

# Supporting Information

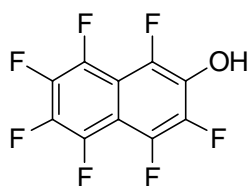
## Flow electrosynthesis for efficient *O*-trifluoromethylation of electron-deficient phenols

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## Synthesis of 1,3,4,5,6,7,8-Heptafluoro-naphthalen-2-ol **1b**



**1b** was prepared based on literature protocol [1]. Octafluoronaphthalene (0.5 g, 1.83 mmol) and KOH (0.24 g, 4.28 mmol) were dissolved in *tert*-butyl alcohol (5 mL) and heated to reflux for 3.5 h followed by evaporation of the solvent under reduced pressure. The residue was acidified with concentrated HCl and extracted with DCM (4 x 20 mL). The combined organic layers were washed with H<sub>2</sub>O and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent gave the desired phenol **1b** as slightly yellow solid. The product was used without further purification.

Yield: 0.49 g (99%).

<sup>13</sup>C{<sup>19</sup>F} NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  = 141.40 (s), 140.70 (s), 140.48 (s), 140.34 (s), 138.96 (s), 137.86 (s), 134.06 (s), 128.98 (s), 107.70 (s), 104.88 (s) ppm.

<sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>):  $\delta$  = -146.74 to -147.01 (m, 1 F, Ar-F), -148.02 to -148.35 (m, 3 F, Ar-F), -153.52 to -153.62 (m, 1H, Ar-F), -156.52 to -156.65 (m, 1 F, Ar-F), -158.50 to -158.60 (m, 1 F, Ar-F) ppm.

GC-MS (EI, 70 eV): *m/z* [M]<sup>+</sup> calc.: 270.0, found: 270.2.

The NMR and mass spectroscopy data are in accordance with literature data [**Fehler! Textmarke nicht definiert.**].

## Screening Experiments

### Current density

Table S1: Results of the screening experiments to determine the optimal current density for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S1): 0.05 mol/l **1a**, 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 ml MeCN/H<sub>2</sub>O 4:1, Q = 2.0 F/mol, electrode configuration: graphite||graphite (1 mm distance), single cell pass reaction.

Current density / mA/cm <sup>2</sup>	Flow rate / ml/min	Reaction time / min	Yield / %
2.5	0.187	134	26
5	0.373	67	31
10	0.746	34	26
15	1.119	22	-

### Total charge amount

Table S2: Results of the screening experiments to determine the optimal charge amount for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S2): 0.05 mol/l **1a**, 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 ml MeCN/H<sub>2</sub>O 4:1, j = 5 mA/cm<sup>2</sup>, electrode configuration: graphite||graphite (1 mm distance), single cell pass reaction.

Charge / F/mol	Flow rate / ml/min	Reaction time / min	Yield / %
1.0	0.746	34	12
2.0	0.373	67	31
3.0	0.249	101	33
4.0	0.187	134	41
5.0	0.149	168	47
6.0	0.124	201	57
8.0	0.093	268	40

### Number of cell passes

Table S3: Results of the screening experiments to determine the optimal number of cell passes for a total charge amount of 6 as well as 8 F/mol for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S3): 0.05 mol/l **1a**, 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 ml MeCN/H<sub>2</sub>O 4:1, j = 5 mA/cm<sup>2</sup>, electrode configuration: graphite||graphite (1 mm distance).

Total charge / F/mol	Cascades	Q/cascade / F/mol	Flow rate / ml/min	Yield / %
6	1	6	0.124	57
	2	3	0.249	62
	3	2	0.373	58
8	1	8	0.093	40
	2	4	0.187	75
	3	2.67	0.280	57

### Electrode distance

Table S4: Results of the screening experiments to determine the optimal electrode distance for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S4): 0.05 mol/l **1a**, 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 ml MeCN/H<sub>2</sub>O 4:1,  $j = 5$  mA/cm<sup>2</sup>,  $Q = 8.0$  F/mol, electrode configuration: graphite||graphite, double cell pass reaction.

