# 2-Substituted 4-(Trifluoromethyl)phenols by Directed *ortho*-Lithiation

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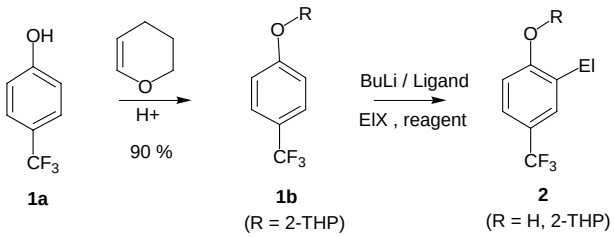
**Abstract:** A broad variety of 2-substituted 4-(trifluoromethyl)phenols can be prepared in a large scale by *o*-lithiation and reaction with electrophiles in good to excellent yields. The key for the selectivity is the superior *ortho*-directing effect of the THP-protected hydroxy group (OTHP) as compared to the $CF_3$-group.

**Key Words:** arylations, electrophilic aromatic substitutions, lithiation, protecting groups, 4-(trifluoromethyl)phenol

In the course of the development of new methods for the synthesis of intermediates for pharmaceuticals we became interested in 2-substituted 4-(trifluoromethyl)phenols. Although usually rather low, the reactivity of the trifluoromethyl group is greatly enhanced in *p*-trifluoromethyl-substituted phenols.[1] Traces of hydrogen fluoride or basic conditions induce polymerization.[2] Reaction with aqueous ammonia furnishes the corresponding nitrile.[3] When 4-(trifluoromethyl)phenol is heated, decomposition is observed at 130 °C.[4] Due to conjugation, 1,6-elimination of hydrogen fluoride and formation of 4-(difluoromethylene)-2,5-cyclohexadiene-1-one seems to be the most prominent reaction.[5] In most cases this elimination is the reason why yields of substitution of 4-(trifluoromethyl)phenols are poor (< 50%).[6,7a,b,8a,b] In other cases very toxic reagents (e.g. anhydrous hydrogen fluoride,[7c,d] chloromethyl methyl ether[8g]) are used or the syntheses are tedious.[8–10]

We became interested in the directed *ortho*-lithiation, a general method which offers the possibility of synthesising all of these derivatives of 4-(trifluoromethyl)phenol selectively, in good yields, short reaction times and convenience of handling. *O*-Tetrahydropyranyl (OTHP) is a very efficient *ortho*-directing group.[11] Due to the stabilising effect, the lithium complexes are stable enough to avoid very low reaction temperatures.[12]

For the preparation of the THP ether **1b** we used a modified procedure.[13] By addition of 4-(trifluoromethyl)phenol (**1a**) to a solution of 3,4-dihyro-2*H*-pyran (DHP) and a catalytic amount of HCl/dioxane in dichloromethane the ether **1b** was obtained in 90% yield (Scheme). Due to its distinct sensitivity to acid, the inverse sequence of addition of DHP to phenol **1a** produced a considerable amount of insoluble solid.




**Scheme**

Compound **1b** was lithiated with butyllithium at –70 °C or with butyllithium/TMEDA at –10 °C or –20 °C and subsequently quenched with an electrophile ElX (Table). Although $CF_3$ is a strongly electron-withdrawing group, it has the least *ortho*-directing aptitude because of its bulkiness. Therefore, the deprotonation occurs at the *ortho*-position relative to the *O*-containing function.[8h,14] The protective group can be removed during workup by addition of HCl/dioxane (entry 1 and 5), an advantage as compared to the methoxymethyl group, which requires a supplementary deprotection step.[8h,15] Moreover, the methoxymethyl group has to be introduced using a highly toxic chloro compound. A very efficient and convenient method for the chlorination of **1b** was the addition of hexachloroethane (entry 6).[16] For the synthesis of the boronic ester **2g** an excess of triisopropyl borate and an inverse sequence of addition was important to prevent a subsequent substitution of a second methoxy group. Transesterification with diethanolamine gave a solid product which could be purified by crystallization (entry 7).[17]

In conclusion, we have developed a versatile method for the synthesis of 2-substituted 4-(trifluoromethyl)phenols in a large scale by *ortho*-lithiation and reaction with a broad variety of electrophiles in good to excellent yields. Reaction times are short. High yields and high selectivity (other regioisomeres were not detected), caused by a superior *o*-directing effect of OTHP compared to the $CF_3$-group, facilitate the purification of the products, and the use of highly toxic chemicals can be omitted.

