Supporting Information

Sustainable Electrochemical Dehydrogenative C(sp^3)−H mono/di-Alkylations

Jin-Yu He,† Wei-Feng Qian,† Yan-Zhao Wang, Chaochao Yao, Nana Wang, Huilin Liu, Bing Zhong, Cuiju Zhu,* and Hao Xu*

College of Chemistry, Central China Normal University

Email: hao.xu@ccnu.edu.cn

Table of content

General Information S-3

Optimization of The Reaction Conditions S-4

General Procedure A: Electroxidative dehydrogenative mono-alkylation S-11

General Procedure B: Electroxidative dehydrogenative di-alkylation S-11

General Procedure C: Electroxidative dehydrogenative alkenylation S-11

Characterization Data of Products S-12

Crystal Data and Structure Refinement for **47**, **4**, **82** S-59

Cyclic Voltammetry Studies S-64

Mechanistic Studies S-70

References S-78

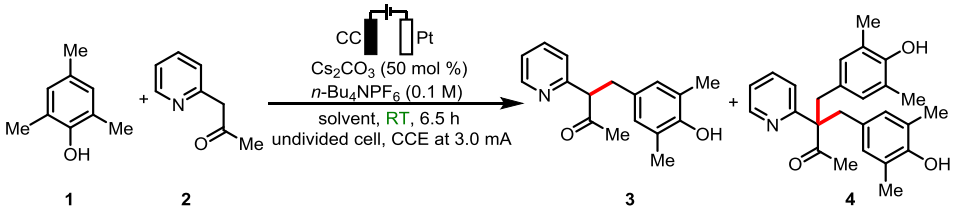
^{1}H, ^{13}C and ^{19}F-NMR Data S-79

General Information

All reactions were carried out under an air atmosphere using 15 mL three-neck flasks. Acetone was purchased from Shanghai SCR company. HFIP was purchased from Bidepharm. Dicarbonyl compounds were purchased from Tansoole. Commercial reagents were used without further purification. Flash column chromatography was performed using 300–400 mesh silica gel. Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker 400 MHz or Varian 600 MHz spectrometer. Chemical shifts (δ) are reported in ppm from the resonance of tetramethyl silane as the internal standard ($CDCl_3$: δ = 7.26 ppm for ^{1}H, TMS: δ = 0 ppm for ^{1}H, δ = 77.16 ppm for ^{13}C). ^{13}C NMR spectra were recorded on 100 MHz or 150 MHz with complete proton decoupling spectrophotometers. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (J) are given in Hertz (Hz). High resolution mass spectra (HRMS) were measured with Bruker micrOTOF II ESI-TOF using a positive electrospray ionization (ESI+).

Optimization of The Reaction Conditions

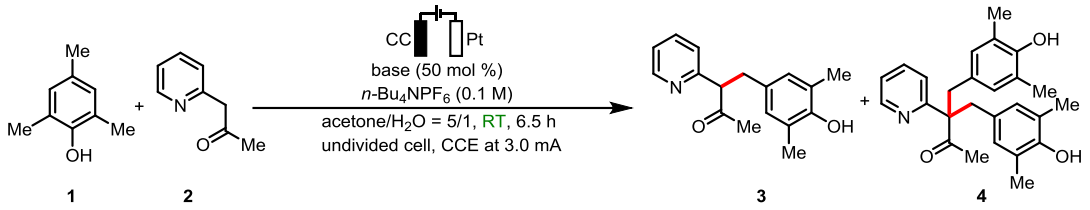
Table S1: Evaluation of solvents[a]



Entry	Solvent (mL)	Yield[b] **3** [%]	Yield[b] **4** [%]
1	acetone/H_2O = 5/1	**85(82)**	---
2	acetone/H_2O = 4/2	53	---
3	DMF/H_2O = 5/1	66	---
4	THF/H_2O = 5/1	24	---
5	MeCN/H_2O = 5/1	68	---
6	acetone = 6	65	---
7	acetone/MeOH = 5/1	45	---
8	acetone/HFIP = 5/1	67	---
9	acetone/TFE = 5/1	33	---
10	HFIP = 6	40	39
11	TFE = 6	27	---
12	MeOH = 6	40	---
13	HFIP/H_2O = 5/1	18	65
14	$CF_3CHFCF_2CH_2OH/H_2O$ = 5/1	43	---
15	$(CF_3)_2CHOCH_3/H_2O$ = 5/1	11	---
16	HFIP/H_2O = 5/1	---	**84(80)**[c]

[a] Reaction conditions: Undivided cell, carbon cloth anode, Pt cathode, **1** (0.4 mmol), **2** (0.2 mmol), Cs_2CO_3 (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), solvent (6 mL), constant current = 3.0 mA, 6.5 h (3.6 F/mol), RT, under air. NMR yield determined by using $C_2H_2Cl_4$ as internal standard. [b]Isolated yield in parentheses. [c] t = 10.0 h.

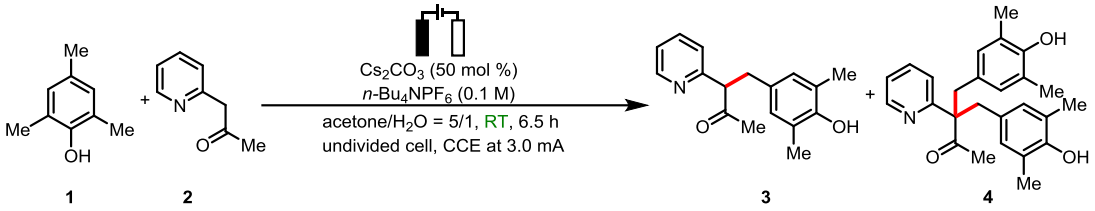
Table S2: Evaluation of base[a]



Entry	Base	Yield[b] **3** [%]	Yield[b] **4** [%]
1	K_2CO_3 as base	75	---
2	NaOH as base	66	--
3	Na_2CO_3 as base	66	--
4	2,6-lutidine as base	76	---
5	quinuclidine as base	68	---
6	without base	56	---

[a] Reaction conditions: Undivided cell, carbon cloth anode, Pt cathode, **1** (0.4 mmol), **2** (0.2 mmol), base (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), acetone/H_2O (5/1, 6 mL), constant current = 3.0 mA, 6.5 h (3.6 F/mol), RT, under air. NMR yield determined by using $C_2H_2Cl_4$ as internal standard. [b] Isolated yield in parentheses.

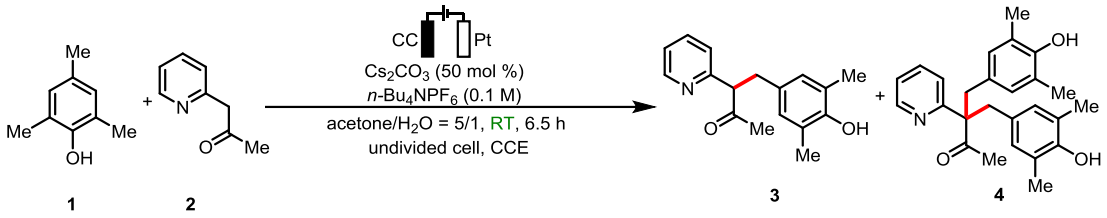
Table S3: Evaluation of electrode[a]



Entry	Electrode	Yield **3** [%]	Yield **4** [%]
1	CC(+)/Ni(-)	75	---
2	Graphite(+)/Pt(-)	58	---
3	Pt(+)/Pt(-)	64	---
4	CC(+)/CC(-)	69	---
5	Graphite(+)/Graphite(-)	44	---

[a] Reaction conditions: Undivided cell, **1** (0.4 mmol), **2** (0.2 mmol), Cs_2CO_3 (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), acetone/H_2O (5/1, 6 mL), constant current = 3.0 mA, 6.5 h (3.6 F/mol), RT, under air. NMR yield determined by using $C_2H_2Cl_4$ as internal standard.

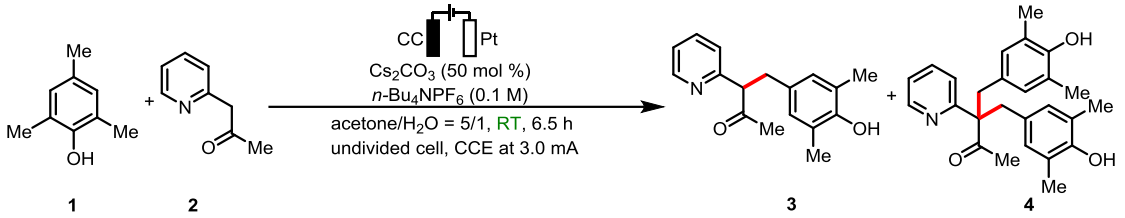
Table S4: Evaluation of electric current[a]



Entry	Electric current	Yield[b] **3** [%]	Yield **4** [%]
1	1.0 mA	87(82)	---
2	3.0 mA	85(82)	---
3	5.0 mA	65	---

[a] Reaction conditions: Undivided cell, carbon cloth anode, Pt cathode, **1** (0.4 mmol), **2** (0.2 mmol), Cs_2CO_3 (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), acetone/H_2O (5/1, 6 mL), CCE, 6.5 h, RT, under air. NMR yield determined by using $C_2H_2Cl_4$ as internal standard. [b] Isolated yield in parentheses.

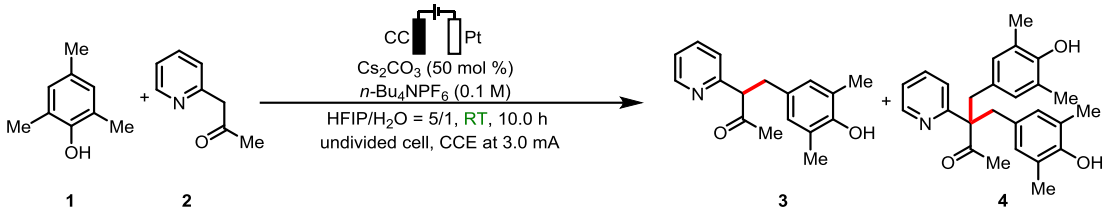
Table S5: Evaluation of other conditions[a]



Entry	Deviation conditions	Yield[b] **3** [%]	Yield **4** [%]
1	*n*-Bu_4NBF_4 as electrolyte	87(82)	---
2	under 40 °C	75	---
3	without electricity	N.R.	---
4	Without electrolyte	**86(80)**	---
5	entry 4 but **2** = 0.4 mmol[c]	83(79)	---

[a] Reaction conditions: Undivided cell, carbon cloth anode, Pt cathode, **1** (0.4 mmol), **2** (0.2 mmol), Cs_2CO_3 (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), acetone/H_2O (5/1, 6 mL), constant current = 3.0 mA, 6.5 h (3.6 F/mol), RT, under air. NMR yield, determined by using $C_2H_2Cl_4$ as internal standard. [b] Isolated yield in parentheses. [c] **1** (0.8 mmol), **2** (0.4 mmol).

Table S6: Evaluation of di-alkylation[a]



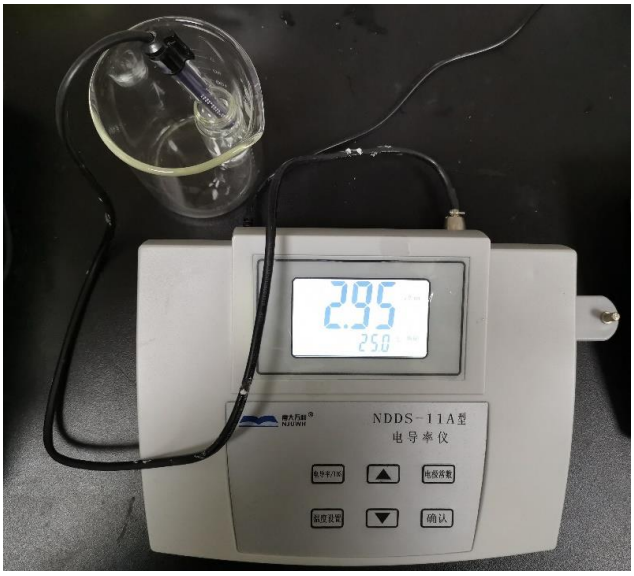
Entry[a]	Deviation conditions	Yield **3** [%]	Yield[b] **4** [%]
1	none	---	84(80)[b]
2	2.0 equiv **1**	---	79(75)
3	K_2CO_3 as base	---	72
4	DIPEA as base	---	75
5	Et_3N as base	---	68
6	without base	41	---
7	acetone/H_2O = 5/1	72	---
8	MeOH/H_2O = 5/1	54	4
9	TFE/H_2O = 5/1	37	26
10	EtOH/H_2O = 5/1	41	14
11	Without *n*-Bu_4NPF_6	---	82
12	entry 11 but CCE = 10.0 mA	---	91(87)[c]
13	entry 7 but CCE = 10.0 mA	65	8[c]
14	entry12 but **2** = 0.4 mmol[d]	---	**(87)**[c]

[a]Reaction conditions: Undivided cell, carbon cloth anode, Pt cathode, **1** (0.5 mmol), **2** (0.2 mmol), Cs_2CO_3 (0.5 equiv.) *n*-Bu_4NPF_6 (0.1 M), solvent (6 mL), constant current = 3.0 mA, 10.0 h (5.6 F/mol), RT, under air. [b] Isolated yield in parentheses. [c] t = 8.0 h. DIPEA= *N*, *N*-diisopropylethylamine.[d] **1** (1.0 mmol), **2** (0.4 mmol).

Table S7: Evaluation of the conductivity of different kind of solutions[a]

Entry	Variation of mixture	Description	Conductivity[b]
1	Acetone/H_2O	solvents	5.1 μS/cm
2	Acetone/H_2O+ *n*-Bu4NPF6	with electrolyte	2850 μS/cm
3	Acetone/H_2O+ Cs_2CO_3	with Cs_2CO_3	135.4 μS/cm
4	Acetone/H_2O+ Cs_2CO_3+ *n*-Bu4NPF6	with electrolyte and Cs_2CO_3	3160μS/cm
5	Acetone/H_2O + **1** + **2**	without Cs_2CO_3	7.44 μS/cm
6	Acetone/H_2O + **1** + **2** + Cs_2CO_3	without electrolyte	248 μS/cm
7	Acetone/H_2O + **1** + **2** + Cs_2CO_3 + *n*-Bu4NPF6	with electrolyte and Cs_2CO_3	3110.0 μS/cm
8	HFIP/H_2O	solvents	2.97 μS/cm
9	HFIP/H_2O + *n*-Bu4NPF6	with electrolyte	970 μS/cm
10	HFIP/H_2O + Cs_2CO_3	with Cs_2CO_3	934 μS/cm
11	HFIP/H_2O + Cs_2CO_3+ *n*-Bu4NPF6	with electrolyte and Cs_2CO_3	717μS/cm
12	HFIP/H_2O + **1** + **2**	without Cs_2CO_3	73.5 μS/cm
13	HFIP/H_2O + **1** + **2** + Cs_2CO_3	without electrolyte	859 μS/cm
14	HFIP/H_2O + **1** + **2** + Cs_2CO_3 + *n*-Bu4NPF6	with electrolyte and Cs_2CO_3	714 μS/cm

[a] Measure conditions: **1** (0.8 mmol), **2** (0.4 mmol), Cs_2CO_3 (0.5 equiv.), acetone/H_2O (5/1, 6 mL), HFIP/H_2O (5/1, 6 mL), *n*-Bu_4NPF_6 (0.1 M), conductivity determined by using xx as internal standard. Conductivity was measured by NDDS-11A Conductivity meter. [b] The data of each entry was measured three times and averaged.



NDDS-11A Conductivity Meter

General Procedure A: Electroxidative dehydrogenative mono-alkylation

The electrocatalysis was carried out in an undivided cell with a carbon clothe anode (15 mm × 15 mm × 0.1 mm) and a platinum cathode (15 mm × 15 mm × 0.2 mm). 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol), 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol) or amines (0.40 mmol) and alcohols (0.40 mmol), and Cs_2CO_3 (65.2 mg, 0.20 mmol) were placed in a 15 mL cell and dissolved in acetone/H_2O (5 mL/1 mL). Electrolysis was performed at RT with a constant current of 3.0 mA maintained for 6.5 h (3.6 F/mol). Then use DCM to wash the electrodes and then the combined solvents were dried over Na_2SO_4. Evaporation of the solvents and purification by column chromatography on silica gel (petroleum ether/EtOAc) yielded the desired products.

General Procedure B: Electroxidative dehydrogenative di-alkylation

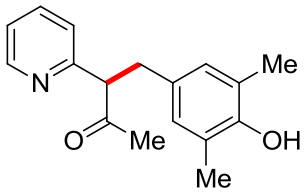
The electrocatalysis was carried out in an undivided cell with a carbon clothe anode (15 mm × 15 mm × 0.1 mm) and a platinum cathode (15 mm × 15 mm × 0.2 mm). 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol), 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol) and Cs_2CO_3 (65.2 mg, 0.20 mmol) were placed in a 15 mL cell and dissolved in HFIP/H_2O (5 mL/1 mL). Electrolysis was performed at r.t with a constant current of 10.0 mA maintained for 6–11 h. Then use DCM to wash the electrodes and then the combined solvents were dried over Na_2SO_4. Evaporation of the solvents and purification by column chromatography on silica gel (petroleum ether/EtOAc) yielded the desired products.

General Procedure C: Electroxidative dehydrogenative alkenylation

The electrocatalysis was carried out in an undivided cell with a carbon clothe anode (10 mm × 10 mm × 0.1 mm) and a platinum cathode (10 mm × 10 mm × 0.2 mm). **3** (107.7 mg, 0.40 mmol) and Cs_2CO_3 (65.2 mg, 0.20 mmol) were placed in a 10 mL cell and dissolved in acetone/H_2O (3 mL/1 mL). Electrolysis was performed at RT with a constant current of 10.0 mA maintained for 3 h (5.6 F/mol). Then use DCM to wash

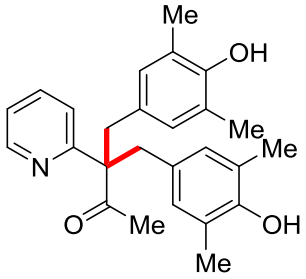
the electrodes and then the combined solvents were dried over Na_2SO_4. Evaporation of the solvents and purification by column chromatography on silica gel (petroleum ether/EtOAc) yielded the desired products.

Characterization Data of Products 3



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (3):

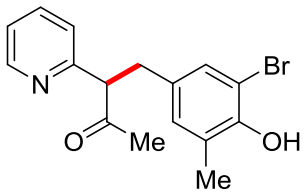
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **3** (86.2 mg, 80%) as a yellow solid. **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.57 (d, J = 4.4 Hz, 1H), 7.61 (dt, J = 7.7, 1.5 Hz, 1H), 7.18–7.14 (m, 2H), 6.68 (s, 2H), 4.74 (brs, 1H), 4.16 (t, J = 7.5 Hz, 1H), 3.32 (dd, J = 13.9, 7.5 Hz, 1H), 2.95 (dd, J = 13.9, 7.5 Hz, 1H), 2.15 (s, 6H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.6, 158.4, 150.9, 149.5, 136.9, 130.6, 129.0, 123.4, 123.3, 122.3, 63.6, 36.6, 30.0, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$ 270.1489, found 270.1488.



3-(4-Hydroxy-3,5-dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (4):

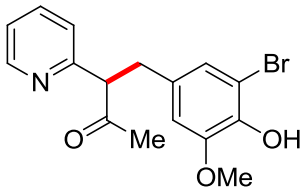
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol) constant current

electrolysis for 8.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **4** (140.2 mg, 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.65 (d, *J* = 4.8 Hz, 1H), 7.60 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.21 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.40 (s, 4H), 4.56 (brs, 2H), 3.25 (d, *J* = 14.4 Hz, 2H), 3.20 (d, *J* = 14.4 Hz, 2H), 2.11 (s, 12H), 2.02 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 209.8, 162.0, 150.8, 149.2, 136.2, 130.6, 128.6, 122.9, 122.4, 122.0, 64.4, 38.5, 28.4, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{30}NO_3$ $[M+H]^+$ 404.2220, found 404.2212.



4-(3-Bromo-4-hydroxy-5-methylphenyl)-3-(pyridin-2-yl)butan-2-one (5):

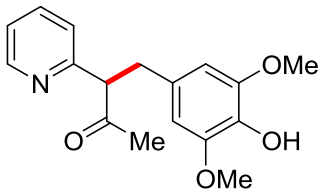
The general procedure A was followed using 2-bromo-4, 6-dimethylphenol (160.9 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **5** (69.5 mg, 52%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.58 (d, *J* = 4.9 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.19–7.16 (m, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.98 (s, 1H), 6.76 (s, 1H), 5.54 (brs, 1H), 4.11 (t, *J* = 7.4 Hz, 1H), 3.31 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.96 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.18 (s, 3H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 158.0, 149.9, 148.9, 137.0, 132.4, 131.2, 129.6, 125.7, 123.4, 122.5, 109.9, 63.7, 36.1, 29.8, 16.8. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{17}NO_2Br$ $[M+H]^+$ 334.0437, found 334.0435.



