Synthesis of Functionalized 6-(Pyridyl)salicylates, Bis(benzophenones), Chlorinated 6*H*-Benzo[*c*]chromen-6-ones, 9*H*-Fluoren-9-ones, Isobenzomorphans and Dibenzo[*b*,*d*]pyrid-6-ones based on New Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes

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Affectionately Dedicated to

My mother who always remain in my heart and soul,

And my beloved nephews Ibraheem and Abdurrafay

CONTENTS

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In the name of Allah, Who is Ubiquitous, Omniscient, Worthy of all praise and Creator of all of us, Who guides in darkness and helps in difficulties. I do obeisance in thanks and gratitude for all His blessings, due to which I was able to accomplish this strenuous task.

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Mirza Arfan Yawer

Abbreviations

Ar	Aromatic
APT	Attached Proton Test
ATCC	American Type Culture Collection
*n*BuLi	*n*-Butylithium
DEPT	Distortionless Enhancement by Polarisation Transfer
EI	Electronic Impact
ESI	Electrospray Ionization
EtOAc	Ethylacetate
HRMS	High Resolution Mass Spectroscopy
IR	Infrared Spectroscopy
LDA	Lithium Diisopropylamide
MS	Mass Spectrometry
Ph	Phenyl
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resonance
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser and Exchange Spectroscopy
Me_3SiOTf	Trimethylsilyl-trifluoromethanesulfonate
Me_3SiCl	Trimethylsilylchloride
mp.	Melting Point
RCM	Ring Closing Metathesis
TBAI	Tetrabutyl Amonium Iodie
TFA	Trifluoroacetic Acid
Tf_2O	Trifluoromethanesulfonic Anhydride
THF	Tetrahydrofurane
TLC	Thin Layer Chromatography
TMS	Trimethylsilane

UV	Ultraviolet Spectroscopy

General introduction

One of the main goal of modern organic chemistry is to develop efficient methods for the synthesis of complex molecules with high chemo-, regio- and stereoselectivity. In addition, the development of new drugs is a great challenge for organic chemists[1]. For example, it is important to develop new antibiotics, due to the increasing problem of resistance of many bacteria against various antibiotics.

In the search for new active ingredients, natural substances often are important lead structures for drug discovery. Thus, it is obvious to construct synthetic compounds or substances which are derived from nature, following the example of nature. The usual procedure for the synthesis of organic compounds is the stepwise formation of individual bonds. However, it would be much more efficient if one could form several bonds in one step without isolating the intermediates, changing the reaction conditions, or adding reagents.[1] It is obvious that this type of reaction would allow to reduce the waste compared to sequential reactions. In addition, the amount of solvents, reagents, adsorbents, and energy would be dramatically decreased. Furthermore the amount of labor would go down. Thus, these reactions would allow an ecologically and economically favourable production. We call this type of transformation a domino reaction[1].

The value of domino and cyclization reaction with masked dianion lies in the heart of organic synthesis and has immense applications. The reactions are often carried out as a one-pot method and can provide an easy access to a large number of natural product analogues. The pharmacological efficiency of these analogues may be better than that of the natural products themselves.

My studies are focussed on the development of new and reliable synthetic strategies and their application for the preparation of natural product analogues and of pharmacologically active carba- and heterocycles. The target structures include pyridyl salicylates, phenanthridinones, chlorinated biaryls, chlorinated dibenzo[*b,d*]pyran-6-ones, chlorinated flourenones, bis(benzophenones) and 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones (isobenzomorphanones). Computational studies for the synthesis of 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones have been carried out in cooperation with Dr. Haijun Jiao, Leibniz institute of catalysis Rostock (LIKAT).

Summary

A significant part of this dissertation has recently been published (see list of publications at the end). The work embodied in this dissertation is concerned with the synthesis of functionalized arenes based on [3+3] cyclocondesations of 1,3-bis(silyloxy)-1,3-butadienes and related transformations and cyclocondensations of aryl-1,3-bis(silyloxy)-1,3-butadienes with isoquinolines and 3-formylchromones.

Synthesis of Functionalized 6-(Pyridyl)salicylates, Bis(benzophenones), Chlorinated 6*H*-Benzo[*c*]chromen-6-ones, 9*H*-Fluoren-9-ones, Isobenzomorphans and Dibenzo[*b*,*d*]pyrid-6-ones based on New Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes

1. This chapter deals with the formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 3-pyridyl-3-silyloxy-2-en-1-ones which afforded regioselective 6-(pyridyl)salicylates **9, 12** and **15** are reported. Further more 3-(pyridyl)-1,3-diones **7, 10** and **13** were prepared by LDA and NaH-mediated reaction of ketones **5** with ethyl (pyridyl)carboxylates **6** are also reported.

2. Chapter two includes the synthesis of functionalized 6(5*H*)-phenanthridinones (dibenzo[*b*,*d*]pyrid-6-ones) **20a-h** based on formal $TiCl_4$ mediated [3+3] cyclocondensation of masked dianions, methodology developed by Chan and coworkers, And subsequent reduction by H_2, Pd/C, lactamization strategy. Synthesis of amino biaryls **21a-b** were also carried out by the reduction of nitro biaryls are presented.

3. In this chapter, I have described the synthesis of functionalized chlorinated biaryls **26a-r** which were prepared by formal 3+3 cyclocondensation of 2-chloro-3-(silyloxy)alk-2-en-1-ones **25a-f** and bis(silylenol ethers) **4a-c**. Furthermore the lactonization of **26m-r** have done in the presence of BBr_3, KO*t*Bu to get biaryl lactones **27a-f**. In addition some of baryls are converted onto respective flourenones **31a-f**. The methodology described here provides an easy and direct route for the synthesis chlorinated biaryls lactones and flourenones.

4. In chapter 4, I have reported the synthesis of bis(benzophenones) **34** by condensation of aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes **32a-l** with 3-formyl-benzopyrylium triflates by ′Michael-retro-Michael-Mukaiyama-aldol′ reaction. This synthesis is carried out under mild conditions and the reactions proceed in acceptable yields with very good regio- and chemoselectivity.

5. This chapter deals with the synthesis of functionalized 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones (isobenzomorphanones) by the condensation of aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes with isoquinolines fallowed by TFA mediate cyclization and subsequent reduction with H_2, Pd/C. In addition a simple rout to synthesis of natural product analogues in excellent yields.

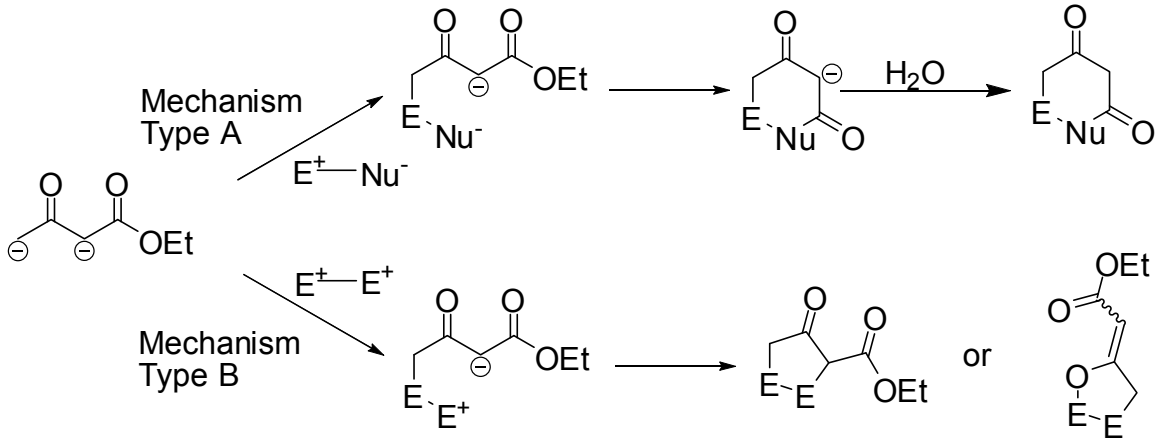
7. This chapter includes the experimental, spectroscopic data and full characterization of all new products has been described.

1. One-pot synthesis of 6-(pyridyl)salicylates based on [3+3] cyclocondensations of 1,3-bis(silyl enol ethers) with 3-pyridyl-3-silyloxy-2-en-1-ones

1.1 Synthesis of 4-alkyl-1,3-bis(trimethylsiloxy)buta-1,3-dienes

1.1.1 Introduction

Dianions represent important building blocks for the regioselective formation of carbon-carbon bonds. Ambident dianions are organic substrates containing two delocalized negative charges. Dianions can be generated by reaction of 1,3-dicarbonyl compounds in the presence of strong base, such as LDA or *n*-BuLi[1]. The functionalization of the terminal carbon atom of 1,3-dicarbonyl compounds by reaction of the corresponding dianions with electrophiles represents an important synthetic method which has been used in the synthesis of natural products. The terminal carbon atom of the dianion can be regioselectively coupled with one equivalent of an electrophile E^+ to give a monoanion which can be subsequently trapped by addition of a second electrophile. Two general mechanistic pathways for *cyclization* reactions of dianions can be discussed as follows[1](Scheme 1-1).



Scheme 1-1: Possible mechanistic pathways for cyclization reactions of 1,3-dicarbonyl dianions. Nu = nucleophile center, E = electrophile center.

Mechanism type A: the dianion can react with monofunctional electrophiles with transposition of a negative charge from the dianion to the electrophile. This carbanion attacks an E^+ centre of the former dianion moiety (e.g. the ester group) to give a cyclic monoanion which is subsequently quenched with water.

Mechanism type B: the dianion can react as a dinucleophile with a dielectrophile. A monoanion is formed, followed by attack of the latter onto a second E^+ center.

Cyclization reactions of dianions with dielectrophiles are synthetically useful. However, problems can arise since both starting materials are highly reactive compounds which have low reactivity matching. In addition, 1,2-dielectrophiles are often rather labile, and reactions with nucleophiles can result in polymerization, decomposition, formation of open-chained products, elimination or SET-process. These intrinsic limitations can be overcome by two ways: a) a proper tuning of the reactivity of dianion and dieletrophile and b) the use of eletroneutral dianion equivalents (masked dianions) in Lewis acid catalyzed reactions.[1]

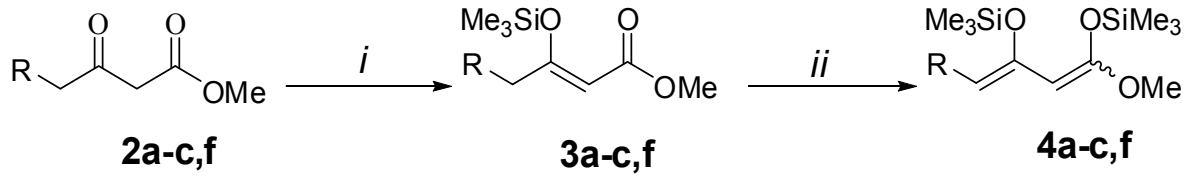
Many studies proved that 1,3-bis(enol silyl ethers) can be considered as equivalents of the corresponding 1,3-dicarbonyl dianions.[2] The chemistry of bis(silyl enol ethers) has been developed during the last two decades.[2d] It is, for example, known that silyl enol ethers can condense with various carbonyl compounds in the presence of Lewis acids.[3] These Lewis-acid-mediated reactions[4](e. g. alkylation and aldol condensation) provide useful alternatives to classical enolate chemistry. In cyclization reactions, 1,3-bis(silyl enol ethers) can react as 1,3-dinucleophiles or, similar to the well-known Danishefsky diene[5], as functionalized butadienes. 1,3-Bis(silyl enol ethers) undergo reactions with electrophiles at the terminal carbon atom followed by reaction of the central carbon or the oxygen atom. Silyl enol ethers can be cleaved with nucleophiles such as MeLi, $LiNH_2$ or $R_4N^+F^-$ to give enolates. These can be reacted with halides (Br_2, Cl_2, I_2) or pseudohalides (PhSCl, PhSeCl, Cl-N=O).[6] Whereas enolates can be alkylated only by primary or secondary halides, silyl enol ethers can be alkylated by tertiary halides.[7]

The preparation of silyl enol ethers mainly follows the procedures reported by Chan and Molander. These syntheses rely on the preparation of mono(silyl enol ethers), Which are subsequently transformed into bis(silyl enol ethers) by deprotonation with LDA and subsequent silylation.[8,9]

In this chapter, I present the synthesis of novel 4-alkyl-1,3-bis(trimethylsilyoxy)-1,3-butadiens following the procedure of Chan.

1.1.2 Results and discussion

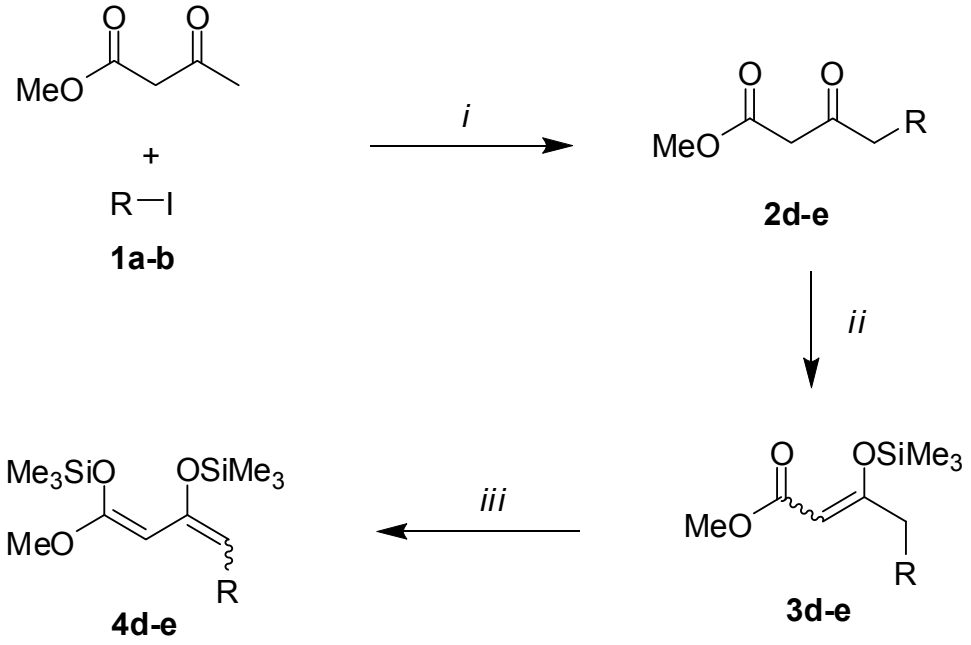
Following the procedures of Chan and Molander, 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4a-c,f** can be prepared from the respective 1,3-dicarbonyl compounds **2a-c,f** in two steps. Treatment of the *β*-ketoesters with NEt_3, Me_3SiCl afforded silyl enol ethers **3a-c,f** Deprotonation of the latter with LDA and subsequent addition of Me_3SiCl afforded the dienes **4a-c,f**.



2a-c,f **3a-c,f** **4a-c,f**

Scheme 1-2: Synthesis of 1,3-bis(silyl enol ethers) **4a-c,f**; *i*: 1) NEt3 (1.5 equiv.); 2) Me3SiCl (1.5 equiv.), C6H6, 20 °C, 12 – 48 h; *ii*: 1) LDA (1.5 equiv.), THF, 0 °C, 2 h; 2) Me3SiCl (1.5 equiv.), –78 → 20 °C, 6 – 12 h.

The synthesis of alkyl-substituted-1,3-bis(silyl enol ether) derivatives require the synthesis of the respective β-ketoesters **2d-e** which was carried out in collaboration with I. Hussain. It is known that the regioselectivities of the reactions of monoanions and dianions generally differ greatly. 1,3-Dicarbonyl monoanions are generally alkylated at the central carbon or at the oxygen atom, whereas the formation of dianions allows the functionalization of the terminal carbon atom. Based on this, the 4-alkyl-3-oxobutanoates **2d-e** were prepared by reactions of the dianion of methyl acetoacetate with the respective alkylhalides **1a-b** (RI). These compounds were transformed, according to a known procedure,[2] into the desired 1,3-bis(silyl enol ethers) **4d-e** via the respective mono(silyl enol ethers) **3d-e** (Scheme 1-3, Table 1-1).



Scheme1-3: Synthesis of alkyl-substituted 1,3-bis(silyl enol ether) derivatives; *i*: 1) 2.5 LDA, THF, 0 °C, 1 h; 2) methyl acetoacetate, **1a-b**, –78 → 20 °C; *ii*: Me_3SiCl (1.5 equiv.), NEt_3 (1.5 equiv.), C_6H_6, 20 °C, 48 h; *iii*: 1) LDA (1.5 equiv.), THF, –78 °C, 1 h; 2) Me_3SiCl (1.5 equiv.), 20 °C, –78 → 20 °C.

All 4-alkyl-1,3-bis(silyl enol ethers) prepared could be stored at suitable conditions (-20 ^{o}C, dry, inert gas atmosphere) for several months without decomposition. The 1,3-bis(silyl enol ethers) **4** of ß-keto esters used in this thesis are listed in the following table.

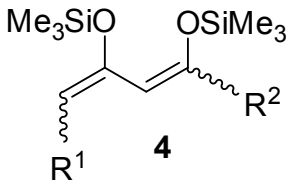


Table 1-1: 1,3-bis(silyl enol ethers) **4** used in this thesis

4	R^1	R^2
a	H	OMe
b	Me	OMe
c	Et	OEt
d	*n*Hex	OMe
e	*n*Oct	OMe
f	Cl	OEt

[a] Yields of isolated products

1.1.3 Conclusions

The application of a the known procedure allows the synthesis of novel 4-alkyl-1,3-bis(silyl enol ethers). These masked dianions are used in the cyclization reactions for synthesis heterocycles and aromatic rings - important building blocks of natural products analogue.

1.2 Synthesis of 6-(pyridyl)salicylates

1.2.1 Introduction

Pyridines are of considerable pharmacological relevance and occur in a variety of natural products.[10] (Pyrid-2-yl)arenes are present in natural 4-azafluorenones (e. g. kinabaline, darienine, and onychine) which exhibit a strong antimicrobial activity.[11] In addition, these are present in 1,6-diazabenzo[*de*]anthracen-7-one natural products, such as sampangin or eupomatidine.[12] The latter were shown to induce apoptosis and are active against human leukemia HL-60 cells.[12] Some years ago, Faizi *et al*. have isolated penduline, isourisoline and pendulamine A, B alkaloids from the Roots of *Polyalthia longifolia* var *pendula*, which possess pronounced antibacterial activity (**Figures 1.1-1.4**).[12]

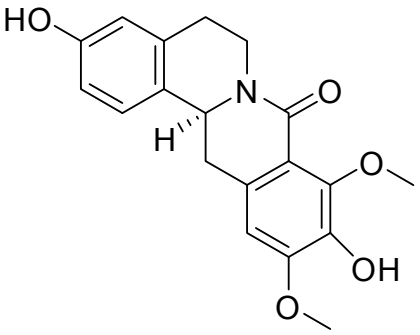


Figure 1.1: Pendulamine A

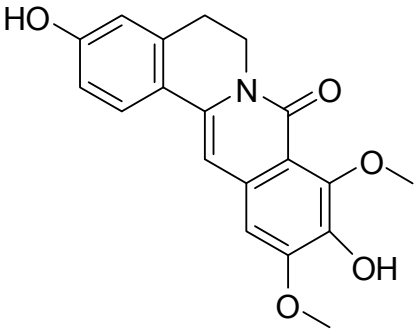


Figure 1.2:Pendulamine B

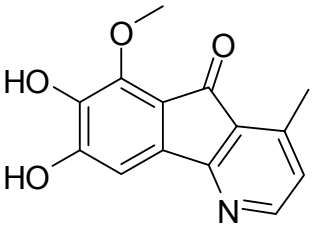


Figure 1.3: Penduline

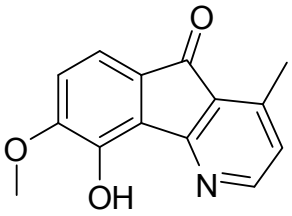


Figure 1.4: Isourlsoline

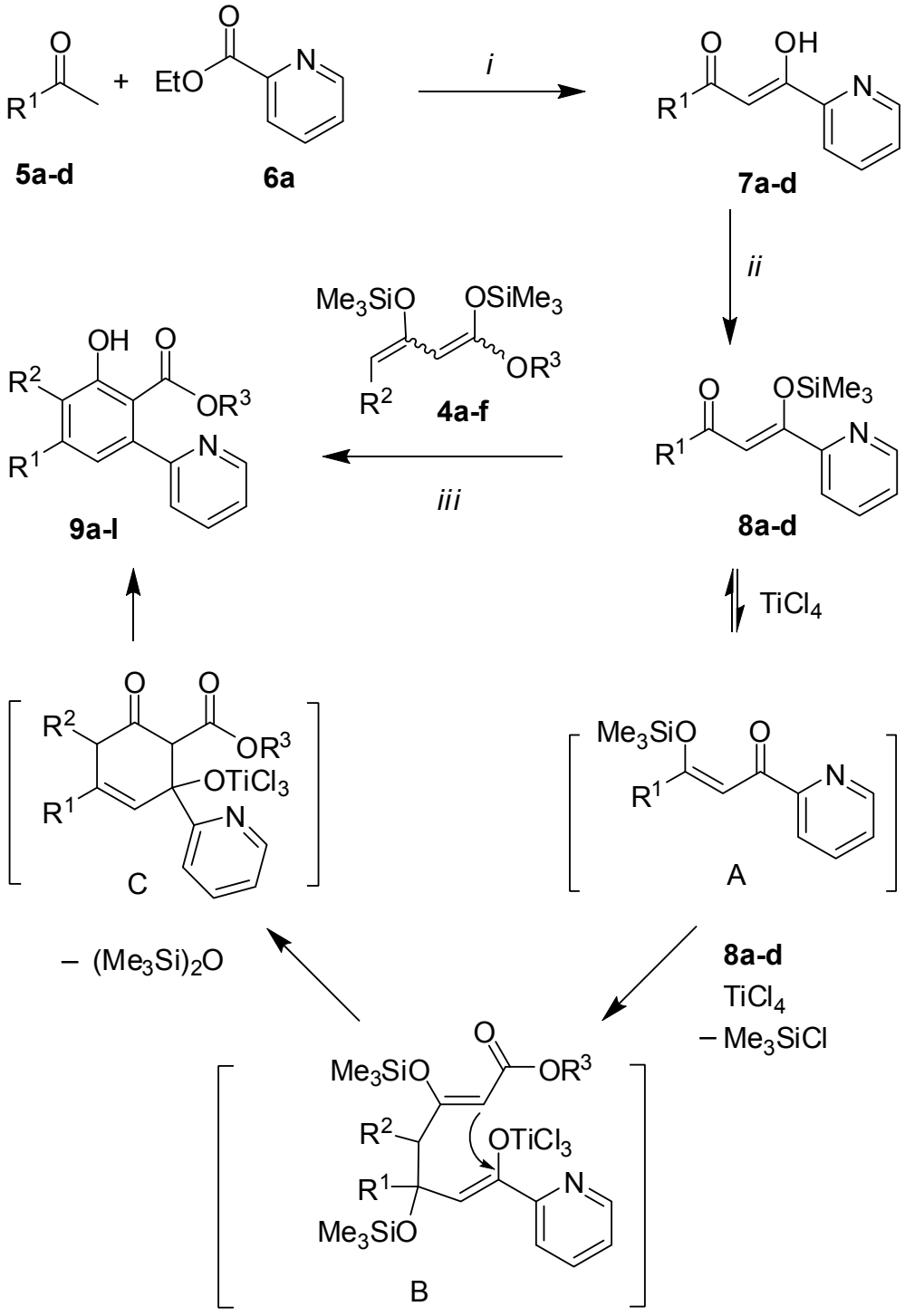
Hetaryl-substituted arenes are available, for example, by palladium(0)-catalyzed cross-coupling reactions.[13] Despite their great synthetic utility, the scope of all these methods is limited by the availability of the starting materials. In fact, the synthesis of more complex aryl halides or triflates by regioselective functionalization of arenes is often rather difficult. In addition, transition metal catalyzed reactions of sterically encumbered substrates often proceed in low yield or not at all. Some years ago, Chan and coworkers reported[2] an elegant approach to salicylates by cyclization of 1,3-bis(silyl enol ethers)[1] with 3-(silyloxy)alk-2-en-1-ones. In recent years, Langer *et al.* reported the application of this method to the synthesis of a variety of functionalized arenes.[14]

Herein, I report a new synthesis of functionalized 3-(pyrid-2-yl)phenols based on formal [3+3] cyclizations of 1,3-bis(silyl enol ethers). These reactions represent what are, to the best of my knowledge, the first [3+3] cyclizations of heterocyclic substrates. From a preparative viewpoint, they offer a convenient and regioselective approach to functionalized and sterically encumbered 6-(pyridyl)salicylates which are not readily available by other methods.

1.2.2 Results and discussion

The 3-(pyrid-2-yl)-1,3-diones **7a-d** were prepared by LDA-mediated reaction of ketones **5a-d** with ethyl (pyrid-2-yl)carboxylate (**6a**). The silylation of **7a-d** afforded the silyl enol ethers **8a-d**. The $TiCl_4$-mediated formal [3+3] cyclization of **8a-d** with 1,3-bis(silyl enol ethers) **4a-f** prepared from the corresponding 1,3-dicarbonyl compounds in two steps[17] – afforded the 6-(pyrid-2-yl)salicylates **9a-l** (Scheme 1-4, Table 1-2). All products were formed with very good regioselectivity. During the optimization of this reaction, the (high) concentration and the temperature played an important role. The cyclization of **7** with **4** proceeds by $TiCl_4$-mediated isomerization of **8** by shift of the silyl group (intermediate **A**), $TiCl_4$-mediated attack of the terminal carbon atom of **4** onto the carbon located next to substituent R^1 to give intermediate **B** (conjugate addition), cyclization (intermediate **C**), and subsequent aromatization.[2, 15] It is noteworthy, that the lone pairs of the nitrogen atom of the pyridine moiety did not hinder the [3+3] cyclization to proceed.

1.2.2.1 Possible mechanism for synthsis of 9a-l



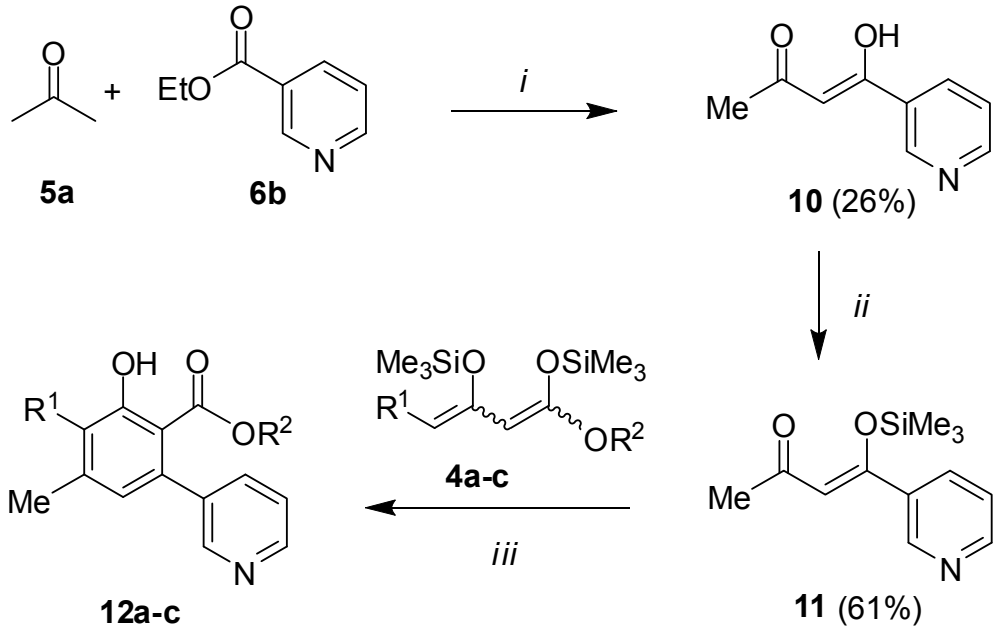
Scheme 1-4: Synthesis of **9a-l**; *i*: LDA (1.5 equiv.), THF; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (3.6 equiv.), C_6H_6, 20 °C, 3 d; *iii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C.

Table 1-2: Synthesis of **9a-l**

8	**4**	**9**	R^1	R^2	R^3	% (**9**)[a]
a	**a**	**a**	Me	H	Me	31
a	**d**	**b**	Me	*n*Hex	Me	30
a	**e**	**c**	Me	*n*Oct	Me	30
a	**f**	**d**	Me	Cl	Et	33
b	**a**	**e**	Et	H	Me	40
b	**b**	**f**	Et	Me	Me	44
b	**c**	**g**	Et	Et	Et	38
b	**d**	**h**	Et	*n*Hex	Me	30
b	**e**	**i**	Et	*n*Oct	Me	30
c	**a**	**j**	*n*Pr	H	Me	33
c	**b**	**k**	*n*Pr	Et	Et	31
d	**a**	**l**	*i*Pr	H	Me	26

[a] Yields of isolated products

The NaH-mediated reaction of acetone (**5a**) with ethyl nicotinate (**6b**) afforded 3-(pyrid-3-yl)-1,3-dione **10**. The silylation of **10** afforded silyl enol ether **11**. The $TiCl_4$-mediated formal [3+3] cyclization of **11** with 1,3-bis(silyl enol ethers) **4a-c** afforded the 6-(pyrid-3-yl)salicylates **12a-c** (Scheme 1-5, Table 1-3).



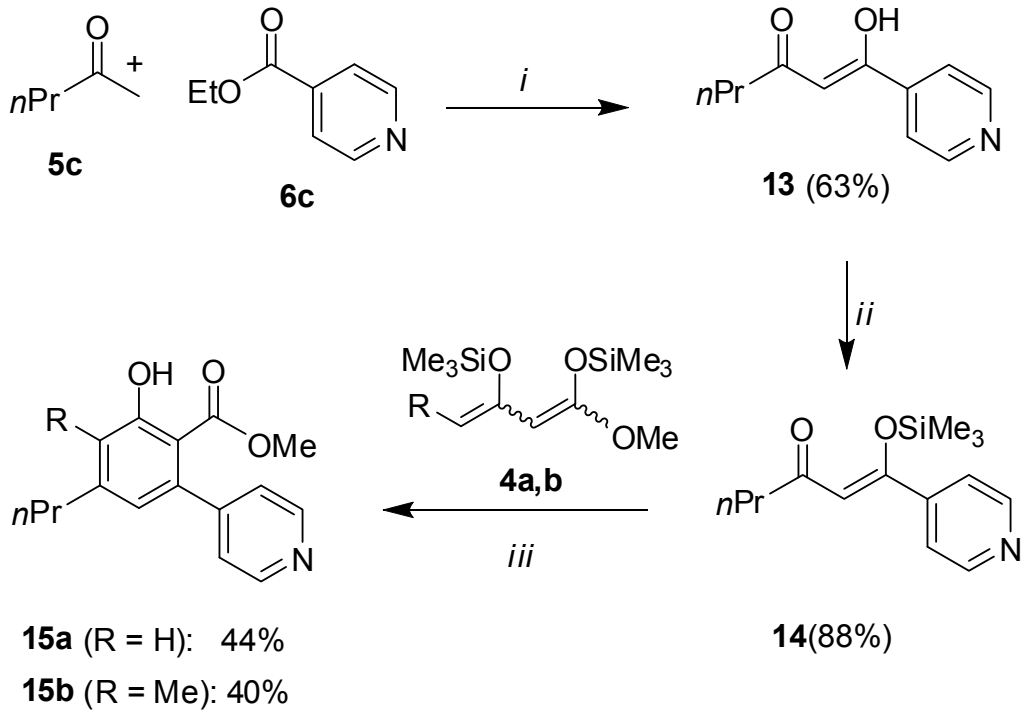
Scheme 1-5: Synthesis of **12a-c**; *i*: NaH (4.0 equiv.), ethyl nicotinate (1 equiv), acetone (2.0 equiv), Et_2O, reflux, 2 h; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (3.6 equiv.), C_6H_6, 20 °C, 3 d; *iii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C.

Table 1-3: Synthesis of **12a-c**

4	**12**	R^1	R^2	% (**12**)[a]
a	**a**	H	Me	44
b	**b**	Me	Me	38
c	**c**	Et	Et	32

[a] Yields of isolated products

The 3-(pyrid-4-yl)-1,3-dione **13** was prepared by LDA-mediated reaction of pentan-2-one (**5c**) with ethyl (pyrid-4-yl)carboxylate (**6c**). The silylation of **13** gave silyl enol ether **14**. The $TiCl_4$-mediated cyclization of **14** with 1,3- bis(silyl enol ethers) **4a,b** afforded the 6-(pyrid-4-yl)salicylates **15a-b** (Scheme 1-6).



Scheme 1-6: Synthesis of **15a-b**; *i*: LDA (1.5 equiv.), THF; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (3.6 equiv.), C_6H_6, 20 °C, 3 d; *iii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C.

1.2.3 Conclusions

In conclusion, a variety of 6-(pyridyl)salicylates were regioselectively prepared by formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 3-pyridyl-3-silyloxy-2-en-1-ones. These reactions represent what are, to the best of our knowledge, the first [3+3] cyclizations of 1,3-bis(silyl enol ethers) with heterocyclic substrates.

2. Synthesis of functionalized 6(5*H*)-phenanthridinones based on a [3+3]-cyclocondensation / lactamization strategy

2.1 Introduction

6(5*H*)-Phenanthridinones (dibenzo[*b*,*d*]pyrid-6-ones) are pharmacologically important molecules which occur in a variety of natural products. This includes, for example, sanguinarinone which shows antiparasitic activity against the dog roundworm, anticoagulant activity, and anti-proliferative activity against leukemia HL-60 cells (Scheme 1).[16] Benzo [*c*] phenanthridine alkaloids including, nitidine (**Figure 2.1**) and sanguinarine (**Figure 2.2**) , have been attractive to synthetic organic chemists and biochemist over last two decades since such compounds have shownintresting biological properties[16d-g] Oxotoddaline has been reported to possess anti-proliferative activity against P-388 and human colon carcinoma HT-29 cells.[17] A number of other pharmacologically active natural products, e. g. cytotoxic oxynitidine,[18] have been reported.[19,20] Recently Cho *et al*.[21j] reported the total synthesis of oxysanguinarine, oxyavicine, oxynitidine and oxyfagaronine alkaloids (**Figure 2.3-2.6**).

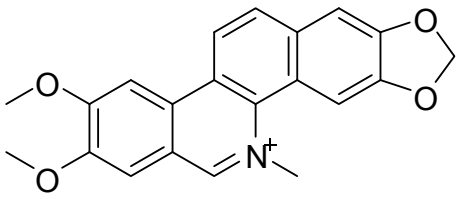


Figure 2.1: Nitidine

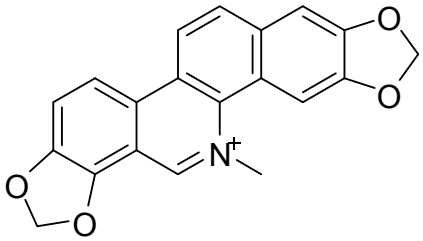


Figure 2.2: Sanguinarine

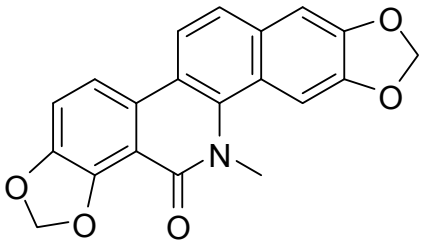


Figure 2.3: Oxysanguinarine

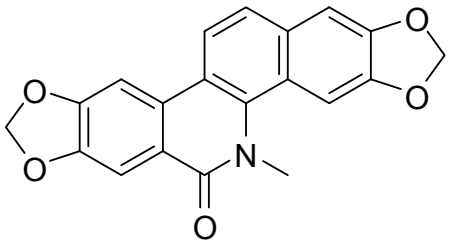


Figure 2.4: Oxyavicine

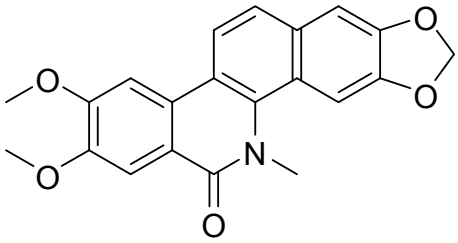


Figure 2.5: Oxynitidine

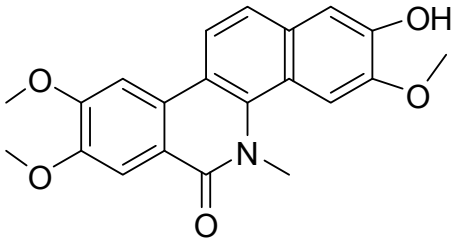


Figure 2.6: Oxyfagaronine

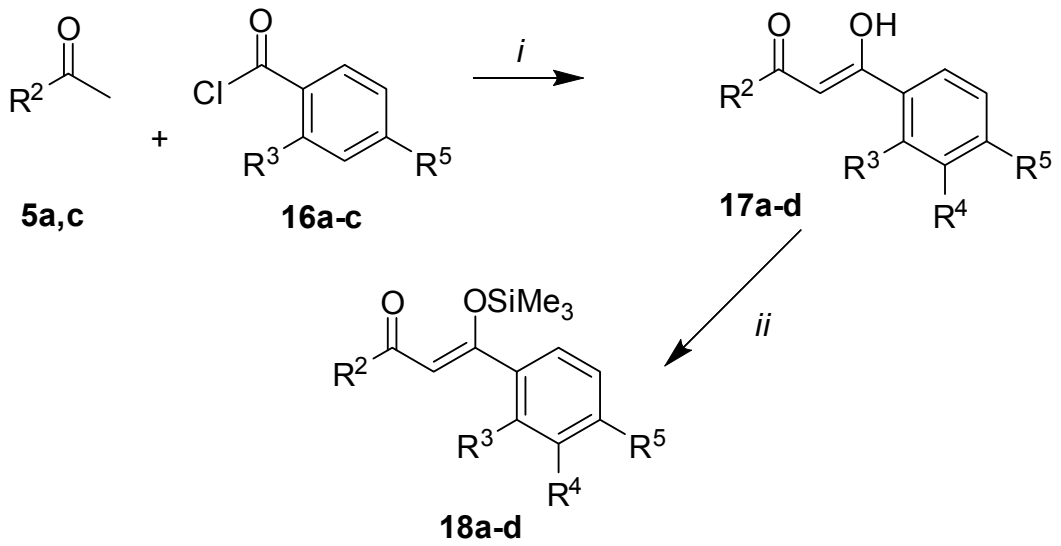
6(5*H*)-Phenanthridinones have been prepared by reductive cyclization of 2-nitro-2'-alkoxycarbonyl-biphenyls under various conditions (including Fe/AcOH, Fe/THF, Zn/HOAc, Raney-Ni, and H_2-Pd/C).[21b] The corresponding biaryls have been prepared by Ullmann-type reactions and by nucleophilic aromatic substitutions.[22] An alternative approach relies on the nitration of appropriate biphenyls.[23] The scope of these reactions is limited by the harsh reaction conditions and by steric effects. In fact, sterically encumbered and highly functionalized derivatives are not readily available by this approach. In addition, the synthesis of the starting materials, highly functionalized arenes, is often not an easy task. These problems can be circumvented by application of a 'building block approach'. To the best of my knowledge, only a single application of this strategy has been reported to date. Ashburn and coworkers reported the synthesis of 2-nitro-2'-alkoxycarbonyl-biphenyls based on [4+2] cycloadditions.[24]

Chan and coworkers were the first to report a convenient synthesis of functionalized phenols by $TiCl_4$-mediated [3+3] cyclization[14] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes[1] with 3-silyloxy-2-en-1-ones. In recent years, Langer *et al.* studied the application of this reaction to the synthesis of various functionalized arenes. Recently, Langer *et al.*[25] reported the synthesis of dibenzo[*b*,*d*]pyran-6-ones based on a [3+3] cyclization / lactonization strategy.

Herein, I wish to report what is, to the best of my knowledge, the first synthesis of 6(5*H*)-phenanthridinones by application of a [3+3]-cyclocondensation / lactamization strategy. Although recently Cho *et al.*[21j] reported the synthesis oxyphenanthridinones, which they synthesised in fourteen steps, and I like to present an efficient methodology to prepare the same skeleton in two steps. Noteworthy, the products are formed with very good regioselectivity and are not readily available by other methods.

2.2 Results and discussion

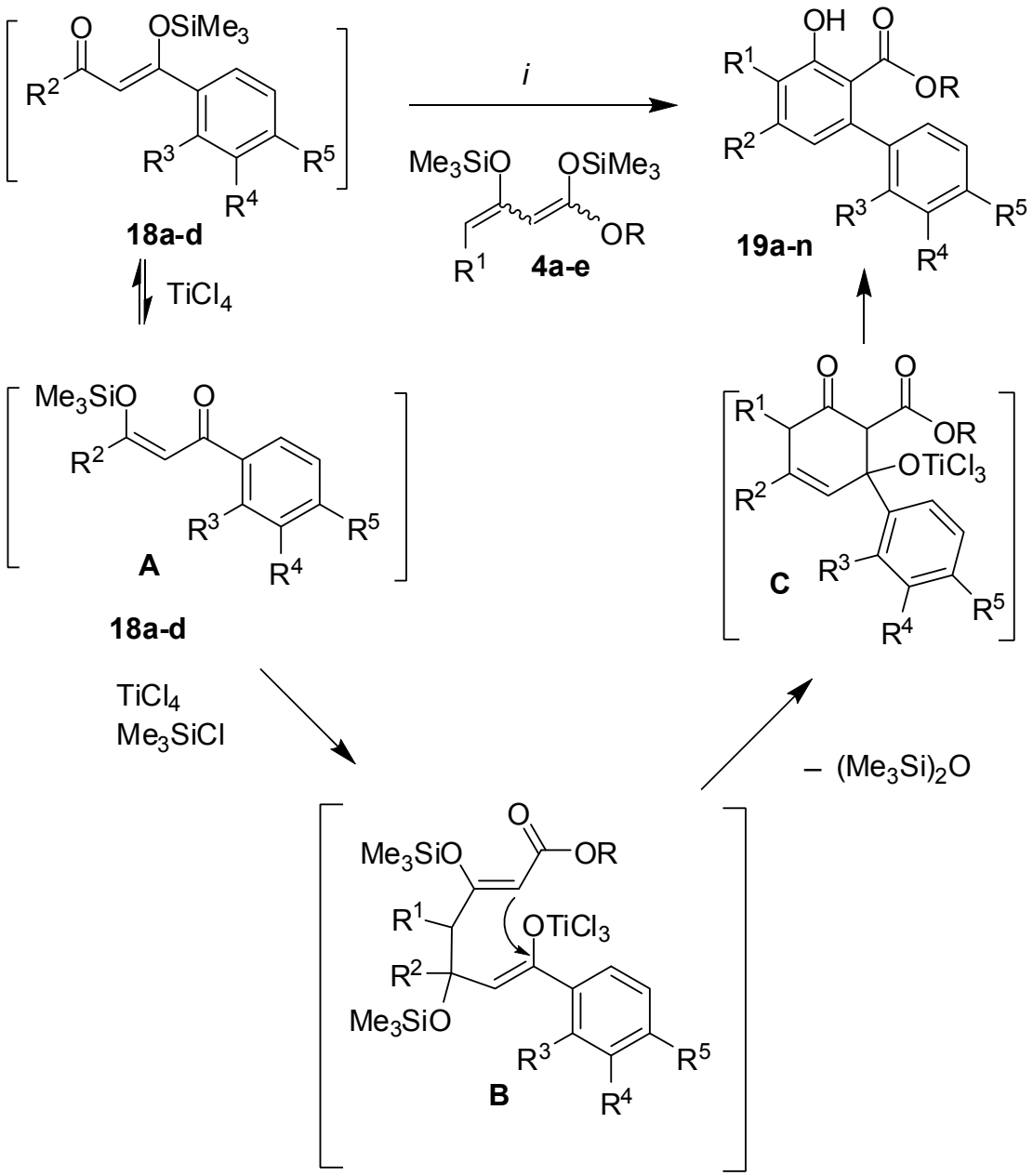
The LDA-mediated condensation of acetone (**5a**) and pentan-2-one (**5c**) with benzoyl chlorides **16a-c** afforded the nitro-substituted benzoylacetones **17a-d** which were transformed into the 1-aryl-1-silyloxy-1-en-3-ones **18a-d** (Scheme 2-1, Table 2-1). The $TiCl_4$-mediated cyclization of **18a-d** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **4a-e**, readily available in two steps from the corresponding β-ketoesters,[2] afforded the novel nitro-substituted biaryls **19a-n** (Scheme 2-2, Table 2-2). All cyclizations proceeded with very good regioselectivity. During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution. The structures of all products were established by spectroscopic methods. The structure of **19m** was independently confirmed by X-ray crystal structure analysis (**Figure 2.7**).[105]



Scheme 2-1: Synthesis of **19a-n**; *i*: LDA (1.5 equiv.), THF; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 3 d.

The regioselective formation of products **19a-n** can be explained, following a mechanism first suggested by Chan,[2] by $TiCl_4$-mediated isomerization of **18** into intermediate type **A**, $TiCl_4$-mediated attack of the terminal carbon atom of 1,3-bis(silyl enol ether) **4** onto the carbon located next to substituent R^1 to give intermediate type **B** (conjugate addition), cyclization (intermediate type **C**), and subsequent aromatization (Scheme 2-2, Table 2-2).

2.2.1 Synthesis of nitro substituted biaryls



Scheme 2-2: Synthesis of **19a-n**; *i*: **18** (1.0 equiv.), **4** (1.1 equiv.), $TiCl_4$, CH_2Cl_2, –78 → 20 °C.

Table 2-1: Synthesis of **17, 18a-d**

5	**16**	**17**	**18**	R^2	R^3	R^4	R^5	% (**17**)[a]	% (**18**)[a]
a	**a**	**a**	**a**	Me	NO_2	H	H	54	91
b	**a**	**b**	**b**	*n*Pr	NO_2	H	H	45	88
a	**b**	**c**	**c**	Me	H	NO_2	H	34	90
a	**c**	**d**	**d**	Me	H	H	NO_2	43	92

[a] Yields of isolated products

Table 2-2: Synthesis of **19a-n**

4	**18**	**19**	R	R^1	R^2	R^3	R^4	R^5	% (**19**)[a]
a	**a**	**a**	Me	H	Me	NO_2	H	H	36
b	**a**	**b**	Me	Me	Me	NO_2	H	H	41
c	**a**	**c**	Et	Et	Me	NO_2	H	H	35
e	**a**	**d**	Me	*n*Oct	Me	NO_2	H	H	40
a	**b**	**e**	Me	H	*n*Pr	NO_2	H	H	48
b	**b**	**f**	Me	Me	*n*Pr	NO_2	H	H	38
c	**b**	**g**	Et	Et	*n*Pr	NO_2	H	H	37
d	**b**	**h**	Me	*n*Hex	*n*Pr	NO_2	H	H	25
a	**c**	**i**	Me	H	Me	H	NO_2	H	32
b	**c**	**j**	Me	Me	Me	H	NO_2	H	50
c	**c**	**k**	Et	Et	Me	H	NO_2	H	37
a	**d**	**l**	Me	H	Me	H	H	NO_2	36
b	**d**	**m**	Me	Me	Me	H	H	NO_2	46
c	**d**	**n**	Me	Et	Me	H	H	NO_2	33

[a] Yields of isolated products

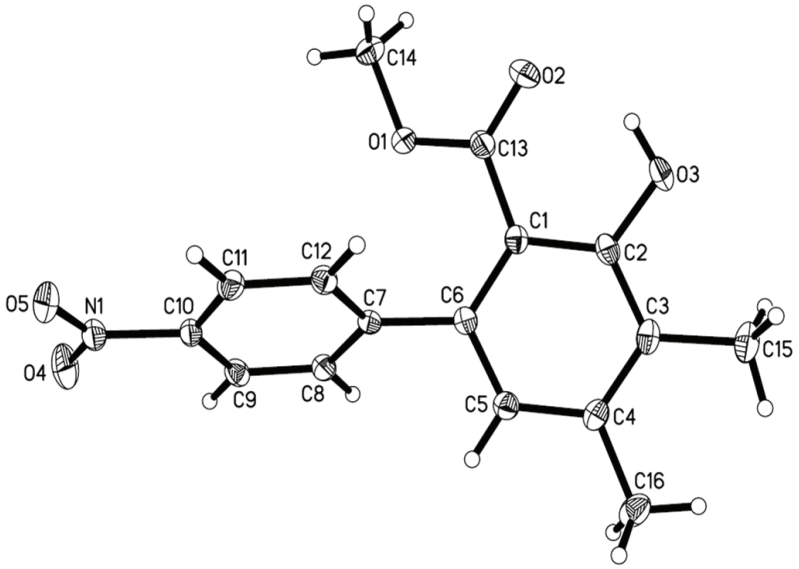
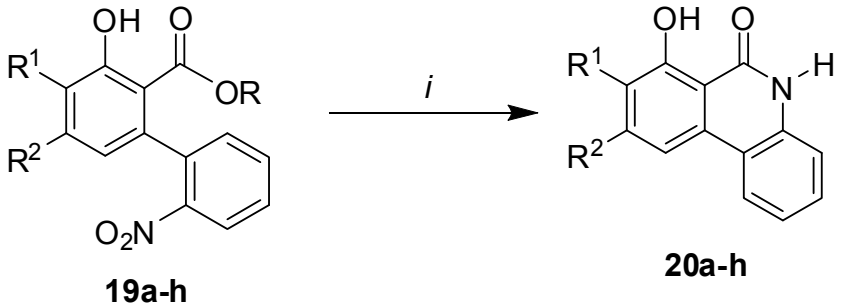


Figure 2.7: Ortep plot of **19m**

The Pd/C-catalyzed hydrogenation of **19a-h** directly afforded the 6(5*H*)-phenanthridinones **20a-h** (Scheme 2-3, Table 2-3). The products are formed by transformation of the nitro into an amino group and subsequent spontaneous lactamization.[26]



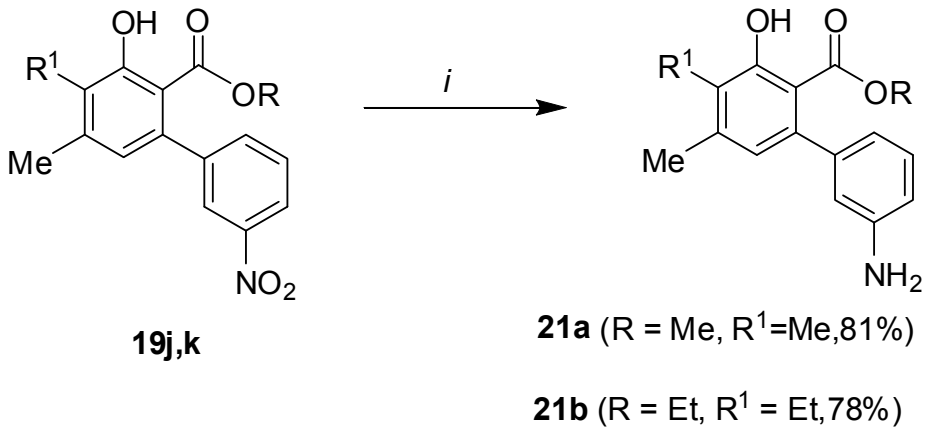
Scheme 2-3: Synthesis of **20a-h**; *i*: H_2, Pd/C (10 mol-%), 25 ^{o}C, 48 h.

Table 2-3: Synthesis of **20a-h**

19	**20**	R	R^1	R^2	% (**20**)[a]
a	**a**	Me	Me	H	64
b	**b**	Me	Me	Me	52
c	**c**	Et	Me	Et	70
d	**d**	Me	Me	*n*-Octyl	69
e	**e**	Me	*n*-Propyl	H	56
f	**f**	Me	*n*-Propyl	Me	50
g	**g**	Et	*n*-Propyl	Et	63
h	**h**	Me	*n*-Propyl	*n*-Hexyl	74

[a] Yields of isolated products

The hydrogenation of 3-nitro-3′-hydroxy-biphenyls **19j** and **19k** afforded the 3-amino-3′-hydroxy-biphenyls **21a** and **21b** (Scheme 2-4). Noteworthy, 3-amino- and 3-nitro-3′-hydroxy-biphenyls are of considerable current interest, due to their wide range of pharmacological properties. This includes, for example, antimalarial activity, binding affinity to C5a receptor (human monocyte cell line U937), inhibition of cyclic nucleotide phosphorodiesterases (PDEs), activity for topoisomerases I and II-mediated DNA cleavage, and anti-hepatitis activity.[26]



19j,k

21a (R = Me, R^1=Me,81%)

21b (R = Et, R^1 = Et,78%)

Scheme 2-4: Synthesis of **21a,b**; *i*: H_2, Pd/C (10 mol-%), 25 °C, 24 h.

2.3. Conclusions

In conclusion, I have reported a regioselective approach to functionalized nitro and amino substituted biaryls and 6(5*H*)-phenanthridinones by application of a [3+3] cyclization / lactamization strategy. The products are not readily available by other methods.

3. Synthesis of chlorinated biaryls, biaryl Lactones and fluorenones based on regioselective [3+3] cyclocondensations of 1,3-bis(silyl enol ethers)

3.1 Introduction

4-Chlorophenols are of considerable pharmacological relevance and occur in a variety of natural products. This includes dibenzo[*b,e*][1,4]dioxepin-11-ones,[27] spirocycles (e. g. aspirochlorins, grisandions, griseofulvins),[28] xanthones (austocystin A),[29] tetracyclins,[30] isochromanones (ochratoxin A), (**Figure 3.1**),[31] terpenes (ascofuranol, ascochlorin),[32] macrocycles (radicicol, bazzanin K),[33] dibenzo[*b,d*]pyran-6-one (graphislactone G),[34] oligosaccharides (flambamycin),[35] benzophenones,[36] polycyles,[37] arenes,[38] and biaryls (ambigol A).[39] They have found many technical and medicinal applications and represent important synthetic building blocks. 2-acyl-4-chlorophenols are found, for example, in the natural product chloratranorin (**Figure 3.2**).[27] Chloroarenes also represent useful starting materials in transition metal catalyzed cross-coupling reactions.[13, 40]

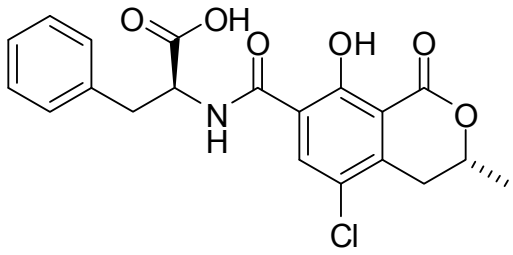


Figure 3.1: Ochratoxin A

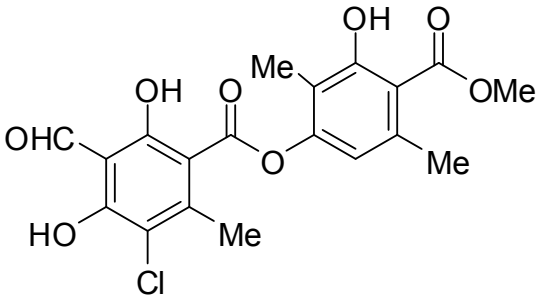


Figure 3.2: Chloratranorin

Classic syntheses of functionalized chlorophenols, based on chlorination of phenols, often suffer from low regioselectivities and yields. Syntheses of 4-chlorophenols based on [4+2] cycloadditions of chloro-substituted buta-1,3-dienes have been reported. For example, Brassard and coworkers reported the synthesis of a chlorinated anthraquinone by [4+2] cycloaddition of 2-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene with a 2-chloronaphthoquinone.[41a] 4-Chlorophenol was also prepared by [4+2] cycloaddition of a chlorinated thiophene with dimethyl acetylenedicarboxylate.[42b] Recently, Langer *et al.* [42] have reported an efficient method for the synthesis of functionalized 4-chlorophenols based on [3+3] cyclizations of 1,3-bis(silyl enol ethers), which can be regarded as electroneutral

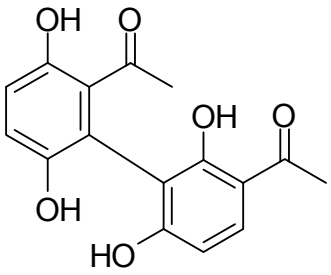
equivalents of 1,3-dicarbonyl dianions and novel 2-chloro-3-(silyloxy)alk-2-en-1-ones. Traditional methodologies rely on the functional group manipulations at aromatic rings, which in many cases was quite difficult to handle and yields were also not satisfactory. In addition, combination of that approach with Suzuki cross-coupling strategy and subsequent BBr_3 mediated lactonization offered access to the synthesis of chloro substituted biaryl lactones.

Herein, I present full details of these studies. With regard to previous work of Langer *et al*.[42a] the preparative scope was considerably extended and a variety of novel chlorinated biaryls were regioselectively prepared. In addition, the synthesis of novel chlorinated biaryl lactones (dibenzo[*b*,*d*]pyran-6-ones) and chlorinated fluorenones, based on regioselective [3+3] cyclizations, is reported. Notably, the functionalized chlorinated arenes reported herein are not readily available by other methods.

