Synthesis of Aryl Chlorides, Aryl Phosphonates, Benzonitriles, Diaryl Sulfides, Biaryl Lactones and Pyrrolocoumarins by Cyclization of 1,3-Bis(silyloxy)-1,3-butadienes with Functionalized 3-Alkoxy-2-en-1-ones and Coumarins

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Eidesstattliche Erklärung

Hiermit erkläre ich, die vorliegende Dissertationsschrift eigenständig und nur unter Verwendung der angegebenen Hilfsmittel und Literaturquellen angefertigt zu haben.

Olumide Foluso Fatunsin

Rostock, 7th April 2010

Affectionately Dedicated to

My dearest Father and Mother for their exceptional love.

Also, to my loving younger brothers and sisters for their cares and support.

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Acknowledgement

*Be thou exalted, **LORD**, in thine own strength; so will we sing and praise thy power. (Psa 21:13). You are worthy O Lord, to receive glory and honour and power; for you have created all things, and for your pleasure they are and were created. (Rev. 4:11). I am really grateful Lord for all you have done for me and blessed be your Holy name.*

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List of used abbreviations

Ar	Aromatic
*n*BuLi	*n*-Butylithium
DEPT	Distortionless Enhancement by Polarisation Transfer
EI	Electronic Ionization
ESI	Electrospray Ionization
EtOAc	Ethyl acetate
HRMS	High Resolution Mass Spectroscopy
IR	Infrared spectroscopy
LDA	Lithium diisopropylamide
MS	Mass Spectrometry
Ph	Phenyl
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resolution
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser and Exchange Spectroscopy
Me_3SiCl	Trimethylsilyl chloride
mp.	Melting point
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy

General Introduction

It is known that humans have used organic compounds and their reactions for thousands of years. Foremost, the discovery of fire was the first encounter with an organic reaction. However, the ancient Egyptians have used organic compounds (indigo and alizarin) to dye cloth and the famous "royal purple" which was also an organic substance obtained from molluscs have been used by the Phoenicians. Ethyl alcohol and the acidic qualities of "soured wine" produced through the fermentation of grapes have been known earlier and also described in the Bible.

As a science, organic chemistry is less than 200 years old and most historians of science date its origin to the early part of the nineteenth century, a time in which an erroneous belief was dispelled.

Scientists began to distinguish between organic compounds and inorganic compounds during the 1780s. Organic compounds were defined as compounds that could be obtained from living organisms, inorganic compounds were those that came from nonliving sources.
A belief called "vitalism" grew and according to this idea, the intervention of a "vital force" was necessary for the synthesis of an organic compound. The chemist believed such synthesis could not take place in the flasks of a chemistry laboratory but only in living organisms.

A number of compounds that were clearly "organic" were synthesized from sources that were clearly "inorganic" between 1828 and 1850. The first of these syntheses was accomplished by Friedrich Wöhler in 1828. Wöhler found that the organic compound urea (a constituent of urine) could be made by evaporating an aqueous solution containing the inorganic compound ammonium cyanate.

Although vitalism disappeared slowly from scientific circles after Wöhler's synthesis, its passing made possible the flowering of the science of organic chemistry that has occurred since 1850.[1] The impact of chemistry plays importance role in our everyday lives although the average citizen may not recognize or appreciate that fact. Recent advances in the chemical sciences are directly responsible for many of the improvements in the standard of living we enjoy. In no area is this truer than in modern medicine, especially as it relates to the development of new drugs.

Millions of organic compounds have been synthesized since and many methods have been developed to access more and more complex chemical structures. Natural products continue to play an important role in discovery and development of new pharmaceuticals, as clinically useful drugs, as starting materials to produce synthetic drugs, or as lead structures

from which a synthetic drug can be designed.[2] A famous example of flavouring compound i.e menthol was extracted from the essential oil of spearmint. At the same time, synthetic compounds not related to natural products play an increasingly important role for drug discovery. Continuous improvements in synthetic methodology have provided a convenient access to a vast array of synthetic substances.

Natural products often represent important lead structures for the development of antibiotics.[3] In fact, a number of natural products exhibit antibiotic activity and since the discovery of penicillin, a large number of antibiotics has been isolated from scores of micro-organisms.[4] This discovery of new important anti-infective compounds includes both plant and animal sources. For example, astemisinin, a sesquiterpene with endoperoxide moiety, was isolated from *Astemisia annua*, a Chinese medicinal plant, which has been used in China for centuries for treatment of malaria. The development of new drugs includes synthetic and semi-synthetic studies, microbial transformations, the biological screening and the study of the mechanism of action[5].

Many natural products have also provided the most important success in the chemotherapy of cancer disease and a number of anticancer drugs represent unmodified natural products isolated from plants or microorganisms:[6] For example, ironotecan which is a camptothecin derivative is a semi synthetic derivative of natural products.

Many important drugs have been developed by a combination of natural product and synthetic chemistry. In this context, combinatorial chemistry provides an ever-increasing pool for evaluation of therapeutic potential; advances in molecular biology will provide insights into the biological processes and, hence, possible targets for the treatment of disease. Bioactive natural products can serve as probes to study these molecular and pharmacological processes.[7]

Interestingly, my studies are focused on the development of new and reliable synthetic strategies and their application to the preparation of natural products analogues, and pharmacologically active carba- and heterocycles. In the present thesis, the synthesis of natural product analogues is studied. These structures include aryl chlorides, aryl phosphonates, benzonitriles, diaryl sulfides, biary lactones and pyrrolocoumarins.

Summary

A significant part of the present dissertation has been recently published. The work presented in this dissertation is concerned with the synthesis of highly functionalized aryl chlorides, aryl phosphonates, benzonitriles, diaryl sulfides, biaryl lactones and pyrrolocoumarins by cyclization of 1,3-bis(silyloxy)-1,3-butadienes with functionalized 3-alkoxy-2-en-1-ones and coumarins.

Synthesis of Aryl Chlorides, Aryl Phosphonates, Benzonitriles, Diaryl Sulfides, Biaryl Lactones and Pyrrolocoumarins by Cyclization of 1,3-Bis(silyloxy)-1,3-butadienes with Functionalized 3-Alkoxy-2-en-1-ones and Coumarins

1. *Regioselective Synthesis of 5-Chlorosalicylates by One-Pot Cyclization of 1,3-bis (trimethylsilyloxy)-1,3-butadienes with 2-Chloro-3-ethoxy-2-alken-1-ones.* This chapter includes the synthesis of a variety of highly substituted 5-chlorosalicylates **7a-q** by one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-buta-dienes with 2-chloro-3-ethoxy-2-alken-1-ones **6a-f**. The reactions proceed with very good regioselectivity.

2. *Regioselective Synthesis of Highly Functionalized Arylphosphonates by Cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-Ethoxy-2-phosphonyl-alk-2-en-1-ones.* In this chapter, an eficient synthesis of highly functionalized arylphosphonates **10a-m** by cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with both aliphatic and aromatic 3-ethoxy-2-phosphonyl-alk-2-en-1-ones **9a-b** were carried out.

3. *First Synthesis of 5-Cyanosalicylates by Formal [3+3] Cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes.* Functionalized benzonitriles are important substructures of various dyes, pharmaceuticals, agrochemicals, herbicides, and pesticides. Herein, the synthesis of 5-cyanosalicylates **13a-ac** by formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with cyano-substituted enones **12a-e** is reported.

4. *Regioselective Synthesis of 5-Arylthio- and 5-Benzylthio-6-phenylsalicylates by One-Pot Cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 2-Arylthio- and 5-Benzylthio-3-ethoxy-2-en-1-ones.* Natural and non-natural diaryl sulfides (diaryl thioethers) are of pharmacological relevance and have been isolated as natural products. I have described in this chapter, the synthesis of variety of 5-arylthio-6-phenylsalicylates **17a-q** by one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 2-arylthio-3-ethoxy-2-en-1-ones **16a-f**.

5. *Synthesis of Chromeno[3,4-b]pyrrol-4(3H)-ones*] *by Cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-3-nitrocoumarin.* Coumarin derivatives constitute the core of a large number of alkaloids and biologically active compounds and this chapter details the synthesis of functionalized chromeno[3,4-b]pyrrol-4(3H)-ones] **20a-k** by $TiCl_4$-mediated reaction of 4-chloro-3-nitrocoumarin **18** with 1,3-bis(silyloxy)-1,3-butadienes and subsequent reduction of the nitro group **19a-k** and cyclization by H_2 and Pd/C.

6. *Regioselective Synthesis of Benzo[c]chromen-6-ones by One-Pot Cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-2-oxo-2H-chromene-3-carbaldehyde*. This chapter includes facile synthesis of functionalized 9-hydroxy-6-oxo-6*H*-benzo[c]chromenes **22a-l** by reaction of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde **21**.

7. *Abstract and the General scheme of this Thesis were outlined in this chapter.*

8. *Experimental part*

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

1 Regioselective Synthesis of 5-Chlorosalicylates by One-Pot Cyclization of 1,3-Bis-(trimethylsilyloxy)-1,3-butadienes with 2-Chloro-3-ethoxy-2-alken-1-ones

1.1 Synthesis of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes

1.1.1 Introduction

The development of new synthetic methods in tackling numerous challenges in the synthesis of complex molecules like production of drugs for medical purposes has received serious setback. Some simple tranformations have been carried out using easy synthetic methods while complex transformations proved difficult or eventual low yields. In addition, the development of molecules with high regio-, chemo-, and stereoselectivity has added to the load of challenges.

The desire of organic chemists is to carry out a reaction in a single step without necessary following the various stepwise procedures like changing reaction conditions, adding reagents or isolating intermediates. However, this method will save cost, reduce the amounts solvents, time and energy used. This type of transformation in single step is what is referred to as Domino reactions.

Interestingly, domino reactions[8] and the reactions of dielectrophiles with dinucleophiles constitute importance concepts for the formation of more than one bond in a single step. Thus, more complex transformations have been made possible. The group of Prof. Langer has focussed on the development of cyclization reactions of dianions[9] and dianion equivalents leading to various biologically relevant ring systems. The reaction of dielectrophiles with dinucleophiles may seems simple but many side reactions usually occur for instance, 1,3-dicarbonyl dianions are only accessible by the use of strong bases.

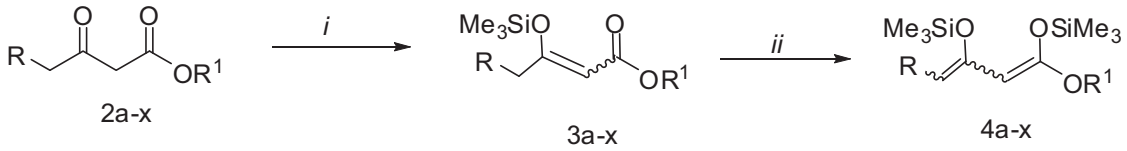
However, dianions represent important building blocks for the regioselective formation of carbon–carbon bonds while ambident dianions are organic substrates containing two delocalized negative charges. Dianions can be generated by reaction of 1,3-dicarbonyl compounds in the presence of strong base, such as *n*-BuLi or LDA [10]. 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.

Recent studies proved that 1,3-bis(silyl enol ethers) can be considered as equivalents of the corresponding 1,3-dicarbonyl dianions.[11] The chemistry of bis silyl enol ethers has been developed during the last two decades.[11b] It is, for example, known that silyl enol ethers can combine with various carbonyl compounds in the presence of Lewis acids.[12] These Lewis acid-mediated reactions[13] (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,[14] 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. They can be reacted with halides or pseudohalides,[15] Whereas enolates can be alkylated only by primary or secondary halides, enol silyl ethers can be alkylated by tertiary halides.[16]

The preparation of 1,3-bis(silyl enol ethers) mainly follows the procedures reported by Chan and Molander. These syntheses rely on the preparation of 1,3-mono(silyl enol ethers) which are subsequently transformed into 1,3-bis(silyl enol ethers) by deprotonation with LDA and subsequent silylation.[17] In this chapter, I present the synthesis of various 1,3-bis(silyl enol ethers) following the procedure of Chan and Molander.

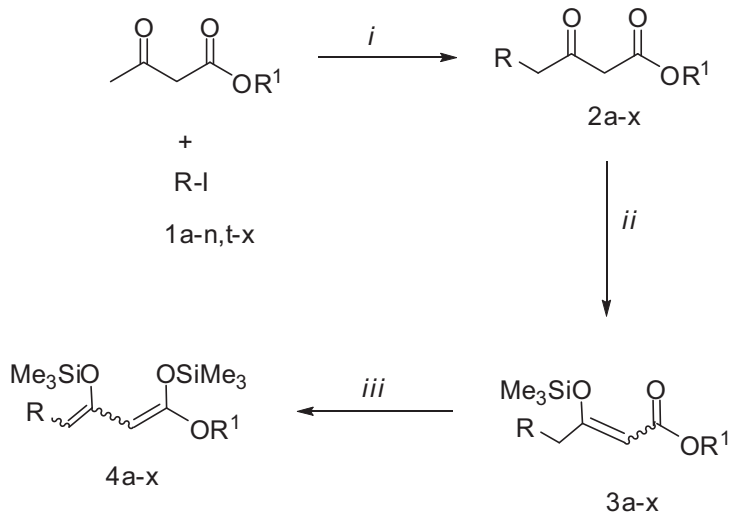
1.1.2 Results and Discussion

With the use of the procedures of Chan and Molander, 1,3-bis(trimethylsilyloxy)-1,3-butadienes **4a-x** were prepared from the respective 1,3-dicarbonyl compounds **2a-x** in two steps, which were commercially available. Treatment of the β-ketoesters with NEt_3, Me_3SiCl afforded 1,3-mono(silyl enol ethers) **3a-x**. Deprotonation of the latter with LDA and subsequent addition of Me_3SiCl afforded the diene **4a-x** (Scheme 1, Table 1)



Scheme 1: Synthesis of 1,3-bis(silyl enol ethers) **4a-x**; *i*) 1) NEt_3 (1.5 equiv.); 2) Me_3SiCl (1.5 equiv.), C_6H_6, 20 °C, 12 - 48 h; *ii*) 1) LDA (1.5 equiv.), THF, 0 °C, 2 h; 2) Me_3SiCl (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 **2a-x**. 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 **2a-x** were prepared by reactions of the dianion of methyl acetoacetate with the respective alkylhalides **1a-n,t-x** (RI). These compounds were transformed, according to a known procedure[18], into the desired 1,3-bis(silyl enol ethers) **4a-x** via the respective mono(silyl enol ethers) **3a-x** (Scheme 2, Table 1).



Scheme 2: Synthesis of alkyl-substituted 1,3-bis(silyl enol ethers) derivatives **4o-s**; *i*: 1) 2.5 LDA, THF, 0 °C, 1 h; 2) **1a-n**, **t-x** –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.

The prepared 4-alkyl-1,3-bis(silyl enol ethers) 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 β-ketoesters used in this thesis are listed in the following table.

Table 1: 1,3-bis(silyl enol ethers) **4a-x**

4	R	R^1
a	H	Me
b	H	Et
c	H	*i*Pr
d	H	$(CH_2)_2OMe$
e	Me	Me
f	Et	Me
g	Et	Et
h	*N*pr	Me
i	*n*Bu	Me
j	*n*Pen	Me
k	*n*Hex	Me
l	*n*Hex	Et
m	*n*Hept	Me
n	*n*Hept	Et
o	*n*Oct	Me
p	*n*Oct	Et
q	*n*Non	Me
r	*n*Dec	Me
s	*n*Dec	Et
t	*i*Pr	Et
u	*i*Pen	Me
v	Cl	Et
w	MeO	Me
x	4-ClC_6H_4	Me

1.1.3 Conclusion

The application of known procedures allowed the synthesis of novel 1,3-bis(silyl enol ethers). These masked dianions are used in this project for cyclization reactions for the synthesis of heterocycles and aromatic rings which represent important building blocks and natural product analogues.

1.2 Synthesis of 5-Chlorosalicylates

1.2.1 Introduction

Aryl chlorides are of genuine importance in synthetic organic chemistry. It has found its usefulness in the field of medicine as lead structures in many pharmacological natural products.[19] In fact, from the standpoint of cost and availability, the aryl chlorides are better than the other aryl halides. The importance of aryl chlorides cannot be overlooked in the area of various antimicrobial activities. For example, griseofulvins[20], a chlorinated molecule has attracted attention because of its antifungal activity and its unique structure. Others with the same core structures like grisandions, spirochlorins and epigriseofulvin have shown clastogenic, cytotoxic and antifungal activities.[20] The aryl chlorides with different core structures are present in many natural products such as austocystin A,[21a,b] which contain xanthone core structure. Moreover, 5-chlorosalicylate core structure my main focus in this chapter, is present in the chlorinated tetracyclins,[21c] the isochromanone ochratoxin A (Figure 1),[21d] and in chloratranorin (Figure 2).[19] Antibacterial and antiviral activities have been reported for geodin, dihydronodulin and 7-chlor-1-*O*-methylemodin.[22a-h]

Guisinol, (Figure 3)[19] an isolate from *Emericella unguis* has been shown to exhibit strong antibacterial activity.

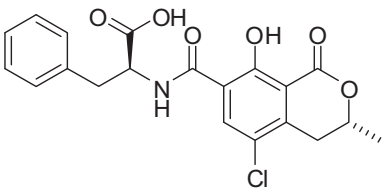


Figure 1. Ochratoxin A

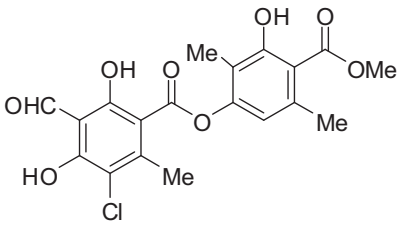


Figure 2. Chloratranorin

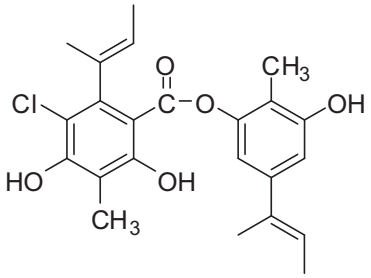


Figure 3. Guisinol

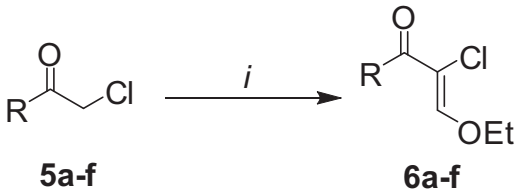
Interestingly, chloroarenes have found an increasing relevance as synthetic building blocks for transition metal-catalysed cross-coupling reactions.[23] Classic syntheses of functionalized aryl chlorides, based on chlorination of arenes, often suffer from low regioselectivities and yields maybe due to the inertness of C-Cl bond. Strategy and employment of chlorinated substrates in cyclization reactions which have been scarcely reported is an alternative strategy. 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.[24] Moreso, the synthesis of a chlorinated phenol by [4+2] cycloaddition of a chlorinated thiophene with dimethyl acetylenedicarboxylate has been reported.[25] Recently, Langer *et al.* have reported [4+2] cycloaddition of 2-chloro-1-methoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene with dimethyl acetylenedicarboxylate.[26]

1,3-bis(trimethylsilyloxy)-1,3-butadienes represent important synthetic building blocks which have been used in formal [3+2], [3+3], [4+2] and [4+3] cyclizations and various other transformations.[11, 27] However, 5-Chlorosalicylates have been prepared by cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 2-chloro-3-silyloxy-2-en-1-ones.[28] A variety of chlorinated hetero- and carbacycles are available by cyclization of 2-chloro-1,3-bis(silyloxy)-1,3-butadienes with various electrophiles.[29] Also, cyclization reactions of 4-chloro-1,3-bis(silyloxy)-1,3-butadienes allow for the synthesis of 3-chlorosalicylates and various other chlorinated arenes and hetarenes.[30]

Herein, I report the synthesis of highly substituted 5-chlorosalicylates by one-pot cyclizations of 1,3-bis-(trimethylsilyloxy)-1,3-butadienes with novel 2-chloro-3-ethoxy-2-alken-1-ones. The reactions proceed with excellent regioselectivity which are not readily available by other method.

1.2.2 Results and Discussion

The reaction of α-chloroketones **5a-f** with triethyl orthoformate and acetic anhydride afforded the novel 2-chloro-3-ethoxy-2-alken-1-ones **6a-f** in 41-81% yields (Scheme 3, Table 2). Noteworthy, the yields of aryl-substituted derivatives **6a-e** were considerably higher than the yield of **6f** and the chloride group proved to be compatible with the reaction conditions.



5a-f **6a-f**

Scheme 3: Synthesis of **6a-f**; *Conditions i*; **5a-f** (1.0 equiv.), $HC(OEt)_3$ (3.0 equiv.), Ac_2O (3.0 equiv.), reflux, 15 h

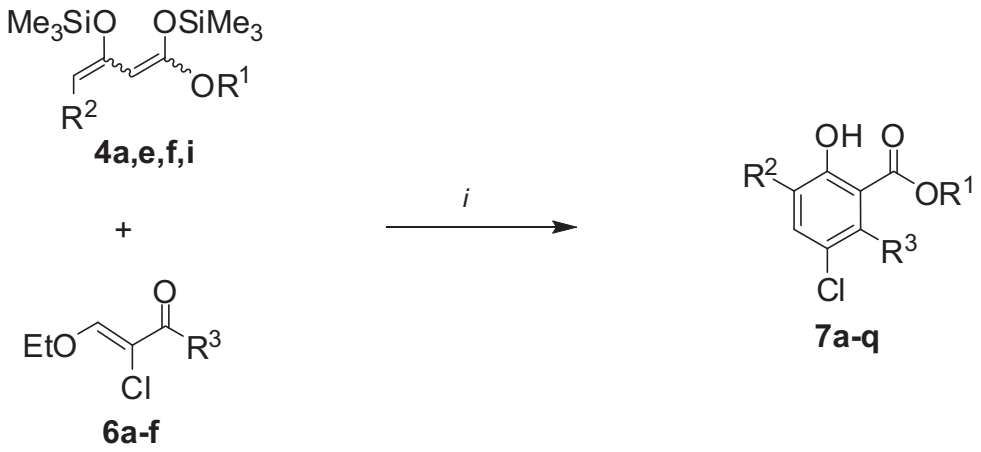
Table 2: Synthesis of **6a-f**

5	R	% (**6**)[a]
a	Ph	76
b	4-FC_6H_4	68
c	4-ClC_6H_4	81
d	2,4-ClC_6H_3	70
e	2,4-FC_6H_3	60
f	Me	41

[a] Yields of isolated products

Furthermore, the $TiCl_4$ (Lewis acid) mediated of 2-chloro-3-ethoxy-2-alken-1-ones **6a-f** with 1,3-bis(silyloxy)-1,3-butadienes **4a,e,f,i**, which are available from the corresponding β-ketoesters in two steps,[11] afforded the novel 5-chlorosalicylates in 35-51% yields (Scheme 4, Table 3). The best yield was observed with methyl 4',6-dichloro-4-ethyl-3-hydroxybiphenyl-2-carboxylate **7i (**51%) which also correspond to the same starting material 2-chloro-1-(4-chlorophenyl)-3-ethoxyprop-2-en-1-one **6c** (81%).

To afford better yields, the reaction was carried out in a highly concentrated solution. However, the yields of 6-aryl-5-chlorosalicylates **7a-p**, which can be regarded as chlorinated biphenyls, were considerably higher than the yield of 6-methyl-5-chlorosalicylate **7q** which was also observed in **6f**. The chloride group proved to be compatible with the reaction conditions and all reactions proceeded with very good regioselectivity in favour of the products containing substituent R^3 located *ortho* to the ester group. The other regioisomer, containing substituent R^3 located *para* to the ester group, were not formed from the inspection of the crude product.



Scheme 4*:* Synthesis of **7a-q** *Conditions*: i: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 12 h

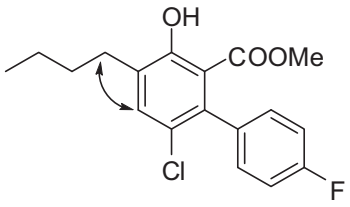
Table 3: Synthesis of **7a-q**

6	**4**	**7**	R^1	R^2	R^3	% (**7**)[a]
a	**a**	**a**	Me	H	Ph	45
a	**e**	**b**	Me	Me	Ph	44
a	**f**	**c**	Me	Et	Ph	46
a	**i**	**d**	Me	*n*Bu	Ph	45
b	**a**	**e**	Me	H	4-FC_6H_4	42
b	**e**	**f**	Me	Me	4-FC_6H_4	40
b	**f**	**g**	Me	Et	4-FC_6H_4	47
b	**i**	**h**	Me	*n*Bu	4-FC_6H_4	49
c	**f**	**i**	Me	Et	4-ClC_6H_4	51
c	**i**	**j**	Me	*n*Bu	4-ClC_6H_4	44
d	**a**	**k**	Me	H	2,4-$Cl_2C_6H_3$	44
d	**f**	**l**	Me	Et	2,4-$Cl_2C_6H_3$	45
d	**i**	**m**	Me	*n*Bu	2,4-$Cl_2C_6H_3$	47
e	**a**	**n**	Me	H	2,4-$F_2C_6H_3$	50
e	**f**	**o**	Me	Et	2,4-$F_2C_6H_3$	49
e	**i**	**p**	Me	*n*Bu	2,4-$F_2C_6H_3$	45
f	**f**	**q**	Me	Et	Me	35

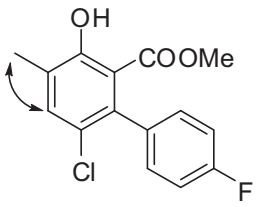
[a] Yields of isolated products

1.2.3 Proof of Structures

For **7a-q**, the one-dimensional ^{1}H NMR spectra are consistent with the products. NOESY experiments were carried out. (Scheme 5).



7h



7f

Scheme 5: Results of NOESY experiments for **7h** and **7f.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

In **7h** the aromatic hydrogen atom at $\delta = 7.28$ correlates with the methylene group giving rise to a triplet at 2.58 ppm.

In **7f** the aromatic hydrogen atom at $\delta = 7.31$ correlates with the methyl group at 2.22 ppm.

1.2.4 Conclusion

In conclusion, I have reported the synthesis of a variety of highly substituted 5-chlorosalicylates by one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-buta-dienes with 2-chloro-3-ethoxy-2-alken-1-ones. The reactions proceed with very good regioselectivity and the products are not readily available by other methods.

2 Regioselective Synthesis of Highly Functionalized Arylphosphonates by Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with 3-Ethoxy-2-phosphonyl-alk-2-en-1-ones

2.1 Introduction

It is known that heterocyclic compounds have high potential as biological active molecules. Likewise, both acyl and aryl phosphonates and their derivatives have various applications. For example, acyclic phosphorus compounds are very efficient pesticides and drugs[31b-c].

They are also important substructures of various dyes.[31a] Certain of the esters of vinylphosphonates have been used to stabilize polymers to heat and light,[31c] and to impart flame and shrinkage resistance to textiles.[31d]

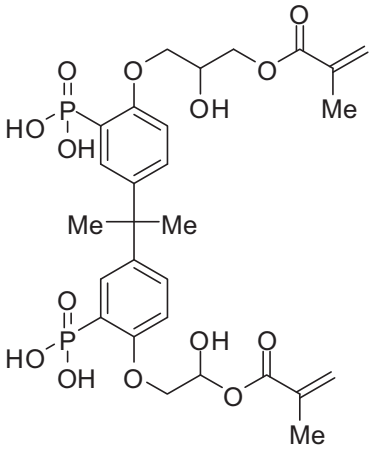


Figure 4. Phosphonic acid

However, aminophosphonic acids, as inhibitors of metabolic processes exert their physiological activity as antibacterial agents, neuroactive compounds, anticancer drugs or pesticides, and their application range from medicine to agriculture. [31e-f]

Arylphosphonates have importance applications in polymer chemistry[32] and as a lead structure in medicinal chemistry.[33] Arylphosphonic acid derivatives play an important role as synthetic intermediates in organic chemistry.[34] Phosphonic acid monomer (Figure 4) is used as monomer for use in dental composites.[35] Also, diphenyl [1-(3-

phenylthioureido)benzyl]phosphonate (Figure 5) found its applications as a herbicide and as a flame retardant in the production of cotton textiles.[36]

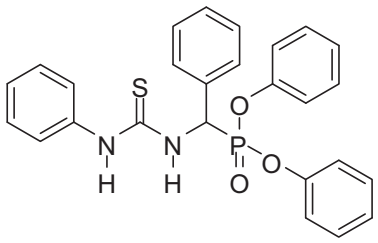


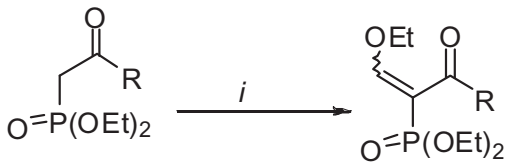
Figure 5. Diphenyl [1-(3-phenylthioureido)benzyl]phosphonate

Different approaches to the synthesis of arylphosphonates have been reported. Classic syntheses of arylphosphonates include, for example, the Friedel–Crafts reaction of aromatics with phosphoric acid derivatives,[37a] Also, the Cu-catalyzed reaction of diazonium salts with phosphorus trichloride has been reported[37b,c] The use of electron-poor aryl halides such as bromoaromatics with the nucleophilic aromatic substitution of sodium dialkylphosphites has equally been reported,[37d] Other reported reactions includes, the nickel(II)- or copper(II)-mediated reaction of trialkyl phosphates with aryl halides,[37e-i] and the reaction of trialkyl phosphites with aromatic Grignard or organolithium compounds.[37j-l] Moreover, a more recent approach to arylphosphonates relies on the palladium-catalyzed reaction of dialkyl phosphates with aryl halides.[38,39] Despite the great usefulness of all these methods for the formation of carbon-phosphorus bonds, they are generally limited by the fact that more complex starting materials, highly functionalized and substituted aryl halides, are not readily available. In fact, the halogenation and functionalization by aromatic electrophilic substitution reactions is often limited by their low *ortho/para* regioselectivity and other side reactions. Most of the C-P bonds forming reactions outlined above have been carried out using simple, sterically unhindered and commercially available substrates.

However, Kouno and coworkers developed a versatile methodology based on the reaction of lithiated vinylphosphonates with electrophiles.[40] and the reactions of these compounds have scarcely been studied so far.[40a,41] Fortunately in recent years, Langer *et al* have studied the synthesis of arenes by titanium(IV)chloride-mediated [3+3] cyclizations[27] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes.[10] Herein, I wish to report the synthesis of highly functionalized arylphosphonates by the cyclocondensation of aliphatic and aromatic 3-ethoxy-2-phosphonyl-alk-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes.

2.2 Results and Discussion

The 1,3-bis(silyloxy)-1,3-butadienes **4a-t** were prepared from the corresponding β-ketoesters in two steps[11,42] Afterwards, vinylphosphonates **9a**[41] and **9b**[40a] were prepared by the reaction of β-ketophosphonates **8a,b** with triethyl orthoformate and acetic anhydride (Scheme 6).



8a,b **9a,9b**

Scheme 6: Synthesis of **9a,b**: *conditions*: *i,* for **9a**: **8a** (1.0 equiv.), $HC(OEt)_3$ (1.2 equiv.), Ac_2O, reflux, 4 h; conditions for **9b**: **8b** (1.8 equiv.) $HC(OEt)_3$, (2.8 equiv.) Ac_2O, reflux, 36 h, then column chromatography; products **9a,b** were isolated as mixtures of *E/Z* isomers

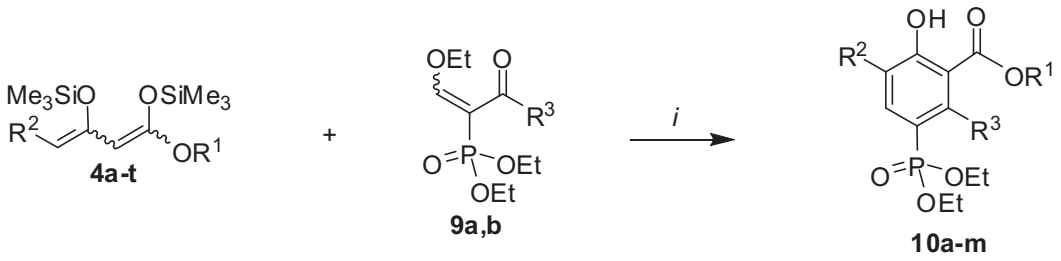
Table 4: Synthesis of **9a,b**

8	R	% (**9**)[a]
a	Me	86
b	Ph	74

[a] Yields of isolated products

The $TiCl_4$-mediated cyclization of vinylphosphonates **9a,b** with dienes **4a-t** afforded the novel arylphosphonates **10a-m** (Scheme 7, Table 5). The reaction was carried out in a highly concentrated solution (2 mL / 1.0 mmol of **9a,b**) for better optimization. The cyclization can be explained by $TiCl_4$-mediated conjugate addition of the terminal carbon atom of the diene to the enone, cyclization by attack of the central carbon atom of the diene to the carbonyl group and subsequent aromatization (before or during the aqueous work up using 10% hydrochloric acid). It is worthy of note that the constitution of the products was proved by 2D NMR studies (HMBC, NOESY, analysis of P-C and P-H coupling constants) and all reactions proceeded with excellent regioselectivity.

In all products, the substituent R^3 is located *ortho* to the ester group but the formation of the other regioisomer, containing the substituent R^3 located *para* to the ester group, was not observed. Similar yields were obtained for reactions of methyl and phenyl substituted vinylphosphonates **9a** and **9b** and the moderate yields accounted for due to the decrease by some hydrolysis and $TiCl_4$-mediated oxidative dimerization of the diene, and by decomposition.



Scheme 7: Synthesis of **10a-m**. *Conditions*: *i*, 1) **9a,b** (1.0 equiv.), **4a-t** (1.1 equiv.), $TiCl_4$ (1.1 equiv.), CH_2Cl_2, −78 → 20 °C, 12 h; 2) HCl (H_2O, 10%)

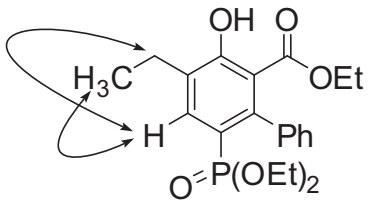
Table 5: Synthesis of **10a-m**

9	**4**	**10**	R^1	R^2	R^3	% (**10**)[a]
a	**a**	**a**	Me	H	Me	48
a	**g**	**b**	Et	Et	Me	52
a	**k**	**c**	Me	*n*Hex	Me	54
a	**o**	**d**	Me	*n*Oct	Me	58
b	**e**	**e**	Me	Me	Ph	56
b	**g**	**f**	Et	Et	Ph	51
b	**h**	**g**	Me	*n*Pr	Ph	53
b	**i**	**h**	Me	*n*Bu	Ph	57
b	**l**	**i**	Et	*n*Hex	Ph	58
b	**n**	**j**	Et	*n*Hept	Ph	55
b	**s**	**k**	Et	*n*Dec	Ph	54
b	**t**	**l**	Et	*i*Pr	Ph	47
b	**p**	**m**	Et	*n*Oct	Ph	54

[a] Yields of isolated products

2.3 Proof of Structures

For **10a-m**, the one-dimensional ^{1}H NMR spectra are consistent with all the products. NOESY and HMBC experiments were carried out. (Scheme 8).



10f

Scheme 8: Results of NOESY experiment for **10f.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

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In **10f** the aromatic hydrogen atom at δ = 7.93 correlates with the ethyl group represented by a triplet at 0.61 ppm and a quartet at 2.68 ppm.

2.4 Conclusion

In conclusion, I have reported a convenient and efficient synthesis of highly functionalized arylphosphonates by what are, to the best of my knowledge, the first cyclocondensation of 3-ethoxy-2-phosphonyl-alk-2-en-1-ones with 1,3-bis(trimethylsilyloxy)-1,3-butadienes, which are not readily available by other methods.

3 First Synthesis of 5-Cyanosalicylates by Formal [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes

3.1 Introduction

Aryl nitriles are of considerable interest as integral parts of dyes, natural products, herbicides, agrochemicals and pharmaceuticals.[43] They represent important building blocks in fine chemical synthesis and my focus in this chapter is on the synthesis of functionalized 5-cyanosalicylates which can be regarded as functionalized 4-cyanophenols. Their substructures are present in a great variety of pharmacologically active compounds; interestingly, 5-Cyanosalicylates and 2-acyl-4-cyanophenols which are the specific derivatives I am focussing in this chapter include, for example, *N*-(3-acetyl-5-cyano-2-hydroxyphenyl)-1*H*-tetrazole-5-carboxamide (Figure 6) which has an antiallergic activity,[44] while other activities like inhibition of HIV-1,[45] anti-dopaminergic,[46] vasorelaxing,[47] inhibition of LTD4-induced contraction of lung membranes,[48] have been reported.

Moreover, 3-cinnamoyl-4-hydroxybenzonitrile (Figure 7) has been reported to contain leukotriene D4 inhibitory activity,[49] Various other usefulness includes antibacterial activity,[50] binding to CHO cell membranes,[51] antagonistic activity against βTC3 cells,[52] inhibition of recombinant human aldehyde reductase,[53] or inhibition of catechol O-methyl-transferase.[54] have also been reported.

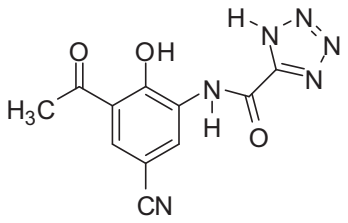


Figure 6. *N*-(3-acetyl-5-cyano-2-hydroxyphenyl)-1*H*-tetrazole-5-carboxamide

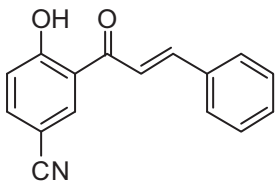


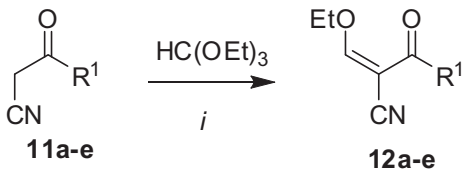
Figure 7. 3-Cinnamoyl-4-hydroxybenzonitrile

In recent years, nitriles have played a crucial role as they can be easily converted into a variety of functional groups such as acids, ketones, oximes and amines.[55b] Various methods for the synthesis of aryl nitriles have been reported.[55a, 56] Substituted 5-cyanosalicylates represent highly functionalized arenes containing a nitrile, ester and hydroxyl group and 5-Cyanosalicylates have been previously prepared by transformation of oximes into nitriles,[57] Other methods includes, cyanation of aryl halides,[58] or Pd(0)-catalyzed reaction of aryl halides with zinc or potassium cyanide,[59] and by Grignard reaction of 4-hydroxy-3,5-diiodo-benzonitrile with carbon dioxide.[60] However, most of the work has concentrated on the inconvenient traditional cyanide sources, which have some severe drawbacks. For example, reactions of *ortho*-substituted aryl halides are often problematic or not possible at all or require the use of toxic thallium reagents.[61] However, the synthesis of the required starting materials, functionalized or highly substituted aryl halides or triflates, can be a difficult and tedious task, due to the low *o*/*p*-regioselectivity of electrophilic substitutions, harsh reaction conditions, and several other drawbacks.

I have developed a new synthesis of functionalized 5-cyanosalicylates by formal [3+3] cyclocondensations[11, 27] of 1,3-bis(silyloxy)-1,3-butadienes[10] with cyano-substituted 3-ethoxy--2-en-1-ones. These reactions provide a convenient and regioselective approach to a variety of 5-cyanosalicylates which are not readily available by other methods.

3.2 Results and Discussion

The starting materials, 2-cyano-3-ethoxy-2-en-1-ones **12a-e** were prepared following a known procedure, [62] by reaction of ketonitriles **11a-e** with triethyl orthoformate and acetic anhydride (Scheme 9, Table 6). 1,3-Bis(silyloxy)-1,3-butadienes **4a-x** were prepared from the corresponding β-ketoesters in two steps.[11]



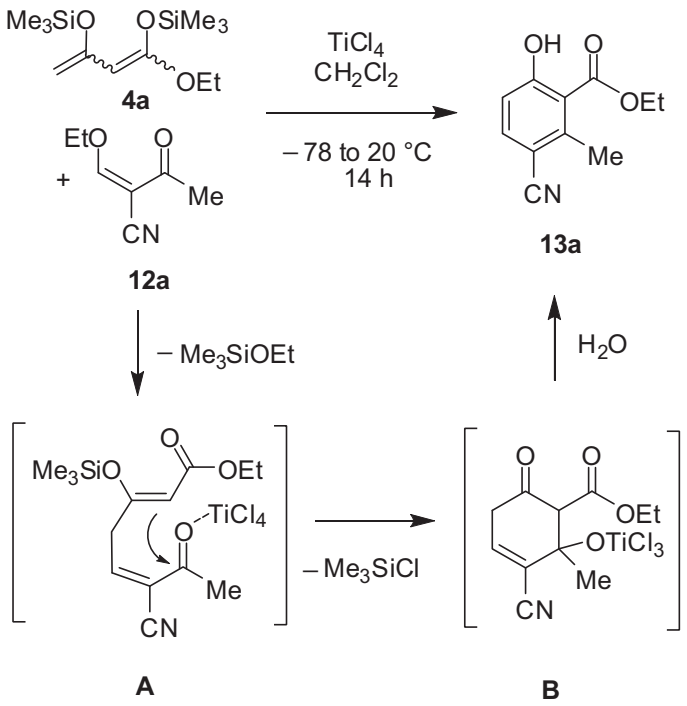
Scheme 9: Synthesis of **12a-e**; *i*: 11a-e (1.0 equiv) $HC(OEt)_3$, (3.0 equiv) Ac_2O, reflux, 2 h

Table 6: Synthesis of 1**2a-e**

12	R^1	% (**12**)[a]
a	Me	100
b	Ph	88
c	4-ClC_6H_4	98
d	4-BrC_6H_4	96
e	4-$(MeO)C_6H_4$	95

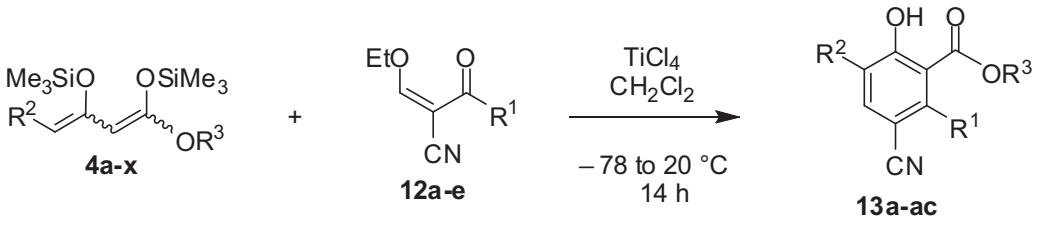
[a] Yields of isolated products

The $TiCl_4$-mediated cyclization of **12a** with **4a** afforded the 5-cyanosalicylate **13a** (Scheme 10). The cyclization proceeded with excellent regioselectivity and the best yield was obtained when the reaction was carried out in a highly concentrated solution. The formation of product **13a** might be explained by $TiCl_4$-mediated conjugate addition of the terminal carbon atom of **4a** to **12a** to give intermediate **A**, cyclization via the central carbon of **4a** to give intermediate **B** (S_N1 reaction), and subsequent aromatization.



Scheme 10: Possible mechanism of the formation of **13a**

The formal [3+3] cyclization of 2-cyano-3-ethoxy-2-en-1-ones **12a-e** with 1,3-bis(silyloxy)-1,3-butadienes **4a-x** afforded the 5-cyanosalicylates **13a-ac** in 33-64% yields (Scheme 11, Table 7). It is noted that the substituent R^1, located next to the carbonyl group of **2a-e,** has some influence on the yields. Better yields were generally obtained for the products **13h-ac** derived from **12b-e**, containing an aryl group, compared to products **13a-g** derived from **12a** which contains a methyl group. Moreover, the best yields were observed for the products derived from chloro- or bromo-substituted enones **12c,d** and the substitution pattern of the diene has no significant influence on the yield.



Scheme 11: Synthesis of **13a-ac**

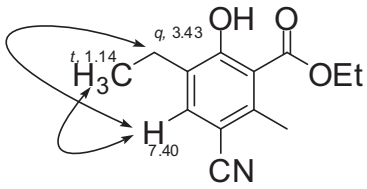
Table 7: Synthesis of **13a-ac**

12	**4**	**13**	R^1	R^2	R^3	%(**13**)[a]
a	**a**	**a**	Me	H	Me	34
a	**b**	**b**	Me	H	Et	33
a	**e**	**c**	Me	Me	Me	35
a	**g**	**d**	Me	Et	Et	34
a	**i**	**e**	Me	*n*Bu	Me	35
a	**k**	**f**	Me	*n*Hex	Me	42
a	**m**	**g**	Me	*n*Hept	Me	34
b	**b**	**h**	Ph	H	Et	45
b	**e**	**i**	Ph	Me	Me	43
b	**g**	**j**	Ph	Et	Et	42
b	**i**	**k**	Ph	*n*Bu	Me	41
b	**m**	**l**	Ph	*n*Hept	Me	42
b	**o**	**m**	Ph	*n*Oct	Me	40
b	**x**	**n**	Ph	4-ClC_6H_4	Me	44
c	**e**	**o**	4-ClC_6H_4	Me	Me	61
c	**g**	**p**	4-ClC_6H_4	Et	Et	62
c	**k**	**q**	4-ClC_6H_4	*n*Hex	Me	64
c	**o**	**r**	4-ClC_6H_4	*n*Oct	Me	59
c	**u**	**s**	4-ClC_6H_4	*i*Pen	Me	62
d	**e**	**t**	4-BrC_6H_4	Me	Me	58
d	**g**	**u**	4-BrC_6H_4	Et	Et	60
d	**k**	**v**	4-BrC_6H_4	*n*Hex	Me	55
d	**o**	**w**	4-BrC_6H_4	*n*Oct	Me	55
d	**q**	**x**	4-BrC_6H_4	*n*Non	Me	57
e	**b**	**y**	4-(MeO)C_6H_4	H	Et	50
e	**e**	**z**	4-(MeO)C_6H_4	Me	Me	51
e	**g**	**aa**	4-(MeO)C_6H_4	Et	Et	49
e	**k**	**ab**	4-(MeO)C_6H_4	*n*Hex	Me	52
e	**o**	**ac**	4-(MeO)C_6H_4	*n*Oct	Me	50

[a] Yields of isolated products

3.3 Proof of Structures

For **13a-ac**, the one-dimensional ^{1}H NMR spectra are consistent with all the products. NOESY and HMBC experiments were carried out (Scheme 12) and the structure of benzonitrile **13b** was independently confirmed by X-ray crystal structure analysis (Figure 8).[95]



13d

Scheme 12: Results of NOESY experiments for **13d.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

In **13d,** the aromatic hydrogen atom at δ = 7.40 correlates with the ethyl group represented by a triplet at 1.14 ppm and a quartet at 3.43 ppm.

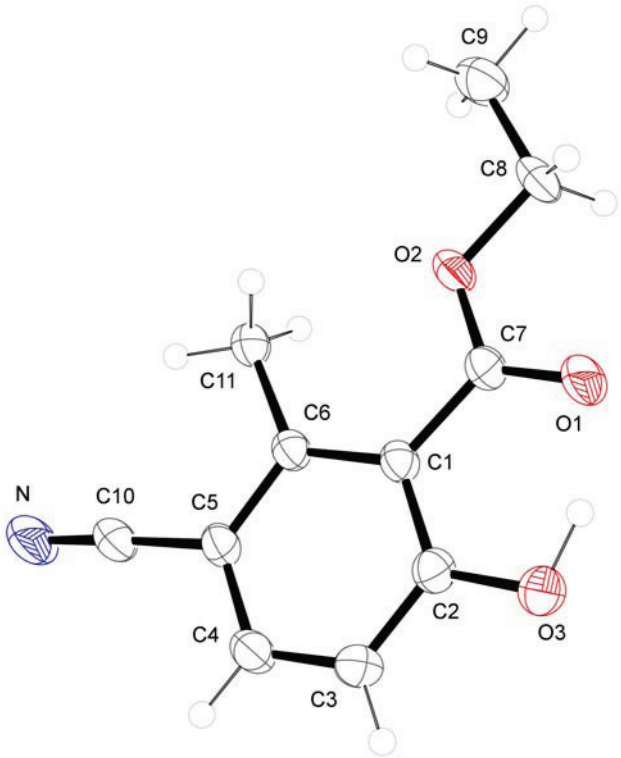


Figure 8. Ortep plot of **13b** (hydrogen at O3 found in the difference map and refined freely)

From the X-ray structure, it is observed that there is an intramolecular bonding between the hydroxyl group and the carbonyl group of the molecule.

3.4 Conclusion

In conclusion, I have reported a convenient and regioselective synthesis of functionalized benzonitriles by what are, to the best of my knowledge, the first formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with cyano-substituted enones. The products are not readily available by other methods.