4-(Trifluoromethyl)phenol (ABCR), trimethyl borate (Aldrich) and trifluoroborane in $Et_2O$ (Aldrich) are commercially available. *N*-Methoxy-*N*-methylpropanamide was a generous gift from Dr. T. Zierke, BASF AG. Petroleum ether used had bp 50−70 °C.

**2-[4-Trifluoromethyl)phenoxy]tetrahydro-2*H*-pyran (1b)**

To a solution of 3,4-dihydro-2*H*-pyran (525 g, 6.25 mol) and HCl in dioxane (1 mL, 4 M) in $CH_2Cl_2$ (1 L) was added dropwise 4-(trifluoromethyl)phenol (**1a**; 400 g, 2.47 mol) at r.t. The reaction was

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**Table** Lithiation of **1b** with BuLi, Temperature and Duration of Lithiation, the Electrophiles (ElX) Added, and Yields of Isolated Products **2**

| Entry | Ligand | T (°C) | t (min) | ElX | Product | El | R | Yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | TMEDA | –10 | 45 | DMF[a] | **2a** | CHO | H | 75 |
| 2 | TMEDA | –10 | 15 | EtCO[NMe(OMe)] | **2b** | EtCO | 2-THP | 62 |
| 3 | TMEDA | –20 | 30 | $Me_3SiCl$ | **2c** | $Me_3Si$ | 2-THP | 90 |
| 4 | TMEDA | –20 | 30 | PhSSPh | **2d** | PhS | 2-THP | 83 |
| 5 | TMEDA | –20 | 30 | $CO_2$[a] | **2e** | $CO_2H$ | H | 53 |
| 6 | – | –70 | 30 | $C_2Cl_6$ | **2f** | Cl | 2-THP | 89 |
| 7 | – | –70 | 45 | B(OPr-*i*)$_3$[b] | **2g** | $B(OC_2H_4)_2NH$ | 2-THP | 68 |

[a] Acidic workup.
[b] Inverse sequence of addition, and subsequent addition of $(HOC_2H_4)_2NH$.

distinctly exothermic. After stirring overnight, the mixture was extracted with an aq solution of $NaHCO_3$ (200 mL) and the organic phase was dried ($Na_2SO_4$) and evaporated. The residue (618 g, GC: 90%, 2.28 mol, 92%) was used in the following step without further purification. It gradually crystallized completely on standing at r.t.; mp 38–39 °C.

HRMS: *m*/*z* calcd for $C_7H_4OF_3^-$ [(M–DHP)$^-$]: 161.0219, found: 161.0220.

EI-NMS (70 eV): *m*/*z* (%) = 246 ([M$^+$], 0.245).

MS (70 eV): *m*/*z* (%) = no [M$^+$], 169 (15), 121 (10), 97 (15), 85 (96), 83 (17), 71 (18), 57 (35), 55 (25), 43 (35), 41 (22), 29 (10), 18 (100), 17 (30).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 1.57 (m, 3 H, THP), 1.80 (m, 2 H, THP), 1.95 (m, 1 H, THP), 3.54 (m, 1 H, THP), 3.80 (m, 1 H, THP), 5.45 (m, 1 H, THP), 7.10 (d, $^3J$ = 8.8 Hz, 2 $H_{arom}$), 7.50 (d, $^3J$ = 8.8 Hz, 2 $H_{arom}$).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = 18.9 (t, $CH_2$-THP), 25.5 (t, $CH_2$-THP), 30.5 (t, $CH_2$-THP), 62.4 (t, CH-$_2$-THP), 96.6 (t, CH-THP), 116.7 (2 d, $CH_{arom}$), 122.4 (q, *J* = 271.2 Hz, $CF_3$), 124.9 (q, $^2J$ = 33.1 Hz, *C*–$CF_3$), 127.1 (2 d, $CH_{arom}$), 160.0 (s, $C_{arom}$–O).

