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Synthesis of functionalized diaryl sulfides based on regioselective one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes

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Abstract

Functionalized diaryl sulfides were prepared based on one-pot cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes.

Keywords: Arenes; Cyclizations; Diaryl sulfides; Silyl enol ethers

1. Introduction

A variety of pharmacologically relevant diaryl sulfides (diaryl thioethers) have been isolated as natural products.[1] Non-natural diaryl sulfides are also of considerable pharmacological relevance. For example, fluorinated diaryl sulfides have been reported to act as serotonin transporter ligands.[2] Most of the known synthetic approaches to diaryl sulfides are based on the formation of a carbon–sulfur bond. Classic syntheses (such as the reaction of copper thiolates with aryl halides or the reduction of aryl sulfones or aryl sulfoxides) are often limited by their harsh conditions, low regioselectivity, narrow preparative scope, use of toxic reagents (such as HMPTA), or by the formation of polysulfides.[3] In recent years, transition metal-catalyzed reactions for the synthesis of diaryl sulfides were developed, which proceed under mild conditions (Buchwald–Hartwig reaction and related transformations).[4,5] Metal-free reactions have also been reported.[6] Despite their great synthetic usefulness, the synthesis of highly substituted and sterically encumbered products by these methods can sometimes be difficult. In addition, the synthesis of the starting materials, substituted arenes and thiophenols, can be a difficult task.

An alternative approach to diaryl sulfides relies on cyclization reactions of arylthio-containing building blocks. In contrast to other methods, this approach relies on the assembly of the arene moiety by formation of two carbon–carbon bonds. Only a few examples of this type of reaction have been reported to date. For example, Hilt and co-workers reported an efficient synthesis of diaryl sulfides by cobalt(I)-catalyzed [4+2] cycloaddition of alkynyl sulfides with 1,3-butadienes.[7] Chan and Prasad reported the synthesis of 2-(thiophenoxy)benzoates based on the cyclization of 1-methoxy-3-thiophenoxy-1-trimethylsilyloxy-1,3-butadiene with 3-siloxy-2-en-1-ones.[8] Diels–Alder reactions of this compound have also been reported.[9] Recently, we reported[10] the synthesis of diaryl sulfides based on formal [3+3] cyclizations[11] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes.[12] These reactions provide a convenient and regioselective approach to sterically encumbered and functionalized diaryl sulfides, which are not readily available by other methods. Herein, full details of the methodology and a comprehensive study of its preparative scope are reported. In addition to the results reported in our preliminary communication, we herein

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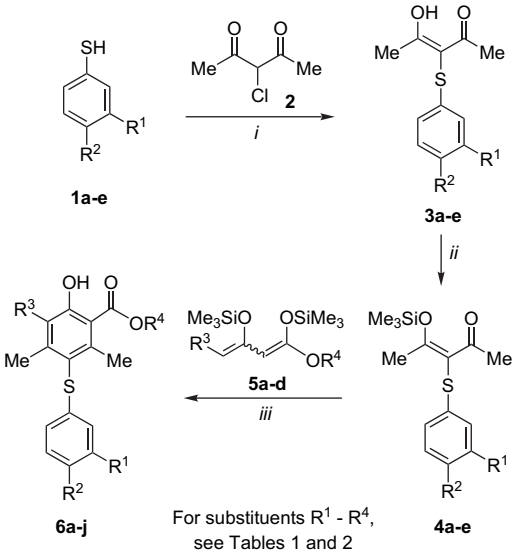
report the synthesis of diaryl sulfides by cyclization of novel 4-thioaryloxy-1,3-bis(trimethylsilyloxy)-1,3-butadienes with 1,1-diacetylcyclopropane, 3-formylchromone and chromone.

2. Results and discussion

The novel 2-thiophenoxy-3-silyloxy-2-en-1-ones **4a–e** were prepared by silylation of 3-(thiophenoxy)pentane-2,4-diones **3a–e**, which are available by reaction of 3-chloropentane-2,4-dione (**2**) with thiophenols **1a–e** (Scheme 1, Table 1).[13] 1,3-Diones **3** are completely enolized in solution and in the solid state. The solid state structures of **3b** and **3c** were confirmed by X-ray crystal structure analyses (Figs. 1 and 2).[14] The $TiCl_4$-mediated formal [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-1,3-dienes **5a–d**, prepared from the corresponding β-ketoesters,[15] afforded the diaryl sulfides **6a–j**.



Scheme 1. Synthesis of **6a–j**. Reagents and conditions: (i) method A: pyridine, MeOH, 0→20 °C, 6 h; method B: piperidine, CH_2Cl_2, MeOH, 0→20 °C, 6 h; (ii) Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h; (iii) $TiCl_4$, CH_2Cl_2, −78→20 °C, 20 h.

The best yields were obtained when the reactions were carried out in a highly concentrated solution and when $TiCl_4$ was employed as the Lewis acid. All structures were established by spectroscopic methods. The structure of **6b** was independently confirmed by X-ray crystal structure analyses (Fig. 3).[14]

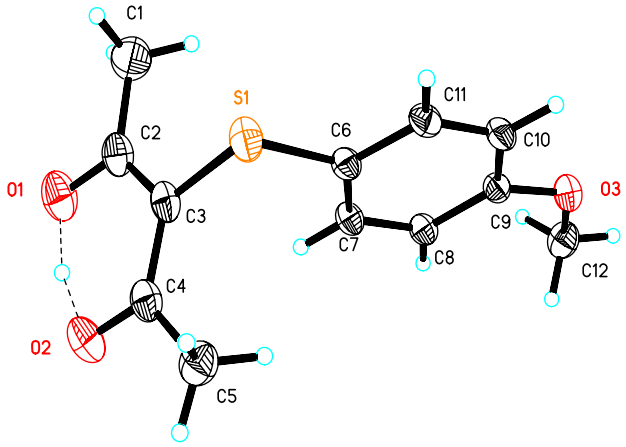


Figure 1. ORTEP plot of **3b** (the position of the H atom between O1 and O1 was calculated from the difference map and refined freely).

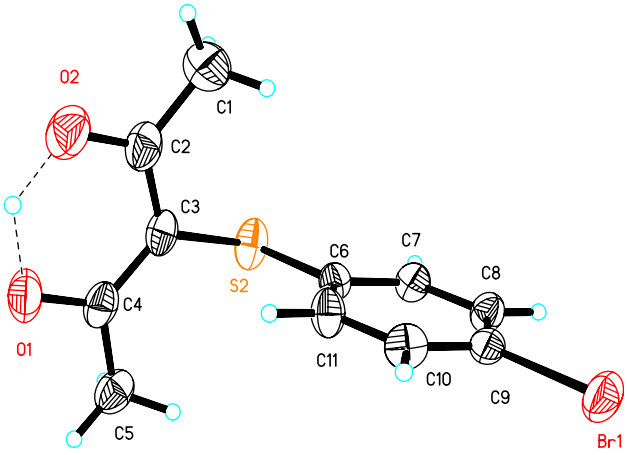


Figure 2. ORTEP plot of **3c** (the position of the H atom between O1 and O1 was calculated from the difference map and refined freely).

The ethyl 4-(thioaryloxy)acetoacetates **7a–d** were prepared by reaction of ethyl 4-chloroacetoacetate with thiophenols **1a–d**, which were transformed into the novel 4-thioaryloxy-1,3-bis(trimethylsilyloxy)-1,3-butadienes **9a–d** (Scheme 2,

Table 1
Synthesis of **6a–j**

Compounds **3** and **4**	Compound **5**	Compound **6**	R^1	R^2	R^3	R^4	%[a] (**3**)[b]	%[a] (**4**)	%[a] (**6**)
a	**a**	**a**	H	H	H	Me	72 (A)	81	48
a	**b**	**b**	H	H	Me	Et			40
a	**c**	**c**	H	H	Et	Et			40
b	**d**	**d**	H	OMe	H	Et	33 (B)	90	43
b	**b**	**e**	H	OMe	Me	Et			35
b	**c**	**f**	H	OMe	Et	Et			38
c	**a**	**g**	H	Br	H	Me	28 (B)	79	36
d	**b**	**h**	H	Me	Me	Et	81 (B)	92	33
e	**a**	**i**	OMe	H	H	Me	73 (B)	81	32
e	**b**	**j**	OMe	H	Me	Et			30

[a] Yields of isolated products.
[b] In brackets: method for the synthesis of **3** (see Section 3).

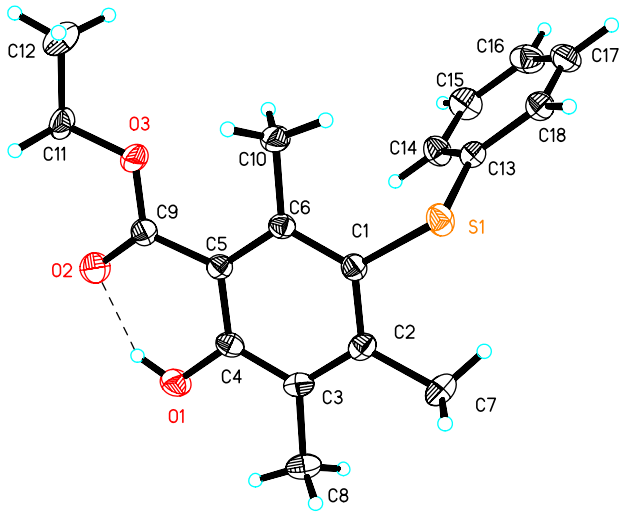
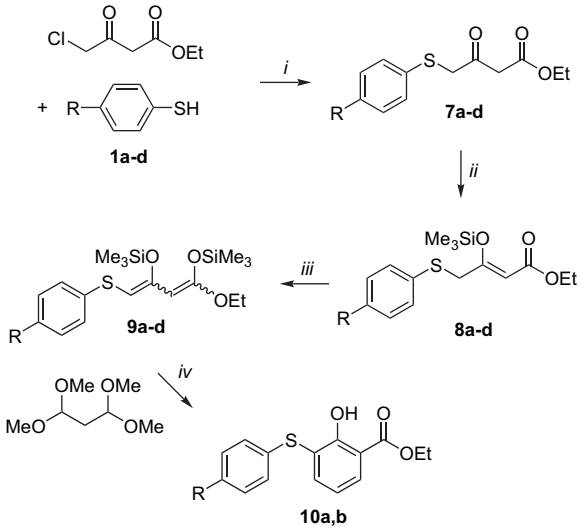


Figure 3. ORTEP plot of **6b**.