4 Regioselective Synthesis of 5-Arylthio- and 5-Benzylthio-6-phenylsalicylates by One-Pot Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes with 2-Arylthio- and 5-Benzylthio-3-ethoxy-2-en-1-ones

4.1 Introduction

Aryl sulfides are of great significance in the field of advanced materials and industrial chemicals such as lubricants, herbicides, organic semiconductors, and high boiling point solvents.[63b-d] They are also key intermediates for the preparation of pharmaceuticals and are common in numerous drugs in therapeutic areas such as diabetes and anti-inflammatory, and Alzheimer's and Parkinson's diseases.[63e-f]

Functionalized natural and non-natural diaryl sulfides (diaryl thioethers) are pharmacologically important and have been isolated as natural products.[64] For example, they are present in dibenzothiophenes, lissoclinotoxins (Figure 9), lissoclibadins, cyclic sulfides, and various other natural products isolated from Streptomyces griseus.[64] Also, fluorinated diaryl sulfides have been reported to act as serotonin transporter ligands.[63a] Diaryl sulfides have been prepared mainly by formation of a carbon-sulphur bond. This includes, for example, the reaction of copper thiolates with aryl halides. An alternative strategy relies on the reduction of aryl sulfones or aryl sulfoxides. In contrast, all these methods are often limited by their harsh and severe conditions, by the formation of polysulfides, preparative scope, use of toxic reagents (such as HMPTA), or low regioselectivity.[65] Mild metal-catalyzed and metal-free reactions for the synthesis of diaryl sulfides have also been reported.[66-68] The synthesis of the starting materials, substituted arenes and thiophenols, can be difficult and these methods are often limited by the fact that highly substituted and sterically encumbered products are not readily available.

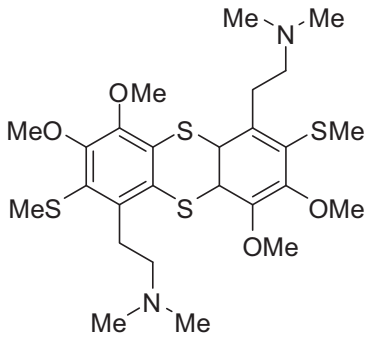
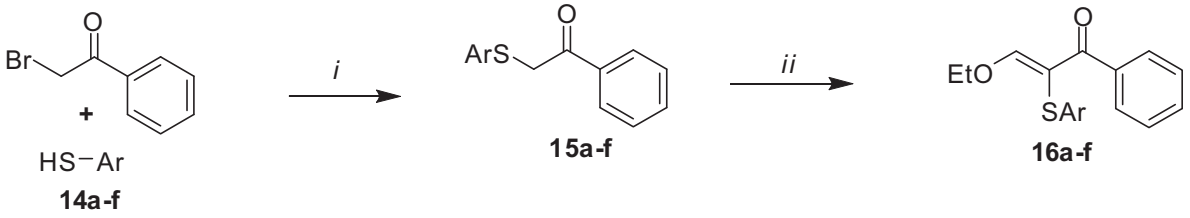


Figure 9. Lissoclinotoxin E

However, the uses of sulphur-containing building blocks in cyclization reactions (building block approach) provide an alternative approach to diaryl sulfides. This approach relies on the assembly of the arene moiety by formation of two carbon-carbon bonds. Hilt and coworkers reported an efficient synthesis of diaryl sulfides by cobalt(I)-catalyzed [4+2] cycloaddition of alkynyl sulfides with 1,3-butadienes.[69] Also, syntheses of 2-arylthio-benzoates and related products by cyclization reactions of arylthio-1-trimethylsilyloxy-1,3-butadienes were reported by Chan *et al,*[11] Langer *et al,* [70] and by others.[71] Recently, Langer *et al* reported[72] the synthesis of 3-and 5-arylthiosalicylates based on formal [3+3] cyclizations[27] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones and 1,1-diacetylcyclopropane.[27] Despite the usefulness of these reactions, they are limited by the fact that, in most cases, only symmetrical 1,3-dielectrophiles can be employed and a methyl group must generally be present at position C-4. In my thesis, I have developed the first synthesis of C-4-unsubstituted 6-aryl-5-arylthio-salicylates by one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 2-arylthio-3-ethoxy-2-en-1-ones.

4.2 Results and Discussion

The novel 2-arylthio-3-ethoxy-2-en-1-ones **16a-f** were prepared by reaction of α-bromoacetophenone with thiophenols **14a-f** to give **15a-f** (Scheme 13, Table 8). The reaction of the latter with triethyl orthoformate and acetic anhydride afforded the 2-arylthio-3-ethoxy-2-en-1-ones **16a-f** in moderate yields.



Scheme 13: Synthesis of **16a-f**; *i*: NaOEt (1.0 equiv.), 2-bromoacetophenone (1.0 equiv.), **14a-f** (1.0 equiv.); *ii*: **15a-f** (1.0 equiv.), $HC(OEt)_3$ (3 equiv.), Ac_2O (3 equiv.), reflux, 15 h at 140 °C; products exist as mixtures of *E/Z* isomers

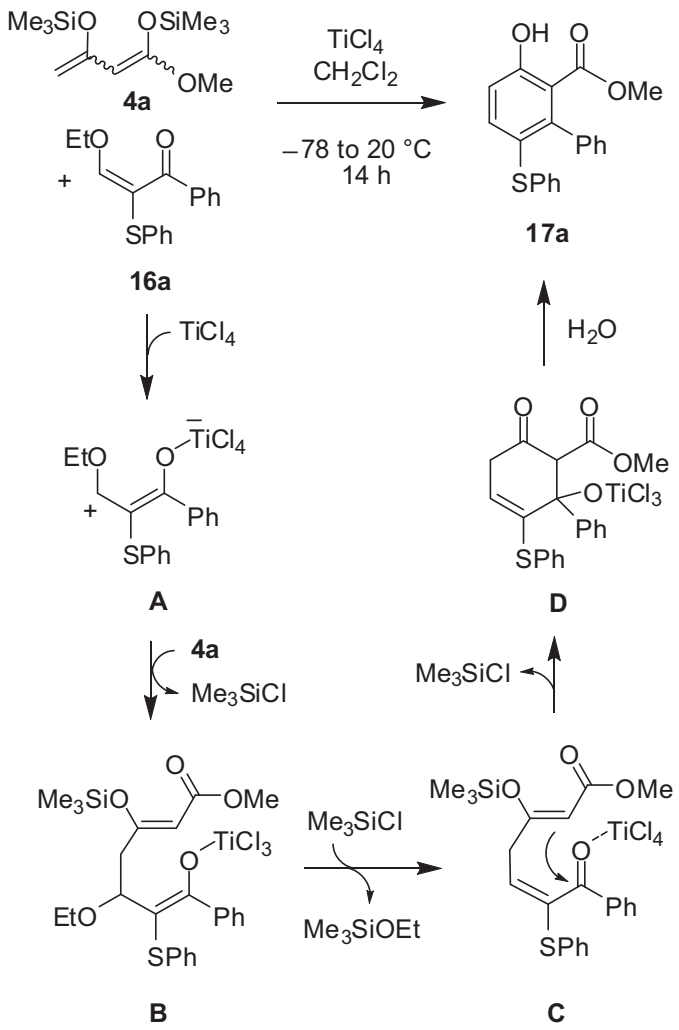
Table 8: Synthesis of **16a-f**

14,15,16	Ar	% (**15**)[a]	% (**16**)[a]
a	Ph	95	41
b	4-MeC_6H_4	98	54
c	4-FC_6H_4	92	55
d	4-$(NO_2)C_6H_4$	99	45
e	$PhCH_2$	99	42
f	2-Naph	96	50

[a] Yields of isolated products

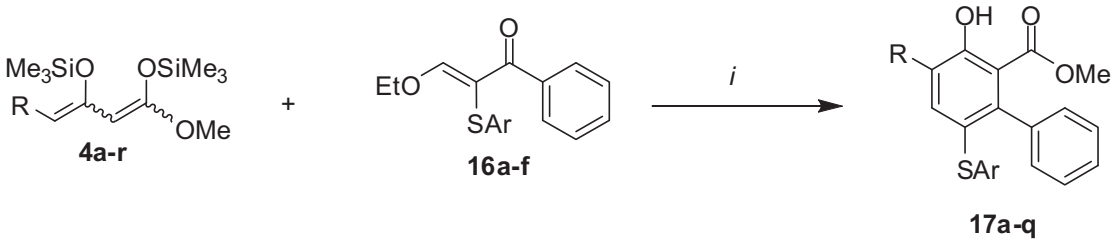
The [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-1,3-diene **4a**, prepared in two steps from methyl acetoacetate, with **16a** afforded the novel 5-phenylthio-6-phenylsalicylate **17a** in 44% yield (Scheme 14). The best yield was obtained when the reaction was carried out in a highly concentrated solution and when $TiCl_4$ was employed as the Lewis acid. It is worth to be noted that the cyclization proceeded with excellent regioselectivity. The moderate yield of **17a** can be explained by practical problems during the chromatographic purification. The formation of the other regioisomer was not observed.

The formation of product **17a** might be explained by reaction of **16a** with $TiCl_4$ to give intermediate **A**, attack of the terminal carbon atom of **4a** onto **A** to give intermediate **B**, formation of intermediate **C**, cyclization via the central carbon (intermediate **D**) and subsequent aromatization. The regioselectivity of the formation of **17a** might be explained by the steric hindrance at the ketone carbonyl group.



Scheme 14: Possible mechanism of the formation of **17a**

The [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-1,3-dienes **4a-r**, prepared in two steps from the corresponding β-ketoesters,[10] with **16a-f** afforded the novel 5-arylthio-6-phenylsalicylates **17a-q** (Scheme 15, Table 9). The reactions could be successfully carried out with 2-arylthio-3-ethoxy-2-en-1-ones containing electron-donating or electron-withdrawing groups. Cyclizations of 1,3-bis(silyloxy)-1,3-butadienes **4b-r**, containing a substituent located at the terminal carbon atom, gave slightly higher yields than the reactions of unsubstituted derivative **4a**. Moreover, the synthesis of product **17p** showed that the method can be successfully applied to the synthesis of 5-benzylthio-salicylates.



Scheme 15: Synthesis of **17a-q**: *Conditions*: i: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 14 h

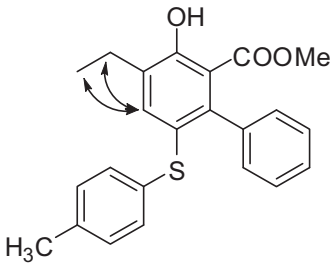
Table 9: Synthesis of **17a-q**

16	4	17	Ar	R	% (**17**)[a]
a	**a**	**a**	Ph	H	44
a	**f**	**b**	Ph	Et	48
a	**o**	**c**	Ph	*n*Oct	51
a	**r**	**d**	Ph	*n*Dec	52
b	**f**	**e**	4-MeC_6H_4	Et	37
b	**r**	**f**	4-MeC_6H_4	*n*Dec	38
c	**e**	**g**	4-FC_6H_4	Me	43
c	**r**	**h**	4-FC_6H_4	*n*Dec	45
d	**a**	**i**	4-$NO_2C_6H_4$	H	35
d	**e**	**j**	4-$NO_2C_6H_4$	Me	48
d	**f**	**k**	4-$NO_2C_6H_4$	Et	40
d	**j**	**l**	4-$NO_2C_6H_4$	*n*Pent	48
d	**k**	**m**	4-$NO_2C_6H_4$	*n*Hex	42
d	**o**	**n**	4-$NO_2C_6H_4$	*n*Oct	45
d	**r**	**o**	4-$NO_2C_6H_4$	*n*Dec	50
e	**f**	**p**	$PhCH_2$	Et	47
f	**f**	**q**	2-Naph	Et	52

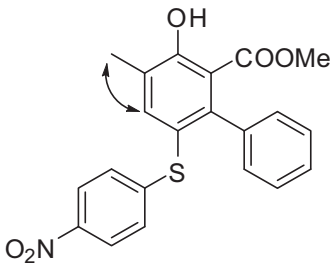
[a] Yields of isolated products

4.3 Proof of Structures

The structures of all products **17a-q** were confirmed by spectroscopic methods (HMBC, NOESY). The structures of products **17a** and **17i**, containing a hydrogen atom located at carbon atom C-3, are evident by the presence of large coupling constants for the two neighbouring hydrogen atoms. The structure of **17j** was independently confirmed by X-ray crystal structure analysis (Figure 10).[95]



17e



17j

Scheme 16: Results of NOESY experiments for **17e** and **17j.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

In **17e** the aromatic hydrogen atom at δ = 7.08 correlates with the ethyl group represented by a triplet at 1.01 ppm and a quartet at 2.49 ppm.

In **17j** the aromatic hydrogen atom at δ = 7.43 correlates with the methyl group at 2.20 ppm.

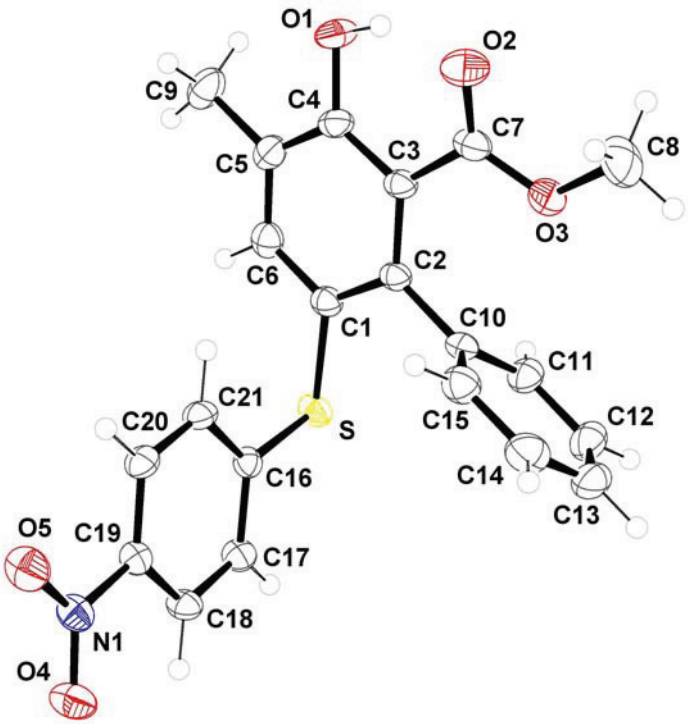


Figure 10. Ortep plot of **17j**

4.4 Conclusion

In conclusion, I have reported the synthesis of variety of 5-arylthio-6-phenylsalicylates prepared by one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 2-arylthio-3-ethoxy-2-en-1-ones. The products are not readily available by other methods.

5 Synthesis of Chromeno[3,4-b]pyrrol-4(3*H*)-ones by Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-3-nitrocoumarin

5.1 Introduction

Heterocycles are cyclic molecules that have an element other than carbon present in the ring (for example, pyridine, furan, thiophene). They are commonly encountered in nature.[1] The chemistry of heterocyclic compounds is one of the broadest and most important branches of organic chemistry. Coumarin and its derivatives have attracted considerable interest because of their various physiological and biochemical properties. They constitute the core of a large number of alkaloids and biologically active compounds. In recent years, several new coumarin derivatives have been found to show strong antibiotic, antitumor, antibacterial, anti-HIV, antifungal, and anti-inflammatory activity.[73] Coumarins are also important in the field of material science and they serve as flourescent labels for the analysis of protein-protein and DNA-protein interactions.[73a]

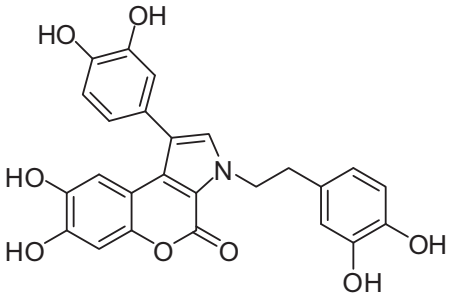


Figure 11. Ningalin B

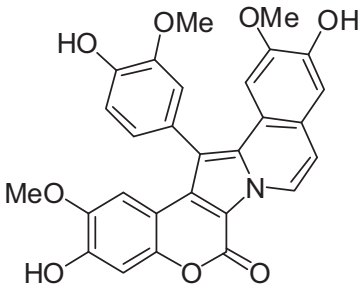


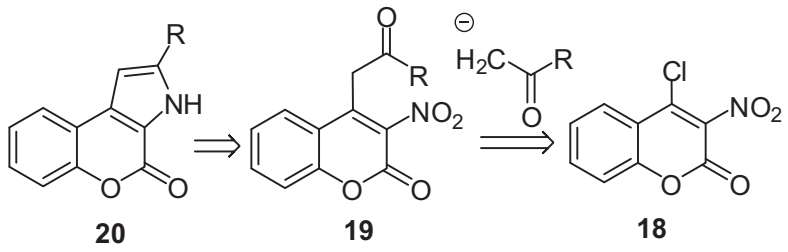
Figure 12. Lamellarin D

A number of strategies for the synthesis of coumarins have been developed to date.[74] The pharmacological and biochemical properties, and therapeutical applications of coumarins depend upon the types of substituents in their basic structure. In this context, pyrrolocoumarin derivatives are of special interest and they are widely spread in nature. For example, ningalin B (Figure 11) and lamellarin D (Figure 12) are two marine alkaloids containing the chromeno[3,4-*b*]pyrrol-4(3*H*)-one subunit. These compounds exhibit a variety of biological properties which include immunomodulatory activity, HIV-1 integrase inhibition, and

cytotoxicity.[75] Due to their pharmacological potential, I developed a new approach to synthesise chromeno[3,4-*b*]pyrrol-4(3*H*)-ones.

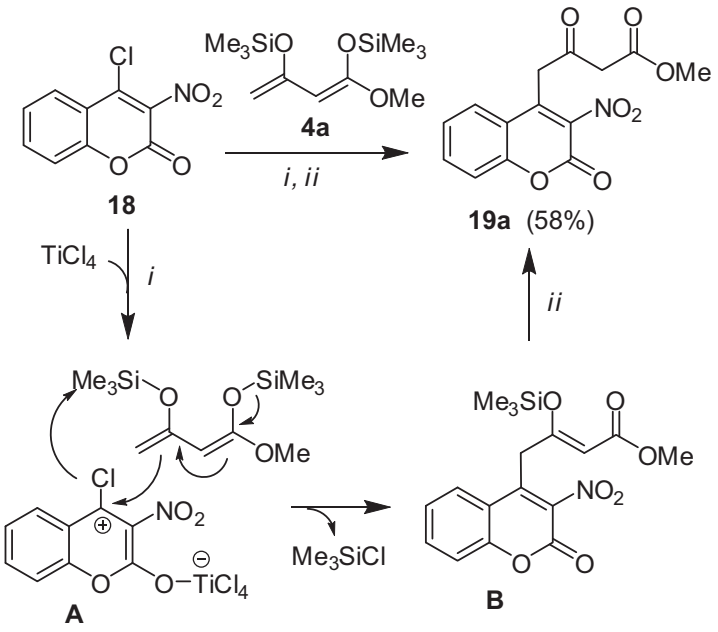
5.2 Results and Discussion

The chromeno[3,4-*b*]-pyrrol-4(3*H*)-one system **20** could be assembled in two steps by reaction of 4-chloro-3-nitrocoumarin (**18**) with an enolate synthon and subsequent reductive cyclization (Scheme 17). 4-Chloro-3-nitrocoumarin is readily available in two steps from 4-hydroxycoumarin (by nitration and subsequent exchange of the OH-group to chlorine). To the best of my knowledge, the strategy outlined above has not been previously employed for the synthesis of chromeno[3,4-*b*]-pyrrol-4(3*H*)-ones. Previous syntheses of these compounds are based on the formation of the pyrrole moiety by Claisen reaction[76] or by Fischer indole synthesis[77] using 3-aminocoumarins as starting materials. Recently, the Sonogashira reaction of 4-chloro-3-nitrocoumarin (**18**) and subsequent reductive cyclization has been reported.[78]



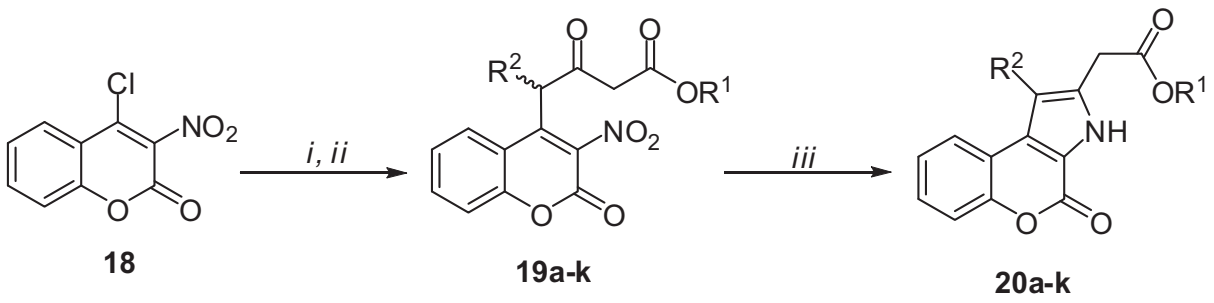
Scheme 17: *Retrosynthetic analysis:* novel strategy for synthesis of chromeno[3,4-*b*]pyrrol-4(3*H*)-ones.

The $TiCl_4$-mediated reaction of **18** with 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**4a**), which can be regarded as a masked dianion,[10] resulted in formation of product **19a** (Scheme 18). However, the best yields were obtained when a stoichiometric ratio of **18**/**4a**/$TiCl_4$ = 1.0/1.1/1.1 was used and when the reaction was carried out in a fairly concentrated solution. The moderate yield (58%) can be explained by practical problems during the chromatographic purification and by partial hydrolysis of the starting materials. The regioselective formation of **19a** can be explained by $TiCl_4$-mediated attack of the terminal carbon atom of the diene to the double bond, extrusion of trimethylchlorosilane to give intermediate **B**, and subsequent hydrolysis of the silyl enol ether during aqueous work-up.



Scheme 18: *Reagents and conditions*: (*i*) $TiCl_4$, CH_2Cl_2, –78 to 20 °C, 14 h; (*ii*) HCl (10%).

The reaction of **18** with dienes **4** afforded products **19b-k** in good yields (Scheme 19, Table 10). Moreover, the hydrogenation of **19a-k**, in the presence of Pd/C (10 mol%) in methanol afforded chromeno[3,4-*b*]pyrrol-4(3*H*)-ones **20a-k** in 39-67% yields. The formation of the products proceeds by reduction of the nitro to an amino group, attack of the latter to the carbonyl group and subsequent extrusion of water. In case of **20i**, the chloride group was cleaved during the reaction.



Scheme 19: *Reagents and conditions:* (i) **4**, $TiCl_4$, CH_2Cl_2, –78 to 20 °C, 14 h; (ii) HCl (10%); (iii) MeOH, H_2, Pd/C 10%, 20 °C, 3 days.

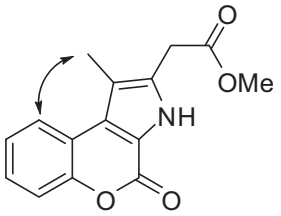
Table 10: Yields of compounds **19a-k** and **20a-k**

19,20	4	R^1	R^2	% (**19**)[a]	% (**20**)[a]
a	**a**	Me	H	58	46
b	**e**	Me	Me	68	51
c	**f**	Me	Et	58	67
d	**h**	Me	*n*Pr	47	42
e	**j**	Me	*n*Pent	43	62
f	**k**	Me	*n*Hex	55	47
g	**p**	Et	*n*Oct	41	40
h	**w**	Me	MeO	41	49
i	**v**	Et	Cl	45	39[b]
j	**d**	$(CH_2)_2OMe$	H	56	44
k	**c**	*i*Pr	H	40	48

[a] Yields refer to pure isolated products; [b] R^2 = H

5.3 Proof of Structures

For **20a-k,** the one-dimensional NMR spectra are consistent with all the products. NOESY and HMBC experiments were carried out and the structure of **20c** was confirmed by an X-ray crystal structure analysis (Figure 13).[95] The chromeno[3,4-*b*]pyrrol-4(3*H*)-one unit has, as expected, a flat structure.



20b

Scheme 20: Results of NOESY experiments for **20b.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

In **20b** the aromatic hydrogen atom at δ = 7.87 - 7.90 correlates with the methyl group at 2.36 ppm.

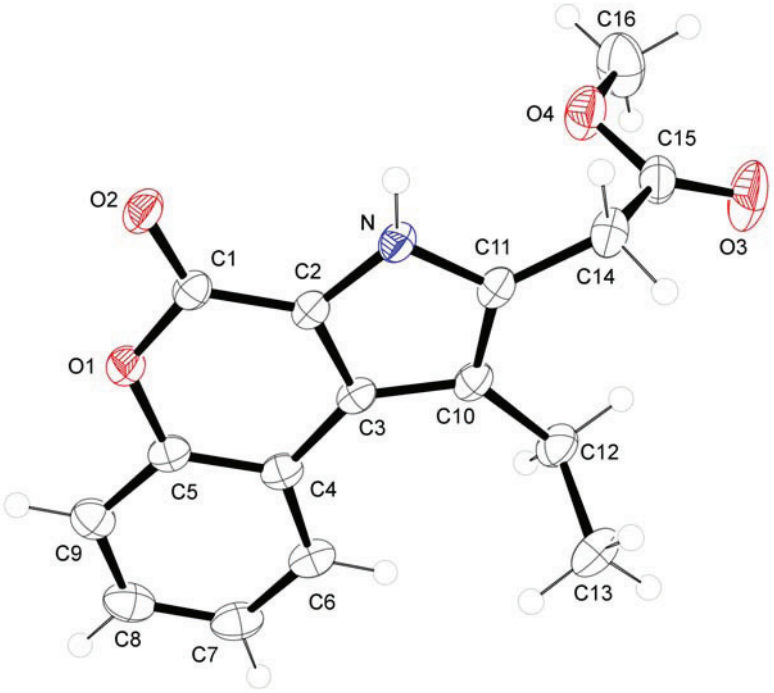


Figure 13. Ortep plot of **20c**

5.4 Conclusion

In conclusion, I have reported a new method for the synthesis of functionalized chromeno[3,4-*b*]pyrrol-4(3*H*)-ones by $TiCl_4$-mediated reaction of 4-chloro-3-nitrocoumarin with 1,3-bis(silyloxy)-1,3-butadienes and subsequent reduction of the nitro group and cyclization. The scope of the new methodology and applications in medicinal chemistry are currently studied in our laboratory.

6 Regioselective Synthesis of Benzo[c]chromen-6-ones by One-Pot Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-2-oxo-2*H*-chromene-3-carbaldehyde

6.1 Introduction

Coumarin and its derivatives are an important class of naturally occurring benzopyrone derivatives with useful pharmacological activity. Much of the coumarins have been explained in the previous chapter but the other important derivative is reported in this chapter. The benzo[c]chromen-6-one core structure represents a highly privileged and biologically relevant molecular scaffold which occurs in many natural products. For example, Autumnariol has been isolated from onions of *Eucomis autumnalis Greab. (Liliaceae)*.[79] and a number of related natural products, such as autumnariniol,[80] alternariol,[81] (Figure 14) and altenuisol[82] have been isolated.[83] 6*H*-Benzo[c]chromen-6-ones have been found to be inhibitors of endothelic cell[84] and oestrogene receptor[85] growth. Both ellagic acid (Figure 15) and coruleoellagic acid have been isolated from plants and they occur as glycosides and aglycons.[86] Moreover, many benzo[d]naphthopyran-6-ones are known as antibiotics and antitumor compounds isolated from *Streptomyces*; this includes, for example, defucogilvocarcin V, gilvocarcins (Figure 16), chrysomycins and ravidomycins.[87]

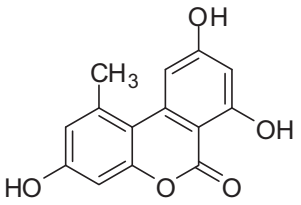


Figure 14. Alternariol

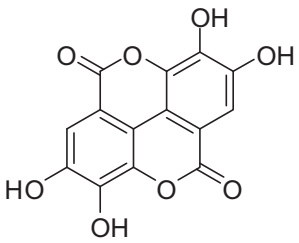


Figure 15. Ellagic acid

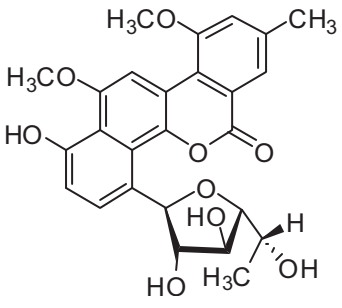
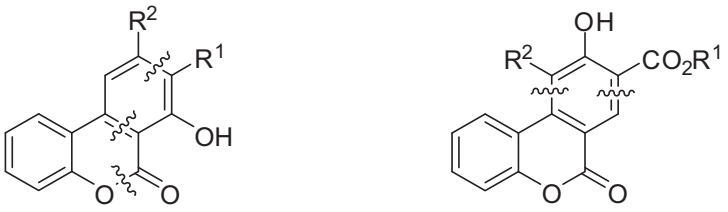


Figure 16. Gilvocarcin M

The first synthetic approach to benzo[c]chromen-6-one was developed in 1929 by Hurtley, based on the cyclization of *o*-bromobenzoic acids with phenols. This method is limited to activated substrates and the yields are often low.[88] Also, Harris and Hay prepared 9-*O*-methylalternariol by condensation of dilithiated 2,4-pentanedione with a protected salicylate and subsequent domino cyclization.[89] In the last 3 decades, a number of syntheses using transition-metal-catalyzed reactions have been reported. For example, 6*H*-benzo[c]chromen-6-ones can be obtained by intramolecular Pd(II)-catalyzed coupling reactions of aryl benzoates.[90] An efficient and versatile synthesis of 6*H*-benzo[c]chromen-6-ones, developed by Snieckus *et al.*, relies on a sequence of directed *ortho*-metalation (DoM) and Suzuki reactions.[91] Zhou *et al.* reported the palladium-catalyzed insertion of carbon oxide into boroxarenes, which are readily synthesized from *ortho*-hydroxybiaryls.[84-88]

Interestingly, during the last 5 years, our group i.e Langer *et al* has been involved in a program dedicated to the exploration of new synthetic methods for the assembling of 6*H*-benzo[c]chromen-6-ones. We have also reported the synthesis of 6*H*-benzo[c]chromen-6-ones by $TiCl_4$ mediated [3+3] cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 3-(2-methoxyphenyl)-3-silyloxy-2-en-1-ones and subsequent BBr_3 mediated lactonization.[92] An alternative approach relies on the Me_3SiOTf mediated reaction of 1,3-bis(silyloxy)-1,3-butadienes with chromones and subsequent NEt_3 mediated domino retro-Michael–aldol–lactonization reaction.[93] Both methods provide an access to functionalized 7-hydroxy-6*H*-benzo[c]chromen-6-ones which may contain a substituent located at carbon atoms C-8 or C-9. The new bonds are formed between carbon atoms C8 and C9 and between C6a and C10a.



Ref. 92 and 93 This present work

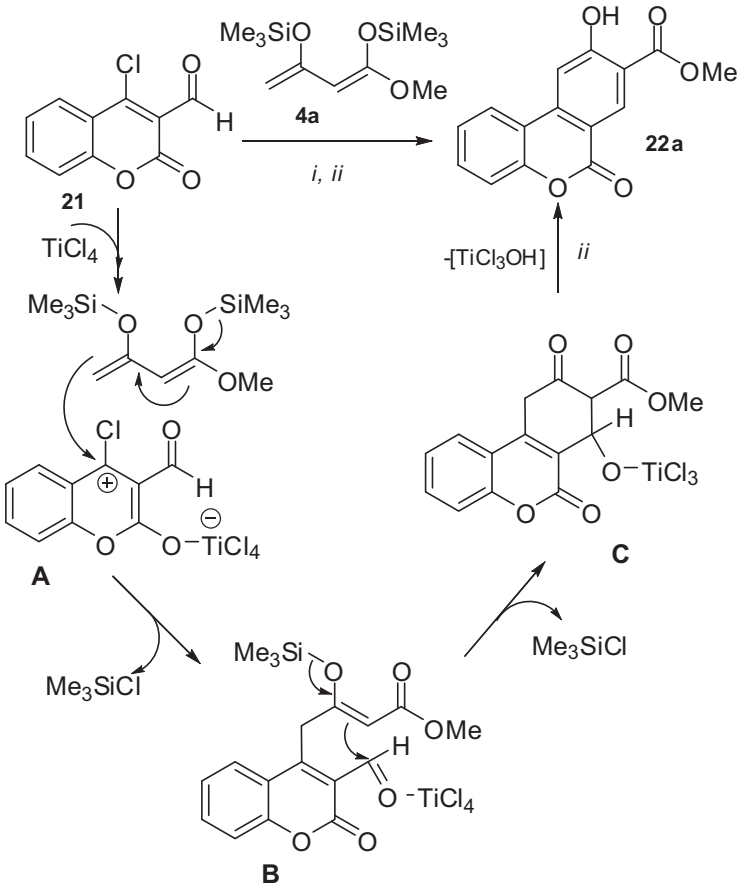
Figure 17. Retrosynthetic analysis

Herein, I hereby report a new synthesis of functionalized 9-hydroxy-6*H*-benzo[c]chromen-6-ones based on the cyclocondentation of 1,3-bis(silyloxy)-1,3-butadienes with 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde. The new bonds of the benzo[c]chromen-6-one system are formed between carbon atoms C7 and C8 and between C10 and C10a. The

reaction of 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde with enolate synthons has not, to the best of my knowledge, been previously reported. In contrast to previously reported syntheses of benzo[c]chromen-6-ones, the approach reported herein allows the assembly of the products in a single step and with a different substitution pattern.

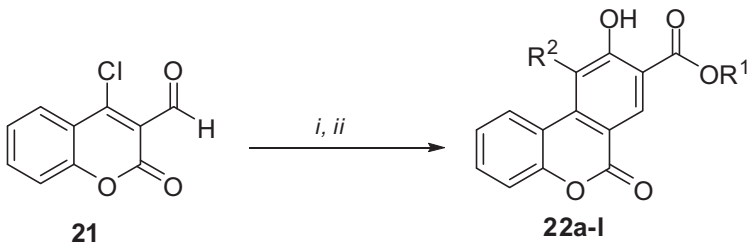
6.2 Results and Discussion

4-Chloro-2-oxo-2*H*-chromene-3-carbaldehyde (**21**) is readily available in one step from commercially available 4-hydroxycoumarin by Vilsmeier-Haack formylation.[94] The $TiCl_4$-mediated reaction of **21** with 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene **4a** (Chan's diene), which can be regarded as a masked dianion,[10] regioselectively afforded 9-hydroxy-6*H*-benzo[*c*]chromen-6-one **22a** (Scheme 21). During the optimization of the reaction conditions, I found out that the best yields were obtained when a stoichiometric ratio of **21**/**4a**/$TiCl_4$ = 1.0/1.1/1.1 was used and also when the reaction was carried out in a fairly concentrated solution. The relatively low yield (40%) can be explained by practical problems during the chromatographic purification and by partial hydrolysis of the starting materials. The formation of product **22a** can be explained by $TiCl_4$ mediated conjugate addition of **4a** to **21** (intermediates **A** and **B**), intramolecular Mukaiyama aldol reaction (intermediate **C**) and aromatization (before or during the aqueous work-up).



Scheme 21: Proposed mechanistic pathway for the [3+3] cyclization of **21** with **4a**. *Conditions*: *i*: $TiCl_4$, CH_2Cl_2, −78 → 20 °C, 14h; *ii*: HCl (10%).

Encouraged by these findings, I have tested the reaction of **21** with a set of substituted 1,3-bis(trimethylsilyloxy)-1,3-butadienes **4**. These reactions lead to the formation of the desired benzo[c]chromen-6-ones **22b-l** in 40-53% yields (Scheme 22, Table 11).



Scheme 22: Synthesis of **22a-l**. *Conditions*: *i*: **4**, $TiCl_4$, CH_2Cl_2, −78 → 20 °C, 14h; *ii*: HCl (10%)

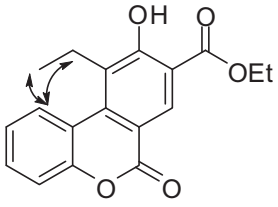
Table 11: Synthesis of 9-hydroxy-6*H*-benzo[c]chromen-6-ones **22a-l**.

22	**4**	R^1	R^2	% (**22**)[a]
a	**a**	Me	H	40
b	**e**	Me	Me	41
c	**g**	Et	Et	52
d	**h**	Me	*n*Pr	44
e	**j**	Me	*n*Pent	47
f	**k**	Me	*n*Hex	50
g	**l**	Et	*n*Hex	45
h	**p**	Et	*n*Oct	47
i	**v**	Et	Cl	41
j	**w**	Me	MeO	44
k	**d**	$(CH_2)_2OMe$	H	53
l	**c**	*i*Pr	H	46

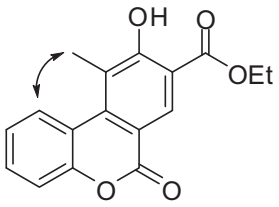
[a] Isolated yields

6.3 Proof of Structures

The structures of all products **22a-l**, were established by spectroscopic methods (NOESY and HMBC, Scheme 23). The structure of **22c** was independently confirmed by X-ray crystal structure analysis (Figure 18).[95]



22c



22b

Scheme 23: Results of NOESY experiments for **22b** and **22c.** Arrows show relevant correlations between hydrogen atoms attached to the carbon atoms indicated.

In **22c** the aromatic hydrogen atom at δ = 8.12 - 8.15 correlates with the ethyl group represented by a triplet at 1.37 - 1.42 ppm and a quartet at 3.12 ppm. In addition, the aromatic hydrogen atom at δ = 8.83 was found to correlates with the ethoxy group represented by a triplet at 1.37 - 1.42 ppm and a quartet at 4.40 ppm.

In **22b** the aromatic hydrogen atom at δ = 8.25 - 8.28 correlates with the methyl group represented by a singlet at 2.69 ppm.

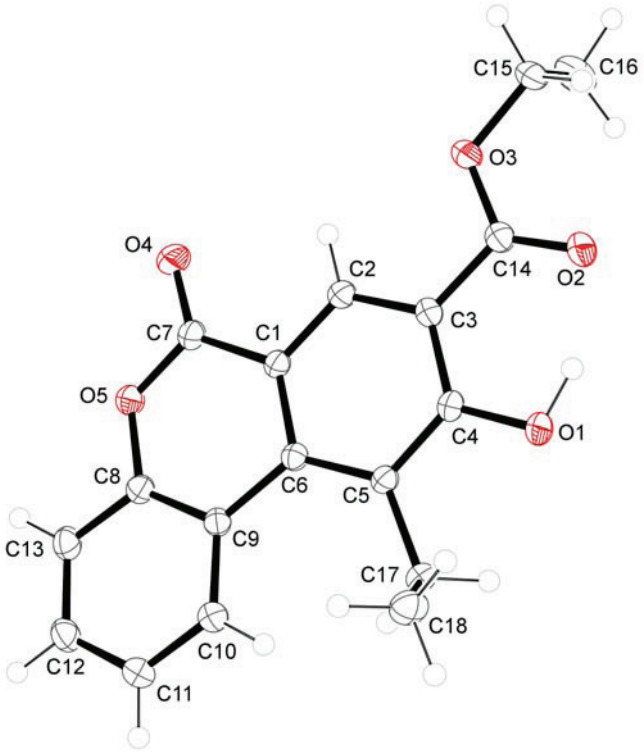


Figure 18. Ortep plot of **22c**

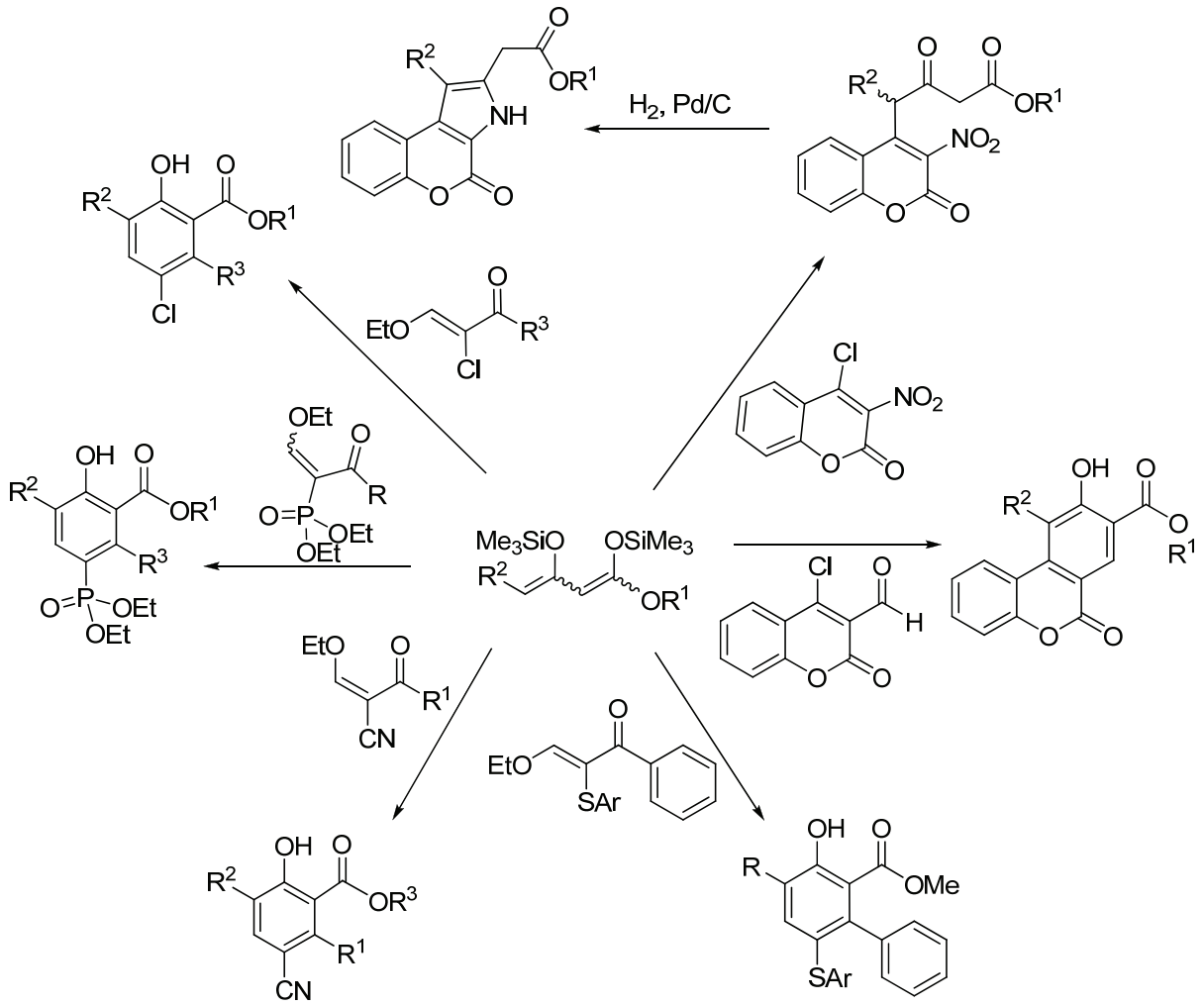
6.4 Conclusion

In summary, I have reported a facile and direct access to functionalized 9-hydroxy-6-oxo-6*H*-benzo[c]chromenes by cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde.

7 Abstract

Regioselective cyclocondensation reactions of 1,3-bis(silyl enol ethers) with different electrophiles provide a convenient approach for the synthesis of various complex carbacycles and heterocycles from simple starting materials. 5-Chlorosalicylates were prepared based on [3+3] cyclizations of 1,3-bis(sily enol ethers) with 2-chloro-3-ethoxy-2-alken-1-ones in an efficient way. Functionalized arylphosphonates were synthesized by $TiCl_4$ mediated [3+3] cyclization reactions of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-ethoxy-2-phosphonyl-alk-2-en-1-ones. Moreover, the synthesis of 5-cyanosalicylates by formal [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes was carried out. The one-pot cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 2-arylthio- and 5-benzylthio-3-ethoxy-2-en-1-ones afforded 5-arylthio- and 5-benzylthio-6-phenylsalicylates. A new synthesis of benzo[*c*]chromen-6-ones by one-pot cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde was developed. Finally, the reaction of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-chloro-3-nitrocoumarin and subsequent reduction using (Pd/C-catalysis) afforded chromeno[3,4-b]pyrrol-4(3*H*)-ones.

Regioselektive Cyclokondensationsreaktionen von 1,3-Bis(silylenolethern) mit verschiedenen Elektrophilen stellen einen geeigneten Zugang für die Synthese mannigfaltiger komplexer Carbacyclen und Heterocyclen ausgehend von einfachen Ausgangssubstanzen dar. 5-Chlorsalicylate sind auf der Basis einer [3+3]-Cyclisierung von 1,3-Bis(silylenolethern) mit 2-Chlor-3-ethoxy-2-alken-1-onen in effizienter Weise synthetisiert worden. Funktionalisierte Arylphosphonate wurden durch eine $TiCl_4$-vermittelte [3+3]-Cyclisierung von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 3-Ethoxy-2-phosphonyl-alk-2-en-1-onen dargestellt. Außerdem wurde die Synthese von 5-Cyanosalicylaten durch formale [3+3]-Cyclokondensation von 1,3-Bis(silyloxy)-1,3-butadienen durchgeführt. Die Ein-Topf-Cyclisierung von 1,3-Bis(silyloxy)-1,3-butadienen mit 2-Arylthio- und 5-Benzythio-3-ethoxy-2-en-1-onen ergab 5-Arylthio- and 5-Benzythio-6-phenylsalicylate. Eine Synthese von Benzo[*c*]chromen-6-onen durch Ein-Topf-Cyclisierung von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 4-Chlor-2-oxo-2*H*-chromen-3-carbaldehyden ist entwickelt worden.
Zusätlich wurden Chromen[3,4-b]pyrrol-4-(3*H*)-onen durch Reaktion von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 4-Chlor-3-nitrocumarinen und anschließende reduktive Cyclisierung mit Pd/C-Katalyse hergestellt.



General Scheme: Some main results of the present thesis

8 Experimental Section

8.1 General: Equipments, chemicals and work technique

^{1}H NMR Spectroscopy:

Bruker: AM 250, Avance 250, AC 250 (250 MHz); ARX 300, Avance 300 (300 MHz); Varian VXR 500 S, Avance 500 (500 MHz); δ = 0.00 ppm for Tetramethylsilane; δ = 2.04 ppm for Acetone-d_6; δ = 7.26 ppm for Deuterochloroform ($CDCl_3$) and δ = 2.50 ppm for DMSO-d_6; 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, Avance 250, AC 250 (62.9 MHz); ARX 300, Avance 300 (75 MHz); Varian VXR 500 S, Avance 500 (125 MHz); δ = 128.00 ppm for Benzene-d_6; δ = 77.00 ppm for $CDCl_3$, δ = 39.7 ppm for DMSO- d_6. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH_3, CH_2, 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 FTCIR, 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, $\lambda = 0.71073$ Å).

Melting points:

Micro heating table HMK 67/1825 Kuestner (Büchi apparatus); Meltingpoints 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 solvents were distilled before use.

TLC:

Merck DC finished foils silica gel 60 F254 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:

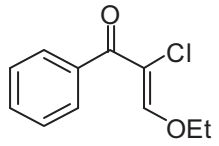
All solvents used were distilled by standard methods. All reactions were carried out under an inert atmosphere, oxygen and humidity exclusion. All of the chemicals are standard, commercially available from Merck®, Aldrich®, Arcos® and others. The order of the characterized connections effected numerically,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

8.2 Procedures and spectroscopic data

General procedure for the synthesis of 6a-f:

To a solution of **5a-f** (1.0 equiv.) in acetic anhydride (3.0 equiv.) was added triethyl orthoformate (3.0 equiv.). The mixture was heated for 15 h at 140 °C. The mixture was dried in vacuo and was purified by chromatography (silica gel, heptanes/ EtOAc) to give **6a-f**.

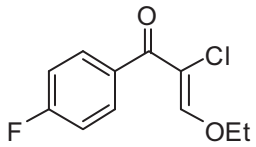
2-Chloro-3-ethoxy-1-phenylprop-2-en-1-one (6a)



Chemical Formula: $C_{11}H_{11}ClO_2$
Exact Mass: 210,045

A mixture of [2-chloro-1-phenylethanone] **5a** (2.0 g, 12.94 mmol), triethyl orthoformate (6.46 mL, 38.82 mmol) and acetic anhydride (3.67 mL, 38.82 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by chromatography (silica gel, *n*-heptane / EtOAc) to give **6a** as a brownish oil (2.1g, 76 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.10 (q, ^3J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.37 - 7.44 (m, 4 H, CH, CH_{Ar}), 7.52 - 7.55 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 66.0 (OCH_2), 113.8 (*C*Cl), 128.7 (2×CH_{Ar}), 128.8 (2×CH_{Ar}), 134.0 (CH_{Ar}), 138.2 (C_{Ar}), 160.5 (*C*H), 189.5 (CO).
IR (neat, cm^{-1}): $\tilde{\nu}$ = 3368 (w), 3062 (w), 2980 (w), 2935 (w), 1747 (m), 1691 (s), 1596 (m), 1449 (m), 1372 (m), 1216 (s), 1181 (m), 1085 (m), 1000 (m), 965 (m), 846 (m), 754 (m), 686 (s), 640 (m), 600 (m), 561 (m). Anal. calcd for $C_{11}H_{11}O_2{}^{35}Cl$: C, 62.66; H, 5.22. Found: C, 62.85; H, 5.03.

