Supporting information

Palladium-Catalyzed Three-Component Carbonylative Synthesis of 2-(Trifluoromethyl)quinazolin-4(3H)-ones from Trifluoroacetimidoyl Chlorides and Amines

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1. General Information

Unless otherwise noted, all reactions were carried out under air atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. 1H NMR spectra were recorded on a Bruker Avance operating at 400 MHz, 13C NMR at 100 MHz and 19F NMR at 377 MHz and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and CDCl₃ (1H NMR δ 7.26, 13C NMR δ 77.16), DMSO - D₆ (1H NMR δ 2.50, 13C NMR δ 39.52) as solvent. All coupling constants (J) are reported in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, dd = double doublet, ddd = double doublet of doublets, t = triplet, dt = double triplet, q = quadruplet, m = multiplet, br = broad. Gas chromatography (GC) analyses were performed on a Shimadzu GC-2014C chromatograph equipped with a FID detector. Mass spectra (MS) were measured on spectrometer by direct inlet at 70 eV. Mass spectroscopy data of the products were collected on an HRMS-TOF instrument or Waters TOFMS GCT Premier using EI or ESI ionization. Melting points were measured with WRR digital point apparatus and not corrected.

1.1 Preparation of Fluorinated Imidoyl Chlorides

A 200 mL two-necked flask equipped with a septum cap, a condenser, and a Teflon coated magnetic stir bar was charged with PPh₃ (34.5 g, 132 mmol), Et₃N (7.3 mL, 53 mmol), CCl₄ (21.1 mL, 220 mmol), and TFA (3.4 mL, 44 mmol). After the solution was stirred for about 10 min (ice bath), amine (53 mmol) dissolved in CCl₄ (21.1 mL, 220 mmol) was added. The mixture was then refluxed under stirring (3 h). After the reaction was completed, residual solid Ph₃PO, PPh₃ and Et₃N-HCl were washed with hexane several times. Then the hexane was filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel or neutral alumina to afford the corresponding trifluoroacetimidoyl chloride product.
1.2 Preparation of TFBen

Formic acid (8.4 mL, 222.8 mmol, 5.0 equiv.) was added to acetic anhydride (16.8 mL, 178.2 mmol, 4.0 equiv.) at rt. The mixture was stirred at 60 °C for 1 h and cooled to rt. The resulting solution was poured into a flask containing 1,3,5-trihydroxybenzene (5.62 g, 44.6 mmol, 1.0 equiv.) and NaOAc (1.83 g, 22.3 mmol, 0.5 equiv.). The mixture was stirred for 4 h in a water bath and then diluted with toluene (100 mL), washed with H₂O (50 mL) twice. The organic phase was kept in fridge (2-8 °C) overnight, then filtered and dried in vacuo to afford the desired product benzene-1,3,5-triyl trifomate (TFBen) (5.1 g, 55%) as a white solid.

2. Experimental Procedures

2.1 Optimization of the Reaction Conditions

2.1.1 Screening of Catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat.</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Pd(OAc)₂</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>69</td>
</tr>
<tr>
<td>3</td>
<td>Pd(PPh₃)₄</td>
<td>71</td>
</tr>
<tr>
<td>4</td>
<td>Pd(CH₃CN)₂Cl₂</td>
<td>91</td>
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<tr>
<td>5</td>
<td>PdCl₂</td>
<td>73</td>
</tr>
<tr>
<td>6</td>
<td>Pd(TFA)₂</td>
<td>95</td>
</tr>
</tbody>
</table>

*Reaction conditions: 1a (0.20 mmol), 2a (0.50 mmol, 2.5 equiv), [M] (5 mol%), PPh₃ (10 mol%), p-cymene (2.0 equiv), base (1.0 mol%), solvents (10 mL), 110 °C, 24 h.*
mol%), Na$_2$CO$_3$ (0.40 mmol, 2.0 equiv), TFBen (1.0 mmol, 5.0 equiv), THF (2.0 mL), 110 °C, 24 h. *Yields determined by GC analysis using dodecane as an internal standard.

### 2.1.2 Screening of Ligands*°

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Yield (%)$^b$</th>
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<tbody>
<tr>
<td>1</td>
<td>Tris(p-methoxyphenyl)phosphine</td>
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</tr>
<tr>
<td>2</td>
<td>Tris(4-fluorophenyl)phosphine</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>Xphos</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>DPPP</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>DPPF</td>
<td>87</td>
</tr>
<tr>
<td>6</td>
<td>Xantphos</td>
<td>90</td>
</tr>
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</table>

*aReaction conditions: 1a (0.20 mmol), 2a (0.50 mmol, 2.5 equiv), Pd(TFA)$_2$ (5 mol%), ligand (10 mol%), Na$_2$CO$_3$ (0.40 mmol, 2.0 equiv), TFBen (1.0 mmol, 5.0 equiv), THF (2.0 mL), 110 °C, 24 h. $^b$Yields determined by GC analysis using dodecane as an internal standard.

### 2.1.3 Screening of Solvents*°

<table>
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<tr>
<th>Entry</th>
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<tr>
<td>1</td>
<td>THF</td>
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</tr>
<tr>
<td>2</td>
<td>1,4-dioxane</td>
<td>97 (95)$^c$</td>
</tr>
<tr>
<td>3</td>
<td>CH$_3$CN</td>
<td>88</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>DMF</td>
<td>85</td>
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</table>

*aReaction conditions: 1a (0.20 mmol), 2a (0.50 mmol, 2.5 equiv), Pd(TFA)$_2$ (5 mol%), PPh$_3$ (10 mol%), Na$_2$CO$_3$ (0.40 mmol, 2.0 equiv), TFBen (1.0 mmol, 5.0 equiv), solvent (2.0 mL), 110 °C, 24 h. $^b$Yields determined by GC analysis using dodecane as an internal standard. $^c$Isolated yield.
### 2.1.4 Screening of Bases\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Yield (%(^b))</th>
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<tr>
<td>1</td>
<td>NaHCO(_3)</td>
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</tr>
<tr>
<td>2</td>
<td>K(_2)CO(_3)</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>NaOAc</td>
<td>95</td>
</tr>
</tbody>
</table>

\(^a\)Reaction conditions: 1\(a\) (0.20 mmol), 2\(a\) (0.50 mmol, 2.5 equiv), Pd(TFA)\(_2\) (5 mol%), PPh\(_3\) (10 mol%), base (0.40 mmol, 2.0 equiv), TFBen (1.0 mmol, 5.0 equiv), 1,4-dioxane (2.0 mL), 110 \(^\circ\)C, 24 h. \(^b\)Yields determined by GC analysis using dodecane as an internal standard.

### 2.1.5 Screening the amount of Pd(TFA)\(_2\) and PPh\(_3\).\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(TFA)(_2)</th>
<th>PPh(_3)</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5 mol%</td>
<td>5 mol%</td>
<td>99 (98)(^c)</td>
</tr>
</tbody>
</table>

\(^a\)Reaction conditions: 1\(a\) (0.20 mmol), 2\(a\) (0.50 mmol, 2.5 equiv), Pd(TFA)\(_2\) (2.5 mol%), PPh\(_3\) (5 mol%), Na\(_2\)CO\(_3\) (0.40 mmol, 2.0 equiv), TFBen (1.0 mmol, 5.0 equiv), 1,4-dioxane (2.0 mL), 110 \(^\circ\)C, 24 h. \(^b\)Yields determined by GC analysis using dodecane as an internal standard. \(^c\)Isolated yield.
2.2 General Procedure for the Synthesis of 3/4

Under N\textsubscript{2} atmosphere, Pd(TFA\textsubscript{2}) (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\textsubscript{3} (2.6 mg, 0.01 mmol, 5 mol%), Na\textsubscript{2}CO\textsubscript{3} (42.2 mg, 0.4 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), 1 (0.2 mmol, 1.0 equiv), 2 (0.5 mmol, 2.5 equiv), 1,4-dioxane (2.0 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 3 or 4.

