Synthesis of Functionalized Salicylates by Formal [3+3] Cyclocondensation of 1,3-Bis(silyloxy)buta-1,3-dienes with 3-Alkoxy-2-en-1-ones

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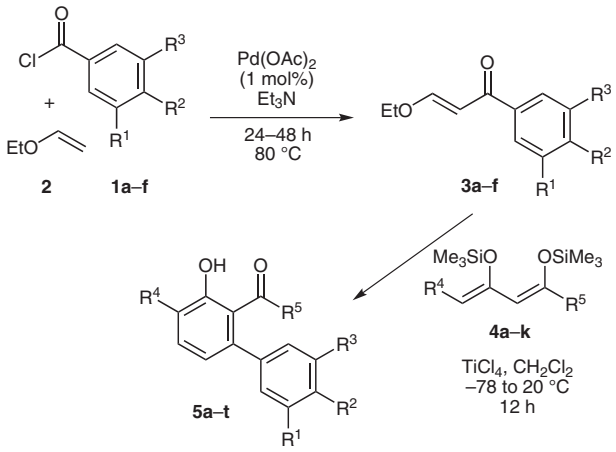
Abstract: The formal [3+3] cyclization of 1,3-bis(silyloxy)buta-1,3-dienes with 1-aryl-3-ethoxyprop-2-en-1-ones, available by Heck reaction of benzoyl chlorides with ethyl vinyl ether, afforded a variety of 6-arylsalicylates. The reaction of the products with concentrated sulfuric acid resulted in the formation of fluorenones. 6-Alkylsalicylates were prepared by cyclization of 1,3-bis(silyloxy)buta-1,3-dienes with aliphatic enones.

Key words: arenes, cyclizations, palladium, regioselectivity, silyl enol ethers

6-Alkyl- and 6-arylsalicylates are of considerable pharmacological importance. Aryl-substituted salicylates can be regarded as functionalized biphenyl derivatives and represent important substructures of pharmacologically relevant natural and non-natural molecules. Examples include cytotoxic and hepatoprotective glycoside esters (e.g., amaroswerin),[1] cancerostatic benzo[1,2-*c*]phenanthridin-14-ones (e.g., sanguinarinone and oxysanguinarine),[2] dibenzo[*b*,*d*]pyran-6-ones (e.g., the antitumor-active graphislactones),[3] simple biaryls,[4] complex macrocycles (e.g., sanguine),[5] dibenzoorthoquinones (e.g., murayaquinone),[6] 9,10-dihydrophenanthrenes (e.g., juncunone),[7] and the cynandiones (exhibiting a considerable in vitro activity against hepatocytes, human bladder carcinoma T-24 cells, epidermoid carcinoma KB cells, and human hepatoma PLC/PRF/5 cells).[8]

Palladium(0)-catalyzed cross-coupling reactions constitute the most widely used synthetic approach to biphenyl derivatives.[9] In general, these methods are broadly applicable. However, the synthesis of sterically encumbered products can be difficult or not possible at all. In addition, the synthesis of the required starting materials, functionalized aryl halides or phenols, can be a difficult and tedious task, due to the low regioselectivity of electrophilic aromatic substitution reactions (e.g., brominations) or due to the low reactivity of electron-poor arenes. An alternative strategy for the synthesis of biphenyls relies on the assembly of the benzene moiety by cyclization reactions. Chan et al. were the first to report[10] the formal [3+3] cyclization[11] of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes[12] with 3-trimethylsilyloxy-2-en-1-ones. In recent years, we have reported the application of this method to the synthesis of a variety of functionalized arenes. Recently, we have reported the synthesis of aryl-substituted salicylates by application of a 'Heck cross-coupling/[3+3] cyclization' strategy.[13] Herein, we report full details of this study. With regard to our preliminary communication, the scope was extended to alkyl-substituted derivatives. In addition, the method was applied to the synthesis of novel functionalized fluorenones. It is worth noting that the sterically encumbered and functionalized arenes prepared are not readily available by other methods.

1-Aryl-3-ethoxyprop-2-en-1-ones **3a**–**f** were prepared, following a known procedure,[14] by Heck reaction of benzoyl chlorides **1a**–**f** with ethyl vinyl ether (**2**) (Scheme 1). The best yields of enones **3** were obtained for **3a**, **3b**, and **3f**. While **3f**, containing three methoxy groups located at the phenyl group, could be isolated in good yield, lower yields were observed for **3d** and **3e** each containing only one methoxy group. 1,3-Bis(trimethylsilyloxy)buta-1,3-dienes **4a**–**k** are available from the corresponding 1,3-dicarbonyl compounds in two steps.[10] The $TiCl_4$-mediated cyclization of **3a**–**f** with 1,3-bis(trimethylsilyloxy)buta-1,3-dienes **4a**–**k** afforded the 6-arylsalicylates **5a**–**t** (Scheme 1, Table 1). All cyclizations proceeded with excellent regioselectivity in favor of the isomers containing the aryl group located *ortho* to the ester group. All products were isomerically pure (ratio >98:2). The regioisomers, containing the aryl group located *para* to the ester group, could not be isolated. The best yields of products **5** were generally obtained when the reaction was carried out



Scheme 1 Synthesis of 6-arylsalicylates **5a**–**t**

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Table 1 Synthesis of 6-Arylsalicylates **5a–t**

3	4	5	R^1	R^2	R^3	R^4	R^5	3 Yield (%)[a]	5 Yield (%)[a]
a	**a**	**a**	H	H	H	H	OMe	49	36
a	**b**	**b**	H	H	H	H	$O(CH_2)_2OMe$	–	30
a	**c**	**c**	H	H	H	Et	OEt	–	43
a	**d**	**d**	H	H	H	*n*-Pr	OMe	–	56
a	**e**	**e**	H	H	H	*n*-C_8H_{17}	OMe	–	70
a	**f**	**f**	H	H	H	$(CH_2)_3Ph$	OMe	–	32
a	**g**	**g**	H	H	H	OMe	OMe	–	20
b	**a**	**h**	H	Cl	H	H	OMe	51	35
b	**c**	**i**	H	Cl	H	Et	OEt	–	25
b	**f**	**j**	H	Cl	H	$(CH_2)_3Ph$	OMe	–	33
b	**g**	**k**	H	Cl	H	OMe	OMe	–	24
c	**a**	**l**	H	NO_2	H	H	OMe	22	30
d	**a**	**m**	H	OMe	H	H	OMe	32	48
d	**h**	**n**	H	OMe	H	Me	OMe	–	48
d	**d**	**o**	H	OMe	H	*n*-Pr	OMe	–	86
e	**a**	**p**	OMe	H	H	H	OMe	30	20
e	**i**	**q**	OMe	H	H	*n*-C_6H_{13}	OMe	–	30
f	**j**	**r**	OMe	OMe	OMe	H	O*i*-Bu	54	31
f	**f**	**s**	OMe	OMe	OMe	$(CH_2)_3Ph$	OMe	–	37
f	**k**	**t**	OMe	OMe	OMe	Me	Et	–	12

[a] Yields of isolated products.

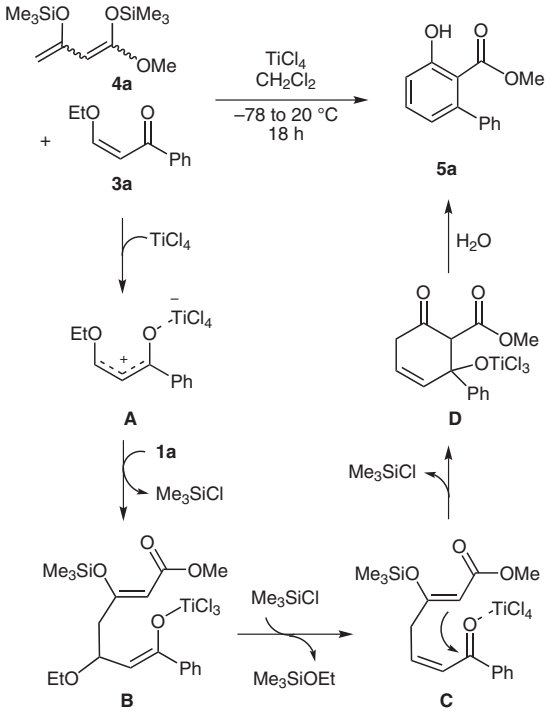
in a highly concentrated solution using stoichiometric amounts of the starting materials.

The regioselective formation of **5a** can be explained by the reaction of **3a** with $TiCl_4$ to give first the allylic cation **A**. The attack of the terminal carbon atom of **4a** onto **A** results in the formation of intermediate **B**. The elimination of (methoxy)trimethylsilane (intermediate **C**) and subsequent cyclization give the intermediate **D**. The elimination of titanium hydroxide and aromatization result in the formation of product **5a** (Scheme 2).

Regarding the [3+3] cyclocondensations, the best yields were obtained for products **5n** and **5o** derived from enone **3d** (containing one methoxy group located at the *para*-position of the phenyl group). Interestingly, the yields of products **5m**–**o**, derived from **3d**, are generally higher than those of the products derived from **3e** (containing one methoxy group located at the *meta*-position) or derived from **3f** (containing three methoxy groups). The yields of products **5h**–**k** and **5l**, containing an electron-withdrawing chloro or nitro group located at the *para*-position of the phenyl group, were generally lower than those of products **5m**–**o**. The yields of the products derived from dienes **4c**–**e**,**i**, containing an alkyl group attached to carbon C-4 of the diene moiety, are generally higher than the yields of those products derived from unsubstituted dienes. The low yield of **5t** can be explained by the generally lower reactivity of 1,3-diketone-derived compared to β-keto ester-derived 1,3-bis(trimethylsilyloxy)buta-1,3-dienes. The Heck reaction of *ortho*-substituted benzoyl chlorides failed to give the corresponding enones. All other attempts to prepare these compounds also failed (e.g., the reaction of *ortho*-substituted acetophenone derivatives with triethyl orthoformate). Therefore, the reaction of *ortho*-substituted 1-aryl-3-ethoxyprop-2-en-1-ones with 1,3-bis(silyloxy)buta-1,3-dienes could not be studied.

