Synthesis of Homophthalates, 2-(Arylsulfonyl)pyridines, 6-(Thien-2-yl)salicylates, Dibenzo[*b*,*d*]pyran-6-ones, Trifluoromethyl- and Fluoro-Substituted Biaryls by [4+2] and [3+3] Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes

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Affectionately Dedicated to

"My parents (Late), Brothers and Sisters"

CONTENTS

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Ibrar Hussain

Abbreviations

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

General introduction

Like all sciences, chemistry has unique place in our pattern of understanding of the universe. It is the science of molecules. But the organic chemsitry is something more. It literally creates itself as it grows. Of course we need to study the molecules of nature both because they are interesting in their own right and because their functions are important to our daily lives. Organic chemistry often studies the life by making new moleculs that give information not available from the molecules actually present in living things. 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.[1] Menthol is the famous example of flavouring compound 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 new antibiotics.[2] In fact, a number of natural products exhibit antibiotic activity. Since the discovery of penicillin, a large number of antibiotics has been isolated from scores of microorganisms.[3] The 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.

Natural products have also provided the most important success in the chemotherapy of cancer disease. A number of anticancer drugs represent unmodified natural products isolated from plants or microorganisms:[5] this includes bleomycin, doxorubicin, mitomycin, paclitaxel (TaxolTM); examples of semi-synthetic derivatives of natural products, which are important anticancer drugs are, for example, ironotecan (a camptothecin derivative), etoposide or tenoposide (a podophyllotoxin derivative). Currently, both a semi-synthetic derivative with improved water solubility, docetaxel (TaxoteneTM) and paclitaxel (TaxolTM) are approved and used clinically in the treatment of ovarian breast cancers.

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.[6]

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 salicylates, dibenzo[*b,d*]pyran-6-ones, fluoroarenes, fluorenones, homophthalates and arylsulfonyl-4-hydroxypyridines.

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 salicylates and dibenzo[*b,d*]pyran-6-ones, based on [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes and cyclization reactions of 1,3-bis(silyloxy)-1,3-butadienes with dimethyl allene-1,3-dicarboxylate and arylsulfonyl cyanides

Synthesis of Homophthalates, 2-(Arylsulfonyl)pyridines,6-(Thien-2-yl)salicylates, Dibenzo[*b*,*d*]pyran-6-ones, Trifluoromethyl- and Fluoro-Substituted Biaryls by [4+2] and [3+3] Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes

1. *One-pot Synthesis of Salicylates based on [3+3] cyclizations of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes and comprison of Regioselectivities.* This chapter includes the synthesis of novel alkyl-substituted 1,3-bis(silyl enol ethers) **5a-v** based on the known procedures. The synthesis of ether-substituted 1,3-bis(silyl enol ethers) is also presented in this chapter. The 1,3-bis(silyl enol ethers) are used as starting materials for the synthesis of 6-(thien-2-yl)- and 6-(fur-2-yl)salicylates **10a-o**, **13a-d** and 4-aryl- and 4-hetaryl-6-(trifluoromethyl)salicylates **16a-o**. In the last, the regioselectivities are compared on the basis of methyl- and trifluoromethyl-substituted derivatives

2. *Synthesis of Biaryls and Dibenzo[b,d]pyran-6-ones based on a [3+3] Cyclization Strategy*. Dibenzo[*b,d*]pyran-6-ones are present in many natural products such as alternariol, autumnariol, autumnariniol and altenuisol. In this chapter, the synthesis of functionalized biaryls **20a-i** is carried out by using the [3+3] cyclization strategy, which are then transformed into the dibenzo[*b,d*]pyran-6-ones **21a-j** by BBr_3 mediated lactonization.

3. *Regioselective Synthesis of Fluorinated Biaryls, 6H-Benzo[c]chromen-6-ones and Fluorenones based on Formal [3+3] Cyclizations of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes.* This chapter includes the synthesis of fluorinated salicylates **26a-w**, by [3+3] cyclization methodology. These salicylates **26a-f** are then transformed into the fluorinated dibenzo[*b,d*]pyran-6-ones **27a-f** by BBr_3 mediated lactonization. Moreover, some salicylates are also transformed into fluorenones **30a-b** and **31a-d**, using the Friedel–Crafts acylation methodolgy.

4. *Synthesis of 4-Hydroxy- and 2,4-Dihydroxy-homophthalates by [4+2] Cycloaddition of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Dimethyl Allene-1,3-dicarboxylate*. In this chapter, the the synthesis of various homophthalates **33a-ab** based on the cycloaddition of dimethyl allene-1,3-dicarboxylate with various 1,3-bis(silyl enol ethers) is carried out.

5. *Synthesis of Functionalized 2-(Arylsulfonyl)-4-hydroxypyridines by Heter-Diels-Alder Reaction of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Arylsulfonyl Cyanides.* This chapter deals with the synthesis of 5-alkyl-, 5-halide-, 5-aryloxy- and 5-thioaryloxy-2-(arylsulfonyl)-4-hydroxypyridines **35a-n** by the hetero-Diels-Alder reaction of substituted 1,3-bis(trimethylsilyloxy)-1,3-butadienes with arylsulfonyl cyanides, thus introducing the substitution pattern at carbon C-3 (or C-5) of the of pyridine using one-pot methodology.

7. *Experimental part*

This chapter includes the procedures and spectroscopic data of all products.

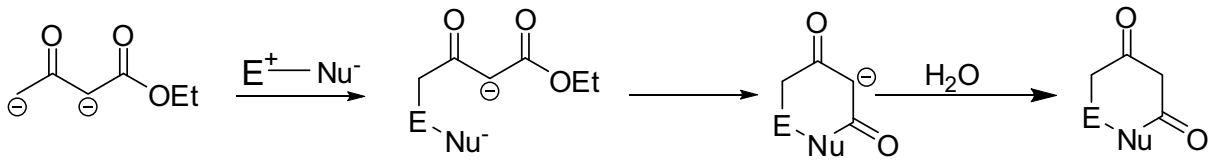
1. One-Pot Synthesis of Salicylates based on Regioselective [3+3] Cyclizations of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes and comparison of Regioselectivities

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

1.1.1. Introduction

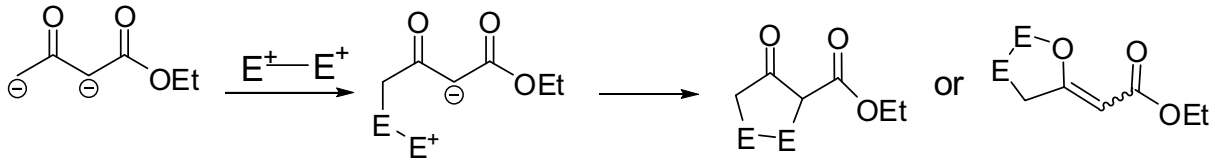
One-pot cyclization of 1,3-dicarbonyl compounds with electrophiles provide a convenient approach to various heterocyclic and carbacyclic ring systems. 1,3-dicarbonyl compounds can react in two ways, free dianions and masked dianions. Dinaion is a specie having two negative charges. Free dianions are generated by reaction of 1,3-dicarbonyl compounds with a strong base, such as LDA or *n*-BuLi.[7] To avoid the high basicity and reactivity of free dianions, these are masked by using some masking agents. 1,3-Bis(silyl enol ethers) commonly known as masked dianions, are considered as the synthetic equivalent of the corresponding 1,3-dicarbonyl compounds.[8] The regioselectivity observed for reactions of free and masked dianions is the same in most of the cases. The terminal carbon atom of 1,3-dicarbonyl compounds is functionalized by reaction of the corresponding dianions with one equivalent of an electrophile E^+, to produce monoanion, which is trapped by the addition of second electrophile. The cyclization reactions of dianions follow the two general mechanistic pathways [7] (Scheme 1-1, Schem 1-2).

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



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

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



Scheme 1-2: Possible mechanism for cyclization reactions of 1,3-dicarbonyl dianions. E = electrophile center

Cyclization reactions of dianions with dielectrophiles are synthetically important. In addition, 1,2-dielectrophiles are often rather labile, and reactions with nucleophiles can often lead to polymerization, decomposition, formation of open-chained products, elimination or SET-process. These limitations can be overcome by two methods: a) a proper tuning of the reactivity of dianion and dieletrophile and b) the use of eletroneutral dianion equivalents (masked dianions) in Lewis acid catalyzed reactions.[7]

Recent studies proved that 1,3-bis(silyl enol ethers) can be considered as equivalents of the corresponding 1,3-dicarbonyl dianions.[8] The chemistry of bis silyl enol ethers has been developed during the last two decades.[8d] It is, for example, known that silyl enol ethers can condense with various carbonyl compounds in the presence of Lewis acids.[9] These Lewis-acid-mediated reactions[10] (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,[11] as functionalized butadienes. 1,3-Bis(silyl enol ethers) undergo reactions with electrophiles at the terminal carbon atom followed by reaction of the central carbon or the oxygen atom. Silyl enol ethers can be cleaved with nucleophiles such as MeLi, $LiNH_2$ or $R_4N^+F^-$ to give enolates. They can be reacted with halides or pseudohalides,[12] Whereas enolates can be alkylated only by primary or secondary halides, enol silyl ethers can be alkylated by tertiary halides.[13]

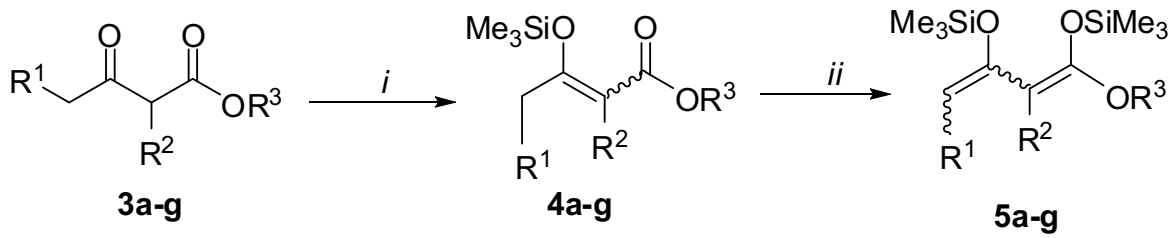
The preparation of 1,3-bis(silyl enol ethers) mainly follows the procedures reported by Chan and Molander. These syntheses rely on the preparation of 1,3-mono(silyl enol ethers)

which are subsequently transformed into 1,3-bis(silyl enol ethers) by deprotonation with LDA and subsequent silylation.[14]

In this chapter, I present the synthesis of various 1,3-bis(silyl enol ethers) following the procedure of Chan, Molander and Simchen.

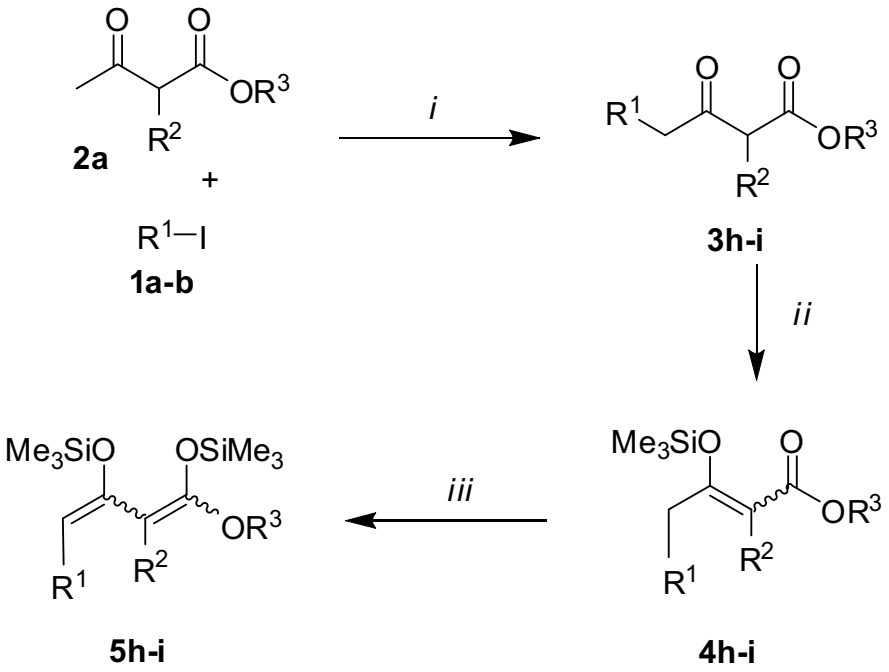
1.1.2. Results and discussion

Following the procedures of Chan and Molander, 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5a-g** were prepared from the respective 1,3-dicarbonyl compounds **3a-g** in two steps, which were commercially available. Treatment of the *β*-ketoesters with NEt_3, Me_3SiCl afforded 1,3-mono(silyl enol ethers) **4a-g**. Deprotonation of the latter with LDA and subsequent addition of Me_3SiCl afforded the diene **5a-g** (Scheme 1-3, Table 1-1).



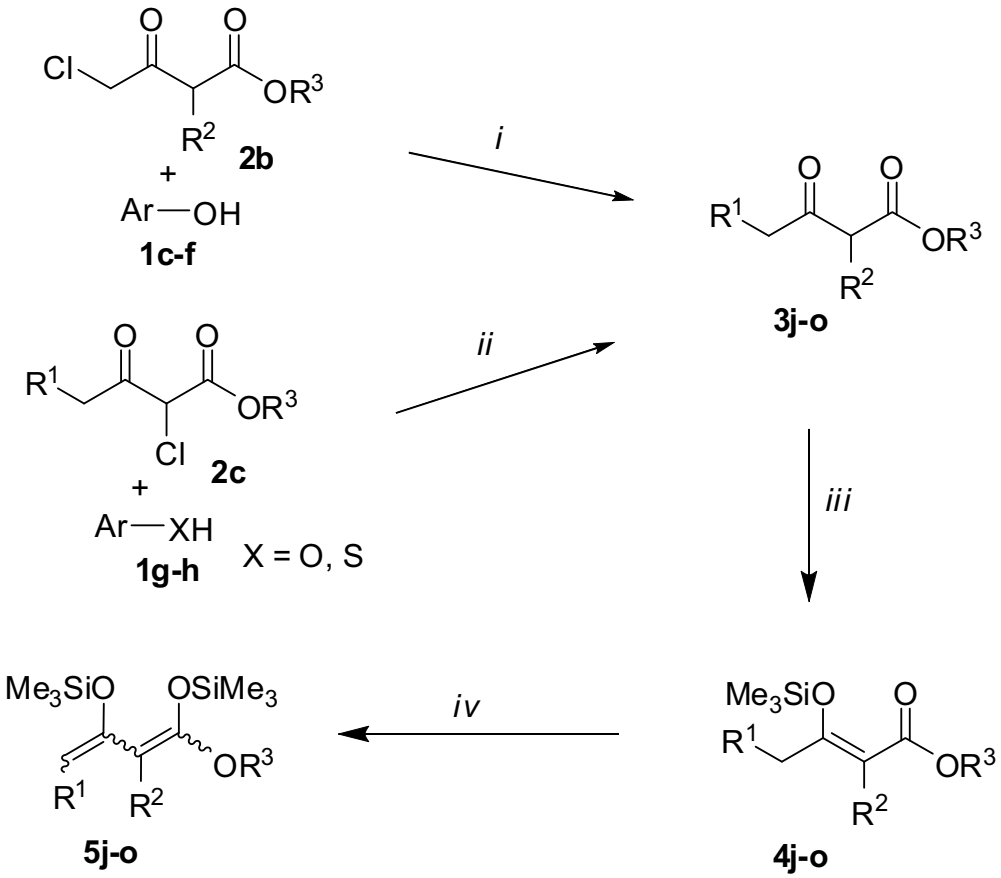
Scheme 1-3: Synthesis of 1,3-bis(silyl enol ethers) **5a-g**; *i*) 1) NEt_3 (1.5 equiv.); 2) Me_3SiCl (1.5 equiv.), C_6H_6, 20 °C, 12 - 48 h; *ii*) 1) LDA (1.5 equiv.), THF, 0 °C, 2 h; 2) Me_3SiCl (1.5 equiv.), –78 → 20 °C, 6 - 12 h.

The synthesis of alkyl-substituted-1,3-bis(silyl enol ether) derivatives, which require the synthesis of the respective *β*-ketoesters **3h-i** was carried out with the collaboration of Yawer *et al*. It is known that the regioselectivities of the reactions of monoanions and dianions generally differ widely. 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 **3h-i** were prepared by reactions of the dianion of ethyl acetoacetate **2a** with the respective alkylhalides **1a-b**. These compounds were transformed, according to a known procedure,[8] into the desired 1,3-bis(silyl enol ethers) **5h-i** via the respective 1,3-mono(silyl enol ethers) **4h-i** (Scheme 1-4, Table 1-1).



Scheme 1-4: Synthesis of alkyl-substituted 1,3-bis(silyl enol ethers) derivatives **5h-i**; *i*: 1) 2.5 LDA, THF, 0 °C, 1 h; 2) **1a-b**, –78 → 20 °C; *ii*: Me_3SiCl (1.5 equiv.), NEt_3 (1.5 equiv.), C_6H_6, 20 °C, 48 h; *iii*: 1) LDA (1.5 equiv.), THF, –78 °C, 1 h; 2) Me_3SiCl (1.5 equiv.), 20 °C, –78 → 20 °C.

In addition, the synthesis of aryloxy-1,3-bis(trimethylsilyloxy)-1,3-butadienes and their application has also been studied. The novel aryloxy- and thioaryloxy-1,3-bis(trimethylsilyloxy)-1,3-butadienes **5j-o** were prepared from the corresponding esters **4j-o** (Scheme 1-5, Table 1-1) by a known procedure.[8] These esters **4j-o**, ethyl 4-aryloxyacetoacetates **4j-m,** ethyl 2-aryloxyacetoacetate **4n** and 2-thioaryloxyacetoacetate **4o** were prepared by base mediated reaction of ethyl 4-chloroacetoacetate **2b** and ethyl 2-chloroacetoacetate **2c**, with the different phenols **1c-f, 1g** and thiophenol **1h** respectively. [15]



Scheme 1-5: Synthesis of aryloxy- and thioaryloxy-1,3-bis(silyl enol ether) derivatives **5j-o**; *i*: KOH, DMSO, 5 h, 20 °C ; *ii*: K_2CO_3, acetone, 2 h, reflux (for X = O); NEt_3, CH_2Cl_2, 30 min, 0 °C (for X = S); *iii*: Me_3SiCl (1.8 equiv.), NEt_3 (1.6 equiv.), C_6H_6, 20 °C, 72 h; *iv*: 1) LDA (1.5 equiv.), THF, –78 °C, 1 h; 2) Me_3SiCl (1.5 equiv.), 20 °C, –78 → 20 °C.

Table 1-1: 1,3-Bis(silyl enol ethers) **5a-o**

5	R^1	R^2	R^3
a	H	H	Me
b	Me	H	Me
c	Et	H	Et
d	H	Cl	Et
e	H	F	Et
f	H	Et	Me
g	Me	Cl	Me
h	*n*Hex	H	Me
i	*n*Oct	H	Me
j	OPh	H	Et
k	O(3-MeC_6H_4)	H	Et
l	O(2-MeC_6H_4)	H	Et
m	O(4-MeC_6H_4)	H	Et
n	H	O(3,5-$Me_2C_6H_3$)	Et
o	H	SPh	Me

1.1.3. Conclusions

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

1.2. Synthesis of 2,4-Bis(trimethylsilyloxy)-1,3-pentadiene

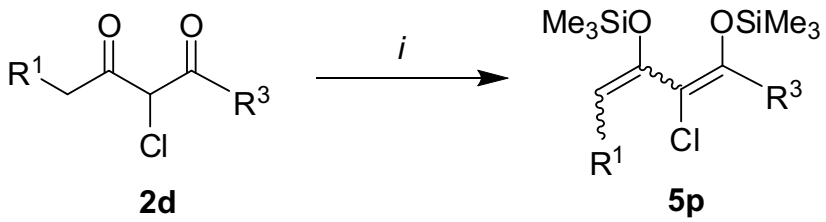
1.2.1. Introduction

A diketone is a molecule containing two ketone groups. 1,3-Diketones, such as acetylacetone, are particularly prone to form stable enols or enolates because of conjugation of the enol or enolate with the other carbonyl group, and the stability gained in forming a six-membered ring, (hydrogen bonded in the case of the enol or containing the counter ion in the

case of the enolate). The masked dianions of 1,3-diketone are of my particular interest. Here in, I wish to report the exciting chemistry of substituted masked dianions of 1,3-diketones. The masking of 1,3-diketone was done using a well known procedure, established by Simchen *et al*.[16] Some substituted 1,3-diketones were also synthesized by the known methods. [15]

1.2.2. Results and discussion

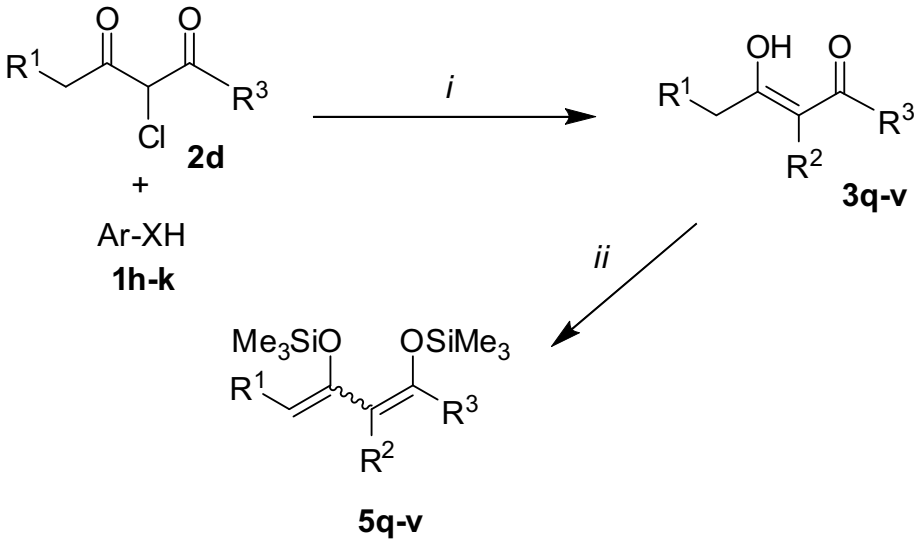
Following the procedure of Simchen *et al*.[16] 2,4-bis(trimethylsilyloxy)-3-chlro-1,3-pentadiene **5p** was prepared from the respective 3-chloropentane-2,4-dione **2d** in one step, which was commercially available. Treatment of 3-chloropentane-2,4-dione with triethylamine and trimethylsilyl-trifluormethansulfonate (TMSOTf) afforded silyl enol ether 2,4-bis(trimethylsilyloxy)-3-chlro-1,3-pentadiene **5p** (Scheme 1-6, Table 1-2).



2d **5p**

Scheme 1-6: Synthesis of 2,4-bis(trimethylsilyloxy)-1,3-pentadiene **5p**; *i:* NEt_3 (2.1 equiv.), Me_3SiOTf (2.1 equiv.), Et_2O, 0 °C, 12 h.

3-(Thioaryloxy)- and 3-(aryloxy)pentane-2,4-diones **5q-v** were prepared, following a known procedure,[15] by reaction of 3-chloropentane-2,4-dione **2d** with thiophenols and phenols respectively **1h-k** (Scheme 1-7, Table 1-2). The silylation of **3q-v** afforded the 3-(thioaryloxy)- and 3-(aryloxy)-2,4-bis(trimethylsilyloxy)-1,3-pentadiene **5q-v**, following the procedure of simchen *et al*.[16]



Scheme 1-7: Synthesis of **5q-v**; *i*: method A: pyridine, MeOH, 0 → 20 °C, 6 h ; method B: piperidine, CH_2Cl_2, MeOH, 0 → 20 °C, 6 h (for X = S); K_2CO_3, acetone, 2 h, reflux (for X = O); *ii*: NEt_3 (2.1 equiv.), Me_3SiOTf (2.1 equiv.), Et_2O, 0 °C, 12 h

Table 1-2: 1,3-Bis(silyl enol ethers) **5p-v**

5	R^1	R^2	R^3
p	H	Cl	Me
q	H	SPh	Me
r	H	S(3-MeC_6H_4)	Me
s	H	S(4-MeC_6H_4)	Me
t	H	O[4-(EtO)C_6H_4]	Me
u	H	O(3-MeC_6H_4)	Me
v	H	O(4-MeC_6H_4)	Me

All of the 1,3-bis(silyl enol ethers) prepared could be stored at suitable conditions (-20 ^oC, dry, inert gas atmosphere) for several months without decomposition.

1.2.3. Conclusions

The application of the known procedures allowed the syntheses of novel 2,4-bis(trimethylsilyloxy)-1,3-pentadienes. These masked dianions are used in the cyclization reactions for synthesis of heterocycles and aromatic rings - important building blocks of natural product analogues.

1.3. One-Pot Synthesis of 6-(Thien-2-yl)salicylates based on Regioselective [3+3] Cyclizations of 1,3-Bis(trimethyl-silyloxy)-1,3-butadienes

1.3.1. Introduction

Heterocyclic biaryls are of considerable pharmacological relevance and represent important lead structures in medicinal chemistry.[17] In this context, highly functionalized 2-(thien-2-yl)benzene derivatives are of special interest. For example, 6-(thien-2-yl)salicylates have been reported to show an in vitro inhibitory activity on guinea-pig detrusor muscle contraction at electrical field stimulation.[18] 2-(Thien-2-yl)benzoates are CAAX peptidomimetics and represent potent inhibitors of farnesyltransferase (Ftase).[19]

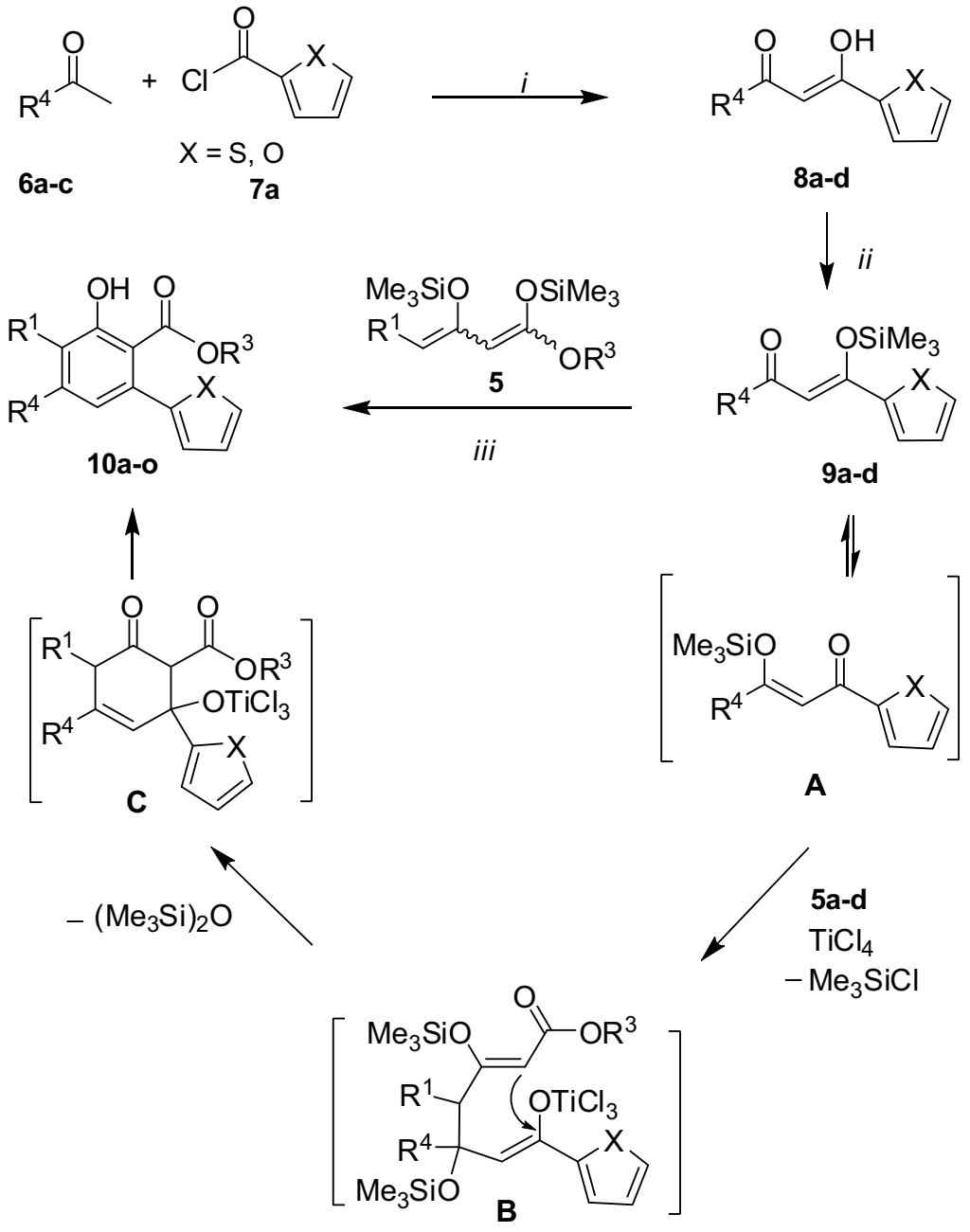
2-(Thien-2-yl)benzoates have been prepared by Grignard reaction of 1-bromo-2-(thien-2-yl)benzene with carbon dioxide[20] and by Stille[21] or Suzuki reactions[22] of 2-halobenzoates or related transition metal-catalyzed cross-coupling reactions.[23] The scope of these methods is often limited by the fact that sterically encumbered substrates often fail to undergo transition metal-catalyzed reactions or the yields are low. Besides, the synthesis of highly substituted and functionalized starting materials is often a difficult task. Based on original work reported by Chan and coworkers,[8a] I have been working on the synthesis of arenes based on formal [3+3] cyclizations of 1,3-bis(silyl enol ethers).[24, 25] Recently, Langer *et al*, eported the first application of this concept to heterocyclic substrates (i. e. pyridines).[26]

Due to the pharmacological relevance of the products, herein, I report synthesis of arenes containing an electron-rich heterocyclic moiety, based on [3+3] cyclization methodology. From a preparative viewpoint, the chemistry reported offers a convenient and regioselective approach to functionalized and sterically encumbered 6-(thien-2-yl)- and 6-(fur-2-yl)salicylates. In fact, the products are not readily available by other methods and have only scarcely been reported so far.[23] Noteworthy, the required starting materials, 3-(thien-2-yl)- and 3-(fur-2-yl)-1,3-diones, are readily available.

1.3.2. Result and Discussion

The 3-(thien-2-yl)- and 3-(fur-2-yl)-1,3-diones **8a-d** were prepared by LDA-mediated reaction of ketones **6a-c** with (thien-2-yl)-and (fur-2-yl)carboxylic acid chloride **7a,b**. The

silylation of **8a-d** afforded the silyl enol ethers **9a-d**. The $TiCl_4$-mediated [3+3] cyclization of **9a-d** with 1,3-bis(silyl enol ethers) **5** (Scheme 1-3 and 1-4, Table 1-1), prepared from the corresponding 1,3-dicarbonyl compounds in two steps,[8c] afforded the 6-(thien-2-yl)salicylates **10a-m** and the 6-(fur-2-yl)salicylates **10n,o** (Scheme 1-8, Table 1-3).



Scheme 1-8: Synthesis of salicylates **10a-o**; *i*: LDA (1.5 equiv.), THF; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72 h; *iii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C

Table 1-3: Synthesis of salicylates **10a-o**

5	**9**	**10**	X	R^1	R^3	R^4	% (**10**) [a]
a	**a**	**a**	S	H	Me	Me	32
b	**a**	**b**	S	Me	Me	Me	33
c	**a**	**c**	S	Et	Et	Me	35
h	**a**	**d**	S	*n*Hex	Me	Me	30
i	**a**	**e**	S	*n*Oct	Me	Me	34
a	**b**	**f**	S	H	Me	Et	35
b	**b**	**g**	S	Me	Me	Et	34
c	**b**	**h**	S	Et	Et	Et	30
h	**b**	**i**	S	*n*Hex	Me	Et	30
a	**c**	**j**	S	H	Me	*n*Pr	40
b	**c**	**k**	S	Me	Me	*n*Pr	47
c	**c**	**l**	S	Et	Et	*n*Pr	42
h	**c**	**m**	S	*n*Hex	Me	*n*Pr	32
a	**d**	**n**	O	H	Me	Et	32
b	**d**	**o**	O	Me	Me	Et	30

[a]Yields of isolated products

The structure of **10b** was independently confirmed by X-ray crystal structure analysis (Figure 1-1).

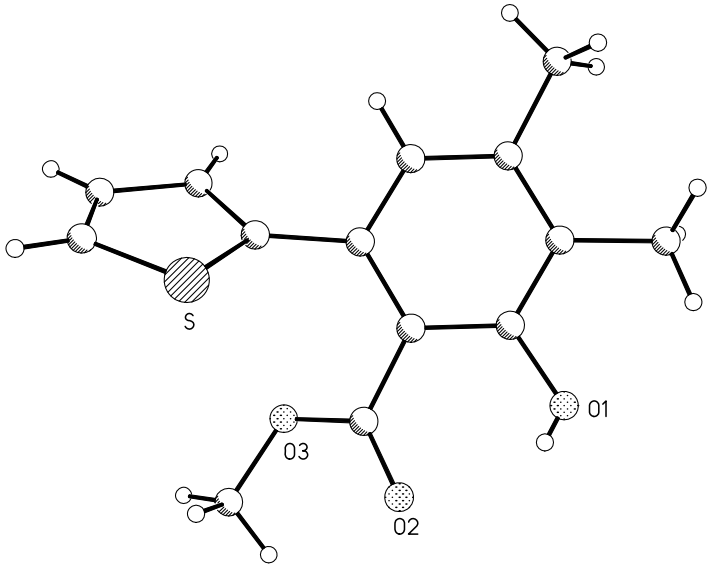
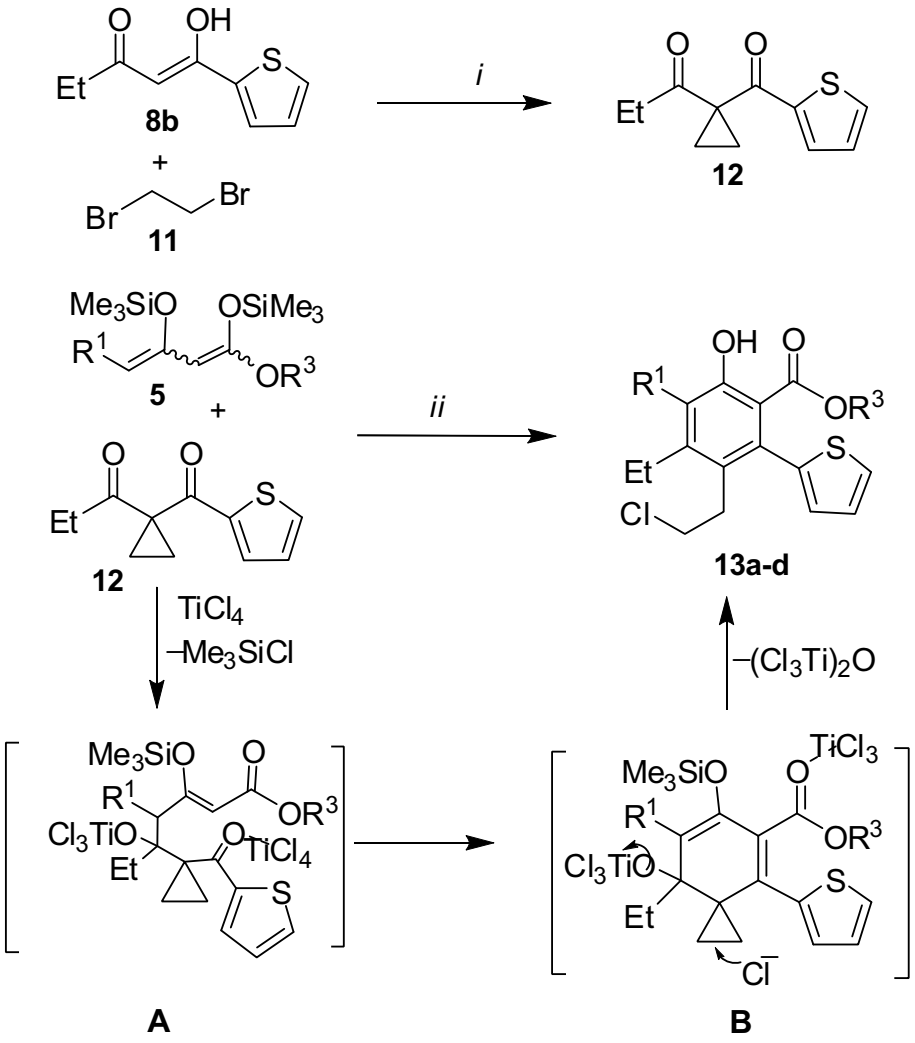


Figure 1-1: ORTEP-plot of **10b**

All products were formed with very good regioselectivity. During the optimization of this reaction, the (high) concentration and the temperature played an important role. The cyclization and the regioselectivity can be explained as follows. The cyclization of **9** with **5** presumably proceeds by $TiCl_4$ mediated isomerization of **9** by shift of the silyl group (intermediate **A**), $TiCl_4$ mediated attack of the terminal carbon atom of **5** onto the carbon located next to substituent R^1 to give intermediate **B** (conjugate addition), cyclization (intermediate **C**), and subsequent aromatization (Scheme 1-8). This mechanism has been previously suggested[8a] by Chan *et al.* for the cyclization of **5a** with 1-phenyl-1-(trimethylsilyloxy)but-1-en-3-one. However, a $TiCl_4$-mediated attack of **5a** onto the carbonyl group of **9a** and subsequent cyclization by an S_N' mechanism with displacement of the Cl_3TiO-group cannot be excluded.

The 1-alkanoyl-1-(thien-2-oyl)cyclopropanes **12** were prepared by reaction of **8b** with 1,2-dibromoethane **11** (Scheme 1-9). The $TiCl_4$-mediated reaction of 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5** (Scheme 1-3 and 1-4, Table 1-1), with **12** afforded the 6-(thien-2-yl)salicylates **13a-d** containing a remote chloride group (Scheme 1-9, Table 1-4). The products are formed by a domino ′[3+3]-cyclization-homo-Michael′ reaction.[27]



Scheme 1-9: Synthesis of salicylates **13a-d**; *i*: K_2CO_3 (4.0 equiv.). DMSO; *ii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h.

Table 1-4: Synthesis of salicylates 13a-d

5	**13**	R^1	R^3	% (**13**) [a]	Regioisomeric ratio Major / Minor
a	a	H	Me	42	100 / 0
b	b	Me	Me	40	95 / 5
c	c	Et	Et	34	80 / 20
d	d	*n*Hex	Me	32	66 / 33

[a] Isolated yields

Two isomers were formed for salicylates **13** (Figure 1-2). The regioselectivity of the isomers were confirmed by COSY and Correlation experiments and the regioisomeric ratio was calculated from the integration of two isomers in ^{1}H NMR spectroscopy. The isomer formed predominantly was considered as major in the regioisomeric ratio.

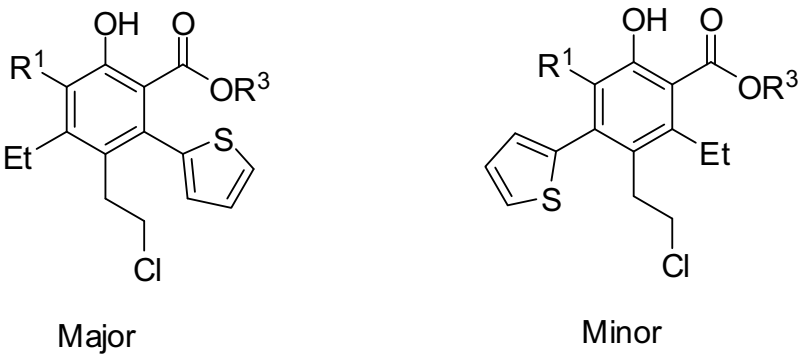


Figure 1-2: Regioisomers of salicylates **13**

In the COSY measurement of **13a**, H–H interactions were found between singlet of the aromatic proton and quartet of the ethyl group resonating at 6.95 (s, 1 H, CH_{Ar}) and 2.92 (q, ^{3}J = 7.4 Hz, 2 H, CH_2CH_3) respectively (Figure 1-3). Similarly the COSY measurement of **13b** showed H–H interactions between triplet of the ethyl group and singlet of the methyl group resonating at 1.13 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3) and 1.88 (s, 3 H, CH_3) respectively. Also H–H interactions were found between singlet of methyl and quartet of ethyl group of **13b** resonating at 1.88 (s, 3 H, CH_3) and 2.86 (q, ^{3}J = 7.5 Hz, 2 H, CH_2CH_3) respectively (Figure 1-3). These interactions confirm that R^1 and ethy group are present at adjacent carbon atoms, thus proving the regioselectivity of the major isomer.

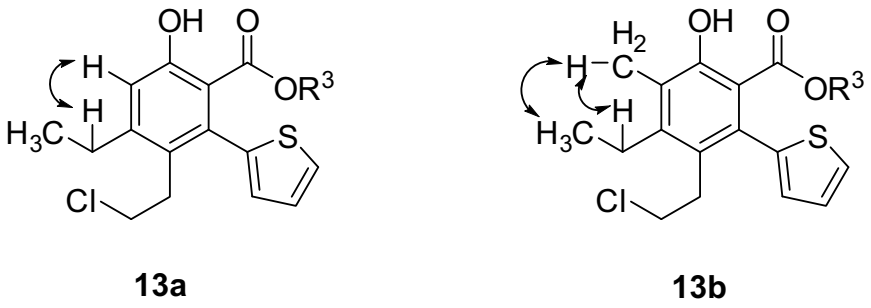


Figure 1-3: Significant COSY interactions of **13a** and **13b**

1.3.3. Conclusion

In conclusion, a variety of sterically encumbered 6-(thien-2-yl)- and 6-(fur-2-yl)salicylates has been regioselectively prepared by Lewis acid mediated [3+3] cyclization of 1,3-bis(silyl enol ethers) with novel 3-(thien-2-yl)- and 3-(fur-2-yl)-3-silyloxy-2-en-1-ones and with 1-alkanoyl-1-(thien-2-oyl)cyclopropanes. These reactions show that arenes containing an electron-rich heterocyclic moiety can be successfully prepared by application of formal [3+3] cyclizations of 1,3-bis(silyl enol ethers).

1.4. Synthesis of 4-Aryl- and 4-Hetaryl-6-(trifluoromethyl)salicylates by Regioselective Cyclization of 1,3-Bis(silyloxy)-1,3-butadienes with 1-Aryl-1-silyloxy-3-(trifluoromethyl)prop-1-en-3-ones

1.4.1. Introduction

The trifluoromethyl group is a very important substituent in organic and medicinal chemistry.[28] Whereas the size of a methyl and a trifluoromethyl group are comparable, the latter possesses a highly electron-withdrawing effect. Therefore, the replacement of a CH_3- by a CF_3-group in a molecule results in a great change of its electronic properties and reactivity. The trifluoromethyl group of drugs plays an important role in drug-receptor interactions and in the *in vivo* transport. In addition, the high chemical and biological stability of the CF_3-group allows to avoid unwanted metabolic transformations. Trifluoromethyl-substituted arenes and hetarenes show an excellent solubility in fluorous biphase systems and supercritical carbon dioxide. Therefore, they are increasingly important ligands in catalytic reactions carried out in these solvent systems.[29] Noteworthy, trifluoromethyl-substituted arenes are present, due to their electronic bias, in several organocatalysts which have been recently developed. [30]

Trifluoromethyl-substituted arenes and hetarenes are available by three strategies: *a*) the fluorination of suitable substrates (‘fluorination method’); *b*) introduction of the CF_3-group into suitable organic substrates (‘trifluoromethylation method’); *c*) cyclization reactions of CF_3-containing organic substrates (‘building block method’). A variety of CF_3-substituted heterocycles have been prepared by trifluoromethylation.[31] However, syntheses of benzene derivatives are rare. Trifluoromethylation reactions include, for example, the SF_4-mediated transformation of carboxylic acids into CF_3-groups, the transformation of CX_3- into CF_3-

groups and the reaction of aryl halides with trifluoromethylcopper. However, the latter is rather unstable and rapidly decomposes in case of slow substitution reactions of 'difficult' substrates. In fact, the preparative scope of trifluoromethylation methods is often limited to specific substrates. In addition, the synthesis of the required highly substituted aromatic starting materials can be a difficult task.

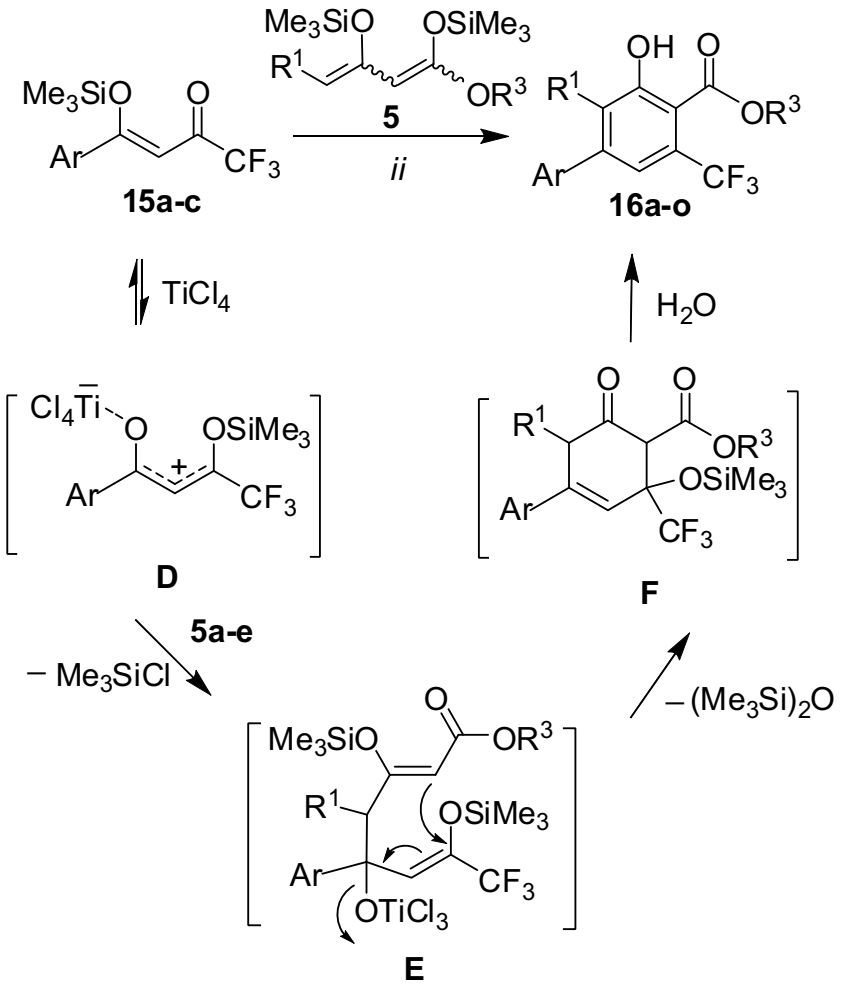
The 'building block method' provides an increasingly important alternative to trifluoromethylation reactions. (Trifluoromethyl)phenols have been prepared based on sequential cyclizations,[32] reactions of metalated (trifluoromethyl)arenes with electrophiles,[33] and Diels-Alder reactions.[34] 3,5-Bis(trifluoromethyl)anilines are available by cyclization of enamines with 1,1,1,5,5,5-hexafluoroacetylacetone.[35] Cyclocondensation reactions of α,β-unsaturated trifluoromethylketones allow a convenient approach to CF_3-substituted heterocycles.[36] However, the synthesis of functionalized benzene derivatives has only scarcely been reported to date.[37] Some years ago, Chan and co workers developed[8a] an elegant approach to phenols based on formal [3+3] cyclizations[24] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes.[25] Recently, Langer *et al* has reported the synthesis of CF_3-substituted phenols by cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 4-ethoxy-1,1,1-trifluoro-3-en-2-ones and 1,1,1-trifluoro-4-(silyloxy)pent-3-en-2-one.[38]

Herein, I want to explore what is, to the best of my knowledge, the first cyclization reactions of 1,3-bis(silyl enol ethers) with 1-aryl-1-trimethylsilyloxy-3-(trifluoromethyl)prop-1-en-3-ones based on [3+3] cyclization strategy. These reactions provide a convenient approach to various 4-aryl- and 4-hetaryl-6-(trifluoromethyl)salicylates. These products are not readily available by other methods.

1.4.2. Results and discussion

The 1-aryl-1-trimethylsilyloxy-3-(trifluoromethyl)prop-1-en-3-ones **15a-c** were prepared by silylation of the corresponding 1,3-diketones **14a-c**, which were commercially available. The $TiCl_4$-mediated cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5** with **15a** afforded the 4-phenyl-6-(trifluoromethyl)salicylates **16a-e** (Scheme 1-10, Table 1-5). The 4-(2-thienyl)-6-(trifluoromethyl)salicylates **16f-j** (Scheme 1-10, Table 1-5) were prepared by cyclization of **5** with **15b**. The cyclization of **5** with **15c** gave the novel 4-(2-furyl)-6-(trifluoromethyl)salicylates **16k-o** (Scheme 1-10, Table 1-5). All cyclization reactions

proceeded with an excellent regioselectivity. Noteworthy, formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 1-aryl- and 1-hetaryl-1-silyloxy-3-(trifluoromethyl)prop-1-en-3-ones have not yet been reported.



Scheme 1-10: Synthesis of salicylates **16a-o**; *i*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72 h; *ii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C

Table 1-5: Synthesis of salicylates **16a-o**

5	**15**	**16**	Ar	R^1	R^3	% (**16**)[a]
a	**a**	**a**	Ph	H	Me	48
b	**a**	**b**	Ph	Me	Me	51
c	**a**	**c**	Ph	Et	Et	37
h	**a**	**d**	Ph	*n*Hex	Me	56
i	**a**	**e**	Ph	*n*Oct	Me	60
a	**b**	**f**	2-Thienyl	H	Me	35
b	**b**	**g**	2-Thienyl	Me	Me	45
c	**b**	**h**	2-Thienyl	Et	Et	44
h	**b**	**i**	2-Thienyl	*n*Hex	Me	34
i	**b**	**j**	2-Thienyl	*n*Oct	Me	37
a	**c**	**k**	2-Furyl	H	Me	40
b	**c**	**l**	2-Furyl	Me	Me	41
c	**c**	**m**	2-Furyl	Et	Et	35
h	**c**	**n**	2-Furyl	*n*Hex	Me	30
i	**c**	**o**	2-Furyl	*n*Oct	Me	35

[a] Yields of isolated products

The regioselectivity of all products was confirmed by the two dimensional NMR spectroscopy (COSY and Correlation). The structures of **16b**, **16f** and **16k** were independently confirmed by X-ray crystal structure analysis (Figure 1-2, 1-3 and 1-4).[116]

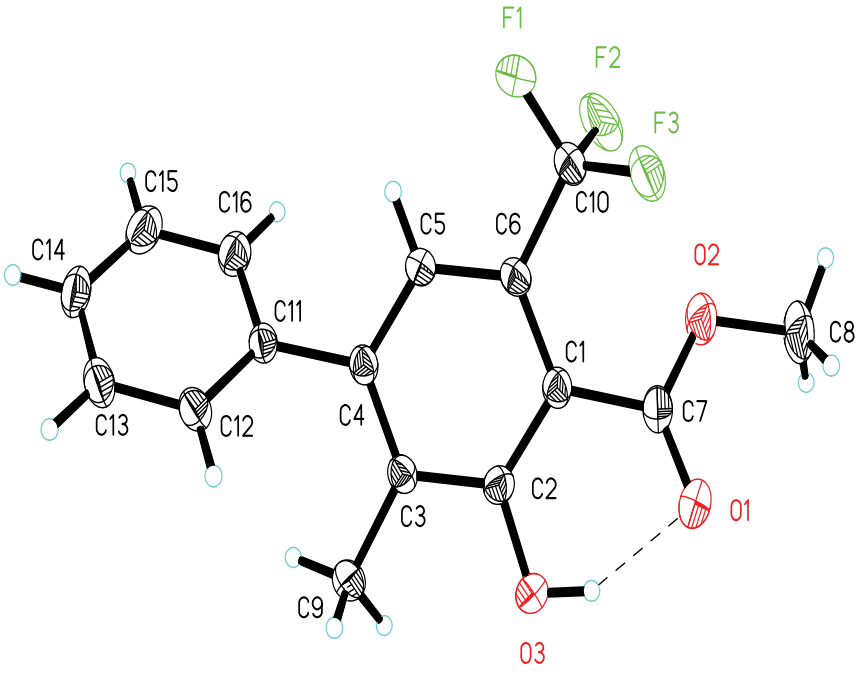


Figure 1-2: ORTEP-plot of **16b**

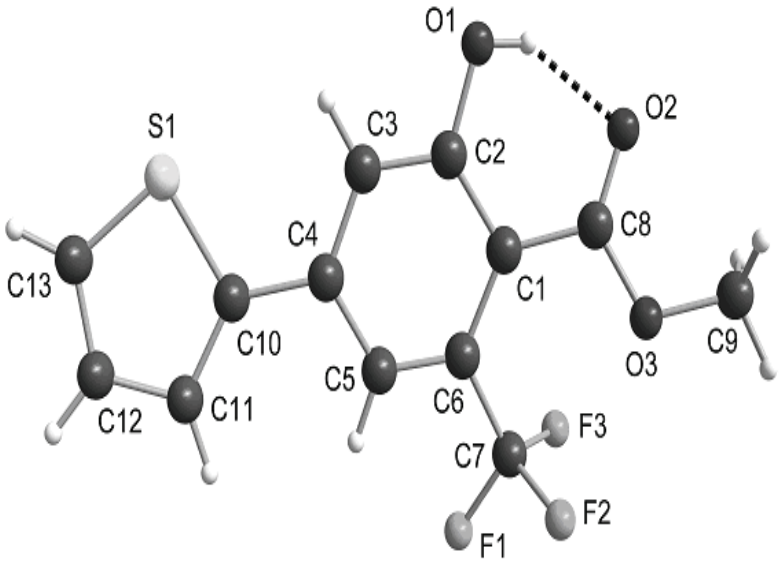


Figure 1-3: ORTEP-plot of **16f**

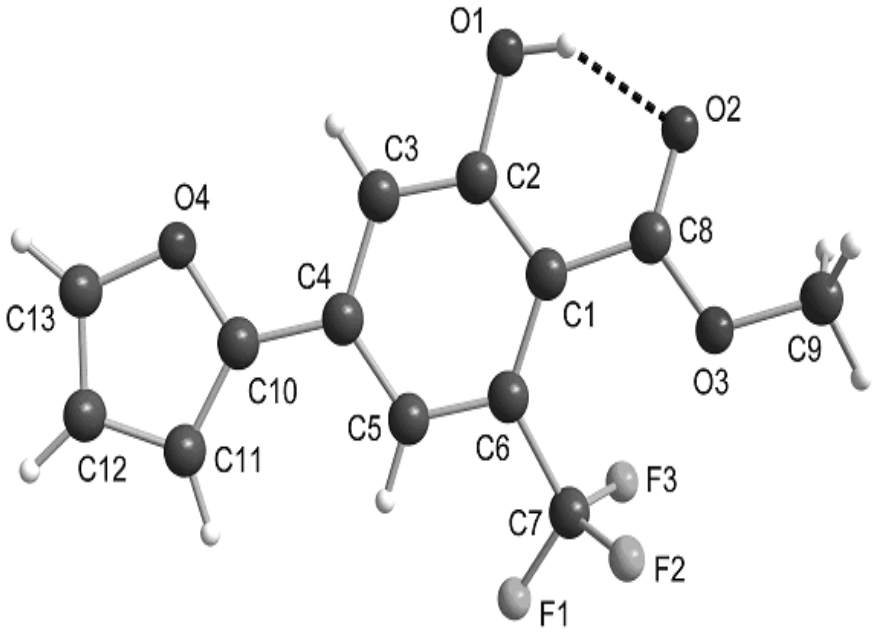
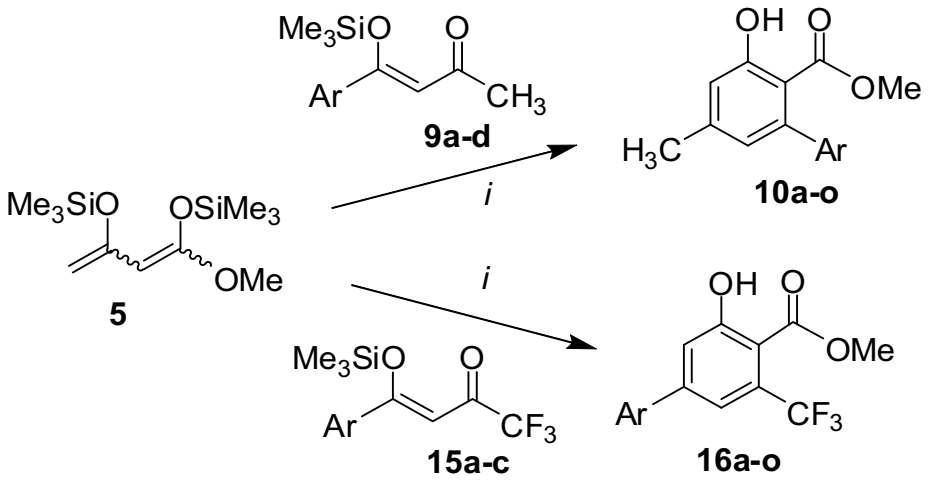


Figure 1-4: ORTEP-plot of **16k**

Noteworthy, the cyclization of 1,3-bis(silyl enol ethers) **5** with alkyl- and CF_3-substituted silyl enol ethers **9** and **15** proceeded with different regioselectivity. This might be explained due to the electron withdrawing effect of CF3 group, and also by comparison of the resonance structures of the cations formed by reaction of $TiCl_4$ with silyl enol ethers **9** and **15** (Scheme 1-11). In case of the CF_3-substituted silyl enol ethers **15**, it can be expected that resonance structure A_1 is predominant over A_2 due to the σ-donating effect of the methyl group. The aryl moiety is expected to be twised out of plane. In contrast, D_2 is expected to be more stable than D_1 due to the cation-destabilizing effect of the CF_3-group (Figure 1-5). The reactions presumably proceed, under kinetic reaction control, by attack of the terminal carbon atom of **5** onto the cationic intermediate which is predominantly present.



Scheme 1-11: Regioselectivity of the cyclization of **5** with **9a** and **15a**: *i*, $TiCl_4$, CH_2Cl_2, –78 → 20 °C

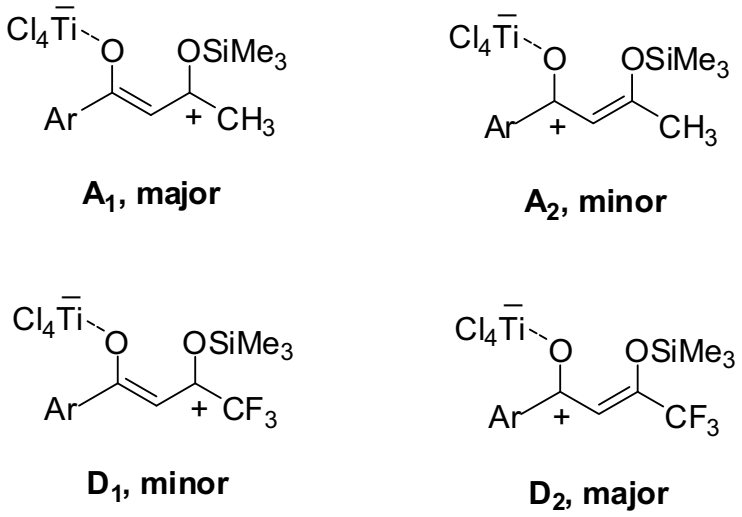


Figure 1-5: Resonance structures of intermediates A and D derived from reaction of $TiCl_4$ with **9** and **15**

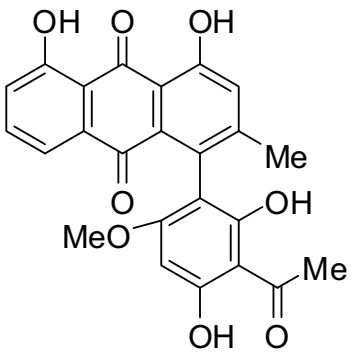
1.4.3. Conclusion

In conclusion, I developed a convenient and regioselective synthesis of 4-aryl- and 4-hetaryl-6-(trifluoromethyl)salicylates by formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 1-aryl- and 1-hetary1-trimethylsilyloxy-3-(trifluoromethyl)prop-1-en-3-ones.

