x}127.7, 2^{x}128.2, 128.6 (d, $J_{C,F}$ = 1.9 Hz), 129.7, 131.4 (d, $J_{C,F}$ =

9.0 Hz), 135.7, 136.4 (d, $J_{C,F}$ = 3.0 Hz), 140.6, 154.1 (d, $J_{C,F}$ = 0.9 Hz), 154.9, 160.6 (d, $^{1}J_{C,F}$ = 250.6 Hz, $C_{Ar}F$), 177.3, 190.6 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -111.2 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 452 ([M]$^+$, 100), 423 (91), 395 (12), 347 (70), 329 (11), 319 (40), 122 (35), 105 (57), 84 (20), 77 (35), 57 (24), 43 (33); HRMS (EI): calcd for $C_{28}H_{21}FN_2O_3$ ([M]$^+$) 452.15307, found 452.15366; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2953 (w), 2921 (w), 2851 (w), 1714 (w), 1651 (m), 1605 (m), 1581 (s), 1564 (s), 1557 (s), 1505 (m), 1481 (m), 1462 (s), 1446 (s), 1436 (m), 1416 (m), 1368 (m), 1328 (m), 1288 (m), 1277 (m), 1249 (s), 1215 (s), 1202 (s), 1177 (m), 1160 (m), 1140 (m), 1102 (m), 1181 (m), 1066 (s), 1047 (m), 1025 (s), 983 (m), 961 (m), 924 (m), 887 (w), 873 (w), 827 (m), 816 (m), 802 (m), 784 (m), 770 (s), 756 (s), 719 (m), 699 (s), 672 (s), 649 (m), 630 (s), 605 (m), 572 (m), 543 (m), 532 (m).

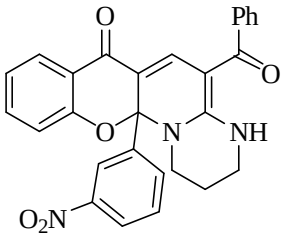
13-Benzoyl-5a-(thiophen-2-yl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26g):



Starting with 3-(2-thenoyl)chromone **6c** (0.256 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26g** was isolated as a yellow solid (0.278 g, 63%), mp 281-283 ºC;

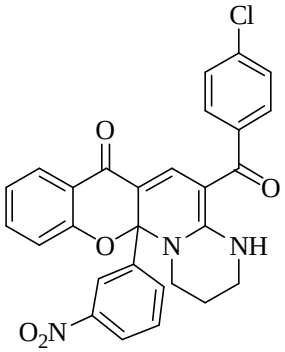
^{1}H NMR (250 MHz, DMSO-d_6): δ = 1.58-1.74 (m, 1H, CH), 1.96-2.11 (m, 1H, CH), 3.34-3.46 (m, 2H, CH), 3.72-3.82 (m, 1H, CH), 3.92-4.03 (m, 1H, CH), 6.93-6.96 (m, 1H, H_{Ar}), 7.03-7.08 (m, 2H, H_{Ar}), 7.21 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 7.50-7.58 (m, 7H, H_{Ar}), 7.62-7.64 (m, 2H, H_{Ar}), 11.58 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.3 (NCH_2), 39.8 (NCH_2), 90.1 and 92.8 (5a-C and 13-C), 109.9, 118.0, 122.2, 122.6, 126.3, 126.8, 127.0, 127.7, 2^{x}127.9, 2^{x}128.3, 129.9, 135.2, 135.6, 140.5, 143.6, 153.7, 154.9, 176.5, 190.8 (C=O); MS (EI, 70 eV) *m/z* (%): 440 ([M]$^+$, 80), 411 (43), 383 (15), 357 (62), 335 (100), 307 (53), 105 (22), 91 (19), 77 (24); HRMS (EI): calcd for $C_{26}H_{20}N_2O_3S$ ([M]$^+$) 440.11891, found 440.11869; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2922 (w), 2852 (w), 1732 (w), 1645 (m), 1600 (m), 1580 (s), 1575 (s), 1564 (s), 1557 (s), 1505 (w), 1482 (m), 1457 (s), 1434 (s), 1381 (m), 1368 (s), 1330 (s), 1297 (m), 1285 (m), 1265 (s), 1244 (s), 1218 (s), 1201 (s), 1174 (m), 1166 (m), 1157 (m), 1136 (s), 1102 (s), 1065 (s), 1043 (m), 1024 (s), 979 (m), 962 (m), 931 (m), 918 (m), 883 (m), 861 (m), 836 (m), 807 (s), 782 (s), 756 (s), 741 (s), 721 (s), 706 (s), 693 (s), 672 (s), 653 (m), 635 (s), 626 (s), 606 (m), 594 (s), 560 (s), 538 (m).

13-Benzoyl-5a-(3-nitrophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26h):



Starting with 3-(3-nitrobenzoyl)chromone **6g** (0.295 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26h** was isolated as a yellow solid (0.359 g, 75%), mp 301-302 ºC; ^{1}H NMR (250 MHz, DMSO-d_6): δ = 1.57-1.74 (m, 1H, CH), 1.95-2.11 (m, 1H, CH), 3.35-3.48 (m, 3H, CH), 3.96-4.08 (m, 1H, CH), 7.05 (td, ^3J = 7.4 Hz, ^5J = 0.8 Hz, 1H, H_{Ar}), 7.40 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.51-7.66 (m, 7H, H_{Ar}), 7.70 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.75 (s, 1H, 12-H), 7.88 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 8.13-8.18 (m, 2H, H_{Ar}), 11.63 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.3 (NCH_2), 39.1 (NCH_2), 91.1 and 92.4 (5a-C and 13-C), 109.1, 118.0, 120.8, 122.3, 122.8, 124.0, 126.4, 2^x127.8, 2^x128.3, 129.9, 130.6, 132.7, 135.8, 136.9, 140.5, 141.6, 147.8, 153.9, 154.7, 176.6, 191.1 (C=O); MS (EI, 70 eV) *m/z* (%): 479 ($[M]^+$, 14), 449 (16), 374 (12), 358 (20), 357 (100), 344 (13), 329 (12), 91 (15), 77 (10); HRMS (EI): calcd for $C_{28}H_{21}N_3O_5$ ($[M]^+$) 479.14757, found 479.14801; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3055 (w), 2919 (w), 2881 (w), 2852 (w), 1989 (w), 1838 (w), 1732 (w), 1650 (m), 1603 (w), 1582 (s), 1562 (s), 1532 (s), 1481 (s), 1459 (s), 1433 (m), 1371 (m), 1339 (s), 1274 (s), 1251 (s), 1224 (m), 1181 (m), 1148 (m), 1100 (m), 1071 (m), 1050 (m), 1026 (m), 971 (m), 902 (w), 881 (w), 853 (w), 829 (m), 816 (m), 780 (m), 765 (s), 740 (s), 712 (s), 651 (m), 632 (s), 608 (m), 579 (m), 548 (w), 534 (w).

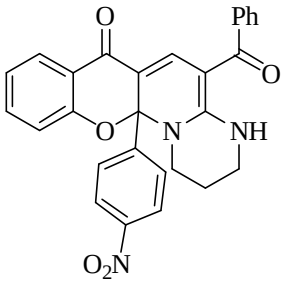
13-(4-Chlorobenzoyl)-5a-(3-nitrophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26i):



Starting with 3-(3-nitrobenzoyl)chromone **6g** (0.295 g, 1.0 mmol) and HKA **24c** (0.237 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26i** was isolated as a yellow solid (0.308 g, 60%), mp 322-323 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.58-1.75 (m, 1H, CH), 1.95-2.11 (m, 1H, CH), 3.34-3.48 (m, 3H, CH), 3.97-4.07 (m, 1H, CH), 7.06 (t, ^3J = 7.2 Hz, 1H, H_{Ar}), 7.40 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 7.54-7.68 (m, 8H, H_{Ar}), 7.88 (d, ^3J = 7.4 Hz, 1H, H_{Ar}), 8.12-8.18 (m, 2H, H_{Ar}), 11.57 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 39.4 (NCH_2), 39.7 (NCH_2), 91.1 and 92.3 (5a-C and 13-C), 109.5, 117.9, 120.7, 122.2, 122.8, 124.0, 126.4, 2^x128.4, 2^x129.7, 130.6, 132.8, 134.6, 135.9, 136.4, 139.2, 141.6, 147.8, 153.8, 154.7, 176.6, 189.5 (C=O); MS (EI, 70 eV) *m/z* (%): 513 ($[M]^+$, 37), 484 (13), 391 (100), 374 (32), 346 (21), 129 (24), 125 (23),

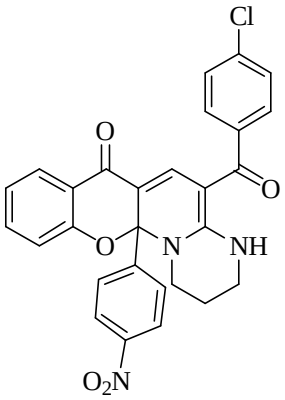
115 (12), 111 (17), 101 (12), 98 (17), 94 (18), 87 (18), 73 (68), 69 (36), 60 (75), 55 (61), 41 (72); HRMS (ESI): calcd for $C_{28}H_{21}{}^{35}ClN_3O_5$ ($[M+H]^+$) 514.11642, found 514.11693, calcd for $C_{28}H_{21}{}^{37}ClN_3O_5$ ($[M+H]^+$) 516.11487, found 516.11522, calcd for $C_{28}H_{20}{}^{35}ClNaN_3O_5$ ($[M+Na]^+$) 536.09837, found 536.09865, calcd for $C_{28}H_{20}{}^{37}ClNaN_3O_5$ ($[M+Na]^+$) 538.09681, found 538.09729; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3030 (w), 2964 (w), 2874 (w), 1652 (w), 1603 (m), 1574 (s), 1558 (s), 1530 (s), 1481 (s), 1470 (m), 1457 (s), 1444 (m), 1434 (m), 1397 (w), 1384 (m), 1341 (s), 1292 (m), 1275 (s), 1250 (s), 1227 (m), 1202 (m), 1191 (m), 1175 (m), 1147 (m), 1099 (m), 1087 (m), 1070 (m), 1047 (w), 1029 (w), 1014 (m), 972 (m), 957 (w), 943 (w), 904 (w), 881 (w), 852 (m), 826 (m), 811 (w), 795 (w), 784 (m), 765 (s), 739 (s), 718 (s), 705 (s), 682 (m), 658 (w), 636 (m), 606 (w), 584 (w), 555 (m).

13-Benzoyl-5a-(4-nitrophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26j):



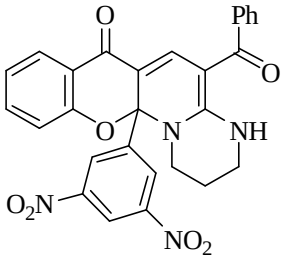
Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26j** was isolated as a yellow solid (0.335 g, 70%), mp 213-214 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.57-1.69 (m, 1H, CH), 1.95-2.09 (m, 1H, CH), 3.35-3.38 (m, 1H, CH), 3.40-3.48 (m, 2H, CH), 3.96-4.05 (m, 1H, CH), 7.05 (td, ^3J = 7.8 Hz, ^4J = 0.9 Hz, 1H, H_{Ar}), 7.35 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.54-7.64 (m, 7H, H_{Ar}), 7.68 (d, ^3J = 8.9 Hz, 2H, H_{Ar}), 7.72 (s, 1H, 12-H), 8.20 (d, ^3J = 8.9 Hz, 2H, H_{Ar}), 11.68 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.3 (NCH_2), 39.1 (NCH_2), 91.4 and 92.4 (5a-C and 13-C), 109.0, 118.0, 122.3, 122.7, 2^x123.9, 126.4, 2^x127.8, 2^x127.9, 2^x128.3, 129.9, 135.8, 136.8, 140.4, 146.2, 147.6, 153.9, 154.7, 176.7, 191.1 (C=O); MS (EI, 70 eV) *m/z* (%): 479 ($[M]^+$, 86), 450 (21), 374 (32), 358 (25), 357 (100), 346 (18); HRMS (ESI): calcd for $C_{28}H_{22}N_3O_5$ ($[M+H]^+$) 480.15540, found 480.15588, calcd for $C_{28}H_{21}NaN_3O_5$ ($[M+Na]^+$) 502.13734, found 502.13772; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3105 (w), 3077 (w), 3045 (w), 3011 (w), 9244 (w), 2873 (w), 2860 (w), 1657 (w), 1606 (w), 1581 (s), 1564 (m), 1518 (m), 1484 (m), 1461 (s), 1439 (m), 1416 (w), 1401 (w), 1374 (m), 1334 (s), 1301 (w), 1289 (m), 1277 (m), 1244 (s), 1222 (m), 1205 (w), 1171 (m), 1142 (m), 1107 (m), 1085 (m), 1072 (m), 1051 (w), 1023 (w), 1010 (w), 1001 (w), 975 (w), 954 (w), 942 (m), 926 (w), 903 (w), 857 (w), 846 (s), 821 (w), 797 (w), 781 (m), 747 (s), 726 (s), 711 (w), 700 (s), 684 (m), 673 (m), 647 (w), 633 (s), 606 (m), 571 (m), 540 (m).

13-(4-Chlorobenzoyl)-5a-(4-nitrophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26k):



Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295 g, 1.0 mmol) and HKA **24c** (0.237 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26k** was isolated as a orange solid (0.319 g, 62%), mp 327-329 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.58-1.69 (m, 1H, CH), 1.99-2.02 (m, 1H, CH), 3.41-3.45 (m, 3H, CH), 3.98-4.03 (m, 1H, CH), 7.05 (t, ^{3}J = 7.4 Hz, 1H, H_{Ar}), 7.36 (d, ^{3}J = 7.9 Hz, 1H, H_{Ar}), 7.59-7.70 (m, 9H, H_{Ar}), 8.17-8.20 (m, 2H, H_{Ar}), 11.61 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.0 (CH_2), 40.2 (NCH_2), 40.5 (NCH_2), 91.3 and 92.3 (5a-C and 13-C), 109.4, 118.0, 122.2, 122.7, 2^{x}123.9, 126.4, 127.8, 2^{x}128.3, 2^{x}129.8, 134.5, 135.8, 136.3, 139.0, 139.1, 146.1, 147.6, 153.8, 154.8, 176.7, 189.5 (C=O); MS (EI, 70 eV) *m/z* (%): 513 ([M]$^{+}$, 42), 484 (18), 391 (100), 374 (43), 346 (21), 125 (11); HRMS (ESI): calcd for $C_{28}H_{21}{}^{35}ClN_3O_5$ ([M+H]$^{+}$) 514.11642, found 514.11701, calcd for $C_{28}H_{21}{}^{37}ClN_3O_5$ ([M+H]$^{+}$) 516.11487, found 516.11543, calcd for $C_{28}H_{20}{}^{35}ClNaN_3O_5$ ([M+Na]$^{+}$) 536.09837, found 536.09876, calcd for $C_{28}H_{20}{}^{37}ClNaN_3O_5$ ([M+Na]$^{+}$) 538.09681, found 538.09723; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3105 (w), 3052 (w), 2874 (w), 1645 (m), 1605 (m), 1577 (s), 1564 (s), 1557 (s), 1520 (s), 1478 (s), 1457 (s), 1435 (s), 1394 (w), 1378 (m), 1361 (w), 1337 (s), 1318 (m), 1285 (m), 1269 (s), 1239 (s), 1209 (s), 1190 (s), 1169 (s), 1142 (s), 1111 (m), 1101 (m), 1083 (m), 1071 (s), 1044 (m), 1030 (w), 1013 (m), 986 (w), 974 (m), 964 (m), 953 (m), 941 (m), 906 (w), 889 (w), 865 (m), 849 (m), 841 (m), 814 (s), 786 (m), 764 (w), 753 (s), 738 (s), 721 (m), 712 (m), 703 (s), 692 (m), 678 (w), 652 (m), 635 (s), 605 (m), 579 (m), 547 (m).

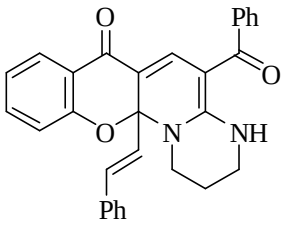
13-Benzoyl-5a-(3,5-dinitrophenyl)-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26l):



Starting with 3-(3,5-dinitrobenzoyl)chromone **6j** (0.340 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26l** was isolated as a red solid (0.461 g, 88%), mp 301-303 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.72-1.76 (m, 1H, CH), 1.98-2.02 (m, 1H, CH), 3.37-3.50 (m, 3H, CH), 4.01-4.07 (m, 1H, CH), 7.09 (t, ^{3}J = 7.4 Hz, 1H, H_{Ar}), 7.47 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 7.51-7.62 (m, 6H, H_{Ar}), 7.66 (td, ^{3}J = 7.7 Hz, ^{4}J = 1.7 Hz, 1H, H_{Ar}), 7.81 (s, 1H, 12-H), 8.47 (d, ^{4}J = 1.0 Hz, 2H, H_{Ar}), 8.71 (t, ^{4}J = 2.0 Hz, 1H, H_{Ar}), 11.59 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.9 (CH_2), 38.4 (NCH_2), 39.2

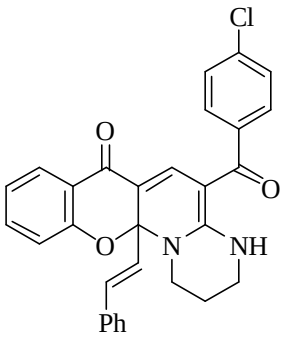
(NCH_2), 90.5 and 92.8 (5a-C and 13-C), 108.3, 117.9, 119.2, 122.2, 123.2, 2ˣ126.1, 126.6, 2ˣ127.8, 2ˣ128.4, 130.2, 136.0, 137.7, 140.4, 143.2, 2ˣ148.4, 153.9, 154.3, 175.9, 191.3 (C=O); MS (EI, 70 eV) *m/z* (%): 524 ($[M]^+$, 20), 419 (11), 357 (100), 329 (11), 91 (7), 44 (10); HRMS (EI): calcd for $C_{28}H_{21}N_4O_7$ ($[M+H]^+$) 525.14048, found 525.14072, calcd for $C_{28}H_{20}NaN_4O_7$ ($[M+Na]^+$) 547.12242, found 547.12187; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3017 (w), 2965 (w), 2883 (w), 2855 (w), 1650 (w), 1607 (w), 1583 (s), 1535 (s), 1481 (s), 1462 (s), 1441 (s), 1368 (m), 1332 (s), 1294 (m), 1274 (s), 1243 (s), 1218 (m), 1199 (m), 1173 (w), 1144 (m), 1104 (m), 1090 (m), 1070 (m), 1047 (m), 1024 (w), 995 (m), 962 (w), 948 (m), 920 (w), 907 (w), 894 (w), 872 (m), 839 (w), 824 (m), 800 (w), 753 (s), 724 (s), 711 (s), 704 (s), 686 (s), 662 (m), 635 (s), 612 (m), 596 (m), 572 (w), 535 (w).

13-Benzoyl-5a-[(*E*)-2-phenylethenyl]-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diazatetraphen-11-one (26m):



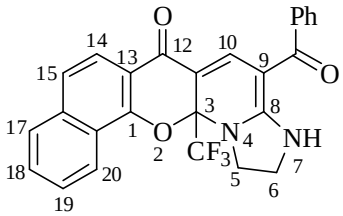
Starting with 3-[(2*E*)-3-phenylprop-2-enoyl]chromone **7** (0.276 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26lm** was isolated as a yellow solid (0.387 g, 84%), mp 186 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.84-1.95 (m, 1H, CH), 2.06-2.16 (m, 1H, CH), 3.39-3.49 (m, 1H, CH), 3.51-3.60 (m, 1H, CH), 3.82-3.92 (m, 1H, CH), 3.93-4.02 (m, 1H, CH), 6.51 (d, ^3J = 15.9 Hz, 1H, =CH), 6.61 (d, ^3J = 15.9 Hz, 1H, =CH), 7.06 (td, J = 0.6 Hz, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.16 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.21-7.31 (m, 3H, H_{Ar}), 7.41-7.44 (m, 2H, H_{Ar}), 7.47-7.57 (m, 6H, H_{Ar}), 7.63 (s, 1H, 12-H), 7.70 (dd, ^4J = 1.6 Hz, ^3J = 7.8 Hz, 1H, H_{Ar}), 11.60 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.3 (CH_2), 38.3 (NCH_2), 39.8 (NCH_2), 91.6 and 92.9 (5a-C and 13-C), 107.6, 117.8, 122.2, 122.4, 126.3, 126.5, 2ˣ127.2, 2ˣ127.9, 2ˣ128.2, 128.5, 2ˣ128.6, 129.7, 132.8, 134.8, 135.0, 136.4, 140.6, 154.0, 154.8, 177.0, 190.7 (C=O); MS (EI, 70 eV) *m/z* (%): 460 ($[M]^+$, 55), 444 (11), 431 (19), 355 (100), 329 (10), 327 (14), 207 (15), 105 (12), 91 (13), 77 (10), 73 (18), 60 (12), 57 (11), 43 (15); HRMS (ESI): calcd for $C_{30}H_{25}N_2O_3$ ($[M+H]^+$) 461.18597, found 461.18169; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 3019 (w), 2954 (w), 2872 (w), 1652 (m), 1605 (m), 1581 (s), 1560 (s), 1483 (s), 1461 (s), 1442 (s), 1384 (m), 1371 (m), 1339 (s), 1321 (m), 1291 (s), 1279 (s), 1246 (s), 1218 (m), 1203 (m), 1152 (m), 1111 (s), 1098 (m), 1064 (m), 1025 (m), 995 (m), 978 (m), 934 (m), 865 (w), 842 (w), 804 (m), 777 (s), 753 (s), 738 (s), 717 (m), 687 (s), 666 (m), 632 (s), 604 (m), 575 (m), 558 (m), 542 (m).

13-(4-Chlorobenzoyl)-5a-[(*E*)-2-phenylethenyl]-1,2,3,4,5a,11-hexahydro-6-oxa-1,5-diaza-tetraphen-11-one (26n):



Starting with 3-[(2*E*)-3-phenylprop-2-enoyl]chromone **7** (0.276 g, 1.0 mmol) and HKA **24c** (0.237 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26n** was isolated as a yellow solid (0.431 g, 87%), mp 254 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.85-1.95 (m, 1H, CH), 2.07-2.17 (m, 1H, CH), 3.39-3.50 (m, 1H, CH), 3.52-3.62 (m, 1H, CH), 3.83-3.92 (m, 1H, CH), 3.93-4.02 (m, 1H, CH), 6.51 (d, ^{3}J = 15.9 Hz, 1H, =CH), 6.60 (d, ^{3}J = 15.9 Hz, 1H, =CH), 7.07 (td, J = 0.8 Hz, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 7.17 (d, ^{3}J = 7.9 Hz, 1H, H_{Ar}), 7.22-7.32 (m, 3H, H_{Ar}), 7.41-7.46 (m, 2H, H_{Ar}), 7.49-7.59 (m, 6H, H_{Ar}), 7.69 (dd, ^{4}J = 1.6 Hz, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 11.51 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.3 (CH_2), 38.3 (NCH_2), 39.8 (NCH_2), 91.6 and 92.6 (5a-C and 13-C), 108.0, 117.7, 122.2, 122.3, 126.3, 126.4, 2^{x}127.2, 2^{x}128.3, 2^{x}128.5, 128.6, 2^{x}129.9, 132.9, 134.5, 134.8, 135.1, 135.9, 139.4, 153.9, 154.9, 177.0, 189.1 (C=O); MS (EI, 70 eV) *m/z* (%): 494 ([M]$^{+}$, 54), 465 (21), 391 (42), 355 (100), 327 (13), 139 (16), 125 (14), 111 (10); HRMS (ESI): calcd for $C_{30}H_{24}{}^{35}ClN_2O_3$ ([M+H]$^{+}$) 495.14700, found 495.14757, calcd for $C_{30}H_{24}{}^{37}ClN_2O_3$ ([M+H]$^{+}$) 497.14552, found 497.14586; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 3030 (w), 2922 (w), 2852 (w), 1648 (w), 1604 (m), 1568 (s), 1480 (s), 1460 (s), 1439 (s), 1394 (w), 1366 (m), 1339 (m), 1319 (w), 1289 (m), 1277 (s), 1261 (w), 1242 (s), 1216 (s), 1202 (s), 1156 (m), 1145 (m), 1108 (s), 1094 (m), 1084 (s), 1062 (s), 1029 (m), 1012 (s), 968 (m), 953 (m), 907 (w), 892 (w), 859 (w), 833 (m), 811 (m), 797 (m), 782 (m), 756 (s), 739 (s), 720 (m), 703 (s), 688 (s), 666 (w), 652 (m), 633 (s), 608 (w), 577 (m), 570 (w), 549 (m).

9-Benzoyl-3-(trifluoromethyl)-2-oxa-4,7-diazapentacyclo[11.8.0.0^{3,11}.0^{4,8}.0^{16,21}]henicosa-1(13),8,10,14,16(21),17,19-heptaen-12-one (26o):

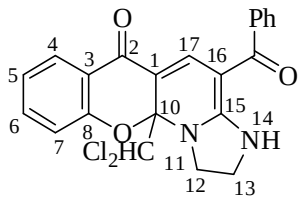


Starting with 3-(trifluoroacetyl)chromone **5a** (0.242 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26o** was isolated as a yellow solid (0.083 g, 18%), mp 292-293 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.99-4.19 (m, 2H, CH), 4.29-4.38 (m, 1H, CH), 4.45-4.54 (m, 1H, CH), 7.44-7.64 (m, 8H, H_{Ar}), 7.83 (d, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 7.99 (d, ^{3}J = 8.6 Hz, 1H, H_{Ar}), 8.14 (s, 1H, 10-H), 8.24 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 9.55 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 43.7 (NCH_2), 44.0 (NCH_2), 88.9 (q, $^{2}J_{C,F}$ = 32.5 Hz), 92.7, 102.1, 122.0, 122.2,

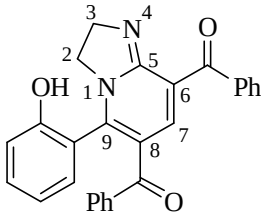
122.6, 123.7, 126.4, 2^{x}128.1, 2^{x}128.3, 2^{x}128.5, 129.1, 131.0, 137.1, 138.9, 141.1, 151.6, 159.5, 176.9, 192.1 (C=O); ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = –80.1 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 462 ([M]$^+$, 6), 394 (24), 393 (100), 105 (5), 77 (6); HRMS (ESI): calcd for $C_{26}H_{18}F_3N_2O_3$ ([M+H]$^+$) 463.12640, found 463.12649, calcd for $C_{26}H_{17}F_3NaN_2O_3$ ([M+Na]$^+$) 485.10835, found 485.10814; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3346 (w), 3085 (w), 3061 (w), 2953 (w), 2923 (w), 2896 (w), 2852 (w), 1650 (m), 1630 (w), 1614 (w), 1558 (s), 1541 (s), 1508 (w), 1490 (m), 1467 (m), 1436 (s), 1409 (w), 1384 (s), 1318 (s), 1273 (m), 1240 (s), 1217 (s), 1189 (s), 1177 (s), 1161 (s), 1133 (s), 1102 (s), 1069 (m), 1030 (s), 1005 (s), 919 (s), 871 (m), 846 (w), 826 (m), 784 (w), 765 (s), 744 (s), 704 (s), 657 (s), 636 (s), 577 (s), 566 (s), 527 (m).

16-Benzoyl-10-(dichloromethyl)-9-oxa-11,14-diazatetracyclo[8.7.0.0^{3,8}.0^{11,15}]heptadeca-1(17),3(8),4,6,15-pentaen-2-one (26p):



Starting with 3-(2,2-dichloroacetyl)chromone **8** (0.257 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **26p** was isolated as a green-brawn solid (0.175 g, 41%), mp 221 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.81-4.03 (m, 2H, CH), 4.19-4.37 (m, 2H, CH), 6.87 (s, 1H, $CHCl_2$), 7.05 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 7.12 (d, ^3J = 7.2 Hz, 1H, H_{Ar}), 7.43-7.58 (m, 6H, H_{Ar}), 7.74-7.78 (m, 2H, H_{Ar}), 9.56 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 43.7 (NCH_2), 43.8 (NCH_2), 77.0 ($CHCl_2$), 91.0 and 93.0 (10-C and 16-C), 103.8, 117.0, 121.8, 122.5, 126.4, 2^{x}127.8, 2^{x}128.3, 130.4, 135,1 139.6, 140.9, 154.2, 158.8, 176.1, 189.6 (C=O); MS (GC, 70 eV) *m/z* (%): 351 ([M-Ph], 44), 323 (100), 295 (11), 164 (11), 105 (11), 77 (50), 51 (14); HRMS (ESI): calcd for $C_{22}H_{17}{}^{35}Cl_2N_2O_3$ ([M+H]$^+$) 427.06101, found 427.06107, calcd for $C_{22}H_{17}{}^{37}Cl_2N_2O_3$ ([M+H]$^+$) 429.05883, found 429.05860, calcd for $C_{22}H_{16}{}^{35}Cl_2NaN_2O_3$ ([M+Na]$^+$) 449.04281, found 449.04302, calcd for $C_{22}H_{16}{}^{37}Cl_2NaN_2O_3$ ([M+Na]$^+$) 451.03993, found 451.04054; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3213 (w), 3068 (w), 2981 (w), 2920 (w), 2851 (w), 1634 (w), 1621 (w), 1602 (w), 1580 (w), 1568 (w), 1539 (s), 1505 (w), 1477 (m), 1460 (m), 1435 (s), 1385 (m), 1325 (s), 1292 (m), 1277 (m), 1233 (m), 1201 (s), 1172 (m), 1151 (m), 1129 (m), 1105 (m), 1074 (m), 1013 (m), 977 (s), 952 (m), 932 (w), 897 (w), 862 (w), 834 (w), 817 (m), 786 (m), 736 (s), 715 (s), 701 (s), 678 (s), 667 (s), 649 (m), 628 (s), 603 (s), 576 (s), 550 (s), 533 (m).

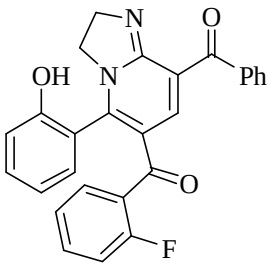
2-{6,8-Dibenzoyl-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl}phenol (27a):



Starting with 3-benzoylchromone **6a** (0.250 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27a** was isolated as a orange solid (0.319 g, 76%), mp 240-241 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.67-3.87 (m, 4H, CH), 6.65-6.74 (m, 2H, H_{Ar}), 7.03 (d, ^{3}J = 7.6 Hz, 1H, H_{Ar}), 7.09 (td, ^{4}J = 1.6 Hz, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 7.25-7.29 (m, 2H, H_{Ar}), 7.35-7.40 (m, 2H, H_{Ar}), 7.49-7.53 (m, 4H, H_{Ar}), 7.62 (tt, ^{4}J = 1.3 Hz, ^{3}J = 7.3 Hz, 1H, H_{Ar}), 7.82-7.85 (m, 2H, H_{Ar}), 10.32 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 47.8 (NCH_2), 52.4 (NCH_2), 113.7, 115.9, 118.6, 118.7, 119.9, 120.3, 2^{x}127.7, 4^{x}128.4, 2^{x}129.2, 129.3, 131.3, 131.5, 132.8, 137.0, 138.7, 141.7, 153.4, 154.2, 192.0 (C=O), 192.3 (C=O); MS (GC, 70 eV) *m/z* (%): 403 ([M-OH], 9), 402 (38), 401 (69), 375 (14), 374 (64), 373 (100), 325 (13), 297 (13), 295 (12), 148 (11), 77 (27); HRMS (ESI): calcd for $C_{27}H_{21}N_2O_3$ ($[M+H]^+$) 421.15467, found 421.15474, calcd for $C_{27}H_{20}NaN_2O_3$ ($[M+Na]^+$) 443.13661, found 443.13685; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 3024 (w), 2972 (w), 2956 (w), 2910 (w), 2883 (w), 2851 (w), 1660 (m), 1642 (m), 1617 (m), 1593 (s), 1504 (m), 1449 (s), 1420 (w), 176 (s), 1337 (w), 1299 (m), 1252 (s), 1217 (s), 1195 (m), 1186 (w), 1171 (m), 1162 (m), 1138 (w), 1117 (m), 1078 (w), 1045 (w), 1034 (w), 1012 (m), 1001 (m), 994 (m), 925 (w), 887 (w), 871 (m), 846 (w), 833 (w), 814 (w), 789 (m), 763 (m), 747 (m), 732 (s), 704 (m), 694 (s), 671 (m), 658 (w), 646 (s), 621 (m), 611 (m), 585 (m), 554 (m), 534 (w).

