Regioselective Synthesis of 4-(Arylsulfanyl)-2-hydroxyhomophthalates by [4 + 2] Cycloaddition of 3-(Arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes with Dimethyl Penta-2,3-dienedioate

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The [4 + 2] cycloaddition of 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes with dimethyl penta-2,3-dienedioate provides a convenient and regioselective approach to a variety of 4-(arylsulfanyl)-2-hydroxyhomophthalates.

1. Introduction. – Allenes are useful building blocks in inter- and intramolecular [4 + 2] cycloadditions [1]. Examples include the synthesis of functionalized phenols by the [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 [2]. 3-Methyl-4-(phenylsulfonyl)phenol was prepared by the reaction of allenylphenylsulfone with *Danishefsky*'s diene [3]. 4-Hydroxy- and 2,4-dihydroxyhomophthalates are available by [4 + 2] cycloaddition of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes with dimethyl penta-2,3-dienedioate [4][5]. This methodology was successfully applied to the synthesis of an analogue of lactonamycin [6], of the N_7-C_{25} fragment of psymberin [7], and of the 4-acetylisocoumarins AGI-7 and sescandelin [8]. Herein, we report what are, to the best of our knowledge, the first [4 + 2] cycloadditions of 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes with dimethyl penta-2,3-dienedioate. These reactions provide a convenient and regioselective approach to a variety of 4-(arylsulfanyl)-2-hydroxyhomophthalates which can be regarded as highly functionalized diaryl sulfides.

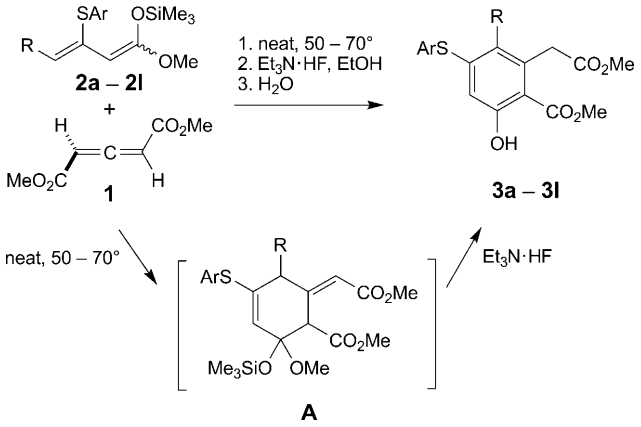
Diaryl sulfides are of considerable pharmacological relevance and occur in several natural products. Examples include the lissoclibadins, dibenzothiophenes, cyclic sulfides, varacins (lissoclinotoxins), and related natural products [9]. Diaryl sulfides are available by reaction of arenes with sulfur[1]) or sulfur dichloride [11], by condensation of organometallic reagents with chlorophenylsulfides [12] or by base-mediated reactions of thiophenols with chloroarenes [13]. However, the competing formation of polysulfides and, in several cases, the low regioselectivities are severe

[1]) For examples, see [10a] and [10b]. For the trifluoromethanesulfonic acid-catalyzed sulfurization of cycloalkanes, see [10c].

drawbacks of these classic synthetic approaches. In recent years, a number of transition metal-catalyzed [14] and metal-free [15] C,S coupling reactions have been developed which allow the formation of diaryl sulfides under mild conditions. However, 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 and tedious task. An alternative approach to diaryl sulfides is based on the use of sulfur-containing building blocks in cyclization reactions. *Hilt* and co-workers reported a convenient approach to diaryl sulfides by a Co^{I}-catalyzed [4 + 2] cycloaddition of alkynyl sulfides with buta-1,3-dienes [16]. Recently, we have studied [17] the synthesis of 3- and 5-(arylsulfanyl)salicylates by $TiCl_4$-mediated formal [3 + 3] cyclizations[2]) of 1,3-bis(silyloxy)-1,3-butadienes[3]) with 3-(silyloxy) 2-en-1-ones [20]. *Chan et al.* [21] and our group [22] reported the synthesis of diaryl sulfides based on cyclization reactions of 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes. Herein, we report, for the first time, the synthesis of 4-(arylsulfanyl)-2-hydroxyhomophthalates by the [4 + 2] cycloaddition of 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes with dimethyl penta-2,3-dienedioate.