4-(3-Bromo-4-hydroxy-5-methoxyphenyl)-3-(pyridin-2-yl)butan-2-one (6):

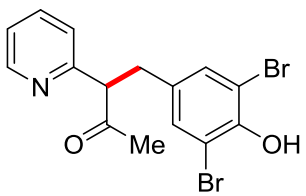
The general procedure A was followed using 2-bromo-6-methoxy-4-methylphenol (173.6 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol).

Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **6** (69.9 mg, 50%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.56 (d, J = 4.4 Hz, 1H), 7.61 (dt, J = 7.8, 1.6 Hz, 1H), 7.17 (dd, J = 7.8, 4.4 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 6.79 (d, J = 1.6 Hz, 1H), 6.44 (d, J = 1.6 Hz, 1H), 4.13 (t, J = 7.6 Hz, 1H), 3.70 (s, 3H), 3.31 (dd, J = 14.0, 7.6 Hz, 1H), 2.99 (dd, J = 14.0, 7.6 Hz, 1H), 2.05 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.7, 157.8, 149.7, 147.1, 141.6, 137.1, 131.9, 124.8, 123.5, 122.5, 111.0, 108.1, 63.4, 56.2, 36.6, 29.8. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{17}NO_3Br$ $[M+H]^+$ 350.0386, found 350.0382.



4-(4-Hydroxy-3,5-dimethoxyphenyl)-3-(pyridin-2-yl)butan-2-one (7):

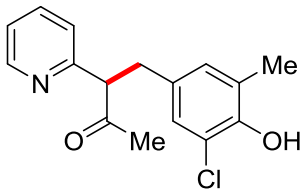
The general procedure A was followed using 2, 6-dimethoxy-4-methylphenol (134.6 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **7** (82.0 mg, 68%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.53 (d, J = 4.2 Hz, 1H), 7.55 (dt, J = 7.8, 1.6 Hz, 1H), 7.13 (dd, J = 7.8, 4.2 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 6.21 (s, 2H), 5.82 (brs, 1H), 4.13 (t, J = 7.6 Hz, 1H), 3.68 (s, 6H), 3.30 (dd, J = 13.8, 7.6 Hz, 1H), 3.00 (dd, J = 13.8, 7.6 Hz, 1H), 2.02 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.0, 158.1, 149.6, 146.8, 136.8, 133.1, 130.1, 123.4, 122.2, 105.6, 63.7, 56.1, 37.4, 29.8. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{20}NO_4$ $[M+H]^+$ 302.1387, found 302.1385.



4-(3, 5-Dibromo-4-hydroxyphenyl)-3-(pyridin-2-yl)butan-2-one (8):

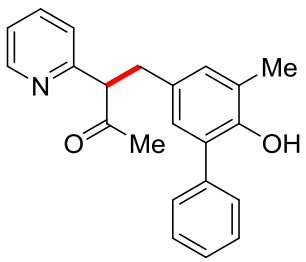
The general procedure A was followed using 2, 6-dibromo-4-methylphenol (212.7 mg,

0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **8** (84.6 mg, 53%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.59 (d, J = 4.8 Hz, 1H), 7.64 (dt, J = 7.8, 1.8 Hz, 1H), 7.20 (dd, J = 7.8, 4.8 Hz, 1H), 7.14 (s, 2H), 7.10 (d, J = 7.8 Hz, 1H), 6.01 (brs, 1H), 4.08 (t, J = 7.4 Hz, 1H), 3.33 (dd, J = 14.0, 7.4 Hz, 1H), 2.98 (dd, J = 14.0, 7.4 Hz, 1H), 2.07 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.2, 157.6, 149.9, 148.5, 137.2, 133.7, 132.6, 123.4, 122.7, 110.3, 63.2, 35.7, 29.7. **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{14}NO_2Br_2$ $[M+H]^+$ 397.9386, found 397.9383.

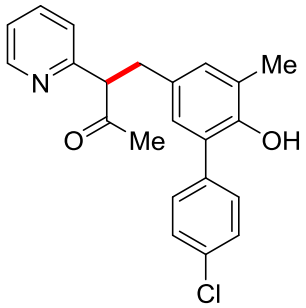


4-(3-Chloro-4-hydroxy-5-methylphenyl)-3-(pyridin-2-yl)butan-2-one (9):

The general procedure A was followed using 2-chloro-4, 6-dimethylphenol (125.3 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **9** (90.8 mg, 78%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.57 (d, J = 4.6 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.17 (dd, J = 7.8, 4.6 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 6.84 (s, 1H), 6.73 (s, 1H), 4.12 (t, J = 7.5 Hz, 1H), 3.31 (dd, J = 14.0, 7.5 Hz, 1H), 2.95 (dd, J = 14.0, 7.5 Hz, 1H), 2.17 (s, 3H), 2.05 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 158.0, 149.9, 148.1, 137.0, 131.7, 130.4, 126.7, 125.8, 123.4, 122.5, 119.4, 63.6, 36.2, 29.8, 16.4. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{17}NO_2Cl$ $[M+H]^+$ 290.0942, found 290.0937.

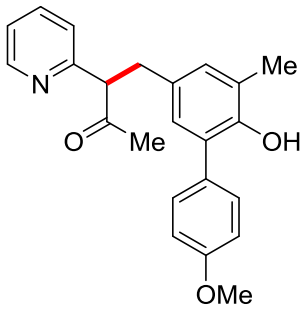


4-(6-Hydroxy-5-methyl-[1,1'-biphenyl]-3-yl)-3-(pyridin-2-yl)butan-2-one (10): The general procedure A was followed using 3,5-dimethyl-[1,1'-biphenyl]-2-ol (158.6 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **10** (70.3 mg, 53%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.55 (d, J = 4.8 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.46–7.42 (m, 2H), 7.37–7.33 (m, 3H), 7.18–7.15 (m, 2H), 6.86 (s, 1H), 6.75 (s, 1H), 4.19 (t, J = 7.5 Hz, 1H), 3.38 (dd, J = 14.0, 7.5 Hz, 1H), 3.03 (dd, J = 14.0, 7.5 Hz, 1H), 2.21 (s, 3H), 2.08 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.2, 158.4, 149.7, 149.1, 137.5, 136.8, 131.1, 130.9, 129.2, 129.1, 128.3, 127.8, 127.6, 124.7, 123.4, 122.3, 63.8, 36.5, 29.8, 16.3. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1645, found 332.1641.



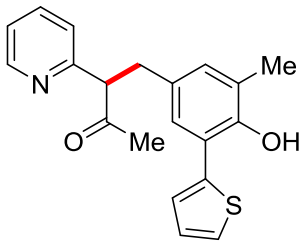
4-(4'-Chloro-6-hydroxy-5-methyl-[1,1'-biphenyl]-3-yl)-3-(pyridin-2-yl)butan-2-one (11):

The general procedure A was followed using 4'-chloro-3, 5-dimethyl-[1, 1'-biphenyl] -2-ol (186.2 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **11** (77.5 mg, 53%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.56 (d, J = 3.9 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.41–7.39 (m, 2H), 7.30–7.26 (m, 2H), 7.19–7.15 (m, 2H), 6.87 (s, 1H), 6.72 (s, 1H), 5.05 (brs, 1H), 4.18 (t, J = 7.5 Hz, 1H), 3.37 (dd, J = 14.4, 7.5 Hz, 1H), 3.03 (dd, J = 14.4, 7.5 Hz, 1H), 2.21 (s, 3H), 2.08 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.1, 158.3, 149.8, 149.1, 136.9, 136.1, 133.7, 131.4, 131.2, 130.6, 129.3, 128.3, 126.6, 124.8, 123.4, 122.4, 63.8, 36.5, 29.8, 16.3. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}NO_2Cl$ $[M+H]^+$ 366.1255, found 366.1253.



4-(6-Hydroxy-4'-methoxy-5-methyl-[1,1'-biphenyl]-3-yl)-3-(pyridin-2-yl)butan-2-one (12):

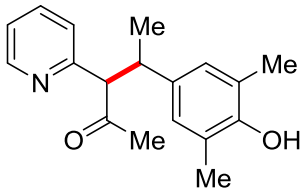
The general procedure A was followed using 4'-methoxy-3, 5-dimethyl-[1, 1'-biphenyl] -2-ol (182.6 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **12** (70.3 mg, 49%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.55 (d, J = 4.8 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.25–7.24 (m, 2H), 7.17–7.13 (m, 2H), 6.96 (d, J = 8.2 Hz, 2H), 6.82 (s, 1H), 6.71 (s, 1H), 5.15 (brs, 1H), 4.17 (t, J = 7.5 Hz, 1H), 3.83 (s, 3H), 3.36 (dd, J = 14.0, 7.5 Hz, 1H), 3.01 (dd, J = 14.0, 7.5 Hz, 1H), 2.19 (s, 3H), 2.07 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.2, 159.3, 158.5, 149.8, 149.2, 136.9, 130.9, 130.8, 130.3, 129.6, 128.3, 127.2, 124.4, 123.5, 122.3, 114.8, 63.9, 55.5, 36.6, 29.9, 16.3. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_3$ $[M+H]^+$ 362.1751, found 362.1747.



4-(4-Hydroxy-3-methyl-5-(thiophen-2-yl)phenyl)-3-(pyridin-2-yl)butan-2-one (13):

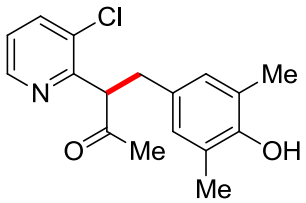
The general procedure A was followed using 2, 4-dimethyl-6-(thiophen-2-yl)phenol (163.4 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **13** (76.9 mg, 57%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.53 (d, J = 4.8 Hz,

1H), 7.60 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 4.8 Hz, 1H), 7.17–7.13 (m, 3H), 7.07–7.05 (m, 1H), 6.91 (s, 1H), 6.81 (s, 1H), 4.17 (t, J = 7.4 Hz, 1H), 3.34 (dd, J = 13.9, 7.4 Hz, 1H), 3.01 (dd, J = 13.9, 7.4 Hz, 1H), 2.19 (s, 3H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.2, 158.1, 149.6, 149.3, 139.3, 136.9, 131.3, 130.9, 128.0, 127.6, 126.0, 125.7, 124.9, 123.4, 122.4, 120.5, 63.5, 36.4, 29.8, 16.4. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{20}NO_2S$ $[M+H]^+$ 338.1209, found 338.1208.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)pentan-2-one (14):

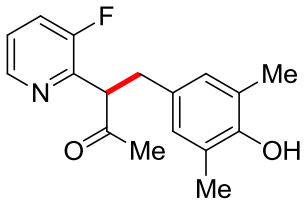
The general procedure A was followed using 4-ethyl-2, 6-dimethylphenol (120.2 mg, 0.80 mmol) and 1-(pyridin-2-yl)propan-2-one (**2**) (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **14** (58.4 mg, 52%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.40 (d, J = 4.3 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 7.6 Hz, 1H), 7.00–6.97 (m, 1H), 6.63 (s, 2H), 4.16 (d, J = 11.0 Hz, 1H), 3.58 (dq, J = 11.0, 6.8 Hz, 1H), 2.21 (s, 3H), 2.07 (s, 6H), 1.29 (d, J = 6.8 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 208.2, 157.4, 150.4, 149.0, 136.5, 135.6, 127.8, 123.8, 122.8, 122.0, 69.0, 40.9, 30.6, 21.7, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1642.



3-(3-Chloropyridin-2-yl)-4-(4-hydroxy-3,5-dimethylphenyl)butan-2-one (16):

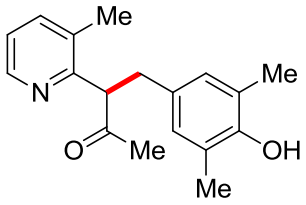
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(3-chloropyridin-2-yl)propan-2-one (67.8 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether /EtOAc: 5/1 to 2/1) yielded **16** (82.6 mg, 68%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.49 (d, J = 4.6 Hz,

1H), 7.64 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.13 (dd, *J* = 8.1, 4.6 Hz, 1H), 6.71 (s, 2H), 4.89 (brs, 1H), 4.63 (t, *J* = 7.2 Hz, 1H), 3.34 (dd, *J* = 14.0, 7.2 Hz, 1H), 3.02 (dd, *J* = 14.0, 7.2 Hz, 1H), 2.14 (s, 6H), 2.04 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 205.8, 155.9, 150.7, 147.7, 137.3, 132.1, 130.7, 129.1, 123.2, 123.0, 59.2, 35.4, 29.6, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2Cl$ $[M+H]^+$ 304.1099, found 304.1097.



3-(3-Fluoropyridin-2-yl)-4-(4-hydroxy-3, 5-dimethylphenyl)butan-2-one (17):

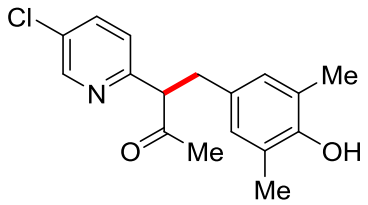
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.8 mmol) and 1-(3-fluoropyridin-2-yl)propan-2-one (61.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether /EtOAc: 5/1 to 2/1) yielded **17** (76.1 mg, 66%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.41 (d, *J* = 4.4 Hz, 1H), 7.33 (t, *J* = 8.8 Hz, 1H), 7.19 (dt, *J* = 8.8, 4.4 Hz, 1H), 6.68 (s, 2H), 4.75 (brs, 1H), 4.42 (t, *J* = 7.4 Hz, 1H), 3.36 (dd, *J* = 13.9, 7.4 Hz, 1H), 3.04 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.13 (s, 6H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 205.7, 157.9 (d, *J* = 257.5 Hz), 150.7, 146.9 (d, *J* = 15.0 Hz), 145.6 (d, *J* = 5.2 Hz), 130.7, 129.2, 123.6 (d, *J* = 3.6 Hz), 123.0, 123.2 (d, *J* = 19.6 Hz), 122.9, 56.6, 35.0, 29.5, 16.0. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ = -124.42. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2F$ $[M+H]^+$ 288.1394, found 288.1393.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(3-methylpyridin-2-yl)butan-2-one (18):

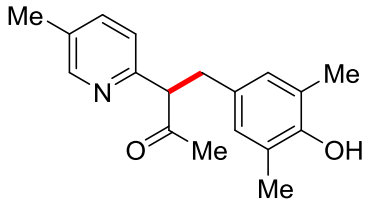
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.8 mmol) and 1-(3-methylpyridin-2-yl)propan-2-one (59.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether /EtOAc: 5/1 to

2/1) yielded **18** (98.3 mg, 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.44 (d, J = 4.4 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.06 (dd, J = 7.5, 4.4 Hz, 1H), 6.56 (s, 2H), 5.03 (brs, 1H), 4.17 (dd, J = 7.9, 6.5 Hz, 1H), 3.34 (dd, J = 13.8, 6.5 Hz, 1H), 2.95 (dd, J = 13.8, 7.9 Hz, 1H), 2.11 (s, 6H), 2.07 (s, 3H), 1.99 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.9, 157.2, 150.7, 147.4, 138.2, 132.6, 131.0, 129.1, 123.0, 122.1, 59.9, 36.0, 28.8, 18.9, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1643.



3-(5-Chloropyridin-2-yl)-4-(4-hydroxy-3,5-dimethylphenyl)butan-2-one (19):

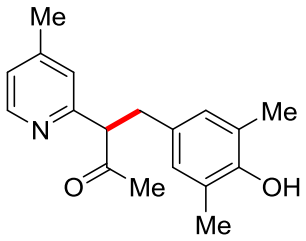
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(5-chloropyridin-2-yl)propan-2-one (67.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **19** (59.5 mg, 49%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.52 (s, 1H), 7.58 (dd, J = 8.4, 1.5 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 6.67 (s, 2H), 4.82 (brs, 1H), 4.16 (t, J = 7.6 Hz, 1H), 3.28 (dd, J = 13.9, 7.6 Hz, 1H), 2.94 (dd, J = 13.9, 7.6 Hz, 1H), 2.15 (s, 6H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.2, 156.6, 150.8, 148.6, 136.6, 130.8, 130.4, 129.1, 124.1, 123.2, 63.1, 36.6, 30.0, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2Cl$ $[M+H]^+$ 304.1098, found 304.1098.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(5-methylpyridin-2-yl)butan-2-one (20):

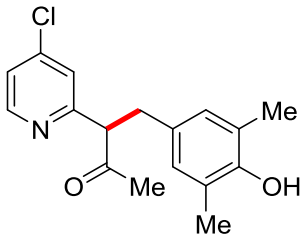
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(5-methylpyridin-2-yl)propan-2-one (59.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to

2/1) yielded **20** (64.6 mg, 57%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.38 (s, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 6.69 (s, 2H), 4.93 (brs, 1H), 4.14 (t, *J* = 8.0 Hz, 1H), 3.30 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.92 (dd, *J* = 13.9, 8.0 Hz, 1H), 2.30 (s, 3H), 2.15 (s, 6H), 2.03 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.8, 155.5, 150.8, 149.9, 137.6, 131.8, 130.8, 129.1, 123.3, 122.6, 63.2, 36.5, 29.9, 18.2, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1648.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(4-methylpyridin-2-yl)butan-2-one (21):

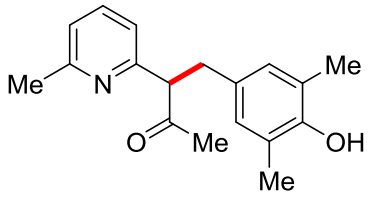
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-methylpyridin-2-yl)propan-2-one (59.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **21** (63.5 mg, 56%)**. ^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.39 (d, *J* = 5.2 Hz, 1H), 7.01 (s, 1H), 6.99 (d, *J* = 5.2 Hz, 1H), 6.70 (s, 2H), 5.56 (brs, 1H), 4.16 (t, *J* = 7.5 Hz, 1H), 3.30 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.91 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.30 (s, 3H), 2.15 (s, 6H), 2.02 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.8, 158.1, 150.9, 149.2, 148.3, 130.8, 129.1, 123.9, 123.4, 63.5, 36.6, 30.0, 21.1, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1646.



3-(4-Chloropyridin-2-yl)-4-(4-hydroxy-3,5-dimethylphenyl)butan-2-one (22):

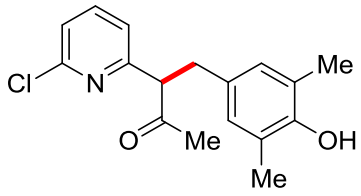
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-chloropyridin-2-yl)propan-2-one (67.9 mg, 0.40 mmol).

Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **22** (70.4 mg, 58%)**.** **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.46 (d, J = 5.7 Hz, 1H), 7.20–7.19 (m, 2H), 6.68 (s, 2H), 4.78 (brs, 1H), 4.16 (t, J = 7.5 Hz, 1H), 3.30 (dd, J = 13.8, 7.5 Hz, 1H), 2.94 (dd, J = 13.8, 7.5 Hz, 1H), 2.16 (s, 6H), 2.07 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.9, 160.0, 150.9, 150.5, 144.9, 130.3, 129.1, 123.7, 123.2, 122.8, 63.5, 36.6, 30.2, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2Cl$ $[M+H]^+$ 304.1098, found 304.1095.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(5-methylpyridin-2-yl)butan-2-one (23):

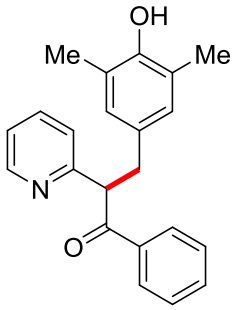
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(6-methylpyridin-2-yl)propan-2-one (59.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **23** (60.1 mg, 53%). **^{1}H-NMR** (600 MHz, $CDCl_3$) δ = 7.50 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.73 (s, 2H), 4.84 (brs, 1H), 4.16 (t, J = 7.4 Hz, 1H), 3.30 (dd, J = 13.9, 7.4 Hz, 1H), 2.92 (dd, J = 13.9, 7.4 Hz, 1H), 2.54 (s, 3H), 2.16 (s, 6H), 2.04 (s, 3H). **^{13}C-NMR** (150 MHz, $CDCl_3$) δ = 207.9, 158.4, 157.8, 150.7, 137.0, 131.0, 129.2, 123.0, 121.8, 119.8, 63.8, 36.7, 30.2, 24.6, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1674.



3-(6-Chloropyridin-2-yl)-4-(4-hydroxy-3,5-dimethylphenyl)butan-2-one (24):

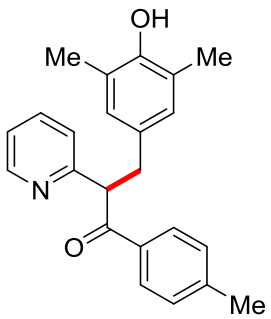
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(6-chloropyridin-2-yl)propan-2-one (67.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to

2/1) yielded **24** (77.8 mg, 64%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.56 (t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.71 (s, 2H), 4.89 (brs, 1H), 4.18 (t, *J* = 7.5 Hz, 1H), 3.27 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.96 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.15 (s, 6H), 2.07 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.2, 159.2, 151.0, 150.8, 139.4, 130.2, 129.1, 123.2, 122.9, 121.6, 63.2, 36.6, 30.2, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2Cl$ $[M+H]^+$ 304.1098, found 304.1097.