3.2 Synthesis of chlorinated biaryls

3.2.1 Introduction

Functionalized biaryls containing a 3-arylsalicylate substructure occur in a variety of pharmacologically relevant natural products. The simple biaryls cynandione A-C (**Figure 3.3**) have been isolated from many plant sources and show a considerable in vitro activity against hepatocytes, human bladder carcinoma T-24 cells, epidermoid carcinoma KB cells, and human hepatoma PLC/PRF/5 cells.[43] Number of natural products, such as knipholone, 6'-*O*-methylknipholone or (+)-asphodelin, contain an anthraquinone moiety.[44] Other compounds, e. g. secalonic acid A or globulixanthone E, contain a bixanthenyl substructure.[45] 3-arylsalicylates are also present in many flavones (e. g. 2,3-dihydroamentoflavone,[45c] bartramiaflavone,[46b] robustaflavone,[45d] dichamanetin).[46d,e] For some derivatives, inhibition of the human liver cathepsin B and K has been reported.[46f,g] The natural product anastatin A (**Figure 3.4**), which contains a hydroxylated dibenzofuran moiety, shows hepatoprotective activity.[13]



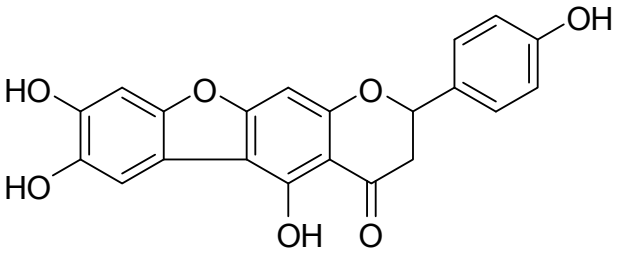
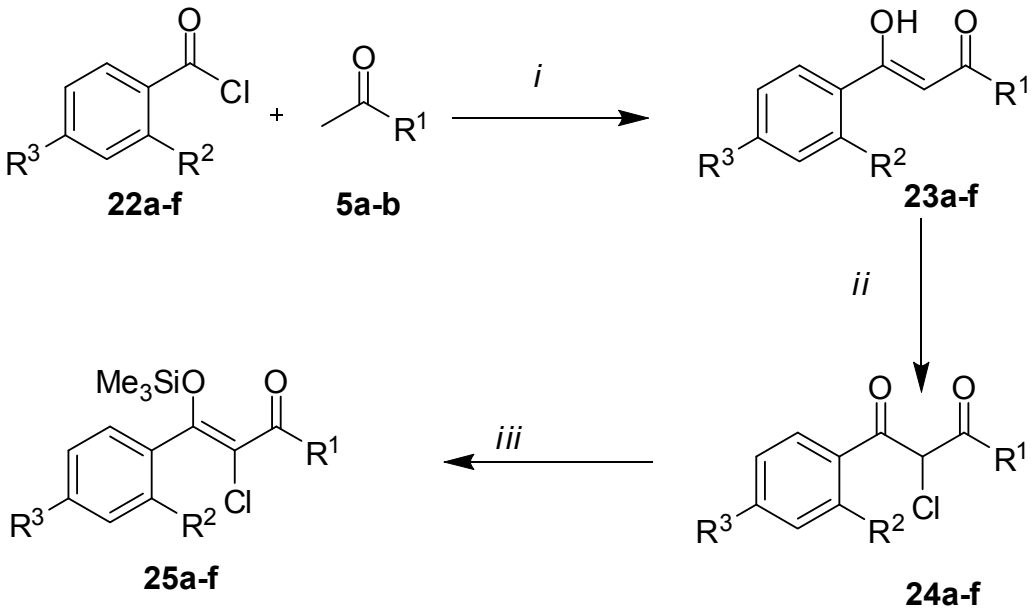


Figure 3.3: Cynandione A-C **Figure 3.4**: Anastatin A

The most important synthetic approach to biaryls relies on palladium(0)-catalyzed cross-coupling reactions.[13] Although these reactions are broadly applicable, the synthesis of sterically encumbered products can be difficult or not possible at all. In addition, the regioselective synthesis of the required aryl halides or triflates can be a very difficult task. Some years ago, Chan *et al.* developed[14b] a convenient approach to salicylates by formal [3+3] cyclizations[14b] of 1,3-bis(trimethylsilyloxy)-1,3-dienes[14a] with 3-trimethylsilyloxy-2-en-1-ones. Recently, Langer *et al*. developed a catalytic variant of this transformation.[48] In my thesis I studied, for the first time, the synthesis of 2-Chloro-3-(silyloxy)alk-2-en-1-ones and their application to the synthesis of functionalized 4-chloro biaryls. The sterically encumbered and functionalized biaryls reported herein are not readily available by other methods.

3.2.2 Results and discussion

2-Chloro-3-(silyloxy)alk-2-en-1-ones **25a-f** were prepared as follows. The LDA mediated reaction of ketones **5a,b** with benzoyl chlorides **22a-f** afforded the 1,3-diketones **23a-f**. The chlorination of the latter with NCS afforded products **24a-f** which were transformed into **25a-f** by silylation (Scheme 3-1, Table 3-1). The $TiCl_4$ mediated cyclization of 1,3-bis(silyl enol ethers) **4a-c,g** with 2-chloro-3-(silyloxy)alk-2-en-1-ones **25a-f** afforded the chlorinated biaryls **26a-r** (Scheme 3-2, Table 3-2). The structures of products **26a** and **26c** were independently confirmed by X-ray crystal structure analyses (**Figures 3.5** and **3.6**).[105]

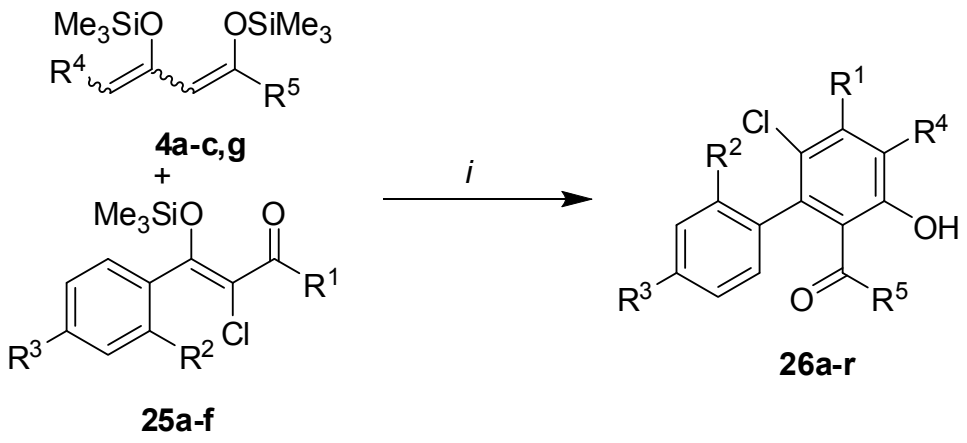


Scheme 3-1: Synthesis of **25a-f**; *i*: LDA (1.5 equiv.), THF; *ii*: NCS (1 equiv.), CCl_4, 75-80 ^oC; *iii*: NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C.

Table 3-1: Synthesis of 2-chloro-3-silyloxy-2-en-1-ones **25a-f**

23,24,25	R^1	R^2	R^3	% (**23**) [a]	% (**24**) [a]	% (**25**) [a]
a	Me	H	H	- [b]	95	90
b	Me	H	F	36	66	80
c	Me	H	Cl	38	52	73
d	Me	Me	H	33	44	72
e	Me	OMe	H	37	47	76
f	*n*Pr	OMe	H	72	81	84

[a] Isolated yields; [b] commercially available



Scheme 3-2: Synthesis of **26a-r**; *i*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h.

Table 3-2: Synthesis of chlorinated biaryls **26a-r**

4	**25**	**26**	R^1	R^2	R^3	R^4	R^5	% (**26**)[a]
a	**a**	**a**	Me	H	H	H	OMe	49
b	**a**	**b**	Me	H	H	Me	OMe	31
g	**a**	**c**	Me	H	H	H	Me	51
c	**a**	**d**	Me	H	H	Et	OEt	43
a	**b**	**e**	Me	H	F	H	OMe	30
b	**b**	**f**	Me	H	F	Me	OMe	48
c	**b**	**g**	Me	H	F	Et	OEt	44
a	**c**	**h**	Me	H	Cl	H	OMe	44
b	**c**	**i**	Me	H	Cl	Me	OMe	34
c	**c**	**j**	Me	H	Cl	Et	OEt	47
a	**d**	**k**	Me	Me	H	H	OMe	26
b	**d**	**l**	Me	Me	H	Me	OMe	40
a	**e**	**m**	Me	OMe	H	H	OMe	47
b	**e**	**n**	Me	OMe	H	Me	OMe	50
c	**e**	**o**	Me	OMe	H	Et	OEt	42
a	**f**	**p**	*n*Pr	OMe	H	H	OMe	34
b	**f**	**q**	*n*Pr	OMe	H	Me	OMe	46
c	**f**	**r**	*n*Pr	OMe	H	Et	OEt	51

[a] Isolated yields

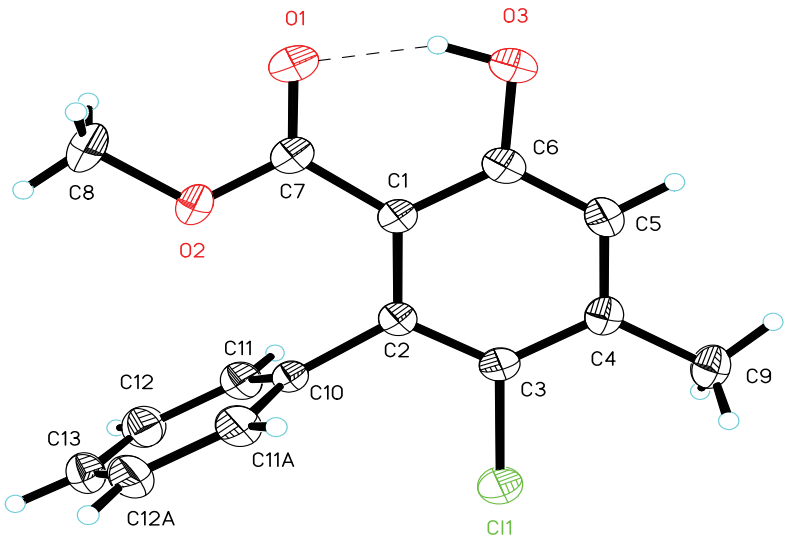


Figure 3.5: Ortep plot of **26a**

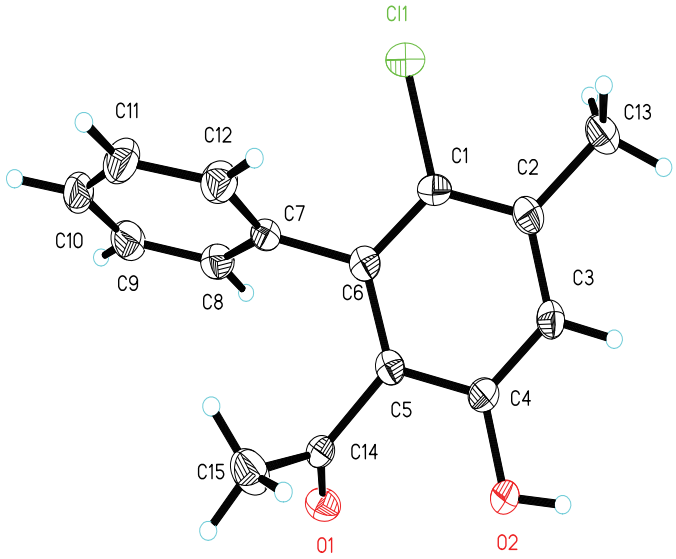


Figure 3.6: Ortep plot of **26c**

3.2.3 Conclusions

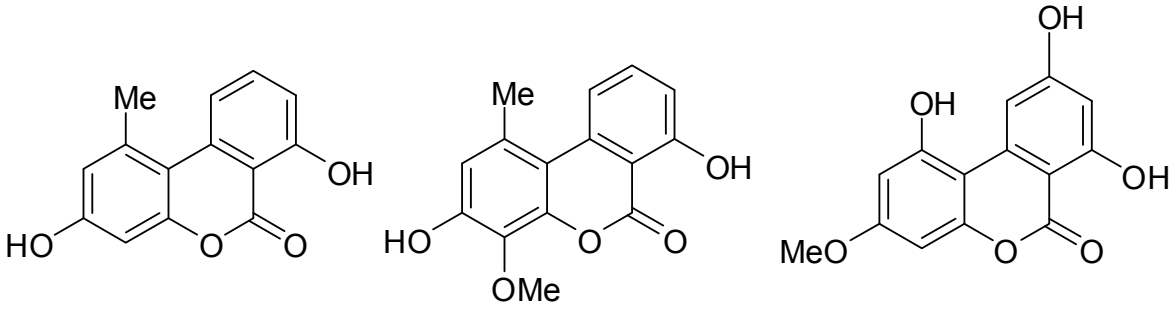
In conclusion, a general method for the regioselective synthesis of chlorinated, sterically encumbered and biaryls by formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 2-chloro-3-(silyloxy)alk-2-en-1-ones was reported. Chlorinated biaryls **26a-r** are isolated in

moderate to good yields. The yields mainly depend on the individual quality of the starting materials and on the handling of each individual experiment.

3.3 Synthesis of biaryl lactones

3.3.1 Introduction

Functionalized dibenzo[*b,d*]pyran-6-ones ('biaryl lactones') occur in a number of natural products such as alternariol, autumnariol, autumnariniol and altenuisol; [44c-e] dibenzo[*b,d*]pyran-6-ones containing an additional lactone bridge are present in ellagic and coruleoellagic acid.[45e,f] benzo[*d*]naphthopyran-6-ones occur in antibiotics and antitumor compounds isolated from *Streptomyces*; this includes, for example, defucogilvocarcin V, gilvocarcins, chrysomycins and ravidomycins.[46h] Some structures, which were isolated from the culture broth of a streptomycete as antitumor substances, were determined as 6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one.[47b] Ravidomycin was extracted from *Streptomyces ravidus* and is mainly active against Gram-positive bacteria including mycobacteria. Ravidomycin also exhibits potent antitumor activity against lymphocytic leukemia, tumor and mammary tumor.[47c] The 6*H*-dibenzo[*b,d*]-pyran-6-one moiety is also present in compounds extracted from *Pteropi faeces* (the species of *Trogopterus xanthipes* Milne-Edwards). These compounds show hyaluronidase inhibitory activity.[47d]



Autumnariol Autumnariniol Alternuisol

Figure 3.7:

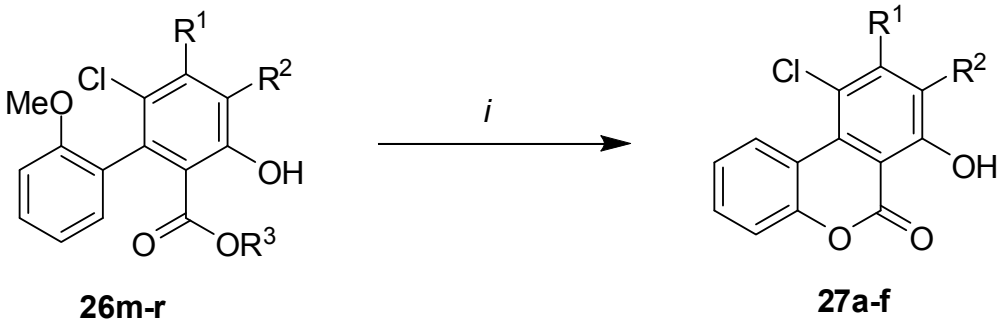
Recently, Langer *et al.* reported the synthesis of 6*H*-benzo[*c*]chromen-6-ones by reaction of 1,3-bis(silyl enol ethers) with benzopyrylium triflates. As recently Langer *et al*. reported the a new approach to 6*H*-benzo[*c*]chromen-6-ones relies on the [3+3] cyclizations of 1,3-bis(silyl

enol ethers) with 1-(2-methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-ones and subsequent lactonization.[25b].

Herein, I wish to report the scope of this methodology to the synthesis of 10-chloro-6*H*-benzo[*c*]chromen-6-ones. The synthesis of this type of chlorinated structure has, to the best of our knowledge, not yet been reported.

3.3.2 Results and discussion

The chlorinated biaryls **26m-r** contain an *ortho*-methoxy group located at one of the aryl groups. Treatment of **26m-r** with borontribromide and subsequent addition of an aqueous solution of potassium *tert*-butanolate, following a protocol recently reported by Langer *et al*.,[25b] afforded the novel chloro-substituted dibenzo[*b*,*d*]pyran-6-ones **27a-f** (Scheme 3-3, Table 3-3). The structure of **27d** was independently confirmed by X-ray crystal structure analyses (**Figure 3.7**).[105]



26m-r **27a-f**

Scheme 3-3: Synthesis of dibenzo[*b*,*d*]pyran-6-ones **27a-f**; *i*: 1) BBr_3 (4 equiv.), CH_2Cl_2, 0 → 20 °C, 18 h; 2) KO*t*Bu, H_2O, 15 min, 20 °C.

Table 3-3: Synthesis of dibenzo[*b*,*d*]pyran-6-ones **27a-f**

26	**27**	R^1	R^2	R^3	% (**27**) [a]
m	**a**	Me	H	Me	73
n	**b**	Me	Me	Me	78
o	**c**	Me	Et	Et	67
p	**d**	*n*Pr	H	Me	88
q	**e**	*n*Pr	Me	Me	54
r	**f**	*n*Pr	Et	Et	48

[a] Isolated yields

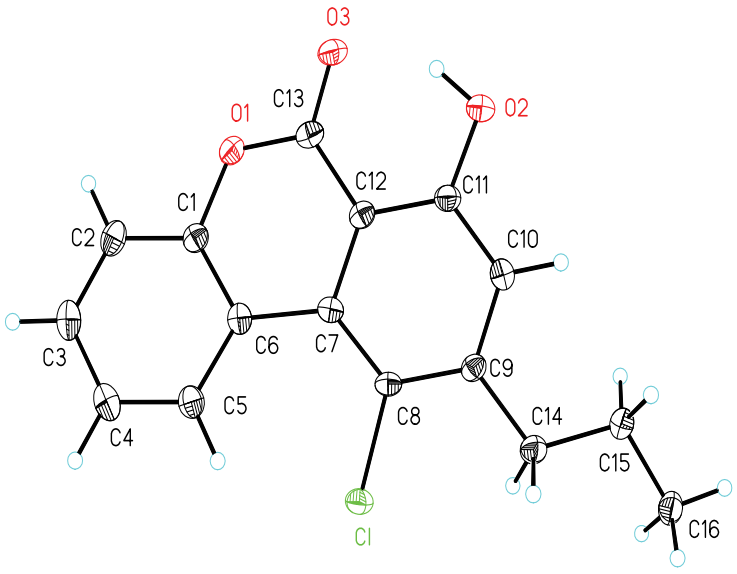


Figure 3.8: Ortep plot of **27d**

3.3.3 Conclusions

In conclusion, I have reported the synthesis of variety of chlorinated 6H-benzo[c]chromen-6-ones based on regioselective [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 2-chloro-3-silyloxy-2-en-1-ones. This approach provides a convenient pathway to synthesis of various functionalized chlorinated lactones which are not readily available by other methods.

3.4 Synthesis of flourenones

3.4.1 Introductuion

1-Hydroxyfluorenones are interesting lead structures in medicinal chemistry and are also present in nature (e. g. in the natural products dengibsin, dengibsinin, and dendroflorin).[49] (**Figures 3.8, 3.9**) Fluorinated fluorenones[50] are of specific interest in current medicinal chemistry. For example, it was shown that 4-fluorofluorenones possess antagonistic in vitro activity to human progesterone receptor B (hPR-B) in cotransfected CV-1 cells (IC50 = 158 nM).[51] Fluorenones have already been prepared, for example, by intramolecular Friedel–Crafts acylations of biaryls.[53] Snieckus and co-workers reported the synthesis of fluorenones based on remote aromatic metalation.[54] Some years ago, the synthesis of fluorenones using a Suzuki coupling/intramolecular Friedel–Crafts acylation sequence has been reported.[55] Recently, Reim *et al* reported an efficient synthetic approach to fluorenones based on a '[3+3] cyclization/Suzuki crosscoupling/Friedel–Crafts acylation' strategy. [52] Chan *et al.* reported the synthesis of 1-hydroxy-3-methylfluorenone by reaction of methyl 6-phenylsalicylate with concentrated sulfuric acid.[2]

Herein, I wish, to report an approach to synthesis of fluorenones and chlorinated fluorenones based on '[3+3] cyclization/Friedel–Crafts acylation' reactions.

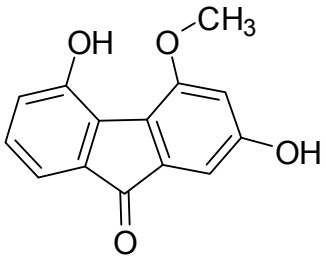


Figure3.8: Dengibsin

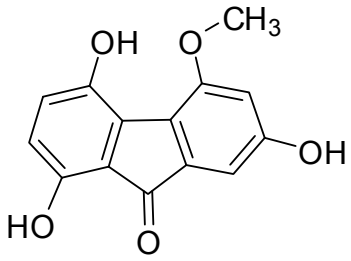
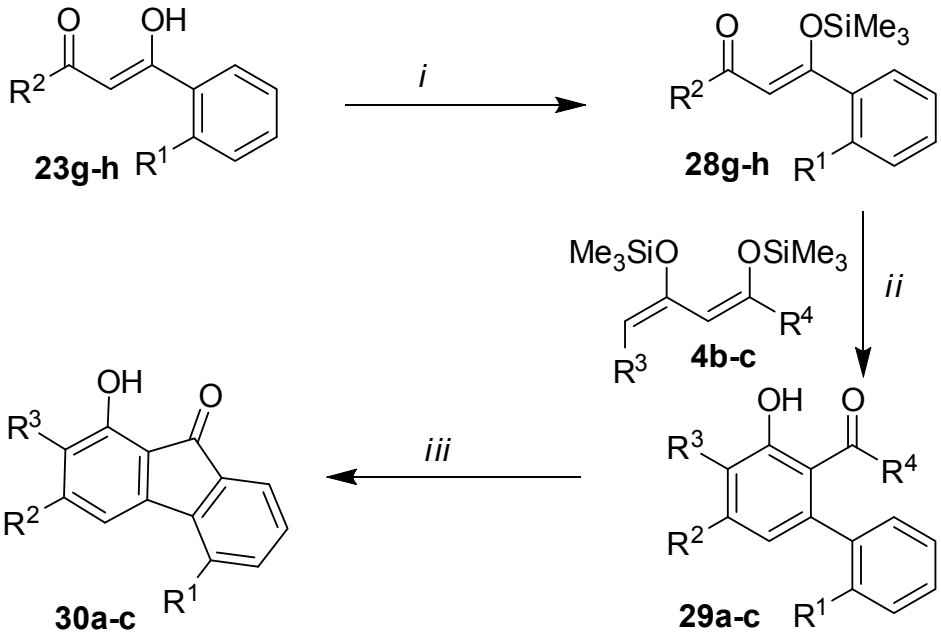


Figure3.9: Dendroflorin

3.4.2 Result and discussion

Aryl-4-(trimethylsilyloxy)but-3-en-2-ones **28g-h**, which were prepared by reaction of 1,3-diketiones **23g-h** with Me_3SiCl/NEt_3. The $TiCl_4$ mediated formal [3+3] cyclization of **28g-h** (Scheme 3-4, Table3-4) with **4b-c** 1,3-bis(silyl enol ethers), **4b-c**– prepared from the

corresponding 1,3-dicarbonyl compounds in one or two steps[14]– afforded the novel biaryls **29a-c** in moderate to good yields. Treatment of the later with concentrated sulfuric acid afforded the fluorenones **30a–c** in high yields (Scheme 3-4, Table 3-4).



Scheme 3-4: Synthesis of **30a-c**; *i*: NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72 h; *ii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C; *iii*: H_2SO4, 20 °C, 1 h.

Table 3-4: Synthesis of fluorenones **30a-c**

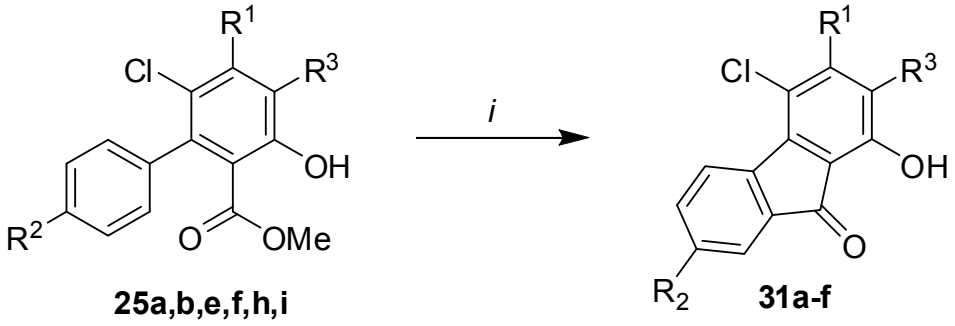
4	**28**	**29**	**30**	R^1	R^2	R^3	R^4	% (**23**)[a]	**% (24)**[a]
b	**g**	**a**	**a**	Cl	Me	Me	OMe	32	80
c	**g**	**b**	**b**	Cl	Me	Et	OEt	35	60
b	**h**	**c**	**c**	F	Me	Me	OMe	32	51

[a] Isolated yields

3.4.3 Chlorinated fluorenones

3.4.3.1 Results and discussion

The reaction of chlorinated biaryls **25a,b,e,f,h,i** with concentrated sulfuric acid afforded the novel chlorinated fluorenones **31a-f** by an intramolecular Friedel-Crafts acylation (Scheme 3-5, Table 3-5). The chloride or fluoride function proved to be compatible with this reaction.



25a,b,e,f,h,i **31a-f**

Scheme 3-5: Synthesis of chlorinated fluorenones **31a-f**; *i*: concd. H_2SO_4, 20 °C, 1 h.

Table 3-5. Synthesis of fluorenones **25a-f**

25	**31**	R^1	R^2	R^3	% (**31**)[a]
a	**a**	Me	H	H	70
b	**b**	Me	H	Me	86
e	**c**	Me	F	H	61
f	**d**	Me	F	Me	55
h	**e**	Me	Cl	H	84
i	**f**	Me	Cl	Me	74

. [a] Isolated yields

3.4.4 Conclusions

In conclusion, I have reported the synthesis of variety of functionalized fluorenones and chlorinated fluorenones, which are to the best of our knowledge, are not readily available by other methods.

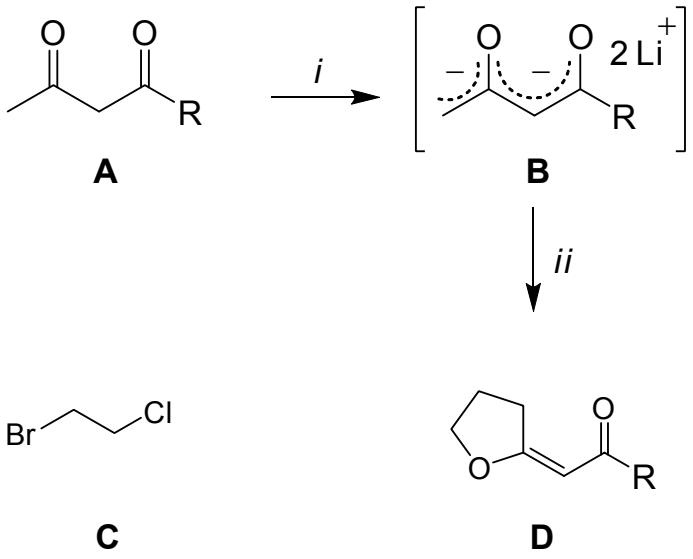
4. Synthesis of 2-benzoyl-4-(2-hydroxybenzoyl)phenols by catalytic domino ′Michael-retro-Michael–Mukaiyama-aldol′ reactions of 1-aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylchromones

4.1 Synthesis of aryl-1,3 -bis(trimethylsilyloxy)-1,3-butadienes

4.1.1 Introduction

The synthesis of relevant organic compounds such as natural products and analogues, drugs, diagnostics, agrochemicals, and other kinds of material is a main topic in academic and industrial chemistry, and it is the connecting point of interdisciplinary research in chemistry, biology, and medicine. The view of synthesis has altered in recent years; there is clearly a change in paradigm. At the beginning, organic chemistry was considered a branch of natural sciences dealing with a specific type of compounds, mainly isolated from living organisms. Even today natural products continue to play an important role in discovery and development of new pharmaceuticals.[56] Since the discovery of penicillin, a large number of antibiotics have been isolated from scores of micro-organisms.[57] Natural products also provide a great help in chemotherapy of cancer. They are an integral part of anticancer drugs e.g. bleomycin, doxorubicin, mitomycin, and paclitaxel.[58] All this pharmacologically and biologically important stuff designed by Mother Nature was not available in bulk quantities which man demanded. Thus the development of new, highly selective methods is still being a main task, to get it in bulk amounts while following the foot steps of nature, but even more important is the search for more efficiency.[59] The relationship between structural complexity and the number of steps in a synthesis must be improved. In addition, synthetic methodology must be designed in a way that it allows access to diversified substance libraries in an automatized way.[60] A general way to improve synthetic eficciency and in addition to give access to a multitude of diversified molecules in solution is the development of multicompound domino reactions, which allow the formation of complex compounds starting from simple substrates. Domino reactions are defined as processes of two or more bond-forming reactions in which a subsequent trans-formation takes place by virtue of the functionalities introduced in a former transformation.[59a,60d,61] The development of cyclization reaction with free[62] and masked dianions,[63] for the development of biologically relevant ring systems, and natural substances,[64] is research priority in the working group prof. Langer.[1] Despite the simplicity of

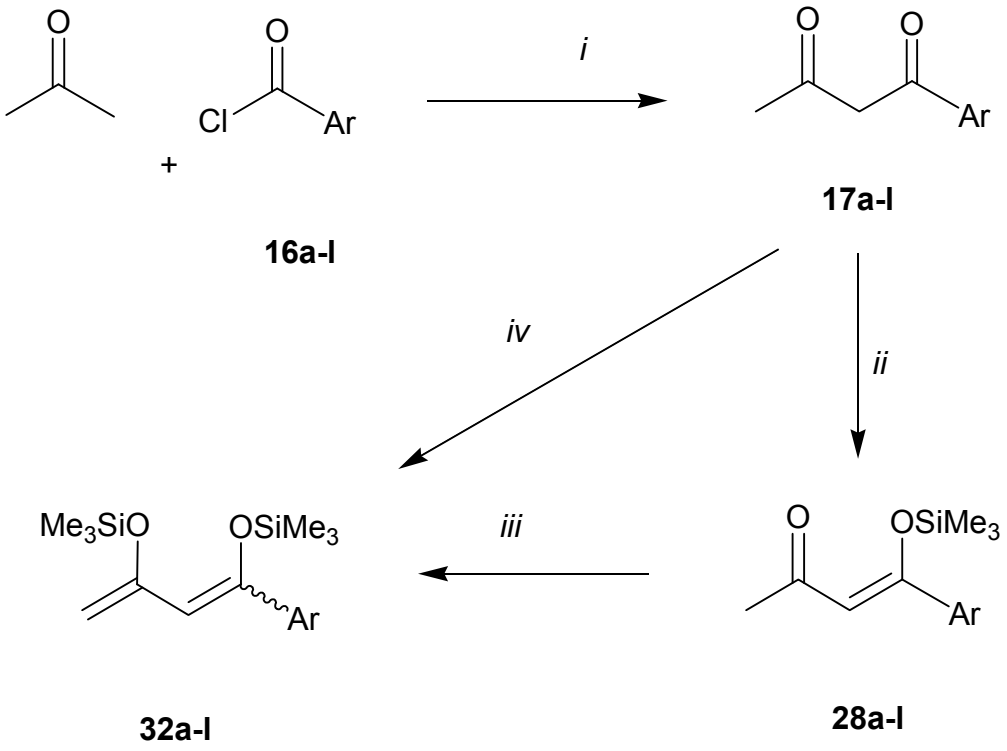
the idea that in the implementation dianions with 1-2 difunctional alkylhalides to cyclic systems, both dianions as many dielectrophiles represent highly reactive compounds, leading to adverse reactions, such as polymerization, reduction of dielectrophile,[65] monoalkylation,[66]eliminations[67] or SET reactions (SET = single-electron-transfer).[68] These problems can be achieved through : (a) optimization of proper tuning of reactivity of dianion and dielectrophile and (b) the use of electroneutral dianions equalivalents (masked dianion) in Lewis acid catalyzed reactions. Masked dianion represent important building blocks. The regioselectivity observed for reactions of true and masked dianions is the same in most cases.



Scheme 4-1: *i*: LDA (2.5 equiv.), THF, 0 °C, 1 h; *ii*: $Br(CH_2)_2Cl$, −78 → 20 °C, 14 h, then reflux, 14 h.

4.1.2 Results and discussion

1,3-Bis(trimethylsilyloxy)-1,3-butadienes **32a-l** are available from the respective 1,3-dicarbonyl compounds **17a-l** in one or two steps. Following the procedures of Danishefsky, Chan and Molander, ester-derived (same for 1,3-diketone) bis(silyl enol ethers) **32a-l** can be prepared by treatment of the respective 1,3-dicarbonyl compound with NEt_3–Me_3SiCl to give the mono(silyl enol ethers) **28a-l** Deprotonation of **28a-l** with LDA and subsequent addition of Me_3SiCl afforded the dienes **32a-l** (Scheme 4-2, Table 4-1).[2] Simchen *et al.* have reported that 1,3-diketone derived bis(silyl enol ethers) can be prepared in one step by treatment of an ether solution of the diketone with NEt_3–Me_3SiOTf (2 equiv).[69]



Scheme 4-2: Synthesis of bis(silylenol ethers) **32a-l**; *i*: LDA,THF (1.5 equiv), acetone (1.0 equiv), acid chloride **16a-l** (1.2equiv.), -78 → 20 ^{o}C; *ii*: Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h; *iii*: LDA, THF, -78 → 20 °C, Me_3SiCl; *iv*: Me_3SiOTf (2.0 equiv), NEt_3, Et_2O, 0→20 °C, 12 h.

Bis(silyl enol ethers) **32a-l** can be stored in most cases at -20 °C for several months without decomposition.

Table 4-1: Products and yields

16	17	28,32	Ar	% (17) [a]	% (28) [a]	% (32) [a]
--	[b]	**a**	Phenyl	[b]	85	74
b	**b**	**b**	4-FC_6H_5	36	80	83
c	**c**	**c**	4-ClC_6H_5	38	80	70
d	**d**	**d**	2-MeC_6H_5	33	88	75
e	**e**	**e**	2-$OMeC_6H_5$	37	79	73
g	**g**	**g**	2-ClC_6H_5	25	75	60
h	**h**	**h**	2-FC_6H_5	35	80	75
i	**i**	**i**	4-$NO_2C_6H_5$	43	92	80
j	**j**	**j**	3,4,5-$OMe_3C_6H_2$	30	70	65
k	**k**	**k**	1-Naph	43	71	70
l	**l**	**l**	2-Naph	62	75	74

[a] Isolated yields; [b] Comercially available

My studies in this chapter are focussed on the synthesis of functionalized carbonyl compounds and of pharmacologically relevant functionalized bis(benzophenones) followed by the synthesis of aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes. I have developed a new methodology for the synthesis of bis(benzophenones) by cyclization reactions of aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-formylchromones.

4.1.3 Conclusions

The application of a the known procedure allows the synthesis of novel aryl-1,3-bis(trimethylsilyloxy)-1,3-butadienes. These masked dianions are used in the cyclization reactions for synthesis heterocycles and aromatic rings - the important building blocks of natural products analogue.

4.2 Synthesis of bis(benzophenones)

4.2.1 Introduction

Functionalized benzophenones occur in a variety of natural products and represent important core structures for the development of pharmaceuticals.[70, 71, 72] For example, 2-hydroxy- and 2-aminobenzophenones are promising candidates for anticancer therapy, due to their antitubulin activity. Functionalized benzophenones also represent important technical products. They are used as photosensitizers[73] and as active ingredients of commercial agents which protect the skin or colour against UV-irradiation.[74] Benzophenones are available by reaction of organometallic reagents with aldehydes and subsequent oxidation. A recent modification of this approach involves the SmI_2 mediated reaction of benzaldehydes with benzylhalides and subsequent oxidation.[75] Other benzophenone syntheses rely on Friedel-Crafts acylations.[76] However, these methods often give unsatisfactory results for the synthesis of functionalized benzophenones (e. g. containing a hydroxy, halide or ester group), due to competing side-reactions. Therefore, the development of new synthetic strategies is of considerable importance in organic and medicinal chemistry.

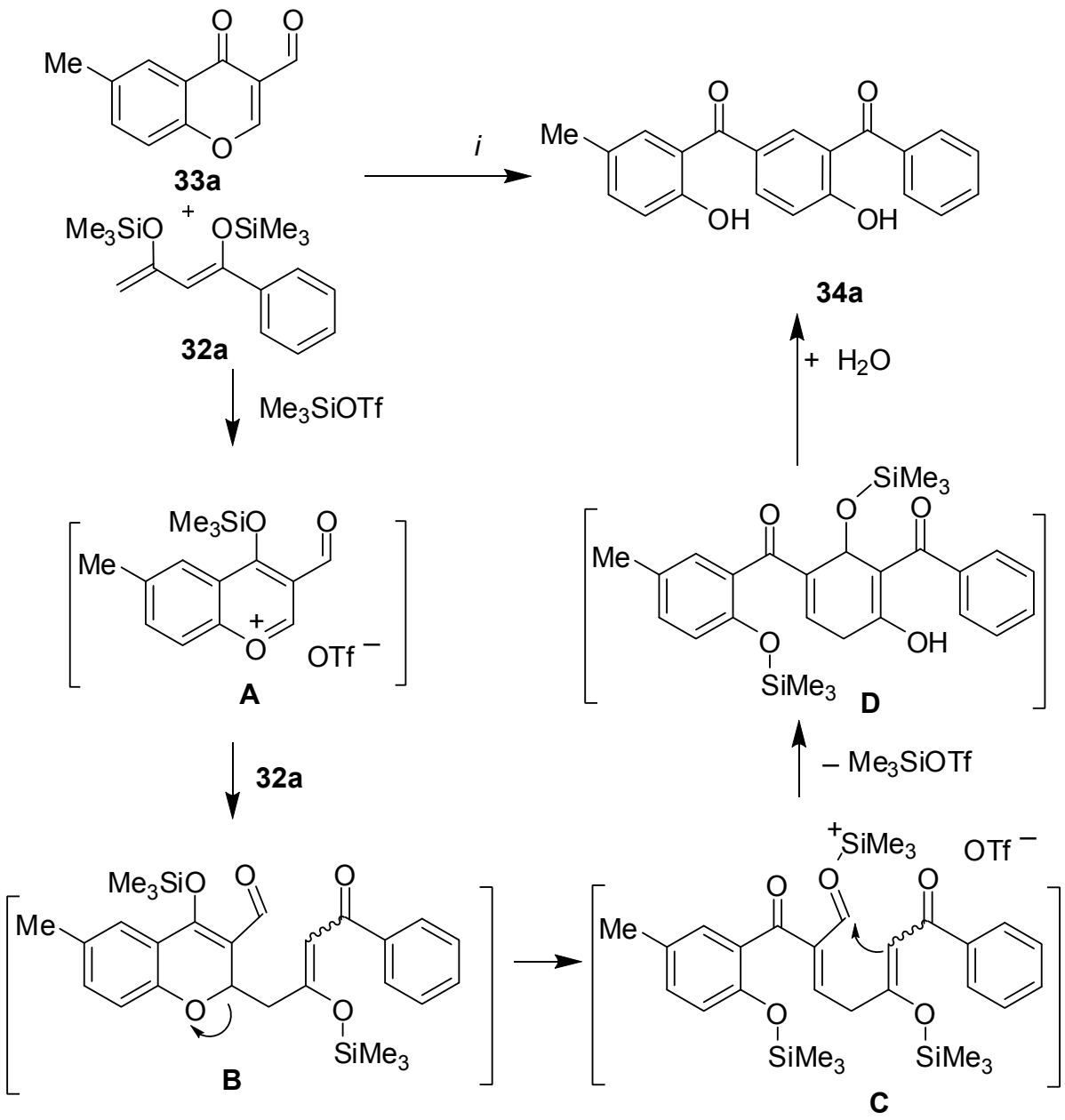
3-Formylchromone represents a useful building block for the synthesis of a great variety of (2-hydroxybenzoyl)heteroarenes.[77] These reactions generally proceed by cyclization of 3-formylchromone with a bis(nucleophile) which involves cleavage of the chromone moiety. Reactions of 3-formylchromone with carbon nucleophiles are relatively rare. For example, the reaction of 3-formylchromones with enamines was reported to give (2-hydroxybenzoyl)pyridines.[78] The reaction of 3-formylchromone with 1,3-dicarbonyl compounds was reported to give open-chain products by simple attack of the central carbon atom of the nucleophile onto the aldehyde (aldol condensation).[79] The employment of acetylacetone resulted in a C,C-cyclization with concurrent cleavage of the chromone moiety to give a benzophenone in low yield.[80] Besides the low yield, the reaction proved to be not general. Recently, Langer *et al*. reported[81] a new approach to 4-(2-hydroxybenzoyl)salicylates based on a new domino reaction of 1,3-bis(silyl enol ethers)[1, 82] with 3-(formyl)benzopyrylium triflates,[83] Which are in situ generated by reaction of 3-formylchromones with trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf). Herein, I wish to report the synthesis of 2-benzoyl-4-(2-hydroxybenzoyl)phenols which can be regarded as functionalized “bis(benzophenones)”. These products are not readily available by other

methods. The reactions reported herein are carried out under mild conditions using catalytic amounts of trimethylsilyl-trifluorosulfonate (Me_3SiOTf).

4.2.3 Results and discussion

The Me_3SiOTf catalyzed reaction of 6-methyl-3-formylchromone (**33a**) with 1-phenyl-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**32a**), readily available from benzoylacetone,[2] afforded the hydroxylated bis(benzophenone) **34a**. The formation of **34a** can be explained by a domino ′Michael-retro-Michael-Mukaiyama-aldol′ reaction (Scheme 4-3). The reaction of 6-methyl-3-formylchromone with Me_3SiOTf afforded the benzopyrylium triflate **A**. The reaction of **A** with the terminal carbon atom of **32a** gave intermediate **B** which underwent a retro-Michael reaction to give the polyketide **C**. An intramolecular aldol reaction gave intermediate **D** which was transformed into **34a** by elimination of siloxane.

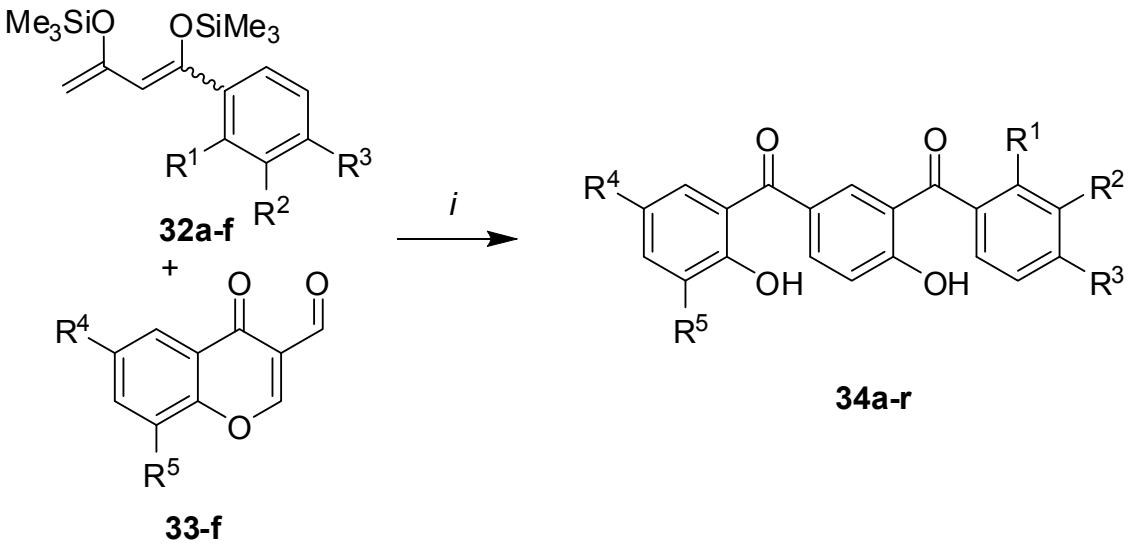
4.2.2.1 Possible mechanism for the synthesis of bis(benzophenones)



Scheme 4-3: Mechanism for the formation of **34a**; *i*: Me_3SiOTf (0.3 equiv.), 20 °C, 10 min; *ii*: 1) **32a** (1.3 equiv.), CH_2Cl_2, 0 → 20 °C, 12 h; 2) HCl (10%).

The cyclization of 1,3-bis(silyl enol ether) **32a** with 6-isopropyl-3-formylchromone (**33b**) and 6,8-dimethyl-3-formylchromone (**32c**) afforded the 2-benzoyl-4-(2-hydroxybenzoyl)phenols **34b** and **34c**, respectively (Scheme 4-4, Table 4-2). The cyclization of 1-(4-fluorophenyl) and 1-(2-fluorophenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**32b,h**) with 3-formylchromones **33b,d,e,f** afforded the fluoro-substituted bis(benzophenones) **34d-g**

and **34m-o** respectively . Products **34h** and **34i** were prepared from 1-(2-methylphenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**32d**). The cyclization of 1-(2-methoxyphenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**32e**) with 3-formylchromones **33a**, **33d**, and **33e** afforded the bis(benzophenones) **34j-l**, respectively. The cyclization of 1-(1-naphthyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**32k**) with 3-formylchromones **33a**, **33b**, and **33e** afforded the 2-benzoyl-4-(2-hydroxybenzoyl)phenols **34p**, **34q**, and **34r**, respectively.



Scheme 4-4: Synthesis of **34a-r**; *i*: 1) Me_3SiOTf (0.3 equiv.) 20 °C, 10 min; *ii*: **32a-f** (1.3 equiv.), CH_2Cl_2, 0 → 20 °C, 12 h; 2) HCl (10%).

Table 4-2: Products and yields

32	**33**	**34**	R^1	R^2	R^3	R^4	R^5	% (**34**) [a]
a	**a**	**a**	H	H	H	Me	H	34
a	**b**	**b**	H	H	H	*i*Pr	H	37
a	**c**	**c**	H	H	H	Me	Me	31
b	**b**	**d**	H	H	F	*i*Pr	H	30
b	**d**	**e**	H	H	F	Cl	H	27
b	**e**	**f**	H	H	F	Br	H	35
b	**f**	**g**	H	H	F	Et	H	37
d	**e**	**h**	Me	H	H	Br	H	39
d	**b**	**i**	Me	H	H	*i*Pr	H	28
e	**a**	**j**	OMe	H	H	Me	H	36
e	**d**	**k**	OMe	H	H	Cl	H	34
e	**e**	**l**	OMe	H	H	Br	H	38
h	**e**	**m**	F	H	H	Br	H	38
h	**b**	**n**	F	H	H	*i*Pr	H	35
h	**d**	**o**	F	H	H	Cl	H	44
k	**b**	**p**	$-(CH)_4-$		H	*i*Pr	H	32
k	**a**	**q**	$-(CH)_4-$		H	Me	H	34
k	**e**	**r**	$-(CH)_4-$		H	Br	H	36
k	**d**	**s**	$-(CH)_4-$		H	Cl	H	36

[a] Isolated yields.

The structure of the products was established by spectroscopic methods. The ^{1}H NMR spectra showed the presence of two low field signals assigned to the intramolecular hydrogen bonds O–H···O. The structures of bis(benzophenones) **34f** and **34m** were independently confirmed by crystal structure analysis (Figures 1 and 2).[105]

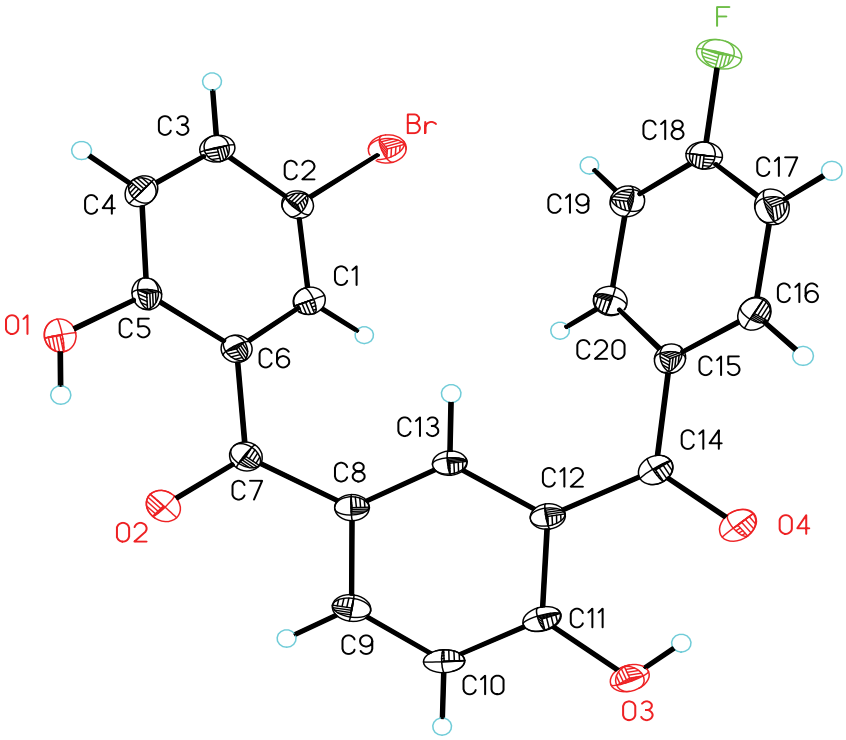


Figure 4-1: ORTEP-Plot of **34f**

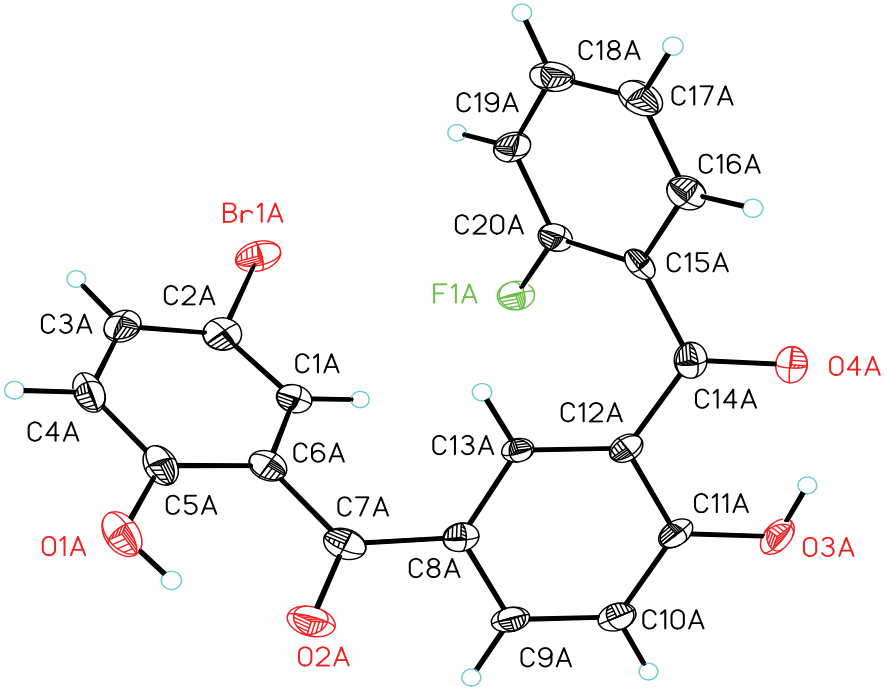


Figure 4-2: ORTEP-Plot of **34m**

4.2.3 Conclusions

In conclusion, I reported the domino reaction of 1-aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylbenzopyrylium triflates which were in situ generated from 3-formylchromones. The products were isolated in only moderate yields. This can be explained by the fact that not all of the 1,3-bis(silyl enol ether) was converted into product. Noteworthy, the reactions reported provide a convenient access to a variety of highly functionalized 2-benzoyl-4-(2-hydroxybenzoyl)phenols under mild conditions. The products are not readily available by other methods.

5. Synthesis of fucntionalized 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-one (isobenzomorphanone) by two-step cyclocondensation of 1,3-bis(strimethylsilyloxy)-1,3-butadienes with ispquinolines

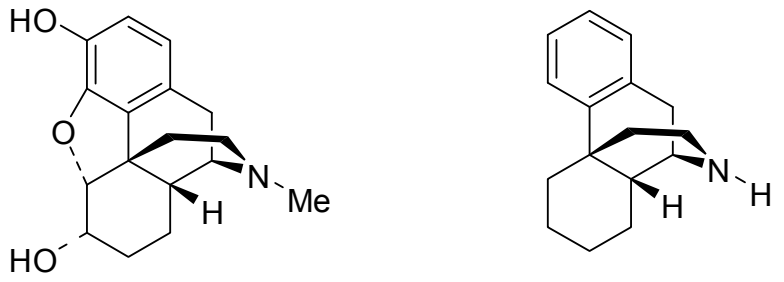
5.1 Introduction

The isoquinoline moiety is present in a variety of pharmacologically active alkaloids.[84] Benzylisoquinoline-type alkaloids, such as papaverine I or reticuline II are isolated from *Papaver*- und *Rauwolfia*-plants and show spasmolytic activity.[85] bis(benzyl)isoquinoline alkaloids include, for example, cycleanine, tetrandrine (antiinflammatory activity), isochondodendrin (sedative activity) and oxyacanthin (sympatholytic activity, adrenalin-antagonist).[84] Tubocurarine is the oldest muscle-relaxing agent and its dichloro derivative is used as a narcotic. Phthalidisoquinoline-alkaloids, isolated from *Papaveraceen*, are characterised by a tetracyclic system containing a γ-lactone moiety. Important examples are, for example, hydrastin and narcotin (noscapin) III. Hydrastin is used as a blood-stanching agent.[84] Noscapin is used as an antitussivic.[86] Synthetic approaches to tetrahydroisoquinoline alkaloids rely on asymmetric Pictet-Spengler-reactions and on Bischler-Napieralski-reactions and subsequent enantioselective reduction.[87] Aporphine-alkaloids contain a fused tetracyclic system. For example, apomorphine IV is used as a strong emetic.[88] Boldine represents a diuretic.[89] Aporphine alkaloids have been prepared, for example, by application of photochemical methods.[90] Pavine- and isopavine-alkaloids, such as dinorargemonine, eschscholtzine, munitagine and pavine, are isolated from *Papaveraceae*, *Berberidaceae*, *Ranunculaceae*, *Lauraceae* and *Menispermaceae* or from callus-cultures of *Cryptocarya Chinensis* and are of considerable pharmacological relevance.[84,91] For example, they show activity against H*erpes simplex* virus type 1[92a] and against tumor necrosis factor production.[92b] Pavine-type alkaloids are synthetically available.[93]

Morphine-alkaloids represent the most important group of naturally occuring isoquinolines.[84] They have been isolated from opium, a crude product mixture which is produced from *Papaver somniferum*. Important natural products include, for example, morphine VI, codein VII, thebaine and heroine[84] which possess a wide range of

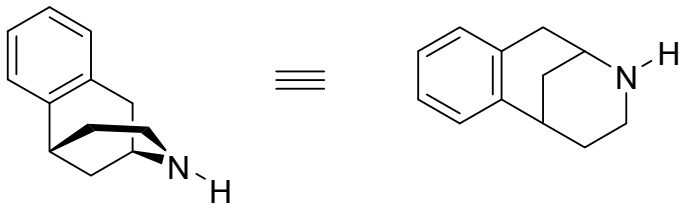
pharmacological activities (e. g. analgetic, sedative, hypnotic, antitussivic, miotic and antidiuretic activity).[84] Morphine, the structure of which was elucidated by Sir Robert Robinson in 1925,[94] is a very important drug for the treatment of pain. The synthesis of morphine-type alkaloids has been reported.[95]

The development of simpler morphine analogues, which show no dependence-producing and other undesirable side-effects, has been the subject of research for many decades. Simpler morphine-like compounds include, for example, morphinan and benzomorphan (i. e., 1,2,3,4,5,6-hexahydro-2,6-methano-3-benzazocine).[96] The first synthesis of a benzomorphan has been reported by Barltrop in 1947.[97] The trivial name "benzomorphan" is derived from the trivial name "morphan" (azabicyclo[3.3.1]nonane). Positional variation of the nitrogen atom leads to various isomers or their derivatives which have been previously synthesized.[98]

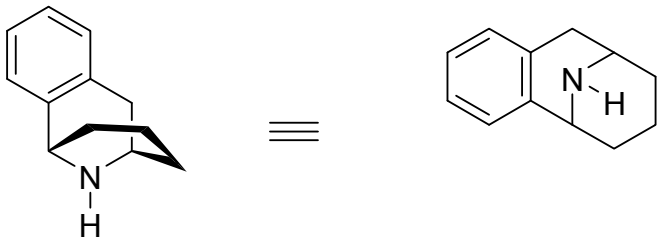


morphine

morphinan

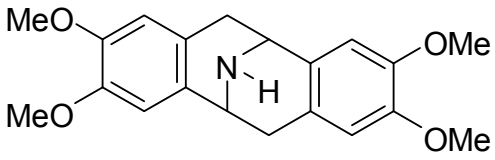


benzomorphan



isobenzomorphan

Figure 5-1: Morphine and some of its simpler analogues



Pavine

Figure 5-2:

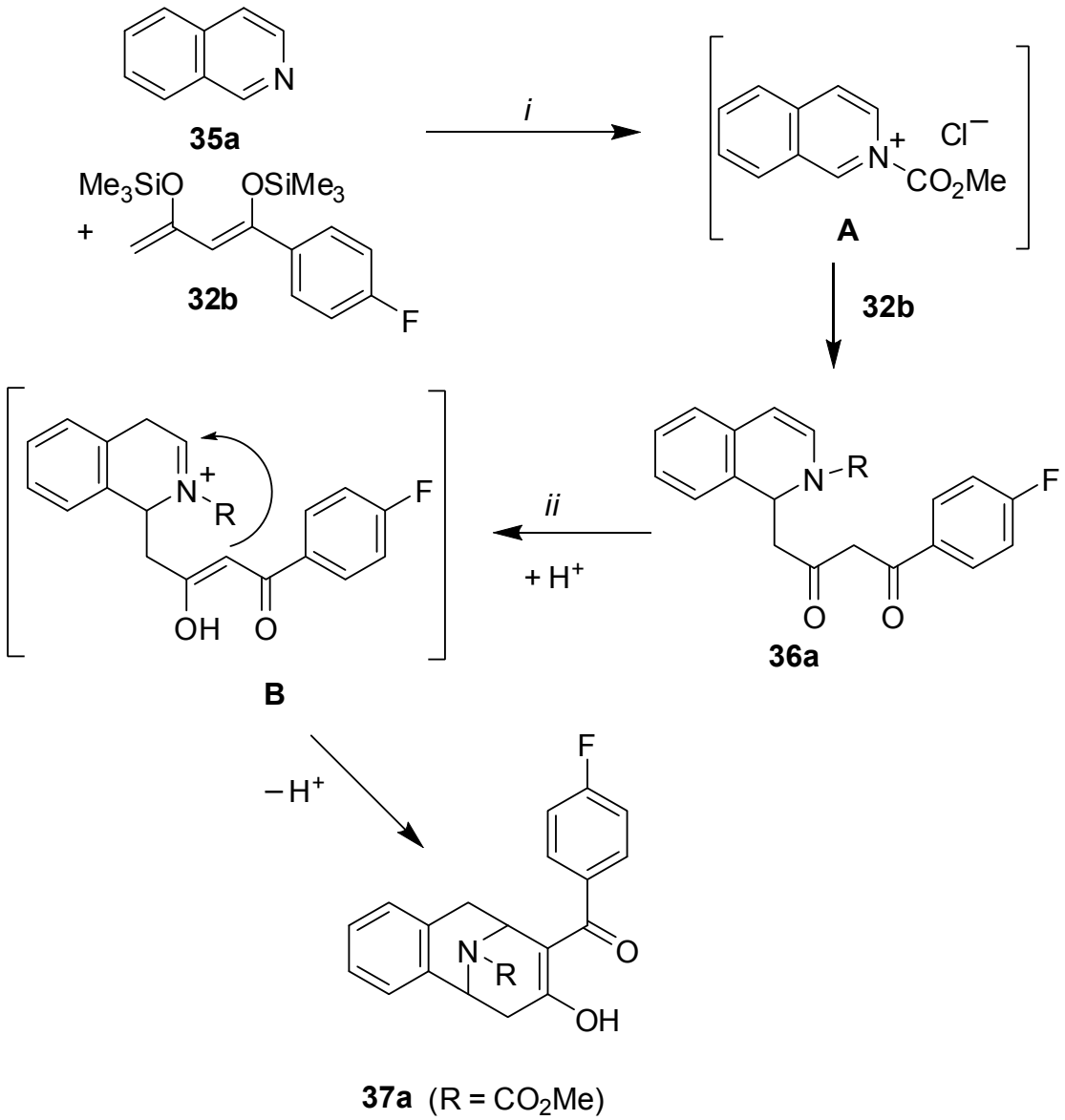
Isobenzomorphans (i. e., 7,8-benzo-9-azabicyclo-[3.3.1]nonanes, 1,2,3,4,5,6-hexahydro-1,5-iminobenzo-cyclooctenes) represent interesting structural isomers of benzomorphans containing an imino-bridge. These compounds are, in a formal sense, simple structural analogues of morphine and are present, for example, in pavine-type alkaloids (Scheme 2). Isobenzomorphans have been prepared by Dieckmann cyclization[99] and by reaction of an acetoneberberine-type enamine with alkyl halides.[100]

Quinolinium- and isoquinolinium salts, generated by alkylation or acylation of quinoline and isoquinoline,[101] are important synthetic building blocks. They have been used, for example, in condensations with Grignard reagents, cyanides (Reissert reaction), trimethylsilylacetonitrile, allylsilanes or silyl enol ethers.[102] In recent years, a number of cyclocondensation reactions of bis(silyl enol ethers) with iminium salts have been reported.[103] Recently, Langer *et al*. have reported[104] a convenient approach to 7,8-benzo-3-hydroxy-9-azabicyclo[3.3.1]non-3-enes, isobenzomorphan derivatives, by condensation of 1,3-bis(silyloxy)-1,3-butadienes[1] with isoquinolinium salts and subsequent acid-mediated cyclization. The products are not readily available by other methods. Herein, I wish to report a comprehensive study of the preparative scope this methodology. In addition, I report, for the first time, the deprotection of the products, the synthesis of the parent 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones by decarboxylation. Some work from this portion will be the part of the Ph.D thesis of Mr. Jörg Peter Gütlein.

