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Synthesis of 2-benzoyl-4-(2-hydroxybenzoyl)phenols by catalytic domino 'Michael–retro-Michael–Mukaiyama-aldol' reactions of 1-aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylchromones

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Abstract

The domino reaction of 1-aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylbenzopyrylium triflates, in situ generated from 3-formylchromones, afforded a variety of 2-benzoyl-4-(2-hydroxybenzoyl)phenols.

1. Introduction

Functionalized benzophenones occur in a variety of natural products and represent important core structures for the development of pharmaceuticals.[1–3] For example, 2-hydroxy- and 2-aminobenzophenones are promising candidates for anticancer therapy, due to their antitubulin activity. Functionalized benzophenones also represent important technical products. They are used as photosensitizers[4] and as active ingredients of commercial agents, which protect the skin or color against UV irradiation.[5] Benzophenones are available by reaction of organometallic reagents with aldehydes and subsequent oxidation. A recent modification of this approach involves the SmI_2 mediated reaction of benzaldehydes with benzylhalides and subsequent oxidation.[6] Other benzophenone syntheses rely on Friedel–Crafts acylations.[7] However, these methods often give unsatisfactory results for the synthesis of functionalized benzophenones (e.g., containing a hydroxy, halide, or ester group), due to competing side reactions. Therefore, the development of new synthetic strategies is of considerable importance in organic and medicinal chemistries.

3-Formylchromone represents a useful building block for the synthesis of a great variety of (2-hydroxybenzoyl)hetarenes.[8] These reactions generally proceed by cyclization of 3-formylchromone with a bis(nucleophile), which involves cleavage of the chromone moiety. Reactions of 3-formylchromone with carbon nucleophiles are relatively rare. For example, the reaction of 3-formylchromones with enamines was reported to give (2-hydroxybenzoyl)pyridines.[9] The reaction of 3-formylchromone with 1,3-dicarbonyl compounds was reported to give open-chain products by simple attack of the central carbon atom of the nucleophile onto the aldehyde (aldol condensation).[10] The employment of acetylacetone resulted in a C,C-cyclization with concurrent cleavage of the chromone moiety to give a benzophenone in low yield.[11] Besides the low yield, the reaction proved to be not general. Recently, we reported[12] a new approach to 4-(2-hydroxybenzoyl)salicylates based on a new domino reaction of 1,3-bis-silyl enol ethers[13,14] with 3-(formyl)benzopyrylium triflates,[15] which are in situ generated by reaction of 3-formylchromones with trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf). Herein, we report the synthesis of 2-benzoyl-4-(2-hydroxybenzoyl)phenols, which can be regarded as functionalized 'bis(benzophenones)'. These products

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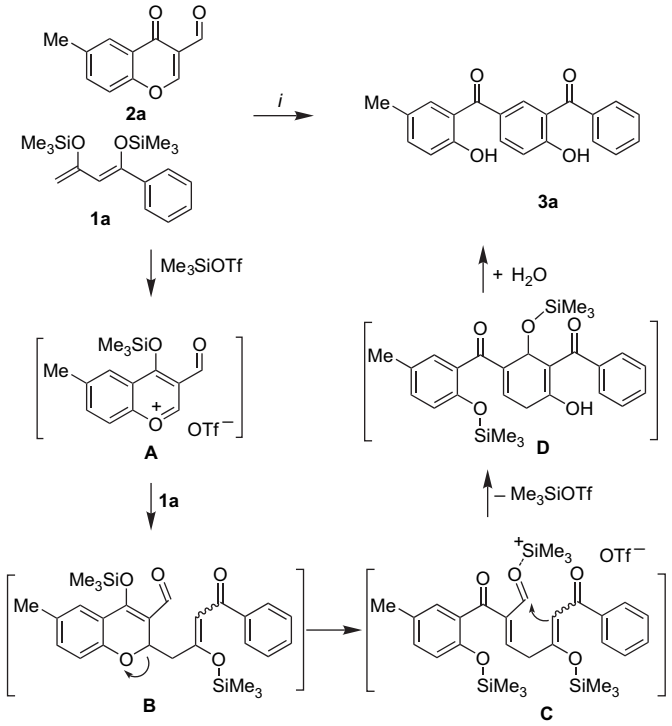
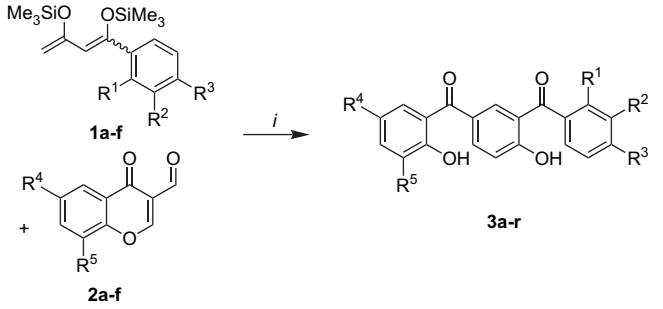
are not readily available by other methods. The reactions reported herein are carried out under mild conditions using catalytic amounts of trimethylsilyl-trifluoromethanesulfonate (Me_3SiOTf).

The Me_3SiOTf catalyzed reaction of 6-methyl-3-formylchromone (**2a**) with 1-phenyl-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**1a**), readily available from benzoylacetone,[16] afforded the hydroxylated bis(benzophenone) **3a**. The formation of **3a** can be explained by a domino 'Michael–retro-Michael–Mukaiyama-aldol' reaction (Scheme 1). The reaction of 6-methyl-3-formylchromone with Me_3SiOTf afforded the benzopyrylium triflate **A**. The reaction of **A** with the terminal carbon atom of **1a** gave intermediate **B**, which underwent a retro-Michael reaction to give the polyketide **C**. An intramolecular aldol reaction gave intermediate **D**, which was transformed into **3a** by elimination of siloxane.



Scheme 1. Mechanism of the formation of **3a**: (i) Me_3SiOTf (0.3 equiv), 20 °C, 10 min; (ii) (1) **1a** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (2) HCl (10%).

The cyclization of 1,3-bis-silyl enol ether **1a** with 6-isopropyl-3-formylchromone (**2b**) and 6,8-dimethyl-3-formylchromone (**2c**) afforded the 2-benzoyl-4-(2-hydroxybenzoyl)phenols **3b** and **3c**, respectively (Scheme 2, Table 1). The cyclization of 1-(2-methoxyphenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1b**) with 3-formylchromones **2a**, **2d**, and **2e** afforded the bis(benzophenones) **3d–f**, respectively. The cyclization of 1-(4-fluorophenyl)- and 1-(2-fluorophenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1c**,**d**) with 3-formylchromones **2b**, **2d**, **2e**, and **2f** afforded the fluoro-substituted bis(benzophenones) **3g–m**. Products **3n** and **3o** were prepared from 1-(2-methylphenyl)-1,3-bis(trimethylsilyloxy)buta-1,3-diene (**1e**). The cyclization of 1-(1-naphthyl)-1,3-bis(trimethylsilyloxy)-buta-1,3-diene (**1f**) with 3-formylchromones **3a**, **3b**, and **3e** afforded the 2-benzoyl-4-(2-hydroxybenzoyl)phenols **3p–3r**, respectively.



