



Synthesis of functionalized triarylmethanes by combination of FeCl₃-catalyzed benzylations of acetylacetone with [3+3] cyclocondensations

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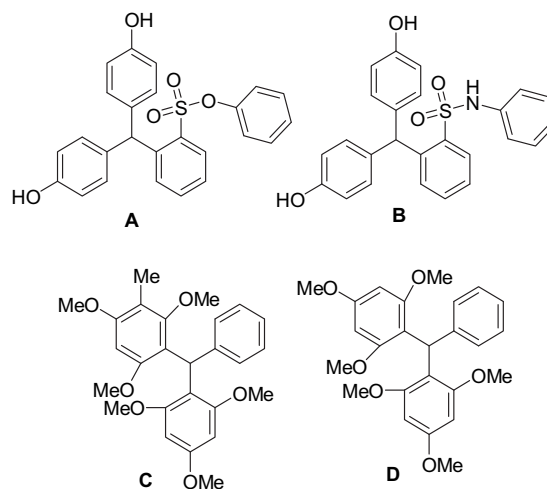
Functionalized triarylmethanes are prepared in two steps by FeCl₃-catalyzed benzylation of acetylacetone to give 3-(diarylmethyl)pentane-2,4-diones and subsequent formal [3+3] cyclization of the latter with 1,3-bis(trimethylsilyloxy)-1,3-dienes.

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1. Introduction

Triarylmethanes are of considerable pharmacological relevance, which includes, for example, oestrogen receptor binding affinity,^{1a} inhibition of hepatic cholesterol,^{1b} inhibition of aldose reductase 2,^{1c} antiproliferative activity,^{1d} antiviral and cytotoxic activity,^{1e} antifungal activity,^{1f} anti-HIV activity,^{1g,h} and CNS activity.¹ⁱ (1,1-Diphenylmethyl)salicylates and related structures have been reported to possess anti-HIV activity,^{3a,1g} and antibacterial activity.^{3b} Naturally occurring triarylmethanes, containing a (1,1-diphenylmethyl)phenol substructure, include molsenone, chamaechromone and a number of related molecules.² Products **A** and **B** were isolated as natural products formed by metabolism of commercial preparations of phenol red, a pH indicator dye often used in cell culture media (Scheme 1).^{1a} The isolation of some substituted triphenylmethanes, such as **C** and **D**, from the leaves of the cajuput tree *Melaleuca quinquenerua* (Myrtaceae) was also reported.²

The scope of classic syntheses of di- and triarylmethanes, based on Friedel–Crafts alkylations, is limited by the drastic reaction conditions and by the formation of regioisomeric mixtures or isomerization products. These problems can be overcome by novel



Scheme 1. Triarylmethane natural products.

FeCl₃·6H₂O-catalyzed Friedel–Crafts type benzylations of arenes using simple benzylic alcohols under mild conditions and with high region- and chemoselectivity.⁴ In this context, FeCl₃-catalyzed conjugate additions of 1,3-dicarbonyl compounds to enones⁵ and condensation of 1,3-dicarbonyl compounds to simple benzylic alcohols have been reported.^{6,7}

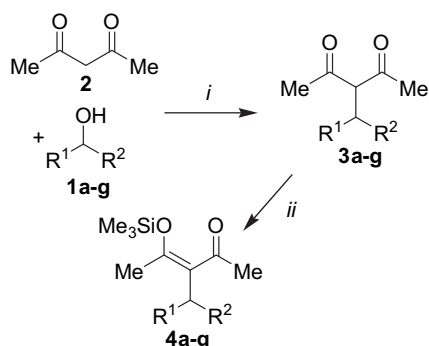
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All attempts to directly prepare sterically encumbered and functionalized triarylmethanes and diarylmethanes, such as 2,6-disubstituted or hydroxylated derivatives, by Fe-catalyzed reaction of arenes with benzylalcohols failed in our hands. In addition, the synthesis of the starting materials, highly substituted and functionalized arenes, proved to be not an easy task. Therefore, we have envisaged an alternative approach to triarylmethanes by development of a building block strategy. Some years ago, Chan et al. developed⁸ a convenient approach to salicylates by formal [3+3] cyclizations⁹ of 1,3-bis(trimethylsilyloxy)-1,3-dienes¹⁰ with 3-trimethylsilyloxy-2-en-1-ones. Recently, we have reported the synthesis of sterically encumbered and functionalized triarylmethanes by a combined FeCl₃-catalyzed benzylation/[3+3] cyclocondensation approach.¹¹ Herein, we report full details and a comprehensive study related to the scope. The products reported herein are not readily available by other methods and have, to the best of our knowledge, not yet been prepared.

2. Results and discussion

The FeCl₃·6H₂O-catalyzed benzylation of acetylacetone (**2**) with benzylalcohols **1a–g**, following conditions reported by Beller et al.,⁶ afforded products **3a–g** in very good yields (Scheme 2, Table 1).¹¹ The silylation of **3a–g** afforded the 3-silyloxy-2-en-1-ones **4a–g**.



Scheme 2. Synthesis of **4a–g**; i: FeCl₃·6H₂O, NO₂CH₃, 50 °C, 4 h; ii: Me₃SiCl, NEt₃, C₆H₆, 20 °C, 72 h.

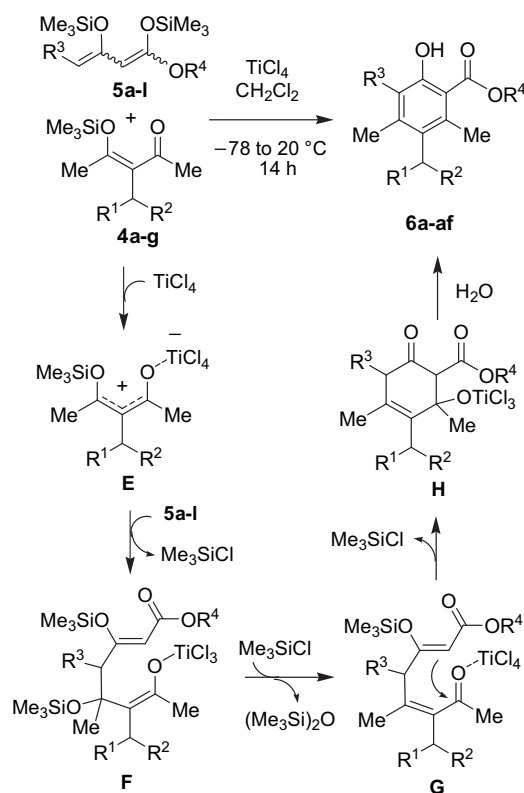
Table 1
Synthesis of **3a–g** and **4a–g**

3,4	R ¹	R ²	% (3) ^a	% (4) ^a
a	Ph	Ph	91	90
b	4-FC ₆ H ₄	4-FC ₆ H ₄	87	89
c	4-ClC ₆ H ₄	4-ClC ₆ H ₄	85	92
d	4-(MeO)C ₆ H ₄	4-(MeO)C ₆ H ₄	88	91
e	Me	Ph	94	81
f	Me	4-BrC ₆ H ₄	95	90
g	Me	4-(MeO)C ₆ H ₄	86	90

^a Isolated yields.

The TiCl₄-mediated formal [3+3] cyclocondensation of **4a–g** with 1,3-bis(silyloxy)-1,3-dienes **5a–l**, available from the corresponding 1,3-dicarbonyl compounds in two steps,⁸ afforded the triarylmethanes **6a–af** (Scheme 3, Table 2). During the optimization, it proved to be important to carry out the reactions in a highly concentrated solution.

The formation of **6a–af** can be explained by reaction of **4a–g** with TiCl₄ to give intermediates **E**. The attack of the terminal carbon atom of **5a–l** onto **E** afforded intermediates **F**. The elimination of hexamethyldisiloxane (intermediates **G**) and subsequent cyclization gave intermediates **H**. The elimination of titanium hydroxide (before or during the aqueous work-up) and aromatization resulted in the formation of products **6a–af**. Due to the symmetrical structure of **E**, the attack of **5a–l** on either terminal



Scheme 3. Possible mechanism of the formation of **6(a–af)**.

Table 2
Synthesis of di- and triarylmethanes **6a–af**

4	5	6	R ¹	R ²	R ³	R ⁴	% (6) ^a
a	a	a	Ph	Ph	H	Me	42
a	b	b	Ph	Ph	H	Et	45
a	c	c	Ph	Ph	H	PhCH ₂	65
a	d	d	Ph	Ph	Me	Me	31
a	e	e	Ph	Ph	Me	Et	40
a	f	f	Ph	Ph	Et	Me	42
a	g	g	Ph	Ph	Et	Et	43
a	h	h	Ph	Ph	<i>n</i> Bu	Me	46
a	i	i	Ph	Ph	<i>n</i> Oct	Me	50
a	j	j	Ph	Ph	<i>n</i> Dec	Me	57
b	a	k	4-FC ₆ H ₄	4-FC ₆ H ₄	H	Me	33
b	b	l	4-FC ₆ H ₄	4-FC ₆ H ₄	H	Et	37
b	c	m	4-FC ₆ H ₄	4-FC ₆ H ₄	H	PhCH ₂	68
b	e	n	4-FC ₆ H ₄	4-FC ₆ H ₄	Me	Et	39
b	f	o	4-FC ₆ H ₄	4-FC ₆ H ₄	Et	Me	41
b	h	p	4-FC ₆ H ₄	4-FC ₆ H ₄	<i>n</i> Bu	Me	53
b	k	q	4-FC ₆ H ₄	4-FC ₆ H ₄	<i>n</i> Non	Me	53
b	j	r	4-FC ₆ H ₄	4-FC ₆ H ₄	<i>n</i> Dec	Me	55
c	a	s	4-ClC ₆ H ₄	4-ClC ₆ H ₄	H	Me	50
c	b	t	4-ClC ₆ H ₄	4-ClC ₆ H ₄	H	Et	53
c	c	u	4-ClC ₆ H ₄	4-ClC ₆ H ₄	H	PhCH ₂	69
c	d	v	4-ClC ₆ H ₄	4-ClC ₆ H ₄	Me	Me	40
c	e	w	4-ClC ₆ H ₄	4-ClC ₆ H ₄	Me	Et	43
c	f	x	4-ClC ₆ H ₄	4-ClC ₆ H ₄	Et	Me	42
c	l	y	4-ClC ₆ H ₄	4-ClC ₆ H ₄	<i>n</i> Pent	Me	53
c	j	z	4-ClC ₆ H ₄	4-ClC ₆ H ₄	<i>n</i> Dec	Me	57
d	a	aa	4-(MeO)C ₆ H ₄	4-(MeO)C ₆ H ₄	H	Me	32
d	b	ab	4-(MeO)C ₆ H ₄	4-(MeO)C ₆ H ₄	H	Et	37
e	a	ac	Me	Ph	H	Me	55
f	c	ad	Me	4-BrC ₆ H ₄	H	PhCH ₂	72
g	b	ae	Me	4-(MeO)C ₆ H ₄	H	Et	46
g	g	af	Me	4-(MeO)C ₆ H ₄	Et	Me	47

^a Isolated yields.

allylic carbon atom would result in the formation of the same products (**6a–af**). The yields depended on the type of substrate employed. The best yields were obtained for those products

derived from diene **5c** (prepared from benzyl acetoacetate). The yields of triarylmethanes derived from C4-unsubstituted dienes **5a,b** were similar to those derived from substituted dienes **5d–f**. The yield of diarylmethanes **6ac–af** were similar to those of triarylmethanes **6a–ab** (comparing the same type of diene and aryl group R²). The aryl groups seem to have no major influence on the yield.

The structures of **6a–af** were established by spectroscopic methods. The structures of **6n**, **6s** and **6ad** were independently confirmed by X-ray crystal structure analyses (Figs. 1–3).¹² Triarylmethanes **6n** and **6s** adopt a propeller-type structure, due to steric interaction of the aryl with the methyl groups. Intramolecular hydrogen bonds O–H...O are observed in solution and in the solid state.

In conclusion, a variety of functionalized and sterically encumbered triarylmethanes were prepared by combination of FeCl₃-catalyzed benzylations of 1,3-diketones and formal [3+3] cyclocondensation reactions. The products are not readily available by other methods.