2-Chloro-3-ethoxy-1-(4-fluorophenyl)prop-2-en-1-one (6b)

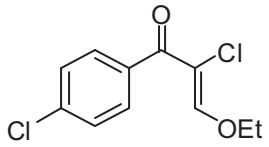


Chemical Formula: $C_{11}H_{10}ClFO_2$
Exact Mass: 228,035

A mixture of [2-chloro-1-(4-fluorophenyl)ethanone] **5b** (2.0 g, 11.59 mmol), triethyl orthoformate (5.79 mL, 34.77 mmol) and acetic anhydride (3.29 mL, 34.77 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by chromatography (silica gel, *n*-heptane / EtOAc) to give **6b** as a brownish oil (1.8 g, 68 %).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, ^3J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.07 (q, ^3J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 6.97 - 7.03 (m, 2 H, CH_{Ar}), 7.27 (s, 1 H, CH), 7.51 - 7.56 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 71.9 (OCH_2), 113.4 (*C*Cl), 115.5 (d, ^2J = 22.0 Hz), 131.2 (d, ^3J = 9.0 Hz), 134.2 (d, ^4J = 3.2 Hz), 159.9 (CH), 164.8 (d, $J_{C,F}$ = 253.0 Hz) ,188.2 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -107.0 IR (neat, cm^{-1}): $\tilde{\nu}$ =

3400 (w), 3114 (w), 3077 (w), 2982 (w), 2939 (w), 1731 (m), 1689 (m), 1596 (s), 1506 (m), 1412 (m), 1372 (m), 1278 (m), 1229 (s), 1155 (s), 1121 (m), 1099 (m), 1010 (m), 913 (m), 841 (s), 759 (m), 687 (m), 631 (m), 609 (m), 599 (m), 561 (m). GC-MS (EI, 70 eV): *m/z* (%) = 230 ([M]$^+$, ^{37}Cl, 9), 228 ([M]$^+$, ^{35}Cl, 29), 199 (36), 165 (7), 123 (100), 107 (8), 95 (39), 75 (15), 29 (7). HRMS (EI): Calcd. for $C_{11}H_{10}O_2{}^{35}ClF$ ([M]$^+$): 228.03479; found: 228.034770.

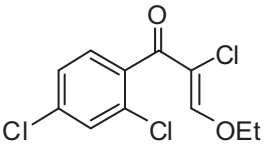
2-Chloro-1-(4-chlorophenyl)-3-ethoxyprop-2-en-1-one (6c)



Chemical Formula: $C_{11}H_{10}Cl_2O_2$
Exact Mass: 244,006

A mixture of [2-chloro-1-(4-chlorophenyl)ethanone] **5c** (2.0 g, 10.58 mmol), triethyl orthoformate (5.29 mL, 31.74 mmol) and acetic anhydride (3.00 mL, 31.74 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by chromatography (silica gel, *n*-heptane / EtOAc) to give **6c** as a brownish oil (2.1 g, 81 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.12 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.32 (s, 1 H, CH), 7.48 - 7.51 (m, 2 H, CH_{Ar}), 7.77 - 7.80 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 65.9 (OCH_2), 113.5 (*C*Cl), 129.2 (2×CH_{Ar}), 130.1 (2×CH_{Ar}), 138.0, 140.4 (C_{Ar}), 160.3 (CH), 188.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2980 (w), 2934 (w), 1747 (m), 1702 (m), 1609 (m), 1588 (s), 1487 (m), 1400 (m), 1372 (m), 1274 (m), 1214 (s), 1176 (m), 1088 (s), 1012 (s), 969 (m), 819 (s), 752 (m), 688 (m), 648 (m), 599 (w), 559 (m). GC-MS (EI, 70 eV): *m/z* (%) = 248 ([M$^+$], ^{37}Cl, ^{37}Cl, 4), 246 ([M$^+$], ^{37}Cl, ^{35}Cl, 22), 244 ([M$^+$], ^{35}Cl, ^{35}Cl, 36), 215 (51), 181 (28), 159 (7), 139 (100), 111 (38), 75 (20), 29 (9). HRMS (EI): Calcd. for $C_{11}H_{10}O_2{}^{35}Cl_2$ ([M]$^+$): 244.00524; found: 244.004846

2-Chloro-1-(2,4-dichlorophenyl)-3-ethoxyprop-2-en-1-one (6d)

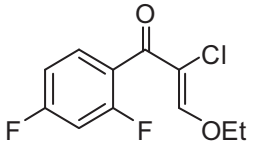


Chemical Formula: $C_{11}H_9Cl_3O_2$
Exact Mass: 277,967

A mixture of [2-chloro-1-(2,4-dichlorophenyl)ethanone] **5d** (2.0 g, 8.95 mmol), triethyl orthoformate (4.47 mL, 26.85 mmol) and acetic anhydride (2.54 mL, 26.85 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by chromatography (silica gel, *n*-heptane / EtOAc) to give **6d** as a brownish oil (1.75 g, 70 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.12 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.16 - 7.39 (m, 4 H, CH, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 72.4 (OCH_2), 114.0 (*C*Cl), 127.2, 129.6, 130.0 (CH_{Ar}), 132.1, 136.4, 136.5 (C_{Ar}), 161.6 (CH), 186.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3095 (w),

3024 (w), 2980 (w), 2932 (w), 2903 (w), 1651 (m), 1602 (m), 1583 (s), 1470 (m), 1440 (m), 1379 (m), 1341 (m), 1297 (s), 1211 (s), 1130 (m), 1090 (m), 1004 (s), 894 (m), 825 (s), 728 (m), 668 (m), 587 (m). GC-MS (EI, 70 eV): *m/z* (%) = 284 ([M^+], ^{37}Cl, ^{37}Cl, ^{37}Cl, 01), 282 ([M^+], ^{37}Cl, ^{37}Cl, ^{35}Cl, 07), 280 ([M^+], ^{37}Cl, ^{35}Cl, ^{35}Cl, 22), 278 ([M^+], ^{35}Cl, ^{35}Cl, ^{35}Cl, 22), 215 (100), 173 (42), 145 (17), 123 (5), 109 (11), 74 (6). (ESI): Calcd. for $C_{11}H_{10}Cl_3O_2$ ([M+H]$^+$): 278.97409; found: 278.97412. Anal. calcd for $C_{11}H_9{}^{35}Cl_3O_2$: C, 47.22; H, 3.22. Found: C, 46.97; H, 2.75.

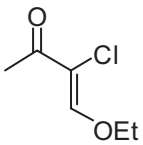
2-Chloro-1-(2,4-difluorophenyl)-3-ethoxyprop-2-en-1-one (6e)



Chemical Formula: $C_{11}H_9ClF_2O_2$
Exact Mass: 246,026

A mixture of [2-chloro-1-(2,4-difluorophenyl)ethanone] **5e** (2.0 g, 10.49 mmol), triethyl orthoformate (5.24 mL, 31.47 mmol) and acetic anhydride (2.97 mL, 31.47 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by chromatography (silica gel, *n*-heptane / EtOAc) to give **6e** as a brownish oil (1.55 g, 60 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.14 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.78 - 6.93 (m, 2 H, CH_{Ar}), 7.30-7.39 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 72.3 (OCH_2), 104.7 (t, J = 25.4 Hz), 111.9 (dd, J = 21.6 Hz, 3.7 Hz), 114.2 (*C*Cl), 123.0 (dd, J = 16.0 Hz, 3.9 Hz), 131.4 (dd, J = 10.1 Hz, 4.5 Hz), 160.8 (CH), 162.0 (dd, $J_{C,F}$ = 347.4 Hz, 253.8 Hz), 162.2 (dd, $J_{C,F}$ = 347.2 Hz, 254.1 Hz), 184.7 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -104.6, -108.4 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3034 (w), 2984 (w), 2984 (w), 2939 (w), 2902 (w), 1744 (w), 1660 (m), 1606 (s), 1499 (m), 1423 (m), 1297 (m), 1269 (m), 1216 (s), 1142 (m), 1087 (s), 1009 (m), 968 (s), 850 (m), 758 (m), 622 (m), 588 (m), 538 (m). GC-MS (EI, 70 eV): *m/z* (%) = 248 ([M^+], ^{37}Cl, 11), 246 ([M^+], ^{35}Cl, 34), 217 (7), 199 (23), 183 (9), 161 (6), 141 (100), 125 (8), 114 (41), 105 (5), 63 (9). HRMS (EI): Calcd. for $C_{11}H_9O_2{}^{35}ClF_2$ ([M]$^+$): 246.02537; found: 246.025692

3-Chloro-4-ethoxybut-3-en-2-one (6f)



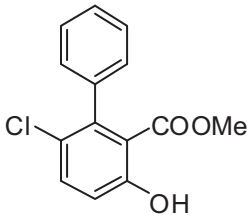
Chemical Formula: $C_6H_9ClO_2$
Exact Mass: 148,029

A mixture of [1-chloropropan-2-one] **5f** (2.0 g, 1.72 mL, 21.61 mmol), triethyl orthoformate (10.80 mL, 64.83 mmol) and acetic anhydride (6.13 mL, 64.83 mmol), was refluxed for 15 hours at 140 °C and the resultant mixture was purified by

chromatography (silica gel, *n*-heptane / EtOAc) to give **6f** as a brownish oil (1.32 g, 41 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (t, ^{3}J = 7.1 Hz, 3 H, OCH_2CH_3), 2.28 (s, 3 H, CH_3). 4.16 (q, ^{3}J = 7.1 Hz, 2 H, OCH_2CH_3), 7.58 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3, 26.5 (CH_3), 71.7 (OCH_2), 112.6 (*C*Cl), 155.6 (CH), 192.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3429 (w), 2982 (w), 2936 (w), 1731 (s), 1674 (m), 1619 (m), 1419 (m), 1373 (m), 1211 (s), 1143 (m), 1068 (m), 997 (m), 936 (m), 861 (m), 731 (m), 677 (m), 597 (m). GC-MS (EI, 70 eV): *m/z* (%) = 150 ([M^+], ^{37}Cl, 10), 148 ([M]$^+$, ^{35}Cl, 31), 120 (22), 120 (22), 105 (100), 43 (23), 29 (12). HRMS (EI): Calcd. for $C_6H_9O_2{}^{35}Cl$ ([M]$^+$): 148.02856; found: 148.028864

General procedure for the synthesis of 7a-q. To a CH_2Cl_2 solution (2 mL per 1 mmol of **6a-f**) of **6a-f** was added **4a,e,f,i** (1.1 mmol) and, subsequently, $TiCl_4$ (1.1 mmol) at -78 °C. The temperature of the solution was allowed to warm to 20 °C during 12 h with stirring. Hydrochloric acid (10 %, 20 mL) was added to the solution and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3×20 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, heptanes / EtOAc) to give **7a-q**.

Methyl 6-chloro-3-hydroxybiphenyl-2-carboxylate (7a)

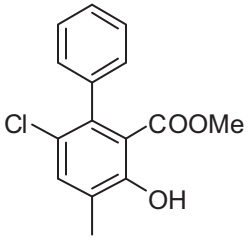


Chemical Formula: $C_{14}H_{11}ClO_3$
Exact Mass: 262,040

Starting with **6a** (0.316 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **7a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.177 g, 45 %).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.32 (s, 3 H, OCH_3), 6.92 (d, ^{3}J = 8.9 Hz, 1 H, CH_{Ar}), 7.05 - 7.08 (m, 2 H, CH_{Ar}), 7.27 - 7.35 (m, 3 H, CH_{Ar}), 7.42 (d, ^{3}J = 8.9 Hz, 1 H, CH_{Ar}), 10.65 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.0 (OCH_3), 113.1 (*C*$COOCH_3$), 117.4 (CH_{Ar}), 124.0 (*C*Cl), 126.2 (CH_{Ar}), 126.6 (2×CH_{Ar}), 127.5 (2×CH_{Ar}), 134.1 (CH_{Ar}), 138.7, 140.8 (C_{Ar}), 159.2 (*C*OH), 169.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2951 (w), 2925 (w), 2852 (w), 1739 (w), 1666 (s), 1593 (m), 1499 (w), 1435 (s), 1334 (m), 1289 (m), 1206 (s), 1135 (m), 1093 (m), 1027 (w), 1000 (w), 963 (m), 825 (m), 770 (m), 748 (s), 698 (s), 690 (s), 635 (m), 610 (m), 573 (m). GC-MS (EI, 70 eV): *m/z* (%) = 264 ([M]$^+$, ^{37}Cl, 21), 262 ([M^+], ^{35}Cl, 68), 230 (100), 202 (63), 168 (11), 139 (81), 113 (6), 87 (7), 69 (8). HRMS

(EI): Calcd. for $C_{14}H_{11}O_3{}^{35}Cl$ ($[M]^+$): 262.03912; found: 262.039159. Anal. calcd for : $C_{14}H_{11}O_3{}^{35}Cl$: C, 63.95; H, 4.19; Found: C, 63.71; H, 4.97.

Methyl 6-chloro-3-hydroxy-4-methylbiphenyl-2-carboxylate (7b)



Chemical Formula: $C_{15}H_{13}ClO_3$
Exact Mass: 276,055

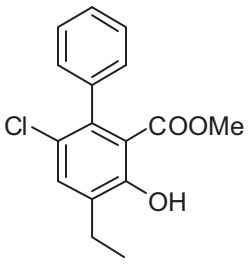
Starting with **6a** (0.316 g, 1.5 mmol) and **4e** (0.453 g, 1.65 mmol), **7b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.183 g, 44 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (s, 3 H, CH_3), 3.25 (s, 3 H, OCH_3), 6.98 - 7.01 (m, 2 H, CH_{Ar}), 7.19 - 7.27 (m, 4 H, CH_{Ar}), 10.83 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.4 (CH_3), 50.5 (OCH_3), 111.9 (*C*$COOCH_3$), 122.7 (*C*Cl), 125.6 (CH_{Ar}), 126.2 (2×CH_{Ar}), 126.5 (C_{Ar}), 127.3 (2×CH_{Ar}), 134.2 (CH_{Ar}), 137.7, 138.6 (C_{Ar}), 157.2 (*C*OH), 169.7 (CO).

IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2951 (w), 2925 (w), 2852 (w), 1664 (s), 1600 (w), 1566 (w), 1499 (w), 1437 (m), 1404 (m), 1378 (m), 1337 (m), 1291 (m), 1239 (s), 1197 (s), 1163 (s), 1072 (w), 986 (w), 968 (m), 884 (w), 806 (m), 746 (m), 697 (s), 680 (m), 562 (m).

GC-MS (EI, 70 eV): *m/z* (%) = 278 ($[M]^+$, ^{37}Cl, 12), 276 ($[M]^+$, ^{35}Cl, 40), 244 (84), 209 (100), 181 (17), 152 (35), 76 (13). HRMS (EI): Calcd. for $C_{15}H_{13}O_3{}^{35}Cl_1$($[M]^+$): 276.05477; found: 276.054923. Anal. calcd for : $C_{15}H_{13}O_3{}^{35}Cl$: C, 65.05; H, 4.70; Found: C, 64.99; H, 5.00.

Methyl 6-chloro-4-ethyl-3-hydroxybiphenyl-2-carboxylate (7c)



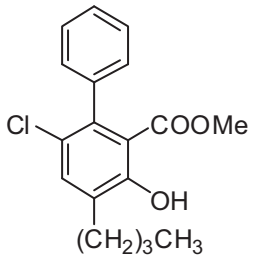
Chemical Formula: $C_{16}H_{15}ClO_3$
Exact Mass: 290,071

Starting with **6a** (0.316 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.201 g, 46 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.55 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.21 (s, 3 H, OCH_3), 6.95 - 6.98 (m, 2 H, CH_{Ar}), 7.16 - 7.24 (m, 4 H, CH_{Ar}), 10.77 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 24.8 (CH_2), 53.9 (OCH_3), 115.4 (*C*$COOCH_3$), 126.3 (*C*Cl), 128.9 (CH_{Ar}), 129.5 (2×CH_{Ar}), 130.6 (2×CH_{Ar}), 135.6 (C_{Ar}), 136.0 (CH_{Ar}), 140.9, 142.0 (C_{Ar}), 160.2 (*C*OH), 173.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2951 (w), 2934 (w), 2874 (w), 1722 (w), 1664 (s), 1599 (m), 1498 (w), 1436 (s), 1408 (s), 1337 (m), 1291 (m), 1253 (m), 1230 (s), 1197 (s),

1161 (s), 1125 (m), 1065 (m), 968 (m), 894 (w), 812 (m), 746 (s), 697 (s), 676 (s), 566 (m). GC-MS (EI, 70 eV): *m/z* (%) = 292 ([M]$^+$, ^{37}Cl, 21), 290 ([M]$^+$, ^{35}Cl, 60), 258 (100), 243 (13), 223 (92), 205 (89), 195 (15), 165 (29), 152 (46), 139 (11), 76 (11). HRMS (EI): Calcd. for $C_{16}H_{15}O_3\,^{35}Cl$ ([M]$^+$): 290.07042; found: 290.070687

Methyl 4-butyl-6-chloro-3-hydroxybiphenyl-2-carboxylate (7d)

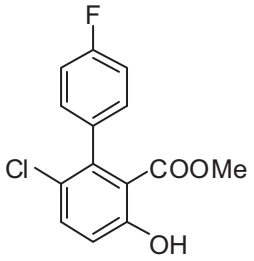


Chemical Formula: $C_{18}H_{19}ClO_3$
Exact Mass: 318,102

Starting with **6a** (0.316 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **7d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.215 g, 45 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_3CH_3$), 1.31 - 1.39 (m, 2 H, CH_2), 1.48 - 1.62 (m, 2 H, CH_2), 2.61 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_2CH_3$), 3.31 (s, 3 H, OCH_3), 7.05 - 7.08 (m, 2 H, CH_{Ar}), 7.25 - 7.30 (m, 4 H, CH_{Ar}), 10.84 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9 (CH_3), 21.6, 28.4, 30.3 (CH_2), 50.9 (OCH_3), 112.5 (CCOOCH$_3$), 123.2 (CCl), 126.0 (CH_{Ar}), 126.6 (2×CH_{Ar}), 127.7 (2×CH_{Ar}), 131.4 (C_{Ar}), 133.8 (CH_{Ar}), 138.0, 139.0 (C_{Ar}), 157.3 (COH), 170.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2953 (m), 2925 (m), 2857 (w), 1665 (m), 1600 (w), 1564 (w), 1498 (w), 1437 (m), 1408 (m), 1337 (m), 1292 (m), 1236 (m), 1197 (m), 1161 (s), 1104 (w), 1072 (w), 989 (w), 885 (w), 810 (m), 747 (m), 697 (s), 677 (m), 631 (m), 572 (w). GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M]$^+$, ^{37}Cl, 10), 318 ([M]$^+$, ^{35}Cl, 34), 286 (15), 251 (65), 244 (33), 233 (16), 209 (100), 181 (15), 165 (13), 152 (57), 69 (23). HRMS (EI): Calcd. for $C_{18}H_{19}O_3\,^{35}Cl$ ([M]$^+$): 318.10172; found: 318.102493

Methyl 6-chloro-4'-fluoro-3-hydroxybiphenyl-2-carboxylate (7e)



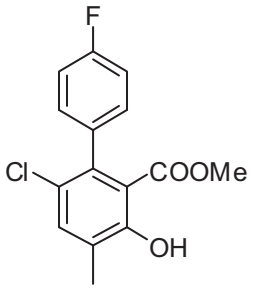
Chemical Formula: $C_{14}H_{10}ClFO_3$
Exact Mass: 280,030

Starting with **6b** (0.343 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **7e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.177 g, 42 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, OCH_3), 6.93 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 7.01 - 7.04 (m, 4 H, CH_{Ar}), 7.42 (d, ^3J = 8.9 Hz, 1 H, CH_{Ar}), 10.70 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.2 (OCH_3), 113.1 (*C*$COOCH_3$), 113.7 (d, ^2J = 25.9 Hz), 117.7 (CH_{Ar}), 124.2 (*C*Cl), 129.2 (d, ^3J = 9.6 Hz), 134.2 (CH_{Ar}), 134.6 (d, ^4J = 4.4 Hz), 139.7 (C_{Ar}), 159.4 (COH), 161.0 (d, $J_{C,F}$ = 295.4 Hz) ,169.5 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -114.9 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3044 (w), 3003 (w), 2953 (w), 2926 (w), 2853 (w), 2045 (w), 1906 (w), 1741 (w), 1667 (m), 1595 (m), 1511 (m), 1437 (s), 1337 (m), 1296 (m), 1206 (s), 1157 (m), 1091 (m), 964 (m), 827 (s), 731 (m), 678 (s), 613 (m), 567 (m). GC-MS (EI, 70 eV): *m/z* (%) = 282 ([M$^+$], ^{37}Cl, 10), 280 ([M$^+$], ^{35}Cl, 30), 248 (100), 220 (33), 185 (8), 157 (50). HRMS (EI): Calcd. for $C_{14}H_{10}O_3{}^{35}ClF$ ([M]$^+$): 280.02970; found: 280.030125

Methyl 6-chloro-4'-fluoro-3-hydroxy-4-methylbiphenyl-2-carboxylate (7f)

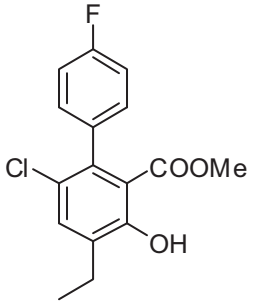


Chemical Formula: $C_{15}H_{12}ClFO_3$
Exact Mass: 294,046

Starting with **6b** (0.343 g, 1.5 mmol) and **4e** (0.453 g, 1.65 mmol), **7f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.177 g, 40 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 3.36 (s, 3 H, OCH_3), 6.99 - 7.10 (m, 4 H, CH_{Ar}), 7.31 (s, 1 H, CH_{Ar}), 10.94 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8 (CH_3), 51.1 (OCH_3), 112.2 (*C*$COOCH_3$), 113.6 (d, ^2J = 25.9 Hz), 123.3 (*C*Cl), 127.2 (C_{Ar}), 129.4 (d, ^3J = 9.6 Hz), 134.6 (CH_{Ar}), 134.9 (d, ^4J = 4.2 Hz), 136.9 (C_{Ar}), 157.8 (COH), 160.9 (d, $J_{C,F}$ = 295.1 Hz) ,169.9 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -115.3 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3041 (w), 2953 (w), 2927 (w), 2855 (w), 1725 (w), 1666 (m), 1606 (m), 1513 (s), 1437 (m), 1331 (m), 1220 (s), 1198 (s), 1158 (s), 1093 (m), 1014 (m), 909 (w), 842 (s), 748 (s), 642 (s), 619 (m), 534 (m). GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M$^+$], ^{37}Cl, 11), 294 ([M$^+$], ^{35}Cl, 32), 262 (73), 227 (100), 199 (19), 170 (38), 85 (9). HRMS (EI): Calcd. for $C_{15}H_{12}O_3{}^{35}ClF$ ([M]$^+$): 294.04535; found: 294.045422

Methyl 6-chloro-4-ethyl-4'-fluoro-3-hydroxybiphenyl-2-carboxylate (7g)



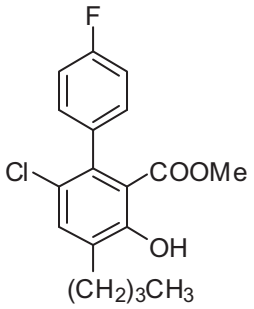
Chemical Formula: $C_{16}H_{14}ClFO_3$
Exact Mass: 308,062

Starting with **6b** (0.343 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.218 g, 47 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.54 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.26 (s, 3 H, OCH_3), 6.89 - 6.92 (m, 4 H, CH_{Ar}), 7.21 (s, 1 H, CH_{Ar}),

10.82 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.6 (CH_3), 24.1 (CH_2), 53.3 (OCH_3), 114.6 (*C*COOCH$_3$), 115.8 (d, ^2J = 22.0 Hz), 125.8 (*C*Cl), 131.6 (d, ^3J = 8.1 Hz), 135.3 (C_{Ar}), 135.4 (CH_{Ar}), 137.2 (d, ^4J = 3.5 Hz), 139.1 (C_{Ar}), 159.7 (COH), 163.2 (d, $J_{C,F}$ = 245.8 Hz) ,172.2 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -115.3 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3041 (w), 2954 (w), 2935 (w), 2875 (w), 1663 (s), 1604 (m), 1566 (w), 1513 (s), 1436 (m), 1412 (m), 1336 (m), 1291 (m), 1217 (s), 1197 (s), 1157 (s), 1093 (m), 1015 (m), 968 (m), 838 (m), 811 (s), 748 (s), 640 (m), 627 (m), 545 (m). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M]$^+$, ^{37}Cl, 17), 308 ([M]$^+$, ^{35}Cl, 55), 276 (79), 261 (15), 241 (100), 223 (54), 213 (17), 183 (23), 170 (37), 157 (10), 85 (7). HRMS (EI): Calcd. for $C_{16}H_{14}O_3{}^{35}ClF$ ([M]$^+$): 308.06100; found: 308.061110

Methyl 4-butyl-6-chloro-4'-fluoro-3-hydroxybiphenyl-2-carboxylate (7h)

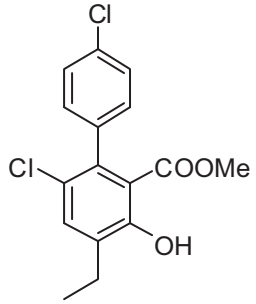


Chemical Formula: $C_{18}H_{18}ClFO_3$
Exact Mass: 336,093

Starting with **6b** (0.343 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **7h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.247 g, 49 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, ^3J = 7.3 Hz, 3 H, (CH$_2$)$_3$*CH$_3$*), 1.29 - 1.36 (m, 2 H, CH_2), 1.47 - 1.57 (m, 2 H, CH_2), 2.58 (t, ^3J = 7.5 Hz, 2 H, *CH$_2$*(CH$_2$)$_2$CH$_3$), 3.34 (s, 3 H, OCH_3), 6.98 - 7.01 (m, 4 H, CH_{Ar}), 7.28 (s, 1 H, CH_{Ar}), 10.88 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 22.6, 29.4, 31.3 (CH_2), 52.1 (OCH_3), 113.5 (*C*COOCH$_3$), 114.6 (d, ^2J = 22.0 Hz), 124.4 (*C*Cl), 130.4 (d, ^3J = 8.0 Hz), 132.8 (C_{Ar}), 134.9 (CH_{Ar}), 135.9 (d, ^4J = 3.5 Hz), 137.9 (C_{Ar}), 158.5 (COH), 162.0 (d, $J_{C,F}$ = 246.0 Hz) ,171.0 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -115.3 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3042 (w), 2954 (w), 2927 (w), 2859 (w), 1665 (m), 1605 (w), 1566 (w), 1513 (m), 1437 (m), 1411 (m), 1336 (m), 1293 (m), 1217 (s), 1197 (s), 1158 (s), 1092 (m), 1016 (m), 989 (w), 885 (w), 809 (s), 748 (s), 647 (m), 627 (m), 553 (w). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M]$^+$, ^{37}Cl, 10), 336 ([M]$^+$, ^{35}Cl, 29), 304 (14), 269 (35), 261 (23), 227 (100), 199 (7), 183 (11), 170 (35), 157 (4). HRMS (EI): Calcd. for $C_{18}H_{18}O_3{}^{35}ClF$ ([M]$^+$): 336.09230; found: 336.091705

Methyl 4',6-dichloro-4-ethyl-3-hydroxybiphenyl-2-carboxylate (7i)

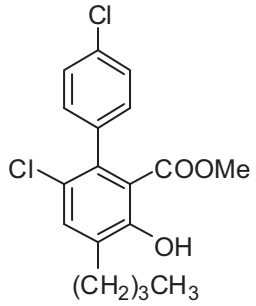


Chemical Formula: $C_{16}H_{14}Cl_2O_3$
Exact Mass: 324,032

Starting with **6c** (0.368 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.249 g, 51 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.55 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.27 (s, 3 H, OCH_3), 6.89 - 6.92 (m, 2 H, CH_{Ar}), 7.18 - 7.22 (m, 3 H, CH_{Ar}), 10.86 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 24.8 (CH_2), 54.0 (OCH_3), 115.1 (*C*$COOCH_3$), 126.3 (*C*Cl), 129.8 (2×CH_{Ar}), 132.1 (2×CH_{Ar}), 134.9, 136.0 (C_{Ar}), 136.1 (CH_{Ar}), 139.6, 140.5 (C_{Ar}), 160.5 (*C*OH), 172.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3043 (w), 2952 (m), 2934 (w), 2874 (w), 2649 (w), 2570 (w), 2280 (w), 2075 (w), 2046 (w), 1931 (w), 1899 (w), 1664 (s), 1602 (m), 1565 (w), 1495 (m), 1436 (s), 1410 (s), 1337 (s), 1290 (m), 1252 (m), 1231 (s), 1197 (s), 1161 (s), 1088 (s), 1016 (s), 967 (m), 895 (m), 836 (s), 802 (s), 756 (s), 730 (s), 632 (m), 590 (s). GC-MS (EI, 70 eV): *m/z* (%) = 328 ([M$^+$], ^{37}Cl, ^{37}Cl, 03), 326 ([M$^+$], ^{37}Cl, ^{35}Cl, 19), 324 ([M$^+$], ^{35}Cl, ^{35}Cl, 30), 292 (51), 257 (100), 229 (8), 186 (11), 165 (17), 152 (6). HRMS (EI): Calcd. for $C_{16}H_{14}O_3{}^{35}Cl_2$ ([M]$^+$): 324.03145; found: 324.031179

Methyl 4-butyl-4',6-dichloro-3-hydroxybiphenyl-2-carboxylate (7j)



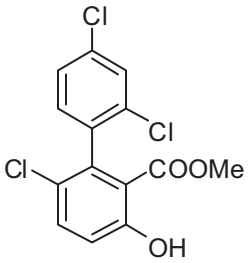
Chemical Formula: $C_{18}H_{18}Cl_2O_3$
Exact Mass: 352,063

Starting with **6c** (0.368 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **7j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.233 g, 44 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_3CH_3$), 1.30 - 1.38 (m, 2 H, CH_2), 1.49 - 1.61 (m, 2 H, CH_2), 2.60 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_2CH_3$), 3.36 (s, 3 H, OCH_3), 6.98 - 7.01 (m, 2 H, CH_{Ar}), 7.27 - 7.30 (m, 3 H, CH_{Ar}), 10.94 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9 (CH_3), 21.5, 28.4, 30.3 (CH_2), 51.1 (OCH_3), 112.2 (*C*$COOCH_3$), 123.2 (*C*Cl), 126.9 (2×CH_{Ar}), 129.1 (2×CH_{Ar}), 132.0, 133.8 (C_{Ar}), 133.9 (CH_{Ar}), 136.7, 137.5 (C_{Ar}), 157.6 (*C*OH), 169.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3044 (w), 2954 (w), 2928 (w), 2860 (w), 1665 (m), 1602 (w), 1566 (w), 1496 (w), 1437 (m), 1338 (m), 1238 (m), 1198 (m), 1162 (m), 1088 (m), 1016 (m), 906 (m), 810 (m), 728 (s), 637 (m), 615 (w), 530 (w). GC-MS (EI, 70 eV): *m/z* (%)

= 356 ([M^+], ^{37}Cl, ^{37}Cl, 03), 354 ([M^+], ^{37}Cl, ^{35}Cl, 16), 352 ([M^+], ^{35}Cl, ^{35}Cl, 24), 320 (7), 285 (35), 277 (16), 243 (100), 186 (16), 152 (8). HRMS (EI): Calcd. for $C_{18}H_{18}O_3{}^{35}Cl_2$ ([$M]^+$): 352.06275; found: 352.063088

Methyl 2',4',6-trichloro-3-hydroxybiphenyl-2-carboxylate (7k)



Chemical Formula: $C_{14}H_9Cl_3O_3$
Exact Mass: 329,962

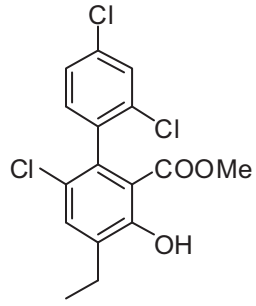
Starting with **6d** (0.419 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **7k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.219 g, 44 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.45 (s, 3 H, OCH_3), 6.96-7.00 (m, 2 H, CH_{Ar}), 7.21 - 7.25 (m, 1 H, CH_{Ar}), 7.41 - 7.48 (m, 2 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.5 (OCH_3), 112.2 (*C*$COOCH_3$), 118.6 (CH_{Ar}), 124.1 (*C*Cl), 125.7, 127.8, 129.7 (CH_{Ar}), 132.7, 132.8 (C_{Ar}), 134.6 (CH_{Ar}), 136.4, 136.7 (C_{Ar}), 160.0 (*C*OH), 169.0 (CO).

IR (neat, cm^{-1}): $\tilde{\nu}$ = 3089 (w), 2953 (w), 2852 (w), 2655 (w), 2540 (w), 1906 (w), 1733 (w), 1668 (s), 1594 (m), 1483 (m), 1437 (s), 1337 (m), 1207 (s), 1103 (m), 1049 (m), 905 (m), 820 (s), 797 (s), 680 (s), 634 (m), 542 (m). GC-MS (EI, 70 eV): *m/z* (%) = 336 ([M^+], ^{37}Cl, ^{37}Cl, ^{37}Cl, 01), 334 ([M^+], ^{37}Cl, ^{37}Cl, ^{35}Cl, 06), 332 ([M^+], ^{37}Cl, ^{35}Cl, ^{35}Cl, 19), 330 ([M^+], ^{35}Cl, ^{35}Cl, ^{35}Cl, 19), 298 (100), 270 (16), 235 (25), 207 (35), 173 (13), 137 (12).

HRMS (EI): Calcd. for $C_{14}H_9O_3{}^{35}Cl_2{}^{37}Cl$ ([$M]^+$): 331.95823; found: 331.958716

Methyl 2',4',6-trichloro-4-ethyl-3-hydroxybiphenyl-2-carboxylate (7l)



Chemical Formula: $C_{16}H_{13}Cl_3O_3$
Exact Mass: 357,993

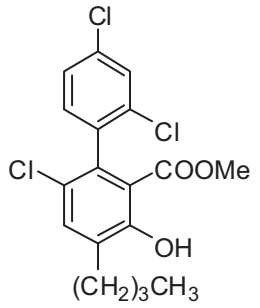
Starting with **6d** (0.419 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.243 g, 45 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.63 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.40 (s, 3 H, OCH_3), 6.93 (d, ^3J = 8.2 Hz, 1 H, CH_{Ar}), 7.15 - 7.20 (m, 1 H, CH_{Ar}), 7.32 - 7.36 (m, 2 H, CH_{Ar}), 11.31 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.2 (CH_3), 22.8 (CH_2), 52.4 (OCH_3), 112.4 (*C*$COOCH_3$), 124.5 (*C*Cl), 126.7, 128.7, 130.9 (CH_{Ar}), 133.6, 133.9 (C_{Ar}), 134.4 (CH_{Ar}), 134.9, 135.0, 137.8 (C_{Ar}), 159.2 (*C*OH), 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3042 (w), 2953 (w), 2933 (w),

2874 (w), 1737 (w), 1665 (s), 1588 (w), 1485 (w), 1437 (m), 1337 (m), 1294 (m), 1198 (m), 1163 (m), 1100 (m), 1009 (w), 907 (m), 808 (s), 730 (s), 648 (m), 600 (w), 554 (w).
GC-MS (EI, 70 eV): *m/z* (%) = 364 ([M^+], ^{37}Cl, ^{37}Cl, ^{37}Cl, 01), 362 ([M^+], ^{37}Cl, ^{37}Cl, ^{35}Cl, 08), 360 ([M^+], ^{37}Cl, ^{35}Cl, ^{35}Cl, 24), 358 ([M^+], ^{35}Cl, ^{35}Cl, ^{35}Cl, 25), 326 (44), 291 (100), 263 (8), 220 (9), 199 (8), 165 (10). HRMS (EI): Calcd. for $C_{16}H_{13}O_3{}^{35}Cl_3$ ([$M]^+$): 357.99248; found: 357.992572

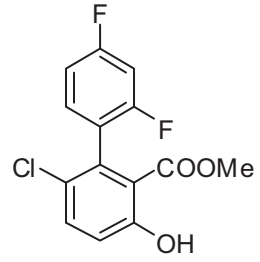
Methyl 4-butyl-2',4',6-trichloro-3-hydroxybiphenyl-2-carboxylate (7m)



Chemical Formula: $C_{18}H_{17}Cl_3O_3$
Exact Mass: 386,024

Starting with **6d** (0.419 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **7m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.273 g, 47 %).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_3CH_3$), 1.31 - 1.39 (m, 2 H, CH_2), 1.49 - 1.60 (m, 2 H, CH_2), 2.62 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_2CH_3$), 3.43 (s, 3 H, OCH_3), 6.96 (d, ^3J = 8.3 Hz, 1 H, CH_{Ar}), 7.18 - 7.23 (m, 1 H, CH_{Ar}), 7.34 - 7.40 (m, 2 H, CH_{Ar}), 11.32 (s, 1 H, OH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 22.6, 29.5, 31.2 (CH_2), 52.4 (OCH_3), 112.5 (CCOOCH$_3$), 124.4 (CCl), 126.7, 128.7, 131.0 (CH_{Ar}), 133.6, 133.8, 133.9, 134.9 (C_{Ar}), 135.2 (CH_{Ar}), 137.8 (C_{Ar}), 159.3 (COH), 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2929 (m), 2860 (w), 1741 (w), 1667 (s), 1587 (w), 1438 (s), 1410 (m), 1338 (m), 1254 (s), 1198 (s), 1162 (s), 1099 (s), 1054 (m), 1003 (m), 945 (m), 809 (s), 794 (s), 749 (s), 638 (m), 558 (w).
GC-MS (EI, 70 eV): *m/z* (%) = 392 ([M^+], ^{37}Cl, ^{37}Cl, ^{37}Cl, 01), 390 ([M^+], ^{37}Cl, ^{37}Cl, ^{35}Cl, 07), 388 ([M^+], ^{37}Cl, ^{35}Cl, ^{35}Cl, 22), 386 ([M^+], ^{35}Cl, ^{35}Cl, ^{35}Cl, 23), 351 (22), 319 (21), 277 (100), 248 (8), 220 (14), 186 (8). HRMS (EI): Calcd. for $C_{18}H_{17}O_3{}^{35}Cl_3$ ([$M]^+$): 386.02378; found: 386.023034

Methyl 6-chloro-2',4'-difluoro-3-hydroxybiphenyl-2-carboxylate (7n)

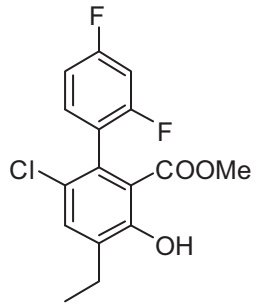


Chemical Formula: $C_{14}H_9ClF_2O_3$
Exact Mass: 298,021

Starting with **6e** (0.370 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **7n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.224 g, 50 %).
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.35 (s, 3 H, OCH_3), 6.68 – 6.79 (m, 2 H, CH_{Ar}), 6.86 – 6.94 (m, 2 H, CH_{Ar}), 7.36 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 10.85 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$,

75 MHz): δ = 52.4 (OCH_3), 103.5 (t, *J* = 25.6 Hz), 110.8 (dd, *J* = 21.3 Hz, 3.7 Hz), 113.8 (*C*$COOCH_3$), 119.6 (CH_{Ar}), 123.5 (dd, *J* = 18.8 Hz, 5.9 Hz), 125.8 (*C*Cl), 131.2 (dd, *J* = 10.6 Hz, 5.9 Hz), 134.6 (C_{Ar}), 135.4 (CH_{Ar}), 160.8 (dd, $J_{C,F}$ = 245.2 Hz, 207.8 Hz), 160.9 (COH), 161.0 (dd, $J_{C,F}$ = 250.0 Hz, 212.3 Hz), 170.1 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -110.5, -111.1 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 2955 (w), 2928 (w), 2854 (w), 1740 (w), 1670 (s), 1594 (m), 1509 (m), 1438 (s), 1335 (m), 1266 (m), 1206 (s), 1137 (s), 1080 (s), 970 (s), 848 (m), 828 (m), 732 (m), 678 (s), 613 (m), 576 (m), 562 (m), 542 (m). GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M^+], ^{37}Cl, 11), 298 ([M^+], ^{35}Cl, 32), 266 (100), 238 (45), 204 (6), 175 (54), 149 (4). HRMS (EI): Calcd. for $C_{14}H_9O_3{}^{35}ClF_2$ ([M]$^+$): 298.02028; found: 298.020663. Anal. calcd for : $C_{14}H_9O_3{}^{35}ClF_2$: C, 56.25; H, 3.01; Found: C, 56.39; H, 3.30.

Methyl 6-chloro-4-ethyl-2',4'-difluoro-3-hydroxybiphenyl-2-carboxylate (7o)



Chemical Formula: $C_{16}H_{13}ClF_2O_3$
Exact Mass: 326,052

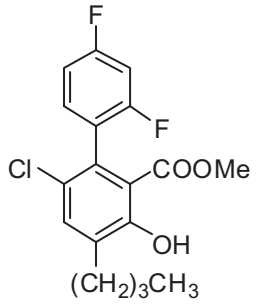
Starting with **6e** (0.370 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7o** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.240 g, 49 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.56 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.34 (s, 3 H, OCH_3), 6.67 - 6.78 (m, 2 H, CH_{Ar}), 6.86 - 6.93 (m, 1 H, CH_{Ar}), 7.26 (s, 1 H, CH_{Ar}), 11.12 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.1 (CH_3), 24.8 (CH_2), 54.3 (OCH_3), 105.3 (t, *J* = 25.7 Hz), 112.6 (dd, *J* = 21.3 Hz, 3.8 Hz), 115.0 (*C*$COOCH_3$), 125.7 (dd, *J* = 20.4 Hz, 7.7 Hz), 127.1 (*C*Cl), 128.9 (C_{Ar}), 133.3 (dd, *J* = 9.4 Hz, 4.8 Hz), 136.3 (CH_{Ar}), 136.9 (C_{Ar}), 161.0 (COH), 162.7 (dd, $J_{C,F}$ = 250.1 Hz, 196.5 Hz), 162.8 (dd, $J_{C,F}$ = 247.5 Hz, 192.7 Hz), 172.6 (CO).

^{19}F NMR (285 MHz, $CDCl_3$): δ = -110.8, -111.1 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 2955 (w), 2876 (w), 1934 (w), 1729 (w), 1667 (m), 1615 (m), 1512 (m), 1434 (m), 1339 (m), 1264 (m), 1217 (s), 1198 (s), 1163 (s), 1138 (s), 1090 (m), 971 (m), 844 (s), 802 (s), 752 (s), 643 (m), 605 (m), 550 (m). GC-MS (EI, 70 eV): *m/z* (%) = 328 ([M^+], ^{37}Cl, 35), 326 ([M^+], ^{35}Cl, 100), 294 (90), 275 (62), 266 (42), 259 (20), 231 (34), 213 (13), 201 (32), 188 (45), 175 (10), 101 (8). HRMS (EI): Calcd. for $C_{16}H_{13}O_3{}^{35}ClF_2$ ([M]$^+$): 326.05158; found: 326.051387

Methyl 4-butyl-6-chloro-2',4'-difluoro-3-hydroxybiphenyl-2-carboxylate (7p)

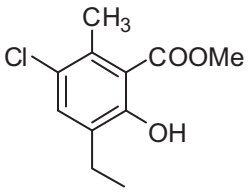


Chemical Formula: $C_{18}H_{17}ClF_2O_3$
Exact Mass: 354,083

Starting with **6e** (0.370 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **7p** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.240 g, 45 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_3CH_3$), 1.31 - 1.38 (m, 2 H, CH_2), 1.51 - 1.59 (m, 2 H, CH_2), 2.61 (t, ^3J = 6.9 Hz, 2 H, $CH_2(CH_2)_2CH_3$), 3.44 (s, 3 H, OCH_3), 6.77 - 6.87 (m, 2 H, CH_{Ar}), 6.95 - 7.03 (m, 1 H, CH_{Ar}), 7.34 (s, 1 H, CH_{Ar}), 11.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9 (CH_3), 21.6, 28.5, 30.2 (CH_2), 51.3 (OCH_3), 102.4 (t, *J* = 25.7 Hz), 109.7 (dd, *J* = 21.3 Hz, 3.7 Hz), 112.1 (*C*$COOCH_3$), 122.8 (dd, *J* = 17.4 Hz, 5.2 Hz), 124.0 (CCl), 126.0 (C_{Ar}), 130.3 (dd, *J* = 9.5 Hz, 4.9 Hz), 132.8 (C_{Ar}), 134.1 (CH_{Ar}), 158.1 (COH), 159.8 (dd, $J_{C,F}$ = 250.2 Hz, 195.2 Hz), 160.1 (dd, $J_{C,F}$ = 268.6 Hz, 214.8 Hz), 169.6 (CO). ^{19}F NMR (285 MHz, $CDCl_3$): δ = -111.5, -111.7 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3081 (w), 2958 (m), 2929 (w), 2860 (w), 1744 (w), 1668 (m), 1616 (m), 1512 (m), 1438 (m), 1338 (m), 1257 (m), 1200 (m), 1138 (s), 1091 (s), 1008 (m), 970 (s), 800 (s), 752 (s), 734 (s), 649 (m), 626 (m), 605 (w), 548 (m). GC-MS (EI, 70 eV): *m/z* (%) = 356 ([M^+], ^{37}Cl, 22), 354 ([M^+], ^{35}Cl, 65), 322 (49), 305 (33), 280 (100), 245 (74), 217 (26), 201 (18), 188 (64). HRMS (EI): Calcd. for $C_{18}H_{17}O_3{}^{35}ClF_2$ ([M]$^+$): 354.08288; found: 354.083135

Methyl 3-chloro-5-ethyl-6-hydroxy-2-methylbenzoate (7q)



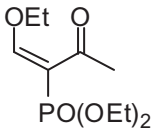
Chemical Formula: $C_{11}H_{13}ClO_3$
Exact Mass: 228,055

Starting with **6f** (0.223 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **7q** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.120 g, 35 %).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.48 (s, 3 H, CH_3), 2.56 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.90 (s, 3 H, OCH_3), 7.22 (s, 1 H, CH_{Ar}), 11.02 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.4, 18.3 (CH_3), 21.7 (CH_2), 51.4 (OCH_3), 112.6 (*C*$COOCH_3$), 124.4 (*C*Cl), 130.6 (C_{Ar}), 133.1 (CH_{Ar}), 133.6 (C_{Ar}), 157.8 (*C*OH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2931 (m), 2874 (w), 2854 (w), 1732 (w), 1661 (s), 1605 (m), 1573 (w), 1436 (s), 1336 (m), 1279 (s), 1235 (m), 1196 (s), 1158 (s), 1053 (m), 998 (m), 844 (m), 803 (s), 733 (m), 664 (s), 531 (w). GC-MS (EI, 70 eV): *m/z* (%) = 230 ([M^+], ^{37}Cl, 12),

228 ([M^+], ^{35}Cl, 34), 196 (69), 181 (12), 168 (100), 153 (8), 133 (7), 115 (12), 103 (9), 89 (9), 77 (14). HRMS (EI): Calcd. for $C_{11}H_{13}O_3{}^{35}Cl$ ([$M]^+$): 228.05477; found: 228.054656

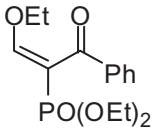
Diethyl 1-ethoxy-3-oxobut-1-en-2-ylphosphonate (9a)



Chemical Formula: $C_{10}H_{19}O_5P$
Exact Mass: 250,097

A mixture of [Diethyl 2-oxopropylphosphonate] **8a** (1.10 g, 1 mL, 5.55 mmol), triethyl orthoformate (1.1 mL, 6.62 mmol) and acetic anhydride (1.5 mL, 16.0 mmol), was stirred for 2 h at 120 °C and subsequently for 2 h at 140 °C. The resulting mixture was distilled to give **9a** as a brownish oil (1.20 g, 86 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 – 1.24 (m, 6 H, 2×OCH_2CH_3), 1.36 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 2.25 (s, 3 H, CH_3), 4.04 – 4.08 (m, 4 H, 2×OCH_2CH_3), 4.23 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.70 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.0, 15.9, 16.0, 20.6 (CH_3), 62.2, 62.4, 73.0 (OCH_2), 107.3 (d, $J_{C,P}$ = 191 Hz), 169.9 (d, $J_{C,P}$ = 25.5 Hz, CH), 195.0 (CO). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 19.64. GC-MS (EI, 70 eV): *m/z* (%) = 250 ([M^+], 5), 235 (47), 221 (12), 207(43), 205 (13), 179 (42), 177 (11), 151 (100), 123 (23), 121 (15), 105 (11), 81 (11), 53 (13), 43 (13), 29 (10). HRMS (EI): Calcd. for $C_{10}H_{19}O_5P$ ([$M]^+$) : 250.09646; found: 250.096662

Diethyl 1-ethoxy-3-oxo-3-phenylprop-1-en-2-ylphosphonate (9b)



Chemical Formula: $C_{15}H_{21}O_5P$
Exact Mass: 312,113

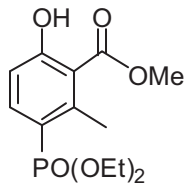
A mixture of [Diethyl 2-oxo-2-phenylethylphosphonate] **8b** (1.50 g, 1.27mL, 5.85 mmol), triethyl orthoformate (1.70 mL, 10.24 mmol) and acetic anhydride (1.56 ml, 16.61 mmol), was stirred for 36 hours at 140 °C , the resultant mixture was cooled to 20 °C and then purified by column chromatography to give **9b** as a brownish oil. (1.350 g, 74 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.21 (t, ^3J = 7.0 Hz, 6 H, 2×OCH_2CH_3), 3.94 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 4.01 - 4.10 (m, 4 H, 2×OCH_2CH_3), 7.34 - 7.48 (m, 5 H, CH_{Ar}), 7.80 - 7.82 (m, 1 H, CH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 16.25 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.1, 16.1, 16.2 (CH_3), 62.3, 62.4, 71.4 (OCH_2), 106.4 (d, $J_{P,C}$ = 189.3 Hz), 128.2 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 133.0 (CH_{Ar}), 137.6 (d, $J_{P,C}$ = 4.3 Hz), 163.5 (d, $J_{P,C}$ = 21.0 Hz, CH), 192.2 (d, $J_{P,C}$ = 4.8 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2982 (w), 2932 (w), 2905 (w), 1716 (w), 1660 (m), 1597 (m), 1448 (m), 1391 (m), 1305 (w), 1244 (s), 1204 (m), 1145 (m), 1050 (m), 1016 (s), 959 (s), 853 (m), 790

(s), 723 (m), 690 (m), 659 (m), 564 (m), 534 (m). GC-MS (EI, 70 eV): *m/z* (%) = 312 ([M^+], 4), 297 (3), 283 (11), 267(53), 239 (25), 211 (17), 183 (21), 159 (14), 151 (34), 129 (45), 105 (100), 77 (54). (ESI): Calcd. for $C_{15}H_{22}O_5P$ ([M+H]$^+$) : 313.1199; found: 313.1198 Anal. calcd for : $C_{15}H_{21}O_5P$: C, 57.69; H, 6.78. Found: C, 57.91; H, 6.76.