2-[8-Benzoyl-6-(2-fluorobenzoyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl]phenol (27b):

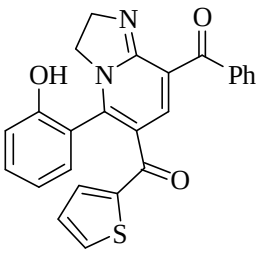


Starting with 3-(2-fluorobenzoyl)chromone **6b** (0.268 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27b** was isolated as a orange solid (0.420 g, 96%), mp 225-227 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.62-3.79 (m, 4H, CH), 6.64 (d, ^{3}J = 7.9 Hz, 1H, H_{Ar}), 6.68 (t, ^{3}J = 7.5 Hz, 1H, H_{Ar}), 6.90-6.93 (m, 1H, H_{Ar}), 6.99 (td, ^{3}J = 7.5 Hz, ^{4}J = 0.9 Hz, 1H, H_{Ar}), 7.04-7.08 (m, 2H, H_{Ar}), 7.23-7.27 (m, 2H, H_{Ar}), 7.51-7.54 (m, 3H, H_{Ar}), 7.63 (tt, ^{3}J = 7.4 Hz, ^{4}J = 1.3 Hz, 1H, H_{Ar}), 7.82-7.84 (m, 2H, H_{Ar}), 10.25 (s, 1H, OH); ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 47.6 (NCH_2), 52.5 (NCH_2), 114.2, 115.3 (d, $J_{C,F}$ = 21.4 Hz), 115.8, 118.6, 119.8, 120.7, 123.6 (d, $J_{C,F}$ = 2.8 Hz), 127.7, 128.3, 2^{x}128.5, 129.0 (d, $J_{C,F}$ = 28.9 Hz), 2^{x}129.2, 131.4, 131.9 (d, $J_{C,F}$ = 8.3 Hz), 133.0, 136.8, 140.6, 153.1, 153.9, 154.7, 158.3 (d, $^{1}J_{C,F}$ = 247.9 Hz, $C_{Ar}F$), 187.8 (C=O), 192.3 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -114.4 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 438 ($[M]^+$, 16), 437

(45), 421 (12), 420 (31), 419 (67), 418 (79), 417 (100), 415 (15), 409 (13), 392 (36), 391 (64), 390 (61), 389 (84), 388 (11), 387 (13), 362 (17), 361 (21), 325 (28), 209 (13), 105 (12), 77 (34); HRMS (ESI): calcd for $C_{27}H_{20}FN_2O_3$ ($[M+H]^+$) 439.14525, found 439.14546; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 3026 (w), 2967 (w), 2915 (w), 2853 (w), 1660 (m), 1648 (w), 1633 (w), 1614 (w), 1595 (m), 1502 (m), 1482 (w), 1451 (m), 1422 (w), 1378 (m), 1337 (w), 1328 (w), 1300 (m), 1273 (m), 1252 (m), 1216 (m), 1172 (w), 1161 (w), 1139 (w), 1116 (m), 1079 (w), 1045 (w), 1033 (w), 1013 (m), 995 (m), 937 (w), 925 (w), 888 (w), 869 (m), 848 (w), 829 (m), 808 (w), 783 (m), 762 (s), 744 (m), 723 (m), 692 (s), 668 (m), 640 (s), 621 (s), 611 (s), 590 (m), 569 (m), 554 (m), 545 (m), 527 (m).

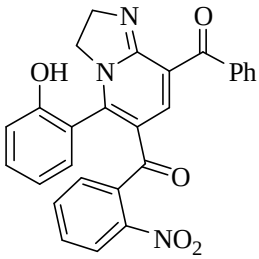
2-[8-Benzoyl-6-(thiophene-2-carbonyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl]phenol (27c):



Starting with 3-(2-thenoyl)chromone **6c** (0.256 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27c** was isolated as a orange solid (0.264 g, 62%), mp 281-283 ºC;

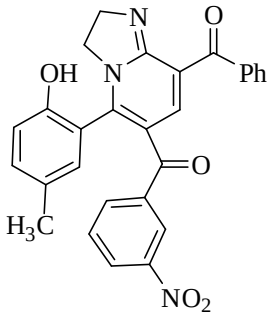
^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.68-3.93 (m, 4H, CH), 6.74 (t, ^3J = 7.5 Hz, 1H, H_{Ar}), 6.84 (d, ^3J = 7.9 Hz, 1H, H_{Ar}), 7.03 (dd, ^3J = 3.8 Hz, ^3J = 4.9 Hz, 1H, H_{Ar}), 7.07 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 7.19 (td, ^3J = 7.8 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 7.46 (s, 1H, 7-H_{Ar}), 7.49-7.54 (m, 2H, H_{Ar}), 7.58 (dd, ^3J = 3.8 Hz, ^4J = 1.1 Hz, 1H, H_{Ar}), 7.62 (tt, ^3J = 7.3 Hz, ^4J = 1.3 Hz, 1H, H_{Ar}), 7.81 (dd, ^4J = 1.1 Hz, ^3J = 4.9 Hz, 1H, H_{Ar}), 7.83-7.86 (m, 2H, H_{Ar}), OH was not detected; ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 47.8 (NCH_2), 52.3 (NCH_2), 114.0, 116.0, 118.8, 119.7, 120.4, 127.8, 2^{x}128.5, 129.1, 2^{x}129.2, 131.3, 132.9, 133.1, 134.0, 137.0, 141.3, 144.0, 152.7, 153.4, 154.4, 183.6 (C=O), 192.3 (C=O); MS (GC, 70 eV) *m/z* (%): 409 ([M-OH], 14), 408 (44), 407 (65), 381 (18), 380 (67), 379 (100), 351 (10), 295 (12), 77 (27); HRMS (ESI): calcd for $C_{25}H_{19}N_2O_3S$ ($[M+H]^+$) 427.11109, found 427.11168, calcd for $C_{25}H_{18}NaN_2O_3S$ ($[M+Na]^+$) 449.09303, found 449.09347; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3065 (w), 2953 (w), 2911 (w), 2883 (w), 2851 (w), 1657 (s), 1615 (s), 1595 (s), 1536 (w), 1503 (s), 1453 (s), 1409 (s), 1376 (s), 1352 (m), 1326 (m), 1300 (m), 1278 (w), 1256 (s), 1234 (m), 1217 (s), 1195 (m), 1182 (m), 1163 (m), 1119 (m), 1080 (w), 1059 (m), 1044 (w), 1034 (m), 1010 (s), 969 (m), 939 (w), 908 (w), 891 (w), 873 (m), 853 (w), 842 (m), 831 (m), 804 (m), 779 (m), 759 (s), 742 (s), 710 (s), 693 (s), 673 (m), 648 (s), 621 (m), 612 (m), 580 (m), 556 (m), 531 (w).

2-[8-Benzoyl-6-(2-nitrobenzoyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl]phenol (27d):



Starting with 3-(2-nitrobenzoyl)chromone **6d** (0.295g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27d** was isolated as a yellow solid (0.363 g, 78%), mp 251-253 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.48-3.64 (m, 2H, CH), 3.72-3.79 (m, 2H, CH), 6.51-6.61 (m, 2H, H_{Ar}), 6.96-7.02 (m, 2H, H_{Ar}), 7.27 (d, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.39 (t, ^3J = 7.7 Hz, 1H, H_{Ar}), 7.47-7.58 (m, 3H, H_{Ar}), 7.66 (t, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.75 (s, 1H, 7-H_{Ar}), 7.81-7.88 (m, 3H, H_{Ar}), 10.23 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 47.7 (NCH_2), 52.6 (NCH_2), 112.7, 115.5, 118.6, 118.7, 119.5, 121.5, 123.8, 128.3, 2^x128.6, 2^x129.3, 129.8, 131.6, 133.1, 133.6, 136.5, 136.7, 139.9, 144.6, 152.8, 153.3, 155.0, 188.0 (C=O), 192.3 (C=O); MS (GC, 70 eV) *m/z* (%): 465 ([M]$^+$, 6), 464 (17), 418 (32), 417 (100), 390 (15), 389 (41), 361 (8), 105 (11), 77 (20), 44 (19); HRMS (ESI): calcd for $C_{27}H_{20}N_3O_5$ ([M+H]$^+$) 466.13963, found 466.13975; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3070 (w), 3051 (w), 2949 (w), 2925 (w), 2876 (w), 2679 (w), 2561 (w), 1662 (m), 1640 (m), 1616 (m), 1589 (s), 1520 (s), 1505 (m), 1471 (w), 1449 (s), 1430 (m), 1375 (s), 1339 (s), 1313 (m), 1293 (s), 1258 (m), 1247 (s), 1223 (s), 1174 (m), 1156 (m), 1107 (w), 1079 (w), 1037 (w), 1012 (m), 997 (m), 975 (w), 945 (m), 926 (w), 867 (w), 856 (w), 836 (w), 811 (w), 798 (m), 789 (s), 760 (s), 711 (s), 688 (s), 679 (s), 654 (m), 639 (m), 614 (m), 586 (m), 554 (m), 545 (m).

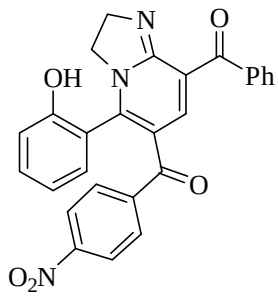
2-[8-Benzoyl-6-(3-nitrobenzoyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl]-4-methylphenol (27e):



Starting with 6-methyl-3-(3-nitrobenzoyl)chromone **6h** (0.309 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27e** was isolated as a yellow solid (0.259 g, 54%), mp 248 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.00 (s, 3H, CH_3), 3.65-3.85 (m, 4H, CH), 6.44 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 6.76 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 6.81 (s, 1H, H_{Ar}), 7.46 (t, ^3J = 7.9 Hz, 1H, H_{Ar}), 7.52-7.55 (m, 2H, H_{Ar}), 7.58 (s, 1H, H_{Ar}), 7.63-7.66 (m, 1H, H_{Ar}), 7.72 (d, ^3J = 7.7 Hz, 1H, H_{Ar}), 7.88 (d, ^3J = 7.3 Hz, 2H, H_{Ar}), 8.05 (s, 1H, H_{Ar}), 8.07 (d, ^3J = 8.2 Hz, ^4J = 1.3 Hz, 1H, H_{Ar}), 10.10 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.5 (CH_3), 47.8 (NCH_2), 52.6 (NCH_2), 113.2, 115.6, 119.3, 121.1, 122.3, 124.9, 127.6, 2^x128.5, 129.2, 2^x129.3, 129.9, 132.2, 133.0, 133.8, 136.8, 140.7, 141.0, 146.4, 151.8, 153.3, 154.0, 190.3 (C=O), 192.3 (C=O); MS (EI, 70 eV) *m/z* (%): 479 ([M]$^+$, 72), 450 (29), 449 (14), 374 (17), 358 (29), 357 (100), 105 (26), 77 (29); HRMS (ESI): calcd for $C_{28}H_{22}N_3O_5$ ([M+H]$^+$) 480.15540, found 480.15555, calcd for $C_{28}H_{21}NaN_3O_5$ ([M+Na]$^+$)

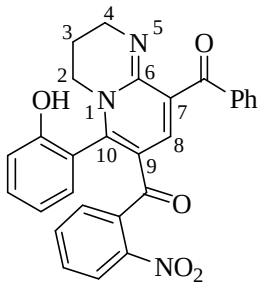
502.13734, found 502.13690; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2913 (w), 2876 (w), 2849 (w), 1664 (m), 1642 (w), 1595 (s), 1526 (s), 1503 (s), 1474 (w), 1435 (m), 1373 (m), 1342 (s), 1285 (s), 1252 (s), 1218 (s), 1196 (s), 1176 (s), 1140 (w), 1118 (s), 1094 (w), 1081 (w), 1042 (w), 1001 (s), 938 (w), 890 (w), 871 (s), 859 (w), 817 (m), 795 (m), 770 (w), 746 (w), 717 (s), 688 (s), 659 (m), 633 (m), 613 (m), 595 (m), 569 (m).

2-[8-Benzoyl-6-(4-nitrobenzoyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-5-yl]phenol (27f):



Starting with 3-(4-nitrobenzoyl)chromone **6i** (0.295g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27f** was isolated as a orange solid (0.237 g, 51%), mp 248-250 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.78 (s, 4H, CH), 6.59-6.67 (m, 2H, H_{Ar}), 7.01-7.06 (m, 2H, H_{Ar}), 7.51-7.59 (m, 5H, H_{Ar}), 7.64 (tt, ^{3}J = 6.8 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 7.85-7.88 (m, 2H, H_{Ar}), 7.98-8.01 (m, 2H, H_{Ar}), 10.38 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 47.8 (NCH_2), 52.5 (NCH_2), 113.5, 116.0, 118.8, 119.9, 120.9, 2^x122.5, 2^x128.5, 2^x129.0, 2^x129.3, 129.8, 131.8, 133.0, 136.8, 140.7, 145.1, 148.0, 153.3, 154.1, 192.3 (C=O); MS (EI, 70 eV) *m/z* (%): 465 ($[M]^+$, 25), 464 (64), 463 (36), 462 (70), 447 (38), 446 (67), 436 (25), 435 (32), 434 (42), 420 (20), 419 (82), 418 (100), 313 (20), 285 (48), 77 (22); HRMS (ESI): calcd for $C_{27}H_{20}N_3O_5$ ($[M+H]^+$) 466.13975, found 466.14014, calcd for $C_{27}H_{19}NaN_3O_5$ ($[M+Na]^+$) 488.12169, found 488.12159; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2943 (w), 2879 (w), 2661 (w), 2559 (w), 2472 (w), 1664 (s), 1651 (m), 1619 (m), 1597 (s), 1566 (w), 1518 (m), 1500 (m), 1453 (s), 1422 (w), 1404 (w), 1380 (m), 1337 (s), 1316 (m), 1301 (s), 1248 (s), 1219 (s), 1195 (m), 1164 (m), 1139 (w), 1106 (w), 1047 (w), 1036 (w), 1012 (m), 996 (m), 945 (w), 925 (w), 863 (m), 851 (m), 831 (w), 805 (w), 789 (s), 777 (w), 765 (s), 747 (m), 733 (m), 698 (s), 685 (m), 652 (m), 627 (m), 587 (m), 556 (m), 538 (w).

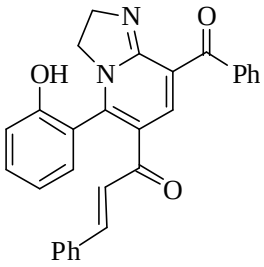
2-[9-Benzoyl-7-(2-nitrobenzoyl)-2*H*,3*H*,4*H*-pyrido[1,2-*a*]pyrimidin-6-yl]phenol (27g):



Starting with 3-(2-nitrobenzoyl)chromone **6d** (0.295g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27g** was isolated as a yellow solid (0.441 g, 92%), mp 224-225 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.63-1.74 (m, 2H, CH), 3.19-3.23 (m, 1H, CH), 3.31-3.45 (m, 3H, CH), 6.45 (d, ^{3}J = 7.9 Hz, 1H, H_{Ar}), 6.60 (t, ^{3}J = 7.3 Hz, 1H, H_{Ar}), 6.95-7.00 (m, 2H, H_{Ar}), 7.20 (dd, ^{3}J = 7.3 Hz, ^{4}J = 1.3 Hz, 1H, H_{Ar}), 7.40 (td, ^{3}J = 7.8 Hz, ^{4}J = 1.3 Hz, 1H, H_{Ar}), 7.45-7.48 (m, 2H, H_{Ar}), 7.51-7.56 (m,

2H, H_{Ar}), 7.64 (t, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.84 (dd, ^3J = 8.1 Hz, ^4J = 0.9 Hz, 1H, H_{Ar}), 7.91-7.93 (m, 2H, H_{Ar}), 10.20 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.2 (CH_2), 43.5 (NCH_2), 46.2 (NCH_2), 113.8, 115.2, 118.8, 118.9, 123.8, 128.2, 128.3, 2^{x}128.6, 2^{x}129.1, 129.7, 129.8, 130.4, 131.7, 133.2, 133.5, 136.4, 136.6, 144.4, 146.8, 154.3, 154.6, 189.7 (C=O), 194.5 (C=O); MS (EI, 70 eV) *m/z* (%): 433 ([M-NO_2], 8), 432 (43), 431 (90), 405 (11), 404 (75), 403 (100), 375 (33), 77 (11); HRMS (ESI): calcd for $C_{28}H_{22}N_3O_5$ ([M+H]$^+$) 480.15579, found 480.15540; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2942 (w), 2849 (w), 2678 (w), 2543 (w), 1668 (m), 1635 (m), 1615 (s), 1603 (s), 1573 (s), 1531 (m), 1519 (s), 1506 (m), 1472 (w), 1450 (s), 1417 (w), 1366 (s), 1344 (s), 1310 (m), 1293 (m), 1250 (s), 1189 (m), 1171 (s), 1156 (m), 1144 (m), 1109 (m), 1087 (m), 1072 (m), 1045 (m), 1020 (m), 970 (m), 954 (m), 932 (m), 877 (m), 853 (m), 826 (w), 805 (w), 789 (m), 773 (w), 755 (s), 740 (s), 716 (m), 706 (s), 689 (s), 680 (s), 650 (w), 636 (m), 610 (m), 596 (m), 557 (w), 530 (w).

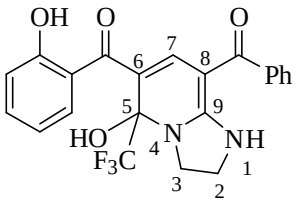
(2*E*)-1-[8-Benzoyl-5-(2-hydroxyphenyl)-2*H*,3*H*-imidazo[1,2-*a*]pyridin-6-yl]-3-phenyl-prop-2-en-1-one (27h):



Starting with 3-[(2*E*)-3-phenylprop-2-enoyl]chromone **7** (0.276 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **27h** was isolated as a yellow solid (0.290 g, 65%), mp 184 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.63-3.69 (m, 1H, CH), 3.76-3.83 (m, 2H, CH), 3.83-3.89 (m, 1H, CH), 6.44 (d, ^3J = 15.7 Hz, 1H, =CH-), 6.86 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.10 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 7.16-7.20 (m, 3H, H_{Ar}), 7.26-7.33 (m, 5H, H_{Ar}), 7.51-7.54 (m, 2H, H_{Ar}), 7.64 (tt, ^3J = 7.4 Hz, ^4J = 1.2 Hz, 1H, H_{Ar}), 7.73 (s, 1H, 7-H_{Ar}), 7.82-7.82 (m, 2H, H_{Ar}), OH was not detected; ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 47.8 (NCH_2), 52.6 (NCH_2), 115.2, 116.8, 188.9, 121.1, 121.2, 124.8, 2^{x}127.8, 2^{x}128.5, 2^{x}128.7, 2^{x}129.2, 129.5, 129.9, 132.0, 132.9, 134.7, 137.0, 140.0, 140.6, 153.2, 153.3, 153.9, 185.3 (C=O), 192.6 (C=O); MS (EI, 70 eV) *m/z* (%): 446 ([M]$^+$, 27), 445 (69), 429 (49), 428 (100), 427 (54), 399 (41), 341 (36), 330 (40), 315 (40), 313 (44), 165 (33), 138 (46), 131 (27), 120 (88), 105 (97), 77 (71), 44 (45); HRMS (ESI): calcd for $C_{29}H_{23}N_2O_3$ ([M+H]$^+$) 447.17032, found 447.17099, calcd for $C_{29}H_{22}NaN_2O_3$ ([M+Na]$^+$) 469.15226, found 469.15173; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 3026 (w), 2924 (w), 2871 (w), 1726 (w), 1645 (w), 1615 (w), 1591 (m), 1574 (m), 1493 (w), 1447 (m), 1422 (w), 1374 (m), 1349 (w), 1319 (w), 1294 (m), 1276 (m), 1201 (s), 1154 (m), 1108 (w), 1070 (w), 1033 (w), 1014 (m), 1000 (m), 975 (m), 860 (w), 832 (w), 817

(w), 802 (w), 752 (s), 731 (s), 694 (s), 666 (s), 653 (m), 642 (s), 587 (w), 562 (s), 537 (m), 530 (m).

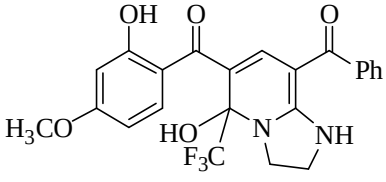
8-Benzoyl-6-(2-hydroxybenzoyl)-5-(trifluoromethyl)-1*H*,2*H*,3*H*,5*H*-imidazolidino-[1,2-*a*]pyridin-5-ol (28a):



Starting with 3-(trifluoroacetyl)chromone **5a** (0.242 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28a** was isolated as a yellow solid (0.202 g, 47%), mp 150-151 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.80-4.00 (m, 4H, CH), 6.76-6.84 (m, 2H, H_{Ar}), 7.12 (dd, ^3J = 7.6 Hz, ^4J = 1.7 Hz, 1H, H_{Ar}), 7.20 (dd, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H_{Ar}), 7.36-7.42 (m, 6H, H_{Ar}), 9.04, 9.46, 9.99 (all three s, 3H, 2OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 42.8 (NCH_2), 43.5 (NCH_2), 84.3 (q, $^2J_{C,F}$ = 32.8 Hz, 5-C), 91.7 (8-C), 105.9, 116.1, 118.8, 125.6, 2^{x}128.0, 2^{x}128.1, 129.4, 130.5, 131.7, 138.6, 148.9, 154.9, 158.0, 188.6 (C=O), 195.2 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –81.6 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 362 ([M-CF_3+H], 17), 361 (80), 345 (12), 344 (73), 343 (100), 268 (19), 267 (88), 265 (12), 105 (19), 89 (11), 78 (28), 71 (12), 69 (11), 63 (29), 57 (19), 45 (17); HRMS (EI): calcd for $C_{22}H_{17}F_3N_2O_4$ ([M]$^+$) 430.11349, found 430.11384; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3311 (w), 3046 (w), 2899 (w), 1619 (m), 1571 (s), 1549 (s), 1506 (m), 1476 (s), 1445 (m), 1395 (m), 1354 (w), 1292 (w), 1277 (w), 1320 (m), 1206 (s), 1167 (s), 1151 (s), 1123 (s), 1033 (s), 1014 (s), 980 (s), 952 (s), 921 (s), 864 (m), 790 (w), 761 (s), 697 (s), 675 (s), 637 (s), 615 (s), 529 (s).

8-Benzoyl-6-(2-hydroxy-4-methoxybenzoyl)-5-(trifluoromethyl)-1*H*,2*H*,3*H*,5*H*-imidazolidino[1,2-*a*]pyridin-5-ol (28b):

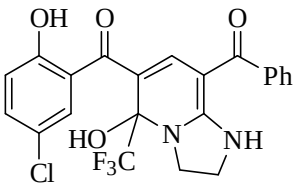


Starting with 7-methoxy-3-(trifluoroacetyl)chromone **5b** (0.272 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28b** was isolated as a yellow solid (0.281 g, 61%), mp 194-196 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.73 (s, 3H, OCH_3), 3.78-4.00 (m, 4H, CH), 6.39 (d, ^4J = 2.3 Hz, 1H, H_{Ar}), 6.45 (dd, ^3J = 8.6 Hz, ^4J = 2.3 Hz, 1H, H_{Ar}), 7.24 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.32 (s, 1H, 7-H), 7.39-7.48 (m, 5H, H_{Ar}), 9.02, 9.45, 10,62 (all three s, 3H, 2OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 42.9 (NCH_2), 43.4 (NCH_2), 55.4 (OCH_3), 84.3 (q, $^2J_{C,F}$ = 32.5 Hz, 5-C), 91.1 (8-C), 101.3, 105.3, 105.7, 116.8, 2^{x}128.1, 2^{x}128.2, 130.5, 132.1, 138.9, 147.2, 157.8, 159.1, 163.2, 188.7 (C=O), 195.6 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –81.4 (s,

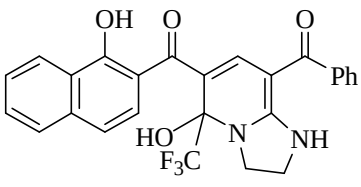
1F, F); MS (EI, 70 eV) *m/z* (%): 391 ([M-CF_3], 14) 375 (14), 374 (65), 373 (100), 267 (54), 203 (12), 187 (10), 99 (13), 84 (11), 69 (15), 57 (14), 44 (22); HRMS (EI): calcd for $C_{23}H_{19}F_3N_2O_5$ ([M]$^+$) 460.12406, found 460.12484; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3328 (w), 3042 (w), 3004 (w), 2963 (w), 2934 (w), 2907 (w), 2838 (w), 1621 (w), 1572 (m), 1547 (m), 1504 (m), 1482 (w), 1440 (w), 1409 (w), 1389 (w), 1363 (w), 1323 (w), 1284 (w), 1240 (m), 1204 (s), 1148 (s), 1099 (s), 1029 (m), 1015 (m), 980 (m), 953 (s), 921 (s), 839 (m), 823 (w), 776 (s), 748 (s), 708 (s), 682 (s), 647 (s), 606 (s), 552 (m), 529 (s).

8-Benzoyl-6-(5-chloro-2-hydroxybenzoyl)-5-(trifluoromethyl)-1*H*,2*H*,3*H*,5*H*-imidazolidino[1,2-*a*]pyridin-5-ol (28c):



Starting with 6-chloro-3-(trifluoroacetyl)chromone **5c** (0.276 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28c** was isolated as a yellow solid (0.223 g, 48%), mp 167 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.78-4.01 (m, 4H, CH), 6.84 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.06 (d, ^4J = 2.7 Hz, 1H, H_{Ar}), 7.22 (dd, ^3J = 8.7 Hz, ^4J = 2.7 Hz, 1H, H_{Ar}), 7.34 (s, 1H, 7-H), 7.37-7.46 (m, 5H, H_{Ar}), 8.78, 9.48, 10.23 (all three s, 3H, 2OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 42.9 (NCH_2), 43.5 (NCH_2), 84.1 (q, $^2J_{C,F}$ = 33.1 Hz, 5-C), 92.6 (8-C), 105.8, 117.8, 122.3, 127.8, 2^{x}128.0, 2^{x}128.1, 128.2, 130.6, 130.8, 138.5, 149.3, 153.4, 157.9, 188.6 (C=O), 192.5 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = –81.4 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 395 ([M-CF_3], 24), 380 (16), 379 (81), 378 (53), 377 (100), 267 (30), 149 (10), 105 (11), 99 (33), 78 (51), 77 (10), 63 (55), 57 (13); HRMS (EI): calcd for $C_{22}H_{16}{}^{35}ClF_3N_2O_4$ ([M]$^+$) 464.07452, found 464.07463; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3274 (w), 1619 (w), 1562 (s), 1496 (m), 1463 (s), 1445 (m), 1395 (m), 1319 (m), 1280 (w), 1247 (m), 1210 (s), 1159 (s), 1099 (s), 1032 (m), 1013 (s), 984 (m), 965 (m), 954 (m), 922 (s), 903 (m), 836 (w), 825 (m), 800 (w), 781 (s), 743 (s), 728 (m), 697 (s), 657 (s), 639 (s), 578 (s), 528 (s).

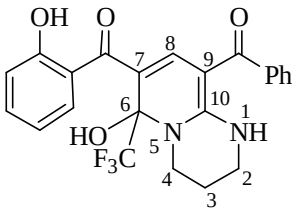
8-Benzoyl-6-(1-hydroxynaphthalene-2-carbonyl)-5-(trifluoromethyl)-1*H*,2*H*,3*H*,5*H*-imidazolidino[1,2-*a*]pyridin-5-ol (28d):



Starting with 3-(trifluoroacetyl)benzo[*h*]chromone **5e** (0.292 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28d** was isolated as a yellow solid (0.163 g, 34%), mp 177-178 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.82-4.04 (m, 4H, CH), 7.31-7.34 (m, 3H, H_{Ar}), 7.37 (s, 1H, 7-H), 7.40-7.47 (m, 4H, H_{Ar}), 7.52-7.64 (m, 2H, H_{Ar}), 7.86 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 8.27 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 8.83, 9.49, 10.76 (all three s, 3H, 2OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 42.9 (NCH_2), 43.3 (NCH_2), 84.4 (q, $^{2}J_{C,F}$ = 32.8 Hz, 5-C), 91.3 (8-C), 104.9, 115.8, 118.3, 123.1, 124.5 (q, $^{1}J_{C,F}$ = 295.7 Hz), 124.6, 125.9, 126.3, 127.6, 2^{x}127.9, 2^{x}128.1, 128.9, 130.3, 135.7, 138.9, 147.4, 156.7, 157.6, 188.9 (C=O), 196.7 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -80.9 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 463 ([M-OH], 11), 462 (40), 411 (26), 395 (28), 394 (84), 393 (100), 391 (11), 268 (12), 267 (74), 231 (18), 196 (12), 105 (20), 77 (17), 69 (12), 57 (12), 44 (16); HRMS (EI): calcd for $C_{26}H_{19}F_3N_2O_4$ ([M]$^{+}$) 480.12914, found 480.12930; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3308 (w), 3049 (w), 2954 (w), 2895 (w), 1614 (w), 1588 (m), 1564 (m), 1549 (m), 1502 (m), 1479 (w), 1451 (m), 1400 (m), 1357 (w), 1318 (w), 1241 (m), 1204 (s), 1193 (s), 1164 (s), 1145 (s), 1128 (s), 1097 (s), 1025 (m), 1015 (m), 998 (m), 955 (m), 923 (s), 882 (m), 830 (m), 803 (m), 794 (m), 760 (s), 745 (s), 698 (s), 658 (s), 610 (m), 593 (s), 581 (s), 556 (s), 536 (s).