5.2. Results and Discussion

The methyl chloroformate-mediated reaction of isoquinoline (**35a**) with 4-(4-fluorophenyl)-2,2,8,8-tetramethyl-6-methylene-3,7-dioxa-2,8-disilanon-4-ene (**32b**), available

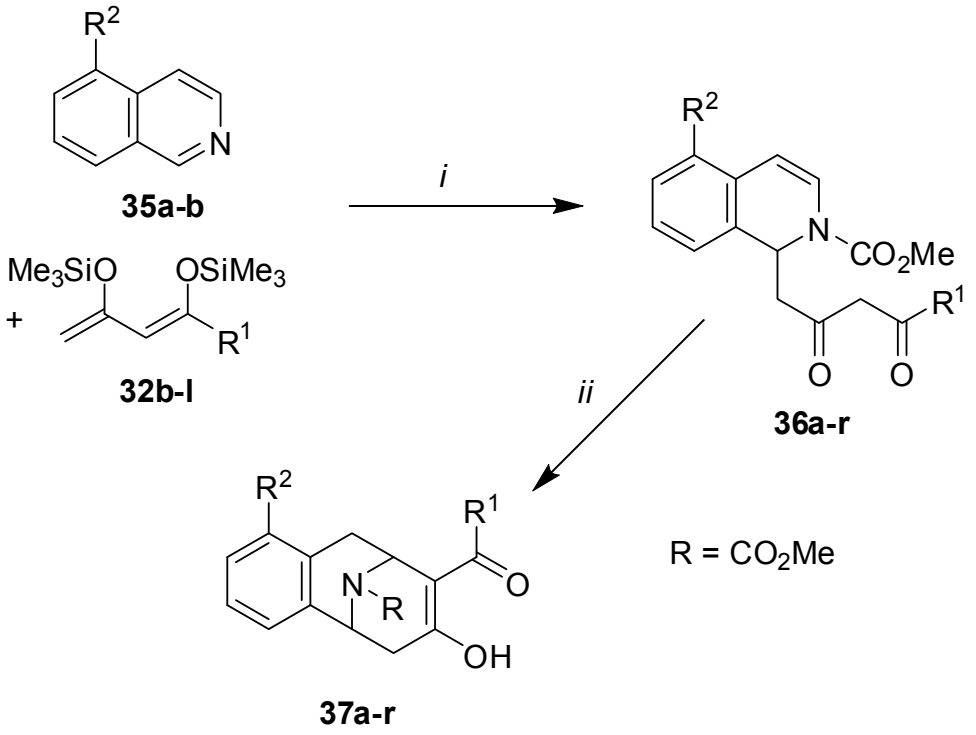
from 4-flourobenzoylacetone,[2] afforded the condensation product **36a** (Scheme 5-1). The reaction proceeds by formation of the isoquinolinium salt **A** and subsequent regioselective attack of the terminal carbon of **32b**. Treatment of **36a** with TFA afforded the 7,8-benzo-3-hydroxy-9-azabicyclo[3.3.1]non-3-ene **37a**. The use of TFA proved to be mandatory; the employment of hydrochloric acid gave unsatisfactory results.



Scheme 5-1: Possible mechanism of the cyclization of aryl-1,3-bis(silyl enol ether) **32b** with **35a**; *i*: **35a** (1.0 equiv.), **32b** (2.0 equiv.), $ClCO_2Me$ (1.2 equiv.), CH_2Cl_2, 0 °C, 2 h, 20 °C, 12 h; *ii*: TFA (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h.

The formation of **37a** proceeds by regioselective attack of the terminal carbon atom of **32b** onto the iminium salt **A** fromed by reaction of **35a** with methyl chloroformate. The TFA-mediated cyclization proceeds by formation of the iminium salt **B** and attack of the enol carbon atom onto the latter. The regioselective cyclization can be explained by the higher thermodynamic stability of the iminium cation **B** compared to the benzylic cation formed by protonation of the other carbon atom of the enamine moiety (by 19.7 kcal/mol at a B3LYP/6-31G* level). Product **37a** is completely present in its enol tautomeric form (which is more stable by 3.3 kcal/mol than the keto form at the same level of theory).

The methyl chloroformate mediated reaction of **35a-c** with aryl-1,3-bis(silyl enol ethers) **32b-l**, prepared from the corresponding 1,3-dicarbonyl compounds, afforded the condensation products **36a-r** which were transformed into the 7,8-benzo-9-azabicyclo[3.3.1]non-3-enes **37a-r** (Scheme 5-2, Table 5-1). All reactions proceeded in moderate to excellent yields. Regarding the cyclization step, better yields were generally obtained for substrates derived from 1,3-diketones compared to those derived from β-ketoesters. This can be explained by the higher extent of enolization of 1,3-diketones compared to β-ketoesters which is important for the TFA-mediated cyclization step. Noteworthy, the synthesis and reactions of pyridine- and thiophene-derived 1,3-bis(silyl enol ethers) **32m** and **32n** has not yet been reported.



Scheme 5-2: Synthesis of **37a-r**; *i*: **35** (1.0 equiv.), **32** (2.0 equiv.), $ClCO_2Me$ (1.2 equiv.), CH_2Cl_2, 0°C, 2 h, 20 °C, 12 h; *ii*: TFA (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h.

Table 5-1: Synthesis of **37a-r**

35	**32**	**36,37**	R^1	R^2	% (**36**) [a]	% (**37**) [a]
a	**b**	**a**	4-FC_6H_4	H	68	67
a	**c**	**b**	4-ClC_6H_4	H	70	69
a	**d**	**c**	2-MeC_6H_4	H	43	72
a	**e**	**d**	2-$(MeO)C_6H_4$	H	68	69
a	**g**	**e**	2-ClC_6H_4	H	58	78
a	**h**	**f**	2-FC_6H_4	Et	76	81
a	**i**	**g**	4-$(NO_2)C_6H_4$	H	43	60
a	**j**	**h**	3,4,5-$(MeO)_3C_6H_2$	H	34	55
a	**k**	**i**	1-Naph	H	41	77
a	**l**	**j**	2-Naph	H	76	70
a	**r**	**k**	2-Pyridyl	H	68	27
a	**s**	**l**	2-Thienyl	H	22	34
b	**c**	**m**	4-ClC_6H_4	NO_2	54	75
b	**b**	**n**	4-FC_6H_4	NO_2	72	55
b	**d**	**o**	2-MeC_6H_4	NO_2	71	96
b	**h**	**p**	2-FC_6H_4	NO_2	41	86
b	**g**	**q**	2-ClC_6H_4	NO_2	56	60
b	**l**	**r**	2-Naph	NO_2	56	63

[a] Yields of isolated products

All structures were proved by spectroscopic methods. Noteworthy, the ^1H and ^{13}C NMR spectra show a splitting of several signals, due to dynamic processes of the carbamate moiety which possesses a significant double bond character. The structures of **37d**, and **37f** were independently confirmed by X-ray crystal structure analyses (**Figures** 5-3, 5-4).[105]

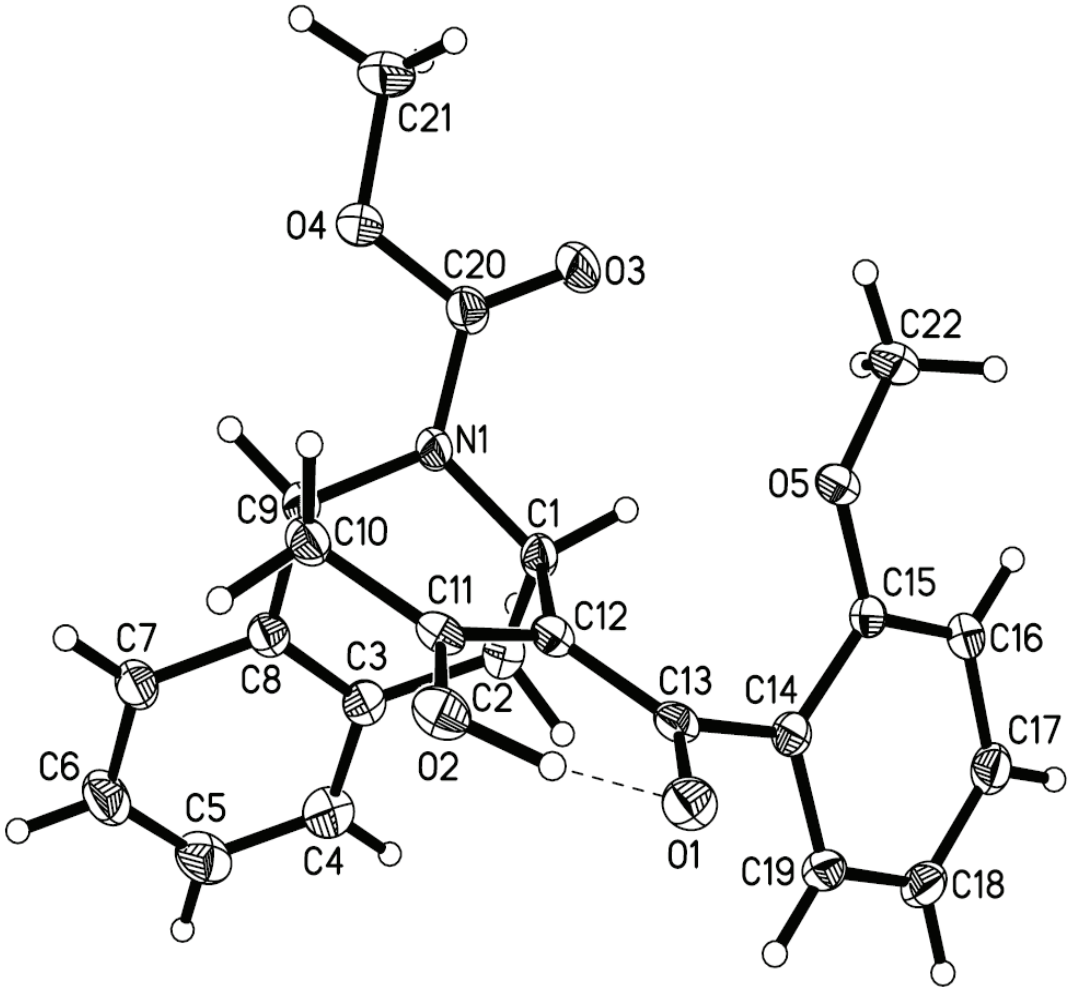


Figure 5-3: Ortep plot of **37d.** The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms.

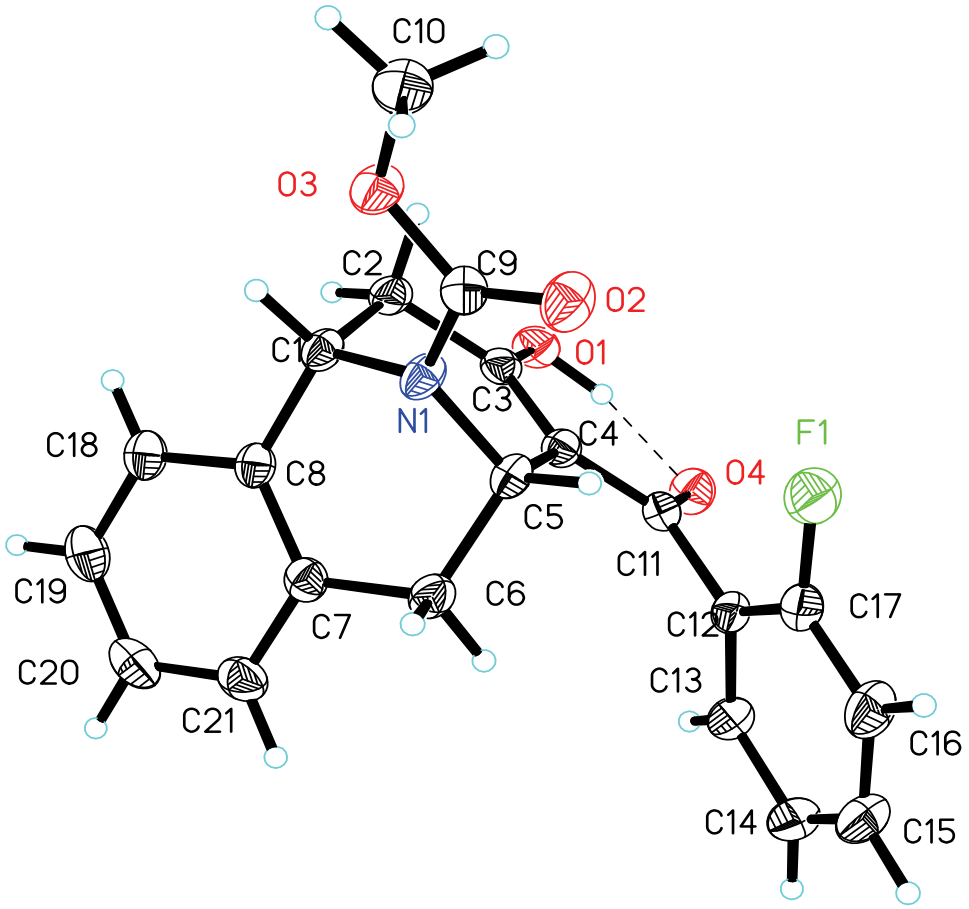
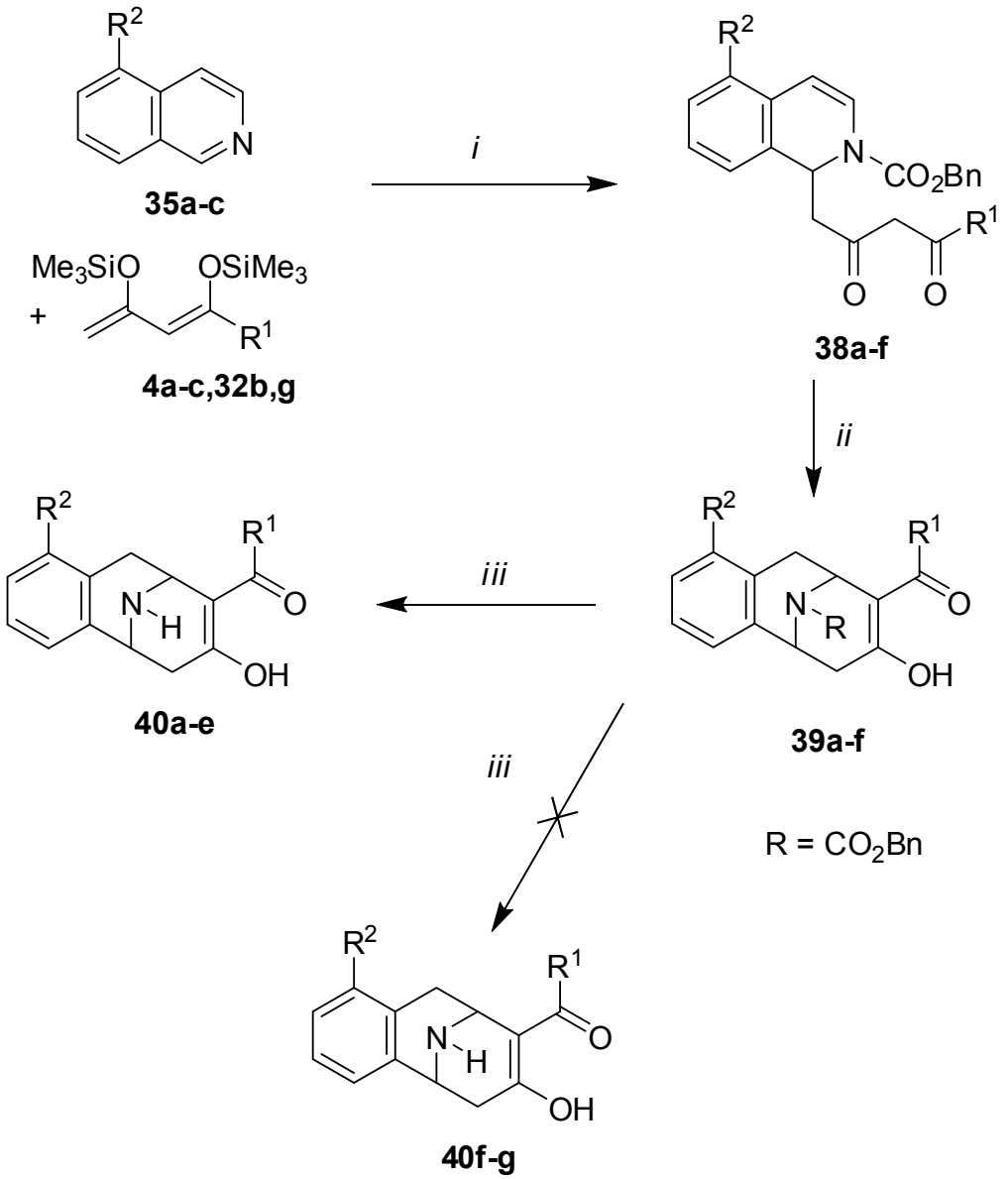


Figure 5-4: Ortep plot of **37f.**The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms.

The reaction of **35a-d** with 1,3-bis(silyl enol ethers) **4a-c** and **32b,g**, in the presence of *benzyl* chloroformate, afforded the condensation products **38a-f** which were transformed into the 7,8-benzo-9-azabicyclo[3.3.1]non-3-enes **39a-f** (Scheme 5-3, Table 5-2). While all attempts to deprotect the methoxycarbonyl-substituted products **37a-ad** proved to be unsuccessful, the deprotection (H_2, Pd/C) of benzyloxycarbonyl-substituted derivatives **39a-e** was possible and gave the desired products **7a-e**, But the conversion of **39 f-g** to **40f-g** was unsuccessful. The hydrogenation of **39a-e** resulted not only in cleavage of the protective group, but also in transformation of the nitro into an amino group. As expected, no splitting of signals was observed for all products **40a-e**, due to the absence of the carbamate moiety.



Scheme 5-3: Synthesis of **40a-g**; *i*: **35** (1.0 equiv.), **4, 32** (2.0 equiv.), $ClCO_2Bn$ (1.2 equiv.), CH_2Cl_2, 0°C, 2 h, 20 °C, 12 h; *ii*: TFA (2.0 equiv.), CH_2Cl_2, 20 °C, 12 h; *iii*;H_2 Pd/C 12 h, 25°C.

Table 5-2: Synthesis of **40a-g**

35	**4**	**38,39,40**	R^1	R^2	% (**38**) [a]	% (**39**) [a]	% (**40**) [a]
a	**a**	**a**	OMe	H	83	37	37
b	**a**	**b**	OMe	NO_2	97	37	
b	**a**	**b**	OMe	NH_2			37
c	**b**	**c**	Me	Br	79	25	
c	**b**	**c**	Me	H			25
a	**c**	**d**	$O(CH_2)_2OMe$	H	80	57	57
a	**b**	**e**	Me	H	55	69	69
a	**32c**	**f**	4-ClC_6H_5	H	81	93	Fail
a	**32g**	**g**	2-ClC_6H_5	H	50	61	Fail

[a] Isolated yields

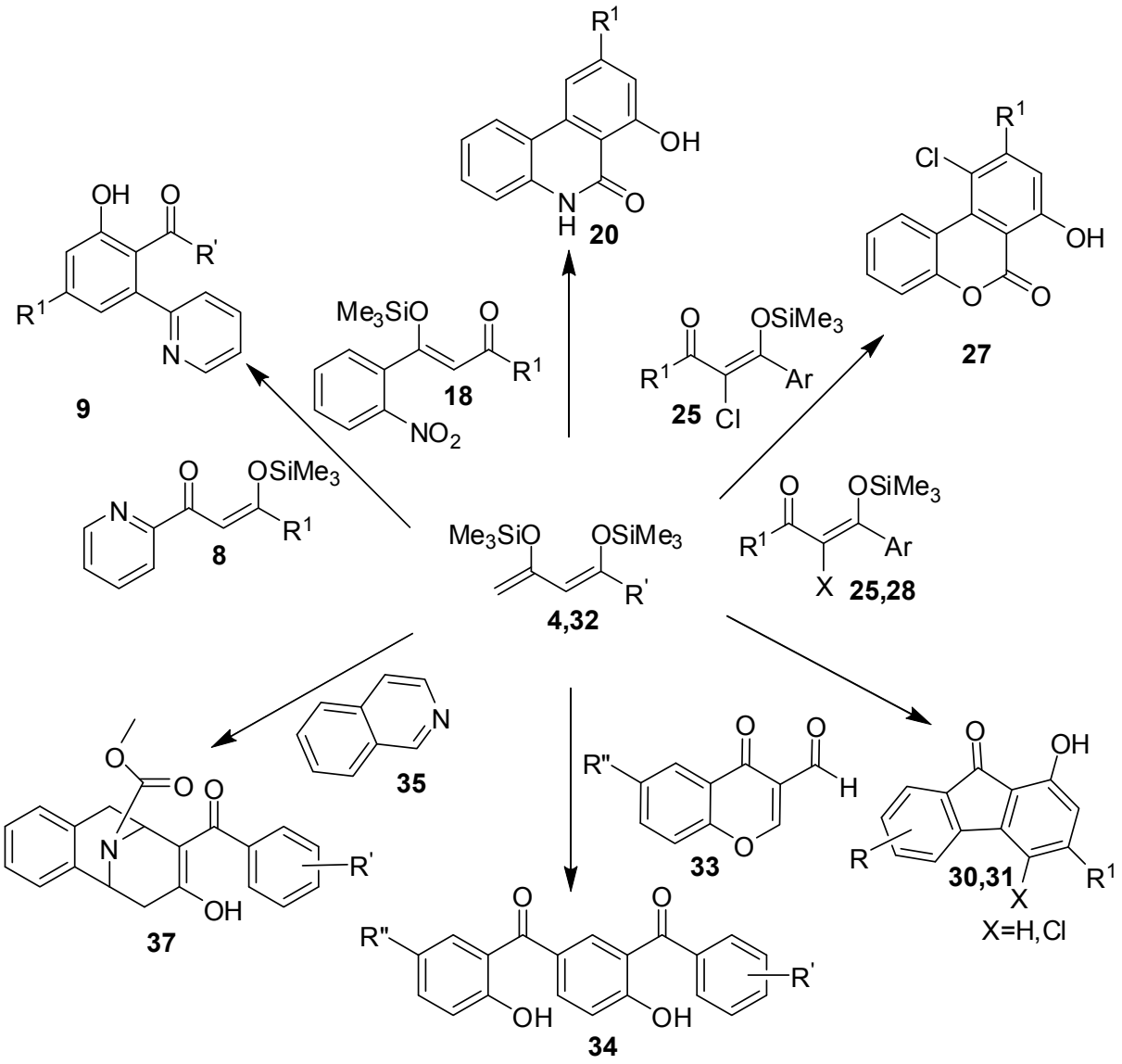
5.3. Conclusions

A great variety of functionalized 7,8-benzo-9-azabicyclo-[3.3.1]nonan-3-ones were prepared by methyl or benzyl chloroformate-mediated condensation of isoquinolines with 1,3-bis(silyloxy)-1,3-butadienes and subsequent TFA-mediated cyclization. The hydroxyl group could be functionalized by Suzuki reactions of the corresponding enol triflates. The N-benzyloxycarbonyl-substituted products were successfully deprotected. The decarboxylation allowed the synthesis of the parent 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones. The products can be regarded as functionalized isobenzomorphans – simple structural analogues of morphine.

6. Abstract

Regioselective cyclocondensation reactions of 1,3-bis(silyl enol ethers) with different mono(silyl enol ethers) provide an elegant approach for the synthesis of various complex carba- and heterocycles from simple starting materials. 6-(Pyridyl)salicylates and biaryls are prepared based on [3+3] cyclocondensations of 1,3-bis(silyl enol ethers) and 1-aryl-1-silyloxy-1-en-3-ones. Subsequently, 2-methoxy- and 2-nitro-substituted biaryls are transformed into biaryl lactones and 6(5*H*)-phenanthridinones based on a lactonization and lactamization strategy, respectively. Furthermore, some of the biaryls are also converted to the respective fluorenones by Friedel–Crafts acylations. The cyclocondensation reaction of aryl-1,3-bis(silyl enol ethers) with 3-formylchromone yielded bis(benzophenones). In addition, functionalized 7,8-benzo-9-azabicyclo[3.3.1]nonan-3-ones (isobenzomorphanons) have been prepared by cyclocondensation of aryl-1.3-bis(silyl enol ethers) with isoquinolines.

Regioselective Cyclokondensationsreaktionen von 1,3-Bis(silylenolethern) mit unterschiedlichen Mono(silylenolethern) bietet einen eleganten Zugang zu einer Vielzahl unterschiedlicher Carba- und Heterocyclen ausgehend von einfachen Startmaterialien. 6-(Pyridyl)salicylate und Biaryle werden durch [3+3] Cyclokondensationen von 1,3-Bis(silylenolethern) und 1-Aryl-1-silyloxy-1-en-3-onen hergestellt. Anschließend werden 2-methoxy- und 2-nitro-substituierte Biaryle in Biaryllactone und 6(5*H*)-Phenanthridinone durch Lactonisierung bzw. Lactamisierung umgewandelt. Außerdem werden Biaryle in Fluorenone durch Friedel–Crafts-Acylierungen umgewandelt. Die Cyclokondensation von Aryl-1,3-bis(silylenolethern) mit 3-Formylchromonen lieferte Bis(benzophenone). Schließlich wurden funktionalisierte 7,8-Benzo-9-azabicyclo[3.3.1]nonan-3-one (Isobenzomorphanone) durch Cyclokondensation von Aryl-1,3-bis(silylenolethern) mit Isoquinolinen synthetisiert.



General Scheme: As the part of this work carried out with bis(silyl enol ethers) and types of formed products (only one substitution pattern is shown for clarity).

6. Experimental Section:

6.1 General: Equipment, chemicals and work technique

^{1}H NMR Spectroscopy: Bruker: AM 250, Bruker ARX 300, Bruker ARX 500; δ = 0.00 ppm for Tetramethylsilane; δ = 2.04 ppm for Acetone d-6; δ = 7.26 ppm for (CDCl3); 2.50 ppm for d-6 DMSO-; Characterization of the signal fragmentations: s = singlet, d = doublet, dd = double of doublet, ddd = doublet of a double doublet, t = triplet, q = quartet, quint = quintet; sext = Sextet, sept = Septet, m = multiplet, br = broadly. Spectra were evaluated according to first order rule. All coupling constants are indicated as (*J*).

^{13}C NMR Spectroscopy: Bruker: AM 250, (62.9 MHz); Bruker: ARX 300, (75 MHz), Bruker: ARX 500, (125 MHz) Ref: 29.84 ± 0.01 ppm and 206.26 ± 0.13 ppm for $(CD_3)_2CO$. δ = 128.00 ppm for Acetone d-6; δ = 77.00 ppm for CDCl3. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH3, CH2, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

Mass Spectroscopy:AMD MS40, AMD 402 (AMD Intectra), Varian MAT CH 7, MAT 731.

High Resolution mass spectroscopy: Finnigan MAT 95 or Varian MAT 311; Bruker FT CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR): Bruker IFS 66 (FT IR), Nicolet 205 FT IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr ,KAP, Nujol, and ATR; Abbreviations for signal allocations: w = weak, m = medium, s = strong, br = broad.

Elementary analysis: LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis: Bruker X8Apex Diffractometer with CCD-Kamera (Mo-K_a und Graphit Monochromator, λ = 0.71073 Å).

Melting points: Micro heating table HMK 67/1825 Kuestner (Büchi apparatus); Melting points are uncorrected.

Column chromatography: Chromatography was performed over Merck silica gel 60 (0,063 - 0,200 mm, 70 - 230 mesh) as normal and/or over mesh silica gel 60 (0,040 - 0,063 mm, 200 - 400 mesh) as Flash Chromatography. All solvent were distilled before use.

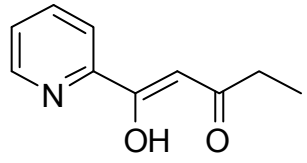
TLC: Merck DC finished foils silica gel 60 F_{254} on aluminum foil and Macherey finished foils Alugram® Sil G/UV_{254}. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

Chemicals and work technique: All solvents for using were distilled by standard methods. All reactions were carried out under an inert atmosphere, oxygen and humidity exclusion. All of the chemicals are standard, commercially available from Merck®, Aldrich®, Arcos® and others. The order of the characterized connections effected numerically, but does not correspond to the order in the main part of dissertation.

6.2. Procedures and Spectroscopic Data

General procedure for the synthesis of 1,3-dicarbonyl compounds 7b-d and 13: To a stirred solution of LDA (75.0 mmol) in THF (1.2 mL/1.0 mmol of LDA) was added ketone **1** (50.0 mmol) at −78 °C. After stirring of the solution for 1 h, **2** or **8** (60.0 mmol) was added. The temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated aqueous solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in *vacuo*. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) to give **3.** Compounds **5a-d** and **6a-c** are commercially available.

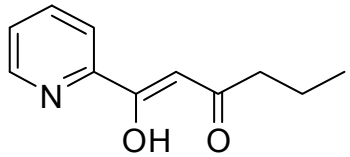
1-Hydroxy-1-(2-pyridyl)-1-penten-3-one (7b):



Starting with LDA (1.5equiv.) in THF (62 mL), 2-butanone (4.4 mL, 50.0 mmol), and **6a** (8.0 mL, 60.0 mmol), **7b** was isolated as a yellow oil (4.76 g, 54%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t,

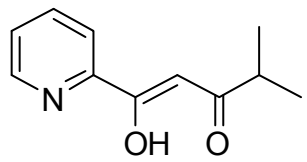
^3J = 7.4 Hz, 3 H, CH_2CH_3), 2.41 (q, ^3J = 7.3, 2 H, CH_2CH_3), 6.73 (s, 1 H, CH), 7.27−7.31 (m, 1 H, CH_{Ar}), 7.68−7.74 (m, 1 H, CH_{Ar}), 7.94−7.98 (m, 1 H, CH_{Ar}), 8.54−8.56 (m, 1 H, CH_{Ar}), 15.61 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.8 (CH_2CH_3), 33.0 (CH_2CH_3), 96.4 (CH), 122.3, 126.4, 137.2, 149.5 (CH_{Ar}), 152.4 (C_{Ar}), 180.6 (COH), 199.6 (C=O). IR (neat cm^{-1}): $\tilde{\nu}$ = 2976 (w), 2879 (w), 1600 (s), 1577 (s), 1563 (s), 1460 (m), 1311 (m), 1240 (m), 1048 (m), 781 (s), 742 (s). GC-MS (EI, 70 eV): *m/z* (%) = 177 ([M^+], 13), 162 (4), 148 (100), 106 (69), 78 (74), 51 (14). HRMS (EI): Calcd. for $C_{10}H_{11}NO_2$: 177.07843; found: 177.07890.

1-Hydroxy-1-(2-pyridyl)-1-hexen-3-one (7c):



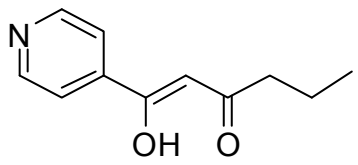
Starting with LDA (1.5 equiv.) in THF (62 mL), 2-pentanone (5.3 mL, 50.0 mmol), and **6a** (8.0 mL, 60.0 mmol), **7c** was isolated as a yellow oil (5.32 g, 56%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.59−1.67 (m, 2 H, $CH_2CH_2CH_3$), 2.35 (t, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 6.73 (s, 1 H, CH), 7.29−7.31 (m, 1 H, CH_{Ar}), 7.71−7.72 (m, 1 H, CH_{Ar}), 7.97 (d, ^3J = 8.0 Hz, 1 H, CH_{Ar}), 8.54 (m, 1 H, CH_{Ar}), 15.68 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 ($CH_2CH_2CH_3$), 19.3 ($CH_2CH_2CH_3$), 41.6 ($CH_2CH_2CH_3$), 97.0 (CH), 122.3, 126.4, 137.3, 149.5 (CH_{Ar}), 152.7 (C_{Ar}), 181.4 (COH), 198.3 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 191 ([M^+], 10), 163 (14), 148 (100), 121 (21), 106 (77), 93 (14), 78.(83), 51 (15), 43 (14). HRMS (EI): Calcd. for $C_{11}H_{13}NO_2$: 191.09408; found: 191.09468.

1-Hydroxy-4-methyl-1-(pyrid-2-yl)pent-1-en-3-one (7d):



Starting with LDA (1.5 equiv.) in THF (62 mL), 3-methyl-2-butanone (5.3 mL, 50.0 mmol), and **6a** (8.0 mL, 60.0 mmol), **7d** was isolated as a yellowish oil (5.653 g, 54%).^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (m, 6 H, $CH(CH_3)_2$), 2.50−2.56 (m, 1 H, $CH(CH_3)_2$), 6.73 ($s_{(br)}$, 1 H, CH), 7.23−7.25 (m, 1 H, CH_{Ar}), 7.64−7.67 (m, 1 H, CH_{Ar}), 7.92 (m, 1 H, CH_{Ar}), 8.51 (m, 1 H, CH_{Ar}), 15.70 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5 ($CH(CH_3)_2$), 38.0 ($CH(CH_3)_2$), 95.0 (CH), 122.1, 125.9, 137.1, 149.1 (CH_{Ar}), 152.5 (C_{Ar}), 181.5 (COH), 202.5 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 191 ([M^+], 11), 148 (100), 121 (22), 106 (37), 93 (4), 78.(80), 43 (40). HRMS (EI): Calcd. for $C_{11}H_{13}NO_2$: 191.09408; found: 191.09466.

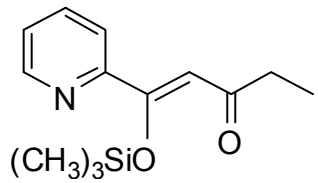
1-Hydroxy-1-(pyrid-4-yl)hex-1-en-3-one (13):



Starting with LDA (1.5 equiv.) in THF (62 mL), 2-pentanone (5.3 mL, 50.0 mmol), **6c** (5.3 mL, 35.0 mmol), **13** was isolated as a yellow solid (4.208 g, 63%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, ^{3}J = 7.4 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.55−1.64 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.33 (t, ^{3}J = 7.5 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 6.13 (s, 1 H, CH), 7.57 (d, ^{3}J = 6.3 Hz, 2 H, CH_{Ar}), 8.61 (d, ^{3}J = 5.3 Hz, 2 H, CH_{Ar}), 15.06 ($s_{(br)}$, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.3 ($CH_2CH_2\mathit{CH_3}$), 18.4 ($CH_2\mathit{CH_2}CH_3$), 41.3 ($\mathit{CH_2}CH_2CH_3$), 96.8 (CH), 120.1 ($2CH_{Ar}$), 141.5 (C_{Ar}), 150.7($2CH_{Ar}$), 178.2 (COH), 199.6 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 191 ([M^+], 18), 163 (19), 148 (100), 121 (9), 106 (27), 93 (4), 78.(20), 51 (15), 43 (10). HRMS (EI): Calcd. for $C_{11}H_{13}NO_2$: 191.09408; found: 191.09411.

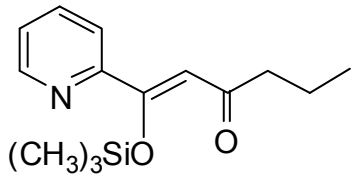
General procedure for the synthesis of silyl enol ethers 8 and 14: To a stirred benzene solution (2.5 mL/1.0 mmol of **7**) of **7** (10.0 mmol) was added triethylamine (16.0 mmol). After stirring of the solution for 2 h, trimethylchlorosilane (36.0 mmol) was added. After stirring of the solution for 72 h, the solvent was removed in *vacuo* and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered under argon atmosphere. The filtrate was concentrated in *vacuo* to give silyl enol ethers **8,** and **14**. Due to the unstable nature of the silyl enol ethers, they were characterized only by NMR spectroscopy.

1-(2-Pyridyl)-1-[(trimethylsilyl)oxy]-1-penten-3-one (8b):



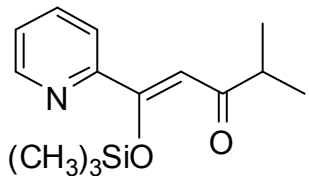
Starting with benzene (38.0 mL), **7b** (4.73 g, 15.3 mmol), triethylamine (6.1 mL, 43.0 mmol) and trimethylchlorosilane (10.51 mL, 83.2 mmol), **8b** was isolated as a reddish oil (5.10 g, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.25 (m, 9 H, $OSi(CH_3)_3$), 1.05−1.08 (m, 3 H, $CH_2\mathit{CH_3}$), 2.80−2.88 (m, 2 H, $\mathit{CH_2}CH_3$), 7.07 (s, 1 H, CH), 7.29−7.31 (m, 1 H, CH_{Ar}), 7.68−7.72 (m, 1 H, CH_{Ar}), 8.02−8.06 (m, 1 H, CH_{Ar}), 8.54−8.56 (m, 1 H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.12 ($Si(CH_3)_3$), 11.1 ($CH_2\mathit{CH_3}$), 27.7 ($\mathit{CH_2}CH_3$), 102.0 (CH), 121.7, 125.9, 136.6, 148.5 (CH_{Ar}), 155.6 (C_{Ar}), 177.3 (C), 188.9 (C=O).

1-(2-Pyridyl)-1-[(trimethylsilyl)oxy]-1-hexen-3-one (8c):



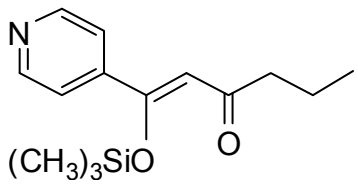
Starting with benzene (69.5 mL), **7c** (5.31 g, 27.8 mmol), triethylamine (6.23 mL, 44.5 mmol) and trimethylchlorosilane (12.6 mL, 100.1 mmol), **8c** was isolated as a reddish oil (6.20 g, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.24−0.29 (m, 9 H, $OSi(CH_3)_3$), 0.87−0.95 (m, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.56−1.66 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.34−2.39 (m, 2 H, $\mathit{CH_2}CH_2CH_3$), 7.26 (s, 1 H, CH), 7.32 (m, 1 H, CH_{Ar}), 7.26−7.36 (m, 1 H, CH_{Ar}), 7.98−8.05 (m, 1 H, CH_{Ar}), 8.54−8.58 (m, 1 H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.09 ($OSi(CH_3)_3$), 13.6 ($CH_2CH_2\mathit{CH_3}$), 20.2 ($CH_2\mathit{CH_2}CH_3$), 30.0 ($\mathit{CH_2}CH_2CH_3$), 102.0 (CH), 120.5, 125.8, 136.6, 148.4 (CH_{Ar}), 155.5 (C_{Ar}), 176.2(C), 188.7 (C=O).

1-(2-Pyridyl)-1-[(trimethylsilyl)oxy]-1-hexen-3-one (8d):



Starting with benzene (38.0 mL), **7d** (5.65 g, 29.5 mmol), triethylamine (6.58 mL, 47.0 mmol) and trimethylchlorosilane (13.4 mL, 106.2 mmol), **8d** was isolated as a reddish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.25 ($OSi(CH_3)_3$), 1.07−1.10 (m, 6 H, $CH\mathit{(CH_3)_2}$), 2.54−2.66 (m, 1 H, $\mathit{CH}(CH_3)_2$), 6.90 (s, 1 H, CH), 7.25−7.30 (m, 1 H, CH_{Ar}), 7.70−7.72 (m, 1 H, CH_{Ar}), 7.97−7.98 (m, 1 H, CH_{Ar}), 8.52 (m, 1 H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3 ($OSi(CH_3)_3$), 10.9 ($CH\mathit{(CH_3)_2}$), 32.2 ($\mathit{CH}(CH_3)_2$), 103.2 (CH), 127.5, 129.2, 129.8, 133.4 (CH_{Ar}), 147.2 (C_{Ar}), 176.5 (C), 185.9 (C=O).

4-Methyl-1-(2-pyridyl)-1-[(trimethylsilyl)oxy]-1-penten-3-one (14):

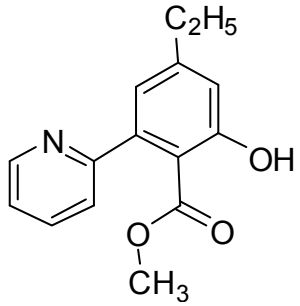


Starting with benzene (65.0 mL), **13** (5.00 g, 26.1 mmol), triethylamine (5.8 mL, 41.8 mmol) and trimethylchlorosilane (11.9 mL, 94.1 mmol), **14** was isolated as a reddish oil (6.05 g, 88%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (m, 9 H, $OSi(CH_3)_3$), 0.70−0.73 (m, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.37−1.44 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.19 (t, ^{3}J = 7.4 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 5.90 (s, 1 H, CH), 7.36−7.42 (m, 2 H, CH_{Ar}), 8.46−8.50 (m, 2 H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ =0.1($Si(CH_3)_3$) 13.0 ($CH_2CH_2\mathit{CH_3}$), 19.5 ($CH_2\mathit{CH_2}CH_3$), 35.5 ($\mathit{CH_2}CH_2CH_3$), 102.6 (CH), 120.1 ($2CH_{Ar}$), 127.4 (C_{Ar}), 149.5 ($2CH_{Ar}$), 176.8 (COH), 187.4 (C=O).

General procedure for the synthesis of salicylates 9e-l, and 15a-b: To a CH_2Cl_2 solution (2 mL/1.0 mmol of **7**) of **7** (1.0 mmol) were added **4** (1.1 mmol) and, subsequently, $TiCl_4$ (1.10

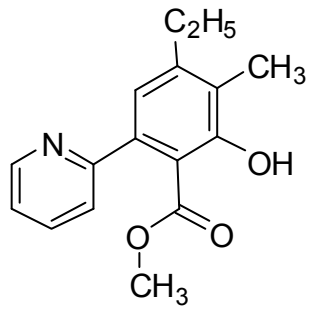
mmol) at −78 °C. The temperature of the solution was allowed to warm to 20 °C during 14 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purifed by chromatography (silica gel, *n*-heptane / EtOAc) to give **9e-l**, and **15a-b**.

Methyl 4-ethyl-2-hydroxy-6-(pyrid-2-yl)benzoate (9e):



Starting with **7b** (0.425 g, 1.67 mmol), **4a** (0.627 g, 1.82 mmol) and $TiCl_4$ (0.20 mL, 1.67 mmol), **9e** was isolated as a reddish highly viscous oil (0.154 g, 40%). ^{1}H NMR(300 MHz, $CDCl_3$): δ = 1.17 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.60 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.39 (s, 3 H, $COOCH_3$), 6.68 (d, ^4J = 1.7 Hz, 1 H, CH_{Ar}), 6.83 (d, ^4J = 1.4 Hz, 1 H, CH_{Ar}), (ddd, ^3J = 6.4 Hz, ^3J = 6.0 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.24 (d, ^3J=7.8 Hz, 1 H, CH_{Ar}), 7.61−7.67 (m, 1 H, CH_{Ar}), 8.53−8.54 (m, 1 H, CH_{Ar}), 10.58 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_2CH_3), 27.8 (CH_2CH_3), 50.7 ($COOCH_3$), 108.4 (C_{Ar}), 115.6 (CH_{Ar}), 120.6 (CH_{Ar}), 121.9 (CH_{Ar}), 122.0, 134.7 (CH_{Ar}), 142.4 (C_{Ar}), 147.4 (CH_{Ar}), 151.1 (C_{Ar}), 159.4 (C_{Ar}) 160.5 (COH_{Ar}), 169.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2970 (w), 2930 (w), 1603 (s), 1578 (s), 1422 (s), 1239 (s), 1214 (s), 1158 (s), 1088 (m), 1056 (m), 818 (m). GC-MS (EI, 70 eV): *m/z* (%) = 257 ([M^+], 32), 225 (61), 211 (8), 197 (11), 182 (100), 154 (10), 127 (8), 84 (9). HRMS (EI): Calcd. for $C_{15}H_{15}NO_3$: 257.10464; found: 257.10461.

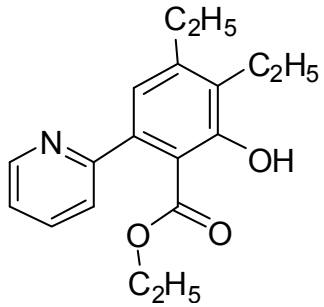
Methyl 4-ethyl-2-hydroxy-3-methyl-6-(pyrid-2-yl)benzoate (9f):



Starting with **7b** (0.374 g, 1.5 mmol), **4b** (0.448 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **9f** was isolated as a reddish highly viscous oil (0.180, 44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, ^3J = 7.7 Hz, 3 H, CH_2CH_3), 2.18 (s, 3 H, CH_3), 2.60 (d, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 3.39 (s, 3 H, $COOCH_3$), 6.67 (s, 1.H, CH_{Ar}), 7.12−7.24 (m, 2.H, CH_{Ar}), 7.59−7.65 (m, 1 H, CH_{Ar}), 8.52 (m, 1 H, CH_{Ar}), 10.80 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.4 (CH_2CH_3), 14.5 (CH_3), 27.4 (CH_2CH_3), 52.1 ($COOCH_3$), 109.2 (C_{Ar}), 121.8, 122.2, 123.4 (CH_{Ar}), 124.7 (C_{Ar}) 136.1 (CH_{Ar}), 140.7 (C_{Ar}), 148.8 (CH_{Ar}), 149.1, 160.0 (C_{Ar}), 161.1 (COH_{Ar}), 171.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2870 (w), 1657 (m), 1364 (m), 1378 (m), 1378 (s), 1260 (m), 1195 (s),

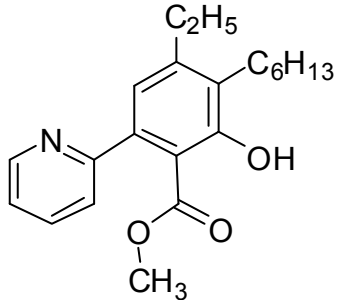
1105 (s), 1009 (m). GC-MS (EI, 70 eV): *m/z* (%) = 271 ([M^+], 35), 239 (100), 224 (23), 211 (20), 196 (20), 182 (10), 167 (17), 154.(7), 84 (7), 78 (5). HRMS (EI): Calcd. for $C_{16}H_{17}NO_3$: 271.12029; found: 271.11995.

Ethyl 3,4-diethyl-2-hydroxy-6-(pyrid-2-yl)benzoate (9g):



Starting with **7b** (0.498 g, 2.0 mmol), **4c** (0.659 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **9g** was isolated as a reddish highly viscous oil (0.230 g, 38%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.24−1.33 (m, 6 H, CH_2CH_3), 2.73−2.87 (m, 4 H, CH_2CH_3), 4.05 (q, ^3J = 7.2 Hz, 2 H, $COOCH_2$), 6.81 (s, 1 H, CH_{Ar}), 7.29−7.33 (m, 1 H, CH_{Ar}), 7.40 (d, ^3J = 7.8 Hz, 1 H, CH_{Ar}), 7.74−7.80 (m, 1 H, CH_{Ar}), 8.66−8.68 (m, 1 H, CH_{Ar}), 11.20 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 (OCH_2CH_3), 14.2, 15.5 (CH_2CH_3), 19.4, 26.5 (CH_2CH_3), 61.1 ($COOCH_2$), 109.5 (C_{Ar}), 121.8, 122.3, 123.4 (CH_{Ar}), 130.8 (C_{Ar}), 136.0 (CH_{Ar}), 140.9 (C_{Ar}), 148.4 (CH_{Ar}), 148.8, 160.2, (C_{Ar}), 161.5 (COH_{Ar}), 171.4 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2965 (w), 2873 (w), 1655 (s), 1587 (m), 1392 (m), 1371 (s), 1273 (s), 1183 (s), 1031 (s), 1031 (m). GC-MS (EI, 70 eV): *m/z* (%) = 299 ([M^+], 44), 253 (100), 238 (70), 224 (25), 210 (13), 167 (14), 117 (8), 78 (5). HRMS (EI): Calcd. for $C_{18}H_{21}NO_3$: 299.15160; found: 299.15122.

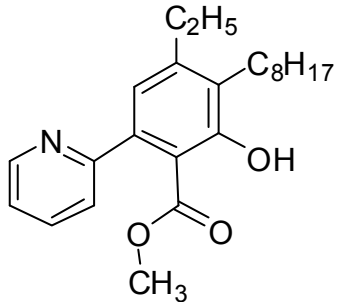
Methyl 4-ethyl-3-hexyl-2-hydroxy-6-(pyrid-2-yl)benzoate (9h):



Starting with **4b** (0.498 g, 2.0 mmol), **4d** (0.751 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **9h** was isolated as a reddish highly viscous oil (0.150 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 ($t_{(br)}$, ^3J = 6.8 Hz, 3 H, $(CH_2)_5CH_3$), 1.12 ($t_{(br)}$, ^3J = 5.5 Hz, 3 H, CH_2CH_3), 1.22−1.28 (m, 8 H, CH_2), 2.64 (t, ^3J = 7.6 Hz, 2 H, $CH_2(C_5H_{11})$, 2.68 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 3.44 (s, 3 H, $COOCH_3$), 6.72 (s, 1.H, CH_{Ar}), 7.17−7.21 (m, 1.H, CH_{Ar}), 7.28−7.31 (m, 1 H, CH_{Ar}), 7.65−7-70 (m, 1 H, CH_{Ar}), 8.56−8.58 (m, 1 H, CH_{Ar}), 10.86 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4 ($C_5H_{11}CH_3$), 15.4 (CH_2CH_3), 23.0, 26.3, 26.6, 29.9, 30.1($(CH_2)_5CH_3$), 33.1 (CH_2CH_3), 52.0 ($COOCH_3$), 109.4 (C_{Ar}), 121.8, 122.4, 123.3 (CH_{Ar}), 129.7 (C_{Ar}) 136.1 (CH_{Ar}), 140.7 (C_{Ar}), 148.7 (CH_{Ar}), 149.6, 160.0 (C_{Ar}), 161.1 (COH_{Ar}), 171.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2852 (w), 1663 (m), 1436 (m), 1397 (m), 1318 (m), 1271 (m), 1195 (s), 1119 (s), 745 (m). GC-MS (EI, 70 eV): *m/z* (%) = 341 ([M^+], 18), 308 (5), 271 (77), 239

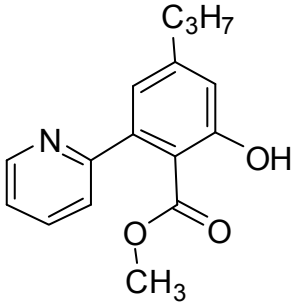
(100), 167 (13), 117 (3), 78 (4), 57 (5), 43 (7). HRMS (EI): Calcd. for $C_{21}H_{27}NO_3$: 341.19855; found: 341.19815.

Methyl 4-ethyl-2-hydroxy-3-octyl-6-(pyrid-2-yl)benzoate (9i):



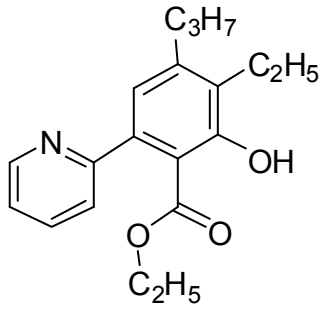
Starting with **7b** (0.498 g, 2.0 mmol), **4e** (0.812 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **9i** was isolated as a dark reddish highly viscous oil (0.220 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80−84 (m, 6 H, CH_3), 1.12−1.27 (m, 12 H, CH_2), 2.59−2.65 (m, 4 H, CH_2), 3.39 (s, 3 H, COO*CH*$_3$), 6.67 (s, 1.H, CH_{Ar}), 7.13−7.17 (m, 1.H, CH_{Ar}), 7.23−7.26 (m, 1 H, CH_{Ar}), 7.61−7.66 (m, 1 H, CH_{Ar}), 8.51−8.54 (m, 1 H, CH_{Ar}), 10.82 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (C_7H_{13}*CH*$_3$), 15.5 (CH_2*CH*$_3$), 22.9, 23.1, 26.3, 26.6, 29.9, 30.0, 30.1, 32.1 (CH_8), 52.0 (COO*CH*$_3$), 109.3 (C_{Ar}), 121.9, 122.4, 123.4 (CH_{Ar}), 129.8 ($2C_{Ar}$) 136.2 (CH_{Ar}), 140.7 (C_{Ar}), 148.7 (CH_{Ar}), 160.0, (C_{Ar}), 161.1 (COH_{Ar}), 171.8 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 2854 (w), 1663 (m), 1436 (m), 1397 (m), 1318 (m), 1270 (m), 1195 (s), 1149 (m), 1010 (m). GC-MS (EI, 70 eV): *m/z* (%) = 369 ([M^+], 11), 341 (30), 310 (5), 271 (94), 252 (60), 239 (100), 177 (13), 127 (4), 78 (4). HRMS (EI): Calcd. for $C_{23}H_{31}NO_3$: 369.22985; found: 369.22968.

Methyl 2-hydroxy-4-propyl-6-(pyrid-2-yl)benzoate (9j):



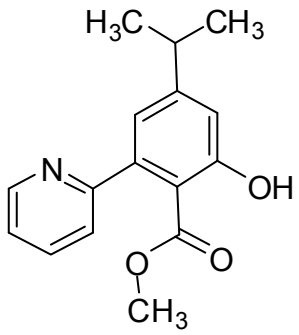
Starting with **7c** (0.527 g, 2.0 mmol), **4a** (0.565 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **9j** was isolated as a reddish highly viscous oil (0.200 g, 33%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_2*CH*$_3$), 1.55−1.63 (m, 2 H, CH_2*CH*$_2CH_3$), 2.51 (t, ^3J = 7.2 Hz, 2 H, *CH*$_2CH_2CH_3$), 3.40 (s, 3 H, COO*CH*$_3$), 6.67 (s, 1 H, CH_{Ar}), 6.80 (s, 1 H, CH_{Ar}), 7.14−7.17 (m, 1 H, CH_{Ar}), 7.24 (d, ^3J = 7.9 Hz, 1 H, CH_{Ar}), 7.61−7.66 (m, 1 H, CH_{Ar}), 8.53−8.54 (m, 1 H, CH_{Ar}), 10.55 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_2CH_2*CH*$_3$), 24.1 (CH_2*CH*$_2CH_3$38.3 (*CH*$_2CH_2CH_3$), 52.1 (COO*CH*$_3$), 109.8 (C_{Ar}), 117.7, 122.1, 123.0, 123.3, 136.1 (CH_{Ar}), 143.6 (C_{Ar}), 148.9 (CH_{Ar}), 150.1, 160.8 (C_{Ar}), 161.1 (COH_{Ar}), 171.2 (C=O)). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3012 (w), 2844 (w), 1662 (s), 1499 (m), 1459 (s), 1378 (s), 1239 (s), 1106 (m), 1074 (m), 1025 (m). GC-MS (EI, 70 eV): *m/z* (%) = 277 ([M^+], 39), 239 (69), 211 (73), 182 (100), 167 (6), 154 (17), 127 (12), 78 (5). HRMS (EI): Calcd. for $C_{16}H_{17}NO_3$: 271.12029; found: 271.12028.