Scheme 2. Synthesis of **3a–r**: (i) Me_3SiOTf (0.3 equiv), 20 °C, 10 min; (ii) (1) **1a–f** (1.3 equiv), CH_2Cl_2, 0→20 °C, 12 h; (2) HCl (10%).

Table 1
Products and yields

1	2	3	R^1	R^2	R^3	R^4	R^5	% (3)[a]
a	**a**	**a**	H	H	H	Me	H	34
a	**b**	**b**	H	H	H	^{i}Pr	H	37
a	**c**	**c**	H	H	H	Me	Me	31
b	**a**	**d**	OMe	H	H	Me	H	36
b	**d**	**e**	OMe	H	H	Cl	H	34
b	**e**	**f**	OMe	H	H	Br	H	38
c	**b**	**g**	H	H	F	^{i}Pr	H	30
c	**d**	**h**	H	H	F	Cl	H	27
c	**e**	**i**	H	H	F	Br	H	35
c	**f**	**j**	H	H	F	Et	H	37
d	**e**	**k**	F	H	H	Br	H	38
d	**b**	**l**	F	H	H	^{i}Pr	H	35
d	**d**	**m**	F	H	H	Cl	H	44
e	**e**	**n**	Me	H	H	Br	H	39
e	**b**	**o**	Me	H	H	^{i}Pr	H	28
f	**b**	**p**	$-(CH)_4-$		H	^{i}Pr	H	32
f	**a**	**q**	$-(CH)_4-$		H	Me	H	34
f	**e**	**r**	$-(CH)_4-$		H	Br	H	36
f	**d**	**s**	$-(CH)_4-$		H	Cl	H	36

[a] Isolated yields.

The structure of the products was established by spectroscopic methods. The ^1H NMR spectra showed the presence of two low field signals assigned to the intramolecular hydrogen bonds O–H···O. The structures of bis(benzophenones) **3i** and **3k** were independently confirmed by crystal structure analysis (Figs. 1 and 2).[17] All bis(benzophenones) **3a–s** show strong UV absorptions (see Section 2) and represent potentially useful photosensitizers.

In conclusion, we reported the domino reaction of 1-aryl-1,3-bis(silyloxy)buta-1,3-dienes with 3-formylbenzopyrylium triflates, which were in situ generated from 3-formylchromones. The products were isolated in only moderate yields. This can be explained by the fact that not all of the 1,3-bis-silyl enol ether was converted into product. Noteworthy, the reactions reported provide a convenient access to a variety of highly functionalized 2-benzoyl-4-(2-hydroxybenzoyl)phenols under mild conditions. The products are not readily available by other methods.

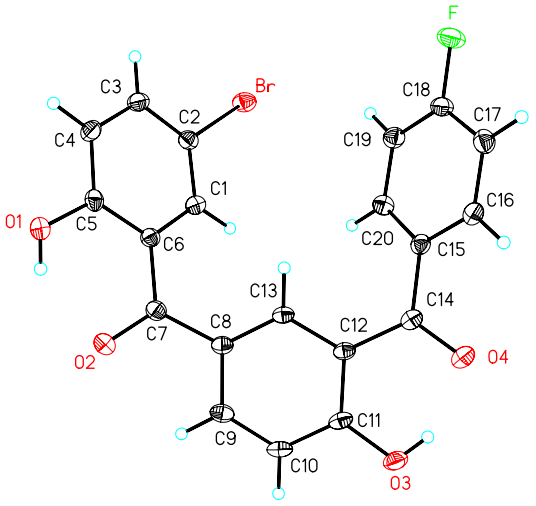


Figure 1. ORTEP plot of **3i**.

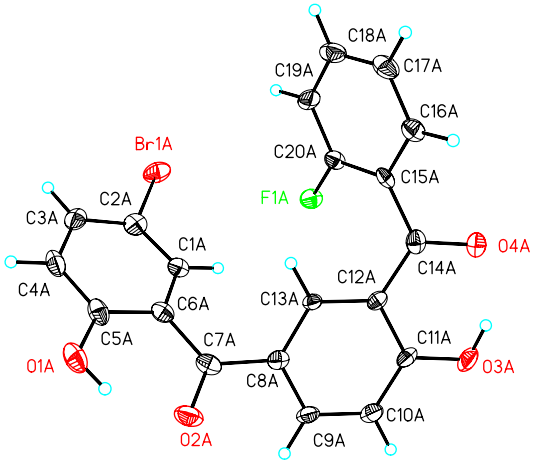


Figure 2. ORTEP plot of **3k**.

2. Experimental section

2.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR, the deuterated solvents indicated were used. Calibration of spectra was carried out on the solvent signals ($CDCl_3$: δ ^{1}H=7.25, δ ^{13}C=77.0; DMSO-d_6: δ ^{1}H=2.50, δ ^{13}C=39.7). The NMR signals were assigned by DEPT and two-dimensional ^{1}H,^{1}H COSY, ^{1}H,^{1}H NOESY, and ^{1}H,^{13}C correlation spectra (HSQC, HMBC). Mass spectrometric data (MS) were obtained by electron ionization (70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected. Formylchromones **2a–f** are commercially available.

2.2. General procedure 1 (synthesis of benzophenones)

To 3-formylchromone **2** (1.0 equiv) was added Me_3SiOTf (0.3 equiv) at 20 °C. After stirring for 10 min, CH_2Cl_2 (8 mL) was added, the solution was cooled to 0 °C, and 1,3-bis-silyl enol ether **1** (1.3 equiv) was added. The mixture was stirred for 12 h at 20 °C and was subsequently poured into an aqueous solution of hydrochloric acid (10%). The organic and the aqueous layers were separated and the latter was extracted with CH_2Cl_2 (3×80 mL). The combined organic layers were washed with water, dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-heptane/CH_2Cl_2=10:1→3:1).

2.2.1. (3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-5-methylphenyl)methanone (**3a**)

Starting with **2a** (188 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1a** (398 mg, 1.3 mmol), **3a** was isolated as a yellow viscous oil (118 mg, 34%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.19 (s, 3H, CH_3), 6.85 (d, J=8.2 Hz, 1H, Ar), 7.09 (d, J=8.7 Hz, 1H, Ar), 7.16–7.26 (m, 2H, Ar), 7.41–7.44 (m, 2H, Ar), 7.48–7.53 (m, 1H, Ar), 7.60–7.63 (m, 2H, Ar), 7.81 (dd, J=8.7, 2.1 Hz, 1H, Ar), 7.94–7.95 (m, 1H, Ar), 11.47 (s, 1H, OH), 12.35 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=19.5 (CH_3), 95.6 (C), 117.3 (CH), 117.4, 117.63 (C), 117.66, 125.9 (CH), 126.7 (C), 127.5 (CH), 127.7 (C), 128.0 (CH), 131.2 (C), 131.3, 131.5, 136.0, 136.1, 136.2 (CH), 159.9, 165.2 (C), 197.7, 200.2 (C=O). IR (neat): $\tilde{\nu}$=3061 (m), 3038 (m), 2959 (s), 2924 (s), 1630 (s), 1590 (s), 1480 (s), 1486 (m), 1408 (m), 1423 (m), 1350 (s), 1290 (s), 1256 (s), 1135 (m), 978 (m), 924 (w), 826 (s), 791 (s), 636 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=221 (4.33), 257 (4.17), 340 (3.69). GC–MS (CI, 70 eV): *m*/*z* (%)=333 ($[M+1]^+$, 100), 285 (10), 257 (10), 225 (10), 189 (10), 93 (20). HRMS (CI) Calcd for $C_{21}H_{17}O_4$ ($[M+1]^+$): 333.1121; found: 333.1116.

