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Concise Synthesis of Dihydrochalcones via Palladium-Catalyzed Coupling of Aryl Halides and 1-Aryl-2-propen-1-ols

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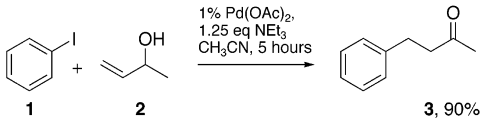
Abstract: An expedient route to substituted dihydrochalcones is reported. The key step is a palladium-assisted arylation of 1-aryl-2-propen-1-ols. This two-step/one-purification process allows the synthesis of a wide range of compounds with original substitution patterns, including polyphenolic derivatives.

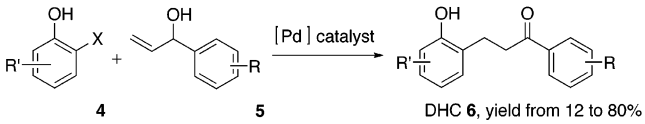
Flavonoids received attention as dietary constituents of potential importance to health. Effects are thought to be due to their antioxidant properties and to involvement in biological pathways.[1] Among the several classes of flavonoids, dihydrochalcones (DHCs) have been reported to demonstrate antifungal, antibacterial,[2] anticancer,[3] and antioxidant[4] properties and have received considerable attention as food sweeteners.[5] DHCs are also useful key synthetic intermediates toward flavenes[6] and anthocyanin-type dyes.[7]

Up to now, DHCs are mostly synthesized through a Claisen−Schmidt condensation[8] followed by reduction of the obtained chalcone, or through the alkaline reduction of a corresponding flavanone.[9] Although widely used, these versatile procedures suffer some drawbacks. In particular, it regularly requires prolonged reaction times,[10] and complete protection of all phenolic functionalities is often necessary to achieve high yields. Alternative pathways to substituted DHCs are scarce.

SCHEME 1. Benzylacetone 3 Synthesis Reported by Heck[11]



SCHEME 2. General Scheme for the Synthesis of DHCs 6 through Palladium-Catalyzed Arylation



In the course of our investigations toward new synthetic routes to flavonoids, we found that a Heck-type reaction would constitute a novel efficient approach to DHCs. In 1976, Heck[11] and Chalk[12] simultaneously reported that arylation of but-3-en-2-ol **2** with iodophenol **1** give benzylacetone **3** (Scheme 1).

Building on these early results, we have initiated further investigations to develop an alternative synthetic route to DHCs **6** from *o*-halophenol **4** and 1-aryl-2-propen-1-ols **5** (Scheme 2).

Vinylation of various aromatic aldehydes **7** affords the desired allylic alcohols **5** in quantitative yields. These derivatives are then arylated, without intermediate purifications, using palladium catalyst in the presence of an aryl halide **4**. The combined vinylation/palladium-mediated arylation proved to be a straightforward entry into substituted DHCs **6**. Various coupling were undertaken.

The reaction conditions, 1% $Pd(OAc)_2$, 1.25 equiv of NEt_3 in CH_3CN (method A), first reported by Heck were successfully applied to the coupling of iodophenol **1** with phenylprop-2-enol **5a** (Table 1). Although the reaction was found to be slow (the reaction time had to be increased to 24 h), the desired product **6a** was obtained with 74% yield (entry 1). Introduction of an *ortho*-phenolic function on the iodoarene resulted as expected in a reduced yield of product at 56%. Although the use of electron-rich haloarenes is known to disfavor Heck-