Scale-up reaction: Under N\textsubscript{2} atmosphere, Pd(TFA\textsubscript{2}) (8.5 mg, 0.025 mmol, 2.5 mol %), PPh\textsubscript{3} (13.0 mg, 005 mmol, 5 mol%), Na\textsubscript{2}CO\textsubscript{3} (211 mg, 2.0 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (420.0 mg, 2.0 mmol, 2.0 equiv), 1a (1.0 mmol, 335.0 mg 1.0 equiv), 2a (2.5 mmol, 190.0 mg, 2.5 equiv), 1,4-dioxane (4.0 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 3 or 4.
2.3 General Procedure for the Synthesis of 5a

Under air atmosphere, Na₂CO₃ (211 mg, 2.0 mmol, 2.0 eq.), 1a (333.0 mg, 1.0 mmol, 1.0 eq.), 2a (182.5 mg, 2.5 mmol, 2.5 eq.), 1,4-dioxane (10.0 mL) (extra dry) were added to a 50 mL round-bottomed flask. Then the tube was sealed and the mixture was stirred at rt. for 2 h. After the reaction was completed, the mixture was slowly cooled to room temperature. After the reaction was completed, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 5a as a yellow solid in 99% yield.

2.4 Late-stage Modification of Natural Complex Molecules

Under N₂ atmosphere, Pd(TFA)₂ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh₃ (2.6 mg, 0.01 mmol, 5 mol%), Na₂CO₃ (42.2 mg, 0.4 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), 1a (0.2 mmol, 1.0 equiv), amine (0.24 mmol, 1.2 equiv), 1,4-dioxane (2.0 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The
Residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 6, 7 and 8 in 57%, 72% and 57% yields, respectively.

2.5 Synthetic Application for the Synthesis of Bioactive Molecule Rutaecarpine

Under N₂ atmosphere, Pd(TFA)₂ (8.5 mg, 0.025 mmol, 2.5 mol %), PPh₃ (13.0 mg, 0.05 mmol, 5 mol %), Na₂CO₃ (211.0 mg, 2.0 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (420.0 mg, 1.0 mmol, 2.0 equiv), 1a (333.0 mg, 1.0 mmol, 1.0 equiv), tryptamine (192.0 mg, 1.2 mmol, 1.2 equiv), 1,4-dioxane (4.0 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 4w in 83% yield.

Compound 4w (357.0 mg, 1.0 mmol, 1.0 eq.) was refluxed in a mixture of acetic acid (3.0 mL) and hydrochloric acid (0.5 mL) for 30 min. The resulting mixture was diluted with water (20 mL) and the solid collected, washed with water, and dried to directly give the product 9 in 97% yield (346.3 mg).

Compound 9 (357.0 mg, 1.0 mmol, 1.0 eq.) was added to a hot well-stirred solution of KOH (297.0 mg, 3.5 mmol, 3.5 equiv) in ethanol (5.0 mL) and water (1.5 mL). The starting material gradually went into solution, and after 10 min a clear solution was obtained from which suddenly rutaecarpine appeared as needles. The reflux was continued for 15 minutes, then the mixture was cooled and the crystals were collected, washed, and dried to directly give the product 10 in 96% yield (275.5 mg).
3 The Mechanistic Investigations

Eq a: Under N₂ atmosphere, Pd(TFA)_2 (1.7 mg, 0.005 mmol, 2.5 mol %), PPh₃ (2.6 mg, 001 mmol, 5 mol%), Na₂CO₃ (42.2 mg, 0.4 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), 1a (0.2 mmol, 66.6 mg, 1.0 equiv), 2a (36.5 mg, 0.5 mmol, 2.5 equiv), TEMPO (62.5 mg, 0.4 mmol, 2.0 eq.) or BHT (88.1mg, 0.4 mmol, 2.0 eq.), 1,4-dioxane (2 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24 h. After the reaction was completed, the mixture was slowly cooled to room temperature. After the reaction was completed, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product 3a as yellow oil in 88% (TEMPO) and 52% (BHT) yield.

Eq b: Under air atmosphere, 5a (74.0 mg, 0.2 mmol, 1.0 eq.), Pd(TFA)_2 (1.7 mg, 0.005 mmol, 2.5 mol %), PPh₃ (2.6 mg, 001 mmol, 5 mol%), Na₂CO₃ (42.2 mg, 0.4 mmol, 2.0 eq), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), 1,4-dioxane (2 mL) (extra dry) were added to an oven-dried 15 mL In-Ex tube. Then the tube was sealed and the mixture was stirred at 110 °C (oil bath) for 24h. After the reaction was completed, the product 3a was observed in 97% yield. (Yields determined by GC analysis using dodecane as an internal standard).
4 Characterization Data of the Corresponding Products

3-Butyl-2-(trifluoromethyl)quinazolin-4(3H)-one (3a)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3a as a yellow oil (52.9 mg, 98%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.31 (d, $J = 7.9$ Hz, 1H), 7.89 - 7.77 (m, 2H), 7.62 - 7.58 (m, 1H), 4.12 (t, $J = 8.1$ Hz, 2H), 1.90 - 1.65 (m, 2H), 1.58 - 1.38 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 161.4, 145.1, 142.2 (q, $J_{(C-F)} = 35.6$ Hz), 134.8, 129.2, 128.4, 127.0, 121.9, 118.3 (q, $J_{(C-F)} = 276.9$ Hz), 45.2, 30.7, 20.2, 13.5.

$^{19}$F NMR (377 MHz, CDCl$_3$) δ -65.8.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{13}$H$_4$F$_3$N$_2$O$^+$, 271.1053, found 271.1060.

3-Butyl-6-methyl-2-(trifluoromethyl)quinazolin-4(3H)-one (3b)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1b (69.4 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3b as a yellow oil. (49.4 mg, 87%).
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.09 (s, 1H), 7.69 (d, \(J = 8.3\) Hz, 1H), 7.62 (d, \(J = 8.3\) Hz, 1H), 4.11 (t, \(J = 8.1\), 2H), 2.51 (s, 3H), 1.72 (m, 2H), 1.59 - 1.36 (m, 2H), 0.97 (t, \(J = 7.4\) Hz, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 161.4, 143.0, 141.5 (q, \(J_{(C-F)} = 35.3\) Hz), 139.8, 136.2, 128.2, 126.4, 121.6, 118.4 (q, \(J_{(C-F)} = 276.8\) Hz), 45.2, 30.7, 21.5, 20.2, 13.6.

\(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -65.7.


3-Butyl-6-fluoro-2-(trifluoromethyl)quinazolin-4(3H)-one (3c)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1c (70.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA\(_2\)) (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\(_3\) (2.6 mg, 0.01 mmol, 5 mol%), Na\(_2\)CO\(_3\) (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.3) to give the titled product 3c as a yellow oil (55.3 mg, 96%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.00 - 7.88 (m, 1H), 7.8 - 7.80 (m, 1H), 7.55 - 7.50 (m, 1H), 4.11 (t, \(J = 8.1\) Hz, 2H), 1.73 (m, 2H), 1.62 - 1.32 (m, 2H), 0.98 (t, \(J = 7.4\) Hz, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 162.4 (d, \(J_{(C-F)} = 252.1\) Hz), 161.2, 160.9, 141.8, 131.2 (d, \(J_{(C-F)} = 8.5\) Hz), 123.6, 123.6 (d, \(J_{(C-F)} = 24.2\) Hz), 118.4 (q, \(J_{(C-F)} = 276.8\) Hz), 112.2 (d, \(J_{(C-F)} = 24.0\) Hz), 45.6, 30.7, 20.3, 13.7.

\(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -65.8, -108.5.

HRMS (ESI): [M+H]+ calcd. for C\(_{13}\)H\(_{13}\)F\(_4\)N\(_2\)O\(_2\), 289.0959, found 289.0970.
3-Butyl-6-chloro-2-(trifluoromethyl)quinazolin-4(3H)-one (3d)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1d (73.4 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.3) to give the titled product 3d as a yellow oil. (56.6 mg, 93%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.25 (s, 1H), 7.74 (d, $J$ = 1.3 Hz, 2H), 4.11 (t, $J$ = 8.1 Hz, 2H), 2.08 - 1.63 (m, 2H), 1.59 - 1.36 (m, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.5, 143.7, 142.6 (q, $J_{(C-F)}$ = 35.8 Hz), 135.4, 130.2, 126.6, 123.1, 118.3 (q, $J_{(C-F)}$ = 277.0 Hz), 45.6, 30.7, 20.3, 13.7.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.8.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{13}$H$_{13}$ClF$_3$N$_2$O$, 305.0663$, found 305.0671.

6-Bromo-3-butyl-2-(trifluoromethyl)quinazolin-4(3H)-one (3e)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1e (82.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3e as a yellow oil. (61.2 mg, 88%).
**1H NMR (400 MHz, CDCl₃)** δ 8.44 (s, 1H), 7.90 (d, J = 2.3 Hz, 1H), 7.68 (d, J = 8.7 Hz, 1H), 4.12 (t, J = 8.1 Hz, 2H), 1.76 - 1.69 (m, 2H), 1.58 - 1.38 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H).

