Universität Rostock Traditio et Innovatio

Synthesis of Hydroxybenzodioates, Aminophenols and Diaryl Selenides by [3+3] Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes with 3-Silyloxy- and 3-Alkoxy-2-en-1-ones

DISSERTATION

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Eidesstattliche Erklärung

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

Mohanad Gh. Shkoor

Rostock, 15th. Sep. 2010

Affectionately Dedicated to

My father and mother, who taught me not to say I can’t, but I will try

My beloved Brothers and Sister, who are always there when I’m in need

My uncles and aunts for their encouragement and care

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In the name of ALLAH, the beneficent, the merciful, who is Ubiquitous, Omniscient, worthy of all praise, without his blessings this work would never been accomplished.

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List of abbreviations:

Å	Angestrom
Ac	Acetyl
Anal.	Elemental analysis
Ar	Aromatic
br. (NMR)	Broad
Calcd.	Calculated
CI	Chemical ionization
CPME	Cyclopentyl methyl ether
<(DHA) (in x-ray analysis)	Angle (Donor-Hydrogen-Acceptor)
d(D-H) (in x-ray analysis)	Distance (Donor-Hydrogen)
d(H...A) (in x-ray analysis)	Distance (Hydrogen-Acceptor)
DMADC	Dimetyl acetylenedicarboxylate
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
d (NMR)	Doublet
dd (NMR)	Doublet of doublets
eq.	Equivalent
Eq.	Equation
ESI	Electrospray ionization
Et	Ethyl
Fig.	Figure
GC.	Gas Chromatography
h	Hour
HIV 1	Human immunodeficiency virus (type 1)
HRMS	High resolution mass spectrometry
Hz	Hertz
^{n}J (NMR)	Coupling constant (over n bonds)
IR	Infrared spectroscopy
K	Temperature (Kelvin)
LDA	Lithium diisopropylamide

m (NMR)	Multiplet
m (IR)	Medium
Me	Methyl
Me_3SiCl = TMSCl	Chlorotrimethylsilane, trimethylsilyl chloride
Me_3SiOTf	Trimethylsilyl trifluoromethanesulfonate
m.p.	Melting point
MS	Mass Spectrometry
NaHMDS	Sodium hexamethyldisilazane
n-Bu	Normal butane
n-Dec	Normal decane
n-Hep	Normal heptane
n-Hex	Normal hexane
NMR	Nuclear magnetic resonance (^{1}H: proton, ^{13}C: Carbon 13)
n-Non	Normal nonane
n-Oct	Normal octane
NOESY	Nuclear overhauser and exchange spectroscopy
NOE	Nuclear overhauser effect.
n-Pen	Normal pentane
n-Pr	Normal propane
ORTEP	Oak ridge thermal ellipsoid plot
OTf	Triflate
Ph	Phenyl
ppm	Parts per million
q (NMR)	Quartet
$(Rh(OH)(cod))_2$	Hydroxy(cyclooctadiene)rhodium(I) dimer
ref.	reference
r.t.	Room temperature
s (NMR)	Singlet
s (IR)	Strong
SET	Single electron transfer
t (NMR)	Triplet
T. (^{o}C)	Temperature (degree Celsius, Centigrade)

t-BuOk	Potassium tertiary butoxide
ter.	tertiary
TfOH	Trifluoromethanesulfonic acid, triflic acid
THF	Tetrahydrofuran
TMS	Tetramethylsilane
w (IR)	Weak

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Preface and talk of the dissertation:

Organic chemistry research is essential in the sustenance of all fields of our daily life. Our clothes, fuel, dyes, medicines, plastics, soap, cosmetics, plastics, polymers and other uncountable substances we use are made up of organic compounds.

Synthetic organic chemistry lies in the core of pharmaceutical industry; it contributes to the synthesis of the isolated biologically active ingredients of natural products and mimics them, in addition, to the preparation of new previously designed compounds that can serve as drugs. For example, the synthesis of penicillin by Sheehan and Henery-Logan [1] and of vancomycin by Nicolaou [2] and independently by Evans [3], in addition to the semi-synthetic process of Taxol by Holton, which allowed Taxol to be used clinically on a large scale [4-6], can be considered as breakthroughs in synthetic organic chemistry.

Due to this essential role in our life, development of new synthetic methods with high chemo, regio- and stereoselectivities accompanied by ecologically and economically favorable production lies in the heart of organic chemistry.

An important category of organic compounds is the group of highly functionalized benzenes. The regioselective synthesis of these compounds is a great challenge for synthetic organic chemists; due to their important roles in organic chemistry, natural product chemistry, analytical chemistry and materials science [7].

The synthesis of highly substituted benzene compounds starting from acyclic precursors, in which the substitution pattern of the final product is governed by the structures and the patterns of the starting materials, received a great interest from synthetic organic chemists. Formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles provide a convenient and regioselective approach to arenes.

This synthetic approach has been extensively explored by our group. In continuation of the contributions of my previous and current colleagues, I have applied this approach for the synthesis of different substituted arenes, which are not easily accessible by other methods, namely: 4-hydroxyisophthalates, 1-hydroxyphthalates, 2-hydroxy-terephthalates, 4-nitro- and 4-aminophenols and diaryl selenides.

My results of this work are published in scientific articles as follows:

1. **Mohanad Shkoor**, Abdolmajid Riahi, Olumide Fatunsin, Ibrar Hussain, Mirza A. Yawer, Mathias Lubbe, Stefanie Reim, Helmut Reinke, Christine Fischer, Peter Langer*, "Diversity-Oriented Synthesis of 1-Hydroxy-2,4-benzodioates by Regioselective [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with 3-Alkoxy- and 3-Silyloxy-2-alkoxycarbonyl-2-en-1-ones", ***Org. Biomol. Chem***. **2009**, *7*, 2182.
2. **Mohanad Shkoor**, Abdolmajid Riahi, Olumide Fatunsin, Mathias Lubbe, Stefanie Reim, Muhammad Sher, Christine Fischer, and Peter Langer*, "Competing regiodirecting effects of ester and aryl groups in [3+3] cyclocondensations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes. Regioselective synthesis of 1-hydroxyphthalates and 2-hydroxy-terphthalates", ***Eur. J. Org. Chem.*** **2010**, 19, 3732.
3. Abdolmajid Riahi, **Mohanad Shkoor**, Rasheed Ahmad Khera, Helmut Reinke, Peter Langer*,"Regioselective synthesis of functionalized 4-nitro- and 4-aminophenols based on formal [3+3] cyclocondensations of 3-ethoxy-2-nitro-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes", ***Tetrahedron Lett.*** **2009***, 50,* 3017.
4. Abdolmajid Riahi, **Mohanad Shkoor**, Olumide Fatunsin, Mirza A. Yawer, Ibrar Hussain, Christine Fischer, and Peter Langer*, "Synthesis of amino- and nitroarenes based on regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes", ***Tetrahedron***, **2009**, *65*, 9300.
5. **Mohanad Shkoor**, Olumide Fatunsin, Abdolmajid Riahi, Alexander Villinger, Peter Langer*, "Synthesis of Functionalized Diaryl Selenides by the First Formal [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with Organoselenium Compounds", ***Tetrahedron Lett***. **2009**, *50*, 5726.

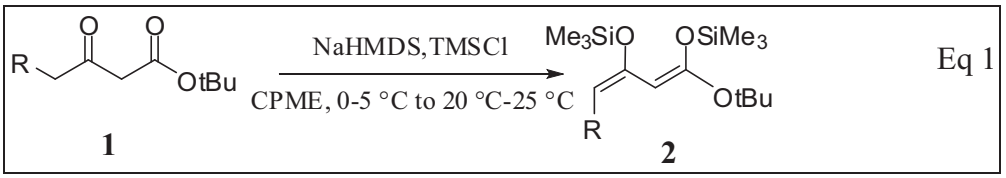
Part 1: Introduction and background:

1.1 1,3-Bis(silyl enol ethers):

The acetoacetate unit is one of the fundamental building blocks in the biogenesis of natural products [9,10]. This fact implies, that 1,3-bis(silyl enol ethers) could be recruited for the synthesis of natural products, especially those including aromatic cores formed from condensation of acetoacetate and derivatives with poly-β-carbonyls.

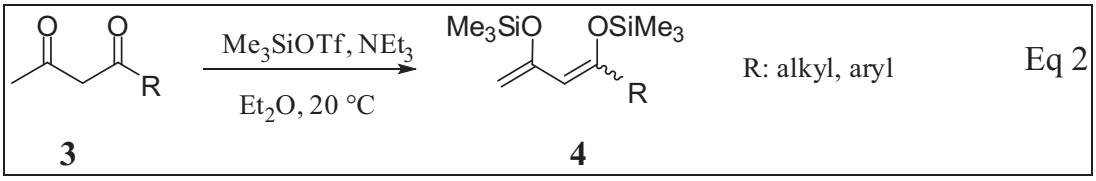
1.1.1 Synthesis of 1,3-bis(silyl enol ethers):

Recently, Tanabe and co-workers [11], have reported a novel regio- and stereoselective synthesis of β-ketoester-derived *tert*-butyl (1*Z*,3*E*)-1,3-bis(TMS) dienol ethers **2** (Eq. 2), in one step using NaHMDS-TMSCl reagent.



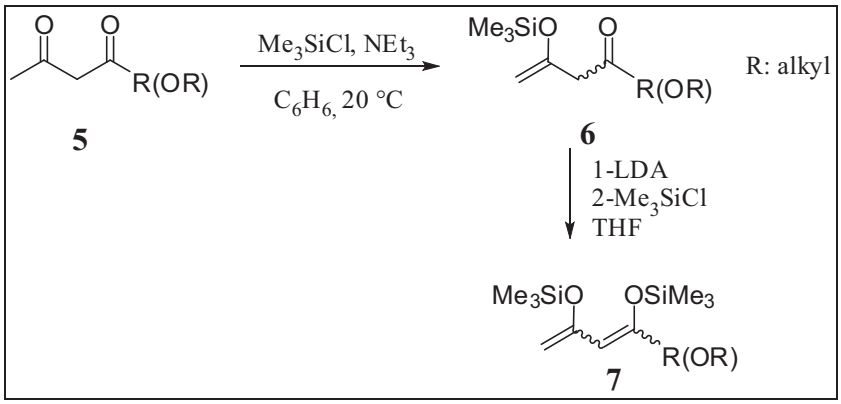
This work was extended by varying the alkoxy group of the ester with a slight modification in the base used therein, thus (1*Z*)- and (1*Z*,3*E*)-1,3-bis(TMS)dienols were steroselectively prepared [12].

Simchen *et al*. [13], reported the one step synthesis of 1,3-bis(sily enol ethers) **4** derived from 1,3-diketones, by treating their ether solution with two equivalents of NEt_3–Me_3SiOTf reagent (Eq. 2). This method lacks substrate generality and requires using expensive reagents.



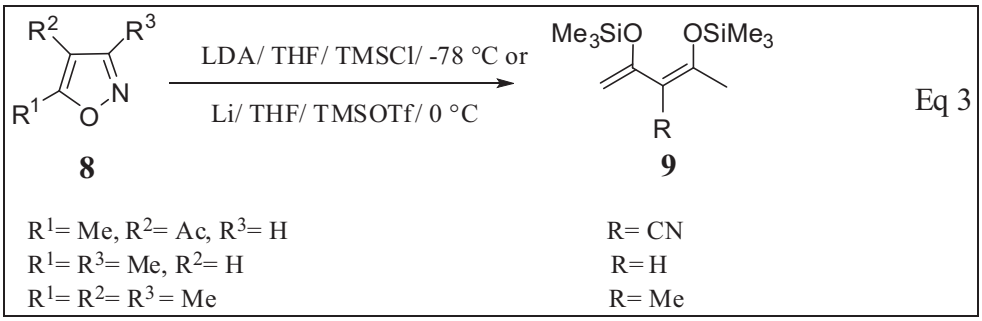
The most widely used synthetic method to produce 1,3-bis(sily enol ethers) was reported by Chan and Molander [14], in which 1,3-dicarbonyl compounds **5** are converted to the

corresponding silyl enol ethers **6** using NEt_3-Me_3SiCl, further silylation, by treating **6** with LDA and subsequent addition of Me_3SiCl to gives **7** (Scheme 1).



Scheme 1: Chan and Molander synthesis of bis(silyl enol ethers).

Barbero *et al*. [15, 16] reported a synthesis of 1,3-diketone-derived bis(silyl enol ethers) **9** by isoxazole ring cleavage and subsequent silylation (Eq. 3).

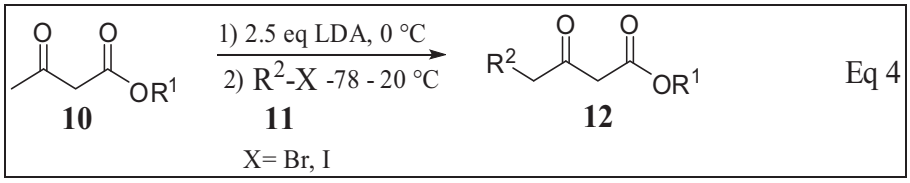


Eq 3

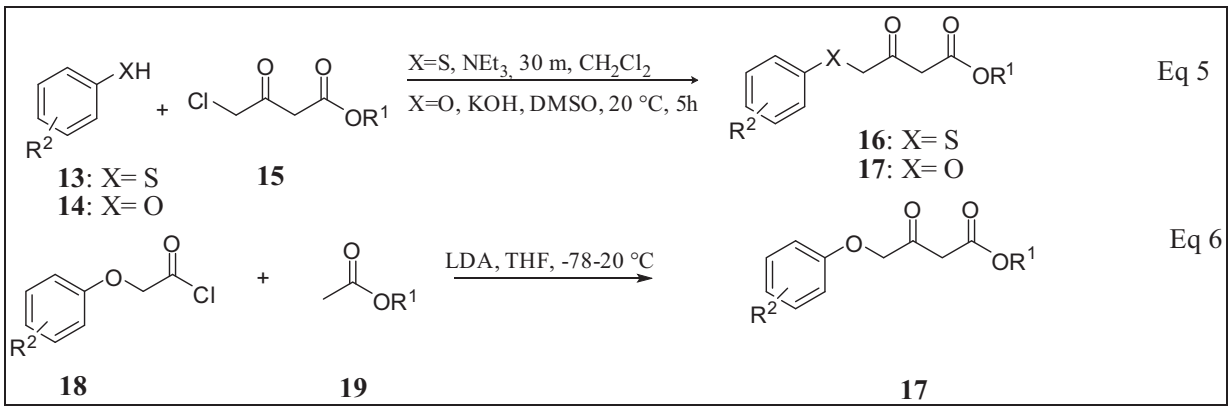
1.1.2 Side chain functionalization of 1,3-bis(silyl enol ethers):

The functionalization of the arenes, resulted from the [3+3] cyclocondensation of 1,3-bis(silyl enol ethers) with dielectrophiles, is goverened by the substitution pattern of both the 1,3-dinucleophile and the 1,3-dielectrophile, however, the functionlization of the side chain of 1,3-bis(silyl enol ether) leads to *ortho*- functionalized phenols, where as the functionlization of the C-2 impedes the aromatization step, and aromatic ring will not form [17].

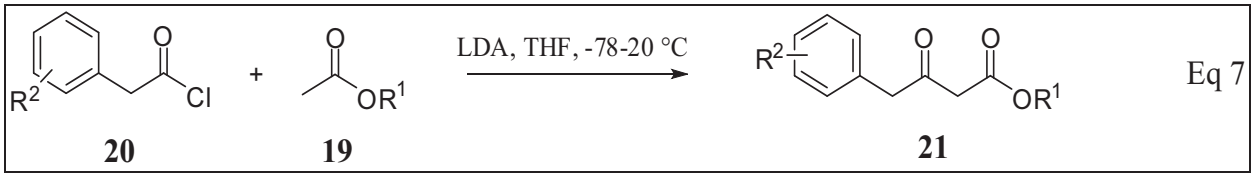
The side chain elongation could be achieved by the reaction of the dianions of alkyl acetoacetates **10** with alkyl bromides or iodides **11** [18] (Eq.4).



Alkyl 4-(thioaryloxy)acetoacetates **16**, were prepared by reaction of alkyl 4-chloroacetoacetates **15** with substituted thiophenols **13**, while alkyl 4-phenoxyacetoacetates **17** were prepared by base mediated reaction of alkyl 4-chloroacetoacetates **15** and functionalized phenols **14** [19, 20] (Eq. 5)**.** Alkyl 4-phenoxyacetoacetates **17** were also prepared by Claisen condensation of alkyl acetates **19** with the corresponding α-aryloxyacetic chlorides **18** [21] (Eq. 6).

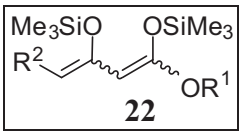


4-Arylacetoacetates **21** were prepared by lithium diisopropylamide mediated reaction of alkyl acetates with the arylacetyl chlorides **20** [22] (Eq. 7).



The β-ketoesters **12**, **15**, **16**, **17** and **21** were then converted to the corresponding 1,3-bis(sily enol ethers).

The 1,3-bis(silyl enol ethers) **22a-u** (Table 1), were prepared and used in the current work.



22

Table 1: Bis(silyl enol ethers) used in current work.

Comp. No.	R^2	R^1
22a	H	Me
22b	H	$(CH_2)_2OMe$
22c	H	CH_2Ph
22d	Me	Me
22e	Me	Et
22f	Et	Me
22g	Et	Et
22h	n-Bu	Me
22i	n-Pen	Me
22j	n-Hex	Me
22k	n-Hep	Me
22l	n-Oct	Me
22m	n-Non	Me
22n	n-Dec	Me
22o	OMe	Me
22p	OPh	Me
22q	$4\text{-}MeC_6H_4$	Me
22r	$4\text{-}ClC_6H_4$	Me
22s	$4\text{-}(MeO)C_6H_4$	Me
22t	$O(2\text{-}MeC_6H_4)$	Et
22u	$O(3\text{-}MeC_6H_4)$	Et
22v	OPh	Et
22w	Cl	Et

Changing the alkyl group of the ester moeity of the dienes **22** affects the physical state of them (viscose to oil), *for example*, in **22w** if R^1 is methyl group the diene will be highly viscous and difficult to handle.

1.1.3 Storage of 1,3-bis(silyl enol ethers):

1,3-Bis(silyl enol ethers) are highly reactive and readily affected by moisture and heat. Due to this high reactivity of 1,3-bis(silyl enol ethers), some precautions should be made in their storage. The freshly prepared 1,3-bis(silyl enol ethers) are stored under inert atmosphere (Argon gas) in cold environment. They can be stored at -30 °C for several months without decomposition or rearrangment.

1.1.4 Reactivity of 1,3-bis(silyl enol ethers):

1,3-Bis(silyl enol ethers), such as 1,3-bis (trimethylsiloxy)-1-methoxybuta-1,3-diene (**22a**), can be regarded as electroneutral equivalents of the dianion **23** (Fig. 1). The *masked* dianion **22a** reacts with electrophiles mostly in the presence of Lewis acids and leads to Michael adducts in its reactions with conjugated carbonyl compounds. This differs from **23**, which is formed and reacted under strong basic conditions. It acts as a hard nucleophile in reactions with conjugated carbonyl compounds to give 1,2-adducts [23, 24].

The fact that reactions of **22a** are conducted under Lewis acids conditions gives more opportunites; electrophiles which are base sensitive could be used, thus 1,3-bis(silyl enol ethers) complement *true* dianions in synthetic organic chemistry.

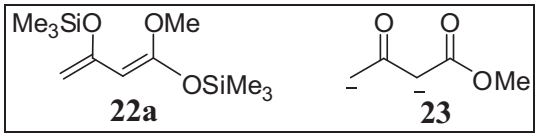


Figure 1: Masked and free dianions of methyl acetoacetate.

Like *true* dianion **23**, *masked* dianions **22** react with electrophiles at their terminal carbon atom (Fig. 2) with difference in reactivity. That could be demonstrated by, for example, reaction of both with bromine. Reaction of **23** gave a mixture of products, while **22a** furnished selectively methyl 4-bromo-3-oxobutanoate in its reaction with one mole of bromine and methyl 2,4-dibromo-3-oxobutanoate with two moles [25]. The nucleophilic reactivity order of the both nucleophilic sites of **22a** doesn't change upon the alkylation of the side chain [17].

In the cases in which the electrophiles are not reactive enough activation by Lewis acids such as titanium tetrachloride is needed [26].

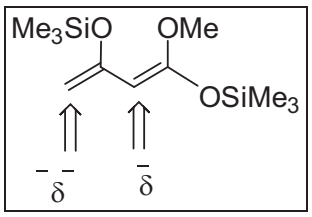
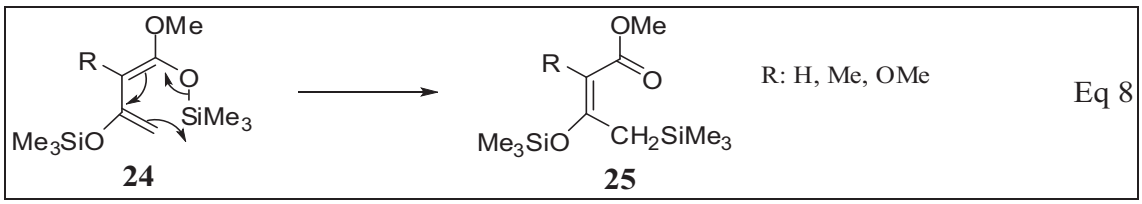


Figure 2: Reactivity of masked dianion **22a**.

Although, the regioselectivites of both dianions and *masked* dianions are the same in most cases, *masked* dianions take the place of the free dianions to avoid their high basicity and reactivity, which lead to many side-reactions such as polymerization, decomposition, deprotonation, formation of open chain products, elimination, or SET-processes (reduction) [27].

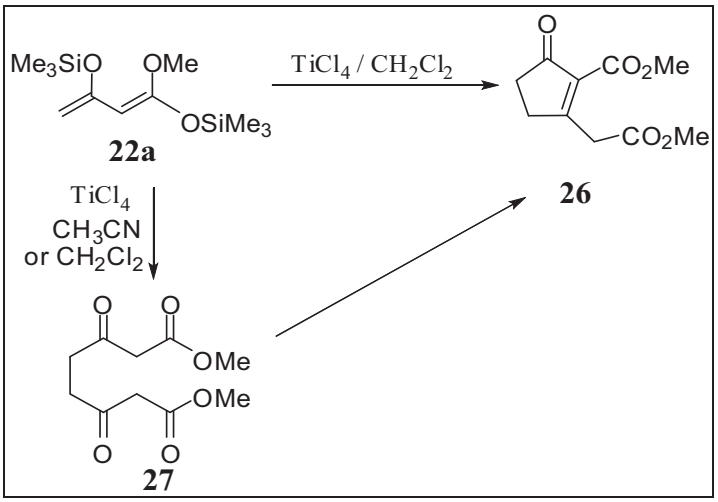
1.1.5 Thermal rearrangement of 1,3-bis(silyl enol ethers):

1,3-Bis(silyl enol ethers) **24**, derived from β-ketoesters with substituents at C2, undergo 1,5 silyl migration from oxygen to carbon to give 4-trimethylsilyl-3-trimethylsilyloxycrotonates **25** (Eq. 8). This occurs upon standing at 20 ºC and involves replacement of a strong O-Si bond with the weaker C-Si, which can be thermodynamically compensated by formation of stable ester carbonyl moiety [28]. Unsubstituted C2 1,3-bis(silyl enol ethers) rearrange in high yields to the corresponding products **25** on heating at 80-120 ºC [29]. The presence of the C2 substituent increases the population of the conformer that undergoes this rearrangement.



1.1.6 Dimerization of 1,3-bis(silyl enol ethers) promoted by $TiCl_4$:

1,3-Bis(silyl enol ethers) undergo oxidative dimerization in the presence of $TiCl_4$ to give **26** or the open chain product **27**, which converts to **26** under $TiCl_4$ activation. $TiCl_4$ acts as an oxidizing agent (Scheme 2) [30-32]. These undesired dimerizations could affect the yields of the [3+3] cyclizations of 1,3-bis(silyl enol ethers).



Scheme 2: Dimerization of **22a** promoted by $TiCl_4$.

1.2 Formal [3+3] cyclization reactions of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles:

One-pot cyclizations of 1,3-dicarbonyl dianions (*true* dianions) and 1,3-bis(silyl enol ethers) *(masked* dianions) with electrophiles provide a convenient strategy to a wide range of heterocyclic and carbacyclic ring systems. Extensive work has been done and still going in these cyclization reactions.

Langer *et al.* reviewed the impressive work in this field: Cyclizations of free and masked 1,3-dicarbonyl dianions with 1,2-dielectrophiles [33], one-pot cyclizations of dinucleophiles with oxalic acid-bis(imidoyl)dichlorides [34], reactions of 1,3-bis(silyl enol ethers) in general [27], syntheses of butenolides by cyclizations of silyl enol ethers with oxalyl chloride [35a] and domino reactions of bis(silyl enol ethers) with 4-silyloxybenzopyrylium triflates [35c] and iminium salts [35d].

In the following work, a strategy based on formal [3+3] cyclization reactions of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles for the synthesis of functionalized arenes was adopted.

The formal [3+3] cyclizations of 1,3-bis(silyl enol ethers) could be performed with different types of 1,3-dielectrophiles, that have different patterns of substituents which provide a powerful tool for the construction of six memebered carbacycles.

The 1,3-dielectrophiles used in formal [3+3] cyclizations with 1,3-bis(silyl enol ethers) could be: 1,3-bis(acetals), 1,3-ketoacetals, 1,3-keto-*S*,*O*-acetals, 3-alkoxy-2-en-1-ones, 3-silyloxy-2-en-1-ones, 1,1-diacylcyclopropanes, 1,1-diacylcyclopentanes and 3-oxoalkanoic acid derivatives [35b]. Lubbe *et al.* have recently reported the first cyclocondensation of 1,3-bis(silyl enol ethers) with 1,1-bis(methylthio)-1-en-3-ones and 3-oxo-orthoesters [36, 37]. Lau *et al*. reported the cyclizations of 1,3-bis(sily enol ethers) with 3-acetyl-5-aryl-4,5-dihydrofurans [38]. Sher *et al*. reported the cyclizations with 3,3-dimethoxypentanoyl chloride [39]. [3+3] cyclizations were also reported with 4-chloro-2-oxo-2*H*-chromene-3-carbaldehyde [40].

The term *formal* is used here to distinguish the cyclizations of 1,3-bis(sily enol ethers) with 1,3-dielectrophiles from the pericyclic cyclizations.

In the current research, two types of 1,3-dielectrophiles were used, namely: ***3-silyloxy-2-en-1-ones*** and ***3-alkoxy-2-en-1-ones***.

1.2.1 Regioselectivity control in the cyclization reactions of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles:

Cyclizations of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles could be simplified as shown in (Fig. 3): fragment 1 represents the 1,3-bis(silyl enol ether) a 1,3-dinucleophile, with C4 more nucleophilic than C2, whereas fragment 2 represents the 1,3-dielectrophile which can be various equivalents of β-dicarbonyl compounds.

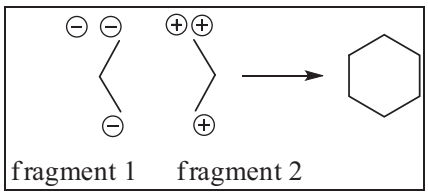


Figure 3: Simplified representation of regioselectivity control in [3+3] cyclizations.

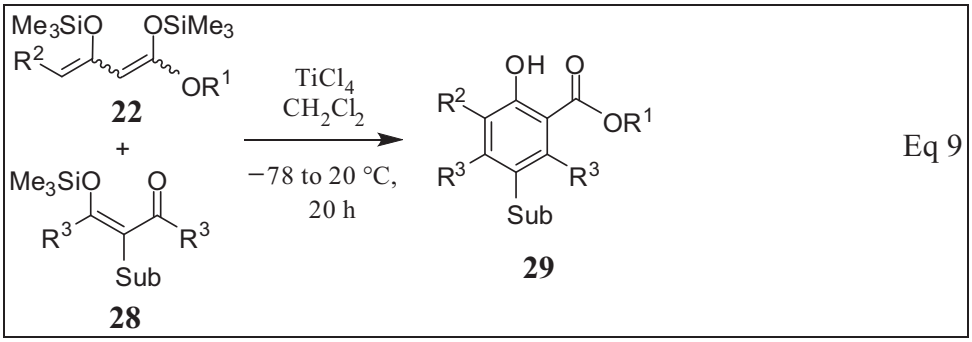
The regiochemistry of these cyclizations is controlled by the differential reactivities of both sites of each fragment. Depending on their experiments in competitive reactions of **22a** with different electrophiles, Chan and co-workers reported that the order of reactivity of electrophiles toward 1,3-bis(sily enol ethers), follows that: aldehyde > conjugate position of β-oxy-α,β-unsaturated ketone~isolated ketone> acetal or monothioacetal> conjugate position of β-oxy-α,β-unsaturated ester or ester carbonyl, thus their attempts to cyclize **22a** with the mono silyl enol ether of its precursor failed [41].

1.2.2 Formal [3+3] cyclization reactions of 1,3-bis(silyl enol ethers) with 3-silyloxy-2-en-1-ones:

The $TiCl_4$ mediated [3+3] cyclocondensation reactions of 1,3-bis(silyl enol ethers) with 3-silyloxy-2-en-1-ones were firstly reported by Chan and co-workers [14a]. When these 3-silyloxy-2-en-1-ones are derived from symmetrical 1,3-diketones, the cyclizations give phenols containing the same substituents located *meta* to the hydroxyl group, via the conjugate addition of the terminal carbon of the 1,3-bis(silyl enol ether) to the conjugate position of 3-silyloxy-2-en-1-ones, followed by cyclization and subsequent aromatization.

Cyclizations of 3-silyloxy-2-en-1-ones derived from unsymmetrical 1,3-dicarbonyl precursors often proceed with low regioselectivity, according to the suggestion Chan [14a], this is a result of the $TiCl_4$-mediated isomerisation of 3-silyloxy-2-en-1-ones (migration of the TMS-group from one oxygen atom to the other), however, some regioselective reactions were reported [14a, 35b].

The mostly used protocol of this strategy is the use of *2-**Sub**-3-silyloxy-2-en-1-ones* **28** derived from symmetrical 1,3-diketones, simplified by (Eq. 9).



Eq 9

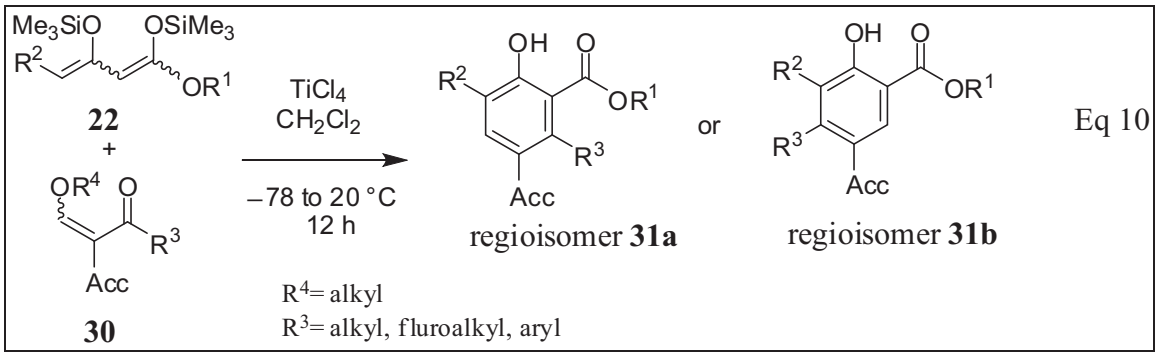
Where ***Sub*** could, *for example*, be: Me [42], $CH(Ph)_2$ [43], CN [44], Ph [45], -N=N-Ph [46], F [47], SPh [19], OPh, Cl [48], Ac [49], OAc [50].

1.2.3 Formal [3+3] cyclization reactions of 1,3-bis(silyl enol ethers) with 3-alkoxy-2-en-1-ones:

Chan and Brownbridge were the first to report a regioselective cyclocondensation of 1,3-bis(silyl enol ether) with 3-alkoxy-2-en-1-one [14a]. Recently, I have been a member in a work-team within our group responsible for the investigation of the scope of the cyclizations of the type 2-acceptor-substituted 3-alkoxy-2-en-1-ones **30**. Some of these cyclizations are still under study at the time of writing of this work.

These cyclizations proceed with high regioselectivity; this might be explained by the fact that these substrates do not undergo $TiCl_4$-mediated isomerisation, for more detailed information about this type of cyclization see [ref. 35b].

This strategy could be simplified as in (Eq. 10).



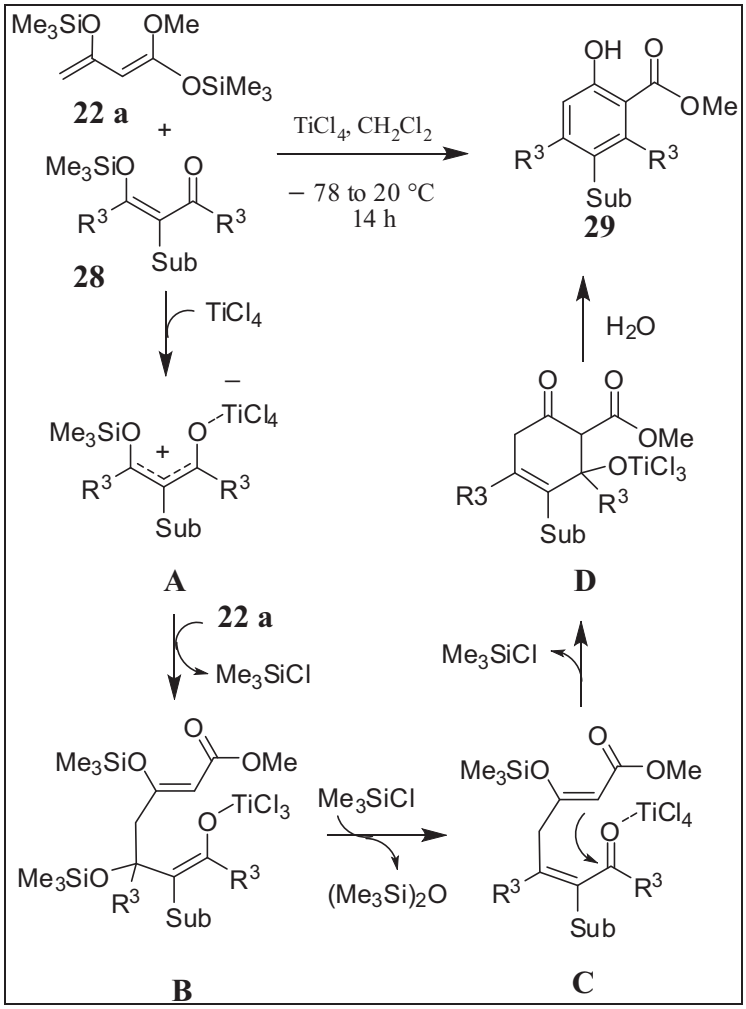
During the course of this research, it was noticed that these cyclizations mostly gave the regioisomer **31a**, resulted from the initial attack of the terminal carbon of the diene onto the conjugate position of **30**.

These acceptor-substituents could be: $-SO_2Ph$ [51], CN [44], $-(CO)CO_2R$, $-(CO)CF_3$ and-(CO)R [52a,b], Cl [53], -SAr [54], $-PO(OEt)_2$ [55] and others, will be included in this manuscript and the rest will be published in the due time.

There are some reported cases in which 3-alkoxy-2-en-1-ones polymerized by $TiCl_4$ [14a], a fact that could affect the yields of their [3+3] cyclizations.

1.2.4 Suggested mechanism of 1,3-bis(silyl enol ether) cyclization with 1,3-dielectrophiles:

Titanium tetrachloride is a Lewis acid which has a great affinity for organic oxygenated compounds. Powerfull activation of carbonyl compounds by $TiCl_4$ allows that silyl enol ethers can readily attack carbonyl compounds to form trimethylsilyl chloride and the titanium salt of the aldol-type products [56]. This fact allows us to draw a *possible* mechanistic pathway for the cycloaromatizations of 1,3-bis(silyl enol ethers) with 3-silyloxy-2-en-1-ones (Scheme 3).

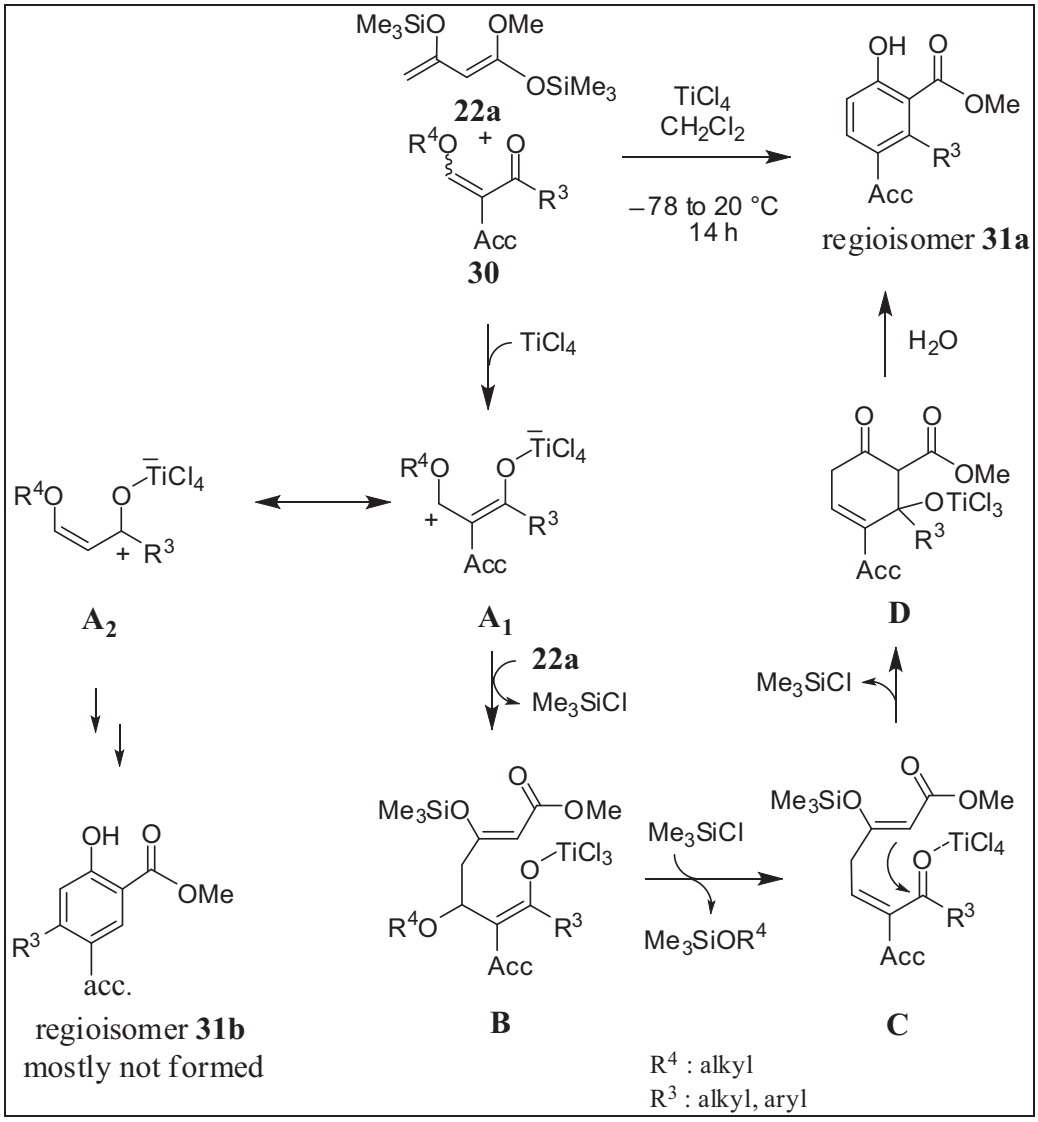


Scheme 3: Suggested mechanism for the cycloaromatization of **22a** with 3-silyloxy-2-en-1-ones.

It is suggested that the reaction starts by reaction of **28** with $TiCl_4$ to give *intermediate **A***, followed be the attack of the terminal carbon atom of **22a** onto **A** to afford *intermediate **B***. The elimination of TMS-siloxane *intermediate **C*** and subsequent cyclization gives *intermediate **D*** (Scheme 3). The elimination of titanium hydroxide (before or during the aqueous work-up) and aromatization results in the formation of **29**.

Due to the symmetrical structure of *intermediate **A***, the attack of **22a** on either terminal allylic carbon atom would result in the formation of the same product.

In analogy to this, a general mechanistic pathway for the cyclocondensation of 1,3-bis(silyl enol ethers) with 3-alkoxy-2-en-1-ones could be also drawn as in Scheme 4.



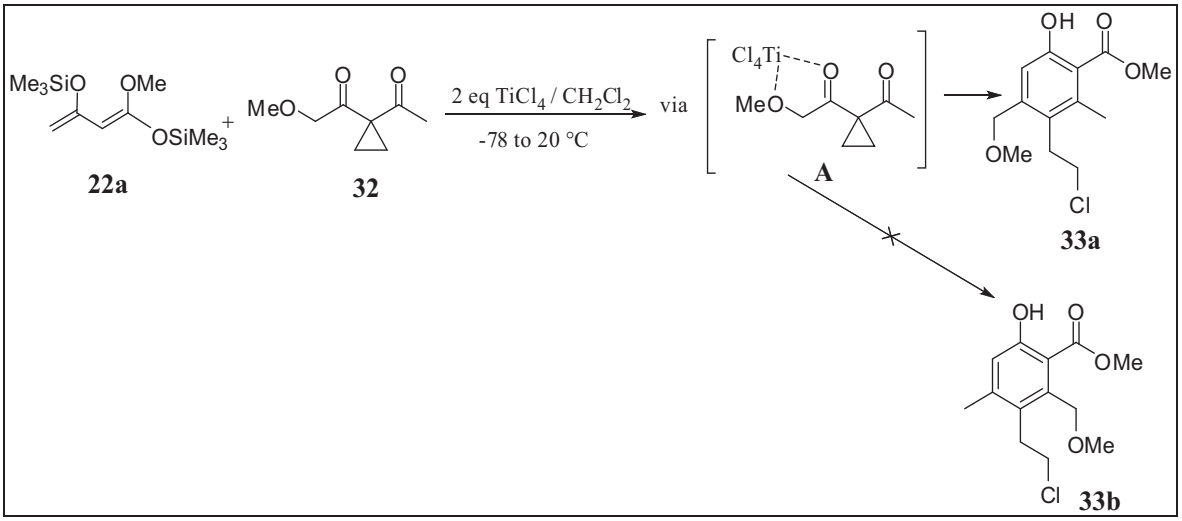
Scheme 4: Suggested mechanism for the cycloaromatization of **22a** with 3-alkoxy-2-en-1-ones.

The formation of product **31a** might be explained by reaction of **30** with $TiCl_4$ to give *intermediate **A**$_1$*, which is in resonance with *intermeidate **A**$_2$*. The regioselectivity might be explained by the steric hindrance of the allylic carbon attached to the alkyl or the aryl group R^3. Cyclization through *intermediate **A**$_1$* (Scheme 4) gives *intermediate **B***, followed by formation of *intermediate **C***. Cyclization via the central carbon *intermediate **D*** and subsequent aromatization gives **31a**.

1.2.5 Regioselectivity tuning. Lewis acid chelation control in [3+3] cyclizations of 1,3-bis(silyl enol ethers) with dielectrophiles:

The ability of Lewis acids to form a five- or a six- membered chelation ring [57, 58] within the 1,3-dielectrophile leads to a selective activation of one of the two electrophilic centers, directing the reaction pathway to form exclusively one of the possible isomers. In case of unsymmetrical 3-silyloxy-2-en-1-ones, the Lewis acid promotes the TMS isomerization to form, exclusively, one isomer, which leads to a regioselective cyclization; this will be discussed in the second part of this manuscript.

The $TiCl_4$ mediated cyclization of alkoxy-substituted 1,1-diacylcyclopropanes **32** with 1,3-bis(trimethylsilyloxy)-1,3-butadiene **22a** furnished exclusively 5-chloroethyl-4-(methoxymethyl)salicylate **33a** (Scheme 5) via chelation of $TiCl_4$ with the methoxy and the neighboring carbonyl group [59, 60]. Chelation effect was also observed in the presence of a neighbouring carbonyl group [52].



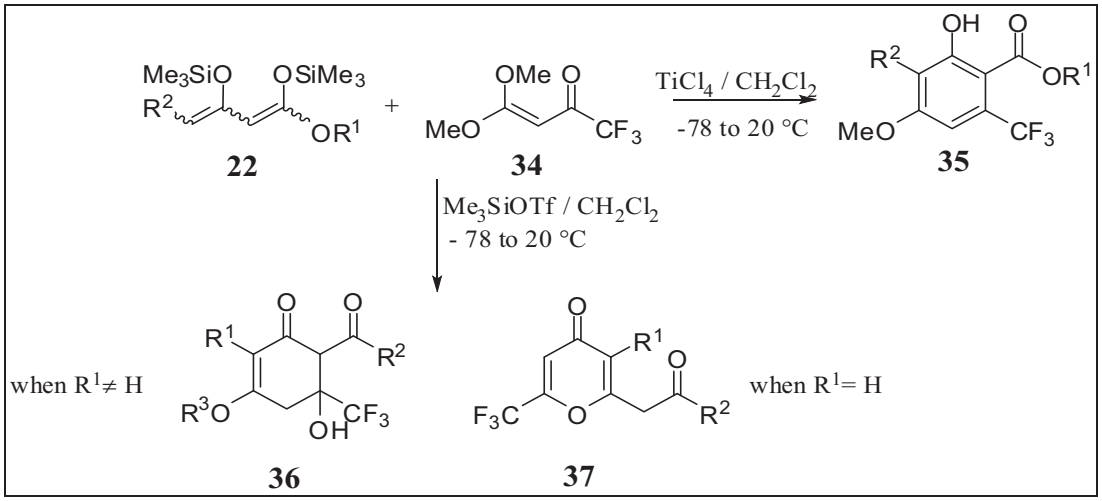
Scheme 5: Lewis acid chelation controlled formation of **33a**.

1.2.6 Influence of the Lewis acid on the outcome of [3+3] cyclizations of 1,3-bis(silyl enol ethers):

The choice of Lewis acid to activate the [3+3] cyclizations of 1,3-bis(silyl enol ethers) can affect the pathway of these reactions. Sher *et al.* reported that $TiCl_4$ mediated cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3,3-dimethoxypentanoyl chloride afforded 4-hydroxysalicylates. But when TMSOTf was used as catalyst 6-hydroxysalicylates were formed [39]. This could be explained by selective activation of electrophilic centers by the Lewis acid. Specific Lewis acids activate specific functional groups.

In other reactions the employment of different Lewis acids gave completely different products. The $TiCl_4$ mediated reaction of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 1,1-dimethoxy-4,4-dichlorobut-1-en-3-one gave 6-dichloromethyl-4-methoxysalicylates. When TMSOTf was employed, functionalized 2-(dichloromethyl)pyran-4-ones were formed in all cases [61].

The $TiCl_4$ mediated formal [3+3] cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes **22** with 4,4-dimethoxy-1,1,1-trifluorobut-3-en-2-one (**34**) gave 4-methoxy-6-(trifluoromethyl)salicylates **35**, while Me_3SiOTf-mediated cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes, containing no substituent located at carbon atom C-4 of the diene, resulted in formation of pyran-4-ones **37** (Scheme 6), while they gave Trifluoromethyl-substituted cyclohexenones **36** when C-4 was substituted [62]. However, the reasons for the influence of the Lewis acid on the regioselectivity of cyclization remain unclear at present.



Scheme 6: Influence of the type of Lewis acid on the regioselectivity of [3+3] cyclocondensations.

1.3 Highly functionalized arenes. Products of [3+3] cyclizations of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles:

Highly functionalized arenes constitute an important class of organic compounds that are widely used in different fields of chemistry.

The "*classical approaches*" for the synthesis of these arenes are based on the direct substitution of an existing benzene scaffold. The most common strategies based on this approach involve: electrophilic [63], or nucleophilic [64] substitution, metal-catalyzed coupling reactions [65], and metalation–functionalization reactions [66].

However, these methods frequently have many drawbacks like: multi-step reaction sequences, low yields, and low positional selectivity of electron-donating or -withdrawing groups and/or from orienting effects of the substituents when applied to the synthesis of highly functionalized arenes.

An efficient alternative approach for the synthesis of highly functionalized arenes is the "*acyclic approach"*, which relies on the construction of the aromatic backbones from acyclic precursors. These annulations include: [3 + 2 + 1] Dötz reaction of Fischer carbene complexes [67], Danheiser alkyne-cyclobutenone [4 + 2] cyclization [68], [4 + 2] cycloaddition of metalacyclopentadienes and alkynes [69], transition metal catalyzed [2 + 2 + 2] and [4 + 2] cycloadditions [70], Yamamoto [4 + 2] benzannulations of o-alkynyl benzaldehydes and alkynes [71], 1,6-electrocyclization reactions [72], [5 + 1] benzannulations between alkenoyl keteneacetals and nitroalkanes [73] and [4 + 2] annulations of Baylis-Hillman adducts [74].

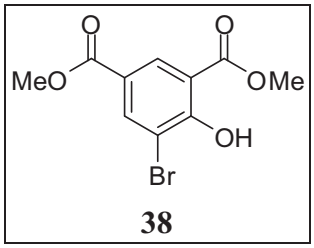
Although these annulations afford variety of substituted arenes, they either lack of substrate generality or require the use of expensive catalysts and involve harsh conditions in some cases.

The $TiCl_4$ mediated [3+3] cyclocondensation reactions of 1,3-bis(silyl enol ethers) with 1,3-dielectrophiles is a strategy which adopts the "*acyclic approach*". Commercially available, easily-accessible building blocks with a wide range of substitution pattern could be used. These regioselective reactions are mostly done in one step under mild conditions with good to excellent yields.

In this Ph.D dissertation, this strategy for the synthesis of some highly functionalized arenes like was utilized: *hydroxybenzodioates*, *4-nitrophenols*, *4-aminophenols* and *diaryl selenides*.

1.3.1 Mono-hydroxybenzodioates:

Functionalized hydroxylated benzoates and benzodioates and their derivatives are of great interest as lead structures in pharmaceutical, industrial and agricultural chemistry and constitute valuable synthetic building blocks in synthetic organic chemistry [75]. Some of these molecules occur in natural products and have interesting pharmacological properties, including: analgesic, antipyretic, antimicrobial and fungicidal (compound **38**) activity and act as inhibitors for some enzymes and inhibitors for the absorption of some steroids, such as, cholestrol and bile acid [76].



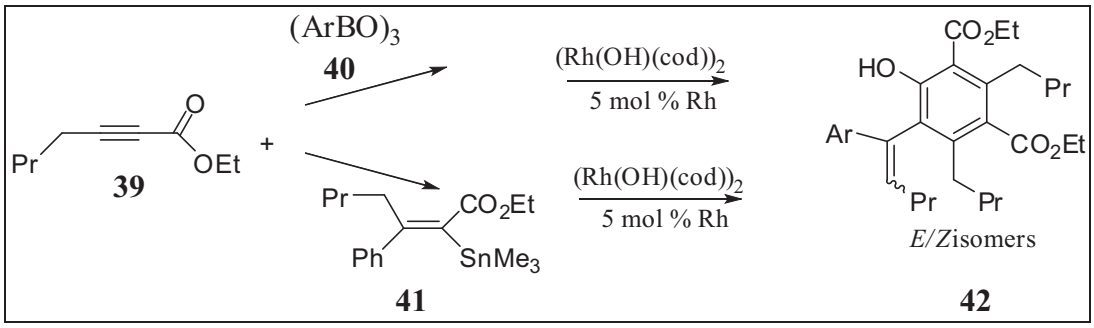
38

Figure 4: Fungicidal agent.

Classically, synthetic approaches to mono-hydroxy benzodioates rely on the oxidations of appropriate benzene derivatives and on the functionalization of phenol or benzoic acid derivatives, including carboxylation of phenols, hydroxylation of aromatic halides and diesters [77- 81].

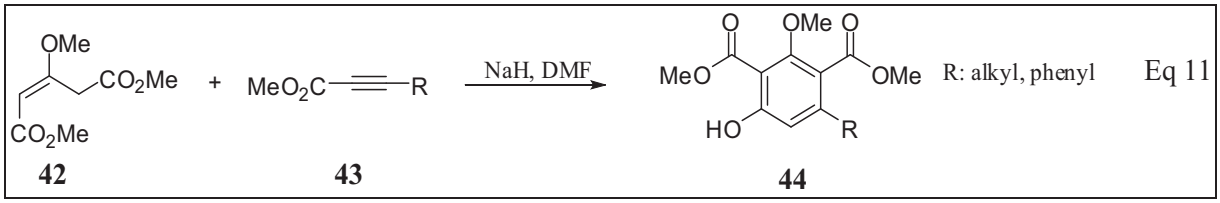
These methods suffer from: poor regioselectivity, harsh reaction conditions which can lead to the destruction of starting precursors. For more complex polyfunctionalized derivatives, highly functionalized or substituted starting materials are not easy accessible.

An alternative approach is based on the annulations of acyclic precursors. Examples of this approach, for the formation of 4-hydroxyisophthaltes, involve: The rhodium catalyzed cyclization reactions (Scheme 7) of alkynoates **39** with alkyl-, aryl-boronic acids and boroxines **40** and tin reagents [82].



Scheme 7: Hayashi and co-workers synthesis of 4-hydroxyisophthalate.

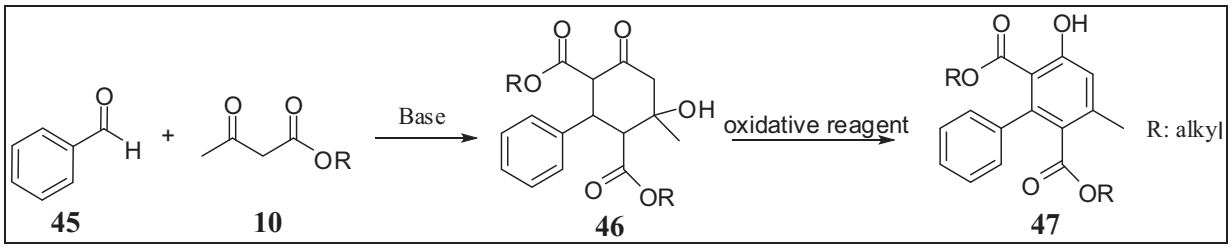
4-Hydroxyisophthalates **44** were also prepared by a Michael addition–Dieckmann cyclization sequence from methyl (*E*)-3-methoxy-4-methoxycarbonylbut-2-enoate (**42**) anion and methyl alkynoates **43** (Eq. 11) and by sodium salt of dimethyl 1,3-acetonedicarboxylate cyclization with acetylenic esters [83].



Cazes *et al.* in their research in the preparation of tetralones, prepared tetralones in which the aromatic rings are 4-hydroxyisophthalte by cyclocondensations of 3-methylcyclohexenones with ethoxymethylenemalonate [84]. Indolylmethyl acetates underwent, upon base-mediated reaction with electron-difficient alkynes, Michael addition followed by intramolecular cyclization and subsequent aromatization and gave substituted carbazoles containing 4-hydroxyisophthaltes and 3-hydroxyphthalates [85].

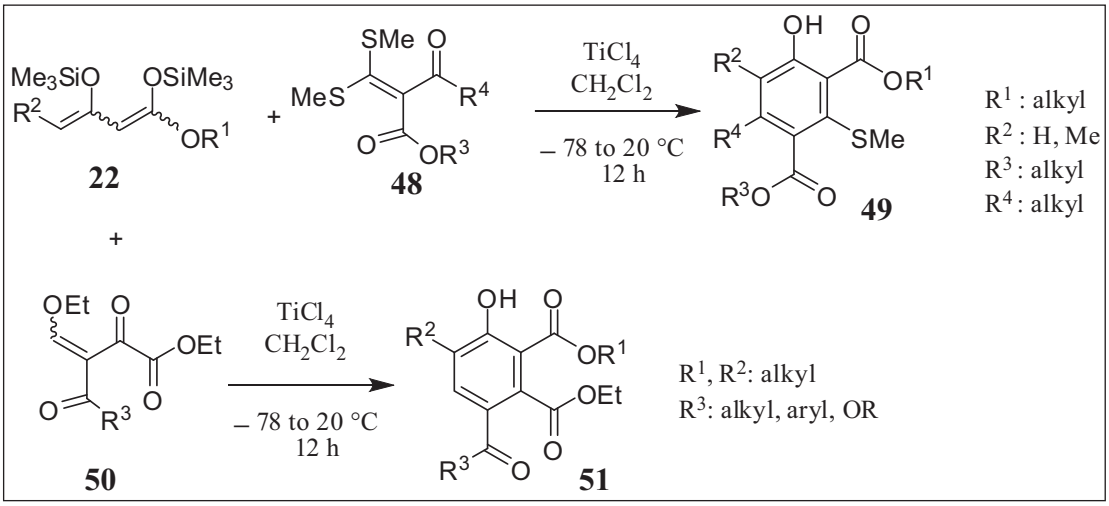
Cyclizations of aromatic aldehydes **45** with β-ketoesters **10** (Scheme 8) followed by oxidative aromatization gave also 4-hydroxisophthalates **47** [86].

4-Hydroxisophthalates were also prepared by oxidative cyclization of ethyl 3-hydroxynon-4-ynoate [87], condensation of methyl 4-(triphenylphosphoranylidene) acetoacetate with methyl 5-methyl-2-(trifluoroacetyl)-2-hexenoate [88] and by [2+2+2] construction of polyfunctionalized cyclohexanones which then underwent aromatization [89].



Scheme 8: Base mediated cyclization of diketoester with aromatic aldehydes.

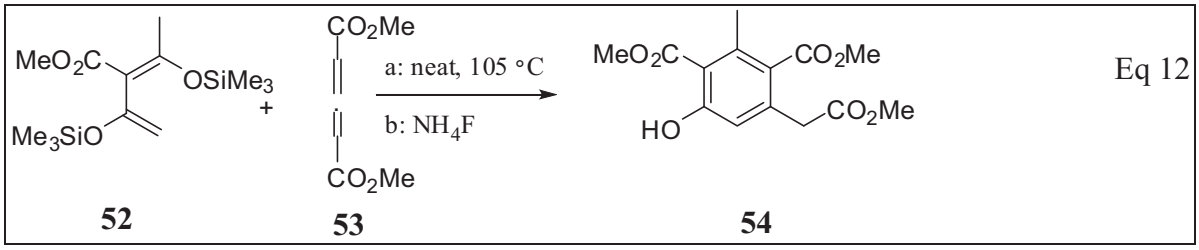
Langer and co-workers reported chealation controlled annulations (Scheme 9) of 1,3-bis(silyl enol ethers) **22** with enones **50** to form hydroxybenzodioates **51** [52a] and with 3-oxo-bis(methylthio)ketenacetale **48** to form isophthaltes **49** [52b].



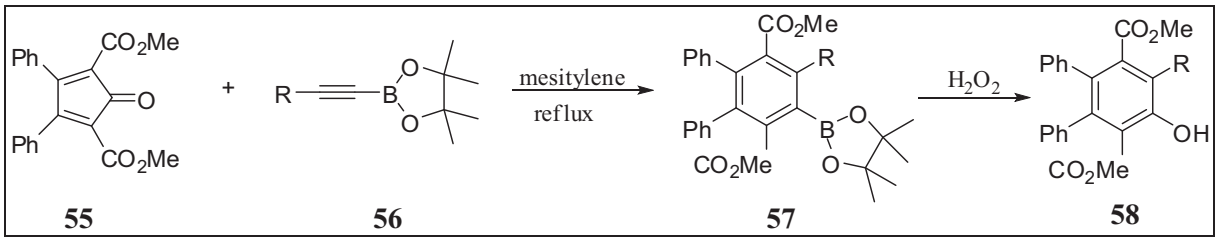
Scheme 9: Langer *et al*. synthesis of hydroxybenzodioates.

"*Acyclic approach*" protocols for the synthesis of 4-hydroxyisophthalates include also cycloaromatization reactions of methyl 4-carbomethoxy-5-methoxy-penta-2,4-dienoate with dimethyl malonate [90] and cyclizations of substituted ethyl 2-(4-oxo-1,4-dihydroquinolin-2-yl)acetates with diethyl(ethoxymethy1ene)malonate to give acridinones containing 4-hydroxyisophthalates [91].

Cycloaddition of 1,3-bis(silyl enol ether) **52** with the allene **53** afforded the isophthalate **54** (Eq. 12) [92].



The Diels-Alder cycloaddition (Scheme 10) of cyclopentadienone **55** with alkynylboronates **56** gave boronic esters **57**, subsequent oxidation gave the 2-hydroxyterephthalates **58** [93].



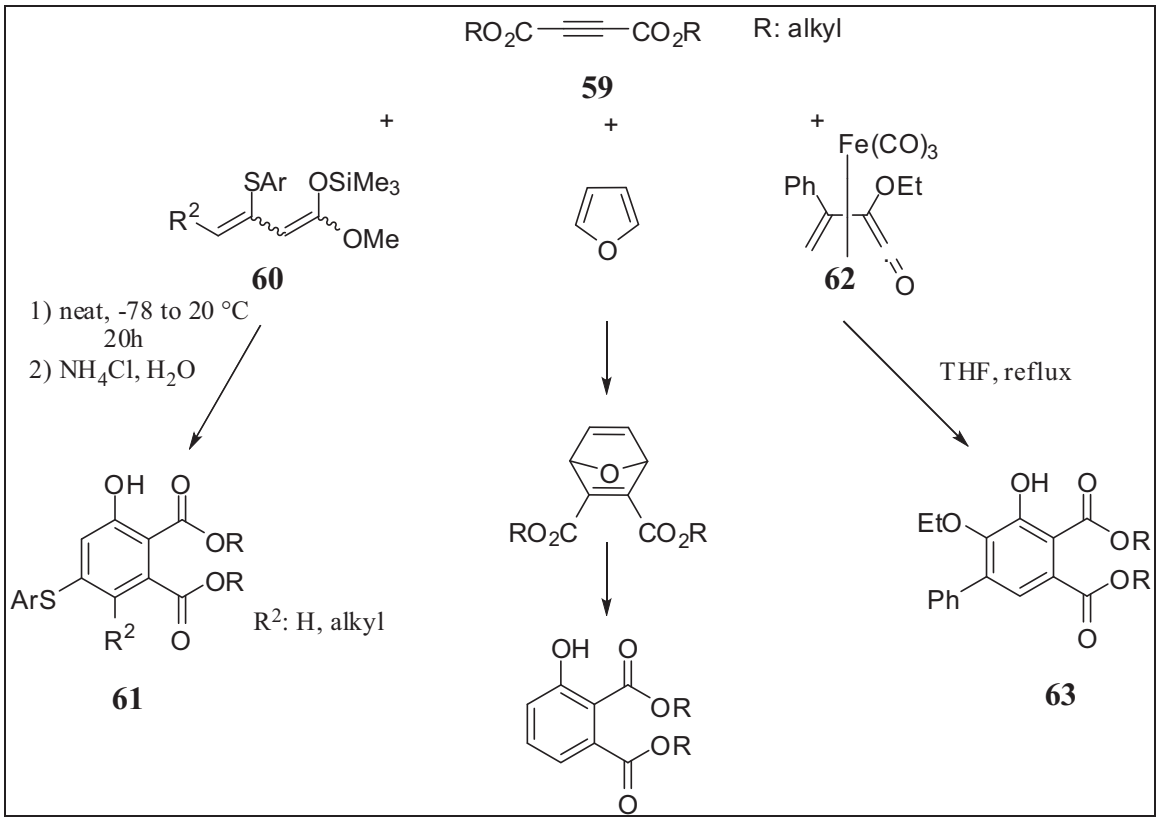
Scheme 10: Synthesis of 2-hydroxyterephthalates by [4+2] annulations.

The syntheses of 3-hydroxyphthalates depend mainly on the annulations of symmetrical dialkyl acetylenedicarboxylates, which provide two vicinal ester moieties in the aromatic ring.

Chan *et al.* and Langer *et al.* reported [4+2] cycloadditions of the dialkylacetylene dicarboxylates **59** (Scheme 11) with substituted butadienes **60** to give the hydroxyphthalates **61** [94].

The Diels-Alder [4+2] cycloadditions of dialkyl acetylenedicarboxylates **59** with substituted and condensed furans were extensively studied [95]. These annulations could be represented in general formula shown in scheme 11. Similar to this, dialkyl acetylenedicarboxylates **59** underwent cyclizations to form 3-hydroxyphthalates, with substituted 3-hydroxy-2-pyrones, substituted furanones [96] and (trialkylsilyl)vinylketenes [97].

Transition metal complexes of vinylketenes undergo annulations to form substituted hydroxyphthalates. Vinylketene complex **62** underwent cyclization (Scheme 11) with **59** and formed phthalate **63** [98]. 3-Hydroxyphthalates were also prepared by dötz annulation [99].



Scheme 11: Diversity-oriented synthesis of 3-hydroxyphthalates.

1.3.2 4-Nitro- and 4-aminophenols:

4-Nitro- and 4-aminophenols are of a great interest in synthetic and pharmaceutical organic chemistry, due to their wide spectrum of biological activities and occurrence in the core structure of many natural products [75a].