9-Benzoyl-7-(2-hydroxybenzoyl)-6-(trifluoromethyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]-pyrimidin-6-ol (28e):

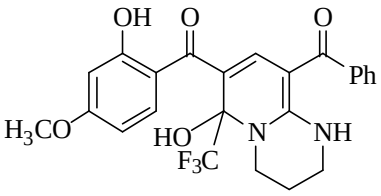


Starting with 3-(trifluoroacetyl)chromone **5a** (0.242 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28e** was isolated as a yellow solid (0.391 g, 88%), mp 177-178 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.81-1.91 (m, 1H, CH), 2.02-2.09 (m, 1H, CH), 3.39-3.48 (m, 1H, CH), 3.55-3.61 (m, 2H, CH), 3.80-3.85 (m, 1H, CH), 6.72-6.80 (m, 2H, H_{Ar}), 7.06 (dd, ^{3}J = 7.6 Hz, ^{4}J = 1.6 Hz, 1H, H_{Ar}), 7.13-7.18 (m, 1H, H_{Ar}), 7.29 (s, 1H, 8-H), 7.36-7.39 (m, 5H, H_{Ar}), 9.88, 10.01, 11.47 (all three s, 3H, 2OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.1 (CH_2), 38.6 (NCH_2), 39.8 (NCH_2), 84.3 (q, $^{2}J_{C,F}$ = 32.7 Hz, 6-C), 94.4 (9-C), 103.8, 116.0, 118.7, 125.0 (q, $^{1}J_{C,F}$ = 296.5 Hz), 125.3, 128.0, 128.3, 129.0, 129.1, 130.4, 131.3, 131.4, 139.1, 149.3, 154.5, 154.8, 190.4 (C=O), 195.6 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -83.9 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 444 ([M]$^{+}$, 9), 397 (12), 376 (45), 375 (92), 357 (42), 282 (41), 281 (100), 105 (19), 91 (12), 77 (13); HRMS (ESI): calcd for $C_{23}H_{20}F_3N_2O_4$ ([M+H]$^{+}$) 445.13697, found 445.13743, calcd for $C_{23}H_{19}F_3NaN_2O_4$ ([M+Na]$^{+}$) 467.11891, found 467.11891; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 2937 (w), 2865 (w), 1733 (w), 1610 (m), 1597 (m), 1575 (m), 1538 (w), 1512 (w), 1475 (m), 1446 (m), 1379 (m), 1351 (w), 1327 (m), 1287 (w), 1263 (m), 1234 (m), 1206 (m), 1173 (s), 1151 (s), 1132 (s), 1074 (m), 1051

(w), 1037 (w), 992 (w), 965 (m), 938 (s), 866 (w), 847 (w), 817 (w), 803 (w), 760 (s), 733 (s), 702 (s), 676 (s), 642 (s), 593 (m), 566 (m), 531 (m).

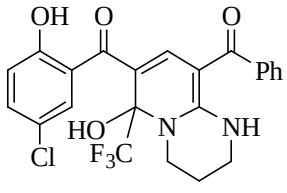
9-Benzoyl-7-(2-hydroxy-4-methoxybenzoyl)-6-(trifluoromethyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]pyrimidin-6-ol (28f):



Starting with 7-methoxy-3-(trifluoroacetyl)chromone **5b** (0.272 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28e** was isolated as a yellow solid (0.341 g, 72%), mp 187-188 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.78-1.94 (m, 1H, CH), 2.00-2.12 (m, 1H, CH), 3.39-3.48 (m, 1H, CH), 3.52-3.63 (m, 2H, CH), 3.70 (s, 3H, OCH_3), 3.77-3.86 (m, 1H, CH), 6.34 (d, ^{4}J = 2.3 Hz, 1H, H_{Ar}), 6.39 (dd, ^{3}J = 8.6 Hz, ^{4}J = 2.3 Hz, 1H, H_{Ar}), 7.12 (dd, ^{3}J = 8.6 Hz, 1H, H_{Ar}), 7.28 (s, 1H, 8-H), 7.39-7.44 (m, 5H, H_{Ar}), 10.03, 10.26, 11.51 (all three s, 3H, 2OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.2 (CH_2), 38.6 (NCH_2), 39.8 (NCH_2), 55.3 (OCH_3), 84.4 (q, $^{2}J_{C,F}$ = 32.5 Hz, 6-C), 93.9 (9-C), 101.3, 103.6, 105.4, 117.2, 2^{x}128.2, 2^{x}128.3, 130.3, 131.5, 139.4, 148.3, 154.7, 157.8, 162.6, 190.5 (C=O), 195.7 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -83.9 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 474 ([M]$^{+}$, 14), 406 (31), 405 (100), 389 (20), 388 (85), 387 (89), 359 (23), 282 (81), 281 (79), 203 (11), 179 (16), 151 (13), 135 (20), 105 (25), 91 (33), 77 (18), 69 (68), 51 (28); HRMS (EI): calcd for $C_{24}H_{21}F_3N_2O_5$ ([M]$^{+}$) 474.13971, found 474.13995; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 3038 (w), 3004 (w), 2926 (w), 2851 (w), 1738 (w), 1598 (m), 1568 (s), 1506 (m), 1473 (w), 1456 (w), 1440 (m), 1423 (w), 1407 (w), 1388 (m), 1369 (m), 1349 (s), 1316 (w), 1294 (w), 1264 (m), 1240 (s), 1225 (s), 1199 (s), 1171 (s), 1155 (s), 1134 (s), 1108 (s), 1076 (m), 1060 (m), 1025 (m), 999 (w), 985 (m), 972 (m), 949 (s), 939 (s), 920 (m), 877 (w), 862 (w), 826 (s), 777 (s), 754 (s), 736 (s), 706 (s), 697 (s), 668 (m), 644 (s), 610 (s), 577 (m), 535 (s).

9-Benzoyl-7-(5-chloro-2-hydroxybenzoyl)-6-(trifluoromethyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]pyrimidin-6-ol (28g):

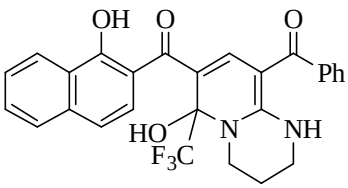


Starting with 6-chloro-3-(trifluoroacetyl)chromone **5c** (0.276 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28g** was isolated as a yellow solid (0.454 g, 95%), mp 171 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.78-1.94 (m, 1H, CH), 2.00-2.13 (m, 1H, CH), 3.42-3.50 (m, 1H, CH), 3.51-3.65 (m, 2H, CH), 3.77-3.88 (m, 1H, CH), 6.80 (d, ^{3}J

= 8.7 Hz, 1H, H_{Ar}), 7.02 (d, ^4J = 1.7 Hz, 1H, H_{Ar}), 7.19 (dd, ^3J = 8.7 Hz, ^4J = 1.7 Hz, 1H, H_{Ar}), 7.25 (s, 1H, 8-H), 7.36-7.40 (m, 5H, H_{Ar}), 9.72, 10.19, 11.42 (all three s, 3H, 2OH and NH); ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 19.0 (CH_2), 38.7 (NCH_2), 39.7 (NCH_2), 84.2 (q, $^2J_{C,F}$ = 32.4 Hz, 6-C), 94.8 (9-C), 103.7, 117.7, 122.2, 124.9 (q, $^1J_{C,F}$ = 296.2 Hz), 127.2, 127.9, 2^{x}128.0, 2^{x}128.1, 130.4, 130.7, 139.1, 149.6, 153.2, 154.8, 190.6 (C=O), 193.0 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -83.8 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 411 ([M-CF_3+2H], 52), 410 (32), 409 (99), 393 (26), 392 (13), 391 (66), 282 (26), 281 (100), 253 (10), 105 (21), 91 (16), 77 (16); HRMS (ESI): calcd for $C_{23}H_{18}{}^{35}ClF_3N_2O_4$ ([M+H]$^+$) 479.09800, found 479.09794, calcd for $C_{23}H_{18}{}^{37}ClF_3N_2O_4$ ([M+H]$^+$) 481.09605, found 481.09590; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3070 (w), 2955 (w), 2919 (w), 2867 (w), 2851 (w), 1600 (m), 1568 (m), 1516 (m), 1462 (m), 1456 (m), 1443 (w), 1405 (m), 1381 (m), 1365 (m), 1318 (w), 1293 (m), 1263 (m), 1231 (m), 1216 (m), 1149 (s), 1130 (s), 1074 (m), 1055 (m), 1025 (m), 998 (m), 980 (w), 942 (s), 907 (m), 874 (w), 848 (w), 836 (m), 817 (w), 783 (s), 743 (m), 724 (m), 701 (s), 642 (s), 596 (m), 555 (m), 534 (m).

9-Benzoyl-7-(1-hydroxynaphthalene-2-carbonyl)-6-(trifluoromethyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]pyrimidin-6-ol (28h):

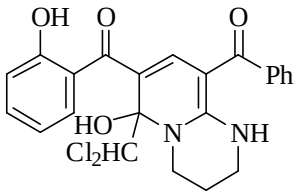


Starting with 3-(trifluoroacetyl)benzo[*h*]chromone **5e** (0.292 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28h** was isolated as a yellow solid (0.385 g, 78%), mp 192-193 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.81-1.97 (m, 1H, CH), 2.01-2.14 (m, 1H, CH), 3.43-3.51 (m, 1H, CH), 3.54-3.67 (m, 2H, CH), 3.80-3.92 (m, 1H, CH), 7.27-7.40 (m, 8H, H_{Ar}), 7.50-7.61 (m, 2H, H_{Ar}), 7.82 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 8.27 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 9.82, 11.00, 11.46 (all three s, 3H, 2OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.2 (CH_2), 38.7 (NCH_2), 39.7 (NCH_2), 84.5 (q, $^2J_{C,F}$ = 32.6 Hz, 6-C), 94.3 (9-C), 103.3, 107.8, 116.8, 118.5, 123.0, 124.6, 125.8, 126.1, 127.6, 2^{x}128.1, 2^{x}128.2, 128.4, 130.2, 135.4, 139.4, 148.6, 154.7, 190.8 (C=O), 196.3 (C=O); ^{19}F NMR (282.4 MHz, DMSO-d_6): δ = -83.6 (s, 1F, F); MS (EI, 70 eV) *m/z* (%): 494 ([M]$^+$, 6), 426 (9), 425 (34), 409 (9), 408 (21), 407 (92), 282 (15), 281 (100), 69 (38), 51 (26); HRMS (EI): calcd for $C_{27}H_{21}F_3N_2O_4$ ([M]$^+$) 494.14479, found 494.14498; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3059 (w), 3027 (w), 2875 (w), 1617 (w), 1589 (m), 1569 (m), 1538 (w), 1515 (m), 1458 (m), 1438 (m), 1405 (m), 1367 (m), 1323 (w), 1289 (w), 1266 (m), 1240 (s), 1208 (m), 1160 (s), 1144 (s), 1130 (s), 1094 (m), 1058 (s), 1024 (m), 1006 (m), 940 (s), 894 (w), 880 (w), 858 (w),

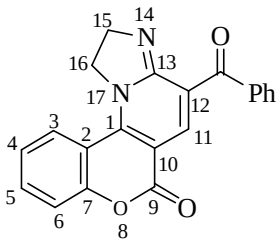
809 (m), 787 (s), 758 (s), 742 (s), 718 (m), 695 (s), 688 (s), 667 (s), 657 (s), 643 (s), 601 (s), 578 (m), 570 (m), 544 (w).

9-Benzoyl-6-(dichloromethyl)-7-(2-hydroxybenzoyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]-pyrimidin-6-ol (28i):



Starting with 3-(2,2-dichloroacetyl)chromone **8** (0.257 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **28i** was isolated as a yellow solid (0.230 g, 50%), mp 150-151 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.90-2.08 (m, 2H, CH), 3.37-3.47 (m, 1H, CH), 3.48-3.59 (m, 2H, CH), 3.99-4.08 (m, 1H, CH), 6.62 (s, 1H, $CHCl_2$), 6.75-6.80 (m, 2H, H_{Ar}), 7.14-7.20 (m, 3H, H_{Ar}), 7.34-7.38 (m, 5H, H_{Ar}), 9.39, 9.81, 11.33 (all three s, 3H, 2OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.3 (CH_2), 38.4 (NCH_2), 39.8 (NCH_2), 78.6 ($CHCl_2$), 88.4 (6-C), 94.8 (9-C), 107.5, 116.3, 118.5, 124.8, 2^{x}127.9, 2^{x}128.3, 129.5, 130.0, 131.5, 139.6, 148.3, 154.9, 155.5, 190.1 (C=O), 195.7 (C=O); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2996 (w), 2954 (w), 2921 (w), 2871 (w), 1612 (m), 1580 (s), 1519 (m), 1477 (m), 1421 (m), 1370 (m), 1345 (w), 1317 (m), 1304 (m), 1268 (m), 1205 (s), 1179 (s), 1145 (s), 1094 (m), 1074 (m), 1056 (m), 1029 (m), 997 (m), 956 (m), 943 (m), 886 (w), 874 (w), 846 (w), 793 (s), 781 (m), 742 (s), 702 (s), 690 (s), 673 (s), 642 (s), 616 (s), 562 (m), 532 (m).

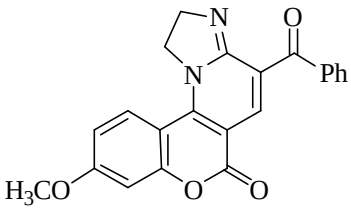
12-Benzoyl-8-oxa-14,17-diazatetracyclo[8.7.0.0^{2,7}.0^{13,17}]heptadeca-1(10),2(7),3,5,11,13-hexaen-9-one (29a):



Starting with 3-(heptafluorobutanoyl)chromone **5q** (0.342 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **29a** was isolated as a red solid (0.311 g, 91%), mp 256-257 ºC; ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C): δ = 4.03 (t, ^3J = 9.6 Hz, 2H, CH), 4.65 (t, ^3J = 9.6 Hz, 2H, CH), 7.43-7.45 (m, 2H, H_{Ar}), 7.50-7.53 (m, 2H, H_{Ar}), 7.60 (s, 1H, 11-H_{Ar}), 7.63 (td, ^4J = 1.2 Hz, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.74 (td, ^4J = 1.2 Hz, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.86-7.88 (m, 2H, H_{Ar}), 8.35 (d, ^3J = 8.6 Hz, 1H, H_{Ar}); ^{13}C NMR (125.6 MHz, DMSO-d_6, 100 °C): δ = 49.9 (NCH_2), 54.1 (NCH_2), 99.0, 112.7, 117.5, 123.9, 124.7, 126.3, 127.8, 2^{x}127.9, 2^{x}128.6, 132.6, 133.1, 135.2, 136.2, 147.9, 153.3, 157.8, 191.4 (C=O); MS (EI, 70 eV) *m/z* (%): 342 ([M]$^+$, 100), 341 (83), 340 (11), 339 (23), 327 (16), 315 (55), 314 (96), 313 (83), 312 (36), 311 (60), 299 (11), 287 (22), 286 (75), 285 (17), 268 (12), 258 (10), 242 (13),

240 (10), 239 (42), 171 (22), 105 (17), 77 (73), 51 (10); HRMS (ESI): calcd for $C_{21}H_{15}N_2O_3$ ($[M+H]^+$) 343.10772, found 343.10788; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3353 (w), 3060 (w), 2961 (w), 2933 (w), 2886 (w), 1715 (w), 1634 (s), 1596 (m), 1562 (s), 1518 (s), 1492 (s), 1449 (m), 1369 (m), 1340 (m), 1300 (m), 1214 (s), 1189 (s), 1176 (s), 1157 (s), 1126 (s), 1048 (m), 1001 (s), 947 (s), 918 (s), 859 (m), 840 (s), 796 (s), 745 (s), 720 (s), 687 (s), 667 (s), 653 (s), 634 (s), 584 (m), 554 (s), 533 (s).

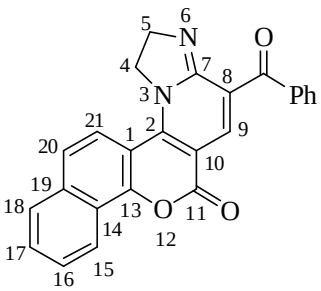
12-Benzoyl-5-methoxy-8-oxa-14,17-diazatetracyclo[8.7.0.0^{2,7}.0^{13,17}]heptadeca-1(10),2(7),3,5,11,13-hexaen-9-one (29b):



Starting with 7-methoxy-3-(trifluoroacetyl)chromone **5b** (0.372 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **29b** was isolated as a red solid (0.115 g, 31%), mp 309-310 ºC;

^{1}H NMR (250 MHz, DMSO-d_6, 100 °C): δ = 3.94 (s, 3H, OCH_3), 4.02 (t, ^3J = 9.6 Hz, 2H, CH), 4.59 (t, ^3J = 9.6 Hz, 2H, CH), 7.00-7.04 (m, 2H, H_{Ar}), 7.47-7.53 (m, 3H, H_{Ar}), 7.60 (s, 1H, 11-H_{Ar}), 7.83-7.87 (m, 2H, H_{Ar}), 8.27 (d, ^3J = 9.7 Hz, 1H, H_{Ar}); ^{13}C NMR (62.9 MHz, DMSO-d_6, 100 °C): δ = 49.1 (NCH_2), 54.0 (NCH_2), 55.6 (OCH_3), 97.0, 101.8, 105.8, 111.8, 123.2, 127.6, 127.7, 2^{x}127.8, 2^{x}128.5, 132.3, 135.8, 136.4, 148.1, 153.3, 155.5, 163.1, 191.3 (C=O); IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3361 (w), 2953 (w), 2884 (w), 1733 (w), 1635 (w), 1611 (w), 1554 (s), 1502 (s), 1412 (s), 1367 (w), 1329 (m), 1276 (m), 1253 (m), 1176 (m), 1153 (s), 1232 (w), 1196 (m), 1186 (m), 1107 (s), 1049 (m), 1020 (m), 997 (m), 964 (w), 951 (w), 930 (w), 918 (w), 881 (w), 843 (m), 796 (s), 755 (s), 727 (s), 709 (s), 692 (s), 659 (s), 645 (s), 623 (s), 588 (s), 554 (s), 534 (s).

8-Benzoyl-12-oxa-3,6-diazapentacyclo[11.8.0.0^{2,10}.0^{3,7}.0^{14,19}]henicosa-1(13),2(10),6,8,14(19),15,17,20-octaen-11-one (29c):

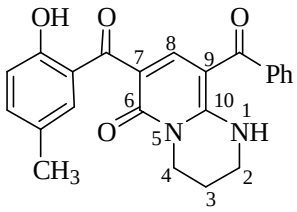


Starting with 3-(heptafluorobutanoyl)benzo[*h*]chromone **5w** (0.392 g, 1.0 mmol) and HKA **24a** (0.207 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **29c** was isolated as a red solid (0.329 g, 84%), mp 337-339 ºC;

^{1}H NMR (500 MHz, DMSO-d_6, 100 °C): δ = 4.06 (t, ^3J = 9.5 Hz, 2H, CH), 4.73 (t, ^3J = 9.5 Hz, 2H, CH), 7.52 (t, ^3J = 7.5 Hz, 2H, H_{Ar}), 7.64 (t, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.67 (s, 1H, 9-H_{Ar}), 7.73-7.80 (m, 2H, H_{Ar}), 7.87-7.90 (m, 3H, H_{Ar}),

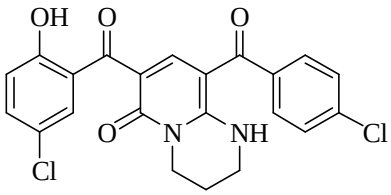
8.04 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 8.33 (d, ^3J = 9.3 Hz, 1H, H_{Ar}), 8.47 (d, ^3J = 8.1 Hz, 1H, H_{Ar}); ^{13}C NMR (125.8 MHz, DMSO-d_6, 100 °C): δ = 49.4 (NCH_2), 53.8 (NCH_2), 98.8, 107.7, 120.6, 121.8, 122.3, 123.0, 124.6, 126.8, 126.9, 2^{x}127.7, 2^{x}128.4, 129.1, 132.3, 134.1, 134.9, 136.2, 148.6, 150.8, 153.1, 157.4, 191.1 (C=O); MS (EI, 70 eV) *m/z* (%): 392 ($[M]^+$, 42), 391 (100), 365 (14), 364 (30), 363 (88), 362 (11), 361 (17), 336 (13), 289 (20), 77 (13); HRMS (ESI): calcd for $C_{25}H_{17}N_2O_3$ ($[M+H]^+$) 393.12337, found 393.12345, calcd for $C_{25}H_{16}NaN_2O_3$ ($[M+Na]^+$) 415.10531, found 415.10520; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3337 (w), 3054 (w), 2926 (w), 2873 (w), 1732 (w), 1633 (m), 1558 (s), 1519 (s), 1497 (s), 1417 (s), 1397 (s), 1355 (m), 1330 (m), 1300 (m), 1280 (m), 1265 (m), 1242 (m), 1204 (s), 1188 (s), 1156 (s), 1095 (s), 1052 (s), 1015 (s), 988 (s), 948 (s), 880 (m), 796 (s), 745 (s), 745 (s), 717 (s), 688 (s), 669 (s), 651 (s), 639 (s), 620 (s), 594 (s), 574 (s).

9-Benzoyl-7-(2-hydroxy-5-methylbenzoyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]pyrimidin-6-one (30a):



Starting with 3-(heptafluorobutanoyl)chromone **5r** (0.356 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **30a** was isolated as a yellow solid (0.295 g, 76%), mp 165-166 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.00-2.06 (m, 2H, CH), 2.19 (s, 3H, CH_3), 3.52-3.55 (m, 2H, CH), 3.89-3.93 (m, 2H, CH), 6.74 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.10-7.13 (m, 2H, H_{Ar}), 7.43-7.55 (m, 5H, H_{Ar}), 7.81 (s, 1H, 8-H_{Ar}), 10.34, 10.96 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.3 (CH_2), 19.9 (CH_3), 38.4 (NCH_2), 39.2 (NCH_2), 97.6 (9-C), 112.0, 116.3, 124.6, 127.1, 2^{x}127.9, 2^{x}128.3, 2^{x}130.6, 133.7, 139.3, 147.4, 155.0, 155.5, 158.4, 193.3 (C=O), 193.9 (C=O); MS (EI, 70 eV) *m/z* (%): 388 ($[M]^+$, 8), 254 (13), 253 (13), 203 (88), 202 (100), 187 (42), 186 (10), 185 (16), 173 (28), 126 (11), 125 (47), 109 (30), 105 (17), 78 (13), 77 (16); HRMS (EI): calcd for $C_{23}H_{20}N_2O_4$ ($[M]^+$) 388.14176, found 388.14250; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3179 (w), 3054 (w), 2983 (w), 2951 (w), 2920 (w), 2876 (w), 1675 (w), 1592 (s), 1557 (s), 1502 (m), 1481 (s), 1442 (m), 1403 (m), 1370 (m), 1344 (m), 1326 (m), 1287 (m), 1276 (m), 1258 (m), 1238 (s), 1204 (s), 1177 (s), 1079 (m), 1050 (m), 1028 (m), 1000 (w), 981 (m), 956 (w), 941 (w), 917 (w), 885 (w), 861 (w), 833 (w), 824 (m), 799 (m), 770 (s), 753 (s), 703 (s), 676 (s), 642 (s), 551 (m), 540 (m).

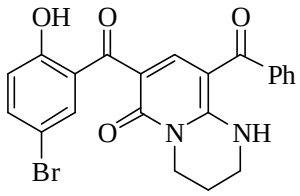
7-(5-Chloro-2-hydroxybenzoyl)-9-(4-chlorobenzoyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]-pyrimidin-6-one (30b):



Starting with 6-chloro-3-(heptafluorobutanoyl)chromone **5t** (0.356 g, 1.0 mmol) and HKA **24c** (0.237 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **30b** was isolated as a yellow solid (0.310 g, 70%), mp 216-217 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.01 (m, 2H, CH), 3.53 (m, 2H, CH), 3.88 (m, 2H, CH), 6.83 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.18 (d, ^4J = 2.4 Hz, 1H, H_{Ar}), 7.27 (dd, ^3J = 8.7 Hz, ^4J = 2.7 Hz, 1H, H_{Ar}), 7.50-7.56 (m, 4H, H_{Ar}), 7.88 (s, 1H, 8-H_{Ar}), 10.21, 10.85 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 18.2 (CH_2), 38.5 (NCH_2), 39.2 (NCH_2), 98.2 (9-C), 111.6, 117.8, 122.1, 2^{x}128.5, 2^{x}129.2, 2^{x}129.9, 131.0, 135.4, 137.9, 147.6, 154.7, 155.1, 158.5, 190.7 (C=O), 192.1 (C=O); MS (EI, 70 eV) *m/z* (%): 442 ([M$^+$], 46), 288 (100), 139 (11), 111 (8); HRMS (ESI): calcd for $C_{22}H_{17}{}^{35}Cl_2N_2O_4$ ([M+H]$^+$) 443.05599, found 443.05675, calcd for $C_{22}H_{17}{}^{37}Cl_2N_2O_4$ ([M+H]$^+$) 445.05353, found 445.05419; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2992 (w), 2873 (w), 1667 (w), 1651 (w), 1588 (s), 1564 (s), 1558 (s), 1503 (m), 1471 (m), 1396 (m), 1371 (m), 1352 (m), 1314 (m), 1292 (m), 1261 (s), 1244 (s), 1205 (s), 1180 (s), 1112 (w), 1088 (m), 1048 (w), 1014 (m), 982 (m), 947 (w), 914 (w), 885 (w), 848 (m), 827 (m), 808 (m), 779 (s), 732 (m), 688 (s), 674 (m), 644 (m), 598 (w), 561 (m), 539 (m).

9-Benzoyl-7-(5-bromo-2-hydroxybenzoyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]pyrimidin-6-one (30c):

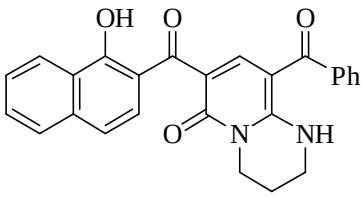


Starting with 6-bromo-3-(heptafluorobutanoyl)chromone **5v** (0.421 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **30c** was isolated as yellow solid (0.344 g, 76%), mp 206-208 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.97-2.06 (m, 2H, CH), 3.50-3.57 (m, 2H, CH), 3.86-3.90 (m, 2H, CH), 6.79 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.26 (d, ^4J = 2.5 Hz, 1H, H_{Ar}), 7.37 (d, ^4J = 2.5 Hz, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.48-7.55 (m, 5H, H_{Ar}), 7.94 (s, 1H, 8-H_{Ar}), 10.25, 10.93 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 18.3 (CH_2), 38.5 (NCH_2), 39.2 (NCH_2), 98.2 (9-C), 109.5, 111.4, 118.3, 2^{x}128.0, 2^{x}128.4, 130.0, 130.7, 131.2, 133.7, 139.2, 147.9, 155.1, 155.2, 158.5, 190.5 (C=O), 193.5 (C=O); MS (EI, 70 eV) *m/z* (%): 452 ([M]$^+$, 39), 255 (17), 254 (100), 253 (99), 105 (8); HRMS (EI): calcd for $C_{22}H_{17}{}^{79}BrN_2O_4$ ([M]$^+$) 452,03662 found 452.03659, calcd for $C_{22}H_{17}{}^{81}BrN_2O_4$ ([M]$^+$) 454,03457 found 454.03485; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w),

2976 (w), 2905 (w), 2869 (w), 1665 (w), 1620 (w), 1596 (s), 1558 (s), 1496 (m), 1463 (s), 1447 (m), 1399 (w), 1373 (m), 1359 (m), 1329 (m), 1310 (m), 1289 (m), 1267 (s), 1238 (s), 1196 (s), 1178 (s), 1122 (m), 1078 (m), 1052 (m), 1020 (w), 1010 (w), 977 (m), 950 (w), 939 (w), 914 (w), 905 (w), 883 (w), 854 (w), 823 (m), 804 (m), 795 (m), 780 (w), 748 (s), 705 (s), 678 (s), 643 (s), 624 (s), 595 (m), 547 (w), 530 (s).

9-Benzoyl-7-(1-hydroxynaphthalene-2-carbonyl)-1*H*,2*H*,3*H*,4*H*,6*H*-pyrido[1,2-*a*]-pyrimidin-6-one (30d):



Starting with 3-(heptafluorobutanoyl)benzo[*h*]chromone **5w** (0.392 g, 1.0 mmol) and HKA **24b** (0.222 g, 1.1 mmol) in 1,4-dioxane (6-7 mL), the product **30d** was isolated as a yellow solid (0.322 g, 76%), mp 268-269 °C;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.07 (s, 2H, CH), 3.57 (s, 2H, CH), 3.96 (m, 2H, CH), 7.30 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.44-7.58 (m, 7H, H_{Ar}), 7.68 (t, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.83-7.88 (m, 2H, H_{Ar}), 8.30 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 10.97, 13.53 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 18.3 (CH_2), 38.4 (NCH_2), 39.8 (NCH_2), 98.1 (9-C), 111.5, 114.0, 117.3, 123.4, 124.3, 125.8, 127.5, 127.7, 2^{x}127.9, 2^{x}128.4, 129.9, 130.6, 136.6, 139.3, 146.9, 155.1, 158.4, 160.4, 193.3 (C=O), 197.2 (C=O); MS (EI, 70 eV) *m/z* (%): 424 ([M]$^+$, 77), 377 (10), 281 (9), 255 (33), 254 (100), 253 (99), 225 (9), 177 (12), 131 (9), 115 (9), 105 (10), 77 (11), 69 (30); HRMS (ESI): calcd for $C_{26}H_{21}N_2O_4$ ([M+H]$^+$) 425.14958, found 425.14982; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2963 (w), 2915 (w), 2875 (w), 1666 (m), 1590 (s), 1567 (s), 1557 (s), 1496 (s), 1456 (s), 1404 (m), 1374 (m), 1359 (s), 1314 (m), 1298 (s), 1249 (s), 1227 (s), 1199 (s), 1169 (s), 1146 (s), 1107 (s), 1080 (m), 1058 (s), 1025 (s), 953 (m), 906 (m), 882 (m), 862 (m), 804 (m), 780 (s), 738 (s), 717 (m), 699 (s), 667 (s), 642 (s), 614 (s), 598 (s), 588 (s), 573 (s), 536 (m).

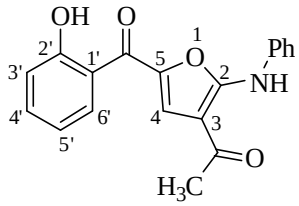
1.2.4 Supplement for Chapter 5

General procedure for the synthesis of compounds 32 and 33:

To a stirred reaction mixture of the corresponding 3-halochromone **9-11** (1.0 mmol) and *β*-ketoamide **31** (1.1 mmol) in dioxane (6-7 mL), DBU (1.3 mmol) was slowly added by syringe at room temperature. Stirring at room temperature was continued until the chromone was consumed

(approximately 3-4 h for 3-chlorochromones **11** and 10-12 h in case of 3-iodochromones **9** and 3-bromochromones **10**). The solvent was distilled off under reduced pressure, and the resulting residue was washed with a diluted aqueous solution of HCl. The formed precipitate was filtered off. In some cases, it was necessary to purify the obtained product by washing with a mixture of isopropanol and heptane (1:10) or by chromatography (silica gel, heptane/ ethyl acetate).

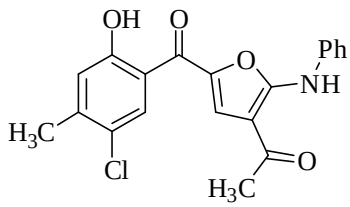
1-{5-[(2-Hydroxyphenyl)carbonyl]-2-(phenylamino)furan-3-yl}ethan-1-one (32a):



Starting with 3-bromochromone **10a** (0.225 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32a** was isolated as a yellow solid (0.279 g, 87%), mp 141-143 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.39 (s, 3H, CH_3), 6.87 (t, ^3J = 7.6 Hz, 1H, H_{Ar}), 6.98 (t, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.12 (t, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.33-7.47 (m, 5H, H_{Ar}), 7.55 (s, 1H, 4-H_{Ar}), 7.98 (dd, ^4J = 1.4 Hz, ^3J = 8.0 Hz, 1H, H_{Ar}), 10.15, 11.81 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.1 (CH_3), 103.5, 118.6, 118.8, 118.9, 2^{x}119.3, 123.0, 124.9, 2^{x}129.7, 130.1, 135.5, 136.3, 141.7, 159.7, 162.6, 182.4 (C=O), 193,4 (C=O); MS (GC, 70 eV) *m/z* (%) 321 ($[M]^+$, 51), 201 (24), 172 (32), 130 (35), 121 (18), 93 (100), 77 (26), 65 (15), 43 (19); HRMS (EI): calcd for $C_{19}H_{15}NO_4$ ($[M]^+$) 321.09956, found 321.09941; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3250 (w), 2922 (w), 2852 (w), 2732 (w), 1651 (m), 1616 (s), 1600 (m), 1575 (m), 1532 (s), 1472 (s), 1436 (m), 1417 (m), 1354 (w), 1323 (m), 1302 (m), 1288 (m), 1235 (m), 1222 (m), 1205 (s), 1181 (s), 1150 (s), 1110 (m), 1064 (w), 1034 (w), 1018 (w), 966 (m), 954 (m), 896 (m), 870 (w), 852 (m), 823 (m), 791 (w), 776 (w), 752 (s), 726 (s), 701 (s), 686 (m), 656 (s), 633 (s), 613 (m), 600 (m), 582 (s), 567 (m), 550 (m).