2. Results and Discussion. – The known 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes **2a** – **2l** were prepared from methyl acetoacetate or methyl 3-oxopentanoate and from the corresponding thiophenols in two steps [22][23]. Dimethyl penta-2,3-dienedioate (**1**) was prepared by a known procedure [24]. The [4 + 2] cycloaddition of **1** with 3-(phenylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-diene **2a** afforded 4-(phenylsulfanyl)-2-hydroxyhomophthalate (**3a**) in 85% yield (*Scheme*).

Scheme. *Synthesis and Possible Mechanism of the Formation of the 4-(Arylsulfanyl)-2-hydroxyhomophthalates* **3a** – **3l**



The best yield was obtained when a stoichiometric ratio of **2a**/**1** 1:1 was used and when the reaction was carried out without solvent (neat). The yield decreased when the reaction was carried out in a toluene solution (at room temperature or at elevated

[2]) For a review of [3 + 3] cyclizations, see [18].

[3]) For a review of 1,3-bis(silyloxy)buta-1,3-dienes, see [19].

temperature). The starting materials were added at 0° and the mixture was subsequently stirred at 50–70° for 12 h. The conversion was not complete when the reaction was carried out at 20° or when the reaction time was decreased. In contrast, a further increase of the temperature (higher than 70°) resulted in decomposition. After stirring for 12 h, an EtOH solution of triethylammonium fluoride (for complete cleavage of the O–Si bond) [25] was added to the solution and, susequently, an aqueous workup was carried out. The reaction presumably proceeds by cycloaddition to give intermediate **A**. Subsequently, cleavage of the silyl ether and elimination of MeOH from the intermediary hemiacetal afforded product **3a** (*Scheme*). It is worth noting that the selective elimination of MeOH (formation of a 2-hydroxyhomophthalate) rather than H_2O (formation of a 2-methoxyhomophthalate) was observed.

The cycloaddition of **1** with 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes **2a**–**2l** afforded the novel 4-(arylsulfanyl)-2-hydroxyhomophthalates **3a**–**3l** in 50–85% yield (*Scheme* and *Table*). 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 Me group located at C-atom C(4) of the diene, due to steric hindrance. The employment of allenes other than **1** proved to be unsuccessful in our hands.

Table. *Synthesis of the 4-(Arylsulfanyl)-2-hydroxyhomophthalates* **3a**–**3l**

Compounds **2** and **3**	R	Ar	Yield of **3** [%][a])
a	H	Ph	85
b	H	4-F–C_6H_4	55
c	H	3-Me–C_6H_4	83
d	H	3-Cl–C_6H_4	60
e	H	4-Me–C_6H_4	83
f	H	Naphthalen-2-yl	80
g	Me	Ph	59
h	Me	4-F–C_6H_4	50
i	H	4-Cl–C_6H_4	65
j	H	4-Et–C_6H_4	80
k	Me	4-Et–C_6H_4	72
l	Me	4-Cl–C_6H_4	55

[a]) Yields of isolated products.

3. Conclusions. – We have reported a convenient and regioselective synthesis of 4-(arylsulfanyl)-2-hydroxyhomophthalates by [4 + 2] cycloadditions of 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes with dimethyl penta-2,3-dienedioate. Due to their polyfunctionalized nature, 4-(arylsulfanyl)-2-hydroxyhomophthalates represent versatile synthetic building blocks.

Experimental Part

General. Column chromatography: silica gel (SiO_2; *Merck*). IR Spectra: *Nicolet 380* FT-IR spectrometer; in cm^{-1}. NMR Spectra: *Bruker AVANCE 300 III* and *Bruker AVANCE 250 II* spectrometer; Me_4Si as internal standard; δ in ppm, J in Hz. EI-MS and HR-EI-MS: *MAT 95-XP* instrument; in m/z.

General Experimental Procedure for the Synthesis of **3a**–**3l**. To neat **2a**–**2l** (1.5 mmol) was added **1** (1.5 mmol) at 0° and the mixture was stirred for 30 min. Subsequently, the mixture was stirred at 50–70° for 12 h. The soln. was allowed to cool to 20°, and an EtOH soln. (2 ml, 96%) of $Et_3N \cdot HF$ (1.5 mmol) was added. The mixture was stirred for 10 min, and subsequently H_2O and CH_2Cl_2 were added. The org. and the aq. layer were separated, and the latter was extracted with CH_2Cl_2 (3×20 ml). The combined org. layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated *in vacuo*, and the residue was purified by chromatography (SiO_2; AcOEt/heptanes 1:9).

