Efficient Copper Catalyzed Trifluoromethylation of Aromatic and Heteroaromatic Iodides: The Beneficial Anchoring Effect of Borates

Zsombor Gonda, Szabolcs Kovács, Csaba Wéber, Tamás Gáti, Attila Mészáros, András Kotschy, Zoltán Novák

Supporting Information
# Table of contents

General .................................................................................................................................................... 3

Experimental Section ................................................................................................................................ 4

   Examination of different catalysts in copper catalyzed trifluoromethylation ........................................ 4

   Determination of water effect on the coupling .......................................................................................... 5

   Examination of potassium (trifluoromethyl)metoxyborates storage-stability ........................................ 6

   Study of catalyst loading for the coupling of 1-iodonaphthalene ........................................................... 7

   Study of ligand effect .................................................................................................................................. 8

   Study of stoichiometry effect on the coupling ........................................................................................... 9

   Temperature effect ..................................................................................................................................... 10

   Study of fluoride source effect .................................................................................................................. 11

   Solvent effect .............................................................................................................................................. 13

Preparation of aryl iodide substrates ........................................................................................................ 14

Study of functional group tolerance of copper catalyzed trifluoromethylation ......................................... 18

General procedure for the preparation of the trifluoromethylated compounds ........................................ 24

References ................................................................................................................................................. 36
General

Unless otherwise indicated, all starting materials were obtained from commercial suppliers, and were used without further purification. Anhydrous DMSO ≥99.9% was used for the couplings, as it was purchased.

Analytical thin-layer chromatography (TLC) was performed on Merck DC pre coated TLC plates with 0.25 mm Kieselgel 60 F_{254}. Visualization was performed with a 254 nm UV lamp. The $^1$H, $^{13}$C and $^{19}$F NMR spectra were recorded on a Bruker Avance-250 spectrometer and in CDCl$_3$ and DMSO-$d_6$. Chemical shifts are expressed in parts per million (δ) using residual solvent protons as internal standards (δ 7.26 for $^1$H, δ 77.0 for $^{13}$C). Coupling constants (J) are reported in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), m (multiplet). Combination gas chromatography and low resolution mass spectrometry was obtained on an Agilent 6890N Gas Chromatograph (30 m x 0.25 mm column with 0.25 µm HP-5MS coating, He carrier gas) and Agilent 5973 Mass Spectrometer (Ion source: EI+, 70eV, 230°C; interface: 300°C). IR spectra were obtained on a Bruker IFS55 spectrometer on a single-reflection diamond ATR unit. All melting points were measured on Büchi 501 apparatus and are uncorrected. High-resolution mass spectra were acquired on an Agilent 6230 time-of-flight mass spectrometer equipped with a Jet Stream electrospray ion source in positive ion mode. Injections of 0.1-0.3 µl were directed to the mass spectrometer at a flow rate 0.5 ml/min (70% acetonitrile-water mixture, 0.1 % formic acid), using an Agilent 1260 Infinity HPLC system. Jet Stream parameters: drying gas (N$_2$) flow and temperature: 10.0 l/min and 325 °C, respectively; nebulizer gas (N$_2$) pressure: 10 psi; capillary voltage: 4000V; sheath gas flow and temperature: 325 °C and 7.5 l/min; TOFMS parameters: fragmentor voltage: 120 V; skimmer potential: 120V; OCT 1 RF Vpp:750 V. Full-scan mass spectra were acquired over the m/z range 100-2500 at an acquisition rate of 250 ms/spectrum and processed by Agilent MassHunter B.03.01 software.
Experimental Section

For the optimization studies we monitored the reactions with GC-MS analysis of samples taken from the reaction mixture at the given reaction time. In the absence of any major side-products the conversions were determined on the basis of the areas of the starting aryl iodide and the product obtained in the GC chromatogram. The conversion was calculated with the following formula: \[ \text{conv \%} = \left( \frac{\text{Area of product}}{\text{Area of product} + \text{Area of Aryl iodide}} \right) \times 100 \]

Examination of different catalysts in copper catalyzed trifluoromethylation

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) catalyst (0.07 mmol), ligand (0.07 mmol), CF$_3$B(OMe)$_3$K (222 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51µL, 0.35 mmol, 1 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 60 °C. The samples were taken after 2, 4, 6, 8 and 20 h, dissolved in Et$_2$O and analyzed by GC-MS.
Determination of water effect on the coupling.

Table 1. Samples were taken after 16 hours to check the sensitivity of the reaction to the manipulation during the sampling.
Examination of potassium (trifluoromethyl)metoxyborates storage-stability

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), CF$_3$B(OMe)$_3$K (222 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, then evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51$\mu$L, 0.35 mmol, 1 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 4 h at 60 °C. The samples were taken after 0, 2, 4 h, dissolved in Et$_2$O and analyzed by GC-MS. This reaction was taken after CF$_3$B(OMe)$_3$K salt isolation 6, 20 and 27 days.

Figure 2.
Study of catalyst loading for the coupling of 1-iodonaphthalene

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (0.0175-0.14 mmol), 1,10-phenanthroline (0.0175-0.14 mmol), KF (61 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51 µL, 0.35 mmol, 1 eq.), B(OMe)$_3$ (109 mg, 117 µL, 1.05 mmol, 3 eq.), TMSCF$_3$ (149.3 mg, 155 µL, 1.05 mmol, 3 eq.) were added via syringe. Solid aryl iodides were weighed directly in the reaction vessel. The resulting orange-brown suspension was stirred for 24 h at 60 °C. The samples were taken after 2, 4 and 24 h dissolved in Et$_2$O and analyzed by GC-MS.

![Conversion vs Time Graph](image)

*Figure 3.*
An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), ligand (0.07 mmol), KF (61 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, then evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51µL, 0.35 mmol, 1 eq.), B(OMe)$_3$ (109 mg, 117µL, 1.05 mmol, 3 eq.), TMSCF$_3$ (149.3 mg, 155 µL, 1.05 mmol, 3 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 60 °C. The samples were taken after 2, 4, 6 and 8 h, dissolved in Et$_2$O and analyzed by GC-MS.

![Conversion vs Time Graph](image)

**Figure 4.**
Study of stoichiometry effect on the coupling

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), KF (20.3-61 mg, 0.35-1.05 mmol 1-3 eq.). The reaction vessel was closed, then evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51 µL, 0.35 mmol, 1 eq.), B(OMe)$_3$ (0-1.05 mmol, 0-3 eq.), TMSCF$_3$ (0.35-1.05 mmol, 1-3 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 60 °C. The samples were taken after 2, 4, 6, 8 and 24 h, dissolved in Et$_2$O and analyzed by GC-MS.

![Figure 5.](image-url)
Temperature effect

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), KF (61 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51\(\mu\)L, 0.35 mmol, 1 eq.), B(OMe)\(_3\) (109 mg, 117\(\mu\)L, 1.05 mmol, 3 eq.), TMSCF\(_3\) (149.3 mg, 155 \(\mu\)L, 1.05 mmol, 3 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 30, 40, 50 and 60 °C. The samples were taken after 2, 4, 6 and 8 h, dissolved in Et\(_2\)O and analyzed by GC-MS.

![Figure 6.](image)

<table>
<thead>
<tr>
<th>B(OR)(_3)</th>
<th>(T)</th>
<th>Time</th>
<th>Conversion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>R=Me, 1eq.</td>
<td>60 °C</td>
<td>18h</td>
<td>70</td>
</tr>
<tr>
<td>R=Me, 3eq.</td>
<td>60 °C</td>
<td>18h</td>
<td>94</td>
</tr>
<tr>
<td>R=Me, 3eq.</td>
<td>50 °C</td>
<td>18h</td>
<td>97</td>
</tr>
<tr>
<td>R=Et, 3eq.</td>
<td>60 °C</td>
<td>18h</td>
<td>95</td>
</tr>
<tr>
<td>R=Et, 3eq.</td>
<td>50 °C</td>
<td>18h</td>
<td>91</td>
</tr>
</tbody>
</table>

Table 2. Determination of temperature effect on the coupling with different borates. (Samples were taken after 18 hours to check the sensitivity of the reaction to the manipulation during the sampling).
Study of fluoride source effect

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), fluoride (1.05 mmol 3 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the 1-iodonaphtalene (88.9 mg, 51 µL, 0.35 mmol, 1 eq.), $\text{B(OMe)}_3$ (109 mg, 117 µL, 1.05 mmol, 3 eq.), TMSCF₃ (149.3 mg, 155 µL, 1.05 mmol, 3 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 60 °C. The samples were taken after 2, 4, 6 and 8 h, dissolved in Et₂O and analyzed by GC-MS.