**2-Hydroxy-5-(trifluoromethyl)benzaldehyde (2a)**
A 2 L round-bottomed flask was filled with TMEDA (241 g, 2.08 mol) and BuLi in hexane (1.3 L, 1.63 M, 2.12 mol) was added to the sirred content over a period of 30 min at –10 °C. After 45 min a melt of **1b** (400 g, GC 92%, 1.5 mol) was added dropwise at –10 °C over a period of 30 min, whereupon the lithium complex precipitated. After 2 h, DMF (152 g, 2.08 mol) was added. A cloudy solution was produced, which after 15 min was added dropwise over a period of 30 min to a solution of HCl (38%, 750 mL) in $H_2O$ (500 mL) at a maximum temperature of 45 °C. There was a rapid evolution of gas. After stirring overnight, the aqueous phase was separated, the organic phase was treated with an HCl/dioxane solution (4 M, 70 mL) and the mixture was once again stirred overnight. The product crystallized on cooling to –30 °C (2–3 h). It was filtered by suction, washed with cold pentane (500 mL) and dried in air to give **2a** (220 g GC: 98.3%, 1.13 mol, 75%) as colorless crystals; mp 60–62 °C.

HRMS: *m*/*z* calcd for $C_8H_4O_2F_3^-$ [(M–H)$^-$]: 189.0168, found: 189.0171.

MS (70 eV): *m*/*z* (%) = 190 ([M$^+$], 94), 189 (100), 172 (20), 161 (30), 144 (20), 113 (10), 69 (12), 28 (25), 18 (10).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, $^3J$ = 9.2 Hz, 1 $H_{arom}$), 7.75 (dd, $^3J$ = 9.2 Hz, $^4J$ = 1.8 Hz, 1 $H_{arom}$), 7.85 (d, $^4J$ = 1.8 Hz, 1 $H_{arom}$), 9.95 (s, 1 H, CHO).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = 118.8 (d, $CH_{arom}$), 120.0 (s, *C*–CHO), 122.5 (q, $^2J$ = 32.8 Hz, *C*–$CF_3$), 125.1 (q, *J* = 271.6 Hz, $CF_3$), 131.2 (d, $CH_{arom}$), 133.5 (d, $CH_{arom}$), 164.0 (s, $C_{arom}$–OH), 196.0 (d, CHO).

**1-[2-(Tetrahydro-2*H*-pyran-2-yloxy)-5-(trifluoromethyl)-phenyl]propan-1-one (2b)**
TMEDA (24 g, 0.207 mol) was placed in a 500 mL round-bottomed flask and while stirring BuLi in hexane (130 mL, 1.63 M, 0.212 mol) was added dropwise at –10 °C over a period of about 30 min. After 15 min a melt of **1b** (40 g, GC 90%, 0.146 mol) was added dropwise at –10 °C over a period of 30 min, whereupon the lithium complex precipitated. After 1 h, *N*-methoxy-*N*-methylpropanamide (24 g, 0.205 mol) was added. A cloudy solution was produced, which after 1 h was added dropwise to a solution of HCl (32%, 60 mL) in $H_2O$ (40 mL). The aqueous phase was separated and extracted with hexane and the organic phases were evaporated. The residue was recrystallized from hexane at –50 °C. The product **2b** (27.3 g, HPLC 96%, 91 mmol, 62%) was obtained as colorless crystals; mp 54–57 °C.

MS (70 eV): *m*/*z* (%) = no [M$^+$], 218 (4), 189 (20), 169 (4), 111 (5), 97 (8), 85 (100), 71 (12), 57 (28), 43 (22), 29 (12), 18 (56).

$^1$H NMR (360 MHz, $CDCl_3$): δ = 1.20 (t, $^3J$ = 7.0 Hz, 3 H, C$H_3$CH$_2$), 1.75 (m, 6 H, THP), 3.05 (q, $^3J$ = 7.0 Hz, 2 H, CH$_3$C$H_2$), 3.65 (m, 1 H, THP), 3.80 (m, 1 H, THP), 5.65 (m, 1 H, THP) 7.30 (d, $^3J$ = 8.8 Hz, 1 $H_{arom}$), 7.67 (dd, $^3J$ = 8.8 Hz, $^4J$ = 2.2 Hz, 1 $H_{arom}$), 7.85 (d, $^4J$ = 2.2 Hz, 1 $H_{arom}$).

$^{13}$C NMR (360 MHz, $CDCl_3$): δ = 8.5 (q, $CH_3$), 18.6 (t, $CH_2$-THP), 24.9 (t, $CH_2$-THP), 30.1 (t, $CH_2$-THP), 37.1 (t, $CH_3CH_2$), 62.2 (t, $CH_2$-THP), 97.0 (d, CH-THP), 115.5 (d, $CH_{arom}$), 123.8 (q, $^2J$ = 33.3 Hz, *C*–$CF_3$), 124.0 (q, *J* = 271.6 Hz, $CF_3$), 127.5 (d, $CH_{arom}$), 129.1 (s, *C*–CHO), 129.8 (d, $CH_{arom}$), 158.2 (s, $C_{arom}$–O), 202.2 (s, C=O).