1-{5-[(5-Chloro-2-hydroxy-4-methylphenyl)carbonyl]-2-(phenylamino)furan-3-yl}ethan-1-one (32b):

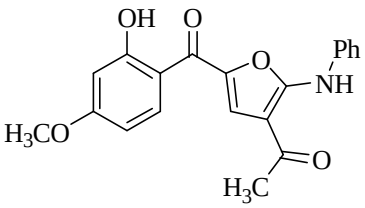


Starting with 3-bromo-6-chloro-7-methylchromone **10c** (0.274 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32b** was isolated as a orange solid (0.365 g, 99%), mp 187-188 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 6.96 (s, 1H, H_{Ar}), 7.18 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.39-7.44 (m, 2H, H_{Ar}), 7.56-7.59 (m, 3H, H_{Ar}), 7.84 (s, 1H, 4-H_{Ar}),

10.23, 10.77 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.7 (CH_3), 27.1 (CH_3), 103.5, 117.4, 2^{x}119.2, 120.5, 123.2, 124.3, 125.0, 2^{x}129.8, 129.9, 136.1, 142.1, 144.8, 159.5, 161.5, 180.5 (C=O), 193.5 (C=O); MS (GC, 70 eV) *m/z* (%): 369 ([M]$^+$, 45), 201 (51), 172 (29), 169 (18), 130 (38), 93 (100), 77 (52), 69 (10), 51 (13), 43 (21); HRMS (EI): calcd for $C_{20}H_{16}{}^{35}ClNO_4$ ([M]$^+$) 369.07624, found 369.07613; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3239 (w), 3203 (w), 3140 (w), 3054 (w), 2952 (w), 2916 (w), 1722 (w), 1713 (w), 1641 (s), 1621 (m), 1601 (m), 1580 (m), 1514 (s), 1478 (s), 1458 (m), 1444 (m), 1384 (w), 1374 (m), 1343 (s), 1320 (m), 1230 (s), 1200 (s), 1166 (s), 1113 (m), 1021 (w), 950 (m), 879 (w), 858 (w), 837 (s), 815 (m), 744 (m), 728 (s), 689 (m), 648 (s), 610 (m), 597 (m), 531 (s).

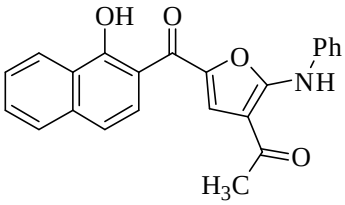
1-{5-[(2-Hydroxy-4-methoxyphenyl)carbonyl]-2-(phenylamino)furan-3-yl}ethan-1-one (32c):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32c** was isolated as a yellow solid (0.344 g, 98%), mp 169-171 ºC;

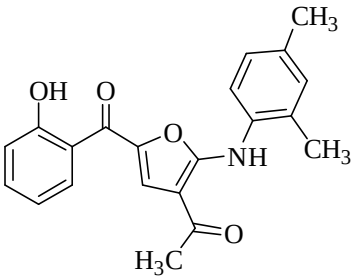
Yield 98%, yellow solid, mp: 169-171 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 4.44-6.47 (m, 2H, H_{Ar}), 7.17 (t, ^3J = 7,5 Hz, 1H, H_{Ar}), 7,40 (t, ^3J = 8.4 Hz, 2H, H_{Ar}), 7.47-7.49 (m, 2H, H_{Ar}), 7.56 (s, 1H, 4-H_{Ar}), 8.01 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 10.15, 12.73 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.1 (CH_3), 55.6 (OCH_3), 101.2, 103.2, 107.7, 112.4, 119.3, 120.3, 121.7, 124.8, 129.1, 129.6, 131.8, 136.4, 141.9, 159.3, 165.7, 166.1, 181.2 (C=O), 193.4 (C=O); MS (GC, 70 eV) *m/z* (%): 351 ([M]$^+$, 57), 259 (23), 258 (100), 243 (43), 217 (33), 216 (12), 201 (18), 188 (13), 172 (26), 161 (10), 151 (45), 130 (45), 128 (10), 108 (11), 93 (84), 77 (37), 69 (14), 51 (10), 43 (20); HRMS (EI): calcd for $C_{20}H_{17}NO_5$ ([M]$^+$) 351.11012, found 351.10989; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3152 (w), 3056 (w), 1681 (m), 1641 (w), 1621 (m), 1592 (s), 1524 (w), 1510 (w), 1486 (w), 1466 (m), 1435 (m), 1411 (m), 1383 (m), 1357 (m), 1296 (m), 1278 (m), 1223 (m), 1206 (s), 1196 (m), 1178 (m), 1153 (m), 1138 (m), 1089 (m), 1031 (w), 1010 (w), 989 (w), 941 (w), 925 (w), 890 (w), 976 (w), 811 (m), 773 (m), 728 (s), 697 (m), 680 (s), 638 (s), 606 (m), 580 (m), 565 (s), 549 (m).

1-{5-[(1-Hydroxynaphthalen-2-yl)carbonyl]-2-(phenylamino)furan-3-yl}ethan-1-one (32d):



Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32d** was isolated as a orange solid (0.197 g, 53%), mp 206-208 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.45 (s, 3H, CH_3), 7.21 (t, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.38-7.48 (m, 3H, H_{Ar}), 7.55-7.63 (m, 3H, H_{Ar}), 7.69 (t, ^3J = 7.0 Hz, 1H, H_{Ar}), 7.91 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 8.04 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 8.12 (s, 1H, 4-H_{Ar}), 8.33 (t, ^3J = 8.2 Hz, 1H, H_{Ar}), 10.27, 13.9 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 27.3 (CH_3), 104.0, 112.4, 118.4, 2^{x}120.5, 123.4, 124.5, 124.8, 2^{x}125.1, 126.1, 127.5, 2^{x}129.3, 129.9, 136.2, 136.6, 140.6, 158.9, 160.9, 181.0 (C=O), 193.0 (C=O); MS (EI, 70 eV) *m/z* (%): 371 ([M]$^+$, 41), 278 (21), 263 (13), 237 (15), 201 (100), 186 (10), 171 (18), 130 (17), 93 (53), 77 (11), 69 (12), 43 (9); HRMS (ESI): calcd for $C_{23}H_{18}NO_4$ ([M+H] $^+$) 372.12303, found 372.12341, calcd for $C_{23}H_{17}NaNO_4$ ([M+Na]$^+$) 394.10498, found 394.10503; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3235 (w), 3065 (w), 2921 (w), 2851 (w), 1641 (w), 1621 (m), 1602 (w), 1574 (m), 1520 (s), 1482 (w), 1455 (m), 1409 (m), 1382 (m), 1350 (m), 1322 (m), 1263 (m), 1243 (s), 1202 (s), 1156 (m), 1145 (m), 1128 (s), 1096 (m), 1062 (w), 1023 (m), 1000 (w), 955 (m), 922 (w), 906 (w), 880 (w), 857 (m), 809 (w), 790 (s), 749 (s), 718 (s), 691 (s), 650 (s), 628 (m), 612 (m), 596 (w), 572 (m), 529 (s).

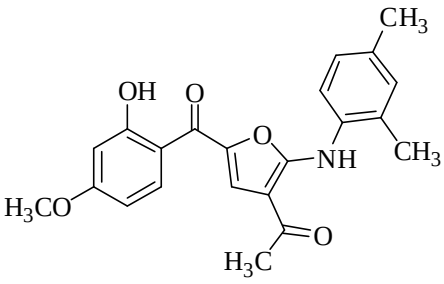
1-{2-[(2,4-Dimethylphenyl)amino]-5-[(2-hydroxyphenyl)carbonyl]furan-3-yl}ethan-1-one (32e):



Starting with 3-bromochromone **10a** (0.225 g, 1.0 mmol), *N*-(2,4-dimethylphenyl)-3-oxobutanamide **31b** (0.226 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32e** was isolated as a orange solid (0.325 g, 93%), mp 141-143 ºC; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.25 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.86-6.98 (m, 2H, H_{Ar}), 7.07-7.11 (m, 2H, H_{Ar}), 7.42 (td, ^3J = 7.8 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 7.54-7.60 (m, 2H, H_{Ar}), 7.75 (s, 1H, 4-H_{Ar}), 10.15, 10.70 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 17.3 (CH_3), 20.4 (CH_3), 27.0 (CH_3), 103.1, 116.9, 118.9, 120.6, 123.1, 123.9, 127.3, 128.6, 129.7, 131.3, 132.4, 133.1, 134.4, 141.5, 157.6, 159.7, 180.5 (C=O), 193.3 (C=O); MS (GC, 70 eV) *m/z* (%): 349 ([M]$^+$, 61), 229 (18), 200 (19), 121 (100), 105 (12), 77 (12), 65 (12), 43 (10); HRMS (EI): calcd for $C_{21}H_{19}NO_4$ ([M]$^+$) 349.13086, found 349.13057; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3097 (w), 3042

(w), 3012 (w), 2959 (w), 2919 (w), 2853 (w), 2731 (w), 1650 (m), 1606 (m), 1565 (m), 1526 (s), 1481 (s), 1435 (m), 1392 (w), 1376 (w), 1349 (m), 1293 (m), 1285 (m), 1264 (w), 1231 (s), 1205 (ss), 1177 (m), 1152 (s), 1134 (m), 1116 (m), 1034 (m), 1018 (m), 956 (m), 932 (m), 889 (m), 866 (w), 842 (s), 805 (s),796 (s), 775 (m),754 (s), 726 (s), 696 (s), 672 (s), 625 (s), 583 (s), 547 (s).

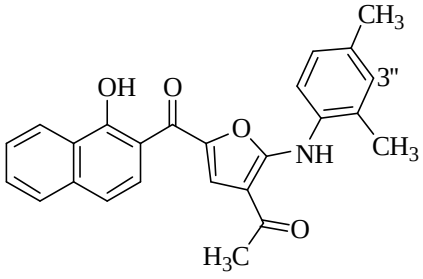
1-{2-[(2,4-Dimethylphenyl)amino]-5-[(2-hydroxy-4-methoxyphenyl)carbonyl]-furan-3-yl}ethan-1-one (32f):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), *N*-(2,4-dimethylphenyl)-3-oxobutanamide **31b** (0.226 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32f** was isolated as a braun solid (0.262 g, 69%), mp 137-139 ºC;

^{1}H NMR (300 MHz,$CDCl_3$): δ = 2.33 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.42-6.47 (m, 2H, H_{Ar}), 7.08-7.10 (m, 2H, H_{Ar}), 7.60 (s, 1H, 4-H_{Ar}), 7.69 (d, ^{3}J = 7.8 Hz, 1H, H_{Ar}), 8.02 (d, ^{3}J = 9.0 Hz, 1H, H_{Ar}), 10.16, 12.84 (both s, 2H, OH and NH); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 17.7 (CH_3), 20.8 (CH_3), 26.9 (CH_3), 55.5 (OCH_3), 101.1, 103.2, 107.7, 112.4, 119.6, 121.9, 127.7, 127.8, 131.7, 131.9, 132.4, 134.8, 141.8, 160.0, 165.6, 166.2, 181.1 (C=O), 193.3 (C=O); MS (GC, 70 eV) *m/z* (%): 379 ([M]$^+$, 22), 217 (20), 151 (20), 121 (100); HRMS (EI): calcd for $C_{22}H_{21}NO_5$ ([M]$^+$) 379.14142, found 379.14136; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3012 (w), 2971 (w), 2920 (w), 2850 (w), 1725 (w), 1710 (w), 1689 (w), 1642 (m), 1607 (m), 1572 (m), 1530 (s), 1502 (m), 1484 (m), 1469 (m), 1442 (m), 1412 (w), 1369 (m), 1355 (m), 1329 (w), 1294 (w), 1243 (s), 1207 (s), 1184 (m), 1162 (w), 1129 (s), 1021 (w), 950 (m), 932 (w), 877 (w), 867 (w), 851 (w), 829 (m), 800 (m), 757 (w), 729 (m), 691 (m), 632 (s), 614 (w), 585 (m), 551 (w).

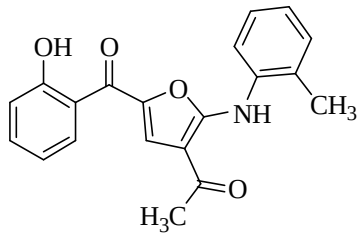
1-{2-[(2,4-Dimethylphenyl)amino]-5-[(1-hydroxynaphthalen-2-yl)carbonyl]furan-3-yl}ethan-1-one (32g):



Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), *N*-(2,4-dimethylphenyl)-3-oxobutanamide **31b** (0.226 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32g** was isolated as a yellow solid (0.303 g, 76%), mp 161-163 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.10 (s, 1H, 3′′-H_{Ar}), 7.15 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 7.28 (d, ^{3}J = 8.1 Hz, 1H, H_{Ar}), 7.54 (dt, ^{3}J = 6.9 Hz, ^{5}J = 0.9 Hz, 1H, H_{Ar}), 7.63 (dt, ^{3}J = 8.1 Hz, ^{4}J = 1.2 Hz, 1H, H_{Ar}), 7.70 (s, 1H, 4-H_{Ar}), 7.76-7.80 (m, 2H, H_{Ar}), 8.06 (d, ^{3}J = 9.0 Hz, 1H, H_{Ar}), 8.48 (d, ^{3}J = 8.3 Hz, 1H, H_{Ar}), 10.20, 14.12 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 17.8 (CH_3), 20.9 (CH_3), 27.0 (CH_3), 103.5, 112.0, 118.2, 119.6, 122.7, 124.4, 124.7, 125.5, 125.9, 127.3, 127.7, 127.8, 130.0, 131.7, 132.4, 134.8, 136.8, 141.9, 160.1, 163.6, 182.0 (C=O), 193.4 (C=O); MS (EI, 70 eV) *m/z* (%): 399 ([M]$^{+}$, 52), 237 (16), 230 (12), 229 (93), 200 (10), 171 (12), 121 (100); HRMS (EI): calcd for $C_{25}H_{21}NO_4$ ([M]$^{+}$) 399.14651, found 399.14623; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3118 (w), 3051 (w), 3015 (w), 2972 (w), 2922 (w), 2860 (w), 1642 (m), 1626 (m), 1611 (w), 1601 (w), 1568 (m), 1528 (s), 1503 (m), 1482 (w), 1461 (s), 1420 (m), 1376 (m), 1354 (m), 1328 (w), 1271 (w), 1244 (s),1205 (s), 1150 (m), 1130 (m), 1117 (m), 1098 (m), 1061 (w), 1025 (w), 999 (w), 958 (m), 931 (w), 920 (w), 874 (m), 802 (m), 787 (s), 754 (s), 732 (m), 716 (m), 660 (w), 631 (s), 587 (w), 572 (m), 551 (w).

1-{5-[(2-Hydroxyphenyl)carbonyl]-2-[(2-methylphenyl)amino]furan-3-yl}ethan-1-one (32h):

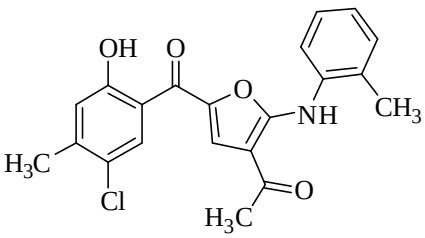


Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), *N*-(2-methylphenyl)-3-oxobutanamide **31c** (0.210 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32h** was isolated as a yellow solid (0.285 g, 85%), mp 109-111 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.31 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 6.89-6.99 (m, 2H, H_{Ar}), 7.14 (td, ^{3}J = 7.4 Hz, ^{4}J = 1.1 Hz, 1H, H_{Ar}), 7.27-7.34 (m, 2H, H_{Ar}), 7.42 (td, ^{3}J = 7.7 Hz, ^{4}J = 1.7 Hz, 1H, H_{Ar}), 7.59 (dd, ^{3}J = 7.7 Hz, ^{4}J = 1.7 Hz, 1H, H_{Ar}), 7.72 (d, ^{3}J = 8.00 Hz, 1H, H_{Ar}), 7.78 (s, 1H, 4-H_{Ar}), 10.23, 10.66 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 17.3 (CH_3), 27.0 (CH_3), 103.2, 116.9, 118.9, 120.3, 123.2,

123.6, 125.0, 127.0, 128.5, 129.6, 130.8, 133.1, 135.0, 141.7, 157.5, 159.5, 180.6 (C=O), 193.5 (C=O); MS (GC, 70 eV) *m/z* (%): 335 ([M]$^+$, 62), 215 (18), 186 (28), 144 (17), 121 (18), 107 (100), 91 (31), 65 (27), 43 (14); HRMS (EI): calcd for $C_{20}H_{17}NO_4$ ([M]$^+$) 335.11521, found 335.11497; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3145 (w), 2969 (w), 2734 (w), 1641 (s), 1615 (m), 1594 (s), 1577 (m), 1538 (s), 1481 (s), 1440 (m), 1403 (m), 1379 (w), 1348 (m), 1324 (m), 1295 (s), 1237 (s), 1216 (s), 1187 (m), 1151 (s), 1112 (m), 1033 (w), 996 (w), 968 (m), 957 (m), 899 (w), 862 (m), 824 (m), 794 (w), 781 (w), 752 (s), 734 (s), 699 (s), 678 (m), 653 (s), 631 (s), 591 (m), 573 (m), 558 (w).

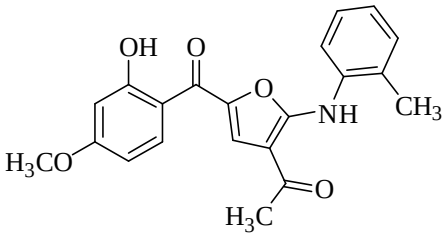
1-{5-[(5-Chloro-2-hydroxy-4-methylphenyl)carbonyl]-2-[(2-methylphenyl)amino]furan-3-yl}ethan-1-one (32i):



Starting with 3-bromo-6-chloro-7-methylchromone **10c** (0.274 g, 1.0 mmol), *N*-(2-methylphenyl)-3-oxobutan-amide **31c** (0.210 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32i** was isolated as a yellow solid (0.379 g, 99%), mp 166-167 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.31 (s, 6H, 2^{x}CH$_3$), 2.40 (s, 3H, CH$_3$), 6.94 (s, 1H, 3′-H$_{Ar}$), 7.14 (t, ^3J = 6.7 Hz, 1H, H$_{Ar}$), 7.31 (m, 2H, H$_{Ar}$), 7.58 (s, 1H, 6′-H$_{Ar}$), 7.70 (d, ^3J = 7.6 Hz, 1H, H$_{Ar}$), 7.84 (s, 1H, 4-H$_{Ar}$), 10.24, 10.84 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.3 (CH$_3$), 19.9 (CH$_3$), 27.1 (CH$_3$), 103.3, 119.3, 120.5, 122.5, 123.0, 124.1, 125.2, 127.0, 128.7, 129.2, 130.9, 134.9, 140.7, 141.7, 156.2, 159.6, 178.7 (C=O), 193.5 (C=O); MS (GC, 70 eV) *m/z* (%): 383 ([M]$^+$, 33), 215 (29), 186 (18), 169 (12), 144 (12), 107 (100), 91 (27), 77 (13), 65 (11), 43 (13); HRMS (ESI): calcd for $C_{21}H_{19}{}^{35}ClNO_4$ ([M+H]$^+$) 384.09971, found 384.09934, calcd for $C_{21}H_{19}{}^{37}ClNO_4$ ([M+H]$^+$) 386.09763, found 386.09792; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3140 (w), 3113 (w), 3027 (w), 2918 (w), 2858 (w), 1641 (s), 1621 (m), 1597 (m), 1574 (m), 1531 (s), 1505 (m), 1479 (m), 1464 (m), 1415 (w), 1372 (m), 1344 (m), 1323 (m), 1307 (m), 1247 (s), 1227 (s), 1178 (m), 1168 (m), 1112 (m), 1049 (w), 1021 (w), 1001 (w), 958 (m), 947 (m), 870 (w), 847 (m), 807 (m), 778 (w), 743 (w), 690 (m), 647 (m), 622 (m), 599 (m), 555 (w), 536 (m).

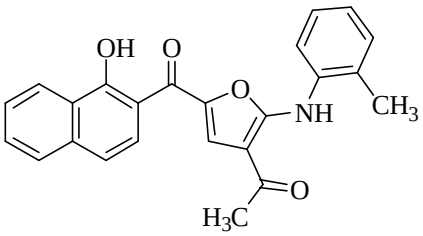
1-{5-[(2-Hydroxy-4-methoxyphenyl)carbonyl]-2-[(2-methylphenyl)amino]furan-3-yl}ethan-1-one (32j):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), *N*-(2-methylphenyl)-3-oxobutanamide **31c** (0.210 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32j** was isolated as a yellow solid (0.358 g, 98%), mp 156-158 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.48-6.51 (m, 2H, H_{Ar}), 7.14 (t, ^3J = 8.1 Hz, 1H, H_{Ar}), 7.31 (t, ^3J = 7.5 Hz, 2H, H_{Ar}), 7.71 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.85 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 7.98 (s, 1H, 4-H_{Ar}), 10.22, 12.11 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.6 (CH_3), 27.3 (CH_3), 55.8 (OCH_3), 101.5, 103.4, 107.0, 113.6, 121.0, 123.8, 125.4, 127.2, 129.1, 131.0, 132.2, 135.2, 141.0, 160.0, 163.4, 164.7, 180.3 (C=O), 193.6 (C=O); MS (GC, 70 eV) *m/z* (%): 365 ($[M]^+$, 32), 258 (18), 217 (19), 186 (11), 151 (25), 144 (12), 107 (100), 91 (25), 65 (13), 43 (12); HRMS (ESI): calcd for $C_{21}H_{20}NO_5$ ($[M+H]^+$) 366.13360, found 366.13368, calcd for $C_{21}H_{19}NaNO_5$ ($[M+Na]^+$) 388.11554, found 388.11563; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3100 (w), 3031 (w), 3014 (w), 2985 (w), 2951 (w), 2917 (w), 2894 (w), 2849 (w), 1639 (s), 1617 (m), 1592 (s), 1574 (s), 1556 (w), 1528 (s), 1503 (s), 1475 (m), 1462 (s), 1430 (m), 1397 (w), 1359 (s), 1322 (m), 1307 (w), 1296 (w), 1254 (s), 1229 (s), 1202 (s), 1183 (m), 1172 (s), 1140 (s), 1128 (s), 1107 (s), 1062 (w), 1048 (w), 1024 (s), 960 (m), 948 (m), 878 (w), 851 (m), 835 (s), 809 (w), 799 (m), 780 (w), 744 (s), 729 (s), 686 (s), 647 (m), 631 (s), 599 (m), 555 (m), 526 (m).

1-{5-[(1-Hydroxynaphthalen-2-yl)carbonyl]-2-[(2-methylphenyl)amino]furan-3-yl}-ethan-1-one (32k):

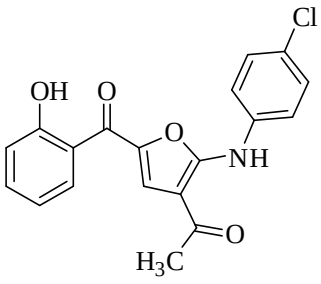


Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), *N*-(2-methylphenyl)-3-oxobutanamide **31c** (0.210 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32k** was isolated as a yellow solid (0.358 g, 93%), mp 166-168 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.14 (t, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.26-7.30 (m, 2H, H_{Ar}), 7.35 (t, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.50-7.56 (m, 1H, H_{Ar}), 7.60-7.65 (m, 1H, H_{Ar}), 7.69 (s, 1H, 4-H_{Ar}), 7.74 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.92 (d, ^3J = 8.1 Hz, 1H, H_{Ar}),

8.03 (d, ^3J = 9.0 Hz, 1H, H_{Ar}), 8.46 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 10.31, 14.12 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 17.6 (CH_3), 26.8 (CH_3), 103.4, 111.7, 118.0, 119.1, 122.3, 124.1, 124.4, 124.7, 125.2, 125.7, 127.1, 127.1, 127.3, 129.8, 130.8, 134.8, 136.6, 141.8, 159.6, 163.4, 182.1 (C=O), 193.3 (C=O); MS (EI, 70 eV) *m/z* (%): 385 ($[M]^+$, 53), 237 (15), 216 (11), 215 (96), 186 (12), 171 (17), 170 (11), 152 (39), 151 (40), 144 (11), 137 (14), 123 (18), 115 (12), 107 (100), 98 (12), 96 (17), 91 (16), 69 (15), 43 (10), 41 (10); HRMS (EI): calcd for $C_{24}H_{19}NO_4$ ($[M]^+$) 385.13086, found 385.13065; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3122 (w), 3067 (w), 2915 (w), 2859 (w), 1643 (s), 1619 (m), 1594 (m), 1573 (m), 1524 (s), 1459 (s), 1415 (m), 1375 (m), 1356 (m), 1328 (w), 1294 (w), 1265 (m), 1243 (s), 1229 (s), 1209 (m), 1194 (m), 1177 (w), 1148 (m), 1129 (m), 1111 (m), 1096 (w), 1050 (w), 1023 (w), 998 (w), 958 (m), 911 (m), 867 (m), 809 (w), 797 (m), 790 (m), 775 (m), 755 (s), 732 (s), 721 (s), 694 (w), 660 (w), 644 (s), 626 (m), 572 (m), 544 (m).

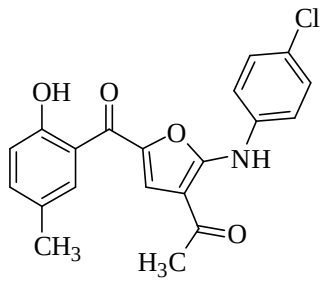
1-{2-[(4-Chlorophenyl)amino]-5-[(2-hydroxyphenyl)carbonyl]furan-3-yl}ethan-1-one (32l):



Starting with 3-iodochromone **9a** (0.272 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32l** was isolated as a braun solid (0.163 g, 46%), mp 175-177 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.39 (s, 3H, CH_3), 6.91-7.00 (m, 2H, H_{Ar}), 7.42-7.45 (m, 3H, H_{Ar}), 7.58-7.60 (m, 3H, H_{Ar}), 7.77 (s, 1H, 4-H_{Ar}), 10.24, 10.64 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 27.3 (CH_3), 103.8, 116.9, 118.9, 2^x121.7, 123.2, 123.4, 128.2, 2^x129.0, 129.7, 133.2, 135.8, 141.8, 157.4, 158.2, 180.7 (C=O), 192.9 (C=O); MS (GC, 70 eV) *m/z* (%): 355 ($[M]^+$, 44), 235 (24), 206 (22), 187 (26), 164 (35), 127 (100), 111 (13), 65 (18), 43 (30); HRMS (ESI): calcd for $C_{19}H_{15}{}^{35}ClNO_4$ ($[M+H]^+$) 356.06841, found 356.06842, calcd for $C_{19}H_{15}{}^{37}ClNO_4$ ($[M+H]^+$) 358.06621, found 358.06626; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3237 (w), 3196 (w), 3154 (w), 3099 (w), 3054 (w), 1643 (w), 1615 (m), 1587 (w), 1574 (m), 1557 (w), 1526 (s), 1505 (m), 1479 (s), 1435 (m), 1417 (m), 1385 (w), 1337 (m), 1295 (m), 1282 (m), 1241 (m), 1229 (m), 1203 (m), 1181 (m), 1155 (s), 1093 (m), 1062 (w), 1034 (w), 1014 (w), 958 (m), 891 (m), 864 (w), 852 (w), 836 (m), 808 (s), 755 (s), 725 (s), 697 (s), 671 (s), 633 (m), 617 (s), 592 (m), 567 (s), 529 (s).

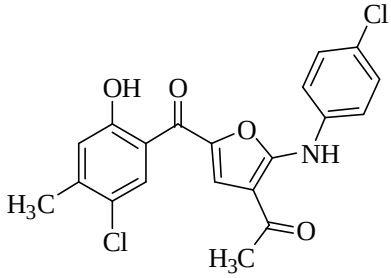
1-{2-[(4-Chlorophenyl)amino]-5-[(2-hydroxy-5-methylphenyl)carbonyl]furan-3-yl}-ethan-1-one (32m):



Starting with 3-bromo-6-methylchromone **10b** (0.239 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32m** was isolated as a yellow solid (0.365 g, 99%), mp 188-190 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.24 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 6.88 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.22 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 7.40-7.43 (m, 3H, H_{Ar}), 7.57-7.59 (m, 2H, H_{Ar}), 7.78 (s, 1H, 4-H_{Ar}), 10.24, 10.61 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 19.9 (CH_3), 27.3 (CH_3), 103.7, 116.8, 2^{x}121.8, 123.3, 127.6, 128.2, 2^{x}129.0, 129.6, 134.1, 135.8, 141.9, 155.6, 155.7, 158.2, 180.8 (C=O), 192.9 (C=O); MS (GC, 70 eV) *m/z* (%): 369 ([M]$^+$, 58), 242 (13), 237 (20), 235 (57), 227 (10), 206 (23), 201 (27), 166 (14), 164 (45), 135 (48), 127 (100), 111 (21), 107 (11), 77 (38), 75 (15), 69 (16), 53 (11), 43 (47); HRMS (EI): calcd for $C_{20}H_{16}{}^{35}ClNO_4$ ([M]$^+$) 369.07624, found 369.07589, calcd for $C_{20}H_{16}{}^{37}ClNO_4$ ([M]$^+$) 371.07329, found 371.07380; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3233 (w), 3190 (w), 2917 (w), 2859 (w), 2710 (w), 1643 (w), 1608 (m), 1567 (m), 1520 (s), 1478 (s), 1418 (m), 1384 (m), 1341 (s), 1324 (s), 1291 (m), 1284 (m), 1253 (m), 1244 (m), 1230 (s), 1213 (s), 1201 (s), 1161 (s), 1107 (m), 1092 (s), 1061 (m), 1027 (w), 1011 (m), 978 (w), 961 (m), 913 (w), 889 (w), 870 (w), 800 (s), 762 (m), 738 (s), 697 (m), 679 (s), 635 (m), 619 (s), 588 (m), 573 (m), 549 (m).