The structures of all products were established by spectroscopic methods. The structure of **5i** was independently confirmed by X-ray crystal structure analysis (Figure 1).[15]

The hydroxyl group of the 6-arylsalicylates can be functionalized by palladium-catalyzed cross-coupling reactions.[16] Biaryl derivative **5a** was transformed into its triflate **6** (Scheme 3). The Suzuki reaction of **6** with phe-



Scheme 2 Regioselectivity of the cyclization of **3a** with **4a**

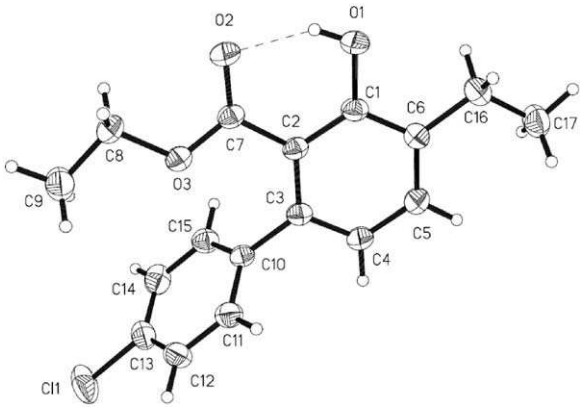
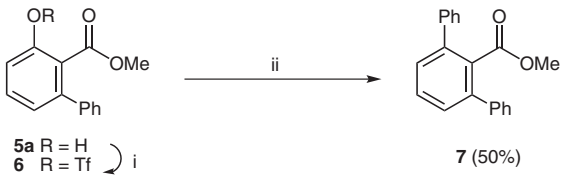


Figure 1 X-ray crystal structure of **5i**



Scheme 3 Synthesis of **7**: *Reagents and conditions*: *i*) Tf_2O, pyridine, –78 to –10 °C; *ii*) $PhB(OH)_2$, K_3PO_4, $Pd(PPh_3)_4$, 1,4-dioxane, 12 h, reflux

nylboronic acid afforded product **7**. The structure of **7** was independently confirmed by X-ray crystal structure analysis (Figure 2).[15]

The bromination of **3a** and **3e** afforded **8a** and **8b**, respectively (Scheme 4, Table 2). The $TiCl_4$-mediated cyclization of **8a**,**b** with 1,3-bis(trimethylsilyloxy)buta-1,3-dienes **4a**,**h**,**l** afforded the 6-aryl-5-bromosalicylates **9a**–**d**. It is noteworthy that these reactions represent what are, to the best of our knowledge, the first [3+3] cyclizations of bromine-containing substrates. The transformations are of synthetic utility, since the bromide group can be further functionalized by palladium(0)-catalyzed cross-coupling reactions and other transformations. Generally, highly substituted brominated arenes are not readily available by electrophilic substitutions, due to the formation of regioisomers. The structure of **9a** was independently confirmed by X-ray crystal structure analysis.[13]

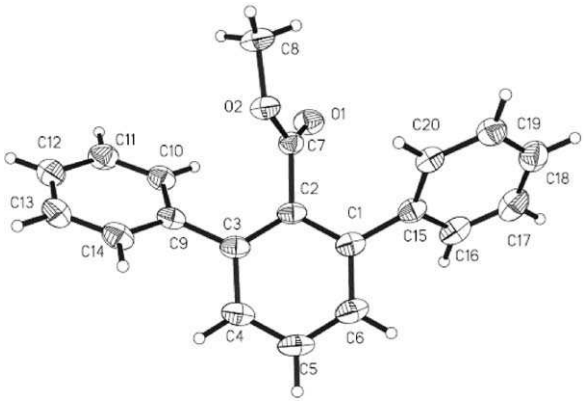
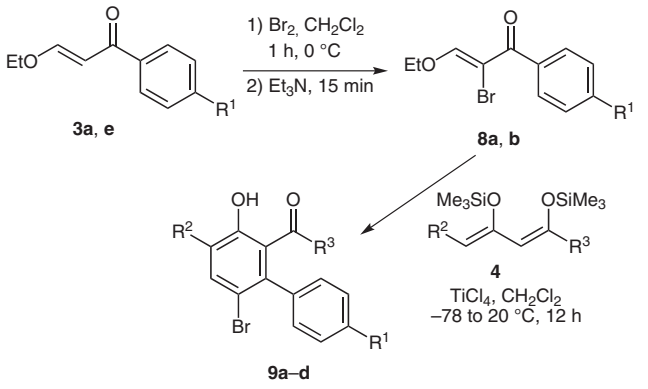


Figure 2 X-ray crystal structure of **7**

The structures of salicylates **5a**,**d**,**e**,**k**, and **9b** were independently confirmed as follows: Treatment of these compounds with concentrated sulfuric acid, following conditions earlier reported by us,[16] resulted in the formation of the novel fluorenones **10a**–**e** in excellent yields (Scheme 5, Table 3). This result indicates that the phenyl

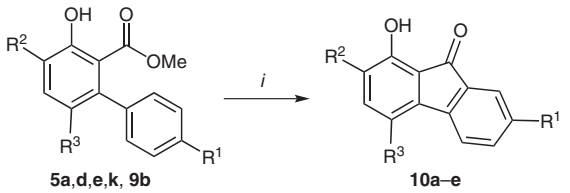


Scheme 4 Synthesis of 6-aryl-5-bromosalicylates **9a**–**d**

Table 2 Synthesis of 6-Aryl-5-bromosalicylates **9a**–**d**

3	8	4	9	R^1	R^2	R^3	**8** Yield (%)[a]	**9** Yield (%)[a]
a	**a**	**a**	**a**	H	H	OMe	61	50
a	**a**	**h**	**b**	H	Me	OMe	–	52
e	**b**	**h**	**c**	MeO	Me	OMe	36	48
e	**b**	**l**	**d**	MeO	H	OEt	–	22

[a] Yields of isolated products.



Scheme 5 Synthesis of fluorenones **10a**–**e**: *Reagents and conditions*: *i*) H_2SO_4, 1 h, 0 °C

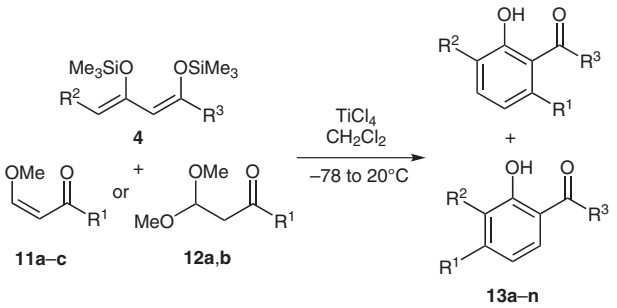
Table 3 Synthesis of **10a**–**e**

Starting material	**10**	R^1	R^2	R^3	**10** Yield (%)[a]
5a	**a**	H	H	H	81
5e	**b**	H	*n*-C_8H_{17}	H	84
5d	**c**	H	*n*-Pr	H	96
5k	**d**	Cl	OMe	H	96
9b	**e**	H	Me	Br	82

[a] Yields of isolated products.

group of the starting material is located *ortho* to the ester group.

The $TiCl_4$-mediated cyclization of 1,3-bis(silyloxy)buta-1,3-dienes **4b**,**g**,**h**,**i**,**m**,**n** with 4-methoxybut-3-en-2-one (**11a**) afforded the 6-methylsalicylates **13a**–**f** (Scheme 6, Table 4). Chan and Brownbridge previously reported the cyclization of **4a** with **11a**.[10a] All products were formed with excellent regioselectivity in favor of the isomer containing the methyl group (R^1) located *ortho* to the ester group.



Scheme 6 Synthesis of phenols **13a**–**n**

The yields of products **13a** and **13f**, derived from dienes containing an alkyl group attached to carbon C-4 of the diene, were higher than those of the products derived from unsubstituted dienes. The cyclization of **4h** with 5-methoxypent-4-en-3-one (**11b**) afforded the 6-ethylsalicylate **13g**. The yield of **13g** was lower than the yield of product **13a** derived from **11a**. In addition, the product was isolated as a 4:1 mixture of regioisomers (the major isomer contains the ethyl group located ortho to the ester group). Product **13h** was isolated as a pure regioisomer, albeit in low yield, from the reaction of **4h** with 6-methoxyhex-5-en-4-one (**11c**).

Table 4 Synthesis of phenols **13a**–**n**

11,**12**	**4**	**13**	R^1	R^2	R^3	**13** Yield (%)[a]	rs[b]
11a	**h**	**a**	Me	Me	OMe	40	>98:2
11a	**g**	**b**	Me	OMe	OMe	38	>98:2
11a	**m**	**c**	Me	H	Me	33	>98:2
11a	**b**	**d**	Me	H	$O(CH_2)_2OMe$	24	>98:2
11a	**n**	**e**	Me	Cl	OEt	15	>98:2
11a	**i**	**f**	Me	*n*-C_6H_{13}	OMe	55	>98:2
11b	**h**	**g**	Et	Me	OMe	30	4:1
11c	**h**	**h**	*n*-Pr	Me	OMe	18	>98:2
12a	**l**	**i**	Et	H	OEt	56	6:1
12a	**m**	**j**	Et	H	Me	46	4:1
12a	**n**	**k**	Et	H	Ph	72	4:1
12a	**k**	**l**	Et	Me	Et	34	4:1
12b	**l**	**m**	*n*-Pr	H	OEt	32	10:1
12b	**g**	**n**	*n*-Pr	OMe	OMe	28	8:1

[a] Yields of isolated products.
[b] Regioselectivity in favor of the isomer containing the alkyl group R^1 located *ortho* to the COR^3 group.

The $TiCl_4$-mediated cyclization of 1,3-bis(silyloxy)buta-1,3-dienes **4g**,**k**–**n** with ketoacetals **12a** and **12b** afforded products **13i**–**n** as mixtures of regioisomers. The ratios vary from 4:1 to 10:1. The major isomers contain the ethyl or propyl group located *ortho* to the ester or acyl group. The yields of the products derived from **12a** are generally higher than the yields of those products derived from **12b**.

In conclusion, we have reported a convenient and regioselective synthesis of 6-alkyl- and 6-arylsalicylates by formal [3+3] cyclizations of 1,3-bis(silyloxy)buta-1,3-dienes with 3-alkoxyprop-2-en-1-ones.

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 data 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.

Heck Reaction of Ethyl Vinyl Ether with Acid Chlorides; 3-Ethoxy-1-phenylpropenone (3a) Typical Procedure[14]

To a mixture of ethyl vinyl ether (2.90 g, 40.0 mmol) and Et_3N (1.20 g, 12.0 mmol) in a pressure tube was added $Pd(OAc)_2$ (20 mg, 0.1 mmol) under argon. The mixture was stirred until a clear yellow solution was formed. To the mixture was added benzoyl chloride (1.20 g, 10.0 mmol) and stirred at 80 °C for 24 h. The mixture was

poured into Et_2O (50 mL) and the solid (Et_3N·HCl) was filtered off. The filtrate was concentrated under reduced pressure and the residue was purified by chromatography (silica gel, heptanes–EtOAc, 10:1 → 5:1) to give **3a** as a slightly yellow oil (3.80 g, 55%).

Biphenyls 5a–t; 3-Hydroxybiphenyl-2-carboxylic Acid Methyl Ester (5a); Typical Procedure

To a CH_2Cl_2 solution (1 mL) of 3-ethoxy-1-phenylpropenone (**3a**; 176 mg, 1.0 mmol) and of **4a** (260 mg, 1.0 mmol) was added a CH_2Cl_2 solution (5 mL) of $TiCl_4$ (0.12 mL, 1.0 mmol) at –78 °C. The temperature of the solution was allowed to warm to 20 °C within 14 h. To the mixture was added CH_2Cl_2 (10 mL) and 10% aq HCl (10 mL). The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (heptanes–EtOAc, 10:1) to give **5a** as a slightly yellow oil (0.081 g, 36%).

IR (neat): 3059 (w), 3028 (w), 2952 (w), 2851 (w), 1735 (w), 1667 (s), 1601 (m), 1571 (m), 1501 (w), 1439 (s), 1343 (m), 1270 (m), 1220 (s), 1172 (m), 1124 (m), 1097 (m), 1065 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.35 (s, 3 H, OCH_3), 6.68 (d, ^3J = 7.5 Hz, 1 H_{arom}), 6.87 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.08–7.30 (m, 6 H_{arom}), 10.49 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.0 (OCH_3), 112.5 (C_{arom}), 117.0, 123.0, 127.2, 128.0, 128.5, 134.0 (CH_{arom}), 143.0, 145.2, 161.7 (C_{arom}), 171.7 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 228 (M^+, 36), 196 (100), 168 (53), 139 (33).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}O_3$ (M^+): 228.0781; found: 228.0786.

3-Hydroxybiphenyl-2-carboxylic Acid Methoxyethyl Ester (5b)

Starting from **3a** (0.352 g, 2.0 mmol) and 1-(2-methoxyethoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4b**; 0.912 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5b** was isolated as a yellow oil (0.082 g, 30%).