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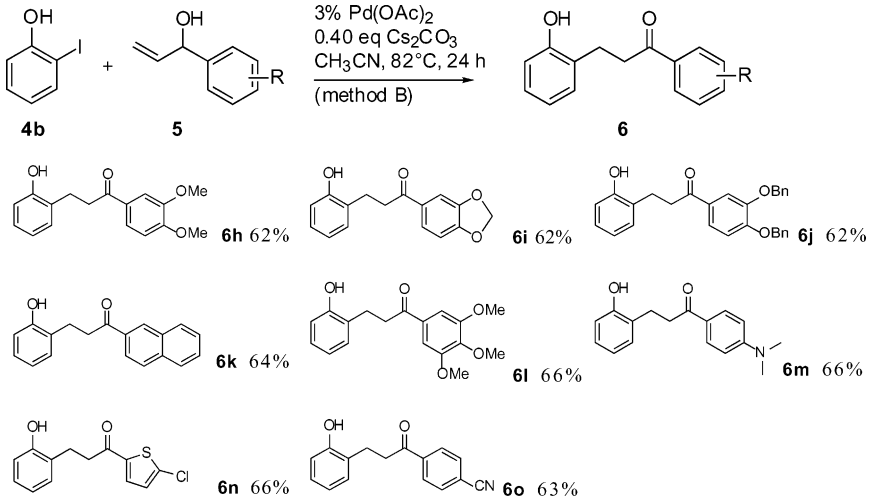
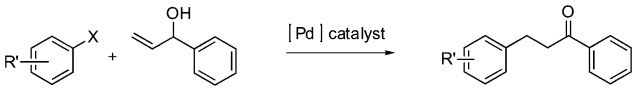
SCHEME 3. Synthesis of Substituted DHCs 6 Using Coupling Conditions B[a]



[a] Isolated yields.

TABLE 1. Coupling of the Phenylprop-2-enol 5a with Various Aryl Halides



Entry	ArX	DHC	Yield(%)[a]	Conditions[b]
1	**1**	**6a**	74%	A
2	**4b**	**6b**	61%	B
3	**4c**	**6c**	70%	B
4	**4d**		0%	A,B
5	**4e**	**6e**	10%	B
6			45%	C
7	**4f**	**6f**	45%	C
8	**4g**	**6g**	12%	C

[a] Isolated yields. [b] Coupling conditions: (method A) 1% $Pd(OAc)_2$, 1.25 equiv of NEt_3, CH_3CN reflux, 24 h; (method B) 3% $Pd(OAc)_2$, 0.40 equiv of Cs_2CO_3, CH_3CN, reflux, 24 h; (method C) 3% Herrmann's catalyst 8, 2.00 equiv of AcONa, $CH_3CN/DMF/H_2O$, 140 °C, 24 h.

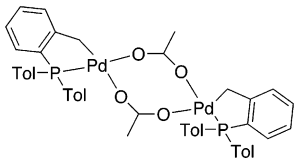
type reaction,[13] we succeeded to improve this result with 3% $Pd(OAc)_2$, by using Cs_2CO_3 as a base in CH_3CN (method B). Under these conditions, we obtained 61% yield of the DHC **6b** (entry 2). The protection of the phenol functionality with an electron-withdrawing *p*-toluenesulfonyl group resulted in a slightly increased yield (entry 3).

However, the presence of an additional phenolic function on the iodoarene caused the reduction of the iodide and no coupling product was observed (entry 4). To extend the reaction to dihydroxylated aryl halides, we studied the coupling reaction using aryl bromide substrates. Since aryl bromides are much less reactive,[14] the reaction time was increased but it did not afford better yields. Therefore, we sought for improved catalytic system. Toward this end, different palladium sources were examined. Other catalysts namely $PdCl_2(PPh_3)_2$, $Pd(dba)_2$, $Pd(PPh_3)_4$, $Pd(OAc)_2/P(o\text{-tol})_3$, $Pd(dppe)_2$, Herrmann catalyst,[15] $PdCl_2$, $PdBr_2$, and $Pd(acac)_2$ gave only poor yields such as conditions A. Investigation of different methods (various bases and solvent) was undertaken. Using the Herrmann's palladacycle **8** at 140 °C with AcONa in a mixture of $CH_3CN/DMF/H_2O$, bromoresorcinol **7e** was arylated in 45% yield while method B afforded only the DHC **6e** in 10% yield (entries 5−6). Bromohydroquinone **4f** (entry 7) and the monoprotected phloroglucinol derivative **4g** (entry 8) were arylated in the same way in reasonable to poor yields.

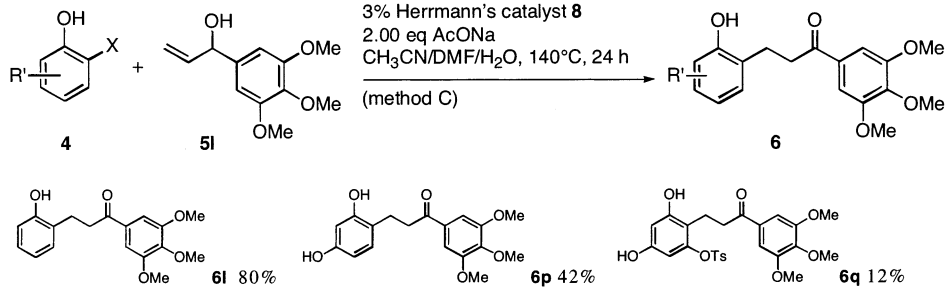
(13) Electron-poor aryl halides oxidatively add to Pd(0) more readily than do the corresponding electron-rich aryl halides. For details on oxidative addition and on Heck reaction, see: (a) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed.; University Science Books, Mill Valley, CA, 1999. (b) Beletskaya, I.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009−3066.