1-{5-[(5-Chloro-2-hydroxy-4-methylphenyl)carbonyl]-2-[(4-chlorophenyl)amino]furan-3-yl}ethan-1-one (32n):

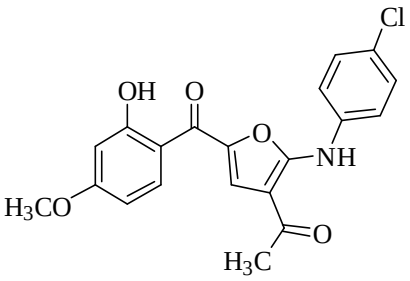


Starting with 3-bromo-6-chloro-7-methylchromone **10c** (0.274 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32n** was isolated as a yellow solid (0.395 g, 98%), mp 214-216 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 6.96 (s, 1H, 3′-H_{Ar}), 7.43-7.48 (m, 2H, H_{Ar}), 7.57-7.61 (m, 3H, H_{Ar}), 7.83 (s, 1H, 4-H_{Ar}), 10.27, 10.78 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 19.9 (CH_3), 27.3 (CH_3), 103.9, 119.2, 2^{x}122.0, 122.7, 123.01, 123.9, 128.4, 2^{x}129.1, 129.2, 135.7, 140.7, 141.8, 156.1, 158.4, 178.8 (C=O), 192.9 (C=O); MS (GC, 70 eV) *m/z* (%): 403 ([M]$^+$, 42), 237

(25), 236 (10), 235 (74), 206 (30), 169 (26), 166 (12), 164 (32), 129 (32), 127 (100), 111 (14), 77 (20), 75 (11), 69 (12), 43 (30); HRMS (ESI): calcd for $C_{20}H_{16}{}^{35}Cl_2NO_4$ ($[M+H]^+$) 404.04509, found 404.04507, calcd for $C_{20}H_{16}{}^{37}Cl_2NO_4$ ($[M+H]^+$) 406.04256, found 406.04260; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3242 (w), 3196 (w), 3109 (w), 2979 (w), 2919 (w), 2855 (w), 1641 (m), 1621 (m), 1573 (m), 1525 (s), 1494 (s), 1373 (m), 1340 (s), 1310 (m), 1247 (s), 1202 (s), 1167 (s), 1118 (m), 1092 (m), 1061 (w), 1011 (m), 968 (w), 947 (m), 880 (w), 842 (m), 803 (m), 742 (m), 690 (m), 634 (w), 618 (m), 592 (m), 546 (m).

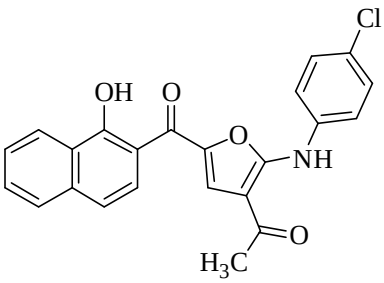
1-{2-[(4-Chlorophenyl)amino]-5-[(2-hydroxy-4-methoxyphenyl)carbonyl]furan-3-yl}-ethan-1-one (32o):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32o** was isolated as a yellow solid (0.181 g, 47%), mp 187-189 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.43 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 6.52-6.56 (m, 2H, H_{Ar}), 7.46 (d, ^3J = 8.7 Hz, 2H, H_{Ar}), 7.59 (d, ^3J = 9.0 Hz, 2H, H_{Ar}), 7.87 (d, ^3J = 8.4 Hz, 1H, H_{Ar}), 7.95 (s, 1H, 4-H_{Ar}), 10.25, 12.08 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 27.5 (CH_3), 55.8 (OCH_3), 101.5, 104.0, 107.0, 113.6, 2^{x}122.1, 123.6, 128.5, 2^{x}129.3, 132.2, 136.0, 141.1, 158.3, 163.3, 164.8, 180.4 (C=O), 193.1 (C=O); MS (GC, 70 eV) *m/z* (%): 385 ($[M]^+$, 37), 258 (100), 243 (40), 235 (12), 217 (46), 206 (15), 188 (12), 166 (11), 164 (35), 151 (53), 129 (23), 127 (63), 111 (16), 75 (10), 69 (17), 43 (29); HRMS (ESI): calcd for $C_{20}H_{17}{}^{35}ClNO_5$ ($[M+H]^+$) 386.07898, found 386.07883, calcd for $C_{20}H_{17}{}^{37}ClNO_5$ ($[M+H]^+$) 388.07688, found 388.07679; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3231 (w), 3119 (w), 3008 (w), 2916 (w), 2849 (w), 1643 (m), 1618 (m), 1573 (m), 1525 (s), 1500 (s), 1438 (m), 1418 (w), 1374 (m), 1351 (m), 1320 (w), 1296 (w), 1245 (s), 1205 (s), 1183 (m), 1136 (s), 1110 (m), 1091 (m), 1061 (w), 1027 (w), 1021 (w), 1013 (w), 952 (s), 881 (w), 834 (s), 806 (m), 757 (w), 722 (m), 706 (w), 694 (w), 694 (m), 675 (w), 638 (m), 619 (m), 593 (w), 562 (s), 528 (w).

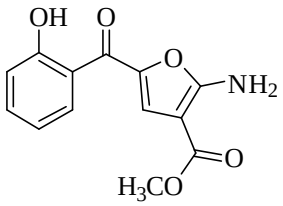
1-{2-[(4-Chlorophenyl)amino]-5-[(1-hydroxynaphthalen-2-yl)carbonyl]furan-3-yl}ethan-1-one (32p):



Starting with 3-iodobenzo[*h*]chromone **9b** (0.322 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32p** was isolated as a yellow solid (0.227 g, 56%), mp 230-232 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (s, 3H, CH_3), 7.27-7.40 (m, 3H, H_{Ar}), 7.45-7.48 (m, 2H, H_{Ar}), 7.53 (t, ^3J = 7.7 Hz, 1H, H_{Ar}), 7.61-7.64 (m, 2H, H_{Ar}), 7.77 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.98 (d, ^3J = 8.8 Hz, 1H, H_{Ar}), 8.46 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 10.19, 13.92 (both s, 2H, OH and NH); ^{13}C NMR (62.3 MHz, $CDCl_3$): δ = 27.1 (CH_3), 103.6, 111.9, 118.3, 2^{x}120.4, 122.3, 124.3, 124.4, 125.4, 126.0, 127.3, 2^{x}129.7, 129.9, 130.2, 135.0, 136.9, 142.1, 159.1, 163.5, 182.2 (C=O), 193.6 (C=O); MS (EI, 70 eV) *m/z* (%): 405 ([M]$^+$, 32), 278 (28), 263 (14), 235 (100), 171 (42), 164 (21), 127 (47), 115 (17), 110 (15), 43 (11); HRMS (ESI): calcd for $C_{23}H_{16}{}^{35}ClNO_4$ ([M-H]$^-$) 404.06951, found 404.07002, calcd for $C_{23}H_{16}{}^{37}ClNO_4$ ([M-H]$^-$) 406.06755, found 406.06784; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3240 (w), 3119 (w), 3049 (w), 2961 (w), 2923 (w), 2853 (w), 1731 (w), 1651 (m), 1620 (m), 1575 (m), 1537 (s), 1494 (m), 1464 (m), 1422 (m), 1385 (m), 1349 (m), 1317 (w), 1271 (m), 1253 (s), 1209 (m), 1181 (w), 1150 (m), 1094 (m), 1062 (w), 1027 (w), 1016 (w), 1004 (m), 962 (m), 925 (w), 863 (m), 803 (s), 787 (m), 751 (m), 723 (m), 712 (m), 691 (w), 650 (w), 637 (m), 619 (m), 571 (m), 547 (m).

Methyl 2-amino-5-[(2-hydroxyphenyl)carbonyl]furan-3-carboxylate (32q):

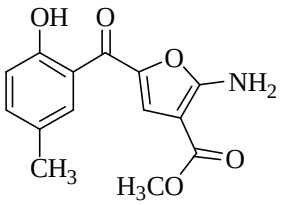


Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32q** was isolated as a yellow solid (0.128 g, 49%), mp 142-144 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.70 (s, 3H, OCH_3), 6.87-6.95 (m, 2H, H_{Ar}), 7.18 (s, 1H, 4-H_{Ar}), 7.38 (td, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, H_{Ar}), 7.53 (dd, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 8.09 (s, 2H, NH_2), 10.59 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 50.9 (OCH_3), 91.2, 116.8, 118.9, 123.4, 125.2, 129.5, 132.8, 140.7, 157.2, 163.2, 164.6, 179.7 (C=O); MS (GC, 70 eV) *m/z* (%): 261 ([M]$^+$, 33), 244 (100), 213 (20), 184 (10), 158 (21), 141 (23), 121 (42), 109 (28), 93 (11), 65 (22), 52 (19), 39 (11); HRMS (EI): calcd for $C_{13}H_{11}NO_5$ ([M]$^+$) 261.06317,

found 261.06323; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3370 (w), 3307 (w), 3244 (w), 3174 (w), 1699 (m), 1668 (m), 1628 (w), 1568 (m), 1557 (m), 1537 (s), 1470 (m), 1427 (w), 1372 (m), 1315 (m), 1287 (m), 1247 (s), 1223 (s), 1182 (m), 1150 (s), 1115 (m), 1093 (m), 1041 (m), 962 (w), 947 (w), 893 (m), 876 (w), 865 (w), 821 (w), 806 (m), 777 (m), 738 (s), 708 (m), 695 (m), 668 (m), 627 (s), 580 (m).

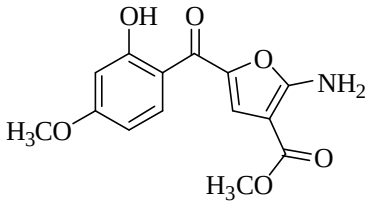
Methyl 2-amino-5-[(2-hydroxy-5-methylphenyl)carbonyl]furan-3-carboxylate (32r):



Starting with 3-bromo-6-methylchromone **10b** (0.239 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32r** was isolated as a yellow solid (0.248 g, 90%), mp 111-113 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.24 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 6.82 (d, ^3J = 8.3 Hz, 1H, 3′-H_{Ar}), 7.17-7.19 (m, 2H, 4′,6′-H_{Ar}), 7.32 (s, 1H, 4-H_{Ar}), 8.08 (s, 2H, NH_2), 10.38 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.0 (CH_3), 50.9 (OCH_3), 91.1, 116.7, 123.1, 125.1, 127.6, 129.4, 133.4, 140.7, 155.0, 163.3, 164.6, 179.9 (C=O); MS (GC, 70 eV) *m/z* (%): 275 ($[M]^+$, 38), 258 (100), 230 (17), 227 (18), 172 (15), 141 (40), 135 (64), 109 (36), 107 (13), 77 (31), 52 (23); HRMS (EI): calcd for $C_{14}H_{13}NO_5$ ($[M]^+$) 275.07882, found 275.07859; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3418 (w), 3368 (w), 3307 (w), 3242 (w), 3152 (w), 2952 (w), 2922 (w), 2860 (w), 1699 (m), 1682 (w), 1674 (w), 1668 (w), 1651 (w), 1627 (m), 1615 (m), 1574 (s), 1568 (s), 1557 (s), 1538 (s), 1531 (s), 1526 (s), 1520 (s), 1480 (s), 1428 (m), 1408 (w), 1371 (w), 1345 (w), 1307 (w), 1285 (s), 1245 (m), 1226 (s), 1165 (s), 1141 (s), 1125 (s), 1090 (m), 1044 (m), 953 (w), 919 (w), 868 (w), 851 (w), 820 (m), 810 (m), 774 (s), 734 (m), 709 (m), 697 (m), 678 (s), 574 (m), 534 (s).

Methyl 2-amino-5-[(2-hydroxy-4-methoxyphenyl)carbonyl]furan-3-carboxylate (32s):

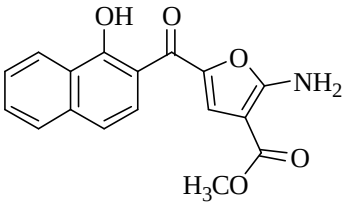


Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32s** was isolated as a braun solid (0.230 g, 79%), mp 116-118 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.72 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 6.47-6.53 (m, 2H, 3′,5′-H_{Ar}), 7.42 (s, 1H, 4-H_{Ar}), 7.87 (d, ^3J = 8.6 Hz, 1H, 6′-H_{Ar}), 8.08 (s, 2H, NH_2), 12.25 (s, 1H, OH); ^{13}C NMR (62.3 MHz, DMSO-d_6): δ = 50.9 (OCH_3), 55.5 (OCH_3), 91.4, 101.3, 106.8, 113.4, 124.6, 131.9, 140.0, 163.2, 163.3, 164.3, 164.4, 179.6 (C=O); MS (GC, 70 eV) *m/z* (%):

291 ([M]$^+$, 30), 274 (100), 259 (11), 246 (26), 243 (24), 231 (18), 188 (12), 151 (46), 109 (13), 108 (10), 52 (13); HRMS (EI): calcd for $C_{14}H_{13}NO_6$ ([M]$^+$) 291.07374, found 291.07358; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3365 (w), 3308 (w), 3234 (w), 3171 (w), 2949 (w), 2843 (w), 2207 (w), 1697 (w), 1672 (w), 1613 (m), 1566 (m), 1529 (s), 1503 (m), 1468 (m), 1453 (w), 1432 (m), 1373 (w), 1328 (w), 1314 (w), 1293 (w), 1251 (s), 1230 (s), 1209 (s), 1185 (s), 1160 (s), 1121 (s), 1097 (s), 1050 (m), 1022 (m), 969 (w), 884 (w), 870 (w), 819 (m), 807 (m), 778 (m), 756 (w), 738 (m), 706 (m), 693 (m), 665 (w), 642 (w), 618 (s), 580 (s), 558 (s).

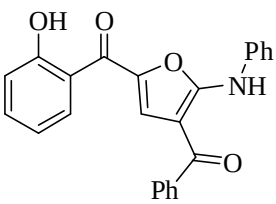
Methyl 2-amino-5-[(1-hydroxynaphthalen-2-yl)carbonyl]furan-3-carboxylate (32t):



Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32t** was isolated as a yellow solid (0.274 g, 88%), mp 192-194 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H, OCH_3), 6.32 (s, 2H, NH_2), 7.26 (d, ^3J = 9.0 Hz, 1H, H_{Ar}), 7.49-7.54 (m, 1H, H_{Ar}), 7.56 (s, 1H, 4-H_{Ar}), 7.58-7.63 (m, 1H, H_{Ar}), 7.74 (d, ^3J = 7.8 Hz, 1H, H_{Ar}), 7.86 (d, ^3J = 9.0 Hz, 1H, H_{Ar}), 8.43 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 13.78 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 51.7 (OCH_3), 93.6, 112.1, 118.5, 2^{x}124.5, 124.8, 125.6, 126.1, 127.5, 130.1, 137.0, 141.3, 163.1, 164.0, 164.7, 182.5 (C=O); MS (EI, 70 eV) *m/z* (%): 311 ([M]$^+$, 59), 295 (21), 294 (100), 266 (15), 263 (23), 197 (25), 196 (24), 171 (59), 170 (45), 142 (10), 141 (88), 115 (24), 114 (29), 109 (52); HRMS (EI): calcd for $C_{17}H_{13}NO_5$ ([M]$^+$) 311.07882, found 311.07879; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 3422 (w), 3310 (w), 3258 (w), 3151 (w), 3055 (w), 2948 (w), 1693 (m), 1623 (m), 1600 (w), 1564 (m), 1536 (m), 1479 (w), 1454 (s), 1427 (m), 1413 (m), 1385 (w), 1317 (w), 1268 (s), 1251 (s), 1210 (m), 1163 (s), 1148 (s), 1105 (m), 1023 (m), 978 (w), 914 (w), 871 (w), 837 (w), 805 (w), 792 (s), 761 (s), 737 (s), 716 (m), 660 (w), 638 (w), 602 (m), 549 (m), 526 (m).

2-{[4-Benzoyl-5-(phenylamino)furan-2-yl]carbonyl}phenol (32u):

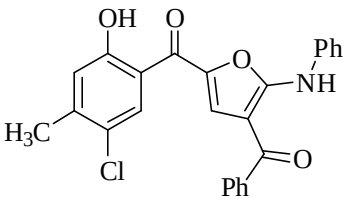


Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32u** was isolated as a yellow solid (0.241 g, 63%), mp 170-172 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.88-6.98 (m, 2H, H_{Ar}), 7.21 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.37-7.47 (m, 4H, H_{Ar}), 7.53-7.66 (m, 6H, H_{Ar}), 7.79-7.81 (m, 2H, H_{Ar}), 10.54, 10.65 (both s, 2H, OH

and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 101.8, 116.8, 119.0, 2^{x}120.4, 123.2, 123.6, 124.7, 2^{x}128.0, 2^{x}128.8, 129.3, 2^{x}129.7, 132.0, 133.1, 136.6, 138.4, 142.1, 157.0, 160.6, 180.6 (C=O), 188.2 (C=O); MS (EI, 70 eV) *m/z* (%): 383 ([M]$^+$, 44), 291 (13), 263 (18), 234 (14), 171 (9), 121 (10), 105 (100), 93 (99), 91 (18), 77 (78), 66 (11), 51 (11); HRMS (EI): calcd for $C_{24}H_{17}NO_4$ ([M]$^+$) 383.11521, found 383.11551; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3051 (w), 1635 (s), 1599 (m), 1587 (m), 1578 (m), 1566 (s), 1542 (s), 1499 (m), 1481 (m), 1470 (m), 1445 (m), 1394 (m), 1351 (w), 1336 (w), 1325 (w), 1299 (m), 1289 (m), 1265 (m), 1245 (s), 1218 (m), 1203 (m), 1178 (m), 1147 (s), 1137 (m), 1103 (w), 1031 (w), 1000 (w), 972 (m), 937 (m), 923 (w), 890 (m), 870 (w), 846 (w), 822 (w), 799 (w), 786 (m), 761 (m), 739 (s), 710 (m), 690 (s), 657 (s), 616 (m), 601 (m), 575 (m), 565 (m), 530 (m).

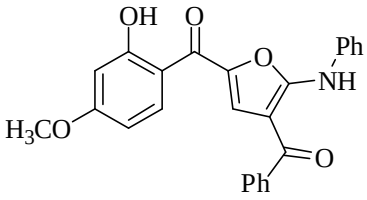
2-{[4-Benzoyl-5-(phenylamino)furan-2-yl]carbonyl}-4-chloro-5-methylphenol (32v):



Starting with 3-bromo-6-chloro-7-methylchromone **10c** (0.274 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32v** was isolated as a yellow solid (0.310 g, 72%), mp 200-202 ºC;

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.40 (s, 3H, CH_3), 6.92 (s, 1H, 3′-H_{Ar}), 7.21-7.26 (m, 1H, H_{Ar}), 7.47-7.56 (m, 7H, H_{Ar}), 7.82-7.84 (m, 3H, H_{Ar}), 8.24 (s, 1H, 4-H_{Ar}), 10.75, 12.17 (both s, 2H, OH and NH); ^{13}C NMR (62.3 MHz, $CDCl_3$): δ = 20.7 (CH_3), 102.3, 117.4, 2^{x}119.5, 120.5, 124.2, 124.3, 125.1, 125.2, 2^{x}128.2, 2^{x}128.8, 2^{x}130.0, 132.2, 136.1, 138.5, 142.4, 144.9, 161.3, 161.6, 180.8 (C=O), 189.7 (C=O); MS (GC, 70 eV) *m/z* (%): 431 ([M]$^+$, 52), 263 (51), 234 (17), 169 (21), 105 (100), 93 (82), 77 (80), 53 (14), 51 (14); HRMS (ESI): calcd for $C_{25}H_{19}{}^{35}ClNO_4$ ([M+H]$^+$) 432.09971, found 432.09984, calcd for $C_{25}H_{19}{}^{37}ClNO_4$ ([M+H]$^+$) 434.09789, found 434.09821; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3234 (w), 3062 (w), 2991 (w), 2949 (w), 2916 (w), 1628 (m), 1594 (w), 1579 (w), 1525 (s), 1495 (m), 1485 (m), 1471 (m), 1455 (w), 1443 (m), 1385 (w), 1369 (w), 1331 (m), 1315 (m), 1312 (m), 1248 (m), 1228 (m), 1200 (w), 1170 (s), 1123 (m), 1114 (m), 1078 (w), 1031 (w), 1014 (w), 1001 (w), 960 (w), 936 (w), 924 (w), 909 (m), 880 (w), 871 (w), 864 (w), 841 (w), 811 (w), 797 (m), 788 (m), 751 (m), 740 (m), 733 (s), 714 (m), 692 (s), 681 (s), 665 (m), 652 (s), 637 (s), 609 (m), 596 (s), 578 (m), 546 (s), 528 (s).

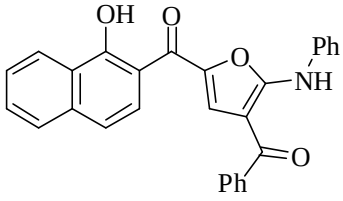
2-{[4-Benzoyl-5-(phenylamino)furan-2-yl]carbonyl}-5-methoxyphenol (32w):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32w** was isolated as a yellow solid (0.285 g, 69%), mp 181-183 ºC;

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.85 (s, 3H, OCH_3), 6.42-6.49 (m, 2H, H_{Ar}), 7.17-7.24 (m, 1H, H_{Ar}), 7.42–7.60 (m, 7H, H_{Ar}), 7.66 (s, 1H, 4-H_{Ar}), 7.79-7.83 (m, 2H, H_{Ar}), 8.01 (d, ^3J = 8.8 Hz, 1H, H_{Ar}), 10.67, 12.74 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.6 (OCH_3), 101.2, 102.0, 107.7, 112.4, 2^{x}119.5, 122.7, 124.9, 2^{x}128.1, 2^{x}128.7, 2^{x}129.7, 131.9, 132.0, 136.4, 138.7, 142.2, 161.2, 165.8, 166.2, 181.4 (C=O), 189.6 (C=O); MS (EI, 70 eV) *m/z* (%): 413 ([M]$^+$, 38), 321 (24), 320 (100), 151 (14), 105 (98), 93 (32), 78 (13), 77 (23), 71 (11), 69 (16), 63 (13), 57 (18), 55 (11), 44 (18), 43 (11); HRMS (EI): calcd for $C_{25}H_{19}NO_5$ ([M]$^+$) 413.12577, found 413.12575; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3266 (w), 3152 (w), 3106 (w), 3055 (w), 3014 (w), 2975 (w), 2917 (w), 2847 (w), 1626 (s), 1601 (m), 1579 (m), 1566 (m), 1526 (s), 1500 (s), 1494 (s), 1469 (m), 1450 (m), 1415 (w), 1362 (m), 1347 (m), 1301 (w), 1249 (s), 1198 (m), 1185 (s), 1167 (m), 1140 (s), 1127 (s), 1081 (m), 1025 (m), 1002 (w), 983 (w), 959 (w), 949 (w), 930 (m), 908 (w), 873 (w), 827 (s), 802 (m), 739 (s), 692 (s), 670 (s), 650 (s), 628 (m), 614 (m), 595 (m), 560 (s), 526 (m).

2-{[4-Benzoyl-5-(phenylamino)furan-2-yl]carbonyl}naphthalen-1-ol (32x):

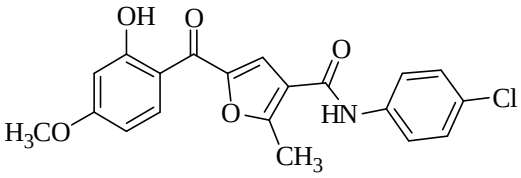


Starting with 3-chloro-7-methoxychromone **11c** (0.211 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **32x** was isolated as a orange solid (0.303 g, 70%), mp 165-167 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.26 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.38 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 7.49 (t, ^3J = 7.9 Hz, 2H, H_{Ar}), 7.55-7.65 (m, 4H, H_{Ar}), 7.65-7.71 (m, 3H, H_{Ar}), 7.75 (s, 1H, 4-H_{Ar}), 7.85-7.91 (m, 3H, H_{Ar}), 7.99 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 8.32 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 10.73, 13.65 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 102.3, 112.6, 118.4, 2^{x}120.9, 123.4, 124.5, 124.7, 125.0, 125.1, 126.1, 127.5, 2^{x}128.2, 2^{x}128.8, 2^{x}129.3, 129.9, 132.1, 136.2, 136.5, 138.3, 141.1, 160.7, 160.8, 181.2 (C=O), 188.1 (C=O); MS (EI, 70 eV) *m/z* (%): 433 ([M]$^+$, 33), 340 (39), 263 (100), 171 (11), 105 (74), 93 (35), 77 (20); HRMS (ESI): calcd for $C_{28}H_{20}NO_4$ ([M+H]$^+$) 434.13868, found 434.13892, calcd for

$C_{28}H_{19}NaNO_4$ ([M+Na]$^+$) 456.12063, found 456.12034; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3275 (w), 3054 (w), 2921 (w), 2851 (w), 1653 (w), 1626 (w), 1597 (w), 1577 (w), 1565 (w), 1524 (s), 1462 (s), 1444 (m), 1410 (m), 1381 (m), 1348 (m), 1337 (m), 1320 (m), 1253 (s), 1206 (m), 1177 (m), 1150 (m), 1125 (m), 1098 (m), 1078 (m), 1026 (m), 995 (m), 941 (m), 930 (m), 917 (m), 891 (m), 867 (m), 851 (m), 809 (m), 787 (m), 752 (s), 738 (s), 721 (s), 689 (s), 667 (s), 648 (s), 625 (s), 599 (s), 581 (m), 569 (s), 549 (s).

_N_-(4-chlorophenyl)-5-[(1-hydroxynaphthalen-2-yl)carbonyl]-2-methylfuran-3-carboxamide (33):



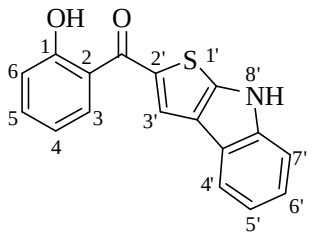
Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), *N*-(4-chlorophenyl)-3-oxobutanamide **31d** (0.233 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (6-7 mL), the product **33** was isolated as a pale yellow solid (0.027 g, 7%), mp 214-216 ºC;
^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.56 (d, ^4J = 2.4 Hz, 1H, H_{Ar}), 6.61 (dd, ^3J = 8.9 Hz, ^4J = 2.5 Hz, 1H, H_{Ar}), 7.40 (dt, ^3J = 8.9 Hz, ^4J = 2.5 Hz, 2H, H_{Ar}), 7.76 (dd, ^3J = 8.9 Hz, ^4J = 2.5 Hz, 2H, H_{Ar}), 8.00-8.04 (m, 2H, H_{Ar}), 10.07, 11.96 (both s, 2H, OH and NH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 14.0 (CH_3), 55.7 (OCH_3), 101.3, 107.2, 113.7, 118.3, 119.7, 2^{x}121.8, 127.4, 2^{x}128.5, 132.6, 137.6, 148.5, 160.6, 162.4, 163.5, 165.1, 181.9 (C=O); MS (GC, 70 eV) *m/z* (%): 385 ([M]$^+$, 36), 260 (15), 259 (100), 258 (87), 243 (15), 217 (24), 151 (47), 129 (15), 127 (42), 109 (99), 108 (10), 43 (14); HRMS (ESI): calcd for $C_{20}H_{17}{}^{35}ClNO_5$ ([M+H]$^+$) 386.07898, found 386.07870, calcd for $C_{20}H_{17}{}^{37}CNO_5$ ([M+H]$^+$) 388.07688, found 388.07690; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3325 (w), 3016 (w), 2923 (w), 2851 (w), 1734 (w), 1713 (w), 1650 (w), 1626 (m), 1606 (m), 1594 (m), 1575 (m), 1531 (m), 1515 (s), 1495 (m), 1454 (w), 1441 (w), 1403 (w), 1371 (s), 1342 (s), 1314 (m), 1294 (w), 1271 (m), 1255 (s), 1223 (m), 1213 (m), 1196 (s), 1177 (m), 1157 (w), 1136 (s), 1093 (w), 1082 (m), 1024 (w), 1016 (m), 999 (m), 962 (s), 894 (w), 874 (m), 853 (m), 835 (s), 815 (s), 760 (m), 735 (w), 711 (w), 698 (m), 685 (m), 656 (m), 634 (w), 623 (s), 611 (m), 596 (w), 534 (m).

General procedure for the synthesis of compound 35:

Method A. To a stirred reaction mixture of the corresponding 3-halochromone **10** or **11** (1.0 mmol) and 3*H*-indole-2-thione **34** (1.1 mmol) in 1,4-dioxane (12 mL), DBU (1.3 mmol) was slowly added by syringe at room temperature. Stirring was continued until the starting 3-halochromone was consumed (TLC control, 3-4 hours). The solvent was distilled off under reduced pressure. The resulting residue was purified by column chromatography (silica gel, heptane/ethyl acetate).

Method B. To a stirred reaction mixture of the corresponding 3-halochromone **9-11** (1.0 mmol) and 3*H*-indole-2-thione **34** (1.1 mmol) in DMF (12 mL), K_2CO_3 (4 mmol) was added at room temperature. Stirring was continued until the chromone was consumed (TLC control, 3-4 hours). The solvent was distilled off under reduced pressure. The resulting residue was purified by column chromatography (silica gel, heptane/ethyl acetate).

2-{8*H*-Thieno[2,3-*b*]indole-2-carbonyl}phenol (35a):



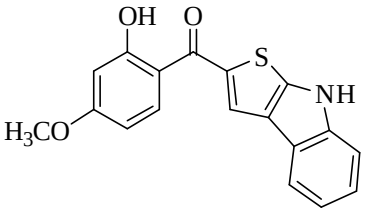
Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), indoline-2-thione **34a** (0.164 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35a** was isolated as a orange solid (0.167 g, 57%), mp 212-213 ºC, (Method A);

Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), indoline-2-thione **34a** (0.164 g, 1.1 mmol) and K_2CO_3 (0.552 g, 4 mmol) in DMF (12 mL), the product **35a** was isolated as a orange solid (0.217 g, 74%), (Method B);

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.94-7.02 (m, 2H, H_{Ar}), 7.14 (td, ^4J = 1.0 MHz, ^3J = 7.5 MHz, 1H, H_{Ar}), 7.27 (td, ^4J = 1.2 MHz, ^3J = 7.6 MHz, 1H, H_{Ar}), 7.41 (td, ^4J = 1.7 MHz, ^3J = 7.8 MHz, 1H, H_{Ar}), 7.50-7.53 (m, 2H, H_{Ar}), 7.90 (d, ^3J = 7.6 MHz, 1H, H_{Ar}), 7.98 (s, 1H, 3′-H_{Ar}), 10.21, 12.09 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 112.0, 116.7, 118.9, 119.8, 120.2, 121.9, 123.5, 125.1, 125.4, 128.6, 129.4, 132.0, 135.7, 142.5, 148.1, 155.9, 188.3 (C=O); MS (GC, 70 eV) *m/z* (%): 293 ([M]$^+$, 42), 261 (20), 260 (100), 174 (14), 173 (93), 172 (29), 128 (16), 65 (14); HRMS (EI): calcd for $C_{17}H_{11}NO_2S$ ([M]$^+$) 293.05050, found 293.05043; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3256 (w), 3079 (w), 3055 (w), 1651 (w), 1623 (w), 1583 (w), 1544 (w), 1504 (m), 1484 (w), 1470 (s), 1446 (m), 1400 (s), 1333 (m), 1312 (w), 1299 (m), 1233 (s), 1215 (s), 1154 (m), 1131 (m), 1115 (m), 1099 (w), 1085 (m), 1035 (w), 1014 (w), 979 (w),

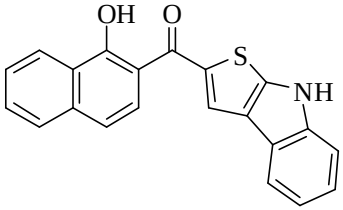
947 (w), 924 (w), 892 (w), 880 (w), 866 (m), 825 (m), 775 (m), 752 (s), 729 (s), 715 (m), 694 (s), 662 (s), 628 (m), 600 (s), 590 (m), 566 (m), 552 (m), 544 (m).