Ethyl 3-ethyl-2-hydroxy-4-propyl-6-(pyrid-2-yl)benzoate (9k):



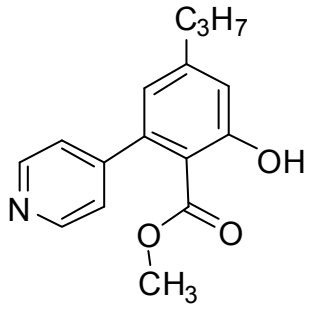
Starting with **7c** (0.527 g, 2.0 mmol), **4b** (0.659 g, 2.2 mmol) and $TiCl_4$ (0.239 mL, 2.2 mmol), **9k** was isolated as a reddish highly viscous oil (0.200 g, 31%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (t, ^3J = 7.0 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 0.91 (t, ^3J = 7.4 Hz, 3 H, $CH_2\mathit{CH_3}$), 1.10 (t, ^3J = 8.5 Hz, 2 H, $CH_2\mathit{CH_3}$), 1.51−1.59 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.53, (t, ^3J = 7.8 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 2.67 (q, ^3J = 7.4 Hz, 2 H, $\mathit{CH_2}CH_3$), 3.89 (q, ^3J = 7.2 Hz, 2 H, $COO\mathit{CH_2}CH_3$), 6.63 (s, 1 H, CH_{Ar}), 6.63 (s, 1 H, CH_{Ar}), 7.17−7.26 (m, 2 H, CH_{Ar}), 7.60−7.65 (m, 1 H, CH_{Ar}), 8.52 (m, 1 H, CH_{Ar}), 11.04 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1 ($CH_2CH_2\mathit{CH_3}$), 12.8 ($CH_2\mathit{CH_3}$), 13.2 ($OCH_2\mathit{CH_3}$), 18.1 ($CH_2\mathit{CH_2}CH_3$), 23.1, ($\mathit{CH_2}CH_2CH_3$), 34.2 ($\mathit{CH_2}CH_3$), 59.7 ($COO\mathit{CH_2}CH_3$), 108.0 (C_{Ar}), 121.7 (CH_{Ar}), 129.7 ($2CH_{Ar}$), 134.7 (C_{Ar}), 145.6 ($2CH_{Ar}$), 158.9 ($2C_{Ar}$), 160.1 ($2C_{Ar}$), 170.2 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2958 (w), 2871 (w), 1658 (m), 1464 (m), 1393 (m), 1371 (m), 1273 (m), 1183 (s), 1110 (s), 1027 (m). GC-MS (EI, 70 eV): *m/z* (%) = 313 ([M^+], 33), 267 (19), 252 (100), 238 (29), 210 (6), 195 (3,), 167 (8), 154 (3) 78 (5). HRMS (EI): Calcd. for $C_{19}H_{23}NO_3$: 313.16725; found: 313.16693.

Methyl 2-hydroxy-4-isopropyl-6-(pyrid-2-yl)benzoate (9l):



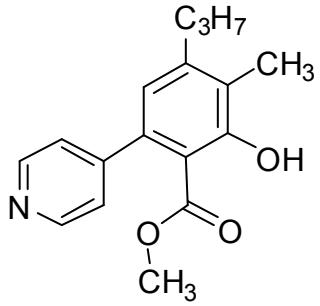
Starting with **7d** (0.527 g, 2.0 mmol), **4a** (0.565 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **9l** was isolated as a reddish highly viscous oil (0.142 g, 26%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, ^3J = 7.1 Hz, 6 H, $CH\mathit{(CH_3)_2}$), 2.75−2.89 (m, 1 H, $\mathit{CH}(CH_3)_2$), 3.41 (s, 3 H, $COO\mathit{CH_3}$), 6.71 (d, ^4J = 1.3 Hz, 1 H, CH_{Ar}), 6.86 (d, ^4J = 1.3 Hz, 1 H, CH_{Ar}), 7.17−7.18 (m, 1 H, CH_{Ar}), 7.26 (d, ^3J = 7.6 Hz, 1 H, CH_{Ar}), 7.64 (ddd, ^3J = 7.8 Hz, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1 H, CH_{Ar}), 8.54 (m, 1 H, CH_{Ar}),10.57 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.7 ($CH\mathit{(CH_3)_2}$), 34.6 ($\mathit{CH}(CH_3)_2$), 52.1 ($COO\mathit{CH_3}$) 109.9 (C_{Ar}), 115.6, 121.1, 122.1, 123.4, 136.2 (CH_{Ar}),143.7 (C_{Ar}) 148.9 (CH_{Ar}), 156.2, 160.9 (C_{Ar}), 162.0 (COH_{Ar}), 177.2 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3109 (w), 2868 (w), 1666 (m), 1601(m), 1423 (m), 1353 (m), 1300 (s), 1270 (s), 1160 (s), 1058 (m), 809 (m). GC-MS (EI, 70 eV): *m/z* (%) = 271 ([M^+], 33), 239 (69), 224 (16), 196 (100), 167 (23), 141.(5), 78 (4). HRMS (EI): Calcd. for $C_{16}H_{17}NO_3$: 271.12029; found: 271.12038.

Methyl 2-hydroxy-4-propyl-6-(pyrid-4-yl)benzoate (15a):



Starting with **14** (0.392 g, 1.5 mmol), **4a** (0.429 g, 1.65 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **15a** was isolated as a reddish highly viscous oil (0.180 g, 44%).^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.54−1.63 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.50 (t, ^3J = 7.2 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.42 (s, 3 H, $COO\mathit{CH_3}$), 6.48 (s, 1 H, CH_{Ar}), 6.82 (s, 1 H, CH_{Ar}), 7.09−7.12 (m, 2 H, CH_{Ar}), 8.54−8.69 (m, 2 H, CH_{Ar}), 10.87 ($s_{(br)}$, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7 ($CH_2CH_2\mathit{CH_3}$), 23.6 ($CH_2\mathit{CH_2}CH_3$), 37.9 ($\mathit{CH_2}CH_2CH_3$), 51.6 ($COO\mathit{CH_3}$), 108.7 (C_{Ar}), 117.4 ($2CH_{Ar}$), 122.7 (CH_{Ar}) 141.6 (C_{Ar}), 148.9 (CH_{Ar}), 150.2 (C_{Ar}), 150.7 ($2CH_{Ar}$), 151.3 (C_{Ar}), 162.2 (COH_{Ar}), 170.5 (C=O). GC-MS (EI, 70 eV): IR (neat, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 2873 (w), 1601 (m), 1577 (s), 1403 (m), 1283 (m), 1086 (m), 11042 (m), 993 (m), 742 (m). MS (EI, 70 eV): *m/z* (%) = 271 ([M^+], 48), 239 (100), 211 (99), 182 (30), 167 (5), 154 (4), 127 (16), 78 (4). HRMS (EI): Calcd. for $C_{16}H_{17}NO_3$: 271.12029; found: 271.11994.

Methyl 2-hydroxy-3-methyl-4-propyl-6-(pyrid-4-yl)benzoate (15b):

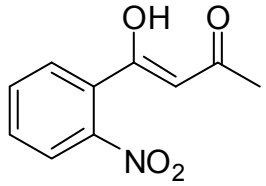


Starting with **14** (0.395 g, 1.5 mmol), **4b** (0.429 g, 1.65 mmol) and $TiCl_4$ (0.180 mL, 1.65 mmol), **15b** was isolated as a reddish highly viscous oil (0.170 g, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (t, ^3J = 6.5 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.48−1.57 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.21 (s, 3 H, CH_3), 2.52 (t, ^3J = 6.0 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.43 (s, 3 H, $COO\mathit{CH_3}$), 6.40 (s, 1.H, CH_{Ar}), 7.11 (m, 1.H, CH_{Ar}), 7.60−7.62 (m, 1.H, CH_{Ar}), 8.69 (m, 2 H, CH_{Ar}), 10.87 ($s_{(br)}$, 1 H, OH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 10.2 ($CH_2CH_2\mathit{CH_3}$), 13.0 (CH_3), 22.2 ($CH_2\mathit{CH_2}CH_3$), 35.0 ($\mathit{CH_2}CH_2CH_3$), 50.6 ($COO\mathit{CH_3}$), 106.7 (C_{Ar}), 121.3 ($3CH_{Ar}$), 124.0, 137.7 (C_{Ar}) 146.7 ($2C_{Ar}$), 149.6 ($2CH_{Ar}$), 159.3 (COH_{Ar}), 170.2 (C=O). GC-MS (EI, 70 eV): IR (neat, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 2871 (w), 1699 (m), 1429 (m), 1398 (m), 1300 (m), 1267 (m), 1200 (s), 1114 (s), 753 (m). MS (EI, 70 eV): *m/z* (%) = 285 ([M^+], 45), 238 (100), 225 (35), 210 (11), 196 (16), 182 (8), 167 (17), 154 (6), 139 (5), 84 (4), 78 (4). HRMS (EI): Calcd. for $C_{17}H_{19}NO_3$: 285.13594; found: 285.13545.

General procedure for the synthesis of aryl-1,3-dicarbonyl compounds17a-d: To a stirred solution of LDA (75.0 mmol) in THF (1.2 mL/1.0 mmol of LDA) was added ketone **5** (50.0 mmol) at −78 °C. After stirring of the solution for 1 h, **16** (60.0 mmol) was added. The

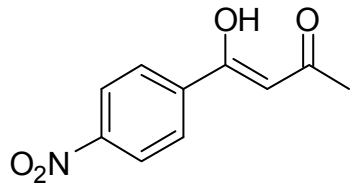
temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated aqueous solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in *vacuo*. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) to give **3.** Compounds **5a-d** and **16a-c** are commercially available.

4-Hydroxy-4-(2-nitrophenyl)but-3-en-2-one(17a):



Starting with LDA (1.5equiv.) in THF (62 mL), **5a** (2.90 mL, 50.0 mmol), and **16a** (7.93 mL, 60.0 mmol), **17b** was isolated as a reddish yellow oil (5.405 g, 54%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, CH_3), 6.16 (s, 1 H, CH), 7.45 ─ 7.60 (m, 3 H, CH_{Ar}), 7.82 (m, 1 H, CH_{Ar}), 15.12 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.2 (CH_3), 99.9 (CH), 124.3, 129.3, 130.0, 133.0 (CH_{Ar}), 134.7, 147.8, (C_{Ar}), 187.1 (COH), 190.2 (C=O). MS (EI 70 eV): *m/z* (%) = 207 ([M]$^+$, 38), 192 (100), 160 (19), 150 (36), 120 (8), 89 (9), 85 (27), 76 (18), 43 (45). HRMS (EI): Calcd. for $C_{10}H_9NO_2$: 207.05261; found: 207.05232.

4-hydroxy-4-(4-nitrophenyl)but-3-en-2-one(17d):

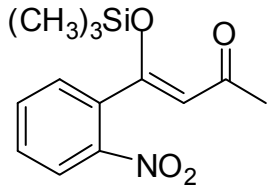


Starting with LDA (1.5equiv.) in THF (62 mL), **5a** (2.90 mL, 50.0 mmol), and **16c** (11.130 g, 60.0 mmol), **17d** was isolated as a yellow solid (4.405 g, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 5.74 (s, 1 H, CH), 7.95 (d, ^3J = 8.7 Hz, 2 H, CH_{Ar}), 8.21 (d, ^3J = 9.0 Hz, 2 H, CH_{Ar}), 15.80 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.0 (CH_3), 98.5 (CH), 124.3 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 140.9, 149.9 (C_{Ar}), 179.8 (COH), 196.6 (C=O). GC_MS (EI 70 eV): *m/z* (%) = 207 ([M]$^+$, 38), 192 (100), 165 (8), 160 (19), 150 (36), 120 (8), 104 (18), 89 (9), 85 (27), 76 (18), 63 (7), 50 (12), 43 (45). HRMS (EI): Calcd. for $C_{10}H_9NO_2$: 207.05261; found: 207.05232.

General procedure for the synthesis of silyl enol ethers 18, 25 and 28: To a stirred benzene solution (2.5 mL/1.0 mmol of **17**) of **17** (10.0 mmol) was added triethylamine (16.0 mmol). After stirring of the solution for 2 h, trimethylchlorosilane (18.0 mmol) was added. After stirring of the solution for 72 h, the solvent was removed in *vacuo* and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered under argon atmosphere. The

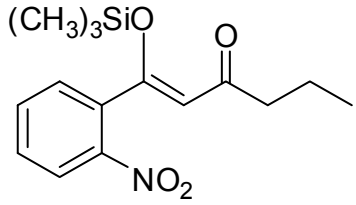
filtrate was concentrated in *vacuo* to give silyl enol ethers **18, 25** and **28**. Due to the unstable nature of the silyl enol ethers, they were characterized only by NMR spectroscopy.

4-(2-nitrophenyl)-4-(trimethylsilyloxy)but-3-en-2-one1(18a):



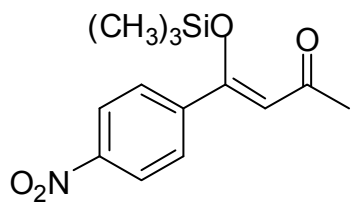
Starting with benzene (90.0 mL), **17a** (6.121 g, 29.54 mmol), triethylamine (6.62 mL, 47.2 mmol) and trimethylchlorosilane (6.67 mL, 53.2 mmol), **18a** was isolated as a reddish oil (7.30 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ =0.05-0.30 (m, 9 H, $Si(CH_3)_3$), 2.15 (s, 3 H, CH_3), 6.06 (s, 1 H, CH), 7.45 ─ 7.60 (m, 3 H, CH_{Ar}), 7.82 (m, 1 H, CH_{Ar}), ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.2 ($Si(CH_3)_3$), 24.5 (CH_3), 98.9 (CH), 124.9, 129.6, 130.5, 133.5 (CH_{Ar}), 134.9, 148.8, (C_{Ar}), 180.1 (COTMS), 191.2 (C=O).

1-(2-nitrophenyl)-1-(trimethylsilyloxy)hex-1-en-3-one(18b):



Starting with benzene (63.0 mL), **17b** (4.83 g, 20.2 mmol), triethylamine (4.50 mL, 43.0 mmol) and trimethylchlorosilane (4.64 mL, 33.1 mmol), **18b** was isolated as a reddish oil(5.60 g, 88%). ^{1}H NMR (250 MHz, $CDCl_3$): δ =0.21-0.43 (m, 9 H, $Si(CH_3)_3$), 1.06 ─ 1.14 (m, 3 H, CH_3), 1.69 ─ 1.85 (m, 2 H, CH_2), 2.43 ─ 2.53 (m, 2 H, CH_2), 5.85 (s, 1 H, CH), 7.50 ─ 8.00 (m, 3 H, CH_{Ar}), 8.07 ─ 8.19 (m, 1 H, CH_{Ar}), ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.2 ($Si(CH_3)_3$), 13.8 (CH_3), 36.4, 39.5 (CH_2), 98.9 (CH), 124.1, 128.1, 129.3, 131.6 (CH_{Ar}), 139.4, 148.3, (C_{Ar}), 178.0 (COTMS), 193.2 (C=O).

4-(4-Nitrophenyl)-4-(trimethylsilyloxy)but-3-en-2-one(18d):

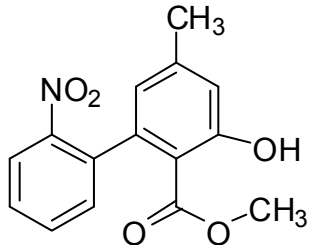


Starting with benzene (52.0 mL), **17d** (4.405 g, 21.3 mmol), triethylamine (4.70 mL, 33.0 mmol) and trimethylchlorosilane (5.09 mL, 37.8 mmol), **18d** was isolated as a yellow solid (5.350 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02-0.22 (m, 9 H, $Si(CH_3)_3$), 2.10 (s, 3 H, CH_3), 6.08 (s, 1 H, CH), 7.80 ─ 7.89 (m, 2 H, CH_{Ar}), 8.09 ─ 8.17 (m, 2 H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.6 ($Si(CH_3)_3$), 24.6 (CH_3), 96.8 (CH), 121.5 ($2CH_{Ar}$), 125.9 ($2CH_{Ar}$), 138.4, 147. (C_{Ar}), 177.2 (COTMS), 194.1 (C=O).

General procedure for the synthesis of salicylates 19a-n: To a CH_2Cl_2 solution of silyl enol ether **18** (1.0 equiv.) and 1,3-bis(silyl enol ether) **4** (1.1 equiv.) was dropwise added $TiCl_4$ (1.1

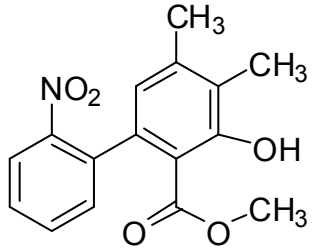
equiv.) at –78 °C under argon atmosphere. The solution was stirred at –78 °C for 30 min and then allowed to warm to 20 °C during 18 h. To the solution was added a saturated aqueous solution of 10 % HCl. The organic layer was separated and the aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography (silica gel, *n*-hexane/EtOAc) to give salicylates **19.**

3-hydroxy-5-methyl-2'-nitro[1,1'-biphenyl]-2-carboxylate (19a):



Starting with bis silyl-enol ether 4**a** (1.145 g, 4.4 mmol), $TiCl_4$ (0.835 g, 4.4 mmol) CH_2Cl_2 (6 mL) and monosilyl enol ether **18a** (1.117 g, 4.0 mmol), **19a** was isolated (0.420 g, 36 %) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.21 (s, 3 H, CH_3), 3.33 (s, 3 H, OCH_3), 6.35 (d, ^4J = 1.9 Hz, 1 H, CH_{Ar}), 6.74 (d, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 7.10 − 7.13 (m, 1 H, CH_{Ar}), 7.36 (ddd, ^3J = 7.4 Hz, ^3J = 7.2 Hz, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 7.47 (ddd, ^3J = 7.5 Hz, ^3J = 7.4 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.92 (dd, ^3J = 8.0 Hz, ^4J = 1.5 Hz, 1 H, Ar), 11.10 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 21.6 (CH_3), 51.9 (OCH_3), 108.4 (C_{Ar}), 118.0, 122.5, 123.6, 127.8, 131.1. 132.4 (CH_{Ar}), 138.2, 140.2, 145.6, 147.8, 162.4 (C_{Ar}), 170.4 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 287 ($[M]^+$, 26), 255 (100), 227 (27), 197 (5), 181 (11), 152 (30), 115 (5), 76 (7). HRMS (EI): Calcd. for $C_{15}H_{13}NO_5$: 287.07882; found: 287.07873.

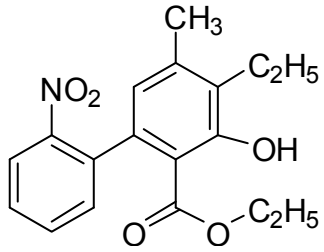
Methyl 3-hydroxy-4,5-dimethyl-2'-nitrobiphenyl-2-carboxylate(19b):



Starting with bis silyl-enol ether **4b** (1.207 g, 4.4 mmol), $TiCl_4$ (0.834 g, 4.4 mmol) CH_2Cl_2 (8 mL) and monosilyl enol ether **18a** (1.117 g, 4.0 mmol), **19b** was isolated (0.500 g, 41%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.10 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 6.35 (s, 1 H, CH_{Ar}), 7.11 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 7.33 (ddd, ^3J = 7.7 Hz, ^3J = 7.6 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.46 (ddd, ^3J = 7.6 Hz, ^3J = 7.5 Hz, ^4J = 1.3 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 8.3 Hz, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 11.47 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.5, 20.5 (CH_3), 51.9 (OCH_3), 108.0 (C_{Ar}), 122.6, 123.5, (CH_{Ar}), 125.0 (C_{Ar}), 127.6, 131.2, 132.3 (CH_{Ar}), 136.9, 138.5, 143.6, 148.0, 160.5 (C_{Ar}), 171.4 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 301 ($[M]^+$, 64), 269 (100), 255 (24), 224 (27), 208 (48), 195 (13), 180 (49), 165 (29),

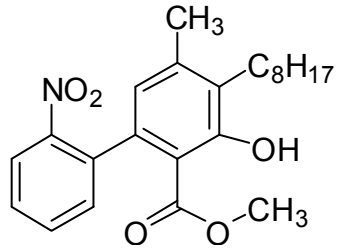
152 (28), 128 (11), 115 (16), 77 (7). HRMS (EI): Calcd. for $C_{16}H_{15}NO_5$: 301.09447; found: 301.09434.

Ethyl 4-ethyl-3-hydroxy-5-methyl-2'-nitrobiphenyl-2-carboxylate(19c):



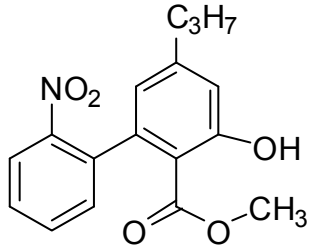
Starting with bis silyl-enol ether **4c** (0.998 g, 3.3 mmol), $TiCl_4$ (0.625 g, 3.3 mmol) CH_2Cl_2 (6 mL) and monosilyl enol ether **18a** (0.789 g, 3.0 mmol), **19c** was isolated (0.350 g, 35 %) as a yellow solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.59 (t, ^3J = 7.4 Hz, 3 H, CH_3), 1.04 (t, ^3J = 7.5 Hz, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 2.61 (m, 2 H, CH_2), 3.82 (q, ^3J = 7.5 Hz, 2 H, OCH_2), 6.32 (s, 1 H, CH_{Ar}), 7.12 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.34 (ddd, ^3J = 8.0 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.45 (ddd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 11.58 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 4.8, 14.8, 21.3 (CH_3), 21.5 (CH_2), 62.8 (OCH_2), 110.0 (C_{Ar}), 124.6, 125.5, 129.4 (CH_{Ar}), 132.8 (C_{Ar}), 133.1, 134.1 (CH_{Ar}), 138.8, 140.8, 144.5, 149.9, 162.5 (C_{Ar}), 172.5 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 329 ($[M]^+$, 100), 283 (80), 255 (24), 238 (32), 222 (78), 207 (40), 194 (99), 165 (64), 152 (29), 139 (13), 115 (18), 77 (13). HRMS (EI): Calcd. for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12546.

Methyl 3-hydroxy-5-methyl-2'-nitro-4-octylbiphenyl-2-carboxylate(19d):



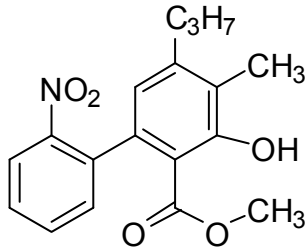
Starting with bis silyl-enol ether **4f** (1.100 g, 3.3 mmol), $TiCl_4$ (0.625 g, 3.3 mmol) CH_2Cl_2 (6 mL) and monosilyl enol ether **18a** (0.789 g, 3.0 mmol), **19d** was isolated (0.476 g, 40 %) as a yellow viscous oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.73 ─ 0.79 (m, 3 H, CH_3), 1.13 ─ 1.30 (m, 12 H, CH_2), 2.18 (s, 3 H, CH_3), 2.52 ─ 2.60 (m, 2 H, CH_2), 3.31 (s, 3 H, OCH_3), 6.32 (s, 1 H, CH_{Ar}), 7.11 (dd, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, CH_{Ar}), 7.33 (ddd, ^3J = 8.0 Hz, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1 H, CH_{Ar}), 7.45 (ddd, ^3J = 7.4 Hz, ^3J = 7.1 Hz, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 11.43 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 16.0, 21.8 (CH_3), 24.6, 28.3, 30.6, 31.2, 31.4, 32.0, 33.8 (CH_2), 53.8 (OCH_3), 110.0 (C_{Ar}), 124.8, 125.4, 129.5 (CH_{Ar}), 131.8 (C_{Ar}), 133.2, 134.1 (CH_{Ar}), 138.9, 140.5, 150.0, 162.5 (C_{Ar}), 172.9 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 399 ($[M]^+$, 100), 353 (49), 340 (13), 306 (17), 268 (69), 225 (84), 208 (80), 194 (58), 180 (27), 165 (65), 152 (21), 115 (10), 77 (5), 43 (18). HRMS (EI): Calcd. for $C_{23}H_{29}NO_5$: 399.20402; found: 399.20336.

Methyl 3-hydroxy-2'-nitro-5-propylbiphenyl-2-carboxylate (19e):



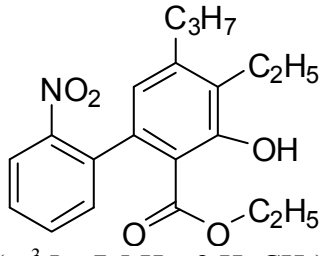
Starting with bis silyl-enol ether **4a** (1.145 g, 4.4 mmol), $TiCl_4$ (0.835 g, 4.4 mmol) CH_2Cl_2 (8 mL) and monosilyl enol ether **18b** (1.229 g, 4.0 mmol), **19e** was isolated (0.607 g, 48 %) as a yellow gummy solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.80 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.47 ─ 1.56 (m, 2 H, CH_2), 2.44 (t, ^3J = 7.0 Hz, 2 H, CH_2), 3.27 (s, 3 H, OCH_3), 6.36 (d, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 6.74 (d, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 7.12 (dd, ^3J = 7.5 Hz, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 7.36 (ddd, ^3J = 7.3 Hz, ^3J = 7.0 Hz, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 7.47 (ddd, ^3J = 7.6 Hz, ^3J = 7.3 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.91 (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1 H, CH_{Ar}), 11.10 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 13.8 (CH_3), 23.4, 37.7 (CH_2), 51.8 (OCH_3), 108.6 (C_{Ar}), 117.3, 122.0, 123.7, 127.8, 131.1, 132.5 (CH_{Ar}), 138.4, 140.3, 147.8, 150.2, 162.4 (C_{Ar}), 170.3 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 315 ($[M]^+$, 47), 269 (100), 255 (17), 240 (11), 227 (14), 197 (10), 181 (18), 165 (16), 152 (31), 115 (19), 77 (8). HRMS (EI): Calcd. for $C_{17}H_{17}NO_5$: 315.11062; found: 315.11032.

Methyl 3-hydroxy-4-methyl-2'-nitro-5-propylbiphenyl-2-carboxylate (19f):



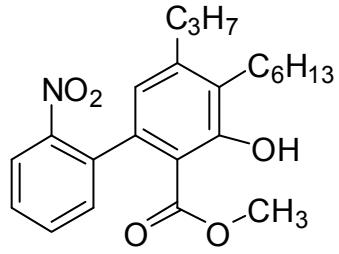
Starting with bis silyl-enol ether **4b** (1.207 g, 4.4 mmol), $TiCl_4$ (0.835 g, 4.4 mmol) CH_2Cl_2 (8 mL) and monosilyl enol ether **4a** (1.229 g, 4.0 mmol), **19f** was isolated (0.500 g, 38 %) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.82 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.41 ─ 1.50 (m, 2 H, CH_2), 2.12(s, 3 H, CH_3), 2.47 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.32 (s, 3 H, OCH_3), 6.34 (s, 1 H, CH_{Ar}), 7.11 (dd, ^3J = 8.7 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.34 (ddd, ^3J = 8.0 Hz, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 7.45 (ddd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 11.49 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 10.3, 12.9 (CH_3), 22.1, 35.0 (CH_2), 50.8 (OCH_3), 107.0 (C_{Ar}), 121.0, 122.6 (CH_{Ar}), 127.7 (CH_{Ar}), 126.5, 130.3, 131.2 (CH_{Ar}), 135.8, 137.6, 146.8, 147.0, 159.8 (CH_{Ar}), 170.1 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 329 ($[M]^+$, 55), 297 (100), 283 (20), 238 (18), 224 (30), 208 (14), 194 (12), 165 (25), 139 (7), 115 (9), 77 (5). HRMS (EI): Calcd. for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12597.

Ethyl 4-ethyl-3-hydroxy-2'-nitro-5-propylbiphenyl-2-carboxylate (19g):



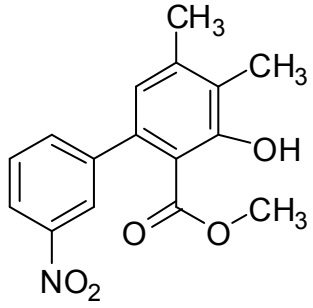
Starting with bis silyl-enol ether **4b** (1.207 g, 4.4 mmol), $TiCl_4$ (0.835 g, 4.4 mmol) CH_2Cl_2 (8 mL) and monosilyl enol ether **4a** (1.229 g, 4.0 mmol), **19f** was isolated (0.500 g, 38 %) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.82 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.41 ─ 1.50 (m, 2 H, CH_2), 2.12(s, 3 H, CH_3), 2.47 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.32 (s, 3 H, OCH_3), 6.34 (s, 1 H, CH_{Ar}), 7.11 (dd, ^3J = 8.7 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.34 (ddd, ^3J = 8.0 Hz, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1 H, CH_{Ar}), 7.45 (ddd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 11.49 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 10.3, 12.9 (CH_3), 22.1, 35.0 (CH_2), 50.8 (OCH_3), 107.0 (C_{Ar}), 121.0, 122.6 (CH_{Ar}), 127.7 (CH_{Ar}), 126.5, 130.3, 131.2 (CH_{Ar}), 135.8, 137.6, 146.8, 147.0, 159.8 (CH_{Ar}), 170.1 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 329 ($[M]^+$, 55), 297 (100), 283 (20), 238 (18), 224 (30), 208 (14), 194 (12), 165 (25), 139 (7), 115 (9), 77 (5). HRMS (EI): Calcd. for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12597.

Methyl 4-hexyl-3-hydroxy-2'-nitro-5-propylbiphenyl-2-carboxylate(19h):



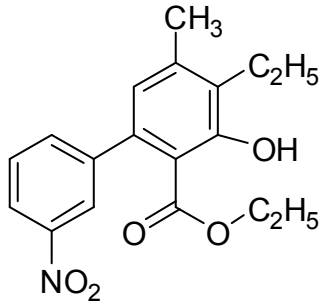
Starting with bis silyl-enol ether **4c** (0.9986 g, 3.2 mmol), $TiCl_4$ (0.625 g, 3.2 mmol) CH_2Cl_2 (6 mL) and monosilyl enol ether **18b** (0.876 g, 3.0 mmol), **19h** was isolated (0.315 g, 26 %) as a yellow oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.59 (t, ^3J = 7.3 Hz, 3 H, CH_3), 0.83 (t, ^3J = 6.5 Hz, 3 H, CH_3), 1.07 (t, ^3J = 7.4 Hz, 3 H, CH_3), 1.39 ─ 1.48 (m, 2 H, CH_2), 2.43 ─ 2.50 (m, 2 H, CH_2), 2.57 ─ 2.66 (m, 2 H, Ch_2), 3.82 (q, ^3J = 6.5 Hz, 2 H, OCH_2), 6.32 (s, 1 H, CH_{Ar}), 7.12 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.34 (ddd, ^3J = 8.0 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.44 (ddd, ^3J = 7.5 Hz, ^3J = 7.4 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.88 (dd, ^3J = 7.6 Hz, ^4J = 1.3 Hz, 1 H, CH_{Ar}), 11.58 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 8.9, 14.4, 15.2 (CH_3), 20.3, 25.1, 36.3 (CH_2), 62.0 (OCH_2), 109.4 (C_{Ar}), 123.1, 124.7, 128.6 (CH_{Ar}), 131.7 (C_{Ar}), 132.4, 133.2 (CH_{Ar}), 137.9, 140.1, 148.1, 149.1, 162.0 (C_{Ar}), 171.8 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 357 ($[M]^+$, 100), 311 (54), 283 (21), 266 (38), 250 (43), 235 (20), 220 (58), 194 (20), 180 (39), 165 (39), 152 (27), 115 (15), 77 (11). HRMS (EI): Calcd. for $C_{20}H_{23}NO_5$: 357.15707; found: 329.15710.

Methyl 3-hydroxy-4,5-dimethyl-3'-nitrobiphenyl-2-carboxylate (19j):



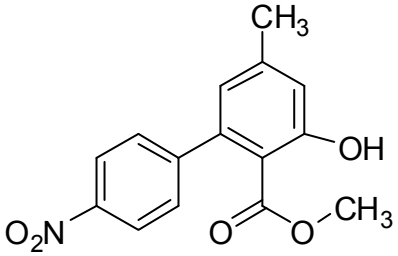
Starting with bis silyl-enol ether 4b (0.598 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **18c** (0.548 g, 2.0 mmol), **19j** was isolated (0.305 g, 50 %) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.09 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 3.36 (s, 3 H, OCH_3), 6.46 (s, 1 H, CH_{Ar}), 7.30 ─ 7.40 (m, 2 H, CH_{Ar}), 7.97 (m, 1 H, CH_{Ar}), 8.03 ─ 8.07 (m, 1 H,CH_{Ar}), 11.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 12.0, 21.3 (CH_3), 52.1 (OCH_3), 108.7 (C_{Ar}), 121.9, 123.5, 124.3 (CH_{Ar}), 125.7 (C_{Ar}), 128.6, 134.9 (CH_{Ar}), 139.0, 144.0, 145.4, 148.1, 160.7, (C_{Ar}), 171.6 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 301 ([M]$^+$, 46), 269 (100), 252 (66), 222 (40), 195 (17), 165 (33), 152 (28), 139 (7), 82 (5). HRMS (EI): Calcd. for $C_{16}H_{15}NO_5$: 301.09444; found: 301.09431.

Ethyl 4-ethyl-3-hydroxy-5-methyl-3'-nitrobiphenyl-2-carboxylate (19k):



Starting with bis silyl-enol ether **4c** (0.659 g, 2.2 mmol), $TiCl_4$ (0.41 g, 2.2 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **18c** (0.548 g, 2.0 mmol), **19k** was isolated (0.250 g, 37 %) as a yellow gummy solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.63 (t, ^3J = 7.7 Hz, 3 H, CH_3), 1.04 (t, ^3J = 7.7 Hz, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 2.62 (q, ^3J = 7.0 Hz, 2 H, CH_2), 3.87 (q, ^3J = 6.0 Hz, 2 H, OCH_2), 6.46 (s, 1 H, CH_{Ar}), 7.37 ─ 7.45 (m, 2 H, CH_{Ar}), 7.99 (m, 1 H, CH_{Ar}), 8.03 ─ 8.07 (m, 1 H, CH_{Ar}), 11.32 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.9, 12.0, 18.4 (CH_3), 18.6 (CH_2), 60.0 (OCH_2), 107.6 (C_{Ar}), 120.3, 122.2, 123.1, 127.2, 130.3 (CH_{Ar}), 133.5, 137.8, 141.6, 144.1, 146.6, 159.3 (C_{Ar}), 169.7 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 329 ([M]$^+$, 58), 283 (92), 266 (100), 236 (23), 209 (30), 194 (8), 178 (11), 165 (41), 152 (16), 139 (7), 115 (6). HRMS (EI): Calcd. for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12659.

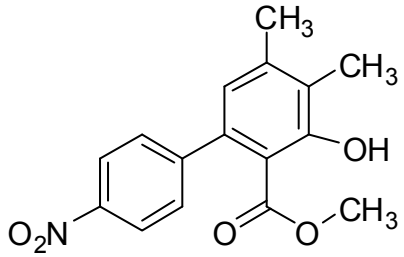
Methyl 3-hydroxy-5-methyl-4'-nitrobiphenyl-2-carboxylate (19l):



Starting with bis silyl-enol ether **4a** (0.568 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **18d** (0.558 g, 4.0 mmol), **19l** was isolated (0.210 g, 36 %) as a colourless solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.23 (s, 3 H, CH_3), 3.36 (s, 3 H, OCH_3), 6.44 (d, ^4J=1.6 Hz, 1 H, CH_{Ar}), 6.77 (d, ^4J=1.3 Hz, 1 H, CH_{Ar}), 7.25 (d, ^3J=8.8 Hz, 2 H, CH_{Ar}), 8.10 (d, ^3J=8.8 Hz, 2 H,

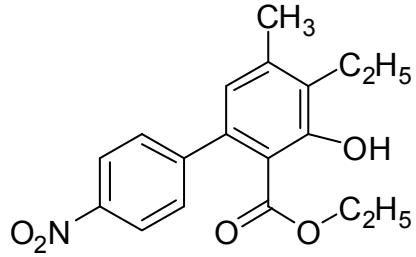
CH_{Ar}), 10.81 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 21.6 (CH_3), 51.7 (OCH_3), 108.6 (C_{Ar}), 118.2 (CH_{Ar}), 122.8 ($2CH_{Ar}$), 123.5 (CH_{Ar}), 129.0 ($2CH_{Ar}$), 142.1, 145.4, 146.9, 149.9, 162.2 (C_{Ar}), 170.0 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 287 ($[M]^+$, 27), 255 (100), 197 (9), 181 (30), 152 (20), 115 (5), 76 (7). HRMS (EI): Calcd. for $C_{15}H_{13}NO_5$: 287.07882; found: 287.07879.

Methyl 3-hydroxy-4,5-dimethyl-4'-nitrobiphenyl-2-carboxylate (19m):



Starting with bis silyl-enol ether **4b** (0.598 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **18d** (0.558 g, 2.0 mmol), **19m** was isolated (0.420 g, 33 %) as a colourless solid. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.16 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3) 3.40 (s, 3 H, OCH_3), 6.49 (s, 1 H, CH_{Ar}), 7.29 (d, ^3J=8.8 Hz, 2 H, CH_{Ar}), 8.14 (d, ^3J=8.8 Hz, 2 H, CH_{Ar}), 11.18 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 11.5, 20.4 (CH_3), 51.7 (OCH_3), 108.2 (C_{Ar}), 122.7 ($2CH_{Ar}$), 123.6 (CH_{Ar}), 125.4 (CH_{Ar}), 129.0 ($2CH_{Ar}$), 138.9, 143.5, 146.6, 150.2, 160.2 (C_{Ar}), 171.1 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 301 ($[M]^+$, 40), 269 (100), 254 (19), 223 (42), 195 (17), 180 (6), 165 (32), 152 (29), 139 (7), 115 (7), 76 (5). HRMS (EI): Calcd. for $C_{16}H_{15}NO_5$: 301.09447; found: 301.09477.

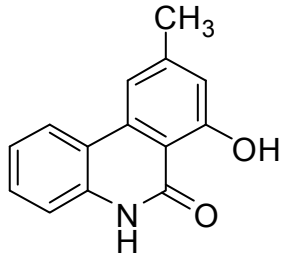
Ethyl 4-ethyl-3-hydroxy-5-methyl-4'-nitrobiphenyl-2-carboxylate (19n):



Starting with bis silyl-enol ether **4c** (0.659 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **18d** (0.558 g, 2.0 mmol), **19n** was isolated (0.420 g, 33 %) as a colourless solid. ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.65 (t, ^3J=7.4 Hz, 3 H, CH_3), 1.09 (t, ^3J=7.5 Hz, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 2.67 (q, ^3J=7.5 Hz, 2 H, CH_2), 3.92 (q, ^3J=7.4 Hz, 2 H, OCH_2), 6.46 (s, 1 H, CH_{Ar}), 7.30 (d, ^3J=8.8 Hz, 2 H, CH_{Ar}), 8.14 (d, ^3J=8.8 Hz, 2 H, CH_{Ar}), 11.27 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 12.9, 13.1, 19.4 (CH_3), 19.6 (CH_2), 61.1 (OCH_2), 108.5 (C_{Ar}), 122.7 ($2CH_{Ar}$), 123.7 (CH_{Ar}), 129.1 ($2CH_{Ar}$), 131.3, 139.1, 142.5, 146.5, 150.5, 160.2 (C_{Ar}), 170.7 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 329 ($[M]^+$, 58), 283 (100), 266 (50), 240 (46), 222 (9), 209 (13), 178 (10), 165 (56), 152 (19), 139 (8), 115 (7), 77 (4). HRMS (EI): Calcd. for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12590.

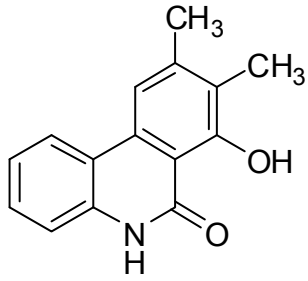
General procedure for the synthesis of 6(5*H*)-phenanthridinones 19a-h: To a stirred methanol suspension (25 mL) of Pd/C (10 mol-%) was added **19a-h** (1.0 equiv.). The mixture was set under a hydrogen atmosphere. After stirring for 48 h at 20 °C, the reaction mixture was filtered (celite) and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes heptanes/EtOAc = 2:1).

7-Hydroxy-9-methyl-6(5*H*)-phenanthridinone (20a).



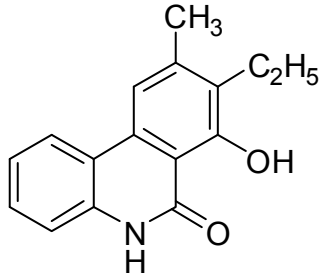
Starting with **19a** (0.429 g, 1.65 mmol), **20a** was isolated (0.200 g, 61%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid.. ^{1}H NMR (DMSO, 250 MHz): δ = 2.45 (s, 3 H, CH_3), 6.82 (s, 1 H, CH_{Ar}), 7.27 − 7.30 (m, 1 H, CH_{Ar}), 7.33 − 7.41 (m, 1 H, CH_{Ar}), 7.49 − 7.55 (m, 1 H, CH_{Ar}), 7.76 (m, 1 H, CH_{Ar}), 8.34 (d, ^{3}J = 7.9 Hz, 1 H, CH_{Ar}), 12.02 ($s_{(br)}$, 1 H, NH), 13.25 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 21.8 (CH_3), 107.9 (C_{Ar}), 113.1 115.0, 116.6 (CH_{Ar}), 118.0 (C_{Ar}), 123.2, 123.6, 128.4 (CH_{Ar}), 129.8, 135.6, 146.0, 159.4 (C_{Ar}), 165.7 (C=O). MS (EI 70 eV): *m/z* (%) = 225 ([M]$^+$, 100), 206 (10), 196 (16), 99 (14), 73 (16), 57 (27), 43 (52). HRMS (EI): Calcd. for $C_{14}H_{11}NO_2$: 225.07853; found: 225.07843.

7-Hydroxy-8,9-dimethylphenanthridin-6(5*H*)-one(20b):



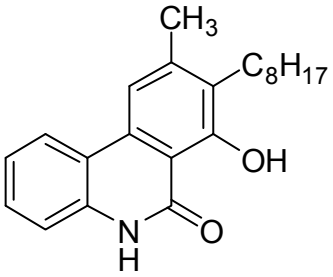
Starting with **19b** (0.504 g, 1.67 mmol), **20a** was isolated (0.200 g, 52%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR (DMSO, 250 MHz): δ = 2.08 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 7.27 − 7.52 (m, 3 H, CH_{Ar}), 7.74 (s, 1 H, CH_{Ar}), 8.34 (d, ^{3}J = 7.5 Hz, 1 H, CH_{Ar}), 11.97 ($s_{(br)}$, 1 H, NH), 13.60 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 10.6, 13.9 (CH_3), 107.3 (C_{Ar}), 112.4, 116.4, 121.3, (CH_{Ar}), 123.0 (C_{Ar}), 123.2, 123.6, 129.2 (CH_{Ar}), 135.1, 148.3, 159.2, (C_{Ar}), 165.6 (C=O). MS (EI 70 eV): *m/z* (%) = 239 ([M]$^+$, 89), 224 (34), 191 (10), 97 (26), 84 (100), 66 (98), 57 (95). Anal.: Calcd for $C_{15}H_{13}NO_2$: C 75.30, H 5.48, N 5.85; found.: C 75.40, H 5.42, N 5.70.

8-Ethyl-7-hydroxy-9-methylphenanthridin-6(5*H*)-one (20c):



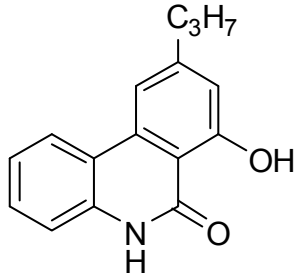
Starting with **19c** (0.137 g, 0.41 mmol), **20c** was isolated (0.070 g, 70%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR (DMSO, 250 MHz): δ = 1.10 (t, ^3J = 8.0 Hz, 3 H, CH_3), 2.47 (s, 3 H, CH_3), 2.68 (q, ^3J = 7.5 Hz, 2 H, CH_2), 7.26 ─ 7.32 (m, 1 H, CH_{Ar}), 7.36 − 7.39 (m, 1 H, CH_{Ar}), 7.46 − 7.52 (m, 1 H, CH_{Ar}), 7.75 (s, 1 H, CH_{Ar}), 8.31 (d, ^3J = 8.4 Hz, 1 H, CH_{Ar}), 11.99 ($s_{(br)}$, 1 H, NH), 13.59 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 13.0, 18.5 (CH_3), 19.8 (CH_2), 107.6 (C_{Ar}), 113.5, 116.5 (CH_{Ar}), 118.3 (C_{Ar}), 123.0, 123.3, (CH_{Ar}), 127.8 (CH_{Ar}), 129.3 (CH_{Ar}), 132.2, 135.2, 143.6, 158.9 (C_{Ar}), 165.8 (C=O). MS (EI 70 eV): *m/z* (%) = 253 ($[M]^+$, 39), 238 (100), 220 (2), 190 (5), 165 (6), 104 (4), 95 (3), 63 (3). HRMS (EI): Calcd. for $C_{16}H_{15}NO_2$: 253.10973; found: 253.10991.

7-Hydroxy-9-methyl-8-octylphenanthridin-6(5*H*)-one (20d):



Starting with **19c** (0.275 g, 0.68 mmol), **20c** was isolated (0.200 g, 69%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR (DMSO/$CDCl_3$, 250 MHz): δ = 0.77 ─ 0.85 (m, 3 H, CH_3), 1.85 ─ 1.24 (m, 8 H, CH_2), 1.41 ─ 1.49 (m, 4 H, CH_2), 2.41 (s, 3 H, Ch_3), 2.60 ─ 2.66 (m, 2 H, CH_2), 7.16 ─ 7.32 (m, 3 H, CH_{Ar}), 7.53 (s, 1 H, CH_{Ar}), 8.12 (d, ^3J = 7.8 Hz, 1 H, CH_{Ar}), 11.70 ($s_{(br)}$, 1 H, NH), 13.44 (s, 1 H, OH). ^{13}C NMR (DMSO/$CDCl_3$, 62 MHz): δ_C = 13.8, 20.1 (CH_3), 22.1, 25.3, 28.4, 28.6, 29.0, 29.3, 31.5 (CH_2), 107.6 (C_{Ar}), 112.8, 112.9, 116.3 (CH_{Ar}), 118.2 (C_{Ar}), 122.6 (CH_{Ar}), 126.6, 126.7 (C_{Ar}), 128.6 (CH_{Ar}), 132.0, 143.2, 159.2 (C_{Ar}), 165.6 (C=O). MS (EI 70 eV): *m/z* (%) = 337 ($[M]^+$, 28), 308 (4), 276 (3), 252 (7), 238 (100), 224 (5), 192 (3), 160 (4) 128 (25), 97 (14), 69 (15). HRMS (EI): Calcd. for $C_{22}H_{27}NO_2$: 337.20363; found: 337.20310.

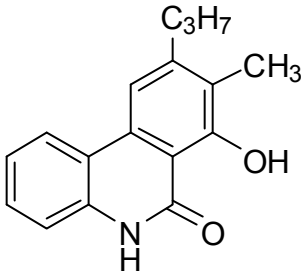
7-Hydroxy-9-propylphenanthridin-6(5*H*)-one (20e):



Starting with **19e** (0.563 g, 1.787 mmol), **20e** was isolated (0.240 g, 56%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR (DMSO, 250 MHz): δ = 0.92 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.63 ─ 1.72 (m, 2 H, CH_2), 2.68 (t, ^3J = 7.1 Hz, 2 H, CH_2), 6.81 ($s_{(br)}$, 1 H, CH_{Ar}), 7.25 − 7.29 (m, 1 H, CH_{Ar}), 7.32 − 7.39 (m, 1 H, CH_{Ar}), 7.47 ─ 7.53 (m, 1 H, CH_{Ar}), 7.74

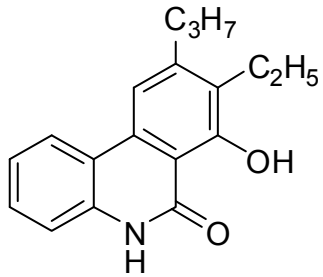
($s_{(br)}$, 1 H, CH_{Ar}), 8.35 (d, ^3J = 7.7 Hz, 1 H, CH_{Ar}), 12.01 ($s_{(br)}$, 1 H, NH), 13.25 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 13.6 (CH_3), 23.6, 38.6 (CH_2), 107.9 (C_{Ar}), 112.3, 114.3, 116.5 (CH_{Ar}), 118.2 (C_{Ar}), 123.1, 123.7, 129.7 (CH_{Ar}), 135.2, 135.5, 150.2, 161.4 (C_{Ar}), 165.7 (C=O). MS (EI 70 eV): *m/z* (%) = 253 ([M]$^+$, 40), 225 (100), 196 (20), 177 (30), 149 (60), 115 (15), 89 (12), 69 (20), 44 (70), 43 (9). HRMS (EI): Calcd. for $C_{16}H_{15}NO_2$: 253.10973; found: 253.10991

7-Hydroxy-8-methyl-9-propylphenanthridin-6(5*H*)-one (20f):



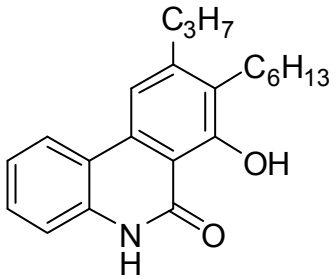
Starting with **19f** (0.480g, 1.45 mmol), **20f** was isolated (0.190 g, 50%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR (DMSO, 250 MHz): δ = 0.90 (t, ^3J = 7.4 Hz, 3 H, CH_3), 1.50 ─ 1.59 (m, 2 H, CH_2), 2.12 (s, 3 H, CH_3), 2.65 (t, ^3J = 7.5 Hz, 2 H, CH_2), 7.18 ─ 7.24 (m, 1 H, CH_{Ar}), 7.28 − 7.32 (m, 1 H, CH_{Ar}), 7.32 − 7.43 (m, 1 H, CH_{Ar}), 7.64 (s, 1 H, CH_{Ar}), 8.25 (d, ^3J = 8.2 Hz, 1 H, CH_{Ar}), 11.89 ($s_{(br)}$, 1 H, NH), 13.55 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 10.5, 13.8 (CH_3), 23.0, 35.9 (CH_2), 107.4 (C_{Ar}), 112.3, 116.6 (CH_{Ar}), 118.5, 121.5 (C_{Ar}), 123.0, 123.3, 129.3 (CH_{Ar}), 131.9, 135.2, 148.6, 159.4 (C_{Ar}), 165.7 (C=O). MS (EI 70 eV): *m/z* (%) = 267 ([M]$^+$, 100), 252 (76), 239 (75), 224 (34), 210 (5), 190 (7), 165 (7), 78 (34), 63 (43), 43 (9). HRMS (EI): Calcd. for $C_{17}H_{17}NO_2$: 267.12535; found: 267.12538.

8-Ethyl-7-hydroxy-9-propylphenanthridin-6(5*H*)-one (20g):



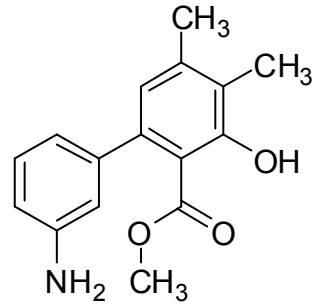
Starting with **19g** (0.202 g, 0.57 mmol), **7a** was isolated (0.100 g, 63%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid..^{1}H NMR (DMSO, 250 MHz): δ = 1.00 (t, ^3J = 8.1 Hz, 3 H, CH_3), 1.13 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.66 (q, ^3J = 7.3 Hz, 2 H, CH_2), 2.66 ─ 2.77 (m, 4 H, CH_2), 7.26 ─ 7.36 (m, 2 H, CH_{Ar}), 7.49 − 7.58 (m, 2 H, CH_{Ar}), 8.34 (d, ^3J = 8.0 Hz, 1 H, CH_{Ar}), 11.90 ($s_{(br)}$, 1 H, NH), 13.62 (s, 1 H, OH). ^{13}C NMR (DMSO, 62 MHz): δ_C = 13.9, 14.0 (CH_3), 18.3, 24.0, 35.0 (CH_2), 107.5 (C_{Ar}), 112.6, 116.6 (CH_{Ar}), 118.4 (C_{Ar}), 123.0, 128.8, 131.3 (CH_{Ar}), 132.3, 135.2, 147.8, 159.2 (C_{Ar}), 165.7 (C=O). MS (EI 70 eV): *m/z* (%) = 281 ([M]$^+$, 100), 238 (76), 207 (12), 224 (30), 190 (7), 165 (5), 78 (40), 63 (23), 43 (8). HRMS (EI): Calcd. for $C_{17}H_{17}NO_2$: 267.12535; found: 267.12538. Anal.: Calcd for $C_{18}H_{19}NO_2$: C 76.84, H 6.81, N 4.98; found.: C 76.90, H 6.60, N 4.90.

8-Hexyl-7-hydroxy-9-propylphenanthridin-6(5*H*)-one (20h):



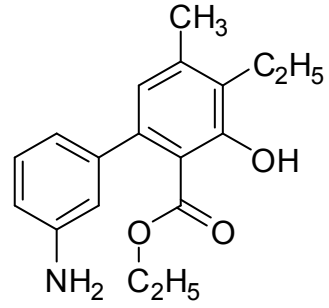
Starting with **19h** (0.250g, 0.62 mmol), **20h** was isolated (0.150 g, 74%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.83 (t, ^{3}J = 7.8 Hz, 3 H, CH_3), 0.99 (t, ^{3}J = 7.5 Hz, 3 H, CH_3), 1.26 ─ 1.48 (m, 8 H, CH_2), 1.60 ─ 1.69 (m, 2 H, CH_2), 2.66 ─ 2.72 (m, 4 H, CH_2), 7.11 ─ 7.15 (m, 1 H, CH_{Ar}), 7.21 − 7.25 (m, 1 H, CH_{Ar}), 7.37 − 7.40 (m, 1 H, CH_{Ar}), 7.48 (s, 1 H, CH_{Ar}), 8.10 (d, ^{3}J = 8.5 Hz, 1 H, CH_{Ar}), 9.49 ($s_{(br)}$, 1 H, NH), 13.92 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.1, 14.2 (CH_3), 22.6, 24.4, 25.8, 29.5, 29.8, 31.7, 36.0 (CH_2), 107.5 (C_{Ar}), 112.0, 112.6, 116.2 (CH_{Ar}), 119.4 (C_{Ar}), 123.2 (CH_{Ar}), 123.5 (C_{Ar}), 127.9 (CH_{Ar}), 129.1, 131.4, 133.5, 148.7 (C_{Ar}), 160.0 (C=O). MS (EI 70 eV): *m/z* (%) = 337 ([M]$^{+}$, 42), 280 (9), 266 (100), 225 (19), 161 (9), 128 (40), 83 (24), 69 (43) 43 (9). HRMS (EI): Calcd. for $C_{22}H_{27}NO_2$: 337.20363; found: 337.20310.

Methyl 2'-amino-3-hydroxy-4,5-dimethylbiphenyl-2-carboxylate (21a):



Starting with **19j** (0.150g, 0.45 mmol), **21a** was isolated (0.110 g, 81%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.13 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 3.41 ($m_{(br)}$, 2 H, NH_2), 3.44 (s, 3 H, OCH_3), 6.40 (s, 1 H, CH_{Ar}), 6.49 − 6.57 (m, 3 H, CH_{Ar}), 7.00 − 7.06 (m, 1 H, CH_{Ar}), 10.86 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 11.4, 20.4 (CH_3), 51.6 (OCH_3), 109.1 (C_{Ar}), 113.3, 114.9, 119.0 (CH_{Ar}), 123.6 (C_{Ar}), 123.8, 128.3, (CH_{Ar}), 141.6, 142.8, 144.2, 145.7, 159.2 (C_{Ar}), 172.0 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 271 ([M]$^{+}$, 72), 239 (100), 224 (87), 210 (13), 196 (21), 180 (6), 167 (13), 135 (5), 115 (5), 98 (6), 65 (4). HRMS (EI): Calcd. for $C_{16}H_{17}NO_3$: 271.12029; found: 271.12050.