2.2.2. (3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-5-isopropylphenyl)methanone (**3b**)

Starting with **2d** (147 mg, 0.67 mmol), Me_3SiOTf (39 mg, 0.18 mmol), and 1,3-bis-silyl enol ether **1a** (270 mg, 0.83 mmol), **3b** was isolated as a yellow viscous oil (81 mg, 37%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.05 (d, J=7.1 Hz, 6H, CH_3), 2.67–2.76 (m, 1H, CH), 6.96 (d, J=8.3 Hz, 1H, Ar), 7.13 (d, J=8.7 Hz, 1H, Ar), 7.27–7.31 (m, 2H, Ar), 7.40–7.45 (m, 2H, Ar), 7.49–7.54 (m, 1H, Ar), 7.60–7.61 (m, 1H, Ar), 7.62–7.63 (m, 1H, Ar), 7.84 (dd, J=8.7, 2.1 Hz, 1H, Ar), 8.01 (m, 1H, Ar), 11.55 (s, 1H, OH), 12.44 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.3 ($2CH_3$), 33.6 (CH), 118.8 (CH), 118.9, 119.0 (C), 129.0 (2CH), 129.0 (2C), 129.3 (2CH), 130.3, 132.8, 135.0, 136.2 (CH), 137.5 (C), 137.6 (CH), 139.4 (C), 161.5, 166.8 (C), 199.1, 201.8 (C=O). IR (KBr): $\tilde{\nu}$=2958 (m), 2922 (m), 2856 (w), 1632 (s), 1598 (s), 1481 (m), 1445 (w), 1355 (s), 1288 (m), 1255 (s), 1115 (w), 981 (w), 949 (w), 840 (w), 794 (m), 635 (w) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.50), 263 (4.47), 341 (3.95). GC–MS (EI, 70 eV): *m*/*z* (%)=360 ($[M]^+$, 75), 345 (20), 281 (11), 225 (10), 197 (11), 172 (10), 163 (43), 147 (100), 101 (6), 77 (20), 51 (4). HRMS (EI) Calcd for $C_{23}H_{20}O_4$ ($[M]^+$): 360.1356; found: 360.1345.

*2.2.3. (3-Benzoyl-4-hydroxyphenyl)-(2-hydroxy-3,5-dimethylphenyl)methanone (**3c**)*

Starting with **5e** (139 mg, 0.6 mmol), Me_3SiOTf (39 mg, 0.18 mmol), and 1,3-bis-silyl enol ether **1a** (239 mg, 0.78 mmol), **3c** was isolated as a yellow solid (70 mg, 31%), mp=116–118 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=2.86 (br s, 6H, CH_3), 7.07 (s, 1H, Ar), 7.10 (m, 2H, Ar), 7.39–7.43 (m, 2H, Ar), 7.47–7.53 (m, 1H, Ar), 7.60–7.63 (m, 2H, Ar), 7.80 (dd, J=8.5, 1.9 Hz, 1H, Ar), 7.93 (m, 1H, Ar), 11.77 (s, 1H, OH), 12.34 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.5, 19.5 (CH_3), 116.9, 117.3 (C), 117.5, 125.9 (CH), 126.0, 126.3 (C), 127.5, 128.0 (CH), 128.1 (2C), 129.0, 131.2, 131.4, 134.6, 136.1, 137.2 (CH), 158.0, 165.1 (C), 198.0, 200.2 (C=O). IR (KBr): $\tilde{\nu}$=2960 (m), 2923 (m), 2867 (w), 1633 (s), 1597 (s), 1433 (m), 1445 (w), 1355 (s), 1318 (w), 1288 (s), 1256 (s), 1215 (s), 1139 (m), 1049 (w), 795 (s) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.51), 262 (4.40), 340 (4.00). GC–MS (EI, 70 eV): m/z (%)=346 ($[M]^+$, 56), 148 (100), 120 (36), 105 (14), 91 (12), 77 (26), 65 (4). HRMS (EI) Calcd for $C_{22}H_{18}O_4$ ($[M]^+$):346.1199; found: 346.1202.

*2.2.4. [4-Hydroxy-3-(2-methoxybenzoyl)phenyl]-(2-hydroxy-5-methylphenyl)methanone (**3d**)*

Starting with **2a** (188 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1b** (437 mg, 1.3 mmol), **3d** was isolated as a yellow viscous oil (131 mg, 36%). ^1H NMR (300 MHz, $CDCl_3$): δ=2.15 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 6.84–6.88 (m, 1H, Ar), 6.96 (d, J=8.5 Hz, 1H, Ar), 7.01 (dd, J=7.6, 1.5 Hz, 1H, Ar), 7.08 (d, J=8.8 Hz, 1H, Ar), 7.18–7.27 (m, 3H, Ar), 7.41 (ddd, J=8.5, 8.5, 1.8 Hz, 1H, Ar), 7.73 (m, 1H, Ar), 7.80 (dd, J=8.8, 2.1 Hz, 1H, Ar), 11.54 (s, 1H, OH), 12.53 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=20.9 (CH_3), 56.2 (OCH_3), 112.2, 118.6, 118.7 (CH), 119.0, 120.0 (C), 121.1 (CH), 127.3, 128.0 (C), 129.1 (CH), 132.7 (C), 132.8, 132.9, 136.5, 137.5, 137.7 (CH), 157.0, 161.2, 166.2 (C), 199.0, 202.3 (C=O). IR (neat): $\tilde{\nu}$=2957 (s), 2934 (s), 2853 (s), 1731 (m), 1670 (w), 1603 (s), 1491 (s), 1446 (s), 1464 (s), 1363 (m), 1286 (m), 1258 (s), 1184 (m), 1163 (m), 1079 (m), 1024 (m), 847 (w), 754 (m), 647 (w) cm^{-1}. MS (EI, 70 eV): m/z (%)=362 ($[M]^+$, 71), 347 (5), 331 (27), 227 (18), 197 (23), 167 (8), 149 (23), 135 (100), 77 (18), 57 (14), 43 (12). HRMS (EI) Calcd for $C_{22}H_{18}O_5$ ($[M]^+$): 362.1149; found: 362.1139.