2. Synthesis of Biaryls and Dibenzo[*b,d*]pyran-6-ones based on a [3+3] Cyclization Strategy

2.1. Introduction

Functionalized biaryls containing a 3-arylsalicylate substructure occur in a variety of pharmacologically relevant natural products. The simple biaryl cynandione has been isolated from many plant sources and shows a considerable in vitro activity against hepatocytes, human bladder carcinoma T-24 cells, epidermoid carcinoma KB cells, and human hepatoma PLC/PRF/5 cells.[39] A natural product, isolated from the roots of such as bulbine-knipholone contains an anthraquinone moiety, showing antiplasmodial activity.[40] Other compounds, e. g. secalonic acid A or globulixanthone E, contain a bixanthenyl substructure.[41] Biaryls are also present in many flavones (e. g. bartramiaflavone, robustaflavone, dichamanetin).[42] For example, robustaflavone which is a naturally occurring compound, is an inhibitor of hepatitis B virus replication in vitro.[42] The natural product anastatin A, which contains a hydroxylated dibenzofuran moiety, shows hepatoprotective activity.[43]



Bulbine-knipholone

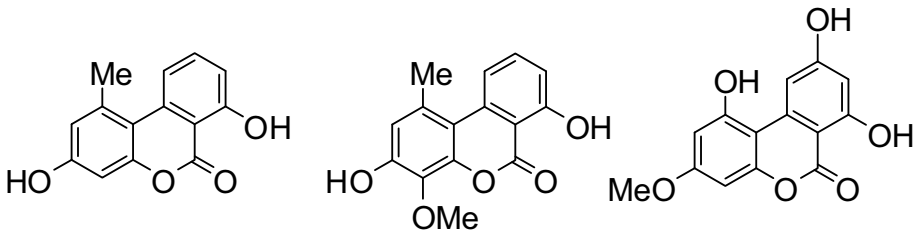
Figure 2-1: A natural product containing biaryl moiety

Functionalized dibenzo[*b,d*]pyran-6-ones ('biaryl lactones') occur in a number of natural products such as alternariol, autumnariol, autumnariniol and altenuisol; [44] dibenzo[*b,d*]pyran-6-ones containing an additional lactone bridge are present in ellagic and coruleoellagic acid.[45] Benzo[*d*]naphthopyran-6-ones occur in antibiotics and antitumor compounds isolated from *Streptomyces*; this includes, for example, defucogilvocarcin V, gilvocarcins, chrysomycins and ravidomycins.[46] Some structures, which were isolated from the culture broth of a

streptomycete as antitumor substances, were determined as 6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one.[47a] Ravidomycin was extracted from *Streptomyces ravidus* and is mainly active against Gram-positive bacteria including mycobacteria. Ravidomycin also exhibits potent antitumor activity against lymphocytic leukemia, tumor and mammary tumor.[47b] The 6*H*-dibenzo[*b,d*]-pyran-6-one moiety is also present in compounds extracted from *Pteropi faeces* (the species of *Trogopterus xanthipes* Milne-Edwards). These compounds show hyaluronidase inhibitory activity.[47c]

Many different methods for the synthesis of biaryllactones have been reported. A classic method for the synthesis of dibenzo[*b,d*]pyran-6-ones relies on the cyclization of o-bromobenzoic acid with phenols. However, the scope of this method is limited to highly activated substrates and the yields are often rather low.[46] Harris and Hay prepared 9-*O*-methylalternariol by condensation of dilithiated 2,4-pentanedione with a protected salicylate and subsequent domino cyclization.[48] Bringmann *et al.* developed an approach to dibenzo[*b,d*]pyran-6-ones by intramolecular Pd(II) catalyzed coupling reactions of ester-linked aryl bromides and phenols.[49] Snieckus and co-workers reported a versatile and efficient synthesis of dibenzo[*b,d*]pyran-6-ones by sequential ′directed ortho metalation (DOM)−Suzuki cross-coupling′ reactions.[46] This approach relies on the preparation of amide-substituted boronic acids by DOM of benzoic amides. Suzuki cross-coupling reactions of the products with aryl bromides afforded biaryls which were transformed into the target molecules by lactonization. Some years ago, Langer *et al.* have reported the synthesis of biaryl lactones by domino 'retro-Michael-aldol-lactonization' reactions.[50] In this method, the regioselective condensation of 1,3-bis(trimethylsilyloxy)-1,3-butadiens with benzopyrylium triflates afforded functionalized 2,3-dihydrobenzopyrans, masked tetraketides, which underwent a domino reaction upon treatment with base. Recently, Nguyen V.T.H. *et al.* reported the synthesis of dibenzo[*b*,*d*]pyran-6-ones based on sequential ′[3+3] cyclization−Suzuki cross-coupling′ reactions.[51] This approach relies on the [3+3] cyclization of 1,3-bis-silyl enol ethers with 3-silyloxyalk-2-en-1-ones, a methodology developed by Chan and co-workers (*vide supra*).[8,52] The functionalized salicylates prepared were transformed into their corresponding aryl triflates which were coupled with boronic acids by Suzuki reactions.[52] The biaryls thus formed were transformed into dibenzo[*b,d*]pyran-6-ones by BBr_3 mediated lactonization.[53]

Herein, I wish to report what is, to the best of my knowledge, a new and simple methodology for the synthesis of dibenzo[*b*,*d*]pyran-6-ones. My approach is based on [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 1-(2-methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-ones. The salicylates prepared were directly transformed into dibenzo[*b,d*]pyran-6-ones by BBr_3 mediated lactonization.

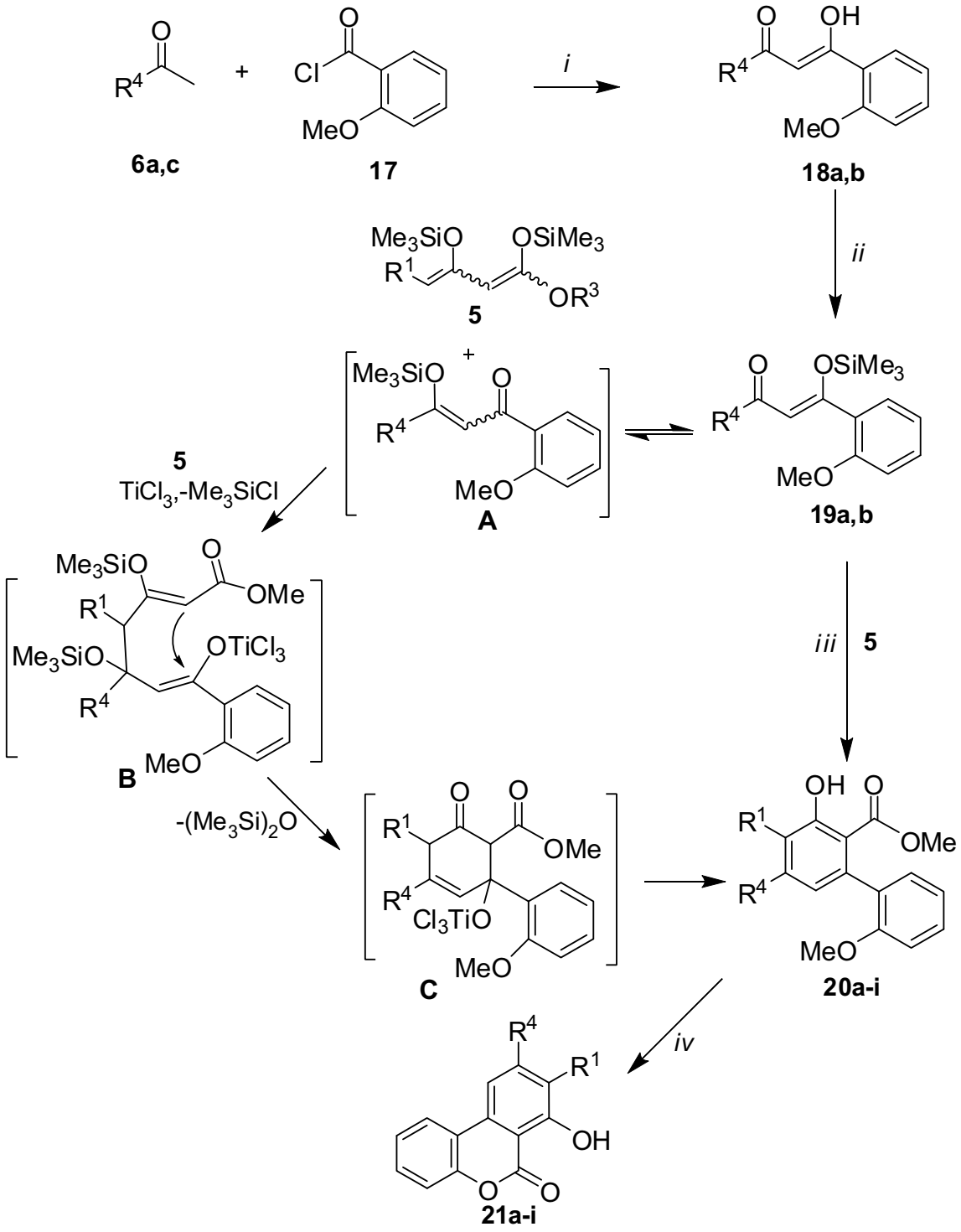


Autumnariol Autumnariniol Alternuisol

Figure 2-2: Some natural products containing dibenzo[*b*,*d*]pyran-6-ones moiety

2.2. Results and discussion

(2-Methoxybenzoyl)acetone **18a** and (2-methoxybenzoyl)butan-2-one **18b** were prepared, by LDA mediated reaction of acetone **6a** and pentan-2-one **6c** with 2-methoxybenzoyl chloride **17**, respectively. The silylation of **18a,b** afforded the silyl enol ethers **19a,b**. The [3+3] cyclization of 1-(2-methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-ones **19a,b** with 1,3-bis(silyl enol ethers) **5** afforded the biaryls **20a-i** with excellent regioselectivity.[54] The regioselectivity can be explained by $TiCl_4$ mediated isomerization of **19a,b** by shift of the trimethylsilyl group from one oxygen atom to the other (intermediate **A**), $TiCl_4$ mediated attack of the terminal carbon atom of the 1,3-bis(silyl enol ether) onto the carbon located next to substituent R^1 to give (intermediate **B**) (conjugate addition), cyclization (intermediate **C**), and subsequent aromatization. Treatment of biaryls **20a-i** with BBr_3 and subsequent addition of an aqueous solution of KO*t*Bu afforded the dibenzo[*b*,*d*]pyran-6-ones **21a-i** (Scheme 2-1, Table 2-1).



Scheme 2-1: Synthesis of dibenzo[*b,d*]pyran-6-ones **21a-i**; *i*: LDA (1.5 equiv.), THF; *ii*: 1) NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72 h; *iii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C; *iv*: 1) BBr_3 (4 equiv.), CH_2Cl_2, 0 → 20 °C, 18 h, 2) KOtBu, H_2O, 15 min, 20 °C

Table 2-1: Synthesis of dibenzo[*b,d*]pyran-6-ones **21a-i**

5	**20,21**	R^1	R^4	% (**20**)[a]	% (**21**)[a]
a	**a**	H	Me	47	92
b	**b**	Me	Me	27	69
c	**c**	Et	Me	34	62
h	**d**	*n*Hex	Me	26	65
i	**e**	*n*Oct	Me	52	60
a	**f**	H	*n*Pr	22	77
b	**g**	Me	*n*Pr	21	73
c	**h**	Et	*n*Pr	30	71
h	**i**	*n*Hex	*n*Pr	32	62

[a] Yields of isolated products,

The structure of all products was established by spectroscopic methods. The structure of **21c** was independently confirmed by X-ray crystal structure analysis (Figure 2-3).[116]

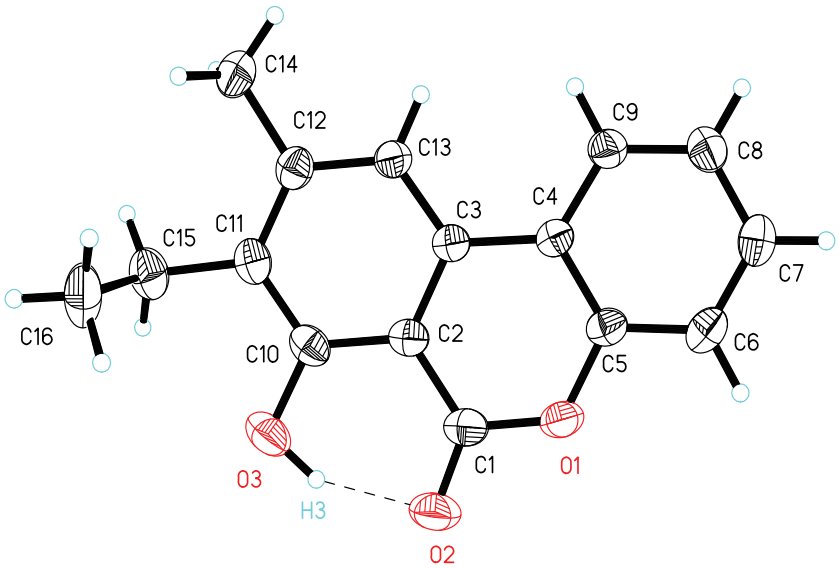


Figure 2-3: ORTEP-plot of **21c** with 50% probability of the thermal ellipsoids

2.3. Conclusions

A new methodology for the synthesis of dibenzo[*b*,*d*]pyran-6-ones based on [3+3] cyclizations of 1,3-bis(silyl enol ethers) has been reported. Known syntheses of dibenzo[*b*,*d*]pyran-6-ones rely on the transition metal catalyzed coupling of two appropriate benzene derivatives and are, thus, limited by the availability of the later. The synthesis of functionalized and heavily substituted benzene derivatives was a difficult task. In contrast to known methods, the methodology reported herein involves the assembly of one of the two benzene moieties during the synthesis. Therefore, products can be prepared which are not readily available by other methods. Notably, this strategy outlined herein, bases on [3+3] cyclizations as the key step. The overall yields of the dibenzo[*b*,*d*]pyran-6-ones are mainly limited by the [3+3] cyclization step which mostly proceeds only in moderate yield. However, the substitution pattern available by the [3+3] cyclization is not readily available by other methods.

3. Regioselective Synthesis of Fluorinated Biaryls, 6*H*-Benzo[*c*]chromen-6-ones and Fluorenones based on Formal [3+3] Cyclizations of 1,3-Bis(Silyl Enol Ethers)

3.1. Synthesis of Fluorinated Biaryls

3.1.1. Introduction

Fluoro group represents, due to its unique stereoelectronic properties, a very important substituent in organic and medicinal chemistry.[29] While the size of the fluoro group is comparable to a hydrogen atom, its high electronegativity results in a dramatic change of the electronic situation and of the reactivity of the molecule. This plays an important role in drug-receptor interactions. Notably, the increased lipophilicity of fluoro-substituted molecules also improves their transport in vivo. It is noteworthy that, due to the high chemical and biological stability of the fluoro group, undesirable metabolic transformations are often avoided. Therefore, the synthesis of fluoro-substituted arenes and hetarenes plays an important role in drug discovery.[29,55] A great variety of pharmaceuticals, such as well known ciprofloxacin, ofloxacin, or norfloxacin, contain a fluoroarene moiety.[56] Aryl fluorides are also present in natural products. This includes, for example, 4-fluoro-zaragozic acid A or fluorinated carbazole alkaloids.[57] Organic fluoro compounds show a very good solubility in fluorophilic solvents. Therefore, they are used as ligands[58] for catalytic reactions in fluorous biphase systems and supercritical carbon dioxide.[59] The unique electronic properties of fluorinated arenes are used also for applications in organocatalysis.[60,61]

Aryl fluorides are available by reaction of arenes with strong electrophilic fluorination agents (such as fluorine or xenon fluorides).[62] However, these reagents are difficult to obtain or handle, dangereous or (in some cases) very expensive. Selectfluor represents an 'easy-to-handle', commercially available electrophilic fluorination agent.[63] However, the fluorination of non-activated arenes was reported to be unsuccessful (low conversion).[63,64] The fluorination of (activated) anisol has been reported to proceed with 72% conversion. However, a 1:1 regioisomeric mixture of 2- and 4-fluoromethoxyphenol was formed.[64] The reaction of Selectfluor with phenols has been reported to give 4-fluorocyclohexadienones.[65] The functionalization of simple fluorinated arenes, such as 4-fluorophenol, by electrophilic substitution reactions has been widely explored.[66] However, these transformations are often

low-yielding and proceed with low regioselectivity. In addition, the synthesis of heavily substituted benzene derivatives is not an easy task. A different approach to aryl fluorides relies on cyclization reactions of fluorinated synthetic building blocks. For example, Shi *et al.* reported the synthesis of aryl fluorides based on [4+2] cycloaddition reactions of 2-fluoro-1-methoxy-3-trimethylsilyloxy-1,3-butadiene, 2-fluoro-3-methoxy-buta-1,3-diene and related dienes with alkenes or alkynes.[67,68]

Herein, I wish to report a convenient approach, which is based on the formal [3+3] cyclization of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles, first reported by Chan and coworkers,[8] provides an efficient way to the various functionalized arenes.[24,25] Recently, I reported the application of this method to the synthesis of aryl fluorides based on [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 2-fluoro-3-silyloxy-2-en-1-ones.[69] Herein, I report full details of these studies. With regard to the preliminary communication, I extended the preparative scope also. In addition, I report the application of this methodology to the synthesis of fluorinated 6*H*-benzo[*c*]chromen-6-ones (biaryl lactones, dibenzo[*b*,*d*]pyran-6-ones) and fluorenones. The chemistry outlined herein offers a convenient and regioselective approach to a variety of functionalised and sterically encumbered aryl fluorides which are not readily available by other methods.

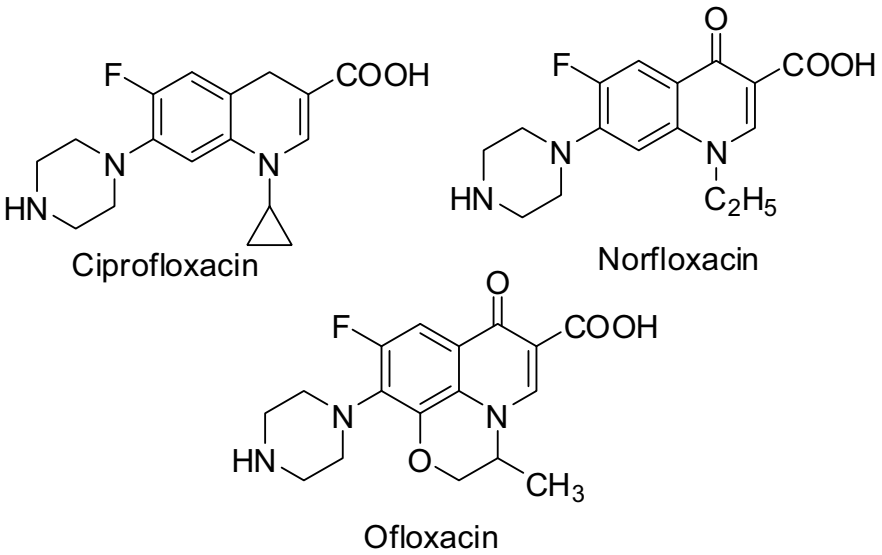
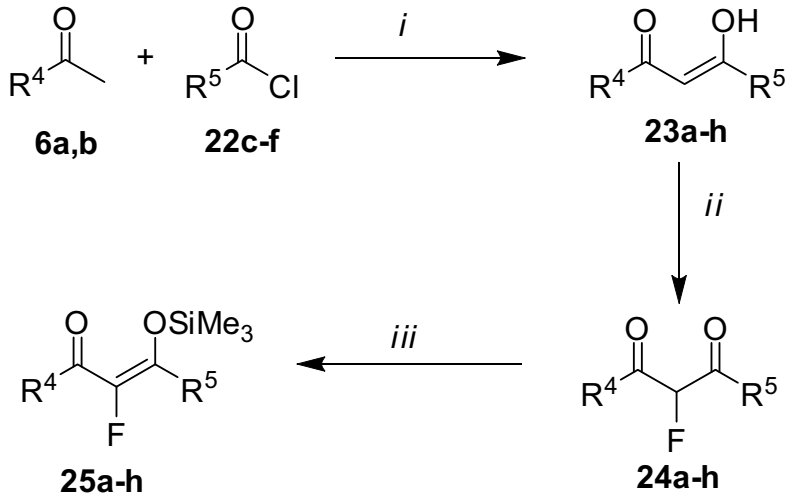


Figure 3-1: Some pharmaceuticals containing fluoroarene moiety

3.1.2. Results and discussion

The compounds **23a,b**[70] have already been reported as **18a,b** in the second chapter. The LDA mediated reaction of ketones **6a,c** with acid chlorides **22c-h** afforded the 1,3-diketones

23c-h. 2-Fluoro-1,3-diones are available by reaction of 1,3-diketones with fluorine,[71] *N*-fluorobis(trifluoromethyl)-sulfonimide,[72] and selectfluor.[73] My starting point was the synthesis of a variety of novel 2-fluoro-1,3-diones which were required for further studies. The reaction of selectfluor with 1,3-diketones **23a-h** afforded the 2-fluoro-1,3-diones **24a-h** which were transformed, by reaction with Me_3SiCl/NEt_3, into the 2-fluoro-3-silyloxy-2-en-1-ones **25a-h** (Scheme 3-1, Table 3-1). The $TiCl_4$ mediated cyclization of 1,3-bis(silyl enol ethers) **5a-c**[8c] with 2-fluoro-3-silyloxy-2-en-1-ones **25a-h** afforded the novel fluorinated biaryls **26a-w** (Scheme 3-2, Table 3-2) in moderate to good yields.

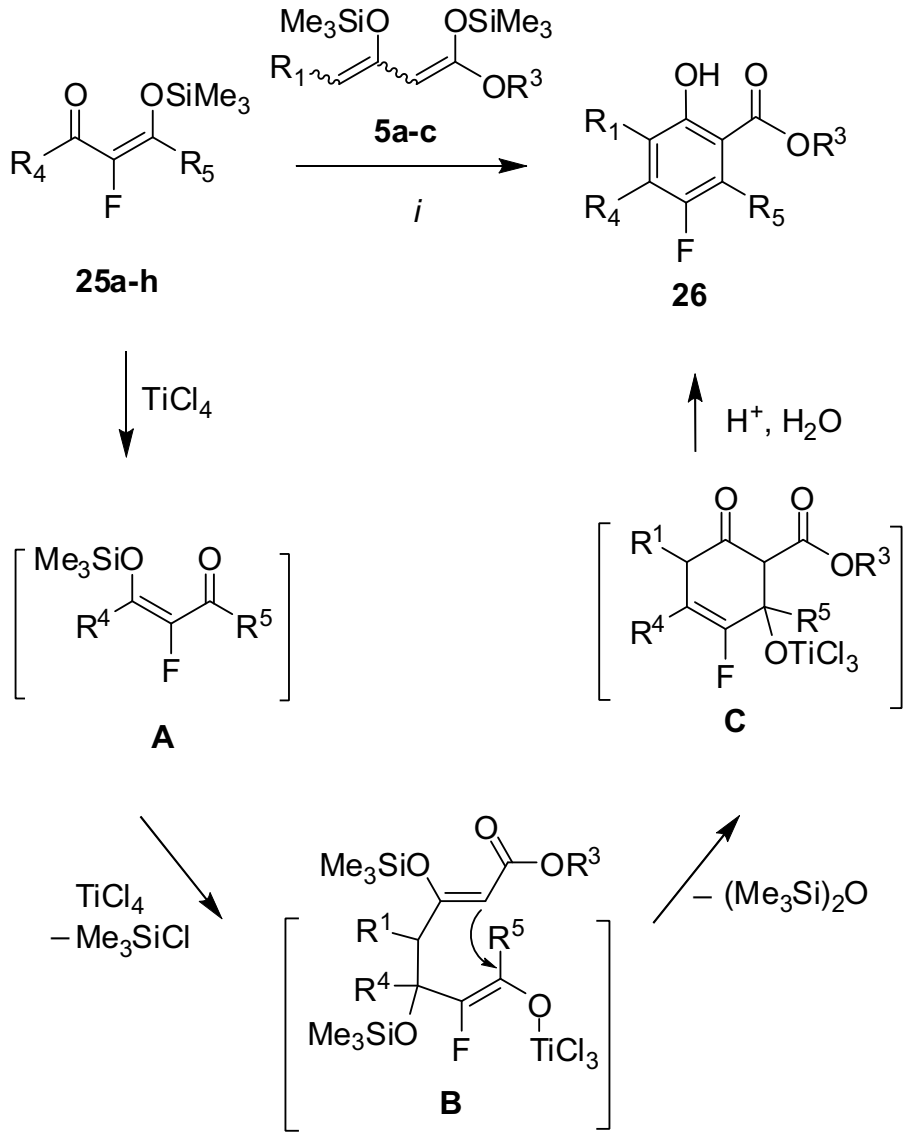


Scheme 3-1: Synthesis of fluorinated sily enol ethers **25a-h**; *i*: LDA (1.5 equiv.), THF; *i*: Selectfluor, CH_3CN; reflux, 4 h; *iii*: NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72h.

Table 3-1: Synthesis of 2-fluoro-3-silyloxy-2-en-1-ones **25a-h**

23,24,25	R^4	R^5	% (**23**) [a]	% (**24**) [a]	% (**25**) [a]
a	Me	2-(MeO)C_6H_4	37	72	99
b	*n*Pr	2-(MeO)C_6H_4	73	90	79
c	Me	2-MeC_6H_4	33	65	44
d	Me	2-ClC_6H_4	25	42	80
e	Me	4-ClC_6H_4	38	58	70
f	Me	4-FC_6H_4	36	46	82
g	Me	1-Naph	43	37	71
h	*n*Pr	2-Naph	62	64	74

[a] Isolated yields;



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

Table 3-2. Synthesis of salicylates **26a-w**

5	**25**	**26**	R^1	R^3	R^4	R^5	% (**26**) [a]
a	**a**	**a**	H	Me	Me	2-(MeO)C_6H_4	44
b	**a**	**b**	Me	Me	Me	2-(MeO)C_6H_4	54
c	**a**	**c**	Et	Et	Me	2-(MeO)C_6H_4	44
a	**b**	**d**	H	Me	*n*Pr	2-(MeO)C_6H_4	35
b	**b**	**e**	Me	Me	*n*Pr	2-(MeO)C_6H_4	34
c	**b**	**f**	Et	Et	*n*Pr	2-(MeO)C_6H_4	55
a	**c**	**g**	H	Me	Me	2-MeC_6H_4	44
b	**c**	**h**	Et	Et	Me	2-MeC_6H_4	40
a	**d**	**i**	H	Me	Me	2-ClC_6H_4	26
b	**d**	**j**	Me	Me	Me	2-ClC_6H_4	38
c	**d**	**k**	Et	Et	Me	2-ClC_6H_4	38
a	**e**	**l**	H	Me	Me	4-ClC_6H_4	30
b	**e**	**m**	Me	Me	Me	4-ClC_6H_4	32
c	**e**	**n**	Et	Et	Me	4-ClC_6H_4	44
a	**f**	**o**	H	Me	Me	4-FC_6H_4	32
b	**f**	**p**	Me	Me	Me	4-FC_6H_4	40
c	**f**	**q**	Et	Et	Me	4-FC_6H_4	35
a	**g**	**r**	H	Me	Me	1-Naph	31
b	**g**	**s**	Me	Me	Me	1-Naph	37
c	**g**	**t**	Et	Et	Me	1-Naph	42
a	**h**	**u**	H	Me	*n*Pr	2-Naph	30
b	**h**	**v**	Me	Me	*n*Pr	2-Naph	34
c	**h**	**w**	Et	Et	*n*Pr	2-Naph	35

[a] Isolated yields

The best yields were obtained when the reaction was carried out in high concentration. The use of Me_3SiOTf or $BF_3{\cdot}OEt_2$, rather than $TiCl_4$, was unsuccessful (no conversion or decomposition, respectively). Notably, products **26a-w** were formed with excellent

regioselectivity. The formation of the opposite regioisomer could not be detected. The results can be explained by the following mechanism:[8c,25] Silyl enol ethers **25** undergo a $TiCl_4$ mediated 1,5-silyl shift to give intermediate **A**. The $TiCl_4$ mediated conjugate addition of the 1,3-bis(silyl enol ethers) **5** onto **A** gave intermediate **B** (Mukaiyama-Michael reaction). The cyclization proceeds by attack of the central carbon of **5** onto the carbonyl group (Mukaiyama-aldol reaction). Aromatization by an elimination reaction (before or during the aqueous work-up) leads to the final product. The yields seem to mainly depend on the quality of the starting materials and on the handling of each individual experiment.

The structures of **26m** and **26n** were independently confirmed by X-ray crystal structure analysis (Figures 3-2, 3-3).[116]

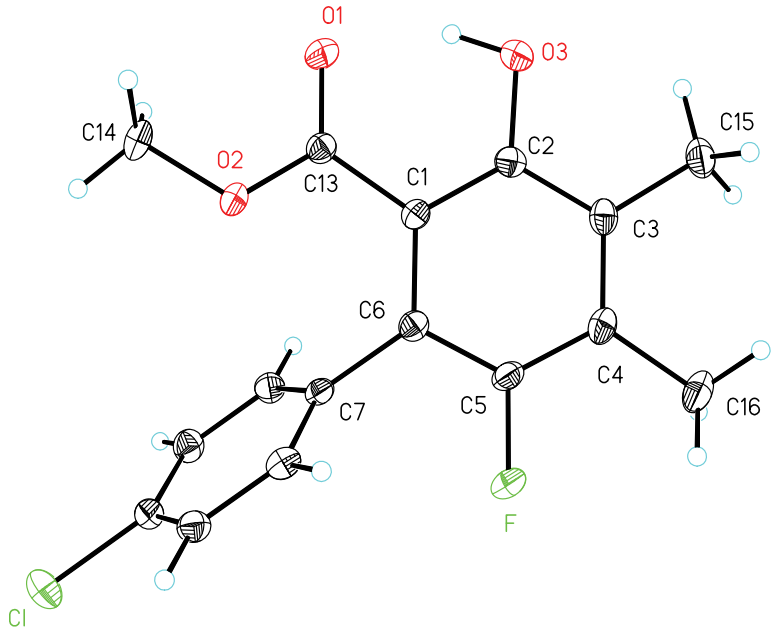


Figure 3-2: ORTEP-plot of **26m**

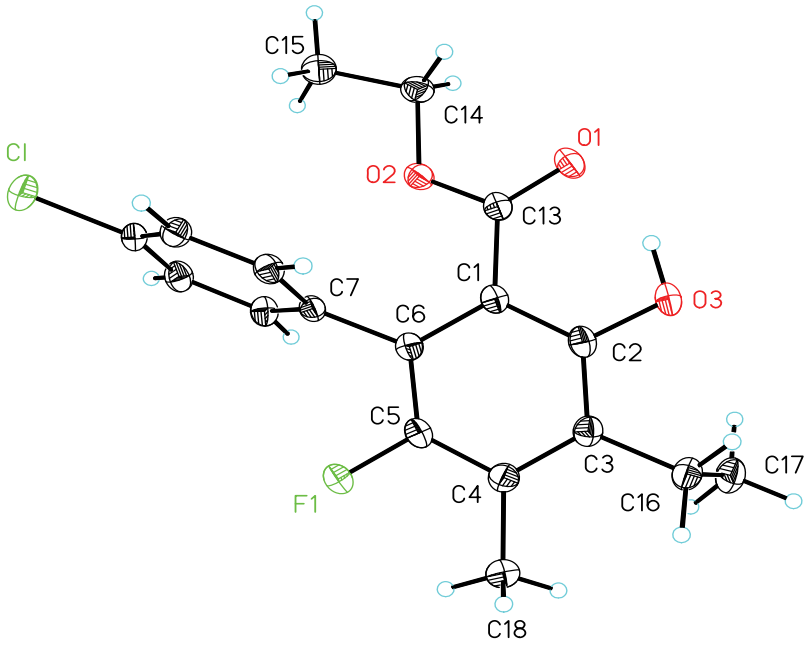


Figure 3-3: ORTEP-plot of **26n**

3.1.3. Conclusions

In conclusion, a variety of regioselective functionalized aryl fluorides, has been synthesized based on one-pot [3+3] cyclization of 1,3-bis(silyl enol ethers) with 2-fluoro-3-silyloxy-2-en-1-ones. These products are not readily available by other methods.

3.2. Fluorinated Lactones

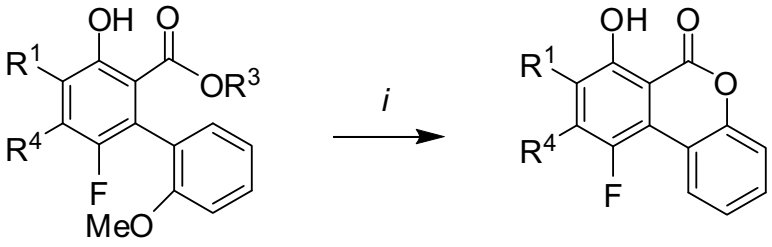
3.2.1. Introduction

As the biological relevance of 6*H*-Benzo[*c*]chromen-6-ones (dibenzo[*b*,*d*]pyran-6-ones, biaryl lactones)[44a,44c,45,74-78] has already been discussed in previous chapter. Recently, Langer *et al.* reported the synthesis of 6*H*-benzo[*c*]chromen-6-ones by reaction of 1,3-bis(silyl enol ethers) with benzopyrylium triflates.[79] As we have reported the recent approach to 6*H*-benzo[*c*]chromen-6-ones relies on the [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 1-(2-methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-ones and subsequent lactonization.[70] Herein, I wish to extend the scope of this methodology to the synthesis of 10-fluoro-6*H*-benzo[*c*]chromen-6-ones. The synthesis of this type of fluorinated core structure has, to the

best of my knowledge, not yet been reported.

3.2.2. Results and discussion

Treatment of biaryls **26a-f** with BBr_3 and subsequent addition of an aqueous solution of potassium *tert*-butanolate (KO*t*Bu) afforded the novel fluorinated dibenzo[*b*,*d*]pyran-6-ones **27a-f** (Scheme 3-3, Table 3-3). The formation of the products proceeded by cleavage of the arylmethyl ether and subsequent base-medaited lactonization. The structure of **27d** was independently confirmed by crystal structure analysis (Figure 3-4).



26a-f **27a-f**

Scheme 3-3: Synthesis of dibenzo[*b*,*d*]pyran-6-ones **27a-f**; *i*: BBr_3 (4.0 equiv.), CH_2Cl_2, 0 → 20 °C, 18 h, *ii*) KO*t*Bu (1M), H_2O, 15 min, 20 °C

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

26	R^1	R^3	R^4	% (**27**)[a]
a	H	Me	Me	91
b	Me	Me	Me	84
c	Et	Et	Me	75
d	H	Me	*n*Pr	47
e	Me	Me	*n*Pr	55
f	Et	Et	*n*Pr	67

[a] Isolated yields

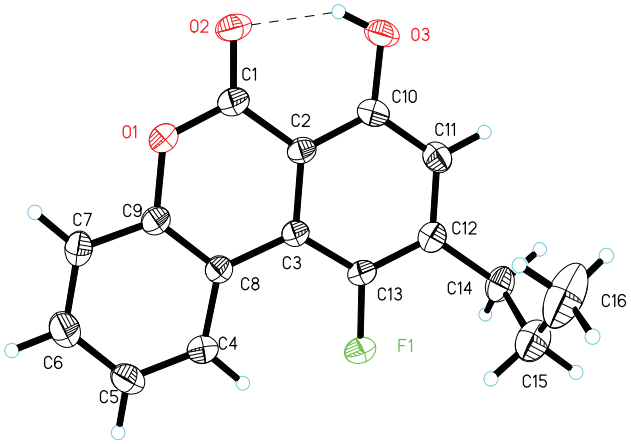


Figure 3-4: ORTEP-plot of **27d**

3.2.3. Conclusions

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

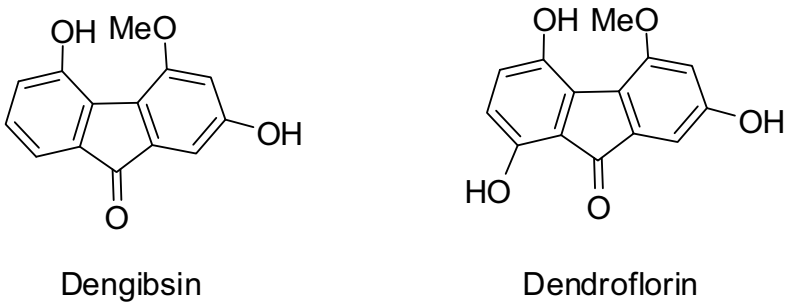
3.3. Fluorenones

3.3.1. Introduction

1-Hydroxyfluorenones are interesting lead structures in medicinal chemistry and are also present in nature (e. g. in the natural products dengibsin, dengibsinin, and dendroflorin).[80] Fluorinated fluorenones[81] are of specific interest in current medicinal chemistry. For example, it was shown that 4-fluorofluorenones possess antagonistic in vitro activity to human progesterone receptor B (hPR-B) in cotransfected CV-1 cells (IC50 = 158 nM).[82] Fluorenones have already been prepared, for example, by intramolecular Friedel–Crafts acylations of biaryls.[83] Snieckus and co-workers reported the synthesis of fluorenones based on remote aromatic metalation.[84] Some years ago, the synthesis of fluorenones using a Suzuki coupling/intramolecular Friedel–Crafts acylation sequence has been reported.[85] Recently, Reim *et al.* reported an efficient synthetic approach to fluorenones based on a '[3+3]

cyclization/Suzuki crosscoupling/Friedel–Crafts acylation' strategy.[86] Chan *et al.* reported the synthesis of 1-hydroxy-3-methylfluorenone by reaction of methyl 6-phenylsalicylate with concentrated sulfuric acid.[8a]

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

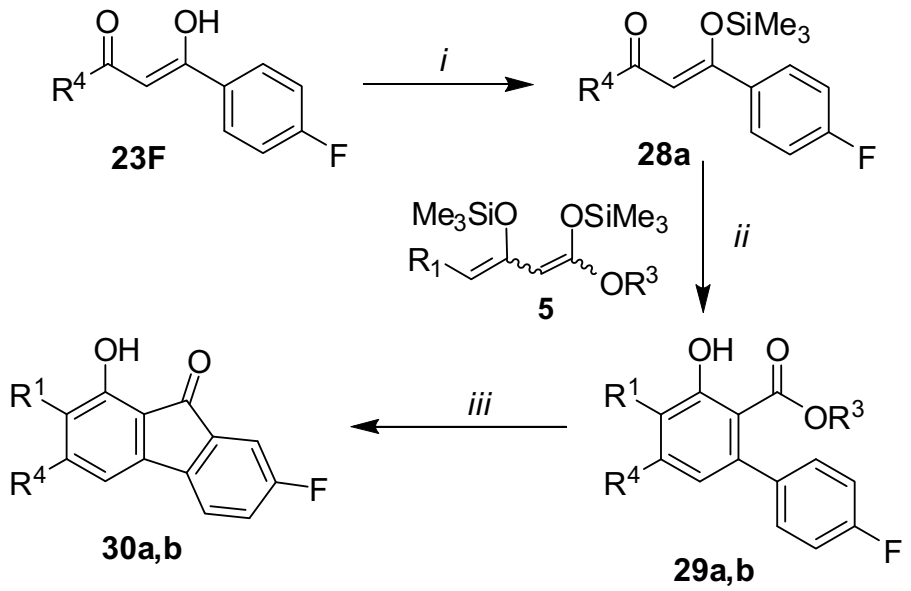


Dengibsin Dendroflorin

Figure 3-5: Some natural products containing fluorenones.

3.3.2. Results and discussion

3-silyloxy-2-en-1-ones **28a**, was prepared by reaction of 1,3-diketone **23f** with Me_3SiCl/NEt_3 (Scheme 3-4, Table 3-4). The $TiCl_4$ mediated formal [3+3] cyclization of **28a** with 1,3-bis(silyl enol ethers) **5a,c** – prepared from the corresponding 1,3-dicarbonyl compounds in one or two steps[8c]– afforded the novel fluorinated biaryls **29a,b** in moderate to good yields. Treatment of the latter with concentrated sulfuric acid afforded the fluorenones **30a,b** in high yields (Scheme 3-4, Table 3-4).



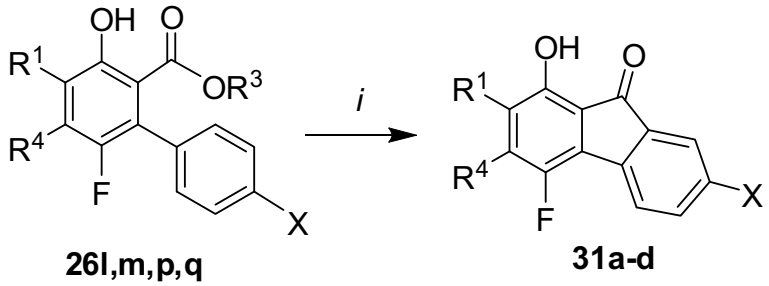
Scheme 3-4: Synthesis of fluorenones **30a,b**; *i*: NEt_3 (1.6 equiv.), Me_3SiCl (1.8 equiv.), C_6H_6, 20 °C, 72 h. *ii*: $TiCl_4$, CH_2Cl_2, –78 → 20 °C. *iii*: H_2SO4, 20 °C, 1 h.

Table 3-4: Synthesis of fluorenones **30a,b**

5	**29**	**30**	R^1	R^3	R^4	% (**29**)[a]	% (**30**)[a]
a	**a**	**a**	H	Me	Me	44	68
c	**a**	**b**	Et	Et	Me	49	76

[a] Isolated yields;

The novel 1-hydroxy-4-fluorofluorenones **31a-d** were obtained in good yields by simple treatment of 6-arylsalicylates **26l,m,p,q** with concentrated sulfuric acid (Scheme 3-5, Table 3-5).



26l,m,p,q **31a-d**

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

Table 3-5: Synthesis of fluorenones **31a-d**

26	**31**	X	R^1	R^3	R^4	% (**31**) [a]
l	**a**	Cl	H	Me	Me	77
m	**b**	Cl	Me	Me	Me	75
p	**c**	F	Me	Me	Me	74
q	**d**	F	Et	Et	Me	69

[a] Isolated yields

3.3.3. Conclusions

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

4. Synthesis of 4-Hydroxy- and 2,4-Dihydroxy-homophthalates by [4+2] Cycloaddition of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Dimethyl Allene-1,3-dicarboxylate

4.1. Introduction

A cycloaddition is a pericyclic chemical reaction, in which two π bonds are lost and two σ bonds are gained, the resulting reaction is a cyclization reaction. This refers to the Diels-Alder a [4 + 2] cycloaddition, which proceeds between a conjugated diene and a dienophile to form a cyclic system.[87] The diene component in the Diels-Alder reaction can be open-chain or cyclic and it can have many different kinds of substituents.[88] The dienophile is usually an electron deficient specie, mostly having the electron withdrawing group conjugated to unsaturated system. Different types of dienes and dienophiles are being used for the cycloaddition reactions. Here in, the masked dianions and allene as a diene and dienophile respectively, are of my particular interest. The synthesis and chemistry of masked dianions has already been discussed in the previous chapters. Allenes represent versatile synthetic building blocks in inter- and intramolecular [4+2] cycloadditions.[89] Synthesis of (−)-Epibatidine and its derivatives has been carried out from chiral allene-1,3-dicarboxylate esters.[90] The [4+2] cycloaddition of 1,3-bis(silyl enol ethers) with allenes has been reported to give functionalized phenols. For example, (*R*)-(+)-lasiodiplodin was prepared based on the cyclization of a cyclic allenylester with 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene.[91] The reaction of allenylphenylsulfone with Danishefsky's diene afforded 3-methyl-4-(phenylsulfonyl)-phenol.[92] Roush and Murphy were the first to report the cycloaddition of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with dimethyl allene-1,3-dicarboxylate.[93] Some years ago, Langer *et al*, has reported the synthesis of various homophthalates based on the cycloaddition of dimethyl allene-1,3-dicarboxylate with various 1,3-bis(silyl enol ethers).[94] Later on, this methodology was successfully applied to the synthesis of an analogue of lactonamycin[95] and of the N_7-C_{25} fragment of psymberin (Scheme 1).[96]

Herein, I report the full details of this methodology and a study related to the preparative scope.

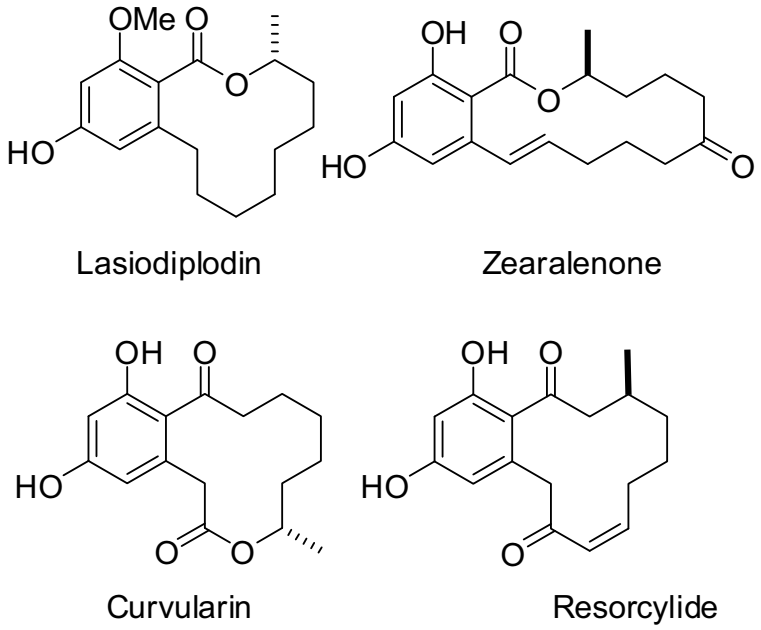


Figure 4-1: Some natural products containing Lasiodiplodin and related structures

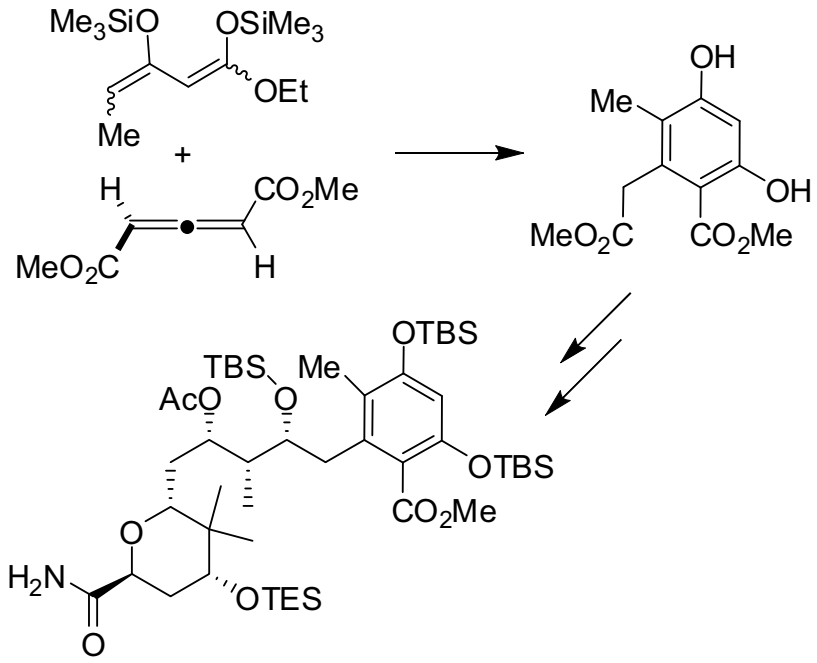
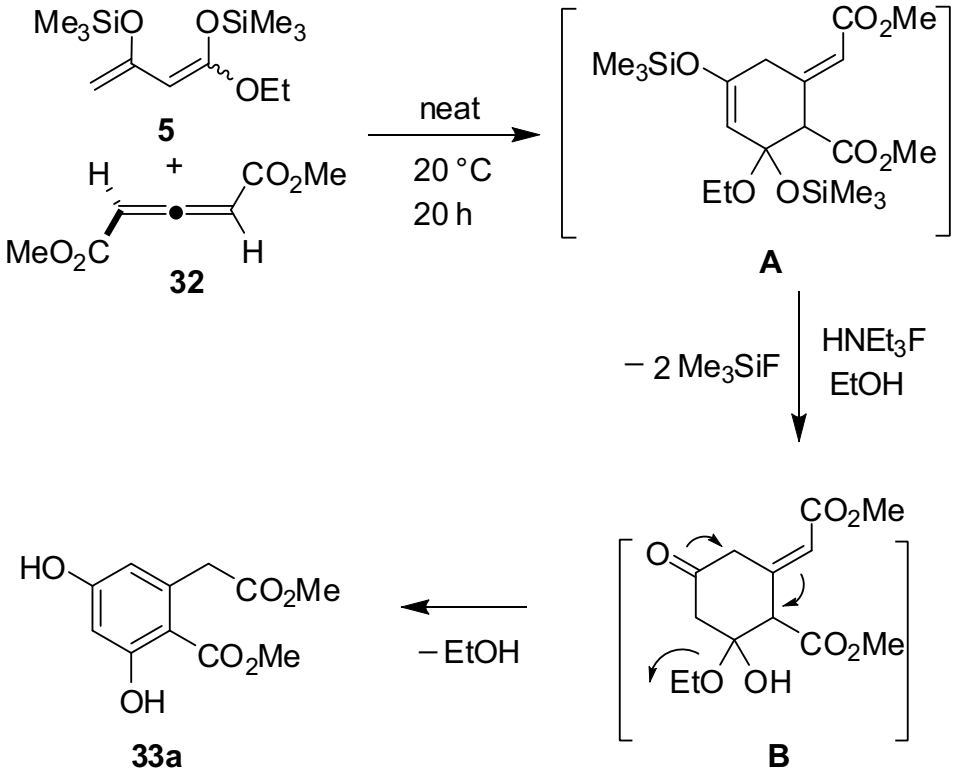


Figure 4-2: Synthesis of the N_7-C_{25} fragment of psymberin by Floreancig and Rech

4.2. Results and discussion

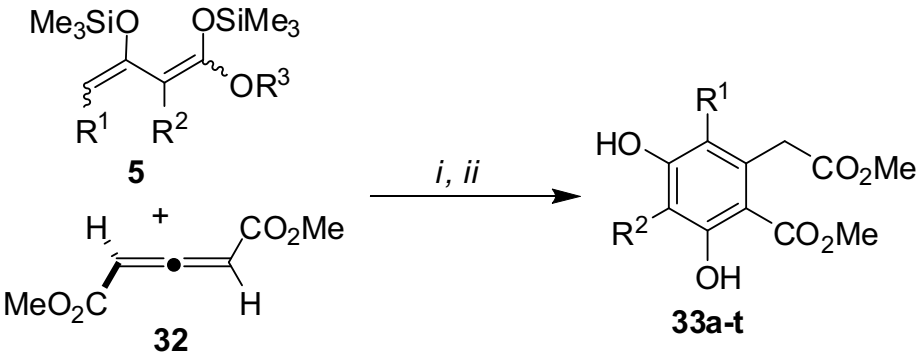
The reaction of 1-ethoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene **5a** (Table 1-1), prepared from ethyl acetoacetate in two steps[8a,8c,24] with dimethyl allene-1,3-dicarboxylate **32**, available from dimethyl acetone-1,3-dicarboxylate,[97] afforded the homophthalate **33a** up to 42% yield (Scheme 4-1, Table 4-1). The best yield was obtained when a mixture of the starting materials (neat) was stirred for 20 h at 20 °C. Subsequently, to the mixture was added an ethanolic solution of triethylammonium fluoride.[98] The formation of **33a** can be explained by [4+2] cycloaddition to give intermediate **A**, cleavage of the Si-O bonds upon addition of triethylammonium fluoride, and subsequent aromatization by extrusion of ethanol intermediate **B**, enolization and migration of the exocyclic double bond. The yield decreased when the reaction was carried out at elevated temperature (40 or 80 °C), or when the reaction was carried in a toluene solution (room temperature or reflux). The yield also decreased when the reaction time was decreased (no complete conversion) or increased (decomposition). The stoichiometry also played an important role. The use of an excess of the dienophile did not result in an increase of the yield.



Scheme 4-1: Possible mechanism of the formation of **33a**

Noteworthy, the selective elimination of ethanol (formation of a 3-hydroxyphenol) rather than water (formation of a 3-ethoxyphenol) was observed. The relatively low yield can be explained by partial decomposition of the quite sensitive diene, due to the long reaction time.

The cycloaddition of **32** with 1-alkoxy-, 1-aryloxy- and 1-thioaryloxy-1,3-bis(trimethylsilyloxy)-1,3-butadienes **5**, prepared in two steps from the corresponding β-ketoesters, afforded the 2,4-dihydroxyhomophthalates **33a-t** (Scheme 4-2, Table 4-1). A wide range of products – including fluoro-, chloro-, alkyl-, methoxy-, benzyloxy-, aryloxy-, arylthio-substituted derivatives – were successfully prepared. Moderate to good yields were obtained for all products (except for **33s**). Noteworthy, the reaction conditions were optimized for each individual experiment (reaction time and temperature, see experimental section).



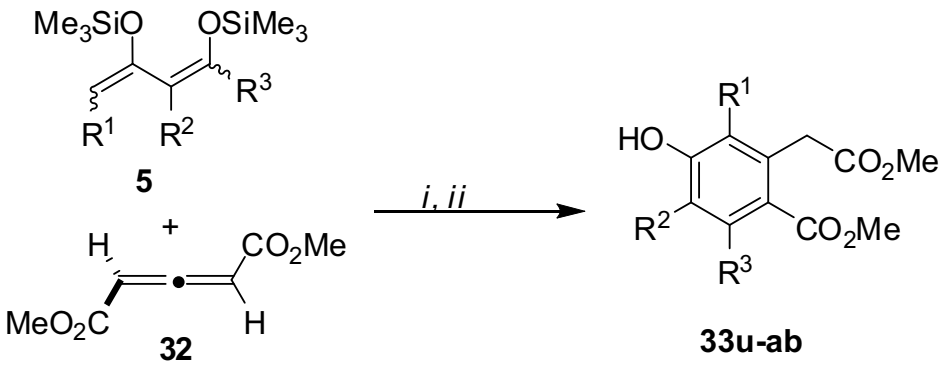
Scheme 4-2: Synthesis of 2,4-dihydroxyhomophthalates **33a-t**; *i*: neat 20-80 °C, 12-18 h. *ii* $HNET_3F$, H_2O

Table 4-1: Synthesis of 2,4-dihydroxyhomophthalates **31a-t**

33	R^1	R^2	R^3	% (**33**) [a]
a	H	H	Et	42
b	H	Et	Et	52
c	H	Cl	Et	64
d	H	F	Et	70
e	H	SPh	Me	50
f	Me	H	Me	51
g	Me	Cl	Me	47
h	Et	H	Et	40
i	Allyl	H	Et	50
j	*n*Bu	H	Et	38
k	*n*Hex	H	Me	52
l	*n*Oct	H	Me	56
m	Bn	H	Et	32
n	OMe	H	Me	34
o	OPh	H	Et	58
p	O(3-MeC_6H_4)	H	Et	48
q	O(2-MeC_6H_4)	H	Et	50
r	O(4-MeC_6H_4)	H	Et	54
s	OBn	H	Et	16
t	SPh	H	Et	41

[a] Isolated yields

The cycloaddition of **32** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5**, available from the corresponding 1,3-diketones, afforded the 4-hydroxyhomophthalates **33u-ab** (Scheme 4-3, Table 4-2). A wide range of products – including chloro-, alkyl- and aryloxy- substituted derivatives – were successfully prepared. All products were formed in moderate yields (except for **3x**). The conditions were, again, optimized for each individual experiment.



Scheme 4-3: Synthesis of 4-hydroxyhomophthalates **33u-ab**; *i*: neat 20-80 °C, 12-18 h. *ii* $HNET_3F$, H_2O

Table 4-2: Synthesis of 4-dihydroxyhomophthalates **33u-ab**

33	R^1	R^2	R^3	% (**33**)[a]
u	H	H	Me	40
v	H	H	Ph	46
w	H	Me	Me	44
x	H	CO_2Me	Me	20
y	H	Cl	Me	42
z	H	O[4-(EtO)C_6H_4]	Me	48
aa	H	O(4-ClC_6H_4)	Me	45
ab	H	O[4-(NC)C_6H_4]	Me	56

[a] Isolated yields

The regioselectivity of all products was confirmed by the two dimensional NMR spectroscopy (COSY and Correlation). The structures of **33b**, **33c** and **33d** were independently confirmed by X-ray crystal structure analyses (Figures 1-3).[116]

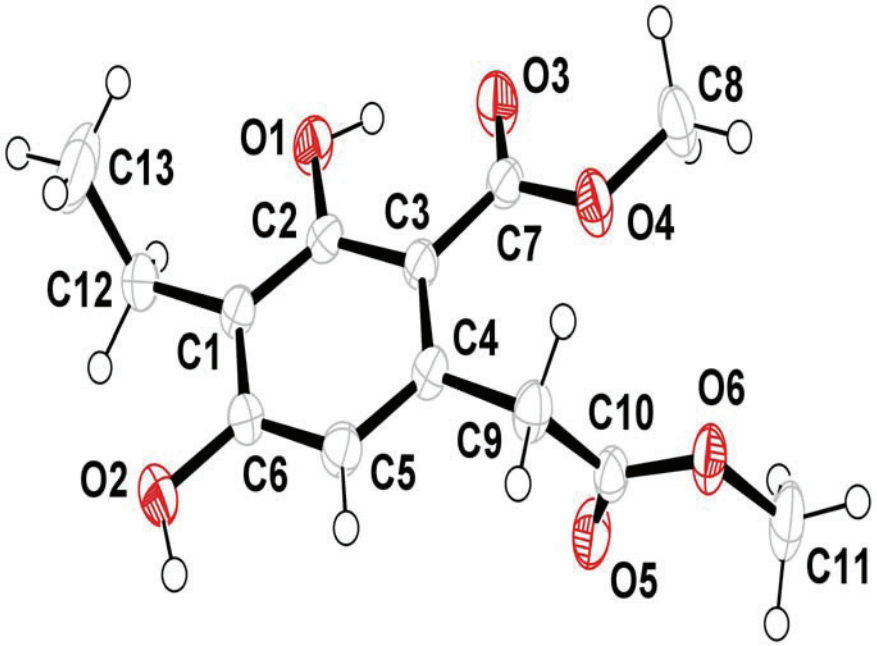


Figure 4-3: ORTEP-plot of **33b**

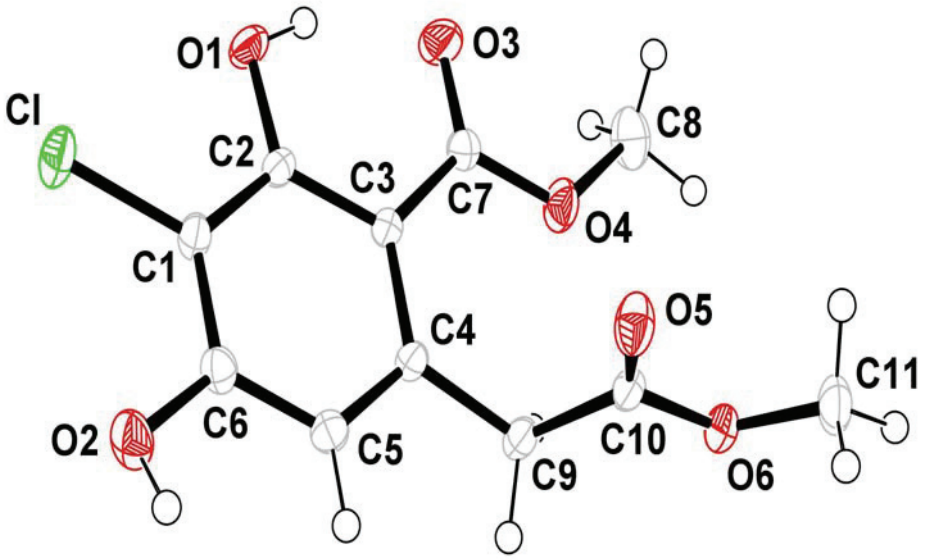


Figure 4-4: ORTEP-plot of **33c**

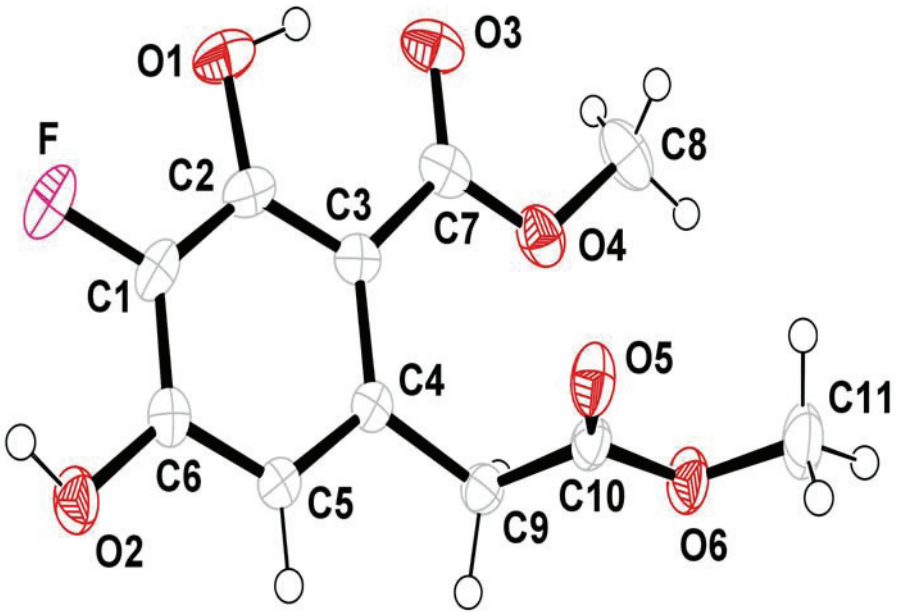


Figure 4-5: ORTEP-plot of **33d**

4.3. Conclusions

In conclusion, a variety of functionalized 4-hydroxy- and 2,4-dihydroxy-homophthalates has been prepared by reaction of 1,3-bis(trimethylsiloxy)-1,3-butadienes with dimethyl allene-1,3-dicarboxylate. These products are not readily available by other methods.