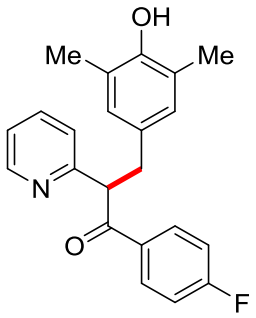
3-(4-Hydroxy-3,5-dimethylphenyl)-1-phenyl-2-(pyridin-2-yl)propan-1-one (25):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-phenyl-2-(pyridin-2-yl)ethan-1-one (78.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **25** (92.7 mg, 70%). **^{1}H-NMR** (400 MHz, $CDCl_3$) = 8.51 (d, *J* = 4.8 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.35–7.29 (m, 3H), 7.10 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.74 (s, 2H), 5.37 (brs, 1H), 5.16 (t, *J* = 7.5 Hz, 1H), 3.47 (dd, *J* = 13.8, 7.5 Hz, 1H), 3.07 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.12 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 198.8, 159.1, 150.9, 149.5, 137.0, 136.8, 133.0, 130.7, 129.2, 129.0, 128.5, 123.2, 122.8, 122.2, 58.4, 38.2, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1645, found 332.1639.



3-(4-Hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)-1-(p-tolyl)propan-1-one (26):

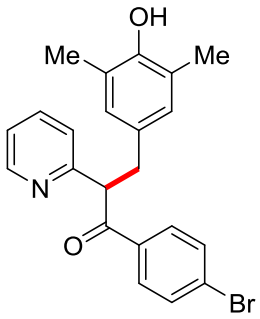
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)-1-(*p*-tolyl)ethan-1-one (84.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **26** (99.2 mg, 72%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 4.4 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.10 (dd, *J* = 7.7, 4.4 Hz, 1H), 6.73 (s, 2H), 5.11 (t, *J* = 7.5 Hz, 1H), 3.46 (dd, *J* = 13.8, 7.5 Hz, 1H), 3.06 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.32 (s, 3H), 2.12 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 198.4, 159.4, 150.8, 149.5, 143.9, 137.0, 134.4, 130.9, 129.3, 129.2, 123.1, 122.8, 122.1, 58.4, 38.2, 21.7, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1802, found 346.1799.



1-(4-Fluorophenyl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (27):

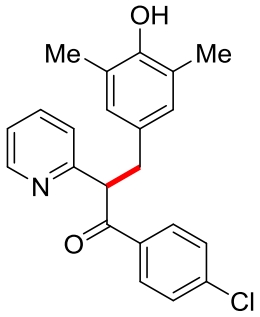
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-fluorophenyl)-2-(pyridin-2-yl)ethan-1-one (86.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **27** (110.5 mg, 79%)**. ^{1}H-NMR** (600 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 5.4 Hz, 1H), 8.02 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.60 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.12 (dd, *J* = 7.9, 5.4 Hz, 1H), 6.99 (t, *J* = 8.9 Hz, 2H), 6.73 (s, 2H), 5.34 (brs, 1H), 5.10 (dd, *J* = 8.0, 6.7 Hz, 1H), 3.46 (dd, *J* = 13.8, 8.0 Hz, 1H), 3.05 (dd, *J* = 13.8, 6.7 Hz, 1H), 2.11 (s, 6H). **^{13}C-NMR** (150 MHz, $CDCl_3$) δ = 197.3, 165.7 (d, *J* = 255.1 Hz), 159.1, 150.9, 149.6, 137.1, 133.2 (d, *J* = 3.0 Hz), 131.7 (d, *J* = 9.3 Hz), 130.7, 129.3, 123.2, 122.7, 122.3, 115.6 (d, *J* = 21.9 Hz), 58.5, 38.1, 16.1. **^{19}F-NMR** (377

MHz, $CDCl_3$) δ = -105.12. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}NO_2F$ $[M+H]^+$ 350.1551, found 350.1551.



1-(4-Bromophenyl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (28):

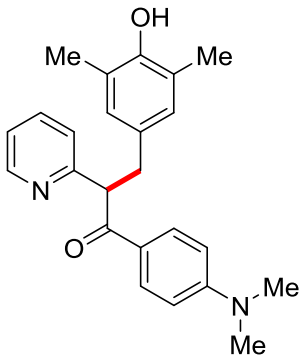
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-bromophenyl)-2-(pyridin-2-yl)ethan-1-one (110.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **28** (130.5 mg, 79%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 4.6 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.59 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.28–7.26 (m, 1H), 7.12 (dd, *J* = 7.8, 4.6 Hz, 1H), 6.72 (s, 2H), 5.30 (brs, 1H), 5.08 (t, *J* = 7.4 Hz, 1H), 3.46 (dd, *J* = 13.9, 7.4 Hz, 1H), 3.05 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.12 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 197.8, 158.9, 150.9, 149.7, 137.1, 135.6, 131.8, 130.7, 130.6, 129.3, 128.3, 123.1, 122.8, 122.3, 58.6, 38.0, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}NO_2Br$ $[M+H]^+$ 410.0750, found 410.0729.



1-(4-Chlorophenyl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (29):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg,

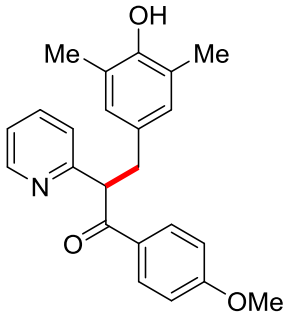
0.80 mmol) and 1-(4-chlorophenyl)-2-(pyridin-2-yl)ethan-1-one (92.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **29** (118.4 mg, 81%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 4.0 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 2H), 7.59 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.12 (ddd, *J* = 7.7, 4.0, 1.4 Hz, 1H), 6.72 (s, 2H), 5.07 (dd, *J* = 8.1, 6.6 Hz, 1H), 5.03 (brs, 1H), 3.45 (dd, *J* = 13.9, 8.1 Hz, 1H), 3.05 (dd, *J* = 13.9, 6.6 Hz, 1H), 2.12 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 197.6, 159.0, 150.8, 149.7, 139.5, 137.1, 135.2, 130.7, 130.5, 129.3, 128.9, 123.1, 122.8, 122.3, 58.7, 38.0, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}NO_2Cl$ $[M+H]^+$ 366.1255, found 366.1241.



1-(4-(Dimethylamino)phenyl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl) propan-1-one (30):

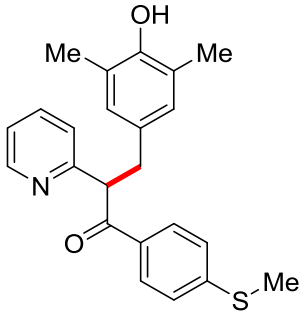
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-(dimethylamino)phenyl)-2-(pyridin-2-yl)ethan-1-one (96.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **30** (113.8 mg, 76%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 5.0 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 2H), 7.56 (dt, *J* = 7.9, 1.7 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 7.9, 5.0 Hz, 1H), 6.75 (s, 2H), 6.55 (d, *J* = 9.0 Hz, 2H), 5.06 (t, *J* = 7.5 Hz, 1H), 4.67 (brs, 1H), 3.45 (dd, *J* = 13.8, 7.5 Hz, 1H), 3.04 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.99 (s, 6H), 2.12 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 196.5, 160.2, 153.4, 150.6, 149.4, 136.8, 131.5, 131.4, 129.3, 124.9, 122.8, 122.6, 121.8, 110.7, 57.9, 40.1, 38.2, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{27}N_2O_2$ $[M+H]^+$

375.2067, found 375.2060.



3-(4-Hydroxy-3,5-dimethylphenyl)-1-(4-methoxyphenyl)-2-(pyridin-2-yl)propan-1-one (31):

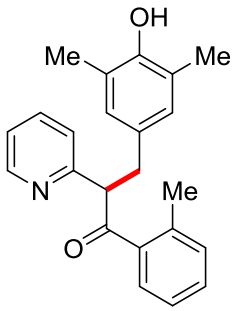
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(4-methoxyphenyl)-2-(pyridin-2-yl)ethan-1-one (90.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **31** (139.3 mg, 96%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.51 (d, J = 5.0 Hz, 1H), 8.00 (d, J = 8.9 Hz, 2H), 7.58 (dt, J = 7.7, 1.9 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.10 (dd, J = 7.7, 5.0 Hz, 1H), 6.82 (d, J = 8.9 Hz, 2H), 6.74 (s, 2H), 5.07 (t, J = 7.4 Hz, 1H), 4.61 (brs, 1H), 3.80 (s, 3H), 3.46 (dd, J = 13.8, 7.4 Hz, 1H), 3.05 (dd, J = 13.8, 7.4 Hz, 1H), 2.13 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 197.3, 163.5, 159.5, 150.9, 149.4, 137.0, 131.4, 130.8, 129.8, 129.2, 123.2, 122.7, 122.1, 113.7, 58.0, 55.4, 38.2, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_3$ $[M+H]^+$ 362.1751, found 362.1744.



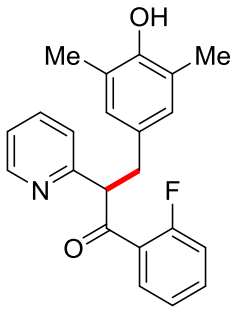
3-(4-Hydroxy-3,5-dimethylphenyl)-1-(4-(methylthio)phenyl)-2-(pyridin-2-yl)propan-1-one (32):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg,

0.80 mmol) and 1-(4-(methylthio)phenyl)-2-(pyridin-2-yl)ethan-1-one (97.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **32** (108.7 mg, 72%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.50 (d, J = 4.1 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 7.8 Hz, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.13–7.08 (m, 3H), 6.73 (s, 2H), 5.54 (brs, 1H), 5.11 (t, J = 7.5 Hz, 1H), 3.46 (dd, J = 13.7, 7.5 Hz, 1H), 3.05 (dd, J = 13.7, 7.5 Hz, 1H), 2.42 (s, 3H), 2.11 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 197.8, 159.3, 150.9, 149.5, 146.0, 137.0, 133.1, 130.8, 129.4, 129.2, 124.9, 123.2, 122.7, 122.1, 58.2, 38.1, 16.1, 14.7. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_2S$ $[M+H]^+$ 378.1522, found 378.1517.

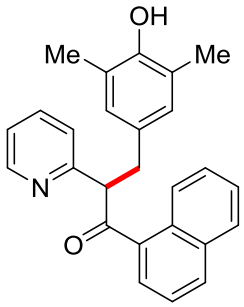


3-(4-Hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)-1-(o-tolyl)propan-1-one (33): The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)-1-(o-tolyl)ethan-1-one (84.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **33** (103.3 mg, 75%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.52 (d, J = 4.8 Hz, 1H), 7.60–7.56 (m, 2H), 7.29–7.22 (m, 2H), 7.12–7.10 (m, 3H), 6.75 (s, 2H), 4.97 (t, J = 7.4 Hz, 1H), 4.83 (brs, 1H), 3.48 (dd, J = 14.0, 7.4 Hz, 1H), 3.05 (dd, J = 14.0, 7.4 Hz, 1H), 2.33 (s, 3H), 2.13 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 202.9, 158.8, 150.9, 149.3, 138.3, 138.2, 136.9, 131.6, 131.1, 130.6, 129.2, 128.6, 125.5, 123.3, 122.9, 122.2, 61.0, 38.2, 20.8, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1802, found 346.1796.



1-(2-Fluorophenyl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (34):

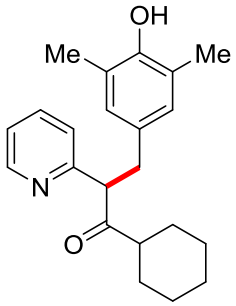
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80) mmol and 1-(2-fluorophenyl)-2-(pyridin-2-yl) ethan-1-one (86.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **34** (97.5 mg, 70%)**.** **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 4.9 Hz, 1H), 7.76 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.54 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.41–7.35 (m, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.13–7.07 (m, 2H), 6.97 (dd, *J* = 11.2, 8.3 Hz, 1H), 6.70 (s, 2H), 4.95 (t, *J* = 7.4 Hz, 1H), 4.77 (brs, 1H), 3.47 (dd, *J* = 13.8, 7.4 Hz, 1H), 3.05 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.13 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 197.6 (d, *J* = 3.8 Hz), 161.0 (d, *J* = 254.6 Hz), 158.5, 150.6, 149.6, 136.6, 134.2 (d, *J* = 9.0 Hz), 131.2 (d, *J* = 2.5 Hz), 130.8, 129.4, 126.4 (d, *J* = 12.4 Hz), 124.4 (d, *J* = 3.5 Hz), 124.0, 122.9, 122.0, 116.6 (d, *J* = 23.6 Hz), 62.1 (d, *J* = 5.5 Hz), 37.8, 16.0. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ = -110.18. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}NO_2F$ $[M+H]^+$ 350.1551, found 350.1544.



3-(4-Hydroxy-3,5-dimethylphenyl)-1-(naphthalen-1-yl)-2-(pyridin-2-yl)propan-1-one (35):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg,

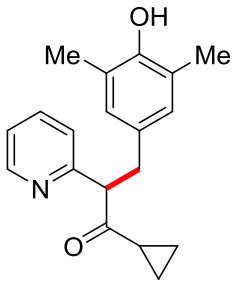
0.80 mmol) and 1-(naphthalen-1-yl)-2-(pyridin-2-yl)ethan-1-one (98.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **35** (114.6 mg, 75%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.34 (d, J = 4.5 Hz, 1H), 8.29 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.36–7.32 (m, 1H), 7.30–7.27 (m, 2H), 7.13 (t, J = 8.0 Hz, 1H), 6.93–6.90 (m, 1H), 6.68 (s, 2H), 5.65 (brs, 1H), 5.09 (dd, J = 8.7, 6.2 Hz, 1H) , 3.48 (dd, J = 13.7, 8.7 Hz, 1H), 3.02 (dd, J = 13.7, 6.2 Hz, 1H), 1.96 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 202.8, 158.8, 151.0, 149.3, 137.0, 136.3, 133.7, 132.4, 130.6, 130.3, 129.3, 128.2, 128.0, 127.7, 126.3, 125.7, 124.3, 123.4, 122.9, 122.2, 61.6, 38.4, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{24}NO_2$ $[M+H]^+$ 382.1802, found 382.1801.



1-Cyclohexyl-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (36):

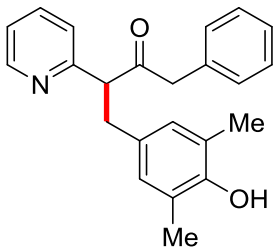
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-cyclohexyl-2-(pyridin-2-yl)ethan-1-one (81.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **36** (112.0 mg, 83%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.53 (d, J = 5.0 Hz, 1H), 7.60 (dt, J = 7.7, 3.9 Hz, 1H), 7.23 (d, J = 7.7 Hz, 1H), 7.15 (dd, J = 7.7, 5.0 Hz, 1H), 6.69 (s, 2H), 4.73 (brs, 1H), 4.36 (dd, J = 8.5, 6.4 Hz, 1H), 3.28 (dd, J = 13.7, 8.5 Hz, 1H), 2.88 (dd, J = 13.7, 6.4 Hz, 1H), 2.34–2.27 (m, 1H), 2.15 (s, 6H), 1.73–1.49 (m, 5H), 1.29–1.20 (m, 1H), 1.15–1.04 (m, 4H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 212.6, 158.7, 150.9, 149.3, 136.9, 130.7, 129.1, 123.3, 122.8, 122.2, 61.5, 51.0, 37.7, 28.3, 27.8, 25.8, 25.7, 25.3, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{28}NO_2$ $[M+H]^+$

338.2115, found 338.2112.



1-Cyclopropyl-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (37):

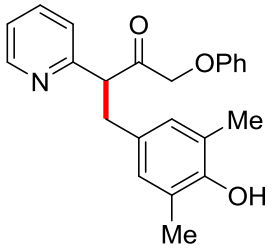
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-cyclopropyl-2-(pyridin-2-yl)ethan-1-one (64.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **37** (92.0 mg, 78%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.56 (d, J = 4.6 Hz, 1H), 7.61 (dt, J = 7.7, 1.7 Hz, 1H), 7.20–7.15 (m, 2H), 6.69 (s, 2H), 5.01 (brs, 1H), 4.32 (t, J = 7.4 Hz, 1H), 3.34 (dd, J = 13.9, 7.4 Hz, 1H), 2.99 (dd, J = 13.9, 7.4 Hz, 1H), 2.14 (s, 6H), 1.96–1.90 (m, 1H), 0.97–0.94 (m, 2H), 0.78–0.68 (m, 2H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 209.4, 158.7, 150.7, 149.5, 136.9, 130.9, 129.2, 123.4, 123.1, 122.2, 63.8, 36.8, 20.9, 16.0, 11.5, 11.4. **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{22}NO_2$ $[M+H]^+$ 296.1645, found 296.1647.



4-(4-Hydroxy-3,5-dimethylphenyl)-1-phenyl-3-(pyridin-2-yl)butan-2-one (38):

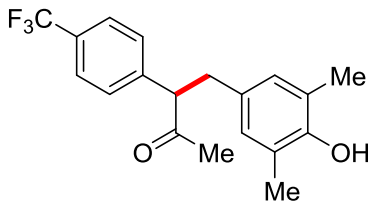
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.8 mmol) and 1-phenyl-3-(pyridin-2-yl)propan-2-one (84.4 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **38** (85.9 mg, 62%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.58 (d, J = 4.5 Hz, 1H), 7.60 (t, J

= 7.6 Hz, 1H), 7.20–7.13 (m, 5H), 6.95–6.93 (m, 2H), 6.62 (s, 2H), 4.63 (brs, 1H), 4.30 (t, *J* = 7.5 Hz, 1H), 3.65 (d, *J* = 15.7 Hz, 1H), 3.58 (d, *J* = 15.7 Hz, 1H), 3.29 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.93 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.13 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.7, 158.4, 150.8, 149.6, 136.9, 133.8, 130.6, 129.7, 129.2, 128.5, 126.8, 123.3, 123.0, 122.4, 62.3, 49.9, 37.1, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1802, found 346.1797.



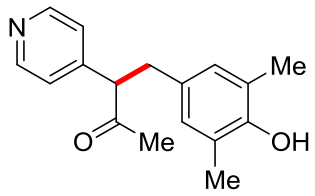
4-(4-Hydroxy-3,5-dimethylphenyl)-1-phenoxy-3-(pyridin-2-yl)butan-2-one (39):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-phenoxy-3-(pyridin-2-yl)propan-2-one (90.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **39** (131.5 mg, 92%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.3 Hz, 1H), 7.61 (dt, *J* = 7.7, 3.9 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.19–7.13 (m, 3H), 6.90 (t, *J* = 7.7 Hz, 1H), 6.73 (s, 2H), 6.60 (d, *J* = 8.2 Hz, 2H), 5.18 (brs, 1H), 4.65 (d, *J* = 17.3 Hz, 1H), 4.49–4.44 (m, 2H), 3.38 (dd, *J* = 13.7, 7.5 Hz, 1H), 3.00 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.16 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 205.2, 157.8, 157.7, 151.0, 149.5, 137.0, 130.2, 129.5, 129.2, 123.4, 123.3, 122.5, 121.5, 114.5, 72.6, 59.3, 36.6, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_3$ $[M+H]^+$ 362.1751, found 362.1748.



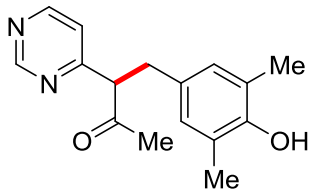
4-(4-Hydroxy-3,5-dimethylphenyl)-3-(4-(trifluoromethyl)phenyl)butan-2-one (40):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.8 mmol) and 1-(4-(trifluoromethyl)phenyl)propan-2-one (81.0 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **40** (66.2 mg, 49%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.57 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 6.65 (s, 2H), 4.65 (brs, 1H), 3.98 (t, J = 7.5 Hz, 1H), 3.30 (dd, J = 13.9, 7.5 Hz, 1H), 2.77 (dd, J = 13.9, 7.5 Hz, 1H), 2.16 (s, 6H), 2.04 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.5, 150.8, 142.7, 130.6, 129.7 (q, J = 32.5 Hz), 129.0 (d, J = 29.4 Hz), 125.8 (q, J = 3.7 Hz), 124.2 (q, J = 272.0 Hz), 123.1, 61.6, 37.9, 30.1, 16.0. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ = -62.49. **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{19}F_3O_2Na$ $[M+Na]^+$ 359.1229, found 359.1233.