*2.2.5. (5-Chloro-2-hydroxyphenyl)-[4-hydroxy-3-(2-methoxybenzoyl)phenyl]methanone (**3e**)*

Starting with **4b** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1b** (437 mg, 1.3 mmol), **6e** was isolated as a yellow viscous oil (121 mg, 34%). ^1H NMR (300 MHz, $CDCl_3$): δ=3.85 (s, 3H, OCH_3), 6.92 (d, J=8.9 Hz, 1H, Ar), 6.97 (d, J=8.4 Hz, 1H, Ar), 7.11 (d, J=8.8 Hz, 1H, Ar), 7.19 (s, 1H, Ar), 7.26 (dd, J=7.5, 2.5 Hz, 1H, Ar), 7.34 (dd, J=8.9, 2.6 Hz, 1H, Ar), 7.39–7.45 (m, 2H, Ar), 7.70–7.71 (m, 1H, Ar), 7.83 (dd, J=8.7, 2.3 Hz, 1H, Ar), 11.60 (s, 1H, OH), 12.58 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=55.0 (OCH_3), 110.9 (CH), 117.9, 118.6 (C), 119.1, 119.9 (CH), 122.2 (C), 125.8 (CH), 126.8 (C), 127.7 (2CH), 130.5 (C), 131.6, 134.9, 135.2, 136.1 (CH), 155.6, 160.4, 165.3 (C), 196.6, 200.8 (C=O). IR (KBr): $\tilde{\nu}$=3433 (w), 2960 (s), 2924 (s), 2853 (s), 1634 (s), 1590 (m), 1465 (m), 1433 (w), 1354 (m), 1281 (w), 1260 (s), 1100 (s), 1019 (s), 802 (s), 754 (w), 637 (w) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.20), 256 (3.97), 337 (3.32). MS (EI, 70 eV): m/z (%)=384 ($[M]^+$, [^{37}Cl], 37), 382 ($[M]^+$, [^{35}Cl], 92), 367 (22), 353 ([^{37}Cl], 51), 351 ([^{35}Cl], 100), 249 ([^{37}Cl], 51), 247 ([^{35}Cl], 24), 210 (32), 197 (96), 157 ([^{37}Cl], 19), 155 ([^{35}Cl], 68), 147 (44), 135 (86), 108 (64), 97 (32), 83 (32), 77 (43), 57 (57), 43 (12). HRMS (EI) Calcd for $C_{21}H_{15}O_5Cl$ ($[M]^+$, ^{35}Cl): 382.0602; found: 382.0602.

*2.2.6. (5-Bromo-2-hydroxyphenyl)[4-hydroxy-3-(2-methoxybenzoyl)phenyl]methanone (**3f**)*

Starting with **2c** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1b** (437 mg, 1.3 mmol), **3f** was isolated as yellow solid (163 mg, 38%), mp=151–152 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=3.78 (s, 3H, OCH_3), 6.86 (d, J=8.5 Hz, 1H, Ar), 6.96–6.99 (m, 2H, Ar), 7.10 (d, J=8.5 Hz, 1H, Ar), 7.26 (dd, J=7.6, 1.9 Hz, 1H, Ar), 7.38–7.48 (m, 2H, Ar), 7.55–7.56 (m, 1H, Ar), 7.70–7.71 (m, 1H, Ar), 7.81 (dd, J=7.4, 2.1 Hz, 1H, Ar), 11.61 (s, 1H, OH), 12.59 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=56.4 (OCH_3), 110.0 (C), 112.4, 119.2 (CH), 119.9, 120.6 (C), 120.9, 121.3 (CH), 127.1, 128.2 (C), 129.1, 133.0, 134.9, 136.6, 137.5, 139.1 (CH), 157.0, 162.2, 166.7 (C), 198.0, 202.2 (C=O). IR (KBr): $\tilde{\nu}$=3441 (m), 2958 (m), 2923 (s), 2852 (m), 1637 (s), 1596 (s), 1480 (m), 1464 (s), 1431 (w), 1342 (m), 1320 (s), 1285 (s), 1160 (w), 1102 (m), 1024 (m), 839 (w), 795 (s) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (3.90), 255 (3.64), 336 (3.19). MS (EI, 70 eV): m/z (%)=428 ($[M]^+$, [^{81}Br], 62), 426 ($[M]^+$, [^{79}Br], 60), 397 ([^{81}Br], 81), 395 ([^{79}Br], 82), 293 ([^{81}Br], 12), 291 ([^{79}Br], 13), 197 (100), 173 (7), 147 (31), 135 (57), 108 (37), 77 (27), 57 (19), 43 (15). HRMS (EI) Calcd for $C_{21}H_{15}O_5Br$ ($[M]^+$, ^{79}Br): 426.0097; found: 426.0088. Anal. Calcd for $C_{21}H_{15}O_5Br$ (426.00, ^{79}Br): C 59.21, H 3.55; found: C 59.29, H 3.89.

*2.2.7. [3-(4-Fluorobenzoyl)-4-hydroxyphenyl]-(2-hydroxy-5-isopropylphenyl)methanone (**3g**)*

Starting with **2d** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1c** (421 mg, 1.3 mmol), **3g** was isolated as a yellow solid (115 mg, 30%), mp=134–136 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=1.06 (d, J=7.1 Hz, 6H, CH_3), 2.72 (m, 1H, CH), 6.92 (d, J=8.4 Hz, 1H, Ar), 7.08–7.13 (m, 3H, Ar), 7.26 (m, 1H, Ar), 7.30 (dd, J=8.5, 2.5 Hz, 1H, Ar), 7.64–7.69 (m, 2H, Ar), 7.84 (dd, J=8.5, 2.1 Hz, 1H, Ar), 7.97–7.98 (m, 1H, Ar), 11.52 (s, 1H, OH), 12.28 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=22.9 ($2CH_3$), 32.7 (CH), 114.8, 115.1, 117.4, 117.6 (CH), 127.8 (C), 128.8, 130.6, 130.7 (CH), 132.2,

132.3 (C), 133.7, 134.4, 136.2 (CH), 138.0, 160.1, 162.5, 165.2, 165.9 (C), 197.5, 198.6 (C=O). IR (neat): $\tilde{\nu}$=3062 (w), 2959 (m), 2871 (m), 1635 (w), 1472 (w), 1201 (w), 1158 (m), 1110 (m), 1073 (m), 871 (m), 852 (m), 793 (m), 638 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.65), 263 (4.50), 340 (4.12). MS (EI, 70 eV): *m/z* (%)=378 ($[M]^+$, 47), 363 (12), 162 (43), 147 (100), 123 (11), 91 (13), 69 (7), 57 (6). HRMS (EI) Calcd for $C_{23}H_{19}O_4F$: 378.1262; found: 378.1257.