5. Synthesis of Functionalized 2-(Arylsulfonyl)-4-hydroxypyridines by Heter-Diels-Alder Reaction of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Arylsulfonyl Cyanides

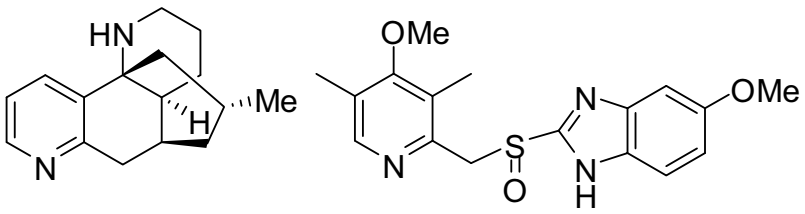
5.1. Introduction

The pyridine ring appears in a range of bioactive compounds, both naturally occurring and synthetic, often in highly substituted form; examples include the lycopodium alkaloids such as lycodine,[99] and the well-known proton pump inhibitor omeprazole, which is used to reduce the production of acid in the stomach. Thiopeptide antibiotics, a class of sulfur containing highly modified cyclic peptides, are of particular interest which are characterised by the presence of a heterocyclic centrepiece consisting of a tri- or tetra-substituted pyridine embedded in a macrocyclic array.[100] Examples of these types of natural products are amythiamicin D[101] and nosiheptide.[102]

Hetero Diels-Alder reaction is of particular interest, as it allows synthesis of heterocyclic framework. In amythiamicin D, the pyridine core was successfully constructesd via a biomimetic hetero-Diels–Alder reaction of a 2-azabutadiene.[101] Ghosez *et al.* reported a versatile method for the preparation of large range of pyridines and dihydropyridines, using 1-azabutadienes in hetero-Diels-Alder reaction.[103] The scope of the hetero-Diels–Alder reaction of 1-azabutadienes has been extended by the discovery of Boger and Blagg that N-sulfonyl-2-(ethoxycarbonyl)-1-aza-1,3-butadienes participate in the [4+2] cycloadditions with electron rich dienophiles.[104] The hetero-Diels–Alder reaction of aldehydes with Danishefsky's diene or related silyl enol ethers has been widely used for the synthesis of pyran derivatives.[103c,105] Ding *et al*. has reported the synthesis of δ-lactones based on the enantioselective hetero-Diels-Alder reaction of electron-rich 1,3-dimethoxy-1-(trimethylsiloxy)butadiene (Brassard's diene) with aldehydes.[106] In contrast, hetero-Diels–Alder reactions of nitriles are relatively rare, due to the low reactivity of nitriles as hetero-dienophiles.[107] Some years ago, Breitmaier and Rüffer reported[108] an efficient synthesis of functionalized pyridines by cyclization of buta-1,3-dienes, including 2-siloxy)buta-1,3-dienes, with highly reactive tosyl cyanide.[109] Pyridines have also been prepared by cyclization of pyran-2-ones with tosyl cyanide with extrusion of carbon dioxide.[110] The 1,3-dipolar cycloaddition of diazomethane with tosyl cyanide has been reported to give 1,2,3-triazines.[111] McClure *et al.* has reported the synthesis of 1-azabicyclo[2.2.2]oct-1-enes by cyclization of 2-(siloxy)cyclohexa-1,3-dienes with tosyl

cyanide.[112] Recently, Langer *et al*. reported the synthesis of 2-(arylsulfonyl)-4-hydroxypyridines,[113] which are of considerable pharmacological importance.[114]

However, the presence of a hydroxyl group at carbon C-3 (or C-5) of the pyridine ring, as in nosiheptide, presents a different challenge.[115] Herein, I report, to the best of my knowledge, a highly functionalized substitution pattern -for example alkyl, halide, aryloxy and thioaryloxy groups- at carbon C-3 (or C-5) position of 4-hyroxypyridines based on hetero-Diels–Alder reaction of 1,3-bis(trimethylsiloxy)buta-1,3-dienes (1,3-bis-silyl enol ethers)[8,24,25] with aryl cyanides. These reactions allow the convenient synthesis of 2-(arylsulfonyl)-4-hydroxypyridines having a wide range of substitution pattern at carbon C-3 (or C-5), which is difficult to achieve by electrophillic substitution reactions of pyridine. The synthesis of highly functionalized 2-(arylsulfonyl)-4-hydroxypyridines has not been yet reported.



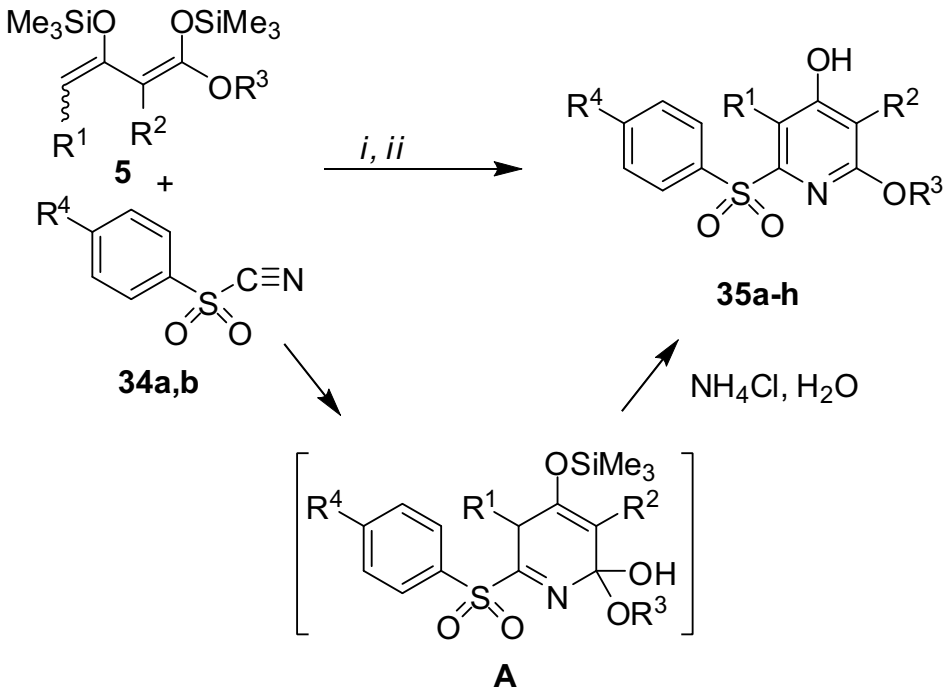
Lycodine Ompeprazole

Figure 5-1: Some novel compounds containing pyridine moiety as central core

5.2. Results and Discussion

The reaction of aryl cyanides **34a,b** with 1,3-bis(trimethylsiloxy)buta-1,3-dienes **5**, readily available from substituted methyl acetoacetate or ethyl acetoacetate, afforded the substituted 4-hydroxy-2-sulfonylpyridines **35a-h** (Scheme 5-1, Table 5-1) in up to 62% yield. The best yields were obtained when a neat mixture of the starting materials was allowed to slowly warm from –78 °C to ambient temperature. A complex mixture was obtained when the reaction was carried out at elevated temperatures or when a solvent was added. An aqueous work-up using NH_4Cl or HCl was necessary. The formation of **35** can be explained by [4+2] cycloaddition to give intermediate **A** and subsequent acid-mediated cleavage of the silyloxy group and aromatization. The reaction times were in the range of 48 to 96 h. In most cases, the reactions were carried out at –78 → 20 °C. Noteworthy, the yields of 4-hydroxy-2-sulfonylpyridines pyridines **35** were very good. This can be explained by the *cisoid*

conformation of 1,3-bis(sily enol ethers) **5** , due to the presence of the substituent located at the *central* carbon atom. The reaction of **34a,b** with 1,3-bis(sily enol ethers) containing a substituent located at the *terminal* carbon atom proved to be unsuccessful, presumably due to steric reasons. The employment of ethoxycarbonyl cyanide rather than **34a,b** proved to be unsuccessful, due to its low reactivity; decomposition was observed under forcing conditions (neat, 120 °C).



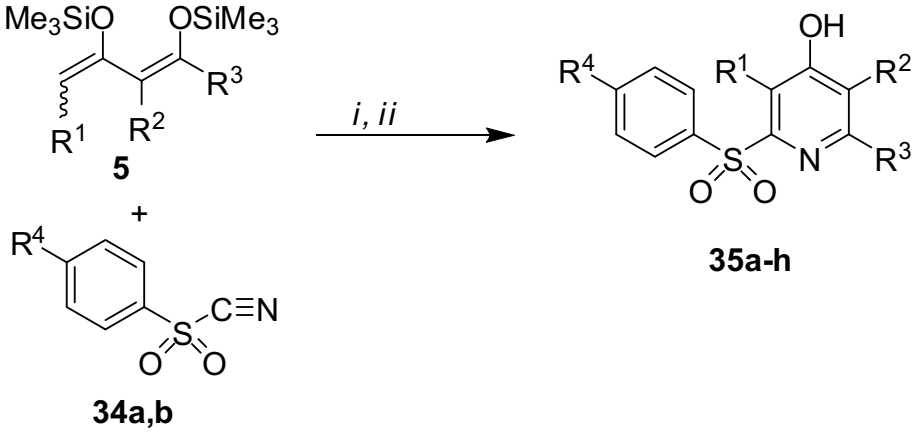
Scheme 5-1: Synthesis of 2-(arylsulfonyl)-4-hydroxypyridines **35a**–**h**; *i*: neat −78 °C to 60 °C, 48 to 96 h. *ii*: aq. 1M NH_4Cl

Table 5-1: Synthesis of 2-(arylsulfonyl)-4-hydroxypyridines **35a-h**

5	**34**	**35**	R^1	R^2	R^3	R^4	% (**35**)[a]
d	**a**	**a**	H	Cl	Et	H	56
e	**a**	**b**	H	F	Et	H	59
f	**a**	**c**	H	Et	Me	H	60
n	**a**	**d**	H	O(2,3-$Me_2C_6H_3$)	Et	H	61
o	**a**	**e**	H	SPh	Me	H	56
d	**b**	**f**	H	Cl	Et	Me	48
e	**b**	**g**	H	F	Et	Me	54
n	**b**	**h**	H	O(2,3-$Me_2C_6H_3$)	Et	Me	62

[a] Isolated yields

The reaction of aryl cyanide **34a,b** with 1,3-bis(trimethylsiloxy)buta-1,3-dienes **5**, readily available from substituted 1,3-diketones, afforded the substituted 4-hydroxy-2-tosylpyridine **35i-n** (Scheme 5-2, Table 5-2) in up to 79% yield, following the same procedure as discussed for **35a-h**.



Scheme 5-2: Synthesis of 2-(arylsulfonyl)-4-hydroxypyridines **35a**–**h**; *i*: neat −78 °C to 60 °C, 48 to 96 h. *ii*: aq. 1M NH_4Cl

Table 5-2: Synthesis of 2-(arylsulfonyl)-4-hydroxypyridines **35i-n**

5	**34**	**35**	R^1	R^2	R^3	R^4	% (**35**)[a]
q	**a**	**i**	H	SPh	CH_3	H	53
r	**a**	**j**	H	S(3-MeC_6H_4)	CH_3	H	79
u	**b**	**k**	H	O(3-MeC_6H_4)	CH_3	CH_3	58
v	**b**	**l**	H	O(4-MeC_6H_4)	CH_3	CH_3	57
q	**b**	**m**	H	SPh	CH_3	CH_3	64
s	**b**	**n**	H	S(4-MeC_6H_4)	CH_3	CH_3	51

[a] Isolated yields

The structures of carbon C-3 (or C-5) substituted 2-(arylsulfonyl)-4-hydroxypyridines **35a–n** were confirmed by spectroscopic methods. The compound **35k** was crystallized as a monohydrate of 2-methyl-3-(m-tolyloxy)-6-tosylpyridin-4-ol. The structures of **35i** and **35k** were independently confirmed by crystal structure analyses (Figures 5-2 and 5-3).[116]

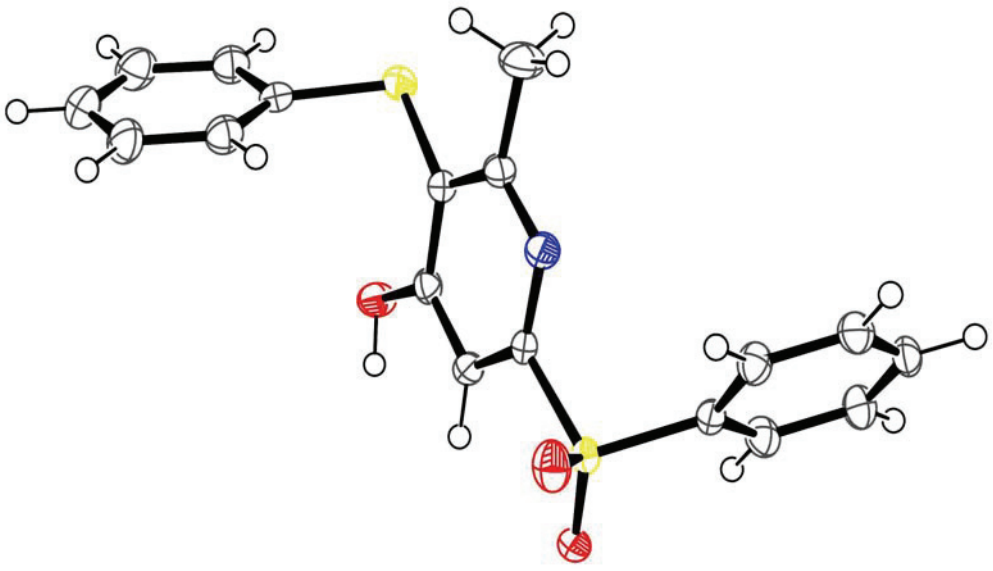


Figure 5-2: ORTEP-plot of **35i**

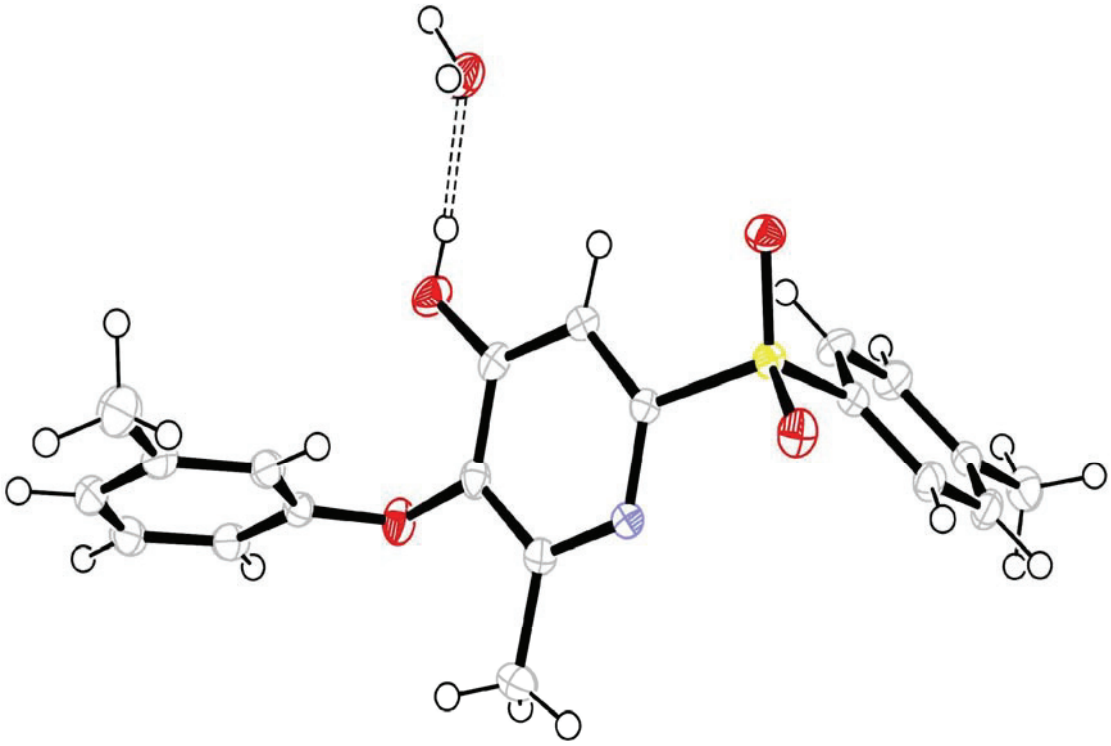


Figure 5-3: ORTEP-plot of **35k**

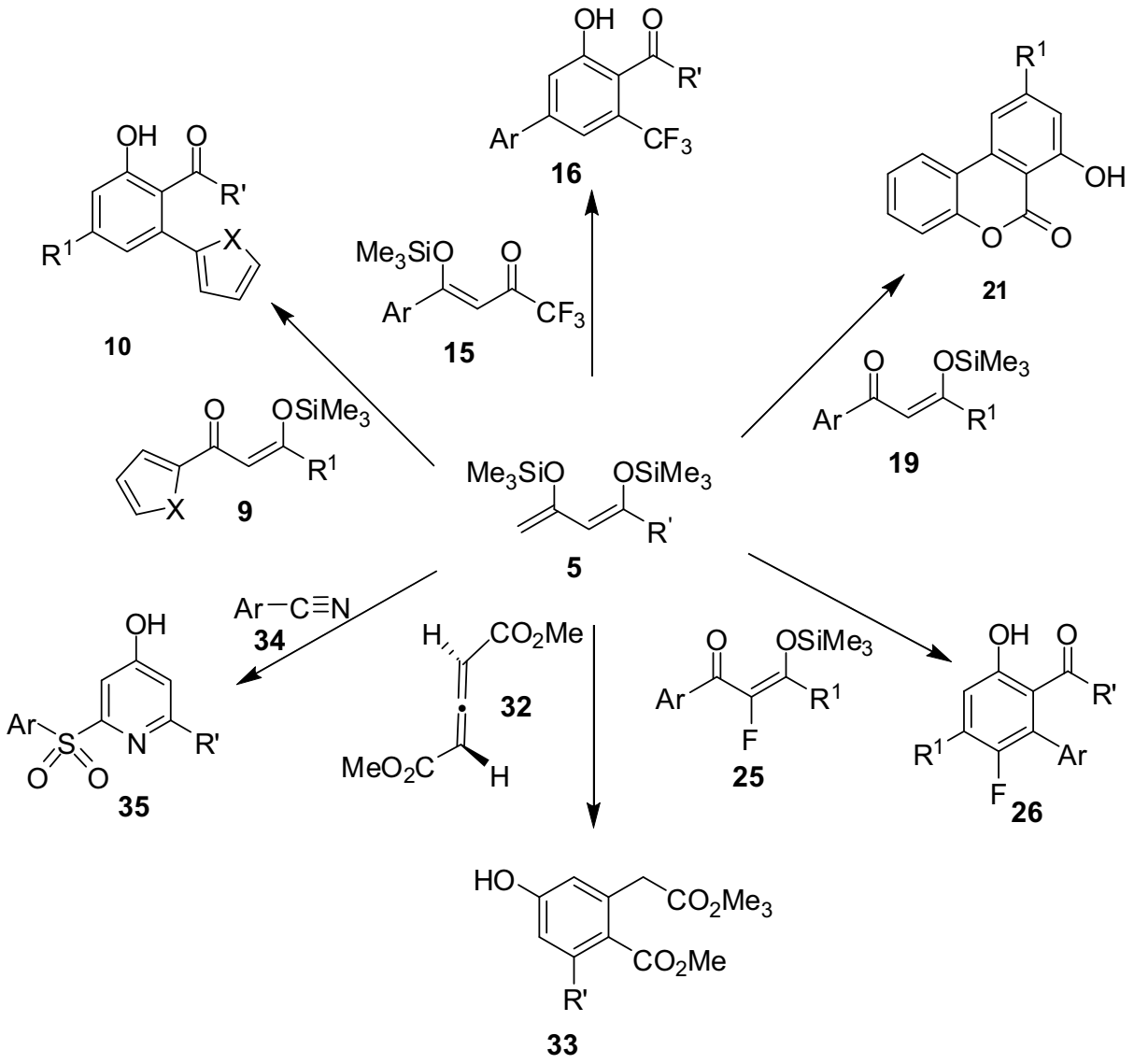
5.3. Conclusions

In conclusion, a variety of functionalized 5-alkyl-, 5-halide-, 5-aryloxy- and 5-thioaryloxy- 2-(arylsulfonyl)-4-hydroxypyridines has been prepared by hetero-Diels-Alder reaction of 1,3-bis(trimethylsiloxy)-1,3-butadienes with arylsulfonyl cyanides. The products are not readily available by other methods.

6. Abstract

One-pot cyclization reactions of 1,3-bis(silyl enol ethers) with the different electrophiles provide a convenient approach for the synthesis of various complex carbacycles and heterocycles from simple starting materials. 6-Hetaryl-salicylates and 4-Aryl and 4-Hetaryl-salicylates were prepared based on [3+3] cyclizations of 1,3-bis(sily enol ethers) in an efficient way. Dibenzo[*b*,*d*]pyran-6-ones were synthesized by formal [3+3] cyclization of 1,3-bis(silyl enol ethers) with 1-(2-methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-ones and subsequent BBr_3-mediated lactonization. Aryl fluorides were synthesized by [3+3] cyclization of 1,3-bis(silyl enol ethers) with 2-fluoro-3-silyloxy-2-en-1-ones. 1,3-Bis(silyl enol ethers) were used efficiently for the synthesis of highly functionalized homomphthalates and 4-hydoxypyridines based on [4+2] cyclization reactions.

Ein-Topf Cyclisierungensreaktionen von 1,3-Bis(silylenolethern) mit unterschiedlichen Elektrophilen ermöglicht einen bequemen Zugang zu einer großem Bandbreite von Carba- und Heterocyclen ausgehend von einfachen Startmaterialien. 6-Hetaryl-salicylate und 4-Aryl und 4-Hetaryl-salicylate wurde durch [3+3] Cyclisierungen von 1,3-Bis(silyenolethern) auf effiziente Weise hergestellt. Weiterhin wurden Dibenzo[*b*,*d*]pyran-6-one durch formale [3+3] Cyclisierungen von 1,3-Bis(silylenolethern) mit 1-(2-Methoxyphenyl)-1-(trimethylsilyloxy)alk-1-en-3-onen und anschließende BBr_3-vermittelte Lactonisierung synthetisiert. Arylfluoride wurden durch [3+3] Cyclisierungen von 1,3-Bis(silylenolethern) mit 2-Fluoro-3-silyloxy-2-en-1-onen hergestellt. 1,3-Bis(silylenolether) wurden weiterhin als Bausteine für die Synthese hochfunktionalisierter Homomphthalate und 4-Hydoxypyridine durch [4+2] Cycloadditionen erfolgreich eingesetzt.



General Scheme: As the part of this work was carried out with 1,3-bis(silyl enol ethers) and types of formed products (more substituents are not taken into the account)

7. Experimental Section:

7.1. General: Equipment, 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 (CDCl3) 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 Acetone d-6; δ = 77.00 ppm for CDCl3, 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: B

ruker 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 solvent were distilled before use.

TLC:

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

Chemicals and work technique:

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

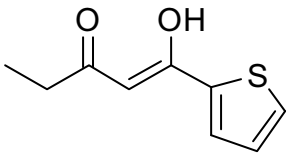
7.2. Procedures and Spectroscopic Data

General procedure for the synthesis of 1,3-dicarbonyl compounds 8, 18, 23:

To a stirred solution of LDA (75.0 mmol) in THF (1.2 mL/1.0 mmol of LDA) was added ketone **6** (50.0 mmol) at −78 °C. After the solution was stirred for 1 h, the acid chloride **7** (60.0 mmol) was added. The temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in *vacuo*. The residue was purified by

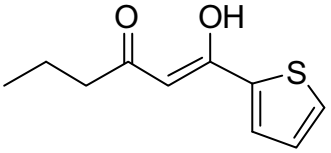
chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) to give **8.** Compounds **6a-c** were commercially available.

1-Hydroxy-1-(2-thienyl)-1-penten-3-one (8b).



Starting with THF (62.5 mL), LDA (75 mmol), 2-butanone **6b** (3.606 g, 50.0 mmol) and 2-thiophenecarbonyl chloride **7a** (8.796 g, 60.0 mmol), **8b** was isolated as a yellowish oil (2.720 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, ^{3}J = 6.6 Hz, 3 H, CH_2CH_3), 2.60 (q, ^{3}J = 7.6 Hz, 2 H, CH_2CH_3), 6.22 (s, 1 H, CH), 7.31−7.33 (m, 1 H, CH_{Hetar}), 7.78 (dd, ^{3}J = 4.9 Hz, ^{4}J = 1.1 Hz, 1 H, CH_{Hetar}), 7.88−7.90 (m, 1 H, CH_{Hetar}), 15.89 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.5 (CH_2CH_3), 31.0 (CH_2CH_3), 95.3 (CH), 128.5, 130.4, 132.6 (CH_{Hetar}), 142.1 (C_{Hetar}), 182.1 (COH), 186.1 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 182 ([M^+], 62), 153 (86), 126 (26), 111 (100), 97 (7), 83 (8), 69 (56), 56 (17), 53 (7), 45 (8), 39 (17), 29 (8). HRMS (EI): Calcd. for $C_9H_{10}O_2S$ [M^+]: 182.03960; found: 182.03933.

1-Hydroxy-1-(2-thienyl)-1-hexen-3-one (8c).



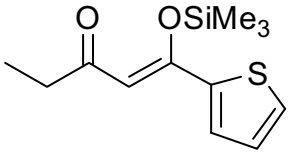
Starting with THF (62.5 mL), LDA (75.0 mmol), 2-pentanone **6c** (4.306 g, 50.0 mmol) and 2-thiophenecarboxylic acid chloride **2** (8.796 g, 60.0 mmol), 3c was isolated as a yellowish oil (2.750 g, 28%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, ^{3}J = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.53−1.61 (m, 2 H, $CH_2CH_2CH_3$), 2.21 (t, ^{3}J = 7.2 Hz, 2 H, $CH_2CH_2CH_3$), 5.91 (s, 1 H, CH), 6.97−7.00 (m, 1 H, CH_{Hetar}), 7.46 (dd, ^{3}J = 4.4 Hz, ^{4}J = 0.9 Hz, 1 H, CH_{Hetar}), 7.56−7.57 (m, 1 H, CH_{Hetar}), 15.62 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.6 ($CH_2CH_2CH_3$), 18.4 ($CH_2CH_2CH_3$), 38.2 ($CH_2CH_2CH_3$), 94.8 (CH), 126.6, 129.1, 131.9 (CH_{Hetar}), 142.6 (C_{Hetar}), 181.0 (COH), 189.1 (CO). GC-MS (EI, 70 eV): m/z (%) = 196 ([M^+], 47), 181 (3), 168 (14), 153 (100), 135 (4), 126 (34), 111 (90), 97 (7), 85 (7), 69 (53), 53 (5), 39 (18). HRMS (EI): Calcd. for $C_{10}H_{12}O_2S$ [M^+]: 196.05525; found: 196.05469.

General procedure for the synthesis of sily enol ethers 9, 15, 19, 25, 28:

To a stirred benzene solution (2.5 mL/1.0 mmol of **8**) of **8** (10.0 mmol) was added triethylamine (16.0 mmol). After the solution was stirred for 2 h, trimethylchlorosilane (18.0 mmol) was added. After the solution was stirred for 72 h, the solvent was removed in *vacuo* and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered

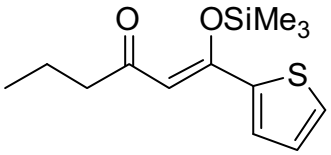
under argon atmosphere. The filtrate was concentrated in *vacuo* to give silyl enol ethers **9**. The compounds **14a-c** were available commercially.

1-(2-Thienyl)-1-[(trimethylsilyl)oxy]-1-penten-3-one (9b).



Starting with benzene (30.0 mL), **8b** (1.821 g, 10.0 mmol), triethylamine (1.619 g, 16.0 mmol) and trimethylchlorosilane (1.738 g, 18.0 mmol), **9b** was isolated as a reddish oil (2.162 g, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.20 (m, 9 H, $Si(CH_3)_3$), 0.98 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3), 2.68 (q, ^{3}J = 7.6 Hz, 2 H, CH_2CH_3), 5.96 (s, 1 H, CH), 6.93−6.95 (m, 1 H, CH_{Hetar}), 7.36−7.38 (m, 1 H, CH_{Hetar}), 7.42−7.44 (m , 1 H, CH_{Hetar}).

1-(2-Thienyl)-1-[(trimethylsilyl)oxy]-1-hexen-3-one (9c).

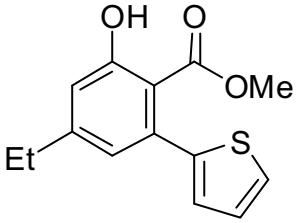


Starting with benzene (73.0 mL), **8c** (4.799 g, 24.5 mmol), triethylamine (3.960 g, 39.1 mmol) and trimethylchlorosilane (4.780 g, 44.0 mmol), **9c** was isolated as a yellowish oil (6.018 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.27 (m, 9 H, $Si(CH_3)_3$), 0.90 (t, ^{3}J = 7.2 Hz, 3 H, $CH_2CH_2CH_3$), 1.53 (m, 2 H, $CH_2CH_2CH_3$), 2.74 (t, ^{3}J = 6.1 Hz, 2 H, $CH_2CH_2CH_3$), 6.08 (s,1 H, CH), 6.97−7.01 (m, 1 H, CH_{Hetar}), 7.43−7.45 (m, 1 H, CH_{Hetar}), 7.49−7.51 (m , 1 H, CH_{Hetar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.3 ($Si(CH_3)_3$), 12.8 ($CH_2CH_2CH_3$), 18.4 ($CH_2CH_2CH_3$), 35.3 ($CH_2CH_2CH_3$), 103.8 (CH), 127.5, 128.8, 132.0 (CH_{Hetar}), 147.3 (C_{Hetar}), 174.8 (C), 181.7 (CO).

General procedure for the synthesis of salicylates 10, 16, 20, 26, 29:

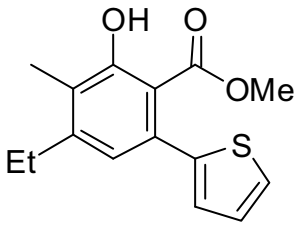
To a CH_2Cl_2 solution (2 mL/1.0 mmol of **9**) of **9** (1.0 mmol) was added **5** (1.1 mmol) and, subsequently, $TiCl_4$ (1.1 mmol) at −78 °C. The temperature of the solution was allowed to warm to 20 °C during 14 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in *vacuo*. The residue was purifed by chromatography (silica gel, *n*-heptane / EtOAc) to give **10**.

Methyl 4-ethyl-2-hydroxy-6-(2-thienyl)benzoate (10f).



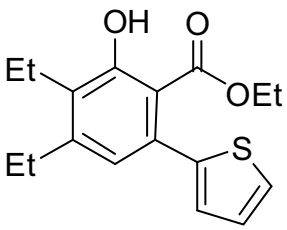
Starting with **9b** (0.448 g, 2.0 mmol), **5a** (0.567 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10f** was isolated as a reddish viscous oil (0.184 g, 35%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 2.53 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.50 (s, 3 H, OCH_3), 6.69 (s, 1 H, CH_{Ar}), 6.77 (s, 1 H, CH_{Ar}), 6.81 (m, 1 H, CH_{Hetar}), 6.91 (dd, ^3J = 5.1 Hz, ^4J = 1.7 Hz, 1 H, CH_{Hetar}), 7.21 (dd, ^3J = 4.9 Hz, ^4J = 1.3 Hz, 1 H, CH_{Hetar}), 10.55 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_2CH_3), 27.7 (CH_2CH_3), 50.8 (OCH_3), 109.0 (CCOOCH$_{3Ar}$), 115.5 (CH_{Ar}), 122.8, 123.9 (CH_{Hetar}), 124.7 (CH_{Ar}), 125.4 (CH_{Hetar}), 135.5, 142.7 (C_{Ar}), 149.7 (C_{Hetar}), 160.5 (COH_{Ar}), 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2967 (s), 2872 (w), 1734 (w), 1664 (s), 1610 (s), 1568 (s), 1440 (s), 1360 (s), 1265 (s), 1160 (m), 1098 (s), 1014 (m), 932 (m), 808 (m), 791 (m), 697 (s).GC-MS (EI, 70 eV): *m/z* (%) = 262 ([M$^+$], 43), 230 (100), 202 (26), 187 (24), 173 (7), 115 (10). HRMS (EI): Calcd. for $C_{14}H_{14}O_3S$ [M$^+$]: 262.0582; found: 262.06562.

Methyl 4-ethyl-2-hydroxy-3-methyl-6-(2-thienyl)benzoate (10g).



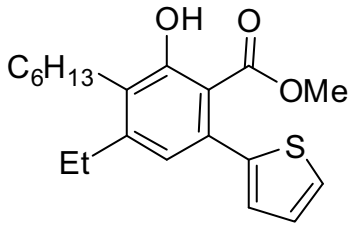
Starting with **9b** (0.448 g, 2.0 mmol), **5b** (0.598 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10g** was isolated as a reddish viscous oil. (0.180 g, 34%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.13 (s, 3 H, CH_3), 2.54 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.48 (s, 3 H, OCH_3), 6.67 (s, 1 H, CH_{Ar}), 6.77−6.79 (m, 1 H, CH_{Hetar}), 6.90 (dd, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1 H, CH_{Hetar}), 7.16 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1 H, CH_{Hetar}), 10.87 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.0 (CH_2CH_3), 14.0 (CH_3), 26.8 (CH_2CH_3), 51.7 (OCH_3), 109.0 (CCOOCH$_{3Ar}$), 123.1 (CH_{Ar}), 123.5, 124.6, 126.3 (CH_{Hetar}), 133.3, 139.7 (C_{Ar}), 144.4 (C_{Hetar}), 148.4 (C_{Ar}), 159.6 (COH_{Ar}), 171.6 (CO). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1663 (s), 1607 (m), 1561 (m), 1261 (s), 1220 (m), 1196 (m), 1160 (m), 1102 (w), 1043 (m), 1007 (m), 848 (m), 806 (m), 766 (w), 649 (s). MS (EI, 70 eV): *m/z* (%) = 276 ([M$^+$], 98), 244 (100), 216 (91), 201 (41), 187 (23), 173 (25), 115 (15), 97 (8), 69 (10), 55 (8), 43 (8). HRMS (CI, positive): Calcd. for $C_{15}H_{17}O_3S$ ([M+1]$^+$): 277.08929; found: 277.08890.

Ethyl 3,4-diethyl-2-hydroxy-6-(2-thienyl)benzoate (10h).



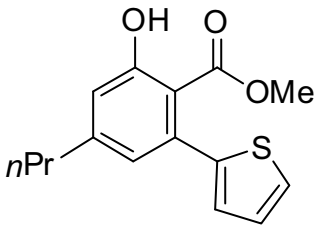
Starting with **9b** (0.448 g, 2.0 mmol), **5c** (0.659 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10h** was isolated as a reddish viscous oil (0.186 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 7.0 Hz, 3 H, CH_2CH_3), 1.09 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.12 (t, ^3J = 7.6 Hz, 3 H, OCH_2CH_3), 2.56 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 2.64 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.96 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 6.67 (s, 1 H, CH_{Ar}), 6.76−6.78 (m, 1 H, CH_{Hetar}), 6.90 (dd, ^3J = 5.1 Hz, ^4J = 1.5 Hz, 1 H, CH_{Hetar}), 7.17 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1 H, CH_{Hetar}), 10.99 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 (CH_2CH_3), 14.4 (CH_2CH_3), 16.6 (OCH_2CH_3), 19.5 (CH_2CH_3), 26.4 (CH_2CH_3), 61.3 (OCH_2CH_3), 110.8 ($CCOOCH_2CH_{3Ar}$), 124.2 (CH_{Ar}), 125.9, 126.1, 127.1 (CH_{Hetar}), 134.0, 139.7 (C_{Ar}), 144.8 (C_{Hetar}), 148.1 (C_{Ar}), 160.4 (COH_{Ar}), 171.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2968 (s), 2874 (m), 1657 (s), 1606 (m), 1559 (m), 1463 (m), 1394 (s), 1322 (m), 1274 (s), 1242 (m), 1220 (s), 1175 (s), 1109 (m), 1030 (m), 870 (w), 812 (m), 694 (s). MS (EI, 70 eV): *m/z* (%) = 304 ([M^+], 47), 258 (100), 229 (31), 215 (52), 201 (6), 187 (7), 171 (13), 153 (6), 97 (11), 81(9), 69 (14), 55 (13), 41 (11). HRMS (EI): Calcd. for $C_{17}H_{20}O_3S$ [M^+]: 304.11277; found: 304.11299.

Methyl 4-ethyl-3-hexyl-2-hydroxy-6-(2-thienyl)-benzoate (10i).



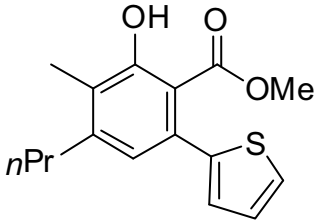
Starting with **9b** (0.425 g, 1.7 mmol), **5h** (0.628 g, 1.8 mmol) and $TiCl_4$ (0.20 mL, 1.8 mmol), **10i** was isolated as a reddish viscous oil (0.156 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t(br), ^3J = 7.0 Hz, 3 H, $CH_2(CH_2)_4CH_3$), 1.03 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.08−1.14 (m, 8 H, $CH_2(CH_2)_4CH_3$), 2.46 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 2.48 (q, ^3J = 8.1 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.41 (s, 3 H, OCH_3), 6.59 (m, 1 H, CH_{Ar}), 6.70 (m, 1 H, CH_{Hetar}), 6.82 (dd, ^3J = 6.4 Hz, ^4J = 1.7 Hz, 1 H, CH_{Hetar}), 7.07−7.09 (m, 1 H, CH_{Hetar}), 10.71 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2 ($(CH_2)_5CH_3$), 20.9 (CH_2CH_3), 23.8, 27.2, 30.4, 30.7, 31.0, 33.1 (CH_2), 53.0 (OCH_3), 111.2 ($CCOOCH_{3Ar}$), 124.9 (CH_{Ar}), 125.9, 126.6, 127.6 (CH_{Hetar}), 130.4, 134.6 (C_{Ar}), 145.8 (C_{Hetar}), 149.3 (C_{Ar}), 160.8 (COH_{Ar}), 172.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2925 (s), 2854 (m), 1661 (s), 1606 (m), 1559 (m), 1439 (s), 1396 (s), 1324 (m), 1263 (s), 1220 (s), 1197 (m), 1162 (m), 1125 (w), 849 (m), 813 (w), 649 (m). GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M^+], 43), 314 (8), 285 (100), 271 (5), 257 (8), 244 (55), 215 (13), 187 (4), 171 (12), 153 (4), 85 (8), 71 (11), 57 (15), 43 (13). HRMS (EI): Calcd. for $C_{20}H_{26}O_3S$ [M^+]: 346.15972; found: 346.15989.

Methyl 2-hydroxy-4-propyl-6-(2-thienyl)benzoate (**10j**).



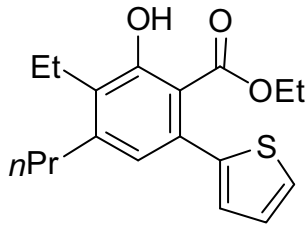
Starting with **9c** (0.536 g, 2.0 mmol), **5a** (0.568 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10j** was isolated as a reddish viscous oil (0.214 g, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.45−1.58 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.42 (t, ^3J = 7.8 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.46 (s, 3 H, OCH_3), 6.62 (s, 1 H, CH_{Ar}), 6.70 (s, 1 H, CH_{Ar}), 6.77 (m, 1 H, CH_{Hetar}), 6.86 (m, 1 H, CH_{Hetar}), 7.15 (d, ^3J = 6.3 Hz, 1H, CH_{Hetar}), 10.57 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7 (CH_3), 23.6, 37.7 (CH_2), 51.7 (OCH_3), 110.2 ($\mathit{C}COOMe_{Ar}$), 117.1, 124.3 (CH_{Ar}), 124.9, 125.6, 126.4 (CH_{Hetar}), 136.7, 143.7 (C_{Ar}), 149.2 (C_{Hetar}), 161.4 (COH_{Ar}), 171.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3012 (w), 2844 (w), 1662 (s), 1499 (m), 1459 (s), 1378 (s), 1239 (s), 1106 (m), 1074 (m), 1025 (m), 806 (m). MS (EI, 70 eV): *m/z* (%) = 276 ([M^+], 60), 244 (100), 229 (5), 216 (97), 187 (24), 160 (10), 115 (20). HRMS (EI): Calcd. for $C_{15}H_{16}SO_3$ [M^+]: 276.08147; found: 276.08178.

Methyl 2-hydroxy-3-methyl-4-propyl-6-(2-thienyl)-benzoate (10k).



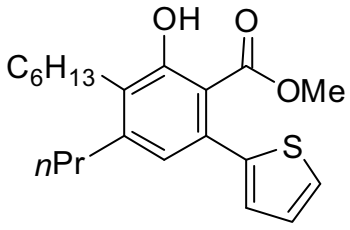
Starting with **9c** (0.537 g, 2.0 mmol), **5b** (0.604 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10k** was isolated as a reddish viscous oil (0.274 g, 47%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.46−1.49 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.14 (s, 3 H, CH_3), 2.49 (t, ^3J = 7.8 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.49 (s, 3 H, OCH_3), 6.66 (s,1 H, CH_{Ar}), 6.78-6.79 (m, 1 H, CH_{Hetar}), 6.90 (dd, ^3J = 5.1 Hz, ^4J = 1.5 Hz, 1H, CH_{Hetar}), 7.17 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1H, CH_{Hetar}), 10.88 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.7 ($CH_2CH_2\mathit{CH_3}$), 14.7 (CH_3), 23.1 ($CH_2\mathit{CH_2}CH_3$), 36.3 ($\mathit{CH_2}CH_2CH_3$), 52.2 (OCH_3), 110.2 ($\mathit{C}COOMe_{Ar}$), 124.8 (CH_{Ar}), 125.9, 126.8, 127.5 (CH_{Hetar}), 133.5, 140.0 (C_{Ar}), 144.6 (C_{Hetar}), 147.5 (C_{Ar}), 160.1 (COH_{Ar}), 172.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2957 (s), 2871 (m), 1662 (s), 1607 (m), 1562 (m), 1438 (s), 1397 (s), 1312 (m), 1266 (s), 1198 (m), 1161 (m), 1011 (w), 849 (w), 807 (m), 747 (w), 697 (m). MS (EI, 70 eV): *m/z* (%) = 290 ([M^+], 72), 258 (100), 229 (18), 215 (25), 202 (55), 187 (13), 171 (13), 158 (4), 128 (9), 115 (10), 89 (3), 77 (4), 45 (3). HRMS (EI): Calcd. for $C_{16}H_{18}O_3S$ [M^+]: 290.09712; found: 290.09699.

Ethyl 3-ethyl-2-hydroxy-4-propyl-6-(2-thienyl)-benzoate (6l).



Starting with **9c** (0.537 g, 2.0 mmol), **5c** (0.659 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10l** was isolated as a reddish viscous oil (0.245 g, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.0 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 0.89 (t, ^3J = 7.2 Hz, 3 H, $CH_2\mathit{CH_3}$), 1.09 (t, ^3J = 7.4 Hz, 3 H, $OCH_2\mathit{CH_3}$), 1.49−1.56 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.50 (t, ^3J = 7.8 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 2.64 (q, ^3J = 7.4 Hz, 2 H, $\mathit{CH_2}CH_3$), 3.96 (q, ^3J = 7.0 Hz, 2 H, $O\mathit{CH_2}CH_3$), 6.66 (s, 1 H, CH_{Ar}), 6.76−6.77 (m, 1 H, CH_{Hetar}), 6.88 (dd, ^3J = 5.1 Hz, ^4J = 1.5 Hz, 1H, CH_{Hetar}), 7.16 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1H, CH_{Hetar}), 10.99 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 ($CH_2CH_2\mathit{CH_3}$), 14.3 ($\mathit{CH_2}CH_3$), 14.6 ($OCH_2\mathit{CH_3}$), 19.6 ($CH_2\mathit{CH_2}CH_3$), 24.5 ($\mathit{CH_2}CH_2CH_3$), 35.5 ($\mathit{CH_2}CH_3$), 61.3 ($O\mathit{CH_2}CH_3$), 110.8 ($\mathit{C}COOCH_2CH_{3Ar}$), 124.8 ($CH_{Ar}$), 125.0, 125.9, 126.7 ($CH_{Hetar}$), 131.0, 133.7 ($C_{Ar}$), 142.6 ($C_{Hetar}$), 144.8 ($C_{Ar}$), 160.2 ($COH_{Ar}$), 171.6 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 318 ([M^+], 62), 272 (100), 257 (64), 244 (18), 229 (45), 216 (7), 201 (7), 187 (5), 171 (14), 153 (4), 115 (7), 97 (3), 77 (3). HRMS (EI): Calcd. for $C_{18}H_{22}O_3S$ [M^+]: 318.12842; found: 318.12842.

Methyl 3-hexyl-2-hydroxy-4-propyl-6-(2-thienyl)-benzoate (10m).

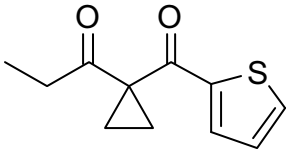


Starting with **9c** (0.537 g, 2.0 mmol), **5h** (0.812 g, 2.2 mmol) and $TiCl_4$ (0.24 mL, 2.2 mmol), **10m** was isolated as a reddish viscous oil (0.273 g, 35%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t(br), ^3J = 4.7 Hz, 3 H, $CH_2(CH_2)_4\mathit{CH_3}$), 0.81 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.08 (m, 8H, $CH_2(\mathit{CH_2})_4CH_3$), 1.39−1.47 (m, 2H, $CH_2\mathit{CH_2}CH_3$), 2.41 (t, ^3J = 7.8 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 2.49 (t, ^3J = 7.4 Hz, 2 H, $\mathit{CH_2}(CH_2)_4CH_3$), 3.41 (s, 3 H, OCH_3), 6.57 (m, 1 H, CH_{Ar}), 6.69−6.71 (m, 1 H, CH_{Hetar}), 6.81 (dd, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1 H, CH_{Hetar}), 7.10 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1 H, CH_{Hetar}), 10.71 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 ($(CH_2)_5\mathit{CH_3}$), 13.2 ($CH_2CH_2\mathit{CH_3}$), 21.6, 23.0, 25.0, 28.5, 28.6, 30.7, 34.2 (CH_2), 50.8 (OCH_3), 108.9 ($\mathit{C}COOCH_{3Ar}$), 123.5 (CH_{Ar}), 123.6, 124.4, 125.4 (CH_{Hetar}), 128.5, 132.1 (C_{Ar}), 143.3 (C_{Hetar}), 145.7 (C_{Ar}), 158.7 (COH_{Ar}), 170.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2927 (s), 2870 (m), 1663 (s), 1605 (m), 1559 (m), 1437 (s), 1396 (s), 1268 (s), 1161 (s), 1114 (w), 1015 (w), 810 (m), 693 (s). MS (EI, 70 eV): *m/z* (%) = 360 ([M^+], 79), 328 (35), 311 (21), 285 (100), 271 (13), 258 (73), 243 (28), 201 (11), 171 (11), 97 (6), 83 (6), 57 (11). HRMS (CI, Positive): Calcd. for $C_{21}H_{29}O_3S$ ([M+1]$^+$): 361.18319; found: 361.18305.

General procedure for the synthesis of 12:

To a stirred dimethylsulfoxide solution (1 mL/1.0 mmol of **8**) of **8** (10.0 mmol) was added potassium carbonate (40.0 mmol) at room temperature. After the solution was stirred for 30 min, 1,2-dibromoethane **11** (20.0 mmol) was added at 20 °C. After the solution was stirred for 12 h, an excess amount of water was added to remove dimethylsulfoxide and the mixture was extracted with dichloromethane. The combined organic layers were dried (Na_2SO_4) and filtered. The filtrate was concentrated in *vacuo*. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) to give **12**.

1-[1-(2-Thienylcarbonyl)cyclopropyl]-1-ethanone (12a).

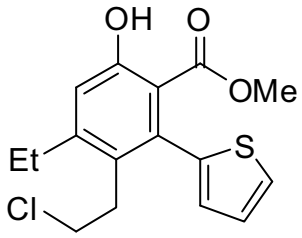


Starting with dimethysulfoxide (17.8 mL), **8b** (3.250 g, 17.840 mmol), K_2CO_3 (9.863 g, 71.4 mmol) and 1,2-dibromoethane **11** (6.704 g, 35.7 mmol), **12a** was isolated as a reddish oil (3.417 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, ^3J = 7.1 Hz, 3 H, CH_2CH_3), 1.34 (t, ^3J = 3.1 Hz, 2 H, CH_2), 1.43 (t, ^3J = 3.2 Hz, 2 H, CH_2), 2.42 (q, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 7.05 (dd, ^3J = 4.9 Hz, ^4J = 1.1 Hz, 1 H, CH_{Hetar}), 7.56−7.58 (m, 1 H, CH_{Hetar}), 7.60−7.62 (m, 1 H, CH_{Hetar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.4 (CH_2CH_3), 16.1 ($2CH_2$), 35.2 (CH_2CH_3), 41.6 (CO*C*CO), 128.2, 133.6, 134.2 (CH_{Hetar}), 143.4 (C_{Hetar}), 188.7, 206.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2977 (w), 1700 (m), 1647 (s), 1512 (w), 1409 (s), 1315 (m), 1233 (m), 1052 (m), 972 (w), 794 (w), 721 (s), 657 (w). GC-MS (EI, 70 eV): *m/z* (%) = 208 ([M^+], 16), 193 (10), 179 (22), 151 (9), 111 (100), 83 (8), 57 (13), 39 (13). HRMS (EI): Calcd. for $C_{11}H_{12}O_2S$ [M^+]: 208.05507; found: 208.05475.

General procedure for the synthesis of salicylates 13:

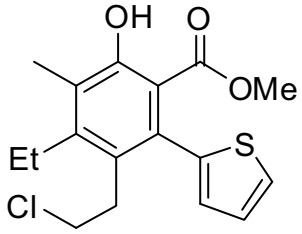
To a CH_2Cl_2 solution (50 mL/1.0 mmol of **12**) of **12** (1.0 mmol) was added **5** (1.1 mmol) and, subsequently, $TiCl_4$ (1.1 mmol) at −78 °C. The temperature of the solution was allowed to warm to 20 °C during 14 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purifed by chromatography (silica gel, *n*-heptane / EtOAc) to give **13**.

Methyl 3-(2-chloroethyl)-4-ethyl-6-hydroxy-2-(thiophen-2-yl)benzoate (13a).



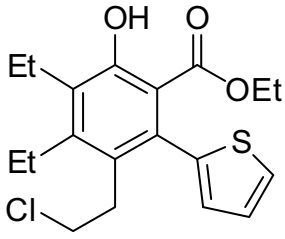
Starting with **12a** (0.312 g, 1.2 mmol), **5a** (0.429 g, 1.6 mmol) and $TiCl_4$ (0.570 mL, 3.0 mmol), **13a** was isolated as a colourless solid (0.204 g, 42%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 2.92 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.08 (t, ^3J = 7.5 Hz, 2 H, CH_2CH_2Cl), 3.36 (t, ^3J = 8.1 Hz, 2 H, CH_2CH_2Cl), 3.92 (s, 3 H, OCH_3), 6.95 (s, 1 H, CH_{Ar}), 6.96 (s, 1 H, CH_{Hetar}), 7.03 (d, ^3J = 5.1 Hz, 1 H, CH_{Hetar}), 7.32 (dd, ^3J = 5.1 Hz, ^4J = 1.2 Hz, 1 H, CH_{Hetar}), 10.42 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 15.9 (CH_2CH_3), 26.6 (CH_2CH_3), 32.9 (CH_2CH_2Cl), 43.4 (CH_2CH_2Cl), 52.5 (OCH_3), 112.6 ($CCOOCH_{3Ar}$), 118.2 (CH_{Ar}), 126.1 (CH_{Hetar}), 126.8 (C_{Ar}), 126.9, 127.0 (CH_{Hetar}), 141.1, 141.3 (C_{Ar}), 145.8 (C_{Hetar}), 159.4 (COH_{Ar}), 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2923 (w), 1661 (s), 1597 (w), 1569 (m), 1434 (s), 1337 (m), 1234 (s), 1203 (s), 1142 (m), 1080 (m), 939 (w), 807 (m), 788 (m), 692 (s). MS (EI, 70 eV): *m/z* (%) = 326 ([M^+], ^{37}Cl, 8), 324 ([M^+], ^{35}Cl, 21), 294 (^{37}Cl, 17), 292 (^{35}Cl, 49), 275 (6), 245 (^{37}Cl, 5), 243 (^{35}Cl, 100), 215 (4), 187 (5), 171 (6), 119 (9), 97 (11), 83 (11), 69 (24), 57 (19). HRMS (EI): Calcd. for $C_{16}H_{17}ClO_3S$ ([M]$^+$, ^{35}Cl): 324.05796; found: 324.05780.

Methyl 3-(2-chloroethyl)-4-ethyl-6-hydroxy-5-methyl-2-(thiophen-2-yl)benzoate (13b).



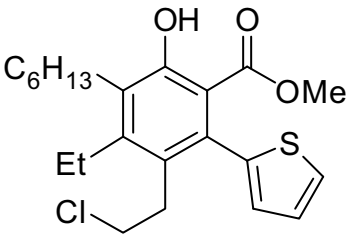
Starting with **12a** (0.312 g, 1.2 mmol), **5b** (0.452 g, 1.7 mmol) and $TiCl_4$ (0.570 mL, 3.0 mmol), **13b** was isolated as a colourless viscous oil (0.200 g, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.13 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.88 (s, 3 H, CH_3), 2.86 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 2.89 (t, ^3J = 7.3 Hz, 2 H, CH_2CH_2Cl), 3.42 (t, ^3J = 6.5 Hz, 2H, CH_2CH_2Cl), 3.92 (s, 3 H, OCH_3), 6.74−6.76 (m, 1 H, CH_{Hetar}), 7.05 (dd, ^3J = 5.2 Hz, ^4J = 1.7 Hz, 1 H, CH_{Hetar}), 7.36 (d, ^3J = 6.2 Hz, 1 H, CH_{Hetar}), 10.71 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.7 (CH_2CH_3), 15.7 (CH_3), 23.3 (CH_2CH_3), 32.8 (CH_2CH_2Cl), 42.8 (CH_2CH_2Cl), 51.5 (OCH_3), 112.0 ($CCOOCH_{3Ar}$), 124.8, 125.7, 126.1 (CH_{Hetar}), 126.7, 139.1, 139.9, 140.8 (C_{Ar}), 140.8 (C_{Hetar}), 157.1 (COH_{Ar}), 170.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 1642 (s), 1567 (w), 1434 (m), 1325 (m), 1236 (s), 1209 (s), 1122 (s), 1035 (m), 814 (s), 716 (s), 666 (m), 554 (m). MS (EI, 70 eV): *m/z* (%) = 340 ([M^+], ^{37}Cl, 17), 338 ([M^+], ^{35}Cl, 36), 308 (^{37}Cl, 33), 306 (^{35}Cl, 100), 289 (7), 271 (7), 257 (68), 243 (51), 229 (7), 214 (5), 177 (10), 161 (7), 135 (6), 111 (8), 97 (12), 83 (13), 69 (21), 57 (24). HRMS (EI): Calcd. for $C_{16}H_{19}ClO_3S$ ([M]$^+$, ^{35}Cl): 338.07361; found: 338.07354.

Ethyl 3-(2-chloroethyl)-2,5-diethyl-6-hydroxy-4-(2-thienyl)benzoate (13c).



Starting with **12a** (0.312 g, 1.2 mmol), **5c** (0.499 g, 1.6 mmol) and $TiCl_4$ (0.570 mL, 3.0 mmol), **13c** was isolated as a colourless oil (0.194 g, 34%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.15 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.38 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.32 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 2.67 (t, ^3J = 7.5 Hz, 2 H, CH_2CH_2Cl), 2.88 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.34 (t, ^3J = 5.0 Hz, 2H, CH_2CH_2Cl), 4.40 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.77 (d, ^3J = 4.6 Hz, 1 H, CH_{Hetar}), 7.04 (dd, ^3J = 5.1 Hz, ^4J = 1.7 Hz, 1 H, CH_{Hetar}), 7.33 (d, ^3J = 6.2 Hz, 1 H, CH_{Hetar}), 10.75 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0, 13.3, (CH_2CH_3), 15.1 (OCH_2CH_3), 18.3 (CH_2CH_3), 23.3 (CH_2CH_2Cl), 32.9 (CH_2CH_3), 42.9 (CH_2CH_2Cl), 60.9 (OCH_2CH_3), 112.5 ($CCOOC_2H_{5Ar}$), 124.6 (CH_{Hetar}), 125.3 (C_{Ar}), 125.9, 126.8 (CH_{Hetar}), 130.9, 138.8, 139.1 (C_{Ar}), 140.8 (C_{Hetar}), 157.1 (COH_{Ar}), 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2963 (w), 1651 (s), 1589 (w), 1446 (w), 1396 (m), 1371 (s), 1277 (s), 1194 (s), 1121 (m), 1018 (m), 814 (w), 693 (s). MS (EI, 70 eV): *m/z* (%) = 368 ([M^+], ^{37}Cl, 18), 366 ([M^+], ^{35}Cl, 55), 341 (15), 344 (56), 322 (^{37}Cl, 38), 320 (^{35}Cl, 100), 287 (34), 271 (23), 257 (61), 243 (19), 228 (10), 213 (5), 177 (94), 161 (60), 149 (40), 129 (22). HRMS (EI): Calcd. for $C_{17}H_{23}ClO_3S$ ([$M]^+$, ^{35}Cl): 366.10509; found: 366.10404.