The known 3-(arylsulfanyl)-1-(trimethylsilyloxy)buta-1,3-dienes **2a**–**2l** were prepared from methyl acetoacetate or methyl 3-oxopentanoate and from the corresponding thiophenols in two steps [22][23]. Dimethyl penta-2,3-dienedioate (**1**) was prepared by a known procedure [24].

Methyl 2-Hydroxy-6-(2-methoxy-2-oxoethyl)-4-(phenylsulfanyl)benzoate (**3a**). Starting with **2a** (420 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3a** was isolated as a highly viscous colorless oil (423 mg, 85%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 3.60 (*s*, MeO); 3.71 (*s*, CH_2); 3.78 (*s*, MeO); 6.43 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.32–7.44 (*m*, 5 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 38.3 (CH_2); 51.9 (MeO); 52.0 (MeO); 109.0 (arom. C); 114.5, 122.0, 129.0 (arom. CH each); 129.9 (2 arom. CH); 130.1 (arom. C); 134.8 (2 arom. CH); 136.6, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 333 (20), 332 (100, M^+), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 332.0711 (M^+, $C_{17}H_{16}O_5S^+$; calc. 332.0712).

Methyl 4-[(4-Fluorophenyl)sulfanyl]-2-hydroxy-6-(2-methoxy-2-oxoethyl)benzoate (**3b**). Starting with **2b** (447 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3b** was isolated as a highly viscous colorless oil (288 mg, 55%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 3.47 (*s*, MeO); 3.63 (*s*, MeO); 3.69 (*s*, CH_2); 6.41(*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.11–7.34 (*m*, 4 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 38.3 (CH_2); 52.9 (MeO); 53.2 (MeO); 109.0 (arom. C); 114.5, 129.0 (arom. CH each); 129.9 (2 arom. CH); 130.1 (arom. C); 134.8 (2 arom. CH); 136.6, 137.5, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 351 (18), 350 (100, M^+), 319 (13), 318 (19), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 350.0616 (M^+, $C_{17}H_{15}FO_5S^+$; calc. 350.0619).

Methyl 2-Hydroxy-6-(2-methoxy-2-oxoethyl)-4-[(3-methylphenyl)sulfanyl]benzoate (**3c**). Starting with **2c** (441 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3c** was isolated as a highly viscous colorless oil (430 mg, 83%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.31 (*s*, Me); 3.60 (*s*, MeO); 3.72 (*s*, CH_2); 3.78 (*s*, MeO); 6.43 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.32–7.44 (*m*, 4 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 21.3 (Me); 42.5 (CH_2); 51.9 (MeO); 52.2 (MeO); 109.0 (arom. C); 113.9, 121.5 (arom. CH each); 130.1 (arom. C); 130.6 (2 arom. CH); 131.1 (2 arom. CH); 135.4, 136.6, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 347 (20), 346 (100, M^+), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 346.0879 (M^+, $C_{18}H_{18}O_5S^+$; calc. 346.0870).

Methyl 4-[(3-Chlorophenyl)sulfanyl]-2-hydroxy-6-(2-methoxy-2-oxoethyl)benzoate (**3d**). Starting with **2d** (471 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3d** was isolated as a highly viscous colorless oil (329 mg, 60%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 3.46 (*s*, MeO); 3.58 (*s*, MeO); 3.68 (*s*, CH_2); 6.42 (*s*, 1 arom. H); 6.48 (*s*, 1 arom. H); 7.11–7.34 (*m*, 4 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 38.3 (CH_2); 52.9 (MeO); 53.2 (MeO); 109.0 (arom. C); 114.5, 129.0 (arom. CH each); 129.9 (2 arom. CH); 130.1 (arom. C); 134.8 (2 arom. CH); 136.6, 137.5, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 368 (37), 367 (18), 366 (100, M^+), 335 (5), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 366.0322 (M^+, $C_{17}H_{15}ClO_5S^+$; calc. 366.0323).