![Figure 7](image-url)
Figure 8.
Solvent effect

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), KF (61 mg, 1.05 mmol 3 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. Solvent (1.0 mL) and the 1-iodonaphthalene (88.9 mg, 51 µL, 0.35 mmol, 1 eq.), B(OMe)₃ (109 mg, 117 µL, 1.05 mmol, 3 eq.), TMSCF₃ (149.3 mg, 155 µL, 1.05 mmol, 3 eq.) were added via syringe. The resulting orange-brown suspension was stirred for 20 h at 30, 40, 50 and 60 °C. The samples were taken after 2 h, dissolved in Et₂O and analyzed by GC-MS.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conversion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>anh. t-BuOH</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>anh toluene</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>anh. MeCN</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>anh dioxane</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>DMA</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>NMP</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>DMF</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>DMF-DMSO 99:1</td>
<td>29</td>
</tr>
<tr>
<td>9</td>
<td>DMF-DMSO 9:1</td>
<td>37</td>
</tr>
<tr>
<td>10</td>
<td>DMF-DMSO 1:1</td>
<td>77</td>
</tr>
<tr>
<td>11</td>
<td>sulpholane</td>
<td>41</td>
</tr>
<tr>
<td>12</td>
<td>anh. DMSO</td>
<td>89</td>
</tr>
<tr>
<td>13</td>
<td>DMSO</td>
<td>8</td>
</tr>
</tbody>
</table>

*Table 3. Copper catalyzed couplings in different solvents.*
Preparation of aryl iodide substrates

Aryl iodides as starting materials which are commercially available were purchased from commercial sources. Hydroxy and amino groups and N-heterocycles were protected according to the literature procedures (benzylation of indole derivatives (1r, 1t), THP protection of 4-iodophenol (1a), dibenzylolation of 4-iodoaniline (1b), trifluoroacetylation of 4-iodoaniline (1c), benzylation of 9-benzyl-3-iodo-9H-carbazole (1x). The properties of the prepared compounds (1H and 13C NMR, MS) are in fully agreement with the described literature data.

![Chemical Structure](attachment:image.png)

1-(4-iodobenzyl)-4-phenyl-1H-1,2,3-triazole

In a 4 mL screw capped vial the terminal acetylene (0.5 mmol) and the azide (0.5 mmol) was measured. 10.00 mL DCM solution of the catalyst was prepared, dissolving 33.8 mg (0.05mmol) of \( \text{C}_3\text{H}_7\text{COOCu(PPPh}_3)_2 \) in the solvent. For the reactions usually 50 µL of the catalyst solution was used, and the total volume of the solvent was 300 µL. The reaction was stirred at room temperature (28 °C) for the indicated time. Then the solvent was evaporated affording the crude product. The products usually proved to be pure enough, but further purifications such as recrystallization of the solid from toluene.

White crystals. Yield: 153 mg (0.425 mmol), 85%. Mp.154-156 °C. \(^1\)H NMR (250 MHz, DMSO): \( \delta = 8.63 \) (s, 1H), 7.86 (d, 2 H, \( J = 7.5 \) Hz), 7.77 (d, 2 H, \( J = 8.25 \) Hz), 7.43 (t, 2 H, \( J = 7.25 \) Hz); 7.37 (d, 1 H, \( J = 7.25 \) Hz), 7.17 (d, 2 H, \( J = 8.25 \) Hz), 5.62 (s, 2H) ppm. \(^13\)C NMR (62.5 MHz, DMSO): \( \delta = 146.6, 137.5, 135.7, 130.5; 130.1; 128.8; 127.9; 125.1; 121.5; 94.4; 52.4 \) ppm. IR (ATR): 3082, 2922, 1483, 1442, 1404, 1221, 1077, 1049, 1007 cm\(^{-1}\). MS (EI, 70 eV): \( m/z \) (%): 361(8, \([M^+]\)), 332 (10), 230 (8), 217 (30), 206 (25), 116 (100), 89 (70). HRMS caleld for \( \text{C}_{15}\text{H}_{13}\text{IN}_3 [M + H]^+ \) 362.0149; found 362.0144.
Methyl 2-iodoisonicotinate (1f)

To a stirred solution, of 2-iodoisonicotinic acid (2 mmol, 1 equiv) in MeOH (4 ml) was added cc. H$_2$SO$_4$ (50 µL). The mixture was refluxed for 16 h. The reaction mixture was diluted with EtOAc (30 mL) and was extracted with saturated NaHCO$_3$ solution (15 mL). The organic phase was washed with brine (15 mL), and dried over anhydrous MgSO$_4$. The solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc, 8:2).

Yellow oil 465 mg (1.77 mmol, yield: 88%). R$_f$: 0.50 (in hexane:EtOAc 8:2), Mp.: 46-48 °C, $^1$H NMR (500 MHz, DMSO) δ 8.58 (dd, $J$ = 5.0, 0.7 Hz, 1H), 8.17 (dd, $J$ = 1.5, 0.8 Hz, 1H), 7.84 (dd, $J$ = 5.0, 1.5 Hz, 1H), 3.89 (s, 3H). $^{13}$C NMR (126 MHz, DMSO) δ 164.19, 152.73, 138.93, 133.63, 122.61, 119.70, 53.51 ppm. IR (ATR) ν$_{max}$ 2953, 1727, 1541, 1434, 1352, 1288, 1258, 1131, 960, 757, 754 cm$^{-1}$. MS (EI, 70 eV): m/z (%): 263 (100, [M$^+$]), 232 (26), 204 (28), 177 (25), 136 (62), 127 (28), 108 (12). HRMS calcd for C$_7$H$_7$INO$_2$ [M+H$^+$] 263.9521 found 263.9516.

General procedure for the benzylation of aril-iodides

To a stirred solution, of aril-iodide (4 mmol, 1 equiv) in DMSO (40 ml) was added KOH (18.4 mmol, 4.6 equiv). The mixture was stirred for 30 min at RT. During this time the color changed from yellow to brown. After, BnBr (4.8 mmol, 1.2 equiv) was added. The reaction mixture was stirred for 2 h and H$_2$O was added. The aqueous phase was extracted with Et$_2$O. The organic phase was washed with brine, and dried over anhydrous MgSO$_4$. The solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexane/EtOAc, 8:2).

3-(Benzyloxy)-2-chloro-6-iodopyridine (1g)

This compound was prepared following the general procedure. Yellow solid 686 mg (1.98 mmol, yield: 99%). R$_f$: 0.49 (in hexane:EtOAc, 8:2) Mp.: 85-86 °C, $^1$H NMR (500 MHz, DMSO) δ 7.80 (d, $J$ = 8.4 Hz, 1H), 7.47 – 7.39 (m, 5H), 7.37 – 7.33 (m, 1H), 5.26 (s, 2H). $^{13}$C NMR (126 MHz, DMSO) δ 150.74, 138.94, 135.64, 134.56, 128.62, 128.28, 127.71, 124.61, 103.05, 70.48 ppm. IR (ATR) ν$_{max}$ 3053, 1423, 1353, 1277, 1073, 997, 823, 717, 690, 462 cm$^{-1}$. MS (EI, 70 eV): m/z (%): 436 (26, [M$^+$]),
1-Benzyl-4-iodo-3,5-diphenylpirazole (1k)

This compound was prepared following the general procedure. White solid, 335 mg (0.77 mmol, yield: 77%). Rf.: 0.56 (in hexane/EtOAc, 8:2) Mp.: 121-122 °C ¹H NMR (500 MHz, DMSO) δ 7.85 – 7.81 (m, 2H), 7.57 – 7.45 (m, 5H), 7.44 – 7.37 (m, 3H), 7.29 – 7.21 (m, 3H), 7.01 – 6.95 (m, 2H), 5.32 (s, 2H) ¹³C NMR (126 MHz, DMSO) δ 150.61, 146.54, 136.95, 132.90, 130.16, 129.57, 129.47, 128.80, 128.55, 128.34, 128.16, 127.86, 127.56, 126.92, 62.10, 53.79 ppm. IR (ATR) νmax 2930, 1451, 1304, 765, 729, 695 cm⁻¹. MS (EI, 70 eV): m/z (%): 436 (39, [M⁺]), 359 (14), 307 (8), 189 (85), 91 (100), 65 (17). HRMS calcd for C₂₂H₁₇IN₂ [M+H]⁺ 437.0515 found 437.0511.