IR (neat): 3057 (w), 3026 (w), 2982 (w), 2927 (w), 2881 (w), 2840 (w), 2819 (w), 1732 (w), 1659 (s), 1598 (m), 1570 (m), 1500 (w), 1449 (m), 1437 (m), 1406 (w), 1375 (m), 1312 (m), 1268 (s), 1215 (s), 1172 (s), 1120 (s), 1094 (s), 1063 (m), 1024 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.95 (t, ^3J = 4.8 Hz, 2 H, CH_2), 3.06 (s, 3 H, OCH_3), 4.02 (t, ^3J = 4.8 Hz, 2 H, CH_2), 6.71 (d, ^3J = 7.4 Hz, 1 H_{arom}), 6.91 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.15–7.35 (m, 6 H_{arom}), 10.51 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 58.6 (OCH_3), 63.8, 69.1 (CH_2), 112.1 (C_{arom}), 116.6, 122.5, 126.6, 127.5, 128.2, 133.6 (CH_{arom}), 142.9, 144.9, 161.3 (C_{arom}), 170.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 272 (M^+, 27), 197 (25), 196 (100), 168 (33), 139 (17).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_4$ (M^+): 272.1043; found: 272.1040.

4-Ethyl-3-hydroxybiphenyl-2-carboxylic Acid Ethyl Ester (5c)

Starting from **3a** (0.176 g, 1.0 mmol) and 1-ethoxy-1,3-bis(trimethylsilyloxy)hexa-1,3-diene (**4c**; 0.302 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5c** was isolated as a colorless solid (0.109 g, 43%); mp 49–51 °C.

IR (neat): 3049 (w), 3022 (w), 2991 (w), 2963 (w), 2931 (w), 2873 (w), 1646 (s), 1615 (w), 1601 (w), 1567 (w), 1498 (w), 1470 (w), 1456(w), 1440 (w), 1417 (m), 1398 (m), 1372 (s), 1340 (m), 1303 (w), 1288 (s), 1240 (s), 1193 (m), 1166 (s), 1150 (w), 1110 (w), 1101 (m), 1063 (w), 1017 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.61 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.13 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.60 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.84 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.61 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.06–7.20 (m, 6 H_{arom}), 10.86 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 12.9 (OCH_2CH_3), 13.6 (CH_2CH_3), 22.9 (CH_2CH_3), 60.9 (OCH_2CH_3), 111.6 (C_{arom}), 121.7, 126.4, 127.5, 128.2 (CH_{arom}), 131.4 (C_{arom}), 132.7 (CH_{arom}), 142.3, 143.3, 159.3 (C_{arom}), 171.4 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 270 (M^+, 57), 225 (16), 224 (76), 223 (20), 209 (42), 207 (18), 206 (100), 181 (24), 178 (16), 165 (18), 153 (209, 152 (40).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_3$ (M^+): 270.1250; found: 270.1253.

3-Hydroxy-4-propylbiphenyl-2-carboxylic Acid Methyl Ester (5d)

Starting from **3a** (0.352 g, 2.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)hepta-1,3-diene (**4d**; 0.906 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5d** was isolated as a yellow oil (0.300 g, 56%).

IR (neat): 3057 (w), 3026 (w), 2955 (m), 2931 (m), 2870 (w), 1661 (s), 1610 (m), 1600 (m), 1567 (m), 1436 (s), 1413 (s), 1343 (m), 1268 (s), 1236 (s), 1195 (s), 1144 (s), 1105 (m), 1073 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, ^3J = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.68 (sext, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 2.67 (t, ^3J = 7.3 Hz, 2 H, $CH_2CH_2CH_3$), 3.47 (s, 3 H, OCH_3), 6.73 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.19–7.36 (m, 6 H_{arom}), 10.79 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.5, 31.9 (CH_2), 51.6 (OCH_3), 111.5 (C_{arom}), 121.8, 126.5, 127.5, 128.1 (CH_{arom}), 129.9 (C_{arom}), 133.8 (CH_{arom}), 142.2, 142.9, 159.2 (C_{arom}), 171.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 270 (M^+, 71), 238 (69), 237 (23), 221 (59), 210 (83), 209 (100), 196 (22), 181 (21), 165 (19), 153 (25), 152 (77), 151 (17).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_3$ (M^+): 270.1250; found: 270.1254.

3-Hydroxy-4-octylbiphenyl-2-carboxylic Acid Methyl Ester (5e)

Starting from **3a** (0.328 g, 2.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)dodeca-1,3-diene (**4e**; 1.117 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5e** was isolated as a yellow oil (0.476 g, 70%).

IR (neat): 3026 (w), 2952 (m), 2922 (s), 2853 (s), 1751 (w), 1714 (w), 1662 (s), 1623 (m), 1601 (w), 1569 (w), 1437 (s), 1414 (m), 1376 (m), 1342 (m), 1312 (m), 1268 (m), 1233 (s), 1196 (m), 1145 (s), 1109 (w), 1072 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 [t, ^3J = 6.7 Hz, 3 H, $CH_2(CH_2)_6CH_3$], 1.25–1.67 [m, 12 H, $CH_2(CH_2)_6CH_3$], 2.68 [t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_6CH_3$], 3.73 (s, 3 H, OCH_3), 6.73 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.19–7.38 (m, 6 H_{arom}), 10.78 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6, 27.2, 29.2, 29.3, 29.6, 31.2, 31.8 (CH_2), 51.6 (OCH_3), 111.5 (C_{arom}), 121.8, 126.5, 127.5, 128.1 (CH_{arom}), 130.2 (C_{arom}), 133.7 (CH_{arom}), 142.9, 159.2, 171.8 (C_{arom}), 206.4 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 340 (M^+, 39), 210 (100), 209 (71), 180 (15), 153 (15), 152 (38).

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{28}O_3$ $(M + H)^+$: 341.2111; found: 341.2109.

3-Hydroxy-4-(3-phenylpropyl)biphenyl-2-carboxylic Acid Methyl Ester (5f)

Starting from **3a** (0.176 g, 1.0 mmol) and 7-methoxy-5,7-bis(trimethylsilyloxy)hepta-4,6-dienylbenzene (**4f**; 0.378 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5f** was isolated as a yellow oil (0.112 g, 32%).

IR (neat): 3083 (w), 3059 (w), 3026 (m), 2949 (m), 2858 (w), 1663 (s), 1601 (m), 1568 (w), 1496 (m), 1437 (s), 1416 (s), 1345 (s), 1270 (s), 1240 (s), 1197 (s), 1151 (s), 1101 (w), 1075 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.87 (m, 2 H, CH_2), 2.60 (m, 4 H, CH_2), 3.34 (s, 3 H, OCH_3), 6.61 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.02–7.25 (m, 11 H_{arom}), 10.69 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 29.6, 30.8, 35.7 (CH_2), 51.6 (OCH_3),111.6 (C_{arom}), 121.8, 125.6, 126.6, 127.5, 128.1, 128.2, 128.4 (CH_{arom}), 129.6 (C_{arom}), 133.7 (CH_{arom}), 142.3, 142.4, 142.9, 159.3 (C_{arom}), 171.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 346 (M^+, 29), 211 (15), 210 (100), 209 (18).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}O_3$ (M^+): 346.1563; found: 346.1567.

3-Hydroxy-4-methoxybiphenyl-2-carboxylic Acid Methyl Ester (5g)

Starting from **3a** (0.176 g, 1.0 mmol) and 1,4-dimethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4g**; 0.290 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5g** was isolated as a yellow oil (0.046 g, 20%).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.52 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 6.78 (d, ^3J = 8.2 Hz, 1 H_{arom}), 7.01 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.21–7.35 (m, 5 H_{arom}), 10.06 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.8, 56.2 (OCH_3), 113.5 (C_{arom}), 114.2, 121.5, 126.6, 127.6, 128.2 (CH_{arom}), 135.6, 142.1, 147.5, 150.1 (C_{arom}), 170.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 49), 227 (22), 226 (100), 225 (23), 180 (18), 139 (18), 127 (37).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_4$ (M^+): 258.0886; found: 258.0892.

4′-Chloro-3-hydroxybiphenyl-2-carboxylic Acid Methyl Ester (5h)

Starting from 1-(4-chlorophenyl)-3-ethoxypropenone (**3b**; 0.209 g, 1.0 mmol) and **4a** (0.260 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5h** was isolated as a yellow oil (0.090 g, 35%).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.46 (s, 3 H, OCH_3), 6.69 (d, ^3J = 7.5 Hz, 1 H_{arom}), 6.95 (d, ^3J = 8.4 Hz, 1 H_{arom}), 7.15 (d, ^3J = 8.4 Hz, 2 H_{arom}), 7.33(d, ^3J = 8.4 Hz, 2 H_{arom}), 7.40 (dd, ^3J = 7.6 Hz, 1 H_{arom}), 10.65 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.8 (OCH_3), 118.8 (C_{arom}), 117.0, 122.4, 127.7, 129.3 (CH_{arom}), 132.8 (C_{arom}) 133.8 (CH_{arom}), 141.2, 143.5, 161.6 (C_{arom}), 171.0 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 264 (M^+, ^{37}Cl, 12), 262 (M^+, ^{35}Cl, 33), 232 (33), 230 (100), 202 (36), 139 (44).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}ClO_3$ (M^+): 262.0391; found: 262.0396.

Anal. Calcd for $C_{14}H_{11}ClO_3$: C, 64.01; H, 4.22. Found: C, 63.66; H, 4.27.

4′-Chloro-4-ethyl-3-hydroxybiphenyl-2-carboxylic Acid Ethyl Ester (5i)

Starting from **3b** (0.420 g, 2.0 mmol) and **4c** (0.906 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5i** was isolated as a yellow oil (0.150 g, 25%).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.25 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.72 (q, ^3J = 7.5 Hz, 2H, CH_2CH_3), 4.01 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.68 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.13–7.41 (m, 5 H_{arom}), 11.08 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.0 (OCH_2CH_3), 13.6 (CH_2CH_3), 22.9 (CH_2CH_3), 61.1 (OCH_2CH_3), 111.2 (C_{arom}), 121.6, 127.6 (CH_{arom}), 128.2 (C, Ar), 129.5 (CH_{arom}), 131.9 (C_{arom}), 132.8 (CH_{arom}), 140.9, 141.8, 159.6 (C_{arom}), 171.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 306 (M^+, ^{37}Cl, 24), 304 (M^+, ^{35}Cl, 69), 259 (49), 258 (43), 257 (100), 230 (18), 223 (79), 195 (21), 165 (33), 152 (38).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{17}ClO_3$ (M^+): 304.0860; found: 304.0864.

4′-Chloro-3-hydroxy-4-(3-phenylpropyl)biphenyl-2-carboxylic Acid Methyl Ester (5j)

Starting from **3b** (0.210 g, 1.0 mmol) and **4f** (0.378 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5j** was isolated as a yellow solid (0.127 g, 33%); mp 65–67 °C.

