Synthesis of functionalized diaryl sulfides by cyclocondensation of 3-arylthio-1-silyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane, dimethyl allene-1,3-dicarboxylate, 1,1-bis(methylthio)-1-en-3-ones and 3-oxo-orthoesters

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Whoever loves to meet God, God loves to meet him.

Sayings of Prophet Muhammad S.A.W

No one who keeps his mind focussed entirely upon himself, can grow large, strong and beautiful in character.

Sayings of Prophet Muhammad S.A.W

Feed the hungry and visit the sick, and free the captive, if he be unjustly confined. Assist any person oppressed, whether Muslim or non-Muslim.

Sayings of Prophet Muhammad S.A.W

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In the name of GOD, Who is Ubiquitous, Omniscient, Worthy of all praise and Creator of all of us, Who guides in darkness and helps in difficulties.

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I dedicate this work to all who help me so much by doing prays and also sincere with me.

The most important is, to say that I have a great debt on my life due to the enormous sacrifices of my parents for their divine love, prayers, constant care, encouragement and continuous support throughout my studies. Whatever, I am, that is because of the countless prayers of my parents, who instilled in me, a charm for education and the value of being organized.

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20 March 1983.

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Affectionately Dedicated to

"My family specially my beloved Parents, my wife, my sisters and brothers as well as all who Prayed for me"

Table of contents **07**

List of used abbreviations **09**

General Introduction **11**

Summary **16**

1 **Synthesis of 3-arylthio-1-silyloxy-1,3-butadienes** **17**

2 Regioselective synthesis of 2-(arylthio)benzoates by the first catalytic [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadieneswith1,1,3,3-tetramethoxypropane **20**

2.1 Introduction 20
2.2 Results and discussion 21
2.3 Conclusions 25

3 Regioselective synthesis of 4-arylthio-2-hydroxy-homophthalates by [4+2] Cycloaddition of 3-arylthio-1-silyloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate **26**

3.1 Introduction 26
3.2 Results and discussion 28
3.3 Conclusions 30

4 Regioselective synthesis of 2-arylthio-4-methoxybenzoates and 2-arylthio 6-(methylthio)benzoates based on formal [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **31**

4.1 Intoduction 31
4.2 Result and discussion 31
4.3 Conclusions 38

5 Experimental Section **39**

5.1 General: equipment, chemicals and work technique 39
5.2 Procedures and spectroscopic data 41

References **80**

Curriculum vitae **83**

List of used abbreviations

Ar	Aromatic
APT	Attached proton test
ATCC	American Type Culture Collection
nBuLi	n-Butylithium
DEPT	Distortionless Enhancement by Polarisation Transfer
EI	Electronic Ionization
ESI	Electrospray Ionization
EtOAc	Ethylacetate
HRMS	High Resolution Mass Spectroscopy
IR	Infrared spectroscopy
LDA	Lithium diisopropylamide
MS	Mass Spectrometry
Ph	Phenyl
NEt_3	Triethylamine
NMR	Nuclear Magnetic Resolution
HMQC	Heteronuclear Multiple Quantum Coherence
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser and Exchange Spectroscopy
Me_3SiOTf	Trimethylsilyl-trifluoro methanesulfonate
Me_3SiCl	Trimethylsilylchloride
mp.	Melting point
RCM	Ring Closing Metathesis

TBAI	Tetrabutyl amonium iodie
TFA	Trifluoroacetic acid
Tf_2O	Trifluoromethanesulfonic anhydride
THF	Tetrahydrofurane
TLC	Thin Layer Chromatography
TMS	Trimethylsilane
UV	Ultraviolet Spectroscopy

Chemistry is considered the central science due to its significant connections and overlaps with other sciences. If a scientific discipline involves matter, chemistry and synthesis play an important role. A large amount of research breakthroughs in physics would not have been possible without the use of principles and methods of chemistry and synthesis. The development of specialised drugs to cure diseases and understanding of biological and geological systems would be unimaginable without the contribution from chemistry.

Garlic and onion are two important species containing organosulfide ingredients (Chart 1). Here are some natural product of biological important organosulfide compounds isolated by garlic and onion.

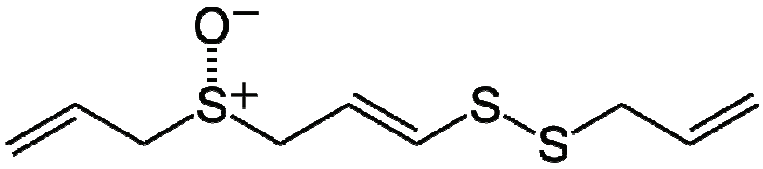


Chart 1. Structure of natural products isolated from onion and garlic

Penicillin represents an organosulfide compound which was among the first antibiotics discovered as natural products from the mold penicillium (Chart 2). Penicillins as well as cephalosporins are called beta-lactam antibiotics.

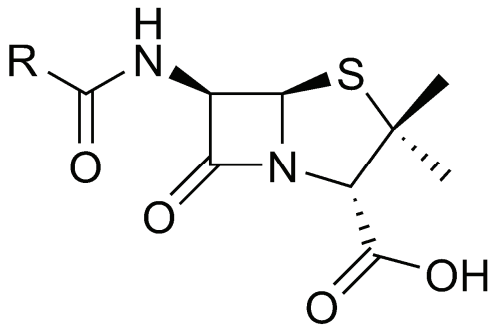


Chart 2. Structure of penicillin

Dapsone represents a water soluble pro-drug for the treatment of Leprosy (Chart 3).

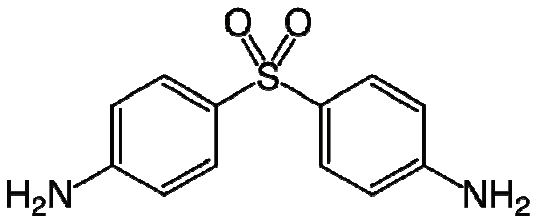


Chart 3. Structure of dapsone

Organosulfide compounds are often associated with foul odours, but ironically many of the sweetest compounds known are organosulfur derivatives.[1] Allicin and ajoene are organosulfide compounds isolated from garlic and are responsible for its odor. It is also obtainable from onions.[2] Nature abounds with organosulfur compounds — sulfur is essential for life. Two of the 20 essential amino acids are organosulfur compounds.[1]

Diaryl sulfides are pharmacologically relevant compounds which occur in a number of natural products. Prominent examples include the lissoclibadins, dibenzothiophenes, cyclic sulfides, varacins (lissoclinotoxins), and related natural products. Sulfide containing compounds are one of the oldest antimicrobial substances in clinical use. One of the most commonly used sulfide-based antibiotics is cotrimoxazole, a combination of sulphamethoxazole (again a sulfide compound) and trimethoprim (which is not sulfide-based). Some more sulfur/sulfonamide-containing drugs are amoxil, generic captopril, prilosec, protonix, zantac, vioxx, clinoril and generic dapsone. Antimicrobial sulfide drugs are bactrim, gantrisin, sultrin, novacet and pediazole and many are used to treat diabetics. [3]

Natural sulfide-containing compounds prevent the browning of fresh-cut fruit and offer a potent alternative to vitamin C. MSM is a sulfur-containing substance that is currently sold on the market primarily for pain control and for its anti-arthritic and anti-inflammatory properties. It is a metabolite of dimethylsulfoxide (DMSO). DMSO represents a widely used dipolar aprotic solvent and also is a key reagent for the synthesis of a range of useful organic molecules.[4]

Chiral sulfoxides have been used in asymmetric synthesis, because Inversion barriers are quite high in the case of simple alkyl or aryl sulfoxides and thus racemisation only occurs above 200 ºC. Sulfones are of great synthetic interest and these typically crystalline compounds find extensive use in organic chemistry. Sulfonamides are used to protect amines as they are extremely stable amine derivatives and have also been found to exhibit useful biological acitivities. Hyperlipidemia constitutes a major etiopathological factor for atherosclerosis. The medicinal value of garlic is best known for its lipid lowering effects and antiatherogenic effects. The mechanism by which lipid-soluble organosulfide

compounds from garlic reduce plasma lipids has not been fully investigated. The author had previously shown that the hepatic activity of β-hydroxy-β-methylglutaryl-CoA (HMG-CoA) reductase, the rate limiting enzyme in cholesterol biosynthesis, and the incorporation of radiolabeled (1, 2 14C), was significantly decreased in rat treated with garlic derived organosulfide compounds. It can be proposed that the antiatherogenic effect of the organosulfide compounds may be attributed to the formation of protein internal disulphide and thus inactivation of the thiol (-SH) group enzymes. For example, the latter include HMG-CoA reductase and the multienzyme complex of fatty acid synthesis. The antiatherogenic effects of these organosulfide compounds can be attributed to such reactions that inhibit HMG-CoA reductase and other lipogenic enzymes. The anticarcinogenic effects of these compounds may also be due to inhibitory reactions on enzymes that activate carcinogens. The present report shows the efficacy of ajoene, a garlic-derived organic trisulfide, for short-term therapy of tinea pedis, ajoene is an alternative, efficient and low-cost antimycotic drug for short-term therapy of tinea pedis. The fact that ajoene can be easily prepared from an alcoholic extract of garlic may make it suitable for Third World public health care.[2]

Onion, apparently via its thiosulphinate and cepaene content, inhibits the production of AA as well as its conversion to pro-inflammatory prostaglandins and leukotrienes. More specifically, onion cepaenes were shown to inhibit COX and LOX activity as well as blood platelet aggregation.The same study also showed that onion extract can decrease the onset and development of tumors as well as have antiasthmatic effects (the latter again via COX inhibition). Allicin inhibited the production of pro-inflammatory cytokine messengers in a study of inflammatory bowel disease, apparently by inactivating the pro-inflammatory factor NF κB via its I

κB inhibitor. By virtue of sulfide-based antioxidants found in garlic, NF κB was maintained in its inactive state, thus preventing synthesis of excess COX/LOX. Onions possess antibacterial properties as well. Although less research is available on the antibacterial activity of onion, it is suggested that S-propenylcysteine sulphoxide is the compound that inhibits antibacterial metabolism by the same mechanism as garlic. Onion extract, the activity of which remained stable for 48h, inhibited Streptococcus mutans, a bacterium that causes strep throat, tonsillitis, bacterial pneumonia, as well as other diseases.[2]

My aim was to develop new methods to synthesize sulfide compounds containing a diaryl sufide moiety. These methods are based on novel formal [3+3] and by [4+2] cyclizations.

Diaryl sulfides are present in important drugs which imitate natural nucleosides (e. g., AZT imitates deoxythymidine) and inhibit the virus from copying its RNA into DNA inside human cells by inhibiting the enzyme 'reverse transcriptase'. This allows to control (to some extent) the disease AIDS.[5] Diaryl sulfides are also important for the development of new drugs against African sleeping sickness and Chagas disease and others. For example, diaryl sulfides with a central anilino moiety, decorated with a flexible N-alkyl side chain bearing a terminal ammonium ion, constitute a known class of inhibitors.[5]

Summary

This dissertation is concerned with the development of new methods for the synthesis of functionalized diarylsulfides. A significant part of this dissertation has recently been published (see list of publications at the end). The work in this dissertation is mainly concerned with the development of new methods for the regioselective synthesis of functionalized diarylsulfides based on novel $TiCl_4$ or Me_3SiOTf mediated formal [3+3] and [4+2] cyclizations.

1. The first chapter contains the synthesis of novel 3-arylthio-1-silyloxy-1,3-butadienes in two steps. The reaction of β-ketoesters with various thiophenols gave 3-(arylthio)alkanoates. The latter were subsequently deprotonated (LDA) and reacted with Me_3SiCl to give 3-arylthio-1-silyloxy-1,3-butadienes.

2. The second chapter includes the regioselective synthesis of 2-(arylthio)benzoates by the first catalytic [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane.

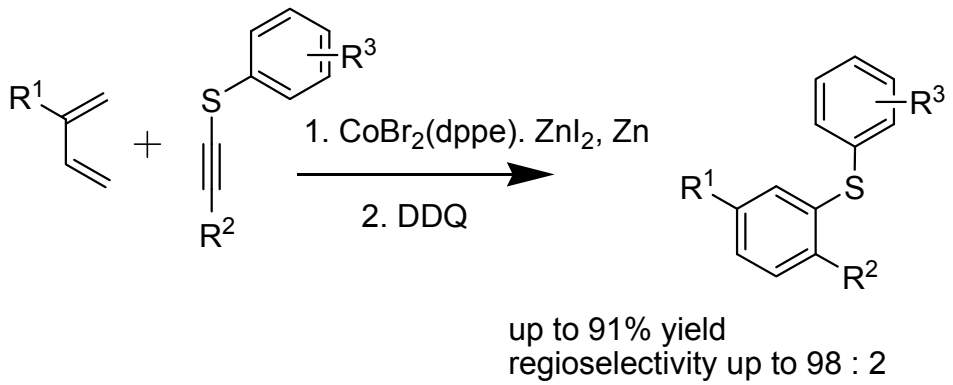
3. The thrid chapter contains the regioselective synthesis of 4-arylthio-2-hydroxy-homophthalates by [4+2] cycloaddition of 3-arylthio-1-silyloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate.

4. The fourth chapter contains the regioselective synthesis of 2-arylthio-4-methoxybenzoates and 2-arylthio-6-(methylthio)benzoates based on formal [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes.

1. Synthesis of 3-arylthio-1-silyloxy-1,3-butadienes

Classic syntheses of diaryl sulfides include, for example, reactions of arenes with sulfide[6] or sulfur dichloride,[7] condensations of Grignard or organolithium reagents with chlorophenyl-sulfides[8] or base-mediated reactions of thiophenols with chloroarenes.[9] The competing formation of polysulfides and low regioselectivities are severe drawbacks of these methods. In contrast, transition metal-catalyzed[10] and metal-free[11] carbon-sulfur coupling reactions allow the synthesis of diaryl sulfides under relatively mild conditions. However, the scope of this approach is limited by the fact that reactions of sterically encumbered substrates are often difficult or not possible at all. In addition, the synthesis of the starting materials, substituted aryl halides or triflates, can be a difficult task.