General procedure for the synthesis of arylphosphonates 10a-m.

To a CH_2Cl_2 solution (2 mL / 1.0 mmol of **9a,b**) of **9a,b** was added **4a-t** (1.1 mmol) and, subsequently, $TiCl_4$ (1.1 mmol) at –78 °C. The temperature of the solution was allowed to warm to 20 °C during 12 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 × 20 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, *n*-heptane / EtOAc) to give **10a-m**.

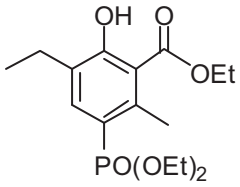
Methyl 3-(diethoxyphosphoryl)-6-hydroxy-2-methylbenzoate (10a)



Chemical Formula: $C_{13}H_{19}O_6P$
Exact Mass: 302.092

Starting with **9a** (0.375 g, 1.5 mmol) and bis silyl-enol ether **4a** (0.429 g, 1.65 mmol), **10a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil. (0.217 g, 48 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (m, 6 H, 2×$OCH_2\mathit{CH_3}$), 2.65 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 3.99 – 4.07 (m, 4 H, 2×$\mathit{OCH_2}CH_3$), 6.83 (dd, $^3J_{H,H}$ = 8.6 Hz, $^4J_{P,H}$ = 3.3 Hz, 1 H, CH_{Ar}), 7.90 (dd, $^3J_{H,H}$ = 14.0 Hz, $^3J_{P,H}$ = 9.0 Hz, 1 H, CH_{Ar}), 11.0 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.2, 16.2, 20.6 (CH_3), 52.5 (OCH_3), 62.0, 62.0 (OCH_2), 114.9 (d, $J_{P,CH}$ = 15.2 Hz, CH_{Ar}), 115.9 (d, $J_{P,C}$ =16.1 Hz), 119.0 (d, $J_{P,C}$ = 193.0 Hz), 139.3 (d, $J_{P,CH}$ = 11.0 Hz, CH_{Ar}), 145.8 (d, $J_{P,C}$ = 13.5 Hz), 164.0 (d, $J_{P,C}$ = 3.4 Hz, *C*OH), 171.2 (d, $J_{P,C}$ = 2.4 Hz, CO). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 19.56 IR (neat, cm^{-1}): $\tilde{\nu}$ = 2920 (m), 2851 (m), 1733 (m), 1660 (w), 1636 (w), 1580 (m), 1456 (m), 1437 (m), 1376 (w), 1308 (m), 1285 (m), 1199 (m), 1161 (m), 1158 (m), 1016 (s), 961 (m), 906 (m), 844 (m), 793 (m), 741 (m), 678 (w), 614 (w), 535 (m). GC-MS (EI, 70 eV): *m/z* (%) = 302 ([$M]^+$, 65), 287 (50), 274 (20), 270 (48), 259 (17), 242 (100), 229 (18), 227 (13), 214 (84), 197 (43), 186 (21), 167 (17), 161 (31), 158 (23), 134 (15), 105 (19), 77 (27), 65 (10), 51 (12), 29 (14). HRMS (EI): Calcd. for $C_{13}H_{19}O_6P$ ([$M]^+$): 302.09138; found: 302.091395.

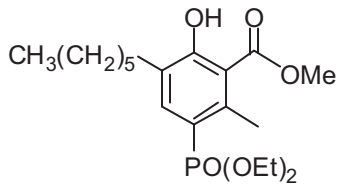
Ethyl 3-(diethoxyphosphoryl)-5-ethyl-6-hydroxy-2-methylbenzoate (10b)



Chemical Formula: $C_{16}H_{25}O_6P$
Exact Mass: 344.139

Starting with **9a** (0.375 g, 1.5 mmol) and bis silyl-enol ether **4g** (0.499 g, 1.65 mmol), **10b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.268 g, 52 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.13 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3), 1.26 (t, ^{3}J = 6.9 Hz, 6 H, 2×OCH_2CH_3), 1.36 (t, ^{3}J = 7.1 Hz, 3 H, OCH_2CH_3), 2.59 (q, ^{3}J = 7.7 Hz, 2 H, CH_2CH_3), 2.65 (s, 3 H, CH_3), 3.98 – 4.09 (m, 4 H, 2×OCH_2CH_3), 4.39 (q, ^{3}J = 7.7 Hz, 2 H, OCH_2CH_3), 7.82 (d, $^{3}J_{P,H}$ = 14.20 Hz, 1 H, CH_{Ar}), 11.39 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 20.46. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.5, 13.1, 15.2, 15.3, 19.9 (CH_3), 21.9 (CH_2), 60.8, 60.9, 61.1 (OCH_2), 113.2 (d, $J_{P,C}$ =16.87 Hz), 117.4 (d, $J_{P,C}$ =192.69 Hz), 128.8 (d, $J_{P,C}$ = 14.15 Hz), 137.7 (d, $J_{P,CH}$ = 11.0 Hz,), 142.6 (d, $J_{P,C}$ = 13.0 Hz), 161.9 (d, $J_{P,C}$ = 3.80 Hz; *C*OH), 170.6 (d, $J_{P,C}$ = 2.71 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2977 (w), 2874 (w), 1728 (m), 1657 (m), 1570 (w), 1444 (m), 1392 (w), 1372 (m), 1290 (m), 1242 (m), 1201 (m), 1177 (m), 1159 (m), 1095 (m), 1047 (m), 1015 (s), 958 (m), 865 (m), 790 (m), 745 (w), 672 (w), 615 (w). GC-MS (EI, 70 eV): *m/z* (%) = 344 ($[M]^+$, 40), 329 (15), 299 (27), 298 (100), 270 (95), 242 (28), 225 (16), 214 (17), 134 (10), 105 (11), 77 (10), 29 (10). HRMS (EI): Calcd. for $C_{16}H_{25}O_6P$ ($[M]^+$): 344.13833; found: 344.138227.

Methyl 3-(diethoxyphosphoryl)-5-hexyl-6-hydroxy-2-methylbenzoate (10c)

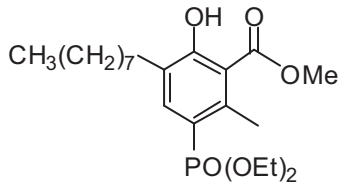


Chemical Formula: $C_{19}H_{31}O_6P$
Exact Mass: 386.186

Starting with **9a** (0.375 g, 1.5 mmol) and bis silyl-enol ether **4k** (0.568 g, 1.65 mmol), **10c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish oil (0.312 g, 54 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.8 (t, ^{3}J = 6.5 Hz, 3 H, $(CH_2)_5CH_3$), 1.16 – 1.20 (m, 6 H, 3×CH_2), 1.25 (t, ^{3}J = 6.9 Hz, 6 H, 2×OCH_2CH_3), 1.46 – 1.56 (m, 2 H, CH_2), 2.55 (t, ^{3}J = 7.9 Hz, 2 H, CH_2), 2.63 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 3.98 – 4.09 (m, 4 H, 2×OCH_2CH_3), 7.80 (d, $^{3}J_{P,H}$ = 13.70 Hz, 1 H, CH_{Ar}), 11.29 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 20.34. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 15.2, 15.3, 19.7 (CH_3), 21.3, 28.2, 28.2, 28.7, 30.6 (CH_2), 51.5 (OCH_3), 60.8, 60.9 (OCH_2), 113.1 (d, $J_{P,C}$ = 17.0 Hz), 117.4 (d, $J_{P,C}$ = 190.0 Hz), 127.6 (d, $J_{P,C}$ = 15.8 Hz), 138.6 (d, $J_{P,CH}$ = 13.2 Hz_r), 142.5 (d, $J_{P,C}$ = 13.2 Hz), 161.8 (d, $J_{P,C}$ = 3.14 Hz; *C*OH), 171.1

(d, $J_{P,C}$ = 2.51 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2925 (w), 2855 (w), 1733 (w), 1662 (w), 1601 (w), 1570 (w), 1436 (m), 1391 (w), 1345 (w), 1294 (w), 1246 (m), 1200 (m), 1160 (m),1096 (m), 1048 (m), 1018 (s), 960 (m), 887 (w), 840 (w), 771 (m), 679 (w), 617 (w), 562 (m). GC-MS (EI, 70 eV): *m/z* (%) = 386 ($[M]^+$, 25), 371 (12), 327 (17), 326 (100), 298 (13), 284 (35), 283 (12), 256 (15), 227 (11), 71 (10), 57 (16), 55 (13), 43 (13), 41 (11). HRMS (EI): Calcd. for $C_{19}H_{31}O_6P$ ($[M]^+$): 386.18528; found: 386.185467.

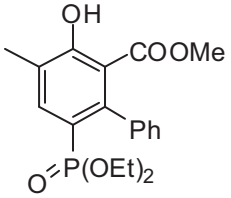
Methyl 3-(diethoxyphosphoryl)-6-hydroxy-2-methyl-5-octylbenzoate (10d)



Chemical Formula: $C_{21}H_{35}O_6P$
Exact Mass: 414.217

Starting with **9a** (0.375 g, 1.5 mmol) and bis silyl-enol ether **4o** (0.614 g, 1.65 mmol), **10d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish oil (0.360 g, 58 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.4 Hz, 3 H, $(CH_2)_7CH_3$), 1.15 – 1.20 (m, 10 H, 5×CH_2), 1.22 – 1.27 (m, 6 H, 2×OCH_2CH_3), 1.46 – 1.56 (m, 2 H, CH_2), 2.55 (t, ^3J = 7.7 Hz, 2 H, CH_2), 2.63 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 3.98 – 4.08 (m, 4 H, 2×OCH_2CH_3), 7.80 (d, $^3J_{P,H}$ = 14.20 Hz, 1 H, CH_{Ar}), 11.29 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 20.35. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 15.2, 15.3, 19.8 (CH_3), 21.6, 28.2, 28.2, 28.4, 28.6, 28.8, 30.8 (CH_2), 51.4 (OCH_3), 60.8, 60.9 (OCH_2), 113.2 (d, $J_{P,C}$ = 18.0 Hz), 117.4 (d, $J_{P,C}$ = 190.4 Hz), 127.6 (d, $J_{P,C}$ = 15.7 Hz), 138.6 (d, $J_{P,CH}$ = 11.2 Hz,), 142.5 (d, $J_{P,C}$ = 12.3 Hz), 161.8 (d, $J_{P,C}$ = 3.57 Hz; *C*OH), 171.1 (d, $J_{P,C}$ = 3.0 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2923 (m), 2853 (w), 1732 (w), 1663 (w), 1601 (w), 1571 (w), 1438 (m), 1391 (w), 1340 (w), 1292 (w), 1245 (m), 1199 (m), 1160 (m), 1096 (w), 1048 (m), 1018 (s), 958 (m), 839 (w), 792 (m), 722 (w), 679 (w), 616 (w), 545 (w). GC-MS (EI, 70 eV): *m/z* (%) = 414 ($[M]^+$, 43), 399 (13), 355 (19), 354 (100), 326 (10), 284 (38), 283 (17), 256 (12), 227 (14). HRMS (EI): Calcd. for $C_{21}H_{35}O_6P$ ($[M]^+$): 414.21658; found: 414.216315.

Methyl 6-(diethoxyphosphoryl)-3-hydroxy-4-methylbiphenyl-2-carboxylate (10e)

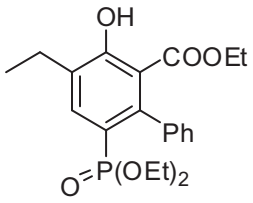


Chemical Formula: $C_{19}H_{23}O_6P$
Exact Mass: 378,123

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4e** (0.453 g, 1.65 mmol), **10e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.318 g, 56 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.0 Hz, 6 H, 2×OCH_2CH_3), 2.18 (s, 3 H, CH_3), 3.20 (s, 3 H, OCH_3), 3.59 –

3.72 (m, 4 H, 2×OCH_2CH_3.), 7.03 – 7.18 (m, 5 H, CH_{Ar}), 7.86 (d, $^3J_{P,H}$ = 13.7 Hz, 1 H, CH_{Ar}), 10.97 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 17.9 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.8, 16.0, 16.1 (CH_3), 52.0 (OCH_3), 61.5, 61.6 (OCH_2), 114.1 (d, $J_{P,C}$ = 16.6 Hz), 118.8 (d, $J_{P,C}$ = 194.8 Hz), 125.7 (d, $J_{P,C}$ = 15.0 Hz), 126.6 (2×CH_{Ar}), 127.1 (CH_{Ar}), 129.2 (2×CH_{Ar}), 139.8 (d, $J_{P,CH}$ = 10.6 Hz), 140.0 (d, $J_{P,C}$ = 4.8 Hz), 146.4 (d, $J_{P,C}$ = 12.4 Hz), 162.1 (d, $J_{P,C}$ = 3.1 Hz, COH), 171.5 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2984 (w), 2953 (w), 2907 (w), 1737 (m), 1729 (m), 1673 (w), 1553 (m), 1297 (m), 1191 (s), 1159 (s), 1127 (s), 1015 (s), 963 (s), 886 (m), 763 (m), 700 (s), 582 (s), 547 (s). GC-MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, 38), 346 (100), 317 (22), 289 (35), 271 (17), 209 (41), 152 (21). HRMS (EI): Calcd. for $C_{19}H_{23}O_6P$ ($[M]^+$): 378.12268; found: 378.122280.

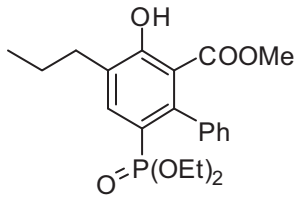
Ethyl 6-(diethoxyphosphoryl)-4-ethyl-3-hydroxybiphenyl-2-carboxylate (10f)



Chemical Formula: $C_{21}H_{27}O_6P$
Exact Mass: 406,155

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4g** (0.499 g, 1.65 mmol), **10f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.311 g, 51 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.06 (t, ^3J = 7.1 Hz, 6 H, 2×OCH_2CH_3), 1.20 (t, ^3J = 7.5 Hz, 3 H, OCH_2CH_3), 2.68 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.67 – 3.82 (m, 6 H, 3×OCH_2CH_3.), 7.13 – 7.32 (m, 5 H, CH_{Ar}), 7.93 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 11.25 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.2 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 13.5, 16.0, 16.1 (CH_3), 23.1 (CH_2), 61.3, 61.5, 61.6 (OCH_2), 114.4 (d, $J_{P,C}$ = 16.5 Hz), 118.9 (d, $J_{P,C}$ = 195.0 Hz), 127.0 (2×CH_{Ar}), 127.7 (CH_{Ar}), 129.4 (2×CH_{Ar}), 131.4 (d, $J_{P,C}$ = 14.4 Hz), 138.3 (d, $J_{P,CH}$ = 10.7 Hz), 140.2 (d, $J_{P,C}$ = 4.9 Hz), 146.3 (d, $J_{P,C}$ = 12.4 Hz), 162.0 (d, $J_{P,C}$ = 3.2 Hz, COH), 171.2 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2977 (w), 2932 (w), 2905 (w), 2874 (w), 2232 (w), 1730 (m), 1659 (m), 1555 (w), 1443 (m), 1374 (m), 1295 (m), 1229 (s), 1182 (s), 1130 (s), 1050 (s), 1020 (s), 959 (s), 827 (m), 762 (w), 729 (s), 699(s), 645 (s), 582 (m), 548 (s). GC-MS (EI, 70 eV): *m/z* (%) = 406 ($[M]^+$, 44), 360 (100), 331 (82), 303 (49), 285 (26), 223 (32), 152 (17). HRMS (EI): Calcd. for $C_{21}H_{27}O_6P$ ($[M]^+$): 406.15398; found: 406.153859.

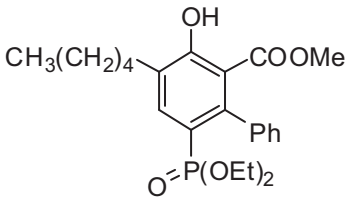
Methyl 6-(diethoxyphosphoryl)-3-hydroxy-4-propylbiphenyl-2-carboxylate (10g)



Chemical Formula: $C_{21}H_{27}O_6P$
Exact Mass: 406,155

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4h** (0.499 g, 1.65 mmol), **10g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.323 g, 53 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_2CH_3$), 1.06 (t, ^3J = 7.2 Hz, 6 H, 2×OCH_2CH_3), 1.59 – 1.66 (m, 2 H, CH_2), 2.62 (t, ^3J = 7.4 Hz, 2 H, $CH_2(CH_2)CH_3$), 3.27 (s, 3 H, OCH_3) 3.66 – 3.76 (m, 4 H, 2×OCH_2CH_3), 7.13 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 10.99 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.0 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 16.0, 16.1 (CH_3), 22.4, 31.9 (CH_2), 52.0 (OCH_3), 61.5, 61.6 (OCH_2), 114.3 (d, $J_{P,C}$ = 16.6 Hz), 118.8 (d, $J_{P,C}$ = 194.9 Hz), 126.6 (2×CH_{Ar}), 127.1 (CH_{Ar}), 129.2 (2×CH_{Ar}), 130.0 (d, $J_{P,C}$ = 14.4 Hz), 139.1 (d, $J_{P,CH}$ = 10.5 Hz), 140.1 (d, $J_{P,C}$ = 4.7 Hz), 146.3 (d, $J_{P,C}$ = 12.5 Hz), 161.8 (d, $J_{P,C}$ = 3.2 Hz, COH), 171.5 (d, $J_{P,C}$ = 2.6 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2959 (w), 2931 (w), 2872 (w), 2234 (w), 1732 (w), 1666 (m), 1538 (m), 1438 (m), 1338 (m), 1302 (m), 1226 (m), 1162 (m), 1130 (m), 1051 (m), 1022 (s), 964 (m), 816 (m), 727 (s), 699 (s), 645 (m), 605 (m), 584 (m), 549 (s). GC-MS (EI, 70 eV): *m/z* (%) = 406 ($[M]^+$, 72), 374 (53), 345 (100), 317 (51), 289 (30), 271 (25), 237 (50), 209 (19), 165 (11), 152 (24). HRMS (EI): Calcd. for $C_{21}H_{27}O_6P$ ($[M]^+$): 406.15398; found: 406.154777.

Methyl 6-(diethoxyphosphoryl)-3-hydroxy-4-pentylbiphenyl-2-carboxylate (10h)

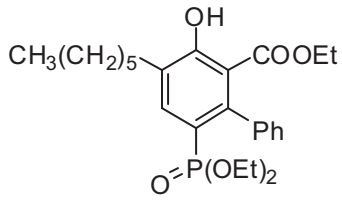


Chemical Formula: $C_{23}H_{31}O_6P$
Exact Mass: 434,186

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4i** (0.546 g, 1.65 mmol), **10h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.371 g, 57 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.84 (t, ^3J = 6.9 Hz, 3 H, $(CH_2)_4CH_3$), 1.06 (t, ^3J = 7.1 Hz, 6 H, 2×OCH_2CH_3), 1.29 – 1.32 (m, 4 H, 2×CH_2), 1.57 – 1.62 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.7 Hz, 2 H, $CH_2(CH_2)_3CH_3$), 3.27 (s, 3 H, OCH_3) 3.66 – 3.76 (m, 4 H, 2×OCH_2CH_3), 7.13 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 10.99 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.1 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 15.0, 15.1 (CH_3), 21.5, 27.9, 28.9, 30.8 (CH_2), 51.0 (OCH_3), 60.5, 60.6 (OCH_2), 113.3 (d, $J_{P,C}$ = 16.6 Hz), 117.8 (d, $J_{P,C}$ = 194.8 Hz), 125.6 (2×CH_{Ar}), 126.1 (CH_{Ar}), 128.2 (2×CH_{Ar}), 129.2 (d, $J_{P,C}$ = 14.4 Hz),

138.1 (d, $J_{P,CH}$ = 10.7 Hz), 139.1 (d, $J_{P,C}$ = 4.7 Hz), 145.3 (d, $J_{P,C}$ = 12.4 Hz), 160.8 (d, $J_{P,C}$ = 3.2 Hz, COH), 170.5 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (m), 2928 (m), 2858 (w), 2232 (w), 1736 (m), 1666 (m), 1556 (w), 1437 (m), 1342 (m), 1297 (m), 1230 (m), 1161 (m), 1130 (m), 1051 (s), 1023 (s), 964 (m), 815 (m), 728 (s), 699 (s), 645 (m), 604 (m), 583 (m), 549 (s).(ESI): Calcd. for $C_{23}H_{32}O_6P$ ($[M+H]^+$): 435.1931; found: 435.194.

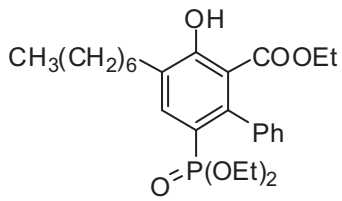
Ethyl 6-(diethoxyphosphoryl)-4-hexyl-3-hydroxybiphenyl-2-carboxylate (10i)



Chemical Formula: $C_{25}H_{35}O_6P$
Exact Mass: 462,217

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4l** (0.592 g, 1.65 mmol), **10i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.402 g, 58 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.2 Hz, 3 H, $(CH_2)_5CH_3$), 0.83 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 1.06 (t, ^3J = 7.1 Hz, 6 H, 2×OCH_2CH_3), 1.23 - 1.30 (m, 6 H, 3×CH_2), 1.53 – 1.61 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.67 – 3.84 (m, 6 H, 3×OCH_2CH_3.), 7.14 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 11.23 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.2 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9, 14.1, 16.0, 16.1 (CH_3), 22.6, 29.2, 29.3, 29.9, 31.7 (CH_2), 61.3, 61.5, 61.6 (OCH_2), 114.2 (d, $J_{P,C}$ = 16.5 Hz), 118.8 (d, $J_{P,C}$ = 194.8 Hz), 126.6 (2×CH_{Ar}), 127.1 (CH_{Ar}), 129.4 (2×CH_{Ar}), 130.2 (d, $J_{P,C}$ = 14.4 Hz), 139.0 (d, $J_{P,CH}$ = 10.6 Hz), 140.3 (d, $J_{P,C}$ = 4.9 Hz), 146.3 (d, $J_{P,C}$ = 12.4 Hz), 162.0 (d, $J_{P,C}$ = 3.2 Hz, COH), 171.2 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2979 (w), 2927 (m), 2857 (w), 2233 (w), 1731 (w), 1660 (m), 1538 (w), 1443 (m), 1374 (m), 1298 (m), 1229 (m), 1184 (m), 1130 (m), 1051 (m), 1021 (s), 962 (m), 794 (m), 728 (s), 698 (m), 644 (w), 605 (w), 584 (w), 549 (m). GC-MS (EI, 70 eV): *m/z* (%) = 462 ($[M]^+$, 69), 416 (56), 388 (100), 359 (48), 346 (98), 317 (63), 289 (46), 271 (20), 209 (37), 180 (13), 152 (12), 105 (19), 43 (10). HRMS (EI): Calcd. for $C_{25}H_{35}O_6P$ ($[M]^+$): 462.21658; found: 462.216324.

Ethyl 6-(diethoxyphosphoryl)-4-heptyl-3-hydroxybiphenyl-2-carboxylate (10j)

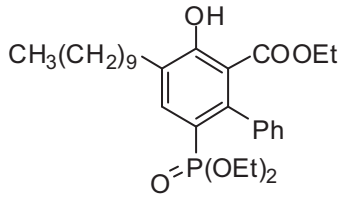


Chemical Formula: $C_{26}H_{37}O_6P$
Exact Mass: 476,233

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4n** (0.615 g, 1.65 mmol), **10j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.393 g, 55 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_6CH_3$), 0.82 (t, ^3J = 6.9 Hz, 3 H,

OCH_2CH_3), 1.06 (t, ^3J = 7.1 Hz, 6 H, 2×OCH_2CH_3), 1.19 – 1.23 (m, 8 H, 4×CH_2), 1.54 – 1.62 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_5CH_3$), 3.68 – 3.81 (m, 6 H, 3×OCH_2CH_3), 7.13 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 11.23 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.2 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.9, 13.1, 15.0, 15.1 (CH_3), 21.7, 28.2, 28.3, 28.6, 28.9, 30.8 (CH_2), 60.3, 60.5, 60.6 (OCH_2), 113.2 (d, $J_{P,C}$ = 16.5 Hz), 117.8 (d, $J_{P,C}$ = 194.8 Hz), 125.6 (2×CH_{Ar}), 126.1 (CH_{Ar}), 128.4 (2×CH_{Ar}), 129.2 (d, $J_{P,C}$ = 14.5 Hz), 138.0 (d, $J_{P,CH}$ = 10.6 Hz), 139.3 (d, $J_{P,C}$ = 4.9 Hz), 145.3 (d, $J_{P,C}$ = 12.2 Hz), 161.0 (d, $J_{P,C}$ = 3.2 Hz, COH), 170.2 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2957 (w), 2926 (m), 2855 (w), 1732 (w), 1660 (m), 1557 (w), 1443 (m), 1374 (m), 1299 (m), 1250 (m), 1184 (m), 1130 (m), 1052 (s), 1022 (s), 968 (m), 796 (s), 731 (m), 699 (m), 645 (w), 606 (w), 584 (w), 551 (m). GC-MS (EI, 70 eV): *m/z* (%) = 476 ([M]$^+$, 24), 462 (47), 430 (22), 416 (38), 388 (66), 359 (47), 346 (100), 317 (65), 303 (11), 289 (49), 271 (19), 209 (34), 44 (27). HRMS (EI): Calcd. for $C_{26}H_{37}O_6P$ ([M]$^+$): 476.23223; found: 476.232197.

Ethyl 4-decyl-6-(diethoxyphosphoryl)-3-hydroxybiphenyl-2-carboxylate (10k)

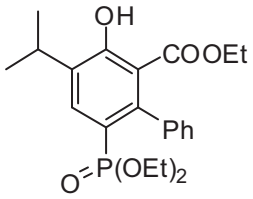


Chemical Formula: $C_{29}H_{43}O_6P$
Exact Mass: 518,280

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4s** (0.661 g, 1.65 mmol), **10k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.420 g, 54 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.60 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_9CH_3$), 0.81 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 1.06 (t, ^3J = 6.9 Hz, 6 H, 2×OCH_2CH_3), 1.16 – 1.34 (m, 14 H, 7×CH_2), 1.53 – 1.61 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.64 – 3.84 (m, 6 H, 3×OCH_2CH_3), 7.13 – 7.25 (m, 5 H, CH_{Ar}), 7.90 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 11.22 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.2 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 14.1, 16.0, 16.1 (CH_3), 22.6, 29.2 (3×CH_2), 29.3, 29.4, 29.6, 29.9, 31.9 (CH_2), 61.3, 61.5, 61.6 (OCH_2), 114.2 (d, $J_{P,C}$ = 16.5 Hz), 118.8 (d, $J_{P,C}$ = 194.9 Hz), 126.6 (2×CH_{Ar}), 127.0 (CH_{Ar}), 129.4 (2×CH_{Ar}), 130.2 (d, $J_{P,C}$ = 14.5 Hz), 139.0 (d, $J_{P,CH}$ = 10.6 Hz), 140.3 (d, $J_{P,C}$ = 4.7 Hz), 146.3 (d, $J_{P,C}$ = 12.4 Hz), 162.0 (d, $J_{P,C}$ = 3.3 Hz, COH), 171.2 (d, $J_{P,C}$ = 2.6 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2925 (m), 2854 (m), 2234 (w), 1732 (w), 1660 (m), 1556 (m), 1443 (m), 1374 (m), 1298 (m), 1229 (s), 1183 (s), 1130 (s), 1052 (s), 1021 (s), 963 (s), 912 (m), 809 (m), 729 (s), 698 (s), 644 (m), 606 (m), 583 (m), 550 (s). GC-MS (EI, 70 eV): *m/z* (%) = 518 ([M]$^+$, 100), 489 (20), 433 (19), 420 (35), 408 (21), 381 (15), 331 (35), 283 (22),

231 (15), 207 (27), 165 (11), 75 (12), 43 (13). HRMS (EI): Calcd. for $C_{29}H_{43}O_6P$ ($[M]^+$): 518.27918; found: 518.276509.

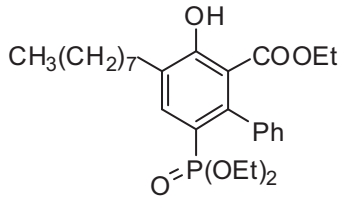
Ethyl 6-(diethoxyphosphoryl)-3-hydroxy-4-isopropylbiphenyl-2-carboxylate (10l)



Chemical Formula: $C_{22}H_{29}O_6P$
Exact Mass: 420,170

Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4t** (0.522 g, 1.65 mmol), **10l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.296 g, 47 %).^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.2 Hz, 3 H, $OCH_2\mathit{CH_3}$), 1.07 (t, ^3J = 7.1 Hz, 6 H, 2×$CH_2\mathit{CH_3}$), 1.21 (t, ^3J = 6.9 Hz, 6 H, 2×CH_3), 3.29 – 3.34 (m, 1 H, $\mathit{CH}(CH_3)_2$), 3.68 – 3.84 (m, 6 H, 3×$\mathit{OCH_2}CH_3$.), 7.15 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 10.29 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.6 Hz. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.9, 15.0, 15.1 (CH_3), 21.0 (2×CH_3), 26.0 (CH), 60.3, 60.4, 60.5 (OCH_2), 113.2 (d, $J_{P,C}$ = 16.5 Hz), 117.8 (d, $J_{P,C}$ = 194.8 Hz), 125.7 (2×CH_{Ar}), 126.0 (CH_{Ar}), 128.4 (2×CH_{Ar}), 129.2 (d, $J_{P,C}$ = 14.5 Hz), 134.6 (d, $J_{P,CH}$ = 10.7 Hz), 139.3 (d, $J_{P,C}$ = 4.9 Hz), 145.3 (d, $J_{P,C}$ = 12.2 Hz), 161.0 (d, $J_{P,C}$ = 3.2 Hz, COH), 170.2 (d, $J_{P,C}$ = 2.5 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2962 (w), 2929 (w), 2872 (w), 2236 (w), 1738 (w), 1659 (w), 1538 (w), 1443 (w), 1373 (m), 1294 (w), 1230 (m), 1186 (m), 1126 (m), 1051 (m), 1022 (s), 964 (m), 800 (m), 728 (s), 699 (m), 646 (m), 585 (w), 548 (m). GC-MS (EI, 70 eV): *m/z* (%) = 420 ($[M]^+$, 53), 374 (66), 345 (100), 317 (42), 299 (17), 237 (31), 223 (11), 165 (20), 152 (8). (ESI): Calcd. for $C_{22}H_{30}O_6P$ ($[M+H]^+$): 421.1775; found: 421.1777.

Ethyl 6-(diethoxyphosphoryl)-3-hydroxy-4-octylbiphenyl-2-carboxylate (10m)



Chemical Formula: $C_{27}H_{39}O_6P$
Exact Mass: 490,248

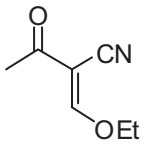
Starting with **9b** (0.468 g, 1.5 mmol) and bis silyl-enol ether **4p** (0.638 g, 1.65 mmol), **10m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil. (0.397 g, 54 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.2 Hz, 3 H, $(CH_2)_7\mathit{CH_3}$), 0.83 (t, ^3J = 6.9 Hz, 3 H, $OCH_2\mathit{CH_3}$), 1.06 (t, ^3J = 7.0 Hz, 6 H, 2×$OCH_2\mathit{CH_3}$), 1.19 – 1.29 (m, 10 H, 5×CH_2), 1.56 – 1.61 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.6 Hz, 2 H, $\mathit{CH_2}(CH_2)_6CH_3$), 3.68 – 3.81 (m, 6 H, 3×$\mathit{OCH_2}CH_3$.), 7.14 – 7.25 (m, 5 H, CH_{Ar}), 7.91 (d, $^3J_{P,H}$ = 13.8 Hz, 1 H, CH_{Ar}), 11.22 (s, 1 H, OH). ^{31}P NMR (250 MHz, $CDCl_3$): δ = 18.2 Hz. ^{13}C NMR ($CDCl_3$, 75

MHz): δ = 12.9, 14.1, 16.0, 16.1 (CH_3), 22.6, 29.2, 29.3, 29.4, 29.7, 29.9, 31.7 (CH_2), 61.3, 61.5, 61.6 (OCH_2), 114.2 (d, $J_{P,C}$ = 16.5 Hz), 118.8 (d, $J_{P,C}$ = 195.0 Hz), 126.7 (2×CH_{Ar}), 127.1 (CH_{Ar}), 129.4 (2×CH_{Ar}), 130.2 (d, $J_{P,C}$ = 14.4 Hz), 139.0 (d, $J_{P,CH}$ = 10.7 Hz), 140.3 (d, $J_{P,C}$ = 4.9 Hz), 146.3 (d, $J_{P,C}$ = 12.2 Hz), 162.0 (d, $J_{P,C}$ = 3.2 Hz, COH), 171.2 (d, $J_{P,C}$ = 2.6 Hz, CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2979 (w), 2956 (w), 2927 (m), 2856 (w), 1732 (m), 1659 (m), 1597 (w), 1552 (w), 1443 (m), 1374 (m), 1298 (m), 1233 (m), 1184 (m), 1130 (m), 1051 (s), 1022 (s), 962 (m), 809 (m), 765 (m), 698 (m), 606 (w), 550 (m). GC-MS (EI, 70 eV): *m/z* (%) = 490 ($[M]^+$, 100), 462 (27), 417 (12), 380 (13), 353 (21), 331 (25), 309 (18), 283 (16), 207 (13), 75 (8). HRMS (EI): Calcd. for $C_{27}H_{39}O_6P$ ($[M]^+$): 490.24788; found: 490.247459.

General procedure for the synthesis of 2-Cyano-3-ethoxy-2-en-1-ones 12a-e:

To an acetic anhydride solution (2.5 mL / 10 mmol of (**11a-e**)) was added ketonitriles **11a-e** (1.0 equiv.) and triethyl orthoformate (3.0 equiv.). The mixture was refluxed for 2 hours. The Ac_2O was removed in vacuo and the solid residue was purified by crystallization from ethanol to give **12a-e**.

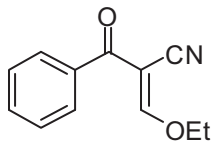
2-(Ethoxymethylene)-3-oxobutanenitrile (12a)



Chemical Formula: $C_7H_9NO_2$
Exact Mass: 139.063

Starting with **11a** [3-oxobutanenitrile] (2.00 g, 24.36 mmol) and triethyl orthoformate (12.17 mL, 73.08 mmol), product was isolated after crystallization from ethanol to give **12a** as a brown crystal (3.387g, 100 %). mp. 70 - 71 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.44 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 2.38 (s, 3 H, CH_3), 4.36 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 8.0 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3, 28.2 (CH_3), 74.1 (OCH_2), 94.4 (*C*CN), 114.4 (CN), 171.8 (CH), 191.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2958 (w), 2922 (m), 2852 (w), 2253 (w), 2226 (w), 1693 (m), 1671 (m), 1612 (s), 1612 (s), 1590 (m), 1469 (w), 1445 (w), 1394 (w), 1383 (w), 1309 (m), 1294 (m), 1232 (s), 1153 (m), 1094 (m), 1075 (m), 999 (m), 957 (m), 908 (m), 877 (m), 784 (w), 728 (m), 648 (w), 638 (m), 624 (m), 608 (m), 537 (w). GC-MS (EI, 70 eV): *m/z* (%) = 139 ($[M^+]$, 50), 124 (8), 111 (21), 96 (100), 83 (81), 68 (93), 52 (10). HRMS (EI): Calcd. for $C_7H_9O_2N$ ($[M]^+$) : 139.06278; found: 139.063030

2-Benzoyl-3-ethoxyacrylonitrile (12b)

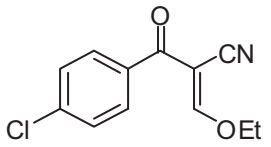


Chemical Formula: $C_{12}H_{11}NO_2$
Exact Mass: 201.079

Starting with **11b** [3-oxo-3-phenylpropanenitrile] (2.00 g, 13.78 mmol) and triethyl orthoformate (6.88 mL, 41.34 mmol), product was isolated after crystallization from ethanol to give **12b** as a brown solid (2.43 g, 88 %). mp. 70 - 71 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 (t, ^3J = 7.2 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.34 (q, ^3J = 7.2 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.40 – 7.52 (m, 3 H, CH_{Ar}), 7.77 – 7.82 (m, 2 H, CH_{Ar}), 8.03 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4 (CH_3), 74.3 (OCH_2), 94.1 (*C*CN), 114.7 (CN), 128.5 (2×CH_{Ar}), 128.7 (2×CH_{Ar}), 133.1 (CH_{Ar}), 136.9 (C_{Ar}), 174.4 (CH), 187.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2985 (w), 2937 (w), 2219 (w), 1645 (m), 1598 (s), 1577 (s), 1492 (w), 1472 (w), 1446 (m), 1393 (m), 1376 (m), 1352 (m), 1301 (m), 1288 (m), 1231 (s), 1180 (m), 1153 (m), 1104 (m), 1004 (m), 922 (m), 909 (m), 870 (w), 796 (w), 716 (m), 698 (m), 670 (m), 611 (w), 555 (w). GC-MS (EI, 70 eV): *m/z* (%) = 201 ([M^+], 13), 200 (14), 183 (2), 172 (19), 158 (2), 145 (3), 116 (3), 105 (100), 89 (5), 77 (43), 51 (13), 29 (7). HRMS (EI): Calcd. for $C_{12}H_{11}O_2N$ ([M]$^+$) : 201.07843; found: 201.078326

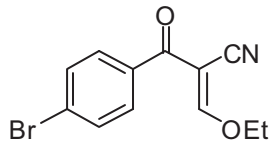
2-(4-Chlorobenzoyl)-3-ethoxyacrylonitrile (12c)



Chemical Formula: $C_{12}H_{10}ClNO_2$
Exact Mass: 235.040

Starting with **11c** [3-(4-chlorophenyl)-3-oxopropanenitrile] (2.00 g, 11.14 mmol) and triethyl orthoformate (5.56 mL, 33.42 mmol), product was isolated after crystallization from ethanol to give **12c** as a pink crystal (2.57 g, 98 %), mp. 95 - 97 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.42 (t, ^3J = 7.2 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.36 (q, ^3J = 7.2 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.37 – 7.41 (m, 2 H, CH_{Ar}), 7.75 – 7.79 (m, 2 H, CH_{Ar}), 8.05 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.4 (CH_3), 73.6 (OCH_2), 92.7 (*C*CN), 113.6 (CN), 128.0 (2×CH_{Ar}), 129.2 (2×CH_{Ar}), 134.1, 138.5 (C_{Ar}), 173.8 (CH), 185.4 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3026 (w), 2982 (w), 2937 (w), 2227 (m), 1921 (w), 1642 (m), 1594 (m), 1487 (m), 1394 (m), 1373 (w), 1354 (m), 1308 (m), 1258 (s), 1180 (m), 1157 (m), 1106 (m), 1090 (m), 1005 (m), 965 (w), 955 (m), 914 (m), 867 (m), 836 (m), 785 (m), 753 (s), 730 (m), 694 (m), 628 (w), 585 (m), 563 (m). GC-MS (EI, 70 eV): *m/z* (%) = 235 ([M^+], ^{35}Cl, 13), 234 ([M^+], ^{37}Cl, 8), 206 (14), 172 (8), 139 (100), 123 (3), 111 (31), 75 (17), 50 (5), 29 (8). HRMS (EI): Calcd. for $C_{12}H_{10}O_2N^{35}Cl$ ([M]$^+$): 235.03946; found: 235.039090

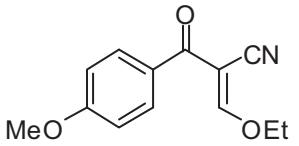
2-(4-Bromobenzoyl)-3-ethoxyacrylonitrile (12d)



Chemical Formula: $C_{12}H_{10}BrNO_2$
Exact Mass: 278.989

Starting with **11d** [3-(4-bromophenyl)-3-oxopropanenitrile] (2.000 g, 8.93 mmol) and triethyl orthoformate (4.46 mL, 26.79 mmol), product was isolated after crystallization from ethanol to give **12d** as a pink crystal (2.40 g, 96 %). mp. 99 - 102 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.42 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.36 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 7.53 – 7.58 (m, 2 H, CH_{Ar}), 7.67 – 7.72 (m, 2 H, CH_{Ar}), 8.05 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.2 (CH_3), 74.4 (OCH_2), 93.5 (*C*CN), 114.4 (CN), 128.1 (C_{Ar}), 130.2 (2×CH_{Ar}), 131.9 (2×CH_{Ar}), 135.5 (C_{Ar}), 174.7 (CH), 186.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3073 (w), 3042 (w), 2920 (w), 2852 (w), 2221 (m), 1921 (w), 1621 (m), 1586 (m), 1537 (m), 1504 (m), 1483 (m), 1384 (m), 1317 (m), 1245 (m), 1184 (m), 1166 (m), 1116 (m), 1071 (m), 1021 (m), 1010 (m), 980 (m), 906 (m), 827 (s), 749 (s), 689 (m), 626 (m), 604 (m), 576 (m), 559 (m), 533 (m). GC-MS (EI, 70 eV): *m/z* (%) = 281 ([M$^+$], ^{81}Br, 16), 279 ([M$^+$], ^{79}Br, 16), 278 (11), 252 (15), 238 (4), 225 (6), 200 (10), 185 (97), 183 (100), 172 (12), 157 (29), 155 (29), 143 (8), 115 (5), 96 (4), 76 (21), 68 (6), 50 (12), 29 (12). HRMS (EI): Calcd. for $C_{12}H_{10}O_2N^{79}Br$ ([M]$^+$): 278.98894; found: 278.988999

3-Ethoxy-2-(4-methoxybenzoyl)acrylonitrile (12e)



Chemical Formula: $C_{13}H_{13}NO_3$
Exact Mass: 231.090

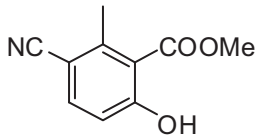
Starting with **11e** [3-(4-methoxyphenyl)-3-oxopropanenitrile] (2.00 g, 11.42 mmol) and triethyl orthoformate (5.70 mL, 34.26 mmol), product was isolated after crystallization from ethanol to give **12e** as a reddish-brown solid (2.50 g, 95 %). mp. 45 - 50 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.41 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 3.80 (s, 3 H, OCH_3), 4.33 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 6.87 – 6.90 (m, 2 H, CH_{Ar}), 7.86 – 7.89 (m, 2 H, CH_{Ar}), 8.02 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 55.6 (OCH_3), 74.0 (OCH_2), 93.6 (*C*CN), 113.8 (2×CH_{Ar}), 115.1 (CN), 131.3 (2×CH_{Ar}), 161.2, 163.7 (C_{Ar}), 174.0 (CH), 185.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 2929 (w), 2844 (w), 2215 (m), 1911 (w), 1738 (w), 1682 (w), 1631 (m), 1597 (m), 1574 (m), 1556 (m), 1504 (m), 1462 (m), 1450 (m), 1423 (m), 1377 (m), 1308 (m), 1255 (s), 1167 (s), 1125 (m), 1022 (s), 974 (m), 960 (m), 838 (s), 812 (m), 800 (m), 751 (m), 700 (m), 632 (m), 605 (m), 541 (m), 531 (m). GC-MS (EI, 70 eV): *m/z* (%) = 231 ([M$^+$], 23), 216 (2), 202 (6), 188 (4), 174 (3), 160 (2), 136 (9), 135

(100), 107 (6), 92 (11), 77 (13), 64 (5), 50 (2). HRMS (EI): Calcd. for $C_{13}H_{13}O_3N$ ($[M]^+$): 231.08899; found: 231.089338

General experimental procedure for the synthesis of 13a-ac.

To a stirred solution of CH_2Cl_2 (3 mL per 1.0 mmol of **12a-e**) of **12a-e** was added **4a-x** (1.1 mmol) and, subsequently $TiCl_4$ (1.1 mmol) at −78 °C under argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C during 14 h with stirring. To the solution was added HCl (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 purified by column chromatography (silica gel, heptanes/ethyl acetate) to give **13a-ac**.

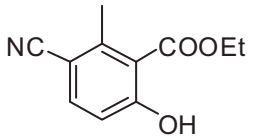
Methyl 3-cyano-6-hydroxy-2-methylbenzoate (13a)



Chemical Formula: $C_{10}H_9NO_3$
Exact Mass: 191,058

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **13a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.097 g, 34 %). mp. 84 - 85 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.71 (s, 3 H, CH_3), 3.95 (s, 3 H, OCH_3), 6.85 (d, ^3J = 8.9 Hz, 1 H, CH_{Ar}), 7.54 (d, ^3J = 8.9 Hz, 1 H, CH_{Ar}), 11.69 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.9 (CH_3), 52.9 (OCH_3), 105.9 (*C*CN), 113.4 (*C*COOCH$_3$), 117.0 (CH_{Ar}), 118.4 (CN), 137.8 (CH_{Ar}), 146.5 (C_{Ar}), 165.7 (*C*OH), 171.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 2927 (w), 2854 (w), 2252 (w), 2222 (w), 1737 (w), 1669 (m), 1590 (m), 1469 (m), 1442 (m), 1385 (w), 1352 (m), 1323 (m), 1303 (m), 1224 (m), 1172 (w), 1135 (w), 1057 (w), 1019 (w), 940 (w), 910 (m), 835 (w), 811 (w), 773 (w), 731 (s), 649 (w), 606 (w), 562 (w). GC-MS (EI, 70 eV): *m/z* (%) = 191 ($[M^+]$, 76), 160 (68), 159 (100), 131 (55), 130 (48), 103 (21), 77 (21), 76 (15), 63 (4), 51 (11). HRMS (EI): Calcd. for $C_{10}H_9O_3N$ ($[M]^+$): 191.05769; found: 191.057322

Ethyl 3-cyano-6-hydroxy-2-methylbenzoate (13b)

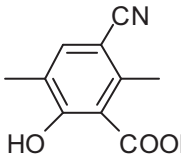


Chemical Formula: $C_{11}H_{11}NO_3$
Exact Mass: 205,074

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4b** (0.446 g, 1.65 mmol), **13b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.101 g, 33 %). mp. 86 - 87 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39(t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 2.72 (s, 3 H, CH_3), 4.42 (q, ^3J=7.3Hz,

2 H, OCH_2CH_3), 6.84 (d, ^3J = 8.8 Hz, 1 H, CH), 7.53 (d, ^3J = 8.9 Hz, 1 H, CH), 11.78 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 20.8 (OCH_2CH_3), 61.7 (OCH_2), 104.8 (*C*CN), 112.6 (*C*COOCH$_2$CH$_3$), 116.0 (CH), 117.4 (CN), 136.7 (CH), 145.5 (*C*CH$_3$), 164.8 (*C*OH), 169.62 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3072 (w), 2991 (w), 2923 (w), 2851 (w), 2777 (w), 2692 (w), 2589 (w), 2224 (w), 1660 (s), 1588 (m), 1570 (w), 1476 (m), 1450 (w), 1398 (m), 1375 (s), 1348(m), 1318(m), 1302 (m), 1231 (s), 1182 (w), 1146 (m), 1108 (w), 1057 (w), 1021 (m), 996 (w), 909 (w), 856 (m), 831 (m), 723 (w), 632 (w), 609 (w), 558 (w). GC-MS (EI, 70eV): *m/z* (%) = 205 (M$^+$, 26), 159 (100), 130 (22), 103 (8), 77 (12), 51 (6). HRMS (EI) Calcd for $C_{11}H_{11}O_3N$ ([M]$^+$): 205.07334; found: 205.073572.

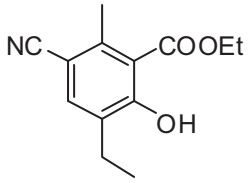
Methyl 3-cyano-6-hydroxy-2,5-dimethylbenzoate (13c)



Chemical Formula: $C_{11}H_{11}NO_3$
Exact Mass: 205.074

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4e** (0.457 g, 1.65 mmol), **13c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.107 g, 35 %). mp. 134 - 136 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 2.66 (s, 3 H, CH_3), 3.93 (s, 3 H, OCH_3), 7.40 (s, 1 H, CH_{Ar}), 11.99 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.6, 21.6 (CH_3), 52.6 (OCH_3), 104.9 (*C*CN), 112.7 (*C*COOCH$_3$), 118.7 (CN), 126.5 (C_{Ar}), 138.2 (CH_{Ar}), 143.7 (C_{Ar}), 164.5 (*C*OH), 171.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2990 (w), 2956 (w), 2926 (w), 2851 (w), 2217 (m), 1667 (s), 1605 (m), 1592 (m), 1580 (m), 1444 (s), 1413 (m), 1377 (m), 1334 (s), 1264 (s), 1199 (s), 1166 (s), 1077 (m), 1019 (m), 979 (m), 910 (m), 889 (m), 803 (s), 770 (m), 688 (m), 659 (m). GC-MS (EI, 70 eV): *m/z* (%) = 205 ([M]$^+$, 37), 174 (25), 173 (100), 145 (90), 144 (20), 116 (19), 91 (11), 90 (14), 89 (19). HRMS (EI): Calcd. for $C_{11}H_{11}O_3N$ ([M]$^+$): 205.07334; found: 205.073468.