IR (neat): 3078 (w), 3057 (w), 3024 (w), 2939 (w), 2917 (w), 2855 (w), 1656 (s), 1612 (w), 1600 (w), 1576 (w), 1493 (m), 1436 (m), 1421 (s), 1396 (w), 1348 (s), 1299 (w), 1279 (s), 1268 (m), 1245 (s), 1201 (m), 1160 (m), 1135 (w), 1100 (w), 1085 (m), 1049 (w), 1025 (w), 1016 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.86 (m, 2 H, CH_2), 2.60 (m, 4 H, CH_2), 3.38 (s, 3 H, OCH_3), 6.38 (s, 1 H_{arom}), 6.55 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.00–7.20 (m, 9 H_{arom}), 10.79 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 29.6, 30.8, 35.6 (CH_2), 51.7 (OCH_3), 111.3 (C_{arom}), 121.7, 125.6, 127.7, 128.2, 128.4, 129.4, 130.1 (CH_{arom}), 132.6 (C_{arom}), 133.8 (CH_{arom}), 141.0, 141.4, 142.3, 159.6 (C_{arom}), 171.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 382 (M^+, ^{37}Cl, 9), 380 (M^+, ^{35}Cl, 29), 244 (35), 209 (100), 97 (23).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{21}ClO_3$ (M^+): 380.1173; found: 380.1177.

4′-Chloro-3-hydroxy-4-methoxybiphenyl-2-carboxylic Acid Methyl Ester (5k)

Starting from **3b** (0.210 g, 1.0 mmol) and **4g** (0.290 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5k** was isolated as a yellow oil (0.070 g, 24%).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.54 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 6.71 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.00 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.16 (d, ^3J = 8.5 Hz, 2 H_{arom}), 7.32 (d, ^3J = 8.5 Hz, 2 H_{arom}), 10.20 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.9, 56.1 (OCH_3), 113.1 (C_{arom}), 114.2, 121.4, 127.7, 129.6 (CH_{arom}), 132.5, 134.1, 140.7, 147.8, 150.5 (C_{arom}), 170.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 294 (M^+, ^{37}Cl, 15), 292 (M^+, ^{35}Cl, 45), 262 (433), 261 (26), 260 (100), 231 (25), 225 (56), 217 (22), 197 (19).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}ClO_4$ (M^+): 292.0496; found: 292.0500.

3-Hydroxy-4′-nitrobiphenyl-2-carboxylic Acid Methyl Ester (5l)

Starting from 3-ethoxy-1-(4-nitrophenyl)propenone (**3c**; 0.209 g, 1.0 mmol) and **4a** (0.260 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5l** was isolated as a yellow oil (0.077 g, 30%).

IR (neat): 3106 (m), 2959 (w), 2849 (w), 1664 8s), 1603 (s), 1573 (m), 1445 (s), 1439 (s), 1347 (s), 1276, 1216 (s), 1174 (s), 1126 (m), 1108 (m), 1065 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.50 (s, 3 H, OCH_3), 6.75 (d, ^3J = 7.5 Hz, 1 H_{arom}), 7.08 (d, ^3J = 8.4 Hz, 1 H_{arom}), 7.39 (d, ^3J = 8.8

Hz, 2 H_{arom}), 7.46 (dd, ^3J = 8.2 Hz, 1 H_{arom}), 8.24 (d, ^3J = 8.8 Hz, 2 H_{arom}), 10.86 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.9 (OCH_3), 111.2 (C_{arom}), 118.1, 122.1, 122.8, 129.0, 134.1 (CH_{arom}), 142.3, 146.8, 149.6, 162.0 (C_{arom}), 170.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 273 (M^+, 35), 241 (100), 213 (20), 139 (41).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}O_5N$ (M^+): 273.0631; found: 273.0631.

3-Hydroxy-4′-methoxybiphenyl-2-carboxylic Acid Methyl Ester (5m)

Starting from 1-(4-methoxyphenyl)-3-ethoxypropenone (**3d**; 0.206 g, 1.0 mmol) and **4a** (0.260 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5m** was isolated as a yellow oil (0.080 g, 48%).

IR (neat): 3172 (w), 3067 (w), 3035 (w), 3010 (w), 2957 (w), 2840 (w), 1709 (w), 1663 (s), 1606 (m), 1570 (m), 1512 (m), 1474 (m), 1434 (s), 1335 (m), 1309 (m), 1261 (m), 1235 (s), 1210 (s), 1176 (s), 1166 (s), 1120 (s), 1095 (m), 1061 (m), 1020 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.53 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.79 (d, ^3J = 7.5 Hz, 1 H_{arom}), 6.90 (d, ^3J = 8.8 Hz, 2 H_{arom}), 6.97 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.16 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.38 (dd, ^3J = 8.8 Hz, 1 H_{arom}), 10.53 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.7, 55.2 (OCH_3), 112.1 (C_{arom}), 113.1, 116.2, 122.6, 129.2, 133.5 (CH_{arom}), 135.0, 144.4, 158.7, 161.2 (C_{arom}), 171.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 43), 227 (17), 226 (100), 198 (30), 183 (22).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_4$ (M^+): 258.0886; found: 258.0886.

3-Hydroxy-4′-methoxy-4-methylbiphenyl-2-carboxylic Acid Methyl Ester (5n)

Starting from **3d** (0.412 g, 2.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene (**4h**; 0.822 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5n** was isolated as a yellow oil (0.260 g, 48%).

IR (neat): 3028 (w), 2995 (w), 2953 (w), 2934 (w), 2836 (w), 1722 (w), 1662 (s), 1609 (m), 1565 (w), 1517 (m), 1482 (w), 1457 (m), 1436 (s), 1405 (m), 1311 (m), 1298 (m), 1286 (m), 1263 (s), 1237 (s), 1191 (m), 1175 (m), 1142 (m), 1112 (m), 1102 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.52 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 6.70 (d, ^3J = 7.6 Hz, 1 H_{arom}), 6.89 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.14 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.26 (d, ^3J = 7.6 Hz, 1 H_{arom}), 10.77 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 15.8 (CH_3), 51.7, 55.2 (OCH_3), 111.4 (C_{arom}), 113.0, 121.8 (CH_{arom}), 125.2 (C_{arom}), 129.2, 134.4 (CH_{arom}), 135.3, 141.8, 158.4, 159.4 (C_{arom}), 171.9 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 272 (M^+, 100), 241 (16), 239 (83), 212 (49), 209 (43), 197 (48), 169 (20), 141 (18), 115 (22).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_4$ (M^+): 272.1043; found: 272.1039.

3-Hydroxy-4′-methoxy-4-propylbiphenyl-2-carboxylic Acid Methyl Ester (5o)

Starting from **3d** (0.412 g, 2.0 mmol) and **4d** (0.906 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **5o** was isolated as a yellow solid (0.520 g, 86%).

IR (neat): 3008 (w), 2955 (s), 2867 (w), 2839 (w), 1650 (s), 1607 (m), 1577 (w), 1565 (w), 1513 (w), 1433 (s), 1418 (s), 1344 (s), 1301 (m), 1272 (s), 1245 (s), 1218 (s), 1192 (s), 1171 (s), 1147 (s), 1108 (m), 1101 (m), 1071 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, ^3J = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.67 (sext, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 2.66 (t, ^3J = 7.8 Hz, 2 H, $CH_2CH_2CH_3$), 3.51 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 6.72 (d, ^3J = 7.6 Hz, 1 H_{arom}), 6.89 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.14 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.25 (d, ^3J = 7.6 Hz, 1 H_{arom}), 10.72 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.5, 31.9 (CH_2), 51.7, 55.2 (OCH_3), 111.6 (C_{arom}), 113.0, 121.8, 129.2 (CH_{arom}), 129.5 (C_{arom}), 133.7 (CH_{arom}), 135.4, 141.8, 158.4, 159.1 (C_{arom}), 172.0 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 300 (M^+, 80), 268 (76), 240 (56), 239 (100), 237 (35), 139 (18).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{20}O_4$ (M^+): 300.1356; found: 300.1352.

3-Hydroxy-3′-methoxybiphenyl-2-carboxylic Acid Methyl Ester (5p)

Starting from 1-(3-methoxyphenyl)-3-ethoxypropenone (**3e**; 0.206 g, 1.0 mmol) and **4a** (0.260 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5p** was isolated as a yellow oil (0.040 g, 20%).

IR (neat): 3053 (w), 2999 (w), 2950 (w), 2834 (w), 1733 (w), 1663 (m), 1598 (m), 1571 (m), 1437 (m), 1337 (m), 1321 (m), 1307 (m), 1278 (m), 1225 (s), 1164 (s), 1120 (m), 1101 (m), 1063 (w), 1039 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 6.78–6.89 (m, 4 H_{arom}), 7.00 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.26 (dd, ^3J = 7.0 Hz, 1 H_{arom}), 7.40 (dd, ^3J = 7.8 Hz, 1 H_{arom}), 10.57 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.7, 55.2 (OCH_3), 112.1 (C_{arom}), 112.4, 113.6, 116.7, 120.8, 122.4, 128.5, 133.6 (CH_{arom}), 144.0, 144.6, 159.0, 161.2 (C_{arom}), 171.3 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 41), 227 (18), 226 (100), 198 (40).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_4$ (M^+): 258.0886; found: 258.0881.

4-Hexyl-3-hydroxy-3′-methoxybiphenyl-2-carboxylic Acid Methyl Ester (5q)

Starting from **3e** (0.206 g, 1.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)deca-1,3-diene (**4i**; 0.344 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5q** was isolated as a yellow oil (0.095 g, 30%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, ^3J = 6.9 Hz, 3 H, CH_3), 1.05–1.56 (m, 8 H, CH_2), 2.55 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.37 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 6.60–6.74 (m, 5 H_{arom}), 7.12 (dd, ^3J = 8.2 Hz, 1 H_{arom}), 10.62 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.6, 29.2, 29.3, 29.8, 31.7 (CH_2), 51.6, 55.2 (OCH_3), 111.5 (C_{arom}), 112.1, 113.6, 120.9, 121.6, 128.4 (CH_{arom}), 130.3 (C_{arom}), 133.6, (CH_{arom}), 141.9, 144.3, 159.0, 159.1 (C_{arom}), 171.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 342 (M^+, 31), 240 (100).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{26}O_4$ (M^+): 342.1825; found: 342.1831.

3-Hydroxy-3′,4′,5′-methoxybiphenyl-2-carboxylic Acid Isobutyl Ester (5r)

Starting from 3-ethoxy-1-(3,4,5-trimethoxyphenyl)propenone (**3f**; 0.266 g, 1.0 mmol) and 1-isobutoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4j**; 0.302 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5r** was isolated as a colorless solid (0.093 g, 31%); mp 90–92 °C.

IR (neat): 2996 (w), 2961 (w), 2937 (w), 2874 (w), 2837 (w), 1644 (m), 1599 (w), 1582 (m), 1510 (w), 1462 (m), 1446 (m), 1432 (w), 1410 (m), 1380 (m), 1354 (m), 1310 (w), 1288 (m), 1250 (s), 1237 (s), 1212 (m), 1179 (m), 1123 (s), 1107 (s), 1063 (w), 1044 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.62 [d, ^3J = 6.7 Hz, 6 H, $CH(CH_3)_2$], 1.45 [tq, ^3J = 6.7 Hz, 1 H, $CH_2CH(CH_3)_2$], 3.80 [d, ^3J = 6.5 Hz, 2 H, $CH_2CH(CH_3)_2$], 3.83 (s, 6 H, OCH_3), 3.80 (s, 3 H, OCH_3), 6.46 (s, 2 H_{arom}), 6.80 (d, ^3J = 7.5 Hz, 1 H_{arom}), 7.00 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.39 (dd, ^3J = 7.6 Hz, 1 H_{arom}), 10.77 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 18.8 [$CH(CH_3)_2$], 27.2 [$CH(CH_3)_2$], 56.1, 60.7 (OCH_3), 71.8 [$CH_2CH(CH_3)_2$], 105.6 (CH_{arom}), 112.3 (C_{arom}), 117.7, 122.4, 133.4 (CH_{arom}), 137.1, 138.7, 144.5, 152.7, 161.4 (C_{arom}), 171.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 360 (M^+, 95), 286 (100), 177 (45).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{24}O_6$ (M^+): 360.1567; found: 360.1562.