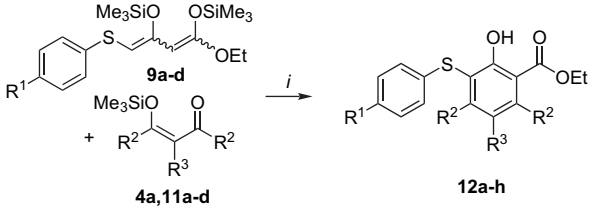
Scheme 2. Synthesis of **10a** and **10b**. Reagents and conditions: (i) NEt_3, CH_2Cl_2, 30 min, 0 °C; (ii) Me_3SiCl, NEt_3, C_6H_6, 20 °C, 72 h; (iii) LDA, THF, −78→20 °C; (iv) method A: $TiCl_4$, CH_2Cl_2, −78→20 °C, 20 h; method B: Me_3SiOTf (0.1 equiv), CH_2Cl_2, −78→20 °C, 20 h.

Table 2
Synthesis of **10a** and **10b**

Compounds **7**–**10**	R	%[a] (**7**)	%[a] (**8**)	%[a] (**9**)	%[a] (**10**)
a	H	80	84	89	31[b] (52)[c]
b	OMe	81	78	85	30 [b] (42)[c]
c	Me	77	85	80	—[d]
d	Cl	84	90	87	—[d]

[a] Yields of isolated products.
[b] Method A.
[c] Method B (see Ref. 12).
[d] Experiment was not carried out.

Table 2). The synthesis of **7a** has been previously reported.[16] The $TiCl_4$-mediated [3+3] cyclization of **9a** and **9b** with 1,1,3,3-tetramethoxypropane afforded the diaryl sulfides **10a** and **10b**, respectively. The employment of catalytic amounts of TMSOTf (0.1 equiv)[17] rather than stoichiometric amounts of $TiCl_4$ resulted in an increase of the yield.



Scheme 3. Synthesis of **12a**–**h**. Reagents and conditions: (i) $TiCl_4$, CH_2Cl_2, −78→20 °C, 20 h.

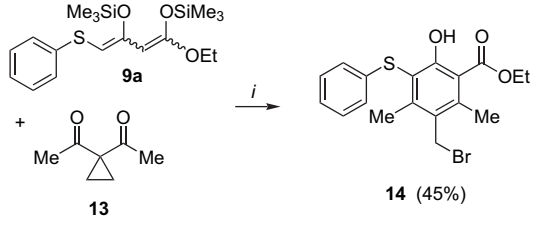
Table 3
Synthesis of **12a**–**h**

Compounds **4a** and **11**	Compound **9**	Compound **12**	R^1	R^2	R^3	%[a] (**12**)
11a	**a**	**a**	H	Me	H	48
11b	**b**	**b**	OMe	Et	H	35
11c	**a**	**c**	H	Me	Cl	37
11d	**a**	**d**	H	Me	Me	33
4a	**a**	**e**	H	Me	PhS	34
4a	**b**	**f**	OMe	Me	PhS	34
11c	**c**	**g**	Me	Me	Cl	30
11c	**d**	**h**	Cl	Me	Cl	34

[a] Yields of isolated products.

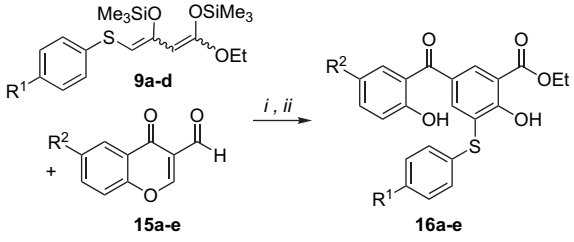
The [3+3] cyclization of 1,3-bis(trimethylsilyloxy)-1,3-dienes **9a**–**d** with 3-silyloxy-2-en-1-ones **4a** and **11a**–**d** afforded the diaryl sulfides **12a**–**h** (Scheme 3, Table 3). Products **12e** and **12f** represent novel 1,3-bis(sulfides).

The $TiBr_4$-mediated cyclization of 1,3-bis(silyloxy)-1,3-diene **9a** with 1,1-diacetylcyclopropane (**13**) afforded the 3-thiophenoxysalicylate **14** containing a remote bromide function (Scheme 4). Its formation can be explained by a domino '[3+3]-cyclization/homo-Michael' reaction.[18]



Scheme 4. Synthesis of **14**. Reagents and conditions: (i) $TiBr_4$, CH_2Cl_2, −78→20 °C, 20 h.

The Me_3SiOTf-catalyzed reaction of 1,3-bis(silyloxy)-1,3-dienes **9a**–**d** with 3-formylchromones **15a**–**e** afforded the highly functionalized diaryl sulfides **16a**–**e** (Scheme 5, Table 4). The



Scheme 5. Synthesis of **16a**–**e**. Reagents and conditions: (i) Me_3SiOTf (0.3 equiv), 20 °C, 10 min; (ii) (1): **9a**–**d** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (2) HCl (10%).

Table 4
Synthesis of **16a–e**

Compound **9**	Compound **15**	Compound **16**	R^1	R^2	%[a] (**16**)
a	**a**	**a**	H	Cl	47
b	**b**	**b**	OMe	Et	38
c	**c**	**c**	Me	Br	45
d	**d**	**d**	Cl	Me	40
d	**e**	**e**	Cl	H	50

[a] Yields of isolated products.

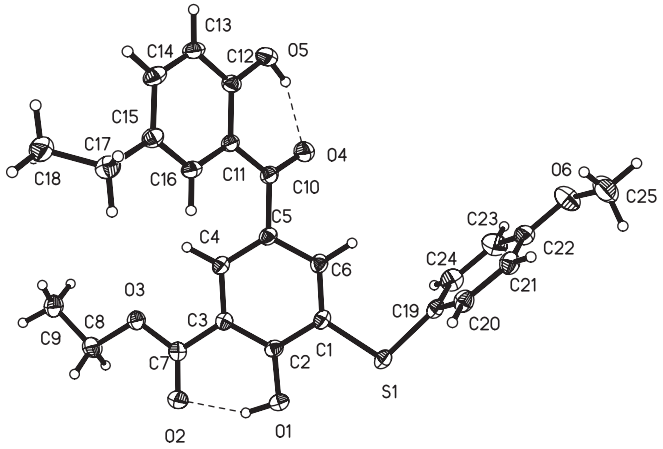
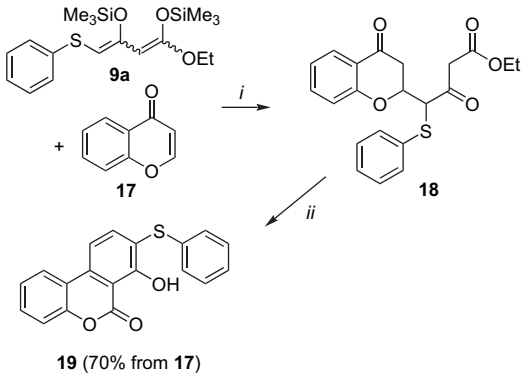


Figure 4. ORTEP plot of **16b** (the hydrogen atom positions at O1 and O5 were calculated from the difference map and refined freely).

products are formed by a domino 'Michael/retro-Michael/Mukaiyama-aldol' reaction.[19] The structure of **16b** was independently confirmed by X-ray crystal structure analysis (Fig. 4).[14]

The Me_3SiOTf-catalyzed reaction of **9a** with chromone (**17**) afforded the condensation product **18**, which was transformed (without purification) into diaryl sulfide **19** by treatment with triethylamine (Scheme 6). The formation of **19** can be explained by a domino 'retro-Michael/aldol/lactonization' reaction.[20]



Scheme 6. Synthesis of **19**. (i) (1) Me_3SiOTf (1.3 equiv), 20 °C, 1 h; (2) **9a** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (3) HCl (10%); (ii) NEt_3 (2.0 equiv), EtOH, 20 °C, 12 h.

In conclusion, a variety of functionalized and sterically encumbered diaryl sulfides were prepared by cyclization reactions of 1,3-bis(trimethylsilyloxy)-1,3-butadienes. The products are not readily available by other methods.

3. Experimental section

3.1. General comments

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H and ^{13}C NMR spectra the deuterated solvents indicated were used. Mass spectrometric (MS) data were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

*3.2. General procedures for the synthesis of 3-thioaryloxy-2,4-pentanediones **3a–e***

Method A. To a stirred pyridine solution (0.1 mL) of 3-chloro-2,4-pentanedione (**2**) (1.0 mmol) was slowly added a mixture of benzenethiol **1** (1.0 mmol) and methanol (0.1 mL) at 0 °C. The mixture was stirred at room temperature for 6 h. Precipitated pyridine hydrochloride was removed by filtration and washed with ether (3×15 mL). The combined filtrates were washed with water (5×25 mL) and dried over Na_2SO_4. The solution was filtered and the solvent of the filtrate was removed under reduced pressure. The residue was purified by chromatography (silica gel, EtOAc/*n*-heptane).

Method B. To a mixture of 3-chloro-2,4-pentanedione (**2**) (1.0 mmol) and benzenethiol **1** (1.0 mmol) was dropwise added (within 10 min) a mixture of piperidine (1.0 mmol) and dichloromethane (0.1 mL) at 0 °C. After stirring for 5 min, MeOH (0.4 mL) was added and the solution was stirred for 6 h at room temperature. Precipitated pyridine hydrochloride was removed by filtration and washed with ether (3×15 mL). The combined filtrates were washed with water (5×25 mL) and dried over Na_2SO_4. The solution was filtered and the solvent of the filtrate was removed under reduced pressure. The residue was purified by chromatography (silica gel, EtOAc/*n*-heptane).