Ethyl 3-cyano-5-ethyl-6-hydroxy-2-methylbenzoate (13d)

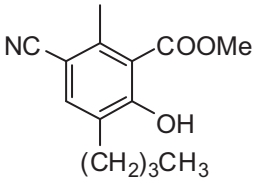


Chemical Formula: $C_{13}H_{15}NO_3$
Exact Mass: 233,105

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4g** (0.498 g, 1.65 mmol), **13d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.119 g, 34 %). mp. 72 - 73 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14 (t, ^3J = 8.1 Hz, 3 H, CH_3), 1.38 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 3.43 (q, ^3J = 8.1 Hz, 2 H, CH_2), 2.68 (s, 3 H, CH_3), 4.41 (q, ^3J = 6.3

Hz, 2 H, O$CH_2$$CH_3$), 7.40 (s, 1 H, CH_{Ar}), 12.10 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.1, 13.2, 20.5 (CH_3), 21.6 (CH_2), 61.6 (OCH_2), 104.0 (*C*CN), 111.9 (*C*COO$CH_2$$CH_3$), 118.0 (CN), 130.9 ($C_{Ar}$), 135.4 ($CH_{Ar}$), 142.7 ($C_{Ar}$), 163.1 (*C*OH), 170.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2975 (w), 2933 (w), 2221 (w), 1658 (m), 1610 (w), 1577 (w), 1559 (w), 1541 (w), 1507 (w), 1437 (m), 1398 (w), 1376 (m), 1352 (w), 1325 (m), 1293 (w), 1265 (w), 1244 (m), 1188 (s), 1086 (w), 1019 (w), 909 (m), 874 (w), 811 (w), 733 (s), 686 (w), 667 (w), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 233 ([M^+], 28), 187 (60), 172 (9), 159 (100), 144 (7), 130 (7), 116 (8), 103 (7), 89 (9), 77 (8), 51 (3), 29 (5). HRMS (EI): Calcd. for $C_{13}H_{15}O_3N$ ([M]$^+$): 233.10464; found: 233.104263

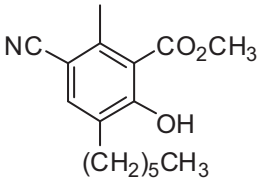
Methyl 3-butyl-5-cyano-2-hydroxy-6-methylbenzoate (13e)



Chemical Formula: $C_{14}H_{17}NO_3$
Exact Mass: 247,121

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **13e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish oil (0.130 g, 35 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_3$*CH_3*), 1.24 - 1.33 (m, 2 H, CH_2), 1.45 - 1.52 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.3 Hz, 2 H, CH_2), 2.65 (s, 3 H, CH_3), 3.93 (s, 3 H, OCH_3), 7.38 (s, 1 H, CH_{Ar}), 11.98 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1, 20.6 (CH_3), 21.6, 28.3, 30.2 (CH_2), 52.0 (OCH_3), 104.1 (*C*CN), 112.0 (*C*COOCH_3), 118.0 (CN), 129.9 (C_{Ar}), 136.3 (CH_{Ar}), 143.0 (C_{Ar}), 163.2 (*C*OH), 170.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2957 (m), 2931 (m), 2862 (w), 2222 (m), 1717 (w), 1666 (s), 1609 (w), 1577 (w), 1559 (w), 1541 (w), 1507 (w), 1456 (m), 1438 (m), 1384 (w), 1354 (m), 1338 (m), 1299 (m), 1262 (w), 1234 (w), 1203 (m), 1171 (m), 1105 (w), 1077 (w), 988 (w), 911 (w), 812 (m), 772 (w), 733 (m), 695 (w), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 247 ([M^+], 32), 215 (29), 198 (16), 186 (19), 173 (100), 159 (3), 145 (36), 130 (5), 116 (11), 103 (6), 89 (19), 77 (6), 63 (4), 51 (3), 39 (5), 29 (3). HRMS (EI): Calcd. for $C_{14}H_{17}O_3N$ ([M]$^+$) : 247.12029; found: 247.119876

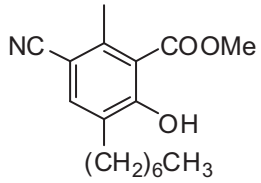
Methyl 3-cyano-5-hexyl-6-hydroxy-2-methylbenzoate (13f)



Chemical Formula: $C_{16}H_{21}NO_3$
Exact Mass: 275,152

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4k** (0.568 g, 1.65 mmol), **13f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.173 g, 42 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.67 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_5CH_3$), 1.06 - 1.13 (m, 6 H, 3×CH_2), 1.31 - 1.42 (m, 2 H, CH_2), 2.39 (t, ^3J = 7.5 Hz, 2 H, CH_2), 2.52 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 7.25 (s, 1 H, CH_{Ar}), 11.83 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 21.6 (CH_3), 22.6, 28.7, 29.0, 29.4, 31.6 (CH_2), 52.8 (OCH_3), 104.9 (*C*CN), 112.7 (*C*$COOCH_3$), 118.7 (CN), 130.7 (C_{Ar}), 137.2 (CH_{Ar}), 143.5, (C_{Ar}), 164.0 (*C*OH), 171.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2927 (m), 2856 (w), 2221 (w), 1665 (m), 1608 (w), 1579 (w), 1438 (m), 1334 (m), 1245 (w), 1201 (m), 1170 (m), 1077 (w), 989 (w), 908 (m), 812 (w), 731 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 275 ($[M]^+$, 37), 244 (12), 243 (29), 226 (13), 215 (15), 214 (33), 200 (13), 187 (13), 186 (22), 174 (20), 173 (100), 145 (36), 144 (15), 116 (11), 89 (19). HRMS (EI): Calcd. for $C_{16}H_{21}NO_3$ ($[M]^+$): 275.15160; found: 275.151528.

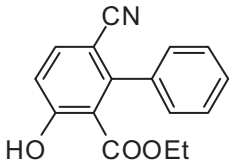
Methyl 3-cyano-5-heptyl-6-hydroxy-2-methylbenzoate (13g)



Chemical Formula: $C_{17}H_{23}NO_3$
Exact Mass: 289,168

Starting with **12a** [2-(ethoxymethylene)-3-oxobutanenitrile] (0.209 g, 1.5 mmol) and **4m** (0.420 g, 1.65 mmol), **13g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.148 g, 34 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 6.7 Hz, 3 H, $(CH_2)_6CH_3$), 1.21 - 1.25 (m, 8 H, 4×CH_2), 1.48 - 1.55 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.4 Hz, 2 H, CH_2), 2.67 (s, 3 H, CH_3), 3.94 (s, 3 H, OCH_3), 7.39 (s, 1 H, CH_{Ar}), 11.98 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 21.6 (CH_3), 22.7, 28.9, 29.1, 29.3, 29.5, 31.8 (CH_2), 52.9 (OCH_3), 104.9 (*C*CN), 112.8 (*C*$COOCH_3$), 118.8 (CN), 130.7 (C_{Ar}), 137.1 (CH_{Ar}), 143.6 (C_{Ar}), 164.0 (*C*OH), 171.7 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2926 (m), 2855 (m), 2222 (w), 1665 (m), 1609 (w), 1579 (w), 1438 (m), 1384 (w), 1354 (m), 1335 (m), 1262 (w), 1238 (w), 1202 (m), 1171 (m), 1122 (w), 1077 (w), 988 (w), 908 (m), 812 (w), 772 (w), 732 (m), 696 (w), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 289 ($[M^+]$, 38), 257 (29), 240 (12), 214 (33), 200 (11), 186 (21), 173 (100), 159 (9), 145 (34), 130 (5), 116 (12), 103 (6), 89 (19), 77 (6), 55 (4), 41 (11). HRMS (EI): Calcd. for $C_{17}H_{23}O_3N$ ($[M]^+$): 289.17507; found: 289.17512

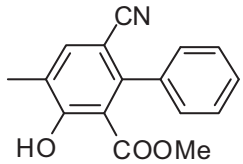
Ethyl 6-cyano-3-hydroxybiphenyl-2-carboxylate (13h)



Chemical Formula: $C_{16}H_{13}NO_3$
Exact Mass: 267.090

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4b** (0.446 g, 1.65 mmol), **13h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.180 g, 45 %). mp. 122 - 124 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.64 (t, ^3J = 8.3 Hz, 3 H, OCH_2CH_3), 3.89 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 7.01 (d, ^3J = 8.2 Hz, 1 H, CH_{Ar}), 7.14 - 7.19 (m, 2 H, CH_{Ph}), 7.34 - 7.37 (m, 3 H, CH_{Ph}), 7.64 (d, ^3J = 8.6 Hz, 1 H, CH_{Ar}), 11.47 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8 (CH_3), 61.9 (OCH_2), 105.7 (*C*CN), 113.5 (*C*$COOCH_2CH_3$), 117.7 (CN), 118.1 (CH_{Ar}), 128.0 (3×CH_{Ph}), 128.3 (2×CH_{Ph}), 137.4 (CH_{Ar}), 138.9, 149.6 (C_{Ar}), 164.7 (*C*OH), 169.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2984 (w), 2939 (w), 2227 (w), 1730 (w), 1668 (m), 1584 (m), 1548 (w), 1462 (m), 1444 (m), 1400 (w), 1376 (m), 1324 (m), 1222 (s), 1140 (w), 1097 (w), 1075 (w), 1013 (w), 910 (w), 836 (w), 759 (m), 731 (m), 716 (m), 699 (m), 645 (w), 598 (w), 550 (w). GC-MS (EI, 70 eV): *m/z* (%) = 267 ([M^+], 34), 221 (100), 193 (41), 164 (21), 139 (11), 114 (3), 88 (2), 63 (3). HRMS (EI): Calcd. for $C_{16}H_{13}O_3N$ ([$M]^+$): 267.08899; found: 267.088732

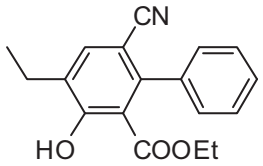
Methyl 6-cyano-3-hydroxy-4-methylbiphenyl-2-carboxylate (13i)



Chemical Formula: $C_{16}H_{13}NO_3$
Exact Mass: 267.090

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4e** (0.457 g, 1.65 mmol), **13i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish solid (0.172 g, 43 %). mp. 105 - 107 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, CH_3), 3.37 (s, 3 H, OCH_3), 7.12 - 7.17 (m, 2 H, CH_{Ph}), 7.30 - 7.35 (m, 3 H, CH_{Ph}), 7.51 (s, 1 H, CH_{Ar}), 11.53 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.7 (CH_3), 52.2 (OCH_3), 104.9 (*C*CN), 112.6 (*C*$COOCH_3$), 118.2 (CN), 127.6 (C_{Ar}), 127.9 (2×CH_{Ph}), 128.1 (3×CH_{Ph}), 137.9 (CH_{Ar}), 138.9, 147.2 (C_{Ar}), 163.1 (*C*OH), 170.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 3027 (w), 2954 (w), 2924 (w), 2217 (w), 1722 (m), 1673 (m), 1594 (w), 1566 (w), 1461 (m), 1434 (s), 1377 (m), 1322 (s), 1259 (m), 1241 (m), 1162 (m), 1076 (m), 1022 (m), 983 (m), 848 (m), 809 (s), 757 (s), 702 (s), 677 (m), 552 (m). GC-MS (EI, 70 eV): *m/z* (%) = 267 ([$M]^+$, 32), 236 (19), 235 (100), 234 (15), 207 (12), 206 (16), 179 (10), 178 (14), 151 (10), 76 (7). HRMS (EI): Calcd. for $C_{16}H_{11}O_3N$ ([$M]^+$): 267.08899; found: 267.088902.

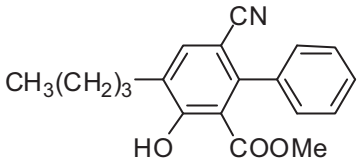
Ethyl 6-cyano-4-ethyl-3-hydroxybiphenyl-2-carboxylate (13j)



Chemical Formula: $C_{18}H_{17}NO_3$
Exact Mass: 295.121

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4g** (0.498 g, 1.65 mmol), **13j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow crystalline solid (0.186 g, 42 %). mp. 47 - 48 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.58 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.15 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.61 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 3.83 (q, ^3J = 6.9 Hz, 2 H, OCH_2CH_3), 7.08 - 7.11 (m, 2 H, CH_{Ph}), 7.25 - 7.29 (m, 3 H, CH_{Ph}), 7.46 (s, 1 H, CH_{Ar}), 11.65 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 13.1 (CH_3), 22.7 (CH_2), 61.6 (OCH_2), 105.1 (*C*CN), 112.8 (*C*$COOCH_2CH_3$), 118.2 (CN), 127.9 (2×CH_{Ph}), 128.0 (CH_{Ph}), 128.2 (2×CH_{Ph}), 133.4 (C_{Ar}), 136.1 (CH_{Ar}), 139.2, 146.9 (C_{Ar}), 162.9 (*C*OH), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2972 (w), 2937 (w), 2877 (w), 2252 (w), 2226 (w), 1663 (s), 1601 (w), 1567 (w), 1445 (m), 1424 (m), 1401 (m), 1376 (m), 1329 (m), 1306 (m), 1269 (w), 1242 (m), 1196 (s), 1147 (m), 1113 (w), 1096 (w), 1067 (w), 1021 (w), 909 (m), 841 (w), 819 (m), 762 (m), 732 (s), 701 (m), 649 (w), 549 (w). GC-MS (EI, 70 eV): *m/z* (%) = 295 ([M^+], 48), 249 (59), 231 (100), 220 (12), 203 (21), 190 (9), 177 (14), 165 (12), 151 (13), 139 (4), 102 (2), 77 (3), 51 (2). HRMS (EI): Calcd. for $C_{18}H_{17}O_3N$ ([$M]^+$): 295.12029; found: 295.120225

Methyl 4-butyl-6-cyano-3-hydroxybiphenyl-2-carboxylate (13k)

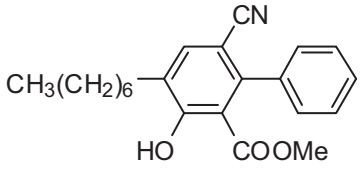


Chemical Formula: $C_{19}H_{19}NO_3$
Exact Mass: 309,136

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4i** (0.522 g, 1.65 mmol), **13k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish viscous oil (0.190 g, 41 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_3CH_3$), 1.26 - 1.35 (m, 2 H, CH_2), 1.46 - 1.55 (m, 2 H, CH_2), 2.59 (t, ^3J = 7.9 Hz, 2 H, CH_2), 3.33 (s, 3 H, OCH_3), 7.08 - 7.13 (m, 2 H, CH_{Ph}), 7.27 - 7.31 (m, 3 H, CH_{Ph}), 8.46 (s, 1 H, CH_{Ar}), 11.45 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 22.5, 29.2, 31.2 (CH_2), 52.2 (OCH_3), 105.2 (*C*CN), 112.7 (*C*$COOCH_3$), 118.1 (CN), 127.9 (2×CH_{Ph}), 128.1 (3×CH_{Ph}), 132.1 (C_{Ar}), 137.0 (CH_{Ar}), 139.1, 146.6 (C_{Ar}), 163.0 (*C*OH), 170.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2920 (w), 2223 (w), 1742 (w), 1663 (m), 1593 (w), 1565 (w), 1494 (w), 1435 (s), 1333 (m), 1314 (m), 1261 (m), 1205 (s), 1170 (m), 1074 (w), 1029 (w), 985 (w), 856 (w), 815 (m), 759 (s), 699 (s), 658 (m), 549 (m). GC-MS (EI, 70 eV): *m/z* (%) = 309 ([$M]^+$, 40), 277 (27), 259

(18), 244 (10), 236 (17), 235 (100), 234 (35), 221 (8), 206 (10), 178 (11), 177 (15), 151 (18). HRMS (EI): Calcd. for $C_{19}H_{19}O_3N$ ($[M]^+$): 309.13594; found: 309.135859.

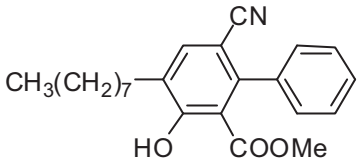
Methyl 6-cyano-4-heptyl-3-hydroxybiphenyl-2-carboxylate (13l)



Chemical Formula: $C_{22}H_{25}NO_3$
Exact Mass: 351,183

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4m** (0.591 g, 1.65 mmol), **13l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish oil (0.221 g, 42 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 7.6 Hz, 3 H, $(CH_2)_6CH_3$), 1.26 - 1.35 (m, 8 H, 4×CH_2), 1.51 – 1.61 (m, 2 H, CH_2), 2.62 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.37 (s, 3 H, OCH_3), 7.12 - 7.17 (m, 2 H, CH_{Ph}), 7.30 - 7.36 (m, 3 H, CH_{Ph}), 7.49 (s, 1 H, CH_{Ar}), 11.49 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 22.6, 28.9, 29.1, 29.4, 29.5, 31.8 (CH_2), 52.2 (OCH_3), 104.9 (*C*CN), 112.7 (*C*$COOCH_3$), 118.1 (CN), 127.9 (2×CH_{Ph}), 128.1 (3×CH_{Ph}), 132.1 (C_{Ar}), 137.1 (CH_{Ar}), 139.1, 147.0 (C_{Ar}), 162.9 (*C*OH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2924 (m), 2854 (w), 2223 (w), 1745 (w), 1664 (m), 1599 (w), 1566 (w), 1439 (m), 1335 (m), 1234 (m), 1204 (s), 1146 (m), 1074 (w), 990 (w), 897 (w), 815 (m), 760 (s), 724 (w), 699 (s), 549 (w). GC-MS (EI, 70 eV): *m/z* (%) = 351 ($[M]^+$, 39), 320 (9), 319 (32), 236 (23), 235 (100), 234 (45), 231 (9), 219 (13), 206 (10), 178 (10), 177 (13), 151 (15), 41 (7). HRMS (EI): Calcd. for $C_{22}H_{25}O_3N$ ($[M]^+$): 351.18290; found: 351.183058.

Methyl 6-cyano-3-hydroxy-4-octylbiphenyl-2-carboxylate (13m)

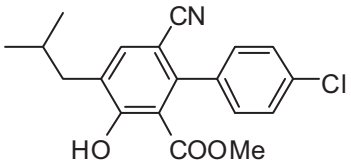


Chemical Formula: $C_{23}H_{27}NO_3$
Exact Mass: 365,199

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4o** (0.614 g, 1.65 mmol), **13m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.219 g, 40 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_7CH_3$), 1.06 - 1.08 (m, 10 H, 5×CH_2), 1.52 - 1.62 (m, 2 H, CH_2), 2.50 (t, ^3J = 7.3 Hz, 2 H, CH_2), 3.46 (s, 3 H, OCH_3), 7.13 - 7.18 (m, 2 H, CH_{Ph}), 7.31 - 7.37 (m, 3 H, CH_{Ph}), 7.50 (s, 1 H, CH_{Ar}), 11.50 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 22.6, 28.8, 29.2, 29.3, 29.4, 29.5, 31.8 (CH_2), 52.2 (OCH_3), 105.0 (*C*CN), 112.7 (*C*$COOCH_3$), 118.1 (CN), 127.9 (2×CH_{Ph}), 128.1 (3×CH_{Ph}), 132.1 (C_{Ar}), 137.0 (CH_{Ar}), 139.0, 147.0 (C_{Ar}), 162.9 (*C*OH), 170.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2923 (m), 2853 (m), 2224 (w), 1749 (w), 1665 (m), 1600 (w), 1567 (w), 1436 (m), 1335 (m), 1234 (m), 1205 (s), 1146 (m), 1074 (w), 999 (w), 907 (w), 816 (m), 760 (s), 727 (w), 700 (s), 549 (w). GC-MS (EI, 70 eV): *m/z* (%) = 365 ($[M]^+$, 21), 333 (29), 236 (26), 235

(100), 234 (47), 231 (13), 222 (11), 221 (10), 219 (24), 218 (12), 207 (15), 206 (18), 190 (11), 179 (11), 178 (17), 177 (18), 152 (12), 151 (25), 129 (20), 116 (39), 101 (12), 98 (10), 97 (11), 85 (11), 81 (9), 71 (20), 69 (32), 57 (42), 55 (34). HRMS (EI): Calcd. for $C_{23}H_{27}O_3N$ ($[M]^+$): 365.19885; found: 365.198427.

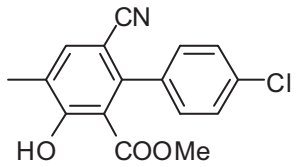
Methyl 4'-chloro-6-cyano-3-hydroxy-4-isobutylbiphenyl-2-carboxylate (13n)



Chemical Formula: $C_{19}H_{18}ClNO_3$
Exact Mass: 343.098

Starting with **12b** [2-benzoyl-3-ethoxyacrylonitrile] (0.302 g, 1.5 mmol) and **4x** (0.612 g, 1.65 mmol), **13n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.227 g, 44 %). mp. 149 - 151 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.40 (s, 3 H, OCH_3), 7.17 - 7.23 (m, 2 H, CH_{Ph}), 7.28 - 7.47 (m, 7 H, $CH_{ClPh,Ph}$), 7.67 (s, 1 H, CH_{Ar}), 11.73 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 53.6 (OCH_3), 106.9 (*C*CN), 114.9 (*C*$COOCH_3$), 118.6 (CN), 128.9 (2×CH_{Ph}), 129.0 (2×CH_{Ph}), 129.3 (CH_{Ph}), 129.6 (2×CH_{ClPh}), 130.7, (C_{Ar}), 131.5 (2×CH_{ClPh}), 134.4, 135.3 (C_{Ar}), 138.7 (CH_{Ar}), 139.4, 149.5 (C_{Ar}), 162.7 (*C*OH), 171.7 (CO). IR (KBr, cm^{-1}) $\tilde{\nu}$ = 3086 (w), 3061 (w), 3027 (w), 2954 (w), 2929 (w), 2852 (w), 2252 (w), 2226 (w), 1737 (w), 1667 (m), 1593 (w), 1553 (w), 1493 (w), 1437 (m), 1393 (m), 1330 (m), 1249 (w), 1208 (m), 1182 (m), 1094 (m), 1081 (w), 1031 (w), 1015 (w), 987 (w), 909 (m), 834 (m), 764 (m), 732 (s), 704 (m), 661 (w), 650 (w), 544 (w). MS (ESI+): calcd. for $C_{21}H_{15}ClNO_3$, $(M+H)^+$: 364.0735; found: 364.07353; Calcd. for $C_{21}H_{14}ClNNaO_3$ (M + Na)+: 386.05544; found: 386.05531.

Methyl 4'-chloro-6-cyano-3-hydroxy-4-methylbiphenyl-2-carboxylate (13o)

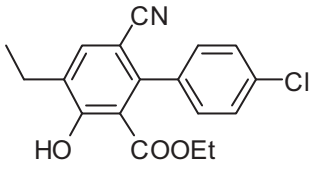


Chemical Formula: $C_{16}H_{12}ClNO_3$
Exact Mass: 301.051

Starting with **12c** [2-(4-chlorobenzoyl)-3-ethoxyacrylonitrile] (0.353 g, 1.5 mmol) and **4e** (0.457 g, 1.65 mmol), **13o** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.275 g, 61 %). mp. 167 - 169 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, CH_3), 3.42 (s, 3 H, OCH_3), 7.06 - 7.10 (m, 2 H, CH_{ClPh}), 7.31 - 7.35 (m, 2 H, CH_{ClPh}), 7.51 (s, 1 H, CH_{Ar}), 11.61 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.7 (CH_3), 51.4 (OCH_3), 103.9 (*C*CN), 111.3 (*C*$COOCH_3$), 116.8 (CN), 127.2 (C_{Ar}), 127.9 (2×CH_{ClPh}), 128.5 (2×CH_{ClPh}), 133.2, 136.3 (C_{Ar}), 136.6 (CH_{Ar}), 144.7 (C_{Ar}), 162.4 (*C*OH), 169.4 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2958 (w), 2848 (w), 2227 (w), 1932 (w), 1837 (w), 1667 (m), 1597 (m), 1557 (w),

1500 (w), 1435 (m), 1353 (m), 1332 (s), 1268 (m), 1203 (m), 1169 (m), 1147 (m), 1042 (w), 1017 (m), 981 (m), 902 (w), 868 (w), 809 (s), 771 (m), 659 (w), 613 (m), 548 (m). GC-MS (EI, 70 eV): *m/z* (%) = 303 ([M^+], ^{37}Cl, 11), 301 ([M^+], ^{35}Cl, 31), 271 (21), 270 (13), 269 (61), 235 (17), 234 (100), 178 (9), 177 (14), 151 (11). HRMS (EI): Calcd. for $C_{16}H_{12}O_3{}^{35}ClN$ ([$M]^+$): 301.5002; found: 301.050144.

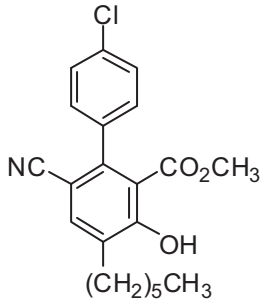
Ethyl 4'-chloro-6-cyano-4-ethyl-3-hydroxybiphenyl-2-carboxylate (13p)



Chemical Formula: $C_{18}H_{16}ClNO_3$
Exact Mass: 329.082

Starting with **12c** [2-(4-chlorobenzoyl)-3-ethoxyacrylonitrile] (0.353 g, 1.5 mmol) and **4g** (0.499 g, 1.65 mmol), **13p** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellowish solid (0.306 g, 62 %). mp. 165 - 167 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 6.7 Hz, 3 H, CH_2CH_3), 1.19 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.65 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.92 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 7.07 - 7.11 (m, 2 H, CH_{ClPh}), 7.31 - 7.34 (m, 2 H, CH_{ClPh}), 7.50 (s, 1 H, CH_{Ar}), 11.77 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9, 13.1 (CH_3), 22.7, 62.0 (CH_2), 104.9 (*C*CN), 112.5 (*C*$COOCH_2H_3$), 117.9 (CN), 128.2 (2×CH_{ClPh}), 129.6 (2×CH_{ClPh}), 133.8, 134.2 (C_{Ar}), 136.1 (CH_{Ar}), 137.7, 145.7 (C_{Ar}), 163.0 (*C*OH), 170.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2978 (w), 2876 (w), 2227 (w), 1910 (w), 1654 (m), 1568 (w), 1498 (m), 1444 (m), 1420 (m), 1374 (m), 1326 (s), 1274 (w), 1223 (m), 1194 (s), 1142 (m), 1111 (w), 1006 (m), 948 (w), 906 (w), 808 (s), 775 (m), 665 (w), 605 (m), 547 (m). GC-MS (EI, 70 eV): *m/z* (%) = 331 ([M^+], ^{37}Cl, 9), 329 ([M^+], ^{35}Cl, 26), 285 (12), 283 (35), 249 (18), 248 (100), 177 (11). HRMS (EI): Calcd. for $C_{18}H_{16}O_3{}^{35}ClN$ ([$M]^+$): 329.08183; found: 329.081140.

Methyl 4'-chloro-6-cyano-4-hexyl-3-hydroxybiphenyl-2-carboxylate (13q)

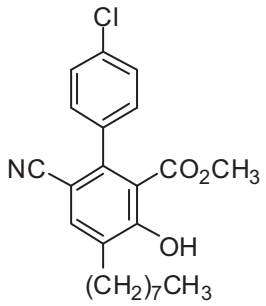


Chemical Formula: $C_{21}H_{22}ClNO_3$
Exact Mass: 371,129

Starting with **12c** [2-(4-chlorobenzoyl)-3-ethoxyacrylonitrile] (0.353 g, 1.5 mmol) and **4k** (0.568 g, 1.65 mmol), **13q** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.357 g, 64 %). mp. 45 - 46 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_5CH_3$), 1.18 - 1.32 (m, 6 H, 3×CH_2), 1.50 - 1.57 (m, 2

H, CH_2), 2.62 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.42 (s, 3 H, OCH_3), 7.07 - 7.10 (m, 2 H, 2×CH_{Ph}), 7.31 - 7.35 (m, 2 H, 2×CH_{Ph}), 7.49 (s, 1 H, CH_{Ar}), 11.59 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.6, 27.8, 28.1, 28.6, 30.7 (CH_2), 51.5 (OCH_3), 103.9 (*C*CN), 111.5 (*C*COOCH$_3$), 116.9 (CN), 127.3 (2×CH_{Ph}), 128.6 (2×CH_{Ph}), 131.7, 133.3 (C_{Ar}), 136.0 (CH_{Ar}), 136.4, 144.5 (C_{Ar}), 162.0 (*C*OH), 169.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2929 (w), 2857 (w), 2225 (w), 1668 (m), 1601 (w), 1575 (w), 1496 (w), 1439 (m), 1397 (w), 1345 (m), 1207 (m), 1171 (w), 1148 (w), 1091 (w), 908 (m), 825 (w), 732 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 373 ([M$^+$], ^{37}Cl, 11), 371 ([M$^+$], ^{35}Cl, 23), 268 (18), 235 (18), 234 (100), 177 (16). HRMS (EI): Calcd. for $C_{21}H_{22}O_3N^{35}Cl$ ([M]$^+$): 371.12827; found: 371.127801.

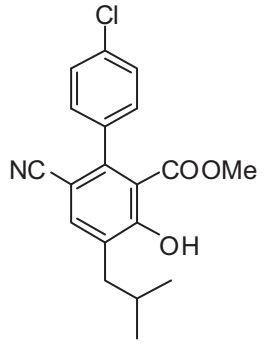
Methyl 4'-chloro-6-cyano-3-hydroxy-4-octylbiphenyl-2-carboxylate (13r)



Chemical Formula: $C_{23}H_{26}ClNO_3$
Exact Mass: 399,160

Starting with **12c** [2-(4-chlorobenzoyl)-3-ethoxyacrylonitrile] (0.353 g, 1.5 mmol) and **4o** (0.614 g, 1.65 mmol), **13r** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish solid (0.354 g, 59 %). mp. 68 - 71 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_7CH_3$), 1.17 - 1.34 (m, 10 H, 5×CH_2), 1.49 - 1.58 (m, 2 H, CH_2), 2.61 (t, ^3J = 7.4 Hz, 2 H, CH_2), 3.42 (s, 3 H, OCH_3), 7.06 - 7.12 (m, 2 H, 2×CH_{Ph}), 7.31 - 7.35 (m, 2 H, 2×CH_{Ph}), 7.51 (s, 1 H, CH_{Ar}), 11.59 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.6, 28.8, 29.2, 29.3, 29.4, 29.6, 31.9 (CH_2), 52.5 (OCH_3), 104.9 (*C*CN), 112.5 (*C*COOCH$_3$), 117.9 (CN), 128.3 (2×CH_{Ph}), 129.5 (2×CH_{Ph}), 132.7, 134.1 (C_{Ar}), 137.0 (CH_{Ar}), 137.4, 145.5 (C_{Ar}), 163.2 (*C*OH), 170.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2925 (m), 2854 (w), 2224 (w), 1666 (m), 1600 (w), 1576 (w), 1496 (w), 1438 (m), 1397 (m), 1342 (m), 1341 (m), 1259 (w), 1206 (m), 1172 (m), 1091 (m), 1016 (w), 990 (w), 906 (m), 816 (w), 730 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 401 ([M$^+$], ^{37}Cl, 11), 399 ([M$^+$], ^{35}Cl, 22), 332 (38), 270 (10), 268 (21), 235 (18), 234 (100), 177 (15). HRMS (EI): Calcd. for $C_{23}H_{26}O_3N^{35}Cl$ ([M]$^+$): 399.15957; found: 399.159574.

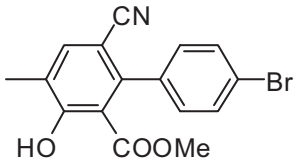
Methyl 4'-chloro-6-cyano-3-hydroxy-4-isobutylbiphenyl-2-carboxylate (13s)



Chemical Formula: $C_{19}H_{18}ClNO_3$
Exact Mass: 343,098

Starting with **12c** [2-(4-chlorobenzoyl)-3-ethoxyacrylonitrile] (0.353 g, 1.5 mmol) and **4u** (0.522 g, 1.65 mmol), **13s** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a light yellow solid (0.319 g, 62 %). mp. 74 - 76 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.89 (d, ^3J = 6.7 Hz, 6 H, 2×CH_3), 1.90 - 1.99 (m, 1 H, *C*H(CH_3)$_2$), 2.51 (d, ^3J = 7.2 Hz, 2 H, CH_2), 3.43 (s, 3 H, OCH_3), 7.08 - 7.13 (m, 2 H, CH_{ClPh}), 7.32 - 7.36 (m, 2 H, CH_{ClPh}), 7.47 (s, 1 H, CH_{Ar}), 11.57 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4 (2×CH_3), 27.0 (*C*H(CH_3)$_2$), 37.8 (CH_2), 51.5 (OCH_3), 103.8 (*C*CN), 111.6 (*C*COOCH$_3$), 116.9 (CN), 127.3 (2×CH_{ClPh}), 128.6 (2×CH_{ClPh}), 130.5, 133.3, 136.4 (C_{Ar}), 137.0 (CH_{Ar}), 144.6 (C_{Ar}), 162.2 (*C*OH), 169.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2928 (m), 2868 (w), 2224 (w), 1741 (w), 1665 (s), 1599 (m), 1575 (w), 1496 (m), 1436 (s), 1397 (m), 1385 (w), 1345 (m), 1325 (m), 1314 (m), 1263 (m), 1204 (s), 1169 (m), 1148 (m), 1089 (s), 1016 (m), 1000 (m), 981 (m), 945 (w), 904 (w), 888 (w), 861 (w), 820 (m), 771 (m), 738 (m), 660 (m), 634 (m), 545 (m). GC-MS (EI, 70 eV): *m/z* (%) = 345 ([M$^+$], ^{37}Cl, 10), 343 ([M$^+$], ^{35}Cl, 29), 277 (20), 276 (100), 270 (16), 268 (44), 234 (39), 177 (24), 151 (5), 130 (2), 88 (2), 43 (5). HRMS (EI): Calcd. for $C_{19}H_{18}O_3N^{35}Cl$ ([M]$^+$): 343.09697; found: 343.096981.

Methyl 4'-bromo-6-cyano-3-hydroxy-4-methylbiphenyl-2-carboxylate (13t)

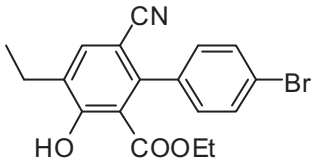


Chemical Formula: $C_{16}H_{12}BrNO_3$
Exact Mass: 345.000

Starting with **12d** [2-(4-bromobenzoyl)-3-ethoxyacrylonitrile] (0.420 g, 1.5 mmol) and **4e** (0.457 g, 1.65 mmol), **13t** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white crystalline solid (0.301 g, 58 %). mp. 199 - 200 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, CH_3), 3.42 (s, 3 H, OCH_3), 7.00 - 7.04 (m, 2 H, CH_{BrPh}), 7.47 (s, 1H, CH_{Ar}), 7.50 - 7.52 (m, 2 H, CH_{BrPh}), 11.61 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.8 (CH_3), 52.6 (OCH_3), 104.9 (*C*CN), 112.2 (*C*COOCH$_3$), 117.8 (CN), 122.5, 128.3 (C_{Ar}), 129.9 (2×CH_{BrPh}), 131.5 (2×CH_{BrPh}), 137.7 (CH_{Ar}), 137.8, 145.4 (C_{Ar}), 163.2 (*C*OH), 170.4 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3082 (w), 2957 (w), 2852 (w), 2227 (m), 1933 (w), 1667 (m), 1591 (w), 1555 (w), 1496 (w), 1435 (m), 1353 (m), 1331 (m), 1267 (m), 1201 (m), 1167 (m), 1146 (m), 1042 (w),

1012 (m), 987 (m), 902 (m), 861 (w), 807 (s), 770 (m), 659 (w), 600 (m), 548 (m). GC-MS (EI, 70 eV): *m/z* (%) = 347 ([M^+], ^{81}Br, 29), 345 ([M^+], ^{79}Br, 29), 316 (10), 315 (60), 314 (12), 313 (60), 235 (20), 234 (100), 206 (12), 178 (10), 177 (19), 151 (17). HRMS (EI): Calcd. for $C_{16}H_{12}O_3{}^{79}BrN$ ([$M]^+$): 344.99951; found: 344.999038.

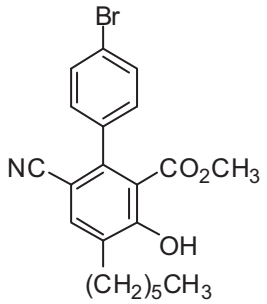
Ethyl 4'-bromo-6-cyano-4-ethyl-3-hydroxybiphenyl-2-carboxylate (13u)



Chemical Formula: $C_{18}H_{16}BrNO_3$
Exact Mass: 373.031

Starting with **12d** [2-(4-bromobenzoyl)-3-ethoxyacrylonitrile] (0.420 g, 1.5 mmol) and **4g** (0.499 g, 1.65 mmol), **13u** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.336 g, 60 %). mp. 197 - 199 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.19 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 2.65 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.93 (q, ^3J = 7.5 Hz, 2 H, OCH_2CH_3), 7.01 - 7.05 (m, 2 H, CH_{BrPh}), 7.47 (s, 1 H, CH_{Ar}), 7.50 - 7.52 (m, 2 H, CH_{BrPh}), 11.78 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9, 13.0 (CH_3), 22.7, 62.0 (CH_2), 104.8 (*C*CN), 112.4 (*C*$COOCH_3$), 117.9 (CN), 122.3 (C_{Ar}), 129.5 (2×CH_{BrPh}), 131.2 (2×CH_{BrPh}), 133.8 (C_{Ar}), 136.0 (CH_{Ar}), 138.2, 145.5 (C_{Ar}), 163.2 (*C*OH), 170.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2970 (w), 2874 (w), 2224 (w), 1898 (w), 1659 (s), 1573 (w), 1492 (w), 1421 (m), 1393 (m), 1327 (s), 1268 (m), 1239 (m), 1190 (s), 1146 (m), 1100 (w), 1004 (m), 906 (w), 809 (s), 727 (m), 652 (w), 599 (m), 547 (m). GC-MS (EI, 70 eV): *m/z* (%) = 375 ([M^+], ^{81}Br, 20), 373 ([M^+], ^{79}Br, 21), 329 (32), 327 (32), 249 (19), 248 (100), 190 (10), 177 (12). HRMS (EI): Calcd. for $C_{18}H_{16}O_3{}^{79}BrN$ ([$M]^+$): 373.03081; found: 373.030467.

Methyl 4'-bromo-6-cyano-4-hexyl-3-hydroxybiphenyl-2-carboxylate (13v)

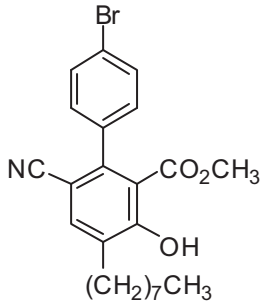


Chemical Formula: $C_{21}H_{22}BrNO_3$
Exact Mass: 415,078

Starting with **12d** [2-(4-bromobenzoyl)-3-ethoxyacrylonitrile] (0.420 g, 1.5 mmol) and **4k** (0.568 g, 1.65 mmol), **13v** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.343 g, 55 %) ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.73 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_7CH_3$), 1.07 - 1.20 (m, 6 H, 3×CH_2), 1.42 - 1.50 (m, 2 H, CH_2), 2.51 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.42 (s, 3 H, OCH_3), 6.90 - 6.95 (m, 2 H, 2×CH_{Ph}), 7.36 - 7.39 (m, 3 H, 3×CH_{Ar}), 11.49 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 23.8, 30.0, 30.3, 30.8, 32.9 (CH_2), 53.7 (OCH_3), 106.0 (*C*CN), 113.6 (*C*$COOCH_3$), 119.1 (CN), 123.6 (C_{Ar}) 131.1, 132.4 (4×CH_{Ph}), 133.9 (C_{Ar}), 138.2 (CH_{Ar}), 139.0, 146.6 (C_{Ar}), 164.2 (*C*OH), 171.7

(CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2927 (m), 2856 (w), 2224 (w), 1666 (m), 1601 (w), 1573 (w), 1493 (w), 1438 (m), 1392 (w), 1340 (m), 1262 (w), 1206 (m), 1171 (w), 1101 (w), 1071 (w), 1013 (w), 908 (m), 817 (w), 770 (w), 730 (s), 649 (w), 621 (w). GC-MS (EI, 70 eV): *m/z* (%) = 417 ([M^+], ^{81}Br, 16), 415 ([M^+], ^{79}Br, 17), 417 (17), 415 ([M]$^+$, 17), 304 (26), 235 (17), 234 (100), 205 (11), 177 (12). HRMS (EI): Calcd. for $C_{21}H_{22}O_3N^{79}Br$ ([M]$^+$): 415.07776; found: 415.077792.

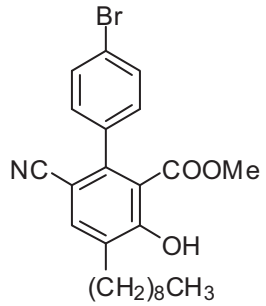
Methyl 4'-bromo-6-cyano-3-hydroxy-4-octylbiphenyl-2-carboxylate (13w)



Chemical Formula: $C_{23}H_{26}BrNO_3$
Exact Mass: 443,110

Starting with **12d** [2-(4-bromobenzoyl)-3-ethoxyacrylonitrile] (0.420 g, 1.5 mmol) and **4o** (0.614 g, 1.65 mmol), **13w** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.367 g, 55 %). mp. 73 - 75 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_7CH_3$), 1.16 - 1.32 (m, 10 H, 5×CH_2), 1.49 - 1.61 (m, 2 H, CH_2), 2.61 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.43 (s, 3 H, OCH_3), 7.01 - 7.05 (m, 2 H, 2×CH_{Ph}), 7.47 - 7.51 (m, 3 H, 3×CH_{Ar}), 11.59 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.6, 28.8, 29.2, 29.4, 29.5, 29.6, 31.8 (CH_2), 52.5 (OCH_3), 104.8 (*C*CN), 112.4 (*C*COOCH$_3$), 117.9 (CN), 122.3 (C_{Ar}) 129.8, 131.3 (4×H_{Ph}), 132.7 (C_{Ar}), 137.0 (CH_{Ar}), 137.8, 145.5 (C_{Ar}), 163.1 (*C*OH), 170.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2924 (m), 2854 (w), 2224 (w), 1667 (m), 1602 (w), 1574 (w), 1493 (w), 1438 (m), 1392 (w), 1339 (m), 1259 (w), 1205 (m), 1172 (m), 1103 (w), 1071 (w), 1012 (w), 906 (m), 817 (w), 770 (w), 728 (s), 649 (w), 548 (w). GC-MS (EI, 70 eV): *m/z* (%) = 445 ([M^+], ^{81}Br, 15), 443 ([M^+], ^{79}Br, 15), 332 (29), 235 (20), 234 (100). HRMS (EI): Calcd. for $C_{23}H_{26}O_3N^{79}Br$ ([M]$^+$): 443.10906; found: 443.109033.

Methyl 4'-bromo-6-cyano-3-hydroxy-4-nonylbiphenyl-2-carboxylate (13x)

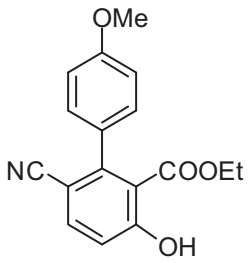


Chemical Formula: $C_{24}H_{28}BrNO_3$
Exact Mass: 457,125

Starting with **12d** [2-(4-bromobenzoyl)-3-ethoxyacrylonitrile] (0.420 g, 1.5 mmol) and **4q** (0.638 g, 1.65 mmol), **13x** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.392 g, 57 %). mp. 65 - 67 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_8CH_3$), 1.18 - 1.24 (m, 12 H, 6×CH_2), 1.51 – 1.59 (m, 2 H, CH_2), 2.62 (t, ^3J = 7.4 Hz, 2 H, CH_2), 3.43 (s, 3 H, OCH_3), 7.01 - 7.05 (m, 2 H,

CH_{BrPh}), 7.48 (s, 1 H, CH_{Ar}), 7.49 - 7.51 (m, 2 H, CH_{BrPh}), 11.60 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.7, 27.8, 28.3, 28.4, 28.5, 28.6, 29.9, 30.9 (CH_2), 51.5 (OCH_3), 103.8 (*C*CN), 111.4 (*C*COOCH$_3$), 116.9 (CN), 121.4 (C_{Ar}), 128.8 (2×CH_{BrPh}), 130.2 (2×CH_{BrPh}), 131.7 (C_{Ar}), 136.0 (CH_{Ar}), 136.9, 144.5 (C_{Ar}), 162.1 (*C*OH), 169.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3333 (w), 2949 (m), 2921 (m), 2871 (m), 2847 (m), 2226 (w), 1911 (w), 1736 (m), 1714 (m), 1639 (w), 1599 (m), 1568 (m), 1493 (w), 1458 (m), 1428 (m), 1403 (m), 1392 (m), 1374 (w), 1356 (w), 1334 (w), 1301 (m), 1257 (m), 1237 (m), 1207 (m), 1187 (m), 1176 (m), 1148 (s), 1125 (m), 1072 (m), 1055 (w), 1038 (w), 1028 (w), 1012 (m), 985 (m), 966 (m), 946 (w), 912 (w), 881 (w), 854 (w), 821 (m), 803 (m), 761 (m), 745 (m), 726 (m), 702 (m), 674 (m), 621 (m), 561 (m), 548 (m). GC-MS (EI, 70 eV): *m/z* (%) = 459 ([M$^+$], ^{81}Br, 41), 457 ([M$^+$], ^{79}Br, 41), 427 (9), 390 (5), 368 (4), 346 (90), 330 (7), 314 (22), 288 (14), 235 (73), 224 (11), 205 (22), 177 (22), 158 (13), 129 (42), 116 (100), 97 (21), 85 (34), 71 (48), 57 (74). HRMS (EI): Calcd. for $C_{24}H_{28}O_3N^{79}Br$ ([M]$^+$): 457.12471; found: 457.124229

Ethyl 6-cyano-3-hydroxy-4'-methoxybiphenyl-2-carboxylate (13y)

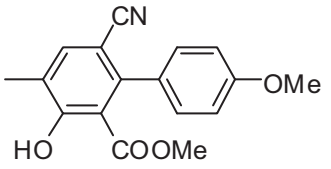


Chemical Formula: $C_{17}H_{15}NO_4$
Exact Mass: 297,100

Starting with **12e** [3-ethoxy-2-(4-methoxybenzoyl)acrylonitrile] (0.347 g, 1.5 mmol) and **4b** (0.453 g, 1.65 mmol), **13y** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.223 g, 50 %), mp. 116 - 117 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.73 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 3.79 (s, 3 H, OCH_3), 3.93 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 6.86 - 6.91 (m, 2 H, CH_{OMePh}), 6.99 (d, ^3J = 8.7 Hz, 1 H, CH_{Ar}), 7.07 - 7.12 (m, 2 H, CH_{OMePh}), 7.62 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 11.36 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 55.4 (OCH_3), 61.9 (OCH_2), 106.1 (*C*CN), 113.5 (2×CH_{OMePh}), 113.9 (*C*COOCH$_2$CH$_3$), 117.9 (CH_{Ar}), 118.0 (CN), 129.4 (2×CH_{OMePh}), 131.2 (C_{Ar}), 137.4 CH_{Ar}), 149.5, 159.8 (C_{Ar}), 164.7 (*C*OH), 170.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3306 (w, br), 3070 (w), 2987 (w), 2959 (w), 2921 (m), 2838 (w), 2537 (w), 2351 (w), 2225 (m), 2175 (w), 2050 (w), 1931 (w), 1682 (m), 1651 (w), 1609 (m), 1570 (m), 1517 (m), 1464 (m), 1455 (m), 1395 (m), 1372 (m), 1311 (m), 1294 (m), 1251 (m), 1174 (s), 1138 (m), 1112 (m), 1096 (m), 1028 (m), 1016 (m), 948 (m), 929 (w), 908 (w), 872 (w), 848 (m), 835 (s), 806 (m), 795 (m), 778 (m), 742 (m), 723 (m), 706 (m), 675 (m), 646 (m), 621 (m), 579 (m), 558 (m), 532 (m). GC- MS (EI, 70 eV): *m/z* (%) = 297 ([M$^+$], 44), 251 (100), 236 (5), 223 (16),

208 (9), 180 (9), 152 (7), 126 (5), 101 (1), 75 (2), 63 (2). HRMS (EI): Calcd. for $C_{17}H_{15}O_4N$ ($[M]^+$): 297.09956; found: 297.099391

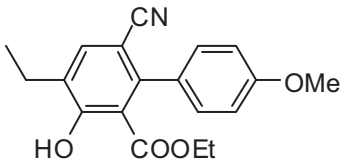
Methyl 6-cyano-3-hydroxy-4'-methoxy-4-methylbiphenyl-2-carboxylate (13z)



Chemical Formula: $C_{17}H_{15}NO_4$
Exact Mass: 297.100

Starting with **12e** [3-ethoxy-2-(4-methoxybenzoyl)acrylonitrile] (0.347 g, 1.5 mmol) and **4e** (0.457 g, 1.65 mmol), **13z** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.227u,n g, 51 %). mp. 85 - 87 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 3.42 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 6.85 - 6.89 (m, 2 H, CH_{OMePh}), 7.05 - 7.09 (m, 2 H, CH_{OMePh}), 7.49 (s, 1 H, CH_{Ar}), 11.43 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.6 (CH_3), 52.4, 55.3 (OCH_3), 105.2 (*C*CN), 112.8 (*C*$COOCH_3$), 113.5 (2×CH_{OMePh}), 118.3 (CN), 127.4 (C_{Ar}), 129.2 (2×CH_{OMePh}), 131.1 (C_{Ar}), 137.7 (CH_{Ar}), 146.9, 159.5 (C_{Ar}), 162.9 (*C*OH), 170.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2958 (w), 2843 (w), 2219 (w), 1659 (m), 1608 (m), 1555 (w), 1515 (m), 1427 (m), 1331 (m), 1308 (s), 1260 (m), 1202 (m), 1176 (m), 1145 (m), 1033 (m), 1019 (m), 983 (m), 902 (m), 862 (w), 808 (s), 767 (m), 661 (w), 648 (m), 535 (m). GC-MS (EI, 70 eV): *m/z* (%) = 297 ($[M^+]$, 45), 266 (19), 265 (100), 264 (12), 250 (11), 222 (9), 166 (9), 140 (8), 39 (8). HRMS (EI): Calcd. for $C_{17}H_{15}O_4N$ ($[M]^+$): 297.09956; found: 297.099657.