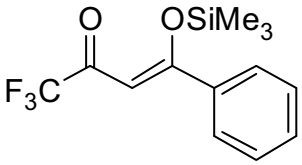
Methyl 3-(2-chloroethyl)-4-ethyl-5-hexyl-6-hydroxy-2-(thiophen-2-yl)benzoate (13d).



Starting with **12a** (0.312 g, 1.2 mmol), **5h** (0.587 g, 1.6 mmol) and $TiCl_4$ (0.570 mL, 3.0 mmol), **13d** was isolated as a colourless oil (0.186 g, 32%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.75 (t (br), ^3J = 7.0 Hz, 3 H, $CH_2(CH_2)_4CH_3$), 1.10 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 1.14−1.16 (m, 8 H, $CH_2(CH_2)_4CH_3$), 1.29−1.32 (m, 2 H, $CH_2(CH_2)_4CH_3$), 2.27 (q, ^3J = 6.1 Hz, 2 H, CH_2CH_3), 2.85 (t, ^3J = 6.2 Hz, 2 H, CH_2CH_2Cl), 3.34 (t, ^3J = 5.5 Hz, 2 H, CH_2CH_2Cl), 3.91 (s, 3 H, OCH_3), 6.75−6.77 (m, 1 H, CH_{Hetar}), 7.03 (dd, ^3J = 5.2 Hz, ^4J = 1.7 Hz, 1 H, CH_{Hetar}), 7.33 (d, ^3J = 6.3 Hz, 1 H, CH_{Hetar}), 10.61 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 $(CH_2)_5CH_3$), 16.0, (CH_2CH_3), 22.4, 23.1, 28.3, 29.8, 29.9, 31.3, 33.9, 43.9 ($8CH_2$), 52.4 (OCH_3), 112.3 ($CCOOC_2H_{5Ar}$), 122.7 (C_{Ar}), 125.3, 125.8, 126.0 (CH_{Hetar}), 130.2, 138.7, 139.4 (C_{Ar}), 140.8 (C_{Hetar}), 157.0 (COH_{Ar}), 170.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2925 (w), 16582 (m), 1590 (w), 1432 (m), 1316 (m), 1202 (m), 1124 (m), 1070 (w), 833 (w), 817 (w), 693 (m). GC−MS (EI, 70 eV): *m/z* (%) = 410 ([M^+], ^{37}Cl, 27), 408 ([M^+], ^{35}Cl, 74), 378 (^{37}Cl, 36), 376 (^{35}Cl, 100),

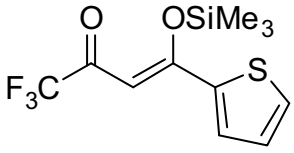
359 (27), 313 (42), 285 (12), 243 (48), 227 (8), 184 (7), 112 (4). HRMS (EI): Calcd. for $C_{22}H_{29}ClO_3S$ ($[M]^+$, ^{35}Cl): 408.15204; found: 408.15396.

1,1,1-trifluoro-4-phenyl-4-[(trimethylsilyl)oxy]-3-buten-2-one (15a).



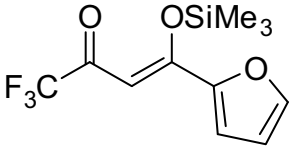
Starting with benzene (60.0 mL), **14a** (5.00 g, 24.6 mmol), triethylamine (3.927 g, 38.8 mmol) and trimethylchlorosilane (2.917 g, 27.0 mmol), **15a** was isolated as a reddish oil (5.729 g, 82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.20 (m, 9 H, $Si(CH_3)_3$), 6.56 (s, 1 H, CH), 7.29−7.34 (m, 3 H, CH_{Ar}), 7.77−7.80 (m, 2 H, CH_{Ar}).

1,1,1-Trifluoro-4-(2-thienyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (15b).



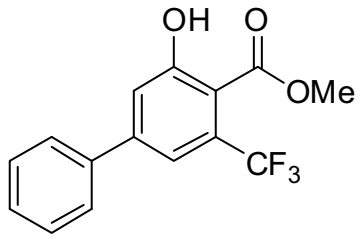
Starting with benzene (45.0 mL), **14b** (3.330 g, 15.0 mmol), triethylamine (2.429 g, 24.0 mmol) and trimethylchlorosilane (2.917 g, 27.0 mmol), **15b** was isolated as a reddish oil (3.175 g, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.24 (m, 9 H, $Si(CH_3)_3$), 6.53 (m, 1 H, CH), 7.04 (m, 1 H, CH_{Heter}), 7.56−7.62 (m, 2 H, CH_{Heter}).

1,1,1-Trifluoro-4-(2-furyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (15c).



Starting with benzene (45.0 mL), **14c** (3.09 g, 15.0 mmol), triethylamine (2.429 g, 24.0 mmol) and trimethylchlorosilane (2.917 g, 27.0 mmol), **15c** was isolated as a reddish oil (3.169 g, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.27 (m, 9 H, $Si(CH_3)_3$), 6.44 (m, 1 H, CH), 6.59 (m, 1 H, CH_{Heter}), 7.12−7.19 (m, 1 H, CH_{Heter}), 7.49−7.54 (m, 1 H, CH_{Heter}).

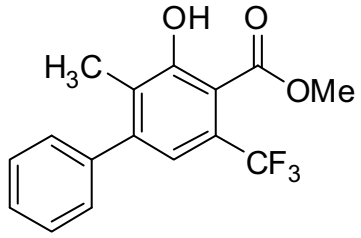
Methyl 3-hydroxy-5-(trifluoromethyl)[1,1'-biphenyl]-4-carboxylate (16a).



Starting with **15a** (0.361 g, 1.5 mmol), **5a** (0.426 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), **16a** was isolated as a colourless solid (0.213 g, 48 %); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 7.24 (m, 1 H, CH_{Ph}), 7.27 (m, 2 H, CH_{Ph}), 7.32 (m, 1 H, CH_{Ar}), 7.37 (m, 1 H, CH_{Ar}), 7.42−7.44 (m, 2 H, CH_{Ph}), 10.55 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.8 (OCH_3), 109.5 ($CCOOCH_{3Ar}$), 118.0 (q, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 116.7 (CH_{Ar}), 119.7 (CH_{Ph}), 123.3 (d, ^1J = 269.7 Hz, CF_3), 127.1 ($2CH_{Ph}$), 129.0 ($2CH_{Ph}$), 130.7 (q, ^2J = 31.6 Hz, $CCF3_{Ar}$), 138.2 (C_{Ph}), 146.7 (C_{Ar}), 162.2 (COH_{Ar}), 169.5 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −58.8 (CF_3). IR (Neat, cm^{-1}):

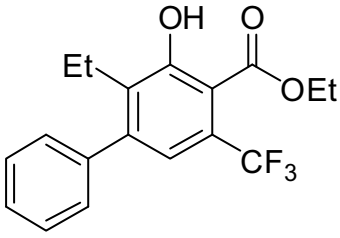
$\tilde{\nu}$ = 1660 (s), 1619 (m), 1452 (s), 1343 (s), 1219 (m), 1136 (s), 966 (m), 882 (m), 694 (m). GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M^+], 49), 265 (27), 264 (100), 263 (22), 236 (43), 208 (8), 188 (18), 139 (13), 118 (6). HRMS (EI): Calcd. for $C_{15}H_{11}F_3O_3$: 296.06548; found: 296.06510.

Methyl 3-hydroxy-2-methyl-5-(trifluoromethyl)[1,1'-biphenyl]-4-carboxylate (16b).



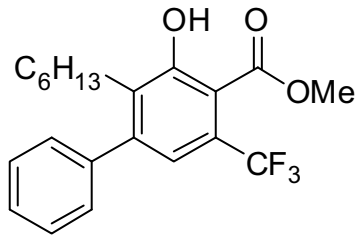
Starting with **15a** (0.361 g, 1.5 mmol), **5b** (0.426 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), **16b** was isolated as a reddish viscous oil (0.237 g, 51 %); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 7.15 (m, 1 H, CH_{Ph}), 7.19 (m, 1 H, CH_{Ar}), 7.22 (m, 1 H, CH_{Ph}), 7.34 (m, 2 H, CH_{Ph}), 7.36 (m, 1 H, CH_{Ph}), 11.09 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_3), 52.8 (OCH_3), 108.6 (*C*COOCH$_{3Ar}$), 120.2 (q, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 123.5 (d, ^1J = 269.0 Hz, CF_3), 127.4 (q, ^2J = 31.6 Hz, *C*CF3$_{Ar}$), 127.9 (CH_{Ph}), 128.3 (2CH_{Ph}), 128.8 (2CH_{Ph}), 130.0 (C_{Ph}), 139.7, 146.9 (C_{Ar}), 160.6 (COH_{Ar}), 170.2 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −58.0 (CF_3). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 2995 (w), 1681 (m), 1609 (w), 1439 (m), 1335 (m), 1274 (s), 1122 (s), 1017 (s), 886 (s), 700 (s). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M^+], 68), 279 (27), 278 (80), 277 (100), 257 (9), 250 (36), 231 (7), 201 (24), 181 (57), 152 (24), 152 (24), 115 (5). HRMS (EI): Calcd. for $C_{16}H_{13}F_3O_3$: 310.08113; found: 310.08062.

Ethyl 2-ethyl-3-hydroxy-5-(trifluoromethyl)[1,1'-biphenyl]-4-carboxylate (16c).



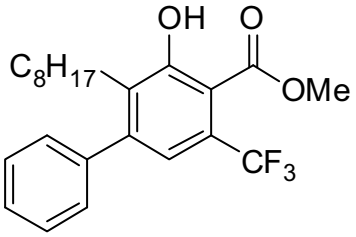
Starting with **15a** (0.360 g, 1.5 mmol), **5h** (0.495 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), **6c** was isolated as a reddish viscous oil (0.187 g, 37 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.32 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.54 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 4.36 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 7.09 (s(br), 1 H, CH_{Ar}), 7.15 (m, 1 H, CH_{Ph}), 7.16−7.19 (m, 2 H, CH_{Ph}), 7.30−7.33 (m, 2 H, CH_{Ph}), 11.13 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.4 (CH_2CH_3), 12.6 (OCH_2CH_3), 19.8 (CH_2CH_3), 62.2 (OCH_2CH_3), 108.3 (*C*COOCH$_2$CH$_{3Ar}$), 119.5 (q, $^3J_{F,\,C}$ = 6.6 Hz, CH_{Ar}), 122.5 (d, $^1J_{F,\,C}$ = 269.0 Hz, CF_3), 125.4 (q, ^2J = 31.6 Hz, *C*CF3$_{Ar}$), 126.7 (CH_{Ph}), 127.2 (2CH_{Ph}), 127.5 (2CH_{Ph}), 134.2 (C_{Ph}), 139.0, 145.7 (C_{Ar}), 159.1 (COH_{Ar}), 168.7 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −57.8 (CF_3). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M^+], 59), 293 (26), 292 (79), 291 (100), 264 (46), 249 (24), 223 (5), 195 (21), 165 (15). HRMS (EI): Calcd. for $C_{18}H_{17}F_3O_3$: 338.11243; found: 338.11274.

Methyl 2-hexyl-3-hydroxy-5-(trifluoromethyl)[1,1'-biphenyl]-4-carboxylate (16d).



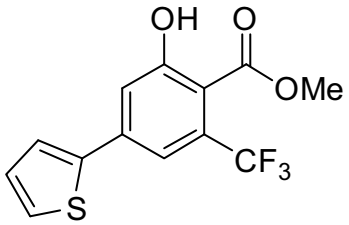
Starting with **15a** (0.360 g, 1.5 mmol), **5h** (0.563 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), 1**6d** was isolated as a reddish viscous oil (0.319 g, 56 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.64 (t(br), ^3J = 7.0 Hz, 3 H, $CH_2(CH_2)_4CH_3$), 0.99−1.34 (m, 8 H, $CH_2(CH_2)_4CH_3$), 2.44 (t, ^3J = 8.0 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.81 (s, 3 H, OCH_3), 7.01 (m, 1 H, CH_{Ar}), 7.08 (m, 1 H, CH_{Ph}), 7.11 (m, 1 H, CH_{Ph}), 7.23 (m, 2 H, CH_{Ph}), 7.25 (m, 1 H, CH_{Ph}), 10.91 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.9 (CH_3), 22.4, 27.3, 29.0, 29.3, 31.3 (CH_2), 52.7 (OCH_3), 109.0 (CCOOCH$_{3Ar}$), 120.5 (q, $^3J_{F,\,C}$ = 6.5 Hz, CH_{Ar}), 123.5 (d, $^1J_{F,\,C}$ = 269.0 Hz, CF_3), 127.4 (q, $^2_{F,\,C}$ = 31.6 Hz, CCF$_{3Ar}$), 127.8 (CH_{Ph}), 128.2 (2CH_{Ph}), 128.6(2CH_{Ph}), 134.2 (C_{Ph}), 140.0, 147.0 (C_{Ar}), 160.4 (COH$_{Ar}$), 170.2 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −57.8 (CF_3). IR (Capillary, cm^{-1}): $\tilde{\nu}$ = 2927(w), 2856 (w), 1671 (m), 1610 (w), 1439 (m), 1336 (m), 1280 (s), 1200 (m), 1177 (s), 1030 (w), 947 (m), 885 (m), 770 (m), 701 (s). GC-MS (EI, 70 eV): *m/z* (%) = 380 ([M$^+$], 55), 349 (31), 348 (100), 347 (49), 331 (13), 278 (40), 277 (62), 250 (28), 229 (5), 201 (23), 181 (28), 152 (16). HRMS (EI): Calcd. for $C_{21}H_{23}O_3F_3$: 380.15938; found: 380.15976.

Methyl 3-hydroxy-2-octyl-5-(trifluoromethyl)[1,1'-biphenyl]-4-carboxylate (16e).



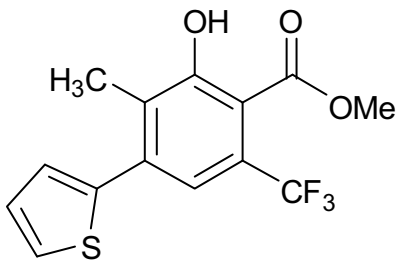
Starting with **15a** (0.360 g, 1.5 mmol), **5i** (0.563 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), 1**6e** was isolated as a reddish viscous oil (0.367 g, 60 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.77 (t(br), ^3J = 6.9 Hz, 3 H, $CH_2(CH_2)_6CH_3$), 1.08−1.39 (m, 12 H, $CH_2(CH_2)_6CH_3$), 2.25 (t, ^3J = 7.8 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.90 (s, 3 H, OCH_3), 7.10 (m, 1 H, CH_{Ar}), 7.16 (m, 1 H, CH_{Ph}), 7.19 (m, 1 H, CH_{Ph}), 7.32 (m, 2 H, CH_{Ph}), 7.25 (m, 1 H, CH_{Ph}), 10.99 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.6, 26.3 (CH_2), 28.0 (3CH_2), 28.6, 30.8 (CH_2), 51.7 (OCH_3), 108.0 (CCOOCH$_{3Ar}$), 119.5 (q, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 122.4 (d, $^1J_{F,\,C}$ = 269.0 Hz, CF_3), 125.8 (q, $^2J_{F,\,C}$ = 31.6 Hz, CCF$_{3Ar}$), 126.7, 126.9, 127.0, 127.2, 127.5 (CH_{Ph}), 133.2 (C_{Ph}), 139.0 (C_{Ar}), 146.0 (C_{Ar}), 159.4 (COH$_{Ar}$), 169.2 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −58.6 (CF_3). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 2854 (w), 1672 (w), 1374 (w), 1257 (s), 1087 (m), 1012 (s), 791 (s). GC-MS (EI, 70 eV): *m/z* (%) = 408 ([M$^+$], 43), 377 (32), 37 (100), 359 (12), 333 (7), 278 (41), 277 (59), 250 (25), 229 (5), 201 (19), 181 (18), 152 (13). HRMS (EI): Calcd. for $C_{23}H_{27}O_3F_3$: 408.19068; found: 408.19180.

Methyl 2-hydroxy-4-(2-thienyl)-6-(trifluoromethyl)benzoate (16f).



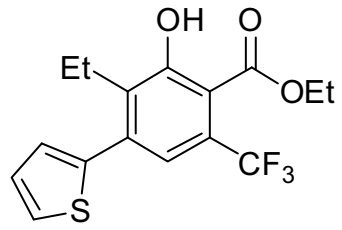
Starting with **15b** (0.442 g, 1.5 mmol), **5a** (0.430 g, 1.6 mmol) and $TiCl_4$ (0.18 mL, 1.6 mmol), **16f** was isolated as a colourless solid (0.160 g, 35%), m.p = 126−128 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, OCH_3), 7.05 (dd, ^3J = 5.1 Hz, ^4J= 1.4 Hz, 1 H, CH_{Heter}), 7.33−7.35 (m, 2 H, CH_{Heter}), 7.37−7.39 (m, 1 H, CH_{Ar}), 7.47 (m, 1 H, CH_{Ar}), 10.86 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 52.8 (OCH_3), 109.2 (CCOOCH_{3Ar}), 116.6 (d, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 117.8 (CH_{Ar}), 123.1 (d, $^1J_{F,\,C}$ = 269.7 Hz, CF3), 125.7, 127.5, 128.5 (CH_{Heter}), 130.5 (d, $^2J_{F,\,C}$ = 31.6 Hz, CCF3$_{Ar}$), 139.7 (C_{Heter}), 141.2 (C_{Ar}), 162.4 (COH_{Ar}), 169.3 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 59.0 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2964 (w), 2857 (w), 1672 (m), 1614 (w), 1440 (m), 1422 (m), 1326 (m), 1228 (w), 1127 (m), 1030 (m), 923 (m), 869 (m), 717 (m). GC-MS (EI, 70 eV): *m/z* (%) = 302 ([M$^+$], 81), 270 (100), 242 (41), 223 (9), 214 (40), 194 (4), 169 (4), 145 (16), 121 (13). HRMS (EI): Calcd. for $C_{13}H_9O_3F_3S$: 302.02190; found: 302.02202.

Methyl 2-hydroxy-3-methyl-4-(2-thienyl)-6-(trifluoromethyl)benzoate (16g).



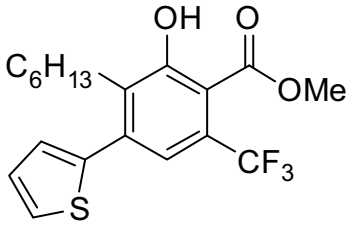
Starting with **15b** (0.442 g, 1.5 mmol), **5b** (0.452 g, 1.6 mmol) and $TiCl_4$ (0.18 mL, 1.6 mmol), **16g** was isolated as a colourless solid (0.215 g, 45%), m.p = 72−74 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 3.92 (s, 3 H, OCH_3), 7.04 (d, $^4J_{H,\,F}$ = 2.2 Hz, 1 H, CH_{Ar}), 7.07 (m, 1 H, CH_{Heter}), 7.30 (m, 1 H, CH_{Heter}), 7.36 (m, 1 H, CH_{Heter}), 11.16 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.8 (CH_3), 51.8 (OCH_3), 107.7 (CCOOCH_{3Ar}), 119.8 (d, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 122.3 (d, $^1J_{F,\,C}$ = 271.5 Hz, CF_3), 125.8 (CH_{Heter}), 126.0 (d, $^2J_{F,\,C}$ = 31.5 Hz, CCF3$_{Ar}$), 126.3, 126.9 (CH_{Heter}), 128.8, 138.3 (C_{Ar}), 139.6 (C_{Heter}), 159.7 (COH_{Ar}), 169.0 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.6 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 2853 (w), 1683 (m), 1606 (w), 1436 (m), 1315 (m), 1275 (s), 1112 (s), 1013 (m), 937 (m), 882 (m), 687 (s). GC-MS (EI, 70 eV): *m/z* (%) = 316 ([M$^+$], 66), 284 (29), 256 (100), 237 (5), 207 (11), 187 (10), 159 (8), 134 (4), 115 (6). HRMS (EI): Calcd. for $C_{14}H_{11}O_3F_3S$: 316.03755; found: 316.03784.

Ethyl 3-ethyl-2-hydroxy-4-(2-thienyl)-6-(trifluoromethyl)benzoate (16h).



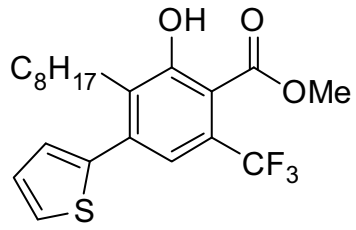
Starting with **15b** (0.442 g, 1.5 mmol), **5c** (0.499 g, 1.6 mmol) and $TiCl_4$ (0.18 mL, 1.6 mmol), **16h** was isolated as a yellow oil (0.230 g, 44%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.34 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.74 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 4.38 (q, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 7.03 (m, 1 H, CH_{Heter}), 7.04 (d, $^4J_{H,F}$ = 1.4 Hz, 1 H, CH_{Ar}), 7.26 (m, 1 H, CH_{Heter}), 7.33−7.35 (m, 1 H, CH_{Heter}), 11.19 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.2 (CH_3), 21.0 (CH_2CH_3), 62.5 (OCH_2CH_3), 109.5 (CCOOCH$_2$CH$_{3Ar}$), 121.2 (d, $^3J_{F,C}$ = 7.5 Hz, CH_{Ar}), 123.3 (d, $^1J_{F,C}$ = 271.5 Hz, CF_3), 126.6 (CH_{Heter}), 127.0 (d, $^2J_{F,C}$ = 31.5 Hz, CCF3$_{Ar}$), 127.3, 127.4 (CH_{Heter}), 136.0, 138.8 (C_{Ar}), 140.5 (C_{Heter}), 160.6 (COH_{Ar}), 169.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2930 (w), 2874 (w), 1666 (m), 1608 (w), 1463 (w), 1372 (m), 1288 (s), 1231 (m), 1137 (s), 1013 (m), 932 (m), 883 (w), 696 (s). GC-MS (EI, 70 eV): *m/z* (%) = 344 ([M$^+$], 45), 298 (15), 270 (100), 255 (4), 222 (4), 207 (6), 171 (5). HRMS (EI): Calcd. for $C_{16}H_{15}O_3F_3S$: 344.07413; found: 344.07710.

Methyl 3-hexyl-2-hydroxy-4-(2-thienyl)-6-(trifluoromethyl)benzoate (16i).



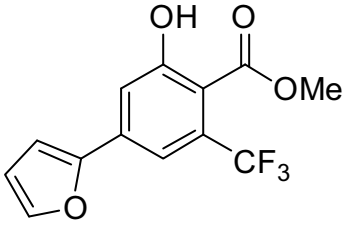
Starting with **15b** (0.442 g, 1.5 mmol), **5h** (0.568 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), **16i** was isolated as a colourless viscous oil (0.196 g, 34 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t(br), ^3J = 6.6 Hz, 3 H, $CH_2(CH_2)_4CH_3$), 1.18−1.51 (m, 8 H, $CH_2(CH_2)_4CH_3$), 2.69 (t, ^3J = 8.2 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.92 (s, 3 H, OCH_3), 7.02 (m, 1 H, CH_{Ar}), 7.04−7.06 (m, 1 H, CH_{Heter}), 7.26 (m, 1 H, CH_{Heter}), 7.35 (dd, ^3J = 4.8 Hz, ^4J = 1.3 Hz, 1 H, CH_{Heter}), 11.05 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.5, 26.6, 28.3, 28.4, 30.4 (CH_2), 51.8 (OCH_3), 108.2 (CCOOCH$_{3Ar}$), 120.2 (q, $^3J_{F,C}$ = 8.2 Hz, CH_{Ar}), 122.4 (d, $^1J_{F,C}$ = 250.4 Hz, CF_3), 125.7(C_{Ar}), 125.6, 126.2, 126.4 (CH_{Heter}), 134.0, 138.1 (C_{Ar}), 139.5 (C_{Heter}), 159.5 (COH_{Ar}), 169.1 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.7 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2928(w), 2849 (w), 1672 (m), 1601 (w), 1439 (m), 1356 (m), 1298 (s), 1198 (m), 1124 (s), 1047 (w), 940 (m), 810 (m), 701 (s). GC-MS (EI, 70 eV): *m/z* (%) = 386 ([M$^+$], 100), 354 (25), 337 (11), 326 (94), 315 (8), 297 (14), 283 (59), 256 (54), 235 (7), 207 (28), 187 (7), 158 (14). HRMS (EI): Calcd. for $C_{19}H_{21}O_3F_3S$: 386.11580; found: 386.11536.

Methyl 2-hydroxy-3-octyl-4-(2-thienyl)-6-(trifluoromethyl)benzoate (16j).



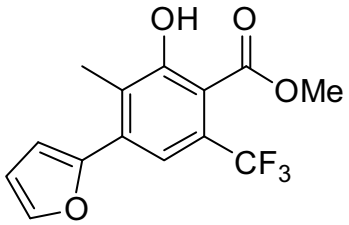
Starting with **15b** (0.442 g, 1.5 mmol), **5i** (0.614 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 1.6 mmol), **16j** was isolated as a colourless viscous oil (0.231 g, 37 %), m.p = 49−50 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.58 (t(br), ^3J = 6.9 Hz, 3 H, $CH_2(CH_2)_6CH_3$), 0.95−1.26 (m, 12 H, $CH_2(CH_2)_6CH_3$), 2.47 (t, ^3J = 8.1 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.70 (s, 3 H, OCH_3), 6.80 (m, 1 H, CH_{Ar}), 6.83 (m, 1 H, CH_{Heter}), 7.04 (m, 1 H, CH_{Heter}), 7.13 (dd, ^3J = 6.3 Hz, ^4J = 1.3 Hz, 1 H, CH_{Heter}), 10.82 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6, 27.6, 29.1, 29.2, 29.4, 29.7, 31.8 (CH_2), 52.8 (OCH_3), 109.2 (CCOOCH$_{3Ar}$), 121.3 (q, $^3J_{F,\,C}$ = 6.7 Hz, CH_{Ar}), 123.3 (d, $^1J_{F,\,C}$ = 271.5 Hz, CF_3), 126.5 (d, $^2J_{F,\,C}$ = 31.5 Hz, CCF3$_{Ar}$), 126.6, 127.2, 127.4 (CH_{Heter}), 135.0, 139.1 (C_{Ar}), 140.5 (C_{Heter}), 160.5 (COH_{Ar}), 170.1 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.7 (CF_3). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 2915(w), 2848 (w), 1669 (m), 1604 (w), 1440 (m), 1338 (m), 1286 (m), 1197 (m), 1125 (s), 1048 (w), 946 (m), 852 (w), 698 (s). GC-MS (EI, 70 eV): *m/z* (%) = 414 ([M$^+$], 100), 382 (30), 365 (12), 297 (16), 284 (33), 283 (63), 269 (74), 256 (48), 235 (7), 207 (24), 158 (12). HRMS (EI): Calcd. for $C_{21}H_{25}O_3F_3S$: 414.14710; found: 414.14684.

Methyl 2-hydroxy-4-(2-furanyl))-6-(trifluoromethyl)benzoate (16k).



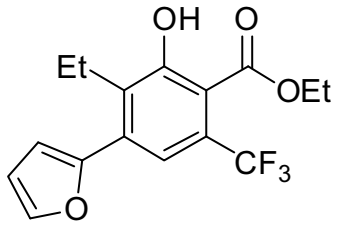
Starting with **15c** (0.556 g, 2.0 mmol), **5a** (0.567 g, 2.2 mmol) and $TiCl_4$ (0.24 ml, 2.2 mmol), **16k** was isolated as a colourless solid (0.231 g, 40 %), m.p = 116−118 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, OCH_3), 6.45 (q, $^4J_{H,\,F}$ = 1.7 Hz, 1 H, CH_{Ar}), 6.78 (dd, ^3J = 4.1 Hz, ^4J = 0.6 Hz, 1 H, CH_{Heter}), 7.37 (m, 1 H, CH_{Heter}), 7.47 (m, 1 H, CH_{Ar}), 7.52 (m, 1 H, CH_{Heter}), 10.84 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.8 (OCH_3), 108.9, 112.2 (CH_{Heter}), 114.7 (q, $^3J_{F,\,C}$ = 6.7 Hz, CH_{Ar}), 115.6 (CH_{Ar}), 117.7 (CCOOCH$_{3Ar}$), 123.1 (d, $^1J_{F,\,C}$ = 271.5 Hz, CF_3), 131.0 (d, $^2J_{F,\,C}$ = 32.2 Hz, CCF3$_{Ar}$), 135.6 (C_{Ar}), 144.0 (CH_{Heter}), 151.2 (C_{Heter}), 162.4 (COH_{Ar}), 169.4 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 59.0 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 2852 (w), 1660 (m), 1621 (w), 1440 (m), 1335 (m), 1290 (m), 1212 (m), 1126 (m), 1016 (m), 904 (m), 802 (m), 760 (m). GC-MS (EI, 70 eV): *m/z* (%) = 286 ([M$^+$], 81), 254 (100), 226 (69), 207 (10), 198 (23), 169 (16), 151 (21), 129 (4), 113 (8), 75 (5). HRMS (EI): Calcd. for $C_{13}H_9O_4F_3$: 286.04474; found: 286.04447.

Methyl 4-(2-furanyl)-2-hydroxy-3-methyl-6-(trifluoromethyl)benzoate (16l).



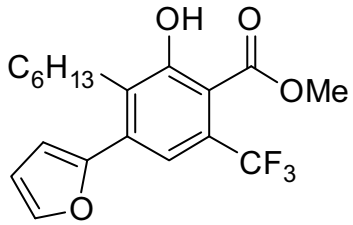
Starting with **15c** (0.4176 g, 1.5 mmol), **5b** (0.452 g, 1.6 mmol) and $TiCl_4$ (0.18 ml, 2.2 mmol), **16l** was isolated as a red solid (0.186 g, 41 %), m.p = 79−82 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.91 (s, 3 H, OCH_3), 6.48 (dd, ^3J = 5.2 Hz, ^4J = 1.8 Hz, 1 H, CH_{Heter}), 6.65−6.67 (m, 1 H, CH_{Heter}), 7.50 (m, 1 H, CH_{Ar}), 7.60 (m, 1 H, CH_{Heter}), 11.21 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.5 (CH_3), 51.8 (OCH_3), 107.1 (*C*COOCH$_{3Ar}$), 110.8, 110.9 (CH_{Heter}), 116.4 (q, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 122.4 (d, $^1J_{F,\,C}$ = 271.5 Hz, CF_3), 124.6 (C_{Ar}), 126.4 (d, $^2J_{F,\,C}$ = 32.2 Hz, *C*CF3$_{Ar}$), 133.6 (C_{Ar}), 142.1 (CH_{Heter}), 150.3 (C_{Heter}), 159.8 (COH_{Ar}), 169.1 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.8 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 2850 (w), 1798 (m), 1658 (m), 1438 (m), 1338 (m), 1282 (s), 1120 (s), 1018 (m), 936 (m), 804 (m), 754 (m). GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M$^+$], 100), 268 (78), 248 (80), 219 (9), 192 (10), 164 (26), 133 (11), 115 (21). HRMS (EI): Calcd. for $C_{14}H_{11}O_4F_3$: 300.06039; found: 300.05967.

Ethyl 3-ethyl-4-(2-furanyl)-2-methyl-6-(trifluoromethyl)benzoate (16m).



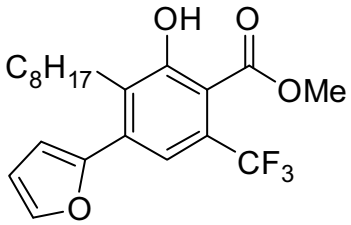
Starting with **15c** (0.556 g, 2.0 mmol), **5c** (0.652 g, 2.2 mmol) and $TiCl_4$ (0.24 ml, 2.2 mmol), **16m** was isolated as a red solid (0.226 g, 35 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.34 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 2.87 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 4.38 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 6.47 (q, $^3J_{H,\,F}$ = 5.1 Hz, 1 H, CH_{Ar}), 6.63 (m, 1 H, CH_{Heter}), 7.50 (m, 1 H, CH_{Heter}), 7.54 (m, 1 H, CH_{Heter}), 11.27 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 12.5 (OCH_2CH_3), 19.6 (CH_2CH_3), 61.5 (OCH_2CH_3), 107.8 (*C*COOCH$_2$*CH*$_{3Ar}$), 109.9, 110.8 (CH_{Heter}), 117.0 (q, $^3J_{F,\,C}$ = 6.8 Hz, CH_{Ar}), 122.4 (d, $^1J_{F,\,C}$ = 269.1 Hz, CF_3), 126.4 (d, $^2J_{F,\,C}$ = 32.2 Hz, *C*CF3$_{Ar}$), 132.7, 133.0 (C_{Ar}), 142.2 (CH_{Heter}), 150.3 (C_{Heter}), 159.9 (COH_{Ar}), 168.7 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.1 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2924 (w), 2853 (w), 1671 (m), 1439 (m), 1336 (m), 1282 (s), 1200 (m), 1131 (s), 1047 (m), 954 (w), 886 (w), 770 (w), 701 (s). GC-MS (EI, 70 eV): *m/z* (%) = 328 ([M$^+$], 61), 282 (29), 254 (100), 234 (7), 207 (7), 177 (7), 128 (7). HRMS (EI): Calcd. for $C_{16}H_{15}O_4F_3$: 328.09170; found: 328.09162.

Methyl 4-(2-furanyl)-3-hexyl-2-methyl-6-(trifluoromethyl)benzoate (16n).



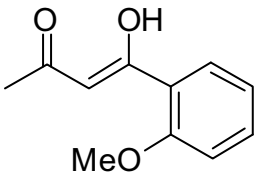
Starting with **15c** (0.556 g, 2.0 mmol), **5h** (0.751 g, 2.2 mmol) and $TiCl_4$ (0.24 ml, 2.2 mmol), **16n** was isolated as a viscous oil (0.222 g, 30 %). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.84 (t, ^3J = 6.8 Hz, 3 H, $CH_2(CH_2)_4CH_3$), 1.23-1.54 (m, 8H, $CH_2(CH_2)_4CH_3$), 2.80 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_4CH_3$), 3.89 (s, 3 H, OCH_3), 6.46 (q, $^4J_{H,\ F}$ = 1.8 Hz, 1 H, CH_{Ar}), 6.58 (m, 1 H, CH_{Heter}), 7.48 (m, 1 H, CH_{Heter}), 7.53 (m, 1 H, CH_{Heter}), 11.14 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.0 (CH_3), 21.6, 26.2, 27.5, 28.6, 30.5 (CH_2), 51.7 (OCH_3), 107.4 (CCOOCH$_{3Ar}$), 109.9, 110.8 (CH_{Heter}), 177.0 (q, $^3J_{F,\ C}$ = 6.8 Hz, CH_{Ar}), 122.4 (d, $^1J_{F,\ C}$ = 269.1 Hz, CF_3), 126.3 (d, $^2J_{F,\ C}$ = 31.6 Hz, CCF3$_{Ar}$), 131.7, 133.3 (C_{Ar}), 142.1 (CH_{Heter}), 150.3 (C_{Heter}), 159.8 (COH_{Ar}), 169.1 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 59.0 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2917 (w), 2849 (w), 1672 (m), 1439 (m), 1336 (m), 1282 (s), 1202 (m), 1133 (s), 948 (w), 880 (w), 739 (w). GC-MS (EI, 70 eV): *m/z* (%) = 370 ([M$^+$], 100), 338 (24), 321 (11), 310 (42), 281 (32), 267 (68), 240 (28), 219 (31), 211 (6), 183 (14), 164 (11), 133 (15), 115 (8). HRMS (EI): Calcd. for $C_{19}H_{21}O_4F_3$: 370.13865; found: 370.13811.

Methyl 4-(2-furanyl)-3-hexyl-2-methyl-6-(trifluoromethyl)benzoate (16o).



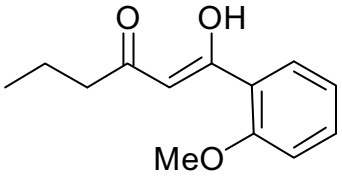
Starting with **15c** (0.556 g, 2.0 mmol), **5i** (0.812 g, 2.2 mmol) and $TiCl_4$ (0.24 ml, 2.2 mmol), **16o** was isolated as a colourless solid (0.280 g, 35 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, ^3J = 6.8 Hz, 3 H, $CH_2(CH_2)_6CH_3$), 1.46−1.54 (m, 12 H, $CH_2(CH_2)_6CH_3$), 2.80 (t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.89 (s, 3 H, OCH_3), 6.44 (q, $^4J_{H,\ F}$ = 4.1 Hz, 1 H, CH_{Ar}), 6.57 (dd, ^3J = 4.1 Hz, ^4J = 0.8 Hz, 1 H, CH_{Heter}), 7.47 (m, 1 H, CH_{Heter}), 7.52 (m, 1 H, CH_{Heter}), 11.12 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6, 27.2, 28.6, 29.2, 29.3, 29.9, 31.8 (CH_2), 52.7 (OCH_3), 108.4 (CCOOCH$_{3Ar}$), 110.9, 111.8 (CH_{Heter}), 118.1 (q, $^3J_{F,\ C}$ = 6.8 Hz, CH_{Ar}), 123.4 (d, $^1J_{F,\ C}$ = 269.0 Hz, CF_3), 127.4 (q, $^2J_{F,\ C}$ = 31.0 Hz, CCF3$_{Ar}$), 132.8, 134.3 (C_{Ar}), 143.1 (CH_{Heter}), 151.4 (C_{Heter}), 160.9 (COH_{Ar}), 170.1 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = − 58.8 (CF_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2917 (w), 2849 (w), 1672 (m), 1439 (m), 1336 (m), 1282 (s), 1202 (m), 1133 (s), 948 (w), 880 (w), 739 (w). GC-MS (EI, 70 eV): *m/z* (%) = 398 ([M$^+$], 100), 366 (42), 338 (8), 267 (76), 219 (37), 183 (12), 133 (11). HRMS (EI): Calcd. for $C_{21}H_{25}O_4F_3$: 398.42021; found: 398.42310.

4-Hydroxy-4-(2-methoxyphenyl)-3-buten-2-one (18a).



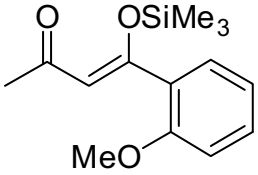
Starting with THF (62.5 mL), LDA (75 mmol), acetone **6a** (2.904 g, 50.0 mmol) and 2-methoxy anisoyl chloride **17** (10.235 g, 60.0 mmol), **18a** was isolated as a yellowish oil (3.550 g, 37%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 3.69 (s, 3 H, OCH_3), 6.28 (s, 1 H, CH), 6.76 (dd, *J* = 8.5 Hz, *J* = 0.9 Hz, 1 H, Ar), 6.84 (ddd, *J* = 7.3 Hz, *J* = 7.3 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.22 (ddd, *J* = 8.5 Hz, *J* = 8.2 Hz, *J* = 1.8 Hz, 1 H, Ar), 7.70 (dd, *J* = 7.6 Hz, *J* = 1.8 Hz, 1 H, Ar), 15.3 (s(br), 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 26.1 (CH_3), 55.4 (OCH_3), 101.9, 111.6, 120.9, 130.8, 133.1 (CH), 134.8, 158.4, 181.3, 194.6 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3005 (w) 2962 (w), 1721 (m), 1603 (s), 1490 (s), 1250 (s), 1164 (m), 1022 (m), 989 (m), 755 (m), 533 (w). MS (EI, 70 eV): *m/z* (%) = 192 ($[M]^+$, 12), 174 (10), 161 (54), 136 (10), 135 (100), 120 (5), 105 (4), 92 (11), 77 (25), 63.1 (5), 51 (5), 43 (11). HRMS (EI): Calcd. for $C_{11}H_{12}O_3$: 192.07810; found: 192.07797. Anal. calcd. for $C_{11}H_{12}O_3$: C 68.73, H 6.29; found: C 69.16, H 6.52.

1-Hydroxy-1-(2-methoxyphenyl)-1-hexen-3-one (18b).



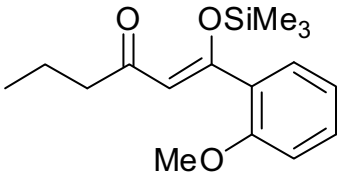
Starting with THF (5 mL), LDA (6.0 mmol), 2-Pentanone **6c** (0.344 g, 4.0 mmol) and 2-methoxy anisoyl chloride **17** (0.818 g, 4.8 mmol), **18a** was isolated as a yellowish oil (0.647 g, 73%, mixture of keto-enol tautomers). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, J = 7.2 Hz, 3 H, CH_3), 1.53-1.61 (m, 2 H, CH_2), 2.26 (t, J = 7.3 Hz, 2 H, CH_2), 3.74 (s, 3 H, OCH_3), 6.32 (s, 1 H, CH), 6.80 (m, 1 H, Ar), 6.88 (dd, J = 7.6 Hz, J = 0.9 Hz, 1 H, Ar), 7.27 (ddd, J = 8.5 Hz, J = 8.4 Hz, J = 1.9 Hz, 1 H, Ar), 7.74 (dd, J = 7.8 Hz, J = 1.9 Hz, 1 H, Ar), 16.2 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 (CH_3), 18.2, 40.2 (CH_2), 54.5 (OCH_3), 100.3, 110.6, 119.6 (CH), 123.2 (C), 128.7, 131.9 (CH), 157.3, 180.5, 196.3 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2963 (m), 2935 (m), 2874 (w), 2839 (w), 1718 (w), 1668 (w), 1604 (s), 1490 (s), 1465 (m), 1293 (m), 1250 (s), 1165 (m), 1067 (w), 1067 (w), 1023 (m), 805 (w), 754 (m). MS (EI, 70 eV): m/z (%) = 220 ($[M]^+$, 7), 202 (4), 189 (23), 177 (24), 135 (100), 120 (3), 105 (2), 92 (8), 77 (17), 63.1 (3), 43 (5). HRMS (EI): Calcd. for $C_{13}H_{16}O_3$: 220.10940; found: 220.10898. Anal. calcd. for $C_{13}H_{16}O_3$: C 70.88, H 7.32; found: C 70.55, H 7.58.

4-(2-Methoxyphenyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (19a).



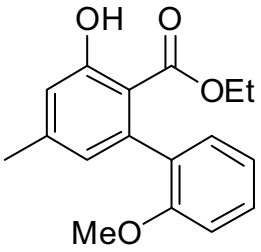
Starting with benzene (37 mL), **18a** (2.854 g, 14.9 mmol), triethylamine (2.406 g, 23.8 mmol) and trimethylchlorosilane (2.905 g, 26.7 mmol), **19b** was isolated as a yellow oil (2.893 g, 73%, mixture of *E/Z*-isomers). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.21 (s, 9 H, $3CH_3$), 2.31 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 6.16 (s, 1 H, CH), 6.84-6.86 (m, 1 H, Ar), 6.90 (dd, *J* = 8.7 Hz, *J* = 1.1 Hz, 1 H, Ar), 7.28-7.30 (m, 1 H, Ar), 7.51 (dd, *J* = 8.7 Hz, *J* = 2.1 Hz, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.16 (3 CH_3), 21.9 (CH_3), 55.1 (OCH_3), 101.3, 111.0, 119.8, 130.5, 131.5 (CH), 132.7, 157.2, 169.7, 191.3 (C).

1-(2-Methoxyphenyl)-1-[(trimethylsilyl)oxy]-1-hexen-3-one (19b).



Starting with benzene (55 mL) of **18b** (5.0 g, 22.7 mmol), triethylamine (3.675 g, 36.3 mmol) and trimethylchlorosilane (4.439 g, 40.8 mmol), **19b** was isolated as a yellowish oil (5.024 g, 75%, mixture of *E/Z*-isomers). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.23 (s, 9 H, $3CH_3$), 0.90 (m, 3 H, CH_3), 1.51-1.59 (m, 2 H, CH_2), 2.72 (t, *J* = 7.6 Hz, CH_3), 3.75 (s, 3 H, OCH_3), 6.15 (s, 1 H, CH), 6.82-6.83 (m, 1 H, Ar), 6.89 (dd, *J* = 6.3 Hz, *J* = 0.5 Hz, 1 H, Ar), 7.26-7.28 (m, 1 H, Ar), 7.53 (dd, *J* = 8.3 Hz, *J* = 1.8 Hz, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.5 (3 CH_3), 13.9 (CH_3), 20.3, 36.2 (CH_2), 55.6 (OCH_3), 101.3, 109.3 (CH), 111.0 (C), 120.2, 120.6, 131.6 (CH), 157.4, 173.3, 191.0 (C).

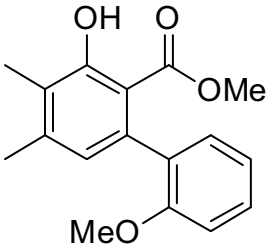
Ethyl 3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (20a).



Starting with **19a** (0.582 g, 2.2 mmol), **5a** (0.659 g, 2.4 mmol) and $TiCl_4$ (0.455 g, 2.4 mmol), **20a** was isolated (0.293 g, 47%) as a colorless solid (mp = 91-93 ºC). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 3.70 (s, 3 H, OCH_3), 3.97 (q, *J* = 7.3 Hz, 2 H, OCH_2CH_3), 6.87-6.58 (m, 1 H, Ar), 6.80-6.81 (m, 1 H, Ar), 6.85 (dd, *J* = 8.1 Hz, *J* = 1.2 Hz, 1 H, Ar), 6.99 (ddd, *J* = 7.3 Hz, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H, Ar), 7.15 (dd, *J* = 7.3 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.32 (ddd, *J* = 8.6 Hz, *J* = 7.3 Hz, *J* = 1.8 Hz, 1 H, Ar), 10.93 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 22.2 (CH_3), 55.6 (OCH_2CH_3), 60.8 (OCH_3), 109.9, 117.2, 120.5 (CH), 122.8 (C) 124.2, 128.4, 129.5 (CH), 140.8, 145.0, 151.6, 156.4, 161.4,171.2 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432(m), 2924 (s), 1655 (s), 1616 (m), 1462 (s), 1278 (m), 1217 (m), 1197 (m), 1107 (m), 1026 (m),

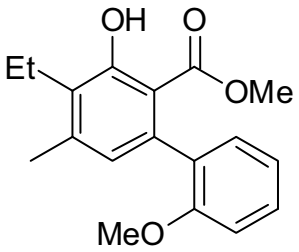
871 (w), 759 (m). MS (EI, 70 eV): *m/z* (%) = 286 (M^+, 40), 255 (2), 240 (100), 211 (15), 197 (22), 169 (11), 152 (7), 141 (7), 115 (9), 77 (2). HRMS (EI): Calcd. for $C_{17}H_{18}O4$: 286.11996; found: 286.120041.

Methyl 3-hydroxy-2'-methoxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (20b).



Starting with **19a** (0.529 g, 2.0 mmol), **5b** (0.604 g, 2.2 mmol) and $TiCl_4$ (0.411 g, 2.2 mmol), **20b** was isolated (0.117 g, 27%) as a yellow viscous oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.09 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 3.36 (s, 3 H, OCH_3), 3.38 (s, 3 Hz, 3 H, OCH_3), 6.60 (s, 1 H, Ar), 6.86 (dd, *J* = 8.2 Hz, *J* = 0.9 Hz, 1 H, Ar), 6.99 (ddd, *J* = 8.1 Hz, *J* = 7.3 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.19 (dd, *J* = 7.3 Hz, *J* = 1.8 Hz, 1 H, Ar), 7.31 (ddd, *J* = 8.2 Hz, *J* = 7.3 Hz, *J* = 1.8 Hz, 1 H, Ar), 11.07 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 20.5, 30.3 (CH_3), 51.4, 55.4 (OCH_3), 109.6, 120.4, 124.2 (CH), 125.5 (C) 128.2, 129.3 (CH), 132.2, 137.0, 143.2, 147.6, 156.1, 158.9, 171.9 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3000 (m), 2954 (m), 2951 (m), 2854 (m), 1657 (s), 1611 (m), 1439 (s), 1393 (s), 1269 (s), 1242 (s), 1195 (m), 1025 (s), 918 (w), 807 (m), 761 (s), 637 (w), 578 (w). MS (EI, 70 eV): *m/z* (%) = 286 (M^+, 35), 254 (64), 239 (100), 223 (40), 211 (22), 181 (27), 165 (16), 152 (16), 131 (27), 115 (12), 77 (18). HRMS (EI): Calcd. for $C_{17}H_{18}O4$: 286.11996; found: 286.119424.

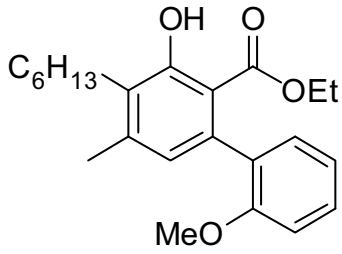
Methyl 4-ethyl-3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (20c).



Starting with **19a** (0.582 g, 2.2 mmol), **5c** (0.692 g, 2.4 mmol) and $TiCl_4$ (0.411 g, 2.2 mmol), **20c** was isolated (0.226 g, 34%) as a colorless solid (mp = 123-125°C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.9 Hz, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 2.68 (q, *J* = 5.8 Hz, 2 H, CH_2), 3.42 (s, 3 Hz, OCH_3), 3.65 (s, 3 H, OCH_3), 6.53 (s, 1 H, Ar), 6.80 (dd, *J* = 8.5 Hz, *J* = 1.2 Hz, 1 H, Ar), 6.94 (ddd, *J* = 8.5 Hz, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H, Ar), 7.14 (dd, *J* = 7.3 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.24 (ddd, *J* = 8.4 Hz, *J* = 6.2 Hz, *J* = 2.1 Hz, 1 H, Ar), 10.92 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.2 (CH_3), 19.7 (CH_2), 19.8 (CH_3), 51.6, 55.6 (OCH_3), 109.7, 120.6 (CH), 123.5 (C), 124.7, 128.4, 129.5 (CH), 130.0, 137.3, 142.6, 144.3, 156.3, 159.0, 172.1 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 2954 (m), 2927 (m), 2870 (w), 1659 (s), 1605 (m), 1438 (s), 1278 (s), 1239 (s), 1197 (m), 1102 (m), 1026 (m), 812 (m), 756 (s), 639 (w), 575 (w). GC-MS (EI, 70 eV): *m/z* (%) = 300.2 (M^+, 71), 268 (78), 253 (100), 250 (40), 239 (11), 237 (71), 225 (16), 223 (7), 181 (17), 152

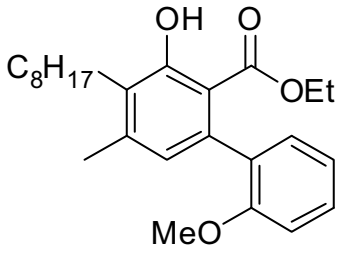
(12), 115 (7), 77 (5). HRMS (EI): Calcd. for $C_{18}H_{20}O4$: 300.13561; found: 300.135117.

Ethyl 4-hexyl-3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (20d).



Starting with the **19a** (0.582 g, 2.2 mmol), **5h** (0.861 g, 2.4 mmol), $TiCl_4$ (0.448 g, 2.4 mmol), **20d** was isolated (0.216 g, 26%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.69 (t, *J* = 7.0 Hz, 3 H, CH_3), 0.83 (t, *J* = 6.4 Hz, 3 H, CH_3), 1.17-1.28 (m, 8 H, CH_2), 2.24 (s, 3 H, CH_3), 2.59 (t, *J* = 8.2 Hz, 2 H CH_2), 3.62 (s, 3 H, OCH_3), 3.89 (q, *J* = 7.3 Hz, 2 H, OCH_2CH_3) 6.57 (s, 1 H, Ar), 6.84 (dd, *J* = 7.3 Hz, *J* = 0.9 Hz, 1 H, Ar), 6.97 (ddd, *J* = 7.3 Hz, *J* = 6.4 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.16 (dd, *J* = 7.3 Hz, *J* = 1.8 Hz, 1 H, Ar), 7.29 (ddd, *J* = 7.3 Hz, *J* = 6.4 Hz, *J* = 1.8 Hz, 1 H, Ar), 10.08 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.9, 14.0, 19.7 (CH_3), 22.6, 26.3, 29.6, 31.2, 31.8 (CH_2), 55.3 (OCH_3), 60.5 (OCH_2CH_3), 109.6 (CH), 110.4 (C), 120.3, 124.3 (CH), 127.9 (C), 128.7, 129.3 (CH), 132.5, 137.2, 142.4, 156.2, 159.1, 171.5 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2926 (s), 2856 (m), 1656 (s), 1610 (m), 1462 (m), 1389 (m), 1270 (s), 1244 (m), 1180 (m), 1109 (m), 1029 (m), 750 (m). GC-MS (EI, 70 eV): *m/z* (%) = 370 (M^+, 64), 324 (45), 309 (68), 307 (35), 254 (60), 253 (54), 239 (100), 223 (43), 181 (15), 115 (4), 77 (2). HRMS (EI): Calcd. for $C_{23}H_{30}O_4$: 370.21386; found: 370.213501.

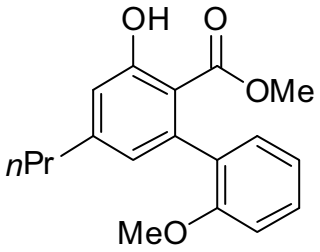
Ethyl 3-hydroxy-2'-methoxy-5-methyl-4-octyl[1,1'-biphenyl]-2-carboxylate (20e).



Starting with **19a** (0.582 g, 2.2 mmol), **5i** (0.928 g, 2.4 mmol), and $TiCl_4$ (0.455 g, 2.4 mmol), **20e** was isolated (0.457 g, 52%) as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.74 (t, *J* = 7.3 Hz, 3 H, CH_3), 0.86 (t(br), *J* = 7.5 Hz, 3 H, CH_3), 1.23-1.37 (m, 12 H, CH_2), 2.30 (s, 3 H, CH_3), 2.64 (t, *J* = 7.6 Hz, 2 H, CH_3), 3.67 (s, 3 H, OCH_3), 3.94 (q, *J* = 6.7 Hz, 2 H, OCH_2CH_3), 6.58 (s, 1 H, Ar), 6.85 (dd, *J* = 7.9 Hz, *J* = 1.2 Hz, 1 H, Ar), 6.98 (ddd, *J* = 7.3 Hz, *J* = 6.9 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.17 (dd, *J* = 7.3 Hz, *J* = 1.8 Hz 1 H, Ar), 7.29 (ddd, *J* = 8.2 Hz, *J* = 7.7 Hz, *J* = 1.8 Hz, 1 H, Ar), 10.99 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.9, 14.1, 19.8 (CH_3), 22.6, 26.9, 28.8, 29.3, 29.5, 30.1, 31.9 (CH_2), 55.3 (OCH_3), 60.5 (OCH_2CH_3), 109.6 (CH), 110.4 (C), 120.2, 124.2 (CH), 127.9 (C), 128.7, 129.3 (CH), 132.5, 137.2, 142.4, 156.2, 159.1, 171.5 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (s), 2926 (s), 2855 (w), 1657 (m), 1610 (m), 1490 (m), 1490 (w), 1389 (m), 1373 (m), 1274 (s), 1243 (m), 1180 (s), 1109 (m), 1036 (m), 750 (w). GC-MS (EI, 70 eV): *m/z* (%) = 398 (M^+, 61), 352 (51), 338 (17), 337 (70), 281 (7), 254

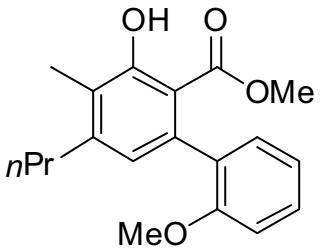
(61), 253 (58), 239 (100), 223 (42), 211 (9), 181 (14), 115 (3), 77 (2), 43 (7). HRMS (EI): Calcd. for $C_{25}H_{34}O_4$: 398.24516; found: 398.24515.

Methyl 3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (20f).



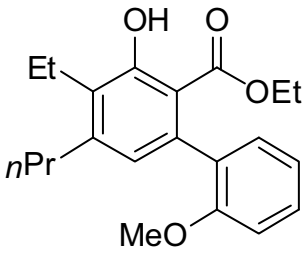
Starting with **19b** (0.585 g, 2.0 mmol), **5a** (0.568 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **20f** was isolated (0.134 g, 22%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.53 (m, 2 H, CH_2), 2.43 (t, *J* = 7.4 Hz, 2 H, CH_2), 3.34 (s, 3 H, OCH_3), 3.56 (s, 3 H, OCH_3), 6.46-6.47 (m, 1 H, Ar), 6.68 (m, 1 H, Ar), 6.72 (dd, *J* = 8.1 Hz, *J* = 0.4 Hz, 1 H, Ar), 6.85 (ddd, *J* = 8.5 Hz, *J* = 7.4 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.05 (dd, *J* = 7.4 Hz, *J* = 1.8 Hz, 1 H, Ar), 7.15 (ddd, *J* = 8.1 Hz, *J* = 8.1 Hz, *J* = 1.9 Hz, 1 H, Ar), 10.60 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.8 (CH_3), 22.7, 37.0 (CH_2), 50.4, 54.4 (OCH_3), 108.8 (CH), 109.8 (C), 115.3, 119.4, 122.5, 127.4, 128.4 (CH), 132.9, 139.3, 148.5, 155.1, 160.0, 170.4 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2961 (m), 2934 (m), 2873 (w), 1665 (s), 1610 (s), 1570 (s), 1491 (m), 1437 (m), 1359 (w), 1269 (s), 1248 (s), 1025 (m), 807 (w), 753 (m). GC-MS (EI, 70 eV): *m/z* (%) = 300 (M^+, 42), 269 (23), 268 (100), 240 (43), 197 (12), 152 (6), 115 (5), 91 (2), 77 (2). HRMS (EI): Calcd. for $C_{18}H_{20}O_4$: 300.13561; found: 300.13695.

Methyl 3-hydroxy-2'-methoxy-4-methyl-5-propyl[1,1'-biphenyl]-2-carboxylate (20g).



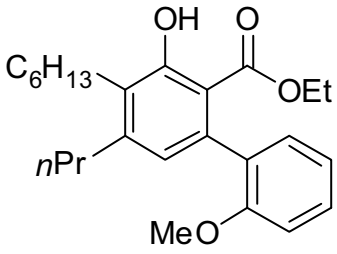
Starting with **19b** (0.585 g, 2.0 mmol), **5b** (0.598 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **20g** was isolated (0.137 g, 21%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.49-1.56 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 2.54 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.40 (s, 3 H, OCH_3), 3.62 (s, 3 H, OCH_3), 6.52 (s, 1 H, Ar), 6.77 (dd, *J* = 8.0 Hz, *J* = 0.9 Hz, 1 H, Ar), 6.91 (ddd, *J* = 7.4 Hz, *J* = 7.4 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.11 (dd, *J* = 7.4 Hz, *J* = 1.7 Hz, 1 H, Ar), 7.20 (ddd, *J* = 8.1 Hz, *J* = 7.4 Hz, *J* = 1.7 Hz, 1 H, Ar), 10.98 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.2, 13.1 (CH_3), 22.2, 35.0 (CH_2), 50.4, 54.4 (OCH_3), 108.7 (CH), 109.2 (C), 119.4, 122.5 (CH), 122.6 (C), 127.2, 128.4 (CH), 131.4, 135.9, 146.3, 155.2, 158.2, 170.9 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2957 (s), 2929 (s), 2871 (m), 1663 (m), 1610 (m), 1584 (w), 1491 (m), 1437 (m), 1267 (s), 1243 (s), 1169 (m), 1029 (m), 810 (m), 752 (m). GC-MS (EI, 70 eV): *m/z* (%) = 314 (M^+, 59), 282 (100), 267 (52), 251 (28), 239 (61), 211 (11), 181 (14), 115 (6), 91 (3), 77 (3). HRMS (EI): Calcd. for $C_{18}H_{22}O_4$: 314.15159; found: 314.15126.

Ethyl 4-ethyl-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (20h).