(14) The lower reactivity of aryl bromides is generally ascribed to their reluctance to oxidatively add to Pd(0). See also ref 13.

(15) Herrmann's catalyst **8**:



SCHEME 4. Synthesis of Substituted DHCs 6 Using Coupling Conditions C[a]



[a] Isolated yields.

Next, we studied the functional group tolerance on the alkenyl moiety, coupling iodophenol **4b**, and various 1-aryl-2-propen-1-ols **5** with method B (Scheme 3). Different aromatic, polycyclic aromatic, and heteroaromatic substitutions were considered. The effect of electronically neutral, donating and withdrawing substituents on the aromatic part is minimal. The yield and the rate of the reactions were not affected. Yields around 65% were easily obtained.

Finally, we have tested reaction conditions C using Herrmann's catalyst **8** with both substrates bearing polyoxygenated substitutions (Scheme 4). We observed the formation of the desired DHCs from 80% to 12% yields. When introducing more phenolic substitutions on the aryl halide part, decreased yields are obtained.

In conclusion, we report herein an expedient alternative route for the synthesis of DHCs and analogues. Our two-step/one-purification process allows the synthesis of a wide range of analogues with original and complex substitution patterns, which can be interesting intermediates toward major flavonoid compounds. Until now, few systems applicable for wide diversification have been developed. Our unprecedented pathway is basically applicable for a range of structures and has permitted the preparation and characterization of novel products.

Experimental Section

General Procedure for the Preparation of Alkenes 5. Vinylmagnesium bromide (1 M in THF, 1 equiv) was added at 0 °C to a solution of aldehyde **7** (1 equiv) in dry THF (0.7 M). The reaction was stirred for 2 h at 0 °C. The mixture was then diluted with diethyl ether and quenched with a saturated NH_4-Cl solution. The organic layer was separated, washed twice with water, dried over anhydrous sodium sulfate, filtered, and concentrated. The residual oil was used without further purification. The yield was quantitative according to the NMR analysis of the crude mixture.

Typical Procedure for the Arylations. Reactions were performed in capped Pyrex tubes under argon and monitored by TLC.

Method A. To a stirred solution of the olefinic reactant **5** (1.25 equiv) in CH_3CN (2 M) were added the aryl halide **4** (1 equiv), triethylamine (1.25 equiv), and $Pd(OAc)_2$ (0.01 equiv). The mixture was heated at 100 °C during 24 h.

Method B. To a stirred solution of the olefinic reactant **5** (1.3 equiv) in CH_3CN (0.7 M) were added the aryl halide **4** (1 equiv), Cs_2CO_3 (0.4 equiv), and $Pd(OAc)_2$ (0.03 equiv). The mixture was heated at 100 °C during 24 h.

Method C. To a stirred solution of AcONa (2.0 equiv) in H_2O/DMF (2/3 0.9 M) were added the olefinic reactant **5** (1.3 equiv) in CH_3CN (1.1 M), the aryl halide **4** (1 equiv), and catalyst **8** (0.03 equiv). The mixture was heated at 140 °C during 24 h.

Workup. The mixture was diluted with AcOEt and quenched with a saturated NH_4Cl solution. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated.

DHCs were purified by silica gel column chromatography with ethyl acetate/hexane mixture as eluant.

1,3-Diphenylpropan-1-one (6a): ^{1}H NMR δ 7.96 (d, 2H, J = 7.3 Hz), 7.57 (t, 1H, J = 7.3 Hz), 7.46 (t, 2H, J = 7.3 Hz), 7.28 (m, 5H), 3.33 (t, 2H, J = 7.5 Hz), 3.09 (t, 2H, J = 7.5 Hz); ^{13}C NMR δ 199.2, 141.3, 136.9, 133.1, 128.6, 128.6, 128.5, 128.1, 126.2, 40.5, 30.2; IR (CsI) 3048, 2920, 1687, 1599, 1582, 1480, 1447 cm^{-1}; MS m/e 211 (13) $[M + H]^+$, 228 (100) $[M + NH_4]^+$; HRMS calcd for $C_{15}H_{14}O$ 210.1045, found 210.1040.