5-Methoxy-2-{8*H*-thieno[2,3-*b*]indole-2-carbonyl}phenol (35b):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), indoline-2-thione **34a** (0.164 g, 1.1 mmol) and K_2CO_3 (0.552 g, 4 mmol) in DMF (12 mL), the product **35b** was isolated as a yellow solid (0.181 g, 56%), mp 228-229 ºC, (Method B); ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.84 (s, 3H, OCH_3), 6.56-6.62 (m, 2H, H_{Ar}), 7.17 (t, ^3J = 7.4 MHz, 1H, H_{Ar}), 7.28 (td, ^4J = 0.9 MHz, ^3J = 7.6 MHz, 1H, H_{Ar}), 7.53 (d, ^3J = 8.1 MHz, 1H, H_{Ar}), 7.84 (d, ^3J = 8.7 MHz, 1H, H_{Ar}), 7.93 (d, ^3J = 7.7 MHz, 1H, H_{Ar}), 8.23 (s, 1H, 3′-H_{Ar}), 11.65 (s, 2H, OH, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 55.5 (OCH_3), 101.5, 106.4, 112.1, 115.4, 119.9, 120.3, 122.0, 123.5, 125.5, 128.1, 132.3, 134.9, 142.6, 147.9, 161.3, 163.9, 187.8 (C=O); MS (EI, 70 eV) *m/z* (%): 323 ([M]$^+$, 21), 291 (17), 290 (100), 173 (34); HRMS (ESI): calcd for $C_{18}H_{14}NO_3S$ ([M+H]$^+$) 324.06889, found 324.06883; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3246 (w), 3079 (w), 3059 (w), 3004 (w), 2982 (w), 2952 (w), 2904 (w), 2835 (w), 2719 (w), 2635 (w), 1633 (m), 1581 (m), 1550 (w), 1504 (s), 1473 (m), 1446 (m), 1396 (m), 1372 (m), 1346 (m), 1314 (w), 1278 (m), 1266 (s), 1237 (s), 1214 (s), 1194 (m), 1156 (m), 1145 (m), 1130 (w), 1101 (m), 1086 (m), 1029 (m), 1015 (w), 966 (w), 922 (w), 866 (w), 842 (m), 823 (w), 801 (w), 784 (m), 767 (m), 748 (w), 729 (s), 708 (w), 692 (s), 640 (w), 617 (m), 591 (s), 562 (w), 542 (w).

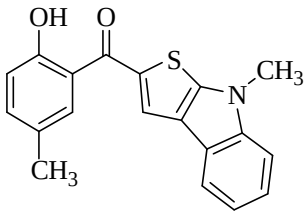
2-{8*H*-Thieno[2,3-*b*]indole-2-carbonyl}naphthalen-1-ol (35c):



Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), indoline-2-thione **34a** (0.164 g, 1.1 mmol) and K_2CO_3 (0.552 g, 4 mmol) in DMF (12 mL), the product **35c** was isolated as a dark yellow solid (0.268 g, 78%), mp 282-284 ºC, (Method B); ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.19 (t, ^3J = 7.4 MHz, 1H, H_{Ar}), 7.30 (t, ^3J = 7.4 MHz, 1H, H_{Ar}), 7.53-7.64 (m, 3H, H_{Ar}), 7.71 (t, ^3J = 7.4 MHz, 1H, H_{Ar}), 7.97 (d, ^3J = 7.8 MHz, 2H, H_{Ar}), 8.08 (d, ^3J = 8.8 MHz, 1H, H_{Ar}), 8.36 (d, ^3J = 8.3 MHz, 1H, H_{Ar}), 8.46 (s, 1H, 3′-H_{Ar}), 12.19, 13.03 (both s, 2H, OH and NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 112.2, 114.2, 118.6, 120.1, 120.4, 122.0, 123.4, 123.8, 124.7, 126.0, 2^{x}126.1, 127.6, 129.1, 129.5, 134.4, 136.0, 142.7, 148.6, 158.9, 188.9 (C=O); MS (EI, 70 eV) *m/z* (%): 343 ([M]$^+$, 37), 311 (10), 310 (49),

174 (22), 173 (100), 172 (21), 155 (10); HRMS (ESI): calcd for $C_{21}H_{14}NO_2S$ ($[M+H]^+$) 344.07398, found 344.07393; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3247 (w), 3077 (w), 3056 (w), 1629 (w), 1600 (w), 1574 (m), 1554 (m), 1502 (m), 1476 (w), 1456 (m), 1445 (m), 1424 (w), 1399 (s), 1333 (m), 1312 (m), 1274 (m), 1257 (w), 1235 (s), 1209 (m), 1190 (m), 1156 (m), 1129 (m), 1089 (m), 1025 (w), 1014 (w), 986 (w), 956 (m), 931 (w), 918 (w), 911 (w), 879 (w), 866 (w), 847 (w), 825 (w), 796 (s), 765 (m), 753 (s), 746 (s), 733 (s), 704 (m), 684 (m), 658 (m), 638 (m), 615 (m), 596 (m), 582 (s), 573 (s), 548 (m), 527 (m).

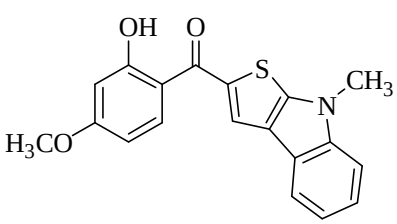
4-Methyl-2-{8-methyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}phenol (35d):



Starting with 3-bromo-6-methylchromone **10b** (0.239 g, 1.0 mmol), 1-methylindoline-2-thione **34b** (0.179 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35d** was isolated as a yellow solid (0.138 g, 43%), mp 141-143 ºC, (Method A);

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.29 (s, 3H, CH_3), 3.92 (s, 3H, NCH_3), 6.90 (d, ^3J = 8.2 MHz, 1H, H_{Ar}), 7.18-7.23 (m, 2H, H_{Ar}), 7.29 (d, ^4J = 1.8 MHz, 1H, H_{Ar}), 7.35 (td, ^4J = 1.2 MHz, ^3J = 7.7 MHz, 1H, H_{Ar}), 7.60 (d, ^3J = 8.2 MHz, 1H, H_{Ar}), 7.94 (d, ^3J = 7.7 MHz, 1H, H_{Ar}), 8.02 (s, 1H, 3′-H_{Ar}), 9.93 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.0 (CH_3), 32.3 (NCH_3), 110.3, 116.6, 120.0, 120.5, 121.9, 123.4, 123.6, 125.1, 127.6, 128.9, 129.4, 132.6, 135.8, 142.9, 150.4, 153.7, 188.1 (C=O); MS (GC, 70 eV) *m/z* (%): 321 ($[M]^+$, 32), 288 (45), 187 (100), 172 (18), 115 (12), 77 (17); HRMS (EI): calcd for $C_{19}H_{15}NO_2S$ ($[M]^+$) 321.08180, found 321.08162; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3046 (w), 2917 (w), 1621 (w), 1575 (w), 1553 (m), 1506 (m), 1495 (m), 1480 (s), 1461 (s), 1429 (m), 1422 (m), 1399 (s), 1385 (s), 1347 (m), 1315 (s), 1287 (m), 1267 (s), 1241 (s), 1211 (s), 1194 (s), 1130 (s), 1089 (m), 1052 (m), 1015 (m), 930 (m), 906 (w), 882 (w), 868 (w), 847 (w), 821 (s), 789 (s), 781 (s), 746 (s), 696 (m), 685 (m), 673 (m), 625 (s), 598 (m), 571 (w), 543 (m), 541 (m).

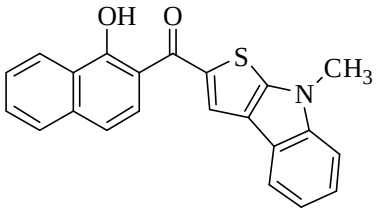
5-Methoxy-2-{8-methyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}phenol (35e):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), 1-methylindoline-2-thione **34b** (0.179 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35e** was isolated as a yellow solid (0.155 g, 46%), mp 158-159 ºC, (Method A);

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 6.44-6.48 (m, 2H, H_{Ar}), 7.14-7.19 (m, 1H, H_{Ar}), 7.26-7.28 (m, 2H, H_{Ar}), 7.73 (d, ^3J = 7.7 Hz, 1H, H_{Ar}), 7.86-7.89 (m, 2H, H_{Ar}), 12.25 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.4 (NCH_3), 55.5 (OCH_3), 101.3, 107.2, 109.4, 113.3, 119.8, 120.7, 122.3, 123.5, 124.2, 127.0, 132.7, 134.7, 143.0, 150.7, 164.8, 165.2, 188.7 (C=O); MS (GC, 70 eV) *m/z* (%): 337 ([M]$^+$, 27), 304 (100), 187 (64), 172 (12), 155 (14); HRMS (ESI): calcd for $C_{19}H_{16}NO_3S$ ([M+H]$^+$) 338.08450, found 338.08450, calcd for $C_{19}H_{15}NaNO_3S$ ([M+Na]$^+$) 360.06650, found 360.06620; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2971 (w), 2930 (w), 2848 (w), 1612 (m), 1573 (m), 1552 (w), 1491 (s), 1454 (s), 1441 (m), 1397 (m), 1364 (s), 1330 (s), 1317 (s), 1297 (m), 1250 (s), 1206 (s), 1172 (m), 1163 (s), 1139 (s), 1126 (s), 1089 (s), 1052 (s), 1023 (s), 1015 (s), 963 (s), 894 (m), 850 (s), 822 (m), 808 (s), 757 (s), 747 (s), 735 (s), 708 (s), 694 (s), 671 (m), 644 (m), 637 (s), 594 (s), 546 (s).

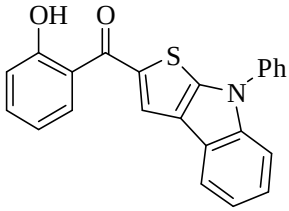
2-{8-Methyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}naphthalen-1-ol (35f):



Starting with 3-chloro-4H-benzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), 1-methylindoline-2-thione **34b** (0.179 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35f** was isolated as a yellow solid (0.196 g, 55%), mp 180-181 ºC, (Method A);

^{1}H NMR (300MHz, DMSO-d_6): δ = 3.93 (s, 3H, NCH_3), 7.24 (td, ^4J = 0.9 MHz, ^3J = 7.5 MHz, 1H, H_{Ar}), 7.37 (td, ^4J = 1.2 MHz, ^3J = 7.7 MHz, 1H, H_{Ar}), 7.53 (d, ^3J = 8.8 MHz, 1H, H_{Ar}), 7.58-7.63 (m, 2H, H_{Ar}), 7.71 (td, ^4J = 1.3 MHz, ^3J = 7.5 MHz, 1H, H_{Ar}), 7.95-8.01 (m, 2H, H_{Ar}), 8.06 (d, ^3J = 8.8 MHz, 1H, H_{Ar}), 8.36 (d, ^3J = 8.3 MHz, 1H, H_{Ar}), 8.47 (s, 1H, 3′-H_{Ar}), 13.01 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.5 (NCH_3), 110.5, 114.1, 118.6, 120.2, 120.7, 121.9, 123.4, 123.7, 124.5, 124.7, 125.7, 126.1, 127.6, 129.4, 129.5, 134.4, 136.0, 143.1, 150.8, 158.9, 188.6 (C=O); MS (EI, 70 eV) *m/z* (%): 357 ([M]$^+$, 30), 324 (21), 187 (100), 172 (11); HRMS (ESI): calcd for $C_{22}H_{16}NO_2S$ ([M+H]$^+$) 358.08963, found 358.08948, calcd for $C_{22}H_{15}NaNO_2S$ ([M+Na]$^+$) 380.07157, found 380.07118; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3047 (w), 2935 (w), 1658 (w), 1642 (w), 1628 (m), 1599 (w), 1574 (m), 1556 (w), 1536 (w), 1508 (m), 1493 (m), 1454 (s), 1425 (m), 1415 (m), 1398 (s), 1380 (s), 1343 (m), 1317 (m), 1277 (m), 1264 (s), 1253 (s), 1210 (m), 1197 (m), 1155 (m), 1139 (m), 1129 (m), 1116 (m), 1091 (m), 1052 (m), 1024 (m), 1017 (m), 953 (m), 919 (w), 883 (m), 865 (m), 843 (m), 820 (m), 804 (m), 791 (m), 772 (s), 756 (m), 733 (s), 717 (s), 704 (m), 686 (m), 658 (m), 637 (m), 605 (m), 586 (s), 572 (m), 546 (m), 532 (m).

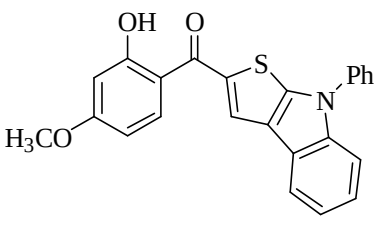
2-{8-Phenyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}phenol (35g):



Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), 1-phenylindoline-2-thione **34c** (0.248 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35g** was isolated as a orange solid (0.221 g, 60%), mp 156-157 ºC, (Method A);

^{1}H NMR (300MHz, DMSO-d_6): δ = 6.98 (td, J = 0.9 MHz, ^{3}J = 7.4 MHz, 1H, H_{Ar}), 7.02 (dd, J = 0.7 MHz, ^{3}J = 8.3 MHz, 1H, H_{Ar}), 7.29 (td, J = 0.9 MHz, ^{3}J = 7.4 MHz, 1H, H_{Ar}), 7.36 (td, ^{4}J = 1.4 MHz, ^{3}J = 7.7 MHz, 1H, H_{Ar}), 7.43 (td, ^{4}J = 1.7 MHz, ^{3}J = 7.7 MHz, 1H, H_{Ar}), 7.51 (dd, ^{4}J = 1.7 MHz, ^{3}J = 7.7 MHz, 1H, H_{Ar}), 7.56 (d, ^{3}J = 7.7 MHz, 2H, H_{Ar}), 7.71 (t, ^{3}J = 7.7 MHz, 2H, H_{Ar}), 7.78-7.81 (m, 2H, H_{Ar}), 8.05 (dd, J = 0.9 MHz, ^{3}J = 7.4 MHz, 1H, H_{Ar}), 8.12 (s, 1H, 3′-H_{Ar}), 10.19 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 110.9, 116.7, 118.9, 120.5, 121.7, 122.7, 2^{x}123.8, 124.3, 125.3, 125.5, 128.1, 128.7, 129.4, 2^{x}130.6, 132.2, 135.9, 137.2, 141.7, 148.8, 155.8, 188.4 (C=O); MS (GC, 70 eV) *m/z* (%): 369 ([M]$^{+}$, 57), 352 (17), 337 (20), 336 (81), 250 (20), 249 (100), 248 (12), 247 (15), 204 (19), 65 (10); HRMS (ESI): calcd for $C_{23}H_{16}NO_2S$ ([M+H]$^{+}$) 370.08963, found 370.08972; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3052 (w), 2921 (w), 2852 (w), 1615 (w), 1579 (m), 1557 (w), 1515 (w), 1500 (m), 1482 (m), 1467 (s), 1452 (m), 1443 (m), 1399 (s), 1373 (m), 1335 (m), 1325 (m), 1299 (m), 1275 (m), 1249 (m), 1210 (s), 1183 (m), 1150 (s), 1130 (m), 1099 (m), 1081 (m), 1035 (w), 1024 (w), 985 (w), 968 (w), 951 (w), 929 (w), 916 (w), 895 (m), 877 (w), 870 (w), 852 (w), 845 (w), 811 (w), 781 (m), 767 (s), 755 (s), 747 (s), 737 (s), 726 (s), 695 (s), 662 (s), 638 (m), 626 (m), 612 (m), 597 (s), 566 (w), 535 (m).

5-Methoxy-2-{8-phenyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}phenol (35h):

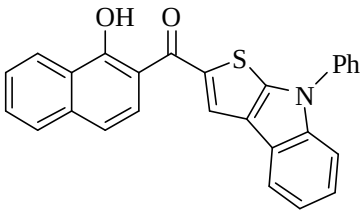


Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), 1-phenylindoline-2-thione **34c** (0.248 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35h** was isolated as a orange solid (0.140 g, 35%); mp 149-150 ºC, (Method A);

^{1}H NMR (250MHz, DMSO-d_6): δ = 3.84 (s, 3H, OCH_3), 6.58-6.63 (m, 2H, H_{Ar}), 7.28-7.40 (m, 2H, H_{Ar}), 7.52-7.59 (m, 2H, H_{Ar}), 7.68-7.85 (m, 5H, H_{Ar}), 8.07 (d, ^{3}J = 7.2 MHz, 1H, H_{Ar}), 8.35 (s, 1H, 3′-H_{Ar}), 11.33 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 55.5 (OCH_3), 101.6, 106.5, 110.8, 110.9, 115.4, 120.5, 121.7, 122.7, 2^{x}123.7, 124.3, 125.7, 128.1, 2^{x}130.5, 132.2, 135.1, 137.3, 141.7, 148.4, 161.1, 164.0, 187.7 (C=O); MS (GC, 70 eV) *m/z* (%): 399 ([M]$^{+}$, 31),

367 (26), 366 (100), 250 (13), 249 (69), 204 (11), 186 (13); HRMS (ESI): calcd for $C_{24}H_{18}NO_3S$ ($[M+H]^+$) 400.10019, found 400.10018; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3054 (w), 3011 (w), 2952 (w), 2921 (w), 2852 (w), 2705 (w), 2659 (w), 1741 (w), 1621 (w), 1595 (w), 1568 (m), 1551 (w), 1515 (w), 1500 (m), 1467 (m), 1452 (m), 1445 (m), 1403 (s), 1384 (m), 1366 (s), 1335 (m), 1324 (m), 1300 (w), 1280 (w), 1253 (s), 1231 (s), 1216 (s), 1204 (s), 1188 (s), 1159 (m), 1144 (m), 1130 (s), 1102 (m), 1082 (s), 1044 (m), 1019 (s), 962 (m), 953 (m), 917 (w), 885 (w), 828 (s), 799 (s), 765 (m), 758 (m), 737 (s), 710 (s), 695 (s), 665 (m), 643 (m), 631 (m), 612 (m), 592 (s), 574 (s).

2-{8-Phenyl-8*H*-thieno[2,3-*b*]indole-2-carbonyl}naphthalen-1-ol (35i):

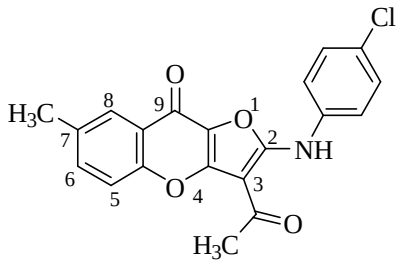


Starting with 3-chlorobenzo[*h*]chromone **11c** (0.231 g, 1.0 mmol), 1-phenylindoline-2-thione **34c** (0.248 g, 1.1 mmol) and DBU (0.20 mL, 1.3 mmol) in 1,4-dioxane (12 mL), the product **35i** was isolated as a orange solid (0.243 g, 58%), mp 164ºC, (Method A); ^{1}H NMR (300MHz, DMSO-d_6): δ = 7.30-7.41 (m, 2H, H_{Ar}), 7.53-7.64 (m, 4H, H_{Ar}), 7.69-7.74 (m, 3H, H_{Ar}), 7.80 (d, ^3J = 7.5 MHz, 2H, H_{Ar}), 7.97 (d, ^3J = 8.1 MHz, 1H, H_{Ar}), 8.05-8.12 (m, 2H, H_{Ar}), 8.36 (d, ^3J = 8.3 MHz, 1H, H_{Ar}), 8.56 (s, 1H, 3′-H_{Ar}), 12.87 (s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 110.9, 114.2, 118.8, 120.6, 121.8, 122.6, 123.4, 2^{x}123.7, 124.5, 124.7, 125.8, 126.1, 126.2, 127.6, 128.2, 129.1, 129.6, 2^{x}130.5, 134.6, 136.1, 137.2, 141.8, 149.0, 158.9, 188.9 (C=O); MS (EI, 70 eV) *m/z* (%): 419 ($[M]^+$, 36), 386 (16), 384 (12), 250 (25), 249 (100); HRMS (ESI): calcd for $C_{27}H_{18}NO_2S$ ($[M+H]^+$) 420.10528, found 420.10519, calcd for $C_{27}H_{17}NaNO_2S$ ($[M+Na]^+$) 442.08722, found 442.08734; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2953 (w), 2922 (w), 2852 (w), 1623 (w), 1593 (w), 1557 (w), 1514 (w), 1496 (m), 1446 (s), 1416 (m), 1399 (s), 1373 (m), 1339 (m), 1317 (m), 1296 (m), 1262 (m), 1250 (s), 1214 (s), 1186 (m), 1159 (m), 1149 (m), 1137 (m), 1095 (m), 1088 (m), 1075 (m), 1023 (m), 960 (m), 938 (w), 917 (m), 908 (m), 871 (w), 848 (m), 834 (m), 810 (m), 792 (m), 763 (s), 748 (s), 738 (s), 724 (s), 693 (s), 669 (m), 657 (m), 643 (m), 627 (m), 613 (m), 596 (w), 583 (s), 574 (s), 530 (m).

General procedure for the synthesis of compound 36a:

To a solution of 2-benzoylfuran **32m** (1.0 mmol) in DCM (10 ml), I_2 (2.0 mmol) was added in solid form. Subsequently, DBU (3.0 mmol) was slowly added by syringe and the mixture was stirred vigorously at room temperature. The progress of the reaction was monitored by TLC. When the starting 2-benzoylfuran **32m** was consumed (≈ 2-3 hour), an aqueous solution of $K_2S_2O_3$ (2 mmol) and K_2CO_3 (2.0 mmol) was added and the solution was extracted with $CHCl_3$ (3 x 15 ml). The combined organic layers were concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (heptane/ethylacetate, 3:1).

3-Acetyl-2-[(4-chlorophenyl)amino]-7-methyl-9*H*-furo[3,2-*b*]chromen-9-one (36a):



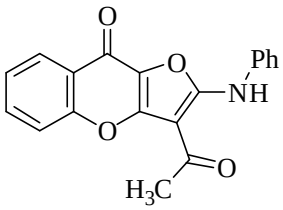
Starting with 1-{2-[(4-chlorophenyl)amino]-5-[(2-hydroxy-5-methylphenyl)carbonyl]furan-3-yl}ethan-1-one **32m** (0.111 g, 0.3 mmol), I_2 (0.152 g, 0.6 mmol) and DBU (0.14 mL, 0.9 mmol) in dichloromethane (2-3 ml), the product **36a** was isolated as a white solid (0.035 g, 32%), mp 228-230 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (s, 3H, CH_3), 2.69 (s, 3H, CH_3), 7.36-7.39 (m, 2H, H_{Ar}), 7.46-7.52 (m, 4H, H_{Ar}), 8.16 (s, 1H, 8-H_{Ar}), 10.61 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.9 (CH_3), 28.7 (CH_3), 93.6, 117.4, 2^{x}121.0, 125.9, 128.8, 2^{x}129.8, 130.5, 133.6, 134.3, 135.2, 152.7, 153.5, 159.6, 162.5, 191.9 (C=O); MS (GC, 70 eV) *m/z* (%): 367 ([M]$^+$, 100), 366 (28), 325 (16), 296 (18), 242 (44), 160 (12), 111 (14), 43 (13); HRMS (ESI): calcd for $C_{20}H_{15}{}^{35}ClNO_4$ ([M+H]$^+$) 368.06841, found 368.06838, calcd for $C_{20}H_{15}{}^{37}ClNO_4$ ([M+H]$^+$) 370.06627, found 370.06631, calcd for $C_{20}H_{14}{}^{35}ClNaNO_4$ ([M+Na]$^+$) 390.05036, found 390.05035, calcd for $C_{20}H_{14}{}^{37}ClNaNO_4$ ([M+Na]$^+$) 392.04822, found 392.04803; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3045 (w), 2923 (w), 2853 (w), 1734 (w), 1709 (w), 1659 (m), 1631 (s), 1615 (s), 1594 (s), 1573 (m), 1562 (s), 1502 (s), 1479 (s), 1435 (s), 1382 (m), 1347 (w), 1313 (w), 1290 (w), 1275 (w), 1251 (m), 1235 (m), 1198 (m), 1145 (w), 1115 (m), 1095 (m), 1060 (w), 1044 (w), 1011 (m), 959 (s), 931 (w), 894 (w), 851 (w), 828 (s), 814 (s), 794 (w), 770 (m), 759 (m), 736 (m), 710 (w), 693 (w), 673 (m), 653 (w), 631 (m), 614 (m), 548 (m).

General procedure for the synthesis of compound 36b-h and 37:

To a stirred mixture of 3-halochromone **10** or **11** (1.0 mmol) and *β*-ketoamide **31** (1.1 mmol) in dioxane (6-7 mL), DBU (1.3 mmol) was added slowly by syringe at room temperature. Stirring was continued until the 3-halochromone was completely consumed (TLC control, 3-4 hours). DCM (10 mL), I_2 (2.0 mmol) and DBU (3.0 mmol) were added, and the mixture was stirred vigorously for 2-3 hours at room temperature. The progress of the reactions was again monitored by TLC. An aqueous solution of $K_2S_2O_3$ (2 mmol) and K_2CO_3 (2.0 mmol) was added, and the solution was extracted with $CHCl_3$ (3 x 15 ml). The combined organic layers were concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, heptane/ ethylacetate = 3:1). In the case of the reaction of 3-bromochromone **10d**, the second step of the reaction was carried out in refluxing DMF.

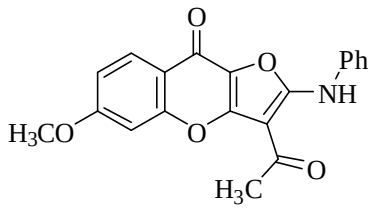
3-Acetyl-2-(phenylamino)-9*H*-furo[3,2-*b*]chromen-9-one (36b):



Starting with 3-bromochromone **10a** (0.225 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **36b** was isolated as a white solid (0.118 g, 37%), mp 258-260 ºC;

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.68 (s, 3H, CH_3), 7.21 (t, ^3J = 7.4 Hz, 1H, H_{Ar}), 7.40-7.48 (m, 3H, H_{Ar}), 7.55-7.58 (m, 3H, H_{Ar}), 7.66 (td, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 8.40 (dd, ^3J = 7.9 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 10.62 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.7 (CH_3), 93.4, 117.6, 2^{x}119.9, 125.1, 125.2, 125.3, 126.4, 128.6, 2^{x}129.7, 132.4, 135.6, 152.9, 155.2, 160.0, 162.2, 191.8 (C=O); MS (GC, 70 eV) *m/z* (%): 319 ([M]$^+$, 100), 318 (37), 277 (20), 248 (20), 228 (27), 146 (11), 77 (31), 76 (9), 43 (13); HRMS (EI): calcd for $C_{19}H_{13}NO_4$ ([M]$^+$) 319.08391, found 319.08370; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3151 (w), 3049 (w), 3014 (w), 1660 (m), 1637 (s), 1620 (s), 1596 (s), 1581 (s), 1555 (s), 1510 (s), 1459 (s), 1426 (s), 1384 (m), 1360 (m), 1326 (m), 1313 (w), 1275 (w), 1251 (m), 1205 (w), 1187 (m), 1143 (m), 1102 (m), 1082 (w), 1062 (w), 1025 (w), 999 (w), 958 (s), 898 (m), 866 (w), 845 (w), 831 (w), 802 (w), 783 (w), 745 (s), 733 (s), 704 (m), 687 (s), 656 (s), 639 (w), 624 (s), 611 (m), 593 (m), 563 (w), 538 (w).

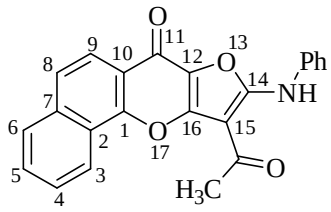
3-Acetyl-6-methoxy-2-(phenylamino)-9*H*-furo[3,2-*b*]chromen-9-one (36c):



Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **36c** was isolated as a white solid (0.098 g, 28%), mp 259-261 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 2.63 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 7.09 (dd, ^3J = 8.8 Hz, ^2J = 2.4 Hz, 1H, H_{Ar}), 7.22-7.29 (m, 2H, H_{Ar}), 7.43-7.58 (m, 4H, H_{Ar}), 8.09 (d, ^3J = 8.8 Hz, 1H, H_{Ar}), 10.41 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 27.9 (CH_3), 55.6 (OCH_3), 92.9, 101.1, 113.0, 117.7, 2^{x}120.5, 124.7, 126.0, 127.2, 2^{x}128.8, 135.4, 151.8, 156.1, 158.8, 160.6, 162.6, 190.0 (C=O); MS (GC, 70 eV) *m/z* (%): 349 ([M]$^+$, 100), 307 (15), 292 (16), 278 (20), 258 (27), 77 (24), 43 (11); HRMS (EI): calcd for $C_{20}H_{15}NO_5$ ([M]$^+$) 349.09447, found 349.09448; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3223 (w), 3065 (w), 3044 (w), 3013 (w), 2990 (w), 2948 (w), 2840 (w), 1660 (w), 1652 (w), 1616 (s), 1602 (s), 1592 (s), 1579 (s), 1553 (m), 1495 (m), 1458 (m), 1441 (s), 1378 (w), 1359 (w), 1346 (w), 1323 (w), 1271 (m), 1244 (s), 1201 (w), 1151 (w), 1133 (w), 1095 (s), 1059 (w), 1023 (m), 953 (s), 903 (w), 877 (w), 856 (m), 826 (w), 801 (w), 761 (m), 747 (s), 737 (s), 714 (m), 688 (s), 649 (m), 621 (m), 610 (s), 589 (s).

15-Acetyl-14-(phenylamino)-13,17-dioxatetracyclo[8.7.0.0^{2,7}.0^{12,16}]heptadeca-1(10),2(7),3,5,8,12(16),14-heptaen-11-one (36d).

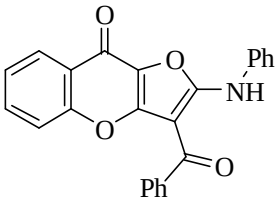


Starting with 3-bromobenzo[*h*]chromone **10d** (0.275 g, 1.0 mmol), acetoacetanilide **31a** (0.195 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **36d** was isolated as a pale yellow solid (0.052 g, 14%), mp 292-294 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 2.82 (s, 3H, CH_3), 7.28 (d, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.46-7.53 (m, 2H, H_{Ar}), 7.58-7.62 (m, 2H, H_{Ar}), 7.78-7.83 (m, 2H, H_{Ar}), 7.96 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 8.09-8.12 (m, 1H, H_{Ar}), 8.20 (d, ^3J = 8.7 Hz, 1H, H_{Ar}), 8.55-8.58 (m, 1H, H_{Ar}), 10.44 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 27.9 (CH_3), 92.8, 119.9, 2^{x}120.4, 120.5, 120.9, 121.6, 124.2, 124.6, 126.9, 127.3, 127.8, 128.1, 2^{x}128.6, 134.3, 135.3, 157.9, 158.9, 160.5, 162.9, 189.6 (C=O); MS (GC, 70 eV) *m/z* (%): 369 ([M]$^+$, 100), 327 (12), 298 (17), 278 (27), 196 (11), 171 (11), 77 (23), 43 (11); HRMS (EI): calcd for $C_{23}H_{15}NO_4$ ([M]$^+$) 369.09956, found 369.09932; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3246 (w), 3205 (w), 3169 (w), 3060 (w), 1665 (m), 1648 (s),

1635 (s), 1619 (s), 1595 (s), 1577 (s), 1556 (m), 1510 (s), 1501 (s), 1459 (m), 1438 (s), 1426 (s), 1378 (m), 1340 (m), 1324 (w), 1267 (w), 1242 (m), 1223 (m), 1188 (w), 1177 (w), 1145 (w), 1110 (w), 1093 (w), 1076 (w), 1060 (w), 1027 (w), 986 (w), 960 (m), 941 (w), 900 (w), 875 (w), 869 (w), 843 (w), 826 (m), 780 (w), 786 (w), 765 (m), 756 (s), 741 (m), 734 (m), 710 (w), 686 (m), 672 (m), 649 (w), 631 (m), 619 (w), 606 (m), 598 (w), 579 (w), 566 (m), 532 (w).