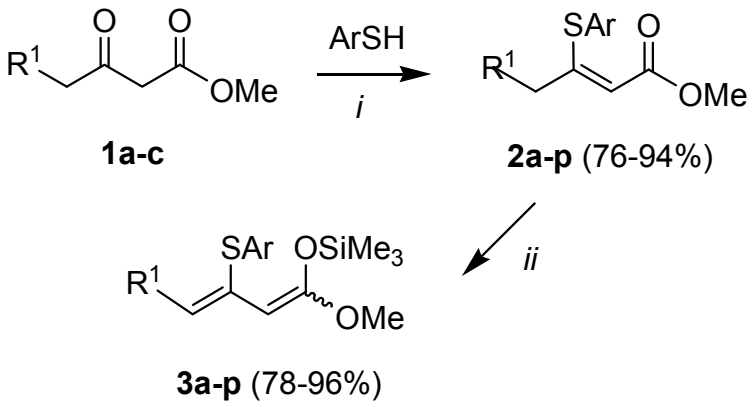
A strategy to circumvent these problems relies on the application of a building block approach using appropriate sulfur-containing substrates in cyclization reactions. Diaryl sulfides have been prepared by cobalt(I)-catalyzed [4+2] cycloaddition of alkynyl sulfides with 1,3-butadienes.[12] (Chart 4).



up to 91% yield
regioselectivity up to 98 : 2

Chart 4. Cobalt(I)-catalyzed Diels-Alder reaction

Thiols and diaryl sulfides have a very bad smell and, therefore, all reactions have to be carried out with great care. The reaction of β-ketoesters **1a-c** with various thiophenols gave, following the procedure reported by Chan *et al.,*[13] the 3-(arylthio)alkanoates **2a-p** (Scheme 1). Deprotonation of **2a-p** (LDA) and subsequent addition of Me_3SiCl afforded, again following the procedure reported by Chan *et al.,*[13] the 3-arylthio-1-silyloxy-1,3-butadienes **3a-p**. The synthesis of **2a** and **3a** has been previously reported.[13] Dienes **3a-p** proved to be unstable and had to be used directly after their preparation.



1a-c **2a-p** (76-94%) **3a-p** (78-96%)

Scheme 1. Synthesis of **3a-p** (for R^1 and Ar, see Table 1); conditions: *i,* P_4O_{10}, CH_2Cl_2, 20 °C, 18 h; *ii*, 1) LDA, THF, –78 °C, 1 h; 2) Me_3SiCl, –78 → 20 °C, 14 h

-

Table 1. Synthesis of **3a-p**

3	R^1	Ar	% **(2)**[a]	% **(3)**[a]
a	H	Ph	90	90
b	H	4-FC_6H_4	80	80
c	H	3-MeC_6H_4	82	87
d	H	3-ClC_6H_4	80	86
e	H	4-MeC_6H_4	85	88
f	H	2-Naph	75	79
g	Me	4-MeC_6H_4	85	83
h	Me	Ph	84	82
i	Me	4-FC_6H_4	74	78
j	Et	Ph	84	83
a	H	Ph	90	90
k	H	4-ClC_6H_4	87	84
l	H	4-$MeOC_6H_4$	84	88
m	H	3-$MeOC_6H_4$	83	88
n	H	4-EtC_6H_4	86	87
o	Me	4-EtC_6H_4	80	80
p	Me	4-ClC_6H_4	77	78

[a] Yields of isolated products

2. Regioselective synthesis of 2-(arylthio)benzoates by the first catalytic [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane

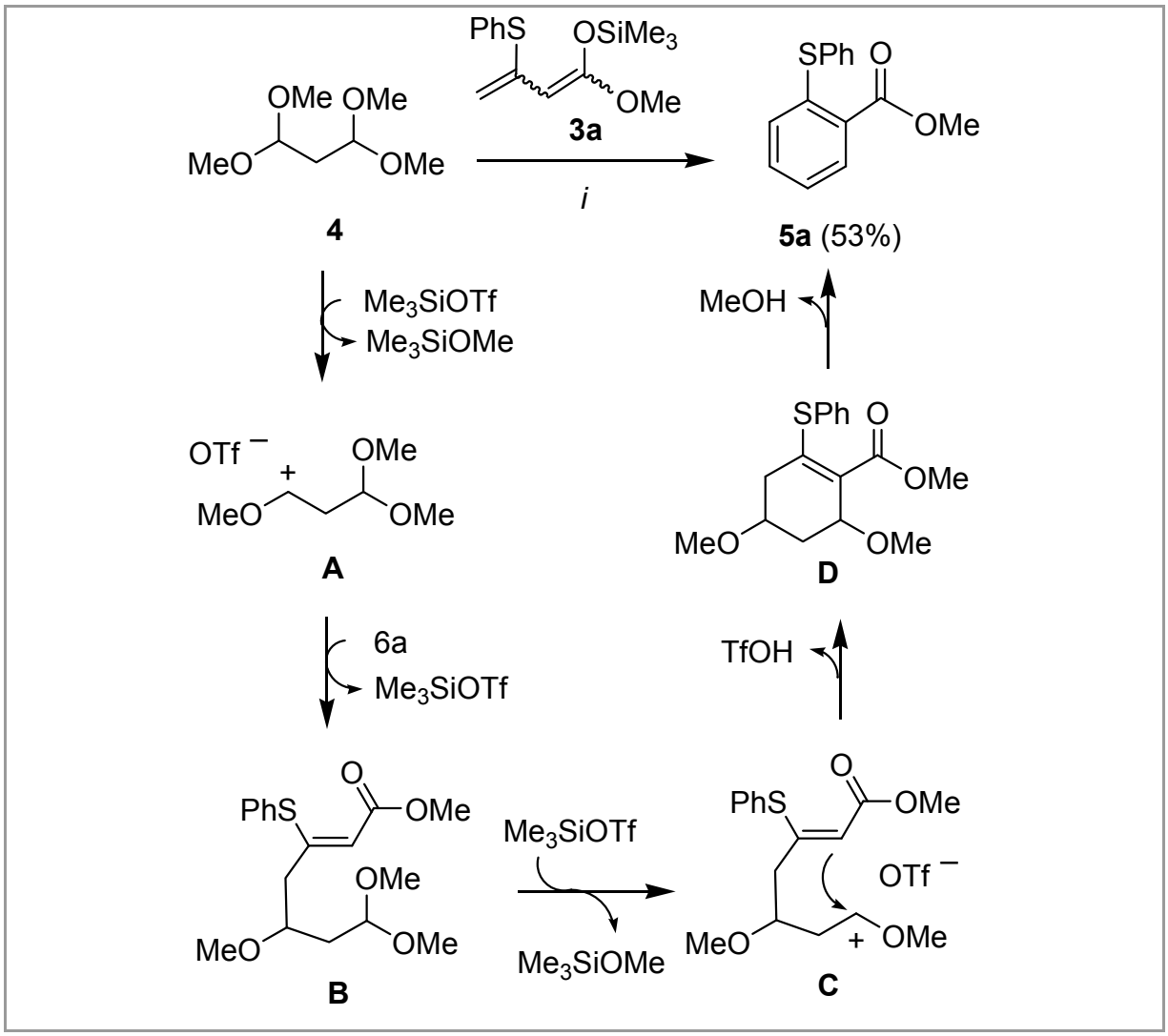
2.1 Introduction

Recently, Langer et al. studied[14] the synthesis of 3- and 5-(arylthio)salicylates by $TiCl_4$-mediated [3+3] cyclizations[15] of 1,3-bis(silyloxy)-1,3-butadienes[16] with 3-silyloxy-2-en-1-ones, a method first developed[17] by Chan and coworkers. The $TiCl_4$-mediated cyclocondensation of 1,3-bis(silyloxy)-1,3-butadienes with 1,1,3,3-tetramethoxypropane and 2-alkyl-1,1,3,3-tetraethoxypropanes has also been reported.[17, 18] Recently, Langer et al. also have developed a catalytic variant of this reaction using trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf) as the catalyst.[19]

Chan *et al*. reported the synthesis of 2-(phenylthio)benzoates by $TiCl_4$-mediated [3+3] cyclization of 3-silyloxy-2-en-1-ones with 3-arylthio-1-trimethylsilyloxy-1,3-butadienes.[20] Again, I have studied the $TiCl_4$-mediated domino ′[3+3] cyclization / homo-Michael′ reaction of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-diacylcyclopropanes.[21] Herein, I communicate a convenient synthesis of 2-(arylthio)benzoates by what are, to the best of my knowledge, the first formal [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane. It is important to note, that these reactions can be carried out using catalytic amounts of Me_3SiOTf. In contrast to the C-S coupling reactions outlined above, my method relies on the assembly of one of the two arene moieties.

2.2 Result and discussions

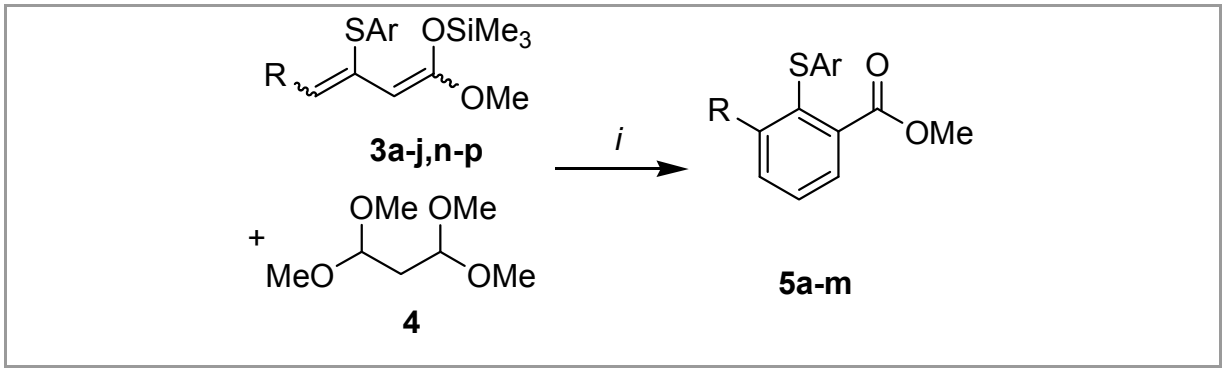
The reaction of 3-phenylthio-1-silyloxy-1,3-butadiene **3a** with 1,1,3,3-tetramethoxypropane **(4)**, in the presence of catalytic amounts of Me_3SiOTf, afforded the 2-(phenylthio)benzoate **5a** (Scheme 2). The best yields were obtained when 0.1 equiv. of Lewis acid was used. The use of 0.2 or 1.0 equiv. of Me_3SiOTf did not result in an increase of the yield. The yields decreased when less than 0.1 equiv. of Lewis acid was employed. The use of 1.0 equiv. of $TiCl_4$ proved to be possible, but again did not increase the yield. The work-up procedure (diluted hydrochloric acid), the temperature (–78 → 20 °C, 20 h), and the concentration (ca. 2 mL of CH_2Cl_2 per **1** mmol of **3a**) proved to be important parameters during the optimization. The high concentration is a significant difference to the procedure reported[19] for the Me_3SiOTf-catalyzed cyclization of 1,3-bis(silyloxy)-1,3-butadienes with **4**. The use of tetraethoxypropane rather than **4** proved to be unsuccessful. The use of trifluoroacetic acid or triflic acid (rather than Me_3SiOTf) failed to give the desired product.



Scheme 2. Possible mechanism of the formation of **5a**; conditions: *i*: 1) Me_3SiOTf (0.1 equiv.), CH_2Cl_2, –78 → 20 °C, 20 h; 2) HCl, H_2O

The formation of **5a** can be explained by Me_3SiOTf-catalyzed formation of oxonium cation A, attack of the terminal carbon atom of **3a** onto A to give intermediate B, Me_3SiOTf-catalyzed formation of oxonium cation C, cyclization to give intermediate D, and subsequent aromatization by extrusion of methanol. The suggested mechanism has not been experimentally proved.

The cyclization of dienes **3a-j,n-p** with **4** afforded the 2-(arylthio)benzoates **5a-m** in moderate yields (Scheme 3, Table 2). Comparable yields were obtained for products **5b,d**, which are derived from dienes containing an electron-withdrawing halogen atom located at the arylthio group, and for products **5a,c,e**.



Scheme 3. Synthesis of **5a-m**; conditions: *i*: 1) Me_3SiOTf (0.1 equiv.), CH_2Cl_2, –78 → 20 °C, 20 h; 2) HCl, H_2O

Table 2: Synthesis of **5a-m**

3	**5**	R	Ar	% **(5)**[a]
a	**a**	H	Ph	53
b	**b**	H	4-FC_6H_4	47
c	**c**	H	3-MeC_6H_4	54
d	**d**	H	3-ClC_6H_4	51
e	**e**	H	4-MeC_6H_4	53
f	**f**	H	2-Naph	33
g	**g**	Me	4-MeC_6H_4	46
h	**h**	Me	Ph	50
i	**i**	Me	4-FC_6H_4	44
j	**j**	Et	Ph	50
n	**k**	H	4-EtC_6H_4	55
o	**l**	Me	4-Et-C_6H_4	45
p	**m**	Me	4-ClC_6H_4	48

[a] Yields of isolated products

2.3 Conclusion

In conclusion, I have reported a convenient approach to 2-(arylthio)benzoates by the first catalytic [3+3] cyclizations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane. The scope and applications of this methodology are currently studied in our laboratory.

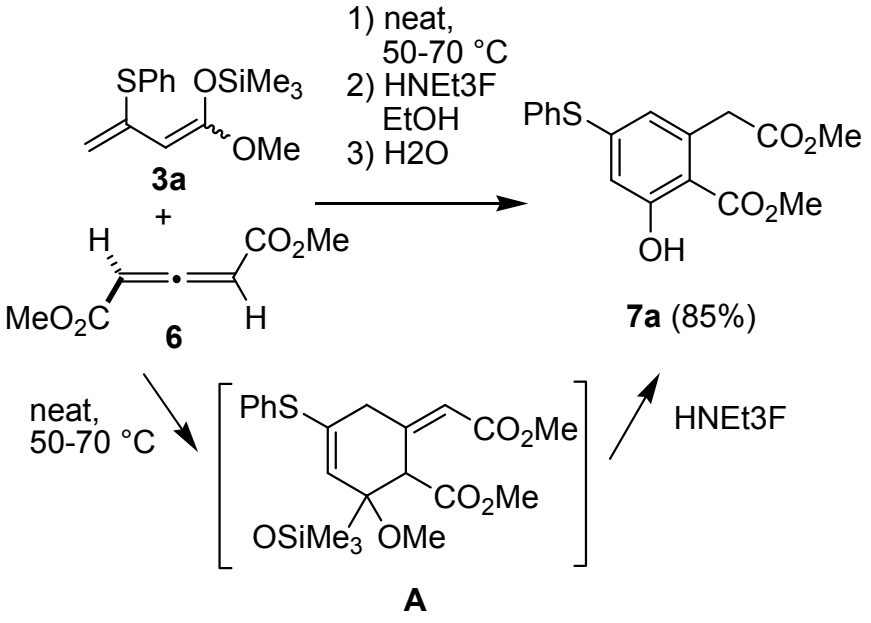
3. Regioselective synthesis of 4-arylthio-2-hydroxy-homophthalates by [4+2] cycloaddition of 3-arylthio-1-silyloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate

3.1 Introduction

Allenes are useful building blocks in inter- and intramolecular [4+2] cycloadditions.[22] Examples include the synthesis of functionalized phenols by [4+2] cycloaddition of 2-silyloxy-1,3-dienes with allenes. For example, the cycloaddition of a cyclic allenylester with 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene is a key step during the synthesis of (R)-(+)-lasiodiplodin.[23] 3-Methyl-4-(phenylsulfonyl)-phenol was prepared by reaction of allenylphenylsulfone with Danishefsky's diene.[24] 4-Hydroxy- and 2,4-dihydroxy-homophthalates are available by [4+2] cycloaddition of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with dimethyl allene-1,3-dicarboxylate.[25,26] This methodology was successfully applied to the synthesis of an analogue of lactonamycin,[27] of the N_7-C_{25} fragment of psymberin,[28] and of the 4-acetylisocoumarins AGI-7 and sescandelin.[29] Herein, I report what are, to the best of my knowledge, the first [4+2] cycloadditions of 3-arylthio-1-trimethylsiloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate. These reactions provide a convenient and regioselective approach to a variety of 4-arylthio-2-hydroxy-homophthalates which can be also regarded as highly functionalized diaryl sulfides.