1-Benzyl-3-iodo-5-methoxy-1H-indole (1t)

This compound was prepared following the general procedure. White solid 352 mg (0.97 mmol, yield: 75%). Rf.: 0.61 (in hexane/EtOAc, 8:2) M.p. at 98-99 °C decomposed, ¹H NMR (500 MHz, DMSO) δ 7.69 (s, 1H), 7.40 (d, J = 8.9 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.26 – 7.17 (m, 3H), 6.81 (dd, J = 8.9, 2.4 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 5.39 (s, 2H), 3.78 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 154.9, 138.4, 133.7, 131.4, 131.0, 129.1, 127.9, 127.6, 113.2, 112.2, 102.1, 55.8, 55.5, 49.9. ppm. IR (ATR) νmax 1617, 1487, 1443, 1357, 1288, 1219, 1175, 1028, 847, 823, 789, 743, 706, 622 cm⁻¹. MS (EI, 70 eV): m/z (%): 363 (45, [M⁺]), 272 (7), 236 (10), 193 (8), 91 (100), 65 (8).
1-Benzyl-4-iodo-1H-indazole (1v)

This compound was prepared following the general procedure. Yellow oil 339 mg (1.02 mmol, yield: 51%). R<sub>f</sub>: 0.59 (in hexane/EtOAc, 8:2), Mp.: 57-58 °C, <sup>1</sup>H NMR (500 MHz, DMSO) δ 7.91 (d, J = 0.9 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.56 (dd, J = 7.2, 0.5 Hz, 1H), 7.32-7.28 (m, 2H), 7.27-7.24 (m, 1H), 7.22-7.20(m, 1H), 7.17 (dd, J = 8.4, 7.2 Hz, 1H), 5.66 (s, 2H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 138.95, 137.19, 135.53, 129.87, 128.59, 128.02, 127.75, 127.63, 127.38, 110.06, 86.64, 52.27 ppm. IR (ATR) ν<sub>max</sub> 3030, 2931, 1372, 1258, 1160, 934, 777, 720, 694, 601 cm<sup>-1</sup>. MS (EI, 70 eV): m/z (%) : 334 (100, [M<sup>+</sup>]), 257 (13), 207 (24), 178 (12), 91 (100), 65 (21). HRMS calcd for C<sub>14</sub>H<sub>12</sub>IN<sub>2</sub>[M+H]<sup>+</sup> 335.0045 found 335.0040.
Study of functional group tolerance of copper catalyzed trifluoromethylation

The goal of this study was the exploration of the functional group tolerance. The reactions were monitored with GC-MS analysis of samples taken from the reaction mixture at the given reaction time. The conversions were determined on the basis of the areas of the starting aryl iodide and the product obtained in the GC chromatogram. The conversion was calculated with the following formula: conv \% = \frac{\text{Area of product}}{\text{Area of product} + \text{Area of Aryl iodide}} \times 100

Procedure: An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (13.3 mg, 0.07 mmol), 1,10-phenanthroline (12.6 mg, 0.07 mmol), KF (61 mg, 1.05 mmol 3 eq.) and the aryl iodide (0.35 mmol, 1 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (1.0 mL) and the aryl iodide (0.35 mmol) (if it isn’t solid), B(OMe)\textsubscript{3} (109 mg, 117 \mu L, 1.05 mmol, 3 eq.), TMSCF\textsubscript{3} (149.3 mg, 155 \mu L, 1.05 mmol, 3 eq.) were added via syringe. Solid aryl iodides were weighed directly in the reaction vessel. The resulting orange-brown suspension was stirred for 24 h at 60 °C. The sample was dissolved in Et\textsubscript{2}O and analyzed by GC-MS.
Conditions: CuI (0.07 mmol), 1,10-phenanthroline (0.07 mmol), KF (1.05 mmol), aryl iodide (0.35 mmol). DMSO (anh, 1.0 mL), B(OMe)$_3$ (1.05 mmol), TMSCF$_3$ (1.05 mmol, 3 eq.), 60 °C, % GC yield.
1-(trifluoromethyl)naphthalene\(^7\)

MS (EI, 70 eV): \(m/z\) (%): 196 (100, [M\(^+\)]), 177 (20), 146 (50), 126 (10), 75 (10).

1,3-dimethyl-2-(trifluoromethyl)benzene\(^8\)

MS (EI, 70 eV): \(m/z\) (%): 174 (55, [M\(^+\)]), 159 (50), 155 (15), 105 (100), 77 (15).

1-isopropyl-2-(trifluoromethyl)benzene\(^9\)

MS (EI, 70 eV): \(m/z\) (%): 188 (40, [M\(^+\)]), 173 (80), 153 (65), 133 (100), 127 (15), 77 (10).

1-methoxy-4-(trifluoromethyl)benzene\(^10\)

MS (EI, 70 eV): \(m/z\) (%): 176 (100, [M\(^+\)]), 157 (45), 145 (45), 133 (50), 127 (20), 113 (30), 107 (10), 96 (20), 76 (10).
1-nitro-4-(trifluoromethyl)benzene\textsuperscript{11}

MS (EI, 70 eV): \( m/z \) (%): 191 (40, \([M^+])\), 172 (10), 145 (100), 125 (20), 95 (20), 75 (20).

3-(trifluoromethyl)benzonitrile\textsuperscript{12}

MS (EI, 70 eV): \( m/z \) (%): 171 (100, \([M^+])\), 152 (60), 145 (5), 121 (55), 102 (15), 75 (20), 69 (10).

1-chloro-2,4-bis(trifluoromethyl)benzene\textsuperscript{13}

MS (EI, 70 eV): \( m/z \) (%): 248 (100, \([M^+])\), 229 (60), 213 (30), 198 (30), 194 (15), 179 (30), 163 (25), 143 (20), 125 (15), 75 (20), 69 (20).

1-bromo-4-(trifluoromethyl)benzene\textsuperscript{14}

MS (EI, 70 eV): \( m/z \) (%): 226 (70), 224 (70, \([M^+])\), 207 (20), 205 (20), 176 (10), 174 (10), 145 (100), 125 (20), 95 (20), 75 (30).
1,1,1-trifluoro-2-(4-(trifluoromethyl)phenyl)propan-2-ol\textsuperscript{15}

MS (EI, 70 eV): \(m/z\) (%): 258 (1, [M\textsuperscript{+}]), 239 (10), 189 (100), 173 (30), 145 (35), 127 (10), 69 (15).

1,1,1-trifluoro-2-(4-iodophenyl)propan-2-ol\textsuperscript{15}

MS (EI, 70 eV): \(m/z\) (%): 316 (40, [M\textsuperscript{+}]), 247 (100), 231 (15), 203 (10), 150 (10), 127 (15), 120 (15), 105 (30), 91 (15), 77 (77), 65 (25).

4-methyl-N-(4-(trifluoromethyl)phenyl)benzenesulfonamide\textsuperscript{16}

MS (EI, 70 eV): \(m/z\) (%): 315 (10, [M\textsuperscript{+}]), 155 (40), 91 (100), 65 (25).