4-Nitrophenols are important building blocks in synthetic organic chemistry, routinely they serve as precursors for the corresponding aminoarenes [100]. They show antifungal [101a], antiandrogenetic [101b], vasodilative [101c], estrogenic [101d] and HIV-1 integrase inhibition [101e] activities (Fig. 5).

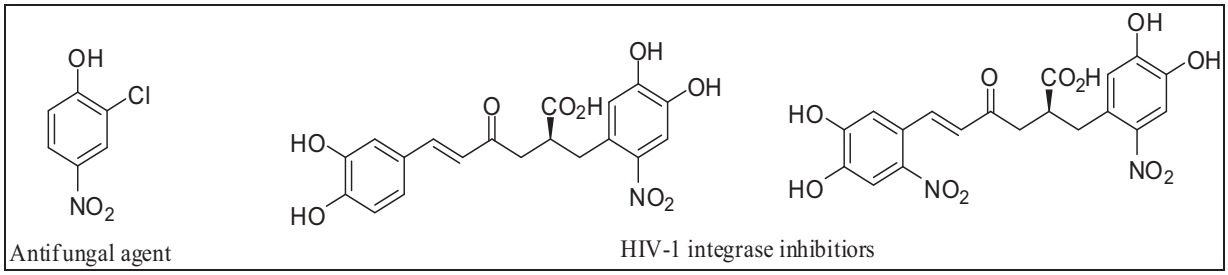
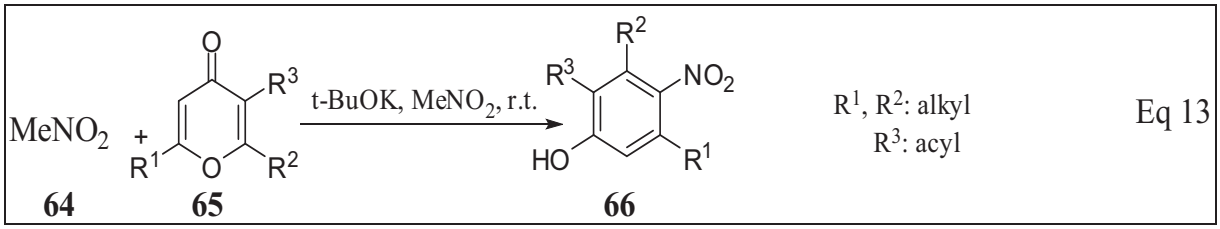


Figure 5: Biologically active nitrophenols.

Classical methods, which start with an existing arene, for the synthesis of 4-nitrophenols involve: catalytic hydroxylation of nitroaryl halides [102], nucleophilic hydroxylation of aromatic nitro compounds [103], oxidation of the corresponding *p*-nitrosophenol [104] and nitration of phenols using different nitrating agents [105].

These methods are accompanied by severe drawbacks. For example, the oxidation of nitrosophenol by using nitric acid results in the evolutoin of toxic nitrogen oxides [99]. The nitration of phenols suffers from the low regioselectivity, overnitration and the oxidation of the substrates. Several side-reactions are possible for functionalized substrates, due to the harsh reaction conditions and steric effects.

"*Acyclic approaches*", which overcome these drawbacks, involve: the base mediated condensations of nitromethane (**64**) (Eq. 13) with 4*H*-pyran-4-ones **65**, which gave 4-nitrophenols **66** [106]. Base mediated cyclocondensations of acetone derivatives with 2-nitromalonaldehyde and 3-nitrochromone also gave substituted nitrophenol [107].



Ariga *et al.* [108] reported the base-mediated cyclization of β-nitroenamine **67** with ketones **68** to give nitrophenols **69** (Eq. 14)

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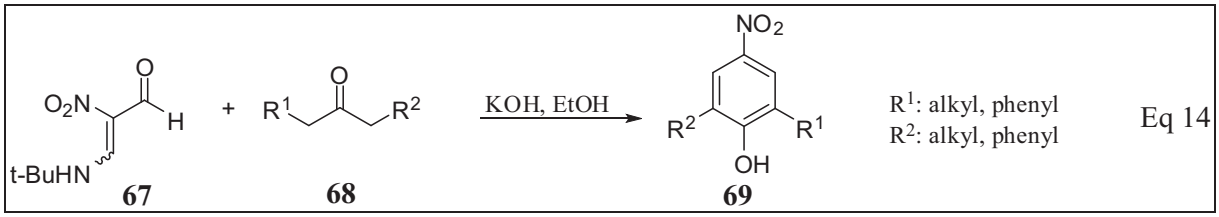
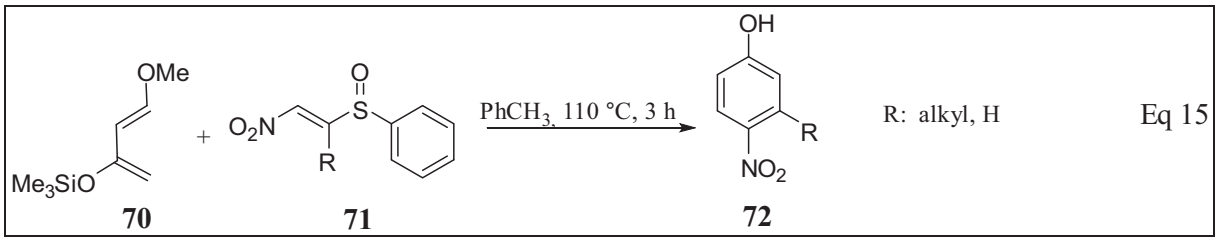
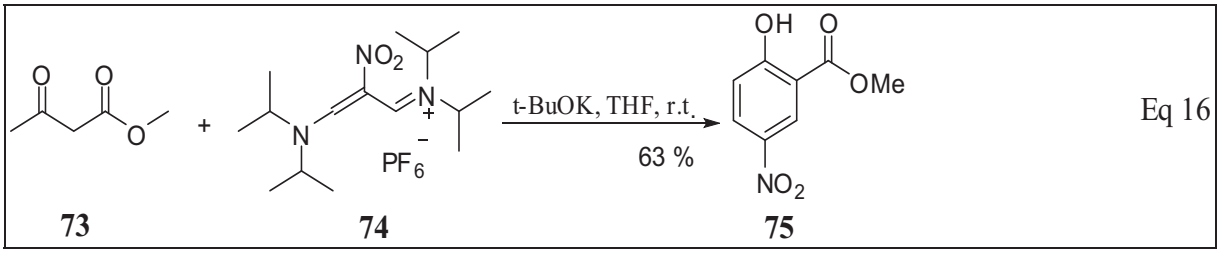


Danishefsky´s diene **70** was cyclized (Eq. 15) with β-sulfinylnitroethylenes **71** in Diels-Alder fashion to give compounds **72** [109].

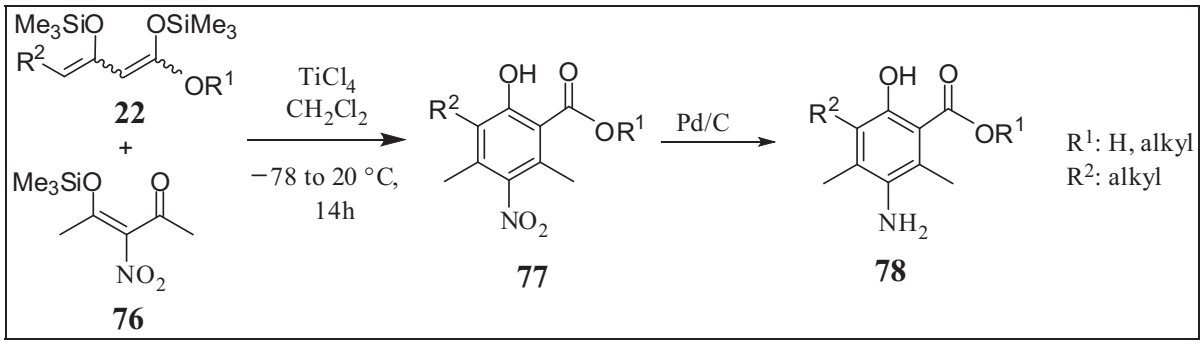


Davies *et al.* reported the synthesis of anilines by addition of ketones to vinamidinium salts. Although they obtained mixtures of anilines and nitrophenols, they isolated 4-nitrophenols in good yields in some cases. For example, methyl acetoacetate (**73**) was reacted with the salt **74** (Eq. 16) to give the nitrophenol **75** in 63% yield [110].



Tebby and co-workers reported the synthesis of nitrophenols by cyclotrimerization of nitroketenes [111].

Nitro- and aminophenols were also prepared by [3+3] cyclization reactions (Scheme 12). Dienes **22** reacted with the nitro substituted 3-silyloxy-2-en-1-one **76** and afforded nitrophenols **77**, subsequent reduction gave aminophenols **78** [112].



Scheme 12: Synthesis of nitro and aminophenols by [3+3] cyclizations and subsequent reduction.

Anilines are important intermediates in synthetic organic chemistry and in industrial applications, like the manufacture of agrochemicals, dyes, pharmaceuticals, and other industrial products [113].

An important class of anilines are fuctionalized 4-aminophenols. A wide range of pharmacological activities have been reported for functionalized 4-aminophenols. *For example*, *N*-(4-hydroxyphenyl)acetamide (**paracetamol**^{R}) (Fig. 6) is well described as analgesic and antipyretic agent [114]. Antimicrobial and antituberculosis activity and several other pharmacological properties have been reported for *N*-(4-ethoxyphenyl)acetamide (**Phenacetin**^{R}**)** [115] (Fig. 6).

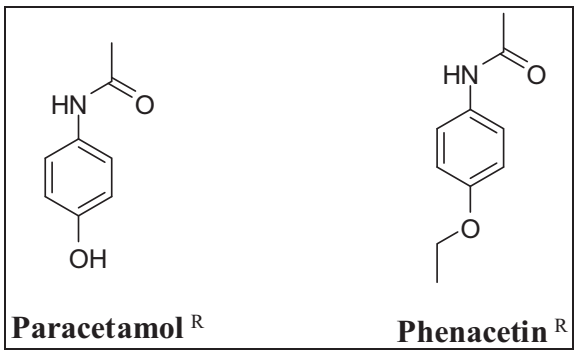


Figure 6: Biologically active aminophenols.

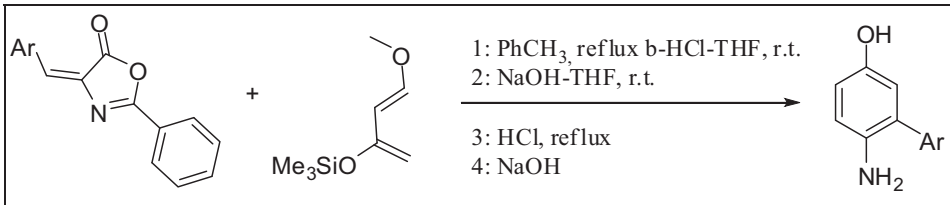
Even simple natural products, such as 3,4-dihydroxy-6-aminobenzoic acid [116a], 2-(3-amino-2,4-dibromo-6-hydroxyphenyl)acetic acid [116b], and 2-amino-4,5-dimethoxybenzoic acid [116c], are of considerable pharmacological relevance. More complex natural products include, for example, popolohuanone D [117], or 3-hydroxy-*N*-(2-hydroxy-4,5-dimethoxy-phenyl)succinamic acid [118]. In addition, the 2-acyl-4-aminophenol substructure is incorporated in a number of polycyclic natural products, such as uncialamycin or alpkinidine [119].

Routinely, amino arenes are prepared by reduction of the corresponding nitro precursors. Extensive research was done in this context, various reductions, reducing agents and catalytic systems were reported [120].

Reduction of aryl 4-azidophenols was also reported to give 4-aminophenols [121]. Direct hydroxylation of aniline also gave 4-aminophenol [122]. Recently catalytic C-N bond formation to produce aminoarenes has attracted a great interest and was applied for the synthesis of aminophenol derivatives [123].

The direct hydroxylation suffers from serious regioisomerization problems. Functionalized azidoarenes could be explosive and difficult to prepare. The syntheses of highly functionalized or sterically encumbered starting haloarenes can be a difficult and tedious task.

An "*acyclic approach*" for the direct synthesis of functionalized 4-aminophenols involves Diels-Alder annulation of Danishefsky's diene **70** (Eq. 17) with **79** to give aminophenols **80**. Actually, this process consists of many steps [124].



79 **70** **80**

Eq 17

1.3.3 Diaryl selenides:

Earlier it was considered, that selenium compounds are only toxic and have no biological value. Nowadays selenium is considered as micronutrient, whose absence causes skeletal and cardiac dysfunction [125]. It is also important for the immune system and for cellular defense against oxidative damage, thus its compounds could be possible candidates to play an important role as anticancer agents [126].

Organoselenium compounds have been tested as antibacterial, antiviral, antifungal, antiparasitic, anti-inflammatory, antihistamine and anticancer agents [127].

Among organoselenium compounds, diaryl selenides have interesting biological and pharmaceutical activities. They have attracted considerable interest because of their potential as anticancer and antioxidant agents [128]. Diaryl selenides **81**, **82**, **83** (Fig. 7) were reported to have antitumor activities [129].

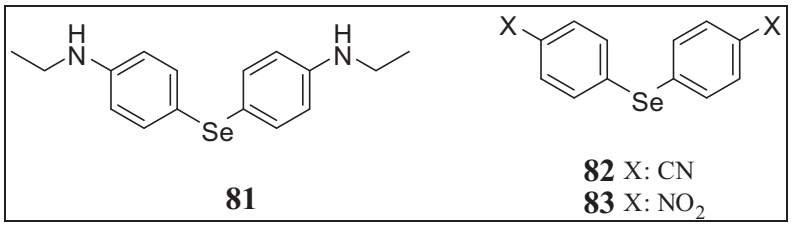


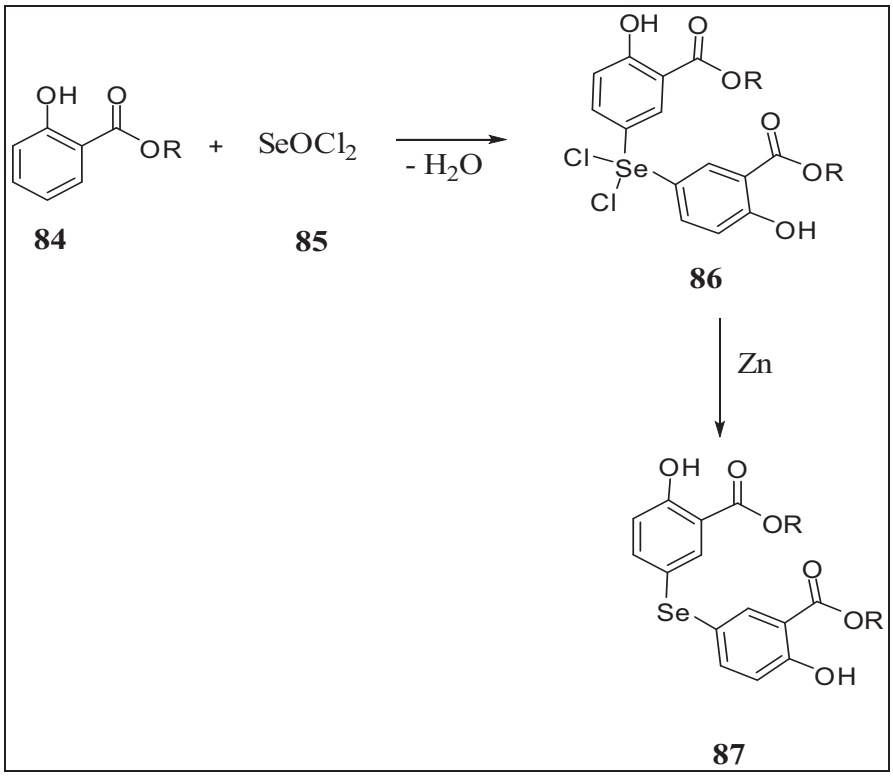
Figure 7: Biologically active diaryl selenides.

In addition, diaryl selenides play an important role in synthetic organic chemistry as key intermediates for the synthesis of a wide range of biologically and pharmacologically active selenium compounds, such as selenonium salts, selenoxides, selenimines and selenide dihalides [130].

Classically, general methods for the synthesis of diaryl selenides rely on the electrophilic substitution by ArSeX (X= Hal, CN, SeAr) using aryllithium, aryl Grignard reagents, diarylmercurials [131], anilines and phenols [132], or nucleophilic reactions of $ArSe^-$ with aryl diazonium salts [133]. The reaction of halobenzenes with phenylselenol (PhSeH) or benzene selenolate anion (PhSeNa) or diphenyl diselenide (PhSeSePh) in the presence of a transition metal catalyst, such as Pd [134], Ni [135], Cu-salt [136] have also been reported. Recently,

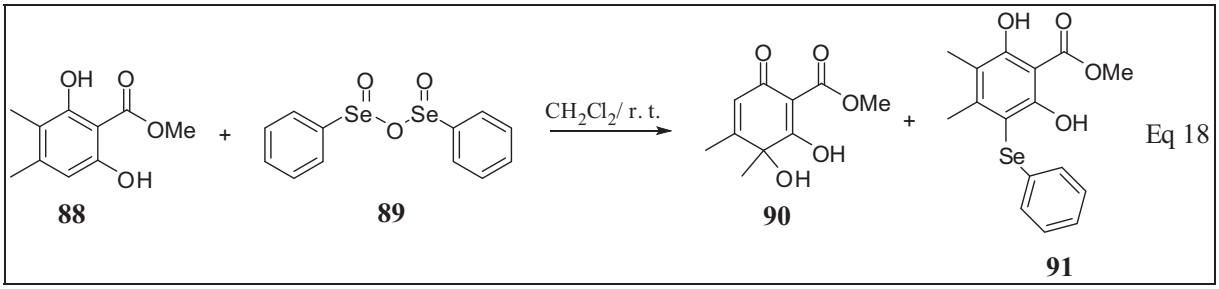
diaryl selenides have been prepared by cross coupling reaction of aryl iodides and $PhSeSnBu_3$ using palladium-based catalysts [137]. In addition, the *p*-toluenesulfonic acid or ammonium peroxosulfate mediated reaction of arenes with diphenyl diselenides were reported to give diaryl selenides [138], while triarylbismuth reacts with diaryldiselenides to form the corresponding diarylselenium compounds [139].

Symmetrical salicylate-derived diaryl-selenides are known and have been prepared by reaction of salicylates **84** with $SeOCl_2$ (**85**) (Scheme 12) and subsequent reduction with zinc to give diaryl selenides **87** [140].



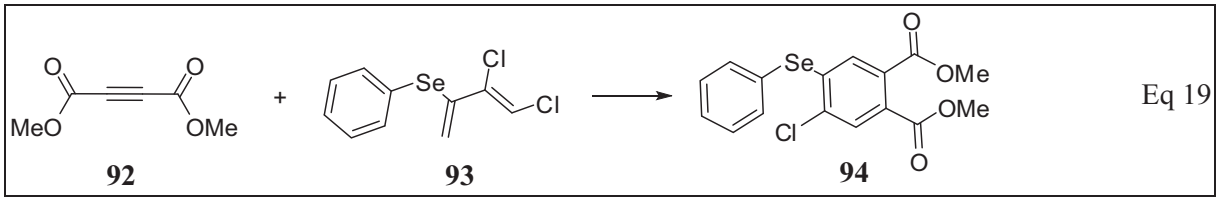
Scheme 13: Synthesis of symmetrical salicylate-derived diaryl selenides.

Barton and coworkers have reported an isolated example of the formation of an unsymmetrical salicylate-derived diaryl-selenide **91** as a side-product (Eq. 18) during their research in the synthesis of tetracycline using benzeneselenic anhydride **89** [141].

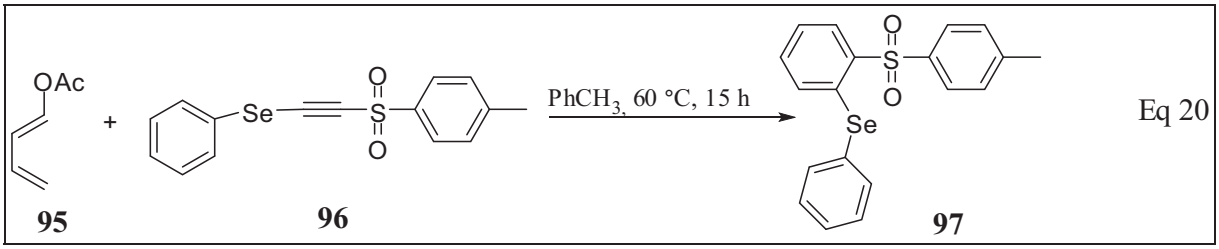


However, these methods suffer many serious disadvantages; *for example*, methods that use starting selenolates involve usage of an excess of these precursors that make the purification of the final products difficult task. To produce the selenolates, excessive amounts of reducing agent are required. Selenols are foul-smelling reagents. Regioselectivity problems are also encountered.

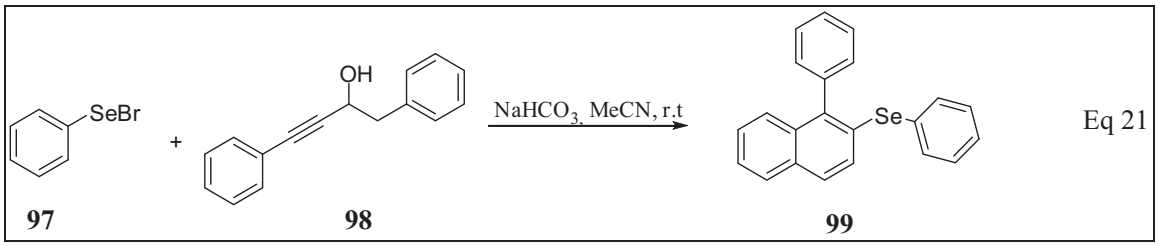
An "*acyclic approach*" for the synthesis of diaryl selenides involves the Diels-Alder annulation of DMADC (**92**) with the substituted diene **93** to give diaryl selenide **94 (**Eq. 19) [142].



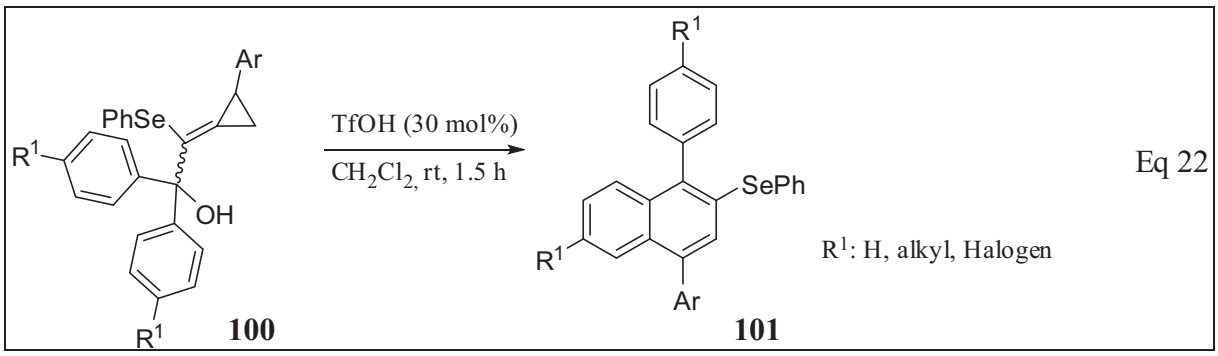
Diels-Alder [4+2] cycloaddition of diene **95** with 1-(phenylseleno)-2-(*p*-tolouenesulfonyl)ethyne (**96**) (Eq. 20) afforded compound **97** in 80% [143].



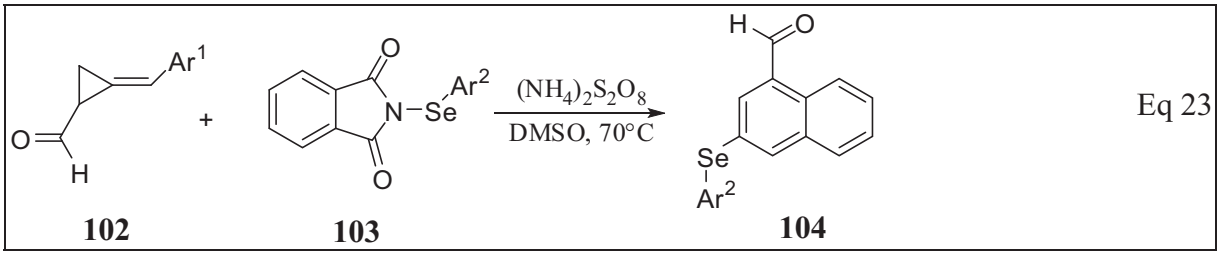
Phenyl naphthyl selenide **99** was prepared by electrophilic cyclization of benzeneselenyl bromide (**97**) (Eq. 21) with alkyne **98** [144].



Substituted phenyl naphthyl selenides **101** were also prepared by treatment of methylenecyclopropanes **100** with trifluoromethanesulfonic acid (Eq. 22) [145].



Another method for the synthesis of phenyl naphthyl selenides **104** relies on radical ring-opening-intramolecular cyclization (Eq. 23) of 2-(arylmethylene)cyclopropylaldehydes **102** using the free radical initiator ammonium persulfate and the selenium source *N*-(phenylseleno)phthalimide **103** [146].



Part 2: Results and discussions:

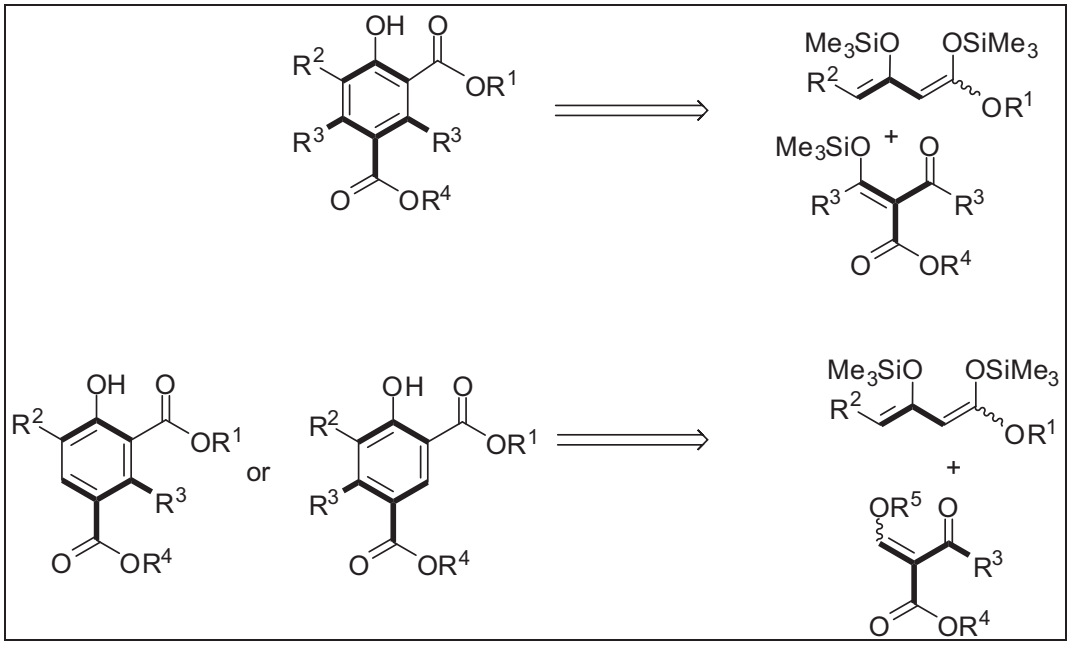
2.1 Diversity-oriented synthesis of 1-hydroxy-2,4-benzodioates by regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 3-alkoxy- and 3-silyloxy-2-alkoxycarbonyl-2-en-1-ones:

In recognition of their importance in different fields of chemistry, my efforts were directed toward the investigation of a suitable and reliable method for the synthesis of 1-hydroxy-2,4-benzodioates.

2.1.1 Target, problems to solve and strategy:

Most of the reported methods for the synthesis of 1-hydroxy-2,4-benzodioates, which adopt the "*acyclic approach*", lack generality of starting materials. I investigated the validity of [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 1,3-dielectrophiles for a regioselective and one step construction of highly functionalized 1-hydroxy-2,4-benzodioates under mild conditions.

My strategy depends on the [3+3] cyclization of functionalized 1,3-bis(silyloxy)-1,3-butadienes with the two substituted 1,3-dielectrophiles: 3-silyloxy-2-en-1-ones and 3-alkoxy-2-en-1-ones. A retrosynthesis of the target molecules could be represented as in (Scheme 14).

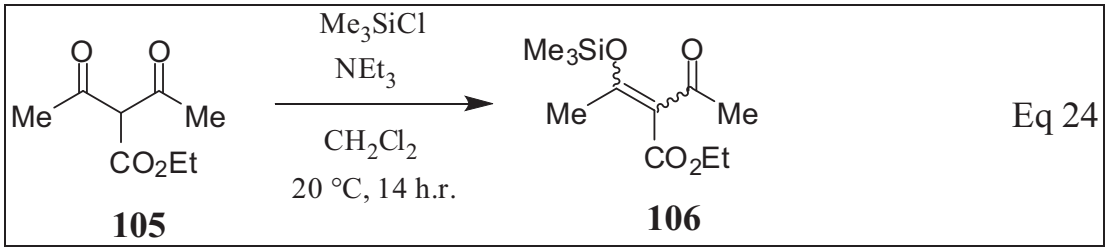


Scheme 14: Retrosynthesis of 1-hydroxy-2,4-benzodioates.

2.1.2 Synthesis of substituted 1-hydroxy-3,5-dimethyl-2,4-benzodioates by [3+3] cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with 2-ethoxycarbonyl-3-silyloxy-2-en-1-one:

Langer *et al.* have reported [147a] preliminary results of the synthesis of 1-hydroxy-3,5-dimethyl-2,4-benzodioates by $TiCl_4$-mediated [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones derived from (symmetrical) ethyl 2-acetylacetoacetate. My target was to extend the preparative scope of this reaction.

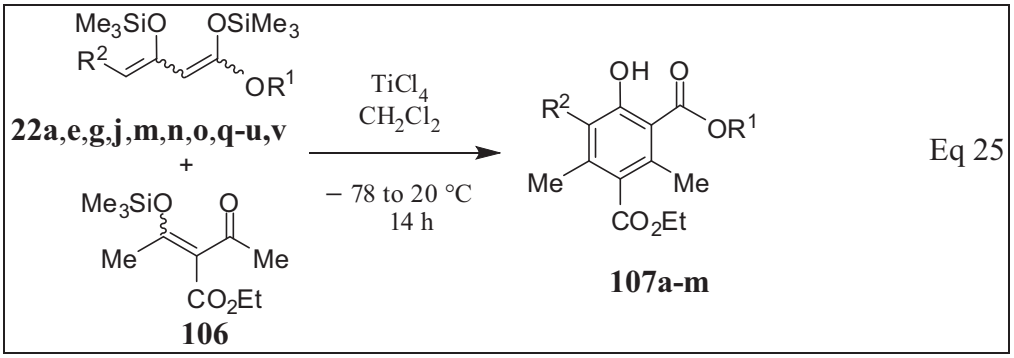
The triethylamine-mediated silylation (Eq. 24) of commercially available ethyl 2-acetylacetoacetate (**105**) with trimethylchlorosilane at room temperature afforded the 2-ethoxycarbonyl-3-silyloxy-2-en-1-one **106** in 87% yield.



Eq 24

The $TiCl_4$-mediated formal [3+3] cyclizations of β-ketoester-derived 1,3-bis(silyloxy)-1,3-butadienes **22a**,**e**,**g**,**j**,**m**,**n**,**o**,**q-u**,**v** with 3-silyloxy-2-en-1-one **106** afforded the 1-hydroxy-2,4-benzodioates **107a-m** (Eq. 25, Table 2) in moderate to good yields.

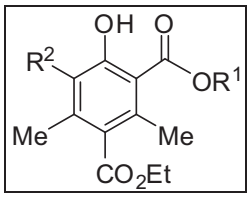
The best yields were obtained when the reactions were done in concentrated solutions (2 ml of CH_2Cl_2/1mmol of **106**) with equivalent ratio of the reactants (**106**/**22**/ $TiCl_4$) (1.0/1.1/1.1). The reactions were done in completely dry argon atmosphere at -78 ^oC using *iso*-propanol-liquid nitrogen bath and allowed to warm to room temperature during 14 hours.



Eq 25

Compounds **107a-m** (Table 2) are 1-hydroxy-2,4-benzodioates with the same substituent on C3 and C5, thus the syntheses of compounds **107a-m** bear no issue of regioselectivity. The cyclization of the 1,3-bis(silyloxy)-1,3-butadienes **22q**,**r**,**s** with **106** afforded the 1-hydroxydimethyl-2,4-benzodioates **107i**,**j**,**k**, respectively. These isophthalates can be considered also as highly substituted biaryls. Compounds **107h**,**l**,**m** could be considered as highly functionalized diaryl ethers.

Functionalized diaryl ethers [21] and biaryls [22] have important biological relevance and occur in many natural products.



107a-m

Table 2: Products and yields **107a-m**.

22	**107**	R^1	R^2	% (**107**)[a]
a	**a**	Me	H	30[b]
e	**b**	Et	Me	48[b]
g	**c**	Et	Et	49[b]
j	**d**	Me	*n*-Hex	35
m	**e**	Me	*n*-Non	40
n	**f**	Me	*n*-Dec	41
o	**g**	Me	OMe	65[b]
v	**h**	Et	OPh	48
q	**i**	Me	4-MeC_6H_4	38
r	**j**	Me	4-ClC_6H_4	37
s	**k**	Me	4-$(MeO)C_6H_4$	34
t	**l**	Et	O(2-MeC_6H_4)	42
u	**m**	Et	O(3-MeC_6H_4)	51

[a] Yields of isolated products, [b] ref. 147a

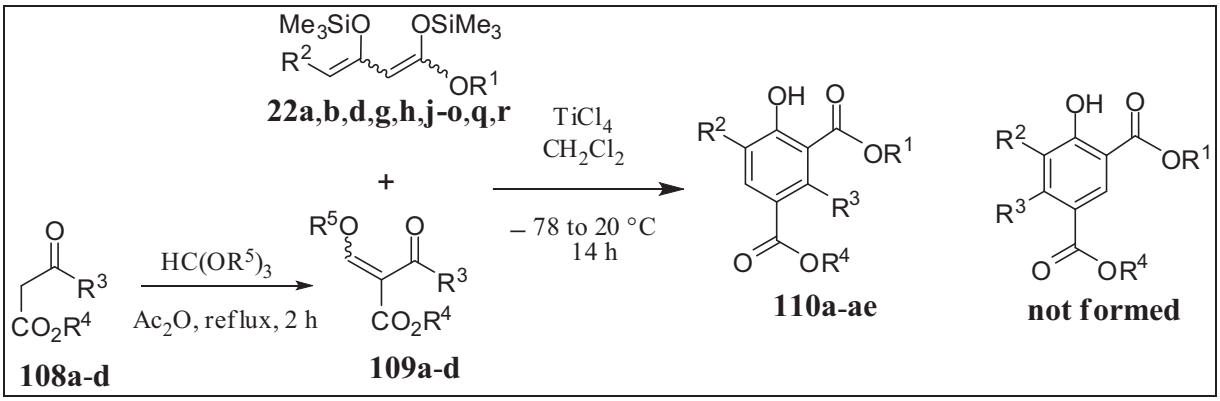
When the side-chain substituted 1,3-bis(silyloxy)-1,3-butadienes **22** were used, the yields increased (albeit not significantly in some cases). The butadiene **22o** gave the best yield [147a]. The lowest yield was observed when **22a** was reacted. My trials to improve the yield, unfortunately, failed. No clear trend for the variation of the yields was observed.

2.1.3 Synthesis of functionalized 1-hydroxy-2,4-benzodioates by [3+3] cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with 3-alkoxy- 2-en-1-ones:

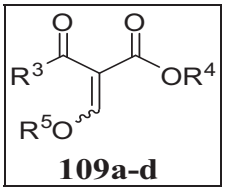
The second protocol of the strategy relies on the use of unsymmetrical 3-alkoxy- 2-en-1-ones, rather than 3-silyoxy-2-en-1-ones for the [3+3] cyclization reactions with 1,3-bis(silyloxy)-1,3-butadienes. This provides another route for the synthesis of the target molecules.

2-Alkoxycarbonyl-3-methoxy-2-en-1-ones **109a-d** were prepared, following known procedures [148, 149], by reflux of β-ketoesters **108a-d** in a mixture of trialkyl orthoformate and acetic anhydride (Scheme 15, Table 3). The syntheses of **109a**,**c**,**d** were reported [149]. The enones **109a-d** were obtained as mixtures of *E/Z* isomers.

The $TiCl_4$-mediated formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes **22a**,**b**,**d**,**g**,**h**,**j-o**,**q**,**r** with 3-alkoxy-2-en-1-ones **109a-d** afforded the 1-hydroxy-2,4-benzodioates **110a-ae** (Scheme 15, Table 5) in 43-60% yields. The other regioisomers were not detected.



Scheme 15: Synthesis of 1-hydroxyl-2,4-benzodioates **110a-ae**.



109a-d

Table 3: Compounds **109a-d** and their yields.

108, **109**	R^3	R^4	R^5	% (**109**)[a]
a	Me	Me	Me	82
b	Et	Me	Me	84
c	*n*-Pr	Me	Me	83
d	Ph	Et	Et	81

[a] Yields of isolated products, for the reported compounds see ref. [149]

2.1.3.1 Optimization of reaction conditions:

The best conditions were obtained when the reaction was carried out using an equivalent ratio (1.0/ 1.1/ 1.1) of (**109a**/ **22d** / $TiCl_4$), in concentrated solution (2 ml of CH_2Cl_2/ 1 mmol of **109a**), at -78 °C followed by slow warming to room temperature during 14 hours. Different parameters were varied to get the optimized conditions (Table 4).

In *trial 1* the decrease of the amount **22d** led to a decrease of the yield. When the amounts of the diene **22d** and **109d** were increased **(***trials 2 and 4* respectively), the yields of the isolated product decreased. This might be a result of the increase of their concentration, which enhances their $TiCl_4$-mediated dimerization and polymerization under the same reaction conditions.

When the reaction was done at 0 °C sudden increase of the heat and decomposition were observed (*trial 5*). Employing other Lewis acids gave complex mixtures which could not be isolated by normal column chromatography (*trials 8, 9, 10*).

Yields decreased when the reaction was carried out in more dilute solution (*trials 11-13*), up to the level that no product was detected when (30 ml/ **109a**) of solvent was used.

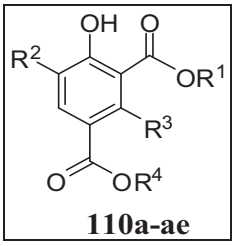
Table 4: Optimization of reaction parameters of the product **110b**.

trial	[**109a**][a]	L.A. [b]	**109a**/**22d**/L.A.	T. (°C)	h.r.[c]	% (**110b**)[a]
1	2	$TiCl_4$	1.0/1.0/1.0	-78-r.t.	14	28
2	2	$TiCl_4$	1.0/2.0/1.0	-78-r.t.	14	31
3	2	$TiCl_4$	1.0/1.0/2.0	-78-r.t.	14	20
4	2	$TiCl_4$	2.0/1.0/1.0	-78-r.t.	14	33
5	2	$TiCl_4$	1.0/1.1/1.1	0-r.t.	14	0
6	**2**	**$TiCl_4$**	**1.0/1.1/1.1**	**-78-r.t.**	**14**	**57**
7	2	$TiCl_4$	1.0/1.1/1.1	-78-r.t.	4	18
8	2	$SnCl_4$	1.0/1.1/1.1	-78-r.t.	14	u. p .[d]
9	2	$BF_3.Et_2O$	1.0/1.1/1.1	-78-r.t.	14	u. p .[d]
10	2	TMSOTf	1.0/1.1/1.1	-78-r.t.	14	u. p .[d]
11	3	$TiCl_4$	1.0/1.1/1.1	-78-r.t.	14	34
12	6	$TiCl_4$	1.0/1.1/1.1	-78-r.t.	14	21
13	10	$TiCl_4$	1.0/1.1/1.1	-78-r.t.	14	7
14	30	$TiCl_4$	1.0/1.1/1.1	-78-r.t.	14	0

[a] ml of CH_2Cl_2/ mmol of **109a**, [b] Lewis acid, [c] time in hours 14 hours= overnight, [d] unidentified products (formation of complex mixture)

2.1.3.2 Preparative scope:

Compounds **110a-ae** (Table 5) are 1-hydroxy-3-substituted-2,4-benzodioates having no substituent on C5. These compounds are unknown to date. Compounds **110j,k,u** and **110ad**,**ae** are considered as highly substituted biaryls and could be synthesized by either: functionalization of the side chain of the diene **22** or by functionalization of enones **109**. This indicates that the variation of both the masked dianions **22** and the dielectrophiles **109** is possible and lead to these functionalized isophthalates.



110a-ae

Table 5: Products and yields of **110a-ae**.

22	109	110	R^1	R^2	R^3	R^4	% (**110**)[a]
a	**a**	**a**	Me	H	Me	Me	43
d	**a**	**b**	Me	Me	Me	Me	57
g	**a**	**c**	Et	Et	Me	Me	50
h	**a**	**d**	Me	*n*-Bu	Me	Me	52
j	**a**	**e**	Me	*n*-Hex	Me	Me	55
k	**a**	**f**	Me	*n*-Hept	Me	Me	51
l	**a**	**g**	Me	*n*-Oct	Me	Me	48
m	**a**	**h**	Me	*n*-Non	Me	Me	52
b	**a**	**i**	$(CH_2)_2OMe$	H	Me	Me	48
q	**a**	**j**	Me	4-MeC_6H_4	Me	Me	53
r	**a**	**k**	Me	4-ClC_6H_4	Me	Me	48
o	**a**	**l**	Me	OMe	Me	Me	52
d	**b**	**m**	Me	Me	Et	Me	52
g	**b**	**n**	Et	Et	Et	Me	50
h	**b**	**o**	Me	*n*-Bu	Et	Me	52
j	**b**	**p**	Me	*n*-Hex	Et	Me	52
k	**b**	**q**	Me	*n*-Hept	Et	Me	51
l	**b**	**r**	Me	*n*-Oct	Et	Me	50
m	**b**	**s**	Me	*n*-Non	Et	Me	51
n	**b**	**t**	Me	*n*-Dec	Et	Me	49
q	**b**	**u**	Me	4-MeC_6H_4	Et	Me	51
d	**c**	**v**	Me	Me	*n*-Pr	Me	51
g	**c**	**w**	Et	Et	*n*-Pr	Me	53

h	**c**	**x**	Me	*n*-Bu	*n*-Pr	Me	51
j	**c**	**y**	Me	*n*-Hex	*n*-Pr	Me	45
k	**c**	**z**	Me	*n*-Hept	*n*-Pr	Me	46
l	**c**	**aa**	Me	*n*-Oct	*n*-Pr	Me	45
m	**c**	**ab**	Me	*n*-Non	*n*-Pr	Me	50
n	**c**	**ac**	Me	*n*-Dec	*n*-Pr	Me	55
d	**d**	**ad**	Me	Me	Ph	Et	58
g	**d**	**ae**	Et	Et	Ph	Et	60

[a] Yields of isolated products

When R^3 was a phenyl group (**110ad** and **ae**) the yields increased. The Yields of products **110b-h** are slightly higher than the yield of **110a**. This could be attributed to the inductive donating effect of the alkyl group which enhances the nucleophilicity of the C4 carbon. No clear systematic trend in the yields was noticed. No clear relation was noticed when R^2 were the same and R^3 changed.

2.1.3.3 Structural proof:

For compound **110a** (Fig. 8) the aromatic protons resonate as doublets at δ = 6.78 ppm and δ = 7.76 ppm with coupling constants ^3J = 8.7 Hz and ^3J = 8.9 Hz, respectively. These large coupling constants indicate that they are *ortho* to each other.

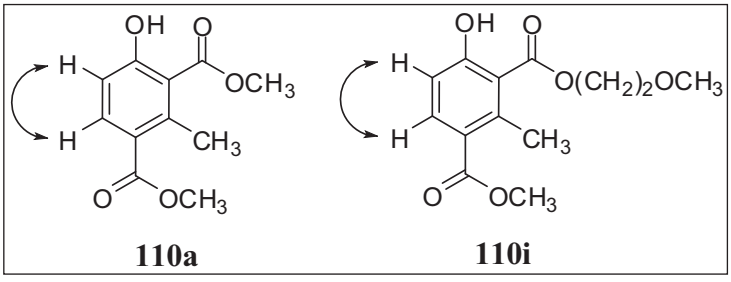


Figure 8: Ortho coupling of **110a** and **110i**.

The same was observed for **110i**: the two aromatic protons resonate at δ = 6.78 ppm and δ =7.78 ppm as doublets with coupling constants ^3J = 8.7 Hz and ^3J = 9.0 Hz.

For other compounds, the elucidation of the structure and the confirmation of the regioselectivity were difficult and had to rely on 2D NMR spectroscopy.

$^{1}H,^{1}H$ NOE experiments were done for compounds **110p** and **110y**. For **110p**, the benzylic protons (at carbon 1) of the hexyl side chain appear as a triplet at δ = 2.53 ppm and correlate with the aromatic proton which appears as a singlet at δ = 7.61 ppm (Fig. 9 and 10). Also, a NOE correlation was observed between this aromatic proton and the protons at carbon 2.

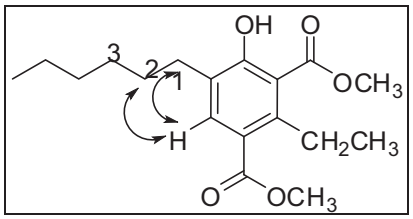


Figure 9: $^{1}H,^{1}H$ NOE correlations of **110p**.

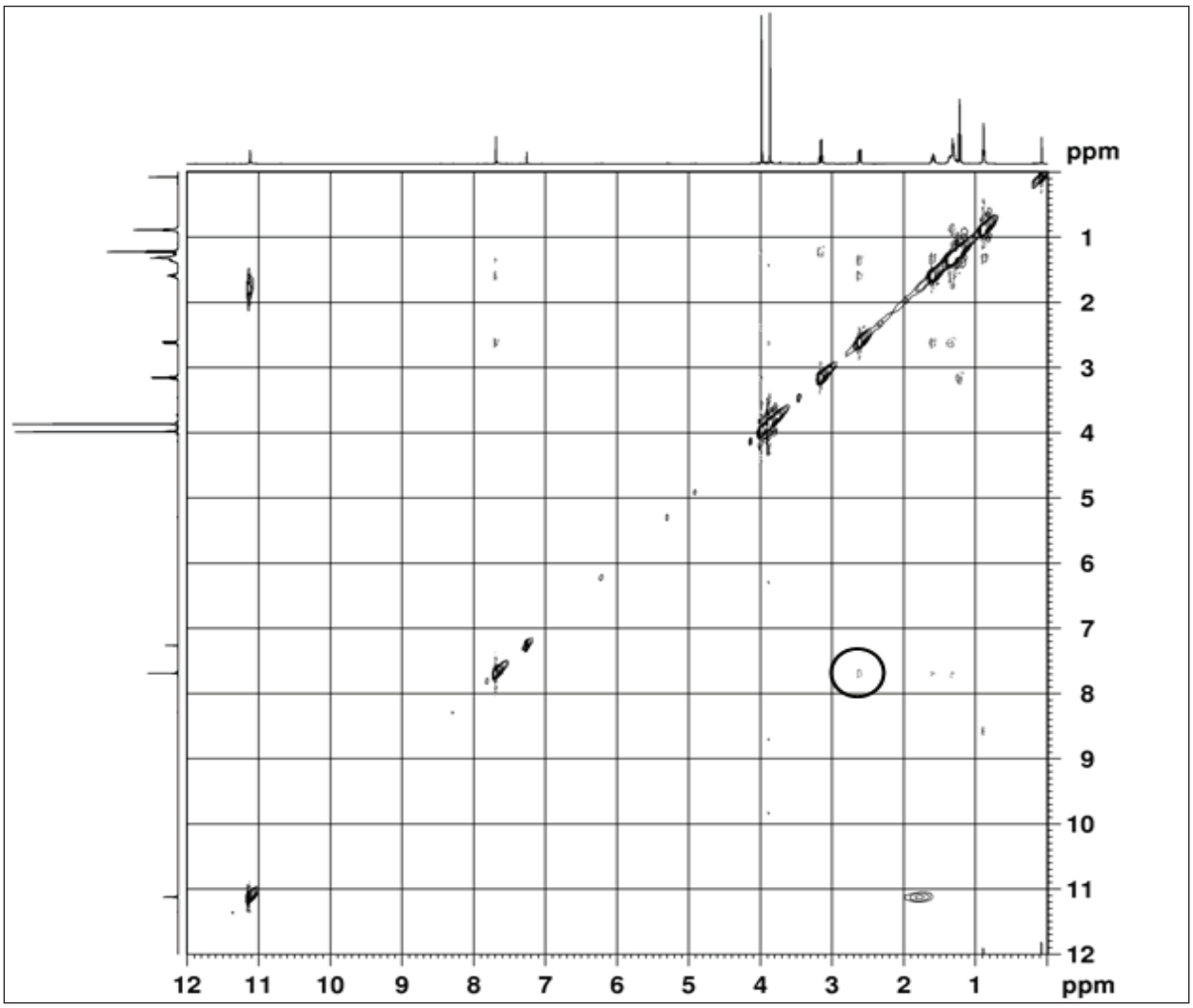


Figure 10: $^{1}H,^{1}H$ NOE Spectrum of **110p**.

In **110y**, a NOE correlation was observed between the benzylic protons which resonate as a triplet at δ = 3.03 ppm and the methyl protons of the propyl side chain which appear at δ = 0.90 ppm. It is useful to assign both benzylic protons groups ($PhCH_2$) (Fig. 11). On the other hand, a NOE correlation was observed between the aromatic proton which resonates at δ = 7.61 ppm and the benzylic protons of carbon 1 which resonate at δ = 2.53 ppm.

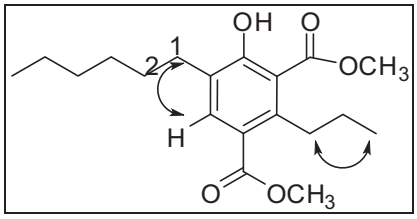


Figure 11: $^{1}H,^{1}H$ NOE correlations of **110y**.

More downfield shifts for aromatic protons in compounds **110j**,**k**,**u** (Fig. 13) were noticed. It might be that these aromatic protons are affected by the anisotropic effect of the aromatic ring on the carbon atom C5 of these phenols.

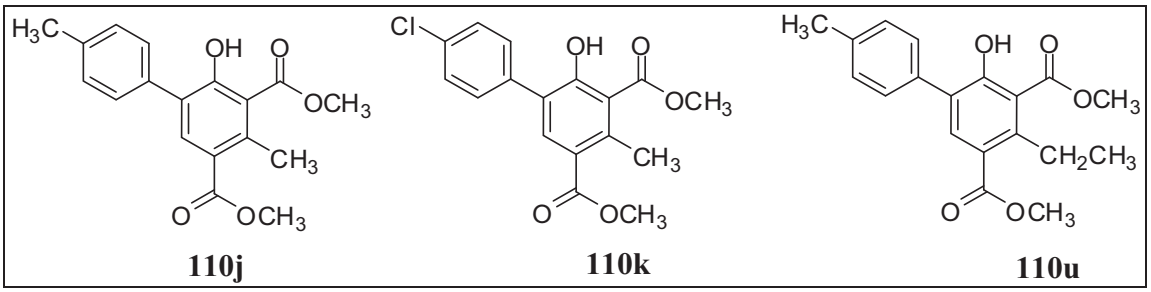


Figure 12: Compounds **110j,k,u**.

The regioselectivity observed here can be explained by steric and electronic factors (see section 1.2.4 and 1.2.1).

2.1.3.4 X-ray analysis:

The structures of both **110b** and **110k** were confirmed by X-ray crystal structure analyses.

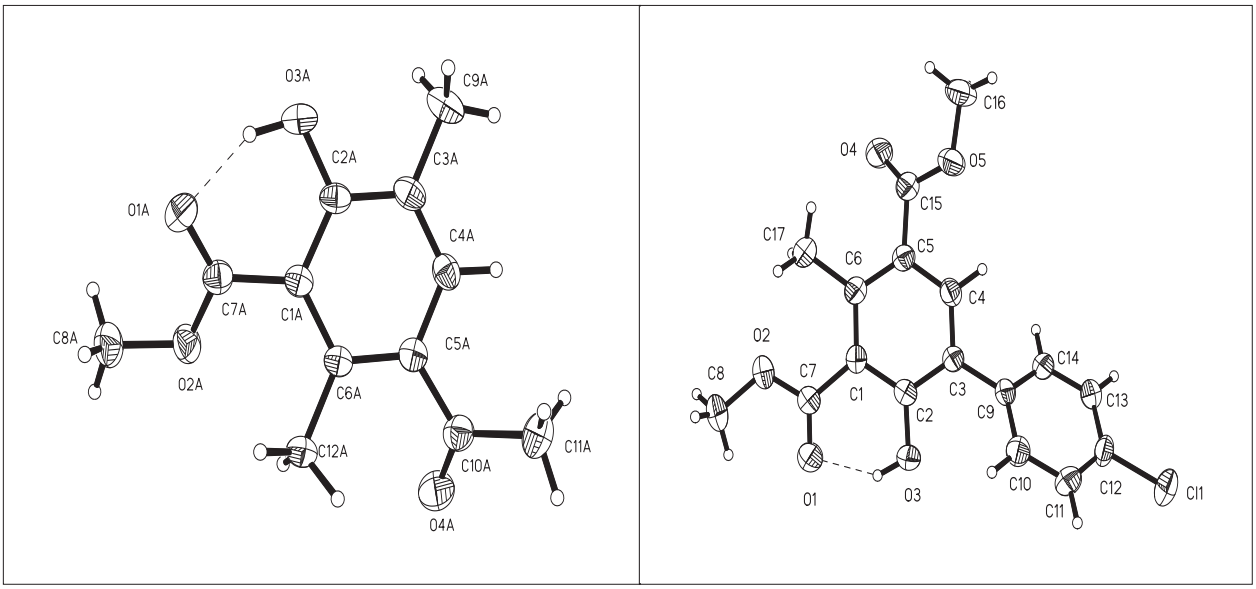


Figure 13: ORTEP plot of one of the two molecules **110b** in the asymmetric unit and **110k** (50% level).

These X-ray structures (Fig. 13) were another proof of the suggested regioselectivity. In both compounds the O-H group is involved in intramolecular hydrogen bonding. In addition, it is involved in intermolecular hydrogen bonding (Fig. 14) in **110k**. The torsion angle between the two aromatic planes in **110k** was calculated to be 39.96^0 (7).

Hydrogen bonding properties: bond lengths between donors and acceptors and the angles are listed for compounds **110b** and **110k** in Tables 6 and 7 respectively.

Table 6: Hydrogen bonds for **110b** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3B)-H(3B)...O(1B)	0.94(2)	1.76(2)	2.6124(16)	149.6(19)
O(3A)-H(3A)...O(1A)	0.96(3)	1.69(3)	2.5772(16)	151(2)

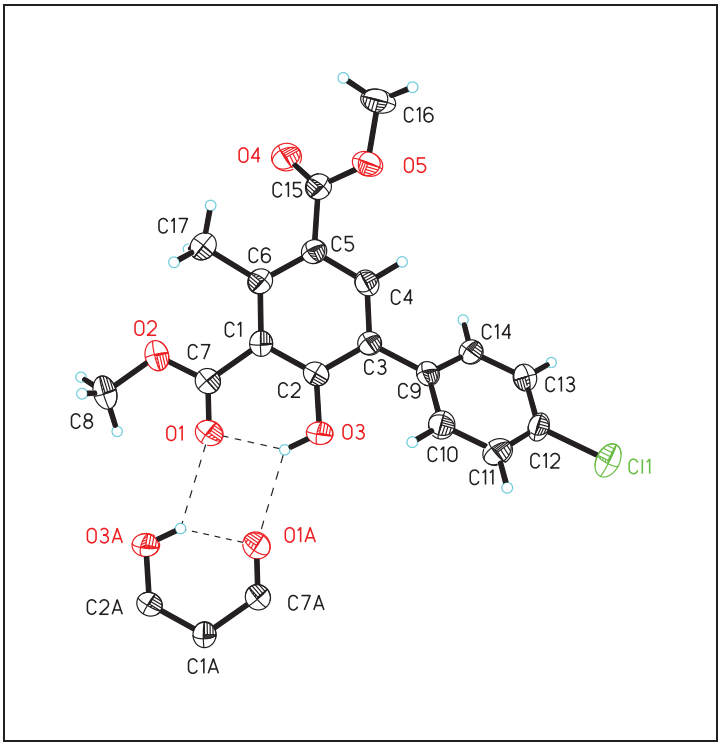


Figure 14: Inter -and intra-molecular hydrogen bonding in **110k**.

Table 7: Hydrogen bonds for **110K** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3O)...O(1)	0.89(4)	1.76(4)	2.508(3)	140(3)
O(3)-H(3O)...O(1)#1	0.89(4)	2.25(3)	2.913(3)	130(3)

2.2 Competing regiodirecting effects of ester and aryl groups in [3+3] cyclocondensations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes. Regioselective synthesis of 3-hydroxy-phthalates and 2-hydroxy-terephthalates:

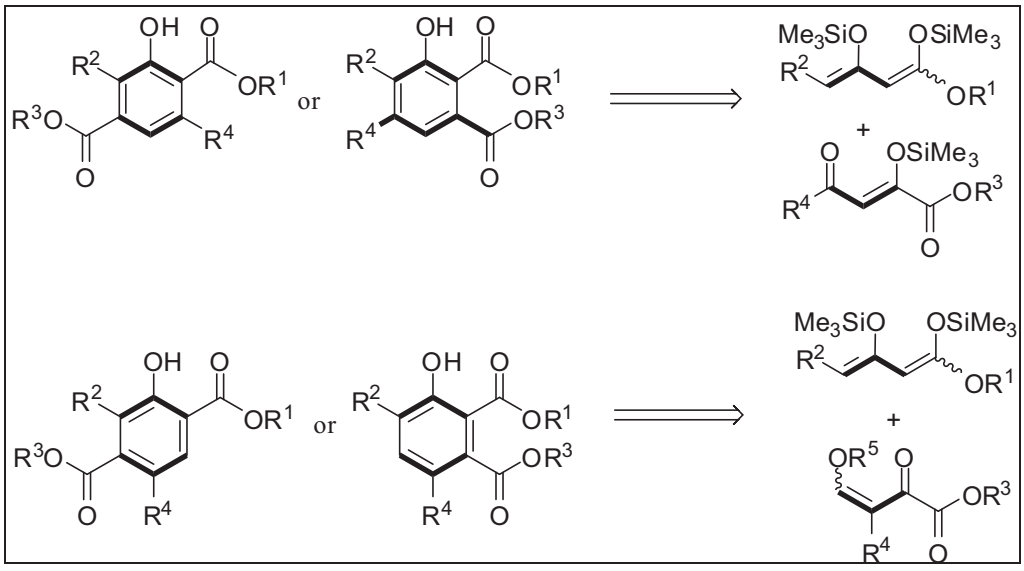
The divergent use of 3-hydroxy-phthalates and 2-hydroxy-terephthalates in various fields of chemistry raises the need to find reliable methods for their synthesis.

2.2.1 Target, problems to solve and strategy:

Few strategies that adopt the "*acyclic approach*" for the synthesis 3-hydroxy-phthalates and 2-hydroxy-terephthalates are reported in literature (see section 1.3.1). However, these methods have many drawbacks such as lack of generality of the starting materials.

I investigated the possibility of synthesis of these arenes by the use of [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 1,3-dielectrophiles. This strategy would offer a direct, regioselective and one step construction of substituted 3-hydroxy-phthalates and 2-hydroxy-terephthalates under mild conditions.

My strategy relies on the [3+3] cyclization of functionalized 1,3-bis(silyloxy)-1,3-butadienes with two types of 1,3-dielectrophiles: 3-silyloxy-2-en-1-ones and 3-alkoxy-2-en-1-ones, a schematic presentation for this strategy is shown in Scheme 16. In the cyclizations with unsymmetrical 3-silyloxy-2-en-1-ones, two regioisomers could be predicted, the same is for unsymmetrical 3-alkoxy-2-en-1-ones.

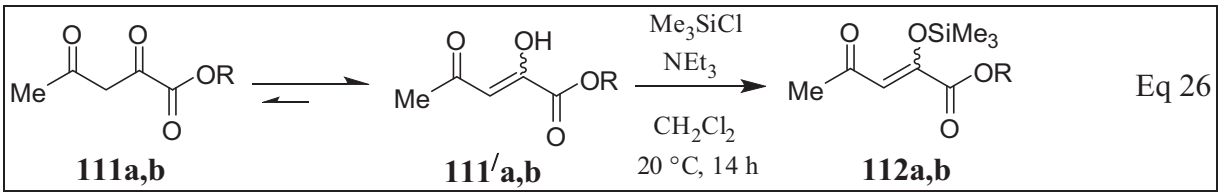


Scheme 16: Retrosynthesis of 3-hydroxy-phthalates and 2-hydroxy-terephthalates.

2.2.2 Synthesis of substituted 3-hydroxyphthalates by [3+3] cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with unsymmetrical 3-(silyloxy)-2-en-1-ones derived from acetylpyruvates:

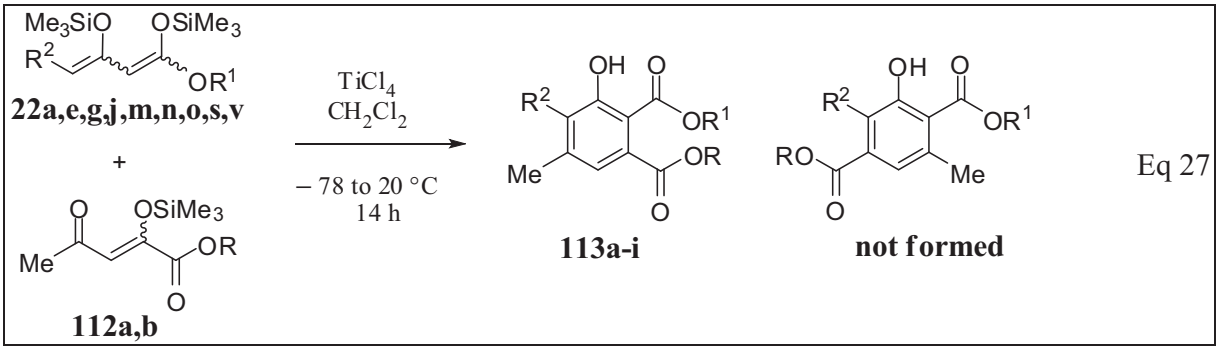
Langer *et al.* reported [147a] preliminary results related to the synthesis of 3-hydroxy-5-methylphthalates based on regioselective chelation-controlled cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 4-silyloxy-2-oxo-3-butenoates, derived from acetylpyruvates. Herein, I report a full and detailed account related to this scope.

4-Silyloxy-2-oxo-3-butenoates **112a**,**b** were prepared in 84% and 81% yields, respectively, by triethylamine-mediated silylation (Eq. 26) of the commercially available acetylpyruvates **111a**,**b**, which exist mainly in their enol form **111′a**,**b** [150].



Eq 26

The $TiCl_4$-mediated formal [3+3] cyclizations (Eq. 27, Table 8) of 1,3-bis(silyloxy)-1,3-butadienes **22a**,**e**,**g**,**j**,**m**,**n**,**o**,**s**,**v** with 4-silyloxy-2-oxo-3-butenoates **112a**,**b** afforded the 3-hydroxy-5-methylphthalates **113a-i**, in good yields. No other regioisomers were detected.



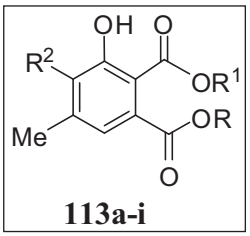
Eq 27

The best yields were obtained when the equivalent ratio of reactants was (**112**/**22**/ $TiCl_4$) (1.0/1.1/1.1), when the reactions were done in a concentrated solution (2 ml of CH_2Cl_2/1 mmol of **112**) under inert atmosphere of argon gas at -78°C using *iso*-propanol-liquid nitrogen bath and when the reactions were allowed to warm to room temperature during 14 hours.

2.2.2.1 Preparative scope:

Compounds **113a-i** (Table 8) are C6 unsubstituted 3-hydroxy-phthalates. Compound **113h** can be considered as a highly functionalized biaryl, while compound **113i** is a functionalized diaryl ether.

The yields of **113a**,**c** were improved from 17%, 22%, respectively [147a] to 43% and 42%. The previous low yields could be due to practical problems or due to the quality of the starting materials, such as the use of old diene or wet solvent or reaction atmosphere.



113a-i

Table 8: Products and yields of **113a-i**.