Starting with **19b** (0.585 g, 2.0 mmol), **5c** (0.660 g, 2.0 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **20h** was isolated (0.203 g, 29%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.59 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.81 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.02 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.40-1.48 (m, 2 H, CH_2), 2.43 (t, *J* = 7.2 Hz, 2 H, CH_2), 2.56 (q, *J* = 7.4 Hz, 2 H, CH_2), 3.51 (s, 3 H, OCH_3), 3.79 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 6.40 (s, 1 H, Ar), 6.64-6.66 (m, 1 H, Ar), 6.78 (ddd, *J* = 7.4 Hz, *J* = 7.2 Hz, *J* = 0.7 Hz, 1 H, Ar), 6.98 (dd, *J* = 7.4 Hz, *J* = 1.7 Hz, 1 H, Ar), 7.09 (ddd, *J* = 8.0 Hz, *J* = 7.6 Hz, *J* = 1.7 Hz, 1 H, Ar), 10.96 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 15.0, 15.2 (CH_3), 20.3, 25.2, 36.4 (CH_2), 56.4 (OCH_3), 61.6 (OCH_2CH_3), 110.9 (CH), 111.5 (C), 121.4, 125.0, 129.1, 130.5 (CH), 130.6, 133.8, 138.4, 147.6, 157.4, 160.4, 172.6 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2961 (s), 2932 (s), 2872 (m), 2835 (w), 1657 (s), 1608 (m), 1560 (w), 1494 (w), 1463 (m), 1395 (m), 1373 (m), 1278 (s), 1245 (s), 1178 (s), 1111 (m), 1029 (m), 788 (m), 751 (m). GC-MS (EI, 70 eV): *m/z* (%) = 342 (M^+, 58), 296 (100), 281 (71), 265 (46), 253 (80), 225 (8), 197 (5), 181 (10), 165 (11), 115 (5), 91 (3), 77 (3). HRMS (EI): Calcd. for $C_{21}H_{26}O_4$: 342.18256; found: 342.18256.

Ethyl 4-hexyl-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (20i).

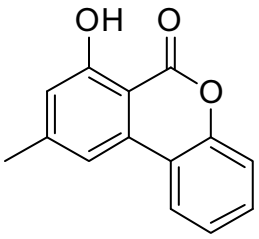


Starting with **19b** (0.292 g, 1.0 mmol), **5h** (0.400 g, 1.1 mmol) and $TiCl_4$ (0.209 g, 1.1 mmol), **20i** was isolated (0.123 g, 32%) by column chromatography (silica gel, *n*-hexane/EtOAc = 40:1 → 20:1) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.68 (t, *J* = 7.0 Hz, 3 H, CH_3), 0.82 (t(br), *J* = 7.2 Hz, 3 H, CH_3), 0.89 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.25-1.52 (m, 10 H, CH_2), 2.51 (t, *J* = 8.3 Hz, 2 H, CH_2), 2.58 (t, *J* = 7.0 Hz, 2 H, CH_2), 3.60 (s, 3 H, CH_3), 3.87 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 6.49 (s, 1 H, Ar), 6.74 (dd, *J* = 8.1 Hz, *J* = 0.9 Hz, 1 H, Ar), 6.88 (ddd, *J* = 7.4 Hz, *J* = 7.4 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.08 (dd, *J* = 7.4 Hz, *J* = 1.7 Hz, 1 H, Ar), 7.20 (ddd, *J* = 8.1 Hz, *J* = 8.0 Hz, *J* = 1.9 Hz, 1 H, Ar), 11.04 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4, 14.5, 14.6 (CH_3), 23.1, 24.4, 26.5, 29.7, 30.0, 32.0, 35.7 (CH_2), 55.7 (OCH_2CH_3), 60.9 (OCH_3), 110.2 (CH), 110.7 (C), 120.7, 123.9, 128.4 (CH), 128.7 (C), 129.9 (CH), 133.1, 137.6, 147.6, 156.7, 159.7, 171.9 (C).). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2957 (s), 2929 (s), 2870 (m), 1658 (s), 1609 (m), 1560 (w), 1463 (m), 1400 (s), 1374 (s), 1270 (s), 1242 (s), 1179 (s), 1179 (s), 1110 (m), 1030 (m),

817 (w), 751 (s). GC-MS (EI, 70 eV): *m/z* (%) = 398 (M^+, 45), 352 (27), 335 (13), 309 (100), 266 (24), 238 (2). HRMS (EI): Calcd. for $C_{25}H_{34}O_4$: 398.24440; found: 398.24516.

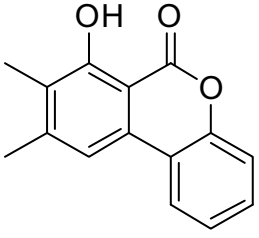
General procedure for synthesis of benzo[*c*]chromen-6-ones 21 and 27: To a CH_2Cl_2 solution of **20** was added BBr_3 at 0 °C. The solution was allowed to warm to 20 °C during 18 h. To the solution was added an aqueous solution of KO*t*Bu (0.1 M) and the solution was stirred for 15 min. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo*. The product **21** was purified by chromatography (silica gel; *n*-hexane/ EtOAc = 20:1) as a colourless solid.

7-Hydroxy-9-methyl-6*H*-benzo[*c*]chromen-6-one (21a).



Starting with **20a** (0.278 g, 0.971 mmol) in CH_2Cl_2 (15 mL), BBr_3 (0.973 g, 3.89 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21a** was isolated as a colourless solid (0.219 g, 92%), mp. = 150-151 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 6.77-6.78 (m, 1 H, Ar), 7.15 (s, 1 H, Ar), 7.21 (dd, *J* = 7.0 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.25-7.27 (m, 1H,Ar), 7.37 (ddd, *J* = 8.3 Hz, *J* = 7.0 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.90 (dd, *J* = 7.9 Hz, *J* = 1.2 Hz, 1 H, Ar), 11.20 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.0 (CH_3), 104.3 (C), 113.5, 117.4, 118.1 (CH), 118.7 (C) 123.7, 125.4, 130.9 (CH), 135.3, 149.4, 151.1, 162.8, 165.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3438 (m), 3068 (m), 2923 (w), 1680 (s), 1627 (s), 1568 (s), 1512 (w), 1456 (m), 1421 (m), 1276 (s), 1235 (s), 1208 (s), 1148 (m), 1078 (s), 842 (m), 750 (s), 511 (m). GC-MS (EI, 70 eV): *m/z* (%) = 226 (M^+, 100), 197 (20), 169 (8), 141 (8), 115 (11), 77 (3). HRMS (EI): Calcd. for $C_{14}H_{10}O_3$: 226.06245; found 226.061951.

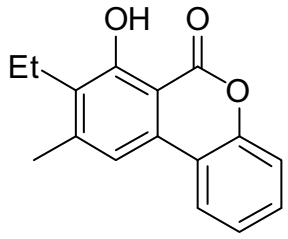
7-Hydroxy-8,9-dimethyl-6*H*-benzo[*c*]chromen-6-one (21b).



Starting with **20b** (0.100 g, 0.349 mmol) in CH_2Cl_2 (10 mL), BBr_3 (0.349 g, 1.39 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **21b** was isolated as a colourless solid (0.058 g, 69%), mp. = 164-166 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 2.39 (s, 3 H, CH_3), 7.18 (s, 1 H, Ar), 7.28 (dd, *J* = 7.6 Hz, *J* = 1.2 Hz, 1 H, Ar), 7.34-7.35 (m, 1 H, Ar), 7.39 (ddd, *J* = 8.5 Hz, *J* = 6.8 Hz, *J* = 1.2 Hz, 1 H, Ar), 7.95 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1 H, Ar), 11.55 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.3, 20.3 (CH_3), 28.6 (CH2), 102.4 (C), 112.2, 116.4 (CH), 117.4 (C), 121.8 (CH) 122.9 (C), 123.8, 128.7 (CH),

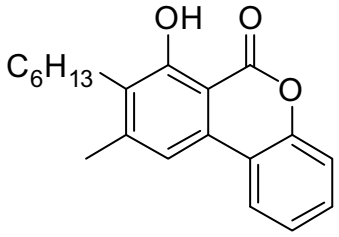
130.5, 146.6, 149.3, 158.9, 164.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (m), 2923 (s), 2852 (m), 1670 (s), 1608 (m), 1560 (m), 1520 (m), 1457 (m), 1410 (m), 1361 (m), 1319 (m), 1280 (s), 1235 (s), 1246 (m), 1175 (m), 1136 (s), 1094 (m), 903 (w), 800 (w), 759 (s), 546 (w). GC-MS (EI, 70 eV): *m/z* (%) = 240 (M^+, 100), 225 (39), 211 (5), 197 (6), 181 (3), 165 (8), 152 (7), 139 (4), 115 (6), 76 (3). HRMS (EI): Calcd. for $C_{15}H_{12}O_3$: 240.07810; found 240.07779.

8-Ethyl-7-hydroxy-9-methyl-6*H*-benzo[*c*]chromen-6-one (21c).



Starting with **20c** (0.100 g, 0.333 mmol) in CH_2Cl_2 (10 mL), BBr_3 (0.334 g, 1.33 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **21c** was isolated as a colourless solid (0.052 g, 62%), mp. = 109-111 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 2.70 (q, *J* = 7.3 Hz, 2 H, CH_2), 7.20 (s, 1 H, Ar), 7.22-7.24 (m, 1 H, Ar), 7.25-7.26 (m, 1 H, Ar), 7.36 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.89 (dd, *J* = 7.9 Hz, *J* = 1.2 Hz, 1 H, Ar), 11.50 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.8 (CH_3), 19.2 (CH_2), 20.4 (CH_3), 103.6 (C), 113.5, 117.4 (CH), 118.3 (C), 122.7, 124.8, 129.7 (CH), 130.5, 131.6, 146.5, 150.3, 159.8, 165.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3437 (m), 2967 (m), 1671 (s), 1622 (m), 1610 (m), 1560 (m), 1453 (m), 1404 (m), 1227 (s), 1177 (m), 1135 (m), 1110 (m), 903 (w), 807 (m), 769 (s). GC-MS (EI, 70 eV): *m/z* (%) = 254 (M^+, 46), 240 (22), 239 (100), 152 (8), 115 (4), 76 (3). HRMS (EI): Calcd. for $C_{16}H_{14}O_3$: 254.09375; found 254.09304.

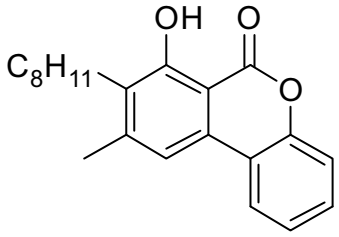
8-Hexyl-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (21d).



Starting with **20d** (0.100 g, 0.270 mmol) in CH_2Cl_2 (10 mL), BBr_3 (0.271 g, 1.079 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **21d** was isolated as a colourless solid (0.061 g, 65%), mp. = 88-90 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (t(br), *J* = 7.0 Hz, 3 H, CH_3), 1.19-1.29 (m, 8 H, CH_2), 2.86 (s, 3 H, CH_3), 3.12 (t, *J* = 7.0 Hz, 2 H, CH_2), 7.19 (s, 1 H, Ar), 7.26 (ddd, *J* = 8.5 Hz, *J* = 8.2 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.29-7.30 (m, 1 H, Ar), 7.38 (ddd, *J* = 7.3 Hz, *J* = 7.0 Hz, *J* = 1.5 Hz, 1 H, Ar),7.94 (dd, *J* = 8.2 Hz, *J* = 1.2 Hz, 1 H, Ar), 11.52 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 19.8 (CH_3), 21.1, 25.1, 27.7, 28.7, 30.7 (CH_2), 102.7 (C), 112.6, 116.6 (CH), 117.6 (C), 121.9, 123.9 (CH), 128.6 (C), 128.7 (CH), 130.8, 145.8, 149.5, 159.2, 164.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2955 (m), 2922 (s), 2853 (m), 1673 (s), 1624 (m), 1609 (m), 1556 (w), 1458 (m), 1404 (m), 1366 (w), 1227 (s), 1179 (m), 1137 (m), 1120 (m), 1037

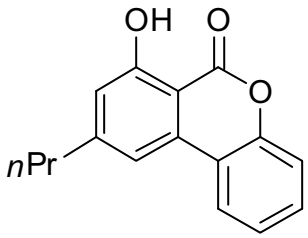
(w), 906 (w), 804 (m), 769 (m), 751 (m), 621 (w). GC-MS (EI, 70 eV): *m/z* (%) = 310 (M^+, 22), 292 (2), 263 (5), 240 (34), 239 (100), 165 (5), 115 (2). HRMS (EI): Calcd. for $C_{20}H_{22}O_3$: 310.15635; found 310.15649.

7-Hydroxy-9-methyl-8-octyl-6*H*-benzo[*c*]chromen-6-one (21e).



Starting with **20e** (0.250 g, 0.627 mmol) in CH_2Cl_2 (20 mL), BBr_3 (0.651 g, 2.509 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21e** was isolated as a colourless solid (0.128 g, 60%), mp. = 87-89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t(br), J = 7.5 Hz, 3 H, CH_3), 1.18-1.21 (m, 12 H, CH_2), 2.37 (s, 3 H, CH_3), 2.63 (t, J = 7.0 Hz, 2 H, CH_2), 7.19 (s, 1 H, Ar), 7.22-7.24 (m, 1 H, Ar), 7.25-7.26 (m, 1 H, Ar), 7.35 (ddd, J = 8.1 Hz, J = 7.0 Hz, J = 1.8 Hz, 1 H, Ar), 7.89 (dd, J = 7.9 Hz, J = 1.2 Hz, 1 H, Ar), 11.46 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 20.6 (CH_3), 22.5, 25.6, 28.5, 29.2, 29.3, 29.8, 31.3 (CH_2), 102.8 (C), 113.4, 117.5, 122.6, 124.7, 129.3 (CH), 129.6, 131.5, 146.6, 147.4, 150.2, 159.9, 165.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2950 (m), 2919 (s), 2850 (s), 1680 (s), 1625 (m), 1610 (m), 1556 (m), 1458 (m), 1405 (m), 1334 (m), 1273 (s), 1178 (m), 1135 (s), 1121 (m), 1045 (w), 906 (w), 757 (s), 625 (w), 550 (w), 471 (w). GC-MS (EI, 70 eV): *m/z* (%) = 338 (M^+, 22), 253 (4), 240 (36), 239 (100), 207 (9), 152 (5), 115 (2), 77(1). HRMS (EI): Calcd. for $C_{22}H_{26}O_3$: 338.18765; found 338.18719.

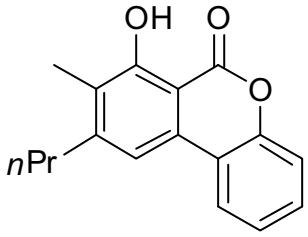
7-Hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (21f).



Starting with **20e** (0.100 g, 0.333 mmol) in CH_2Cl_2 (8 mL), BBr_3 (0.336 g, 1.341 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21f** was isolated as a colourless solid (0.065 g, 77%), mp. = 97-99 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t , J = 7.2 Hz, 3 H, CH_3), 1.63-1.70 (m, 2 H, CH_2), 2.64 (t, J = 7.4 Hz, 2 H, CH_2), 6.84-6.85 (m, 1 H, Ar), 7.19 (s. 1 H, Ar), 7.27 (dd, J = 8.3 Hz, J = 0.7 Hz, 1 H, Ar), 7.32 (dd, J = 8.4 Hz, J = 0.9 Hz, 1 H, Ar). 7.41 (ddd, J = 8.4 Hz, J = 6.8 Hz, J = 1.7 Hz, 1 H, Ar), 7.97 (dd, J = 8.3 Hz, J = 1.7 Hz, 1 H, Ar), 11.22 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, (CH_3), 24.3, 39.2 (CH_2), 104.5 (C), 112.9, 116.8, 118.1 (CH), 118.8 (C), 123.6, 125.3, 130.8 (CH), 135.3, 151.1, 154.0, 162.8, 165.7 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (m), 3139 (w), 2962 (m), 2931 (m), 2872 (w), 1678 (s), 1625 (s), 1565 (s), 1511 (w), 1424 (s), 1319 (m), 1226 (s), 1104 (w), 1071 (s), 835 (w), 767 (s), 715 (m). GC-MS (EI, 70 eV): *m/z* (%) = 254 (M^+, 65), 239 (14), 226 (100), 211 (2), 197 (13), 181 (11), 165 (5), 152 (10), 139 (7), 127 (3), 115 (10),

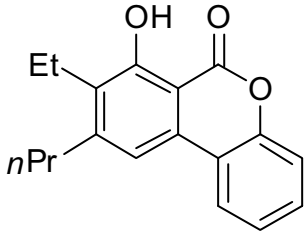
76 (3). HRMS (EI): Calcd. for $C_{16}H_{14}O_3$: 254.09375; found 254.09365.

7-Hydroxy-8-methyl-9-propyl-6*H*-benzo[*c*]chromen-6-one (21g).



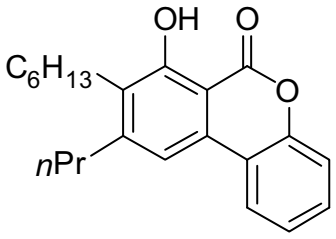
Starting with **20g** (0.076 g, 0.241 mmol) in CH_2Cl_2 (7 mL), BBr_3 (0.242 g, 0.964 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21g** was isolated as a colourless solid (0.047 g, 73%), mp. = 113-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t , *J* = 7.2 Hz, 3 H, CH_3), 1.57-1.65 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 2.67 (t, *J* = 7.6 Hz, 2 H, CH_2), 7.19 (s, 1 H, Ar), 7.28 (dd, *J* = 8.3 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.33 (m(br), 1 H, Ar), 7.38 (ddd, *J* = 8.7 Hz, *J* = 8.1 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.96 (dd, *J* = 8.0 Hz, *J* = 1.7 Hz, 1 H, Ar), 11.57 (s, 1 H, OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.1, 14.1 (CH_3), 23.3, 36.7 (CH_2), 103.5 (C), 112.6, 117.6 (CH), 118.6 (C), 122.9 (CH), 124.2 (C), 124.9, 129.8 (CH), 131.7, 150.4, 151.5, 160.4, 165.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3065 (m), 2965 (s), 2924 (s), 2853 (s), 1668 (s), 1624 (w), 1607 (m), 1516 (w), 1427 (m), 1326 (w), 1271 (s), 1157 (m), 1146 (m), 801 (m), 767 (s). GC-MS (EI, 70 eV): *m/z* (%) = 268 (M^+, 100), 253 (48), 240 (74), 225 (37), 181 (5), 152 (12), 115 (7), 89 (3) 76 (3). HRMS (EI): Calcd. for $C_{17}H_{16}O_3$: 268.10940; found 268.10923.

8-Ethyl-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (21h).



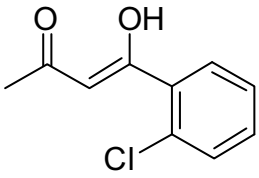
Starting with **20h** (0.084 g, 0.246 mmol) in CH_2Cl_2 (7 mL), BBr_3 (0.246 g, 0.981 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21h** was isolated as a colourless solid (0.049 g, 71%), mp. = 96-98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t , *J* = 7.4 Hz, 3 H, CH_3), 1.12 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.59-1.67 (m, 2 H, CH_2, 2.67 (q, *J* = 8.0 Hz, 2 H, CH_2), 2.72 (t, *J* = 7.6 Hz, 2 H, CH_2), 7.18 (s, 1 H, Ar), 7.26 (dd, *J* = 8.0 Hz, *J* = 0.7 Hz, 1 H, Ar), 7.32-7.34 (m, 1 H, Ar), 7.37 (ddd, *J* = 8.7 Hz, *J* = 7.0 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.95 (dd, *J* = 7.9 Hz, *J* = 1.7 Hz, 1 H, Ar), 11.54 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 13.1 (CH_3),18.0, 23.3, 34.9 (CH_2), 102.6 (C), 111.7, 116.5 (CH), 117.6 (C), 121.8, 123.8, 128.8 (CH), 129.3, 130.8, 149.4, 149.9, 159.4, 164.8 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2963 (s), 2930 (m), 2870 (m), 1669 (s), 1621 (m), 1609 (m), 1557 (m), 1468 (m), 1404 (m), 1332 (m), 1249 (s), 1139 (s), 1005 (w), 806 (w), 750 (s). GC-MS (EI, 70 eV): *m/z* (%) = 282 (M^+, 72), 267 (100), 254 (6), 239 (36), 226 (21), 208 (5), 181 (7), 165 (11), 115 (4), 89 (2) 76 (3). HRMS (EI): Calcd. for $C_{18}H_{18}O_3$: 282.12505; found 282.12507.

8-Hexyl-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (21i).



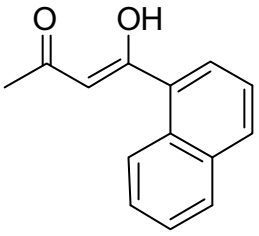
Starting with **20i** (0.067 g, 0.168 mmol) in CH_2Cl_2 (6 mL), BBr_3 (0168 g, 0.672 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **21i** was isolated as a colourless solid (0.035 g, 62%), mp. = 78-80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t(br), *J* = 7.6 Hz, 3 H, CH_3), 0.98 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.18-1.26 (m, 10 H, CH_2), 1.61 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.66 (t, *J* = 7.6, 2 H, CH_2), 7.18 (s, 1 H, Ar), 7.27 (dd, *J* = 7.6 Hz, *J* = 0.9 Hz, 1 H, Ar), 7.32 (m, 1 H, Ar), 7.37 (ddd, *J* = 8.5 Hz, *J* = 7.0 Hz, *J* = 1.5 Hz, 1 H, Ar), 7.95 (dd, *J* = 8.2 Hz, *J* = 1.5 Hz, 1 H, Ar), 11.54 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0, 13.2 (CH_3), 21.6, 23.2, 24.8, 28.4, 28.6, 30.6, 35.0 (CH_2), 102.5 (C), 111.7, 116.5 (CH), 117.6 (C), 121.8, 123.8 (CH), 128.2 (C), 128.8 (CH), 130.7, 149.4, 150.1, 159.4, 164.8 (C). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 2961 (s), 2924 (s), 2852 (m), 1683 (w), 1622 (w), 1611 (w), 1462 (w), 1409 (w), 1268 (s), 1122 (s), 1021 (m), 864 (w), 803 (m), 789 (m), 670 (w). GC-MS (EI, 70 eV): *m/z* (%) =338 (M^+, 34), 320 (5), 295 (12), 281 (10), 267 (100), 239 (28), 207 (9), 165 (18), 149 (13), 125 (18), 111 (30), 83 (50), 69 (60), 57 (80). HRMS (EI): Calcd. for $C_{22}H_{26}O_3$: 338.18765; found 338.18733.

4-(2-Chlorophenyl)-4-hydroxy-3-buten-2-one (23d).



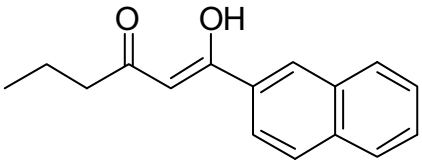
Starting with LDA (75 mmol), acetone **6a** (2.904 g, 50.0 mmol) and 2-chlorobenzoyl chloride 22d (10.501 g, 60.0 mmol) in THF (62.5 mL), **23d** (2.514 g, 25 %) was isolated as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.09 (s, 3 H, CH_3), 5.95 (s, 1 H, CH), 7.23 (m, 1 H, CH_{Clph}), 7.27 (m, 1 H, CH_{Clph}), 7.32 (m, 1 H, CH_{Clph}), 7.48 (m, 1 H, CH_{Clph}), 15.64 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.8 (CH_3), 102.2 (CH), 127.4, 130.3 (CH_{Clph}), 130.6 (C_{Clph}), 131.1, 132.1 (CH_{Clph}), 135.9 (C_{Clph}), 185.0 (COH), 193.1 (*C*OCH_3). (IR (neat, cm^{-1}): $\tilde{\nu}$ = 2964 (w), 1762 (m), 1602 (s), 1434 (s), 1291 (m), 1099 (m), 1046 (s), 952 (m), 766 (s), 535 (w). MS (EI, 70 eV): *m/z* (%) = 196 ([M]$^+$, [^{37}Cl] 1), 181 (10), 161 (100), 139 (26), 111 (11), 85 (9), 75 (10), 69 (15), 43 (13). HRMS (EI): Calcd. for $C_{10}H_9ClO_2$ ([M]$^+$, ^{35}Cl): 196.02856; found: 196.02830.

4-Hydroxy-4-(1-naphthyl)-3-buten-2-one (23g).



Starting THF(62.5 mL), LDA (65.5 mmol), acetone **6a** (2.904 g, 50.0 mmol) and 1-naphthoyl chloride **22g** (11.400 g, 60.0 mmol), **23g** (4.563 g, 43 %) was isolated as a yellow viscous oil.^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CO*CH$_3$*), 6.14 (s, 1 H, CH), 7.45-7.62 (m, 4 H, CH_{Napth}), 7.88−8.07 (m, 2 H, CH_{Napth}), 8.48−8.52 (m, 1 H, CH_{Napth}), 16.14 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.8 (CO*CH$_3$*), 97.4 (CH), 125.1, 125.2, 126.7, 126.8, 127.7, 128.9 (CH_{Napth}), 130.5 (C_{Napth}), 132.4 (CH_{Napth}), 134.2, 134.6 (C_{Napth}), 189.6 (COH), 197.3 (*C*OCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2927 (w), 1745 (s), 1715 (s), 1590 (s), 1472 (m), 1435 (s), 1360 (m), 1292 (s), 1254 (m), 1119 (m), 1053 (m), 964 (w), 845 (w), 765 (m), 742 (m), 606 (w). MS (EI, 70 eV): *m/z* (%) = 212 ([M]$^+$, 99), 197 (56), 179 (43), 169 (72), 155 (85), 141 (26), 127 (100), 115 (14), 101 (9), 85 (18), 77 (14), 69 (31), 63 (9), 51 (6), 43 (27).

1-Hydroxy-1-(2-naphthyl)-1-hexen-3-one (23h).



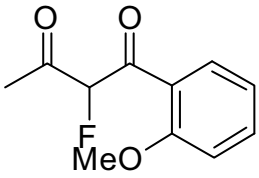
Starting with THF (62.5 mL), LDA (65.5 mmol), 2-Pentanone **6c** (4.306 g, 50.0 mmol) and 2-naphthoyl chloride **22f** (11.400 g, 60.0 mmol), **23h** was isolated as a yellowish oil (7.449 g, 62 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_2*CH$_3$*), 1.56−1.64 (m, 2 H, CH_2*CH$_2$*CH_3), 2.28 (t, ^{3}J = 7.6 Hz, 2 H, *CH$_2$*CH_2CH_3), 6.18 (s, 1 H, CH), 7.35−7.39 (m, 2 H, CH_{Napth}), 7.66−7.70 (m, 2 H, CH_{Napth}), 7.73 (m, 1 H, CH_{Napth}), 7.74 (m, 1 H, CH_{Napth}), 8.27 (s, 1 H, CH_{Napth}), 16.21 (s(br), 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.4 (CH_2CH_2*CH$_3$*), 18.1 (CH_2*CH$_2$*CH_3) , 40.0 (*CH$_2$*CH_2CH_3), 95.3 (CH), 121.1, 125.5 (CH_{Napth}), 126.5, 126.8 (C_{Napth}), 126.9, 127.2, 128.1 (CH_{Napth}), 131.1 (C_{Napth}), 131.6, 134.0 (CH_{Napth}), 182.1 (COH), 195.5 (*C*$OCH_2CH_2CH_3$). (IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2960 (m), 2873 (w), 1631 (s), 1465 (m), 1386 (m), 1278 (w), 1152 (w), 953 (w), 781 (s), 746 (w). MS (EI, 70 eV): *m/z* (%) = 240 ([M]$^+$, 82), 211 (22), 197 (100), 170 (19), 155 (95), 127 (67), 101 (5), 77 (9), 69 (77), 43 (10). HRMS (EI): Calcd. for $C_{16}H_{16}O_2$: 240.11448; found: 240.11470.

General procedure for the synthesis of fluorinated 1,3-dicarbonyl compounds 24.

A stirred solution of **23** (16 mmol) and selectfluor (16 mmol) in acetonitrile (2 mL/1 mmol of 23) was refluxed for 4 h. After cooling, the precipitate was filtered off, and the filtrate was diluted with water. The organic layer was separated and the aqueous layer was repeatedly

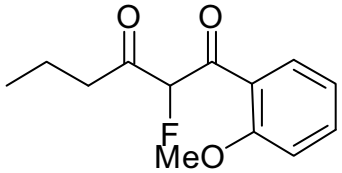
extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography (silica gel, *n*-heptane/dichloromethane) to give the fluorinated 1,3-dicarbonyl compunds **24.**

2-Fluoro-1-(2-methoxyphenyl)-1,3-butanedione (24a).



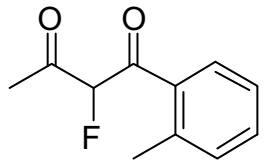
Starting with **23a** (3.088 g, 16.1 mmol) and selectfluor (5.695 g, 16.1 mmol) in acetonitrile (32 mL), **24a** (2.500 g, 73%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 6.06 (d, $^2J_{H,F}$ = 48.0 Hz, 1 H, CH), 6.86-6.89 (m, 2 H, CH_{An}), 7.43 (m, 1 H, CH_{An}), 7.55 (m, 1 H, CH_{An}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1 ($CO\mathit{CH_3}$), 55.8 (OCH_{3An}), 97.9 (d, ^1J = 194.9 Hz, $CO\mathit{C}FCOCH_3$), 112.1, 121.5 (CH_{An}), 125.0 ($COCH_{3An}$), 131.7 (CH_{An}), 135.5 (d, ^4J = 3.5 Hz, CH_{An}), 170.1 (d, ^3J = 26.9 Hz, C_{An}), 193.4 (d, ^2J = 21.0 Hz, *C*OCFCOCH3), 199.6 (d, ^2J = 22.5 Hz, COCF*C*OCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −191.1 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2960 (m), 2874 (w), 1726 (s), 1600 (s), 1489 (s), 1301 (s), 1254 (s), 1163 (m), 1081 (s), 962 (w), 757 (s). MS(EI, 70 eV): *m/z* (%) = 210 ([M^+], 50), 135 (100), 120 (2), 108 (2), 92 (11), 77 (22), 63 (4), 43 (8). HRMS (EI): Calcd. for $C_{16}H_{11}FO_3$: 210.06867; found: 286.06820.

2-Fluoro-1-(2-methoxyphenyl)-1,3-hexanedione (24b).



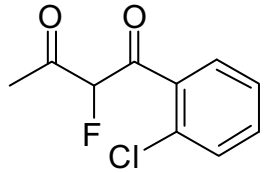
Starting with **23b** (0.881 g, 4.0 mmol) and selectfluor (1.417 g, 4.0 mmol) in acetonitrile (8 mL), **24b** (0.808 g, 90%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.55−1.63 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.58 (t(br), ^3J = 7.2 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.82 (s, 3 H, $OC\mathit{H_3}$), 5.93 (d, $^2J_{H,F}$ = 45.9 Hz, 1 H, CH), 6.96 (d, ^3J = 8.5 Hz, 1 H, CH_{An}), 7.01 (d, ^3J = 7.6 Hz, 1 H, CH_{An}), 7.46−7.52 (m, 1 H, CH_{An}), 7.62-7.66 (m, 1 H, CH_{An}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 ($COCH_2CH_2\mathit{CH_3}$), 16.6 (d, ^4J = 1.2 Hz, $COCH_2\mathit{CH_2}CH_3$), 40.9 ($CO\mathit{CH_2}CH_2CH_3$), 55.9 (OCH_{3An}), 97.8 (d, ^1J = 194.9 Hz, $CO\mathit{C}FCOCH_2CH_2CH_3$), 112.1, 121.4 ($CH_{An}$), 125.1 ($\mathit{C}OCH_{3An}$), 131.0, 135.4 ($CH_{An}$), 169.7 (d, ^3J = 27.0 Hz, C_{An}), 193.4 (d, ^2J = 20.6 Hz, *C*OCFCOCH$_2$CH$_2$CH3), 201.8 (d, ^2J = 21.5 Hz, COCF*C*OCH$_2$CH$_2$CH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −192.8 (CF). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2966 (s), 2877 (m), 1731 (s), 1686 (s), 1599 (s), 1486 (s), 1438 (s), 1290 (s), 1248 (s), 1163 (s), 1019 (s), 971 (m), 759 (s), 651 (m). MS (EI, 70 eV): *m/z* (%) = 238 (M^+, 3), 207 (10), 168 (5), 135 (100), 92 (8) 77 (16), 64 (3), 43 (10). HRMS (EI): Calcd. for $C_{13}H_{15}FO_3$: 238.09997; found: 238.09972.

2-Fluoro-1-(2-methylphenyl)-1,3-butanedione (24c).



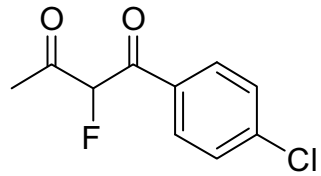
Starting with **23c** (2.0618 g, 12.6 mmol) and selectfluor (4.4 g, 12.6 mmol) in acetonitrile (25 mL), **24c** (1.123 g, 46%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s(br), 3 H, CH_3), 2.42 (s, 3 H, CH_{3An}), 5.75 (d, $^{2}J_{H,F}$ = 50.1 Hz, 1 H, CH), 7.21 (m, 1 H, CH_{Tol}), 7.33 (m, 1 H, CH_{Tol}), 7.35 (m, 1 H, CH_{Tol}), 7.60 (m, 1 H, CH_{Tol}).. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CO*CH₃*), 28.6 (CH_{3Tol}), 95.8 (d, ^{1}J = 196.5 Hz, CO*C*FCOCH$_3$), 124.6 (CH $_{Tol}$), 127.1 (*C*$CH_{3\ Tol}$), 131.2, 131.6 (CH $_{Tol}$), 139.7 (d, ^{4}J = 3.6 Hz, CH $_{Tol}$), 165.1 (C $_{Tol}$), 172.0 (d, ^{2}J = 20.7 Hz, *C*OCFCOCH3), 187.1 (d, ^{2}J = 22.8 Hz, COCF*C*OCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −187.1 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2929 (m), 1713 (s), 1692 (s), 1602 (m), 1571 (m), 1457 (m), 1296 (s), 1101 (m), 958 (w), 765 (m). MS (EI, 70 eV): *m/z* (%) = 194 ([M$^+$], 5), 179 (39), 159 (5), 131 (12), 119 (100), 103 (6), 91 (66), 77 (5), 65 (17), 51 (5), 43 (19), 39 (6). HRMS (EI): Calcd. for $C_{11}H_{11}FO_2$: 194.07376; found: 194.07356.

1-(2-Chlorophenyl)-2-fluoro-1,3-butanedione (24d).



Starting with **23d** (0.393 g, 2.0 mmol) and selectfluor (0.708 g, 2.0 mmol) in acetonitrile (4 mL), **24d** (0.180 g, 42%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 5.79 (d, $^{2}J_{H,F}$ = 49.3 Hz, 1 H, CH), 7.29 (m, 1 H, CH_{ClPh}), 7.31 (m, 1 H, CH_{ClPh}), 7.39 (m, 1 H, CH_{ClPh}), 7.55 (m, 1 H, CH_{ClPh}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0 (CO*CH₃*), 96.0 (d, ^{1}J = 198.9 Hz, CO*C*FCOCH3), 123.1, 124.5 (CH_{ClPh}), 125.7 (*C*Cl_{ClPh}), 127.7, 133.6 (CH_{ClPh}), 168.7 (d, ^{3}J = 24.6 Hz, C_{ClPh}), 191.8 (d, ^{2}J = 20.3 Hz, *C*OCFCOCH$_3$), 199.1 (d, ^{2}J = 22.7 Hz, COCF*C*OCH$_3$).^{19}F NMR (235 MHz, $CDCl_3$): δ = −190.2 (CF). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3420 (w), 2925 (w), 1735 (s), 1683 (s), 1509 (s), 1358 (m), 1286 (s), 1122 (m), 1063 (m), 970 (w), 780 (s).

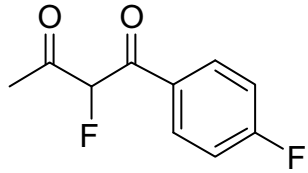
1-(4-Chlorophenyl)-2-fluoro-1,3-butanedione (24e).



Starting with 23e (3.933 g, 20.0 mmol) and selectfluor (7.085 g, 20.0 mmol) in acetonitrile (40 mL), **24e** (2.5 g, 58%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 5.90 (d, $^{2}J_{H,F}$ = 49.9 Hz, 1 H, CH), 7.36 (m, 2 H, CH_{ClPh}), 7.79 (m, 2 H, CH_{ClPh}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3106 (w), 1924 (w)1740 (m), 1689 (s), 1590 (s), 1488 (m), 1360 (s), 1179 (s), 1093 (s), 836 (s), 729 (m). MS (EI, 70 eV): *m/z* (%) = 216 ([M]$^+$, [^{37}Cl], 5), 214 ([M]$^+$, [^{35}Cl], 15), 199 (3), 179 (13), 159 (3), 141 ([M]$^+$, [^{37}Cl], 34), 139

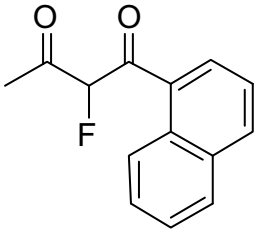
([M]$^+$, [^{35}Cl], 100), 113 ([M]$^+$, [^{37}Cl], 14), 111 ([M]$^+$, [^{35}Cl], 41), 87 (6), 75 (20), 50 (6), 43 (23). HRMS (EI): Calcd. for $C_{10}H_8ClFO_2$ ([M]$^+$,^{35}Cl): 214.01914; found: 214.01846.

2-Fluoro-1-(4-fluorophenyl)-1,3-butanedione (24f).



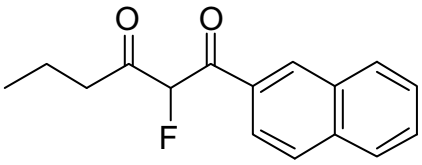
Starting with **23f** (0.360 g, 2.0 mmol) and selectfluor (0.708 g, 2.0 mmol) in acetonitrile (4 mL), **24f** (0.185 g, 46%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 5.90 (d, $^2J_{H,F}$ = 50.1 Hz, 1 H, CH), 7.07 (m, 2 H, CH_{FPh}), 7.96−7.98 (m, 2 H, CH_{FPh}).^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7 (CO*CH$_3$*), 96.6 (d, ^{1}J = 198.0 Hz, CO*C*FCOCH3), 115.1 (d, ^3J = 22.2 Hz, $2CH_{FPh}$), 128.9 (d, ^3J = 4.4 Hz, C_{FPh}), 131.6 (d, ^4J = 3.3 Hz, $2CH_{FPh}$), 165. 5 (d, ^1J = 256.2 Hz, CF_{FPh}), 187.7 (d, ^2J = 19.2 Hz, *C*OCFCOCH$_3$), 199.4 (d, ^2J = 23.6 Hz, COCF*C*OCH$_3$). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3079 (m), 2929 (m), 1738 (s), 1693 (s), 1599 (s), 1507 (s), 1414 (s), 1360 (s), 1240 (s), 1160 (s), 1013 (m), 851 (s), 610 (m). MS (EI, 70 eV): *m/z* (%) = 198 ([M$^+$], 12), 183 (4), 123 (100), 107 (3), 95 (42), 75 (15), 43 (17). HRMS (EI): Calcd. for $C_{10}H_8F_2O_2$: 198.04869; found: 198.139023.

2-Fluoro-1-(1-naphthyl)-1,3-butanedione (24g).



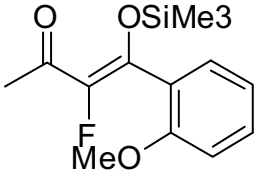
Starting with **23g** (0.480 g, 2.0 mmol) and selectfluor (0.708 g, 2.0 mmol) in acetonitrile (4 mL), **24g** (0.193 g, 37%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 5.84 (d, $^2J_{H,F}$ = 49.9 Hz, 1 H, CH), 7.37−7.39 (m, 4 H, CH_{Napth}), 7.82−7.86 (m, 2 H, CH_{Napth}), 8.51−8.54 (m, 1 H, CH_{Napth}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5 (CO*CH3*), 97.5 (d, ^1J = 200.4 Hz, CO*C*FCOCH$_3$), 127.1, 130.3, 130.5, 130.9 (CH_{Napth}), 131.8, 132.1 (C_{Napth}), 132.2, 132.8, 133.4 (CH_{Napth}), 167.7 (d, ^3J = 26.8 Hz, C_{Napth}), 188.8 (d, ^2J = 28.4 Hz, *C*OCFCOCH$_3$), 199.5 (d, ^2J = 23.1 Hz, COCF*C*OCH$_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −185.6 (CF). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3400 (br(w)), 3072 (w), 2927 (w), 1716 (s), 1590 (s), 1472 (m), 1435 (s), 1360 (m), 1291 (m), 1126 (m), 1053 (m), 743 (s). MS (EI, 70 eV): *m/z* (%) = 230 ([M$^+$], 25), 210 (5), 195 (5), 167 (12), 155 (100), 139 (12), 127 (82), 101 (5), 77 (7), 43 (11).

2-Fluoro-1-(2-naphthyl)-1,3-hexanedione (24h).



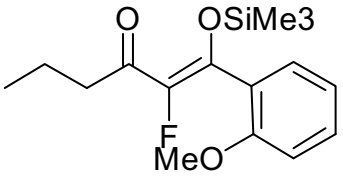
Starting with **23h** (0.480 g, 2.0 mmol) and selectfluor (0.708 g, 2.0 mmol) in acetonitrile (4 mL), **24h** (0.331 g, 64%) was isolated as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, ^{3}J = 7.6 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.49−1.57 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.58 (t(br), ^{3}J = 8.0 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 5.84 (d, $^{2}J_{H,F}$ = 48.4 Hz, 1 H, CH), 7.78-7.81 (m, 4 H, CH_{Napth}), 8.41 (m, 1 H, CH_{Napth}), 8.49 (m, 2 H, CH_{Napth}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 ($COCH_2CH_2\mathit{CH_3}$), 16.6 (d, ^{4}J = 1.6 Hz, $COCH_2\mathit{CH_2}CH_3$), 40.5 ($CO\mathit{CH_2}CH_2CH_3$), 97.1 (d, ^{1}J = 197.7 Hz, $CO\mathit{C}FCOCH_2CH_2CH_3$), 124.5 (d, ^{4}J = 197.7 Hz, CH_{Napth}), 127.4 , 128.2, 129.1, 129.8, 130.4 (CH_{Napth}), 132.6 (C_{Napth}), 133.0 (CH_{Napth}), 136.5 (C_{Napth}), 165.7 (d, ^{3}J = 19.7 Hz, C_{Napth}), 190.6 (d, ^{2}J = 18.9 Hz, $\mathit{C}OCFCOCH_2CH_2CH_3$), 203.2 (d, ^{2}J = 22.6 Hz, $COCF\mathit{C}OCH_2CH_2CH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −190.7 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2965 (m), 2876 (w), 1732 (m), 1686 (s), 1629 (s), 1596 (m), 1467 (m), 1281 (m), 1126 (m), 1098 (m), 864 (w), 755 (m). MS (EI, 70 eV): *m/z* (%) = 258 ([M^+], 27), 229 (12), 215 (5), 188 (19), 155 (100), 127 (54), 101 (3), 71 (10), 43 (15), HRMS (EI): Calcd. for $C_{16}H_{15}FO_2$: 258.10506; found: 258.10470.

3-Fluoro-4-(2-methoxyphenyl)-4-(silyloxy)-3-buten-2-one (25a).



Starting with benzene (30 mL), **24a** (2.502 g, 11.9 mmol), triethylamine (1.926 g, 19.0 mmol) and trimethylchlorosilane (2.326 g, 21.4 mmol), **25a** was isolated as a yellowish oil (3.322 g, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10-0.11 (m, 9 H, $Si(CH_3)_3$), 1.90 (s, 3 H, CH_3), 3.73 (s, 3 H, $OC\mathit{H_3}$), 6.87 (m, 1 H, CH_{An}), 6.90 (m, 1 H, CH_{An}), 7.12−7.14 (m, 1 H, CH_{An}) 7.32 (m, 1 H, CH_{An}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 ($OSi(\mathit{CH_3})_3$), 25.8 ($CO\mathit{CH_3}$), 55.0 ($CO\mathit{CH_3}_{An}$), 110.6, 120.0 (CH_{An}), 123.4 ($\mathit{C}OCH_{3An}$), 130.3, 131.1 (CH_{An}), 143.3 (C), 145.8 (d, ^{1}J = 240.4 Hz, CF), 156.7 (C_{An}), 190. 3 (d, ^{2}J = 27.5 Hz, $\mathit{C}OCH_3$).

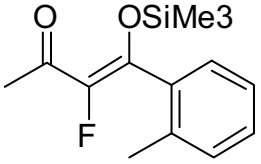
2-Fluoro-1-(2-methoxyphenyl)-1-(silyloxy)-1-hexen-3-one (25b).



Starting with benzene (39 mL), **24b** (3.079 g, 12.9 mmol), triethylamine (2.090 g, 20.6 mmol) and trimethylchlorosilane (2.524 g, 23.2 mmol), **25b** was isolated as a yellowish oil (3.163 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (m, 9 H, $Si(CH_3)_3$), 0.76 (t, ^{3}J = 7.4 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.44−1.47 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.30 (t(br), ^{3}J = 7.2 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 3.71 (s, 3 H, $OC\mathit{H_3}$), 6.83 (d, ^{3}J = 8.2 Hz, 1 H, CH_{An}),

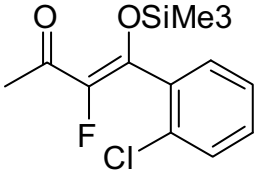
6.90 (d, ^{3}J = 7.6 Hz, 1 H, CH_{An}), 7.11 (dd, ^{3}J = 7.6 Hz, ^{4}J = 1.7 Hz, 1 H, CH_{An}), 7.31 (dd, ^{3}J = 7.6 Hz, ^{4}J = 0.9 Hz, 1 H, CH_{An}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (OSi(CH_3)$_3$), 13.1 ($COCH_2CH_2CH_3$), 16.6 (d, ^{4}J = 1.2 Hz, $COCH_2CH_2CH_3$), 40.7 ($COCH_2CH_2CH_3$), 54.8 ($COCH_3$), 110.5, 119.8 (CH_{An}), 123.6 (COCH3$_{An}$), 130.2, 130.7 (CH_{An}), 134.6 (C), 145.6 (d, ^{1}J = 243.2 Hz, CF), 156.6 (d, ^{3}J = 9.9 Hz, C_{An}), 193.2 (d, ^{2}J = 28.5 Hz, CO$CH_2CH_2CH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −145.9 (CF).

2-Fluoro-3-methyl-1-(2-methylphenyl)-1,3-butadienyloxy(trimethyl)silane (25c).



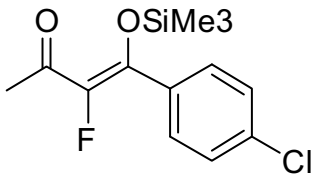
Starting with benzene (18 mL), **24c** (1.123 g, 5.8 mmol), triethylamine (0.936 g, 9.2 mmol) and trimethylchlorosilane (1.131 g, 10.5 mmol), **25c** was isolated as a yellowish oil (1.001 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (m, 9 H, Si(CH_3)$_3$), 2.11 (s, 3 H, CH_{3Tol}), 7.12 (m, 2 H, CH_{Tol}), 7.18 (m, 2 H, C_{Tol}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (OSi(CH_3)$_3$), 18.5 ($COCH_3$), 27.1 (CH_{3Tol}), 125.1, 127.6, 128.8, 129.8 (CH_{Tol}), 131.0 ($C$$CH_{3Tol}$), 136.0 (d, ^{3}J = 2.7 Hz, C_{Tol}), 143.5 (C), 145.6 (d, ^{1}J = 241.0 Hz, CFCOCH$_3$), 189.2 (d, ^{2}J = 24.4 Hz, COCH$_3$).

4-(2-Chlorophenyl)-3-fluoro-4-(silyloxy)-3-buten-2-one (25d).



Starting with benzene (26 mL), **24d** (2.281 g, 10.6 mmol), triethylamine (1.719 g, 17.0 mmol) and trimethylchlorosilane (2.076 g, 19.1 mmol), **25d** was isolated as a yellowish oil (2.432 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (m, 9 H, Si(CH_3)$_3$), 1.97 (s, 3 H, CH_3), 7.38 (m, 1 H, CH_{ClPh}), 7.40 (m, 1 H, CH_{ClPh}), 7.50 (m, 1 H, CH_{ClPh}), 7.54 (m, 1 H, CH_{ClPh}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (OSi(CH_3)$_3$), 27.6 ($COCH_3$), 126.2, 129.1, 130.1, 131.8 (CH_{ClPh}), 132.5, 133.4 (C_{ClPh}), 143.5 (d, ^{2}J = 12.6 Hz, C), 145.2 (d, ^{1}J = 244.7 Hz, CFCOCH$_3$), 190.1 (d, ^{2}J = 29.7 Hz, COCH$_3$).

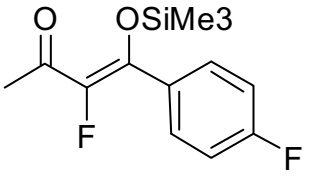
4-(4-Chlorophenyl)-3-fluoro-4-(silyloxy)-3-buten-2-one (25e).



Starting with benzene (35 mL), **24e** (2.511 g, 11.6 mmol), triethylamine (1.885 g, 18.6 mmol) and trimethylchlorosilane (2.277 g, 18.6 mmol), **25e** was isolated as a yellowish oil (2.183 g, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.13 (m, 9 H, Si(CH_3)$_3$), 2.09 (s, 3 H, CH_3), 7.19 (m, 2 H, CH_{ClPh}), 7.56 (m, 2 H, CH_{ClPh}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.1 (OSi(CH_3)$_3$), 19.0 ($COCH_3$), 127.7, 129.7, 129.8, 130.0 (CH_{ClPh}), 135.4 (C), 137.4

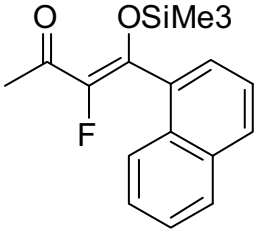
(*C*Cl$_{ClPh}$), 144.7 (d, ^{1}J = 237.4 Hz, *C*FCOCH$_3$), 149.9 (d, ^{3}J = 12.1 Hz, C$_{ClPh}$) 185.1 (d, ^{2}J = 29.4 Hz, *C*OCH$_3$).

3-Fluoro-4-(4-fluorophenyl)-4-(silyloxy)-3-buten-2-one (25f).



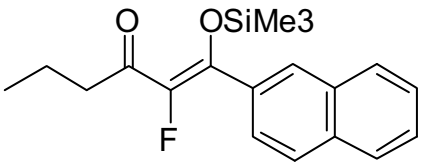
Starting with benzene (26 mL), **24f** (2.064 g, 10.4 mmol), triethylamine (1.684 g, 16.7 mmol) and trimethylchlorosilane (2.034 g, 18.7 mmol), **25f** was isolated as a yellowish oil (2.306 g, 82%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.23 (m, 9 H, Si(CH$_3$)$_3$), 2.20 (s, 3 H, CH$_3$), 7.03 (m, 2 H, CH$_{FPh}$), 7.76-7.78 (m, 2 H, CH$_{FPh}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 0.4 (OSi(*CH$_3$*)$_3$), 19.0 (CO*CH$_3$*), 114.6 (d, ^{2}J = 21.5 Hz, 2CH$_{FPh}$), 130.8 (d, ^{2}J = 6.9 Hz, 2CH$_{FPh}$), 144.8 (d, ^{1}J = 237.9 Hz, *C*FCOCH$_3$), 146.4 (C), 149.7 (d, ^{3}J = 12.2 Hz, C$_{FPh}$), 164.5 (d, ^{1}J = 252.5 Hz, CF$_{FPh}$), 185.5 (d, ^{2}J = 29.1 Hz, COCF*C*OCH$_3$). ^{19}F NMR (235 MHz, CDCl$_3$): δ = −144.1 (CF).

4-(1-Naphthyl)-4-[(trimethylsilyl)oxy]-3-buten-2-one (25g).



Starting with benzene (24 mL), **24g** (2.425 g, 9.4 mmol), triethylamine (1.520 g, 15.0 mmol) and trimethylchlorosilane (1.836 g, 16.9 mmol), **25g** was isolated as a yellowish oil (2.016 g, 71%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.16 (m, 9 H, Si(CH$_3$)$_3$), 1.94 (s(br), 3 H, CH$_3$), 7.56 (m, 4 H, CH$_{Napth}$), 7.92 (m, 3 H, CH$_{Napth}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 0.1 (OSi(*CH$_3$*)$_3$), 27.2 (CO*CH$_3$*), 124.1, 124.4, 125.6, 125.7 (CH$_{Napth}$), 126.3 (d, ^{3}J = 11.8 Hz, C$_{Napth}$), 126.4 (CH$_{Napth}$), 127.2, 127.8 (C$_{Napth}$), 127.9, 129.7 (CH$_{Napth}$), 144.3 (C), 145.9 (d, ^{1}J = 242.6 Hz, *C*FCOCH$_3$), 189.8 (d, ^{2}J = 26.7 Hz, *C*OCH$_3$).

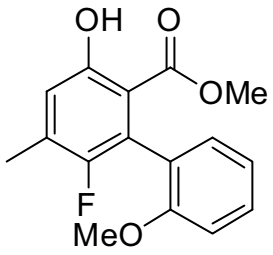
2-Fluoro-1-(2-naphthyl)-1-(silyloxy)-1-hexen-3-one (25h).



Starting with benzene (19 mL), **24h** (1.9155 g, 7.4 mmol), triethylamine (1.200 g, 11.8 mmol) and trimethylchlorosilane (1.449 g, 13.3 mmol), **25h** was isolated as a yellowish oil (1.813 g, 74%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.10−0.24 (m, 9 H, Si(CH$_3$)$_3$), 0.91 (t, ^{3}J = 7.2 Hz, 3 H, CH$_2$CH$_2$*CH$_3$*), 1.54−1.62 (m, 2 H, CH$_2$*CH$_2$*CH$_3$), 2.57 (t(br), ^{3}J = 8.5 Hz, 2 H, *CH$_2$*CH$_2$CH$_3$), 7.37 (m, 1 H, CH$_{Napth}$), 7.39 (m, 1H, CH$_{Napth}$), 7.69−7.78 (m, 4 H, CH$_{Napth}$), 8.26 (m, 1H, CH$_{Napth}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ = 0.1 (OSi(*CH$_3$*)$_3$), 13.1 (COCH$_2$CH$_2$*CH$_3$*), 19.6 (d, ^{4}J = 2.7 Hz, COCH$_2$*CH$_2$*CH$_3$), 33.3 (CO*CH$_2$*CH$_2$CH$_3$), 124.4, 127.0, 127.1, 127.3, 128.7, 128.8, 129.7

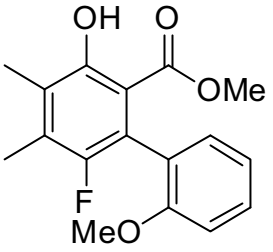
(CH_{Napth}), 131.7, 134.4 (C_{Napth}), 134.5 (C), 145.0 (d, ^1J = 238.4 Hz, *C*FCOCH$_2$CH$_2$CH$_3$), 152.8 (d, ^3J = 10.7 Hz, C_{Napth}), 186.9 (d, ^2J = 29.7 Hz, *C*OCH$_2$CH$_2$CH$_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −142.9 (CF).

Methyl 6-fluoro-3-hydroxy-2'-methoxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26a).



Starting with **25a** (0.847 g, 3.0 mmol), **5a** (0.852 g, 3.3 mmol) and $TiCl_4$ (0.620 g, 3.3 mmol), **26a** was isolated as a colorless solid (0.383 g, 44%), (mp = 105−107 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s(br), 3 H, CH_3), 3.37 (s, 3 H, OC*H*$_3$), 3.65 (s, 3 H, COO*CH*$_3$), 6.85 (d, $^4J_{H,F}$ = 8.1 Hz, 1 H, CH_{Ar}), 6.92 (dd, ^3J = 7.4 Hz, ^4J = 0.9 Hz, 1 H, CH_{An}), 7.01−7.04 (m, 1H, CH_{An}), 7.19−7.23 (m, 1 H, CH_{An}), 7.25−7.28 (m, 1 H, CH_{An}), 10.57 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (d, ^3J = 3.6 Hz, CH_3), 50.6 (O*CH*$_{3An}$), 54.4 (COO*CH*$_3$), 109.2 (d, ^3J = 9.6 Hz, CH_{Ar}), 110.0 (*C*COOCH$_{3Ar}$), 117.8 (d, ^4J = 4.2 Hz, CH_{An}), 119.0 (CH_{An}), 123.6 (*C*OCH$_{3An}$), 124.8 (d, ^2J = 19.5 Hz, *C*CF$_{Ar}$), 127.9, 129.2 (CH_{An}), 132.1 (d, ^2J = 21.5 Hz, *C*CH3$_{Ar}$), 150.6 (d, ^1J = 233.0 Hz, CF_{Ar}), 155.4 (C_{An}), 156.2 (d, ^4J = 2.1 Hz, COH_{Ar}), 169.7 (d, ^4J = 2.1 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.9 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3012 (w), 2844 (w), 1662 (s), 1499 (m), 1459 (s), 1378 (s), 1239 (s), 1106 (m), 1074 (m), 1025 (m), 806 (m). MS (EI, 70 eV): *m/z* (%) = 290 ([M$^+$], 50), 258 (100), 241 (6), 229 (26), 187 (10), 159 (6), 133 (8). HRMS (EI): Calcd. for $C_{16}H_{15}FO_4$: 290.09489; found: 290.09473.

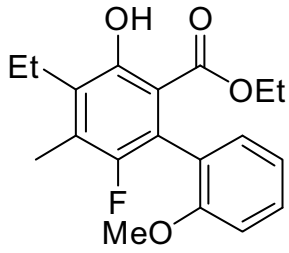
Methyl 6-fluoro-3-hydroxy-2'-methoxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26b).



Starting with **25a** (0.847 g, 3.0 mmol), **5b** (0.898 g, 3.3 mmol) and $TiCl_4$ (0.620 g, 3.3 mmol), **26b** was isolated a colorless solid (0.494 g, 54%), (mp = 98−100 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s(br), 6 H, CH_3), 3.36 (s, 3 H, OC*H*$_{3An}$), 3.64 (s, 3 H, COO*CH*$_3$), 6.84 (dd, ^3J = 8.1 Hz, ^4J = 0.9 Hz, 1 H, CH_{An}), 6.91 (dd, ^3J = 7.4 Hz, ^4J = 1.1 Hz, 1 H, CH_{An}), 7.01−7.04 (m, 1H, CH_{An}), 7.23 (ddd, ^3J = 8.1 Hz, ^3J = 8.1 Hz, ^4J = 1.8 Hz, 1 H, CH_{An}), 10.91 (s, 1 H, OH_{Ar}) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.7 (d, ^4J = 2.3 Hz, CH_3), 11.1 (d, ^3J = 5.8 Hz, *C*CH$_{3Ar}$), 50.6 (O*CH*$_{3An}$), 54.6 (COO*CH*$_3$), 108.6 (d, ^3J = 2.9 Hz, *C*COOCH$_{3Ar}$), 109.1, 119.0 (CH_{An}), 121.6 (d, ^2J = 20.4 Hz, *C*CF$_{Ar}$), 124.0 (*C*OCH$_{3An}$), 125.0 (d, ^3J = 3.4 Hz, C_{An}), 124.0 (CH_{An}), 129.4 (d, ^4J = 1.7 Hz, CH_{An}), 130.4 (d, ^2J = 19.8 Hz, FC*C*CH$_{3Ar}$), 150.2 (d, ^1J = 232.2 Hz, CF_{Ar}), 154.5 (d, ^3J = 1.7 Hz, *C*CH$_{3Ar}$), 155.5 (COH_{Ar}), 170.3 (d, ^4J = 3.3 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.8 (CF). IR (KBr,

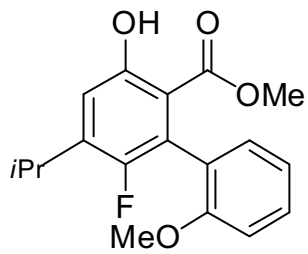
cm^{-1}): $\tilde{\nu}$ = 3016 (w), 2960 (m), 2841 (w), 1660 (s), 1621 (m), 1499 (m), 1437 (s), 1340 (s), 1248 (s), 1228 (s), 1095 (s), 903 (m), 805 (s), 749 (s). MS (EI, 70 eV): *m/z* (%) = 304 (M^+, 39), 272 (71), 257 (100), 241 (60), 229 (22), 213 (9), 199 (10), 183 (14), 165 (12), 149 (40), 112 (16), 97 (21), 83 (30), 69 (65), 57 (64). HRMS (EI): Calcd. for $C_{17}H_{17}FO_4$: 304.11054; found: 304.10978. Anal. calcd. for $C_{17}H_{17}FO_4$: C 67.09, H 5.63; found: C 67.22, 5.62.

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



Starting with **25a** (0.424 g, 1.5 mmol), **5a** (0.357 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26c** was isolated as a colorless solid (0.220 g, 33%), (mp = 81−83 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.64 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.09 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.19 (s(br), 3 H, CH_3), 2.68 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.64 (s, 3 H, OCH_{3An}), 3.86 (q, ^3J = 7.2 Hz, 2 H, $COOCH_2CH_3$), 6.82 (d, ^3J = 8.4 Hz, 1 H, CH_{An}), 6.86−6.91 (m, 1 H, CH_{An}), 6.99 (d, ^3J = 7.4 Hz, 1H, CH_{An}), 7.23 (ddd, ^3J = 8.1 Hz, ^3J = 7.4 Hz, ^4J = 1.7 Hz, 1 H, CH_{An}), 10.99 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.4 (CH_2CH_3), 11.9 ($COOCH_2CH_3$), 12.0 (d, ^3J = 11.2 Hz, CH_3), 18.6 (d, ^4J = 1.6 Hz, CH_2CH_3), 54.5 (OCH_{3An}), 59.7 ($COOCH_2CH_3$), 109.0 (d, ^3J = 2.9 Hz, $CCOOCH_2CH_{3Ar}$), 109.3, 119.1 (CH_{An}), 121.5 (d, ^2J = 20.4 Hz, CCF_{Ar}), 124.0 ($COCH3_{An}$), 127.5 (CH_{An}), 129.4 (d, ^4J = 1.7 Hz, CH_{An}), 129.6 (d, ^2J = 19.2 Hz, CCH_{3Ar}), 130.9 (d, ^3J = 3.5 Hz, C_{An}), 150.4 (d, ^1J = 232.1 Hz, CF_{Ar}), 154.5 (d, ^3J = 1.7 Hz, CCH_2CH_{3Ar}), 155.7(COH_{Ar}), 169.9 (d, ^4J = 3.4 Hz, $COOCH_2CH3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.5 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3420 (w(br)), 3058 (w), 2970 (m), 2933 (m), 2873 (m), 1653 (s), 1615 (m), 1499 (m), 1466 (m), 1398 (s), 1326 (s), 1276 (s), 1243 (s), 1225 (s), 1080 (m), 1029 (m), 752 (s). MS (EI, 70 eV): *m/z* (%) = 332 ([M^+], 44), 286 (86), 271 (75), 255 (100), 228 (8), 213 (9), 199 (17), 183 (16), 152 (9), 133 (6), 69 (12). HRMS (EI): Calcd. for $C_{19}H_{21}FO_4$: 332.14184; found: 332.14174. Anal. calcd. for $C_{19}H_{21}FO_3$: C 68.66, H 6.36; found: C 68.83, 6.81.

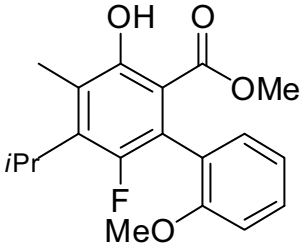
Methyl 6-fluoro-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (26d).



Starting with **25b** (0.621 g, 2.0 mmol), **5a** (0.568 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **26d** was isolated as a colorless solid (0.229 g, 35%), (mp = 67−70 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2CH_3$), 1.53 (m, 2 H, $CH_2CH_2CH_3$), 2.48 (t(br), ^3J = 7.2 Hz, 2 H, $CH_2CH_2CH_3$), 3.31 (s,

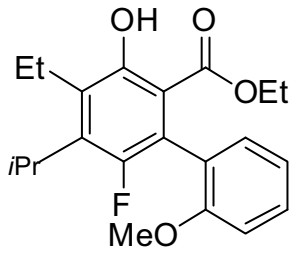
3 H, OCH_{3An}), 3.58 (s, 3 H, COOCH_3), 6.71 (d, $^4J_{H,F}$ = 6.4 Hz, 1 H, CH_{Ar}), 6.79 (dd, ^3J = 8.1 Hz, ^4J = 0.7 Hz, 1 H, CH_{An}), 6.85 (ddd, ^3J = 7.4 Hz, ^3J = 7.4 Hz, ^4J = 0.9 Hz, 1 H, CH_{An}), 6.97 (m, 1H, CH_{An}), 7.18 (ddd, ^3J = 8.1 Hz, ^3J = 8.1 Hz, ^4J = 1.7 Hz, 1 H, CH_{An}), 10.50 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 ($CH_2CH_2CH_3$), 21.6 (d, ^4J = 1.1 Hz, $CH_2CH_2CH_3$), 30.5 (d, ^3J = 2.2 Hz, $CH_2CH_2CH_3$), 50.6 (OCH_{3An}), 54.5 (COOCH_3), 109.3 (CH_{An}), 109.8 (d, ^3J = 2.3 Hz, CCOOCH$_2$CH$_{3Ar}$), 116.9 (d, ^3J = 2.9 Hz, CH_{Ar}), 119.1 (CH_{An}), 123.7 (COCH3$_{An}$), 124.9 (d, ^2J = 19.8 Hz, CCF$_{Ar}$), 127.8 (CH_{An}), 129.3 (d, ^4J = 1.7 Hz, CH_{An}), 136.5 (d, ^2J = 19.8 Hz, CCH$_2$CH$_2$CH$_{3Ar}$), 150.4 (d, ^1J = 233.8 Hz, CF_{Ar}), 155.5 (COH_{Ar}), 156.3 (d, ^3J = 2.9 Hz, C_{An}), 169.8 (d, ^4J = 2.9 Hz, COOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −128.2 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2959 (s), 2873 (m), 1669 (s), 1622 (m), 1583 (w), 1499 (m), 1435 (s), 1332 (s), 1239 (s), 1110 (m), 1028 (m), 847 (m), 752 (s). GC-MS (EI, 70 eV): *m/z* (%) = 318 ([M$^+$], 36), 286 (100), 258 (29), 243 (4), 229 (5), 215 (9), 186 (4), 159 (5), 133 (3). HRMS (EI): Calcd. for $C_{18}H_{19}FO_4$: 318.12619; found: 318.12680.

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



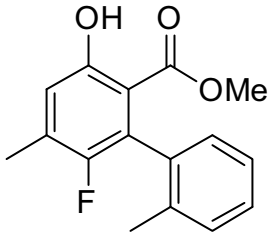
Starting with **25b** (0.621 g, 2.0 mmol), **5b** (0.598 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **26e** was isolated as a colorless solid (0.228 g, 34%) , (mp = 62-64 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.44 (m, 2 H, $CH_2CH_2CH_3$), 2.13 (s, 3 H, CH_3), 2.54 (t(br), ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 3.30 (s, 3 H, OCH_{3An}), 3.58 (s, 3 H, COOCH_3), 6.78 (d, ^4J = 7.6 Hz, 1 H, CH_{An}), 6.84 (ddd, ^3J = 7.4 Hz, ^3J = 7.4 Hz, ^4J = 0.9 Hz, 1 H, CH_{An}), 6.98 (m, 1H, CH_{An}), 7.17 (ddd, ^3J = 8.1 Hz, ^3J = 8.1 Hz, ^4J = 1.7 Hz, 1 H, CH_{An}), 10.85 (s, 1 H, OH_{Ar}) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 (d, ^4J = 2.3 Hz, CH_3), 15.9 ($CH_2CH_2CH_3$), 24.5 ($CH_2CH_2CH_3$), 30.5 (d, ^3J = 3.6 Hz, $CH_2CH_2CH_3$), 53.5 (OCH_{3An}), 57.5 (COOCH_3), 111.8 (d, ^3J = 2.9 Hz, CCOOCH$_3$), 112.2, 122.0 (CH_{An}), 124.6 (d, ^2J = 21.0 Hz, CCF$_{Ar}$), 127.0 (COCH3$_{An}$), 127.6 (d, ^3J = 4.0 Hz, C_{An}), 130.6 (CH_{An}), 132.4 (d, ^4J = 1.7 Hz, CH_{An}), 137.8 (d, ^2J = 19.2 Hz, CCH$_2$CH$_2$CH$_{3Ar}$), 153.3 (d, ^1J = 232.1 Hz, CF_{Ar}), 157.6 (COH_{Ar}), 158.1 (d, ^3J = 2.3 Hz, CCH3$_{Ar}$), 173.3 (d, ^4J = 2.9 Hz, COOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −127.1 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (m(br)), 3009 (w), 2956 (m), 1659 (s), 1616 (m), 1500 (w), 1411 (s), 1338 (s), 1266 (s), 1220 (s), 1137 (m), 1025 (m), 750 (m). GC-MS (EI, 70 eV): *m/z* (%) = 332 ([M$^+$], 47), 300 (100), 285 (27), 269 (13), 257 (38), 241 (17), 199 (10), 133 (3). HRMS (EI): Calcd. for $C_{19}H_{21}FO_4$: 332.14184; found: 332.14206.

Ethyl 4-ethyl-6-fluoro-3-hydroxy-2'-methoxy-5-propyl[1,1'-biphenyl]-2-carboxylate (26f).



Starting with **25b** (0.467 g, 1.5 mmol), **5c** (0.499 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol **26f** was isolated as a colorless oil (0.286 g, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.59 (t, ^3J = 7.0 Hz, 3 H, $CH_2CH_2CH_3$), 0.86 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.07 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 1.46 (m, 2 H, $CH_2CH_2CH_3$), 2.53 (q, ^3J = 7.8 Hz, 2 H, CH_2CH_3), 2.62 (s(br), ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 3.58 (s, 3 H, OCH_{3An}), 3.80 (q, ^3J = 7.0 Hz, 2 H, $COOCH_2CH_3$), 6.77 (dd, ^3J = 8.1 Hz, ^4J = 0.7 Hz, 1 H, CH_{An}), 6.83 (ddd, ^3J = 7.4 Hz, ^3J = 7.4 Hz, ^4J = 1.1 Hz, 1 H, CH_{An}), 6.96 (dd, ^3J = 7.4 Hz, ^4J = 1.1 Hz, 1 H, CH_{An}), 7.17 (ddd, ^3J = 8.1 Hz, ^3J = 8.1 Hz, ^4J = 1.7 Hz, 1 H, CH_{An}), 10.91 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_2CH_3), 15.8 ($CH_2CH_2CH_3$), 16.0 ($COOCH_2CH_3$), 21.5 (d, ^4J = 1.6 Hz, CH_2CH_3), 25.4 (d, ^4J = 1.1 Hz, $CH_2CH_2CH_3$), 30.2 (d, ^3J = 3.3 Hz, $CH_2CH_2CH_3$), 57.7 (OCH_{3An}), 62.6 ($COOCH_2CH_3$), 112.1 (d, ^3J = 2.9 Hz, $CCOOCH_2CH_{3Ar}$), 112.3, 120.0 (CH_{An}), 124.8 (d, ^2J = 20.9 Hz, CCF_{Ar}), 127.4 ($COCH3_{An}$), 130.4 (CH_{An}), 132.4 (d, ^4J = 1.7 Hz, CH_{An}), 133.4 (d, ^3J = 3.5 Hz, C_{An}), 137.1 (d, ^3J = 18.6 Hz, $CCH_2CH_2CH_{3Ar}$), 153.4 (d, ^1J = 232.7 Hz, CF_{Ar}), 157.7 (d, ^3J = 1.7 Hz, CCH_2CH_{3Ar}), 158.6 (COH_{Ar}), 172.8 (d, ^4J = 2.5 Hz, $COOCH_2CH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.8 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2958 (s), 2870 (m), 1655 (s), 1616 (m), 1503 (m), 1468 (m), 1415 (m), 1399 (m), 1246 (s), 1233 (s), 1097 (m), 750 (s). GC-MS (EI, 70 eV): *m/z* (%) = 360 ([M^+], 56), 314 (100), 299 (50), 283 (67), 271 (31), 199 (8). HRMS (EI): Calcd. for $C_{21}H_{25}FO_4$: 360.17314; found: 360.17255.

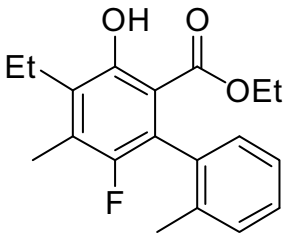
Methyl 6-fluoro-3-hydroxy-2',5-dimethyl[1,1'-biphenyl]-2-carboxylate (26g).



Starting with **25c** (0.360 g, 1.5 mmol), **5a** (0.426 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26g** was isolated as a colorless viscous oil (0.180 g, 44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (s(br), 3 H, CH_{3Tol}), 2.30 (s(br), 3 H, CH_3), 3.41 (s, 3 H, $COOCH_3$), 6.84 (d, $^4J_{H,F}$ = 6.4 Hz, 1 H, CH_{Ar}), 6.97 (d, ^3J = 7.4 Hz, 1 H, CH_{Tol}), 7.21 (m, 1 H, CH_{Tol}), 7.22−7.24 (m, 2 H, CH_{Tol}), 10.79 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.8 (d, ^3J = 3.6 Hz, CH_{3Tol}), 20.1 (CH_3), 50.3 ($COOCH_3$), 110.3 (d, ^3J = 2.7 Hz, $CCOOCH_{3Ar}$), 118.9 (d, ^3J = 4.3 Hz, CH_{Ar}), 125.5, 127.8, 128.9 (CH_{Tol}), 129.4 (CCH_{3Tol}), 129.6 (d, ^4J = 3.5 Hz, CH_{Tol}), 133.9 (d, ^2J = 21.5 Hz, CCF_{Ar}), 136.0 (d, ^2J = 13.9 Hz, CCH_{3Ar}), 139.6 (C_{Tol}), 151.8 (d, ^1J = 232.7 Hz, CF_{Ar}), 158.2 (d, ^4J = 2.3 Hz, COH_{Ar}), 171.1 (d, ^4J = 2.9 Hz,

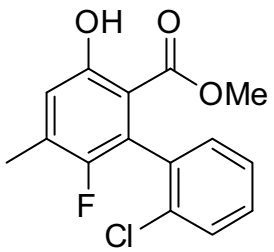
*C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.8 (CF_{Ar}). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2925 (m), 2875 (w), 1669 (s), 1624 (w), 1437 (m), 1334 (m), 1240 (s), 1221 (s), 1077 (m), 846 (m), 755 (m), 644 (w). GC-MS (EI, 70 eV): *m/z* (%) = 274 ([M^+], 29), 242 (100), 214 (10), 199 (11), 183 (6), 171 (16), 136 (3). HRMS (EI): Calcd. for $C_{16}H_{15}FO_3$: 274.09997; found: 274.10009.

Ethyl 4-ethyl-6-fluoro-3-hydroxy-2',5-dimethyl[1,1'-biphenyl]-2-carboxylate (26h).



Starting with **25c** (0.360 g, 1.5 mmol), **5c** (0.495 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol) CH_2Cl_2 (3 mL), **26h** was isolated as a colorless viscous oil (0.185 g, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (t, ^3J = 7.0 Hz, 3 H, CH_2CH_3), 1.23 (t, ^3J = 7.4 Hz, 3 H, $COOCH_2CH_3$), 2.12 (s, 3 H, CH_{3Tol}), 2.32 (s(br), 3 H, CH_{3Ar}), 2.82 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.95 (q, ^3J = 7.0 Hz, 2 H, $COOCH_2CH_3$), 7.03 (d, ^3J = 7.4 Hz, 1 H, CH_{Tol}), 7.17−7.23 (m, 1 H, CH_{Tol}), 7.26−7.28 (m, 2 H, CH_{Tol}), 11.29 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8 (d, ^3J = 6.1 Hz, CH_{3Tol}), 13.2 (CH_2CH_3), 13.5 ($COOCH_2CH_3$), 20.0 (d, ^4J = 2.2 Hz, CH_2CH_3), 20.2 (CH_{3Tol}), 61.3 ($COOCH_2CH_3$), 109.7 (d, ^3J = 2.9 Hz, CCOOCH$_2$CH$_{3Ar}$), 125.5 (CH_{Tol}), 126.3 (CCH$_{3Tol}$), 126.6 (C_{Tol}), 127.6 (CH_{Tol}), 129.1 (d, ^4J = 1.1 Hz, CH_{Tol}), 129.5 (CH_{Tol}), 131.3 (d, ^2J = 19.8 Hz, CCF$_{Ar}$), 132.3 (d, ^3J = 3.5 Hz, CCH$_2$CH$_{3Ar}$), 136.5 (d, ^2J = 19.5 Hz, CCH$_{3Ar}$), 151.6 (d, ^1J = 231.0 Hz, CF_{Ar}), 156.5 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.1 (d, ^4J = 3.2 Hz, COOCH$_2$CH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.5 (CF_{Ar}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2926 (s), 2855 (w), 1661 (s), 1616 (w), 1456 (m), 1374 (m), 1328 (m), 1272 (m), 1226 (s), 1214 (s), 1170 (w), 1038 (w), 759 (m), 734 (m), 450 (w). GC-MS (EI, 70 eV): *m/z* (%) = 316 ([M^+], 39), 270 (43), 255 (100), 237 (11), 213 (4), 183 (12), 165 (6). HRMS (EI): Calcd. for $C_{19}H_{21}FO_3$: 316.14692; found: 316.14730.

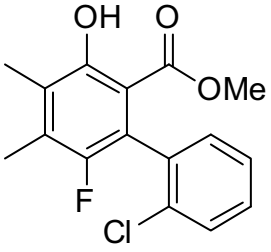
Methyl 2'-chloro-6-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26i).



Starting with **25d** (0.429 g, 1.5 mmol), **5a** (0.426 g, 1.6 mmol), $TiCl_4$ (0.310 g, 1.6 mmol), **26i** was isolated as a reddish oil (0.118 g, 26%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s(br), 3 H, CH_3), 3.38 (s, 3 H, $COOCH_3$), 6.81 (d, $^4J_{H,\ F}$ = 6.6 Hz, 1 H, CH_{Ar}), 7.06−7.08 (m, 1 H, CH_{ClPh}), 7.19−7.22 (m, 2 H, CH_{ClPh}), 7.34−7.37 (m, 1 H, CH_{ClPh}), 10.82 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4 (d, ^3J = 3.9 Hz, CH_3), 51.0 ($COOCH_3$), 108.7 (d, ^3J = 1.7 Hz, CCOOCH$_{3Ar}$), 118.7 (d, ^3J = 3.4 Hz, CH_{Ar}), 125.2 (d, ^2J = 19.8 Hz, CCF$_{Ar}$), 127.7 (3CH$_{Ph}$), 129.4 (d, ^4J = 1.1 Hz, CH_{Ph}), 132.1 (d, ^3J = 1.1 Hz, C_{Ph}), 132.7 (d, ^2J = 21.0 Hz, CCH$_{3Ar}$), 133.9 (CCl$_{ClPh}$), 150.4 (d, ^1J = 234.4 Hz, CF_{Ar}), 156.9 (d, ^4J

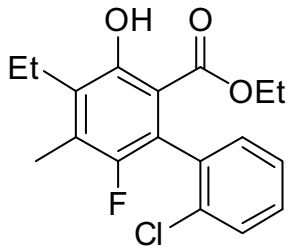
= 2.3 Hz, COH_{Ar}), 169.3 (d, ^4J = 2.9 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.4 (CF). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1674 (s), 1632 (w), 1376 (s), 1331 (s), 1215 (s), 1074 (m), 858 (m), 760 (s). GC-MS (EI, 70 eV): *m/z* (%) = GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M^+], [^{37}Cl], 3), 294 ([M^+], [^{35}Cl], 9), 259 (100), 234 (15), 199 (21), 170 (24), 151 (4), 129 (4), 85 (9), 75 (4). HRMS (EI): Calcd. for $C_{15}H_{12}ClFO_3$ ([M]$^+$, ^{35}Cl): 294.04535; found: 294.04604.

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



Starting with **25d** (0.429 g, 1.5 mmol), **5b** (0.448 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26j** was isolated by column chromatography as a colorless solid (0.177 g, 38%), (mp = 76-78 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s(br), 6 H, CH_3), 3.38 (s, 3 H, COO*CH*$_3$), 7.06−7.09 (m, 2 H, CH_{ClPh}), 7.18−7.21 (m, 2 H, CH_{ClPh}), 11.19 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3 (d, ^4J = 2.9 Hz, CH_3), 12.6 (d, ^3J = 5.2 Hz, *CH*$_3$), 52.4 (COO*CH*$_3$), 109.0 (d, ^3J = 2.6 Hz, *C*COOCH$_{3Ar}$), 123.8 (d, ^2J = 21.0 Hz, *C*CF$_{Ar}$), 126.5 (d, ^4J = 1.1 Hz, CH_{ClPh}), 127.5 (d, ^3J = 3.5 Hz, CCH_{3Ar}), 128.9, 129.1, 131.0 (CH_{ClPh}), 132.3 (d, ^2J = 19.8 Hz, *C*CH$_{3Ar}$), 133.7 (d, ^3J = 1.1 Hz, C_{ClPh}), 135.7 (CCl_{ClPh}), 151.5 (d, ^1J = 232.1 Hz, CF_{Ar}), 156.7 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.4 (d, ^4J = 3.4 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.4 (CF). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M^+], [^{37}Cl], 5), 308 ([M^+], [^{35}Cl], 15), 273 (38), 241 (100), 213 (7), 183 (15), 170 (9), 136 (5), 82 (3). HRMS (EI): Calcd. for $C_{16}H_{16}ClFO_3$ ([M]$^+$, ^{35}Cl): 308.06100; found: 308.06159.

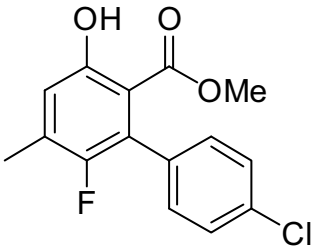
Ethyl 2'-chloro-4-ethyl-6-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26k).



Starting with **25d** (0.405 g, 1.5 mmol), **5c** (0.494 g, 1.6 mmol), $TiCl_4$ (0.310 g, 1.6 mmol), **26k** was isolated as a reddish viscous oil (0.192 g, 38%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.49 (t, ^3J = 7.2 Hz, 3 H, CH_2*CH*$_3$), 0.93 (t, ^3J = 7.6 Hz, 3 H, $COOCH_2$*CH*$_3$), 2.20 (s(br), 3 H, CH_3), 2.52 (q, ^3J = 7.4 Hz, 2 H, *CH*$_2$CH$_3$), 3.72 (q, ^3J = 7.0 Hz, 2 H, COO*CH*$_2$CH$_3$), 6.90−6.93 (m, 1 H, CH_{ClPh}), 6.99−7.06 (m, 2 H, CH_{ClPh}), 7.16−7.19 (m, 1 H, CH_{ClPh}), 11.12 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8 (d, ^3J 5.8 Hz, C*CH*$_3$), 13.2 (CH_2*CH*$_3$), 13.4 ($COOCH_2$*CH*$_3$), 20.1 (d, ^4J = 2.3 Hz, *CH*$_2$CH$_3$), 61.4 (COO*CH*$_2$CH$_{3Ar}$), 109.4 (d, ^3J = 2.3 Hz, *C*COOCH$_2$CH$_{3Ar}$), 123.9 (d, ^2J = 21.0 Hz, *C*CF$_{Ar}$), 126.4, 128.8, 129.1 (CH_{ClPh}), 131.0 (d, ^4J = 1.7 Hz, CH_{ClPh}), 131.6 (d, ^2J = 19.2 Hz, *C*CH$_{3Ar}$), 133.3 (d, ^3J = 2.9 Hz, *C*CH$_2$CH$_{3Ar}$), 133.9 (d, ^3J = 1.1 Hz, C_{ClPh}), 136.1 (*C*Cl$_{ClPh}$), 151.6 (d, ^1J = 232.7 Hz, CF$_{Ar}$), 156.6 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.0 (d, ^4J = 2.9 Hz, *C*OOCH$_2$CH$_3$). ^{19}F NMR (235

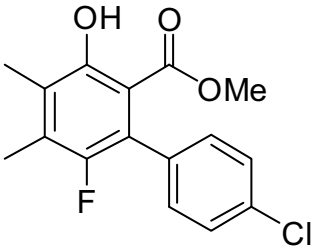
MHz, $CDCl_3$): δ = −125.1 (CF). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M^+], [^{37}Cl], 4), 336 ([M^+], [^{35}Cl], 14), 301 (27), 292 ([^{37}Cl], 5), 290 ([^{35}Cl], 16), 275 ([^{37}Cl], 4), 273 ([^{35}Cl], 11), 255 (100), 247 (4), 207 (4), 183 (15), 170 (4). HRMS (EI): Calcd. for $C_{18}H_{18}ClFO_3$ ([$M]^+$, ^{35}Cl): 336.09230; found: 336.09156.

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



Starting with **25e** (0.574 g, 2.0 mmol), **5a** (0.568 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **26l** was isolated as a colorless solid (0.171 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s(br), 3 H, CH_3), 3.39 (s, 3 H, COO*C*H_3), 6.78 (d, $^4J_{H,F}$ = 6.4 Hz, 1 H, CH_{Ar}), 7.03−7.06 (m, 2 H, CH_{ClPh}), 7.27−7.30 (m, 2 H, CH_{ClPh}), 11.59 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (d, ^3J = 3.7 Hz, CH_3), 50.8 (COO*C*H_3), 108.8 (d, ^3J = 1.7 Hz, *C*COOCH_{3Ar}), 118.3 (d, ^3J = 3.5 Hz, CH_{Ar}), 126.8 (d, ^4J = 1.1 Hz, 2 CH_{ClPh}), 127.3 (d, ^2J = 19.2 Hz, *C*CF_{Ar}), 129.2 (2CH_{ClPh}), 132.3 (d, ^2J = 14.5 Hz, *C*CH_{3Ar}), 132.6 (C_{ClPh}), 133.1 (*C*Cl_{ClPh}), 150.5 (d, ^1J = 234.3 Hz, CF_{Ar}), 156.6 (d, ^4J = 1.8 Hz, COH_{Ar}), 169.5 (d, ^4J = 2.9 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −127.4 (CF). GC-MS (EI, 70 eV): *m/z* (%) = 296 ([M^+], [^{37}Cl], 11), 294 ([M^+], [^{35}Cl], 31), 264 ([^{37}Cl], 32), 262 ([^{35}Cl], 100), 236 ([^{37}Cl], 8), 234 ([^{35}Cl], 24), 199 (11), 170 (24), 151 (3), 85 (9). HRMS (EI): Calcd. for $C_{15}H_{12}ClFO_3$ ([$M]^+$, ^{35}Cl): 294.04535; found: 294.04581.

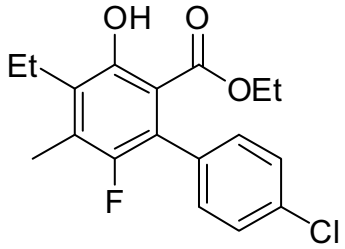
Methyl 4'-chloro-6-fluoro-3-hydroxy-4,5-dimethyl[1,1'-biphenyl]-2-carboxylate (26m).



Starting with **25e** (0.574 g, 2.0 mmol), **5b** (0.598 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **26m** was isolated as a yellowish solid (0.198 g, 32%), (mp = 87−92 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14 (s(br), 6 H, CH_3), 3.35 (s, 3 H, COO*C*H_3), 6.99−7.02 (m, 2 H, CH_{ClPh}), 7.22−7.25 (m, 2 H, CH_{ClPh}), 10.89 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2 (d, ^4J = 2.9 Hz, CH_3), 12.5 (d, ^3J = 5.8 Hz, C*C*H_{3Ar}), 52.2 (COO*C*H_3), 109.2 (d, ^3J = 2.9 Hz, *C*COOCH_{3Ar}), 125.4 (d, ^2J = 19.8 Hz, *C*CF_{Ar}), 127.0 (d, ^3J = 3.4 Hz, *C*CH_{3Ar}), 128.2 (2CH_{ClPh}), 130.8 (2CH_{ClPh}), 132.1 (d, ^2J = 19.8 Hz, *C*CH_{3Ar}), 133.3 (C_{ClPh}), 135.0 (*C*Cl_{ClPh}), 151.6 (d, ^1J = 232.7 Hz, CF_{Ar}), 156.3 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.5 (d, ^4J = 2.9 Hz, *C*OOCH3). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.4 (CF). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M^+], [^{37}Cl], 10), 308 ([M^+], [^{35}Cl], 30), 278 ([^{37}Cl], 19), 276 ([^{35}Cl], 54), 261 (7), 241 (100), 233 (6), 213 (8), 183 (15), 170 (12), 136 (5). HRMS (EI): Calcd. for $C_{15}H_{10}{}^{35}ClFO_2$: 276.03479; found: 276.03481. HRMS (EI): Calcd. for $C_{16}H_{14}ClFO_3$ ([$M]^+$,

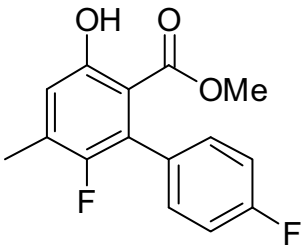
^{35}Cl): 308.06100; found: 308.06178.

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



Starting with **25e** (0.574 g, 2.0 mmol),**5c** (0.660 g, 2.2 mmol) and $TiCl_4$ (0.414 g, 2.2 mmol), **26n** was isolated as a yellowish solid (0.297 g, 44%), (mp = 73−75 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (t, ^3J = 7.0 Hz, 3 H, CH_2CH_3), 1.09 (t, ^3J = 7.4 Hz, 3 H, $COOCH_2CH_3$), 2.20 (s(br), 3 H, CH_3), 2.69 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.89 (q, ^3J = 7.2 Hz, 2 H, $COOCH_2CH_3$), 7.03−7.07 (m, 2 H, CH_{ClPh}), 7.25−7.30 (m, 2 H, CH_{ClPh}), 11.01 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.7 (CH_2CH_3), 13.3 (d, ^3J = 9.0 Hz, CH_3), 14.3 ($COOCH_2CH_3$), 20.0 (d, ^3J = 2.3 Hz, CH_2CH_3), 61.5 ($COOCH_2CH_3$), 109.6 (d, ^3J = 2.4 Hz, $CCOOCH_2CH_{3Ar}$), 125.7 (d, ^2J = 20.4 Hz, CCF_{Ar}), 128.1 ($2CH_{ClPh}$), 130.0 ($2CH_{ClPh}$), 131.3 (d, ^2J = 19.2 Hz, CCH_{3Ar}), 133.0 (d, ^3J = 2.9 Hz, CCH_2CH_{3Ar}), 133.3 (C_{ClPh}), 135.3 (CCl_{ClPh}), 151.7 (d, ^1J = 232.7 Hz, CF_{Ar}), 156.3 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.1 (d, ^4J = 2.9 Hz, $COOCH_2CH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.0 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2973 (m), 2875 (w), 1660 (s), 1616 (w), 1797 (m), 1395 (s), 1375 (s), 1331 (s), 1226 (s), 1106 (m), 1086 (s), 1017 (m), 823 (s), 810 (m), 514 (m). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M$^+$], [^{37}Cl], 10), 336 ([M$^+$], [^{35}Cl], 29), 292 ([^{37}Cl], 14), 290 ([^{35}Cl], 40), 275 (12), 255 (100), 237 (8), 212 (3), 183 (17), 170 (4). HRMS (EI): Calcd. for $C_{18}H_{18}ClFO_3$ ([M]$^+$,^{35}Cl): 336.09230; found: 336.09218.

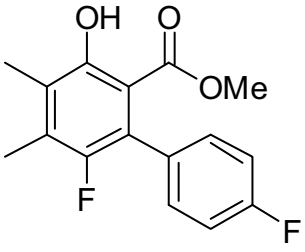
Methyl 4',6-difluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26o).



Starting with **25f** (0.405 g, 1.5 mmol), **5a** (0.426 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26o** was isolated as a colorless viscous oil (0.135 g, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.20 (s(br), 3 H, CH_3), 3.38 (s, 3 H, $COOCH_3$), 6.77 (d, $^4J_{H,F}$ = 6.4 Hz, 1 H, CH_{Ar}), 6.96−7.01 (m, 2 H, CH_{FPh}), 7.04−7.09 (m, 2 H, CH_{FPh}), 10.57 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (d, ^3J = 3.9 Hz, CH_3), 50.8 ($COOCH_3$), 109.0 (d, ^3J = 1.7 Hz, $CCOOCH_{3Ar}$), 113.6 (d, ^2J = 21.9 Hz, $2CH_{FPh}$), 118.1 (d, ^3J = 4.4 Hz, CH_{Ar}), 127.5 (d, ^2J = 19.2 Hz, CCF_{Ar}), 129.4 (d, ^4J = 1.7 Hz, CH_{FPh}), 129.6 (d, ^4J = 1.1 Hz, CH_{FPh}), 130.5 (d, ^3J = 3.4 Hz, C_{FPh}), 132.4 (d, ^2J = 21.5 Hz, CCH_{3Ar}), 150.7 (d, ^1J = 233.8 Hz, CF_{Ar}), 156.6 (d, ^4J = 1.7 Hz, COH_{Ar}), 161.1 (d, ^1J = 244.3 Hz, CF_{FPh}), 169.6 (d, ^4J = 2.9 Hz, $COOCH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −127.5 (CF_{Ar}), −115.5 (CF_{FPh}). GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M$^+$], 32), 246 (100), 218 (41), 201 (3), 189 (16), 170 (8),

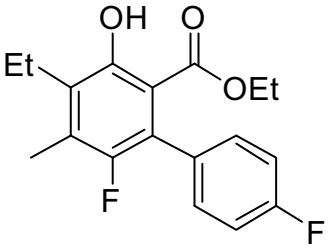
151 (3), 133 (2), 85 (4). HRMS (EI): Calcd. for $C_{15}H_{12}F_2O_3$: 278.07490; found: 278.07532.

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



Starting with **25f** (0.405 g, 1.5 mmol), **5b** (0.448 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26p** was isolated as a colorless viscous oil (0.177 g, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s(br), 6 H, CH_3), 3.32 (s, 3 H, COO*CH*$_3$), 6.92−6.96 (m, 2 H, CH_{FPh}), 6.99−7.03 (m, 2 H, CH_{FPh}), 10.86 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.2 (d, ^4J = 2.3 Hz, CH_3), 12.5 (d, ^3J = 5.7 Hz, C*CH*$_3$), 52.1 (COO*CH*$_3$), 109.5 (d, ^3J = 2.5 Hz, *C*COOCH$_{3Ar}$), 114.9 (d, ^2J = 21.4 Hz, 2CH_{FPh}), 125.7 (d, ^2J = 20.4 Hz, *C*CF_{Ar}), 126.9 (d, ^3J = 3.6 Hz, C_{FPh}), 131.0 (d, ^4J = 1.8 Hz, CH_{FPh}), 131.1 (d, ^4J = 1.2 Hz, CH_{FPh}), 132.0 (d, ^2J = 19.5 Hz, *C*CH_{3Ar}), 132.4 (d, ^3J = 3.5 Hz, *C*CH_{3Ar}), 151.8 (d, ^1J = 231.9 Hz, CF_{Ar}), 155.8 (d, ^4J = 1.8 Hz, COH_{Ar}), 162.5 (d, ^1J = 244.1 Hz, CF_{FPh}), 171.6 (d, ^4J = 3.1 Hz, *C*OOCH3).^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.5 (CF_{Ar}), −115.5 (CF_{FPh}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2926 (m), 2875 (w), 1665 (s), 1616 (w), 1515 (s), 1440 (s), 1334 (s), 1259 (m), 1219 (s), 1174 (m), 1096 (m), 1015 (m), 833 (m), 805 (m), 586 (m). GC-MS (EI, 70 eV): *m/z* (%) = 292 ([M^+], 64), 260 (100), 245 (81), 231 (9), 217 (43), 183 (17), 170 (5), 151 (3). HRMS (EI): Calcd. for $C_{16}H_{14}F_2O_3$: 292.09055; found: 292.09034.

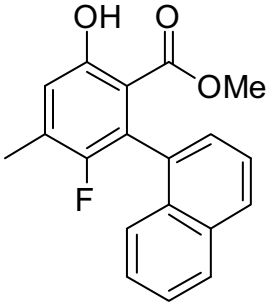
Ethyl 4-ethyl-4',6-difluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (26q).



Starting with **25f** (0.405 g, 1.5 mmol), **5c** (0.495 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26q** was isolated as a colorless viscous oil (0.170 g, 35%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (t, ^3J = 7.2 Hz, 3 H, CH_2*CH*$_3$), 1.09 (t, ^3J = 7.4 Hz, 3 H, COOCH$_2$*CH*$_3$), 2.19 (s(br), 3 H, CH_3), 2.69 (q, ^3J = 7.4 Hz, 2 H, *CH*$_2$CH$_3$), 3.88 (q, ^3J = 7.0 Hz, 2 H, COO*CH*$_2$CH$_3$), 6.95−7.02 (m, 2 H, CH_{FPh}), 7.04−7.11 (m, 2 H, CH_{FPh}), 11.00 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8 (d, ^3J = 2.3 Hz, CH_3), 13.4 (CH_2*CH*$_3$), 13.5 (COOCH$_2$*CH*$_3$), 20.0 (d, ^4J = 2.3 Hz, *CH*$_2$CH$_3$), 61.4 (COO*CH*$_2$CH$_3$), 109.8 (d, ^3J = 1.7 Hz, *C*COOCH$_2$CH$_{3Ar}$), 114.7, 115.7 (CH_{FPh}), 125.9 (d, ^2J = 20.4 Hz, *C*CF_{Ar}), 131.0 (d, ^2J = 1.1 Hz, CH_{FPh}), 131.1 (d, ^2J = 2.3 Hz, CH_{FPh}), 131.3 (d, ^2J = 20.4 Hz, *C*CF_{Ar}), 132.7 (d, ^3J = 3.5 Hz, C_{FPh}), 132.8 (d, ^3J = 2.9 Hz, *C*CH_2CH_{Ar}), 151.9 (d, ^1J = 232.7 Hz, CF_{Ar}), 156.2 (d, ^4J = 1.7 Hz, COH_{Ar}), 162.5 (d, ^1J = 243.7 Hz, CF_{FPh}), 171.2 (d, ^4J = 3.5 Hz, *C*$OOCH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.1 (CF_{Ar}), −115.9 (CF_{FPh}). GC-MS (EI, 70 eV): *m/z* (%) = 320 ([M^+], 64), 274 (88), 256 (100), 231 (34), 201 (24), 183 (23), 170 (6), 151

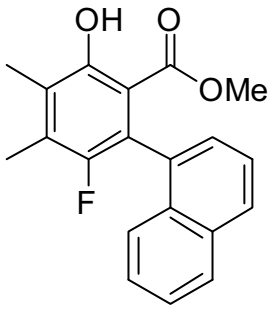
(4), 133 (3). HRMS (EI): Calcd. for $C_{18}H_{18}F_2O_3$: 320.17071; found: 320.12229.

Methyl 3-fluoro-6-hydroxy-4-methyl-2-(1-naphthyl)benzoate (26r).



Starting with **25g** (0.454 g, 1.5 mmol), **5a** (0.426 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26r** was as a reddish solid(0.135 g, 31%), (mp = 119−121 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s(br), 3 H, CH_3), 3.01 (s, 3 H, COO*CH*$_3$), 6.88 (dd, ^3J = 6.6 Hz, ^4J = 0.7 Hz, 1 H, CH_{Napth}), 7.17 (dd, ^3J = 7.0 Hz, ^4J = 1.3 Hz, 1 H, CH_{Napth}), 7.29−7.32 (m, 1 H, CH_{Napth}), 7.35 (m, 1 H, CH_{Ar}), 7.37−7.39 (m, 1 H, CH_{Napth}), 7.41−7.44 (m, 1 H, CH_{Napth}), 7.76−7.81 (m, 2 H, CH_{Napth}), 10.82 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (d, ^3J = 3.5 Hz, CH_3), 50.6 (COO*CH*$_3$), 109.7 (d, ^3J = 2.3 Hz, *C*COOCH$_{3Ar}$), 118.4 (d, ^3J = 3.5 Hz, CH_{Ar}), 123.9, 124.1, 124.5, 125.0, 125.1, 126.6 (CH_{Napth}), 126.7 (d, ^2J = 15.7 Hz, *C*CF$_{Ar}$), 127.1 (CH_{Napth}), 131.1, 132.1, 132.5 (C_{Napth}), 132.7 (d, ^2J = 12.2 Hz, FC*C*CH$_{3Ar}$), 151.1 (d, ^1J = 233.8 Hz, CF_{Ar}), 156.9 (d, ^4J = 2.3 Hz, COH_{Ar}), 169.6 (d, ^4J = 2.9 Hz, *C*OOCH$_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.6 (CF_{Ar}). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1665 (m), 1463 (s), 1376 (s), 1335 (m), 1225 (m), 1080 (w), 953 (w), 789 (m), 551 (w). GC-MS (EI, 70 eV): *m/z* (%) = 310 ([M$^+$], 38), 278 (100), 249 (18), 233 (8), 220 (15), 155 (3), 110 (10). HRMS (EI): Calcd. for $C_{19}H_{15}FO_3$: 310.09997; found: 310.10006.

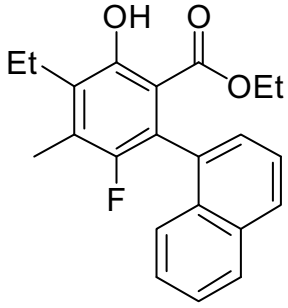
Methyl 3-fluoro-6-hydroxy-4,5-dimethyl-2-(1-naphthyl)benzoate (26s).



Starting with **25g** (0.454 g, 1.5 mmol), **5b** (0.448 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26s** was isolated as a reddish solid (0.180 g, 37%), (mp = 88−91 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s(br), 3 H, CH_3), 2.17 (s(br), 3 H, CH_3), 2.92 (s, 3 H, COO*CH*$_3$), 7.10 (dd, ^3J = 7.0 Hz, ^4J = 1.1 Hz, 1 H, CH_{Napth}), 7.19−7.19 (m, 1 H, CH_{Napth}), 7.30−7.32 (m, 2 H, CH_{Napth}), 7.66−7.72 (m, 3 H, CH_{Napth}), 11.15 (s, 1 H, OH_{Ar}) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (d, ^4J = 2.3 Hz, CH_3), 13.4 (d, ^3J = 5.8 Hz, C*CH*$_3$), 52.8 (COO*CH*$_3$), 111.0 (d, ^3J = 2.9 Hz, *C*COOCH$_{3Ar}$), 125.7 (d, ^2J = 21.5 Hz, *C*CF$_{Ar}$), 126.2, 126.4, 126.7, 127.1 (CH_{Napth}), 127.5 (d, ^4J = 1.1 Hz, CH_{Napth}), 127.9 (d, ^3J = 3.4 Hz, *C*CH$_{3Ar}$), 128.6, 129.3 (CH_{Napth}), 133.1 (d, ^2J = 19.8 Hz, *C*CH$_{3Ar}$), 133.5, 134.4, 135.3 (CH_{Napth}), 152.9 (d, ^1J = 231.5 Hz, CF_{Ar}), 155.5 (d, ^4J = 1.7 Hz, COH_{Ar}), 172.4 (d, ^4J = 2.9 Hz, *C*OOCH$_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −124.0 (CF). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1664 (s), 1457 (s), 1377 (s), 1339 (s), 1260 (s), 1226 (s), 1098 (m), 924 (w), 779 (s), 432 (w).GC-MS (EI, 70 eV): *m/z* (%) = 324 ([M$^+$], 36), 292 (100), 277 (18), 249 (10), 233 (8),

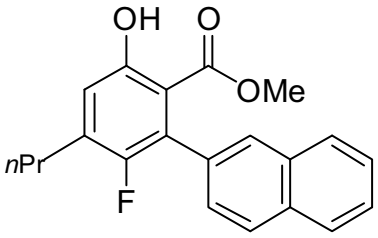
220 (17), 162 (4), 110 (8). HRMS (EI): Calcd. for $C_{20}H_{17}FO_3$: 324.11562; found: 324.11546.

Ethyl 3-ethyl-5-fluoro-2-hydroxy-4-methyl-6-(1-naphthyl)benzoate (26t).



Starting with **25g** (0.454 g, 1.5 mmol), **5c** (0.495 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26t** was isolated as a reddish solid (0.223 g, 42%), (mp = 68−72 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.16 (t, ^3J = 7.5 Hz, 3 H, $COOCH_2CH_3$), 2.56 (s(br), 3 H, CH_{3Ar}), 2.68 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.58 (q, ^3J = 7.3 Hz, 2 H, $COOCH_2CH_3$), 7.11 (m, 1 H, CH_{Napth}), 7.21−7.26 (m, 4 H, CH_{Napth}), 7.68−7.76 (m, 2 H, CH_{Napth}), 11.10 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9 (d, ^3J = 5.6 Hz, CH_{3Ar}), 12.6 (CH_2CH_{3Ar}), 13.5 ($COOCH_2CH_{3Ar}$), 20.1 (d, ^4J = 1.6 Hz, CH_2CH_{3Ar}), 61.1 ($COOCH_2CH_{3Ar}$), 110.4 (d, ^3J = 2.3 Hz, $CCOOCH_2CH_{3Ar}$), 125.0 (d, ^2J = 21.5 Hz, CCF_{Ar}), 125.4 (d, ^4J = 1.1 Hz, CH_{Napth}), 125.8, 125.9, 126.2, 126.6, 127.7, 128.4 (CH_{Napth}), 131.5 (d, ^2J = 19.2 Hz, CCH_{3Ar}), 132.9 (d, ^3J = 2.9 Hz, CCH_2CH_{3Ar}), 133.1, 133.6 (C_{Napth}), 134.8 (d, ^4J = 1.1 Hz, CCH_{3Ar}), 152.3 (d, ^1J = 231.5 Hz, CF_{Ar}), 156.6 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.1 (d, ^4J = 3.5 Hz, $COOCH_{3Ar}$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −124.0 (CF). IR (Nujol, cm^{-1}): $\tilde{\nu}$ = 1663 (s), 1460 (s), 1357 (s), 1327 (m), 1206 (m), 1109 (w), 1041 (w), 790 (m), 641 (w). GC-MS (EI, 70 eV): *m/z* (%) = 352 ([M^+], 36), 306 (34), 291 (100), 273 (5), 220 (13), 162 (2), 110 (2). HRMS (EI): Calcd. for $C_{22}H_{21}FO_3$: 352.14692; found: 352.14689.

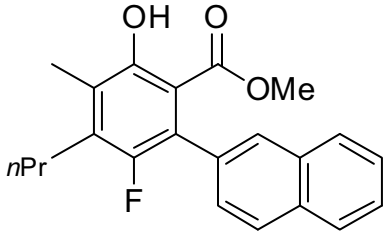
Methyl 3-fluoro-6-hydroxy-2-(2-naphthyl)-4-propylbenzoate (26u).



Starting with **25h** (0.495 g, 1.5 mmol), **5a** (0.424 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26u** was isolated as a colorless viscous oil (0.143 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.54−1.62 (m, 2 H, $CH_2CH_2CH_3$), 2.53 (t, ^3J = 7.4 Hz, 2 H, $CH_2CH_2CH_3$), 3.21 (s, 3 H, $COOCH_3$), 6.80 (d, $^4J_{H,F}$ = 6.3 Hz, 1 H, CH_{Ar}), 7.22 (dd, , ^3J = 8.4 Hz, ^4J = 1.7 Hz, 1 H, CH_{Napth}), 7.37−7.40 (m, 2 H, CH_{Napth}), 7.58 (m, 1 H, CH_{Napth}), 7.71−7.77 (m, 3 H, CH_{Napth}), 10.58 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 ($CH_2CH_2CH_3$), 23.1 (d, ^4J = 1.1 Hz, $CH_2CH_2CH_3$), 32.0 (d, ^3J = 1.7 Hz, $CH_2CH_2CH_3$), 52.1 ($COOCH_3$), 110.7 (d, ^3J = 1.7 Hz, $CCOOCH_{3Ar}$), 118.7 (d, ^4J = 2.8 Hz, CH_{Napth}), 125.6 (CH_{Napth}), 126.4 (d, ^3J = 5.2 Hz, CH_{Ar}), 127.3, 128.1, 128.4, 129.7 (CH_{Napth}), 129.9, 130.2 (C_{Napth}), 131.3 (CH_{Napth}), 132.9 (d, ^3J = 1.7 Hz, C_{Napth}), 133.5 (d, ^3J = 19.2 Hz, CCF_{Ar}), 138.2

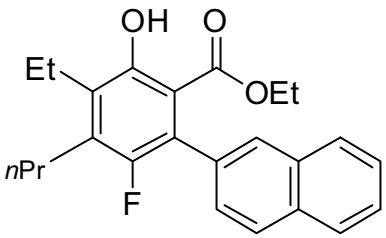
(d, ^3J = 19.8 Hz, *C*$CH_2CH_2CH_{3Ar}$), 152.0 (d, ^1J = 234.4 Hz, CF_{Ar}), 158.0 (d, ^4J = 2.0 Hz, COH_{Ar}), 171.2 (d, ^4J = 2.9 Hz, *C*$OOCH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −128.8 (CF). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2960 (s), 2872 (w), 1668 (s), 1619 (w), 1437 (s), 1332 (s), 1234 (s), 1092 (m), 819 (m), 787 (m), 746 (m), 478 (m). GC-MS (EI, 70 eV): *m/z* (%) = 338 ([M^+], 50), 306 (100), 278 (44), 249 (31), 220 (32), 207 (5), 169 (6), 125 (5), 110 (9). HRMS (EI): Calcd. for $C_{21}H_{19}FO_3$: 338.13127; found: 338.13136.

Methyl 3-fluoro-6-hydroxy-5-methyl-2-(2-naphthyl)-4-propylbenzoate (26v).



Starting with **25h** (0.495 g, 1.5 mmol), **5b** (0.448 g, 1.6 mmol), $TiCl_4$ (0.310 g, 1.6 mmol) **26v** was isolated as a colorless solid (0.180 g, 34%), (mp = 87−90 ºC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_2*CH_3*), 1.39−1.52 (m, 2 H, CH_2*CH_2*CH_3), 2.16 (s, 3 H, CH_3), 2.55 (t(br), ^3J = 7.4 Hz, 2 H, *CH_2*CH_2CH_3), 3.16 (s, 3 H, COO*CH_3*), 7.18 (dd, ^3J = 8.3 Hz, ^4J = 1.5 Hz, 1 H, CH_{Napth}), 7.31−7.34 (m, 2 H, CH_{Napth}), 7.54 (m, 1 H, CH_{Napth}), 7.65−7.72 (m, 3 H, CH_{Napth}), 10.89 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.2 (d, ^4J = 2.3 Hz, CH_3), 12.6 (CH_2CH_2*CH_3*), 21.8 (d, ^4J = 1.1 Hz, CH_2*CH_2*CH_3), 27.8 (d, ^3J = 3.9 Hz, *CH_2*CH_2CH_3), 50.9 (COO*CH_3*), 107.9 (d, ^3J = 2.9 Hz, *C*$COOCH_{3Ar}$), 124.4, 124.5 (CH_{Napth}), 124.7 (d, ^2J = 19.8 Hz, *C*CF_{Ar}), 125.1 (*C*CH_{3Ar}), 125.4, 126.2, 126.3, 126.3, 126.5 (CH_{Napth}), 130.9, 131.6, 132.1 (C_{Napth}), 134.6 (d, ^2J = 19.2 Hz, *C*$CH_2CH_2CH_{3Ar}$), 150.4 (d, ^1J = 232.7 Hz, CF_{Ar}), 154.7 (d, ^4J = 1.7 Hz, COH_{Ar}), 169.9 (d, ^4J = 3.5 Hz, *C*$OOCH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −127.7 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2959 (m), 2871 (w), 1664 (s), 1617 (w), 1440 (s), 1414 (s), 1331 (s), 1264 (s), 1224 (s), 1115 (w), 1017 (m), 895 (w), 819 (m), 744 (m), 475 (m). GC-MS (EI, 70 eV): *m/z* (%) = 352 ([M^+], 47), 320 (100), 305 (37), 292 (15), 277 (20), 249 (4), 220 (17), 176 (7), 146 (6), 116 (5). HRMS (EI): Calcd. for $C_{22}H_{21}FO_3$: 352.14692; found: 352.14732.

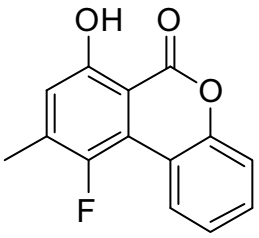
Ethyl 3-ethyl-5-fluoro-2-hydroxy-6-(2-naphthyl)-4-propylbenzoate (26w).



Starting with **25h** (0.495 g, 1.5 mmol), **5c** (0.484 g, 1.6 mmol) and $TiCl_4$ (0.310 g, 1.6 mmol), **26w** was isolated (0.204 g, 35%) by column chromatography (silica gel, *n*-heptane/EtOAc = 30:1 → 20:1) as a colorless viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.31 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_2*CH_3*), 0.91 (t, ^3J = 7.2 Hz, 3 H, *CH_2*CH_3), 1.13 (t, ^3J = 7.4 Hz, 3 H, $COOCH_2$*CH_3*),

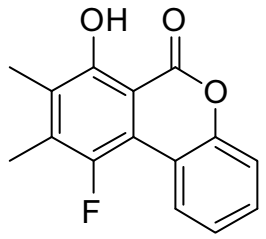
1.45−1.58 (m, 2 H, $CH_2CH_2CH_3$), 2.59 (t(br), ^3J = 8.0 Hz, 2 H, $CH_2CH_2CH_3$), 2.67 (t, ^3J = 8.0 Hz, 2 H, CH_2CH_3), 3.74 (q, ^3J = 7.2 Hz, 2 H, $COOCH_2CH_3$), 7.25 (dd, ^3J = 8.3 Hz, ^4J = 1.5 Hz, 1 H, CH_{Napth}), 7.35−7.40 (m, 2 H, CH_{Napth}), 7.57 (m, 1 H, CH_{Napth}), 7.68−7.79 (m, 3 H, CH_{Napth}), 11.00 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 ($CH_2CH_2CH_3$), 14.4 (CH_2CH_3), 14.7 ($COOCH_2CH_3$), 20.0 (d, ^4J = 1.6 Hz, $CH_2CH_2CH_3$), 23.9 (d, ^4J = 1.1 Hz, CH_2CH_3), 28.8 (d, ^3J = 3.3 Hz, $CH_2CH_2CH_3$), 61.3 ($COOCH_2CH_3$), 110.2 (d, ^3J = 2.9 Hz, $CCOOCH_2CH_{3Ar}$), 126.1, 126.3 (CH_{Napth}), 127.0 (d, ^2J = 20.4 Hz, CCF_{Ar}), 127.3, 128.0 (CH_{Napth}), 128.1 (d, ^4J = 1.6 Hz, CH_{Napth}), 128.2 (d, ^4J = 1.1 Hz, CH_{Napth}), 128.2 (CH_{Napth}), 132.3 (d, ^3J = 3.5 Hz, CCH_2CH_{3Ar}), 132.8, 133.4 (C_{Napth}), 134.3 (d, ^4J = 1.1 Hz, C_{Napth}), 135.9 (d, ^2J = 18.6 Hz, $FCCCH_2CH_2CH_{3Ar}$), 152.1 (d, ^1J = 232.7 Hz, CF_{Ar}), 156.5 (d, ^4J = 1.7 Hz, COH_{Ar}), 171.3 (d, ^4J = 3.5 Hz, $COOCH_2CH_3$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −127.4 (CF). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2964 (s), 2873 (m), 1660 (s), 1613 (m), 1507 (m), 1416 (s), 1373 (s), 1328 (s), 1257 (s), 1243 (s), 1210 (s), 1164 (m), 1030 (m), 819 (m), 749 (s), 477 (m). GC-MS (EI, 70 eV): *m/z* (%) = 380 ([M^+], 65), 334 (100), 305 (10), 291 (39), 273 (37), 246 (5), 176 (5), 152 (3), 131 (3), 116 (3). HRMS (EI): Calcd. for $C_{24}H_{25}FO_3$: 380.17822; found: 380.17793.

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



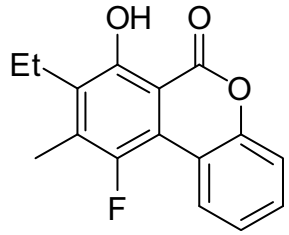
Starting with **26a** (0.060 g, 0.21 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.207 g, 0.83 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27a** was isolated as a colourless solid (0.046 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s(br), 3 H, CH_3), 6.81 (d, $^4J_{H,F}$ = 5.9 Hz, 1 H, CH_{Ar}), 7.24−7.26 (m, 1 H, CH_{An}), 7.28 (m, 1H, CH_{An}), 7.38−7.43 (m, 1 H, CH_{An}), 8.35−8.39 (m, 1 H, CH_{An}), 11.21 (s, 1 H, OH) . ^{13}C NMR (62 MHz, $CDCl_3$): δ = 15.7 (d, ^3J = 6.2 Hz, CH_3), 103.4 (d, ^3J = 3.7 Hz, CCO_{Ar}), 115.4 (d, ^3J = 5.2 Hz, CH_{An}), 117.2 (CH_{An}), 118.3 (d, ^{3}J = 4.9 Hz, CH_{An}), 120.5 (d, ^{3}J = 11.2 Hz, C_{An}), 125.2 (d, ^4J = 2.5 Hz, CH_{Ar}), 127.4 (d, ^2J = 22.9 Hz, C_{Ar}), 130.3 (d, ^4J = 2.5 Hz, CH_{An}), 136.8 (d, ^2J = 20.5 Hz, CCH_{3Ar}), 149.9 (CO_{An}), 150.5 (d, ^1J = 241.1 Hz, CF_{Ar}), 158.1 (d, ^4J = 2.5 Hz, COH_{Ar}), 164.5 (d, ^4J = 3.1 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.7 (CF_{Ar}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2853 (w), 1672 (s), 1607 (m), 1455 (w), 1432 (w), 1278 (m), 1206 (s), 1104 (m), 1065 (m), 758 (s). MS (EI, 70 eV): *m/z* (%) = 244 ([M^+], 100), 229 (17), 216 (11), 196 (9), 159 (9), 133 (12), 69 (5), 57 (4). HRMS (EI): Calcd. for $C_{14}H_{19}FO_3$: 244.05302; found: 244.05258.

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



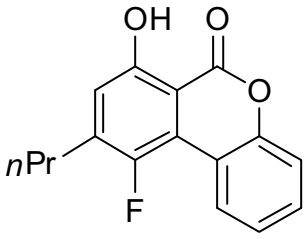
Starting with **26b** (0.060 g, 0.20 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.197 g, 0.78 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27b** was isolated as a colourless solid (0.043 g, 84%), mp. = 151−154 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 2.28 (s(br), 3 H, CH_3), 7.25−7.28 (m, 2H, CH_{An}), 7.36−7.42 (m, 1H, CH_{An}), 8.35−8.40 (m, 1H, CH_{An}), 11.60 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.7 (d, ^4J = 2.2 Hz, CH_3), 12.3 (d, ^3J = 7.8 Hz, CH_3), 102.5 (d, ^3J = 5.2 Hz, CCO$_{Ar}$), 116.3 (d, ^3J = 5.2 Hz, C_{An}), 117.2 (CH_{An}), 117.7 (d, ^2J = 12.8 Hz, CCF$_{Ar}$), 125.2 (CH_{An}), 126.3 (d, ^3J = 4.0 Hz, CCH$_{3Ar}$), 127.4 (CH_{An}), 129.8 (d, ^4J = 2.3 Hz, CH_{An}), 135.3 (d, ^2J = 19.2 Hz, CCH$_{3Ar}$), 149.8 (CO$_{An}$), 150.3 (d, ^1J = 241.1 Hz, CF$_{Ar}$), 156.4 (d, ^4J = 1.7 Hz, COH$_{Ar}$), 165.1 (d, ^4J = 3.4 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.4 (CF$_{Ar}$). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2962 (m), 2925 (m), 2854 (w), 1677 (s), 1622 (w), 1606 (m), 1440 (s), 1335 (m), 1270 (s), 1179 (s), 1095 (s), 1228 (s), 1022 (m), 799 (s), 757 (s). GC-MS (EI, 70 eV): *m/z* (%) = 258 ([M$^+$], 100), 243 (25), 229 (4), 215 (3), 199 (3), 183 (4), 170 (4), 152 (3). HRMS (EI): Calcd. for $C_{15}H_{11}FO_3$: 258.06867; found: 258.06807.