**13C NMR (101 MHz, CDCl₃)** δ 160.4, 144.0, 142.7 (q, J(C-F) = 35.8 Hz), 138.2, 130.3, 129.8, 123.3, 118.4 (q, J(C-F) = 277.0 Hz), 45.7, 45.6, 30.8, 20.3, 13.7.

**19F NMR (377 MHz, CDCl₃)** δ -65.8.

**HRMS (ESI):** [M+H]+ calcd. for C₁₄H₁₃BrF₃N₂O⁺, 349.0158, found 349.0162.

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3-Butyl-2,6-bis(trifluoromethyl)quinazolin-4(3H)-one (3f)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1f (80.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)₂ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh₃ (2.6 mg, 0.01 mmol, 5 mol%), Na₂CO₃ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.3) to give the titled product 3f as a yellow oil (62.9 mg, 93%).

**1H NMR (400 MHz, CDCl₃)** δ 8.59 (s, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 4.14 (t, J = 8.1 Hz, 2H), 1.74 (m, 2H), 1.55 - 1.34 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H).

**13C NMR (101 MHz, CDCl₃)** δ 160.8, 147.3, 144.3 (q, J(C-F) = 35.9 Hz), 133.9, 131.2 (q, J(C-F) = 33.6 Hz), 129.6, 125.1, 123.5 (q, J(C-F) = 272.8 Hz), 122.1, 118.3 (q, J(C-F) = 277.4 Hz), 45.7, 30.8, 20.3, 13.6.

**19F NMR (377 MHz, CDCl₃)** δ -62.7, 66.0.

**HRMS (ESI):** [M+H]+ calcd. for C₁₄H₁₃F₆N₂O⁺, 339.0927, found 339.0933.
3-Butyl-7-methyl-2-(trifluoromethyl)quinazolin-4(3H)-one (3g)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1g (69.4 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3g as a yellow oil (50.6 mg, 89%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.17 (d, $J$ = 8.2 Hz, 1H), 7.58 (s, 1H), 7.40 (d, $J$ = 7.4 Hz, 1H), 4.10 (t, $J$ = 8.1 Hz, 2H), 2.50 (s, 3H), 1.95 - 1.60 (m, 2H), 1.60 - 1.32 (m, 2H), 0.97 (t, $J$ = 7.4 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.4, 146.1, 145.3, 142.4 (q, $J$$_{(C-F)}$ = 35.5 Hz), 130.8, 128.3, 126.9, 119.6, 118.5 (q, $J$$_{(C-F)}$ = 277.0 Hz), 45.2, 30.9, 21.9, 20.3, 13.7.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.8.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{14}$H$_{16}$F$_3$N$_2$O, 285.1209, found 285.1218.

3-Butyl-7-fluoro-2-(trifluoromethyl)quinazolin-4(3H)-one (3h)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1h (70.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via
flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.3) to give the titled product 3h as a yellow oil. (52.4 mg, 91%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] \( \delta \) 8.15 - 8.11 (m, 1H), 7.27 - 7.24 (m, 1H), 7.15 - 7.10 (m, 1H), 3.92 (t, \( J = 8.1 \) Hz, 2H), 1.57 - 1.49 (m, 2H), 1.45 - 1.19 (m, 2H), 0.78 (t, \( J = 7.4 \) Hz, 3H).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] \( \delta \) 166.7 (d, \( J_{(C-F)} = 256.0 \) Hz), 160.8, 147.3 (d, \( J_{(C-F)} = 13.2 \) Hz), 143.6 (q, \( J_{(C-F)} = 35.7 \) Hz), 129.9 (d, \( J_{(C-F)} = 10.1 \) Hz), 118.8, 118.3 (q, \( J_{(C-F)} = 277.3 \) Hz), 118.2 (d, \( J_{(C-F)} = 23.4 \) Hz), 114.0 (d, \( J_{(C-F)} = 22 \) Hz), 45.5, 30.8, 20.3, 13.7.

\[ ^19F \text{ NMR (377 MHz, CDCl}_3 \] \( \delta \) -65.9, -101.8.

HRMS (ESI): [M+H]+ calcd. for C\(_{13}\)H\(_{13}\)F\(_3\)N\(_2\)O\(^+\), 289.0959, found 289.0967.

3-Butyl-7-chloro-2-(trifluoromethyl)quinazolin-4(3H)-one (3i)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1i (73.4 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)\(_2\) (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\(_3\) (2.6 mg, 0.01 mmol, 5 mol%), Na\(_2\)CO\(_3\) (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.3) to give the titled product 3i as a yellow oil. (51.1 mg, 84%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] \( \delta \) 8.22 (s, 1H), 7.79 (d, \( J = 1.9 \) Hz, 1H), 7.53 (d, \( J = 8.6 \) Hz, 1H), 4.10 (t, \( J = 8.1 \) Hz, 2H), 1.89 - 1.61 (m, 2H), 1.59 - 1.37 (m, 2H), 0.98 (t, \( J = 7.4 \) Hz, 3H).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] \( \delta \) 160.9, 146.1, 143.5 (q, \( J_{(C-F)} = 35.8 \) Hz), 141.3, 129.9, 128.5, 128.1, 120.4, 118.3 (q, \( J_{(C-F)} = 277.3 \) Hz), 46.0, 30.8, 20.3, 13.7.

\[ ^19F \text{ NMR (377 MHz, CDCl}_3 \] \( \delta \) -66.0.

HRMS (ESI): [M+H]+ calcd. for C\(_{13}\)H\(_{13}\)ClF\(_3\)N\(_2\)O\(^+\), 305.0663, found 305.0670.
7-Bromo-3-butyl-2-(trifluoromethyl)quinazolin-4(3H)-one (3j)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1j (82.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)_2 (1.7 mg, 0.005 mmol, 2.5 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3j as a yellow oil (62.6 mg, 90%).

^1H NMR (400 MHz, CDCl_3) δ 8.16 (s, 1H), 8.00 (d, J = 1.8 Hz, 1H), 7.71 (d, J = 8.5, 1H), 4.11 (t, J = 8.1 Hz, 2H), 1.77 - 1.69 (m, 2H), 1.57 - 1.37 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H).

^13C NMR (101 MHz, CDCl_3) δ 161.1, 146.1, 143.5 (q, J_{C-F} = 36.1 Hz), 132.8, 131.3, 129.7, 128.5, 120.8, 118.3 (q, J_{C-F} = 277.3 Hz), 45.5, 30.8, 20.3, 13.7.

^19F NMR (377 MHz, CDCl_3) δ -65.9.

HRMS (ESI): [M+H]^+ calcd. for C_{13}H_{13}BrF_3N_2O^+, 349.0158, found 349.0166.

3-Butyl-6,8-dichloro-2-(trifluoromethyl)quinazolin-4(3H)-one (3k)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1k (80.2 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)_2 (1.7 mg, 0.005 mmol, 2.5 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3k as a white solid (55.4 mg, 82%).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.19 (s, 1H), 7.86 (s, 1H), 4.13 (t, $J = 8.1$ Hz, 2H), 1.82 - 1.63 (m, 2H), 1.59 - 1.33 (m, 2H), 0.99 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.1, 143.0 (q, $J_{(C-F)} = 36.3$ Hz), 140.9, 135.3, 135.1, 134.6, 125.4, 124.2, 118.2 (q, $J_{(C-F)} = 277.4$ Hz), 45.9, 30.7, 20.3, 13.7.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.8.

M.p. 121 - 122 °C

HRMS (ESI): $[M+H]^+$ calcd. for C$_{13}$H$_{12}$F$_3$N$_2$O$^+$, 339.0273, found 339.0284.

3-Butyl-2-(difluoromethyl)quinazolin-4(3H)-one (3l)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1l (63.0 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3l as a yellow oil. (48.4 mg, 96%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.30 (d, $J = 9.0$ Hz, 1H), 7.78 (t, $J = 6.9$ Hz, 1H), 7.71 (d, $J = 7.7$ Hz, 1H), 7.56 (t, $J = 8.0$ Hz, 1H), 6.60 (t, $J = 53.6$ Hz, 1H), 4.18 (t, $J = 8.1$ Hz, 2H), 1.98 - 1.57 (m, 2H), 1.56 - 1.33 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.8, 146.8 (t, $J_{(C-F)} = 26.1$ Hz), 146.1, 134.6, 128.8, 128.0, 127.0, 121.9, 114.8 (q, $J_{(C-F)} = 245.8$ Hz), 44.4, 30.9, 20.3, 13.7.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -115.3, -115.4.