*2.2.8. (5-Chloro-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (**3h**)*

Starting with **2b** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1c** (421 mg, 1.3 mmol), **3h** was isolated as a yellow viscous oil (101 mg, 27%). ^1H NMR (300 MHz, $CDCl_3$): δ=6.95 (d, *J*=8.7 Hz, 1H, Ar), 7.06–7.09 (m, 1H, Ar), 7.11–713 (m, 1H, Ar), 7.17 (d, *J*=7.1 Hz, 1H, Ar), 7.38 (dd, *J*=8.7, 2.5 Hz, 1H, Ar), 7.49–7.50 (m, 1H, Ar), 7.63–7.68 (m, 1H, Ar), 7.72–7.75 (m, 1H, Ar), 7.84 (dd, *J*=8.6, 2.1 Hz, 1H, Ar), 7.96–7.97 (m, 1H, Ar), 11.51 (s, 1H, OH), 12.39 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=113.5, 113.9 (CH), 117.5 (C), 118.0 (CH), 118.5 (C), 119.2 (2CH), 122.3, 126.9, 127.4 (C), 131.7 (2CH), 134.7, 135.05 (CH), 135.08 (C), 135.9 (CH), 160.3, 165.6 (C), 195.5, 199.1 (C=O). IR (KBr): $\tilde{\nu}$=2960 (w), 2925 (w), 1626 (s), 1581 (s), 1468 (m), 1255 (s), 1217 (s), 841 (s), 796 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.30), 259 (4.06), 338 (3.64). MS (CI, 70 eV): *m/z* (%)=373 ($[M+1]^+$, [^{37}Cl], 10), 371 ($[M+1]^+$, [^{35}Cl], 20), 342 ([^{37}Cl], 14), 340 ([^{35}Cl], 28), 285 (18), 229 (20), 177 (100), 111 (8), 85 (12), 69 (20). HRMS (CI) Calcd for $C_{20}H_{12}O_4ClF$ ($[M+1]^+$, ^{35}Cl): 371.3142; found: 371.3143.

*2.2.9. (5-Bromo-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (**3i**)*

Starting with **2c** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1c** (421 mg, 1.3 mmol), **3i** was isolated as yellow solid (146 mg, 35%), mp=118–120 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=6.89 (d, *J*=8.9 Hz, 1H, Ar), 7.14–7.19 (m, 3H, Ar), 7.50 (dd, *J*=8.9, 2.4 Hz, 1H, Ar), 7.65 (m, 1H, Ar), 7.67–7.72 (m, 2H, Ar), 7.86 (dd, *J*=8.5, 2.1 Hz, 1H, Ar), 7.90–7.91 (m, 1H, Ar), 11.50 (s, 1H, OH), 12.33 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=110.6 (C), 116.3, 116.6 (CH), 118.5 (C), 119.8 (CH), 120.6 (C), 121.1 (CH), 128.3 (C), 132.1, 132.2 (CH), 133.4, 133.5 (C), 135.0, 136.0, 137.5, 139.2 (CH), 162.2, 167.1 (C), 197.9, 199.8 (C=O). IR (KBr): $\tilde{\nu}$=3069 (w), 2956 (m), 2900 (w), 1627 (s), 1585 (s), 1466 (s), 1341 (m), 1287 (m), 1253 (s), 1213 (s), 1072 (m), 843 (s), 610 (w) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.30), 259 (4.06), 338 (3.64). MS (EI, 70 eV): *m/z* (%)=416 ($[M]^+$, [^{81}Br], 100), 414 ($[M]^+$, [^{79}Br], 100), 319 (7), 243 (12), 216 ([^{81}Br], 80), 214 ([^{79}Br], 80), 200 ([^{81}Br], 96), 198 ([^{79}Br], 96), 172 (10), 147 (67), 123 (75), 95 (55), 57 (25). HRMS (EI) Calcd for $C_{20}H_{12}O_4BrF$ ($[M]^+$, ^{79}Br): 413.9897; found: 413.9897.

*2.2.10. (5-Ethyl-2-hydroxyphenyl)-[3-(4-fluorobenzoyl)-4-hydroxyphenyl]methanone (**3j**)*

Starting with **2f** (202 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1c** (421 mg, 1.3 mmol), **3j** was isolated as yellow viscous oil (135 mg, 37%). ^1H NMR (300 MHz, $CDCl_3$): δ=1.06 (t, *J*=7.6 Hz, 3H, CH_3), 2.48 (q, *J*=7.8 Hz, 2H, CH_2), 6.89–6.92 (m, 1H, Ar), 7.09–7.14 (m, 3H, Ar), 7.25–7.29 (m, 2H, Ar), 7.65–7.70 (m, 2H, Ar), 7.82–7.85 (m, 1H, Ar), 7.95–7.96 (m, 1H, Ar), 11.50 (s, 1H, OH), 12.24 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=16.9 (CH_3), 29.2 (CH_2), 116.2, 116.5 (CH), 118.8 (C), 118.9, 119.0 (CH), 129.2 (2CH), 131.6, 132.1 (C), 132.2 (CH), 133.6 (C), 134.7 (2CH), 135.7 (CH), 136.6, 137.6, 161.5, 166.5 (C), 199.0, 200.0 (C=O). IR (neat): $\tilde{\nu}$=3063 (w), 2964 (m), 2930 (m), 2872 (w), 1631 (s), 1599 (s), 1481 (s), 1409 (w), 1351 (s), 1292 (s), 1255 (s), 1214 (s), 1157 (s), 1073 (w), 882 (w), 844 (s), 612 (w) cm^{-1}. MS (CI, 70 eV): *m/z* (%)=365 ($[M+1]^+$, 100), 340 (10), 303 (7), 243 (8), 177 (20), 149 (25), 133 (20), 96 (10). HRMS (CI) Calcd for $C_{22}H_{18}O_4F$ ($[M+H]^+$): 365.11836; found: 365.11842.

*2.2.11. (5-Bromo-2-hydroxyphenyl)-[3-(2-fluorobenzoyl)-4-hydroxyphenyl]methanone (**3k**)*

Starting with **2c** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1d** (421 mg, 1.3 mmol), **3k** was isolated as yellow solid (155 mg, 38%), mp=105 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=6.86 (d, *J*=8.3 Hz, 1H, Ar), 7.14 (d *J*=8.7 Hz, 1H, Ar), 7.18–7.23 (m, 1H, Ar), 7.25–7.28 (m, 1H, Ar), 742–7.46 (m, 1H, Ar), 7.47 (m, 1H, Ar), 7.49–7.51 (m, 1H, Ar), 7.65–7.66 (m, 1H, Ar), 7.74–7.76 (m, 1H, Ar), 7.88 (dd, *J*=8.5, 2.3 Hz, 1H, Ar), 11.55 (s, 1H, OH), 12.36 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=110.6 (C), 116.8, 117.1 (CH), 119.2 (C), 119.7 (CH), 120.5 (C), 120.9, 125.6 (CH), 128.5, 130.5 (C), 134.9, 136.2, 136.3, 138.0, 139.2 (CH), 139.3, 162.2, 166.8 (C), 197.8, 198.6 (C=O). IR (neat): $\tilde{\nu}$=3054 (w), 2956 (s), 2924 (s), 2852 (s), 1629 (s), 1590 (s), 1465 (s), 1418 (s), 1418 (s), 1304 (m), 1253 (s), 1208 (s), 1122 (s), 927 (m), 844 (s), 763 (s), 629 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.50), 256 (4.23), 340 (3.79). MS (EI, 70 eV): *m/z* (%)=416 ($[M]^+$, [^{81}Br], 97), 414 ($[M]^+$, [^{79}Br], 97), 397 ([^{81}Br], 6), 395 ([^{79}Br], 6), 216 ([^{81}Br], 71), 214 ([^{79}Br], 71), 199 ([^{81}Br], 100), 197 ([^{79}Br], 100), 147 (47), 123 (51), 95 (22), 57 (11). HRMS (EI) Calcd for $C_{20}H_{12}O_4BrF$ ($[M]^+$, ^{79}Br): 413.9897; found: 413.9891.