112	22	113	R	R^1	R^2	% (**113**)[a]
a	**a**	**a**	Me	Me	H	43[b]
a	**e**	**b**	Me	Et	Me	32
a	**g**	**c**	Me	Et	Et	42[b]
b	**j**	**d**	Et	Me	*n*-Hex	37
b	**m**	**e**	Et	Me	*n*-Non	42
b	**n**	**f**	Et	Me	*n*-Dec	42
a	**o**	**g**	Me	Me	OMe	45[b]
b	**s**	**h**	Et	Me	4-(MeO)C_6H_4	39
b	**v**	**i**	Et	Et	OPh	40
b	**w**	**j**	Et	Et	Cl	0

[a] Yields of isolated products, [b] ref. 147a

The highest yield was obtained when **22o** was used. No clear systematic trend for the yields was observed. When the diene **22w** was used no aromatic compound was isolated. This could be due to the electron withdrawing inductive effect of the chlorine atom, which decreases the nucleophilicity of the terminal carbon atom.

2.2.2.2 Structural proof:

The ($PhCH_3$) protons in compound **113h** (Fig. 15) are more downfield shifted than the other derivatives, they resonate at δ = 2.51 ppm. This could be due to the anisotropic effect of the neighboring aromatic ring.

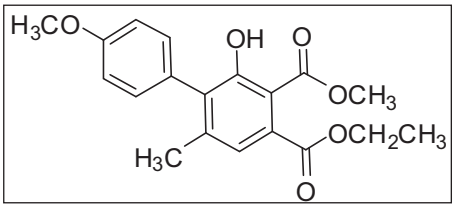


Figure 15: The phthalate **113h**.

$^1H,^1H$ NOE experiments were done for compounds **113b** and **113h** in my recent work, it was also done for **113c** as well [147] (Fig. 16). These experiments confirmed the suggested regioselectivity. Both $PhCH_3$ proton groups in **113b**, which resonate at δ = 2.26 ppm and 2.39 ppm, correlate with each other (Fig. 16). In addition, there is a NOE correlation between the aromatic proton which resonates at δ = 6.94 ppm and the methyl group appears as a singlet at δ = 2.39 ppm.

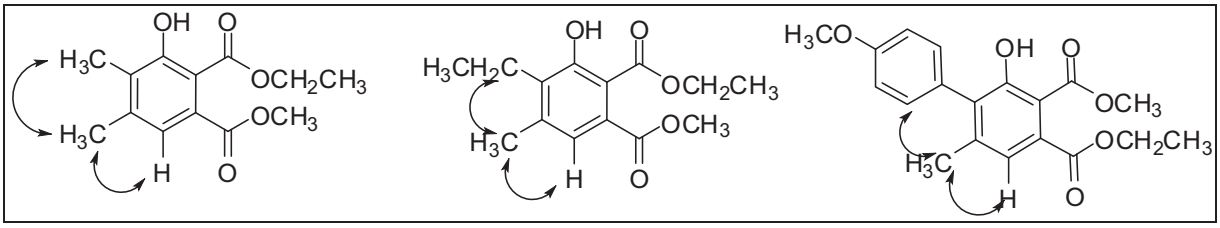
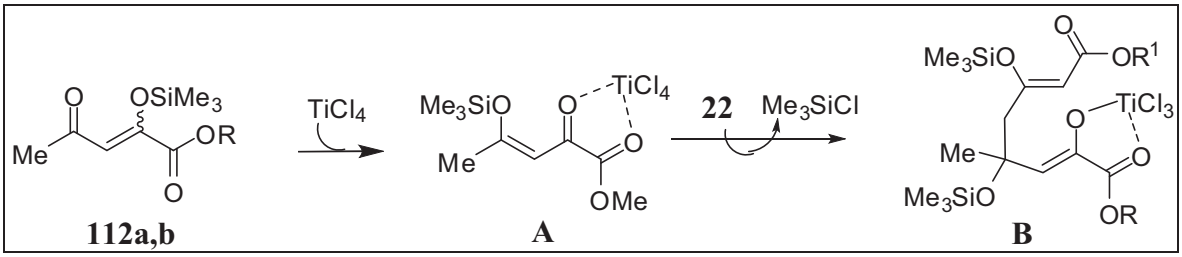


Figure 16: $^1H,^1H$ NOE correlations of **113b, 113c** and **113h**.

The regioselectivity might be explained by $TiCl_4$-assisted migration of the TMS group of **112** (Scheme 17) and formation of *intermediate **A*** as a result of the chelation of $TiCl_4$ with the neighbouring oxygen atoms.

The reaction of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones usually proceeds by attack of the terminal carbon atom of the diene onto the double bond of the 3-silyloxy-2-en-1-one in a conjugate addition fashion *intermediate* **B**. The π-donating effect of the silyloxy group increases the electron density (and thus decreases the electrophilicity) of the carbonyl group of the enone moiety. Therefore, conjugate addition is observed.



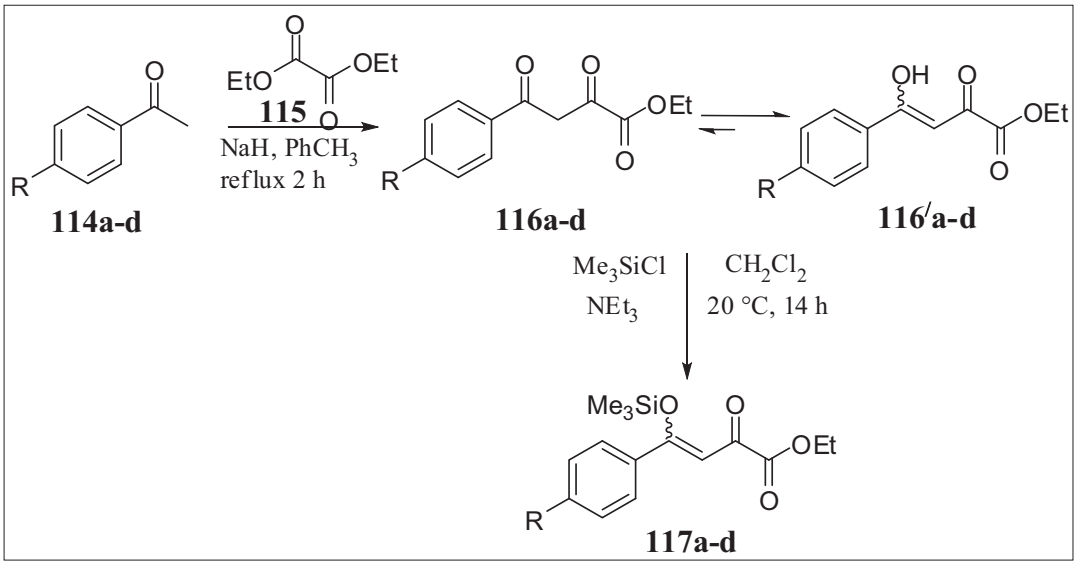
112a,b **A** **B**

Scheme 17: Me_3Si migration promoted by $TiCl_4$ chelation ring formation in the cyclization of **112**.

2.2.3 Synthesis of substituted 2-hydroxy-terephthalates by [3+3] cyclocondensation of 1,3-Bis(silyloxy)-1,3-butadienes with unsymmetrical 3-(silyloxy)-2-en-1-ones derived from benzoylpyruvates:

In continuation of the cyclization of unsymmetrical 3-(silyloxy)-2-en-1-ones derived from acetylpyruvates, I studied also the cyclizations of 3-(silyloxy)-2-en-1-ones derived from benzoylpyruvates.

The reaction of various substituted acetophenones **114a-d** with diethyl oxalate (**115**) (Scheme 18, Table 9), in the presence of sodium hydride (60% in oil), afforded the 2,4-diketoesters **116a–d** [151] in excellent yields, which were by triethylamine-mediated silylation converted to the corresponding 3-silyloxy-2-en-1-ones **117a-d**.



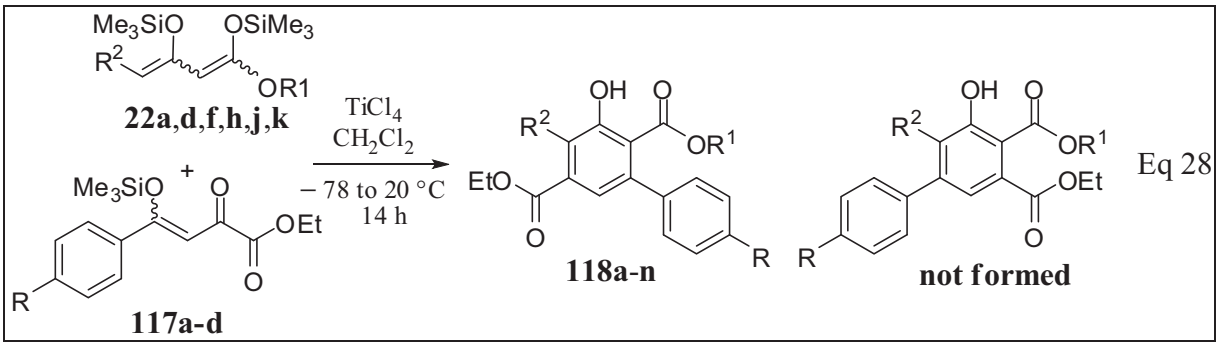
Scheme 18: Synthesis of the enones **117a-d**.

Table 9: Products **116** and **117**.

114, 116, 117	R	% (**116**)[a]	% (**117**)[a]
a	H	94	89
b	Me	95	84
c	NO_2	92	94
d	Br	95	91

[a] Yields of isolated products.

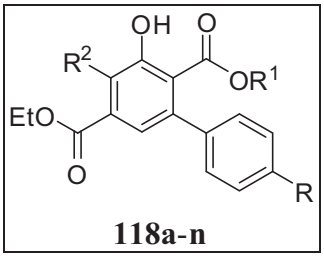
The $TiCl_4$-mediated formal [3+3] cyclization (Eq. 28, Table 10) of 1,3-bis(silyloxy)-1,3-butadienes **22a**,**d**,**f**,**h**,**j**,**k** with the 3-(silyloxy)-2-en-1-ones **117a-d**, derived from benzoylpyruvates, afforded the 6-aryl-2-hydroxy-terephthalates **118a-n**.



Eq 28

The cyclizations were done using optimized parameters: the equivalent ratio of reactants was (**117**/**22**/ $TiCl_4$) (1.0/1.1/1.1). The reactions were done under inert atmosphere in concentrated solutions (2 ml of extra dry CH_2Cl_2/1 mmol of **117**).

Compounds **118a-n** (Table 10) are 6-aryl-2-hydroxy-terephthalates having no substituent on C5. These compounds could be also considered as substituted biaryls. Compounds **118h**,**i** are nitro-substituted biaryls, which can be intermediates for amino-substituted biaryls. Both classes of compounds have wide applications in medicinal and pharmaceutical chemistry [152].



118a-n

Table 10: Products **118a-n**.

22	117	118	R	R^1	R^2	% (**118**)[a]
a	**a**	**a**	H	Me	H	43
d	**a**	**b**	H	Me	Me	49
f	**a**	**c**	H	Me	Et	50
h	**a**	**d**	H	Me	*n*-Bu	46
a	**b**	**e**	Me	Me	H	44
d	**b**	**f**	Me	Me	Me	46
f	**b**	**g**	Me	Me	Et	46
d	**c**	**h**	NO_2	Me	Me	66
f	**c**	**i**	NO_2	Me	Et	67
a	**d**	**j**	Br	Me	H	53
d	**d**	**k**	Br	Me	Me	55
f	**d**	**l**	Br	Me	Et	59
j	**d**	**m**	Br	Me	*n*-Hex	50
k	**d**	**n**	Br	Me	*n*-Hept	50
p	**a**	**o**	H	Me	OPh	0
w	**c**	**p**	NO_2	Et	Cl	0

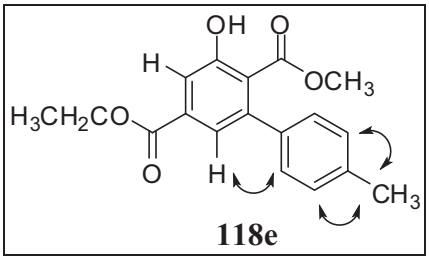
[a] Yields of isolated products.

The yields varied according to the electron withdrawing inductive effect of the substituent located the 6-aryl moieties. Generally, the yields increased as the withdrawing inductive effect of this substituent increased NO_2 > Br > H > Me. The latter increase the electrophilicity

of the carbonyl. Trials to cyclise both dienes **22p** and **22w** failed, even with Ar-NO_2 substituted enones.

2.2.3.1 Structural proof:

$^1H,^1H$ NOE experiments were done for compound **118e** (Fig. 17). It was found that the $PhCH_3$ protons, which resonate as a singlet at δ = 2.33 ppm, correlate with the aromatic protons which appear as a multiplet in the range δ =7.09 - 7.13 ppm (Fig. 18). Thus, it was useful to assign the aromatic protons of the toulene ring. The aromatic protons, which appear as multiplet at δ =7.04 - 7.08 ppm, correlate with only one aromatic proton of the phenol ring which resonate as a doublet at δ =7.39 ppm. A correlation, which supposed to be observed in the hypothetic isomer of **118e** with the other doublet at δ =7.55 ppm, was not observed. This observation cancelled the possibility of the hypothetic regioisomer of **118e**. Moreover, the coupling constants observed for the phenol protons (1.6 and 1.7 Hz) indicate *meta* couplings.



118e

Figure 17: $^1H,^1H$ NOE correlations of **118e**.

Similarly, coupling constants observed for the phenol protons for compounds **118a** and **118j** (1.7 and 1.8 Hz) indicate *meta* couplings.

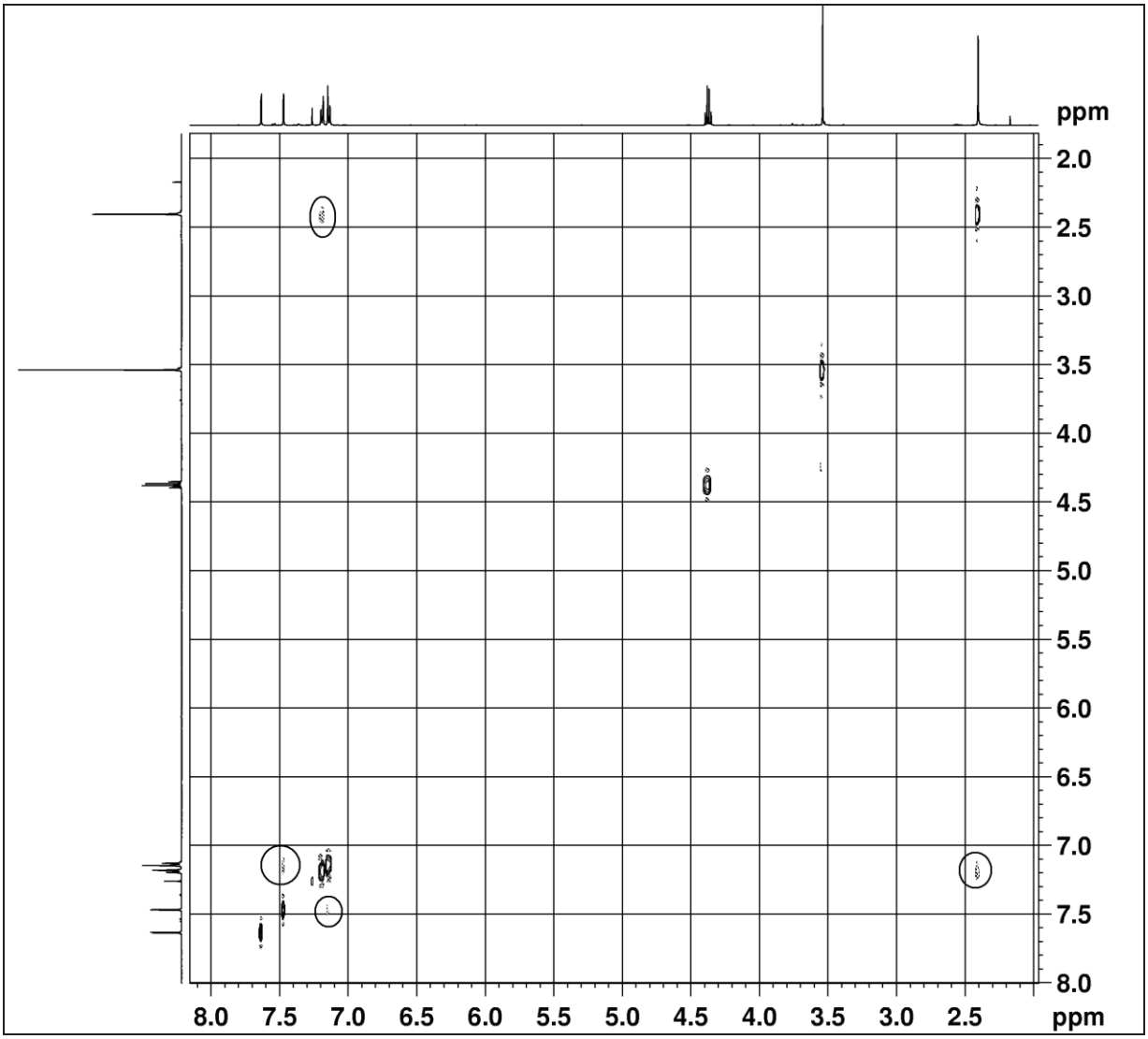


Figure 18: $^{1}H,^{1}H$ NOE spectrum of **118e**.

The signals (^{1}H NMR) of the methyl group of the CO_2Me moiety of terephthalates **118** (δ = 3.36 – 3.47 ppm) are generally slightly shifted upfield compared to the corresponding signals of isophthalates **107**, **110** and **113**. This can be explained by the fact that the CO_2Me groups of terephthalates **118** are located in the anisotropic cone (Fig. 19) of the neighboring aryl group.

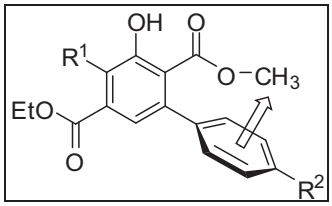


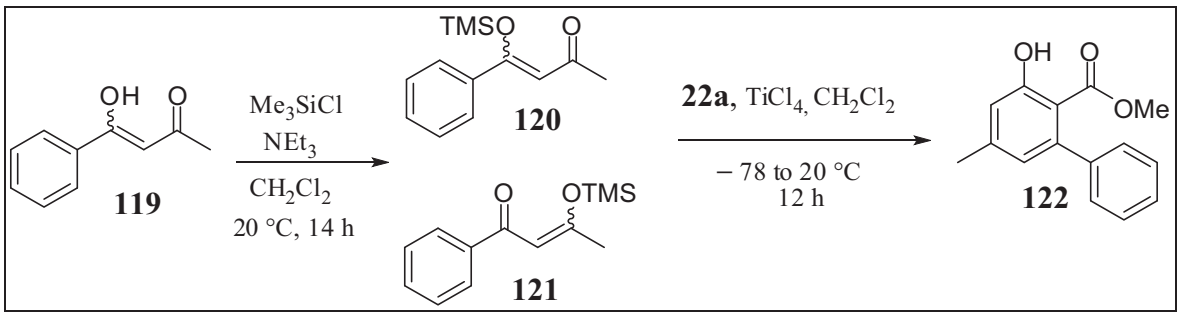
Figure 19: Location of the CO_2Me group in the anisotropic cone of the neighboring aryl group of **118a-n**.

The regioselectivity observed in the [3+3] cyclizations of 3-(silyloxy)-2-en-1-ones **117a-d**, derived from benzoylpyruvates, is different form that observed acetylpyruvates **112a**,**b**. The aryl group of **118a-n** is located in *ortho*-position to the ester group, while the methyl group of **113a-i** is located *para* to the ester group.

Chan and Brownbridge reported [14a] that the reaction of **22a** with 4-phenyl-4-(trimethylsilyloxy)but-3-en-2-one **120**, prepared from benzoylacetone (**119**) (Scheme 19), afforded methyl 6-phenyl-4-methylsalicylate **122** (the phenyl group of which is located *ortho* to the ester group).

This result was explained by $TiCl_4$-mediated isomerization of the TMS group of 4-phenyl-4-(trimethylsilyloxy)but-3-en-2-one **120** to give 1-phenyl-3-(trimethylsilyloxy)but-2-en-1-one **121** (or its titanium-complex) and subsequent conjugate addition of the terminal carbon atom of **22a** onto the enone.

Similarly, it is expected that **117a-d** underwent this isomerisation, followed by conjugate addition of the terminal carbon atom of dienes **22**.



Scheme 19: $TiCl_4$-mediated isomerization of the TMS group in 4-phenyl-4-(trimethylsilyloxy)but-3-en-2-ones.

This might be explained by an energetically favourable interaction of Ti(IV) with the neighbouring phenyl group. The regioselective formation of **118a-n** shows that this effect successfully competes with the chelation discussed above for the synthesis of products **113a-i**. The tendency of the aryl group to be located in *ortho*-position to the ester group is obviously higher than the tendency of the pyruvate-derived ester group to be located *ortho* to the diene-derived ester group.

2.2.3.2 X-ray analysis:

Another proof of the regioselectivity came from the X-ray crystal structure analyses (Fig. 20 and 21) of compounds **118h**, **118m**, respectively.

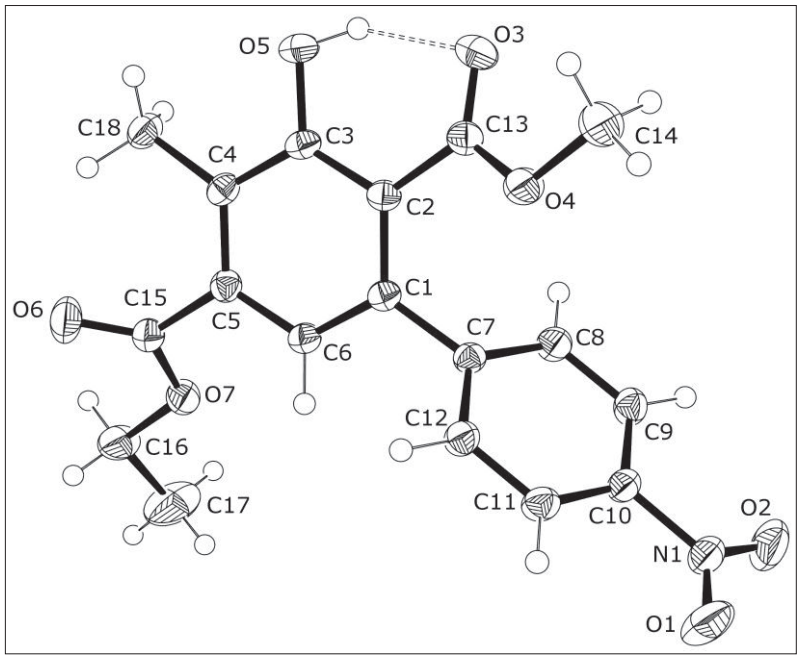


Figure 20: ORTEP plot of **118h** (50% level).

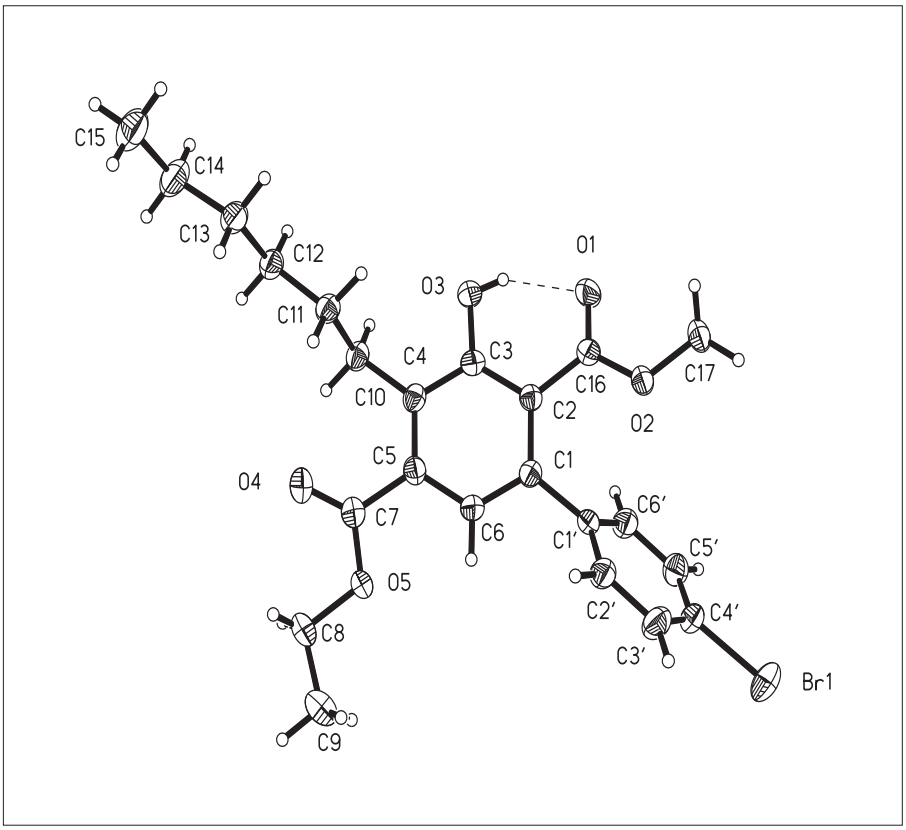


Figure 21: ORTEP plot **118m** (50% level).

In both compounds, the OH group is involved in intramolecular hydrogen bonding (Tables 11 and 12). In **118h**, the torsion angle between the two aromatic planes is 60.17 $(3)^0$ and between the NO_2 group and the phenyl group the torsion angle is 9.96 $(12)^0$. This indicates that the nitro group is almost in the plane of the aromatic ring. In compound **118m**, the torsion angle between the two aromatic planes is 54.66 $(6)^0$.

Table 11: Hydrogen bonds for **118h** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O5—H5···O3	0.90 (2)	1.74 (2)	2.5610 (12)	150.5 (17)

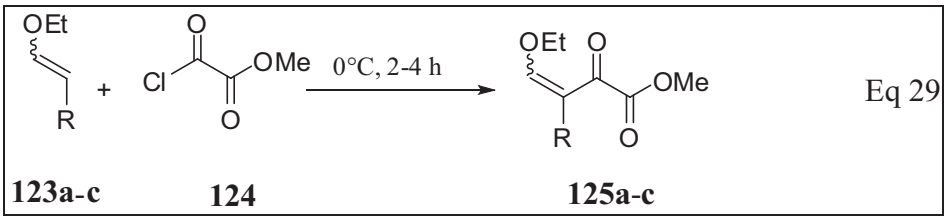
Table 12: Hydrogen bonds for **118m** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3O)...O(1)	0.77(3)	1.85(3)	2.541(2)	151(3)

2.2.4 Synthesis of substituted 2-hydroxy-terephthalates and 3-hydroxyphthalates by [3+3] cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with substituted 4-ethoxy-2-oxo-3-butenoates:

The protocol then was extended toward the utilization of 4-alkoxy-, rather than 4-silyloxy-2-oxo-3-butenoates in the formal [3+3] cyclization reactions with 1,3-bis(silyloxy)-1,3-butadienes. This provides another method for the synthesis of the target molecules.

The treatment of the enol ethers **123a-c** with methyl 2-chloro-2-oxoacetate (**124**) afforded, following a known procedure [153], the substituted 4-ethoxy-2-oxo-3-butenoates **125a-c** (Eq. 29, Table 13), which were isolated as mixtures of *E/Z* isomers. The synthesis of the derivative **125a** has been previously reported [153].



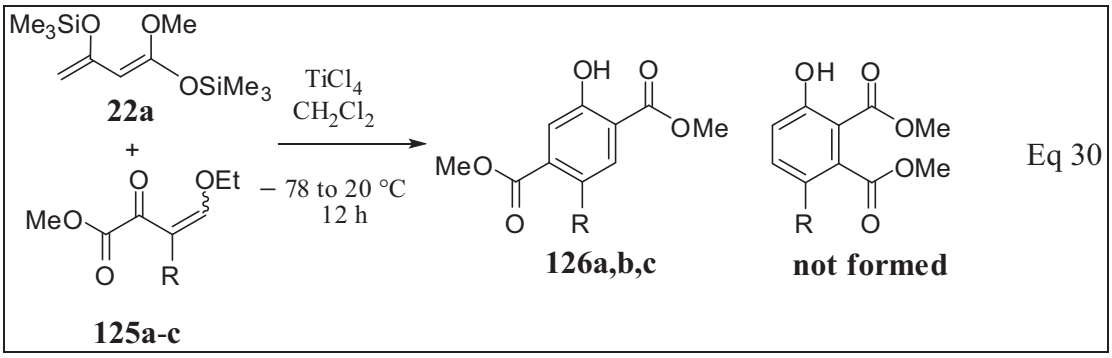
Eq 29

Table 13: Products and yields **125a-c**.

123,**124**	R	% (**124**)[a]
a	H	82
b	Me	97
c	Et	95

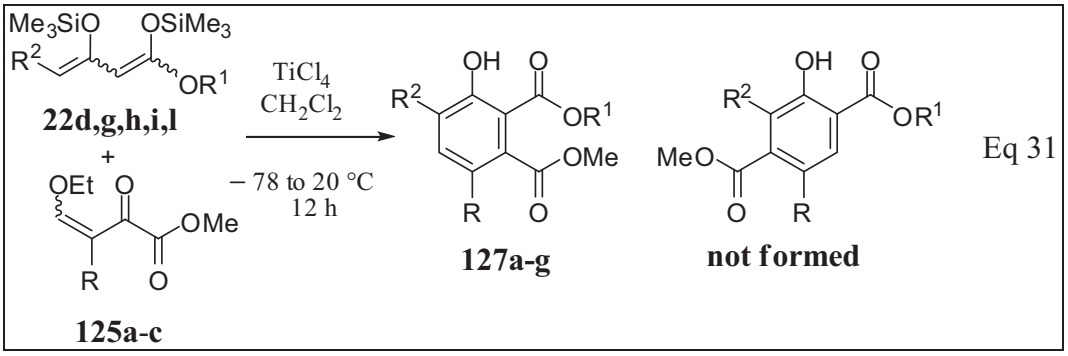
[a] Yields of isolated products

The $TiCl_4$-mediated formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadiene **22a** with 4-ethoxy-2-oxo-3-butenoates **125a-c** gave 2-hydroxyterephthalates **126a-c** (Eq. 30, Table 14). The formation of the other regioisomers was not observed. The reaction proceeds by attack of the terminal carbon atom of the diene **22a** onto the carbonyl group and subsequent cyclization followed by aromatization.



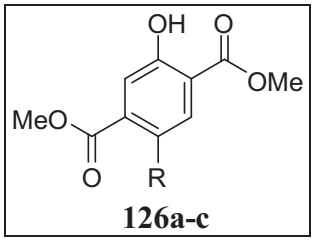
Eq 30

In contrast, $TiCl_4$-mediated [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes **22d**,**g**,**h**,**i**,**l**, which have a substituent at C4, with 4-ethoxy-2-oxo-3-butenoate **125a-c** gave 3-hydroxyphthalates **127a-g** (Eq. 31, Table 15). The products were formed with very good regioselectivity. The formation of the other regioisomers, 2-hydroxyterephthalates, was not observed.



Eq 31

Compounds **126a-c** (Table 14) are 2-hydroxyterephthalates having no substituent located at C3 and C6. Compounds **127a-g** (Table 15) are substituted 3-hydroxyphthalates having no substituents at C5. Both categories of molecules are considered as functionalized salicylates.

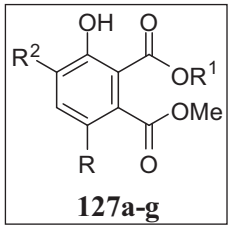


126a-c

Table 14: Products and yields **126a-c**.

125,126	R	% (126)[a]
a	H	40
b	Me	45
c	Et	47

[a] Yields of isolated products



127a-g

Table 15: Products and yields of **127a-g**.

22	125	127	R	R^1	R^2	% (127)[a]
d	**a**	**a**	H	Me	Me	42
g	**a**	**b**	H	Et	Et	45
h	**a**	**c**	H	Me	*n*-Bu	43
l	**a**	**d**	H	Me	*n*-Oct	45
d	**b**	**e**	Me	Me	Me	45
i	**b**	**f**	Me	Me	*n*-Pent	46
d	**c**	**g**	Et	Me	Me	48

[a] Yields of isolated products

2.2.4.1 Structural proof:

The terephthalate **126a** was previously prepared by anodic monohydroxylation of dimethyl terephthalate in 47% yield [81]. the obtained spectroscopic data are in full agreement with those reported. The comparison of these data with those reported for **126a** [81] and for its phthalate regioisomer, reported also in the literature [96d], confirmed the structure for **126a**.

The structure of terephthalate **126b** was confirmed by the two singlets observed at δ = 7.41 ppm and 7.62 ppm (Fig. 22), the same also was noticed for **126c**. The phthalate regioisomers of **126b** [154] and **126c** [95e] are known and their spectroscopic data are, as expected, different from terephthalates **126b** and **126c**.

The regioselectivity noticed for compounds **126a-c** could be explained by the higher electrophilicity of the carbonyl group located next to the ester group, which also forms a chelate with $TiCl_4$.

The change of the regioselectivity in the formation of compounds **127a-g** might be explained by steric reasons (interaction of substituent R^2 with the ester group of the enone).

Compound **127e** was previously reported and its spectroscopic data are in agreement with the obtained data [96f].

3-Hydroxyphthalates **127a-g** show a singlet at approx. 7.10 ppm which can be assigned to proton H-5 located *meta* to the ester group. In contrast, the signals of protons located *ortho* to an ester group are generally shifted more downfield.

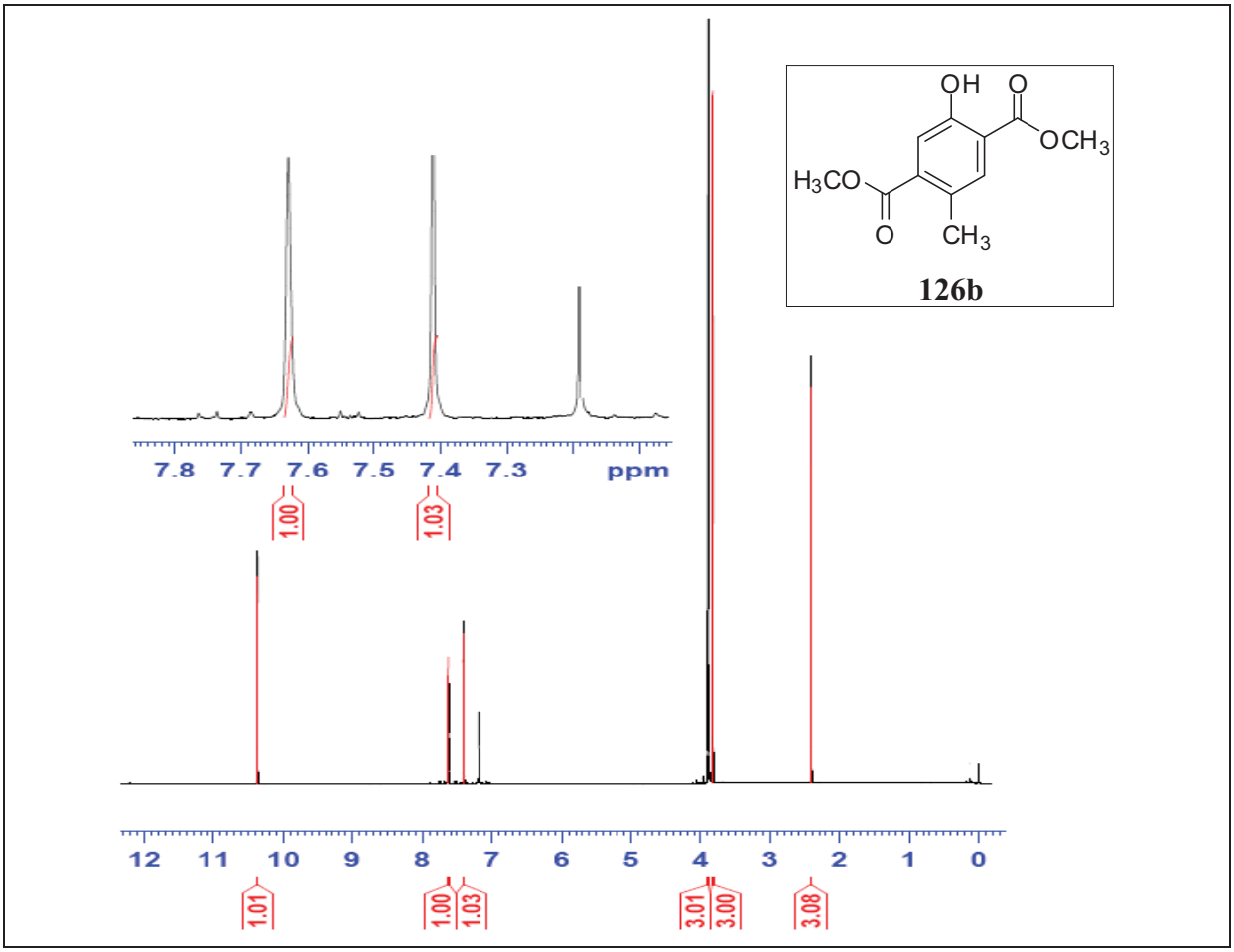


Figure 22: ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **126b**.

^{1}H,^{1}H NOE experiments were performed for compounds **127g** and **127e**. For **127g**, it was observed that the aromatic proton, which resonates at δ = 7.13 ppm as a singlet, correlates with the $PhCH_3$ protons (Fig. 23 and 24), which resonate at δ = 2.19 ppm as a singlet. In addition it correlates with both groups of protons of the ethyl side chain $Ph\mathit{CH_2CH_3}$.

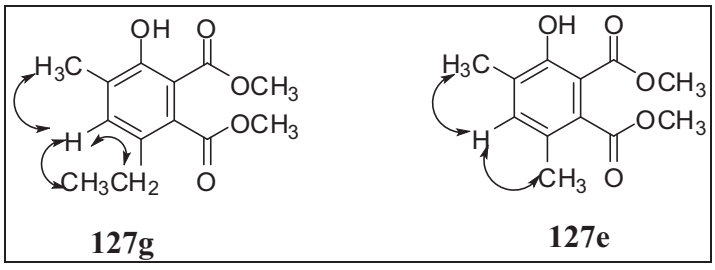


Figure 23: ^{1}H,^{1}H NOE correlations of **127g** and **127e**.

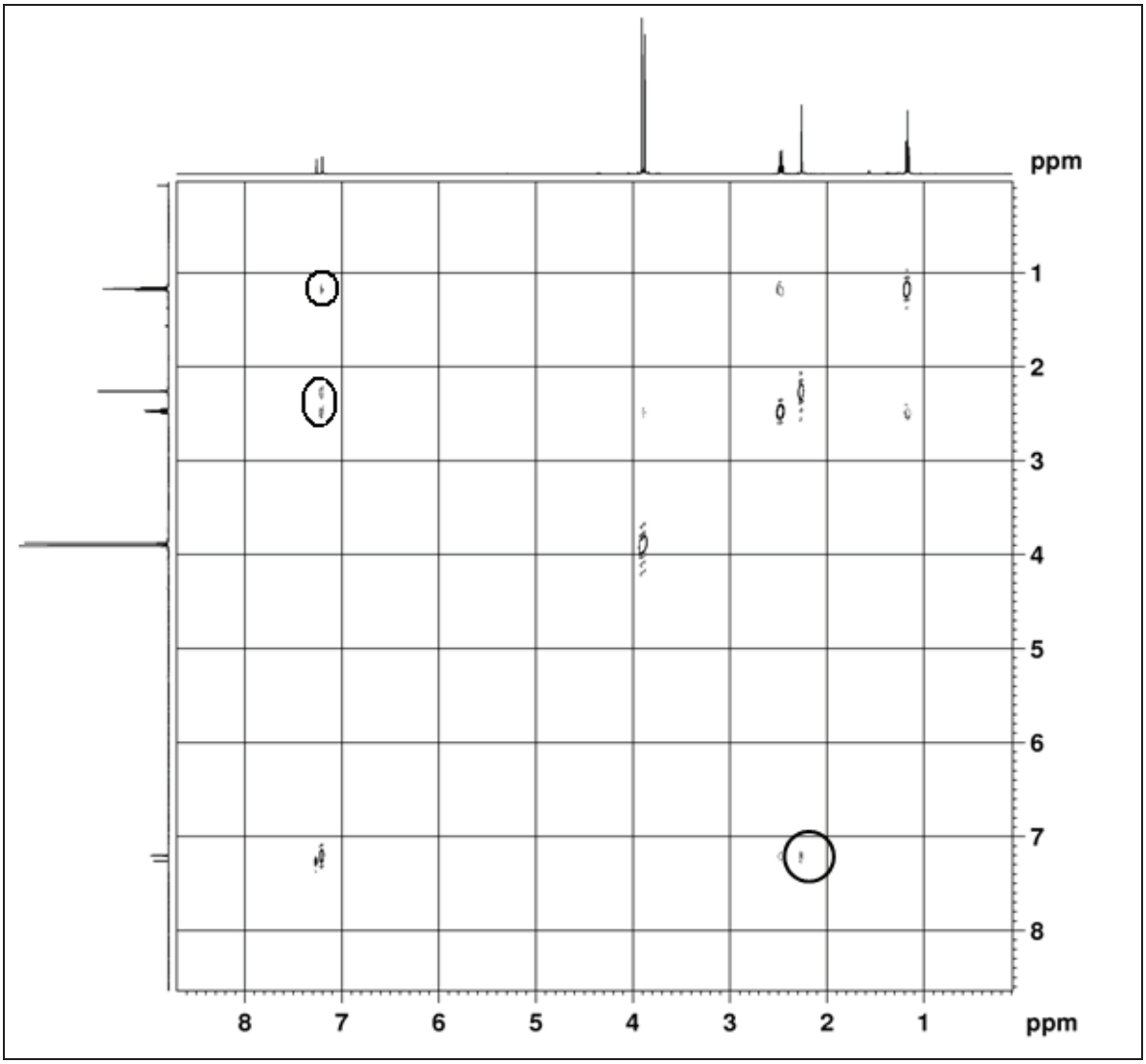


Figure 24: $^{1}H,^{1}H$ NOE Spectrum of **127g**.

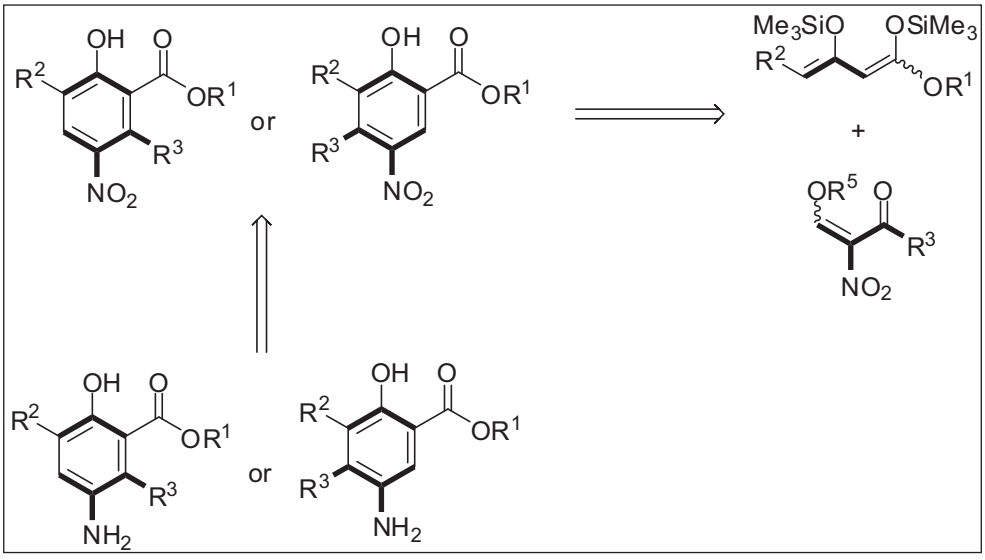
2.3 Regioselective synthesis of functionalized 4-nitro- and 4-aminophenols based on formal [3+3] cyclocondensations of 3-ethoxy-2-nitro-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes:

The great importance of 4-nitro- and 4-aminophenols in pharmaceutical and natural product chemistry has attracted my attention to find a new synthetic method for their regioselective and reliable synthesis.

2.3.1 Target, problems to solve and strategy:

Hefner *et al.* have reported [3+3] cyclocondensation of symmetrical nitro substitited 3-silyloxy-2-en-1-one with 1,3-bis(silyloxy)-1,3-butadienes [112] to give nitrophenols followed by reduction to get 4-aminophenols. The scope of the reaction was limited to symmetrical substrates. My task was to develop a more versatile protocol.

My approach is based on the cyclization of unsymmetrical 3-alkoxy-2-nitro-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes (Scheme 20) to give functionalized 4-nitrophenols under mild conditions, followed by the catalytic reduction of these nitrophenols to get 4-aminophenols.



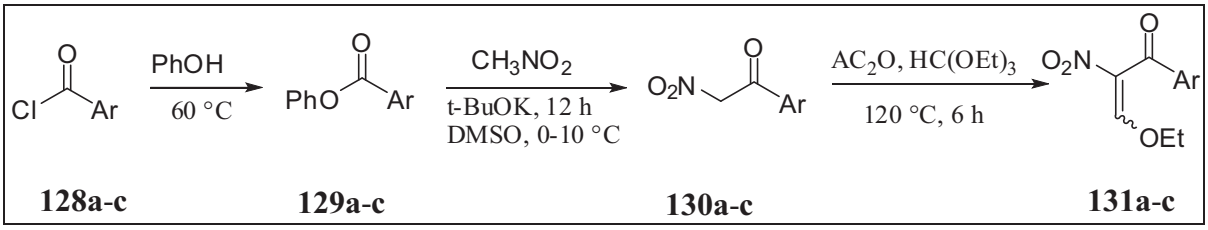
Scheme 20: Retrosynthesis of 4-nitro- and 4-aminophenols.

2.3.2 Regioselective synthesis of functionalized 4-nitro- and 4-aminophenols by formal [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 3-ethoxy-2-nitro-2-en-1-ones and subsequent catalytic hydrogenation:

Aryl phenolates **129a-c** were previously reported [155] and were synthesized from the corresponding aroyl chlorides **128a-c** [156].

The base mediated reactions of **129a-c** with nitromethane [157] gave the α-nitroacetophenones **130a-c**, (Scheme 21, Table 16), which have also been earlier reported [157,158].

The reflux of **130a-c** in a mixture of triethyl orthoformate and acetic anhydride afforded the 3-ethoxy-2-nitro-2-en-1-ones **131a-c** as mixtures of *E/Z* regioisomers (Scheme 21, Table 16).



Scheme 21: Synthesis of 3-alkoxy-2-nitro-2-en-1-ones **131a-c**.

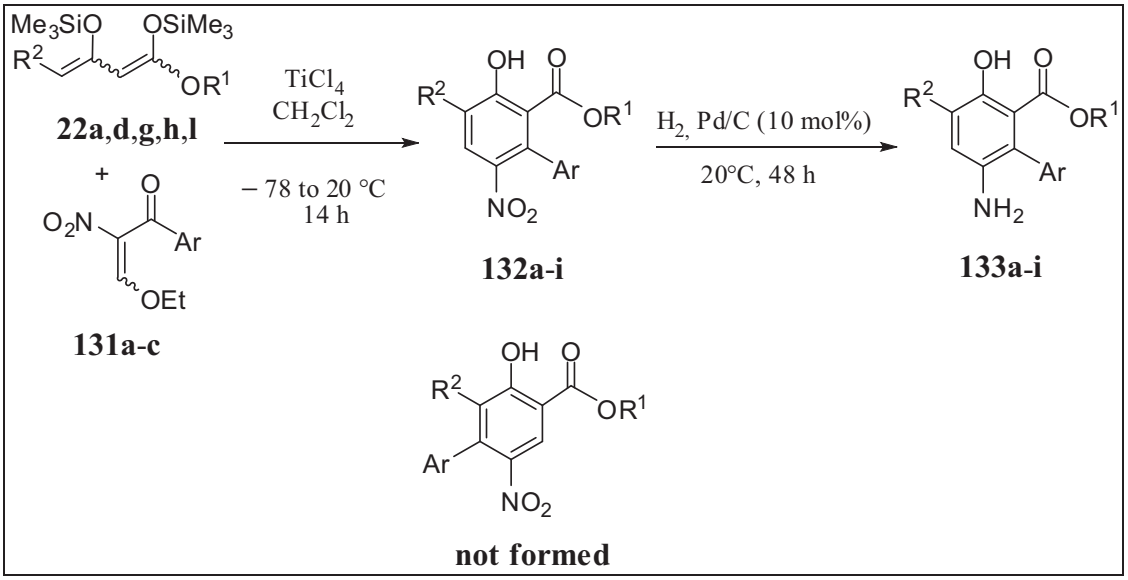
Table 16: Products and yields of **131a-c**.

129,**130**, **131**	Ar	%(**131**)[a]
a	Ph	81
b	2-MeC_6H_4	81
c	2-ClC_6H_4	82

[a] Yields of isolated products

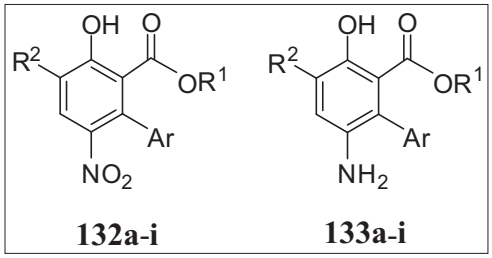
The $TiCl_4$-mediated formal [3+3]cyclizations of 1,3-bis(silyloxy)-1,3-butadienes **22a**,**d**,**g**,**h**,**l** with 3-ethoxy-2-nitro-2-en-1-ones **131a-c** (Scheme 22, Table 17) gave 4-nitrophenols **132a-i** in good to very good yields. The other regioisomers were not formed.

The hydrogenation of the nitrophenols **132a-i**, catalyzed by Pd/C (10 mol%) (Scheme 22, Table 17), afforded the corresponding aminophenols **133a-i** in excellent yields.



Scheme 22: Synthesis of 4-nitro- and 4-aminophenols **132a-i**, **133a-i**.

Compounds **132a-i** are 4-nitrophenols. They can be also considered as functionalized biaryls. Furthermore, they are nitro-biaryls, which were reported to possess a wide spectrum of pharmaceutical applications [107]. Compounds **133a-i** are the corresponding amino derivatives of **132a-i**. These compounds could be starting substrates for many synthetic targets. The synthesis of 3-alkyl-4-nitro and 3-alkyl-4-aminophenols is now under investigation.



132a-i **133a-i**

Table 17: Products and yields of **132a-i** and **133a-i**.

131	22	132, 133	Ar	R^1	R^2	% (132)[a]	% (133)[a]
a	**a**	**a**	Ph	Me	H	56	86
a	**d**	**b**	Ph	Me	Me	57	85
a	**g**	**c**	Ph	Et	Et	65	96
a	**h**	**d**	Ph	Me	*n*-Bu	58	91
a	**l**	**e**	Ph	Me	*n*-Oct	62	90
b	**a**	**f**	2-MeC_6H_4	Me	H	68	90
b	**d**	**g**	2-MeC_6H_4	Me	Me	72	89
c	**a**	**h**	2-ClC_6H_4	Me	H	56	88
c	**d**	**i**	2-ClC_6H_4	Me	Me	70	89

[a] Yields of isolated products.

Generally, the yields increased when a C4-substituted diene was used. No regular effect on the yield was observed with variation of the aryl group. Excellent yields of the aminophenols were obtained.

2.3.2.1 Structural proof:

$^1H,^1H$ NOE experiments were done for compounds **132b** and **132d**. For **132d**, it was observed that the aromatic proton, which resonates at δ = 7.68 ppm as a singlet, correlates with the Ph*CH*$_2$ protons (Fig. 25 and 26) which resonate at δ = 2.64 ppm as a triplet. In addition, it correlates with CH_2 protons of the butyl side chain $PhCH_2CH_2$.

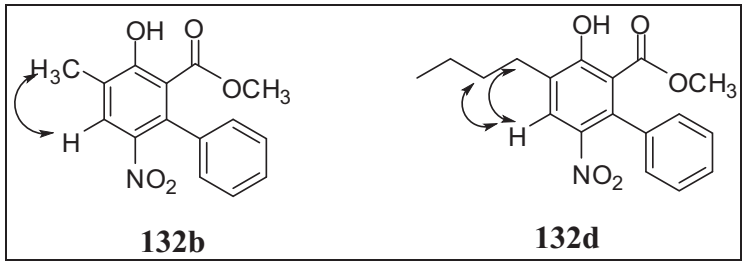


Figure 25: $^{1}H, ^{1}H$ NOE correlations of **132b** and **132d**.

It was noticed from ^{1}H NMR spectroscopy that the OH groups in compounds **132a-i** resonate in the range (δ = 11.07-11.79) ppm, while for compounds **133a-i** they appear in the range of δ = 9.98-10.42 ppm. This difference could be attributed to the electron withdrawing nature of the nitro group, the donating effect of the amino group as well as the presence of the intermolecular hydrogen bonding. The NH_2 protons appear as broad singlets in the range of δ = 3.02-3.09 ppm. Generally, OCH_3 groups in compounds **133a-i** are slightly more downfield shifted than those of the corresponding amino derivatives.

In the ^{13}C NMR spectra, the carbon of the C-OH group in compounds **132a-i** appear in the range of δ = 162.0-164.4 ppm, while for compounds **133a-i**, they appear between δ = 152.8-154.7 ppm.

The aromatic protons of the phenol rings of **132a** resonate at δ = 7.02 and 7.82 ppm as doublets with coupling constants ^{3}J = 9.0 Hz and ^{3}J = 8.9 Hz which are assigned for *ortho*-coupling. The same was noticed for both **132f** and **132h**.

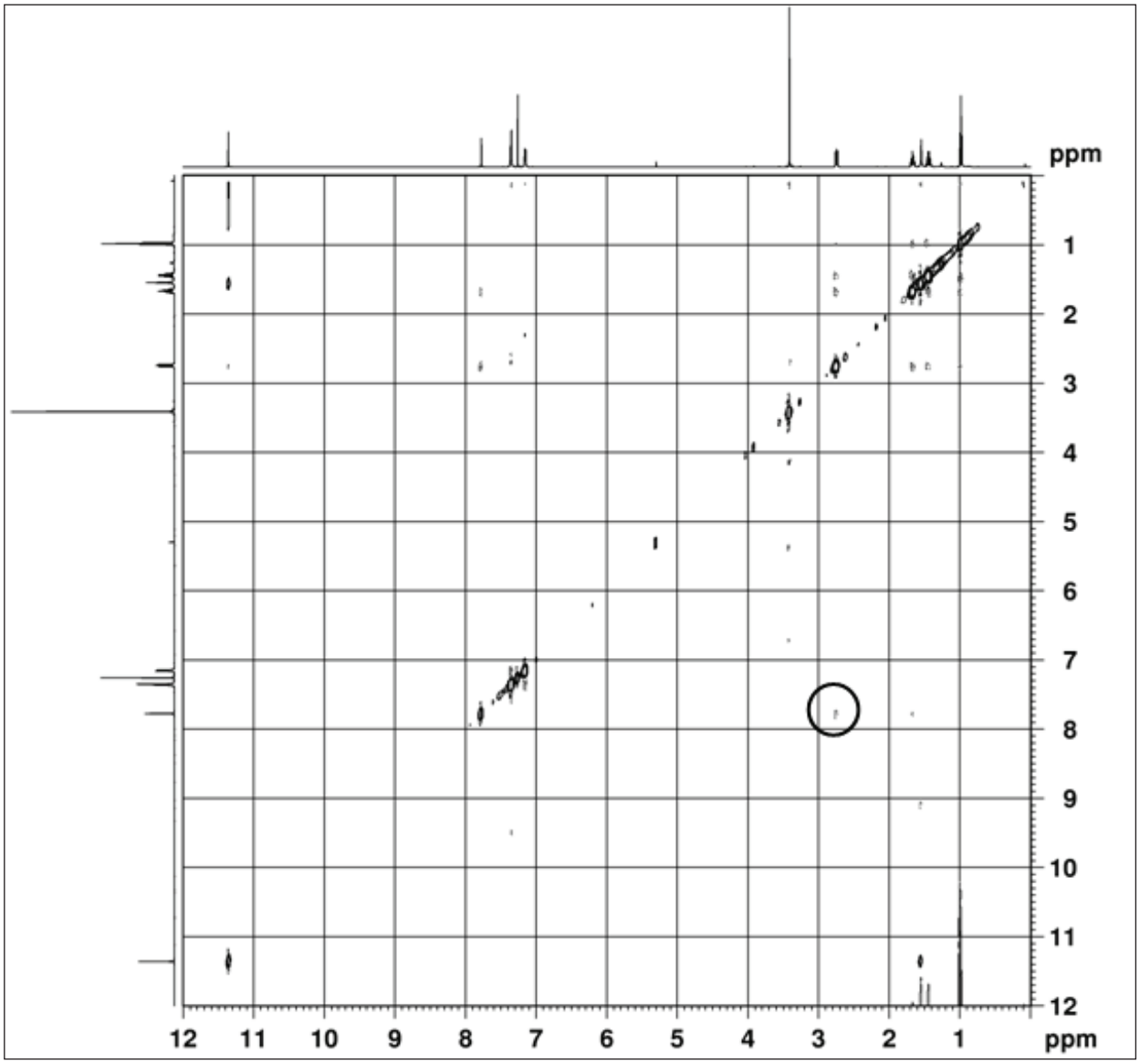


Figure 26: $^{1}H,^{1}H$ NOE Spectrum of **132d**.

The regioselectivity observed here resulted from the initial addition of the C4 nucleophilic center of the diene to the conjugate position of the enone.

2.3.2.2 X-ray analysis:

Another proof of the regioselectivity came from the X-ray crystal structure analyses (Fig. 27) of compounds **132i**.

The reported bond lengths NO are: d(N-O) =1.45 °A and d(N=O) =1.17 °A [159], for compound **132i** the bond lengths are: d (O(4)-N(1)) = 1.2255(17) °A and d ((5)-N(1)) = 1.2211(19) °A, which lies between the values for the single and double bond. This is due to the partial double bond character of NO in NO_2.

The O-H group in compound **132i** is involved in both inter- and intramolecular hydrogen bonding (Fig. 28, Table 18).

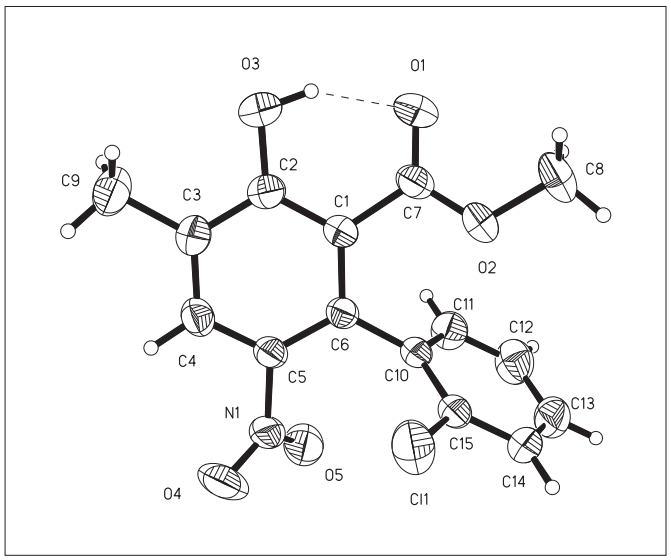


Figure 27: ORTEP plot of **132i** and (50% level).

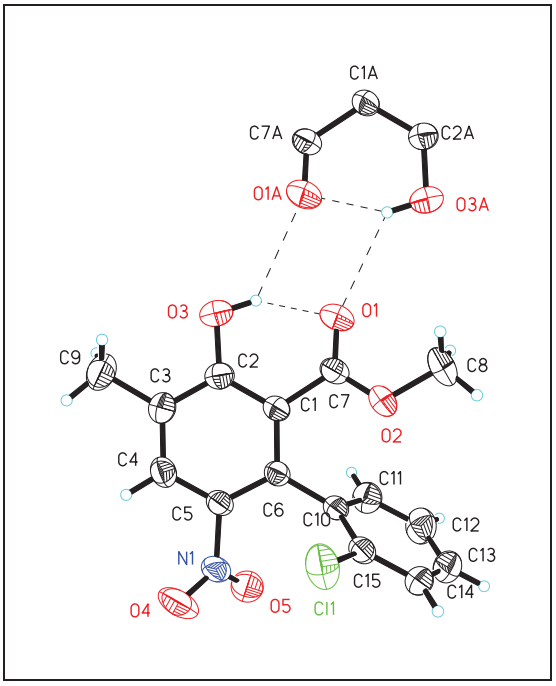


Figure 28: Inter -and intra-molecular hydrogen bonding in **132i**.

Table 18: Hydrogen bonds for **132i** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3O)...O(1)	0.91(3)	1.81(3)	2.6299(18)	150(3)
O(3)-H(3O)...O(1)#1	0.91(3)	2.60(3)	3.2021(17)	125(2)

There are four symmetry independent molecules in the asymmetric unit of **133a** (Fig. 29, 30 and 31**)** which form a very special network of hydrogen bonds.

The molecules can be distinguished by the help of the angles between their aromatic rings or the dihedral angle of the respective atoms (Table 19).

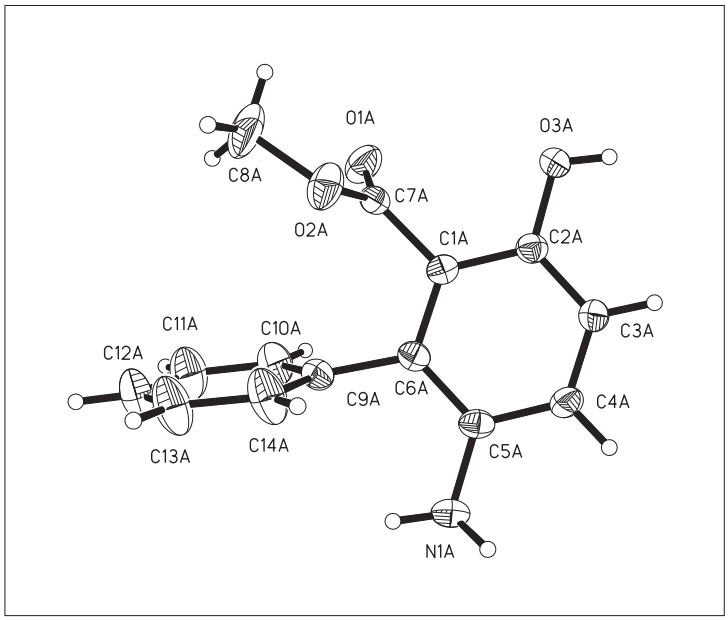


Figure 29: ORTEP plot of molecule A (1 of the four symmetry independent molecules) in **133a**.

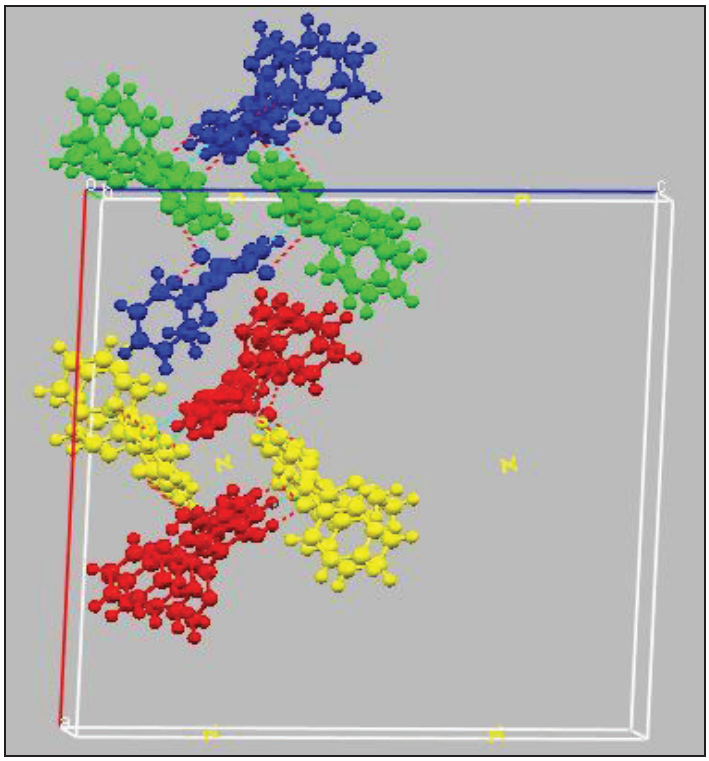


Figure 30: Crystal structure of **133a** (view almost along the b- and screw axis, molecules A: green, B: blue, C: red, D: yellow).

Table 19: Differences between the four symmetry independent molecules in **133a** with estimated standard deviations in parentheses.