3-Hydroxy-3′,4′,5′-trimethoxy-4-(3-phenylpropyl)biphenyl-2-carboxylic Acid Methyl Ester (5s)

Starting from **3f** (0.266 g, 1.0 mmol) and **4f** (0.378 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5s** was isolated as a yellow oil (0.160 g, 37%).

IR (neat): 3060 (w), 3025 (w), 2999 (m), 2936 (m), 2858 (w), 2836 (w), 1663 (s), 1585 (s), 1510 (m), 1496 (m), 1437 (s), 1409 (s), 1351 (s), 1285 (m), 1252 (s), 1195 (m), 1168 (m), 1127 (s), 1008 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (m, 2 H, CH_2), 2.73 (m, 4 H, CH_2), 3.54 (s, 3 H, OCH_3), 3.84 (s, 6 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.44 (s, 2 H_{arom}), 6.76 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.16–7.32 (m, 6 H_{arom}), 10.70 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 30.0, 31.2, 36.0 (CH_2), 52.2, 56.5, 61.3 (OCH_3), 105.9 (CH_{arom}), 112.2 (C_{arom}), 122.0, 126.1, 128.6, 128.8 (CH_{arom}), 130.1 (C_{arom}), 134.1 (CH_{arom}), 137.3, 139.0, 142.6, 142.7, 153.0, 159.5 (C_{arom}), 172.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 436 (M^+, 100), 300 (91), 269 (87).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{28}O_6$ (M^+): 436.1880; found: 436.1879.

1-(3-Hydroxy-3′,4′,5′-trimethoxy-4-methylbiphenyl-2-yl)propan-1-one (5t)

Starting from **3f** (0.266 g, 1.0 mmol) and 3,5-bis(trimethylsilyloxy)hepta-2,4-diene (**4k**; 0.272 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **5t** was isolated as a brownish solid (0.040 g, 12%); mp 68–70 °C.

IR (neat): 3443 (br), 2938 (s), 2837 (w), 1628 (s), 1584 (s), 1508 (s), 1462 (s), 1379 (m), 1351 (m), 1267 (s), 1238 (s), 1183 (w), 1166 (m), 1128 (s), 1049 (m), 1007 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.18 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 2.29 (s, 3 H, CH_3), 3.86 (s, 6 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.51 (s, 2 H_{arom}), 6.80 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.14 (d, ^3J = 7.6 Hz, 1 H_{arom}), 11.02 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 9.5 (CH_2CH_3), 15.8 (CH_3), 36.2 (CH_2CH_3), 56.1, 61.0 (OCH_3), 106.1, 121.0 (CH_{arom}), 126.1 (C_{arom}), 134.1 (CH_{arom}), 137.7, 137.8, 141.3, 153.3, 158.0 (C_{arom}), 211.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 330 (M^+, 100), 301 (38), 299 (21), 286 (15), 271 (16), 270 (58).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{22}O_5$ (M^+): 330.1461; found: 330.1461.

[1,1′;3′,1″]Terphenyl-2-carboxylic Acid Methyl Ester (7)

To a CH_2Cl_2 solution (3 mL) of **5a** (0.070 g, 0.3 mmol) were slowly added pyridine and Tf_2O (0.36 mmol) at –78 °C. The mixture was stirred for 4 h and subsequently purified by chromatography (silica gel, CH_2Cl_2) to give **6**. A dioxane solution (5 mL) of **6** (0.29 mmol), $PhB(OH)_2$ (0.37 mmol), anhyd K_3PO_4 (0.46 mmol), and $Pd(PPh_3)$ (0.01 mmol) was stirred for 14 h in a pressure tube at 60 °C. To the mixture was added aq NH_4Cl (20 mL) and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes–EtOAc, 20:1) to give **7** as a colorless solid (0.043 g, 50%); mp 140–150 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.52 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 6.70 (d, ^3J = 7.6 Hz, 1 H_{arom}), 6.89 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.14 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.26 (d, ^3J = 7.6 Hz, 1 H_{arom}), 10.77 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 51.7 (OCH_3), 127.5, 128.2, 128.3, 128.8, 129.3 (CH_{arom}), 132.8, 140.3, 140.5 (C_{arom}), 169.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 288 (M^+, 52), 258 (20), 257 (100), 228 (28), 226 (16).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{16}O_2$ (M^+): 288.1144; found: 288.1141.

Bromination of 3a,e to 8a,b

To a CH_2Cl_2 solution (5 mL) of **3a**,**e** (2.0 mmol) was slowly added a CH_2Cl_2 solution (5 mL) of Br_2 (2.0 mmol) at 0 °C using a dropping funnel. After stirring for 1 h, H_2O (20 mL) was added, the organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes–EtOAc, 10:1).

6-Bromo-3-hydroxybiphenyl-2-carboxylic Acid Ethyl Ester (9a)

The reaction was carried out following the typical procedure as given for the synthesis of **5a**–**t**. Starting from **3a** (0.253 g, 1.0 mmol) and **4a** (0.260 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **9a** was prepared via the intermediate bromide **8a** as a yellow solid (0.122 g, 50%), mp 68–70 °C.

IR (neat): 3070 (w), 3024 (w), 3000 (w), 2947 (w), 2849 (w), 1662 (s), 1589 (m), 1537 (w), 1496 (w), 1433 (s), 1332 (s), 1282 (m), 1228 (m), 1205 (s), 1134 (m), 1114 (m), 1092 (m), 1070 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.39 (s, 3 H, OCH_3), 6.93 (d, ^3J = 8.9 Hz, 1 H_{arom}), 7.09–7.13 (m, 2 H_{arom}), 7.34–7.43 (m, 3 H_{arom}), 7.68 (d, ^3J = 7.6 Hz, 1 H_{arom}), 10.78 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 52.0 (OCH_3), 114.3, 114.6 (C_{arom}), 118.7, 127.1, 127.6, 128.3, 138.0 (CH_{arom}), 141.7, 143.6, 160.8 (C_{arom}), 170.5 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 308 (M^+, ^{81}Br, 32), 306 (M^+, ^{79}Br, 31), 276 (100), 274 (94), 249 (20), 246 (23), 139 (64).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}BrO_3$ (M^+): 305.9886; found: 305.9889.

6-Bromo-3-hydroxy-4′-methoxybiphenyl-2-carboxylic Acid Ethyl Ester (9b)

The reaction was carried out following the typical procedure as given for the synthesis of **5a**–**t**. Starting from **3a** (0.284 g, 1.0 mmol) and **4h** (0.274 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **9b** was prepared via the intermediate bromide **8a** as a yellow solid (0.060 g, 22%); mp 96–98 °C.

IR (neat): 3211 (br), 3088 (w), 3030 (w), 2997 (w), 2960 (w), 2935 (w), 2838 (w), 1892 (w), 1693 (s), 1608 (m), 1570 (m), 1514 (m), 1464 (m), 1434 (s), 1392 (m), 1370 (m), 1339 (m), 1312 (m), 1286 (s), 1225 (s), 1171 (s), 1141 (m), 1116 (m), 1104 (m), 1086 (m), 1031 (s), 1007 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 3.85 (s, 3 H, OCH_3), 3.91 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.89–6.92 (m, 4 H_{arom}), 7.04 (d, ^3J = 8.8 Hz, 1 H_{arom}), 7.66 (d, ^3J = 8.9 Hz, 1 H_{arom}), 10.86 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.0 (OCH_2CH_3), 55.2 (OCH_3), 61.3 (OCH_2CH_3), 113.0 (CH, Ar), 114.8, 115.2 (C_{arom}), 118.5, 129.6 (CH_{arom}), 134.4 (C_{arom}), 137.8 (CH_{arom}), 143.4, 158.8, 160.8 (C_{arom}), 170.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 352 (M^+, ^{81}Br, 33), 350 (M^+, ^{79}Br, 33), 307 (16), 306 (99), 305 (17), 304 (100), 169 (15).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}BrO_4$ (M^+): 350.0148; found: 350.0149.

6-Bromo-3-hydroxy-4-methylbiphenyl-2-carboxylic Acid Methyl Ester (9c)

The reaction was carried out following the typical procedure as given for the synthesis of **5a**–**t**. Starting from **3e** (0.423 g, 1.5 mmol) and **4h** (0.411 g, 1.5 mmol) in CH_2Cl_2 (5 mL), **9c** was prepared via the intermediate bromide **8b** as a yellow oil (0.166 g, 52%).

IR (neat): 3057 (w), 3024 (w), 2950 (w), 2924 (w), 2851 (w), 1661 (s), 1599 (w), 1567 (w), 1498 (w), 1435 (m), 1402 (m), 1378 (w), 1355 (m), 1287 (m), 1235 (s), 1195 (s), 1161 (s), 1072 (w), 1016 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 3.21 (s, 3 H, OCH_3), 6.92–7.25 (m, 5 H_{arom}), 7.41 (s, 1 H_{arom}), 10.85 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 15.6 (CH_3), 51.9 (OCH_3), 113.5, 113.9 (C_{arom}), 127.0, 127.5 (CH_{arom}), 128.2 (C_{arom}), 128.6, 138.5 (CH_{arom}), 141.0, 142.0, 159.2 (C_{arom}), 170.9 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 322 (M^+, ^{81}Br, 33), 320 (M^+, ^{79}Br, 36), 290 (80), 289 (19), 288 (81), 210 (18), 209 (100), 153 (27), 152 (51).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}BrO_3$ (M^+): 320.0042; found: 320.0034.

6-Bromo-3-hydroxy-4′-methoxy-4-methylbiphenyl-2-carboxylic Acid Methyl Ester (9d)

The reaction was carried out following the typical procedure as given for the synthesis of **5a**–**t**. Starting from **3e** (0.284 g, 1.0 mmol) and **4l** (0.274 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **9d** was prepared via the intermediate bromide **8b** as a yellow solid (0.160 g, 48%); mp 83–85 °C.

IR (neat): 3032 (w), 3003 (w), 2955 (w), 2923 (w), 2837 (w), 1713 (w), 1655 (m), 1606 (m), 1513 (m), 1462 (m), 1429 (m), 1401 (m), 1377 (m), 1337 (m), 1308 (m), 1283 (m), 1240 (s), 1228 (s), 1191 (m), 1174 (m), 1156 (m), 1145 (m), 1108 (m), 1018 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 3.43 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.91 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.03 (d, ^3J = 8.8 Hz, 2 H_{arom}), 7.56 (s, 1 H_{arom}), 10.91 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 15.6 (CH_3), 52.1, 55.1 (OCH_3), 112.9 (CH_{arom}), 113.8, 114.5, 127.9 (C, Ar), 129.7 (CH_{arom}), 134.3 (C, Ar), 138.3 (CH_{arom}), 140.6, 158.5, 159.0 (C, Ar), 171.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 352 (M^+, ^{81}Br, 47), 350 (M^+, ^{79}Br, 47), 321 (16), 320 (99), 319 (22), 318 (100), 240 (19), 239 (95), 168 (16), 139 (29).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}BrO_4$ (M^+): 350.0148; found: 350.0150.