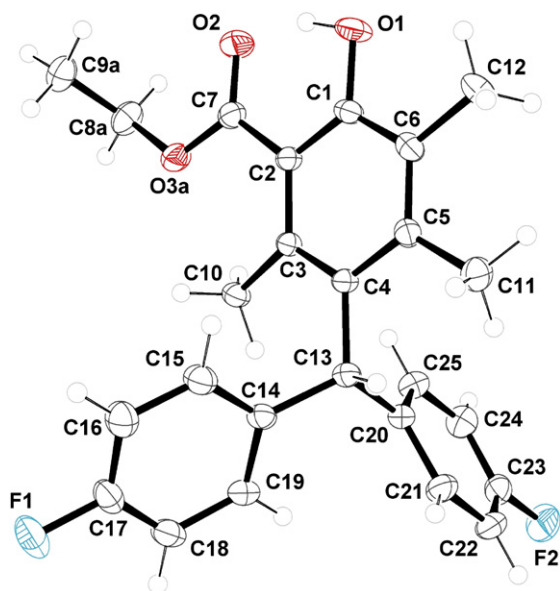


Figure 1. Ortep plot of **6n**.

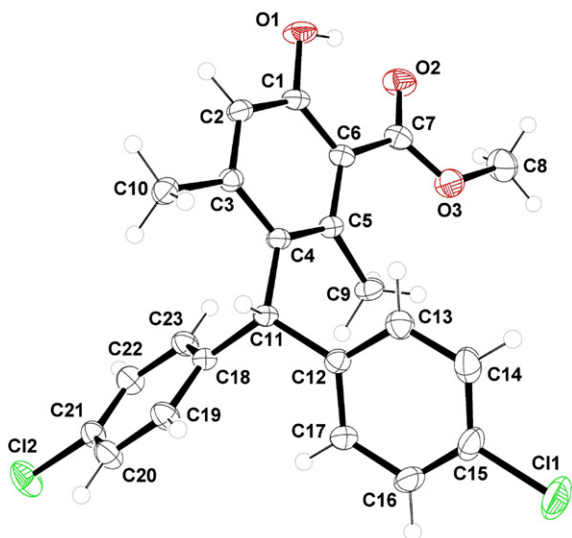


Figure 2. Ortep plot of **6s**.

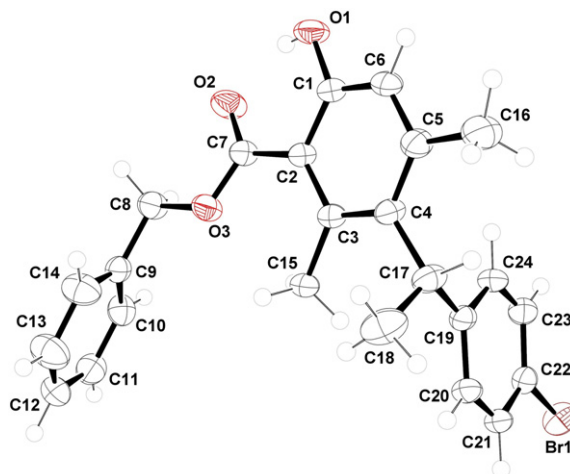


Figure 3. Ortep plot of **6ad**.

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 ¹³C NMR spectra the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, isobutane) or electrospray ionization (ESI). For preparative scale chromatography silica gel 60 (0.063–0.200 mm, 70–230 mesh) was used.

3.1.1. General procedure for the synthesis of 3-substituted pentane-2,4-diones (3a–g). In a pressure tube, FeCl₃·6H₂O (5 mol %), **1a–g** (5.0 mmol) and acetylacetone (20.0 mmol) were dissolved in 10 mL of nitromethane. After stirring for 4 h at 50 °C, the reaction was quenched with water followed by extraction with dichloromethane. The combined organic layers were dried over Na₂SO₄. Then, products **3a–g** were purified by column chromatography (heptanes/ethyl acetate=1:1).

3.1.2. 3-Benzhydrylpentane-2,4-dione (3a). Starting with FeCl₃·6H₂O (0.067 g, 5 mol %), **1a** (0.92 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (1.21 g, 91%). ¹H NMR (250 MHz, CDCl₃): δ=2.02 (s, 6H, CH₃), 4.75 (d, *J*=11.5 Hz, CH), 4.84 (d, *J*=11.6 Hz, CH), 7.17–7.29 (m, 10H, CH_{Ar}). ¹³C NMR (62 MHz, CDCl₃): δ=29.6 (CH₃), 51.2, 74.5 (CH), 127.0, 127.7, 128.9 (CH_{Ar}), 141.2 (C_{Ar}), 202.9 (CO). (IR (KBr), cm⁻¹): 3081 (w), 3019 (w), 2962 (w), 2925 (w), 2870 (w), 1651 (s), 1598 (m), 1563 (m), 1494 (m), 1444 (m), 1603 (s), 1507 (s), 1297 (m), 1246 (s), 1159 (m), 1095 (m), 1014 (w), 849 (s), 786 (s), 506 (w). MS (EI, 70 eV): *m/z* (%)=266 ([M]⁺, 64), 251 (45), 165 (43), 148 (34), 143 (100), 129 (6), 95 (48), 85 (15), 75 (26), 69 (54), 50 (45), 43 (26). HRMS (EI): Calcd for C₁₈H₁₈O₂ ([M]⁺): 266.13068; found: 266.130655.

3.1.3. 3-(Bis(4-fluorophenyl)methyl)pentane-2,4-dione (3b). Starting with FeCl₃·6H₂O (0.067 g, 5 mol %), **1b** (1.10 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3b** was isolated as a white crystalline solid (1.31, 87%), mp 102–104 °C. ¹H NMR (250 MHz, CDCl₃): δ=2.02 (s, 6H, CH₃), 4.65 (d, *J*=11.7 Hz, CH), 4.82 (d, *J*=11.6 Hz, CH), 6.95–7.01 (m, 4H, CH_{Ar}), 7.19–7.24 (m, 4H, CH_{Ar}). ¹³C NMR (62 MHz, CDCl₃): δ=29.6 (CH₃), 49.5, 74.8 (CH), 115.9 (d, *J*_{C,F}=21.6 Hz, CH_{Ar}), 129.2 (d, *J*_{C,F}=8.1 Hz, CH_{Ar}), 136.9 (d, *J*_{C,F}=3.1 Hz, C_{Ar}), 162.2 (d, *J*_{C,F}=245.8 Hz, C_{Ar}), 202.4 (CO). (IR (KBr), cm⁻¹): 2954 (w), 2922 (w), 2855 (w), 1650 (s), 1661 (m), 1573 (m), 1612 (s), 1527

(m), 1297, 1245 (m), 1212 (s), 1134 (m), 1023 (w), 1014 (m), 848 (s), 788 (s), 545 (w). MS (EI, 70 eV): m/z (%)=302 ($[M]^+$, 64), 287 (66), 259 (6), 183 (100), 109 (16), 95 (48), 85 (14), 75 (50), 69 (54), 50 (45), 43 (53). HRMS (EI): Calcd for $C_{18}H_{16}F_2O_2$ ($[M]^+$): 302.11184; found: 302.111765.

3.1.4. 3-(Bis(4-chlorophenyl)methyl)pentane-2,4-dione (3c). Starting with $FeCl_3 \cdot 6H_2O$ (0.067 g, 5 mol%), **1c** (1.26 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3c** was isolated as a white crystalline solid (1.41, 85%), mp 142–144 °C. 1H NMR (250 MHz, $CDCl_3$): δ =2.01 (s, 6H, CH_3), 4.63 (d, J =11.8 Hz, 1H, CH), 4.79 (d, J =11.7 Hz, 1H, CH), 7.14–7.18 (m, 4H, CH_{Ar}), 7.22–7.27 (m, 4H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ =29.6 (CH_3), 49.7, 74.9 (CH), 114.2, 128.6 (CH_{Ar}), 133.7, 158.3 (C_{Ar}), 203.2 (CO). (IR (KBr), cm^{-1}): 2928 (w), 2855 (w), 1735 (w), 1659 (s), 1609 (s), 1407 (m), 1324 (m), 1309 (m), 1297 (s), 1254 (m), 1243 (m), 1158 (m), 1088 (m), 1022 (w), 846 (s), 754 (s), 554 (w). MS (EI, 70 eV): m/z (%)=334 ($[M]^+$, 84), 319 (34), 291 (65), 165 (54), 135 (6), 123 (43), 109 (100), 96 (48), 87 (11), 75 (67), 69 (26), 50 (5), 43 (23). HRMS (EI): Calcd for $C_{18}H_{16}Cl_2O_2$ ($[M]^+$): 334.05274; found: 334.052365.

3.1.5. 3-(Bis(4-methoxyphenyl)methyl)pentane-2,4-dione (3d). Starting with $FeCl_3 \cdot 6H_2O$ (0.067 g, 5 mol%), **1d** (1.22 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3d** was isolated as a white crystalline solid (1.43 g, 88%), mp 125–127 °C. 1H NMR (250 MHz, $CDCl_3$): δ =1.92 (s, 6H, CH_3), 3.67 (s, 6H, OCH_3), 4.54 (d, J =11.8 Hz, 1H, CH), 4.63 (d, J =11.7 Hz, 1H, CH), 6.70–6.73 (m, 4H, CH_{Ar}), 7.06–7.09 (m, 4H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ =29.6 (CH_3), 49.7 (CH), 55.1 (OCH_3), 74.9 (CH), 114.2, 128.6 (CH_{Ar}), 133.7, 158.3 (C_{Ar}), 203.2 (CO). (IR (KBr), cm^{-1}): 2951 (w), 2928 (w), 2830 (w), 1608 (s), 1547 (m), 1287 (m), 1246 (s), 1159 (m), 1145 (m), 1095 (s), 1014 (w), 849 (s), 743 (m), 506 (w). MS (EI, 70 eV): m/z (%)=326 ($[M]^+$, 64), 283 (34), 265 (66), 238 (100), 183 (32), 108 (63), 95 (48), 85 (13), 75 (24), 69 (53), 50 (25), 43 (53). HRMS (EI): Calcd for $C_{20}H_{22}O_4$ ($[M]^+$): 326.15181; found: 326.151265.

3.1.6. 3-(1-Phenylethyl)pentane-2,4-dione (3e). Starting with $FeCl_3 \cdot 6H_2O$ (0.067 g, 5 mol%), **1e** (0.61 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3e** was isolated as a white crystalline solid (0.96, 94%), mp 112–114 °C. 1H NMR (250 MHz, $CDCl_3$): δ =1.19 (d, J =7.0 Hz, 3H, CH_3), 1.80 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 3.55–3.63 (m, 1H, CH), 4.02 (d, J =11.5 Hz, 1H, CH), 7.13 (–CH), 126.9, 127.2, 128.7 (CH_{Ar}), 143.0 (C_{Ar}), 203.3, 203.4 (CO). (IR (KBr), cm^{-1}): 2950 (w), 2927 (w), 2829 (w), 1608 (s), 1547 (m), 1605 (s), 1534, 1434, 1389 (m), 1283 (m), 1254 (w), 1146 (m), 1097 (s), 1033 (w), 845 (s), 785 (s), 576 (w). MS (EI, 70 eV): m/z (%)=204 ($[M]^+$, 44), 189 (34), 175 (36), 138 (46), 125 (100), 109 (65), 95 (48), 85 (11), 75 (20), 69 (50), 43 (23). HRMS (EI): Calcd for $C_{13}H_{16}O_2$ ($[M]^+$): 204.11503; found: 204.115651.

3.1.7. 3-(1-(4-Bromophenyl)ethyl)pentane-2,4-dione (3f). Starting with $FeCl_3 \cdot 6H_2O$ (0.067 g, 5 mol%), **1f** (1.00 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3f** was isolated as a white crystalline solid (1.35, 95%), mp 112–114 °C. 1H NMR (250 MHz, $CDCl_3$): δ =1.11 (d, J =7.0 Hz, 3H, CH_3), 1.79 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 3.44–3.56 (m, 1H, CH), 3.92 (d, J =11.7 Hz, 1H, CH), 6.98–7.01 (m, 2H, CH_{Ar}), 7.33–7.36 (m, 2H, CH_{Ar}). ^{13}C NMR (62 MHz, $CDCl_3$): δ =20.6, 29.5, 29.7 (CH_3), 39.6, 76.4 (CH), 120.7 (C_{Ar}), 129.0, 131.9 (CH_{Ar}), 142.1 (C_{Ar}), 202.9, 203.0 (CO).