Methyl 2-Hydroxy-6-(2-methoxy-2-oxoethyl)-4-[(4-methylphenyl)sulfanyl]benzoate (**3e**). Starting with **2e** (441 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3e** was isolated as a highly viscous colorless oil (430 mg, 83%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.32 (*s*, Me); 3.60 (*s*, MeO); 3.72 (*s*, CH_2); 3.78 (*s*, MeO); 6.43 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.32–7.44 (*m*, 4 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 21.3 (Me); 42.5 (CH_2); 51.9 (MeO); 52.2 (MeO); 109.0 (arom. C); 113.9, 121.5 (arom. CH each); 130.1 (arom. C); 130.6 (2 arom. CH); 131.1 (2 arom. CH); 135.4, 136.6, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 347 (20), 346 (100, M^+), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 346.0879 (M^+, $C_{18}H_{18}O_5S^+$; calc. 346.0870).

Methyl 2-Hydroxy-6-(2-methoxy-2-oxoethyl)-4-[(naphthalen-2-yl)sulfanyl]benzoate (**3f**). Starting with **2f** (495 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3f** was isolated as a highly viscous colorless oil (458 mg, 80%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 3.60 (*s*, MeO); 3.72 (*s*, CH_2); 3.79 (*s*, MeO); 6.43 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.32–7.45 (*m*, 7 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 41.1 (CH_2); 51.9 (MeO); 52.0 (MeO); 109.0 (arom. C); 114.8, 122.2, 129.0 (arom. CH each); 129.9, 130.0 (2 arom. CH each); 130.1 (arom. C); 134.4 (2 arom. CH); 136.6, 138.4, 139.2, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 383 (11), 382 (51, M^+), 322 (9), 317 (16), 316 (31), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 382.0870 (M^+, $C_{21}H_{18}O_5S^+$; calc. 382.0870).

Methyl 6-Hydroxy-2-(2-methoxy-2-oxoethyl)-3-methyl-4-(phenylsulfanyl)benzoate (**3g**). Starting with **2g** (441 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3g** was isolated as a highly viscous colorless oil (306 mg, 59%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.32 (*s*, Me); 3.53 (*s*, MeO); 3.67 (*s*, MeO); 3.77 (*s*, CH_2); 6.49 (*s*, 1 arom. H); 7.32–7.63 (*m*, 5 arom. H); 10.77 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 15.8 (Me); 38.2 (CH_2); 51.0 (MeO); 52.2 (MeO); 109.2 (arom. C); 112.9 (arom. CH); 125.4 (arom. C); 129.9, 135.3 (2 arom. CH each); 135.4 (arom. CH); 140.5, 145.6, 146.3, 155.8 (arom. C each); 165.5, 169.0 (2 CO). EI-MS (70 eV): 347 (20), 346 (100, M^+), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 346.0879 (M^+, $C_{18}H_{18}O_5S^+$; calc. 346.0870).

Methyl 4-[(4-Fluorophenyl)sulfanyl]-6-hydroxy-2-(2-methoxy-2-oxoethyl)-3-methylbenzoate (**3h**). Starting with **2h** (468 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3h** was isolated as a highly viscous colorless oil (273 mg, 50%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.32 (*s*, Me); 3.53 (*s*, MeO); 3.71 (*s*, MeO); 3.82 (*s*, CH_2); 6.49 (*s*, 1 arom. H); 7.22–7.48 (*m*, 4 arom. H); 10.77 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 15.9 (Me); 37.5 (CH_2); 51.0 (MeO); 52.2 (MeO); 110.2 (arom. C); 111.5 (arom. CH); 125.4 (arom. C); 129.9, 135.3 (2 arom. CH each); 140.5, 150.8, 151.5, 155.8, 159.0 (arom. C each); 165.5, 169.0 (2 CO). EI-MS (70 eV): 365 (18), 364 (100, M^+), 333 (23), 332 (64), 305 (34), 304 (89), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 364.0770 (M^+, $C_{18}H_{17}FO_5S^+$; calc. 364.0775).

Methyl 4-[(4-Chlorophenyl)sulfanyl]-2-hydroxy-6-(2-methoxy-2-oxoethyl)benzoate (**3i**). Starting with **2i** (471 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3i** was isolated as a highly viscous colorless oil (357 mg, 65%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 3.47 (*s*, MeO); 3.59 (*s*, MeO); 3.69 (*s*, CH_2); 6.43 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.11–7.34 (*m*, 4 arom. H); 11.26 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 38.3 (CH_2); 52.9 (MeO); 53.2 (MeO); 109.0 (arom. C); 114.5, 129.0 (arom. CH each); 129.9 (2 arom. CH); 130.1 (arom. C); 134.8 (2 arom. CH); 136.6, 137.5, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 368 (37), 367 (18), 366 (100, M^+), 334 (21), 273 (23), 272 (56), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 366.0322 (M^+, $C_{17}H_{15}ClO_5S^+$; calc. 366.0323).