Dimethyl allene-1,3-dicarboxylate **(6)** was prepared according to a known procedure.[30] The [4+2] cycloaddition of 6 with 3-phenylthio-1-trimethylsilyloxy-1,3-butadiene **3a** afforded 4-phenylthio-2-hydroxy-homophthalate **(8a)** in 85% yield (Scheme 1). The best yield was obtained when a stoichiometric ratio of 3a/p = 1:1

was used and when the reaction was carried out without solvent (neat). The yield decreased when the reaction was carried in a toluene solution (room temperature or at elevated temperature). The starting materials were added at 0 °C and the mixture was subsequently stirred at 50-70 °C for 12 h. The conversion was not complete when the reaction was carried out at 20 °C or when the reaction time was decreased. In contrast, a further increase of the temperature (higher than 70 °C) resulted in decomposition. After stirring for 12 h, to the solution was added an ethanol solution of triethylammonium fluoride (for complete cleavage of the O-Si bond) and, susequently, an aqueous work-up was carried out.



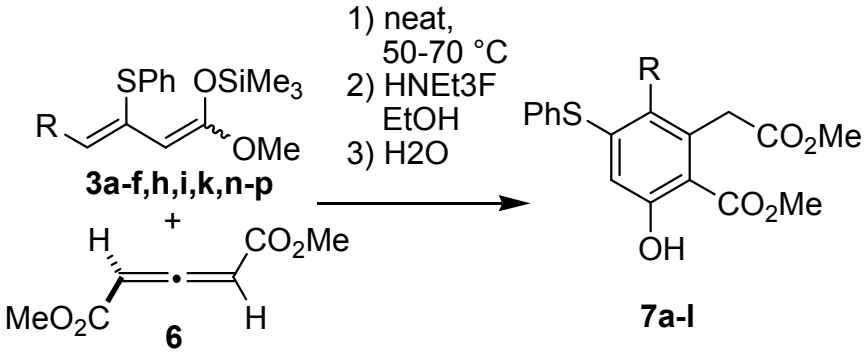
Scheme 4. Possible mechanism of the formation of **7a**

The reaction presumably proceeds by cycloaddition to give intermediate A. Subsequently, cleavage of the silyl ether and elimination of methanol from the intermediaryhemiacetal afforded product **7a** (Scheme 4). It is worth noting that the

selective elimination of methanol (formation of a 2-hydroxy-homophthalate) rather than water (formation of a 2-methoxy-homophthalate) was observed.

3.2 Result and discussion

The cycloaddition of **6** with 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **3a-f,h,i,k,n-p** afforded the novel 4-arylthio-2-hydroxyhomophthalates **7a-l** in 50-85% yield (Scheme 5, Table 3). A wide range of products could be successfully prepared. The best yields were obtained for products derived from dienes containing an electron-rich aryl group. The yields slightly dropped for dienes containing a methyl group located at carbon atom C-4 of the diene, due to steric hindrance.



Scheme 5. Synthesis of 2,4-dihydroxyhomophthalates **7a-l**

Table 3. Synthesis of 4-arylthio-2-hydroxy-homophthalates **7a-l**

3	**7**	R	Ar	% **(7)** [a]
a	**a**	H	Ph	85
b	**b**	H	4-FC_6H_4	55
c	**c**	H	3-MeC_6H_4	83
d	**d**	H	3-ClC_6H_4	60
e	**e**	H	4-MeC_6H_4	83
f	**f**	H	2-Naphthyl	80
h	**g**	Me	Ph	59
i	**h**	Me	4-FC_6H_4	50
k	**i**	H	4-ClC_6H_4	65
n	**j**	H	4-EtC_6H_4	80
o	**k**	Me	4-EtC_6H_4	72
p	**l**	Me	4-ClC_6H_4	55

[a] Yields of isolated products

3.3 Conclusion

In conclusion, I have reported a convenient and regioselective synthesis of 4-arylthio-2-hydroxy-homophthalates by [4+2] cycloadditions of 3-arylthio-1-trimethylsiloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate. Due to their polyfunctionalized nature, 4-arylthio-2-hydroxy-homophthalates represent versatile synthetic building blocks. The chemistry of these products is currently being studied.

4 Regioselective synthesis of 2-arylthio-4-methoxybenzoates and 2-arylthio-6-(methylthio)benzoates based on formal [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes

4.1 Introduction

Recently, Langer *et al.,* at have studied the synthesis of 4-methoxysalicylates by cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 3-oxo-orthoesters.[31] Herein, I report a convenient synthesis of 2-arylthio-4-methoxybenzoates by what are, to the best of my knowledge, the first [3+3] cyclocondensations of 3-oxo-orthoesters with 3-arylthio-1-trimethylsilyloxy-1,3-butadienes. This method provides a regioselective approach to a wide range of novel diaryl sulfides which are not readily available by other methods. In contrast to the C-S coupling reactions outlined above, my method relies on the assembly of one of the two arene moieties.

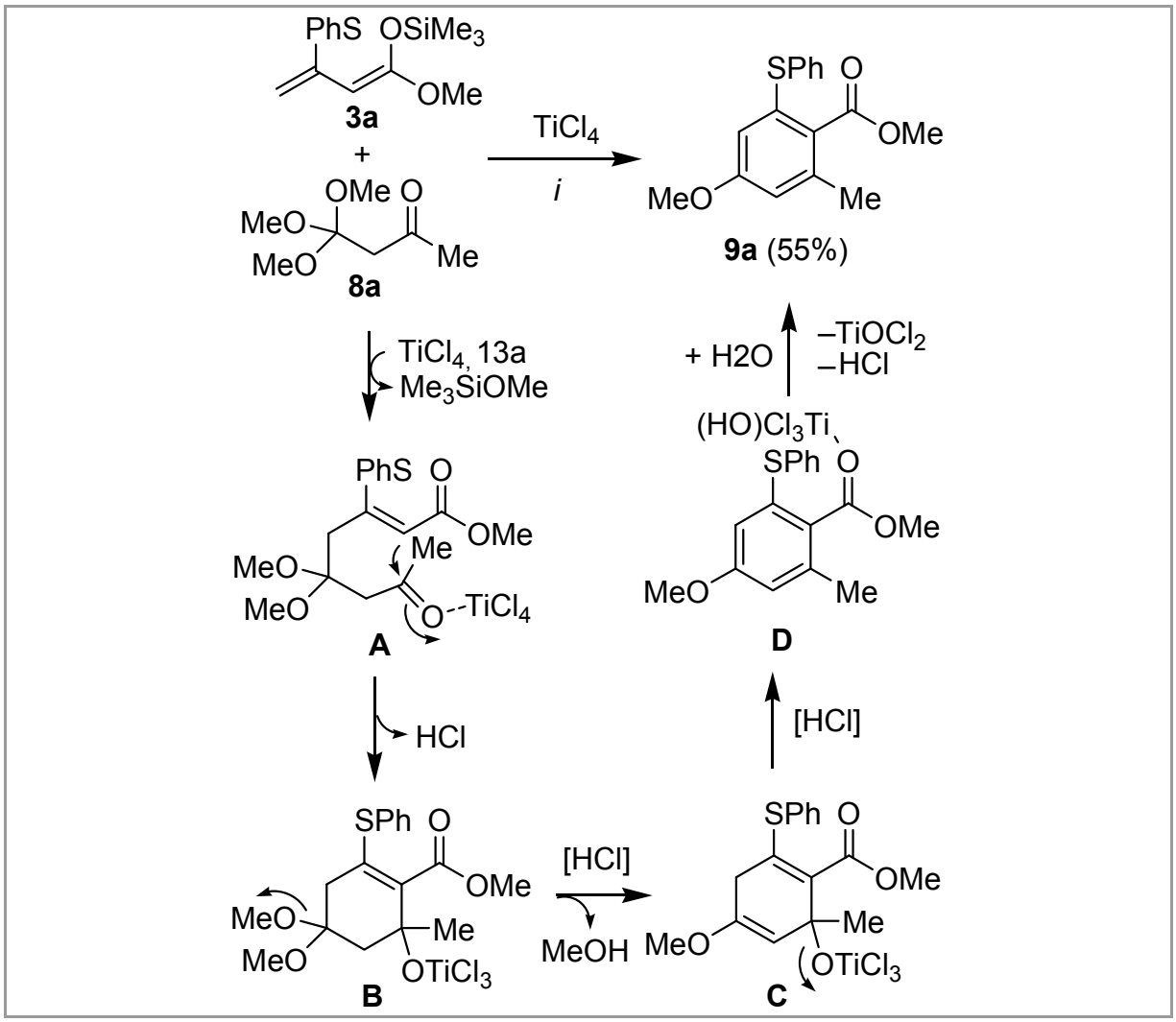
The known 3-oxo-orthoesters **8a,b** were prepared, following literature procedures, by condensation of 1,1-dichloroethene with acetyl and propionyl chloride, respectively, and subsequent reaction of the 3,3,3-trichloro-ketones thus formed with methanol.[32]

4.2 Results and Discussion

The known 3-oxo-orthoesters **8a,b** were prepared, according to literature procedures,[25] by condensation of 1,1-dichloroethene with acetyl and propionyl chloride, respectively, to give 3,3,3-trichloroketones which were subsequently transformed into the products by reaction with methanol. The known 3-arylthio-1-

trimethylsilyloxy-1,3-butadienes **3a-e,h,k,n,o** were prepared from methyl acetoacetate, methyl 3-oxopentanoate and various thiophenols in two steps.[26]

The $TiCl_4$-mediated cyclization of **8a** with 3-phenylthio-1-trimethylsilyloxy-1,3-butadiene **3a** afforded 2-phenylthio-4-methoxybenzoate **9a** (Scheme 6). The cyclization proceeded with very good regioselectivity. The formation of 2-phenylthio-6-methoxybenzoate, a regioisomer of **9a**, was not observed. The best yields were obtained when a stoichiometric ratio of **3a/1a**/$TiCl_4$ = 1.0/1.5/1.5 was used and when the reaction was carried out in a fairly concentrated solution **(8a)** = 0.33 M). The relatively low yield (55%) can be explained by practical problems during the chromatographic purification and by partial hydrolysis of the starting materials.

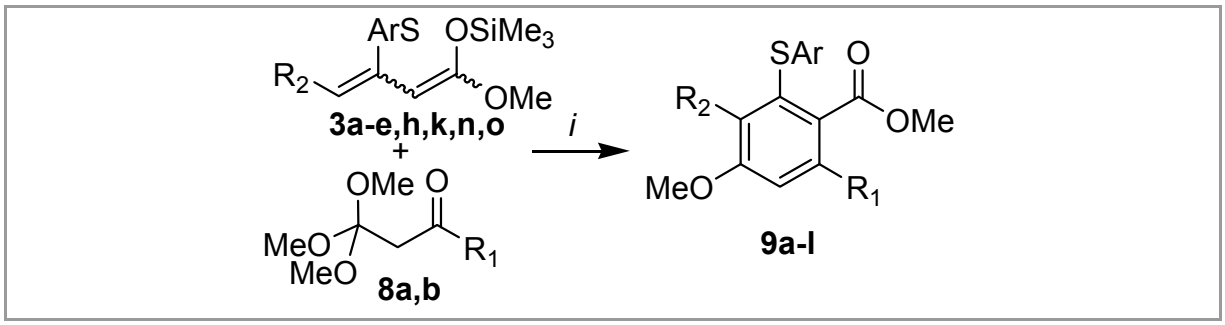


Scheme 6. Possible mechanism of the formation of arene **9a**; *i*: 1) $TiCl_4$ (1.0 equiv.), CH_2Cl_2, –78 → 20 °C, 20 h; 2) HCl (10%)

The formation of **9a** can be explained by the mechanism depicted in Scheme 6. The $TiCl_4$-mediated attack of diene **3a** to the orthoester gives intermediate A. The attack of the central carbon atom of **3a** onto the carbonyl group results in cyclization (intermediate B). Aromatization (intermediates C and D) and hydrolysis (during the aqueous work up) provide the final product. The cyclization might

proceed also by $TiCl_4$-mediated extrusion of methanol from **8a** to give 4,4-dimethoxy-3-buten-2-one, conjugate addition of the terminal carbon atom of **3a** onto the latter and subsequent cyclization. This process would follow a mechanism earlier suggested for the cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-alkoxy-2-en-1-ones.[26]

The $TiCl_4$-mediated cyclization of 3-oxo-orthoesters **8a,b** with 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **3a-e,h,k,n,o** gave the novel 2-arylthio-4-methoxybenzoates **9a-** (Scheme 7, Table 4).