Molecule	Angle between aromatic rings	Dihedral angle
A(green)	76.45(0.09)	C1A-C6A-C9A-C10A: 73.27(0.26)
B(blue)	58.55(0.09)	C15B-C20B-C23B-C24B: 57.49(0.24)
C(red)	66.93(0.07)	C29C-C34C-C37C-C42C: -64.03(0.23)
D(yellow)	68.92(0.08)	C43D-C48D-C51D-C52D: 67.95(0.24)

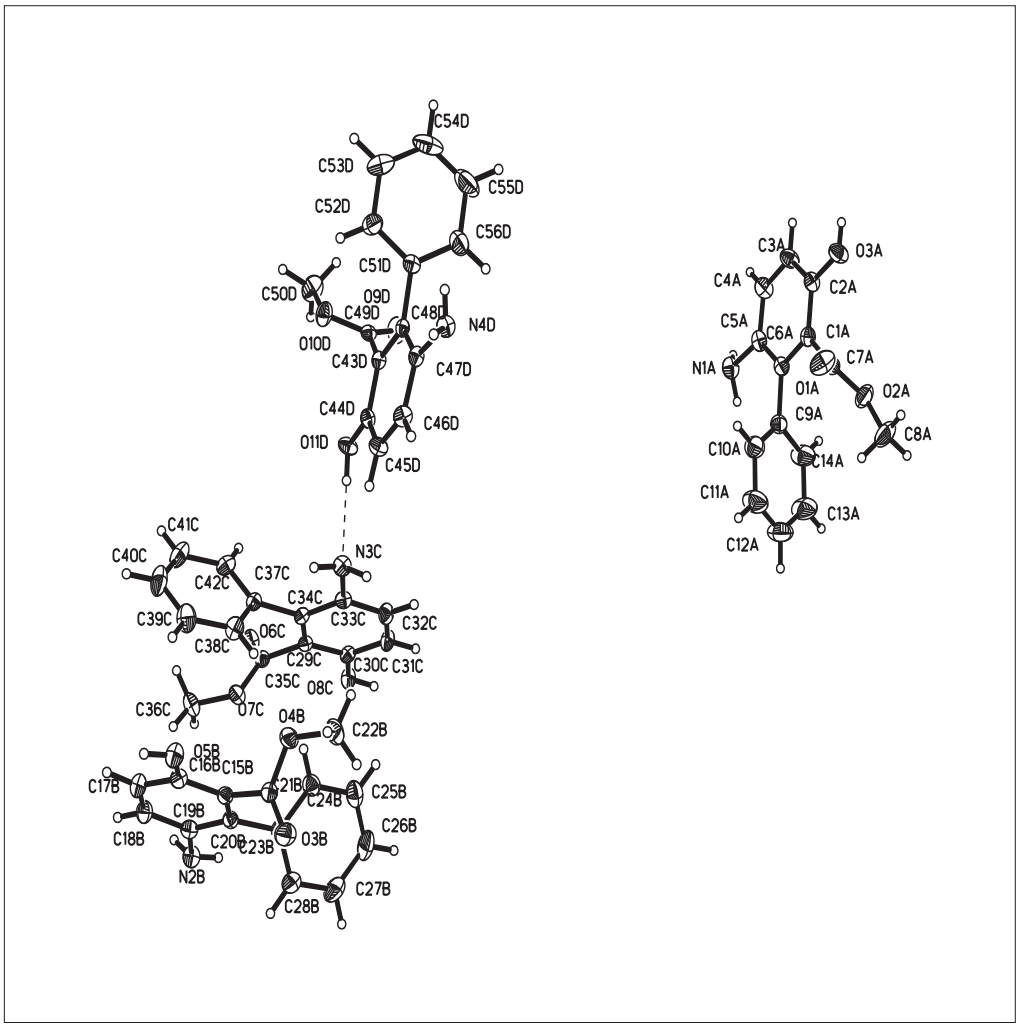


Figure 31: ORTEP plot of the asymmetric unit of **133a**.

Although there is a total of 12 different bond lengths for the hydrogen bonds, there are only five different symmetry operators for generating equivalent atoms in neighboring molecules.

This means that there are some common patterns of hydrogen bond types (Table 20). All four molecules form rows of hydrogen bonded molecules along the b-axis via the hydrogen atoms of the amino groups as donor and the carbonyl oxygen atoms of the next molecule as acceptor.

The OH-protons point in any case to the nitrogen of the amino group of a neighbor molecule. This is done in pairs, *i.e*. the OH group in an **A** molecule points to the N-atom in molecule **B** (the symmetry code being x+1, y-1, z), the OH in **B** to a nitrogen in a neighboring molecule **A** with symmetry code -x+1, y-1/2, -z+1/2 thus forming tubes of hydrogen bonded molecules around a screw axis. In a similar manner **C** and **D** type molecules are arranged about another screw axis. However, since there is an inter-molecular hydrogen bond between H12D of the OH group in molecule **D** and the nitrogen N3C in molecule **C** of the same asymmetric unit, only three symmetry operators ($1, $3 and $4) are needed here.

Unfortunately the position of the OH protons could not be elucidated from the difference map. Therefore in this case there is no estimated standard deviation for the distances D-H, H…A and the angle DHA. On the other hand all hydrogen atoms of the four amino groups could be taken from the difference map.

Table 20: Distances (Å) and angles (deg) for the hydrogen bonds in **133a** with estimated standard deviations in parentheses.

Involved atoms	D-H	H…A	D…A	Angle DHA
O3A-H3A...N2B_$1[a]	0.82	2.05	2.865(2)	169.8
N1A-H1NA...O1A_$2	0.91(3)	2.20(3)	2.844(3)	127(2)
N1A-H2NA...O3A_$2	0.89(3)	2.32(3)	3.167(2)	159(3)
O6B-H6B...N1A_$3	0.82	2.02	2.840(2)	175.1
N2B-H2NB...O4B_$2	0.84(3)	2.47(3)	3.068(3)	129(2)
N2B-H1NB...O6B_$2	0.89(3)	2.22(3)	3.095(2)	168(3)
O9C-H9C...N4D_$4	0.82	2.06	2.877(2)	171.2
N3C-H2NC...O9C_$5	0.91(3)	2.30(3)	3.170(2)	160(2)
N3C-H1NC...O7C_$5	0.88(3)	2.17(3)	2.807(2)	129(2)
O12D-H12D...N3C	0.82	2.01	2.828(2)	174.6
N4D-H2ND...O12D_$5	0.87(3)	2.30(3)	3.163(2)	168(3)
N4D-H1ND...O10D_$5	0.81(3)	2.46(3)	2.976(2)	122(2)

[a]The symmetry codes can be seen from (Table 21)

Table 21: Operators and symmetry codes for generating equivalent atoms or molecules.

Operator	symmetry code
$1	x+1, y-1, z
$2	x, y+1, z
$3	-x+1, y-1/2, -z+1/2
$4	-x+1, y+3/2, -z+1/2
$5	x, y-1, z

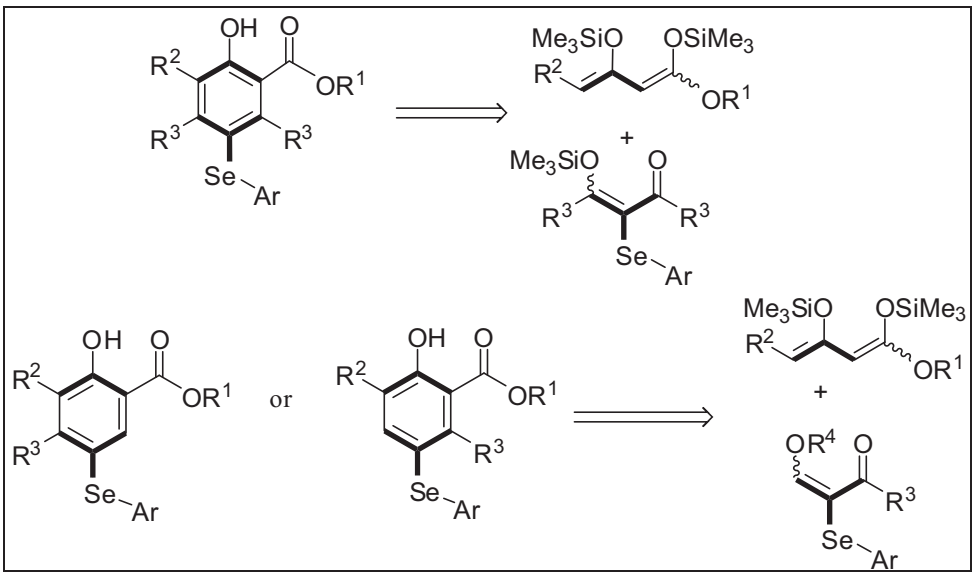
2.4 Synthesis of functionalized diaryl selenides by the first [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with organoselenium compounds:

Diaryl selenides play an important role in pharmaceutical chemistry; this was reviewed [127b]. Finding reliable methods for the direct synthesis of highly functionalized diaryl selenides is a demanding task.

2.4.1 Target, problems to solve and strategy:

The few reported methods for the synthesis of diaryl selenides starting with "acyclic precursors" suffer from the fact that the availability of these starting precursors is a tedious task and their substitution pattern is limited.

My strategy to overcome the previous drawbacks rely on the construction of these functionalized arenes by [3+3] cyclization reactions (Scheme 23) of 1,3-bis(silyloxy)-1,3-butadienes with phenylselanyl substituted 3-silyloxy-2-en-1-ones and 3-alkoxy-2-en-1-ones.

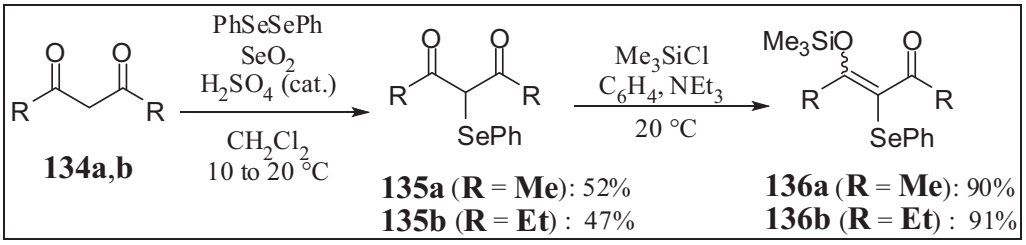


Scheme 23: Retrosynthesis of diaryl selenides.

2.4.2 Synthesis of functionalized diaryl selenides by [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with symmetrical 3-silyloxy-2-phenylselanyl-2-en-1-ones:

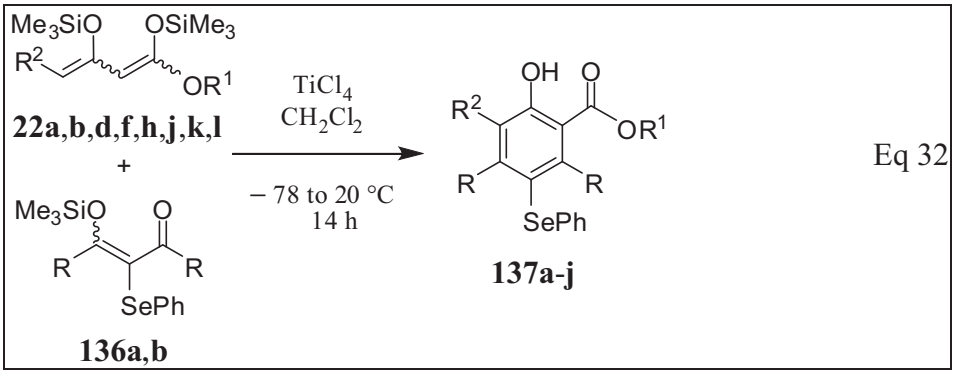
The sulfuric acid catalyzed reaction of diketones **134a**,**b** with selenium dioxide and diphenyl diselenide (Scheme 24) afforded the phenylselanyl-substituted 1,3-diketones **135a**,**b** in relatively good yields.

The synthesis of **135a** has been previously reported [160]. The base mediated silylation of **135a**,**b** (Scheme 24) using chlorotrimethylsilane as a silylating agent afforded the novel phenylselanyl substituted 3-silyloxy-3-en-1-ones **136a**,**b** in high yields.



Scheme 24: Synthesis of 3-silyloxy-2-phenylselanyl-2-en-1-ones.

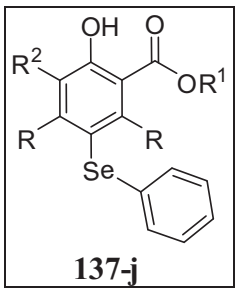
The formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes **22a,b,d,f,h,j,k,l** with symmetrical 3-silyloxy-2-phenylselenayl-2-en-1-ones **136a**,**b**, mediated by $TiCl_4$ (Eq. 32, Table 20), afforded the diaryl selenides **137a-j** in good to very good yields.



Eq 32

These cyclizations were done using the equivalent ratio of reactants (**136**/**22**/ $TiCl_4$) (1.0/1.1/1.1), in concentrated solutions (2 ml of extra dry CH_2Cl_2/1 mmol of **136**).

Compounds **137a-j** could be considered as unsymmetrical diaryl selenides. These 4-(phenylselanyl)phenols have the same substituents at C3 and C5.



137-j

Table 22: Products and yields of **137a-j**.

136	22	137	R	R^2	R^1	%(**137**)[a]
a	**a**	**a**	Me	H	Me	59
a	**b**	**b**	Me	H	$CH_2CH_2OCH_3$	57
a	**d**	**c**	Me	Me	Me	68
a	**f**	**d**	Me	Et	Me	70
a	**h**	**e**	Me	n-But	Me	69
a	**j**	**f**	Me	n-Hex	Me	62
a	**k**	**g**	Me	n-Hep	Me	62
a	**l**	**h**	Me	n-Oct	Me	59
b	**a**	**i**	Et.	H	Me	56
b	**b**	**j**	Et.	H	$CH_2CH_2OCH_3$	55
b	**c**	**k**	Et	H	$CH_2C_6H_5$	0
a	**w**	**l**	Me	Cl	Et	0
b	**o**	**m**	Et	OMe	Me	0

[a] Yields of isolated products

Generally, when C4-substituted dienes were used, the yields increased. No regular dependence of the yield on the side chain length of the diene was noticed. Trials to cyclize the dienes **22c**,**w**,**o** failed and the starting precursors were recovered. Yields also were relatively low when **136b** was used as dielectrophile. This could be due to steric factors.

No issue of regioselectivity is encountered here.

My attempts to prepare unsymmetrical 3-alkoxy-2-phenylselanyl-2-en-1-ones, unfortunately, failed.

2. 4.2.1 X-ray analysis:

The structure of **137b** was confirmed by X-ray crystal structure analyses (Fig. 32, Table 23). The OH group is involved in intramolecular hydrogen bonding.

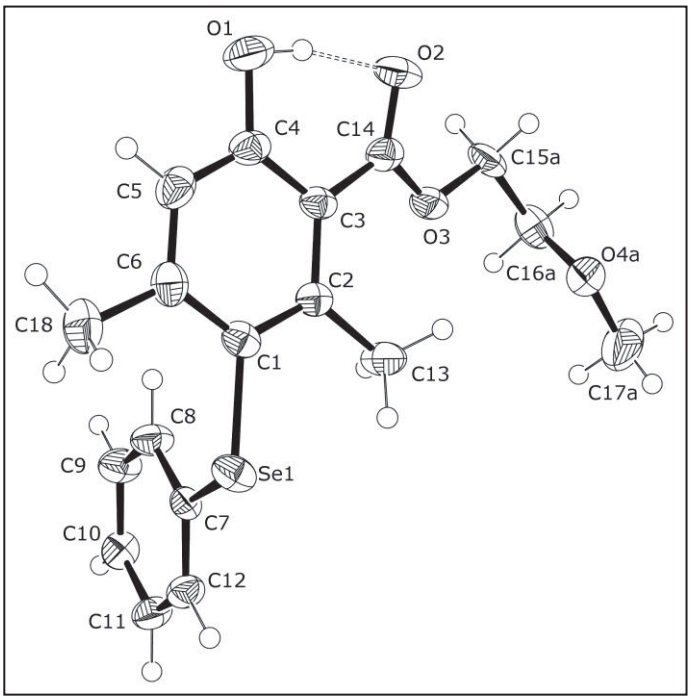


Figure 32: ORTEP plot of **137b** and (50% level).

The angle C16A—O4A—C17A was found to be 113.1 (7) °, while its for C7—Se1—C1 100.73 (10)°. The dihedral angle (C7—Se1—C1—C6) is 100.4 (2) °.

Table 23: Hydrogen bonds for **137b** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)	0.87 (4)	1.69(4)	2.536 (3)	165 (3)

Part 3: Experimental part:

3.1 General: Equipment, chemicals and work techniques:

3.1.1 ^{1}H NMR spectroscopy:

Bruker: AM 250, Avance 250, AC 250 (250 MHz); ARX 300, Avance 300 (300 MHz); Varian VXR 500 S, Avance 500 (500 MHz); δ = 0.00 ppm for Tetramethylsilane; δ = 2.04 ppm for Acetone d-6; δ = 7.26 ppm for Deuterochloroform ($CDCl_3$) and δ = 2.50 ppm for DMSO- d_6; Multiplicities are given as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signals. More complex coupling patterns are represented by combinations of the respective symbols. For example, td indicates a triplet of doublets with the larger coupling constant associated with the first symbol (here: triplet). Spectra were evaluated according to first order rule. All coupling constants are indicated as (*J*).

3.1.2 ^{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 $CDCl_3$, δ = 39.7 ppm for DMSO- d_6. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH_3, CH_2, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

3.1.3 Mass spectrometry (MS):

AMD MS40, Varian MAT CH 7, MAT 731 (EI, 70 eV), Intecta AMD 402 (EI, 70 eV and CI), Finnigan MAT 95 (CI, 200 eV).

3.1.4 High resolution mass spectroscopy:

Finnigan MAT 95 or Varian MAT 311; Bruker FTCIR, AMD 402 (AMD Intectra).

3.1.5 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.

3.1.6 Elementary analysis:

LECO CHNS-932, Thermoquest Flash EA 1112.

3.1.7 X-ray crystal structure analysis:

Bruker X8Apex Diffractometer with CCD-Kamera (Mo-K_a und Graphit Monochromator, $\lambda = 0.71073$ Å). The space group is determined by the XPREP program and the structures were solved via the SHELX-97 program package. Refinements were carried out according to the minimum square error method.

3.1.8 Melting points:

Micro heating table HMK 67/1825 Kuestner (Büchi Apparatus), Leitz Labolux 12 Pol with heating table Mettler FP 90. Melting points are uncorrected.

3.1.9 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.

3.1.10 Thin layer chromatography (TLC):

Merck Kieselgel 60 F254 on aluminium foil from Macherey-Nagel. Detection was carried out under UV light at 254 nm and 365 nm. As colourizing reagent the following mixtures were used: 1-2/100 p-Anisaldehyde or vanillin, 10/100 glacial acetic acid, 5/100 sulphuric acid, 83-84/100 methanol.

3.2 Chemicals and work techniques:

All solvents for using were distilled by standard methods. All reactions were carried out under an inert atmosphere, oxygen and humidity exclusion. Schlenk techniques were applied. 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 the dissertation.

3.3 Procedures:

3.3.1 General procedure for the [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with dielectrophiles; synthesis of 107a-m, 110a-ae, 113a-i, 118a-n, 126a-c, 127a-g, 132a-i and 137a-j:

To a CH_2Cl_2 solution (2 mL / 1.0 mmol of the dielectrophile) of the dielectrophile (1.0 equiv.) was added **22** (1.1 equiv.) and, subsequently, $TiCl_4$ (1.1equiv.) 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 later 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 product the products.

3.3.2 General procedure for the synthesis of 1-hydroxy2,4-benzodioates 109b,c:

β-Ketoester was added to a mixture of triethyl orthoformate and acetic anhydride and the mixture was heated under reflux for 2 hours. The mixture was purified by distillation to give **109b**,**c**

3.3.3 General procedure for the synthesis of alkyl 4-ethoxy-2-oxo-3-butbutenoates 125a-c:

To alkyl vinyl ether **123a-c** (2.0 equiv.) is dropwise added during 20 minutes methyl chlorooxoacetate (1.0 equiv.) under Argon at 0 °C. The mixture was stirred for at 0 °C for 3 h. The temperature was allowed to warm to 20 °C during 15 h with stirring. The mixture was distilled in vacuo, to give **125a-c**. The synthesis of **125a** has been previously reported [153].

3.3.4 General procedure for the synthesis of 3-ethoxy-2-nitro-1-phenylprop-2-en-1-ones 131a-c:

To a solution of **130a-c** in acetic anhydride (2.0 equiv / 1.0 equiv of **130a-c**) was added triethyl orthoformiate (1.2 equiv). The solution was stirred at 120 °C for 6 h. The solvent was concentrated in vacuo and the residue was purified by chromatography (silica gel, heptanes / EtOAc) to give **131a-c**.

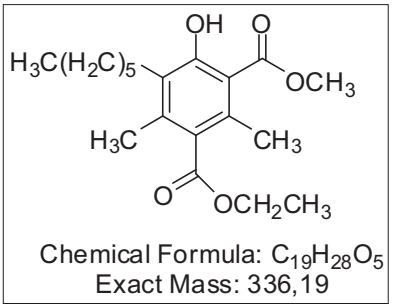
3.3.5 General procedure for the synthesis of 4-aminophenols 133a-i:

To a methanol suspension (25 mL/1 mmol of **132a-i**) of **132a-i** (1.0 equiv.) or an ethanol suspension of **132c** (1.0 equiv.) was added Pd/C (10 mol-%, 0.1 equiv.). The mixture was set under a hydrogen atmosphere. After stirring for 48 h at 20 °C, the reaction mixture was filtered (Celite) and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/EtOAc = 2:1).

3.4 Spectroscopic data of the synthesized compounds:

1-Ethyl 3-methyl 5-hexyl-4-hydroxy-2,6-imethylisophthalate (107d):

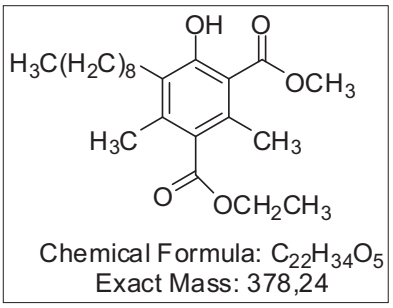
Starting with **106** (0.489 g, 2.0 mmol) and **22j** (0.758 g, 2.2 mmol), **107d** was isolated after chromatography (silica gel, heptanes/EtOAc) as a colourless viscous oil (0.236 g, 35%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t(br), ^{3}J = 7.4 Hz, 3 H, CH_3), 1.19 − 1.25 (m, 8 H, 4 CH_2), 1.31 (t, ^{3}J = 7.6 Hz, 3 H, OCH_2CH_3), 2.16 (s, 3 H, $PhCH_3$), 2.34 (s, 3 H, $PhCH_3$), 2.59 (t, ^{3}J = 7.4 Hz, 2 H, $PhCH_2$), 3.88 (s, 3 H, OCH_3), 4.32 (q, ^{3}J = 7.6 Hz, 2 H, OCH_2CH_3), 11.40 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2, 15.3, 18.0, 21.0 (CH_3), 23.7, 27.3, 29.7, 32.4, 34.4 (CH_2), 53.6 (OCH_3), 62.3 (OCH_2CH_3), 111.1, 129.3, 130.0, 135.1, 140.0 (C_{Ar}), 161.9 (COH), 171.8, 173.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2962 (m), 1723 (m), 1663 (m), 1439 (m), 1394 (m), 1229 (s), 1194 (s), 1151 (s), 1101 (m), 1033 (m), 844 (w), 723 (w). GC-MS (EI, 70 eV): *m/z* (%) = 336 ([M^+], 49), 289 (100), 276 (87), 259 (19), 234 (54), 206 (31), 187 (43), 178 (13), 159 (6), 91 (9), 77 (8), 43 (7). HRMS (EI): Calcd. for $C_{19}H_{28}O_5$: 336.19313; found: 336.19263.

1-Ethyl 3-methyl 4-hydroxy-2,6-dimethyl-5-nonylisophthalate (107e):

Starting with **106** (0.489 g, 2.0 mmol) and **22m** (0.851 g, 2.2 mmol), **107e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.302 g, 40%).

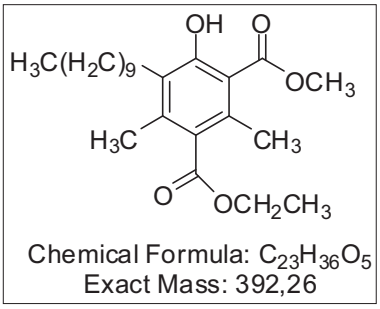


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^{3}J = 7.3 Hz, 3 H, $(CH_2)_8CH_3$), 1.19 - 1.24 (m, 14 H, 7 CH_2), 1.31 (t, ^{3}J = 7.3 Hz, 3 H, OCH_2CH_3), 2.15 (s, 3 H, $PhCH_3$), 2.34 (s, 3 H, $PhCH_3$), 2.57 (t, ^{3}J = 6.7 Hz, 2 H, $PhCH_2$), 3.87 (s, 3 H, OCH_3), 4.30 (q, ^{3}J = 7.1 Hz, 2 H, OCH_2CH_3), 11.48 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 16.8, 20.0 (CH_3), 22.6, 26.1, 28.8, 29.3, 29.5, 29.6, 29.9, 31.8 (CH_2), 52.2 (OCH_3), 61.3 (OCH_2), 109.9 ($CCOOCH_3$), 128.1 ($COOC_2H_5$), 128.8, 133.8, 138.8 (C_{Ar}), 160.7 (COH), 170.6, 172.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2922 (m), 2852 (w), 1725 (m), 1657 (m), 1598 (w), 1572 (w), 1439 (m), 1411 (w), 1362 (m), 1328 (m), 1267 (m), 1217 (s), 1192 (m), 1155 (m), 1123 (m), 1094 (w), 1073 (w), 1033 (m), 972 (w), 858 (w), 809 (m), 756 (w), 684 (w), 662 (w), 580 (w), 541 (w). GC-MS (EI, 70 eV): *m/z* (%) = 378 ([$M]^+$, 52), 333 (20), 332 (118), 331 (100), 329

(17), 318 (29), 301 (10), 275 (14), 235 (10), 234 (60), 233 (38), 206 (41), 187 (24). HRMS (EI): Calcd. for $C_{22}H_{34}O_5$ ($[M]^+$): 378.240088; found: 378.239837.

1-Ethyl 3-methyl 5-decyl-4-hydroxy-2,6-dimethylisophthalate (107f):

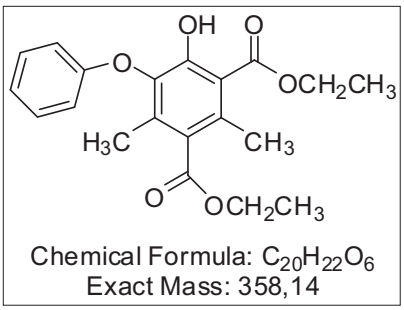
Starting with **106** (0.489 g, 2.0 mmol) and **22n** (0.882 g, 2.2 mmol), **107f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.321 g, 41%).



^{1}H NMR (250 MHz, $CDCl_3$) : δ = 0.80 (t, ^3J = 7.3 Hz, 3 H, $(CH_2)_9CH_3$), 1.13 - 1.23 (m, 16 H, 8 CH_2), 1.30 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 2.15 (s, 3 H, $PhCH_3$), 2.33 (s, 3 H, $PhCH_3$), 2.57 (t, ^3J = 6.7 Hz, 2 H, $PhCH_2$), 3.87 (s, 3 H, OCH_3), 4.30 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 11.47 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 16.8, 20.0 (CH_3), 22.6, 26.1, 28.8, 29.3, 29.5, 29.6, 29.6, 29.9, 31.8 (CH_2), 52.2 (OCH_3), 61.3 (OCH_2), 109.9 ($CCOOCH_3$), 128.1 ($COOC_2H_5$), 128.8, 133.8, 138.9 (C_{Ar}), 160.7 (COH), 170.6 172.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2922 (m), 2852 (w), 1725 (m), 1657 (m), 1597 (w), 1572 (w), 1439 (m), 1409 (w), 1362 (m), 1328 (m), 1264 (m), 1216 (s), 1191 (m), 1155 (m), 1123 (m), 1093 (w), 1070 (w), 1033 (m), 959 (w), 858 (w), 808 (m), 761 (w), 721(w), 685 (w), 662 (w), 580 (w), 539 (w). GC-MS (EI, 70 eV): *m/z* (%) = 392 ($[M]^+$, 42), 347 (23), 346 (24), 345 (100), 343 (22), 332 (17), 315 (10), 275 (13), 261 (10), 235 (10), 234 (51), 233 (38), 206 (40), 177 (11), 43 (13). HRMS (EI): Calcd. for $C_{23}H_{36}O_5$ ($[M]^+$): 392.25573; found: 392.255696.

Diethyl 4-hydroxy-2,6-dimethyl-5-phenoxyisophthalate (107h):

Starting with **106** (0.489 g, 2.0 mmol) and **22v** (0.807 g, 2.2 mmol), **107h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a reddish viscous oil (0.344 g, 48%).

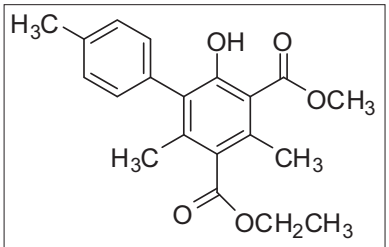


^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 1.34 (t, ^3J = 7.6 Hz, 3 H, OCH_2CH_3), 2.07 (s, 3 H, $PhCH_3$), 2.42 (s, 3 H, $PhCH_3$), 4.33 (q, ^3J = 7.3 Hz, 2 H, OCH_2CH_3), 4.37 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 6.76 (d, ^3J = 7.4 Hz, 2 H, CH_{Ar}), 6.89 (m, 1 H, CH_{Ar}), 6.94 (m, 2 H, CH_{Ar}), 11.27 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 12.7 , 13.1 19.0, 19.2 (CH_3), 60.1, 61.1 (OCH_2CH_3), 110.6 ($CCOOC_2H_5$), 113.6 (2 CH_{Ar}), 115.2 (CH_{Ar}), 128.7 ($CCOOC_2H_5$), 130.7 (2 CH_{Ar}), 130.9, 132.6, 137.9, 154.9 (C_{Ar}), 156.5 (COH), 168.2, 169.9 (CO).IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (w), 1722 (s), 1658 (m), 1489 (m), 1367 (m), 1261 (m), 1215 (s), 1046 (s), 749 (s), 688 (m).GC-MS (EI, 70 eV): *m/z* (%) = 358 ($[M^+]$,

63), 312 (64), 283 (100), 267 (21), 240 (12), 211 (6), 181 (5), 161 (11), 105 (61), 77 (22). HRMS (EI): Calcd. for $C_{20}H_{22}O_6$: 358.14109; found: 358.14174.

3-Ethyl 5-methyl 6-hydroxy-2,4,4'-trimethylbiphenyl-3,5-dicarboxylate (107i):

Starting with **106** (0.489 g, 2.0 mmol) and **22q** (0.771 g, 2.2 mmol), **107i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.260 g, 38%).

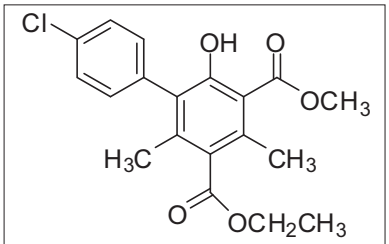


Chemical Formula: $C_{20}H_{22}O_5$
Exact Mass: 342,15

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 1.90 (s, 3 H, $PhCH_3$), 2.27 (s, 3 H, $PhCH_3$), 2.36 (s, 3 H, $PhCH_3$), 3.83 (s, 3 H, OCH_3), 4.26 (q, ^3J = 7.0 Hz, 2 H, OCH_2CH_3), 6.94 - 6.97 (m, 2 H, CH_{Ar}), 7.02 - 7.08 (m, 2 H, CH_{Ar}), 11.18 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 18.2, 20.1, 21.2 (CH_3), 52.3 (OCH_3), 61.2 (OCH_2), 110.6 ($CCOOCH_3$), 128.8 (C_{Ar}), 129.0 ($CCOOC_2H_5$), 129.2 (2 CH_{Ar}), 129.7 (2 CH_{Ar}), 133.0 (C_{Ar}), 135.8, 137.0, 139.5 (C_{Ar}), 160.1 (COH), 170.1, 171.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2929 (w), 2871 (w), 1721 (m), 1658 (m), 1598 (w), 1568 (w), 1513 (w), 1438 (m), 1363 (w), 1330 (m), 1213 (s), 1203 (s), 1098 (m), 1075 (w), 1035 (m), 958 (w), 923 (w), 842 (w), 821 (w), 809 (m), 760 (w), 729 (w), 710 (w), 686 (w), 666 (w), 611 (w), 580 (w), 539 (w). GC-MS (EI, 70 eV): *m/z* (%) = 342 ($[M]^+$, 50), 310 (100), 297 (17), 282 (22), 265 (13), 253 (12), 236 (11), 209 (16), 165 (14), 119 (5), 43 (5). HRMS (EI): Calcd. for $C_{20}H_{22}O_5$ ($[M]^+$): 342.14618; found: 342.146101.

3-Ethyl 5-methyl 4'-chloro-6-hydroxy-2,4-dimethyl-biphenyl-3,5-dicarboxylate (107j):

Starting with **106** (0.489 g, 2.0 mmol) and **22r** (0.816 g, 2.2 mmol), **107j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.270 g, 37%).



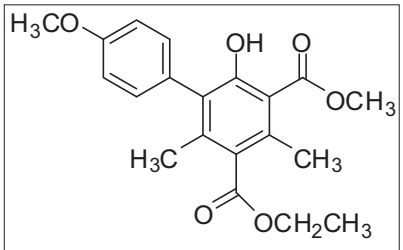
Chemical Formula: $C_{19}H_{19}ClO_5$
Exact Mass: 362,09

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 1.78 (s, 3 H, $PhCH_3$), 2.27 (s, 3 H, $PhCH_3$), 3.74 (s, 3 H, OCH_3), 4.16 (q, ^3J = 6.9 Hz, 2 H, OCH_2CH_3), 6.89 - 6.93 (m, 2 H, 2 CH_{Ar}), 7.02 - 7.08 (m, 2 H, 2 CH_{Ar}), 11.26 (S, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.1, 19.1, 21.2 (CH_3), 53.3 (OCH_3), 62.2 (OCH_2), 111.5 ($CCOOCH_3$), 128.7 (C_{Ar}), 129.6 (2 CH_{Ar}), 129.9 ($CCOOC_2H_5$), 132.2 (2 CH_{Ar}), 134.3, 135.5, 137.4, 140.3 (C_{Ar}), 160.0 (COH), 170.8, 172.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2930 (w), 2871 (w), 1722 (m), 1658 (m), 1604 (w), 1591 (w), 1571 (w), 1491 (w), 1438 (m), 1408 (w), 1363 (w), 1329 (m), 1204 (s), 1100 (m),

1086 (m), 1034 (m), 1014 (m), 985 (w), 957 (w), 831 (m), 809 (m), 758 (w), 689 (w), 665 (w), 612 (w), 579 (w). GC-MS (EI, 70 eV): *m/z* (%) = 364 ([M^+], ^{37}Cl, 12), 362 ([M^+], ^{35}Cl, 39), 332 (^{37}Cl, 29), 331 (23), 330 (^{35}Cl, 100), 317 (15), 302 (18), 285 (12), 274 (8), 165 (14), 128 (6), 86 (9), 43 (5). HRMS (EI): Calcd. for $C_{19}H_{19}ClO_5$ ([$M]^+$, ^{35}Cl): 362.09155; found: 362.090638.

3-Ethyl 5-methyl 6-hydroxy-4'-methoxy-2,4-dimethyl-biphenyl-3,5-dicarboxylate (107k):

Starting with **106** (0.489 g, 2.0 mmol) and **22s** (0.807 g, 2.2 mmol), **107k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.245 g, 34%).

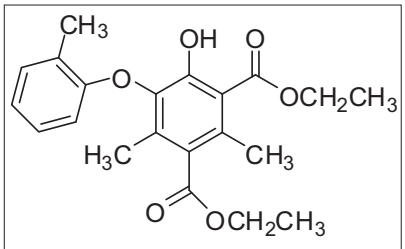


Chemical Formula: $C_{20}H_{22}O_6$
Exact Mass: 358,14

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.96 (s, 3 H, $PhCH_3$), 2.42 (s, 3 H, $PhCH_3$), 3.77 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.32 (q, ^3J = 6.9 Hz, 2 H, OCH_2CH_3), 6.88 - 6.93 (m, 2 H, 2 CH_{Ar}), 7.02 - 7.08 (m, 2 H, 2 CH_{Ar}), 11.26 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.2, 18.2, 20.1 (CH_3), 52.3, 55.3 (OCH_3), 61.2 (OCH_2), 110.6 (*C*$COOCH_3$), 113.9 (2 CH_{Ar}), 128.1 (C_{Ar}), 128.7 (*C*$COOC_2H_5$), 128.9 (C_{Ar}), 130.9 (2 CH_{Ar}), 135.8, 139.7 (C_{Ar}), 158.8 (C_{Ar}), 160.2 (COH), 170.2, 171.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3033 (w), 2995 (w), 2953 (w), 2906 (w), 2835 (w), 1719 (m), 1656 (w), 1608 (w), 1509 (s), 1439 (m), 1364 (w), 1331 (m), 1300 (w), 1242 (s), 1207 (s), 1174 (s), 1100 (m), 1073 (w), 1030 (s), 985 (w), 956 (w), 830 (m), 810 (m), 764 (w), 686 (w), 637 (w), 581 (w), 555 (w), 526 (m). GC-MS (EI, 70 eV): *m/z* (%) = 358 ([$M]^+$, 5), 326 (10), 270 (21), 121 (100), 78 (6). HRMS (EI): Calcd. for $C_{20}H_{22}O_6$ ([$M]^+$): 358.14109; found: 358.140227.

Diethyl 4-hydroxy-2,6-dimethyl-5-(2-tolyloxy)isophthalate (107l):

Starting with **106** (0.489 g, 2.0 mmol) and **22t** (0.837 g, 2.2 mmol), **107l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a reddish viscous oil (0.312 g, 42%).



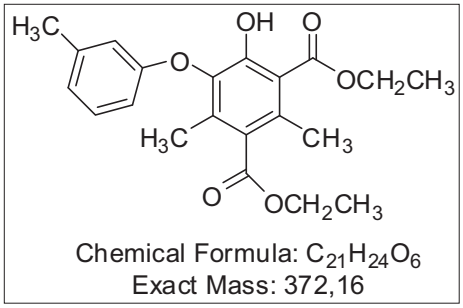
Chemical Formula: $C_{21}H_{24}O_6$
Exact Mass: 372,16

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.35 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.05 (s, 3 H, $PhCH_3$), 2.24 (s, 3 H, $PhCH_3$), 2.43 (s, 3 H, $PhCH_3$), 4.35 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 4.38 (q, ^3J = 7.6 Hz, 2 H, OCH_2CH_3), 6.54 (s, 1 H, CH_{Ar}), 6.56 (m, 2 H, 2 CH_{Ar}), 6.75 (d, ^3J = 7.5 Hz, 1 H, CH_{Ar}), 11.20 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 15.6, 16.0, 16.1,

21.9, 23.3 (CH_3), 63.2, 64.0 (CH_2), 113.1 (CH_{Ar}), 114.2 (C_{Ar}), 117.1, 124.7, 130.5 (CH_{Ar}), 131.3 135.4, 136.8, 140. 9, 141.6 (C_{Ar}), 157.8 (COH), 159.4 (C_{Ar}), 171.1, 172.8 (CO).
IR (neat, cm^{-1}): $\tilde{\nu}$ = 2979 (m), 1723 (s), 1658 (s), 1586 (m), 1444 (s), 1367 (m), 1321 (s), 1218 (s), 1139 (s), 1032 (s), 939 (m), 771 (m), 686 (m). MS (EI, 70 eV): *m/z* (%) = 372 ([M^+], 33), 326 (49), 297 (84), 281 (12), 254 (13), 225 (4), 119 (100). HRMS (EI): Calcd. for $C_{21}H_{24}O_6$: 372.15673; found: 372.15665.

Diethyl 4-hydroxy-2,6-dimethyl-5-(3-tolyloxy)isophthalate (107m):

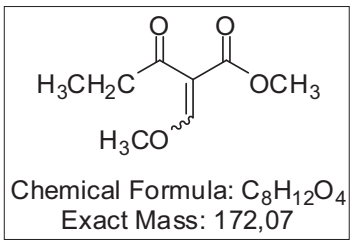
Starting with **106** (0.489 g, 2.0 mmol) and **22u** (0.837 g, 2.2 mmol), **107m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a reddish viscous oil (0.382 g, 51%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 1.35 (t, ^3J = 7.6 Hz, 3 H, OCH_2CH_3), 2.07 (s, 3 H, $PhCH_3$), 2.22 (s, 3 H, $PhCH_3$), 2.42 (s, 3 H, $PhCH_3$), 4.36 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 4.38 (q, ^3J = 7.6 Hz, 2 H, OCH_2CH_3), 6.56 (m, 2 H, 2 CH_{Ar}), 6.72 (d, ^3J = 7.6 Hz, 1 H, CH_{Ar}), 7.06 (m, 1 H, CH_{Ar}), 11.25 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.7, 14.1, 14.2, 20.0, 21.4 (CH_3), 61.4, 61.8 (CH_2), 111.5 (CH_{Ar}), 112.3 (C_{Ar}), 115.3, 122.8 (CH_{Ar}), 128.6 (C_{Ar}), 129.2 (CH_{Ar}), 133.5, 135.0, 139.0, 139.7 (C_{Ar}), 155.9 (COH), 157.5 (C_{Ar}), 169.3, 170.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 1660 (s), 1619 (m), 1452 (s), 1343 (s), 1219 (m), 1136 (s), 966 (m), 882 (m), 694 (m). MS (EI, 70 eV): *m/z* (%) = 372 ([M^+], 28), 326 (52), 297 (66), 254 (28), 119 (100). HRMS (EI): Calcd. for $C_{21}H_{24}O_6$: 372.15673; found: 372.15665.

Methyl 2-(methoxymethylene)-3-oxopentanoate (109b):

Methyl 3-oxopentanoate (1.3 ml, 10 mmol), was reacted with a mixture of triethyl orthoformate (2.5 mL) and acetic anhydride (2.5 mL). Distillation gave **109b** as a brownish oil (1.44 g, 84%, mixture of geometric isomers, only NMR data of the major isomer are listed).

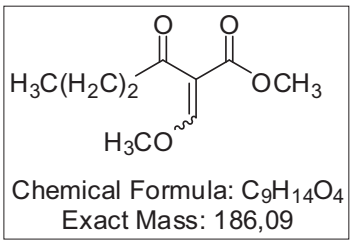


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.94 (t, ^3J =7.2 Hz, 3 H, CH_3), 2.61 (q, ^3J =7.3 Hz, 2 H, CH_2), 3.60 (s, 3 H, OMe), 3.66 (s, 3H, OMe), 7.79 (s, 1 H, CH_{olf}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 8.2 (CH_3), 35.8 (CH_2), 54.4, 62.0 (OCH_3), 112.1 (C), 165.1 (CH_{olf}), 171.9 (CO), 203.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2355 (w), 2249 (w), 2125 (w), 2003 (w), 1961 (w), 1711 (w), 1629 (w), 1450 (w), 1283 (w) 1126 (w), 1052 (s),

1024 (s), 1005 (s), 819 (m), 757 (m), 622 (m). GC-MS (EI, 70 eV): m/z (%) = 172([M]+, 40), 143 (81), 85 (18), 75 (100), 59 (11), 57 (13), 55 (11), 54 (16), 53 (13), 29 (20). HRMS (EI): Calcd. for $C_8H_{12}O_4$: 172.07301; found: 172.072814.

Methyl 2-(methoxymethylene)-3-oxohexanoate (109c):

Methyl 3-oxohexanoate (1.4 ml, 9.9 mmol) was reacted with a mixture of triethyl orthoformate (2.5 mL) and acetic anhydride (2.5 mL). Distillation gave **109c** as a brownish oil (1.53 g, 83%, mixture of geometric isomers, only NMR data of the major isomer are listed).

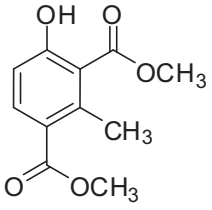


Chemical Formula: $C_9H_{14}O_4$
Exact Mass: 186,09

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, ^3J =7.2 Hz, 3 H, CH_3), 1.43 - 1.50 (m, 2 H, CH_2), 2.62 (t, ^3J =7.2 Hz, 2 H, CH_2), 3.63 (s, 3 H, OMe), 3.67 (s, 3 H, OMe), 7.79 (s, 1 H, CH_{olf}).^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.3 (CH_3), 17.4, 44.3 (CH_2), 54.1, 61.3 (OCH_3), 112.5 (C), 165.2 (CH_{olf}), 171.0, 201.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3437 (w), 2960 (w), 2250 (w), 2124 (w), 1711 (w), 1630 (w), 1439 (w), 1378 (w), 1274 (w), 1129 (w), 1052 (s), 1024 (s), 1004 (s), 820 (m), 757 (m), 622 (m). GC-MS (EI, 70 eV): m/z (%) = 186([M]+, 3), 155 (22), 143 (93), 85 (16), 75 (100), 59 (10), 55(13), 54 (15), 43 (16), 41 (15). HRMS (EI): Calcd. for $C_9H_{14}O_4$: 186.08866; found: 186.088376.

Dimethyl 4-hydroxy-2-methylisophthalate (110a):

Starting with **109a** (0.237 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **110a** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.144 g, 43%), m.p. = 88 - 90 °C.

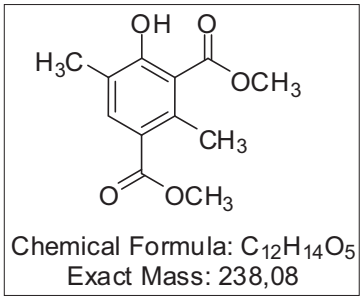


Chemical Formula: $C_{11}H_{12}O_5$
Exact Mass: 224,07

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.63 (s, 3 H, $PhCH_3$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 6.78 (d, ^3J = 8.7 Hz, 1 H, CH_{Ar}), 7.76 (d, ^3J = 8.9 Hz, 1 H, CH_{Ar}), 10.98 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.0 (CH_3), 52.0, 52.5 (OCH_3), 114.5 (CCOOCH$_3$), 115.2 (CH_{Ar}), 123.9 (CCOOCH$_3$), 135.8 (CH_{Ar}), 143.6 (C_{Ar}), 163.9 (COH), 168.0, 171.7 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3339 (w), 2989 (w), 2959 (w), 2924 (w), 2853 (w), 1715 (m), 1688 (m), 1651 (m), 1583 (m), 1537 (m), 1430 (m), 1386 (m), 1321 (m), 1243 (m), 1195 (s), 1151 (s), 1050 (m), 1018 (m), 960 (m), 944 (m), 858 (m), 797 (s), 754 (m), 707 (s), 652 (m), 560 (m). GC-MS (EI, 70 eV): *m/z* (%) = 224 ($[M]^+$, 31), 193 (30), 192 (100), 161 (56), 160 (26), 149 (13), 133 (12), 132 (12), 105 (10), 77 (15), 51 (11). HRMS (EI): Calcd. for $C_{11}H_{12}O_5$ ($[M]^+$): 224.06792; found: 224.067341.

Dimethyl 4-hydroxy-2,5-dimethylisophthalate (110b):

Starting with **109a** (0.237 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **110b** was isolated after chromatography (silica gel, heptanes/EtOAc) as a white solid (0.205 g, 57%), m.p. = 110 - 112°C.

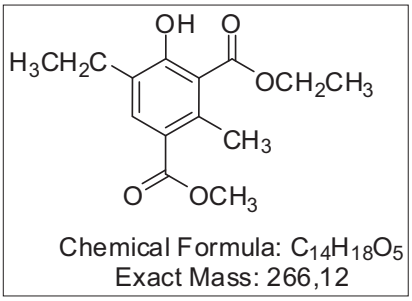


Chemical Formula: $C_{12}H_{14}O_5$
Exact Mass: 238,08

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, $PhCH_3$), 2.60 (s, 3 H, $PhCH_3$), 3.78 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.75 (s, 1 H, CH_{Ar}), 11.22 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.7, 19.8 (CH_3), 51.9, 52.4 (OCH_3), 113.7 (*C*$COOCH_3$), 123.0 (C_{Ar}), 124.0 (*C*$COOCH_3$), 136.3 (CH_{Ar}), 140.6 (C_{Ar}), 162.4 (COH) 168.2, 172.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3349 (w), 2992 (w), 2953 (w), 2931 (w), 2853 (w), 1716 (m), 1693 (m), 1667 (m), 1579 (m), 1537 (m), 1434 (m), 1384 (w), 1330 (m), 1229 (m), 1190 (s), 1144 (s), 1049 (m), 1013 (m), 959 (m), 855 (m), 796 (s), 745 (m), 702 (m), 651 (m), 606 (m). GC-MS (EI, 70 eV): *m/z* (%) = 238 ($[M]^+$, 33), 207 (33), 206 (100), 178 (65), 175 (31), 163 (26), 91 (16), 65 (12). HRMS (EI): Calcd. for $C_{12}H_{14}O_5$ ($[M]^+$): 238.08358; found: 238.083755.

3-Ethyl 1-methyl 5-ethyl-4-hydroxy-2-methylisophthalate (110c):

Starting with **109a** (0.237 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **110c** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.200 g, 50%).

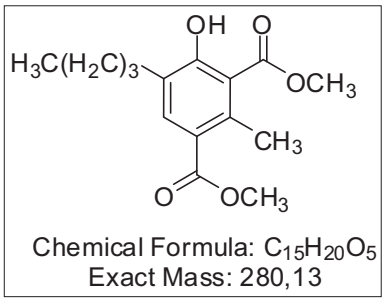


Chemical Formula: $C_{14}H_{18}O_5$
Exact Mass: 266,12

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.05 (t, ^3J = 7.5 Hz, 3 H, CH_2*CH_3*), 1.27 (t, ^3J = 6.7 Hz, 3 H, OCH_2*CH_3*), 2.48 (q, ^3J = 7.3 Hz, 2 H, *CH_2*CH_3), 2.52 (s, 3 H, $PhCH_3$), 3.71 (s, 3 H, OCH_3), 4.30 (q, ^3J = 7.0 Hz, 2 H, O*CH_2*CH_3), 7.55 (s, 1 H, CH_{Ar}), 11.21 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.5, 14.1, 19.9 (CH_3), 23.1 (CH_2), 52.0 (OCH_3), 62.2 (OCH_2), 114.3 (*C*$COOC_2H_5$), 123.4 (*C*$COOCH_3$), 129.8 (C_{Ar}), 134.9 (CH_{Ar}), 140.8 (C_{Ar}), 162.5 (COH), 168.5, 171.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2967 (w), 2874 (w), 1718 (m), 1655 (m), 1580 (w), 1429 (m), 1396 (w), 1372 (m), 1326 (m), 1261 (m), 1227 (s), 1199 (s), 1154 (s), 1095 (w), 1043 (m), 1019 (m), 959 (w), 844 (w), 809 (m), 780 (m), 743 (w), 650 (m), 535 (w). GC-MS (EI, 70 eV): *m/z* (%) = 266 ($[M]^+$, 25), 221 (17), 220 (63), 193 (12), 192 (100), 189 (15), 177 (10), 77 (11), 29 (7). HRMS (EI): Calcd. for $C_{14}H_{18}O_5$ ($[M]^+$): 266.11488; found: 266.115159.

Dimethyl 5-butyl-4-hydroxy-2-methylisophthalate (110d):

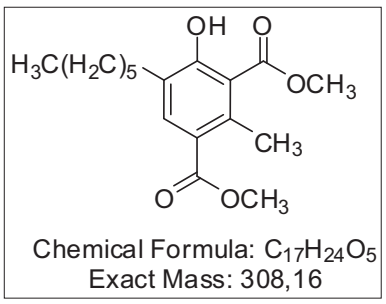
Starting with **109a** (0.237 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **110d** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.218 g, 52%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, ^{3}J = 7.5 Hz, 3 H, CH_3), 1.25 – 1.35 (m, 2 H, CH_2), 1.48 – 1.53 (m, 2 H, CH_2), 2.54 (t, ^{3}J = 7.5 Hz, 2 H, $PhCH_2$), 2.58 (s, 3 H, $PhCH_3$), 3.79 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.21 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9, 18.9 (CH_3), 21.5, 28.9, 30.4 (CH_2), 50.9, 51.5 (OCH_3), 113.0 (*C*$COOCH_3$), 122.1 (C_{Ar}), 127.6 (*C*$COOCH_3$), 134.8 (CH_{Ar}), 139.6 (C_{Ar}), 161.1 (COH), 167.4, 171.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3024 (w), 2989 (w), 2957 (w), 2932 (w), 2865 (w), 1713 (s), 1659 (m), 1608 (w), 1579 (w), 1431 (s), 1377 (w), 1337 (m), 1259 (m), 1228 (s), 1199 (s), 1152 (s), 1049 (m), 994 (m), 962 (m), 894 (m), 872 (w), 808 (m), 767 (m), 653 (m), 544 (w). GC-MS (EI, 70 eV): *m/z* (%) = 280 ($[M]^+$, 34), 249 (20), 248 (19), 231 (15), 220 (39), 219 (18), 217 (14), 207 (12), 206 (100), 205 (23), 189 (19), 178 (40), 173 (34), 91 (10), 77 (11). HRMS (EI): Calcd. for $C_{15}H_{20}O_5$ ($[M]^+$): 280.13053; found: 280.130756.

Dimethyl 5-hexyl-4-hydroxy-2-methylisophthalate (110e):

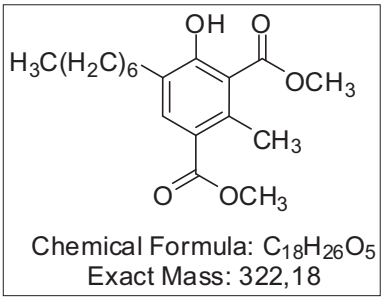
Starting with **109a** (0.237 g, 1.5 mmol) and **22J** (0.569 g, 1.65 mmol), **110e** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.254 g, 55%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.72 (t, ^{3}J = 7.5 Hz, 3 H, CH_3), 1.11 – 1.20 (m, 6 H, 3 CH_2), 1.40 – 1.47 (m, 2 H, CH_2), 2.44 (t, ^{3}J = 7.5 Hz, 2 H, $PhCH_2$), 2.51 (s, 3 H, $PhCH_3$), 3.71 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 7.54 (s, 1 H, CH_{Ar}), 11.13 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 19.8 (CH_3), 22.6, 29.1, 29.2, 29.7, 31.7 (CH_2), 51.9, 52.4 (OCH_3), 113.9 (*C*$COOCH_3$), 123.1 (C_{Ar}), 128.7 (*C*$COOCH_3$), 135.7 (CH_{Ar}), 140.5 (C_{Ar}), 162.0 (COH), 168.3, 172.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2926 (w), 2856 (w), 1719 (m), 1659 (m), 1608 (w), 1580 (w), 1432 (m), 1335 (m), 1227 (s), 1194 (s), 1150 (s), 1045 (m), 990 (m), 961 (w), 886 (w), 808 (m), 779 (m), 725 (w), 651 (m), 555 (w). GC-MS (EI, 70 eV): *m/z* (%) = 308 ($[M]^+$, 37), 277 (23), 276 (20), 259 (16), 248 (40), 247 (31), 245 (11), 233 (13), 220 (10), 219 (17), 217 (14), 207 (16), 206 (100), 205 (33), 178 (35), 173 (42), 91 (10), 77 (10), 43 (8). HRMS (EI): Calcd. for $C_{17}H_{24}O_5$ ($[M]^+$): 308.16183; found: 308.161283.

Dimethyl 5-hexyl-4-hydroxy-2-methylisophthalate (110f):

Starting with **109a** (0.237 g, 1.5 mmol) and **22k** (0.592 g, 1.65 mmol), **110f** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.246 g, 51%).

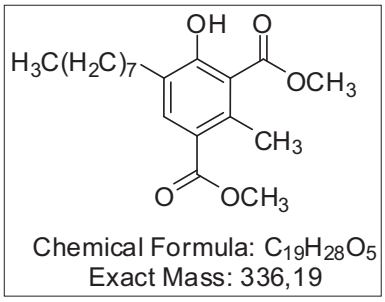


Chemical Formula: $C_{18}H_{26}O_5$
Exact Mass: 322,18

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.78 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.18 – 1.22 (m, 8 H, 4 CH_2), 1.48 – 1.54 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 2.58 (s, 3 H, $PhCH_3$), 3.79 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.22 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 18.8 (CH_3), 21.6, 27.7, 27.8, 28.2, 28.7, 30.8 (CH_2), 50.9, 51.4 (OCH_3), 112.9 (*C*$COOCH_3$), 122.1 (C_{Ar}), 127.6 (*C*$COOCH_3$), 134.7 (CH_{Ar}), 139.6 (C_{Ar}), 161.1 (COH), 167.4, 171.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3400 (w), 2952 (w), 2923 (w), 2853 (w), 1720 (m), 1659 (m), 1610 (w), 1579 (w), 1433 (m), 1379 (w), 1336 (m), 1228 (s), 1195 (s), 1152 (s), 1046 (m), 997 (w), 889 (w), 809 (m), 779 (m), 723 (w), 651 (m), 553 (w). GC-MS (EI, 70 eV): *m/z* (%) = 322 ($[M]^+$, 33), 291 (23), 290 (19), 273 (14), 262 (32), 247 (29), 233 (11), 231 (14), 219 (17), 207 (17), 206 (100), 205 (33), 178 (33), 173 (40), 91 (10), 77 (9), 43 (10), 29 (8). HRMS (EI): Calcd. for $C_{18}H_{26}O_5$ ($[M]^+$): 322.17748; found: 322.177264.

Dimethyl 4-hydroxy-2-methyl-5-octylisophthalate (110g):

Starting with **109a** (0.237 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **110g** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.241 g, 48%).

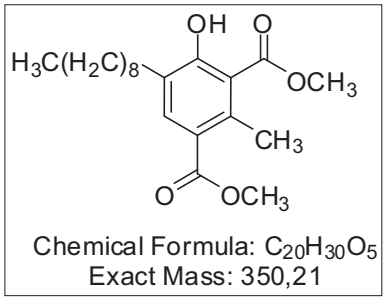


Chemical Formula: $C_{19}H_{28}O_5$
Exact Mass: 336,19

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.15 – 1.23 (m, 10 H, 5 CH_2), 1.51 – 1.53 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.7 Hz, 2 H, $PhCH_2$), 2.59 (s, 3 H, $PhCH_3$), 3.80 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.21 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 19.8 (CH_3), 22.6, 29.2, 29.4, 29.5, 29.6, 29.7, 31.8 (CH_2), 51.9, 52.4 (OCH_3), 113.9 (*C*$COOCH_3$), 123.1 (C_{Ar}), 128.8 (*C*$COOCH_3$), 135.7 (CH_{Ar}), 140.6 (C_{Ar}), 162.0 (COH), 168.4, 172.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2924 (w), 2853 (w), 1720 (m), 1699 (m), 1605 (w), 1552 (w), 1434 (m), 1377 (w), 1336 (m), 1229 (s), 1202 (s), 1153 (s), 1045 (m), 996 (w), 911 (w), 809 (m), 759 (m), 700 (m), 652 (w), 566 (w). GC-MS (EI, 70 eV): *m/z* (%) = 336 ($[M]^+$, 35), 305 (20), 304 (14), 287 (13), 276 (32), 247 (34), 245 (17), 233 (12), 219 (18), 207 (15), 206 (100), 205 (30), 178 (33), 173 (39), 91 (11), 43 (10), 41 (10), 29 (7). HRMS (EI): Calcd. for $C_{19}H_{28}O_5$ ($[M]^+$): 336.19313; found: 336.193115.

Dimethyl 4-hydroxy-2-methyl-5-nonylbenzene-1,3-dioate (110h):

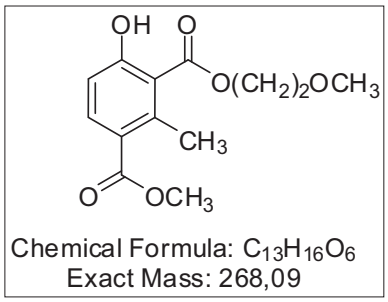
Starting with **109a** (0.237 g, 1.5 mmol) and **22m** (0.638 g, 1.65 mmol), **110h** was isolated after chromatography (silica gel, heptanes/EtOAc) as a white solid (0.273 g, 52%), m.p. 56 - 57 °C.



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.19 – 1.26 (m, 12 H, 6 CH_2), 1.47 – 1.55 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.2 Hz, 2 H, $PhCH_2$), 2.59 (s, 3 H, $PhCH_3$), 3.80 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.20 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1, 18.8 (CH_3), 21.6, 28.2, 28.3, 28.4, 28.5, 28.7, 29.9, 30.9 (CH_2), 50.9, 51.4 (OCH_3), 112.9 (*C*$COOCH_3$), 122.1 (*C*$COOCH_3$), 127.6 (C_{Ar}), 134.7 (CH_{Ar}), 139.6 (C_{Ar}), 161.0 (COH), 167.3, 171.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3000 (w), 2954 (m), 2914 (m), 2851 (m), 1709 (m), 1665 (m), 1607 (w), 1579 (m), 1471 (m), 1437 (w), 1426 (w), 1382 (w), 1335 (m), 1252 (w), 1229 (s), 1210 (s), 1194 (s), 1149 (s), 1045 (m), 1003 (m), 986 (m), 972 (m), 961 (m), 920 (m), 887 (s), 802 (m), 791 (m), 781 (m), 743 (m), 714 (m), 659 (m), 610 (m), 561 (w). GC-MS (EI, 70 eV): *m/z* (%) = 350 ([M^+], 34), 319 (20), 290 (24), 259 (15), 247 (27), 233 (10), 219 (15), 206 (100), 192 (9), 173 (39), 163 (7), 147 (6), 119 (3), 91 (7), 77 (7), 55 (4), 41 (10). HRMS (EI): Calcd. for $C_{20}H_{30}O_5$ ([M]$^+$): 350.20878; found: 350.208651.

3-(2-Methoxyethyl) 1-methyl 4-hydroxy-2-methylbenzene-1,3-dioate (110i):

Starting with **109a** (0.237 g, 1.5 mmol) and **22b** (0.502 g, 1.65 mmol), **110i** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.193 g, 48%).

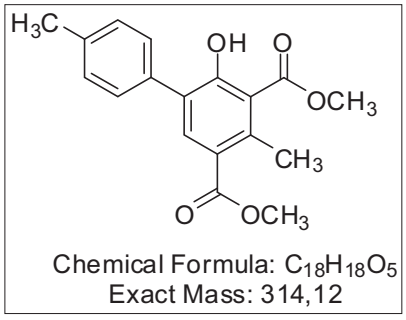


^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.66 (s, 3 H, $PhCH_3$), 3.36 (s, 3 H, OCH_3), 3.66 (t, ^3J = 4.9 Hz, 2 H,$OCH_2CH_2OCH_3$), 3.80 (s, 3 H, OCH_3), 4.47 (t, ^3J = 4.7 Hz, 2 H, $OCH_2CH_2OCH_3$), 6.78 (d, ^3J = 8.7 Hz, 1 H, CH_{Ar}), 7.78 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 10.51 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.6 (CH_3), 52.7, 59.6 (OCH_3), 65.2, 70.5 (OCH_2), 115.9 (CH_{Ar}), 116.0 (C_{Ar}), 124.7 (*C*$COOCH_3$), 136.5 (CH_{Ar}), 144.3 (C_{Ar}), 164.0 (COH), 168.6, 171.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3281 (w), 2951 (w), 2924 (w), 2851 (w), 1716 (m), 1661 (w), 1588 (m), 1470 (w), 1434 (w), 1378 (w), 1315 (w), 1224 (m), 1200 (m), 1048 (s), 1028 (s), 955 (m), 868 (m), 834 (m), 804 (m), 783 (m), 709 (m), 653 (m), 608 (m), 543 (m). GC-MS (EI, 70 eV): *m/z* (%) = 268 ([M^+], 17), 237 (8), 192 (100), 161 (32), 133

(5), 105 (6), 77 (7), 59 (11), 45 (5). HRMS (EI): Calcd. for $C_{13}H_{16}O_6$ ($[M]^+$): 268.09414; found: 268.094150.

Dimethyl 2-hydroxy-4,4'-dimethylbiphenyl-3,5-dicarboxylate (110j):

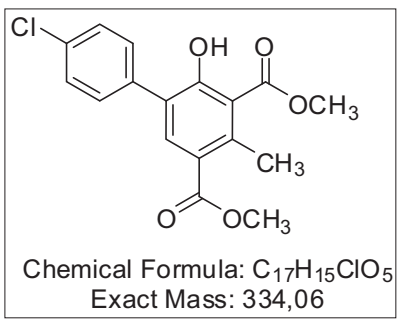
Starting with **109a** (0.237 g, 1.5 mmol) and **22q** (0.578 g, 1.65 mmol), **110j** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.250 g, 53 %), m.p. = 83 - 85 °C.