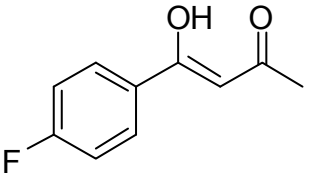
Ethyl 2'-amino-4-ethyl-3-hydroxy-5-methylbiphenyl-2-carboxylate (21b):



Starting with **19k** (0.250g, 0.82 mmol), **21b** was isolated (0.184 g, 78%) by column chromatography (silica gel, heptanes/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.74 (t, ^{3}J=7.4 Hz, 3 H, CH_3), 1.07 (t, ^{3}J=7.5 Hz, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 2.63 (q, ^{3}J=7.4 Hz, 2 H, CH_2), 3.42 ─ 3.60 (($m_{(br)}$, 2 H, NH_2), 3.93 (q, ^{3}J=7.5 Hz, 2 H, OCH_2), 6.44 ─ 6.48 (m,

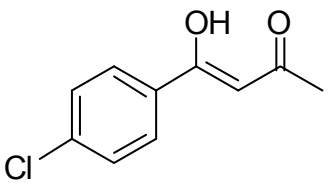
1 H, CH_{Ar}), 6.49 − 6.54 (m, 3 H, CH_{Ar}), 6.96 − 7.03 (m, 1 H, CH_{Ar}), 10.95 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 13.1, 13.2, 19.4 (CH_3), 19.6 (CH_2), 60.7 (OCH_2), 109.0 (C_{Ar}), 113.2, 115.1, 119.0, 123.9, 128.3 (CH_{Ar}), 129.6, 141.8, 141.9, 144.4, 145.7, 159.3 (C_{Ar}), 171.5 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 299 ($[M]^+$, 96), 253 (64), 238 (100), 220 (34), 210 (16), 180 (15), 152 (7), 128 (5), 90 (7), 65 (3). HRMS (EI): Calcd. for $C_{18}H_{21}NO_3$: 299.15160; found: 299.15146.

4-(4-Fluorophenyl)-4-hydroxy-3-buten-2-one (23b):



To a stirred solution of LDA (75 mmol) in THF (62 mL) was added acetone (2.904 g, 50.0 mmol) at -78 °C. After the solution was stirred for 1 h, 4-florobenzoyl chloride (9.51 g, 60.0 mmol) was added. The temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with ethylacetate (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/EtOAc 30:1 → 20:1) to give **23b** as a colorless solid (3.9 g, 36%) mp = 48-49 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 6.04 (s, 1 H, CH), 7.04 (m, 2 H, CH), 7.81 (m, 2 H, CH), 16.07 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4 (CH_3), 95.3 (CH), 114 (d, ^3J = 21.8 Hz, 2CH), 128.4 (d, ^2J = 8.9 Hz, 2CH), 130.3 (d, ^4J = 2.9 Hz, C), 164.3 (d, ^1J = 252.0 Hz, CF), 181.9 (C), 191.8 (C=O). (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1603 (s), 1507 (s), 1297(m), 1246 (s), 1159 (m), 1095 (m), 1014 (w), 849 (s), 786 (s), 506 (w). MS (EI, 70 eV): *m/z* (%) = 180 ($[M]^+$, 64), 165 (66), 138 (6), 123 (100), 109 (6), 95 (48), 85 (11), 75 (20), 69 (50), 50 (5), 43 (23). HRMS (EI): Calcd. for $C_{10}H_9FO_2$ ($[M]^+$): 180.05811; found: 180.05765.

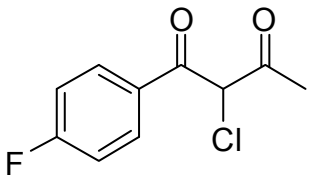
4-(4-Chlorophenyl)-4-hydroxy-3-buten-2-one (23c):



To a stirred solution of LDA (75 mmol) in THF (62 mL) was added acetone (2.904 g, 50.0 mmol) at -78 °C. After the solution was stirred for 1 h, 4-chlorobenzoyl chloride (10.5 g, 60.0 mmol) was added. The temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with ethylacetate (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in

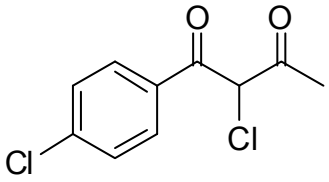
vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/EtOAc 30:1 → 20:1) to give **23c** as a light yellow solid (3.762 g, 38%) mp = 66-68 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3 H, CH_3), 6.06 (s, 1 H, CH), 7.33 (m, 1 H, CH), 7.35 (m, 1 H, CH), 7.72 (m, 1 H, CH), 7.75 (m, 1 H, CH), 16.01 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.1 (CH_3), 96.9 (CH), 128.7 (2CH), 129.3 (2CH), 133.7, 138.9, 182.6 (C), 194.1 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3075 (m), 2847 (m), 1594 (s), 1547 (s), 1486 (s), 1284 (m), 1113 (m), 1093 (s), 1012 (s), 840 (m), 779 (s), 437 (m). MS (EI, 70 eV): *m/z* (%) = 198 ([M]$^+$, [^{37}Cl], 34), 196 ([M]$^+$, [^{35}Cl]), 69), 181 (87), 161 (26), 154 (8), 139 (100), 111 (44), 101 (5), 89 (13), 85 (25), 75 (36), 69 (79), 63 (6), 50 (11), 43 (36). HRMS (EI): Calcd. for $C_{10}H_9ClO_2$ ([M]$^+$, [^{35}Cl]): 196.02856; found: 196.02870.

2-Chloro-1-(4-flourophenyl)butane-1,3-dione (24b):



A mixture of **23b** (4.11 g, 22.8 mmol) and NCS (3.09 g, 22.8 mmol) in CCl_4 (50 mL) was heated at reflux for 4 h. After cooling, the precipitate of succinimide was filtered off and water was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 30:1 → 20:1) to give **24b** as dark yellow oil (3.25 g, 66%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.29 (s, 3 H, CH_3), 5.46 (s, 1 H, CH), 7.06-7.09 (m, 2 H, Ar), 7.92-7.97 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 25.6 (CH_3), 63.2 (CH), 115.1, 115.3, 131.2, 131.3 (CH), 163.7, 167.7 (C), 187.3, 197.6 (C=O). GC-MS (EI 70 eV): *m/z* (%) = 216 ([M]$^+$, [^{37}Cl], 12), 214 ([M]$^+$, [^{35}Cl], 4),, 199 (4), 172 (114), 123 (100), 95 (39), 75 (13), 43 (19). HRMS (EI): Calcd. for $C_{10}H_8ClFO_2$ ([M]$^+$, [^{35}Cl]): 214.01914; found: 214.01824.

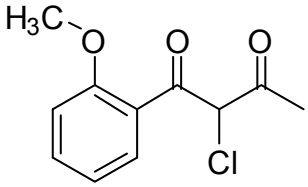
3-Chloro-4-(4-chlorophenyl)butane-1,3-dione (24c):



A mixture of **23c** (4.38 g, 22.3 mmol) and NCS (3.02 g, 22.3 mmol) in CCl_4 (49 mL) was heated at reflux for 4 h. After cooling, the precipitate of succinimide was filtered off and water was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 30:1 → 20:1) to give **24c** as yellowish oil (2.60 g, 52%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.31 (s, 3 H, CH_3), 5.43 (s, 1 H, CH), 7.42 (m, 2 H, CH_3), 7.84-

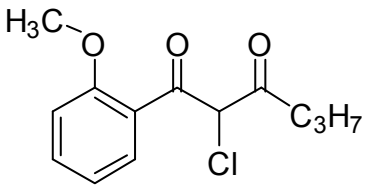
7.87 (m, 2 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 27.0 (CH_3), 64.5 (CH), 128.7 (C), 129.7 (2CH), 131.1 (2CH), 141.6 (C), 189.1, 198.9 (C=O). GC-MS (EI, 70 eV) : *m/z* (%) = 234 ($[M]^+$, [2x^{37}Cl], 1), 232 ($[M]^+$, [^{37}Cl], [^{35}Cl], 6), 230 ($[M]^+$, [2x^{35}Cl], 10), 215 (3), 188 (13), 139 (100), 111 (38), 75 (21), 43 (26). HRMS (EI): Calcd. for $C_{10}H_8Cl_2O_2$ ($[M]^+$, [2x^{35}Cl]): 229.98959; found: 229.98919.

2-Chloro-1-(2-methoxyphenyl)butane-1,3-dione (24e).



A mixture of **23e** (4.80 g, 25.0 mmol) and NCS (3.33 g, 25 mmol) in CCl_4 (55 mL) was heated at reflux for 4 h. After cooling, the precipitate of succinimide was filtered off and water was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 30:1 → 20:1) to give **24e** as yellow oil (2.67 g, 47%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.26 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 5.56 (s, 1 H, CH), 6.88 (d, *J*=8.4 Hz, 1 H, Ar), 6.91-6.96 (m, 1 H, Ar), 7.40-7.46 (m, 1 H, Ar), 7.74 (dd, *J*=7.6 Hz, *J*= 1.9 Hz 1 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 26.0, (CH_3), 54.5 (OCH_3), 66.9 (CH), 110.8, 120.4 (CH), 123.4 (C), 130.4, 134.3 (CH), 157.4 (C), 189.3, 196.3 (C=O). GCMS (EI, 70 eV): *m/z* (%) = 228 ($[M]^+$, [^{37}Cl], 3), 226, ($[M]^+$, [^{35}Cl], 1), 197 (^{37}Cl, 8), 195 (^{35}Cl, 24), 135 (100), 108 (7), 92 (9), 77 (21), 63 (5). HRMS (EI): Calcd. for $C_{10}H_9ClO_2$:($[M]^+$, [^{35}Cl]):226.03912 found: 226.03926

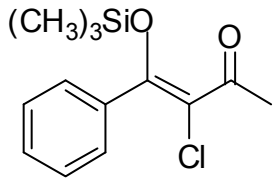
2-Chloro-1-(2-methoxyphenyl)hexane-1,3-dione (24f).



A mixture of **23f** (4.00 g, 18 mmol) and NCS (2.41 g, 18 mmol) in CCl_4 (40 mL) was heated at reflux for 4 h. After cooling, the precipitate of succinimide was filtered off and water was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 30:1 → 20:1) to give **24f** as yellowish oil (3.72 g, 81%). ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.80 (t, J= 7.4 Hz, 3 H, CH_3), 1.48-1.58 (m, 2 H, CH_2), 2.51-2.58 (m, 2 H, CH_2), 3.73 (s, 3 H, OCH_3), 5.64 (s, 1 H, CH), 6.83-6.86 (m, 1 H, Ar), 6.87-6.92 (m, 1 H, Ar), 7.36-7.42 (m, 1 H, Ar), 7.71 (dd, *J*=7.8 Hz, *J*=1.7 Hz, 1 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.6 (CH_3), 15.0, 39.5 (CH_2), 55.6 (OCH_3), 65.8, 110.0,

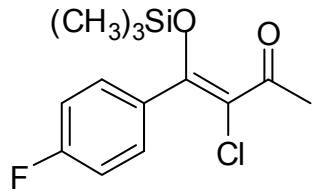
119.3 (CH), 122.6 (C), 129.5, 133.5 (CH), 156.5 (C), 188.5, 197.6 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 2926 (w), 1665 (s), 1618 (w), 1440 (s), 1344 (s), 1177 (s), 1094 (m), 805 (s). GCMS (EI, 70 eV) : *m/z* (%) = 256 ($[M]^+$, [^{37}Cl], 6), 254 ($[M]^+$, [^{35}Cl]), 12), 223 (79), 184 (59), 135 (100), 92 (46), 77 (76), 43 (64). HRMS (EI): Calcd. for $C_{13}H_{15}ClO_3$ ($[M]^+$, [^{35}Cl]): 254.07042; found: 254.07013.

3-Chloro-4-phenyl-4-[(trimethylsilyl)oxy]-3-buten-2-one (25a):



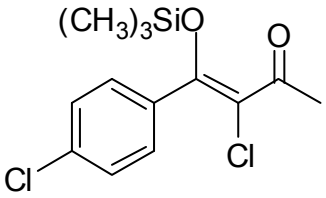
Starting with benzene (120ml), **24a** (9.50 g, 48.3 mmol), triethylamine (10.71 mL, 77.3 mmol). And trimethylchlorosilane (10.98 mL, 86.9 mmol), **25a** as a dark yellow oil (10.10, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.26 (s, 9 H, CH_3), 1.99 (s, 3 H, CH_3), 7.33-7.36 (m, 2 H, Ar), 7.40-7.43 (m, 1 H, Ar), 7.70-7.73 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 0.5, 0.7, 1.9, 21.4 (CH_3), 111.6 (CCl), 128.1 (2CH), 129.1 (2CH), 132.4 (CH), 137.7, 157.4 (C), 191.8 (C=O).

3-Chloro-4-(4-fluorophenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (25b):



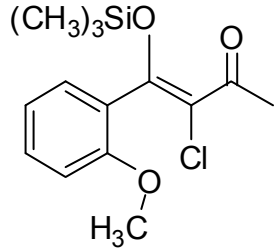
To a stirred benzene solution (45 mL), **24b** (3.25 g, 15.11 mmol), triethylamine (3.38 mL, 24.17 mmol). and trimethylchlorosilane (3.43 mL, 27.2 mmol), **25b** as reddish yellow oil (3.50 g, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.24 (s, 9 H, CH_3), 1.91 (s, 3 H, CH_3), 7.00-7.03 (m, 2 H, Ar), 7.72-7.76 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 0.6, 0.8, 1.9, 21.4 (CH_3), 111.4 (C), 115.2, 115.5, 131.9, 132.1 (CH), 157.9, 163.7, 167.3 (C), 188.4 (C=O).

3-Chloro-4-(4-chlorophenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (25c):



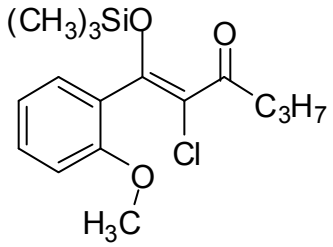
To a stirred benzene solution (33 mL), **24c** (2.607 g, 11.27 mmol), triethylamine (2.52 mL, 18.0 mmol). and trimethylchlorosilane (2.56 mL, 20.3 mmol), **25c** as reddish yellow oil (2.51 g, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.24 (s, 9 H, CH_3), 2.01 (s, 3 H, CH_3), 7.29 (m, 2 H, Ar), 7.62-7.65 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 0.8, 0.9, 2.0, 21.6 (CH_3), 111.6 (C), 128.6 (2CH), 130.8 (2CH), 136.3, 138.9, 158.6 (C), 190.9 (C=O).

3-Chloro-4-(2-methylphenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (25d):



To a stirred benzene solution (13.8 mL), **24d** (1.16 g, 5.5 mmol), triethylamine (1.23 mL, 8.84 mmol), trimethylchlorosilane (1.25 mL, 9.9 mmol), **25d** as reddish yellow oil (1.13 g, 72%).^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.20 (s, 9 H, CH_3), 2.14 (s, 3 H, CH_3), 2.57 (s, 3 H, CH_3),728 (m, 1 H, Ar), 7.35 (m, 1 H, Ar), 7.47 (m, 1 H, Ar), 7.48 (m, 1 H, Ar), . ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 0.4, 1.1, 2.1, 25.7 (CH_3), 108.4 (C), 125.6, 127.5, 130.1, 130.5, (CH), 134.8, 135.4, 182.6 (C), 195.3 (C=O).

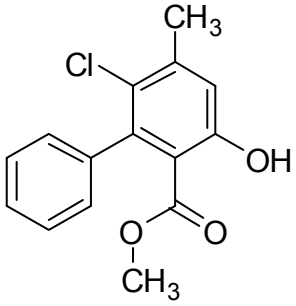
3-Chloro-4-(2-methoxyphenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (25e):



To a stirred benzene solution (35.3 mL), **24f** (2.67 g, 11.7 mmol), triethylamine (2.64 mL, 18.8 mmol), trimethylchlorosilane (2.67 mL, 21.19 mmol), **25e** as reddish yellow oil (2.70 g, 76%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.02 (s, 9 H, CH_3), 1.96 (s, 3 H, CH_3), 3.72(s, 3 H, OCH_3), 6.85-6.88 (m, 1 H, Ar), 7.10-7.12 (m, 1 H, Ar), 7.30-7.33 (m, 1 H, Ar), 7.70-7.81 (m, 1 H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 0.2 ($3CH_3$),

General procedure for the synthesis of biaryls 26a-r: To a CH_2Cl_2 solution of silyl enol ether **25** (1.0 equiv.) and 1,3-bis(silyl enol ether) **4** (1.1 equiv.) was dropwise added $TiCl_4$ (1.1 equiv.) at –78 °C under argon atmosphere. The solution was stirred at –78 °C for 30 min and then allowed to warm to 20 °C during 18 h. To the solution was added a saturated aqueous solution of 10 % HCl. The organic layer was separated and the aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography (silica gel, *n*-hexane/EtOAc) to give salicylates **26.**

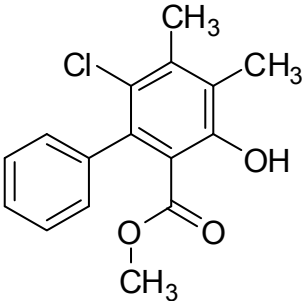
Methyl 5-chloro-2-hydroxy-4-methyl-6-phenylbenzoate (26a):



Starting with bis-silyl enol ether **4a** (0.429 g, 1.65 mmol), $TiCl_4$ (0.313 g, 1.65 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25a** (0.403 g, 1.5 mmol), **26a** was isolated (0.204 g, 49%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.28 (s, 3 H, CH_3), 3.24 (s, 3 H, OCH_3), 6.82 (s, 1 H, Ar), 6.99 (dd, *J* = 7.4 Hz, *J* = 1.5

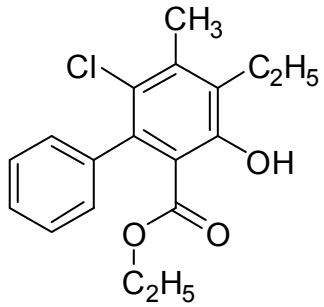
Hz, 2 H, Ar), 7.20-7.23 (m, 2 H, Ar), 7.25-7.28 (m, 1 H, Ar) 10.67 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 20.2 (CH_3), 54.4 (OCH_3), 110.4 (CH), 124.3 (C), 125.5 (CH), 126.1 (2CH), 127.0 (2CH), 139.0, 140.6, 142.2, 158.3 (C), 169.2 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M]$^+$, [^{37}Cl], 10), 276 ([M]$^+$, [^{35}Cl], 30), 246 ([^{37}Cl], 33), 244 ([^{35}Cl], 100), 216 (22), 181 (10), 152 (27), 76 (14). HRMS (EI): Calcd. for $C_{15}H_{13}ClO_3$ ([M]$^+$, [^{35}Cl]): 276.05477; found: 276.05475.

Methyl 6-chloro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26b):



Starting with bis-silyl enol ether **4b** (0.452 g, 1.65 mmol), $TiCl_4$ (0.313 g, 1.65 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25a** (0.403 g, 1.5 mmol), **26b** was isolated (0.133 g, 31%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.19 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 6.99-7.02 (m, 2 H, Ar), 7.21-7.24 (m, 2 H, Ar), 7.26-7.29 (m, 1 H, Ar), 11.03 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.6, 17.1 (CH_3), 50.8 (OCH_3), 110.0, 124.6, 125.0 (C), 125.7 (CH), 126.4 (2CH), 127.6 (2CH), 137.9, 139.5, 140.7, 156.8 (C), 170.2 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 3025 (w), 2951 (m), 1655 (s), 1244 (s), 1200 (s), 1175 (s), 1014 (m), 708 (s). GC-MS (EI, 70 eV): *m/z* (%) = 292 ([M]$^+$, [^{37}Cl], 11), 290 ([M]$^+$, [^{35}Cl],, 33), 260 ([^{37}Cl], 19), 258 ([^{35}Cl], 57), 223 (100), 195 (10), 165 (21) 82 (8). HRMS (EI): Calcd. for $C_{16}H_{15}ClO_3$ ([M]$^+$, [^{35}Cl],): 290.07042; found: 290.07028.

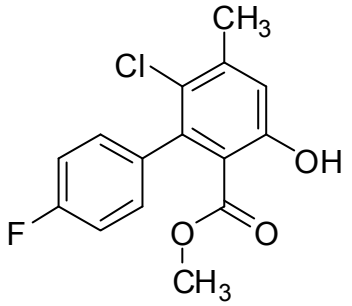
Ethyl 6-chloro-4-ethyl-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26d).



Starting with bis-silyl enol ether **4c** (0.452 g, 1.65 mmol), $TiCl_4$ (0.313 g, 1.65 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25a** (0.403 g, 1.5 mmol), **11d** was isolated (0.205 g, 43%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.56 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.04 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 2.71 (q, *J* = 7.4 Hz, 2 H, CH_2), 3.77 (q, *J* = 7.2 Hz, 2 H, OCH_2), 6.99-7.03 (m, 2 H, Ar), 7.19-7.21 (m, 2 H, Ar), 7.25-7.28, (m, 1 H, Ar), 11.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.8, 12.1, 16.3 (CH_3), 19.2 (CH_2), 59.9 (OCH_2), 110.2, 124.9 (C), 125.6 (CH), 126.4 (2CH), 127.7 (2CH), 130.9, 138.1, 140.0, 140.2, 156.9 (C), 169.8 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M]$^+$, [^{37}Cl], 18), 318 ([M]$^+$, [^{35}Cl], 54), 274 ([^{37}Cl], 27), 272 ([^{35}Cl], 79),

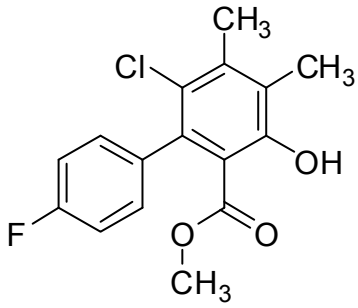
259, ([^{37}Cl], 4), 257 ([^{35}Cl], 13), 237 (81), 219 (100) 165 (42). 115 (6), 77 (5). HRMS (EI): Calcd. for $C_{18}H_{19}ClO_3$ ([M]$^+$, [^{35}Cl]): 318.10172; found: 318.101231.

Methyl 6-chloro-4'-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26e):



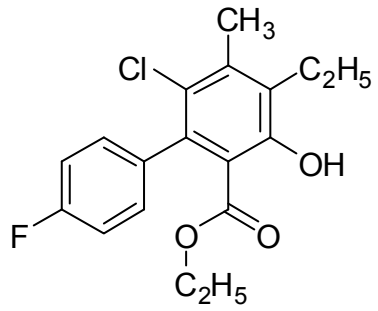
Starting with bis-silyl enol ether **4a** (0.429 g, 1.65 mmol), $TiCl_4$ (0.,313 g, 1.65 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25b** (0.430 g, 1.5 mmol), **26e** was isolated (0.125 g, 28%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 122-124 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.26 (s, 3 H, CH_3), 3.28 (s, 3 H, OCH_3), 6.81 (s, 1 H, Ar), 6.93 (m, 2H, Ar), 6.95 (m, 2 H, Ar), 10.70 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 20.6 (CH_3) 50.9 (OCH_3), 110.8 (C), 113.4, 113.7, 118.3 (CH), 124.8 (C), 128.4, 128.6 (CH), 135.3, 139.9, 142.9, 162.5, 162.7 (C), 169.5 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2853 (w), 1671 (s), 1515 (s), 1362 (s), 1235 (s), 1166 (s), 1014 (m), 809 (s). GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M]$^+$, [^{37}Cl], 12), 294 ([M]$^+$, [^{35}Cl], 36), 262 (100), 234(36), 199 (14), 170 (31) 85 (13). HRMS (EI): Calcd. for $C_{15}H_{12}ClFO_3$ ([M]$^+$, [^{35}Cl]): 294.04535; found: 294.045720.

Methyl 6-chloro-4'-fluoro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26f).



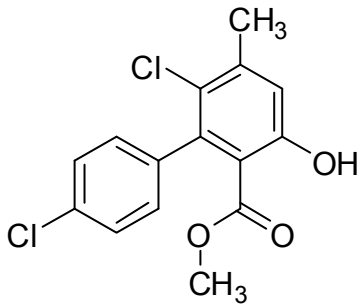
Starting with bis-silyl enol ether **4b** (0.452 g, 1.65 mmol), $TiCl_4$ (0.313 g, 1.65 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25b** (0.430 g, 1.5 mmol), **26f** was isolated (0.224 g, 48%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 65-68 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.20 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 6.97 (m, 2H, Ar), 6.99 (m, 2 H, Ar), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.7, 17.1 (CH_3), 50.9 (OCH_3), 110.0 (C), 113.3, 113.6 (CH), 125.3 (C), 129.2, 129.3 (CH), 135.8, 136.8, 140.9, 157.0, 159.1, 162.4 (C), 170.1 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2960 (m), 1659 (s), 1511 (s), 1470 (s), 1245 (s), 1015 (s), 806 (w). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M]$^+$, [^{37}Cl], 10), 308 ([M]$^+$, [^{35}Cl], 32), 276 (59), 241 (100), 213 (13), 183 (21), 91 (5). HRMS (EI): Calcd. for $C_{16}H_{14}ClFO_3$ ([M]$^+$, [^{35}Cl]): 308.06100; found: 308.060892.

Ethyl 5-chloro-3-ethyl-2-hydroxy-4-methyl-6-(4-fluorophenyl)benzoate (26g).



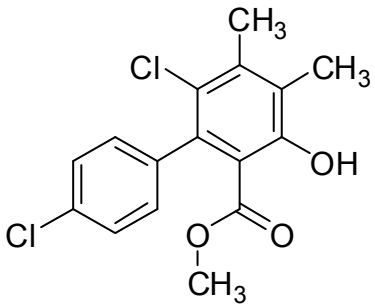
Starting with bis-silyl enol ether **4c** (0.499 g, 1.65 mmol), $TiCl_4$ (0.313 g, 1.65 mmol) CH_2Cl_2 (3 mL) and silyl enol ether **25b** (0.430 g, 1.5 mmol), **26g** was isolated (0.219 g, 44%), by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a light red solid (mp = 73-75 ºC). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.55 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.24 (s, 3 H, CH_3), 2.62 (q, *J* = 7.5 Hz, 2 H, CH_2), 3.73 (q, *J* = 7.2 Hz, 2 H, OCH_2), 6.86 (m, 2 H, Ar), 6.88 (m, 2 H, Ar), 11.11 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 12.9, 13.1, 17.4 (CH_3), 20.4 (CH_2), 61.2 (OCH_2), 111.3 (C), 114.3, 114.6, 130.3, 130.4 (CH), 132.3, 137.1, 138.0, 141.2, 158.0, 160.3, 163.6 (C), 170.7 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2970 (m), 2927 (m), 1655 (s), 1511 (s), 1376 (s), 1233 (s), 1217 (s), 1187 (s), 810 (w). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M]$^+$, [^{37}Cl], 18), 336 ([M]$^+$, [^{35}Cl], 54), 290 (82), 255 (100), 237 (86), 183 (43), 170 (82), 133 (6), 91 (2), 51 (2). HRMS (EI): Calcd. for $C_{18}H_{18}ClFO_3$ ([M]$^+$, [^{35}Cl]): 336.09230; found: 336.09188.

Methyl 4',6-dichloro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate(26h):



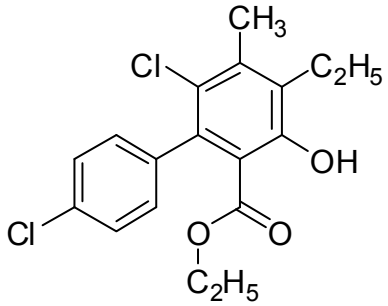
Starting with bis-silyl enol ether **4a** (0.567 g, 2.18 mmol), $TiCl_4$ (0.413 g, 2.18 mmol) CH_2Cl_2 (3 mL) and silyl enol ether **25c** (0.606 g, 2.00 mmol), **26h** was isolated (0.275 g, 44%), by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 80-82 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.29 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 6.85 (m, 1 H, Ar), 6.93-6.96 (m, 2 H, Ar), 7.24-7.27 (m, 2 H, Ar), 10.76 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 21.5 (CH_3), 51.9 (OCH_3), 111.5 (C), 119.4 (CH), 125.6 (C), 127.8 (2CH), 129.8 (2CH), 132.8, 138.8, 140.6, 144.0, 159.8 (C), 170.3 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$= 2952 (m), 2923 (w), 1671 (s), 1452 (s), 1229 (s), 1190 (s), 1018 (s), 820 (w). GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M]$^+$, [2x^{37}Cl], 3), 312 ([M]$^+$, [^{37}Cl], [^{35}Cl], 18), 310 ([M]$^+$, [2x^{35}Cl], 28), 278 (100), 250 (13), 215 (15), 187 (8), 152 (9), 93 (8), 76 (9). HRMS (EI): Calcd. for $C_{15}H_{12}Cl_2O_3$([M]$^+$, [2x^{35}Cl]): 310.01580; found: 310.01625.

Methyl 4',6-dichloro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26i).



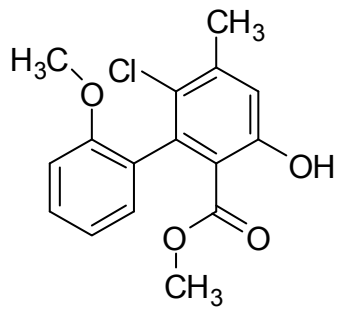
Starting with bis-silyl enol ether **4b** (0.598 g, 2.18 mmol), $TiCl_4$ (0.413 g, 2.18 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25c** (0.606 g, 2.00 mmol), **11i** was isolated (0.220 g, 34%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a light yellow solid, mp = 95-97 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.23 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 3.34 (s, 3 H, OCH_3), 6.96-6.99 (m, 2 H, Ar), 7.27-7.29 (m, 2 H, Ar), 11.12 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 13.1, 18.6 (CH_3), 52.4 (OCH_3), 111.2, 126.0, 126.9 (C), 128.2 (2CH), 130.5 (2CH), 131.1, 138.0, 139.8, 142.4, 158.5 (C), 171.4 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2957 (m), 2927 (w), 1660 (s), 1441 (s), 1244 (s), 1202 (s), 1016 (s), 809 (m). GC-MS (EI, 70 eV): *m/z* (%) = 328 ($[M]^+$, $[2x^{37}Cl]$, 4), 326 ($[M]^+$, $[^{37}Cl]$, $[^{35}Cl]$, 17), 324 ($[M]^+$, $[2x^{35}Cl]$,, 27), 292 (53), 257 (100), 229(11), 165 (25), 99 (5), 82 (12). HRMS (EI): Calcd. for $C_{16}H_{14}Cl_2O_3$: 324.03145 ($[M]^+$, $[2x^{35}Cl]$): found: 324.031296.

Ethyl 4',6-dichloro-4-ethyl-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26j).



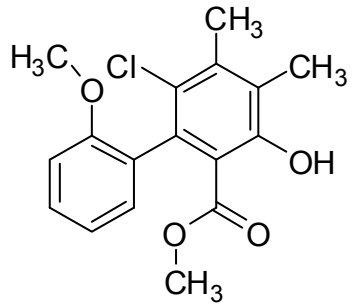
Starting with bis-silyl enol ether **4c** (0.659 g, 2.18 mmol), $TiCl_4$ (0.413 g, 2.18 mmol), CH_2Cl_2 (3 mL) and silyl enol ether **25c** (0.606 g, 2.00 mmol), **26j** was isolated (0.335 g, 47%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 94-96 ºC.^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.67 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.09 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.74 (q, *J* = 7.4 Hz, 2 H, CH_2), 3.85 (q, *J* = 7.2 Hz, 2 H, OCH_2), 6.97-6.99 (m, 2 H, Ar), 7.26-7.29 (m, 2 H, Ar), 11.25 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 12.8, 13.0, 17.4 (CH_3), 20.3 (CH_2), 61.2 (OCH_2), 110.9, 125.7 (C), 127.7 (2CH), 130.1 (2CH), 132.4, 132.6, 137.7, 139.6, 141.2, 158.0 (C), 170.6 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3431 (w), 2966 (m), 2929 (m), 1672 (s), 1382 (s), 1305 (s), 1219 (s), 1101 (m), 186 (m). MS (EI, 70 eV): *m/z* (%) = 356 ($[M]^+$, $[2x^{37}Cl]$, 3), 354 ($[M]^+$, $[^{37}Cl]$, $[^{35}Cl]$, 16), 352 ($[M]^+$, $[2x^{35}Cl]$, 25), 306 (35), 271 (100), 199 (4), 165 (15) 152 (4). 82 (2). HRMS (EI): Calcd. for $C_{18}H_{18}Cl_2O_3$ ($[M]^+$, $[2x^{35}Cl]$): 352.06275 ; found: 352.06340.

Methyl 6-chloro-3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26m):



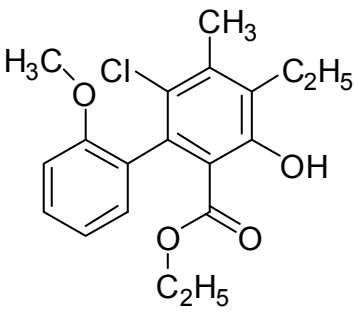
Starting with bis-silyl enol ether **4a** (0.573 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol), CH_2Cl_2 (4 mL) and silyl enol ether **25e** (0.597 g, 2.00 mmol), **26m** was isolated (0.285 g, 47%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.28 (s, 3 H, CH_3), 3.28 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 6.80 (m, 1H, Ar), 6.81-6.83 (m, 1 H, Ar), 6.84, (m, 1 H, Ar), 6.85-6.86, (m, 1 H, Ar), 7.18-7.24, (m, 1 H, Ar), 10.76 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 20.68 (CH_3), 50.8, 54.7 (OCH_3), 109.4 (CH), 111.0 (C), 118.0 (CH), 118.1 (C), 119.1 (CH), 125.1 (C), 127.7, 128.6 (CH), 137.8, 142.8, 155.2, 158.8 (C), 169.6 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 308 ($[M]^+$, [^{37}Cl], 12), 306 ($[M]^+$, [^{35}Cl], 37), 274 (100), 245 (8), 231 (8), 211 (8), 183 (7), 168 (11), 139 (10), 91 (3), 76 (6). HRMS (EI): Calcd. for $C_{16}H_{15}ClO_4$ ($[M]^+$, [^{35}Cl]): 306.06534; found: 306.06620.

Methyl 6-chloro-3-hydroxy-2'-methoxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26n):



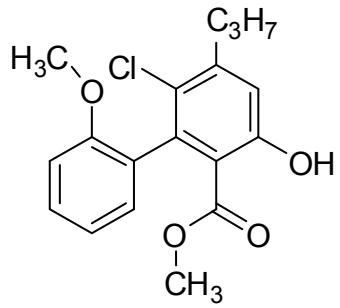
Starting with bis-silyl enol ether **4b** (0.604 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol), CH_2Cl_2 (4 mL) and silyl enol ether **25e** (0.597 g, 2.00 mmol), **26n** was isolated (0.319 g, 50%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 78-80 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.16 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3), 3.27 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 6.79-6.82 (m, 1 H, Ar), 6.83-6.87 (m, 2 H, Ar), 7.16-7.22, (m, 1 H, Ar), 11.10 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.7, 17.2 (CH_3), 50.8, 54.7 (OCH_3), 109.3 (CH), 110.2 (C), 119.1 (CH), 125.0, 125.1 (C), 127.5, 128.7 (CH), 129.1, 134.7, 140.8, 155.3, 157.0 (C), 170.2 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2953 (m), 2923 (m), 1668 (s), 1436 (s), 1293 (s), 1200 (s), 1015 (m), 744 (s). GC-MS (EI, 70 eV): *m/z* (%) = 322 ($[M]^+$, [^{37}Cl], 17), 320 ($[M]^+$, [^{35}Cl], 56), 288 (100), 273 (32), 257 (97), 181 (19), 165 (13), 152 (13), 115 (5), 76 (7). HRMS (EI): Calcd. for $C_{17}H_{17}ClO_4$ ($[M]^+$, [^{35}Cl]): 320.08099; found: 320.081273.

Ethyl 6-chloro-4-ethyl-3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26o):

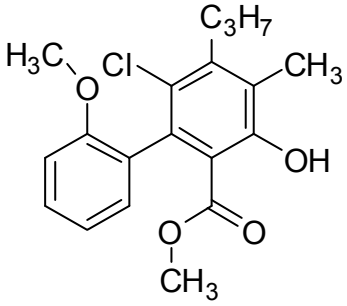


Starting with bis-silyl enol ether **4c** (0.665 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol), CH_2Cl_2 (4 mL) and silyl enol ether **25e** (0.597 g, 2.00 mmol), **26o** was isolated (0.290 g, 42%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 90-92 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.63 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.09 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.73 (q, *J* = 7.4 Hz, 2 H, CH_2), 3.66 (m, 3 H, OCH_3), 3.83 (q, *J* = 7.1 Hz, 2 H, OCH_2), 6.82-6.85 (m, 1 H, Ar), 6.86-6.88 (m, 2 H, Ar), 7.21-7.27 (m, 1 H, Ar), 11.24 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.9, 12.1, 16.4 (CH_3), 19.4 (CH_2), 54.6 (OCH_3), 59.9 (OCH_2), 109.3 (CH), 110.5 (C), 119.1 (CH), 125.3 (C), 127.4, 128.7 (CH), 129.4, 130.8, 134.8, 140.0, 155.5, 157.0 (C), 169.9 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2971 (m), 2958 (m), 2871 (m), 1649 (s), 1299 (s), 1233 (s), 1114 (s), 1030 (s), 811 (w). GC-MS (EI 70, eV): *m/z* (%) = 350 ([M]$^+$, [^{37}Cl], 15), 348 ([M]$^+$, [^{35}Cl], 46), 302 (74), 287 (19), 271 (100), 249 (16), 224 (7), 181 (11), 165 (12), 115 (4), 77 (2). HRMS (EI): Calcd. for $C_{19}H_{21}ClO_4$ ([M]$^+$, [^{35}Cl]): 348.11229; found: 348.11171.

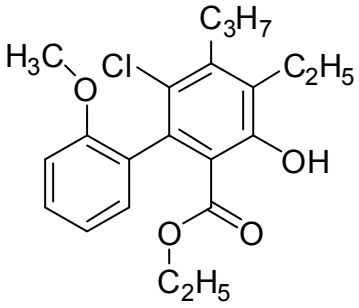
Methyl 6-chloro-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (26p):



Starting with bis-silyl enol ether **4a** (0.573 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol), CH_2Cl_2 (4 mL) and silyl enol ether **25f** (0.653 g, 2.00 mmol), **26p** was isolated (0.229 g, 34%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a slightly yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.87 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.50-1.62 (m, 2 H, CH_2), 2.52-2.65 (m, 2 H, CH_2), 3.27 (m, 3 H, OCH_3), 3.60 (s, 3 H, OCH_3), 6.79 (s, 1 H, Ar), 6.82 (m, 1 H, Ar), 6.83-6.85 (m, 2 H, Ar), 7.17-7.23 (m, 1 H, Ar), 10.73 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 12.9 (CH_3), 21.2, 35.7 (CH_2), 50.8, 54.7 (OCH_3), 109.4 (CH), 111.1(C), 117.2 (CH), 117.3 (C), 119.1 (CH), 124.7 (C), 127.6, 128.7 (CH), 138.0, 146.6, 155.3, 158.8 (C), 169.6 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 336 ([M]$^+$, [^{37}Cl], 12), 334 ([M]$^+$, [^{35}Cl], 37), 302 (100), 274 (43), 230 (10), 181 (5), 152 (9) 139 (8). HRMS (EI): Calcd. for $C_{18}H_{19}ClO_4$ ([M]$^+$, [^{35}Cl): 334.09664; found: 334.09699.

Methyl 6-chloro-3-hydroxy-2'-methoxy-4-methyl-5-propyl[1,1'-biphenyl]-2-carboxylate (26q): 

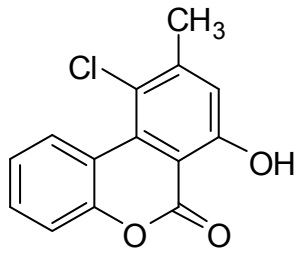
Starting with bis-silyl enol ether **4b** (0.604 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol) CH_2Cl_2 (4 mL) and silyl enol ether **25f** (0.653 g, 2.00 mmol), **26q** was isolated (0.325 g, 47%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a slightly yellow viscous oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.41-1.49 (m, 2 H, CH_2), 2.17 (s, 3 H, CH_3), 2.67-2.74 (m, 2 H, CH_2), 3.25 (m, 3 H, OCH_3), 3.59 (s, 3 H, OCH_3), 6.78 (d, *J* = 8.1 Hz, 1 H, Ar), 6.82-6.83 (m, 2 H, Ar), 7.14-7.20 (m, 1 H, Ar), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 4.8, 14.2 (CH_3), 16.3, 38.0 (CH_2), 53.7, 57.6 (OCH_3), 112.3 (CH), 113.3 (C), 122.0 (CH), 127.6, 127.8 (C), 130.4, 131.7 (CH), 132.1, 137.9, 147.7, 158.3, 160.2 (C), 173.1 (C=O). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3000 (w), 2958 (s), 2931 (m), 2872 (m), 1663 (s), 1249 (s), 1218 (s), 1104 (m), 1028 (s), 808 (m). MS (EI, 70 eV): *m/z* (%) = 350 ($[M]^+$, [^{37}Cl], 13), 348 ($[M]^+$, [^{35}Cl], 37), 316 (100), 301 (15), 285 (14), 257 (21), 181 (11), 165 (7), 69 (13). HRMS (EI): Calcd. for $C_{19}H_{21}ClO_4$ ($[M]^+$, [^{35}Cl]): 348.11229; found: 348.11170.

Ethyl 6-chloro-4-ethyl-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (26r): 

Starting with bis-silyl enol ether **4c** (0.665 g, 2.20 mmol), $TiCl_4$ (417 g, 2.20 mmol) CH_2Cl_2 (4 mL) and monosilyl enol ether **25f** (0654. g, 2.00 mmol), **26r** was isolated (0.384 g, 51%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless solid, mp = 79-81 ºC. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.64 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.13 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.47-1.54 (m, 2 H, CH_2), 2.67-2.69 (m, 2 H, CH_2), 2.72-2.76 (m, 2 H, CH_2), 3.67 (s, 3 H, OCH_3), 3.83 (q, *J* = 7.2 Hz, 2 H, OCH_2), 6.84 (d, *J* = 8.1 Hz, 1 H, Ar), 6.87-6.89 (m, 2 H, Ar), 7.22-7.28, (m, 1 H, Ar), 11.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.9, 13.2, 13.5 (CH_3), 19.3, 21.9, 32.4 (CH_2), 54.7 (OCH_3), 59.9 (OCH_2), 109.4 (CH), 110.7 (C), 119.1 (CH), 124.9 (C), 127.4, 128.8 (CH), 129.5, 130.5, 135.1, 144.1, 155.5, 157.3 (C), 169.8 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (w), 2959 (s), 2932 (s), 2870 (m), 1652 (s), 1392 (s), 1243 (s), 1185 (s), 1049 (m), 801 (w). MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, [^{37}Cl], 14), 376 ($[M]^+$, [^{35}Cl], 42), 330 (100), 299 (84), 287 (7), 271 (8), 181 (9), 165 (6), 131 (8), 69 (19), 43 (12). HRMS (EI): Calcd. for $C_{21}H_{25}ClO_4$ ($[M]^+$, [^{35}Cl]): 376.14359; found: 376.142978.

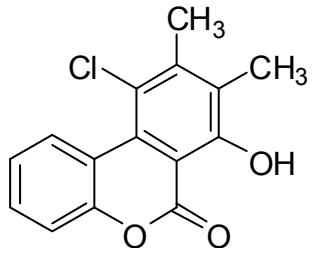
General procedure for synthesis of benzo[*c*]chromen-6-ones 27a-f by lactonization with BBr_3: To a CH_2Cl_2 solution of **26** was added BBr_3 at 0 °C. The solution was allowed to warm to 20 °C during 18 h. To the solution was added an aqueous solution of KO*t*Bu (0.1 M) and the solution was stirred for 15 min. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The product was purified by chromatography (silica gel; *n*-hexane/ EtOAc = 20:1) as a colourless solid.

10-Chloro-7-hydroxy-9-methyl-6*H*-benzo[*c*]chromen-6-one (27a):



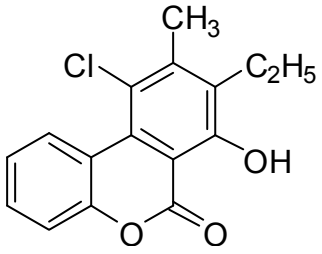
Starting with **26m** (0.104 g, 0.31 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.339 g, 1.35 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27a** was isolated as a colourless solid (0.063 g, 73%), mp. 107-110 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.45 (s, 3 H, CH_3), 6.96 (s, 1 H, Ar), 7.27-7.30 (m, 2 H, Ar), 7.41-7.46 (m, 1 H, Ar), 9.24-9.27 (m, 1 H, Ar), 11.78 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 21.0 (CH_3), 104.0 (C), 115.7 (CH), 116.1 (C), 117.2 (CH), 119.1 (C), 122.5, 125.8, 128.8 (CH), 129.3, 147.0, 148.5, 159.1 (C), 163.2 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3026 (w), 2957 (w), 2924 (w), 1667 (s), 1265 (s), 1218 (s), 1102 (s), 1031 (s), 763 (s). GC-MS (EI, 70 eV): *m/z* (%) = 262 ([M]$^+$, [^{35}Cl], 33), 260 ([M]$^+$, [^{35}Cl], 100), 225 (26), 197 (13), 169 (8), 139 (10), 112 (14) 69 (5). HRMS (EI): Calcd. for $C_{14}H_9ClO_3$ ([M]$^+$, [^{35}Cl]): 260.02347; found: 260.02249.

10-Chloro-7-hydroxy-8,9-dimethyl-6*H*-benzo[*c*]chromen-6-one (27b):



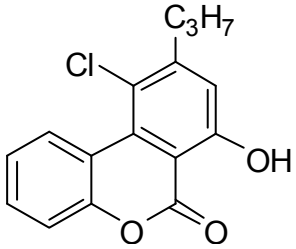
Starting with **26n** (0.129 g, 0.37 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.374 g, 1.49 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27b** was isolated as a colourless solid (0.080 g, 78 %), mp. 154-156 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.23 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 7.22-7.24 (m, 1 H, Ar), 7.26 (m, 1 H, Ar), 7.36-7.42 (m, 1 H, Ar), 9.17 (dd, *J* = 8.4 Hz, *J* = 2.1Hz, 1 H, Ar), 12.18 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 10.9, 16.9 (CH_3), 102.9 (C), 115.5 (CH), 116.2, 119.3 (C), 123.3 (CH), 124.7 (C), 125.8 (CH), 126.4 (C), 128.2 (CH), 145.1, 148.2, 157.3 (C), 163.6 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3446 (w), 2925 (m), 2851 (m), 1669 (s), 1597 (s), 1397 (s), 1254 (s), 1168 (s), 1113 (m), 780 (s). GC-MS (EI, 70 eV): *m/z* (%) = 276 ([M]$^+$, [^{37}Cl], 33), 274 ([M]$^+$, [^{35}Cl], 100), 259 (7), 239 (16), 211 (7), 181 (6), 165 (6), 152 (8), 115 (4), 76 (5). HRMS (EI): Calcd. for $C_{15}H_{11}ClO_3$ ([M]$^+$, [^{35}Cl]): 274.03912; found: 274.03900.

10-Chloro-8-ethyl-7-hydroxy-9-methyl-6*H*-benzo[*c*]chromen-6-one (27c):



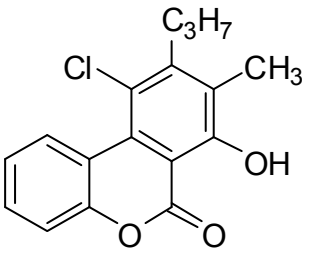
Starting with **26o** (0.110 g, 0.31 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.315 g, 1.26 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27c** was isolated as a colourless solid (0.060 g, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.06 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 2.71 (q, *J* = 7.4 Hz, 2 H, CH_2), 7.17-7.18 (m, 1 H, Ar), 7.21 (m, 1 H, Ar), 7.32-7.37 (m, 1 H, Ar), 9.08-9.11 (m, 1 H, Ar), 12.12 (s, 1 H, OH). ^{13}C NMR($CDCl_3$, 75 MHz): δ_C = 13.4, 18.6 (CH_3), 20.8 (CH_2), 105.4 (C), 117.8 (CH), 118.5, 121.8 (C), 124.6, 128.0 (CH), 128.8 (C), 130.5 (CH), 132.9, 146.8, 150.5, 159.5 (C), 165.9 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2969 (m), 2928 (m), 1663 (s), 1393 (s), 1242 (s), 1166 (s), 1116 (m), 758 (m). GC-MS (EI, 70 eV): *m/z* (%) = 290 ([M]$^+$, [^{37}Cl], 16), ,288 ([M]$^+$, [^{35}Cl], 49), 273 (100), 245 (3), 181 (7), 165 (6), 152 (7), 126 (3), 76 (5). HRMS (EI): Calcd. for $C_{16}H_{13}ClO_3$ ([M]$^+$, [^{35}Cl]): 288.05477; found: 288.05465.

10-Chloro-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (27d):



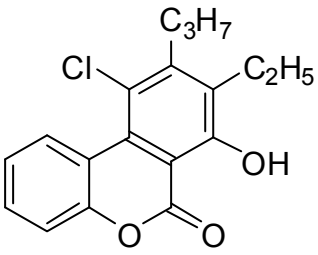
Starting with **26p** (0.107 g, 0.32 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0..320 g, 1.27 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27d** was isolated as a colourless crystaline (0.078 g, 88%), mp. 115-117 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.56-1.68 (m, 2 H, CH_2), 2.69-2.75 (m, 2 H, CH_2), 6.89 (s, 1 H, Ar), 7.21-7.22 (m, 1 H, Ar), 7.25 (m, 1 H, Ar), 7.36-7.42 (m, 1 H, Ar), 9.18-9.21 (m, 1 H, Ar),11.73 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.3 (CH_3), 22.7, 37.9 (CH_2), 106.3 (C), 117.9 (CH), 118.5 (C), 118.9 (CH), 121.0 (C), 124.7, 128.2, 131.1 (CH), 131.8, 150.0, 153.0, 161.4 (C), 165.4 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2965 (m), 2931 (m), 2876 (m), 1675 (s), 1606 (m), 1421 (s), 1232 (s), 1216 (s), 1105 (w), 765 (s). GC-MS (EI, 70 eV): *m/z* (%) = 290 ([M]$^+$, [^{37}Cl], 33), 288 ([M]$^+$, [^{35}Cl], 100), 260 (94), 253 (16), 225 (38), 197 (13), 181 (10), 168 (14), 152 (18), 139 (23), 126 (6), 75 (5). HRMS (EI): Calcd. for $C_{16}H_{13}ClO_3$ ([M]$^+$, [^{35}Cl]): 288.05477; found: 288.05478.

10-Chloro-7-hydroxy-8-methyl-9-propyl-6*H*-benzo[*c*]chromen-6-one (27e):



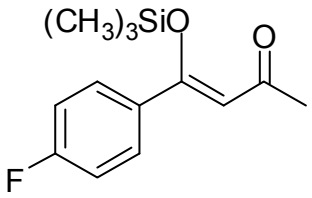
Starting with **26q** (0.129 g, 0.37 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.320 g, 1.27 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27e** was isolated as a light brown solid (0.060 g, 54%), mp. = 98-100 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.01 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.49-1.54 (m, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 2.83-2.89 (m, 2 H, CH_2), 7.23-7.24 (m, 1 H, Ar), 7.27 (m, 1 H, Ar), 7.36-7.42 (m, 1 H, Ar), 9.20 (d, *J* = 8.9 Hz, 1 H, Ar), 12.20 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 11.4, 13.4 (CH_3), 20.6, 33.1 (CH_2), 104.0 (C), 116.4 (CH), 117.3, 119.8 (C), 123.2, 126.8 (CH), 127.3, 127.7 (C), 129.1 (CH), 149.2, 149.9, 158.6 (C), 164.6 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2968 (m), 2925 (m), 2861 (m), 1671 (s), 1598 (m), 1394 (s), 1259 (s), 1221 (m), 1166 (s), 774 (s). GC-MS (EI, 70 eV): *m/z* (%) = 304 ([M]$^+$, [^{37}Cl], 33), 302 ([M]$^+$, [^{35}Cl], 100), 274 (52), 267 (22), 239 (44), 181 (16), 152 (17), 115 (5), 76 (5). HRMS (EI): Calcd. for $C_{17}H_{15}ClO_3$ ([M]$^+$, [^{35}Cl]): 302.07042; found: 302.07123.

10-Chloro-8-ethyl-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (27f):



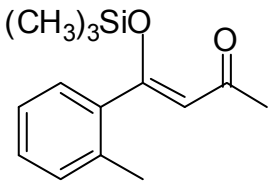
Starting with **26r** (0.200 g, 0.51 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.513 g, 2.12 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27f** was isolated as a light red solid (0.080 g, 48%), mp. = 98-100 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.03 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.13 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.55-1.60 (m, 2 H, CH_2), 2.75 (q, *J* = 7.4 Hz, 2 H, CH_2), 2.83-2.88 (m, 2 H, CH_2), 7.24-7.25 (m, 1 H, Ar), 7.27-7.28 (m, 1 H, Ar), 7.37-7.42 (m, 1 H, Ar), 9.20-9.23 (m, 1 H, Ar), 12.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 14.1, 14.9 (CH_3), 20.8, 23.1, 34.1 (CH_2), 105.7 (C), 117.8 (CH), 118.7, 121.4 (C), 124.6, 128.3 (CH), 129.4 (C), 130.6 (CH), 132.8, 150.6, 150.8, 160.0 (C), 166.1 (C=O). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2928 (m), 2869 (m), 1677 (s), 1597 (w), 1383 (s), 1243 (s), 1215 (s), 1116 (s), 753 (s). GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M]$^+$, [^{35}Cl], 33), 316 ([M]$^+$, [^{35}Cl], 100), 302 (8), 301 (40), 273.1 (51), 205 (7), 165 (4), 76 (4). HRMS (EI): Calcd. for $C_{18}H_{17}ClO_3$ ([M]$^+$, [^{35}Cl]): 316.08607; found: 316.08636.

1-(4-fluorophenyl)-3-methyl-1,3-butadienyl]oxy}(trimethyl)silane(28b):



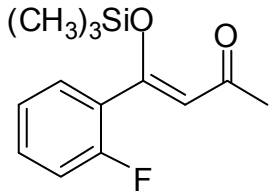
To a stirred benzene solution (83 mL), **17b** (5.01 g, 27.8 mmol), triethylamine (6.236 mL, 16.0 mmol), trimethylchlorosilane (6.326 mL, 18.0 mmol) was isolated **28b** as yellowish oil (6.055 g , 88 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.11 (m, 9 H, $3CH_3$), 2.18 (s , 3 H, CH_3), 6.03 (s, 1 H, CH), 6.79-6.88 (m, 2 H, Ar), 7.63-7.67 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.22 ($3CH_3$), 21.7 (CH_3), 104.6 (CH), 115.2 (2CH), 130.0 (2CH), 136.4, 166.5, 171.0 (C), 188.6 (C=O).

4-(2-methylphenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (28d):



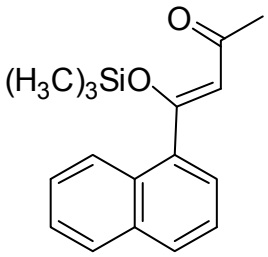
To a stirred benzene solution (90 mL), **17d** (4.769 g, 27.06 mmol), triethylamine (6.068 mL, 43.3 mmol). and trimethylchlorosilane (6.150 mL, 48.7 mmol) was isolated **38d** as yellowish oil (5.961 , 88.8 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.18 (m, 9 H, $3CH_3$), 2.48 (s (br), 3 H, CH_3), 2.58 (s (br), 3 H, CH_3), 6.01 (s (br), 1 H, CH), 7.33 (m, 1 H, CH_{Ar}), 7.35 (m, 1 H, CH_{Ar}), 7.38-7.39 (m, 1 H, CH_{Ar}), 7.51-7.55 (m, 1 H,CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.5 ($3CH_3$), 21.3 (CH_3), 108.4 (CH), 125.3, 128.2, 129.4, 130.9 (CH_{Ar}), 135.1, 141.5 (C_{Ar}), 170.2 (CO_{TMS}) 194.7 (C=O).

4-(2-fluorophenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (28g):



To a stirred benzene solution (90 mL), **17g** (5.405 g, 30.0 mmol), triethylamine (6.727 mL, 48.0 mmol). and trimethylchlorosilane (6.821 mL, 54.0 mmol) was isolated **28g** as yellowish oil (6.056 , 80 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.24 (s, 9 H, $3CH_3$), 2.33 (s, 3 H, CH_3), 5.99 (s, 1 H, CH), 6.93-6.99 (m, 1 H, Ar), 7.01-7.04 (m, 1 H, Ar), 7.10-7.13 (m, 1 H, Ar), 7.66-7.72 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, 0.4, 1.8, 22.2 (CH_3), 101.4, 108.6, 116.2, 128.2, 130.6 (CH), 133.2, 158.9, 162.6 (C) 194.7 (C=O).

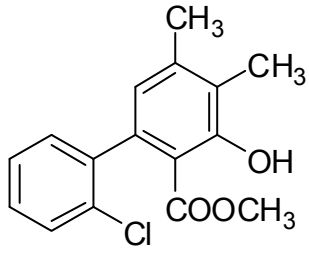
4-(5,8-dihydro-1-naphthalenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one(28k):



To a stirred benzene solution (30 mL) **17k** (2.1222 g, 10.0 mmol), triethylamine (2.24 mL, 16.0 mmol), trimethylchlorosilane (2.240 mL, 18.0 mmol) was isolated **28k** as yellowish oil (1.990 g , 70 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.23 (s, 9 H, $3CH_3$), 2.80 (s, 3 H, CH_3), 6.44 (s, 1 H, CH), 7.69-7.71 (m, 1 H, Ar), 7.83-7.86 (m, H, Ar), 7.99 (dd, *J*=6.8 Hz, *J*=1.1 Hz, 1 H, Ar), 8.11 (m, 1 H, Ar), 8.15-8.19 (m, 1 H, Ar), 8.46-8.54 (m, 1 H, Ar), 8.74-8.81 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4 ($3CH_3$), 21.9 (CH_3), 109.4, 124.7, 125.7, 126.6, 126.8, 128.3, 130.0, 130.7 (CH), 133.4, 133.7, 140.1, 171.0 (C), 194.3 (C=O).