3-(2-Hydroxyphenyl)-1-phenylpropan-1-one (6b): ^{1}H NMR δ 7.99 (dd, 2H, J = 7.2, 1.5 Hz), 7.57 (dd, 1H, J = 7.2, 1.5 Hz), 7.45 (t, 2H, J = 7.2 Hz), 7.16 (d, 1H, J = 7.3 Hz), 7.14 (t, 1H, J = 7.3 Hz), 6.95 (d, 1H, J = 7.3 Hz), 6.86 (t, 1H, J = 7.3 Hz), 3.46 (t, 2H, J = 6.1 Hz), 3.07 (t, 2H, J = 6.1 Hz); ^{13}C NMR δ 202.0, 154.4, 136.0, 133.7, 130.5, 128.6, 128.3, 127.9, 127.7, 120.6, 117.3, 40.3, 23.5; IR (CsI) 3355, 3068, 2929, 1670, 1596, 1581, 1490, 1455, 1365, 1235 cm^{-1}; MS m/e 227 (5) $[M + H]^+$, 244 (100) $[M + NH_4]^+$, 470 (38) $[2M + NH_4]^+$; HRMS calcd for $C_{15}H_{14}O_2$ 226.0994, found 226.0980.

3-(2-Tosyloxyphenyl)-1-phenylpropan-1-one (6c): ^{1}H NMR δ 7.93 (dd, 2H, J = 7.1 Hz), 7.75 (d, 2H, J = 8.1 Hz), 7.56 (t, 1H, J = 7.1 Hz), 7.49 (t, 2H, J = 7.1 Hz), 7.28 (d, 2H, J = 8.1 Hz), 7.22 (m, 4H), 3.14 (t, 2H, J = 7.6 Hz), 2.88 (t, 2H, J = 7.6 Hz), 2.38 (s, 3H); ^{13}C NMR δ 198.8, 148.0, 145.4, 136.6, 134.4, 133.0 (CH), 130.9 (CH), 129.8 (CH), 128.6 (CH), 128.3 (CH), 128.0 (CH), 127.5 (CH), 127.2 (CH), 122.4 (CH), 38.8 (CH_2), 24.5 (CH_2), 21.6 (CH_3); IR (CsI) 3063, 2925, 1686, 1597, 1488, 1449, 1372, 1193, 1180, 1086 cm^{-1}; MS m/e 398 (100) $[M + NH_4]^+$; HRMS calcd for $C_{22}H_{20}O_4S$, 380.1082 found 380.1070.

3-(2,4-Dihydroxyphenyl)-1-phenylpropan-1-one (6e): ^{1}H NMR δ 7.99 (d, 1H, J = 7.1 Hz), 7.59 (t, 1H, J = 7.1 Hz), 7.46 (t, 2H, J = 7.1 Hz), 6.97 (d, 1H, J = 8.0 Hz), 6.42 (d, 1H, J = 2.5 Hz), 6.36 (dd, 1H, J = 8.0 Hz, J = 2.5 Hz), 3.42 (t, 2H, J = 5.8 Hz), 2.96 (t, 2H, J = 5.8 Hz); ^{13}C NMR δ 202.5, 155.5, 136.0, 133.9 (CH), 131.3 (CH), 128.7(CH), 128.4 (CH), 120.1, 107.9 (CH), 104.5 (CH), 40.7 (CH_2), 22.7 (CH_2); IR (CsI) 3341, 2925, 2854, 1667, 1619, 1598, 1510, 1449, 1296, 1209, 1160, 1103 cm^{-1}; MS m/e 260 (100) $[M + NH_4]^+$; HRMS calcd for $C_{15}H_{14}O_3$ 242.0943 ,found 242.0940.