HRMS (ESI): $[M+H]^+$ calcd. for C$_{13}$H$_{12}$F$_2$N$_2$O$^+$, 253.1147, found 253.1156.
3-Butyl-2-(chlorodifluoromethyl)quinazolin-4(3H)-one (3m)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1m (70.0 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, $R_f = 0.3$) to give the titled product 3m as a yellow oil. (46.9 mg, 82%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.30 (d, $J = 8.0$ Hz, 1H), 7.99 - 7.67 (m, 2H), 7.60 - 7.56 (m, 1H), 4.21 (t, $J = 8.1$ Hz, 2H), 1.70 - 1.73 (m, 2H), 1.57 - 1.33 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.8, 145.6 (q, $J_{(C-F)} = 28.3$ Hz), 145.1, 134.9, 129.2, 128.5, 127.1, 123.4, 120.5 (q, $J_{(C-F)} = 293.7$ Hz), 45.7, 30.7, 20.3, 13.7.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -54.3.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{13}$H$_{14}$ClF$_2$N$_2$O, 287.0757, found 287.0767.

3-Butyl-2-(perfluoroethyl)quinazolin-4(3H)-one (3n)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1n (76.6 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 m mol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, $R_f = 0.3$) to give the titled product 3n as a yellow oil. (55.7 mg, 87%).
1H NMR (400 MHz, CDCl3) δ 8.32 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 8.1 Hz, 1H), 7.77 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.3 Hz, 1H), 4.17 (t, J = 8.1 Hz, 2H), 1.98 - 1.65 (m, 2H), 1.58 - 1.36 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H).

13C NMR (101 MHz, CDCl3) δ 161.5, 144.8, 142.0 (t, J(C-F) = 27.5 Hz) 134.6, 129.4, 128.5, 126.9, 122.0, 118.3 (qt, J(C-F) = 285.9 Hz, J(C-F) = 33.9 Hz), 111.0 (d, J(C-F) = 36.3 Hz), 44.9, 30.8, 20.2, 13.6.

19F NMR (377 MHz, CDCl3) δ -79.6, -109.8.


3-Butyl-2-(perfluoropropyl)quinazolin-4(3H)-one (3o)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1o (86.6 mg, 0.2 mmol, 1.0 eq.), amine 2a (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)2 (1.7 mg, 0.005 m mol, 2.5 mol%), PPh3 (2.6 mg, 0.01 mmol, 5 mol%), Na2CO3 (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 3o as a yellow oil. (62.2 mg, 84%).

1H NMR (400 MHz, CDCl3) δ 8.31 (d, J = 7.7 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.60 (t, J = 6.9 Hz, 1H), 4.15 (t, J = 8.1 Hz, 2H), 2.04 - 1.65 (m, 2H), 1.61 - 1.28 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H).

13C NMR (101 MHz, CDCl3) δ 161.6, 144.9, 142.4 (t, J(C-F) = 27.2 Hz), 142.1, 134.8, 129.5, 128.5, 127.1, 122.1, 118.2 (qt, J(C-F) = 19.6 Hz, J(C-F) = 33.8 Hz), 112.7 (q, J(C-F) = 276.3 Hz), 45.2, 31.1, 20.3, 13.7.

19F NMR (377 MHz, CDCl3) δ -77.7, -107.0, -121.9.

3-Propyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4a)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2b (29.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 m mol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4a as a yellow oil. (50.7 mg, 99%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (d, $J$ = 7.9 Hz, 1H), 7.97 - 7.73 (m, 2H), 7.62 - 7.58 (m, 1H), 4.08 (t, $J$ = 8.0 Hz, 2H), 2.22 - 1.57 (m, 2H), 1.02 (t, $J$ = 7.4 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.5, 145.2, 142.4 (q, $J_{(C-F)}$ = 35.6 Hz), 134.9, 129.3, 128.6, 127.1, 122.0, 118.4 (q, $J_{(C-F)}$ = 277.0 Hz), 47.0, 22.2, 11.3.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.8.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{12}$H$_{12}$F$_3$N$_2$O, 257.0896, found 257.0905.

3-Pentyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4b)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2c (44.0 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 m mol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4b as a yellow oil. (56.3 mg, 99%).
1H NMR (400 MHz, CDCl3) δ 8.31 (d, J = 8.2 Hz, 1H), 7.97 - 7.63 (m, 2H), 7.71 - 7.42 (m, 1H), 4.11 (t, J = 8.1 Hz, 2H), 1.77 - 1.72 (m, 2H), 1.55 - 1.25 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H).

13C NMR (101 MHz, CDCl3) δ 161.5, 145.2, 142.4 (q, J(C-F) = 35.6 Hz), 134.9, 129.3, 128.6, 127.1, 122.0, 118.4 (q, J(C-F) = 277.0 Hz), 45.6, 29.1, 28.5, 22.3, 14.0.

19F NMR (377 MHz, CDCl3) δ -65.8.

HRMS (ESI): [M+H]+ calcd. for C17H22F3N2O, 327.1697, found 327.1687.

3-Octyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4c)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2d (64.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)2 (1.7 mg, 0.005 m mol, 2.5 mol %), PPh3 (2.6 mg, 0.01 mmol, 5 mol%), Na2CO3 (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product 4c as a yellow oil. (61.3 mg, 94%).

1H NMR (400 MHz, CDCl3) δ 8.31 (d, J = 8.1 Hz, 1H), 7.91 - 7.76 (m, 2H), 7.62 - 7.57 (m, 1H), 4.11 (t, J = 8.0 Hz, 2H), 1.97 - 1.50 (m, 2H), 1.57 -1.36 (m, 2H), 1.37 - 1.22 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H).

13C NMR (101 MHz, CDCl3) δ 161.5, 145.2, 142. (q, J(C-F) = 35.6 Hz), 134.9, 129.3, 128.6, 127.1, 122.0, 118.5 (q, J(C-F) = 277.0 Hz), 45.7, 31.9, 29.3, 29.2, 28.8, 27.0, 22.7, 14.2.

19F NMR (377 MHz, CDCl3) δ -65.8.

HRMS (ESI): [M+H]+ calcd. for C17H22F3N2O, 327.1697, found 327.1687.
3-Decyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4d)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2e (78.7 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.4) to give the titled product 4d as a white solid (65.9 mg, 93%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.32 (d, $J$ = 7.8 Hz, 1H), 7.91 - 7.76 (m, 2H), 7.62 - 7.58 (m, 1H), 4.11 (t, $J$ = 8.1 Hz, 2H), 1.82 - 1.69 (m, 2H), 1.52 - 1.37 (m, 2H), 1.37 - 1.23 (m, 12H), 0.87 (t, $J$ = 6.8 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.5, 145.2, 142.4 (q, $J_{(C-F)}$ = 35.6 Hz), 134.9, 129.3, 128.6, 127.1, 122.1, 118.5 (q, $J_{(C-F)}$ = 277.0 Hz), 45.6, 32.0, 29.6, 29.4, 29.2, 28.8, 27.1, 22.8, 14.2.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.8.

M.p. 71 - 72 °C


3-Isobutyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4e)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2f (36.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via
flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4e as a yellow oil. (48.1 mg, 89%).

**1H NMR (400 MHz, CDCl3)** δ 8.31 (d, J = 7.4 Hz, 1H), 7.93 - 7.75 (m, 2H), 7.63 - 7.59 (m, 1H), 4.04 (d, J = 7.5 Hz, 2H), 2.54 - 2.09 (m, 1H), 0.93 (d, J = 6.8 Hz, 6H).

**13C NMR (101 MHz, CDCl3)** δ 162.0, 144.8, 142.5 (q, J_{C-F} = 34.4 Hz), 134.7, 129.3, 128.3, 126.8, 123.3, 118.7 (q, J_{C-F} = 277.1 Hz), 53.4, 19.7.

**19F NMR (377 MHz, CDCl3)** δ -64.7.

**HRMS (ESI):** [M+H]+ calcd. for C_{13}H_{14}F_3N_2O^+, 271.1053, found 271.1062.

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3-Isopropyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4f)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2g (29.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)_2 (1.7 mg, 0.005 mmol, 2.5 mol %), PPh₃ (2.6 mg, 0.01 mmol, 5 mol%), Na₂CO₃ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4e as a yellow oil. (43 mg, 84%).

**1H NMR (400 MHz, CDCl3)** δ 8.27 (d, J = 7.9 Hz, 1H), 8.05 - 7.69 (m, 2H), 7.60 - 7.56 (m, 1H), 4.66 - 4.56 (m, 1H), 1.70 (d, J = 6.7 Hz, 6H).