*3.2.1. 3-Thiophenoxy-2,4-pentanedione (**3a**)*

Method A. Starting with 3-chloro-2,4-pentanedione (5.5 mL, 48.9 mmol), thiophenol (5.0 mL, 48.9 mmol), pyridine (3.9 mL, 48.9 mmol) and methanol (4.9 mL), **3a** was isolated as a colourless oil (7.30 g, 72%). ^1H NMR (250 MHz, $CDCl_3$): δ=2.26 (s, 6H, CH_3), 7.01 (dd, 2H, J=1.2, 8.2 Hz, ArH), 7.07 (m, 1H, ArH), (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.7 (2C, CH_3), 102.0 (C), 125.0 (2C, CH), 125.6 (CH), 129.6 (2C, CH), 138.1 (C), 198.7 (2C); IR (neat): $\tilde{\nu}$=3072 (m), 2925 (m), 2853 (w), 1725 (m), 1582 (s), 1478 (s), 1259 (s), 1069 (m), 739 (s), 690 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 208.1 (M^+, 100), 166.1 (30), 147.1 (25), 123.1 (16), 103.1 (18), 88 (13), 43.1 (54); elemental analysis: calcd (%) for $C_{11}H_{12}O_2S$ (208.0): C 63.43, H 5.81; found: C 62.9, H 6.40.

*3.2.2. 3-(4-Methoxythiophenoxy)-2,4-pentanedione (**3b**)*

Method B. Starting with 3-chloro-2,4-pentanedione (3.8 mL, 33.3 mmol), 4-methoxythiophenol (4.1 mL, 33.3 mmol),

piperidine (3.3 mL, 33.3 mmol), CH_2Cl_2 (3 mL) and methanol (13.5 mL), **3b** was isolated as a colourless solid (2.80 g, 33%), mp=88 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.32 (s, 6H, CH_3), 3.75 (s, 3H, OCH_3), 6.81 (d, 2H, J=9.1 Hz, ArH), 7.01 (d, 2H, J=9.1 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.3 (2C, CH_3), 55.2 (CH_3), 102.9 (C), 114.8 (2C, CH), 126.8 (2C, CH), 128.3, 157.8 (C), 197.9 (2C); IR (KBr): $\tilde{\nu}$=2998 (m), 2961 (m), 2836 (w), 1492 (s), 1294 (s), 1172 (s), 1330 (s), 910 (w), 819 (s), 516 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 238 (M^+, 57), 196 (6), 151 (7), 108.1 (100), 59.1 (4), 43.1 (39); elemental analysis: calcd (%) for $C_{12}H_{14}O_3S$ (238.06): C 60.48, H 5.92; found: C 60.71, H 5.99.

3.2.3. 3-(4-Bromothiophenoxy)-2,4-pentanedione (**3c**)

Method B. Starting with 3-chloro-2,4-pentanedione (1.5 mL, 13.2 mmol), 4-bromothiophenol (2.50 g, 13.2 mmol), piperidine (1.3 mL, 13.2 mmol), CH_2Cl_2 (1.3 mL) and methanol (5 mL), **3c** was isolated as a colourless solid (1.00 g, 28%), mp=79 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.29 (s, 6H, CH_3), 6.92 (d, 2H, J=8.8 Hz, ArH), 7.35 (d, 2H, J=8.9 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.7 (2C, CH_3), 101.5, 119.2 (C), 126.6 (2C, CH), 132.6 (2C, CH), 137.4 (C), 198.7 (2C); IR (KBr): $\tilde{\nu}$=3433 (w), 1557 (s), 1472 (s), 1386 (s), 1256 (w), 1020 (m), 909 (w), 809 (s), 479 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 288 (M^+, ^{81}Br, 98), 286 (M^+, ^{79}Br, 96), 246 (43), 244 (41), 192 (40), 164.1 (42), 117 (33), 88 (27), 43.1 (100); elemental analysis: calcd (%) for $C_{11}H_{11}BrO_2S$ (285.96): C 46.01, H 3.86; found: C 45.98, H 3.94.

3.2.4. 3-(4-Methylthiophenoxy)-2,4-pentanedione (**3d**)

Method B. Starting with 3-chloro-2,4-pentanedione (9.1 mL, 80.5 mmol), 4-methylthiophenol (10.00 g, 80.5 mmol), piperidine (8 mL, 80.5 mmol), CH_2Cl_2 (6 mL) and methanol (30 mL), **3d** was isolated as a colourless solid (14.50 g, 81%), mp=56 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.27 (s, 3H, CH_3), 2.31 (s, 6H, CH_3), 6.96 (d, 2H, J=8.2 Hz, ArH), 7.07 (d, 2H, J=8.0 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.3 (2C, CH_3), 55.6 (CH_3), 101.1 (C), 110.9 (2C, CH), 117.3, 130.4 (CH), 139.6, 160.7 (C), 198.7 (2C); IR (KBr): $\tilde{\nu}$=3073 (w), 2918 (w), 1576 (s), 1399 (s), 1259 (m), 1085 (w), 1016 (s), 909 (m), 806 (s), 506 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 222.1 (M^+, 100), 180.1 (27), 146.1 (17), 117.1 (25), 88.1 (27), 43.1 (51); elemental analysis: calcd (%) for $C_{12}H_{12}O_2S$ (222.07): C 64.83, H 6.35; found: C 64.94, H 6.31.

3.2.5. 3-(3-Methoxythiophenoxy)-2,4-pentanedione (**3e**)

Method B. Starting with 3-chloro-2,4-pentanedione (3.85 mL, 34.1 mmol), 3-methoxythiophenol (4.23 mL, 34.1 mmol), piperidine (3.38 mL, 34.1 mmol), CH_2Cl_2 (3 mL) and methanol (13 mL), **3e** was isolated as a colourless oil (5.90 g, 73%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.30 (s, 6H, CH_3), 3.75 (s, 3H, OCH_3), 6.60 (m, 1H, ArH), 6.63 (br d, 1H, J=7.6 Hz, ArH), 6.66 (s, 1H, ArH), 7.16 (t, 1H, J=7.6 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.1 (CH_3), 24.8 (2C, CH_3), 102.4 (C), 125.3 (2C, CH), 130.3 (CH), 134.5, 135.5 (C), 198.6 (2C); IR (neat): $\tilde{\nu}$=3061 (w), 2958 (m), 2835 (m), 1590 (s), 1425 (s), 1182 (m), 857 (m), 686 (s), 534 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 238.1 (M^+, 100), 196.1 (50), 153.1 (32), 108.1 (24), 88.1 (18), 43.1 (9); elemental analysis: calcd (%) for $C_{12}H_{14}O_3S$ (238.06): C 60.48, H 5.92; found: C 60.01, H 5.88.

3.3. General procedure for the synthesis of diaryl thioethers **6a–j** and **12a–h**

To a dichloromethane solution (2 mL/mmol) of **4** (1.0 mmol) and **5** (1.0 mmol) was added $TiCl_4$ (1.0 mmol) at −78 °C. The solution was allowed to warm to ambient temperature within 20 h. To the solution was added a saturated solution of $NaHCO_3$ (15 mL). The organic and the aqueous layers were separated and the latter was extracted with diethyl ether (3×20 mL). The filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc/*n*-heptane=1:4).

3.3.1. Methyl 4,6-dimethyl-5-(thiophenoxy)salicylate (**6a**)

Starting with 3-(silyloxy)alk-2-en-1-one **4a** (200 mg, 0.7 mmol), 1,3-bis(silyl enol ether) **5a** (185 mg, 0.71 mmol) and $TiCl_4$ (0.08 mL, 0.71 mmol), **6a** was isolated as a colourless solid (99 mg, 48%), mp=83 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.40 (s, 3H, CH_3), 2.72 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 6.89 (d, 2H, J=8.2 Hz, ArH), 6.76 (s, 1H, ArH), 6.91 (s, 1H, ArH), 7.05 (br t, 1H, J=7.2 Hz, ArH), 7.18 (br t, 1H, J=7.4 Hz, ArH), 11.17 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4, 2.7, 52.3 (CH_3), 112.4 (C), 117.7 (CH), 122.7 (C), 124.6 (CH), 125.2 (2C, CH), 128.9 (2C, CH), 138.2, 147.1, 151.4, 162.5, 171.8 (C); IR (KBr): $\tilde{\nu}$=3061 (m), 2954 (m), 1663 (s), 1478 (s), 1360 (s), 1233 (s), 1187 (m), 1024 (m), 947 (w), 740 (s), 690 (m), 629 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 288.1 (M^+, 57), 256.1 (100), 185.1 (7), 91 (6); elemental analysis: calcd (%) for $C_{16}H_{16}O_3S$ (288.08): C 66.64, H 5.59; found: C 66.81, H 5.68.

3.3.2. Ethyl 3,4,6-trimethyl-5-(thiophenoxy)salicylate (**6b**)

Starting with 3-(siloxy)alk-2-en-1-one **4a** (200 mg, 0.71 mmol), 1,3-bis(silyl enol ether) **5b** (204 mg, 0.7 mmol) and $TiCl_4$ (0.08 mL, 0.7 mmol), **6b** was isolated as a colourless solid (90 mg, 40%), mp=122 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.42 (t, 3H, J=7.1 Hz, CH_3), 2.24 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.74 (s, 3H, CH_3), 4.44 (q, 2H, J=7.1 Hz, OCH_2), 6.90 (m, 2H, ArH), 7.06 (br t, 1H, J=7.3 Hz, ArH), 7.18 (m, 2H, ArH), 11.52 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=12.7, 14.1, 19.5, 21.6 (CH_3), 61.8 (CH_2), 112.0, 122.5, 123.9 (C), 124.5 (CH), 125.2 (2C, CH), 128.9 (2C, CH), 138.7, 143.7, 149.1, 160.6, 171.9 (C); IR (KBr): $\tilde{\nu}$=3069 (m), 2980 (m), 1644 (s), 1548 (m), 1395 (s), 1343 (s), 1146 (s), 1083 (m), 1025 (s), 868 (w), 735 (s), 688 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 316 (M^+, 38), 270 (100), 242 (20), 165 (10), 77 (11); elemental analysis: calcd (%) for $C_{18}H_{20}O_3S$ (316.11): C 68.33, H 6.37; found: C 68.23, H 6.48.