Ethyl 6-cyano-4-ethyl-3-hydroxy-4'-methoxybiphenyl-2-carboxylate (13aa)

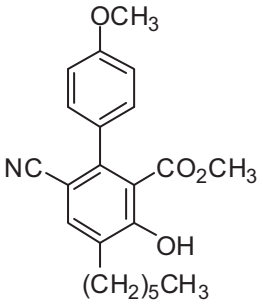


Chemical Formula: $C_{19}H_{19}NO_4$
Exact Mass: 325.131

Starting with **12e** [3-ethoxy-2-(4-methoxybenzoyl)acrylonitrile] (0.347 g, 1.5 mmol) and **4g** (0.499 g, 1.65 mmol), **13aa** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.237 g, 49 %). mp. 54 - 56 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.19 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 2.65 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 3.92 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 3.77 (s, 3 H, OCH_3), 6.85 - 6.88 (m, 2 H, CH_{OMePh}), 7.06 - 7.09 (m, 2 H, CH_{OMePh}), 7.49 (s, 1 H, CH_{Ar}), 11.60 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9, 13.2 (CH_3), 22.7 (CH_2), 55.3 (OCH_3), 62.0 (OCH_2), 105.2 (*C*CN), 112.9 (*C*$COOCH_3$), 113.5 (2×CH_{OMePh}), 118.3 (CN), 129.2 (2×CH_{OMePh}), 132.5 (C_{Ar}), 133.8 (C_{Ar}), 136.9 (CH_{Ar}), 146.9, 159.8 (C_{Ar}), 163.0 (*C*OH), 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2968 (w),

2875 (w), 2223 (w), 1658 (m), 1608 (m), 1566 (w), 1515(s), 1434 (m), 1399 (m), 1373 (m), 1326 (m), 1302 (m), 1268 (m), 1239 (s), 1189 (s), 1145 (s), 1109 (m), 1065 (w), 1030 (m), 906 (w), 808 (s), 770 (m), 643 (w), 534 (m). GC-MS (EI, 70 eV): *m/z* (%) = 325 ([M^+], 84), 280 (23), 279 (100), 264 (29), 262 (12), 261 (52), 251 (10), 250 (10), 249 (12), 248 (60), 247 (12), 246 (30), 236 (15), 208 (9), 193 (8), 177 (8), 165 (9), 152 (8), 29 (9). HRMS (EI): Calcd. for $C_{19}H_{19}O_4N$ ([$M]^+$): 325.13086; found: 325.130617

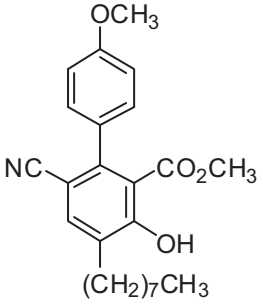
Methyl 6-cyano-4-hexyl-3-hydroxy-4'-methoxybiphenyl-2-carboxylate (13ab)



Chemical Formula: $C_{22}H_{25}NO_4$
Exact Mass: 367,178

Starting with **12e** [3-ethoxy-2-(4-methoxybenzoyl)acrylonitrile] (0.347 g, 1.5 mmol) and **4k** (0.568 g, 1.65 mmol), **13ab** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.286 g, 52 %). mp. 43 - 44 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_5CH_3$), 1.18 - 1.32 (m, 6 H, 3×CH_2), 1.50 - 1.59 (m, 2 H, CH_2), 2.61 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.40 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 6.83 - 6.88 (m, 2 H, 2×CH_{Ph}), 7.04 - 7.09 (m, 2 H, 2×CH_{Ph}), 7.46 (s, 1 H, CH_{Ar}), 11.39 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.6, 28.8, 29.1, 29.5, 31.6 (CH_2), 52.4, 55.2 (OCH_3), 105.6 (*C*CN), 113.0 (*C*$COOCH_3$), 113.5 (2×CH_{Ph}), 118.4 (CN), 129.4 (2×CH_{Ph}), 131.1, 131.8 (C_{Ar}), 137.0 (CH_{Ar}), 146.6, 159.4 (C_{Ar}), 162.7 (*C*OH), 170.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2927 (m), 2856 (w), 2223 (w), 1746 (w), 1665 (m), 1609 (m), 1579 (w), 1516 (m), 1436 (m), 1337 (m), 1289 (m), 1247 (s), 1205 (m), 1176 (m), 1147 (m), 1110 (w), 1034 (w), 906 (m), 830 (m), 768 (w), 728 (s), 649 (m). GC-MS (EI, 70 eV): *m/z* (%) = 368 (17), 367 ([$M]^+$, 85), 336 (13), 335 (54), 266 (17), 265 (100), 264 (44), 234 (22). HRMS (EI): Calcd. for $C_{22}H_{25}O_4N$ ([$M]^+$): 367.17781; found: 367.177574.

Methyl 6-cyano-3-hydroxy-4'-methoxy-4-octylbiphenyl-2-carboxylate (13ac)



Chemical Formula: $C_{24}H_{29}NO_4$
Exact Mass: 395,210

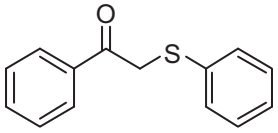
Starting with **12e** [3-ethoxy-2-(4-methoxybenzoyl)acrylonitrile] (0.347 g, 1.5 mmol) and **4o** (0.614 g, 1.65 mmol), **13ac** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.297 g, 50 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_7CH_3$), 1.17 - 1.32 (m, 10 H, 5×CH_2), 1.50 - 1.59 (m, 2 H, CH_2), 2.61

(t, ^{3}J = 7.5 Hz, 2 H, CH_2), 3.42 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 6.84 - 6.90 (m, 2 H, 2×CH_{Ph}), 7.05 - 7.11 (m, 2 H, 2×CH_{Ph}), 7.48 (s, 1 H, CH_{Ar}), 11.49 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.6, 27.9, 28.2, 28.3, 28.4, 28.6, 30.9 (CH_2), 51.3, 54.3 (OCH_3), 104.1 (*C*CN), 111.9 (*C*$COOCH_3$), 112.4 (2×CH_{Ph}), 117.4 (CN), 128.4 (2×CH_{Ph}), 130.1, 130.8 (C_{Ar}), 136.1 (CH_{Ar}), 145.5, 158.4 (C_{Ar}), 161.7 (*C*OH), 170.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2924 (m), 2854 (w), 2223 (w), 1665 (m), 1609 (m), 1516 (m), 1436 (s), 1339 (m), 1290 (m), 1247 (s), 1205 (m), 1175 (m), 1034 (m), 991 (w), 906 (m), 829 (m), 767 (w), 729 (s), 649 (m), 536 (w). GC-MS (EI, 70 eV): *m/z* (%) = 396 (21), 395 ($[M]^+$, 97), 364 (14), 363 (56), 266 (17), 265 (100), 264 (50), 234 (21). HRMS (EI): Calcd. for $C_{24}H_{29}NO_4$ ($[M]^+$): 395.20911; found: 395.209162.

General procedure for the synthesis of 15a-f:

To a suspension of sodium ethoxide (1.0 equiv.) in ethanol (0.7ml / 1mmol NaOEt), was added the (**14a-f**) substituted thiophenol (1.0 equiv.) at 25 °C followed by portionwise addition of 2-bromoacetophenone (1.0 equiv.). The mixture was refluxed for 10 minutes and then poured into 2 L of ice. Filtration of the suspension gave the respective products **15a-f**.

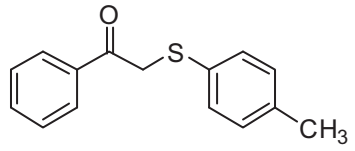
1-Phenyl-2-(phenylthio)ethanone (15a)



Chemical Formula: $C_{14}H_{12}OS$
Exact Mass: 228,061

Starting with NaOEt (1.361 g, 20 mmol), **14a** (2.20 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15a** was isolated as a brown semi-solid (4.286 g, 93 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.20 (s, 2 H, CH_2), 7.13 - 7.24 (m, 3 H, CH_{Ar}), 7.29 - 7.33 (m, 2 H, CH_{Ar}), 7.36 - 7.41 (m, 2 H, CH_{Ar}), 7.48 - 7.53 (m, 1 H, CH_{Ar}), 7.85 - 7.89 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 41.2 (CH_2), 127.1 (CH_{Ar}), 128.7 (4×CH_{Ar}), 129.1 (2×CH_{Ar}), 130.6 (2×CH_{Ar}), 133.5 (CH_{Ar}), 134.8, 135.4 (C_{Ar}), 194.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3339 (w), 3057 (w), 2902 (w), 1675 (s), 1596 (m), 1579 (m), 1480 (m), 1447 (m), 1438 (m), 1412 (w), 1394 (w), 1317 (m), 1273 (s), 1197 (m), 1158 (m), 1088 (m), 1024 (m), 999 (m), 932 (w), 906 (w), 843 (w), 736 (s), 685 (s), 641 (s), 616 (m), 555 (m). GC-MS (EI, 70 eV): *m/z* (%) = 228 ($[M]^+$, 39), 123 (8), 105 (100), 77 (32), 65 (6), 51 (10). HRMS (EI): Calcd. for $C_{14}H_{12}OS$ ($[M]^+$): 228.06034; found: 228.060346.

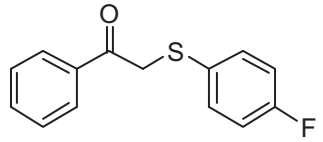
1-Phenyl-2-(p-tolylthio)ethanone (15b)



Chemical Formula: $C_{15}H_{14}OS$
Exact Mass: 242,077

Starting with NaOEt (1.361 g, 20 mmol), **14b** (2.484 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15b** was isolated as a brown semi-solid (4.773 g, 98 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 4.19 (s, 2 H, CH_2), 6.94 - 6.96 (m, 1 H, CH_{Ar}), 7.09 - 7.13 (m, 3 H, CH_{Ar}), 7.35 - 7.40 (m, 2 H, CH_{Ar}), 7.47 - 7.52 (m, 1 H, CH_{Ar}), 7.85 - 7.88 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.3 (CH_3), 41.3 (CH_2), 127.5, 128.0 (CH_{Ar}), 128.6 (2×CH_{Ar}), 128.7 (2×CH_{Ar}), 128.9, 131.2, 133.4 (CH_{Ar}), 134.5, 135.5, 138.9 (C_{Ar}), 194.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3340 (w), 3055 (w), 2918 (w), 2732 (w), 1675 (s), 1593 (m), 1475 (m), 1447 (m), 1317 (m), 1273 (s), 1195 (m), 1134 (m), 1035 (w), 987 (m), 854 (m), 748 (m), 685 (s), 641 (m), 623 (w), 610 (w), 557 (m). GC-MS (EI, 70 eV): *m/z* (%) = 242 ($[M]^+$, 45), 137 (14), 105 (100), 91 (9), 77 (30), 65 (7), 51 (7). HRMS (EI): Calcd. for $C_{15}H_{14}OS$ ($[M]^+$): 242.07599; found: 242.076514

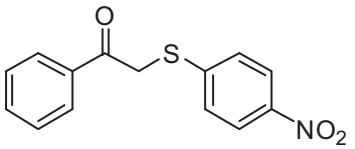
2-(4-Fluorophenylthio)-1-phenylethanone (15c)



Chemical Formula: $C_{14}H_{11}FOS$
Exact Mass: 246,051

Starting with NaOEt (1.361 g, 20 mmol), **14c** (2.563 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15c** was isolated as a light-brown oil (4.554 g, 92 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.22 (s, 2 H, CH_2), 6.97 - 7.03 (m, 2 H, CH_{Ar}), 7.39 - 7.44 (m, 2 H, CH_{Ar}), 7.46 - 7.52 (m, 2 H, CH_{Ar}), 7.59 - 7.64 (m, 1 H, CH_{Ar}), 7.93 - 7.96 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 42.1 (CH_2), 116.2 (d, $^{2}J_{C,F}$ = 22.0 Hz), 128.7 (4×CH_{Ar}), 129.4 (d, $^{4}J_{C,F}$ = 3.1 Hz), 133.5 (CH_{Ar}), 133.9 (d, $^{3}J_{C,F}$ = 8.2 Hz), 135.3 (C_{Ar}), 162.5 (d, $^{1}J_{C,F}$ = 247.8 Hz), 193.9 (CO). ^{19}F NMR (285 MHz, $CDCl_3$); δ = -113.5 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3338 (w), 3062 (w), 2905 (w), 1675 (s), 1589 (m), 1580 (m), 1489 (s), 1448 (m), 1396 (m), 1274 (m), 1221 (s), 1196 (s), 1156 (m), 1090 (m), 1000 (m), 932 (w), 826 (m), 748 (m), 687 (s), 646 (m), 625 (m), 557 (m). GC-MS (EI, 70 eV): *m/z* (%) = 246 ($[M]^+$, 30), 141 (4), 127 (5), 105 (100), 83 (6), 77 (33), 51 (8). HRMS (EI): Calcd. for $C_{14}H_{11}OFS$ ($[M]^+$): 246.05092; found: 246.050909

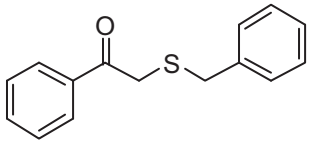
2-(4-Nitrophenylthio)-1-phenylethanone (15d)



Chemical Formula: $C_{14}H_{11}NO_3S$
Exact Mass: 273,046

Starting with NaOEt (1.361 g, 20 mmol), **14d** (3.104 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15d** was isolated as a brown solid (5.438 g, 99 %). mp. 150 - 152 °C ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.37 (s, 2 H, CH_2), 7.33 - 7.36 (m, 2 H, CH_{Ar}), 7.41 - 7.46 (m, 3 H, CH_{Ar}), 7.90 - 7.93 (m, 2 H, CH_{Ar}), 8.03 - 8.06 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 39.1 (CH_2), 124.0 (2×CH_{Ar}), 127.2 (2×CH_{Ar}), 128.6 (2×CH_{Ar}), 128.9 (2×CH_{Ar}), 134.0 (CH_{Ar}), 134.9, 145.4, 145.7 (C_{Ar}), 192.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3370 (w), 3094 (w), 3062 (w), 2918 (w), 2850 (w), 1677 (m), 1594 (m), 1575 (s), 1502 (s), 1448 (m), 1392 (m), 1334 (s), 1276 (m), 1196 (m), 1108 (m), 1069 (m), 988 (m), 906 (w), 852 (m), 755 (m), 737 (s), 680 (s), 623 (m), 610 (m), 566 (m), 537 (m). GC-MS (EI, 70 eV): *m/z* (%) = 273 ([M]$^+$, 8), 105 (100), 77 (30), 51 (6). HRMS (EI): Calcd. for $C_{14}H_{11}O_3NS$ ([M]$^+$): 273.04542; found: 273.045738**.**

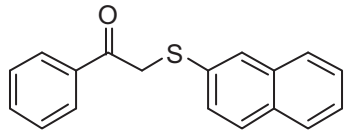
2-(Benzylthio)-1-phenylethanone (15e)



Chemical Formula: $C_{15}H_{14}OS$
Exact Mass: 242,077

Starting with NaOEt (1.361 g, 20 mmol), **14e** (2.484 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15e** was isolated as a semi-brown solid (4.828 g, 99 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (s, 2 H, CH_2), 3.79 (s, 2 H, CH_2), 7.28 - 7.32 (m, 2 H, CH_{Ar}), 7.34 - 7.38 (m, 3 H, CH_{Ar}), 7.46 - 7.52 (m, 2 H, CH_{Ar}), 7.57 - 7.62 (m, 1 H, CH_{Ar}), 7.94 - 7.98 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 35.9, 36.1 (CH_2), 127.3 (CH_{Ar}), 128.5 (2×CH_{Ar}), 128.6 (2×CH_{Ar}), 128.7 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 133.3 (CH_{Ar}), 135.4, 137.3 (C_{Ar}), 194.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3648 (w), 3327 (w), 3083 (w), 3059 (w), 3027 (w), 2919 (w), 2626 (w), 2321 (w), 1964 (w), 1900 (w), 1813 (w), 1766 (w), 1670 (s), 1596 (m), 1579 (m), 1493 (m), 1447 (m), 1417 (w), 1315 (m), 1275 (s), 1197 (m), 1130 (m), 1071 (m), 1013 (m), 932 (w), 803 (w), 748 (m), 698 (s), 686 (s), 645 (m), 618 (w), 588 (w), 561 (m). GC-MS (EI, 70 eV): *m/z* (%) = 242 ([M]$^+$, 15), 120 (70), 105 (100), 91 (45), 77 (39), 65 (12), 51 (11). HRMS (EI): Calcd. for $C_{15}H_{14}OS$ ([M]$^+$): 242.07599; found: 242.076303

2-(Naphthalen-2-ylthio)-1-phenylethanone (15f)



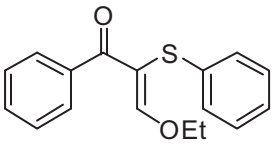
Chemical Formula: $C_{18}H_{14}OS$
Exact Mass: 278,077

Starting with NaOEt (1.361 g, 20 mmol), **14f** (3.205 g, 20 mmol), and 2-bromoacetophenone (4.00 g, 20 mmol), **15f** was isolated as a semi-brown solid (5.389 g, 96 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.29 (s, 2 H, CH_2), 7.35 - 7.40 (m, 5 H, CH_{Ar}), 7.63 - 7.75 (m, 5 H, CH_{Ar}), 7.86 - 7.89 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 41.2 (CH_2), 126.2, 126.6, 127.4, 127.7, 128.0, 128.6 (CH_{Ar}), 128.7 (4×CH_{Ar}), 128.9 (CH_{Ar}), 132.2 (C_{Ar}), 133.5 (CH_{Ar}), 133.7, 134.0, 135.5 (C_{Ar}), 194.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3328 (w), 3104 (w), 3052 (w), 2985 (w), 2943 (w), 2902 (w), 2853 (w), 1971 (w), 1954 (w), 1916 (w), 1828 (w), 1686 (m), 1668 (m), 1621 (m), 1578 (m), 1498 (m), 1446 (m), 1417 (w), 1338 (w), 1270 (m), 1194 (m), 1130 (m), 1068 (m), 1012 (m), 941 (m), 846 (m), 814 (s), 738 (s), 686 (s), 651 (m), 626 (m), 599 (w), 553 (m). GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M]$^{+}$, 88), 173 (29), 129 (11), 115 (20), 105 (100), 77 (26), 51 (6). HRMS (EI): Calcd. for $C_{18}H_{14}OS$ ([M]$^{+}$): 278.07599; found: 278.076186

General procedure for the synthesis of 16a-f:

To a solution of **15a-f** (1.0 equiv.) in acetic anhydride (3.0 equiv.) was added triethyl orthoformate (3.0 equiv.). The mixture was refluxed for 15 h at 140 °C. The mixture was dried in vacuo and purified by chromatography (silica gel, heptanes/ EtOAc) to give **16a-f**

3-Ethoxy-1-phenyl-2-(phenylthio)prop-2-en-1-one (16a)

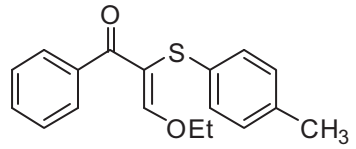


Chemical Formula: $C_{17}H_{16}O_2S$
Exact Mass: 284,087

Starting with **15a** (2.00 g, 8.76 mmol), triethyl orthoformate (3.90 g, 26.28 mmol), and acetic anhydride (2.68 g, 26.28 mmol), **16a** was isolated as a yellowish oil (1.013 g, 41 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, ^{3}J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.09 (q, ^{3}J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 6.99 - 7.04 (m, 1 H, CH_{Ar}), 7.09 - 7.12 (m, 1 H, CH_{Ar}), 7.13 - 7.19 (m, 3 H, CH_{Ar}), 7.28 - 7.34 (m, 2 H, CH_{Ar}), 7.38 - 7.44 (m, 1 H, CH_{Ar}), 7.55 - 7.58 (m, 3 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 71.8 (OCH_2), 112.3 (C), 125.7 (CH_{Ar}), 128.1 (4×CH_{Ar}), 128.7 (2×CH_{Ar}), 128.8 (2×CH_{Ar}), 131.5 (CH_{Ar}), 135.8, 138.9 (C_{Ar}), 166.4 (C), 193.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2981 (w), 2935 (w), 2895 (w), 1644 (m), 1588 (s), 1475 (m), 1439 (m), 1390 (m), 1297 (m), 1212 (s), 1178 (m), 1089 (m), 1009 (m), 892 (m), 822 (m), 737 (m), 688 (s), 657 (s), 616 (m), 577 (m), 541 (m).

GC-MS (EI, 70 eV): *m/z* (%) = 284 ([M]$^+$, 100), 255 (6), 149 (10), 135 (6), 121 (15), 105 (90), 77 (46), 51 (10). HRMS (EI): Calcd. for $C_{17}H_{16}O_2S$ ([M]$^+$): 284.08655; found: 284.085992

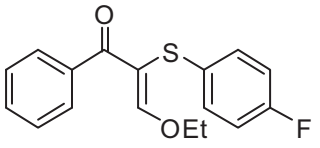
3-Ethoxy-1-phenyl-2-(p-tolylthio)prop-2-en-1-one (16b)



Chemical Formula: $C_{18}H_{18}O_2S$
Exact Mass: 298,103

Starting with **15b** (2.00 g, 8.25 mmol), triethyl orthoformate (3.67 g, 24.75 mmol), and acetic anhydride (2.53 g, 24.75 mmol), **16b** was isolated as a yellowish oil (1.333 g, 54 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, ^3J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 2.18 (s, 3 H, CH_3), 4.10 (q, ^3J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 6.96 - 7.00 (m, 2 H, CH_{Ar}), 7.28 - 7.34 (m, 2 H, CH_{Ar}), 7.38 - 7.43 (m, 2 H, CH_{Ar}), 7.53 - 7.58 (m, 3 H, CH_{Ar}), 7.82 - 7.85 (m, 1 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4, 21.3 (CH_3), 71.7 (OCH_2), 112.3 (C), 125.1, 126.6, 127.7, 128.1, 128.6, 128.8, 128.9, 131.5, 133.9 (CH_{Ar}), 135.4, 138.4, 139.0 (CH_{Ar}), 166.3 (CH), 192.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2980 (w), 2930 (w), 1749 (m), 1703 (m), 1645 (m), 1591 (s), 1447 (m), 1370 (m), 1272 (m), 1214 (s), 1180 (m), 1085 (m), 1011 (m), 893 (m), 822 (m), 755 (m), 687 (s), 658 (m), 617 (w), 562 (m), 542 (w). GC-MS (EI, 70 eV): *m/z* (%) = 298 ([M]$^+$, 100), 149 (12), 135 (11), 123 (9), 105 (88), 91 (9), 77 (40), 51 (6). HRMS (EI): Calcd. for $C_{18}H_{18}O_2S$ ([M]$^+$): 298.10220; found: 298.101601

3-Ethoxy-2-(4-fluorophenylthio)-1-phenylprop-2-en-1-one (16c)

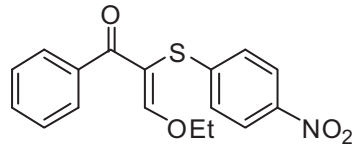


Chemical Formula: $C_{17}H_{15}FO_2S$
Exact Mass: 302,078

Starting with **15c** (2.00 g, 8.12 mmol), triethyl orthoformate (3.61 g, 24.36 mmol), and acetic anhydride (2.49 g, 24.36 mmol), **16c** was isolated as a brownish oil (1.351 g, 55 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.09 (q, ^3J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 6.79 - 6.85 (m, 2 H, CH_{Ar}), 7.16 - 7.21 (m, 2 H, CH_{Ar}), 7.29 - 7.34 (m, 2 H, CH_{Ar}), 7.39 - 7.44 (m, 1 H, CH_{Ar}), 7.48 (s, 1 H, CH), 7.52 - 7.56 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4 (CH_3), 71.8 (OCH_2), 113.2 (C), 115.8 (d, $^2J_{C,F}$ = 22.0 Hz), 128.2 (2×CH_{Ar}), 128.8 (CH_{Ar}), 130.7 (d, $^4J_{C,F}$ = 3.8 Hz), 131.1 (d, $^3J_{C,F}$ = 8.1 Hz), 130.7 (C_{Ar}), 131.6 (CH_{Ar}), 138.9 (C_{Ar}), 161.6 (d, $^1J_{C,F}$ = 245.5 Hz), 165.9 (CH), 193.3 (CO). ^{19}F NMR (285 MHz, $CDCl_3$); δ = -116.5. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2982 (w), 2936 (w), 2896 (w), 2816 (w), 1749 (w), 1704 (w), 1644 (m), 1586 (s), 1487 (s), 1445 (m), 1392 (m), 1334 (w), 1272 (m), 1212 (s), 1153

(m), 1086 (m), 1010 (s), 928 (w), 822 (m), 755 (w), 657 (m), 625 (m), 562 (w). GC-MS (EI, 70 eV): *m/z* (%) = 302 ($[M]^+$, 100), 273 (5), 127 (12), 105 (94), 77 (43), 51 (7). HRMS (EI): Calcd. for $C_{17}H_{15}O_2FS$ ($[M]^+$): 302.07713; found: 302.077385

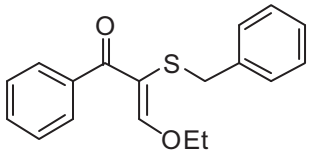
3-Ethoxy-2-(4-nitrophenylthio)-1-phenylprop-2-en-1-one (16d)



Chemical Formula: $C_{17}H_{15}NO_4S$
Exact Mass: 329,072

Starting with **15d** (2.00 g, 7.32 mmol), triethyl orthoformate (3.25 g, 21.96 mmol), and acetic anhydride (2.24 g, 21.96 mmol), **16d** was isolated as a yellowish oil (1.078 g, 45 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.15 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.19 - 7.22 (m, 2 H, CH_{Ar}), 7.34 - 7.39 (m, 2 H, CH_{Ar}), 7.43 - 7.48 (m, 1 H, CH_{Ar}), 7.58 - 7.61 (m, 2 H, CH_{Ar}), 7.74 (s, 1 H, CH_{Ar}), 7.97 - 8.00 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4 (CH_3), 72.5 (OCH_2), 109.3 (C), 123.9 (2×CH_{Ar}), 126.2 (2×CH_{Ar}), 128.4 (2×CH_{Ar}), 128.8 (2×CH_{Ar}), 132.0 (CH_{Ar}), 138.4, 145.2, 146.4 (C_{Ar}), 168.7 (CH), 192.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3272 (w), 3092 (w), 3011 (w), 2951 (w), 2891 (w), 2605 (w), 2440 (w), 1672 (m), 1643 (m), 1592 (m), 1574 (s), 1558 (s), 1500 (s), 1471 (m), 1386 (m), 1332 (s), 1314 (s), 1217 (s), 1175 (s), 1109 (m), 1013 (s), 934 (m), 910 (s), 844 (s), 794 (m), 717 (s), 697 (s), 681 (s), 659 (m), 645 (s), 625 (m), 565 (m), 541 (m). GC-MS (EI, 70 eV): *m/z* (%) = 329 ($[M]^+$, 68), 300 (8), 255 (6), 197 (6), 165 (6), 105 (100), 77 (27), 50 (7). HRMS (EI): Calcd. for $C_{17}H_{15}O_4NS$ ($[M]^+$): 329.07163; found: 329.071842

2-(Benzylthio)-3-ethoxy-1-phenylprop-2-en-1-one (16e)

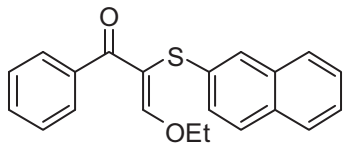


Chemical Formula: $C_{18}H_{18}O_2S$
Exact Mass: 298,103

Starting with **15e** (2.00 g, 8.25 mmol), triethyl orthoformate (3.67 g, 24.76 mmol), and acetic anhydride (2.53 g, 24.76 mmol), **16e** was isolated as a yellowish oil (1.033 g, 42 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 3.90 - 3.97 (m, 4 H, CH_2,OCH_2CH_3), 7.13 - 7.19 (m, 5 H, CH_{Ar}), 7.26 - 7.28 (m, 4 H, CH_{Ar}), 7.36 - 7.41 (m, 2 H, CH_{Ar}).^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 36.7 (CH_2), 71.3 (OCH_2), 112.3 (C), 126.8 (CH_{Ar}), 128.0 (2×CH_{Ar}), 128.1 (2×CH_{Ar}), 128.8 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 131.2 (CH_{Ar}), 138.3, 139.3 (C_{Ar}), 166.1 (CH), 193.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 3028 (w), 2978 (w), 2924 (w), 1750 (w), 1704 (w), 1672 (m), 1596 (m), 1492 (m), 1447 (m), 1340 (m), 1275 (m), 1217 (m), 1179 (m),

1071 (m), 1014 (m), 967 (m), 843 (m), 765 (m), 696 (s), 687 (s), 646 (m), 618 (m), 563 (m), 540 (m). GC-MS (EI, 70 eV): *m/z* (%) = 298 ([M]$^+$, 34), 252 (30), 147 (51), 131 (10), 105 (79), 91 (100), 77 (49), 65 (13), 51 (8), 39 (8). HRMS (EI): Calcd. for $C_{18}H_{18}O_2S$ ([M]$^+$): 298.10220; found: 298.102566

3-Ethoxy-2-(naphthalen-2-ylthio)-1-phenylprop-2-en-1-one (16f)



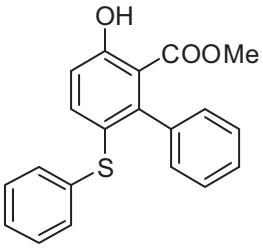
Chemical Formula: $C_{21}H_{18}O_2S$
Exact Mass: 334,103

Starting with **15f** (2.00 g, 7.18 mmol), triethyl orthoformate (3.19 g, 21.54 mmol), and acetic anhydride (2.20 g, 21.54 mmol), **16f** was isolated as a yellowish oil (1.201 g, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.11 (q, ^3J = 7.1 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.26 - 7.43 (m, 7 H, CH_{Ar}), 7.58 - 7.67 (m, 6 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.4 (CH_3), 71.8 (OCH_2), 112.1 (C), 125.4, 126.2, (CH_{Ar}), 126.3 (2×CH_{Ar}), 127.1, 127.6 (CH_{Ar}), 128.1 (2×CH_{Ar}), 128.3 (CH_{Ar}), 128.8 (2×CH_{Ar}), 131.5 (CH_{Ar}), 131.7, 133.3, 133.7, 138.9 (C_{Ar}), 166.5 (CH), 193.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3053 (w), 2979 (w), 2930 (w), 1749 (m), 1703 (m), 1644 (m), 1587 (m), 1500 (m), 1446 (m), 1339 (m), 1268 (m), 1215 (s), 1132 (m), 1086 (m), 1012 (m), 940 (m), 847 (m), 811 (s), 743 (m), 688 (s), 632 (m), 617 (m), 601 (m), 575 (m), 541 (m). GC-MS (EI, 70 eV): *m/z* (%) = 334 ([M]$^+$, 100), 159 (12), 115 (16), 105 (76), 77 (31). HRMS (EI): Calcd. for $C_{21}H_{18}O_2S$ ([M]$^+$): 334.10220; found: 334.102183

General procedure for the synthesis of 17a-q.

To a solution (3mL/ of **16a-f**) of **16a-f** was added **4a-r** (1.1 mmol) and, subsequently, $TiCl_4$ (1.1 mmol) at -78 °C. The temperature of the solution was allowed to warm to 20 °C during the 14 h with stirring. Hydrochloric acid (10 %, 20mL) was added to the solution and both the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3×20mL). The combined organic layers were dried (Na_2SO_4), filtered and filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes / EtOAc) to give **17a-q.**

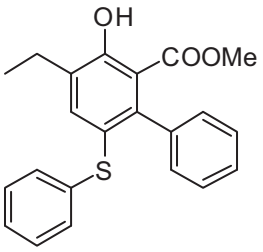
Methyl 3-hydroxy-6-(phenylthio)biphenyl-2-carboxylate (17a)



Chemical Formula: $C_{20}H_{16}O_3S$
Exact Mass: 336,082

Starting with **16a** (0.427 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **17a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.222 g, 44 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.23 (s, 3 H, OCH_3), 6.83 (d, ^3J = 8.8 Hz, 1 H, CH_{Ar}), 6.92 - 6.95 (m, 4 H, CH_{Ar}), 6.99 - 7.05 (m, 3 H, CH_{Ar}), 7.14 - 7.17 (m, 3 H, CH_{Ar}), 7.28 (d, ^3J = 8.8 Hz, 1 H, CH_{Ar}), 10.67 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.0 (OCH_3), 113.9 (*C*$COOCH_3$), 118.2 (CH_{Ar}), 126.1 (C_{Ar}), 126.4, 127.0 (CH_{Ar}), 127.4 (2×CH_{Ar}), 128.5 (2×CH_{Ar}), 128.9 (2×CH_{Ar}), 130.0 (2×CH_{Ar}), 137.3 (C_{Ar}), 139.1 (CH_{Ar}), 140.7, 146.1 (C_{Ar}), 161.1 (*C*OH), 171.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 3021 (w), 2950 (w), 2850 (w), 2659 (w), 2536 (w), 1943 (w), 1880 (w), 1739 (w), 1663 (s), 1582 (m), 1496 (w), 1435 (s), 1335 (m), 1288 (m), 1208 (s), 1155 (m), 1094 (m), 1024 (m), 964 (m), 828 (m), 737 (s), 698 (s), 688 (s), 612 (m), 575 (m). GC-MS (EI, 70 eV): *m/z* (%) = 336 ($[M]^+$, 46), 304 (100), 275 (8), 247 (17), 215 (8), 171 (17), 139 (10). HRMS (EI): Calcd. for $C_{20}H_{16}O_3S$ ($[M]^+$): 336.08147; found: 336.081073

Methyl 4-ethyl-3-hydroxy-6-(phenylthio)biphenyl-2-carboxylate (17b)

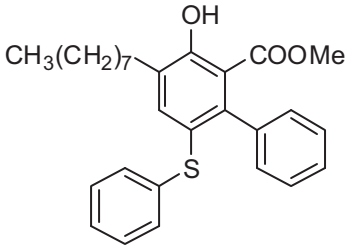


Chemical Formula: $C_{22}H_{20}O_3S$
Exact Mass: 364,113

Starting with **16a** (0.427 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **17b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.263 g, 48 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.50 (q, ^3J = 7.7 Hz, 2 H, CH_2CH_3), 3.19 (s, 3 H, OCH_3), 6.84 - 6.90 (m, 4 H, CH_{Ar}), 6.96 - 7.03 (m, 2 H, CH_{Ar}), 7.08 - 7.12 (m, 5 H, CH_{Ar}), 10.89 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.7 (CH_3), 24.1 (CH_2), 53.1 (OCH_3), 114.6 (*C*$COOCH_3$), 125.6 (C_{Ar}), 127.1, 128.0 (CH_{Ar}), 128.5 (2×CH_{Ar}), 129.8 (2×CH_{Ar}), 130.0 (2×CH_{Ar}), 130.3 (2×CH_{Ar}), 134.4,139.3 (C_{Ar}), 140.2 (CH_{Ar}), 142.2, 145.6 (C_{Ar}), 160.7 (*C*OH), 172.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 3023 (w), 2963 (m), 2951 (m), 2933 (w), 2874 (w), 1933 (w), 1701 (m), 1661 (s), 1598 (m), 1477 (m), 1436 (s), 1409 (m), 1338 (m), 1290 (m), 1229 (s), 1196 (s), 1161 (s), 1065 (m), 1024 (m), 968 (m), 907 (m), 841 (m), 815 (m), 737 (s), 697 (s), 689 (s), 628 (m), 569 (w), 530 (m). GC-MS (EI, 70 eV): *m/z* (%) = 364 ($[M]^+$, 34), 332 (100), 223 (37), 205 (11),

184 (7), 165 (14), 110 (9), 78 (11), 63 (9), 40 (31). HRMS (EI): Calcd. for $C_{22}H_{20}O_3S$ ($[M]^+$): 364.11277; found: 364.112680

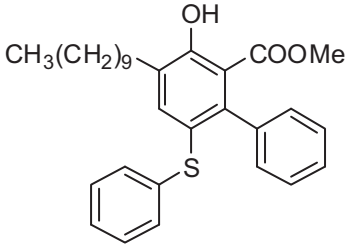
Methyl 3-hydroxy-4-octyl-6-(phenylthio)biphenyl-2-carboxylate (17c)



Chemical Formula: $C_{28}H_{32}O_3S$
Exact Mass: 448,207

Starting with **16a** (0.427 g, 1.5 mmol) and **4o** (0.615 g, 1.65 mmol), **17c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.344 g, 51 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_7CH_3$), 1.07 - 1.12 (m, 10 H, 5×CH_2), 1.39 - 1.43 (m, 2 H, CH_2), 2.45 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.19 (s, 3 H, OCH_3), 6.84 - 6.90 (m, 4 H, CH_{Ar}), 6.95 - 7.03 (m, 3 H, CH_{Ar}), 7.08 - 7.11 (m, 4 H, CH_{Ar}), 10.87 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 23.9, 30.2, 30.3, 30.5, 30.6, 30.9, 33.1 (CH_2), 53.0 (OCH_3), 114.6 (CCOOCH$_3$), 125.4 (C_{Ar}), 127.0, 128.0 (CH_{Ar}), 128.4 (2×CH_{Ar}), 129.8 (2×CH_{Ar}), 130.0 (2×CH_{Ar}), 130.2 (2×CH_{Ar}), 133.1, 139.4 (C_{Ar}), 141.1 (CH_{Ar}), 142.2, 145.6 (C_{Ar}), 160.7 (COH), 172.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3024 (w), 2952 (m), 2923 (m), 2853 (m), 1934 (w), 1703 (m), 1663 (m), 1598 (w), 1477 (w), 1437 (s), 1410 (m), 1340 (m), 1234 (s), 1197 (m), 1161 (m), 1024 (m), 905 (w), 842 (m), 813 (m), 749 (m), 698 (s), 629 (m), 616 (w), 596 (w), 572 (w), 532 (w). GC-MS (EI, 70 eV): *m/z* (%) = 448 ($[M]^+$, 21), 416 (15), 340 (72), 308 (81), 291 (10), 210 (100), 181 (16), 152 (28), 129 (17), 116 (37), 71 (9), 57 (16), 43 (15). HRMS (EI): Calcd. for $C_{28}H_{32}O_3S$ ($[M]^+$): 448.20667; found: 448.206838

Methyl 4-decyl-3-hydroxy-6-(phenylthio)biphenyl-2-carboxylate (17d)

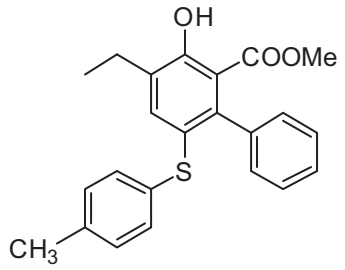


Chemical Formula: $C_{30}H_{36}O_3S$
Exact Mass: 476,239

Starting with **16a** (0.427 g, 1.5 mmol) and **4r** (0.661 g, 1.65 mmol), **17d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.372 g, 52 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_9CH_3$), 1.07 - 1.10 (m, 14 H, 7×CH_2), 1.37 - 1.43 (m, 2 H, CH_2), 2.45 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.19 (s, 3 H, OCH_3), 6.84 - 6.90 (m, 4 H, CH_{Ar}), 7.00 - 7.12 (m, 7 H, CH_{Ar}), 10.87 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.7, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7, 29.9, 31.9 (CH_2), 51.9 (OCH_3), 113.4 (CCOOCH$_3$), 124.2 (C_{Ar}), 125.8, 126.7, 127.2, 127.6, 128.1, 128.6 (CH_{Ar}), 128.8 (2×CH_{Ar}), 129.0 (2×CH_{Ar}), 131.9, 138.2 (C_{Ar}), 139.9 (CH_{Ar}), 141.0, 144.4 (C_{Ar}), 159.5

(*C*OH), 171.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3024 (w), 2951 (m), 2922 (s), 2852 (m), 1938 (w), 1745 (w), 1663 (m), 1598 (w), 1582 (w), 1477 (m), 1437 (s), 1410 (m), 1340 (m), 1292 (m), 1234 (m), 1197 (m), 1162 (m), 1072 (m), 1024 (m), 999 (m), 909 (w), 842 (w), 813 (m), 737 (s), 698 (s), 689 (s), 631 (w), 596 (w), 572 (w), 531 (w). GC-MS (EI, 70 eV): *m/z* (%) = 476 ($[M]^+$, 14), 444 (11), 368 (35), 336 (77), 318 (9), 304 (52), 210 (100), 182 (18), 152 (16), 129 (11), 116 (22), 43 (17). HRMS (EI): Calcd. for $C_{30}H_{36}O_3S$ ($[M]^+$): 476.23797; found: 476.238503

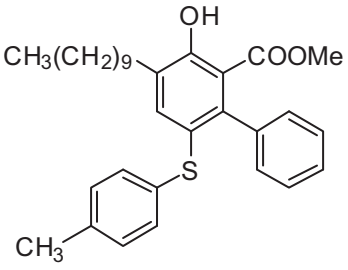
Methyl 4-ethyl-3-hydroxy-6-(p-tolylthio)biphenyl-2-carboxylate (17e)



Chemical Formula: $C_{23}H_{22}O_3S$
Exact Mass: 378,129

Starting with **16b** (0.448 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **17e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.210 g, 37 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.07 (s, 3 H, CH_3), 2.49 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.20 (s, 3 H, OCH_3), 6.65 - 6.73 (m, 2 H, CH_{Ar}), 6.87 - 6.91 (m, 3 H, CH_{Ar}), 7.08 (s, 1 H, CH_{Ar}), 7.10 - 7.13 (m, 4 H, CH_{Ar}), 10.87 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8, 22.5 (CH_3), 24.1 (CH_2), 53.1 (OCH_3), 114.5 (*C*$COOCH_3$), 125.9 (C_{Ar}), 127.6, 128.0, 128.1 (CH_{Ar}), 128.5 (2×CH_{Ar}), 128.8, 129.2 (CH_{Ar}), 129.9 (2×CH_{Ar}), 134.3, 134.8, 139.8 (C_{Ar}), 140.0 (CH_{Ar}), 142.2, 145.3 (C_{Ar}), 160.6 (*C*OH), 172.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 3025 (w), 2963 (m), 2932 (m), 2908 (w), 2873 (w), 1934 (w), 1731 (m), 1662 (s), 1592 (m), 1574 (m), 1436 (s), 1413 (m), 1342 (m), 1289 (m), 1231 (s), 1197 (m), 1163 (m), 1080 (m), 1027 (m), 970 (m), 907 (w), 845 (m), 815 (m), 774 (m), 750 (m), 699 (s), 689 (m), 629 (w). GC-MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, 38), 346 (100), 254 (17), 223 (62), 205 (13), 184 (9), 165 (25), 124 (12), 105 (11), 91 (31), 77 (16), 44 (30). HRMS (EI): Calcd. for $C_{23}H_{22}O_3S$ ($[M]^+$): 378.12842; found: 378.128189

Methyl 4-decyl-3-hydroxy-6-(p-tolylthio)biphenyl-2-carboxylate (17f)

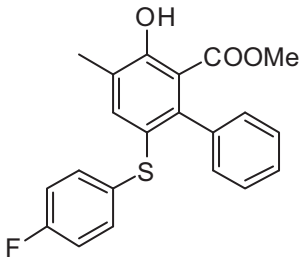


Chemical Formula: $C_{31}H_{38}O_3S$
Exact Mass: 490,254

Starting with **16b** (0.448 g, 1.5 mmol) and **4r** (0.661 g, 1.65 mmol), **17f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.280 g, 38 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_9CH_3$), 1.07 - 1.10 (m, 14 H, 7×CH_2), 1.38 - 1.47 (m, 2 H, CH_2), 2.06 (s, 3 H, CH_3), 2.45 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.19

(s, 3 H, OCH_3), 6.65 - 6.69 (m, 2 H, CH_{Ar}), 6.87 - 6.90 (m, 3 H, CH_{Ar}), 7.07 - 7.12 (m, 5 H, CH_{Ar}), 10.86 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3, 22.5 (CH_3), 23.9, 30.3, 30.5, 30.6, 30.7, 30.8, 30.9, 31.1, 33.1 (CH_2), 53.0 (OCH_3), 114.5 (*C*$COOCH_3$), 125.7 (C_{Ar}), 127.5, 128.0 (CH_{Ar}), 128.4 (2×CH_{Ar}), 128.8, 129.3 (CH_{Ar}), 129.8 (2×CH_{Ar}), 131.0 (CH_{Ar}), 133.0, 138.9, 139.7 (C_{Ar}), 140.8 (CH_{Ar}), 142.2, 145.3 (C_{Ar}), 160.6 (*C*OH), 172.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 3025 (w), 2951 (m), 2922 (s), 2852 (m), 1934 (w), 1749 (w), 1716 (w), 1704 (w), 1662 (s), 1592 (m), 1574 (w), 1437 (s), 1412 (m), 1339 (m), 1291 (m), 1234 (s), 1197 (m), 1162 (m), 1073 (w), 998 (m), 908 (w), 844 (m), 813 (m), 767 (m), 749 (m), 698 (s), 631 (w), 595 (w), 542 (w). GC-MS (EI, 70 eV): *m/z* (%) = 490 ($[M]^+$, 5), 458 (6), 336 (32), 223 (11), 210 (100), 181 (19), 152 (29), 129 (14), 116 (31), 91 (16), 71 (16), 43 (33). HRMS (EI): Calcd. for $C_{31}H_{38}O_3S$ ($[M]^+$): 490.25362; found: 490.254117

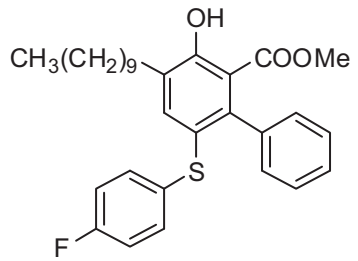
Methyl 6-(4-fluorophenylthio)-3-hydroxy-4-methylbiphenyl-2-carboxylate (17g)



Chemical Formula: $C_{21}H_{17}FO_3S$
Exact Mass: 368,088

Starting with **16c** (0.454 g, 1.5 mmol) and **4e** (0.453 g, 1.65 mmol), **17g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.238 g, 43 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_3), 3.30 (s, 3 H, OCH_3), 6.94 - 6.99 (m, 4 H, CH_{Ar}), 7.18 - 7.25 (m, 6 H, CH_{Ar}), 10.98 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.9 (CH_3), 50.9 (OCH_3), 112.2 (*C*$COOCH_3$), 115.0 (d, $^2J_{C,F}$ = 21.9 Hz), 125.9, 126.3 (CH_{Ar}), 126.4 (C_{Ar}), 126.6, 127.1, 127.7 (CH_{Ar}), 131.1 (d, $^3J_{C,F}$ = 8.1 Hz), 131.4 (d, $^4J_{C,F}$ = 3.2 Hz), 138.4 (CH_{Ar}), 139.8, 141.9, 142.6 (C_{Ar}), 158.6 (*C*OH), 160.7 (d, $^1J_{C,F}$ = 246.5 Hz),170.4 (CO). ^{19}F NMR (285 MHz, $CDCl_3$); δ = -115.6 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3059 (w), 3025 (w), 2951 (w), 2926 (w), 2902 (w), 2854 (w), 1729 (w), 1664 (m), 1613 (w), 1599 (w), 1488 (m), 1437 (m), 1408 (m), 1338 (m), 1280 (m), 1243 (s), 1228 (s), 1197 (m), 1155 (m), 1086 (m), 1013 (m), 943 (w), 827 (s), 809 (s), 760 (m), 698 (s), 678 (m), 628 (m), 595 (w), 564 (w), 548 (w). GC-MS (EI, 70 eV): *m/z* (%) = 368 ($[M]^+$, 28), 336 (100), 240 (11), 209 (26), 184 (10), 152 (15), 128 (7). HRMS (EI): Calcd. for $C_{21}H_{17}O_3FS$ ($[M]^+$): 368.08769; found: 368.088033