3.1.8. 3-(1-(4-Methoxyphenyl)ethyl)pentane-2,4-dione (3g). Starting with $FeCl_3 \cdot 6H_2O$ (0.067 g, 5 mol%), **1g** (0.76 g, 5.0 mmol), acetylacetone (2.0 g, 20.0 mmol), **3g** was isolated as a white crystalline solid (1.01, 86%), mp 138–140 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.11 (d, J =6.9 Hz, 3H, CH_3), 1.76 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 3.41–3.53 (m, 1H, CH), 3.70 (s, 3H, OCH_3), 3.91 (d, J =11.7 Hz, 1H, CH), 6.73–6.77 (m, 2H, CH_{Ar}), 7.01–7.04 (m, 2H, CH_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ =20.9, 29.6, 29.8, 39.7 (CH_3), 55.2 (OCH_3), 76.6 (CH), 114.6, 128.2 (CH_{Ar}), 134.9, 158.4 (C_{Ar}), 203.5, 203.6 (CO). (IR (KBr), cm^{-1}): 2957 (w), 2935 (w), 2834 (w), 1712 (s), 1554, 1529, 1456, 1324 (m), 1277 (s), 1246 (s), 1157 (m), 1095 (s), 1056 (w), 847 (s), 773 (s), 645 (w). MS (EI, 70 eV): m/z (%)=234 ($[M]^+$, 64), 165 (66), 138 (6), 123 (100), 109 (6), 95 (48), 85 (11), 75 (20), 69 (50), 50 (5), 43 (23). HRMS (EI): Calcd for $C_{14}H_{18}O_2$ ($[M]^+$): 234.12559; found: 234.125855.

3.1.9. General procedure for the synthesis of silyl enol ethers (4a–g). To a stirred benzene solution (2.5 L/1.0 mol of **3a–g**), of (5.0 mmol) and triethylamine (7.5 mmol) was added. After stirring of the solution for 2 h, trimethylchlorosilane (9.0 mmol) was added. After stirring of the solution for 72 h, the solvent was removed in vacuo and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered under argon atmosphere. The filtrate was concentrated in vacuo to give silyl enol ethers **4a–g**. Due to their unstable nature, compounds **4** could only be characterized by 1H NMR spectroscopy.

3.1.10. 3-Benzhydryl-4-(trimethylsilyloxy)pent-3-en-2-one (4a). Starting with benzene (12.5 mL), **3a** (1.33 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4a** was isolated as a reddish oil (1.52 g, 90%). 1H NMR (250 MHz, $CDCl_3$): δ =0.19 (s, 9H, 3 CH_3), 1.91 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 5.48 (s, 1H, CH), 7.17–7.27 (m, 10H, CH_{Ar}).

3.1.11. 3-(Bis(4-fluorophenyl)methyl)-4-(trimethylsilyloxy)-pent-3-en-2-one (4b). Starting with benzene (12.5 mL), **3a** (1.51 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4a** was isolated as a reddish oil (1.66 g, 89%). 1H NMR (250 MHz, $CDCl_3$): δ =0.19 (s, 9H, CH_3), 2.02 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 5.55 (s, 1H, CH), 7.01–7.22 (m, 2H, CH_{Ar}), 7.19–7.31 (m, 4H, CH_{Ar}).

3.1.12. 3-(Bis(4-chlorophenyl)methyl)-4-(trimethylsilyloxy)-pent-3-en-2-one (4c). Starting with benzene (12.5 mL), **3a** (1.67 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4a** was isolated as a reddish oil (1.87 g, 92%). 1H NMR (250 MHz, $CDCl_3$): δ =0.18 (s, 9H, CH_3), 2.01 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 5.68 (s, 1H, CH), 7.85–7.89 (m, 2H, CH_{Ar}), 7.89–7.96 (m, 2H, CH_{Ar}).

3.1.13. 3-(Bis(4-methoxyphenyl)methyl)-4-(trimethylsilyloxy)-pent-3-en-2-one (4d). Starting with benzene (12.5 mL), **3d** (1.63 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4a** was isolated as a reddish oil (1.81 g, 91%). 1H NMR (250 MHz, $CDCl_3$): δ =0.16 (s, 9H, CH_3), 3.79 (s, 6H, OCH_3), 5.39 (s, 1H, CH), 6.96–7.06 (m, 4H, CH_{Ar}), 7.35–7.45 (m, 4H, CH_{Ar}).

3.1.14. 3-(1-Phenylethyl)-4-(trimethylsilyloxy)pent-3-en-2-one (4e). Starting with benzene (12.5 mL), **3e** (1.02 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4e** was isolated as a reddish oil (1.12 g, 81%). 1H NMR (250 MHz, $CDCl_3$): δ =0.15 (m, 9H, CH_3), 1.28 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.43 (d, J =8.6 Hz, 3H, CH_3), 4.12 (q, J =8.1 Hz, 1H, CH), 6.82–7.22 (m, 4H, CH_{Ar}).

3.1.15. 3-(1-(4-Bromophenyl)ethyl)-4-(trimethylsilyloxy)pent-3-en-2-one (4f). Starting with benzene (12.5 mL), **3f** (1.00 g, 5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4f** was isolated as a reddish oil (1.60 g, 90%). 1H NMR (250 MHz, $CDCl_3$): δ =0.17 (m, 9H, CH_3), 1.44 (d, J =8.7 Hz, 3H, CH_3), 1.62 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 4.11 (q, J =8.6 Hz, 1H, CH), 7.07–7.11 (m, 4H, CH_{Ar}).

3.1.16. 3-(1-(4-Methoxyphenyl)ethyl)-4-(trimethylsilyloxy)pent-3-en-2-one (4g). Starting with benzene (12.5 mL), **3g** (0.76 g,

5.0 mmol), triethylamine (0.76 g, 7.5 mmol) and trimethylchlorosilane (0.98 g, 9.0 mmol), **4g** was isolated as a reddish oil (1.53 g, 90%). ¹H NMR (250 MHz, CDCl₃): δ=0.16 (m, 9H, CH₃), 1.42 (d, *J*=8.6 Hz, 3H, CH₃), 1.64 (s, 3H, CH₃), 1.73 (s, 3H, CH₃), 3.89 (s, 3H, OCH₃), 4.12 (q, *J*=8.2 Hz, 1H, CH), 7.06–7.12 (m, 2H, CH_{Ar}), 7.16–7.20 (m, 2H, CH_{Ar}).

3.1.17. General procedure for the synthesis of 6(a–af). To a CH₂Cl₂ solution (2 L/1.0 mol of **4a–g**) of **4a–g** was added **5a–l** (1.1 mmol) and, subsequently, TiCl₄ (1.1 mmol) at –78 °C. The temperature of the solution was allowed to warm to 20 °C during 14 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH₂Cl₂ (3×20 mL). The combined organic layers were dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/EtOAc) to give **6(a–af)**.

3.1.18. Methyl 3-diphenylmethyl-6-hydroxy-2,4-dimethylbenzoate (6a). Starting with **4a** (0.510 g, 1.5 mmol) and **5a** (0.429 g, 1.65 mmol), **6a** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.22 g, 42%). ¹H NMR (300 MHz, CDCl₃): δ=1.98 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 3.79 (s, 3H, OCH₃), 5.92 (s, 1H, CH), 6.65 (s, 1H, CH_{Ar}), 6.99–7.21 (m, 10H, CH_{Ar}), 10.51 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=20.3, 21.7 (CH₃), 49.7 (CH), 52.0 (OCH₃), 111.7 (C_{Ar}), 117.8 (CH_{Ar}), 126.0, 128.2, 129.1 (CH_{Ar}), 132.2, 139.3, 141.0, 144.3 (C_{Ar}), 158.8 (C_{OH}), 170.9 (CO). IR (neat, cm⁻¹): 3084 (w), 3026 (w), 2959 (w), 2918 (w), 1663 (s), 1599 (m), 1564 (m), 1492 (m), 1435 (m), 1341 (m), 1265 (m), 1210 (m), 1143 (m), 1069 (m), 942 (m), 914 (w), 857 (m), 801 (m), 736 (m), 719 (s), 696 (s), 613 (m), 571 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=346 (M⁺, 66), 315 (34), 314 (100), 299 (21), 285 (14), 237 (18), 167 (14), 166 (24), 165 (49), 115 (10). HRMS (EI): calcd for C₂₃H₂₂O₃ [M]⁺: 346.15635; found: 346.156966.

3.1.19. Ethyl 3-diphenylmethyl-6-hydroxy-2,4-dimethylbenzoate (6b). Starting with **4a** (0.510 g, 1.5 mmol) and **5b** (0.452 g, 1.65 mmol), **6b** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.242 g, 45%). ¹H NMR (300 MHz, CDCl₃): δ=1.19 (t, *J*=7.1 Hz, 3H, OCH₂CH₃), 1.90 (s, 3H, CH₃), 2.03 (s, 3H, CH₃), 4.22 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 5.85 (s, 1H, CH), 6.57 (s, 1H, CH_{Ar}), 6.95–7.12 (m, 10H, CH_{Ar}), 10.52 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=13.1, 20.2, 21.7 (CH₃), 49.7 (CH), 60.5 (OCH₂CH₃), 111.8 (C_{Ar}), 116.8, 124.9, 127.1, 128.0 (CH_{Ar}), 132.1, 139.3, 141.1, 144.2 (C_{Ar}), 158.9 (C_{OH}), 170.5 (CO). IR (neat, cm⁻¹): 3082 (w), 3058 (w), 2961 (w), 2924 (w), 2871 (w), 1726 (w), 1654 (m), 1598 (m), 1568 (w), 1492 (m), 1449 (w), 1370 (m), 1258 (s), 1224 (m), 1141 (m), 1068 (s), 1013 (s), 860 (m), 799 (s), 736 (w), 696 (s), 622 (m), 578 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=360 (M⁺, 88), 315 (66), 314 (100), 299 (26), 285 (15), 271 (10), 237 (33), 209 (10), 167 (35), 166 (26), 165 (51). HRMS (EI): calcd for C₂₄H₂₄O₃ [M]⁺: 360.17200; found: 360.171717.

3.1.20. Benzyl 3-diphenylmethyl-6-hydroxy-2,4-dimethylbenzoate (6c). Starting with **4a** (0.510 g, 1.5 mmol) and **5c** (0.555 g, 1.65 mmol), **6c** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.410 g, 65%). ¹H NMR (300 MHz, CDCl₃): δ=1.95 (s, 3H, CH₃), 2.10 (s, 3H, CH₃), 5.27 (s, 2H, OCH₂), 6.65 (s, 1H, CH), 6.98–7.19 (m, 10H, CH_{Ar}), 7.24–7.29 (m, 5H, CH_{Ar}), 10.51 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=21.4, 22.8 (CH₃), 50.7 (CH), 67.3 (OCH₂), 112.6 (C_{Ar}), 117.9, 126.0, 128.2, 128.4, 128.5, 128.6, 129.0 (CH_{Ar}), 133.2, 135.1, 140.4, 142.0, 145.6 (C_{Ar}), 160.0 (C_{OH}), 171.3 (CO). IR (neat, cm⁻¹): 3082 (w), 3058 (w), 3023 (w), 2973 (w), 2928 (w), 1729 (w), 1654 (s), 1598 (m), 1566 (m), 1493 (m), 1450 (m), 1379 (m), 1320 (m), 1289 (m), 1260 (m), 1209 (s), 1141 (m), 1140 (s), 1064 (s), 1026 (m), 969 (w), 949 (w), 908 (w), 850 (m), 800 (m), 748 (m), 734 (m), 717 (m), 694 (s), 614 (m), 578 (m) cm⁻¹.

MS (EI, 70 eV): *m/z* (%)=422 (M⁺, 6), 314 (19), 288 (36), 287 (10), 273 (40), 211 (12), 195 (17), 178 (10), 167 (27), 166 (34), 165 (61), 152 (16), 115 (10), 92 (20), 91 (100), 89 (10), 79 (13), 78 (14), 77 (18), 65 (22), 63 (10), 55 (10), 51 (12), 44 (36), 43 (13), 41 (14). HRMS (EI): calcd for C₂₉H₂₆O₃ [M]⁺: 422.18765; found: 422.188014.