Scheme 7. Synthesis of arenes **9a-l**; *i*: 1) $TiCl_4$ (1.0 equiv.), CH_2Cl_2, –78 → 20 °C, 20 h; 2) HCl (10%)

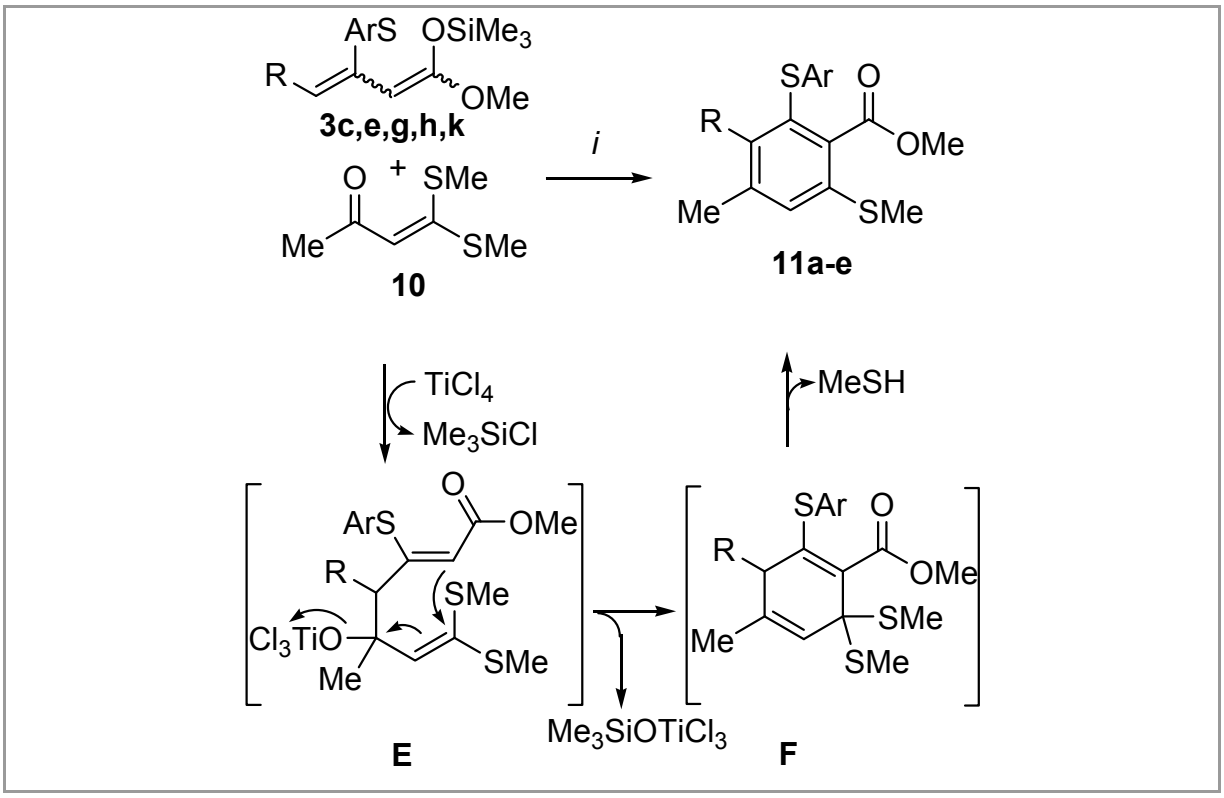
Table 4. Synthesis of **9a-l**

8	**3**	**9**	R^1	R^2	Ar	% **(9)** [a]
a	**a**	**a**	Me	H	Ph	55
a	**b**	**b**	Me	H	4-FC_6H_4	40
a	**c**	**c**	Me	H	3-MeC_6H_4	50
a	**d**	**d**	Me	H	3-ClC_6H_4	46
a	**e**	**e**	Me	H	4-MeC_6H_4	51
a	**h**	**f**	Me	Me	Ph	45
a	**k**	**g**	Me	H	4-ClC_6H_4	46
a	**n**	**h**	Me	H	4-EtC_6H_4	45
a	**o**	**i**	Me	Me	4-EtC_6H_4	35
b	**d**	**j**	Et	H	3-ClC_6H_4	37
b	**e**	**k**	Et	H	4-MeC_6H_4	38
b	**k**	**l**	Et	H	4-ClC_6H_4	40

[a] Yields of isolated products

Various substituents can be introduced at carbon atoms C3 and C6 of the benzoate moiety (substituents R^1 and R^2) and at the arylthio group. The yields of the products **9h,o**, derived from dienes **3h,o** containing a substituent located at the terminal carbon atom, are lower than the yields of the other products. The yields of the products derived from **8a** are slightly higher than the yields of the producrts derived from **8b**. The substituents located at the aryl group of the diene seems to have no major influence on the yield. The moderate yields can be explained by problems during the chromatographic purification and by partial hydrolysis of the starting materials. In some reactions a small amount of hydrolyzed starting material was recovered.

Recently, Langer *et al;* have reported the synthesis of 6-(methylthio)salicylates by cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones.[31] Based on these results I studied related cyclization reactions of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes. The cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **3c,e,g,h,k** with 1,1-bis(methylthio)-1-en-3-one 10[32] afforded the novel 2-arylthio-6-(methylthio)benzoates **11a-e** in 37-55% yield (Scheme 8, Table 5). The formation of products **11** might be explained by $TiCl_4$-mediated attack of the diene onto the carbonyl group of **10** to give intermediate E, formation of an allylic cation and cyclization (intermediate F). The extrusion of MeSH leads to the final product.



Scheme 8. Synthesis of arenes **11a-e** Conditions: *i*, 1) $TiCl_4$, –78 → 20 °C, 20 h; 2) HCl (10%).

-

Table 5. Synthesis of **11a-e**

3	**11**	R	Ar	% **(11)**[a]
c	**a**	H	3-MeC_6H_4	37
e	**b**	H	4-MeC_6H_4	55
g	**c**	Me	4-MeC_6H_4	51
h	**d**	Me	Ph	48
k	**e**	H	4-ClC_6H_4	49

[a] Yields of isolated products

4.3 Conclusion

In conclusion, I have reported the synthesis of 2-arylthio-4-methoxybenzoates by cyclocondensation of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-oxo-orthoesters. In addition, I have reported the synthesis of 2-arylthio-6-(methylthio)benzoates by cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones. The chemistry reported herein provides a regioselective approach to a wide range of novel diaryl sulfides which are not readily available by other methods.

Experimental Section

4.1 General: Equipments, chemicals and work techniques

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

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

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

High Resolution mass spectroscopy: Finnigan MAT 95 or Varian MAT 311; Bruker.

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.

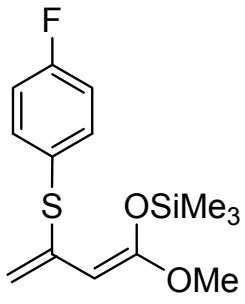
X-ray crystal structure analysis: Bruker X8Apex Diffractometer with CCD-Kamera (Mo-Ka und Graphit Monochromator, λ = 0.71073 Å).56

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

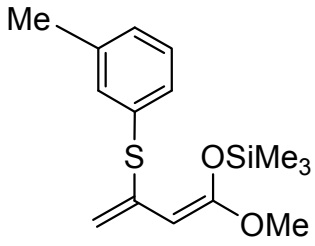
TLC: Merck DC finished foils silica gel 60 F254 on aluminum foil and Macherey finished foils Alugram® Sil G/UV254. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

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

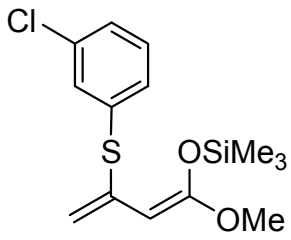
General procedure for the synthesis of 3-arylthio-1-silyloxy-1,3-butadienes 3b-p: To a THF solution (1.2 mL / mmol of **2**) of diisopropylamine (DIPA) (84.5 mmol) was added nBuLi (84.5 mmol) at 0 °C. After stirring for 45 min, **2** (65.0 mmol) was added at -78 °C. After stirring for 1 h, TMSCl (97.5 mmol) was added at -78 °C and the solution was allowed to warm to 20 °C during 18 h with stirring. The solvent was removed in vacuo. To the residue was added heptane and the mixture was filtered under inert atmosphere. The filtrate was concentrated in vacuo to give products 3 which were used without further purification. Due to their unstable nature, products 3 have been used directly after their preparation and have been characterized only by ^{1}H NMR spectroscopy. The products are isolated as mixtures of E/Z isomers. Only the signals of the major isomer are listed.



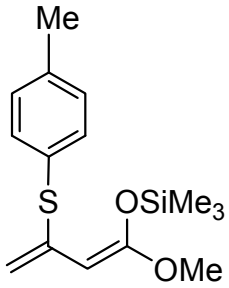
(1-Methoxy-3-(4-fluorophenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3b): Starting with **2b** (14,700 mg, 65.0 mmol), DIPA (8,500 mg, 84.5 mmol), nBuLi (5,400 mg, 84.5 mmol) and TMSCl (10,500 mg, 97.5 mmol), **3b** was isolated as a highly viscous oil (15,500 mg, 80%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19 (s, 9H, TMS), 3.38 (s, 3H, OCH_3), 3.49 (s, 2H, CH_2), 5.34 (s, 1H, CH), 7.08-7.51 (m, 4H, ArH).



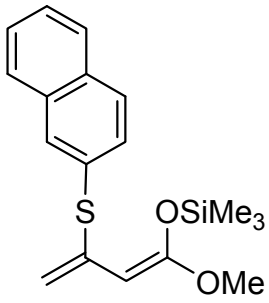
(1-Methoxy-3-(3-methylphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3c): Starting with **2c** (14,400 mg, 65.0 mmol), DIPA (8,500 mg, 84.5 mmol), nBuLi (5,400 mg, 84.5 mmol) and TMSCl (10,500 mg, 97.5 mmol), **3c** was isolated as a highly viscous oil (16,600 mg, 87%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 (s, 9H, TMS), 2.12 (s, 3H, CH_3), 3.35 (s, 3H, OCH_3), 3.48 (s, 2H, CH_2), 5.27 (s, 1H, CH), 7.02-7.38 (m, 4H, ArH).



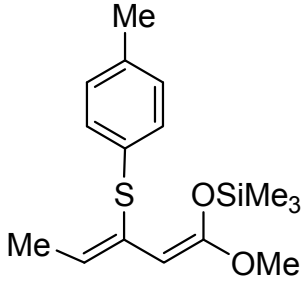
(1-Methoxy-3-(3-chlorophenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3d): Starting with **2d** (15,700 mg, 65.0 mmol), DIPA (8,500 mg, 84.5 mmol), nBuLi (5,400 mg, 84.5 mmol) and TMSCl (10,500 mg, 97.5 mmol), **3d** was isolated as a highly viscous oil (17,500 mg, 86%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.21 (s, 9H, TMS), 3.49 (s, 2H, CH_2), 5.32 (s, 1H, CH), 7.04-7.37 (m, 4H, ArH).



(1-Methoxy-3-(4-methylphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3e): Starting with **2e** (14,400 mg, 65.0 mmol), DIPA (8,500 mg, 84.5 mmol), nBuLi (5,400 mg, 84.5 mmol) and TMSCl (10,500 mg, 97.5 mmol), **3e** was isolated as a highly viscous oil (16,700 mg, 88%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 (s, 9H, TMS), 2.14 (s, 3H, CH_3), 3.37 (s, 3H, OCH_3), 3.48 (s, 2H, CH_2), 5.27 (s, 1H, CH), 7.02-7.38 (m, 4H, ArH).

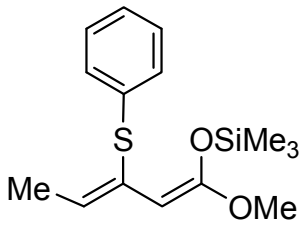


(1-Methoxy-3-(naphth-2-ylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3f): Starting with **2f** (10.4 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3f** was isolated as a highly viscous oil (13.2 g, 79%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19 (s, 9H, TMS), 3.32 (s, 3H, OCH_3), 3.46 (s, 2H, CH_2), 5.29 (s, 1H, CH), 7.01-7.51 (m, 7H, ArH).

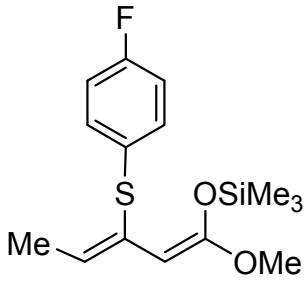


(1-Methoxy-3-(4-methylphenylsulfanyl)penta-1,3-dienyloxy)trimethylsilane (3g): Starting with **2g** (15.3 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3g** was isolated as

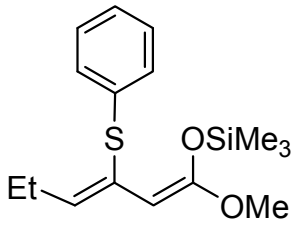
a highly viscous oil (16.5 g, 83%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 9H, TMS), 1.72 (s, 3H, CH_3), 2.08 (d, 3H, CH_3), 3.15 (s, 3H, OCH_3), 6.03 (q, 1H, CH), 6.84 (s, 1H, CH), 6.92-7.28 (m, 4H, ArH).



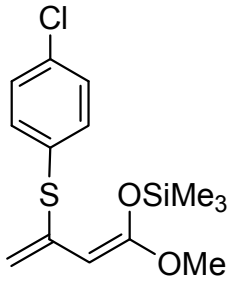
(1-Methoxy-3-(phenylsulfanyl)penta-1,3-dienyloxy)-trimethylsilane (3h): Starting with **2h** (14.4 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3h** was isolated as a highly viscous oil (15,600 mg, 82%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 9H, TMS), 2.12 (d, 3H, CH_3), 3.17 (s, 3H, OCH_3), 6.06 (q, 1H, CH), 6.84 (s, 1H, CH), 6.92-7.28 (m, 5H, ArH).



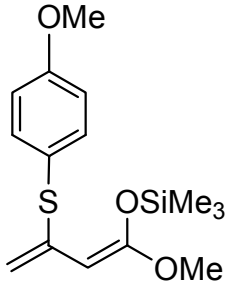
(1-Methoxy-3-(4-fluorophenylsulfanyl)penta-1,3-dienyloxy)trimethylsilane (3i): Starting with **2i** (15.6 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3i** was isolated as a highly viscous oil (15.8 g, 78%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 9H, TMS), 2.08 (d, 3H, CH_3), 3.15 (s, 3H, OCH_3), 6.05 (q, 1H, CH), 6.84 (s, 1H, CH), 6.92-7.28 (m, 4H, ArH).



(1-Methoxy-3-(phenylsulfanyl)hexa-1,3-dienyloxy)-trimethylsilane (3j): Starting with **2j** (15.3 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3j** was isolated as a highly viscous oil (16.5 g, 83%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 9H, TMS), 2.08 (m, 2H, CH_2), 2.6 (t, 3H, CH_3), 3.15 (s, 3H, OCH_3), 6.05 (t, 1H, CH), 6.54 (s, 1H, CH), 6.92-7.30 (m, 5H, ArH).