3.3.3. Ethyl 4,6-dimethyl-3-ethyl-5-(thiophenoxy)salicylate (**6c**)

Starting with 3-(silyloxy)alk-2-en-1-one **4a** (200 mg, 0.7 mmol), 1,3-bis(silyl enol ether) **5c** (214 mg, 0.7 mmol) and $TiCl_4$ (0.08 mL, 0.7 mmol), **6c** was isolated as a yellow highly

viscous oil (90 mg, 40%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.04 (t, 3H, J=7.4 Hz, CH_3), 1.32 (t, 3H, J=7.1 Hz, CH_3), 2.40 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 2.68 (q, 2H, J=7.4 Hz, OCH_2), 4.35 (q, 2H, J=7.1 Hz, OCH_2), 6.82 (dd, 2H, J=1.5, 8.3 Hz, ArH), 6.97 (br t, 1H, J=7.3 Hz, ArH), 7.10 (br t, 2H, J=7.4 Hz, ArH), 11.38 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=12.1, 13.1, 17.6 (CH_3), 19.4 (CH_2), 20.5 (CH_3), 60.8 (CH_2), 111.1, 121.6 (C), 123.4 (CH), 124.1 (2C, CH), 127.8 (2C, CH), 129.0, 137.7, 142.9, 147.4, 159.4, 170.9 (C); IR (neat): $\tilde{\nu}$=3057 (m), 2970 (s), 2873 (m), 1732 (w), 1653 (s), 1583 (s), 1551 (s), 1439 (s), 1230 (s), 1084 (m), 866 (w), 813 (m), 689 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 330.2 (M^+, 63), 284.1 (100), 256.1 (24), 139 (9), 165.1 (7), 91.1 (8); HRMS (EI): calcd for $C_{19}H_{22}O_3S$ $[M^+]^+$: 330.12828, found 330.12842.

3.3.4. Ethyl 4,6-dimethyl-5-(4-methoxythiophenoxy)-salicylate (*6d*)

Starting with 3-(silyloxy)alk-2-en-1-one **4b** (300 mg, 0.96 mmol), 1,3-bis(silyl enol ether) **5d** (263 mg, 0.96 mmol) and $TiCl_4$ (0.1 mL, 0.96 mmol), **6d** was isolated as a colourless solid (138 mg, 43%), mp=77 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.38 (t, 3H, J=7.0 Hz, CH_3), 2.39 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 4.40 (q, 2H, J=7.1 Hz, OCH_2), 6.73 (d, 2H, J=9.1 Hz, ArH), 6.81 (s, 1H, ArH), 6.84 (d, 2H, J=9.1 Hz, ArH), 11.10 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.1, 20.5, 22.1, 54.3 (CH_3), 60.8 (CH_2), 111.4 113.7 (2C, CH), 116.5 (CH), 123.0 (C), 126.3 (2C, CH), 127.9, 145.8, 150.0, 156.5, 161.3, 170.3 (C); IR (KBr): $\tilde{\nu}$=2991 (m), 2954 (m), 2833 (m), 1653 (s), 1558 (m), 1494 (s), 1450 (s), 1341 (s), 1286 (s), 1125 (w), 871 (m), 623 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 332.1 (M^+, 84), 286 (100), 243 (10), 218 (11), 178 (8) 139 (7), 91 (6); elemental analysis: calcd (%) for $C_{18}H_{20}O_4S$ (332.10): C 65.04, H 6.06; found: C 64.78, H 6.19.

3.3.5. Ethyl 3,4,6-trimethyl-5-(4-methoxythiophenoxy)-salicylate (*6e*)

Starting with 3-(silyloxy)alk-2-en-1-one **4b** (300 mg, 0.96 mmol), 1,3-bis(silyl enol ether) **5b** (277 mg, 0.96 mmol) and $TiCl_4$ (0.1 mL, 0.96 mmol), **6e** was isolated as a colourless oil (116 mg, 35%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.32 (t, 3H, J=7.1 Hz, CH_3), 2.14 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 4.34 (q, 2H, J=7.0 Hz, OCH_2), 6.67 (d, 2H, J=8.8 Hz, ArH), 6.78 (d, 2H, J=8.8 Hz, ArH), 11.39 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=11.7, 13.1, 18.6, 20.7, 54.2 (CH_3), 60.8 (CH_2), 110.9, 113.6 (2C, CH), 122.8, 122.9 (C), 126.2 (2C, CH), 128.4, 142.3, 147.9, 156.3, 159.1, 170.9 (C); IR (KBr): $\tilde{\nu}$=2978 (m), 2835 (m), 1645 (s), 1572 (s), 1491 (s), 1343 (s), 1287 (s), 1183 (s), 1099 (m), 868 (w), 800 (m), 621 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 346 (M^+, 83), 300 (100), 278 (14), 246 (23), 196 (26), 108 (36), 77 (14); elemental analysis: calcd (%) for $C_{19}H_{22}O_4S$ (345.11): C 65.87, H 6.40; found: C 65.71, H 6.59.

3.3.6. Ethyl 4,6-dimethyl-3-ethyl-5-(4-methoxythiophenoxy)-salicylate (*6f*)

Starting with 3-(silyloxy)alk-2-en-1-one **4b** (400 mg, 1.3 mmol), 1,3-bis(silyl enol ether) **5c** (387 mg, 1.3 mmol) and $TiCl_4$ (0.15 mL, 1.3 mmol), **6f** was isolated as a colourless highly viscous oil (175 mg, 38%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.09 (t, 3H, J=7.4 Hz, CH_3), 1.37 (t, 3H, J=7.0 Hz, CH_3), 2.47 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 2.73 (q, 2H, J=7.3 Hz, OCH_2), 3.71 (s, 3H, OCH_3), 4.40 (q, 2H, J=7.1 Hz, OCH_2), 6.73 (d, 2H, J=9.1 Hz, ArH), 6.83 (d, 2H, J=9.1 Hz, ArH), 11.38 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.2, 14.1, 18.7 (CH_3), 20.4 (CH_2), 21.7, 55.2 (CH_3), 61.7 (CH_2), 112.1 (C), 114.6 (2C, CH), 124.0 (C), 127.1 (2C, CH), 129.3, 129.9, 143.5, 148.2, 157.3, 160.2, 171.9 (C); IR (neat): $\tilde{\nu}$=2968 (m), 2834 (m), 1729 (w), 1652 (s), 1592 (s), 1437 (s), 1372 (s), 1260 (s), 1108 (s), 865 (w), 820 (s), 622 (m), 516 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 360 (M^+, 83), 300 (100), 286 (33), 271 (10), 178 (9), 57 (6); elemental analysis: calcd (%) for $C_{20}H_{24}O_4S$ (360.13): C 66.64, H 6.71; found: C 66.04, H 6.97.

3.3.7. Methyl 4,6-dimethyl-5-(4-bromothiophenoxy)-salicylate (*6g*)

Starting with 3-(silyloxy)alk-2-en-1-one **4c** (200 mg, 0.55 mmol), 1,3-bis(silyl enol ether) **5a** (144 mg, 0.55 mmol) and $TiCl_4$ (0.06 mL, 0.55 mmol), **6g** was isolated as a colourless solid (73 mg, 36%), mp=114 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.32 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 6.68 (d, 2H, J=8.5 Hz, ArH), 6.80 (s, 1H, ArH), 7.20 (d, 2H, J=8.5 Hz, ArH), 11.10 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=20.3, 21.9, 51.3 (CH_3), 11.5, 116.8 (C), 117.1 (CH), 121.1 (C), 12.7 (2C, CH), 130.9 (2C, CH), 136.5, 146.1, 150.2, 161.7, 170.6 (C); IR (KBr): $\tilde{\nu}$=3068 (w), 2953 (m), 1660 (s), 1594 (s), 1472 (s), 1355 (s), 1230 (s), 1188 (m), 1005 (s), 944 (w), 824 (w), 807 (s), 503 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 368 (M^+, ^{81}Br, 49), 366 (M^+, ^{79}Br, 48), 336 (100), 334 (95), 184 (11), 127 (6), 91 (11); elemental analysis: calcd (%) for $C_{16}H_{15}BrO_3S$ (365.99): C 52.33, H 4.12; found: C 52.18, H 4.31.

3.3.8. Ethyl 3,4,6-trimethyl-5-(4-methylthiophenoxy)-salicylate (*6h*)

Starting with 3-(silyloxy)alk-2-en-1-one **4d** (500 mg, 1.8 mmol), 1,3-bis(silyl enol ether) **5b** (520 mg, 1.8 mmol) and $TiCl_4$ (0.2 mL, 1.8 mmol), **6h** was isolated as a colourless solid (188 mg, 33%), mp=75 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.33 (t, 3H, J=7.1 Hz, CH_3), 2.15 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 4.35 (q, 2H, J=7.3 Hz, CH_2), 6.72 (d, 2H, J=8.2 Hz, ArH), 6.92 (d, 2H, J=8.2 Hz, ArH), 11.41 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=12.9, 14.3, 19.7, 20.9, 21.7 (CH_3), 61.9 (CH_2), 112.4, 123.3, 124.0 (C), 125.4 (2C, CH), 129.8 (2C, CH), 134.4, 135, 143.7, 149.2, 160.6, 172.1 (C); IR (KBr): $\tilde{\nu}$=3015 (w), 2936 (m), 1647 (s), 1551 (m), 1490 (s), 1392 (s), 1288 (s), 1185 (s), 1100 (m), 1014 (m), 868 (w), 801 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 330.1 (M^+, 70), 284.1 (100), 256 (17), 241 (41), 165 (7), 91 (11); elemental analysis: calcd (%) for $C_{19}H_{22}O_3S$ (330.12): C 69.06, H 6.71; found: C 68.89, H 6.98.

*3.3.9. Methyl 4,6-dimethyl-5-(3-methoxythiophenoxy)-salicylate (**6i**)*

Starting with 3-(silyloxy)alk-2-en-1-one **4e** (500 mg, 1.7 mmol), 1,3-bis(silyl enol ether) **5a** (455 mg, 1.7 mmol) and $TiCl_4$ (0.18 mL, 1.7 mmol), **6i** was isolated as a colourless solid (174 mg, 32%), mp=78 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.28 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.32 (m, 1H, ArH), 6.37 (m, 1H, ArH), 6.48 (br m, 1H, ArH), 6.74 (s, 1H, ArH), 6.97 (t, 1H, J=8.1 Hz, ArH), 11.01 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=21.4, 23.1, 52.4, 55.2 (CH_3), 109.8, 110.7 (CH), 112.2 (C), 117.4, 117.5 (CH), 122.3 (C), 129.5 (CH), 139.5, 147.0, 151.2, 159.9, 162.4, 171.6 (C); IR (KBr): $\tilde{\nu}$=3002 (w), 2947 (m), 1663 (s), 1591 (s), 1474 (s), 1357 (s), 1229 (s), 1110 (m), 1046 (s), 877 (w), 847 (w), 768 (s), 686 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 318 (M^+, 59), 286 (100), 256 (17), 225 (10), 179 (16), 91 (8), 57 (8); elemental analysis: calcd (%) for $C_{17}H_{18}O_4S$ (318.09): C 64.13, H 5.70; found: C 64.41, H 5.93.