Electrode distance / mm	Flow rate / ml/min	Reaction time / min	Yield / %
1	0.187	268	75
0.5	0.187	268	90

### Concentration of supporting electrolyte

Table S5: Results of the screening experiments to determine the optimal concentration of supporting electrolyte NaClO<sub>4</sub> for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S5): 0.05 mol/l **1a**, 0.2 mol/l **2** in 25 ml MeCN/H<sub>2</sub>O 4:1,  $j = 5$  mA/cm<sup>2</sup>,  $Q = 8.0$  F/mol, electrode configuration: graphite||graphite (0.5 mm distance), double cell pass reaction.

c(electrolyte) / mol/l	Flow rate / ml/min	Reaction time / min	Yield / %
0	0.187	268	58
0.05	0.187	268	68
0.1	0.187	268	67
0.2	0.187	268	90
0.3	0.187	268	83

### Concentration of starting materials **1a/2**

Table S6: Results of the screening experiments to determine the optimal concentration of starting material for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S6): 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 ml MeCN/H<sub>2</sub>O 4:1,  $j = 5$  mA/cm<sup>2</sup>,  $Q = 8.0$  F/mol, electrode configuration: graphite||graphite (0.5 mm distance), double cell pass reaction.

c(phenol <b>1a</b> / <b>2</b> ) / mol/l	Flow rate / ml/min	Reaction time / min	Yield / %
0.05 / 0.2	0.187	268	90
0.1 / 0.4	0.094	536	77

## Electrode configuration

Table S7: Results of the screening experiments to determine the optimal electrode materials for the electrochemical *O*-trifluoromethylation of pentafluorophenol **1a**. Reaction conditions (constant for all experiments in Table S6): 0.05 mol/l **1a**, 0.2 mol/l **2**, 0.2 mol/l NaClO<sub>4</sub> in 25 mL MeCN/H<sub>2</sub>O 4:1, *j* = 5 mA/cm<sup>2</sup>, *Q* = 8.0 F/mol, electrode distance: 0.5 mm, double cell pass reaction.

Electrodes	Flow rate / ml/min	Reaction time / min	Yield / %
Graphite    graphite	0.187	268	90
Graphite    stainless steel	0.187	268	90
Glassy carbon    stainless steel	0.187	268	85
BDD    stainless steel	0.187	268	-

## Mechanistic Investigations

It was found that for the reaction to proceed well, the oxidation potentials of the respective phenols has to be close to the one of the Langlois reagent [2]. E.g., pentachlorophenol (1.00 V) and pentafluorophenol (1.07 V) show a good overlap with the oxidation signal of the Langlois reagent (1.33 V, see Figure S1 a)), whereby pentafluorophenol exhibits a slightly higher oxidation potential and leads to better yields of the corresponding trifluoromethyl ether. In contrast, the oxidation potential of pentakis(trifluoromethyl)phenol is much higher (1.50 V) and therefore shows almost no overlap with the oxidation signal of NaSO<sub>2</sub>CF<sub>3</sub>, resulting in no formation of the trifluoromethyl ether. Based on these results, we have proposed a mechanism in which the corresponding phenol and NaSO<sub>2</sub>CF<sub>3</sub> are oxidized simultaneously at the anode, leading to a co-evolution of phenoxy radicals and CF<sub>3</sub> radicals, which recombine to the desired trifluoromethyl ether. For the cathode reaction, the formation of molecular hydrogen by reduction of protons is suggested, in accordance with previous reports [3,4].