Fluorenones 10a–e; General Procedure

To **5a**,**e**,**d**,**k**, or **9b** (0.25 mmol) was added concd H_2SO_4 (3 mL) at 0 °C and the mixture was stirred for 1–24 h until the conversion was complete (TLC control). The mixture was poured into ice water (50 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, length = 5 cm, diameter = 1 cm, EtOAc–heptanes, 1:5).

1-Hydroxyfluoren-9-one (10a)

Starting from 3-hydroxybiphenyl-2-carboxylic acid methyl ester (**5a**; 0.060 g, 0.26 mmol), **10a** was isolated as a brownish solid (0.041 g, 81%); mp 100–105 °C.

IR (KBr): 3354 (br), 3044 (w), 2956 (w), 2920 (w), 2850 (w), 1952 (w), 1926 (w), 1895 (w), 1861 (w), 1823 (w), 1682 (s), 1615 (m), 1595 (s), 1587 (s), 1482 (w), 1467 (s), 1453 (s), 1436 (s), 1381 (w), 1321 (m), 1306 (m), 1282 (s), 1203 (s), 1168 (s), 1161 (s), 1129 (s), 1107 (s), 1073 (s), 1037 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75 (d, ^3J = 8.4 Hz, 1 H_{arom}), 7.02 (d, ^3J = 7.1 Hz, 1 H_{arom}), 7.26–7.38 (m, 2 H_{arom}), 7.47–7.51 (m, 2 H_{arom}), 7.62 (d, ^3J = 7.3 Hz, 1 H_{arom}).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 112.8 (CH_{arom}), 117.4 (C, Ar), 118.1, 121.0, 124.0, 129.0 (CH_{arom}), 134.2 (C, Ar), 134.6, 137.4 (CH_{arom}), 143.8, 144.1, 157.3 (C, Ar), 196.3 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 196 (M^+, 100), 168 (52), 139 (42).

HRMS (EI): *m*/*z* calcd for $C_{13}H_8O_2$ (M^+): 196.0518; found: 196.0522.

1-Hydroxy-2-octylfluoren-9-one (10b)

Starting from 3-hydroxy-4-octylbiphenyl-2-carboxylic acid methyl ester (**5e**; 0.274 g, 0.80 mmol), **10b** was isolated as an orange solid (0.210 g, 84%); mp 18–22 °C.

IR (KBr): 3367 (w), 2921 (s), 2852 (s), 1712 (m), 1685 (s), 1651 (w), 1622 (m), 1600 (m), 1576 (w), 1466 (s), 1455 (s), 1435 (m), 1371 (m), 1348 (m), 1318 (m), 277 (m), 1171 (s), 1125 (m), 1108 (m), 1038 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 [t, ^3J = 6.8 Hz, 3 H, $CH_2(CH_2)_6CH_3$], 1.17–1.63 [m, 12 H, $CH_2(CH_2)_6CH_3$], 2.59 [t, ^3J = 7.6 Hz, 2 H, $CH_2(CH_2)_6CH_3$], 6.94 (d, ^3J = 7.2 Hz, 1 H_{arom}), 7.16–7.27 (m, 2 H_{arom}), 7.45 (d, ^3J = 3.8 Hz, 2 H_{arom}), 7.60 (d, ^3J = 7.3 Hz, 1 H_{arom}).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6, 27.4, 29.2, 29.7, 31.7, 31.8, 30.9 (CH_2), 112.5 (CH_{arom}), 117.2 (C_{arom}), 120.6, 123.9, 128.5, (CH_{arom}), 132.8 (C_{arom}), 134.5, 137.1 (CH_{arom}), 141.3, 144.4, 155.9, 196.8 (C_{arom}), 213.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 308 (M^+, 33), 290 (20), 210 (78), 209 (100).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{24}O_2$ (M^+): 308.1770; found: 308.1764.

1-Hydroxy-2-propylfluoren-9-one (10c)

Starting from 3-hydroxy-4-propylbiphenyl-2-carboxylic acid methyl ester (**5d**; 0.260 g, 0.96 mmol), **10c** was isolated as a yellow solid (0.220 g, 96%); mp 50–52 °C.

IR (KBr): 3341 (w), 3054 (w), 2949 (m), 2927 (s), 2927 (m), 2902 (m), 2865 (m), 1677 (s), 1625 (m), 1598 (s), 1556 (w), 1537 (w), 1495 (w), 1467 (m), 1453 (m), 1431 (s), 1345 (s), 1293 (m), 1293 (m), 1262 (m), 1238 (m), 1197 (s), 1168 (s), 1160 (m), 1146 (m), 1104 (m), 1073 (m), 1013 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 1.65 (sext, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 2.59 (t, ^3J = 7.2 Hz, 2 H, $CH_2CH_2CH_3$), 6.95 (d, ^3J = 7.2 Hz, 1 H_{arom}), 7.17–7.28 (m, 2 H_{arom}), 7.45 (d, ^3J = 4.6 Hz, 2 H_{arom}), 7.61 (d, ^3J = 7.3 Hz, 1 H_{arom}).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.8 (CH_3), 22.7, 30.9 (CH_2), 112.5 (CH_{arom}), 117.1 (C_{arom}), 120.6, 123.9, 128.5, (CH_{arom}), 132.5,

134.3 (C_{arom}), 134.5, 137.1 (CH_{arom}), 141.3, 144.3, 155.8 (C_{arom}), 196.7 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 238 (M^+, 34), 210 (19), 209 (100), 152 (29).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}O_2$ (M^+): 238.0988; found: 238.0991.

7-Chloro-1-hydroxy-2-methoxyfluoren-9-one (10d)

Starting from 4′-chloro-3-hydroxy-4-methoxybiphenyl-2-carboxylic acid methyl ester (**5k**; 0.060 g, 0.20 mmol), **10d** was isolated as a red solid (0.050 g, 96%); mp 150–152 °C.

IR (KBr): 3408 (m), 3093 (w), 2945 (w), 2919 (w), 2849 (w), 2832 (w), 1731 (w), 1681 (s), 1651 (m), 1621 (m), 1593 (m), 1557 (w), 1497 (m), 1463 (s), 1456 (s), 1438 (s), 1423 (s), 1360 (w), 1320 (w), 1296 (s), 1280 (s), 1239 (s), 1212 (s), 1193 (s), 1166 (s), 1116 (s), 1086 (s), 1073 (s), 1055 (s), 1012 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 6.77 (d, ^3J = 7.8 Hz, 1 Harom), 6.86 (d, ^3J = 7.8 Hz, 1 H_{arom}), 7.28 (d, ^3J = 8.0 Hz, 1 H_{arom}), 7.34 (d, ^3J = 8.0 Hz, 1 H_{arom}), 7.49 (d, ^4J = 1.8 Hz, 1 H_{arom}).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 112.8, 116.6 (CH_{arom}), 118.1 (C_{arom}), 121.3, 124.3 (CH_{arom}), 133.8, 133.8 (C_{arom}), 134.2 (CH_{arom}), 136.0, 142.6, 147.5, 149.6, (C_{arom}), 194.2 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 262 (M^+, ^{37}Cl, 33), 260 (M^+, ^{35}Cl, 98), 231 (38), 219 (34), 217 (100), 214 (29), 126 (35).

HRMS (EI): *m*/*z* calcd for $C_{14}H_9ClO_3$ (M^+): 260.0234; found: 260.0232.

4-Bromo-1-hydroxy-2-methylfluoren-9-one (10e)

Starting from 6-bromo-3-hydroxy-4-methyl-biphenyl-2-carboxylic acid methyl ester (**9b**; 0.120 g, 0.38 mmol), **10e** was isolated as a yellow solid (0.090 g, 82%); mp 130–135 °C.

IR (KBr): 3316 (m), 3064 (w), 3050 (w), 2947 (w), 2929 (m), 2853 (w), 2731 (m), 1679 (s), 1620 (s), 1600 (s), 1583 (s), 1557 (w), 1485 (m), 1464 (s), 1444 (s), 1419 (s), 1377 (w), 1351 (s), 1309 (m), 1276 (s), 1236 (s), 1197 (m), 1168 (s), 1112 (s), 1078 (m), 1032 (s), 1012 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 7.26–7.34 (m, 2 H_{arom}), 7.52 (dd, ^3J = 7.6 Hz, 1 H_{arom}), 7.64 (d, ^3J = 7.8 Hz, 1 H_{arom}), 8.2 (d, ^3J = 7.6 Hz, 1 H_{arom}).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.4 (CH_3), 107.2, 118.6 (C_{arom}), 123.3, 124.0, 128.9 (CH_{arom}), 130.4, 134.1 (C_{arom}), 134.7 (CH_{arom}), 138.6 (C_{arom}), 141.4 (CH_{arom}), 143.3, 155.4, (C_{arom}), 195.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 290 (M^+, ^{81}Br, 97), 288 (M^+, ^{79}Br, 100), 209 (81), 152 (31).

HRMS (EI): *m*/*z* calcd for $C_{14}H_9BrO_2$ (M^+): 287.9780; found: 287.9773.

Salicylate Esters 13a–n; General Procedure

To a CH_2Cl_2 solution (1 mL) of **4** (3.0 mmol) and **11** or **12** (2.0 mmol) was added a CH_2Cl_2 solution (1 mL) of $TiCl_4$ (0.24 mL, 2.0 mmol) at –78 °C. The solution was allowed to warm to 20 °C during 14 h with stirring. To the solution were added CH_2Cl_2 (10 mL) and aq 10% HCl (10 mL). The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (heptanes–EtOAc, 10:1).

2-Hydroxy-3,6-dimethylbenzoic Acid Methyl Ester (13a)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene (**4h**; 0.274 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13a** was isolated (0.080 g, 40%) as a colorless solid; mp 38–41 °C.

IR (neat): 3031 (w), 2962 (m), 2905 (w), 1667 (m), 1616 (w), 1585 (w), 1447 (w), 1411 (w), 1380 (w), 1347 (w), 1289 (w), 1259 (s), 1196 (w), 1147 (m), 1095 (s), 1054 (s), 1023 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 2.50 (s, 3 H, CH_3), 3.95 (s, 3 H, OCH_3), 6.55 (d, ^3J = 7.5 Hz, 1 H_{arom}), 7.08 (d, ^3J = 7.5 Hz, 1 H_{arom}), 11.55 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 15.7, 23.8 (CH_3), 52.0 (OCH_3), 111.5 (C_{arom}), 122.0 (CH_{arom}), 124.1 (C_{arom}), 135.0 (CH_{arom}), 138.4, 161.0 (C_{arom}), 172.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 180 (M^+, 47), 149, (23), 148 (91), 120 (100), 91 (50).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{12}O_3$ (M^+): 180.0781; found: 180.0785.

2-Hydroxy-3-methoxy-6-methylbenzoic Acid Methyl Ester (13b)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 1,4-dimethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4g**; 0.290 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13b** was isolated as a yellow oil (0.075 g, 38%).

IR (neat): 3432 (w), 3031 (w), 3000, w), 2955 (m), 2937 (m), 2837 (w), 1730 (m), 1663 (s), 1617 (w), 1583 (m), 1492 (m), 1436 (s), 1384 (w), 1351 (m), 1323 (m), 1294 (s), 1246 (s), 1201 (m), 1172 (w), 1154 (m), 1067 (s), 1047 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, CH_3), 3.87 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 6.46 (d, ^3J = 8.2 Hz, 1 H_{arom}), 6.89 (d, ^3J = 8.2 Hz, 1 H_{arom}), 11.27 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 23.1 (CH_3), 52.1, 56.1 (OCH_3), 112.7 (C_{arom}), 115.3, 121.3 (CH_{arom}), 131.6, 146.6, 152.5 (C_{arom}), 172.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 196 (M^+, 60), 165 (40), 164 (100), 163 (17), 136 (90), 135 (45), 134 (29), 121 (41).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{12}O_4$ (M^+): 196.0730; found: 196.0733.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.03; H, 6.34.