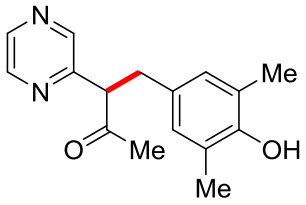
4-(4-Hydroxy-3,5-dimethylphenyl)-3-(pyridin-4-yl)butan-2-one (41):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(pyridin-4-yl)propan-2-one (54.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **41** (89.4 mg, 83%) as white solid. **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.52 (s, 2H), 7.15 (d, J = 4.0 Hz, 2H), 6.63 (s, 2H), 3.91 (t, J = 7.5 Hz, 1H), 3.27 (dd, J = 13.8, 7.5 Hz, 1H), 2.76 (dd, J = 13.8, 7.5 Hz, 1H), 2.16 (s, 6H), 2.04 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 151.2, 149.9, 147.8, 129.9, 129.0, 123.8, 123.6, 61.1, 37.6, 30.2, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$ 270.1489, found 270.1490.



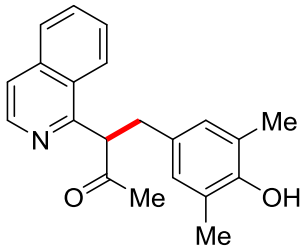
4-(4-Hydroxy-3, 5-dimethylphenyl)-3-(pyrimidin-4-yl)butan-2-one (42):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)-1-(pyridin-4-yl)ethan-1-one (54.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **42** (72.4 mg, 67%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 9.15 (d, J = 1.2 Hz, 1H), 8.61 (d, J = 5.2 Hz, 1H), 7.19 (dd, J = 5.2, 1.2 Hz, 1H), 6.67 (s, 2H), 5.25 (brs, 1H), 4.15 (t, J = 7.6 Hz, 1H), 3.28 (dd, J = 13.9, 7.6 Hz, 1H), 2.97 (dd, J = 13.9, 7.6 Hz, 1H), 2.15 (s, 6H), 2.10 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.1, 166.8, 158.8, 157.2, 151.1, 129.5, 129.0, 123.4, 120.9, 63.2, 36.4, 30.3, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$ 271.1441, found 271.1441.



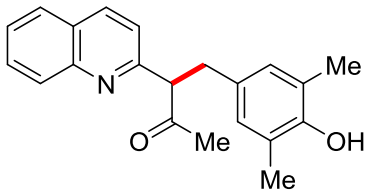
4-(4-Hydroxy-3,5-dimethylphenyl)-3-(pyrazin-2-yl)butan-2-one (43):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(pyrazin-2-yl)propan-2-one (54.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **43** (70.3 mg, 65%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.55 (t, J = 2.6 Hz, 1H), 8.45 (d, J = 2.6 Hz, 1H), 8.39 (s, 1H), 6.64 (s, 2H), 4.81 (brs, 1H), 4.17 (t, J = 7.6 Hz, 1H), 3.34 (dd, J = 13.9, 7.6 Hz, 1H), 3.00 (dd, J = 13.9, 7.6 Hz, 1H), 2.14 (s, 6H), 2.10 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.4, 154.2, 151.1, 144.9, 144.4, 143.0, 129.5, 128.9, 123.6, 61.2, 36.3, 29.8, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$ 271.1441, found 271.1435.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-(isoquinolin-1-yl)butan-2-one (44):

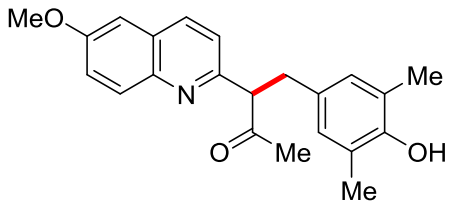
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(isoquinolin-1-yl)propan-2-one (74.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **44** (114.5 mg, 90%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.53 (d, J = 5.6 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 8.5 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 5.6 Hz, 2H), 6.73 (s, 2H), 5.02 (brs, 1H), 4.88 (t, J = 7.4 Hz, 1H), 3.57 (dd, J = 14.1, 7.4 Hz, 1H), 3.16 (dd, J = 14.1, 7.4 Hz, 1H), 2.11 (s, 6H), 2.04 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 158.4, 150.8, 142.1, 136.6, 131.1, 130.2, 129.1, 127.7, 127.6, 127.5, 124.8, 123.1, 120.3, 60.4, 36.1, 28.7, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{22}NO_2$ $[M+H]^+$ 320.1645, found 320.1643.



4-(4-Hydroxy-3, 5-dimethylphenyl)-3-(quinolin-2-yl)butan-2-one (45):

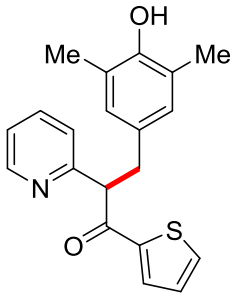
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(quinolin-2-yl)propan-2-one (74.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **45** (103.2 mg, 81%). **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.15 (d, J = 8.6 Hz, 1H), 7.99 (s, 1H), 7.87 (d, J = 8.6 Hz, 1H), 7.36 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 2.8 Hz, 1H), 6.66 (s, 2H), 4.40 (t, J = 7.5 Hz, 1H), 3.85 (s, 3H), 3.23 (dd, J = 14.1, 7.5 Hz, 1H), 2.98 (dd, J = 14.1, 7.5 Hz, 1H), 2.02 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 158.4, 150.8, 142.1, 136.6, 131.1, 130.2, 129.1, 127.7, 127.6, 127.5, 124.8, 123.1, 120.3,

60.4, 36.1, 28.7, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{22}NO_2$ $[M+H]^+$ 320.1645, found 320.1639.



4-(4-Hydroxy-3, 5-dimethylphenyl)-3-(6-methoxyquinolin-2-yl)butan-2-one (46):

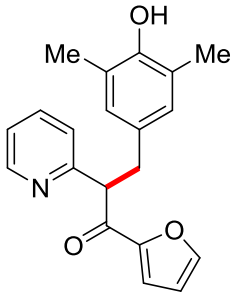
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(6-methoxyquinolin-2-yl)propan-2-one (86.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **46** (97.6 mg, 70%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.00–7.96 (m, 2H), 7.36 (dt, J = 9.3, 2.4 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.05 (t, J = 2.4 Hz, 1H), 6.76 (s, 2H), 4.84 (brs, 1H), 4.37 (t, J = 7.5 Hz, 1H), 3.93 (s, 3H), 3.41 (dd, J = 13.7, 7.5 Hz, 1H), 3.03 (dd, J = 13.7, 7.5 Hz, 1H), 2.15 (s, 6H), 2.07 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.8, 157.8, 156.1, 150.8, 144.1, 135.8, 130.8, 130.6, 129.2, 128.3, 123.2, 122.5, 120.9, 105.2, 64.3, 55.7, 36.6, 30.2, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{24}NO_3$ $[M+H]^+$ 350.1751, found 350.1746.



3-(4-Hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)-1-(thiophen-2-yl)propan-1-one (47):

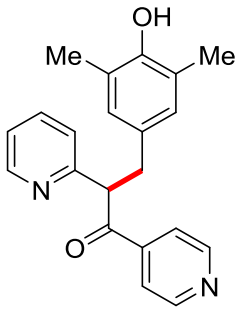
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)-1-(thiophen-2-yl)ethan -1-one (81.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **47** (90.8 mg, 67%)**. ^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.50 (d, J = 4.9 Hz,

1H), 7.77 (d, *J* = 3.8 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 4.9 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.14–7.11 (m, 1H), 6.94 (t, *J* = 4.9 Hz, 1H), 6.75 (s, 2H), 5.73 (brs, 1H), 4.99 (t, *J* = 7.5 Hz, 1H), 3.46 (dd, *J* = 13.8, 7.5 Hz, 1H), 3.06 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.11 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 191.7, 159.0, 150.8, 149.5, 144.4, 137.0, 134.2, 133.4, 130.7, 129.3, 128.3, 123.1 , 122.7, 122.3, 59.9, 38.0, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{20}NO_2S$ $[M+H]^+$ 338.1209, found 338.1204.



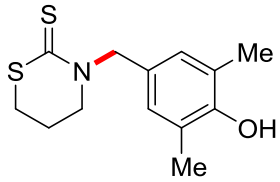
1-(Furan-2-yl)-3-(4-hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propan-1-one (48):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-(furan-2-yl)-2-(pyridin-2-yl)ethan-1-one (74.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **48** (102.6 mg, 80%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 5.6 Hz, 1H), 7.60 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.43–7.42 (m, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 3.6 Hz, 1H), 7.12 (ddd, *J* = 7.9, 5.6, 0.9 Hz, 1H), 6.74 (s, 2H), 6.35 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.92 (brs, 1H), 4.91 (dd, *J* = 8.5, 6.5 Hz, 1H), 3.44 (dd, *J* = 13.8, 8.5 Hz, 1H), 3.04 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.11 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 187.4, 158.6, 152.3, 151.0, 149.3, 147.0, 137.0, 130.4, 129.2, 123.4, 122.9, 122.3, 119.2, 112.3, 58.4, 37.5, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{20}NO_3$ $[M+H]^+$ 322.1438, found 322.1438.



3-(4-Hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)-1-(pyridin-4-yl)propan-1-one (49):

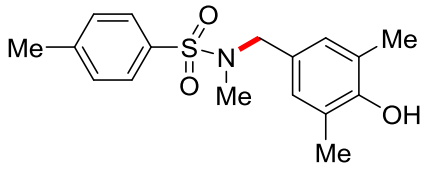
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)-1-(pyridin-4-yl)ethan-1-one (79.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **49** (104.0 mg, 81%). **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.68 (dd, J = 4.6, 1.5 Hz, 2H), 8.40 (d, J = 4.8 Hz, 1H), 7.95 (s, 1H), 7.77 (dd, J = 4.6, 1.5 Hz, 2H), 7.66 (dt, J = 7.8, 1.9 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.15 (dd, J = 7.8, 4.8 Hz, 1H), 6.66 (s, 2H), 5.23 (t, J = 7.5 Hz, 1H), 3.30 (dd, J = 13.8, 7.5 Hz, 1H), 2.93 (dd, J = 13.8, 7.5 Hz, 1H), 2.04 (s, 6H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ = 198.2, 158.4, 151.3, 150.6, 149.3, 142.5, 136.9, 129.3, 128.8, 124.1, 123.8, 122.1, 121.6, 57.0, 36.5, 16.6. **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{21}N_2O_2$ $[M+H]^+$ 333.1598, found 333.1590.



3-(4-Hydroxy-3,5-dimethylbenzyl)-1,3-thiazinane-2-thione (50):

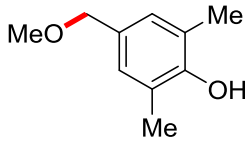
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1, 3-thiazinane-2-thione (53.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 20/1) yielded **50** (66.6 mg, 62%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.98 (s, 2H), 5.23 (s, 2H), 4.69 (brs, 1H), 3.41 (t, J = 6.0 Hz, 2H), 2.96 (t, J = 6.0 Hz, 2H), 2.23 (s, 6H), 2.20–2.14 (m, 2H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ =190.3, 152.8, 128.1, 126.0, 124.4, 56.4, 49.0, 31.7, 22.7, 16.7. **HR-MS** (ESI) *m/z* calcd for $C_{13}H_{17}NOS_2Na$ $[M+Na]^+$ 290.0644,

found 290.0629.



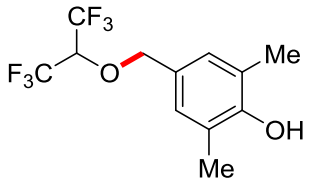
***N*-(4-hydroxy-3,5-dimethylbenzyl)-*N*,4-dimethylbenzenesulfonamide (51):**

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and *N*,4-dimethylbenzenesulfonamide (74.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **51** (90.7 mg, 71%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.71 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 6.88 (s, 2H), 4.72 (brs, 1H), 3.97 (s, 2H), 2.55 (s, 3H), 2.45 (s, 3H), 2.21 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 152.0, 143.5, 134.4, 129.8, 128.9, 127.6, 126.9, 123.3, 53.8, 34.2, 21.6, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{21}NO_3SNa$ $[M+Na]^+$ 342.1134, found 342.1132.



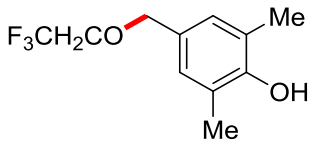
4-(Methoxymethyl)-2,6-dimethylphenol (52):

The general procedure was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and MeOLi (15.2 mg, 0.4 mmol) as substrate, acetone/MeOH (5.0/1.0) as solvent. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 20/1) yielded **52** (57.9 mg, 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.95 (s, 2H), 4.93 (brs, 1H), 4.33 (s, 2H), 3.37 (s, 3H), 2.23 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 152.0, 129.4, 128.7, 123.4, 74.7, 57.8, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{10}H_{14}O_2Na$ $[M+Na]^+$ 189.0886, found 189.0887. The analytical data are in accordance to those reported in the literature.[1]



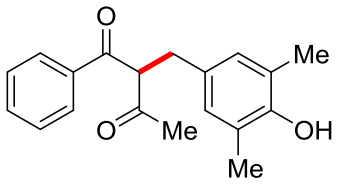
4- {**[(1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy]methyl**} **-2,6-dimethylphenol (53):**

The general procedure was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) as substrate, Cs_2CO_3 (130.3 mg, 0.4 mmol) as base, HFIP (6.0 mL) as solvent. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 20/1) yielded **53** (105.3 mg, 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.02 (s, 2H), 4.86 (brs, 1H), 4.76 (s, 2H), 4.19–4.10 (m, 1H), 2.28 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 153.1, 129.9, 126.2, 123.6, 121.9 (qd, J = 284.3, 3.6 Hz), 75.9, 73.7 (p, J = 32.1 Hz), 15.8. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ = -73.40. **HR-MS** (ESI) *m/z* calcd for $C_{12}H_{13}O_2F_6$ $[M+H]^+$ 303.0814, found 303.0817.



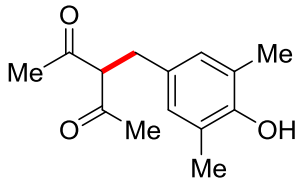
2, 6-Dimethyl-4-((2, 2, 2-trifluoroethoxy)methyl)phenol (54):

The general procedure was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol), Cs_2CO_3 (130.3 mg, 0.4 mmol) as base, acetone/TFE (5.0/1.0) as solvent. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 20/1) yielded **54** (70.8 mg, 76%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.00 (s, 2H), 4.91 (brs, 1H), 4.57 (s, 2H), 3.83 (q, J = 8.5 Hz, 2H), 2.27 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 152.4, 129.0, 127.9, 124.3 (q, J = 279.3 Hz), 123.5, 74.1, 66.7 (q, J = 33.8 Hz), 15.8. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ= -73.71. **HR-MS** (ESI) *m/z* calcd for $C_{11}H_{13}O_2F_3Na$ $[M+Na]^+$ 257.0760, found 257.0759.



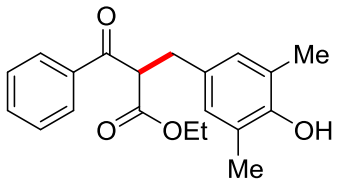
2-(4-Hydroxy-3,5-dimethylbenzyl)-1-phenylbutane-1,3-dione (55):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-phenylbutane-1, 3-dione (64.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **55** (71.7 mg, 60%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 6.79 (s, 2H), 4.78 (t, J = 7.0 Hz, 1H), 3.24–3.13 (m, 2H), 2.16 (s, 6H), 2.13 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 204.2, 196.1, 151.1, 136.5, 133.8, 129.7, 129.0, 128.9, 128.8, 123.4, 65.3, 34.1, 28.7, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{20}O_3Na$ $[M+Na]^+$ 319.1305, found 319.1297.



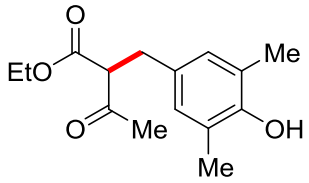
3-(4-Hydroxy-3, 5-dimethylbenzyl)pentane-2,4-dione (56):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and pentane-2, 4-dione (40.0 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **56** in enol form (49.7 mg, 53%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 16.78 (s, 1H), 6.72 (s, 2H), 4.77 (brs, 1H), 3.53 (s, 2H), 2.22 (s, 6H), 2.08 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 192.1, 150.8, 131.0, 127.5, 123.4, 108.8, 32.1, 23.4, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{18}O_3Na$ $[M+Na]^+$ 257.1148, found 257.1152.



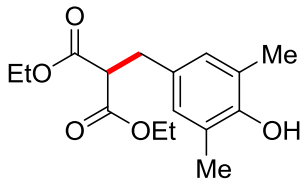
Ethyl-2-(4-hydroxy-3, 5-dimethylbenzyl)-3-oxo-3-phenylpropanoate (57):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and pentane-2,4-dione (76.9 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **57** (91.4 mg, 70%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.97 (d, J = 7.4 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 6.83 (s, 2H), 4.59 (t, J = 7.2 Hz, 1H), 4.14–4.08 (m, 2H), 3.25–3.15 (m, 2H), 2.17 (s, 6H), 1.13 (t, J = 7.1 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 194.9, 169.6, 151.1, 136.2, 133.6, 129.7, 129.0, 128.7, 123.3, 61.5, 56.6, 34.0, 16.0, 14.0. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{22}O_4Na$ $[M+Na]^+$ 349.1410, found 349.1406.



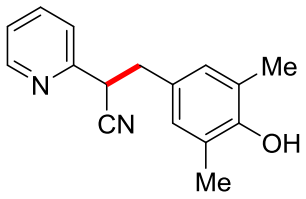
Ethyl-2-(4-hydroxy-3, 5-dimethylbenzyl)-3-oxobutanoate (58):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and ethyl 3-oxobutanoate (52.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **58** (51.5 mg, 49%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.77 (s, 2H), 4.70 (brs, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.72 (t, J = 7.6 Hz, 1H), 3.02 (d, J = 7.6 Hz, 2H), 2.19 (s, 6H), 2.18 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 203.2, 169.4, 151.1, 129.5, 128.9, 123.3, 61.8, 61.5, 33.3, 29.7 16.0, 14.1. **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{20}O_4Na$ $[M+Na]^+$ 287.1254, found 287.1249.



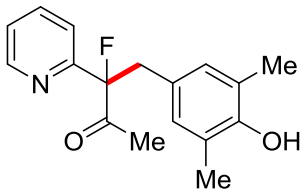
Diethyl 2-(4-hydroxy-3,5-dimethylbenzyl)malonate (59):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and diethyl malonate (64.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **59** (80.0 mg, 68%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.79 (s, 2H), 4.95 (brs, 1H), 4.19–4.13 (m, 4H), 3.59 (t, J = 7.8 Hz, 1H), 3.08 (d, J = 7.8 Hz, 2H), 2.18 (s, 6H), 1.21 (t, J = 7.0 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 169.2, 151.1, 129.2, 129.0, 123.2, 61.5, 54.3, 34.0, 16.0, 14.1. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{20}O_3Na$ $[M+Na]^+$ 317.1359, found 317.1351.



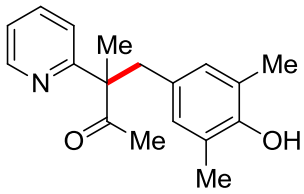
3-(4-Hydroxy-3,5-dimethylphenyl)-2-(pyridin-2-yl)propanenitrile (60):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 2-(pyridin-2-yl)acetonitrile (47.2 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **60** (57.5 mg, 57%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.62 (d, J = 4.6 Hz, 1H), 7.68 (dt, J = 7.8, 1.8 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 7.26 (t, J = 4.6 Hz, 1H), 6.77 (s, 2H), 4.17 (dd, J = 9.1, 5.6 Hz, 1H), 3.21 (dd, J = 13.6, 5.6 Hz, 1H), 3.09 (dd, J = 13.6, 9.1 Hz, 1H), 2.18 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 154.9, 151.7, 149.9, 137.4, 129.4, 127.8, 123.5, 123.2, 122.3, 119.9, 42.6, 39.7, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{17}N_2O$ $[M+H]^+$ 253.1335, found 253.1334.



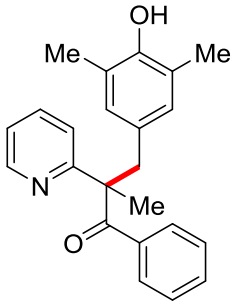
3-Fluoro-4-(4-hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (61):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-fluoro-1-(pyridin-2-yl)propan-2-one (61.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **61** (86.2 mg, 75%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.65 (d, J = 4.6 Hz, 1H), 7.68 (dt, J = 7.8, 1.7 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.24 (dd, J = 7.8, 4.6 Hz, 1H), 6.72 (s, 2H), 4.62 (brs, 1H), 3.57 (dd, J = 27.7, 14.7 Hz, 1H), 3.38 (dd, J = 24.8, 14.7 Hz, 1H), 2.15 (s, 6H), 2.12 (d, J = 4.8 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 205.4 (d, J = 29.3 Hz), 156.3 (d, J = 26.4 Hz), 151.3, 149.2, 136.9, 130.7, 125.7, 123.2, 122.9, 120.2 (d, J = 8.8 Hz), 102.6 (d, J = 188.2 Hz), 41.1 (d, J = 20.3 Hz), 26.2, 16.0. **^{19}F-NMR** (377 MHz, $CDCl_3$) δ = -164.04. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}NO_2F$ $[M+H]^+$ 288.1394, found 288.1390.