Methyl 4-[(4-Ethylphenyl)sulfanyl]-2-hydroxy-6-(2-methoxy-2-oxoethyl)benzoate (**3j**). Starting with **2j** (462 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3j** was isolated as a highly viscous colorless oil (432 mg, 80%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.19 (*t*, $J = 7.2$, *Me*CH_2); 2.61 (*q*, $J = 7.2$, Me*CH*$_2$); 3.59 (*s*, MeO); 3.71 (*s*, CH_2); 3.77 (*s*, MeO); 6.41 (*s*, 1 arom. H); 6.49 (*s*, 1 arom. H); 7.11–7.38 (*m*, 4 arom. H); 11.28 (*s*, OH). ^{13}C-NMR

(63 MHz, $CDCl_3$): 14.2 (Me); 27.4 (CH_2); 36.5 (CH_2); 50.9 (MeO); 51.2 (MeO); 109.0 (arom. C); 113.0 (arom. CH); 127.9 (2 arom. CH); 130.1 (arom. CH); 134.8 (2 arom. CH); 136.6, 137.5, 138.5, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 361 (22), 360 (100, M^+), 301 (16), 273 (23), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 360.1026 (M^+, $C_{19}H_{20}O_5S^+$; calc. 360.1026).

Methyl 4-[(4-Ethylphenyl)sulfanyl]-6-hydroxy-2-(2-methoxy-2-oxoethyl)-3-methylbenzoate (**3k**). Starting with **2k** (483 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3k** was isolated as a highly viscous colorless oil (404 mg, 72%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.19 (*t*, $J = 7.1$, *Me*CH_2); 2.23 (*s*, Me); 2.61 (*q*, $J = 7.1$, Me*CH*$_2$); 3.64 (*s*, MeO); 3.79 (*s*, MeO); 3.89 (*s*, CH_2); 6.49 (*s*, 1 arom. H); 7.11–7.44 (*m*, 4 arom. H); 11.28 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 14.2 (Me); 15.0 (Me); 27.4 (CH_2); 36.5 (CH_2); 50.9 (MeO); 51.2 (MeO); 109.0 (arom. C); 113.0 (arom. CH); 127.9 (2 arom. CH); 130.1 (arom. C); 134.8 (2 arom. CH); 136.6, 137.5, 138.5, 147.3, 163.3 (arom. C each); 170.8, 171.6 (2 CO). EI-MS (70 eV): 376 (22), 374 (100, M^+), 334 (21), 273 (23), 258 (13), 257 (62), 240 (22), 213 (11), 184 (27), 51 (8). HR-EI-MS: 374.0322 (M^+, $C_{20}H_{22}O_5S^+$; calc. 374.0323).

Methyl 4-[(4-Chlorophenyl)sulfanyl]-6-hydroxy-2-(2-methoxy-2-oxoethyl)-3-methylbenzoate (**3l**). Starting with **2l** (492 mg, 1.5 mmol) and **1** (234 mg, 1.5 mmol), **3l** was isolated as a highly viscous colorless oil (313 mg, 55%). IR (neat): 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*. ^{1}H-NMR (250 MHz, $CDCl_3$): 2.34 (*s*, Me); 3.53 (*s*, MeO); 3.69 (*s*, MeO); 3.79 (*s*, CH_2); 6.49 (*s*, 1 arom. H); 7.22–7.48 (*m*, 4 arom. H); 10.77 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 16.2 (Me); 38.2 (CH_2); 51.0 (MeO); 52.2 (MeO); 109.2 (arom. C); 112.9 (arom. CH); 125.4 (arom. C); 129.9, 135.3 (2 arom. CH each); 140.5, 145.6, 151.5, 155.8, 159.0 (arom. C each); 165.5, 169.0 (2 CO). EI-MS (70 eV): 381 (17), 380 (100, M^+), 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). HR-EI-MS: 380.0476 (M^+, $C_{18}H_{17}ClO_5S^+$; calc. 380.0480).

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