1-(2-Hydroxy-6-methylphenyl)ethanone (13c)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 2,4-bis(trimethylsilyloxy)penta-1,3-diene (**4m**; 0.244 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13c** was isolated as a yellow oil (0.050 g, 33%).

IR (neat): 3342 (b), 3061 (w), 2964 (w), 2929 (w), 2855 (w), 1688 (m), 1624 (s), 1606 (s), 1464 (s), 1446 (s), 1381 (m), 1361 (m), 1326 (s), 1287 (s), 1255 (s), 1213 (s), 1165 (m), 1101 (w), 1055 (w), 1034 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.60 (s, 3 H, CH_3), 2.67 (s, 3 H, CH_3), 6.72 (d, ^3J = 7.7 Hz, 1 H_{arom}), 6.84 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.27 (t, ^3J = 8.0 Hz, 1 H_{arom}), 12.29 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 24.4, 33.3 (CH_3), 116.5 (CH_{arom}), 121.6, (C_{arom}), 123.0, 134.6 (CH_{arom}), 139.4, 162.7 (C_{arom}), 206.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 150 (M^+, 35), 135 (100).

HRMS (EI): *m*/*z* calcd for $C_9H_{10}O_2$ (M^+): 150.0675; found: 150.0678.

2-Hydroxy-6-methylbenzoic Acid 2-Methoxyethyl Ester (13d)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 1-(2-methoxyethoxy)-1,3-bis(trimethylsilyloxy)buta-1,3-di-

ene (**4b**; 0.304 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13d** was isolated as a yellow oil (0.051 g, 24%).

IR (neat): 3408 (w), 3058 (w), 2971 (m), 2933 (m), 2892 (m), 2822 (w), 1730 (w), 1661 (s), 1608 (m), 1579 (m), 1459 (m), 1445 (m), 1407 (w), 1376 (m), 1292 (m), 1253 (s), 1215 (s), 1166 (m), 1120 (s), 1079 (m), 1033 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, CH_3), 3.42 (s, 3 H, OCH_3), 3.73 (t, ^3J = 4.7 Hz, 2 H, CH_2), 4.51 (t, ^3J = 4.7 Hz, 2 H, CH_2), 6.71 (d, ^3J = 8.1 Hz, 1 H_{arom}), 6.83 (d, ^3J = 8.8 Hz, 1 H_{arom}), 7.26 (t, ^3J = 3.9 Hz, 1 H_{arom}), 11.07 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 23.8 (CH_3), 58.9 (OCH_3), 64.1, 70.0 (CH_2), 112.4 (C_{arom}), 115.5, 122.9, 134.2 (CH_{arom}), 141.5, 162.6 (C_{arom}), 171.3 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 210 (M^+, 21), 135 (30), 134 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{14}O_4$ (M^+): 210.0886; found: 210.0890.

3-Chloro-2-hydroxy-6-methylbenzoic Acid Ethyl Ester (13e)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 4-chloro-1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4n**; 0.214 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13e** was isolated (0.032 g, 15%) as a yellow solid; mp 54–56 °C.

IR (neat): 3430 (w), 3301 (w), 3065 (w), 3009 (w), 2985 (m), 2939 (m), 2870 (w), 2822 (w), 2744 (w), 2624 (w), 2586 (w), 1911 (w), 1662 (s), 1600 (m), 1564 (w), 1468 (m), 1455 (m), 1424 (s), 1374 (s), 1344 (m), 1298 (s), 1254 (s), 1209 (s), 1160 (m), 1126 (m) 1108 (m), 1020 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.63 (s, 3 H, CH_3), 4.46 (t, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.67 (d, ^3J = 8.1 Hz, 1 H_{arom}), 7.37 (d, ^3J = 8.1 Hz, 1 H_{arom}), 11.93 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.1 (CH_3), 23.8 (OCH_2CH_3), 62.1 (OCH_2CH_3), 113.6, 119.9 (C_{arom}), 122.8, 134.0 (CH_{arom}), 140.0, 158.1 (C_{arom}), 171.4 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 216 (M^+, ^{37}Cl, 8), 214 (M^+, ^{35}Cl, 22), 169 (24), 168 (100).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{11}ClO_3$ (M^+): 214.0391; found: 214.0391.

Anal. Calcd for $C_{10}H_{11}ClO_3$: C, 55.96; H, 5.17. Found: C, 55.79; H, 5.40.

3-Hexyl-2-hydroxy-6-methylbenzoic Acid Methyl Ester (13f)

Starting from 4-methoxybut-3-en-2-one (**11a**; 0.100 g, 1.0 mmol) and 1-ethoxy-1,3-bis(trimethylsilyloxy)deca-1,3-diene (**4i**; 0.344 g, 1.0 mmol) in CH_2Cl_2 (5 mL), **13f** was isolated as a yellow oil (0.138 g, 55%).

IR (neat): 3094 (w), 3034 (w), 2955 (s), 2929 (s), 2857 (s), 1751 (w), 1715 (w), 1660 (s), 1614 (m), 1582 (w), 1438 (s), 1417 (s), 1349 s), 1288 (s), 1256 (s), 1240 (s9, 1196 (m), 1146 (s), 1053 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 [t, ^3J = 7.1 Hz, 3 H, $CH_2(CH_2)_4CH_3$], 1.25–1.60 [m, 8 H, $CH_2(CH_2)_4CH_3$], 2.50 (s, 3 H, CH_3), 2.61 [t, ^3J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 3.96 (s, 3 H, OCH_3), 6.64 (d, ^3J = 7.6 Hz, 1 H_{arom}), 7.14 (d, ^3J = 7.6 Hz, 1 H_{arom}), 11.52 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.1, 22.6 (CH_3), 23.8, 29.2, 29.3, 29.7, 31.7 (CH_2), 51.9 (OCH_3), 111.6 (C_{arom}), 122.0 (CH_{arom}), 128.8 (C_{arom}), 134.2 (CH_{arom}), 138.3, 160.7 (C_{arom}), 172.6 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 250 (M^+, 48), 190 (62), 161 (34), 148 (92), 147 (100), 120 (35).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{22}O_3$ (M^+): 250.1563; found: 250.1567.

6-Ethyl-2-hydroxy-3-methylbenzoic Acid Methyl Ester (13g)

Starting from 1-methoxypent-1-en-3-one (**11b**; 0.228 g, 2.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene (**4h**; 0.822 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13g** was isolated as a mixture of regioisomers (rs = 4:1, 0.115 g, 30%). The spectroscopic data are listed for the major isomer.

IR (neat): 3152 (w), 2966 (w), 2953 (w), 2875 (w), 1728 (w), 1668 (s), 1617 (m), 1575 (w), 1497 (w), 1438 (s), 1416 (m), 1378 (m), 1438 (s), 1281 (s), 1262 (s), 1242 (s), 1233 (s), 1195 (s), 1174 (m), 1149 (s), 1102 (m), 1093 (m), 1058 (w), 1031 (m), 1010 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 2.21 (s, 3 H, CH_3), 2.65 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 3.92 (s, 3 H, OCH_3), 6.70 (d, ^3J = 8.2 Hz, 1 H_{arom}), 7.62 (d, ^3J = 8.2 Hz, 1 H_{arom}), 11.08 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 10.6 (CH_3), 14.1 (CH_2CH_3), 27.0 (CH_2CH_3), 62.0 (OCH_3), 109.3 (C_{arom}), 119.0 (CH_{arom}), 123.9 (C_{arom}), 126.7 (CH_{arom}), 150.7, 159.8 (C_{arom}), 171.0 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 194 (M^+, 38), 163 (21), 162 (100), 134 (50).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{14}O_3$ (M^+): 194.0937; found: 194.0945.

2-Hydroxy-3-methyl-6-propylbenzoic Acid Methyl Ester (13h)

Starting from 1-ethoxyhex-1-en-3-one (**11c**; 0.284 g, 2.0 mmol) and 1-methoxy-1,3-bis(trimethylsilyloxy)penta-1,3-diene (**4h**; 0.822 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13h** was isolated as a yellow oil (0.080 g, 18%).

IR (neat): 3151 (w), 2955 (m), 2932 (w), 2817 (w), 1727 (w), 1668 (s), 1616 (m), 1575 (w), 1497 (w), 1438 (s), 1413 (m), 1378 (m), 1328 (m), 1282 (m), 1271 (m), 1247 (s), 1195 (s), 1175 (m), 1149 (s), 1106 (m), 1045 (w), 1009 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.97 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 1.59 (sext, ^3J = 7.7 Hz, 2 H, $CH_2CH_2CH_3$), 2.20 (s, 3 H, CH_3), 2.60 (t, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CH_3$), 3.92 (s, 3 H, OCH_3), 6.68 (d, ^3J = 8.2 Hz, 1 H_{arom}), 7.60 (d, ^3J = 8.2 Hz, 1 H_{arom}), 11.08 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 10.8 (CH_3), 14.0 (CH_2CH_3), 23.1 ($CH_2CH_2CH_3$), 36.1 ($CH_2CH_2CH_3$), 52.0 (OCH_3), 109.3 (C_{arom}), 119.9 (CH_{arom}), 124.2 (C_{arom}), 126.4 (CH_{arom}), 149.2, 159.9 (C_{arom}), 171.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 208 (M^+, 44), 177 (20), 176 (79), 161 (100), 148 (46), 119 (20).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{16}O_3$ (M^+): 208.1094; found: 208.1093.

2-Ethyl-6-hydroxybenzoic Acid Ethyl Ester (13i)

Starting from 1,1-dimethoxypentan-3-one (**12a**; 0.292 g, 2.0 mmol) and 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4l**; 0.822 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13i** was isolated as a mixture of regioisomers (rs = 6:1, 0.220 g, 56%). The spectroscopic data are listed for the major isomer.

IR (neat): 3165 (w), 2968 (w), 2935 (w), 2874 (w), 1666 (s), 1621 (m), 1572 (m), 1500 (m), 1462 (m), 1398 (m), 1371 (m), 1330 (m), 1293 (m), 1255 (s), 1212 (s), 1172 (w), 1150 (s), 1093 (s), 1069 (m), 1058 (m), 1015 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.40 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 2.63 (q, ^3J = 7.5 Hz, 2 H, CH_2CH_3), 4.38 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.69–6.1 (m, 2 H_{arom}), 7.04 (d, ^3J = 8.8 Hz, 1 H_{arom}), 10.80 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.2 (OCH_2CH_3), 14.8 (CH_2CH_3), 29.0 (CH_2CH_3), 61.1 (OCH_2CH_3), 110.2 (C_{arom}), 116.4, 119.1, 129.7 (CH_{arom}), 151.5, 161.6 (C_{arom}), 170.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 194 (M^+, 34), 149 (22), 148 (100), 91 (25).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{14}O_3$ (M^+): 194.0937; found: 194.0938.

1-(2-Ethyl-6-hydroxyphenyl)ethanone (13j)

Starting from 1,1-dimethoxypentan-3-one (**12a**; 0.292 g, 2.0 mmol) and 2,4-bis(trimethylsilyloxy)penta-1,3-diene (**4m**; 0.734 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13j** was isolated as a mixture of regioisomers (rs = 4:1, 0.152 g, 46%). The spectroscopic data are listed for the major isomer.