*3.3.10. Ethyl 3,4,6-trimethyl-5-(3-methoxythiophenoxy)-salicylate (**6j**)*

Starting with 3-(silyloxy)alk-2-en-1-one **4e** (500 mg, 1.7 mmol), 1,3-bis(silyl enol ether) **5b** (490 mg, 1.7 mmol) and $TiCl_4$ (0.18 mL, 1.7 mmol), **6j** was isolated as a colourless oil (177 mg, 30%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.33 (t, 3H, J=7.1 Hz, CH_3), 2.15 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 4.35 (q, 2H, J=7.1 Hz, OCH_2), 6.38 (m, 1H, ArH), 6.42 (m, 1H, ArH), 6.52 (br m, 1H, ArH), 7.02 (t, 1H, J=8.2 Hz, ArH), 11.44 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=11.7, 13.1, 18.5, 20.5, 54.1 (CH_3), 60.8 (CH_2), 108.8, 109.9 (CH), 110.9 (C), 116.5 (CH), 121.2, 122.9 (C), 128.7 (CH), 139.2, 142.8, 148.1, 159.0, 159.6, 170.9 (C); IR (KBr): $\tilde{\nu}$=3058 (w), 2933 (s), 1729 (w), 1652 (s), 1590 (s), 1475 (s), 1376 (s), 1283 (s), 1242 (s), 1181 (s), 1045 (s), 860 (s), 686 (m), 566 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 346 (M^+, 80), 300 (100), 256 (17), 257 (20), 164 (6), 69 (13), 57 (5); elemental analysis: calcd (%) for $C_{19}H_{22}O_4S$ (346.12): C 65.87, H 6.40; found: C 65.47, H 6.64.

*3.4. General procedure for the synthesis of ethyl 4-(thioaryloxy)acetoacetates **7a–b***

A solution of 4-chloroacetoacetate (1.0 mmol), NEt_3 (1.05 mmol) and thiophenol **1** (1.03 mmol) in CH_2Cl_2 (2 mL) was stirred at 0 °C for 30 min. The reaction mixture was diluted with EtOAc and washed with an aqueous solution of NaOH (1 M), hydrochloric acid (1 M) and brine. The combined organic layers were dried (Na_2SO_4), filtered and the solvent of the filtrate was removed under reduced pressure. The residue was purified by chromatography (silica gel, EtOAc/*n*-heptane).

*3.4.1. Ethyl 4-(thiophenoxy)acetoacetate (**7a**)*

Starting with 4-chloroacetoacetate (10 mL, 73 mmol), thiophenol (7.7 mL, 75.5 mmol), NEt_3 (10.7 mL, 76.7 mmol) and dichloromethane (146 mL), **7a** was isolated as a colourless oil (13.80 g, 80%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.26 (t, 3H, J=7.1 Hz, CH_3), 3.63 (s, 2H, CH_2), 3.81 (s, 2H, CH_2), 4.18 (q, 2H, J=7.1 Hz, OCH_2), 7.23–7.27 (m, 2H, ArH), 7.29–7.31 (m, 1H, ArH), 7.32–7.37 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.4 (CH_3), 44.3, 46.9, 61.9 (CH_2), 127.6 (CH), 129.6 (2C, CH), 130.2 (2C, CH), 134.4, 167.4, 198.3 (C); IR (neat): $\tilde{\nu}$=3059 (w), 2982 (m), 2937 (w), 1743 (s), 1716 (s), 1583 (m), 1439 (m), 1320 (s), 1188 (s), 1026 (s), 741 (s), 691 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 238 (M^+, 40), 192 (18), 166 (5), 150 (53), 123 (100), 110 (29), 77 (16), 65 (10); elemental analysis: calcd (%) for $C_{12}H_{14}O_3S$ (238): C 60.48, H 5.92; found: C 59.90, H 5.91.

*3.4.2. Ethyl 4-(4-methoxythiophenoxy)acetoacetate (**7b**)*

Starting with 4-chloroacetoacetate (3.3 mL, 24.2 mmol), thiophenol (3 mL, 25 mmol), NEt_3 (3.6 mL, 25.5 mmol) and dichloromethane (50 mL), **7b** was isolated as a colourless oil (5.40 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.11 (t, 3H, J=7.1 Hz, CH_3), 3.48 (s, 2H, CH_2), 3.52 (s, 2H, CH_2), 3.62 (s, 3H, OCH_3), 4.02 (q, 2H, J=7.0 Hz, OCH_2), 6.68 (d, 2H, J=8.9 Hz, ArH), 7.10 (d, 2H, J=8.7 Hz, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.4 (CH_3), 46.2, 46.9 (CH_2), 55.6 (CH_3), 61.8 (CH_2), 115.2 (2C, CH), 124.5 (C), 134.3 (2C, CH), 159.2 (C), 167.7 (C), 198.2 (C); IR (neat): $\tilde{\nu}$=2981 (m), 2939 (w), 2837 (w), 1743 (s), 1714 (s), 1592 (s), 1495 (s), 1367 (m), 1284 (s), 1181 (s), 1029 (s), 828 (m), 638 (w), 525 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 268 (M^+, 24), 222 (16), 196 (26), 180 (12), 153 (100), 139 (28), 109 (39), 96 (10), 69 (20); elemental analysis: calcd (%) for $C_{13}H_{16}O_3S$: C 59.19, H 6.01; found: C 58.34, H 6.34.

*3.4.3. Ethyl 4-(4-methylthiophenoxy)acetoacetate (**7c**)*

Starting with 4-chloroacetoacetate (5.3 mL, 39.0 mmol), thiophenol (5.00 g, 40.2 mmol), NEt_3 (5.7 mL, 41.0 mmol) and dichloromethane (78 mL), **7c** was isolated as a colourless oil (7.8 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.16 (t, 3H, J=7.1 Hz, CH_3), 2.22 (s, 3H, CH_3), 3.53 (s, 2H, CH_2), 3.65 (s, 2H, CH_2), 4.07 (q, 2H, J=7.0 Hz, OCH_2), 7.01 (d, 2H, J=8.1 Hz, ArH), 7.17 (d, 2H, J=8.2 Hz, ArH); ^{13}C NMR (75 MHz): δ=14.4, 21.4 (CH_3), 42.2, 43.6, 61.8 (CH_2), 130.4 (2C, CH), 130.8 (2C, CH), 131.5, 137.9, 167.4, 198.3 (C); IR (neat): $\tilde{\nu}$=2981 (m), 2924 (w), 1744 (s), 1715 (s), 1652 (w), 1494 (m), 1320 (s), 1186 (s), 1030 (s), 942 (w), 800 (s), 733 (w); MS (EI, 70 eV): *m/z* (%): 252 (M^+, 30), 206 (15), 164 (28), 137 (100), 119 (9), 91 (24), 77 (7), 45 (28); elemental analysis: calcd (%) for $C_{13}H_{16}O_3S$ (252.0): C 61.88, H 6.39; found: C 61.40, H 6.34.

*3.4.4. Ethyl 4-(4-methylthiophenoxy)acetoacetate (**7d**)*

Starting with 4-chloroacetoacetate (13.8 mL, 101.1 mmol), 4-chlorothiophenol (15.00 g, 104.0 mmol), NEt_3 (14.7 mL, 106.1 mmol) and dichloromethane (202 mL), **7d** was isolated as a colourless oil (23.8 g, 84%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.21 (t, 3H, J=7.0 Hz, CH_3), 3.58 (s, 2H, CH_2), 3.76 (s, 2H, CH_2), 4.11 (q, 2H, J=7.4 Hz, OCH_2), 7.23 (m, 4H, ArH); ^{13}C NMR (62 MHz): δ=14.1 (CH_3), 44.0, 46.5, 61.5 (CH_2), 129.3

(2C, CH), 130.8 (2C, CH), 132.7, 133.2, 172.2, 197.7 (C); IR (neat): $\tilde{\nu}$=2982 (m), 2937 (w), 1743 (s), 1716 (s), 1653 (w), 1478 (s), 1321 (s), 1250 (m), 1188 (m), 1095 (s), 815 (m), 744 (w); MS (EI, 70 eV): *m/z* (%): 274 (M^+, ^{37}Cl, 1), 272 (M^+, ^{35}Cl, 3), 200 (5), 184 (3), 157 (13), 88 (29), 86 (92), 84 (100), 51 (74); HRMS (EI): calcd for $C_{12}H_{13}O_3ClS$ [M^{++}, ^{35}Cl]: 272.02660, found 272.02684.

3.4.5. Ethyl 3-(thiophenoxy)salicylate (**10a**)

Starting with tetramethoxy (0.26 mL, 1.57 mmol), 1,3-bis-(silyl enol ether) **9a** (600 mg, 1.57 mmol) and $TiCl_4$ (0.17 mL, 1.57 mmol), **10a** was isolated as a highly viscous oil (133 mg, 31%). ^1H NMR (300 MHz, $CDCl_3$): δ=1.34 (t, 3H, *J*=7.1 Hz, CH_3), 4.34 (q, 2H, *J*=7.0 Hz, OCH_2), 6.74 (t, 1H, *J*=7.7 Hz, ArH), 7.17–7.27 (m, 5H, ArH), 7.29–7.31 (m, 1H, ArH), 7.69–7.73 (dd, 1H, *J*=1.5, 8.0 Hz, ArH), 11.39 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.1 (CH_3), 60.7 (CH_2), 111.8 (C), 118.3 (CH), 123.0 (C), 126.2, 128.0 (CH), 128.2 (2C, CH), 130.2 (2C, CH), 133.0 (C), 136.8 (CH), 158.8, 169.1 (C); IR (neat): $\tilde{\nu}$=3074 (w), 2983 (m), 2936 (w), 1669 (s), 1601 (m), 1428 (s), 1318 (s), 1251 (s), 1188 (s), 1023 (m), 752 (s), 690 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 274 (M^+, 66), 228 (100), 200 (14), 171 (37), 139 (5), 95 (6), 51 (4); elemental analysis: calcd (%) for $C_{15}H_{14}O_3S$ (274.07): C 65.67, H 5.14; found: C 65.23, H 5.13.