^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, $PhCH_3$), 2.65 (s, 3 H, $PhCH_3$), 3.80 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 7.15 – 7.19 (m, 2 H, 2 CH_{Ar}), 7.34 – 7.37 (m, 2 H, 2 CH_{Ar}), 7.83 (s, 1 H, CH_{Ar}), 11.04 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.9, 20.2 (CH_3), 51.0, 51.6 (OCH_3), 114.3 (*C*$COOCH_3$), 122.6 (*C*$COOCH_3$), 126.9 (C_{Ar}), 128.0 (2 CH_{Ar}), 128.2 (2 CH_{Ar}), 132.6 (C_{Ar}), 135.4 (CH_{Ar}), 136.4, 141.0 (C_{Ar}), 159.5 (COH), 167.0, 171.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3027 (w), 3012 (w), 2953 (w), 2924 (w), 2853 (w), 1771 (w), 1718 (m), 1684 (w), 1663 (m), 1653 (m), 1636 (w), 1616 (w), 1608 (w), 1576 (w), 1558 (w), 1540 (w), 1533 (w), 1516 (w), 1507 (w), 1497 (w), 1489 (w), 1472 (w), 1456 (w), 1436 (m), 1399 (w), 1338 (m), 1240 (m), 1209 (m), 1103 (w), 1052 (w), 1028 (w), 958 (w), 910 (w), 822 (w), 783 (w), 733 (m), 668 (w), 650 (w), 617 (w), 608 (w), 567 (w), 541 (w). GC-MS (EI, 70 eV): *m/z* (%) = 314 ($[M^+]$, 42), 282 (100), 267 (5), 251 (14), 239 (16), 222 (13), 195 (14), 165 (13), 152 (12), 132 (12), 119 (29), 105 (18), 91 (19), 69 (22), 57 (29), 43 (20). HRMS (EI): Calcd. for $C_{18}H_{18}O_5$ ($[M]^+$): 314.11488; found: 314.114827.

Dimethyl 4'-chloro-2-hydroxy-4-methylbiphenyl-3,5-dicarboxylate (110k):

Starting with **109a** (0.237 g, 1.5 mmol) and **22r** (0.612 g, 1.65 mmol), **110k** was isolated after chromatography (silica gel, heptanes/EtOAc) as a brownish crystals (0.241 g, 48%), m.p. = 160 - 161 °C.

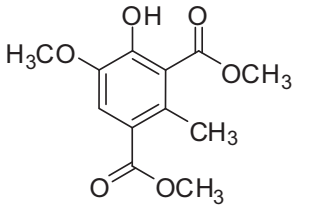


^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.65 (s, 3 H, $PhCH_3$), 3.80 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 7.28 – 7.33 (m, 2 H, 2 CH_{Ar}), 7.38 – 7.43 (m, 2 H, 2 CH_{Ar}), 7.81 (s, 1 H, CH_{Ar}), 11.36 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.1 (CH_3), 51.1, 51.7 (OCH_3), 114.0 (*C*$COOCH_3$), 122.9 (*C*$COOCH_3$), 125.6 (C_{Ar}), 127.4 (2 CH_{Ar}), 129.6 (2 CH_{Ar}), 132.6, 134.0 (C_{Ar}), 135.4 (CH_{Ar}), 141.8 (C_{Ar}), 159.7 (COH), 166.8, 171.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3000 (w), 2951 (w), 1716 (m), 1662 (m), 1603 (m), 1579

(m), 1562 (w), 1492 (m), 1439 (m), 1425 (m), 1389 (m), 1375 (m), 1323 (m), 1301 (m), 1239 (m), 1194 (s), 1171 (s), 1105 (m), 1085 (m), 1051 (m), 1025 (m), 1010 (m), 949 (m), 926 (m), 876 (m), 825 (m), 806 (m), 782 (m), 771 (m), 746 (m), 719 (m), 675 (m), 650 (m), 629 (m), 613 (m), 540 (m). GC-MS (EI, 70 eV): *m/z* (%) = 336 ([M^+], ^{37}Cl, 6), 334 ([M^+], ^{35}Cl, 17), 302 (100), 296 (20), 270 (12), 242 (7), 215 (4), 152 (11), 125 (8), 104 (6), 86 (10), 43 (9). HRMS (EI): Calcd. for $C_{17}H_{15}O_5Cl$ ([$M]^+$): 334.06025; found: 334.059873.

Dimethyl 4-hydroxy-5-methoxy-2-methylbenzene-1,3-dioate (110l):

Starting with **109a** (0.237 g, 1.5 mmol) and **22o** (0.360 g, 1.7 mmol), **110l** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.198 g, 52%).

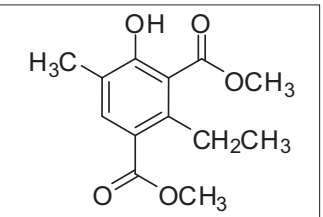


Chemical Formula: $C_{12}H_{14}O_6$
Exact Mass: 254,08

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.45 (s, 3 H, $PhCH_3$), 3.76 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 7.32 (s, 1 H, CH_{Ar}), 9.41 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.7 (CH_3), 52.0, 52.6, 56.2 (OCH_3), 115.5 (CH_{Ar}), 117.6 (*C*$COOCH_3$), 122.3 (*C*$COOCH_3$), 133.4, 145.3 (C_{Ar}), 151.6 (COH), 167.7, 170.4 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3400 (w), 3001 (w), 2951 (w), 2842 (w), 1713 (m), 1662 (m), 1610 (w), 1587 (m), 1492 (m), 1433 (m), 1385 (w), 1357 (m), 1305 (m), 1282 (m), 1200 (s), 1167 (s), 1082 (s), 1048 (m), 1029 (s), 959 (m), 914 (w), 886 (m), 858 (w), 806 (w), 780 (m), 730 (m), 688 (w), 671 (w), 647 (w), 621 (w), 592 (w), 553 (w). GC-MS (EI, 70 eV): *m/z* (%) = 254 ([M^+], 38), 222 (100), 207 (4), 194 (53), 179 (20), 163 (11), 147 (18), 136 (15), 119 (5), 107 (3), 92 (7), 77 (10), 64 (5), 53 (5), 39 (5). HRMS (EI): Calcd. for $C_{12}H_{14}O_6$ ([$M]^+$): 254.07849; found: 254.078254.

Dimethyl 2-ethyl-4-hydroxy-5-methylisophthalate (110m):

Starting with **109b** (0.258 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **110m** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.196 g, 52%).



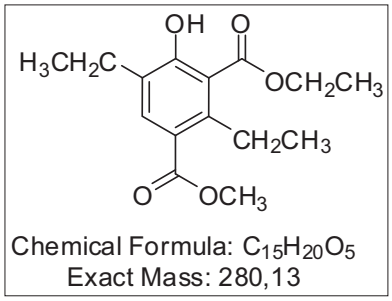
Chemical Formula: $C_{13}H_{16}O_5$
Exact Mass: 252,10

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14 (t, ^3J = 7.7 Hz, 3 H, CH_2CH_3), 2.21 (s, 3 H, $PhCH_3$), 3.09 (q, ^3J = 7.1 Hz, 2 H, CH_2CH_3), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.63 (s, 1 H, CH_{Ar}), 11.14 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8, 15.0 (CH_3), 24.2 (CH_2), 50.9, 51.5 (OCH_3), 112.2 (*C*$COOCH_3$), 121.5 (C_{Ar}), 123.4 (*C*$COOCH_3$), 136.0 (CH_{Ar}), 145.6 (C_{Ar}), 161.4 (COH), 167.3, 171.2 (CO).

IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2930 (w), 2854 (w), 1719 (m), 1658 (m), 1610 (w), 1578 (w), 1432 (m), 1380 (w), 1333 (m), 1300 (m), 1277 (m), 1225 (s), 1192 (s), 1149 (s), 1071 (m), 1017 (m), 983 (m), 886 (w), 813 (m), 776 (m), 732 (m), 675 (m), 644 (m). GC-MS (EI, 70 eV): *m/z* (%) = 252 ($[M]^+$, 32), 221 (27), 220 (100), 189 (24), 177 (11), 170 (12), 161 (11), 160 (19), 133 (9), 132 (10), 103 (9), 77 (14). HRMS (EI): Calcd. for $C_{13}H_{16}O_5$ ($[M]^+$): 252.09923; found: 252.099203.

3-Ethyl 1-methyl 2,5-diethyl-4-hydroxyisophthalate (110n):

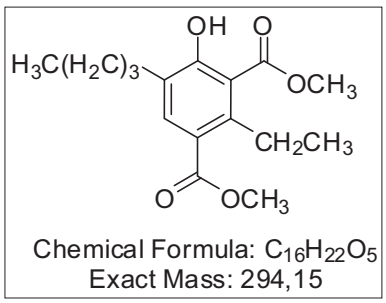
Starting with **109b** (0.258 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **110n** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.210 g, 50%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.11 - 1.19 (m, 6 H, 2 CH_3), 1.37 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 2.58 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.11 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 4.39 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 7.63 (s, 1 H, CH_{Ar}), 11.22 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.4, 13.9, 15.2 (CH_3), 21.9, 23.9, 50.9 (CH_2), 61.1 (OCH_2), 112.4 ($CCOOC_2H_5$), 121.6 ($CCOOCH_3$), 129.0 (C_{Ar}), 134.0 (CH_{Ar}), 145.3 (C_{Ar}), 161.0 (COH), 167.3, 170.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2968 (w), 2935 (w), 2875 (w), 1722 (m), 1657 (m), 1608 (w), 1578 (w), 1429 (w), 1373 (w), 1323 (w), 1274 (m), 1229 (m), 1200 (m), 1156 (w), 1093 (w), 1061 (w), 1021 (w), 979 (w), 909 (w), 847 (w), 818 (w), 733 (m), 648 (w). GC-MS (EI, 70 eV): *m/z* (%) = 280 ($[M]^+$, 36), 249 (11), 235 (23), 234 (100), 206 (17), 203 (20), 191 (16), 175 (11), 174 (37), 147 (15), 146 (16), 91 (13), 77 (10). HRMS (EI): Calcd. for $C_{15}H_{20}O_5$ ($[M]^+$): 280.13053; found: 280.130632.

Dimethyl 5-butyl-2-ethyl-4-hydroxyisophthalate (110o):

Starting with **109b** (0.258 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **110o** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.229 g, 52%).

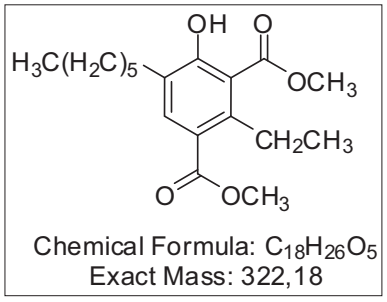


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_3CH_3$), 1.14 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.25 – 1.34 (m, 2 H, CH_2), 1.45 – 1.54 (m, 2 H, CH_2), 2.55 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.08 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.78 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 16.0

(CH_3), 22.6, 25.1, 29.6, 31.4 (CH_2), 51.9, 52.5 (OCH_3), 113.4 (*C*$COOCH_3$), 122.6 (C_{Ar}), 128.8 (*C*$COOCH_3$), 135.9 (CH_{Ar}), 146.4 (C_{Ar}), 162.0 (COH), 168.2, 172.1 (CO).
IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2930 (w), 2873 (w), 2256 (w), 1721 (m), 1662 (m), 1606 (w), 1579 (w), 1434 (m), 1337 (w), 1276 (m), 1228 (m), 1202 (m), 1153 (w), 1068 (w), 986 (w), 908 (m), 816 (w), 732 (s), 648 (w). GC-MS (EI, 70 eV): *m/z* (%) = 294 ($[M]^+$, 47), 263 (27), 262 (41), 247 (12), 245 (23), 233 (18), 231 (20), 221 (14), 220 (100), 219 (26), 203 (55), 192 (13), 187 (28), 160 (15), 159 (11), 131 (11), 103 (12), 91 (13), 77 (14). HRMS (EI): Calcd. for $C_{16}H_{22}O_5$ ($[M]^+$): 294.14618; found: 294.146337.

Dimethyl 2-ethyl-5-hexyl-4-hydroxyisophthalate (110p):

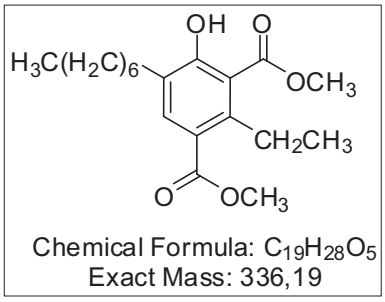
Starting with **109b** (0.258 g, 1.5 mmol) and **22j** (0.569 g, 1.65 mmol), **110p** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.251 g, 52%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.13 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.21 – 1.29 (m, 6 H, 3 CH_2), 1.46 – 1.53 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 2.99 (q, ^3J = 7.3 Hz, 2 H, $PhCH_2$), 3.78 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 16.0, (CH_3), 22.6, 25.0, 29.1, 29.2, 29.8, 31.7 (CH_2), 51.9, 52.5 (OCH_3), 113.3 (*C*$COOCH_3$), 122.6 (C_{Ar}), 128.8 (*C*$COOCH_3$), 135.9 (CH_{Ar}), 146.4 (C_{Ar}), 161.9 (COH), 168.2, 172.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2927 (w), 2856 (w), 2255 (w), 1719 (m), 1660 (m), 1606 (w), 1578 (w), 1433 (m), 1334 (m), 1272 (m), 1227 (s), 1200 (s), 1151 (m), 1087 (w), 1068 (w), 1047 (w), 992 (w), 906 (s), 816 (w), 729 (s), 648 (m). GC-MS (EI, 70 eV): *m/z* (%) = 323 (10), 322 ($[M]^+$, 50), 291 (28), 290 (38), 273 (25), 262 (11), 261 (43), 259 (16), 247 (11), 234 (11), 233 (21), 231 (49), 221 (16), 220 (100), 219 (31), 205 (10), 192 (14), 187 (31), 160 (15), 131 (11), 103 (11), 91 (12), 77 (11). HRMS (EI): Calcd. for $C_{18}H_{26}O_5$ ($[M]^+$): 322.17748; found: 322.177229.

Dimethyl 2-ethyl-5-heptyl-4-hydroxyisophthalate (110q):

Starting with **109b** (0.258 g, 1.5 mmol) and **22k** (0.592 g, 1.65 mmol), **110q** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.257 g, 51%).

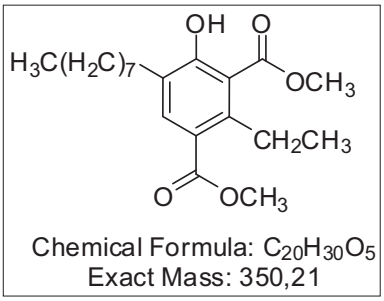


Chemical Formula: $C_{19}H_{28}O_5$
Exact Mass: 336,19

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.14 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.20 – 1.27 (m, 8 H, 4 CH_2), 1.49 – 1.54 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.08 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1, 16.0, (CH_3), 22.6, 25.1, 29.1, 29.2, 29.4, 29.8, 31.8 (CH_2), 51.9, 52.5 (OCH_3), 113.2 (*C*$COOCH_3$), 122.7 (C_{Ar}), 129.0 (*C*$COOCH_3$), 136.2 (CH_{Ar}), 146.6 (C_{Ar}), 162.3 (COH), 168.4, 172.2 (CO).
IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2927 (m), 2855 (w), 2258 (w), 1722 (m), 1662 (m), 1606 (w), 1579 (w), 1434 (m), 1335 (w), 1275 (m), 1228 (m), 1202 (m), 1152 (w), 1069 (w), 990 (w), 908 (m), 816 (w), 733 (m), 648 (w). GC-MS (EI, 70 eV): *m/z* (%) = 337 (10), 336 ($[M]^+$, 45), 305 (26), 304 (35), 287 (24), 275 (10), 273 (15), 262 (10), 261 (41), 247 (11), 246 (49), 234 (10), 233 (20), 221 (18), 220 (100), 205 (10), 192 (15), 161 (10), 160 (13), 159 (11), 131 (11), 103 (10), 91 (11), 43 (10). HRMS (EI): Calcd. for $C_{19}H_{28}O_5$ ($[M]^+$): 336.19313; found: 336.193054.

Dimethyl 2-ethyl-4-hydroxy-5-octylisophthalate (110r):

Starting with **109b** (0.258 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **110r** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellow oil (0.263 g, 50%).



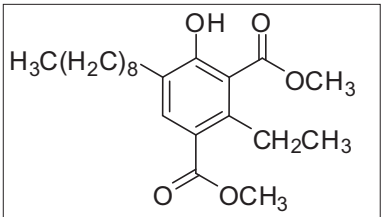
Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350,21

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.13 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.22 – 1.36 (m, 10 H, 5 CH_2), 1.47 – 1.56 (m, 2 H, CH_2), 2.52 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.06 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.7, 15.9, (CH_3), 22.1, 25.1, 28.9, 29.0, 29.2, 29.3, 29.8, 31.6 (CH_2), 51.6, 52.4 (OCH_3), 112.8 (*C*$COOCH_3$), 121.7 (C_{Ar}), 128.7 (*C*$COOCH_3$), 135.9 (CH_{Ar}), 146.1 (C_{Ar}), 161.9 (COH), 167.7, 171.9 (CO).
IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2925 (m), 2854 (w), 2255 (w), 1745 (w), 1711 (w), 1658 (m), 1604 (w), 1569 (w), 1462 (w), 1329 (w), 1231 (w), 1153 (w), 908 (m), 845 (w), 734 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 350 (10), 318 (12), 228 (28), 220 (20), 155 (10), 130 (10), 129 (44), 116 (100), 111 (11), 101 (10), 98 (11), 97 (15), 95 (12), 85 (21), 83 (16), 81

(17), 71 (30), 69 (40), 57 (43), 55 (26), 43 (32), 41 (19). HRMS (ESI, [M-H)$^-$]): Calcd. for $C_{20}H_{29}O_5$: 349.20205; found: 349.20192.

Dimethyl 2-ethyl-4-hydroxy-5-nonylbenzene-1,3-dioate (110s):

Starting with **109b** (0.258 g, 1.5 mmol) and **22m** (0.638 g, 1.65 mmol), **110s** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellow oil (0.278 g, 51%).

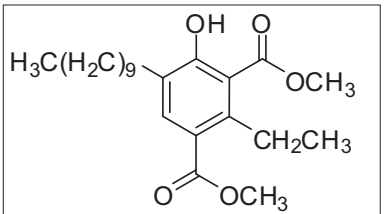


Chemical Formula: $C_{21}H_{32}O_5$
Exact Mass: 364,22

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 6.5 Hz, 3 H, CH_3), 1.14 (t, ^3J = 7.0 Hz, 3 H, CH_3), 1.18 – 1.25 (m, 12 H, 6 CH_2), 1.49 – 1.54 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.0 Hz, 2 H, $PhCH_2$), 3.08 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.80 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.2, 15.1 (CH_3), 21.7, 24.1, 26.4, 28.2, 28.3, 28.5, 28.8, 30.3, 30.8 (CH_2), 50.9, 51.5 (OCH_3), 112.3 (*C*COOCH$_3$), 121.6 (*C*COOCH$_3$), 127.8 (C_{Ar}), 135.0 (CH_{Ar}), 145.5 (C_{Ar}), 161.0 (COH), 167.4, 171.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2925 (s), 2854 (m), 1749 (w), 1717 (m), 1662 (m), 1617 (w), 1577 (w), 1559 (w), 1540 (w), 1507 (w), 1456 (w), 1436 (m), 1331 (w), 1273 (w), 1229 (m), 1203 (m), 1153 (w), 1070 (w), 994 (w), 909 (m), 817 (w), 734 (m), 668 (w), 649 (w). GC-(EI, 70 eV): *m/z* (%) = 364 ([M$^+$], 47), 332 (49), 315 (19), 273 (41), 242 (21), 220 (100), 187 (21), 160 (9), 129 (26), 116 (54), 97 (12), 85 (7), 69 (11), 57 (14), 43 (16). HRMS (EI): Calcd. for $C_{21}H_{32}O_5$ ([M]$^+$): 364.22443; found: 364.223933.

Dimethyl 5-decyl-2-ethyl-4-hydroxybenzene-1,3-dioate (110t):

Starting with **109b** (0.258 g, 1.5 mmol) and **22n** (0.661 g, 1.65 mmol), **110t** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellow oil (0.278 g, 49%).



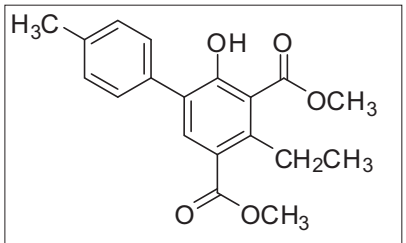
Chemical Formula: $C_{22}H_{34}O_5$
Exact Mass: 378,24

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.6 Hz, 3 H, CH_3), 1.13 (t, ^3J = 8.6 Hz, 3 H, CH_3), 1.16 – 1.24 (m, 14 H, 7 CH_2), 1.46 – 1.54 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.08 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.62 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1, 15.3 (CH_3), 21.8, 24.2, 28.2, 28.3, 28.4, 28.5, 28.6, 28.7, 28.8, 30.9, (CH_2), 50.8, 51.5 (OCH_3), 112.5 (*C*COOCH$_3$), 121.8 (*C*COOCH$_3$), 127.9 (C_{Ar}), 134.9 (CH_{Ar}), 145.5 (C_{Ar}), 161.0 (COH), 167.4, 171.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 2925 (s), 2854 (m), 1723 (m), 1663 (m), 1608 (w), 1578 (w), 1435 (m), 1336 (m), 1275 (m), 1228 (m), 1203 (m), 1153 (m), 1069 (w),

995 (w), 909 (m), 817 (w), 734 (m), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 378 ([M^+], 43), 363 (3), 346 (48), 329 (19), 311 (11), 287 (40), 275 (9), 261 (36), 233 (19), 220 (100), 207 (63), 187 (21), 160 (9), 115 (32), 95 (11), 73 (21), 55 (13), 43 (16). HRMS (EI): Calcd. for $C_{22}H_{34}O_5$ ([$M]^+$): 378.24008; found: 378.240020.

Dimethyl 4-ethyl-2-hydroxy-4'-methylbiphenyl-3,5-dicarboxylate (110u):

Starting with **109b** (0.258 g, 1.5 mmol) and **22q** (0.578 g, 1.65 mmol), **110u** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light red oil (0.250 g, 51%).

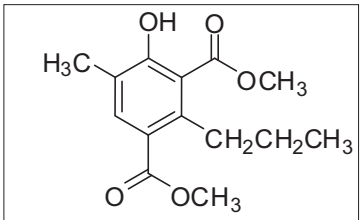


Chemical Formula: $C_{19}H_{20}O_5$
Exact Mass: 328,13

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.31 (s, 3 H, $PhCH_3$), 3.11 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.79 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 7.15 - 7.19 (m, 2 H, 2 CH_{Ar}), 7.33 - 7.36 (m, 2 H, 2 CH_{Ar}), 7.82 (s, 1 H, CH_{Ar}), 10.60 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.9, 21.2 (CH_3), 25.2 (CH_2), 52.0, 52.7 (OCH_3), 115.2 ($CCOOCH_3$), 122.9 (C_{Ar}), 127.9 ($CCOOCH_3$), 129.1 (2 CH_{Ar}), 129.5 (2 CH_{Ar}), 133.5 (C_{Ar}), 136.5 (CH_{Ar}), 137.5, 147.5 (C_{Ar}), 160.0 (COH), 167.7, 171.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2950 (w), 2874 (w), 1719 (m), 1660 (m), 1605 (m), 1561 (m), 1514 (w), 1431 (m), 1397 (m), 1332 (m), 1293 (m), 1231 (s), 1198 (s), 1174 (s), 1081 (m), 1029 (m), 961 (m), 932 (m), 822 (m), 778 (m), 745 (m), 680 (w), 656 (m), 539 (m). GC-MS (EI, 70 eV): *m/z* (%) = 328 ([$M]^+$, 40), 297 (47), 296 (100), 253 (12), 165 (7). HRMS (EI): Calcd. for $C_{19}H_{20}O_5$ ([$M]^+$): 328.13053; found: 328.130425.

Dimethyl 4-hydroxy-5-methyl-2-propylisophthalate (110v):

Starting with **109c** (0.279 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **110v** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light red oil (0.203 g, 51%).



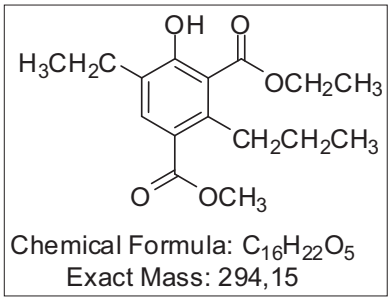
Chemical Formula: $C_{14}H_{18}O_5$
Exact Mass: 266,12

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_3CH_3$), 1.41 – 1.50 (m, 2 H, $CH_2CH_2CH_3$), 2.10 (s, 3 H, $PhCH_3$), 2.98 (t, ^3J = 8.2 Hz, 2 H, $CH_2CH_2CH_3$), 3.73 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 7.58 (s, 1 H, CH_{Ar}), 11.09 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.5, 15.8 (CH_3), 22.3, 33.6 (CH_2), 51.9, 52.6 (OCH_3), 113.2 ($CCOOCH_3$), 122.9 (C_{Ar}), 124.4 ($CCOOCH_3$), 136.8 (CH_{Ar}), 145.2 (C_{Ar}), 162.4 (COH), 168.3, 172.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2927 (w), 2855 (w), 1720 (m), 1658 (m), 1609 (w), 1580 (w), 1432 (m), 1379 (w), 1331 (m), 1265 (m), 1222 (s), 1192 (s), 1150 (s), 1063 (m), 1017 (m),

985 (m), 912 (w), 843 (w), 813 (m), 760 (m), 731 (m), 678 (w), 647 (w). GC-MS (EI, 70 eV): *m/z* (%) = 266 ([M]$^+$, 28), 235 (29), 234 (100), 219 (12), 203 (24), 187 (14), 178 (14), 177 (9), 175 (11), 163 (9), 157 (8), 147 (9), 91 (10), 77 (8). HRMS (EI): Calcd. for $C_{14}H_{18}O_5$ ([M]$^+$): 266.11488; found: 266.114914.

3-Ethyl 1-methyl 5-ethyl-4-hydroxy-2-propylisophthalate (110w):

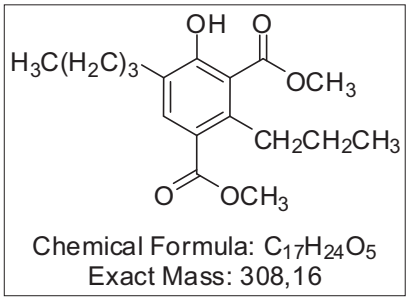
Starting with **109c** (0.279 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **110w** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.233 g, 53%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.76 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_2CH_3$), 0.99 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.23 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3), 1.32 – 1.47 (m, 2 H, $CH_2CH_2CH_3$), 2.44 (q, ^3J = 7.6 Hz, 2 H, $PhCH_2CH_3$), 2.91 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2CH_2$), 3.65 (s, 3 H, OCH_3), 4.25 (q, ^3J = 7.6 Hz, 2 H, OCH_2CH_3), 7.48 (s, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8, 15.3, 15.8 (CH_3), 24.2, 26.5, 34.9 (CH_2), 53.2 (OCH_3), 63.4 (OCH_2CH_3), 114.7 (CCOOCH$_2$CH$_3$), 124.1 (C_{Ar}), 131.3 (CCOOCH$_3$), 136.3 (CH_{Ar}), 146.1 (C_{Ar}), 163.4 (COH), 169.7, 173.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2963 (w), 2933 (w), 2872 (w), 2255 (w), 1716 (m), 1655 (m), 1607 (w), 1578 (w), 1428 (w), 1396 (w), 1373 (w), 1321 (w), 1298 (w), 1263 (w), 1223 (s), 1154 (m), 1097 (w), 1054 (w), 1020 (w), 971 (w), 906 (m), 868 (w), 845 (w), 818 (w), 729 (s), 648 (w), 581 (w). GC-MS (EI, 70 eV): *m/z* (%) = 294 ([M]$^+$, 38), 263 (14), 249 (22), 248 (100), 233 (17), 230 (14), 217 (21), 215 (11), 198 (17), 192 (48), 191 (11), 177 (12), 173 (12), 171 (13), 115 (10), 91 (13), 77 (10). HRMS (EI): Calcd. for $C_{16}H_{22}O_5$ ([M]$^+$): 294.14618; found: 294.146042.

Dimethyl 5-butyl-4-hydroxy-2-propylisophthalate (110x):

Starting with **109c** (0.279 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **110x** was isolated after chromatography (silica gel, heptanes/EtOAc) as a light yellowish oil (0.236 g, 51%).

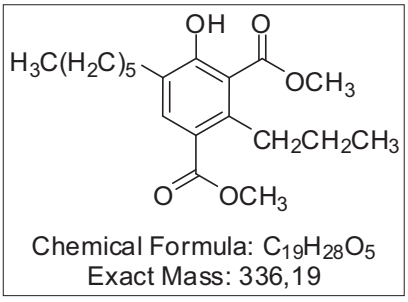


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.82 - 0.93 (m, 6 H, 2 CH_3), 1.25 – 1.35 (m, 2 H, $(CH_2)_2CH_2CH_3$), 1.45 – 1.55 (m, 4 H, 2 CH_2), 2.54 (t, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.03 (t, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 14.6 (CH_3), 22.6, 25.3, 29.5, 31.4, 33.6 (CH_2), 51.9, 52.5 (OCH_3), 113.4 (CCOOCH$_3$), 122.8 (C_{Ar}), 128.7 (CCOOCH$_3$),

135.9 (CH_{Ar}), 145.0 (C_{Ar}), 161.9 (COH), 168.3, 172.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2930 (w), 2871 (w), 2255 (w), 1719 (m), 1661 (m), 1606 (w), 1579 (w), 1434 (m), 1335 (w), 1297 (w), 1265 (w), 1226 (m), 1199 (m), 1153 (m), 1088 (w), 1063 (w), 999 (w), 907 (m), 816 (w), 731 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 309 (10), 308 ($[M]^+$, 54), 277 (36), 276 (41), 259 (30), 247 (20), 245 (38), 235 (13), 234 (100), 233 (29), 219 (11), 217 (53), 216 (19), 202 (11), 201 (17), 191 (13), 187 (10), 184 (10), 178 (22), 173 (14), 115 (16), 91 (14), 77 (12). HRMS (EI): Calcd. for $C_{17}H_{24}O_5$ ($[M]^+$): 308.16183; found: 308.162084.

Dimethyl 5-hexyl-4-hydroxy-2-propylisophthalate (110y):

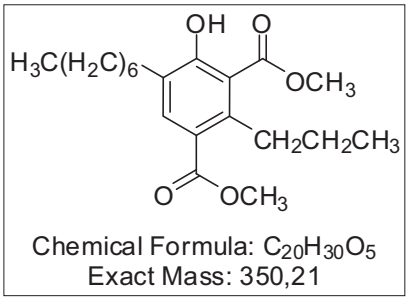
Starting with **109c** (0.279 g, 1.5 mmol) and **22j** (0.569 g, 1.65 mmol), **110y** was isolated after chromatography (silica gel, heptanesEtOAc) as a yellowish oil (0.227 g, 45%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_5CH_3$), 0.90 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_2CH_3$), 1.17 – 1.32 (m, 6 H, 3 CH_2), 1.43 – 1.56 (m, 4 H, 2 CH_2), 2.53 (t, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.03 (t, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.78 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.6 (CH_3), 22.6, 25.3, 29.1, 29.2, 29.8, 31.7, 33.6 (CH_2), 51.9, 52.6 (OCH_3), 113.7 (CCOOCH$_3$), 122.9 (C_{Ar}), 128.8 (CCOOCH$_3$), 136.0 (CH_{Ar}), 145.0 (C_{Ar}), 162.3 (COH), 168.4, 172.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2927 (m), 2857 (w), 2255 (w), 1720 (m), 1660 (m), 1606 (w), 1579 (w), 1433 (m), 1331 (w), 1298 (w), 1261 (w), 1226 (s), 1199 (s), 1152 (m), 1092 (w), 1062 (w), 995 (w), 972 (w), 907 (m), 816 (w), 731 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 337 (34), 336 ($[M]^+$, 98), 306 (19), 305 (91), 304 (96), 303 (14), 289 (21), 288 (13), 287 (75), 276 (23), 275 (89), 274 (14), 273 (76), 262 (18), 261 (37), 249 (11), 248 (54), 247 (72), 246 (17), 245 (87), 244 (13), 235 (55), 234 (100), 233 (88), 229 (12), 219 (22), 217 (14), 216 (32), 215 (32), 206 (11), 205 (13), 203 (18), 202 (23), 201 (44), 192 (13), 191 (24), 189 (11), 187 (14), 184 (14), 178 (37), 175 (18), 174 (12), 173 (22), 159 (11), 157 (14), 147 (12), 146 (10), 145 (13), 115 (12), 91 (12). HRMS (EI): Calcd. for $C_{19}H_{28}O_5$ ($[M]^+$): 336.19313; found: 336.192594.

Dimethyl 5-heptyl-4-hydroxy-2-propylisophthalate (110z):

Starting with **109c** (0.279 g, 1.5 mmol) and **22k** (0.592 g, 1.65 mmol), **110z** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.242 g, 46%).

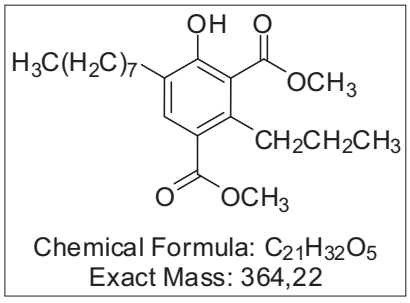


Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350,21

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, ^3J = 7.6 Hz, 3 H, $(CH_2)_6CH_3$), 0.91 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_2CH_3$), 1.13 – 1.30 (m, 8 H, 4 CH_2), 1.45 – 1.58 (m, 4 H, 2 CH_2), 2.54 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.03 (t, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.6 (CH_3), 22.7, 25.4, 29.1, 29.5, 29.6, 29.8, 31.8, 33.6 (CH_2), 51.9, 52.5 (OCH_3), 113.6 (CCOOOCH$_3$), 122.8 (C_{Ar}), 128.8 (CCOOOCH$_3$), 135.8 (CH_{Ar}), 145.0 (C_{Ar}), 162.1 (COH), 168.4, 172.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2926 (m), 2855 (w), 1720 (m), 1661 (m), 1607 (w), 1578 (w), 1434 (m), 1329 (w), 1298 (w), 1262 (w), 1226 (s), 1199 (m), 1152 (w), 1093 (w), 1063 (w), 994 (w), 908 (w), 816 (w), 732 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 351 (13), 350 ($[M]^+$, 56), 319 (41), 318 (43), 301 (34), 289 (10), 287 (36), 276 (12), 275 (50), 262 (10), 261 (12), 259 (43), 248 (11), 247 (25), 235 (17), 234 (100), 233 (44), 219 (11), 216 (12), 203 (11), 202 (12), 201 (21), 191 (14), 178 (22), 173 (14), 145 (10). HRMS (EI): Calcd. for $C_{20}H_{30}O_5$ ($[M]^+$): 350.20878; found: 350.208521.

Dimethyl 4-hydroxy-5-octyl-2-propylisophthalate (110aa):

Starting with **109c** (0.279 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **110aa** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.246 g, 45%).



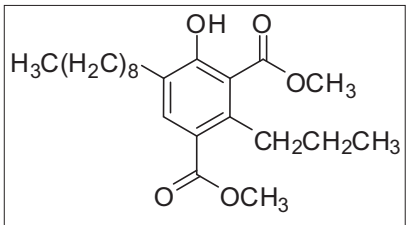
Chemical Formula: $C_{21}H_{32}O_5$
Exact Mass: 364,22

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 7.4 Hz, 3 H, $(CH_2)_7CH_3$), 0.90 (t, ^3J = 7.6 Hz, 3 H, $(CH_2)_2CH_3$), 1.17 – 1.30 (m, 10 H, 5 CH_2), 1.46 – 1.57 (m, 4 H, 2 CH_2), 2.53 (t, ^3J = 7.6 Hz, 2 H, $PhCH_2$), 3.03 (t, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.6 (CH_3), 22.6, 25.3, 29.1, 29.2, 29.4, 29.5, 29.8, 31.8, 33.6 (CH_2), 51.8, 52.5 (OCH_3), 113.7 (CCOOOCH$_3$), 123.1 (C_{Ar}), 129.0 (CCOOOCH$_3$), 136.1 (CH_{Ar}), 145.4 (C_{Ar}), 162.1 (COH), 168.2, 172.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2926 (m), 2855 (w), 2256 (w), 1721 (w), 1662 (m), 1606 (w), 1579 (w), 1434 (m), 1331 (w), 1298 (w), 1262 (w), 1227 (m), 1200 (m), 1152 (w), 1094 (w), 1062 (w), 995 (w), 908 (m), 817 (w), 733 (s), 649 (w). GC-MS (EI, 70 eV): *m/z* (%) = 364

([M]$^+$, 47), 333 (42), 332 (73), 315 (28), 301 (33), 289 (11), 276 (21), 275 (74), 273 (53), 261 (13), 248 (17), 247 (32), 235 (26), 234 (100), 233 (69), 228 (16), 219 (14), 217 (11), 216 (22), 215 (10), 203 (13), 202 (16), 201 (32), 191 (14), 185 (11), 184 (11), 179 (11), 178 (25), 175 (14), 173 (17), 158 (10), 157 (12), 155 (13), 147 (10), 145 (10), 130 (11), 129 (45), 117 (13), 116 (85), 115 (11), 101 (10), 98 (11), 91 (11), 85 (19), 83 (12), 81 (10), 71 (30), 69 (25), 57 (42), 55 (23). HRMS (EI): Calcd. for $C_{21}H_{32}O_5$ ([M]$^+$): 364.22443; found: 364.224478.

Dimethyl 4-hydroxy-5-nonyl-2-propylbenzene-1,3-dioate (110ab):

Starting with **109c** (0.279 g, 1.5 mmol) and **22m** (0.638 g, 1.65 mmol), **110ab** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.284 g, 50%).

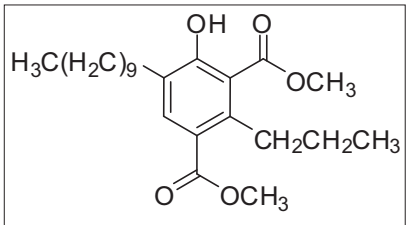


Chemical Formula: $C_{22}H_{34}O_5$
Exact Mass: 378,24

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.4 Hz, 3 H, $(CH_2)_8CH_3$), 0.91 (t, ^3J = 7.5 Hz, 3 H, $(CH_2)_2CH_3$), 1.15 – 1.26 (m, 14 H, 7 CH_2), 1.52 – 1.54 (m, 2 H, CH_2), 2.54 (t, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.00 – 3.06 (m, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 13.9 (CH_3), 21.9, 24.4, 26.1, 28.2, 28.3, 28.5, 28.8, 30.3, 30.9 32.6 (CH_2), 50.9, 51.5 (OCH_3), 112.6 (*C*$COOCH_3$), 121.9 (*C*$COOCH_3$), 127.9 (C_{Ar}), 135.1 (CH_{Ar}), 144.2 (C_{Ar}), 161.2 (COH), 167.6, 171.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (m), 2925 (s), 2854 (m), 1722 (m), 1662 (m), 1608 (w), 1578 (w), 1435 (m), 1330 (w), 1299 (w), 1262 (m), 1227 (s), 1200 (m), 1153 (m), 1094 (w), 1063 (w), 995 (w), 908 (m), 817 (w), 733 (s), 650 (w). GC-MS (EI, 70 eV): *m/z* (%) = 378 ([M$^+$], 50), 368 (5), 346 (57), 329 (21), 275 (40), 242 (22), 234 (100), 201 (17), 178 (18), 158 (12), 129 (37), 116 (78), 97 (16), 85 (12), 69 (17), 57 (23), 43 (21). HRMS (EI): Calcd. for $C_{22}H_{34}O_5$ ([M]$^+$): 378.24008; found: 378.239947.

Dimethyl 5-decyl-4-hydroxy-2-propylbenzene-1,3-dioate (110ac):

Starting with **109c** (0.279 g, 1.5 mmol) and **22n** (0.661 g, 1.65 mmol), **110ac** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.323 g, 55%).



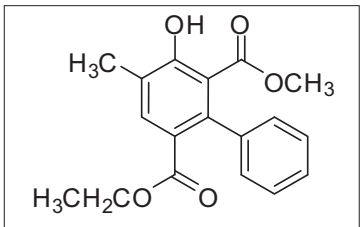
Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392,26

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.5 Hz, 3 H, $(CH_2)_9CH_3$), 0.91 (t, ^3J = 7.2 Hz, 3 H, $(CH_2)_2CH_3$), 1.16 – 1.26 (m, 16 H, 8 CH_2), 1.49 – 1.54 (m, 2 H, CH_2), 2.53 (t, ^3J = 7.7 Hz, 2 H, $PhCH_2$), 3.01 – 3.06 (m, 2 H, $PhCH_2$), 3.79 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 7.61 (s, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9,

14.7 (CH_3), 22.7, 25.2, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 29.8, 31.9, 33.8 (CH_2), 51.9, 52.7 (OCH_3), 113.3 (*C*$COOCH_3$), 122.9 (*C*$COOCH_3$), 128.8 (C_{Ar}), 136.0 (CH_{Ar}), 145.1 (C_{Ar}), 162.0 (COH), 168.4, 172.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2954 (m), 2955 (m), 2854 (m), 1723 (m), 1662 (m), 1606 (w), 1579 (w), 1434 (m), 1331 (w), 1298 (w), 1261 (w), 1227 (m), 1200 (m), 1152 (w), 1095 (w), 1061 (w), 996 (w), 908 (w), 817 (w), 734 (m), 650 (w). GC-MS (EI, 70 eV): *m/z* (%) = 392 ([M^+], 50), 360 (43), 343 (20), 301 (30), 275 (31), 247 (20), 234 (100), 219 (8), 201 (15), 178 (18), 145 (7), 116 (12), 91 (5), 69 (4), 55 (7), 43 (11). HRMS (EI): Calcd. for $C_{23}H_{36}O_5$ ([M]$^+$): 392.25573; found: 392.255638.

6-Ethyl 2-methyl 3-hydroxy-4-methylbiphenyl-2,6-dicarboxylate (110ad):

Starting with **109d** (0.372 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **110ad** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.272 g, 58%).

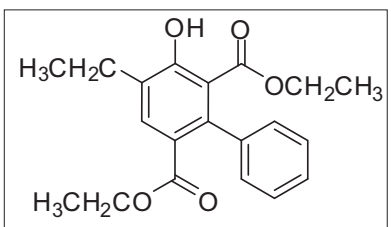


Chemical Formula: $C_{18}H_{18}O_5$
Exact Mass: 314,12

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 2.24 (s, 3 H, $PhCH_3$), 3.89 (s, 3 H, OCH_3), 4.14 (q, ^3J = 7.5 Hz, 2 H, OCH_2CH_3), 7.02 - 7.06 (m, 3 H, 3 CH_{Ar}), 7.33 - 7.36 (m, 2 H, 2 CH_{Ar}), 7.88 (s, 1 H, CH_{Ar}), 11.04 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 15.8 (CH_3), 51.9 (OCH_3), 61.4 (OCH_2), 112.7 (*C*$COOCH_3$), 123.9 (*C*$COOC_2H_5$), 126.0 (C_{Ar}), 128.2 (CH_{Ar}), 128.4 (2 CH_{Ar}), 128.7 (2 CH_{Ar}), 133.7 (CH_{Ar}), 135.6, 135.9 (C_{Ar}), 167.5 (COH), 171.4, 173.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3059 (w), 2981 (w), 2953 (w), 2905 (w), 2872 (w), 1737 (m), 1686 (m), 1662 (m), 1597 (m), 1578 (m), 1494 (w), 1381 (w), 1366 (m), 1264 (m), 1193 (s), 1148 (s), 1076 (m), 1022 (m), 998 (m), 942 (w), 870 (w), 814 (m), 755 (m), 687 (s), 647 (m), 572 (m). GC-MS (EI, 70 eV): *m/z* (%) = 314 ([M^+, 51), 283 (20), 282 (100), 254 (22), 253 (96), 237 (27), 210 (12), 209 (47), 208 (23), 181 (10), 153 (15), 152 (10). HRMS (EI): Calcd. for $C_{18}H_{18}O_5$ ([M]$^+$): 314.11488; found: 314.114952.

Diethyl 4-ethyl-3-hydroxybiphenyl-2,6-dicarboxylate (110ae):

Starting with **109d** (0.372 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **110ae** was isolated after chromatography (silica gel, heptanes/EtOAc) as yellowish oil (0.308 g, 60%).



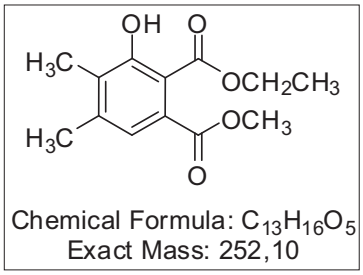
Chemical Formula: $C_{20}H_{22}O_5$
Exact Mass: 342,15

^{1}H NMR (300 MHz, $CDCl_3$) : δ = 0.57 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 0.77 (t, ^3J = 7.4 Hz, 3 H, OCH_2CH_3) , 1.16 (t, ^3J = 7.3 Hz, 3 H, $PhCH_2CH_3$), 2.61 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2CH_3$), 3.74 – 3.85(m, 4 H, 2 OCH_2CH_3), 6.99 – 7.04 (m, 2 H, 2 CH_{Ar}), 7.17 - 7.19 (m, 3 H, 3 CH_{Ar}), 7.62 (s, 1 H,

CH_{Ar}), 11.17 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 13.4, 13.6 (CH_3), 22.9, 60.7, 61.3 (CH_2), 113.0 (*C*COOCH$_3$), 124.5 (*C*COOC$_2$H$_5$), 126.6 (CH_{Ar}), 127.1 (2 CH_{Ar}), 128.3 (2 CH_{Ar}), 131.9 (CH_{Ar}), 134.4, 141.2, 142.3 (C_{Ar}), 161.5 (COH), 168.4, 171.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2978 (w), 2935 (w), 2874 (w), 2254 (w), 1708 (m), 1657 (m), 1602 (w), 1571 (w), 1443 (m), 1398 (w), 1367 (m), 1329 (m), 1306 (m), 1281 (m), 1265 (m), 1214 (s), 1178 (s), 1125 (m), 1095 (w), 1066 (w), 1020 (m), 907 (m), 884 (w), 866 (w), 819 (w), 763 (w), 728 (s), 698 (s), 669 (w), 648 (w). GC-MS (EI, 70 eV): *m/z* (%) = 342 ($[M]^+$, 35), 297 (16), 296 (51), 268 (19), 267 (100), 251 (12), 223 (36), 222 (11), 165 (13), 152 (13). HRMS (EI): Calcd. for $C_{20}H_{22}O_5$ ($[M]^+$) : 342.14618; found: 342.146145.

2-Ethyl 1-methyl 3-hydroxy-4,5-dimethylphthalate (113b):

Starting with **112a** (0.433 g, 2.0 mmol) and **22e** (0.635 g, 2.2 mmol), **113b** was isolated as a reddish viscous oil (0.161 g, 32%).

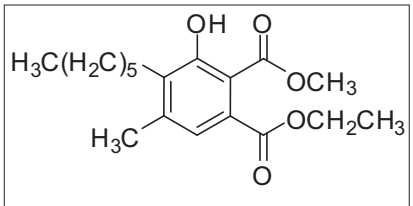


Chemical Formula: $C_{13}H_{16}O_5$
Exact Mass: 252,10

^1H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.6 Hz, 3 H, OCH$_2$*CH$_3$*), 2.26 (s, 3 H, PhCH$_3$), 2.39 (s, 3 H, PhCH$_3$), 3.85 (s, 3H, OCH$_3$), 4.24 (q, ^3J = 7.4 Hz, 2 H, *OCH$_2$*CH$_3$), 6.94 (s, 1 H, CH_{Ar}), 11.54 (s, 1H, OH).^{13}C NMR (62 MHz, $CDCl_3$): δ = 11.5, 13.4, 21.6 (CH_3), 51.3 (OCH$_3$), 60.2 (OCH$_2$), 112.4 (C_{Ar}), 121.4 (CH_{Ar}), 124.0, 134.7, 136.7 (C_{Ar}), 160.3 (COH), 166.7, 171.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 1660 (s), 1619 (m), 1452 (s), 1343 (s), 1219 (m), 1136 (s), 966 (m), 882 (m), 694 (m). MS (EI, 70 eV): *m/z* (%) = 252 ([M$^+$], 55), 220 (100), 207 (37), 192 (87), 175 (13), 164 (82), 147 (17), 119 (15), 91 (25), 77 (11), 65 (18). HRMS (EI): Calcd. for $C_{13}H_{16}O_5$: 252.10056; found: 252.09998.

1-Ethyl 2-methyl 4-hexyl-3-hydroxy-5-methylphthalate (113d):

Starting with **112b** (0.461 g, 2.0 mmol) and **22j** (0.758 g, 2.2 mmol), **113d** was isolated as a reddish viscous oil (0.238 g, 37%).



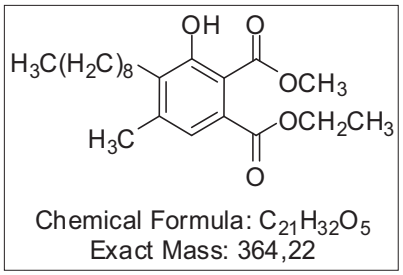
Chemical Formula: $C_{18}H_{26}O_5$
Exact Mass: 322,18

^1H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t(br), ^3J = 7.1 Hz, 3 H, CH_3), 1.02−1.25 (m, 8 H, CH_2), 1.31 (t, ^3J = 7.6 Hz, 3 H, OCH$_2$*CH$_3$*), 2.24 (s, 3 H, PhCH$_3$), 2.58 (t, ^3J = 7.4 Hz, 2 H, PhCH$_2$), 3.81 (s, 3 H, OCH$_3$), 4.25 (q, ^3J = 7.2 Hz, 2 H, *OCH$_2$*CH$_3$), 6.69 (s, 1 H, CH_{Ar}), 10.84 (s, 1 H, OH).

^{13}C NMR (62 MHz, $CDCl_3$): δ = 15.2, 15.4 (CH_3), 23.7 (CH_2), 25.1 (CH_3), 28.3, 30.3, 30.1, 32.7 (CH_2), 34.4 (OCH_3), 64.4 (OCH_2CH_3), 114.8 (C_{Ar}), 123.7 (CH_{Ar}), 130.8, 137.1, 139.1 (C_{Ar}), 162.4 (COH), 168.4, 173.4 (CO). MS (EI, 70 eV): *m/z* (%) = 322 ([M^+], 20), 290 (7), 261 (11), 233 (5), 220 (100), 206 (32), 192 (32), 174 (8), 161 (6), 148 (7), 119 (8), 91 (6), 69 (7). HRMS (EI): Calcd. for $C_{18}H_{26}O_5$: 322.17747; found: 322.17730.

1-Ethyl 2-methyl 3-hydroxy-5-methyl-4-nonylphthalate (113e):

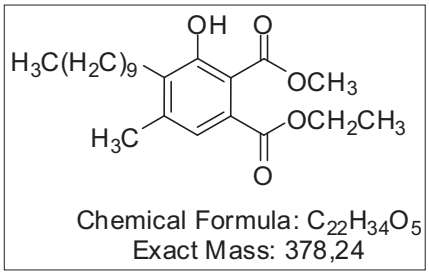
Starting with **112b** (0.461 g, 2.0 mmol) and **22m** (0.851 g, 2.2 mmol), **113e** was isolated as a yellowish oil (0.306 g, 42%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 6.3 Hz, 3 H, CH_3), 1.16-1.19 (m, 14 H, $7CH_2$), 1.32 (t, ^3J = 6.7 Hz, 3 H, OCH_2CH_3), 2.44 (s, 3 H, $PhCH_3$), 2.53 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 4.29 (q, ^3J = 7.5 Hz, 2 H, OCH_2CH_3), 6.12 (s, 1 H, CH_{Ar}), 11.84 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 13.1, 21.6 (CH_3), 22.7, 25.9, 28.5, 29.0, 29.3, 29.6, 30.8, 31.8 (CH_2), 50.7 (OCH_3), 60.3 (OCH_2), 112.9 (C_{Ar}), 121.4 (CH_{Ar}), 128.6, 134.8, 144.3, (C_{Ar}), 159.9 (COH), 165.0, 171.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3336 (w), 3107 (w), 2953 (w), 2919 (m), 2848 (w), 1725 (w), 1660 (w), 1612 (m), 1493 (w), 1462 (m), 1415 (m), 1284 (m), 1259 (m), 1201 (m), 1225 (m), 1089 (m), 1014 (m), 977 (m), 840 (w), 795 (s), 754 (m), 722 (w), 682 (w), 622 (w), 551 (w). GC-MS (EI, 70 eV): *m/z* (%) = 364 ([$M]^+$, 22), 260 (19), 259 (100), 192 (12), 191 (34). HRMS (EI): Calcd. for $C_{21}H_{32}O_5$ ([$M]^+$): 364.22443; found: 364.224257.

1-Ethyl 2-methyl 4-decyl-3-hydroxy-5-methylphthalate (113f):

Starting with **112b** (0.461 g, 2.0 mmol) and **22n** (0.882 g, 2.2 mmol), **113f** was isolated as a yellowish oil (0.318 g, 42%).

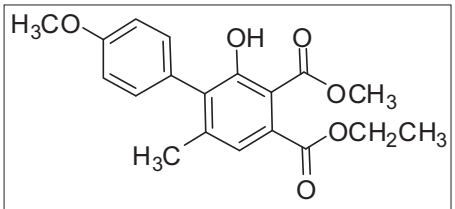


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.80 (t, ^3J = 6.7 Hz, 3 H, CH_3), 1.16-1.19 (m, 16 H, 8 CH_2), 1.32 (t, ^3J = 6.2 Hz, 3 H, OCH_2CH_3), 2.44 (s, 3 H, $PhCH_3$), 2.76 (t, ^3J = 7.2 Hz, 2 H, $PhCH_2$), 3.89 (s, 3 H, OCH_3), 4.29 (q, ^3J = 6.2 Hz, 2 H, OCH_2CH_3), 6.94 (s, 1 H, CH_{Ar}), 11.54 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 13.2, 21.6 (CH_3), 22.8, 25.9, 26.2, 28.2, 28.4, 28.5, 29.0, 30.8, 31.8 (CH_2), 51.3 (OCH_3), 60.2 (OCH_2), 112.6 (C_{Ar}), 121.4 (CH_{Ar}), 128.6, 134.7, 136.8 (C_{Ar}), 160.2 (COH), 166.9, 171.2 (CO).

IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2922 (s), 2852 (m), 1724 (m), 1662 (m), 1624 (w), 1561 (w), 1445 (m), 1395 (m), 1367 (m), 1298 (m), 1229 (s), 1193 (m), 1148 (m), 1104 (m), 1058 (m), 1011 (m), 843 (m), 800 (m), 780 (m), 721 (w), 602 (w). GC-MS (EI, 70 eV): *m/z* (%) = 378 ($[M]^+$, 21), 274 (20), 273 (100), 192 (12), 191 (32). HRMS (EI): Calcd. for $C_{22}H_{34}O_5$ ($[M]^+$): 378.24008; found: 378.239759.

4-Ethyl 3-methyl 2-hydroxy-4'-methoxy-6-methylbiphenyl-3,4-dicarboxylate (113h):

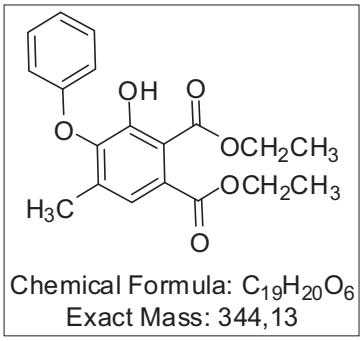
Starting with **112b** (0.461 g, 2.0 mmol) and **22s** (0.807 g, 2.2 mmol), **113h** was isolated as a yellowish oil (0.268 g, 39 %).



^{1}HNMR (250 MHz, $CDCl_3$) : δ = 1.27 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.51 (s, 3 H, $PhCH_3$), 3.76 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 3.99 (q, ^3J = 6.2 Hz, 2 H, OCH_2CH_3), 6.76 (s, 1 H, CH_{Ar}), 6.85 - 6.88 (m, 2 H, CH_{Ar}), 7.10 - 7.12 (m, 2 H, CH_{Ar}), 11.43 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.6, 19.0 (CH_3), 51.4, 54.2 (OCH_3), 60.1 (OCH_2), 112.5 (C_{Ar}), 113.1 ($2CH_{Ar}$), 121.2 (CH_{Ar}), 127.0, 129.1 (C_{Ar}), 129.4 (2 CH_{Ar}), 129.8, 136.2, 157.6 (C_{Ar}), 159.2 (COH), 170.4, 170.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2953 (w), 2931 (w), 2871 (w), 2836 (w), 1720 (w), 1661 (w), 1608 (m), 1510 (m), 1438 (w), 1392 (w), 1368 (w), 1299 (w), 1243 (s), 1193 (w), 1174 (m), 1156 (m), 1109 (w), 1078 (w), 1031 (m), 969 (w), 902 (w), 831 (m), 788 (w), 689 (w), 643 (w), 597 (w), 578 (w). GC-MS (EI, 70 eV): *m/z* (%) = 344 ($[M]^+$, 53), 313 (21), 312 (100), 283 (18), 256 (13), 239 (8), 211 (6), 197 (5), 149 (7), 135 (10), 121 (12), 73 (12). HRMS (EI): Calcd. for $C_{19}H_{20}O_6$ ($[M]^+$): 344.125; found: 344.071546.

Diethyl 3-hydroxy-5-methyl-4-phenoxyphthalate (113i):

Starting with **112b** (0.461 g, 2.0 mmol) and **22v** (0.807 g, 2.2 mmol), **113i** was isolated as a reddish viscous oil (0.275 g, 40%).

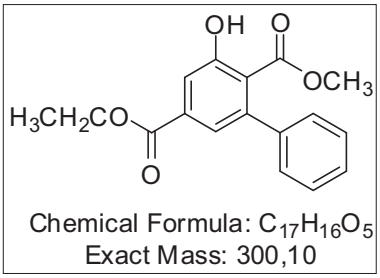


^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.27 (t, ^3J = 7.5 Hz, 3 H, OCH_2CH_3), 2.42 (s, 3 H, $PhCH_3$), 4.01 (q, ^3J = 7.6 Hz, 2 H, OCH_2CH_3), 4.28 (q, ^3J = 7.4 Hz, 2 H, OCH_2CH_3), 6.66 (m, 1 H, CH_{Ar}), 6.67 − 6.83 (m, 2 H, 2 CH_{Ar}), 7.04 (m, 1 H, CH_{Ar}), 7.07 − 7.08 (m, 2 H, CH_{Ar}), 11.16 (s, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ = 13.7, 14.1, 23.6 (CH_3), 61.4, 62.3 (CH_2), 114.8 ($2CH_{Ar}$), 116.4 (C_{Ar}), 121.7, 122.2 (CH_{Ar}), 129.3 (CH_{Ar}),

129.8, 132.1, 137.1, 140.0 (C_{Ar}), 156.3 (COH), 158.4 (C_{Ar}), 165.1, 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2980 (w), 1727 (m), 1661 (m), 1489 (m), 1412 (m), 1371 (m), 1296 (m), 1236 (s), 1016 (s), 747 (m), 687 (m). GC-MS (EI, 70 eV): *m/z* (%) = 344 ([M^+], 63), 298 (38), 269 (8), 253 (20), 226 (100), 197 (13), 177 (5), 148 (6), 121 (6), 105 (48).

5-Ethyl 2-methyl 3-hydroxybiphenyl-2,5-dicarboxylate (118a):

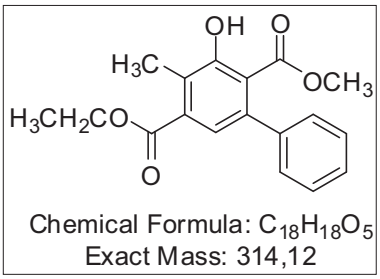
Starting with **117a** (0.439 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **118a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish oil, (0.194 g, 43%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (t, ^3J = 7.5 Hz, 3 H, CH_3), 3.43 (s, 3 H, OCH_3), 4.31 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 7.14 - 7.18 (m, 2 H, CH_{Ar}), 7.26 - 7.33 (m, 3 H, CH_{Ar}), 7.39 (d, ^4J = 1.7 Hz, 1 H, CH_{Ar}), 7.57 (d, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 10.41 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 14.33 (CH_3), 52.19 (OCH_3), 60.38 (OCH_2) 115.51 (C_{Ar}), 117.67, 122.90, 127.16 (CH_{Ar}), 127.75 (2 CH_{Ar}), 128.13 (2 CH_{Ar}), 134.76, 141.93, 145.00 (C_{Ar}), 160.96 (COH), 165.38, 170.82 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 3026 (w), 2959 (w), 2904 (w), 1713 (s), 1671 (s), 1611 (m), 1567 (m), 1497 (w), 1433 (m), 1410 (m), 1367 (m), 1341 (m), 1321 (m), 1307 (w), 1264 (m), 1238 (s), 1201 (s), 1155 (m), 1139 (m), 1113 (m), 1081 (m), 1025 (m), 982 (m), 948 (m), 922 (w), 892 (m), 870 (w), 828 (m), 806 (m), 766 (s), 699 (s), 666 (m), 648 (m), 621 (m), 607 (m), 563 (m). GC-MS (EI, 70 eV): *m/z* (%) = 300 ([$M]^+$, 28), 269 (20), 268 (100), 196 (12), 195 (14), 168 (10), 139 (20). HRMS (EI): Calcd. for $C_{17}H_{16}O_5$ ([$M]^+$): 300.09923; found: 300.099353.

5-Ethyl 2-methyl 3-hydroxy-4-methylbiphenyl-2,5-dicarboxylate (118b):

Starting with **117a** 0.439 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **118b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil, (0.231 g, 49%).

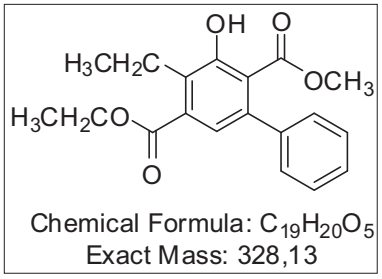


^{1}H NMR (300 MHz, $CDCl_3$) : δ = 1.24 (t, ^3J = 7.5 Hz, 3 H, CH_3), 2.35 (s, 3 H, $PhCH_3$), 3.36 (s, 3 H, OCH_3), 4.24 (q, ^3J = 7.4 Hz, 2 H, OCH_2), 7.06 (s, 1 H, CH_{Ar}), 7.11 - 7.18 (m, 2 H, CH_{Ar}), 7.21 - 7.27 (m, 3 H, CH_{Ar}), 10.82 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 12.71, 14.34 (CH_3), 51.96 (OCH_3), 60.37 (OCH_2) 113.34 (C_{Ar}), 122.36 (CH_{Ar}), 126.75 (C_{Ar}), 126.95 (CH_{Ar}), 127.78 (2 CH_{Ar}), 128.13 (2 CH_{Ar}), 135.43, 141.49, 142.28 (C_{Ar}), 159.98 (COH), 167.47, 171.51 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2952 (w), 2929 (w), 2871 (w), 1723 (s), 1665 (s), 1600 (w),

1561 (w), 1499 (w), 1437 (m), 1394 (m), 1380 (m), 1367 (m), 1341 (m), 1298 (m), 1261 (s), 1230 (s), 1194 (s), 1158 (s), 1138 (m), 1095 (s), 1049 (s), 1003 (m), 967 (m), 937 (m), 843 (m), 810 (m), 800 (m), 785 (m), 759 (m), 699 (s), 628 (w), 613 (m), 581 (w). GC-MS (EI, 70 eV): *m/z* (%) = 315 (11), (314 ($[M]^+$, 53), 283 (21), 282 (100), 281 (13), 269 (23), 254 (13), 253 (57), 226 (19), 210 (15), 209 (24), 197 (16), 182 (17), 181 (23), 153 (17), 152 (32), 151 (10). HRMS (EI): Calcd. for $C_{18}H_{18}O_5$ ($[M]^+$): 314.11488; found: 314.114942.

5-Ethyl 2-methyl 4-ethyl-3-hydroxybiphenyl-2,5-dicarboxylate (118c):

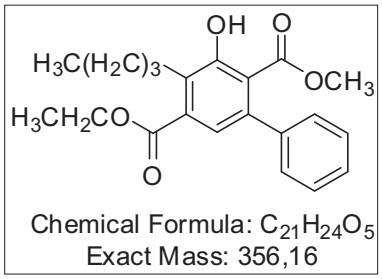
Starting with **117a** (0.439 g, 1.5 mmol) and **22f** (0.476 g, 1.65 mmol), **118c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish oil, (0.246 g, 50%).