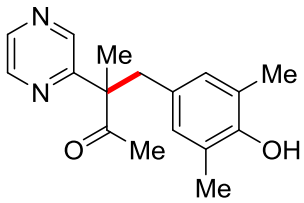
4-(4-Hydroxy-3,5-dimethylphenyl)-3-methyl-3-(pyridin-2-yl)butan-2-one (62):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 3-(pyridin-2-yl)butan-2-one (59.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **62** (94.0 mg, 83%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.59 (d, J = 4.4 Hz, 1H), 7.56 (dt, J = 7.6, 1.9 Hz, 1H), 7.16 (dd, J = 7.6, 4.4 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H), 6.20 (s, 2H), 3.21 (d, J = 13.6 Hz, 1H), 3.07 (d, J = 13.6 Hz, 1H), 2.04 (s, 6H), 1.96 (s, 3H), 1.41 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 210.4, 162.2, 150.8, 149.1, 136.4, 130.4, 128.7, 122.6, 121.9, 121.8, 59.4, 42.4, 26.8, 20.0, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO_2$ $[M+H]^+$ 284.1645, found 284.1644.



3-(4-Hydroxy-3,5-dimethylphenyl)-2-methyl-1-phenyl-2-(pyridin-2-yl)propan-1-one (63) :

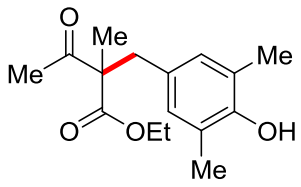
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 1-phenyl-2-(pyridin-2-yl)propan-1-one (84.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **63** (76.8 mg, 55%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.57 (d, J = 4.0 Hz, 1H), 7.58 (dt, J = 7.8, 1.6 Hz, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.23 (t, J = 7.5 Hz, 2H), 7.18–7.15 (m, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.19 (s, 2H), 4.52 (s, 1H), 3.40 (d, J = 13.6 Hz, 1H), 3.32 (d, J = 13.6 Hz, 1H), 2.05 (s, 6H), 1.60 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 202.0, 163.3, 150.7, 149.4, 136.5, 136.4, 131.8, 131.0, 129.8, 128.7, 128.1, 122.2, 122.1, 121.8, 58.2, 44.5, 22.6, 15.9. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1802, found 346.1799.



4-(4-Hydroxy-3,5-dimethylphenyl)-3-methyl-3-(pyrazin-2-yl)butan-2-one (64):

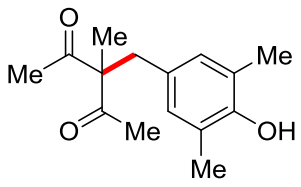
The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 3-(pyrazin-2-yl)butan-2-one (60.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **64** (61.9 mg, 54%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.60 (s, 1H), 8.47 (s, 1H), 8.28 (s, 1H), 6.23 (s, 2H), 5.03 (brs, 1H), 3.22 (d, J = 13.8 Hz, 1H), 3.12 (d, J = 13.8 Hz, 1H), 2.06 (s, 6H), 2.02 (s, 3H), 1.52 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 209.0, 158.1, 151.1, 143.9, 143.5, 142.7, 130.5, 128.0, 122.7, 58.4, 42.5, 27.2, 19.9, 16.0. **HR-MS** (ESI) *m/z* calcd

for $C_{17}H_{20}N_2O_2Na$ $[M+Na]^+$ 307.1417, found 307.1413.



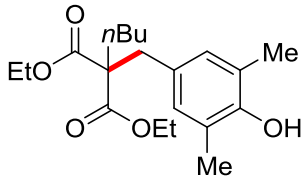
Ethyl 2-(4-hydroxy-3,5-dimethylbenzyl)-2-methyl-3-oxobutanoate (65):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and ethyl 2-methyl-3-oxobutanoate (57.7 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **65** (68.0 mg, 61%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.68 (s, 2H), 4.72 (brs, 1H), 4.22–4.15 (m, 2H), 3.13 (d, J = 13.9 Hz, 1H), 2.91 (d, J = 13.9 Hz, 1H), 2.17 (s, 6H), 2.16 (s, 3H), 1.27 (s, 3H), 1.27 (t, J = 6.8 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.0, 172.8, 151.2, 130.4, 127.8, 122.8, 61.4, 61.1, 39.8, 26.7, 19.1, 16.0, 14.2. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{22}O_4Na$ $[M+Na]^+$ 301.1410, found 301.1409.



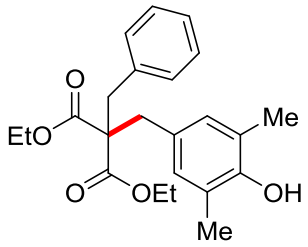
3-(4-Hydroxy-3, 5-dimethylbenzyl)-3-methylpentane-2,4-dione (66):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 3-methylpentane-2,4-dione (45.6 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **66** (58.7 mg, 59%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.66 (s, 2H), 4.61 (brs, 1H), 3.04 (s, 2H), 2.18 (s, 6H), 2.11 (s, 6H), 1.28 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.6, 151.2, 130.4, 127.9, 122.9, 67.6, 39.6, 27.5, 18.4, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{20}O_3Na$ $[M+Na]^+$ 271.1305, found 271.1303.



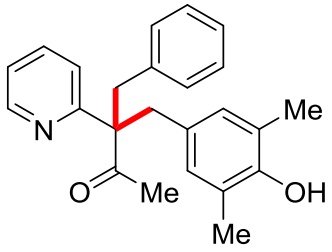
Diethyl 2-butyl-2-(4-hydroxy-3, 5-dimethylbenzyl)malonate (67):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and diethyl 2-butylmalonate (86.5 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **67** (97.0 mg, 69%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 6.66 (s, 2H), 4.80 (brs, 1H), 4.21–4.18 (m, 4H), 3.10 (s, 2H), 2.15 (s, 6H), 1.79–1.75 (m, 2H), 1.37–1.30 (m, 2H), 1.25 (t, J = 7.1 Hz, 6H), 1.27–1.24 (m, 2H), 0.92 (t, J = 7.1 Hz, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 171.7, 151.3, 130.1, 127.6, 122.8, 61.2, 59.0, 37.0, 31.2, 26.3, 22.9, 16.0, 14.2, 14.0. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{30}O_5Na$ $[M+Na]^+$ 373.1985, found 373.1985.



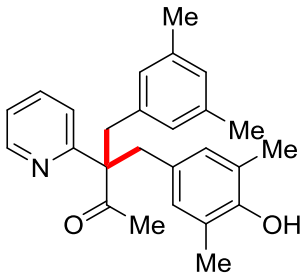
Diethyl 2-benzyl-2-(4-hydroxy-3, 5-dimethylbenzyl)malonate (68):

The general procedure A was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and diethyl 2-benzylmalonate (100.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **68** (104.8 mg, 68%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.28–7.17 (m, 5H), 6.76 (s, 2H), 4.65 (brs, 1H), 4.14–4.08 (m, 4H), 3.19 (s, 2H), 3.11 (s, 2H), 2.19 (s, 6H), 1.18 (t, J = 7.4 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 171.3, 151.3, 136.7, 130.4, 130.3, 128.2, 127.6, 126.9, 122.8, 61.3, 60.4, 39.0, 38.4, 16.1, 14.0. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{29}O_5$ $[M+H]^+$ 385.2010, found 385.2011.



3-Benzyl-4-(4-hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (69):

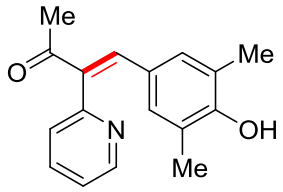
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 4-phenyl-3-(pyridin-2-yl)butan-2-one (90.1 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **69** (115.7 mg, 80%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.64 (d, J = 4.0 Hz, 1H), 7.59 (dt, J = 7.8, 1.9 Hz, 1H), 7.21 (dd, J = 7.8, 4.0 Hz, 1H), 7.16–7.14 (m, 3H), 7.03 (d, J = 7.8 Hz, 1H), 6.85–6.83 (m, 2H), 6.44 (s, 2H), 4.66 (brs, 1H), 3.42 (d, J = 14.4 Hz, 1H), 3.35 (d, J = 14.4 Hz, 1H), 3.30 (d, J = 14.6 Hz, 1H), 3.25 (d, J = 14.6 Hz, 1H), 2.12 (s, 6H), 2.01 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 209.6, 161.6, 150.9, 149.3, 137.5, 136.2, 130.5, 130.4, 128.4, 128.0, 126.4, 122.8, 122.5, 122.1, 64.3, 39.4, 38.6, 28.3, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{26}NO_2$ $[M+H]^+$ 360.1958, found 360.1958.



3-(3,5-Dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (70):

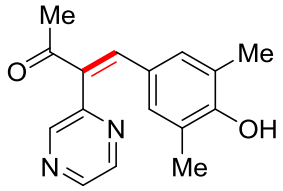
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and 4-(3, 5-dimethylphenyl)-3-(pyridin-2-yl)butan-2-one (101.3 mg, 0.40 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **70** (85.3 mg, 55%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.66 (d, J = 4.8 Hz, 1H), 7.61 (dt, J = 7.8, 1.9 Hz, 1H), 7.21 (dd, J = 7.8, 4.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.80 (s, 1H), 6.40 (s, 4H), 4.49 (brs, 1H), 3.33–3.19 (m, 4H), 2.18 (s, 6H), 2.12 (s, 6H), 2.03 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 209.5, 162.0, 150.8, 149.2, 137.2, 137.2 , 136.1, 130.6,

128.6, 128.3, 128.0, 122.9, 122.4, 122.0, 64.3, 39.2, 38.5, 28.3, 21.4, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{30}NO_2$ $[M+H]^+$ 388.2271, found 388.2264.



4-(4-Hydroxy-3, 5-dimethylphenyl)-3-(pyridin-2-yl)but-3-en-2-one (71):

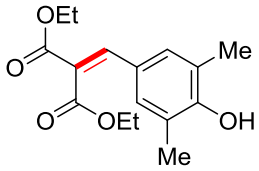
The general procedure C was followed using **3** (107.7 mg, 0.4mmol) and Cs_2CO_3 (65.2 mg, 0.2mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1) yielded **71** (93.3 mg, 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 5.0 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.59 (s, 1H), 7.30 (dd, *J* = 7.8, 5.0 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.44 (s, 2H), 2.31 (s, 3H), 1.98 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 198.4, 157.1, 154.8, 149.9, 141.8, 137.3, 137.2, 131.8, 125.7, 123.9, 122.7, 27.4, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.1332, found 268.1332.



E/*Z* = 9:1

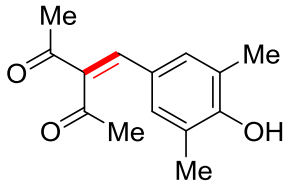
4-(4-Hydroxy-3, 5-dimethylphenyl)-3-(pyrazin-2-yl)but-3-en-2-one (72):

The general procedure C was followed using **43** (108.1 mg, 0.40 mmol) and Cs_2CO_3 (65.2 mg, 0.2 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1) yielded **72** (89.3 mg, 83%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.71 (s, 0.10 H, *Z*), 8.68 (s, 0.90 H, *E*), 8.54 (s, 0.90 H, *E*), 8.50 (s, 0.10 H, *Z*), 8.42 (s, 0.10 H, *Z*), 8.39 (s, 0.90 H, *E*), 7.75 (s, 0.90 H, *E*), 7.45 (s, 0.10 H, *Z*), 7.03 (s, 0.20 H, *Z*), 6.49 (s, 1.80 H, *E*), 5.77 (brs, 1H), 2.41 (s, 2.70 H, *E*), 2.37 (s, 0.30 H, *Z*), 2.22 (s, 0.60 H, *Z*), 2.03 (s, 5.40H, *E*). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 198.0, 155.1, 153.2, 146.6, 144.6, 144.2, 142.9, 134.6, 131.8, 125.2, 123.9, 45.6, 27.1, 16.2. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{17}N_2O_2$ $[M+H]^+$ 269.1285, found 269.1280.



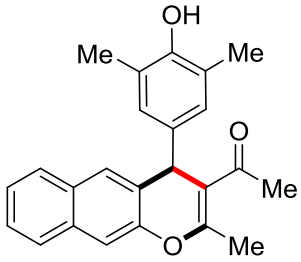
Diethyl 2-(4-hydroxy-3,5-dimethylbenzylidene)malonate (73):

The general procedure C was followed using **59** (117.7 mg, 0.40 mmol) and Cs_2CO_3 (65.2 mg, 0.2 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **73** (99.7 mg, 85%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.60 (s, 1H), 7.08 (s, 2H), 4.35 (q, J = 7.0 Hz, 2H), 4.27 (q, J = 7.0 Hz, 2H), 2.20 (s, 6H), 1.32 (q, J = 7.0 Hz, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 167.6, 164.8, 155.2, 142.6, 130.8, 124.8, 123.8, 123.0, 61.7, 61.6, 16.0, 14.3, 14.0. **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{21}O_5$ $[M+H]^+$ 293.1384, found 293.1384.



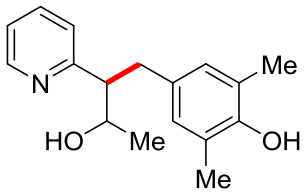
3-(4-Hydroxy-3, 5-dimethylbenzylidene)pentane-2,4-dione (74):

The general procedure C was followed using **56** (93.7 mg, 0.40 mmol) and Cs_2CO_3 (65.2 mg, 0.2 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **74** (76.4 mg, 82%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.36 (s, 1H), 7.02 (s, 2H), 5.83 (brs, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.21 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 207.0, 197.0, 155.5, 140.9, 140.0, 131.0, 124.6, 124.2, 31.7, 26.3, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{16}O_3Na$ $[M+Na]^+$ 255.0992, found 255.0985.



1-(1-(4-Hydroxy-3,5-dimethylphenyl)-3-methyl-1H-benzo[f]chromen-2-yl)ethan-1-one (75):

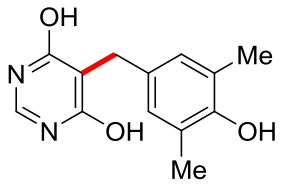
The $CHCl_3$ solution (1.0 mL) was added 3-(4-hydroxy-3,5-dimethylbenzylidene) pentane-2,4-dione **74** (70.0 mg, 0.3 mmol), naphthalen-2-ol (47.6mg, 0.33 mmol) and *p*-TSA (5.7 mg, 0.03 mmol). The reaction mixture was refluxed for 2 days. Then the mixture cooled to room temperature. H_2O (10 mL) was added and extracted with diethyl ether (3×10 mL), then the organic phase was washed with H_2O (3×10 mL), and then dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography on silica gel (petroleum ether/EtOAc: 15:1 to 8:1) yielded **75** (51.7 mg, yield: 48%).[2] **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.06 (d, J = 8.2 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 6.88 (s, 2H), 5.53 (s, 1H), 5.21 (brs, 1H), 2.46 (s, 3H), 2.39 (s, 3H), 2.11 (s, 6H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ = 198.6, 156.6, 151.8, 147.0, 136.0 , 130.9, 130.4, 128.6, 127.7, 126.9, 124.7, 124.1, 123.4, 118.0, 117.1, 116.4, 36.8, 30.5, 19.5, 16.9. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{23}O_3$ $[M+H]^+$ 359.1641, found 359.1629.



4-(3-Hydroxy-2-(pyridin-2-yl)butyl)-2,6-dimethylphenol (76):

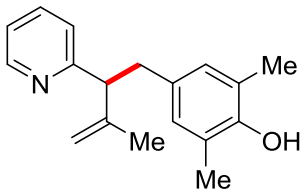
Sodium borohydride (22.7 mg, 0.6 mmol) was added to anhydrous methanol (3.0 mL) solution of **3** (80.8 mg, 0.3 mmol) under a nitrogen atmosphere, and the mixture was stirred for 0.5 h at 0 °C. A saturated aqueous NH_4Cl solution (10 mL) was added, then extracted with EtOAc (3×10 mL), and then dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography on silica gel (petroleum ether/EtOAc: 2/1) yielded **76** (79.7 mg, 97%).[3] **^{1}H-NMR** analysis [integration of pyridyl α-H resonances at 4.07 (major) and 4.24 (minor) ppm] or the unpurified reaction indicated a 2.7:1 d.r. **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.51 (d, J = 4.5 Hz, 1.00H), 7.53 (t, J = 7.4 Hz, 0.73H), 7.42 (t, J = 7.4 Hz, 0.27H), 7.15–7.08 (m, 1.00H), 6.93 (d, J = 7.4 Hz, 0.73H), 6.68–6.66 (m, 1.73H), 6.48 (s, 0.54H), 5.31 (brs, 1.00H), 4.24 (d, J = 6.4 Hz, 0.27H), 4.07 (dd, J = 6.4, 2.5 Hz, 0.73H), 3.09 (dd, J = 13.2, 7.6 Hz, 1.00H), 2.94–2.80 (m, 2.00H), 2.16 (s, 4.38H), 2.11 (s, 1.62H), 1.28 (d, J = 6.4 Hz, 0.81H), 1.04 (d, J = 6.4 Hz, 2.19H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ = 163.6, 163.2, 150.7, 150.5, 148.6, 148.5, 136.6, 136.1, 131.7, 131.6, 129.3, 129.1, 125.1, 124.2, 123.2, 123.1, 121.6, 69.8, 69.2, 54.4, 54.3, 39.3, 34.2, 22.9, 20.4, 16.2, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{22}NO_2$ $[M+H]^+$ 272.1645, found 272.1641.



5-(4-Hydroxy-3,5-dimethylbenzyl)pyrimidine-4,6-diol (77):

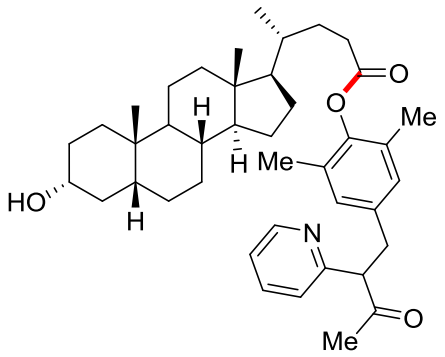
The anhydrous methanol (0.8 mL) solution was added NaOMe (81.0 mg, 1.5 mmol) and amidine hydrochloride (48.3 mg, 0.6 mmol) under a nitrogen atmosphere, and the mixture was stirred for 1.0 h. Then 0.5 mL THF was added to dilute the solution. Then the THF/methanol solution (0.5 mL/0.8 mL) of **59** (88.3 mg, 0.3 mmol) was added to the mixture. The mixture was stirred at ambnent temperature for 6.0 h. After the reaction cooled to room temperature, evaporation of the solvent, acidified with 1 M HCl and cooled to 0 ℃ for 30 minutes, a solid was formed, which was isolated by vacuum filtration and washed three times with H_2O and then dried under high vacuum. Purification by column chromatography on silica gel (DCM/MeOH: 5/1) yielded **77** (45.2 mg, 61%).[4] **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 11.70 (brs, 2H), 7.91 (s, 1H), 6.75 (s, 2H), 3.41 (s, 2H), 2.08 (s, 6H). **^{1}H-NMR** (400 MHz, MeOH- d_4) δ = 9.48 (s, 1H), 8.40 (s, 2H), 5.13 (s, 2H), 3.70 (s, 6H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ = 164.3, 151.0, 147.0, 131.4, 128.1, 123.6, 102.9, 27.1, 16.7. **HR-MS** (ESI) *m/z* calcd for $C_{13}H_{15}N_2O_3$ $[M+H]^+$ 247.1077, found 247.1067.