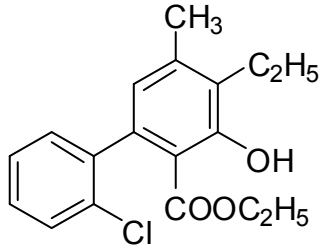
General procedure for the synthsis of flourenone 29a-c and 31a-f: Conc. sulfuric acid (12 mL) was added to **29** (1.00 mmol) and the solution was stirred for 1 h. Then water was added and aqueous solution was extracted with CH_2Cl_2 (3 x 50 mL). The organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 30:1 → 20:1) to give **29** and **31**.

Methyl 2'-chloro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (29a):



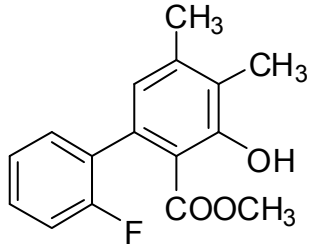
Starting with **4b** (0.603 g, 2.2 mmol), **28g** (0.535 g, 2.0 mmol) and TiCl4 (0.417 g, 2.2 mmol), **29a** was isolated (0.190 g, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 3.38 (s, 3 H, OCH_3), 6.42 (s, 1 H, CH_{Ar}), 7.06-7.10 (m, 1 H, CH_{Ar}), 7.12-7.16 (m, 2 H, CH), 7.25-7.28 (m, 1 H, CH_{Ar}), 11.34 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 20.9 (CH_3), 52.5 (OCH_3), 109.5 (C_{Ar}), 124.1 (CH_{Ar}), 125.1 (C_{Ar}), 126.6, 128.3, 128.9, 130.2 (CH_{Ar}), 133.1, 138.5, 142.4, 143.8 (C_{Ar}), 160.3 (COH_{Ar}), 171.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2958 (s), 2870 (m), 1655 (s), 1616 (m), 1503 (m), 1468 (m), 1415 (m), 1399 (m), 1246 (s), 1233 (s), 1097 (m), 750 (s). GC-MS (EI, 70 eV): *m/z* (%) = 290 ([M^+], 9), 255 (57), 240 (5), 223 (100), 195 (9), 165 (18), 152 (14), 128 (6). HRMS (EI): Calcd. for $C_{16}H_{15}ClO_3$: 290.07042; found: 290.07117.

Ethyl 2'-chloro-4-ethyl-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (29b):



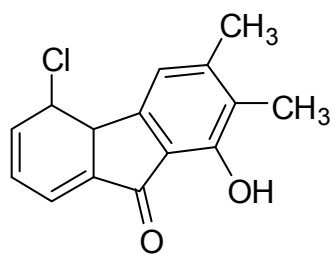
Starting with **4c** (0.651 g, 2.2 mmol), **28g** (0.535 g, 2.0 mmol) and TiCl4 (0.417 g, 2.2 mmol), **29b** was isolated (0.224 g, 35%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.66 (t, ^{3}J = 7.5 Hz, 3 H, CH_2CH_3), 1.08 (t, ^{3}J = 7.4 Hz, 3 H, OCH_2CH_3), 2.23 (s, 3 H, CH_3), 2.58-2.79 (m, 2 H, CH_2CH_3), 3.81-3.91 (m, 2 H, OCH_2CH_3), 6.40 (s, 1 H, CH_{Ar}), 7.07-7.10 (m, 1 H, CH_{Ar}), 7.11-7.15 (m, 2 H, CH), 7.24-7.27 (m, 1 H, CH_{Ar}), 11.47 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 18.4 (OCH_2CH_3), 18.5 (CH_3), 18.6 (CH_2CH_3), 59.8 (OCH_2CH_3), 108.3 (C_{Ar}), 122.8 , 126.7, 127.4, 128.8, 129.5 (CH_{Ar}), 131.9, 137.3, 141.4, 141.5 (C_{Ar}), 158.9 (COH_{Ar}), 170.0 (COGC-MS (EI, 70 eV): *m/z* (%) = 318 ([M^+], 10), 283 (50), 272 (11), 255 (17), 237 (100), 165 (21), 152 (6). HRMS (EI): Calcd. for $C_{18}H_{19}ClO_3$: 318.10172; found: 318.102.

Methyl 2'-fluoro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (29c):



Starting with **4b** (0.452 g, 1.65 mmol), **28h** (0.412 g, 1.5 mmol) and TiCl4 (0.313 g, 1.65 mmol), **29c** was isolated as a yellow solid (0.150 g, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3), 3.43 (s, 3 H, OCH_3), 6.51 (s, 1 H, CH_{Ar}), 6.90-6.96 (m, 1 H, CH_{Ar}), 7.04-7.07 (m, 1 H, CH_{Ar}), 7.11-7.22 (m, 2 H, CH_{Ar}), 11.27 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.5, 20.4 (CH_3), 51.7 (OCH_3), 109.3 (C_{Ar}), 114.4 (d, ^{2}J = 21.9 Hz, CH_{Ar}), 123.6 (d, ^{3}J = 3.9 Hz, CH_{Ar}), 124.3 (CH_{Ar}), 124.8 (C_{Ar}), 128.6 (d, ^{3}J = 7.8 Hz, CH_{Ar}), 130.1 (d, ^{3}J = 3.9 Hz, CH_{Ar}), 130.8 (d, ^{2}J = 8.5 Hz, C_{Ar}), 134.4, 143.4 (C_{Ar}), 159.7 (d, ^{1}J = 240.9 Hz, CF_{Ar}), 159.9 (COH_{Ar}), 171.6 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 274 ([M^+], 45), 242 (100), 227 (58), 213 (10), 199 (59), 183 (12), 170 (16). HRMS (EI): Calcd. for $C_{16}H_{15}FO_3$: 274.09997; found: 274.09978.

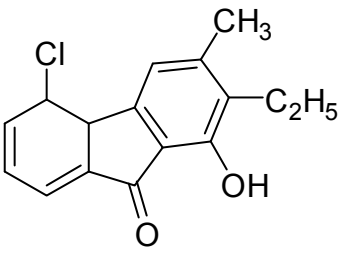
5-Chloro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (30a):



Conc. sulfuric acid (1.5 mL) and **29a** (31 mg, 0.12 mmol) **30a** was isolated as yellow solid (25 mg, 80%).^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 7.05-7:11 (m, 1 H, CH_{Ar}), 7.26-7.29 (m, 2 H, CH_{Ar}), 7.41 (dd, ^{3}J = 7.3 Hz, ^{4}J = 1.0 Hz, 1 H, CH_{Ar}), 8.65 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.6, 21.2 (CH_3), 115.0 (C_{Ar}), 118.8, 122.0 (CH_{Ar}), 126.3 (C_{Ar}), 129.3 (CH_{Ar}),

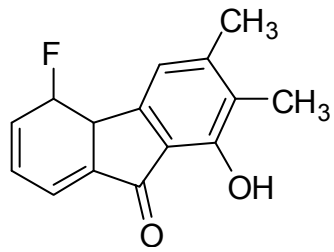
129.4 (C_{Ar}), 135.6 (CH_{Ar}), 136.9, 138.9, 140.4, 147.3 (C_{Ar}), 156.0 (COH_{Ar}), 194.8 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 258 ([M^+], 100), 243 (59), 215 (12), 195 (8), 176 (11), 165 (22), 152 (14). HRMS (EI): Calcd. for $C_{15}H_{11}ClO_2$: 258.04421; found: 258.04370

5-Chloro-2-ethyl-1-hydroxy-3-methyl-9*H*-fluoren-9-one (30b):



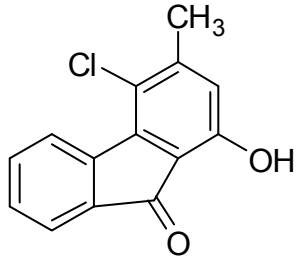
Conc. sulfuric acid (301 mL) and **29b** (80 mg, 0.30 mmol) **30b** was isolated as yellow solid (57 mg, 60%).^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (t, ^3J = 7.8 Hz, 3 H, CH_2CH_3), 2.25 (s, 3 H, CH_3), 2.54 (q, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 7.02-7.08 (m, 1 H, CH_{Ar}), 7.22-7.26 (m, 2 H, CH_{Ar}), 7.38 (dd, ^3J = 8.0 Hz, ^4J = 0.9 Hz,1 H, CH_{Ar}), 8.61 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (CH_2CH_3), 28.2 (CH_2CH_3), 20.1 (CH_3), 115.2 (C_{Ar}), 119.2, 121.9, 129.3 (CH_{Ar}), 129.5, 132.5 (C_{Ar}), 135.5 (CH_{Ar}), 137.0, 139.0, 140.2, 146.4 (C_{Ar}), 156.0 (COH_{Ar}), 194.8 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 272 ([M^+], 40), 257 (100), 229 (7), 189 (4), 165 (15). HRMS (EI): Calcd. for $C_{16}H_{13}ClO_2$: 272.05986; found: 272.05940.

5-Fluoro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (30c):



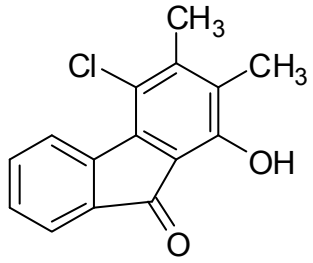
Conc. sulfuric acid (4.8 mL) and **29c** (111 mg, 0.41 mmol) **30c** was isolated as yellow solid (50 mg, 51%). ^{1}H NMR (300 MHz, CDCl3): δ = 2.04 (s, 3 H, CH3), 2.21 (s, 3 H, CH3), 6.88 (s, 1 H, CHAr), 7.00-7.18 (m, 2 H, CHAr), 7.29-7.32 (m, 1 H, CHAr), 8.51 (s, 1 H, OH) . 13C NMR (62 MHz, CDCl3): δ = 10.6, 21.0 (CH3), 114.7 (CAr), 118.6 (d, 4J = 4.1 Hz, CHAr), 119.7 (d, 4J = 3.4 Hz, CHAr), 122.2 (d, 2J = 19.6 Hz, CHAr), 125.9 (CAr), 129.7 (d, 2J = 17.6 Hz, CHAr), 130.2 (d, 3J = 5.9 Hz, CHAr), 137.3 (d, 3J = 4.4 Hz, CAr), 137.4 (CAr), 147.5 (CAr), 155.9 (COHAr), 157.6 (d, 1J = 253.5 Hz, CFAr), 195.0 (d, 4J = 2.6 Hz, CO. GC-MS (EI, 70 eV): m/z (%) = 242 ([M+], 100), 227 (81), 213 (9), 199 (22), 183 (12), 170 (16). HRMS (EI): Calcd. for C15H11FO2 : 242.07376; found: 242.07375

4-Chloro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (31a):



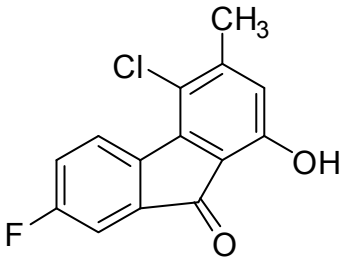
Conc. sulfuric acid (8.5 mL) and **26a** (195 mg, 0.71 mmol) **31a** was isolated as yellow solid (70 mg, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 6.57 (s, 1 H, Ar), 7.18-7.25 (m, 1 H, Ar), 7.38-7.44 (m, 1 H, Ar), 7.55 (d, *J* = 7.2 Hz, 1 H, Ar), 8.03 (d, *J* = 7.6 Hz, 1 H, Ar), 8.43 (s, 1 H OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 117.5 (C), 120.5 (CH), 122.0 (C), 124.4, 124.8, 129.6 (CH), 135.0 (C), 135.1 (CH), 139.9, 143.3, 147.9. 156.0 (C), 195.2 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 246 ([M]$^+$, [^{37}Cl], 50), 244 ([M]$^+$, [^{35}Cl], 100), 216 (10), 181 (21), 152 (37), 126 (3), 90 (7), 76 (17). HRMS (EI): Calcd. for $C_{14}H_9ClO_2$ ([M]$^+$, [^{35}Cl]): 244.02856; found: 244.02847.

4-Chloro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (31b):



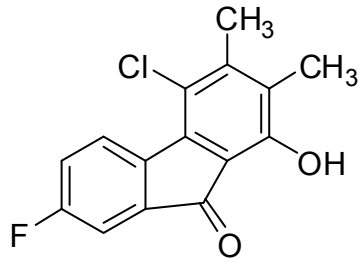
Conc. sulfuric acid (3.1 mL) and **26b** (74 mg, 0.27 mmol) **31b** was isolated as yellow solid (60 mg, 86%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.07 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 7.11-7.22 (m, 1 H, Ar), 7.36-7.42 (m, 1 H, Ar), 7.50-7.53 (m, 1 H, Ar), 7.96-7.99 (m, 1 H, Ar), 8.76 (s, 1 H OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 11.8, 17.1 (CH_3), 116.0, 122.0 (C), 123.8, 124.1 (CH), 127.9 (C), 128.7 (CH), 134.3 (C), 134.5 (CH), 136.5, 143.3, 144.9, 154.3 (C), 195.5 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 260 ([M]$^+$, [^{37}Cl], 50), 258 ([M]$^+$, [^{35}Cl], 100), 243 (12), 223 (29), 195 (11), 176 (9), 165 (27), 152 (12) 139 (6), 115 (5), 82 (8). HRMS (EI): Calcd. for $C_{15}H_{11}ClO_2$ ([M]$^+$, [^{35}Cl]): 258.04421; found: 258.04414.

4-Chloro-7-fluoro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (31c):



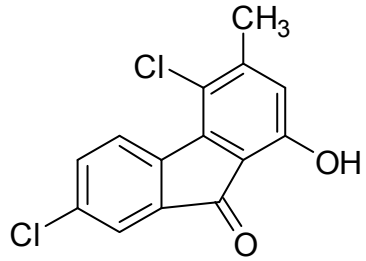
Conc. sulfuric acid (2.31 mL) and **26e** (57 mg, 0.19 mmol), **31c** was isolated as yellow solid (30 mg, 61%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 6.58 (s, 1 H, Ar), 7.06-7.13 (m, 1 H, Ar), 7.09 (dd, *J* = 7.2 Hz, *J* = 2.4 Hz, 1 H, Ar), 8.01-8.05 (m, 1 H, Ar), 8.33 (s, 1 H OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.9 (CH_3), 110.5 (CH), 116.3, 118.9 (C), 119.7, 120.4, 124.7 (CH), 135.9, 137.6, 137.9, 147.1, 154.7 (C), 162.5 (d, ^{1}J = 251.1 Hz, CF), 192.2 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 264 ([M]$^+$, [^{37}Cl], 50), 262 ([M]$^+$, [^{35}Cl], 100), 234 (15), 199 (13), 152 (7), 132 (7), 110 (8), 99 (11), 84 (11). HRMS (EI): Calcd. for $C_{14}H_8ClFO_2$ ([M]$^+$, [^{35}Cl]): 262.01914; found: 262.01903.

4-Chloro-7-fluoro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (31d):



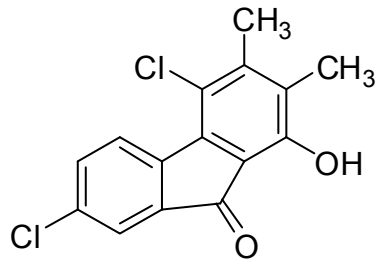
Conc. sulfuric acid (3.06 mL) and **26f** (79 mg, 0.25 mmol), **31d** was isolated as yellow solid (38 mg, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 6.98-7.05 (m, 1 H, Ar), 7.13-7.18 (m, 1 H, Ar), 7.85-7.89 (m, 1 H, Ar), 8.58 (s, 1 H OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.8, 15.2 (CH_3), 109.6 (CH), 114.3 (C), 118.3 (CH), 119.6 (C), 123.5 (CH), 125.8, 133.9, 134.8, 136.9, 148.4, 152.4 (C), 161.5 (d, ^{1}J = 251.0 Hz, CF), 191.7 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M]$^{+}$, [^{37}Cl], 50), 276 ([M]$^{+}$, 100), 261 (16), 241 (31), 213 (12), 183 (25), 170 (11), 138 (6), 91 (7). HRMS (EI): Calcd. for $C_{15}H_{10}ClFO_2$ ([M]$^{+}$, [^{35}Cl]): 276.03479; found: 276.03433.

4,7-Dichloro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (31e):



Conc. sulfuric acid (3.3 mL) and **26h** (85 mg, 0.27 mmol), **31e** was isolated as yellow solid (65 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 6.63 (s, 1 H, Ar), 7.44 (dd, *J* = 8.1 Hz, *J* = 2.1 Hz, 1 H, Ar), 7.53 (m, 1 H, Ar), 8.00 (d, *J* = 8.0 Hz, 1 H, Ar), 8.35 (s, 1 H OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 117.4 (C), 120.8 (CH), 122.2 (C), 124.7, 125.8, 135.4 (CH), 135.9, 136.6, 139.2, 141.4, 148.5, 156.2 (C), 193.7 (C=O). GC-MS (EI, 70 eV): *m/z* (%) = 282 ([M]$^{+}$, [2x^{37}Cl], 15), 280 ([M]$^{+}$, [^{37}Cl], [^{35}Cl], 65), 278 ([M]$^{+}$, [2x^{35}Cl] 100), 251 (11), 215 (12), 186 (24), 152 (57), 137 (8/), 123 (12) 107 (21), 93 (17), 75 (9). HRMS (EI): Calcd. for $C_{14}H_8Cl_2O_2$ ([M]$^{+}$, [2x^{35}Cl]): 277.98959; found: 277.98973.

4,7-Dichloro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (31f):



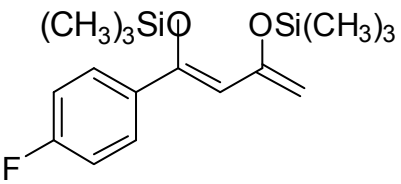
Conc. sulfuric acid (2.76 mL) and **26i** (74 mg, 0.23 mmol), **31f** was isolated as yellow solid (50 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 7.36 (dd, *J* = 8.1 Hz, *J* = 2.1 Hz, 1 H, Ar), 7.49-7.50 (m, 1 H, Ar), 7.94-7.97 (m, 1 H, Ar), 8.58 (s, 1 H OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 17.6 (CH_3), 116.5, 123.1 (C), 124.6, 125.7

(CH), 128.8 (C), 134.4 (C), 135.3, 136.3, 136.5, 141.8, 145.9, 154.9 (C), 194.4 (C=O).GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M]$^+$, [2x^{37}Cl], 15),294 ([M]$^+$, [^{37}Cl], [^{35}Cl], 65), 292 ([M]$^+$, [2x^{35}Cl], 277 (10), 257 (15), 229 (9), 199 (5), 165 (11), 150 (6), 111 (7), 82 (10).

General procedure for synthesis of Aryl-1,3-Bis(silylenol ehters) (32a-l):

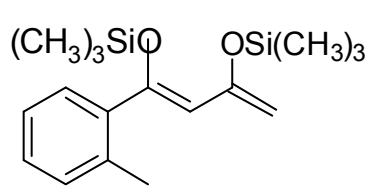
The reaction was carried out analogously to a known procedure. To a stirred THF solution (30 mL) of LDA (36 mmol, 1.5 equiv) was added **28** (7.788 g, 24.0 mmol) at -78 °C. After the solution was stirred for 1 h, trimethylchlorosilane (4.548 mL, 36 mmol) was added. The solution was allowed to warm to room temperature during 12 h with stirring. The solvent was removed in vacuo, and to the residue was added hexane (100 mL) to give asuspension. The latter was filtered under argon atmosphere. The filtrate was distilled in vacuo to give **32.**The compounds were used directly after there preparation.

4-(4-fluorophenyl)-2,2,8,8-tetramethyl-6-methylene-3,7-dioxa-2,8-disila-4-nonene (32b):



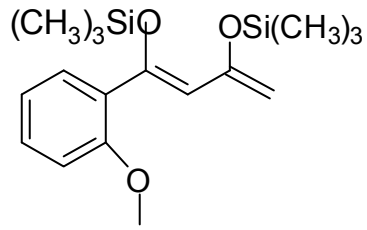
To a stirred THF solution (30 mL) of LDA (36 mmol, 1.5 equiv), **28b** (7.788 g, 24.0 mmol), trimethylchlorosilane (4.548 mL, 36 mmol) **32b** was isolated a dark red oil (6.490 g, 83 %): The compound was used directly after its preparation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.01-0.09 (m, 9 H, $3CH_3$), 0.12 (m, 9 H, $3CH_3$), 4.36-4.37 (m, 1 H, CH_2), 4.79-4.81 (m, 1 H, CH_2), 5.30-5.31 (s, 1 H, CH), 6.78-6.87 (m, 2 H, Ar), 7.30-7.34 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, ($3CH_3$), 0.8 ($3CH_3$), 95.8 (CH_2), 109.1 (CH), 114.9 (2CH), 128.0 (2CH), 135.5, 150.0, 152.8, 161.1(C).

2,2,8,8-tetramethyl-6-methylene-4-(2-methylphenyl)-3,7-dioxa-2,8-disila-4-nonene (32d):



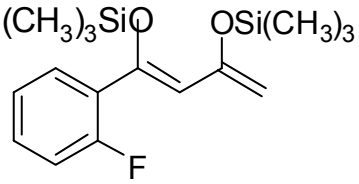
To a stirred THF solution (25 mL) of LDA (30 mmol, 1.5 equiv), **28d** (4.967 g, 20.0 mmol), trimethylchlorosilane (3.789 mL, 30.0 mmol) **32d** was isolated as a dark red oil (4.808 g, 75 %): The compound was used directly after its preparation.^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.13-0.20 (s, 9 H, $3CH_3$), 0.31-0.36 (s, 9 H, $3CH_3$), 2.50 (s, 3 H, CH_3), 4.59-4.60 (m, 1 H, CH_2), 5.11 (m, 1 H, CH_2), 5.12-5.18 (s, 1 H, CH), 7.24-7.25 (m, 1 H, Ar), 7.27 (m, 1 H, Ar), 7.28-7.30 (m, 1 H, Ar), 7.32-7.38 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4, ($3CH_3$), 0.5 ($3CH_3$), 20.2 (CH_3) ,95.1 (CH_2), 111.1, 125.5, 128.4, 129.0, 130.3 (CH), 136.1, 136.5, 139.6, 152.8 (C).

4-(2-methoxyphenyl)-2,2,8,8-tetramethyl-6-methylene-3,7-dioxa-2,8-disila-4-nonene



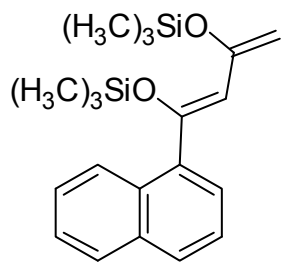
(32e): To a stirred THF solution (21.6 mL) of LDA (26 mmol, 1.3 equiv), **28e** (5.284 g, 20.0 mmol), trimethylchlorosilane (3.789 mL, 30.0 mmol) **32e** was isolated as a reddish yellow oil (4.70 g, 70%): The compound was used directly after its preparation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 (s, 9 H, $3CH_3$), 0.35 (s, 9 H, $3CH_3$), 3.79 (s, 3 H, OCH_3), 4.60 (d, *J*=1.7 Hz, 1 H, CH_2), 5.14 (s, 1 H, CH_2), 5.39 (d, *J*=1.7 Hz, 1 H, CH_2), 6.96-7.00 (m, 1 H, Ar), 7.02-7.06 (m, 1 H, Ar), 7.35-7.39 (m, 1 H, Ar), 7.42-7.45 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5, 0.6, 0.7, 0.8, 0.9, 2.3 (CH_3), 55.6 (OCH_3), 95.6 (CH_2), 111.5, 111.8, 120.6, 129.9, 130.6 (CH), 131.4, 132.4, 149.8, 153.0 (C).

4-(2-fluorophenyl)-2,2,8,8-tetramethyl-6-methylene-3,7-dioxa-2,8-disila-4-nonene (32g):



To a stirred THF solution (25 mL) of LDA (30 mmol, 1.5 equiv), **28g** (5.046 g, 20.0 mmol), trimethylchlorosilane (3.789 mL, 30.0 mmol) **32g** was isolated as a dark red oil (4.868 g, 75 %): The compound was used directly after its preparation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19-0.20 (s, 9 H, $3CH_3$), 0.34-0.37 (s, 9 H, $3CH_3$), 4.61-4.63 (m, 1 H, CH_2), 5.10-5.11 (m, 1 H, CH_2), 5.54-5.55 (s, 1 H, CH), 7.01-7.17 (m, 1 H, Ar), 7.19-7.22 (m, 1 H, Ar), 7.31-7.38 (m, 1 H, Ar), 7.51-7.56 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3, ($3CH_3$), 0.6 ($3CH_3$), 96.4 (CH_2), 113.0, 116.2, 123.8, 127.4, 130.0 (CH), 146.1, 152.6, 157.9 161.1 (C).

4-(5,8-dihydro-1-naphthalenyl)-2,2,8,8-tetramethyl-6-methylene-3,7-dioxa-2,8-disila-4-

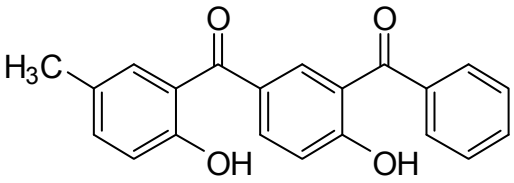


nonene(32k): To a stirred THF solution (8.75 mL) of LDA (10.5 mmol, 1.5 equiv) **28k** (1.990 g, 10.0 mmol), trimethylchlorosilane (1.062 mL, 10.5 mmol) 32k was iosolated as a dark yellow viscos (1.7828 g, 71.4 %): The compound was used directly after its preparation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.28 (s, 9 H, $3CH_3$), 0.66 (s, 9 H, $3CH_3$), 4.94 (m, 1 H, CH_2), 5.51 (s, 1 H, CH_2), 5.68 (m, 1 H, CH_2), 7.85-7.86 (m, 2 H, Ar), 7.89-7.92 (m, 2 H, Ar), 8.19-8.23 (m, 2 H, Ar), 8.64-8.67 (m, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.4 ($3CH_3$), 0.6 ($3CH_3$), 95.3 (CH_2), 112.0, 126.0, 126.3, 126.6, 128.6, 129.0, 130.9, 131.6 (CH), 133.7, 134.0, 137.8, 152.1, 152.9 (C).

General procedure 1 (synthesis of benzophenones) 34a-s:

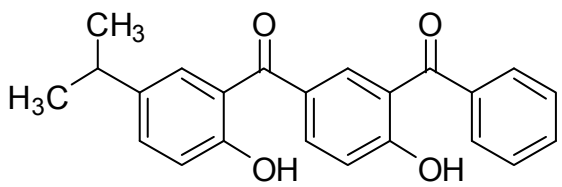
To 3-formylchromone **33** (1.0 equiv.) was added Me_3SiOTf (0.3 equiv.) at 20 °C. After stirring for 10 min CH_2Cl_2 (8 mL) was added, the solution was cooled to 0 °C and the 1,3-bis-silyl enol ether **32** (1.3 equiv.) was added. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-heptane/ CH_2Cl_2 = 10:1 → 3:1).

(3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-5-methylphenyl)methanone (34a):



Starting with **33a** (188 mg 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32a** (398 mg, 1.3mmol), **34a** was isolated as a yellow viscous oil (118 mg, 34%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, CH_3), 6.85 (d, *J* = 8.2 Hz, 1 H, CH_{Ar}), 7.09 (d, *J* = 8.7 Hz, 1 H, CH_{Ar}), 7.16-7.26 (m, 2 H, CH_{Ar}), 7.41-7.44 (m, 2 H, CH_{Ar}), 7.48-7.53 (m, 1 H, CH_{Ar}), 7.60-7.63 (m, 2 H, CH_{Ar}), 7.81 (dd, *J* = 8.7 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 7.94-7.95(m, 1 H, CH_{Ar}), 11.47 (s, 1 H, OH), 12.35 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5 (CH_3), 95.6 (C), 117.3 (CH_{Ar}), 117.4, 117.63 (C_{Ar}), 117.66, 125.9 (CH_{Ar}), 126.7 (C), 127.5 (CH_{Ar}), 127.7 (C_{Ar}), 128.0 (CH), 131.2 (C), 131.3, 131.5, 136.0, 136.1, 136.2 (CH), 159.9, 165.2 (C), 197.7, 200.2 (C=O). IR (neat): $\tilde{\nu}$ = 3061 (m), 3038 (m), 2959 (s), 2924 (s), 1630 (s), 1590 (s), 1480 (s), 1486 (m), 1408 (m), 1423 (m), 1350 (s), 1290 (s), 1256 (s), 1135 (m), 978 (m), 924 (w), 826 (s), 791 (s), 636 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = .221 (4.33), 257 (4.17), 340 (3.69). GC-MS (CI, 70 eV): *m/z* (%) = 333 ([M+1]$^+$, 100), 285 (10), 257 (10), 225 (10), 189 (10), 93 (20). HRMS (CI): Calcd. for $C_{21}H_{17}O_4$ ([M+1]$^+$): 333.1121; found: 333.1116.

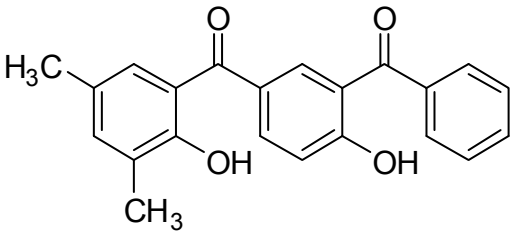
(3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-5-isopropylphenyl)methanone (34b):



Starting with **33b** (147 mg, 0.67 mmol), Me_3SiOTf (39 mg, 0.18 mmol) and 1,3-bis-silyl enol ether **32a** (270 mg, 0.83 mmol), **34b** was isolated as a yellow viscous oil (81 mg, 37%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (d, *J* = 7.1 Hz, 6 H, CH_3), 2.67-2.76 (m, 1 H, CH),

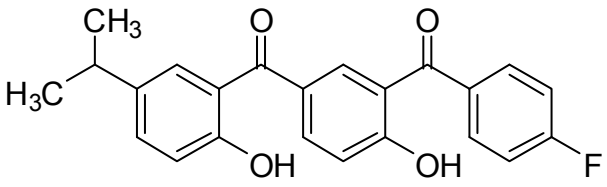
6.96 (d, J = 8.3 Hz, 1 H, CH_{Ar}), 7.13 (d, J = 8.7 Hz, 1 H, CH_{Ar}), 7.27-7.31 (m, 2 H, CH_{Ar}), 7.40-7.45 (m, 2 H, CH_{Ar}), 7.49-7.54 (m, 1 H, CH_{Ar}), 7.60-7.61 (m, 1 H, CH_{Ar}), 7.62-7.63 (m, 1 H, A CH_{Ar}), 7.84 (dd, J = 8.7 Hz, J = 2.1 Hz, 1 H, CH_{Ar}), 8.01(m, 1 H, CH_{Ar}), 11.55 (s, 1 H, OH), 12.44 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ =24.3 ($2CH_3$), 33.6 (CH), 118.8, (CH_{Ar}), 118.9, 119.0 (C_{Ar}), 129.0 ($2CH_{Ar}$), 129.0 ($2C_{Ar}$), 129.3 ($2CH_{Ar}$), 130.3, 132.8, 135.0, 136.2 (CH_{Ar}), 137.5 (C_{Ar}), 137.6 (CH_{Ar}), 139.4 (C_{Ar}), 161.5, 166.8 (C_{Ar}), 199.1, 201.8 (C=O). IR (KBr): $\tilde{\nu}$ = 2958 (m), 2922 (m), 2856 (w), 1632 (s), 1598 (s), 1481 (m), 1445 (w), 1355 (s), 1288 (m), 1255 (s), 1115 (w), 981 (w), 949 (w), 840 (w), 794 (m), 635 (w) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.50), 263 (4.47), 341 (3.95). GC-MS (EI, 70 eV): *m/z* (%) = 360 ($[M]^+$, 75), 345 (20), 281 (11), 225 (10), 197 (11), 172 (10), 163 (43) 147 (100), 101 (6), 77 (20), 51 (4). HRMS (EI): Calcd. for $C_{23}H_{20}O_4$ ($[M]^+$): 360.1356; found: 360.1345.

(3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-3,5-dimethylphenyl)methanone (3c):



Starting with **33c** (139 mg, 0.6 mmol), Me_3SiOTf (39 mg, 0.18 mmol) and 1,3-bis-silyl enol ether **32a** (239 mg, 0.78 mmol), **34c** was isolated as a yellow solid (70 mg, 31%), m.p. = 116-118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.86 (br s, 6 H, CH_3), 7.07 (s, 1 H, CH_{Ar}), 7.10 (m, 2 H, CH_{Ar}), 7.39-7.43 (m, 2 H, CH_{Ar}), 7.47 - 7.53 (m, 1 H, CH_{Ar}), 7.60-7.63 (m, 2 H, CH_{Ar}), 7.80 (dd, J = 8.5 Hz, J = 1.9 Hz, 1 H, CH_{Ar}), 7.93 (m, 1 H, CH_{Ar}), 11.77 (s, 1 H, OH), 12.34 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 19.5 (CH_3), 116.9, 117.3, (C_{Ar}), 117.5, 125.9 (CH_{Ar}), 126.0, 126.3 (C_{Ar}), 127.5, 128.0 (CH_{Ar}), 128.1 ($2C_{Ar}$), 129.0, 131.2, 131.4, 134.6, 136.1, 137.2 (CH_{Ar}), 158.0, 165.1 (C_{Ar}), 198.0, 200.2 (C=O). IR (KBr): $\tilde{\nu}$ = 2960 (m), 2923 (m), 2867 (w), 1633 (s), 1597 (s), 1433 (m), 1445 (w), 1355 (s), 1318 (w), 1288 (s), 1256 (s), 1215 (s), 1139 (m), 1049 (w), 795 (s) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.51), 262 (4.40), 340 (4.00). GC-MS (EI, 70 eV): *m/z* (%) = 346 ($[M]^+$, 56), 148 (100), 120 (36), 105 (14), 91 (12), 77 (26), 65 (4). HRMS (EI): Calcd. for $C_{22}H_{18}O_4$ ($[M]^+$):346.1199; found: 346.1202.

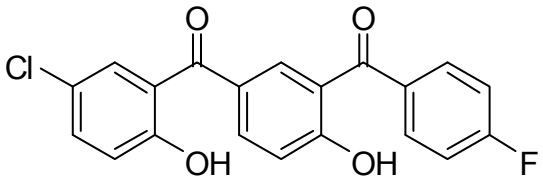
[3-(4-Fluorobenzoyl)-4-hydroxyphenyl]-(2-hydroxy-5-isopropylphenyl)methanone (34d):



Starting with **33b** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32b** (421 mg, 1.3 mmol), **34d** was isolated as a yellow solid (115 mg, 30%), m.p. = 134-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (d, J = 7.1 Hz, 6 H, CH_3),

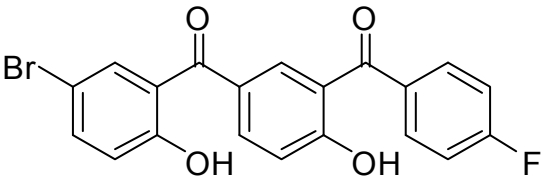
2.72 (m, 1 H, CH), 6.92 (d, J = 8.4 Hz, 1 H, CH_{Ar}), 7.08-7.13 (m, 3 H, CH_{Ar}), 7.26 (m, 1 H, CH_{Ar}), 7.30 (dd, J = 8.5 Hz, J = 2.5 Hz, 1 H, CH_{Ar}) , 7.64-7.69 (m, 2 H, CH_{Ar}), 7.84 (dd, J = 8.5 Hz, J = 2.1 Hz, 1 H, CH_{Ar}), 7.97-7.98 (m, 1 H, CH_{Ar}), 11.52 (s, 1 H, OH), 12.28 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.9 ($2CH_3$), 32.7 (CH), 114.8, 115.1, 117.4, 117.6 (CH_{Ar}), 127.8, (C_{Ar}), 128.8, 130.6, 130.7 (CH_{Ar}), 132.2, 132.3 (C_{Ar}), 133.7, 134.4, 136.2 (CH_{Ar}), 138.0, 160.1, 162.5, 165.2, 165.9 (C_{Ar}), 197.5, 198.6 (C=O). IR (neat): $\tilde{\nu}$ = 3062 (w), 2959 (m), 2871 (m), 1635 (w), 1472 (w), 1201 (w), 1158 (m), 1110 (m), 1073 (m), 871 (m), 852 (m), 793 (m), 638 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.65), 263 (4.50), 340 (4.12). MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, 47), 363 (12), 162 (43), 147 (100), 123 (11), 91 (13), 69 (7), 57 (6). HRMS (EI): Calcd. for $C_{23}H_{19}O_4F$: 378.1262; found: 378.1257.

(5-Chloro-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (34e):



Starting with **33d** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32b** (421 mg, 1.3 mmol), **34e** was isolated as a yellow viscous oil (101 mg, 27%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.95(d, J = 8.7 Hz, 1 H, CH_{Ar}), 7.06-7.09 (m, 1 H, CH_{Ar}), 7.11-713 (m, 1 H, CH_{Ar}), 7.17 (d, J = 7.1 Hz, 1 H, CH_{Ar}), 7.38 (dd, J = 8.7 Hz, J = 2.5 Hz, 1 H, CH_{Ar}), 7.49-7.50 (m, 1 H, CH_{Ar}), 7.63-7.68, (m, 1 H, CH_{Ar}), 7.72-7.75 (m, 1 H, CH_{Ar}), 7.84 (dd, J = 8.6 Hz, J = 2.1 Hz, 1 H, CH_{Ar}), 7.96-7.97 (m, 1 H, CH_{Ar}), 11.51 (s, 1 H, OH), 12.39 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 113.5, 113.9 (CH), 117.5 (C_{Ar}), 118.0 (CH_{Ar}), 118.5 (C_{Ar}), 119.2 ($2CH_{Ar}$), 122.3, 126.9, 127.4 (C_{Ar}), 131.7 ($2CH_{Ar}$), 134.7, 135.05 (CH_{Ar}), 135.08 (C_{Ar}), 135.9 (CH_{Ar}), 160.3, 165.6 (C_{Ar}), 195.5, 199.1 (C=O). IR (KBr): $\tilde{\nu}$ = 2960 (w), 2925 (w), 1626 (s), 1581 (s), 1468 (m), 1255 (s), 1217 (s), 841 (s), 796 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.30), 259 (4.06), 338 (3.64). MS (CI, 70 eV): *m/z* (%) = 373 ($[M+1]^+$, [^{37}Cl], 10), 371 ($[M+1]^+$, [^{35}Cl], 20), 342([^{37}Cl], 14), 340 ([^{35}Cl], 28), 285 (18), 229 (20), 177 (100), 111 (8), 85 (12), 69 (20). HRMS (CI): Calcd. for $C_{20}H_{12}O_4ClF$ ($[M+1]^+$, ^{35}Cl): 371.3142; found: 371.3143.

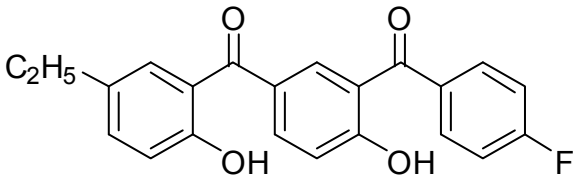
(5-Bromo-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (34f):



Starting with **33e** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3mmol) and 1,3-bis-silyl enol ether **32b** (421 mg, 1.3 mmol), **34f** was isolated as yellow solid (146 mg, 3 5%), m.p. =

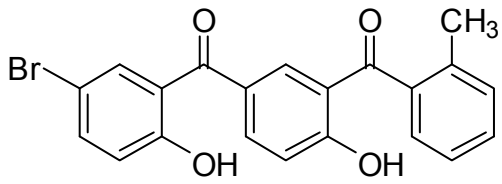
118-120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.89 (d, *J* = 8.9 Hz, 1 H, CH_{Ar}), 7.14-7.19 (m, 3 H, CH_{Ar}), 7.50 (dd, *J* = 8.9 Hz, *J* = 2.4 Hz, 1 H, CH_{Ar}), 7.65 (m, 1 H, CH_{Ar}), 7.67-7.72 (m, 2 H, CH_{Ar}), 7.86 (dd, *J* = 8.5 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 7.90-7.91 (m, 1 H, CH_{Ar}), 11.50 (s, 1H, OH), 12.33 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.6 (C_{Ar}), 116.3, 116.6 (CH_{Ar}), 118.5 (C_{Ar}), 119.8 (CH_{Ar}), 120.6 (C_{Ar}), 121.1 (CH_{Ar}), 128.3 (C_{Ar}), 132.1, 132.2 (CH_{Ar}), 133.4, 133.5 (C_{Ar}), 135.0, 136.0, 137.5, 139.2 (CH_{Ar}), 162.2, 167.1 (C_{Ar}), 197.9, 199.8 (C=O). IR (KBr): $\tilde{\nu}$ = 3069 (w), 2956 (m), 2900 (w), 1627 (s), 1585 (s), 1466 (s), 1341 (m), 1287 (m), 1253 (s), 1213 (s), 1072 (m), 843 (s), 610 (w) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.30), 259 (4.06), 338 (3.64). MS (EI, 70 eV): *m/z* (%) = 416 ($[M]^+$, [^{81}Br], 100), 414 ($[M]^+$, [^{79}Br], 100), 319 (7), 243 (12), 216 ([^{81}Br], 80), 214 ([^{79}Br], 80), 200 ([^{81}Br], 96), 198 ([^{79}Br], 96), 172 (10), 147 (67), 123 (75), 95 (55), 57 (25). HRMS (EI): Calcd. for $C_{20}H_{12}O_4{}^{79}BrF$ ($[M]^+$, ^{81}Br): 413.9897; found: 413.9897.

(5-Ethyl-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (34g):



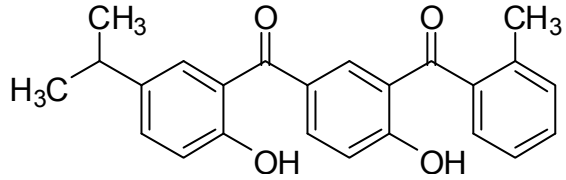
Starting with **33f** (202 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32b** (421 mg, 1.3 mmol), **34g** was isolated as yellow viscous (135 mg, 37%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.48 (q, *J* = 7.8 Hz, 2 H, CH_2), 6.89-6.92 (m, 1 H, CH_{Ar}), 7.09-7.14 (m, 3 H, CH_{Ar}), 7.25-7.29 (m, 2 H, CH_{Ar}), 7.65-7.70 (m, 2 H, CH_{Ar}), 7.82-7.85 (m, 1 H, CH_{Ar}), 7.95-7.96 (m, 1 H, CH_{Ar}), 11.50 (s, 1H, OH), 12.24 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.9 (CH_3), 29.2 (CH_2), 116.2, 116.5 (CH_{Ar}), 118.8 (C_{Ar}), 118.9, 119.0 (CH_{Ar}), 129.2 ($2CH_{Ar}$), 131.6, 132.1 (C_{Ar}), 132.2 (CH_{Ar}), 133.6 (C_{Ar}), 134.7 ($2CH_{Ar}$), 135.7 (CH_{Ar}), 136.6, 137.6, 161.5, 166.5 (C_{Ar}), 199.0, 200.0 (C=O). IR (neat): $\tilde{\nu}$ = 3063 (w), 2964 (m), 2930 (m), 2872 (w), 1631 (s), 1599 (s), 1481 (s), 1409 (w), 1351 (s), 1292 (s), 1255 (s), 1214 (s), 1157 (s), 1073 (w), 882 (w), 844 (s), 612 (w) cm^{-1}. MS (CI, 70 eV): *m/z* (%) = 365 ($[M+1]^+$, (100), 340 (10), 303 (7), 243 (8), 177 (20), 149 (25), 133 (20), 96 (10). HRMS (CI): Calcd. for $C_{22}H_{18}O_4F$ ($[M]^+$): 365.11836; found: 365.11842.

(5-Bromo-2-hydroxyphenyl)-[4-hydroxy-3-(2-methylbenzoyl)phenyl]methanone (3h):



Starting with **33e** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32d** (416 mg, 1.3 mmol), **34h** was isolated as a yellow solid (160 mg, 39%), m.p. = 119-121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 6.84 (d, *J* = 8.7 Hz, 1 H, CH_{Ar}), 7.13 (d, *J* = 7.7 Hz, 1 H, CH_{Ar}), 7.17 (m, 1 H, CH_{Ar}), 7.25-7.26 (m, 1 H, CH_{Ar}), 7.28 (m, 1 H, CH_{Ar}), 7.30-7.33 (m, 1 H, CH_{Ar}), 7.44 (dd, *J* = 8.9 Hz, *J* = 2.5 Hz, 1 H, CH_{Ar}), 7.52-7.53 (m, 1 H, CH_{Ar}), 7.64-7.65 (m, 1 H, CH_{Ar}), 7.83 (dd, *J* = 8.5 Hz, *J* = 2.3 Hz, 1 H, CH_{Ar}), 11.54 (s, 1 H, OH), 12.68 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 110.5, 119.4 (C_{Ar}), 119.6 (CH_{Ar}), 120.5 (CH_{Ar}), 121.0, 126.0, 127.8 (CH_{Ar}), 128.3 (C_{Ar}), 131.2, 131.7, 134.9 (CH_{Ar}), 136.2, 136.5, 136.9 (C_{Ar}), 137.8, 139.1 (CH_{Ar}), 162.2, 167.2 (C_{Ar}), 197.8, 204.4 (C=O). IR (KBr): $\tilde{\nu}$ = 3431 (w), 3064 (w), 3022 (w), 2957 (w), 2924 (w), 2854 (w), 1632 (s), 1597 (s), 1463 (s), 1381 (m), 1319 (s), 1255 (s), 1237 (m), 1209 (s), 1101 (w), 992 (w), 931 (m), 769 (m), 769 (s), 708 (w), 652 (w) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 252 (4.52), 330 (4.18). MS (EI, 70 eV): *m/z* (%) = 412 ([M]$^+$, [^{81}Br], 52), 410 ([M]$^+$, [^{79}Br], 51), 397 ([^{81}Br], 16), 395 ([^{79}Br], 17), 340 (2), 267 (15), 237 (11), 211 (100), 199 ([^{81}Br], 33), 197 ([^{79}Br], 31), 194 (22), 161 (10), 147 (22), 119 (52), 91 (63), 69 (22). HRMS (EI): Calcd. for $C_{21}H_{15}O_4Br$ ([M]$^+$, ^{79}Br): 410.0148; found: 410.0140.

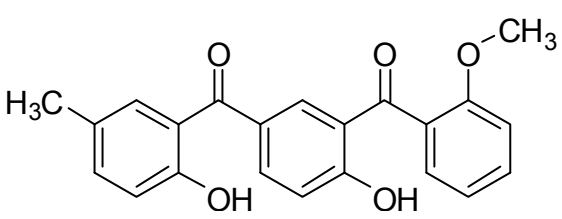
(2-Hydroxy-5-isopropylphenyl)-[4-hydroxy-3-(2-methylbenzoyl)phenyl]methanone (34i):



Starting with **33b** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32d** (416 mg, 1.3 mmol), **34i** was isolated as a yellow solid (105 mg, 28%), m.p. = 138-140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 7.1 Hz, 6 H, CH_3), 2.26 (s, 3 H, CH_3), 2.61-2.75 (m, 1 H, CH), 6.88 (d, *J* = 8.5 Hz, 1 H, CH_{Ar}), 7.12 (d, *J* = 8.7 Hz, 1 H, CH_{Ar}), 7.17 (m, 1 H, CH_{Ar}), 7.18-7.19 (m, 2 H, CH_{Ar}), 7.22 (s, 1 H, CH_{Ar}), 7.24-7.25 (m, 1 H, CH_{Ar}), 7.27-7.31 (m, 1 H, CH_{Ar}), 7.68 (m, 1 H, CH_{Ar}) 7.84 (dd, *J* = 8.5 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 11.56 (s, 1 H, OH), 12.65 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.0 (CH_3), 24.3 ($2CH_3$), 33.6 (CH), 118.8, 119.2 (CH_{Ar}), 119.5 (C_{Ar}), 125.9, 127.7 (CH_{Ar}), 129.3 (C_{Ar}), 130.3, 131.0, 131.6, 135.0 (CH_{Ar}), 135.1, 136.0 (C_{Ar}), 136.2 (CH_{Ar}), 137.2 (C_{Ar}), 138.1 (CH_{Ar}), 139.4, 161.6, 166.8 (C_{Ar}), 199.0, 204.6 (C=O). IR (KBr): $\tilde{\nu}$ = 3430 (w), 3055 (w), 3029 (w), 2961 (m), 2924 (m), 2872 (w), 1632 (s), 1593 (s), 1483 (s), 1356 (s), 1316 (s),

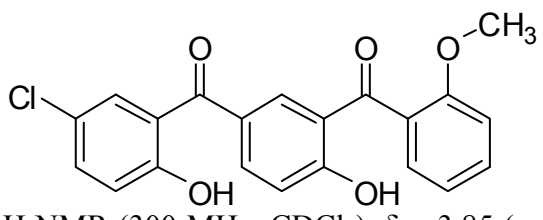
1256 (s), 1211 (s), 1140 (w), 1118 (w), 1097 (w), 981 (w), 900(w), 846 (w), 794 (s), 636 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 255 (4.20), 339 (3.80). MS (EI, 70 eV): *m/z* (%) = 374 ($[M]^+$, 78), 359 (19), 316 (3), 139 (5), 211 (16), 172 (8), 163 (48), 162 (46), 147 (100), 119 (10), 97 (8), 91 (26), 83 (10), 69 (18), 57 (16). HRMS (EI): Calcd. for $C_{24}H_{22}O_4$ ($[M]^+$): 374.1513; found: 374.1505.

[4-Hydroxy-3-(2-methoxybenzoyl)phenyl]-(2-hydroxy-5-methylphenyl)methanone (3j):



Starting with **33a** (188 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32e** (437 mg, 1.3 mmol), **34j** was isolated as a yellow viscous oil (131 mg, 36%). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 3.72 (s, 3 H, OCH_3), 6.84-6.88 (m, 1 H, CH_{Ar}), 6.96 (d, *J* = 8.5 Hz, 1 H, CH_{Ar}), 7.01 (dd, *J* = 7.6 Hz, *J* = 1.5 Hz, 1 H, CH_{Ar}), 7.08 (d, *J* = 8.8 Hz, 1 H, CH_{Ar}), 7.18-7.27 (m, 3 H, CH_{Ar}), 7.41 (ddd, *J*= 8.5 Hz, *J* = 8.5 Hz, *J* = 1.8 Hz, 1 H, CH_{Ar}), 7.73 (m, 1H, CH_{Ar}), 7.80 (dd, *J* = 8.8 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 11.54 (s, 1 H, OH), 12.53 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 (CH_3), 56.2 (OCH_3), 112.2, 118.6, 118.7 (CH_{Ar}), 119.0, 120.0 (C_{Ar}), 121.1 (CH_{Ar}), 127.3, 128.0, (C_{Ar}), 129.1 (CH_{Ar}), 132.7, (C_{Ar}), 132.8, 132.9, 136.5, 137.5, 137.7 (CH_{Ar}), 157.0, 161.2, 166.2 (C_{Ar}), 199.0, 202.3 (C=O). IR (neat): $\tilde{\nu}$ = 2957 (s), 2934 (s), 2853 (s), 1731 (m), 1670 (w), 1603 (s), 1491 (s), 1446 (s), 1464 (s), 1363 (m), 1286 (m), 1258 (s), 1184 (m), 1163 (m), 1079 (m), 1024 (m), 847 (w), 754 (m), 647 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 362 ($[M]^+$, 71), 347 (5), 331 (27), 227 (18), 197 (23), 167 (8), 149 (23), 135 (100), 77 (18), 57 (14), 43 (12). HRMS (EI): Calcd. for $C_{22}H_{18}O_5$ ($[M]^+$): 362.1149; found: 362.1139.

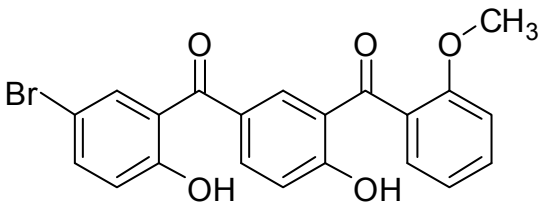
(5-Chloro-2-hydroxyphenyl)-[4-hydroxy-3-(2-methoxybenzoyl)phenyl]methanone (34k):



Starting with **33d** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32e** (437 mg, 1.3 mmol), **34k** was isolated as a yellow viscous oil (121 mg, 34%). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 6.92 (d, *J* = 8.9 Hz, 1 H, CH_{Ar}), 6.97 (d, *J* = 8.4 Hz, 1 H, CH_{Ar}), 7.11 (d, *J* = 8.8 Hz, 1 H, CH_{Ar}), 7.19 (s, 1 H, CH_{Ar}), 7.26 (dd, *J* = 7.5 Hz, *J* = 2.5 Hz, 1 H, CH_{Ar}), 7.34 (dd, *J* = 8.9 Hz, , *J* = 2.6 Hz 1 H, CH_{Ar}), 7.39-7.45 (m, 2 H, CH_{Ar}), 7.70-7.71 (m, 1 H, CH_{Ar}), 7.83 (dd, *J*= 8.7 Hz, *J* = 2.3 Hz, 1 H, CH_{Ar}), 11.60 (s, 1 H, OH), 12.58 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.0 (OCH_3), 110.9 (CH),

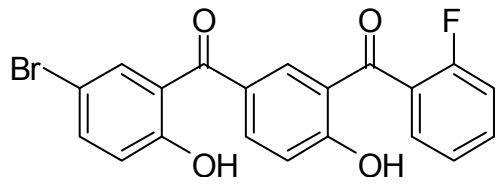
117.9, 118.6 (C_{Ar}), 119.1, 119.9 (CH_{Ar}), 122.2 (C_{Ar}), 125.8 (CH_{Ar}), 126.8 (C_{Ar}), 127.7 ($2CH_{Ar}$), 130.5 (C_{Ar}), 131.6, 134.9, 135.2, 136.1 (CH_{Ar}), 155.6, 160.4, 165.3 (C_{Ar}), 196.6, 200.8 (C=O). IR (KBr): $\tilde{\nu}$ = 3433 (w), 2960 (s), 2924 (s), 2853 (s), 1634 (s), 1590 (m), 1465 (m), 1433 (w), 1354 (m), 1281 (w), 1260 (s), 1100 (s), 1019 (s), 802 (s), 754 (w), 637 (w) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.20), 256 (3.97), 337 (3.32). MS (EI 70 eV): *m/z* (%) = 384 ($[M]^+$, [^{37}Cl], 37), 382 ($[M]^+$, ^{35}Cl], 92), 367 (22), 353 ([^{37}Cl], 51), 351, ([^{35}Cl], 100), 249 ([^{37}Cl], 51), 247, ([^{35}Cl], 24), 210 (32), 197 (96), 157 ([^{37}Cl], 19), 155 ([^{35}Cl], (68), 147 (44), 135 (86), 108 (64), 97 (32), 83 (32), 77 (43), 57 (57), 43 (12). HRMS (EI): Calcd. for $C_{21}H_{15}O_5Cl$ ($[M]^+$, ^{35}Cl): 382.0602; found: 382.0602.

(5-Bromo-2-hydroxyphenyl)[4-hydroxy-3-(2-methoxybenzoyl)phenyl]methanone (34l):



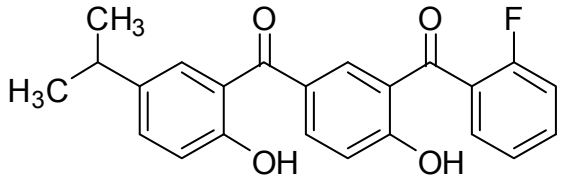
Starting with **33e** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32e** (437mg, 1.3 mmol), **33l** was isolated as yellow solid (163 mg, 38%), m.p. = 151-152 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 6.86 (d, *J* = 8.5 Hz, 1 H, CH_{Ar}), 6,96-6.99 (m, 2 H, CH_{Ar}), 7.10 (d, *J* = 8.5 Hz, 1 H, CH_{Ar}), 7.26 (dd, *J* = 7.6 Hz, *J* = 1.9 Hz, 1 H, CH_{Ar}), 7.38-7.48 (m, 2 H, CH_{Ar}), 7.55-7.56 (m, 1 H, CH_{Ar}), 7.70-7.71(m, 1 H, CH_{Ar}), 7.81 (dd, *J* = 7.4 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 11.61 (s, 1 H, OH), 12.59 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.4 (OCH_3), 110.0 (C_{Ar}), 112.4, 119.2 (CH_{Ar}), 119.9, 120.6 (C_{Ar}), 120.9, 121.3 (CH_{Ar}), 127.1, 128.2 (C_{Ar}), 129.1, 133.0, 134.9, 136.6, 137.5, 139.1 (CH_{Ar}), 157.0, 162.2, 166.7 (C_{Ar}), 198.0, 202.2 (C=O). IR (KBr): $\tilde{\nu}$ = 3441 (m), 2958 (m), 2923 (s), 2852 (m), 1637 (s), 1596 (s), 1480 (m), 1464 (s), 1431 (w), 1342 (m), 1320 (s), 1285 (s), 1160 (w), 1102 (m), 1024 (m), 839 (w), 795 (s) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (3.90), 255 (3.64), 336 (3.19). MS (EI, 70 eV): *m/z* (%) = 428 ($[M]^+$, [^{81}Br], 62), 426 ($[M]^+$, [^{79}Br], 60), 397 [^{81}Br], 81), 395 ([^{79}Br], 82), 293 ([^{81}Br], 12), 291([^{79}Br], 13), 197 (100), 173 (7), 147 (31), 135 (57), 108 (37), 77 (27), 57 (19), 43 (15). HRMS (EI): Calcd. for $C_{21}H_{15}O_5Br$ ($[M]^+$, ^{79}Br): 426.0097; found: 426.0088. Anal.: calcd. for $C_{21}H_{15}O_5Br$ (426.00, ^{79}Br): C 59.21, H 3.55 found: C 59.29, H 3.89.