**Trimethyl[2-(tetrahydro-2*H*-pyran-2-yloxy)-5-(trifluoromethyl)phenyl]silane (2c)**
To a stirred mixture of TMEDA (2.9 g, 25 mmol) and BuLi in hexane (15.9 mL, 15%, 26 mmol) in a 100 mL round-bottomed flask at –20 °C was added dropwise a solution of **1b** (5.0 g, HPLC: 98%, 19.9 mmol) in THF (10 mL). After 30 min, chloro(trimethyl)silane (2.63 g, 24 mmol) and after 2 h $H_2O$ (5 mL) were added. The mixture was allowed to warm up to 20 °C and the phases were separated. The organic phase was washed once with brine and the

combined aqueous phases were washed with *tert*-butyl methyl ether (3 × 5 mL). The organic phases were combined, dried ($Na_2SO_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, petroleum ether–*tert*-butyl methyl ether, 5:1). The title compound (5.8 g, HPLC: 98%, 17.9 mmol, 90%) was obtained as a colorless solid; mp 43–46 °C.

MS (70 eV): *m*/*z* (%) = no [$M^+$], 251 (5), 219 (5), 203 (7), 169 (7), 85 (100), 67 (6), 57 (12), 41 (7), 18 (17).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.35 (s, 9 H, TMS), 1.85 (m, 6 H, THP), 3.65 (m, 1 H, THP), 3.85 (m, 1 H, THP), 5.50 (m, 1 H, THP), 7.17 (d, $^3J$ = 8.5 Hz, 1 $H_{arom}$), 7.55 (dd, $^3J$ = 8.5 Hz, $^4J$ = 2.4 Hz, 1 $H_{arom}$), 7.60 (d, $^4J$ = 2.4 Hz, 1 $H_{arom}$).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = –1.0 (q, 3 $CH_3$), 18.5 (t, CH-$_2$-THP), 25.1 (t, CH-$_2$-THP), 30.1 (t, CH-$_2$-THP), 61.7 (t, CH-$_2$-THP), 96.0 (d, CH--THP), 112.5 (d, $CH_{arom}$), 123.1 (q, $^2J$ = 32.0 Hz, *C*–$CF_3$), 124.7 (q, *J* = 271.5 Hz, $CF_3$), 128.2 (d, $CH_{arom}$), 128.8 (s, $C_{arom}$–Si), 131.8 (d, $CH_{arom}$), 164.2 (s, $C_{arom}$–O).

### 2-[2-(Phenylsulfanyl)-4-(trifluoromethyl)phenoxy]tetrahydro-2*H*-pyran (2d)

To a stirred mixture of TMEDA (2.9 g, 25 mmol) and BuLi in hexane (15.9 mL, 15%, 26 mmol) in a 100 mL round-bottomed flask was added dropwise a solution of **1b** (5.0 g, HPLC: 98%, 19.9 mmol) in THF (10 mL) at –20 °C. After 30 min, (phenyldisulfanyl)benzene (4.8 g, 22 mmol) and after 2 h, $H_2O$ (5 mL) were added. The mixture was allowed to warm up to 20 °C and the phases were separated. The organic phase was washed once with brine and the combined aqueous phases were washed with *tert*-butyl methyl ether (3 × 5 mL). The organic phases were combined, dried ($Na_2SO_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, petroleum ether–*tert*-butyl methyl ether, 24: 1) to afford **2d** (6.35 g (HPLC: 92.3%, 16.6 mmol, 83%) as a colorless solid; mp 72–73 °C.