3-(2,5-Dihydroxyphenyl)-1-phenylpropan-1-one (6f): ^{1}H NMR δ 7.89 (d, 2H, J = 7.5 Hz), 7.48 (t, 1H, J = 7.5 Hz), 7.36 (t, 2H, J = 7.5 Hz), 6.59 (s, 1H), 6.57 (dd, 1H, J = 8.4, 2.6 Hz), 6.47 (dd, 1H, J = 8.4, 2.8 Hz), 3.27 (t, 2H, J = 7.0 Hz), 2.87 (t, 2H, J = 7.0 Hz); ^{13}C NMR δ 201.6, 149.7, 149.5, 147.5, 136.3, 133.2, 128.4, 128.0, 116.5, 115.7, 113.8, 39.3, 24.7; IR (CsI) 3355, 1669, 1597, 1509, 1449, 1364, 1207; MS m/e 243 (100) $[M + H]^+$ 260 (10) $[M + NH_4]^+$; HRMS calcd for $C_{15}H_{14}O_3$ 242.0943 ,found 242.0945.

3-(2,4-Dihydroxy-6-tosyloxyphenyl)-1-phenylpropan-1-one (6g): ^{1}H NMR δ 7.98 (d, 2H, J = 7.2 Hz), 7.75 (d, 2H, J = 8.2 Hz), 7.60 (t, 1H, J = 7.2 Hz), 7.46 (t, 2H, J = 7.2 Hz), 7.30 (d, 2H, J = 8.2 Hz), 6.32 (s, 1H), 6.17 (s, 1H), 3.46 (t, 2H, J = 5.4 Hz), 2.97 (t, 2H, J = 5.4 Hz), 2.46 (s, 3H); ^{13}C NMR δ 203.4,

155.7, 148.8, 145.4, 135.8, 134.0, 129.9, 129.8, 128.7, 128.4, 128.36, 114.2, 103.0, 102.5, 38.5, 21.7, 16.7; MS *m/e* 413 (5) [M + H]$^+$ 430(100) [M + NH$_4$]$^+$; HRMS calcd for $C_{22}H_{20}O_6S$ 412.0981 found 412.0980.

3-(2-Hydroxyphenyl)-1-(3,4-dimethoxyphenyl)propan-1-one (6h): ^{1}H NMR δ 8.20 (bs, 1H), 7.61 (dd, 1H, J = 8.6, 2.2 Hz), 7.54 (d, 1H, J = 2.2 Hz), 7.13 (d, 1H, J = 7.2 Hz), 7.11 (t, 1H, J = 7.2 Hz), 6.90 (d, 1H, J = 7.2 Hz), 6.87 (d, 1H, J = 8.6 Hz), 6.85 (t, 1H, J = 7.2 Hz), 3.94 (s, 3H), 3.92 (s, 3H), 3.42 (t, 2H, J = 6.1 Hz), 3.03 (t, 2H, J = 6.1 Hz); ^{13}C NMR δ 200.4, 154.5, 153.7, 148.9, 130.5, 129.2, 127.9, 123.2, 120.5, 117.3, 110.2, 109.9, 56.0, 55.9, 39.8, 23.6; IR (CsI) 3320, 2936, 1656, 1594, 1586, 1516, 1456, 1419, 1270, 1153, 1022 cm^{-1}; MS *m/e* 287 (100) [M + H]$^+$, 304 (3) [M + NH$_4$]$^+$; HRMS calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1190

3-(2-Hydroxyphenyl)-1-(3,4-methylenedioxyphenyl)propan-1-one (6i): ^{1}H NMR δ 8.10 (bs, 1H), 7.61 (dd, 1H, J = 8.2, 1.9 Hz), 7.44 (d, 1H, J = 1.9 Hz), 7.10 (m, 2H), 6.92 (m, 2H), 6.87 (d, 1H, J = 8.2 Hz), 6.03 (s, 2H), 3.36 (t, 2H, J = 6.0 Hz), 3.01 (t, 2H, J = 6.0 Hz); ^{13}C NMR δ 199.9, 154.4, 152.2, 148.1, 130.5, 127.8, 124.8, 120.5, 117.2, 107.9, 107.8, 101.9, 40.0, 23.6; IR (CsI) 3332, 3077, 2903, 1662, 1603, 1489, 1444, 1358, 1295, 1254, 1112, 1039 cm^{-1}; MS *m/e* 271 (12) [M + H]$^+$, 293 (100); HRMS calcd for $C_{16}H_{14}O_4$ 270.0892, found 270.0881.