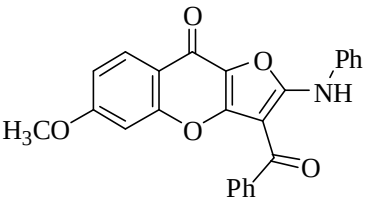
3-Benzoyl-2-(phenylamino)-9*H*-furo[3,2-*b*]chromen-9-one (36e):



Starting with 3-chlorochromone **11a** (0.181 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **36e** was isolated as a white solid (0.160 g, 42%), mp 223-225 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.22-7.32 (m, 2H, H_{Ar}), 7.43-7.53 (m, 3H, H_{Ar}), 7.57-7.73 (m, 6H, H_{Ar}), 7.88-7.92 (m, 2H, H_{Ar}), 8.19 (dd, ^3J = 7.9 Hz, ^4J = 1.6 Hz, 1H, H_{Ar}), 10.79 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 92.1, 117.0, 2^{x}120.9, 124.3, 124.4, 124.8, 125.0, 2^{x}127.4, 127.5, 2^{x}127.6, 2^{x}128.8, 121.5, 132.1, 135.4, 138.2, 151.2, 154.1, 160.6, 160.8, 186.9 (C=O); MS (GC, 70 eV) *m/z* (%): 381 ([M]$^+$, 100), 352 (21), 248 (20), 105 (63), 77 (51), 51 (9); HRMS (ESI): calcd for $C_{24}H_{16}NO_4$ ([M+H]$^+$) 382.10738, found 382.10739; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 1660 (m), 1633 (m), 1610 (m), 1591 (m), 1579 (m), 1555 (s), 1497 (m), 1469 (w), 1457 (m), 1421 (s), 1348 (m), 1336 (m), 1323 (m), 1310 (m), 1275 (w), 1263 (s), 1206 (m), 1186 (m), 1162 (m), 1145 (w), 1104 (m), 1079 (w), 1027 (w), 1001 (w), 987 (m), 960 (w), 934 (w), 911 (m), 897 (s), 873 (w), 843 (w), 823 (w), 800 (w), 784 (m), 744 (s), 691 (s), 684 (s), 665 (s), 657 (s), 637 (m), 614 (m), 592 (s), 570 (w), 536 (w), 531 (w).

3-Benzoyl-6-methoxy-2-(phenylamino)-9*H*-furo[3,2-*b*]chromen-9-one (36f):

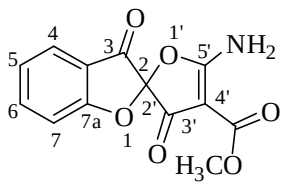


Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), 3-oxo-*N*,3-diphenylpropanamide **31f** (0.263 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **36f** was isolated as a pale yellow solid (0.086 g, 21%), mp 249-251 ºC;

^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.87 (s, 3H, OCH_3), 6.65 (d, ^4J = 2.3 Hz, 1H, H_{Ar}), 7.06 (dd, ^3J = 8.9 Hz, ^4J = 2.3 Hz, 1H, H_{Ar}), 7.28 (t, ^3J = 7.3 Hz, 1H, H_{Ar}), 7.46-7.52 (m, 2H, H_{Ar}), 7.58-7.63 (m, 4H, H_{Ar}), 7.68 (d, ^3J = 7.1 Hz, 1H, H_{Ar}), 7.88-7.91 (m, 2H, H_{Ar}), 8.09 (d, ^3J = 8.8

Hz, 1H, H_{Ar}), 10.72 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 55.3 (OCH_3), 92.1, 100.8, 112.5, 117.8, 2^{x}120.6, 124.7, 126.0, 2^{x}127.3, 127.4, 2^{x}127.5, 2^{x}128.7, 131.3, 135.4, 138.1, 150.7, 155.6, 160.2, 160.8, 162.4, 186.8 (C=O); MS (GC, 70 eV) *m/z* (%): 411 ([M]$^+$, 100), 410 (50), 382 (21), 278 (28), 105 (75), 77 (56), 51 (7); HRMS (ESI): calcd for $C_{25}H_{18}NO_5$ ([M+H]$^+$) 412.11795, found 412.11770, calcd for $C_{25}H_{17}NaNO_5$ ([M+Na]$^+$) 434.09989, found 434.09988; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3046 (w), 3004 (w), 2922 (w), 2852 (w), 1660 (m), 1631 (s), 1618 (s), 1592 (s), 1577 (m), 1568 (m), 1553 (s), 1506 (m), 1494 (m), 1455 (m), 1435 (m), 1418 (m), 1381 (m), 1368 (m), 1347 (w), 1334 (w), 1317 (w), 1278 (m), 1267 (m), 1245 (m), 1212 (m), 1197 (w), 1187 (w), 1165 (m), 1153 (w), 1143 (w), 1110 (s), 1099 (m), 1045 (w), 1028 (m), 988 (m), 941 (w), 905 (m), 889 (w), 870 (m), 843 (s), 821 (m), 811 (w), 791 (m), 748 (s), 738 (s), 715 (m), 696 (s), 680 (s), 667 (s), 637 (m), 625 (m), 614 (w), 590 (m), 579 (m), 547 (w).

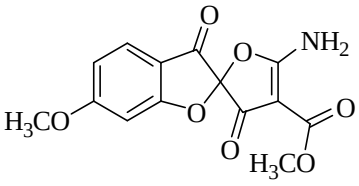
Methyl 5'-amino-3,3'-dioxo-3*H*,3'*H*-spiro[1-benzofuran-2,2'-furan]-4'-carboxylate (37a):



Starting with 3-bromochromone **10a** (0.225 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **37a** was isolated as a white solid (0.083 g, 30%), mp 292-294 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.69 (s, 3H, OCH_3), 7.33 (t, ^3J = 7.5 Hz, 1H, 5-H_{Ar}), 7.46 (d, ^3J = 8.3 Hz, 1H, 7-H_{Ar}), 7.89 (d, ^3J = 7.6 Hz, 1H, 4-H_{Ar}), 7.91 (td, ^3J = 7.8 Hz, ^4J = 1.2 Hz, 1H, 6-H_{Ar}), 9.11 (s, 1H, NH), 10.15 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 50.7 (OCH_3), 84.4, 101.7 (2-C), 113.5, 118.0, 124.4, 125.3, 140.7, 162.6, 171.4 (7a-C), 178.0 (5′-C), 180.8 (3′-C), 192.1 (3-C); MS (EI, 70 eV) *m/z* (%): 275 ([M]$^+$, 23), 151 (15), 150 (100), 121 (11), 105 (25), 68 (12), 44 (18); HRMS (ESI): calcd for $C_{13}H_{10}NO_6$ ([M+H]$^+$) 276.05026, found 276.05037; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3451 (w), 3101 (w), 3028 (w), 2962 (w), 1743 (m), 1729 (m), 1671 (m), 1640 (s), 1616 (s), 1492 (s), 1477 (s), 1460 (s), 1362 (w), 1323 (m), 1304 (m), 1237 (m), 1231 (m), 1202 (m), 1170 (m), 1153 (m), 1107 (w), 1012 (s), 1007 (s), 902 (w), 866 (m), 812 (w), 799 (m), 785 (m), 759 (s), 727 (m), 712 (w), 692 (m), 631 (s), 569 (w).

Methyl 5'-amino-6-methoxy-3,3'-dioxo-3*H*,3'*H*-spiro[1-benzofuran-2,2'-furan]-4'-carboxylate (37b):



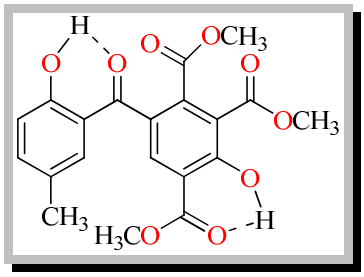
Starting with 3-chloro-7-methoxychromone **11b** (0.211 g, 1.0 mmol), methyl 2-carbamoylacetate **31e** (0.129 g, 1.1 mmol), DBU (0.20 mL, 1.3 mmol), 1,4-dioxane (6-7 mL), I_2 (0.508 g, 2.0 mmol) and DBU (0.45 mL, 3.0 mmol) in dichloromethane (10 mL), the product **37b** was isolated as a white solid (0.084 g, 27%), mp 294-296 ºC;

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.69 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.86 (dd, ^3J = 8.7 Hz, ^4J = 2.0 Hz, 1H, 5-H_{Ar}), 7.02 (d, ^4J = 1.9 Hz, 1H, 7-H_{Ar}), 7.67 (d, ^3J = 8.7 Hz, 1H, 4-H_{Ar}), 9.06 (s, 1H, NH), 10.10 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 50.7 (OCH_3), 56.8 (OCH_3), 84.4, 97.3, 102.7 (2-C), 110.8, 113.4, 126.4, 162.7, 169.6 (6-C), 174.1 (7a-C), 178.0 (5′-C), 181.0 (3′-C), 189.0 (3-C); MS (EI, 70 eV) *m/z* (%): 305 ([M]$^+$, 27), 181 (14), 180 (100), 165 (11), 151 (15), 135 (27), 78 (15), 68 (13), 63 (19), 59 (13), 44 (28); HRMS (ESI): calcd for $C_{14}H_{12}NO_7$ ([M+H]$^+$) 306.06083 found 306.06078, calcd for $C_{14}H_{11}NaNO_7$ ([M+Na]$^+$) 328.04277 found 328.04291; IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3381 (w), 3084 (w), 3024 (w), 2964 (w), 2844 (w), 1724 (m), 1689 (m), 1644 (s), 1626 (s), 1590 (m), 1501 (s), 1460 (w), 1454 (w), 1445 (m), 1424 (w), 1348 (m), 1297 (m), 1282 (m), 1265 (m), 1218 (w), 1188 (w), 1182 (w), 1158 (m), 1139 (s), 1120 (s), 1050 (m), 1023 (m), 1009 (s), 959 (w), 930 (w), 867 (w), 840 (w), 827 (w), 797 (m), 775 (w), 766 (m), 755 (w), 730 (w), 661 (m), 634 (s), 555 (w).

Supplement 2

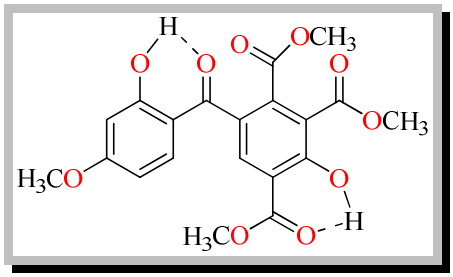
Crystallographic data

Crystal data and structure refinement for 13b:



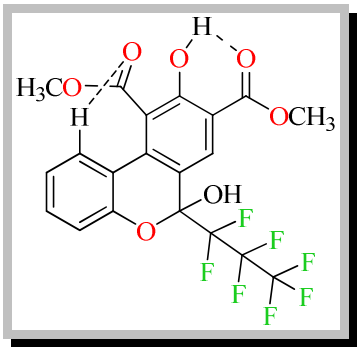
Identification code	is_is52	
Empirical formula	$C_{20}H_{18}O_9$	
Formula weight	402.34 g/mol	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.9975 (8)Å	α = 107.022 (8)°
	b = 10.6797 (11)Å	β = 99.434 (8)°
	c = 11.4242 (17)Å	γ = 111.650 (5)°
Volume	928.83 (19) $Å^3$	
Z	2	
Calculated density	1.439 mg/m^3	
Absorption coefficient	0.115 mm^{-1}	
F(000)	420	
Crystal size	0.27 × 0.20 × 0.04 mm^3	
Θ range for data collection	3.3 - 28.0°	
Limiting indices	-12≤h≤12, -14≤k≤14, -15≤l≤15	
Reflections collected	18251	
Indepent reflections	5026 [*R*(int) = 0.035]	
Completeness to Θ = 29.50°	97.1%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9954 and 0.9696	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5026/0/274	
Goodness-of-fit on F^2	1.052	
Final R indices [I > σ2(I)]	R1 = 0.0465, wR2 = 0.1176	
R indices (all data)	R1 = 0.0820, wR2 = 0.1294	
Largest diff. peak and hole	0.33 and -0.21 e $Å^{-3}$	

Crystal data and structure refinement for 13c:



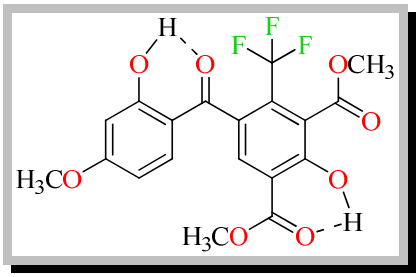
Identification code	is_is73	
Empirical formula	$C_{20}H_{18}O_{10}$	
Formula weight	418.34 g/mol	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	*Pbca*	
Space group (Hall)	-P 2ac 2ab	
Unit cell dimensions	a = 11.3807 (5)Å	α = 90.00°
	b = 8.1698 (4)Å	β = 90.00°
	c = 40.6850 (16)Å	γ = 90.00°
Volume	3782.8 (3) $Å^3$	
Z	8	
Calculated density	1.469 mg/m^3	
Absorption coefficient	0.120 mm^{-1}	
F(000)	1744	
Crystal size	0.80 × 0.48 × 0.25 mm^3	
Θ range for data collection	2.7 - 30.3°	
Limiting indices	-15≤h≤15, -11≤k≤11, -56≤l≤55	
Reflections collected	41068	
Indepent reflections	5272 [*R*(int) = 0.048]	
Completeness to Θ = 29.50°	99.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9707 and 0.9103	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5272/0/284	
Goodness-of-fit on F^2	1.090	
Final R indices [I > σ2(I)]	R1 = 0.0516, wR2 = 0.1209	
R indices (all data)	R1 = 0.0611, wR2 = 0.1248	
Largest diff. peak and hole	0.39 and -0.26 e $Å^{-3}$	

Crystal data and structure refinement for 14o:



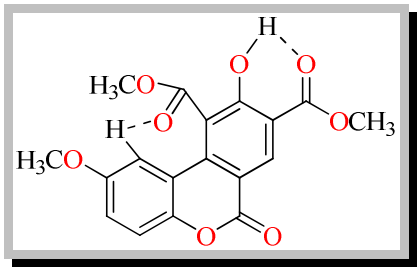
Identification code	is_is82	
Empirical formula	$C_{20}H_{13}F_7O_7$	
Formula weight	498.30 g/mol	
Temperature	173 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1$	
Space group (Hall)	P 2yb	
Unit cell dimensions	a = 10.7404 (19)Å	α = 90.00º
	b = 7.6871 (15)Å	β = 91.526 (12)º
	c = 12.188 (2)Å	γ = 90.00º
Volume	1005.9 (3) $Å^3$	
Z	2	
Calculated density	1.645 mg/m^3	
Absorption coefficient	0.164 mm^{-1}	
F(000)	504	
Crystal size	0.80 × 0.12 × 0.05 mm^3	
Θ range for data collection	4.990 - 61.299°	
Limiting indices	-15≤h≤14, -7≤k≤10, -17≤l≤17	
Reflections collected	11496	
Indepent reflections	5141 [*R*(int) = 0.028]	
Completeness to Θ = 30.00°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9918 and 0.8798	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5141/1/317	
Goodness-of-fit on F^2	1.025	
Final R indices [I > σ2(I)]	R1 = 0.0397, wR2 = 0.0895	
R indices (all data)	R1 = 0.0564, wR2 = 0.0975	
Largest diff. peak and hole	0.25 and -0.22 e $Å^{-3}$	

Crystal data and structure refinement for 15:



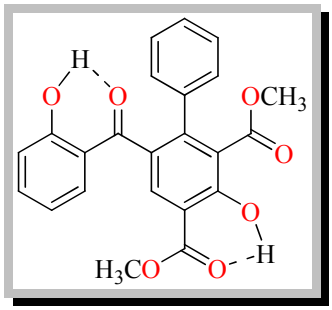
Identification code	is_is752	
Empirical formula	$C_{19}H_{15}F_3O_8$	
Formula weight	428.31 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 8.5463 (5)Å	α = 90.00º
	b = 17.9015 (12)Å	β = 107.863 (3)º
	c = 12.7567 (8)Å	γ = 90.00º
Volume	1857.6 (2) $Å^3$	
Z	4	
Calculated density	1.532 mg/m^3	
Absorption coefficient	0.138 mm^{-1}	
F(000)	880	
Crystal size	0.44 × 0.10 × 0.07 mm^3	
Θ range for data collection	2.28 - 25.14°	
Limiting indices	-12≤h≤10, -25≤k≤25, -17≤l≤17	
Reflections collected	26427	
Indepent reflections	5391 [*R*(int) = 0.064]	
Completeness to Θ = 30.00°	99.6%	
Absorption correction	Multi-scan	
Max. and min. transmission		
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5391/0/281	
Goodness-of-fit on F^2	1.042	
Final R indices [I > σ2(I)]	R1 = 0.0469, wR2 = 0.1009	
R indices (all data)	R1 = 0.0867, wR2 = 0.1192	
Largest diff. peak and hole	0.31 and -0.30 e $Å^{-3}$	

Crystal data and structure refinement for 16:



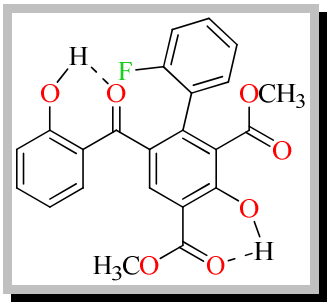
Identification code	ah_is388_1	
Empirical formula	$C_{18}H_{14}O_8$	
Formula weight	358.29 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 8.1090 (5)Å	α = 90.00º
	b = 16.4208 (9)Å	β = 100.506 (3)º
	c = 12.1650 (7)Å	γ = 90.00º
Volume	1592.69 (16) $Å^3$	
Z	4	
Calculated density	1.494 Mg/m^3	
Absorption coefficient	0.119 mm^{-1}	
F(000)	744	
Crystal size	0.24 × 0.18 × 0.13 mm^3	
Θ range for data collection	2.84 - 29.60°	
Limiting indices	-11≤h≤11, -23≤k≤19, -13≤l≤16	
Reflections collected	21690	
Indepent reflections	4560 [*R*(int) = 0.048]	
Completeness to Θ = 29.85°	99.6%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7459 and 0.6834	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4560/0/243	
Goodness-of-fit on F^2	1.045	
Final R indices [I > σ2(I)]	R1 = 0.0432, wR2 = 0.1075	
R indices (all data)	R1 = 0.0650, wR2 = 0.1205	
Largest diff. peak and hole	0.34 and -0.21 e $Å^{-3}$	

Crystal data and structure refinement for 17a:



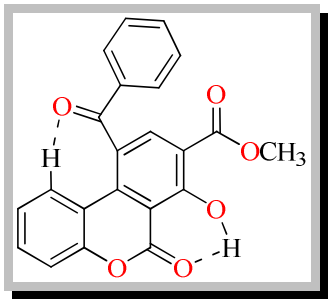
Identification code	ch_is2001	
Empirical formula	$C_{23}H_{18}O_7$	
Formula weight	406.37 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.4746 (4)Å	α = 65.728 (2)°
	b = 10.2347 (4)Å	β = 71.993 (2)°
	c = 11.4323 (4)Å	γ = 82.309 (2)°
Volume	961.06 (6) $Å^3$	
Z	2	
Calculated density	1.404 mg/m^3	
Absorption coefficient	0.105 mm^{-1}	
F(000)	424	
Crystal size	0.25 × 0.15 × 0.09 mm^3	
Θ range for data collection	4.4 - 61.8°	
Limiting indices	-13≤h≤13, -14≤k≤14, -16≤l≤16	
Reflections collected	27835	
Indepent reflections	6112 [*R*(int) = 0.052]	
Completeness to Θ = 31.00°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9906 and 0.9743	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6112/0/281	
Goodness-of-fit on F^2	1.032	
Final R indices [I > σ2(I)]	R1 = 0.0461, wR2 = 0.1131	
R indices (all data)	R1 = 0.0700, wR2 = 0.1280	
Largest diff. peak and hole	0.34 and -0.22 e $Å^{-3}$	

Crystal data and structure refinement for 17b



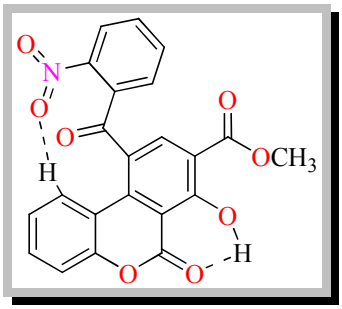
Identification code	is_is93	
Empirical formula	$C_{23}H_{17}FO_7$	
Formula weight	424.37 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	*C*2/*c*	
Space group (Hall)	-C 2yc	
Unit cell dimensions	a = 22.8935 (6)Å	α = 90.00º
	b = 8.2045 (2)Å	β = 98.132 (1)º
	c = 21.6152 (5)Å	γ = 90.00º
Volume	4019.15 (17) $Å^3$	
Z	8	
Calculated density	1.403 mg/m^3	
Absorption coefficient	0.110 mm^{-1}	
F(000)	1760	
Crystal size	0.27 × 0.24 × 0.07 mm^3	
Θ range for data collection	2.6 - 30.5°	
Limiting indices	-31≤h≤32, -11≤k≤9, -30≤l≤30	
Reflections collected	21758	
Indepent reflections	5845 [*R*(int) = 0.035]	
Completeness to Θ = 30.00°	99.6%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9923 and 0.9708	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5845/0/290	
Goodness-of-fit on F^2	1.047	
Final R indices [I > σ2(I)]	R1 = 0.0492, wR2 = 0.1252	
R indices (all data)	R1 = 0.0772, wR2 = 0.1353	
Largest diff. peak and hole	0.89 and -0.44 e $Å^{-3}$	

Crystal data and structure refinement for 18a:



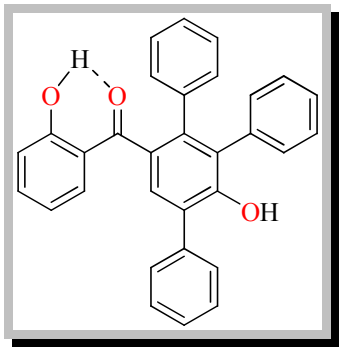
Identification code	av_is2002	
Empirical formula	$C_{22}H_{14}O_6$	
Formula weight	374.33 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.0894 (4)Å	α = 95.198 (2)°
	b = 8.8477 (4)Å	β = 97.489 (2)°
	c = 11.6944 (5)Å	γ = 90.900 (2)°
Volume	826.12 (7) $Å^3$	
Z	2	
Calculated density	1.505 mg/m^3	
Absorption coefficient	0.111 mm^{-1}	
F(000)	388	
Crystal size	0.20 × 0.18 × 0.08 mm^3	
Θ range for data collection	4.6 - 60.2°	
Limiting indices	-11≤h≤10, -12≤k≤12, -16≤l≤16	
Reflections collected	16616	
Indepent reflections	4647 [*R*(int) = 0.027]	
Completeness to Θ = 30.00°	96.5%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9912 and 0.9782	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4657/0/258	
Goodness-of-fit on F^2	1.043	
Final R indices [I > σ2(I)]	R1 = 0.0436, wR2 = 0.1064	
R indices (all data)	R1 = 0.0703, wR2 = 0.1233	
Largest diff. peak and hole	0.38 and -0.24 e $Å^{-3}$	

Crystal data and structure refinement for 18d:



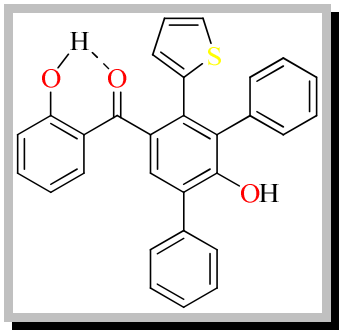
Identification code	av_is149	
Empirical formula	$C_{22}H_{13}NO_8$	
Formula weight	419.33 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.6996 (3)Å	α = 87.360 (2)°
	b = 9.4687 (3)Å	β = 71.996 (1)°
	c = 11.8581 (4)Å	γ = 77.073 (1)°
Volume	905.14 (5) $Å^3$	
Z	2	
Calculated density	1.539 mg/m^3	
Absorption coefficient	0.119 mm^{-1}	
F(000)	432	
Crystal size	0.44 × 0.13 × 0.10 mm^3	
Θ range for data collection	4.4 - 65.1°	
Limiting indices	-12≤h≤13, -14≤k≤14, -17≤l≤17	
Reflections collected	23897	
Indepent reflections	6501 [*R*(int) = 0.023]	
Completeness to Θ = 32.50°	99.4%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9882 and 0.9493	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6501/0/285	
Goodness-of-fit on F^2	1.043	
Final R indices [I > σ2(I)]	R1 = 0.0453, wR2 = 0.1158	
R indices (all data)	R1 = 0.0571, wR2 = 0.1239	
Largest diff. peak and hole	0.38 and -0.28 e $Å^{-3}$	

Crystal data and structure refinement for 20c:



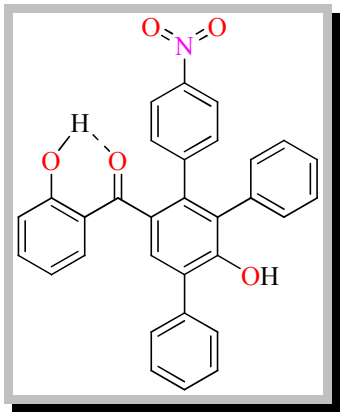
Identification code	av_is2081_b	
Empirical formula	$C_{31}H_{22}O_3$	
Formula weight	442.49 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 18.3936 (4) Å	α = 90.00º
	b = 5.9331 (1) Å	β = 96.666 (2)º
	c = 21.3185 (5) Å	γ = 90.00º
Volume	2310.78 (8) $Å^3$	
Z	4	
Calculated density	1.272 mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	928	
Crystal size	0.56 × 0.07 × 0.06 mm^3	
Θ range for data collection	5.5 - 60.7°	
Limiting indices	-24≤h≤26, -6≤k≤8, -30≤l≤30	
Reflections collected	26898	
Indepent reflections	7113 [*R*(int) = 0.054]	
Completeness to Θ = 30.67°	99.2%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9952 and 0.9561	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7113/0/315	
Goodness-of-fit on F^2	1.008	
Final R indices [I > σ2(I)]	R1 = 0.0577, wR2 = 0.1041	
R indices (all data)	R1 = 0.1228, wR2 = 0.1310	
Largest diff. peak and hole	0.30 and -0.26 e $Å^{-3}$	

Crystal data and structure refinement for 20d:



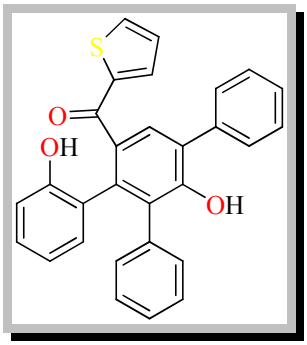
Identification code	av_is1761	
Empirical formula	$C_{29}H_{20}O_3S$	
Formula weight	448.51 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 18.4149 (9)Å	α = 90.00º
	b = 5.8081 (3)Å	β = 96.645 (3)º
	c = 21.3309 (12)Å	γ = 90.00º
Volume	2266.1 (2) $Å^3$	
Z	4	
Calculated density	1.315 mg/m^3	
Absorption coefficient	0.172 mm^{-1}	
F(000)	936	
Crystal size	0.85 × 0.06 × 0.05 mm^3	
Θ range for data collection	4.7 - 52.8°	
Limiting indices	-25≤h≤24, -7≤k≤6, -29≤l≤29	
Reflections collected	28745	
Indepent reflections	6003 [*R*(int) = 0. 115]	
Completeness to Θ = 29.00°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9914 and 0.8675	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6003/8/319	
Goodness-of-fit on F^2	1.029	
Final R indices [I > σ2(I)]	R1 = 0.0612, wR2 = 0.1038	
R indices (all data)	R1 = 0.1405, wR2 = 0.1322	
Largest diff. peak and hole	0.26 and -0.29 e $Å^{-3}$	

Crystal data and structure refinement for 20f:



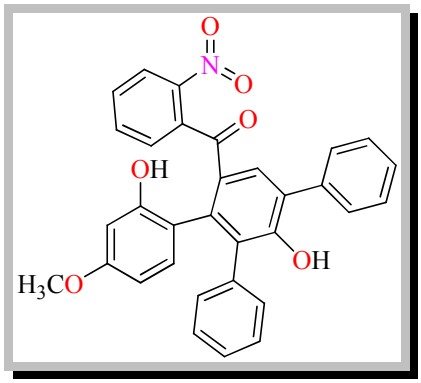
Identification code	ch_is209	
Empirical formula	$C_{31}H_{21}NO_5$	
Formula weight	487.49 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	*Fdd*2	
Space group (Hall)	F 2 -2d	
Unit cell dimensions	a = 36.4369 (12)Å	α = 90.00º
	b = 40.2125 (14)Å	β = 90.00º
	c = 6.8319 (2)Å	γ = 90.00º
Volume	10010.2 (6) $Å^3$	
Z	16	
Calculated density	1.294 mg/m^3	
Absorption coefficient	0.088 mm^{-1}	
F(000)	4064	
Crystal size	0.51 × 0.09 × 0.07 mm^3	
Θ range for data collection	4.6 - 52.7°	
Limiting indices	-48≤h≤43, -52≤k≤52, -9≤l≤8	
Reflections collected	43251	
Indepent reflections	5916 [*R*(int) = 0.061]	
Completeness to Θ = 28.00°	99.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9939 and 0.9564	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5916/1/342	
Goodness-of-fit on F^2	1.089	
Final R indices [I > σ2(I)]	R1 = 0.0519, wR2 = 0.0914	
R indices (all data)	R1 = 0.0894, wR2 = 0.1055	
Largest diff. peak and hole	0.18 and -0.22 e $Å^{-3}$	

Crystal data and structure refinement for 21b:



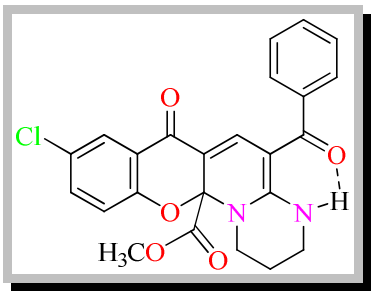
Identification code	is_is1762	
Empirical formula	$C_{29}H_{20}O_3S$	
Formula weight	448.51 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	*Pbca*	
Space group (Hall)	-P 2ac 2ab	
Unit cell dimensions	a = 7.6625 (7)Å	α = 90.00°
	b = 22.434 (2)Å	β = 90.00°
	c = 25.438 (3)Å	γ = 90.00°
Volume	4372.9 (7) $Å^3$	
Z	8	
Calculated density	1.363 mg/m^3	
Absorption coefficient	0.178 mm^{-1}	
F(000)	1872	
Crystal size	0.60 × 0.17 × 0.03 mm^3	
Θ range for data collection	4.8 - 44.1°	
Limiting indices	-9≤h≤5, -29≤k≤23, -32≤l≤31	
Reflections collected	29592	
Indepent reflections	5009 [*R*(int) = 0.112]	
Completeness to Θ = 27.50°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9947 and 0.9005	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5009/0/306	
Goodness-of-fit on F^2	1.003	
Final R indices [I > σ2(I)]	R1 = 0.0646, wR2 = 0.1225	
R indices (all data)	R1 = 0.1469, wR2 = 0.1549	
Largest diff. peak and hole	0.31 and -0.45 e $Å^{-3}$	