MS (70 eV): *m*/*z* (%) = 354 (1) [$M^+$], 270 (85) [$M^+$–THP], 200 (20), 171 (18), 85 (100), 77 (18), 67 (20), 57 (27), 41 (35)29 (25).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 1.70 (m, 6 H, THP), 3.55 (m, 1 H, THP), 3.70 (m, 1 H, THP), 5.55 (m, 1 H, THP), 7.20 (d, $^3J$ = 8.5 Hz, 1 $H_{arom}$), 7.30 (m, 6 $H_{arom}$), 7.43 (dd, $^3J$ = 8.5 Hz, $^4J$ = 1.8 Hz, 1 $H_{arom}$).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = 17.9 (t, $CH_2$-THP), 25.0 (t, $CH_2$-THP), 29.9 (t, $CH_2$-THP), 61.6 (t, $CH_2$-THP), 96.3 (d, CH-THP), 114.3 (d, $CH_{arom}$), 123.9 (q, $^2J$ = 271.6 Hz, *C*–$CF_3$), 124.0 (q, $^2J$ = 32.8 Hz, $CF_3$), 125.2 (d, $CH_{arom}$), 126.7 (s, $C_{arom}$–S), 127.7 (d, 2 $CH_{arom}$), 129.4 (d, 2 $CH_{arom}$), 132.0 (d, 2 $CH_{arom}$), 133.4 (s, $C_{arom}$–S), 156.8 (s, $C_{arom}$–O).

### 2-Hydroxy-5-(trifluoromethyl)isophthalic Acid (2e)

To a stirred mixture of TMEDA (2.9 g, 25 mmol) and BuLi in hexane (15.9 mL, 15%, 26 mmol) in a 100 mL round-bottomed flask was added dropwise a solution of **1b** (5.0 g, HPLC: 98%, 19.9 mmol) in THF (10 mL) at –20 °C. After 30 min, gaseous $CO_2$ dried by passage through a $P_2O_5$ cartridge was bubbled through the mixture for 30 min. The mixture was allowed to warm to 20 °C overnight and then $H_2O$ (5 mL), concd HCl (8 mL) and *tert*-butyl methyl ether (10 mL) were added. A small amount of (0.4 g) colorless solid 2-hydroxy-5-(trifluoromethyl)isophthalic acid was filtered off by suction. The phases were separated, the organic phase washed once with brine and the combined aqueous phases washed with *tert*-butyl methyl ether (3 × 5 mL). The organic phases were combined, dried ($Na_2SO_4$) and evaporated in vacuo. The residue was purified by column chromatography (silica gel, petroleum ether–*tert*-butyl methyl ether, 95:5, + 0.1 mL AcOH/100 mL of eluent) and extraction under basic conditions with *tert*-butyl methyl ether and under acid conditions with $CH_2Cl_2$. The product **2e** (2.2 g, HPLC: 97,8%, 14.5 mmol, 53%) was obtained as a colorless solid; mp 149–151 °C.

MS (70 eV): *m*/*z* (%) = 206 (53) [$M^+$], 188 (100), 160 (76), 132 (20), 63 (28), 18 (65).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.06 (d, $^3J$ = 8.5 Hz, 1 $H_{arom}$), 7.67 (dd, $^3J$ = 8.5 Hz, $^4J$ = 2.4 Hz, 1 $H_{arom}$), 8.16 (d, $^4J$ = 2.4 Hz, 1 $H_{arom}$), 10.60 (s, 1 H, $CO_2H$).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = 113.0 (s, *C*–$CO_2H$), 118.0 (d, $CH_{arom}$), 121.1 (q, $^2J$ = 33.5 Hz, *C*–$CF_3$), 124.0 (q, *J* = 271.2 Hz, $CF_3$), 128.2 (d, $CH_{arom}$), 131.8 (d, $CH_{arom}$), 164.4 (s, $C_{arom}$–O), 171.8 (s, $CO_2H$).

### 2-[2-Chloro-4-(trifluoromethyl)phenoxy]tetrahydro-2*H*-pyran (2f)

To a stirred solution of BuLi in hexane (14.7 mL, 15%, 24 mmol) in a 100 mL round-bottomed flask at –70 °C was added dropwise a solution of **1b** (5 g, HPLC: 98%, 19.9 mmol) in THF (40 mL). After 30 min, a solution of hexachloroethane (9.5 g, 40 mmol) in THF (20 mL) was added at –70 °C. After 4 h, the mixture was allowed to warm up to 20 °C and it was evaporated the next day. The residue was taken up in petroleum ether and the insoluble salts were separated by filtration. After evaporation of the solvent from the filtrate, the product was purified by column chromatography (silica gel, petroleum ether–*tert*-butyl methyl ether, 9: 1); 5.2 g (HPLC: 95%, 17.6 mmol, 89%); colorless oil.