1-(3,4-Bis-benzyloxyphenyl)-3-(2-hydroxyphenyl)propan-1-one (6j): ^{1}H NMR δ 8.14 (bs, 1H), 7.62 (s,1H), 7.57 (dd, 1H, J = 8.4, 1.9 Hz), 7.39 (m, 11H), 7.10 (d, 1H, J = 7.5 Hz), 6.92 (d, 1H, J = 8.4 Hz), 6.85 (t, 1H, J = 7.5 Hz), 5.23 (s, 2H), 5.18 (s, 2H), 3.35 (t, 2H, J = 5.8 Hz), 3.00 (t, 2H, J = 5.8 Hz); ^{13}C NMR δ 200.4, 154.6, 153.7, 148.6, 136.6, 136.3, 130.5, 129.5, 128.6, 128.55, 128.1, 128.0, 127.4, 127.0, 123.5, 120.6, 117.6, 113.8, 112.8, 71.1, 70.8, 40.0, 23.4; IR (CsI) 3320, 3064, 3035, 2935, 1658, 1591, 1512, 1456, 1428, 1269, 1147, 1020 cm^{-1}; MS *m/e* 439 (11) [M + H]$^+$, 456 (100) [M + NH$_4$]$^+$; HRMS calcd for $C_{29}H_{26}O_4$ 438.1831, found 438.1828.

3-(2-Hydroxyphenyl)-1-naphthalen-2-ylpropan-1-one (6k): ^{1}H NMR δ 8.52 (s, 1H), 7.86 (m, 5H), 7.56 (m, 2H), 7.16 (d, 1H, J = 7.6 Hz), 7.13 (t, 1H, J = 7.6 Hz), 6.94 (d, 1H, J = 7.6 Hz), 6.89 (t, 1H, J = 7.6 Hz), 3.61 (t, 2H, J = 5.9 Hz), 3.11 (t, 2H, J = 5.9 Hz); ^{13}C NMR δ 201.9, 154.5, 135.8, 133.4, 132.3, 130.6, 130.3, 129.6, 128.8, 128.5, 128.0, 127.8, 126.9, 123.7, 120.7, 117.4, 40.4, 23.6; IR(CsI) 3331, 3058, 2930, 1665, 1626, 1594, 1456, 1372, 1276, 1239, 1184 cm^{-1}; MS *m/e* 277 (31) [M + H]$^+$, 299 (100); HRMS calcd for $C_{19}H_{16}O_2$ 276.1150, found 276.1145.

3-(2-Hydroxyphenyl)-1-(3,4,5-trimethoxyphenyl)propan-1-one (6l): ^{1}H NMR δ 7.88 (bs, 1H), 7.25 (s, 2H), 7.11 (m, 2H), 6.91 (d, 1H, J = 7.3 Hz), 6.86 (t, 1H, J = 7.3 Hz), 3.90 (bs, 9H), 3.41 (t, 2H, J = 5.5 Hz), 3.04 (t, 2H, J = 5.5 Hz); ^{13}C NMR δ 200.6, 154.4, 153.0, 143.2, 131.3, 130.6 (CH), 128.0 (CH), 127.7, 120.7 (CH), 117.3 (CH), 105.9 (CH), 61.0 (CH_3), 56.3 (CH_3), 40.2 (CH_2), 23.7 (CH_2); IR(CsI) 3421, 2940, 2838, 1663, 1586, 1506, 1457, 1414, 1330, 1235, 1127 cm^{-1}; MS *m/e* 317 (63) [M + H]$^+$, 334 (100) [M + NH$_4$]$^+$; HRMS calcd for $C_{18}H_{20}O_5$ 316.1311 found 316.1307.

1-(4-Dimethylaminophenyl)-3-(2-hydroxyphenyl)propan-1-one (6m): ^{1}H NMR δ 8.90 (bs, 1H), 7.89 (d, 2H, J = 9.1 Hz), 7.10 (m, 2H), 6.88 (m, 2H), 6.62 (d, 2H, J = 9.1 Hz), 3.37 (t, 2H, J = 5.7 Hz), 3.06 (s, 6H), 3.02 (t, 2H, J = 5.7 Hz); ^{13}C NMR δ 199.7, 154.9, 153.8, 130.7, 130.5, 128.4, 127.8, 123.8, 120.3, 117.7, 110.5, 39.9, 39.6, 23.5; IR (CsI) 3198, 2902, 1595, 1545, 1487, 1378, 1254, 1183; MS *m/e* 252 (20), 270 (100) [M + H]$^+$; HRMS calcd for $C_{17}H_{19}NO_2$ 269.1416, found 269.1413.