2,6-Dimethyl-4-(3-methyl-2-(pyridin-2-yl)but-3-en-1-yl)phenol (78):

The anhydrous THF (3.0 mL) solution of methyltriphenylphosphonium bromide (238.5 g, 0.66 mmol) at 0 ℃ was added *n*-BuLi (0.3 mL, 2.5 M, 0.66 mmol) dropwise under a nitrogen atmosphere, and the mixture was stirred for 1 h. After adding **3** (81.0 mg, 0.3

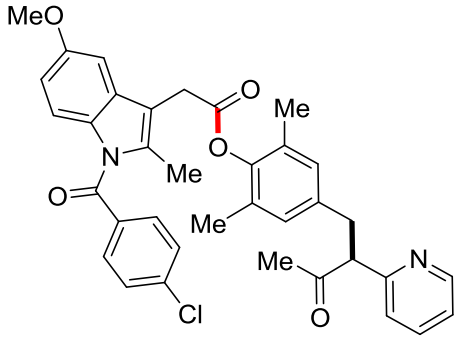
mmol), the mixture was stirred at room temperature for 3 h. A saturated aqueous NH_4Cl solution (10 mL) was added, then extracted with EtOAc (3×10 mL), and then dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1) yielded **78** (45.7 mg, 57%).[5] **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 4.8 Hz, 1H), 7.54 (dt, *J* = 7.6, 1.8 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.08 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.67 (s, 2H), 4.99 (brs, 1H), 4.94 (s, 1H), 4.87 (s, 1H), 3.73 (t, *J* = 7.6 Hz, 1H), 3.14 (dd, J = 13.8, 7.6 Hz, 1H), 3.05 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.14 (s, 6H), 1.66 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 162.7, 150.4, 149.1, 146.6, 136.3, 132.0, 129.1, 123.1, 122.9, 121.4, 111.9, 56.7, 37.8, 21.4, 16.1. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}NO$ $[M+H]^+$ 268.1696, found 268.1698.



2,6-Dimethyl-4-(3-oxo-2-(pyridin-2-yl)butyl)phenyl-(*4R*)-4-((*3R,5R,8R,10S,13R,14S*, 17R)-3-hydroxy-10,13-dimethylhexadecahydro-*1H*-cyclopenta[a]phenanthren-17-yl) pentanoate (79):

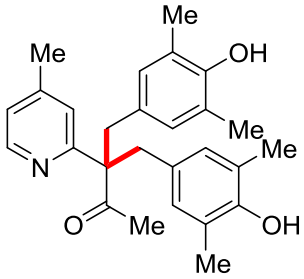
The DCM solution (3.0 mL) was added Lithocholic acid (112.9 mg, 0.3 mmol), **3** (0.36 mmol, 96.9 mg), EDCI (68.8 mg, 0.36 mmol), DMAP (7.4 mg, 0.6 mmol) at room temperature, the mixture was stirred for 0.5 h. H_2O (30 mL) was added, then extracted with DCM (3×20 mL), and then dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography on silica gel (petroleum ether/EtOAc: 3/1) yielded **79** (114.0 mg, yield: 60%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 4.7 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.16–7.11 (m, 2H), 6.74 (s, 2H), 4.15 (t, *J* = 7.4 Hz, 1H), 3.62–3.57 (m, 1H), 3.35 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.97 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.62–2.55 (m, 1H), 2.50-2.42 (m, 1H), 2.05 (s, 3H), 2.02 (s, 6H), 1.97–1.92 (m, 2H), 1.89–1.81 (m, 2H), 1.79–1.73 (m, 2H), 1.70–1.62 (m, 1H), 1.57–1.55 (m, 1H), 1.50–1.47 (m, 2H),

1.43–1.29 (m, 8H), 1.26–1.21 (m, 3H), 1.17–1.08 (m, 3H), 1.06–1.01 (m, 3H), 0.96 (d, *J* = 6.2 Hz, 3H), 0.90 (s, 3H), 0.63 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.9, 172.1, 158.3, 149.8, 146.6, 136.9, 136.7, 129.9, 129.2, 123.4, 122.3, 71.8, 63.5, 56.6, 56.1, 42.8, 42.1, 40.5, 40.2, 36.6, 36.5, 35.9, 35.4, 34.6, 31.3, 31.0, 30.6, 29.8, 28.2, 27.3, 26.5, 24.2, 23.4, 20.9, 18.3, 16.4, 12.1. **HR-MS** (ESI) *m/z* calcd for $C_{41}H_{58}NO_4$ $[M+H]^+$ 628.4360, found 628.4345.



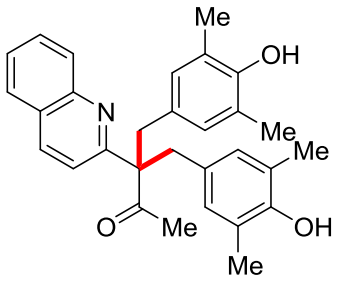
2,6-Dimethyl-4-(3-oxo-2-(pyridin-2-yl)butyl)phenyl-2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (80):

The DCM solution (3.0 mL) was added Indometacin (107.3 mg, 0.3 mmol), **3** (0.36 mmol, 96.9 mg), EDCI (68.8 mg, 0.36 mmol), DMAP (7.4 mg, 0.6 mmol) at room temperature, the mixture was stirred for 0.5 h. H_2O (30 mL) was added, then extracted with DCM (3× 20 mL), and then dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography on silica gel (petroleum ether/EtOAc: 3/1) yielded **80** (158.5 mg, yield: 87%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 4.4 Hz, 1H), 7.63 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.61–7.56 (m, 1H), 7.45 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.16–7.14 (m, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 2.8 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 1H), 6.73 (s, 2H), 6.68 (dd, *J* = 9.0, 2.8 Hz, 1H), 4.13 (d, *J* = 7.4 Hz, 1H), 3.90 (s, 2H), 3.81 (s, 3H), 3.35 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.97 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.44 (s, 3H), 2.04 (s, 3H), 1.93 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.7, 168.6, 168.3, 158.2, 156.1, 149.8, 146.5, 139.4, 137.0, 136.8, 136.1, 133.8, 131.2, 130.8, 130.5, 129.7, 129.2, 123.3, 122.3, 115.0, 112.2, 111.9, 101.2, 63.5, 55.7, 36.5, 30.1, 29.7, 16.2, 13.4. **HR-MS** (ESI) *m/z* calcd for $C_{36}H_{33}N_2O_5ClNa$ $[M+Na]^+$ 631.1970, found 631.1961.



3-(4-Hydroxy-3,5-dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-3-(4-methylpyridin-2-yl)butan-2-one (81):

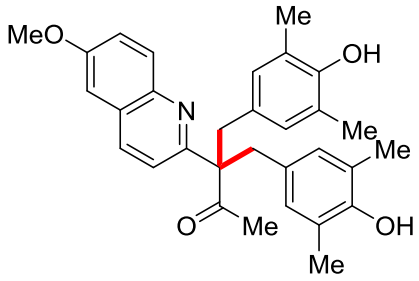
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol) and 1-(4-methylpyridin-2-yl)propan-2-one (59.7 mg, 0.40 mmol), constant current electrolysis for 6.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **81** (94.1 mg, 56%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.50 (d, J = 4.8 Hz, 1H), 7.05 (d, J = 4.8 Hz, 1H), 6.88 (s, 1H), 6.39 (s, 4H), 5.24 (brs, 2H), 3.25 (d, J = 14.4 Hz, 2H), 3.20 (d, J = 14.4 Hz, 2H), 2.30 (s, 3H), 2.12 (s, 12H), 2.06 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 210.4, 161.6, 150.8, 148.8, 147.3, 130.5, 128.4, 123.8, 122.9, 122.6, 64.2, 38.2, 28.2, 21.1, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{32}NO_3$ $[M+H]^+$ 418.2377, found 418.2369.



3-(4-Hydroxy-3,5-dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-3-(quinolin-2-yl)butan-2-one (82):

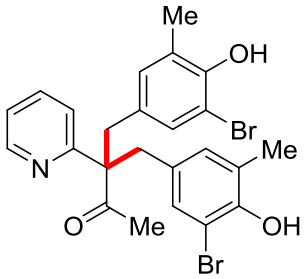
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol) and 1-(quinolin-2-yl)propan-2-one (74.1 mg, 0.40 mmol), constant current electrolysis for 6.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **82** (137.3 mg, 76%). **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.27 (d, J = 8.7 Hz, 1H), 8.00–7.96 (m, 4H), 7.75 (t, J = 7.8 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H), 6.36 (s, 4H), 3.25 (s, 4H), 1.97 (s, 12H), 1.95 (s, 3H).

^{13}C-NMR (100 MHz, DMSO-d_6) δ = 208.6, 162.4, 151.9, 147.2, 136.4, 130.6, 130.1, 129.2, 128.1, 127.8, 127.0, 126.9, 123.8, 121.5, 65.2, 38.6, 28.6, 17.0. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{32}NO_3$ $[M+H]^+$ 454.2377, found 454.2369.



3-(4-Hydroxy-3,5-dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-3-(6-methoxyquinolin-2-yl)butan-2-one (83):

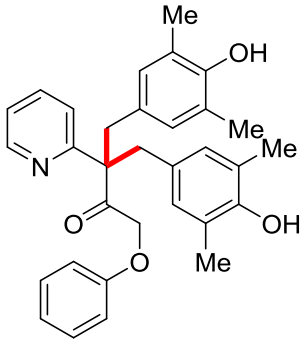
The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol) and 1-(6-methoxyquinolin-2-yl)propan-2-one (74.1 mg, 0.40 mmol), constant current electrolysis for 8.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **83** (108.8 mg, 56%). **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.17 (d, J = 8.8 Hz, 1H), 7.98 (brs, 2H), 7.88 (d, J = 8.8 Hz, 1H), 7.39–7.37 (m, 2H), 7.27 (d, J = 8.8 Hz, 1H), 6.33 (s, 4H), 3.89 (s, 3H), 3.20 (s, 4H), 1.97 (s, 12H), 1.92 (s, 3H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ = 208.3, 159.2, 157.3, 151.4, 142.8, 134.9, 130.3, 130.2, 127.7, 127.5, 123.4, 122.0, 121.2, 105.5, 64.4, 55.5, 38.1, 28.0, 16.6. **HR-MS** (ESI) *m/z* calcd for $C_{31}H_{34}NO_4$ $[M+H]^+$ 484.2482, found 484.2470.



3-(3-Bromo-4-hydroxy-5-methylbenzyl)-4-(3-bromo-4-hydroxy-5-methylphenyl)-3-(pyridin-2-yl)butan-2-one (84):

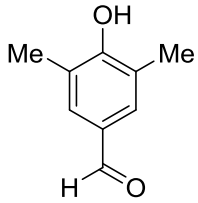
The general procedure B was followed using 2-bromo-4, 6-dimethylphenol (201.1 mg, 1.0 mmol) and 1-(pyridin-2-yl)propan-2-one (54.1 mg, 0.40 mmol), constant current

electrolysis for 7.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **84** (113.8 mg, 53%). **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.85 (brs, 2H), 8.58 (d, J = 4.8 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.33 (dd, J = 7.6, 4.8 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 6.65 (s, 2H), 6.46 (s, 2H), 3.11 (s, 4H), 2.09 (s, 6H), 1.94 (s, 3H). **^{13}C-NMR** (100 MHz, DMSO-d_6) δ = 207.8, 160.8, 150.1, 148.8, 136.6, 131.9, 131.5, 129.4, 126.1, 122.7, 122.4, 110.3, 63.8, 37.6, 27.8, 17.2. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{24}O_3Br$ $[M+H]^+$ 532.0117, found 532.0122.



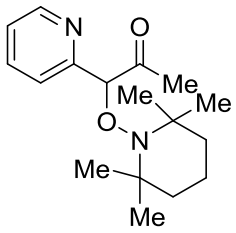
3-(4-Hydroxy-3,5-dimethylbenzyl)-4-(4-hydroxy-3,5-dimethylphenyl)-1-phenoxy-3-(pyridin-2-yl)butan-2-one (85):

The general procedure B was followed using 2, 4, 6-trimethylphenol (**1**) (136.2 mg, 1.0 mmol) and 1-phenoxy-3-(pyridin-2-yl)propan-2-one (90.8 mg, 0.40 mmol) constant current electrolysis for 11.0 h. Purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1 to 2/1) yielded **85** (110.0 mg, 59%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.58 (d, J = 4.3 Hz, 1H), 7.60 (t, J = 7.3 Hz, 1H), 7.20–7.16 (m, 3H), 7.09 (d, J = 8.0 Hz, 1H), 6.91 (t, J = 7.3 Hz, 1H), 6.66 (d, J = 8.0 Hz, 2H), 6.46 (s, 4H), 4.62 (brs, 2H), 4.59 (s, 2H), 3.38 (d, J = 14.1 Hz, 2H), 3.29 (d, J = 14.1 Hz, 2H), 2.11 (s, 12H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 161.7, 158.1, 150.9, 149.0, 136.1, 130.8, 129.4, 128.2, 122.6, 122.5, 122.0, 121.3, 114.7, 72.0, 63.3, 39.0, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{20}O_3$ $[M+H]^+$ 319.1305, found 319.1297. **HR-MS** (ESI) *m/z* calcd for $C_{32}H_{34}NO_4$ $[M+H]^+$ 496.2482, found 496.2470.



4-Hydroxy-3, 5-dimethylbenzaldehyde (89):

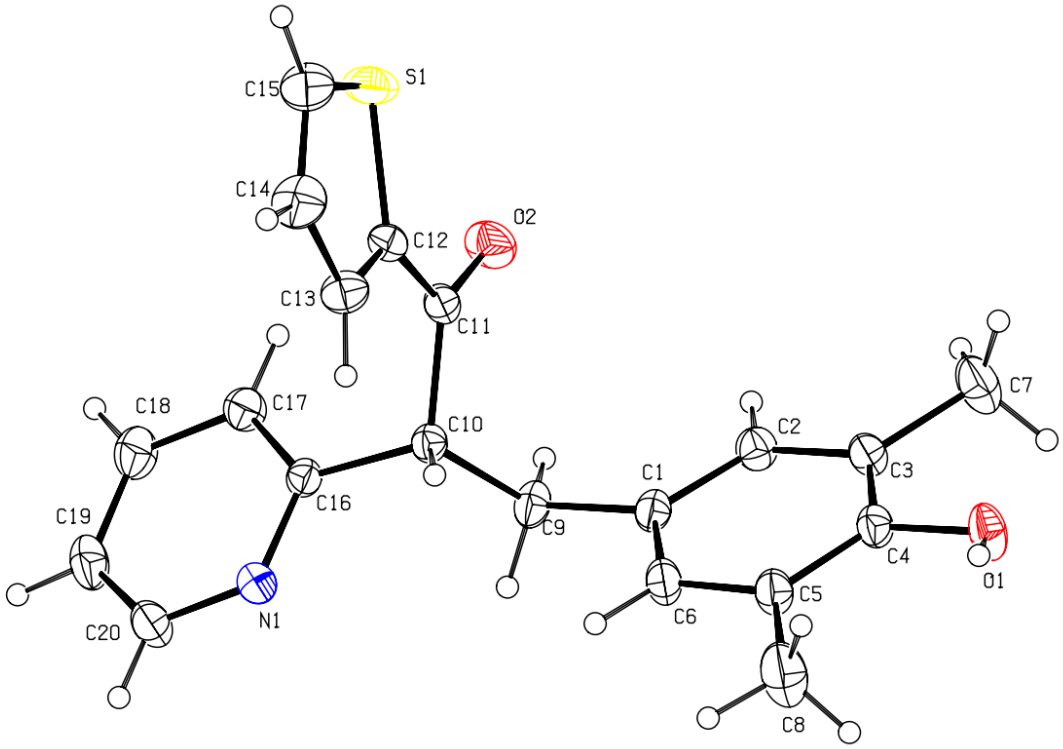
An acetone/H_2O solution (5/1) was added 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) under air atmosphere. The reaction mixture was stirred and electrolyzed at a constant current of 3.0 mA under room temperature. The reaction was dried over Na_2SO_4 and purification by column chromatography on silica gel (petroleum ether/EtOAc: 5/1) yielded **89** (20.2 mg, 17%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 9.80 (s, 1H), 7.54 (s, 2H), 2.31 (s, 6H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 192.0, 158.7, 131.2, 129.1, 124.2, 16.0. **HR-MS** (ESI) *m/z* calcd for $C_9H_{11}O_2$ $[M+H]^+$ 151.0754, found 151.0779. The analytical data are in accordance to those reported in the literature. [6]



1-(Pyridin-2-yl)-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-one (91):

The general procedure A was followed using 1-(pyridin-2-yl)propan-2-one (**2**) (54.0 mg, 0.40 mmol), 2, 4, 6-trimethylphenol (**1**) (109.0 mg, 0.80 mmol) and TEMPO (125.0 mg, 0.80 mmol). Purification by column chromatography on silica gel (petroleum ether/EtOAc: 10/1 to 3/1) yielded **91** (4.1 mg, <5%). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.57 (d, J = 4.0 Hz, 1H), 7.70 (t, J = 7.4 Hz, 1H), 7.50 (d, J = 7.4 Hz, 1H), 7.22–7.19 (m, 1H), 5.36 (s, 1H), 2.24 (s, 3H), 1.56–1.40 (m, 6H), 1.25 (s, 3H), 1.12 (s, 6H), 0.61 (s, 3H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ = 206.8, 157.9, 149.4, 136.8, 122.8, 122.2, 96.3, 40.2, 33.4, 33.3, 27.0, 20.4, 17.1. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{27}N_2O_2$ $[M+H]^+$ 151.0754, found 151.0751.

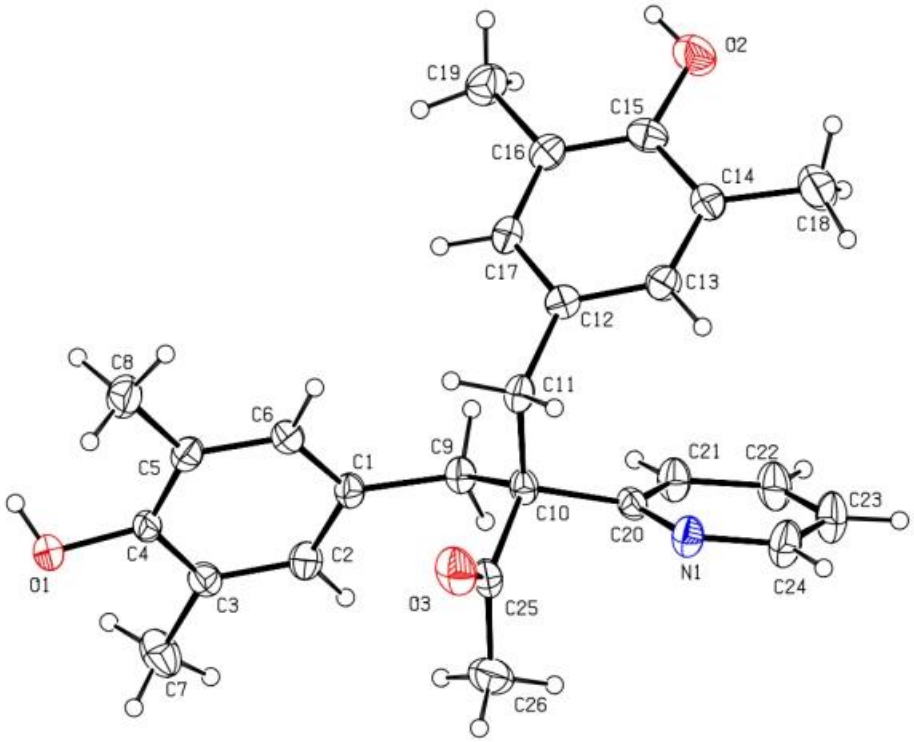
Crystal Data and Structure Refinement for 47, 4, 82:



X Ray structure of **47**
CCDC 2118128

Crystal data and structure refinement for **47**		
Identification code	210618a_0m	
Empirical formula	$C_{20}H_{19}NO_2S$	
Formula weight	37.42	
Temperature	296(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 26.979(4) Å	a= 90°
	b = 9.2286(12) Å	b= 102.602(2)°
	c = 14.3392(19) Å	g = 90°
Volume	3484.1(8) $Å^3$	
Z	8	
Density (calculated)	1.287 Mg/m^3	
Absorption coefficient	0.197 mm^{-1}	
F(000)	1424	

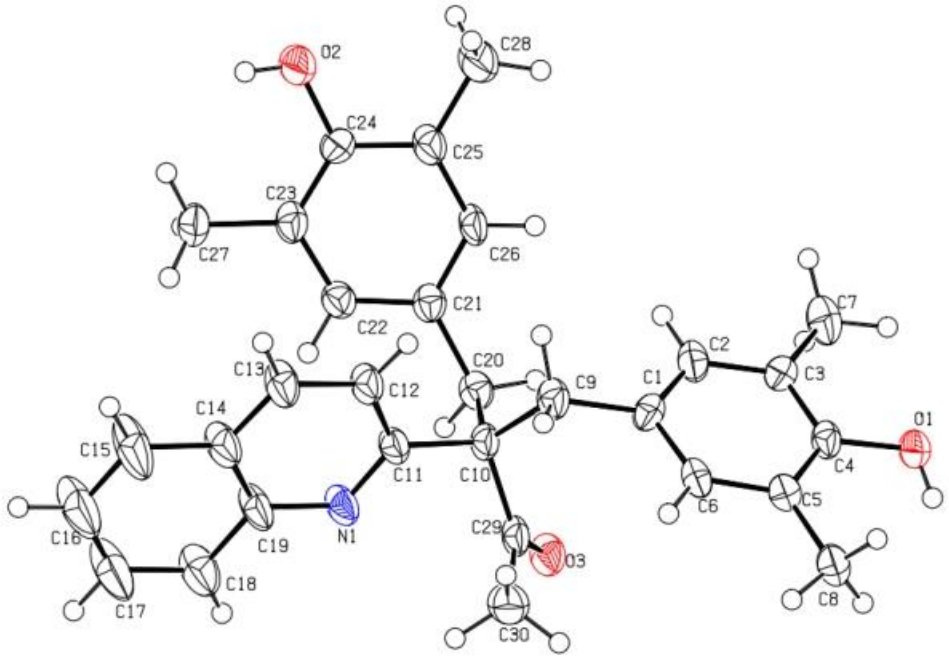
Crystal size	0.3 x 0.2 x 0.2 mm^3
Theta range for data collection	1.547 to 32.030°
Index ranges	-39<=h<=39, -13<=k<=13, -20<=l<=20
Reflections collected	18183
Independent reflections	5678 [R(int) = 0.0238]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7463 and 0.6664
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5678 / 0 / 220
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1228
R indices (all data)	R1 = 0.0609, wR2 = 0.1375
Extinction coefficient	n/a
Largest diff. peak and hole	0.321 and -0.219 e.$Å^{-3}$