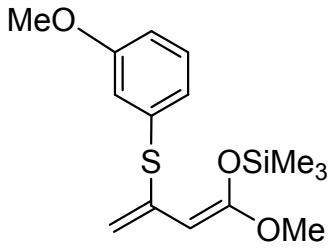


(1-Methoxy-3-(4-chlorophenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3k): Starting with **2k** (15.7 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3k** was isolated as a highly viscous oil (17.1 g, 84%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 (s, 9H, TMS), 3.49 (s, 2H, CH_2), 5.32 (s, 1H, CH), 7.04-7.39 (m, 4H, ArH).

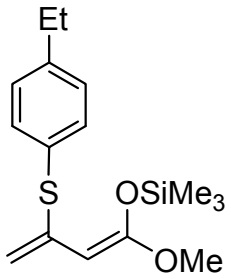


(1-Methoxy-3-(4-methoxyphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3l): Starting with **2l** (15.18 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3l** was isolated as a highly viscous oil (17.6 g, 88%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 (s, 9H,

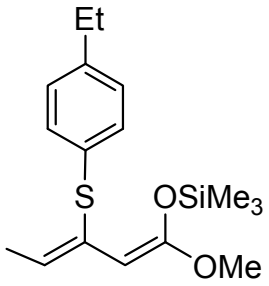
TMS), 3.34 (s, 3H, OCH_3), 3.37 (s, 3H, OCH_3), 3.48 (s, 2H, CH_2), 5.27 (s, 1H, CH), 7.02-7.38 (m, 4H, ArH).



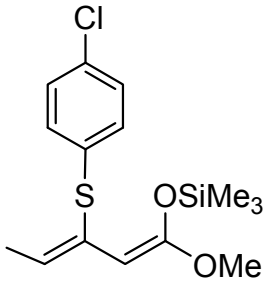
(1-Methoxy-3-(3-methoxyphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3m): Starting with **2m** (15.18 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3m** was isolated as a highly viscous oil (17.6 g, 88%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.17 (s, 9H, TMS), 3.35 (s, 3H, OCH_3), 3.37 (s, 3H, OCH_3), 3.48 (s, 2H, CH_2), 5.27 (s, 1H, CH), 7.02-7.38 (m, 4H, ArH).



(1-Methoxy-3-(4-ethylphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3n): Starting with **2n** (15.3 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3n** was isolated as a highly viscous oil (17.3 g, 87%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.17 (s, 9H, TMS), 1.16 (t, *j = 7.5*, 3H, $CH_2\mathit{CH_3}$), 2.52 (q, *j = 7.5*, 2H, $\mathit{CH_2}CH_3$), 3.45 (s, 3H, OCH_3), 3.59 (s, 2H, CH_2), 5.07 (s, 1H, CH), 7.00-7.40 (m, 4H, ArH).



(1-Methoxy-3-(4-ethylphenylsulfanyl)penta-1,3-dienyloxy)trimethylsilane (3o): Starting with **2o** (16,250 mg, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (10.5 g, 97.5 mmol), **3o** was isolated as a highly viscous oil (16.7 g, 80%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 (s, 9H, TMS), 0.98 (t, j = 7.5, 3H, CH_2CH_3), 1.72 (d, 3H, CH_3), 2.37 (q, j = 7.5, 2H, CH_2CH_3), 3.16 (s, 3H, OCH_3), 6.04 (q, 1H, CH), 6.83 (s 1H, CH), 6.86-7.40 (m, 4H, ArH).



(1-Methoxy-3-(4-ethylphenylsulfanyl)penta-1,3-dienyloxy)trimethylsilane (3p): Starting with **2p** (16.61 g, 65.0 mmol), DIPA (8.5 g, 84.5 mmol), nBuLi (5.4 g, 84.5 mmol) and TMSCl (105 g, 97.5 mmol), **3p** was isolated as a highly viscous oil (16.6 g, 78%, isomeric ratio = 3:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.05 (s, 9H, TMS), 1.72 (d, 3H, CH_3), 3.16 (s, 3H, OCH_3), 6.04 (q, 1H, CH), 6.83 (s 1H, CH), 6.86-7.40 (m, 4H, ArH).

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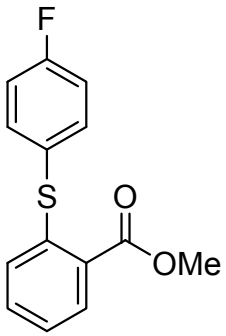
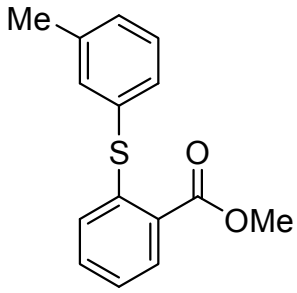
General Procedure

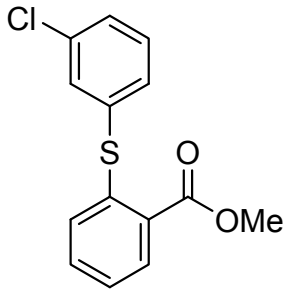
General experimental procedure for the synthesis of **5a-m:** To a dichloromethane solution (2 mL / mmol of 6) of 6 (1.5 mmol) and of 1,1,3,3-tetramethoxypropane (1.0 mmol) was added TMSOTf (0.1 mmol) at –78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added a diluted aqueous solution of HCl (15 mL). The organic and the aqueous layer were separated and the latter was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography.



2-(4-Fluorophenylsulfanyl)benzoic acid methyl ester (5b): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3b** (447 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5b** was isolated as a highly viscous colourless oil (184 mg, 47%); ^{1}H NMR (250 MHz, CDCl3): δ = 3.89 (s, 3H, OCH_3), 6.69-7.89 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 52.0 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm–1; GC-MS (EI, 70 eV): m/z (%): 263 (17), 262 (M^+ 100), 232 (12), 231 (77), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{14}H_{11}O_2FS$ [M^+]: 262.04583, found 262.046008.

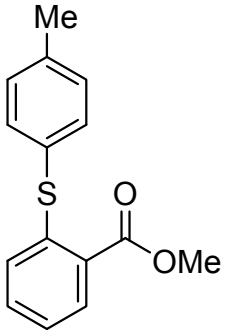


2-(*m*-Tolylsulfanyl)benzoic acid methyl ester (5c): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3c** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5c** was isolated as a highly viscous colourless oil (208 mg, 54%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.33 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 6.72-7.41 (m, 8H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.3 (CH_3), 52.0 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm–1; GC-MS (EI, 70 eV): m/z (%): 259 (34), 258 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.05525, found 258.05570.

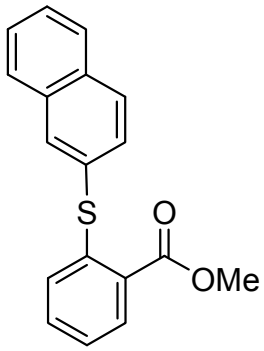


2-(3-Chlorophenylsulfanyl)benzoic acid methyl ester (5d): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3d** (471 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5d** was isolated as a highly viscous colourless oil (212 mg, 51%); ^{1}H NMR (250 MHz, CDCl3): δ = 3.87 (s, 3H, OCH_3), 6.77-7.92 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 51.2 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR

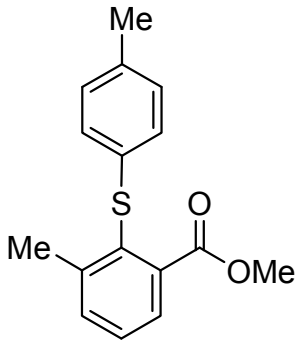
(neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1432 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 280 (31), 279 (12), 278 (M^+ 100), 249 (18), 247 (54), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{14}H_{11}O_2ClS$ [M^+]: 278.01628, found 278.016068.



2-(*p*-Tolylsulfanyl)benzoic acid methyl ester (5e): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3e** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5e** was isolated as a highly viscous colourless oil (205 mg, 53%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.34 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 6.72-7.94 (m, 8H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.3 (CH_3), 52.1 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 259 (34), 258 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.05525, found 258.05570.

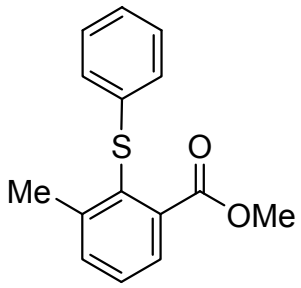


2-(Naphth-2-ylsulfanyl)benzoic acid methyl ester (5f): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3f** (495 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5f** was isolated as a highly viscous colourless oil (145 mg, 33%); ^{1}H NMR (250 MHz, CDCl3): δ = 3.91 (s, 3H, OCH_3), 6.72-8.01 (m, 11H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 52.2 (OCH_3), 124.4, 126.7 (CH_{Ar}), 126.8 (C_{Ar}), 127.0, 127.7, 127.8, 127.9, 129.4 (CH_{Ar}), 129.9 (C_{Ar}), 131.0, 131.8, 132.3 (CH_{Ar}), 133.2, 13.9(C_{Ar}), 135.2 (CH_{Ar}), 143.0 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 296 (17), 294 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{18}H_{14}O_2S$ [M^+]: 294.05525, found 294.05570.

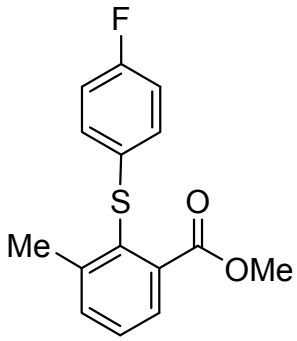


3-Methyl-2-(4-methylcyclohexa-1,5-dienylsulfanyl) benzoic acid methyl ester (5g): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3g** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5g** was isolated as a highly viscous colourless oil (187mg, 46%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.12 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 6.82-7.44 (m, 7H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9, 20.1 (CH_3), 51.3 (OCH_3), 125.2 (CH_{Ar}), 126.9 (2C CH_{Ar}), 127.5 (CH_{Ar}), 128.7 (2C CH_{Ar}), 131.8 (CH_{Ar}),136.3, 138.4, 143.0, 144.6, 144.9 (C_{Ar}), 167.9 (C); IR

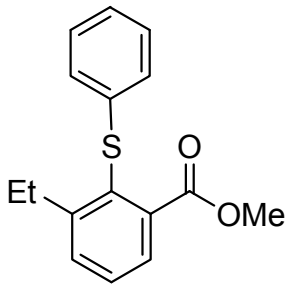
(neat): $\tilde{\nu}$ = 3055 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 273 (18), 272 (M^+ 100), 241 (29), 240 (22), 239 (15), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.08655 found 272.086163



2-(Cyclohexa-1,5-dienylsufanyl)-3-methylbenzoic acid methyl ester (5h): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3h** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5h** was isolated as a highly viscous colourless oil (193 mg, 50%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.30 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), .7.12-7.74 (m, 8H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.2 (CH_3), 52.3 (OCH_3), 124.5 (C_{Ar}), 125.5, 126.4 (CH_{Ar}), 127.5, 128.8 (2C CH_{Ar}), 129.1, 132.9 (CH_{Ar}), 136.3, 138.4, 143.0 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 259 (17), 258 (M^+ 100), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.07090, found 258.070812.

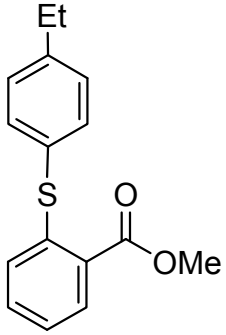


2-(4-Fluorocyclohexa-1,5-dienylsulfanyl)-3-methylbenzoic acid methayl ester (5i): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3i** (468 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5i** was isolated as a highly viscous colourless oil (182 mg, 44%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.25 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), .6.72-7.54 (m, 7H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.2 (CH_3), 51.3 (OCH_3), 114.8, 115.1 (CH_{Ar}), 124.5 (C_{Ar}), 125.4, 128.0, 128.7, 128.8 (CH_{Ar}), 129.1, 129.9 (C_{Ar}), 132.0 (CH_{Ar}), 143.1, 144.2 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm–1; GC-MS (EI, 70 eV): m/z (%): 277 (16), 276 (M^+ 100), 345 (40), 244 (24), 243 (60), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{13}O_2FS$ [M^+]: 276.06148 found 276.061274.



(3-Ethyl-2-phenylsulfanyl)benzoic acid methyl ester (5j): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3j** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5j** was isolated as a highly viscous colourless oil (204 mg, 50%); ^{1}H NMR (250 MHz, CDCl3): δ = 1.06 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.72 (q, J = 7.5 Hz, 2H, CH_2CH_3), 3.66 (s, 3H, OCH_3), 6.98-7.34 (m, 8H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.9 (CH_3), 27.3 (CH_2), 52.2 (OCH_3), 125.4 (CH_{Ar}), 126.3 (C_{Ar}), 126.4 (CH_{Ar}), 127.3, 128.8 (2C CH_{Ar}), 129.0

(C_{Ar}), 129.2, 131.1 (CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 273 (18), 272 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.05025, found 258.050701.



2-(4-Ethylcyclohexa-1,5-dienylsulfanyl)benzoic acid methyl ester (5k): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3n** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5k** was isolated as a highly viscous colourless oil (224 mg, 55%); ^{1}H NMR (250 MHz, CDCl3): δ = 1.11 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.71 (q, J = 7.5 Hz, 2H, CH_2CH_3), 3.86 (s, 3H, OCH_3), 6.73-7.94 (m, 8H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.3 (CH_3), 28.5 (CH_2), 52.1 (OCH_3), 124.4 (CH_{Ar}), 126.3 (C_{Ar}), 126.6 (CH_{Ar}), 128.5 (2C CH_{Ar}), 129.0 (C_{Ar}), 130.5, 132.2 (CH_{Ar}), 135.8 (2C CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 273 (19), 272 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.05025, found 258.050701.