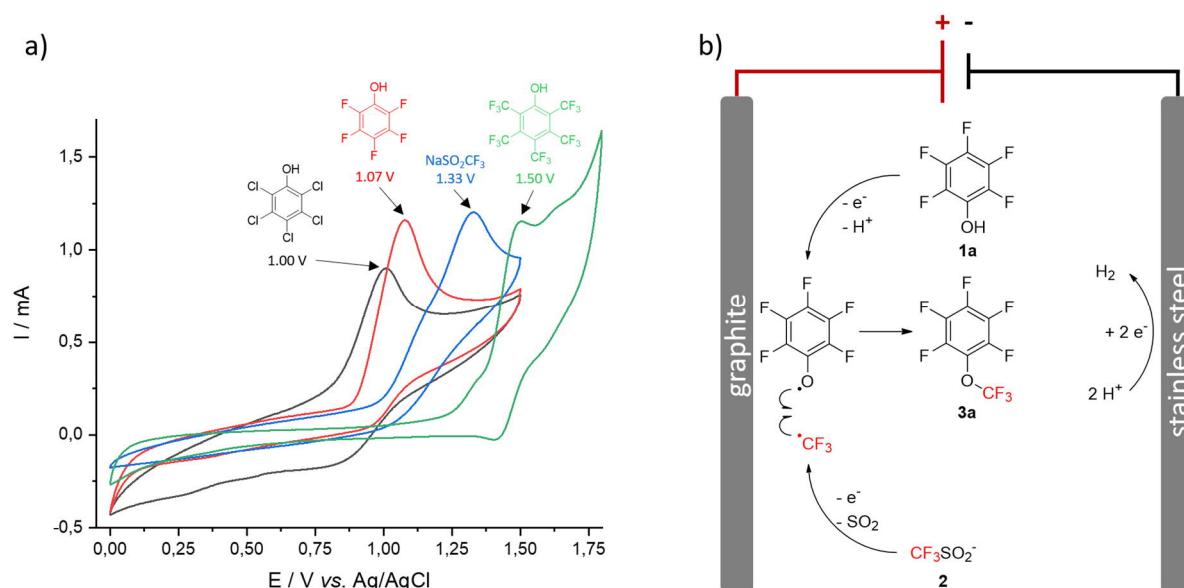
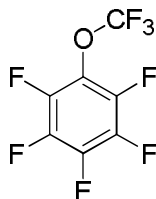


Figure S1: a) Cyclic voltammograms of different electron-poor phenols and the Langlois reagent. b) Proposed mechanism: co-evolution of phenoxy radicals and CF<sub>3</sub> radicals, followed by a radical recombination, resulting in the desired trifluoromethyl ether.

## Synthesis of Aryl trifluoromethyl ethers 3a-e

### Octafluoroanisole 3a



According to the general procedure, 230 mg **1a** (1.25 mmol) were employed. Due to high volatility of product **3a**, complete removal of the solvent was not possible. The yield was determined by  $^{19}\text{F}$  NMR spectroscopy using fluorobenzene as internal standard. Recording of  $^{13}\text{C}$  NMR spectra was not possible due low concentration of **3a** in solution.

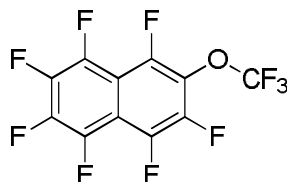
Yield: 90%.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -60.06$  (t,  $J = 7.0$  Hz, Ar- $\text{OCF}_3$ ),  $-151.37$  to  $-151.52$  (m, 2 F, Ar-F),  $-154.35$  (t,  $J = 21.5$  Hz, 1 F, Ar-F),  $-160.58$  to  $-160.79$  (m, 2 F, Ar-F) ppm.

GC-MS (EI, 70 eV):  $m/z$   $[\text{M}]^+$  calc.: 252.0 found: 252.2.

The NMR and mass spectroscopy data are in accordance with literature data [2].

### 1,2,3,4,5,6,8-Heptafluoro-7-(trifluoromethoxy)naphthalene 3b



The synthesis of **3e** was performed as stated in the general procedure with 340 mg of **1b** (1.25 mmol). The crude product was purified by column chromatography (eluent: dichloromethane). **3b** was obtained as a slightly yellow solid.

Yield: 73% (0.31 g).

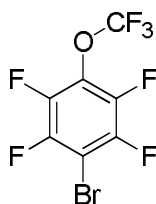
$^{13}\text{C}\{^{19}\text{F}\}$  NMR (126 MHz,  $\text{CDCl}_3$ ):  $\delta = 142.27, 141.71, 141.39, 141.22, 140.33, 139.39, 138.71, 116.48, 110.22, 107.40$  ppm.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -59.52$  (t,  $J = 7.5$  Hz, Ar- $\text{OCF}_3$ ),  $-132.51$  to  $-132.88$  (m, 1 F, Ar-F),  $-143.38$  to  $-143.58$  (m, 1 F, Ar-F),  $-144.83$  to  $-145.28$  (m, 2 F, Ar-F),  $-146.89$  to  $-147.02$  (m, 1 F, Ar-F),  $-151.36$  to  $-151.48$  (m, 1 F, Ar-F),  $-153.37$  to  $-153.52$  (m, 1 F, Ar-F) ppm.