3.1.21. Methyl 3-diphenylmethyl-6-hydroxy-2,4,5-trimethylbenzoate (6d). Starting with **4a** (0.510 g, 1.5 mmol) and **5d** (0.452 g, 1.65 mmol), **6d** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.167 g, 31%). ¹H NMR (300 MHz, CDCl₃): 1.91 (s, 3H, CH₃), 2.10 (s, 6H, CH₃), 3.81 (s, 3H, OCH₃), 5.99 (s, 1H, CH), 7.00–7.21 (m, 10H, CH_{Ar}), 10.77 (s, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz): δ=18.0, 20.0, 28.6 (CH₃), 50.1 (CH), 50.9 (OCH₃), 111.0, 122.2 (C_{Ar}), 124.8, 127.0, 128.0 (CH_{Ar}), 132.0, 135.7, 141.4, 142.7 (C_{Ar}), 156.8 (C_{OH}), 171.6 (CO). IR (neat, cm⁻¹): 3082 (w), 3060 (w), 3024 (w), 2953 (w), 2923 (w), 2853 (w), 1648 (s), 1596 (m), 1563 (m), 1492 (m), 1433 (m), 1394 (m), 1343 (m), 1311 (m), 1231 (s), 1205 (s), 1169 (m), 1097 (m), 1049 (m), 1022 (m), 947 (w), 841 (m), 799 (m), 738 (m), 697 (s), 622 (m), 615 (m), 585 (m) 578 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=360 (M⁺, 34), 329 (24), 328 (100), 300 (14), 285 (20), 223 (12), 222 (11), 179 (10), 178 (10), 167 (16), 166 (12), 165 (36), 152 (10), 91 (10). HRMS (EI): calcd for C₂₄H₂₄O₃ [M]⁺: 360.17200; found: 360.171717.

3.1.22. Ethyl 3-diphenylmethyl-6-hydroxy-2,4,5-trimethylbenzoate (6e). Starting with **4a** (0.510 g, 1.5 mmol) and **5e** (0.476 g, 1.65 mmol), **6e** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.234 g, 40%). ¹H NMR (300 MHz, CDCl₃): 1.18 (t, *J*=7.1 Hz, 3H, OCH₂CH₃), 1.79 (s, 3H, CH₃), 2.00 (s, 3H, CH₃), 2.03 (s, 3H, CH₃), 4.20 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 5.90 (s, 1H, CH), 6.91–7.12 (m, 10H, CH_{Ar}), 10.73 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=13.4, 15.2, 20.2, 22.1 (CH₃), 52.2 (CH), 62.6 (OCH₂CH₃), 113.3, 124.4 (C_{Ar}), 127.0, 129.2, 130.2 (CH_{Ar}), 134.0, 137.9, 143.6, 144.7 (C_{Ar}), 159.0 (C_{OH}), 173.3 (CO). IR (neat, cm⁻¹): 3082 (w), 3060 (w), 3023 (w), 2981 (w), 2927 (w), 1727 (w), 1642 (s), 1596 (m), 1563 (m), 1492 (m), 1442 (m), 1379 (m), 1230 (s), 1195 (m), 1081 (m), 1025 (m), 802 (m), 721 (m), 695 (s), 665 (m), 580 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=374 (M⁺, 32), 329 (28), 328 (100), 327 (10), 300 (16), 285 (20), 223 (12), 222 (11), 179 (10), 178 (10), 167 (32), 166 (14), 165 (43), 152 (12), 91 (11). HRMS (EI): calcd for C₂₅H₂₆O₃ [M]⁺: 374.18765; found: 374.187695.

3.1.23. Methyl 3-diphenylmethyl-5-ethyl-6-hydroxy-2,4-dimethylbenzoate (6f). Starting with **4a** (0.510 g, 1.5 mmol) and **5f** (0.476 g, 1.65 mmol), **6f** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.235 g, 42%). ¹H NMR (300 MHz, CDCl₃): 1.04 (t, *J*=7.4 Hz, 3H, CH₂CH₃), 1.96 (s, 3H, CH₃), 2.09 (s, 3H, CH₃), 2.61 (q, *J*=7.3 Hz, 2H, CH₂CH₃), 5.97 (s, 1H, CH), 6.94–7.26 (m, 10H, CH_{Ar}), 10.81 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=12.3, 17.6, 20.1 (CH₃), 18.9 (CH₂CH₃), 50.2 (CH), 60.1 (OCH₃), 111.3 (C_{Ar}), 124.7, 127.2, 128.5 (CH_{Ar}), 128.2, 132.2, 135.8, 141.5, 141.6 (C_{Ar}), 156.9 (C_{OH}), 171.3 (CO). IR (neat, cm⁻¹): 3082 (w), 3057 (w), 3021 (w), 2964 (w), 2928 (w), 2873 (w), 1728 (w), 1651 (s), 1598 (m), 1563 (m), 1494 (m), 1444 (m), 1371 (m), 1262 (m), 1224 (m), 1190 (s), 1104 (m), 1031 (m), 807 (m), 745 (m), 728 (m), 670 (s), 624 (w), 600 (m), 583 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=374 (M⁺, 33), 329 (26), 328 (43), 327 (100), 300 (12), 285 (10), 179 (15), 178 (17), 167 (30), 166 (16), 165 (44), 152 (14), 91 (13). HRMS (EI): calcd for C₂₅H₂₆O₃ [M]⁺: 374.18765; found: 374.187686.

3.1.24. Ethyl 3-diphenylmethyl-5-ethyl-6-hydroxy-2,4-dimethylbenzoate (6g). Starting with **4a** (0.510 g, 1.5 mmol) and **5g** (0.476 g, 1.65 mmol), **6g** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.250 g, 43%). ¹H NMR (300 MHz, CDCl₃): 1.03 (t, *J*=7.4 Hz, 3H, CH₂CH₃), 1.28 (t, *J*=7.2 Hz, 3H, OCH₂CH₃), 1.95 (s, 3H, CH₃), 2.10 (s, 3H, CH₃), 2.63 (q, *J*=7.4 Hz,

2H, CH₂CH₃), 4.31 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 6.00 (s, 1H, CH), 7.02–7.21 (m, 10H, CH_{Ar}), 10.79 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=12.3, 13.1, 17.1, 20.1 (CH₃), 18.9 (CH₂CH₃), 50.2 (CH), 60.4 (OCH₂CH₃), 111.3 (C_{Ar}), 124.8, 127.1, 128.1 (CH_{Ar}), 128.3, 132.1, 135.9, 141.5, 141.8 (C_{Ar}), 156.8 (C_{OH}), 171.1 (CO). IR (neat, cm⁻¹): 3083 (w), 3058 (w), 3022 (w), 2963 (w), 2929 (w), 2871 (w), 1726 (w), 1651 (s), 1597 (m), 1562 (m), 1493 (m), 1443 (m), 1370 (m), 1261 (m), 1223 (m), 1188 (s), 1106 (m), 1033 (m), 805 (m), 743 (m), 726 (m), 698 (s), 622 (w), 599 (m), 584 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=388 (M⁺, 46), 343 (30), 342 (100), 341 (17), 314 (22), 299 (15), 251 (10), 236 (12), 179 (12), 178 (11), 167 (56), 166 (13), 165 (39), 152 (15), 115 (10), 91 (22), 77 (10), 43 (12). HRMS (ESI-Tof): calcd for C₂₆H₂₈O₃ [M+H]⁺: 388.20384; found: 387.20297.

3.1.25. Methyl 3-diphenylmethyl-5-butyl-6-hydroxy-2,4-dimethylbenzoate (6h). Starting with **4a** (0.510 g, 1.5 mmol) and **5h** (0.521 g, 1.65 mmol), **6h** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.277 g, 46%). ¹H NMR (300 MHz, CDCl₃): δ=0.75 (t, *J*=6.9 Hz, 3H, (CH₂)₂(CH₂)CH₃), 1.21–1.31 (m, 4H, 2×CH₂), 1.84 (s, 3H, CH₃), 1.95 (s, 3H, CH₃), 2.49 (t, *J*=7.1 Hz, CH₂(CH₂)₂CH₃), 3.69 (s, 3H, OCH₃), 5.89 (s, 1H, CH), 6.90–7.09 (m, 10H, CH_{Ar}), 10.62 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=15.1, 19.5, 22.4 (CH₃), 24.2, 27.7, 30.8 (CH₂), 52.3 (CH), 53.1 (OCH₃), 113.3 (C_{Ar}), 127.0, 129.3, 130.3 (CH_{Ar}), 130.6, 134.3, 138.0, 143.6, 144.3 (C_{Ar}), 159.1 (C_{OH}), 173.8 (CO). IR (neat, cm⁻¹): 3083 (w), 3058 (w), 3022 (w), 2952, 2870 (w), 2855 (w), 1737 (w), 1655 (s), 1596 (w), 1493 (w), 1437 (s), 1348 (w), 1313 (w), 1231 (w), 1200 (s), 1115 (w), 1044 (w), 1022 (w), 965 (w), 842 (w), 805 (w), 746 (w), 725 (w), 697 (s), 582 (w) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=402 (M⁺, 100), 371 (26), 370 (83), 369 (12), 355 (24), 353 (22), 342 (15), 341 (14), 328 (37), 327 (25), 285 (10), 279 (16), 167 (15), 165 (14). HRMS (EI): calcd for C₂₇H₃₀O₃ [M]⁺: 402.21895; found: 402.218714.

3.1.26. Methyl 3-diphenylmethyl-6-hydroxy-2,4-dimethyl-5-octylbenzoate (6i). Starting with **4a** (0.510 g, 1.5 mmol) and **5i** (0.614 g, 1.65 mmol), **6i** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.343 g, 50%). ¹H NMR (300 MHz, CDCl₃): δ=0.70 (t, *J*=7.1 Hz, 3H, (CH₂)₆(CH₂)CH₃), 1.05–1.08 (m, 10H, 5×CH₂), 1.24–1.29 (m, 2H, CH₂), 1.84 (s, 3H, CH₃), 1.95 (s, 3H, CH₃), 2.48 (t, *J*=7.2 Hz, 2H, CH₂(CH₂)₅CH₃), 3.70 (s, 3H, OCH₃), 5.89 (s, 1H, CH), 6.90–7.12 (m, 10H, CH_{Ar}), 10.61 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=15.2, 19.5, 22.4 (CH₃), 27.9, 30.3, 30.4, 30.5, 30.6, 31.2, 33.0 (CH₂), 52.3 (s, 1H, CH), 53.1 (OCH₃), 113.3 (C_{Ar}), 127.0, 129.3 (CH_{Ar}), 130.0 (C_{Ar}), 130.3 (CH_{Ar}), 134.3, 138.0, 143.6, 144.3 (C_{Ar}), 159.0 (C_{OH}), 173.8 (CO). IR (neat, cm⁻¹): 3082 (w), 3059 (w), 3023 (w), 2952 (m), 2922 (m), 2852 (m), 1933 (w), 1701 (w), 1657 (s), 1597 (m), 1493 (m), 1437 (s), 1350 (w), 1292 (m), 1245 (m), 1200 (s), 1119 (m), 1048 (m), 1029 (m), 965 (w), 919 (w), 841 (m), 806 (m), 746 (m), 724 (m), 697 (s), 623 (m), 583 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=458 (M⁺, 84), 427 (33), 426 (100), 425 (16), 411 (19), 409 (26), 370 (10), 369 (29), 355 (14), 341 (22), 336 (16), 335 (76), 329 (14), 328 (67), 327 (44), 301 (12), 300 (28), 299 (10), 285 (23), 251 (10), 249 (11), 223 (16), 222 (14), 221 (11), 209 (14), 179 (15), 178 (18), 168 (11), 167 (65), 166 (15), 165 (37), 152 (13), 105 (10), 91 (30), 41 (10). HRMS (EI): calcd for C₃₁H₃₈O₃ [M]⁺: 458.28155; found: 458.281976.

3.1.27. Methyl 3-diphenylmethyl-5-decyl-6-hydroxy-2,4-dimethylbenzoate (6j). Starting with **4a** (0.510 g, 1.5 mmol) and **5j** (0.661 g, 1.65 mmol), **6j** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.415 g, 57%). ¹H NMR (300 MHz, CDCl₃): δ=0.70 (t, *J*=6.8 Hz, 3H, (CH₂)₈CH₂CH₃), 1.07–1.12 (m, 14H, 7×CH₂), 1.24–1.29 (m, 2H, CH₂), 1.84 (s, 3H, CH₃), 1.95 (s, 3H, CH₃), 2.48 (t, *J*=7.2 Hz, 2H, CH₂(CH₂)₈CH₃), 3.70 (s, 3H, OCH₃), 5.89 (s, 1H, CH), 6.90–7.09 (m, 10H, CH_{Ar}), 10.61 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=15.2, 19.5, 22.4 (CH₃), 23.8, 27.9, 30.3, 30.5, 30.6, 30.8,

30.9, 31.2, 33.0 (CH₂), 52.3 (CH), 53.1 (OCH₃), 113.3 (C_{Ar}), 127.0, 129.3 (CH_{Ar}), 129.4 (C_{Ar}), 130.3 (CH_{Ar}), 134.3, 138.0, 143.6, 144.3 (C_{Ar}), 159.0 (C_{OH}), 173.8 (CO). IR (neat, cm⁻¹): 3059 (w), 3023 (w), 2952 (m), 2921 (s), 2852 (m), 1933 (w), 1752 (m), 1703 (m), 1656 (s), 1598 (m), 1493 (m), 1438 (s), 1377 (w), 1322 (m), 1293 (m), 1229 (m), 1201 (s), 1120 (m), 1047 (m), 1030 (m), 959 (w), 903 (w), 841 (m), 806 (m), 746 (m), 724 (m), 698 (s), 623 (m), 615 (m), 583 (m) cm⁻¹. HRMS (ESI): calcd for C₃₃H₄₃O₃ [M+H]⁺: 487.32067; found: 487.32048.