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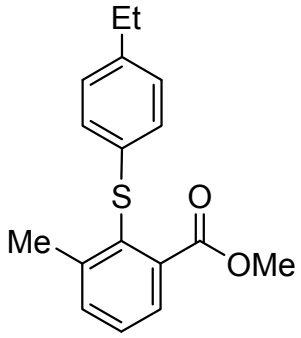
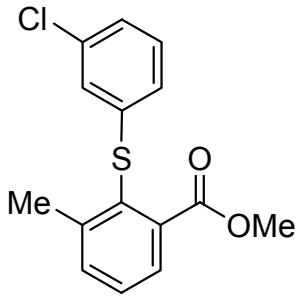


2-(4-Ethylcyclohexa-1,5-dienylsulfanyl)-4-methylbenzoic acid methyl ester (5l): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3o** (483 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5l** was isolated as a highly viscous colourless oil (193 mg, 45%); ^{1}H NMR (250 MHz, CDCl3): δ = 1.09 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.28 (s, 3H, CH_3), 2.42 (q, J = 7.5 Hz, 2H, CH_2CH_3), 3.78 (s, 3H, OCH_3), 6.90-7.34 (m, 7H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.4 (CH_2CH_3), 20.3 (CH_3), 27.3 (CH_2 CH_3), 51.3 (OCH_3), 125.2 (CH_{Ar}), 126.9, 127.4 (2C CH_{Ar}), 127.6 (CH_{Ar}), 129.7 (C_{Ar}), 131.1 (CH_{Ar}), 132.7, 138.2, 140.8, 142.8 (C_{Ar}), 168.0 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 287 (18), 286 (M^+ 100), 271 (17), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{17}H_{18}O_2S$ [M^+]: 286.10220, found286.102313.



2-(3-Chlorocyclohexa-1,5-dienylsulfanyl)-3-methylbenzoic acid methyl ester (5m): Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **3p** (492 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5m** was isolated as a highly viscous colourless oil (210 mg, 48%); ^{1}H NMR (250 MHz, CDCl3): δ = 2.33 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.82-7.53 (m, 7H, ArH) ; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.2

(CH_3), 51.3 (OCH_3), 124.5 (C_{Ar}), 125.5 (CH_{Ar}), 126.5 (C_{Ar}), 127.6, 128.0 (2C CH_{Ar}), 128.3, 132.0 (CH_{Ar}), 136.3, 138.4, 143.0 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s) 530 (m) cm−1; GC-MS (EI, 70 eV): m/z (%): 294 (39), 293 (17), 292 (M^+ 100), 261 (35), 260 (15), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{13}O_2ClS$ [M^+]: 292.03193, found 292.032066

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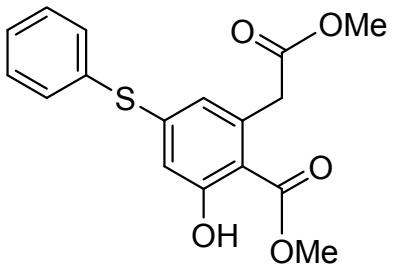
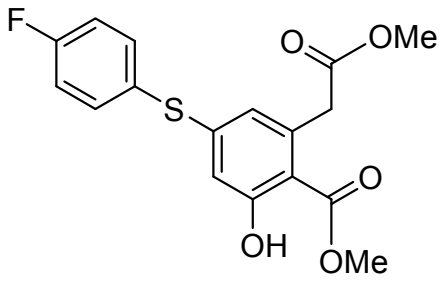
General experimental procedure for the synthesis of 7a-l: To neat **10a-l** (1.5 mmol) was added **9** (1.5 mmol) at 0 °C and the mixture was stirred for 30 min. Subsequently, the mixture was stirred at 50-70 °C for 12 h. The solution was allowed to cool to 20 °C and an ethanol solution (2 mL, 96%) of triethylammonium fluoride (1.5 mmol) was added. The mixture for stirred for 10 min and subsequently water and dichloromethane were added. The organic and the aqueous layer were separated and the latter was extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc / heptanes = 1:9).

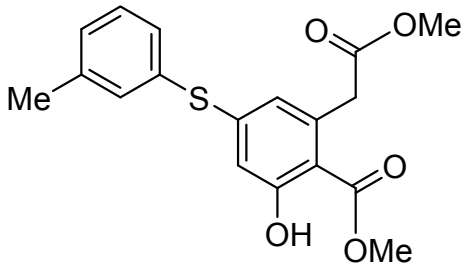


2-Hydroxy-6-methoxycarbonylmethyl-4-(phenylsulfanyl)benzoic acid methyl ester (7a): Starting with **3a** (420 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7a** was isolated as a highly viscous colourless oil (423 mg, 85%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.60 (s, 3H, OCH_3), 3.71 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 6.43(s, 1H, ArH), 6.49 (s, 1H, ArH), 7.32-7.44 (m, 5H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 38.3 (CH_2), 51.9 (OCH_3), 52.0 (OCH_3), 109.0 (C_{Ar}), 114.5, 122.0, 129.0 (CH_{Ar}), 129.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689

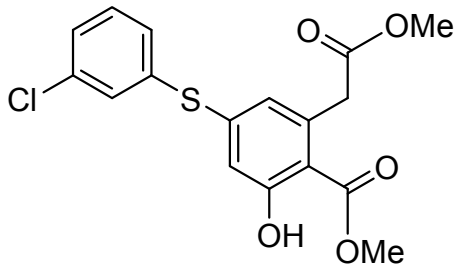
(s), 562 (m); MS (EI, 70 eV): m/z (%) = 333 (20), 332 (M^+, 100), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{17}H_{16}O_5S$ [M^+]: 332.07129, found: 332.071093.



4-(4-Fluorophenylsulfanyl)-2-hydroxy-6-(methoxycarbonylmethyl)benzoic acid methyl ester (7b): Starting with **13b** (447 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7b** was isolated as a highly viscous colourless oil (288 mg, 55%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.47 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 3.69 (s, 2H, CH_2), 6.41(s, 1H, ArH), 6.49 (s, 1H, ArH), 7.11-7.34 (m, 4H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 38.3 (CH_2), 52.9 (OCH_3), 53.2 (OCH_3), 109.0 (C_{Ar}), 114.5, 129.0 (CH_{Ar}), 129.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 137.5, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 351 (18), 350 (M^+, 100), 319 (13), 318 (19), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{17}H_{15}O_5SF$ [M^+]: 350.06187, found: 350.061584.

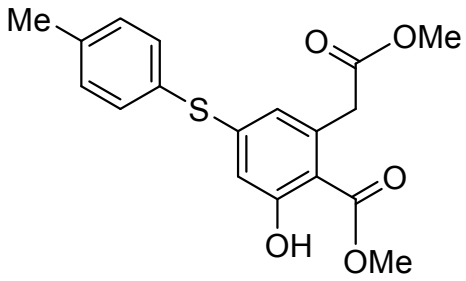


2-Hydroxy-6-methoxycarbonylmethyl-4-(*m*-tolylsulfanyl)benzoic acid methyl ester (7c): Starting with **3c** (441 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7c** was isolated as a highly viscous colourless oil (430 mg, 83%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.31 (s, 3H, CH_3), 3.60 (s, 3H, OCH_3), 3.72 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 6.43(s, 1H, ArH), 6.49 (s, 1H, ArH), 7.32-7.44 (m, 4H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.3 (CH_3), 42.5 (CH_2), 51.9 (OCH_3), 52.2 (OCH_3), 109.0 (C_{Ar}), 113.9, 121.5 (CH_{Ar}), 130.6 ($2CH_{Ar}$), 130.1 (C_{Ar}), 131.1 ($2CH_{Ar}$), 135.4, 136.6, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1321 (s), 1256 (s), 1194 (s), 1163 (s), 1123 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 347 (20), 346 (M^+, 100), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{18}H_{18}O_5S$ [M^+]: 346.08695, found: 346.08788.



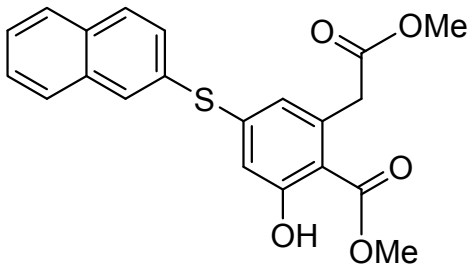
4-(3-Chlorophenylsulfanyl)-2-hydroxy-6-(methoxycarbonylmethyl)benzoic acid methyl ester (7d): Starting with **3d** (471 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7d** was isolated as a highly viscous colourless oil (329 mg, 60%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.46 (s, 3H, OCH_3), 3.58 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2), 6.42 (s, 1H, ArH), 6.48 (s, 1H, ArH), 7.11-7.34 (m, 4H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ

= 38.3 (CH_2), 52.9 (OCH_3), 53.2 (OCH_3), 109.0 (C_{Ar}), 114.5, 129.0 (CH_{Ar}), 129.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 137.5, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 368 (37), 367 (18), 366 (M^+, 100), 335 (5), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{17}H_{15}O_5SCl$ [M^+]: 366.03232, found: 366.032168.



2-Hydroxy-6-(methoxycarbonylmethyl)-4-(*p*-tolylsulfanyl)benzoic acid methyl ester (7e): Starting with **3e** (441 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7e** was isolated as a highly viscous colourless oil (430 mg, 83%); ^1H NMR (250 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 3.60 (s, 3H, OCH_3), 3.72 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 6.43(s, 1H, ArH), 6.49 (s, 1H, ArH), 7.32-7.44 (m, 4H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.3 (CH_3), 42.5 (CH_2), 51.9 (OCH_3), 52.2 (OCH_3), 109.0 (C_{Ar}), 113.9, 121.5 (CH_{Ar}), 130.6 ($2CH_{Ar}$), 130.1 (C_{Ar}), 131.1 ($2CH_{Ar}$), 135.4, 136.6, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1321 (s), 1256 (s), 1194 (s), 1163 (s), 1123 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 347

(20), 346 (M^+, 100), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{18}H_{18}O_5S$ [M^+]: 346.08695, found: 346.08788.



2-Hydroxy-6-(methoxycarbonylmethyl)-4-(2-naphthylsulfanyl)benzoic acid methyl ester (7f): Starting with **3f** (495 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7f** was isolated as a highly viscous colourless oil (458 mg, 80%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.60 (s, 3H, OCH_3), 3.72 (s, 2H, CH_2), 3.79 (s, 3H, OCH_3), 6.43(s, 1H, ArH), 6.49 (s, 1H, ArH), 7.32-7.45 (m, 7H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 41.1 (CH_2), 51.9 (OCH_3), 52.0 (OCH_3), 109.0 (C_{Ar}), 114.8, 122.2, 129.0 (CH_{Ar}), 129.9, 130.0 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.4 ($2CH_{Ar}$), 136.6, 138.4, 139.2, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2995 (w), 2951 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 688 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 383 (11), 382 ((M^+ 51), 322 (9), 317(16), 316 (31), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{21}H_{18}O_5S$ [M^+]: 382.08695, found: 382.087016.

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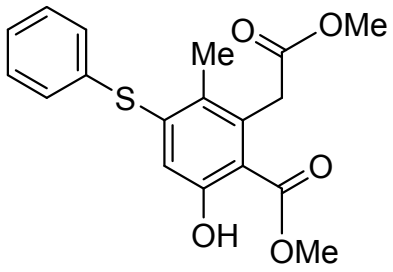
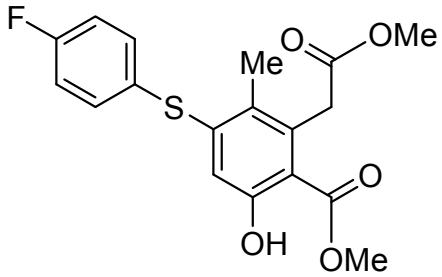
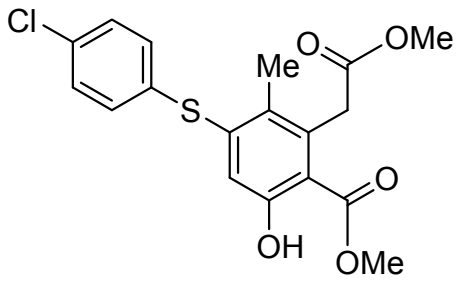


6-Hydroxy-2-(methoxycarbonylmethyl)-3-methyl-4-(phenylsulfanyl)benzoic acid methyl ester (7g): Starting with **3h** (441 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7g** was isolated as a highly viscous colourless oil (306 mg, 59%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.77 (s, 2H, CH_2), 6.49 (s, 1H, ArH), 7.32-7.63 (m, 5H, ArH), 10.77 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.8 (CH_3), 38.2 (CH_2), 51.0 (OCH_3), 52.2 (OCH_3), 109.2 (C_{Ar}), 112.9 (CH_{Ar}), 125.4 (C_{Ar}), 129.9, 135.3 ($2CH_{Ar}$), 135.4 (CH_{Ar}), 140.5, 145.6, 146.3, 155.8 (C_{Ar}), 165.5, 169.0 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 347 (20), 346 (M^+, 100), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{18}H_{18}O_5S$ [M^+]: 346.08695, found: 346.08788.



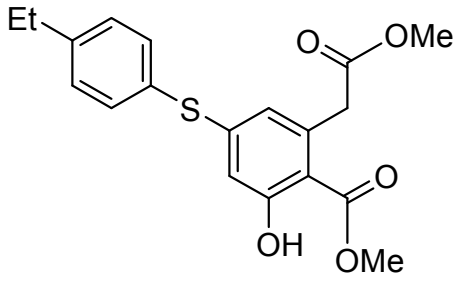
4-(4-Fluorophenylsulfanyl)-6-hydroxy-2-(methoxycarbonylmethyl)-3-methylbenzoic acid methyl ester (7h): Starting with **3i** (468 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7h** was isolated as a highly viscous colourless oil (273 mg, 50%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.82 (s, 2H, CH_2), 6.49 (s, 1H, ArH), 7.22-7.48 (m, 4H, ArH), 10.77 (s, 1H, OH); ^{13}C NMR (63

MHz, $CDCl_3$): δ = 15.9 (CH_3), 37.5 (CH_2), 51.0 (OCH_3), 52.2 (OCH_3), 110.2 (C_{Ar}), 111.5 (CH_{Ar}), 125.4 (C_{Ar}), 129.9, 135.3 ($2CH_{Ar}$), 140.5, 150.8, 151.5, 155.8, 159.0 (C_{Ar}), 165.5, 169.0 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1438 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 962 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 365 (18), 364 (M^+, 100), 333 (23), 332 (64), 305 (34), 304 (89), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{18}H_{17}O_5FS$ [M^+]:364.07752, found: 364.076969.



4-(4-Chlorophenylsulfanyl)-2-hydroxy-6-(methoxycarbonylmethyl)benzoic acid methyl ester (7i): Starting with **3k** (471 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7i** was isolated as a highly viscous colourless oil (357 mg, 65%); ^1H NMR (250 MHz, $CDCl_3$): δ = 3.47 (s, 3H, OCH_3), 3.59 (s, 3H, OCH_3), 3.69 (s, 2H, CH_2), 6.43 (s, 1H, ArH), 6.49 (s, 1H, ArH), 7.11-7.34 (m, 4H, ArH), 11.26 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 38.3 (CH_2), 52.9 (OCH_3), 53.2 (OCH_3), 109.0 (C_{Ar}), 114.5, 129.0 (CH_{Ar}), 129.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 137.5, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 368 (37), 367 (18), 366 (M^+, 100), 334

(21), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{17}H_{15}O_5SCl$ [M^+]: 366.03232, found: 366.032168.



4-(4-Ethylphenylsulfanyl)-2-hydroxy-6-(methoxycarbonylmethyl)benzoic acid methyl ester (7j): Starting with **3n** (462 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7j** was isolated as a highly viscous colourless oil (432 mg, 80%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, 3H, CH_2CH_3), 2.61 (q, 2H, CH_2), 3.59 (s, 3H, OCH_3), 3.71 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3), 6.41 (s, 1H, ArH), 6.49 (s, 1H, ArH), 7.11-7.38(m, 4H, ArH), 11.28 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.2 (CH_3), 27.4 (CH_2), 36.5 (CH_2), 50.9 (OCH_3), 51.2 (OCH_3), 109.0 (C_{Ar}), 113.0, (CH_{Ar}), 127.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 137.5, 138.5, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 361 (22), 360 (M^+, 100), 301 (16), 273 (23), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{19}H_{20}O_5S$ [M^+]: 360.10260, found: 360.102549.

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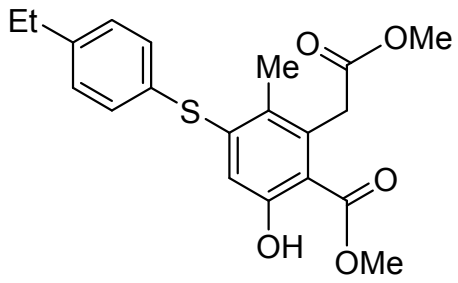
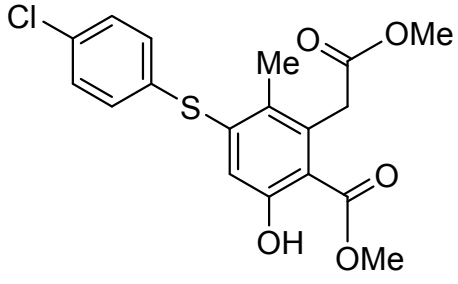


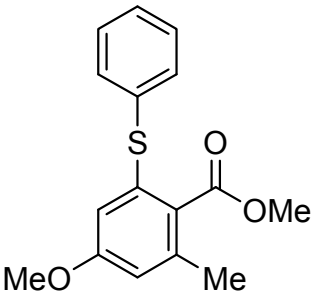
6-Hydroxy-2-(methoxycarbonylmethyl)-3-methyl-4-(*p*-ethylphenylsulfanyl)benzoic acid methyl ester (7k): Starting with **3o** (483 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7k** was isolated as a highly viscous colourless oil (404 mg, 72%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (t, 3H, CH_2CH_3), 2.23 (s, 3H, CH_3), 2.61 (q, 2H, CH_2), 3.64 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.89 (s, 2H, CH_2), 6.49 (s, 1H, ArH), 7.11-7.44 (m, 5H, ArH), 11.28 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.2 (CH_3), 15.0 (CH_3), 27.4 (CH_2), 36.5 (CH_2), 50.9 (OCH_3), 51.2 (OCH_3), 109.0 (C_{Ar}), 113.0, (CH_{Ar}), 127.9 ($2CH_{Ar}$), 130.1 (C_{Ar}), 134.8 ($2CH_{Ar}$), 136.6, 137.5, 138.5, 147.3, 163.3 (C_{Ar}), 170.8, 171.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1436 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 952 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 376 (22), 374 (M^+, 100), 334 (21), 273 (23), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{20}H_{22}O_5S$ [M^+]: 374.03232, found: 374.032168.



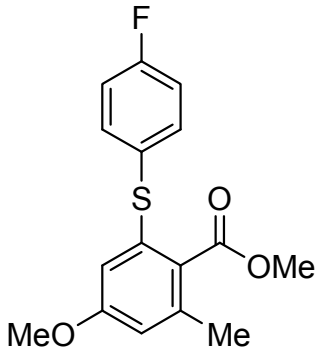
4-(4-Chlorophenylsulfanyl)-6-hydroxy-2-(methoxycarbonylmethyl)-3-methylbenzoic acid methyl ester (7l): Starting with **3p** (492 mg, 1.5 mmol) and **6** (234 mg, 1.5 mmol), **7l** was isolated as a highly viscous colourless oil (313 mg, 55%); ^{1}H NMR (250 MHz,

$CDCl_3$): δ = 2.34 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.79 (s, 2H, CH_2), 6.49 (s, 1H, ArH), 7.22-7.48 (m, 4H, ArH), 10.77 (s, 1H, OH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 16.2 (CH_3), 38.2 (CH_2), 51.0 (OCH_3), 52.2 (OCH_3), 109.2 (C_{Ar}), 112.9 (CH_{Ar}), 125.4 (C_{Ar}), 129.9, 135.3 ($2CH_{Ar}$), 140.5, 145.6, 151.5, 155.8, 159.0 (C_{Ar}), 165.5, 169.0 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2996 (w), 2950 (w), 2846 (w), 1736 (s), 1659 (s), 1599 (s), 1552 (m), 1474 (m), 1438 (s), 1320 (s), 1256 (s), 1194 (s), 1163 (s), 1122 (s), 1088 (m), 1067 (m), 1022 (m), 998 (m), 962 (m), 895 (s), 843 (m), 745 (m), 705 (s), 689 (s), 562 (m); MS (EI, 70 eV): m/z (%) = 381 (17), 380 (M^+, 100), 350 (23), 349 (21), 348 (62), 322 (29), 321 (30), 320 (79), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8); HRMS (EI): calcd for $C_{18}H_{17}O_5ClS$ [M^+]: 380.04797, found: 380.047626.

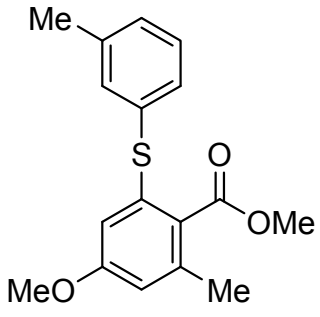
General experimental procedure for the synthesis of 9a-l. To a dichloromethane solution (3 mL / mmol of 1) of **2** (1.5 mmol) and of **1** (2.25 mmol) was added $TiCl_4$ (2.25 mmol) at –78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added hydrochloric acid (10%, 25 mL). The organic and the aqueous layer were separated and the latter was extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc / n-heptane = 1:9).



2-Methoxy-4-methyl-6-(phenylsulfanyl)benzoic acid methyl ester (9a): Starting with **3a** (420mg, 1.5 mmol), **8a** (364 mg, 2.25 mmol), **9a** was isolated as a highly viscous oil (238 mg, 55%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 3.57 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 6.44-7.22 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.0 (CH_3), 50.7 (OCH_3), 51.0 (OCH_3), 110.2 ($2CH_{Ar}$), 129.1 (2C), 129.5, 130.7, 132.5 (CH_{Ar}), 135.9 ($2CH_{Ar}$), 139.6 (2C), 160.5, 165.8 (C); IR (neat): $\tilde{\nu}$ = 3400 (w), 3056 (w), 2992 (w), 2948n(w), 2922 (w), 2850 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1571 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 m); MS (EI, 70 eV): m/z (%) = 289 (18), 288 (M^+, 100), 272 (12), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 185 (10), 184 (17); HRMS (EI): calcd for $C_{16}H_{16}O_3S$ [M^+]: 288.09612, found: 288.097152.

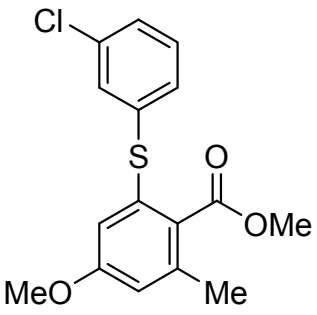


2-Methoxy-4-methyl-6-(4-fluorophenylsulfanyl)benzoic acid methyl ester (9b): Starting with **3b** (447 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9b** was isolated as a highly viscous oil (183 mg, 40%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.59 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 6.37-7.29 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.4 (CH_3), 51.9 (OCH_3), 55.2 (OCH_3), 113.8, 114.4, 116.2, 116.6 (CH_{Ar}), 127.1 , 129.7, 129.8 (C), 134.7, 134.9 (CH_{Ar}), 137.2, 138.6, 160.3, 168.6 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2999(w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959(m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 307 (14), 306 (M^+ 79), 276 (10), 275 (57), 274 (30), 273 (100), 260 (12), 232 (14), 203 (10), 202 (10), 189 (10), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SF$ [M^+]: 306.04622, found: 306.046232.



2-Methoxy-4-methyl-6-(3-methylphenylsulfanyl)benzoic acid methyl ester (9c): Starting with **3c** (441 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9c** was isolated as a gummy compound (227 mg, 50%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 3.59 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 6.49-7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.3 (CH_3), 21.2 (CH_3), 51.9 (OCH_3), 52.2 (OCH_3), 114.1, 114.5, 128.5, 129.0, 129.3 (CH_{Ar}), 132.2 (C), 132 (CH_{Ar}), 134.4, 136.8, 138.3, 139.0, 160.2,

168.8 (C); IR (neat): $\tilde{\nu}$ = 3435 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1571 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 303 (19), 302 (M^+, 100), 272 (11), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ [M^+]: 302.09712, found: 302.097152.



2-Methoxy-4-methyl-6-(3-chlorophenylsulfanyl)benzoic acid methyl ester (9d): Starting with **3d** (471 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9d** was isolated as a highly viscous oil (222 mg, 46%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.64 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 6.58-7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.3 (CH_3), 52.0 (OCH_3), 55.3 (OCH_3), 115.6 ($2CH_{Ar}$), 127.2 , 128.9, 130.0, 130.4 (CH_{Ar}), 134.1, 134.5, 134.7, 137.9, 138.5, 160.3, 168.6 (C); IR (neat): $\tilde{\nu}$ =3055 (w), 2999(w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959(m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 324 (26), 323 (13), 322 (M^+ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SCl$ (M^+): 322.04249, found: 322.042435.

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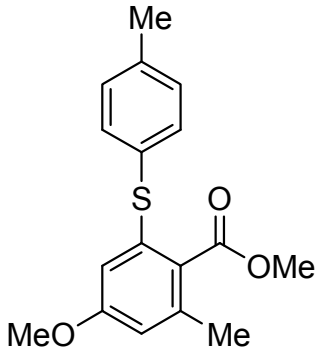
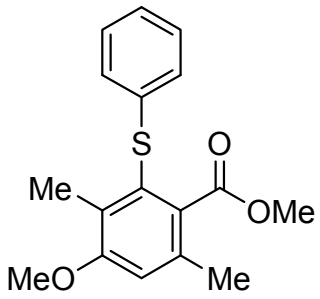
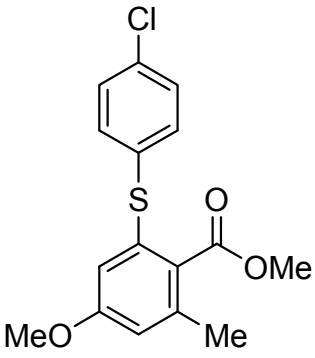


2-Methoxy-4-methyl-6-(4-methylphenylsulfanyl)benzoic acid methyl ester (9e): Starting with **3e** (441 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9e** was isolated as a highly viscous oil (231 mg, 51%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 3.59 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 6.49-7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.4 (CH_3), 21.1 (CH_3), 51.9 (OCH_3), 52.2 (OCH_3), 114.1, 114.5, 128.5, 129.0, 129.3 (CH_{Ar}), 132.2 (C), 132 (CH_{Ar}), 134.4, 136.8, 138.3, 139.0, 160.2, 168.8 (C); IR (neat): $\tilde{\nu}$ = 3434 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 303 (19), 302 (M^+, 100), 272 (11), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ [M^+]: 302.09712, found: 302.097152.

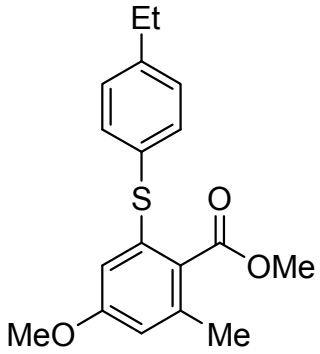


6-Methoxy-3,4-dimethyl-2-(phenylsulfanyl)benzoic acid methyl ester (9f): Starting with **3h** (441 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9f** was isolated as highly viscous oil (167 mg, 37%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 3.72 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 6.66-7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 13.3 (CH_3), 19.7 (CH_3), 52.0 (OCH_3), 55.6 (OCH_3), 112.9, 125.3 (CH_{Ar}), 127.2, 128.7 ($2CH_{Ar}$), 129.3, 129.5, 129.9, 133.5,

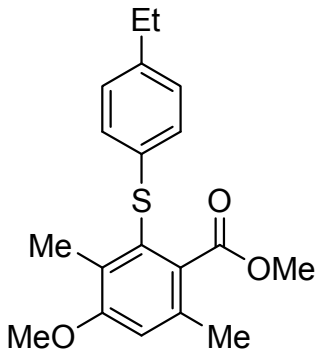
137.3, 158.4, 169.6 (C); IR (neat): $\tilde{\nu}$ = 3434 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 303 (13), 302 (M^+, 70), 272 (11), 271 (61), 270 (21), 269 (100), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ [M^+]: 302.09712, found: 302.097133.