^{1}H NMR (300 MHz, $CDCl_3$) : δ = 1.17 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.30 (t, ^3J = 7.3 Hz, 3 H, CH_3), 2.88 (q, ^3J = 7.3Hz, 2 H, $PhCH_2$), 3.41 (s, 3 H, OCH_3), 4.29 (q, ^3J = 7.2Hz, 2 H, OCH_2), 7.07 (s, 1 H, CH_{Ar}), 7.13 - 7.17 (m, 2 H, CH_{Ar}), 7.22 - 7.31 (m, 3 H, CH_{Ar}), 10.81 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 13.06, 13.20 (CH_3), 19.45 ($PhCH_2$), 50.90 (OCH_3), 60.31 (OCH_2) 112.50 (C_{Ar}), 121.49, 125.94 (CH_{Ar}), 126.70 (2 CH_{Ar}), 127.14 (2 CH_{Ar}), 131.29, 134.30, 140.69, 141.22 (C_{Ar}), 159.13 (COH), 166.83, 170.47 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3025 (w), 2953 (w), 2934 (w), 2874 (w), 1723 (s), 1665 (s), 1600 (w), 1558 (w), 1495 (w), 1437 (m), 1390 (m), 1367 (m), 1346 (m), 1283 (m), 1247 (s), 1222 (s), 1193 (s), 1157 (s), 1138 (m), 1076 (s), 1028 (m), 1007 (m), 966 (m), 947 (m), 887 (w), 844 (m), 815 (m), 800 (m), 785 (m), 759 (m), 699 (s), 627 (w), 581 (w). GC-MS (EI, 70 eV): *m/z* (%) = 329 (21), (328 ($[M]^+$, 100), 297 (22), 296 (94), 295 (22), 283 (35), 268 (39), 276 (67), 253 (19), 251 (11), 249 (23), 240 (11), 225 (19), 224 (35), 223 (28), 221 (13), 197 (49), 196 (42), 195 (25), 194 (10), 167 (10), 166 (14), 165 (51), 153 (12), 152 (34), 151 (11), 139 (14), 129 (11), 115 (12). HRMS (EI): Calcd. for $C_{19}H_{20}O_5$ ($[M]^+$) : 328.13053; found: 328.130470**.**

5-Ethyl 2-methyl 4-butyl-3-hydroxybiphenyl-2,5-dicarboxylate (118d):

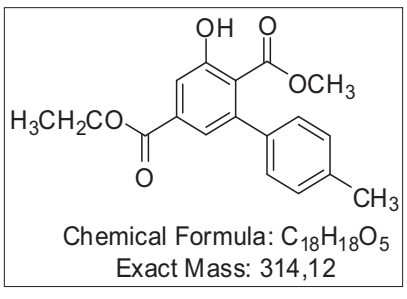
Starting with **117a** (0.439 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **118d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil, (0.245 g, 46%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.7 Hz, 3 H, CH_3), 1.30 (t, ^3J = 7.8 Hz, 3 H, CH_3), 1.35 - 1.40 (m, 2 H, CH_2), 1.49 - 1.57 (m, 2 H, CH_2), 2.87 (q, ^3J = 7.5Hz, 2 H, $PhCH_2$), 3.41 (s, 3 H, OCH_3), 4.28 (q, ^3J = 7.2Hz, 2 H, OCH_2), 7.07 (s, 1 H, CH_{Ar}), 7.13 - 7.17 (m, 2 H, CH_{Ar}), 7.24 - 7.30 (m, 3 H, CH_{Ar}), 10.81 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 13.02, 13.24 (CH_3), 22.10, 28.67, 30.93 (CH_2) 50.91 (OCH_3), 60.53 (OCH_2) 112.55 (C_{Ar}), 121.40, 125.93 (CH_{Ar}), 126.74 (2 CH_{Ar}), 127.14 (2 CH_{Ar}), 130.20, 134.46, 140.66, 141.28 (C_{Ar}), 158.75 (COH), 166.61, 170.42 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 3026 (w), 2954 (m), 2925 (m), 2856 (m), 1724 (s), 1666 (s), 1600 (m), 1555 (w), 1438 (m), 1391 (m), 1367 (m), 1345 (m), 1316 (m), 1290 (m), 1262 (s), 1232 (s), 1194 (s), 1156 (s), 1138 (m), 1092 (s), 1030 (m), 1007 (m), 964 (m), 921 (w), 911 (w), 887 (w), 846 (m), 814 (w), 760 (m), 699 (s), 653 (w), 631 (w), 583 (w). GC-MS (EI, 70 eV): *m/z* (%) = (356 ($[M]^+$, 38), 296 (13), 254 (10), 253 (41), 252 (20), 251 (100), 225 (10), 224 (17), 209 (13), 152 (14). HRMS (EI): Calcd. for $C_{21}H_{24}O_5$ ($[M]^+$): 356.16183; found: 356.162654.

5-Ethyl 2-methyl 3-hydroxy-4'-methylbiphenyl-2,5-dicarboxylate (118e):

Starting with **117b** (0.460 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **118e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.207 g, 44%).

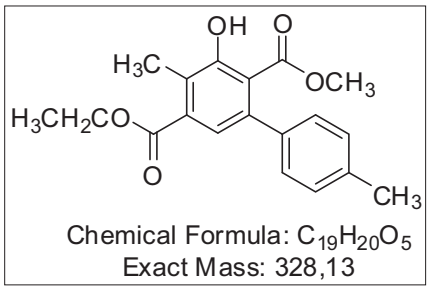


^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.33 (s, 3 H, $PhCH_3$), 3.46 (s, 3 H, OCH_3), 4.30 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 7.04 - 7.08 (m, 2 H, CH_{Ar}), 7.09 - 7.13 (m, 2 H, CH_{Ar}), 7.39 (d, ^4J = 1.6 Hz, 1 H, CH_{Ar}), 7.55 (d, ^4J = 1.7 Hz, 1 H, CH_{Ar}), 10.31 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 13.26, 20.10 (CH_3), 51.12 (OCH_3), 60.31 (OCH_2) 114.68 (C_{Ar}), 116.37, 122.02 (CH_{Ar}), 126.92 (2 CH_{Ar}), 127.50 (2 CH_{Ar}), 133.73, 136.00, 138.00, 144.07 (C_{Ar}), 159.84 (COH), 164.48, 169.92 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3305 (w), 2952 (w), 2870 (w), 1720 (s), 1669 (s), 1610 (w), 1567 (m), 1515 (w), 1492 (w), 1437 (m), 1402 (m), 1369 (m), 1343 (m), 1314 (m), 1236 (s), 1198 (s), 1112 (s), 1079

(m), 1022 (s), 976 (m), 949 (m), 892 (m), 863 (w), 831 (m), 806 (m), 770 (s), 726 (m), 707 (m), 649 (w), 625 (m), 614 (m), 583 (m), 558 (w). GC-MS (EI, 70 eV): *m/z* (%) = 314 ($[M]^+$, 37), 283 (24), 282 (100), 254 (10), 210 (12), 209 (10), 153 (14), 152 (10). HRMS (EI): Calcd. for $C_{18}H_{18}O_5$ ($[M]^+$): 314.11488; found: 314.114722.

5-Ethyl 2-methyl 3-hydroxy-4,4'-dimethylbiphenyl-2,5-dicarboxylate (118f):

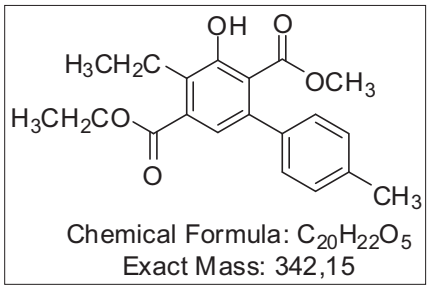
Starting with **117b** (0.460 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **118f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish oil, (0.227 g, 46%).



^{1}HNMR (300 MHz, $CDCl_3$): δ = 1.29 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.32(s, 3 H, $PhCH_3$), 2.40 (s, 3 H, $PhCH_3$), 3.45 (s, 3 H, OCH_3), 4.29 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 7.02 - 7.06 (m, 2 H, CH_{Ar}), 7.08 - 7.11 (m, 3 H, CH_{Ar}), 10.79 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 12.68, 14.24, 21.20 (CH_3), 51.96 (OCH_3), 61.32 (OCH_2) 113.47 (C_{Ar}), 122.51 (CH_{Ar}), 126.42 (C_{Ar}), 128.04 (2 CH_{Ar}), 128.43 (2 CH_{Ar}), 135.39, 136.63, 139.23, 141.50 (C_{Ar}), 159.77 (COH), 167.47, 171.75 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2951 (w), 2924 (w), 2854 (w), 1723 (s), 1664 (s), 1606 (w), 1561 (w), 1517 (w), 1436 (m), 1392 (m), 1367 (m), 1340 (m), 1312 (w), 1297 (w), 1261 (s), 1229 (s), 1194 (s), 1157 (s), 1137 (s), 1111 (m), 1048 (s), 1003 (m), 932 (w), 888 (w), 847 (m), 821 (m), 809 (m), 782 (m), 723 (m), 624 (w), 600 (w), 545 (w). GC-MS (EI, 70 eV): *m/z* (%) = 329 (12), (328 ($[M]^+$, 56), 297 (21), 296 (100), 283 (21), 281 (10), 268 (10), 267 (49), 253 (39), 240 (11), 224 (10), 223 (27), 196 (13), 195 (14), 165 (18), 152 (18). HRMS (EI): Calcd. for $C_{19}H_{20}O_5$ ($[M]^+$): 328.13053; found: 328.130451.

5-Ethyl 2-methyl 4-ethyl-3-hydroxy-4'-methylbiphenyl-2,5-dicarboxylate (118g):

Starting with **117b** (0.460 g, 1.5 mmol) and **22f** (0.476 g, 1.65 mmol), **118g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish oil, (0.236 g, 46%).

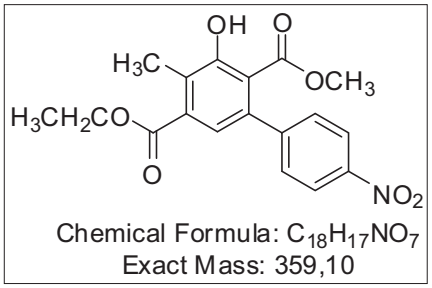


^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15 (t, ^3J = 7.6Hz, 3 H, CH_3), 1.30 (t, ^3J = 7.5 Hz, 3 H, CH_3), 2.32 (s, 3 H, $PhCH_3$), 2.87 (q, ^3J = 7.6Hz, 2 H, $PhCH_2$), 3.45 (s, 3 H, OCH_3), 4.29 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 7.01 - 7.11 (m, 5 H, $5CH_{Ar}$), 10.72 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 13.10, 13.22 (CH_3), 19.55 (CH_2), 20.17 (CH_3), 50.95 (OCH_3), 60.37 (OCH_2) 112.64 (C_{Ar}), 121.50 (CH_{Ar}), 127.00 (2 CH_{Ar}), 127.42 (2 CH_{Ar}), 131.04, 134.33, 135.63, 138.23, 140.71 (C_{Ar}), 158.56 (COH), 166.67, 170.58 (CO).

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3023 (w), 2971 (w), 2933 (w), 2874 (w), 1723 (s), 1664 (s), 1604 (m), 1555 (w), 1517 (w), 1437 (m), 1389 (m), 1367 (m), 1344 (m), 1312 (w), 1282 (m), 1247 (s), 1222 (s), 1193 (s), 1156 (s), 1137 (m), 1111 (w), 1075 (s), 1030 (m), 1007 (m), 967 (w), 949 (m), 908 (w), 888 (w), 846 (w), 823 (m), 784 (m), 723 (w), 709 (w), 670 (w), 654 (w), 627 (w), 598 (w), 567 (w). GC-MS (EI, 70 eV): *m/z* (%) = 343 (22), (342 ($[M]^+$, 98), 311 (23), 310 (100), 309 (16), 297 (31), 295 (30), 282 (25), 281 (49), 267 (38), 265 (10), 263 (26), 254 (13), 239 (14), 238 (28), 237 (32), 235 (10), 211 (33), 210 (37), 209 (18), 179 (10), 178 (12), 166 (16), 165 (38), 153 (10), 152 (14). HRMS (EI): Calcd. for $C_{20}H_{22}O_5$ ($[M]^+$): 342.14618; found: 342.146471.

5-Ethyl 2-methyl 3-hydroxy-4-methyl-4'-nitrobiphenyl-2,5-dicarboxylate (118h):

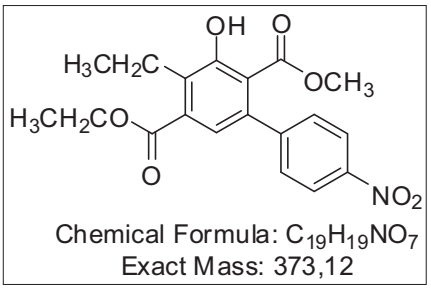
Starting with **117c** (0.506 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **118h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale yellowish solid, m.p. = 123-125, (0.356 g, 66%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.3 Hz, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 3.39 (s, 3 H, OCH_3), 4.25 (q, ^3J = 7.4 Hz, 2 H, OCH_2), 6.99 (s, 1 H, CH_{Ar}), 7.24 - 7.28 (m, 2 H, CH_{Ar}), 8.09 - 8.13 (m, 2 H, CH_{Ar}), 11.13 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 11.48, 12.85 (CH_3), 50.83 (OCH_3), 60.18 (OCH_2) 110.90 (C_{Ar}), 120.52 (CH_{Ar}), 121.58 ($2CH_{Ar}$), 127.12 (C_{Ar}) 127.71 (2 CH_{Ar}), 134.37, 137.57, 145.50, 147.74 (C_{Ar}), 159.35 (COH), 165.62, 169.25 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3115 (w), 3053 (w), 2988 (w), 2954 (m), 2906 (w), 2849 (w), 1730 (s), 1671 (s), 1594 (m), 1567 (w), 1513 (m), 1471 (w), 1435 (m), 1393 (m), 1377 (m), 1366 (m), 1342 (s), 1312 (m), 1194 (s), 1166 (s), 1137 (m), 1105 (m), 1050 (m), 1002 (s), 936 (m), 898 (w), 840 (s), 809 (s), 789 (s), 747 (s), 701 (s), 656 (w), 617 (w), 586 (m), 559 (m). GC-MS (EI, 70 eV): *m/z* (%) = (395 ([M]+, 44), 328 (21), 327 (100), 314 (18), 299 (11), 298 (38), 271 (18), 255 (17), 254 (9), 253 (10), 242 (22), 227 (13), 226 (15), 152 (17), 151 (12), 139 (10). HRMS (EI): Calcd. for $C_{18}H_{17}O_7N$ ($[M]^+$) : 359.09995; found: 359.100038

5-Ethyl 2-methyl 4-ethyl-3-hydroxy-4'-nitrobiphenyl-2,5-dicarboxylate (118i):

Starting with **117c** (0.506 g, 1.5 mmol) and **22f** (0.476 g, 1.65 mmol), **118i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.375 g, 67%), m.p. = 90-92 °C.

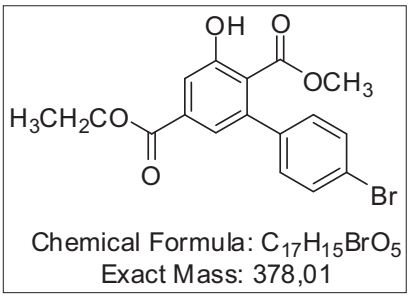


Chemical Formula: $C_{19}H_{19}NO_7$
Exact Mass: 373,12

^{1}HNMR (250 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.7 Hz, 3 H, CH_3), 1.31 (t, ^3J = 7.7 Hz, 3 H, CH_3), 2.90 (q, ^3J = 7.2 Hz, 2 H, $PhCH_2$), 3.45 (s, 3 H, OCH_3), 4.31 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 7.00 (s, 1 H, CH_{Ar}), 7.28 - 7.34 (m, 2 H, CH_{Ar}), 8.14 - 8.20 (m, 2 H, CH_{Ar}), 11.12 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 250 MHz): δ = 12.95, 13.19 (CH_3), 19.65 (CH_2), 51.34 (OCH_3), 60.70 (OCH_2) 111.80 (C_{Ar}), 121.16 (CH_{Ar}), 122.12 (2 CH_{Ar}), 128.36 (2 CH_{Ar}), 133.16, 134.60, 138.44, 146.11, 148.27 (C_{Ar}), 159.79 (COH), 166.27, 169.63 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 3049 (w), 2963 (m), 2930 (m), 2871 (m), 2852 (m), 2450 (w), 2357 (w), 2123 (w), 2123 (w), 1935 (w), 1804 (w), 1730 (s), 1669 (s), 1594 (m), 1562 (m), 1504 (s), 1446 (m), 1412 (m), 1390 (m), 1345 (s), 1315 (m), 1290 (m), 1257 (s), 1227 (s), 1195 (s), 1153 (s), 1135 (s), 1106 (s), 1074 (s), 1062 (s), 1027 (m), 1008 (m), 970 (m), 944 (s), 897 (m), 852 (s), 913 (m), 776 (s), 749 (s), 702 (s), 672 (m), 644 (w), 622 (m), 588 (m), 573 (m). GC-MS (EI, 70 eV): *m/z* (%) = 374 (22), (373 ($[M]^+$, 100), 342 (20), 341 (84), 328 (38), 314 (14), 313 (74), 312 (57), 298 (16), 296 (13), 295 (10), 285 (10), 270 (23), 269 (60), 268 (13), 267 (12), 243 (10), 242 (68), 241 (38), 240 (22), 239 (13), 223 (12), 222 (14), 221 (51), 220 (10), 194 (11), 193 (10), 166 (10), 165 (42), 164 (13), 163 (12), 152 (15), 151 (10), 139 (15). HRMS (EI): Calcd. for $C_{19}H_{19}O_7N$ ($[M]^+$): 373.11560; found: 373.115597.

5-Ethyl 2-methyl 4'-bromo-3-hydroxybiphenyl-2,5-dicarboxylate (118j):

Starting with **117d** (0.557 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **118j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale brownish oil (0.301 g, 53%).



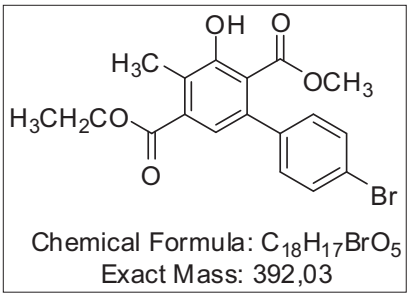
Chemical Formula: $C_{17}H_{15}BrO_5$
Exact Mass: 378,01

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.0 Hz, 3 H, CH_3), 3.43(s, 3 H, OCH_3), 4.25 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 6.97 - 7.01 (m, 2 H, CH_{Ar}), 7.28 (d, ^4J = 1.7 Hz, 1 H, CH_{Ar}), 7.36 - 7.41 (m, 2 H, CH_{Ar}), 7.54 (d, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 10.47 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.2 (CH_3), 52.2 (OCH_3), 61.6 (OCH_2), 115.1 (C_{Ar}), 118.2 (CH_{Ar}), 121.4 (C_{Ar}), 122.7 (CH_{Ar}), 129.8 (2 CH_{Ar}), 130.9 (2 CH_{Ar}), 135.0, 140.9, 143.6, (C_{Ar}),

161.3 (COH), 165.2, 170.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 2980 (w), 2953 (w), 2905 (w), 2872 (w), 2852 (w), 1721 (m), 1672 (m), 1611 (m), 1571 (m), 1493 (m), 1439 (m), 1392 (m), 1345 (m), 1238 (s), 1200 (s), 1114 (s), 1069 (m), 1023 (m), 1010 (m), 948 (m), 881 (m), 835 (m), 807 (m), 770 (m), 681 (m), 622 (m), 574 (m). GC-MS (EI, 70 eV): *m/z* (%) = 378 ([M^+], ^{79}Br, 28), 349 (18), 348 (100), 276 (7), 194 (16), 139 (14). HRMS (EI, 70 eV): Calcd. for $C_{17}H_{15}O_5Br$ ([M]$^+$, ^{79}Br): 378.00974; found: 378.009529.

5-Ethyl 2-methyl 4'-bromo-3-hydroxy-4-methylbiphenyl-2,5-dicarboxylate (118k):

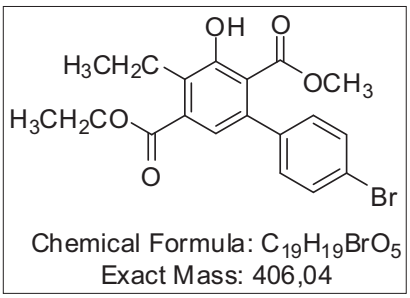
Starting with **117d** (0.557 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **118k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale brownish oil, (0.323g, 55%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.40 (s, 3 H, $PhCH_3$), 3.47(s, 3 H, OCH_3), 4.30 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 7.00 - 7.05 (m, 3 H, CH_{Ar}), 7.40 - 7.44 (m, 2 H, CH_{Ar}), 10.99 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.7, 13.2 (CH_3), 51.1 (OCH_3), 60.4 (OCH_2), 111.9, 120.1 (C_{Ar}), 121.2 (CH_{Ar}), 126.3 (C_{Ar}), 128.8 (2 CH_{Ar}), 129.8 (2 CH_{Ar}), 134.6, 139.2, 140.2 (C_{Ar}), 159.3 (COH), 166.3, 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3046 (w), 2979 (w), 2952 (w), 2904 (w), 2873 (w), 1722 (m), 1665 (m), 1607 (m), 1567 (w), 1492 (w), 1437 (m), 1390 (m), 1367 (m), 1342 (m), 1305 (m), 1261 (s), 1230 (s), 1194 (s), 1157 (s), 1137 (m), 1071 (m), 1048 (s), 1009 (s), 933 (m), 918 (m), 889 (w), 828 (m), 782 (m), 742 (m), 724 (m), 665 (m), 618 (w), 588 (m), 557 (w). GC-MS (EI, 70 eV): *m/z* (%) = 392 ([M^+], ^{79}Br, 47), 360 (100), 333 (30), 304 (15), 253 (55), 196 (12), 180 (9), 152 (38), 139 (10), 104 (8), 76 (11). HRMS (EI): Calcd. for $C_{18}H_{17}O_5Br$ ([M]$^+$, ^{79}Br): 392.02539; found: 392.025473.

5-Ethyl 2-methyl 4'-bromo-4-ethyl-3-hydroxybiphenyl-2,5-dicarboxylate (118l):

Starting with **117d** (0.557 g, 1.5 mmol) and **22f** (0.476 g, 1.65 mmol), **118l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a pale brownish oil (0.359 g, 59%).

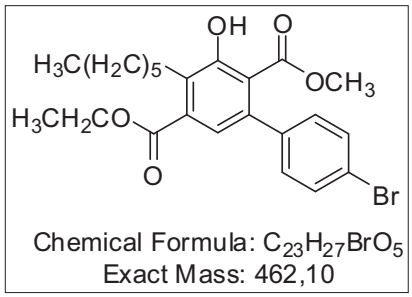


^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.31 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.88 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.47(s, 3 H, OCH_3), 4.30 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 7.01 - 7.05 (m, 3 H, CH_{Ar}), 7.40 - 7.44 (m, 2 H, CH_{Ar}), 10.94 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 13.2 (CH_3), 19.6 (CH_2), 51.1 (OCH_3), 60.4 (OCH_2),

112.1, 120.1 (C_{Ar}), 121.2 (CH_{Ar}), 128.8 (2 CH_{Ar}), 129.8 (2 CH_{Ar}), 131.8, 134.5, 139.4, 140.2 (C_{Ar}), 159.0 (COH), 166.4, 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2972 (w), 2954 (w), 2935 (w), 2875 (w), 2854 (w), 1723 (m), 1665 (m), 1605 (m), 1567 (w), 1490 (w), 1437 (m), 1387 (m), 1368 (m), 1347 (m), 1309 (m), 1282 (m), 1248 (s), 1222 (s), 1194 (m), 1158 (s), 1075 (s), 1029 (m), 1009 (m), 967 (m), 948 (m), 890 (w), 830 (m), 784 (m), 734 (m), 721 (m), 665 (m), 620 (w), 587 (m), 560 (w). GC-MS (EI, 70 eV): *m/z* (%) = 406 ([M^+], ^{79}Br, 92), 376 (98), 348 (32), 331 (16), 302 (34), 275 (50), 249 (17), 221 (89), 194 (21), 165 (72), 152 (24), 128 (7), 82 (11). HRMS (EI): Calcd. for $C_{19}H_{19}O_5Br$ ([$M]^+$, ^{79}Br): 406.04104; found: 406.041136.

5-Ethyl 2-methyl 4'-bromo-4-hexyl-3-hydroxybiphenyl-2,5-dicarboxylate (118m):

Starting with **117d** (0.557 g, 1.5 mmol) and **22j** (0.569 g, 1.65 mmol), **118m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a brownish oil (0.347 g, 50%).

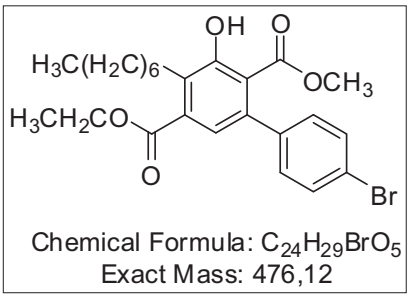


Chemical Formula: $C_{23}H_{27}BrO_5$
Exact Mass: 462,10

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67-0.75 (m, 6 H, 2CH_3), 1.16 – 1.20 (m, 6 H, 3CH_2), 1.40 – 1.46 (m, 2 H, CH_2), 2.74 (t, ^3J = 7.7 Hz, 2 H, CH_2), 3.36 (s, 3 H, OCH_3), 4.19 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 6.90 – 6.94 (m, 3 H, CH_{Ar}), 7.29 - 7.34 (m, 2 H, CH_{Ar}), 10.83 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.3, 15.5 (CH_3), 23.9, 28.2, 31.0, 32.8, 32.9, (CH_2), 53.3 (OCH_3), 62.6 (OCH_2), 114.2, 122.3 (C_{Ar}), 123.4 (CH_{Ar}), 131.0 (2 CH_{Ar}), 132.0 (2 CH_{Ar}), 133.0, 136.8, 141.5, 142.4 (C_{Ar}), 161.3 (COH), 168.7, 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2926 (m), 2855 (w), 1934 (w), 1725 (m), 1667 (m), 1605 (w), 1566 (w), 1554 (w), 1492 (w), 1437 (m), 1388 (m), 1368 (m), 1347 (m), 1313 (w), 1248 (m), 1231 (m), 1195 (m), 1155 (m), 1099 (m), 1071 (m), 1010 (m), 953 (m), 920 (w), 843 (m), 785 (m), 720 (m), 673 (w), 663 (w), 628 (w), 588 (w). GC-MS (EI, 70 eV): *m/z* (%) = 462 ([M^+], ^{79}Br, 42), 419 (10), 357 (100), 331 (42), 302 (13), 278 (17), 253 (26), 196 (19), 152 (17). HRMS (EI): Calcd. for $C_{23}H_{27}O_5Br$ ([$M]^+$, ^{79}Br): 462.10364; found: 462.104001.

5-Ethyl 2-methyl 4'-bromo-4-heptyl-3-hydroxybiphenyl-2,5-dicarboxylate (118n):

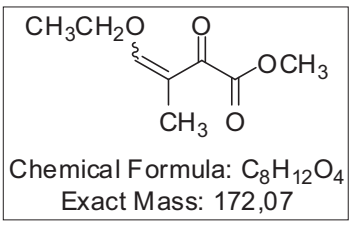
Starting with **117d** (0.557 g, 1.5 mmol) and **22k** (0.592 g, 1.65 mmol), **13n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a brownish oil, (0.357 g, 50%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78-0.83 (m, 6 H, $2CH_3$), 1.28 – 1.33 (m, 8 H, $4CH_2$), 1.35 – 1.39 (m, 2 H, CH_2), 2.84 (t, ^{3}J = 7.4 Hz, 2 H, CH_2), 3.47(s, 3 H, OCH_3), 4.29 (q, ^{3}J = 7.1 Hz, 2 H, OCH_2), 7.00 - 7.04 (m, 3 H, CH_{Ar}), 7.40 - 7.44 (m, 2 H, CH_{Ar}), 10.93 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.1, 13.2 (CH_3), 21.6, 26.3, 28.1, 28.7, 30.3, 30.8 (CH_2), 51.7 (OCH_3), 60.4 (OCH_2), 112.0, 120.1 (C_{Ar}), 121.2 (CH_{Ar}), 128.8 (2 CH_{Ar}), 129.8 (2 CH_{Ar}), 130.7, 134.6, 139.3, 140.2 (C_{Ar}), 159.1 (COH), 166.7, 170.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2972 (w), 2954 (w), 2935 (w), 2875 (w), 2854 (w), 1723 (m), 1665 (m), 1605 (m), 1567 (w), 1490 (w), 1437 (m), 1387 (m), 1368 (m), 1347 (m), 1309 (m), 1282 (m), 1248 (s), 1222 (s), 1194 (m), 1158 (s), 1075 (s), 1029 (m), 1009 (m), 967 (m), 948 (m), 890 (w), 830 (m), 784 (m), 734 (m), 721 (m), 665 (m), 620 (w), 587 (m), 560 (w). GC-MS (EI, 70 eV): *m/z* (%) = 476 ([M^+], ^{79}Br, 30), 416 (7), 373 (100), 333 (30), 292 (18), 253 (17), 196 (11), 152 (9). HRMS (EI): Calcd. for $C_{24}H_{29}O_5Br$ ([$M]^+$, ^{79}Br): 476.11929; found: 476.119450.

Methyl 4-ethoxy-3-methyl-2-oxobut-3-butenoate (125b):

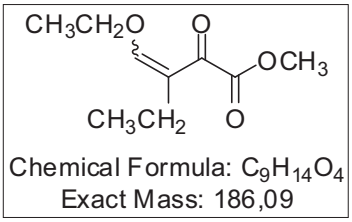
Starting with **123b** (11.75 mL, 106.1 mmol) and methyl chlorooxoacetate (4.89 mL, 53.1 mmol), the product was collected after drying under vacuum as a reddish oil (8.86 g, 97%).



^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33 (t, ^{3}J = 7.1 Hz, 3 H, OCH_2CH_3), 1.70 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 4.14 (q, ^{3}J= 7.1 Hz, 2 H, OCH_2CH_3), 7.54 (s, 1 H, CH_{olf}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 7.4, 15.2 (CH_3), 52.4 (OCH_3), 71.3 (OCH_2), 114.7 (C), 164.6 (CO), 165.7 (CH_{olf}), 185.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2985 (w), 2956 (w), 2903 (w), 2254 (w), 2254 (w), 1731 (m), 1617 (s), 1476 (w), 1437 (w), 1388 (w), 1369 (w), 1330 (w), 1210 (s), 1146 (m), 1108 (m), 1049 (m), 1025 (m), 971 (m), 910 (m), 845 (w), 824 (w), 779 (w), 726 (s), 647 (w). GC-MS (EI, 70 eV): *m/z* (%) = 172 ([M^+], 3), 144 (1), 113 (82), 85 (100), 83 (5), 55 (5), 39 (4), 29 (20). HRMS (EI): Calcd. for $C_8H_{12}O_4$ ([$M]^+$):172.07301; found: 172.073090

Methyl 3-(ethoxymethylene)-2-oxopentanoate (125c):

Starting with **123c** (13.64 mL, 106.1 mmol) and methyl chlorooxoacetate (4.89 mL, 53.1 mmol), the product was collected after drying under vacuum as a redish oil (9.38 g, 95%).

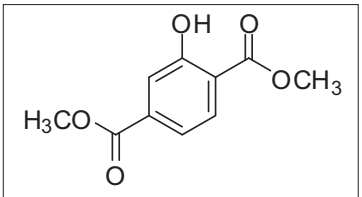


Chemical Formula: $C_9H_{14}O_4$
Exact Mass: 186,09

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.31 (t, ^3J= 7.1 Hz, 3 H, OCH_2CH_3), 2.24 (q, ^3J= 7.5 Hz, 2 H, CH_2CH_3), 3.79 (s, 3 H, OCH_3), 4.12 (q, ^3J= 7.5 Hz, 2 H, OCH_2CH_3), 7.46 (s, 1 H, CH_{olf}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.6, 15.0 (CH_3), 16.0 (CH_2), 52.3 (OCH_3), 71.1 (OCH_2), 120.7 (C), 164.5 (CO), 165.7 (CH_{olf}), 185.3 (CO). IR neat, cm^{-1}): $\tilde{\nu}$ = 2970 (w), 2937 (w), 2878 (w), 1731 (m), 1652 (w), 1615 (s), 1456 (w), 1439 (w), 1388 (w), 1370 (w), 1321 (m), 1301 (m), 1273 (m), 1207 (s), 1146 (m), 1108 (m), 1083 (s), 1021 (m), 965 (m), 898 (m), 871 (m), 798 (w), 777 (w), 732 (m), 706 (m), 648 (w), 547 (w). GC-MS (EI, 70 eV): *m/z* (%) = 186 ([M^+], 4), 127 (100), 99 (90), 83 (4), 69 (4), 53 (7), 43 (10), 29 (6). HRMS (ESI): Calcd. for $C_9H_{15}O_4$ ([M+H]$^+$): 187.09649; found: 187.09595

Dimethyl 2-hydroxyterephthalate (126a):

Starting with **125a** (0.237 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **126a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.127 g, 40%) m.p. 88-91 °C.

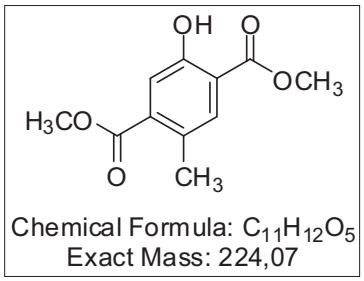


Chemical Formula: $C_{10}H_{10}O_5$
Exact Mass: 210,05

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.45 (dd, ^3J = 8.1 Hz, ^4J = 1.6 Hz,1 H, CH_{Ar}), 7.56 - 7.57 (m, 1 H, CH_{Ar}), 7.83 (d, ^3J = 8.4 Hz, 1 H, CH_{Ar}), 10.67 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.4, 51.6 (OCH_3), 114.6 (C_{Ar}), 117.9, 118.6, 129.0 (CH_{Ar}), 135.4 (C_{Ar}), 160.3 (COH), 164.9, 168.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3115 (w), 3079 (w), 2959 (w), 2916 (m), 2848 (m), 1725 (m), 1678 (s), 1579 (m), 1504 (m), 1435 (m), 1393 (w), 1343 (m), 1297 (s), 1209 (s), 1104 (s), 980 (m), 953 (m), 923 (m), 845 (w), 823 (m), 795 (m), 750 (s), 706 (m), 690 (s), 570 (m), 564 (m). GC-MS (EI, 70 eV): *m/z* (%) = 210 ([$M]^+$, 42), 178 (100), 147 (10), 120 (10), 119 (63), 63 (12). HRMS (EI): Calcd. for $C_{10}H_{10}O_5$ ([$M]^+$): 210.05227; found: 210.052499.

Dimethyl 2-hydroxy-5-methylterephthalate (126b):

Starting with **125b** (0.258 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **126b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.150 g, 45%).

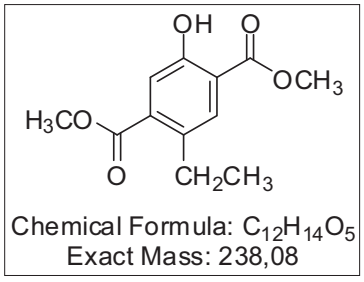


Chemical Formula: $C_{11}H_{12}O_5$
Exact Mass: 224,07

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, $PhCH_3$), 3.83 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 7.41 (s, 1 H, CH_{Ar}), 7.62 (s, 1 H, CH_{Ar}), 10.37 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.3 (CH_3), 51.1, 51.5 (OCH_3), 113.7 (C_{Ar}), 118.4 (CH_{Ar}), 128.5 (C_{Ar}), 131.2 (CH_{Ar}), 139.3 (C_{Ar}), 157.0 (COH), 166.0, 168.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3112 (w), 2956 (w), 2922 (m), 2852 (w), 1723 (m), 1682 (m), 1619 (w), 1572 (w), 1388 (w), 1435 (m), 1387 (w), 1368 (w), 1287 (m), 1249 (m), 1205 (m), 1192 (m), 1102 (s), 1046 (m), 1016 (m), 958 (m), 910 (w), 888 (w), 849 (w), 784 (s), 740 (m), 676 (m), 603 (w), 578 (w). GC-MS (EI, 70 eV): *m/z* (%) = 224 ($[M]^+$, 46), 193 (39), 192 (100), 133 (24), 132 (32), 77 (10), 51 (9). HRMS (EI): Calcd. for $C_{11}H_{12}O_5$ ($[M]^+$): 224.06792; found: 224.067938.

Dimethyl 5-ethyl-2-hydroxyterephthalate (126c):

Starting with **125c** (0.279 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **126c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.168 g, 47%).

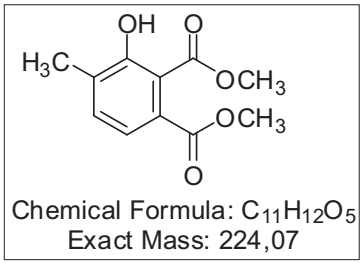


Chemical Formula: $C_{12}H_{14}O_5$
Exact Mass: 238,08

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.79 (q, ^3J = 8.4 Hz, 2 H, $PhCH_2$), 3.83 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.34 (s, 1 H, CH_{Ar}), 7.65 (s, 1 H, CH_{Ar}), 10.39 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8 (CH_3), 25.6 (CH_2), 51.1, 51.5 (OCH_3), 113.7 (C_{Ar}), 118.3, 129.9 (CH_{Ar}), 134.4, 135.2 (C_{Ar}), 157.9 (COH), 168.8, 168.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3205 (w), 2957 (w), 2929 (w), 2872 (w), 1729 (m), 1682 (m), 1636 (w), 1572 (w), 1487 (m), 1439 (m), 1375 (w), 1319 (w), 1281 (m), 1203 (s), 1103 (s), 1066 (m), 961 (m), 908 (w), 844 (w), 794 (m), 759 (m), 697 (m), 647 (w), 622 (w). GC-MS (EI, 70 eV): *m/z* (%) = 238 ($[M]^+$, 45), 223 (9), 206 (100), 191 (56), 174 (11), 146 (27), 133 (8), 119 (7), 91 (11), 65 (6). HRMS (EI): Calcd. for $C_{12}H_{14}O_5$ ($[M]^+$): 238.08358; found: 238.083603.

Dimethyl 3-hydroxy-4-methylphthalate (127a):

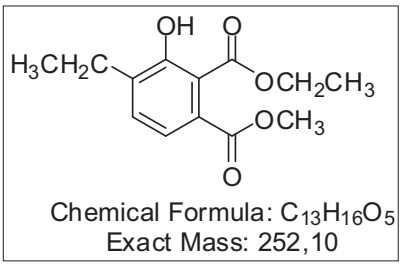
Starting with **125a** (0.237 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **127a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.141 g, 42%), m.p. 76 - 78 °C.



^{1}HNMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, $PhCH_3$), 3.83 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 7.17 (d, ^{3}J = 7.6 Hz, 1 H, CH_{Ar}), 7.64 (d, ^{3}J = 8.3 Hz, 1 H, CH_{Ar}), 11.11 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.45 (CH_3), 51.2, 51.5 (OCH_3), 112.4 (C_{Ar}), 118.3, 125.6 (CH_{Ar}), 126.9, 136.2 (C_{Ar}), 159.3 (COH), 166.4, 169.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3152 (w), 2954 (w), 2924 (m), 2852 (w), 1724 (m), 1674 (m), 1616 (w), 1573 (w), 1439 (m), 1380 (w), 1327 (m), 1285 (m), 1249 (s), 1191 (m), 1148 (s), 1098 (m), 1050 (s), 1006 (m), 966 (w), 910 (w), 869 (w), 821 (w), 803 (m), 755 (s), 728 (m), 644 (w), 578 (w). GC-MS (EI, 70 eV): *m/z* (%) = 224 ($[M]^+$, 40), 193 (29), 192 (47), 165 (10), 164 (100), 133(13), 105 (14), 77 (12), 51 (10). HRMS (EI): Calcd. for $C_{11}H_{12}O_5$ ($[M]^+$): 224.06792; found: 224.068299.

2-Ethyl 1-methyl 4-ethyl-3-hydroxyphthalate (127b):

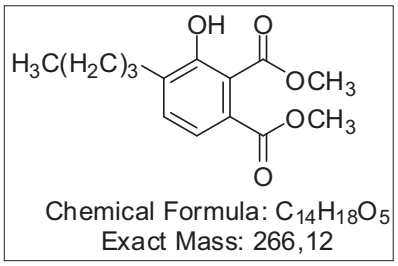
Starting with **125a** (0.237 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **127b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.170 g, 45%).



^{1}HNMR (300 MHz, $CDCl_3$): δ = 0.78 (t, ^{3}J = 7.5 Hz, 3 H, CH_2CH_3), 1.18 (t, ^{3}J = 7.2 Hz, 3 H, OCH_2CH_3), 2.84 (q, ^{3}J = 8.4 Hz, 2 H, $PhCH_2$), 3.84 (s, 3 H, OCH_3), 4.33 (q, ^{3}J = 7.8 Hz, 2 H, OCH_2CH_3), 7.11 (d, ^{3}J = 8.4 Hz, 1 H, CH_{Ar}), 7.65 (d, ^{3}J = 8.0 Hz, 1 H, CH_{Ar}), 11.18 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 13.1 (CH_3), 19.3 (CH_2), 51.2 (OCH_3), 60.7 (OCH_2), 112.8 (C_{Ar}), 118.1, 125.7 (CH_{Ar}), 132.4 (C_{Ar}), 135.9 (C_{Ar}), 159.2 (COH), 166.7, 169.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3133 (w), 2956 (w), 2923 (m), 2853 (w), 1727 (m), 1673 (m), 1615 (w), 1572 (w), 1461 (m), 1398 (w), 1372 (m), 1330 (m), 1291 (s), 1267 (m), 1240 (s), 1222 (m), 1148 (s), 1077 (s), 1018 (m), 952 (w), 864 (w), 806 (m), 757 (s), 732 (m), 644 (w), 577 (w). GC-MS (EI, 70 eV): *m/z* (%) = 252 ($[M]^+$, 30), 221 (11), 207 (10), 206 (10), 191 (11), 179 (12), 178 (100), 146 (28), 91 (11). HRMS (EI): Calcd. for $C_{13}H_{16}O_5$ ($[M]^+$): 252.09923; found: 252.098543.

Dimethyl 4-butyl-3-hydroxyphthalate (127c):

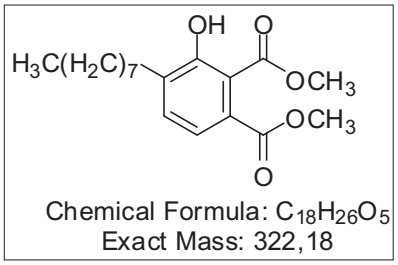
Starting with **125a** (0.237 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **127c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.171 g, 43%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, ^{3}J = 6.8 Hz, 3 H, CH_3), 1.30 - 1.32 (m, 2 H, CH_2), 1.46 - 1.48 (m, 2 H, CH_2), 2.83 (t, ^{3}J = 7.7 Hz, 2 H, $PhCH_2$), 3.83 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 7.11 (d, ^{3}J = 8.2 Hz, 1 H, CH_{Ar}), 7.64 (d, ^{3}J = 8.0 Hz, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.9 (CH_3), 22.0, 29.3, 30.9 (CH_2), 51.2, 51.5 (OCH_3), 112.5 (C_{Ar}), 118.1, 125.7 (CH_{Ar}), 131.3 (C_{Ar}), 136.2 (C_{Ar}), 159.2 (COH), 166.7, 169.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3152 (w), 2954 (m), 2924 (m), 2854 (m), 1727 (m), 1677 (m), 1616 (w), 1572 (w), 1440 (m), 1366 (w), 1335 (m), 1296 (m), 1252 (s), 1199 (m), 1149 (s), 1093 (s), 1025 (m), 958 (w), 841 (m), 806 (m), 758 (s), 722 (m), 659 (w), 578 (w). GC-MS (EI, 70 eV): *m/z* (%) = 266 ($[M]^+$, 60), 235 (33), 233 (12), 224 (17), 223 (36), 207 (41), 206 (56), 205 (23), 192 (24), 191 (100), 176 (12), 175 (81), 174 (23), 173 (11), 164 (52), 145 (11), 133 (20), 131 (10), 105 (13), 104 (12), 77 (15). HRMS (EI): Calcd. for $C_{14}H_{18}O_5$ ($[M]^+$): 266.11488; found: 266.114803.

Dimethyl 3-hydroxy-4-octylphthalate (127d):

Starting with **125a** (0.237 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **127d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.217 g, 45%).

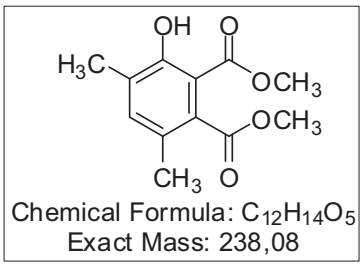


^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^{3}J = 6.9 Hz, 3 H, CH_3), 1.30 - 1.37 (m, 10 H, 5 CH_2), 1.48 - 1.54 (m, 2 H, CH_2), 2.81 (t, ^{3}J = 7.8 Hz, 2 H, $PhCH_2$), 3.83 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 7.11 (d, ^{3}J = 8.2 Hz, 1 H, CH_{Ar}), 7.64 (d, ^{3}J = 8.5 Hz, 1 H, CH_{Ar}), 11.08 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0 (CH_3), 21.6, 26.2, 28.2, 28.3, 28.6, 30.8, 30.8 (CH_2), 51.2, 51.6 (OCH_3), 112.5 (C_{Ar}), 118.3, 125.7 (CH_{Ar}), 131.3, 136.2 (C_{Ar}), 159.2 (COH), 166.6, 169.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 2922 (s), 2853 (m), 1727 (m), 1678 (m), 1619 (w), 1441 (m), 1376 (w), 1336 (w), 1291 (m), 1254 (m), 1229 (s), 1193 (m), 1148 (m), 1101 (m), 1026 (m), 841 (m), 803 (m), 759 (m), 721 (m), 660 (w), 578 (w). GC-MS (EI, 70 eV): *m/z* (%) = 322 ($[M]^+$, 53), 291 (27), 289 (16), 264 (16), 263 (85), 247 (22), 232 (17), 231 (97), 224 (28), 223 (45), 205 (27), 192 (41), 191 (100), 178 (14), 177 (14), 173 (12), 165 (10), 164

(42), 160 (10), 133 (16), 105 (10), 77 (10), 41 (12). HRMS (EI): Calcd. for $C_{18}H_{26}O_5$ ($[M]^+$): 322.17748; found: 322.177861.

Dimethyl 3-hydroxy-4,6-dimethylphthalate (127e):

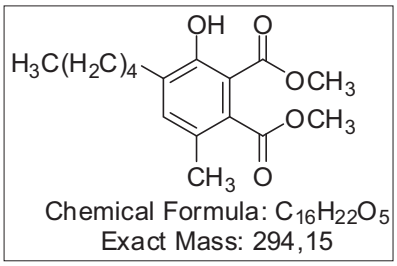
Starting with **125b** (0.258 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **127e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless solid (0.160 g, 45%), m.p. 53-54.



^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, $PhCH_3$), 2.14 (s, 3 H, $PhCH_3$), 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 7.46 (s, 1 H, CH_{Ar}), 10.86 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.6, 17.6 (CH_3), 51.1, 51.4 (OCH_3), 110.8 (C_{Ar}), 122.6, 123.1 (C_{Ar}), 127.1 (CH_{Ar}), 139.6 (C_{Ar}), 157.0 (COH), 168.4, 169.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2953 (m), 2922 (s), 2852 (m), 1735 (m), 1677 (m), 1618 (w), 1440 (m), 1378 (w), 1343 (m), 1283 (m), 1259 (m), 1233 (s), 1204 (m), 1146 (s), 1094 (m), 1052 (m), 1020 (m), 840 (w), 795 (s), 755 (m), 722 (m), 610 (w), 563 (w). GC-MS (EI, 70 eV): *m/z* (%) = 238 ($[M]^+$, 45), 207 (38), 206 (65), 179 (12), 178 (100), 147 (12), 91 (11). HRMS (EI): Calcd. for $C_{12}H_{14}O_5$ ($[M]^+$): 238.08358; found: 238.0833769.

Dimethyl 3-hydroxy-6-methyl-4-pentylphthalate (127f):

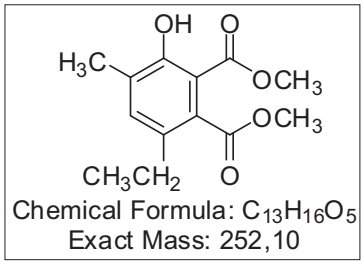
Starting with **125b** (0.258 g, 1.5 mmol) and **22i** (0.546 g, 1.65 mmol), **127f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.203 g, 46%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^3J = 6.6 Hz, 3 H, CH_3), 1.23 - 1.29 (m, 4 H, $2CH_2$), 1.47 - 1.57 (m, 2 H, CH_2), 2.12 (s, 3 H, $PhCH_3$), 2.54 (t, ^3J = 7.7 Hz, 2 H, $PhCH_2$), 3.81 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 7.08 (s, 1 H, CH_{Ar}), 10.92 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.0, 17.4 (CH_3), 21.6, 27.7, 28.8, 30.6 (CH_2), 50.8, 51.9 (OCH_3), 107.8, 124.1, 130.9, 131.8 (C_{Ar}), 136.2 (CH_{Ar}), 157.1 (COH), 168.8, 168.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2928 (w), 2859 (w), 1735 (m), 1672 (m), 1610 (w), 1587 (w), 1433 (s), 1342 (m), 1253 (s), 1207 (s), 1179 (m), 1160 (m), 1097 (w), 1049 (m), 992 (w), 962 (w), 898 (w), 869 (w), 846 (w), 801 (m), 744 (m), 650 (w), 529 (w). GC-MS (EI, 70 eV): *m/z* (%) = 294 ($[M]^+$, 24), 263 (20), 247 (19), 219 (31), 206 (100), 148 (8), 91 (5). HRMS (ESI): Calcd. for $C_{16}H_{23}O_5$ ($[M+H]^+$): 295.154 ; found: 295.1532.

Dimethyl 6-ethyl-3-hydroxy-4-methylphthalate (127g):

Starting with **125c** (0.279 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **127g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish oil (0.181 g, 48%).

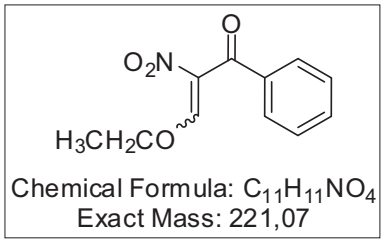


Chemical Formula: $C_{13}H_{16}O_5$
Exact Mass: 252,10

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, ^3J = 7.5 Hz, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 2.40 (q, ^3J = 7.7 Hz, 2 H, $PhCH_2$), 3.81 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 7.13 (s, 1 H, CH_{Ar}), 10.98 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.8, 14.9 (CH_3), 24.9 (CH_2), 51.2, 51.8 (OCH_3), 107.1, 127.6, 130.3, 130.4 (C_{Ar}), 135.7 (CH_{Ar}), 157.3 (COH), 168.6, 168.9 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3116 (w), 2953 (w), 2875 (w), 1732 (s), 1672 (s), 1612 (w), 1588 (w), 1431 (m), 1378 (m), 1351 (m), 1277 (s), 1255 (m), 1204 (s), 1177 (s), 1160 (s), 1046 (m), 988 (m), 895 (m), 867 (w), 805 (m), 789 (m), 734 (m), 639 (m), 563 (m). GC-MS (EI, 70 eV): *m/z* (%) = 252 ($[M]^+$, 30), 220 (100), 205 (16), 188 (18), 162 (40), 134 (27), 103 (10), 91 (8), 77 (13). HRMS (EI): Calcd. for $C_{13}H_{16}O_5$ ($[M]^+$): 252.09923; found: 252.099036.

3-Ethoxy-2-nitro-1-phenylprop-2-en-1-one (131a):

Starting with **130a** (1.7 g, 10.0 mmol), triethyl orthoformiate (2.0 ml, 12.0 mmol) and acetic anhydride (1.9 ml, 20 mmol), **131a** was isolated as a redish viscos oil (1.8 g, 81%).

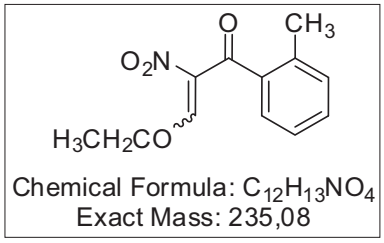


Chemical Formula: $C_{11}H_{11}NO_4$
Exact Mass: 221,07

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.0 Hz, 3 H, OCH_2CH_3), 4.20 (q, ^3J= 6.9 Hz, 2 H, OCH_2CH_3), 7.37 - 7.42 (m, 3 H, CH_{Ar}), 7.76 - 7.79 (m, 2 H, CH_{Ar}), 8.28 (s, 1 H, CH_{olf}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 74.2 (OCH_2), 128.1 (C), 128.8 (2 CH_{Ar}), 129.0 (2 CH_{Ar}), 134.1 (CH_{Ar}), 135.9 (C_{Ar}), 164.1 (CH_{olf}), 185.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2935 (w), 1778 (w), 1674 (m), 1597 (w), 1562 (w), 1535 (m), 1500 (m), 1449 (w), 1338 (w), 1300 (m), 1222 (m), 1153 (w), 1124 (w), 1001 (w), 908 (m), 873 (w), 728 (s), 689 (m), 648 (w). MS (EI 70 eV): *m/z* (%) = 221 ($[M]^+$, 8), 128 (12), 105 (100), 100 (41), 94 (16), 7 (70), 72 (17), 51 (19), 29 (11). HRMS (EI): Calcd. for $C_{11}H_{11}NO_4$: 221.06826; found: 221.068910.

3-Ethoxy-2-nitro-1-o-tolylprop-2-en-1-one (131b):

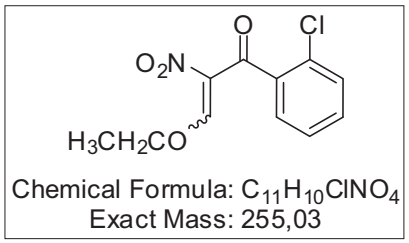
Starting with **130b** (1.8 g, 10.0 mmol), triethyl orthoformiate (2.0 ml, 12.0 mmol) and acetic anhydride (1.9 ml, 20 mmol), **131b** was isolated as a red oil (1.9 g, 81%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, ^{3}J = 7.1 Hz, 3 H, $OCH_2\mathit{CH_3}$), 2.33 (s, 3 H, CH_3), 4.20 (q, ^{3}J = 7.0 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.15 - 7.18 (m, 2 H, CH_{Ar}), 7.31 - 7.39 (m, 2 H, CH_{Ar}), 8.23 (s, 1 H, CH_{olf}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 20.8 (CH_3), 74.3 (OCH_2), 121.8 (C), 125.7, 127.0, 131.0, 133.0 (CH_{Ar}), 136.9, 139.6 (C_{Ar}), 161.6 (CH_{olf}), 187.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 2927 (w), 1698 (m), 1634 (m), 1561 (m), 1532 (m), 1456 (m), 1367 (m), 1300 (m), 1219 (s), 1163 (m), 1094 (m), 1002 (m), 909 (m), 873 (m), 839 (w), 796 (w), 731 (s), 696 (w), 649 (m). HRMS (EI): Calcd. for $C_{12}H_{13}NO_4$: 235.08456; found: 235.084510.

1-(2-Chlorophenyl)-3-ethoxy-2-nitroprop-2-en-1-one (131c):

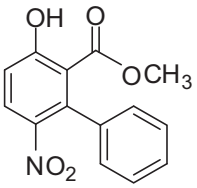
Starting with **130c** (2.0 g, 10.0 mmol), triethyl orthoformate (2.0 ml, 12.0 mmol) and acetic anhydride (1.9 ml, 20 mmol), **131c** was isolated as a redish viscos oil (2.1 g, 82%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, ^{3}J = 7.0 Hz, 3 H, $OCH_2\mathit{CH_3}$), 4.27 (q, ^{3}J = 6.9 Hz, 2 H, $O\mathit{CH_2}CH_3$), 7.29 - 7.30 (m, 1 H, CH_{Ar}), 7.34 - 7.35 (m, 2 H, CH_{Ar}), 7.49 - 7.51 (m, 1 H, CH_{Ar}), 8.29 (s, 1 H, CH_{olf}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 75.1 (OCH_2), 126.6 (C), 128.9, 130.1, 131.9 (CH_{Ar}), 132.3 (C_{Ar}), 132.4 (CH_{Ar}), 136.4 (C_{Ar}), 160.0 (CH_{olf}), 184.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2930 (w), 1777 (w), 1683 (m), 1587 (m), 1560 (s), 1523 (m), 1470 (m), 1368 (m), 1319 (m), 1212 (m), 1163 (m), 1064 (m), 1037 (m), 917 (m), 816 (m), 739 (s), 684 (m), 606 (m), 583 (w), 549 (w). HRMS (EI): Calcd. for $C_{11}H_{10}ClNO_4$: 255.02986; found: 255.02985.

Methyl 3-hydroxy-6-nitrobiphenyl-2-carboxylate (132a):

Starting with **131a** (0.332 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **132a** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.230 g, 56%), m.p. = 137-138 °C.

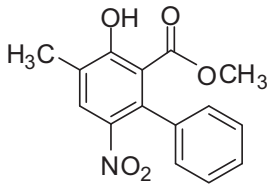


Chemical Formula: $C_{14}H_{11}NO_5$
Exact Mass: 273,06

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.35 (s, 3 H, OCH_3), 7.02 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 7.07 - 7.10 (m, 2 H, CH_{Ph}), 7.27-7.31 (m, 3 H, CH_{Ph}), 7.82 (d, ^3J = 8.9 Hz, 1 H, CH_{Ar}), 11.07 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.5 (OCH_3), 113.6 (*C*$COOCH_3$), 117.7, 127.7, 127.7, 127.7, 127.8, 127.8, 128.5 (CH_{Ar}), 133.7, 136.2, 139.0 (C_{Ar}), 163.8 (COH), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3086 (w), 3062 (w), 2954 (w), 1735 (w), 1670 (m), 1599 (w), 1576 (w), 1525 (m), 1501 (w), 1442 (m), 1324 (m), 1220 (m), 1156 (w), 1132 (m), 1095 (w), 1074 (w), 1026 (w), 970 (w), 907 (m), 837 (w), 813 (w), 769 (w), 727 (s), 698 (m), 672 (m), 648 (w), 584 (w). GC-MS (EI, 70 eV): *m/z* (%) = 273 ($[M]^+$, 80), 242 (17), 241 (100), 224 (15), 213 (25), 212 (13), 196 (14), 185 (18), 184 (11), 183 (13), 159 (16), 157 (11), 155 (20), 140 (15), 139 (66), 138 (10), 129 (25), 128 (14), 127 (19), 115 (10), 113 (10), 102 (10), 77 (12), 63 (11). HRMS (EI): Calcd. for $C_{14}H_{11}O_5N$ ($[M]^+$): 273.06317; found: 273.063020.

Methyl 3-hydroxy-4-methyl-6-nitrobiphenyl-2-carboxylate (132b):

Starting with **131a** (0.332 g, 1.5 mmol) and **22d** (0.457 g, 1.65 mmol), **132b** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.245 g, 57%), m.p. = 57-59 °C.



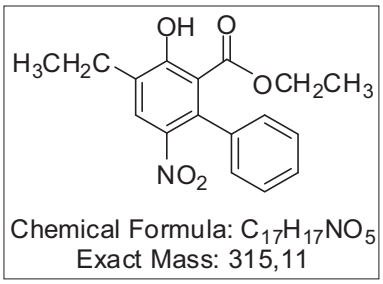
Chemical Formula: $C_{15}H_{13}NO_5$
Exact Mass: 287,08

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 3.33 (s, 3 H, OCH_3), 7.05 - 7.08 (m, 2 H, CH_{Ph}), 7.26 - 7.29 (m, 3 H, CH_{Ph}), 7.71 (s, 1H, CH_{Ar}), 11.33 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.9 (CH_3), 52.4 (OCH_3), 112.6 (*C*$COOCH_3$), 127.6 (CH_{Ar}), 127.7 ($2CH_{Ar}$), 127.9 (3 CH_{Ar}), 133.2, 136.3, 136.6, 142.6 (C_{Ar}), 162.3 (COH), 170.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3062 (w), 2958 (w), 1737 (w), 1665 (m), 1574 (w), 1526 (m), 1495 (w), 1441 (m), 1373 (m), 1302 (m), 1251 (m), 1200 (m), 1170 (m), 1129 (m), 1070 (m), 1031 (w), 1001 (w), 983 (w), 902 (w), 864 (w), 812 (w), 778 (m), 727 (m), 696 (m), 663 (m), 610 (m), 574 (m). GC-MS (EI, 70 eV): *m/z* (%) = 287 ($[M]^+$, 80), 256 (17), 255 (100), 239 (15), 238 (75),

209 (15), 208 (76), 180 (10), 129 (14), 127 (10), 115 (14), 77 (10). HRMS (EI): Calcd. for $C_{15}H_{13}O_5N$ ($[M]^+$): 287.07882; found: 287.078935.

Ethyl 4-ethyl-3-hydroxy-6-nitrobiphenyl-2-carboxylate (132c):

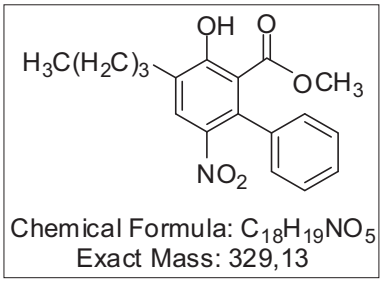
Starting with **131a** (0.332 g, 1.5 mmol) and **22g** (0.499 g, 1.65 mmol), **132c** was isolated after chromatography (silica gel, heptanes/EtOAc) as a viscos yellowish oil (0.306 g, 65%).



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.52 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.12 (t, ^3J = 7.5 Hz, 3 H, OCH_2CH_3), 2.59 (q, ^3J= 7.5 Hz, 2 H, CH_2CH_3), 3.75 (q, ^3J= 7.5 Hz, 2 H, OCH_2CH_3), 6.96 -7 .0 (m, 2 H, CH_{Ph}), 7.16 - 7.18 (m, 3 H, CH_{Ph}), 7.61 (s, 1 H, CH_{Ar}), 11.42 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 13.0 (CH_3), 22.8, 61.8 (CH_2), 112.8 (CCOOCH$_3$), 127.6 (CH_{Ar}), 127.7 (2 CH_{Ar}), 128.1 (3 CH_{Ar}), 133.3, 136.2, 136.8, 142.8 (C_{Ar}), 162.2 (COH), 170.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3002 (w), 2963 (w), 1737 (w), 1657 (m), 1600 (w), 1567 (w), 1512 (m), 1443 (m), 1329 (m), 1298 (m), 1241 (m), 1191 (s), 1149 (m), 1063 (m), 1018 (m), 968 (w), 900 (m), 822 (m), 803 (m), 733 (s), 695 (s), 668 (s), 621 (m), 581 (m), 524 (m). GC-MS (EI, 70 eV): *m/z* (%) = 315 ($[M]^+$, 54), 270 (10), 269 (50), 253 (19), 252 (100), 223 (18), 222 (89), 165 (22), 152 (21), 129 (8). HRMS (EI): Calcd. for $C_{17}H_{17}O_5N$ ($[M]^+$): 315.11012; found: 315.110219.

Methyl 4-butyl-3-hydroxy-6-nitrobiphenyl-2-carboxylate (132d):

Reaction starting with **131a** (0.332 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **132d** was isolated after chromatography (silica gel, heptanes/EtOAc) as a viscos yellowish oil (0.285 g, 58%).

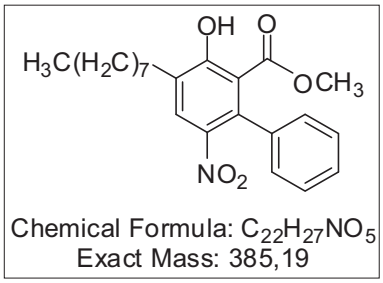


^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.28-1.40 (m, 2 H, CH_2), 1.52 - 1.62 (m, 2 H, CH_2), 2.64 (t, ^3J = 7.2 Hz, 2 H, $PhCH_2$), 3.31 (s, 3 H, OCH_3), 7.04-7.07 (m, 2 H, CH_{Ph}), 7.23 - 7.27 (m, 3 H, CH_{Ph}), 7.68 (s, 1 H, CH_{Ar}), 11.27 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 22.5, 29.4, 31.0 (CH_2), 52.4 (OCH_3), 112.9 (CCOOCH$_3$), 127.6 (CH_{Ar}), 127.7 (2 CH_{Ar}), 127.9 (2 CH_{Ar}), 128.9 (CH_{Ar}), 132.1, 136.2, 136.6, 142.7 (C_{Ar}), 162.0 (COH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 3006 (w), 2952 (w), 1674 (m), 1581 (w), 1531 (w), 1438 (m), 1380 (w), 1356 (m), 1311 (s), 1232 (m), 1140

(m), 1090 (m), 1030 (w), 940 (w), 914 (m), 850 (w), 808 (m), 771 (m), 732 (m), 698 (s), 671 (m), 628 (m), 608 (m). GC-MS (EI, 70 eV): *m/z* (%) = 329 ($[M]^+$, 48), 281 (12), 280 (59), 255 (18), 239 (15), 238 (100), 209 (10), 208 (36), 180 (10), 152 (21). HRMS (EI): Calcd. for $C_{18}H_{19}O_5N$ ($[M]^+$): 329.12577; found: 329.125828.

Methyl 3-hydroxy-6-nitro-4-octylbiphenyl-2-carboxylate (132e):

Starting with **131a** (0.332 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **132e** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.357 g, 62%).