X Ray structure of **4**
CCDC 2118167

Crystal data and structure refinement for **4**

Identification code	210914a_0m
Empirical formula	$C_{26}H_{29}NO_3$
Formula weight	403.50
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 1 21 1
Unit cell dimensions	a = 8.0026(11) Å a= 90°
	b = 15.666(2) Å b= 93.268(3)°
	c = 8.8626(12) Å g = 90°
Volume	1109.3(3) $Å^3$
Z	2
Density (calculated)	1.208 Mg/m^3
Absorption coefficient	0.078 mm^{-1}
F(000)	432
Crystal size	0.12 x 0.1 x 0.1 mm^3
Theta range for data collection	2.302 to 28.905°
Index ranges	-10<=h<=10, -21<=k<=20, -11<=l<=11
Reflections collected	11828
Independent reflections	5485 [R(int) = 0.0357]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7458 and 0.6961
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5485 / 1 / 278
Goodness-of-fit on F^2	1.004
Final R indices [I>2sigma(I)]	R1 = 0.0555, wR2 = 0.0955
R indices (all data)	R1 = 0.1044, wR2 = 0.1114
Absolute structure parameter	0.4(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.149 and -0.192 $e.Å^{-3}$



X Ray structure of **82**
CCDC 2118129

Crystal data and structure refinement for **82**		
Identification code	210924n_0m	
Empirical formula	$C_{30}H_{31}NO_3$	
Formula weight	453.56	
Temperature	100(2) K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.224(4) Å	a= 90°
	b = 14.043(7) Å	b= 90°
	c = 21.164(10) Å	g = 90°
Volume	2444(2) $Å^3$	
Z	4	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.396 mm^{-1}	
F(000)	968	

Crystal size	0.1 x 0.03 x 0.02 mm^3
Theta range for data collection	3.286 to 52.499°
Index ranges	-9<=h<=9, -14<=k<=16, -23<=l<=25
Reflections collected	10751
Independent reflections	4142 [R(int) = 0.0750]
Completeness to theta = 52.499°	98.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7512 and 0.5269
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4142 / 0 / 315
Goodness-of-fit on F^2	1.099
Final R indices [I>2sigma(I)]	R1 = 0.0694, wR2 = 0.1734
R indices (all data)	R1 = 0.1001, wR2 = 0.2070
Absolute structure parameter	-0.4(3)
Extinction coefficient	0.0026(10)
Largest diff. peak and hole	0.312 and -0.331 e.$Å^{-3}$

Cyclic Voltammetry Studies

Unless otherwise noted, the cyclic voltammograms were recorded on a CHI 700E instrument using a glassy carbon disk working electrode (diameter, 3 mm), a Pt wire auxiliary electrode, a SCE reference electrode, and a scan rate of 100 mV/s.

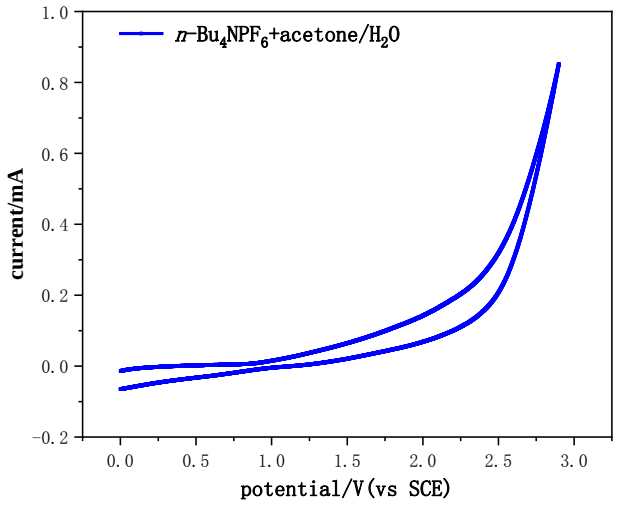


Figure S1. Cyclic voltammogram of *n*-Bu_4NPF_6 (0.1 M) in acetone/H_2O (5/1).

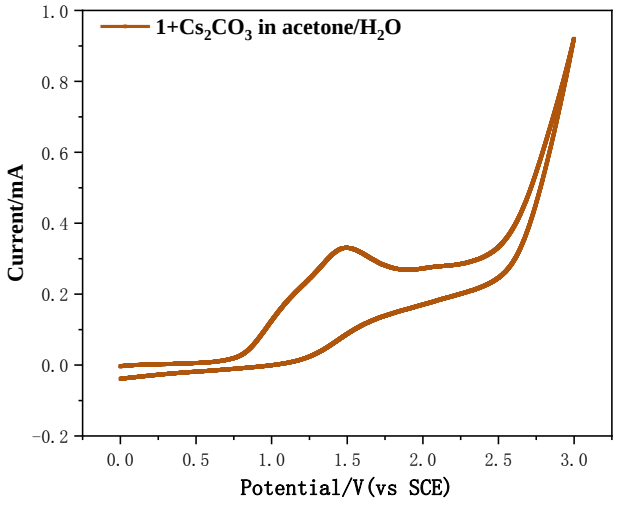


Figure S2. Cyclic voltammogram of **1** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in acetone/H_2O (5/1). E_{oxi} = 1.49 V *vs.* SCE.

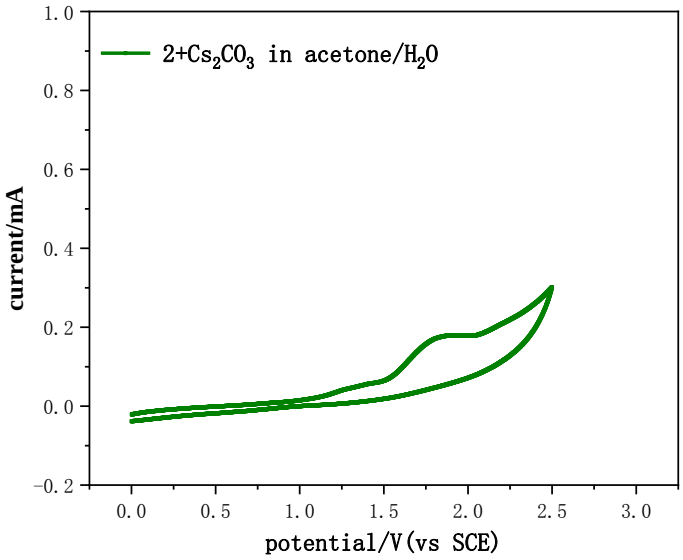


Figure S3. Cyclic voltammogram of **2** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in acetone/H_2O (5/1). E_{oxi} = 1.80 V *vs.* SCE.

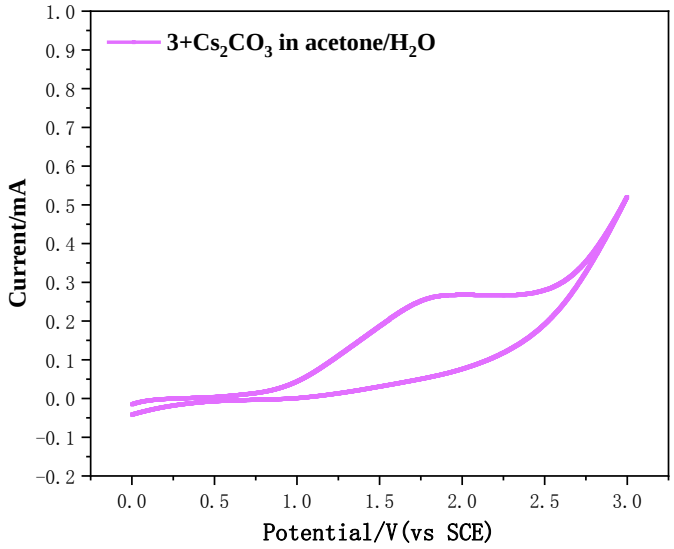


Figure S4. Cyclic voltammogram of **3** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in acetone/H_2O (5/1). E_{oxi} = 1.83 V *vs.* SCE.

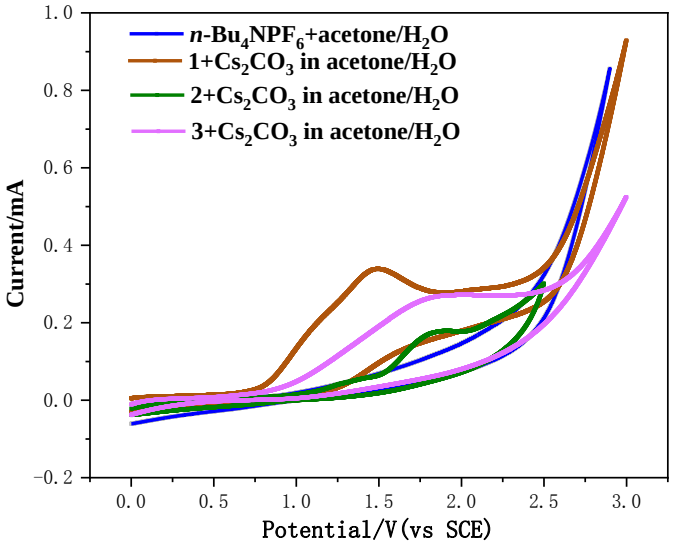


Figure S5. Cyclic voltammograms of *n*-Bu_4NPF_6 (0.1 M) in acetone/H_2O (5/1) in (blank, blue line), substrate **1**+Cs_2CO_3 (brown line), **2**+Cs_2CO_3 (green line), product **3**+Cs_2CO_3 (purple line). Reference electrode: SCE in 3M KCl in H_2O. Scan rate = 100 mV/s.

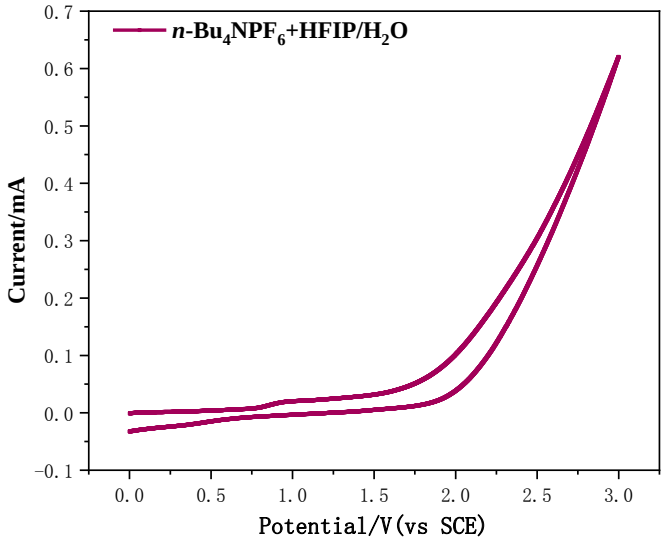


Figure S6. Cyclic voltammogram of *n*-Bu_4NPF_6 (0.1 M) in HFIP/H_2O (5/1).

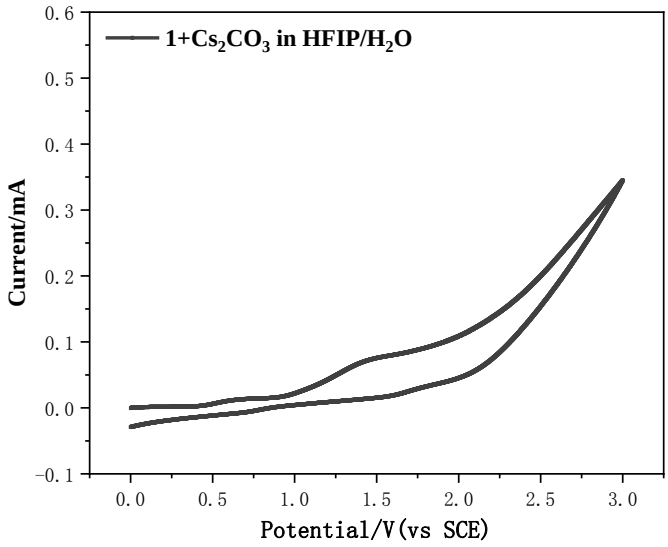


Figure S7. Cyclic voltammogram of **1** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in HFIP/H_2O (5/1). E_{oxi} = 1.44 V *vs*. SCE.

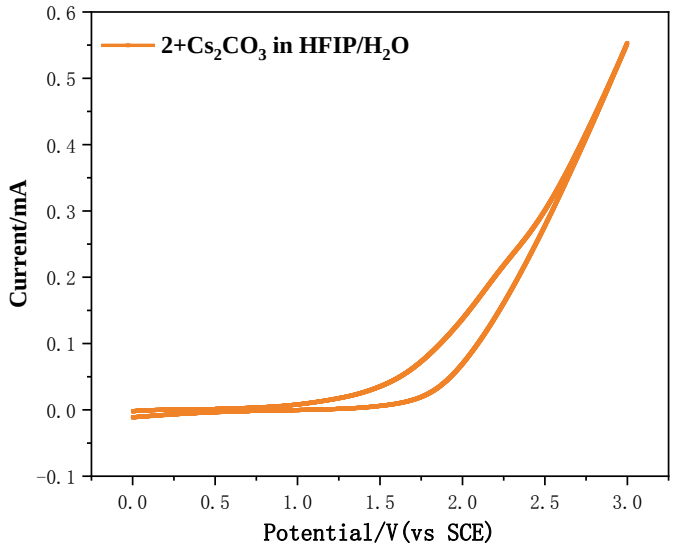


Figure S8. Cyclic voltammogram of **2** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in HFIP/H_2O (5/1). E_{oxi} = 2.26 V *vs*. SCE.

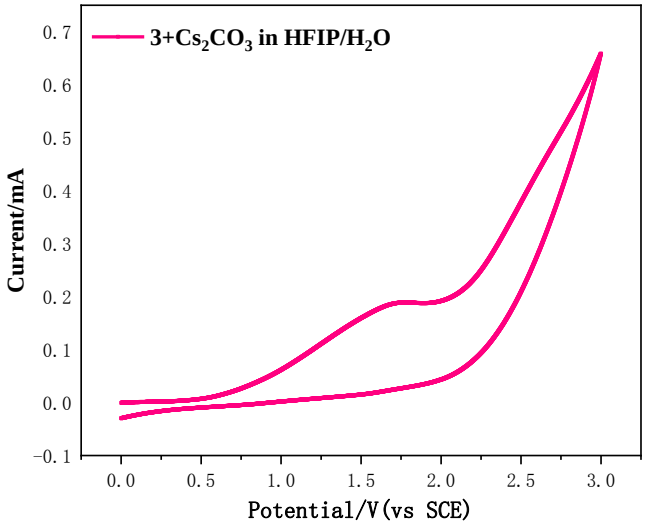


Figure S9. Cyclic voltammogram of **3** (0.4 mmol) in an electrolyte of *n*-Bu_4NPF_6 (0.1 M) and Cs_2CO_3 (0.2 mmol) in HFIP/H_2O (5/1). E_{oxi} = 1.73 V *vs*. SCE.

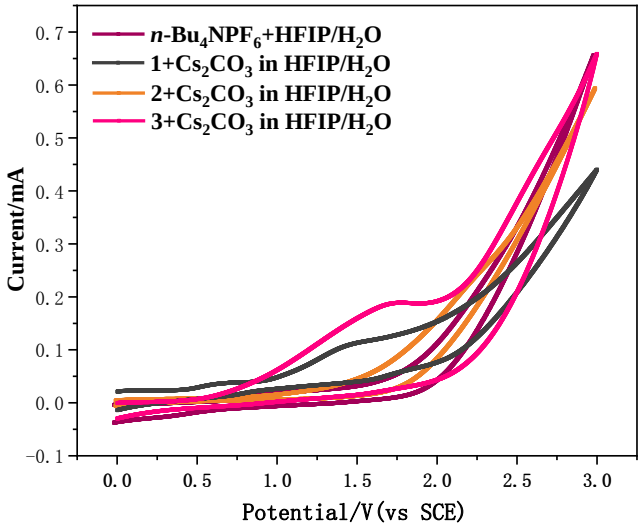


Figure S10. Cyclic voltammograms of *n*-Bu_4NPF_6 (0.1 M) in HFIP/H_2O (5/1) in (blank, dark red line), substrate **1**+Cs_2CO_3 (black line), **2**+Cs_2CO_3 (orange line), product **3**+Cs_2CO_3 (pink line). Reference electrode: SCE in 3M KCl in H_2O. Scan rate = 100 mV/s.

Mechanistic Studies

The effect of HFIP to substrate **2**:

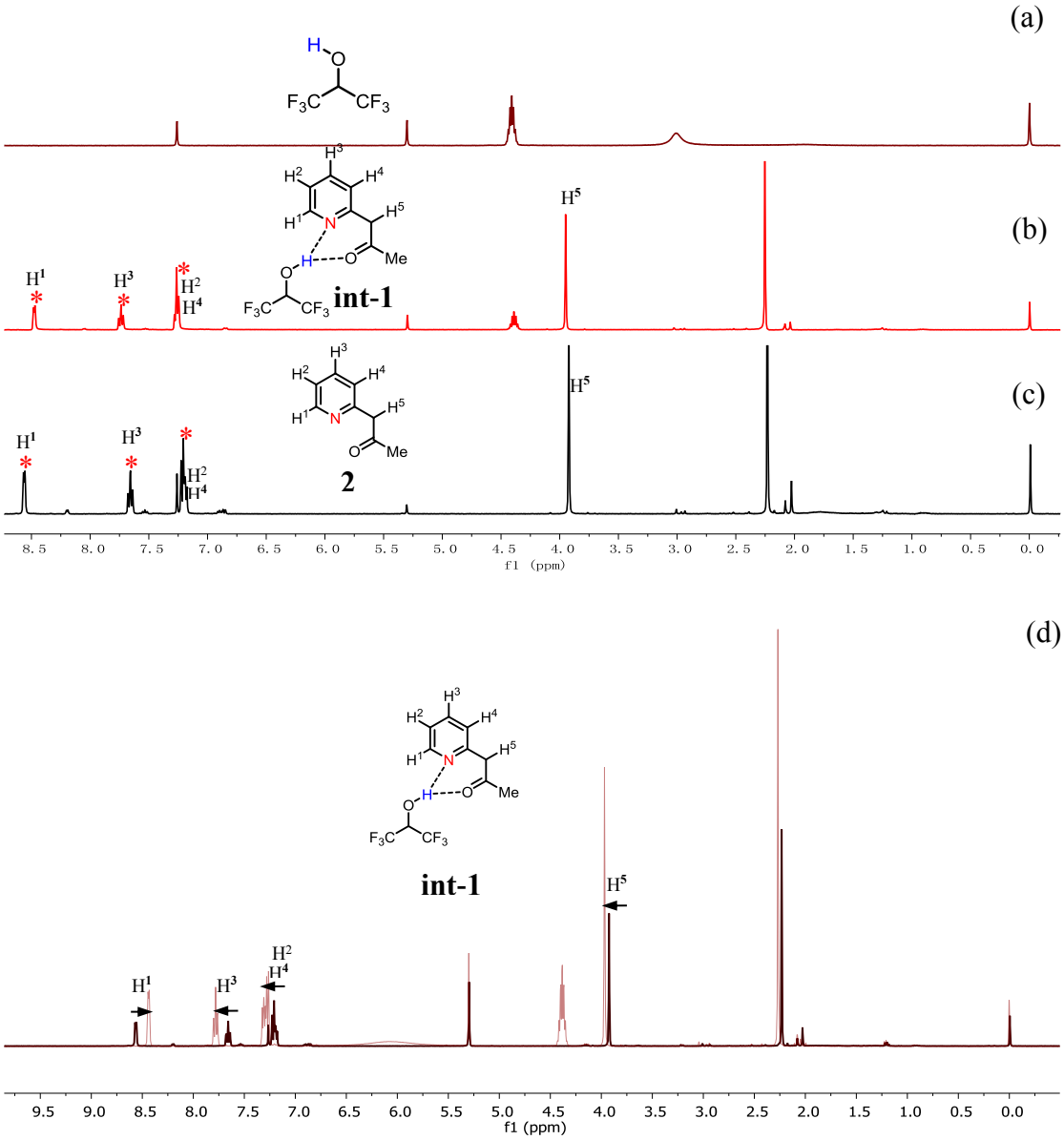


Figure S11. ^{1}H-NMR Spectrum of (a) HFIP, (b) 1:1 mixture of HFIP:**1**, (c) **1**, (d) overlap picture of (b) and (c).