3.4.6. Ethyl 3-(4-methoxythiophenoxy)salicylate (**10b**)

Starting with 1,1,3,3-tetramethoxypropane (0.26 mL, 1.6 mmol), 1,3-bis(silyl enol ether) **9b** (648 mg, 1.6 mmol) and $TiCl_4$ (0.17 mL, 1.6 mmol), **10b** was isolated as a highly viscous oil (143 mg, 30%). ^1H NMR (300 MHz, $CDCl_3$): δ=1.23 (t, 3H, *J*=7.1 Hz, CH_3), 3.63 (s, 3H, OCH_3), 4.23 (q, 2H, *J*=7.2 Hz, OCH_2), 6.55 (t, 1H, *J*=7.8 Hz, ArH), 7.73 (d, 2H, *J*=8.9 Hz, ArH), 6.82–6.86 (dd, 1H, *J*=2.1, 7.6 Hz, ArH), 7.25 (d, 2H, *J*=8.7 Hz, ArH), 7.47–7.50 (dd, 1H, *J*=1.7, 8.0 Hz, ArH), 11.28 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.8, 55.7 (CH_3), 62.3 (CH_2), 112.5 (C), 115.5 (2C, CH), 119.6 (C), 122.9, 127.6 (CH), 127.7 (CH), 134.6 (CH), 136.2 (2C, CH), 158.5, 160.4, 170.6 (C); IR (KBr): $\tilde{\nu}$=3074 (w), 2987 (m), 2942 (w), 2835 (w), 1670 (s), 1569 (m), 1492 (s), 1372 (s), 1289 (s), 1180 (s), 1023 (s), 831 (s), 760 (s), 731 (m), 527 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 304.1 (M^+, 68), 258.1 (100), 243.1 (6), 215.1 (9), 187.1 (16), 159.1 (4), 115.1 (7), 95.1 (6), 63.1 (3); elemental analysis: calcd (%) for $C_{16}H_{16}O_4S$ (304.08): C 63.14, H 5.30; found: C 63.14, H 5.37.

3.4.7. Ethyl 4,6-dimethyl-3-(thiophenoxy)salicylate (**12a**)

Starting with 3-(silyloxy)alk-2-en-1-one **11a** (400 mg, 2.3 mmol), 1,3-bis(silyl enol ether) **9a** (887 mg, 2.3 mmol) and $TiCl_4$ (0.25 mL, 2.3 mmol), **12a** was isolated as a colourless solid (336 mg, 48%), mp=79 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=1.34 (t, 3H, *J*=7.1 Hz, CH_3), 2.33 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 4.35 (q, 2H, *J*=7.3 Hz, OCH_2), 6.66 (s, 1H, ArH), 6.94–6.97 (dd, 2H, *J*=1.5, 8.2 Hz, ArH), 7.01 (m, 1H, ArH), 7.09–7.13 (m, 2H, ArH), 11.75 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.0, 21.5, 23.7 (CH_3), 61.6 (CH_2), 111.5, 116.9 (C), 124.8, 124.9 (CH), 125.9 (2C, CH), 128.6 (2C, CH), 137.2, 142.4, 150.2, 163.4, 172.4 (C); IR (KBr): $\tilde{\nu}$=3054 (w), 2959 (w), 2935 (m), 2935 (m), 2809 (w), 2742 (w), 1639 (s), 1605 (s), 1476 (s), 1447 (s), 1376 (s), 1296 (s), 1259 (s), 1211 (s), 1108 (w), 1015 (m), 820 (m), 741 (s), 459 (w); MS (EI, 70 eV): *m/z* (%): 302.1 (M^+, 61), 256.1 (100), 241.1 (22), 184.1 (14), 165.1 (5), 128 (5), 91.1 (7); elemental analysis: calcd (%) for $C_{17}H_{18}O_3S$ (302.1): C 67.52, H 6.00; found: C 67.48, H 6.24.

3.4.8. Ethyl 4,6-diethyl-3-(4-methoxythiophenoxy)salicylate (**12b**)

Starting with 3-(silyloxy)alk-2-en-1-one **11b** (400 mg, 2.0 mmol), 1,3-bis(silyl enol ether) **9b** (824 mg, 2.0 mmol) and $TiCl_4$ (0.22 mL, 2.0 mmol), **12b** was isolated as a highly viscous oil (251 mg, 35%). ^1H NMR (300 MHz, $CDCl_3$): δ=1.06–1.18 (m, 6H, CH_3), 1.35 (t, 3H, *J*=7.1 Hz, CH_3), 2.78–2.83 (m, 4H, CH_2), 3.67 (s, 3H, OCH_3), 4.35 (q, 2H, *J*=7.2 Hz, OCH_2), 6.68 (d, 2H, *J*=8.9 Hz, ArH), 6.99 (d, 2H, *J*=8.7 Hz, ArH), 7.11 (s, 1H, ArH), 11.07 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.4, 15.5, 16.3 (CH_3), 28.7, 29.7 (CH_2), 55.7 (CH_3), 62.1 (CH_2), 112.0 (C), 124.8 (CH), 114.9 (2C, CH), 117.4 (C), 122.5 (CH), 128.3 (C), 129.1 (2C, CH), 148.4, 155.3, 158.3, 162.5, 171.2 (C); IR (neat): $\tilde{\nu}$=3375 (w), 2963 (s), 2930 (s), 2872 (m), 1728 (s), 1653 (s), 1595 (s), 1493 (s), 1374 (s), 1247 (s), 1107 (s), 1070 (m), 947 (w), 820 (m), 525 (w); MS (EI, 70 eV): *m/z* (%): 360.2 (M^+, 65), 314.1 (100), 281.2 (10), 207 (7), 163 (13), 135 (15), 77 (7); HRMS (EI): calcd for $C_{20}H_{24}O_4S$ [M^+]$^+$: 360.13898, found 360.138235.

3.4.9. Ethyl 5-chloro-4,6-dimethyl-3-(thiophenoxy)salicylate (**12c**)

Starting with 3-(siloxy)alk-2-en-1-one **11c** (339 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **9a** (573 mg, 1.5 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **12c** was isolated as a highly viscous oil (222 mg, 37%). ^1H NMR (250 MHz, $CDCl_3$): δ=1.34 (t, 3H, *J*=7.0 Hz, CH_3), 2.48 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 4.35 (q, 2H, *J*=7.1 Hz, CH_2), 6.89 (d, 1H, *J*=1.4 Hz, ArH), 7.12 (m, 2H, ArH), 7.18 (m, 2H, ArH), 9.41 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.1, 19.6, 20.4 (CH_3), 62.1 (CH_2), 116.6 (C), 117.4 (C), 125.8 (C), 126.4 (2C, CH), 127.5 (CH), 128.9 (2C, CH), 135.5, 138.6, 146.0, 157.2 (C), 169.1 (C=O); IR (KBr): $\tilde{\nu}$=3387 (w), 3058 (w), 2982 (m), 2932 (w), 1730 (m), 1657 (m), 1582 (m), 1478 (m), 1439 (m), 1372 (s), 1219 (s), 1023 (m), 793 (m), 689 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 338 (M^+, ^{37}Cl, 14), 336 (M^+, ^{35}Cl, 48), 290 (100), 275 (14), 261 (9), 184 (12); HRMS (EI): calcd for $C_{17}H_{17}O_3ClS$ [M]$^+$: 336.05814, found 336.05807.

3.4.10. Ethyl 4,5,6-trimethyl-3-(thiophenoxy)salicylate (**12d**)

Starting with 3-(siloxy)alk-2-en-1-one **11d** (308 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **9a** (573 mg, 1.5 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **12d** was isolated as a highly viscous oil (173 mg, 33%). ^1H NMR (250 MHz, $CDCl_3$):

δ=1.33 (t, 3H, J=7.0 Hz, CH_3), 2.12 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 4.35 (q, 2H, J=7.1 Hz, CH_2), 6.95 (m, 1H, ArH), 7.09 (m, 2H, ArH), 7.13 (m, 2H, ArH), 8.63 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.2, 16.4, 18.6, 19.1 (CH_3), 61.6 (CH_2), 115.1 (C), 116.9 (C), 125.4 (C), 126.1 (2C, CH), 128.3 (CH), 129.0 (2C, CH), 136.2, 138.2, 145.5, 155.4 (C), 169.6 (C=O); IR (KBr): $\tilde{\nu}$=3394 (m), 3057 (w), 2981 (m), 2929 (m), 1727 (s), 1654 (m), 1582 (s), 1478 (m), 1439 (m), 1374 (m), 1272 (m), 1228 (s), 1178 (s), 1045 (m), 1023 (m), 739 (s), 689 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 316 (M^+, 42), 270 (100), 255 (22), 241 (9), 184 (5), 165 (7), 105 (6); HRMS (EI): calcd for $C_{18}H_{20}O_3S$ $[M]^+$: 316.11277, found 316.11321.

3.4.11. Ethyl 4,6-dimethyl-3-(4-methoxythiophenoxy)-5-(thiophenoxy)salicylate (12e)

Starting with 3-(siloxy)alk-2-en-1-one **4a** (400 mg, 1.41 mmol), 1,3-bis(silyl enol ether) **9b** (582 mg, 1.41 mmol) and $TiCl_4$ (0.15 mL, 1.41 mmol), **12e** was isolated as a highly viscous oil (212 mg, 34%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.33 (t, 3H, J=7.1 Hz, CH_3), 2.34 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 4.34 (q, 2H, J=7.1 Hz, OCH_2), 6.68 (d, 2H, J=8.9 Hz, ArH), 6.73–6.81 (m, 5H, ArH), 7.32 (d, 2H, J=8.9 Hz, ArH), 11.12 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.5, 21.9, 24.8, 55.7 (CH_3), 62.2 (CH_2), 112.9 (C), 115.1 (2C, CH), 118.0 (CH), 124.5 (C), 127.7 (2C, CH), 128.1, 128.8 (2C), 133.0 (2C, CH), 147.2, 151.4, 157.9, 160.3, 162.8, 171.7 (C); IR (Nujol): $\tilde{\nu}$=2954 (s), 2925 (s), 2855 (s), 2932 (s), 1653 (m), 1591 (s), 1492 (s), 1461 (s), 1372 (s), 1245 (m), 1106 (m), 1034 (s), 871 (s), 802 (w), 620 (w), 522 (m), 423 (w).