GC-MS (EI, 70 eV):  $m/z$   $[\text{M}]^+$  calc.: 338.0 found: 338.3.

The NMR and mass spectroscopy data are in accordance with literature data [2].

### 1-Bromo-2,3,5,6-tetrafluoro-4-(trifluoromethoxy)benzene **3c**



**3c** was prepared in agreement with the general procedure with 310 mg **1c** (1.25 mmol). Due to high volatility of product **3c**, complete removal of the solvent was not possible. The yield was determined by  $^{19}\text{F}$  NMR spectroscopy using fluorobenzene as internal standard. Recording of  $^{13}\text{C}$  NMR spectra was not possible due to low concentration of **3c** in solution.

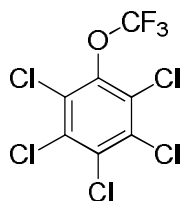
Yield: 79%.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -59.70$  (t,  $J = 7.3$  Hz, Ar- $\text{OCF}_3$ ),  $-131.18$  to  $-131.28$  (m, 2 F, Ar-F),  $-150.32$  to  $-150.47$  (m, 2 F, Ar-F) ppm.

GC-MS (EI, 70 eV):  $m/z$   $[\text{M}]^+$  calc.: 311.9 found: 312.3.

The NMR and mass spectroscopy data are in accordance with literature data [2].

### 1,2,3,4,5-Pentachloro-6-(trifluoromethoxy)benzene **3d**



In accordance with the general procedure, 330 mg **1d** (1.25 mmol) were employed. The crude product was purified by column chromatography (eluent: dichloromethane). **3d** was obtained as a slightly yellow solid.

Yield: 54% (0.23 g).

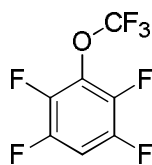
$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ ):  $\delta = 142.24$  (q,  $^3J_{\text{CF}} = 2.2$  Hz), 133.26, 132.63, 129.22, 120.54 (q,  $^1J_{\text{CF}} = 265.0$  Hz,  $\text{OCF}_3$ ) ppm.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -55.56$  (s, 3 F, Ar- $\text{OCF}_3$ ) ppm.

GC-MS (EI, 70 eV):  $m/z$   $[\text{M}]^+$  calc.: 331.8 found: 332.2.

The NMR and mass spectroscopy data are in accordance with literature data [2].

### 1,2,4,5-Tetrafluoro-3-(trifluoromethoxy)benzene **3e**



According to the general procedure, 210 mg **1e** (1.25 mmol) were employed. Due to high volatility of product **3e**, complete removal of the solvent was not possible. The yield was determined by  $^{19}\text{F}$  NMR spectroscopy using fluorobenzene as internal standard. Recording of  $^{13}\text{C}$  NMR spectra was not possible due to low concentration of **3e** in solution.

Yield: 67%.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.12$  (tt,  $J = 9.7$  Hz, 7.0 Hz, 1 H) ppm.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -60.51$  (t,  $J = 7.1$  Hz, Ar-OCF<sub>3</sub>), -138.25 to -138.35 (m, 2 F, Ar-F), -155.93 to -156.04 (m, 2 F, Ar-F) ppm.

GC-MS (EI, 70 eV):  $m/z$  [M]<sup>+</sup> calc.: 234.0 found: 234.2.

The NMR and mass spectroscopy data are in accordance with literature data [2].



## References

- [1] M. Karsch, H. Lund, A. Schulz, A. Villinger, K. Voss, Molecular networks based on CN coordination bonds, *Eur. J. Inorg. Chem.* 33 (2012) 5542-5553.
- [2] J. Bernd, P. Werner, M. Zeplichal, A. Terfort, Electrochemical *O*-trifluoromethylation of electron-deficient phenols, *Electrochem. Commun.* 133 (2021) 107165.
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- [4] Y. Deng, F. Lu, S. You, T. Xia, Y. Zheng, C. Lu, G. Yang, Z. Chen, M. Gao, A. Lei, External-oxidant-free electrochemical oxidative trifluoromethylation of arenes using  $\text{CF}_3\text{SO}_2\text{Na}$  as the  $\text{CF}_3$  source, *Chin. J. Chem.* 37 (2019) 817-820.