MS (70 eV): *m*/*z* (%) = 280 (>1) [$M^+$], 198 (30), 196 (100), 177 (34), 146 (16), 132 (18), 85 (39), 84 (34), 55 (22).

$^1$H NMR (400 MHz, $CDCl_3$): δ = 1.85 (m, 6 H, THP), 3.60 (m, 1 H, THP), 3.80 (m, 1 H, THP), 5.57 (m, 1 H, THP), 7.26 (d, $^3J$ = 8.5 Hz, 1 $H_{arom}$), 7.45 (dd, $^3J$ = 8.5 Hz, $^4J$ = 1.8 Hz, 1 $H_{arom}$), 7.65 (d, $^4J$ = 1.8 Hz, 1 $H_{arom}$).

$^{13}$C NMR (400 MHz, $CDCl_3$): δ = 18.1 (t, $CH_2$-THP), 25.1 (t, $CH_2$-THP), 30.0 (t, $CH_2$-THP), 61.9 (t, $CH_2$-THP), 96.7 (d, CH-THP), 116.0 (d, $CH_{arom}$), 122.3 (q, *J* = 271.5 Hz, $CF_3$), 124.0 (s, $C_{arom}$–Cl), 124.3 (q, $^2J$ = 33.3 Hz, *C*–$CF_3$), 125.0 (d, $CH_{arom}$), 127.5 (d, $CH_{arom}$), 155.2 (s, $C_{arom}$–O).

### 2-(1,3,6,2-Dioxazaborocan-2-yl)-4-(trifluoromethyl)phenyl Tetrahydro-2*H*-pyran-2-yl Ether (2g)

To a solution of **1b** (5 g, HPLC: 98%, 19.9 mmol) in THF (100 mL) in a 250 mL round-bottomed flask was added dropwise a solution of BuLi in hexane (27 mL, 15%, 44 mmol) at –70 °C. After 45 min, this solution was slowly added dropwise to a mixture of triisopropyl borate (15.04 g, 80 mmol) and THF (40 mL) at –70 °C. After 1.5 h, the mixture was allowed to warm up to 20 °C and was evaporated on a rotary evaporator. The residue was taken up in toluene (100 mL) and the insoluble components were filtered. The filtrate was reduced to 50 mL by evaporation and treated with diethanolamine (2.1 g, 20 mmol). After a short time the product crystallized. The slurry of crystals was taken up in *tert*-butyl methyl ether (50 mL), filtered by suction, washed with *tert*-butyl methyl ether and dried to give **2g** (4.9 g, HPLC: 98.4%, 13.4 mmol, 68%) as a colorless solid; mp 192 °C.

MS (70 eV): *m*/*z* (%) = no [$M^+$], 275 (18), 244 (20), 114 (61), 85 (100), 67 (22), 57 (29), 55 (22), 43 (17), 41 (48), 27 (30).

$^1$H NMR (360 MHz, $CDCl_3$): δ = 1.78 (m, 6 H, THP), 2.80 (m, 2 H, $NCH_2CH_2$), 3.30 (m, 1 H, THP), 3.55 (m, 2 H, $NCH_2CH_2$), 3.80 (m, 1 H, THP), 4.00 (m, 4 H, $NCH_2CH_2$), 5.20 (m, 1 H, THP), 6.15 (br s, 1 H, NH), 7.04 (d, $^3J$ = 8.8 Hz, 1 $H_{arom}$), 7.45 (dd, $^3J$ = 8.5 Hz, $^4J$ = 2.2 Hz, 1 $H_{arom}$), 7.94 (d, $^4J$ = 2.2 Hz, 1 $H_{arom}$).

$^{13}$C NMR (360 MHz, $CDCl_3$): δ = 21.9 (t, $CH_2$-THP), 25.4 (t, $CH_2$-THP), 32.0 (t, $CH_2$-THP), 51.7 (t, $CH_2$N), 52.2 (t, $CH_2$N), 63.0 (t, $CH_2$-THP), 63.4 (t, $CH_2$OB), 66.3 (t, $CH_2$OB), 101.6 (d, CH-THP), 115.6 (d, $CH_{arom}$), 125.2 (q, *J* = 271.2 Hz, $CF_3$), 125.8 (q, $^2J$ = 31.7 Hz, *C*–$CF_3$), 126.3 (d, $CH_{arom}$), 132.2 (d, $CH_{arom}$), 132.2 (s, $C_{arom}$–B), 162.8 (s, $C_{arom}$–O).

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