*2.2.12. [3-(2-Fluorobenzoyl)-4-hydroxyphenyl]-(2-hydroxy-5-isopropylphenyl)methanone (**3l**)*

Starting with **2d** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1d** (421 mg, 1.3 mmol), **3l** was isolated as a yellow solid (130 mg, 35%), mp=105–107 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=0.86 (d, *J*=7.1 Hz, 6H, CH_3), 2.25 (m, 1H, CH), 6.75 (d, *J*=8.5 Hz, 1H, Ar), 6.95–6.98 (m, 1H, Ar), 7.01–7.07 (m, 3H, Ar), 7.12 (dd, *J*=8.5, 2.3 Hz, 1H, Ar), 7.23–7.28 (m, 1H, Ar), 7.33–7.38 (m, 1H, Ar), 7.70–7.72 (m, 2H, Ar), 11.34 (s,

1H, OH), 12.30 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.9, 25.0 (CH_3), 34.2 (CH), 117.3, 117.6, 119.4, 120.0 (CH), 120.5 (C), 124.0 (CH), 125.0 (C), 125.7 (CH), 126.4, 126.7, 130.1 (C), 131.0, 135.6, 136.5, 139.9 (CH), 140.1, 161.6, 167.0 (C), 199.4, 199.6 (C=O). IR (KBr): $\tilde{\nu}$=3431 (w), 2960 (m), 2924 (w), 2868 (w), 1634 (s), 1612 (s), 1588 (s), 1483 (s), 1357 (s) 1251 (s), 1212 (s), 840 (m), 765 (s), 634 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=218 (4.30), 258 (3.95), 339 (3.33). MS (EI, 70 eV): *m/z* (%)=378 ([M]$^+$, 13), 343 (5), 163 (25), 162 (29), 147 (100), 123 (68), 121 (7), 91 (31), 69 (14), 57 (19), 41 (19). HRMS (EI) Calcd for $C_{23}H_{19}O_4F$ ([M]$^+$): 378.1262; found: 378.1257.

2.2.13. (5-Chloro-2-hydroxyphenyl)-[3-(2-fluorobenzoyl)-4-hydroxyphenyl]methanone (**3m**)

Starting with **2b** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1d** (421 mg, 1.3 mmol), **3m** was isolated as a yellow solid (163 mg, 44%), mp=123–125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.91 (d, *J*=8.9 Hz, 1H, Ar), 7.14 (d, *J*=8.7 Hz, 1H, Ar), 7.18–7.19 (m, 1H, Ar), 7.22–7.25 (m, 1H, Ar), 7.35 (dd, *J*=8.9, 2.6 Hz, 1H, Ar), 7.42–7.45 (m, 1H, Ar), 7.46–7.50 (m, 1H, Ar), 7.53 (m, 1H, Ar), 7.75–7.77 (m, 1H, Ar), 7.89 (dd, *J*=8.9, 2.1 Hz, 1H, Ar), 11.53 (s, 1H, OH), 12.34 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=117.5, 117.8 (CH), 119.9, 120.0 (C), 120.6, 121.3, 124.6 (CH), 126.4, 126.6, 129.3 (C), 131.1, 132.8 (CH), 134.9 (C), 135.0, 137.2, 138.8 (CH), 162.5, 167.5 (C), 198.5, 199.3 (C=O). IR (neat): $\tilde{\nu}$=3077 (w), 2956 (s), 2924 (s), 2853 (s), 1675 (s), 1633 (s), 1598 (s), 1466 (s), 1417 (s), 1253 (s), 1208 (s), 1140 (s), 1097 (m), 950 (m), 844 (s), 763 (s) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=221 (4.41), 258 (4.27), 340 (3.82). MS (EI, 70 eV): *m/z* (%)=372 ([M]$^+$, [^{37}Cl], 38), 370 ([M]$^+$, [^{37}Cl], 100), 340 ([^{37}Cl], 8), 338 ([^{35}Cl], 10), 267 (26), 243 (10), 216 (51), 197 (20), 177 (19), 155 (96), 147 (33), 123 (42), 95 (25), 57 (27). HRMS (EI) Calcd for $C_{20}H_{12}O_4ClF$ ([M]$^+$, ^{35}Cl): 370.0403; found: 370.0402.

2.2.14. (5-Bromo-2-hydroxyphenyl)-[4-hydroxy-3-(2-methylbenzoyl)phenyl]methanone (**3n**)

Starting with **2c** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1e** (416 mg, 1.3 mmol), **3n** was isolated as a yellow solid (160 mg, 39%), mp=119–121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.25 (s, 3H, CH_3), 6.84 (d, *J*=8.7 Hz, 1H, Ar), 7.13 (d, *J*=7.7 Hz, 1H, Ar), 7.17 (m, 1H, Ar), 7.25–7.26 (m, 1H, Ar), 7.28 (m, 1H, Ar), 7.30–7.33 (m, 1H, Ar), 7.44 (dd, *J*=8.9, 2.5 Hz, 1H, Ar), 7.52–7.53 (m, 1H, Ar), 7.64–7.65 (m, 1H, Ar), 7.83 (dd, *J*=8.5, 2.3 Hz, 1H, Ar), 11.54 (s, 1H, OH), 12.68 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=20.5 (CH_3), 110.5, 119.4 (C), 119.6 (CH), 120.5 (CH), 121.0, 126.0, 127.8 (CH), 128.3 (C), 131.2, 131.7, 134.9 (CH), 136.2, 136.5, 136.9 (C), 137.8, 139.1 (CH), 162.2, 167.2 (C), 197.8, 204.4 (C=O). IR (KBr): $\tilde{\nu}$=3431 (w), 3064 (w), 3022 (w), 2957 (w), 2924 (w), 2854 (w), 1632 (s), 1597 (s), 1463 (s), 1381 (m), 1319 (s), 1255 (s), 1237 (m), 1209 (s), 1101 (w), 992 (w), 931 (m), 769 (m), 769 (s), 708 (w), 652 (w) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=252 (4.52), 330 (4.18). MS (EI, 70 eV): *m/z* (%)=412 ([M]$^+$, [^{81}Br], 52), 410 ([M]$^+$, [^{79}Br], 51), 397 ([^{81}Br], 16), 395 ([^{79}Br], 17), 340 (2), 267 (15), 237 (11), 211 (100), 199 ([^{81}Br], 33), 197 ([^{79}Br], 31), 194 (22), 161 (10), 147 (22), 119 (52), 91 (63), 69 (22). HRMS (EI) Calcd for $C_{21}H_{15}O_4Br$ ([M]$^+$, ^{79}Br): 410.0148; found: 410.0140.