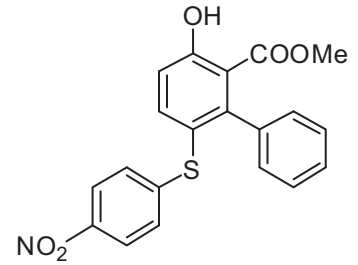
Methyl 4-decyl-6-(4-fluorophenylthio)-3-hydroxybiphenyl-2-carboxylate (17h)



Chemical Formula: $C_{30}H_{35}FO_3S$
Exact Mass: 494,229

Starting with **16c** (0.454 g, 1.5 mmol) and **4r** (0.661 g, 1.65 mmol), **17h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.334 g, 45 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_9CH_3$), 1.07 - 1.10 (m, 14 H, 7×CH_2), 1.38 - 1.42 (m, 2 H, CH_2), 2.44 (t, ^3J = 7.4 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.19 (s, 3 H, OCH_3), 6.69 - 6.74 (m, 2 H, CH_{Ar}), 6.83 - 6.89 (m, 4 H, CH_{Ar}), 7.11 - 7.13 (m, 4 H, CH_{Ar}), 10.84 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 23.9, 30.3, 30.5, 30.6, 30.7 (CH_2), 30.8 (2×CH_2), 30.9, 33.1 (CH_2), 53.1 (OCH_3), 114.6 (*C*$COOCH_3$), 117.1 (d, $^2J_{C,F}$ = 22.0 Hz), 126.3 (C_{Ar}), 127.8 (CH_{Ar}), 128.5 (2×CH_{Ar}), 129.9 (2×CH_{Ar}), 133.1 (d, $^3J_{C,F}$ = 8.0 Hz), 133.8 (d, $^4J_{C,F}$ = 3.3 Hz), 134.9 (C_{Ar}), 140.1 (CH_{Ar}), 142.1, 144.8 (C_{Ar}), 160.5 (*C*OH), 162.9 (d, $^1J_{C,F}$ = 246.0 Hz), 172.7 (CO). ^{19}F NMR (285 MHz, $CDCl_3$); δ = -115.7 IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3025 (w), 2951 (m), 2922 (s), 2852 (m), 1935 (w), 1873 (w), 1746 (w), 1704 (w), 1663 (m), 1589 (m), 1556 (w), 1488 (s), 1437 (s), 1409 (m), 1339 (m), 1292 (m), 1227 (s), 1197 (m), 1155 (s), 1085 (w), 1012 (w), 999 (m), 883 (w), 822 (m), 749 (m), 698 (s), 626 (m), 598 (w), 573 (w). GC-MS (EI, 70 eV): *m/z* (%) = 494 ($[M]^+$, 100), 462 (79), 377 (12), 335 (29), 240 (26), 209 (99), 152 (6), 128 (6). HRMS (EI): Calcd. for $C_{30}H_{35}O_3FS$ ($[M]^+$): 494.22855; found: 494.229150

Methyl 3-hydroxy-6-(4-nitrophenylthio)biphenyl-2-carboxylate (17i)

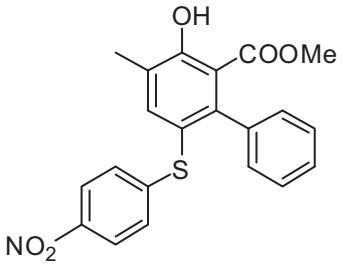


Chemical Formula: $C_{20}H_{15}NO_5S$
Exact Mass: 381,067

Starting with **16d** (0.494 g, 1.5 mmol) and **4a** (0.430 g, 1.65 mmol), **17i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.200 g, 35 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.33 (s, 3 H, OCH_3), 6.88 - 6.93 (m, 4 H, CH_{Ar}), 7.06 (d, ^3J = 8.7 Hz, 1 H, CH_{Ar}), 7.17 - 7.19 (m, 3 H, CH_{Ar}), 7.60 (d, ^3J = 8.7 Hz, 1 H, CH_{Ar}), 7.91 - 7.94 (m, 2 H, CH_{Ar}), 11.03 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.2 (OCH_3), 113.6 (*C*$COOCH_3$), 118.0 (CH_{Ar}), 120.1 (C_{Ar}), 122.8 (2×CH_{Ar}), 125.1 (2×CH_{Ar}), 126.3 (CH_{Ar}), 126.4 (2×CH_{Ar}), 127.0 (2×CH_{Ar}), 139.3 (C_{Ar}), 141.1 (CH_{Ar}), 144.1, 148.2, 148.5 (C_{Ar}), 161.9 (*C*OH), 169.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3093 (w), 3060 (w), 3024 (w), 2959 (w), 2924 (w), 2852 (w), 1737 (w), 1666 (m), 1574 (m), 1510 (m), 1476 (w), 1437 (m), 1334 (s), 1259 (m),

1214 (m), 1083 (m), 1012 (m), 902 (w), 852 (m), 796 (m), 741 (m), 700 (m), 643 (w), 625 (w), 613 (w), 575 (w), 544 (w). GC-MS (EI, 70 eV): *m/z* (%) = 381 ($[M]^+$, 39), 349 (100), 319 (24), 303 (7), 274 (7), 247 (10), 202 (6), 171 (23), 139 (13). HRMS (EI): Calcd. for $C_{20}H_{15}O_5NS$ ($[M]^+$): 381.06654; found: 381.066907

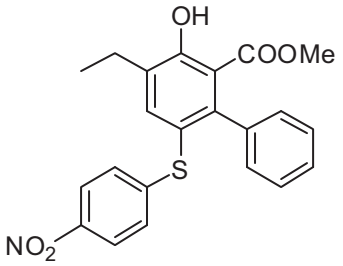
Methyl 3-hydroxy-4-methyl-6-(4-nitrophenylthio)biphenyl-2-carboxylate (17j)



Chemical Formula: $C_{21}H_{17}NO_5S$
Exact Mass: 395,083

Starting with **16d** (0.494 g, 1.5 mmol) and **4e** (0.453 g, 1.65 mmol), **17j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a crystalline solid (0.285 g, 48 %). mp. 124 - 126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3H, CH_3), 3.26 (s, 3 H, OCH_3), 6.81 - 6.87 (m, 4 H, CH_{Ar}), 7.08 - 7.13 (m, 3 H, CH_{Ar}), 7.43 (s, 1H, CH_{Ar}), 7.83 - 7.88 (m, 2 H, CH_{Ar}), 11.20 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8 (CH_3), 51.1 (OCH_3), 112.7 (*C*COOMe), 118.8 (C_{Ar}), 122.8 (2×CH_{Ar}), 124.9 (2×CH_{Ar}), 126.0 (CH_{Ar}), 126.2 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 127.5, 139.5 (C_{Ar}), 141.5 (CH_{Ar}), 144.0, 146.0, 148.7 (C_{Ar}), 160.5 (*C*OH), 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3101 (w), 3088 (w), 3059 (w), 3021 (w), 2952 (w), 2922 (w), 2903 (w), 2855 (w), 1723 (w), 1713 (w), 1668 (m), 1592 (m), 1572 (m), 1499 (m), 1475 (m), 1439 (m), 1398 (m), 1326 (s), 1243 (s), 1196 (s), 1158 (s), 1108 (m), 1018 (m), 945 (m), 884 (m), 846 (s), 810 (s), 743 (s), 678 (s), 624 (m), 542 (m); GC-MS (EI, 70 eV): *m/z* (%) = 395 ($[M]^+$, 27), 363 (100), 333 (25), 316 (5), 219 (38), 209 (21), 184 (9), 152 (10), 129 (10), 93 (6), 73 (12); HRMS (EI): Calcd. for $C_{21}H_{17}NO_5S$ ($[M]^+$): 395.07547; found: 395.0754

Methyl 4-ethyl-3-hydroxy-6-(4-nitrophenylthio)biphenyl-2-carboxylate (17k)

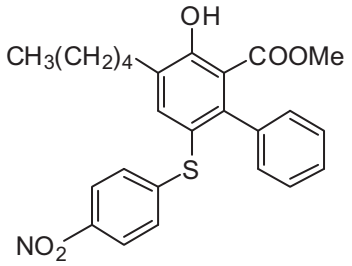


Chemical Formula: $C_{22}H_{19}NO_5S$
Exact Mass: 409,098

Starting with **16d** (0.494 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **17k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.246 g, 40 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.68 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.32 (s, 3 H, OCH_3), 6.86 - 6.93 (m, 4 H, CH_{Ar}), 7.13 - 7.19 (m, 3 H, CH_{Ar}), 7.48 (s, 1 H, CH_{Ar}), 7.88 - 7.94 (m, 2 H, CH_{Ar}), 11.25 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.5 (CH_3), 21.9 (CH_2), 51.1 (OCH_3), 113.0 (*C*COOCH$_3$), 119.0 (C_{Ar}), 122.8 (2×CH_{Ar}), 124.9 (2×CH_{Ar}), 126.1 (CH_{Ar}), 126.2 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 133.2, 139.6 (C_{Ar}), 140.0

(CH_{Ar}), 143.9, 146.0, 148.7 (C_{Ar}), 160.1 (*C*OH), 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3107 (w), 3089 (w), 3062 (w), 3025 (w), 2961 (w), 2929 (w), 2851 (w), 1659 (m), 1593 (m), 1575 (m), 1556 (w), 1504 (m), 1476 (m), 1434 (m), 1407 (m), 1353 (m), 1332 (s), 1260 (m), 1197 (m), 1109 (m), 1016 (m), 926 (m), 853 (m), 787 (m), 740 (s), 699 (s), 650 (m), 625 (m), 565 (m), 542 (m). GC-MS (EI, 70 eV): *m/z* (%) = 409 ($[M]^+$, 30), 377 (100), 347 (49), 254 (15), 223 (70), 205 (31), 184 (12), 165 (26), 129 (12), 93 (12), 69 (8). HRMS (EI): Calcd. for $C_{22}H_{19}O_5NS$ ($[M]^+$): 409.09784; found: 409.098809

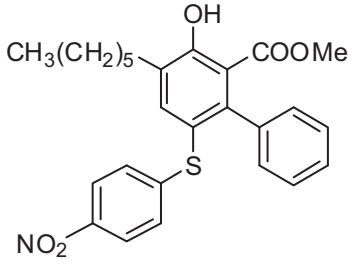
Methyl 3-hydroxy-6-(4-nitrophenylthio)-4-pentylbiphenyl-2-carboxylate (17l)



Chemical Formula: $C_{25}H_{25}NO_5S$
Exact Mass: 451,145

Starting with **16d** (0.494 g, 1.5 mmol) and **4j** (0.546 g, 1.65 mmol), **17l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.325 g, 48 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_4CH_3$), 1.26 - 1.30 (m, 4 H, 2×CH_2), 1.56 - 1.61 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_3CH_3$), 3.31 (s, 3 H, OCH_3), 6.86 - 6.93 (m, 4 H, CH_{Ar}), 7.15 - 7.19 (m, 3 H, CH_{Ar}), 7.46 (s, 1 H, CH_{Ar}), 7.89 - 7.92 (m, 2 H, CH_{Ar}), 11.23 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0 (CH_3), 21.5, 27.8, 28.7, 30.6 (CH_2), 51.1 (OCH_3), 113.0 (*C*$COOCH_3$), 118.9 (C_{Ar}), 122.8 (2×CH_{Ar}), 124.9 (2×CH_{Ar}), 126.1 (CH_{Ar}), 126.3 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 132.0, 139.6 (C_{Ar}), 140.8 (CH_{Ar}), 143.9, 146.0, 148.8 (C_{Ar}), 160.1 (*C*OH), 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3024 (w), 2952 (w), 2926 (w), 2857 (w), 1746 (w), 1711 (w), 1662 (m), 1632 (w), 1594 (m), 1577 (m), 1512 (m), 1438 (m), 1409 (m), 1333 (s), 1296 (m), 1233 (m), 1198 (m), 1162 (m), 1109 (m), 1011 (m), 952 (w), 852 (m), 812 (m), 750 (m), 699 (m), 681 (m), 626 (w), 543 (w). GC-MS (EI, 70 eV): *m/z* (%) = 451 ($[M]^+$, 64), 419 (70), 402 (10), 389 (40), 363 (11), 346 (46), 265 (25), 240 (22), 209 (100), 152 (11). HRMS (EI): Calcd. for $C_{25}H_{25}O_5NS$ ($[M]^+$): 451.14480; found: 451.145724

Methyl 4-hexyl-3-hydroxy-6-(4-nitrophenylthio)biphenyl-2-carboxylate (17m)

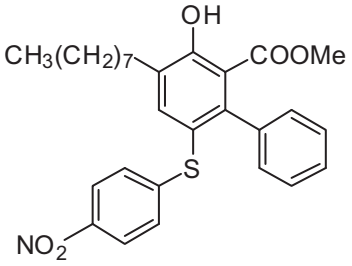


Chemical Formula: $C_{26}H_{27}NO_5S$
Exact Mass: 465,161

Starting with **16d** (0.494 g, 1.5 mmol) and **4k** (0.569 g, 1.65 mmol), **17m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.293 g, 42 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_5CH_3$), 1.08 - 1.19 (m, 6 H, 3×CH_2), 1.40 - 1.50 (m, 2

H, CH_2), 2.53 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.21 (s, 3 H, OCH_3), 6.76 - 6.83 (m, 4 H, CH_{Ar}), 7.03 - 7.08 (m, 3 H, CH_{Ar}), 7.36 (s, 1 H, CH_{Ar}), 7.79 - 7.83 (m, 2 H, CH_{Ar}), 11.13 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 23.8, 30.3, 30.4, 31.0, 32.8 (CH_2), 53.3 (OCH_3), 115.2 (*C*$COOCH_3$), 121.1 (C_{Ar}), 125.0 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 128.3 (CH_{Ar}), 128.5 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 134.2, 141.8 (C_{Ar}), 143.0 (CH_{Ar}), 146.1, 148.2, 151.0 (C_{Ar}), 162.3 (*C*OH), 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3059 (w), 3024 (w), 2953 (w), 2926 (m), 2855 (w), 2258 (w), 1932 (w), 1664 (m), 1594 (w), 1578 (m), 1514 (w), 1438 (m), 1409 (m), 1333 (s), 1234 (m), 1198 (m), 1161 (m), 1110 (w), 1085 (m), 1010 (w), 907 (m), 851 (m), 839 (m), 768 (m), 729 (s), 698 (s), 681 (m), 648 (m), 626 (w), 544 (w). GC-MS (EI, 70 eV): *m/z* (%) = 465 ($[M]^+$, 100), 403 (24), 346 (80), 316 (9), 279 (22), 209 (96), 152 (11). HRMS (EI): Calcd. for $C_{26}H_{27}O_5NS$ ($[M]^+$): 465.16827; found: 465.16793

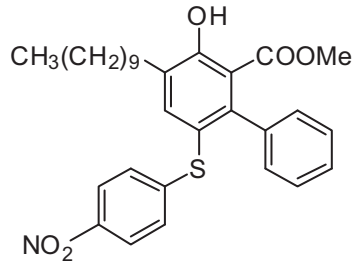
Methyl 3-hydroxy-6-(4-nitrophenylthio)-4-octylbiphenyl-2-carboxylate (17n)



Chemical Formula: $C_{28}H_{31}NO_5S$
Exact Mass: 493,192

Starting with **16d** (0.494 g, 1.5 mmol) and **4o** (0.615 g, 1.65 mmol), **17n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.333 g, 45 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 6.9 Hz, 3 H, $(CH_2)_7CH_3$), 1.17 - 1.22 (m, 10 H, 5×CH_2), 1.53 - 1.60 (m, 2 H, CH_2), 2.63 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.31 (s, 3 H, OCH_3), 6.86 - 6.93 (m, 3 H, CH_{Ar}), 7.15 - 7.19 (m, 4 H, CH_{Ar}), 7.46 (s, 1 H, CH_{Ar}), 7.90 - 7.93 (m, 2 H, CH_{Ar}), 11.23 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.6, 28.1, 28.3, 28.4, 28.6, 28.7, 30.8 (CH_2), 51.1 (OCH_3), 113.0 (*C*$COOCH_3$), 118.8 (C_{Ar}), 122.8 (2×CH_{Ar}), 124.9 (2×CH_{Ar}), 126.1 (CH_{Ar}), 126.3 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 132.0, 139.6 (C_{Ar}), 140.8 (CH_{Ar}), 143.9, 146.0, 148.8 (C_{Ar}), 160.1 (*C*OH), 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 2923 (m), 2853 (m), 1746 (w), 1714 (w), 1664 (m), 1627 (w), 1595 (w), 1579 (w), 1516 (m), 1438 (m), 1408 (m), 1334 (s), 1233 (m), 1198 (m), 1162 (m), 1085 (m), 1011 (m), 909 (w), 852 (m), 814 (m), 741 (m), 699 (m), 681 (m), 626 (w), 543 (w). GC-MS (EI, 70 eV): *m/z* (%) = 493 ($[M]^+$, 6), 463 (90), 431 (100), 405 (10), 374 (12), 333 (16), 307 (23), 253 (16), 240 (89), 221 (23), 209 (98), 184 (22), 152 (35), 124 (55), 105 (22), 93 (56), 55 (51). HRMS (EI): Calcd. for $C_{28}H_{31}O_5NS$ ($[M]^+$): 493.18502; found: 493.18489

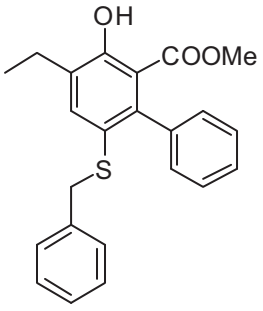
Methyl 4-decyl-3-hydroxy-6-(4-nitrophenylthio)biphenyl-2-carboxylate (17o)



Chemical Formula: $C_{30}H_{35}NO_5S$
Exact Mass: 521,224

Starting with **16d** (0.494 g, 1.5 mmol) and **4r** (0.661 g, 1.65 mmol), **17o** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.391 g, 50 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_9CH_3$), 1.07 - 1.11 (m, 14 H, 7×CH_2), 1.40 - 1.50 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.4 Hz, 2 H, $CH_2(CH_2)_8CH_3$), 3.21 (s, 3 H, OCH_3), 6.76 - 6.82 (m, 4 H, CH_{Ar}), 7.05 - 7.09 (m, 3 H, CH_{Ar}), 7.36 (s, 1 H, CH_{Ar}), 7.79 - 7.82 (m, 2 H, CH_{Ar}), 11.12 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3 (CH_3), 23.9, 30.3, 30.5, 30.6, 30.7, 30.8, 30.9, 31.0, 33.1 (CH_2), 53.3 (OCH_3), 115.2 (CCOOCH$_3$), 121.0 (C_{Ar}), 125.0 (2×CH_{Ar}), 127.1 (2×CH_{Ar}), 128.3 (CH_{Ar}), 128.5 (2×CH_{Ar}), 129.3 (2×CH_{Ar}), 134.2, 141.8 (C_{Ar}), 143.0 (CH_{Ar}), 146.1, 148.2, 151.0 (C_{Ar}), 162.3 (COH), 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2922 (m), 2852 (m), 1934 (w), 1748 (w), 1704 (w), 1664 (m), 1594 (w), 1578 (m), 1515 (m), 1438 (m), 1408 (m), 1334 (s), 1233 (m), 1198 (m), 1163 (m), 1085 (m), 1010 (m), 909 (w), 851 (m), 814 (m), 741 (m), 698 (m), 681 (m), 626 (w), 543 (w). GC-MS (EI, 70 eV): *m/z* (%) = 521 ([M]$^+$, 97), 489 (50), 472 (11), 459 (22), 404 (13), 362 (29), 346 (44), 335 (19), 240 (17), 209 (100), 180 (7), 152 (9), 116 (21), 101 (9). HRMS (EI): Calcd. for $C_{30}H_{35}O_5NS$ ([M]$^+$): 521.23087; found: 521.23025

Methyl 6-(benzylthio)-4-ethyl-3-hydroxybiphenyl-2-carboxylate (17p)

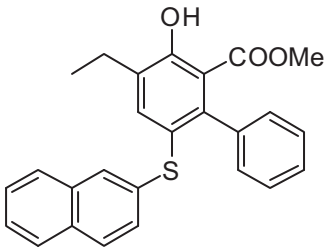


Chemical Formula: $C_{23}H_{22}O_3S$
Exact Mass: 378,129

Starting with **16e** (0.448 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **17p** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.267 g, 47 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.48 (s, 2 H, CH_2), 2.57 (q, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 3.28 (s, 3 H, OCH_3), 6.93 - 6.97 (m, 4 H, CH_{Ar}), 7.18 - 7.23 (m, 7 H, CH_{Ar}), 10.85 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.5 (CH_3), 21.8, 39.2 (CH_2), 50.8 (OCH_3), 112.1 (CCOOCH$_3$), 125.7, 125.9 (CH_{Ar}), 126.2 (2×CH_{Ar}), 126.6, 127.1 (C_{Ar}), 127.3 (2×CH_{Ar}), 127.5 (CH_{Ar}), 127.9 (2×CH_{Ar}), 128.4 (CH_{Ar}), 136.4, 136.5 (C_{Ar}), 137.0 (CH_{Ar}), 140.1 (C_{Ar}), 157.7 (COH), 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 3027 (w), 2963 (w), 2932 (w), 2873 (w), 1935 (w), 1728 (w), 1662 (m), 1597 (m), 1494 (w), 1435 (m), 1337 (m), 1276 (m), 1230 (m), 1196 (m), 1160 (m), 1069 (m), 1013 (m),

969 (m), 843 (m), 748 (m), 696 (s), 646 (m), 629 (m), 562 (m). GC-MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, 2), 346 (5), 255 (8), 120 (50), 105 (100), 91 (94), 77 (51), 65 (22), 51 (18). HRMS (EI): Calcd. for $C_{23}H_{22}O_3S$ ($[M]^+$): 378.12842; found: 378.12826

Methyl 4-ethyl-3-hydroxy-6-(naphthalen-2-ylthio)biphenyl-2-carboxylate (17q)



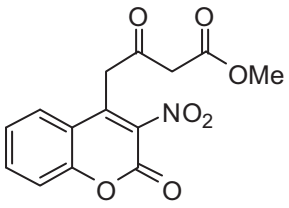
Chemical Formula: $C_{26}H_{22}O_3S$
Exact Mass: 414,129

Starting with **16f** (0.502 g, 1.5 mmol) and **4f** (0.476 g, 1.65 mmol), **17q** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as yellowish oil (0.324 g, 52 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.47 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.20 (s, 3 H, OCH_3), 6.89 - 6.99 (m, 3 H, CH_{Ar}), 7.07 - 7.10 (m, 3 H, CH_{Ar}), 7.22 - 7.28 (m, 4 H, CH_{Ar}), 7.45 - 7.49 (m, 2 H, CH_{Ar}), 7.55 - 7.58 (m, 1 H, CH_{Ar}), 10.93 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8 (CH_3), 24.2 (CH_2), 53.1 (OCH_3), 114.6 (*C*$COOCH_3$), 125.5 (C_{Ar}), 126.9, 127.7, 128.1, 128.4 (CH_{Ar}), 128.5 (2×CH_{Ar}), 128.8, 128.9, 129.4, 129.6, (CH_{Ar}), 129.8 (2×CH_{Ar}), 133.0, 134.6, 134.9, 136.7 (C_{Ar}), 140.2 (CH_{Ar}), 142.2, 145.6 (C_{Ar}), 160.8 (*C*OH), 172.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3052 (w), 3024 (w), 2963 (w), 2950 (w), 2932 (w), 2873 (w), 1932 (w), 1698 (w), 1660 (s), 1591 (m), 1499 (w), 1435 (m), 1337 (m), 1290 (m), 1229 (s), 1195 (m), 1161 (m), 1063 (m), 967 (m), 847 (m), 743 (s), 697 (s), 628 (m), 600 (m), 529 (m). GC-MS (EI, 70 eV): *m/z* (%) = 414 ($[M]^+$, 37), 382 (100), 254 (35), 223 (40), 160 (31), 128 (47), 77 (9), 63 (7), 44 (8). HRMS (EI): Calcd. for $C_{26}H_{22}O_3S$ ($[M]^+$): 414.12842; found: 414.128590

The General procedure for the synthesis of compounds 19a-19k.

To a stirred dichloromethane solution (2 mL /1 mmol of starting materials) of 4-chloro-3-nitrocoumarin **18** (1.0 equiv) and 1,3-bis(silyl enol ether) **4** (1.1 equiv) was added $TiCl_4$ (1.1 equiv) at −78 °C under an argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C in the period of 14 h. To the solution was added hydrochloric acid (10 %, 20 mL) and the mixture was extracted with dichloromethane (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, *n*-heptane/ EtOAc) to give **19a-19k**

Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxobutanoate (19a)

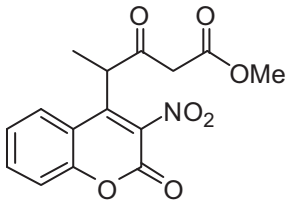


Chemical Formula: $C_{14}H_{11}NO_7$
Exact Mass: 305,054

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4a** (0.430 g, 1.65 mmol), **19a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.266 g, 58 %). mp. 153 - 155 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.20

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.67 (s, 3 H, OCH_3), 3.92 (s, 2H, CH_2), 4.49 (s, 2H, CH_2), 7.49 - 7.60 (m, 2 H, CH_{Ar}), 7.80 - 7.83 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 41.3, 48.3 (CH_2), 52.0 (OCH_3), 117.0 (C_{Ar}), 117.1, 125.6, 127.9, 134.6 (CH_{Ar}), 137.5, 143.2 (C_{Ar}), 151.8 (CO), 152.8 (C_{Ar}), 167.1, 197.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3438 (w), 3270 (w), 2249 (w), 2124 (w), 1738 (w), 1536 (w), 1053 (s), 1024 (s), 1006 (s), 927 (w), 820 (m), 757 (m), 730 (w), 644 (w), 622 (w), 613 (w). (ESI): Calcd. for $C_{14}H_{12}NO_7$ ($[M+H]^+$): 306.06083; found: 306.06049.

Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxopentanoate (19b)

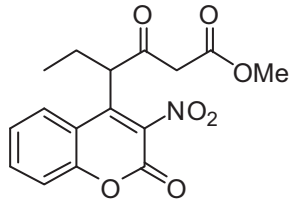


Chemical Formula: $C_{15}H_{13}NO_7$
Exact Mass: 319,069

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4e** (0.453 g, 1.65 mmol), **19b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.324 g, 68 %). mp. 135 - 137 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.21

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.60 (d, ^3J = 7.0 Hz, 3 H, CH_3), 3.35 (d, ^2J = 16.0 Hz, 1H, CH_2), 3.50 (d, ^2J = 16.0 Hz, 1H, CH_2), 3.61 (s, 3 H, OCH_3), 4.00 (q, ^3J = 7.0 Hz, 1 H, CH), 7.30 - 7.42 (m, 2 H, CH_{Ar}), 7.51 - 7.54 (m, 1 H, CH_{Ar}), 7.61 - 7.66 (m, 1 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.0 (CH_3), 47.0 (CH_2), 48.2 (CH), 52.7 (OCH_3), 115.3 (C_{Ar}), 118.3, 126.0, 126.9 (CH_{Ar}), 128.0 (C_{Ar}), 134.4 (CH_{Ar}), 144.3 (C_{Ar}), 152.6 (CO), 152.7 (C_{Ar}), 166.4, 198.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3117 (w), 3079 (w), 3045 (w), 2992 (w), 2962 (w), 2929 (w), 1732 (s), 1704 (s), 1605 (m), 1536 (s), 1436 (m), 1362 (m), 1323 (m), 1282 (s), 1155 (m), 1070 (m), 1030 (m), 989 (s), 872 (m), 835 (m), 767 (s), 693 (m), 657 (m), 580 (m), 547(m). (ESI): Calcd. for $C_{15}H_{13}NNaO_7$ ($[M+Na]^+$): 342.0584; found: 342.0591. Anal. calcd for $C_{15}H_{13}NO_7$: C, 56.43; H, 4.08; N, 4.39. Found: C, 56.94; H, 4.36; N, 4.21.

Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxohexanoate (19c)

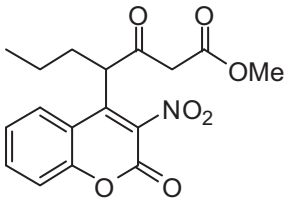


Chemical Formula: $C_{16}H_{15}NO_7$
Exact Mass: 333,085

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4f** (0.476 g, 1.65 mmol), **19c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.288 g, 58 %). mp. 99 - 100 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.32

^{1}H NMR (250 MHz, $CDCl_3$) : δ = 0.86 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.81 - 1.97 (m, 1 H, $CHCH_2CH_3$), 2.31 - 2.45 (m, 1 H, $CHCH_2CH_3$), 3.35 (d, ^2J = 16.1 Hz, 1H, CH_2), 3.54 (d, ^2J = 16.1 Hz, 1H, CH_2), 3.59 (s, 3 H, OCH_3), 3.67 - 3.78 (m, 1 H, CH), 7.28 - 7.41 (m, 2 H, CH_{Ar}), 7.59 - 7.66 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.1 (CH_3), 22.9, 47.4 (CH_2), 52.6 (OCH_3), 56.0 (CH), 115.5 (C_{Ar}), 118.2, 126.0, 127.2 (CH_{Ar}), 128.1 (C_{Ar}), 134.4 (CH_{Ar}), 142.8 (C_{Ar}), 152.6 (CO), 152.7 (C_{Ar}), 166.4, 198.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2975 (w), 2957 (w), 2923 (w), 2877 (w), 1737 (s), 1719 (s), 1605 (m), 1544 (s), 1436 (m), 1362 (m), 1327 (m), 1245 (s), 1148 (s), 1069 (m), 1047 (m), 994 (m), 899 (m), 837 (m), 774 (m), 755 (s), 656 (s), 590 (m), 561(m), 533 (m). (ESI): Calcd. for $C_{16}H_{16}NO_7$ ($[M+H]^+$): 334.09213; found: 334.09214. Anal. calcd for $C_{16}H_{15}NO_7$: C, 57.66; H, 4.51; N, 4.20. Found: C, 57.52; H, 4.50; N, 4.06.

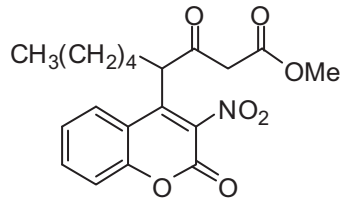
Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxoheptanoate (19d)



Chemical Formula: $C_{17}H_{17}NO_7$
Exact Mass: 347,101

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4h** (0.499 g, 1.65 mmol), **19d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.243 g, 47 %). R_f (*n*-heptane/EtOAc 4:1) = 0.33 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_2CH_3$), 1.08 - 1.29 (m, 2 H, CH_2), 1.65 - 1.78 (m, 1 H, $CHCH_2CH_2CH_3$), 2.23 - 2.35 (m, 1 H, $CHCH_2CH_2CH_3$), 3.29 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.49 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.55 (s, 3 H, OCH_3), 3.77 - 3.81 (m, 1 H, CH), 7.33 - 7.43 (m, 2 H, CH_{Ar}), 7.54 - 7.70 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.7 (CH_3), 21.1, 31.6, 47.4 (CH_2), 52.6 (OCH_3), 54.3 (CH), 115.6 (C_{Ar}), 118.2, 126.2, 127.2 (CH_{Ar}), 128.2 (C_{Ar}), 134.4 (CH_{Ar}), 143.1 (C_{Ar}), 152.6 (CO), 152.8 (C_{Ar}), 166.4, 198.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2960 (w), 2933 (w), 2874 (w), 1733 (s), 1604 (s), 1537 (s), 1448 (m), 1367 (m), 1320 (m), 1244 (m), 1139 (m), 1055 (s), 966 (m), 858 (m), 757 (s), 646 (m), 583 (m). (ESI): Calcd. for $C_{17}H_{16}NO_7$ ($[M-H]^+$): 346.0932; found: 346.0935.

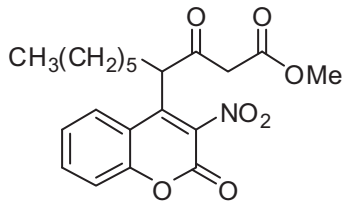
Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxononanoate (19e)



Chemical Formula: $C_{19}H_{21}NO_7$
Exact Mass: 375,132

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4j** (0.546 g, 1.65 mmol), **19e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.242 g, 43 %). R_f (*n*-heptane/EtOAc 4:1) = 0.49 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.77 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_4CH_3$), 1.16 - 1.21 (m, 6 H, 3×CH_2), 1.71 - 1.84 (m, 1 H, $CHCH_2(CH_2)_3CH_3$), 2.29 - 2.39 (m, 1 H, $CHCH_2(CH_2)_3CH_3$), 3.34 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.54 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.59 (s, 3 H, OCH_3), 3.80 - 3.85 (m, 1 H, CH), 7.28 - 7.41 (m, 2 H, CH_{Ar}), 7.59 - 7.65 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.8 (CH_3), 22.2, 27.4, 29.6, 31.3, 47.4 (CH_2), 52.6 (OCH_3), 54.6 (CH), 115.6 (C_{Ar}), 118.2, 126.0, 127.3 (CH_{Ar}), 128.3 (C_{Ar}), 134.4 (CH_{Ar}), 143.2 (C_{Ar}), 152.6 (CO), 152.8 (C_{Ar}), 166.4, 198.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 2930 (w), 2859 (w), 2258 (w), 1735 (s), 1605 (m), 1540 (s), 1449 (m), 1369 (m), 1245 (m), 1199 (m), 1063 (m), 907 (m), 844 (w), 760 (m), 726 (s), 648 (m), 583 (m). (ESI): Calcd. for $C_{19}H_{22}NO_7$ ($[M+H]^+$): 376.1391; found: 376.1395.

Methyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxodecanoate (19f)

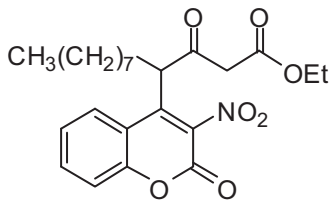


Chemical Formula: $C_{20}H_{23}NO_7$
Exact Mass: 389,147

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4k** (0.569 g, 1.65 mmol), **19f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a reddish-brown oil (0.321 g, 55 %). R_f (*n*-heptane/EtOAc 4:1) = 0.50 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.77 (t, ^3J = 6.8 Hz, 3 H, $(CH_2)_5CH_3$), 1.15 - 1.21 (m, 8 H, 4×CH_2), 1.71 - 1.84 (m, 1 H, $CH_2(CH_2)_4CH_3$), 2.31 - 2.39 (m, 1 H, $CH_2(CH_2)_4CH_3$), 3.34 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.54 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.60 (s, 3 H, OCH_3), 3.80 - 3.84 (m, 1 H, CH), 7.28 - 7.41 (m, 2 H, CH_{Ar}), 7.59 - 7.65 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 22.4, 27.7, 28.9, 29.6, 31.3, 47.4 (CH_2), 52.6 (OCH_3), 54.6 (CH), 115.6 (C_{Ar}), 118.2, 126.0, 127.3 (CH_{Ar}), 128.2 (C_{Ar}), 134.4 (CH_{Ar}), 143.2 (C_{Ar}), 152.6 (CO), 152.8 (C_{Ar}), 166.4, 198.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2927 (m), 2856 (w), 1733 (s), 1604 (m), 1539 (s), 1449 (m), 1369 (m), 1322 (m), 1245 (m), 1198 (m), 1060 (m), 908 (m), 758 (s), 730 (m), 656 (m), 583 (m). (ESI): Calcd. for $C_{20}H_{24}NO_7$ ($[M+H]^+$): 390.1547; found:

390.1546. Anal. calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95; N, 3.60. Found: C, 61.15; H, 5.92; N, 3.55.

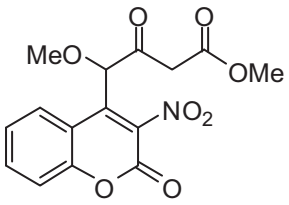
Ethyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxododecanoate (19g)



Chemical Formula: $C_{23}H_{29}NO_7$
Exact Mass: 431,194

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4p** (0.638 g, 1.65 mmol), **19g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a reddish-brown oil (0.265 g, 41 %). R_f (*n*-heptane/EtOAc 4:1) = 0.51 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, ^3J = 7.0 Hz, 3 H, $(CH_2)_7CH_3$), 1.12 - 1.19 (m, 12 H, 6 × CH_2, 3H, OCH_2CH_3), 1.72 - 1.84 (m, 1 H, $CHCH_2(CH_2)_6CH_3$), 2.29 - 2.40 (m, 1 H, $CHCH_2(CH_2)_6CH_3$), 3.32 (d, ^2J = 16.0 Hz, 1 H, CH_2), 3.52 (d, ^2J = 16.0 Hz, 1 H, CH_2), 3.82 - 3.86 (m, 1 H, CH), 4.06 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.28 - 7.40 (m, 2 H, CH_{Ar}), 7.60 - 7.65 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 14.0 (CH_3), 22.6, 27.8, 29.1 (2×CH_2), 29.2, 29.6, 31.7, 47.6 (CH_2), 54.6 (CH), 61.8 (OCH_2), 115.6 (C_{Ar}), 118.2, 125.9, 127.4 (CH_{Ar}), 127.5 (C_{Ar}), 134.4 (CH_{Ar}), 143.2 (C_{Ar}), 152.6 (CO), 152.8 (C_{Ar}), 166.0, 198.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2925 (m), 2855 (m), 1736 (s), 1605 (m), 1540 (s), 1450 (m), 1368 (m), 1244 (m), 1138 (m), 1057 (m), 1026 (m), 908 (m), 858 (m), 758 (s), 731 (s), 647 (m), 583 (m). ESI): Calcd. for $C_{23}H_{30}NO_7$ ($[M+H]^+$): 432.2017; found: 432.2017. Anal. calcd for $C_{23}H_{29}NO_7$: C, 64.02; H, 6.77; N, 3.25. Found: C, 64.39; H, 6.80; N, 3.04.

Methyl 4-methoxy-4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxobutanoate (19h)

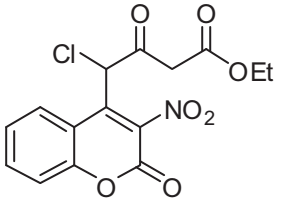


Chemical Formula: $C_{15}H_{13}NO_8$
Exact Mass: 335,064

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4w** (0.479 g, 1.65 mmol), **19h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.207 g, 41 %). mp 144 - 146 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.21 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.48 (s, 3 H, OCH_3), 3.54 (d, ^2J = 14.6 Hz, 1 H, CH_2), 3.61 (d, ^2J = 16.6 Hz, 1 H, CH_2), 3.79 (s, 3 H, OCH_3), 5.33 (s, 1 H, CH), 7.42 - 7.48 (m, 2 H, CH_{Ar}), 7.70 - 7.83 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 45.0 (CH_2), 52.6, 59.9 (OCH_3), 82.0 (CH), 116.2 (C_{Ar}), 117.6, 125.8, 127.3 (CH_{Ar}), 128.3 (C_{Ar}), 134.4 (CH_{Ar}), 142.5 (C_{Ar}), 152.3 (CO), 153.0 (C_{Ar}), 167.4, 198.3 (CO). IR (neat, cm^{-1}):

$\tilde{\nu}$ = 3099 (w), 3035 (w), 2954 (w), 2896 (w), 2839 (w), 1737 (s), 1721 (s), 1602 (m), 1539 (s), 1447 (m), 1333 (s), 1279 (s), 1136 (m), 1099 (s), 1051 (m), 999 (s), 890 (s), 835 (w), 784 (m), 756 (s), 659 (m), 629 (m), 558 (m), 530 (m). (ESI): Calcd. for $C_{15}H_{13}NNaO_8$ ($[M+Na]^+$): 358.0533; found: 358.0541.

Ethyl 4-chloro-4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxobutanoate (19i)

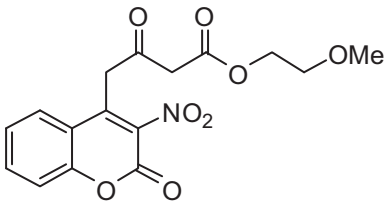


Chemical Formula: $C_{15}H_{12}ClNO_7$
Exact Mass: 353,030

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4v** (0.510 g, 1.65 mmol), **19i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.240 g, 45 %). mp. 135 - 137 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.22

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.07 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 3.53 (d, ^2J = 16.4 Hz, 1 H, CH_2), 3.69 (d, ^2J = 16.4 Hz, 1 H, CH_2), 4.00 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 5.08 (s, 1 H, CH), 7.17 - 7.26 (m, 2 H, CH_{Ar}), 7.47 - 7.53 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 45.5 (CH_2), 56.7 (CH), 62.4 (OCH_2), 114.2 (C_{Ar}), 118.0, 125.8, 127.9 (CH_{Ar}), 128.1 (C_{Ar}), 134.8 (CH_{Ar}), 140.2, 152.3 (C_{Ar}), 152.9, 165.7, 192.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2982 (w), 2939 (w), 2907 (w), 1732 (s), 1737 (s), 1604 (m), 1541 (s), 1450 (m), 1399 (w), 1367 (s), 1322 (m), 1240 (m), 1198 (m), 1095 (m), 1022 (m), 909 (m), 757 (s), 728 (s), 648 (m), 583 (m), 544 (m). (ESI): Calcd. for $C_{15}H_{13}ClNO_7$ ($[M+H]^+$): 354.0375; found: 354.0382.

2-Methoxyethyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxobutanoate (19j)



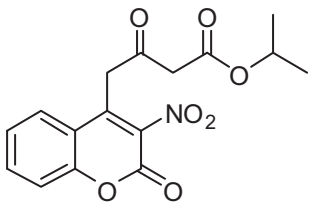
Chemical Formula: $C_{16}H_{15}NO_8$
Exact Mass: 349,080

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4d** (0.502 g, 1.65 mmol), **19j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.291 g, 56 %). mp 126 - 128 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.20

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.32 (s, 3 H, OCH_3), 3.58 (t, ^3J = 4.6 Hz, 2 H, $OCH_2CH_2OCH_3$), 3.63 (s, 2 H, CH_2), 4.21 (s, 2 H, CH_2), 4.30 (t, ^3J = 4.6 Hz, 2 H, $OCH_2CH_2OCH_3$), 7.33 - 7.38 (m, 2 H, CH_{Ar}), 7.60 - 7.68 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 41.7, 48.7 (CH_2), 59.0 (OCH_3), 64.8, 70.0 (OCH_2), 117.2 (C_{Ar}), 117.6, 125.9, 127.1 (CH_{Ar}), 128.3 (C_{Ar}), 134.6 (CH_{Ar}), 142.1 (C_{Ar}), 152.6 (CO), 152.7 (C_{Ar}), 166.9, 194.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3078 (w), 3051 (w), 3002 (w), 2964 (w), 2941 (w), 2834 (w),

1740 (m), 1723 (s), 1605 (m), 1542 (m), 1450 (m), 1368 (m), 1310 (m), 1178 (m), 1129 (m), 1078 (m), 990 (m), 870 (m), 761 (s), 653 (m), 586 (m), 546 (m). (ESI): Calcd. for $C_{16}H_{15}NNaO_8$ ($[M+Na]^+$): 372.069; found: 372.0695. Anal. calcd for $C_{16}H_{15}NO_8$: C, 55.02; H, 4.33; N, 4.01. Found: C, 55.48; H, 4.04; N, 3.93.

Isopropyl 4-(3-nitro-2-oxo-2H-chromen-4-yl)-3-oxobutanoate (19k)



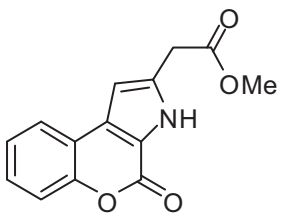
Chemical Formula: $C_{16}H_{15}NO_7$
Exact Mass: 333,085

Reaction started with **18** [4-chloro-3-nitrocoumarin] (0.338 g, 1.5 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene **4c** (0.476 g, 1.65 mmol), **19k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.200 g, 40 %). mp. 96 - 98 °C. R_f (*n*-heptane/EtOAc 4:1) = 0.31 ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23 (s, 3 H, OCH_3), 1.25 (s, 3 H, OCH_3), 3.55 (s, 2 H, CH_2), 4.19 (s, 2 H, CH_2), 5.01 - 5.10 (m, 1 H, CH), 7.33 - 7.38 (m, 2 H, CH_{Ar}), 7.60 - 7.65 (m, 2 H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.7 (2×CH_3), 41.9, 49.0 (CH_2), 70.1 (CH), 117.2 (C_{Ar}), 117.6, 125.9, 127.1 (CH_{Ar}), 128.1 (C_{Ar}), 134.5 (CH_{Ar}), 142.0 (C_{Ar}), 152.6 (CO), 152.7 (C_{Ar}), 166.5, 195.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 2937 (w), 2258 (w), 1721 (s), 1605 (m), 1537 (s), 1450 (m), 1371 (m), 1257 (m), 1199 (m), 1100 (s), 1068 (m), 963 (m), 908 (m), 801 (m), 758 (s), 728 (s), 648 (m), 587 (m), 531 (m). (ESI): Calcd. for $C_{16}H_{16}NO_7$ ($[M+H]^+$): 334.0921; found: 334.0919.

The General procedure for synthesis of chromeno[3,4-b]pyrrol-4(3H)-ones (20a-20k).

In a 50 mL one neck round Schlenk flask under a flow of dry argon 1 mmol of coumpound **19** and 0.05 g of 10 % Pd/C were placed. Afterwards, 25 mL of absolute degassed methanol was added. The system was washed three times with hydrogen and the hydrogenation was conducted with the help of a glass burette under the atmospheric pressure. After the 3 eq. of hydrogen was absorbed, the mixture was kept 3 days at r.t. till the spot of the product was appeared on the TLC. The reaction mixture was filtered through a Celite pad of 2-3 cm and the Celite was washed few times with methanol. The solvent was removed under reduced pressure and the residue was purified by preparative chromatography on silica gel, using heptanes/EtOAc.

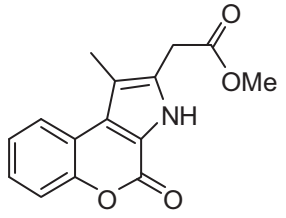
Methyl 2-(4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20a)



Chemical Formula: $C_{14}H_{11}NO_4$
Exact Mass: 257,069

Starting with **19a** (0.216 g, 0.71 mmol), **20a** was isolated (0.084 g, 46 %) by column chromatography (silica gel, Heptane/EtOAc) as yellowish oil. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.67 (s, 3 H, OCH_3), 3.89 (s, 2 H, CH_2), 6.79 (s, 1 H, CH), 7.32 - 7.43 (m, 3 H, CH_{Ar}), 7.92 - 7.94 (m, 1 H, CH_{Ar}), 12.60 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 32.9 (CH_2), 52.0 (OCH_3), 103.0 (CH), 115.7 (C_{Ar}), 116.7 (CH_{Ar}), 117.6 (C_{Ar}), 123.5, 124.2, 127.7 (CH_{Ar}), 129.1, 136.9, 150.7 (C_{Ar}), 153.8, 169.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3452 (w), 2249 (w), 2124 (w), 1716 (w), 1053 (s), 1024 (s), 1005 (s), 820 (m), 757 (m), 622 (w), 613 (w). GC-MS (EI, 70 eV): *m/z* (%) = 257 ([M]$^+$, 79), 198 (100), 170 (12), 140 (6), 115 (11). HRMS (EI): Calcd. for $C_{14}H_{11}O_4N$ ([M]$^+$): 257.06826; found: 257.068265.

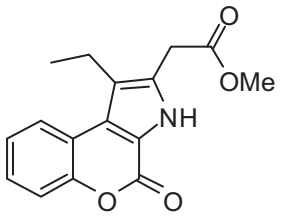
Methyl 2-(1-methyl-4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20b)



Chemical Formula: $C_{15}H_{13}NO_4$
Exact Mass: 271,084

Starting with **19b** (0.100 g, 0.31 mmol), **20b** was isolated (0.043 g, 51 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 211 - 213 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 3.70 (s, 3H, OCH_3), 3.77 (s, 2 H, CH_2), 7.23 - 7.37 (m, 3 H, CH_{Ar}), 7.87 - 7.90 (m, 1 H, CH_{Ar}), 10.26 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.0 (CH_3), 31.3 (CH_2), 52.6 (OCH_3), 113.5, 116.2 (C_{Ar}), 117.5 (CH_{Ar}), 119.1 (C_{Ar}), 123.3, 124.2, 127.3 (CH_{Ar}), 127.5 (C_{Ar}), 132.1, 151.3 (C_{Ar}), 155.5, 169.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3220 (m), 2953 (w), 2919 (m), 2851 (w), 1730 (m), 1692 (s), 1592 (m), 1504 (m), 1428 (m), 1340 (m), 1276 (s), 1199 (s), 1170 (m), 1147 (s), 1110 (m), 1043 (m), 998 (m), 981 (s), 894 (m), 812 (m), 749 (s), 737 (s), 660 (m), 621 (m), 567 (m), 536 (m). GC-MS (EI, 70 eV): *m/z* (%) = 271 ([M]$^+$, 60), 212 (100), 198 (3), 184 (7), 128 (5). HRMS (EI): Calcd. for $C_{15}H_{14}NO_4$ ([M+H]$^+$): 272.0917; found: 272.0923.