3.1.28. Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6k). Starting with **4b** (0.564 g, 1.5 mmol) and **5a** (0.429 g, 1.65 mmol), **6k** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.188 g, 33%). ¹H NMR (300 MHz, CDCl₃): δ=1.98 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 3.82 (s, 3H, OCH₃), 5.84 (s, 1H, CH), 6.68 (s, 1H, CH_{Ar}), 6.86–6.99 (m, 8H, CH_{Ar}), 10.50 (s, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz): δ=21.2, 22.6 (CH₃), 49.3 (CH), 52.0 (OCH₃), 112.9 (C_{Ar}), 115.1 (d, *J*_{C,F}=21.1 Hz, CH_{Ar}), 118.0 (CH_{Ar}), 130.5 (d, *J*_{C,F}=7.5 Hz, CH_{Ar}), 132.8 (C_{Ar}), 137.5 (d, *J*_{C,F}=3.5 Hz, C_{Ar}), 140.1, 145.0 (C_{Ar}), 160.0 (C_{OH}), 161.2 (d, *J*_{C,F}=245.0 Hz, C_{Ar}), 171.8 (CO). ¹⁹F NMR (282 MHz, CDCl₃): δ=-116.8. IR (neat, cm⁻¹): 2949 (w), 2918 (w), 2850 (w), 1650 (s), 1661 (m), 1573 (m), 1503 (s), 1468 (m), 1440 (m), 1349 (m), 1299 (m), 1229 (s), 1155 (m), 1072 (m), 955 (m), 865 (m), 830 (m), 795 (m), 724 (m) 648 (m), 609 (m), 555 (m), 529 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=382 (M⁺, 57), 351 (35), 350 (100), 335 (30), 321 (15), 255 (18), 203 (18), 202 (15), 201 (28), 184 (10), 183 (24). HRMS (EI): calcd for C₂₃H₂₀O₃F₂ [M]⁺: 382.13750; found: 382.137228.

3.1.29. Ethyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6l). Starting with **4b** (0.564 g, 1.5 mmol) and **5b** (0.452 g, 1.65 mmol), **6l** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.220 g, 37%), mp 76–77 °C. ¹H NMR (300 MHz, CDCl₃): δ=1.28 (t, *J*=7.1 Hz, 3H, OCH₂CH₃), 1.97 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 4.30 (t, *J*=7.1 Hz, 2H, OCH₂CH₃), 5.84 (s, 1H, CH), 6.65 (s, 1H, CH_{Ar}), 6.85–7.18 (m, 8H, CH_{Ar}), 10.59 (s, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz): δ=14.1, 21.2, 22.7 (CH₃), 49.3 (CH), 61.6 (OCH₂CH₃), 113.0 (C_{Ar}), 115.0 (d, *J*_{C,F}=21.1 Hz, CH_{Ar}), 118.0 (CH_{Ar}), 130.3 (d, *J*_{C,F}=7.5 Hz, CH_{Ar}), 132.7 (C_{Ar}), 137.6 (d, *J*_{C,F}=3.1 Hz, C_{Ar}), 140.1, 145.0 (C_{Ar}), 160.0 (C_{OH}), 161.1 (d, *J*_{C,F}=245.0 Hz, C_{Ar}), 171.3 (CO). ¹⁹F NMR (282 MHz, CDCl₃): δ=-116.8. IR (neat, cm⁻¹): 3039 (w), 2994 (w), 2954 (w), 2922 (w), 2851 (w), 1727 (w), 1650 (s), 1598 (m), 1536 (m), 1503 (s), 1463 (m), 1393 (m), 1333 (m), 1292 (m), 1268 (m), 1220 (s), 1210 (s), 1157 (m), 1074 (m), 1013 (m), 863 (m), 829 (m), 794 (m), 723 (m) 640 (m), 592 (m), 528 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=396 (M⁺, 45), 351 (32), 350 (100), 335 (20), 321 (12), 255 (13), 203 (16), 202 (12), 201 (20), 183 (20). HRMS (EI): calcd for C₂₄H₂₂O₃F₂ [M]⁺: 396.15315; found: 396.153067.

3.1.30. Benzyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6m). Starting with **4b** (0.564 g, 1.5 mmol) and **5c** (0.555 g, 1.65 mmol), **6m** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless solid (0.466 g, 68%), mp 112–113 °C. ¹H NMR (300 MHz, CDCl₃): δ=1.99 (s, 3H, CH₃), 2.12 (s, 3H, CH₃), 5.33 (s, 2H, OCH₂), 5.87 (s, 1H, CH_{Ar}), 6.70 (s, 1H, CH_{Ar}), 6.89–7.01 (m, 8H, CH_{Ar}), 7.30–7.37 (m, 5H, CH_{Ar}), 10.56 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=21.3, 22.7 (CH₃), 49.3 (CH), 67.4 (OCH₂), 112.8 (C_{Ar}), 114.6 (d, *J*_{C,F}=21.2 Hz, CH_{Ar}), 118.5 (CH_{Ar}), 128.5 (d, *J*_{C,F}=7.7 Hz, CH_{Ar}), 128.6 (C_{Ar}), 137.5 (d, *J*_{C,F}=3.1 Hz, C_{Ar}), 140.2, 145.2 (C_{Ar}), 160.1 (C_{OH}), 161.1 (d, *J*_{C,F}=245.1 Hz, C_{Ar}), 171.1 (CO). ¹⁹F NMR (282 MHz, CDCl₃): δ=-116.8. IR (neat, cm⁻¹): 3070 (w), 3035 (w), 2979 (w), 2931 (w), 2884 (w), 1649 (s), 1598 (m), 1574 (m), 1500 (s), 1426 (m), 1381 (m), 1316 (m), 1292 (m), 1217 (s), 1175 (s), 1145 (m), 1067 (m), 1029 (m), 1012 (m), 953 (m), 860 (m), 829 (m), 817 (m), 794 (s), 748 (s), 698 (s), 647 (m), 598 (m), 528 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=458 (M⁺, 18), 350 (34), 91

(100). HRMS (ESI): calcd for $C_{29}H_{25}O_3F_2$ $[M+H]^+$: 459.17663; found: 459.17593.

3.1.31. Ethyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (6n). Starting with **4b** (0.564 g, 1.5 mmol) and **5e** (0.476 g, 1.65 mmol), **6n** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.239 g, 39%), mp 63–64 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.29 (t, J =7.1 Hz, 3H, OCH_2CH_3), 1.88 (s, 3H, CH_3), 2.10 (s, 6H, $2\times CH_3$), 4.32 (q, J =7.1 Hz, 2H, OCH_2CH_3), 5.90 (s, 1H, CH), 6.86–6.99 (m, 8H, CH_{Ar}), 10.83 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =12.2, 14.1, 19.0, 21.0 (CH_3), 49.7 (OCH_3), 61.5 (OCH_2CH_3), 112.3 (C_{Ar}), 115.0 (d, $J_{C,F}$ =21.0 Hz, CH_{Ar}), 123.5 (C_{Ar}), 130.4 (d, $J_{C,F}$ =7.8 Hz, CH_{Ar}), 132.5, 136.5 (C_{Ar}), 137.5 (d, $J_{C,F}$ =3.2 Hz, C_{Ar}), 143.2 (C_{Ar}), 159.5 (C_{OH}), 160.4 (d, $J_{C,F}$ =244.6 Hz, C_{Ar}), 172.0 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ =–117.0. IR (neat, cm^{-1}): 3070 (w), 3035 (w), 2979 (w), 2931 (w), 2884 (w), 1649 (s), 1598 (m), 1574 (m), 1500 (s), 1426 (m), 1381 (m), 1316 (m), 1292 (m), 1217 (s), 1175 (s), 1145 (m), 1067 (m), 1029 (m), 1012 (m), 953 (m), 860 (m), 829 (m), 817 (m), 794 (s), 748 (s), 698 (s), 647 (m), 598 (m), 528 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=410 (M^+ , 30), 365 (29), 364 (100), 336 (22), 321 (28), 241 (18), 240 (10), 203 (26), 202 (11), 201 (25), 197 (11), 196 (11), 183 (32), 109 (16), 91 (14), 44 (21), 43 (18). HRMS (ESI): calcd for $C_{25}H_{24}O_3F_2$ $[M]^+$: 410.16880; found: 410.169602.

3.1.32. Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-ethylbenzoate (6o). Starting with **4b** (0.564 g, 1.5 mmol) and **5f** (0.476 g, 1.65 mmol), **6o** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.251 g, 41%), mp 82–83 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.03 (t, J =7.4 Hz, 3H, CH_2CH_3), 1.94 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.63 (q, J =7.4 Hz, 2H, CH_2CH_3), 3.82 (s, 3H, OCH_3), 5.90 (s, 1H, CH), 6.86–6.99 (m, 8H, CH_{Ar}), 10.73 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =12.3, 16.9, 18.9 (CH_3), 20.2 (CH_2CH_3), 48.8 (CH), 51.0 (OCH_3), 111.3 (C_{Ar}), 114.0 (d, $J_{C,F}$ =21.2 Hz, CH_{Ar}), 128.5 (C_{Ar}), 129.4 (d, $J_{C,F}$ =7.7 Hz, CH_{Ar}), 131.7, 135.7 (C_{Ar}), 136.8 (d, $J_{C,F}$ =3.2 Hz, C_{Ar}), 141.6 (C_{Ar}), 156.9 (C_{OH}), 161.1 (d, $J_{C,F}$ =244.7 Hz, C_{Ar}), 171.4 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ =–117.0. IR (neat, cm^{-1}): 2961 (w), 2929 (w), 2873 (w), 2852 (w), 1732 (w), 1656 (s), 1599 (m), 1563 (w), 1504 (s), 1439 (m), 1398 (m), 1350 (m), 1293 (m), 1258 (s), 1223 (m), 1201 (m), 1157 (s), 1096 (m), 1014 (s), 953 (m), 861 (m), 832 (m), 795 (s), 699 (s), 643 (m), 601 (w), 567 (m), 530 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=410 (M^+ , 46), 380 (10), 379 (32), 378 (100), 377 (16), 363 (14), 353 (21), 352 (67), 351 (10), 350 (31), 338 (24), 337 (86), 336 (12), 335 (25), 324 (16), 323 (45), 321 (18), 257 (14), 241 (12), 227 (17), 226 (14), 203 (15), 202 (20), 201 (24), 196 (15), 189 (10), 183 (25), 109 (12). HRMS (EI): calcd for $C_{25}H_{24}O_3F_2$ $[M]^+$: 410.16880; found: 410.169602.

3.1.33. Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-butylbenzoate (6p). Starting with **4b** (0.564 g, 1.5 mmol) and **5h** (0.521 g, 1.65 mmol), **6p** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.348 g, 53%), mp 116–117 °C. 1H NMR (300 MHz, $CDCl_3$): δ =0.75 (t, J =6.9 Hz, 3H, $(CH_2)_2CH_2CH_3$), 1.21–1.28 (m, 4H, $2\times CH_2$), 1.83 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 2.49 (t, J =7.3 Hz, 2H, $CH_2(CH_2)_2CH_3$), 3.71 (s, 3H, OCH_3), 5.79 (s, 1H, CH), 6.75–6.88 (m, 8H, CH_{Ar}), 10.62 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =15.2, 18.2, 21.2 (CH_3), 23.1, 26.5, 31.3 (CH_2), 49.8 (CH), 52.08 (OCH_3), 113.5 (C_{Ar}), 116.1 (d, $J_{C,F}$ =21.2 Hz, CH_{Ar}), 129.6 (C_{Ar}), 131.5 (d, $J_{C,F}$ =7.7 Hz, CH_{Ar}), 133.9, 137.8 (C_{Ar}), 139.1 (d, $J_{C,F}$ =3.2 Hz, C_{Ph}), 144.0 (C_{Ar}), 159.2 (C_{OH}), 162.3 (d, $J_{C,F}$ =244.7 Hz, C_{Ar}), 173.6 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ =–117.0. IR (neat, cm^{-1}): 3034 (w), 2954 (w), 2927 (w), 2871 (w), 2858 (w), 1737 (m), 1655 (m), 1504 (s), 1438 (m), 1397 (m), 1350 (m), 1293 (m), 1223 (s), 1200 (s), 1157 (s), 1115 (m), 1044 (m), 1015 (m), 881 (m), 832 (m), 807 (m), 796 (s), 731 (s), 670 (m), 639 (m), 603 (m), 567 (s), 529 (m) cm^{-1} .