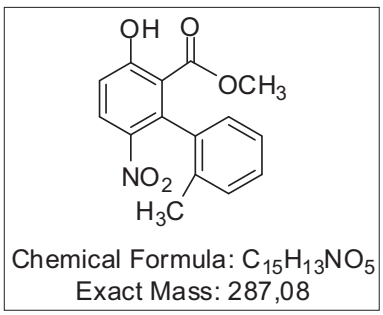


Chemical Formula: $C_{22}H_{27}NO_5$
Exact Mass: 385,19

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.08 - 1.15 (m, 10 H, 5 CH_2), 1.43 - 1.55 (m, 2 H, CH_2), 2.56 (t, ^3J = 7.0 Hz, 2 H, $PhCH_2$), 3.23 (s, 3 H, OCH_3), 6.96-6.99 (m, 2 H, CH_{Ph}), 7.17 - 7.19 (m, 3 H, CH_{Ph}), 7.60 (s, 1H, CH_{Ar}), 11.19 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.6, 28.8, 29.2, 29.3, 29.4, 29.6, 31.8 (CH_2), 52.3 (OCH_3), 112.9 (*C*$COOCH_3$), 127.6 (CH_{Ar}), 127.4 (2 CH_{Ar}), 127.9 (2 CH_{Ar}), 128.9 (CH_{Ar}), 132.1, 136.2, 136.6, 142.7 (C_{Ar}), 162.0 (COH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 2952 (w), 2923 (m), 1666 (m), 1570 (w), 1526 (m), 1437 (m), 1336 (s), 1250 (m), 1164 (m), 1126 (m), 1074 (w), 1029 (w), 964 (w), 914 (w), 843 (w), 814 (m), 754 (m), 733 (m), 697 (s), 669 (m), 612 (w). GC-MS (EI, 70 eV): *m/z* (%) = 385 ($[M]^+$, 64), 337 (23), 336 (95), 255 (16), 254 (15), 239 (21), 238 (100), 209 (12), 208 (29), 180 (10), 152 (16). HRMS (EI): Calcd. for $C_{12}H_{27}O_5N$ ($[M]^+$): 385.18837; found: 385.188315.

Methyl 3-hydroxy-2'-methyl-6-nitrobiphenyl-2-carboxylate (132f):

Starting with **131b** (0.353 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **132f** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.292 g, 68%), m.p. = 74 –76 °C.



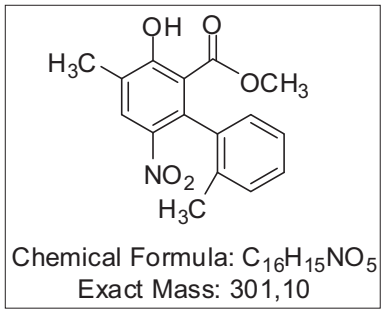
Chemical Formula: $C_{15}H_{13}NO_5$
Exact Mass: 287,08

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, CH_3), 3.28 (s, 3 H, OCH_3), 6.96 (d, ^3J = 8.4 Hz, 1 H, CH_{Ar}), 7.11 - 7.15 (m, 3 H, CH_{Ar}), 7.28 - 7.33 (m, 1 H, CH_{Ar}), 7.93 (d, ^3J = 8.4 Hz, 1 H, CH_{Ar}), 11.33 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.8 (CH_3), 52.6 (OCH_3), 113.1 (*C*$COOCH_3$), 117.9, 125.2 (CH_{Ar}), 128.3 (2 CH_{Ar}), 129.1, 130.0 (CH_{Ar}), 132.9, 135.9, 139.0, 141.3 (C_{Ar}), 164.4 (COH), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2954 (w), 2649

(w), 1673 (m), 1598 (m), 1575 (m), 1518 (m), 1490 (m), 1441 (m), 1313 (s), 1313 (s), 1268 (m), 1232 (s), 1221 (s), 1173 (m), 1132 (m), 1086 (m), 1052 (m), 1034 (w), 964 (m), 912 (m), 832 (m), 814 (m), 763 (m), 733 (s), 689 (m), 658 (m), 593 (m), 531 (m). GC-MS (EI, 70 eV): *m/z* (%) = 287 ($[M]^+$, 27), 270 (14), 269 (15), 256 (17), 239 (19), 238 (100), 237 (21), 228 (52), 226 (14), 181 (15), 153 (25), 127 (13), 115 (20), 63 (9). HRMS (EI): Calcd. for $C_{15}H_{13}O_5N$ ($[M]^+$): 287.07882; found: 287.078912.

Methyl 3-hydroxy-2',4-dimethyl-6-nitrobiphenyl-2-carboxylate (132g):

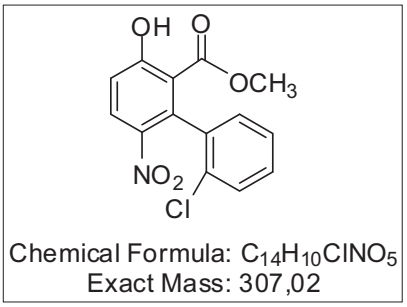
Starting with **131b** (0.353 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **132g** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.324 g, 72%), m.p. = 70 –72 °C.



^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 3.34 (s, 3 H, OCH_3), 6.82 - 6.84 (m, 1 H, CH_{Ar}), 7.03 - 7.16 (m, 3 H, CH_{Ar}), 7.79 (s, 1 H, CH_{Ar}), 11.63 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 15.9, 19.9 (CH_3), 52.6 (OCH_3), 112.2 (*C*$COOCH_3$), 125.2, 127.3 (CH_{Ar}), 127.7 (C_{Ar}), 128.8, 129.0, 130.1 (CH_{Ar}), 136.0, 136.2, 136.3, 142.3 (C_{Ar}), 163.0 (COH), 170.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2953 (w), 2854 (w), 1664 (m), 1573 (m), 1523 (m), 1494 (w), 1380 (m), 1334 (s), 1285 (m), 1254 (s), 1202 (s), 1166 (m), 1133 (m), 1133 (m), 1104 (m), 1041 (w), 1018 (m), 964 (m), 899 (m), 871 (w), 813 (m), 753 (m), 723 (s), 661 (m), 589 (m), 531 (m). GC-MS (EI, 70 eV): *m/z* (%) = 301 ($[M]^+$, 29), 384 (12), 383 (10), 270 (17), 254 (15), 252 (100), 251 (21), 242 (41), 240 (12), 239 (31), 238 (54), 225 (13), 222 (63), 211 (11), 195 (10), 194 (16), 168 (12), 166 (23), 165 (62), 153 (14), 151 (11), 139 (14), 128 (12), 115 (23), 82 (12), 77 (10). HRMS (EI): Calcd. for $C_{16}H_{15}O_5N$ ($[M]^+$): 301.09447; found: 301.093882.

Methyl 2'-chloro-3-hydroxy-6-nitrobiphenyl-2-carboxylate (132h):

Starting with **131c** (0.383 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **132h** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.258 g, 56%), m.p. = 101–103 °C.

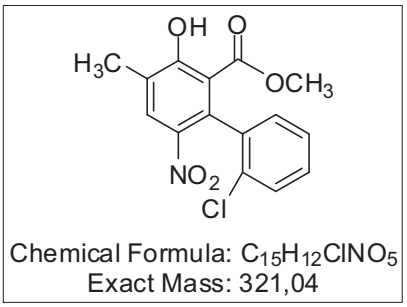


Chemical Formula: $C_{14}H_{10}ClNO_5$
Exact Mass: 307,02

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.41 (s, 3 H, OCH_3), 6.92–7.02 (m, 1 H, CH_{Ar}), 7.09 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 7.17-7.20 (m, 1 H, CH_{Ar}), 7.22 - 7.25 (m, 1 H, CH_{Ar}), 7.35 - 7.38 (m, 1 H, CH_{Ar}), 8.01 (d, ^3J = 9.0 Hz, 1 H, CH_{Ar}), 11.52 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 52.8 (OCH_3), 113.0 (*C*$COOCH_3$), 118.6, 126.4, 128.7, 128.7, 129.2, 130.4 (CH_{Ar}), 132.9, 135.8, 136.5, 142.3 (C_{Ar}), 164.8 (COH), 169.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3073 (w), 2952 (w), 1673 (m), 1599 (m), 1578 (m), 1519 (m), 1480 (w), 1440 (s), 1323 (s), 1230 (m), 1204 (s), 1127 (m), 1049 (m), 968 (m), 914 (m), 841 (m), 811 (m), 750 (s), 737 (s), 698 (s), 644 (m), 592 (w). GC-MS (EI, 70 eV): *m/z* (%) = 307 ([M]$^+$, 10), 273 (15), 272 (100), 241 (10), 240 (66), 226 (12), 212 (18), 184 (15), 173 (10). HRMS (EI): Calcd. for $C_{14}H_{10}O_5NCl$ ([M]$^+$): 307.02420; found: 307.024320.

Methyl 2'-chloro-3-hydroxy-4-methyl-6-nitrobiphenyl-2-carboxylate (132i):

Starting with **131c** (0.383 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **132i** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.337 g, 70%), m.p. = 100-102 °C.

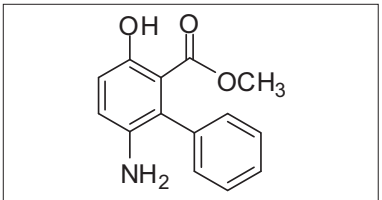


Chemical Formula: $C_{15}H_{12}ClNO_5$
Exact Mass: 321,04

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 3.40 (s, 3 H, OCH_3), 6.99 (dd, ^3J = 6.9 Hz, ^4J = 1.8 Hz, 1 H, CH_{Ar}), 7.15 - 7.26 (m, 2 H, CH_{Ar}), 7.35 (dd, ^3J = 7.7 Hz, ^4J = 1.5 Hz, 1 H, CH_{Ar}), 7.90 (s, 1 H, CH_{Ar}), 11.79 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.0 (CH_3), 52.8 (OCH_3), 112.0 (*C*$COOCH_3$), 126.4 (CH_{Ar}), 128.5 (C_{Ar}), 128.6, 128.8, 129.0, 130.5 (CH_{Ar}), 133.0, 133.8, 136.2, 141.6 (C_{Ar}), 163.4 (COH), 170.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2853 (w), 1731 (w), 1664 (s), 1574 (m), 1521 (m), 1429 (m), 1378 (m), 1341 (s), 1265 (s), 1200 (s), 1128 (m), 1057 (m), 98 (m), 946 (w), 899 (m), 859 (w), 810 (m), 754 (m), 739 (s), 698 (s), 657 (m), 630 (m), 534 (w). GC-MS (EI, 70 eV): *m/z* (%) = 321 ([M]$^+$, 10), 287 (17), 286 (100), 255 (12), 254 (77), 226 (12), 198 (17), 152 (24), 139 (10). HRMS (EI): Calcd. for $C_{15}H_{12}O_5NCl$ ([M]$^+$): 321.03985; found: 321.039927.

Methyl 6-amino-3-hydroxybiphenyl-2-carboxylate (133a):

Starting with **132a** (0.130 g, 0.476 mmol), **133a** was isolated (0.099 g, 86%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish solid, m.p. = 95 - 97 °C.

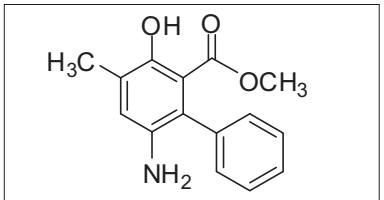


Chemical Formula: $C_{14}H_{13}NO_3$
Exact Mass: 243,09

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.02 (br, 2 H, NH_2), 3.30 (s, 3 H, OCH_3), 6.82-6.84 (m, 2 H, CH_{Ar}), 7.08 - 7.11 (m, 2 H, CH_{Ph}), 7.22 - 7.35 (m, 3 H, CH_{Ph}), 10.07 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.6 (OCH_3), 112.5 (*C*$COOCH_3$), 117.7, 123.1, 127.0, (CH_{Ar}), 127.5 (C_{Ar}), 128.5 (2 CH_{Ar}), 128.9 (2 CH_{Ar}), 136.9, 139.1 (C_{Ar}), 154.7 (COH), 171.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3742 (w), 3060 (w), 2922 (w), 2788 (w), 2671 (w), 1721 (s), 1586 (m), 1488 (m), 1455 (m), 1433 (m), 1348 (m), 1302 (m), 1277 (s), 1239 (m), 1217 (s), 1158 (m), 1110 (m), 1087 (m), 1029 (w), 982 (m), 949 (m), 911 (m), 871 (m), 807 (m), 776 (m), 750 (m), 730 (m), 719 (s), 698 (s), 646 (m), 613 (m), 549 (m). GC-MS (EI, 70 eV): *m/z* (%) = 243 ($[M]^+$, 32), 212 (16), 211 (100), 183 (24), 155 (15), 154 (67), 128 (16), 127 (10), 77 (10). HRMS (EI): Calcd. for $C_{14}H_{13}O_3N$ ($[M]^+$): 243.08899; found: 243.089209.

Methyl 6-amino-3-hydroxy-4-methylbiphenyl-2-carboxylate (133b):

Starting with **132b** (0.140 g, 0.487 mmol), **133b** was isolated (0.107 g, 85%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish oil.

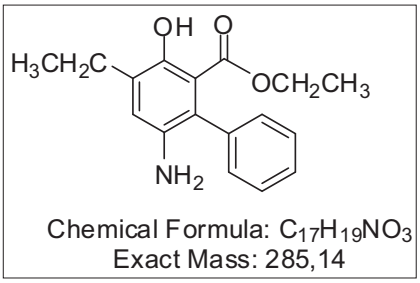


Chemical Formula: $C_{15}H_{15}NO_3$
Exact Mass: 257,11

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_3), 3.09 (br, 2 H, NH_2), 3.28 (s, 3 H, OCH_3), 6.73 (s, 1 H, CH_{Ar}), 7.06-7.09 (m, 2 H, CH_{Ar}), 7.22 - 7.25 (m, 1 H, CH_{Ar}), 7.29 - 7.34 (m, 2 H, CH_{Ar}), 10.36 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.3 (CH_3), 51.5 (OCH_3), 111.7 (*C*$COOCH_3$), 124.2 (CH_{Ar}), 125.0 (C_{Ar}), 126.8 (CH_{Ar}), 128.4 (2 CH_{Ar}), 129.3 (2 CH_{Ar}), 132.5, 136.0, 139.4 (C_{Ar}), 153.1 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3444 (w), 3057 (w), 2924 (w), 2851 (w), 1726 (w), 1658 (m), 1587 (m), 1499 (w), 1434 (m), 1347 (m), 1306 (m), 1280 (m), 1208 (s), 1149 (m), 1106 (m), 1072 (m), 1023 (m), 983 (m), 907 (m), 863 (m), 802 (m), 764 (m), 730 (s), 700 (s), 689 (s), 645 (m), 565 (m). GC-MS (EI, 70 eV): *m/z* (%) = 257 ($[M]^+$, 33), 226 (17), 225 (100), 197 (24), 169 (11), 168 (53), 167 (14), 154 (12), 128 (9). HRMS (EI): Calcd. for $C_{15}H_{15}O_3N$ ($[M]^+$): 257.10464; found: 257.104582.

Ethyl 6-amino-4-ethyl-3-hydroxybiphenyl-2-carboxylate (133c):

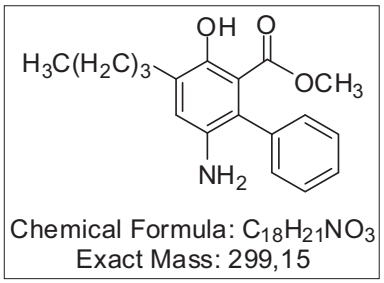
Starting with **132c** (0.130 g, 0.412 mmol), **133c** was isolated (0.113 g, 96%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish oil.



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.58 (t, ^{3}J = 7.0 Hz, 3 H, CH_2CH_3), δ = 1.17 (t, ^{3}J = 7.6 Hz, 3 H, OCH_2CH_3), 2.60 (q, ^{3}J= 7.6 Hz, 2 H, CH_2CH_3), 3.09 (br, 2 H, NH_2), 3.81 (q, ^{3}J= 7.0 Hz, 2 H, OCH_2CH_3), 6.76 (s, 1 H, CH_{Ar}), 7.08 - 7.11 (m, 2 H, CH_{Ar}), 7.21 - 7.34 (m, 3 H, CH_{Ar}), 10.58 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 13.7 (CH_3), 23.0 (CH_2), 60.6 (OCH_2), 111.8 ($CCOOCH_3$), 122.5 (CH_{Ar}), 125.1 (C_{Ar}), 126.7 (CH_{Ar}), 128.4 (2 CH_{Ar}), 129.1 (2 CH_{Ar}), 132.7, 136.0, 139.7 (C_{Ar}), 153.0 (COH), 171.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3447 (w), 3056 (w), 2964 (w), 2872 (w), 1654 (m), 1611 (m), 1585 (m), 1496 (w), 1429 (m), 1371 (m), 1326 (m), 1264 (m), 1205 (s), 1149 (m), 1106 (m), 1065 (m), 1014 (m), 968 (w), 909 (m), 853 (m), 803 (m), 762 (m), 731 (m), 699 (s), 681 (m), 645 (m), 569 (m). GC-MS (EI, 70 eV): *m/z* (%) = 285 ($[M]^+$, 30), 240 (17), 239 (100), 221 (11), 211 (13), 196 (25), 167 (11). HRMS (EI): Calcd. for $C_{17}H_{19}O_3N$ ($[M]^+$): 285.13594; found: 285.135726.

Methyl 6-amino-4-butyl-3-hydroxybiphenyl-2-carboxylate (133d):

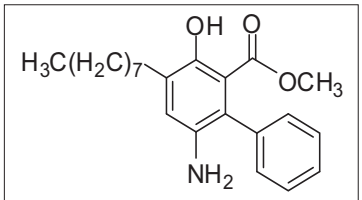
Starting with **132d** (0.130 g, 0.395 mmol), **133d** was isolated (0.108 g, 91%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish oil.



^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, ^{3}J = 6.7 Hz, 3 H, CH_3), 1.15 - 1.18 (m, 2 H, CH_2), 1.50 - 1.59 (m, 2 H, CH_2), 2.56 (t, ^{3}J = 7.6 Hz, 2 H, $PhCH_2$), 3.06 (br, 2 H, NH_2), 3.29 (s, 3 H, OCH_3), 6.75 (s, 1 H, CH_{Ar}), 7.07 - 7.12 (m, 2 H, CH_{Ar}), 7.21 - 7.25 (m, 1 H, CH_{Ar}), 7.32 - 7.36 (m, 2 H, CH_{Ar}), 10.35 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9 (CH_3), 22.5, 29.4, 31.0 (CH_2), 51.4 (OCH_3), 112.0 ($CCOOCH_3$), 123.5 (CH_{Ar}), 125.0 (C_{Ar}), 126.7 (CH_{Ar}), 128.5 (2 CH_{Ar}), 129.1 (2 CH_{Ar}), 131.4, 136.0, 139.5 (C_{Ar}), 152.8 (COH), 171.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3454 (w), 3055 (w), 2922 (m), 2851 (w), 1660 (m), 1598 (m), 1493 (w), 1433 (m), 1315 (m), 1263 (m), 1207 (s), 1152 (m), 1108 (m), 1071 (w), 998 (w), 920 (w), 871 (w), 809 (w), 764 (m), 721 (m), 700 (s), 683 (m), 647 (m), 569 (m). HRMS (EI): Calcd. for $C_{18}H_{21}O_3N$ ($[M]^+$): 299.15299; found: 299.152209.

Methyl 6-amino-3-hydroxy-4-octylbiphenyl-2-carboxylate (133e):

Starting with **132e** (0.150 g, 0.389 mmol), **133e** was isolated (0.124 g, 90%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish oil.

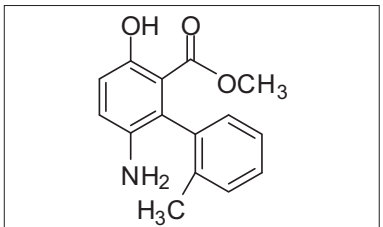


Chemical Formula: $C_{22}H_{29}NO_3$
Exact Mass: 355,21

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 6.5 Hz, 3 H, CH_3), 1.17 - 1.25 (m, 10 H, 5 CH_2), 1.51 - 1.61 (m, 2 H, CH_2), 2.56 (t, ^3J = 7.8 Hz, 2 H, $PhCH_2$), 3.08 (br, 2 H, NH_2), 3.28 (s, 3 H, OCH_3), 6.74 (s, 1 H, CH_{Ar}), 7.07 - 7.11 (m, 2 H, CH_{Ar}), 7.20-7.25 (m, 1 H, CH_{Ar}), 7.30 - 7.35 (m, 2 H, CH_{Ar}), 10.34 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.1 (CH_3), 22.6, 29.3, 29.5, 29.5, 29.6, 30.3, 31.9 (CH_2), 51.5 (OCH_3), 111.9 (*C*$COOCH_3$), 123.4 (CH_{Ar}), 125.1 (C_{Ar}), 126.8 (CH_{Ar}), 128.4 (2 CH_{Ar}), 129.0 (2 CH_{Ar}), 131.5, 135.9, 139.4 (C_{Ar}), 152.9 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3455 (w), 3056 (w), 2922 (m), 2852 (w), 1659 (m), 1599 (m), 1497 (w), 1434 (m), 1317 (m), 1263 (m), 1208 (s), 1150 (m), 1108 (m), 1071 (w), 997 (w), 919 (w), 881 (w), 804 (w), 764 (m), 721 (m), 700 (s). GC-MS (EI, 70 eV): *m/z* (%) = 355 ($[M]^+$, 65), 324 (27), 323 (100), 322 (11), 306 (12), 266 (25), 252 (18), 324 (27), 323 (100), 322 (11), 306 (12), 266 (25), 252 (18), 238 (27), 225 (41), 224 (47), 209 (10), 208 (10), 197 (10), 196 (30), 180 (11), 168 (23), 167 (21), 41 (10). HRMS (EI): Calcd. for $C_{22}H_{29}O_3N$ ($[M]^+$): 355.21420; found: 355.214070.

Methyl 6-amino-3-hydroxy-2'-methylbiphenyl-2-carboxylate (133f):

Starting with **132f** (0.120 g, 0.418 mmol), **133f** was isolated (0.097 g, 90%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish viscos oil.



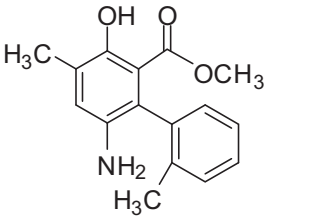
Chemical Formula: $C_{15}H_{15}NO_3$
Exact Mass: 257,11

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 3.02 (br, 2 H, NH_2), 3.31 (s, 3 H, OCH_3), 6.68 (d, ^3J = 8.0 Hz, 1 H, CH_{Ar}), 6.92 - 6.94 (m, 1 H, CH_{Ar}), 7.18 - 7.23 (m, 3 H, CH_{Ar}), 8.0 (d, ^3J = 8.2 Hz, 1 H, CH_{Ar}), 9.98 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.5 (CH_3), 51.7 (OCH_3), 112.1 (*C*$COOCH_3$), 117.6, 123.8, 126.1, 127.4 (CH_{Ar}), 127.8 (C_{Ar}), 128.9, 129.9 (CH_{Ar}), 135.3, 136.2, 138.1 (C_{Ar}), 153.5 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3451 (w), 3060 (w), 2921 (w), 2851 (w), 1664 (m), 1598 (m), 1489 (w), 1463 (m), 1436 (m), 1411 (w), 1335 (m), 1312 (m), 1287 (m), 1212 (s), 1119 (m), 1087 (m), 1037 (m), 982 (w), 913 (m), 806 (m), 757 (m), 734 (s), 689 (m), 624 (m), 565 (m). GC-MS

(EI, 70 eV): *m/z* (%) = 257 ([M]$^+$, 39), 226 (17), 225 (100), 169 (15), 168 (50), 167 (10), 154 (10), 115 (9). HRMS (EI): Calcd. for $C_{15}H_{15}O_3N$ ([M]$^+$): 257.10464; found: 257.104502.

Methyl 6-amino-3-hydroxy-2',4-dimethylbiphenyl-2-carboxylate (133g):

Starting with **132g** (0.140 g, 0.465 mmol), **133g** was isolated (0.112 g, 89%) by column chromatography (silica gel, heptanes/EtOAc) as a yellowish oil.

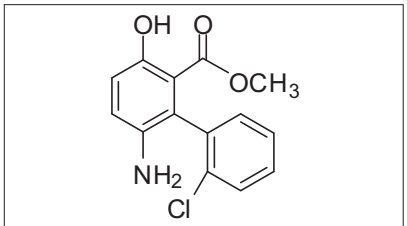


Chemical Formula: $C_{16}H_{17}NO_3$
Exact Mass: 271,12

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 3.04 (br, 2 H, NH_2), 3.30 (s, 3 H, OCH_3), 6.77 (s, 1 H, CH_{Ar}), 6.88 - 6.91 (m, 1 H, CH_{Ar}), 7.12 - 7.18 (m, 3 H, CH_{Ar}), 10.61 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.0, 19.5 (CH_3), 51.6 (OCH_3), 111.3 (*C*$COOCH_3$), 124.3 (CH_{Ar}), 124.5 (C_{Ar}), 126.0 (CH_{Ar}), 126.6 (C_{Ar}), 127.2, 128.8, 129.7 (CH_{Ar}), 135.5, 136.4, 138.6 (C_{Ar}), 153.5 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3447 (w), 3057 (w), 2920 (w), 2850 (w), 1726 (w), 1658 (m), 1610 (m), 1456 (m), 1434 (s), 1377 (m), 1342 (m), 1284 (m), 1208 (s), 1150 (m), 1101 (m), 1023 (m), 983 (m), 909 (w), 869 (m), 804 (m), 758 (s), 728 (s), 678 (m), 645 (m), 578 (m). GC-MS (EI, 70 eV): *m/z* (%) = 271 ([M]$^+$, 39), 240 (17), 239 (100), 183 (10), 182 (25), 168 (30), 167 (13). HRMS (EI): Calcd. for $C_{16}H_{17}O_3N$ ([M]$^+$): 271.12029; found: 271.120370.

Methyl 6-amino-2'-chloro-3-hydroxybiphenyl-2-carboxylate (133h):

Starting with **132h** (0.120 g, 0.390 mmol), **133h** was isolated (0.095 g, 88%) by column chromatography (silica gel, heptanes/EtOAc) as a brown oil.



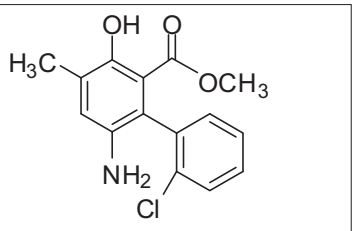
Chemical Formula: $C_{14}H_{12}ClNO_3$
Exact Mass: 277,05

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (br, 2 H, NH_2), 3.30 (s, 3 H, OCH_3), 6.85 (d, ^3J = 8.0 Hz, 1 H, CH_{Ar}), 7.09 - 7.11 (m, 2 H, CH_{Ar}), 7.23 - 7.28 (m, 2 H, CH_{Ar}), 7.32 - 7.37 (m, 2 H, CH_{Ar}), 10.29 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.6 (OCH_3), 112.4 (*C*$COOCH_3$), 117.7, 123.3, 127.0 (CH_{Ar}), 127.8 (C_{Ar}), 128.5, 128.5, 128.8 (CH_{Ar}), 135.5, 136.4, 139.0 (C_{Ar}), 154.8 (COH), 171.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3445 (w), 3056 (w), 2950 (w), 2850 (w), 1728 (w), 1663 (m), 1594 (m), 1463 (m), 1435 (s), 1335 (m), 1285 (m), 1209 (s), 1092 (m), 1027 (m), 982 (m), 805 (m), 759 (m), 732 (m), 700 (s), 626 (m), 580 (m). GC-MS (EI, 70 eV): *m/z* (%) = 277 ([M]$^+$, 42), 246 (14), 245 (100), 211 (19), 210 (59), 183

(10), 182 (52), 154 (62), 153 (13), 127 (14), 77 (11). HRMS (EI): Calcd. for $C_{14}H_{12}O_3NCl$ ($[M]^+$): 277.05002; found: 277.050203.

Methyl 6-amino-2'-chloro-3-hydroxy-4-methylbiphenyl-2-carboxylate (133i):

Starting with **132i** (0.120 g, 0.373 mmol), **133i** was isolated (0.097 g, 89%) by column chromatography (silica gel, heptanes/EtOAc) as a brown oil.

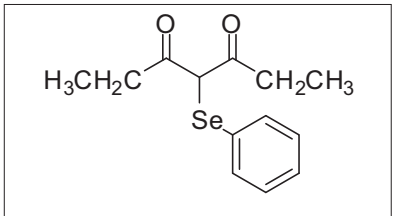


Chemical Formula: $C_{15}H_{14}ClNO_3$
Exact Mass: 291,07

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, CH_3), 3.02 (br, 2 H, NH_2), 3.29 (s, 3 H, OCH_3), 6.78 (s, 1 H, CH_{Ar}), 7.07 - 7.10 (m, 1 H, CH_{Ar}), 7.23 - 7.26 (m, 1 H, CH_{Ar}), 7.30 - 7.35 (m, 2 H, CH_{Ar}), 10.42 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.0 (CH_3), 51.5 (OCH_3), 111.7 (*C*$COOCH_3$), 124.3 (CH_{Ar}), 125.3 (C_{Ar}), 126.8 (CH_{Ar}), 127.8 (C_{Ar}), 128.4 (2 CH_{Ar}), 129.0 (CH_{Ar}), 132.5, 135.5, 139.2 (C_{Ar}), 153.4 (COH), 171.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3447 (w), 3056 (w), 2949 (w), 2851 (w), 1731 (w), 1658 (m), 1612 (m), 1599 (m), 1498 (w), 1434 (s), 1377 (m), 1280 (m), 1206 (s), 1149 (m), 1105 (m), 1072 (m), 1005 (m), 983 (m), 919 (w), 803 (m), 763 (m), 700 (s), 644 (m), 588 (m). GC-MS (EI, 70 eV): *m/z* (%) = 257 ($[M]^+$, 33), 226 (17), 225 (100), 197 (22), 168 (49), 167 (14), 154 (11). HRMS (EI): Calcd. for $C_{15}H_{14}O_3NCl$ ($[M]^+$): 291.07029; found: 291.070370.

4-(Phenylselanyl)heptane-3,5-dione 136b:

To a suspension of selenium dioxide(1.11 gm, 10 mmol) in 35 ml of dichloromethane containing diphenyl diselenide(6.24 gm, 20 mmol) and a catalytic amount of sulfuric acid(0.11 ml, 2 mmol) was added 3,5-heptanedione (2.31 ml, 17 mmol) at 10°C. The mixture was stirred overnight, the reaction mixture was poured in dichloromethane (100 ml) and washed with saturated aqueous sodium hydrogen carbonate (20 ml% 2). The organic layer was dried (sodium sulfate) and evaporated to yellowish oil, which was purified by silica gel column chromatography to afford 4-(phenylselanyl)heptane-3,5-dione as a yellowish oil (1.33 gm, 47 %).



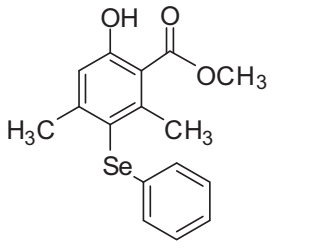
Chemical Formula: $C_{13}H_{16}O_2Se$
Exact Mass: 284,03

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.02 (t, ^3J = 7.4 Hz, 6 H, 2 CH_3), 2.71 (q, ^3J = 7.6Hz, 4 H, 2 CH_2), 7.07 - 7.12 (m, 2H, 2 CH_{Ar}), 7.13 - 7.20 (m,3H, 3 CH_{Ar}), one H is missing. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 13.9 (CH_3), 31.2, 31.3 (CH_2), 112.45 (C), 125.0 (CH_{Ar}), 126.6, 128.3 (2 CH_{Ar}),

130.5 (C_{Ar}), 197.0, 200.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 2976 (w), 2937 (w), 2877 (w), 1695 (m), 1575 (m), 1557 (m), 1475 (m), 1458 (m), 1436 (m), 1401 (m), 1375 (m), 1337 (m), 1296 (m), 1240 (m), 1187 (m), 1156 (m), 1099 (m), 1064 (m), 1019 (m), 997 (m), 886 (w), 847 (m), 805 (m), 731 (s), 688 (s), 666 (m), 614 (w).MS (GC-MS, 70 eV): *m/z* (%): 284 (M^+, 43), 282 (10), 280 (22), 255 (14), 254 (11), 253 (13), 230 (23), 228 (21), 226 (14), 225 (13), 224 (14), 172 (11), 171 (43), 170 (11), 168 (21), 159 (14), 158 (13), 157 (24), 156 (17), 155 (11), 154 (15), 149 (12), 129 (17), 128 (14), 118 (10), 99 (23), 91 (29), 77 (22), 58 (11), 57 (100), 55 (14), 51 (12), 50 (16), 43 (17), 39 (10), 29 (40).HRMS (EI): Calcd. for $C_{13}H_{16}O_2Se$: 284.031191; found: 284.03100

Methyl 6-hydroxy-2,4-dimethyl-3-(phenylselanyl)benzoate (137a):

Starting with **136a** (0.491 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **137a** was isolated sfter column chromatography (ethyl acetate/heptanes) as a colorless oil (0.297 g, 59%).

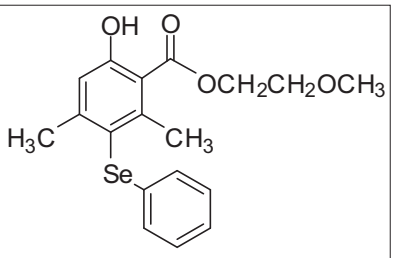


Chemical Formula: $C_{16}H_{16}O_3Se$
Exact Mass: 336,03

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 2.66 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.75 (s, 1 H, CH_{Ar}), 6.94 - 6.98 (m, 2 H, 2 CH_{Ar}), 7.05 - 7.14 (m, 3 H, 3 CH_{Ar}), 10.91 (s, 1 H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4, 25.7 (CH_3), 52.3 (OCH_3), 112.2 (C_{Ar}), 117.3 (CH_{Ar}), 123.1 (C_{Ar}), 125.5 (CH_{Ar}), 128.2, 129.2 (2 CH_{Ar}), 133.4, 146.6, 151.2 (C_{Ar}), 162.4 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2950 (w), 2922 (w), 2852 (w), 1730 (w), 1689 (w), 1656 (s), 1631 (m), 1593 (m), 1475 (m), 1375 (w), 1348 (s), 1298 (s), 1223 (s), 1186 (s), 1125 (s), 1101 (s), 1064 (s), 1020 (m), 997 (m), 947 (w), 858 (w), 801 (m), 731 (s), 688 (m), 664 (m), 589 (m).MS (GC-MS, 70 eV): *m/z* (%): 338 (16), 337 (15), 336 (M^+, 79), 334 (40), 333 (15), 332 (15), 306 (21), 305 (23), 304 (100), 303 (17), 302 (52), 301 (23), 300 (20), 224 (25), 196 (15), 195 (12), 168 (13), 167 (21), 165 (10), 152 (11), 119 (12), 91 (25), 77 (12), 65 (13), 51 (10).HRMS (EI): Calcd. for $C_{16}H_{16}O_3Se$: 336.02592; found: 336.025935.

Methoxyethyl 6-hydroxy-2,4-dimethyl-3-(phenylselanyl)benzoate (137b):

Starting with **136a** (0.491 g, 1.5 mmol) and **22b** (0.502 g, 1.65 mmol), **137b** was isolated after column chromatography (ethyl acetate/heptanes) as a white solid m.p. 60-62 (0.324 g, 57%).

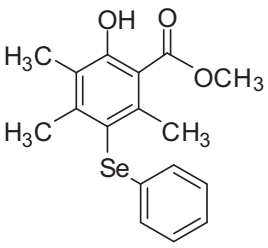


Chemical Formula: $C_{18}H_{20}O_4Se$
Exact Mass: 380,05

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 2.73 (s, 3 H, CH_3), 3.32 (s, 3 H, OCH_3), 3.61 - 3.65 (m, 2 H, CH_2), 4.41 - 4.45 (m, 2 H, CH_2), 6.79 (s, 1 H, CH_{Ar}), 6.95 - 6.98 (m, 2 H, 2 CH_{Ar}), 7.01 - 7.10 (m, 3 H, 3 CH_{Ar}), 10.57 (s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.5, 25.9 (CH_3), 59.0 (OCH_3), 64.3, 70.3 (CH_2), 112.7 (C_{Ar}), 117.6 (CH_{Ar}), 123.6 (C_{Ar}), 125.7 (CH_{Ar}), 128.4, 129.3 (2 CH_{Ar}), 133.4, 147.0, 151.4 (C_{Ar}), 161.9 (COH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3392 (w), 3054 (w), 2923 (w), 2881 (w), 2819 (w), 1728 (w), 1654 (s), 1593 (m), 1576 (m), 1556 (m), 1475 (m), 1449 (m), 1437 (m), 1372 (m), 1342 (m), 1295 (m), 1224 (s), 1199 (m), 1187 (m), 1130 (m), 1107 (m), 1092 (m), 1064 (m), 1020 (s), 997 (m), 859 (m), 801 (m), 732 (s), 688 (m), 623 (m), 589 (m), 538 (w). MS (GC-MS, 70 eV): *m/z* (%): 380 (M^+, 38), 378 (18), 306 (19), 305 (21), 304 (100), 303 (15), 302 (48), 301 (19), 300 (17), 248 (10), 224 (34), 196 (25), 195 (16), 181 (11), 168 (14), 167 (24), 165 (13), 158 (15), 155 (12), 154 (10), 153 (12), 152 (15), 148 (16), 119 (13), 91 (40), 82 (15), 80 (16), 79 (13), 78 (60), 77 (33), 76 (10), 69 (17), 67 (12), 65 (19), 59 (17), 51 (19), 50 (11), 45 (34), 44 (42), 43 (15), 41 (10).HRMS (EI): Calcd. for $C_{18}H_{20}O_4Se$: 380.05213; found: 380.051850.

Methyl 2-hydroxy-3,4,6-trimethyl-5-(phenylselanyl)benzoate (137c):

Starting with **136a** (0.491 g, 1.5 mmol) and **22d** (0.453 g, 1.65 mmol), **137c** was isolated sfter coloumn chromatography (ethyl acetate/heptanes) as a colorless oil (0.356 g, 68%).



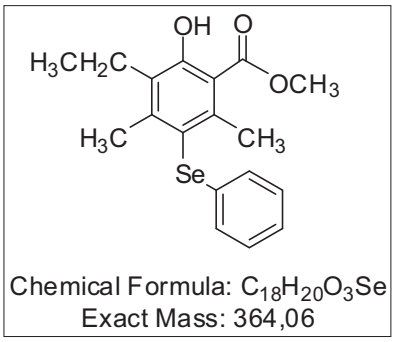
Chemical Formula: $C_{17}H_{18}O_3Se$
Exact Mass: 350,04

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 2.64 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 6.89 - 6.96 (m, 2 H, 2 CH_{Ar}), 6.98 - 7.06 (m, 3 H, 3 CH_{Ar}), 11.16 (s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 22.5, 24.7 (CH_3), 52.4 (OCH_3), 111.8, 123.6, (C_{Ar}), 125.7 (CH_{Ar}), 128.3, 129.2 (2 CH_{Ar}), 131.5, 133.8, 143.2, 148.0 (C_{Ar}), 160.5 (COH), 172.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2950 (w), 2872 (w), 1727 (w), 1652 (s), 1576 (m), 1546 (m), 1475 (m), 1437 (s), 1377 (m), 1344 (m), 1279 (m), 1263 (m), 1235 (s), 1194 (m), 1159 (m), 1095 (m), 1067 (m), 1020 (s), 997 (m),

846 (m), 805 (m), 731 (s), 687 (m), 665 (m), 594 (w).MS (GC-MS, 70 eV): *m/z* (%): 352 (13), 351 (14), 350 (M^+, 65), 348 (34), 347 (12), 346 (11), 320 (19), 318 (100), 317 (16), 316 (48), 315 (23), 314 (18), 181 (12), 166 (10), 165 (12), 133 (12), 105 (16), 103 (10), 91 (10), 78 (10), 77 (26). HRMS (EI): Calcd. for $(M-H)^-$:$C_{17}H_{17}O_3Se$: 349.03493; found: 349.03493.

Methyl 3-ethyl-2-hydroxy-4,6-dimethyl-5-(phenylselanyl)benzoate (137d):

Starting with **136a** (0.491 g, 1.5 mmol) and **22f** (0.476 g, 1.65 mmol), **137d** was isolated after column chromatography (ethyl acetate/heptanes) as a pale yellowish oil (0.381 g, 70%).

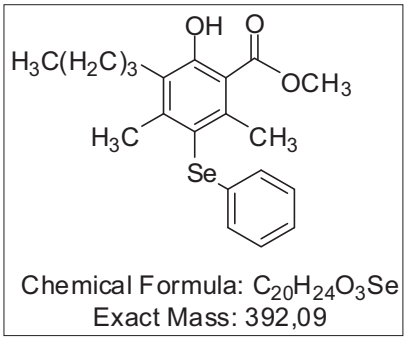


Chemical Formula: $C_{18}H_{20}O_3Se$
Exact Mass: 364,06

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.13 (t, ^3J = 7.4 Hz, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 2.62 (s, 3 H, CH_3), 2.89 (q, ^3J = 7.3 Hz, 2 H, $PhCH_2$), 3.83 (s, 3 H, OCH_3), 6.88 - 6.97 (m, 2 H, 2 CH_{Ar}), 6.96 - 7.07(m, 3 H, 3 CH_{Ar}), 11.17 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (CH_3), 20.7 (CH_2), 21.5, 24.7 (CH_3), 52.2 (OCH_3), 111.9, 123.6 (C_{Ar}), 125.3 (CH_{Ar}), 128.0, 129.1 (2 CH_{Ar}), 131.5, 133.8, 143.2, 148.2 (C_{Ar}), 160.2 (COH), 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2952 (w), 2871 (w), 1726 (w), 1654 (s), 1576 (m), 1544 (w), 1475 (m), 1436 (s), 1374 (m), 1344 (m), 1274 (m), 1257 (s), 1226 (s), 1194 (m), 1158 (m), 1106 (m), 1067 (m), 1020 (m), 997 (w), 989 (w), 848 (m), 808 (m), 731 (s), 687 (m), 665 (m), 631 (w), 579 (w). MS (GC-MS, 70 eV): *m/z* (%): 364 (M^+, 7), 279 (13), 167 (32), 150 (11), 149 (100), 71 (12), 70 (11), 57 (16).HRMS (EI): Calcd. for $C_{18}H_{20}O_3Se$: 364.05722; found: 364.056964.

Methyl 3-butyl-2-hydroxy-4,6-dimethyl-5-(phenylselanyl)benzoate (137e):

Starting with **136a** (0.491 g, 1.5 mmol) and **22h** (0.522 g, 1.65 mmol), **137a** was isolated after column chromatography (ethyl acetate/heptanes) as a pale yellowish oil (0.405g, 69%).



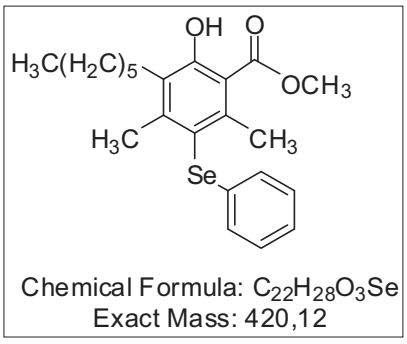
Chemical Formula: $C_{20}H_{24}O_3Se$
Exact Mass: 392,09

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.18 - 1.21 (m, 2 H, CH_2), 1.37 - 1.40 (m, 2 H, CH_2), 2.48 (s, 3 H, CH_3), 2.54 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 2.68 (s, 3 H, CH_3), 3.86 (s, 3 H, OCH_3), 6.86 - 6.96 (m, 2 H, 2 CH_{Ar}), 6.97-7.10 (m, 3 H, 3 CH_{Ar}), 11.15 (s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 21.8 (CH_3), 23.1 (CH_2), 24.6 (CH_3), 27.2, 31.2 (CH_2), 52.3 (OCH_3), 111.7, 123.6 (C_{Ar}), 125.3 (CH_{Ar}), 128.0 (2 CH_{Ar}), 128.5 (C_{Ar}), 129.1 (2 CH_{Ar}), 133.7, 143.2, 148.5 (C_{Ar}),

160.4 (COH), 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2953 (m), 2869 (w), 1728 (m), 1654 (s), 1577(m), 1545 (w), 1494 (w), 1475 (w), 1436 (s), 1374 (m), 1350 (m), 1277 (m), 1262 (m), 1233 (s), 1194 (m), 1157 (m), 1115 (m), 1080 (w), 1055 (w), 1021 (m), 997 (w), 963 (w), 895 (m), 852 (m), 807 (s), 731 (s), 688 (m), 665 (m), 631 (w), 575 (w).MS (GC-MS, 70 eV): 266 (29), 264 (65), 262 (30), 260 (10), 230 (10), 186 (13), 183 (12), 169 (14), 158 (15), 157 (37), 156 (10), 155 (22), 154 (10), 105 (17), 99 (100), 78 (23), 77 (24), 71 (52), 69 (10), 55 (14), 51 (11), 43 (71), 41 (22), 39 (10). HRMS (EI): Calcd. for M-H)$^-$:$C_{20}H_{23}O_3Se$: 391.08189; found: 391.08163.

Methyl 3-hexyl-2-hydroxy-4,6-dimethyl-5-(phenylselanyl)benzoate (137f):

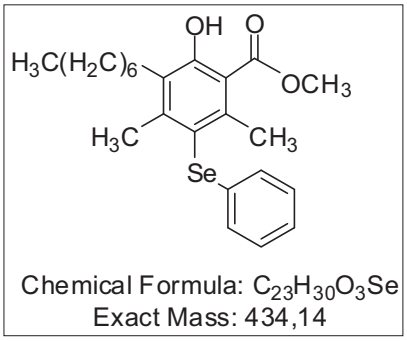
Starting with **136a** (0.491 g, 1.5 mmol) and **22j** (0.569 g, 1.65 mmol), **137f** was isolated after column chromatography (ethyl acetate/heptanes) as a yellowish oil (0.390 g, 62%).



^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.34-1.40 (m, 6 H, 3 CH_2), 1.50 - 1.55 (m, 2 H, CH_2), 2.61 (s, 3 H, CH_3), 2.78 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 2.81 (s, 3 H, CH_3), 4.00 (s, 3 H, OCH_3), 6.98 - 7.12 (m, 2 H, 2 CH_{Ar}), 7.16-7.27 (m, 3 H, 3 CH_{Ar}), 11.31 (s, 1 H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.0 (CH_3), 22.7 (CH_2), 24.8 (CH_3), 27.3, 28.9, 30.0, 31.9, (CH_2), 52.3 (OCH_3), 111.9, 123.6 (C_{Ar}), 125.4 (CH_{Ar}), 128.1 (2 CH_{Ar}), 128.6 (C_{Ar}), 129.2 (2 CH_{Ar}), 133.8, 143.3, 148.3 (C_{Ar}), 160.2 (COH), 172.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2952 (m), 2923 (m), 1747 (w), 1655 (s), 1575(m), 1541 (w), 1472 (w), 1435 (s), 1377 (m), 1347 (m), 1271 (m), 1227 (s), 1189(m), 1150 (m), 1117 (m), 1067 (w), 1056 (w), 1021 (m), 995 (w), 958 (w), 891 (m), 849 (m), 807 (s), 729 (s), 688 (m), 666 (m), 631 (w), 575 (w). HRMS (EI): Calcd. for $C_{23}H_{30}O_3Se$: 420.11636; found: 420.116371.

Methyl 3-heptyl-2-hydroxy-4,6-dimethyl-5-(phenylselanyl)benzoate (137g):

Starting with **136a** (0.491 g, 1.5 mmol) and **22k** (0.592g, 1.65 mmol), **137a** was isolated after column chromatography (ethyl acetate/heptanes) as a yellowish oil (0.403 g, 62%).

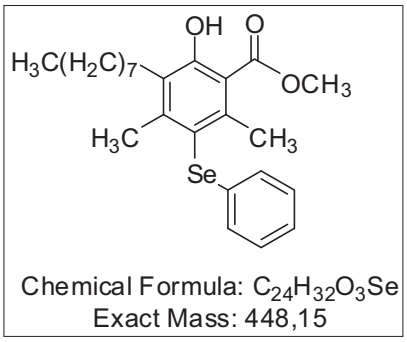


Chemical Formula: $C_{23}H_{30}O_3Se$
Exact Mass: 434,14

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.33 - 1.43 (m, 8 H, 4 CH_2), 1.52 - 1.56 (m, 2 H, CH_2), 2.63 (s, 3 H, CH_3), 2.80 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 2.84 (s, 3H, CH_3), 4.01 (s, 3H, OCH_3), 7.11 - 7.15 (m, 2 H, 2 CH_{Ar}), 7.18 - 7.28 (m, 3 H, 3 CH_{Ar}), 11.30 (s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 21.9 (CH_3), 22.6 (CH_2), 24.7 (CH_3),27.2, 28.9, 29.3, 29.9, 31.9, (CH_2), 52.2 (OCH_3), 111.8, 123.7 (C_{Ar}), 125.3 (CH_{Ar}), 128.0 (2 CH_{Ar}), 128.5 (C_{Ar}), 129.1 (2 CH_{Ar}), 133.8, 143.2, 148.4 (C_{Ar}), 160.3 (COH), 172.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 2952 (m), 2922 (m), 1749 (w), 1655 (s), 1577(m), 1545 (w), 1475 (w), 1437 (s), 1375 (m), 1350 (m), 1275 (m), 1229 (s), 1194 (m), 1158 (m), 1119 (m), 1067 (w), 1057 (w), 1021 (m), 997 (w), 958 (w), 895 (m), 852 (m), 807 (s), 731 (s), 688 (m), 666 (m), 631 (w), 575 (w).MS (GC-MS, 70 eV): 434 (M^+, 26), 432 (12), 402 (17), 318 (11), 239 (11), 214 (44), 211 (12), 196 (10), 172 (11), 158 (22), 153 (12), 141 (10), 140 (10), 130 (19), 129 (80), 117 (12), 116 (100), 101 (20), 99 (11), 98 (20), 97 (17), 96 (12), 85 (37), 83 (12), 71 (60), 69 (31), 59 (11), 57 (82), 56 (12), 55 (43), 43 (62), 41 (39). HRMS (EI): Calcd. for $C_{23}H_{30}O_3Se$: 434.13547; found: 434.135841.

Methyl 2-hydroxy-4,6-dimethyl-3-octyl-5-(phenylselanyl)benzoate (137h):

Starting with **136a** (0.491 g, 1.5 mmol) and **22l** (0.615 g, 1.65 mmol), **137h** was isolated after column chromatography (ethyl acetate/heptanes) as a yellowish oil (0.396 g, 59%).



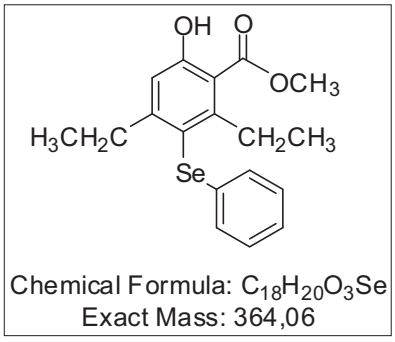
Chemical Formula: $C_{24}H_{32}O_3Se$
Exact Mass: 448,15

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.34 - 1.47 (m, 10 H, 5 CH_2), 1.51 - 1.57 (m, 2 H, CH_2), 2.62 (s, 3 H, CH_3), 2.82 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 2.82 (s, 3 H, CH_3), 4.03 (s, 3 H, OCH_3), 7.10 - 7.14 (m, 2 H, 2 CH_{Ar}), 7.17-7.29 (m, 3 H, 3 CH_{Ar}), 11.31 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 21.9 (CH_3), 22.7 (CH_2), 23.8 (CH_3), 27.5, 29.0, 29.5, 29.7, 30.0, 31. 8 (CH_2), 52.2 (OCH_3), 111.9, 123.8 (C_{Ar}), 125.4 (CH_{Ar}), 128.0 (2 CH_{Ar}), 128.6 (C_{Ar}), 129.2 (2 CH_{Ar}), 133.9, 143.2, 148.5 (C_{Ar}), 160.4 (COH), 172.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2952 (m), 2921 (s), 2851

(m), 1655 (s), 1577(m), 1545 (w), 1475 (w), 1437 (s), 1375 (m), 1351 (m), 1262 (m), 1231 (s), 1194 (m), 1157 (m), 1119 (m), 1065 (w), 1053 (w), 1021 (m), 998 (w), 962 (w), 895 (m), 847 (m), 807 (s), 731 (s), 688 (m), 666 (m), 614 (w), 597 (w). MS (GC-MS, 70 eV): 450 (10), 449 (11), 448 (M^+, 48), 446 (23), 418 (17), 416 (30), 414 (15), 401 (11), 399 (11), 371 (16), 359 (10), 329 (10), 326 (13), 325 (13), 323 (11), 318 (23), 317 (14), 316 (13), 315 (14), 292 (16), 288 (14), 287 (10), 279 (10), 260 (13), 246 (15), 245 (100), 243 (13), 239 (13), 237 (10), 197 (11), 196 (20), 195 (20), 175 (11), 163 (11), 162 (78), 161 (68), 160 (10), 155 (13), 135 (10), 134 (14), 133 (11), 116 (12), 105 (10), 103 (10), 97 (13), 91 (17), 85 (25), 79 (11), 78 (13), 77 (16), 71 (35), 69 (19), 67 (10), 57 (49), 55 (27), 43 (37), 41 (27). HRMS (EI): Calcd. for $C_{24}H_{32}O_3Se$: 448.151620; found: 448.15112.

Methyl 2,4-diethyl-6-hydroxy-3-(phenylselanyl)benzoate (137i):

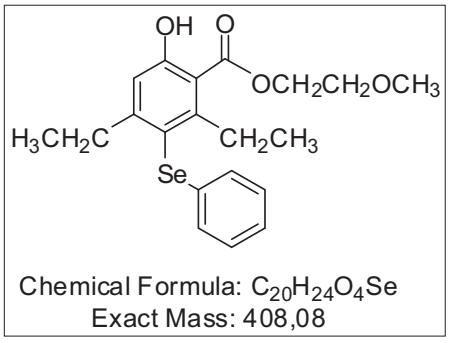
Starting with **136b** (0.533 g, 1.5 mmol) and **22a** (0.430 g, 1.65 mmol), **137i** was isolated after column chromatography (ethyl acetate/heptanes) as a colorless oil (0.305 g, 56%).



^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.98 - 1.05 (m, 6 H, 2 CH_3), 2.69 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.15 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.84 (s, 3 H, OCH_3), 6.77 (s, 1 H, CH_{Ar}), 6.85-6.89 (m, 2 H, 2 CH_{Ar}), 6.90 -7.04 (m, 3 H, 3 CH_{Ar}), 10.85 (s, 1 H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, 16.1 (CH_3), 30.1, 31.3 (CH_2), 52.5 (OCH_3), 111.8 (C_{Ar}), 116.1(CH_{Ar}), 121.6 (C_{Ar}), 125.3 (CH_{Ar}), 127.6, 129.1 (2 CH_{Ar}), 134.5, 152.7, 157.0 (C_{Ar}), 162.8 (COH), 171.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2964 (w), 2931 (w), 2871 (w), 1731 (w), 1657 (s), 1592 (m), 1577 (m), 1555 (w), 1475 (m), 1435 (m), 1347 (m), 1318 (m), 1302 (m), 1244 (m), 1216 (s), 1099 (s), 1067 (m), 1020 (m), 997 (w), 962 (w), 938 (m), 866 (m), 808 (m), 730 (s), 688 (m), 665 (w). MS (GC-MS, 70 eV): *m/z* (%): 366 (M^+, 13), 365 (13), 364 (63), 362 (33), 361 (12), 360 (12), 334 (20), 333 (21), 332 (100), 331 (13), 330 (51), 329 (20), 328 (19), 252 (10), 91 (12), 77 (11). HRMS (EI): Calcd. for $C_{18}H_{20}O_3Se$: 364.05722; found: 364.057718.

2-Methoxyethyl 2,4-diethyl-6-hydroxy-3-(phenylselanyl)benzoate (137j):

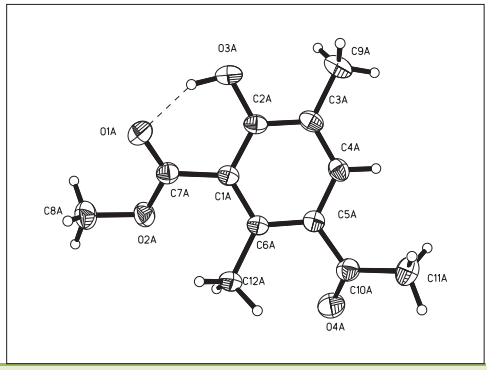
Starting with **136b** (0.533 g, 1.5 mmol) and **22b** (0.502 g, 1.65 mmol), **137j** was isolated after column chromatography (ethyl acetate/heptanes) as a pale yellowish solid m.p. 73-75 (0.336 g, 55%).



^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.91 - 1.01 (m, 6 H, 2 CH_3), 2.63 (q, ^3J = 7.4 Hz, 2 H, $PhCH_2$), 3.06 (q, ^3J = 7.5 Hz, 2 H, $PhCH_2$), 3.20 (s, 3 H, OCH_3), 3.51 - 3.54 (m, 2 H, CH_2), 4.30 - 4.34 (m, 2 H, CH_2), 6.69 (s, 1 H, CH_{Ar}), 6.83 - 6.88 (m, 2 H, 2 CH_{Ar}), 6.88 - 6.97 (m, 3 H, 3 CH_{Ar}), 10.39 (s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 16.3 (CH_3), 29.7, 31.2 (CH_2), 58.5 (CH_3), 64.0, 69.8 (CH_2), 112.5 (C_{Ar}), 116.1(CH_{Ar}), 121.6 (C_{Ar}), 125.2 (CH_{Ar}), 127.6, 129.1 (2 CH_{Ar}), 134.6, 152.8, 156.9 (C_{Ar}), 162.1 (COH), 170.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3399 (w), 3055 (w), 2964 (w), 2928 (w), 2872 (w), 1892 (w), 1777 (w), 1729 (m), 1656 (s), 1592 (m), 1577 (m), 1553 (w), 1475 (m), 1436 (m), 1398 (m), 1341 (m), 1298 (s), 1243 (m), 1216 (s), 1199 (s), 1185 (s), 1086 (s), 1020 (m), 998(w), 981 (w), 867 (m), 838 (m), 808 (m), 730 (s), 688 (s), 665 (m). MS (GC-MS, 70 eV): *m/z* (%): 408 (M^+, 25), 407 (27), 406 (100), 405 (16), 404 (52), 403 (20), 402 (19),330 (18), 329 (37),328 (61), 327 (47),326 (37),325 (38),324 (16),281 (18), 253 (10),249 (16),248 (17),247 (29),207 (21), 115 (13),91 (10),77 (15), 75 (37).HRMS (EI): Calcd. for $C_{20}H_{24}O_4Se$: 408.08343; found: 408.083839.

3.5 X-Ray crystal structural analysis:

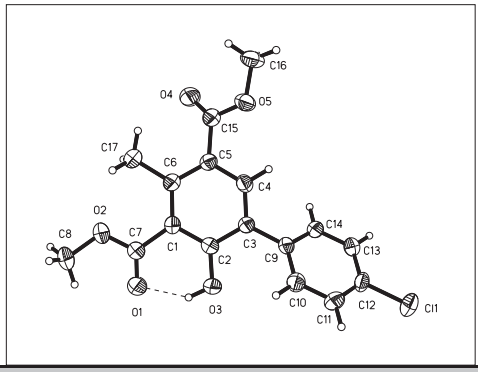
Table 24: Crystal data and structure refinement **110b**.



Empirical formula	$C_{12}H_{14}O_4$	
Formula weight	222.23	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 7.4507(4) Å	α= 77.052(4)°.
	b = 10.6081(6) Å	β= 78.918(3)°.
	c = 14.7549(9) Å	γ = 81.775(3)°.
Volume	1109.24(11) $Å^3$	
Z	4	
Density (calculated)	1.331 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	472	
Crystal size	0.59 x 0.15 x 0.05 mm^3	

ΘΘ range for data collection	1.44 to 30.65°.
Index ranges	-9≤h≤10, -15≤k≤15, -20≤l≤21
Reflections collected	29877
Independent reflections	6765 [R(int) = 0.0356]
Completeness to Θ = 30.65°	98.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9950 and 0.9435
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6765 / 0 / 305
Goodness-of-fit on F^2	1.017
Final R indices [I>2σ(I)]	R1 = 0.0503, wR2 = 0.1178
R indices (all data)	R1 = 0.0949, wR2 = 0.1407
Largest diff. peak and hole	0.325 and -0.228 e.$Å^{-3}$

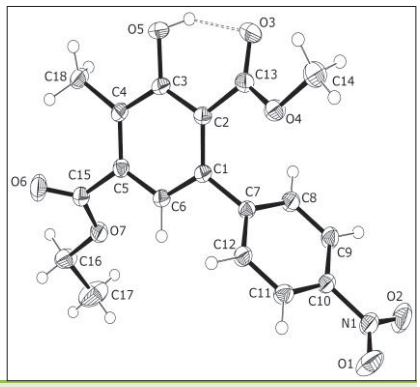
Table 25: Crystal data and structure refinement for **110k**.



Empirical formula	$C_{17}H_{15}ClO_5$	
Formula weight	334.74	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 4.0186(2) Å	α= 90°.
	b = 33.9422(15) Å	β= 98.435(3)°.
	c = 11.3074(5) Å	γ = 90°.
Volume	1525.65(12) $Å^3$	
Z	4	
Density (calculated)	1.457 Mg/m^3	
Absorption coefficient	0.274 mm^{-1}	
F(000)	696	
Crystal size	0.55 x 0.08 x 0.06 mm^3	
Θ range for data collection	2.18 to 24.54°.	
Index ranges	-4≤h≤4, -39≤k≤25, -13≤l≤13	
Reflections collected	8127	
Independent reflections	2550 [R(int) = 0.0781]	

Completeness to Θ = 24.54°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9837 and 0.8639
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2550 / 1 / 216
Goodness-of-fit on F^2	0.899
Final R indices [I>2σ(I)]	R1 = 0.0437, wR2 = 0.0895
R indices (all data)	R1 = 0.0857, wR2 = 0.1008
Largest diff. peak and hole	0.334 and -0.348 e.$Å^{-3}$

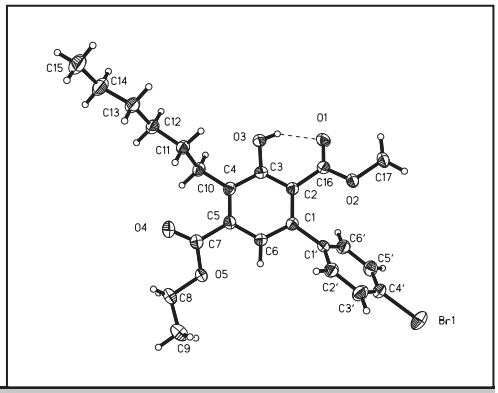
Table 26: Crystal data and structure refinement for **118h**.



Empirical formula	$C_{18}H_{17}NO_7$	
Formula weight	359.33	
Temperature	T = 173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	'P -1'	
Space group (Hall)	'-P 1'	
Unit cell dimensions	a = 7.7885(5)Å	α= 108.560(2)°.
	b = 11.1657(13)Å	β= 108.363(2)°.
	c = 11.2899(8) Å	γ = 97.584(2)°.
Volume	853.42(13) $Å^3$	
Z	2	
Density (calculated)	1.398Mg/m^3	
Absorption coefficient	0.109mm^{-1}	
F(000)	376	
Crystal size	0.73 × 0.35 × 0.17mm^3	
Θ range for data collection	2.0 to 30.0°.	
Index ranges	-10≤h≤10, -15≤k≤15, -15≤l≤15	
Reflections collected	13214	
Independent reflections	4870 [R(int) = 0.036]	

Completeness to Θ = 29.00°	98.3%
Absorption correction	multi-scan (*SADABS*; Sheldrick, 2004)
Max. and min. transmission	0.925and 0.982
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4102 / 0 / 242
Goodness-of-fit on F^2	1.10
Final R indices [I>2σ(I)]	R1 = 0.046, wR2 = 0.137
R indices (all data)	R1 = 0.0541, wR2 = 0.144
Largest diff. peak and hole	0.428 and -0.321 e.$Å^{-3}$

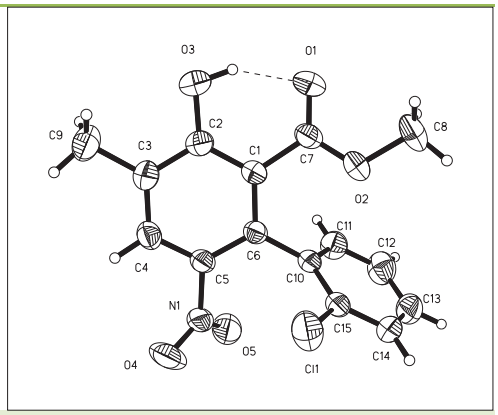
Table 27: Crystal data and structure refinement for **118m.**



Empirical formula	$C_{23}H_{27}BrO_5$	
Formula weight	463.36	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 4.6786(2) Å	α= 70.466(2)°.
	b = 15.1674(6) Å	β= 87.482(3)°.
	c = 16.2811(7) Å	γ = 88.334(2)°.
Volume	1087.67(8) $Å^3$	
Z	2	
Density (calculated)	1.415 Mg/m^3	
Absorption coefficient	1.920 mm^{-1}	
F(000)	480	
Crystal size	0.66 x 0.10 x 0.09 mm^3	
Θ range for data collection	4.61 to 30.00°.	
Index ranges	-6≤h≤6, -21≤k≤21, -22≤l≤22	
Reflections collected	22474	

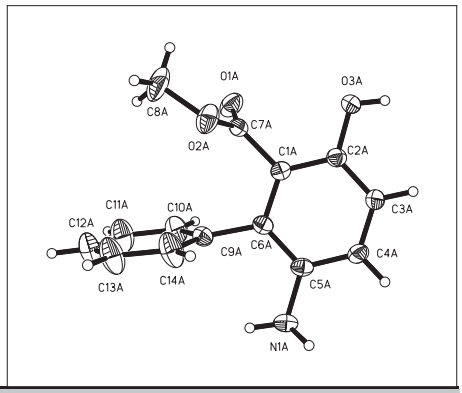
Independent reflections	6209 [R(int) = 0.0375]
Completeness to Θ = 30.00°	97.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8461 and 0.3638
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6209 / 0 / 269
Goodness-of-fit on F^2	1.007
Final R indices [I>2σ(I)]	R1 = 0.0395, wR2 = 0.0810
R indices (all data)	R1 = 0.0813, wR2 = 0.0969
Largest diff. peak and hole	0.385 and -0.316 e.$Å^{-3}$

Table 28: Crystal data and structure refinement for **132i**.

Empirical formula	$C_{15}H_{12}ClNO_5$	
Formula weight	321.71	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group (H.-M.)	$P\bar{1}$	
Space group (Hall)	-P 1	
Unit cell dimensions	a = 8.0110(2) Å	α= 98.145(2)°.
	b = 9.6287(3) Å	β= 107.553(2)°.
	c = 10.6550(3) Å	γ = 103.766(2)°.
Volume	740.61(4) Å3	
Z	2	
Density (calculated)	1.443 Mg/m3	
Absorption coefficient	0.281 mm-1	
F(000)	332	
Crystal size	0.98 x 0.96 x 0.41 mm3	
Θ range for data collection	2.67 to 30.00°.	
Index ranges	-11≤h≤11, -13≤k≤13, -14≤l≤14	
Reflections collected	23731	

Independent reflections	4287 [R(int) = 0.0176]
Completeness to Θ = 30.00°	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8935 and 0.7704
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4287 / 0 / 206
Goodness-of-fit on F2	1.060
Final R indices [I>2σ(I)]	R1 = 0.0406, wR2 = 0.1132
R indices (all data)	R1 = 0.0485, wR2 = 0.1272
Extinction coefficient	0.012(4)
Largest diff. peak and hole	0.291 and -0.373 e.Å-3

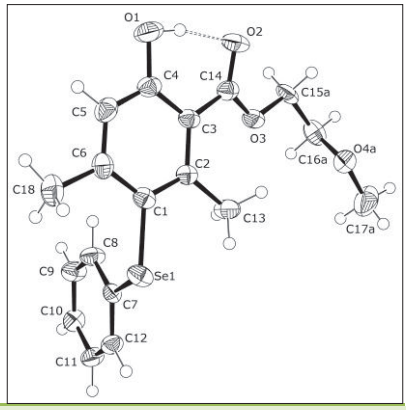
Table 29: Crystal data and structure refinement for **133a**.



Empirical formula	$C_{14}H_{13}NO_3$	
Formula weight	243.25	
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 = 25.215(5) Å	α= 90°.
	b = 7.6790(15) Å	β= 91.99(3)°.
	c = 25.030(5) Å	γ = 90°.
Volume	4843.5(17) $Å^3$	
Z	16	
Density (calculated)	1.334 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	2048	
Crystal size	0.7 x 0.26 x 0.14 mm^3	
Θ range for data collection	2.87 to 30.00°.	
Index ranges	-34≤h≤35, -10≤k≤10, -35≤l≤35	
Reflections collected	52571	

Independent reflections	14030 [R(int) = 0.0390]
Completeness to Θ = 30.00°	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9877 and 0.9406
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	14030 / 0 / 689
Goodness-of-fit on F^2	1.087
Final R indices [I>2σ(I)]	R1 = 0.0626, wR2 = 0.1539
R indices (all data)	R1 = 0.0872, wR2 = 0.1719
Largest diff. peak and hole	0.504 and -0.305 e.$Å^{-3}$

Table 30: Crystal data and structure refinement for **137b**.



Empirical formula	$C_{18}H_{20}O_4Se$	
Formula weight	M_r = 379.30	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group (H.-M.)	$P2_1/n$	
Space group (Hall)	-P 2yn	
Unit cell dimensions	a = 11.593 (2) Å	α= 90.00°.
	b = 17.836 (4) Å	β= 94.40 (3)
	c = 16.587 (3) Å	γ = 90.00°.
Volume	3419.4 (12) $Å^3$	
Z	8	
Density (calculated)	1.474 Mg m^{-3}	
Absorption coefficient	2.213 mm^{-1}	
F(000)	1552	
Crystal size	0.58 × 0.34 × 0.09 mm^3	
Θ range for data collection	4.2°° to 29.0°.	
Index ranges	-15≤h≤10, -15≤k≤24, -22≤l≤22	

Reflections collected	35127
Independent reflections	8942 [R(int) = 0.041]
Completeness to Θ = 29.00°	98.4%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.826and 0.360
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6553 / 0/ 454
Goodness-of-fit on F^2	1.07
Final R indices [I>2σ(I)]	R1 = 0.042, wR2 = 0.0984
R indices (all data)	R1 = 0.0696, wR2 = 0.105
Largest diff. peak and hole	1.09and −0.71 e.$Å^{-3}$

References:

[1]. (a) J. Sheehan, K. Henery-Logan, *J. Am. Chem. Soc.* **1957**, *79*, 1262; (b) J. Sheehan, K. Henery-Logan, *J. Am. Chem. Soc.* **1959**, *81*, 3089.

[2]. (a) K. Nicolaou, S. Natarajan, H. Li, N. Jain, R. Hughes, M. Solomon, J. Ramanjulu, C. Boddy, M. Takayanagi, *Angew. Chem.* **1998**, *110*, 2872; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 2708; (b) K. Nicolaou, N. Jain, S. Natarajan, R. Hughes, M. Solomon, H. Li, J. Ramanjulu, M. Takayanagi, A. Koumbis, T. Brando, *Angew. Chem.* **1998**, *110*, 2879; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 2714; (c) K. Nicolaou, M. Takayanagi, N. Jain, S. Natarajan, M. Takayanagi, A. Koumbis, T. Brando, J. Ramanjulu, *Angew. Chem.* **1998**, *110*, 2881; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 2717.

[3]. (a) D. Evans, M. Wood, B. Trotter, T. Richardson, J. Barrow, J. Katz, *Angew. Chem.* **1998**, *110*, 2864; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 2700; (b) D. Evans, C. Dinsmore, P. Watson, M. Wood, T. Richardson, B. Trotter, J. Katz, *Angew. Chem.* **1998**, *110*, 2868; *Angew. Chem.*, *Int. Ed. Engl.* **1998**, *37*, 2704.

[4]. R. Holton, C. Somoza, H. Kim, F. Liang, R. Biediger, P. Boatman, M. Shindo, C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1597.

[5]. R. Holton, H. Kim, C. Somoza, F. Liang, R. Biediger, P. Boatman, M. Shindo, C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1599.

[6]. R. Holton, R. Juo, H. Kim, A. Williams, S. Harusawa, R. Lowenthal, S. Yogai, *J. Am. Chem. Soc.* **1988**, *110*, 6558.

[7]. D. Astruc, *Modern Arene Chemistry*, Wiley-VCH: Weinheim, Germany, **2002**.

[8]. For a review, see: S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901.

[9]. J. Richard and J. Hehdrickson, *The biosynthesis of steroids, terpenes and acetogenins*, Banjamin, Newyork, USA, **1964**.

[10]. T. Harris, C. Harris, *Tetrahedron*, **1977**, *33*, 2159.

[11]. T. Okabayashi, A. Iida, K. Takai, Y. Nawate, T. Misaki, Y. Tanabe, *J. Org. Chem.* **2007**, *72*, 8142.

[12]. K. Takai, Y. Nawate, T. Okabayashi, H. Nakatsuji, A. Iida, Y. Tanabe, *Tetrahedron*, **2009**, *65*, 5596.

[13]. K. Kraegloh, G. Simchen, *Synthesis*, **1981**, 30.

[14]. (a) T. Chan and P. Brownbridge, *J. Am. Chem. Soc.* **1980**, *102*, 3534; (b) G. Molander, K. Cameron, *J. Am. Chem. Soc.* **1993**, *115*, 830; (c) H. Hagiwara, K. Kimura, H. Uda, *J. Chem. Soc.*, *Chem. Commun.* **1986**, 860; (d) D. Cameron, G. Feutrill, P. Perlmutter, *Aust. J. Chem.* **1982**, *35*, 1469.

[15]. A. Barbero, C. Garcia, B. Gonzalez, F. Pulido, J. Rincon, *Synthesis*, *1997*, 628.

[16]. A. Barbero, F. Pulido, *Synthesis*, **2004**, 401.

[17]. T. Chan, P. Brownbridge, *Tetrahedron*, **1981**, *37*, 387.
[18]. (a) V. Nguyen, E. Bellur, B. Appel, P. Langer, *Synthesis*, **2006**, 2865; (b) V. Nguyen, E. Bellur, B. Appel, P. Langer, *Synthesis*, **2006**, 1103.
[19]. M. Rashid, N. Rasool, M. Adeel, H. Reinke, C. Fischer, P. Langer, *Tetrahedron,* **2008**, *64*, 3782.
[20]. M. Rashid, H. Reinke, P. Langer, *Tetrahedron Lett*. **2007**, *48*, 2321.
[21]. M. Rashid, N. Rasool, M. Adeel, C. Fischer, H. Reinke, A. Spannenberg, P. Langer, *Tetrahedron*, **2008**, *64*, 529.
[22]. M. Adeel, M. Rashid, N. Rasool, R. Ahmad, A. Villinger, H. Reinke, C. Fischer, P. Langer, *Synthesis*, **2009**, 243.
[23]. P. Brownbridge, T. Chan, *Tetrahedron Lett*. **1979**, *46*, 4437.
[24]. S. Hucken, *Ph.D. Thesis*, University of British Columbia, **1973**.
[25]. T. Chan, P. Brownbridge, *J. C. S. Chem. Comm*. **1979**, 578.
[26]. T. Mukaiyama, K. Banno, V. Narasaka, *J. Am. Chem. Soc*. **1974**, *96*, 7503.
[27]. See, review: P. Langer, Synthesis, **2002**, 441.
[28]. E. Colvin, *Chem. Soc. Rev.* **1978**, *7*, 15.
[29]. (a) G. Anderson, D. Cameron, G. Feutrill, R. Read, *Tetrahedron Lett*. **1981**, *22*, 4347; (b) For a 1,3 O-C silyl rearrangement, see: E. Corey, C. Rücker, *Tetrahedron Lett*. **1984**, 4345; (c) K. Yamamoto, S. Suzuki, J. Tsuji, *Chem. Lett.* **1978**, 649.
[30]. P. Brownbridge, T. Chan M. Brook G. Kang, *Can. J. Chem*. **1983**, *61*, 688.
[31]. S. Inaba, I. Ojima, *Tetrahedron Lett*. **1977**, 3634.
[32]. K. Hirai, I. Ojima, *Tetrahedron Lett*. **1977**, 785.
[33]. Reviews (a) P. Langer, *Chem. Eur. J*. **2001**, *7*, 3858; (b) P. Langer, W. Freiberg, *Chem. Rev*. **2004**, *104*, 4125.
[34]. Review: P. Langer, M. Doring, Eur. *J. Org. Chem*. **2002**, 221.
[35]. Reviews: (a) P. Langer, *Synlett*, **2006**, 3369; (b) H. Feist, P. Langer, Synthesis, **2007**, 327; (c) P. Langer, *Synlett*, **2007**, 1016; (d) P. Langer, *Eur. J. Org. Chem.* **2007**, 2233.
[36]. M. Lubbe, R. Klassen, T. Trabhardt, A. Villinger, P. Langer, *Synlett*, **2008**, 2331.
[37]. M. Lubbe, J. P. Gütlein, H. Reinke, P. Langer, *Synlett*, **2008**, 2671.
[38]. M. Lau, P. Langer, *Tetrahedron Lett*. **2008**, *49*, 5618.
[39]. M. Sher, P. Langer, *Synlett*, **2008**, 1050.
[40]. O. Fatunsin, V. Iaroshenko, S. Dudkin, S. Mkrtchyan, A. Villinger, P. Langer, *Tetrahedron Lett*. **2010**, 51, 4693.
[41]. P. Brownbridge, T. Chan, M. Brook, G. Kang, *Can. J. Chem.* **1983**, *61*, 688.
[42]. S. Reim, M. Lau, M. Adeel, I. Hussain, M. Yawer, A. Riahi, Z. Ahmed, C. Fischer, H. Reinke, P. Langer, *Synthesis*, **2009**, 445.
[43]. R. Ahmad, A. Riahi, P. Langer, *Tetrahedron Lett*. **2009**, *50*, 1490.

[44]. (a) O. Fatunsin, M. Shkoor, A. Riahi, R. Dede, H. Reinke, P. Langer, *Synlett*, **2009**, 201; (b) A. Riahi, O. Fatunsin, M. Shkoor, R. Dede, H. Reinke, C. Fischer, P. Langer, *Synthesis*, **2009**, 1623.

[45]. A. Ali, I. Ullah, M. Sher, A. Villinger, P. Langer, *Tetrahedron Lett*. **2009**, *50*, 118.

[46]. J. Hefner, P. Langer, *Tetrahedron Lett*. **2008**, *49*, 2262.

[47]. (a) I. Hussain, M. Yawer, M. Lau, T. Pundt, C. Fischer, H. Reinke, H. Görls, P. Langer, *Eur. J. Org. Chem.* **2008**, 503; (b) T. Pundt, M. Lau, I. Hussain, M. Yawer, H. Reinke, P. Langer, *Tetrahedron Lett*. **2007**, *48*, 2745.

[48]. (a) Z. Ahmed, P. Langer, *Tetrahedron Lett*. **2006**, *47*, 417; (b) M. Sher, Z. Ahmed, M. Rashid, C. Fischer, A. Spannenberg, P. Langer, *Tetrahedron*, **2007**, *63*, 4929; (c) Z. Ahmed, P. Langer, *Synlett*, **2006**, 3361; (d) M. Yawer, I. Hussain, S. Reim, Z. Ahmed, E. Ullah, I. Iqbal, C. Fischer, H. Reinke, H. Görls, P. Langer, *Tetrahedron*, **2007**, *63*, 12562.

[49]. R. Dede, P. Langer, *Tetrahedron Lett*. **2004**, *45*, 9177.

[50]. Z. Ahmed, C. Fischer, A. Spannenberg, P. Langer, *Tetrahedron*, **2006**, *62*, 4800.

[51]. (a) A. Riahi, M. Shkoor, O. Fatunsin, M. Lubbe, H. Reinke, P. Langer, *Tetrahedron Lett.* **2009**, *50*, 115; (b) M. Shkoor, A. Riahi, O. Fatunsin, H. Reinke, C. Fischer, P. Langer, *Synthesis,* **2009**, 2223.

[52]. (a) A. Riahi, M. Shkoor, O. Fatunsin, R. Khera, C. Fischer, P. Langer, *Org. Biomol. Chem.* **2009**, *7*, 4248; (b) M. Lubbe, Ph.D dissertation, University of Rostock, **2009**.

[53]. O. Fatunsin, M. Shkoor, S. Toguem, A. Riahi, O. Aiyelaagbe, E. Akintayo, C. Fischer, P. Langer, *Synlett*, **2010**, 1963.

[54]. O. Fatunsin, M. Shkoor, A. Riahi, M. Hussain, M. Sher, A. Villinger, C. Fischer, P. Langer, *Helv. Chim. Acta,* **2010**, *93*, 1610.

[55]. O. Fatunsin, M. Shkoor, A. Riahi, P. Langer, *Synlett*, **2010**, 1525.

[56]. T. Mukaiyama, *Angew. Chem.* **1977**, *89*, 858; *Angew. Chem.*, *Int. Ed. Engl.* **1977**, *16*, 817.

[57]. For reviews of chelation control in Lewis acid-mediated reactions, see: (a) H. Yamamoto, *Lewis Acid Chemistry*: *A Practical Approach*, Oxford University Press: Oxford, **1999**; (b) R. Mahrwald, *Chem. Rev*. **1999**, *99*, 1095; (c) M. Santelli, J. Pons, *Lewis Acids and Selectivity in Organic Synthesis*, CRC Press: Boca Raton, **1996**; (d) S. Shambayati, S. Schreiber, *In Comprehensive Organic Synthesis*, B. Trost, I. Fleming, Eds. Pergamon, Oxford, **1991**, Vol. 1, 283.

[58]. Chelation control has been reported for the [4 + 3] annulation reaction of benzyloxy-substituted 1,4-dicarbonyl compounds with bis(silyl enol ethers): G. Molander, P. Eastwood, *J. Org. Chem*. **1996**, *61*, 1910.

[59]. J. Hefner, P. Langer, *Tetrahedron Lett*. **2008**, *49*, 4470.
[60]. V. Karapetyan, S. Mkrtchyan, J. Hefner, C. Fischer, P. Langer, *J. Org. Chem.* **2010**, 75, 809.
[61]. V. Karapetyan, S. Mkrtchyan, G. Ghazaryan, A. Villinger, C. Fischer, P. Langer, *Tetrahedron*, **2009**, *65*, 9271.
[62]. A. Bunescu, S. Reimann, M. Lubbe, A. Spannenberg, P. Langer, *J. Org. Chem.* **2009**, *74*, 5002.
[63]. R. Taylor, *Electrophilic Aromatic Substitution*, Wiley, New York, **1990.**
[64]. J. Zoltewicz, *Top. Curr. Chem.* **1975**, *59*, 33.
[65]. J. Hassan, M. Se´vignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359.
[66]. W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673 and references cited therein
[67]. (a) K. Dötz, P. Tomuschat, *Chem. Soc. Rev.* **1999**, *28*, 187; (b) H. Wang, J. Huang, W. Wulff, A. Rheingold, *J. Am. Chem. Soc.* **2003**, *125*, 8980; (c) A. Vorogushin, W. Wulff, H. Hansen, *J. Am. Chem. Soc*. **2002**, *124*, 6512.
[68]. (a) R. Danheiser, R. Brisbois, J. Kowalczyk, R. Miller, *J. Am. Chem. Soc.* **1990**, *112*, 3093; (b) R. Danheiser, S. Gee, *J. Org. Chem*. **1984**, *49*, 1672.
[69]. (a) Z. Xi, K. Sato, Y. Gao, J. Lu, T. Takahashi, *J. Am. Chem. Soc*. **2003**, *125*, 9568; (b) T. Takahashi, M. Ishikawa, S. Huo, *J. Am. Chem. Soc*. **2002**, *124*, 388.
[70]. (a) L. Bonaga, H. Zhang, A. Moretto, H. Ye, D.Gauthier, J. Li, G. Leo, B. Maryanoff, *J. Am. Chem. Soc*. **2005**, 127, 3473; (b) For a selected review, see, ref. [8].
[71]. (a) N. Asao, T. Nogami, S. Lee, Y. Yamamoto, *J. Am. Chem. Soc*. **2003**, *125*, 10921; (b) N. Asao, K. Takahashi, S. Lee, T. Kasahara, Y. Yamamoto, *J. Am. Chem. Soc*. **2002**, *124*, 12650; (c) N. Asao, H. Aikawa, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 7458.
[72]. (a) S. Serra, C. Fuganti, A. Moro, *J. Org. Chem*. **2001**, *66*, 7883; (b) P. Turnbull, H. Moore, *J. Org. Chem*. **1995**, *60*, 644.
[73]. (a) X. Bi, D. Dong, Q. Liu, W. Pan, L. Zhao, B. Li, *J. Am. Chem. Soc*. **2005**, *127*, 4578; (b) O. Barun, S. Nandi, K. Panda, H. Ila, H. Junjappa, *J. Org. Chem.* **2002**, *67*, 5398.
[74]. M. Lee, K. Lee, S. Gowrisankar, J. Kim, *Tetrahedron Lett*. **2006**, *47*, 1355.
[75]. (a) *Römpp Lexikon Naturstoffe* (W. Steglich, B. Fugmann, S. Lang-Fugmann, eds.), Thieme, Stuttgart, **1997**; (b) S. Cabiddu, C. Fattuoni, C. Floris, G. Gelli, S. Melis, F. Sotgiu, *Tetrahedron*, **1990**, *46*, 861; (c) R. Fusco, F. Sannicolo, *J. Org. Chem.* **1981**, *46*, 83; (d) J. Pinhey, P. Xuan, *Aust. J. Chem.* **1988**, *41*, 69; (e) W. Bonner, J. De Graw, *Tetrahedron,* **1962**, *18*, 1295.

[76]. (a) G. Chesher, H. Collier, F. Robinson, E. Taylor, S. Hunt, J. Jones, A. Lindsey, *Nature*, **1955**, *175*, 206; (b) E. Piscopo, M. Diurno, M. Cataldi, G. Scala, F. Aliberti, *Boll. Soc. Ital. Biol. Sper*. **1985**, *61*, 199; Chem. Abstr. 103:51071; (c) O. Maksimov, M. Khasina, *Lekarstvennye Sredstva Dal'nego Vostoka*, **1972**, *11*, 140; Chem. Abst. 84:12952; (d) Y. Hiraiwa, M. Ida, T. Kudo, T. Morinaka, K. Chikauchi, K. Mori, *Metallo-β-lactamase inhibitor*, Patent. No. WO 2008016007; Chem. Abstr. 148:246360; (e) T. Iwasaki, K. Kondo, T. Nishitani, T. Kuroda, K. Hirakoso, A. Ohtani, K. Takashima, *Chem. Pharm. Bull*. **1995**, *43*, 1701.

[77]. See ref. [71] and (a) A. Birch, J. Wright, *J. Aust. J. Chem.* **1969**, *22*, 2635; (b) K. Parker, D. Spero, K. Koziski, *J. Org. Chem.* **1987**, *52*, 183; (c) R. Hill, R. Carlson, *J. Org. Chem.* **1965**, *30*, 2414.

[78]. (a) K. Nicolaou, C. Claiborne, K. Paulvannan, M. Postema, R. Guy, *Chem. Eur. J.* **1997**, *3*, 399; (b) O. House, C. B. Hudson, *J. Org. Chem.* **1970**, *35*, 647; (c) J. Elix, D. Chester, K. Gaul, J. Parker, J. Wardlaw, *Aust. J. Chem.* **1989**, *42*, 1191; (d) J. Elix, C. Barclay, J. Wardlaw, A. Archer, S. Yu, G. Kantvilas, *Aust. J. Chem.* **1999**, *52*, 837.

[79]. (a) T. Iijima, T. Yamaguchi, *Journal of Molecular Catalysis A: Chemical*, **2008**, *295*, 52; (b) Y. Suzuki, T. Hattori, T. Okuzawa, S. Miyano, *Chem. Lett.* **2002**, *31*, 102 and references therein; (c) B. Chen, M. Bednarz, J. Sundeen, Z. Zhang, T. Caulfield, G. Bisacchi, *Organic Preparations and Procedures International*, **1999**, *31*, 106.

[80]. (a) J. Ritter, *Process for the preparation of hydroxy aromatic acids by treatment of halogenated aromatic acids with aqueous base in the presence of a copper source and an amine ligand***.** Patent No. US7335791, **2008**; Chem. Abstr. 148:284903; (b) J. Ritter, *Process for the synthesis of hydroxy aromatic acids*, Patent No. US 20080125604, **2008**; Chem. Abst. 149:11996; (c) Y. Miura, E. Torres, C. Panetta, *J. Org. Chem.* **1988**, *53*, 439.

[81]. K. Fujimoto, Y. Tokuda, H. Maekawa, Y. Matsubara, T. Mizuno, I. Nishiguchi, *Tetrahedron*, **1996**, *52*, 3889.

[82]. Y. Yasuhara, T. Nishimura, T. Hayashi, *Chem. Comm*. **2010**, *46*, 2130.

[83]. (a) A. Zuniga, L. Sanchez, L. Maldonado, M. Ortega, J. Zarraga, *Synthesis*, **2005**, 2293; (b) A. Zuniga, L. Maldonado, E. Barrios, A. Lucas, *Synth. Commun.* **1998**, *28*, 3461.

[84]. M. Tabouzat, A. El Louzi, M. Ahmar, B. Cazes, *Synlett*, **2009**, 1405.

[85]. N. Ramesh, G. Rajeshwaran, A. Mohanakrishnan, *Tetrahedron,* **2009**, *65*, 3592.

[86]. A. Sharma, J. Pandey, R. Tripathi, *Tetrahedron Lett*. **2009**, *50*, 1812.

[87]. K. Hirofumi, I. Hironori, *Chinese Journal of Chemistry*, **2008**, *26*, 1944.

[88]. S. Hegde, R. Bryant, *Synth. Commun.* **1993**, *23*, 2753.

[89]. G. Posner, E. Shulman-Roskes, *J. Org. Chem.* **1989**, *54*, 3514.
[90]. M. Nantz, P. Fuchs, *Synth. Commun.* **1987**, *17*, 761.
[91]. L. Deady, D. Werden, *J. Org. Chem.* **1987**, *52*, 3930.
[92]. (a) C. Cox, T. Siu, S. Danishefsky, *Angew. Chem.* **2003**, *115*, 5783; *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 5625; (b) P. Langer, B. Kracke, *Tetrahedron Lett*. **2000**, *41*, 4545.
[93]. J. Moore, M. York, J. Harrity, *Synlett*, **2005**, 860.
[94]. (a) T. Chan, C. Prasad, *J. Org. Chem.* **1986**, *51*, 3012; (b) I. Iqbal, M. Imran, P. Langer, *Synthesis*, **2009**, 2430; (c) G. Kang, T. Chan, *Can. J. Chem.* **1985**, *63*, 3102.
[95]. See, *for example*, (a) I. Medimagh, S. Marque, D. Prim, S. Chatti, *Heterocycles*, **2009**, *78*, 679; (b) R. Ram, N. Kumar, *Tetrahedron*, **2008**, *64*, 10267; (c) R. Ram, N. Kumar, *Tetrahedron Lett*. **2008**, *49*, 799; (d) V. Nair, K. Abhilash, *Synthesis*, **2005**, 1967; (e) A. Moreno, M. Gomez, E. Vazquez, A. Hoz, A. Ortiz, P. Prieto, J. Mayoral, E. Pires, *Synlett*, **2004**, 1259; (f) A. Padwa, C. Straub, *J. Org. Chem.* **2003**, *68*, 227; (g) M. Bobosiková, W. Clegg, S. Coles, M. Dandárová, M. Hursthouse, T. Kiss, A. Krutosiková, T. Liptaj, N. Prónayová, C. Ramsden, *J. Chem. Soc. Perkin Transactions 1*, **2001**, *7*, 680; (h) A. Amarasekara, W. Pathmasiri, *Bulletin of the Chemical Society of Japan*, **2000**, *73*, 395; (i) A. Padwa, M. Dimitroff, A. Waterson, T. Wu, *J. Org. Chem.* **1997**, *62*, 4088.
[96]. (a) T. Komiyama, Y. Takaguchi, S. Tsuboi, *Synth. Commun.* **2007**, *37*, 531; (b) K. Iio, A. Okajima, Y. Takeda, K. Kawaguchi, B. Whelan, S. Akai, Y. Kita, *Arkivoc*, **2003**, *8*, 144; (c) J. Epsztajn, A. Jozwiak, A. Szczesniak, *J. Chem. Soc. Perkin Transactions 1: Organic and Bio-Organic Chemistry*, **1998**, *16*, 2563; (c) F. Smith, R. Atigadda, *Journal of Heterocyclic Chemistry*, **1991**, *28*, 1813; (d) T. Ziegler, M. Layh, F. Effenberger, *Chem. Ber.* **1987**, *120*, 1347; (e) A. Allen, P. Marquand, R. Burton, K. Villeneuve, W. Tam, *J. Org. Chem.* **2007**, *72*, 7849; (f) P. Vogel, B Willham, H. Prinzbach, *Helv. Chim. Acta* **1969**, *52*, 584.
[97]. J. Loebach, M. Bennet, R. Danheiser, *J. Org. Chem.* **1998**, *63*, 8380.
[98]. N. Darbasie, W. Schnatter, K. Warner, N. Manolache, *Tetrahedron Lett*. **2006**, *47*, 963 and references therein.
[99]. J. Barluenga, F. Aznar, I. Gutiérrez, A. Martín, S. García-Granda, M. Baragaño, *J. Am. Chem. Soc.* **2000**, *122*, 1314.
[100]. N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, NewYork, **2001**.
[101]. (a) S. Dahl, A. Kaplen, *J. Am. Leather Chem. Assoc*. **1958**, *53*, 103; (b) C. Li, S. Taneda, A. Suzuki, C. Furuta, G. Watanabe, K. Taya, *Eur. J. Pharmacol.* **2006**, *543*, 194; (c) K. Yoki, K. Kamata, N. Toda, H. Hayashi, K. Seki, S. Taneda, S. Yoshino, A. Sakushima, M. Sakata, A. Suzuki, *Biol. Pharm. Bull.*

2003, *26*, 394; (d) N. Bitsch, C. Dudas, W. Koerner, K. Failing, S. Biselli, G. Rimkus, H. Brunn, *Arch. Environ. Contam. Toxicol.* **2002**, *43*, 257; (e) K. Ramkumar, E. Serrao, S. Odde, N. Neamati, *Medicinal Research Reviews*, *HIV-1 integrase inhibitors: 2007-2008 update*, **2010**, *30*, 6, 890; (f) A. Api, R. Gudi, *Mutat. Res.* **2000**, *464*, 263; (g) L. Lehman-McKeeman, D. Caudill, J. Vassallo, R. Pearce, A. Madan, A. Parkinson, *Toxicol. Lett.* **1999**, *111*, 105.

[102]. (a) D. Zhao, N. Wu, S. Zhang, P. Xi, X. Su, J. Lan, J. You, *Angew. Chem.* **2009**, *121*, 8885; *Angew. Chem., Int. Ed. Engl.* **2009**, *48*, 8729; (b) A. Tlili, N. Xia, F. Monnier, M. Taillefer, *Angew. Chem.* **2009**, *121*, 8881; *Angew. Chem., Int. Ed. Engl.* **2009**, *48*, 8725; (c) A. Sergeev, T. Schulz, C. Torborg, A. Spannenberg, H. Neumann, M. Beller, *Angew. Chem.* **2009**, *121*, 9555; *Angew. Chem., Int. Ed. Engl.* **2009**, *48*, 7595; (d) M. Makosza, K. Sienkiewicz, *J. Org. Chem.* **1998**, *63*, 4199.

[103]. T. Brose, F. Holzscheiter, G. Mattersteig, W. Pritzkow, V. Voerckel, *Journal für Praktische Chemie/Chemiker-Zeitung*, **1992**, *334*, 497.

[104]. G. Suboch, E. Belyaev, *Pharmaceutical Chemistry Journal*, **2000**, *34*, 215 and references therein

[105]. (a) P. Zeegers, *J. Chem. Edu.* **1993**, *70*, 1036; (b) L. Delaude, P. Laszlo, K. Smith, *Acc. Chem. Res.* **1993**, *26*, 607; (c) H. Pervas, S. Onysiuka, L. Rees, J. Rooney, G. Suckling, *Tetrahedron*, **1988**, *44*, 4555; (c) H. Firouzabadi, N. Iranpoor, M. Zolfigol, *Synth. Commun.* **1997**, *27*, 3301; (d) N. Iranpoor, H. Firouzabadi, M. Zolfigol, *Synth. Commun.* **1998**, *28*, 2773; (e) M. Zolfigol, N. Iranpoor, H. Firouzabadi, *Orient. J. Chem.* **1998**, *14*, 369 and references cited therein; (f) R. Maleski, *Synth. Commun.* **1995**, *25*, 2327 and references cited therein; (g) B. Beake, R. Moodie, *J. Chem.* Soc. *Perkin Trans. 2*, **1998**, *1*, 1 and references cited therein; (h) G. Subach, E. Belyaev, *Russ. J. Org. Chem.* **1998**, *34*, 288; (i) R. Rajagopal, K. Srinivasan, *Synth. Commun*. **2003**, *33*, 961; (j) A. Zolfigol, E. Madrakian, E. Ghaemi, *Synlett*. **2003**, 2222; (k) A. Hajipour, A. Ruoho, *Tetrahedron Lett*. **2005**, *46*, 8307; (l) J. Selvam, V. Suresh, K. Rajesh, S. Reddy, Y. Venkateswarlu, *Tetrahedron Lett*. **2006**, *47*, 2507; (m) V. Anuradha, P. Srinivas, P. Aparna, J. Rao, *Tetrahedron Lett*. **2006**, *47*, 4933; (n) W. Yin, M. Shi, *Tetrahedron*, **2005**, *61*, 10861.

[106]. (a) M. Lang, *Organic Syntheses*, **2002**, *78*, 113; (b) F. Eiden, G. Patzelt, H. Buchborn, *Archiv der Pharmazie*, (Weinheim, Germany), **1989**, *322*, 589.

[107]. (a) K. Akira, H. Hasegawa, S. Baba, *Journal of Labelled Compounds & Radiopharmaceuticals*, **1995**, *36*, 845; (b) C. Reichardt, A. Roechling, G. Schaefer, *J. Phys. Org. Chem.* **2003**, *16*, 682; (c) P. Dijkstra, M. Ptasinska, D. Reinhoudt, H. Den Hertog, J. Eerden, S. Harkema, D. Zeeuw, *J. Org. Chem.* **1987**, *52*, 4913; (d) L. Werbel, P. Cook, E. Elslager, J. Hung, J. Johnson, S. Kesten, D. McNamara, D. Ortwine, D. Worth, *Journal of Medicinal*

Chemistry, **1986**, *29*, 924; (e) L. Marshall, K. Cable, N. Botting, *Tetrahedron*, **2009**, *65*, 8165; (f) G. Haas, J. Stanton, T. Winkler, *Journal of Heterocyclic Chemistry*, **1981**, *18*, 619.

[108]. Y. Nakaike, Y. Kamijo, S. Mori, M. Tamura, N. Nishiwaki, M. Ariga, *J. Org. Chem.* **2005**, *70*, 10169.

[109]. (a) N. Ono, A. Kamimura, A. Kaji, *J. Org. Chem*. **1988**, *53*, 251; (b) M. Jung, D. Grove, *J. Chem. Soc. Chem. Comm.* **1987**, *10*, 753.

[110]. I, Davies, J. Marcoux, J. Kuethe, M. Lankshear, J. Taylor, N. Tsou, P. Dormer, D. Hughes, K. Houk, V. Guner, *J. Org. Chem*. **2004**, *69*, 1298.

[111]. D. Efremov, P. Zavlin, N. Essentseva, J. Tebby, *J. Chem. Soc. Perkin Transactions 1: Organic and Bio-Organic Chemistry*, **1994**, *21*, 3163.

[112]. J. Hefner, Ph.D. dissertation, University of Rostock, **2009**.

[113]. (a) K. Weissermel, H. Arpe, *Industrial Organic Chemistry*, Wiley-VCH, Weinheim, **1997**; (b) S. A. Lawrence, *Amines: Synthesis Properties, and Application*, Cambridge University Press, Cambridge, **2004**.

[114]. S. Mitchell, *Kirk-Othmer Encyclopaedia of Chemical Technology*, 4th ed. Wiley-Interscience, New York, **1992**, *2*, 481.

[115]. (a) L. Nadin, M. Murray, *Biochem. Pharmacol.* **1999**, *58*, 1201; (b) K. Fent, C. Escher, D. Caminada, *Reprod. Toxicol.* **2006**, *22*, 175; (c) S. Khamdang, M. Takeda, R. Noshiro, S. Narikawa, A. Enomoto, N. Anzai, P. Piyachaturawat, H. Endou, *J. Pharmacol. Exp. Ther.* **2002**, *303*, 534; (d) S. Gobec, P. Brozic, T. Rizner, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5170 ; (e) T. Tran, E. Saheba, A. Arcerio, V. Chavez, Q. Li, L. Martinez, T. Primm, *Bioorg. Med. Chem.* **2004**, *12*, 4809.

[116]. a) K. Alvi, B. Nair, C. Gallo, D. Baker, *J. Antibiot.* **1997**, *50*, 264; b) M. de Oliveira, J. Oliveira, F. Galetti, A. de Souza, C. Silva, E. Hajdu, S. Peixinho, R. Berlinck, *Planta Med.* **2006**, *72*, 437; c) J. Lee, A. Chubb, E. Moman, B. McLoughlin, C. Sharkey, J. Kelly, K. Nolan, M. Devocelle, D. Fitzgerald, *Org. Biomol. Chem.* **2005**, *3*, 3678.

[117]. K. Alvi, M. Diaz, P. Crews, D. Slate, R. Lee, R. Moretti, *J. Org. Chem.* **1992**, *57*, 6604.

[118]. L. Ismail, P. Lorenz, F. Stermitz, *J. Nat. Prod.* **1998**, *61*, 1174.

[119]. (a) J. Davies, H. Wang, T. Taylor, K. Warabi, X. Huang, R. Andersen, *Org. Lett.* **2005**, *7*, 5233; (b) Z. Thale, T. Johnson, K. Tenney, P. Wenzel, E. Lobkovsky, J. Clardy, J. Media, H. Pietraszkiewicz, F. Valeriote, P. Crews, *J. Org. Chem.* **2002**, *67*, 9384.

[120]. (a) K Doxsee, M. Feigel, K. Stewart, J. Canary, C. Knobler, D. Cram, *J. Am. Chem. Soc.* **1987**, *109*, 3098; (b) C. Merlic, S. Motamed, B. Quinn, *J. Org. Chem*. **1995**, *60*, 3365; (c) A. Tafesh, J. Weiguny, *Chem. Rev*. **1996**, *96*, 2035; (d) Y. Liu, Y. Lu, M. Prashad, O. Repic, T. Blacklock, *Adv. Synth. Catal*.

2005, *347*, 217; (e) J. Seyden-Penne, *Reductions by the Alumino and Borohydrides in Organic Synthesis*, 2nd ed. Wiley-VCH, New York, **1997**; (f) M. Hudlicky, *Reductions in Organic Chemistry*, Ellis Horwood, Chichester, **1984**; (g) C. Rode, M. Vaidya, R. Chaudhari, *Organic Process Research & Development*, **1999**, *3*, 465; (h) R. Rahaim, R. Maleczka, *Synthesis,* **2006**, 3316; see also ref. [95].

[121]. A. Kamal, K. Ramana, H. Ankati, A. Ramana, *Tetrahedron Lett*. **2002**, *43*, 38, 6861; (b) S. Ram, K. Chary, D. Iyengar, *Synth. Commun.* **2000**, *30*, 4495; and references therein.

[122]. J. Jacquesy, M. Jouannetaud, G. Morellet, Y. Vidal, *Tetrahedron Lett*. **1984**, *25*, 1479.

[123]. (a) T. Schulz, C. Torborg, S. Enthaler, B. Schaeffner, A. Dumrath, A. Spannenberg, H. Neumann, A. Boerner, M. Beller, *Chem. Eur. J.* **2009**, *15*, 4528; (b) R. Kleppinger, C. Lillya, C. Yang, *J. Am. Chem. Soc.* **1997**, *119*, 4097; (c) Mohanakrishnan, A. K.; Srinivasan, P. C. *J. Org. Chem.* **1995**, *60*, 1939; (d) J. Xie, X. Zhu, M. Huang, F. Meng, W. Chen, Y. Wan, *Eur. J. Org. Chem.* **2010**, 3219.

[124]. A. Avenoza, J. Busto, C. Cativiela, J. Peregrina, *Synthesis*, **1995**, 671.

[125]. (a) V. Young, *Engl. J. Med,* **1981**, *304***,** 1228; (b) M. Alaejos, C. Romero, *Chem. Rev.* **1995**, *95*, 227; (c) S. Sathe, A. Mason, R. Rodibaugh, C. Weaver, *J. Agric. Food Chem.* **1992**, *40*, 2084.

[126]. M. Axley, A. Bock, T. Stadtman, *Proc. Natl. Acad. Sci. U.S.A.***1991**, *88*, 8450.

[127]. R. Shamberger, *Biochemistry of Selenium*, E. Frieden, Ed., Plenum Press, **1983**, Ch. 7; (b) G. Mugesh,W. du Mont, H. Sies, *Chem. Rev*. **2001**, *101*, 2125.

[128]. (a) L. Clark, G. Combs, B. Turnbull, E. Slate, D. Chalker, J. Chow, L. Davis, R. Glover, G. Graham, E. Gross, A. Krongrad, J. Lesher, K. Park, B. Sanders, C. Smith, R. Taylor, *J. Am. Med. Assoc*. **1996**, *276*, 1957; (b) E. Block, S. Bird, J. Tyson, P. Uden, X. Zhang, E. Denoyer, *Phosphorus Sulfur and Silicon and the Related Elements,* **1998**, *136*, 1; (c) K. El-Bayoumy, *Nutr. Cancer*, **2001**, *40*, 4; (d) C. Ip, H. Ganther, *Carcinogenesis,* **1992**, *13*, 1167; (e) C. Ip, *J. Am. Coll. Toxicol*. **1987**, *5*, 7; (f) C. Ip, *J. Nutr.* **1998**, *128*, 1845; (g) C. Ip, D. Lisk, H. Ganther, H. Thompson, *J. Anticancer Res*. **1997**, *17*, 3195.

[129]. J. Hu, L. Engman, I. Cotgreave, *Carcinogenesis,* **1995**, *16*, 1815.

[130]. (a) C. Paulmier, *In Selenium Reagents and Intermediates in Organic Synthesis*, J. Baldwin, Ed., Pergamon Press, Oxford, **1986**, p. 4; (b) *Organoselenium Chemistry*, D. Liotta, Ed. Wiley-Interscience, New York, **1987**; (c) *Comprehensive Organic Chemistry*, A. Krief, Ed., Pergamon,

Oxford, **1991**; (d) *Organoselenium Chemistry*, A. Krief, Ed. Springer-Verlag, Berlin, **1988**.

[131]. (a) B. Greenberg, E. Gould, W. Burlant, *J. Am. Chem. Soc*. **1965**, *78*, 4028; (b) T. Campbell, J. McCullough, *J. Am. Chem. Soc*. **1945**, *67*, 1965.

[132]. (a) H. Rheinboldt, M. Perrier, *Bull. Soc. Chim. Fr.* **1955**, 445; (b) H. Rheinboldt, M. Perrier, *Bull. Soc. Chim. Fr.* **1956**, 251; (c) F. Ayorinde, *Tetrahedron Lett*. **1983**, *24*, 2077; (d) P. Southwell-Kelly, I. Johnstone, E. Cole, *Phosphorous Sulfur 1,* **1976**, 261.

[133]. (a) S. Keimatsu, K. Yokota, *J. Pharm. Soc. Jpn.* **1930**, *50*, 531; (b) S. Keimatsu, K. Yokota, S. Suzuki, *J. Pharm. Soc. Jpn.* **1932**, *52*, 961; (c) M. Evers, L. Christiaens, M. Renson, *J. Org. Chem.* **1986**, *51*, 5196.

[134]. (a) B. Ranu, K. Chattopadhyay, S. Banerjee, *J. Org. Chem.* **2006**, *71*, 423; (b) M. Bonaterra, S. Martin, R. Rossi, *Tetrahedron Lett.* **2006**, *47*, 3511; (c) S. Fukuzawa, D. Tanihara, S. Kikuchi, *Synlett*, **2006**, 2145; (d) I. Beletskaya, A. Sigeev, A. Peregudov, P. Petrovskii, *J. Organomet. Chem.* **2000**, *605*, 96.

[135]. (a) C. Millois, P. Diaz, *Org. Lett.* **2000**, *2*, 1705; (b) H. Cristau, B. Chabaud, R. Labaudiniere, H. Christol, *Organometallics*, **1985**, *4*, 657.

[136]. (a) A. Braga, T. Barcellos, M. Paixao, A. Deobald, M. Godoi, H. Stefani, R. Cella, A. Sharma, *Organometallics*, **2008**, *27*, 4009; (b) L. Wang, M. Wang, F. Huang, *Synlett*, **2005**, 2007; (c) N. Taniguchi, *J. Org. Chem.* **2007**, *72*, 1241; (d) D. Chang, W. Bao, *Synlett*, **2006**, 1786; (e) N. Taniguchi, T. Onami, *J. Org. Chem.* **2004**, *69*, 915; (f) Z. Wang, H. Mo, W. Bao, *Synlett*, **2007**, 91; (g) N. Taniguchi, *Synlett*, **2005**, 1687; (h) S. Kumar, L. Engman, *J. Org. Chem.* **2006**, *71*, 5400; (i) R. Gujadhur, D. Venkataraman, *Tetrahedron Lett.* **2003**, *44*, 81; (j) T. Ogawa, K. Hayami, H. Suzuki, *Chem. Lett.* **1989**, 769; (k) N. Taniguchi, T. Onami, *Synlett*, **2003**, 829.

[137]. Y. Nishiyama, K. Tokunaga, N. Sonoda, *Org*. *Lett*. **1999**, *1*, 1725; see also ref. [128 d]

[138]. S. Hayashi, H. Wada, T. Ueno, W. Nakanishi, *J. Org. Chem.* **2006**, *71*, 5574; see also ref. [120 c].

[139]. T. Arnauld, D. Barton, J. Normant, *J. Org. Chem*. **1992**, *64*, 3722.

[140]. R. Nelson, R. Schroeder, W. Bunting, *J. Am. Chem. Soc*. **1933**, *55*, 801.

[141]. D. Barton, S. Ley, P. Magnus, M. Rosenfeld, *J. Chem. Soc. Perkin Trans. 1*. **1977**, 567.

[142]. G. Han, G. Huang, *Chinese Chemical Letters*, **1994**, *5*, 99.

[143]. T. Back, D. Wehrli, *Synlett*, **1995**, 1123.

[144]. X. Zhang, S. Sarkar, R. Larock, *J. Org. Chem.* **2006**, *71*, 236.

[145]. M. Shi, J. Lu, *J. Org. Chem*. **2006**, *71*, 1920.

[146]. M. Miao, X. Huang, *J. Org. Chem*. **2009**, *74*, 5636.

[147]. (a) S. Reim, M. Lubbe, P. Langer, *Tetrahedron Lett*. **2006**, *47*, 6751; (b) M. Lubbe, Diploma dissertation, University of Rostock, **2006**.
[148]. G. Doleschall, P. Seres, *J. Chem. Soc. Perkin Trans. 1,* **1988**, 1875.
[149]. for the synthesis of **109a,c,d** see (a) L. Crombie, D. Games, A. James, *J. Chem. Soc. Perkin Trans. 1*, **1979**, 464; (b) R. Ife, C. Leuch, T. Brown, *Preparation and formulation of 4-amino-3-acylquinolines derivatives and their use as inhibitorsnof gastric acid secretion*, Patent No. EP 330485, **1989**; Chem. Abstr. 112:158073 (c) B. Baker, H. Shapiro, *Journal of Medicinal Chemistry*, **1963**, *6*, 664, respectively
[150]. L. Foley, *J. Org. Chem.* **1985**, *50*, 5204.
[151]. (a) A. K. Roy, S. Batra, *Synthesis*, **2003**, 2325; (b) Z. Chen, B. Zhou, H. Cai, W. Zhu, X. Zou, *Green Chemistry*, **2009**, *11*, 275.
[152]. A. Riahi, M. Shkoor, O. Fatunsin, M. Yawer, I. Hussain, C. Fischer, P. Langer, *Tetrahedron,* **2009**, *65*, 9300; and references therein.
[153]. L. F. Tietze, H. Meier, E. Voß, *Synthesis* **1988**, 274.
[154]. (a) A. G. Schultz, S. A. Hardinger, *J. Org. Chem.* **1991**, *56*, 1105; (b) A. Allen, P. Marquand, R. Burton, K. Villeneuve, W. Tam, *J. Org. Chem.* **2007**, *72*, 7849.
[155]. for **129a**,**b** see H. N. Roya, A. H. Al Mamuna, *Synth. Commun.* **2006**, *36*. 2975, for **129c** see H. Yoshida, Y, Mimura, J. Ohshita, A. Kunai, *Chem. Comm*. **2007**, *23*, 2405.
[156]. S. Nakamatsu, K. Yoshizawa, S. Toyota, F. Toda, I. Matijasic, *Org. Biomol. Chem.* **2003**, *1*, 2231.
[157]. G. Field, S. Zally, *Synthesis*, **1979**, 295.
[158]. M, Ashwell, R. Jackson, *Synthesis*, **1988**, 229.
[159]. Hollemann-Wiberg, *Lehrbuch der Anorganischen Chemie*, 101. Auflage, Walter de Gruyter, Berlin, **1995**, Anhang V.
[160]. N. Miyoshi, T. Yamamoto, N. Kambe, S. Murai, N. Sonoda, *Tetrahedron Lett*. **1982**, *46*, 4813.

Abstract:

Cyclization reactions of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 1,3-dielectrophiles, provide a powerful tool for the synthesis of highly substituted arenes. They proceed with high regioselectivity.

A diversity-oriented, convenient and regioselective synthesis of a great variety of 1-hydroxy-2,4-benzodioates (4-hydroxyisophthalates) by the first formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy- and 3-alkoxy-2-alkoxycarbonyl-2-en-1-ones is reported.

The synthesis of 3-hydroxy-5-methylphthalates is achieved by regioselective chelation-controlled cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 4-silyloxy-2-oxo-3-butenoates derived from acetylpyruvates. The employment of silylated benzoyl- instead of acetylpyruvates results in a change of the regioselectivity and formation of 6-aryl-2-hydroxy-terephthalates. The regiodirecting effect of the aryl group is stronger than the one of the pyruvate-derived ester group. The cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 4-ethoxy-2-oxo-3-butenoates, readily available by condensation of enol ethers with methyl 2-chloro-2-oxoacetate, afforded 3-hydroxyphthalates and 2-hydroxyterephthalates depending on the substitution pattern of the diene.

Highly functionalized 4-nitro- and 4-aminophenols are synthesized by [3+3] cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-ethoxy-2-nitro-2-en-1-ones and subsequent reduction of the resulting nitrophenols.

Various functionalized unsymmetrical diaryl selenides containing a salicylate substructure are prepared by [3+3] cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-silyloxy-2-phenylselenayl-2-en-1-ones.

Keywords:

Silyl enol ether, Arenes, Cyclization, Regioselectivity, Selenide.

Abstract:

Cyclisierungsreaktionen von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 1,3-Dielektrophilen stellen eine bedeutende Möglichkeit zur Synthese von mehrfach substituierten Arenen dar. Sie laufen unter hoher Regioselektivität ab.

Es wird über neue Beiträge auf dem Gebiet der Synthese von mehrfach funktionalisierten Arenen ausgehend von acyclischen Verbindungen berichtet.

Durch die ersten formellen [3+3] Cyclisierungen von 1,3-Bis(silyloxy)-1,3-butadienen mit 3-Silyloxy- und 3-Alkoxy-2-alkoxycarbonyl-2-en-1-onen wurden eine Reihe von gerichteten, milden und regioselektiven Synthesen für eine Vielzahl an 1-Hydroxy-2,4-benzodioaten (4-Hydroxyisophthalaten) erschlossen.

Es wird außerdem über die Synthese von 3-Hydroxy-5-methylphthalaten durch regioselektive chelat-kontrollierte Cyclisierung von 1,3-Bis(silyloxy)-1,3-butadienen mit 4-Silyloxy-2-oxo-3-butenoaten berichtet, die von Acetylpyruvaten abgeleitet sind. Der Einsatz von silylierten Benzoyl- anstelle von Acetylpyruvaten führt zu einer Änderung der Regioselektivität, so dass es zur Bildung von 6-Aryl-2-hydroxy-terephthalaten kommt. Der regiodirigierende Effekt der Arylgruppe ist stärker als der der Pyruvat-Ester-Gruppe. Die Cyclisierung von 1,3-Bis(silyloxy)-1,3-butadienen mit 4-Ethoxy-2-oxo-3-butenoaten, die durch Kondensation von Enolethern mit Methyl-2-chlor-2-oxoacetat erhalten werden, ergab 3-Hydroxyphthalate und 2-Hydroxyterephthalate in Abhängigkeit vom Substitutionsmuster des Diens.

Zusätzlich wurde die regioselektive Synthese von mehrfach funktionalisierten 4-Nitro- und 4-Aminophenolen basierend auf [3+3] Cyclokondensation von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 3-Ethoxy-2-nitro-2-en-1-onen und anschließender Reduktion der erhaltenen Nitrophenole untersucht.

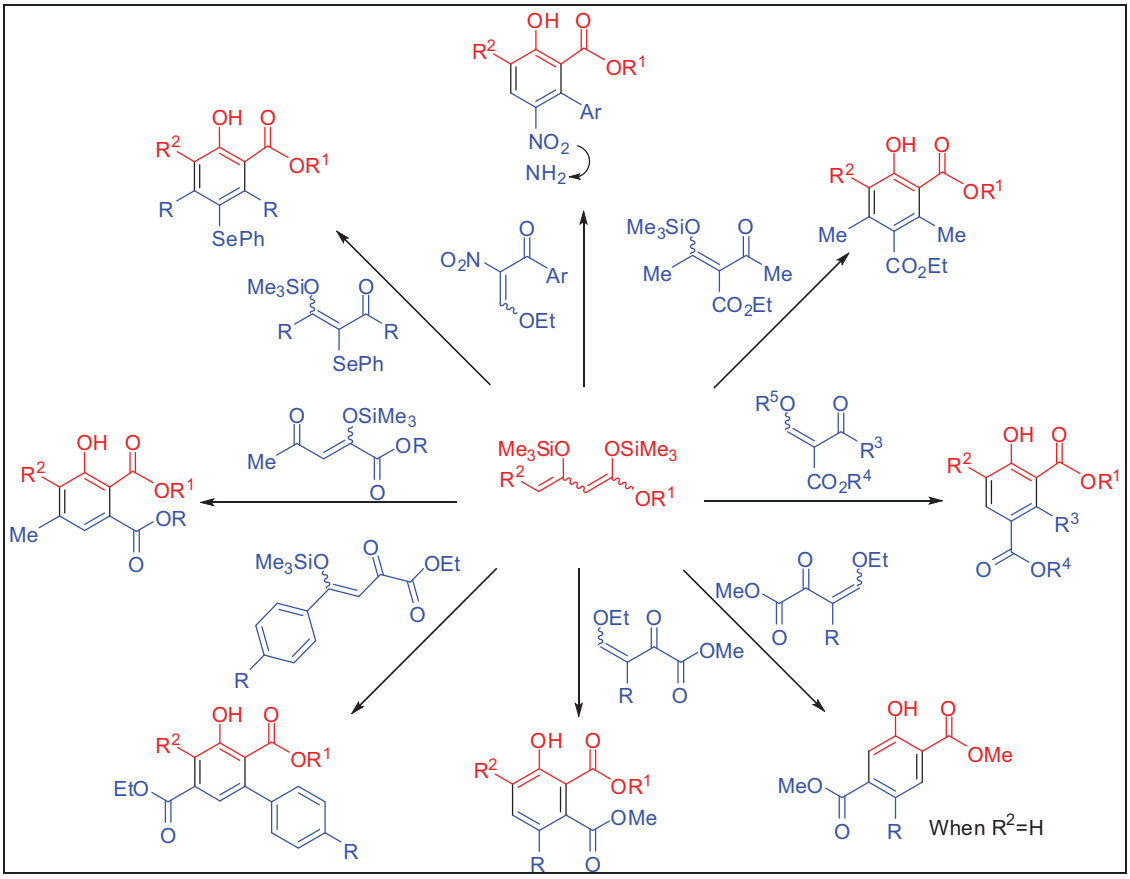
Schließlich wurde durch Cyclokondensation von 1,3-Bis(trimethylsilyloxy)-1,3-butadienen mit 3-Silyloxy-2-phenylselenayl-2-en-1-onen eine Synthese für verschiedene

funktionalisierte unsymmetrische Diarylselenide entwickelt, welche eine Salicylat-Substruktur enthalten.

Schlüsselwörter:

Silylenolether, Arene, Cyclisierungen, Regioselektivität, Selenide.

Graphical Abstarct:



Scheme 25: Graphical abstract.

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– Languages

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Institution:	Institute of Chemistry, University of Rostock, Germany
Subject:	Organic Chemistry
Degree:	**Ph.D.** (Dr. rer. nat.), (1.3) Magna cum laude (very good)
Duration:	October 2007- January 2011

Dissertation:"Synthesis of Hydroxybenzodioates, Aminophenols and Diaryl Selenides by [3+3] Cyclizations of 1, 3-Bis (silyloxy)-1, 3-butadienes with 3-Silyloxy- and 3-Alkoxy-2-en-1-ones".

Supervisor: **Prof. Dr. Peter Langer**

Institution:	Yarmouk University, Irbid, Jordan
Subject:	Science (Chemistry)
Degree:	**M.Sc.** GPA (88.6%), (Excellent), rank 1st
Duration:	April 2003-Dec. 2005

Thesis:" Synthesis and Biological Activity of some new 5- Sulphanyl–4-nitroimidazole Derivatives".

Supervisor: **Prof. Dr. Mahmoud Al-Talib**

Co-Advisor: **Prof. Dr. Hasan Tashtoush**

Institution:	Al-alBayt University, Mafraq, Jordan
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Degree:	**B.Sc.** GPA (78.53%) (Very good), rank 3rd
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– Awards and Scholarships

- Yarmouk University Academic Distinction Award, June 2006.
- (Landesgraduierten-scholarship), State of Mecklenburg-Vorpommern, Federal Republic of Germany, May 2008- Oct. 2010.
- Teaching and research assistantships during Master studies.

- Experiences

Period: May 2006 – Oct. 2007

Editorial Secretary of Jordan Journal of Chemistry

Period: During Master studies:

Teaching Assistantships:

- Chem. 105 General Chemistry lab (1).
- Chem. 106 General Chemistry lab (2).
- Systematic Identification of Organic Compounds.

– Memberships:

German Chemical Society (GDCh-Mitgliedsnummer: 97488).

– Research Interests:

Field: Synthetic Organic Chemistry.

- Cycloadditions of dianions with dielectrophiles
- Synthesis of functionalized Arenes starting from acyclic precursors
- Palladium catalyzed couplings

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– Publications

2011

1. Ghazwan A. Salman, Ahmed Mahal, **Mohanad Shkoor**, Munawar Hussain, Alexander Villinger, Peter Langer "Regioselective Suzuki-Miyaura Reactions of the Bis(triflate) of 1,2,3,4-Tetrahydro-9,10-dihydroxyanthracen-1-one" ***Tetrahedron Lett.*** **2011**, *52*, 3, 392.

2010

2. **Mohanad Shkoor**, Olumide Fatunsin, Abdolmajid Riahi, Mathias Lubbe, Stefanie Reim, Muhammad Sher, Christine Fischer, Peter Langer " Competing regiodirecting effects of ester and aryl groups in [3+3] cyclocondensations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes. Regioselective synthesis of 1-hydroxyphthalates and 2-hydroxy-terphthalates" ***Eur. J. Org. Chem.*** **2010**, 19, 3732.
3. Olumide Fatunsin, Viktor O. Iaroshenko, Sergii Dudkin, **Mohanad Shkoor**, Dmitro Volochnyuk, Ashot Gevorgyan, Peter Langer "Synthesis of Chromeno[3,4-*b*]pyrrol-4(3*H*)-ones by Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with 4-Chloro-3-nitrocoumarin" ***Synlett,*** **2010**, 1533.
4. Olumide Fatunsin, **Mohanad Shkoor**, Serge-Mithérand Tengho Toguem, Abdolmajid Riahi, Olapeju O. Aiyelaagbe, Emmanuel Akintayo, Christine Fischer, Peter Langer "Regioselective Synthesis of 5-Chlorosalicylates by One-Pot Cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 2-Chloro-3-ethoxy-2-alken-1-ones" ***Synlett*** **2010**, 1963.
5. Ihsan Ullah, Muhammad Sher, Asad Ali, Rasheed Ahmad Khera, Muhammad Nawaz, **Mohanad Shkoor**, Inam Iqbal, Muhammad Imran, Alexander Villinger, Christine Fischer, Peter Langer "Synthesis of Sterically Encumbered Biaryls based on a 'Copper(I)-Catalyzed Arylation / [3+3] Cyclocondensation' Strategy " ***Tetrahedron***, **2010**, *66*, 3824.
6. Olumide Fatunsin, **Mohanad Shkoor**, Abdolmajid Riahi, Munawar Hussain, Muhammad Sher, Alexander Villinger, Christine Fischer, Peter Langer "Regioselective Synthesis of 5-Arylthio- and 5-Benzylthio-6-phenylsalicylates by One-Pot Cyclizations of 1,3-Bis(silyloxy)-1,3-butadienes with 2-Arylthio- and 5-Benzylthio-3-ethoxy-2-en-1-ones" ***Helv. Chim. Acta***, **2010**, *93*, 1610.
7. Olumide Fatunsin, **Mohanad Shkoor**, Abdolmajid Riahi, Peter Langer " Regioselective Synthesis of Highly Functionalized Arylphosphonates by Cyclocondensation of 1,3-Bis(trimethylsilyloxy)-1,3-butadienes with 3-Ethoxy-2-phosphonyl-alk-2-en-1-ones" ***Synlett***, **2010**, 1525.

2009

8. **Mohanad Shkoor**, Abdolmajid Riahi, Olumide Fatunsin, Ibrar Hussain, Mirza A. Yawer, Mathias Lubbe, Stefanie Reim, Helmut Reinke, Christine Fischer, Peter Langer "Diversity-Oriented Synthesis of 1-Hydroxy-2,4-benzodioates by Regioselective [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with 3-Alkoxy- and 3-Silyloxy-2-alkoxycarbonyl-2-en-1-ones" ***Org. Biomol. Chem***. **2009**, *7*, 2182.

9. **Mohanad Shkoor**, Abdolmajid Riahi, Olumide Fatunsin, Helmut Reinke, Christine Fischer, Peter Langer "Diversity-oriented synthesis of functionalized diaryl-sulfones by regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 2-arylsulfonyl-3-ethoxy-2-en-1-ones" ***Synthesis***, **2009**, 2223.

10. **Mohanad Shkoor**, Olumide Fatunsin, Abdolmajid Riahi, Alexander Villinger, Peter Langer "Synthesis of Functionalized Diaryl Selenides by the First Formal [3+3] Cyclocondensations of 1,3-Bis(silyloxy)-1,3-butadienes with Organoselenium Compounds" ***Tetrahedron Lett.*** **2009**, *50*, 5726.

11. Abdolmajid Riahi, **Mohanad Shkoor**, Rasheed Ahmad Khera, Helmut Reinke, Peter Langer "Regioselective synthesis of functionalized 4-nitro- and 4-aminophenols based on formal [3+3] cyclocondensations of 3-ethoxy-2-nitro-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes" ***Tetrahedron Lett.*** **2009**, *50*, 3017.

12. Abdolmajid Riahi, **Mohanad Shkoor**, Rasheed Ahmad Khera, Helmut Reinke, Peter Langer "Regioselective synthesis of functionalized 4-nitro- and 4-aminophenols based on formal [3+3] cyclocondensations of 3-ethoxy-2-nitro-2-en-1-ones with 1,3-bis(silyloxy)-1,3-butadienes" ***Tetrahedron Lett.*** **2009**, *50*, 3017.

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

14. Abdolmajid Riahi, **Mohanad Shkoor**, Olumide Fatunsin, Peter Langer **"**Regioselective synthesis of 4-acyl-1-hydroxy-2,3-benzodioates by chelation-controlled [3+3] annulation of 3-acyl-4-ethoxy-2-oxo-3-enoates with 1,3-bis(trimethylsilyloxy)-1,3-butadienes" ***Org. Biomol. Chem.*** **2009**, *7*, 4248.

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

16. Mahmoud Al-Talib, Dalia Al-Saad, **Mohanad Shkoor**, Hasan Tashtoush "Efficient Synthesis of 2-Aroyl-3-Alkoxy-2,3-Dihydrothiazolo[2,3-c][1,2,4]Triazol-5(6H)-ones" ***Jordan Journal of Chemistry***, **2009**, *4*, 317.

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

2007

18. Hasan Tashtoush, Yaseen Al-Soud, Ahmed Maslat, **Mohanad Shkoor**, Mahmoud Al-Talib "Synthesis and Biological Activity of some new 5-Sulphanyl–4-nitroimidazole Derivatives" ***Jordan Journal of Chemistry***, **2007**, *2*, 11.