2.2.15. (2-Hydroxy-5-isopropylphenyl)-[4-hydroxy-3-(2-methylbenzoyl)phenyl]methanone (**3o**)

Starting with **2d** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1d** (416 mg, 1.3 mmol), **3o** was isolated as a yellow solid (105 mg, 28%), mp=138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.04 (d, *J*=7.1 Hz, 6H, CH_3), 2.26 (s, 3H, CH_3), 2.61–2.75 (m, 1H, CH), 6.88 (d, *J*=8.5 Hz, 1H, Ar), 7.12 (d, *J*=8.7 Hz, 1H, Ar), 7.17 (m, 1H, Ar), 7.18–7.19 (m, 2H, Ar), 7.22 (s, 1H, Ar), 7.24–7.25 (m, 1H, Ar), 7.27–7.31 (m, 1H, Ar), 7.68 (m, 1H, Ar) 7.84 (dd, *J*=8.5, 2.1 Hz, 1H, Ar), 11.56 (s, 1H, OH), 12.65 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=20.0 (CH_3), 24.3 ($2CH_3$), 33.6 (CH), 118.8, 119.2 (CH), 119.5 (C), 125.9, 127.7 (CH), 129.3 (C), 130.3, 131.0, 131.6, 135.0 (CH), 135.1, 136.0 (C), 136.2 (CH), 137.2 (C), 138.1 (CH), 139.4, 161.6, 166.8 (C), 199.0, 204.6 (C=O). IR (KBr): $\tilde{\nu}$=3430 (w), 3055 (w), 3029 (w), 2961 (m), 2924 (m), 2872 (w), 1632 (s), 1593 (s), 1483 (s), 1356 (s), 1316 (s), 1256 (s), 1211 (s), 1140 (w), 1118 (w), 1097 (w), 981 (w), 900 (w), 846 (w), 794 (s), 636 (m) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=255 (4.20), 339 (3.80). MS (EI, 70 eV): *m/z* (%)=374 ([M]$^+$, 78), 359 (19), 316 (3), 139 (5), 211 (16), 172 (8), 163 (48), 162 (46), 147 (100), 119 (10), 97 (8), 91 (26), 83 (10), 69 (18), 57 (16). HRMS (EI) Calcd for $C_{24}H_{22}O_4$ ([M]$^+$): 374.1513; found: 374.1505.

2.2.16. (2-Hydroxy-5-isopropylphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (**3p**)

Starting with **2d** (216 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1f** (463 mg, 1.3 mmol), **3p** was isolated as a yellow viscous oil (130 mg, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.90 (d, *J*=6.9 Hz, 6H, CH_3), 2.44–2.56 (m, 1H, CH), 7.11 (m, 1H, Ar), 7.16–7.18 (m, 1H, Ar), 7.19–7.22 (m, 1H, Ar), 7.41–7.44 (m, 1H, Ar), 7.45 (m, 1H, Ar), 7.47 (m, 2H, Ar), 7.48–7.52 (m, 1H, Ar), 7.74–7.75 (m, 1H, Ar), 7.82–7.84 (m, 1H, Ar), 7.85–7.86 (m, 1H, Ar), 7.87–7.89 (m, 1H, Ar), 7.92 (dd, *J*=7.6, 1.2 Hz, 1H, Ar), 11.52 (s, 1H, OH), 12.73 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.9 ($2CH_3$), 33.4 (CH), 118.7, 119.3 (CH), 120.0 (C), 124.7, 125.2, 126.7, 127.2, 128.0, 129.0 (CH), 129.3 (C), 130.2 (CH), 130.6 (C), 131.8 (CH), 134.1, 134.9 (C), 135.0, 136.3, 138.2 (CH), 139.6, 161.5, 166.9, 189.6 (C), 198.8, 204.0 (C=O). IR (neat): $\tilde{\nu}$=3058 (m), 2959 (s), 2926 (m), 2870 (m), 1630 (s), 1589 (s), 1508 (m), 1480 (s), 1354 (s), 1296 (m), 1252 (s), 1211 (s), 1146 (m), 1129 (w), 1045 (w), 908 (m), 843 (s), 793 (s), 733 (s) cm^{-1}. GC–MS (EI, 70 eV): *m/z* (%)=410 ([M]$^+$, 86), 395 (16), 247 (14), 197 (17), 163 (49), 147 (100), 127 (30), 91 (19),

65 (5). HRMS (EI) Calcd for $C_{27}H_{22}O_4$ ([M]$^+$): 410.1513; found: 410.1512.

2.2.17. (2-Hydroxy-5-methylphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (**3q**)

Starting with **2a** (188 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1f** (463 mg, 1.3 mmol), **3q** was isolated as a yellow solid (130 mg, 34%), mp=112–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$), δ=2.00 (s, 3H, CH_3), 6.77 (d, J=8.4 Hz, 1H, Ar), 7.06–7.07 (m, 1H, Ar), 7.08–7.11 (m, 1H, Ar), 7.13 (m, 1H, Ar), 7.41–7.42 (m, 1H, Ar), 7.43 (m, 1H, Ar), 7.44–7.47 (m, 2H, Ar), 7.68–7.69 (m, 1H, Ar), 7.78–7.80 (m, 1H, Ar), 7.81–7.82 (m, 1H, Ar), 7.83–7.85 (m, 1H, Ar), 7.89 (dd, J=7.6, 1.5 Hz, 1H, Ar), 11.42 (s, 1H, OH), 12.65 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=19.3 (CH_3), 117.2 (CH), 117.3 (C), 117.7 (CH), 118.6 (C), 123.2, 123.8, 125.4, 125.8, 126.6, 127.5 (CH), 127.7, 129.1 (C), 130.4, 131.2 (CH), 132.2, 133.5 (C), 135.0, 136.1, 136.7 (CH), 159.8, 165.4, 188.1 (C), 197.3, 202.4 (C=O). UV–vis (nm, CH_3CN): λ_{max} (log ε)=222 (4.88), 256 (4.32), 341 (4.02). GC–MS (CI, 70 eV): m/z (%)=383 ([M+1]$^+$, 100), 305 (5), 267 (4), 229 (3), 177 (5), 122 (3), 88 (3). HRMS (CI) Calcd for $C_{25}H_{19}O_4$ ([M+1]$^+$): 383.1278: found: 383.1297.