8-Ethyl-10-fluoro-7-hydroxy-9-methyl-6*H*-benzo[*c*]chromen-6-one (27c).



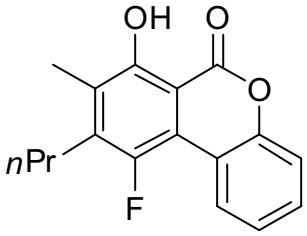
Starting with **26c** (0.060 g, 0.18 mmol) in CH_2Cl_2 (5 mL), BBr_3 (0.180 g, 0.72 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27c** was isolated as a colourless solid (0.037 g, 75%), mp. = 119−121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 2.34 (s(br), 3 H, CH_3), 2.74 (q, ^3J = 7.2 Hz, 2 H, CH_2CH_3), 7.19 (m, 1 H, CH_{An}), 7.29−7.30 (m, 1 H, CH_{An}), 7.37−7.43 (m, 1 H, CH_{An}), 8.39−8.43 (m, 1 H, CH_{An}), 11.60 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.7 (d, ^3J = 8.7 Hz, CH_3), 11.9 (CH_2CH_3), 18.5 (d, ^4J = 2.3 Hz, CH_2CH_3), 103.4 (d, ^3J = 4.4 Hz, CCO$_{Ar}$), 115.5 (d, ^3J = 5.2 Hz, C_{An}), 116.3 (CH_{An}), 117.1 (d, ^2J = 12.8 Hz, CCF$_{Ar}$), 124.2, 126.5 (CH_{An}), 128.9 (d, ^4J = 2.3 Hz, CH_{An}), 131.3 (d, ^3J = 3.5 Hz, CCH$_2$CH$_{3Ar}$), 133.8 (d, ^2J = 14.9 Hz, CCH$_{3Ar}$), 148.0 (CO$_{An}$), 148.3 (d, ^1J = 241.0 Hz, CF$_{Ar}$), 155.4 (d, ^4J = 1.7 Hz, COH$_{Ar}$), 164.4 (d, ^4J = 3.4 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −124.7 (CF$_{Ar}$). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2967 (m), 2876 (w), 1672 (s), 1608 (m), 1563 (w), 1413 (s), 1339 (s), 1287 (s), 1268 (s), 1178 (s), 1164 (s), 872 (m), 768 (s), 738 (m). MS (EI, 70 eV): *m/z* (%) = 272 ([M$^+$], 42), 257 (100), 229 (2), 170 (4), 152 (3), 133 (2). HRMS (EI): Calcd. for $C_{16}H_{13}FO_3$: 272.08432; found: 272.08386.

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



Starting with **26d** (0.148 g, 0.46 mmol) in CH_2Cl_2 (8 mL), BBr_3 (0.465 g, 1.85 mmol) and KO*t*Bu (20 mL, 0.1 M aqueous solution), **27d** was isolated as a colourless solid (0.060 g, 47%), mp. = 88−90°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.57−1.70 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.65 (t(br), ^3J = 7.2 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 6.82 (d, $^4J_{H,F}$ = 5.7 Hz, 1 H, CH_{Ar}), 7.24−7.26 (m, 1 H, CH_{An}), 7.27 (m, 1 H, CH_{An}), 7.37−7.43 (m, 1H, CH_{An}), 8.37−8.41 (m, 1 H, CH_{An}), 11.22 (s, 1 H, OH) .^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 ($CH_2CH_2\mathit{CH_3}$), 21.7 (d, ^4J = 1.1 Hz, $CH_2\mathit{CH_2}CH_3$), 30.8 (d, ^3J = 3.9 Hz, $\mathit{CH_2}CH_2CH_3$), 102.7 (d, ^3J = 4.0 Hz, $\mathit{C}CO_{Ar}$), 115.3 (d, ^3J = 5.2 Hz, C_{An}), 116.7 (d, ^3J = 3.4 Hz, CH_{Ar}), 120.0 (d, ^2J = 12.2 Hz, $\mathit{C}CF_{Ar}$), 124.3, 126.5, 126.8 (CH_{An}), 129.4 (d, ^4J = 1.1 Hz, CH_{An}), 140.3 (d, ^2J = 19.2 Hz, $\mathit{C}CH_2CH_2CH_{3Ar}$), 148.5 (d, ^1J = 243.2 Hz, CF_{Ar}), 149.1 (CO_{An}), 157.4 (d, ^4J = 2.0 Hz, COH_{Ar}), 163.8 (d, ^4J = 2.9 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −125.7 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2965 (m), 2870 (m), 1700 (s), 1629 (m), 1569 (m), 1447 (m), 1435 (s), 1276 (s), 1203 (s), 1106 (s), 952 (w), 756 (s), 735 (m). GC-MS (EI, 70 eV): *m/z* (%) = 272 ([M^+], 100), 257 (10), 244 (96), 215 (21), 199 (10), 183 (3), 170 (11), 157 (7), 133 (9). HRMS (EI): Calcd. for $C_{18}H_{19}FO_4$: 272.08432; found: 272.08412.

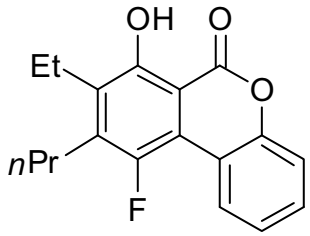
10-Fluoro-7-hydroxy-8-methyl-9-propyl-6*H*-benzo[*c*]chromen-6-one (27e).



Starting with **26e** (0.100 g, 0.30 mmol) in CH_2Cl_2 (8 mL), BBr_3 (0.30 g, 1.20 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27e** was isolated as a colourless solid (0.052 g, 60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.44−1.60 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.14 (s, 3 H, CH_3), 2.70 (t(br), ^3J = 7.6 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 7.23 (m, 1H, CH_{An}), 7.25 (m, 1H, CH_{An}), 7.33−7.39 (m, 1H, CH_{An}), 8.46−8.78 (m, 1H, CH_{An}), 11.60 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.4 (d, ^4J = 2.2 Hz, CH_3), 13.1 ($CH_2CH_2\mathit{CH_3}$), 21.5 (d, ^4J = 1.9 Hz, $CH_2\mathit{CH_2}CH_3$), 27.7 (d, ^3J = 5.4 Hz, $\mathit{CH_2}CH_2CH_3$), 101.7 (d, ^3J = 5.2 Hz, $\mathit{C}CO_{Ar}$), 115.4 (d, ^3J = 5.2 Hz, C_{An}), 116.2 (CH_{An}), 116.9 (d, ^2J = 12.8 Hz, $\mathit{C}CF_{Ar}$), 124.2 (CH_{An}), 125.4 (d, ^3J = 4.0 Hz, $\mathit{C}CH_{3Ar}$), 126.5 (CH_{An}), 128.8 (d, ^4J = 2.3 Hz, CH_{An}), 138.7 (d, ^2J = 18.0 Hz, $\mathit{C}CH_2CH_2CH_{3Ar}$), 148.9 ($CO_{An}$), 149.4 (d, ^1J = 241.4 Hz, CF_{Ar}), 155.8 (d, ^4J = 1.7 Hz, COH_{Ar}), 164.2 (d, ^4J = 3.4 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.9 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2968 (s), 2926 (s), 2853 (m), 1678 (s), 1604 (m), 1456 (m), 1426 (s), 1339 (m), 1281 (s), 1178 (s), 1119 (m), 871 (m), 763

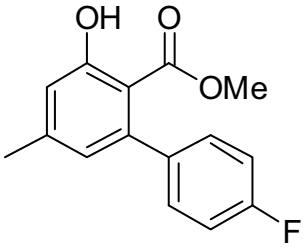
(s), 729 (m). GC-MS (EI, 70 eV): *m/z* (%) = 286 ([M^+], 100), 271 (47), 258 (47), 243 (12), 229 (6), 215 (2), 199 (7), 183 (6), 170 (7), 152 (5), 133 (4). HRMS (EI): Calcd. for $C_{17}H_{15}FO_3$: 286.09997; found: 286.09965.

8-Ethyl-10-fluoro-7-hydroxy-9-propyl-6*H*-benzo[*c*]chromen-6-one (27f).



Starting with **26f** (0.124 g, 0.35 mmol) in CH_2Cl_2 (6 mL), BBr_3 (0.124 g, 0.35 mmol) and KO*t*Bu (10 mL, 0.1 M aqueous solution), **27f** was isolated as a colourless solid (0.069 g, 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, ^3J = 7.2 Hz, 3 H, $CH_2CH_2\mathit{CH_3}$), 1.13 (t, ^3J = 7.2 Hz, 3 H, $CH_2\mathit{CH_3}$), 1.51−1.64 (m, 2 H, $CH_2\mathit{CH_2}CH_3$), 2.70 (q, ^3J = 8.2 Hz, 2 H, $\mathit{CH_2}CH_3$), 2.75 (t(br), ^3J = 8.3 Hz, 2 H, $\mathit{CH_2}CH_2CH_3$), 7.24−7.29 (m, 2 H, CH_{An}), 7.36−7.42 (m, 1 H, CH_{An}), 8.39−8.43 (m, 1 H, CH_{An}), 11.62 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7 ($CH_2\mathit{CH_3}$), 13.2 ($CH_2CH_2\mathit{CH_3}$), 18.5 (d, ^4J = 1.6 Hz, CH_2CH_3), 22.5 (d, ^4J = 1.1 Hz, $CH_2\mathit{CH_2}CH_3$), 27.7 (d, ^3J = 5.8 Hz, $\mathit{CH_2}CH_2CH_3$), 102.0 (d, ^3J = 4.6 Hz, $\mathit{C}CO_{Ar}$), 115.5 (d, ^3J = 5.2 Hz, C_{An}), 116.3 (CH_{An}), 117.1 (d, ^2J = 12.8 Hz, $\mathit{C}CF_{Ar}$), 124.2, 126.5 (CH_{An}), 128.9 (d, ^4J = 1.7 Hz, CH_{An}), 131.1 (d, ^3J = 3.5 Hz, $\mathit{C}CH_2CH_{3Ar}$), 138.3 (d, ^2J = 18.0 Hz, $\mathit{C}CH_2CH_2CH_{3Ar}$), 149.0 ($CO_{An}$), 149.7 (d, ^1J = 242.0 Hz, CF_{Ar}), 155.8 (d, ^4J = 1.1 Hz, COH_{Ar}), 164.4 (d, ^4J = 3.5 Hz, CO).^{19}F NMR (235 MHz, $CDCl_3$): δ = −126.3 (CF). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2961 (s), 2929 (m), 2870 (m), 1686 (s), 1608 (m), 1410 (s), 1336 (m), 1278 (m), 1171 (s), 1114 (s), 1092 (m), 891 (w), 752 (s). GC-MS (EI, 70 eV): *m/z* (%) = 300 ([M^+], 100), 285 (74), 272 (7), 257 (70), 244 (18), 229 (5), 199 (7), 183 (8), 170 (6), 152 (3), 133 (3). HRMS (EI): Calcd. for $C_{18}H_{17}FO_3$: 300.11562; found: 300.11481.

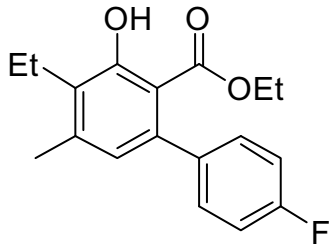
Methyl 4'-fluoro-3-hydroxy-5-methyl[1,1'-biphenyl]-2-carboxylate (29a).



Starting with **28a** (0.378 g, 1.5 mmol), **5a**(0.429 g, 1.6 mmol) and $TiCl_4$ (0.312 g, 1.6 mmol, **29a** was isolated as a colorless oil (0.114 g, 44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 3.41 (s, 3 H, OCH_3), 6.49 (s, 1 H, CH_{Ar}), 6.74 (s, 1 H, CH_{Ar}), 6.92-9.98 (m, 2 H, CH), 6.83 (s, 2 H, CH), 10.74 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 50.5 (OCH_3), 108.2 (C_{Ar}), 113.4 (d, ^2J = 21.5 Hz, $2CH_{Ar}$), 116.1, 123.0 (CH_{Ar}), 128.5 (d, ^3J = 8.0 Hz, $2CH_{Ar}$), 137.8 (d, ^4J = 3.5 Hz, C_{Ar}), 142.5, 143.9 (C_{Ar}), 160.9 (d, ^1J = 219.5 Hz, CF_{Ar}), 162.5 (COH_{Ar}), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2948 (s), 2895 (m), 1675 (s), 1616 (m), 1493 (m), 1458 (m), 1405 (m), 1399 (m), 1254 (s), 1219 (s), 1068 (m), 748 (s). GC-MS (EI, 70 eV): *m/z* (%) = 260 ([M^+], 34), 228 (100), 200 (46),

171 (21), 157 (6), 146 (4). HRMS (EI): Calcd. for $C_{15}H_{13}FO_3$: 260.08432; found: 260.08383.

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

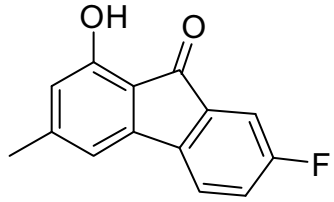


Starting with **28a** (0.378 g, 1.5 mmol), **5c** (0.484 g, 1.6 mmol) and $TiCl_4$ (0.312 g, 1.6 mmol, **29b** was isolated as a colorless oil (0.132 g, 44%).^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.73 (t, ^3J = 7.2 Hz, 3 H, CH_2CH_3), 1.09 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.25 (s, 3 H, CH_3), 2.66 (q, ^3J = 7.4 Hz, 2 H, CH_2CH_3), 3.91 (q, ^3J = 7.3 Hz, 2 H,OCH_2CH_3), 6.49 (s, 1 H, CH_{Ar}), 6.91-6.97 (m, 2 H, CH_{Ar}), 7.08-7.11 (m, 2 H, CH_{Ar}), 7.24-7.27 (m, 1 H, CH_{Ar}), 11.14 (s, 1 H, OH) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 18.4 (OCH_2CH_3), 18.5 (CH_3), 28.6 (CH_2CH_3), 59.8 (OCH_2CH_3), 108.3 (C_{Ar}), 113.2 (d, ^2J = 21.1 Hz, $2CH_{Ar}$), 123.2 (CH_{Ar}), 128.7 (C_{Ar}), 129.0 (d, ^3J = 8.0 Hz, $2CH_{Ar}$), 136.6 (C_{Ar}), 138.4 (d, ^4J = 3.3 Hz, C_{Ar}), 141.1 (C_{Ar}), 158.7 (COH_{Ar}), 160.8 (d, ^1J = 244.0 Hz, CF_{Ar}), 170.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2958 (s), 2870 (m), 1655 (s), 1616 (m), 1503 (m), 1468 (m), 1415 (m), 1399 (m), 1246 (s), 1233 (s), 1097 (m), 750 (s). GC-MS (EI, 70 eV): *m/z* (%) = 302 ([M^+], 53), 256 (73), 241 (100), 223 (10), 213 (57), 199 (8), 183 (29). HRMS (EI): Calcd. for $C_{18}H_{19}FO_3$: 302.13127; found: 302.13190.

General procedure for synthesis of fluorenones 30 and 31:

A solution of **29** (1 mmol) in concentrated sulfuric acid (12 mL) was stirred at room temperature for one hour. To the solution was added water and it was stirred for further 15 minutes. The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in *vacuo*. The product was purified by chromatography (silica gel; *n*-heptane/ EtOAc = 20:1) to give **30**.

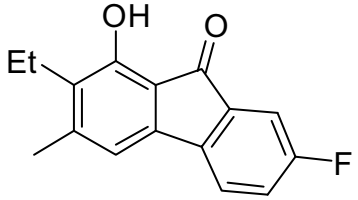
7-fluoro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (30a).



Starting with **29a** (0.114 g, 0.438 mmol) and conc. sulfuric acid (2.307 mL), **30a** was isolated as a yellow oil (0.156 g, 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 6.45 (s, 1 H, CH_{Ar}), 6.74 (s, 1 H, CH_{Ar}), 7.01-7.09 (m, 1 H, CH_{Ar}), 7.21 (dd, ^3J = 7.4 Hz, ^4J = 3.0 Hz, 1 H, CH_{Ar}), 7.34 (dd, ^3J = 7.5 Hz, ^4J = 4.5 Hz, 1 H, CH_{Ar}), 8.15 (s, 1 H, OH) . ^{13}C NMR (62 MHz, $CDCl_3$): δ = 22.5 (CH_3), 111.4 (d, ^2J = 23.9 Hz, CH_{Ar}), 114.1, 117.7 (CH_{Ar}), 120.4 (d, ^2J = 25.3 Hz, CH_{Ar}), 122.0 (d, ^3J = 7.5 Hz, CH_{Ar}), 129.4 (C_{Ar}), 137.2

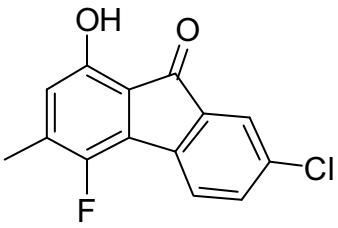
(d, ^{3}J = 8.5 Hz, C_{Ar}), 139.6 (d, ^{4}J = 2.4 Hz, C_{Ar}), 143.4, 149.9 (C_{Ar}), 157.5 (COH_{Ar}), 163.4 (d, ^{1}J = 247.4 Hz, CF_{Ar}), 194.0 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 228 ([M^{+}], 100), 199 (36), 170 (26), 151 (3), 100 (5), 85 (9). HRMS (EI): Calcd. for $C_{14}H_9FO_2$: 228.05811; found: 228.057995.

2-Ethyl-7-fluoro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (30b).



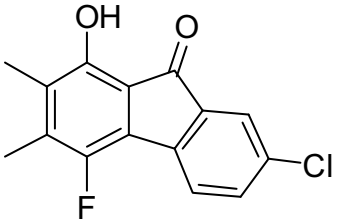
Starting with **29b** (0.132 g, 0.437 mmol) and conc. sulfuric acid (2.340 mL), **30b** was isolated as a yellow viscous oil (0.194 g, 76%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, ^{3}J = 7.6 Hz, 3 H, $CH_2\mathit{CH_3}$), 2.26 (s, 3 H, CH_3), 2.56 (q, ^{3}J = 7.4 Hz, 2 H, $\mathit{CH_2}CH_3$), 6.57 (s, 1 H, CH_{Ar}), 7.03 (ddd, ^{3}J = 8.2 Hz, ^{3}J = 6.3 Hz, ^{4}J = 0.5 Hz,1 H, CH_{Ar}), 7.19 (m, 1 H, CH_{Ar}), 7.29 (m, 1 H, CH_{Ar}), 8.42 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.2 ($CH_2\mathit{CH_3}$), 18.3 (CH_3), 28.2 ($\mathit{CH_2}CH_3$), 109.6 (d, ^{2}J = 23.1 Hz, CH_{Ar}), 111.9 (C_{Ar}), 113.1 (CH_{Ar}), 118.4 (d, ^{2}J = 22.9, CH_{Ar}), 119.7 (d, ^{3}J = 8.6 Hz, CH_{Ar}), 126.4, 129.7 (C_{Ar}), 135.0 (d, ^{3}J = 6.8 Hz, C_{Ar}), 138.0 (d, ^{4}J = 3.7 Hz, C_{Ar}), 144.7 (C_{Ar}), 154.0 (COH_{Ar}), 161.2 (d, ^{1}J = 245.5 Hz, CF_{Ar}), 192.7 (d, ^{4}J = 1.8 Hz, CO). GC-MS (EI, 70 eV): *m/z* (%) = 256 ([M^{+}], 42), 241 (100), 213 (8), 183 (12), 170 (7). HRMS (EI): Calcd. for $C_{16}H_{13}FO_2$: 256.08941; found: 256.08976.

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



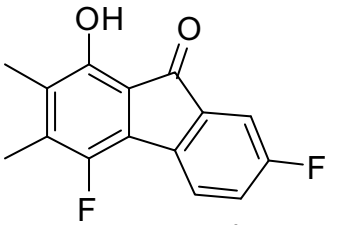
Starting with **26l** (0.031 g, 0.105 mmol) and conc. Sulfuric acid (1.2 mL), **31a** was isolated as a yellow solid (0.021 g, 77 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (d, $^{4}J_{H,F}$ = 1.3 Hz, 3 H, CH_3), 6.52 (d, ^{3}J = 5.9 Hz, 1 H, CH_{Ar}), 7.18 (m, 1 H, CH_{ClPh}), 7.38 (d, ^{3}J = 8.0 Hz, 1 H, CH_{ClPh}), 7.52 (m, 1 H, CH_{ClPh}), 8.02 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.0 (d, ^{3}J = 4.0 Hz, CH_3), 112.3 (d, ^{2}J = 24.0 Hz, $\mathit{C}CH_{3Ar}$), 116.4 (d, ^{3}J = 4.6 Hz, C_{ClPh}), 121.1 (CH_{ClPhr}), 124.9 (d, ^{4}J = 1.7 Hz, CH_{ClPh}), 125.2 (d, ^{3}J = 3.5 Hz, CH_{Ar}), 134.6 (CH_{ClPh}), 136.3 (C_{ClPh}), 138.4 (d, ^{2}J = 19.0 Hz, C_{Ar}), 145.0 (C_{Ar}), 152.4 (C_{ClPh}), 153.8 (COH_{Ar}), 163.6 (d, ^{1}J = 250.5 Hz, CF_{Ar}), 193.7 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −131.7 (CF_{Ar}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3423 (br, m), 2973 (m), 2851 (w), 1698 (s), 1636 (w), 1605 (m), 1456 (m), 1310 (m), 1270 (m), 1180 (s), 1088 (m), 793 (m), 580 (w). GC-MS (EI, 70 eV): *m/z* (%) = 264 ([M^{+}], [^{37}Cl], 34), 262 ([M^{+}], [^{35}Cl], 100), 235 ([^{37}Cl], 3), 233 ([^{35}Cl], 8), 199 (13), 170 (23), 151 (3), 131 (3), 99 (6), 85 (9). HRMS (EI): Calcd. for $C_{14}H_8ClFO_2$ ([$M]^{+}$, ^{35}Cl): 262.01914; found: 262.01891.

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



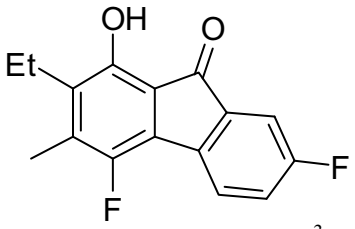
Starting with **26m** (0.036 g, 0.12 mmol) and conc. Sulfuric acid (1.390 mL), **31b** was isolated as a yellow solid (0.024 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 (s, 3 H, CH_3), 2.12 (s(br), 3 H, CH_3), 7.33 (dd, ^{3}J = 8.0 Hz, ^{4}J = 1.9 Hz, 1 H, CH_{ClPh}), 7.42 (m, 1 H, CH_{ClPh}), 7.46 (d, ^{3}J = 1.8 Hz, 1 H, CH_{ClPh}), 8.32 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.5 (d, ^{4}J = 1.7 Hz, CH_3), 12.5 (d, ^{3}J = 5.2 Hz, CH_3), 115.4 (d, ^{3}J = 5.2 Hz, $C$$CH_{3Ar}$), 123.5 (d, ^{2}J = 17.4 Hz, $C$$CH_{3Ar}$), 124.7, 125.2 ($CH_{ClPh}$), 129.3 (d, ^{4}J = 2.3 Hz, C_{ClPh}), 134.7 (d, ^{2}J = 28.5 Hz, C_{Ar}), 134.9 (CH_{ClPh}), 136.0 (C_{ClPh}), 136.2 (d, ^{3}J = 5.8 Hz, C_{ClPh}), 140.1 (C_{Ar}), 150.5 (d, ^{1}J = 244.9 Hz, CF_{Ar}), 152.5 (COH_{Ar}), 194.3 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −129.5 (CF_{Ar}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3414 (br, s), 2923 (m), 2852 (m), 1696 (s), 1636 (w), 1604 (m), 1453 (s), 1382 (w), 1288 (s), 1274 (s), 1170 (s), 1078 (m), 1021 (m), 878 (w), 793 (m), 743 (m), 629 (m). GC-MS (EI, 70 eV): *m/z* (%) = 278 ([M^+], [^{37}Cl], 37), 276 ([M^+], [^{35}Cl], 100), 263 ([^{37}Cl], 12), 261 ([^{35}Cl], 40), 235 ([^{37}Cl], 3), 233 ([^{35}Cl], 10), 213 (5), 207 (23), 183 (17), 170 (11), 138 (6), 91 (11). HRMS (EI): Calcd. for $C_{15}H_{10}ClFO_2$ ([$M]^+$, ^{35}Cl): 276.03479; found: 276.03481.

4,7-Difluoro-1-hydroxy-2,3-dimethyl-9*H*-fluoren-9-one (31c).



Starting with **26p** (0.078g, 0.27 mmol) and conc. sulfuric acid (3.2 mL), **31c** was isolated as a yellow solid (0.069 g, 74 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3), 2.01 (d, $^{4}J_{H,F}$ = 2.1 Hz, 3 H, CH_3), 7.00 (ddd, ^{3}J = 8.5 Hz, ^{3}J = 8.7 Hz, ^{4}J = 2.5 Hz, 1 H, CH_{FPh}), 7.14 (dd, ^{3}J = 7.2 Hz, ^{4}J = 2.4 Hz, 1 H, CH_{FPh}), 7.38 (dd, ^{3}J = 8.1 Hz, ^{4}J = 2.5 Hz, 1 H, CH_{FPh}), 8.24 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.4 (d, ^{4}J = 1.7 Hz, CH_3), 12.4 (d, ^{3}J = 5.8 Hz, CH_3), 112.0 (d, ^{2}J = 22.7 Hz, CH_{FPh}), 115.8 (d, ^{3}J = 5.2 Hz, $C$$CH_{3Ar}$), 121.1 (d, ^{2}J = 22.7 Hz, $C$$CH_{3Ar}$), 123.5 (d, ^{3}J = 18.6 Hz, CH_{FPh}), 125.3 (CH_{FPh}), 128.5 (d, ^{3}J = 1.1 Hz, C_{FPh}), 136.0 (d, ^{2}J = 16.3 Hz, C_{Ar}), 136.7 (d, ^{3}J = 8.1 Hz, C_{FPh}), 137.6 (d, ^{3}J = 1.7 Hz, C_{Ar}), 150.2 (d, ^{1}J = 244.3 Hz, CF_{FPh}), 152.4 (COH_{Ar}), 163.3 (d, ^{1}J = 248.4 Hz, CF_{Ar}), 194.0 (d, ^{4}J = 2.3 Hz, CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −131.1 (CF_{Ar}), −111.9 (CF_{FPh}). GC-MS (EI, 70 eV): *m/z* (%) = 260 ([M^+], 100), 245 (51), 231 (7), 217 (13), 201 (9), 183 (14), 130 (4). HRMS (EI): Calcd. for $C_{15}H_{10}F_2O_2$: 260.06434; found: 260.06394.

2-Ethyl-4,7-difluoro-1-hydroxy-3-methyl-9*H*-fluoren-9-one (31d).

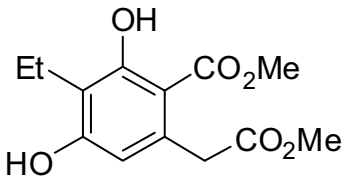


Starting with **26q** (0.037 mg, 0.12 mmol) and conc. sulfuric acid (1.38 mL), **31d** was isolated as a yellow solid (0.022 g, 69 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3), 2.16 (s, 3 H, CH_3), 2.57 (q, ^{3}J = 7.4 Hz, 2 H, CH_2CH_3), 7.06 (ddd, ^{3}J = 8.5 Hz, ^{3}J = 8.5 Hz, ^{4}J = 2.4 Hz, 1 H, CH_{FPh}), 7.20 (dd, ^{3}J = 5.1 Hz, ^{4}J = 0.3 Hz, 1 H, CH_{FPh}), 7.48 (dd, ^{3}J = 8.1 Hz, ^{4}J = 3.6 Hz, 1 H, CH_{FPh}), 8.31 (s, 1 H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 9.5 (CH_2CH_3), 11.2 (CH_3), 17.0 (d, ^{4}J = 2.3 Hz, CH_2CH_3), 109.6 (d, ^{2}J = 23.3 Hz, CH_{FPh}), 113.8 (CCH_2CH_{3Ar}), 118.8 (d, ^{2}J = 22.7 Hz, CH_{FPh}), 121.4 (d, ^{4}J = 16.3 Hz, CCH_{3FPh}), 123.2 (CH_{FPh}), 126.3 (C_{Ar}), 133.1 (d, ^{2}J = 17.4 Hz, C_{Ar}), 134.6 (C_{FPh}), 135.4 (C_{FPh}), 148.1 (d, ^{1}J = 244.3 Hz, C_{FPh}), 150.1 (COH_{Ar}), 161.0 (d, ^{1}J = 248.4 Hz, CF_{Ar}), 191.9 (CO). ^{19}F NMR (235 MHz, $CDCl_3$): δ = −129.8 (CF_{Ar}), − 111.8 (CF_{FPh}). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3445 (br, m), 2975 (w), 2939 (m), 2852 (w), 1684 (s), 1603 (w), 1485 (m), 1265 (m), 1095 (m), 837 (w), 598 (w). GC-MS (EI, 70 eV): *m/z* (%) = 274 ([M^+], 43), 259 (100), 231 (6), 201 (8), 183 (7), 122 (2). HRMS (EI): Calcd. for $C_{16}H_{12}FO_2$: 274.07999; found: 274.07954.

General procedure for the synthesis of homophthalates 33.

To neat allene **32** (1.0 mmol) was added neat diene **5** (1.25 mmol)1 at 0 °C under argon atmosphere. The reaction mixture was stirred at 0 °C for 30 minutes and then the solution was stirred at 20−40 °C for several hours. To the mixture was added an ethanolic solution (96%, 2 mL) of triethylammonium fluoride (1.5 mmol). The solution was diluted with water and repeatedly extracted with diethyl ether or dicholoromethane. 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 / EtOAc or petroleum ether / diethyl ether = 1:1) to give product **33**.

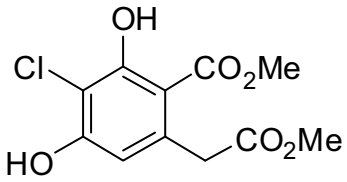
Methyl 3-ethyl-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate (33b).



Starting with **5f** (0.361 g, 1.25 mmol), **32** (0.156 g, 1.0 mmol), triethylammonium fluoride (0.242 g, 1.5 mmol) was added, **33b** was isolated as a yellow viscous oil (0.139 g, 52%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, CD_3OD): δ = 0.98 (t, ^{3}J = 7.4 Hz, 3 H, CH_2CH_3), 2.53 (q, ^{3}J = 7.4 Hz, 2 H, CH_2CH_3), 3.58 (s, 3 H, $COOCH_3$), 3.67 (s, 2 H, CH_2COOCH_3), 3.71 (s, 3 H, CH_2COOCH_3), 6.13 (s, 1 H, CH_{Ar}). ^{13}C NMR (62 MHz,

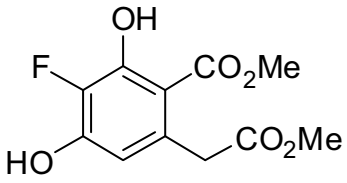
CD_3OD): δ = 13.4 (CH_2CH_3), 16.8 (CH_2CH_3), 43.2 (CH_2COOCH_3), 52.6 ($COOCH_3$), 52.7 (CH_2COOCH_3), 104.6(C_{Ar}), 113.1 (CH_{Ar}), 117.8, 136.0 (C_{Ar}), 161.1, 163.9 (COH_{Ar}), 172.6 ($COOCH_3$), 174.2 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3285 (w), 2961 (w), 1699 (s), 1646 (m), 1604 (m), 1439 (m), 1275 (s), 1193 (s), 1156 (s), 1051 (m), 984 (m), 839 (m), 746 (m). GC-MS (EI, 70 eV): *m/z* (%) = 268 ([M^+], 33), 250 (5), 236 (30), 222 (10), 208 (19), 189 (22), 176 (100), 148 (8), 91 (6), 77 (6).

Methyl 3-chloro-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate (33c).



Starting with **5d** (0.386 g, 1.25 mmol), **32** (0.156 g, 1.0 mmol), and triethylammonium fluoride (0.242 g, 1.5 mmol) was added, **33c** was isolated as a yellow viscous oil (0.177 g, 64%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, CD_3OD): δ = 3.67 (s, 3 H, $COOCH_3$), 3.82 (s, 2 H, CH_2COOCH_3), 3.85 (s, 3 H, CH_2COOCH_3), 6.38 (s, 1 H, CH_{Ar}). ^{13}C NMR (62 MHz, CD_3OD): δ = 43.0 (CH_2COOCH_3), 52.4 ($COOCH_3$), 52.4 (CH_2COOCH_3), 106.2 (C_{Ar}), 113.5 (CH_{Ar}), 137.6 ($2C_{Ar}$), 159.6, 161.6 (COH_{Ar}), 172.3 ($COOCH_3$), 173.8 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3226 (w), 2958 (w), 1698 (m), 1654 (m), 1435 (m), 1319 (m), 1235 (s), 1189 (s), 1076 (m), 959 (m), 800 (m), 687 (m). GC-MS (EI, 70 eV): *m/z* (%) = 276 ([M^+], ^{37}Cl, 16), 274 ([M^+], ^{35}Cl, 48), 244 (^{37}Cl, 20), 242 (^{35}Cl, 42), 216 (^{37}Cl, 37), 214 (^{35}Cl, 100), 201 (^{37}Cl, 24), 199 (^{35}Cl, 76), 185 (13), 171 (8), 155 (33). HRMS (EI): Calcd. for $C_{11}H_{11}O_6Cl$ ([M^+], ^{35}Cl): 274.02387; found: 274.02379.

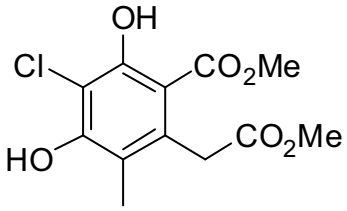
Methyl 3-fluoro-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate (33d).



Starting with **5e** (0.920 g, 2.5 mmol), **32** (0.312 g, 2.0 mmol), and triethylammonium fluoride (0.483 g, 3.0 mmol) was added, **33d** was isolated as a red solid (0.361 g, 70%), mp. = 148−156 °C. Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, CD_3OD): δ = 2.36 (s, 3 H, $COOCH_3$), 2.47 (s, 2 H, CH_2COOCH_3), 2.54 (s, 3 H, CH_2COOCH_3), 5.04 (d, ^4J = 7.6 Hz, 1 H, CH_{Ar}). ^{13}C NMR (62 MHz, CD_3OD): δ = 42.6 (CH_2COOCH_3), 52.4 ($COOCH_3$), 52.5 (CH_2COOCH_3), 106.7 (C_{Ar}), 114.2 (d, ^3J = 1.3 Hz, CH_{Ar}), 126.3 (C_{Ar}), 133.8 (d, ^3J = 4.1 Hz, C_{Ar}), 140.6 (d, ^1J = 234.3 Hz, CF_{Ar}), 150.8 (d, ^2J = 9.6 Hz, COH_{Ar}), 153.6 (d, ^2J = 10.3 Hz, COH_{Ar}), 171.9 ($COOCH_3$), 174.0 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3231 (w), 2956 (w), 1706 (s), 1657 (m), 1597 (m), 1437 (s), 1324 (m), 1249 (s), 1199 (s), 1105 (m), 1059 (m), 979 (s), 844 (m), 743 (s). GC-MS (EI, 70 eV): *m/z* (%) = 258 ([M^+], 49), 226 (63), 198 (90), 183 (100), 169 (13), 155 (8), 139 (39), 110 (5), 83 (11). HRMS (EI):

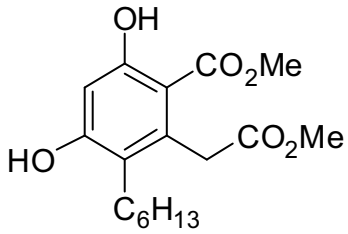
Calcd. for $C_{11}H_{11}FO_6$: 258.05342; found: 258.05382.

Methyl 3-chloro-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-5-methylbenzoate (33g).



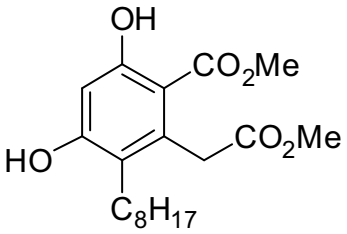
Starting with **5g** (0.386 g, 1.25 mmol), **32** (0.156 g, 1.0 mmol), and triethylammonium fluoride (0.242 g, 1.5 mmol), **33g** was isolated as a yellow solid (0.135 g, 47%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.64 (s, 3 H, COO*CH*$_3$), 3.83 (s, 3 H, CH_2CO*OCH*$_3$), 3.88 (s, 2 H, *CH*$_2$COOCH$_3$), 6.21 (br, 1 H, OH), 11.88 (br, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.2 (CH_3), 37.2 (*CH*$_2$COOCH$_3$), 52.0 (CO*OCH*$_3$), 52.4 (CH_2CO*OCH*$_3$), 106.4, 107.1, 117.1, 134.4, 154.7, 157.4 (C_{Ar}), 171.1 (*CO*OCH$_3$), 171.2 (CH_2*CO*OCH$_3$). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3256 (w), 2956 (w), 1716 (s), 1648 (m), 1577 (m), 1436 (m), 1326 (s), 1216 (s), 1165 (s), 1001 (m), 962 (m), 808 (m). GC-MS (EI, 70 eV): *m/z* (%) = 290 ([M$^+$], ^{37}Cl, 16), 288 ([M$^+$], ^{35}Cl, 49), 258 (^{37}Cl, 18), 256 (^{35}Cl, 48), 230 (^{37}Cl, 37), 228 (^{35}Cl, 100), 215 (^{37}Cl, 29), 213 (^{35}Cl, 90), 196 (17), 105 (6), 77 (20). HRMS (EI): Calcd. for $C_{12}H_{13}O_6Cl$ ([M$^+$], ^{35}Cl): 288.03952; found: 288.03964.

Methyl 3-hexyl-4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-benzoate (33k).



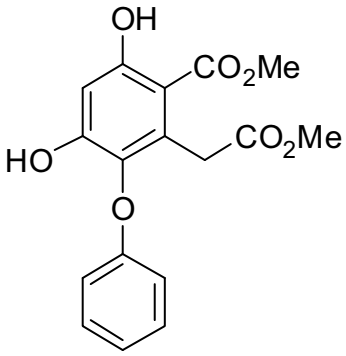
Starting with **5h** (0.557 g, 1.5 mmol), **32** (0.187 g, 1.2 mmol), and triethylammonium fluoride (0.290 g, 1.8 mmol), **33k** was isolated as a colourless solid (0.170 g, 52%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.8 Hz, 3 H, $CH_2(CH_2)_4$*CH*$_3$), 1.20−1.26 (m, 8 H, CH_2*(CH*$_2$*)*$_4$$CH_3$), 2.43 (t, ^3J = 6.8 Hz, 2 H, *CH*$_2$(CH_2)$_4$$CH_3$), 3.69 (s, 3 H, COO*CH*$_3$), 3.80 (s, 3 H, CH_2CO*OCH*$_3$), 3.87 (s, 2 H, *CH*$_2$COOCH$_3$), 6.10 (s, 1 H, CH_{Ar}), 6.56 (s, 1 H, OH_{Ar}), 11.16 (s(br), 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 ((CH_2)$_5$*CH*$_3$), 22.6, 26.1, 29.5, 29.8, 31.7 ((*CH*$_2$)$_5$$CH_3$), 36.8 (*CH*$_2$COOCH$_3$), 51.8 (CO*OCH*$_3$), 52.2 ($CH_2CO$*OCH*$_3$), 102.9 ($CH_{Ar}$), 105.5, 128.3, 134.8 ($C_{Ar}$), 159.9, 162.4 ($COH_{Ar}$), 171.1 (*CO*OCH$_3$), 173.4 ($CH_2$*CO*OCH$_3$). GC-MS (EI, 70 eV): *m/z* (%) = 324 ([M$^+$], 33), 292 (24), 253 (25), 221 (100), 189 (80), 163 (20), 134 (5), 105 (5), 69 (12). HRMS (EI): Calcd. for $C_{17}H_{24}O_6$: 324.15674; found: 324.15600.

Methyl 4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-3-octylbenzoate (33l).



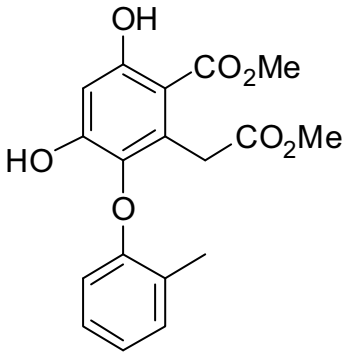
Starting with **5i** (0.465 g, 1.25 mmol), **32** (0.156 g, 1.0 mmol), and triethylammonium fluoride (0.242 g, 1.5 mmol), **33l** was as a colourless viscous oil (0.197 g, 56%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 (t, ^{3}J = 6.3 Hz, 3 H, $CH_2(CH_2)_6CH_3$), 1.18 (m, 12 H, $CH_2(CH_2)_6CH_3$), 3.63 (t, ^{3}J = 5.8 Hz, 2 H, $CH_2(CH_2)_6CH_3$), 3.69 (s, 3 H, $COOCH_3$), 3.79 (s, 3 H, CH_2COOCH_3), 3.86 (s, 2 H, CH_2COOCH_3), 6.08 (s, 1 H, CH_{Ar}), 6.92 (s, 1 H, OH_{Ar}), 11.16 (s, 1 H, OH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 ($(CH_2)_7CH_3$), 22.5, 26.0, 29.2, 29.4, 29.7, 29.8, 31.8 ($(CH_2)_5CH_3$), 36.7 (CH_2COOCH_3), 51.7 ($COOCH_3$), 52.1 (CH_2COOCH_3), 102.8 (CH_{Ar}), 105.2, 123.3, 134.6 (C_{Ar}), 160.1, 162.3 (COH_{Ar}), 171.0 ($COOCH_3$), 173.5 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3281 (w), 2923 (w), 2847 (w), 1701 (m), 1651 (m), 1592 (m), 1438 (w), 1329 (m), 1253 (s), 1194 (s), 1152 (s), 1096 (w), 971 (m), 841 (m), 673 (m). GC-MS (EI, 70 eV): *m/z* (%) = 352 ([M^+], 43), 321 (15), 279 (5), 253 (98), 221 (100), 189 (14), 163 (13). HRMS (EI): Calcd. for $C_{19}H_{28}O_6$: 352.18804; found: 352.18813.

Methyl 4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-3-phenoxy-benzoate (33o).



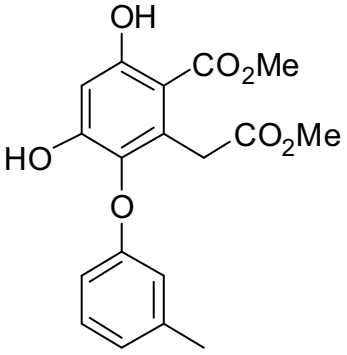
Starting with **5j** (0.630 g, 1.8 mmol), **32** (0.225 g, 1.4 mmol), and triethylammonium fluoride (0.348 g, 2.2 mmol), **33o** was isolated as a yellow viscous oil (0.278 g, 58%). Reaction time: 18 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.48 (s, 3 H, $COOCH_3$), 3.78 (s, 2 H, CH_2COOCH_3), 3.79 (s, 3 H, CH_2COOCH_3), 6.54 (s(br), 1 H, CH_{Ar}), 6.78−6.82 (m, 3 H, CH_{Ph}), 6.97−7.00 (m, 1 H, CH_{Ph}), 7.17−7.20 (m, 1 H, CH_{Ph}), 7.24 (s(br), 1 H, OH_{Ar}), 11.45 (s(br), 1 H, OH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 34.2 (CH_2COOCH_3), 51.8 ($COOCH_3$), 51.9 (CH_2COOCH_3), 103.9 (CH_{Ar}), 105.4 (C_{Ar}), 114.9 ($2CH_{Ph}$), 123.1 (CH_{Ph}), 129.9 ($2CH_{Ph}$), 130.4, 133.9 (C_{Ar}), 154.8 (C_{Ph}), 157.1, 162.4 (COH_{Ar}), 170.7 ($COOCH_3$), 171.2 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3350 (w), 2952 (w), 1734 (m), 1658 (m), 1589 (m), 1489 (m), 1436 (m), 1329 (m), 1154 (s), 1022 (m), 978 (m), 750 (s), 688 (s), 540 (m). MS (EI, 70 eV): *m/z* (%) = 332 ([M^+], 100), 300 (70), 268 (43), 240 (84), 212 (32), 191 (16), 171 (13), 109 (12), 77 (17), 69 (33). HRMS (EI): calcd. for $C_{17}H_{16}O_7$: 332.08905; found: 332.08918.

Methyl 4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-3-(2-methyl-phenoxy)benzoate (33p).



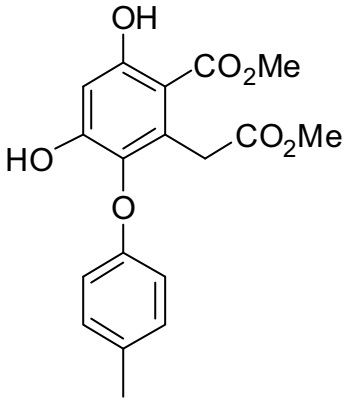
Starting with **5l** (0.657 g, 1.8 mmol), **32** (0.225 g, 1.4 mmol), and triethylammonium fluoride (0.348 g, 2.2 mmol), **33p** was isolated as a yellow viscous oil (0.249 g, 50%). Reaction time: 17 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_{3Tol}), 3.42 (s, 3 H, CO*OCH*$_3$), 3.71 (s, 2 H, *CH*$_2$COOCH$_3$), 3.72 (s, 2 H, CH$_2$COO*CH3*), 6.02 (s(br), 1 H, OH_{Ar}), 6.32 (d, ^{3}J = 6.8 Hz, 1 H, CH_{Tol}), 6.49 (s, 1 H, CH_{Ar}), 6.80−6.86 (m, 1 H, CH_{Tol}), 7.06−7.09 (m, 2 H, CH_{Tol}), 11.38 (s(br), 1 H, OH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 16.1 (CH_{3Tol}), 34.1 (*CH*$_2$COOCH$_3$), 51.7 (CO*OCH*$_3$), 51.9 (CH$_2$CO*OCH*$_3$), 103.8 (CH_{Ar}), 105.3 (C_{Ar}), 112.4, 122.6 (CH_{Tol}), 126.0 (C_{Ar}), 127.1 (C_{Tol}), 130.1, 131.4 (CH_{Tol}), 134.2 (C_{Tol}), 154.8 (C_{Ar}), 155.2, 162.2 (COH_{Ar}), 170.7 (*CO*OCH$_3$), 171.2 (CH$_2$*CO*OCH$_3$). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3368 (w), 2952 (w), 1735 (s), 1658 (m), 1592 (m), 1489 (m), 1435 (m), 1329 (m), 1222 (s), 1187 (s), 1018 (m), 983 (m), 844 (m), 750 (s). MS (EI, 70 eV): *m/z* (%) = 346 ([M$^+$], 100), 314 (56), 282 (22), 271 (44), 254 (42), 226 (13), 193 (29), 105 (8), 91 (21). HRMS (EI): calcd. for $C_{18}H_{18}O_7$: 346.10470; found: 346.10437.

Methyl 4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-3-(3-methyl-phenoxy)benzoate (33q).



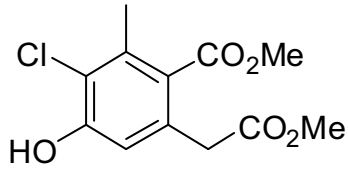
Starting with **5k** (0.951 g, 2.5 mmol), **32** (0.312 g, 2.0 mmol), and triethylammonium fluoride (0.242 g, 3.0 mmol), **33q** was isolated as a slightly yellow solid 0.336 g, 48%), m.p = 130−133 °C. Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_{3Tol}), 3.43 (s, 3 H, CO*OCH*$_3$), 3.71 (s, 3 H, CH$_3$COO*CH*), 3.73 (s, 2 H, *CH*$_2$COOCH$_3$), 6.14 (s(br), 1 H, OH_{Ar}), 6.47 (s, 1 H, CH_{Ar}), 6.50−6.54 (m, 2 H, CH_{Tol}), 6.72 (d, ^{3}J = 7.6 Hz, 1 H, CH_{Tol}), 7.01 (d, ^{3}J = 8.4 Hz, 1 H, CH_{Tol}), 11.39 (s(br), 1 H, OH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.3 (CH_{3Tol}), 34.1 (*CH*$_2$COOCH$_3$), 51.7 (CO*OCH*$_3$), 51.8 (CH$_2$CO*OCH*$_3$), 103.8 (CH_{Ar}), 105.1 (C_{Ar}), 111.8, 115.4, 123.7, 129.5 (CH_{Tol}), 130.3 (*C*CH3$_{Tol}$), 134.1, 140.1 (C_{Ar}), 154.9 (C_{Tol}), 157.1, 162.2 (COH_{Ar}), 170.7 (*CO*OCH$_3$), 171.4 (CH$_2$*CO*OCH$_3$). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3239 (w), 2948 (w), 1700 (s), 1655 (m), 1595 (m), 1438 (m), 1328 (m), 1228 (s), 1180 (s), 1105 (m), 983 (m), 844 (m), 770 (s). GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M$^+$], 100), 314 (51), 282 (35), 271 (51), 254 (39), 226 (19), 191 (18), 157 (4), 129 (8), 91 (18). HRMS (EI): calcd. for $C_{18}H_{18}O_7$: 346.10470; found: 346.10525.

Methyl 4,6-dihydroxy-2-(2-methoxy-2-oxoethyl)-3-(4-methylphenoxy)benzoate (33r).



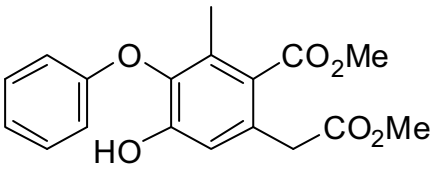
Starting with **5m** (0.951 g, 2.5 mmol), **32** (0.312 g, 2.0 mmol), and triethylammonium fluoride (0.483 g, 3.0 mmol), **33r** was as a brown solid (0.380 g, 54 %), m.p. = 116−124 °C. Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, CD_3OD): δ = 2.15 (s, 3 H, CH_{3Tol}), 3.46 (s, 3 H, CO*OCH₃*), 3.73 (s, 3 H, CH_2COOCH_3), 3.78 (s, 2 H, CH_2COOCH_3), 4.77 (s(br), 1 H, OH_{Ar}), 6.37 (s, 1 H, CH_{Ar}), 6.59 (d, ^{3}J = 8.5 Hz, 2 H, CH_{Tol}), 6.93 (d, ^{3}J = 8.4 Hz, 2 H, CH_{Tol}). ^{13}C NMR (62 MHz, CD_3OD): δ = 20.5 (CH_{3Tol}), 34.6 (CH_2COOCH_3), 52.3 (CO*OCH₃*), 52.5 (CH_2CO*OCH₃*), 104.4 (CH_{Ar}), 105.1 (C_{Ar}), 115.7 ($2CH_{Tol}$), 130.7 ($2CH_{Tol}$), 132.0 (C_{Ar}), 132.2 (*C*$CH3_{Tol}$), 136.4 (C_{Ar}), 157.3 (COH_{Ar}), 157.8 (C_{Tol}), 162.8 (COH_{Ar}), 172.1 (*CO*OCH_3), 173.5 (CH_2*CO*OCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3268 (w), 2434 (w), 1702 (m), 1645 (m), 1610 (m), 1507 (m), 1440 (m), 1341 (m), 1217 (s), 1102 (m), 990 (m), 821 (s), 773 (m). GC-MS (EI, 70 eV): *m/z* (%) = 346 ([M^+], 100), 314 (30), 282 (32), 271 (49), 254 (43), 239 (35), 239 (35), 191 (15), 157 (5), 129 (9), 91 (16), 69 (21). HRMS (EI): Calcd. for $C_{18}H_{18}O_7$: 346.10470; found: 346.10523.

Methyl 3-chloro-4-hydroxy-6-(2-methoxy-2-oxoethyl)-2-methylbenzoate (33y).



Starting with **5p** (0.349 g, 1.25 mmol), **32** (0.156 g, 1.0 mmol), and triethylammonium fluoride (0.242 g, 1.5 mmol), **33y** was isolated as a reddish viscous oil (0.114 g, 42%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 3.59 (s, 2 H, CH_2COOCH_3), 3.61 (s, 3 H, CO*OCH₃*), 3.62 (s, 1 H, OH_{Ar}), 3.66 (s, 3 H, CH_2CO*OCH₃*), 6.32 (s, 1 H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 26.3 (CH_3), 35.6 (CH_2COOCH_3), 51.7 (CO*OCH₃*), 51.8 (CH_2CO*OCH₃*), 82.7(C_{Ar}), 124.3 (CH_{Ar}), 144.4, 165.2, 165.2 (C_{Ar}), 170.1 (COH_{Ar}), 198.9 (2CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3002 (w), 2954 (w), 1731 (s), 1649 (w), 1435 (m), 1356 (m), 1327 (m), 1252 (m), 1166 (s), 1012 (m), 859 (w). GC-MS (EI, 70 eV): *m/z* (%) = 274 ([M^+], ^{37}Cl, 9), 272 ([M^+], ^{35}Cl, 25), 242 (^{37}Cl, 40), 240 (^{35}Cl, 100), 211 (^{37}Cl, 15), 209 (^{35}Cl, 46), 197 (5), 180 (6), 154 (4), 125 (5), 89 (11), 77 (6). HRMS (EI): calcd. for $C_{12}H_{13}ClO_5$ ([M^+], ^{35}Cl): 272.04460; found: 272.04423.

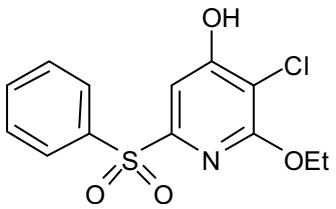
Methyl 4-hydroxy-6-(2-methoxy-2-oxoethyl)-2-methyl-3-phenoxybenzoate (33z). Starting with **5t** (0.761 g, 2.0 mmol), **32** (0.251 g, 1.6 mmol), and triethylammonium fluoride (0.241 g, 1.5 mmol), **33z** was isolated as a red viscous oil (0.359 g, 48%). Reaction time: 14 h (40 °C). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, ^{3}J = 6.9 Hz, 3 H, OCH_2CH_3), 2.07 (s, 3 H, CH_{3Ar}), 3.57 (s, 3 H, $COOCH_3$), 3.61 (s, 3 H, CH_2COOCH_3), 3.71 (s, 2 H, CH_2COOCH_3), 3.86 (q, ^{3}J = 6.9 Hz, 2 H, OCH_2CH_3), 6.38 (s, 1 H, CH_{Ar}), 6.68 (m, 2 H, CH_{Ph}), 6.70 (m, 2 H, CH_{Ph}), 6.78 (s, 1 H, OH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 14.7 (CH_{3Ar}), 25.9 (OCH_2CH_3), 34.2 (CH_2COOCH_3), 51.5 ($COOCH_3$), 51.9 (CH_2COOCH_3), 63.7 (OCH_2CH_3), 95.2 (C_{Ar}), 115.3 ($2CH_{Ph}$), 115.8 (C_{Ar}), 117.3 ($2CH_{Ph}$), 127.5 (CH_{Ar}), 145.1, 147.8 (C_{Ar}), 150.3, 154.5 (C_{Ph}), 165.5 (COH_{Ar}), 170.4 ($COOCH_3$), 201.5 (CH_2COOCH_3). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3434 (w), 2953 (w), 1735 (s), 1502 (s), 1435 (m), 1194 (s), 1140 (m), 1044 (m), 825 (m), 774 (w). GC-MS (EI, 70 eV): *m/z* (%) = 374 ([M^+], 46), 342 (81), 313 (100), 299 (3), 271 (7), 253 (6). HRMS (EI): Calcd. for $C_{20}H_{22}O_7$: 374.13600; found: 374.13532.



General Procedure for the synthesis of 2-(Arylsulfonyl)-4-hydroxypyridines 35:

To the arylsulfonyl cyanide **34** (1.0 eq) was added dropwise the 1,3-bis-silyl enol ether **5** (2.0-2.5 eq) at -78 °C. The mixture was warmed up to 45−60 °C during 48−96 h with stirring. To the mixture was added the solution of ammonium chloride (1M, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in *vacuo*. The residue was purifed by chromatography (silica gel, *n*-heptane / EtOAc) to give **35**.

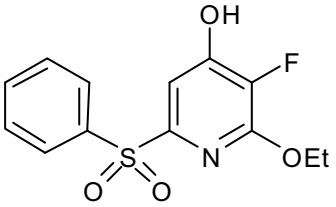
3-Chloro-2-ethoxy-6-(phenylsulfonyl)pyridin-4-ol (35a).



Starting with **34a** (0.167 g, 1.0 mmol) and 5d 1 (0.617 g, 2.0 mmol), **35a** was isolated as yellow viscous oil (0.175 g, 56%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, ^{3}J = 7.1 Hz, 3 H, OCH_2CH_3), 4.27 (q, ^{3}J = 7.1 Hz, 2 H, OCH_2CH_3), 7.19 (s(br), 1 H, OH_{Heter}), 7.44−7.49 (m, 2 H, CH_{Ph}), 7.52 (m, 1 H, CH_{Ph}), 7.55 (s, 1 H, CH_{Heter}), 7.96 (dd, ^{3}J = 8.4 Hz, ^{4}J = 1.5 Hz, 2 H, CH_{Ph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (OCH_2CH_{3Heter}), 64.1 (OCH_2CH_3), 105.6 (CH_{Heter}), 106.9 (C_{Heter}), 128.9 ($2CH_{Ph}$), 129.0 ($2CH_{Ph}$), 133.8 (CH_{Ph}), 138.4 (C_{Ph}), 153.6 (COH_{Heter}), 159.9, 160.4 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3312 (w), 1731 ((br), w), 1608 (m), 1417 (m), 1385 (m), 1347 (m), 1304 (m), 1251 (m),

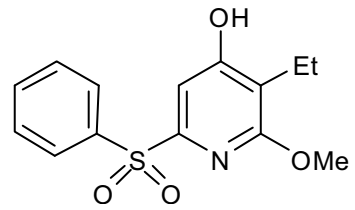
1159 (m), 1093 (s), 1076 (s), 840 (s), 725 (s), 592 (s). HRMS (ESI): Calcd. for $C_{13}H_{12}ClNO_4S$ ($[M+H]^+$, ^{35}Cl) : 314.02483; found: 314.02486, ($[M+Na]^+$, ^{35}Cl) : 336.006433; found: 336.00678.

2-Ethoxy-3-fluoro-6-(phenylsulfonyl)pyridin-4-ol (35b).



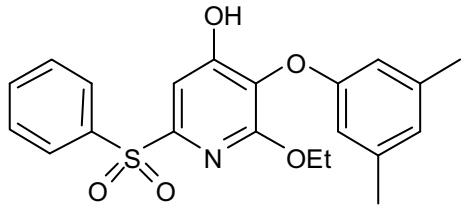
Starting with **34a** (0.167 g, 1.0 mmol) and **5e** 1 (0.589 g, 2.0 mmol), **35b** was isolated as red solid (0.179 g, 59%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 4.26 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 7.19 (s(br), 1 H, OH_{Heter}), 7.43 (m, 1 H, CH_{Heter}), 7.46−7.50 (m, 2 H, CH_{Ph}), 7.53−7.56 (m, 1 H, CH_{Ph}), 7.95 (dd, ^3J = 8.4 Hz, ^4J = 1.5 Hz, 2 H, CH_{Ph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (OCH_2CH_3), 63.6 (OCH_2CH_3), 107.8 (CH_{Heter}), 128.9 ($2CH_{Ph}$), 129.0 ($2CH_{Ph}$), 133.8 (CH_{Ph}), 136.8 (d, ^1J = 252.4 Hz, CF_{Heter}), 138.4 (C_{Ph}), 149.4 (d, ^4J = 6.7 Hz, C_{Heter}), 151.3 (d, ^2J = 10.2 Hz, COH_{Heter}), 153.8 (d, ^2J = 9.9 Hz, C_{Heter}). ^{19}F NMR (235 MHz, $CDCl_3$): −162.05 (CF_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3354 (w), 1576 (m), 1440 (m), 1353 (m), 1317 (m), 1149 (s), 1076 (m), 1022 (m), 740 (s), 724 (s), 682 (s), 585 (s). HRMS (ESI): Calcd. for $C_{13}H_{12}FNO_4S$ ($[M+H]^+$) : 298.05438; found: 298.05413, ([M+Na) : 320.03652; found: 320.03633.