MS (EI, 70 eV): m/z (%)=438 (M^+ 100), 407 (28), 406 (72), 389 (24), 378 (18), 377 (16), 365 (10), 364 (40), 363 (28), 321 (13), 297 (15), 203 (21), 201 (12), 183 (14), 109 (12). HRMS (ESI): calcd for $C_{27}H_{29}O_3F_2$ $[M+H]^+$: 439.20065; found: 439.20975.

3.1.34. Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-nonylbenzoate (6q). Starting with **4b** (0.564 g, 1.5 mmol) and **5k** (0.614 g, 1.65 mmol), **6q** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.402 g, 53%), mp 147–148 °C. 1H NMR (300 MHz, $CDCl_3$): δ =0.70 (t, J =7.0 Hz, 3H, $(CH_2)_7CH_2CH_3$), 1.09–1.16 (m, 12H, $6\times CH_2$), 1.27–1.31 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 2.48 (t, J =7.1 Hz, 2H, $CH_2(CH_2)_7CH_3$), 3.71 (s, 3H, OCH_3), 5.79 (s, 1H, CH), 6.75–6.88 (m, 8H, CH_{Ar}), 10.67 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =15.2, 23.8, 27.9 (CH_3), 28.3, 30.3, 30.5, 30.7, 30.8, 30.9, 31.2, 33.0 (CH_2), 51.0 (CH), 53.2 (OCH_3), 113.5 (C_{Ar}), 116.1 (d, $J_{C,F}$ =21.2 Hz, CH_{Ar}), 129.6 (C_{Ar}), 131.5 (d, $J_{C,F}$ =7.7 Hz, CH_{Ar}), 133.9, 137.8 (C_{Ar}), 139.1 (d, $J_{C,F}$ =3.4 Hz, C_{Ar}), 143.9 (C_{Ar}), 159.2 (C_{OH}), 162.3 (d, $J_{C,F}$ =244.7 Hz, C_{Ph}), 173.6 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ =–117.1. IR (neat, cm^{-1}): 2952 (w), 2922 (w), 2853 (w), 1751 (m), 1654 (m), 1558 (s), 1506 (m), 1446 (m), 1351 (m), 1227 (s), 1157 (s), 1148 (m), 1030 (m), 1016 (m), 841 (m), 798 (m), 778 (m), 721 (m), 667 (m), 628 (w), 568 (m), 530 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=508 (M^+ 100), 473 (18), 405 (16), 381 (20), 377 (18), 365 (19), 364 (51), 336 (14), 276 (13), 275 (76), 183 (10), 109 (16), 57 (13), 43 (14). HRMS (ESI): calcd for $C_{32}H_{38}F_2O_3$ $[M+H]^+$: 509.2789; found: 509.2787.

3.1.35. Methyl 3-(bis(4-fluorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-decylbenzoate (6r). Starting with **4b** (0.564 g, 1.5 mmol) and **5j** (0.661 g, 1.65 mmol), **6r** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.429 g, 55%), mp 161–162 °C. 1H NMR (300 MHz, $CDCl_3$): δ =0.75 (t, J =6.8 Hz, 3H, $(CH_2)_8CH_2CH_3$), 1.08–1.12 (m, 14H, $7\times CH_2$), 1.17–1.25 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 2.48 (t, J =7.2 Hz, 2H, $CH_2(CH_2)_8CH_3$), 3.71 (s, 3H, OCH_3), 5.78 (s, 1H, CH_{Ar}), 6.76–6.89 (m, 8H, CH_{Ar}), 10.61 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =15.2, 19.4, 22.4 (CH_3), 23.8, 27.9, 28.3, 30.3, 30.5, 30.7, 30.8, 31.2, 33.0 (CH_2), 51.0 (CH), 53.2 (OCH_3), 113.5 (C_{Ar}), 116.1 (d, $J_{C,F}$ =21.1 Hz, CH_{Ar}), 129.6 (C_{Ar}), 131.5 (d, $J_{C,F}$ =8.2 Hz, CH_{Ar}), 133.9, 137.8 (C_{Ar}), 139.1 (d, $J_{C,F}$ =3.0 Hz, C_{Ar}), 144.0 (C_{Ar}), 159.2 (C_{OH}), 162.3 (d, $J_{C,F}$ =245.0 Hz, C_{Ar}), 173.6 (CO). ^{19}F NMR (282 MHz, $CDCl_3$): δ =–117.0. IR (neat, cm^{-1}): 2952 (w), 2922 (w), 2853 (w), 1751 (m), 1658 (m), 1600 (m), 1505 (s), 1437 (m), 1399 (m), 1351 (m), 1294 (m), 1225 (s), 1201 (m), 1157 (s), 1120 (m), 1048 (m), 1015 (m), 907 (m), 840 (m), 797 (s), 733 (m), 671 (m), 628 (m), 568 (s), 530 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=522 (100) (M^+ 100), 490 (83), 473 (17), 405 (15), 381 (23), 377 (14), 365 (11), 364 (51), 363 (34), 336 (13), 321 (11), 276 (12), 275 (80), 203 (59), 201 (10), 183 (11), 109 (14), 57 (10), 43 (13). HRMS (ESI): calcd for $C_{33}H_{41}O_3F_2$ $[M+H]^+$: 523.29465; found: 522.29452.

3.1.36. Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6s). Starting with **4c** (0.614 g, 1.5 mmol) and **5a** (0.429 g, 1.65 mmol), **6s** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.311 g, 50%), mp 95–97 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.98 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 5.82 (s, 1H, CH), 6.66 (s, 1H, CH_{Ar}), 6.90–7.19 (m, 8H, CH_{Ar}), 10.53 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =20.4, 21.6 (CH_3), 48.6 (CH), 51.0 (OCH_3), 111.9 (C_{Ar}), 117.0, 127.4, 129.3 (CH_{Ar}), 131.0, 131.2, 139.1, 139.2, 144.0 (C_{Ar}), 159.0 (C_{OH}), 170.7 (CO). IR (neat, cm^{-1}): 2961 (w), 2918 (w), 1663 (s), 1599 (m), 1564 (m), 1492 (m), 1435 (m), 1341 (m), 1265 (m), 1210 (m), 1143 (m), 1069 (m), 942 (m), 914 (w), 857 (m), 801 (m), 736 (m), 719 (s), 696 (s), 613 (m), 571 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=415 (M^+ , 17), 414 (78), 386 (17), 385 (28), 384 (93), 383 (48), 382 (100), 369 (10), 367 (15), 347 (22), 319 (12), 271 (21), 239 (10), 237 (12), 235 (28), 201 (10), 199 (31), 179

(14), 178 (11), 165 (50). HRMS (ESI): calcd for $C_{23}H_{19}Cl_2O_3$ $[M-H]^+$: 413.07188; found: 413.07167.

3.1.37. Ethyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6t). Starting with **4c** (0.614 g, 1.5 mmol) and **5b** (0.452 g, 1.65 mmol), **6t** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a white solid (0.340 g, 53%), mp 117–118 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.29 (t, J =7.1 Hz, 3H, OCH_2CH_3), 1.97 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 4.31 (q, J =7.1 Hz, 2H, OCH_2CH_3), 5.82 (s, 1H, CH), 6.66 (s, 1H, CH_{Ar}), 6.91–6.94 (m, 4H, CH_{Ar}), 7.16–7.19 (m, 4H, CH_{Ar}), 10.63 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ =13.1, 20.3, 21.7 (CH_3), 48.6 (CH), 55.6 (OCH_3), 60.6 (OCH_2CH_3), 112.0 (C_{Ar}), 117.0, 127.4, 129.0 (CH_{Ar}), 129.3, 131.0, 131.1 (C_{Ar}), 139.2, 143.9 (C_{Ar}), 159.2 (C_{OH}), 170.3 (CO). IR (neat, cm^{-1}): 2981 (w), 2958 (w), 2923 (w), 2852 (w), 1647 (s), 1596 (m), 1572 (m), 1487 (s), 1463 (m), 1395 (s), 1371 (m), 1321 (m), 1292 (m), 1224 (s), 1178 (m), 1143 (m), 1089 (s), 1067 (m), 1009 (s), 861 (m), 815 (m), 784 (m), 734 (m), 686 (m), 627 (m), 593 (m), 583 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=429 (M^+ , 10), 428 (38), 386 (12), 385 (20), 384 (67), 383 (32), 382 (100), 367 (10), 347 (19), 239 (10), 237 (11), 236 (10), 235 (23), 201 (12), 199 (31), 180 (10), 179 (16), 178 (13), 166 (11), 165 (57), 164 (10), 156 (10), 125 (11), 91 (12), 77 (10), 67 (10), 36 (12). HRMS (ESI): calcd for $C_{24}H_{22}Cl_2O_3$ $[M-H]^+$: 428.08732; found: 428.08796.

3.1.38. Benzyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6u). Starting with **4c** (0.614 g, 1.5 mmol) and **5c** (0.429 g, 1.65 mmol), **6u** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.507 g, 69%), mp 137–138 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.95 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 5.28 (s, 2H, OCH_2), 5.80 (s, 1H, CH), 6.66 (CH_{Ar}), 6.89–6.93 (m, 4H, CH_{Ar}), 7.14–7.18 (m, 4H, CH_{Ar}), 7.26–7.31 (m, 5H, CH), 10.54 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ =21.4, 22.8 (CH_3), 49.6 (CH), 67.4 (OCH_2), 112.8 (C_{Ar}), 118.1, 128.2, 128.4, 128.6, 128.7, 130.3 (CH_{Ar}), 132.0, 133.2, 135.0, 140.1, 140.2, 145.2 (C_{Ar}), 160.2 (C_{OH}), 171.1 (CO). IR (neat, cm^{-1}): 3031 (w), 2979 (w), 2928 (w), 1660 (s), 1598 (m), 1567 (m), 1487 (m), 1462 (m), 1387 (m), 1341 (m), 1270 (m), 1257 (m), 1231 (m), 1208 (m), 1144 (m), 1089 (m), 1068 (s), 1012 (m), 949 (w), 838 (m), 801 (m), 749 (m), 737 (m), 693 (s), 636 (m), 583, 539 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=490 (M^+ , 60), 401 (10), 399 (16), 385 (15), 384 (75), 383 (28), 382 (100), 165 (15), 92 (22), 91 (40), 57 (13), 54 (16), 43 (11). HRMS (EI): calcd for $C_{29}H_{25}Cl_2O_3$ $[M+H]^+$: 491.11996; found: 491.11201.

3.1.39. Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (6v). Starting with **4c** (0.614 g, 1.5 mmol) and **5d** (0.452 g, 1.65 mmol), **6v** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.255 g, 40%), mp 113–114 °C. 1H NMR (300 MHz, $CDCl_3$): 1.89 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.88 (s, 1H, CH), 6.92–6.95 (m, 4H, CH_{Ar}), 7.16–7.19 (m, 4H, CH_{Ar}), 10.81 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ =13.0, 21.6, 28.6 (CH_3), 49.0 (CH), 51.1 (OCH_3), 111.2, 116.4 (C_{Ar}), 127.4, 129.3, 130.8 (CH_{Ar}), 134.0, 137.9, 143.6, 144.7 (C_{Ar}), 159.0 (C_{OH}), 173.3 (CO). IR (neat, cm^{-1}): 2921 (w), 2852 (w), 1731 (w), 1659 (s), 1592 (m), 1565 (m), 1489 (m), 1456 (m), 1439 (m), 1398 (m), 1377 (m), 1347 (m), 1280 (m), 1260 (m), 1201 (m), 1164 (m), 1091 (m), 1013 (m), 925 (w), 822 (m), 756 (w), 698 (m), 596 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=429 (10), 428 (38), 400 (10), 399 (15), 398 (62), 397 (26), 396 (100), 199 (11), 57(32). HRMS (ESI): calcd for $C_{24}H_{22}Cl_2O_3$ $[M-H]^+$: 427.08732; found: 427.08657.