(5-Bromo-2-hydroxyphenyl)-[3-(2-fluorobenzoyl)-4-hydroxyphenyl]methanone (34m):



Starting with **33e** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32g** (421 mg, 1.3 mmol), **34m** was isolated as yellow solid (155 mg, 38%), m.p. = 105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86 (d, *J* = 8.3 Hz, 1 H, CH_{Ar}), 7.14 (d *J* = 8.7 Hz, 1 H, CH_{Ar}), 7.18-7.23 (m, 1 H, CH_{Ar}), 7.25-7.28 (m, 1 H, CH_{Ar}), 742-7.46 (m, 1 H, CH_{Ar}), 7.47 (m, 1H, CH_{Ar}), 7.49-7.51 (m, 1H, CH_{Ar}), 7.65-7.66 (m, 1H, CH_{Ar}), 7.74-7.76 (m, 1 H, CH_{Ar}), 7.88 (dd, *J* = 8.5 Hz, *J* = 2.3 Hz, 1 H, CH_{Ar}), 11.55 (s, 1 H, OH), 12.36 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 110.6 (C_{Ar}), 116.8, 117.1 (CH_{Ar}), 119.2 (C_{Ar}), 119.7 (CH_{Ar}), 120.5 (C_{Ar}), 120.9, 125.6 (CH_{Ar}), 128.5, 130.5 (C_{Ar}), 134.9, 136.2, 136.3, 138.0, 139.2 (CH_{Ar}), 139.3, 162.2, 166.8 (C_{Ar}), 197.8, 198.6 (C=O). IR (neat): $\tilde{\nu}$ = 3054 (w), 2956 (s), 2924 (s), 2852 (s), 1629 (s), 1590 (s), 1465 (s), 1418 (s), 1418 (s), 1304 (m), 1253 (s), 1208 (s), 1122 (s), 927 (m), 844 (s), 763 (s), 629 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 218 (4.50), 256 (4.23), 340 (3.79). MS (EI, 70 eV): *m/z* (%) = 416 ([M]$^+$, [^{81}Br], 97), 414 ([M]$^+$, [^{79}Br], 97), 397 ([^{81}Br], 6), 395 ([^{79}Br], 6), 216 ([^{81}Br], 71), 214 ([^{79}Br], 71), 199 ([^{81}Br], 100), 197 ([^{79}Br], 100), 147 (47), 123 (51), 95 (22), 57 (11). HRMS (EI): Calcd. for $C_{20}H_{12}O_4BrF$ ([M]$^+$, ^{79}Br): 413.9897; found: 413.9891.

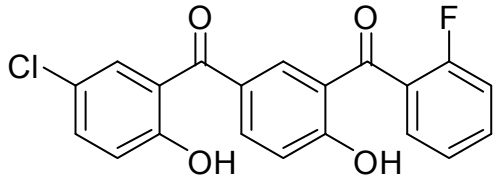
[3-(2-Fluorobenzoyl)-4-hydroxyphenyl]-(2-hydroxy-5-isopropylphenyl)methanone (34n):



Starting with **33b** (216 mg, 1.0 mmol), Me_3SiOTf (66mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32g** (421 mg, 1.3 mmol), **34g** was isolated as a yellow solid (130 mg, 35%), m.p. = 105-107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 7.1 Hz, 6 H, CH_3), 2.25 (m, 1 H, CH), 6.75 (d, *J* = 8.5 Hz, 1 H, CH_{Ar}), 6.95-6.98 (m, 1 H, CH_{Ar}), 7.01-7.07 (m, 3 H, CH_{Ar}), 7.12 (dd, *J* = 8.5 Hz, *J* = 2.3, 1 H, CH_{Ar}), 7.23-7.28 (m, 1 H, CH_{Ar}), 7.33-7.38 (m, 1 H, CH_{Ar}), 7.70-7.72 (m, 2 H, CH_{Ar}), 11.34 (s, 1 H, OH), 12.30 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.9, 25.0 (CH_3), 34.2 (CH), 117.3, 117.6, 119.4, 120.0 (CH) $_{Ar}$, 120.5 (C), 124.0 (CH_{Ar}), 125.0 (C_{Ar}), 125.7 (CH_{Ar}), 126.4, 126.7, 130.1 (C_{Ar}), 131.0, 135.6, 136.5, 139.9 (CH_{Ar}), 140.1, 161.6, 167.0 (C_{Ar}), 199.4, 199.6 (C=O). IR (KBr): $\tilde{\nu}$ = 3431 (w), 2960 (m), 2924 (w), 2868 (w), 1634 (s), 1612 (s), 1588 (s), 1483 (s), 1357 (s) 1251 (s), 1212 (s), 840 (m), 765 (s), 634 (m) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = . MS (EI, 70 eV): *m/z* (%) =

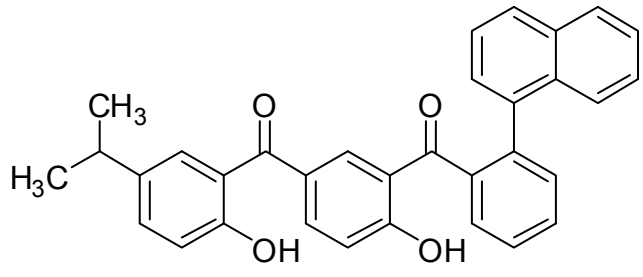
378 ([M]$^+$,13), 343 (5), 163 (25), 162 (29), 147 (100), 123 (68), 121 (7), 91 (31), 69 (14), 57 (19), 41 (19). HRMS (EI): Calcd. for $C_{23}H_{19}O_4F$ ([M]$^+$): 378.1262; found: 378.1257.

(5-Chloro-2-hydroxyphenyl)-[3-(2-fluorobenzoyl)-4-hydroxyphenyl]methanone (34o).



Starting with **33d** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32g** (421 mg, 1.3 mmol), **34o** was isolated as a yellow solid (163 mg, 44%), m.p. = 123-125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.91 (d, *J* = 8.9 Hz, 1 H, CH_{Ar}), 7.14 (d, *J* = 8.7 Hz, 1 H, CH_{Ar}), 7.18-7.19 (m, 1 H, CH_{Ar}), 7.22-7.25 (m, 1 H, CH_{Ar}), 7.35 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1 H, CH_{Ar}), 7.42-7.45 (m, 1 H, CH_{Ar}), 7.46-7.50 (m, 1H, CH_{Ar}), 7.53 (m, 1 H, CH_{Ar}), 7.75-7.77 (m, 1 H, CH_{Ar}), 7.89 (dd, *J* = 8.9 Hz, *J* = 2.1 Hz, 1 H, CH_{Ar}), 11.53 (s, 1 H, OH), 12.34 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 117.5, 117.8 (CH_{Ar}), 119.9, 120.0 (C_{Ar}), 120.6, 121.3, 124.6 (CH_{Ar}), 126.4, 126.6, 129.3 (C_{Ar}), 131.1, 132.8 (CH_{Ar}), 134.9 (C_{Ar}), 135.0, 137.2, 138.8 (CH_{Ar}), 162.5, 167.5 (C_{Ar}), 198.5, 199.3 (C=O). IR (neat): $\tilde{\nu}$ = 3077 (w), 2956 (s), 2924 (s), 2853 (s), 1675 (s), 1633 (s), 1598 (s), 1466 (s), 1417 (s), 1253 (s), 1208 (s), 1140 (s), 1097 (m), 950 (m), 844 (s), 763 (s) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 221 (4.41), 258 (4.27), 340 (3.82). MS (EI, 70 eV): *m/z* (%) = 372 ([M]$^+$, [^{37}Cl], 38), 370 ([M]$^+$, [^{37}Cl], 100), 340 ([^{37}Cl], 8), 338 ([^{35}Cl],10), 267 (26), 243 (10), 216 (51), 197 (20), 177 (19), 155 (96), 147 (33), 123 (42), 95 (25), 57 (27). HRMS (EI): Calcd. for $C_{20}H_{12}O_4ClF$ ([M]$^+$,^{37}Cl): 370.0403; found: 370.0402.

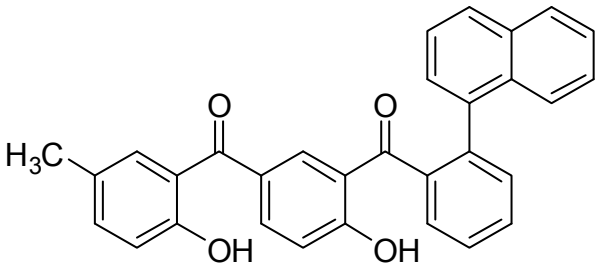
(2-Hydroxy-5-isopropylphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (34p):



Starting with **33b** (216mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32k** (463 mg, 1.3 mmol), **34p** was isolated as a yellow viscous oil (130 mg, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.9 Hz 6 H, CH_3), 2.44-2.56 (m, 1 H, (CH), 7.11 (m, 1 H, CH_{Ar}), 7.16-7.18 (m, 1 H, CH_{Ar}), 7.19-7.22 (m, 1 H, CH_{Ar}), 7.41-7.44 (m, 1 H, CH_{Ar}), 7.45 (m, 1 H, CH_{Ar}), 7.47 (m, 2 H, CH_{Ar}), 7.48-7.52 (m, 1 H, CH_{Ar}), 7.74-7.75 (m, 1 H, CH_{Ar}), 7.82-7.84 (m, 1 H, CH_{Ar}), 7.85-7.86 (m, 1 H, CH_{Ar}), 7.87-7.89 (m, 1 H, CH_{Ar}), 7.92 (dd, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H, CH_{Ar}), 11.52 (s, 1 H, OH), 12.73 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.9 ($2CH_3$), 33.4 (CH), 118.7,

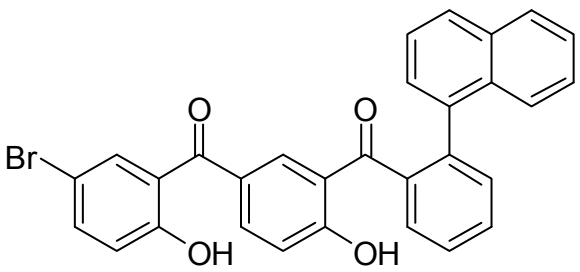
119.3 (CH_{Ar}), 120.0 (C_{Ar}), 124.7, 125.2, 126.7, 127.2, 128.0, 129.0 (CH_{Ar}), 129.3 (C_{Ar}), 130.2 (CH_{Ar}), 130.6 (C_{Ar}), 131.8 (CH_{Ar}), 134.1, 134.9 (C_{Ar}), 135.0, 136.3, 138.2 (CH_{Ar}), 139.6, 161.5, 166.9, 189.6 (C_{Ar}), 198.8, 204.0 (C=O). IR (neat): $\tilde{\nu}$ = 3058 (m), 2959 (s), 2926 (m), 2870 (m), 1630 (s), 1589 (s), 1508 (m), 1480 (s), 1354 (s), 1296 (m), 1252 (s), 1211 (s), 1146 (m), 1129 (w), 1045 (w), 908 (m), 843 (s), 793 (s), 733 (s) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 410 ($[M]^+$, 86), 395 (16), 247 (14), 197 (17), 163 (49), 147 (100), 127 (30), 91 (19), 65 (5). HRMS (EI): Calcd. for $C_{27}H_{22}O_4$ ($[M]^+$): 410.1513; found: 410.1512.

(2-Hydroxy-5-methylphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (34q):



Starting with **33a** (188 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32k** (463 mg, 1.3 mmol), **34q** was isolated as a yellow solid (130 mg, 34%), m.p. = 112-114 °C. ^1H NMR (300 MHz, $CDCl_3$), δ = 2.00 (s, 3 H, CH_3), 6.77 (d, *J* = 8.4 Hz, 1 H, CH_{Ar}), 7.06-7.07 (m, 1 H, CH_{Ar}), 7.08-7.11 (m, 1 H, CH_{Ar}), 7.13 (m, 1 H, CH_{Ar}), 7.41-7.42 (m, 1 H, CH_{Ar}), 7.43 (m, 1 H, CH_{Ar}), 7.44-7.47 (m, 2 H, CH_{Ar}), 7.68-7.69 (m, 1 H, CH_{Ar}), 7.78-7.80 (m, 1 H, CH_{Ar}), 7.81-7.82 (m, 1 H, CH_{Ar}), 7.83-7.85 (m, 1 H, CH_{Ar}), 7.89 (dd, *J* = 7.6 Hz, *J* = 1.5 Hz, 1 H, CH_{Ar}), 11.42 (s, 1 H, OH), 12.65 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3 (CH_3), 117.2 (CH_{Ar}), 117.3 (C_{Ar}), 117.7 (CH_{Ar}), 118.6 (C_{Ar}), 123.2, 123.8, 125.4, 125.8, 126.6, 127.5 (CH_{Ar}), 127.7, 129.1 (C_{Ar}), 130.4, 131.2 (CH_{Ar}), 132.2, 133.5 (C_{Ar}), 135.0, 136.1, 136.7 (CH_{Ar}), 159.8, 165.4, 188.1 (C_{Ar}), 197.3, 202.4 (C=O). UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 222 (4.88), 256 (4.32), 341 (4.02. GC-MS (CI 70 eV): *m/z* (%) = 383 ($[M+1]^+$,100), 305 (5), 267 (4), 229 (3), 177 (5), 122 (3), 88 (3). HRMS (CI): Calcd. for $C_{25}H_{19}O_4$ ($[M+1]^+$): 383.1278: found: 383.1297.

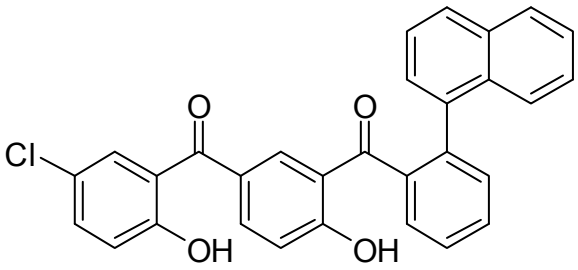
(5-Bromo-2-hydroxyphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (3r):



Starting with **33e** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32k** (463 mg, 1.3 mmol), **34r** was isolated as a yellow solid (166 mg, 36%), m.p. = 125-127 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 8.9 Hz, 1 H, CH_{Ar}), 7.14-7.15 (m, 1 H, CH_{Ar}), 7.17 (s, 1 H, CH_{Ar}) 7.38 (m, 1 H, CH_{Ar}), 7.41-7.43 (m, 1 H, CH_{Ar}),

7.44-7.45 (m, 1 H, CH_{Ar}), 7.49-750 (m, 1 H, CH_{Ar}), 7.52-7.53 (m, 1 H, CH_{Ar}), 7.71-7.72 (m, 1 H, CH_{Ar}), 7.80-7.82 (m, 1 H, CH_{Ar}), 7.83-7.84 (m, 1 H, CH_{Ar}), 7.85-7.88 (m, 1 H, CH_{Ar}), 7.92 (dd, J = 7.3 Hz, J = 1.9 Hz, 1 H, CH_{Ar}), 11.46 (s, 1 H, OH), 12.74 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.1 (C_{Ar}), 118.2 (CH_{Ar}), 118.5, 119.0 (C_{Ar}), 119.5, 123.3, 123.8, 125.7, 125.8, 126.6 (CH_{Ar}), 126.8 (C_{Ar}), 127.6 (CH_{Ar}), 129.2 (C_{Ar}), 130.7 (CH_{Ar}), 132.8, 133.1 (C_{Ar}), 133.5, 135.1, 136.5, 137.7 (CH_{Ar}), 160.7, 165.9 (C_{Ar}), 196.4, 202.2 (C=O). IR (KBr): $\tilde{\nu}$ = 3047 (w), 2957 (w), 2924 (w), 2853 (w), 1626 (s), 1588 (s), 1507 (w), 1464 (s), 1336 (s), 1251 (s), 1209 (s), 1045 (w), 915 (s), 777 (s) cm^{-1}. UV-Vis (nm, CH_3CN): λ_{max} (lg ε) = 257 (3.89), 339 (3.48). GC-MS (EI 70 eV): *m/z* (%) = 448 ($[M]^+$, [^{81}Br], 89), 446 ($[M]^+$, [^{79}Br], 90), 368 (6), 249 ([^{81}Br], 89), 247 ([^{79}Br], 89), 231 (13), 155 (35), 128 (100), 63 (10). HRMS (EI): Calcd. for $C_{24}H_{15}O_4{}^{79}Br$: 446.0148 ($[M]^+$, ^{79}Br): found: 446.0161.

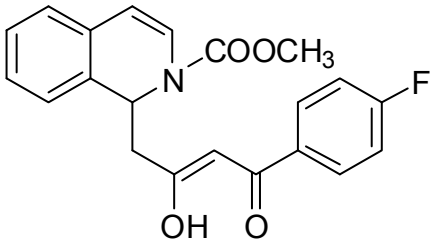
(5-Chloro-2-hydroxyphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (34s):

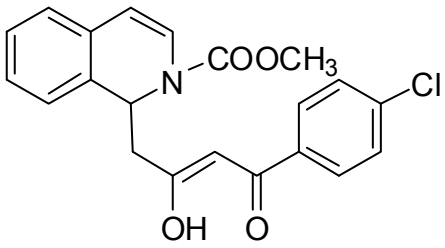


Starting with **33d** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol) and 1,3-bis-silyl enol ether **32k** (463 mg, 1.3 mmol), **34s** was isolated as a yellow viscous oil (144 mg, 36%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.84 (d, J = 8.1 Hz, 1 H, CH_{Ar}), 7.15-7.16 (m, 1 H, CH_{Ar}), 7.18 (s, 1 H, CH_{Ar}), 7.28 (dd, J = 8.9 Hz, J = 2.5 Hz, 1 H, CH_{Ar}), 7.35 (m, 1 H, CH_{Ar}), 7.44-7-47 (m, 2 H, CH_{Ar}), 7.51-7.52 (m, 1 H, CH_{Ar}), 7.53 (s, 1 H, CH_{Ar}), 7.71-7.72 (m, 1 H, CH_{Ar}), 7.81-7.83 (m, 1 H, CH_{Ar}), 7.85-7.86 (m, 1 H, CH_{Ar}), 7.91-7.95 (m, 1 H, CH_{Ar}), 11.45 (s, 1 H, OH), 12.73 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 119.6 (CH_{Ar}), 119.8, 120.0 (C_{Ar}), 120.5 (CH_{Ar}), 123.6 (C_{Ar}), 124.7, 125.2 (CH_{Ar}), 127.3 ($2CH_{Ar}$), 128.1 (CH_{Ar}), 128.3 (C_{Ar}), 129.0 (CH_{Ar}), 130.6 (C_{Ar}), 131.9, 132.1 (CH_{Ar}), 134.2, 134.6 (C_{Ar}), 136.3, 136.6, 137.9 (CH_{Ar}), 161.7, 167.3 (C_{Ar}), 197.9, 203.6 (C=O). MS (CI, 70 eV): *m/z* (%) = 405 ($[M+1]^+$, [^{37}Cl], 50), 403 ($[M+1]^+$, [^{37}Cl], 100), 285 (10), 257 (12), 229 (10), 177 (13), 125 (14), 97 (15), 85 (20), 69 (21). HRMS (CI): Calcd. for $C_{24}H_{16}O_4{}^{35}Cl$ ($[M+1]^+$, ^{37}Cl): 403.0732; found: 403.0731.

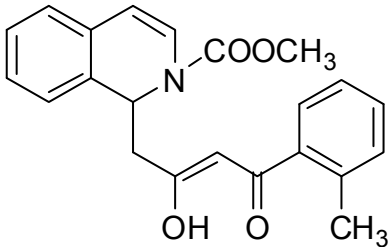
General procedure for the synthesis of 36a-r and 38f-g: To a CH_2Cl_2 solution (40 mL) of isoquinoline (0.520 g, 4.0 mmol) was added the 1,3-bis-silyl enol ether (8.0 mmol) and methyl chloroformate (0.460 g, 4.8 mmol) at 0 °C. The solution was stirred for 2 h at 0 °C and for 12 h at 20 °C. A saturated aqueous solution of ammonium chloride (20 mL) was added and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1).

1-[(*Z*)-4-(4-Fluorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2-(methoxycarbonyl)-isoquinolinium (36a): Starting with isoquinoline (0.258 g, 2.00 mmol), **32b** (0.973 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36a** was prepared as an orange red solid (0.450 g, 68%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.39 – 2.72 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.67 (s, 3 H, COO*CH3*, isomer 1, isomer 2), 5.77 (m, 1 H, NCH, isomer 1, isomer 2), 5.80 (m, 1 H, COCH, isomer 1, isomer 2), 5.84 – 5.91 (m, 1 H, CH, isomer 1, isomer 2), 6.73 (d, ^3J = 7.8 Hz, 1 H, CH, isomer 1), 6.73 (d, ^3J = 7.8 Hz, 1 H, CH, isomer 2), 6.96 – 7.16 (m, 6 H, CH_{Ar}), 7.68 – 7.74 (m, 2 H, CH_{Ar}), 15.90 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 44.5/44.8 (NCH*CH2*), 54.2/54.4 (OCH_3), 54.5/55.0 (NCH), 98.4/98.5 (COO*CH3*), 110.0/110.3 (CH), 116.8/117.0 (d, ^2J = 20.2 Hz, $2CH_{Ar}$), 125.3 (CH), 125.9/126.0, 127.2/127.4, 128.2, 129.2/129.3 (CH_{Ar}), 130.7 (d, ^3J = 6.5 Hz, $2CH_{Ar}$), 130.8/130.9, 131.1/131.3, 132.3/132.4 (C_{Ar}), 154.3/154.9 (COH), 166.4/166.5 (d, ^1J = 250.5 Hz, CF_{Ar}), 184.9/185.7, 190.8/191.4 (CO); GC-MS (EI, 70 eV): *m*/*z* (%) = 367 (M^+, 1), 276 (2), 201 (2), 188 (100), 144 (25), 129 (10), 103 (7), 59 (5); HRMS (EI): Calcd. for $C_{21}H_{18}FNO_4$: 367.12144; found: 367.12160.



1-[(*Z*)-4-(4-Chlorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2(1*H*)-Isoquinoline-carboxylic acid methyl ester (36b): 

Starting with isoquinoline (0.258 g, 2.00 mmol), **32c** (1.023 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36b** was prepared as a red gummy solid (0.530 g, 70%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.46 – 2.63 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.65 (s, 3 H, $COOCH_3$, isomer 1), 3.67 (s, 3 H, $COOCH_3$, isomer 2), 5.66 (m, 1 H, NCH, isomer 1, isomer 2), 5.78 – 5.79 (m, 1 H, COCH, isomer 1, isomer 2), 5.85 – 5.90 (m, 1 H, CH, isomer 1, isomer 2), 6.74 (d, ^{3}J = 7.6 Hz, 1 H, CH, isomer 1), 6.91 (m, 1 H, CH, isomer 2), 6.98 – 7.07 (m, 4 H, CH_{Ar}), 7.26 (d, ^{3}J = 7.8 Hz, 2 H, CH_{Ar}), 7.61 (d, ^{3}J = 7.9 Hz, 2 H, CH_{Ar}), 15.90 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.7/43.9 (NCH*CH_2*), 53.1 (NCH), 53.3/53.9 (COO*CH_3*), 97.4/97.5, 108.7/109.0, 124.1 (CH), 124.7/124.8, 125.9/126.1, 127.0, 128.0/128.1 (CH_{Ar}), 128.3 (2CH), 128.7/128.8 ($2CH_{Ar}$), 129.8/130.0, 131.0/131.1, 133.2, 138.4/138.7 (C_{Ar}), 153.0/153.6 (COH), 182.8/183.7, 190.5/191.1 (CO); IR (neat): $\tilde{\nu}$ = 3106 (w), 3066 (w), 2997 (w), 2950 (s), 1704 (s), 1590 (s), 1079 (s), 775 (m), 750 (s), 671 (w) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 383 (M^+, 2), 292 (5), 201 (3), 188 (100), 144 (33), 129 (12), 103 (6), 77 (3); HRMS (EI): Calcd. for $C_{21}H_{18}ClNO_4$: 383.09189; found: 383.09167.

1-[(*Z*)-2-Hydroxy-4-(2-methylphenyl)-4-oxo-2-butenyl]-2(1*H*)-isoquinoline carboxylic acid methyl ester (36c): 

Starting with isoquinoline (0.258 g, 2.00 mmol), **32d** (0.961 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36c** was prepared as a yellow solid (0.300 g, 43%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.47 (s, 3 H, CH_3, isomer 1, isomer 2), 2.51 – 2.83 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.82 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.68 (s, 1 H, COC*H*, isomer 1, isomer 2), 5.77 – 5.92 (m, 1 H, NCH, isomer 1, isomer 2), 6.02 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1, isomer 2), 6.86 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1), 7.05 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 2), 7.09 – 7.40 (m, 8 H, CH_{Ar}), 15.98 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 21.9 (CH_3), 44.8/45.0 (NCH*CH_2*), 54.6/54.7 (COO*CH_3*), 54.9/55.5 (NCH), 103.1 (CH), 110.1/110.5 (CH), 125.6 (CH), 126.2/126.3, 127.0/127.2, 127.4/127.6, 128.5, 129.4/129.5, 129.6/129.7 (CH_{Ar}), 131.3/131.5 (C_{Ar}), 132.1/132.2, 132.5/132.6 (CH_{Ar}), 132.7/132.8, 137.3/137.4, 138.4 (C_{Ar}), 154.5/155.1 (COH), 190.6, 191.2/191.6 (CO); GC-MS

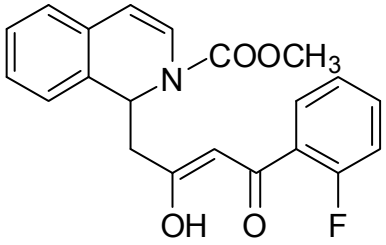
(EI, 70 eV): *m*/*z* (%) = 363 (M^+, 1), 272 (1), 188 (100), 144 (21), 129 (8), 103 (6), 91 (5), 59 (4); HRMS (EI): Calcd. for $C_{22}H_{21}NO_4$: 363.14610; found: 363.14600.

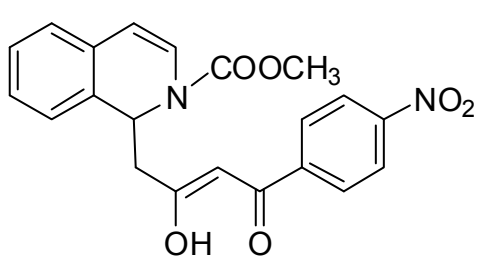
1-[(*Z*)-2-hydroxy-4-(2-methoxyphenyl)-4-oxo-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36d): Starting with isoquinoline (0.258 g, 2.00 mmol), **32e** (1.009 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36d** was prepared as a reddish highly viscous oil (0.450 g, 68%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.65 –2.83 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.75 (s, 3 H, OCH_3, isomer 1, isomer 2), 3.84 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.73 – 5.86 (m, 1 H, NCH, isomer 1, isomer 2), 5.89 – 5.99 (m, 1 H, COCH, isomer 1, isomer 2), 6.24 – 6.29 (m, 1 H, CH, isomer 1&2), 6.81 – 6.89 (m, 1 H, CH, Isomer 1&2), 6.93 – 7.18 (m, 6 H, CH_{Ar}) 7.31 – 7.43 (m, 1 H, CH_{Ar}), 7.79 (m, 1 H, CH_{Ar}), 16.15 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 44.1/44.4 (NCH*CH2*), 53.1/53.4 (OCH_3), 53.4 (NCH), 54.1/55.5 (COO*CH*$_3$), 102.7, 108.8/109.0, 111.6 (CH), 120.6, 124.2/124.8 (CH_{Ar}), 125.2 (C_{Ar}), 126.1/126.3, 127.1, 127.9/128.0, 129.9/130.1, 130.7 (CH_{Ar}), 131.4/131.6 (C_{Ar}), 133.0/133.2 (CH_{Ar}), 134.5 (C_{Ar}), 153.1/153.8 (*C*OCH_3), 158.4 (COH), 182.4/183.5, 190.8/191.5 (CO); GC-MS (EI, 70 eV): *m*/*z* (%) = 379 (M^+, 1), 201 (1), 188 (100), 144 (23), 129 (8), 103 (5), 77 (6), 59 (4); HRMS (EI): Calcd. for $C_{22}H_{21}NO_5$: 379.14142; found: 379.14158.

1-[(*Z*)-4-(2-Chlorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2(1*H*)-isoquinoline carboxylic acid methyl ester (36e): Starting with isoquinoline (0.258 g, 2.00 mmol), **32g** (1.023 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36e** was prepared as a yellow oil (0.450 g, 58%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.45 – 2.77 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.78 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.72 – 5.77 (m, 1 H, NCH, isomer 1, isomer 2), 5.82 (s, 1 H, COCH, isomer 1), 5.88 (s, 1 H, COCH, isomer 2), 5.97 (d, ^3J = 7.5 Hz, 1 H, CH, isomer 1, isomer 2), 6.80 (d, ^3J = 7.5 Hz, 1 H, CH, isomer 1), 6.99 (d, ^3J = 7.5 Hz, 1 H, CH, isomer 2), 7.04 – 7.20 (m, 4 H, CH_{Ar}), 7.29 – 7.48 (m, 4 H, CH_{Ar}), 15.52 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.9/44.2 (NCH*CH2*), 53.8/53.9 (COO*CH*$_3$), 54.0/54.7 (NCH),

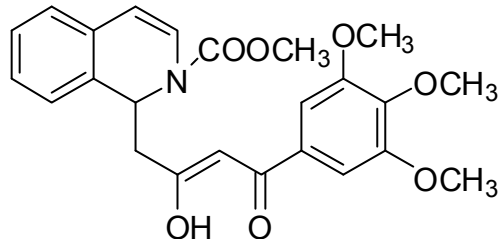
103.2/103.3, 109.4/109.6, 124.7/125.2 (CH), 125.3/125.4, 125.5, 126.7, 127.4, 127.7, 128.6/128.7, 130.4 (CH_{Ar}), 130.6 (C_{Ar}), 131.1/131.2, 131.6/131.7 (C_{Ar}), 132.1/132.3 (CH_{Ar}), 136.2 (C_{Ar}), 153.6/154.2 (COH), 186.2/187.4, 189.5/190.0 (CO); MS (EI, 70 eV): *m*/*z* (%) = 383 (M^+, 1), 292 (2), 201 (2), 188 (100), 144 (23), 129 (10), 103 (6), 77 (3); HRMS (EI): Calcd. for $C_{21}H_{18}ClNO_4$: 383.09189; found: 383.09167.

1-[(*Z*)-4-(2-Fluorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2(1*H*)isoquinolinecarboxylic acid methyl ester (36f): Starting with isoquinoline (0.258 g, 2.00 mmol), **32h** (0.973 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36f** was prepared as a deep reddish viscous oil (0.561 g, 76%, mp. = 165-168 ^oC). ^1H NMR (250 MHz, $CDCl_3$,): δ = 2.41 – 2.74 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.36 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.64− 5.69 (m, 1 H, NCH, isomer 1), 5.77 − 5.80 (m, 1 H, NCH, isomer 2), 5.86 − 5.89 (m, 1 H, COCH, isomer 1, isomer 2), 6.00 – 6.02 (m, 1 H, CH, isomer 1, isomer 2), 6.73 (d, ^3J = 7.5 Hz, 1 H, CH, isomer 1), 6.92 (d, ^3J = 7.5 Hz, 1 H, CH, isomer 2), 6.98 – 7.11 (m, 6 H, CH_{Ar}), 7.31 – 7.33 (m, 1 H, CH_{Ar}), 7.77 6.73 (ddd, ^3J = 7.7 Hz, ^3J = 7.7 Hz, ^4J = 1.8 Hz,1 H, CH_{Ar}), 15.91 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 44.9/45.3 (NCH*CH2*), 54.1/54.3 (NCH), 54.5/55.0 (COO*CH3*), 103.1/103.5, 109.9/110.1 (CH), 117.4 (d, ^2J = 16.2 Hz, CH_{Ar}), 124.0/124.2 (CH), 125.2/125.4 (CH_{Ar}), 125.9 (d, ^3J = 6.1 Hz, CH_{Ar}),127.0/127.2, 128.1 (CH_{Ar}), 129.1 (d, ^3J = 7.2 Hz, CH_{Ar}), 129.6 (d, ^4J = 1.8 Hz, CH_{Ar}),131.0 (CH_{Ar}), 132.2/132.3, 134.5, 134.6/134.8 (C_{Ar}), 154.1/154.6 (COH), 162.0 (d, ^1J = 253.8 Hz, CF_{Ar}), 180.6/181.3, 193.0/193.3 (CO); IR (neat): ν = 3108 (w), 3078 (w), 2996 (w), 2969 (w), 1519 (s), 1434 (s), 1110 (s), 643 (m), 776 (s) cm^{-1}; GCMS (EI, 70 eV): *m*/*z* (%) = 367 (M^+, 5), 188 (100), 144 (28), 129 (22), 103 (12), 59 (8). HRMS (EI): Calcd. for $C_{21}H_{18}O_4FN$: 367.12144; found: 367.12076.



1-[(*Z*)-2-Hydroxy-4-(4-nitrophenyl)-4-oxo-2-butenyl]-2(1*H*)-isoquinolinecarboxylic acid methyl ester (36g): 

Starting with isoquinoline (0.258 g, 2.00 mmol), **32i** (1.054 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36g** was prepared as a yellow solid (0.300 g, 43%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.47 – 2.65 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.62 (s, 3 H, OCH_3, isomer 1), 3.66 (s, 3 H, OCH_3, isomer 2), 5.63 (t(br), ^{3}J = 7.6 Hz, 1 H, NCH, isomer 1, isomer 2), 5.70 – 5.85 (m, 1 H, NCH, isomer 1, isomer 2), 5.90 (s(br), 1 H, COC*H*, isomer 1, isomer 2), 6.69 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1), 6.87 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 2), 6.96 – 7.12 (m, 4 H, CH_{Ar}), 7.79 (d, ^{3}J = 7.8 Hz , 2 H, CH_{Ar}), 8.12 (d, ^{3}J = 7.8 Hz , 2 H, CH_{Ar}), 15.58 – 15.71 (m(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 44.5 (NCH*C*H_2), 53.3/53.5 (NCH), 53.9 (O*C*H_3), 98.7, 108.9/109.2, 123.7 (CH), 124.2 (2CH_{Ar}), 124.9/125.0, 126.0/126.2 (CH_{Ar}), 127.2 (C_{Ar}), 127.8 (2CH_{Ar}), 127.9/128.2, 128.3/129.9 (CH_{Ar}), 130.5/130.9, 140.3, 149.8 (C_{Ar}), 153.2/153.6 (COH), 179.8/180.9, 193.1/193.9 (CO); IR (neat): $\tilde{\nu}$ = 3108 (w), 3078 (w), 2994 (w), 2969 (w), 1519 (s), 1434 (s), 1110 (s), 645 (m), 777 (s), 751 (w) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 394 (M^+, 2), 365 (2), 319 (3), 188 (100), 144 (75), 129 (49), 103 (16); HRMS (EI): Calcd. for $C_{21}H_{18}N_2O_6$: 394.11594; found: 394.11602.

1-[(*Z*)-2-Hydroxy-4-oxo-4-(3,4,5-trimethoxyphenyl)-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36h): 

Starting with isoquinoline (0.258 g, 2.00 mmol), **32j** (1.185 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36h** was prepared as a yellow highly viscous oil (0.300 g, 34%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.46 – 2.69 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.68 (s, 3 H, COO*CH3*, isomer 1), 3.70 (s, 3 H, COO*CH3*, isomer 2), 3.70 (m, 9 H, OCH3 isomer 1&2), 5.68 (m, 1 H, NCH, isomer 1, isomer 2), 5.76 – 5.85 (m, 1 H, COCH, isomer 1, isomer 2), 5.92 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1, isomer 2), 6.75 (d, ^{3}J = 7.6 Hz, 1 H, CH, isomer 1) 6.92 (m, 1 H, CH, isomer 2), 6.97 – 7.22 (m, 6 H, CH_{Ar}), 16.01 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 41.3/41.7 (NCH*CH2*), 51.3/51.5 (NCH), 54.3 (3OCH_3), 58.9 (COO*CH3*), 95.3/95.5, 102.6, 106.9/107.107.1 (CH), 122.3, 122.8/122.9, 124.1/124.3 (CH_{Ar}), 125.0 (C_{Ar}), 126.0/126.1, 128.0/128.2 (CH_{Ar}), 128.4 (C_{Ar}), 129.2/129.3 (CH_{Ar}), 140.0/140.1 (C_{Ar}), 151.2 (3*C*OCH_{3Ar}),

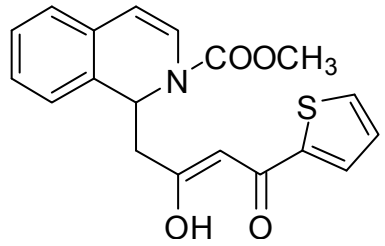
151.8 (COH), 183.0/183.8, 186.6/187.1 (CO); IR (neat): ν = 2997 (w), 2951 (w), 2939 (w), 2836 (w), 1709 (s), 1570 (s), 1119 (s), 999 (s), 773 (s) cm^{-1}; HRMS (EI): Calcd. for $C_{24}H_{25}O_7N$: 439.16255; found: 439.16281.

1-[(*Z*)-2-Hydroxy-4-(2-naphthyl)-4-oxo-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36i): Starting with isoquinoline (0.258 g, 2.00 mmol), **32k** (1.05 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36i** was prepared as a reddish highly viscous oil (0.325 g, 41% mp. = 86-88 ^{o}C). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.35 – 2.69 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.65 (s, 3 H, $COOCH_3$, isomer 1), 3.67 (s, 3 H, $COOCH_3$, isomer 2), 5.66 (s, 1 H, COCH, isomer 1, isomer 2), 5.73 – 5.78 (m, 1 H, NCH, isomer 1, isomer 2), 5.86 (d, ^{3}J = 7.7 Hz, 1 H, CH, isomer 1, isomer 2), 6.70 (d, ^{3}J = 7.7 Hz, 1 H, CH, isomer 1), 6.87 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 2), 6.94 – 7.10 (m, 4 H, CH_{Ar}), 7.30 – 7.46 (m, 4 H, CH_{Ar}), 7.69 – 7.78 (m, 2 H, CH_{Ar}), 8.16 – 7.20 (m, 1 H, CH_{Ar}), 15.98 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.2/43.4 (NCH*CH2*), 53.3/53.4 (COO*CH*$_3$), 53.6/54.2 (NCH), 102.7/102.8, 124.2, 1024.7 (CH), 124.8/124.9, 125.4/125.5, 126.1, 126.3, 127.0 (CH_{Ar}), 127.1 ($2CH_{Ar}$), 127.3, 128.1/128.2, 128.4, 130.0 (CH_{Ar}), 130.2, 131.1/131.2, 131.7/131.9, 133.7, 134.3/134.4 (C_{Ar}), 153.2/153.1 (COH), 188.5/189.0, 189.5/190.4 (CO); IR (neat): ν = 3054 (w), 2952 (w), 2926 (w), 2849 (w), 1710 (s), 1593 (s), 1118 (s), 972 (m), 772 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 399 (M^+, 1), 308 (1), 212 (1), 188 (100), 155 (4), 144 (18), 129 (7), 103 (5), 77 (2), 59 (3); HRMS (EI): Calcd. for $C_{25}H_{21}NO_4$: 399.14720; found: 399.14691.

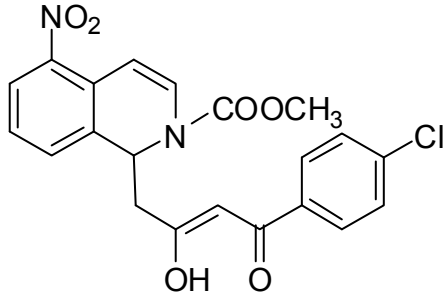
1-[(*Z*)-2-Hydroxy-4-(2-naphthyl)-4-oxo-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36j): Starting with isoquinoline (0.258 g, 2.00 mmol), **32l** (1.05 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36ju** was prepared as a reddish solid (0.561 g, 76% mp. = 122-125 ^{o}C). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.43 – 2.73 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.64 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.63 – 5.69 (m, 1 H, NCH, isomer 1, isomer 2), 5.75 (s, 1 H, COCH, isomer 1), 5.79 (s, 1 H, COCH,

isomer 2), 5.93 – 6.01 (m, 1 H, CH, isomer 1, isomer 2), 6.61 (d, ^3J = 7.5 Hz, 1 H, CH_{Ar}, isomer 1), 6.91 (d, ^3J = 7.5 Hz, 1 H, CH_{Ar}, isomer 2), 6.95 – 7.11 (m, 4 H, CH_{Ar}), 7.39 – 7.44 (m, 2 H, CH_{Ar}), 7.69 – 7.81 (m, 4 H, CH_{Ar}), 8.21 (m, 1 H, CH_{Ar}), 15.95 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.9/44.2 (NCH*CH2*), 53.3/53.4 (NCH), 53.6/54.0 (COO*CH3*), 97.9, 108.9/109.1, 123.1 (CH), 124.2, 124.8, 126.1/126.3, 126.7, 127.1, 127.7, 128.1, 128.3, 128.4 (CH_{Ar}), 129.3 ($2CH_{Ar}$), 130.0/130.1, 131.2/131.3, 132.1/132.2, 132.6, 135.3 (C_{Ar}), 153.2/153.1 (COH), 184.1/184.8, 190.6/190.9 (CO); IR (neat): ν = 3052 (w), 3027 (w), 2955 (w), 2918 (w), 1714 (s), 1633 (m), 1116 (s), 972 (w), 783 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 399 (M^+, 1), 308 (1), 188 (100), 144 (20), 127 (6), 103 (5), 59 (3); HRMS (EI): Calcd. for $C_{25}H_{21}NO_4$: 399.14651; found: 399.14696.

1-[(*Z*)-2-Hydroxy-4-oxo-4-(2-pyridyl)-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36k): Starting with isoquinoline (0.258 g, 2.00 mmol), **32r** (1.009 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36k** was prepared as a reddish highly viscous oil (0.450 g, 68%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.46 – 2.77(m, 2 H, NCHC*H2*, isomer 1, isomer 2), 3.64 (s, 3 H, COO*CH3*, isomer 1, isomer 2), 5.65 – 5.71 (m, 1 H, NCH, isomer 1, isomer 2), 5.80 – 5.90 (m, 1 H, CH, isomer 1, isomer 2), 6.62 (s, 1 H, COCH, isomer 1, isomer 2), 6.73 (d, ^3J = 7.2 Hz, 1 H, CH, isomer 1), 6.89 (d, ^3J = 7.2 Hz, 1 H, CH, isomer 2), 6.91 – 7.08 (m, 4 H, CH_{Ar}), 7.26 – 7.29 (m, 1 H, CH_{Ar}), 7.65 – 7.70 (m, 1 H, CH_{Ar}), 7.92 – 7.96 (m, 1 H, CH_{Ar}), 8.51 – 7.70 (m, 1 H, CH_{Ar}), 15.56 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.8/44.2 (NCH*CH2*), 53.1/53.2 (OCH_3), 53.5/53.8 (NCH), 98.0, 108.8/109.1, 122.1 (CH), 124.2, 124.8/124.9, 126.1/126.2 (CH_{Ar}), 126.4, 127.0/127.1 (C_{Ar}), 128.0, 129.9/130.1 (CH_{Ar}), 131.3 (C_{Ar}), 137.1 (CH_{Ar}), 148.8/149.1 (C_{Ar}), 151.9 (CH_{Ar}), 153.1/153.6 (COH), 182.0/182.5, 192.0/192.2 (CO); IR (neat): ν = 3106 (w), 3055 (w), 2952 (w), 2851 (w), 1709 (s), 1564 (s), 1119 (s), 772 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 350 (M^+, 5), 274 (3), 188 (100), 144 (56), 129 (19, 103 (9), 78 (10), 59 (7); HRMS (EI): Calcd. for $C_{20}H_{18}N_2O_4$: 350.12611; found: 350.12617.

1-[(*Z*)-2-Hydroxy-4-oxo-4-(2-thienyl)-2-butenyl]-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36l): 

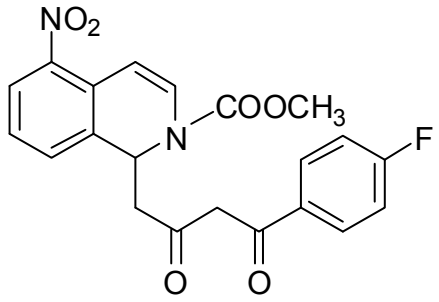
Starting with isoquinoline (0.258 g, 2.00 mmol), **32s** (0.937 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36l** was prepared as a reddish highly viscous oil (0.150 g, 22%, mp. = 70- 72 ^{o}C). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.07 – 2.42 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.42 (s, 3 H, COO*CH3*, isomer 1, isomer 2), 5.36– 5.41 (m, 1 H, NCH, isomer 1, isomer 2), 5.47 (s, 1 H, COCH, isomer 1, isomer 2), 5.54 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1), 5.65 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 2), 6.48 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 1), 6.66 (d, ^{3}J = 7.5 Hz, 1 H, CH, isomer 2), 6.71 – 6.91 (m, 5 H, CH_{Ar}), 7.24 (m, 2 H, CH_{Ar}), 16.01 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 42.4/42.9 (NCH*CH2*), 53.6/53.7 (NCH), 53.9/54.4 (OCH_3), 98.0, 109.2/109.4, 124.5 (CH), 125.1/125.2, 126.4/126.6, 127.4/127.5, 128.4/128.5, 128.6/128.7 (CH_{Ar}), 130.2/130.4 (C_{Ar}), 130.7/131.1 (CH_{Ar}), 131.4/131.5 (C_{Ar}), 132.9/133.2 (CH_{Ar}), 142.0/142.2 (C_{Ar}), 153.6/154.1 (COH), 182.6/183.0, 184.4/184.9 (CO); IR (neat): ν = 3112 (w), 3034 (w), 2972 (w), 2826 (w), 1698 (s), 1598 (s), 1158 (s), 954 (s), 774 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%) = 355 (M^+, 36), 337 (18), 264 (92), 188 (100), 170 (15), 170 (15), 144 (18), 11 (86), 83 (8), 59 (14); HRMS (EI): Calcd. for $C_{19}H_{17}NO_4S$: 355.08728; found: 355.08637.

1-[(*Z*)-4-(4-Chlorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2-(methoxycarbonyl)-5-nitro-isoquinoline (36m): 

Starting with 5-nitroisoquinoline (0.348 g, 2.00 mmol), **32c** (1.023 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36m** was prepared as a red gummy solid (0.486 g, 54%, mp. = 166-170 ^{o}C). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.71 – 2.73 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.76 (s, 3 H, $COOCH_3$, isomer 1&2), 5.78 (m, 1 H, NCH, isomer 1, isomer 2), 5.84 (m, 1 H, COCH, isomer 1, isomer 2), 6.56 – 6.68 (m, 1 H, CH, isomer 1&2), 6.99 − 7.02 (m, 1 H, CH isomer 1&2), 7.14 − 7.20 (m, 2 H, CH_{Ar}), 7.29 – 7.35 (m, 2 H, CH_{Ar}), 7.65 − 7.69 (m, 2 H, CH_{Ar}), 7.79 − 7.83(m, 1 H, CH_{Ar}), 15.87 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.9 (NCH*CH2*), 53.9 (NCH), 54.7 (COO*CH3*), 98.4, 103.8, 125.6, (CH), 127.7, (CH_{Ar}), 129.4

($2CH_{Ar}$), 129.9 ($2CH_{Ar}$). 131.4 (CH_{Ar}), 132.2 (C_{Ar}), 133.133.9 (CH_{Ar}), 134.1 ($2C_{Ar}$), 139.9, 145.4 (C_{Ar}), 153.5 (COH), 184.1/184.8, 190.5/191.0 (CO); IR (neat): ν = 3035 (w), 3011 (w), 2957 (w), 2855 (w), 1711 (s), 1590 (s), 1223 (s), 1098 (s), 762 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 430 ([M^+], ^{37}Cl, 2), 428 ([M^+], ^{35}Cl, 6), 246 (2), 233 (100), 187 (15), 158 (25), 143 (80), 128 (15), 59 (34); HRMS (EI): Calcd. for $C_{21}H_{17}ClNO_6$ ([M^+], ^{35}Cl): 428.07697; found: 428.07756.

1-[4-(4-Fluorophenyl)-2,4-dioxobutyl]-2(1*H*)-isoquinolinecarboxylic acid methyl ester (36n): Starting with nitroisoquinoline (0.348 g, 2.00 mmol), **32b** (0.973 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36n** was prepared as an orange red solid (0.590 g, 72%, mp. = 150-153 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.51 – 2.61 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.69 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.77 (m, 1 H, NCH, isomer 1, isomer 2), 5.82 (s, 1 H, COCH, isomer 1, isomer 2), 6.55 – 6.62 (m, 1 H, CH, isomer 1, isomer 2), 6.95 (m, 1 H, CH, isomer 1, isomer 2), 6.97 – 7.00 (m, 2 H, CH_{Ar}), 7.08 – 7.14 (m, 1 H, CH_{Ar}), 7.24 – 7.26 (m, 1 H, CH_{Ar}), 7.67 – 7.77 (m, 3 H, CH_{Ar}), 15.52 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 43.9/44.2 (NCH*CH2*), 54.2 (NCH), 55.0 (COO*CH₃*), 98.5, 104.0 (CH), 117.0 (d, ^2J = 17.9 Hz, $2CH_{Ar}$), 125.9 (CH), 127.9, 130.1 (CH_{Ar}), 130.8 (d, ^4J = 2.2 Hz, $2CH_{Ar}$), 132.1/132.2 (CH_{Ar}), 132.7, 134.4, 145.7 (C_{Ar}), 153.8/154.3 (COH), 166.5 (d, ^1J = 209.6 Hz, CF_{Ar}), 185.1/185.7, 189.9/190.4 (CO); IR (neat): ν = 3110 (w), 3030 (w), 2971 (w), 2836 (w), 1695 (s), 1597 (s), 1155 (s), 951 (s), 771 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 414 (M^+, 50), 343 (25), 281 (10), 195 (100), 165 (12), 123 (70).



1-[(*Z*)-2-Hydroxy-4-(2-methylphenyl)-4-oxo-2-butenyl]-5-nitro-2(1*H*)-isoquinolinecarboxylic acid methyl ester (36o): Starting with 6-nitroisoquinoline (0.348 g, 2.00 mmol), **32d** (0.961 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36o** was prepared as a yellow gummy solid (0.580 g, 71%). ^{1}H NMR (300 MHz, $CDCl_3$,): δ = 2.48 (s, 3 H, CH_3, isomer 1, isomer 2), 2.65 – 2.81 (m, 2 H, NCHC*H*$_2$, isomer 1, isomer 2), 3.89 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.72 (s, 1 H, COC*H*, isomer 1, isomer 2), 5.90 – 6.00 (m, 1 H, NCH, isomer 1, isomer 2), 6.70 – 6.76 (m, 1 H, CH, isomer 1, isomer 2), 7.10 – 7.13 (m, 1 H, CH, isomer 1, isomer 2), 7.23 – 7.45 (m, 6 H, CH_{Ar}), 7.92 (d, ^{3}J = 6.7 Hz , 1 H, CH_{Ar}), 15.89 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 22.0 (CH_3), 44.2/44.3 (NCH*CH2*), 54.5 (NCH), 54.2 (COO*CH3*), 103.1, 104.0, 126.0 (CH), 126.5 (C_{Ar}), 127.2, 128.1, 129.7, 130.3, 130.8, 132.4, 132.9 (CH_{Ar}), 134.7, 137.0, 138.6, 145.8, (C_{Ar}), 153.9/154.5 (COH), 189.8/190.4, 190.7/191.5 (CO); IR (neat): ν = 3065 (w), 3015 (w), 2954 (w), 2928 (w), 1716 (s), 1519 (s), 1265 (s), 966 (s), 759 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 408 (M^+, 35), 393 (14), 340 (15), 271 (28), 210 (33), 195 (53), 177 (30), 135 (12), 123 (100), 111 (18), 69 (63), 57 (86), 43 (58).

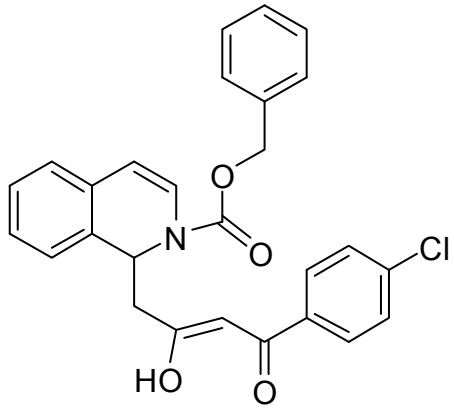
1-[(*Z*)-4-(2-Fluorophenyl)-2-hydroxy-4-oxo-2-butenyl]-2-(methoxycarbonyl)-5-nitro-isoquinoline (36p): Starting with 5-nitroisoquinoline (0.348 g, 2.00 mmol), **32h** (0.973 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36p** was prepared as a yellow solid (0.345 g, 41%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.70 – 2.73 (m, 2 H, NCHC*H*$_2$, isomer 1, isomer 2), 3.76 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.79− 5.89 (m, 1 H, NCH, isomer 1,isomer 2), 6.01 (m, 1 H, COCH, isomer 1, isomer 2), 6.58 – 6.71 (m, 1 H, CH, isomer 1&2), 6.99 – 7.02 (m, 1 H, CH, isomer 1, isomer 2), 7.07 − 7.21 (m, 3 H, CH, CH_{Ar}), 7.32 – 7.42 (m, 2 H, CH_{Ar}), 7.81 − 7.85 (m, 2 H, CH_{Ar}), 15.83 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.2/43.4 (NCH*CH2*), 52.9/53.4 (NCH), 53.6/53.8 (COO*CH3*), 102.1 (CH), 102.3 (d, ^{3}J = 12.0 Hz, CH_{Ar}), 102.5 (CH), 116.6 (d, ^{2}J = 21.0 Hz, CH_{Ar}), 124.5 (d, ^{4}J = 3.0 Hz, CH_{Ar}), 124.7 (CH), 126.7, 127.1, 127.3/128.8, 130.0 (CH_{Ar}), 131.3/131.5, 133.3, 133.9, 144.5 (CH_{Ar}), 153.0 (COH), 161.5 (d, ^{1}J = 247.4 Hz, CF_{Ar}), 180.0, 191.3 (CO); GC-MS (EI, 70 eV): *m*/*z* (%) = 414 (M^+, 50), 343 (30), 281 (15), 255 (10), 195 (100), 123 (99).

1-[(*Z*)-4-(2-Chlorophenyl)-2-hydroxy-4-oxo-2-butenyl]-5-nitro-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36q): Starting with 6-nitroisoquinoline (0.348 g, 2.00 mmol), **32g** (0.961 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36q** was prepared as a orange solid (0.520 g, 56%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.45 – 2.61 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.69 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.69 (s, 1 H, COCH, isomer 1, isomer 2), 5.75 – 5.80 (m, 1 H, NCH, isomer 1, isomer 2), 6.49 – 6.60 (m, 1 H, CH, isomer 1, isomer 2), 6.80 – 6.92 (m, 1 H, CH, isomer 1, isomer 2), 7.05 – 7.26 (m, 5 H, CH_{Ar}), 7.32 – 7.35 (m, 1 H, CH_{Ar}), 7.74 (dd, ^{3}J = 7.5 Hz, ^{4}J = 1.0 Hz, 1 H, CH_{Ar}), 15.30 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.2/43.5 (NCH*CH2*), 53.7 (NCH), 54.4 (COO*CH3*), 103.4, 125.3 (CH), 125.7 (C_{Ar}), 127.4 (CH), 127.5, 129.3, 130.0, 130.4, 131.3, 131.8, 132.2 (CH_{Ar}), 132.5, 133.8, 136.0, 145.1 (C_{Ar}), 153.2/153.6 (COH), 186.7/187.4, 188.6/188.9 (CO); IR (neat): ν = 3067 (w), 3002 (w), 2954 (w), 2851 (w), 1719 (s), 1604 (s), 1519 (s), 1115 (m), 967 (s), 759 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 430 ([M^+], ^{37}Cl, 1), 428 ([M^+], ^{35}Cl, 3), 246 (2), 233 (100), 187 (15), 158 (25), 143 (80), 128 (15), 59 (34); HRMS (EI): Calcd. for $C_{21}H_{17}ClNO_6$ ([M^+], ^{35}Cl): 428.07697; found: 428.07756.

1-[(*Z*)-2-Hydroxy-4-(2-naphthalenyl)-4-oxo-2-butenyl]-5-nitro-2(1*H*)-isoquinoline-carboxylic acid methyl ester (36r): Starting with nitroisoquinoline (0.348 g, 2.00 mmol), **32l** (0.973 g, 3.00 mmol) and methyl chloroformate (0.226 g, 2.40 mmol), **36r** was prepared as an yellow solid (0.500 g, 56%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.73 – 2.76 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 3.75 (s, 3 H, $COOCH_3$, isomer 1, isomer 2), 5.82 – 5.91 (m, 1 H, CH, isomer 1, isomer 2), 6.01 – 6.06 (m, 1 H, NCH, isomer 1, isomer 2), 6.59 – 6.70 (m, 1 H, COCH, isomer1&2), 7.15 (m, 1 H, CH, isomer 1, isomer 2), 7.33 (d, ^{3}J = 7.7 Hz, 1 H, CH_{Ar}), 7.45 – 7.51 (m, 2 H, CH_{Ar}), 7.76 – 7.86 (m, 6 H, CH_{Ar}), 8.27 (m, 1 H, CH_{Ar}), 16.05 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.0 (NCH*CH2*), 53.1/53.4 (NCH), 53.8 (COO*CH3*), 97.9, 102.8, 122.9 (CH), 124.7 (CH_{Ar}), 125.1 (C_{Ar}), 126.7, 126.8, 127.7 (CH_{Ar}), 128.3 ($2CH_{Ar}$), 128.5 (CH_{Ar}), 128.7 (C_{Ar}), 129.3 (CH_{Ar}), 129.5 (C_{Ar}), 131.4, 131.7 (CH_{Ar}), 132.6, 133.3, 135.3 (C_{Ar}), 144.5 (COH),

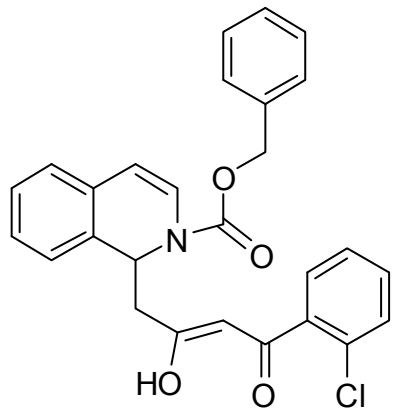
184.4/184.6, 189.6/189.8 (CO); IR (neat): ν□ = 1704 (w), 1615 (m), 1521 (w), 1185 (w), 977 (w), 761 (w) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 444 (M^+, 2), 410 (2), 233 (100), 203 (36), 155 (11), 143 (35), 127 (14), 69 (18); HRMS (EI): Calcd. for $C_{25}H_{20}N_2O_4$: 444.13159; found: 444.13132.

Benzyl 1-(4-(4-chlorophenyl)-2-hydroxy-4-oxobut-2-enyl)isoquinoline-2(1H)-carboxylate (38f).



Starting with Isoquinoline (0.258 g, 2.00 mmol), **32c** (1.023 g, 3.00 mmol) and benzyl chloroformate (0.409 g, 2.40 mmol), **38f** was isolated as a reddish viscous oil (0.563 g, 61%). ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.34 – 2.67 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 5.03 – 5.06 (m, 2 H, $COOCH_2$, isomer 1, isomer 2), 5.61 – 5.63 (m, 1 H, COCH, isomer 1, isomer 2), 5.66 – 5.75 (m, 1 H, NCH, isomer 1, isomer 2), 5.85 – 5.88 (m, 1 H, CH, isomer 1, isomer 2), 6.70 – 6.73 (m, 1 H, CH, isomer 1, isomer 2), 6.94 – 6.99 (m, 4 H, CH_{Ar}), 7.07 – 7.25 (m, 7 H, CH_{Ar}), 7.52 – 7.59 (m, 2 H, CH_{Ar}), 15.83 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.7/44.0 (NCH*CH_2*), 53.5/54.0 (NCH), 68.2 (COO*CH_2*), 97.4/97.5, 109.0/109.1, 124.1 (CH), 124.7/124.8, 125.0, 126.1, 126.2, 127.1, 127.2 (CH_{Ar}), 128.1/128.2 ($2CH_{Ar}$), 128.2/128.3,(CH_{Ar}), 128.5 ($2CH_{Ar}$), 128.8/128.9, 129.9 (CH_{Ar}), 130.1, 131.1/131.2, 133.3/133.4, 135.4/135.7, 138.7/138.8 (C_{Ar}), 152.6/153.1 (COH), 183.2/183.9, 190.3/190.9 (CO); IR (neat): ν = 3103 (w), 3060 (w), 2990 (w), 2900 (s), 1702 (s), 1595 (s), 1070 (s), 770 (m), 752 (s), 675 (w) cm^{-1}; Anal. Calcd for $C_{27}H_{22}ClNO_4$ (459.96): C 70.50, H 4.82,. Found: C 70.469, H 4.919.

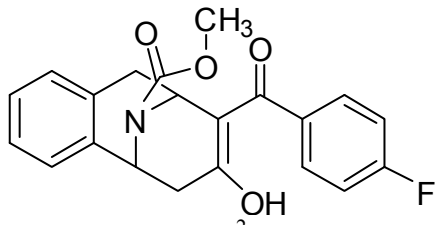
Benzyl 1-(4-(2-chlorophenyl)-2-hydroxy-4-oxobut-2-enyl)isoquinoline-2(1H)-carboxylate (38g).



Starting with Isoquinoline (0.258 g, 2.00 mmol), **32g** (1.023 g, 3.00 mmol) and benzyl chloroformate (0.409 g, 2.40 mmol), **38g** was isolated as a reddish viscous oil (0.624 g, 67%).. ^{1}H NMR (250 MHz, $CDCl_3$,): δ = 2.61 – 2.84 (m, 2 H, NCHCH_2, isomer 1, isomer 2), 5.00 – 5.018 (m, 2 H, $COOCH_2$, isomer 1, isomer 2), 5.65 (s, 1 H, COCH, isomer 1, isomer 2), 5.71 – 5.73 (m, 1 H, NCH, isomer 1, isomer 2), 5.82 – 5.85 (m, 1 H, CH, isomer 1, isomer 2), 6.69 – 6.72

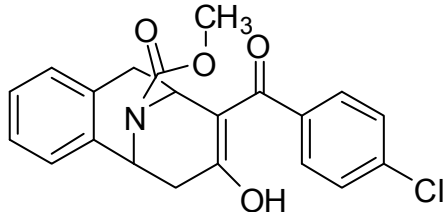
(m, 1 H, CH, isomer 1, isomer 2), 6.90 – 7.08 (m, 3 H, CH_{Ar}), 7.13 – 7.32 (m, 10 H, CH_{Ar}), 15.840 (s(br), 1 H, OH); ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 43.8/44.2 (NCH*CH_2*), 54.1/54.6 (NCH), 68.7 (COO*CH_2*), 103.2/103.3, 109.5/109.9, 124.6 (CH), 125.2, 125.4, 125.5, 126.5, 126.7, 127.4, 127.7, 127.8, 128.7, 128.8, 129.1, 130.4, 130.6 (CH_{Ar}), 131.1/131.2, 131.6, 131.7, 132.1/132.3, 136.0/136.3 (C_{Ar}), 153.0/153.7 (COH), 186.6/186.7, 189.1/189.9 (CO); IR (neat): ν = 3108 (w), 3062 (w), 2995 (w), 2900 (s), 1706 (s), 1593 (s), 1077 (s), 779 (m), 750 (s), 671 (w) cm^{-1}; Anal. Calcd for $C_{27}H_{22}ClNO_4$ (459.96): C 70.50, H 4.82, N 3.05. Found: C 70.20, H 4.85, 2.80.

General procedure for the synthesis of 37a-r and 39a-g: To a CH_2Cl_2 solution (6 mL) of **3** (1.5 mmol) was added TFA (3.0 mmol) and the solution was stirred for 12 h at 20 °C. For **4a-ad**: a saturated aqueous solution of sodium bicarbonate (2 mL) was added and the organic and the aqueous layers were separated. The latter was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. For **4a-ad** and **6a-e**: The residue was purified by chromatography (silica gel, hexane → hexane/EtOAc = 2:1). The product was dried for 16 h at 50 °C and 0.01 mbar to remove hydrolyzed **2**. Due to the amide resonance and formation of *E/Z*-isomers, doubling of some signals was observed. In all products, the 1,3-dicarbonyl moiety resides in the enolic form.

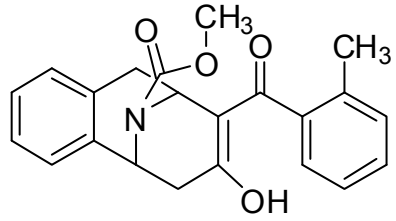
Methyl 10-(4-fluorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37a): 

Starting with **36a** (0.164 g, 0.43 mmol) and TFA (0.87 g, 0.09 mmol), **37a** was isolated as a colourless solid (0.110 g, 67%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.23 (d, ^2J = 16.5 Hz, 1 H, CH*CH_2*), 2.48 (d, ^2J = 18.0 Hz, 1 H, CH*CH_2*), 2.89 – 3.12 (m, 2 H, CHC*H_2*), 3.69 (s, 3 H, CO_2CH_3, isomer 1&2), 5.31 − 5.45 (m, 1 H, NCH), 5.50 – 5.72 (m, 1 H, NCH), 6.88 (m, 1 H, CH_{Ar}), 7.03 − 7.15 (m, 5 H, CH_{Ar}), 7.44 – 7.52 (m, 2 H, CH_{Ar}), 16.28(s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.7/35.1, 40.7/41.1 (CH*C*H$_2$), 45.2/45.8, 48.2/49.0 (NCH), 53.0/53.1 (CO_2*CH_3*), 109.2 (C), 116.1 (d, ^2J = 25.0 Hz, 2CH_{Ar}), 126.4/126.7, 127.5/127.6, 129.1/129.2 (CH_{Ar}), 129.5 (d, ^3J = 9.5 Hz, 2CH_{Ar}), 130.7/131.2 (CH_{Ar}), 131.6/131.7, 132.7/132.8, 135.9/136.0 (C_{Ar}), 154.7 (C-OH), 163.9 (d, ^1J = 248.0 Hz, CF_{Ar}), 187.1/187.9, 188.7/188.9 (C=O); IR (neat): ν = 2957 (w), 2935 (w), 2919 (w), 2851 (w), 1691 (s), 1446 (s), 1235 (s),

1022 (s), 758 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%) = 376 ([M^+], 22), 349 (17), 276 (100), 188 (39), 144 (15), 123 (50), 115 (12), 95 (16), 77 (5), 59(10). HRMS (EI): Calcd. for $C_{21}H_{18}O_4NF$: 367.12144; found: 367.12113.

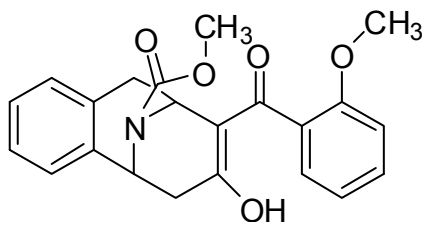
Methyl 10-(4-chlorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37b): 

Starting with **36b** (0.420 g, 1.09 mmol) and TFA (0.249 g, 2.10 mmol), **37b** was isolated as a colourless solid (0.290 g, 69%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.15 (d, ^2J = 17.0 Hz, 1 H, CHCH_2), 2.42 (d, ^2J= 19.5, Hz, 1 H, CHCH_2), 2.82 – 3.06 (m, 2 H, CHCH_2), 3.63 ($s_{(br)}$, 3 H, CO_2CH_3, isomer 1&2), 5.25 − 5.39 (m, 1 H, NCH), 5.41 – 5.62 (m, 1 H, NCH), 6.82 − 6.85 (m, 1 H, CH_{Ar}), 6.93 − 7.06 (m, 3 H, CH_{Ar}), 7.31 − 7.43 (m, 4 H, CH_{Ar}), 16.17 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.2, 40.9/41.2 (CHCH_2), 45.1/45.7, 48.4/49.0 (NCH), 53.0/53.4 (CO_2CH_3), 109.3 (C), 126.4, 126.7/126.8, 127.6/127.7, 128.3, 128.6, 129.2, 129.7/129.9, 130.7 (CH_{Ar}), 131.1, 134.9, 135.8, 136.8 (C_{Ar}), 154.3/154.6 (C-OH), 187.4/188.1, 188.6/188.9 (C=O); IR (neat): ν□ = 3034 (w), 3000 (w), 2990 (w), 2838 (w), 1691 (s), 1447 (s), 1313 (s), 1023 (s), 759 (s) cm^{-1}; GC-MS (EI, 70 eV): *m/z* (%) = 385 ([M^+], ^{37}Cl, 8), 383 ([M^+], ^{35}Cl, 21), 294 (^{37}Cl, 33), 383 (^{35}Cl, 100), 188 (68), 139 (51), 111 (25), 91 (6), 59 (11); HRMS (EI): Calcd. for $C_{21}H_{18}O_4ClN$, ([M^+], ^{35}Cl): 383.09189; found: 383.09192.

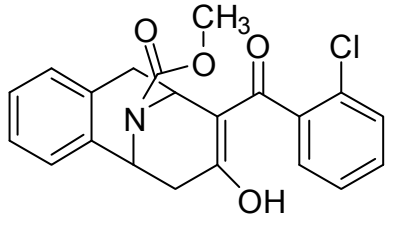
Methyl 11-hydroxy-10-(2-methylbenzoyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37c): 

Starting with **36c** (0.277 g, 0.76 mmol) and TFA (0.173 g, 1.50 mmol), **37c** was isolated as a colourless solid (0.201 g, 72%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.21 − 2.23 (m, 1 H, CHCH_2), 2.25 (s, 3H, CH_3), 2.49 (d, ^2J = 17.5, 1 H, CHCH_2), 2.78 – 2.86 (m, 1 H, CHCH_2), 2.98 – 3.13 (m, 1 H, CHCH_2), 3.65 (s, 3 H, CO_2CH_3, isomer 1&2), 5.08 – 5.28 (m, 1 H, NCH), 5.32 – 5.47 (m, 1 H, NCH), 6.89 – 6.91 (m, 1 H, CH_{Ar}), 7.01 – 7.10 (m, 3 H, CH_{Ar}), 7.14 – 7.29 (m, 4 H, CH_{Ar}), 16.20 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 17.0/17.1 (CH_3), 32.5/32.9, 39.1/39.5 (CHCH_2), 43.5/44.2, 46.6/47.1 (NCH), 50.9 (CO_2CH_3), 108.0 (C), 124.0, 124.2 (C_{Ar}), 124.4, 124.7, 125.7, 127.5, 127.7, 128.9, 129.2, 129.7 (CH_{Ar}), 132.4, 133.8/134.0 (C_{Ar}), 152.4 (C-OH), 186.1/186.8, 188.9/189.3 (C=O); GC-MS (EI, 70

eV): *m*/*z* (%) = 363 ([M^+], 24), 345 (11), 272 (100), 218 (14), 188 (13), 180 (26), 119 (26), 77(5), 65 (9); HRMS (EI): Calcd. for $C_{22}H_{21}O_4N$: 363.14651; found: 363.14570.

Methyl 11-hydroxy-10-(2-methoxybenzoyl)-13-azatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6,8,10-pentaene-13-carboxylate (37d): 

Starting with **36d** (0.210 g, 0.553 mmol) and TFA (0.126 g, 1.107 mmol), **37d** was isolated as a colourless solid (0.190 g, 69%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.23 (d, ^2J= 17.5 Hz. 1 H, CHCH_2), 2.46 (d, ^2J= 17.5 Hz, 1 H, CHCH_2), 2.77 – 2.88 (m, 1 H, CHCH_2), 2.99 − 3.12 (m,1 H, CHCH_2), 3.64 (s, 3H, OCH_3), 3.83 (s, 3 H, CO_2CH_3, isomer 1&2), 5.19 – 5.31 (m, 1 H, NCH), 5.34 – 5.43 (m, 1 H, NCH), 6.86 – 7.18 (m, 7 H, CH_{Ar}), 7.33 – 7.39 (m, 1 H, CH_{Ar}), 16.03 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.4/34.9, 40.3/40.7 (CH*C*H_2), 45.3/45.9, 48.3/48.9 (NCH), 52.4 (OCH_3), 55.4/55.6 (CO_2*C*H_3), 110.8 (C), 111.3/111.5, 120.9/121.0, 126.5/126.6, 127.4/127.5, 128.1, 129.5/129.8 (CH_{Ar}), 131.5/131.6 ($2CH_{Ar}$), 132.1, 136.2, 136.3, 154.2/154.4 (C_{Ar}), 155.0/155.3 (C-OH), 184.5/185.0, 190.9/191.3 (C=O); IR (neat): *v* = 2956 (w), 2925 (w), 2910 (w), 2841 (w), 1693 (s), 1442 (s), 1225 (s), 1012 (s), 750 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 379 ([M^+], 27), 361 (13), 330 (7), 288 (100), 258 (6), 212 (8), 188 (30), 135 (59), 115 (14), 77(21), 59 (7); HRMS (EI): Calcd. for $C_{22}H_{21}O_5N$: 379.14142; found: 379.14091.

Methyl 10-(2-chlorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6,8,10-pentaene-13-carboxylate (37e): 

Starting with **36e** (0.350 g, 0.911 mmol) and TFA (0.2079 g, 1.823 mmol), **37e** was isolated as a colourless solid (0.274 g, 78%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.37 (d, ^2J = 16.1 Hz. 1 H, CHCH_2), 2.51 (d, ^2J = 18.9 Hz, 1 H, CHCH_2), 2.84− 2.90 (m,1 H, CHCH_2), 3.01 – 3.15 (m, 1 H, CHCH_2), 3.67 (s, 3 H, CO_2CH_3, isomer 1&2), 5.11 – 5.25 (m, 1 H, NCH), 5.35 – 5.46 (m, 1 H, NCH), 6.96 (m, 1 H, CH_{Ar}), 7.04 – 7.19 (m, 3 H, CH_{Ar}), 7.34 – 7.47 (m, 4 H, CH_{Ar}), 15.88 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.2/34.8, 40.6/41.1 (CH*C*H_2), 45.5/46.2, 48.3/49.0 (NCH), 50.9 (CO_2*C*H_3), 110.1 (C), 126.3 (C_{Ar}), 126.6/126.7, 127.7 (CH_{Ar}), 127.6/127.7 (C_{Ar}), 127.9, 128.8, 129.6/129.9, 130.4/130.7, 130.9, 131.0 (CH_{Ar}), 131.6, 135.9/136.0 (C_{Ar}), 154.6 (C-OH), 186.6/187.0, 189.1 (C=O); GC-MS

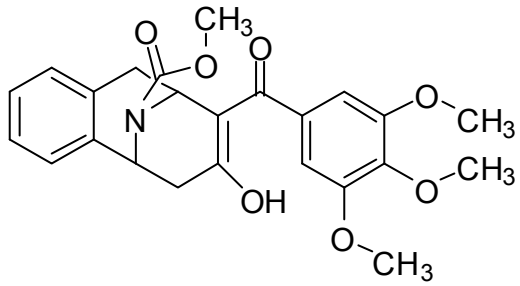
(EI, 70 eV): *m*/*z* (%) = 385 ([M^+], Cl^{37} 7), 383 ([M^+], Cl^{35} 20), 365 (11), 348 (10), 330 (12), 292 (100), 212 (10), 188 (20), 139 (30), 115 (12), 77(5); HRMS (EI): Calcd. for $C_{21}H_{18}O_4NCl$: 383.09189 ([M^+], Cl^{35}); found: 383.09184

Methyl 10-(2-fluorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37f): Starting with **36f** (0.430 g, 1.17 mmol) and TFA (0.226 g, 2.34 mmol), **37f** was isolated as a light yellow solid (0.350 g, 81%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.24 (d, ^2J = 19.5 Hz, 1 H, CHC*H*$_2$), 2.49 (d, ^2J = 18.0, 1 H, CHC*H*$_2$), 2.87 – 2.98 (m, 1 H, CHC*H*$_2$), 3.06 – 3.12 (m, 1 H, CHC*H*$_2$), 3.66 (s, 3 H, CO_2CH_3, isomer 1&2), 5.18 – 5.30 (m, 1 H, NCH), 5.37 – 5.44 (m, 1 H, NCH), 6.90 – 7.23 (m, 8 H, CH_{Ar}), 15.93 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.6/35.1, 40.6/41.1 (CH*C*H$_2$), 45.2/45.8, 48.3/48.9 (NCH), 52.9 (CO_2*CH*$_3$), 110.7 (C), 116.4/116.7 (2CH_{Ar}), 124.7 (d, ^4J = 3.1 Hz, CH_{Ar}), 126.3 (C_{Ar}), 126.6/126.7, (CH_{Ar}), 127.5 (d, ^3J = 7.2 Hz, CH_{Ar}), 128.6, 129.6/129.9 (CH_{Ar}), 131.0/131.4 (C_{Ar}), 132.1 (d, ^3J =7.9 Hz, CH_{Ar}), 135.9/136.0 (C_{Ar}), 154.4/154.5 (C-OH), 158.0/158.2 (d, ^1J = 245.0 Hz, CF_{Ar}), 186.4/186.8, 186.9/187.3 (C=O); IR (neat): *v* = 2957 (w), 2930 (w), 2915 (w), 2848 (w), 1693 (s), 1448 (s), 1210 (s), 1022 (s), 754 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 367 ([M^+], 70), 349 (45), 276 (100), 258 (20), 188 (73), 123 (83), 95 (37), 57(32).; HRMS (EI): Calcd. for $C_{21}H_{18}O_4NF$: 367.12144; found: 367.12106

Methyl 11-hydroxy-10-(4-nitrobenzoyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37g): Starting with **36g** (0.169 g, 0.43 mmol) and TFA (0.097 g, 085 mmol), **37g** was isolated as a colourless solid (0.100 g, 60%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.19 (d, ^2J = 16.1 Hz, 1 H, CHC*H*$_2$), 2.53 (d, ^2J = 19.0, Hz, 1 H, CHC*H*$_2$), 2.91 – 3.17 (m, 2 H, CHC*H*$_2$), 3.71 (s, 3 H, CO_2CH_3, isomer 1&2), 5.22 − 5.41 (m, 1 H, NCH), 5.46 – 5.59 (m, 1 H, NCH), 6.90 − 6.93 (s, 1 H, CH_{Ar}), 7.05 − 7.15 (s, 3 H, CH_{Ar}), 7.61 − 7.71 (m, 2 H, CH_{Ar}), 8.30 − 8.33 (m, 2 H, CH_{Ar}),16.05 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.9/35.3, 40.8/41.3 (CH*C*H$_2$), 45.0/45.7, 48.3/49.0 (NCH), 53.1/53.4 (CO_2*CH*$_3$), 109.5 (C), 124.2 (2CH_{Ar}), 124.4, 126.7/126.9, 127.8/127.9, 128.2, 129.6/129.9, 130.3 (CH_{Ar}), 130.7, 135.6, 142.0, 148.8 (C_{Ar}), 154.6 (C-OH), 187.3/187.6, 188.3/189.0

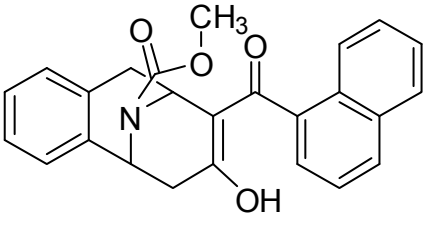
(C=O); MS (EI, 70 eV): *m*/*z* (%) = 394 ([M^+], 19), 376 (23), 346 (6), 303 (100), 273 (30), 188 (92), 180 (19), 120 (71), 92 (12), 73 (11), 57 (20).; HRMS (EI): Calcd. for $C_{21}H_{18}O_6N_2$: 394.11594; found: 394.11665.

Methyl 11-hydroxy-10-(3,4,5-trimethoxybenzoyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37h):



Starting with **36h** (0.180 g, 0.41 mmol) and TFA (0.093 g, 0.82 mmol), **37h** was isolated as a colourless solid (0.100 g, 55%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.29 (d, ^2J = 15.7 Hz, 1 H, CH*CH*$_2$), 2.46 (d, ^2J = 15.5, Hz, 1 H, CH*CH*$_2$), 2.73 – 2.99 (m, 1 H, CHC*H*$_2$), 3.09 – 3.18 (m, 1 H, CHC*H*$_2$), 3.70 (s, 3 H, CO_2CH_3, isomer 1), 3.73 (s, 3 H, CO_2CH_3, isomer 2) 3.83 − 3.87 ($m_{(br)}$, 9 H, OCH_3, isomer 1&2), 5.14 − 5.45 (m, 1 H, NCH), 5.60 – 5.90 (m, 1 H, NCH), 6.70 (s, 1 H, CH_{Ar}), 6.78 (s, 1 H, CH_{Ar}), 7.00 − 7.19 (m, 4 H, CH_{Ar}), 16.21 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.9/35.3, 40.5/40.9 (CH*C*H$_2$), 45.1/45.8, 48.4/49.0 (NCH), 53.0 (OCH_3), 56.2/56.3 (CO_2*CH*$_3$), 61.0, 64.2/64.4 (OCH_3), 108.9/109.1 (C), 126.4/126.6, 127.2/127.3, 127.5/127.6, 129.5/129.7, 129.9/130.0, 130.4/130.5 (CH_{Ar}), 131.7/131.8, 135.5/135.9, 139.9, 153.0, 153.5, 154.4 (C_{Ar}), 154.7 (C-OH), 186.9/187.0, 190.4/190.5 (C=O); MS (EI, 70 eV): *m*/*z* (%) = 439 ([M^+], 80), 348 (100), 294 (25), 212(7), 188 (61), 85 (8), 71 (12), 57 (22); HRMS (EI): Calcd. for $C_{24}H_{25}O_7N$: 439.16255; found: 439.16281

Methyl 11-hydroxy-10-(1-naphthoyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37i):



Starting with **36i** (0.115 g, 0.28 mmol) and TFA (0.067 g, 0.57 mmol), **37i** was isolated as a colourless solid (0.080 g, 70%, mp. = 154-156 ^{o}C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.00 − 2.07 (m, 1 H, CHC*H*$_2$), 2.53 (d, ^2J = 15.0 Hz, 1 H, CH*CH*$_2$), 2.59 – 2.69 (m, 1 H, CHC*H*$_2$), 3.04 − 3.19 (m,1 H, CHC*H*$_2$), 3.56 (s, 3 H, CO_2CH_3, isomer 1), 3.63 (s, 3 H, CO_2CH_3, isomer 2), 5.18 (m, 1 H, NCH), 5.31 – 5.43 (m, 1 H, NCH), 6.75 (m, 1 H, CH_{Ar}), 7.01 – 7.15 (m, 3 H, CH_{Ar}), 7.38 – 7.50 (m, 4 H, CH_{Ar}), 7.67 (m, 1 H, CH_{Ar}), 7.83− 7.91 (m, 2 H, CH_{Ar}), 16.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.2, 41.1/41.6 (CH*C*H$_2$), 45.7/46.2, 48.5/49.1 (NCH), 52.9/53.4 (CO_2*CH*$_3$), 110.9 (C), 124.5/124.6, 124.7,

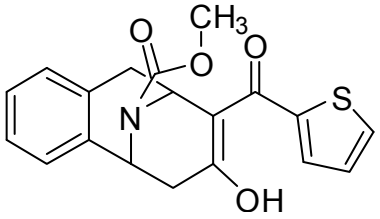
125.1, 126.4 (CH_{Ar}), 126.9 ($2CH_{Ar}$), 127.1/127.3, 127.5/127.6, 128.5, 129.5, 129.8 (CH_{Ar}), 130.2, 131.1, 131.7, 133.3/133.6, 135.9/136.0 (C_{Ar}), 154.5 (C-OH), 188.6, 190.1/190.5 (C=O); GC-MS (EI, 70 eV): *m*/*z* (%) = 399 ([M^+], 50), 382 (10), 356 (15), 308 (100), 280 (41), 253 (19), 212 (20), 188 (12), 155 (44), 127 (4); HRMS (EI): Calcd. for $C_{25}H_{21}O_4N$: 399.14651; found: 399.14617.

Methyl 11-hydroxy-10-(2-naphthoyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37j): Starting with **36j** (0.399 g, 1.00 mmol) and TFA (0.228 g, 2.00 mmol), **37j** was isolated as a slightly yellow solid (0.307 g, 77%, mp. = 166-168 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.33 (d, ^2J = 15.5 Hz, 1 H, CHCH_2), 2.60 (d, ^2J = 18.5 Hz, 1 H, CHCH_2), 3.01 – 3.34 (m, 1 H, CHCH_2), 3.35 − 3.51 (m,1 H, CHCH_2), 3.72 (s, 3 H, CO_2CH_3, isomer 1), 3.83 (s, 3 H, CO_2CH_3, isomer 2), 5.25 − 5.44 (m, 1 H, NCH), 5.79 – 5.96 (m, 1 H, NCH), 6.94 − 7.24 (m, 4 H, CH_{Ar}), 7.56 – 7.71 (m, 2 H, CH_{Ar}), 7.85 – 8.13 (m, 4 H, CH_{Ar}), 8.20 (s, 1 H, CH_{Ar}), 16.18 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.3, 40.8/41.2 (CHCH_2), 45.2/45.8, 48.4/49.1 (NCH), 53.0/53.1 (CO_2CH_3), 109.1 (C), 123.7/123.8, 126.3/126.4, 126.6, 126.9, 127.0, 127.2, 127.4, 127.6/127.7, 127.8/127.9, 128.8/128.9, 129.7/129.9 (CH_{Ar}), 130.9, 131.4, 132.6, 133.9/134.1, 135.9/136.1 (C_{Ar}), 154.7 (C-OH), 187.1/187.1, 189.8/190.3 (C=O IR (neat): ν = 3061 (w), 3042 (w), 2956 (w), 2849 (w), 1699 (s), 1443 (s), 1219 (s), 1006 (s), 750 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 399 ([M^+], 63), 382 (12), 356 (5), 308 (100), 280 (11), 253 (19), 212 (23), 188 (15), 155 (44), 127 (42), 116(27), 91 (10), 59 (12); HRMS (EI): Calcd. for $C_{25}H_{21}O_4N$: 399.14651; found: 399.14617.

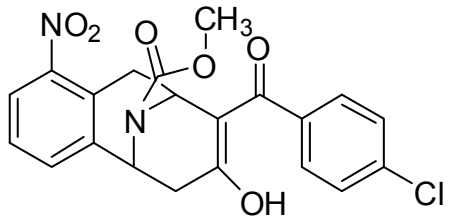
Methyl 11-hydroxy-10-(2-pyridinylcarbonyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37k): Starting with **36k** (0.300 g, 0.85 mmol) and TFA (0.195 g, 1.71 mmol), **37k** was isolated as a yellow oil (0.080g, 27%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.49 (d, ^2J = 17.9 Hz, 1H, CHCH_2), 2.78 − 2.85 (m, 1H, CHCH_2), 3.01 – 3.16 (m, 1 H, CHCH_2), 3.18 − 3.29 (m,1 H, CHCH_2), 3.66 (s, 3 H, CO_2CH_3, isomer 1&2), 5.34 − 5.48 (m, 1 H, NCH), 5.81 – 6.05 (m, 1

H, NCH), 6.94 − 7.07 (m, 4 H, CH_{Ar}), 7.43 – 7.47 (m, 1 H, CH_{Ar}), 7.86 – 7.95 (m, 1 H, CH_{Ar}), 8.08 − 8.14 (s, 1 H, CH_{Ar}), 8.54 (m, 1 H, CH_{Ar}), 15.59 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 35.0, 40.9/41.4 (CH*C*H_2), 45.8/46.3, 48.6/49.1 (NCH), 52.8 (CO_2*C*H_3), 111.1 (C), 124.7, 125.3, 126.2/126.5, 127.2/127.4, 129.6, 130.0, 133.0, 133.4 (CH_{Ar}), 136.3/136.4, 138.2, 138.6 (C_{Ar}), 154.4/154.8 (C-OH), 183.2, 192.2 (C=O); GC-MS (EI, 70 eV): *m*/*z* (%) = 350 ([M^+], 34), 275 (4), 259 (100), 188 (66), 162 (7), 144 (9), 106 (11), 78 (28), 59 (4); HRMS (EI): Calcd. for $C_{20}H_{18}O_4N_2$: 350.12611; found: 350.12604.

Methyl 11-hydroxy-10-(2-thienylcarbonyl)-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37l): Starting with **36l** (0.120 g, 0.35 mmol) and TFA (0.045 g, 0.40 mmol), **37l** was isolated as a reddish viscous oil (0.041g, 34%, mp. = 37-40 ^{o}C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.45− 2.47 (m, 1 H, CH*C*H_2 isomer 1), 2.51 − 2.54 (m, 1 H, CH*C*H_2 isomer 2), 2.76 (d, ^2J= 15.0 Hz, 1 H, CH*C*H_2 isomer 1), 2.83 (d, ^2J= 15.0 Hz, 1 H, CH*C*H_2 isomer 2), 3.01− 3.21 (m, 1 H, CH*C*H_2 isomer 1&2), 3.32− 3.40 (m, 1 H, CH*C*H_2 isomer 1&2), 3.69 (s, 3 H, CO_2CH_3, isomer 1), 3.74 (s, 3 H, CO_2CH_3, isomer 2), 5.36 − 5.40 (m, 1 H, NCH isomer 1&2), 5.87 – 6.03 (m, 1 H, NCH isomer 1&2), 6.97 − 7.18 (m, 5 H, CH_{Ar}), 7.61 – 7.77 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.4, 40.9/41.3 (CH*C*H_2), 45.0/45.7, 48.2/48.7 (NCH), 53.0 (CO_2*C*H_3), 108.1 (C), 126.3/126.7, 127.3/127.6, 128.5, 129.7/130.0, 131.7/131.9, 133.0, 133.8 (CH_{Ar}), 135.4, 136.4, 140.3 (C_{Ar}), 154.6/155.1 (C-OH), 178.8/179.4, 187.2/188.1 (C=O); IR (neat): ν = 3097 (w), 2990 (w), 2948 (w), 2851 (w), 1690 (s), 1448 (s), 1249 (s), 1022 (s), 749 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 355 ([M^+], 36), 337 (15), 264 (86), 188 (100), 180 (37), 170 (10), 144 (15), 111 (68), 97 (19), 83 (21), 69 (25), 57 (29); HRMS (EI): Calcd. for $C_{19}H_{17}NO_4S$: 355.08728; found: 355.08729.

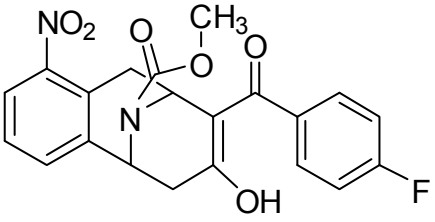


Methyl 10-(4-chlorobenzoyl)-11-hydroxy-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37m): Starting with **36m** (0.399 g, 1.00 mmol) and TFA (0.229 g, 2.01 mmol), **37m** was isolated as a light yellow solid (0.300g, 75%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.48 (d, ^2J =



19.0 Hz, 1 H, CHCH_2), 2.58 (d, ^2J = 18.0 Hz, 1 H, CHCH_2), 3.05 – 3.27 (m, 2 H, CHCH_2), 3.67 (s, 3 H, CO_2CH_3, isomer 1), 3.74 (s, 3 H, CO_2CH_3, isomer 2), 5.17 − 5.44 (m, 1 H, NCH), 5.54 – 5.81 (m, 1 H, NCH), 7.29 − 7.45 (m, 5 H, CH_{Ar}), 7.79 – 7.89 (m, 2 H, CH_{Ar}), 16.13 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 32.6/33.0, 40.4/40.8 (CHCH_2), 44.3/45.0, 48.4/49.1 (NCH), 53.3/53.4 (CO_2CH_3), 108.9 (C), 124.3, 127.3/127.4, 128.2/128.3, 128.5, (CH_{Ar}), 129.3 ($2CH_{Ar}$), 130.2 (CH_{Ar}), 131.1/131.8, 134.4, 137.3, 138.8, 149.9 (C_{Ar}), 154.3 (C-OH), 185.9/186.5, 189.5/189.6 (C=O); IR (neat): ν = 3082 (w), 3009 (w), 2954 (w), 2852 (w), 1699 (s), 1445 (s), 1221 (s), 1013 (s), 768 (s) cm^{-1}; GCMS (EI, 70 eV): *m*/*z* (%) = 430 ([M^++1], ^{37}Cl, 1), 428 ([M^++1], ^{35}Cl, 3), 390 (100), 312 (35), 256 (30), 210 (10); HRMS (EI): Calcd. for $C_{21}H_{17}O_6N_2$: ([M^+], ^{35}Cl), 428.07697; found: 428.07755.

Methyl 10-(4-fluorobenzoyl)-11-hydroxy-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37n): Starting with **36n** (0.396 g, 1.04 mmol) and TFA (0.237 g, 2.08 mmol), **37n** was isolated as a colourless solid (0.220g, 55%, mp. = 150-153 ^{o}C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.42 (d, ^2J = 15.0 Hz, 1 H, CHCH_2), 2.53 (d, ^2J = 15.8 Hz, 1 H, CHCH_2), 2.99 – 3.23 (m, 2 H, CHCH_2), 3.62 (s, 3 H, CO_2CH_3, isomer 1), 3.68 (s, 3 H, CO_2CH_3, isomer 2), 5.12 − 5.38 (m, 1 H, NCH), 5.49 – 5.74 (m, 1 H, NCH), 7.03 − 7.09 (m, 2 H, CH_{Ar}), 7.26 − 7.50 (m, 3 H, CH_{Ar}), 7.74 – 7.88 (m, 2 H, CH_{Ar}), 16.09 ($m_{(br)}$, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 32.6/33.0, 40.4/40.7 (CHCH_2), 44.3/45.0, 48.4/49.1 (NCH), 53.2/53.4 (CO_2CH_3), 108.7/108.9 (C), 116.3 (d, ^2J = 21.0 Hz, $2CH_{Ar}$), 124.4/124.7, 127.2/127.3, 127.9/128.3 (CH_{Ar}), 129.2 (d, ^3J = 8.4 Hz, CH_{Ar}), 129.5 (d, ^3J = 10.0 Hz, CH_{Ar}), 131.5/131.7, 132.3, 138.3/138.8, 148.9/149.8 (C_{Ar}), 154.4 (C-OH), 162.1 (d, ^1J = 241.8 Hz, CF_{Ar}), 185.6/186.4, 189.5/189.8 (C=O); IR (neat): ν = 3079 (w), 3002 (w), 2954 (w), 2815 (w), 1698 (s), 1444 (s), 1224 (s), 1032 (s), 784 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 412 ([M^+], 11), 382 (10), 364 (28), 276 (100), 233 (69), 203 (35), 180 (13), 123 (99), 95 (34); HRMS (EI): Calcd. for $C_{21}H_{18}O_6N_2F$: 412.10652; found: 412.10666.



Methyl 11-hydroxy-10-(2-methylbenzoyl)-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37o): Starting with **36o** (0.410 g, 1.09 mmol) and TFA (0.248 g, 2.18 mmol), **37o** was isolated as a colourless solid (0.355g, 69%. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.18 (s, 3 H, CH_3), 2.49 (d, ^{2}J = 15.0 Hz, 1 H, CH*CH*$_2$), 2.52 (d, ^{2}J = 15.1, Hz, 1 H, CH*CH*$_2$), 2.92 – 2.98 (m, 2 H, CHC*H*$_2$), 3.70 (s, 3 H, CO_2CH_3, isomer 1&2), 5.13 − 5.32 (m, 1 H, NCH), 5.41 – 5.55 (m, 1 H, NCH), 7.11 − 7.34 (m, 6 H, CH_{Ar}), 7.75 − 7.79 (m, 1 H, CH_{Ar}), 16.17 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 18.8/19.0 (CH_3), 32.0/32.4, 40.7/41.2 (CH*C*H$_2$), 44.7/45.3, 48.6/49.3 (NCH), 53.2 (CO_2*CH*$_3$), 109.4/109.6 (C), 124.1 (CH_{Ar}), 125.9 (C_{Ar}), 126.2, 127.4, 128.3, 130.2, 131.1, 131.5/131.8 (CH_{Ar}), 134.2, 135.2, 138.8/138.9, 149.9/150.1 (C_{Ar}), 154.1/154.3 (C-OH), 186.7/187.3, 191.8/192.2 (C=O); HRMS (EI): Calcd. for $C_{22}H_{20}O_6N_2$: 408.13159; found: 408.13276.

Methyl 10-(2-fluorobenzoyl)-11-hydroxy-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37p): Starting with **36p** (0.210 g, 0.55 mmol) and TFA (0.125 g, 1.10 mmol), **37p** was isolated as a slightly yellow solid (0.180 g, 86%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.50 (d, ^{2}J= 15.8 Hz, 1 H, CH*CH*$_2$), 2.60 (d, ^{2}J= 15.8 Hz, 1 H, CH*CH*$_2$), 3.05 – 3.20 (m, 2 H, CHC*H*$_2$), 3.72 (s, 3 H, CO_2CH_3, isomer 1&2), 5.30 − 5.43 (m, 1 H, NCH), 5.46 – 5.57 (m, 1 H, NCH), 7.15 − 7.34 (m, 5 H, CH_{Ar}), 7.43 (m, 1 H, CH_{Ar}), 7.78 – 7.82 (m, 1 H, CH_{Ar}), 15.89 ($s_{(br)}$, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 32.2/32.8, 40.2/40.7 (CH*C*H$_2$), 44.3/45.0, 48.2/49.0 (NCH), 53.2 (CO_2*CH*$_3$), 110.4 (C), 116.4/116.8, 124.3, 125.1, 127.3 (CH_{Ar}), 128.3 (C_{Ar}), 128.4 (d, ^{2}J = 16.5 Hz, CH_{Ar}), 129.1 (CH_{Ar}), 131.6 (d, ^{4}J = 2.3 Hz, CH_{Ar}), 132.5 (d, ^{3}J = 8.2 Hz, CH_{Ar}) 139.0 ($2C_{Ar}$), 149.6 (C_{Ar}), 154.4 (C-OH), 185.5/185.8, 187.5 (C=O); MS (CI, 70 eV): *m*/*z* (%) = 413 ([M^+1], 23), 393 (24), 363 (15), 233 (100), 203 (15); HRMS (CI): Calcd. for $C_{21}H_{19}O_6N_2F$: 413.10652; found: 413.10666.

Methyl 10-(2-chlorobenzoyl)-11-hydroxy-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37q): Starting with **36q** (0.416 g, 1.05 mmol) and TFA (0.239 g, 2.09 mmol), **37q** was isolated as a light yellow solid (0.205 g, 60%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.45 (d, ^{2}J = 16.7 Hz. 1 H, CHCH_2), 2.66 (d, ^{2}J = 14.6 Hz, 1 H, CHCH_2), 2.94− 3.10 (m, 2 H, CHCH_2), 3.64 (s, 3 H, CO_2CH_3, isomer 1&2), 5.09 – 5.24 (m, 1 H, NCH), 5.37 – 5.50 (m, 1 H, NCH), 7.14 (m, 1 H, CH_{Ar}), 7.27 – 7.42 (m, 5 H, CH_{Ar}), 7.72 – 7.76 (m, 1 H, CH_{Ar}), 15.78 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 31.9/32.5, 40.2/40.7 (CHCH_2), 44.6/45.2, 48.4/49.1 (NCH), 53.2 (CO_2CH_3), 109.6 (C), 124.2, 127.4, 127.7, 127.9, 128.3, 130.5, 131.3 (CH_{Ar}), 131.7, 133.1, 135.1, 139.0, 149.9 (C_{Ar}), 154.3 (C-OH), 185.8, 189.8 (C=O); IR (neat): v = 3011 (w), 1990 (w), 2956 (w), 2849 (w), 1698 (s), 1443 (s), 1219 (s), 1029 (s), 731 (s) cm^{-1}; GC-MS (CI, 70 eV): *m*/*z* (%) = 431 ([M$^+$+1], ^{37}Cl, 3), 429 ([M$^+$+1], ^{35}Cl, 10), 391 (100), 313 (30), 257 (35), 211 (20); HRMS (EI): Calcd. for $C_{21}H_{17}O_6N_2Cl$: ([M$^+$], ^{35}Cl), 428.07697; found: 428.07755.

Methyl 11-hydroxy-10-(2-naphthoyl)-6-nitro-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (37r): Starting with **36r** (0.443 g, 1.00 mmol) and TFA (0.228 g, 2.00 mmol), **37r** was isolated as a yellowish solid (0.280 g, 63%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.49 (d, ^{2}J = 17.5 Hz, 1 H, CHCH_2), 2.61 (d, ^{2}J = 19.0 Hz, 1 H, CHCH_2), 3.02 – 3.11 (m, 2 H, CHCH_2), 3.73 (s, 3 H, CO_2CH_3, isomer 1&2), 5.41− 5.56 (m, 1 H, NCH), 5.70 – 5.91 (m, 1 H, NCH), 7.18 (m, 1 H, CH_{Ar}), 7.21 – 7.36 (m, 2 H, CH_{Ar}), 7.46 – 7.53 (m, 3 H, CH_{Ar}), 7.75 − 8.03 (m, 4 H, CH_{Ar}), 16.22 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.2, 41.1/41.6 (CHCH_2), 45.7/46.2, 48.5/49.1 (NCH), 52.9/53.4 (CO_2CH_3), 110.9 (C), 124.5/124.6, 124.7, 125.1, 126.4 (CH_{Ar}), 126.9 (2CH_{Ar}), 127.1/127.3, 127.5/127.6, 128.5, 129.5, 129.8 (CH_{Ar}), 130.2, 131.1, 131.7, 133.3/133.6, 135.9/136.0 (C_{Ar}), 154.5 (C-OH), 188.6, 190.1/190.5 (C=O); IR (neat): v = 3033 (w), 3014 (w), 2958 (w), 2852 (w), 1702 (s), 1528 (s), 1340 (s), 1029 (s), 771 (s) cm^{-1}; GC-MS (EI, 70 eV): *m*/*z* (%) = 444 ([M$^+$], 10), 425 (16), 385 (10), 308 (90), 257 (13), 233 (37), 180 (40), 155 (100), 143 (29), 125 (43), 59 (11); HRMS (EI): Calcd. for $C_{25}H_{20}O_6N_2$: 444.13159; found: 444.13172.

Benzyl 10-(4-chlorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (39f): Starting with **38f** (0.200 g, 0.43 mmol) and TFA (0.869 g, 0.69 mmol), **39f** was isolated as a yellowish gummy solid (0.163 g, 81%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.20 – 2.29 (m, 1 H, CH*CH*$_2$), 2.45 – 2.52 (m, 1 H, CH*CH*$_2$), 2.91 – 3.17 (m, 2 H, CHC*H*$_2$), 5.37 – 5.48 (m, 1 H, NCH), 5.22 (s, 2 H, CO_2CH_2, isomer 1&2), 5.47− 5.73 (m, 1 H, NCH), 7.15 – 7.50 (m, 13 H, CH_{Ar}), 16.05 ($s_{(br)}$, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.8/35.3, 40.7/41.2 (CH*C*H$_2$), 45.1/45.8, 48.5/49.1 (NCH), 67.3/67.9 (CO_2*CH*$_2$), 109.4 (C), 126.4/136.6, 126.4/126.6, 126.7/126.8 (CH_{Ar}), 127.6/127.7 ($2CH_{Ar}$), 128.1/128.3, 128.4/128.6,128.65/128.7 (CH_{Ar}), 129.0/129.1 ($2CH_{Ar}$), 129.6/129.8, 130.5, 131.1, 132.0/132.1(CH_{Ar}), 133.5/133.8, 134.7/134.8, 135.9/136.1, 136.7, 137.1 (C_{Ar}), 153.7/154.1 (C-OH), 187.4/187.9, 188.4/188.9 (C=O); MS (EI, 70 eV): 461 ([M^++1], ^{37}Cl, 3), 459 ([M^++1], ^{35}Cl, 8), 434 (4), 375 (7), 324 (17), 264 (5), 212 (10), 181 (6), 138 (26), 111 (19), 91 (100), 69 (32), 57 (51), 44 (86); HRMS (EI): Calcd. for $C_{27}H_{22}O_4NCl$: ([M^+], ^{35}Cl), 459.12313; found: 459.12318.

Benzyl 10-(2-chlorobenzoyl)-11-hydroxy-13-azatricyclo[7.3.1.0^{2,7}]trideca-2,4,6,8,10-pentaene-13-carboxylate (39g). Starting with **38g** (0.424 g, 0.923 mmol) and TFA (0.210 g, 2.10 mmol), **39g** was isolated as a gummy solid (0.212 g, 50%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.31 – 2.56 (m, 2 H, CH*CH*$_2$), 2.83 – 3.18 (m, 2 H, CHC*H*$_2$), 5.00 – 5.18 (m, 1 H, NCH), 5.22 (s, 2 H, CO_2CH_2, isomer 1&2), 5.27− 5.46 (m, 1 H, NCH), 6.97 – 7.11 (m, 4 H, CH_{Ar}), 7.29 – 7.37 (m, 9 H, CH_{Ar}), 15.70 ($s_{(br)}$, 1 H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C = 34.3/34.8, 40.6/40.9 (CH*C*H$_2$), 45.5/46.1, 48.4/49.0 (NCH), 67.7 (CO_2*CH*$_2$), 110.0 (C), 126.3, 126.6, 126.8/126.9, 127.2, 127.6/127.7, 127.9, 128.1, 128.2/128.3, 128.5, 128.6 , 129.7, 129.9, 130.4 (CH_{Ar}), 131.1, 131.6, 135.4, 135.8, 136.3 (C_{Ar}), 154.2 (C-OH), 187.0, 189.4 (C=O); MS (EI, 70 eV): 461 ([M^++1], ^{37}Cl, 8), 459 ([M^++1], ^{35}Cl, 23), 444 (8), 414 (2), 368 (18), 324 (65), 288 (114), 212 (21), 198 (21), 161 (18), 129 (34), 91 (100), 57 (18), 44 (80); HRMS (EI): Calcd. for $C_{27}H_{22}O_4NCl$: ([M^+], ^{35}Cl), 459.12367; found: 459.12341.

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X-Ray Crystals Data

Data for compound 19m Chapter 2:

data_ ks 709m

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_chemical_name_systematic
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_chemical_melting_point ?
_chemical_formula_moiety ?
_chemical_formula_sum ' C16 H15 N O5'

_chemical_formula_weight 301.29

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_atom_type_description
_atom_type_scat_dispersion_real
_atom_type_scat_dispersion_imag
_atom_type_scat_source
'C' 'C' 0.0033 0.0016
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'H' 'H' 0.0000 0.0000
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'N' 'N' 0.0061 0.0033
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'O' 'O' 0.0106 0.0060
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting monoclinic
_symmetry_space_group_name_H-M P2(1)/n

loop_
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'-x+1/2, y+1/2, -z+1/2'
'-x, -y, -z'
'x-1/2, -y-1/2, z-1/2'

_cell_length_a 13.539(3)
_cell_length_b 7.6294(15)
_cell_length_c 13.870(3)
_cell_angle_alpha 90.00
_cell_angle_beta 98.50(3)
_cell_angle_gamma 90.00
_cell_volume 1417.0(5)
_cell_formula_units_Z 4
_cell_measurement_temperature 200(2)
_cell_measurement_reflns_used all
_cell_measurement_theta_min ?
_cell_measurement_theta_max ?

_exptl_crystal_description prism
_exptl_crystal_colour colourless
_exptl_crystal_size_max 0.50
_exptl_crystal_size_mid 0.45
_exptl_crystal_size_min 0.30
_exptl_crystal_density_meas ?
_exptl_crystal_density_diffrn 1.412
_exptl_crystal_density_method 'not measured'
_exptl_crystal_F_000 632
_exptl_absorpt_coefficient_mu 0.106
_exptl_absorpt_correction_type none
_exptl_absorpt_correction_T_min ?
_exptl_absorpt_correction_T_max ?
_exptl_absorpt_process_details ?

Data for compound 26a Chapter 3:

Table 1. Crystal data and structure refinement for ah137cl.

Identification code	ah137cl
Empirical formula	$C_{15}H_{13}Cl\ O_3$
Formula weight	276.70
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group (H.-M.)	Pnma
Space group (Hall)	-P 2ac 2n

Unit cell dimensions	a = 14.3783(6) Å	α= 90°.
	b = 6.9445(4) Å	β= 90°.
	c = 13.1845(6) Å	γ = 90°.
Volume	1316.47(11) $Å^3$	
Z	4	
Density (calculated)	1.396 Mg/m^3	
Absorption coefficient	0.291 mm^{-1}	
F(000)	576	
Crystal size	0.98 x 0.29 x 0.08 mm^3	
θ range for data collection	2.10 to 29.99°.	
Index ranges	-20≤h≤19, -9≤k≤8, -18≤l≤16	
Reflections collected	10853	
Independent reflections	1960 [R(int) = 0.0363]	
Completeness to θ = 29.99°	94.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9777 and 0.7639	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1960 / 0 / 113	
Goodness-of-fit on F^2	1.054	
Final R indices [I>2σ(I)]	R1 = 0.0388, wR2 = 0.1048	
R indices (all data)	R1 = 0.0523, wR2 = 0.1171	
Extinction coefficient	0.003(2)	
Largest diff. peak and hole	0.423 and -0.243 $e.Å^{-3}$	

Data for compound 27d Chapter 3:

Table 1. Crystal data and structure refinement for fo3174.

Identification code	FO3174	
Empirical formula	C16 H13 Cl O3	
Formula weight	288.71	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 17.9894(10) Å	α= 90°.
	b = 6.8769(3) Å	β= 90°.
	c = 20.6852(13) Å	γ = 90°.
Volume	2559.0(2) $Å^3$	
Z	8	

Density (calculated)	1.499 Mg/m^3
Absorption coefficient	0.302 mm^{-1}
F(000)	1200
Crystal size	0.05 x 0.05 x 0.04 mm^3
Theta range for data collection	2.26 to 27.48°.
Index ranges	-23<=h<=22, -8<=k<=8, -26<=l<=25
Reflections collected	19690
Independent reflections	2929 [R(int) = 0.1290]
Completeness to theta = 27.48°	99.9 %
Absorption correction	NONE
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2929 / 0 / 186
Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0551, wR2 = 0.1123
R indices (all data)	R1 = 0.1348, wR2 = 0.1418
Largest diff. peak and hole	0.385 and -0.421 $e.Å^{-3}$

Data for compound 34f Chapter 4:

Table 1. Crystal data and structure refinement for **34f (FO3176)**.

Identification code	FO3176	
Empirical formula	C20 H12 Br F O4	
Formula weight	415.21	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 7.5626(2) Å	α= 90°.
	b = 19.2580(5) Å	β= 90°.
	c = 22.4319(4) Å	γ = 90°.
Volume	3266.99(13) $Å^3$	
Z	8	
Density (calculated)	1.688 Mg/m^3	
Absorption coefficient	2.551 mm^{-1}	
F(000)	1664	
Crystal size	0.04 x 0.04 x 0.02 mm^3	
Theta range for data collection	2.79 to 27.48°.	
Index ranges	-9<=h<=9, -25<=k<=24, -28<=l<=29	
Reflections collected	21125	

Independent reflections	3734 [R(int) = 0.0517]
Completeness to theta = 27.48°	99.8 %
Absorption correction	NONE
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3734 / 0 / 243
Goodness-of-fit on F^2	1.006
Final R indices [I>2sigma(I)]	R1 = 0.0324, wR2 = 0.0759
R indices (all data)	R1 = 0.0506, wR2 = 0.0841
Largest diff. peak and hole	0.376 and -0.530 e.$Å^{-3}$

Data for compound 34m Chapter 4:

Table 1. Crystal data and structure refinement for **34m (FO3180)**.

Identification code	FO3180	
Empirical formula	C20 H12 Br F O4	
Formula weight	415.21	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	Pc	
Unit cell dimensions	a = 9.0722(4) Å	α= 90°.
	b = 26.1738(5) Å	β= 73.646(2)°.
	c = 7.3483(3) Å	γ = 90°.
Volume	1674.29(11) $Å^3$	
Z	4	
Density (calculated)	1.647 Mg/m^3	
Absorption coefficient	2.489 mm^{-1}	
F(000)	832	
Crystal size	0.04 x 0.04 x 0.04 mm^3	
Theta range for data collection	2.34 to 27.56°.	
Index ranges	-11<=h<=11, -33<=k<=28, -9<=l<=9	
Reflections collected	10672	
Independent reflections	6004 [R(int) = 0.0948]	
Completeness to theta = 27.56°	97.0 %	
Absorption correction	NONE	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6004 / 2 / 469	
Goodness-of-fit on F^2	1.070	
Final R indices [I>2sigma(I)]	R1 = 0.0756, wR2 = 0.1838	

R indices (all data)	R1 = 0.1035, wR2 = 0.2105
Absolute structure parameter	0.018(18)
Largest diff. peak and hole	1.483 and -0.886 e.Å^{-3}

Data for compound 37d Chapter 5:

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_chemical_formula_moiety ?
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_chemical_formula_weight 379.40

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_atom_type_description
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_atom_type_scat_source
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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'H' 'H' 0.0000 0.0000
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'N' 'N' 0.0061 0.0033
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'O' 'O' 0.0106 0.0060
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'x+1/2, -y+1/2, -z'

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_cell_length_b 12.8998(4)
_cell_length_c 16.4167(4)
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_cell_angle_beta 90.00
_cell_angle_gamma 90.00
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_cell_measurement_reflns_used all
_cell_measurement_theta_min ?
_cell_measurement_theta_max ?

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Data for compound 37f Chapter 5:

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'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

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_cell_angle_beta                 90.00
_cell_angle_gamma                90.00
_cell_volume                    1694.15(14)
_cell_formula_units_Z            4
_cell_measurement_temperature     200(2)
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_cell_measurement_theta_max       ?
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_exptl_crystal_density_method     'not measured'
_exptl_crystal_F_000              768
_exptl_absorpt_coefficient_mu     0.107
_exptl_absorpt_correction_type    numerical
_exptl_absorpt_correction_T_min   0.8326
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_exptl_absorpt_process_details    ?

_exptl_absorpt_correction_T_max   ?
_exptl_absorpt_process_details    ?
```

Curriculum vitae

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PUBLICATIONS:

1 ***Mirza Arfan yawer***, Ibrar Hussain, Jörg-Peter Güzlein, Andreas Schmidt, Haijun Jiao Hemut Reinke, Anke Spannerberg and Peter Langer*, ***Eur. J.Org. Chem,* 2008**. (in press). "Synthesis of Functionalized Isobenzomorphans by Two-Step Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Isoquinolines".

2 ***Mirza Arfan Yawer***, Ibrar Hussain, Inam Iqbal, Anke Spannerberg and Peter Langer*, ***Tetrahedron Lett.* 2008**, 4467–4469. **"**Synthesis of Functionalized Dibenzo[*b*,*d*]pyrid-6-ones based on a [3+3]-Cyclocondensation / Lactamization Strategy".

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Declaration/Erklärung

Here by I declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the University of Rostock nor to any other scientific Institution for the purpose of doctorate. Further more, I declare that I have written this work by myself and that I have not used any other sources, other than mentioned earlier in this work.

Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion eingereicht wurde.

Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe

I hereby apply irrevocably to take oral examination in the form of a private viva voce and a public presentation.

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Mirza Arfan Yawer