3-Ethyl-2-methoxy-6-(phenylsulfonyl)pyridin-4-ol (35c).



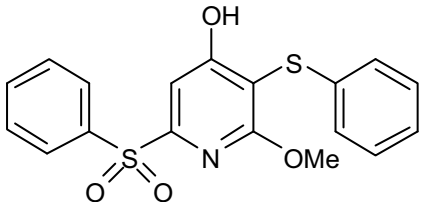
Starting with **34a** (0.188 g, 1.0 mmol) and **5f** 1 (0.576 g, 2.0 mmol), **35c** was isolated as yellow viscous oil (0.176 g, 60%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, CD_3OD): δ = 0.97 (t, ^3J = 7.9 Hz, 3 H, CH_2CH_3), 2.46 (q, ^3J = 7.7 Hz, 2 H, CH_2CH_3), 3.24 (s, 3 H, OCH_{3Heter}), 6.97 (s, 1 H, CH_{Heter}), 7.32−7.35 (m, 3 H, CH_{Ph}), 7.78 (d, ^3J = 9.8 Hz, 2 H, CH_{Ph}). ^{13}C NMR (75 MHz, CD_3OD): δ = 12.7 (CH_2CH_3), 17.3 (CH_2CH_3), 50.0 (OCH_{3Heter}), 104.9 (CH_{Heter}), 118.1 (C_{Heter}), 129.5 ($2CH_{Ph}$), 130.9 ($2CH_{Ph}$), 137.7 (CH_{Ph}), 146.5 (C_{Ph}), 151.5 (COH_{Heter}), 164.7, 165.3 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3417 (w), 2933 (w), 1726 (m), 1613 (m), 1413 (m), 1319 (s), 1267 (s), 1146 (s), 1083 (s), 904 (w), 812 (m), 674 (s), 592 (s). MS (EI, 70 eV): *m/z* (%) = 293 ($[M]^+$, 100), 229 (96), 186 (8), 160 (14), 139 (64), 91 (37), 69 (26). HRMS (ESI): Calcd. for $C_{14}H_{15}NO_4S$ ($[M+H]^+$) : 294.07946; found: 294.07964, ($[M+Na]^+$) : 316.06140; found: 316.06148.

3-(3,5-dimethylphenoxy)-2-ethoxy-6-(phenylsulfonyl)pyridin-4-ol (35d).



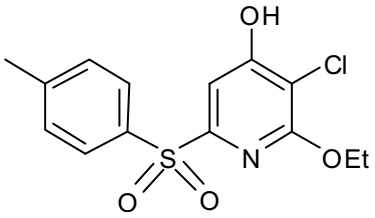
Starting with **34a** (0.167 g, 1.0 mmol) and **5n** 1 (0.756 g, 2.0 mmol), **35d** was isolated as yellow viscous oil (0.243 g, 61%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.99 (t, ^{3}J = 7.0 Hz, 3 H, OCH_2CH_3), 2.14 (s, 6 H, CH_{3Xyl}), 4.16 (q, ^{3}J = 7.0 Hz, 2 H, OCH_2CH_3), 6.37 (s, 2 H, CH_{Xyl}), 6.59 (s, 1 H, CH_{Xyl}), 6.77 (s(br), 1 H, OH_{Heterl}), 7.45−7.48 (m, 2 H, CH_{Ph}), 7.48 (s, 1 H, CH_{Heter}), 7.51 (m, 1 H, CH_{Ph}), 7.98 (dd, ^{3}J = 8.5 Hz, ^{4}J = 1.5 Hz, 2 H, CH_{Ph}).^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1 (OCH_2CH_3), 19.3 ($2CH_{3Xyl}$), 61.2 (OCH_2CH_3), 104.8 (CH_{Heter}), 111.1 ($2CH_{Ph}$), 122.9 (CH_{Xyl}), 125.9 (C_{Heter}), 126.9 ($2CH_{Ph}$), 127.1 ($2CH_{Xyl}$), 131.7 (CH_{Ph}), 136.7 (C_{Xyl}), 137.5 (C_{Ph}), 148.8 ($2C_{Xyl}$), 154.5 (COH_{Heter}), 155.1, 155.6 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3324 (w), 1592 (s), 1468 (m), 1429 (m), 1305 (m), 1132 (s), 1095 (m), 997 (m), 831 (m), 724 (s), 679 (s), 594 (s). HRMS (ESI): Calcd. for $C_{21}H_{21}NO_5S$ ($[M+H]^+$) : 400.12132; found: 400.12108, ($[M+Na]^+$) : 422.10299; found: 422.10326.

2-Methoxy-6-(phenylsulfonyl)-3-(phenylthio)pyridin-4-ol (35e).



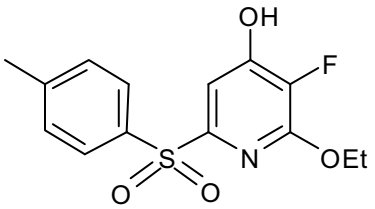
Starting with **34a** (0.167 g, 1.0 mmol) and **5o** 1 (0.746 g, 2.0 mmol), **35e** was isolated as yellow solid (0.210 g, 56%); Reaction conditions: 96 h, 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, OCH_{3Heter}), 7.02 (m, 1 H, CH_{Ph}), 7.05 (m, 1 H, CH_{Ph}), 7.15 (m, 2 H, CH_{Ph}), 7.18 (m, 2 H, CH_{Ph}), 7.45 (s, 1 H, CH_{Heter}), 7.47 (m, 1 H, CH_{Heter}), 7.50 (s(br), 1 H, OH_{Heter}), 7.54−7.57 (m, 1 H, CH_{Ph}), 8.01 (d, ^{3}J = 6.9 Hz, 2 H, CH_{Ph}).. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.1 (OCH_{3Heter}), 104.7 (CH_{Heter}), 125.2 (C_{Heter}), 127.1 (CH_{Ph}), 128.1 ($2CH_{Ph}$), 125.9 ($2CH_{Ph}$), 129.2 ($2CH_{Ph}$), 129.3 ($2CH_{Ph}$), 132.6, 137.3 (C_{Ph}), 133.8 (CH_{Ph}), 138.3 (C_{Ph}), 157.4 (COH_{Heter}), 164.9, 166.5 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3246 (w), 1625 (m), 1559 (w), 1503 (m), 1445 (m), 1385 (m), 1301 (s), 1142 (s), 1076 (s), 906 (m), 724 (s), 600 (s). HRMS (ESI): Calcd. for $C_{18}H_{15}NO_4S_2$ ($[M+H]^+$) : 374.05153; found: 374.05163, ($[M+Na]^+$) : 396.03360; found: 396.03347.

3-chloro-2-ethoxy-6-tosylpyridin-4-ol (35f).



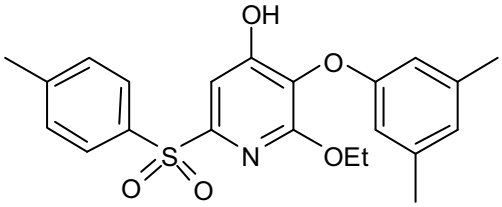
Starting with **34b** (0.094 g, 1.0 mmol) and BISY (0.617 g, 2.0 mmol), **35f** was isolated as red viscous oil (0.156 g, 48%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, ^{3}J = 7.8 Hz, 3 H, $OCH_2\mathit{CH_3}$), 2.35 (s, 3 H, CH_{3Tol}), 4.28 (q, ^{3}J = 6.8 Hz, 2 H, OCH_2CH_3), 7.19 (s, 1 H, CH_{Heter}), 7.24 (d, ^{3}J = 8.1 Hz, 2 H, CH_{Tol}), 7.42 (s(br), 1 H, OH_{Heterl}), 7.84 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}).^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 ($OCH_2\mathit{CH_{3Heter}}$), 21.6 ($CH_{3Tol}$), 64.0 ($OCH_2CH_3$), 105.4 ($CH_{Heter}$), 106.7 ($C_{Heter}$), 129.1 ($2CH_{Tol}$), 129.6 ($2CH_{Tol}$), 135.5, 144.8 ($C_{Tol}$), 153.9 ($COH_{Heter}$), 159.8, 160.3 ($C_{Heter}$). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 1594 (m), 1415 (m), 1338 (m), 1252 (m), 1115 (s), 1078 (s), 840 (s), 676 (s), 589 (s). MS (CI, Positive, 70 eV): *m/z* (%) = 330 ($[M+1]^+$, ^{37}Cl, 35), 328 ($[M+1]^+$, ^{35}Cl, 100), 299 (4), 279 (2), 257 (5), 233 (3), 219 (3), 193 (3), 177 (4), 141 (5), 125 (5), 81 (^{37}Cl, 11), 79 (^{35}Cl, 97), 71 (17). HRMS (ESI): Calcd. for $C_{14}H_{14}ClNO_4S$ ($[M+H]^+$, ^{35}Cl) : 328.04048; found: 328.04058, ($[M+Na]^+$, ^{35}Cl) : 350.02243; found: 350.0039.

2-ethoxy-3-fluoro-6-tosylpyridin-4-ol (35g).



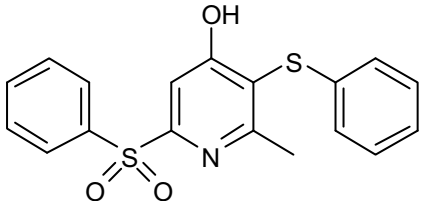
Starting with **34b** (0.188 g, 1.0 mmol) and **5e** (0.589 g, 2.0 mmol), **35g** was isolated as red viscous oil (0.178 g, 54%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^{3}J = 6.8 Hz, 3 H, $OCH_2\mathit{CH_3}$), 2.35 (s, 3 H, CH_{3Tol}), 4.27 (q, ^{3}J = 6.8 Hz, 2 H, OCH_2CH_3), 7.23 (s(br), 1 H, OH_{Heter}), 7.27 (d, ^{3}J = 8.1 Hz, 2 H, CH_{Tol}), 7.46 ($d_{H,F}$, ^{4}J = 5.0 Hz, 1 H, CH_{Heter}), 7.82 (d, ^{3}J = 8.5 Hz, 2 H, CH_{Tol}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 ($OCH_2\mathit{CH_3}$), 21.6 (CH_{3Tol}), 63.5 (OCH_2CH_3), 107.6 (CH_{Heter}), 128.9 ($2CH_{Tol}$), 129.6 ($2CH_{Tol}$), 135.5 (C_{Tol}), 137.8 (d, ^{1}J = 251.9 Hz, CF_{Heter}), 144.8 (C_{Tol}), 149.7 (d, ^{4}J = 6.2 Hz, C_{Heter}), 151.3 (d, ^{2}J = 9.9 Hz, COH_{Heter}), 153.7 (d, ^{2}J = 9.9 Hz, C_{Heter}). ^{19}F NMR (235 MHz, $CDCl_3$): −162.63 (CFHeter). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3255 (w), 1624 (m), 1505 (m), 1425 (m), 1383 (m), 1261 (s), 1140 (m), 1084 (m), 811 (m), 686 (m), 600 (m). MS (CI, Positive, 70 eV): *m/z* (%) = 312 ($[M+1]^+$, 100), 247 (8), 219 (6), 177 (3), 119 (11), 69 (7). HRMS (ESI): Calcd. for $C_{14}H_{14}FNO_4S$ ($[M+H]^+$) : 312.07003; found: 312.06950, ($[M+Na]^+$) : 334.05198; found: 334.05194.

3-(3,5-dimethylphenoxy)-2-ethoxy-6-tosylpyridin-4-ol (35h).



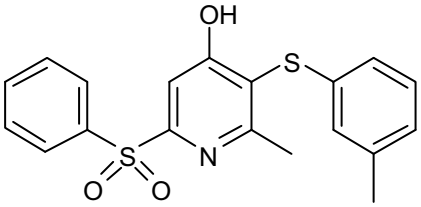
Starting with **34b** (0.188 g, 1.0 mmol) and **5n** (0.757 g, 2.0 mmol), **35h** was isolated as red viscous oil (0.253 g, 62%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, CD_3OD): δ = 0.97 (t, ^{3}J = 7.3 Hz, 3 H, OCH_2CH_3), 2.29 (s, 6 H, CH_{3Xyl}), 2.52 (s, 3 H, CH_{3Tol}), 4.28 (q, ^{3}J = 7.4 Hz, 2 H, OCH_2CH_3), 6.54 (s, 2 H, CH_{Xyl}), 6.72 (s, 1 H, CH_{Xyl}), 7.26 (s, 1 H, CH_{Heterl}), 7.51 (d, ^{3}J = 8.0 Hz, 2 H, CH_{Tol}), 8.01 (d, ^{3}J = 8.3 Hz, 2 H, CH_{Tol}).^{13}C NMR (75 MHz, CD_3OD): δ = 14.2 (OCH_2CH_{3Heter}), 21.3 ($2CH_{3Xyl}$), 21.4 (CH_{3Tol}), 62.7 (OCH_2CH_{3Heter}), 106.7 (CH_{Heter}), 113.8 ($2CH_{Xyl}$), 124.9 (CH_{Xyl}), 129.6 ($2CH_{Tol}$), 131.0 ($2CH_{Tol}$), 140.3 (C_{Tol}), 143.3 ($2C_{Xyl}$), 149.6 (C_{Tol}), 158.4 (C_{Heter}), 159.7 (C_{Xyl}), 159.9, 160.4 (C_{Heter}), 170.8 (COH_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3248 (w), 2952 (w), 1632 (s), 1436 (m), 1309 (m), 1178 (s), 1092 (m), 1035 (m), 952 (w), 805 (s), 696 (s). HRMS (ESI): Calcd. for $C_{20}H_{19}NO_4S$ ($[M+1]^+$) : 414.13784; found: 414.13769, ($[M+Na]^+$) : 436.47982; found: 436.47842.

2-Methy-6-(phenylsulfonyl)-3-(phenylthio)pyridin-4-ol (35i).



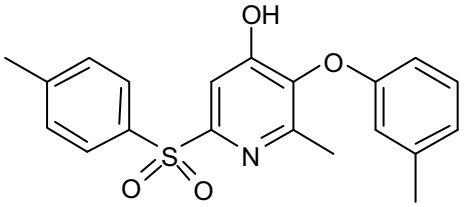
Starting with **34a** (0.167 g, 1.0 mmol) and **5q** 1 (0.704 g, 2.0 mmol), **35i** was isolated as yellow viscous oil (0.189 g, 53%); Reaction conditions: 96 h, 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, CH_{3Heter}), 6.89 (dd, ^{3}J = 8.2 Hz, ^{4}J = 1.9 Hz, 2 H, CH_{Tol}), 7.10(m, 3 H, CH_{Tol}), 7.38 (s(br), 1 H, OH_{Heter}), 7.47 (m, 3 H, CH_{Tol}), 7.59 (s, 1 H, CH_{Heter}), 7.95 (dd, ^{3}J = 8.4 Hz, ^{4}J = 1.5 Hz, 2 H, CH_{Tol}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 20.4 (CH_{3Heter}), 108.17 (CH_{Heter}), 117.7 (C_{Ph}), 126.1 (C_{Heter}), 127.1 ($2CH_{Ph}$), 129.1 ($2CH_{Ph}$), 129.6 ($2CH_{Ph}$), 129.9 ($2CH_{Ph}$), 133.9 ($2CH_{Ph}$), 138.5 (C_{Ph}), 159.1, 165.5 (C_{Heter}), 165.6 (COH_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3249 (w), 1562 (m), 1446 (m), 1397 (m), 1307 (m), 1156 (s), 1082 (m), 905 (s), 721 (s), 684 (m), 601 (s). GC-MS (EI, 70 eV): *m/z* (%) = 357 ($[M]^+$, 4), 292 (100), 252 (4), 216 (6), 147 (6), 109 (24), 77 (19), 65 (7), 51 (10). HRMS (EI): Calcd. for $C_{18}H_{15}NO_3S_2$: 357.04879; found: 357.04863.

2-methyl-6-(phenylsulfonyl)-3-(*m*-tolylthio)pyridin-4-ol (35j).



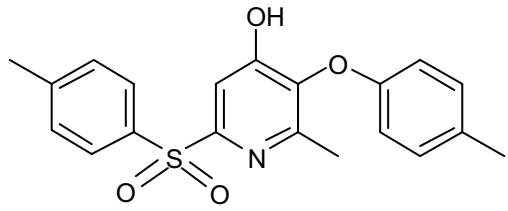
Starting with **34a** (0.167 g, 1.0 mmol) and **5r** 1 (0.733 g, 2.0 mmol), **35j** was isolated as yellow viscous oil (0.296 g, 79%); Reaction conditions: 96 h, 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_{3Tol}), 2.48 (s, 3 H, CH_3, CH_{3Heter}), 6.82 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}), 6.98 (d, ^{3}J = 8.1 Hz, 1 H, CH_{Ph}), 7.45 (m, 1 H, CH_{Tol}), 7.48 (m, 1 H, CH_{Ph}), 7.55 (s(br), 1 H, OH_{Heter}), 7.63 (m, 1 H, CH_{Heter}), 7.52 (m, 1 H, CH_{Tol}), 8.00 (dd, ^{3}J = 8.1 Hz, ^{4}J = 1.5 Hz, 1 H, CH_{Ph}).^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.9 (CH_{3Tol}), 21.9 (CH_{3Heter}), 105.9 (CH_{Heter}), 113.2, 116.3 (C_{Heter}), 126.0 ($2CH_{Ph}$), 126.7 (CH_{Tol}), 127.1 ($2CH_{Tol}$), 127.2 (CH_{Tol}), 127.9 (C_{Ph}), 128.4 ($2CH_{Ph}$), 131.8 (CH_{Ph}), 135.5 (C_{Tol}), 136.6 (C_{Tol}), 157.0 (COH_{Heter}), 163.4 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3377 (w), 2921 (w), 1561 (m), 1491 (m), 1446 (m), 1396 (m), 1306 (m), 1155 (s), 1081 (m), 1015 (w), 905 (s), 803 (m), 722 (s), 684 (m), 600 (s). GC-MS (CI, Positive, 70 eV): *m/z* (%) = 371 ($[M]^+$, 14), 306 (100), 292 (5), 274 (4), 216 (5), 186 (3), 135 (6), 123 (27), 91 (8), 77 (24), 65 (4), 45 (7). HRMS (EI): Calcd. for $C_{19}H_{17}NO_3S_2$ ($[M]^+$) : 371.06444; found: 371. 06407.

2-methyl-3-(*m*-tolyloxy)-6-tosylpyridin-4-ol (35k).



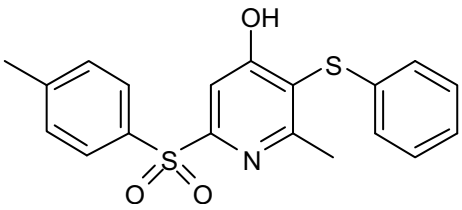
Starting with **34b** (0.141 g, 0.750 mmol) and **5u** (0.525 g, 1.5 mmol), **35k** was isolated as colourless solid (0.240 g, 58%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.16 (s, 3 H, CH_{3Tol}), 2.18 (s, 3 H, CH_{3Tol}), 2.32 (s, 3 H, CH_{3Heter}), 6.47 (m, 1 H, CH_{Tol}), 6.53 (s, 1 H, CH_{Heter}), 6.75 (d, ^{3}J = 7.3 Hz, 1 H, CH_{Tol}), 7.00−7.06 (m, 2 H, CH_{Tol}), 7.21 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}), 7.62 (s(br), 1 H, OH_{Heter}), 7.82 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}).^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.1 (CH_{3Heter}), 19.4, 19.7 (CH_{3Tol}), 108.9 (CH_{Heter}), 109.9, 113.6, 121.9 (CH_{Tol}), 126.9 ($2CH_{Tol}$), 127.5 (CH_{Tol}), 127.8 ($2CH_{Tol}$), 133.9, 137.8 (C_{Tol}), 138.2 (C_{Heter}), 142.9 (C_{Tol}), 152.2 (C_{Heter}), 152.6 (C_{Tol}), 154.3 (COH_{Heter}), 179.3 (C_{Heter}). GC-MS (CI, Positive, 70 eV): *m/z* (%) = 370 ($[M+1]^+$, 100), 305 (58), 291 (4), 232 (8), 69 (24). HRMS (ESI): Calcd. for $C_{20}H_{19}NO_4S$ ($[M+H]^+$) : 370.11076; found: 370.11067, ($[M+Na]^+$) : 392.09270; found: 392.09270.

2-methyl-3-(*p*-tolyloxy)-6-tosylpyridin-4-ol (35l).



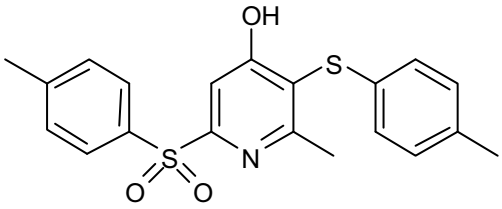
Starting with **34b** (0.141 g, 0.75 mmol) and **5v** (0.525 g, 1.75 mmol), **35l** was isolated as yellow solid (0.210 g, 57%); Reaction conditions: 48 h, 45 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_{3Tol}), 2.21 (s, 3 H, CH_{3Tol}), 2.34 (s, 3 H, CH_{3Heter}), 6.61 (d, ^{3}J = 8.5 Hz, 2 H, CH_{Tol}), 6.98 (d, ^{3}J = 8.3 Hz, 2 H, CH_{Tol}), 7.19 (s, 1 H, CH_{Heter}), 7.24 (d, ^{3}J = 8.1 Hz, 2 H, CH_{Tol}), 7.64 (s(br), 1 H, OH_{Heter}), 7.86 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.1, 21.6 (CH_{3Tol}), 30.9 (CH_{3Heter}), 110.3 (CH_{Heter}), 113.8 (C_{Tol}), 114.7 ($2CH_{Tol}$), 128.9 ($2CH_{Tol}$), 129.7 ($2CH_{Tol}$), 129.9 (C_{Tol}), 130.4 ($2CH_{Tol}$), 130.7 (C_{Tol}), 132.7, 136.0, 139.6 (C_{Heter}), 144.7 (C_{Tol}), 154.7 (COH_{Heter}). MS (EI, 70 eV): *m/z* (%) = 369 ($[M]^+$, 1), 320 (1), 305 (100), 288 (10), 214 (13), 186 (9), 139 (8), 107 (9), 91 (45), 65 (16). HRMS (ESI): Calcd. for $C_{20}H_{19}NO_4S$ ($[M+H]^+$) : 370.11076; found: 370.11207, ($[M+Na]^+$) : 392.09270; found: 392.09732.

2-Methyl-3-(phenylthio)-6-tosylpyridin-4-ol (35m).



Starting with **34b** (0.188 g, 1.0 mmol) and **5q** (0.705 g, 2.0 mmol), **35m** was isolated as colorless oil (0.240 g, 64%); Reaction conditions: 96 h, 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_{3Tol}), 2.41 (s, 3 H, CH_{3Heter}), 6.80 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}), 7.02−7.06 (m, 3 H, CH_{Ph}), 7.09 (s(br), 1 H, OH_{Heter}), 7.18 (d, ^{3}J = 8.0 Hz, 2 H, CH_{Ph}), 7.55 (s, 1 H, CH_{Heter}), 7.82 (d, ^{3}J = 8.3 Hz, 2 H, CH_{Tol}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.6 (CH_{3Tol}), 23.7 (CH_{3Heter}), 108.1 (CH_{Heter}), 117.7 (C_{Ph}), 126.9 (CH_{Ph}), 127.3 ($2CH_{Tol}$), 129.1 ($2CH_{Ph}$), 129.5 ($2CH_{Ph}$), 129.8 ($2CH_{Tol}$), 132.7 (C_{Tol}), 135.5 (C_{Heter}), 145.1 (C_{Tol}), 159.2 (COH_{Heter}), 165.3, 165.8 (C_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 1552 (w), 1396 (m), 1316 (m), 1152 (s), 1081 (s), 905 (m), 728 (s), 678 (s), 590 (s). GC-MS (EI, 70 eV): *m/z* (%) = 371 ($[M]^+$, 1), 306 (100), 292 (3), 266 (6), 230 (4), 214 (3), 190 (4), 147 (5), 109 (22), 91 (17), 77 (6), 65 (14). HRMS (EI): Calcd. for $C_{19}H_{17}NO_3S_2$: 371.06444; found: 371.06400.

2-methyl-3-(*p*-tolylthio)-6-tosylpyridin-4-ol (35n).



Starting with **34b** (0.188 g, 1.0 mmol) and **5s** (0.733 g, 2.0 mmol), **35n** was isolated as colorless oil (0.200 g, 51%); Reaction conditions: 96 h, 60 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_{3Tol}), 2.31 (s, 3 H, CH_{3Tol}), 2.45 (s, 3 H, CH_{3Heter}), 6.85 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}), 6.94 (d, ^{3}J = 8.1 Hz, 2 H, CH_{Tol}), 7.22 (d, ^{3}J = 8.0 Hz, 2 H, CH_{Tol}), 7.60 (s, 1 H, CH_{Heter}), 7.76 (s(br), 1 H, OH_{Heter}), 7.85 (d, ^{3}J = 8.2 Hz, 2 H, CH_{Tol}). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 20.9, 21.6 (CH_{3Tol}), 23.9 (CH_{3Heter}), 107.7 (CH_{Heter}), 118.0 (C_{Tol}), 127.9 ($2CH_{Tol}$), 128.8 ($2CH_{Tol}$), 129.1 ($2CH_{Tol}$), 129.7 ($2CH_{Tol}$), 135.6, 137.3 (C_{Tol}), 130.7 (C_{Tol}), 144.8, 159.5, 165.1 (C_{Heter}), 165.4 (COH_{Heter}). IR (Neat, cm^{-1}): $\tilde{\nu}$ = 3279 (w), 1583 (m), 1546 (m), 1490 (m), 1393 (m), 1306 (m), 1154 (s), 1124 (s), 1076 (s), 964 (w), 799 (s), 680 (s). MS (EI, 70 eV): *m/z* (%) = 385 ($[M]^+$, 13), 320 (100), 306 (7), 280 (11), 228 (11), 160 (6), 135 (10), 123 (45), 91 (38), 79 (12), 65 (9), 45 (13). HRMS (EI): Calcd. for $C_{20}H_{19}NO_3S_2$: 385.08009; found: 385.07955.

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address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk.

Data for X-Ray Crystal Structures

Data for compound 16b (chapter 1):

Table 1. Crystal data and structure refinement for ah216.

Identification code	ah216	
Empirical formula	$C_{16}\ H_{13}\ F_3\ O_3$	
Formula weight	310.26	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group (H.-M.)	Pbca	
Space group (Hall)	-P 2ac 2ab	
Unit cell dimensions	a = 8.1866(6) Å	α= 90°.
	b = 7.9746(6) Å	β= 90°.
	c = 42.350(3) Å	γ = 90°.
Volume	2764.8(3) $Å^3$	
Z	8	
Density (calculated)	1.491 Mg/m^3	
Absorption coefficient	0.129 mm^{-1}	
F(000)	1280	
Crystal size	0.68 x 0.61 x 0.31 mm^3	
Θ range for data collection	2.67 to 30.00°.	
Index ranges	-9≤h≤11, -11≤k≤9, -27≤l≤59	
Reflections collected	17499	
Independent reflections	4026 [R(int) = 0.0285]	
Completeness to Θ = 30.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9612 and 0.9177	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4026 / 0 / 206	
Goodness-of-fit on F^2	1.134	
Final R indices [I>2σ(I)]	R1 = 0.0616, wR2 = 0.1402	
R indices (all data)	R1 = 0.0682, wR2 = 0.1437	
Extinction coefficient	0.0010(7)	
Largest diff. peak and hole	0.411 and -0.403 $e.Å^{-3}$	

Data for compound 16f (chapter 1):

CHEMICAL DATA

```
_chemical_name_systematic
;
Methyl 4-(thien-2-yl)-6-trifluormethyl-salicylate
;
_chemical_name_common            ?
_chemical_melting_point          ?
_chemical_formula_moiety         ?
_chemical_formula_sum
 'C13 H9 F3 O3 S'
_chemical_formula_weight         302.26

# CRYSTAL DATA

_symmetry_cell_setting           orthorhombic
_symmetry_space_group_name_H-M    'P n a 2 1'
_symmetry_space_group_name_Hall   'P 2c -2n'
_symmetry_Int_Tables_number      33

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

_cell_length_a                   13.840(3)
_cell_length_b                   4.9310(10)
_cell_length_c                   35.860(7)
_cell_angle_alpha                90.00
_cell_angle_beta                 90.00
_cell_angle_gamma                90.00
_cell_volume                     2447.3(9)
_cell_formula_units_Z            8
_cell_measurement_temperature    173(2)
_cell_measurement_reflns_used    2049
_cell_measurement_theta_min      5.978
_cell_measurement_theta_max      44.283

_exptl_crystal_description       needle
_exptl_crystal_colour            colourless
_exptl_crystal_size_max          0.90
_exptl_crystal_size_mid          0.09
_exptl_crystal_size_min          0.06
_exptl_crystal_density_meas      ?
_exptl_crystal_density_diffrn    1.641
_exptl_crystal_density_method    'not measured'
_exptl_crystal_F_000             1232
_exptl_absorpt_coefficient_mu    0.307
_exptl_absorpt_correction_type   'multi-scan'
_exptl_absorpt_correction_T_min  0.7696
_exptl_absorpt_correction_T_max  0.9818
```

_exptl_absorpt_process_details '(SADABS; Sheldrick, 2004)'

Data for compound 16k (chapter 1):

CHEMICAL DATA

_chemical_name_systematic
;
Methyl 4-(fur-2-yl)-6-trifluormethyl-salicylate
;
_chemical_name_common ?
_chemical_melting_point ?
_chemical_formula_moiety ?
_chemical_formula_sum
'C13 H9 F3 O4'
_chemical_formula_weight 286.20

loop_
_atom_type_symbol
_atom_type_description
_atom_type_scat_dispersion_real
_atom_type_scat_dispersion_imag
_atom_type_scat_source
'C' 'C' 0.0033 0.0016
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'H' 'H' 0.0000 0.0000
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'O' 'O' 0.0106 0.0060
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'F' 'F' 0.0171 0.0103
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

CRYSTAL DATA

_symmetry_cell_setting orthorhombic
_symmetry_space_group_name_H-M 'P n a 2 1'
_symmetry_space_group_name_Hall 'P 2c -2n'
_symmetry_Int_Tables_number 33

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

_cell_length_a 13.851(3)
_cell_length_b 4.8284(10)
_cell_length_c 35.183(7)
_cell_angle_alpha 90.00
_cell_angle_beta 90.00

_cell_angle_gamma 90.00
_cell_volume 2353.0(8)
_cell_formula_units_Z 8
_cell_measurement_temperature 173(2)
_cell_measurement_reflns_used 1347
_cell_measurement_theta_min 6.001
_cell_measurement_theta_max 45.365

_exptl_crystal_description needle
_exptl_crystal_colour colourless
_exptl_crystal_size_max 0.81
_exptl_crystal_size_mid 0.09
_exptl_crystal_size_min 0.05
_exptl_crystal_density_meas ?
_exptl_crystal_density_diffrn 1.616
_exptl_crystal_density_method 'not measured'
_exptl_crystal_F_000 1168
_exptl_absorpt_coefficient_mu 0.149
_exptl_absorpt_correction_type 'multi-scan'
_exptl_absorpt_correction_T_min 0.8885
_exptl_absorpt_correction_T_max 0.9926
_exptl_absorpt_process_details '(SADABS; Sheldrick, 2004)'

Data for compound 21c (chapter 2):

Table 1. Crystal data and structure refinement for ah54.

Identification code	ah54	
Empirical formula	C_{16} H_{14} O_3	
Formula weight	254.27	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/c$	
Space group (Hall)	-P 2ybc	
Unit cell dimensions	a = 12.3408(2) Å	α= 90°.
	b = 12.8642(2) Å	β= 98.0890(10)°.
	c = 7.74600(10) Å	γ = 90°.
Volume	1217.48(3) $Å^3$	
Z	4	
Density (calculated)	1.387 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	536	
Crystal size	0.43 x 0.25 x 0.21 mm^3	
Θ range for data collection	3.09 to 29.00°.	
Index ranges	-16≤h≤16, -17≤k≤17, -10≤l≤10	

Reflections collected	16584
Independent reflections	3176 [R(int) = 0.0264]
Completeness to Θ = 29.00°	97.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9803 and 0.9601
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3176 / 0 / 178
Goodness-of-fit on F^2	1.030
Final R indices [I>2σ(I)]	R1 = 0.0400, wR2 = 0.1088
R indices (all data)	R1 = 0.0508, wR2 = 0.1219
Largest diff. peak and hole	0.286 and -0.169 e.$Å^{-3}$

Data for compound 26m (chapter 3):

Table 1. Crystal data and structure refinement for **FO3175**.

Identification code	FO3175	
Empirical formula	C16 H14 Cl F O3	
Formula weight	308.72	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 9.2577(3) Å	α= 90°.
	b = 11.9231(5) Å	β= 107.529(3)°.
	c = 13.5991(6) Å	γ = 90°.
Volume	1431.37(10) $Å^3$	
Z	4	
Density (calculated)	1.433 Mg/m^3	
Absorption coefficient	0.285 mm^{-1}	
F(000)	640	
Crystal size	0.05 x 0.04 x 0.04 mm^3	
Theta range for data collection	2.92 to 27.49°.	
Index ranges	-12<=h<=11, -15<=k<=15, -15<=l<=17	
Reflections collected	9370	
Independent reflections	3267 [R(int) = 0.0401]	
Completeness to theta = 27.49°	99.4 %	
Absorption correction	NONE	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3267 / 0 / 197	

Goodness-of-fit on F^2	1.016
Final R indices [I>2sigma(I)]	R1 = 0.0422, wR2 = 0.1017
R indices (all data)	R1 = 0.0717, wR2 = 0.1160
Largest diff. peak and hole	0.224 and -0.279 e.Å^{-3}

Data for compound 26n (chapter 3):

Table 1. Crystal data and structure refinement for fo3171.

Identification code	FO3171	
Empirical formula	C18 H18 Cl F O3	
Formula weight	336.77	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.5963(6) Å	α= 81.374(4)°.
	b = 9.5216(10) Å	β= 89.582(5)°.
	c = 12.1083(11) Å	γ = 70.703(5)°.
Volume	816.39(13) Å^3	
Z	2	
Density (calculated)	1.370 Mg/m^3	
Absorption coefficient	0.256 mm^{-1}	
F(000)	352	
Crystal size	0.05 x 0.05 x 0.05 mm^3	
Theta range for data collection	2.64 to 27.44°.	
Index ranges	-9<=h<=9, -12<=k<=11, -15<=l<=15	
Reflections collected	5631	
Independent reflections	3672 [R(int) = 0.0337]	
Completeness to theta = 27.44°	98.5 %	
Absorption correction	NONE	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3672 / 0 / 215	
Goodness-of-fit on F^2	0.973	
Final R indices [I>2sigma(I)]	R1 = 0.0521, wR2 = 0.1208	
R indices (all data)	R1 = 0.0954, wR2 = 0.1470	
Largest diff. peak and hole	0.203 and -0.268 e.Å^{-3}	

Data for compound 33b (chapter 4):

```
# CHEMICAL DATA

_chemical_name_systematic
```

```
;
Methyl 3-ethyl-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate
;
_chemical_name_common              ?
_chemical_melting_point            ?
_chemical_formula_moiety           ?
_chemical_formula_sum
 'C13 H16 O6'
_chemical_formula_weight           268.26

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

_symmetry_cell_setting             orthorhombic
_symmetry_space_group_name_H-M     'P b c n'
_symmetry_space_group_name_Hall    '-P 2n 2ab'
_symmetry_Int_Tables_number        60

# CRYSTAL DATA

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

_cell_length_a                     15.714(3)
_cell_length_b                     8.2090(16)
_cell_length_c                     20.299(4)
_cell_angle_alpha                  90.00
_cell_angle_beta                   90.00
_cell_angle_gamma                  90.00
_cell_volume                       2618.5(9)
_cell_formula_units_Z              8
_cell_measurement_temperature      173(2)
_cell_measurement_reflns_used      5726
_cell_measurement_theta_min        4.775
_cell_measurement_theta_max        67.845

_exptl_crystal_description         plate
_exptl_crystal_colour              colourless
_exptl_crystal_size_max            0.58
_exptl_crystal_size_mid            0.53
_exptl_crystal_size_min            0.15
_exptl_crystal_density_meas        ?
_exptl_crystal_density_diffrn      1.361
_exptl_crystal_density_method      'not measured'
_exptl_crystal_F_000               1136
```

```
_exptl_absorpt_coefficient_mu     0.109
_exptl_absorpt_correction_type    'multi-scan'
_exptl_absorpt_correction_T_min   0.9396
_exptl_absorpt_correction_T_max   0.9839
_exptl_absorpt_process_details    '(SADABS; Sheldrick, 2004)'


# EXPERIMENTAL DATA  ?

_exptl_special_details
;
 ?
;

_diffrn_ambient_temperature       173(2)
_diffrn_radiation_wavelength      0.71073
_diffrn_radiation_type            MoK\a
_diffrn_radiation_source          'sealed tube'
_diffrn_radiation_monochromator   graphite
_diffrn_measurement_device_type   'Bruker-Nonius Apex X8-CCD-
diffractometer'
_diffrn_measurement_method        '\w scans'
_diffrn_detector_area_resol_mean  ?
_diffrn_standards_number          ?
_diffrn_standards_interval_count  ?
_diffrn_standards_interval_time   ?
_diffrn_standards_decay_%         ?
_diffrn_reflns_number             15044
_diffrn_reflns_av_R_equivalents   0.0217
_diffrn_reflns_av_sigmaI/netI     0.0170
_diffrn_reflns_limit_h_min        -16
_diffrn_reflns_limit_h_max        20
_diffrn_reflns_limit_k_min        -10
_diffrn_reflns_limit_k_max        10
_diffrn_reflns_limit_l_min        -22
_diffrn_reflns_limit_l_max        26
_diffrn_reflns_theta_min          2.59
_diffrn_reflns_theta_max          27.50
_diffrn_measured_fraction_theta_max    0.997
_diffrn_reflns_theta_full              27.50
_diffrn_measured_fraction_theta_full   0.997
_reflns_number_total              3003
_reflns_number_gt                 2463
_reflns_threshold_expression      >2sigma(I)

_computing_data_collection        'Bruker Apex v2.0-2'
_computing_cell_refinement        'Bruker Apex v2.0-2'
_computing_data_reduction         'Bruker SAINT'
_computing_structure_solution     'SHELXS-97 (Sheldrick, 1997)'
_computing_structure_refinement   'SHELXL-97 (Sheldrick, 1997)'
_computing_molecular_graphics     'ORTEP-3 (Farrugia, 1997)'
_computing_publication_material   'SHELXL-97'
```

Data for compound 33c (chapter 4):

```
# CHEMICAL DATA

_chemical_name_systematic
;
Methyl 3-chloro-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate
;
_chemical_name_common             ?
```

```
_chemical_melting_point           ?
_chemical_formula_moiety          ?
_chemical_formula_sum
 'C11 H11 Cl O6'
_chemical_formula_weight          274.65

loop_
 _atom_type_symbol
 _atom_type_description
 _atom_type_scat_dispersion_real
 _atom_type_scat_dispersion_imag
 _atom_type_scat_source
 'C'  'C'   0.0033   0.0016
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'H'  'H'   0.0000   0.0000
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'O'  'O'   0.0106   0.0060
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'Cl'  'Cl'   0.1484   0.1585
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting            monoclinic
_symmetry_space_group_name_H-M    'C 2/c'
_symmetry_space_group_name_Hall   '-C 2yc'
_symmetry_Int_Tables_number       15

# CRYSTAL DATA

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

_cell_length_a                    21.914(4)
_cell_length_b                    8.1480(16)
_cell_length_c                    15.168(3)
_cell_angle_alpha                 90.00
_cell_angle_beta                  119.34(3)
_cell_angle_gamma                 90.00
_cell_volume                      2360.8(8)
_cell_formula_units_Z             8
_cell_measurement_temperature     173(2)
_cell_measurement_reflns_used     5466
_cell_measurement_theta_min       5.520
_cell_measurement_theta_max       72.131

_exptl_crystal_description        block
_exptl_crystal_colour             colourless
_exptl_crystal_size_max           0.45
_exptl_crystal_size_mid           0.45
_exptl_crystal_size_min           0.35
_exptl_crystal_density_meas       ?
_exptl_crystal_density_diffrn     1.545
_exptl_crystal_density_method     'not measured'
_exptl_crystal_F_000              1136
_exptl_absorpt_coefficient_mu     0.341
_exptl_absorpt_correction_type    'multi-scan'
```

```
_exptl_absorpt_correction_T_min   0.8617
_exptl_absorpt_correction_T_max   0.8900
_exptl_absorpt_process_details    '(SADABS; Sheldrick, 2004)'

# EXPERIMENTAL DATA

_exptl_special_details
;
 ?
;

_diffrn_ambient_temperature       173(2)
_diffrn_radiation_wavelength      0.71073
_diffrn_radiation_type            MoK\a
_diffrn_radiation_source          'sealed tube'
_diffrn_radiation_monochromator   graphite
_diffrn_measurement_device_type   'Bruker-Nonius Apex X8-CCD-
diffractometer'
_diffrn_measurement_method        '\w scans'
_diffrn_detector_area_resol_mean  ?
_diffrn_standards_number          ?
_diffrn_standards_interval_count  ?
_diffrn_standards_interval_time   ?
_diffrn_standards_decay_%         ?
_diffrn_reflns_number             18626
_diffrn_reflns_av_R_equivalents   0.0157
_diffrn_reflns_av_sigmaI/netI     0.0144
_diffrn_reflns_limit_h_min        -35
_diffrn_reflns_limit_h_max        34
_diffrn_reflns_limit_k_min        -8
_diffrn_reflns_limit_k_max        13
_diffrn_reflns_limit_l_min        -22
_diffrn_reflns_limit_l_max        25
_diffrn_reflns_theta_min          2.72
_diffrn_reflns_theta_max          36.23
_diffrn_measured_fraction_theta_max    0.918
_diffrn_reflns_theta_full              36.23
_diffrn_measured_fraction_theta_full   0.918
_reflns_number_total              5232
_reflns_number_gt                 4525
_reflns_threshold_expression      >2sigma(I)

_computing_data_collection        'Bruker Apex v2.0-2'
_computing_cell_refinement        'Bruker Apex v2.0-2'
_computing_data_reduction         'Bruker SAINT'
_computing_structure_solution     'SHELXS-97 (Sheldrick, 1997)'
_computing_structure_refinement   'SHELXL-97 (Sheldrick, 1997)'
_computing_molecular_graphics     'ORTEP-3 (Farrugia, 1997)'
_computing_publication_material   'SHELXL-97'
```

Data for compound 33d (chapter 4):

```
# CHEMICAL DATA

_chemical_name_systematic
;
Methyl 3-fluoro-2,4-dihydroxy-6-(2-methoxy-2-oxoethyl)-benzoate
;
_chemical_name_common             ?
_chemical_melting_point           ?
_chemical_formula_moiety          'C11 H11 F O6'
```

```
_chemical_formula_sum
 'C11 H11 F O6'
_chemical_formula_weight          258.20

loop_
 _atom_type_symbol
 _atom_type_description
 _atom_type_scat_dispersion_real
 _atom_type_scat_dispersion_imag
 _atom_type_scat_source
 'C'  'C'   0.0033   0.0016
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'H'  'H'   0.0000   0.0000
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'O'  'O'   0.0106   0.0060
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'F'  'F'   0.0171   0.0103
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting            triclinic
_symmetry_space_group_name_H-M    'P -1'
_symmetry_space_group_name_Hall   '-P 1'
_symmetry_Int_Tables_number       2


# CRYSTAL DATA

loop_
 _symmetry_equiv_pos_as_xyz
 'x, y, z'
 '-x, -y, -z'

_cell_length_a                    7.5980(15)
_cell_length_b                    7.7540(16)
_cell_length_c                    10.764(2)
_cell_angle_alpha                 107.65(3)
_cell_angle_beta                  96.61(3)
_cell_angle_gamma                 109.78(3)
_cell_volume                      551.6(3)
_cell_formula_units_Z             2
_cell_measurement_temperature     173(2)
_cell_measurement_reflns_used     4774
_cell_measurement_theta_min       5.887
_cell_measurement_theta_max       59.193

_exptl_crystal_description        block
_exptl_crystal_colour             colourless
_exptl_crystal_size_max           0.23
_exptl_crystal_size_mid           0.14
_exptl_crystal_size_min           0.10
_exptl_crystal_density_meas       ?
_exptl_crystal_density_diffrn     1.554
_exptl_crystal_density_method     'not measured'
_exptl_crystal_F_000              268
_exptl_absorpt_coefficient_mu     0.138
_exptl_absorpt_correction_type    'multi-scan'
_exptl_absorpt_correction_T_min   0.9690
_exptl_absorpt_correction_T_max   0.9864
_exptl_absorpt_process_details    '(SADABS; Sheldrick, 2004)'

# EXPERIMENTAL DATA

_exptl_special_details
```

```
;
 ?
;

_diffrn_ambient_temperature       173(2)
_diffrn_radiation_wavelength      0.71073
_diffrn_radiation_type            MoK\a
_diffrn_radiation_source          'sealed tube'
_diffrn_radiation_monochromator   graphite
_diffrn_measurement_device_type   'Bruker-Nonius Apex X8-CCD-
diffractometer'
_diffrn_measurement_method        '\w scans'
_diffrn_detector_area_resol_mean  ?
_diffrn_standards_number          ?
_diffrn_standards_interval_count  ?
_diffrn_standards_interval_time   ?
_diffrn_standards_decay_%         ?
_diffrn_reflns_number             13356
_diffrn_reflns_av_R_equivalents   0.0227
_diffrn_reflns_av_sigmaI/netI     0.0179
_diffrn_reflns_limit_h_min        -9
_diffrn_reflns_limit_h_max        9
_diffrn_reflns_limit_k_min        -10
_diffrn_reflns_limit_k_max        10
_diffrn_reflns_limit_l_min        -13
_diffrn_reflns_limit_l_max        13
_diffrn_reflns_theta_min          2.95
_diffrn_reflns_theta_max          27.50
_diffrn_measured_fraction_theta_max    0.995
_diffrn_reflns_theta_full              27.50
_diffrn_measured_fraction_theta_full   0.995
_reflns_number_total              2513
_reflns_number_gt                 2020
_reflns_threshold_expression      >2sigma(I)

_computing_data_collection        'Bruker Apex v2.0-2'
_computing_cell_refinement        'Bruker Apex v2.0-2'
_computing_data_reduction         'Bruker SAINT'
_computing_structure_solution     'SHELXS-97 (Sheldrick, 1997)'
_computing_structure_refinement   'SHELXL-97 (Sheldrick, 1997)'
_computing_molecular_graphics     'ORTEP-3 (Farrugia, 1997)'
_computing_publication_material   'SHELXL-97'
```

Data for compound 35i (chapter 5):

```
# CHEMICAL DATA
_chemical_name_systematic
;
 ?
;
_chemical_name_common             ?
_chemical_melting_point           ?
_chemical_formula_moiety          'C18 H15 N O3 S2'
_chemical_formula_sum
 'C18 H15 N O3 S2'
_chemical_formula_weight          357.43

loop_
 _atom_type_symbol
 _atom_type_description
 _atom_type_scat_dispersion_real
```

```
 _atom_type_scat_dispersion_imag
 _atom_type_scat_source
 'C'  'C'   0.0033   0.0016
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'H'  'H'   0.0000   0.0000
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'N'  'N'   0.0061   0.0033
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'O'  'O'   0.0106   0.0060
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'S'  'S'   0.1246   0.1234
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'


# CRYSTAL DATA

_symmetry_cell_setting            monoclinic
_symmetry_space_group_name_H-M    'P 21/n'
_symmetry_space_group_name_Hall   '-P 2yn'
_symmetry_Int_Tables_number       14

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

_cell_length_a                    9.3830(19)
_cell_length_b                    5.9990(12)
_cell_length_c                    29.850(6)
_cell_angle_alpha                 90.00
_cell_angle_beta                  98.42(3)
_cell_angle_gamma                 90.00
_cell_volume                      1662.1(6)
_cell_formula_units_Z             4
_cell_measurement_temperature     173(2)
_cell_measurement_reflns_used     2847
_cell_measurement_theta_min       4.409
_cell_measurement_theta_max       54.817

_exptl_crystal_description        block
_exptl_crystal_colour             colourless
_exptl_crystal_size_max           0.43
_exptl_crystal_size_mid           0.20
_exptl_crystal_size_min           0.05
_exptl_crystal_density_meas       ?
_exptl_crystal_density_diffrn     1.428
_exptl_crystal_density_method     'not measured'
_exptl_crystal_F_000              744
_exptl_absorpt_coefficient_mu     0.336
_exptl_absorpt_correction_type    'multi-scan'
_exptl_absorpt_correction_T_min   0.8689
_exptl_absorpt_correction_T_max   0.9834
_exptl_absorpt_process_details    '(SADABS; Sheldrick, 2004)'
```

Data for compound 35k (chapter 5):

```
# CHEMICAL DATA

_chemical_name_systematic
;
```

```
 ?
;
_chemical_name_common             ?
_chemical_melting_point           ?
_chemical_formula_moiety          ?
_chemical_formula_sum
 'C20 H21 N O5 S'
_chemical_formula_weight          387.44

loop_
 _atom_type_symbol
 _atom_type_description
 _atom_type_scat_dispersion_real
 _atom_type_scat_dispersion_imag
 _atom_type_scat_source
 'C'  'C'   0.0033   0.0016
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'H'  'H'   0.0000   0.0000
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'N'  'N'   0.0061   0.0033
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'O'  'O'   0.0106   0.0060
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
 'S'  'S'   0.1246   0.1234
 'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting            monoclinic
_symmetry_space_group_name_H-M    'C 2/c'
_symmetry_space_group_name_Hall   '-C 2yc'
_symmetry_Int_Tables_number       15

# CRYSTAL DATA

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

_cell_length_a                    26.319(5)
_cell_length_b                    9.903(2)
_cell_length_c                    17.239(3)
_cell_angle_alpha                 90.00
_cell_angle_beta                  123.40(3)
_cell_angle_gamma                 90.00
_cell_volume                      3751.1(13)
_cell_formula_units_Z             8
_cell_measurement_temperature     173(2)
_cell_measurement_reflns_used     7494
_cell_measurement_theta_min       5.659
_cell_measurement_theta_max       70.541

_exptl_crystal_description        block
_exptl_crystal_colour             colourless
_exptl_crystal_size_max           0.37
_exptl_crystal_size_mid           0.25
_exptl_crystal_size_min           0.21
_exptl_crystal_density_meas       ?
```

```
_exptl_crystal_density_diffrn     1.372
_exptl_crystal_density_method     'not measured'
_exptl_crystal_F_000              1632
_exptl_absorpt_coefficient_mu     0.204
_exptl_absorpt_correction_type    'multi-scan'
_exptl_absorpt_correction_T_min   0.9283
_exptl_absorpt_correction_T_max   0.9584
_exptl_absorpt_process_details    '(SADABS; Sheldrick, 2004)'


# EXPERIMENTAL DATA

_exptl_special_details
;
 ?
;

_diffrn_ambient_temperature       173(2)
_diffrn_radiation_wavelength      0.71073
_diffrn_radiation_type            MoK\a
_diffrn_radiation_source          'sealed tube'
_diffrn_radiation_monochromator   graphite
_diffrn_measurement_device_type   'Bruker-Nonius Apex X8-CCD-
diffractometer'
_diffrn_measurement_method        '\w scans'
_diffrn_detector_area_resol_mean  ?
_diffrn_standards_number          ?
_diffrn_standards_interval_count  ?
_diffrn_standards_interval_time   ?
_diffrn_standards_decay_%         ?
_diffrn_reflns_number             33165
_diffrn_reflns_av_R_equivalents   0.0223
_diffrn_reflns_av_sigmaI/netI     0.0184
_diffrn_reflns_limit_h_min        -36
_diffrn_reflns_limit_h_max        36
_diffrn_reflns_limit_k_min        -13
_diffrn_reflns_limit_k_max        13
_diffrn_reflns_limit_l_min        -24
_diffrn_reflns_limit_l_max        19
_diffrn_reflns_theta_min          2.38
_diffrn_reflns_theta_max          30.00
_diffrn_measured_fraction_theta_max    0.999
_diffrn_reflns_theta_full              30.00
_diffrn_measured_fraction_theta_full   0.999
_reflns_number_total              5454
_reflns_number_gt                 4696
_reflns_threshold_expression      >2sigma(I)

_computing_data_collection        'Bruker Apex v2.0-2'
_computing_cell_refinement        'Bruker Apex v2.0-2'
_computing_data_reduction         'Bruker SAINT'
_computing_structure_solution     'SHELXS-97 (Sheldrick, 1997)'
_computing_structure_refinement   'SHELXL-97 (Sheldrick, 1997)'
_computing_molecular_graphics     'ORTEP-3 (Farrugia, 1997)'
_computing_publication_material   'SHELXL-97'
```

Curriculum Vitae

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  Title: *Synthesis of Homophthalates, 2-(Arylsulfonyl)pyridines, 6-(Thien-2-yl)salicylates, Dibenzo[b,d]pyran-6-ones, Trifluoromethyl- and Fluoro-Substituted Biaryls by [4+2] and [3+3] Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes*

- HEJ Research Institute of Chemistry, University of Karachi, Pakistan
  Research Fellow, Supramolecular Chemistry, **2004-2006**
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- **Master of Science,** Chemistry, **2003**
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Scholarships & Awards:

- Split Ph.D Scholarship from Higher Education Commission of Pakistan (Jan 2005 to July 2008)
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Advanced Courses Attented:

1- Advanced Course in "X-Ray Crystallography" at H.E.J Research Institute of Chemistry, University of Karachi, Pakistan (May 2005).
2- Four full fledge courses in Advanced Organic Chemistry with "A" grade at H.E.J Research institute of Chemistry, University of Karachi, Pakistan (May 2004-Nov.2004.
3- A Course on "Polymer Characterization and Carbon Nanotubes" at H.E.J Research Institute of Chemistry, University of Karachi, Pakistan (Jan. 2005).
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Research Publications:

1- ***Ibrar Hussain,*** Mirza A. Yawer, Matthias Lau, Thomas Pundt, Christine Fischer, Helmut Reinke, Helmar Görls, Peter Langer, *Eur. J.Org. Chem*. **2008**, 503-508. "Regioselective Synthesis of Fluorinated Phenols, Biaryls, 6H-Benzo[c]chromen-6-ones and Fluorenones based on Formal [3+3] Cyclizations of 1,3-Bis(Silyl Enol Ethers)".
2- ***Ibrar Hussain***, Van Thi Hong Nguyen, Mirza Arfan Yawer, Tuan Thanh Dang, Christine Fischer, Helmut Reinke, Peter Langer, *J. Org. Chem.* **2007**, *72*, 6255-6258. "Synthesis of Dibenzo[b,d]pyran-6-ones based on [3+3] Cyclizations of 1,3-Bis(Silyl Enol Ethers) with 3-Silyloxy-2-en-1-ones".
3- ***Ibrar Hussain***, Mirza Arfan Yawer, Abdolmajid Riahi, Alexander Villinger, Christine Fischer, Helmar Görls, Peter Langer, *Org. Bio.Mol. (submitted)*. "One-Pot Synthesis of 6-(Thien-2-yl)- and 6-(Fur-2-yl)salicylates based on Regioselective [3+3] Cyclizations of 1,3-Bis(trimethyl-silyloxy)-1,3-butadienes".
4- ***Ibrar Hussain***, Mirza Arfan Yawer, Bettina Appel, Muhammad sher, Ahmad S.A. Mahal, Alexander Villinger and Peter Langer, *Org. Bio.Mol. (submitted). "*Synthesis of 4-Hydroxy- and 2,4-Dihydroxy-homophthalates by [4+2] Cycloaddition of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Dimethyl Allene-1,3-dicarboxylate".
5- ***Ibrar Hussain***, Mirza Arfan Yawer, Alexander Villinger and Peter Langer, *Org. Bio.Mol. (submitted). "*Synthesis of 4-Hydroxypyridines by Hetero-Diels-Alder Reaction of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Arylsulfonyl Cyanide. *Manuscript in Preparation".*

6- Mirza A. Yawer, ***Ibrar Hussain***, Inam Iqbal, Anke Spannenberg, and Peter Langer, *Tetrahedron Letters.* (accepted). "Synthesis of Functionalized Dibenzo[*b*,*d*]pyrid-6-ones based on a [3+3]-Cyclocondensation / Lactamization Strategy".

7- Mirza A. Yawer, ***Ibrar Hussain***, Andreas Schmidt, Jörg-Peter Gütlein, Haijun Jiao, Helmut Reinke, and Peter Langer, *Chem. Eur. J* (submitted). "Synthesis of Functionalized Isobenzomorphans by Two-Step Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with Isoquinolines".

8- Mirza Arfan Yawer, ***Ibrar Hussain***, Stefanie Reim, Zafar Ahmed, Ehsan Ullah, Inam Iqbal, Christine Fischer, Helmut Reinke, Helmar Görls, and Peter Langer, *Tetrahedron* **2007**, *63*, 12562-12575. "Regioselective Synthesis of 4-Chlorophenols, 10-Chloro-7-hydroxy-6H-benzo[c]chromen-6-ones and 4-Chloro-1-hydroxy-9H-fluoren-9-ones based on [3+3] Cyclizations of 1,3-Bis(silyloxy)-1,3-dienes with 2-Chloro-3-silyloxy-2-en-1-ones".

9- Mirza A. Yawer, ***Ibrar Hussain***, Christine Fischer, Helmar Görls, Peter Langer, *Tetrahedron* **2008**, in print (Symposium-in-print). "Synthesis of 2-Benzoyl-4-(2-hydroxybenzoyl)phenols by Catalytic Domino ′Michael-Retro-Michael-Mukaiyama-Aldol′ Reactions of 1-Aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylchromones".

10- Thomas Pundt, Matthias Lau, ***Ibrar Hussain***, Mirza, A. Yawer, Helmut Reinke, Peter Langer, *Tetrahedron Lett.* **2007**, *48*, 2745-2747. "One-Pot Synthesis of Aryl Fluorides by [3+3] Cyclization of 1,3-Bis(Silyl Enol Ethers) with 2-Fluoro-3-silyloxy-2-en-1-ones."

11- Rüdiger Dede, Lars Michaelis, Dilver Fuentes, Mirza A. Yawer, ***Ibrar Hussain***, Christine Fischer, Peter Langer, *Tetrahedron* **2007**, *63*, 12547-12561. "Synthesis of 4-Alkoxycarbonyl-butenolides by Uncatalyzed One-Pot Cyclization of 1,3-Bis(silyloxy)alk-1-enes with Oxalyl Chloride".

12- Mirza Arfan Yawer, abdolmajid Riahi, Muhammad Adeel, ***Ibrar Hussain***, Christine Fischer, Peter Langer. *Synthesis* **2008**. (accepted). "One-pot synthesis of 6-(pyridyl)salicylates by formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 3-pyridyl-3-silyloxy-2-en-1-ones"

Declaration/Erklärung

Here by I declare that this work has so for neither submitted to the Faculty of Mathematics and Natural Sciences at the University of Rostock nor to any other scientific Institution for the purpose of doctorate. Further more, I declare that I have written this work by myself and that I have not used any other sources, other than mentioned earlier in this work.
Hiermit erkläre ich, daß diese Arbeit bisher von mir weder an der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock noch einer anderen wissenschaftlichen Einrichtung zum Zwecke der Promotion
Eingereicht wurde.
Ferner erkläre ich, dass ich diese Arbeit selbständig verfasst und keine anderen als die darin angegebenen Hilfsmittel benutzt habe

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

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Ibrar Hussain