2-Methoxy-4-methyl-6-(4-chlorophenylsulfanyl)benzoic acid methyl ester (9g): Starting with **3k** (471 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9g** was isolated as a highly viscous oil (222 mg, 46%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 3.65 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 6.58-7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.3 (CH_3), 52.0 (OCH_3), 55.3 (OCH_3), 115.6 ($2CH_{Ar}$), 127.2 , 128.9, 130.0, 130.4 (CH_{Ar}), 134.1, 134.5, 134.7, 137.9, 138.5, 160.3, 168.6 (C); IR (neat): $\tilde{\nu}$ =3055 (w), 2999(w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1561 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959(m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 324 (26), 323 (13), 322 (M^+ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SCl$ [M^+]: 322.04249, found: 322.042436

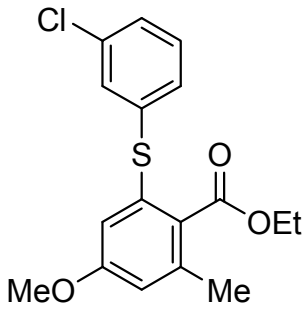


2-Methoxy-4-methyl-6-(4-ethylphenylsulfanyl)benzoic acid methyl ester (9h): Starting with **3n** (462 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9h** was isolated as a highly viscous oil (213 mg, 45%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14 (t, J = 7.6, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.54 (q, J = 7.6, 2 H, CH_2), 3.56 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 6.39-7.26 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.3 (CH_3), 19.4 (CH_3), 27.2 (CH_2CH_3), 50.9 (OCH_3), 54.1 (OCH_3), 112.6, 113.0 (CH_{Ar}), 125.9 (C), 127.8 ($2CH_{Ar}$), 129.9 (C), 131.9 ($2CH_{Ar}$), 136.8, 137.4, 143.3, 159.2, 167.7 (C); IR (neat): $\tilde{\nu}$ = 3070 (w), 3023 (w), 2959 (w), 2930 (w), 2870 (w), 1911 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 317 (20), 316 (M^+, 100), 285 (45), 284 (17), 283 (51), 269 (13), 256 (10), 255 (40), 121 (26), 186 (11), 184 (15); HRMS (EI): calcd for $C_{18}H_{20}O_3S$ [M^+]: 316.11277, found: 316.112934.



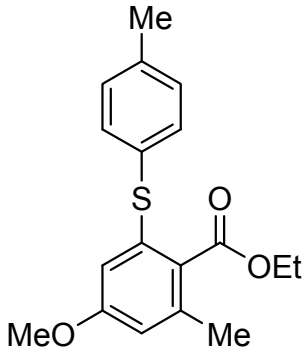
6-Methoxy-3,4-dimethyl-2-(4-ethylphenylsulfanyl) benzoic acid methyl ester (9i): Starting with **3o** (483 mg, 1.5 mmol) and **8a** (364 mg, 2.25 mmol), **9i** was isolated as a highly viscous oil (173 mg, 35%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10 (t, J = 7.6, 3 H, CH_3), 2.11 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 2.48 (q, J = 7.6, 2H, CH_2), 3.73 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 6.94-7.18 (m, 5H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 12.3, (CH_3), 14.4

(CH_3), 18.7 (CH_3), 27.3 (CH_2), 51.0 (OCH_3), 54.6 (OCH_3), 111.7 (CH_{Ar}), 126.6, 127.3 ($2CH_{Ar}$), 127.5, 128.3, 128.6, 132.3, 132.8, 134.9, 157.3, 168.5 (C); IR (neat): $\tilde{\nu}$ = 2962 (w), 2928 (w), 2872 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 331 (20), 330 (M^+, 98), 272 (11), 271 (61), 270 (21), 269 (100), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{19}H_{22}O_3S$ [M^+]: 330.12842, found: 330.128242.



2-(3-Chlorophenylsulfanyl)-4-ethyl-6-methoxybenzoic acid methyl ester (9j): Starting with **3d** (471 mg, 1.5 mmol) and **8b** (396 mg, 2.25 mmol), **9j** was isolated as a highly viscous oil (186 mg, 37%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.55 (t, 3 H, CH_3), 2.56 (q, J = 7.6, 2 H, CH_2), 3.65 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 6.58-7.23 (m, 6 H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.3 (CH_3), 27.1 (CH_2), 52.0 (OCH_3), 55.3 (OCH_3), 114.4, 115.8, 127.1, 128.6 (CH_{Ar}), 129.7 (C), 130.0, 130.1 (CH_{Ar}), 134.1, 135.6, 138.1, 144.4, 160.5, 168.7 (C); IR (neat): $\tilde{\nu}$ =3055 (w), 2999(w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959(m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 338 (26), 337 (13), 336 (M^+ 70), 293 (29), 292 (17), 291

(83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{17}H_{17}O_3SCl$ [M^+]: 336.05814, found: 336.057409.



2-(4-Methylphenylsulfanyl)-4-ethyl-6-methoxybenzoic acid methyl ester (9k): Starting with **3e** (441 mg, 1.5 mmol) and **8b** (396 mg, 2.25 mmol), **9k** was isolated as a highly viscous oil (180 mg, 38%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14 (t, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 2.57 (q, J = 7.6, 2 H, CH_2), 3.59 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 6.41-7.25 (m, 6 H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.3 (CH_3), 20.1 (CH_3), 26.1 (CH_2), 50.9 (OCH_3), 54.1 (OCH_3), 111.8, 112.6 (CH_{Ar}), 126.0 (C), 128.8, 131.7 ($2CH_{Ar}$), 132.3, 136.1, 136.9, 143.3, 159.3, 167.9 (C); IR (neat): $\tilde{\nu}$ =3055 (w), 2999(w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959(m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 316 (M^+, 45), 285 (23), 284 (20), 383 (100), 269 (31), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{18}H_{20}O_3S$ (M^+): 316.11277, found: 316.112679.

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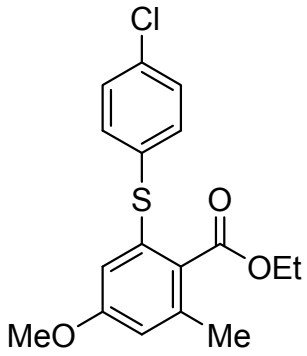
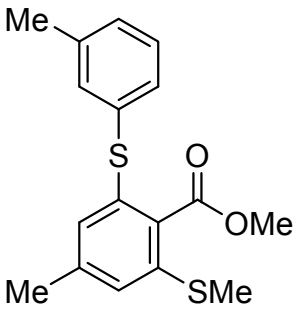
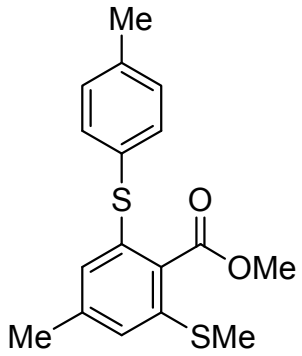


2-(4-Chlorophenylsulfanyl)-4-ethyl-6-methoxybenzoic acid methyl ester (9l): Starting with **3k** (471 mg, 1.5 mmol) and **8b** (396 mg, 2.25 mmol), **9l** was isolated as a highly viscous oil (201 mg, 40%); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.55 (t, 3 H, CH_3), 2.56 (q, J = 7.6, 2 H, CH_2), 3.65 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 6.58-7.23 (m, 6 H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.3 (CH_3), 27.1 (CH_2), 52.0 (OCH_3), 55.3 (OCH_3), 114.4, 115.8, 127.1, 128.6 (CH_{Ar}), 129.7 (C), 130.0, 130.1 (CH_{Ar}), 134.1, 135.6, 138.1, 144.4, 160.5, 168.7 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 958 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): m/z (%) = 338 (26), 337 (13), 336 (M^+ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{17}H_{17}O_3SCl$ [M^+]: 336.05814, found: 336.057409.

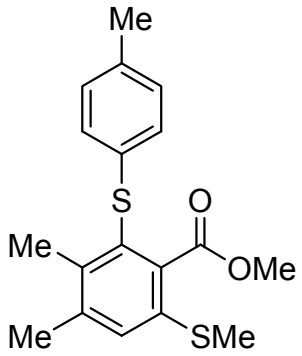
General experimental procedure for the synthesis of diaryl sulfides 11a-e: To a dichloromethane solution (6 mL / mmol of 4) of **2** (1.5 mmol) and of **4** (1.5 mmol) was added $TiCl_4$ (2.25 mmol) at –78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added a hydrochloric acid (10%, 25 mL). The organic and the aqueous layer were separated and the latter was extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc / n-heptane = 1:9).



4-Methyl-2-methylsulfanyl-6-(3-tolylsulfanyl)benzoic acid methyl ester (11a): Starting with **3c** (441 mg, 1.5 mmol), **10** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **11a** was isolated as a highly viscous oil (248 mg, 52%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3), 2.39 (s, 3 H, SCH_3), 3.82 (s, 3 H, OCH_3), 6.80-7.20 (m, 6 H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.4 (CH_3), 21.1 (CH_3), 21.3 (SMe), 52.2 (OMe), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1606 (m), 1581 (m), 1476 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 954 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%) = 319 (20), 318 (M^+ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ [M^+]: 318.07427, found: 318.07489.

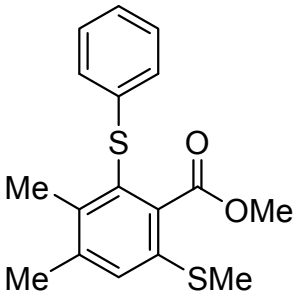


4-Methyl-2-methylsulfanyl-6-(4-tolylsulfanyl)benzoic acid methyl ester (11b): Starting with **3e** (441 mg, 1.5 mmol), **10** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **11b** was isolated as a highly viscous oil (262 mg, 55%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 2.39 (s, 3 H, SCH_3), 3.82 (s, 3 H, OCH_3), 6.80-7.19 (m, 6 H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.4 (CH_3), 21.2 (CH_3), 21.3 (SCH_3), 52.2 (OCH_3), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (C); IR (neat): $\tilde{\nu}$ = 3056 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1727 (s), 1606 (m), 1581 (m), 1476 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 954 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%) = 319 (20), 318 (M^+ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (16), 195 (17), 63 (3); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ [M^+]: 318.07427, found: 318.07489.

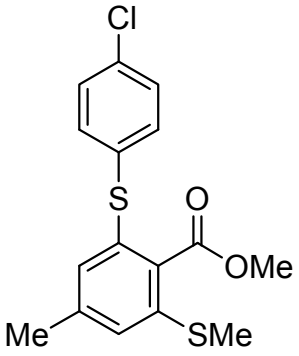


3,4-Dimethyl-6-methylsulfanyl-2-(4-tolylsulfanyl)-benzoic acic methyl ester (11c): Starting with **3g** (462 mg, 1.5 mmol), **10** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **11c** was isolated as a highly viscous oil (184 mg, 37%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 2.39 (s, 3 H, SCH_3), 3.85 (s, 3 H, OCH_3), 6.91-7.30 (m, 5 H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.0 (CH_3), 21.0 (CH_3), 21.3 (SCH_3), 52.3 (OCH_3), 127.3, 128.6, 128.9, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6,

134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.8 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%) = 333 (21), 332 (M^+ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ [M^+]: 3320.08992, found: 332.090382.



3,4-Dimethyl-6-methylsulfanyl-2-(phenylsulfanyl)benzoic acic methyl ester (11d): Starting with **3h** (441 mg, 1.5 mmol), **10** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **11d** was isolated as a highly viscous oil (190 mg, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 2.39 (s, 3 H, SCH_3), 3.85 (s, 3 H, OCH_3), 6.91-7.30 (m, 6 H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.0 (CH_3), 21.1 (CH_3), 21.3 (SMe), 52.3 (OMe), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.8 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%) = 319 (21), 318 (M^+ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ [M^+]: 318.07427, found: 318.075053.



4-Chloro-2-methylsulfanyl-6-(4-tolylsulfanyl)benzoic acid methyl ester (11e): Starting with **3k** (472 mg, 1.5 mmol), **10** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **11e** was isolated as a highly viscous oil (244 mg, 45%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 2.39 (s, 3 H, SCH_3), 3.85 (s, 3 H, OCH_3), 6.80-7.30 (m, 6 H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 21.1 (CH_3), 21.3 (SCH_3), 52.3 (OCH_3), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (C); IR (neat): $\tilde{\nu}$ = 3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%) = 340 (24), 338 (M^+ 71), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{16}H_{15}O_2S_2Cl$ [M^+]: 338.3496, found: 338.33908.

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Curriculum Vitae

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Publications

1. **Muhammad Imran**, Inam Iqbal, Peter Langer*, *Synlett* **2009**, in print. “Regioselective Synthesis of 2-Arylthio-4-(methoxy)benzoates by the First [3+3] Cyclocondensations of 3-Arylthio-1-silyloxy -1,3-butadienes with 3-Oxo-orthoesters”.

2. **Muhammad Imran**, Inam Iqbal and Peter Langer*, submitted to *Tetrahedron Lett*. “Synthesis of 4-Arylthio-2-hydroxy-homophthalates by [4+2] cycloaddition of 3-arylthio-1-trimethylsiloxy-1,3-butadienes with dimethyl allene-1,3-dicarboxylate“

3. **Muhammad Imran**, Inam Iqbal, Nasir Rasool, Muhammad A. Rashid and Peter Langer*, *Synlett* **2008**, 2708-2710. “Regioselective Synthesis of 2-Thiophenoxybenzoates by the First Catalytic [3+3] Cyclocondensations of 1-Trimethylsilyloxy-3-thiophenoxy-1,3-butadienes with 1,1,3,3-Tetramethoxypropane”.

4. Inam Iqbal, **Muhammad Imran** and Peter Langer*, submitted to *Tetrahedron.* “Regioselective Synthesis of 2-Arylthio-4-methoxybenzoates and 2-Arylthio-6-(methylthio)benzoates based on Formal [3+3] Cyclocondensations of 3-Arylthio-1-trimethylsilyloxy-1,3-butadienes”

5. Inam Iqbal, **Muhammad Imran**, Nasir Rasool, Muhammad A. Rashid, Munawar Hussain, Alexander Villinger, Christine Fischer and Peter Langer*, in print *Tetrahedron.* “Functionalized 2-(arylthio)benzoates are prepared by formal [3+3]

cyclizations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-silyloxy-2-en-1-ones and 1,1-diacylcyclopropanes.''

6. Inam Iqbal, **Muhammad Imran** and Peter Langer*, *Synthesis* **2009**, efirst. "Synthesis of 5-Arylthio-3-hydroxyphthalates by the First [4+2] Cycloadditions of 3-Arylthio-1-silyloxy-1,3-butadienes with Dimethyl Acetylenedicarboxylate".

7. Inam Iqbal, **Muhammad Imran**, Alexander Villinger and Peter Langer*, *Synthesis* **2009**, 297-305. "Regioselective Synthesis of Functionalized 2-(Arylthio)-benzoates by the First [3+3] Cyclizations of 3-Arylthio-1-silyloxy-1,3-butadienes with 3-Alkoxy-2-en-1-ones".

8. Muhammad A. Rashid, Nasir Rasool, Inam Iqbal, **Muhammad Imran** and Peter Langer*, *Tetrahedron Lett.* **2008**, *49*, 2466-2468. "Regioselective Synthesis of Functionalized 2-(Phenylthio)benzoates by ′[3+3] Cyclization / Homo-Michael′ Reactions of 1-Methoxy-1-trimethylsilyloxy-3-phenylthio-1,3-butadienes with 1,1-Diacylcyclopropanes".

Declaration/Erklärung

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

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

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

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

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Muhammad Imran