2.2.18. (5-Bromo-2-hydroxyphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (**3r**)

Starting with **2c** (253 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1f** (463 mg, 1.3 mmol), **3r** was isolated as a yellow solid (166 mg, 36%), mp=125–127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.79 (d, J=8.9 Hz, 1H, Ar), 7.14–7.15 (m, 1H, Ar), 7.17 (s, 1H, Ar) 7.38 (m, 1H, Ar), 7.41–7.43 (m, 1H, Ar), 7.44–7.45 (m, 1H, Ar), 7.49–750 (m, 1H, Ar), 7.52–7.53 (m, 1H, Ar), 7.71–7.72 (m, 1H, Ar), 7.80–7.82 (m, 1H, Ar), 7.83–7.84 (m, 1H, Ar), 7.85–7.88 (m, 1H, Ar), 7.92 (dd, J=7.3, 1.9 Hz, 1H, Ar), 11.46 (s, 1H, OH), 12.74 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=109.1 (C), 118.2 (CH), 118.5, 119.0 (C), 119.5, 123.3, 123.8, 125.7, 125.8, 126.6 (CH), 126.8 (C), 127.6 (CH), 129.2 (C), 130.7 (CH), 132.8, 133.1 (C), 133.5, 135.1, 136.5, 137.7 (CH), 160.7, 165.9 (C), 196.4, 202.2 (C=O). IR (KBr): $\tilde{\nu}$=3047 (w), 2957 (w), 2924 (w), 2853 (w), 1626 (s), 1588 (s), 1507 (w), 1464 (s), 1336 (s), 1251 (s), 1209 (s), 1045 (w), 915 (s), 777 (s) cm^{-1}. UV–vis (nm, CH_3CN): λ_{max} (log ε)=257 (3.89), 339 (3.48). GC–MS (EI, 70 eV): m/z (%)=448 ([M]$^+$, [^{81}Br], 89), 446 ([M]$^+$, [^{79}Br], 90), 368 (6), 249 ([^{81}Br], 89), 247 ([^{79}Br], 89), 231 (13), 155 (35), 128 (100), 63 (10). HRMS (EI) Calcd for $C_{24}H_{15}O_4Br$: 446.0148 ([M]$^+$, ^{79}Br): found: 446.0161.

2.2.19. (5-Chloro-2-hydroxyphenyl)-[4-hydroxy-3-(1-naphthoyl)phenyl]methanone (**3s**)

Starting with **2d** (208 mg, 1.0 mmol), Me_3SiOTf (66 mg, 0.3 mmol), and 1,3-bis-silyl enol ether **1f** (463 mg, 1.3 mmol), **3s** was isolated as a yellow viscous oil (144 mg, 36%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.84 (d, J=8.1 Hz, 1H, Ar), 7.15–7.16 (m, 1H, Ar), 7.18 (s, 1H, Ar),), 7.28 (dd, J=8.9, 2.5 Hz, 1H, Ar), 7.35 (m, 1H, Ar), 7.44–7.47 (m, 2H, Ar), 7.51–7.52 (m, 1H, Ar), 7.53 (s, 1H, Ar), 7.71–7.72 (m, 1H, Ar), 7.81–7.83 (m, 1H, Ar), 7.85–7.86 (m, 1H, Ar), 7.91–7.95 (m, 1H, Ar), 11.45 (s, 1H, OH), 12.73 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=119.6 (CH), 119.8, 120.0 (C), 120.5 (CH), 123.6 (C), 124.7, 125.2 (CH), 127.3 (2CH), 128.1 (CH), 128.3 (C), 129.0 (CH), 130.6 (C), 131.9, 132.1 (CH), 134.2, 134.6 (C), 136.3, 136.6, 137.9 (CH), 161.7, 167.3 (C), 197.9, 203.6 (C=O). MS (CI, 70 eV): m/z (%)=405 ([M+1]$^+$, [^{37}Cl], 50), 403 ([M+1]$^+$, [^{37}Cl], 100), 285 (10), 257 (12), 229 (10), 177 (13), 125 (14), 97 (15), 85 (20), 69 (21). HRMS (CI) Calcd for $C_{24}H_{16}O_4Cl$ ([M+1]$^+$, ^{35}Cl): 403.0732; found: 403.0731.

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References and notes

1. Liou, J.-P.; Chang, J.-Y.; Chang, C.-W.; Chang, C.-Y.; Mahindroo, N.; Kuo, F.-M.; Hsieh, H.-P. *J. Med. Chem.* **2004**, *47*, 2897.
2. Liou, J.-P.; Chang, C.-W.; Song, J. S.; Yang, Y. S.; Yeh, C. F.; Tseng, H. Y.; Lo, Y. K.; Chang, C.-L.; Chang, C.-M.; Hsieh, H.-P. *J. Med. Chem.* **2002**, *45*, 2556.
3. Pettit, G. R.; Toki, B.; Herald, D. L.; Verdier-Pinard, P.; Boyd, M. R.; Hamel, E.; Pettit, R. K. *J. Med. Chem.* **1998**, *41*, 1688.
4. Cai, X.; Sakamoto, M.; Fujitsuka, M.; Majima, T. *Chem.—Eur. J.* **2005**, *11*, 6471 and references cited therein.
5. Langhals, H.; Fuchs, K. *Chem. Unserer Zeit* **2004**, *38*, 98 and references cited therein.
6. Shiue, J.-S.; Lin, M.-H.; Fang, J.-M. *J. Org. Chem.* **1997**, *62*, 4643.
7. Buchta, E.; Egger, H. *Chem. Ber.* **1957**, *90*, 2760.
8. For reviews on 3-formylchromone, see: (a) Ellis, G. P. *The Chemistry of Heterocyclic Compounds*; Weisberger, A., Ed.; Interscience: New York, NY, 1977; Vol 35, p 921; (b) Ghosh, C. K.; Ghosh, C. *Indian J. Chem.* **1997**, *36B*, 968.
9. Heber, D. *Synthesis* **1978**, 691.
10. (a) Ghosh, C. K.; Khan, S. *Synthesis* **1981**, 903; (b) Hass, G.; Stanton, J. L.; von Sprecher, A.; Wenk, P. *J. Heterocycl. Chem.* **1981**, *18*, 607; (c) Prousek, J. *Collect. Czech. Chem. Commun.* **1991**, 1361; (d) Ghosh, C. K.; Bandyopadhyay, C.; Biswas, S.; Chakravarty, A. K. *Indian J. Chem., Sect. B* **1990**, *29*, 814.
11. Bandyopadhyay, C.; Sur, K. R.; Patra, R. *J. Chem. Res., Synop.* **1998**, *12*, 802.
12. (a) Langer, P.; Appel, B. *Tetrahedron Lett.* **2003**, 7921; (b) Appel, B.; Rotzoll, S.; Reinke, H.; Langer, P. *Eur. J. Org. Chem.* **2006**, 3638.
13. For a review on 1,3-bis-silyl enol ethers, see: Langer, P. *Synthesis* **2002**, 441.
14. For a review on domino reactions of 1,3-bis-silyl enol ethers with benzopyrylium triflates, see: Langer, P. *Synlett* **2007**, 1016.
15. Lee, Y.-G.; Ishimaru, K.; Iwasaki, H.; Ohkata, K.; Akiba, K. *J. Org. Chem.* **1991**, *56*, 2058.
16. Molander, G. A.; Cameron, K. O. *J. Am. Chem. Soc.* **1993**, *115*, 830.
17. CCDC-650038 (**3i**) and CCDC-650039 (**3k**) 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.