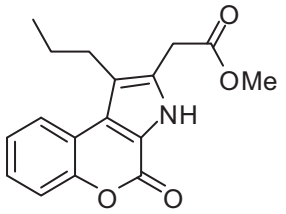
Methyl 2-(1-ethyl-4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20c)



Chemical Formula: $C_{16}H_{15}NO_4$
Exact Mass: 285,100

Starting with **19c** (0.100 g, 0.31 mmol), **20c** was isolated (0.060 g, 67 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 199 - 201 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.22. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.79 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.68 (s, 3 H, OCH_3), 3.78 (s, 2H, CH_2), 7.21 - 7.38 (m, 3 H, CH_{Ar}), 7.82 - 7.85 (m, 1 H, CH_{Ar}), 10.44 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8 (CH_3), 18.3, 31.3 (CH_2), 52.6 (OCH_3), 116.3 (C_{Ar}), 117.6 (CH_{Ar}), 118.8, 120.4 (C_{Ar}), 123.3, 124.3 (CH_{Ar}), 126.8 (C_{Ar}), 127.3 (CH_{Ar}), 132.0, 151.2 (C_{Ar}), 155.6, 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3218 (w), 2966 (w), 2951 (w), 2931 (w), 2875 (w), 1738 (m), 1681 (s), 1674 (s), 1610 (m), 1555 (m), 1456 (m), 1424 (m), 1301 (m), 1253 (m), 1230 (m), 1148 (s), 1114 (m), 1013 (s), 984 (s), 850 (m), 739 (s), 713 (s), 659 (m), 631 (s), 586 (m), 546 (w). GC-MS (EI, 70 eV): *m/z* (%) = 285 ([M]$^+$, 100), 270 (39), 238 (7), 226 (82), 212 (42), 182 (8), 167 (10). HRMS (EI): Calcd. for $C_{16}H_{16}NO_4$ ([M+H]$^+$): 286.1074; found: 286.1076.

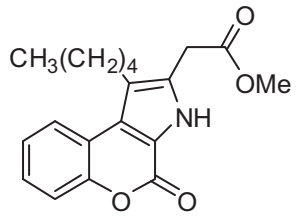
Methyl 2-(4-oxo-1-propyl-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20d)



Chemical Formula: $C_{17}H_{17}NO_4$
Exact Mass: 299,116

Starting with **19d** (0.200 g, 0.58 mmol), **20d** was isolated (0.072 g, 42 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 192 - 193 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_2CH_3$), 1.55 - 1.63 (m, 2 H, CH_2), 2.71 (t, ^3J = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 3.66 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2), 7.22 - 7.37 (m, 3 H, CH_{Ar}), 7.76 - 7.80 (m, 1 H, CH_{Ar}), 10.76 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 23.4, 27.1, 31.5 (CH_2), 52.5 (OCH_3), 116.3 (C_{Ar}), 117.6 (CH_{Ar}), 118.8, 118.9 (C_{Ar}), 123.3, 124.3 (CH_{Ar}), 126.9 (C_{Ar}), 127.2 (CH_{Ar}), 132.8, 151.1 (C_{Ar}), 155.8, 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3206 (m), 3041 (w), 2956 (m), 2933 (w), 2874 (w), 1737 (m), 1682 (s), 1587 (w), 1461 (m), 1427 (m), 1287 (m), 1222 (m), 1154 (m), 1006 (m), 983 (m), 854 (m), 739 (s), 693 (m), 634 (m), 593 (m), 540 (m). GC-MS (EI, 70 eV): *m/z* (%) = 299 ([M]$^+$, 69), 270 (100), 240 (14), 212 (48), 182 (9). HRMS (EI): Calcd. for $C_{17}H_{17}O_4N$ ([M]$^+$): 299.11521; found: 299.114763. Anal. calcd for $C_{17}H_{17}O_4N$: C, 68.21; H, 5.72; N, 4.68. Found: C, 67.76; H, 5.86; N, 4.33.

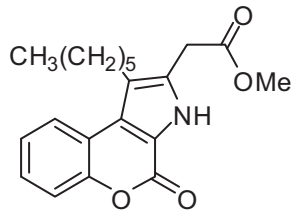
Methyl 2-(4-oxo-1-pentyl-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20e)



Chemical Formula: $C_{19}H_{21}NO_4$
Exact Mass: 327,147

Starting with **19e** (0.180 g, 0.48 mmol), **20e** was isolated (0.097 g, 62 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 169 - 170 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.22. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 6.9 Hz, 3 H, $(CH_2)_4CH_3$), 1.28 - 1.32 (m, 4 H, 2 × CH_2), 1.52 - 1.57 (m, 2 H, CH_2), 2.72 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_3CH_3$), 3.66 (s, 3 H, OCH_3), 3.80 (s, 2 H, CH_2), 7.22 - 7.37 (m, 3 H, CH_{Ar}), 7.77 - 7.80 (m, 1 H, CH_{Ar}), 10.78 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0 (CH_3), 21.5, 24.1, 29.0, 30.5, 30.7 (CH_2), 51.5 (OCH_3), 115.3 (C_{Ar}), 116.5 (CH_{Ar}), 117.9, 118.1 (C_{Ar}), 122.3, 123.3 (CH_{Ar}), 125.9 (C_{Ar}), 126.2 (CH_{Ar}), 131.7, 150.1 (C_{Ar}), 154.8, 169.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3221 (m), 3140 (w), 3073 (w), 3039 (w), 3000 (w), 2954 (m), 2922 (m), 2858 (m), 1729 (m), 1691 (s), 1556 (m), 1464 (m), 1436 (m), 1340 (m), 1284 (m), 1263 (m), 1203 (s), 1145 (s), 1114 (m), 1040 (m), 981 (s), 897 (m), 744 (s), 667 (m), 586 (m), 545 (w). GC-MS (EI, 70 eV): *m/z* (%) = 327 ($[M]^+$, 55), 270 (100), 254 (10), 238 (12), 212 (61), 198 (8). HRMS (EI): Calcd. for $C_{19}H_{21}O_4N$ ($[M]^+$): 327.14651; found: 327.146281.

Methyl 2-(1-hexyl-4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20f)

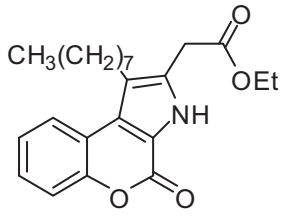


Chemical Formula: $C_{20}H_{23}NO_4$
Exact Mass: 341,163

Starting with **19f** (0.244 g, 0.63 mmol), **20f** was isolated (0.101 g, 47 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 157 - 159 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.22. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 6.9 Hz, 3 H, $(CH_2)_5CH_3$), 1.23 - 1.34 (m, 6 H, 3 × CH_2), 1.53 - 1.59 (m, 2 H, CH_2), 2.73 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.69 (s, 3 H, OCH_3), 3.78 (s, 2 H, CH_2), 7.23 - 7.38 (m, 3 H, CH_{Ar}), 7.78 - 7.82 (m, 1 H, CH_{Ar}), 10.40 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0 (CH_3), 22.6, 25.2, 29.3, 30.3, 31.4, 31.6 (CH_2), 52.6 (OCH_3), 116.4 (C_{Ar}), 117.6 (CH_{Ar}), 118.9, 119.1 (C_{Ar}), 123.3, 124.3 (CH_{Ar}), 126.8 (C_{Ar}), 127.2 (CH_{Ar}), 132.3, 151.2 (C_{Ar}), 155.6, 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3225 (m), 3143 (w), 3073 (w), 3040 (w), 2950 (m), 2923 (m), 2859 (m), 1727 (m), 1694 (s), 1558 (m), 1463 (m), 1433 (m), 1340 (m), 1280 (m), 1202 (s), 1146 (s), 1114 (m), 1041 (m), 982 (m), 823 (m), 742 (s), 726 (m), 667 (m), 623 (m), 576 (w), 556 (w). GC-MS (EI, 70 eV): *m/z* (%) = 341 ($[M]^+$, 53), 270 (100), 238 (12), 212 (57), 198 (8). HRMS

(EI): Calcd. for $C_{20}H_{23}O_4N$ ($[M]^+$): 341.16216; found: 341.161634. Anal. calcd for $C_{20}H_{23}O_4N$: C, 70.36; H, 6.79; N, 4.10. Found: C, 69.82; H, 6.93; N, 3.85.

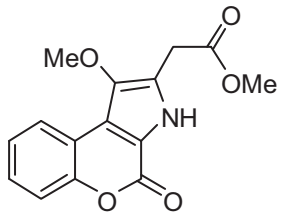
Ethyl 2-(1-octyl-4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20g)



Chemical Formula: $C_{23}H_{29}NO_4$
Exact Mass: 383,210

Starting with **19g** (0.182 g, 0.42 mmol), **20g** was isolated (0.065 g, 40 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 109 - 110 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.29. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.9 Hz, 3 H, $(CH_2)_7CH_3$), 1.17 - 1.34 (m, 10 H, 5 × CH_2, 3 H, OCH_2CH_3), 1.52 - 1.57 (m, 2 H, CH_2), 2.72 (t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.77 (s, 2 H, CH_2), 4.13 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.22 - 7.36 (m, 3 H, CH_{Ar}), 7.77 - 7.80 (m, 1 H, CH_{Ar}), 10.69 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (2 × CH_3), 21.6, 24.2, 28.3, 28.4, 28.6, 29.3, 30.6, 30.8 (CH_2), 60.6 (OCH_2), 115.3 (C_{Ar}), 116.5 (CH_{Ar}), 117.9, 118.0 (C_{Ar}), 122.3, 123.2 (CH_{Ar}), 125.8 (C_{Ar}), 126.1 (CH_{Ar}), 131.8, 150.2 (C_{Ar}), 154.7, 168.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3214 (m), 2954 (w), 2920 (m), 2869 (w), 2848 (w), 1726 (m), 1686 (s), 1556 (w), 1464 (m), 1366 (m), 1284 (m), 1191 (s), 1166 (m), 1143 (s), 1115 (m), 1041 (m), 982 (m), 908 (m), 856 (m),744 (s), 724 (s), 668 (m), 625 (m), 594 (w), 554 (w), 543 (w). GC-MS (EI, 70 eV): *m/z* (%) = 383 ($[M]^+$, 58), 296 (16), 284 (100), 238 (15), 212 (62), 198 (9). (ESI): Calcd. for $C_{23}H_{30}NO_4$ ($[M+H]^+$): 384.2169; found: 384.2175.

Methyl 2-(1-methoxy-4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20h)

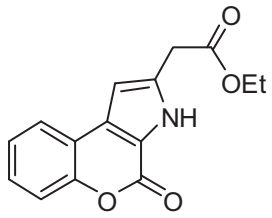


Chemical Formula: $C_{15}H_{13}NO_5$
Exact Mass: 287,079

Starting with **19h** (0.100 g, 0.30 mmol), **20h** was isolated (0.042 g, 49 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 186 - 188 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.69 (s, 2 H, CH_2), 3.82 (s, 6 H, 2 × OCH_3), 7.25 - 7.33 (m, 3 H, CH_{Ar}), 7.94 - 7.97 (m, 1 H, CH_{Ar}), 10.47 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.2 (CH_2), 52.6, 62.7 (OCH_3), 112.9, 117.1 (C_{Ar}), 117.2 (CH_{Ar}), 120.2 (C_{Ar}), 123.9, 124.5 (CH_{Ar}), 126.0 (C_{Ar}), 127.7 (CH_{Ar}), 140.5, 150.8 (C_{Ar}), 155.5, 169.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3227 (m), 3071 (w), 2994 (w), 2951 (w), 2929 (w), 2835 (w), 1781 (w), 1735 (s), 1679 (s), 1560 (m), 1486 (m), 1434 (m), 1355 (m), 1311 (m), 1242 (s), 1149

(s), 1126 (s), 1002 (s), 979 (s), 911 (m), 861 (m), 748 (m), 731 (s), 650 (m), 594 (m), 538 (m). GC-MS (EI, 70 eV): *m/z* (%) = 287 ($[M]^+$, 100), 228 (88), 213 (43), 185 (13), 144 (8). (ESI): Calcd. for $C_{15}H_{14}NO_5$ ($[M+H]^+$): 288.0866; found: 288.0869.

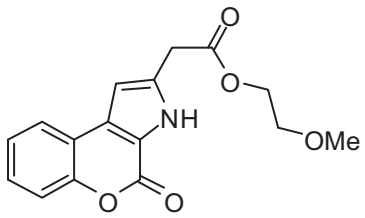
Ethyl 2-(4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20i)



Chemical Formula: $C_{15}H_{13}NO_4$
Exact Mass: 271,084

Starting with **19i** (0.150 g, 0.42 mmol), **20i** was isolated (0.045 g, 39 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 170 - 172 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 3.84 (s, 2 H, CH_2), 4.17 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 6.54 (s, 1 H, CH), 7.21 - 7.33 (m, 3 H, CH_{Ar}), 7.65 - 7.68 (m, 1 H, CH_{Ar}), 10.62 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 32.6 (CH_2), 60.7 (OCH_2), 101.9 (CH), 115.8 (C_{Ar}), 116.3 (CH_{Ar}), 116.8 (C_{Ar}), 122.2, 123.3, 126.9 (CH_{Ar}), 129.3, 134.9, 150.3 (C_{Ar}), 154.5, 168.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3200 (m), 3125 (m), 2976 (w), 2929 (w), 1946 (w), 1914 (w), 1800 (w), 1736 (m), 1683 (s), 1562 (m), 1502 (m), 1433 (m), 1334 (m), 1294 (m), 1174 (s), 1166 (s), 1113 (s), 1027 (m), 977 (m), 826 (m), 786 (m), 748 (s), 694 (m), 625 (m), 576 (m), 543 (m). GC-MS (EI, 70 eV): *m/z* (%) = 271 ($[M]^+$, 71), 198 (100), 170 (14), 115 (11). (ESI): Calcd. for $C_{15}H_{14}NO_4$ ($[M+H]^+$): 272.0917; found: 272.0921.

2-Methoxyethyl 2-(4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20j)

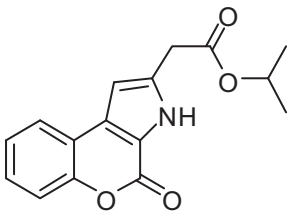


Chemical Formula: $C_{16}H_{15}NO_5$
Exact Mass: 301,095

Starting with **19j** (0.100 g, 0.29 mmol), **20j** was isolated (0.038 g, 44 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 136 - 138 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, OCH_3), 3.58 (t, ^3J = 4.7 Hz, 2 H, $OCH_2CH_2OCH_3$), 3.87 (s, 2 H, CH_2), 4.29 (t, ^3J = 4.6 Hz, 2 H, $OCH_2CH_2OCH_3$), 6.53 (s, 1 H, CH), 7.22 - 7.33 (m, 3 H, CH_{Ar}), 7.65 - 7.67 (m, 1 H, CH_{Ar}), 10.49 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 33.6 (CH_2), 59.0 (OCH_3), 64.4, 70.0 (OCH_2), 102.9 (CH) 117.0 (C_{Ar}), 117.3 (CH_{Ar}), 117.8 (C_{Ar}), 123.2, 124.2, 127.9 (CH_{Ar}), 130.2, 135.3, 151.4 (C_{Ar}), 155.3, 169.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3201 (m), 2958 (w), 2923 (w), 2853 (w), 1734 (m), 1688 (s), 1561 (w), 1502 (m), 1434 (w), 1336 (w), 1293 (s), 1173

(m), 1115 (m), 1032 (m), 977 (m), 874 (m), 750 (s), 694 (m), 625 (w), 579 (w), 542 (w). GC-MS (EI, 70 eV): *m/z* (%) = 301 ($[M]^+$, 64), 225 (78), 198 (100), 170 (19), 140 (12), 115 (20). (ESI): Calcd. for $C_{16}H_{16}NO_5$ ($[M+H]^+$): 302.1023; found: 302.1023.

Isopropyl 2-(4-oxo-3,4-dihydrochromeno[3,4-b]pyrrol-2-yl)acetate (20k)



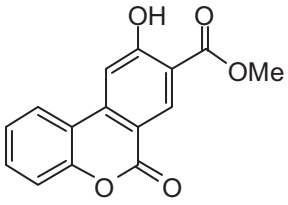
Chemical Formula: $C_{16}H_{15}NO_4$
Exact Mass: 285,100

Starting with **19k** (0.108 g, 0.32 mmol), **20k** was isolated (0.044 g, 48 %) by column chromatography (silica gel, Heptane/EtOAc) as a white solid. mp. 161 - 163 °C. R_f (*n*-heptane/EtOAc 1: 1) = 0.20. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (s, 3 H, OCH_3), 1.22 (s, 3 H, OCH_3), 3.81 (s, 2 H, CH_2), 4.97 - 5.07 (m, 1 H, *CH*(CH_3)$_2$), 6.54 (s, 1 H, CH), 7.21 - 7.32 (m, 3 H, CH_{Ar}), 7.65 - 7.68 (m, 1 H, CH_{Ar}), 10.80 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.7 (2 × CH_3), 33.9 (CH_2), 69.3 (*CH*(CH_3)$_2$), 102.8 (CH), 116.7 (C_{Ar}), 117.3 (CH_{Ar}), 117.9 (C_{Ar}), 123.3, 124.3, 127.9 (CH_{Ar}), 130.4, 136.3, 151.3 (C_{Ar}), 155.6, 169.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3211 (m), 3121 (w), 2989 (w), 2927 (w), 2851 (w), 1720 (s), 1687 (s), 1561 (m), 1502 (m), 1435 (m), 1358 (m), 1290 (m), 1201 (s), 1164 (s), 1108 (s), 1080 (s), 974 (s), 820 (m), 764 (m), 753 (s), 737 (s), 692 (m), 626 (m), 593 (m), 583 (m), 546 (m). GC-MS (EI, 70 eV): *m/z* (%) = 285 ($[M]^+$, 58), 243 (22), 198 (100), 170 (12), 140 (7), 115 (13), 43 (13). HRMS (EI): Calcd. for $C_{16}H_{15}O_4N$ ($[M]^+$): 285.09956; found: 285.099566. Anal. calcd for $C_{16}H_{15}O_4N$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.00; H, 5.44; N, 4.52.

The General procedure for the synthesis of Benzo[c]chromen-6-ones 22a-l.

To a stirred dichloromethane solution (2 mL / 1 mmol of starting materials) of 4-Chloro-2-oxo-2*H*-chromene-3-carbaldehyde **21** (1.0 equiv) and 1,3-bis(silyl enol ether) **4** (1.1 equiv) was added $TiCl_4$ (1.1 equiv) at −78 °C under an argon atmosphere. The temperature of the reaction mixture was allowed to rise to 20 °C in the period of 14 h. To the solution was added hydrochloric acid (10 %, 20 mL) and the mixture was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, *n*-heptane/ EtOAc) to give **22a-l.**

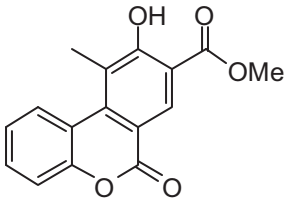
Methyl 9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22a)



Chemical Formula: $C_{15}H_{10}O_5$
Exact Mass: 270,053

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4a** (0.430 g, 1.65 mmol), **22a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.162 g, 40 %). mp. 238 - 239 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.95 (s, 3 H, OCH_3), 7.19 - 7.50 (m, 4 H, CH_{Ar}), 7.89 (s, 1 H, CH_{Ar}), 8.87 (s, 1 H, CH_{Ar}), 11.30 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.9 (OCH_3), 108.4 (CH_{Ar}), 112.2 (*C*$COOCH_3$), 112.8, 116.0 (C_{Ar}), 117.0, 122.7, 123.7, 131.0, 134.0 (CH_{Ar}), 140.0, 151.1 (C_{Ar}), 159.2 (*C*OH), 164.6, 168.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3014 (w), 2960 (w), 2923 (w), 2851 (w), 1728 (m), 1674 (m), 1597 (m), 1442 (m), 1348 (m), 1326 (m), 1236 (m), 1189 (s), 1117 (m), 1067 (m), 1037 (m), 967 (m), 920 (m), 877 (m), 797 (s), 740 (s), 731 (s), 686 (s), 631 (s), 621 (s), 529 (m). GC-MS (EI, 70 eV): *m/z* (%) = 270 ([M]$^+$, 81), 238 (100), 210 (71), 182 (13), 154 (8), 126 (25), 91 (8). HRMS (EI): Calcd. for $C_{15}H_{10}O_5$ ([M]$^+$): 270.05227; found: 270.052630.

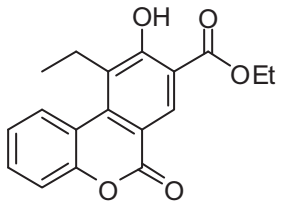
Methyl 9-hydroxy-10-methyl-6-oxo-6H-benzo[c]chromene-8-carboxylate (22b)



Chemical Formula: $C_{16}H_{12}O_5$
Exact Mass: 284,068

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4e** (0.453 g, 1.65 mmol), **22b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.179 g, 42 %). mp. 232 - 234 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.69 (s, 3 H, CH_3), 3.96 (s, 3 H, OCH_3), 7.24 - 7.48 (m, 3 H, CH_{Ar}), 8.25 - 8.28 (m, 1 H, CH_{Ar}), 8.87 (s, 1 H, CH_{Ar}), 11.83 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.3 (CH_3), 51.9 (OCH_3), 111.2 (*C*$COOCH_3$), 113.0, 116.2 (C_{Ar}), 117.1 (CH_{Ar}), 118.1, 121.8 (C_{Ar}), 123.0, 127.2, 129.9, 131.1 (CH_{Ar}), 151.1 (C_{Ar}), 160.0 (*C*OH), 163.5, 169.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 3008 (w), 2960 (w), 1858 (w), 1722 (s), 1668 (s), 1590 (m), 1438 (m), 1378 (m), 1292 (m), 1245 (s), 1213 (s), 1088 (s), 1014 (s), 990 (s), 863 (w), 796 (s), 756 (s), 654 (m), 588 (w), 528 (m). GC-MS (EI, 70 eV): *m/z* (%) = 284 ([M]$^+$, 55), 252 (35), 224 (100), 195 (5), 168 (10), 139 (22). HRMS (EI): Calcd. for $C_{16}H_{12}O_5$ ([M]$^+$): 284.06792; found: 284.068651.

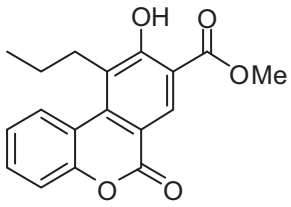
Ethyl 10-ethyl-9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22c)



Chemical Formula: $C_{18}H_{16}O_5$
Exact Mass: 312,100

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4g** (0.499 g, 1.65 mmol), **22c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.244 g, 52 %). mp. 197 - 198 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 - 1.42 (m, 6 H, 2×CH_3), 3.12 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 4.40 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.23 - 7.46 (m, 3 H, CH_{Ar}), 8.12 - 8.15 (m, 1 H, CH_{Ar}), 8.83 (s, 1 H, CH_{Ar}), 11.89 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.6, 13.2 (CH_3), 19.9 (CH_2), 61.3 (OCH_2), 111.5 (CCOOC$_2$H$_5$), 112.9 (C_{Ar}), 117.2 (CH_{Ar}), 117.6 (C_{Ar}), 123.2, 126.6 (CH_{Ar}), 127.7 (C_{Ar}), 129.9, 131.3 (CH_{Ar}), 137.5, 150.9 (C_{Ar}), 160.1 (COH), 163.8, 168.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3089 (w), 2983 (w), 2967 (w), 2937 (w), 2875 (w), 1864 (w), 1727 (m), 1663 (m), 1604 (m), 1555 (m), 1455 (m), 1403 (m), 1341 (m), 1264 (s), 1205 (s), 1155 (m), 1115 (m), 1054 (m), 990 (m), 890 (m), 804 (s), 750 (s), 652(m), 591 (m), 562 (m), 536 (m). GC-MS (EI, 70 eV): *m/z* (%) = 312 ([M]$^+$, 48), 265 (12), 251 (13), 238 (100), 223 (8), 152 (10), 139 (12). HRMS (EI): Calcd. for $C_{18}H_{16}O_5$ ([M]$^+$): 312.09923; found: 312.099590

Methyl 9-hydroxy-6-oxo-10-propyl-6H-benzo[c]chromene-8-carboxylate (22d)

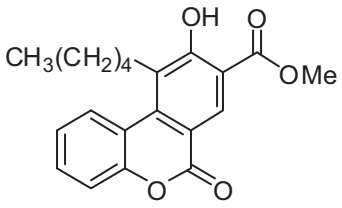


Chemical Formula: $C_{18}H_{16}O_5$
Exact Mass: 312,100

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4h** (0.499 g, 1.65 mmol), **22d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.206 g, 44 %). mp. 222 - 223 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_2CH_3$), 1.75 - 1.83 (m, 2 H, CH_2), 3.03 (t, ^3J = 8.2 Hz, 2 H, $CH_2(CH_2)CH_3$), 3.95 (s, 3 H, OCH_3), 7.23 - 7.46 (m, 3 H, CH_{Ar}), 8.03 - 8.06 (m, 1 H, CH_{Ar}), 8.84 (s, 1 H, CH_{Ar}), 11.77 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.3 (CH_3), 20.3, 28.6 (CH_2), 51.9 (OCH_3), 111.3 (CCOOCH$_3$), 113.1 (C_{Ar}), 117.3 (CH_{Ar}), 117.6 (C_{Ar}), 123.2, 126.5 (CH_{Ar}), 126.8 (C_{Ar}), 129.9, 131.4 (CH_{Ar}), 137.7, 151.0 (C_{Ar}), 160.0 (COH), 163.7, 169.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 2959 (m), 2927 (m), 2871 (w), 2853 (w), 1732 (s), 1670 (s), 1604 (m), 1433 (m), 1347 (m), 1278 (m), 1242 (s), 1203 (s), 1110 (m), 1065 (m), 997 (m), 850 (w), 798 (s), 751 (s), 686 (w), 655 (w), 612 (w), 563 (w).

GC-MS (EI, 70 eV): *m/z* (%) = 312 ($[M]^+$, 64), 283 (59), 251 (100), 237 (9), 223 (10), 195 (10), 139 (28). HRMS (EI): Calcd. for $C_{18}H_{16}O_5$ ($[M]^+$): 312.09923; found: 312.098589.

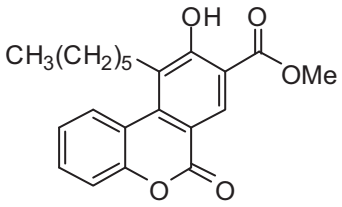
Methyl 9-hydroxy-6-oxo-10-pentyl-6H-benzo[c]chromene-8-carboxylate (22e)



Chemical Formula: $C_{20}H_{20}O_5$
Exact Mass: 340,131

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4j** (0.546 g, 1.65 mmol), **22e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.240 g, 47 %). mp. 143 - 145 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 7.1 Hz, 3 H, $(CH_2)_4CH_3$), 1.36 - 1.51 (m, 4 H, 2 × CH_2), 1.70 - 1.81 (m, 2 H, CH_2), 3.04 (t, ^3J = 8.2 Hz, 2 H, $CH_2(CH_2)_3CH_3$), 3.94 (s, 3 H, OCH_3), 7.22 - 7.46 (m, 3 H, CH_{Ar}), 8.05 - 8.08 (m, 1 H, CH_{Ar}), 8.83 (s, 1 H, CH_{Ar}), 11.76 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.3, 26.5, 26.6, 31.1 (CH_2), 51.9 (OCH_3), 111.2 (CCOOCH$_3$), 113.1 (C_{Ar}), 117.2 (CH_{Ar}), 117.6 (C_{Ar}), 123.1, 126.6 (CH_{Ar}), 126.9 (C_{Ar}), 129.9, 131.3 (CH_{Ar}), 137.6, 151.0 (C_{Ar}), 160.0 (COH), 163.7, 169.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3051 (w), 2959 (w), 2929 (w), 2870 (w), 2850 (w), 1729 (m), 1669 (m), 1604 (m), 1556 (m), 1431 (m), 1347 (m), 1280 (m), 1243 (s), 1211 (s), 1191 (m), 1112 (m), 1050 (m), 915 (m), 856 (w), 801 (m), 748 (s), 738(s), 654 (m), 606 (m), 567 (m). GC-MS (EI, 70 eV): *m/z* (%) = 340 ($[M]^+$, 63), 283 (71), 270 (12), 251 (100), 224 (19), 195 (9), 139 (22). HRMS (EI): Calcd. for $C_{20}H_{20}O_5$ ($[M]^+$): 340.13053; found: 340.130745. Anal. calcd for $C_{20}H_{20}O_5$: C, 71.10; H, 5.64. Found: C, 70.57; H, 5.92.

Methyl 10-hexyl-9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22f)

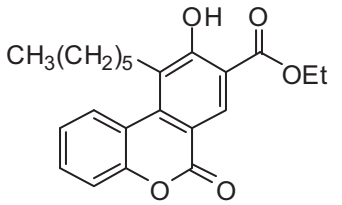


Chemical Formula: $C_{21}H_{22}O_5$
Exact Mass: 354,147

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4k** (0.569 g, 1.65 mmol), **22f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.266 g, 50 %). mp. 126 - 128 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.87 (t, ^3J = 7.0 Hz, 3 H, $(CH_2)_5CH_3$), 1.31 - 1.53 (m, 6 H, 3 × CH_2), 1.70 - 1.77 (m, 2 H, CH_2), 3.04 (t, ^3J = 8.1 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.94 (s, 3 H, OCH_3), 7.22 - 7.46 (m, 3 H, CH_{Ar}), 8.05 - 8.08 (m, 1 H, CH_{Ar}), 8.83 (s, 1 H, CH_{Ar}), 11.76 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 21.6, 26.7, 26.8, 28.5, 30.5 (CH_2), 51.9 (OCH_3),

111.2 (*C*COOCH$_3$), 113.1 (C$_{Ar}$), 117.2 (CH$_{Ar}$), 117.6 (C$_{Ar}$), 123.1, 126.6 (CH$_{Ar}$), 126.9 (C$_{Ar}$), 129.9, 131.3 (CH$_{Ar}$), 137.6, 151.0 (C$_{Ar}$), 160.0 (*C*OH), 163.7, 169.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3088 (w), 2956 (w), 2923 (m), 2855 (w), 2253 (w), 1729 (m), 1669 (m), 1588 (m), 1431 (m), 1346 (m), 1240 (m), 1209 (m), 1109 (m), 1047 (m), 993 (m), 907 (s), 805 (m), 730 (s), 653 (m), 605 (m), 569 (m). GC-MS (EI, 70 eV): *m/z* (%) = 354 ([M]$^+$, 57), 294 (35), 283 (69), 270 (15), 251 (100), 224 (20), 139 (23). HRMS (EI): Calcd. for C$_{21}$H$_{22}$O$_5$ ([M]$^+$): 354.14618; found: 354.145924.

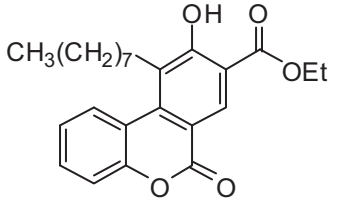
Ethyl 10-hexyl-9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22g)



Chemical Formula: C$_{22}$H$_{24}$O$_5$
Exact Mass: 368,162

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4l** (0.592 g, 1.65 mmol), **22g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.248 g, 45 %). mp. 98 - 100 °C ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.88 (t, ^3J = 6.9 Hz, 3 H, (CH$_2$)$_5$*CH$_3$*), 1.33 - 1.55 (m, 6 H, 3 × CH$_2$, 3H, OCH$_2$*CH$_3$*), 1.71 - 1.80 (m, 2 H, CH$_2$), 3.07 (t, ^3J = 8.1 Hz, 2 H, *CH$_2$*(CH$_2$)$_4$CH$_3$), 4.41 (q, ^3J = 7.2 Hz, 2 H, O*CH$_2$*CH$_3$), 7.23 - 7.48 (m, 3 H, CH$_{Ar}$), 8.08 - 8.12 (m, 1 H, CH$_{Ar}$), 8.87 (s, 1 H, CH$_{Ar}$), 11.92 (s, 1 H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 13.1, 13.2 (CH$_3$), 21.6, 26.7, 26.8, 28.5, 30.5 (CH$_2$), 61.3 (OCH$_2$), 111.5 (*C*COOCH$_2$CH$_3$), 113.0 (C$_{Ar}$), 117.2 (CH$_{Ar}$), 117.7 (C$_{Ar}$), 123.1, 126.6 (CH$_{Ar}$), 126.9 (C$_{Ar}$), 129.9, 131.3 (CH$_{Ar}$), 137.5, 150.9 (C$_{Ar}$), 160.1 (*C*OH), 163.9, 168.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3086 (w), 2957 (m), 2926 (m), 2855 (w), 1734 (s), 1669 (s), 1604 (m), 1557 (m), 1462 (m), 1399 (m), 1282 (m), 1238 (s), 1207 (s), 1111 (m), 1016 (s), 955 (m), 800 (s), 749 (s), 739 (s), 654 (m), 610 (w), 567 (w). GC-MS (EI, 70 eV): *m/z* (%) = 368 ([M]$^+$, 52), 339 (17), 321 (8), 297 (67), 251 (100), 224 (21), 139 (20). (ESI): Calcd. for C$_{22}$H$_{25}$O$_5$ ([M+H]$^+$): 369.1697; found: 369.1703.

Ethyl 9-hydroxy-10-octyl-6-oxo-6H-benzo[c]chromene-8-carboxylate (22h)

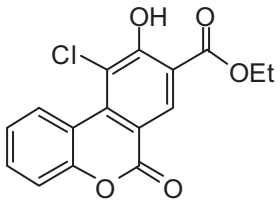


Chemical Formula: C$_{24}$H$_{28}$O$_5$
Exact Mass: 396,194

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4p** (0.638 g, 1.65 mmol), **22h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.280 g, 47 %). mp. 82 - 83 °C ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.84 (t, ^3J = 6.9 Hz, 3 H, (CH$_2$)$_7$*CH$_3$*), 1.21 - 1.54 (m, 10 H, 5 × CH$_2$, 3H, OCH$_2$*CH$_3$*), 1.70 - 1.83 (m, 2 H,

CH_2), 3.06 (t, ^3J = 8.1 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 4.41 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.23 - 7.48 (m, 3 H, CH_{Ar}), 8.08 - 8.11 (m, 1 H, CH_{Ar}), 8.87 (s, 1 H, CH_{Ar}), 11.92 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 14.2 (CH_3), 22.7, 27.7, 27.8 (CH_2), 29.3 (2 × CH_2), 29.9, 31.9 (CH_2), 62.3 (OCH_2), 112.5 (CCOOCH$_2$CH$_3$), 114.0 (C_{Ar}), 118.2 (CH_{Ar}), 118.7 (C_{Ar}), 124.1, 127.6 (CH_{Ar}), 127.9 (C_{Ar}), 130.9, 132.3 (CH_{Ar}), 138.5, 151.9 (C_{Ar}), 161.1 (COH), 164.9, 169.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3085 (w), 2999 (w), 2949 (m), 2919 (m), 2861 (m), 2847 (m), 1954 (w), 1925 (w), 1874 (w), 1728 (s), 1668 (m), 1588 (m), 1554 (m), 1441 (m), 1377 (m), 1267 (s), 1240 (s), 1208 (s), 1135 (m), 1110 (m), 1017 (m), 957 (m), 865 (m), 794 (m), 750 (s), 654 (m), 604 (m), 572 (m), 530 (m). GC-MS (EI, 70 eV): *m/z* (%) = 396 ([M]$^+$, 55), 367 (18), 349 (8), 297 (68), 251 (100), 195 (8), 139 (14). (ESI): Calcd. for $C_{24}H_{29}O_5$ ([M+H]$^+$): 397.2015; found: 397.2016.

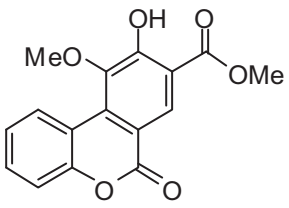
Ethyl 10-chloro-9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22i)



Chemical Formula: $C_{16}H_{11}ClO_5$
Exact Mass: 318,030

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4v** (0.510 g, 1.65 mmol), **22i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellow solid (0.196 g, 41 %). mp. 176 - 178 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.42 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.45 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.30 - 7.54 (m, 3 H, CH_{Ar}), 8.91 (s, 1 H, CH_{Ar}), 9.31 - 9.34 (m, 1 H, CH_{Ar}), 12.30 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1 (CH_3), 62.0 (OCH_2), 112.3 (CCOOCH$_2$CH$_3$), 113.5, 116.1 (C_{Ar}), 117.0 (CH_{Ar}), 117.7 (C_{Ar}), 123.3, 127.0, 131.2, 131.5 (CH_{Ar}), 136.1, 151.0 (C_{Ar}), 158.9 (COH), 161.5, 168.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3141 (w), 3076 (w), 2984 (w), 2961 (w), 2925 (w), 2851 (w), 1731 (s), 1672 (m), 1548 (m), 1440 (m), 1402 (m), 1328 (m), 1285 (m), 1234 (s), 1200 (s), 1120 (m), 1092 (s), 1005 (s), 951 (m), 804 (s), 754 (s), 735 (s), 647 (m), 579 (m), 563 (m). GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M]$^+$, ^{37}Cl, 15), 318 ([M]$^+$, ^{35}Cl, 42), 272 (100), 244 (16), 209 (7), 153 (7), 125 (9). HRMS (EI): Calcd. for $C_{16}H_{11}O_5{}^{35}Cl$ ([M]$^+$): 318.02895; found: 318.028498.

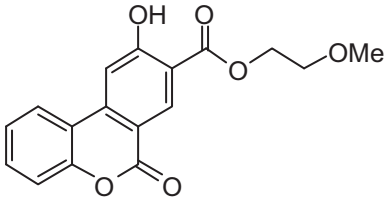
Methyl 9-hydroxy-10-methoxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22j)



Chemical Formula: $C_{16}H_{12}O_6$
Exact Mass: 300,063

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4w** (0.479 g, 1.65 mmol), **22j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.198 g, 44 %). mp. 213 - 215 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.95 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 7.25 - 7.49 (m, 3 H, CH_{Ar}), 8.74 (s, 1 H, CH_{Ar}), 8.90 - 8.93 (m, 1 H, CH_{Ar}), 11.52 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.0, 58.8 (OCH_3), 112.3 (*C*$COOCH_3$), 112.8, 115.9 (C_{Ar}), 116.7, 123.9, 127.2, 128.3, 130.5 (CH_{Ar}), 131.3, 144.2, 150.6 (C_{Ar}), 159.0 (*C*OH), 159.4, 168.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3079 (w), 2955 (w), 2927 (w), 2850 (w), 2254 (w), 1725 (s), 1679 (s), 1604 (s), 1543 (s), 1446 (m), 1346 (m), 1296 (s), 1240 (s), 1212 (s), 1111 (s), 1038 (m), 938 (m), 909 (m), 803 (m), 749 (s), 729 (s), 655 (m), 626 (m), 570 (w), 537 (m). GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M]$^+$, 76), 268 (67), 240 (100), 225 (46), 157 (16), 125 (12), 113 (13). HRMS (EI): Calcd. for $C_{16}H_{12}O_6$ ([M]$^+$): 300.06284; found: 300.063372.

2-Methoxyethyl 9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22k)

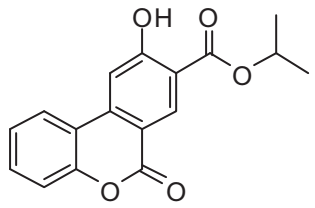


Chemical Formula: $C_{17}H_{14}O_6$
Exact Mass: 314,079

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4d** (0.502 g, 1.65 mmol), **22k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pink solid (0.250 g, 53 %). mp. 142 - 144 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.38 (s, 3 H, OCH_3), 3.71 (t, ^3J = 4.7 Hz, 2 H, CH_2), 4.50 (t, ^3J = 4.6 Hz, 2 H, CH_2), 7.25 - 7.51 (m, 4 H, CH_{Ar}), 7.90 - 7.93 (m, 1 H, CH_{Ar}), 8.91 (s, 1 H, CH_{Ar}), 11.32 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 59.1 (OCH_3), 65.1, 69.9 (OCH_2), 109.4 (CH_{Ar}), 113.2 (*C*$COOCH_2CH_2OCH_3$), 113.8, 117.0 (C_{Ar}), 118.0, 123.7, 124.7, 132.0, 135.1 (CH_{Ar}), 141.0, 152.1 (C_{Ar}), 160.2 (*C*OH), 165.7, 169.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 3004 (w), 2929 (w), 2901 (w), 2850 (w), 2834 (w), 1729 (s), 1673 (m), 1599 (m), 1559 (m), 1450 (m), 1382 (m), 1324 (m), 1242 (m), 1190 (m), 1117 (m), 1070 (m), 1024 (m), 951 (w), 863 (w), 798 (m), 751 (s), 689 (m), 622 (w), 588 (w), 538 (w). GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M]$^+$, 57), 256 (22), 238 (100), 210 (33), 155 (12), 126 (18), 59 (17). HRMS (EI): Calcd.

for $C_{17}H_{14}O_6$ ($[M]^+$): 314.07849; found: 314.078148. Anal. calcd for $C_{17}H_{14}O_6$: C, 64.97; H, 4.49. Found: C, 65.33; H, 4.26.

Isopropyl 9-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (22l)



Chemical Formula: $C_{17}H_{14}O_5$
Exact Mass: 298,084

Reaction started with **21** [4-chloro-2-oxo-2H-chromene-3-carbaldehyde] (0.313 g, 1.5 mmol) and bis silyl-enol ether **4c** (0.476 g, 1.65 mmol), **22l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.206 g, 46 %). mp. 199 - 200 °C ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 5.22 - 5.33 (m, 1 H, *CH*(CH_3)$_2$), 7.25 - 7.51 (m, 4 H, CH_{Ar}), 7.90 - 7.94 (m, 1 H, CH_{Ar}), 8.87 (s, 1 H, CH_{Ar}), 11.57 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.8 (2 × CH_3), 69.6 (CH), 108.3 (CH_{Ar}), 112.0 (*C*COOCH(CH_3)$_2$), 113.4, 116.1 (C_{Ar}), 117.0, 122.7, 123.7, 130.9, 133.9 (CH_{Ar}), 139.8, 151.1 (C_{Ar}), 159.4 (*C*OH), 164.9, 167.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3073 (w), 2987 (w), 2923 (w), 2851 (w), 1725 (s), 1667 (m), 1565 (m), 1449 (m), 1375 (m), 1320 (m), 1253 (s), 1190 (s), 1099 (s), 1067 (s), 956 (m), 906 (m), 798 (s), 754 (s), 736 (m), 685 (m), 628 (m), 547 (m), 533(w). GC-MS (EI, 70 eV): *m/z* (%) = 298 ($[M]^+$, 31), 256 (34), 238 (100), 210 (33), 182 (7), 126 (16). HRMS (EI): Calcd. for $C_{17}H_{14}O_5$ ($[M]^+$): 298.08358; found: 298.083635.

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X-Ray Crystals Data

Data for compound 13b in Chapter 3 (Fig 8)

Table 1: Crystal data and structure refinement for av_of86.

Identification code	av_of86	
Empirical formula	$C_{11}H_{11}NO_3$	
Formula weight	205.21	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P-1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.1772(7) Å	α = 88.615(7)°.
	b = 7.6028(8) Å	β = 71.709(7)°.
	c = 9.9549(10) Å	γ = 85.719(7)°.
Volume	514.32(9) $Å^3$	
Z	2	
Density (calculated)	1.325 Mg/m^3	
Absorption coefficient	0.097 mm^{-1}	
F(000)	216	
Crystal size	0.27 x 0.17 x 0.13 mm^3	
Reflections collected	12386	
Independent reflections	2908 [R(int) = 0.0300]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2117 / 0 / 142	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2σ(I)]	R1 = 0.0474, wR2 = 0.1277	
R indices (all data)	R1 = 0.0690, wR2 = 0.1496	

Data for compound 17j in Chapter 4 (Fig 10)

Table 2: Crystal data and structure refinement for av_of205.

Identification code	av_of205c1	
Empirical formula	$C_{21}H_{17}NO_5S$	
Formula weight	395.42	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P-1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.7866(3) Å	α = 69.638(2)°.
	b = 11.3088(4) Å	β = 79.219(2)°.
	c = 11.9248(5) Å	γ = 77.349(2)°.
Volume	953.47(6) $Å^3$	
Z	2	
Density (calculated)	1.377 Mg/m^3	
Absorption coefficient	0.203 mm^{-1}	
F(000)	412	
Crystal size	0.41 x 0.28 x 0.18 mm^3	
Reflections collected	18635	
Independent reflections	5027 [R(int) = 0.0217]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4373 / 0 / 259	
Goodness-of-fit on F^2	1.072	
Final R indices [I>2σ(I)]	R1 = 0.0356, wR2 = 0.1009	
R indices (all data)	R1 = 0.0420, wR2 = 0.1047	

Data for compound 20c in Chapter 5 (Fig 13)

Table 3: Crystal data and structure refinement for av_of384.

Identification code	av_of384
Empirical formula	$C_{16}H_{15}NO_4$

Formula weight	285.29	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	P-1	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.326(6) Å	α = 74.02(2)°.
	b = 8.216(8) Å	β = 87.278(15)°.
	c = 11.749(9) Å	γ = 86.66(2)°.
Volume	678.3(10) $Å^3$	
Z	2	
Density (calculated)	1.397 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	300	
Crystal size	0.43 x 0.17 x 0.11 mm^3	
Reflections collected	14264	
Independent reflections	3918 [R(int) = 0.0331]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2952 / 0 / 196	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2σ(I)]	R1 = 0.0442, wR2 = 0.1190	
R indices (all data)	R1 = 0.0623, wR2 = 0.1282	

Data for compound 22c in Chapter 6 (Fig 18)

Table 4: Crystal data and structure refinement for av_of425.

Identification code	av_of425
Empirical formula	$C_{18}H_{16}NO_5$
Formula weight	312.31
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	P-1
Space group (Hall)	-P 1

Unit cell dimensions	a = 7.741(5) Å	α = 108.281(13)°.
	b = 8.452(4) Å	β = 97.68(3)°.
	c = 11.562(5) Å	γ = 93.343(13)°.
Volume	707.8(6) $Å^3$	
Z	2	
Density (calculated)	1.465 Mg/m^3	
Absorption coefficient	0.107 mm^{-1}	
F(000)	328	
Crystal size	0.94 x 0.12 x 0.12 mm^3	
Reflections collected	15536	
Independent reflections	4095 [R(int) = 0.0213]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3483 / 0 / 214	
Goodness-of-fit on F^2	1.063	
Final R indices [I>2σ(I)]	R1 = 0.0395, wR2 = 0.1158	
R indices (all data)	R1 = 0.0475, wR2 = 0.1220	

Curriculum Vitae

List of Publications:

1. **Olumide Fatunsin**, Abdolmajid Riahi, Mohanad Shkoor, Rüdiger Dede, Helmut Reinke, Peter Langer, *Synlett* **2009**, 201-204. "First Synthesis of Functionalized Benzonitriles by Formal [3+3] Cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes".

2. **Olumide Fatunsin**, Mohanad Shkoor, Abdolmajid Riahi, Munawar Hussain, Muhammad Sher, Alexander Villinger, Christine Fischer, Peter Langer, *Helv. Chim. Acta* **2010**, (accepted). "Regioselective Synthesis of 5-Arylthio- and 5-Benzylthio-6-phenylsalicylates by One-Pot Cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 2-Arylthio- and 5-Benzylthio-3-ethoxy-2-en-1-ones".

3. **Olumide Fatunsin**, Viktor O. Iaroshenko, Sergii Dudkin, Mohanad Shkoor, Dmutro Volochnyuk, Ashot Gevorgyan, Peter Langer, *Synlett* **2010**, 1533-1535 "Efficient Synthesis of Chromeno[3,4-b]pyrrol-4(3*H*)-ones by Cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-3-nitrocoumarin".

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10. Abdolmajid Riahi, Mohanad Shkoor, **Olumide Fatunsin**, Mirza A. Yawer, Ibrar Hussain, Christine Fischer, and Peter Langer, *Tetrahedron* **2009**, *65*, 9300-9315. "Synthesis of amino- and nitroarenes based on regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes".

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14. Abdolmajid Riahi, Mohanad Shkoor, **Olumide Fatunsin**, Mathias Lubbe, Helmut Reinke, Peter Langer, *Tetrahedron Lett.* **2009**, *50*, 115-117. "First synthesis of 4-(arylsulfonyl)phenols by regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 2-arylsulfonyl-3-ethoxy-2-en-1-ones".

15. Esen Bellur, Mirza A. Yawer, Ibrar Hussain, Abdolmajid Riahi, **Olumide Fatunsin**, Christine Fischer, Peter Langer, *Synthesis* **2009**, 227-242. "Synthesis of 3-Acylpyrroles, 3-(Alkoxycarbonyl)pyrroles, 6,7-Dihydro-1*H*-indol-4(5*H*)-ones and 3-Benzoylpyridines based on Staudinger-Aza-Wittig Reactions of 1,3-Dicarbonyl Compounds with 2- and 3-Azido-1,1-dialkoxyalkanes".

16. Rasheed Ahmad Khera, Rasheed Ahmad, Ihsan Ullah, Obaid-Ur-Rahman Abid, **Olumide Fatunsin**, Muhammad Sher, Alexander Villinger, Peter Langer, *Helv. Chim. Acta* **2010**, (accepted). "Cyclization *versus* Elimination Reactions of 5-Aryl-5-hydroxy-1,3-diones. One-pot Synthesis of 6-Aryl-2,3-dihydro-4*H*-pyran-4-ones".

Declaration/Erklärung

I hereby declare that this work has so far neither been 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. Furthermore, 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.

_____

Olumide Foluso Fatunsin