Table S8: The pyridyl proton shifts of **2:**

entry	H^1	H^3	H^2, H^4 (m, 2H)	H^5
2	**8.56**	**7.66**	**7.20**	**3.92**
2 in HFIP	**8.44**	**7.78**	**7.29**	**3.97**

The effect of HFIP to product **3**:

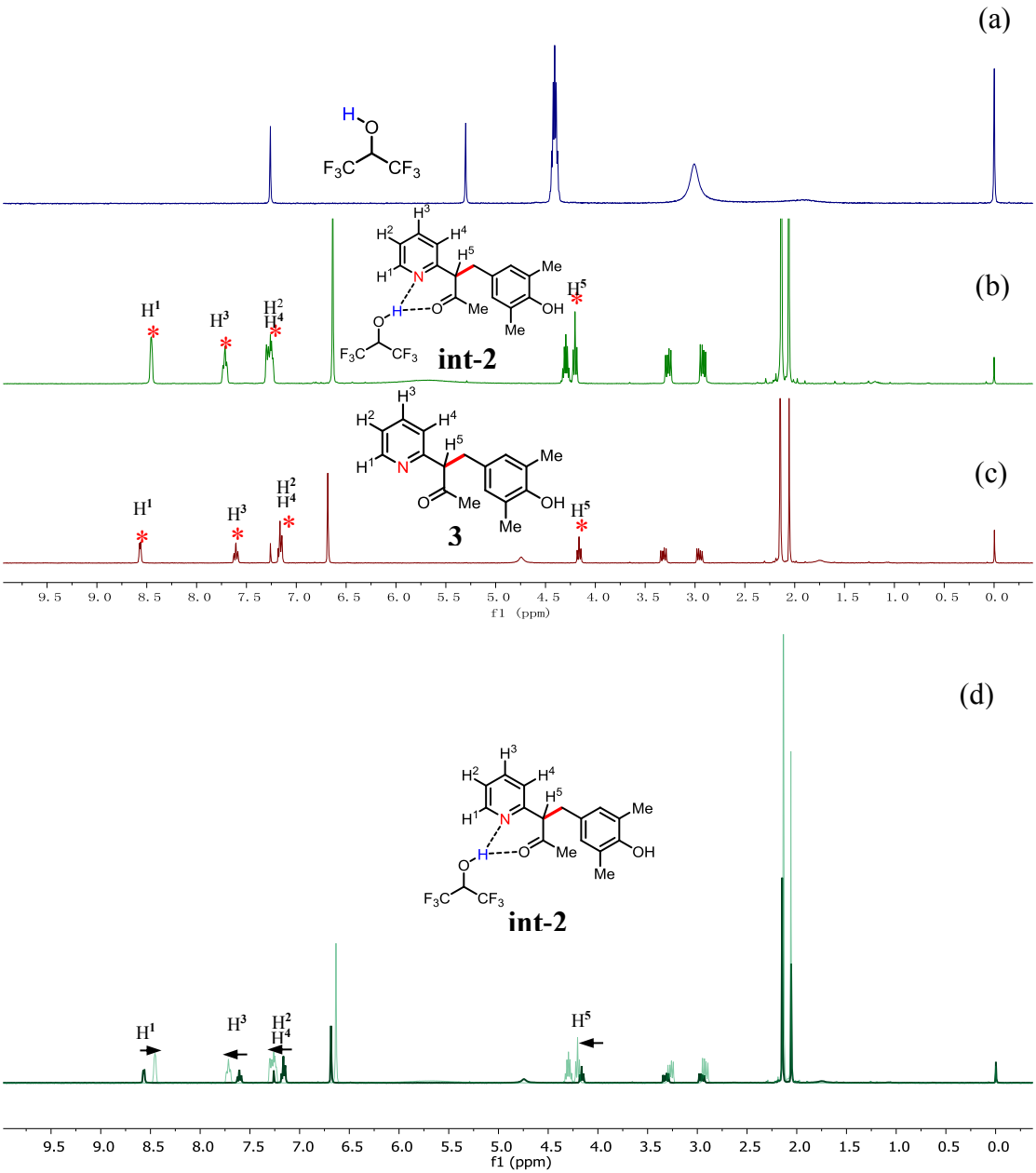
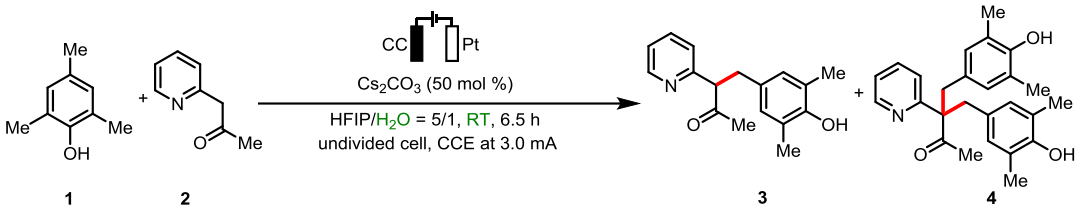


Figure S12. ^{1}H-NMR Spectrum of (a) HFIP, (b) 1:1 mixture of HFIP:**3**, (c) **3**, (d) overlap picture of (b) and (c).

Table S9: The pyridyl proton shifts of **3:**

entry	H^1	H^3	H^2, H^4 (m, 2H)	H^5
3	**8.57**	**7.61**	**7.16**	**4.16**
3 in HFIP	**8.46**	**7.72**	**7.28**	**4.20**



^{1}H-NMR monitoring experiments:

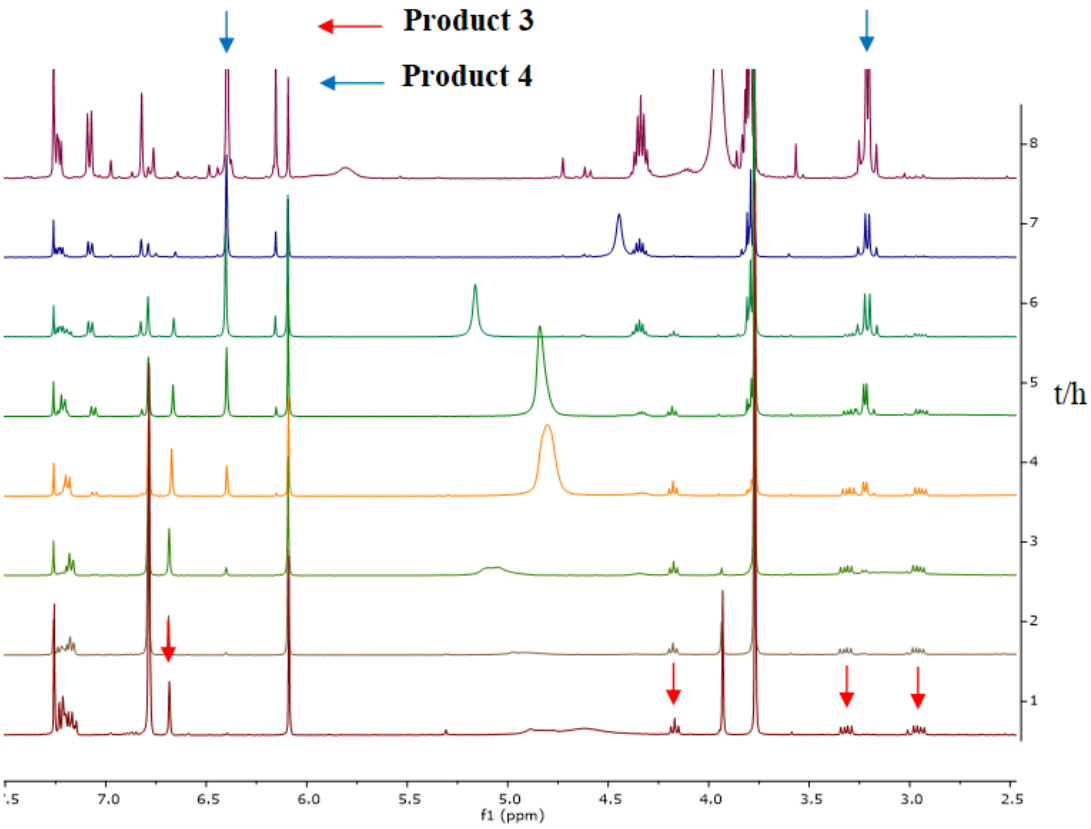


Figure S13. Monitoring the di-alkylation reaction

Time (h) / Yield (%)	0	1	2	3	4	5	6	7	8
3	0	46	63	67	72	49	11	3	1
4	0	0	4	17	25	50	77	84	88

(a)

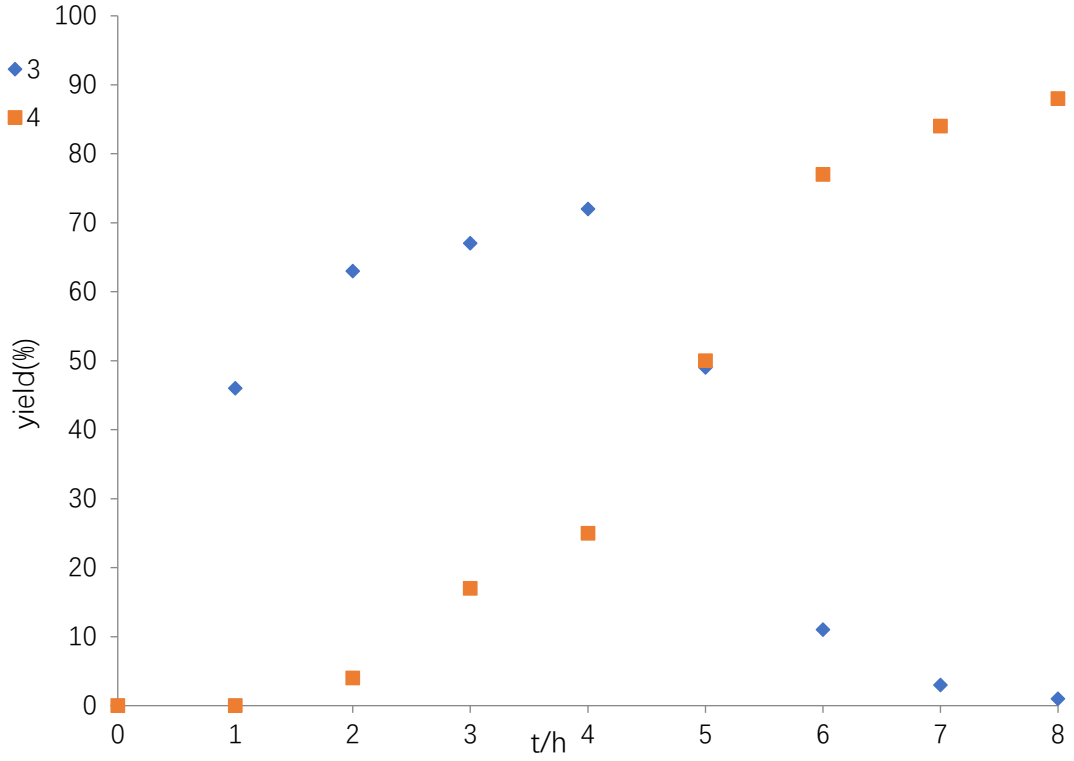
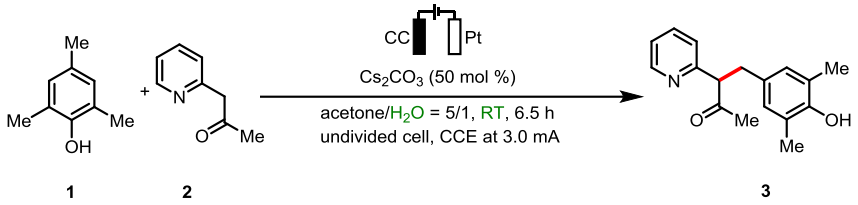


Figure S14. Conversion determined by **^{1}H-NMR** analysis using 1,3,5-trimethoxy benzene as the internal standard. (a) Reaction profile of the formation of product **3** and **4**.



1 2 3

^{1}H-NMR monitoring experiments:

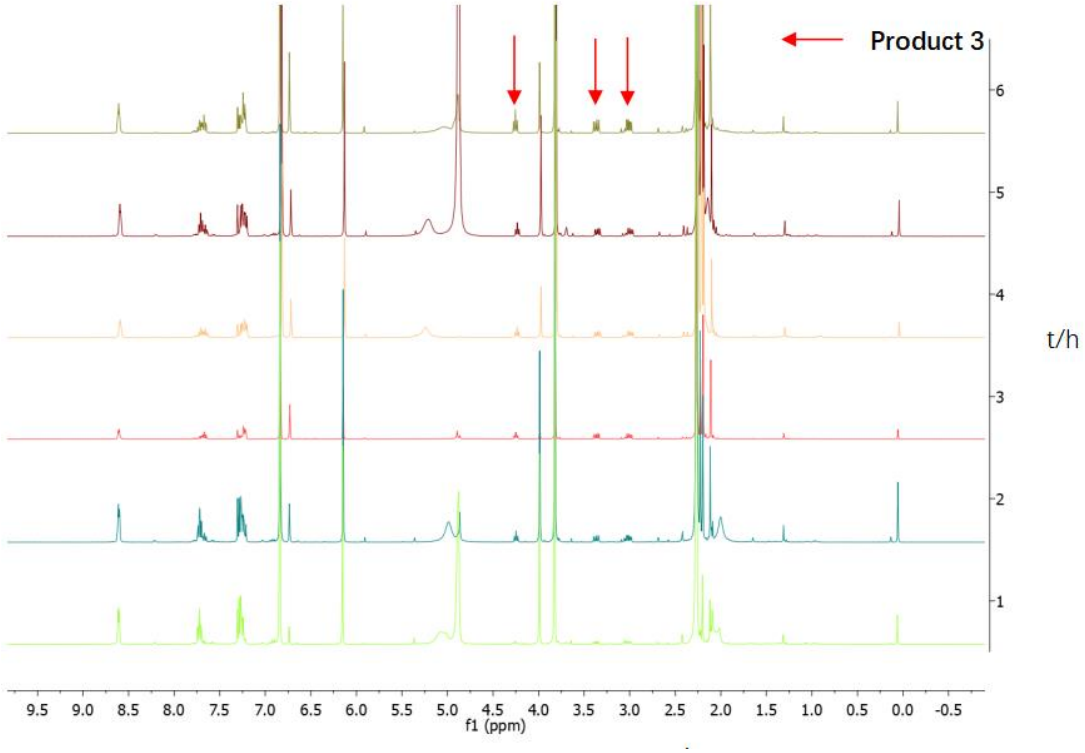


Figure S15. Monitoring the mono-alkylation reaction

Time (h)	Yield of **3** (%)	Current efficiency (%)
0	0	0
1	12	86
2	24	87
3	39	93
4	51	91
5	63	90
6	72	86

Table S10: Yield and current efficiency

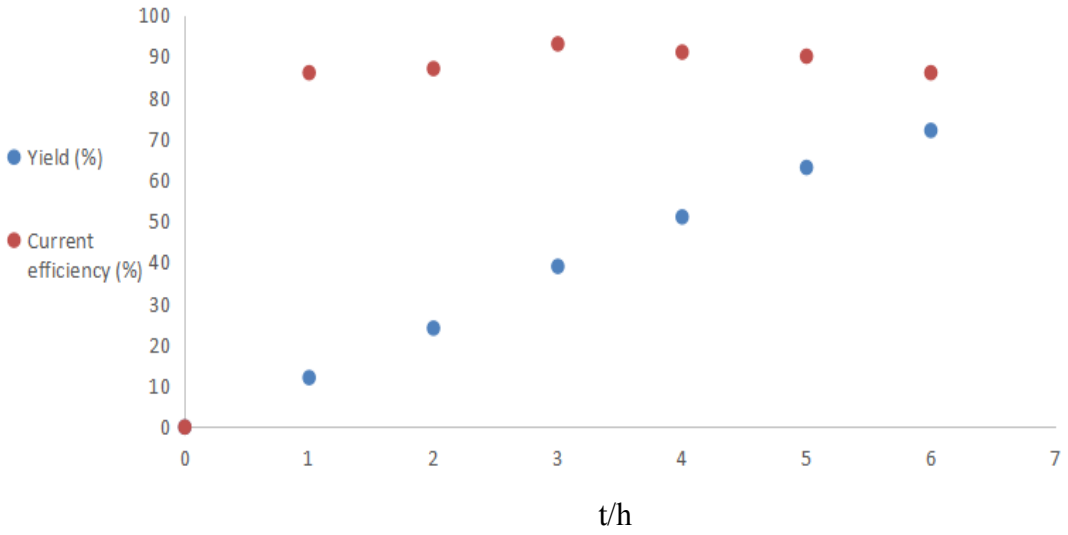
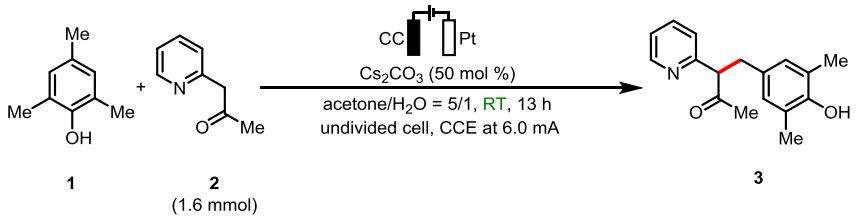


Figure S16. Conversion determined by ^{1}**H-NMR** analysis using 1,3,5-trimethoxy benzene as the internal standard.

Recycle and reuse the base:



Procedure: After the reaction (1.6 mmol scale) completed, the mixture was evaporated in vacuo for removing acetone, subsequently extracted with DCM (3× 5 mL). The aqueous phase was transferred into an undivided cell again and reused for the next reaction. This procedure was repeated three times.

Run	1st	2nd	3rd	4th
Yield of **3** (%)	78%	72%	66%	53%

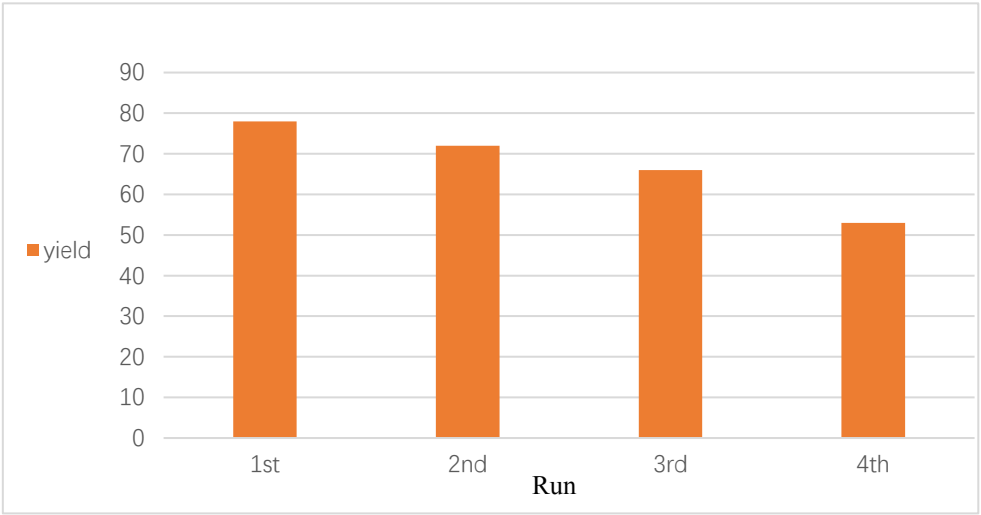


Figure S17. Yield of **3**.

References

[1] M. Uyanik, K. Nishioka, R. Kondo, K. Ishihara, *Nat. Chem.*, **2020**, *12*, 353–362.

[2] R. Kshatriya, D. Kambale, S. Mali, V. P. Jejurkar, P. Lokhande, H. K. Chaudhari, S. Saha, *ChemistrySelect*. **2019**, *4*, 7943–7948.

[3] Z. Wu, T. Li, Y. Ding, A. Hu, *ACS Appl. Polym. Mater*. **2020**, *2, 5414–5422*.

[4] R. J. Armstrong, M. D. Smith, *Angew. Chem. Int., Ed.*, **2014**, *53*, 12822–12826.

[5] J. Cao, D. Lv, F. Yu, M.-F. Chiou, Y. Li, H. Bao, *Org. Lett.*, **2021**, *23*, 3184–3189.

[6] J.-A. Jiang, C. Chen, J.-G. Huang, H.-W. Liu, S. Cao, Y.-F. Ji, *Green Chem.*, **2014**, *16*, 1248–1254.