IR (neat): 3033 (w), 2967 (w), 2932 (w), 2874 (w), 2726 (w), 1636 (s), 1621 (s), 1570 (m), 1502 (m), 1453 (w), 1421 (m), 1363 (s), 1323 (s), 1301 (m), 1274 (m), 1256 (s), 1221 (s), 1193 (m), 1164 (m), 1148 (m), 1136 (w), 1057 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.59 (s, 3 H, CH_3), 2.63 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 6.71–6.80 (m, 2 H_{arom}), 6.63 (d, ^3J = 8.1 Hz, 1 H_{arom}), 12.29 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.6 (CH_2CH_3), 26.4 (CH_3), 29.0 (CH_2CH_3), 117.1 (CH_{arom}), 117.6 (C_{arom}), 119.0, 130.6 (CH_{arom}), 154.1, 162.5 (C_{arom}), 203.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 164 (M^+, 47), 149 (100).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{12}O_2$ (M^+): 164.0831; found: 164.0833.

(2-Ethyl-6-hydroxyphenyl)phenylmethanone (13k)

Starting from 1,1-dimethoxypentan-3-one (**12a**; 0.292 g, 2.0 mmol) and [1,3-bis(trimethylsilyloxy)buta-1,3-dienyl]benzene (**4n**; 0.919 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13k** was isolated as a mixture of regioisomers (rs = 4:1, 0.324 g, 72%). The spectroscopic data are listed for the major isomer.

IR (neat): 3057 (w), 3033 (w), 2966 (w), 2932 (w), 2873 (w), (1625 (s), 1598 (s), 1574 (s), 1497 (m), 1445 (m), 1414 (m), 1333 (s), 1299 (m), 1255 (s), 1225 (s), 1178 (m), 1160 (m), 1120 (m), 1096 (w), 1073 (w), 1027 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.67 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 6.70 (d, ^3J = 8.2 Hz, 1 H_{arom}), 6.89 (d, ^3J = 8.8 Hz, 1 H_{arom}), 7.48–7.68 (m, 6 H_{arom}), 12.14 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.6 (CH_2CH_3), 29.1 (CH_2CH_3), 117.0 (C_{arom}), 117.2, 118.7, 128.2, 129.0, 131.6, 133.5, 138.1 (CH_{arom}), 154.1, 163.5 (C_{arom}), 201.0 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 226 (M^+, 82), 225 (100), 149 (46).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_2$ (M^+): 226.0910; found: 226.0909.

1-(6-Ethyl-2-hydroxy-3-methylphenyl)propan-1-one (13l)

Starting from 1,1-dimethoxypentan-3-one (**12a**; 0.292 g, 2.0 mmol) and 3,5-bis(trimethylsilyloxy)hepta-2,4-diene (**4k**; 0.816 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13l** was isolated as a mixture of regioisomers (rs = 4:1, 0.130 g, 34%). The spectroscopic data are listed for the major isomer.

IR (neat): 2968 (w), 2938 (w), 2876 (w), 1629 (s), 1574 /w), 1495 (w), 1454 (w), 1410 (m), 1373 (m), 1298 (m), 1275 (m), 1258 (m), 1230 (s), 1211 (m), 1140 (w), 1096 (m), 1051 (m), 1035 (m), 1009 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 1.23 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 2.20 (s, 3 H, CH_3), 2.65 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 3.00 (q, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 6.71 (d, ^3J = 8.2 Hz, 1 H_{arom}), 7.55 (d, ^3J = 8.2 Hz, 1 H_{arom}), 12.79 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 8.4 (CH_2CH_3), 10.4 (CH_3), 14.1 (CH_2CH_3), 27.1, 31.3 (CH_2CH_3), 116.5 (C_{arom}), 118.6 (CH_{arom}), 124.7 (C_{arom}), 126.9 (CH_{arom}), 151.3, 160.8 (C_{arom}), 206.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 192 (M^+, 19), 163 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{16}O_2$ (M^+): 192.1144; found: 192.1143.

2-Hydroxy-6-propylbenzoic Acid Ethyl Ester (13m)

Starting from 1,1-dimethoxyhexan-3-one (**12b**; 0.320 g, 2.0 mmol) and 1-ethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4l**; 0.822 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13m** was isolated as a mixture of regioisomers (rs = 10:1, (0.134 g, 32%). The spectroscopic data are listed for the major isomer.

IR (neat): 3165 (w), 2960 (w), 2932 (w), 2872 (w), 1667 (s), 1622 (m), 1573(m), 1501 (w), 1464 (m), 1398 (w), 1371 (m), 1329 (m), 1303 (m), 1291 (m), 1277 (m), 1249 (s), 1208 (s), 1173 (w), 1150 (s), 1094 (s), 1015 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 1.40 (t, ^3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.65 (sext, ^3J = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 2.56 (t, ^3J = 7.3 Hz, 2 H, $CH_2CH_2CH_3$), 4.39 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH_3), 6.67–6.79 (m, 2 H_{arom}), 7.74 (d, ^3J = 8.1 Hz, 1 H_{arom}), 10.79 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 13.7 (OCH_2CH_3), 14.1 (CH_2CH_3), 23.8 ($CH_2CH_2CH_3$), 38.1 ($CH_2CH_2CH_3$), 61.1 (OCH_2CH_3), 110.2 (C_{arom}), 117.0, 119.7, 129.6 (CH_{arom}), 151.5, 161.6 (C_{arom}), 170.1 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 208 (M^+, 43), 163 (27), 162 (100), 134 (92), 105 (34).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{16}O_3$ (M^+): 208.1094; found: 208.1094.

2-Hydroxy-3-methoxy-6-propylbenzoic Acid Methyl Ester (13n)

Starting from 1,1-dimethoxyhexan-3-one (**12b**; 0.320 g, 2.0 mmol) and 1,4-dimethoxy-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**4g**; 0.870 g, 3.0 mmol) in CH_2Cl_2 (5 mL), **13n** was isolated as a mixture of regioisomers (rs = 8:1, 0.167 g, 28%). The spectroscopic data are listed for the major isomer.

IR (neat): 3152 (w), 2957 (m), 2933 (w), 2871 (w), 1672 (s), 1616 (w), 1573 (w), 1498 (w), 1438 (s), 1414 (m), 1322 (s), 1292 (m), 1322 (s), 1292 (m), 1253 (s), 1199 (s), 1153 (m), 1093 (w), 1068 (w), 1045 (m), 1034 (m), 1010 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 1.62 (sext, ^3J = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 2.63 (t, ^3J = 7.5 Hz, 2 H, $CH_2CH_2CH_3$), 3.88 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 6.68 (d, ^3J = 8.3 Hz, 1 H_{arom}), 7.49 (d, ^3J = 8.2 Hz, 1 H_{arom}), 10.89 (s, 1 H, OH).

^{13}C NMR (250 MHz, $CDCl_3$): δ = 14.0 (CH_2CH_3), 23.4 ($CH_2CH_2CH_3$), 32.7 ($CH_2CH_2CH_3$), 52.1, 60.4 (OCH_3), 111.3 (C_{arom}), 119.8, 124.1 (CH_{arom}), 143.2, 146.2, 155.1 (C_{arom}), 170.7 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 224 (M^+, 46), 193 (20), 192 (100), 177 (75), 164 (40), 163 (16).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{16}O_4$ (M^+): 224.1043; found: 224.1039.

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References

(1) (a) Kawahara, N.; Masuda, K.; Sekita, S.; Satake, M. *Chem. Pharm. Bull.* **2001**, *49*, 771. (b) Inouye, H.; Nakamura, Y. *Tetrahedron* **1971**, *27*, 1951. (c) Kanamori, H.; Sakamoto, I.; Mizuta, M.; Tanaka, O. *Chem. Pharm. Bull.* **1986**, *34*, 1663. (d) Lacaille-Dubois, M.-A.; Galle, K.; Wagner, H. *Planta Med.* **1996**, *62*, 365. (e) Kawahara, N.; Masuda, K.; Sekita, S.; Satake, M. *Chem. Pharm. Bull.* **2001**, *49*, 771. (f) Li, J.-C.; Feng, L.; Sun, B.-H.; Ikeda, T.; Nohara, T. *Biol. Pharm. Bull.* **2005**, *28*, 534.

(2) (a) Shamma, M.; Tomlinson, H. H. *J. Org. Chem.* **1978**, *43*, 2852. (b) Ishii, H.; Ishikawa, T.; Ishikawa, Y.-i.; Sakamoto, M.; Ishikawa, M.; Takahashi, T. *Chem. Pharm. Bull.* **1984**, *32*, 2984. (c) Matsuhashi, R.; Satou, T.; Koike, K.; Yokosuka, A.; Mimaki, Y.; Sashida, Y.; Nikaido, T. *Planta Med.* **2002**, *68*, 169.

(3) (a) Holker, J. S. E.; O'Brien, E.; Simpson, T. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1365. (b) Stinson, E. E.; Moreau, R. A. *Phytochemistry* **1986**, *25*, 2721. (c) Abe, H.; Nishioka, K.; Takeda, S.; Arai, M.; Takeuchi, Y.; Harayama, T. *Tetrahedron Lett.* **2005**, *46*, 3197. (d) Zhang, H.-W.; Huang, W.-Y.; Song, Y.-C.; Chen, J.-R.; Tan, R.-X. *Helv. Chim. Acta* **2005**, *88*, 2861. (e) Tanahashi, T.; Kuroishi, M.; Kuwahara, A.; Nagakura, N.; Hamada, N. *Chem. Pharm. Bull.* **1997**, *45*, 1183.

(4) (a) Kamisuki, S.; Takahashi, S.; Mizushina, Y.; Hanashima, S.; Kuramochi, K.; Kobayashi, S.; Sakaguchi, K.; Nakata, T.; Sugawara, F. *Tetrahedron* **2004**, *60*, 5695. (b) Uchida, R.; Tomoda, H.; Dong, Y.; Omura, S. *J. Antibiot.* **1999**, *52*, 572. (c) Khan, K. A.; Shoeb, A. *Phytochemistry* **1984**, *23*, 765.

(5) (a) Takechi, M.; Tanaka, Y.; Takehara, M.; Nonaka, G.-I.; Nishioka, I. *Phytochemistry* **1985**, *24*, 2245. (b) Tanaka, T.; Tachibana, H.; Nonaka, G.-i.; Nishioka, I.; Hsu, F.-L. *Chem. Pharm. Bull.* **1993**, *41*, 1214. (c) Yokozawa, T.; Chen, C. P.; Tanaka, T.; Kitani, K. *Biochem. Pharmacol.* **2002**, *63*, 853.

(6) Gould, S. J.; Melville, C. R.; Chen, J. *Tetrahedron* **1997**, *53*, 4561.

(7) Miles, D. H.; Randle, S.; Shakir, R.; Atwood, J. L. *J. Org. Chem.* **1981**, *46*, 2813.

(8) Lin, Y.-L.; Wu, Y.-M.; Kuo, Y.-H. *Phytochemistry* **1997**, *45*, 1057.

(9) *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, .

(10) (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.

(11) For a review of 1,3-bis(trimethylsilyloxy)buta-1,3-dienes in general, see: Langer, P. *Synthesis* **2002**, 441.

(12) For a review of [3+3] cyclizations, see: Feist, H.; Langer, P. *Synthesis* **2007**, 327.

(13) Mroß, G.; Reinke, H.; Langer, P. *Synlett* **2008**, 963.

(14) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 4257.

(15) CCDC-725263 and CCDC-725731 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(16) Reim, S.; Lau, M.; Langer, P. *Tetrahedron Lett.* **2006**, *47*, 6903.