3.4.12. Ethyl 4,6-dimethyl-3,5-(dithiophenoxy)salicylate (12f)

Starting with 3-(siloxy)alk-2-en-1-one **4a** (400 mg, 1.41 mmol), 1,3-bis(silyl enol ether) **9a** (539 mg, 1.41 mmol) and $TiCl_4$ (0.15 mL, 1.41 mmol), **12f** was isolated as a highly viscous oil (196 mg, 34%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.27 (t, 3H, J=7.0 Hz, CH_3), 2.51 (s, 6H, CH_3), 4.30 (q, 2H, J=7.1 Hz, OCH_2), 6.76–6.80 (dd, 2H, J=1.2, 8.2 Hz, ArH), 6.88–6.92 (m, 2H, ArH), 6.94–7.09 (m, 6H, ArH), 9.37 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.1, 20.6, 21.4 (CH_3), 62.0 (CH_2), 116.7, 116.8, 124.5 (C), 124.8 (CH), 125.2 (2C, CH), 125.6 (CH), 126.2 (2C, CH), 128.9 (2C, CH), 129.0 (2C, CH), 135.1, 137.7, 146.6, 154.2, 159.1, 169.2 (C); IR (KBr): $\tilde{\nu}$=3373 (s), 3057 (s), 2981 (s), 2932 (s), 2869 (m), 1728 (s), 1653 (s), 1439 (s), 1121 (s), 998 (m), 857 (m), 738 (s), 689 (s), 582 (w), 471 (w); MS (EI, 70 eV): *m/z* (%): 410 (M^+, 69), 364 (100), 340 (44), 290 (18), 253 (12), 219 (12), 177 (74), 161 (48), 109 (35), 83 (56), 57 (93), 43 (54); HRMS (EI): calcd for $C_{23}H_{22}O_3S_2$ $[M^+]^+$: 410.10049, found 410.09973.

3.4.13. Ethyl 5-chloro-4,6-dimethyl-3-(4-methylthiophenoxy)salicylate (12g)

Starting with 3-(siloxy)alk-2-en-1-one **11c** (339 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **9c** (594 mg, 1.5 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **12g** was isolated as a colourless solid (166 mg, 30%), mp=79 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.34 (t, 3H, J=7.0 Hz, CH_3), 2.20 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 4.32 (q, 2H, J=7.2 Hz, CH_2), 6.86–6.90 (m, 2H, ArH), 6.94–6.97 (m, 2H, ArH), 9.21 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=12.9, 18.4, 19.3, 19.9 (CH_3), 61.0 (OCH_2), 115.9, 116.9 (C), 125.9 (2C, CH), 126.1 (C), 128.9 (2C, CH), 130.8, 134.8, 137.2, 144.6, 155.8 (C), 167.9 (C=O); IR (KBr): $\tilde{\nu}$=2986 (w), 2962 (w), 2917 (w), 1727 (w), 1644 (m), 1573 (w), 1565 (w), 1491 (m), 1434 (m), 1371 (m), 1277 (m), 1213 (s), 1013 (s), 804 (s), 583 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 352 (M^+, ^{37}Cl, 16), 350 (M^+, 43), 304 (100), 289 (9), 269 (15), 213 (6), 198 (6), 119 (7); HRMS (EI): calcd for $C_{18}H_{19}O_3ClS$ (M^+, ^{35}Cl): 350.07379, found 350.07338.

3.4.14. Ethyl 5-chloro-4,6-dimethyl-3-(4-chlorothiophenoxy)salicylate (12h)

Starting with 3-(siloxy)alk-2-en-1-one **11c** (339 mg, 1.65 mmol), 1,3-bis(silyl enol ether) **9d** (625 mg, 1.5 mmol) and $TiCl_4$ (0.18 mL, 1.65 mmol), **12h** was isolated as a colourless solid (206 mg, 34%), mp=100 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.35 (t, 3H, J=7.4 Hz, CH_3), 2.52 (s, 6H, $2CH_3$), 4.32 (q, 2H, J=7.4 Hz, CH_2), 6.91 (d, 2H, J=8.9 Hz, ArH), 7.09 (d, 2H, J=8.9 Hz, ArH), 9.90 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.1, 19.9, 20.5 (CH_3), 62.3 (OCH_2), 115.8, 117.4 (C), 127.7 (2C, CH), 129.1 (2C, CH), 131.6, 134.5, 139.2, 146.5, 158.1 (C), 169.5 (C=O); IR (neat): $\tilde{\nu}$=3065 (w), 2990 (w), 2956 (w), 2922 (m), 1727 (m), 1644 (s), 1564 (w), 1528 (w), 1473 (s), 1423 (m), 1372 (s), 1298 (w), 1276 (s), 1214 (s), 1090 (s), 1009 (s), 865 (w), 814 (s), 735 (m), 684 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 374 ($[M]^+$, $[2\times^{37}Cl]$, 6), 372 ($[M]^+$, $[^{37}Cl]$, $[^{35}Cl]$, 28), 370 ($[M]^+$, $[2\times^{35}Cl]$, 41), 324 (100), 309 (15), 289 (14), 261 (8), 198 (8), 144 (10); HRMS (EI): calcd for $C_{17}H_{16}O_3Cl_2S$ ($[M]^+$, $[2\times^{35}Cl]$): 370.01917, found 370.073380.

3.4.15. Ethyl 4,6-dimethyl-5-(2-bromoethyl)-3-(thiophenoxy)salicylate (14)

Starting with 1,1-diacetylcyclopropane (**13**) (500 mg, 3.9 mmol), 1,3-bis(silyl enol ether) **9a** (2.200 g, 5.5 mmol), $TiBr_4$ (1.400 g, 3.9 mmol) and CH_2Cl_2 (110 mL), **14** was isolated as a yellowish highly viscous compound (715 mg, 45%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.32 (t, 3H, J=7.1 Hz, CH_3), 2.34 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.15 (m, 2H, CH_2), 3.30 (m, 2H, CH_2), 4.36 (q, 2H, J=7.1 Hz, CH_2), 6.92 (m, 2H, ArH), 7.05 (m, 1H, ArH), 7.15 (m, 2H, ArH), 8.67 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.2, 17.8, 18.5 (CH_3), 29.4, 34.2, 61.7 (CH_2), 116.3, 117.7 (C), 125.7 (CH), 126.2 (2C CH), 129.1 (2C CH), 129.2 (C), 133.6, 138.5, 145.8, 156.4, 169.2 (C); IR (neat): $\tilde{\nu}$=3386 (s), 2979 (s), 2934 (m), 1728 (s), 1655 (s), 1582 (s), 1478 (s), 1373 (s), 1228 (s), 1048 (m), 739 (m), 690 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 410 (M^+, ^{81}Br, 59), 408 (M^+, ^{79}Br, 57), 364 (100), 329 (18), 283 (85), 269 (24), 77 (12); HRMS (EI): calcd for $C_{19}H_{21}O_3BrS$ ($[M+1]^{++}$): 408.03893, found 408.03884.

3.5. General procedure for the synthesis of benzophenones *16a–e*

Me_3SiOTf (0.3 equiv) was added to 3-formylchromone (1.0 equiv) at 20 °C. After stirring for 10 min, CH_2Cl_2 (8 mL) was added, the solution was cooled to 0 °C and 1,3-bis(silyl enol ether) (1.3 equiv) was added. The mixture was stirred at 20 °C for 12 h and was subsequently poured into an aqueous solution of HCl (10%). The organic and the aqueous layers were separated and the latter was extracted three times with 15 mL of CH_2Cl_2. The combined organic layers were washed with 25 mL of brine and dried over Na_2SO_4. The solution was filtered and the solvent of the filtrate was removed under reduced pressure. The residue was purified by chromatography (silica gel, EtOAc/*n*-heptane).

3.5.1. Ethyl 5-(2-hydroxy-3-chlorobenzoyl)-3-(thiophenoxy)salicylate (*16a*)

Starting with 3-formylchromone **15a** (400 mg, 1.91 mmol), 1,3-bis(silyl enol ether) **9a** (806 mg, 2.1 mmol) and Me_3SiOTf (0.1 mL, 0.57 mmol), **16a** was isolated as a colourless solid (385 mg, 47%), mp=104 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.33 (t, 3H, J=7.1 Hz, CH_3), 4.38 (q, 2H, J=7.2 Hz, CH_2), 6.86 (dd, 1H, J=0.8, 8.3 Hz, ArH), 7.16–7.34 (m, 6H, ArH), 7.41 (dd, 2H, J=1.7, 8.2 Hz, ArH), 8.02 (d, 1H, J=2.2 Hz, ArH), 11.53 (s, 1H, OH), 11.89 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=12.9 (CH_3), 61.3 (CH_2), 111.2, 118.3 (C), 118.9 (CH), 122.2, 126.5, 127.2, 127.6 (C), 128.6 (CH), 128.7 (2C, CH), 130.0, 130.5 (CH), 132.4 (2C, CH), 133.8, 134.9 (CH), 160.2, 160.5, 168.4, 196.4 (C); IR (KBr): $\tilde{\nu}$=3073 (w), 2958 (w), 2854 (w), 1661 (s), 1576 (s), 1473 (s), 1314 (s), 1290 (s), 1195 (m), 1022 (m), 864 (m), 787 (s), 690 (s), 418 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 430 (M^+, ^{37}Cl, 40), 428 (M^+, ^{35}Cl, 95), 382 (100), 302 (5), 228 (18) 200 (10), 171 (17), 155 (21), 99 (5); HRMS (EI): calcd for $C_{22}H_{17}ClO_5S$ [M^{++}, ^{35}Cl]: 428.04744, found 428.04797.