3.1.40. Ethyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4,5-trimethylbenzoate (6w). Starting with **4c** (0.614 g, 1.5 mmol) and **5e** (0.476 g, 1.65 mmol), **6w** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.285 g, 43%), mp 111–112 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.19 (t, J =7.1 Hz, 3H, OCH_2CH_3), 1.78

(s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 4.22 (q, J =7.1 Hz, 2H, OCH_2CH_3), 5.78 (s, 1H, CH), 6.82–6.85 (m, 4H, CH_{Ar}), 7.06–7.09 (m, 4H, CH_{Ar}), 10.77 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ =12.2, 14.1, 19.0, 21.0 (CH_3), 50.0 (CH), 61.6 (OCH_2CH_3), 112.3, 123.6 (C_{Ar}), 128.4, 130.3 (CH_{Ar}), 131.8, 136.5, 139.5, 140.5, 143.2 (C_{Ar}), 158.1 (C_{OH}), 171.9 (CO). IR (neat, cm^{-1}): 3070 (w), 3035 (w), 2979 (w), 2931 (w), 2884 (w), 1649 (s), 1598 (m), 1574 (m), 1500 (s), 1426 (m), 1381 (m), 1316 (m), 1292 (m), 1217 (s), 1175 (s), 1145 (m), 1067 (m), 1029 (m), 1012 (m), 953 (m), 860 (m), 829 (m), 817 (m), 794 (s), 748 (s), 698 (s), 647 (m), 598 (m), 528 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=442 (M^+ , 10), 414 (13), 413 (21), 412 (63), 411 (30), 410 (100), 384 (16), 382 (28), 367 (13), 285 (12), 285 (12), 165 (15), 71 (11), 69 (12), 57 (14), 57 (11), 43 (16). HRMS (ESI): calcd for $C_{25}H_{23}Cl_2O_3$ $[M-H]^+$: 441.10297; found: 441.10289.

3.1.41. Methyl 3-(bis(4-chlorophenyl)methyl)-5-ethyl-6-hydroxy-2,4-dimethylbenzoate (6x). Starting with **4c** (0.614 g, 1.5 mmol) and **5f** (0.476 g, 1.65 mmol), **6x** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.278 g, 42%), mp 127–128 °C. 1H NMR (300 MHz, $CDCl_3$): δ =1.02 (t, J =7.4 Hz, 3H, OCH_2CH_3), 1.94 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.63 (q, J =7.4 Hz, 2H, OCH_2CH_3), 3.82 (s, 3H, OCH_3), 5.88 (s, 1H, CH), 6.92–6.95 (m, 4H, CH_{Ar}), 7.16–7.19 (m, 4H, CH_{Ar}), 10.77 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =12.3, 17.0, 19.0, 20.3 (CH_3), 28.6 (CH_2), 49.1 (CH), 51.1 (OCH_3), 111.3 (C_{Ar}), 127.4 (CH_{Ar}), 128.6 (C_{Ar}), 129.3 (CH_{Ar}), 130.8, 131.1, 135.7, 139.5, 141.5 (C_{Ar}), 157.0 (C_{OH}), 171.4 (CO). IR (neat, cm^{-1}): 2953, 2927 (w), 2871 (w), 2854 (w), 1731 (w), 1656 (s), 1593 (m), 1561 (m), 1489 (s), 1439 (m), 1350 (m), 1324 (m), 1290 (m), 1223 (m), 1178 (m), 1106 (m), 1091 (m), 1013 (s), 877 (w), 807 (m), 781 (m), 705 (m), 653 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=443 (M^+ , 10), 442 (42), 414 (10), 413 (17), 412 (63), 411 (31), 410 (100), 384 (17), 382 (27), 367 (12), 285 (13), 285 (13), 165 (14), 71 (10), 69 (10), 57 (16), 57 (10), 43 (17). HRMS (EI): calcd for $C_{25}H_{24}Cl_2O_3$ $[M+H]^+$: 444.18023; found: 444.18011.

3.1.42. Methyl 3-(bis(4-chlorophenyl)methyl)-6-hydroxy-2,4-dimethyl-5-pentylbenzoate (6y). Starting with **4c** (0.614 g, 1.5 mmol) and **5i** (0.545 g, 1.65 mmol), **6y** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.385 g, 53%), mp 131–132 °C. 1H NMR (300 MHz, $CDCl_3$): δ =0.86 (t, J =6.9 Hz, 3H, $(CH_2)_4CH_3$), 1.18–1.23 (m, 4H, $2 \times CH_2$), 1.31–1.38 (m, 2H, CH_2), 1.93 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.59 (t, J =7.3 Hz, 2H, $CH_2(CH_2)_3CH_3$), 3.82 (s, 3H, OCH_3), 5.87 (s, 1H, CH), 6.91–6.94 (m, 4H, CH_{Ar}), 7.16–7.19 (m, 4H, CH_{Ar}), 10.75 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ =12.9, 13.1, 17.2 (CH_3), 20.3, 21.6, 22.0, 25.5, 28.6 (CH_2), 49.1 (s, 1H, CH), 51.0 (OCH_3), 111.2, 127.3 (C_{Ar}), 127.4, 129.3 (CH_{Ar}), 130.8, 131.1, 135.7, 139.5, 141.7, 144.3 (C_{Ar}), 157.2 (C_{OH}), 171.4 (CO). IR (neat, cm^{-1}): 3059 (w), 3023 (w), 2952 (m), 2922 (m), 2852 (m), 1933 (w), 1701 (w), 1657 (s), 1597 (m), 1493 (m), 1437 (s), 1350 (w), 1292 (m), 1245 (m), 1200 (s), 1119 (m), 1048 (m), 1029 (m), 965 (w), 919 (w), 841 (m), 806 (m), 746 (m), 724 (m), 697 (s), 623 (m), 583 (m) cm^{-1} . MS (EI, 70 eV): m/z (%)=484 (100), 439 (17), 423 (11), 411 (15), 409 (12), 399 (33), 398 (48), 397 (10), 396 (36), 395 (20), 368 (15), 355 (17), 285 (14), 257 (18), 235 (30), 201 (15), 199 (14), 166 (12), 165 (32), 139 (14), 127 (12), 97 (17), 95 (10), 85 (15), 71 (19), 67 (22), 57 (37), 56 (10), 43 (30). HRMS (EI): calcd for $C_{28}H_{30}Cl_2O_3$ $[M+H]^+$: 485.15723; found: 485.12623.

3.1.43. Methyl 3-(bis(4-chlorophenyl)methyl)-5-decyl-6-hydroxy-2,4-dimethylbenzoate (6z). Starting with **4c** (0.614 g, 1.5 mmol) and **5j** (0.661 g, 1.65 mmol), **6z** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.474 g, 57%), mp 141–142 °C. 1H NMR (300 MHz, $CDCl_3$): δ =0.70 (t, J =6.9 Hz, 3H, $CH_2(CH_2)_8CH_3$), 1.03–1.08 (m, 14H, $7 \times CH_2$), 1.23–1.30 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.48 (t, J =7.0 Hz, 2H, $CH_2(CH_2)_8CH_3$), 3.71 (s, 3H, OCH_3), 5.77 (s, 1H, CH), 6.81–6.84 (m, 4H, CH_{Ar}), 7.05–7.08 (m, 4H,

(CH_{Ar}), 10.65 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=15.2, 19.4, 22.5 (CH₃), 23.8, 28.0, 28.3, 30.3, 30.5, 31.2 (CH₂), 51.3 (CH), 53.2 (OCH₃), 113.5 (C_{Ar}), 129.6, 131.5 (CH_{Ar}), 133.0, 133.3, 137.8, 141.7, 144.0 (C_{Ar}), 159.3 (C_{OH}), 173.6 (CO). IR (neat, cm⁻¹): 2952 (m), 2922 (s), 2852 (m), 1933 (w), 1745 (m), 1702 (m), 1658 (s), 1594 (m), 1562 (m), 1489 (m), 1455 (m), 1437 (m), 1377 (w), 1323 (m), 1278 (m), 1244 (m), 1235 (s), 1201 (m), 1178 (m), 1120 (w), 1091 (m), 1013 (m), 906 (w), 840 (s), 807 (m), 766 (m), 732 (m), 627 (m), 578 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=555 (M⁺, 22), 54 (69), 526 (12), 525 (22), 524 (62), 523 (40), 522 (89), 521 (10), 509 (11), 507 (27), 505 (19), 457 (10), 439 (16), 437 (22), 423 (10), 411 (12), 409 (17), 40 (10) 399 (31) 398 (45) 397 (100), 396 (45), 395 (30), 370 (13), 369 (15) 368 (19), 355 (12), 353 (10), 333 (10), 285 (13), 257 (14), 256 (15), 243 (17), 237 (21), 235 (32), 201 (14), 199 (12), 180 (10), 178 (10), 166 (10), 165 (30), 139 (12), 127 (10), 125 (24), 97 (14), 95 (1), 85 (12), 83 (16), 81 (13), 71 (17), 69 (20), 67 (12), 57 (31), 56 (11), 55 (29), 45 (12), 44 (57) 43 (52) 41 (29). HRMS (EI): calcd for C₃₃H₄₁Cl₂O₃ [M+H]⁺: 555.2364; found: 555.2454.

3.1.44. Methyl 3-(bis(4-methoxyphenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6aa). Starting with **4d** (0.600 g, 1.5 mmol) and **5a** (0.429 g, 1.65 mmol), **6aa** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.194 g, 32%), mp 119–120 °C. ¹H NMR (300 MHz, CDCl₃): 1.98 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 3.72 (s, 3H, OCH₃), 3.81 (s, 6H, OCH₃), 5.81 (s, 1H, CH), 6.64 (s, 1H, CH_{Ar}), 6.72–6.75 (m, 2H, CH_{Ar}), 6.90–6.93 (m, 2H, CH_{Ar}), 10.47 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=21.2, 22.7 (CH₃), 49.1 (CH), 52.0 (OCH₃), 65.2 (s, 6H, OCH₃), 112.7 (C_{Ar}), 117.7, 129.9, 133.6 (CH_{Ar}), 133.6, 134.4, 140.2, 145.3, 157.7 (C_{Ar}), 159.7 (C_{OH}), 172.0 (CO). IR (neat, cm⁻¹): 3027 (w), 2997 (w), 2951 (w), 2834 (w), 1728 (w), 1658 (s), 1606 (m), 1568 (m), 1506 (s), 1461 (m), 1438 (m), 1347 (m), 1286 (s), 1240 (m), 1172 (s), 1029 (s), 949 (m), 854 (m), 802 (m), 778 (m), 700 (m), 640 (m), 573 (m) cm⁻¹. HRMS (ESI): calcd for C₂₅H₂₆O₅ [M+H]⁺: 407.1853; found: 407.18548.

3.1.45. Ethyl 3-(bis(4-methoxyphenyl)methyl)-6-hydroxy-2,4-dimethylbenzoate (6ab). Starting with **4d** (0.600 g, 1.5 mmol) and **5b** (0.452 g, 1.65 mmol), **6ab** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a yellowish solid (0.232 g, 37%), mp 121–122 °C. ¹H NMR (300 MHz, CDCl₃): 1.28 (t, *J*=7.1 Hz, 3H, OCH₂CH₃), 1.97 (s, 3H, CH₃), 2.10 (s, 3H, CH₃), 3.72 (s, 6H, OCH₃), 4.30 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 5.81 (s, 1H, CH), 6.64 (s, 1H, CH_{Ar}), 6.72–6.75 (m, 2H, CH_{Ar}), 6.90–6.94 (m, 2H, CH_{Ar}), 10.56 (s, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz): δ=14.1, 21.1, 22.8 (CH₃), 49.1 (CH), 55.2 (OCH₃), 61.2 (OCH₃), 61.4 (OCH₂CH₃), 112.9 (C_{Ar}), 113.5, 117.8, 129.9 (CH_{Ar}), 134.4, 140.2, 145.2, 157.7 (C_{Ar}), 159.7 (C_{OH}), 171.5 (CO). IR (neat, cm⁻¹): 2952 (w), 2930 (w), 2833 (w), 1726 (w), 1651 (s), 1606 (m), 1581 (m), 1568 (m), 1506 (s), 1461 (m), 1393 (m), 1371 (m), 1324 (m), 1298 (m), 1240 (s), 1227 (s), 1172 (s), 1142 (s), 1109 (m), 1068 (m), 1029 (s), 838 (m), 800 (m), 778 (m), 724 (m), 700 (m), 640 (m), 608 (m) cm⁻¹. HRMS (ESI): calcd for C₂₆H₂₉O₅ [M+H]⁺: 421.19372; found: 421.18461.