Crystal data and structure refinement for 21e:



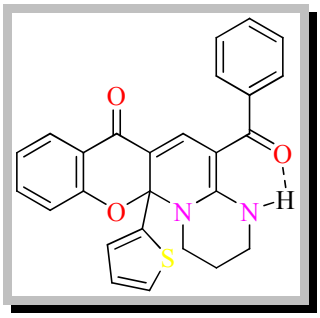
Identification code	is_is163	
Empirical formula	$C_{32}H_{23}NO_6$	
Formula weight	517.51	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	*Pbca*	
Space group (Hall)	-P 2ac 2ab	
Unit cell dimensions	a = 16.0280 (12)Å	α = 90.00º
	b = 14.4028 (12)Å	β = 90.00º
	c = 21.1809 (18)Å	γ = 90.00º
Volume	4889.6 (7) $Å^3$	
Z	8	
Calculated density	1.406 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	2160	
Crystal size	0.41 × 0.23 × 0.11 mm^3	
Θ range for data collection	2.7 - 27.4°	
Limiting indices	-20≤h≤20, -18≤k≤18, -27≤l≤27	
Reflections collected	45522	
Indepent reflections	5615 [*R*(int) = 0.100]	
Completeness to Θ = 27.50°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9893 and 0.9611	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5615/27/393	
Goodness-of-fit on F^2	1.032	
Final R indices [I > σ2(I)]	R1 = 0.0553, wR2 = 0.1514	
R indices (all data)	R1 = 0.0823, wR2 = 0.1638	
Largest diff. peak and hole	0.34 and -0.24 e $Å^{-3}$	

Crystal data and structure refinement for 25f:



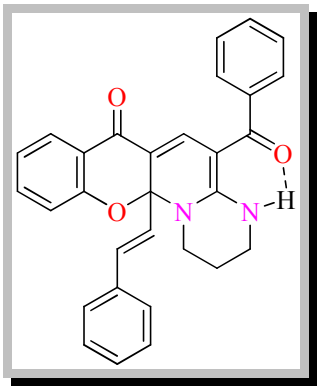
Identification code	is_is246	
Empirical formula	$C_{24}H_{19}ClN_2O_5$	
Formula weight	450.86 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.4502 (3)Å	α = 68.214 (3)°
	b = 11.0719 (5)Å	β = 82.026 (3)°
	c = 14.3255 (7)Å	γ = 71.014 (3)°
Volume	1037.37 (8) $Å^3$	
Z	2	
Calculated density	1.443 mg/m^3	
Absorption coefficient	0.225 mm^{-1}	
F(000)	468	
Crystal size	0.19 × 0.17 × 0.08 mm^3	
Θ range for data collection	6.1 - 65.5°	
Limiting indices	-11≤h≤10, -16≤k≤16, -21≤l≤21	
Reflections collected	37516	
Indepent reflections	7499 [*R*(int) = 0.049]	
Completeness to Θ = 32.50°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9822 and 0.9585	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7499/0/294	
Goodness-of-fit on F^2	1.004	
Final R indices [I > σ2(I)]	R1 = 0.0487, wR2 = 0.1007	
R indices (all data)	R1 = 0.0970, wR2 = 0.1214	
Largest diff. peak and hole	0.39 and -0.44 e $Å^{-3}$	

Crystal data and structure refinement for 26g:



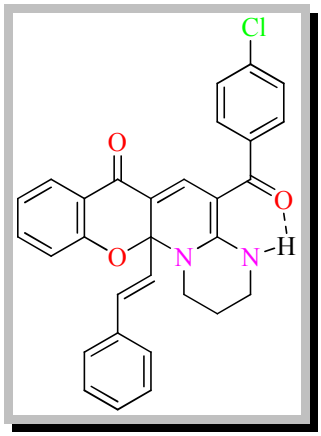
Identification code	ch_is255	
Empirical formula	$C_{26}H_{20}N_2O_3S$	
Formula weight	440.50 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 7.8696 (2)Å	α = 90.00º
	b = 16.2835 (5)Å	β = 95.653 (2)º
	c = 16.1443 (5)Å	γ = 90.00º
Volume	2058.74 (10) $Å^3$	
Z	4	
Calculated density	1.421 mg/m^3	
Absorption coefficient	0.019 mm^{-1}	
F(000)	920	
Crystal size	0.36 × 0.21 × 0.06 mm^3	
Θ range for data collection	5.6 - 61.1°	
Limiting indices	-11≤h≤11, -23≤k≤19, -23≤l≤23	
Reflections collected	33282	
Indepent reflections	6557 [*R*(int) = 0.052]	
Completeness to Θ = 31.00°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9887 and 0.9346	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6557/0/312	
Goodness-of-fit on F^2	1.028	
Final R indices [I > σ2(I)]	R1 = 0.0501, wR2 = 0.1038	
R indices (all data)	R1 = 0.0877, wR2 = 0.1203	
Largest diff. peak and hole	0.33 and -0.24 e $Å^{-3}$	

Crystal data and structure refinement for 26m:



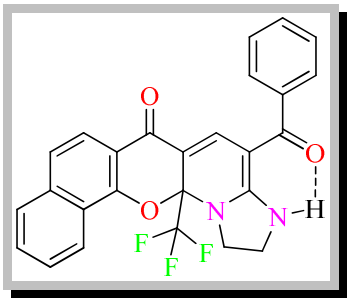
Identification code	is_is252	
Empirical formula	$C_{30}H_{24}N_2O_3$	
Formula weight	460.51 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 10.2821 (12)Å	α = 107.939 (6)°
	b = 10.3291 (12)Å	β = 98.029 (6)°
	c = 13.0613 (14)Å	γ = 115.540 (6)°
Volume	1129.2 (2) $Å^3$	
Z	2	
Calculated density	1.354 mg/m^3	
Absorption coefficient	0.088 mm^{-1}	
F(000)	484	
Crystal size	0.28 × 0.10 × 0.06 mm^3	
Θ range for data collection	4.8 - 49.7°	
Limiting indices	-12≤h≤12, -11≤k≤12, -16≤l≤16	
Reflections collected	15811	
Indepent reflections	4235 [*R*(int) = 0.066]	
Completeness to Θ = 26.00°	95.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9947 and 0.9758	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4235/0/321	
Goodness-of-fit on F^2	1.001	
Final R indices [I > σ2(I)]	R1 = 0.0565, wR2 = 0.1216	
R indices (all data)	R1 = 0.1164, wR2 = 0.1512	
Largest diff. peak and hole	0.27 and -0.26 e $Å^{-3}$	

Crystal data and structure refinement for 26n:



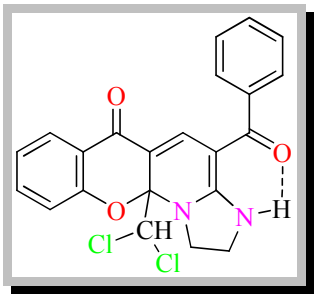
Identification code	is_is264	
Empirical formula	$C_{30}H_{23}ClN_2O_3$	
Formula weight	494.95 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 8.1449 (2)Å	α = 90.00º
	b = 12.9178 (3)Å	β = 93.823 (1)º
	c = 22.4376 (4)Å	γ = 90.00º
Volume	2355.50 (9) $Å^3$	
Z	4	
Calculated density	1.396 mg/m^3	
Absorption coefficient	0.199 mm^{-1}	
F(000)	1032	
Crystal size	0.48 × 0.10 × 0.06 mm^3	
Θ range for data collection	4.8 - 60.3°	
Limiting indices	-11≤h≤11, -18≤k≤18, -29≤l≤32	
Reflections collected	36329	
Indepent reflections	7489 [*R*(int) = 0.047]	
Completeness to Θ = 31.00°	99.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9881 and 0.9104	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7489/0/329	
Goodness-of-fit on F^2	1.007	
Final R indices [I > σ2(I)]	R1 = 0.0475, wR2 = 0.0944	
R indices (all data)	R1 = 0.0928, wR2 = 0.1134	
Largest diff. peak and hole	0.35 and -0.26 e $Å^{-3}$	

Crystal data and structure refinement for 26o:



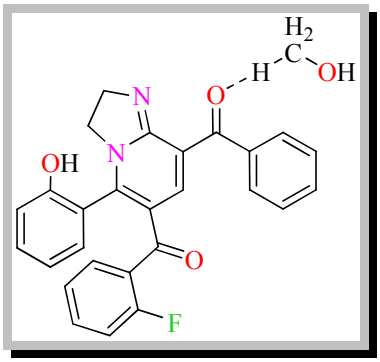
Identification code	is_is4602	
Empirical formula	$C_{26}H_{17}F_3N_2O_3$	
Formula weight	462.41 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 7.4706 (7)Å	α = 90.00º
	b = 19.1877 (17)Å	β = 95.507 (4)º
	c = 14.3379 (11)Å	γ = 90.00º
Volume	2045.8 (3) $Å^3$	
Z	4	
Calculated density	1.501 mg/m^3	
Absorption coefficient	0.117 mm^{-1}	
F(000)	952	
Crystal size	0.27 × 0.08 × 0.04 mm^3	
Θ range for data collection	2.9 - 21.3°	
Limiting indices	-7≤h≤9, -18≤k≤24, -18≤l≤18	
Reflections collected	22066	
Indepent reflections	4507 [*R*(int) = 0.085]	
Completeness to Θ = 27.09°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7455 and 0.6852	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4507/3/324	
Goodness-of-fit on F^2	1.000	
Final R indices [I > σ2(I)]	R1 = 0.0539, wR2 = 0.0903	
R indices (all data)	R1 = 0.1384, wR2 = 0.1185	
Largest diff. peak and hole	0.23 and -0.28 e $Å^{-3}$	

Crystal data and structure refinement for 26p:



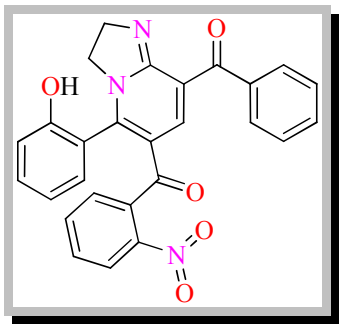
Identification code	is_2701	
Empirical formula	$C_{22}H_{16}Cl_2N_2O_3$	
Formula weight	427.27 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 9.9068 (6)Å	α = 114.988 (3)°
	b = 10.0544 (6)Å	β = 100.724 (3)°
	c = 10.9014 (7)Å	γ = 100.864 (3)°
Volume	922.51 (10) $Å^3$	
Z	2	
Calculated density	1.538 mg/m^3	
Absorption coefficient	0.381 mm^{-1}	
F(000)	440	
Crystal size	0.21 × 0.16 × 0.08 mm^3	
Θ range for data collection	5.2 - 62.0°	
Limiting indices	-13≤h≤13, -14≤k≤14, -15≤l≤15	
Reflections collected	20836	
Indepent reflections	5335 [*R*(int) = 0.027]	
Completeness to Θ = 30.00°	99.3%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9702 and 0.9243	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5335/0/226	
Goodness-of-fit on F^2	1.019	
Final R indices [I > σ2(I)]	R1 = 0.0388, wR2 = 0.0880	
R indices (all data)	R1 = 0.0582, wR2 = 0.0975	
Largest diff. peak and hole	0.38 and -0.28 e $Å^{-3}$	

Crystal data and structure refinement for 27b:



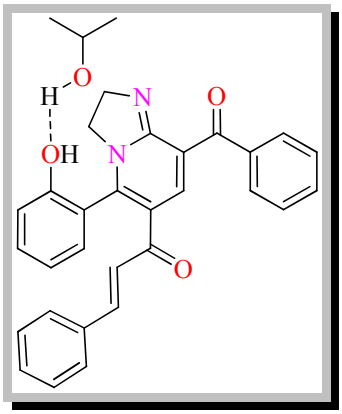
Identification code	is_is404
Empirical formula	$C_{27}H_{19}FN_2O_3 \cdot CH_4O$
Formula weight	470.48 g/mol
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group (H.-M.)	*Pbca*
Space group (Hall)	-P 2ac 2ab
Unit cell dimensions	a = 13.6829 (4)Å α = 90.00º
	b = 13.6968 (5)Å β = 90.00º
	c = 24.0304 (7)Å γ = 90.00º
Volume	4503.6 (2) $Å^3$
Z	8
Calculated density	1.388 mg/m^3
Absorption coefficient	0.098 mm^{-1}
F(000)	1968
Crystal size	0.60 × 0.23 × 0.10 mm^3
Θ range for data collection	2.3 - 29.4°
Limiting indices	-18≤h≤18, -18≤k≤16, -32≤l≤32
Reflections collected	61437
Indepent reflections	5973 [*R*(int) = 0.072]
Completeness to Θ = 29.00°	99.8%
Absorption correction	Multi-scan
Max. and min. transmission	0.7461 and 0.7002
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5973/21/347
Goodness-of-fit on F^2	1.023
Final R indices [I > σ2(I)]	R1 = 0.0554, wR2 = 0.1169
R indices (all data)	R1 = 0.0979, wR2 = 0.1394
Largest diff. peak and hole	0.30 and -0.38 e $Å^{-3}$

Crystal data and structure refinement for 27d:



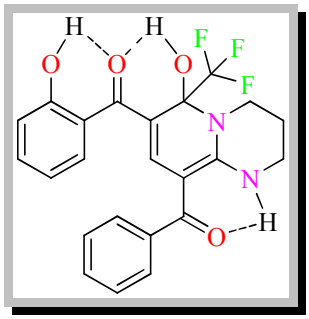
Identification code	is_is268	
Empirical formula	$C_{27}H_{19}N_3O_5$	
Formula weight	465.45 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 12.1392 (3)Å	α = 90.00º
	b = 13.7350 (3)Å	β = 96.476 (1)º
	c = 13.1589 (3)Å	γ = 90.00º
Volume	2180.01 (9) $Å^3$	
Z	4	
Calculated density	1.418 mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	968	
Crystal size	0.26 × 0.19 × 0.17 mm^3	
Θ range for data collection	2.4 - 30.7°	
Limiting indices	-17≤h≤15, -14≤k≤19, -18≤l≤17	
Reflections collected	32868	
Indepent reflections	6327 [*R*(int) = 0.057]	
Completeness to Θ = 30.00°	99.5%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7463 and 0.6916	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6327/0/317	
Goodness-of-fit on F^2	1.014	
Final R indices [I > σ2(I)]	R1 = 0.0538, wR2 = 0.1092	
R indices (all data)	R1 = 0.1129, wR2 = 0.1328	
Largest diff. peak and hole	0.31 and -0.28 e $Å^{-3}$	

Crystal data and structure refinement for 27h:



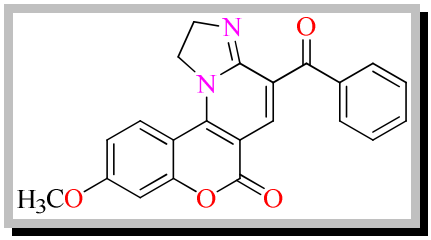
Identification code	av_is405	
Empirical formula	$C_{29}H_{22}N_2O_3 \cdot 0.5(C_3H_8O)$	
Formula weight	476.53 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	C 2/c	
Space group (Hall)	-C 2yc	
Unit cell dimensions	a = 24.3897(15)Å	α = 90.00º
	b = 14.4367 (9) Å	β = 95.522 (4)°
	c = 14.2172 (9) Å	γ = 90.00 º
Volume	4982.7 (5) $Å^3$	
Z	8	
Calculated density	1.270 mg/m^3	
Absorption coefficient	0.08 mm^{-1}	
F(000)	2008	
Crystal size	0.08 × 0.08 × 0.02 mm^3	
Θ range for data collection	2.8 - 20.6 °	
Limiting indices	-29≤h≤29, -17≤k≤16, -17≤l≤17	
Reflections collected	23255	
Indepent reflections	4642 [*R*(int) = 0.118]	
Completeness to Θ = 25.50°	99.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7453 and 0.6574	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4642 /1/345	
Goodness-of-fit on F^2	1.001	
Final R indices [I > σ2(I)]	R1 = 0.0591, wR2 = 0.1142	
R indices (all data)	R1 = 0.1486, wR2 = 0.1550	
Largest diff. peak and hole	0.32 and -0.24 e $Å^{-3}$	

Crystal data and structure refinement for 28e:



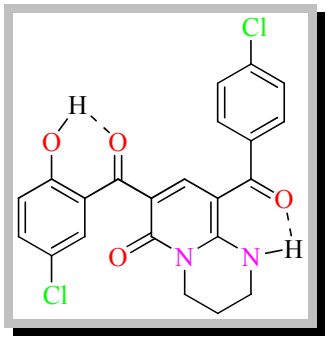
Identification code	is_is4061	
Empirical formula	$C_{23}H_{19}F_3N_2O_4$	
Formula weight	444.40 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	*P* -1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 11.4582 (2)Å	α = 91.229 (1)°
	b = 11.8588 (2)Å	β = 111.145 (1)°
	c = 15.5620 (3)Å	γ = 91.826 (1)°
Volume	1969.97 (6) $Å^3$	
Z	4	
Calculated density	1.498 mg/m^3	
Absorption coefficient	0.122 mm^{-1}	
F(000)	920	
Crystal size	0.25 × 0.21 × 0.16 mm^3	
Θ range for data collection	2.5 - 30.6°	
Limiting indices	-16≤h≤16, -16≤k≤16, -21≤l≤21	
Reflections collected	44219	
Indepent reflections	11474 [*R*(int) = 0.038]	
Completeness to Θ = 30.00°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7463 and 0.6857	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11474/0/601	
Goodness-of-fit on F^2	1.008	
Final R indices [I > σ2(I)]	R1 = 0.0468, wR2 = 0.0932	
R indices (all data)	R1 = 0.0855, wR2 = 0.1123	
Largest diff. peak and hole	0.35 and -0.22 e $Å^{-3}$	

Crystal data and structure refinement for 29b:



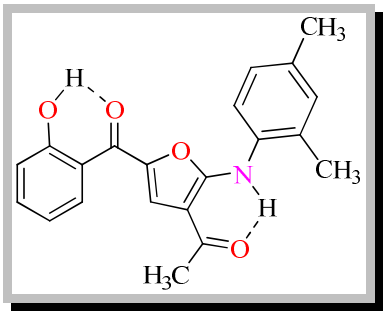
Identification code	ah_is4594	
Empirical formula	$C_{22}H_{16}N_2O_4$	
Formula weight	372.37 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 15.2230 (4)Å	α = 90.00º
	b = 6.7516 (1)Å	β = 104.295 (1)º
	c = 16.7885 (4)Å	γ = 90.00º
Volume	1672.09 (6) $Å^3$	
Z	4	
Calculated density	1.479 mg/m^3	
Absorption coefficient	0.103 mm^{-1}	
F(000)	776	
Crystal size	0.22 × 0.20 × 0.04 mm^3	
Θ range for data collection	2.5 - 30.5°	
Limiting indices	-20≤h≤16, -8≤k≤6, -21≤l≤22	
Reflections collected	20211	
Indepent reflections	4019 [*R*(int) = 0.045]	
Completeness to Θ = 28.00°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7462 and 0.6950	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4019/0/254	
Goodness-of-fit on F^2	1.027	
Final R indices [I > σ2(I)]	R1 = 0.0860, wR2 = 0.0920	
R indices (all data)	R1 = 0.0860, wR2 = 0.1090	
Largest diff. peak and hole	0.25 and -0.25 e $Å^{-3}$	

Crystal data and structure refinement for 30b:



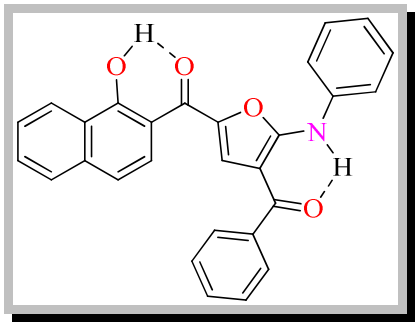
Identification code	is_is2451	
Empirical formula	$C_{22}H_{16}Cl_2N_2O_4 \cdot H_2O$	
Formula weight	461.28 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 14.6744 (16)Å	α = 90.00º
	b = 7.8448 (9)Å	β = 104.472 (5)º
	c = 18.406 (2)Å	γ = 90.00º
Volume	2051.7 (4) $Å^3$	
Z	4	
Calculated density	1.493 mg/m^3	
Absorption coefficient	0.355 mm^{-1}	
F(000)	952	
Crystal size	0.25 × 0.21 × 0.04 mm^3	
Θ range for data collection	4.6 - 46.8°	
Limiting indices	-17≤h≤17, -8≤k≤9, -21≤l≤21	
Reflections collected	16757	
Indepent reflections	3576 [*R*(int) = 0.054]	
Completeness to Θ = 25.00°	98.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9859 and 0.9164	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3576/0/279	
Goodness-of-fit on F^2	0.992	
Final R indices [I > σ2(I)]	R1 = 0.0502, wR2 = 0.1030	
R indices (all data)	R1 = 0.0937, wR2 = 0.1154	
Largest diff. peak and hole	0.34 and -0.44 e $Å^{-3}$	

Crystal data and structure refinement for 32e:



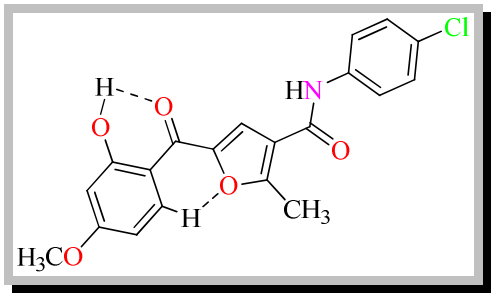
Identification code	is_is29d1_c	
Empirical formula	$C_{21}H_{19}NO_4$	
Formula weight	349.37 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	*Aba*2	
Space group (Hall)	A 2 -2ac	
Unit cell dimensions	a = 53.4482 (16)Å	α = 90.00º
	b = 16.9847 (5)Å	β = 90.00º
	c = 7.5348 (3)Å	γ = 90.00º
Volume	6840.1 (4) $Å^3$	
Z	16	
Calculated density	1.357 mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	2944	
Crystal size	0.30 × 0.20 × 0.10 mm^3	
Θ range for data collection	5.0 - 50.1 °	
Limiting indices	-69≤h≤69, -22≤k≤21, -9≤l≤9	
Reflections collected	15265	
Indepent reflections	6289 [*R*(int) = 0.038]	
Completeness to Θ = 28.00°	92.4%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9906 and 0.9723	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6289 /1/491	
Goodness-of-fit on F^2	1.033	
Final R indices [I > σ2(I)]	R1 = 0.0458, wR2 = 0.0854	
R indices (all data)	R1 = 0.0619, wR2 = 0.0926	
Largest diff. peak and hole	0.21 and -0.23 e $Å^{-3}$	

Crystal data and structure refinement for 32x:



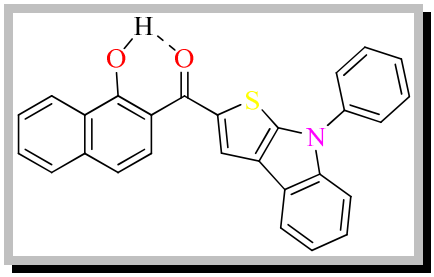
Identification code	is_is361	
Empirical formula	$C_{28}H_{19}NO_4$	
Formula weight	433.44 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 15.6057 (3)Å	α = 90.00º
	b = 13.4479 (2)Å	β = 94.359 (1)º
	c = 9.9275 (2)Å	γ = 90.00º
Volume	2077.40 (7) $Å^3$	
Z	4	
Calculated density	1.386 mg/m^3	
Absorption coefficient	0.093 mm^{-1}	
F(000)	904	
Crystal size	0.30 × 0.24 × 0.18 mm^3	
Θ range for data collection	5.1 - 61.5°	
Limiting indices	-23≤h≤17, -20≤k≤18, -13≤l≤14	
Reflections collected	34884	
Indepent reflections	7154 [*R*(int) = 0.036]	
Completeness to Θ = 31.90°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9834 and 0.9726	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7154/0/306	
Goodness-of-fit on F^2	1.024	
Final R indices [I > σ2(I)]	R1 = 0.0492, wR2 = 0.1052	
R indices (all data)	R1 = 0.0929, wR2 = 0.1249	
Largest diff. peak and hole	0.32 and -0.25 e $Å^{-3}$	

Crystal data and structure refinement for 33:



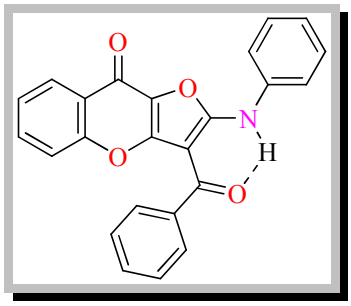
Identification code	is_is3801	
Empirical formula	$C_{20}H_{16}ClNO_5 \cdot C_2H_6OS$	
Formula weight	463.92 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/m$	
Space group (Hall)	-P 2yb	
Unit cell dimensions	a = 9.7020 (2)Å	α = 90.00º
	b = 6.8943 (1)Å	β = 91.201 (1)º
	c = 16.0179 (3)Å	γ = 90.00º
Volume	1071.18 (3) $Å^3$	
Z	2	
Calculated density	1.438 mg/m^3	
Absorption coefficient	0.316 mm^{-1}	
F(000)	484	
Crystal size	0.28 × 0.27 × 0.13 mm^3	
Θ range for data collection	4.9 - 70.7°	
Limiting indices	-14≤h≤14, -10≤k≤10, -23≤l≤23	
Reflections collected	18612	
Indepent reflections	3979 [*R*(int) = 0.022]	
Completeness to Θ = 32.00°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9601 and 0.9168	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3979/0/192	
Goodness-of-fit on F^2	1.025	
Final R indices [I > σ2(I)]	R1 = 0.0382, wR2 = 0.1038	
R indices (all data)	R1 = 0.0465, wR2 = 0.1126	
Largest diff. peak and hole	0.47 and -0.37 e $Å^{-3}$	

Crystal data and structure refinement for 35i:



Identification code	is_is447	
Empirical formula	$C_{27}H_{17}NO_2S$	
Formula weight	419.48 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 10.4820 (5)Å	α = 90.00º
	b = 9.7696 (4)Å	β = 105.020 (2)º
	c = 19.8471 (8)Å	γ = 90.00º
Volume	1963.00 (15) $Å^3$	
Z	4	
Calculated density	1.419 mg/m^3	
Absorption coefficient	0.191 mm^{-1}	
F(000)	872	
Crystal size	0.44 × 0.30 × 0.22 mm^3	
Θ range for data collection	2.9 - 32.5°	
Limiting indices	-15≤h≤15, -12≤k≤14, -30≤l≤28	
Reflections collected	32487	
Indepent reflections	7065 [*R*(int) = 0.028]	
Completeness to Θ = 32.50°	99.5%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7464 and 0.6868	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7065/0/284	
Goodness-of-fit on F^2	1.032	
Final R indices [I > σ2(I)]	R1 = 0.0407, wR2 = 0.1086	
R indices (all data)	R1 = 0.0537, wR2 = 0.1206	
Largest diff. peak and hole	0.39 and -0.21 e $Å^{-3}$	

Crystal data and structure refinement for 36e:



Identification code	is_is411	
Empirical formula	$C_{24}H_{15}NO_4$	
Formula weight	381.37 g/mol	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	$P2_12_12_1$	
Space group (Hall)	P 2ac 2ab	
Unit cell dimensions	a = 4.9114 (4)Å	α = 90.00º
	b = 9.9314 (7)Å	β = 90.00º
	c = 36.687 (3)Å	γ = 90.00º
Volume	1789.5 (2) $Å^3$	
Z	4	
Calculated density	1.416 mg/m^3	
Absorption coefficient	0.097 mm^{-1}	
F(000)	792	
Crystal size	0.99 × 0.10 × 0.04 mm^3	
Θ range for data collection	4.7 - 44.1°	
Limiting indices	-6≤h≤6, -13≤k≤13, -49≤l≤48	
Reflections collected	18306	
Indepent reflections	4548 [*R*(int) = 0.072]	
Completeness to Θ = 28.50°	100%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9961 and 0.9099	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4548/0/267	
Goodness-of-fit on F^2	1.010	
Final R indices [I > σ2(I)]	R1 = 0.0480, wR2 = 0.0925	
R indices (all data)	R1 = 0.0937, wR2 = 0.1105	
Largest diff. peak and hole	0.20 and -0.20 e $Å^{-3}$	

List of abbreviations

A	Absorption
AMP	Adenosine monophosphate
Ar	Aromatic
ATP	Adenosine triphosphate
d	Day
2D	Two-dimensional
CN	Nitrile
COSY	Correlation spectroscopy
DABCO	1,4-Diazabicyclo[2.2.2]octane
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMF	*N*,*N*-Dimethylformamide
DMF-DMA	*N*,*N*-Dimethylformamide dimethyl acetal
DNA	Deoxyribonucleic acid
ε	Extinction coefficient
EI	Electron ionization
ESI	Electrospray ionization
Et	Ethyl
GC	Gas chromatography
GTP	Guanosine-5'-triphosphate
h	Hour
H_{Ar}	Aromatic hydrogen atom
HCl	Hydrochloric acid
HIV	Human immunodeficiency virus
HKA	Heterocyclic ketene aminal
HMBC	Heteronuclear multiple bond correlation
HRMS	High resolution mass spectroscopy
Hz	Hertz

IR	Infrared spectroscopy
IMPDH	Inosine-5′-monophosphate dehydrogenase
J	Coupling constant
λ	Wavelength
Me	Methyl
MeCN	Acetonitrile
MS	Mass spectrometry
mp	Melting point
NAD	Nicotinamide adenine dinucleotide
NMR	Nuclear magnetic resonance
Nu	Nucleophile
Ph	Phenyl
r. t.	Room temperature
R^F	Polyfluoroalkyl group
RNA	Ribonucleic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
UV	Ultraviolet
*	Chiral atom (centre)

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List of publications

1. Viktor O. Iaroshenko,* Satenik Mkrtchyan, Dmitriy M. Volochnyuk, Peter Langer,* Vyacheslav Ya. Sosnovskikh,* Dmytro Ostrovskyi, Sergii Dudkin, Anton V. Kotljarov, Mariia Miliutina, **Iryna Savych**, Andrei A. Tolmachev, *Synthesis* **2010**, 2749-2759.

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3. **Iryna Savych**, Tim Gläsel, Alexander Villinger, Vyacheslav Ya. Sosnovskikh, Viktor O. Iaroshenko,* Peter Langer,* *Org. Biomol. Chem.*, **2014**, DOI: 10.1039/C4OB01730G.

Poster contributions to academic conferences

1. **Iryna Savych**, Alexander Villinger, Vyacheslav Ya. Sosnovskikh, Peter Langer,* Viktor O. Iaroshenko,* - *"Reactions of 3-acylchromones with dimethyl 1,3-acetonedicarboxylate and 1,3-diphenylacetone: one-pot synthesis of functionalized 2-hydroxybenzophenones, 6H-benzo[c]chromenes and benzo[c]coumarins*" - 15th JCF-Frühjahrssymposium, 6th-9th March, **2013**, Berlin, Germany.

2. **Iryna Savych**, Tim Gläsel, Alexander Villinger, Viktor O. Iaroshenko,* Peter Langer,* - *"Efficient Synthesis of Functionalized 2-Salicyloylfurans and Furo[3,2-b]chromen-9-ones based on One-Pot Cyclizations of 3-Halochromones"* - 16th JCF-Frühjahrssymposium 26th-29th March, **2014**, Jena, Germany.