1-(5-Chlorothiophen-2-yl)-3-(2-hydroxyphenyl)propan-1-one (6n): ^{1}H NMR δ 7.53 (d, 1H, J = 4.0 Hz), 7.12 (t, 1H, J = 7.2 Hz), 7.11 (d, 1H, J = 7.2 Hz), 6.95 (d, 1H, J = 4.0 Hz), 6.87 (m, 2H), 3.30 (t, 2H, J = 6.2 Hz), 3.01 (t, 2H, J = 6.2 Hz); ^{13}C NMR δ 193.5, 154.3, 141.6, 140.5, 132.3 (CH), 130.5 (CH), 128.1 (CH), 127.7 (CH), 127.3, 120.8 (CH), 117.3 (CH), 39.9 (CH_2), 23.6 (CH_2); IR (CsI) 3376, 3098, 2932, 1646, 1456, 1418, 1325, 1238, 1214, 1011 cm^{-1}; MS *m/e* 267 (100) [M + H]$^+$, 269 (35); HRMS calcd for $C_{13}H_{11}ClO_2S$ 266.0168, found 266.0167.

1-(4-Cyanophenyl)-3-(2-hydroxyphenyl)propan-1-one (6o): ^{1}H NMR δ 8.04 (d, 2H, J = 8.8 Hz), 7.74 (d, 2H, J = 8.8 Hz), 7,13 (m, 2H), 6.88 (m, 2H), 3.41 (t, 2H, J = 6.6 Hz), 3.05 (t, 2H, J = 6.6 Hz); ^{13}C NMR δ 200.1, 154.0, 139.1, 132.4, 130.5, 128.5, 127.9, 127.0, 121.8, 120.7, 117.7, 116.5, 40.0, 23.9; IR (CsI) 3421, 3067, 2933, 2232, 1686, 1608, 1594, 1504, 1490, 1456, 1405, 1364, 1294, 1233, 1205, 1099, 982, 843, 758 cm^{-1}; MS *m/e* 252 (21) [M + H]$^+$, 274 (100); HRMS calcd for $C_{16}H_{13}NO_2$ 251.0946, found 251.0944.

3-(2,4-Dihydroxyphenyl)-1-(3,4,5-trimethoxyphenyl)propan-1-one (6p): ^{1}H NMR δ 7.22 (s, 2H), 6.92 (d, 1H, J = 8.1 Hz), 6.43 (d, 1H, J = 3.7 Hz), 6.35 (dd, 1H, J = 8.1 Hz, J = 3.7 Hz), 3.90 (s, 3H), 3.87 (s, 6H), 3.33 (t, 2H, J = 6.2 Hz), 2.93 (t, 2H, J = 6.2 Hz); ^{13}C NMR δ 201.2, 155.7, 155.2, 152.9, 131.3, 119.7, 107.9, 105.9, 104.2, 60.9, 56.2, 40.2, 23.4; IR (CsI) 3411, 2920, 1660, 1619, 1588, 1507, 1459, 1416, 1331, 1155, 1127 cm^{-1}; MS *m/e* 333 (100) [M + H]$^+$; HRMS calcd for $C_{18}H_{20}O_6$ (M$^{\bullet+}$) 332.1260, found 332.1260.

3-(2,4-Dihydroxy-6-tosyloxyphenyl)-1-(3,4,5-trimethoxyphenyl)propan-1-one (6q): ^{1}H NMR δ 8.80 (bs, 1H), 7.80 (d, 2H, J = 7.9 Hz), 7.34 (d, 2H, J = 7.9 Hz), 7.24 (s, 2H), 6.35 (s, 1H), 6.09 (s, 1H), 3.90 (s, 9H), 3.40 (t, 2H, J = 5.5 Hz), 2.84 (t, 2H, J = 5.5 Hz), 2.43 (s, 3H); ^{13}C NMR δ 202.1, 156.7, 155.5, 153.0, 149.6, 145.7, 143.3, 133.1, 131.0, 130.0, 128.2, 113.7, 106.0, 103.6, 101.6, 60.9, 56.3, 38.6, 21.6, 17.1; MS *m/e* 503 (100) [M + H]$^+$; HRMS calcd for $C_{25}H_{26}O_9S$ (M$^{\bullet+}$) 502.1298, found 502.1297.

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Supporting Information Available: General experimental methods and ^{1}H/^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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