**13C NMR (101 MHz, CDCl3)** δ 162.0, 144.8, 142.5 (q, J_{C-F} = 34.4 Hz), 134.7, 129.3, 128.3, 126.8, 123.3, 118.7 (q, J_{C-F} = 277.1 Hz), 53.4, 19.7.

**19F NMR (377 MHz, CDCl3)** δ -64.7.

**HRMS (ESI):** [M+H]+ calcd. for C_{12}H_{12}F_3N_2O^+, 257.0896, found 257.0903.
3-(tert-Butyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4g)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2h (29.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4g as a yellow oil (40 mg, 74%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J = 6.6$ Hz, 1H), 7.24 - 7.19 (m, 1H), 6.73 - 6.63 (m, 2H), 1.52 (s, 9H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 150.0, 140.9 (q, $J_{(C-F)} = 28.9$ Hz), 140.7, 138.6, 128.4, 123.9, 120.4, 116.8 (q, $J_{(C-F)} = 291.4$ Hz), 52.7, 28.6.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.3.

HRMS (ESI): [M+H]$^+$ calcd. for C$_{13}$H$_{14}$F$_3$N$_2$O, 271.1053, found 271.1069.

3-Cyclopropyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4h)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2i (28.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4h as a white solid (46.2 mg, 91%).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (d, $J = 7.6$ Hz, 1H), 7.78 - 7.72 (m, 2H), 7.58 - 7.59 (m, 1H), 3.14 (s, 1H), 1.30 - 1.31 (m, 2H), 1.01 - 0.97 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.5, 144.7, 144.3, 134.9, 129.3, 128.4, 127.0, 122.4, 118.5 (q, $J_{(C,F)} = 277.4$ Hz), 27.8, 9.5.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -64.1.

M.p. 121 - 122 °C

HRMS (ESI): [M+H]+ calcd. for C$_{12}$H$_{16}$F$_3$N$_2$O, 255.0740, found 255.0748.

![Structure](image)

3-Cyclohexyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4i)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2j (49.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4i as a yellow oil (55.1 mg, 93%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.27 (d, $J = 7.8$ Hz, 1H), 7.84 - 7.75 (m, 2H), 7.60 - 7.56 (m, 1H), 4.16 - 7.09 (m, 1H), 3.01 - 2.49 (m, 2H), 1.94 - 1.88 (m, 2H), 1.78 - 1.69 (m, 4H), 1.37 - 1.32 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.1, 144.7, 142.7 (q, $J_{(C,F)} = 34.3$ Hz), 134.7, 129.3, 128.3, 126.9, 123.3, 118.7 (q, $J_{(C,F)} = 277.1$ Hz), 62.0, 28.8, 26.6, 25.1.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -64.6.

HRMS (ESI): [M+H]+ calcd. for C$_{15}$H$_{16}$F$_3$N$_2$O, 297.1209, found 297.1215.
3-((3s,5s,7s)-Adamantan-1-yl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4j)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2k (75.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4j as a white solid (41.1 mg, 59%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.17 (d, $J = 8.2$ Hz, 1H), 8.01 (d, $J = 8.4$ Hz, 1H), 7.87 (t, $J = 7.7$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 2.46 (d, $J = 1.8$ Hz, 6H), 2.31 - 2.27 (m, 3H), 1.81 - 1.68 (m, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.5, 151.7 (q, $J_{(C-F)} = 36.1$ Hz), 150.6, 134.2, 128.6, 128.5, 124.3, 120.0 (q, $J_{(C-F)} = 275.6$ Hz), 118.0, 85.1, 41.4, 36.4, 31.3.

$^{19}$F NMR (377 MHz, CDCl$_3$) δ -70.9.

M.p. 162 - 163 °C

HRMS (ESI): [M+H]$^+$ calcd. for C$_{19}$H$_{20}$F$_3$N$_2$O$^+$, 349.1522, found 349.1531.

3-Benzyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4k)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2l (53.6 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via
flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4k as a white solid (57.2 mg, 94%).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{)} \delta 8.34 (d, J = 8.1 Hz, 1H), 7.92 - 7.79 (m, 2H), 7.65 - 7.61 (m, 1H), 7.33 - 7.28 (m, 3H), 7.19 - 7.19 (d, J = 7.2 Hz, 2H), 5.45 (s, 2H). \]

\[ \text{13C NMR (101 MHz, CDCl}_3\text{)} \delta 161.6, 145.2, 142.5 (q, J_{(C-F)} = 35.7 Hz), 137.5, 135.1, 132.6, 129.5, 129.4, 128.7, 127.4, 126.5, 122.1, 118.3 (q, J_{(C-F)} = 277.4 Hz), 47.9, 21.2. \]

\[ \text{19F NMR (377 MHz, CDCl}_3\text{)} \delta -65.1. \]

M.p. 97 - 98 °C

HRMS (ESI): [M+H]+ calcd. for C_{16}H_{12}F_{3}N_{2}O^{+}, 305.0896, found 305.0903.

3-(4-Methylbenzyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4l)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2m (60.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)_{2} (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\textsubscript{3} (2.6 mg, 0.01 mmol, 5 mol%), Na\textsubscript{2}CO\textsubscript{3} (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4l as a white solid (55.3 mg, 87%).

\[ \text{1H NMR (400 MHz, CDCl}_3\text{)} \delta 8.34 (d, J = 7.8 Hz, 1H), 7.95 - 7.77 (m, 2H), 7.64 - 7.60 (m, 1H), 7.19 - 6.99 (m, 4H), 5.41 (s, 2H), 2.31 (s, 3H). \]

\[ \text{13C NMR (101 MHz, CDCl}_3\text{)} \delta 161.6, 145.2, 142.5 (q, J_{(C-F)} = 35.7 Hz), 137.5, 135.1, 132.6, 129.5, 129.4, 128.7, 127.4, 126.5, 122.1, 118.3 (q, J_{(C-F)} = 277.4 Hz), 47.9, 21.2. \]

\[ \text{19F NMR (377 MHz, CDCl}_3\text{)} \delta -65.1. \]

M.p. 101 - 102 °C

HRMS (ESI): [M+H]+ calcd. for C_{17}H_{14}F_{3}N_{2}O^{+}, 319.1053, found 319.1060.
3-(4-Chlorobenzyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4m)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2n (70.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4m as a white solid (58.8 mg, 81%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.33 (d, $J = 8.0$ Hz, 1H), 7.87 (d, $J = 3.6$ Hz, 2H), 7.66 - 7.62 (m, 1H), 7.28 (d, $J = 8.5$ Hz, 2H), 7.14 (d, $J = 8.5$ Hz, 2H), 5.39 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 161.6, 145.1, 142.2 (q, $J_{(C-F)} = 35.8$ Hz), 135.4, 134.1, 133.7, 129.7, 129.0, 128.8, 128.0, 127.5, 122.0, 118.3 (q, $J_{(C-F)} = 277.3$ Hz), 47.5.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -65.2.

M.p. 110 - 111 °C

HRMS (ESI): [M+H]$^+$ calcd. for C$_{16}$H$_{11}$ClF$_3$N$_2$O$^+$, 339.0507, found 339.0511.

3-(3-Bromobenzyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4n)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2o (92.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via
flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4n as a white solid (70.3 mg, 92%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.33 (d, \(J = 8.0\) Hz, 1H), 7.87 (d, \(J = 4.4\) Hz, 2H), 7.66 - 7.63 (m, 1H), 7.40 (d, \(J = 7.9\) Hz, 1H), 7.33 (s, 1H), 7.18 (t, \(J = 7.8\) Hz, 1H), 7.10 (d, \(J = 7.8\) Hz, 1H), 5.40 (s, 2H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 161.5, 145.1, 142.1 (q, \(J\)\(_{C-F}\) = 39.8 Hz), 137.9, 135.4, 131.0, 130.3, 129.7, 129.5, 128.8, 127.5, 125.1, 122.9, 121.9, 118.3 (q, \(J\)\(_{C-F}\) = 275.5 Hz), 47.3.

\(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -65.2.

M.p. 109 - 110 °C

HRMS (ESI): [M+H]+ calcd. for C\(_{16}\)H\(_{11}\)BrF\(_3\)N\(_2\)O\(_2\), 383.0001, found 383.0004.