4-phenyl-1-(4-(trifluoromethyl)benzyl)-1H-1,2,3-triazole\textsuperscript{17}

MS (EI, 70 eV): \(m/z\) (%): 303 (5, [M\textsuperscript{+}]), 274 (10), 159 (45), 116 (100), 109 (20), 89 (25).
2-(trifluoromethyl)pyrazine$^{18}$

MS (EI, 70 eV): $m/z$ (%): 148 (100, [M$^+$]), 129 (20), 121 (25), 94 (15), 79 (15), 75 (25), 69 (15), 52 (50).

3-(trifluoromethyl)pyridine$^{19}$

MS (EI, 70 eV): $m/z$ (%): 147 (80, [M$^+$]), 127 (60), 120 (20), 97 (25), 78 (80), 75 (55), 69 (50), 51 (100).

2-methyl-5-(trifluoromethyl)thiophene$^{20}$

MS (EI, 70 eV): $m/z$ (%): 166 (80, [M$^+$]), 147 (25), 115 (20), 97 (100), 69 (25).
General procedure for the preparation of the trifluoromethylated compounds

An oven-dried test tube with a septum cap and a stir bar was charged with copper(I) iodide (76 mg, 0.4 mmol), 1,10-phenanthroline (72 mg, 0.4 mmol), KF (348 mg, 6 mmol, 3 eq.) and the aryl iodide (2.00 mmol, 1 eq.). The reaction vessel was closed, than evacuated and refilled with argon or nitrogen three times. DMSO (4.0 mL) and the aryl iodide (2.00 mmol) (if it isn’t solid), B(O(trimethyl)s) (623 mg, 6 mmol, 3 eq.), TMSCF3 (854 mg, 887 µL, 6 mmol, 3 eq.) were added via syringe. Solid aryl iodides were weighed directly in the reaction vessel. The resulting orange-brown suspension was stirred for 24 h at 60 °C. After cooling to ambient temperature, the orange solution was diluted with Et2O (10 mL) and washed with 1n HCl (25 mL). Acidic washing was omitted for basic products. The washing was re-extracted with Et2O (2 × 5 mL) and the combined organic layer was washed with conc. ammonia (25%, 25 mL) to remove traces of copper salts. The washing was re-extracted with Et2O (2 × 5 mL) and the combined organic layer were washed with brine (15 mL) and dried over MgSO4 and concentrated. The crude product was purified by flash column chromatography, if not noted otherwise.

2-(4-(Trifluoromethyl)phenoxy)tetrahydro-2H-pyran (4a)

The general procedure was followed. Yellow solid 329 mg (1.34 mmol, yield: 67%). Rf: 0.69 (in hexane:EtOAc 20:1) Mp.: 14 °C, 1H NMR (250 MHz, CDCl3): δ = 7.53 (d, 2H, J = 8.53 Hz), 7.12 (d, 2H, J = 8.37 Hz), 5.48(s, 1H), 3.90-3.80 (m, 1H), 3.65-3.57 (m, 1H), 2.00-1.55 (m, 6H), 13C NMR (62.5 MHz, CDCl3): δ = 159.2 (q, JCF = 1.38 Hz), 127.1 (q, JCF = 3.68 Hz), 124.8 (q, JCF = 271.17 Hz), 123.9 (q, JCF = 32.63 Hz), 116.8, 96.6, 62.4, 30.5, 25.5, 18.9, 19F NMR (235 MHz): δ = -62.00 ppm. IR (ATR) νmax 2947, 2876, 1615, 1517, 1321, 1244, 1159, 1105, 1064, 1036, 957, 836, 646, 600, 508 cm⁻1. MS (EI, 70 eV): m/z (%): 246 (1, [M⁺]), 162 (20), 143 (20), 112 (10), 85 (100).
**N,N-diBenzy1-4-(trifluoromethyl)aniline (4b)**

The general procedure was followed. Yellow white solid 231 mg (0.68 mmol, yield: 68%). Rf: 0.68 (in hexane:EtOAc 10:1) Mp. 98-101 °C, 1H NMR (250 MHz, CDCl3): 7.39-7.22 (m, 12H), 6.72 (d, 2H, J = 8.67 Hz), 4.69 (s, 4H), 13C NMR (62.5 MHz, CDCl3): 151.7, 137.9, 129.2, 127.6, 126.9 (q, JCF = 3.68 Hz), 126.8, 111.9, 54.6, 19F NMR (235 MHz): -61.40 ppm. IR (ATR) νmax 2922, 2857, 1615, 1528, 1449, 1351, 1246, 1197, 1154, 1111, 1069, 961, 800, 723, 692 cm⁻¹. MS (EI, 70 eV): m/z (%): 341 (20, [M⁺]), 322 (2), 250 (10), 172 (5), 145 (10), 91 (100).

![Image of N,N-diBenzy1-4-(trifluoromethyl)aniline (4b)](image)

**2,2,2-Trifluoro-N-(4-(trifluoromethyl)phenyl)acetamide (4c)**

The general procedure was followed. Yellow white solid 308 mg (1.2 mmol, yield: 60%). Rf: 0.66 (in hexane:EtOAc 4:1) Mp. 124-127 °C, 1H NMR (250 MHz, DMSO-d₆): 11.6 (s, 1H), 7.84 (dd, 4H, J₁ = 30.56, J₂ = 8.77 Hz), 13C NMR (62.5 MHz, DMSO-d₆): 155.5, 140.4, 138.0, 136.6, 126.6, 122.6, 120.7, 118.1, 19F NMR (235 MHz): -62.66, -75.29 ppm. IR (ATR) νmax 2424, 1702, 1321, 1266, 1204, 1152, 1109, 1064, 997, 834, 723 cm⁻¹. MS (EI, 70 eV): m/z (%): 257 (70, [M⁺]), 238 (20), 188 (80), 168 (20), 145 (100), 113 (20), 69 (40).

![Image of 2,2,2-Trifluoro-N-(4-(trifluoromethyl)phenyl)acetamide (4c)](image)

**Methyl 2-(trifluoromethyl)benzoate (4d)**

The general procedure was followed. Colorless oil 132.8 mg (0.65 mmol, yield: 33 %). Rf: 0.69 (in hexane:EtOAc 10:1) 1H NMR (250 MHz, CDCl3): 7.68-7.60 (m, 2H), 7.49-7.45 (m, 2H), 3.82 (s, 3H), 13C NMR (62.5 MHz, CDCl3): 167.1, 131.6 (q, JCF = 3.2Hz), 131.1, 131.0 (q, JCF = 46.4 Hz), 130.1, 128.7 (q, JCF = 97.0 Hz), 126.5 (q, JCF = 16.1 Hz), 123.7 (q, JCF = 820.0 Hz), 52.6, 19F NMR (235 MHz): -61.19 ppm. IR (ATR) νmax 2957, 1735, 1435, 1310, 1296, 1263, 1135, 1103, 1053, 1035, 958, 767, 719, 684, 646, 597 cm⁻¹. MS (EI, 70 eV): m/z (%): 204 (20, [M⁺]), 185 (10), 173 (100), 145 (70), 125 (10), 95 (10), 75 (10).

![Image of Methyl 2-(trifluoromethyl)benzoate (4d)](image)
**N,N-Diethyl-4-(trifluoromethyl)benzamide (4e)**

The general procedure was followed. Yellow oil 198 mg (0.81 mmol, yield: 81%). R<sub>f</sub>: 0.38 (in hexane:EtOAc 2:1) <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.57 (d, 2H, J = 8.06 Hz), 7.39 (d, 2H, J = 6.32 Hz), 3.45 (q, 2H, J = 6.63 Hz), 3.11 (q, 2H, J = 6.63 Hz), 1.15 (t, 3H, J = 6.32 Hz), 1.00 (t, 3H, J = 6.32 Hz). <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ = 170.1, 141.2, 131.3 (q, J<sub>CF</sub> = 32.63 Hz), 127.0, 125.7 (q, J<sub>CF</sub> = 3.68 Hz), 124.1 (q, J<sub>CF</sub> = 272.08 Hz), 43.6, 39.7, 14.4, 13.1. <sup>19</sup>F NMR (235 MHz): δ = -63.30 ppm. MS (EI, 70 eV): m/z (%) = 244 (30, [M+H]+), 226 (5), 173 (100), 145 (60), 125 (10), 95 (10). IR (ATR) ν<sub>max</sub> 2976, 2937, 1629, 1429, 1321, 1286, 1164, 1122, 1095, 1062, 845, 610 cm<sup>-1</sup>. MS (EI, 70 eV): m/z (%) = 244 (25, [M+H]+), 226 (5), 173 (100), 145 (60), 125 (5), 95 (5).

**Methyl 2-((trifluoromethyl)isonicotinate (4f)**

The general procedure was followed. Yellow oil 120 mg (0.59 mmol, yield: 59%). R<sub>f</sub>: 0.51 (in hexane:EtOAc 8:2) <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 8.71 (d, 1H, J = 5.06 Hz), 8.05 (s, 1H), 7.87 (dd, 1H, J = 4.90 Hz, J = 0.95 Hz), 3.82 (s, 3H). <sup>13</sup>C NMR (126 MHz, DMSO) δ 163.9, 151.8, 147.4 (q, J = 34.5 Hz), 139.1, 126.4, 121.3 (q, J = 274.1 Hz), 119.3 (q, J = 2.8 Hz), 53.2. <sup>19</sup>F NMR (235 MHz, CDCl<sub>3</sub>): δ = -68.14 ppm. IR (ATR) ν<sub>max</sub> 2960, 1734, 1441, 1330, 1256, 1130, 1082, 764, 697 cm<sup>-1</sup>. MS (EI, 70 eV): m/z (%) = 205 (82, [M+H]+), 186 (35), 174 (100), 146 (61), 136 (12), 69 (25). HRMS calcd for C<sub>8</sub>H<sub>7</sub>F<sub>3</sub>NO<sub>2</sub> [M+H]+ 206.1419 found 206.0424.

**3-(Benzyloxy)-2-chloro-6-(trifluoromethyl)pyridine (4g)**

The general procedure was followed. Yellow solid 266 mg (0.93 mmol, yield: 93%). R<sub>f</sub>: 0.47 (in hexane:EtOAc 8:2) Mp.: 82-83 °C, <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ = 7.55 (d, 1H, J = 8.4 Hz), 7.44-7.39 (m, 5H), 7.30 (d, 1H, J = 8.4 Hz), 5.25 (s, 2H), ppm. <sup>13</sup>C NMR (126 MHz, DMSO) δ 153.0, 139.9, 136.9 (q, J = 35.6 Hz), 135.3, 128.7, 128.4, 127.8, 122.5, 122.0 (q, J = 2.5 Hz), 121.1 (q, J = 272.9 Hz), 70.9. <sup>19</sup>F NMR (235 MHz): δ = -62.92 ppm. IR (ATR) ν<sub>max</sub> 1569, 1342, 1254, 1180, 1110,
Methyl 2-chloro-4-(trifluoromethyl)nicotinate (4h)

The general procedure was followed. Slightly yellow oil, 170 mg (0.71 mmol, yield: 71%).

\[ \text{R}_{f} = 0.67 \text{ (in hexane:EtOAc 8:2)} \]

$^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 8.64 (d, 1H, $J = 5.05$ Hz), 7.54 (d, 1H, $J = 5.21$ Hz), 4.00 (s, 3H) $^1$C NMR (126 MHz, DMSO) $\delta$ 163.7, 152.8, 147.5, 136.2 (q, $J = 33.9$ Hz), 125.9 (q, $J = 2.4$ Hz), 121.55 (q, $J = 275.0$ Hz), 120.08 (q, $J = 3.9$ Hz), 53.94 (s).

$^{19}$F NMR (235 MHz): $\delta$ = -62.84 ppm.

IR (ATR) $\nu_{\text{max}}$ 2959, 1744, 1567, 1379, 1314, 1271, 1141, 1062, 835, 683 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 287 (3, [M$^+$]), 168 (7), 148 (10), 91 (100), 65 (21). HRMS calcd for C$_{13}$H$_{10}$ClF$_3$NO [M+H]$^+$ 288.0403 found 288.0398.

4-Methyl-2-(methylthio)-6-(trifluoromethyl)pyrimidine (4i)$^{26}$

The general procedure was followed. Yellow oil 131 mg (0.63 mmol, yield: 90%).

\[ \text{R}_{f} = 0.67 \text{ (in hexane:EtOAc 8:2)} \]

$^1$H NMR (500 MHz, DMSO) $\delta$ 7.63 (s, 1H), 2.55 (s, 3H), 2.54 (s, 3H). $^1$C NMR (126 MHz, DMSO) $\delta$ 172.53, 171.35, 153.71 (q, $J = 35.1$ Hz), 120.52 (q, $J = 275.2$ Hz), 112.33 (q, $J = 2.7$ Hz), 24.02, 13.56.$^{19}$F NMR (235 MHz, CDCl$_3$): $\delta$ = -70.86 ppm. IR (ATR) $\nu_{\text{max}}$ 2933, 1737, 1585, 1392, 1271, 1143, 1115, 848, 708, 550 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 239 (23, [M$^+$]), 208 (100), 180 (31), 160 (6), 69 (13). HRMS calcd for C$_7$H$_8$F$_3$N$_2$S [M+H]$^+$ 209.0360 found 209.0351.

1-Benzyl-4-(trifluoromethyl)-1H-pyrazole (4j)$^{27}$

The general procedure was followed. The conversion after 24h was 87%. The remaining iodide was transformed with Sonogashira reaction with 2-methyl-3-butyn-2-ol. After the trifluoromethylation the tube was opened, CuI (2 mg), Pd(PPh$_3$)$_3$Cl$_2$ (2 mg), 2-methyl-3-butyn-2-ol (50 µl) and diisopropyl amine (250 µl) was added to the reaction mixture. The tube was sealed, refilled with argon and the
mixture was stirred at 60 °C additional 16h. The work up and the purification step was the same as it is described in the general procedure.

Yellow oil 136 mg (0.60 mmol, yield: 60%). Rf.: 0.54 (in hexane:EtOAc 8:2) 1H NMR (250 MHz, CDCl3): δ = 7.66(s, 1H), 7.54(s, 1H), 7.31-7.29(m, 3H), 7.19-7.16(m, 2H), 5.23(s, 4H). 13C NMR (126 MHz, DMSO) δ 136.9 (q, J = 2.6 Hz), 136.6, 130.5 (q, J = 3.6 Hz), 128.7, 127.8, 123.0 (q, J = 265.5 Hz), 111.7 (q, J = 37.3 Hz), 55.2. 19F NMR (235 MHz): δ = -56.80 ppm. IR (ATR) νmax 3035, 1574, 1400, 1231, 1192, 1110, 967, 738, 693, 681 cm⁻¹. MS (EI, 70 eV): m/z (%): 226 (48, [M+]), 225 (100), 207 (13), 149 (10), 91 (43). HRMS calcd for C11H10F3N2 [M+H]⁺ 227.0796 found 227.0786.

1-Benzyl-3,5-diphenyl-4-(trifluoromethyl)-1H-pyrazole (4k)

The general procedure was followed. The conversion after 24h was 35%. The tube was opened and 3 eq. KF, 3 eq. B(OMe)3 and 3 eq. TMSCF3 were added again to the reaction mixture. The tube was sealed, refilled with argon and the mixture was stirred at 60 °C additional 16h (55% conv.) then the addition of the reactants was repeated. After the third run the conversion was 68%. The work up and was the same as in the general procedure. The crude product was purified with preparative HPLC.

Yellow solid 92 mg (0.24 mmol, yield: 34%). Rf.: 0.56 (in hexane:EtOAc 8:2) Mp.: 123-124 °C, 1H NMR (500 MHz, DMSO) δ 7.61 (d, J = 6.9 Hz, 2H), 7.57 – 7.41 (m, 8H), 7.29-7.25 (m, 3H), 7.03 – 6.95 (m, 2H), 5.23 (s, 3H). 13C NMR (126 MHz, DMSO) δ 149.3, 144.9, 136.7, 132.2, 130.5, 130.2, 129.3, 129.2, 129.1, 129.0, 128.8, 128.20, 128.17, 127.6, 122.98 (q, J = 209.1, 125.7 Hz), 107.78 (d, J = 19.3 Hz), 53.31. 19F NMR (235 MHz): δ = -52.63 ppm. IR (ATR) νmax 1496, 1466, 1338, 1228, 1174, 1147, 1121, 1100, 1075, 987, 782, 744, 723, 697 cm⁻¹. MS (EI, 70 eV): m/z (%): 378 (47, [M⁺]), 301 (25), 259 (8), 189 (15), 91 (100), 65 (11). HRMS calcd for C15H13ClNO [M+H]⁺ 379.1422 found 379.1428.

1-(Trifluoromethyl)isoquinoline (4l)

The general procedure was followed. Slightly yellow oil 162 mg (0.82 mmol, yield: 82%). Rf.: 0.54 (in hexane:EtOAc 8:2) 1H NMR (250 MHz, CDCl3): δ = 8.58 (d, 1H, J = 5.7 Hz), 8.29 (d, 1H, J = 8.5 Hz), 7.91 (d, 1H, J = 7.6 Hz), 7.82 (d, 1H, J = 5.7 Hz), 7.80-7.67 (m, 2H) ppm. 13C NMR (126 MHz,
DMSO) $\delta$ 144.6 (q, $J = 32.5$ Hz), 140.8, 136.8, 131.4, 129.7, 128.0, 125.3, 123.7, 123.5 (q, $J = 2.9$ Hz), 122.2 (q, $J = 276.3$ Hz). $^{19}$F NMR (235 MHz): $\delta$ = -63.45 ppm. IR (ATR) $\nu_{\text{max}}$ 3062, 1587, 1301, 1255, 1168, 1115, 986, 830, 747, 656 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 197 (100, [M$^+$]), 178 (8), 147 (8), 128 (90), 101 (23), 75 (11), 69 (10). HRMS calcd for C$_{10}$H$_7$F$_3$N [M+H]$^+$ 198.0531 found 198.0526.

6-(Trifluoromethyl)quinoline (4m)$^{28}$

The general procedure was followed. Yellow solid 252 mg (0.64 mmol, yield: 64%). $R_f$: 0.51 (in hexane:EtOAc 2:1) Mp. 37-39 °C (lit.:39 °C, $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 9.02 (q, 1H, $J = 4.3$ Hz), 8.23 (q, 2H, $J = 13.7$ Hz), 8.13 (s, 1H), 7.87 (d, 1H, $J = 9.0$ Hz), 7.47 (q, 1H, $J = 12.6$ Hz), $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$ = 152.8, 149.5, 137.1, 131.1, 127.6, 126.1, 125.5, 125.4, 122.6, 122.1, $^{19}$F NMR (235 MHz): $\delta$ = -62.84 ppm. IR (ATR) $\nu_{\text{max}}$ 2925, 1466, 1336, 1296, 1192, 1158, 1144, 1109, 1062, 900, 846, 798, 740 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 197(100, [M$^+$]), 178 (20), 147 (35), 128 (20), 101 (10), 75 (15).

3-Bromo-2-(trifluoromethyl)quinoline (4n)

The general procedure was followed. Yellow solid 90 mg (0.32 mmol, yield: 32%). $R_f$: 0.62 (in hexane:EtOAc 8:2) Mp.: 73-74 °C, $^1$H NMR (500 MHz, DMSO) $\delta$ 9.12 (s, 1H), 8.18 (d, $J = 8.4$ Hz, 1H), 8.12 (d, $J = 8.1$ Hz, 1H), 7.99-7.96 (m, 1H), 7.90-7.83 (m, 1H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 144.40, 143.67 (q, $J = 33.4$ Hz), 143.59, 132.34, 130.80, 130.16, 129.80, 127.87, 120.84 (q, $J = 161.7$ Hz), 111.8, $^{19}$F NMR (235 MHz): $\delta$ = -66.39 ppm. IR (ATR) $\nu_{\text{max}}$ 1459, 1430, 1302, 1174, 1130, 1109, 965, 922, 786, 759, 744, 743, 633, 609, 567 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 277 (100, [M+2$^+$]), 275 (100, [M$^+$]), 206 (53), 196 (37), 176 (21), 146 (29), 127 (69), 101 (34), 75 (19). HRMS calcd for C$_{10}$H$_6$BrF$_3$N [M+H]$^+$ 275.9636 found 275.9612.
4-Chloro-6-(trifluoromethyl)quinoline (4o)

The general procedure was followed. Yellow solid 221 mg (0.95 mmol, yield: 95%). Rf.: 0.34 (in hexane:EtOAc 8:2) Mp.: 21-22 °C, 1H NMR (250 MHz, CDCl₃): δ = 8.89 (d, 1H, J = 4.7 Hz), 8.54 (s, 1H ), 8.24 (d, 1H, J = 8.9 Hz), 7.21-7.92 (dd, H, J = 8.9 Hz, J = 1.9 Hz), 7.59 (d, 2H, J = 4.7 Hz) ppm. 13C NMR (126 MHz, DMSO) δ 153.3, 149.5, 142.2, 131.57, 128.0 (q, J = 32.3 Hz), 126.12 (q, J = 2.9 Hz), 124.92, 123.8 (q, J = 272.5 Hz). 19F NMR (235 MHz): δ = -62.92 ppm. IR (ATR) νmax 3033, 1631, 1562, 1427, 1364, 1307, 1070, 848, 829, 678 cm⁻¹. MS (EI, 70 eV): m/z (%): 231 (100, [M⁺]), 212 (13), 196 (48), 181 (10), 169 (19), 99 (11), 69 (17). HRMS calcd for C₁₁H₆ClF₃N [M+H⁺] 232.0141 found 232.0144.

7-Chloro-4-(trifluoromethyl)quinoline (4p)

The general procedure was followed. Yellow solid 343 mg (74 mmol, yield: 74%). Rf.: 0.43 (in hexane:EtOAc 10:1) Mp. 64-65 °C, 1H NMR (250 MHz, CDCl₃): δ = 9.04 (d, 1H, J = 4.3 Hz), 8.2 (d, 1H, J = 2.1 Hz), 8.06 (dd, 1H, J₁ = 1.9 Hz J₂ = 9.2 Hz), 7.68 (d, 1H, J = 4.3 Hz), 7.63 (dd, 1H, J₁ = 2.1 Hz J₂ = 9.1 Hz), 13C NMR (62.5 MHz, CDCl₃): δ = 150.7, 149.3, 136.3, 134.4 (q, JCF = 95.5 Hz), 129.4, 129.3, 125.3 (q, JCF = 6.9 Hz), 121.1 (q, JCF = 20.1Hz), 118.0 (q, JCF = 16.1 Hz), 19F NMR (235 MHz): δ = -61.91 ppm. IR (ATR) νmax 2924, 1607, 1501, 1322, 1286, 1187, 1160, 1147, 1118, 1074, 978, 883, 822, 700 cm⁻¹. MS (EI, 70 eV): m/z (%) 231 (100, [M⁺]), 196 (50), 176 (20), 126 (10), 99 (20).

8-(Benzyloxy)-5-chloro-7-(trifluoromethyl)quinoline (4q)

The general procedure was followed. Slightly yellow solid 270 mg (0.80 mmol, yield: 80%). Rf.: 0.66 (in hexane:EtOAc 8:2) Mp.: 49-50 °C, 1H NMR (250 MHz, CDCl₃): δ = 9.08 (dd, 1H, J = 4.11 J =
1.58 Hz), 8.61 (dd, 1H, J = 8.60 J = 1.65 Hz), 7.80 (s, 1H), 7.67-7.63 (m, 3H), 7.45-7.36 (m, 3H), 5.62 (s, 2H) ppm. $^{13}$C NMR (126 MHz, DMSO) $\delta$ 153.4, 151.5, 142.5, 136.8, 133.2, 128.9, 128.4, 128.2, 128.1, 125.3, 124.9, 123.0 (q, J = 273.5 Hz), 122.4 (q, J = 4.9 Hz), 121.0 (q, J = 30.5 Hz), 77.2. $^{19}$F NMR (235 MHz): $\delta$ = -61.00 ppm. IR (ATR) $\nu_{max}$ 1596, 1497, 1449, 1356, 1323, 1272, 1215, 1130, 1081, 1040, 843, 705, 650 cm$^{-1}$. MS (EI, 70 eV): m/z (%): 337 (10, [M]+), 316 (12), 231 (21), 218 (10), 183 (14), 168 (24), 91 (100). HRMS calcd for C$_{17}$H$_{12}$ClF$_3$NO [M+H]$^+$ 338.0560 found 338.0559.

1-Benzyl-7-(trifluoromethyl)-1H-indole (4r)$^{31}$

The general procedure was followed. Yellow solid 164 mg (0.60 mmol, yield: 72%). $R_f$: 0.77 (in hexane:EtOAc 20:1) Mp. 30 °C (lit.): 45-47 °C, $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 7.89 (d, 1H, J = 7.9 Hz), 7.62 (d, 1H, J = 7.6 Hz), 7.42-7.29 (m, 4H), 7.20 (t, 1H, J = 7.7 Hz), 7.01 (d, 1H, J = 3.2 Hz), 7.05-7.02 (m, 2H), 7.70 (d, 2H, J = 3.3 Hz), 5.56 (s, 2H), $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$ = 138.0 (q, $J_{CF}$ = 3.2 Hz), 131.7 (q, $J_{CF}$ = 3.2 Hz) 131.6, 131.2, 128.6, 128.4, 127.8, 127.6, 127.4, 126.8, 126.6, 125.6 (q, $J_{CF}$ = 3.7 Hz), 120.9 (q, $J_{CF}$ = 19.3 Hz), 118.4, 113.2 (q, $J_{CF}$ = 96.5 Hz), 103.3, 51.8 (q, $J_{CF}$ = 16.1 Hz), $^{19}$F NMR (235 MHz): $\delta$ = -55.83 ppm. IR (ATR) $\nu_{max}$ 1432, 1296, 1162, 1105, 1088, 1066, 963, 799, 720, 693 cm$^{-1}$. MS (EI, 70 eV): m/z (%): 275 (20, [M$^+$]), 91 (100).

1-Benzyl-5-(trifluoromethyl)-1H-indole (4s)$^{32}$

The general procedure was followed. Yellow solid 307 mg (1.1 mmol, yield: 88%). $R_f$: 0.74 (in hexane:EtOAc 20:1) Mp. 80-84 °C, $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 7.95 (s, 1H), 7.41-7.27 (m, 5H), 7.09 (d, 1H, J = 3.2 Hz), 7.10-7.06 (m, 2H), 6.62 (d, 1H, J = 3.2 Hz), 5.31 (s, 2H), $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$ = 137.5 (q, $J_{CF}$ = 0.9 Hz), 136.8, 130.0, 128.9, 128.0, 127.9, 126.7, 121.9 (q, $J_{CF}$ = 95.2 Hz), 118.7 (q, $J_{CF}$ = 12.9 Hz), 118.4 (q, $J_{CF}$ = 10.6 Hz), 109.9, 102.7, 50.3, $^{19}$F NMR (235 MHz): $\delta$ = -60.75 ppm. IR (ATR) $\nu_{max}$ 2923, 1440, 1347, 1324, 1285, 1183, 1162, 1094, 1050, 891, 803, 730 cm$^{-1}$. MS (EI, 70 eV): m/z (%): 275 (20, [M$^+$]), 91 (100). HRMS calcd for C$_{16}$H$_{13}$F$_3$N [M+H]$^+$ 276.1000 found 276.0997.
1-Benzyl-5-methoxy-3-(trifluoromethyl)-1H-indole (4t)

The general procedure was followed. White solid 83.5 mg (0.27 mmol, yield: 27 %). Rf.: 0.50 (in hexane:EtOAc 8:1), Mp. 65-67 °C, 1H NMR (250 MHz, CDCl3): δ = 7.41 (s, 1H), 7.34-7.29 (m, 3H), 7.17-7.12 (m, 4H), 6.91 (dd, 1H, J1 = 9.2 Hz, J2 = 2.3 Hz), 5.29 (s, 2H), 3.87 (s, 3H), 13C NMR (62.5 MHz, CDCl3): δ = 155.3, 136.1, 131.5, 129.0, 128.1, 128.1 (q, JCF = 5.0 Hz), 126.9, 124.9 (q, JCF = 2.3 Hz), 113.9, 111.3, 105.9 (q, JCF = 36.7 Hz), 100.9, 55.8, 50.7, 19F NMR (235 MHz): δ = -57.48 ppm. IR (ATR) νmax 2956, 2939, 2836, 1552, 1491, 1436, 1279, 1252, 1187, 1122, 1092, 1029, 877, 825, 804, 746, 726, 705, 661, 638, 495, 425 cm⁻¹. MS (EI, 70 eV): m/z (%): 286 (2), 276 (100, [M⁺]), 257 (15), 207 (60), 199 (40), 91 (43), 65 (14). HRMS calcd for C17H15F3NO [M+H]+ 306.1106 found 306.1092.

1-Benzyl-3-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridine (4u)

The general procedure was followed. Slightly yellow solid 260 mg (0.94 mmol, yield: 94%). Rf.: 0.60 (in hexane:EtOAc 8:2) Mp.: 52-53 °C, 1H NMR (250 MHz, CDCl3): δ = 8.25 (dd, 1H, J = 4.66 Hz, J = 1.50 Hz), 7.86 (d, 2H, J = 7.90 Hz), 7.32(s, 1H), 7.15-6.99 (m, 6H), 5.31(s, 2H), 13C NMR (126 MHz, DMSO) δ 146.6, 144.6, 137.4, 129.9 (q, J = 5.0 Hz), 128.7, 127.7, 127.5, 127.4, 124.1 (q, J = 265.8 Hz), 117.8, 115.7 (q, J = 2.2 Hz), 102.5 (q, J = 37.1 Hz), 47.6. 19F NMR (235 MHz): δ = -57.49 ppm. IR (ATR) νmax 3062, 1604, 1550, 1456, 1271, 1175, 1081, 770, 691 cm⁻¹. MS (EI, 70 eV): m/z (%): 276 (100, [M⁺]), 257 (15), 207 (60), 199 (40), 91 (43), 65 (14). HRMS calcd for C15H12F2N2 [M+H]^+ 277.0953 found 277.0948.

1-Benzyl-4-(trifluoromethyl)-1H-indazole (4v)

The general procedure was followed. Yellow oil 180 mg (0.65 mmol, yield: 87%). Rf.: 0.59 (in hexane:EtOAc 8:2) 1H NMR (250 MHz, CDCl3): δ = 8.21 (s, 1H), 7.56-7.20 (m, 8H), 5.66 (s, 2H)
ppm$^{13}$C NMR (126 MHz, DMSO) $\delta$ 139.8, 137.0, 131.0, 128.6, 127.7, 127.4, 125.9, 124.2 (q, $J = 272.0$ Hz), 120.9 (q, $J = 33.1$ Hz), 118.8 (q, $J = 1.9$ Hz), 118.7 (q, $J = 4.8$ Hz), 114.8, 52.1.$^{19}$F NMR (235 MHz): $\delta$ = -61.89 ppm. IR (ATR) $\nu_{\text{max}}$ 3034, 1616, 1452, 1320, 1114, 935, 791, 723, 694 cm$^{-1}$.

MS (EI, 70 eV): $m/z$ (%): 276 (65, [M$^+$]), 257 (13), 199 (23), 137 (12), 91 (100), 65 (25). HRMS calcd for C$_{15}$H$_{12}$F$_3$N$_2$ [M+H]$^+$ 277.0953 found 277.0950.

7-Benzyl-4-chloro-5-(trifluoromethyl)-7H-pyrrolo[2,3-d]pyrimidine (4w)

The general procedure was followed. Yellow oil 43 mg (0.69 mmol, yield: 27%). $R_f$: 0.41 (in hexane:EtOAc 8:2) Mp.: 89-90 °C, $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.78 (s, 1H), 7.62 (s, 1H), 7.39-7.34 (m, 3H), 7.29 (dd, $J = 7.8$, 1.8 Hz, 2H), 5.49 (s, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 152.25, 152.11, 151.95, 135.00, 129.74 (q, $J = 5.8$ Hz), 129.24, 128.76, 128.01, 122.14 (q, $J = 266.8$ Hz), 113.28, 105.55 (q, $J = 39.1$ Hz), 48.90. $^{19}$F NMR (235 MHz): $\delta$ = -55.95 ppm. IR (ATR) $\nu_{\text{max}}$ 1598, 1540, 1442, 1364, 1317, 1247, 1184, 1122, 975, 953, 886, 856, 758, 701, 663, 612 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 311 (50, [M$^+$]), 242 (13), 234 (8), 91 (100), 65 (26). HRMS calcd for C$_{14}$H$_{10}$ClF$_3$N$_3$ [M+H]$^+$ 312.0515 found 312.0520.

9-Benzyl-3-(trifluoromethyl)-9H-carbazole (4x)

The general procedure was followed. Yellow solid 282 mg (0.87 mmol, yield: 87%). $R_f$: 0.74 (in hexane:EtOAc 8:1) Mp.: 78-80 °C, $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.44 (s, 1H), 8.19 (d, 1H $J = 7.78$ Hz), 7.69 (d, 1H $J = 8.53$ Hz), 7.53 (t, 1H $J = 8.03$ Hz), 7.43 (dd, 2H $J_1 = 8.28$ Hz, $J_2 = 2.76$ Hz), 7.37-7.28 (m, 4H), 7.16-7.14 (m, 2H), 5.53 (s, 2H), $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$ = 142.1, 141.3, 136.5, 128.9, 127.8, 126.9, 126.4, 125.34 (q, $J_{CF} = 271.43$ Hz), 122.6 (q, $J_{CF} = 8.07$ Hz), 121.6 (q, $J_{CF} = 32.28$ Hz), 120.7, 120.2, 117.9 (q, $J_{CF} = 3.67$ Hz), 109.4, 109.0, 47.1, $^{19}$F NMR (235 MHz): $\delta$ = -60.55 ppm. IR (ATR) $\nu_{\text{max}}$ 2926, 1600, 1466, 1451, 1326, 1270, 1206, 1136, 1098, 1049, 830, 792, 766, 742 cm$^{-1}$. MS (EI, 70 eV): $m/z$ (%): 325 (20, [M$^+$]), 234 (2), 165 (1), 91 (100), HRMS calcd for C$_{20}$H$_{15}$F$_3$N [M+H]$^+$ 326.1157 found 326.1145.

9-Benzyl-3-(trifluoromethyl)-9H-carbazole (4x)
2-Methyl-5-(trifluoromethyl)benzofuran (4y)

The general procedure was followed. Colorless oil 301 mg (0.75 mmol, yield: 75%). Rf: 0.88 (in hexane:EtOAc 8:1) ¹H NMR (250 MHz, CDCl₃): δ = 7.75 (s, 1H), 7.47 (m, 2H), 6.43 (s, 1H), 2.48 (s, 3H). ¹³C NMR (62.5 MHz, CDCl₃): δ = 157.5, 156.1, 131.5, 129.3, 126.7, 124.3, 122.6, 120.2 (q, JCF = 11.03 Hz), 117.7 (q, JCF = 12.40 Hz), 110.9, 102.8, 14.0. ¹⁹F NMR (235 MHz): δ = -60.81 ppm. IR (ATR) νmax: 2924, 1603, 1449, 1443, 1327, 1285, 1177, 1159, 1114, 1051, 941, 888, 815, 792 cm⁻¹. MS (EI, 70 eV): m/z (%): 200 (70, [M⁺]), 199 (100), 181 (20), 151 (30), 131 (35), 103 (20), 77 (20).

3-(Trifluoromethyl)dibenzo[b,d]furan (4z)

The general procedure was followed. White solid 202 mg (0.86 mmol, yield: 86%). Rf: 0.90 (in hexane:EtOAc 8:1) Mp. 92-93 °C (lit.: 97 °C). ¹H NMR (250 MHz, CDCl₃): δ = 8.22 (s, 1H), 7.97 (d, 1H J = 8.37 Hz), 7.71 (d, 1H J = 9.95 Hz) 7.65-7.59 (m, 2H), 7.53 (t, 1H J = 14.37 Hz), 7.40 (t, 1H J = 15.43 Hz). ¹³C NMR (62.5 MHz, CDCl₃): δ = 158.0, 157.1, 135.9, 129.9, 128.6, 124.8, 124.6 (q, JCF = 11.03 Hz), 123.7, 123.5, 121.3, 118.6 (q, JCF = 11.95 Hz), 112.4, 112.4. ¹⁹F NMR (235 MHz): δ = -61.34 ppm. IR (ATR) νmax: 2923, 1452, 1352, 1330, 1318, 1367, 1161, 1096, 1051, 897, 827, 770, 753 cm⁻¹. MS (EI, 70 eV): m/z (%): 200 (70, [M⁺]), 199 (100), 181 (20), 151 (30), 131 (35), 103 (20), 77 (20).

2-Ethyl-4-(trifluoromethyl)benzo[b]thiophene (4aa)

The general procedure was followed. Yellow oil 158 mg (0.69 mmol, yield: 69%). Rf: 0.86 (in hexane:EtOAc 20:1) ¹H NMR (250 MHz, CDCl₃): δ = 7.83 (d, 1H, J = 8.0 Hz), 7.53 (d, 1H, J = 7.6 Hz), 7.21-7.16 (m, 2H), 2.80 (q, 2H J = 23.5 Hz), 1.31 (t, 3H J = 7.6 Hz). ¹³C NMR (62.5 MHz, CDCl₃): δ = 141.2, 136.6, 134.4, 127.1, 124.3, 123.8, 122.4, 122.0, 118.4, 24.7, 15.8. ¹⁹F NMR (235 MHz): δ = -62.07 ppm. IR (ATR) νmax: 2971, 1458, 1316, 1219, 1149, 1113, 1060, 833, 783, 739, 711 cm⁻¹. MS (EI, 70 eV): m/z (%): 200 (70, [M⁺]), 199 (100), 181 (20), 151 (30), 131 (35), 103 (20), 77 (20).
cm\(^{-1}\). MS (EI, 70 eV): \(m/z\) (%): 230 (30, [M\(^+\)]), 215 (100), 196 (5), 182 (10), 165 (0), 151 (20), 115 (10), 69 (10). HRMS calcd for C\(_{11}\)H\(_{10}\)F\(_3\)S [M+H]\(^+\) 231.0455 found 231.0450.

2-(Trifluoromethyl)-9H-fluorene (4ab)

The general procedure was followed. Yellow solid 99 mg (0.21 mmol, yield: 21%). R\(_f\): 0.91 (in hexane:EtOAc 10:1) Mp. 85-86 °C (lit.): 80-82 °C. \(^1\)H NMR (250 MHz, CDCl\(_3\)): \(\delta = 7.86\) (t, 2H \(J = 7.50\) Hz), 7.80 (s, 1H), 7.63 (dd, 2H \(J_1 = 21.83, J_2 = 7.78\) Hz), 7.45-7.35 (m, 2H), 3.97 (s, 3H). \(^{13}\)C NMR (62.5 MHz, CDCl\(_3\)): \(\delta = 145.1, 143.8, 143.4, 140.3, 128.0, 127.1, 125.2, 124.6\) (q, \(J_{CF} = 271.43\) Hz), 124.8 (q, \(J_{CF} = 4.40\) Hz), 121.9 (q, \(J_{CF} = 3.68\) Hz), 120.6, 119.9, 36.9. \(^{19}\)F NMR (235 MHz): \(\delta = -62.17\) ppm. IR (ATR) \(\nu_{\text{max}}\) 1426, 1326, 1283, 1159, 1102, 1061, 882, 839, 773, 739 cm\(^{-1}\). MS (EI, 70 eV): \(m/z\) (%): 234 (50, [M\(^+\)]), 215 (5), 183 (10), 165 (100), 139 (5), 107 (10).
References

5 Milen, Matyas; Grun, Alajos; Balint, Erika; Dancso, András; Keglevich, Gyorgy; Synth. Commun. 2010, 40, 2291.