3.5.2. Ethyl 5-(2-hydroxy-3-ethylbenzoyl)-3-(4-methoxythiophenoxy)salicylate (*16b*)

Starting with 6-ethyl-3-formylchromone **15b** (500 mg, 2.47 mmol), 1,3-bis(silyl enol ether) **9b** (10.17 g, 2.47 mmol) and Me_3SiOTf (0.15 mL, 0.86 mmol), **16b** was isolated as a colourless solid (422 mg, 38%), mp=124 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.06 (t, 3H, J=7.5 Hz, CH_3), 1.29 (t, 3H, J=7.0 Hz, CH_3), 2.40 (q, 2H, J=7.7 Hz, CH_2), 3.60 (s, 3H, O*CH*$_3$), 4.34 (q, 2H, J=7.2 Hz, CH_2), 6.82 (m, 3H, ArH), 7.13–7.25 (m, 3H, ArH), 7.38 (d, 2H, J=8.8 Hz, ArH), 7.96 (d, 1H, J=2.0 Hz, ArH), 11.50 (s, 1H, OH), 11.80 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=14.1, 15.8 (CH_3), 27.9 (CH_2), 55.3 (CH_3), 62.1 (CH_2), 111.6 (C), 115.4 (2C, CH), 118.2 (CH), 118.5, 120.7 (C), 129.1 (CH), 129.1, 129.3 (C), 131.4, 133.5 (CH), 134.2 (C), 136.1 (CH), 136.5 (2C, CH), 160.5, 160.6, 161.0, 169.8, 198.6 (C); IR (ATR): $\tilde{\nu}$=2994 (w), 2912 (w), 2839 (w), 1677 (s), 1588 (s), 1349 (s), 1241 (s), 1217 (s), 1166 (s), 1019 (m), 833 (m), 810 (m), 670 (m), 567 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 452 (M^+, 100), 406 (97), 258 (31), 230 (6), 177 (10), 149 (49), 111 (24), 83 (36), 57 (62); elemental analysis: calcd (%) for $C_{25}H_{24}O_6S$ (452.52): C 66.35, H 5.35; found: C 66.58, H 5.37.

3.5.3. Ethyl 5-(2-hydroxy-3-bromobenzoyl)-3-(4-methylthiophenoxy)salicylate (*16c*)

Starting with 6-bromo-3-formylchromone **15c** (380 mg, 1.5 mmol), 1,3-bis(silyl enol ether) **9c** (594 mg, 1.5 mmol) and Me_3SiOTf (0.08 mL, 0.45 mmol), **16c** was isolated as a colourless solid (329 mg, 45%), mp=125 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.33 (t, 3H, J=7.0 Hz, CH_3), 2.24 (s, 3H, CH_3), 4.36 (q, 2H, J=7.1 Hz, CH_2), 6.81 (d, 1H, J=9.4 Hz, ArH), 7.12 (d, 2H, J=7.9 Hz, ArH), 7.18 (d, 1H, J=2.0 Hz, ArH), 7.32 (d, 2H, J=10.1 Hz, ArH), 7.41–7.45 (m, 2H, J=10.1 Hz, ArH), 7.98 (d, 1H, J=2.2 Hz, ArH), 11.47 (s, 1H, OH), 11.86 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=11.9, 19.1 (CH_3), 60.2 (CH_2), 108.0, 110.0, 117.9 (C), 118.3 (CH), 124.7, 126.1, 126.7 (C), 127.0 (CH), 128.6 (2C, CH), 131.6 (CH), 132.2 (2C, CH), 132.5, 136.5 (CH), 137.1, 159.0, 159.6, 167.5, 195.4 (C); IR (ATR): $\tilde{\nu}$=3017 (w), 2982 (w), 2865 (w), 1627 (s), 1568 (s), 1467 (s), 1398 (s), 1285 (s), 1163 (s), 1018 (s), 996 (m), 836 (m), 736 (s), 613 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 488 (M^+, ^{81}Br, 100), 486 (M^+, ^{79}Br, 92), 442 (87), 440 (78), 242 (25), 199 (20), 125 (12), 111 (20), 57 (45); elemental analysis: calcd (%) for $C_{23}H_{19}BrO_5S$ (486.01): C 56.68, H 3.93; found: C 56.12, H 4.40.

3.5.4. Ethyl 5-(2-hydroxy-3-methylbenzoyl)-3-(4-chlorothiophenoxy)salicylate (*16d*)

Starting with 6-methyl-3-formylchromone **15d** (255 mg, 1.35 mmol), 1,3-bis(silyl enol ether) **9d** (566 mg, 1.35 mmol) and Me_3SiOTf (0.07 mL, 0.40 mmol), **16d** was isolated as a colourless solid (240 mg, 40%), mp=98 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.32 (t, 3H, J=7.1 Hz, CH_3), 2.13 (s, 3H, CH_3), 4.38 (q, 2H, J=7.1 Hz, CH_2), 6.85 (d, 1H, J=8.5 Hz, ArH), 7.10 (d, 1H, J=1.4 Hz, ArH), 7.16–7.29 (m, 5H, ArH), 7.51 (d, 1H, J=2.0 Hz, ArH), 8.09 (d, 1H, J=2.2 Hz, ArH), 11.47 (s, 1H, OH), 11.86 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.0, 21.4 (CH_3), 63.4 (CH_2), 113.5 (C), 119.2 (CH), 119.3, 126.3, 128.7, 130.2 (C), 130.6 (2C, CH), 131.7 (CH), 132.2 (C), 133.2 (CH), 134.5 (2C, CH), 135.2 (C), 138.2, 138.3 (CH), 161.9, 163.1, 170.6, 199.2 (C); IR (ATR): $\tilde{\nu}$=2994 (w), 2919 (w), 2855 (w), 1628 (s), 1581 (s), 1412 (s), 1377 (s), 1218 (s), 1190 (m), 1090 (m), 994 (m), 815 (m), 666 (m), 536 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 444 (M^+, ^{37}Cl, 31), 442 (M^+, ^{35}Cl, 86), 396 (100), 308 (10), 262 (40), 205 (10), 171 (10), 135 (42), 69 (50); HRMS (EI): calcd for $C_{23}H_{19}ClO_5S$ [M^{++}, ^{35}Cl]: 442.06469, found 442.06362.

3.5.5. Ethyl 5-(2-hydroxybenzoyl)-3-(4-chlorothiophenoxy)salicylate (*16e*)

Starting with 3-formylchromone **15e** (500 mg, 2.87 mmol), 1,3-bis(silyl enol ether) **9d** (12.01 g, 2.87 mmol) and Me_3SiOTf (0.15 mL, 0.86 mmol), **16e** was isolated as a highly

viscous oil (385 mg, 47%). ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.32 (t, 3H, J=7.2 Hz, CH_3), 4.38 (q, 2H, J=7.2 Hz, CH_2), 6.74 (m, 1H, ArH), 6.95 (dd, 1H, J=0.9, 8.3 Hz, ArH), 7.18–7.43 (m, 6H, ArH), 7.50 (d, 1H, J=1.8 Hz, ArH), 8.09 (d, 1H, J=2.0 Hz, ArH), 11.57 (s, 1H, OH), 11.85 (s, 1H, OH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=15.0 (CH_3), 63.4 (CH_2), 113.4 (C), 119.5, 119.6 (CH), 119.7, 126.4, 130.0 (C), 130.6 (2C, CH), 131.7 (CH), 132.2 (C), 133.5 (CH), 134.5 (2C, CH), 135.2 (C), 137.3, 138.3 (CH), 163.2, 163.9, 170.5, 199.2 (C); IR (ATR): $\tilde{\nu}$=2979 (w), 2906 (w), 2871 (w), 1670 (s), 1623 (s), 1575 (s), 1338 (s), 1236 (s), 1184 (s), 1091 (m), 987 (m), 816 (m), 792 (m), 561 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 430 (M^+, ^{37}Cl, 36), 428 (M^+, ^{35}Cl, 81), 382 (100), 262 (16), 205 (9), 205 (10), 171 (11), 121 (71), 65 (14); HRMS (EI): calcd for $C_{22}H_{17}ClO_5S$ [M^{++}, ^{35}Cl]: 428.04840, found 428.04797.

3.6. Synthesis of 7-hydroxy-6H-benzo[c]chromen-6-one **19**

Me_3SiOTf (1.3 equiv) was added to chromone (1.0 equiv) at 20 °C. After stirring for 1 h, CH_2Cl_2 (8 mL) was added. The solution was cooled to 0 °C and 1,3-bis(silyl enol ether) (1.3 equiv) was added. The mixture was stirred at 20 °C for 12 h and was subsequently poured into an aqueous solution of HCl (10%). The organic and the aqueous layers were separated, the latter was extracted three times with 15 mL of CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4. The solution was filtered and the solvent of the filtrate was removed under reduced pressure to give crude **18**. To an EtOH solution (10 mL) of crude **18** was added NEt_3 (2.0 equiv) and the mixture was stirred for 12 h at 20 °C. Hydrochloric acid (1 M) was added, the organic and the aqueous layers were separated and the latter was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4. The solution was filtered and the solvent of the filtrate was removed under reduced pressure. The residue was purified by chromatography (silica gel, EtOAc/*n*-heptane) to give **19**.

3.6.1. 8-Thiophenoxy-7-hydroxy-6H-benzo[c]chromen-6-one (**19**)

Starting with chromone **17** (310 mg, 2.1 mmol), 1,3-bis(silyl enol ether) **9a** (1.05 g, 2.7 mmol), Me_3SiOTf (0.48 mL, 2.7 mmol) and NEt_3 (0.58 mL, 4.2 mmol), **19** was isolated as a colourless solid (461 mg, 68%), mp=178 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.20–7.28 (m, 5H, ArH), 7.35–7.42 (m, 5H, ArH), 7.86 (dd, 1H, J=1.9, 8.5 Hz, ArH), 11.8 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=105.9 (C), 112.5, 117.6 (CH), 118.1 (C), 123.1 (CH), 124.3 (C), 125.3, 127.9 (CH), 129.4 (2C, CH), 130.6 (CH), 132.2 (2C, CH), 132.9, 133.6 (C), 138.2 (CH), 150.4, 159.7, 165.4 (C); IR (KBr): $\tilde{\nu}$=3068 (w), 3046 (w), 1673 (w), 1606 (s), 1555 (m), 1422 (s), 1320 (m), 1271 (s), 1150 (s), 1025 (w), 830 (m), 759 (s), 691 (m), 456 (w) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 320 (M^+, 100), 302 (5), 288 (5), 258 (4), 215 (3), 143 (5), 77 (3); HRMS (EI): calcd for $C_{19}H_{12}O_3S$ [$M]^+$: 320.05025, found 320.05017.

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