3-(Thiophen-2-ylmethyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4o)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2p (59.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)\(_2\) (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\(_3\) (2.6 mg, 0.01 mmol, 5 mol%), Na\(_2\)CO\(_3\) (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4o as a white solid (55.2 mg, 89%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.36 (d, \(J = 7.8\) Hz, 1H), 7.90 - 7.72 (m, 2H), 7.64 - 7.60 (m, 1H), 7.24 (d, \(J = 5.1\) Hz, 1H), 7.15 (d, \(J = 3.3\) Hz, 1H), 6.98 - 6.91 (m, 1H), 5.53 (s, 2H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 161.6, 145.0 141.6 (q, \(J\)\(_{C-F}\) = 35.9 Hz), 137.0, 135.2, 129.6, 128.7, 128.4, 127.3, 126.7, 126.5, 122.0, 118.4 (q, \(J\)\(_{C-F}\) = 277.4 Hz), 43.4.

\(^{19}\)F NMR (377 MHz, CDCl\(_3\)) \(\delta\) -64.6.

M.p. 98 - 99 °C
HRMS (ESI): [M+H]+ calcd. for C_{14}H_{10}F_{3}N_{2}OS+, 311.0460, found 311.0465.

3-Phenyl-2-(trifluoromethyl)quinazolin-4(3H)-one (4p)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2q (46.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4p as a white solid (48.7 mg, 84%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.33 (d, J = 7.8 Hz, 1H), 7.99 - 7.80 (m, 2H), 7.65 (t, J = 8.1 Hz, 1H), 7.60 - 7.50 (m, 3H), 7.30 - 4.32 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 161.8, 145.4, 142.4 (q, $J_{(C-F)}$ = 35.5 Hz), 135.3, 134.9, 130.1, 129.7, 129.4, 129.2, 128.8, 127.5, 122.3, 118.0 (q, $J_{(C-F)}$ = 277.5 Hz).

$^{19}$F NMR (377 MHz, CDCl$_3$) δ -64.0.

M.p. 121 - 122 °C

HRMS (ESI): [M+H]+ calcd. for C$_{15}$H$_{10}$F$_3$N$_2$O$,^+$, 291.0740, found 291.0752.

3-(4-Methoxyphenyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4q)
General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride \textbf{1a} (66.6 mg, 0.2 mmol, 1.0 eq.), amine \textbf{2r} (61.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product \textbf{4q} as a white solid (51.2 mg, 80%).

**$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.33 (d, $J = 7.8$ Hz, 1H), 8.13 - 7.82 (m, 2H), 7.62 - 7.66 (m, 1H), 7.21 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.9$ Hz, 2H), 3.88 (s, 3H).**

**$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.2, 160.6, 145.4, 142.7 (q, $J_{(C,F)} = 35.0$ Hz), 135.3, 130.3, 129.6, 128.8, 127.6, 127.2, 122.3, 118.0 (q, $J_{(C,F)} = 277.5$ Hz), 114.7, 55.7.**

**$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -64.1.**

**M.p.** 177 - 178 °C

**HRMS (ESI):** [M+H]$^+$ calcd. for C$_{16}$H$_{12}$F$_3$N$_2$O$_2^+$, 321.0845, found 321.0852.

3-(4-Bromophenyl)-2-(trifluoromethyl)quinazolin-4(3$H$)-one (\textbf{4r})

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride \textbf{1a} (66.6 mg, 0.2 mmol, 1.0 eq.), amine \textbf{2s} (85.8 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product \textbf{4r} as a white solid (64.0 mg, 87%).

**$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.32 (d, $J = 8.4$ Hz, 1H), 7.98 - 7.79 (m, 2H), 7.69 - 7.58 (m, 3H), 7.19 (d, $J = 8.2$ Hz, 2H).**
13C NMR (101 MHz, CDCl3) δ 161.6, 145.2, 141.9 (q, J_{(C-F)} = 35.6 Hz), 135.5, 133.9, 132.8, 130.9, 129.9, 128.9, 127.6, 124.5, 122.1, 117.9 (q, J_{(C-F)} = 277.6 Hz).

19F NMR (377 MHz, CDCl3) δ -63.9.

M.p. 154 - 155 °C

HRMS (ESI): [M+H]+ calcd. for C_{15}H_{9}BrF_{3}N_{2}O+, 368.9845, found 368.9851.

3-(o-Tolyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4s)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2t (53.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol %), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4s as a white solid (49.9 mg, 82%).

1H NMR (400 MHz, CDCl3) δ 8.36 (d, J = 7.8 Hz, 1H), 7.93 - 7.88 (m, 2H), 7.66 (t, J = 8.2 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.40 - 7.34 (m, 2H), 7.21 (d, J = 7.8 Hz, 1H), 2.13 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 161.1, 145.5, 142.5 (q, J_{(C-F)} = 35.4 Hz), 137.0, 135.4, 134.0, 131.1, 130.4, 129.7, 129.2, 128.9, 127.6, 127.0, 122.2, 117.9 (q, J_{(C-F)} = 277.4 Hz), 17.6.

19F NMR (377 MHz, CDCl3) δ -65.5.

M.p. 122 - 123 °C

HRMS (ESI): [M+H]+ calcd. for C$_{16}$H$_{12}$F$_3$N$_2$O+, 305.0896, found 305.0904.
3-(Naphthalen-1-yl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4t)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1\textit{a} (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2\textit{u} (71.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)\textsubscript{2} (1.7 mg, 0.005 mmol, 2.5 mol %), PPh\textsubscript{3} (2.6 mg, 0.01 mmol, 5 mol%), Na\textsubscript{2}CO\textsubscript{3} (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 4\textit{t} as a white solid (61.2 mg, 90%).

$^{1}$H NMR (400 MHz, CDCl\textsubscript{3}) $\delta$ 8.38 (d, $J = 8.0$ Hz, 1H), 8.00 - 7.95 (m, 1H), 7.98 (t, $J = 7.5$ Hz, 2H), 7.93 (t, $J = 7.7$ Hz, 1H), 7.69 (t, $J = 7.5$ Hz, 1H), 7.61 (t, $J = 7.8$ Hz, 1H), 7.55 (t, $J = 6.9$ Hz, 1H), 7.51 - 7.48 (m, 2H), 7.43 (d, $J = 8.3$ Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl\textsubscript{3}) $\delta$ 161.6, 145.6, 143.1 (q, $J_{(C-F)} = 35.4$ Hz), 135.5, 134.3, 131.7, 130.9, 130.7, 129.8, 129.0, 128.8, 127.9, 127.8, 127.5, 126.9, 125.2, 122.2, 121.8, 117.9 (q, $J_{(C-F)} = 277.9$ Hz).

$^{19}$F NMR (377 MHz, CDCl\textsubscript{3}) $\delta$ -64.8.

M.p. 164 - 165 °C

HRMS (ESI): [M+H]+ calcd. for C\textsubscript{19}H\textsubscript{12}F\textsubscript{3}N\textsubscript{2}O\textsuperscript{+}, 341.0896, found 341.0905.

3-(Naphthalen-2-yl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4u)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1\textit{a} (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2\textit{v} (71.5 mg, 0.5 mmol, 2.5 eq.), Pd(TFA)\textsubscript{2} (1.7 mg, 0.005 mmol, 2.5 mol %),
PPh₃ (2.6 mg, 0.01 mmol, 5 mol%), Na₂CO₃ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 4u as a white solid (62.6 mg, 82%).

1H NMR (400 MHz, CDCl₃) δ 8.36 (d, J = 7.9 Hz, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.98 - 7.87 (m, 4H), 7.82 (s, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.64 - 7.54 (m, 2H), 7.38 (d, J = 8.6 Hz, 1H).

13C NMR (101 MHz, CDCl₃) δ 162.1, 145.4, 142.5 (q, J(C-F) = 35.7 Hz), 135.4, 133.7, 133.3, 132.4, 129.7, 129.5, 128.9, 128.5, 128.4, 128.1, 127.7, 127.6, 127.1, 126.3, 122.3, 118.1 (q, J(C-F) = 277.4 Hz).

19F NMR (377 MHz, CDCl₃) δ -63.8.

M.p. 168 - 169 °C


3,3'-(Ethane-1,2-diyl)bis(2-(trifluoromethyl)quinazolin-4(3H)-one) (4v)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (133.2 mg, 0.4 mmol, 2.0 eq.), amine 2w (12.0 mg, 0.2 mmol, 1.0 eq.), Pd(TFA)₂ (3.4 mg, 0.01 mmol, 5 mol %), PPh₃ (5.2 mg, 0.02 mmol, 10 mol%), Na₂CO₃ (84.8 mg, 0.8 mmol, 4.0 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.2) to give the titled product 4v as a white solid (62.7 mg, 69%).

1H NMR (400 MHz, CDCl₃) δ 8.12 (d, J = 8.1 Hz, 2H), 7.92 - 7.75 (m, 4H), 7.57 - 7.53 (m, 2H), 4.68 (s, 4H).

13C NMR (101 MHz, CDCl₃) δ 162.1, 144.9, 141.7 (q, J(C-F) = 35.8 Hz), 135.2, 129.6, 128.7, 127.1, 121.6, 118.2 (q, J(C-F) = 276.9 Hz), 45.6.

19F NMR (377 MHz, CDCl₃) δ -65.4, -65.5.

M.p. 216 - 217 °C
HRMS (ESI): [M+H]+ calcd. for C_{20}H_{13}F_{6}N_{4}O_{2}^+, 455.0937, found 455.0941.

(Z)-N-Butyl-2,2,2-trifluoro-N’-(2-iodophenyl)acetimidamide (5a)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (333 mg, 1.0 mmol, 1.0 eq.), amine 2a (183 mg, 2.5 mmol, 2.5 eq.), Na_{2}CO_{3} (106 mg, 1.0 mmol, 5.0 eq.) and 1,4-dioxane (5 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product 5a as yellow oil (366.3 mg, 99%).

{\textbf{1H NMR (400 MHz, (CD}_{3}\text{SO})}} \delta \ 8.01 \ (s, 1H), 7.76 \ (d, \ J = 6.7 \ Hz, 1H), 7.26 \ (t, \ J = 7.0 \ Hz, 1H), 6.78 \ (d, \ J = 7.1 \ Hz, 1H), 6.73 \ (t, \ J = 7.6 \ Hz, 1H), 3.31 - 2.73 \ (m, 2H), 1.71 - 1.39 \ (m, 2H), 1.39 - 1.11 \ (m, 2H), 0.97 - 0.71 \ (m, 3H).

{\textbf{13C NMR (101 MHz, (CD}_{3}\text{SO})}} \delta \ 149.7, 141.8 \ (q, \ J_{C-F} = 27.0 \ Hz), 137.9, 128.4, 123.7, 120.4, 117.3 \ (q, \ J_{C-F} = 35.4 \ Hz), 92.6, 41.0, 30.4, 19.5, 13.5.

{\textbf{19F NMR (377 MHz, (CD}_{3}\text{SO})}} \delta -64.2, -74.1.

HRMS (ESI): [M+H]+ calcd. for C_{12}H_{15}F_{3}N_{2}^+, 371.0227, found 371.0235.

2-(4-Oxo-2-(trifluoromethyl)quinazolin-3(4H)-yl)isoindoline-1,3-dione (6)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2x (38.9 mg, 0.24 mmol, 1.2 eq.), Pd(TFA)_{2} (1.7 mg, 0.005 mmol, 2.5 mol %), PPh_{3} (2.6 mg, 0.01 mmol, 5 mol%), Na_{2}CO_{3} (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via
flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.2) to give the titled product 6 as a white solid (40.9 mg, 57%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (d, $J$ = 7.8 Hz, 1H), 8.04 - 8.02 (m, 2H), 7.94 (d, $J$ = 4.2 Hz, 2H), 7.92 - 7.90 (m, 2H), 7.75 - 7.62 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.8, 157.6, 144.8, 142.0 (q, $J_{(C-F)}$ = 37.0 Hz), 136.2, 135.7, 130.3, 129.6, 128.0, 125.0, 122.1, 117.3 (q, $J_{(C-F)}$ = 277.4 Hz).

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -68.4.

M.p. 147 - 149 °C

HRMS (ESI): [M+H]$^+$ calcd. for C$_{17}$H$_9$F$_3$N$_3$O$_3$, 360.0591, found 360.0598.

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2y (36.8 mg, 0.24 mmol, 1.2 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, Rf = 0.2) to give the titled product 7 as a white solid (50.4 mg, 72%).

$^1$H NMR (400 MHz, DMSO) $\delta$ 8.91 (s, 1H), 8.78 (s, 1H), 8.25 (d, $J$ = 7.8 Hz, 1H), 7.95 (t, $J$ = 7.5 Hz, 1H), 7.84 (d, $J$ = 8.0 Hz, 1H), 7.73 (t, $J$ = 7.5 Hz, 1H), 6.75 - 6.58 (m, 2H), 6.50 (d, $J$ = 7.8 Hz, 1H), 4.11 (t, $J$ = 8.0 Hz, 2H), 2.79 (t, $J$ = 10.0 Hz, 2H).

$^{13}$C NMR (101 MHz, DMSO) $\delta$ 160.6, 145.4, 144.5, 144.1, 141.5 (q, $J_{(C-F)}$ = 35.0 Hz), 135.2, 129.6, 128.4, 128.1, 126.5, 121.6, 119.2, 118.2 (q, $J_{(C-F)}$ = 277.5 Hz), 115.8, 46.7, 33.4.

$^{19}$F NMR (377 MHz, DMSO) $\delta$ -64.9.

M.p. 179- 180 °C

HRMS (ESI): [M+H]$^+$ calcd. for C$_{17}$H$_{14}$F$_3$N$_2$O$_3^+$, 351.0951, found 351.0954.
3-((1R,4aS,10aR)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (8)

General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (66.6 mg, 0.2 mmol, 1.0 eq.), amine 2z (68.5 mg, 0.24 mmol, 1.2 eq.), Pd(TFA)$_2$ (1.7 mg, 0.005 mmol, 2.5 mol%), PPh$_3$ (2.6 mg, 0.01 mmol, 5 mol%), Na$_2$CO$_3$ (42.4 mg, 0.4 mmol, 2 eq.), TFBen (210.0 mg, 1 mmol, 5.0 eq.) and 1,4-dioxane (2 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.2) to give the titled product 8 as a white solid (55.0 mg, 57%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.28 (d, $J = 7.9$ Hz, 1H), 7.87 - 7.77 (m, 2H), 7.62 - 7.58 (m, 1H), 7.15 (d, $J = 8.2$ Hz, 1H), 7.00 (d, $J = 8.1$ Hz, 1H), 6.94 (s, 1H), 3.03 - 3.00 (m, 2H), 2.94 - 2.75 (m, 1H), 2.25 (d, $J = 12.9$ Hz, 1H), 2.04 - 2.00 (m, 1H), 1.93 - 1.87 (m, 1H), 1.76 - 1.63 (m, 2H), 1.65 - 1.53 (m, 1H), 1.45 - 1.33 (m, 1H), 1.30 - 1.26 (m, 6H), 1.23 (d, $J = 6.9$ Hz, 6H), 1.09 (s, 3H), 0.90 - 0.86 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.1, 147.3, 145.8, 144.8, 143.4 (q, $J_{(C,F)} = 34.7$ Hz), 134.9, 134.7, 129.4, 128.3, 127.5, 127.0, 124.1, 124.0, 122.0, 118.4 (q, $J_{(C,F)} = 277.9$ Hz), 77.2, 55.1, 48.1, 40.1, 38.1, 36.0, 33.6, 30.4, 29.8, 25.9, 24.1, 22.8, 19.9, 18.6.

$^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -62.3.

M.p. 221 - 222 °C

HRMS (ESI): [M+H]$^+$ calcd. for C$_{29}$H$_{34}$F$_3$N$_2$O$^+$, 483.2618, found 483.2622.

3-(2-(1H-Indol-3-yl)ethyl)-2-(trifluoromethyl)quinazolin-4(3H)-one (4w)
General Procedure was followed with (2-iodophenyl)trifluoroacetimide chloride 1a (333.0 mg, 1.0 mmol, 1.0 eq.), amine 2aa (192.5 mg, 1.2 mmol, 1.2 eq.), Pd(TFA)$_2$ (8.5 mg, 0.025 mmol, 2.5 mol %), PPh$_3$ (13 mg, 0.05 mmol, 5 mol%), Na$_2$CO$_3$ (212 mg, 2.0 mmol, 2 eq.), TFBen (420.0 mg, 2.0 mmol, 2.0 eq.) and 1,4-dioxane (5 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 10:1, Rf = 0.2) to give the titled product 4w as a white solid (296.3 mg, 83%).

$^1$H NMR (400 MHz, DMSO) $\delta$ 10.98 (s, 1H), 8.35 - 8.22 (m, 1H), 7.96 - 7.91 (m, 1H), 7.84 (t, $J = 6.9$ Hz, 1H), 7.78 - 7.66 (m, 2H), 7.39 (d, $J = 8.0$ Hz, 1H), 7.26 (s, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 7.03 (t, $J = 7.4$ Hz, 1H), 4.26 (t, $J = 8.0$ Hz, 2H), 3.12 (t, $J = 8.0$ Hz, 2H).

$^{13}$C NMR (101 MHz, DMSO) $\delta$ 160.8, 144.5, 141.6 (q, $J_{C,F} = 35.0$ Hz), 136.3, 135.1, 129.5, 128.1, 127.0, 126.5, 123.1, 121.7, 121.1, 118.6, 118.2 (q, $J_{C,F} = 277.0$ Hz), 118.0, 111.6, 110.1, 45.8, 24.1.

$^{19}$F NMR (377 MHz, DMSO) $\delta$ -64.8.

M.p. 179-180 ºC

HRMS (ESI): [M+H]+ calcd. for C$_{19}$H$_{15}$F$_3$N$_3$O$^+$, 358.1162, found 358.1167.


General Procedure was followed with 4w (357.0 mg, 1 mmol, 1.0 eq.), HOAc (3 mL) and HCl (0.5 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 5:1, Rf = 0.2) to give the titled product 9 as a white solid (346.3 mg, 97%).

$^1$H NMR (400 MHz, DMSO) $\delta$ 10.97 (s, 1H), 7.78 (d, $J = 7.1$ Hz, 1H), 7.75 (s, 1H), 7.59 - 7.54 (m, 2H), 7.39 (t, $J = 7.7$ Hz, 1H), 7.24 (t, $J = 7.5$ Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 6.91 - 6.83 (m, 2H), 5.16 - 5.11 (m, 1H), 3.26 (t, $J = 12.5$ Hz, 1H), 2.96 (d, $J = 19.3$ Hz, 1H), 2.88 - 2.71 (m, 1H).

$^{13}$C NMR (101 MHz, DMSO) $\delta$ 161.4, 143.8, 136.9, 133.9, 127.7, 125.5 (q, $J_{C,F} = 300.1$ Hz), 124.9, 124.7, 123.1, 119.5, 119.1, 119.0, 114.8, 114.7, 112.2, 112.1, 37.1, 19.8.

$^{19}$F NMR (377 MHz, DMSO) $\delta$ -75.9.
M.p. 265 - 266 °C

HRMS (ESI): [M+H]+ calcd. for C$_{19}$H$_{15}$F$_3$N$_3$O$, 358.1162$, found 358.1169.

![Chemical structure](image1)


General Procedure was followed with 9 (357.0 mg, 1.0 mmol, 1.0 eq.), KOH (200.0 mg), EtOH (5.0 mL) and H$_2$O (1.5 mL). Upon completion the mixture was cooled and the crystals were collected, washed, and dried to give the titled product 10 as a white solid (275.5 mg, 96%).

$^1$H NMR (400 MHz, CDCl$_3$) δ 9.91 (s, 1H), 8.33 (d, $J = 7.8$ Hz, 1H), 7.71 - 7.65 (m, 1H), 7.65 - 7.59 (m, 2H), 7.47 - 7.37 (m, 1H), 7.24 - 7.26 (m, 2H), 7.18 - 7.14 (m, 1H), 4.59 (t, $J = 6.9$ Hz, 2H), 3.23 (t, $J = 6.9$ Hz, 2H).

$^{13}$C NMR (101 MHz, DMSO) δ 161.1, 147.8, 145.7, 139.1, 134.8, 127.6, 127.0, 126.9, 126.4, 125.4, 125.2, 121.2, 120.4, 120.2, 118.3, 113.0, 41.3, 19.4.

M.p. 255 - 256 °C

HRMS (ESI): [M+H]+ calcd. for C$_{18}$H$_{14}$N$_3$O$+$ 288.1131, found 288.1144.

![Chemical structure](image2)

Benzene-1,3,5-triyl triformate (TFBen)

General Procedure was followed with Formic acid (8.4 mL, 222.8 mmol, 5.0 equiv.), acetic anhydride (16.8 mL, 178.2 mmol, 4.0 equiv.), 1,3,5-trihydroxybenzene (5.62 g, 44.6 mmol, 1.0 equiv.) and NaOAc (1.83 g, 22.3 mmol, 0.5 equiv.). The mixture was stirred for 4 h in a water bath and then diluted with toluene (100 mL), washed with H$_2$O (50 mL) twice. Keep the organic phase in fridge (2-8 °C) overnight. Then filtered and dried in vacuo to afford the desired product benzene-1,3,5-triyl triformate (TFBen) (5.1 g, 55%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.24 (s, 3H), 6.97 (s, 3H).
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 158.1, 150.3, 112.6.

5 References


6 Copy of $^1$H, $^{13}$C and $^{19}$F NMR Spectra of Products

$^1$H NMR 400 MHz, CDCl$_3$

$^{13}$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^{1}$H NMR 400 MHz, CDCl$_3$

$^{13}$C NMR 101 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$F NMR 377 MHz, CDCl$_3$
$\text{3d}$

$^{13}\text{C NMR 101 MHz, CDCl}_3$

$\text{3d}$

$^{19}\text{F NMR 377 MHz, CDCl}_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{1}$H NMR 400 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
49

3g

$^1$H NMR 400 MHz, CDCl$_3$

3g

$^{13}$C NMR 101 MHz, CDCl$_3$
$\text{^19F NMR 377 MHz, CDCl}_3$

$\text{^1}H \text{ NMR 400 MHz, CDCl}_3$
$3h$

$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 101 MHz, CDCl$_3$
$\text{F NMR 377 MHz, CDCl}_3$

$\text{H NMR 400 MHz, CDCl}_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
3k

$^1$H NMR 400 MHz, CDCl$_3$

3k

$^{13}$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$F NMR 377 MHz, CDCl$_3$
4a

$^{13}$C NMR 101 MHz, CDCl$_3$

4a

$^{19}$F NMR 377 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^{13}$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
4d

$^{1}H$ NMR 400 MHz, CDCl$_3$

4d

$^{13}C$ NMR 101 MHz, CDCl$_3$
\textbf{4d}

$^{19}$F NMR 377 MHz, CDCl$_3$

\textbf{4e}

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
4f
\( ^{19}F \) NMR 377 MHz, CDCl\textsubscript{3}

4g
\( ^{1}H \) NMR 400 MHz, CDCl\textsubscript{3}
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
4h

$^1$H NMR 400 MHz, CDCl$_3$

$^{13}$C NMR 101 MHz, CDCl$_3$
**4h**

$^{19}$F NMR 377 MHz, CDCl$_3$

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**4i**

$^1$H NMR 400 MHz, CDCl$_3$
**S75**

**13C NMR 101 MHz, CDCl₃**

- 152.28, 144.77, 143.24, 134.30, 132.90, 131.28, 123.28, 122.87, 117.47, 114.61

**19F NMR 377 MHz, CDCl₃**

- -61.56, -28.81, -28.81
$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 101 MHz, CDCl$_3$
\[ ^1\text{H NMR 400 MHz, CDCl}_3 \]

\[ ^1\text{C NMR 101 MHz, CDCl}_3 \]
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^4$H NMR 400 MHz, CDCl$_3$

$^1$H NMR 101 MHz, CDCl$_3$

$^13$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
4q

$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
**4r**

$^{19}$F NMR 377 MHz, CDCl$_3$

**4s**

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{19}F$ NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl$_3$

$^{19}$F NMR 377 MHz, CDCl$_3$
$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 101 MHz, CDCl$_3$
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$\text{S96}$
$^1$H NMR 400 MHz, (CD$_3$)$_2$SO

$^{13}$C NMR 101 MHz, (CD$_3$)$_2$SO
$^{19}$F NMR 377 MHz, CDCl$_3$

$^1$H NMR 400 MHz, CDCl$_3$
$^{13}$C NMR 101 MHz, CDCl₃

$^{19}$F NMR 377 MHz, CDCl₃
$^{13}$C NMR 101 MHz, DMSO

$^1$H NMR 400 MHz, DMSO
$^1$H NMR 400 MHz, DMSO

$^1$F NMR 377 MHz, DMSO
$^1$H NMR 377 MHz, DMSO

$^1$C NMR 101 MHz, DMSO

$^{19}$F NMR 377 MHz, DMSO
$^{1}H$ NMR 400 MHz, CDCl$_3$

$^{13}C$ NMR 101 MHz, DMSO
TFBen

$^1$H NMR 400 MHz, CDCl$_3$

TFBen

$^{13}$C NMR 101 MHz, CDCl$_3$
$^{1}H$ NMR 400 MHz, DMSO

$^{13}C$ NMR 101 MHz, DMSO
$^{19}$F NMR 377 MHz, DMSO

5a

Structure of 5a