3.1.46. Methyl 6-hydroxy-2,4-dimethyl-3-(1-phenylethyl)benzoate (6ac). Starting with **4e** (0.417 g, 1.5 mmol) and **5a** (0.429 g, 1.65 mmol), **6ac** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.233 g, 55%). ¹H NMR (300 MHz, CDCl₃): 1.58 (d, *J*=7.0 Hz, 3H, CH₃), 2.12 (s, 3H, CH₃), 2.14 (s, 3H, CH₃), 3.82 (s, 3H, OCH₃), 4.57 (q, *J*=7.4 Hz, 1H, CH), 6.63 (s, 1H, CH_{Ar}), 7.04–7.11 (m, 3H, CH_{Ar}), 10.41 (s, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz): δ=17.2, 20.1, 22.1 (CH₃), 37.6 (CH), 51.9 (OCH₃), 112.7 (C_{Ar}), 117.6, 125.4, 126.3, 128.2 (CH_{Ar}), 135.9, 139.2, 144.5, 145.4 (C_{Ar}), 159.4 (C_{OH}), 172.0 (CO). IR (neat, cm⁻¹): 3083 (w), 3024 (w), 2953 (w), 2876 (w), 1729 (w), 1659 (s), 1600 (m), 1570 (m), 1494 (m), 1460 (m), 1439 (m), 1348 (m), 1327 (m), 1266 (m), 1227 (s), 1195 (m), 1154 (m), 1072 (m), 1020 (m), 950 (w), 859 (w), 804 (m), 723 (m), 698 (m), 647 (m), 565 (w) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=284 (M⁺, 54), 253 (26), 252 (95), 238 (19), 237 (100), 166 (11),

165 (21). HRMS (EI): calcd for C₁₈H₂₀O₃ [M]⁺: 284.14070; found: 284.140521.

3.1.47. Benzyl 3-(1-(4-bromophenyl)ethyl)-6-hydroxy-2,4-dimethylbenzoate (6ad). Starting with **4f** (0.535 g, 1.5 mmol) and **5c** (0.429 g, 1.65 mmol), **6ad** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a solid (0.475 g, 72%), mp 147–148 °C. ¹H NMR (300 MHz, CDCl₃): 1.53 (d, *J*=7.2 Hz, 3H, CH₃), 2.10 (s, 3H, CH₃), 2.12 (s, 3H, CH₃), 4.45 (q, *J*=7.2 Hz, 1H, CH), 5.28 (s, 2H, OCH₂), 6.63 (s, 1H, CH_{Ar}), 6.89–6.92 (m, 2H, CH_{Ar}), 7.26–7.30 (m, 7H, CH_{Ar}), 10.45 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=16.3, 19.3, 21.1 (CH₃), 36.2 (CH), 66.3 (OCH₂), 111.7, 116.7 (CH_{Ar}), 118.1 (C_{Ar}), 128.1, 128.5, 128.6, 128.7, 131.2 (CH_{Ar}), 134.1, 138.2, 143.3, 143.4 (C_{Ar}), 158.7 (C_{OH}), 170.0 (CO). IR (neat, cm⁻¹): 3063 (w), 3034 (w), 2941 (w), 2880 (w), 1650 (s), 1596 (m), 1567 (m), 1482 (m), 1463 (m), 1453 (m), 1383 (m), 1343 (m), 1328 (m), 1291 (m), 1222 (s), 1162 (m), 1069 (m), 1017 (m), 1005 (s), 909 (w), 866 (w), 843 (w) 817 (m), 749 (m), 733 (m), 698 (s), 644 (m), 582 (m), 546 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=440 (M⁺, 3), 438 (3), 291 (10), 289 (11), 195 (10), 92 (13), 91 (100), 77 (10), 65 (12), 44 (12). HRMS (EI): calcd for C₂₄H₂₃O₃Br⁷⁹ [M]⁺: 438.08251; found: 438.082911, calcd for C₂₄H₂₃O₃Br⁸¹ [M]⁺: 440.08046; found: 440.081149.

3.1.48. Ethyl 6-hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2,4-dimethylbenzoate (6ae). Starting with **4g** (0.462 g, 1.5 mmol) and **5b** (0.452 g, 1.65 mmol), **6ae** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.225 g, 46%). ¹H NMR (300 MHz, CDCl₃): 1.26 (d, *J*=7.1 Hz, 3H, OCH₂CH₃), 1.53 (d, *J*=7.2 Hz, 3H, CH₃), 2.09 (s, 3H, CH₃), 2.14 (s, 3H, CH₃), 3.67 (s, 3H, OCH₃), 4.28 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 4.48 (q, *J*=7.2 Hz, 1H, CH), 6.59 (s, 1H, CH_{Ar}), 6.69–6.72 (m, 2H, CH_{Ar}), 6.92–6.95 (m, 2H, CH_{Ar}), 10.44 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=14.1, 17.5, 20.0, 22.1 (CH₃), 36.8 (CH), 55.2 (OCH₃), 112.9 (C_{Ar}), 113.6 (CH_{Ar}), 117.5 (C_{Ar}), 127.31 (CH_{Ar}), 135.8, 137.4, 139.2, 144.1, 157.3 (C_{Ar}), 159.3 (C_{OH}), 171.5 (CO). IR (neat, cm⁻¹): 2975 (w), 2935 (w), 2834 (w), 1736 (w), 1655 (s), 1607 (m), 1568 (m), 1509 (s), 1462 (m), 1393 (m), 1370 (m), 1299 (m), 1242 (s), 1224 (s), 1117 (m), 1153 (m), 1074 (m), 1030 (m), 953 (w), 859 (w), 830 (m), 755 (m), 743 (m), 607 (m), 562 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=328 (M⁺, 40), 313 (21), 283 (16), 282 (45), 268 (18), 267 (100). HRMS (EI): calcd for C₂₀H₂₄O₄ [M]⁺: 328.16691; found: 328.167020.

3.1.49. Methyl 5-ethyl-6-hydroxy-3-(1-(4-methoxyphenyl)ethyl)-2,4-dimethylbenzoate (6af). Starting with **4g** (0.462 g, 1.5 mmol) and **5f** (0.476 g, 1.65 mmol), **6af** was isolated after chromatography (silica gel, *n*-heptane/EtOAc) as a colourless oil (0.240 g, 47%). ¹H NMR (300 MHz, CDCl₃): 1.03 (t, *J*=7.4 Hz, 3H, CH₂CH₃), 1.18 (s, 3H, CH₃), 1.57 (d, *J*=7.2 Hz, 3H, CH₃), 1.58 (s, 3H, CH₃), 2.63 (q, *J*=7.4 Hz, 2H, CH₂CH₃), 3.71 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 4.59 (q, *J*=7.2 Hz, 1H, CH_{Ar}), 6.71–6.74 (m, 2H, CH_{Ar}), 6.94–6.98 (m, 2H, CH_{Ar}), 10.54 (s, 1H, OH). ¹³C NMR (CDCl₃, 62 MHz): δ=12.3, 16.1, 16.7, 18.8 (CH₃), 28.6 (CH₂), 36.1 (CH), 50.9 (OCH₃), 54.2 (OCH₃), 112.6, 126.2 (CH_{Ar}), 134.7, 136.8, 140.9, 156.0 (C_{Ar}), 156.3 (C_{OH}), 171.6 (CO). IR (neat, cm⁻¹): 2953 (w), 2925 (w), 2871 (w), 2853 (w), 2871 (w), 2853 (w), 1736 (w), 1655 (s), 1596 (m), 1562 (m), 1509 (s), 1438 (m), 1398 (m), 1371 (m), 1303 (m), 1274 (m), 1244 (s), 1176 (s), 1106 (m), 1033 (m), 1008 (m), 951 (w), 829 (m), 807 (m), 732 (m), 636 (m), 566 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%)=342 (M⁺, 95), 327 (21), 311 (28), 310 (100), 309 (10), 296 (14), 295 (69), 284 (13), 283 (15), 282 (70), 281 (10), 269 (26), 267 (39), 253 (11), 239 (11), 238 (16), 209 (10), 155 (10), 135 (11), 127 (11), 119 (13), 105 (10), 77 (11), 32 (12). HRMS (EI): calcd for C₂₁H₂₆O₄ [M]⁺: 342.18256; found: 342.182444.

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References and notes

- (a) Bindal, R. D.; Golab, J. T.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 7861; (b) Jendralla, H.; Granzer, E.; Kerekjarto, B. v.; Krause, R.; Schacht, U. *J. Med. Chem.* **1991**, *34*, 2962; (c) Costantino, L.; Ferrari, A. M.; Gamberini, M. C.; Rastelli, G. *Bioorg. Med. Chem.* **2002**, *10*, 3923; (d) Al-Qawasmeh, R. A.; Lee, Y.; Cao, M.-Y.; Gu, X.; Vassilakos, A.; Wright, J. A.; Young, A. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 347; (e) Mibu, N.; Yokomizo, K.; Uyeda, M.; Sumoto, K. *Chem. Pharm. Bull.* **2003**, *51*, 1325; (f) Schultz, T. W.; Sinks, G. D.; Cronin, M. T. D. *Environ. Toxicol.* **2002**, *17*, 14; (g) Wang, P.; Kozlowski, J.; Cushman, M. J. *Org. Chem.* **1992**, *57*, 3861; (h) Long, Y.-Q.; Jiang, X.-H.; Dayam, R.; Sanchez, T.; Shoemaker, R.; Sei, S.; Neamati, N. *J. Med. Chem.* **2004**, *47*, 2561; (i) Matulenko, M. A.; Surber, B.; Fan, L.; Kolasa, T.; Nakane, M.; Terranova, M. A.; Uchic, M. E.; Miller, L. N.; Chang, R.; Donnelly-Roberts, D. L.; Namovic, M. T.; Moreland, R.; Brioni, J. D.; Stewart, A. O. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5095.
- (a) Bai, L.; Masukawa, N.; Yamaki, M.; Takagi, S. *Phytochemistry* **1998**, *47*, 1637; (b) Jin, C.; Michetich, R. G.; Daneshtalab, M. *Phytochemistry* **1999**, *50*, 505; (c) Bindal, R. D.; Katzenellenbogen, J. A. *J. Med. Chem.* **1988**, *31*, 1978; (d) Seligmann, O.; Wagner, H. *Tetrahedron* **1981**, *37*, 2601.
- (a) Cushman, M.; Kanamathareddy, S.; De Clerq, E.; Schols, D.; Goldman, M. E.; Bowen, J. A. *J. Med. Chem.* **1991**, *34*, 337; (b) Parmar, V. S.; Bisht, K. S.; Jain, R.; Singh, S.; Sharma, S. K.; Gupta, S.; Malhotra, S.; Tyagi, O. D.; Vardhan, A.; Pati, H. N. *Indian J. Chem., Sect. B* **1996**, *35*, 220.
- (a) Jovel, I.; Mertins, K.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem.* **2005**, *117*, 3981; *Angew. Chem., Int. Ed.* **2005**, *44*, 3913; (b) Mertins, K.; Jovel, I.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem.* **2005**, *117*, 242; *Angew. Chem., Int. Ed.* **2005**, *44*, 238.
- (a) Christoffers, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3141; (b) Christoffers, J. *Eur. J. Org. Chem.* **1998**, *7*, 1259; (c) Christoffers, J.; Oertling, H. *Tetrahedron* **2000**, *56*, 1339.
- Kischel, J.; Mertins, K.; Michalik, D.; Zapf, A.; Beller, M. *Adv. Synth. Catal.* **2007**, *349*, 865.
- (a) Bisaro, F.; Prestat, G.; Vitale, M.; Poli, G. *Synlett* **2002**, 1823; (b) Gullickson, G. C.; Lewis, D. E. *Aust. J. Chem.* **2003**, *56*, 385; (c) Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem.* **2006**, *118*, 807; *Angew. Chem., Int. Ed.* **2006**, *45*, 793; (d) Rueping, M.; Nachtsheim, B. J.; Ieawsuwan, W. *Adv. Synth. Catal.* **2006**, *348*, 1033; (e) Yao, X.; Li, C. *J. Am. Chem. Soc.* **2004**, *126*, 6884; (f) Yao, X.; Li, C. *J. Org. Chem.* **2005**, *70*, 5752; (g) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem.* **2006**, *118*, 2667; *Angew. Chem., Int. Ed.* **2006**, *45*, 2605.
- (a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534; (b) Brownbridge, P.; Chan, T.-H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688.
- Review of [3+3] cyclizations: Feist, H.; Langer, P. *Synthesis* **2007**, 327.
- Review of 1,3-bis(trimethylsilyloxy)-1,3-dienes: Langer, P. *Synthesis* **2002**, 441.
- Ahmad, R.; Riahi, A.; Langer, P. *Tetrahedron Lett.* **2009**, *50*, 1490.
- CCDC-756115, 756116, and 756117 contain all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk.