

# **CHEMISTRY**

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## **A EUROPEAN JOURNAL**

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### **Supporting Information**

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#### **A Modular Synthesis of Teraryl-Based $\alpha$ -Helix Mimetics, Part 1: Synthesis of Core Fragments with Two Electron-Poorly Differentiated Leaving Groups**

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## 1 General Experimental Aspects, Materials and Methods

NMR spectra were recorded on a Bruker Avance III 300 MHz FT NMR spectrometer (300.36 MHz (<sup>1</sup>H), 75.53 MHz (<sup>13</sup>C)), or on a Varian Unity Inova 500 MHz NB high resolution FT NMR spectrometer (499.76 MHz (<sup>1</sup>H), 125.67 MHz (<sup>13</sup>C)) at 27°C. Chemical shifts  $\delta$  [ppm] are referenced to residual protonated solvent signals as internal standard [ $D_6$ ]DMSO:  $\delta$  = 2.50 ppm (<sup>1</sup>H), 39.52 ppm (<sup>13</sup>C) and CDCl<sub>3</sub>:  $\delta$  = 7.26 ppm (<sup>1</sup>H), 77.16 ppm (<sup>13</sup>C).<sup>[1]</sup> Signal multiplicities are abbreviated as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), dt (doublet of triplet), q (quadruplet), dq (doublet of quadruplet), sept (septet), m (multiplet) with the prefix b in case of broad signals. Superscript abbreviations are used as follows: H<sup>Ar</sup> (phenyl), H<sup>Naph</sup> (naphthyl), H<sup>BPin</sup> (boronic acid pinacol ester), and H<sup>Phth</sup> (phthalimide); abbreviation C<sub>q</sub> is used for quaternary carbon atoms. <sup>13</sup>C NMR resonances were assigned by APT or DEPT or <sup>2</sup>D-HSQC and -HMBC experiments. NMR signals for the residues of the terarylic-systems mimicking amino acids are superscripted with the common 3-letter-code.

GC-MS measurements were performed on an Agilent Technologies 7890A (G3440A) GC system equipped with an Agilent Technologies J&W GC-column HP-5MS ((5%-phenyl)-methylpolysiloxane; length: 30 m; inner-diameter: 0.250 mm; film: 0.25  $\mu$ m) at a constant helium flow rate (He 5.0; Air Liquide; “Alphagaz”; 1.085 mL/min; average velocity 41.6 cm/sec) in split mode 1/175 (inlet temperature: 250°C; injection volume: 2.0  $\mu$ L; sample concentration: ~0.5 mg/mL in ethyl acetate (EtOAc), methanol (MeOH), dichloromethane (DCM), or diethyl ether (Et<sub>2</sub>O)). The GC was coupled to a 5975C inert mass sensitive detector with triple-axis detector (MSD, EI, 70 eV; transfer line: 300°C; MS source: 240°C; MS quad: 180°C), with a solvent delay of 2.60 min. Two general gradients MP\_50\_S (initial temperature: 50°C, 1.0 min; linear ramp: 40°C/min; final temperature: 300°C; final time: 5.0 min; post run 1.0 min; detecting range: 50.0 to 550.0 amu), or MP\_100\_L (initial temperature: 100°C, 1.0 min; linear ramp: 50°C/min; final temperature: 300°C; final time: 12.0 min; post run 1.0 min; detecting range: 100.0 to 600.0 amu) were applied.

When reactions were monitored by GC-MS, the samples were prepared using a microscale workup. This means, an aliquot was taken from the reaction mixture, quenched with ~1 mL aqueous solution and ~1 mL DCM, EtOAc, or Et<sub>2</sub>O. After proper mixing and phase separation, the organic layer was collected, dried over MgSO<sub>4</sub> and filtered through cotton in a Pasteur-pipette. Reaction mixtures containing transition metals were additionally filtered

## General Experimental Aspects, Material and Methods

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through a short pad of silica gel (~1 cm) over cotton in a Pasteur-pipette (eluted with EtOAc or MeOH).

Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60-F<sub>254</sub> and spots were visualized by UV-light ( $\lambda = 254$  and/or 366 nm), or by treatment with cerium ammonium molybdate solution (CAM) (CAM: 2.0 g Ce(IV)SO<sub>4</sub>, 50 g (NH<sub>4</sub>)<sub>2</sub>MoO<sub>4</sub>, 50 mL concentrated H<sub>2</sub>SO<sub>4</sub> in 400 mL water), followed by warming with a heat gun.

Flash column chromatography was performed using silica gel 60 Å (35-70 µm particle size) from Acros Organics at an air pressure of ~1.5 bar. A 20 to 100-fold excess of silica gel was used with respect to the amount of dry raw material (exact values are given in experimental procedures). The stationary phase was filled in an appropriate sized column resulting in a pad of 15-25 cm silica gel. The column was equilibrated with the solvent or solvent mixture, and the sample was loaded onto the pad by diluting the crude product with the eluent. If the crude product was not good soluble in the eluent, the sample was dissolved in a proper solvent (MeOH or EtOAc), and the double amount of silica gel (or Celite®545, particle size 0.02-0.1 mm) was added, followed by removing the solvent using a rotary evaporator and drying in vacuo. The mobile phase was forced through the column by means of a rubber bulb pump.

For semi-preparative HPLC a Knauer Smartline Instrument with Autosampler 3800, Manager 5000, Pump 1000, UV Diode Array Detector 2600, and Fraction Collector Teledyne Isco Foxy Jr. FC100 modules were used. Semi-preparative HPLC was carried out utilizing a Macherey-Nagel VP 125/21 Nucleodur 100-5 C18 ec column with a VP 20/16 Nucleodur C18 ec pre-column at a flow rate of 16 mL/min, or a Macherey-Nagel VP 125/21 Nucleosil 120-5 C4 ec column with a VP 20/16 Nucleosil C8 ec pre-column at the same flow rate.

Analytical HPLC analysis was performed applying an Agilent Technologies 1200 Series (G1379B Degasser, G1312B Binary Pump SL, G1367C High Performance Autosampler SL, G1330 FC/ALS Thermostat, G1316B Thermostatted Column Compartment SL, G1365C Multiple Wavelength Detector SL) with an Agilent Technologies 6120 quadrupole LC/MS Detector with a G1918B Electrospray Ionization Source. Analytical HPLC was carried out utilizing a Macherey-Nagel EC 150/4 Nucleodur 100-5 C18 ec with a CC 8/4 Nucleodur 100-5 C18 ec pre-column, or a Macherey-Nagel EC 150/4 Nucleosil 120-5 C4 ec with a CC 8/4 Nucleosil 120-5 C4 ec pre-column, in ESI-positive mode.

For analytical purposes and HPLC and/or semi-preparative HPLC, demineralized water was additionally purified by filtering through a 0.2 µm cellulose nitrate membrane filter.

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High Resolution Mass Spectrometry (HRMS) was performed on an Agilent Technologies 7890A (G3440A) GC system equipped with an Agilent Technologies J&W GC-column DB-5MS (length: 30 m; inner-diameter: 0.250 mm; film: 0.25 µm) at a constant helium flow. The GC was coupled to a Waters GCT Premier Micromass. For Direct Inlet (DI-EI) only the Waters GCT Premier Micromass unit was used.

Melting points were determined on a “Mel-Temp” melting-point apparatus (Electrothermal) and are given uncorrected.

Boiling points (b.p.<sup>exp.</sup>, b.p.<sup>lit.</sup>) are listed in torr (if not otherwise mentioned).

Chemicals were purchased from Sigma-Aldrich, Fisher Scientific, Merck, or Alfa Aesar. All compounds were used without further purification unless otherwise noted.

Thionyl chloride ( $\text{SOCl}_2$ ) and acetone were distilled prior to use, also tetrahydrofuran (THF) and  $\text{Et}_2\text{O}$  were distilled, to get rid of the stabilizer 2,6-di-*tert*-butyl-4-methylphenol (BHT).

Palladium(II) acetate ( $\text{Pd}(\text{OAc})_2$ ) was recrystallized under reflux from absolute, degassed glacial acetic acid (~25 mL/g) and was filtered under inert conditions. After drying in vacuo, the catalyst was stored under an atmosphere of argon at -28°C.<sup>[2]</sup>

For determination of concentration of the *n*-butyl lithium solution in *n*-hexane (*n*-BuLi) a procedure according to KOFRON and BACLAWSKI was used.<sup>[3]</sup> To 250 mg 2,2-diphenylacetic acid, dissolved in 10 mL absolute THF, *n*-BuLi was added dropwise, until a colour change from colourless to yellow was detected. The added amount of *n*-BuLi corresponds to the amount of 2,2-diphenylacetic acid. The titre determination was accomplished before every use of the *n*-BuLi solution.

Ethanol (EtOH) was dried over sodium (Na) and diethyl phthalate. After inert distillation EtOH was stored over 3 Å molecular sieves in an amber glass Schlenk-flask under an atmosphere of argon. DCM, and MeOH were dried over  $\text{CaH}_2$  and distilled under an argon atmosphere before use. Acetonitrile (ACN) was dried over NaH and after inert distillation stored over 3 Å molecular sieves in an amber glass Schlenk-flask under an argon atmosphere.  $\text{Et}_2\text{O}$ , 1,2-dimethoxyethane (1,2-DME), 1,4-dioxane, and THF were dried by heating at reflux under an atmosphere of argon over Na, until benzophenone indicated dryness by a deep blue colour. Absolute  $\text{Et}_2\text{O}$ , 1,2-DME, 1,4-dioxane, and THF were stored over 4 Å molecular sieves in an amber glass Schlenk-flask under an argon atmosphere. Molecular sieves were activated by filling a 500 mL round-bottomed flask to one third of its volume with molecular sieves (Sigma-Aldrich, beads, 8-12 mesh) and heating the flask in a heating mantle (~150°C) under oil pump vacuum for ~3 days, followed by cooling to room temperature under an

## General Experimental Aspects, Material and Methods

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atmosphere of argon. When referring to "oil pump vacuum" the applied pressure is usually in the region of  $10^{-2}$ - $10^{-3}$  mbar by using a rotary vane pump.

Degassing of reaction mixtures or solvents was performed by subjecting the accordant vessel to vacuum and refilling with an inert gas. This procedure was repeated at least three times (vacuum/gas cycles). Alternatively, degassing was carried out by passing a stream of argon through the reaction mixture/solvent. This means, a balloon filled with argon was placed on a syringe with needle, and the needle was punched through a septum and dipped into the reaction mixture. Additionally the vessel was immersed in an ultrasonic bath.

When working at a temperature of 0°C, an ice-water bath served as the cooling agent. Temperatures of -4°C to -18°C were adjusted with ice/MeOH mixtures, and -78°C was achieved by a dry ice/acetone mixture. For reactions requiring cryogenic temperatures over several hours, a cryostat was used.

The workup of hydrogenation experiments utilizing metal-catalysts was performed by filtering off the catalyst, using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

## 2 Experimental Procedures and Analytical Data

### 2.1 Synthesis of the Triflate Core Fragments

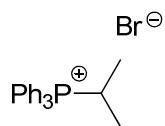
#### 2.1.1 Representative procedure for the iodination of phenol derivatives

In a 25 mL one-neck round-bottom flask 1.0 eq of the corresponding phenol derivative **16** was dissolved in acetic acid and 1.0 eq iodine monochloride (ICl) was added at room temperature. In some cases additionally ICl was added, to ensure quantitative conversion. The reaction mixture was quenched with 100 mL 0.5 M NaHCO<sub>3</sub> solution and the aqueous phase was extracted with DCM (3x50 mL). The combined organic layers were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (25%, 3x100 mL), followed by saturated NaCl solution (1x100 mL). After drying over MgSO<sub>4</sub>, the solvent was removed under reduced pressure, and the crude product was purified by flash column chromatography.

#### 2.1.2 Representative procedure for synthesis of the triflate derivatives from the corresponding phenols

In a flame dried and argon flushed Schlenk-flask 1.0 eq of the corresponding phenol derivative **17** was dissolved in pyridine. After cooling the solution to 0°C trifluoromethanesulfonic anhydride (Tf<sub>2</sub>O) was carefully added. After stirring 5 min at 0°C, the solution was allowed to warm to room temperature and stirred until quantitative conversion was detected by TLC. 60 mL Et<sub>2</sub>O were added and the organic phase was washed with H<sub>2</sub>O (3x30 mL), followed by extracting the combined aqueous layers with Et<sub>2</sub>O (2x30 mL). The organic phases were washed with 1 M HCl (2x60 mL) and saturated NaCl solution (1x60 mL), dried over MgSO<sub>4</sub> and concentrated in vacuo. The crude product was purified by flash column chromatography.

#### 2.1.3 Isopropyltriphenylphosphonium bromide (**18a**)



**18a**

A Teflon®-coated autoclave-flask was charged with 15.0 g triphenylphosphine (PPh<sub>3</sub>) (57.2 mmol, 1.0 eq) and 19.0 mL isopropyl bromide (24.9 g, 200 mmol, 3.5 eq). The autoclave was sealed and heated to 150°C (~12 bar). After 23 h the reaction mixture was allowed to cool to room temperature, and the resulting pale orange solid was subsequently

## Experimental Procedures and Analytical Data

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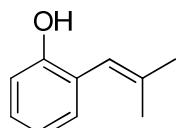
thoroughly washed with THF (4x25 mL) and Et<sub>2</sub>O (2x25 mL). After filtration and drying of the filter cake, compound **18a** was isolated as a colourless powder.<sup>[4]</sup>

**Yield:** 20.51 g (93%), colourless solid, C<sub>21</sub>H<sub>22</sub>BrP [385.28 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 8.01-7.95 (m, 6 H; H<sup>Ar</sup>), 7.78-7.65 (m, 9 H; H<sup>Ar</sup>), 5.62-5.47 (m, 1 H; CH), 1.33 (dd, <sup>3</sup>J(H,P) = 19.0 Hz, <sup>3</sup>J(H,H) = 6.8 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 134.8 (d, <sup>4</sup>J(C,P) = 3 Hz; C<sup>Ar</sup>), 134.1 (d, <sup>3</sup>J(C,P) = 9 Hz; C<sup>Ar</sup>), 130.6 (d, <sup>2</sup>J(C,P) = 12 Hz; C<sup>Ar</sup>), 117.8 (d, <sup>1</sup>J(C,P) = 83 Hz; C<sup>Ar</sup>), 21.5 (d, <sup>1</sup>J(C,P) = 46 Hz; CH), 16.4 (d, <sup>2</sup>J(C,P) = 2 Hz; CH<sub>3</sub>) ppm; **m.p.**<sup>exp.</sup> = 235-238°C (m.p.<sup>lit.</sup> = 237.5-238.5°C).<sup>[4]</sup>

Analytical data are in accordance with those reported.<sup>[5]</sup>

### 2.1.4 2-(2-Methylprop-1-en-1-yl)phenol (**19a**)



**19a**

In a flame dried 500 mL three-neck round-bottom flask equipped with reflux condenser and argon-inlet 23.3 g (60.3 mmol, 2.3 eq) phosphonium-salt **18a** were suspended in 175 mL absolute, degassed toluene. In a second flame dried Schlenk-flask 6.88 g (61.1 mmol, 2.3 eq) KOtBu were suspended in 44 mL absolute, degassed THF. This colourless suspension was cannulated to the phosphonium-salt suspension **18a** and stirred for 60 min at 50°C. After some minutes the suspension became a dark red solution. Meanwhile in another flame dried Schlenk-flask 2.80 mL (3.20 g, 26.2 mmol, 1.0 eq) salicylaldehyde (**16h**) were dissolved in 35 mL absolute, degassed toluene. The dark red phosphonium-salt solution **18a** was cooled to -78°C and the salicylaldehyde solution (**16h**) was added *via* cannula. During the cannulation the reaction mixture became brighter and a pale yellow precipitate was formed. The suspension was stirred overnight at room temperature and stirred at 80°C until complete conversion was detected by GC-MS. The red-brown suspension was quenched with 60 mL saturated NH<sub>4</sub>Cl solution. The phases were separated; the aqueous phase was diluted with 120 mL water and extracted with Et<sub>2</sub>O (3x120 mL). The combined organic layers were washed with saturated NaCl solution (1x300 mL), dried over MgSO<sub>4</sub>, filtered and concentrated to dryness under reduced pressure. The brown crude product was purified by distillation.<sup>[6]</sup>

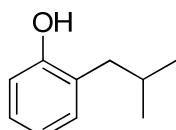
**Yield:** 2.47 g (64%), yellow oil, C<sub>10</sub>H<sub>12</sub>O [148.09 g/mol].

## Experimental Procedures and Analytical Data

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.17 (dt, <sup>3</sup>J(H,H) = 8.0 Hz, <sup>4</sup>J(H,H) = 1.3 Hz, 1 H; H<sup>Ar</sup>), 7.08-7.05 (m, 1 H; H<sup>Ar</sup>), 6.92-6.87 (m, 2 H; H<sup>Ar</sup>), 6.14 (s, 1 H; CH), 5.09 (bs, 1 H; OH), 1.96 (d, <sup>4</sup>J(H,H) = 1.2 Hz, 3 H; CH<sub>3</sub>), 1.70 (d, <sup>4</sup>J(H,H) = 1.0 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 152.9 (C<sub>q</sub>; C<sup>Ar</sup>), 140.7 (C<sub>q</sub>; CH=C(CH<sub>3</sub>)<sub>2</sub>), 130.0 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 124.8 (C<sub>q</sub>; C<sup>Ar</sup>), 120.3 (C<sup>Ar</sup>), 118.8 (CH), 115.0 (C<sup>Ar</sup>), 26.0 (CH<sub>3</sub>), 19.6 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 4.79 min; m/z (%): 148 (92) [M<sup>+</sup>], 133 (100) [M<sup>+</sup>-CH<sub>3</sub>], 105 (63) [M<sup>+</sup>-C<sub>3</sub>H<sub>8</sub>]; **b.p.**<sup>exp.</sup> = 45°C, 0.1 torr (**b.p.**<sup>lit.</sup> = 104°C, 15 torr).<sup>[7]</sup>

Analytical data are in accordance with those reported.<sup>[8]</sup>

### **2.1.5 2-Isobutylphenol (16c)**



**16c**

In an argon flushed 250 mL three-neck round-bottom flask equipped with argon-inlet 2.40 g phenol derivative **19a** (16.2 mmol, 1.0 eq) were dissolved in 120 mL MeOH. To this yellow solution 240 mg palladium on activated charcoal (Pd/C) (10 wt%) were added.\* After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (6x), the reaction mixture was stirred for 3 h at room temperature. After filtering off the catalyst (5x3 cm SiO<sub>2</sub>, eluent: MeOH) and evaporating the solvent using a rotary evaporator, the crude product was purified by distillation.<sup>†</sup>

**Yield:** 1.85 g (77%), colourless oil, C<sub>10</sub>H<sub>12</sub>O [150.22 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.13-7.07 (m, 2 H; H<sup>Ar</sup>), 6.88 (dt, <sup>3</sup>J(H,H) = 7.5 Hz, <sup>4</sup>J(H,H) = 1.1 Hz, 1 H; H<sup>Ar</sup>), 6.79-6.76 (m, 1 H; H<sup>Ar</sup>), 4.67 (s, 1 H; OH), 2.50 (d, <sup>3</sup>J(H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>), 2.04-1.86 (m, 1 H; CH), 0.95 (d, <sup>3</sup>J(H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 153.7 (C<sub>q</sub>; C<sup>Ar</sup>), 131.4 (C<sup>Ar</sup>), 127.6 (C<sub>q</sub>; C<sup>Ar</sup>), 127.2 (C<sup>Ar</sup>), 120.7 (C<sup>Ar</sup>), 115.4 (C<sup>Ar</sup>), 39.4 (CH<sub>2</sub>), 29.0 (CH), 22.7 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 4.90 min; m/z (%): 150 (39) [M<sup>+</sup>], 107 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>8</sub>]; **b.p.**<sup>exp.</sup> = 45°C, 0.2 torr, (**b.p.**<sup>lit.</sup> = 45-50°C, 1 torr).<sup>[9]</sup>

Analytical data are in accordance with those reported.<sup>[10]</sup>

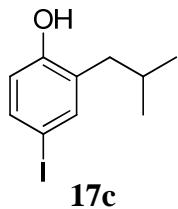
\* Palladium on activated charcoal, moistened with water, 5% Pd basis (based on dry substance), Aldrich 75992.

† The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

## Experimental Procedures and Analytical Data

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### **2.1.6 4-Iodo-2-isobutylphenol (17c)**



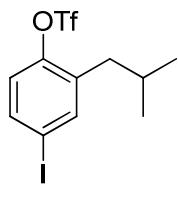
Compound **17c** was prepared according to procedure 2.1.1 from 1.50 g phenol derivative **16c** (10.0 mmol, 1.0 eq) in 14 mL acetic acid and 500  $\mu$ L ICl (1.62 g, 10.0 mmol, 1.0 eq). After 24 h 200  $\mu$ L ICl (648 mg, 3.99 mmol, 0.4 eq) were additionally added and quantitative conversion was detected after further 24 h. After flash column chromatography (cyclohexane/EtOAc = 12/1,  $R_f$  = 0.20, CAM), compound **17c** was isolated as a pale orange powder.<sup>[11]</sup>

**Yield:** 2.35 g (85%), pale orange powder,  $C_{10}H_{13}IO$  [276.11 g/mol].

**$^1H$  NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.38-7.33 (m, 2 H; H<sup>Ar</sup>), 6.54 (d,  $^3J$  (H,H) = 8.2 Hz, 1 H; H<sup>Ar</sup>), 4.71 (bs, 1 H; OH), 2.41 (d,  $^3J$  (H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>), 1.97-1.83 (m, 1 H; CH), 0.92 (d,  $^3J$  (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm;  **$^{13}C$  NMR** (76 MHz, CDCl<sub>3</sub>):  $\delta$  = 153.7 (C<sub>q</sub>; C<sup>Ar</sup>), 139.8 (C<sup>Ar</sup>), 135.9 (C<sup>Ar</sup>), 130.6 (C<sub>q</sub>; C<sup>Ar</sup>), 117.7 (C<sup>Ar</sup>), 82.8 (C<sub>q</sub>; C<sup>Ar</sup>), 39.0 (CH<sub>2</sub>), 29.0 (CH), 22.6 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 6.26 min;  $m/z$  (%): 276 (73) [ $M^+$ ], 233 (100) [ $M^+ - C_3H_8$ ], 107 (17) [ $M^+ - C_3H_8I$ ]; **m.p.**<sup>exp.</sup> = 62-63°C.

Analytical data are in accordance with those reported.<sup>[11]</sup>

### **2.1.7 4-Iodo-2-isobutylphenyl trifluoromethanesulfonate (3c)**



**3c**

Compound **3c** was prepared according to procedure 2.1.2 from 2.20 g phenol derivative **17c** (7.97 mmol, 1.0 eq) in 9 mL pyridine and 2.10 mL Tf<sub>2</sub>O (2.47 g, 8.76 mmol, 1.1 eq). Quantitative conversion was detected after 24 h. After flash column chromatography (cyclohexane,  $R_f$  = 0.50, CAM), compound **3c** was isolated as a pale yellow oil.

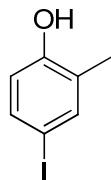
**Yield:** 2.97 g (91%), pale yellow oil,  $C_{11}H_{12}F_3IO_3S$  [408.18 g/mol].

## Experimental Procedures and Analytical Data

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**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.63-7.57 (m, 2 H; H<sup>Ar</sup>), 6.99 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 2.52 (d, <sup>3</sup>J (H,H) = 7.3 Hz, 2 H; CH<sub>2</sub>), 2.01-1.83 (m, 1 H; CH), 0.92 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 148.3 (C<sub>q</sub>; C<sup>Ar</sup>), 141.0 (C<sup>Ar</sup>), 137.0 (C<sub>q</sub>; C<sup>Ar</sup>), 136.9 (C<sup>Ar</sup>), 123.2 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 320 Hz; CF<sub>3</sub>), 93.2 (C<sub>q</sub>; C<sup>Ar</sup>), 39.1 (CH<sub>2</sub>), 29.3 (CH), 22.4 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.98 min; m/z (%): 408 (59) [M<sup>+</sup>], 233 (100) [M<sup>+</sup>-C<sub>4</sub>H<sub>8</sub>F<sub>3</sub>O<sub>2</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 407.9504; found: 407.9510.

### 2.1.8 4-Iodo-2-methylphenol (**17a**)



**17a**

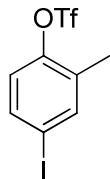
Compound **17a** was prepared according to procedure 2.1.1 from 2.00 g *o*-cresole (**16a**) (18.5 mmol, 1.0 eq) in 25 mL acetic acid and 1.11 mL ICl (3.60 g, 22.2 mmol, 1.2 eq). After 24 h again 250 μL ICl (810 mg, 4.99 mmol, 0.3 eq) were added and quantitative conversion was detected after 27 h. After flash column chromatography (cyclohexane/EtOAc = 10/1, R<sub>f</sub> = 0.27, CAM) compound **17a** was isolated as a pale brown powder.

**Yield:** 4.03 g (93%), pale brown powder, C<sub>7</sub>H<sub>7</sub>IO [234.03 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.43 (d, <sup>4</sup>J (H,H) = 1.4 Hz, 1 H; H<sup>Ar</sup>), 7.35 (dd, <sup>3</sup>J (H,H) = 8.4 Hz, <sup>4</sup>J (H,H) = 1.9 Hz, 1 H; H<sup>Ar</sup>), 6.54 (d, <sup>3</sup>J (H,H) = 8.4 Hz, 1 H; H<sup>Ar</sup>), 4.78 (s, 1 H; OH), 2.20 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 153.8 (C<sub>q</sub>; C<sup>Ar</sup>), 139.6 (C<sup>Ar</sup>), 136.0 (C<sup>Ar</sup>), 126.9 (C<sub>q</sub>; C<sup>Ar</sup>), 117.3 (C<sup>Ar</sup>), 82.8 (C<sub>q</sub>; C<sup>Ar</sup>), 15.6 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.64 min; m/z (%): 234 (100) [M<sup>+</sup>], 107 (25) [M<sup>+</sup>-I]; **m.p.<sup>exp.</sup>** = 65-66°C (m.p.<sup>lit.</sup> = 65-67°C).<sup>[12]</sup>

Analytical data are in accordance with those reported.<sup>[12]</sup>

**2.1.9 4-Iodo-2-methylphenyl trifluoromethanesulfonate (3a)**



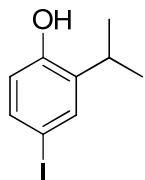
**3a**

Compound **3a** was prepared according to procedure 2.1.2 from 3.26 g phenol derivative **17a** (13.9 mmol, 1.0 eq) in 17 mL pyridine and 4.10 mL Tf<sub>2</sub>O (4.80 g, 17.0 mmol, 1.2 eq). Quantitative conversion was detected after 24 h. After flash column chromatography (cyclohexane, R<sub>f</sub> = 0.46, CAM) compound **3a** was isolated as a colourless oil.

**Yield:** 3.85 g (76%), colourless oil, C<sub>8</sub>H<sub>6</sub>F<sub>3</sub>IO<sub>3</sub>S [366.10 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.66 (d, <sup>4</sup>J(H,H) = 1.5 Hz, 1 H; H<sup>Ar</sup>), 7.58 (dd, <sup>3</sup>J(H,H) = 8.6 Hz, <sup>4</sup>J(H,H) = 1.8 Hz, 1 H; H<sup>Ar</sup>), 6.98 (d, <sup>3</sup>J(H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 2.34 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 148.5 (C<sub>q</sub>; C<sup>Ar</sup>), 141.1 (C<sup>Ar</sup>), 136.9 (C<sup>Ar</sup>), 133.5 (C<sub>q</sub>; C<sup>Ar</sup>), 123.2 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J(C,F) = 320 Hz; CF<sub>3</sub>), 93.2 (C<sub>q</sub>; C<sup>Ar</sup>), 16.2 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.46 min; *m/z* (%): 366 (73) [M<sup>+</sup>], 233 (100) [M<sup>+</sup>-CF<sub>3</sub>O<sub>2</sub>S], 106 (10) [M<sup>+</sup>-CF<sub>3</sub>IO<sub>2</sub>S].

**2.1.10 4-Iodo-2-isopropylphenol (17b)**



**17b**

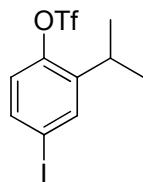
Compound **17b** was prepared according to procedure 2.1.1 from 2.00 g 2-isopropylphenole (**16b**) (14.7 mmol, 1.0 eq) in 20 mL acetic acid and 884 μL ICl (2.86 g, 17.6 mmol, 1.2 eq). After 24 h 125 μL ICl (405 mg, 2.49 mmol, 0.2 eq) were additionally added and quantitative conversion was detected after 27 h. After flash column chromatography (cyclohexane/EtOAc = 12/1, R<sub>f</sub> = 0.23, CAM) compound **17b** was isolated as a dark yellow oil.

**Yield:** 3.38 g (88%), dark yellow oil, C<sub>9</sub>H<sub>11</sub>IO [262.09 g/mol].

## Experimental Procedures and Analytical Data

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.45 (d, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.34 (dd, <sup>3</sup>J (H,H) = 8.4 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 6.52 (d, <sup>3</sup>J (H,H) = 8.4 Hz, 1 H; H<sup>Ar</sup>), 4.73 (bs, 1 H; OH), 3.14 (sept, <sup>3</sup>J (H,H) = 6.9 Hz, 1 H; CH), 1.23 (d, <sup>3</sup>J (H,H) = 6.9 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 152.8 (C<sub>q</sub>; C<sup>Ar</sup>), 137.5 (C<sub>q</sub>; C<sup>Ar</sup>), 135.6 (C<sup>Ar</sup>), 117.7 (C<sup>Ar</sup>), 83.5 (C<sub>q</sub>; C<sup>Ar</sup>), 27.2 (CH), 22.5 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.04 min; m/z (%): 262 (97) [M<sup>+</sup>], 247 (100) [M<sup>+</sup>-CH<sub>3</sub>], 120 (45) [M<sup>+</sup>-CH<sub>3</sub>I].

### **2.1.11 4-Iodo-2-isopropylphenyl trifluoromethanesulfonate (3b)**



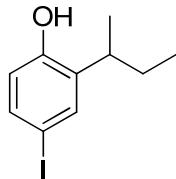
**3b**

Compound **3b** was prepared according to procedure 2.1.2 from 2.58 g phenol derivative **17b** (9.84 mmol, 1.0 eq) in 12 mL pyridine and 2.61 mL Tf<sub>2</sub>O (3.06 g, 10.8 mmol, 1.1 eq). Quantitative conversion was detected after 3 h. After flash column chromatography (cyclohexane, R<sub>f</sub> = 0.49, CAM) compound **3b** was isolated as a colourless oil.

**Yield:** 2.59 g (67%), colourless oil, C<sub>10</sub>H<sub>10</sub>F<sub>3</sub>IO<sub>3</sub>S [394.15 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.69 (d, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.57 (dd, <sup>3</sup>J (H,H) = 8.6 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 6.97 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 3.22 (sept, <sup>3</sup>J (H,H) = 6.8 Hz, 1 H; CH), 1.25 (d, <sup>3</sup>J (H,H) = 6.9 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 147.1 (C<sub>q</sub>; C<sup>Ar</sup>), 143.8 (C<sub>q</sub>; C<sup>Ar</sup>), 137.3 (C<sup>Ar</sup>), 136.7 (C<sup>Ar</sup>), 123.2 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 320 Hz; CF<sub>3</sub>), 93.8 (C<sub>q</sub>; C<sup>Ar</sup>), 27.3 (CH), 23.1 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.71 min; m/z (%): 394 (85) [M<sup>+</sup>], 134 (100) [M<sup>+</sup>-CF<sub>3</sub>IO<sub>2</sub>S], 119 (14) [M<sup>+</sup>-C<sub>2</sub>H<sub>3</sub>F<sub>3</sub>IO<sub>2</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 393.9348; found: 393.9339.

### **2.1.12 2-sec-Butyl-4-iodophenol (17d)**



**17d**

Compound **17d** was prepared according to procedure 2.1.1 from 2.00 g 2-sec-butylphenole (**16d**) (13.4 mmol, 1.0 eq) in 20 mL acetic acid and 806 μL ICl (2.61 g, 16.1 mmol, 1.2 eq).

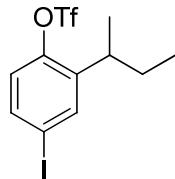
## Experimental Procedures and Analytical Data

After 24 h again 200  $\mu$ L ICl (648 mg, 3.99 mmol, 0.3 eq) were added and quantitative conversion was detected after 27 h. After flash column chromatography (cyclohexane/EtOAc = 12/1,  $R_f$  = 0.11, CAM) compound **17d** was isolated as a pale brown oil.

**Yield:** 2.80 g (76%), pale brown oil,  $C_{10}H_{13}IO$  [276.11 g/mol].

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  = 7.41 (d,  $^4J(H,H)$  = 2.1 Hz, 1 H;  $H^{Ar}$ ), 7.33 (dd,  $^3J(H,H)$  = 8.4 Hz,  $^4J(H,H)$  = 2.2 Hz, 1 H;  $H^{Ar}$ ), 6.53 (d,  $^3J(H,H)$  = 8.4 Hz, 1 H;  $H^{Ar}$ ), 4.76 (bs, 1 H; OH), 2.95-2.83 (m, 1 H; CH), 1.66-1.52 (m, 2 H;  $CH_2$ ), 1.21 (d,  $^3J(H,H)$  = 6.9 Hz, 3 H;  $CH_3$ ), 0.86 (t,  $^3J(H,H)$  = 7.4 Hz, 3 H;  $CH_3$ ) ppm;  **$^{13}C$  NMR** (76 MHz,  $CDCl_3$ , APT):  $\delta$  = 153.1 ( $C_q$ ;  $C^{Ar}$ ), 136.4 ( $C_q$ ;  $C^{Ar}$ ), 136.2 ( $C^{Ar}$ ), 135.5 ( $C^{Ar}$ ), 117.7 ( $C^{Ar}$ ), 83.5 ( $C_q$ ;  $C^{Ar}$ ), 34.1 (CH), 29.8 ( $CH_2$ ), 20.4 ( $CH_3$ ), 12.2 ( $CH_3$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 6.27 min;  $m/z$  (%): 276 (58) [ $M^+$ ], 247 (100) [ $M^+ - C_2H_5$ ], 120 (45) [ $M^+ - C_2H_5I$ ]; **HRMS** (EI): calcd for  $[M^+]$ : 276.0011; found: 276.0019.

### **2.1.13 2-(*sec*-Butyl)-4-iodophenyl trifluoromethanesulfonate (3d)**



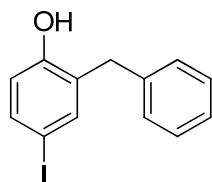
**3d**

Compound **3d** was prepared according to procedure 2.1.2 from 2.80 g phenol derivative **17d** (10.1 mmol, 1.0 eq) in 12 mL pyridine and 2.70 mL  $Tf_2O$  (3.15 g, 11.2 mmol, 1.1 eq). Quantitative conversion was detected after 3 h. After flash column chromatography (cyclohexane,  $R_f$  = 0.68, CAM) compound **3d** was isolated as a colourless oil.

**Yield:** 3.23 g (78%); colourless oil,  $C_{11}H_{12}F_3IO_3S$  [408.18 g/mol].

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  = 7.64 (d,  $^4J(H,H)$  = 2.2 Hz, 1 H;  $H^{Ar}$ ), 7.57 (dd,  $^3J(H,H)$  = 8.6 Hz,  $^4J(H,H)$  = 2.2 Hz, 1 H;  $H^{Ar}$ ), 6.98 (d,  $^3J(H,H)$  = 8.6 Hz, 1 H;  $H^{Ar}$ ), 3.02-2.90 (m, 1 H; CH), 1.65-1.57 (m, 2 H;  $CH_2$ ), 1.23 (d,  $^3J(H,H)$  = 6.9 Hz, 3 H;  $CH_3$ ), 0.85 (t,  $^3J(H,H)$  = 7.4 Hz, 3 H;  $CH_3$ ) ppm;  **$^{13}C$  NMR** (76 MHz,  $CDCl_3$ , APT):  $\delta$  = 147.6 ( $C_q$ ;  $C^{Ar}$ ), 142.9 ( $C_q$ ;  $C^{Ar}$ ), 137.6 ( $C^{Ar}$ ), 136.6 ( $C^{Ar}$ ), 123.2 ( $C^{Ar}$ ), 118.7 (q,  $^1J(C,F)$  = 320 Hz;  $CF_3$ ), 93.8 ( $C_q$ ;  $C^{Ar}$ ), 34.2 (CH), 30.6 ( $CH_2$ ), 21.0 ( $CH_3$ ), 12.1 ( $CH_3$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 5.93 min;  $m/z$  (%): 408 (68) [ $M^+$ ], 379 (21) [ $M^+ - C_2H_5$ ], 246 (23) [ $M^+ - C_3H_5F_3O_2S$ ]; **HRMS** (EI): calcd for  $[M^+]$ : 407.9504; found: 407.9530.

### 2.1.14 2-Benzyl-4-iodophenol (**17e**)



**17e**

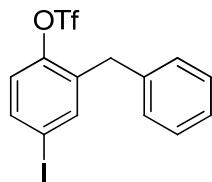
Compound **17e** was prepared according to procedure 2.1.1 from 2.00 g 2-benzylphenole (**16e**) (19.0 mmol, 1.0 eq) in 12 mL acetic acid and 1.14 mL ICl (3.70 g, 22.8 mmol, 1.0 eq). After 24 h 191  $\mu$ L ICl (620 mg, 3.80 mmol, 0.2 eq) were additionally added and quantitative conversion was detected after 27 h. After flash column chromatography (cyclohexane/EtOAc = 8/1,  $R_f$  = 0.31, CAM) compound **17e** was isolated as a brown powder.<sup>[11]</sup>

**Yield:** 4.70 g (80%); brown powder, C<sub>13</sub>H<sub>11</sub>IO [310.13 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.26-7.23 (m, 2 H; H<sup>Ar</sup>, overlapping), 7.18-7.12 (m, 2 H; H<sup>Phe</sup>), 7.10-7.04 (m, 3H; H<sup>Phe</sup>), 6.40 (d, <sup>3</sup>J (H,H) = 8.1 Hz, 1 H; H<sup>Ar</sup>), 4.63 (bs, 1 H; OH), 3.77 (s, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT):  $\delta$  = 153.8 (C<sub>q</sub>; C<sup>Ar</sup>), 139.5 (C<sup>Ar</sup>), 139.1 (C<sub>q</sub>; C<sup>Phe</sup>), 136.7 (C<sup>Ar</sup>), 130.0 (C<sub>q</sub>; C<sup>Ar</sup>), 128.9 (C<sup>Phe</sup>), 128.8 (C<sup>Phe</sup>), 126.8 (C<sup>Phe</sup>), 118.2 (C<sup>Ar</sup>), 83.1 (C<sub>q</sub>; C<sup>Ar</sup>), 36.2 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 7.47 min; *m/z* (%): 310 (100) [ $M^+$ ], 232 (31) [ $M^+ - C_6H_5$ ], 183 (13) [ $M^+ - I$ ]; **m.p.**<sup>exp.</sup> = 35-37°C.

Analytical data are in accordance with those reported.<sup>[11]</sup>

### 2.1.15 2-Benzyl-4-iodophenyl trifluoromethanesulfonate (**3e**)



**3e**

Compound **3e** was prepared according to procedure 2.1.2 from 4.60 g phenol derivative **17e** (14.8 mmol, 1.0 eq) in 20 mL pyridine and 4.00 mL Tf<sub>2</sub>O (4.68 g, 16.6 mmol, 1.1 eq). Quantitative conversion was detected after 18 h. After flash column chromatography (cyclohexane,  $R_f$  = 0.28, CAM) compound **3e** was isolated as a colourless oil.

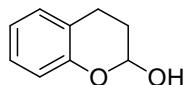
**Yield:** 5.62 g (86%); yellow oil, C<sub>14</sub>H<sub>10</sub>F<sub>3</sub>IO<sub>3</sub>S [442.19 g/mol].

## Experimental Procedures and Analytical Data

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**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.42 (dd, <sup>3</sup>J (H,H) = 8.6 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.32 (d, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.16-7.04 (m, 3 H; H<sup>Phe</sup>), 6.99-6.96 (m, 2 H; H<sup>Phe</sup>), 6.83 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 3.82 (s, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 147.9 (C<sub>q</sub>; C<sup>Ar</sup>), 140.8 (C<sup>Ar</sup>), 137.7 (C<sub>q</sub>; C<sup>Phe</sup>), 137.5 (C<sup>Ar</sup>), 136.6 (C<sub>q</sub>; C<sup>Ar</sup>), 129.2 (C<sup>Phe</sup>), 129.0 (C<sup>Phe</sup>), 127.1 (C<sup>Phe</sup>), 123.3 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 320 Hz; CF<sub>3</sub>), 93.5 (C<sub>q</sub>; C<sup>Ar</sup>), 35.6 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 7.13 min; m/z (%): 442 (100) [M<sup>+</sup>], 309 (51) [M<sup>+</sup>-CF<sub>3</sub>O<sub>2</sub>S], 181 (23) [M<sup>+</sup>-CF<sub>3</sub>IO<sub>2</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 441.9348; found: 441.9337.

### **2.1.16 Chroman-2-ol (21)**



**21**

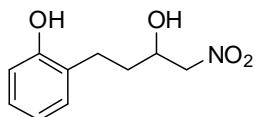
In an flame dried and argon flushed 250 mL three-neck round-bottom flask equipped with argon inlet and dropping funnel 5.00 g dihydrocoumarin (**20**) (33.7 mmol, 1.0 eq) were dissolved in 100 mL toluene. The solution was cooled to -78°C and 37.0 mL DIBALH (5.26 g, 37.0 mmol, 1.1 eq) were added drop wise over a period of 60 min. The reaction was stirred until full conversion (2 h) and then was quenched with 20 mL H<sub>2</sub>O. The white suspension was warmed up to room temperature and the colourless precipitate was filterer over celite®. The phases were separated and the aqueous phase was extracted with Et<sub>2</sub>O (1x200mL). The filter cake was stirred with 200 mL Et<sub>2</sub>O and filtered again. The combined organic phases were washed with H<sub>2</sub>O (1x200mL) and saturated NaCl-solution (1x200mL). Then the combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum.

**Yield:** 4.83 g (95%); yellow oil, C<sub>9</sub>H<sub>10</sub>O<sub>2</sub> [150.17 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.15-7.07 (m, 2 H; H<sup>Ar</sup>), 6.92-6.82 (m, 2 H; H<sup>Ar</sup>), 5.62 (t, <sup>3</sup>J (H,H) = 3.2 Hz, 1 H; CH), 3.27 (s, 1 H; OH), 3.05-2.94 (m, 1 H; CH<sub>2</sub>), 2.76-2.67 (m, 1 H; CH<sub>2</sub>), 2.06-1.99 (m, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 152.1 (C<sub>q</sub>; C<sup>Ar</sup>), 129.4 (C<sup>Ar</sup>), 127.5 (C<sup>Ar</sup>), 122.2 (C<sub>q</sub>; C<sup>Ar</sup>), 121.0 (C<sup>Ar</sup>), 117.0 (C<sup>Ar</sup>), 92.3 (CH), 27.2 (CH<sub>2</sub>), 20.4 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.28 min; m/z (%): 150 (26) [M<sup>+</sup>], 131 (100) [M<sup>+</sup>-OH], 107 (23) [M<sup>+</sup>-C<sub>2</sub>H<sub>2</sub>O], 77 (30) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>O<sub>2</sub>].<sup>[13]</sup>

Analytical data are in accordance with those reported.<sup>[13]</sup>

**2.1.17 2-(3-Hydroxy-4-nitrobutyl)phenol (19c)**



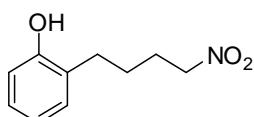
**19c**

In a flame dried and argon flushed Schlenk-flask 4.00 g lactole **21** (26.6 mmol, 1.0 eq) were dissolved in 14.5 mL nitromethane. 3.70 mL Et<sub>3</sub>N (2.70 g, 26.6 mmol, 1.0 eq) were added to the yellow solution and the reaction mixture was heated to reflux temperature. When quantitative conversion was reached (3 h) the reaction mixture was cooled to room temperature and 50 mL saturated NaHCO<sub>3</sub>-solution were added. The aqueous phase was extracted with ethylacetate (3x50 mL) and the combined organic layers were washed with saturated NaCl-solution (1x40 mL). Then they were dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (cyclohexane/EtOAc = 10/1, R<sub>f</sub> = 0.18, CAM).

**Yield:** 3.54 g (69%); pale yellow oil, C<sub>10</sub>H<sub>13</sub>NO<sub>4</sub> [211.21 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.13-7.05 (m, 2 H; H<sup>Ar</sup>), 6.89 (t, <sup>3</sup>J (H,H) = 7.4 Hz, 1 H; H<sup>Ar</sup>), 6.82 (d, <sup>3</sup>J (H,H) = 8.1 Hz, 1 H; H<sup>Ar</sup>), 4.82-4.74 (m, 1 H; CH), 4.71-4.64 (m, 1 H; CH<sub>2</sub>), 4.54 (dd, <sup>2</sup>J (H,H) = 12.5 Hz, <sup>3</sup>J (H,H) = 3.8 Hz, 1 H; CH<sub>2</sub>), 3.01-2.78 (m, 2 H; CH<sub>2</sub>), 2.15-2.05 (m, 1 H; CH<sub>2</sub>), 1.93-1.80 (m, 1 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 153.4 (C<sub>q</sub>; C<sup>Ar</sup>), 129.6 (C<sup>Ar</sup>), 127.8 (C<sup>Ar</sup>), 121.2 (C<sup>Ar</sup>) 121.0 (C<sub>q</sub>; C<sup>Ar</sup>), 117.1 (C<sup>Ar</sup>), 78.9 (CH<sub>2</sub>), 72.1 (CH), 24.7 (CH<sub>2</sub>), 24.0 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.23 min (elimination product); *m/z* (%): 193 (57) [M<sup>+</sup>], 146 (36) [M<sup>+</sup>-NO<sub>2</sub>], 131 (100) [M<sup>+</sup>-HNO<sub>3</sub>], 107 (37) [M<sup>+</sup>-C<sub>3</sub>H<sub>4</sub>NO<sub>2</sub>]; **HRMS** (EI): calcd for [M-H<sub>2</sub>O]<sup>+</sup>: 193.0739; found: 193.0728.

**2.1.18 2-(4-Nitrobutyl)phenol (16g)**



**16g**

In an flame dried and argon flushed 100 mL three-neck round-bottom flask equipped with argon inlet and reflux condenser 2.21 g phenol derivative **19c** (11.4 mmol, 1.0 eq) were dissolved in 75.0 mL methanol. To this yellow solution 2.27 g NaCNBH<sub>3</sub> (36.1 mmol, 3.2 eq) were added and heated to reflux temperature for 24 h. The reaction was cooled to room temperature and quenched with 20 mL HCl (0.1 M). Toxic gases were neutralized over a

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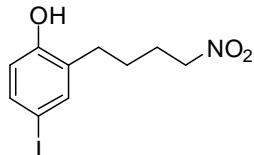
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KMnO<sub>4</sub>-solution. When no more gas is built methanol was removed in vacuum. The oily residue was dissolved in 20 mL DCM and washed with H<sub>2</sub>O (1x20 mL). The aqueous phase was reextracted with DCM (2x20 mL) and the combined organic layers were washed with saturated NaHCO<sub>3</sub> solution. Then they were dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (cyclohexane/EtOAc = 3/1, R<sub>f</sub> = 0.31, CAM).

**Yield:** 1.43 g (64%); yellow oil, C<sub>10</sub>H<sub>13</sub>NO<sub>3</sub> [195.22 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.13-7.07 (m, 2 H; H<sup>Ar</sup>), 6.88 (t, <sup>3</sup>J (H,H) = 7.4 Hz, 1 H; H<sup>Ar</sup>), 6.74 (d, <sup>3</sup>J (H,H) = 8.1 Hz, 1 H; H<sup>Ar</sup>), 4.41 (t, <sup>3</sup>J (H,H) = 6.9 Hz, 2 H; CH<sub>2</sub>NO<sub>2</sub>), 2.68 (t, <sup>3</sup>J (H,H) = 7.4 Hz, 2 H; CH<sub>2</sub>), 2.11-2.01 (m, 2 H; CH<sub>2</sub>), 1.77-1.67 (m, 2 H; CH<sub>2</sub>) ppm;  
**<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 153.6 (C<sub>q</sub>; C<sup>Ar</sup>), 130.5 (C<sup>Ar</sup>), 127.6 (C<sup>Ar</sup>), 127.5 (C<sub>q</sub>; C<sup>Ar</sup>), 121.1 (C<sup>Ar</sup>), 115.4 (C<sup>Ar</sup>), 75.7 (CH<sub>2</sub>NO<sub>2</sub>), 29.2 (CH<sub>2</sub>), 27.0 (CH<sub>2</sub>), 26.4 (CH<sub>2</sub>) ppm;  
**GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.60 min; m/z (%): 195 (13) [M<sup>+</sup>], 107 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>NO<sub>2</sub>], 91 (23) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>NO<sub>3</sub>], 77 (36) [M<sup>+</sup>-C<sub>4</sub>H<sub>9</sub>NO<sub>3</sub>]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 195.0895; found: 195.0898.

### **2.1.19 4-Iodo-2-(4-nitrobutyl)phenol (17g)**



**17g**

In an argon flushed Schlenk-flask 1.11 g phenol derivative **16g** (5.66 mmol, 1.0 eq) were dissolved in 5 mL acetic acid. 1.16 g ICl (7.14 mmol, 1.3 eq) dissolved in 5 mL acetic acid were added to the yellow solution. The now red-brown solution was heated to 40°C until full conversion (4 h). The reaction mixture was diluted with 50 mL DCM and washed with saturated NaHCO<sub>3</sub>-solution (1x50 mL). The aqueous phase was reextracted with DCM (3x50 mL). The combined organic layers were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>-solution (50%, 2x50 mL) and saturated NaCl-solution (1x100 mL). Then they were dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (cyclohexane/EtOAc = 5/1, R<sub>f</sub> = 0.12, CAM).

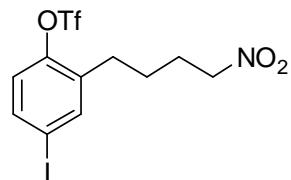
**Yield:** 1.38 g (76%); orange oil, C<sub>10</sub>H<sub>12</sub>INO<sub>3</sub> [321.11 g/mol].

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**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.38-7.34 (m, 2 H; H<sup>Ar</sup>), 6.52 (d, <sup>3</sup>J (H,H) = 8.1 Hz, 1 H; H<sup>Ar</sup>), 5.01 (s, 1 H; OH), 4.41 (t, <sup>3</sup>J (H,H) = 6.9 Hz, 2 H; CH<sub>2</sub>NO<sub>2</sub>), 2.62 (t, <sup>3</sup>J (H,H) = 7.5 Hz, 2 H; CH<sub>2</sub>), 2.09-1.99 (m, 2 H; CH<sub>2</sub>), 1.74-1.64 (m, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 153.6 (C<sub>q</sub>; C<sup>Ar</sup>), 139.0 (C<sup>Ar</sup>), 136.3 (C<sup>Ar</sup>), 130.5 (C<sub>q</sub>; C<sup>Ar</sup>), 117.6 (C<sup>Ar</sup>), 83.0 (C<sub>q</sub>; C<sup>Ar</sup>), 75.6 (CH<sub>2</sub>NO<sub>2</sub>), 28.9 (CH<sub>2</sub>), 27.0 (CH<sub>2</sub>), 26.3 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.60 min; m/z (%): 195 (13) [M<sup>+</sup>], 107 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>NO<sub>2</sub>], 91 (23) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>NO<sub>3</sub>], 77 (36) [M<sup>+</sup>-C<sub>4</sub>H<sub>9</sub>NO<sub>3</sub>]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 320.9862; found: 320.9871.

### **2.1.20 4-Iodo-2-(4-nitrobutyl)phenyl trifluoromethanesulfonate (3g)**



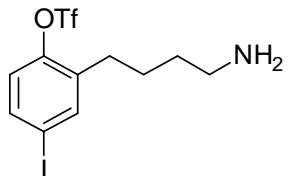
**3g**

Compound **3g** was prepared according to procedure 2.1.2 from 1.11 mg phenol derivative **17g** (3.47 mmol, 1.0 eq) in 10 mL pyridine and 920 μL Tf<sub>2</sub>O (1.08 g, 3.81 mmol, 1.1 eq). Quantitative conversion was detected after 90 min. After flash column chromatography (cyclohexane/Et<sub>2</sub>O = 20/1, R<sub>f</sub> = 0.30, CAM) compound **3g** was isolated as yellow oil.

**Yield:** 1.18 g (75%); yellow oil, C<sub>11</sub>H<sub>11</sub>F<sub>3</sub>INO<sub>5</sub>S [453.17 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.65-7.60 (m, 2 H; H<sup>Ar</sup>), 7.00 (d, <sup>3</sup>J (H,H) = 8.4 Hz, 1 H; H<sup>Ar</sup>), 4.20 (t, <sup>3</sup>J (H,H) = 6.9 Hz, 2 H; CH<sub>2</sub>NO<sub>2</sub>), 2.71 (t, <sup>3</sup>J (H,H) = 7.8 Hz, 2 H; CH<sub>2</sub>), 2.12-2.02 (m, 2 H; CH<sub>2</sub>), 1.78-1.68 (m, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 147.9 (C<sub>q</sub>; C<sup>Ar</sup>), 140.1 (C<sup>Ar</sup>), 137.5 (C<sup>Ar</sup>), 136.4 (C<sub>q</sub>; C<sup>Ar</sup>), 123.5 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 327 Hz; CF<sub>3</sub>), 93.6 (C<sub>q</sub>; C<sup>Ar</sup>), 75.2 (CH<sub>2</sub>NO<sub>2</sub>), 29.1 (CH<sub>2</sub>), 26.9 (CH<sub>2</sub>), 26.6 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 7.41 min; m/z (%): 453 (21) [M<sup>+</sup>], 365 (26) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>NO<sub>2</sub>], 131 (87) [M<sup>+</sup>-CF<sub>3</sub>INO<sub>5</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 452.9355; found: 452.9353.

### 2.1.21 2-(4-aminobutyl)-4-iodophenyl trifluoromethanesulfonate (3i)



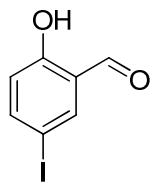
**3i**

In an argon flushed Schlenk-flask 969 mg **3g** (2.14 mmol, 1.0 eq) and 597 mg Fe-powder (10.7 mmol, 5.0 eq) were suspended in 10 mL HCl (2 M). Quantitative conversion was detected by HPLC-MS after 4.5 h. The reaction mixture was neutralized with NaOH (2 M) and diluted with 20 mL ethylacetate. The precipitate was filtered off and the phases were separated. The aqueous phase was extracted with ethylacetate (2x50 mL) and the combined organic layers were washed with saturated NaCl-solution (1x50 mL). Then they were dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (EtOAc/MeOH/Et<sub>3</sub>N = 8/1/1, R<sub>f</sub> = 0.24, CAM).

**Yield:** 325 g (36%); yellow oil, C<sub>11</sub>H<sub>11</sub>F<sub>3</sub>INO<sub>3</sub>S [423.19 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.66 (d, <sup>4</sup>J(H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.58 (dd, <sup>3</sup>J(H,H) = 8.4 Hz, <sup>4</sup>J(H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 6.97 (d, <sup>3</sup>J(H,H) = 8.7 Hz, 1 H; H<sup>Ar</sup>), 3.12 (s, 2 H; NH<sub>2</sub>), 2.81-2.63 (m, 4 H; CH<sub>2</sub>), 1.67-1.57 (m, 4 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 148.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.3 (C<sup>Ar</sup>), 137.5 (C<sub>q</sub>; C<sup>Ar</sup>), 137.1 (C<sup>Ar</sup>), 123.3 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J(C,F) = 327 Hz; CF<sub>3</sub>), 93.5 (C<sub>q</sub>; C<sup>Ar</sup>), 41.5 (CH<sub>2</sub>NH<sub>2</sub>), 32.2 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 27.1 (CH<sub>2</sub>) ppm; **HRMS** (EI): calcd for [M<sup>+</sup>]: 422.9613; found: 422.9638.

### 2.1.22 2-Hydroxy-5-iodobenzaldehyde (17h)



**17h**

In an argon flushed Schlenk-flask 2.20 mL salicylaldehyde (**16h**) (2.52 g, 20.6 mmol, 1.0 eq) were dissolved in 20 mL glacial acetic acid. 1.23 mL ICl (3.99 g, 24.58 mmol, 1.2 eq) were added and the brown solution was stirred for 24 h at 40°C. To achieve quantitative conversion, three times 0.5 eq ICl (total: 1.55 mL, 5.03 g, 31.0 mmol, 1.5 eq) were added every further 24 h. After quantitative conversion the reaction mixture was quenched with

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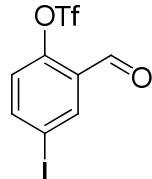
100 mL 0.5 M NaHCO<sub>3</sub> solution and 100 mL DCM were added. After phase separation the aqueous phase was extracted with DCM (3x50 mL). The combined organic layers were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (25%, 2x100 mL) and saturated NaCl solution (1x100 mL). Finally the organic phase was dried over MgSO<sub>4</sub>, the solvent was removed in vacuo and the crude product was purified by flash column chromatography (cyclohexane/EtOAc = 200/1, R<sub>f</sub> = 0.20, CAM).<sup>[14]</sup>

**Yield:** 4.74 g (93%); pale yellow powder, C<sub>7</sub>H<sub>5</sub>IO<sub>2</sub> [248.02 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 10.94 (s, 1 H; CHO), 9.83 (s, 1 H; OH), 7.84 (d, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.76 (dd, <sup>3</sup>J (H,H) = 8.8 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 6.80 (d, <sup>3</sup>J (H,H) = 8.8 Hz, 1 H; H<sup>Ar</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 195.5 (CHO), 161.3 (C<sub>q</sub>; C<sup>Ar</sup>), 145.4 (C<sup>Ar</sup>), 142.0 (C<sup>Ar</sup>), 122.7 (C<sub>q</sub>; C<sup>Ar</sup>), 120.3 (C<sup>Ar</sup>), 80.5 (C<sub>q</sub>; C<sup>Ar</sup>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.48 min; m/z (%): 248 (100) [M<sup>+</sup>], 219 (6) [M<sup>+</sup>-CHO], 202 (3) [M<sup>+</sup>-CH<sub>2</sub>O<sub>2</sub>]; **m.p.**<sup>exp.</sup> = 97-99°C (m.p.<sup>lit.</sup> = 97-98°C).<sup>[15]</sup>

Analytical data are in accordance with those reported.<sup>[14]</sup>

### **2.1.23 2-Formyl-4-iodophenyl trifluoromethanesulfonate (3h)**



**3h**

In a flame dried and argon flushed Schlenk-flask 2.00 g phenol derivative **17h** (8.06 mmol, 1.0 eq) were dissolved in 7.00 mL DCM and 976 μL pyridine (957 mg, 12.1 mmol, 1.5 eq). The pale yellow solution was cooled to 0°C. After cooling to 0°C 3.90 mL Tf<sub>2</sub>O (4.55 mL, 16.1 mmol, 2.0 eq) were added and was allowed to warm to room temperature after 5 min. After quantitative conversion (4 h) the brown reaction mixture was diluted with 100 mL DCM and the organic phase was washed with 100 mL H<sub>2</sub>O. The aqueous phase was extracted with DCM (2x100 mL) and the combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was removed under reduced pressure. The brown, oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 40/1, R<sub>f</sub> = 0.26 CAM).<sup>[16]</sup>

**Yield:** 3.20 g (71%), yellow oil, C<sub>8</sub>H<sub>4</sub>F<sub>3</sub>IO<sub>3</sub>S [380.08 g/mol].

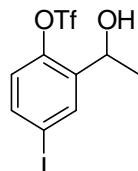
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 10.18 (s, 1 H; CHO), 8.29 (d, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 8.02 (dd, <sup>3</sup>J (H,H) = 8.6 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.16 (d, <sup>3</sup>J (H,H) = 8.7 Hz, 1 H;

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$\text{H}^{\text{Ar}}$ ) ppm;  **$^{13}\text{C}$  NMR** (76 MHz,  $\text{CDCl}_3$ ):  $\delta = 185.1$  (CHO), 149.8 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 144.7 ( $\text{C}^{\text{Ar}}$ ), 139.6 ( $\text{C}^{\text{Ar}}$ ), 129.8 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 124.4 ( $\text{C}^{\text{Ar}}$ ), 118.7 (q,  $^1\text{J}(\text{C},\text{F}) = 321$  Hz;  $\text{CF}_3$ ), 93.7 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_\text{R} = 5.98$  min;  $m/z$  (%): 380 (100) [ $M^+$ ], 247 (54) [ $M^+ - \text{CF}_3\text{O}_2\text{S}$ ], 219 (24) [ $M^+ - \text{C}_2\text{HF}_3\text{O}_3\text{S}$ ].

### **2.1.24 2-(1-hydroxyethyl)-4-iodophenyl trifluoromethanesulfonate (3l)**



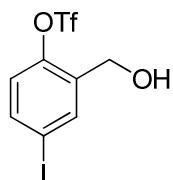
**3l**

In a flame dried and argon flushed Schlenk-flask 69.1 mg Mg (2.84 mmol, 1.2 eq) were prepared and stirred for 20 min without solvent. Then it was suspended in 5 mL  $\text{Et}_2\text{O}$  and 180  $\mu\text{L}$  iodomethane (403 mg, 2.84 mmol, 1.2 eq) dissolved in 5 mL  $\text{Et}_2\text{O}$  were added. The reaction mixture was refluxed till the whole Mg was dissolved (30 min). The colourless suspension was added drop by drop to a solution of **3h** in 10 mL  $\text{Et}_2\text{O}$ . The pale yellow suspension kept stirring until quantitative conversion was detected by TLC. After 5 h the reaction was diluted with 100 mL  $\text{Et}_2\text{O}$  and washed with 1 M HCl (1x100 mL), saturated  $\text{NaHCO}_3$  solution (1x100 mL) and saturated NaCl solution. The organic layer was tried over  $\text{MgSO}_4$ , filtered and the solvent was removed in vacuum. The yellow, oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 10/1,  $R_f = 0.21$ , CAM).

**Yield:** 882 mg (94%), pale yellow solid,  $\text{C}_9\text{H}_8\text{F}_3\text{IO}_4\text{S}$  [396.12 g/mol].

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 8.02$  (d,  $^4\text{J}(\text{H},\text{H}) = 2.1$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 7.67 (dd,  $^3\text{J}(\text{H},\text{H}) = 8.6$  Hz,  $^4\text{J}(\text{H},\text{H}) = 2.3$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 6.98 (d,  $^3\text{J}(\text{H},\text{H}) = 8.4$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 5.16 (q,  $^3\text{J}(\text{H},\text{H}) = 6.4$  Hz, 1 H; CH), 2.04 (bs, 1 H; OH), 1.50 (d,  $^3\text{J}(\text{H},\text{H}) = 6.6$  Hz, 3 H;  $\text{CH}_3$ ) ppm;  **$^{13}\text{C}$  NMR** (76 MHz,  $\text{CDCl}_3$ ):  $\delta = 145.9$  ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 140.8 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 138.3 ( $\text{C}^{\text{Ar}}$ ), 137.2 ( $\text{C}^{\text{Ar}}$ ), 123.1 ( $\text{C}^{\text{Ar}}$ ), 118.6 (q,  $^1\text{J}(\text{C},\text{F}) = 322$  Hz;  $\text{CF}_3$ ), 94.0 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 64.1 (CH), 24.2 ( $\text{CH}_3$ ) ppm; **m.p.<sup>exp.</sup>** = 37-40°C; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_\text{R} = 6.24$ ;  $m/z$  (%): 382 (49) [ $M^+$ ], 249 (14) [ $M^+ - \text{CF}_3\text{O}_2\text{S}$ ], 122 (11) [ $M^+ - \text{CF}_3\text{IO}_2\text{S}$ ]; **HRMS** (EI): calcd for [ $M^+$ ]: 395.9140; found: 395.9135.

**2.1.25 2-(Hydroxymethyl)-4-iodophenyl trifluoromethanesulfonate (3j)**



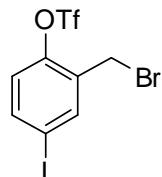
**3j**

In a flame dried and argon flushed Schlenk-flask 920 mg aldehyde **3h** (2.42 mmol, 1.0 eq) were dissolved in 4.5 mL absolute DCM. This solution was cooled to -78°C and 3.23 mL diisobutylaluminium hydride (DIBALH) (1.5 M in toluene) (688 mg, 4.84 mmol, 2.0 eq) were carefully added. After stirring for 30 min at -78°C the bright yellow solution was allowed to warm to room temperature and kept stirring until quantitative conversion was detected by GC-MS. After 16 h the reaction mixture was quenched with 50 mL MeOH and 50 mL H<sub>2</sub>O. A fine, pale yellow precipitate was formed. The suspension was filtered through Celite®, 100 mL DCM were added to the filtrate and the phases were separated. The aqueous phase was extracted with DCM (4x50 mL) and the combined organic layers were dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure and the yellow, oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 5/1, R<sub>f</sub> = 0.32, CAM).

**Yield:** 506 mg (55%), pale yellow powder, C<sub>8</sub>H<sub>6</sub>F<sub>3</sub>IO<sub>4</sub>S [382.10 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.97 (d, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.70 (dd, <sup>3</sup>J (H,H) = 8.6 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 7.01 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 4.76 (s, 2 H; CH<sub>2</sub>), 1.96 (bs, 1 H; OH) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 146.7 (C<sub>q</sub>; C<sup>Ar</sup>), 138.9 (C<sup>Ar</sup>), 138.5 (C<sup>Ar</sup>), 135.9 (C<sub>q</sub>; C<sup>Ar</sup>), 123.2 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 320 Hz; CF<sub>3</sub>), 93.7 (C<sub>q</sub>; C<sup>Ar</sup>), 59.1 (CH<sub>2</sub>) ppm; **m.p.**<sup>exp.</sup> = 28-30°C; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.24; *m/z* (%): 382 (49) [M<sup>+</sup>], 249 (14) [M<sup>+</sup>-CF<sub>3</sub>O<sub>2</sub>S], 122 (11) [M<sup>+</sup>-CF<sub>3</sub>IO<sub>2</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 381.8984; found: 381.8989.

**2.1.26 2-(Bromomethyl)-4-iodophenyl trifluoromethanesulfonate (22)**



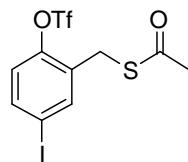
**22**

In an argon flushed 250 two-neck round-bottom flask equipped with argon inlet 700 mg alcohol **3j** (1.83 mmol, 1.0 eq) were dissolved in 100 mL DCM. A catalytic amount of DMF was added. 215  $\mu$ L thionylbromide (571 mg, 2.75 mmol, 1.5 eq) were added drop wise. The brownish solution was stirred 16 h and after full conversion the reaction mixture was diluted with 50 mL DCM. The solution was washed with saturated NaHCO<sub>3</sub>-solution (1x100mL) and saturated NaCl-solution (1x100mL). The organic layer was dried over MgSO<sub>4</sub>, filtered and the solvent was removed in vacuum. The oily crude product was purified by flash column chromatography (cyclohexane, R<sub>f</sub> = 0.36, CAM).

**Yield:** 339 mg (42%), pale yellow oil, C<sub>8</sub>H<sub>5</sub>BrF<sub>3</sub>IO<sub>3</sub>S [444.99 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.87 (d, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.72 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.06 (d, <sup>3</sup>J (H,H) = 8.4 Hz, 1 H; H<sup>Ar</sup>), 4.43 (s, 2 H; CH<sub>2</sub>), ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>):  $\delta$  = 147.1 (C<sub>q</sub>; C<sup>Ar</sup>), 141.1 (C<sup>Ar</sup>), 139.6 (C<sup>Ar</sup>), 133.0 (C<sub>q</sub>; C<sup>Ar</sup>), 123.6 (C<sup>Ar</sup>), 118.7 (q, <sup>1</sup>J (C,F) = 327 Hz; CF<sub>3</sub>), 93.3 (C<sub>q</sub>; C<sup>Ar</sup>), 24.5 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.30; *m/z* (%): 444 (20) [M<sup>+</sup>], 365 (100) [M<sup>+</sup>-Br], 311 (17) [M<sup>+</sup>-CF<sub>3</sub>O<sub>2</sub>S], 332 (24) [M<sup>+</sup>-CBrF<sub>3</sub>O<sub>2</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 443.8140; found: 443.8143.

**2.1.27 S-5-iodo-2-(((trifluoromethyl)sulfonyl)oxy)benzyl ethanethioate (3k)**



**3k**

In a flame dried and argon flushed Schlenk-flask 300 mg bromo-derivative **22** (674  $\mu$ mol, 1.0 eq) were dissolved in 2 mL absolute THF. 205 mg K<sub>2</sub>CO<sub>3</sub> (1.28 mmol, 2.2 eq) and 57.8  $\mu$ L thioacetic acid (61.6 mg, 809  $\mu$ mol, 1.2 eq) were added. The colourless suspension was stirred at room temperature until full conversion. Full conversion was detected by

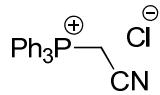
## Experimental Procedures and Analytical Data

GC-MS after 60 min. Then the reaction mixture was neutralized with HCl (1 M, 1 mL) and diluted with 20 mL H<sub>2</sub>O. The aqueous phase was extracted with DCM (3x20 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated in vacuum. The oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 50/1, R<sub>f</sub> = 0.27, CAM).

**Yield:** 245 mg (82%), colourless oil, C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>IO<sub>4</sub>S<sub>2</sub> [440.20 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.82 (d, <sup>4</sup>J (H,H) = 1.8 Hz, 1 H; H<sup>Ar</sup>), 7.65 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.01 (d, <sup>3</sup>J (H,H) = 8.7 Hz, 1 H; H<sup>Ar</sup>), 4.11 (s, 2 H; CH<sub>2</sub>), 2.38 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 194.1 (C<sub>q</sub>; COOMe) 147.5 (C<sub>q</sub>; C<sup>Ar</sup>), 140.8 (C<sup>Ar</sup>), 138.5 (C<sup>Ar</sup>), 133.3 (C<sub>q</sub>; C<sup>Ar</sup>), 123.2 (C<sup>Ar</sup>), 118.6 (q, <sup>1</sup>J (C,F) = 318 Hz; CF<sub>3</sub>), 93.3 (C<sub>q</sub>; C<sup>Ar</sup>), 30.4 (CH<sub>3</sub>), 27.1 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.84; m/z (%): 440 (57) [M<sup>+</sup>], 397 (24) [M<sup>+</sup>-C<sub>2</sub>H<sub>3</sub>O], 291 (91) [M<sup>+</sup>-CF<sub>3</sub>O<sub>3</sub>S]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 439.8861; found: 439.8857.

### 2.1.28 (Cyanomethyl)triphenylphosphonium chloride (18b)



**18b**

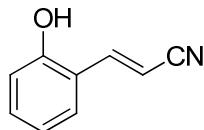
In a flame dried and argon flushed Schlenk-flask 9.00 g PPh<sub>3</sub> (34.4 mmol, 1.0 eq) were dissolved in 50 mL absolute, degassed toluene. 4.35 mL 2-chloroacetonitrile (5.18 g, 58.6 mmol, 2.0 eq) were added to the colourless solution. The reaction mixture was stirred under reflux and after 24 h a colourless precipitate was formed. The suspension was cooled to room temperature and the precipitate was collected by filtration and washed with Et<sub>2</sub>O (2x10 mL).<sup>[17]</sup>

**Yield:** 11.5 g (99%), colourless powder, C<sub>20</sub>H<sub>17</sub>ClNP [337.78 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 8.01-7.81 (m, 15 H; H<sup>Ar</sup>), 6.20 (d, <sup>2</sup>J (H,P) = 15.9 Hz, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT): δ = 135.9 (d, <sup>4</sup>J (C,P) = 3 Hz; C<sup>Ar</sup>), 133.8 (d, <sup>3</sup>J (C,P) = 11 Hz; C<sup>Ar</sup>), 130.5 (d, <sup>2</sup>J (C,P) = 13 Hz; C<sup>Ar</sup>), 116.3 (d, <sup>1</sup>J (C,P) = 89 Hz; C<sup>Ar</sup>), 112.9 (d, <sup>2</sup>J (C,P) = 9 Hz; CN), 14.3 (d, <sup>1</sup>J (C,P) = 55 Hz; CH<sub>2</sub>) ppm; **m.p.**<sup>exp.</sup> = 263°C, decomposition (m.p.<sup>lit.</sup> = 265-267°C, decomposition).<sup>[18]</sup>

Analytical data are in accordance with those reported.<sup>[18]</sup>

**2.1.29 3-(2-Hydroxyphenyl)acrylonitrile (19b)**



**19b**

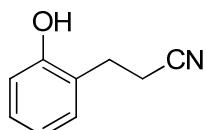
In a flame dried and argon flushed 500 mL three-neck round-bottom flask equipped with reflux condenser, and two argon-inlets 12.5 g **18b** (36.9 mmol, 1.5 eq) were suspended in 120 mL absolute THF. After cooling the suspension to 0°C, 4.13 g KO*t*Bu (36.9 mmol, 1.5 eq) were added. The pale yellow reaction mixture was stirred at 50°C and after 60 min the suspension was cooled again to 0°C. 2.61 mL salicylaldehyde (**16h**) (3.00 g, 24.6 mmol, 1.0 eq) were added and the brown suspension was heated to 80°C. After quantitative conversion (20 h) the reaction mixture was cooled to room temperature and quenched with 120 mL saturated NH<sub>4</sub>Cl solution. The aqueous phase was extracted with DCM (3x100 mL) and the combined organic layers were washed with saturated NaCl solution (1x200 mL), dried over MgSO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and the brown, oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 3/1, R<sub>f</sub> = 0.22, CAM).

**Yield:** 3.43 g (96%), orange powder, C<sub>9</sub>H<sub>7</sub>NO [145.16 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.63 (d, <sup>3</sup>J (H,H) = 16.8 Hz, 1 H; CH), 7.35 (dd, <sup>3</sup>J (H,H) = 7.8 Hz, <sup>4</sup>J (H,H) = 1.2 Hz 1 H; C<sup>Ar</sup>), 7.29 (dt, <sup>3</sup>J (H,H) = 8.1 Hz, <sup>4</sup>J (H,H) = 1.6 Hz, 1 H; C<sup>Ar</sup>), 6.95 (dt, <sup>3</sup>J (H,H) = 7.7 Hz, <sup>4</sup>J (H,H) = 0.6 Hz, 1 H; C<sup>Ar</sup>), 6.86 (d, <sup>3</sup>J (H,H) = 8.1 Hz, 1 H; C<sup>Ar</sup>), 6.30 (s, 1 H; OH), 6.17 (d, <sup>3</sup>J (H,H) = 16.8 Hz, 1H; CH) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 155.4 (C<sub>q</sub>; C<sup>Ar</sup>), 147.3 (CH), 132.4 (C<sup>Ar</sup>), 129.6 (C<sup>Ar</sup>), 121.1 (C<sup>Ar</sup>), 121.1 (C<sub>q</sub>; C<sup>Ar</sup>), 119.2 (C<sub>q</sub>; CN), 116.6 (C<sup>Ar</sup>), 96.8 (CH) ppm; **m.p.**<sup>exp.</sup> = 124-128°C (m.p.<sup>lit.</sup> = 126-127°C);<sup>[19]</sup> **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.20 min; *m/z* (%): 145 (31) [M<sup>+</sup>], 118 (100) [M<sup>+</sup>-CN], 51 (7) [M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>O].

Analytical data are in accordance with those reported.<sup>[20]</sup>

### 2.1.30 3-(2-Hydroxyphenyl)propanenitrile (**16f**)



**16f**

An argon flushed 500 mL three-neck round-bottom flask, equipped with argon-inlet, was charged with 3.40 g (23.4 mmol, 1.0 eq) phenol derivative **19b** and dissolved in 190 mL MeOH. 680 mg palladium(II) hydroxide on activated charcoal (Pd(OH)<sub>2</sub>/C) (20 wt%) were added to the orange reaction mixture.\* After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (6x), the reaction mixture was stirred for 24 h at room temperature. After filtering off the catalyst (5x3 cm SiO<sub>2</sub>, eluent: MeOH) and evaporating the solvent using a rotary evaporator, the crude product was purified by flash column chromatography (cyclohexane/EtOAc = 5/1, R<sub>f</sub> = 0.13, CAM).†

**Yield:** 2.30 g (67%), pale brown oil, C<sub>9</sub>H<sub>9</sub>NO [147.17 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.17-7.11 (m, 2 H; H<sup>Ar</sup>), 6.89 (dt, <sup>3</sup>J(H,H) = 7.5 Hz, <sup>4</sup>J(H,H) = 1.0 Hz, 1 H; H<sup>Ar</sup>), 6.75 (d, <sup>3</sup>J(H,H) = 7.9 Hz, 1 H; H<sup>Ar</sup>), 5.59 (bs, 1 H; OH), 2.98 (t, <sup>3</sup>J(H,H) = 7.4 Hz, 2 H; CH<sub>2</sub>), 2.69 (t, <sup>3</sup>J(H,H) = 7.3 Hz, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 153.9 (C<sub>q</sub>; C<sup>Ar</sup>), 130.7 (C<sup>Ar</sup>), 128.7 (C<sup>Ar</sup>), 124.7 (C<sub>q</sub>; C<sup>Ar</sup>), 121.0 (C<sup>Ar</sup>), 119.8 (C<sub>q</sub>; CN), 115.5 (C<sup>Ar</sup>), 26.9 (CH<sub>2</sub>), 17.5 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.82 min; m/z (%): 147 (29) [M<sup>+</sup>], 107 (100) [M<sup>+</sup>-C<sub>2</sub>H<sub>2</sub>N], 91 (9) [M<sup>+</sup>-C<sub>2</sub>H<sub>3</sub>NO].

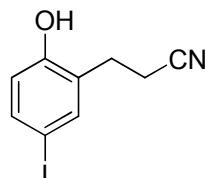
Analytical data are in accordance with those reported.<sup>[21]</sup>

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\* Palladium hydroxide on activated charcoal, moistened with water, 15-20% Pd basis (based on dry substance), Fluka 76063.

† The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

### 2.1.31 3-(2-Hydroxy-5-iodophenyl)propanenitrile (17f)



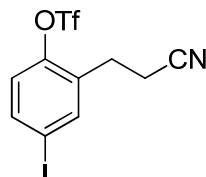
**17f**

Compound **17f** was prepared according to procedure 2.1.1 from 1.00 g 3-(2-hydroxyphenyl)-propanenitrile (**16f**) (6.79 mmol, 1.0 eq) in 10 mL acetic acid and 1.10 g ICl (6.79 mmol, 1.0 eq). After 24 h quantitative conversion was detected by GC-MS. Compound **17f** was used in the next step without further purification.\*

**Yield:** 1.25 g (67%), brown oil, C<sub>9</sub>H<sub>8</sub>INO [273.07 g/mol].

**TLC:** R<sub>f</sub> = 0.15 (cyclohexane/EtOAc = 5/1, CAM); **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 7.13 min; m/z (%): 272 (80) [M<sup>+</sup>], 233 (100) [M<sup>+</sup>-C<sub>2</sub>H<sub>2</sub>N], 146 (13) [M<sup>+</sup>-I], 106 (17) [M<sup>+</sup>-C<sub>2</sub>H<sub>2</sub>IN]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 272.9651; found: 272.9670.

### 2.1.32 2-(2-Cyanoethyl)-4-iodophenyl trifluoromethanesulfonate (3f)



**3f**

Compound **3f** was prepared according to procedure 2.1.2 from 870 mg phenol derivative **17f** (3.19 mmol, 1.0 eq) in 4 mL pyridine and 845 μL Tf<sub>2</sub>O (989 mg, 3.50 mmol, 1.1 eq). Quantitative conversion was detected after 2 h. After flash column chromatography (cyclohexane/Et<sub>2</sub>O = 10/1, R<sub>f</sub> = 0.20, CAM) compound **3f** was isolated as a pale yellow solid.

**Yield:** 893 mg (69%), pale yellow solid, C<sub>10</sub>H<sub>7</sub>F<sub>3</sub>INO<sub>3</sub>S [405.13 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.75-7.69 (m, 2 H; H<sup>Ar</sup>), 7.06 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 3.02 (t, <sup>3</sup>J (H,H) = 7.3 Hz, 2 H; CH<sub>2</sub>), 2.69 (t, <sup>3</sup>J (H,H) = 7.3 Hz, 2H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 147.5 (C<sub>q</sub>; C<sup>Ar</sup>), 140.3 (C<sup>Ar</sup>), 138.8 (C<sup>Ar</sup>), 133.1 (C<sub>q</sub>; C<sup>Ar</sup>), 123.7 (C<sup>Ar</sup>), 118.6 (q, <sup>1</sup>J (C,F) = 320 Hz; CF<sub>3</sub>), 118.0 (C<sub>q</sub>; CN), 93.8 (C<sub>q</sub>; C<sup>Ar</sup>), 25.9 (CH<sub>2</sub>), 17.7 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.65 min; m/z (%): 405 (47) [M<sup>+</sup>], 272

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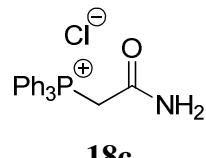
\* During flash column chromatography, a deiodination of compound **17f** was observed.

## Experimental Procedures and Analytical Data

(53)  $[M^+ - CF_3O_2S]$ , 145 (100)  $[M^+ - CF_3IO_2S]$ ; **m.p.**<sup>exp.</sup> = 46-50°C; **HRMS** (EI): calcd for  $[M^+]$ : 404.9143; found: 404.9145.

## 2.2 Synthesis of the Diazonium Core Fragments

### 2.2.1 (2-Amino-2-oxoethyl)triphenylphosphonium chloride (18c)



**18c**

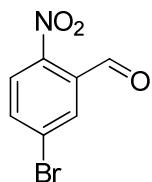
In a flame dried 50 mL two-neck round-bottom flask with reflux condenser and argon-inlet 7.86 g PPh<sub>3</sub> (30.0 mmol, 1.05 eq) and 2.67 g 2-chloroacetamide (28.6 mmol, 1.0 eq) were dried in vacuo. The dried starting materials were suspended in 33 mL freshly distilled nitromethane, and the mixture was stirred for 19 h at 105°C. The pale yellow solution was allowed to cool to room temperature, and the formed colourless precipitate was isolated by filtration, washed with EtOAc (2x10 mL), Et<sub>2</sub>O (1x15 mL) and dried in vacuo.<sup>[22]</sup>

**Yield:** 9.93 g (98%), colourless powder, C<sub>20</sub>H<sub>19</sub>ClNOP [355.80 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 8.43 (bs, 1 H; CONH<sub>2</sub>), 7.90-7.71 (m, 15 H; H<sup>Ar</sup>), 7.62 (bs, 1 H; CONH<sub>2</sub>), 5.13 (d, <sup>2</sup>J(H,P) = 14.9 Hz, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO): δ = 165.0 (d, <sup>2</sup>J(C,P) = 5 Hz; CONH<sub>2</sub>), 134.7 (d, <sup>4</sup>J(C,P) = 3 Hz; C<sup>Ar</sup>), 133.8 (d, <sup>3</sup>J(C,P) = 11 Hz; C<sup>Ar</sup>), 129.9 (d, <sup>2</sup>J(C,P) = 13 Hz; C<sup>Ar</sup>), 119.1 (d, <sup>1</sup>J(C,P) = 89 Hz; C<sup>Ar</sup>), 31.2 (d, <sup>1</sup>J(C,P) = 58 Hz; CH<sub>2</sub>) ppm; **m.p.**<sup>exp.</sup> = 215-218°C (m.p.<sup>lit.</sup> = 227-229°C).<sup>[23]</sup>

Analytical data are in accordance with those reported.<sup>[22]</sup>

### 2.2.2 5-Bromo-2-nitrobenzaldehyde (6)



**6**

At 0°C 5 mL HNO<sub>3</sub> (60-70% solution in H<sub>2</sub>O) and 10 mL H<sub>2</sub>SO<sub>4</sub> (96% solution in H<sub>2</sub>O) were mixed in a 100 mL round-bottom flask, and 4.12 g 3-bromobenzaldehyde (**5**) (22.3 mmol, 1.0 eq) were added in small portions. During the addition a yellow/orange precipitate was formed, and after 30 min at 0°C, the suspension was stirred for 45 min at room temperature.

## Experimental Procedures and Analytical Data

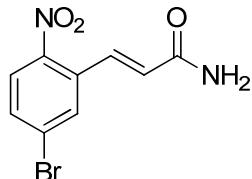
The mixture was poured into 60 mL ice cold saturated NaHCO<sub>3</sub> solution and extracted with EtOAc (3x25 mL). The combined yellow organic layers were washed with saturated NaHCO<sub>3</sub> solution until the pH of the aqueous phase was ~8-9 and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and evaporation of the solvent, the dark-orange crude product was purified by flash column chromatography (230 g SiO<sub>2</sub>, 31x4.5 cm, cyclohexane/EtOAc = 9/1, R<sub>f</sub> = 0.31).<sup>[24]</sup>

**Yield:** 4.26 g (83%), pale yellow solid, C<sub>7</sub>H<sub>4</sub>BrNO<sub>3</sub> [230.02 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 10.41 (s, 1 H; CHO), 8.06 (d, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>), 8.03 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 7.88 (dd, <sup>3</sup>J (H,H) = 8.6 Hz, <sup>4</sup>J (H,H) = 2.2 Hz, 1 H; H<sup>Ar</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 186.9 (CHO), 148.2 (C<sub>q</sub>; C<sup>Ar</sup>), 136.6 (C<sup>Ar</sup>), 132.8 (C<sup>Ar</sup>), 132.7 (C<sub>q</sub>; C<sup>Ar</sup>), 129.7 (C<sub>q</sub>; C<sup>Ar</sup>), 126.3 (C<sup>Ar</sup>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.41 min; *m/z* (%): 231 (1) [M<sup>+</sup>], 229 (1) [M<sup>+</sup>], 201 (67) [M<sup>+</sup>-O<sub>2</sub>], 199 (68) [M<sup>+</sup>-O<sub>2</sub>], 184 (23) [M<sup>+</sup>-HNO<sub>2</sub>], 182 (23) [M<sup>+</sup>-HNO<sub>2</sub>], 173 (96) [C<sub>5</sub>H<sub>2</sub>BrNO<sup>+</sup>], 171 (100) [C<sub>5</sub>H<sub>2</sub>BrNO<sup>+</sup>]; **m.p.**<sup>exp.</sup> = 62-66°C (m.p.<sup>lit.</sup> = 63-66°C).<sup>[24]</sup>

Analytical data are in accordance with those reported.<sup>[25]</sup>

### 2.2.3 (*E*)-3-(5-Bromo-2-nitrophenyl)acrylamide (7)



7

In a flame dried 100 mL two-neck round-bottom flask with argon-inlet 1.66 g (2-amino-2-oxoethyl)triphenylphosphonium chloride (**18c**) (4.67 mmol, 1.05 eq) and 524 mg KOtBu (4.67 mmol, 1.05 eq) were suspended under ice/NaCl cooling in 40 mL absolute, degassed MeOH. After 20 min 1.02 g 5-bromo-2-nitrobenzaldehyde (**6**) (4.43 mmol, 1.0 eq) were added in one portion, and after 45 min stirring at -2°C the mixture was concentrated to dryness without further workup. The salmon-coloured crude product was recrystallized from 190 mL MeOH/EtOAc (70/25), and after hot filtration the formed pale yellow crystals were isolated by filtration.\*

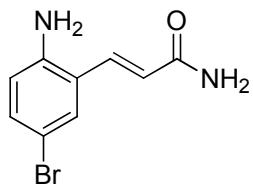
**Yield:** 1.08 g (90%), pale yellow fine crystals/wool, C<sub>9</sub>H<sub>7</sub>BrN<sub>2</sub>O<sub>3</sub> [271.07 g/mol].

\* Only the *E*-isomer crystallized under chosen conditions.

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**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 8.00 (d, <sup>3</sup>J (H,H) = 8.7 Hz, 1 H; H<sup>Ar</sup>), 7.97 (d, <sup>4</sup>J (H,H) = 2.0 Hz, 1 H; H<sup>Ar</sup>), 7.84 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.63 (d, <sup>3</sup>J (H,H) = 15.6 Hz, 1 H; CH), 7.61 (bs, 1 H; CONH<sub>2</sub>, overlapping), 7.35 (bs, 1 H; CONH<sub>2</sub>), 6.66 (d, <sup>3</sup>J (H,H) = 15.6 Hz, 1 H; CH) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT): δ = 165.5 (C<sub>q</sub>; CONH<sub>2</sub>), 147.1 (C<sub>q</sub>; C<sup>Ar</sup>), 133.0 (CH), 132.8 (C<sup>Ar</sup>), 132.4 (C<sub>q</sub>; C<sup>Ar</sup>), 131.3 (C<sup>Ar</sup>), 128.5 (CH), 127.4 (C<sub>q</sub>; C<sup>Ar</sup>), 126.7 (C<sup>Ar</sup>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 7.35 min, m/z (%): 226 (100) [M<sup>+</sup>–H<sub>2</sub>NO<sub>2</sub>], 224 (94) [M<sup>+</sup>–H<sub>2</sub>NO<sub>2</sub>], 145 (19) [M<sup>+</sup>–BrNO<sub>2</sub>]; **m.p.**<sup>exp.</sup> = 242–248°C (decomposition).

### 2.2.4 (*E*)-3-(2-Amino-5-bromophenyl)acrylamide (**8**)



**8**

In a flame dried 250 mL two-neck round-bottom flask with argon-inlet 3.74 g (*E*)-3-(5-bromo-2-nitrophenyl)acrylamide (**7**) (13.8 mmol, 1.0 eq) and 3.27 g tin powder (325 mesh) (27.6 mmol, 2.0 eq) were dried in vacuo. After back-flushing with argon, 100 mL degassed acetic acid (96% in water) were added, and the deep-greyish suspension was stirred under exclusion of light at room temperature until full conversion (~2d) was detected by GC-MS (mini-workup: saturated NaOH/EtOAc/MgSO<sub>4</sub>). During the reaction a colour change from grey over green to yellow was observed. After quantitative conversion the reaction mixture was concentrated under reduced pressure to a half, and the pale yellow suspension was quenched with saturated NaOH solution. After heating to 55°C the aqueous phase was filtered, and the warm aqueous phase was extracted with EtOAc (4x50 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and after removing the solvent under reduced pressure, compound **8** was isolated as a yellow powder.

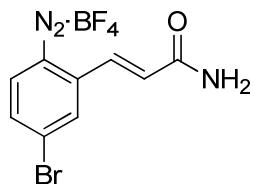
**Yield:** 3.32 g (quant.), bright-yellow solid, C<sub>9</sub>H<sub>9</sub>BrN<sub>2</sub>O [241.08 g/mol].

**TLC:** R<sub>f</sub> = 0.20 (EtOAc, tailing); **<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 7.51 (d, <sup>3</sup>J (H,H) = 15.7 Hz, 1 H; CH), 7.40 (bs, 1 H; CONH<sub>2</sub>, overlapping), 7.39 (d, <sup>4</sup>J (H,H) = 2.3 Hz, 1 H; H<sup>Ar</sup>), 7.15 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.3 Hz, 1 H; H<sup>Ar</sup>), 7.05 (bs, 1 H; CONH<sub>2</sub>), 6.64 (d, <sup>3</sup>J (H,H) = 8.7 Hz, 1 H; H<sup>Ar</sup>), 6.42 (d, <sup>3</sup>J (H,H) = 15.6 Hz, 1 H; CH), 5.61 (bs, 2 H; Ar-NH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT): δ = 167.0 (C<sub>q</sub>; CONH<sub>2</sub>), 146.8 (C<sub>q</sub>;

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$C^{Ar}$ ), 133.8 (CH), 132.4 ( $C^{Ar}$ ), 128.4 ( $C^{Ar}$ ), 121.9 ( $C^{Ar}$ ), 120.7 (C<sub>q</sub>;  $C^{Ar}$ ), 118.1 (CH), 107.0 (C<sub>q</sub>;  $C^{Ar}$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 7.60 min;  $m/z$  (%): 242 (35) [ $M^+$ ], 240 (36) [ $M^+$ ], 226 (54) [ $M^+-NH_2$ ], 224 (62) [ $M^+-NH_2$ ], 198 (13) [ $M^+-CH_2NO$ ], 196 (15) [ $M^+-CH_2NO$ ], 117 (61) [ $M^+-CH_2BrNO$ ]; **m.p.**<sup>exp.</sup> = 195-197°C.

### **2.2.5 (E)-2-(3-Amino-3-oxoprop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (2a)**



**2a**

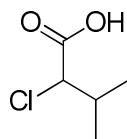
In a flame dried 500 mL two-neck round-bottom flask with argon-inlet 3.32 g (E)-3-(2-amino-5-bromophenyl)acrylamide (**8**) (13.8 mmol, 1.0 eq) were dissolved in 250 mL absolute, degassed THF. After cooling to -45°C, 2.08 mL boron trifluoride ethyl etherate ( $BF_3\cdot Et_2O$ ) (2.39 g, 16.8 mmol, 1.2 eq) were added to the orange-yellow solution, followed by addition of 3.64 mL *tert*-butyl nitrite (90%, pure) (2.82 g, 27.4 mmol, 2.0 eq). The reddish-brown suspension was stirred at -15°C for 3.5 h, and after warming to -5°C for additional 11 h. The reaction mixture was concentrated at -5°C to half of its volume (~130 mL), before adding 130 mL absolute, degassed *n*-hexane (-5°C). The formed skin-coloured precipitate was collected by filtration, and after drying, air stable compound **2a** was isolated.\*

**Yield:** 4.09 g (87%), pale yellow, skin-coloured solid,  $C_9H_7BBrF_4N_3O$  [339.88 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO):  $\delta$  = 8.65 (d, <sup>3</sup>*J*(H,H) = 8.8 Hz, 1 H;  $H^{Ar}$ ), 8.56 (s, 1 H;  $H^{Ar}$ ), 8.21 (d, <sup>3</sup>*J*(H,H) = 8.7 Hz, 1 H;  $H^{Ar}$ ), 7.81 (bs, 1 H; CONH<sub>2</sub>), 7.61 (d, <sup>3</sup>*J*(H,H) = 15.4 Hz, 1 H; CH), 7.58 (bs, 1 H; CONH<sub>2</sub>, overlapping), 7.13 (d, <sup>3</sup>*J*(H,H) = 15.6 Hz, 1 H; CH) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT):  $\delta$  = 164.9 (C<sub>q</sub>; CONH<sub>2</sub>), 139.5 (C<sub>q</sub>;  $C^{Ar}$ ), 136.5 (C<sub>q</sub>;  $C^{Ar}$ ), 134.5 (CH), 134.3 ( $C^{Ar}$ ), 133.1 ( $C^{Ar}$ ), 131.6 ( $C^{Ar}$ ), 128.7 (CH), 113.7 (C<sub>q</sub>;  $C^{Ar}$ ) ppm; **m.p.**<sup>exp.</sup> = 141-143°C (spontaneous decomposition).

\* HRMS (DI-EI) gave no unambiguous results because of decomposition during heating process.

### 2.2.6 2-Chloro-3-methylbutanoic acid (**23**)



**23**

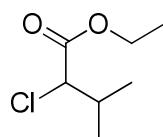
In a flame dried 500 mL three-neck round-bottom flask equipped with dropping funnel, thermometer and argon-inlet 8.00 g L-valine (68.3 mmol, 1.0 eq) were dissolved in 160 mL 5 M HCl. The colourless solution was cooled to -5°C and a precooled solution of 5.70 g NaNO<sub>2</sub> (82.0 mol, 1.2 eq) in 30 mL water was added dropwise under vigorous stirring and efficient cooling, so that the temperature of the reaction mixture is kept below 5°C. After 5 h stirring at -5°C the reaction was allowed to warm to room temperature and stirred overnight. After 20 h 8.00 g solid Na<sub>2</sub>CO<sub>3</sub> (75.5 mmol, 1.1 eq) were added in small portions to prevent foaming. The aqueous phase was extracted with Et<sub>2</sub>O (4x200 mL) and the combined organic layers was washed with saturated NaCl solution (1x400 mL), dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The pale yellow crude product was purified by distillation.<sup>[26]</sup>

**Yield:** 4.83 g (52%), colourless oil, C<sub>5</sub>H<sub>9</sub>ClO<sub>2</sub> [136.03 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 11.24 (bs, 1 H; OH), 4.20 (d, <sup>3</sup>J (H,H) = 6.1 Hz, 1 H; CHCl), 2.44-2.29 (m, 1 H; CH), 1.09 (d, <sup>3</sup>J (H,H) = 6.7 Hz, 3 H; CH<sub>3</sub>, overlapping), 1.07 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 175.6 (C<sub>q</sub>; COOH), 64.1 (CHCl), 32.6 (CH), 19.8 (CH<sub>3</sub>), 18.0 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 4.07 min; *m/z* (%): 101 (3) [M<sup>+</sup>-Cl], 94 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>]; **b.p.**<sup>exp.</sup> = 110°C, 0.06 torr, (b.p.)<sup>lit.</sup> = 103-105°C, 10 torr).<sup>[26]</sup>

Analytical data are in accordance with those reported.<sup>[27]</sup>

### 2.2.7 Ethyl 2-chloro-3-methylbutanoate (**9**)



**9**

In an argon flushed 250 mL two-neck round-bottom flask equipped with argon-inlet 4.60 g carboxylic acid **23** (33.9 mmol, 1.0 eq) were dissolved in 120 mL ethanol. The colourless

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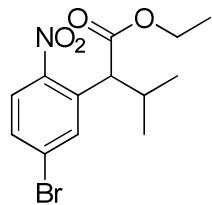
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solution was cooled to 0°C and 3.00 mL SOCl<sub>2</sub> (4.84 g, 40.7 mmol, 1.2 eq) were carefully added. The reaction mixture was stirred overnight at room temperature and after 16 h the solvent and not reacted SOCl<sub>2</sub> were removed under reduced pressure by distillation. The yellow, oily residue was dissolved in 100 mL EtOAc and washed with 0.1 M HCl (3x50 mL). The organic layer was dried over MgSO<sub>4</sub>, filtered and the solvent was removed by using a rotary evaporator. The crude product was purified by distillation.

**Yield:** 3.60 g (64%), colourless oil, C<sub>7</sub>H<sub>13</sub>ClO<sub>2</sub> [164.63 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 4.23 (q, <sup>3</sup>J (H,H) = 7.1 Hz, 2 H; CH<sub>2</sub>), 4.09 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 1 H; CHCl), 2.37-2.21 (m, 1 H; CH), 1.29 (t, <sup>3</sup>J (H,H) = 7.1 Hz, 3 H; CH<sub>3</sub>), 1.03 (d, <sup>3</sup>J (H,H) = 6.7 Hz, 3 H; CH<sub>3</sub>, overlapping), 1.02 (d, <sup>3</sup>J (H,H) = 6.7 Hz, 3 H; CH<sub>3</sub>) ppm;  
**<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 169.6 (C<sub>q</sub>; COOH), 64.4 (CHCl), 62.0 (CH<sub>2</sub>), 32.8 (CH), 19.7 (CH<sub>3</sub>), 18.2 (CH<sub>3</sub>), 14.2 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 3.85 min; m/z (%): 165 (1) [M<sup>+</sup>], 12 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>6</sub>], 94 (71) [M<sup>+</sup>-C<sub>5</sub>H<sub>11</sub>]; **b.p.**<sup>exp.</sup> = 55°C, 8 torr.

### 2.2.8 Ethyl 2-(5-bromo-2-nitrophenyl)-3-methylbutanoate (10)



**10**

After drying of 8.88 g KOtBu (79.1 mmol, 2.4 eq) in a flame dried 250 mL Schlenk-flask, 100 mL absolute, degassed THF were added and the colourless suspension was cooled to -40°C. In a second flame dried Schlenk-flask 6.66 g 1-bromo-4-nitrobenzol (33.0 mmol, 1.0 eq) and 6.51 g ethylester **9** (39.6 mmol, 1.2 eq) were suspended in 50 mL absolute, degassed THF. With a cannula the yellow suspension **9** was transferred to the KOtBu suspension and during cannulation the colour turned into a deep violet. The reaction mixture was stirred 4 h at -40°C and after quantitative conversion the reaction was neutralized with 100 mL 1 M HCl by forming a bright yellow suspension. The aqueous phase was extracted with EtOAc (3x200 mL) and the combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was removed by using a rotary evaporator. The brown crude product was purified by flash column chromatography (cyclohexane/EtOAc = 100/1, R<sub>f</sub> = 0.55, CAM).

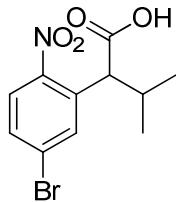
**Yield:** 5.80 g (53%), yellow powder, C<sub>13</sub>H<sub>16</sub>BrNO<sub>2</sub> [330.17 g/mol].

## Experimental Procedures and Analytical Data

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**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.91 (d, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 7.64 (d, <sup>3</sup>J (H,H) = 8.6 Hz, 1 H; H<sup>Ar</sup>), 7.52 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>), 4.24-4.03 (m, 2 H; CH<sub>2</sub>), 3.87 (d, <sup>3</sup>J (H,H) = 10.4 Hz, 1 H; CH), 2.41-2.28 (m, 1 H; CH), 1.22 (t, <sup>3</sup>J (H,H) = 7.1 Hz, 3 H; CH<sub>3</sub>), 1.07 (d, <sup>3</sup>J (H,H) = 6.5 Hz, 3 H; CH<sub>3</sub>), 0.76 (d, <sup>3</sup>J (H,H) = 6.8 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 172.4 (C<sub>q</sub>; COOH), 149.6 (C<sub>q</sub>; C<sup>Ar</sup>), 134.7 (C<sub>q</sub>; C<sup>Ar</sup>), 132.9 (C<sup>Ar</sup>), 131.3 (C<sup>Ar</sup>), 127.4 (C<sub>q</sub>; C<sup>Ar</sup>), 125.6 (C<sup>Ar</sup>), 61.4 (CH<sub>2</sub>), 52.3 (CH), 32.9 (CH), 21.3 (CH<sub>3</sub>), 20.1 (CH<sub>3</sub>), 14.2 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.84 min; m/z (%): 283 (100) [M<sup>+</sup>-NO<sub>2</sub>], 255 (46) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>NO<sub>2</sub>]; **m.p.**<sup>exp.</sup> = 85-87°C; **HRMS** (EI): calcd for [M<sup>+</sup>]: 329.0263; found: 329.0271.

### **2.2.9 2-(5-Bromo-2-nitrophenyl)-3-methylbutanoic acid (11)**



**11**

In a 100 mL round-bottom flask 7.01 g ethylester **10** (21.2 mmol, 1.0 eq) were dissolved in 15 mL 1,4-dioxane. 12.4 mL 2 M NaOH solution were added to the pale yellow solution and the colour turned into a dark brown. The reaction was stirred at 50°C and complete conversion was detected by TLC (cyclohexane/EtOAc/AcOH = 500/100/1, R<sub>f</sub> = 0.21, CAM) after 20 h. The solvent was removed under reduced pressure and the brown residue was redissolved in 200 mL 1 M HCl. The aqueous phase was extracted with DCM (3x200 mL) and the combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was removed by using the rotary evaporator. The brown crude product was purified by flash column chromatography (cyclohexane/EtOAc/AcOH = 500/100/1, R<sub>f</sub> = 0.21, CAM), affording compound **11** as pale yellow solid.

**Yield:** 6.41 g (71%), pale yellow solid, C<sub>11</sub>H<sub>12</sub>BrNO<sub>4</sub> [302.12 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 9.09 (bs, 1 H; COOH), 7.84 (d, <sup>4</sup>J (H,H) = 2.0 Hz, 1 H; H<sup>Ar</sup>), 7.68 (d, <sup>3</sup>J (H,H) = 8.7 Hz, 1 H; H<sup>Ar</sup>), 7.55 (dd, <sup>3</sup>J (H,H) = 8.7 Hz, <sup>4</sup>J (H,H) = 2.0 Hz, 1 H; H<sup>Ar</sup>), 3.91 (d, <sup>3</sup>J (H,H) = 10.3 Hz, 1 H; CH), 2.43-2.27 (m, 1 H; CH), 1.12 (d, <sup>3</sup>J (H,H) = 6.5 Hz, 3 H; CH<sub>3</sub>), 0.77 (d, <sup>3</sup>J (H,H) = 6.7 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 177.7 (C<sub>q</sub>; COOH), 149.5 (C<sub>q</sub>; C<sup>Ar</sup>), 134.0 (C<sub>q</sub>; C<sup>Ar</sup>), 133.1 (C<sup>Ar</sup>), 131.7 (C<sup>Ar</sup>), 127.6 (C<sub>q</sub>; C<sup>Ar</sup>), 125.8 (C<sup>Ar</sup>), 52.4 (CH), 32.5 (CH), 21.4 (CH<sub>3</sub>), 20.1 (CH<sub>3</sub>) ppm; **m.p.**<sup>exp.</sup> = 137-140°C; **HRMS** (DI-EI): calcd for [M<sup>+</sup>]: 300.9950; found: 300.9975.

### 2.2.10 4-Bromo-2-isobutyl-1-nitrobenzene (12)



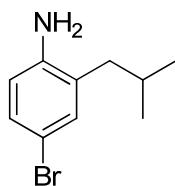
**12**

In a flame dried 100 mL Schlenk-flask 1.71 g carboxylic acid **11** (5.66 mmol, 1.0 eq) and 782 mg K<sub>2</sub>CO<sub>3</sub> (5.66 mmol, 1.0 eq) were suspended in 17 mL absolute DMF. The reaction mixture was stirred at 50°C and quantitative conversion was detected after 24 h. The dark brown suspension was allowed to cool to room temperature. During neutralization of the reaction mixture with 120 mL 0.25 M HCl, a colour change from brown to orange was observed. The aqueous phase was extracted with Et<sub>2</sub>O (3x100 mL) and the combined organic layers were washed with saturated NaCl solution (2x100 mL), dried over MgSO<sub>4</sub>, filtered and the solvent was removed under reduced pressure. The yellow crude product was purified by flash column chromatography (cyclohexane/EtOAc = 100/1, R<sub>f</sub> = 0.24, UV).

**Yield:** 1.30 g (89%), pale yellow oil, C<sub>10</sub>H<sub>12</sub>BrNO<sub>2</sub> [258.11 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.76 (d, <sup>3</sup>J (H,H) = 8.9 Hz, 1 H; H<sup>Ar</sup>), 7.49-7.46 (m, 2 H; H<sup>Ar</sup>), 2.77 (d, <sup>3</sup>J (H,H) = 7.1 Hz, 2 H; CH<sub>2</sub>), 1.97-1.83 (m, 1 H; CH), 0.92 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 148.6 (C<sub>q</sub>; C<sup>Ar</sup>), 138.7 (C<sub>q</sub>; C<sup>Ar</sup>), 135.6 (C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 127.3 (C<sub>q</sub>; C<sup>Ar</sup>), 126.4 (C<sup>Ar</sup>), 41.7 (CH<sub>2</sub>), 29.6 (CH), 22.5 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.05 min; *m/z* (%): 257 (1) [M<sup>+</sup>], 241 (21) [M<sup>+</sup>-O], 200 (100) [M<sup>+</sup>-C<sub>4</sub>H<sub>9</sub>].

### 2.2.11 4-Bromo-2-isobutylaniline (13)



**13**

In a 100 mL round-bottom flask 1.30 g nitrobenzene derivative **12** (5.04 mmol, 1.0 eq) were dissolved in 85 mL glacial acetic acid. 1.80 g tin-powder (15.2 mmol, 3.0 eq) were added and the grey suspension was stirred 48 h at room temperature. After removing of the acetic acid under reduced pressure, the oily residue was cooled to 0°C and neutralized with saturated NaOH solution (pH ~7-8). To the neutralized aqueous phase 100 mL EtOAc were added to redissolve the precipitated organic crude product. The insoluble inorganic salts were filtered

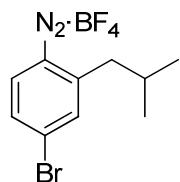
## Experimental Procedures and Analytical Data

off using a pad of Celite®. After phase separation the aqueous phase was extracted with EtOAc (3x100 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was removed by using a rotary evaporator. The yellow, oily crude product was purified by flash column chromatography (cyclohexane/EtOAc = 8/1, R<sub>f</sub> = 0.21, UV).

**Yield:** 1.07 g (93%), light brown oil, C<sub>10</sub>H<sub>14</sub>BrN [228.13 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.13-7.10 (m, 2 H; H<sup>Ar</sup>), 6.56-6.53 (m, 1 H; H<sup>Ar</sup>), 3.57 (bs, 2 H; NH<sub>2</sub>), 2.32 (d, <sup>3</sup>J (H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>), 2.00-1.82 (m, 1 H; CH), 0.95 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 143.5 (C<sub>q</sub>; C<sup>Ar</sup>), 133.2 (C<sup>Ar</sup>), 129.7 (C<sup>Ar</sup>), 128.2 (C<sub>q</sub>; C<sup>Ar</sup>), 117.3 (C<sup>Ar</sup>), 110.4 (C<sup>Ar</sup>), 40.8 (CH<sub>2</sub>), 27.9 (CH), 22.8 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.07 min; *m/z* (%): 227 (30) [M<sup>+</sup>], 184 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>], 105 (10) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>Br]; **HRMS** (EI): calcd for [M<sup>+</sup>]: 227.0310; found: 227.0315.

### **2.2.12 4-Bromo-2-isobutylbenzenediazonium tetrafluoroborate (2b)**



**2b**

A 25 mL round-bottom flask was charged with 222 mg aniline derivative **13** (973 μmol, 1.0 eq) and to the precooled starting material 10 mL HBF<sub>4</sub> (48%) were carefully added. In a second round-bottom flask 67.0 mg NaNO<sub>2</sub> (973 μmol, 1.0 eq) were dissolved in 100 μL H<sub>2</sub>O and cooled to 0°C and the cold NaNO<sub>2</sub> solution was slowly added to the cold HBF<sub>4</sub> solution. During the addition of the NaNO<sub>2</sub> solution a brown precipitate was formed and the temperature was controlled to be beneath 5°C. The solution was stirred for 30 min at 0°C and after allowing to warm up to room temperature for further 2 h. The formed precipitate was filtered off and washed with Et<sub>2</sub>O (3x1 mL). During the treatment with Et<sub>2</sub>O brown impurities were dissolved and the off white residue was dried in vacuo.\*

**Yield:** 18 mg (6%), off white powder, C<sub>10</sub>H<sub>12</sub>BBrF<sub>4</sub>N<sub>2</sub> [326.02 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 7.42-7.39 (m, 2 H; H<sup>Ar</sup>), 7.09-7.06 (m, 1 H; H<sup>Ar</sup>), 2.47 (d, <sup>3</sup>J (H,H) = 7.5 Hz, 2 H; CH<sub>2</sub>, overlapping), 1.99-1.83 (m, 1 H; CH), 0.88 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO): δ = 134.5 (C<sub>q</sub>; C<sup>Ar</sup>), 134.3 (C<sub>q</sub>;

\* HRMS (DI-EI) gave no unambiguous results because of decomposition during heating process.

$C^{Ar}$ ), 133.3 ( $C^{Ar}$ ), 129.9 ( $C^{Ar}$ ), 123.1 ( $C^{Ar}$ ), 116.8 ( $C_q$ ;  $C^{Ar}$ ), 38.7 ( $CH_2$ ), 27.4 ( $CH$ ), 22.1 ( $CH_3$ ) ppm.

## **2.3 Synthesis of the Phenyl Boronic Acid Derivatives**

### **2.3.1 Representative procedure for the formation of boronic acid pinacol ester derivatives from the corresponding bromo-phenyl derivatives**

A flame dried and argon flushed 100 mL Schlenk-flask was charged with 1.0 eq phenyl-bromide derivative, 1.1 eq bis(pinacolato)diboron ( $B_2Pin_2$ ), 2.0-3.0 eq potassium acetate (KOAc), and 3-5 mol% [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with DCM ( $PdCl_2(dppf)\cdot DCM$ ). After drying of the starting materials in vacuo and back-flushing with argon, the starting materials were suspended in absolute, degassed DMF, and the orange mixture was stirred at 80°C. The reaction was monitored by GC-MS, after filtering a small aliquot of the reaction mixture through a small pad of  $SiO_2$  and eluting with EtOAc. After quantitative conversion the reddish-brown suspension was filtered through a small pad of silica gel (~2x3 cm) and eluted with MeOH. After evaporation to dryness under reduced pressure, the crude product was purified by flash column chromatography (eluents are indicated).

### **2.3.2 Representative procedure for formation of potassium trifluoroborate derivatives from corresponding phenyl boronic acids or -esters**

A 100 mL round-bottom flask was charged with 1.0 eq boronic acid pinacol ester (or boronic acid) and 3.0 eq hydrogen potassium fluoride ( $KHF_2$ ). A premixed MeOH/H<sub>2</sub>O solution (volume ratios are given) was added, and the colourless solution was stirred at room temperature for the indicated time. After quantitative conversion (disappearance of the starting material on TLC) the colourless suspension was evaporated under reduced pressure to dryness, and the crude product was dissolved in acetone and precipitated by dropwise addition of Et<sub>2</sub>O (typically twice of the volume of acetone). After filtration and washing of the precipitate with Et<sub>2</sub>O, pure colourless potassium trifluoroborate salt was isolated.

### 2.3.3 Potassium trifluoro(*m*-tolyl)borate (**4'a**)



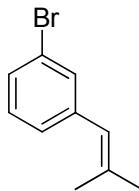
**4'a**

Compound **4'a** was prepared according to procedure 2.3.2 from 728 mg *m*-tolylboronic acid (5.35 mmol, 1.0 eq) and 1.25 g KHF<sub>2</sub> (16.0 mmol, 3.0 eq) in 15 mL MeOH/H<sub>2</sub>O (2/1). The BPin/BF<sub>3</sub>K exchange was completed after 2 h. After removing the solvent under reduced pressure, the colourless solid was redissolved in 12 mL acetone and precipitated with 25 mL Et<sub>2</sub>O.

**Yield:** 1.00 g (94%), colourless solid, C<sub>7</sub>H<sub>7</sub>BF<sub>3</sub>K [198.03 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 7.14-7.09 (m, 2 H; H<sup>Ar</sup>), 6.97 (t, <sup>3</sup>J(H,H) = 7.3 Hz, 1 H; H<sup>Ar</sup>), 6.83 (d, <sup>3</sup>J(H,H) = 7.3 Hz, 1 H; H<sup>Ar</sup>), 2.22 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT): δ = 134.3 (C<sub>q</sub>; C<sup>Ar</sup>), 132.3 (C<sup>Ar</sup>), 128.4 (C<sup>Ar</sup>), 126.1 (C<sup>Ar</sup>), 125.5 (C<sup>Ar</sup>), 21.4 (CH<sub>3</sub>) ppm; **\* m.p.**<sup>exp.</sup> = 243-246°C (m.p.<sup>lit.</sup> = 243-248°C).<sup>[28]</sup>

### 2.3.4 1-Bromo-3-(2-methylprop-1-en-1-yl)benzene (**24a**)



**24a**

A flame dried 250 mL Schlenk-flask was charged with 10.9 g isopropyltriphenylphosphonium bromide (**18a**) (28.4 mmol, 1.2 eq) and 100 mL absolute, degassed THF were added. After cooling to -35°C, a suspension of 3.45 g potassium *tert*-butoxide (KO*t*Bu) (30.7 mmol, 1.3 eq) in 20 mL absolute, degassed THF were added dropwise. Immediately a colour change from white to dark-red was observed, and the reaction mixture was allowed to warm to room temperature. After stirring for 10 min at room temperature, followed by heating to 50°C for 1 h, the mixture was cooled to -55°C, and 2.77 mL 3-bromobenzaldehyde (4.38 g, 23.7 mmol, 1.0 eq) in 20 mL absolute THF were added dropwise (2 drops/min). The suspension was stirred for 2.5 h at -55°C, followed by warming to room temperature overnight. The reaction was monitored by GC-MS, after filtering a small aliquot of the

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\* Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the trifluoroborate function was not observed.

## Experimental Procedures and Analytical Data

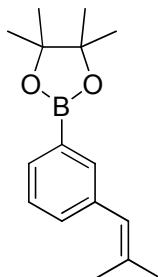
reaction mixture through a small pad of  $\text{SiO}_2$  and eluting with cyclohexane. After quantitative conversion the mixture was quenched with 30 mL saturated  $\text{NH}_4\text{Cl}$  solution, subsequently followed by adding 50 mL  $\text{H}_2\text{O}$ . The aqueous phase was extracted with  $\text{Et}_2\text{O}$  (3x75 mL), and the combined yellow organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to dryness. The yellow residue was suspended in cyclohexane, and the insoluble triphenylphosphine oxide ( $\text{Ph}_3\text{P}=\text{O}$ ) was filtered off and washed with cyclohexane (2x20 mL). Product **24a** was isolated as a colourless oil after flash column chromatography (252 g  $\text{SiO}_2$ , 19x6 cm, cyclohexane,  $R_f = 0.65$ ).

**Yield:** 4.34 g (87%), colourless oil,  $\text{C}_{10}\text{H}_{11}\text{Br}$  [211.10 g/mol].

**$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.37\text{-}7.30$  (m, 2 H;  $\text{H}^{\text{Ar}}$ ), 7.20-7.12 (m, 2 H;  $\text{H}^{\text{Ar}}$ ), 6.20 (s, 1 H; CH), 1.90 (s, 3 H;  $\text{CH}_3$ ), 1.85 (s, 3 H;  $\text{CH}_3$ ) ppm,  **$^{13}\text{C NMR}$**  (76 MHz,  $\text{CDCl}_3$ , APT):  $\delta = 141.0$  ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 137.2 ( $\text{C}_q$ ;  $\text{CH}=\text{C}(\text{CH}_3)_2$ ), 131.7 ( $\text{C}^{\text{Ar}}$ ), 129.7 ( $\text{C}^{\text{Ar}}$ ), 128.9 ( $\text{C}^{\text{Ar}}$ ), 127.5 ( $\text{C}^{\text{Ar}}$ ), 124.0 (CH), 122.3 ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 27.0 ( $\text{CH}_3$ ), 19.5 ( $\text{CH}_3$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R = 4.93$  min;  $m/z$  (%): 212 (5) [ $M^+$ ], 210 (5) [ $M^+$ ], 131 (75) [ $M^+ - \text{Br}$ ], 116 (87) [ $M^+ - \text{CH}_3\text{Br}$ ], 91 (100) [ $\text{C}_7\text{H}_7^+$ ].

Analytical data are in accordance with those reported.<sup>[29]</sup>

### **2.3.5 4,4,5,5-Tetramethyl-2-(3-(2-methylprop-1-en-1-yl)phenyl)-1,3,2-dioxaborolane (4d)**



**4d**

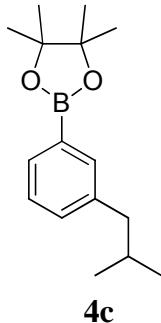
Compound **4d** was prepared according to procedure 2.3.1 from 1.58 g 1-bromo-3-(2-methylprop-1-en-1-yl)benzene (**24a**) (7.48 mmol, 1.0 eq), 2.09 g  $\text{B}_2\text{Pin}_2$  (8.23 mmol, 1.1 eq), 1.47 g  $\text{KOAc}$  (15.0 mmol, 2.0 eq), and 183 mg  $\text{PdCl}_2(\text{dpf})\cdot\text{DCM}$  (220  $\mu\text{mol}$ , 3 mol%) in 15 mL absolute, degassed DMF. A complete Br/BPin exchange was detected after  $\sim 17$  h and the black and oily crude product was purified by flash column chromatography (130 g  $\text{SiO}_2$ , 16x5 cm, cyclohexane/EtOAc = 100/3,  $R_f = 0.31$ ).

## Experimental Procedures and Analytical Data

**Yield:** 1.76 g (91%), pale yellow-green liquid, which become a solid upon standing, C<sub>16</sub>H<sub>23</sub>BO<sub>2</sub> [258.16 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.66-7.62 (m, 2 H; H<sup>Ar</sup>), 7.34-7.32 (m, 2 H; H<sup>Ar</sup>), 6.28 (bs, 1 H; CH), 1.90 (d, <sup>4</sup>J (H,H) = 0.8 Hz, 3 H; CH<sub>3</sub>), 1.86 (d, <sup>4</sup>J (H,H) = 0.8 Hz, 3 H; CH<sub>3</sub>), 1.35 (s, 12 H; CH<sub>3</sub><sup>BPin</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 138.2 (C<sub>q</sub>; C<sup>Ar</sup>), 135.6 (C<sub>q</sub>; CH=C(CH<sub>3</sub>)<sub>2</sub>), 135.4 (C<sup>Ar</sup>), 132.3 (C<sup>Ar</sup>), 131.6 (C<sup>Ar</sup>), 127.6 (C<sup>Ar</sup>), 125.2 (CH), 83.9 (C<sub>q</sub>; C<sup>BPin</sup>), 26.9 (CH<sub>3</sub>), 25.0 (CH<sub>3</sub><sup>BPin</sup>), 19.5 (CH<sub>3</sub>) ppm; \* **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.17 min; m/z (%): 258 (100) [M<sup>+</sup>], 243 (21) [M<sup>+</sup>-CH<sub>3</sub>], 158 (71) [M<sup>+</sup>-C<sub>6</sub>H<sub>12</sub>O], 143 (39) [M<sup>+</sup>-C<sub>7</sub>H<sub>15</sub>O]; **m.p.**<sup>exp.</sup> = 67-68°C; **HRMS** (EI): calcd (m/z) for [M<sup>+</sup>]: 258.1794; found: 258.1814.

### 2.3.6 2-(3-Isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**)



**4c**

In a 100 mL two-neck round-bottom flask with two argon-inlets 1.69 g 2-(3-isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4d**) (6.55 mmol, 1.0 eq) were dissolved in 20 mL MeOH. To this pale yellow solution 74.0 mg platinum(IV) oxide (PtO<sub>2</sub>) (330 μmol, 5 mol%) were added. After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (3x), the reaction mixture was stirred overnight (~10 h) at room temperature. The catalyst was removed by filtration (small pad SiO<sub>2</sub>, eluent: MeOH), and the solvent was removed under reduced pressure using a rotary evaporator.<sup>†</sup> After flash column chromatography (66 g SiO<sub>2</sub>, 22x3 cm, cyclohexane/EtOAc = 50/1, R<sub>f</sub> = 0.36), product **4c** was isolated as a colourless liquid.

**Yield:** 1.62 g (95%), colourless liquid, C<sub>16</sub>H<sub>25</sub>BO<sub>2</sub> [260.18 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.65-7.60 (m, 2 H; H<sup>Ar</sup>), 7.29-7.23 (m, 2 H; H<sup>Ar</sup>, overlapping), 2.48 (d, <sup>3</sup>J (H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>), 1.98-1.80 (m, 1 H; CH), 1.35 (s, 12 H;

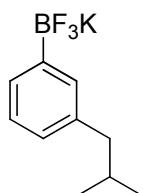
\* Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the boronic acid pinacol ester function was not observed.

<sup>†</sup> The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

## Experimental Procedures and Analytical Data

$\text{CH}_3^{\text{BPin}}$ ), 0.90 (d,  $^3J(\text{H},\text{H}) = 6.6$  Hz, 6 H;  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR (76 MHz,  $\text{CDCl}_3$ , APT):  $\delta = 141.1$  ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 135.5 ( $\text{C}^{\text{Ar}}$ ), 132.3 ( $\text{C}^{\text{Ar}}$ ), 132.3 ( $\text{C}^{\text{Ar}}$ ), 127.6 ( $\text{C}^{\text{Ar}}$ ), 83.8 ( $\text{C}_q$ ;  $\text{C}^{\text{BPin}}$ ), 45.5 ( $\text{CH}_2$ ), 30.4 (CH), 25.0 ( $\text{CH}_3^{\text{BPin}}$ ), 22.6 ( $\text{CH}_3$ ) ppm;  $^{\text{*GC-MS}}$  (EI, 70 eV; MP\_50\_S):  $t_R = 5.93$  min;  $m/z$  (%): 260 (22) [ $M^+$ ], 245 (26) [ $M^+ - \text{CH}_3$ ], 217 (80) [ $M^+ - \text{C}_3\text{H}_7$ ], 203 (14) [ $M^+ - \text{C}_4\text{H}_9$ ], 161 (81) [ $\text{C}_9\text{H}_{10}\text{BO}_2^+$ ]; HRMS (EI): calcd ( $m/z$ ) for [ $M^+$ ]: 260.1951; found: 260.1955.

### 2.3.7 Potassium trifluoro(3-isobutylphenyl)borate (4'b)



**4'b**

Compound **4'b** was prepared according to procedure 2.3.2 from 716 mg 2-(3-isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**) (2.75 mmol, 1.0 eq) and 645 mg  $\text{KHF}_2$  (8.26 mmol, 3.0 eq) in 60 mL  $\text{MeOH}/\text{H}_2\text{O}$  (3/1). The  $\text{BPin}/\text{BF}_3\text{K}$  exchange was completed overnight ( $\sim 16$  h). After removing the solvent under reduced pressure, the colourless solid was redissolved in 15 mL acetone, and after filtration and evaporation, the colourless residue was used in the next step without further purification.

**Yield:** 658 mg (quant.), colourless solid,  $\text{C}_{10}\text{H}_{13}\text{BF}_3\text{K}$  [240.11 g/mol].

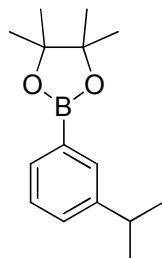
$^1\text{H}$  NMR (300 MHz,  $[\text{D}_6]\text{DMSO}$ ):  $\delta = 7.14\text{-}7.12$  (m, 2 H;  $\text{H}^{\text{Ar}}$ ), 6.98 (t,  $^3J(\text{H},\text{H}) = 7.4$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 6.80 (d,  $^3J(\text{H},\text{H}) = 7.4$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 2.35 (d,  $^3J(\text{H},\text{H}) = 7.1$  Hz, 2 H;  $\text{CH}_2$ ), 1.87-1.69 (m, 1 H; CH), 0.86 (d,  $^3J(\text{H},\text{H}) = 6.6$  Hz, 6 H;  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR (76 MHz,  $[\text{D}_6]\text{DMSO}$ , APT):  $\delta = 138.2$  ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 132.2 ( $\text{C}^{\text{Ar}}$ ), 128.8 ( $\text{C}^{\text{Ar}}$ ), 125.9 ( $\text{C}^{\text{Ar}}$ ), 125.5 ( $\text{C}^{\text{Ar}}$ ), 45.3 ( $\text{CH}_2$ ), 29.8 (CH), 22.3 ( $\text{CH}_3$ ) ppm;  $^{\dagger, \ddagger, \ddot{\ddagger}}$  m.p.<sup>exp.</sup> = 96-100°C; HRMS (DI-EI): calcd ( $m/z$ ) for [ $M^+ - \text{FK}$ ]: 182.1080; found: 182.1090.

<sup>\*</sup> Signal for the quaternary *ipso*-aromatic carbon ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ) at the boronic acid pinacol ester function was not observed.

<sup>†</sup> Signals for the free pinacol were also observed.

<sup>‡</sup> Signal for the quaternary *ipso*-aromatic carbon ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ) at the trifluoroborate function was not observed.

**2.3.8 2-(3-Isopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4e)**



**4e**

In a flame dried 100 mL Schlenk-flask 1.57 mL 1-bromo-3-isopropylbenzene (2.02 g, 10.2 mmol, 1.0 eq), 2.21 mL 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (HBPin) (1.95 g, 15.2 mmol, 1.5 eq), and 4.24 mL absolute triethylamine (3.08 g, 30.4 mmol, 3.0 eq) were dissolved in 25 mL absolute ACN. After degassing the deep red suspension, 249 mg PdCl<sub>2</sub>(dppf)·DCM (330 µmol, 3 mol%) were added, and the reaction mixture was stirred at 80°C until full conversion was detected by GC-MS (~19 h; mini workup: SiO<sub>2</sub>, EtOAc). The reaction was quenched with 20 mL H<sub>2</sub>O, and the aqueous phase was extracted with EtOAc (3x50 mL). The combined yellow organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was removed under reduced pressure. The deep brown crude product was purified by flash column chromatography (100 g SiO<sub>2</sub>, 18x2.5 cm, cyclohexane/EtOAc = 98/2, R<sub>f</sub> = 0.33, CAM).

**Yield:** 1.57 g (63%), colourless oil, which become a semi-solid upon standing, C<sub>15</sub>H<sub>23</sub>BO<sub>2</sub> [246.15 g/mol].

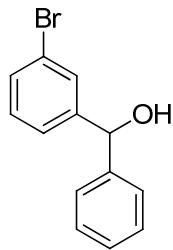
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.69-7.64 (m, 2 H; H<sup>Ar</sup>), 7.37-7.29 (m, 2 H; H<sup>Ar</sup>), 2.94 (sept, <sup>3</sup>J(H,H) = 6.9 Hz, 1 H; CH), 1.36 (s, 12 H; CH<sub>3</sub><sup>BPin</sup>), 1.27 (d, <sup>3</sup>J(H,H) = 6.9 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 148.2 (C<sub>q</sub>; C<sup>Ar</sup>), 133.0 (C<sup>Ar</sup>), 132.5 (C<sup>Ar</sup>), 129.5 (C<sup>Ar</sup>), 127.9 (C<sup>Ar</sup>), 83.8 (C<sub>q</sub>; C<sup>BPin</sup>), 34.3 (CH), 25.0 (CH<sub>3</sub><sup>BPin</sup>), 24.2 (CH<sub>3</sub>) ppm; \* **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.94 min; m/z (%): 246 (51) [M<sup>+</sup>], 231 (100) [M<sup>+</sup>-CH<sub>3</sub>], 203 (14) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>], 173 (2) [M<sup>+</sup>-C<sub>5</sub>H<sub>13</sub>], 147 (71) [C<sub>8</sub>H<sub>8</sub>BO<sub>2</sub><sup>+</sup>]; **m.p.**<sup>exp.</sup> = <30°C.

Analytical data are in accordance with those reported.<sup>[30]</sup>

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\* Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the boronic acid pinacol ester function was not observed.

### 2.3.9 (3-Bromophenyl)(phenyl)methanol (**24b**)



**24b**

In a flame dried 100 mL three-neck round-bottom flask with reflux condenser, dropping funnel and argon-inlet, 433 mg magnesium turnings (17.8 mmol, 1.1 eq) were suspended in 15 mL absolute Et<sub>2</sub>O. A solution of 2.80 g bromobenzene (17.8 mmol, 1.1 eq) in 10 mL absolute Et<sub>2</sub>O were added dropwise to the magnesium turnings and stirred under reflux for 30 min. The brown Grignard-suspension was added to a 100 mL two-neck round-bottom flask containing a solution of 3.00 g 3-bromobenzaldehyde (16.2 mmol, 1.0 eq) in 10 mL absolute Et<sub>2</sub>O. The resulting yellow suspension was stirred under reflux for further 30 min. Under ice cooling the yellow mixture was quenched with 20 mL saturated NH<sub>4</sub>Cl solution, and the aqueous phase was extracted with Et<sub>2</sub>O (3x35 mL). The combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and after evaporating the solvent under reduced pressure, compound **24b** was isolated after flash column chromatography (157 g SiO<sub>2</sub>, 27x4 cm, cyclohexane/EtOAc = 9/1, R<sub>f</sub> = 0.30).<sup>[31]</sup>

**Yield:** 2.79 g (65%), colourless oil, which become a solid upon standing, C<sub>13</sub>H<sub>11</sub>BrO [263.13 g/mol].

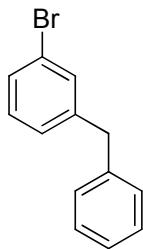
**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ = 7.57 (s, 1 H; H<sup>Ar</sup>), 7.39 (d, <sup>3</sup>J(H,H) = 7.9 Hz, 1 H; H<sup>Ar</sup>), 7.36-7.34 (m, 4 H; H<sup>Ar</sup>), 7.32-7.27 (m, 2 H; H<sup>Ar</sup>), 7.20 (t, <sup>3</sup>J(H,H) = 7.8 Hz, 1 H; H<sup>Ar</sup>), 5.80 (s, 1 H; CH), 1.90 (bs, 1 H; OH) ppm; <sup>\*[31-32]</sup> **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>): δ = 146.1 (C<sub>q</sub>; C<sup>Ar</sup>), 143.3 (C<sub>q</sub>; C<sup>Ar</sup>), 130.7 (C<sup>Ar</sup>), 130.2 (C<sup>Ar</sup>), 129.6 (C<sup>Ar</sup>), 128.8 (C<sup>Ar</sup>), 128.1 (C<sup>Ar</sup>), 126.7 (C<sup>Ar</sup>), 125.2 (C<sup>Ar</sup>), 122.8 (C<sub>q</sub>; C<sup>Ar</sup>), 75.8 (CH) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 7.00 min; *m/z* (%): 264 (13) [M<sup>+</sup>], 262 (14) [M<sup>+</sup>], 183 (27) [M<sup>+</sup>-Br], 165 (15) [M<sup>+</sup>-H<sub>2</sub>BrO], 105 (100) [C<sub>7</sub>H<sub>5</sub>O<sup>+</sup>], 77 (67) [C<sub>6</sub>H<sub>5</sub><sup>+</sup>]; **m.p.**<sup>exp.</sup> = 36-38°C (m.p.<sup>lit.</sup> = 44.5-45°C).<sup>[33]</sup>

Analytical data are in accordance with those reported.<sup>[31]</sup>

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\* Several publication report the signal for the alcohol function as a doublet at ~2.50 ppm.

**2.3.10 1-Benzyl-3-bromobenzene (24c)**



**24c**

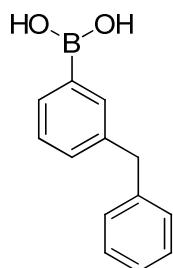
In a 100 mL two-neck round-bottom flask with reflux condenser and argon-inlet, 277 mg lithium aluminium hydride (LAH) (7.30 mmol, 1.9 eq) and 1.02 g aluminium trichloride ( $\text{AlCl}_3$ ) (7.65 mmol, 2.0 eq) were suspended in 15 mL absolute  $\text{Et}_2\text{O}$ . At -20°C a solution of 1.01 g (3-bromophenyl)(phenyl)methanol (**24b**) (3.84 mmol, 1.0 eq) in 10 mL absolute  $\text{Et}_2\text{O}$  were added dropwise. After complete addition the pale blue suspension was stirred under reflux and allowed to cool to room temperature after 1 h. The reaction was quenched with 9 mL  $\text{EtOAc}$ , followed by carefully diluting with 14 mL of 20% aqueous  $\text{H}_2\text{SO}_4$  solution. The grey suspension was extracted with  $\text{Et}_2\text{O}$  (3x35 mL), and the combined organic layers were washed with water (1x50 mL). After drying over  $\text{Na}_2\text{SO}_4$ , filtration and evaporation of the solvent under reduced pressure, the crude product was purified by flash column chromatography (64 g  $\text{SiO}_2$ , 21x3 cm, cyclohexane,  $R_f = 0.46$ ).<sup>[31]</sup>

**Yield:** 920 mg (97%), colourless oil,  $\text{C}_{13}\text{H}_{11}\text{Br}$  [247.13 g/mol].

**$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.36\text{-}7.31$  (m, 4 H;  $\text{H}^{\text{Ar}}$ ), 7.27-7.23 (m, 1 H;  $\text{H}^{\text{Ar}}$ , overlapping), 7.21-7.19 (m, 2 H;  $\text{H}^{\text{Ar}}$ ), 7.17-7.13 (m, 2 H;  $\text{H}^{\text{Ar}}$ ), 3.97 (s, 2 H;  $\text{CH}_2$ ) ppm;  **$^{13}\text{C NMR}$**  (126 MHz,  $\text{CDCl}_3$ ):  $\delta = 143.6$  ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 140.3 ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 132.0 ( $\text{C}^{\text{Ar}}$ ), 130.1 ( $\text{C}^{\text{Ar}}$ ), 129.4 ( $\text{C}^{\text{Ar}}$ ), 129.0 ( $\text{C}^{\text{Ar}}$ ), 128.7 ( $\text{C}^{\text{Ar}}$ ), 127.7 ( $\text{C}^{\text{Ar}}$ ), 126.5 ( $\text{C}^{\text{Ar}}$ ), 122.7 ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 41.7 ( $\text{CH}_2$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R = 6.42$  min;  $m/z$  (%): 248 (37) [ $M^+$ ], 246 (38) [ $M^+$ ], 167 (100) [ $M^+ \text{- Br}$ ], 91 (7) [ $\text{C}_7\text{H}_7^+$ ].

Analytical data are in accordance with those reported.<sup>[31]</sup>

**2.3.11 (3-Benzylphenyl)boronic acid (**25a**)**



**25a**

In a 250 mL Schlenk-flask 3.69 g 1-benzyl-3-bromobenzene (**24c**) (14.9 mmol, 1.0 eq) were dissolved in 80 mL absolute THF. The colourless solution was cooled to -78°C, and 10.0 mL *n*-BuLi (1.64 M, 16.40 mmol, 1.1 eq) were added. Immediately a colour change to pale red was observed, and after 1 h the colour changes to pale yellow. In a second 250 mL Schlenk-flask a solution of 10.0 mL triisopropyl borate ( $B(OiPr)_3$ ) (8.10 g, 43.1 mmol, 2.9 eq) in 20 mL absolute THF was prepared, and the lithium mixture was added after 3 h. After stirring for 1.5 h at -78°C, the colourless solution was allowed to warm room temperature, and the reaction was quenched with 25 mL 5% aqueous HCl solution. The aqueous phase was extracted with Et<sub>2</sub>O (3x25 mL), and the colourless combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and removing the solvent under reduced pressure, compound **25a** was isolated after flash column chromatography (80 g SiO<sub>2</sub>, 25x3 cm, cyclohexane/EtOAc = 65/35, R<sub>f</sub> = 0.27).

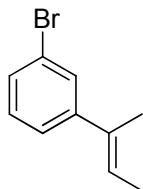
**Yield:** 1.61 g (51%), colourless solid, C<sub>13</sub>H<sub>13</sub>BO<sub>2</sub> [212.05 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.92-7.88 (m, 2 H; H<sup>Ar</sup>), 7.31-7.23 (m, 2 H; H<sup>Ar</sup>, overlapping), 7.19-7.04 (m, 5 H; H<sup>Ar</sup>), 3.96 (s, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 141.2 (C<sub>q</sub>; C<sup>Ar</sup>), 140.7 (C<sub>q</sub>; C<sup>Ar</sup>), 136.2 (C<sup>Ar</sup>), 133.7 (C<sup>Ar</sup>), 133.5 (C<sup>Ar</sup>), 129.1 (C<sup>Ar</sup>), 128.7 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 126.3 (C<sup>Ar</sup>), 42.0 (CH<sub>2</sub>) ppm; <sup>\*</sup> **m.p.**<sup>exp.</sup> = 104-108°C.

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<sup>\*</sup> Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the boronic acid function was not observed.

**2.3.12 (*E/Z*)-1-Bromo-3-(but-2-en-2-yl)benzene (**24d**)**



**24d**

In a flame dried 250 mL three-neck round-bottom flask with reflux condenser, dropping funnel and argon-inlet, 1.84 g magnesium turnings (75.7 mmol, 1.0 eq) were suspended in 20 mL absolute Et<sub>2</sub>O. A solution of 9.19 g bromoethane (84.3 mmol, 1.1 eq) in 50 mL absolute Et<sub>2</sub>O were added dropwise to the magnesium turnings, and the mixture was stirred under reflux for 30 min. A solution of 15.1 g 1-(3-bromophenyl)ethanone (75.6 mmol, 1.0 eq) in 50 mL absolute Et<sub>2</sub>O were added, and the yellow suspension was stirred under reflux until full conversion was detected by GC-MS. The mixture was quenched with 50 mL 5% aqueous HCl solution, and after separation, the organic layer was washed with saturated NaHCO<sub>3</sub> solution. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was removed under reduced pressure. Pure intermediate 2-(3-bromophenyl)butan-2-ol (**24'd**) was isolated after flash column chromatography (cyclohexane/EtOAc = 9/2, R<sub>f</sub> = 0.30).<sup>[34]</sup> The pale yellow crude intermediate **24'd** was placed in a micro-distillation apparatus together with 100 µL of concentrated sulphuric acid. The formed water was distilled off, before the product was isolated at 31–32°C (0.1 torr). Compound **25d** was isolated as a mixture of the corresponding *E*- and *Z*-isomer (*E/Z* = 6/4).<sup>[35]</sup>

**Yield:** 8.31 g (52%), colourless liquid, C<sub>10</sub>H<sub>11</sub>Br [211.10 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.51–7.10 (m, 5 H; H<sup>Ar</sup>), 5.87 (dq, <sup>3</sup>J(H,H) = 6.9 Hz, <sup>4</sup>J(H,H) = 1.3 Hz, 0.6 H; CH(*E*)), 5.58 (dq, <sup>3</sup>J(H,H) = 6.9 Hz, <sup>4</sup>J(H,H) = 1.4 Hz, 0.4 H; CH(*Z*)), 2.00 (bs, 3 H; CH<sub>3</sub>), 1.80 (dd, <sup>3</sup>J(H,H) = 6.9 Hz, <sup>4</sup>J(H,H) = 0.8 Hz, 1.8 H; CH<sub>3</sub>(*E*)), 1.59 (dd, <sup>3</sup>J(H,H) = 6.9 Hz, <sup>4</sup>J(H,H) = 1.5 Hz, 1.2 H; CH<sub>3</sub>(*Z*)) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 146.3 (C<sub>q</sub>; C<sup>Ar</sup>), 144.2 (C<sub>q</sub>; C<sup>Ar</sup>), 135.6 (C<sub>q</sub>; C=CH), 134.5 (C<sub>q</sub>; C=CH), 131.2 (C<sup>Ar</sup>), 129.8 (C<sup>Ar</sup>), 129.6 (C<sup>Ar</sup>), 129.4 (C<sup>Ar</sup>), 128.8 (C<sup>Ar</sup>), 126.9 (C<sup>Ar</sup>), 124.3 (CH), 124.0 (CH), 122.8 (C<sup>Ar</sup>), 122.6 (C<sub>q</sub>; C<sup>Ar</sup>), 122.3 (C<sub>q</sub>; C<sup>Ar</sup>), 25.3 (CH<sub>3</sub>), 15.5 (CH<sub>3</sub>), 15.0 (CH<sub>3</sub>), 14.5 (CH<sub>3</sub>) ppm; **\* GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub><sup>Pro(*E*)</sup> = 5.37 min; *m/z* (%): 212 (36) [M<sup>+</sup>], 210 (35) [M<sup>+</sup>], 197 (3) [M<sup>+</sup>–CH<sub>3</sub>], 195 (3) [M<sup>+</sup>–CH<sub>3</sub>], 157 (1) [C<sub>6</sub>H<sub>4</sub>Br<sup>+</sup>], 155 (1) [C<sub>6</sub>H<sub>4</sub>Br<sup>+</sup>], 131

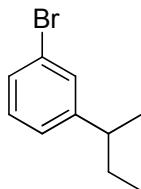
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\* NMR spectra showed both isomers (*E/Z*); unambiguously assignment of the signals was not possible.

## Experimental Procedures and Analytical Data

(100) [ $M^+ - \text{Br}$ ], 116 (83) [ $M^+ - \text{CH}_3\text{Br}$ ];  $t_{\text{R}}^{\text{Pro}(Z)} = 4.99$  min;  $m/z$  (%): 212 (38) [ $M^+$ ], 210 (37) [ $M^+$ ], 197 (3) [ $M^+ - \text{CH}_3$ ], 195 (3) [ $M^+ - \text{CH}_3$ ], 157 (1) [ $\text{C}_6\text{H}_4\text{Br}^+$ ], 155 (1) [ $\text{C}_6\text{H}_4\text{Br}^+$ ], 131 (100) [ $M^+ - \text{Br}$ ], 116 (81) [ $M^+ - \text{CH}_3\text{Br}$ ]; b.p.<sup>exp.</sup> = 31-32°C, 0.1 torr (b.p.<sup>lit.</sup> = 110-112°C, 17 torr).<sup>[35]</sup>

### 2.3.13 1-Bromo-3-(sec-butyl)benzene (24e)



**24e**

A 100 mL three-neck round-bottom flask equipped with two argon-inlets was charged with 8.31 g (*E/Z*)-1-bromo-3-(but-2-en-2-yl)benzene (**24d**) (39.4 mmol, 1.0 eq) and 20 mL absolute EtOH were added. To this colourless solution 41 mg PtO<sub>2</sub> (180 µmol, 0.5 mol%) were added, and the reaction mixture was stirred for 7 h at room temperature under hydrogen atmosphere (after evacuating and back-flushing with hydrogen gas (3x)). The catalyst was removed by filtration (small pad SiO<sub>2</sub>, eluent: MeOH), and the solvent was removed under reduced pressure using a rotary evaporator.\* After flash column chromatography (80 g SiO<sub>2</sub>, 26x3 cm, cyclohexane,  $R_f = 0.74$ ), compound **24e** was isolated as a colourless liquid.<sup>[35]</sup>

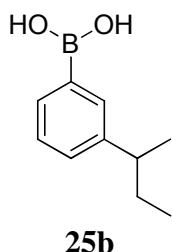
**Yield:** 6.38 g (76%), colourless liquid, C<sub>10</sub>H<sub>13</sub>Br [213.11 g/mol].

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>):  $\delta = 7.33$ -7.30 (m, 2 H; H<sup>Ar</sup>), 7.16 (t, <sup>3</sup>J(H,H) = 7.6 Hz, 1 H; H<sup>Ar</sup>), 7.11 (d, <sup>3</sup>J(H,H) = 7.7 Hz, 1 H; H<sup>Ar</sup>), 2.61-2.53 (m, 1 H; CH), 1.62-1.56 (m, 2 H; CH<sub>2</sub>), 1.23 (d, <sup>3</sup>J(H,H) = 6.9 Hz, 3 H; CH<sub>3</sub>), 0.83 (t, <sup>3</sup>J(H,H) = 7.4 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>):  $\delta = 150.2$  (C<sub>q</sub>; C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 130.0 (C<sup>Ar</sup>), 129.0 (C<sup>Ar</sup>), 125.9 (C<sup>Ar</sup>), 122.5 (C<sub>q</sub>; C<sup>Ar</sup>), 41.7 (CH), 31.2 (CH<sub>2</sub>), 21.8 (CH<sub>3</sub>), 12.3 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_{\text{R}} = 4.94$  min;  $m/z$  (%): 214 (21) [ $M^+$ ], 212 (21) [ $M^+$ ], 199 (1) [ $M^+ - \text{CH}_3$ ], 197 (1) [ $M^+ - \text{CH}_3$ ], 185 (85) [ $M^+ - \text{C}_2\text{H}_5$ ], 183 (88) [ $M^+ - \text{C}_2\text{H}_5$ ], 171 (10) [ $M^+ - \text{C}_3\text{H}_8$ ], 169 (10) [ $M^+ - \text{C}_3\text{H}_8$ ], 133 (6) [ $M^+ - \text{Br}$ ], 104 (100) [ $M^+ - \text{C}_2\text{H}_5\text{Br}$ ].

Analytical data are in accordance with those reported.<sup>[36]</sup>

\* The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

**2.3.14 (3-(*sec*-Butyl)phenyl)boronic acid (**25b**)**



In a 250 mL Schlenk-flask 3.20 g 1-bromo-3-(*sec*-butyl)benzene (**24e**) (15.0 mmol, 1.0 eq) were dissolved in 100 mL absolute THF. The colourless solution was cooled to -78°C and 10.1 mL *n*-BuLi (1.64 M, 16.5 mmol, 1.1 eq) were added. In a second 250 mL Schlenk-flask a solution of 10.4 mL (B(O*i*Pr)<sub>3</sub>) (8.47 g, 45.0 mmol, 3.0 eq) in 20 mL absolute THF was prepared, subsequently the colourless lithium mixture was added dropwise and stirring was continued for 1.5 h at -78°C. The colourless solution was allowed to warm to room temperature, and the reaction was quenched with 30 mL 5% aqueous HCl solution. The aqueous phase was extracted with Et<sub>2</sub>O (3x30 mL), and the colourless combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and removing the solvent under reduced pressure, compound **25b** was isolated after flash column chromatography (65 g SiO<sub>2</sub>, 24x3 cm, cyclohexane/EtOAc = 8/2, R<sub>f</sub> = 0.25).

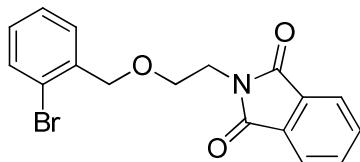
**Yield:** 1.93 g (72%), colourless solid, C<sub>10</sub>H<sub>15</sub>BO<sub>2</sub> [178.04 g/mol].

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ = 8.11 (d, <sup>3</sup>J(H,H) = 6.9 Hz, 1 H; H<sup>Ar</sup>), 8.07 (s, 1 H; H<sup>Ar</sup>), 7.49-7.41 (m, 2 H; H<sup>Ar</sup>), 2.80-2.72 (m, 1 H; CH), 1.75-1.69 (m, 2 H; CH<sub>2</sub>), 1.35 (d, <sup>3</sup>J(H,H) = 7.0 Hz, 3 H; CH<sub>3</sub>), 0.91 (t, <sup>3</sup>J(H,H) = 7.4 Hz, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>): δ = 147.2 (C<sub>q</sub>; C<sup>Ar</sup>), 134.5 (C<sup>Ar</sup>), 133.4 (C<sup>Ar</sup>), 131.5 (C<sup>Ar</sup>), 128.1 (C<sup>Ar</sup>), 41.8 (CH), 31.4 (CH<sub>2</sub>), 22.1 (CH<sub>3</sub>), 12.5 (CH<sub>3</sub>) ppm; <sup>\* m.p.</sup><sup>exp.</sup> = 50-53°C.

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<sup>\*</sup> Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the boronic acid function was not observed.

**2.3.15 2-((2-Bromobenzyl)oxy)ethyl)isoindoline-1,3-dione (24f)**



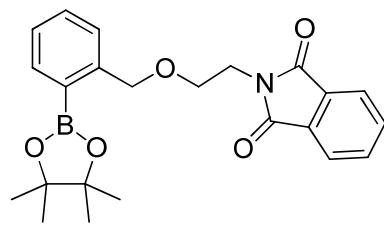
**24f**

In a flame dried and argon flushed 100 mL Schlenk-flask 1.41 g sodium hydride (NaH) (60% dispersion in mineral oil) (35.3 mmol, 1.3 eq) were suspended in 26 mL absolute DMF at 0°C. A solution of 5.35 g 2-(2-hydroxyethyl)isoindoline-1,3-dione (28.0 mmol, 1.0 eq) in 18 mL DMF was slowly added, and after stirring for 30 min at 40°C a solution of 7.00 g 2-bromobenzyl bromide (28.0 mmol, 1.0 eq) in 15 mL absolute DMF were added to the colourless reaction mixture and warmed to 70°C for 1.5 h. After cooling down to room temperature, the suspension was quenched with 250 mL H<sub>2</sub>O and extracted with EtOAc (3x100 mL). The pale yellow crude product was purified by flash column chromatography (240 g SiO<sub>2</sub>, 20x6 cm, cyclohexane/EtOAc = 8/2, R<sub>f</sub> = 0.31). Alternatively the crude can be purified by recrystallization from cyclohexane/THF (15/3).

**Yield:** 6.04 g (60%), colourless solid, C<sub>17</sub>H<sub>14</sub>BrNO<sub>3</sub> [360.20 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.88-7.82 (m, 2 H; H<sup>Phth</sup>), 7.74-7.70 (m, 2 H; H<sup>Phth</sup>), 7.46 (dd, <sup>3</sup>J (H,H) = 7.9 Hz, <sup>4</sup>J (H,H) = 0.9 Hz, 1 H; H<sup>Ar</sup>), 7.40 (bd, <sup>3</sup>J (H,H) = 6.9 Hz, 1 H; H<sup>Ar</sup>), 7.23 (dt, <sup>3</sup>J (H,H) = 7.6 Hz, <sup>4</sup>J (H,H) = 0.8 Hz, 1 H; H<sup>Ar</sup>, overlapping), 7.09 (dt, <sup>3</sup>J (H,H) = 7.8 Hz, <sup>4</sup>J (H,H) = 1.6 Hz, 1 H; H<sup>Ar</sup>), 4.58 (s, 2 H; CH<sub>2</sub>), 3.98 (t, <sup>3</sup>J (H,H) = 5.6 Hz, 2 H; CH<sub>2</sub>), 3.81 (t, <sup>3</sup>J (H,H) = 5.6 Hz, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 168.4 (C<sub>q</sub>; C=O<sup>Phth</sup>), 137.4 (C<sub>q</sub>; C<sup>Ar</sup>), 134.1 (C<sup>Phth</sup>), 132.5 (C<sup>Ar</sup>), 132.3 (C<sub>q</sub>; C<sup>Phth</sup>), 129.1 (C<sup>Ar</sup>), 129.0 (C<sup>Ar</sup>), 127.5 (C<sup>Ar</sup>), 123.4 (C<sup>Phth</sup>), 122.6 (C<sub>q</sub>; C<sup>Ar</sup>), 72.2 (CH<sub>2</sub>), 67.6 (CH<sub>2</sub>), 37.7 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 9.18 min; m/z (%): 361 (1) [M<sup>+</sup>], 359 (1) [M<sup>+</sup>], 280 (2) [M<sup>+</sup>-Br], 190 (10) [C<sub>10</sub>H<sub>8</sub>NO<sub>3</sub><sup>+</sup>], 171 (19) [C<sub>7</sub>H<sub>6</sub>Br<sup>+</sup>], 169 (20) [C<sub>7</sub>H<sub>6</sub>Br<sup>+</sup>], 160 (100) [C<sub>9</sub>H<sub>6</sub>NO<sub>2</sub><sup>+</sup>]; **m.p.**<sup>exp.</sup> = 86-88°C; **HRMS** (EI): calcd (m/z) for [M<sup>+</sup>]: 359.0157; found: 359.0173.

**2.3.16 2-((2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)oxy)ethyl)isoindoline-1,3-dione (**4a**)**



**4a**

Compound **4a** was prepared according to procedure 2.3.1 from 1.51 g 2-((2-bromobenzyl)oxy)ethyl)isoindoline-1,3-dione (**24f**) (4.19 mmol, 1.0 eq), 1.17 g  $B_2Pin_2$  (4.61 mmol, 1.1 eq), 1.24 g KOAc (12.6 mmol, 3.0 eq), and 103 mg  $PdCl_2(dppf)\cdot DCM$  (130  $\mu$ mol, 3 mol%) in 20 mL absolute, degassed DMF. The Br/BPin exchange was completed overnight. The black, oily crude product was purified by flash column chromatography (90 g  $SiO_2$ , 30x3 cm, cyclohexane/EtOAc = 8/2,  $R_f$  = 0.40).

**Yield:** 1.38 g (81%), colourless solid,  $C_{23}H_{26}BNO_5$  [407.27 g/mol].

**$^1H$  NMR** (300 MHz,  $CDCl_3$ ):  $\delta$  = 7.86-7.81 (m, 2 H;  $H^{Phth}$ ), 7.74 (bd,  $^3J(H,H)$  = 7.7 Hz, 1 H;  $H^{Ar}$ ), 7.71-7.67 (m, 2 H;  $H^{Phth}$ ), 7.41-7.32 (m, 2 H;  $H^{Ar}$ ), 7.21 (dt,  $^3J(H,H)$  = 7.3 Hz,  $^4J(H,H)$  = 1.2 Hz, 1 H;  $H^{Ar}$ ), 4.80 (s, 2 H;  $CH_2$ ), 3.95 (t,  $^3J(H,H)$  = 5.9 Hz, 2 H;  $CH_2$ ), 3.76 (t,  $^3J(H,H)$  = 5.9 Hz, 2 H;  $CH_2$ ), 1.33 (s, 12 H;  $CH_3^{BPin}$ ) ppm;  **$^{13}C$  NMR** (76 MHz,  $CDCl_3$ , APT):  $\delta$  = 168.4 ( $C_q$ ;  $C=O^{Phth}$ ), 144.5 ( $C_q$ ;  $C^{Ar}$ ), 135.8 ( $C^{Ar}$ ), 134.0 ( $C^{Phth}$ ), 132.3 ( $C_q$ ;  $C^{Phth}$ ), 131.1 ( $C^{Ar}$ ), 127.7 ( $C^{Ar}$ ), 126.8 ( $C^{Ar}$ ), 123.3 ( $C^{Phth}$ ), 83.8 ( $C_q$ ;  $C^{BPin}$ ), 72.1 ( $CH_2$ ), 67.1 ( $CH_2$ ), 37.8 ( $CH_2$ ), 25.0 ( $CH_3^{BPin}$ ) ppm; \* **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R$  = 10.62 min;  $m/z$  (%): 407 (<1) [ $M^+$ ], 217 (8) [ $C_{13}H_{18}BO_2^+$ ], 190 (8) [ $C_{10}H_8NO_3^+$ ], 174 (78) [ $C_{10}H_8NO_2^+$ ], 160 (100) [ $C_9H_6NO_2^+$ ]; **m.p.**<sup>exp.</sup> = 73-75°C; **HRMS** (EI): calcd ( $m/z$ ) for [ $M^+$ ]: 407.1908; found: 407.1933.

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\* Signal for the quaternary *ipso*-aromatic carbon ( $C_q$ ;  $C^{Ar}$ ) at the boronic acid pinacol ester function was not observed.

**2.3.17 1-Bromo-3-(but-3-en-1-yl)benzene (24g)**



**24g**

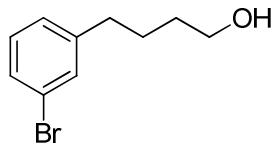
In a flame dried 100 mL three-neck round-bottom flask with argon-inlet, reflux condenser, and dropping funnel 1.07 g magnesium turnings (44.0 mmol, 1.1 eq) were suspended in 30 mL absolute Et<sub>2</sub>O. A solution of 3.98 mL allyl bromide (5.56 g, 46.0 mmol, 1.15 eq) in 10 mL absolute Et<sub>2</sub>O was slowly added in a dropwise manner. After complete addition (~15 min) the reaction mixture was heated under reflux for 3 h. In a second flame dried 250 mL three-neck round-bottom flask with reflux condenser and argon-inlet a colourless solution of 10.0 g 3-bromobenzyl bromide (40.0 mmol, 1.0 eq) in 50 mL absolute THF was prepared. The pale brown Grignard-suspension was allowed to cool to room temperature and was transferred *via* cannula to the colourless, ice cooled benzyl bromide solution, whereby a colourless precipitate was formed. After complete addition the reaction mixture was heated under reflux overnight. After cooling down to room temperature, the colourless suspension was quenched with 45 mL 2 M H<sub>2</sub>SO<sub>4</sub> solution at ~0°C and extracted with Et<sub>2</sub>O (2x50 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was removed under reduced pressure. The pale yellow crude product was used in the next step without further purification. A pure sample was obtained after flash column chromatography (cyclohexane, R<sub>f</sub> = 0.56) as a pale yellow liquid.

**Yield:** 8.34 g (99%), pale yellow liquid, C<sub>10</sub>H<sub>11</sub>Br [211.10 g/mol].

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ = 7.35-7.32 (m, 2 H; H<sup>Ar</sup>), 7.17-7.11 (m, 2 H; H<sup>Ar</sup>), 5.87-5.79 (m, 1 H; CH), 5.05 (dd, <sup>3</sup>J(H,H) = 17.1 Hz, <sup>4</sup>J(H,H) = 1.4 Hz, 1 H; CH=CH<sub>2</sub>), 5.00 (dd, <sup>3</sup>J(H,H) = 10.2 Hz, <sup>4</sup>J(H,H) = 0.4 Hz, 1 H; CH=CH<sub>2</sub>), 2.69 (t, <sup>3</sup>J(H,H) = 7.8 Hz, 2 H; CH<sub>2</sub>), 2.36 (dd, <sup>3</sup>J(H,H) = 15.0 Hz, <sup>3</sup>J(H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>): δ = 144.3 (C<sub>q</sub>; C<sup>Ar</sup>), 137.6 (CH), 131.6 (C<sup>Ar</sup>), 130.0 (C<sup>Ar</sup>), 129.1 (C<sup>Ar</sup>), 127.3 (C<sup>Ar</sup>), 122.5 (C<sub>q</sub>; C<sup>Ar</sup>), 115.5 (CH=CH<sub>2</sub>), 35.3 (CH<sub>2</sub>), 35.1 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 5.06 min; *m/z* (%): 212 (6) [M<sup>+</sup>], 210 (6) [M<sup>+</sup>], 171 (97) [M<sup>+</sup>-C<sub>3</sub>H<sub>5</sub>], 169 (100) [M<sup>+</sup>-C<sub>3</sub>H<sub>5</sub>], 131 (52) [M<sup>+</sup>-Br], 90 (28) [C<sub>7</sub>H<sub>6</sub><sup>+</sup>].

Analytical data are in accordance with those reported.<sup>[37]</sup>

**2.3.18 4-(3-Bromophenyl)butan-1-ol (24h)**



**24h**

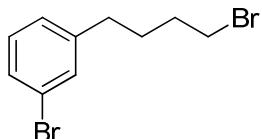
In a flame dried 250 mL Schlenk-flask 4.17 g 9-borabicyclo[3.3.1]nonane dimer (9-BBN) (17.1 mmol, 0.75 eq) were suspended in 80 mL *n*-hexane. A solution of 4.81 g 1-bromo-3-(but-3-en-1-yl)benzene (**24g**) (22.8 mmol, 1.0 eq) dissolved in 50 mL *n*-hexane was slowly added. The mixture was stirred at room temperature overnight, followed by addition of 6 M NaOH (3.80 mL, 22.8 mmol, 1.0 eq) and 7.48 mL H<sub>2</sub>O<sub>2</sub> (35 wt%) (2.97 g, 87.3 mmol, 3.8 eq). The mixture was stirred at 50°C overnight, and after cooling to room temperature the organic layer was separated and washed subsequently with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (1x30 mL), water (1x30 mL), and brine (1x30 mL). The aqueous extracts were combined, saturated with Na<sub>2</sub>CO<sub>3</sub>, filtered and reextracted with Et<sub>2</sub>O (3x50 mL). All organic fractions were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (250 g SiO<sub>2</sub>, 20x6 cm, cyclohexane/EtOAc = 75/25, R<sub>f</sub> = 0.24), to achieve product **24h** as a pale yellow oil.

**Yield:** 4.46 g (85%), pale yellow oil, C<sub>10</sub>H<sub>13</sub>BrO [229.11 g/mol].

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ = 7.34-7.30 (m, 2 H; H<sup>Ar</sup>), 7.16-7.09 (m, 2 H; H<sup>Ar</sup>), 3.66 (t, <sup>3</sup>J (H,H) = 6.4 Hz, 2 H; CH<sub>2</sub>), 2.62 (t, <sup>3</sup>J (H,H) = 7.6 Hz, 2 H; CH<sub>2</sub>), 1.72-1.65 (m, 2 H; CH<sub>2</sub>), 1.62-1.56 (m, 2 H; CH<sub>2</sub>), 1.43 (bs, 1 H; OH) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>): δ = 144.8 (C<sub>q</sub>; C<sup>Ar</sup>), 131.6 (C<sup>Ar</sup>), 130.0 (C<sup>Ar</sup>), 129.0 (C<sup>Ar</sup>), 127.2 (C<sup>Ar</sup>), 122.5 (C<sub>q</sub>; C<sup>Ar</sup>), 62.8 (CH<sub>2</sub>), 35.4 (CH<sub>2</sub>), 32.3 (CH<sub>2</sub>), 27.5 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 6.16 min, *m/z* (%): 230 (12) [M<sup>+</sup>], 228 (15) [M<sup>+</sup>], 184 (98) [M<sup>+</sup>-C<sub>2</sub>H<sub>6</sub>O], 182 (100) [M<sup>+</sup>-C<sub>2</sub>H<sub>6</sub>O], 171 (36) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>O], 169 (36) [M<sup>+</sup>-C<sub>3</sub>H<sub>7</sub>O], 131 (86) [M<sup>+</sup>-H<sub>2</sub>BrO].

Analytical data are in accordance with those reported; in literature [D<sub>6</sub>]DMSO was used.<sup>[38]</sup>

### 2.3.19 1-Bromo-3-(4-bromobutyl)benzene (**24i**)



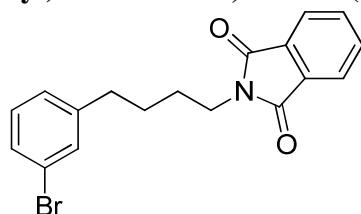
**24i**

A 100 mL flame dried Schlenk-flask was charged with 4.46 g 4-(3-bromophenyl)butan-1-ol (**24h**) (19.5 mmol, 1.0 eq). Under external ice cooling, 4.53 mL tribromophosphine ( $\text{PBr}_3$ ) (13.0 g, 48.2 mmol, 2.5 eq) were carefully added. After stirring at room temperature for 50 min, the reaction mixture was poured onto crushed ice. The aqueous solution was adjusted to pH ~8 (saturated  $\text{NaHCO}_3$  solution) and extracted with DCM (3x60 mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (80 g  $\text{SiO}_2$ , 28x3 cm, cyclohexane,  $R_f = 0.43$ ), to achieve product **24i** as a pale yellow oil.

**Yield:** 5.20 g (91%), pale yellow oil,  $\text{C}_{10}\text{H}_{12}\text{Br}_2$  [292.01 g/mol].

**$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.33$  (s, 1 H;  $\text{H}^{\text{Ar}}$ ), 7.32 (d,  $^3J(\text{H},\text{H}) = 6.8$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ , overlapping), 7.15 (t,  $^3J(\text{H},\text{H}) = 8.0$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 7.10 (d,  $^3J(\text{H},\text{H}) = 7.6$  Hz, 1 H;  $\text{H}^{\text{Ar}}$ ), 3.42 (t,  $^3J(\text{H},\text{H}) = 6.6$  Hz, 2 H;  $\text{CH}_2$ ), 2.62 (t,  $^3J(\text{H},\text{H}) = 7.6$  Hz, 2 H;  $\text{CH}_2$ ), 1.91-1.86 (m, 2 H;  $\text{CH}_2$ ), 1.80-1.74 (m, 2 H;  $\text{CH}_2$ ) ppm;  **$^{13}\text{C NMR}$**  (126 MHz,  $\text{CDCl}_3$ ):  $\delta = 144.3$  ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 131.6 ( $\text{C}^{\text{Ar}}$ ), 130.1 ( $\text{C}^{\text{Ar}}$ ), 129.2 ( $\text{C}^{\text{Ar}}$ ), 127.2 ( $\text{C}^{\text{Ar}}$ ), 122.6 ( $\text{C}_q$ ;  $\text{C}^{\text{Ar}}$ ), 34.8 ( $\text{CH}_2$ ), 33.6 ( $\text{CH}_2$ ), 32.2 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S):  $t_R = 6.41$  min;  $m/z$  (%): 294 (7) [ $M^+$ ], 292 (14) [ $M^+$ ], 290 (7) [ $M^+$ ], 171 (97) [ $M^+ - \text{C}_3\text{H}_6\text{Br}$ ], 169 (100) [ $M^+ - \text{C}_3\text{H}_6\text{Br}$ ], 131 (12) [ $M^+ - \text{HBr}_2$ ].

### 2.3.20 2-(4-(3-Bromophenyl)butyl)isoindoline-1,3-dione (**24j**)



**24j**

In a flame dried 25 mL Schlenk-flask 1.44 g 1-bromo-3-(4-bromobutyl)benzene (**24i**) (4.93 mmol, 1.0 eq) were suspended in 10 mL absolute DMF, and after degassing 1.18 g potassium phthalimide (KNPhth) (6.37 mmol, 1.3 eq) were added in one portion. The pale yellow reaction mixture was stirred overnight at 80°C and subsequently quenched with 5 mL

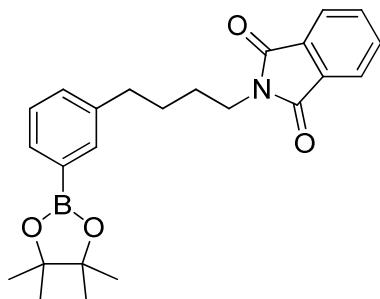
## Experimental Procedures and Analytical Data

5% aqueous NaHCO<sub>3</sub> solution. The pH of the aqueous phase was adjusted with saturated NaHCO<sub>3</sub> solution to ~8-9 and extracted with EtOAc (3x25 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was removed under reduced pressure on a rotary evaporator. The crude yellow oily product was purified by flash column chromatography (210 g SiO<sub>2</sub>, 28x5 cm, cyclohexane/EtOAc = 8/2, R<sub>f</sub> = 0.39).

**Yield:** 1.62 g (92%), colourless solid, C<sub>18</sub>H<sub>16</sub>BrNO<sub>2</sub> [358.23 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.85-7.82 (m, 2 H; H<sup>Phth</sup>), 7.72-7.69 (m, 2 H; H<sup>Phth</sup>), 7.31 (d, <sup>4</sup>J (H,H) = 1.4 Hz, 1 H; H<sup>Ar</sup>), 7.30 (dd, <sup>3</sup>J (H,H) = 6.9 Hz, <sup>4</sup>J (H,H) = 1.4 Hz, 1 H; H<sup>Ar</sup>, overlapping), 7.15-7.07 (m, 2 H; H<sup>Ar</sup>), 3.71 (t, <sup>3</sup>J (H,H) = 6.8 Hz, 2 H; CH<sub>2</sub>), 2.62 (t, <sup>3</sup>J (H,H) = 7.3 Hz, 2 H; CH<sub>2</sub>), 1.77-1.58 (m, 4 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>): δ = 168.6 (C<sub>q</sub>; C=O<sup>Phth</sup>), 144.4 (C<sub>q</sub>; C<sup>Ar</sup>), 134.0 (C<sup>Phth</sup>), 132.2 (C<sub>q</sub>; C<sup>Phth</sup>), 131.6 (C<sup>Ar</sup>), 130.0 (C<sup>Ar</sup>), 129.1 (C<sup>Ar</sup>), 127.2 (C<sup>Ar</sup>), 123.3 (C<sup>Phth</sup>), 122.5 (C<sub>q</sub>; C<sup>Ar</sup>), 37.8 (CH<sub>2</sub>), 35.2 (CH<sub>2</sub>), 28.5 (CH<sub>2</sub>), 28.2 (CH<sub>2</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 8.65 min; m/z (%): 359 (10) [M<sup>+</sup>], 357 (10) [M<sup>+</sup>], 278 (1) [M<sup>+</sup>-Br], 188 (20) [C<sub>11</sub>H<sub>10</sub>NO<sub>2</sub><sup>+</sup>], 171 (13) [C<sub>7</sub>H<sub>6</sub>Br<sup>+</sup>], 169 (14) [C<sub>7</sub>H<sub>6</sub>Br<sup>+</sup>], 160 (100) [C<sub>9</sub>H<sub>6</sub>NO<sub>2</sub><sup>+</sup>]; **m.p.**<sup>exp.</sup> = 89-91°C; **HRMS** (EI): calcd (m/z) for [M<sup>+</sup>]: 357.0364; found: 357.0387.

### **2.3.21 2-(4-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**4b**)**



**4b**

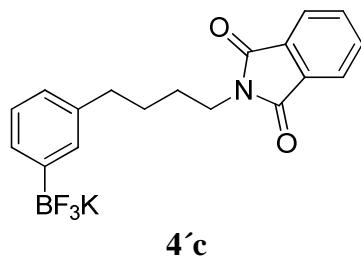
Compound **4b** was prepared according to procedure 2.3.1 from 2.55 g 2-(4-(3-bromophenyl)-butyl)isoindoline-1,3-dione (**24j**) (7.12 mmol, 1.0 eq), 1.99 g B<sub>2</sub>PIn<sub>2</sub> (7.84 mmol, 1.1 eq), 1.40 g KOAc (14.3 mmol, 2.0 eq), and 174 mg PdCl<sub>2</sub>(dpff)-DCM (210 μmol, 3 mol%) in 30 mL absolute, degassed DMF. The Br/BPin exchange was completed after ~17 h. The black crude product was purified by flash column chromatography (206 g SiO<sub>2</sub>, 27x5 cm, cyclohexane/EtOAc = 85/15, R<sub>f</sub> = 0.32), to achieve product **4b** as a colourless solid. Alternatively the crude product can be purified by recrystallization from cyclohexane (~6 mL/g, reflux).

## Experimental Procedures and Analytical Data

**Yield:** 2.72 g (94%), colourless solid, C<sub>24</sub>H<sub>28</sub>BNO<sub>4</sub> [405.29 g/mol].

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ = 7.83-7.80 (m, 2 H; H<sup>Phth</sup>), 7.70-7.67 (m, 2 H; H<sup>Phth</sup>), 7.63-7.61 (m, 2 H; H<sup>Ar</sup>), 7.30-7.27 (m, 2 H; H<sup>Ar</sup>, overlapping), 3.70 (t, <sup>3</sup>J(H,H) = 6.9 Hz, 2 H; CH<sub>2</sub>), 2.65 (t, <sup>3</sup>J(H,H) = 7.4 Hz, 2 H; CH<sub>2</sub>), 1.74-1.64 (m, 4 H; CH<sub>2</sub>), 1.34 (s, 12 H; CH<sub>3</sub><sup>BPin</sup>) ppm; **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>, DEPT): δ = 168.5 (C<sub>q</sub>; C=O<sup>Phth</sup>), 141.3 (C<sub>q</sub>; C<sup>Ar</sup>), 134.8 (C<sup>Ar</sup>), 133.9 (C<sup>Phth</sup>), 132.4 (C<sup>Ar</sup>), 132.2 (C<sub>q</sub>; C<sup>Phth</sup>), 131.5 (C<sup>Ar</sup>), 127.8 (C<sup>Ar</sup>), 123.2 (C<sup>Phth</sup>) 83.8 (C<sub>q</sub>; C<sup>BPin</sup>), 37.9 (CH<sub>2</sub>), 35.5 (CH<sub>2</sub>), 28.9 (CH<sub>2</sub>), 28.4 (CH<sub>2</sub>), 25.0 (CH<sub>3</sub><sup>BPin</sup>) ppm; \* **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 10.26 min; m/z (%): 405 (5) [M<sup>+</sup>], 305 (77) [M<sup>+</sup>-C<sub>6</sub>H<sub>12</sub>O], 202 (100) [M<sup>+</sup>-C<sub>12</sub>H<sub>12</sub>NO<sub>2</sub>], 160 (66) [C<sub>9</sub>H<sub>6</sub>NO<sub>2</sub><sup>+</sup>]; **m.p.**<sup>exp.</sup> = 96-99°C; **HRMS** (EI): calcd (m/z) for [M<sup>+</sup>]: 405.2116; found: 405.2135.

### 2.3.22 Potassium (3-(4-(1,3-dioxoisindolin-2-yl)butyl)phenyl)trifluoroborate (4'c)



Compound **4'c** was prepared according to procedure 2.3.2 from 739 mg 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**4b**) (1.82 mmol, 1.0 eq) and 427 mg KHF<sub>2</sub> (5.47 mmol, 3.0 eq) in 30 mL MeOH/H<sub>2</sub>O (1/1). The BPin/BF<sub>3</sub>K exchange was completed after ~16 h. After evaporation to dryness the colourless solid was redissolved in 7 mL acetone, and after filtration and evaporation, the colourless residue was used in the next step without further purification.

**Yield:** 700 mg (quant.), colourless solid, C<sub>18</sub>H<sub>16</sub>BF<sub>3</sub>KNO<sub>2</sub> [385.23 g/mol].

**<sup>1</sup>H NMR** (300 MHz, [D<sub>6</sub>]DMSO): δ = 7.88-7.81 (m, 4 H; H<sup>Phth</sup>), 7.11 (d, <sup>3</sup>J(H,H) = 8.6 Hz, 2 H; H<sup>Ar</sup>), 6.96 (t, <sup>3</sup>J(H,H) = 7.3 Hz, 1 H; H<sup>Ar</sup>), 6.82 (d, <sup>3</sup>J(H,H) = 7.4 Hz, 1 H; H<sup>Ar</sup>), 3.60 (t, <sup>3</sup>J(H,H) = 6.7 Hz, 2 H; CH<sub>2</sub>), 2.52-2.47 (m, 2 H; CH<sub>2</sub>, overlapping), 1.64-1.49 (m, 4 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, [D<sub>6</sub>]DMSO, APT): δ = 167.9 (C<sub>q</sub>; C=O<sup>Phth</sup>), 139.0 (C<sub>q</sub>; C<sup>Ar</sup>), 134.3 (C<sup>Phth</sup>), 131.6 (C<sub>q</sub>; C<sup>Phth</sup>), 131.5 (C<sup>Ar</sup>), 128.8 (C<sup>Ar</sup>), 126.1 (C<sup>Ar</sup>), 124.8 (C<sup>Ar</sup>), 123.0

\* Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the boronic acid pinacol ester function was not observed.

## Experimental Procedures and Analytical Data

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(C<sup>Phth</sup>), 37.3 (CH<sub>2</sub>), 35.2 (CH<sub>2</sub>), 28.7 (CH<sub>2</sub>), 27.8 (CH<sub>2</sub>) ppm; \* m.p.<sup>exp.</sup> = 56-59°C; **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>-FK]: 327.1245; found: 327.1263.

## **2.4 Synthesis of Terphenyls using the Diazonium Approach**

### **2.4.1 Representative procedure for diazonium coupling with diazonium tetrafluoroborates and potassium trifluoroborate derivatives**

A flame dried and argon flushed 100 mL Schlenk-flask was charged with 1.0 eq diazonium tetrafluoroborate, 1.2 eq potassium trifluoroborate derivative and 5-6 mol% Pd(OAc)<sub>2</sub>. After drying in vacuo and back-flushing with argon the Schlenk-flask was cooled (temperatures are given), and cold absolute, degassed MeOH was added *via* cannula to the reaction mixture. The orange-brown suspension was stirred for the indicated time and temperature. The reaction was monitored by GC-MS, after filtering a small aliquot of the reaction mixture through a small pad of SiO<sub>2</sub> and eluting with MeOH. After quantitative conversion the reaction mixture was concentrated to dryness without further workup, and the crude product was purified by flash column chromatography (eluents are denoted).

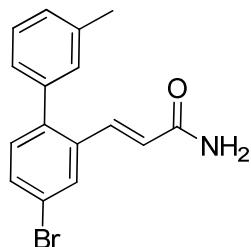
### **2.4.2 Representative procedure for Suzuki-coupling with aryl halides and aryl boronic acid or boronic acid pinacol ester derivatives**

A flame dried and argon flushed 50 mL Schlenk-flask was charged with 1.0 eq aryl halide derivative, 1.0-1.2 eq aryl boronic acid (or pinacol ester), 2.0 eq caesium fluoride (CsF), and 3-5 mol% PdCl<sub>2</sub>(dppf)-DCM. After drying of the starting materials in vacuo and back-flushing with argon, absolute, degassed 1,2-DME was added, and the orange suspension was heated to 80°C. The reaction was monitored by GC-MS, after filtering a small aliquot of the reaction mixture through a small pad of SiO<sub>2</sub> and eluting with MeOH. After quantitative conversion the beige suspension was filtered through a small pad of silica gel (2x3 cm) and eluted with MeOH. The solvent was removed under reduced pressure, and the crude product was purified by flash column chromatography (eluents are indicated for each experiment).

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\* Signal for the quaternary *ipso*-aromatic carbon (C<sub>q</sub>; C<sup>Ar</sup>) at the trifluoroborate function was not observed.

**2.4.3 (*E*)-3-(4-Bromo-3'-methyl-[1,1'-biphenyl]-2-yl)acrylamide (26a)**



**26a**

Compound **26a** was prepared according to procedure 2.4 from 200 mg (*E*)-2-(3-amino-3-oxo-prop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (**2a**) (590 µmol, 1.0 eq), 140 mg potassium trifluoro(*m*-tolyl)borate (**4'a**) (710 µmol, 1.2 eq), and 7 mg Pd(OAc)<sub>2</sub> (31 µmol, 5 mol%) in 20 mL absolute, degassed MeOH at -78°C. The mixture was allowed to warm to 9°C within 9.5 h and further stirred at room temperature (~9 h) completing the reaction. The crude product was purified by flash column chromatography (71 g SiO<sub>2</sub>, 24x3 cm, cyclohexane/EtOAc = 1/1, R<sub>f</sub> = 0.26), to achieve product **26a** as a colourless solid.\*

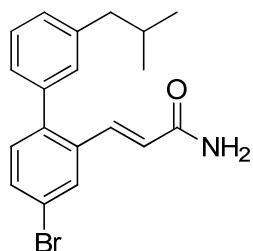
**Yield:** 102 mg (55%), colourless solid, C<sub>16</sub>H<sub>14</sub>BrNO [316.19 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.77 (d, <sup>4</sup>J (H,H) = 1.9 Hz, 1 H; H<sup>Ar</sup>), 7.53 (d, <sup>3</sup>J (H,H) = 15.9 Hz, 1 H; CH), 7.51 (dd, <sup>3</sup>J (H,H) = 8.1 Hz, <sup>4</sup>J (H,H) = 2.1 Hz, 1 H; H<sup>Ar</sup>, overlapping), 7.32-7.26 (m, 1 H; H<sup>Ar</sup>), 7.22-7.17 (m, 2 H; H<sup>Ar</sup>), 7.07-7.03 (m, 2 H; H<sup>Ar</sup>), 6.37 (d, <sup>3</sup>J (H,H) = 15.7 Hz, 1 H; CH), 5.92 (bs, 1 H; CONH<sub>2</sub>), 5.77 (bs, 1 H; CONH<sub>2</sub>), 2.38 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (300 MHz, CDCl<sub>3</sub>, APT): δ = 167.6 (C<sub>q</sub>; CONH<sub>2</sub>), 141.9 (C<sub>q</sub>; C<sup>Ar</sup>), 140.1 (CH), 138.9 (C<sub>q</sub>; C<sup>Ar</sup>), 138.3 (C<sub>q</sub>; C<sup>Ar</sup>), 134.8 (C<sub>q</sub>; C<sup>Ar</sup>), 132.4 (C<sup>Ar</sup>), 132.2 (C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 129.5 (C<sup>Ar</sup>), 128.8 (C<sup>Ar</sup>), 128.5 (C<sup>Ar</sup>), 126.9 (C<sup>Ar</sup>), 122.0 (CH), 121.6 (C<sub>q</sub>; C<sup>Ar</sup>), 21.6 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 8.49 min; *m/z* (%): 317 (1) [M<sup>+</sup>], 315 (1) [M<sup>+</sup>], 273 (11) [M<sup>+</sup>-CH<sub>2</sub>NO], 271 (12) [M<sup>+</sup>-CH<sub>2</sub>NO], 192 (100) [M<sup>+</sup>-CH<sub>2</sub>BrNO]; **m.p.**<sup>exp.</sup> = 83-86°C.

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\* No molecular peak was found by HRMS (EI).

#### 2.4.4 (*E*)-3-(4-Bromo-3'-isobutyl-[1,1'-biphenyl]-2-yl)acrylamide (26b)



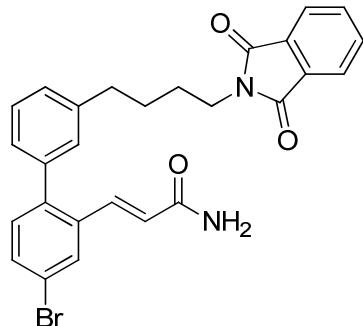
**26b**

Compound **26b** was prepared according to procedure 2.4 from 680 mg (*E*)-2-(3-amino-3-oxo-prop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (**2a**) (2.00 mmol, 1.0 eq), 576 mg potassium trifluoro(3-isobutylphenyl)borate (**4b**) (2.40 mmol, 1.2 eq), and 23 mg Pd(OAc)<sub>2</sub> (0.10 mmol, 5 mol%) in 50 mL absolute, degassed MeOH. After addition at -35°C the mixture was slowly allowed to warm to 5°C in the cooling bath (4 h) and stirred overnight at 5°C. The crude product was purified by flash column chromatography (80 g SiO<sub>2</sub>, 36x3 cm, cyclohexane/EtOAc = 6/4, R<sub>f</sub> = 0.29), to achieve compound **26b** as a pale yellow solid.

**Yield:** 346 mg (48%), pale yellow solid, C<sub>19</sub>H<sub>20</sub>BrNO [358.27 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.77 (d, <sup>4</sup>J (H,H) = 1.9 Hz, 1 H; H<sup>Ar</sup>), 7.54 (d, <sup>3</sup>J (H,H) = 15.8 Hz, 1 H; CH), 7.52 (dd, <sup>3</sup>J (H,H) = 8.2 Hz, <sup>4</sup>J (H,H) = 2.0 Hz, 1 H; H<sup>Ar</sup>, overlapping), 7.32 (t, <sup>3</sup>J (H,H) = 7.6 Hz, 1 H; H<sup>Ar</sup>), 7.23 (d, <sup>3</sup>J (H,H) = 8.3 Hz, 1 H; H<sup>Ar</sup>), 7.17 (d, <sup>3</sup>J (H,H) = 7.6 Hz, 1 H; H<sup>Ar</sup>), 7.09-7.04 (m, 2 H; H<sup>Ar</sup>), 6.37 (d, <sup>3</sup>J (H,H) = 15.7 Hz, 1 H; CH), 5.75 (bs, 2 H; CONH<sub>2</sub>), 2.50 (d, <sup>3</sup>J (H,H) = 7.2 Hz, 2 H; CH<sub>2</sub>), 1.97-1.79 (m, 1 H; CH), 0.92 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 167.4 (C<sub>q</sub>; CONH<sub>2</sub>), 142.1 (C<sub>q</sub>; C<sup>Ar</sup>), 142.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.3 (CH), 138.7 (C<sub>q</sub>; C<sup>Ar</sup>), 134.9 (C<sub>q</sub>; C<sup>Ar</sup>), 132.4 (C<sup>Ar</sup>), 132.2 (C<sup>Ar</sup>), 130.5 (C<sup>Ar</sup>), 129.7 (C<sup>Ar</sup>), 128.9 (C<sup>Ar</sup>), 128.4 (C<sup>Ar</sup>), 127.1 (C<sup>Ar</sup>), 122.0 (CH), 121.6 (C<sub>q</sub>; C<sup>Ar</sup>), 45.5 (CH<sub>2</sub>), 30.4 (CH), 22.5 (CH<sub>3</sub>) ppm; **GC-MS** (EI, 70 eV; MP\_50\_S): t<sub>R</sub> = 9.25 min; m/z (%): 359 (4) [M<sup>+</sup>], 357 (3) [M<sup>+</sup>], 315 (17) [M<sup>+</sup>-CH<sub>2</sub>NO], 313 (17) [M<sup>+</sup>-CH<sub>2</sub>NO], 271 (31) [M<sup>+</sup>-C<sub>4</sub>H<sub>10</sub>NO], 269 (30) [M<sup>+</sup>-C<sub>4</sub>H<sub>10</sub>NO], 234 (63) [M<sup>+</sup>-CH<sub>2</sub>BrNO], 191 (99) [C<sub>6</sub>H<sub>8</sub>BrNO<sup>+</sup>], 189 (100) [C<sub>6</sub>H<sub>8</sub>BrNO<sup>+</sup>]; **m.p.**<sup>exp.</sup> = 155-157°C; **HRMS** (EI): calcd (m/z) for [M<sup>+</sup>]: 357.0728; found: 357.0742.

**2.4.5 (*E*)-3-(4-Bromo-3'-(4-(1,3-dioxoisindolin-2-yl)butyl)-[1,1'-biphenyl]-2-yl)acrylamide (26c)**



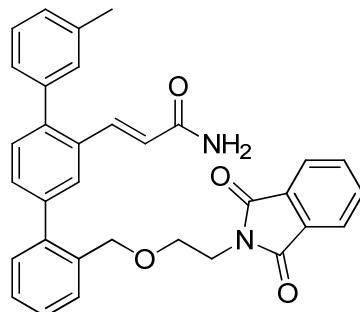
**26c**

Compound **26c** was prepared according to procedure 2.4 from 340 mg (*E*)-2-(3-amino-3-oxo-prop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (**2a**) (1.00 mmol, 1.0 eq), 462 mg potassium (3-(4-(1,3-dioxoisindolin-2-yl)butyl)phenyl)trifluoroborate (**4'c**) (1.20 mmol, 1.2 eq), and 11 mg Pd(OAc)<sub>2</sub> (49 μmol, 5 mol%) in 25 mL absolute, degassed MeOH. After addition at -20°C and warming to 0°C after 1 h, the reaction mixture was stirred overnight at 0°C. After complete conversion the crude product was purified by flash column chromatography (60 g SiO<sub>2</sub>, 25x3 cm, cyclohexane/EtOAc = 3/7, R<sub>f</sub> = 0.43), to achieve product **26c** as a colourless solid.

**Yield:** 247 mg (49%), colourless solid, C<sub>27</sub>H<sub>23</sub>BrN<sub>2</sub>O<sub>3</sub> [503.39 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.85-7.79 (m, 2 H; H<sup>Phth</sup>), 7.76 (d, <sup>4</sup>J(H,H) = 1.9 Hz, 1 H; H<sup>Ar</sup>), 7.72-7.68 (m, 2 H; H<sup>Phth</sup>), 7.54-7.49 (m, 2 H; H<sup>Ar</sup>, CH), 7.33-7.16 (m, 3 H; H<sup>Ar</sup>), 7.09-7.06 (m, 2 H; H<sup>Ar</sup>), 6.37 (d, <sup>3</sup>J(H,H) = 15.7 Hz, 1 H; CH), 5.82 (bs, 2 H; CONH<sub>2</sub>), 3.71 (t, <sup>3</sup>J(H,H) = 6.6 Hz, 2 H; CH<sub>2</sub>), 2.68 (t, <sup>3</sup>J(H,H) = 6.8 Hz, 2 H; CH<sub>2</sub>), 1.71 (bs, 4 H; CH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 168.6 (C<sub>q</sub>; C=O<sup>Phth</sup>), 167.5 (C<sub>q</sub>; CONH<sub>2</sub>), 142.4 (C<sub>q</sub>; C<sup>Ar</sup>), 141.7 (C<sub>q</sub>; C<sup>Ar</sup>), 140.1 (CH), 139.0 (C<sub>q</sub>; C<sup>Ar</sup>), 134.9 (C<sub>q</sub>; C<sup>Ar</sup>), 134.0 (C<sup>Phth</sup>), 132.4 (C<sup>Ar</sup>), 132.3 (C<sub>q</sub>; C<sup>Phth</sup>), 132.2 (C<sup>Ar</sup>), 129.9 (C<sup>Ar</sup>), 129.7 (C<sup>Ar</sup>), 128.6 (C<sup>Ar</sup>), 128.2 (C<sup>Ar</sup>), 127.3 (C<sup>Ar</sup>), 123.3 (C<sup>Phth</sup>), 122.3 (CH), 121.6 (C<sub>q</sub>; C<sup>Ar</sup>), 38.0 (CH<sub>2</sub>), 35.4 (CH<sub>2</sub>), 28.7 (CH<sub>2</sub>), 28.1 (CH<sub>2</sub>) ppm; **m.p.**<sup>exp.</sup> = 164-166°C; **HRMS** (DI-EI): calcd (m/z) for [M<sup>+</sup>]: 502.0892; found: 502.0925.

**2.4.6 (*E*)-3-(2''-((2-(1,3-Dioxoisooindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)acrylamide (14a)**



**14a**

Compound **14a** was prepared according to procedure 2.4.2 from 182 mg (*E*-3-(4-bromo-3'-methyl-[1,1'-biphenyl]-2-yl)acrylamide (**26a**) (0.58 mmol, 1.0 eq), 281 mg 2-(2-((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)oxy)ethyl)isoindoline-1,3-dione (**4a**) (0.69 mmol, 1.2 eq), 175 mg CsF (1.15 mmol, 2.0 eq), and 24 mg PdCl<sub>2</sub>(dppf)·DCM (29 μmol, 5 mol%) in 20 mL absolute, degassed 1,2-DME at 80°C. The aryl-aryl coupling was completed within 15 h. After flash column chromatography (70 g SiO<sub>2</sub>, 24x3 cm, cyclohexane/EtOAc = 4/6, R<sub>f</sub> = 0.30), product **14a** was isolated as a colourless solid.

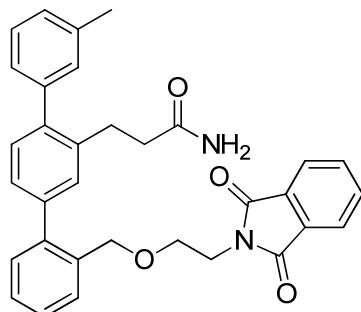
**Yield:** 237 mg (79%), colourless solid, C<sub>33</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub> [516.59 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.82 (bs, 3 H; H<sup>Phth</sup>, H<sup>Ar</sup>), 7.71 (bs, 3 H; H<sup>Phth</sup>, CH), 7.46 (d, <sup>3</sup>J(H,H) = 7.0 Hz, 1 H; H<sup>Ar</sup>), 7.35 (bs, 7 H; H<sup>Ar</sup>), 7.20-7.14 (m, 3 H; H<sup>Ar</sup>, CH), 6.71 (bs, 1 H; CONH<sub>2</sub>), 6.50 (bs, 1 H; CONH<sub>2</sub>), 4.44 (s, 2 H; CH<sub>2</sub>), 3.94-3.93 (m, 2 H; CH<sub>2</sub>), 3.77-3.76 (m, 2 H; CH<sub>2</sub>), 2.41 (s, 3 H; CH<sub>3</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 168.6 (C<sub>q</sub>; C=O<sup>Phth</sup>), 142.0 (C<sub>q</sub>; C<sup>Ar</sup>), 141.7 (C<sub>q</sub>; C<sup>Ar</sup>), 141.4 (C<sup>Ar</sup>), 139.9 (C<sub>q</sub>; C<sup>Ar</sup>), 139.8 (C<sub>q</sub>; C<sup>Ar</sup>), 138.1 (C<sub>q</sub>; C<sup>Ar</sup>), 134.7 (C<sub>q</sub>; C<sup>Ar</sup>), 134.2 (CH), 132.5 (C<sub>q</sub>; C<sup>Ar</sup>), 132.1 (C<sub>q</sub>; C<sup>Phth</sup>), 130.6 (C<sup>Ar</sup>), 130.5 (C<sup>Ar</sup>), 130.4 (C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 128.5 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 127.8 (C<sup>Ar</sup>), 127.7 (C<sup>Ar</sup>), 127.2 (C<sup>Ar</sup>), 123.5 (CH), 71.5 (CH<sub>2</sub>), 67.0 (CH<sub>2</sub>), 38.1 (CH<sub>2</sub>), 21.7 (CH<sub>3</sub>) ppm; <sup>\*</sup> **m.p.**<sup>exp.</sup> = 69-74°C; **HRMS** (DI-EI): calcd (m/z) for [M<sup>+</sup>]: 516.2049; found: 516.2054.

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\* No signal for the quaternary carbon atom of the amide function (C<sub>q</sub>; CONH<sub>2</sub>) was observed, should be visible at ~168.1 ppm. It might be overlapping with the signal of the quaternary carbon atom of the phthalimide moiety (C<sub>q</sub>; C=O<sup>Phth</sup>).

**2.4.7 3-(2''-((2-(1,3-Dioxoisindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (15a)**



**15a**

In a 50 mL two-neck round-bottom flask with two argon-inlets 193 mg (*E*-3-(2''-((2-(1,3-dioxoisindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)acrylamide (**14a**) (0.37 mmol, 1.0 eq) were dissolved in 60 mL MeOH and 19 mg (Pd(OH)<sub>2</sub>/C) (10 wt%) were added to the pale yellow solution.\* After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (3x), the reaction mixture was stirred overnight (~17 h) at room temperature. After filtering off the catalyst (5x3 cm SiO<sub>2</sub>, eluent: MeOH) and evaporating the solvent using a rotary evaporator, compound **15a** was isolated as a pale yellow solid.<sup>†</sup> The product was used in the next step without further purification.

**Yield:** 164 mg (85%), pale yellow solid, C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub> [518.60 g/mol].

**TLC:** R<sub>f</sub> = 0.23 (cyclohexane/EtOAc = 4/6); **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.82-7.81 (m, 2 H; H<sup>Phth</sup>), 7.71-7.70 (m, 2 H; H<sup>Phth</sup>), 7.48-7.45 (m, 1 H; H<sup>Ar</sup>), 7.35-7.27 (m, 5 H; H<sup>Ar</sup>, overlapping), 7.18 (bs, 5 H; H<sup>Ar</sup>), 5.68 (bs, 1 H; CONH<sub>2</sub>), 5.45 (bs, 1 H; CONH<sub>2</sub>), 4.48 (s, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.90 (t, <sup>3</sup>J(H,H) = 5.2 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.69 (t, <sup>3</sup>J(H,H) = 5.2 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.02 (bs, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.41 (bs, 5 H; CH<sub>2</sub><sup>Gln</sup>, CH<sub>3</sub><sup>Ala</sup>, overlapping) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 168.5 (C<sub>q</sub>; C=O<sup>Phth</sup>), 141.8 (C<sub>q</sub>; C<sup>Ar</sup>), 141.2 (C<sub>q</sub>; C<sup>Ar</sup>), 141.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.0 (C<sub>q</sub>; C<sup>Ar</sup>), 138.0 (C<sub>q</sub>; C<sup>Ar</sup>), 137.8 (C<sub>q</sub>; C<sup>Ar</sup>), 135.1 (C<sub>q</sub>; C<sup>Ar</sup>), 134.1 (C<sup>Phth</sup>), 132.2 (C<sub>q</sub>; C<sup>Phth</sup>), 130.2 (C<sup>Ar</sup>), 130.1 (C<sup>Ar</sup>), 130.1 (C<sup>Ar</sup>), 129.5 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.9 (C<sup>Ar</sup>), 127.5 (C<sup>Ar</sup>), 127.1 (C<sup>Ar</sup>), 126.3 (C<sup>Ar</sup>), 123.4 (C<sup>Phth</sup>), 71.0 (CH<sub>2</sub><sup>Lys</sup>), 67.0

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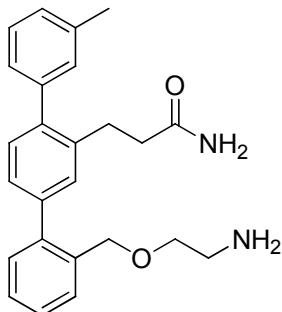
\* Palladium hydroxide on activated charcoal, moistened with water, 15-20% Pd basis (based on dry substance), Fluka 76063.

<sup>†</sup> The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

## Experimental Procedures and Analytical Data

(CH<sub>2</sub><sup>Lys</sup>), 37.8 (CH<sub>2</sub><sup>Lys</sup>), 37.2 (CH<sub>2</sub><sup>Gln</sup>), 29.0 (CH<sub>2</sub><sup>Gln</sup>), 21.7 (CH<sub>3</sub><sup>Ala</sup>) ppm; \* **m.p.**<sup>exp.</sup> = 58-57°C; **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 518.2206; found: 518.2217.

### **2.4.8 3-(2'-(2-Aminoethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (1a)**



**1a**

In a 25 mL round-bottom flask 46 mg 3-(2'-(2-(1,3-dioxoisooindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (**15a**) (89 µmol, 1.0 eq) were dissolved in 2 mL MeOH. After addition of 43 µL H<sub>2</sub>NNH<sub>2</sub>·H<sub>2</sub>O (44 mg, 0.88 mmol, 10.0 eq) the pale yellow solution was stirred until full conversion was monitored by TLC. The colourless suspension was concentrated under reduced pressure to dryness, and the crude product was purified by flash column chromatography (3.5 g SiO<sub>2</sub>, 9x1 cm, MeOH, R<sub>f</sub> = 0.10), to achieve compound **1a** as a colourless solid.

**Yield:** 28 mg (80%), colourless solid, C<sub>25</sub>H<sub>28</sub>N<sub>2</sub>O<sub>2</sub> [388.50 g/mol].

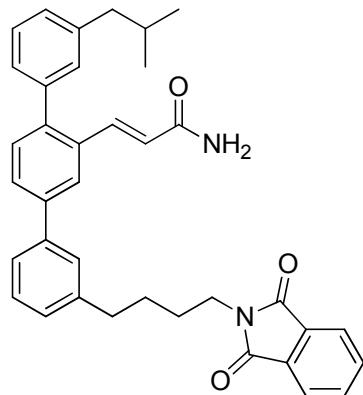
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.54-7.51 (m, 1 H; H<sup>Ar</sup>), 7.40-7.30 (m, 5 H; H<sup>Ar</sup>), 7.26 (bs, 2 H; H<sup>Ar</sup>), 7.18-7.15 (m, 3 H; H<sup>Ar</sup>), 6.08 (bs, 1 H; CONH<sub>2</sub>), 5.54 (bs, 1 H; CONH<sub>2</sub>), 4.47 (s, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.51 (t, <sup>3</sup>J(H,H) = 5.1 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.00 (t, <sup>3</sup>J(H,H) = 8.1 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.88 (t, <sup>3</sup>J(H,H) = 5.0 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.41 (s, 3 H; CH<sub>3</sub><sup>Ala</sup>), 2.37 (t, <sup>3</sup>J(H,H) = 8.1 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>, overlapping), 1.89 (bs, 2 H; NH<sub>2</sub>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 174.8 (C<sub>q</sub>; CONH<sub>2</sub>), 141.9 (C<sub>q</sub>; C<sup>Ar</sup>), 141.2 (C<sub>q</sub>; C<sup>Ar</sup>), 141.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.1 (C<sub>q</sub>; C<sup>Ar</sup>), 138.1 (C<sub>q</sub>; C<sup>Ar</sup>), 137.9 (C<sub>q</sub>; C<sup>Ar</sup>), 135.3 (C<sub>q</sub>; C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 130.1 (C<sup>Ar</sup>), 130.1 (C<sup>Ar</sup>), 130.0 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.2 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.6 (C<sup>Ar</sup>), 127.1 (C<sup>Ar</sup>), 126.3 (C<sup>Ar</sup>), 72.3 (CH<sub>2</sub><sup>Lys</sup>), 71.4 (CH<sub>2</sub><sup>Lys</sup>), 41.9 (CH<sub>2</sub><sup>Lys</sup>), 37.2 (CH<sub>2</sub><sup>Gln</sup>), 29.2 (CH<sub>2</sub><sup>Gln</sup>), 21.6 (CH<sub>3</sub><sup>Ala</sup>) ppm; **m.p.**<sup>exp.</sup> = 107-109°C; **HPLC** (Nucleodur, ESI<sup>+</sup>): t<sub>R</sub> = 12.58 min; *m/z*: 389

\* No signal for the quaternary carbon atom of the amide function (C<sub>q</sub>; CONH<sub>2</sub>) was observed, should be visible at ~168.1 ppm. It might be overlapping with the signal of the quaternary carbon atom of the phthalimide moiety (C<sub>q</sub>; C=O<sup>Phth</sup>).

## Experimental Procedures and Analytical Data

[ $M^+ + H$ ], 411 [ $M^+ + Na$ ];  $\lambda_{max} = 210, 222, 294$  nm; \* **HRMS** (DI-EI): calcd ( $m/z$ ) for [ $M^+$ ]: 388.2151; found: 388.2190.

### **2.4.9 (E)-3-(3''-(4-(1,3-Dioxoisoindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1''-terphenyl]-2'-yl)acrylamide (14b)**



**14b**

Compound **14b** was prepared according to procedure 2.4.2 from 100 mg (*E*-3-(4-bromo-3'-isobutyl-[1,1'-biphenyl]-2-yl)acrylamide (**26b**) (0.28 mmol, 1.0 eq), 124 mg 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**4b**) (0.31 mmol, 1.1 eq), 85 mg CsF (0.56 mmol, 2.0 eq), and 7 mg PdCl<sub>2</sub>(dpff)-DCM (9 μmol, 3 mol%) in 12 mL absolute, degassed 1,2-DME at 80°C. The aryl-aryl coupling was completed within 10 h. The crude product was purified by flash column chromatography (9 g SiO<sub>2</sub>, 18x1.5 cm, cyclohexane/EtOAc = 1/1, R<sub>f</sub> = 0.26), to achieve product **14b** as a colourless solid.

**Yield:** 132 mg (85%), colourless solid, C<sub>37</sub>H<sub>36</sub>N<sub>2</sub>O<sub>3</sub> [556.69 g/mol].

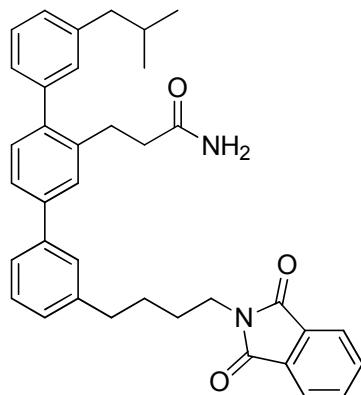
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.88-7.82 (m, 3 H; H<sup>Phth</sup>, CH), 7.75-7.62 (m, 4 H; H<sup>Phth</sup>, H<sup>Ar</sup>), 7.46-7.42 (m, 3 H; H<sup>Ar</sup>), 7.39-7.33 (m, 2 H; H<sup>Ar</sup>), 7.20-7.14 (m, 4 H; H<sup>Ar</sup>, overlapping), 6.57 (d, <sup>3</sup>J (H,H) = 15.7 Hz, 1 H; CH), 5.86 (bs, 1 H; CONH<sub>2</sub>), 5.79 (bs, 1 H; CONH<sub>2</sub>), 3.75 (t, <sup>3</sup>J (H,H) = 6.2 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.76 (bs, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.53 (d, <sup>3</sup>J (H,H) = 7.1 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 1.98-1.85 (m, 1 H; CH<sup>Leu</sup>), 1.78-1.76 (m, 4 H; CH<sub>2</sub><sup>Lys</sup>), 0.95 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub><sup>Leu</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT): δ = 168.7 (C<sub>q</sub>; C=O<sup>Phth</sup>), 168.0 (C<sub>q</sub>; CONH<sub>2</sub>), 142.7 (C<sub>q</sub>; C<sup>Ar</sup>), 142.1 (C<sub>q</sub>; C<sup>Ar</sup>), 142.0 (C<sub>q</sub>; C<sup>Ar</sup>), 141.6 (CH), 140.6 (C<sub>q</sub>; C<sup>Ar</sup>), 140.5 (C<sub>q</sub>; C<sup>Ar</sup>), 139.5 (C<sub>q</sub>; C<sup>Ar</sup>), 134.1 (C<sup>Phth</sup>), 133.2 (C<sub>q</sub>; C<sup>Ar</sup>), 132.2 (C<sub>q</sub>; C<sup>Phth</sup>), 131.2 (C<sup>Ar</sup>), 130.8

\* MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 1.0 mL/min 0.0-1.0 min: 30% MeOH const., 1.0-4.0 min: 37% MeOH lin. gradient, 4.0-10.0 min.: 37% MeOH const., 10.0-10.5 min: 70% MeOH lin. gradient, 10.5-15.0 min: 70% MeOH const., 15.0-15.5 min: 30% MeOH lin. gradient, 15.5-25.0 min: 30% MeOH const.

## Experimental Procedures and Analytical Data

(C<sup>Ar</sup>), 129.1 (C<sup>Ar</sup>), 128.6 (C<sup>Ar</sup>), 128.4 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.3 (C<sup>Ar</sup>), 127.2 (C<sup>Ar</sup>), 125.7 (C<sup>Ar</sup>), 124.8 (C<sup>Ar</sup>), 123.4 (C<sup>Phth</sup>), 121.1 (CH), 45.6 (CH<sub>2</sub><sup>Leu</sup>), 38.0 (CH<sub>2</sub><sup>Lys</sup>), 35.4 (CH<sub>2</sub><sup>Lys</sup>), 30.4 (CH<sup>Leu</sup>), 28.5 (CH<sub>2</sub><sup>Lys</sup>), 28.3 (CH<sub>2</sub><sup>Lys</sup>), 22.6 (CH<sub>3</sub><sup>Leu</sup>) ppm; **m.p.**<sup>exp.</sup> = 168-170°C; **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 566.2726; found: 556.2737.

### **2.4.10 3-(3''-(4-(1,3-Dioxoisoindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (15b)**



**15b**

In a 50 mL two-neck round-bottom flask with two argon-inlets 87 mg (*E*-3-(3''-(4-(1,3-dioxoisoindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14b**) (0.16 mmol, 1.0 eq) were dissolved in a mixture of 32 mL MeOH/EtOH (11/5) and 9 mg Pd(OH)<sub>2</sub>/C (10 wt%) were added to this colourless solution.\* After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (3x), the reaction mixture was stirred for 23 h at room temperature. After the catalyst was filtered off (3x3 cm SiO<sub>2</sub>, eluent: MeOH), the solvent was removed under reduced pressure, and product **15b** was isolated as a colourless solid.<sup>†</sup> The product was used in the next step without further purification.

**Yield:** 81 mg (91%), colourless solid, C<sub>37</sub>H<sub>38</sub>N<sub>2</sub>O<sub>3</sub> [558.71 g/mol].

**TLC:** R<sub>f</sub> = 0.43 (cyclohexane/EtOAc = 6/4); **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.85-7.81 (m, 2 H; H<sup>Phth</sup>), 7.73-7.69 (m, 2 H; H<sup>Phth</sup>), 7.54-7.42 (m, 4 H; H<sup>Ar</sup>), 7.37-7.27 (m, 3 H; H<sup>Ar</sup>), 7.18-7.14 (m, 4 H; H<sup>Ar</sup>), 5.36 (bs, 1 H; CONH<sub>2</sub>), 5.20 (bs, 1 H; CONH<sub>2</sub>), 3.74 (t, <sup>3</sup>J(H,H) = 6.5 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.05 (t, <sup>3</sup>J(H,H) = 6.5 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.74 (t, <sup>3</sup>J(H,H) = 6.8 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.53 (d, <sup>3</sup>J(H,H) = 7.1 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 2.36 (t, <sup>3</sup>J(H,H) = 6.5 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 1.97-1.84 (m, 1 H; CH<sup>Leu</sup>), 1.76-1.74 (m, 4 H; CH<sub>2</sub><sup>Lys</sup>), 0.93 (d, <sup>3</sup>J(H,H) = 6.6 Hz, 6 H;

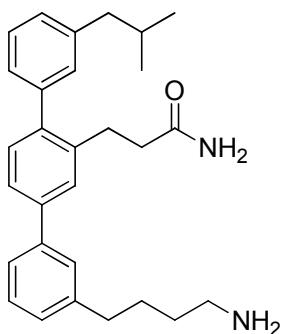
\* Palladium hydroxide on activated charcoal, moistened with water, 15-20% Pd basis (based on dry substance), Fluka 76063.

<sup>†</sup> The catalyst was filtered off using a pad of Celite® or SiO<sub>2</sub> under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with H<sub>2</sub>O and stored in a glass bottle covered with water.

## Experimental Procedures and Analytical Data

$\text{CH}_3^{\text{Leu}}$ ) ppm;  **$^{13}\text{C}$  NMR** (76 MHz,  $\text{CDCl}_3$ , APT):  $\delta = 174.6$  ( $\text{C}_\text{q}$ ;  $\text{CONH}_2$ ), 168.6 ( $\text{C}_\text{q}$ ;  $\text{C}=\text{O}^{\text{Phth}}$ ), 142.7 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.9 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.1 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.1 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 140.9 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 140.7 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 138.5 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 134.0 ( $\text{C}^{\text{Phth}}$ ), 132.3 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Phth}}$ ), 130.8 ( $\text{C}^{\text{Ar}}$ ), 130.1 ( $\text{C}^{\text{Ar}}$ ), 128.9 ( $\text{C}^{\text{Ar}}$ ), 128.2 ( $\text{C}^{\text{Ar}}$ ), 128.1 ( $\text{C}^{\text{Ar}}$ ), 127.7 ( $\text{C}^{\text{Ar}}$ ), 127.4 ( $\text{C}^{\text{Ar}}$ ), 126.6 ( $\text{C}^{\text{Ar}}$ ), 125.2 ( $\text{C}^{\text{Ar}}$ ), 124.8 ( $\text{C}^{\text{Ar}}$ ), 123.3 ( $\text{C}^{\text{Phth}}$ ), 45.6 ( $\text{CH}_2^{\text{Leu}}$ ), 37.9 ( $\text{CH}_2^{\text{Gln}}$ ), 37.1 ( $\text{CH}_2^{\text{Lys}}$ ), 35.6 ( $\text{CH}_2^{\text{Gln}}$ ), 30.5 ( $\text{CH}^{\text{Leu}}$ ), 29.3 ( $\text{CH}_2^{\text{Lys}}$ ), 28.8 ( $\text{CH}_2^{\text{Lys}}$ ), 28.3 ( $\text{CH}_2^{\text{Lys}}$ ), 22.5 ( $\text{CH}_3^{\text{Leu}}$ ) ppm; **m.p.**<sup>exp.</sup> = 118-120°C; **HRMS** (DI-EI): calcd (*m/z*) for  $[M^+]$ : 558.2883; found: 558.2883.

### **2.4.11 3-(3''-(4-Aminobutyl)-3-isobutyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (1b)**



**1b**

In a 25 mL round-bottom flask 53 mg 3-(3''-(4-(1,3-dioxoisindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (**15b**) (95 µmol, 1.0 eq) were dissolved in 5 mL MeOH. After addition of 46 µL  $\text{H}_2\text{NNH}_2\text{-H}_2\text{O}$  (47 mg, 0.95 mmol, 10.0 eq) the colourless solution was stirred until full conversion was detected by TLC. The colourless solution was stirred for 13 h. Because of slow conversion, 46 µL  $\text{H}_2\text{NNH}_2\text{-H}_2\text{O}$  (47 mg, 0.95 mmol, 10.0 eq) were additionally added, and the solution was further stirred for 3 days. Afterwards, the colourless suspension was concentrated under reduced pressure to dryness. Purification by flash column chromatography (5.4 g  $\text{SiO}_2$ , 14x1 cm, MeOH,  $R_f = 0.09$ ) afforded compound **1b** as a pale yellow oil.

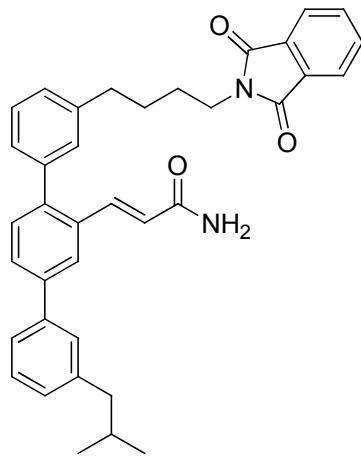
**Yield:** 40 mg (98%), pale yellow oil,  $\text{C}_{29}\text{H}_{36}\text{N}_2\text{O}$  [428.61 g/mol].

**$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.49$  (bs, 1 H;  $\text{H}^{\text{Ar}}$ ), 7.46-7.39 (m, 3 H;  $\text{H}^{\text{Ar}}$ ), 7.34-7.22 (m, 3 H;  $\text{H}^{\text{Ar}}$ , overlapping), 7.14-7.10 (m, 4 H;  $\text{H}^{\text{Ar}}$ ), 5.63 (bs, 1 H;  $\text{CONH}_2$ ), 5.29 (bs, 1 H;  $\text{CONH}_2$ ), 2.99 (t,  $^3J(\text{H},\text{H}) = 7.9$  Hz, 2 H;  $\text{CH}_2^{\text{Gln}}$ ), 2.72-2.63 (m, 4 H;  $\text{CH}_2^{\text{Lys}}$ ), 2.49 (d,  $^3J(\text{H},\text{H}) = 7.1$  Hz, 2 H;  $\text{CH}_2^{\text{Leu}}$ ), 2.28 (t,  $^3J(\text{H},\text{H}) = 7.9$  Hz, 2 H;  $\text{CH}_2^{\text{Gln}}$ ), 2.20 (bs, 2 H;  $\text{NH}_2$ , overlapping), 1.93-1.80 (m, 1 H;  $\text{CH}^{\text{Leu}}$ ), 1.72-1.62 (m, 2 H;  $\text{CH}_2^{\text{Lys}}$ ), 1.54-1.45 (m, 2 H;  $\text{CH}_2^{\text{Lys}}$ ), 0.89 (d,  $^3J(\text{H},\text{H}) = 6.6$  Hz, 6 H;  $\text{CH}_3^{\text{Leu}}$ ) ppm;  **$^{13}\text{C}$  NMR** (76 MHz,  $\text{CDCl}_3$ , APT):  $\delta = 174.8$  ( $\text{C}_\text{q}$ ;  $\text{CONH}_2$ ), 143.0 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.9 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.1 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.0 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 140.9

## Experimental Procedures and Analytical Data

(C<sub>q</sub>; C<sup>Ar</sup>), 140.7 (C<sub>q</sub>; C<sup>Ar</sup>), 138.6 (C<sub>q</sub>; C<sup>Ar</sup>), 130.8 (C<sup>Ar</sup>), 130.1 (C<sup>Ar</sup>), 128.9 (C<sup>Ar</sup>), 128.2 (C<sup>Ar</sup>), 128.2 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.6 (C<sup>Ar</sup>), 127.3 (C<sup>Ar</sup>), 126.5 (C<sup>Ar</sup>), 125.1 (C<sup>Ar</sup>), 124.7 (C<sup>Ar</sup>), 45.5 (CH<sub>2</sub><sup>Leu</sup>), 42.0 (CH<sub>2</sub><sup>Lys</sup>), 37.1 (CH<sub>2</sub><sup>Gln</sup>), 35.9 (CH<sub>2</sub><sup>Lys</sup>), 33.0 (CH<sub>2</sub><sup>Lys</sup>), 30.4 (CH<sup>Leu</sup>), 29.3 (CH<sub>2</sub><sup>Gln</sup>), 28.8 (CH<sub>2</sub><sup>Lys</sup>), 22.5 (CH<sub>3</sub><sup>Leu</sup>) ppm; **HPLC** (Nucleodur, ESI<sup>+</sup>): t<sub>R</sub> = 15.28 min; *m/z*: 429 [M<sup>+</sup>+H], 451 [M<sup>+</sup>+Na]; λ<sub>max</sub> = 210, 230, 294 nm; <sup>\*</sup> **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 428.2828; found: 428.2786.

### **2.4.12 (E)-3-(3-(4-(1,3-Dioxoisooindolin-2-yl)butyl)-3''-isobutyl-[1,1':4',1''-terphenyl]-2'-yl)acrylamide (14c)**



**14c**

Compound **14c** was prepared according to procedure 2.4.2 from 88 mg (*E*-3-(4-bromo-3'-(4-(1,3-dioxoisooindolin-2-yl)butyl)-[1,1'-biphenyl]-2-yl)acrylamide (**26c**) (0.17 mmol, 1.0 eq), 55 mg 2-(3-isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**) (0.21 mmol, 1.2 eq), 54 mg CsF (0.36 mmol, 2.0 eq), and 4 mg PdCl<sub>2</sub>(dpff)-DCM (5 μmol, 3 mol%) in 10 mL absolute, degassed 1,2-DME at 80°C. The aryl-aryl coupling was completed after 15 h, and purification by flash column chromatography (9.5 g SiO<sub>2</sub>, 17x1.5 cm, cyclohexane/EtOAc = 1/1, R<sub>f</sub> = 0.25) afforded product **14c** as a pale yellow solid.

**Yield:** 90 mg (95%), pale yellow solid, C<sub>37</sub>H<sub>36</sub>N<sub>2</sub>O<sub>3</sub> [556.69 g/mol].

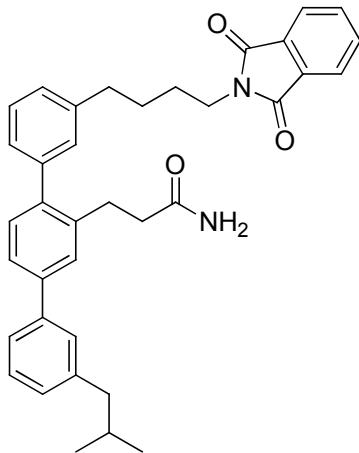
**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.84-7.81 (m, 3 H; H<sup>Phth</sup>, CH), 7.70-7.62 (m, 4 H; H<sup>Phth</sup>, H<sup>Ar</sup>), 7.47-7.30 (m, 5 H; H<sup>Ar</sup>), 7.19-7.15 (m, 4 H; H<sup>Ar</sup>), 6.44 (d, <sup>3</sup>J(H,H) = 15.8 Hz, 1 H; CH), 5.71 (bs, 2 H; CONH<sub>2</sub>), 3.72 (t, <sup>3</sup>J(H,H) = 6.2 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.71 (t, <sup>3</sup>J(H,H) = 6.4 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.57 (d, <sup>3</sup>J(H,H) = 7.1 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 2.01-1.90 (m, 1 H; CH<sup>Leu</sup>), 1.74-1.72

\* MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 1.0 mL/min 0.0-1.0 min: 30% MeOH const., 1.0-4.0 min: 37% MeOH lin. gradient, 4.0-10.0 min.: 37% MeOH const., 10.0-10.5 min: 70% MeOH lin. gradient, 10.5-15.0 min: 70% MeOH const., 15.0-15.5 min: 30% MeOH lin. gradient, 15.5-25.0 min: 30% MeOH const.

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(m, 4 H;  $\text{CH}_2^{\text{Lys}}$ ), 0.95 (d,  ${}^3J(\text{H},\text{H}) = 6.6$  Hz, 6 H;  $\text{CH}_3^{\text{Leu}}$ ) ppm;  **$^{13}\text{C}$  NMR** (76 MHz,  $\text{CDCl}_3$ , APT):  $\delta = 168.7$  ( $\text{C}_\text{q}$ ;  $\text{C}=\text{O}^{\text{Phth}}$ ), 168.1 ( $\text{C}_\text{q}$ ;  $\text{CONH}_2$ ), 142.5 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 142.2 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.7 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 141.5 (CH), 140.9 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 140.2 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 139.8 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 134.0 ( $\text{C}^{\text{Phth}}$ ), 133.3 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Ar}}$ ), 132.3 ( $\text{C}_\text{q}$ ;  $\text{C}^{\text{Phth}}$ ), 131.1 ( $\text{C}^{\text{Ar}}$ ), 130.1 ( $\text{C}^{\text{Ar}}$ ), 128.8 ( $\text{C}^{\text{Ar}}$ ), 128.6 ( $\text{C}^{\text{Ar}}$ ), 128.5 ( $\text{C}^{\text{Ar}}$ ), 128.5 ( $\text{C}^{\text{Ar}}$ ), 128.1 ( $\text{C}^{\text{Ar}}$ ), 127.9 ( $\text{C}^{\text{Ar}}$ ), 127.5 ( $\text{C}^{\text{Ar}}$ ), 125.8 ( $\text{C}^{\text{Ar}}$ ), 124.6 ( $\text{C}^{\text{Ar}}$ ), 123.3 ( $\text{C}^{\text{Phth}}$ ), 121.7 (CH), 45.7 ( $\text{CH}_2^{\text{Leu}}$ ), 38.0 ( $\text{CH}_2^{\text{Lys}}$ ), 35.5 ( $\text{CH}_2^{\text{Lys}}$ ), 30.4 ( $\text{CH}^{\text{Leu}}$ ), 28.8 ( $\text{CH}_2^{\text{Lys}}$ ), 28.2 ( $\text{CH}_2^{\text{Lys}}$ ), 22.6 ( $\text{CH}_3^{\text{Leu}}$ ) ppm; **m.p.**<sup>exp.</sup> = 63-67°C; **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 506.2726; found: 556.2740.

### **2.4.13 3-(3-(4-(1,3-Dioxoisooindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)-propanamide (15c)**



**15c**

In a 50 mL two-neck round-bottom flask with two argon-inlets 75 mg (*E*)-3-(3-(4-(1,3-dioxoisooindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14c**) (0.13 mmol, 1.0 eq) were dissolved in 10 mL MeOH and 8 mg  $\text{Pd}(\text{OH})_2/\text{C}$  (10 wt%) were added to the pale yellow solution.\* After ensuring hydrogen atmosphere by evacuating and back-flushing with hydrogen gas (3x), the reaction mixture was stirred for 1.5 d at room temperature. Due to slow conversion additional 8 mg  $\text{Pd}(\text{OH})_2/\text{C}$  (10 wt%) were added, and after further 2 d of stirring at room temperature, the catalyst was filtered off (3x3 cm  $\text{SiO}_2$ , eluent: MeOH). The solvent was removed under reduced pressure, and compound **15c** was isolated as a pale yellow solid.<sup>†</sup> The product was used in the next step without further purification.

**Yield:** 70 mg (96%), pale yellow solid,  $\text{C}_{37}\text{H}_{38}\text{N}_2\text{O}_3$  [558.71 g/mol].

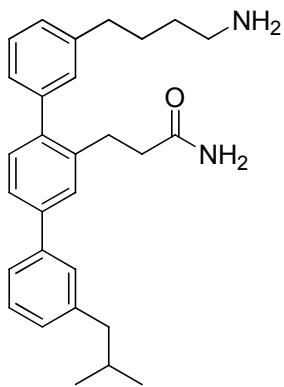
\* Palladium hydroxide on activated charcoal, moistened with water, 15-20% Pd basis (based on dry substance), Fluka 76063.

<sup>†</sup> The catalyst was filtered off using a pad of Celite® or  $\text{SiO}_2$  under inert conditions and eluted with MeOH. The hydrogenation catalyst was washed with  $\text{H}_2\text{O}$  and stored in a glass bottle covered with water.

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**TLC:**  $R_f = 0.33$  (cyclohexane/EtOAc = 4/6); **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.83\text{-}7.79$  (m, 2 H; H<sup>Phth</sup>), 7.72-7.68 (m, 2 H; H<sup>Phth</sup>), 7.55-7.28 (m, 7 H; H<sup>Ar</sup>), 7.18-7.13 (m, 4 H; H<sup>Ar</sup>), 5.46 (bs, 1 H; CONH<sub>2</sub>), 5.36 (bs, 1 H; CONH<sub>2</sub>), 3.72 (t, <sup>3</sup>J(H,H) = 6.2 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 3.04 (t, <sup>3</sup>J(H,H) = 8.0 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.72 (t, <sup>3</sup>J(H,H) = 6.3 Hz, 2 H; CH<sub>2</sub><sup>Lys</sup>), 2.55 (d, <sup>3</sup>J(H,H) = 7.2 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 2.34 (t, <sup>3</sup>J(H,H) = 8.0 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.00-1.86 (m, 1 H; CH<sup>Leu</sup>), 1.73-1.71 (m, 4 H; CH<sub>2</sub><sup>Lys</sup>), 0.95 (d, <sup>3</sup>J(H,H) = 6.6 Hz, 6 H; CH<sub>3</sub><sup>Leu</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT):  $\delta = 174.7$  (C<sub>q</sub>; CONH<sub>2</sub>), 168.7 (C<sub>q</sub>; C=O<sup>Phth</sup>), 142.4 (C<sub>q</sub>; C<sup>Ar</sup>), 142.2 (C<sub>q</sub>; C<sup>Ar</sup>), 141.4 (C<sub>q</sub>; C<sup>Ar</sup>), 140.9 (C<sub>q</sub>; C<sup>Ar</sup>), 140.8 (C<sub>q</sub>; C<sup>Ar</sup>), 140.6 (C<sub>q</sub>; C<sup>Ar</sup>), 138.6 (C<sub>q</sub>; C<sup>Ar</sup>), 134.1 (C<sup>Phth</sup>), 132.2 (C<sub>q</sub>; C<sup>Phth</sup>), 130.8 (C<sup>Ar</sup>), 129.3 (C<sup>Ar</sup>), 128.7 (C<sup>Ar</sup>), 128.5 (C<sup>Ar</sup>), 128.4 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.4 (C<sup>Ar</sup>), 126.8 (C<sup>Ar</sup>), 125.2 (C<sup>Ar</sup>), 124.6 (C<sup>Ar</sup>), 123.4 (C<sup>Phth</sup>), 45.7 (CH<sub>2</sub><sup>Leu</sup>), 38.0 (CH<sub>2</sub><sup>Lys</sup>), 37.1 (CH<sub>2</sub><sup>Gln</sup>), 35.4 (CH<sub>2</sub><sup>Lys</sup>), 30.4 (CH<sup>Leu</sup>), 29.4 (CH<sub>2</sub><sup>Gln</sup>), 28.7 (CH<sub>2</sub><sup>Lys</sup>), 28.3 (CH<sub>2</sub><sup>Lys</sup>), 22.6 (CH<sub>3</sub><sup>Leu</sup>) ppm; **m.p.**<sup>exp.</sup> = 48-50°C; **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 558.2883; found: 558.2925.

### 2.4.14 3-(3-(4-Aminobutyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (1c)



**1c**

In a 25 mL round-bottom flask 58 mg 3-(3-(4-(1,3-dioxoisindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**15c**) (0.10 mmol, 1.0 eq) were dissolved in 4 mL MeOH. After adding 50  $\mu$ L H<sub>2</sub>NNH<sub>2</sub>·H<sub>2</sub>O (52 mg, 1.04 mmol, 10.0 eq) the colourless solution was stirred for 3 d until full conversion was monitored by TLC, followed by evaporating the solvent under reduced pressure. Flash column chromatography (5.5 g SiO<sub>2</sub>, 15x1 cm, MeOH, R<sub>f</sub> = 0.08) afforded compound **1c** as a pale yellow oil.

**Yield:** 34 mg (79%), pale yellow oil, C<sub>29</sub>H<sub>36</sub>N<sub>2</sub>O [428.61 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta = 7.50$  (bs, 1 H; H<sup>Ar</sup>), 7.47-7.22 (m, 6 H; H<sup>Ar</sup>), 7.15-7.10 (m, 4 H; H<sup>Ar</sup>), 5.77 (bs, 1 H; CONH<sub>2</sub>), 5.63 (bs, 1 H; CONH<sub>2</sub>), 2.99 (t, <sup>3</sup>J(H,H) = 8.1 Hz, 2 H; CH<sub>2</sub><sup>Gln</sup>), 2.68-2.63 (m, 4 H; CH<sub>2</sub><sup>Lys</sup>), 2.52 (d, <sup>3</sup>J(H,H) = 7.2 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 2.28 (t,

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$^3J$  (H,H) = 8.1 Hz, 2 H;  $\text{CH}_2^{\text{Gln}}$ ), 2.06 (bs, 2 H; NH<sub>2</sub>), 1.96-1.81 (m, 1 H; CH<sup>Leu</sup>), 1.71-1.61 (m, 2 H; CH<sub>2</sub><sup>Lys</sup>), 1.49-1.39 (m, 2 H; CH<sub>2</sub><sup>Lys</sup>), 0.91 (d,  $^3J$  (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub><sup>Leu</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>, APT):  $\delta$  = 174.8 (C<sub>q</sub>; CONH<sub>2</sub>), 142.4 (C<sub>q</sub>; C<sup>Ar</sup>), 142.4 (C<sub>q</sub>; C<sup>Ar</sup>), 141.3 (C<sub>q</sub>; C<sup>Ar</sup>), 141.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.8 (C<sub>q</sub>; C<sup>Ar</sup>), 140.6 (C<sub>q</sub>; C<sup>Ar</sup>), 138.7 (C<sub>q</sub>; C<sup>Ar</sup>), 130.7 (C<sup>Ar</sup>), 129.4 (C<sup>Ar</sup>), 128.7 (C<sup>Ar</sup>), 128.5 (C<sup>Ar</sup>), 128.3 (C<sup>Ar</sup>), 128.2 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.4 (C<sup>Ar</sup>), 126.7 (C<sup>Ar</sup>), 125.2 (C<sup>Ar</sup>), 124.6 (C<sup>Ar</sup>), 45.7 (CH<sub>2</sub><sup>Leu</sup>), 41.9 (CH<sub>2</sub><sup>Lys</sup>), 37.0 (CH<sub>2</sub><sup>Gln</sup>), 35.6 (CH<sub>2</sub><sup>Lys</sup>), 32.5 (CH<sub>2</sub><sup>Lys</sup>), 30.4 (CH<sup>Leu</sup>), 29.3 (CH<sub>2</sub><sup>Gln</sup>), 28.6 (CH<sub>2</sub><sup>Lys</sup>), 22.6 (CH<sub>3</sub><sup>Leu</sup>) ppm; **HPLC** (Nucleodur, ESI<sup>+</sup>): t<sub>R</sub> = 16.60 min; *m/z*: 429 [M<sup>+</sup>+H], 451 [M<sup>+</sup>+Na];  $\lambda_{\text{max}} = 210, 230, 294$  nm; <sup>\*</sup> **HRMS** (DI-EI): calcd (*m/z*) for [M<sup>+</sup>]: 428.2828; found: 428.2852.

## 2.5 Synthesis of Terphenyls using the Triflate Approach

### 2.5.1 Representative procedure for the synthesis of teraryls by consecutive double Suzuki-Coupling

A flame dried two-neck round-bottom flask with argon-inlet was charged with 1.0 eq of the corresponding boronic acid derivative, 2.0 eq CsF<sup>†</sup>, and 5 mol% PdCl<sub>2</sub>(dpff)-DCM. After drying in vacuo, a solution of 1.0 eq trifluoromethanesulfonate **3** in absolute, degassed 1,2-DME was added. After additional degassing, the reaction mixture was stirred at 80°C until full conversion was detected by TLC. The typically brown suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluents are denoted) and the filtrate was concentrated to dryness using a rotary evaporator.

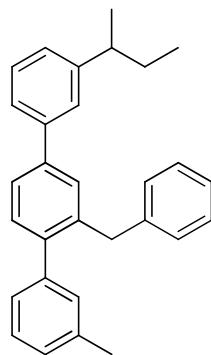
Another flame dried two-neck round-bottom flask with argon-inlet was charged with 1.0-1.2 eq of the second boronic acid pinacol ester **4**, 2.0-3.0 eq caesium carbonate (Cs<sub>2</sub>CO<sub>3</sub>)<sup>†</sup>, and 5 mol% PdCl<sub>2</sub>(dpff)-DCM. After drying in vacuo, a solution of the previously prepared crude intermediate (4-(pyridin-3-yl)phenyl trifluoromethanesulfonate derivative) in 5 mL absolute, degassed 1,2-DME were added. After additional degassing, the reaction mixture was stirred at 80°C overnight. The typically black suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluent: 100 mL MeOH) and after concentrating to dryness, the crude product was purified by flash column chromatography. To obtain highly pure substrate, the product was purified by semi-preparative HPLC.

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<sup>\*</sup> MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 1.0 mL/min 0.0-1.0 min: 30% MeOH const., 1.0-4.0 min: 37% MeOH lin. gradient, 4.0-10.0 min.: 37% MeOH const., 10.0-10.5 min: 70% MeOH lin. gradient, 10.5-15.0 min: 70% MeOH const., 15.0-15.5 min: 30% MeOH lin. gradient, 15.5-25.0 min: 30% MeOH const.

<sup>†</sup> CsF and Cs<sub>2</sub>CO<sub>3</sub> were dried overnight at 60°C in vacuo prior to use.

### 2.5.2 2'-Benzyl-3''-(*sec*-butyl)-3-methyl-1,1':4',1''-terphenyl (**1d**)



**1d**

Compound **1d** was prepared according to procedure 2.5.1 from 81 mg (3-(*sec*-butyl)phenyl)boronic acid (**25b**) (452 µmol, 1.0 eq), 137 mg CsF (905 µmol, 2.0 eq) and 19 mg PdCl<sub>2</sub>(dppf)·DCM (23 µmol, 5 mol%) in 2.00 mL 1,2-DME and 200 mg 2-benzyl-4-iodophenyl trifluoromethanesulfonate (**3e**) (452 µmol, 1.0 eq) in 1.00 mL 1,2-DME. After 2 h the brown suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluent: 100 mL MeOH), and the filtrate was concentrated to dryness (203 mg, quant., crude).

The second Suzuki-coupling was performed with 74 mg *m*-tolylboronic acid (452 µmol, 1.0 eq), 295 mg Cs<sub>2</sub>CO<sub>3</sub> (905 µmol, 2.0 eq) and 18.5 mg PdCl<sub>2</sub>(dppf)·DCM (23 µmol, 5 mol%) in 1.5 mL 1,2-DME and 203 mg of the previously prepared crude intermediate (452 µmol, 1.0 eq) in 1.5 mL absolute, degassed 1,2-DME. A quantitative conversion was confirmed by TLC (cyclohexane, R<sub>f</sub> = 0.18) after stirring at 80°C for 24 h, and the black suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluent: 100 mL MeOH). The crude product was purified by flash column chromatography (20 g SiO<sub>2</sub>, 16x2 cm, cyclohexane, R<sub>f</sub> = 0.18), to achieve compound **1d** as a pale yellow oil (149 mg, 84%).<sup>\*</sup> After preparative HPLC (Nucleosil)<sup>†</sup> product **1d** was isolated as a colourless, highly viscous oil.

**Yield:** 104 mg (59%), colourless oil, C<sub>30</sub>H<sub>30</sub> [390.56 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.57-7.06 (m, 16 H; H<sup>Ar</sup>, H<sup>Phe</sup>), 4.07 (s, 2 H; CH<sub>2</sub><sup>Phe</sup>), 2.70 (h, <sup>3</sup>J(H,H) = 7.0 Hz, 1 H; CH<sup>Ile</sup>), 2.39 (s, 3 H; CH<sub>3</sub><sup>Ala</sup>), 1.73-1.64 (m, 2 H; CH<sub>2</sub><sup>Ile</sup>), 1.32 (d, <sup>3</sup>J(H,H) = 6.9 Hz, 3 H; CH<sub>3</sub><sup>Ile</sup>), 0.90 (t, <sup>3</sup>J(H,H) = 7.4 Hz, 3 H; CH<sub>3</sub><sup>Ile</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 148.3 (C<sub>q</sub>; C<sup>Ar</sup>), 141.6 (C<sub>q</sub>; C<sup>Ar</sup>), 141.5 (C<sub>q</sub>; C<sup>Ar</sup>), 141.4 (C<sub>q</sub>; C<sup>Ar</sup>), 141.0 (C<sub>q</sub>; C<sup>Ar</sup>), 140.7 (C<sub>q</sub>; C<sup>Ar</sup>), 138.6 (C<sub>q</sub>; C<sup>Ar</sup>), 137.7 (C<sub>q</sub>; C<sup>Phe</sup>), 130.7 (C<sup>Ar</sup>), 130.3 (C<sup>Ar</sup>), 129.3

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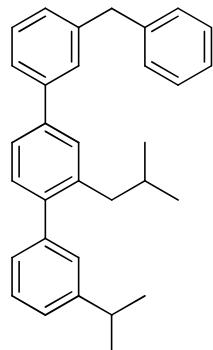
<sup>\*</sup> Analytical HPLC indicated a product purity ≥ 85%.

<sup>†</sup> MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 16 mL/min: 0.0 min: 79% MeOH const., 0.0-7.0 min: 82% MeOH lin. gradient, 7.0-15.0 min: 82% MeOH const., 15.0-15.5 min: 100% MeOH lin. gradient, 15.5-20.0 min: 100% MeOH const., 20.0-20.5 min: 79% MeOH lin. gradient, 20.5-25.0 min: 79% MeOH const.

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(C<sup>Ar</sup>), 129.0 (C<sup>Phe</sup>), 128.8 (C<sup>Ar</sup>), 128.4 (C<sup>Phe</sup>), 128.1 (C<sup>Ar</sup>), 127.8 (C<sup>Ar</sup>), 126.5 (C<sup>Phe</sup>), 126.2 (C<sup>Ar</sup>), 126.1 (C<sup>Ar</sup>), 125.9 (C<sup>Ar</sup>), 125.1 (C<sup>Ar</sup>), 124.8 (C<sup>Ar</sup>), 41.9 (CH<sup>Ile</sup>), 39.4 (CH<sub>2</sub><sup>Phe</sup>), 31.3 (CH<sub>2</sub><sup>Ile</sup>), 22.0 (CH<sub>3</sub><sup>Ile</sup>), 21.6 (CH<sub>3</sub><sup>Ala</sup>), 12.5 (CH<sub>3</sub><sup>Ile</sup>) ppm; **GC-MS** (EI, 70 eV; MP\_100\_L): t<sub>R</sub> = 9.82 min; m/z (%): 390 (100) [M<sup>+</sup>], 361 (53) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>]; **HPLC** (Nucleosil, ESI<sup>+</sup>): t<sub>R</sub> = 7.15 min; λ<sub>max</sub> = 234, 252, 281 nm; <sup>\*</sup> **HRMS** (DI-EI): calcd for [M<sup>+</sup>]: 390.2347; found: 390.2346.

### 2.5.3 3"-Benzyl-2'-isobutyl-3-isopropyl-1,1':4',1"-terphenyl (**1e**)



**1e**

Compound **1e** was prepared according to procedure 2.5.1 from 104 mg (3-benzylphenyl)-boronic acid (**25a**) (490 µmol, 1.0 eq), 149 mg CsF (980 µmol, 2.0 eq) and 20 mg PdCl<sub>2</sub>(dppf)·DCM (25 µmol, 5 mol%) in 2.0 mL 1,2-DME and 200 mg 4-iodo-2-isobutyl-phenyl trifluoromethanesulfonate (**3c**) (490 µmol, 1.0 eq) in 1.0 mL 1,2-DME. After 2 h the brown suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluent: 100 mL MeOH), and the filtrate was concentrated to dryness (222 mg, 101%, crude).

The second Suzuki-coupling was performed with 145 mg 2-(3-isopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4e**) (589 µmol, 1.2 eq), 320 mg Cs<sub>2</sub>CO<sub>3</sub> (980 µmol, 2.0 eq) and 20.4 mg PdCl<sub>2</sub>(dppf)·DCM (25 µmol, 5 mol%) in 1.5 mL 1,2-DME and 220 mg of the previously prepared crude intermediate (490 µmol, 1.0 eq) in 1.5 mL absolute, degassed 1,2-DME. A quantitative conversion was confirmed by TLC (cyclohexane, R<sub>f</sub> = 0.15) after stirring at 80°C for 24 h, and the black suspension was filtered through a pad of SiO<sub>2</sub> (3x2 cm, eluent: 100 mL MeOH). The crude product was purified by flash column chromatography (20 g SiO<sub>2</sub>, 16x2 cm, cyclohexane, R<sub>f</sub> = 0.15), to achieve compound **1e** as a pale yellow oil

<sup>\*</sup> MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 0.7 mL/min: 0.0 min: 74% MeOH const., 0.0-8.0 min: 77% MeOH lin. gradient, 8.0-12.0 min.: 77% MeOH const., 12.0-12.5 min: 100% MeOH lin. gradient, 12.5-15.0 min: 100% MeOH const., 15.0-15.5 min: 74% MeOH lin. gradient, 15.5-17.0 min: 74% MeOH const.

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(173 mg, 85%).<sup>\*</sup> After preparative HPLC (Nucleosil)<sup>†</sup> product **1e** was isolated as a colourless, highly viscous oil.

**Yield:** 110 mg (54%), colourless oil, C<sub>32</sub>H<sub>34</sub> [418.61 g/mol].

**<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ = 7.50-7.12 (m, 16 H; H<sup>Ar</sup>, H<sup>Phe</sup>), 4.07 (s, 2 H; CH<sub>2</sub><sup>Phe</sup>), 2.96 (sept, <sup>3</sup>J (H,H) = 6.8 Hz, 1 H; CH<sup>Val</sup>), 2.56 (d, <sup>3</sup>J (H,H) = 7.2 Hz, 2 H; CH<sub>2</sub><sup>Leu</sup>), 1.82-1.64 (m, 1 H; CH<sup>Leu</sup>), 1.29 (d, <sup>3</sup>J (H,H) = 6.9 Hz, 6 H; CH<sub>3</sub><sup>Val</sup>), 0.77 (d, <sup>3</sup>J (H,H) = 6.6 Hz, 6 H; CH<sub>3</sub><sup>Leu</sup>) ppm; **<sup>13</sup>C NMR** (76 MHz, CDCl<sub>3</sub>): δ = 148.6 (C<sub>q</sub>; C<sup>Ar</sup>), 141.9 (C<sub>q</sub>; C<sup>Ar</sup>), 141.8 (C<sub>q</sub>; C<sup>Ar</sup>), 141.7 (C<sub>q</sub>; C<sup>Ar</sup>), 141.5 (C<sub>q</sub>; C<sup>Ar</sup>), 141.2 (C<sub>q</sub>; C<sup>Ar</sup>), 140.0 (C<sub>q</sub>; C<sup>Phe</sup>), 139.7 (C<sub>q</sub>; C<sup>Ar</sup>), 130.6 (C<sup>Ar</sup>), 129.1 (C<sup>Phe</sup>), 129.0 (C<sup>Ar</sup>), 128.9 (C<sup>Ar</sup>), 128.6 (C<sup>Phe</sup>), 128.1 (C<sup>Ar</sup>), 128.0 (C<sup>Ar</sup>), 127.9 (C<sup>Ar</sup>), 127.7 (C<sup>Ar</sup>), 127.0 (C<sup>Ar</sup>), 126.3 (C<sup>Phe</sup>), 125.1 (C<sup>Ar</sup>), 125.0 (C<sup>Ar</sup>), 124.5 (C<sup>Ar</sup>), 42.4 (CH<sub>2</sub><sup>Phe</sup>), 42.2 (CH<sub>2</sub><sup>Leu</sup>), 34.3 (CH<sup>Val</sup>), 29.9 (CH<sup>Leu</sup>), 24.2 (CH<sub>3</sub><sup>Val</sup>), 22.6 (CH<sub>3</sub><sup>Leu</sup>) ppm; **GC-MS** (EI, 70 eV; MP\_100\_L): t<sub>R</sub> = 11.52 min; m/z (%): 418 (100) [M<sup>+</sup>]; **HPLC** (Nucleosil, ESI<sup>+</sup>): t<sub>R</sub> = 7.00 min; λ<sub>max</sub> = 233, 252, 281 nm;<sup>‡</sup> **HRMS** (DI-EI): calcd for [M<sup>+</sup>]: 418.2661; found: 418.2667.

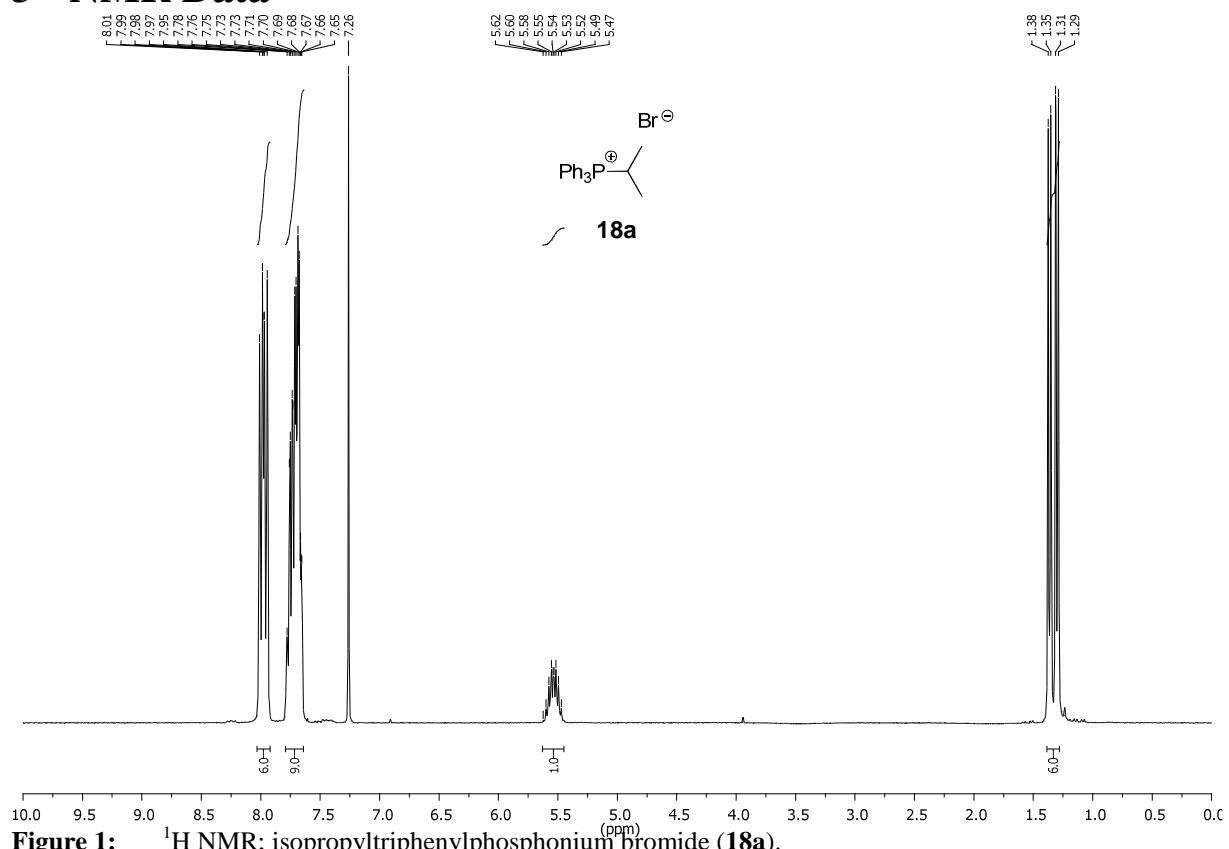
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<sup>\*</sup> Analytical HPLC indicated a product purity ≥ 85%.

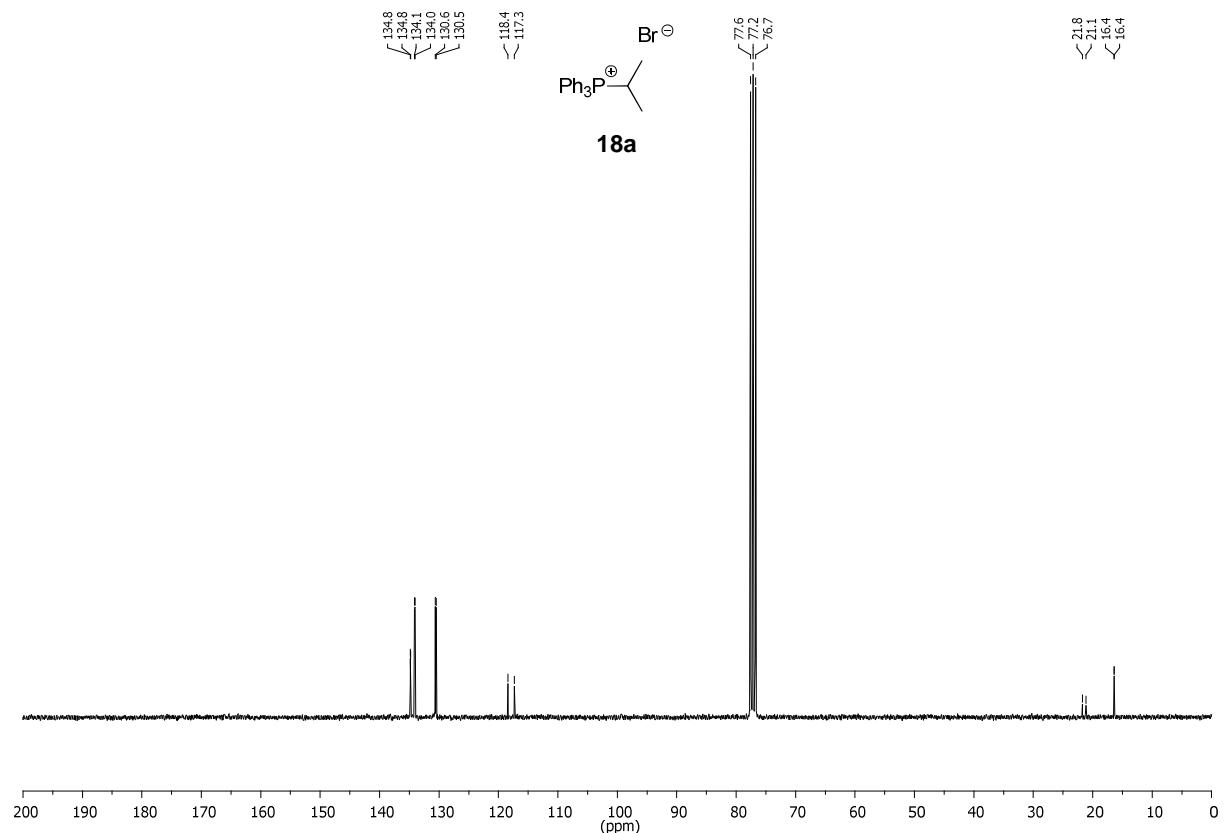
<sup>†</sup> MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 16 mL/min: 0.0 min: 74% MeOH const., 0.0-5.0 min: 85% MeOH lin. gradient, 5.0-12.0 min: 95% MeOH lin. gradient, 12.0-12.5 min: 100% MeOH lin. gradient, 12.5-21.0 min: 100% MeOH const., 21.0-21.5 min: 74% MeOH lin. gradient, 21.5-25.0 min: 74% MeOH const.

<sup>‡</sup> MeOH/water gradient with 1.0% (v/v) HCOOH at a flow rate of 0.7 mL/min: 0.0 min: 74% MeOH const., 0.0-10.0 min: 77% MeOH lin. gradient, 10.0-14.0 min.: 77% MeOH const., 14.0-14.5 min: 100% MeOH lin. gradient, 14.5-17.0 min: 100% MeOH const., 17.0-17.5 min: 74% MeOH lin. gradient, 17.5-19.0 min: 74% MeOH const.

### 3 NMR Data



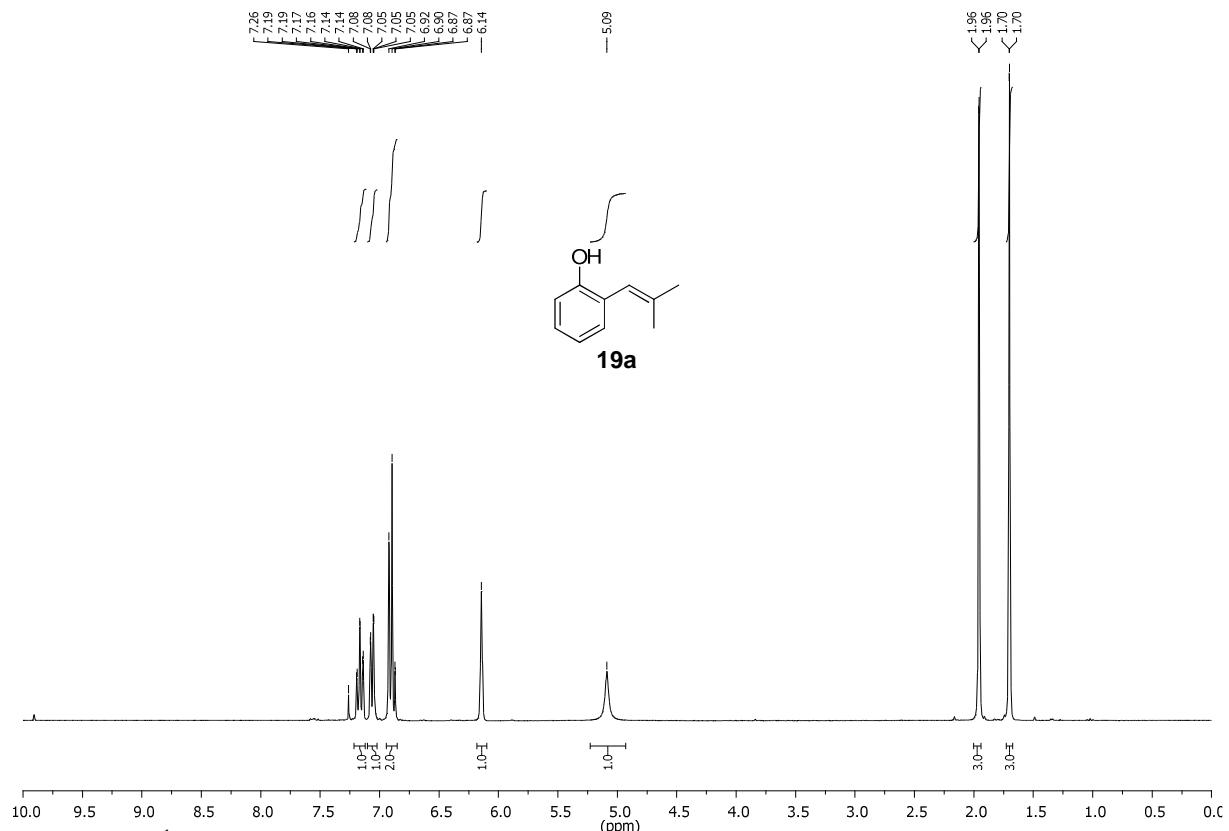
**Figure 1:** <sup>1</sup>H NMR; isopropyltriphenylphosphonium bromide (**18a**).



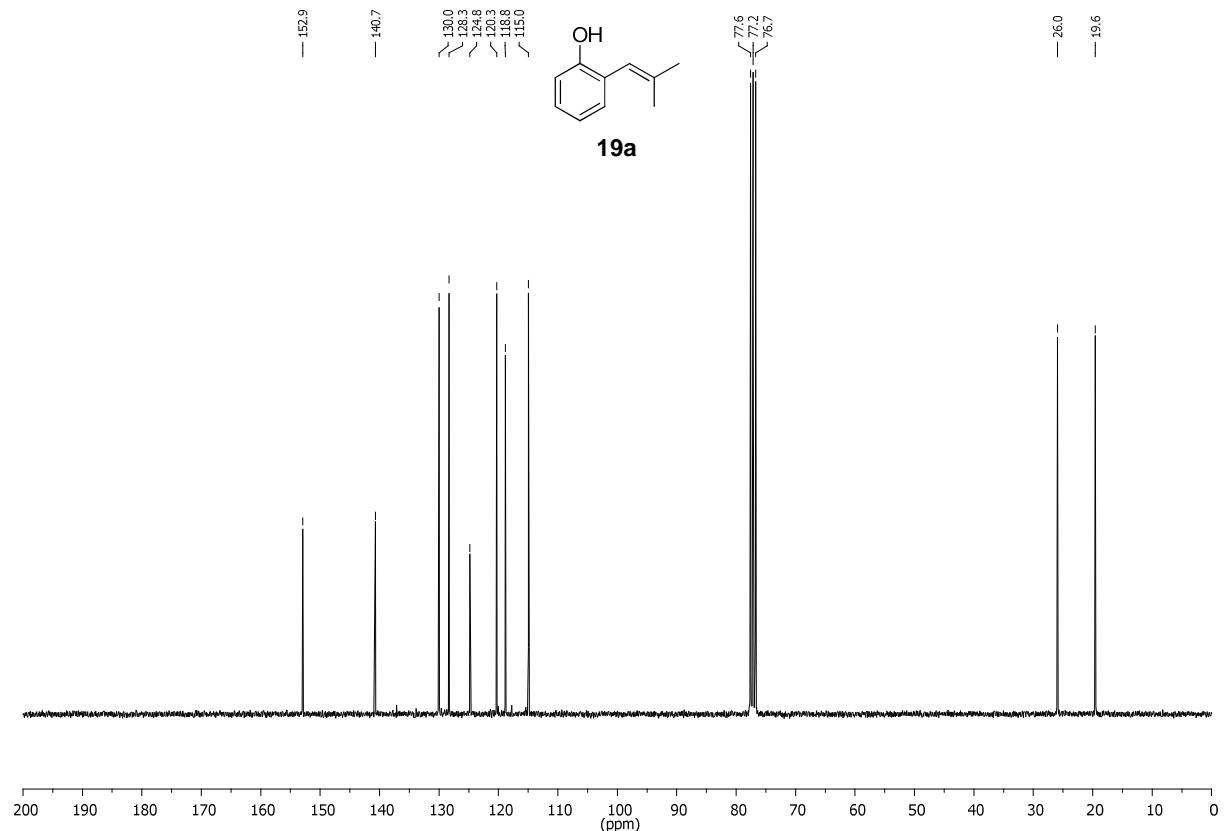
**Figure 2:** <sup>13</sup>C NMR; isopropyltriphenylphosphonium bromide (**18a**).

## NMR Data

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**Figure 3:** <sup>1</sup>H NMR; 2-(2-methylprop-1-en-1-yl)phenol (**19a**).



**Figure 4:** <sup>13</sup>C NMR; 2-(2-methylprop-1-en-1-yl)phenol (**19a**).

## NMR Data

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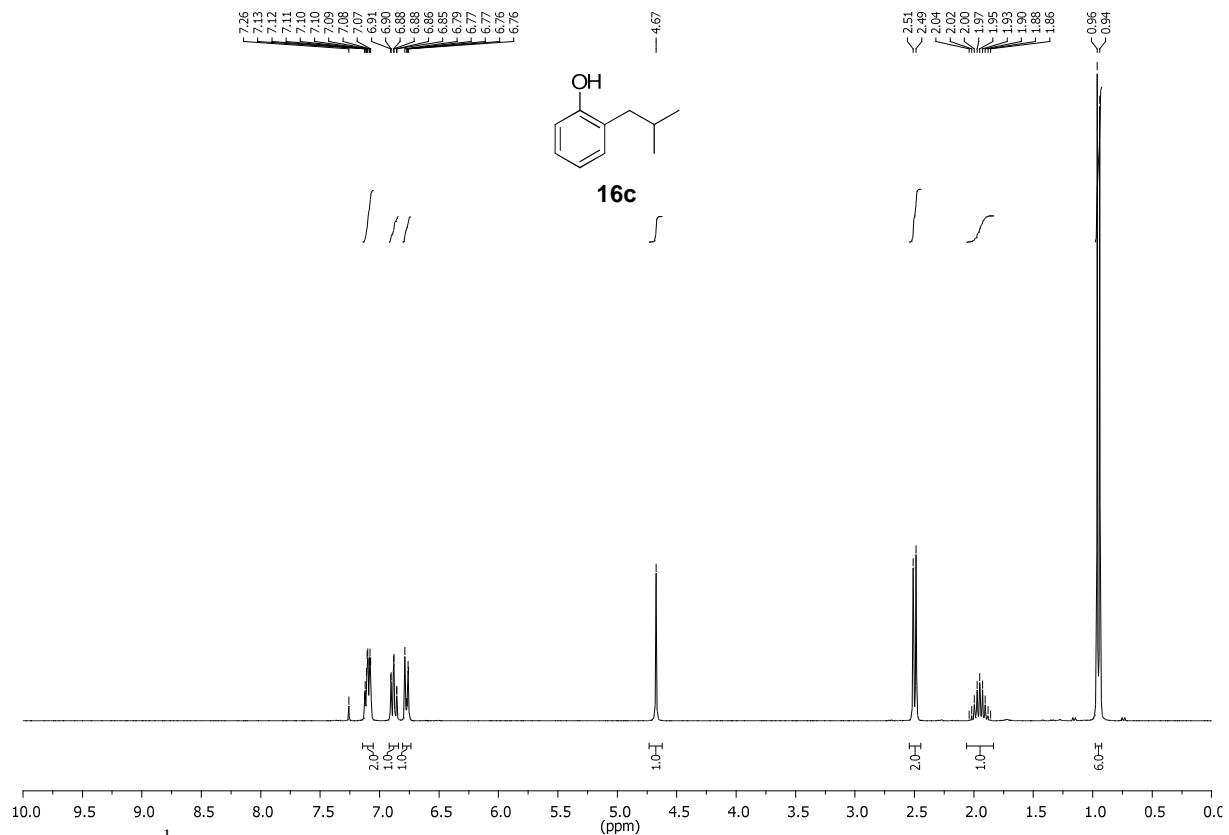


Figure 5: <sup>1</sup>H NMR; 2-isobutylphenol (**16c**).

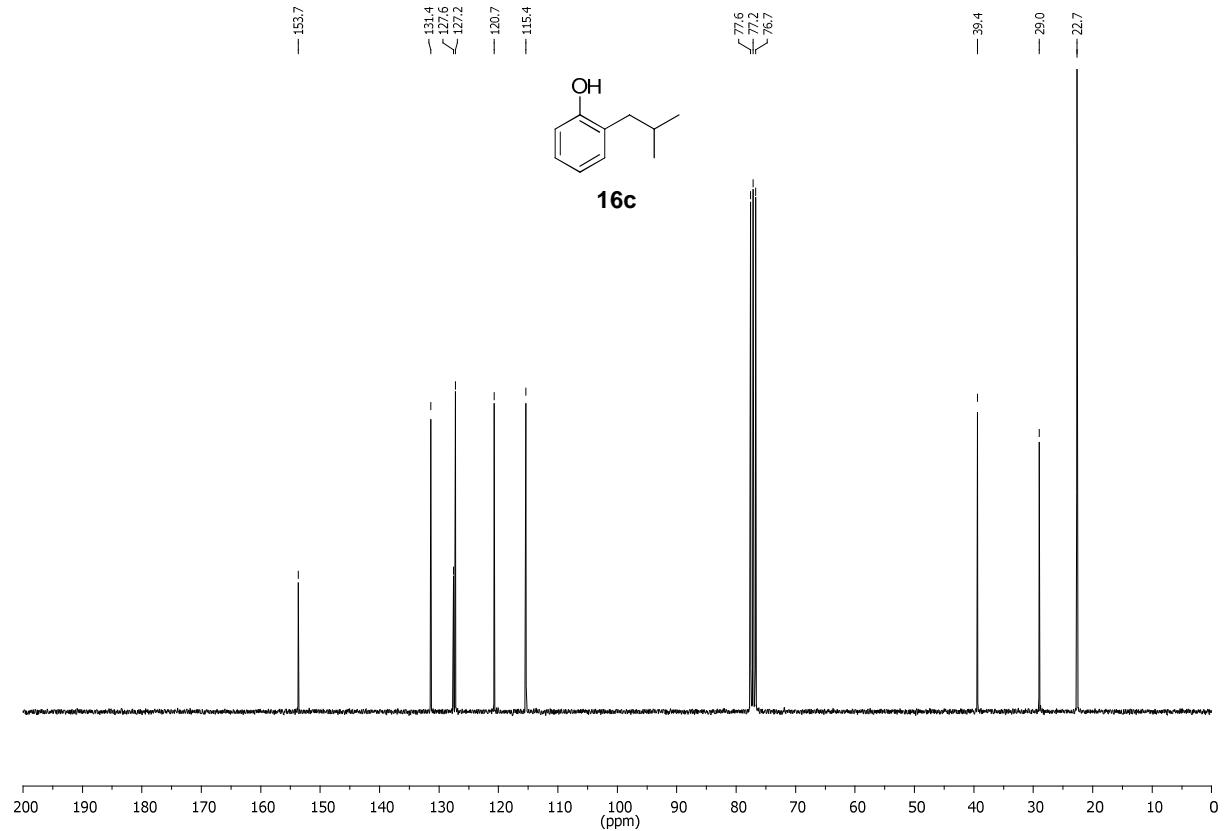


Figure 6: <sup>13</sup>C NMR; 2-isobutylphenol (**16c**).

## NMR Data

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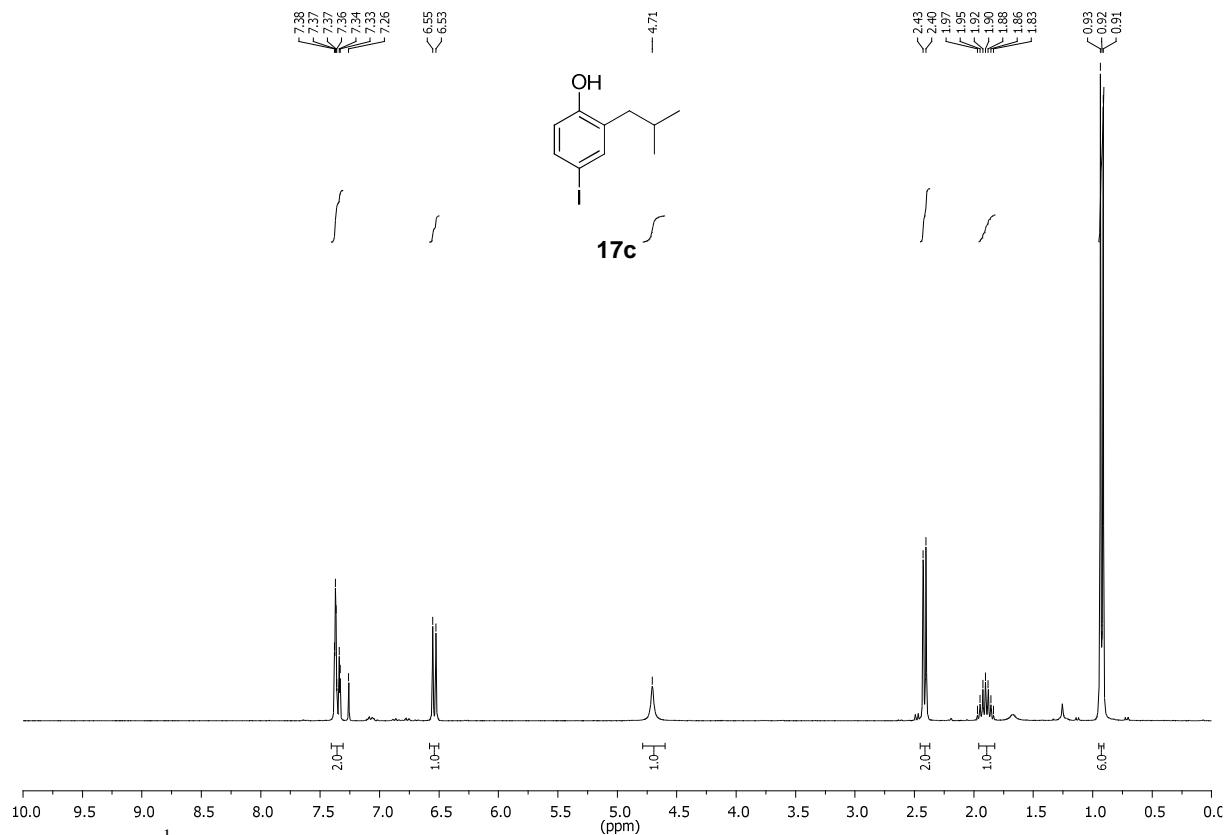


Figure 7: <sup>1</sup>H NMR; 4-iodo-2-isobutylphenol (17c).

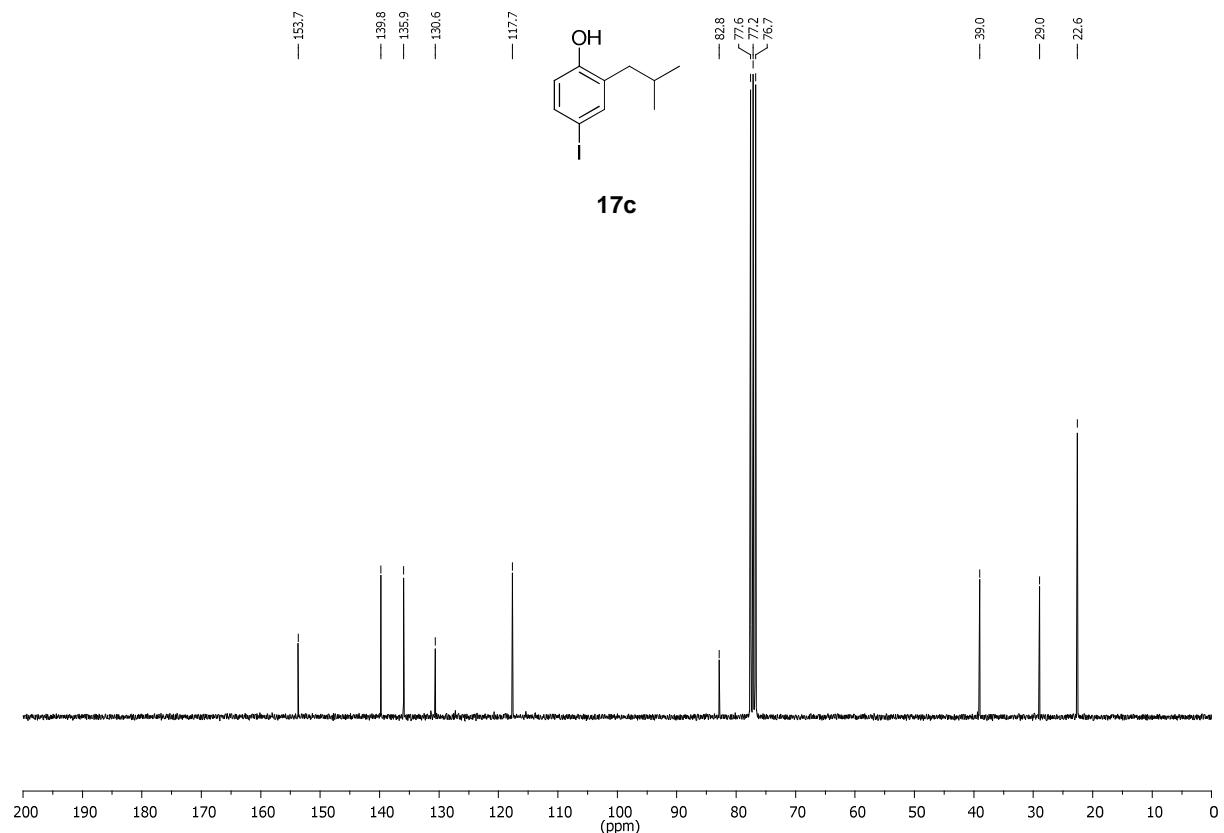
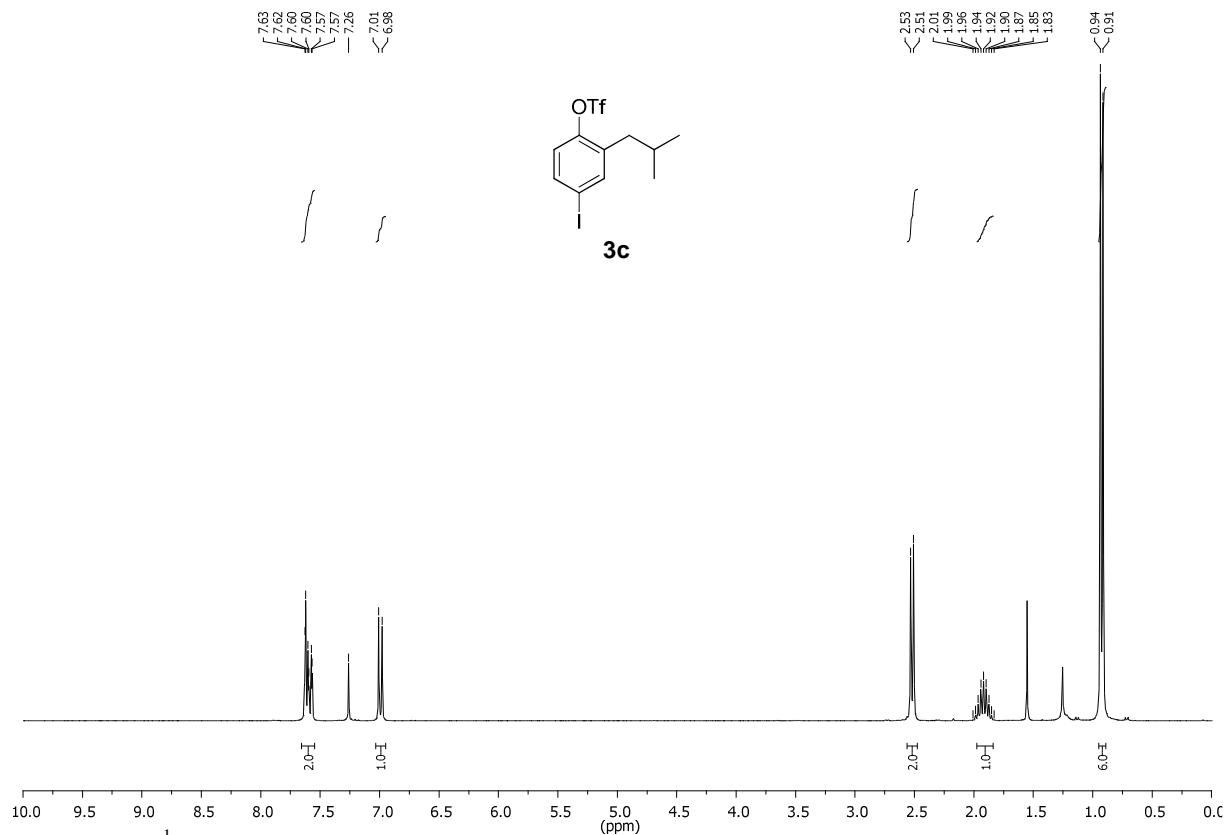


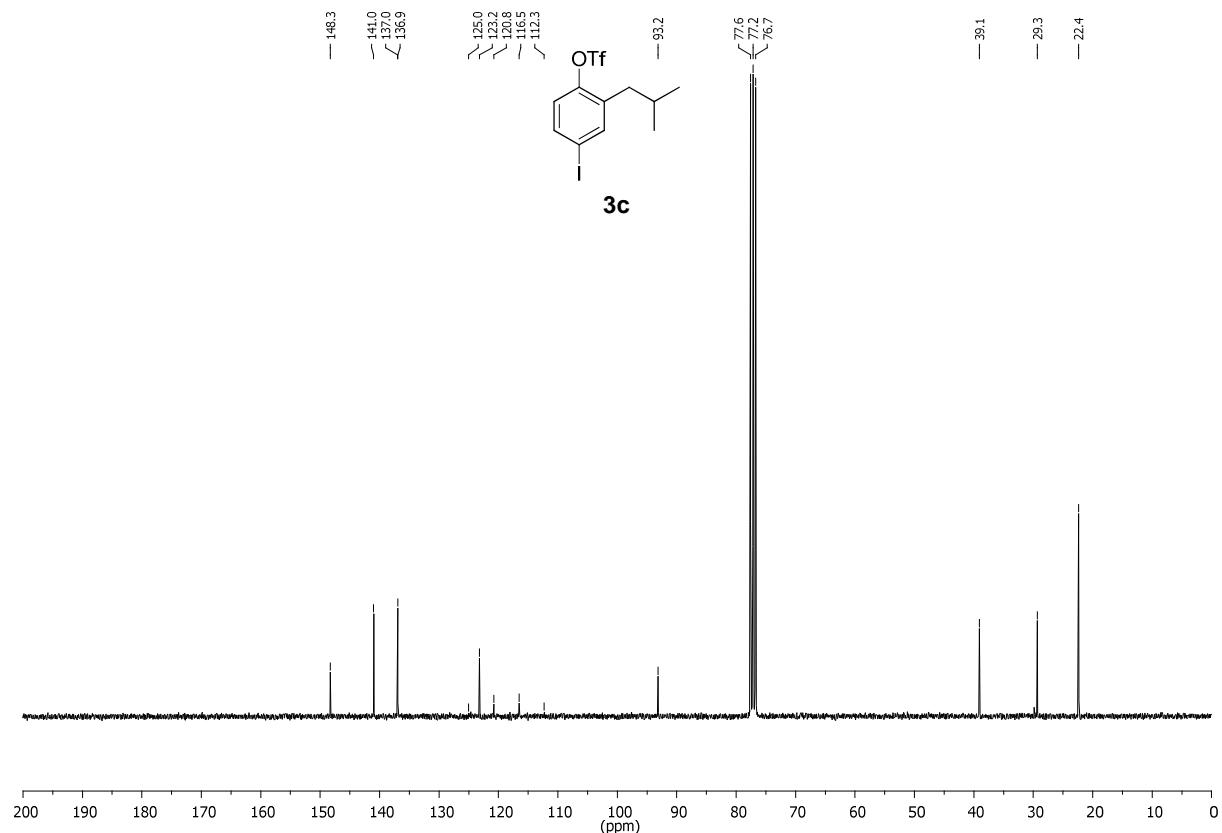
Figure 8: <sup>13</sup>C NMR; 4-iodo-2-isobutylphenol (17c).

## NMR Data

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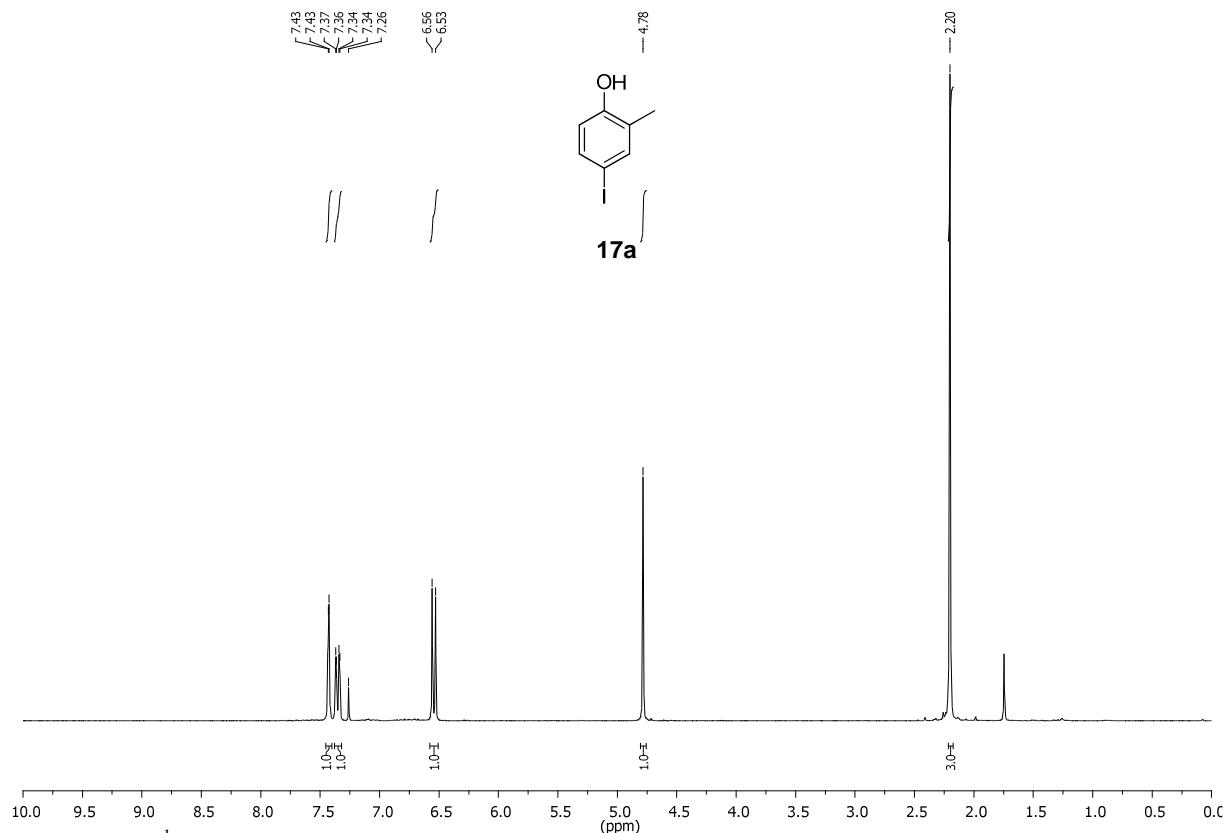
**Figure 9:** <sup>1</sup>H NMR; 4-iodo-2-isobutylphenyl trifluoromethanesulfonate (**3c**).



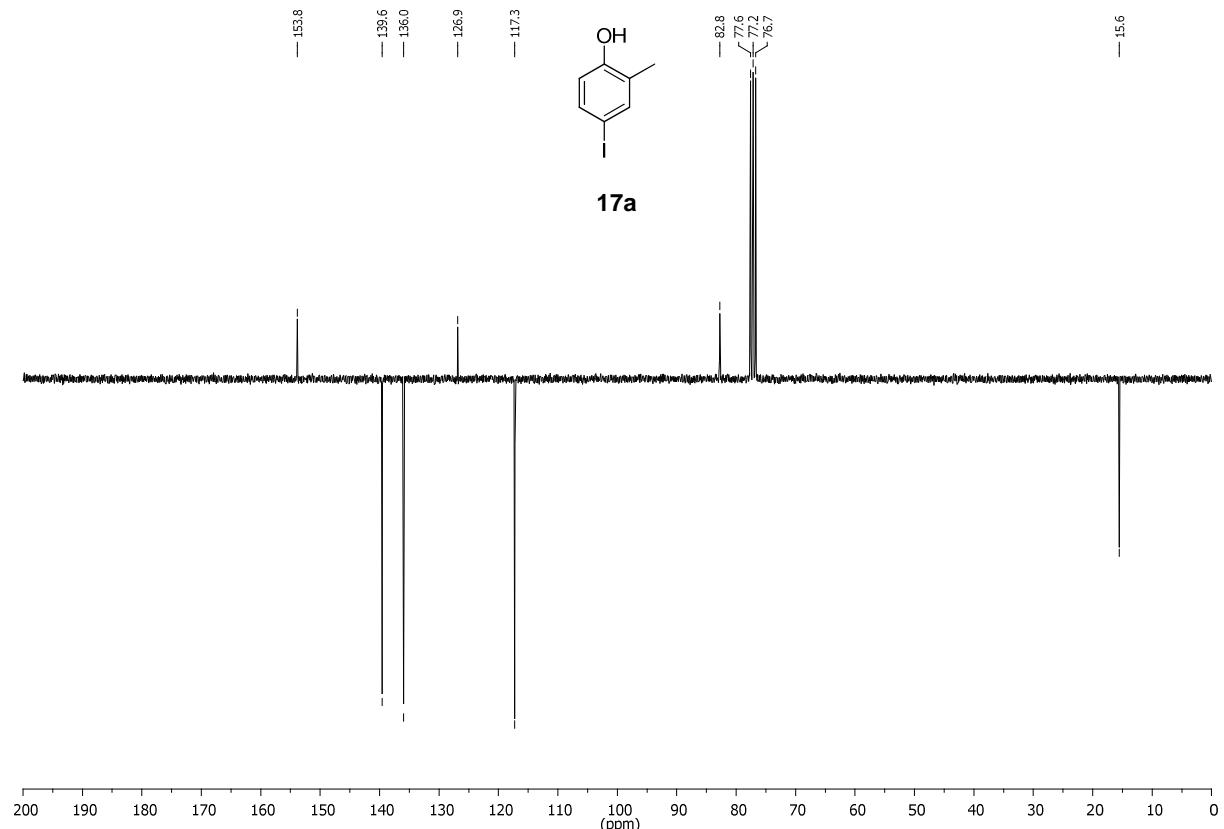
**Figure 10:** <sup>13</sup>C NMR; 4-iodo-2-isobutylphenyl trifluoromethanesulfonate (**3c**).

## NMR Data

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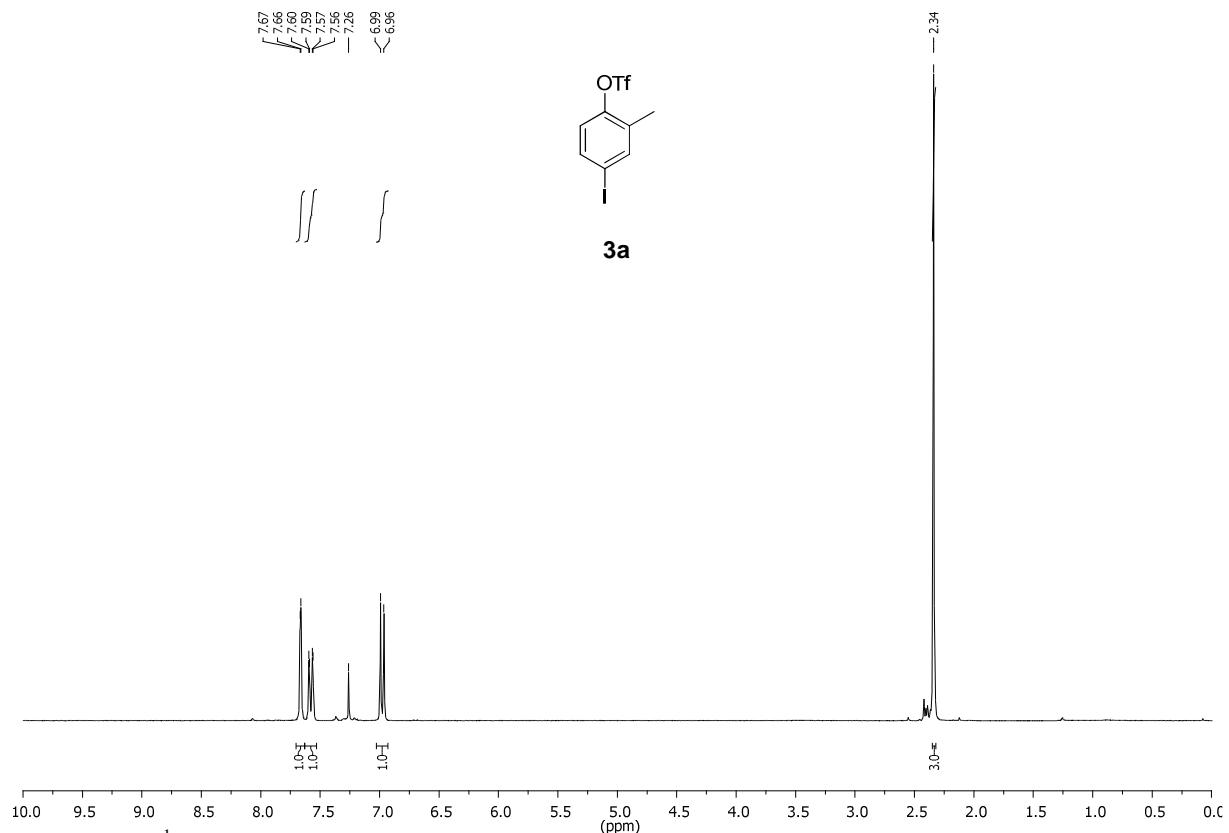
**Figure 11:** <sup>1</sup>H NMR; 4-iodo-2-methylphenol (**17a**).



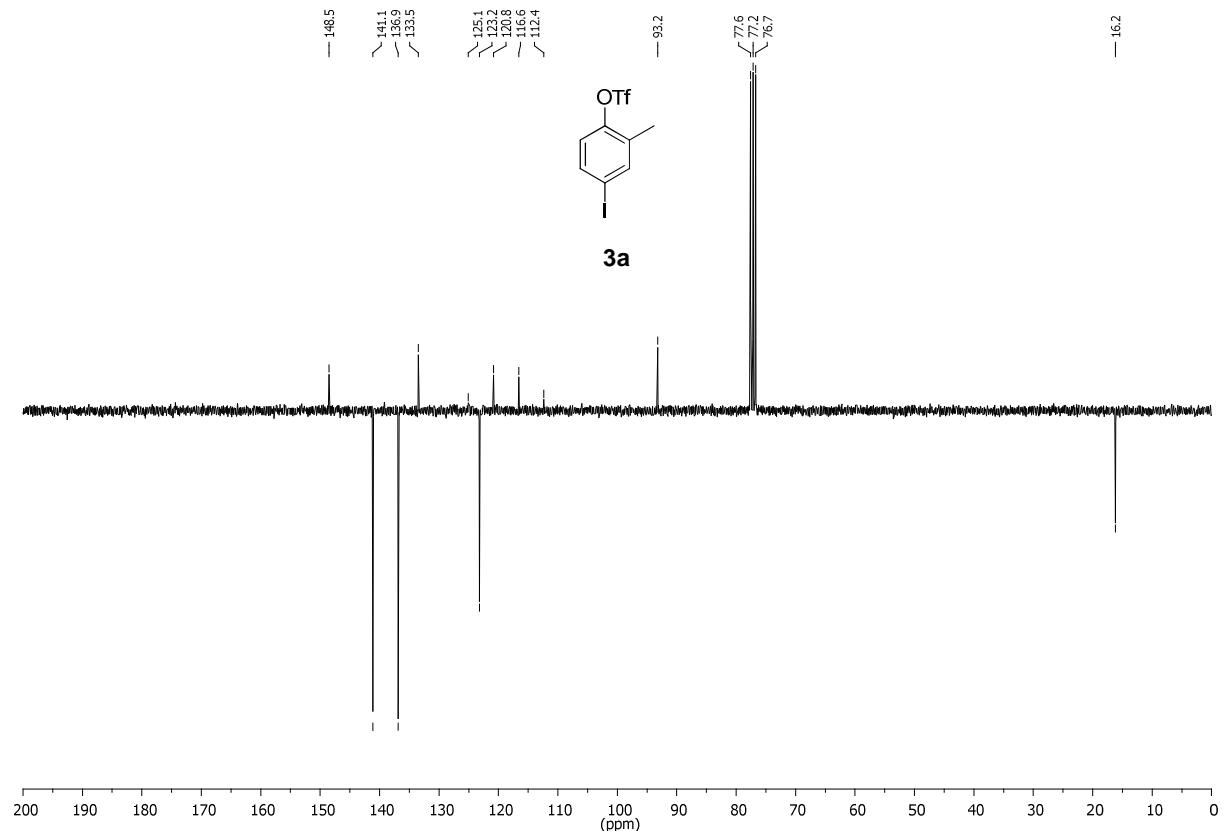
**Figure 12:** <sup>13</sup>C NMR, APT; 4-iodo-2-methylphenol (**17a**).

## NMR Data

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**Figure 13;** <sup>1</sup>H NMR; 4-iodo-2-methylphenyl trifluoromethanesulfonate (**3a**).



**Figure 14:** <sup>13</sup>C NMR, APT; 4-iodo-2-methylphenyl trifluoromethanesulfonate (**3a**).

## NMR Data

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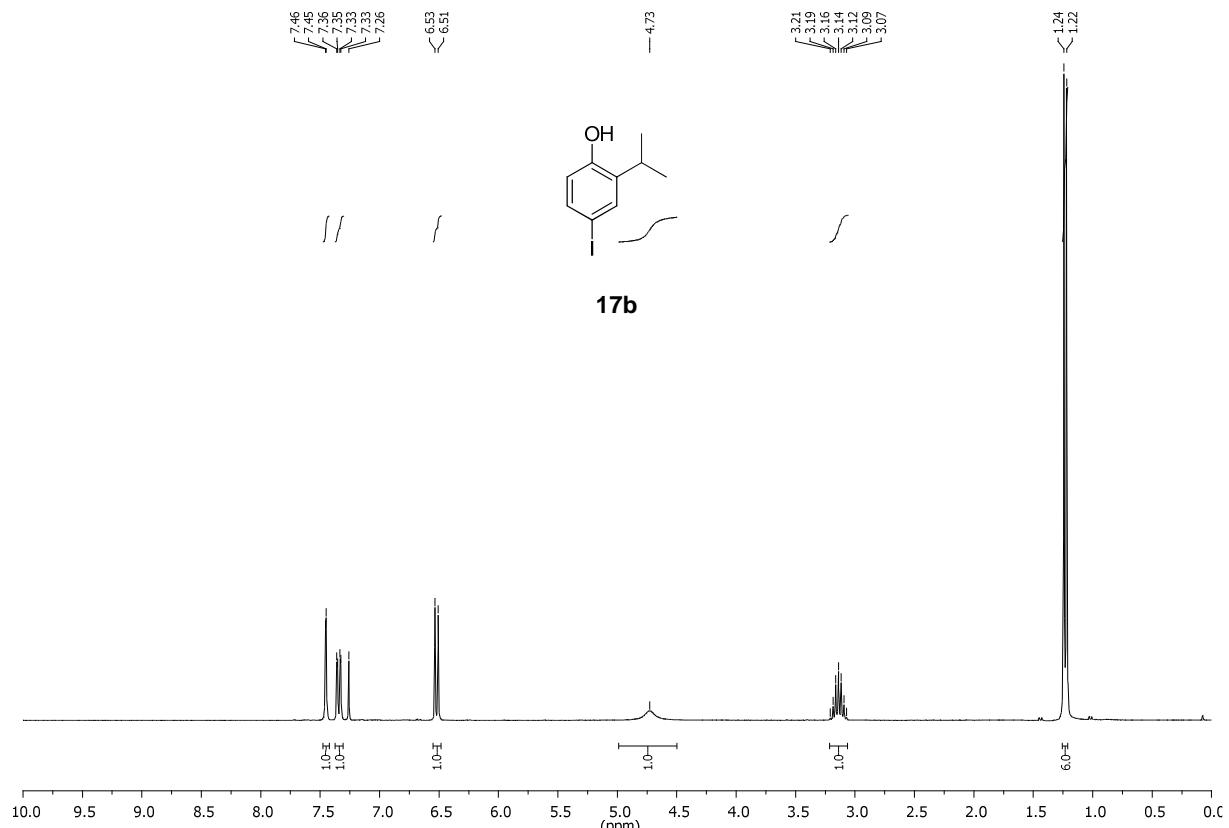


Figure 15: <sup>1</sup>H NMR; 4-iodo-2-isopropylphenol (17b).

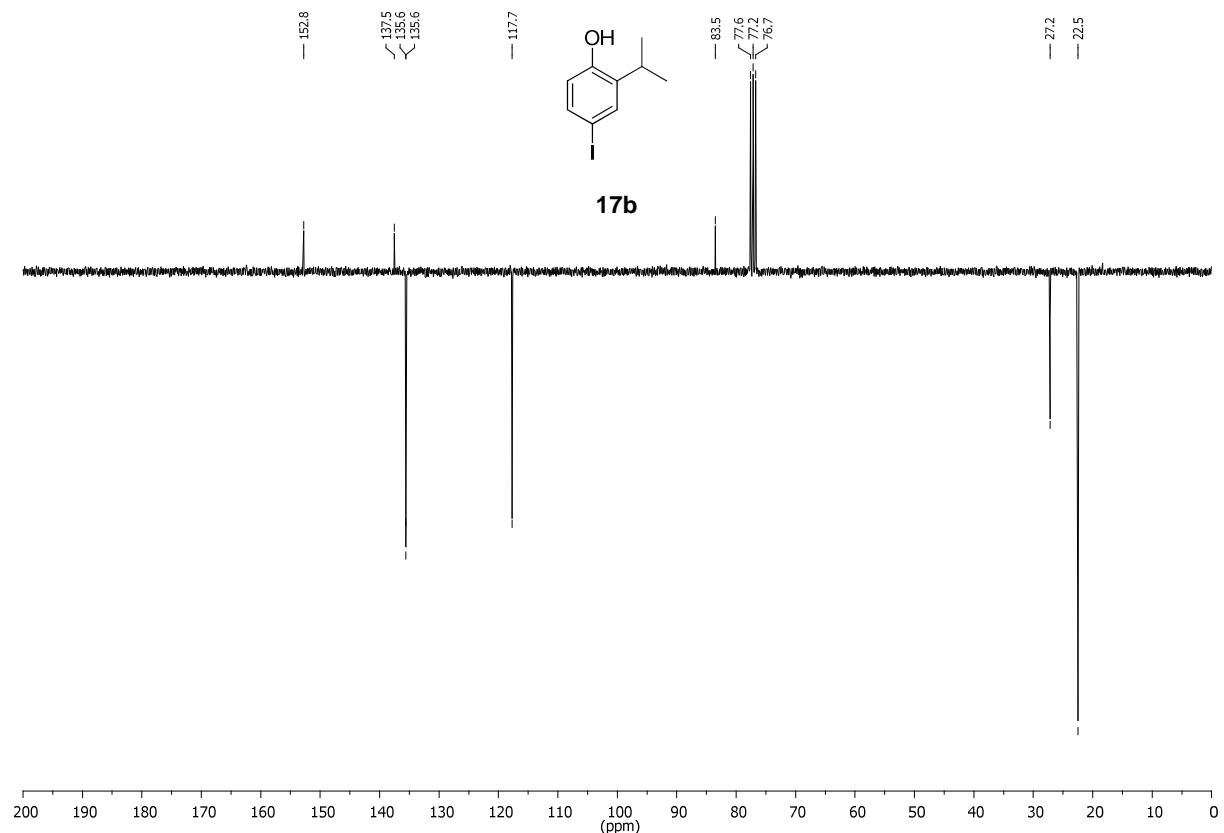
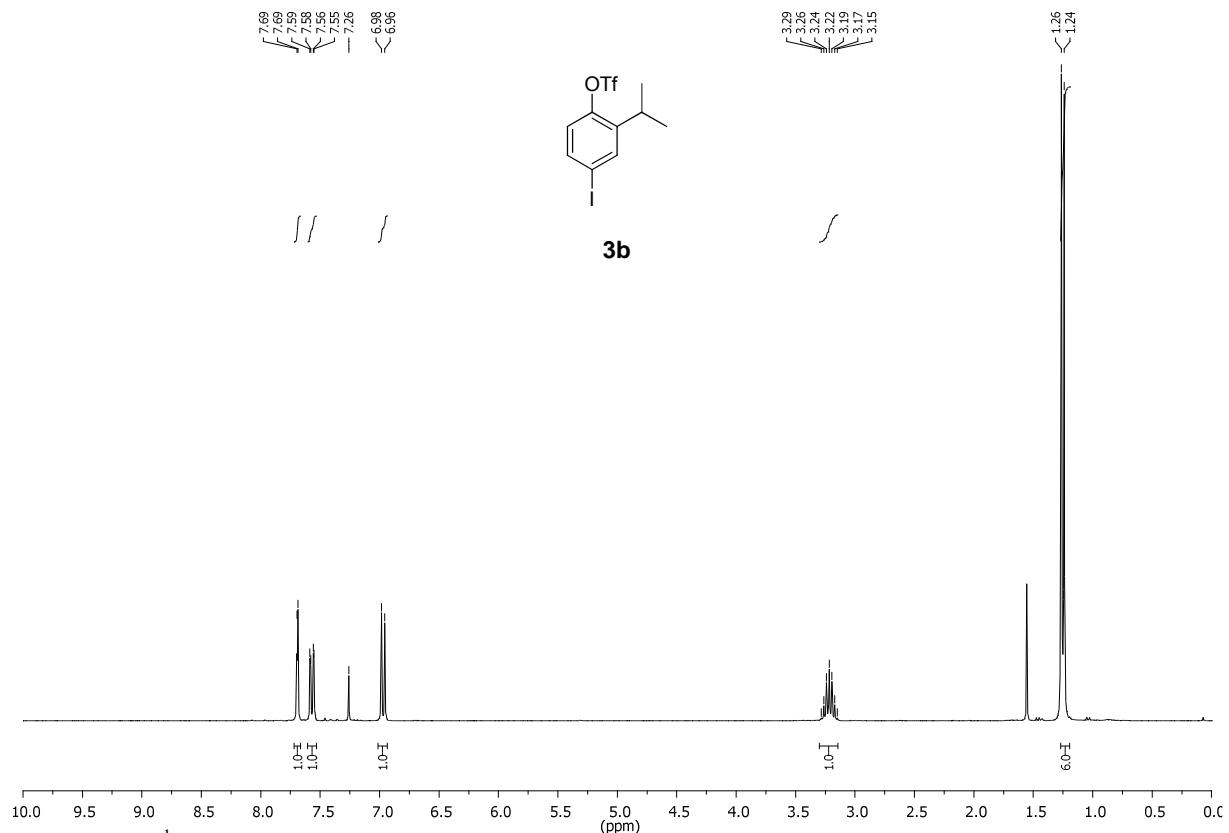


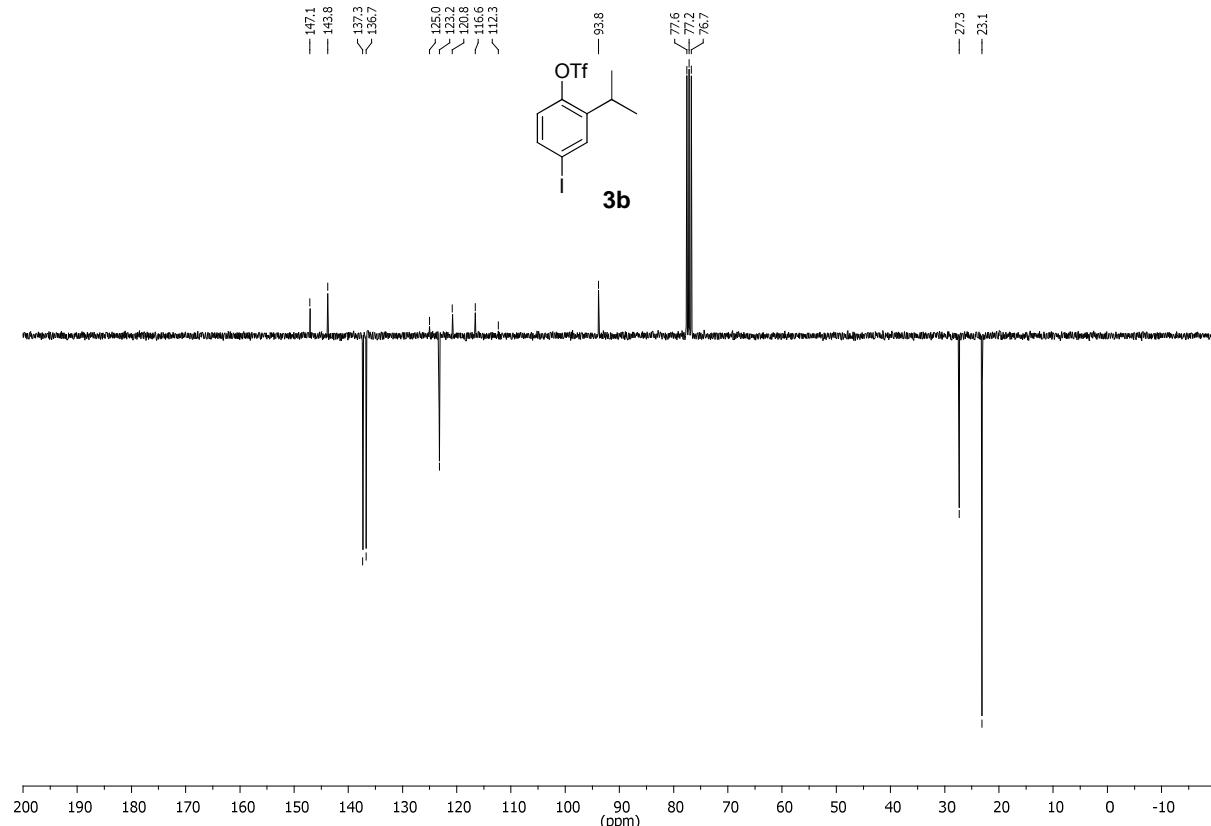
Figure 16: <sup>13</sup>C NMR, APT; 4-iodo-2-isopropylphenol (17b).

## NMR Data

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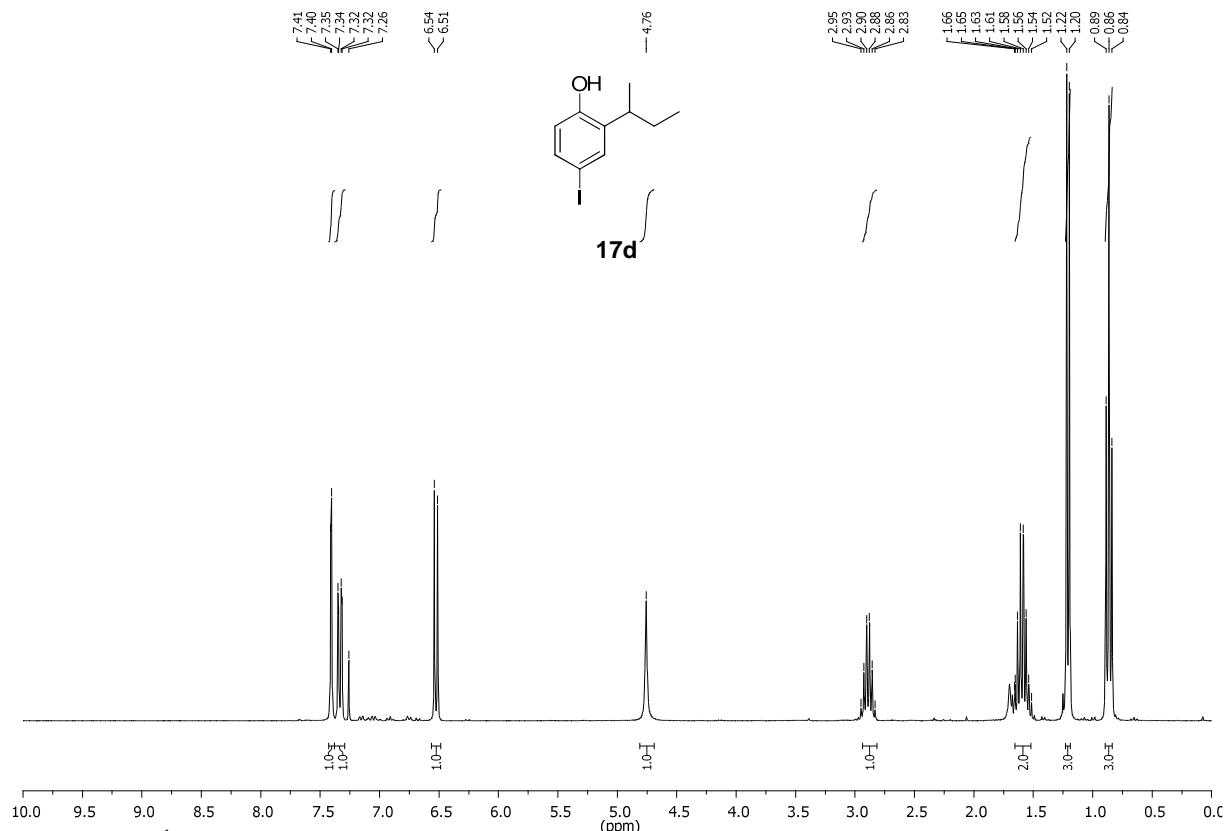
**Figure 17:** <sup>1</sup>H NMR; 4-iodo-2-isopropylphenyl trifluoromethanesulfonate (**3b**).



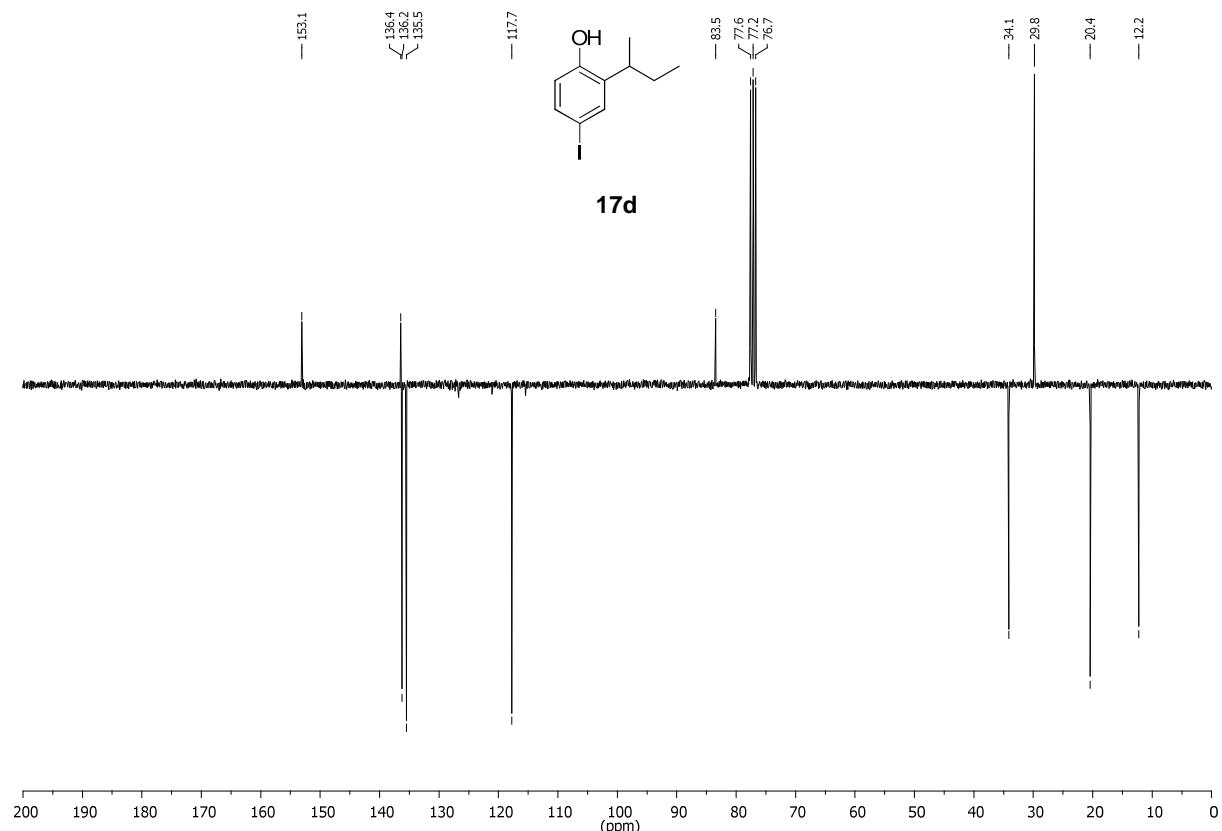
**Figure 18:** <sup>13</sup>C NMR, APT; 4-iodo-2-isopropylphenyl trifluoromethanesulfonate (**3b**).

## NMR Data

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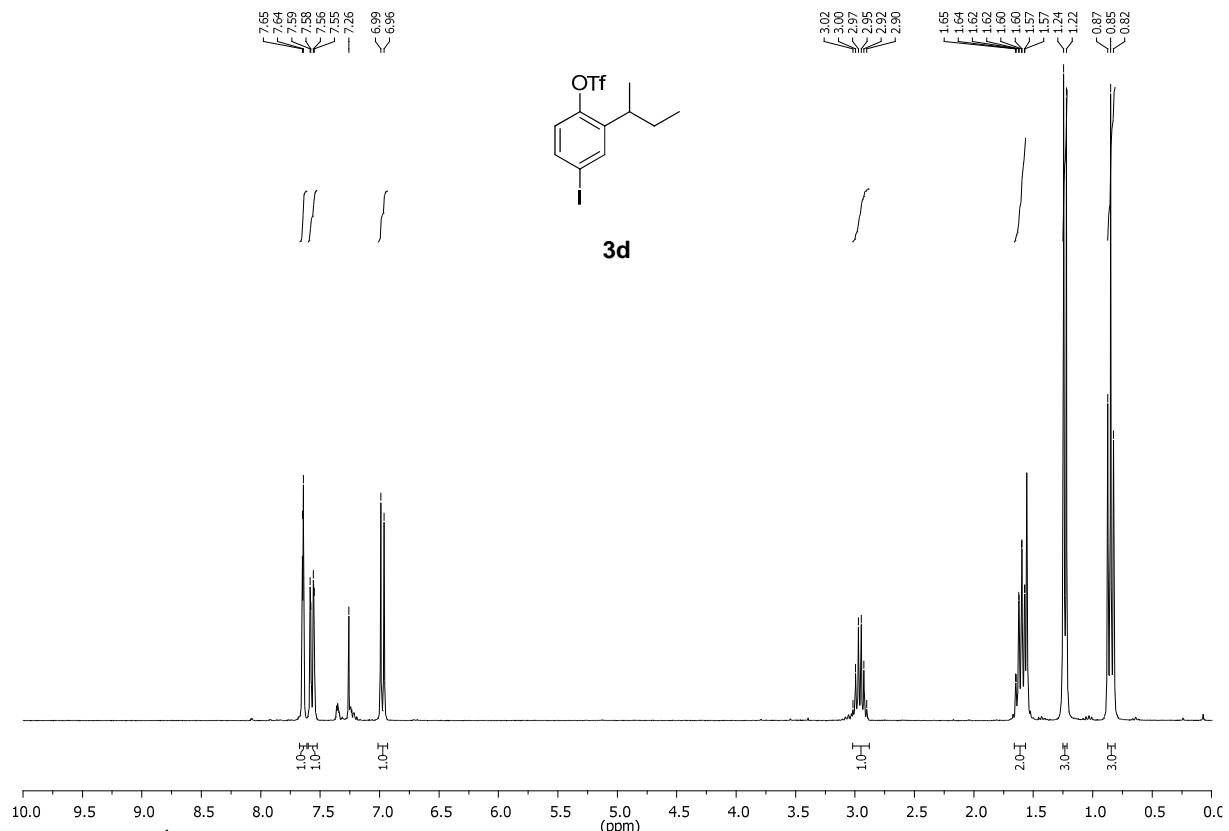
**Figure 19:** <sup>1</sup>H NMR; 2-sec-butyl-4-iodophenol (**17d**).



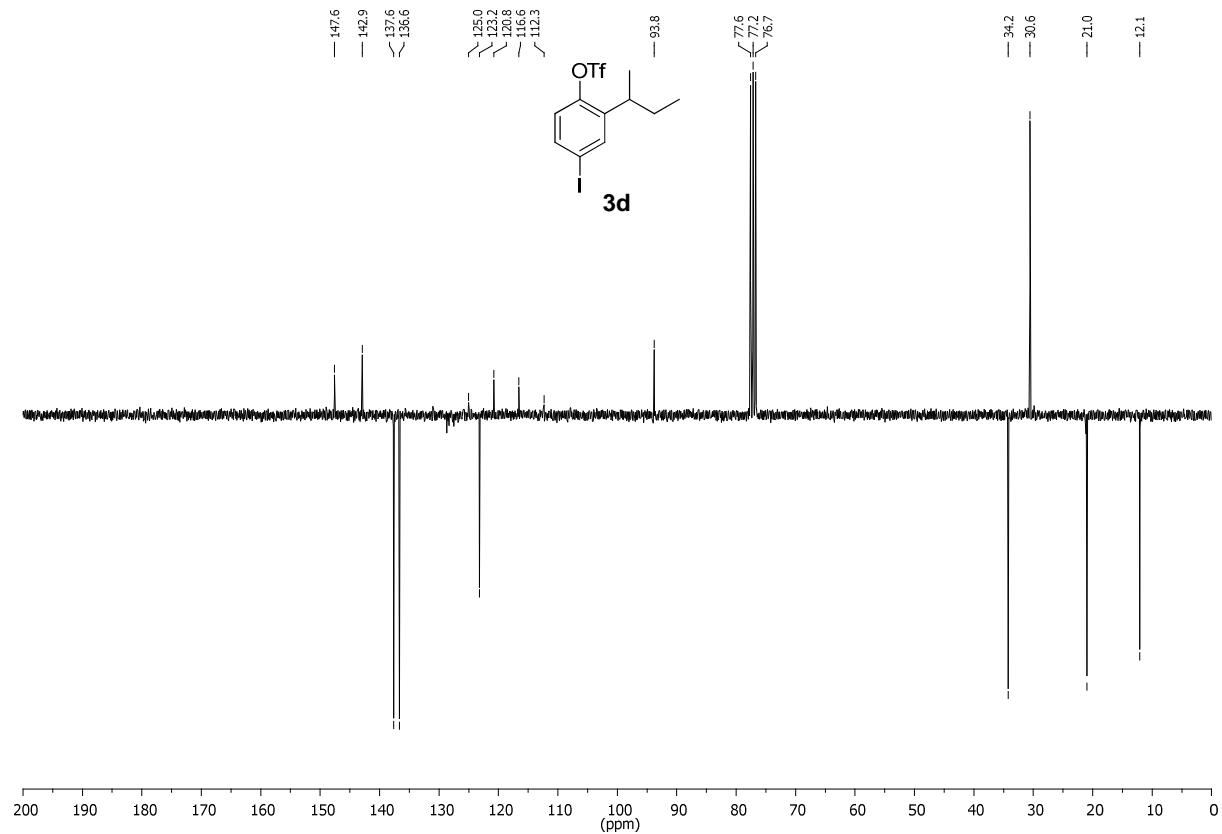
**Figure 20:** <sup>13</sup>C NMR, APT; 2-sec-butyl-4-iodophenol (**17d**).

## NMR Data

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**Figure 21:** <sup>1</sup>H NMR; 2-(*sec*-butyl)-4-iodophenyl trifluoromethanesulfonate (**3d**).



**Figure 22:** <sup>13</sup>C NMR, APT; 2-(*sec*-butyl)-4-iodophenyl trifluoromethanesulfonate (**3d**).

## NMR Data

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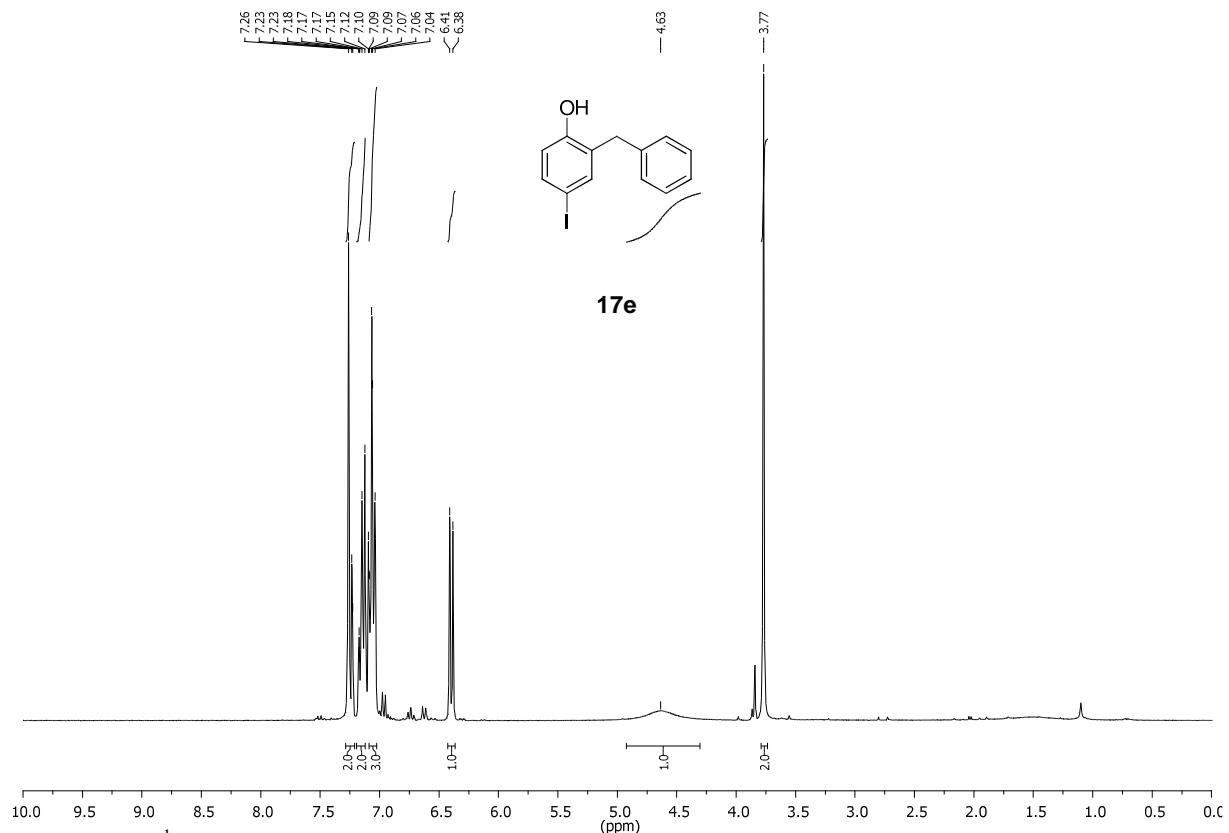


Figure 23: <sup>1</sup>H NMR; 2-benzyl-4-iodophenol (17e).

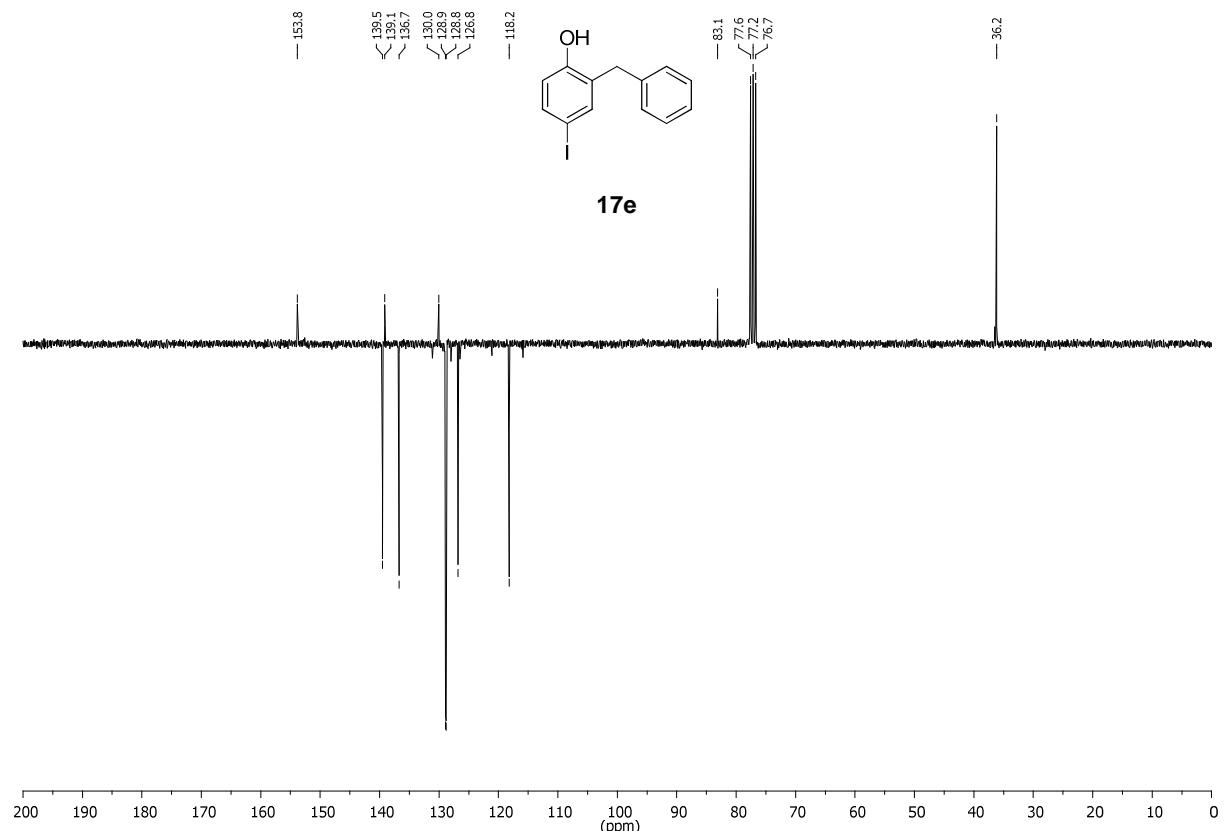
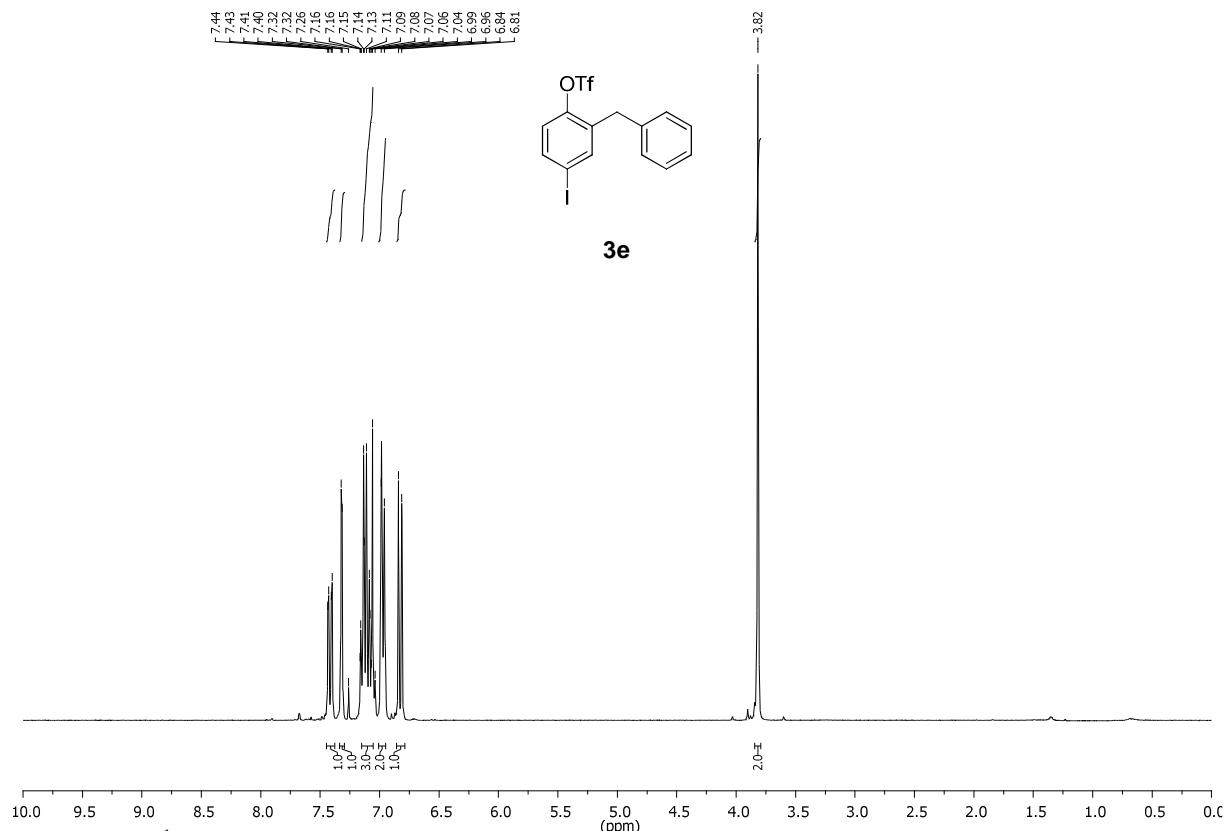


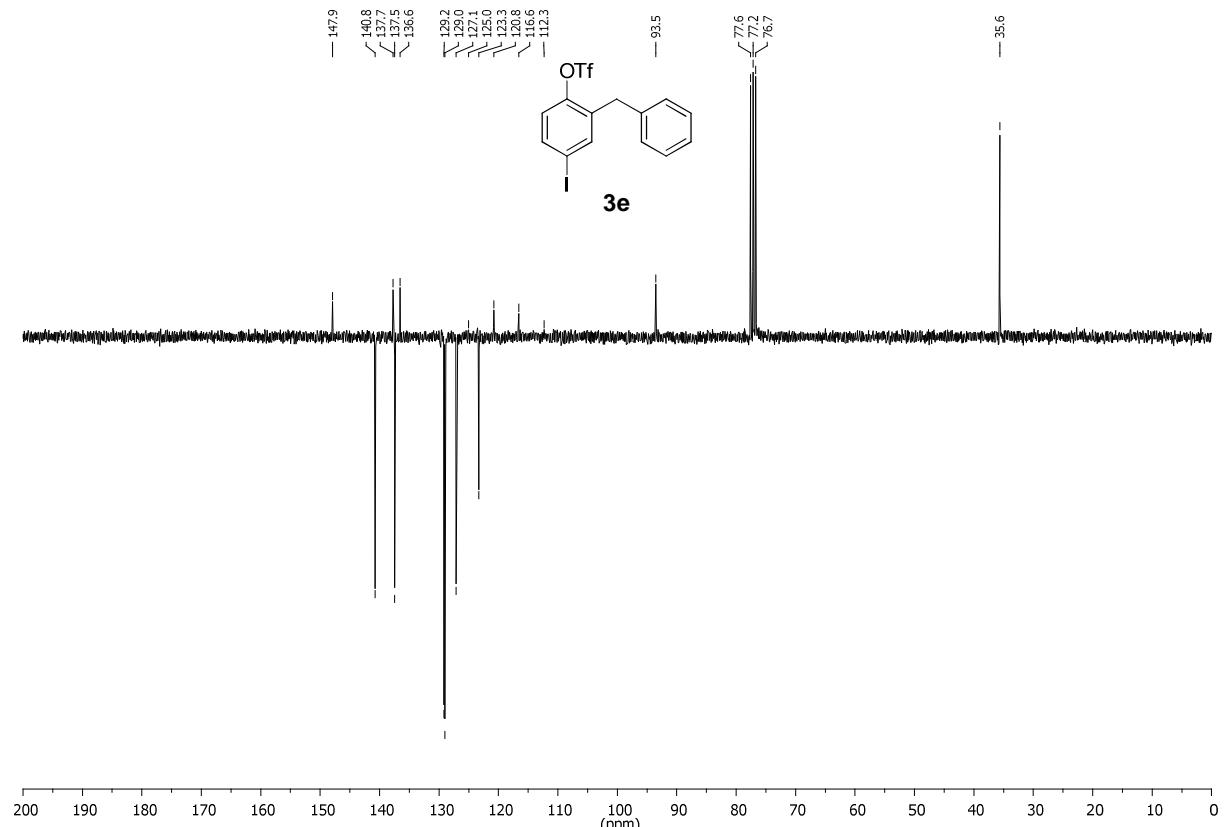
Figure 24: <sup>13</sup>C NMR, APT; 2-benzyl-4-iodophenol (17e).

## NMR Data

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**Figure 25:** <sup>1</sup>H NMR; 2-benzyl-4-iodophenyl trifluoromethanesulfonate (**3e**).



**Figure 26:** <sup>13</sup>C NMR, APT; 2-benzyl-4-iodophenyl trifluoromethanesulfonate (**3e**).

## NMR Data

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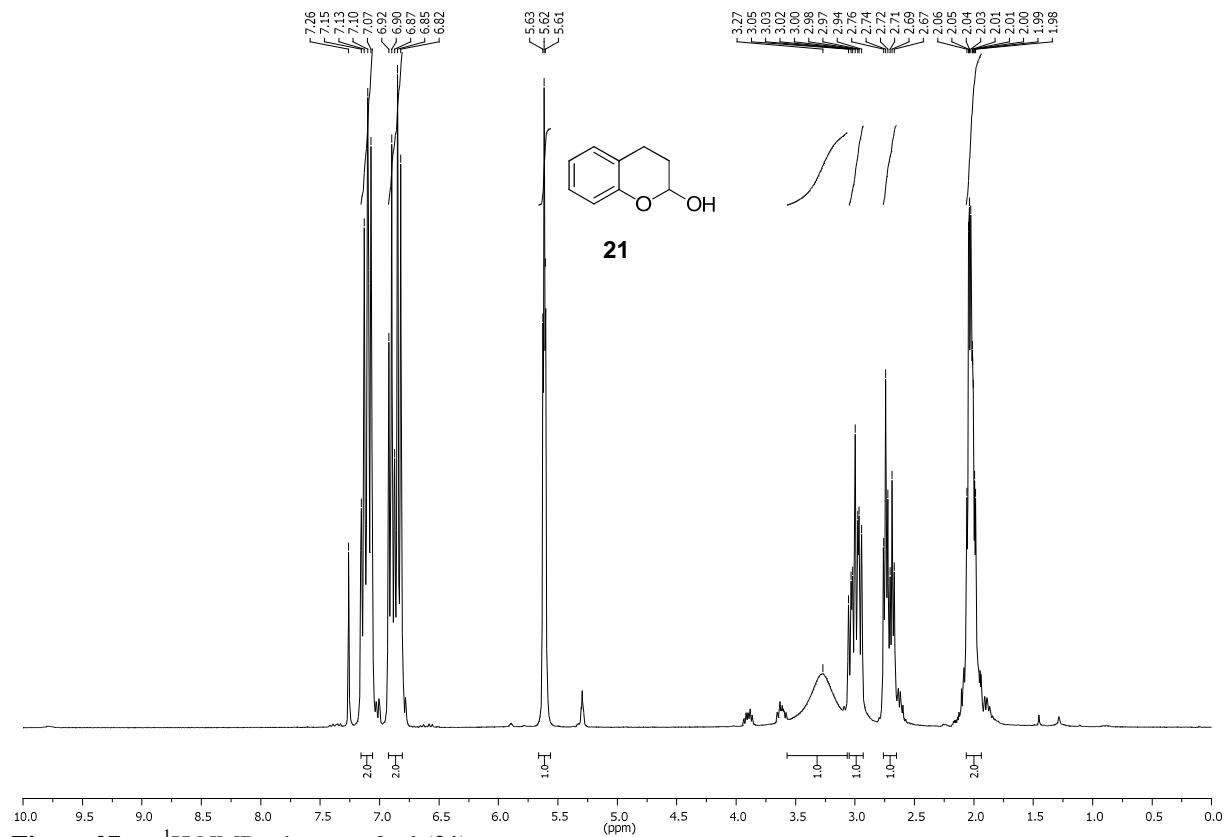


Figure 27:  $^1\text{H}$  NMR; chroman-2-ol (**21**).

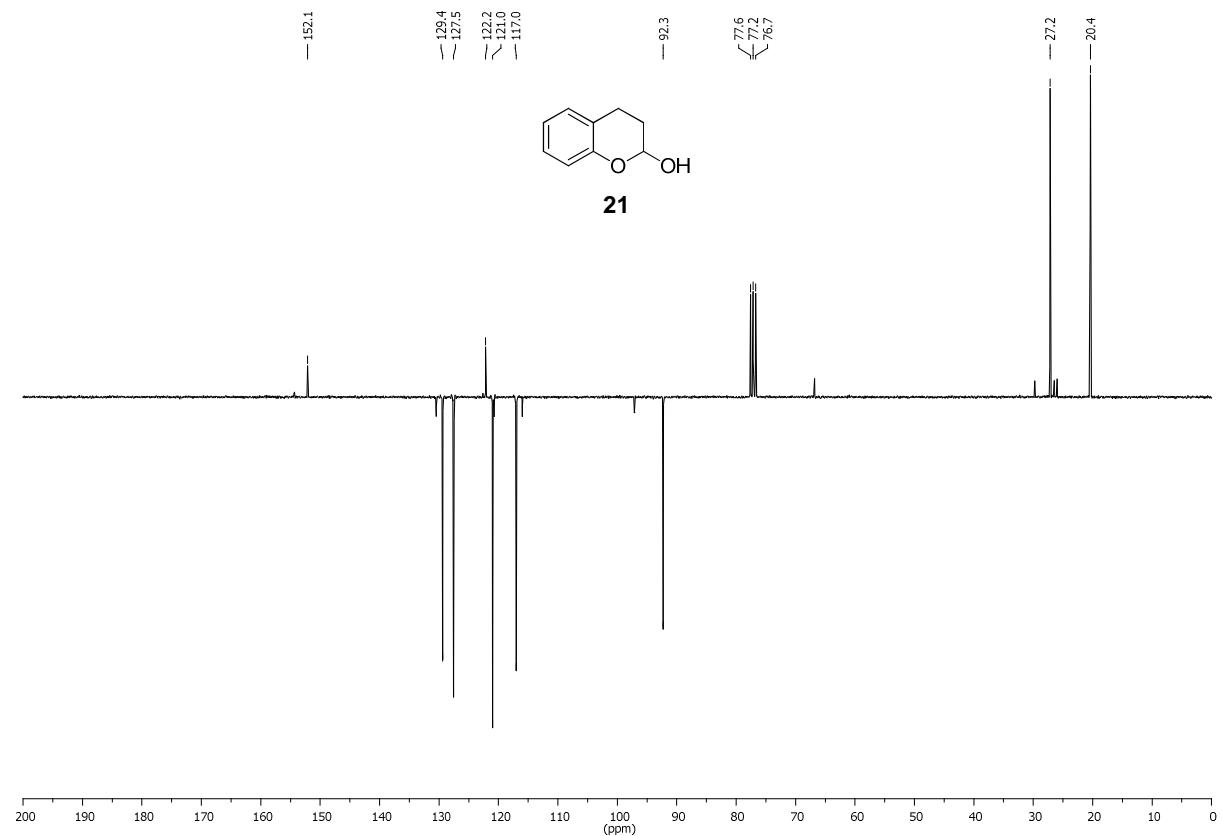
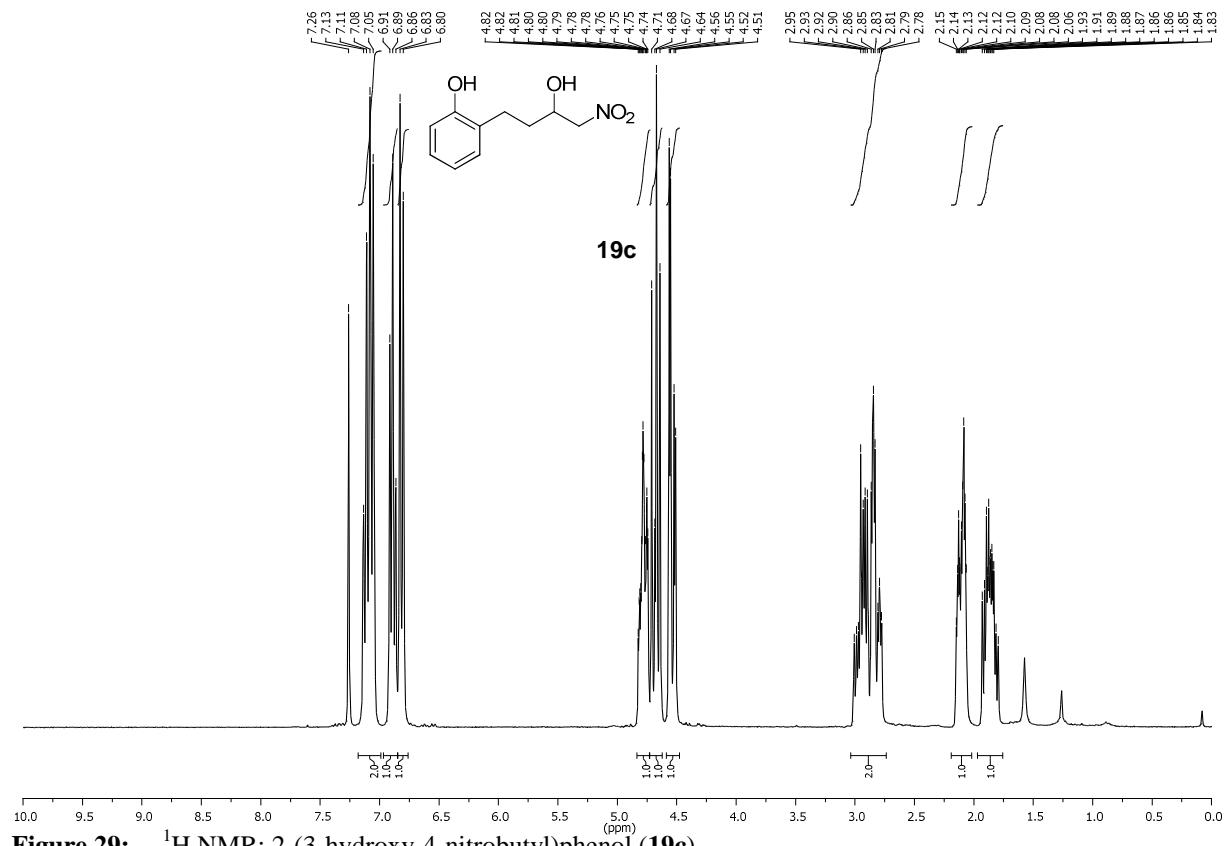


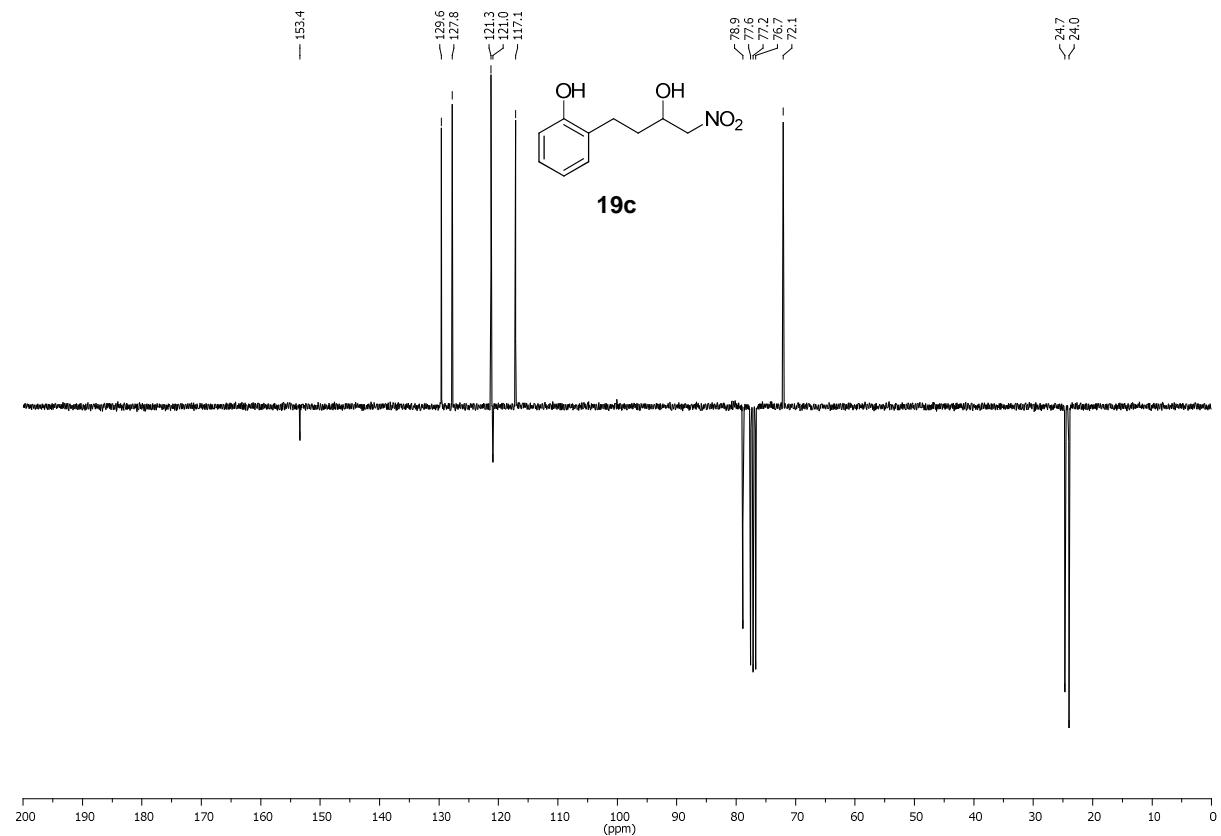
Figure 28:  $^{13}\text{C}$  NMR, APT; chroman-2-ol (**21**).

## NMR Data

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**Figure 29:**  $^1\text{H}$  NMR; 2-(3-hydroxy-4-nitrobutyl)phenol (**19c**).



**Figure 30:**  $^{13}\text{C}$  NMR, APT; 2-(3-hydroxy-4-nitrobutyl)phenol (**19c**).

## NMR Data

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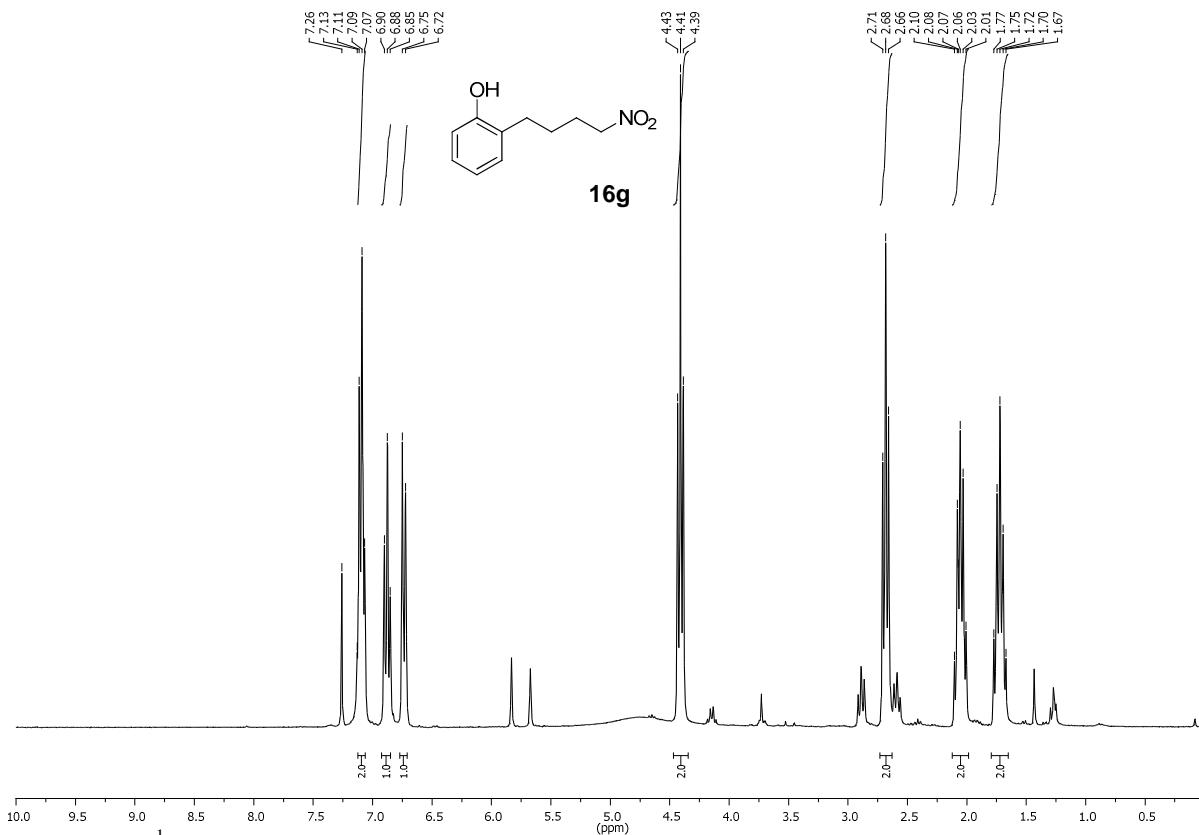


Figure 31: <sup>1</sup>H NMR; 2-(4-nitrobutyl)phenol (16g).

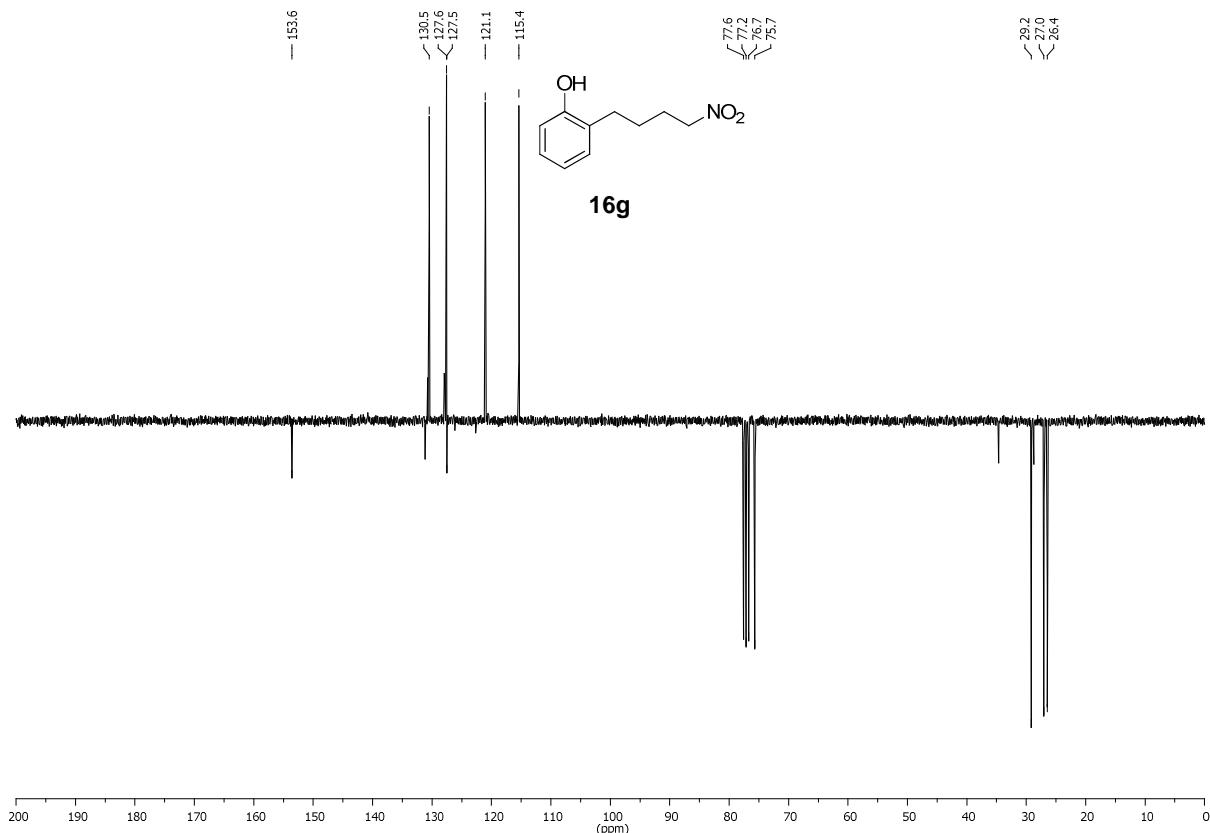
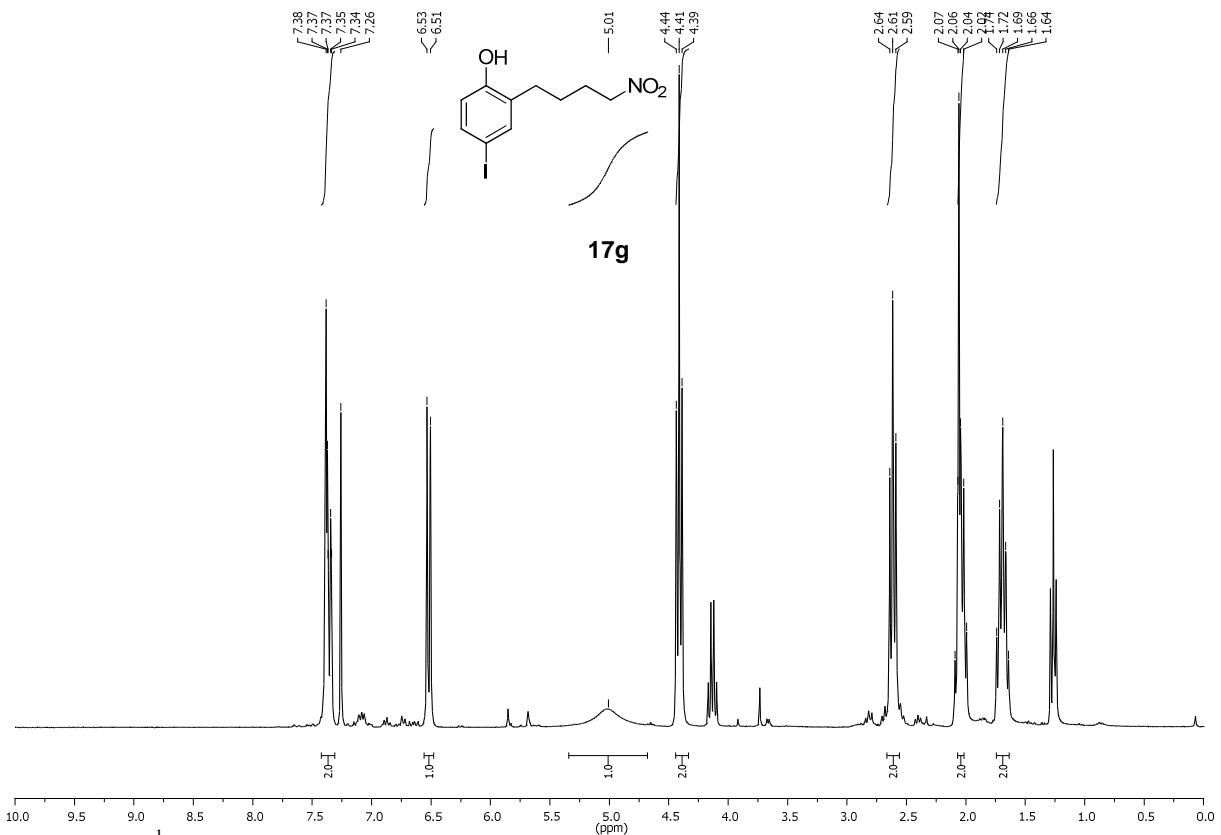


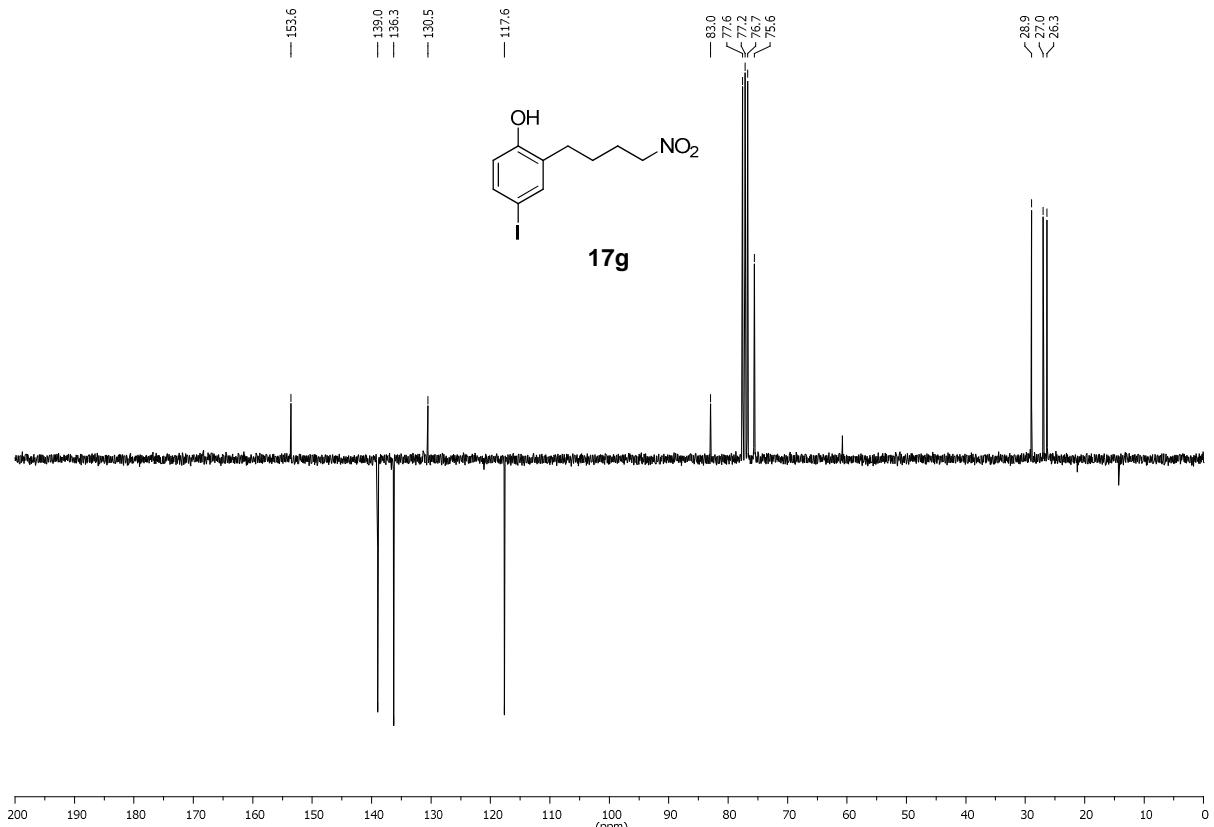
Figure 32: <sup>13</sup>C NMR, APT; 2-(4-nitrobutyl)phenol (16g).

## NMR Data

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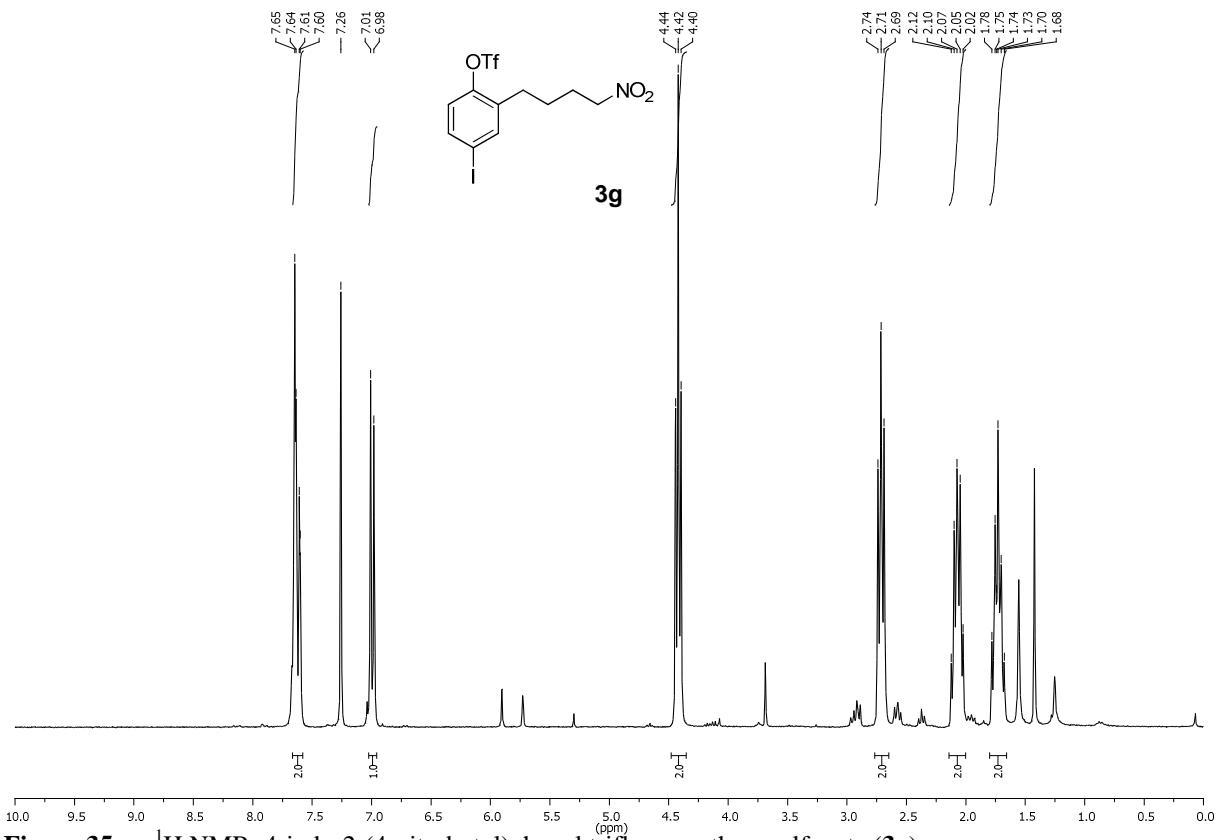
**Figure 33:**  $^1\text{H}$  NMR; 4-iodo-2-(4-nitrobutyl)phenol (**17g**).



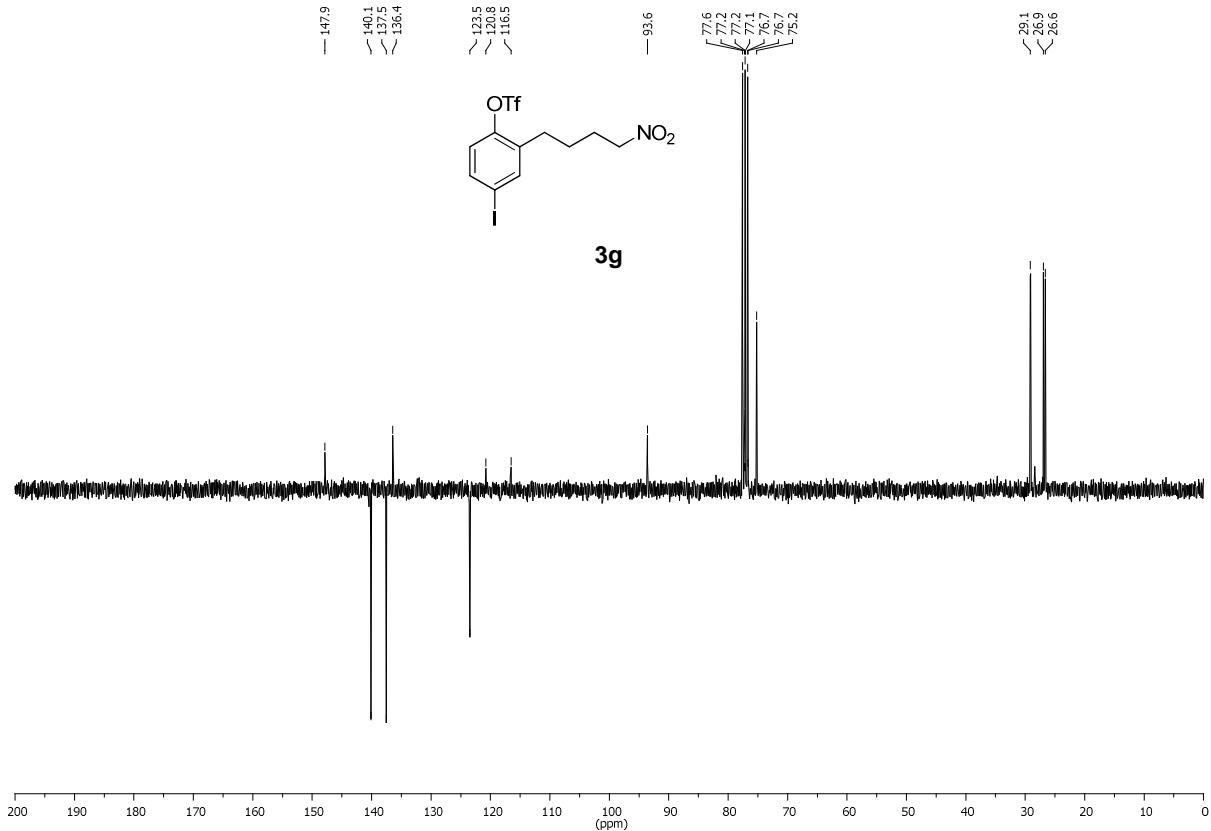
**Figure 34:**  $^{13}\text{C}$  NMR, APT; 4-iodo-2-(4-nitrobutyl)phenol (**17g**).

## NMR Data

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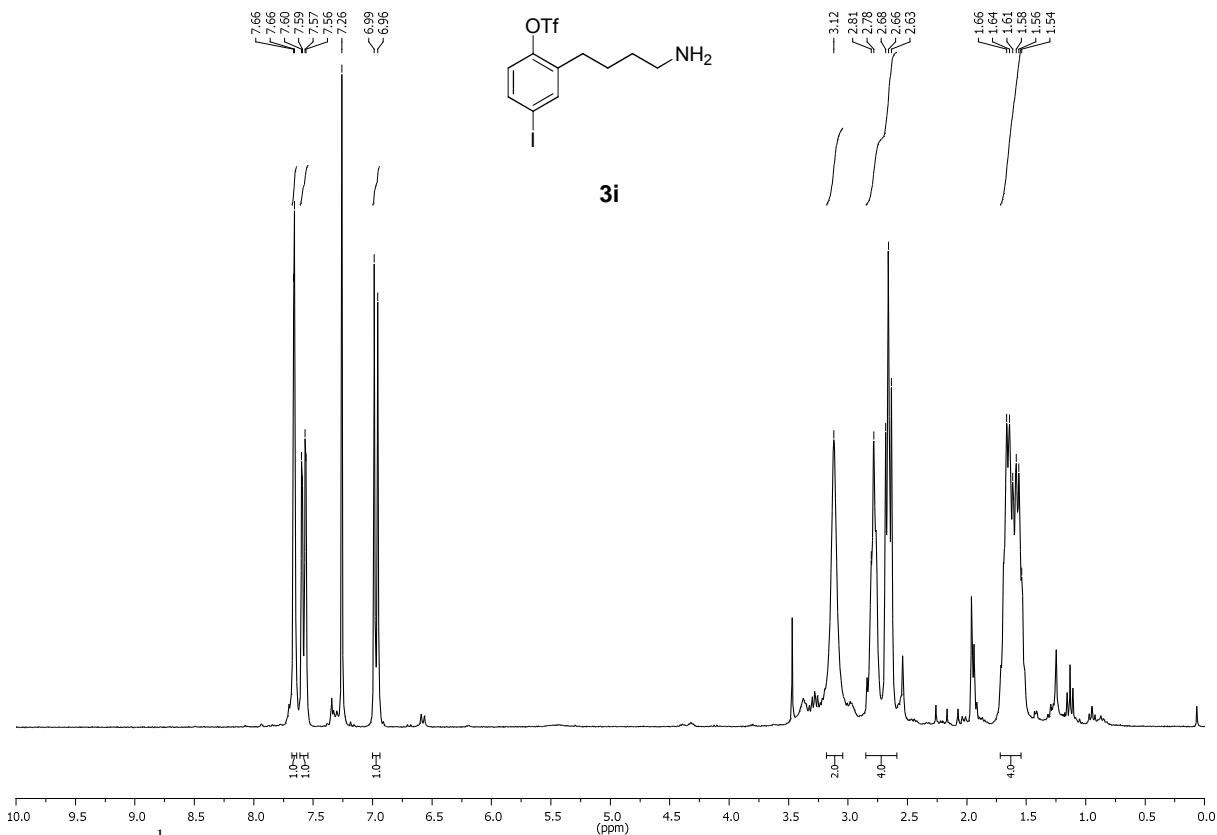
**Figure 35:**  $^1\text{H}$  NMR; 4-iodo-2-(4-nitrobutyl)phenyl trifluoromethanesulfonate (**3g**).



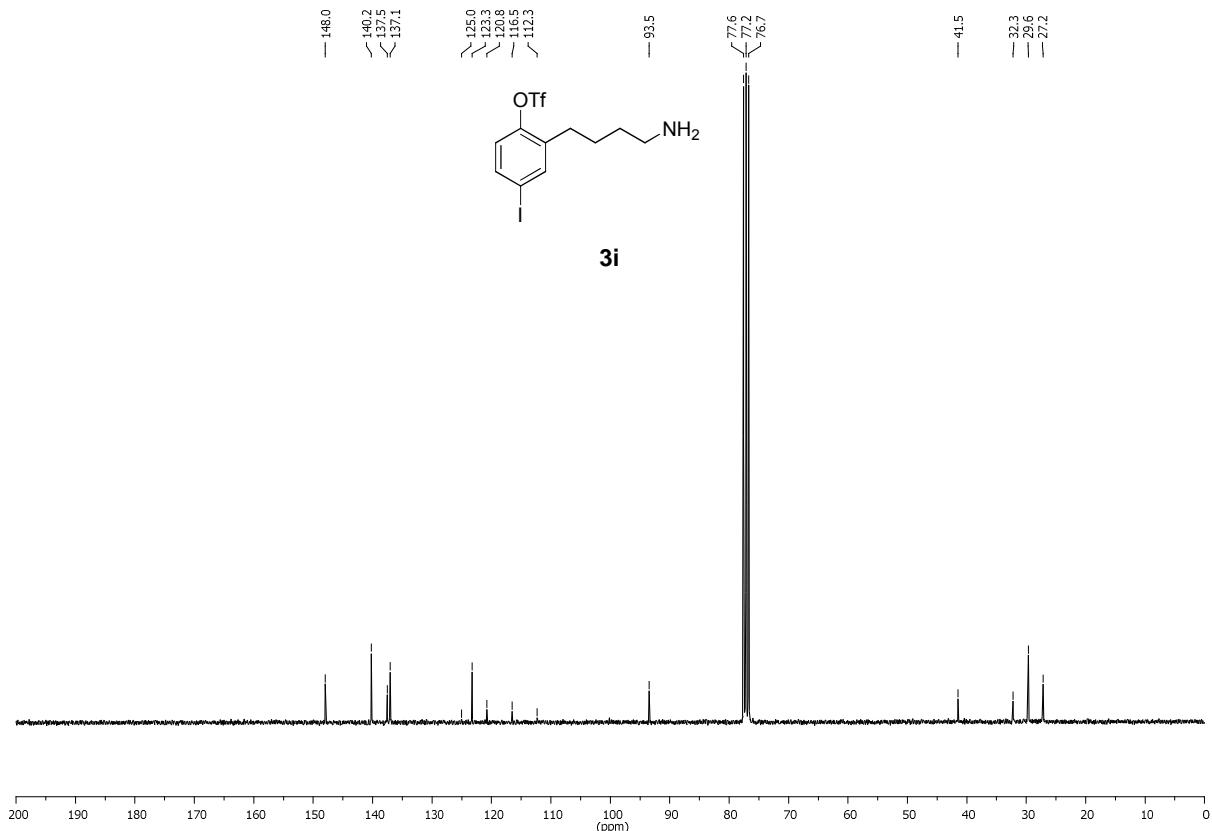
**Figure 36:**  $^{13}\text{C}$  NMR, APT; 4-iodo-2-(4-nitrobutyl)phenyl trifluoromethanesulfonate (**3g**).

## NMR Data

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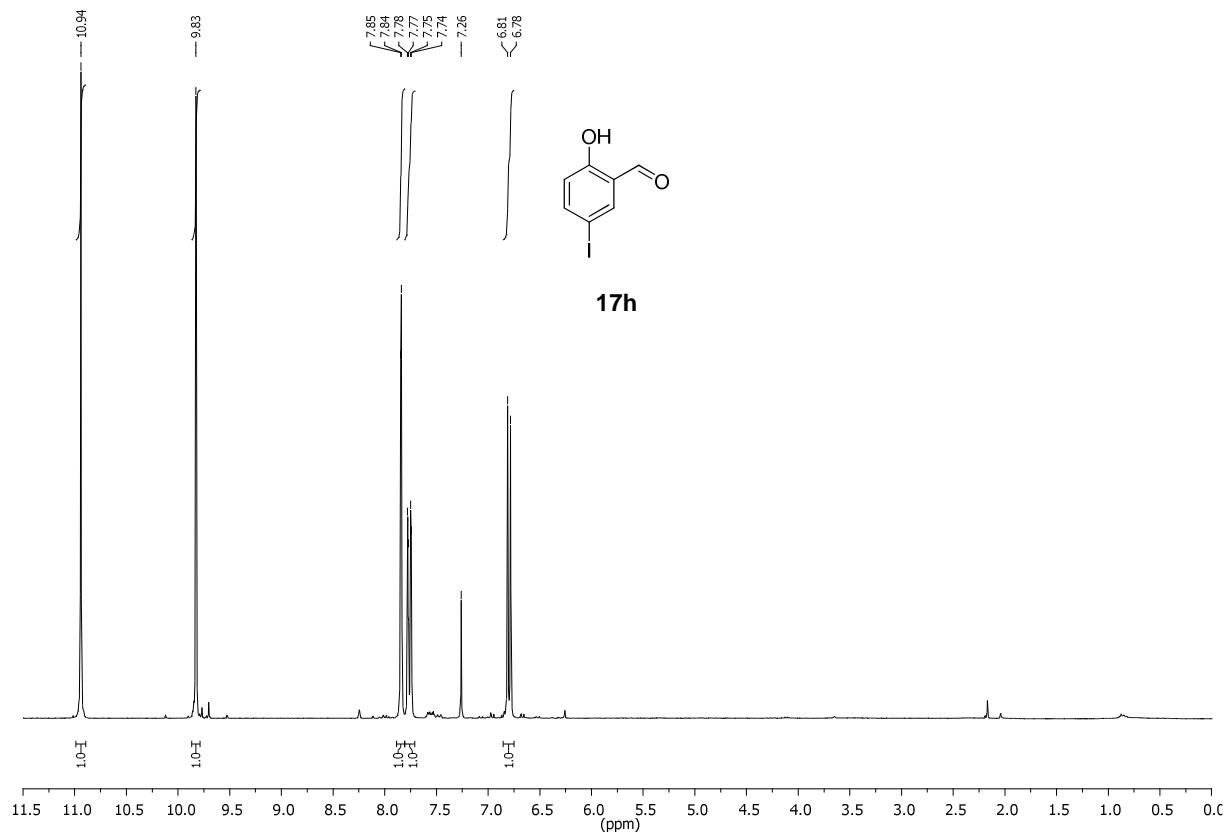
**Figure 37:** <sup>1</sup>H NMR; 2-(4-aminobutyl)-4-iodophenyl trifluoromethanesulfonate (**3i**).



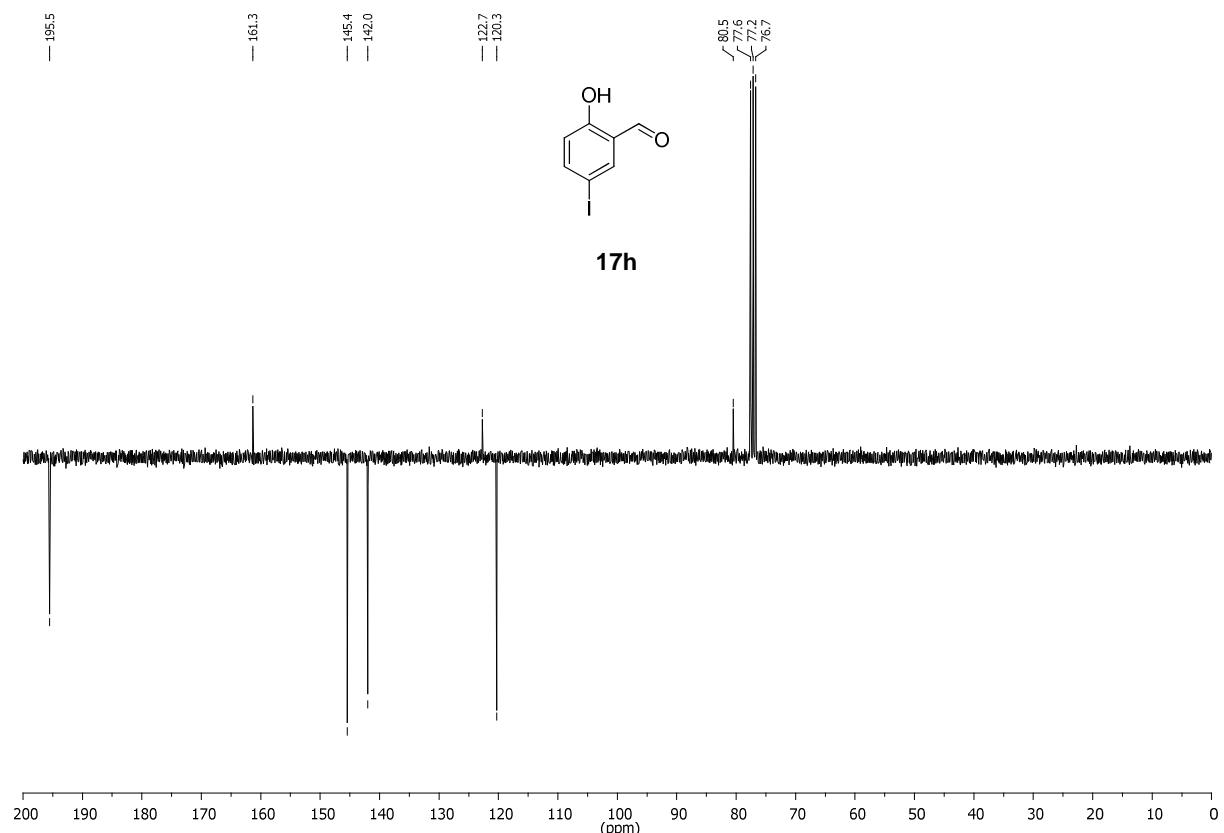
**Figure 38:** <sup>13</sup>C NMR; 2-(4-aminobutyl)-4-iodophenyl trifluoromethanesulfonate (**3i**).

## NMR Data

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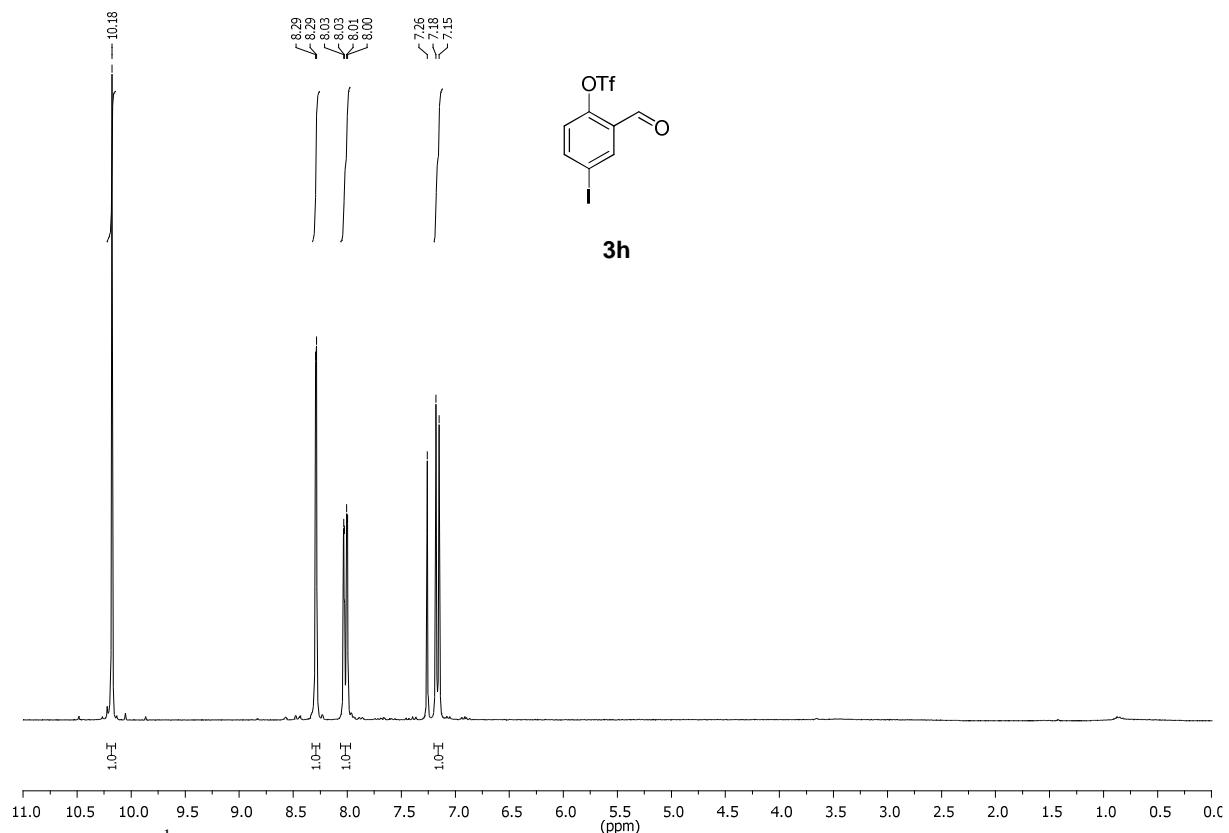
**Figure 39:** <sup>1</sup>H NMR; 2-hydroxy-5-iodobenzaldehyde (17h).



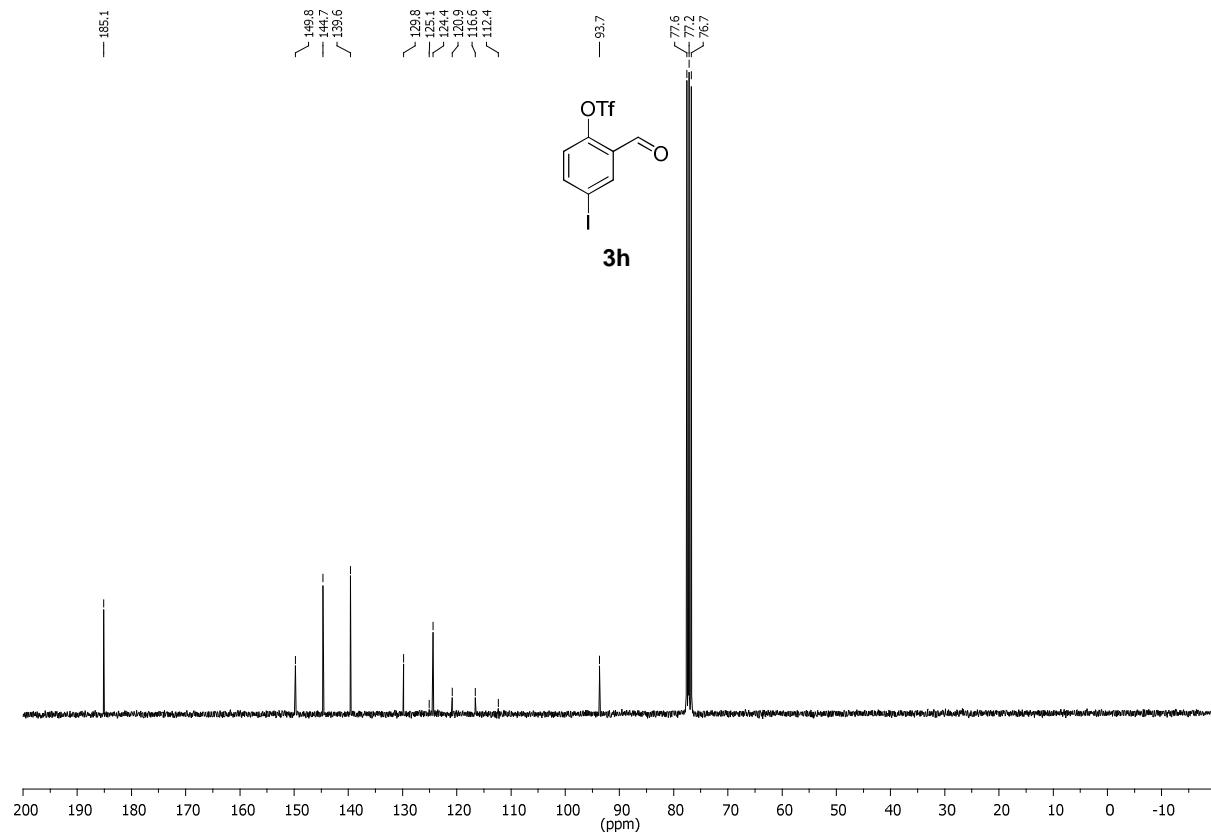
**Figure 40:** <sup>13</sup>C NMR, APT; 2-hydroxy-5-iodobenzaldehyde (17h).

## NMR Data

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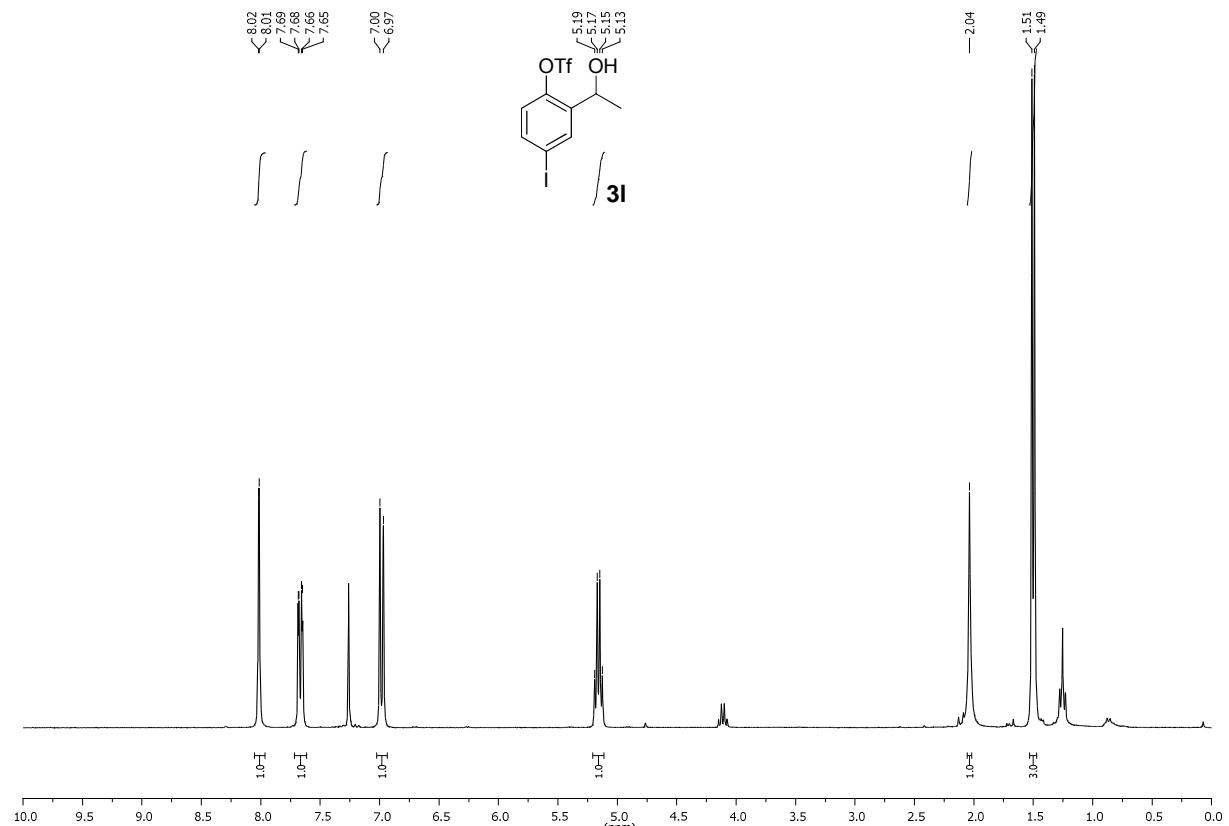
**Figure 41:** <sup>1</sup>H NMR; 2-formyl-4-iodophenyl trifluoromethanesulfonate (**3h**).



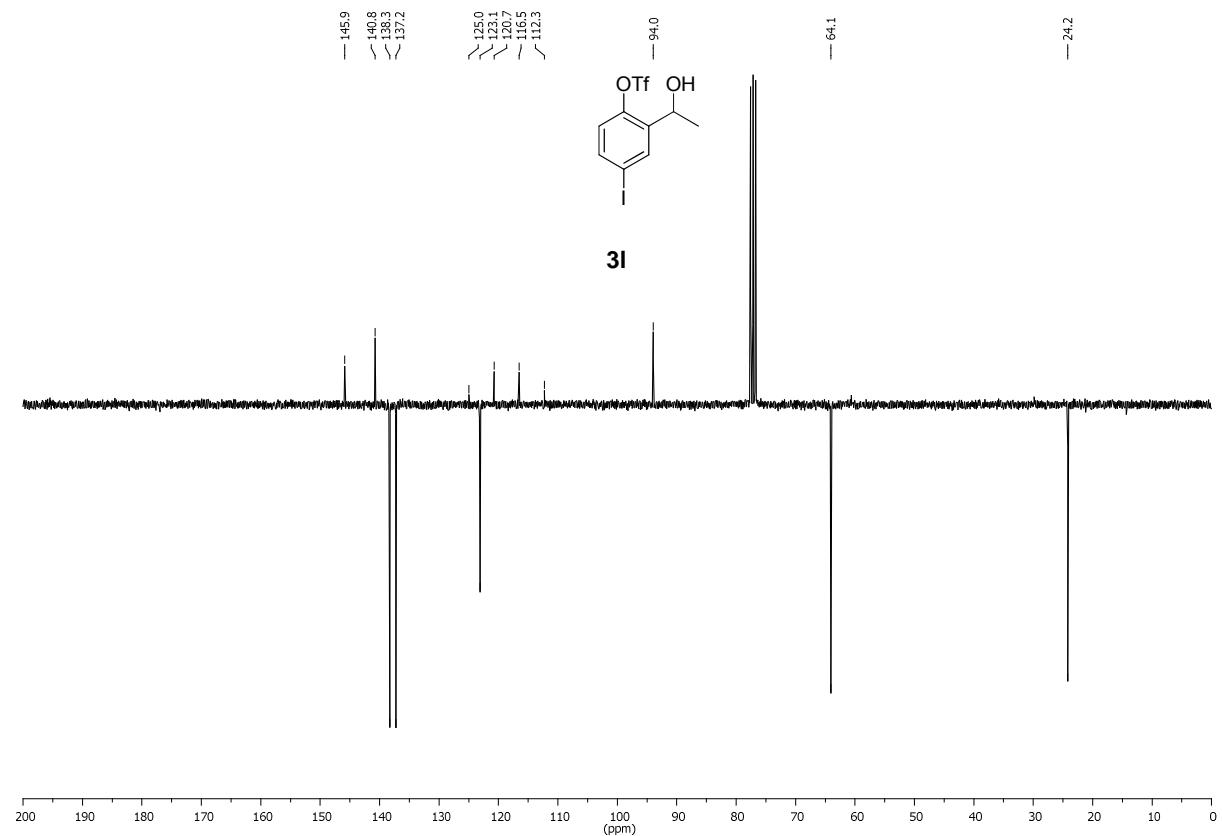
**Figure 42:** <sup>13</sup>C NMR; 2-formyl-4-iodophenyl trifluoromethanesulfonate (**3h**).

## NMR Data

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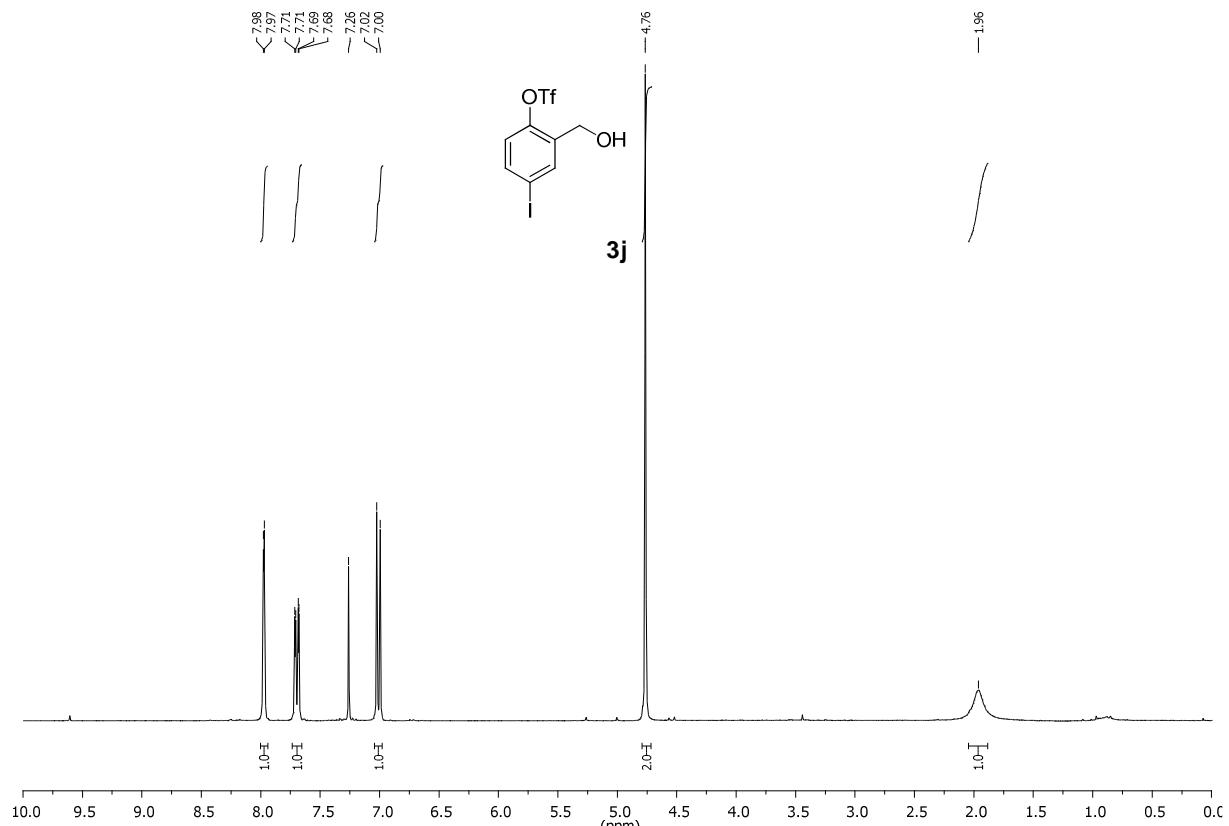
**Figure 43:**  $^1\text{H}$  NMR; 2-(1-hydroxyethyl)-4-iodophenyl trifluoromethanesulfonate (**3l**).



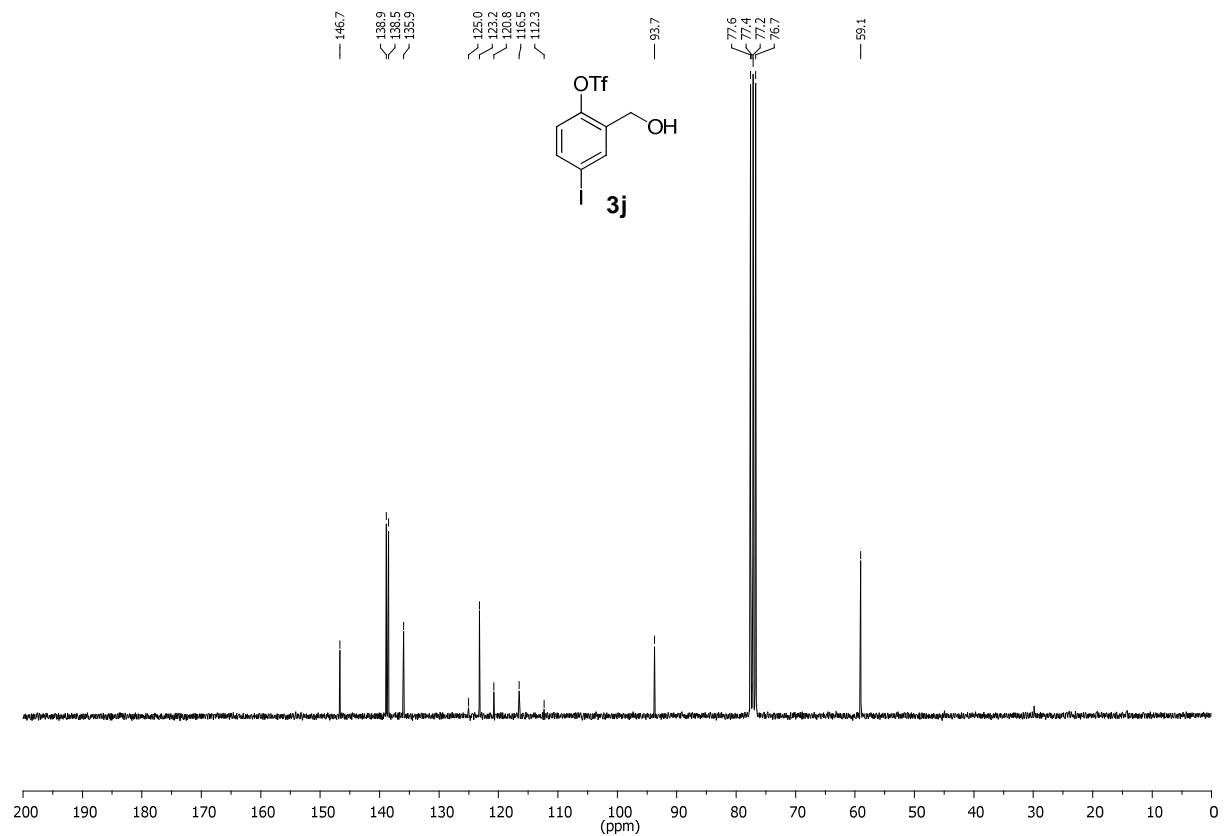
**Figure 44:**  $^{13}\text{C}$  NMR, APT; 2-(1-hydroxyethyl)-4-iodophenyl trifluoromethanesulfonate (**3l**).

## NMR Data

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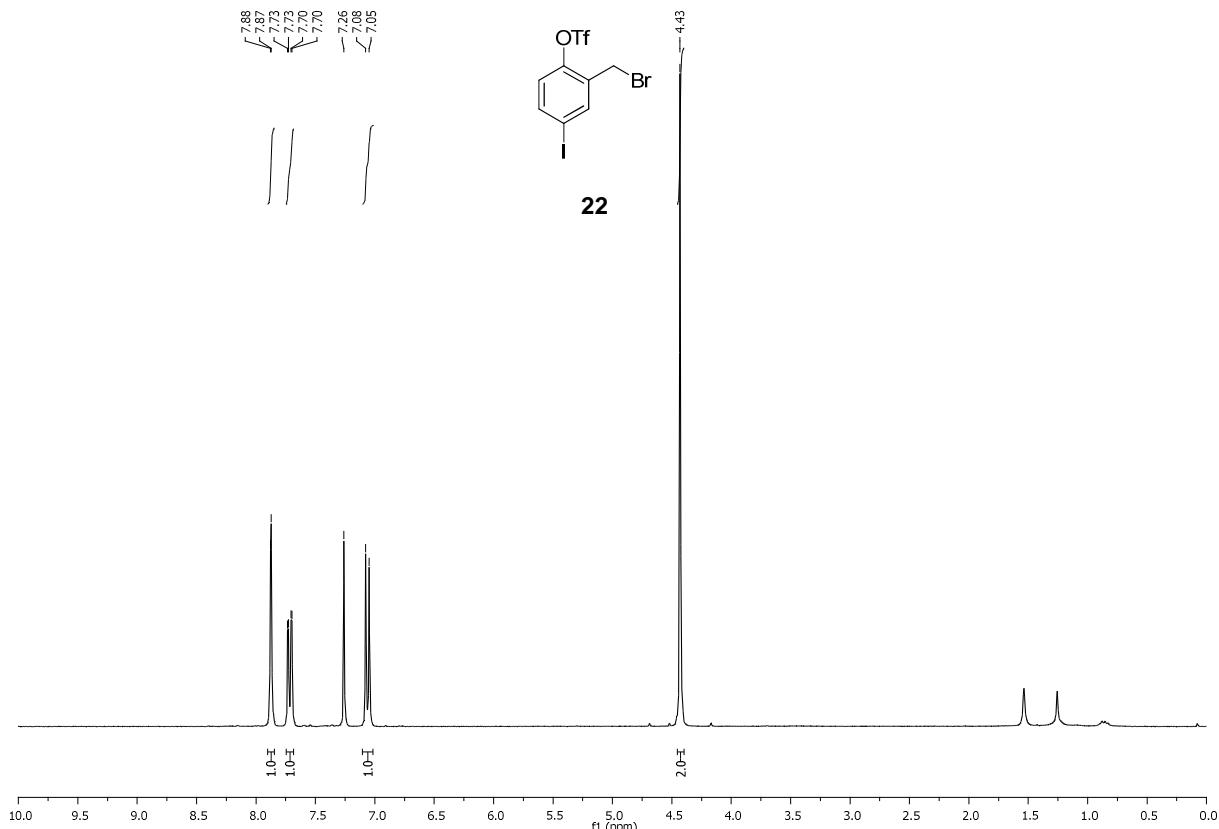
**Figure 45:** <sup>1</sup>H NMR; 2-(hydroxymethyl)-4-iodophenyl trifluoromethanesulfonate (**3j**).



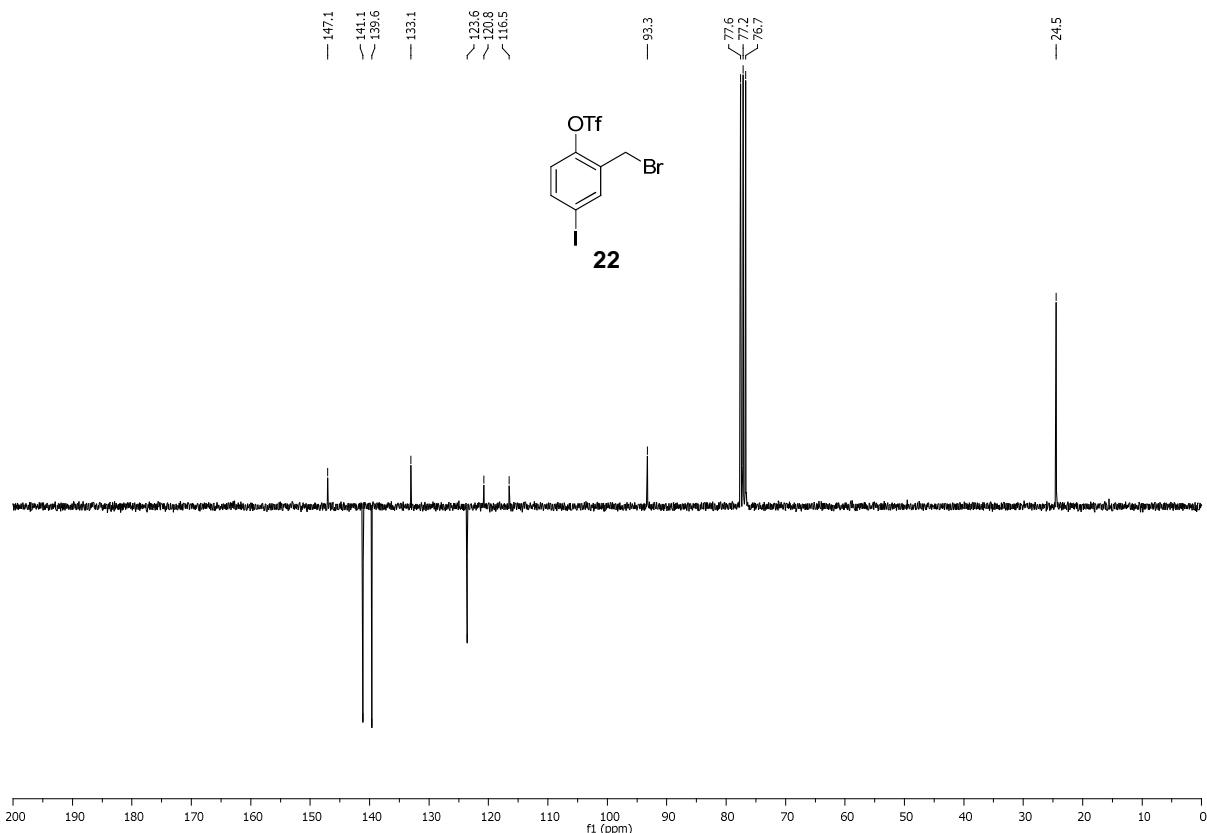
**Figure 46:** <sup>13</sup>C NMR; 2-(hydroxymethyl)-4-iodophenyl trifluoromethanesulfonate (**3j**).

## NMR Data

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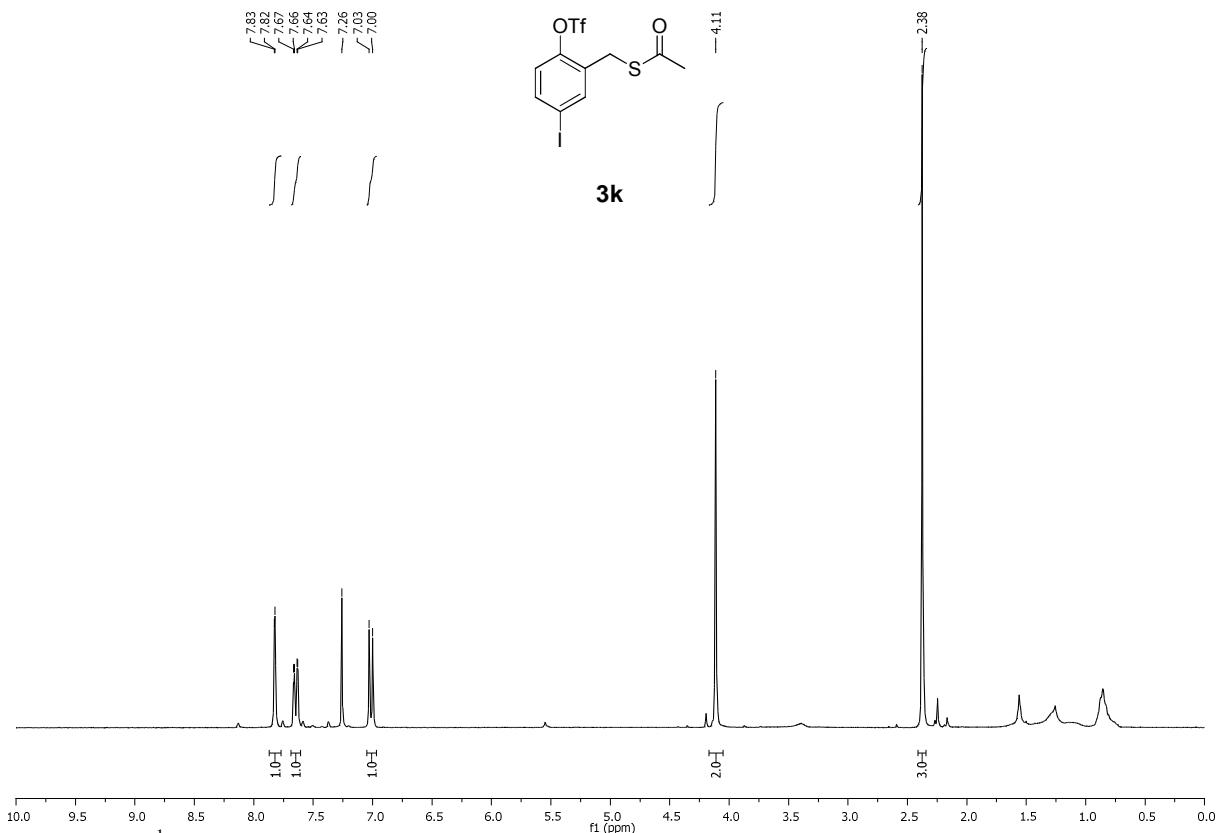
**Figure 47:** <sup>1</sup>H NMR; 2-(bromomethyl)-4-iodophenyl trifluoromethanesulfonate (**22**).



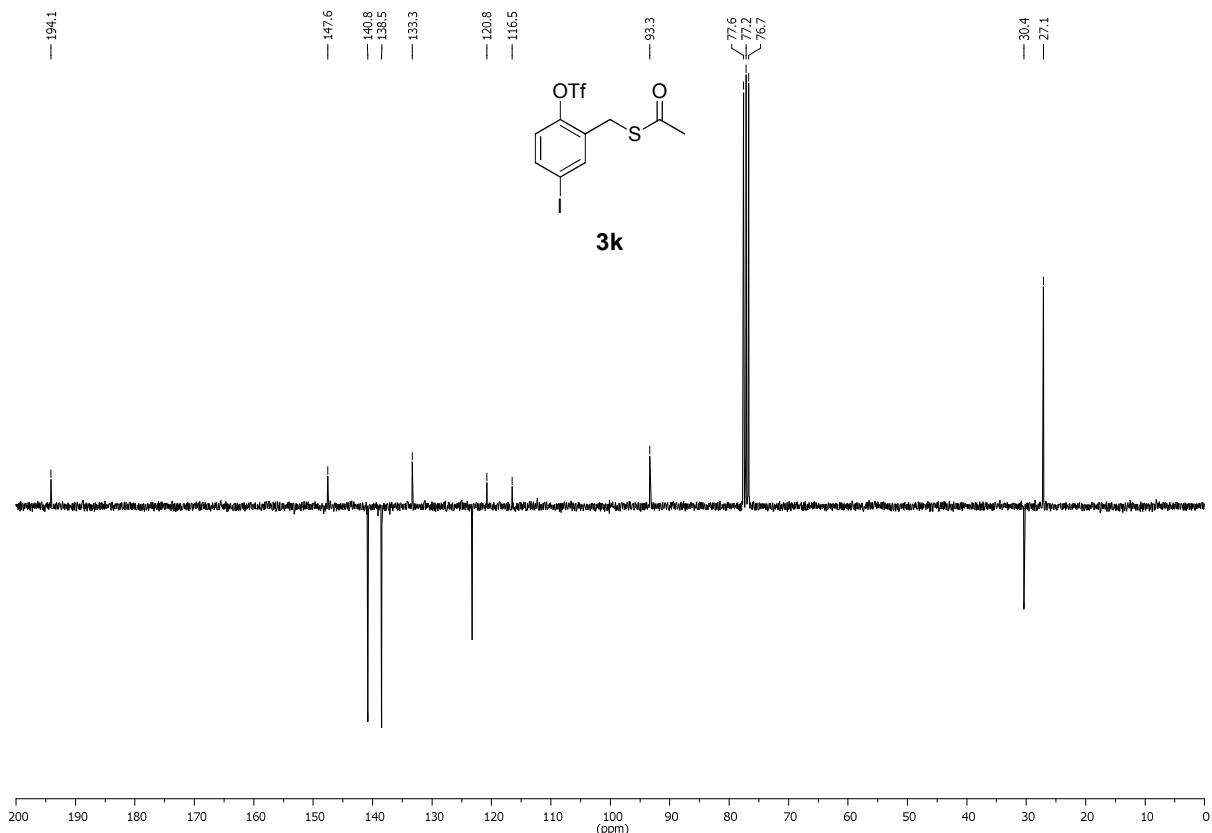
**Figure 48:** <sup>13</sup>C NMR, APT; 2-(bromomethyl)-4-iodophenyl trifluoromethanesulfonate (**22**).

## NMR Data

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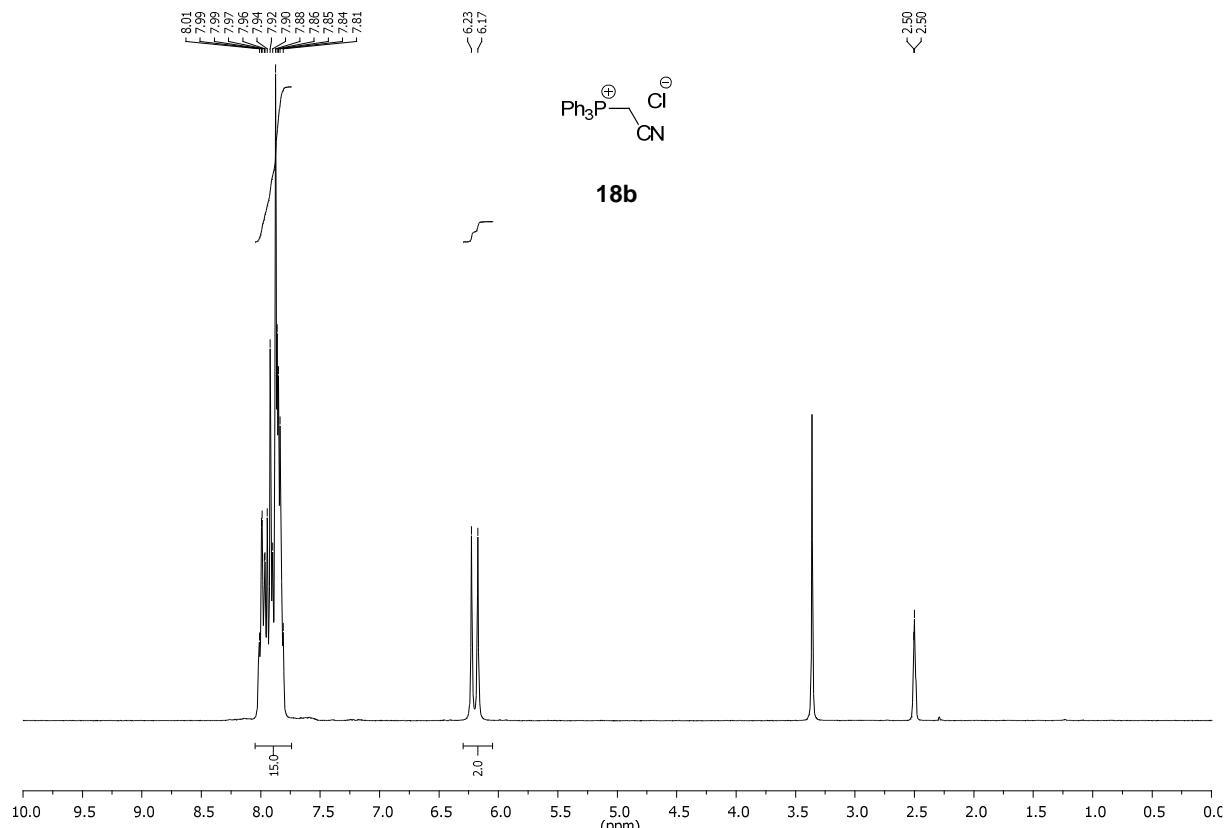
**Figure 49:** <sup>1</sup>H NMR; S-5-iodo-2-((trifluoromethyl)sulfonyloxy)benzyl ethanethioate (**3k**).



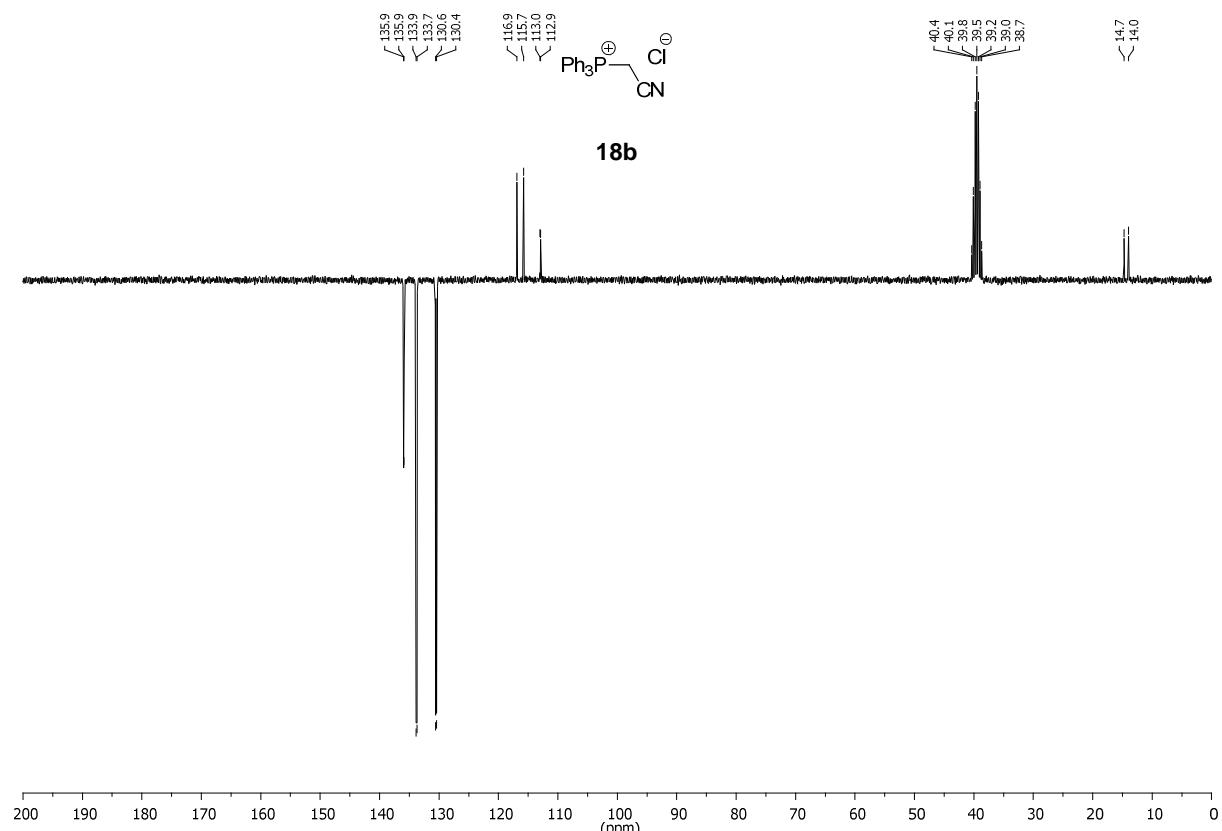
**Figure 50:** <sup>13</sup>C NMR, APT; S-5-iodo-2-((trifluoromethyl)sulfonyloxy)benzyl ethanethioate (**3k**).

## NMR Data

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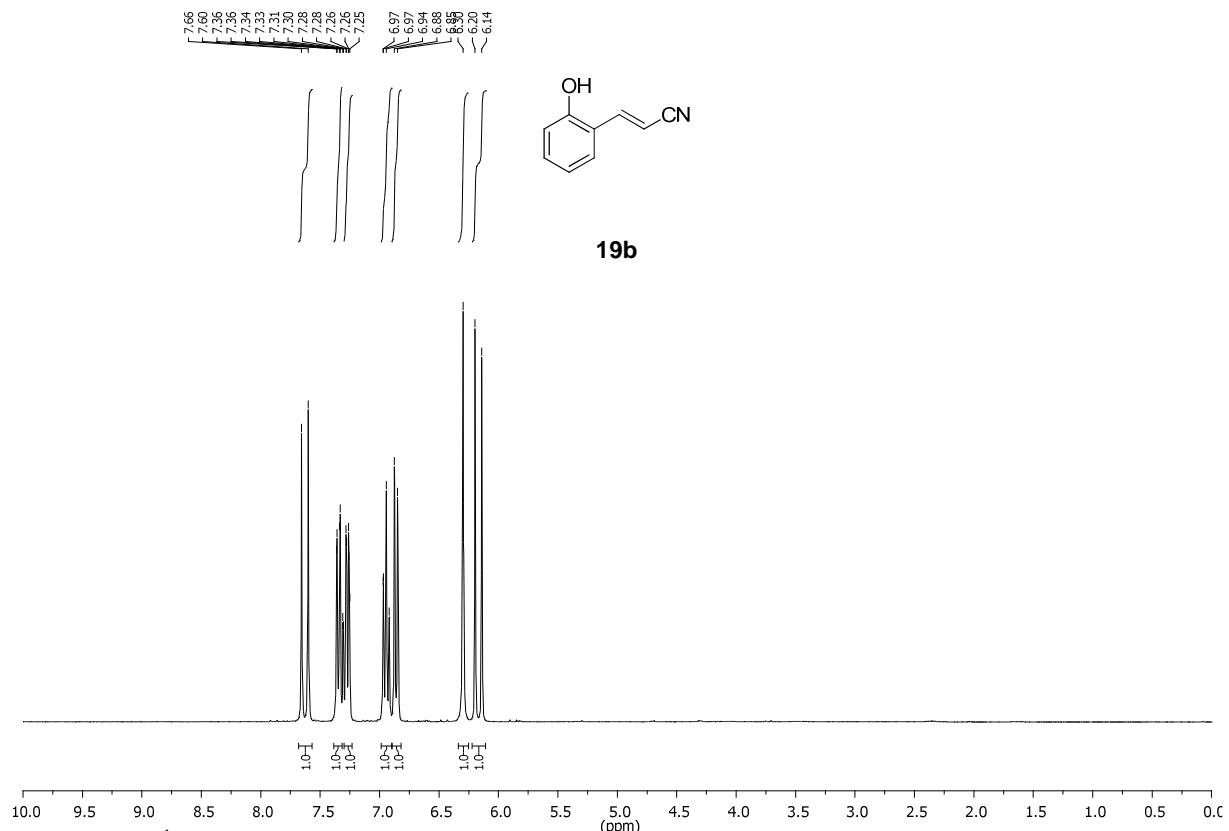
**Figure 51:** <sup>1</sup>H NMR; (cyanomethyl)triphenylphosphonium chloride (**18b**).



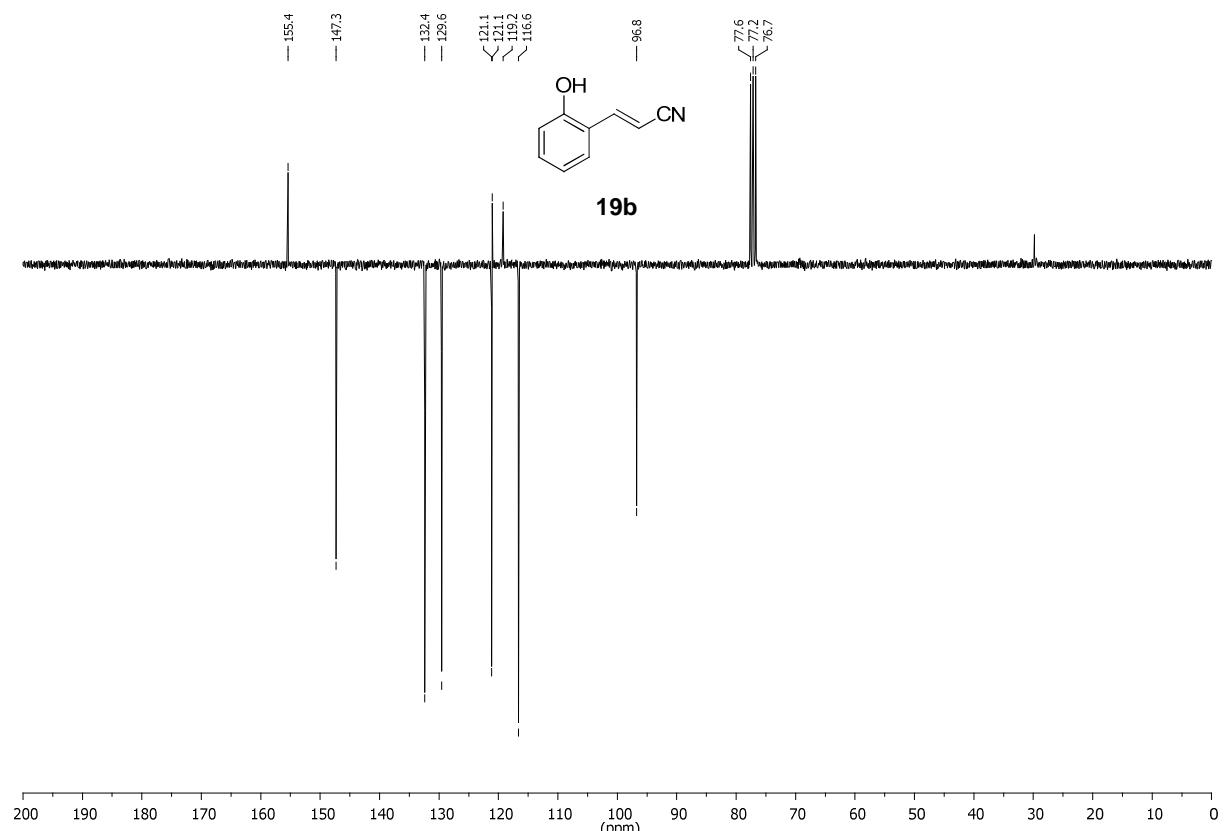
**Figure 52:** <sup>13</sup>C NMR, APT; (cyanomethyl)triphenylphosphonium chloride (**18b**).

## NMR Data

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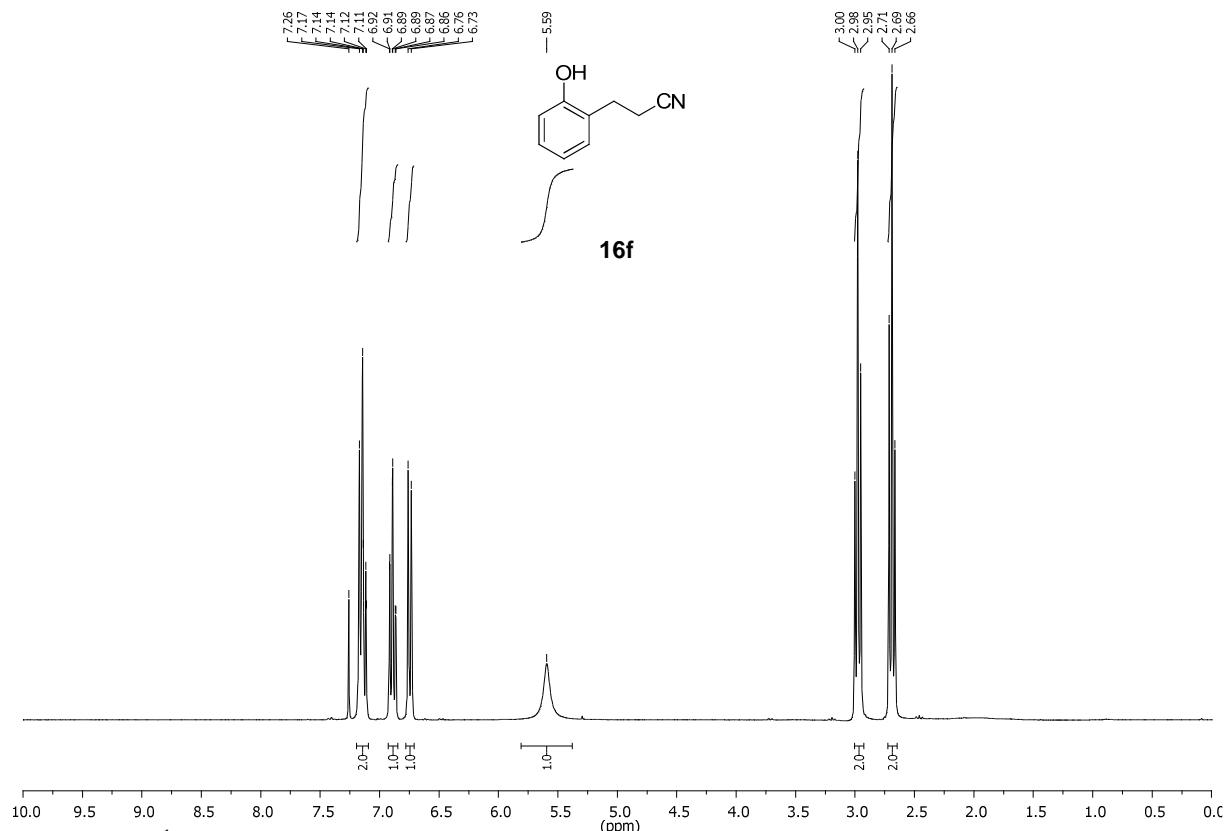
**Figure 53:** <sup>1</sup>H NMR; 3-(2-hydroxyphenyl)acrylonitrile (**19b**).



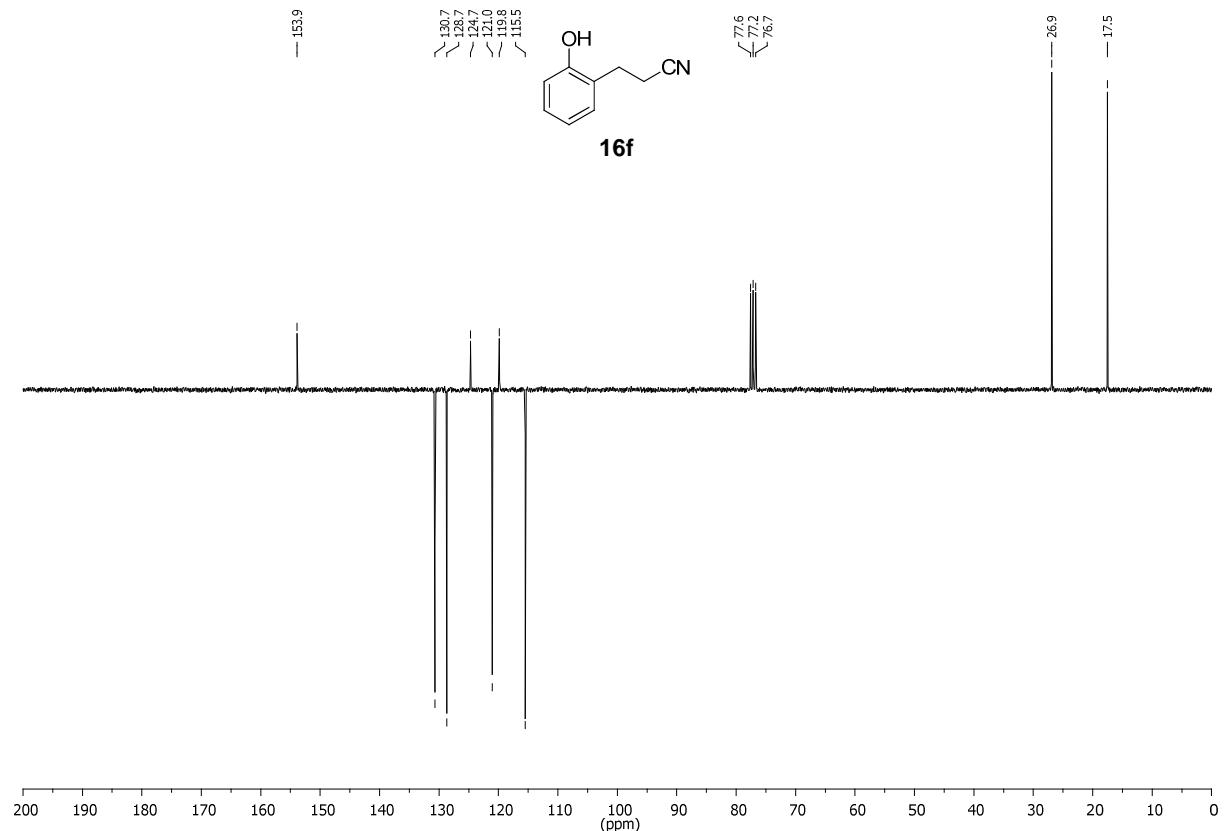
**Figure 54:** <sup>13</sup>C NMR, APT; 3-(2-hydroxyphenyl)acrylonitrile (**19b**).

## NMR Data

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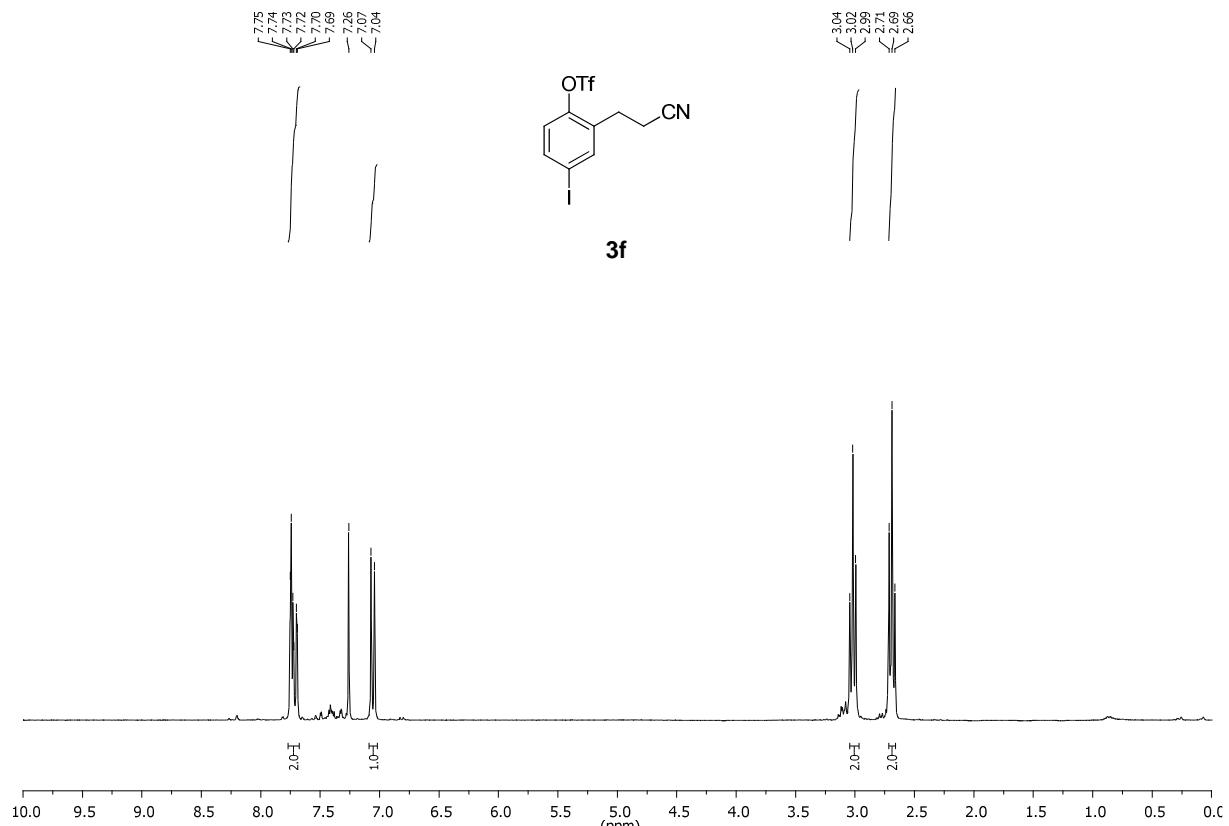
**Figure 55:** <sup>1</sup>H NMR; 3-(2-hydroxyphenyl)propanenitrile (**16f**).



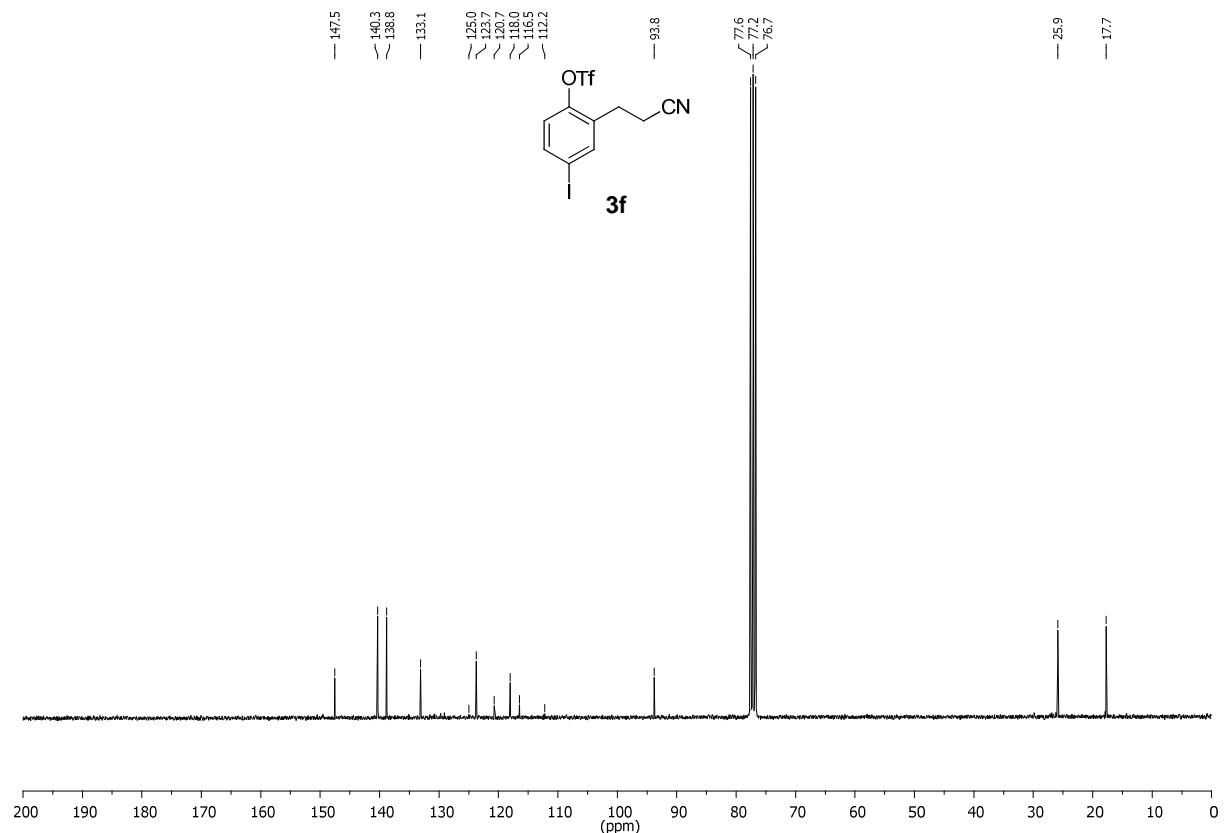
**Figure 56:** <sup>13</sup>C NMR, APT; 3-(2-hydroxyphenyl)propanenitrile (**16f**).

## NMR Data

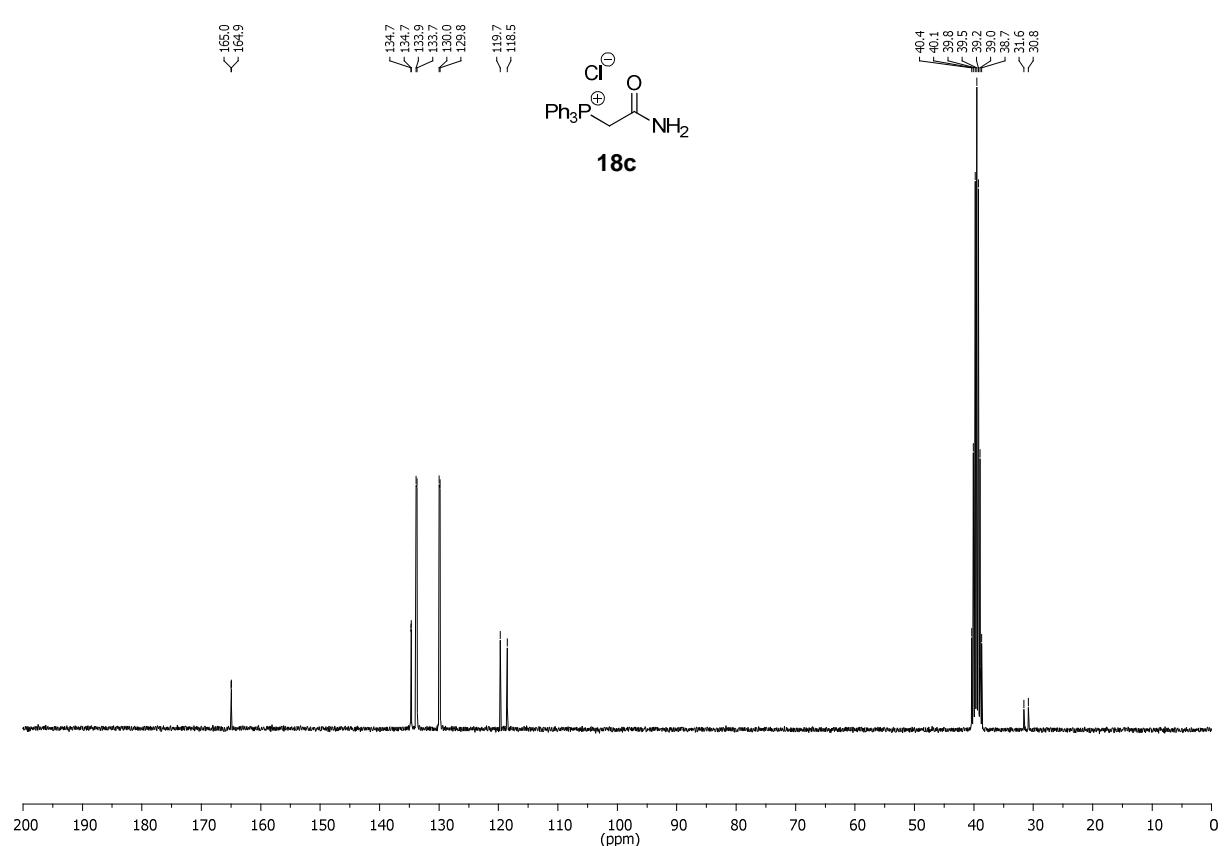
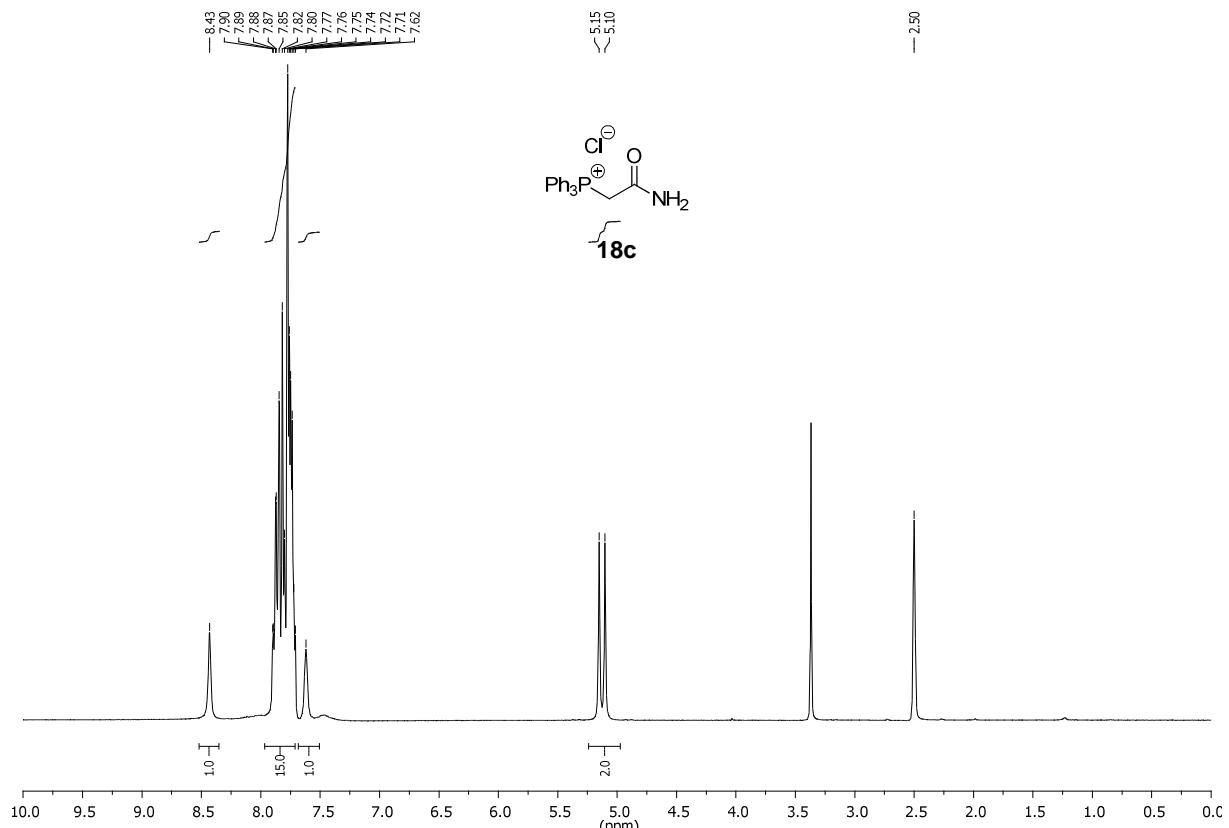
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**Figure 57:** <sup>1</sup>H NMR; 2-(2-cyanoethyl)-4-iodophenyl trifluoromethanesulfonate (**3f**).

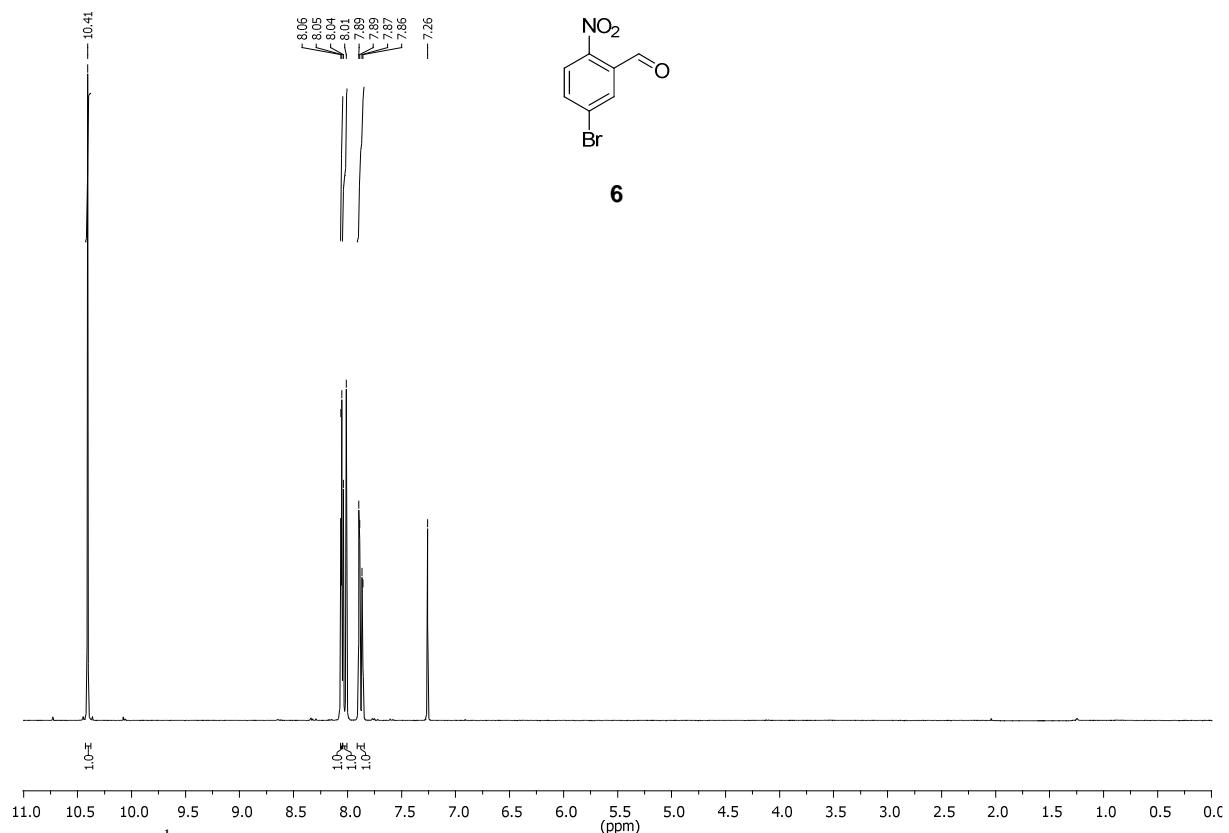


**Figure 58:** <sup>13</sup>C NMR; 2-(2-cyanoethyl)-4-iodophenyl trifluoromethanesulfonate (**3f**).

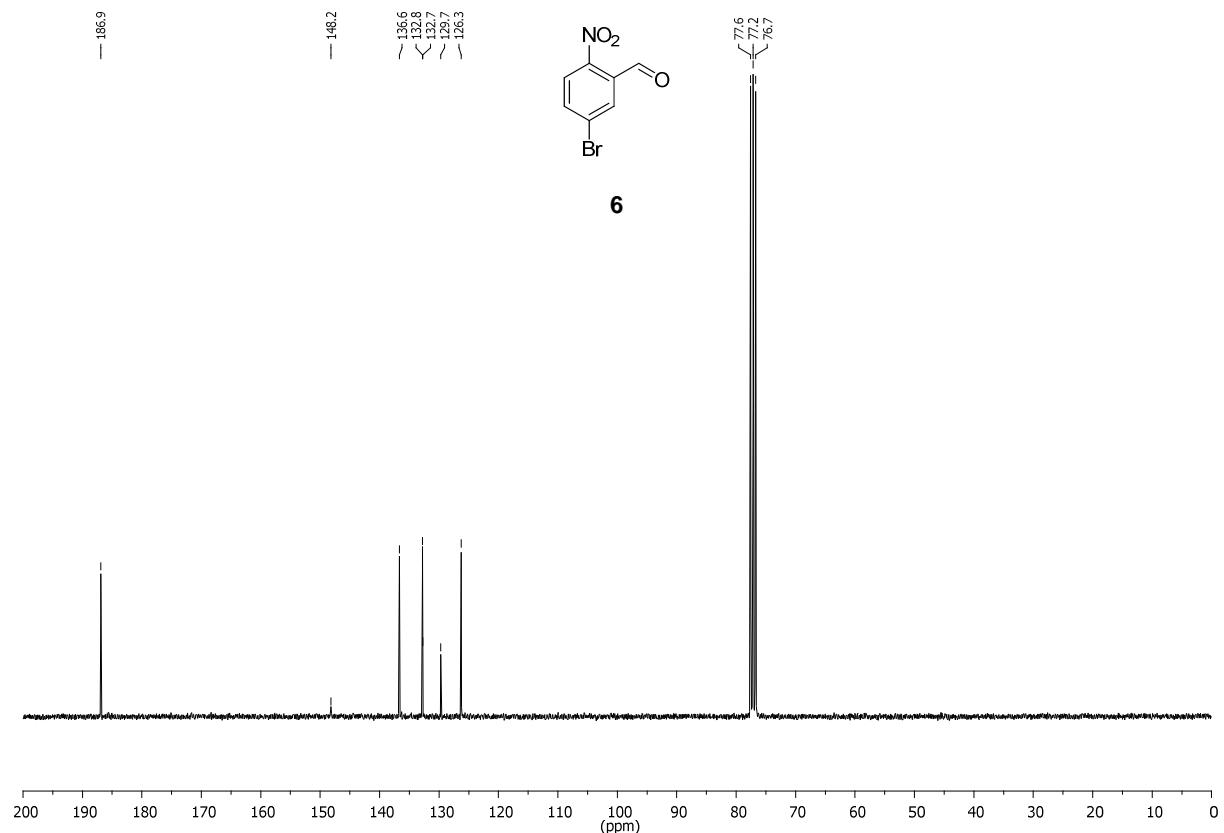


## NMR Data

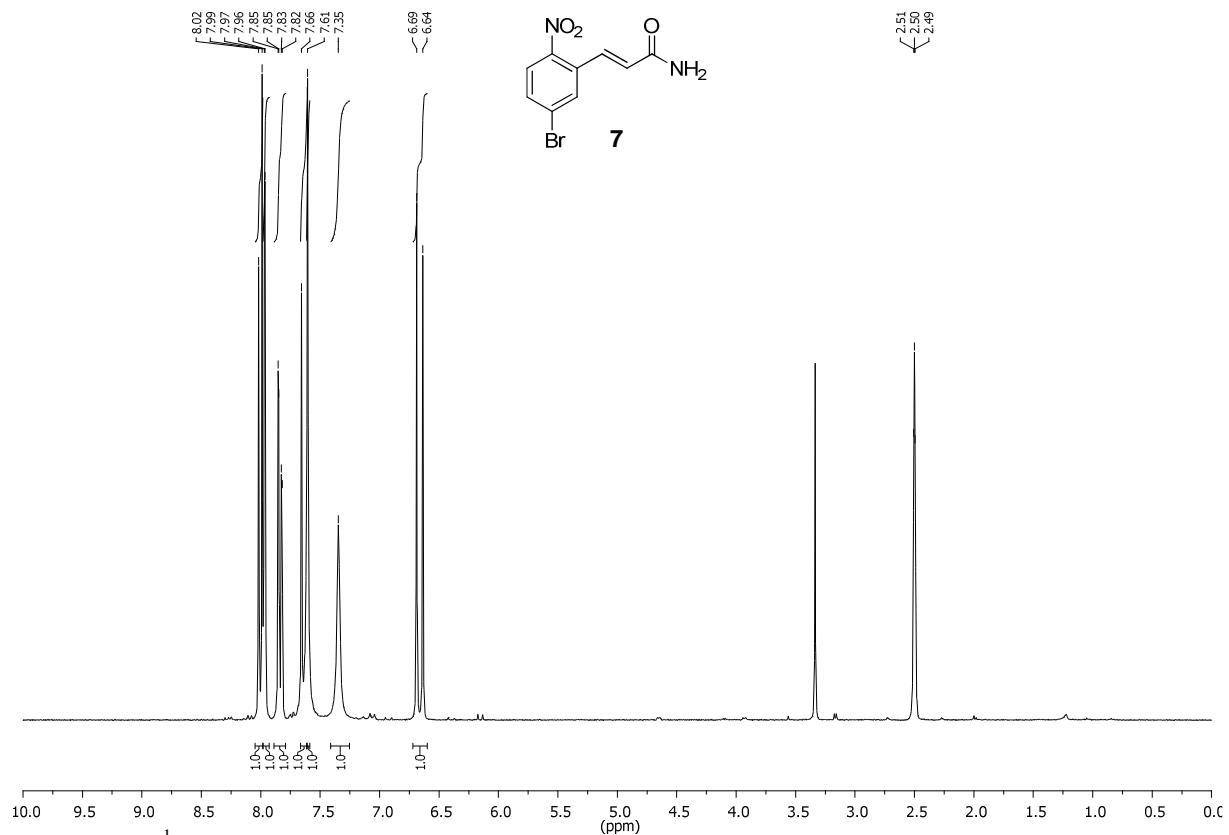
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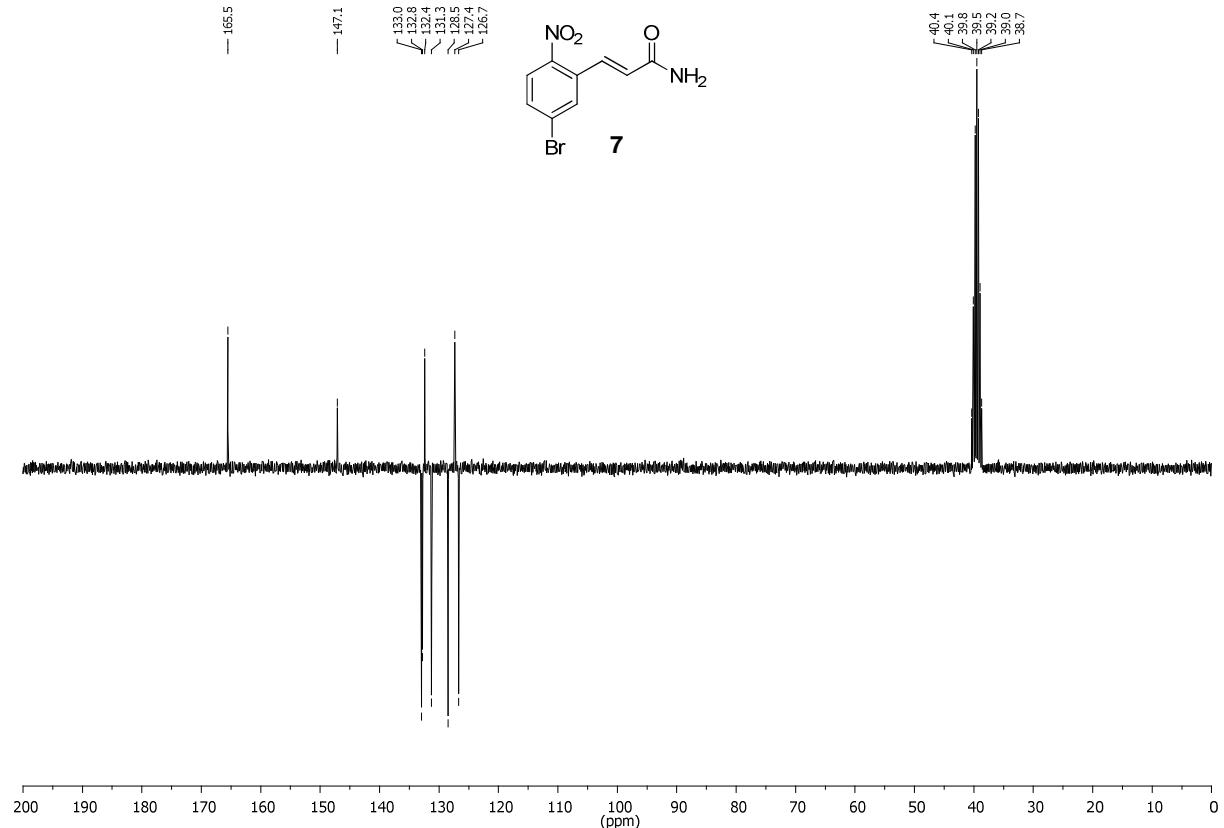
**Figure 61:** <sup>1</sup>H NMR; 5-bromo-2-nitrobenzaldehyde (**6**).



**Figure 62:** <sup>13</sup>C NMR; 5-bromo-2-nitrobenzaldehyde (**6**).



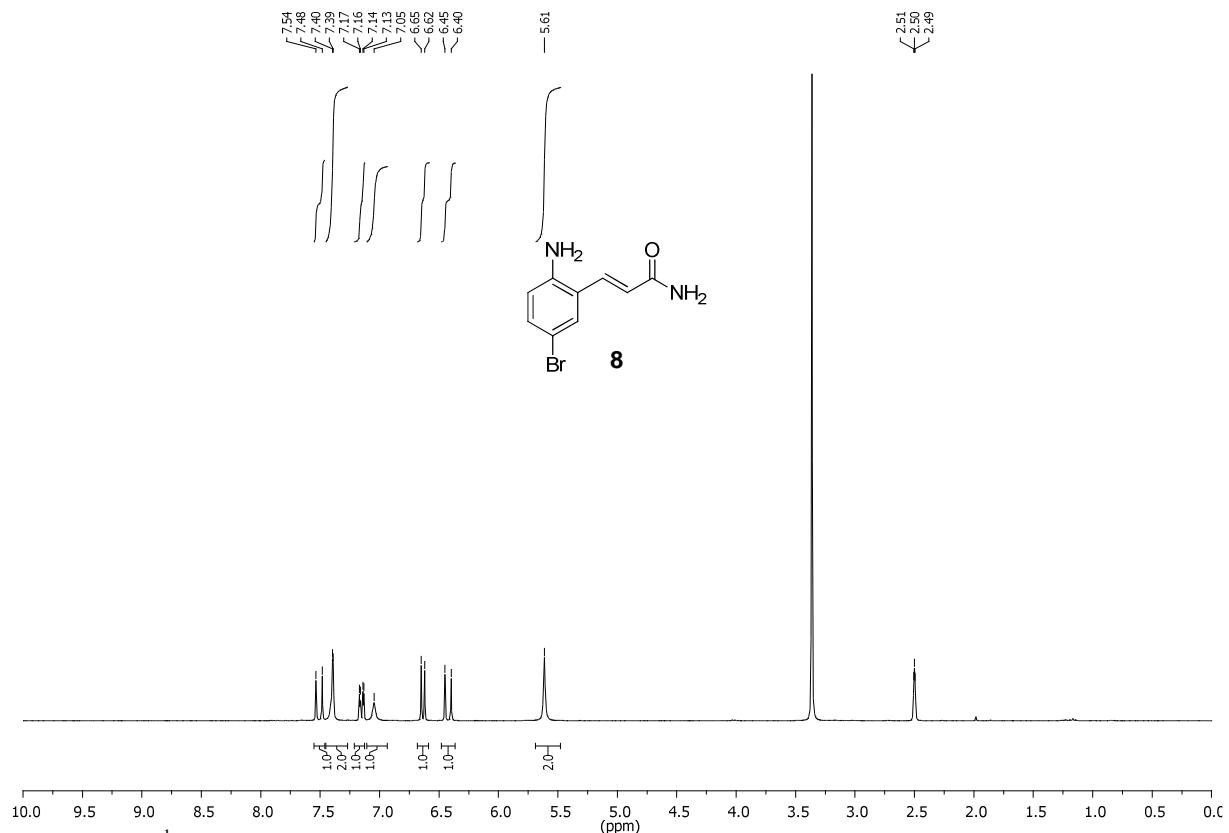
**Figure 63:**  $^1\text{H}$  NMR; (*E*)-3-(5-bromo-2-nitrophenyl)acrylamide (**7**).



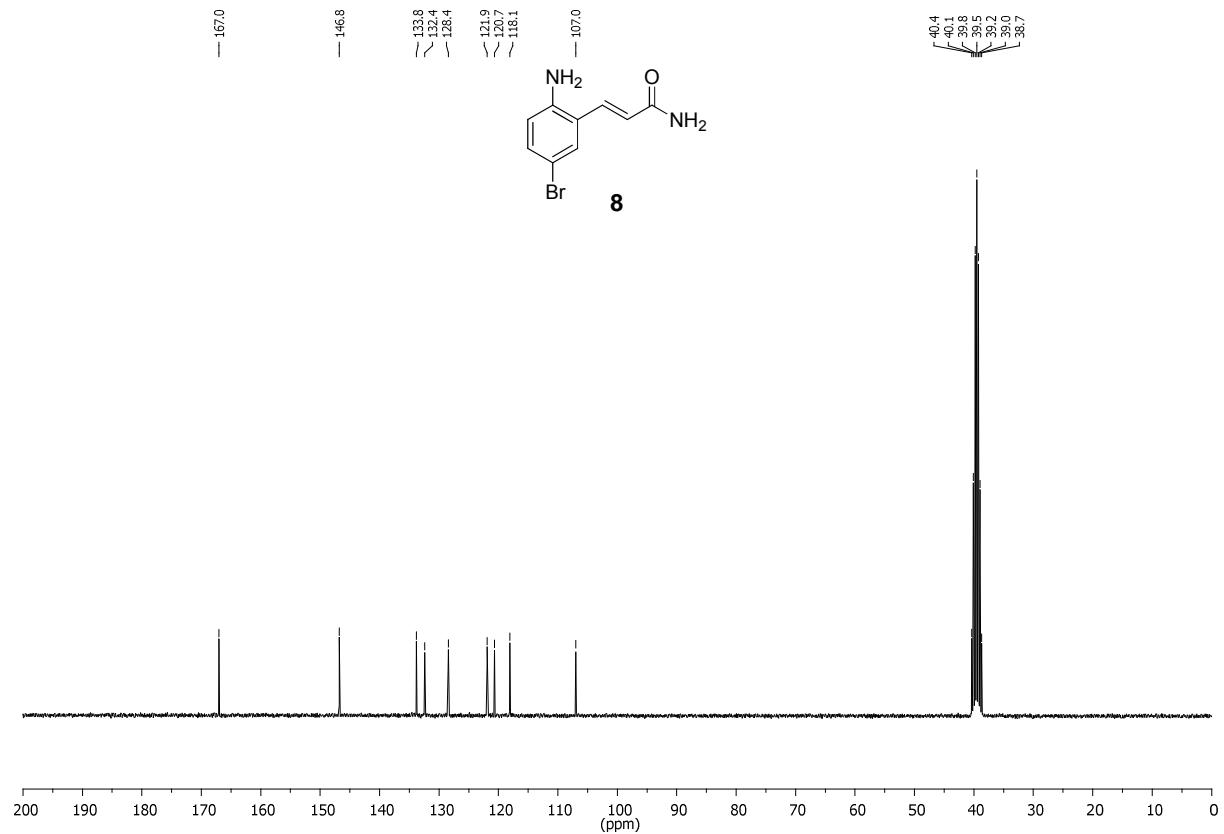
**Figure 64:**  $^{13}\text{C}$  NMR, APT; (*E*-3-(5-bromo-2-nitrophenyl)acrylamide (**7**)).

## NMR Data

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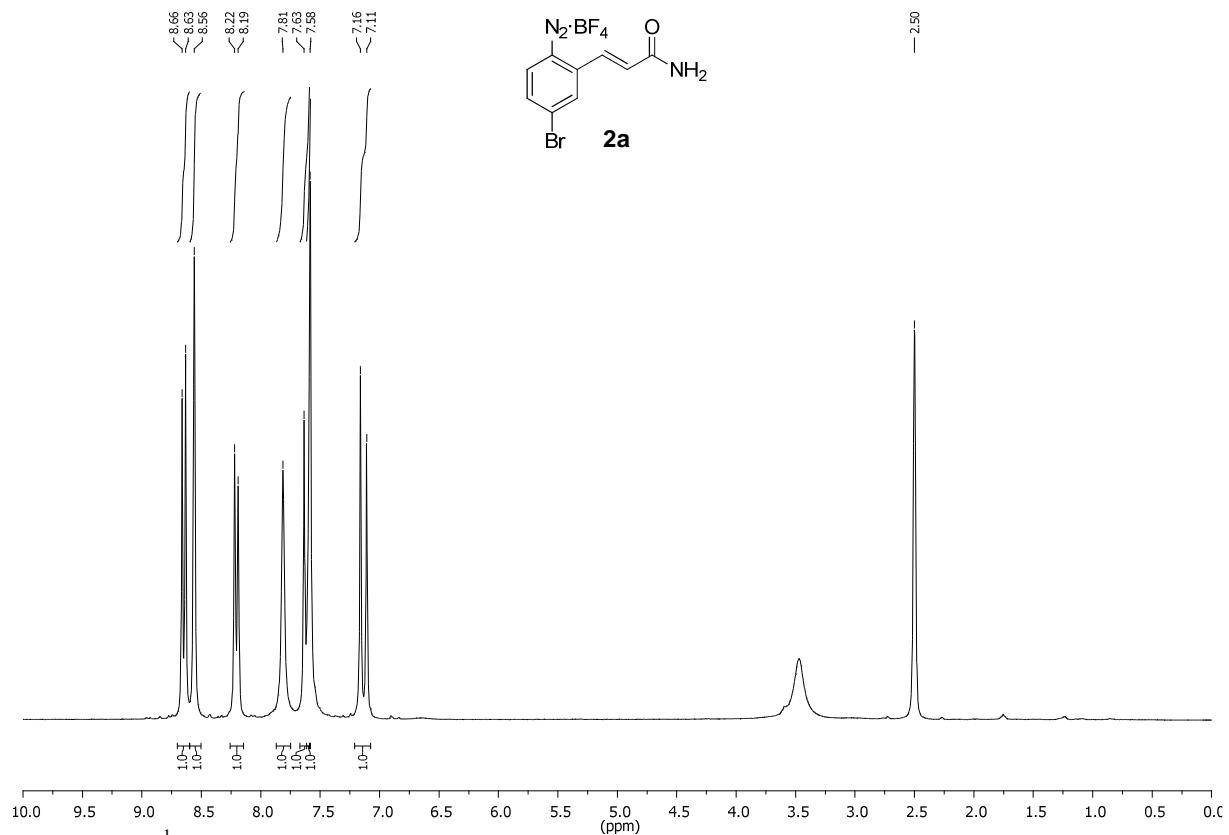
**Figure 65:** <sup>1</sup>H NMR; (*E*)-3-(2-amino-5-bromophenyl)acrylamide (**8**).



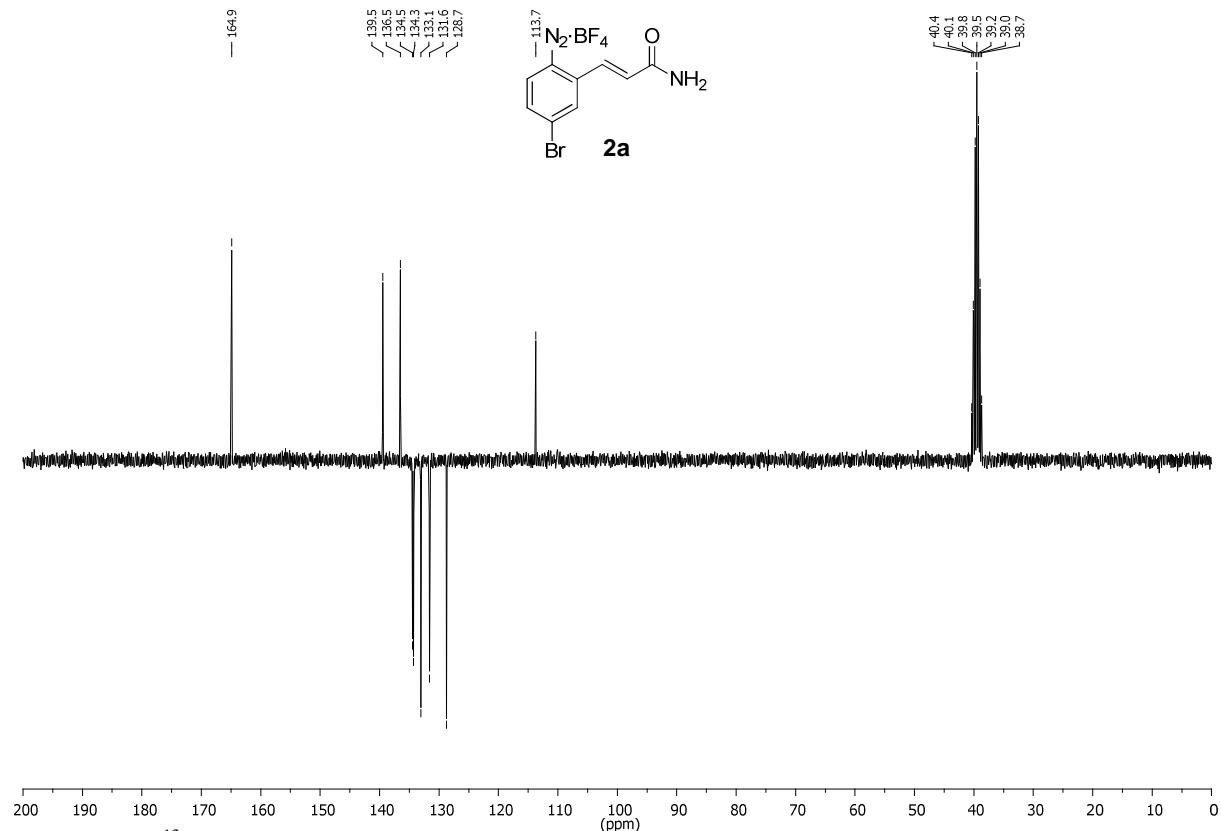
**Figure 66:** <sup>13</sup>C NMR; (*E*)-3-(2-amino-5-bromophenyl)acrylamide (**8**).

## NMR Data

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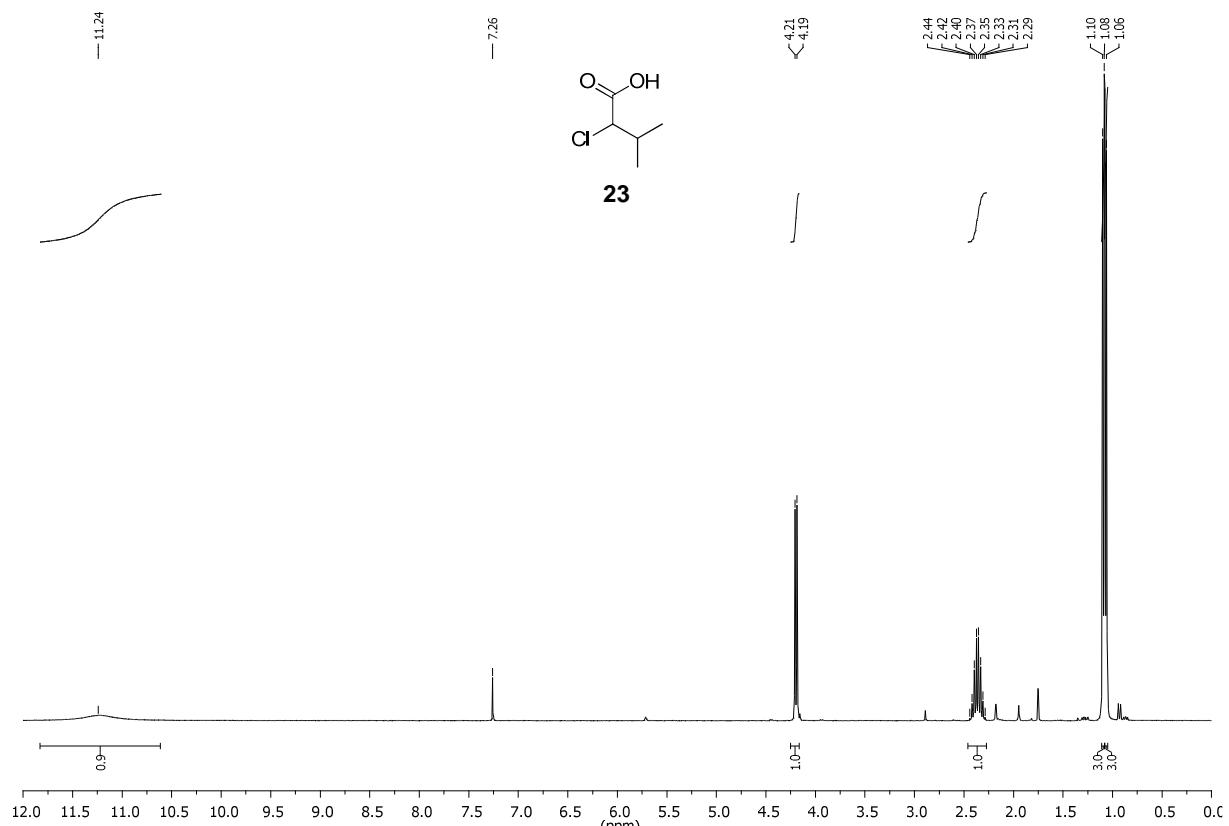
**Figure 67:** <sup>1</sup>H NMR; (*E*)-2-(3-amino-3-oxoprop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (**2a**).



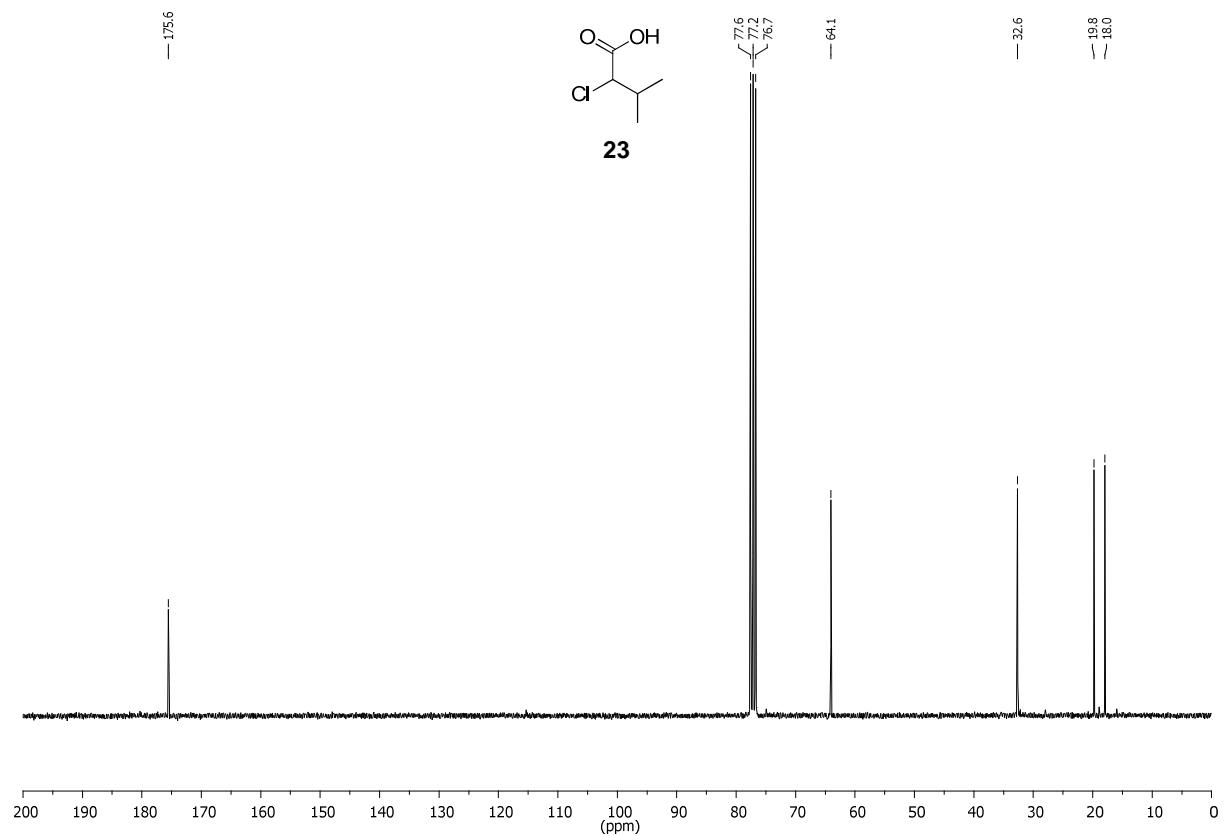
**Figure 68:** <sup>13</sup>C NMR, APT; (*E*)-2-(3-amino-3-oxoprop-1-en-1-yl)-4-bromobenzenediazonium tetrafluoroborate (**2a**).

## NMR Data

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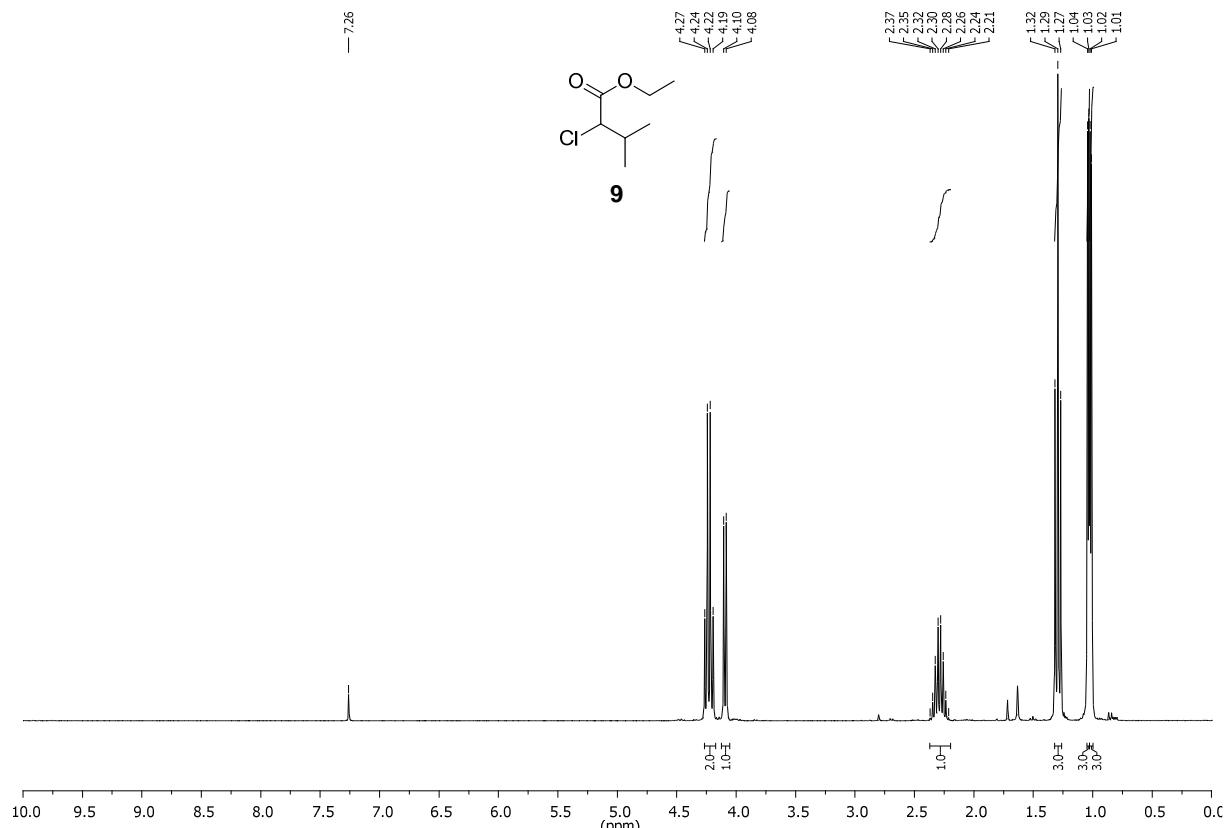
**Figure 69:** <sup>1</sup>H NMR; 2-chloro-3-methylbutanoic acid (**23**).



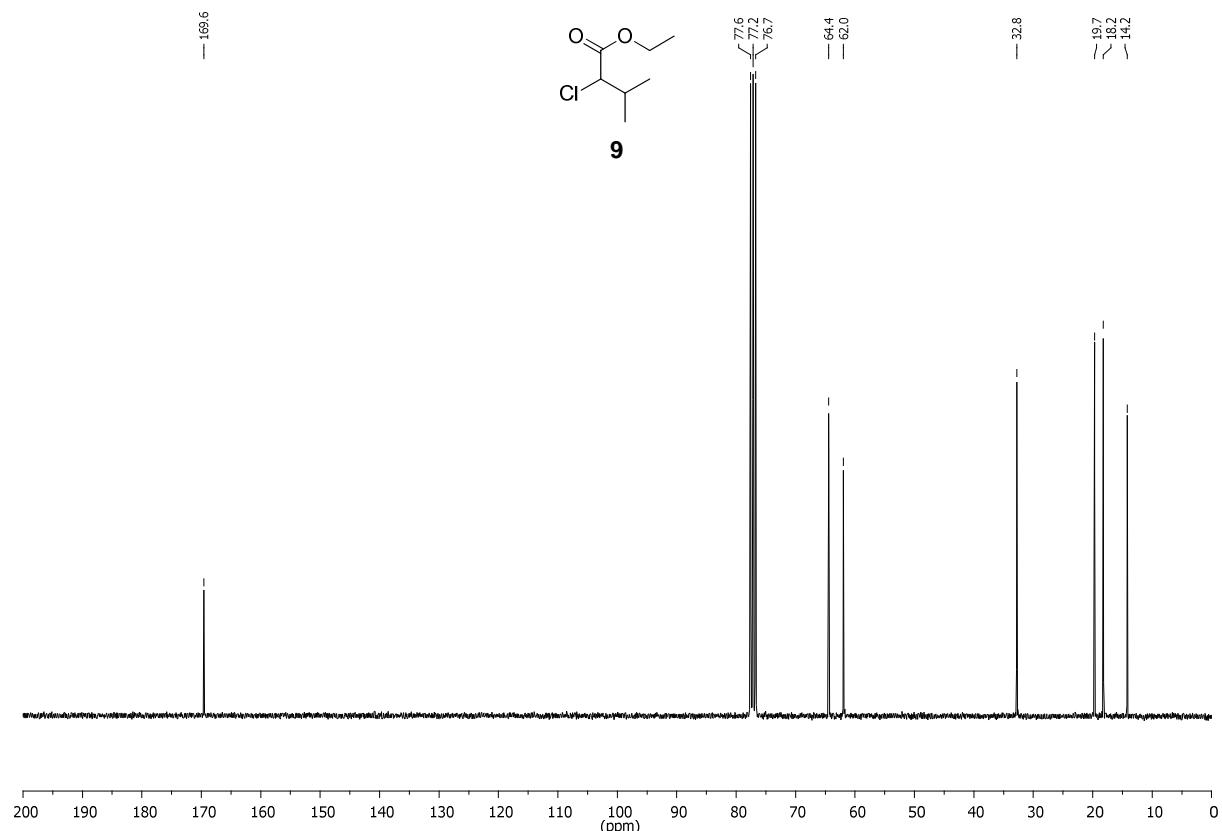
**Figure 70:** <sup>13</sup>C NMR; 2-chloro-3-methylbutanoic acid (**23**).

## NMR Data

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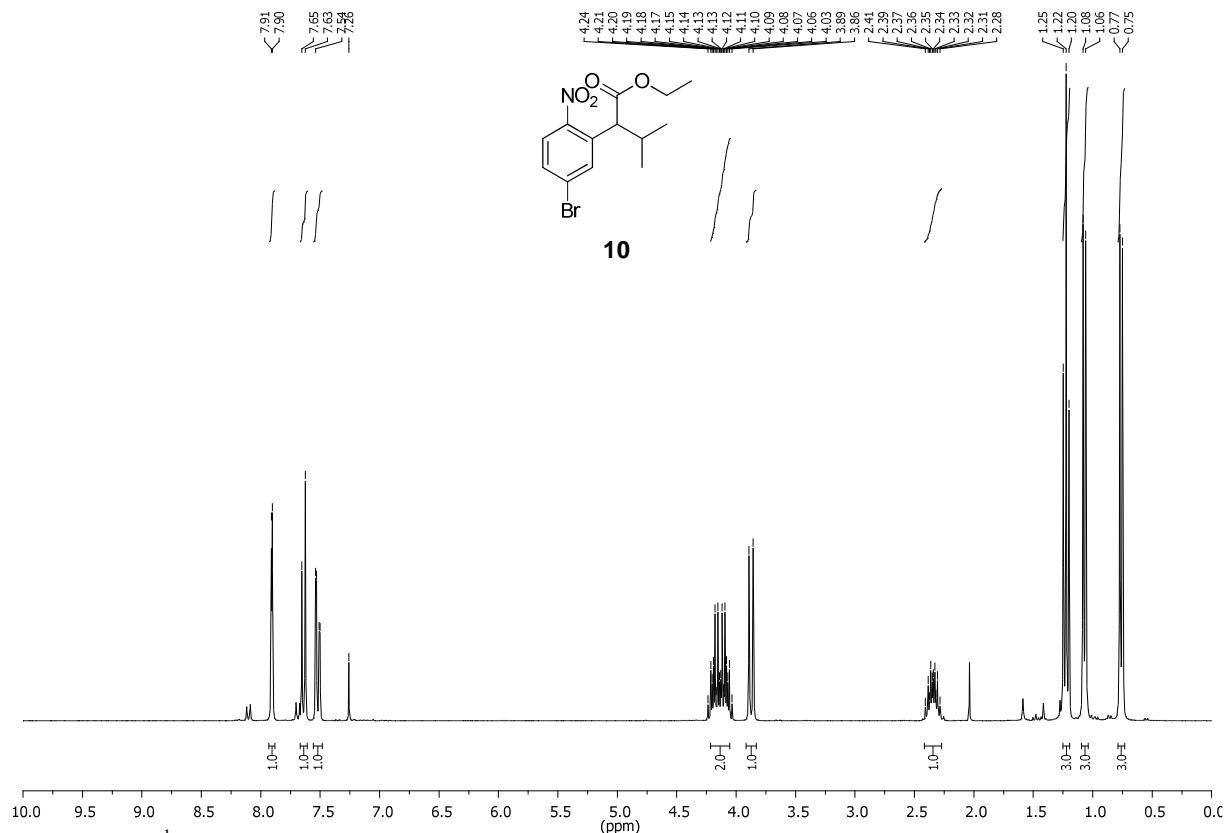
**Figure 71:** <sup>1</sup>H NMR; ethyl 2-chloro-3-methylbutanoate (**9**).



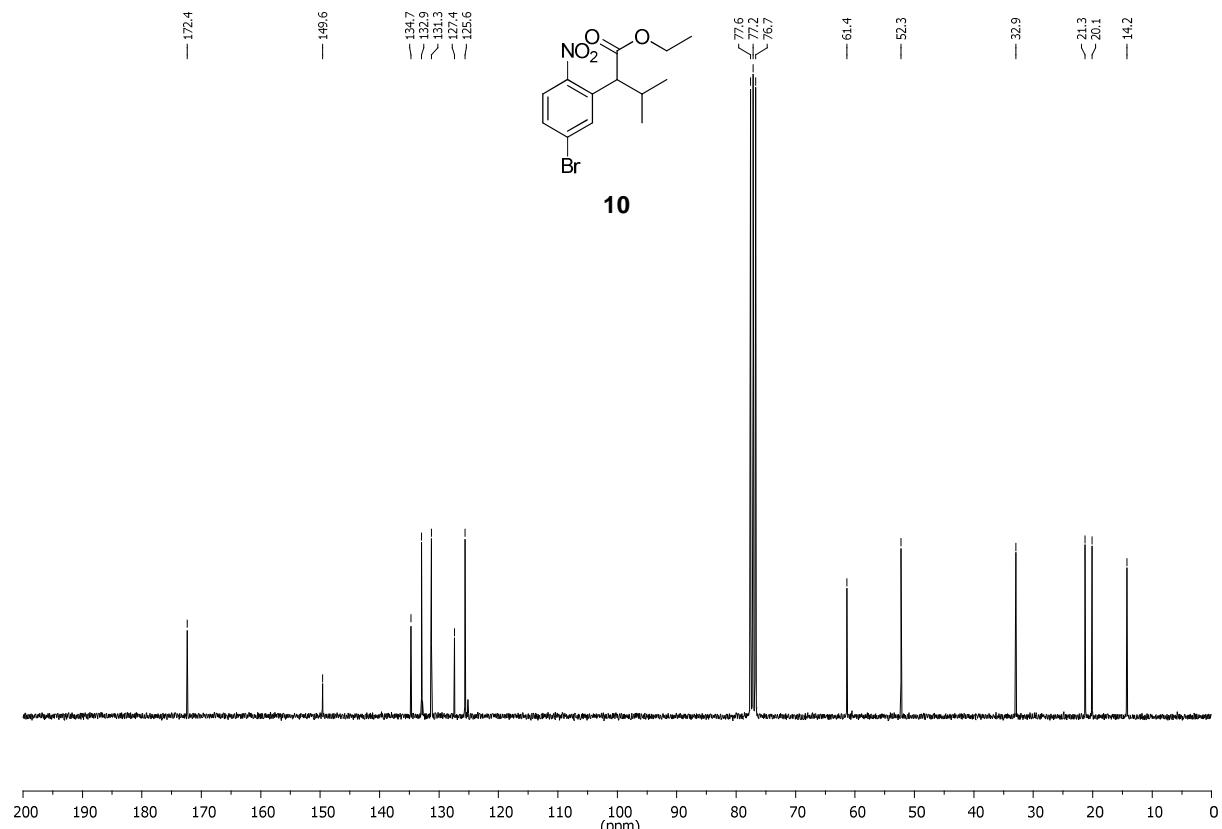
**Figure 72:** <sup>13</sup>C NMR; ethyl 2-chloro-3-methylbutanoate (**9**).

## NMR Data

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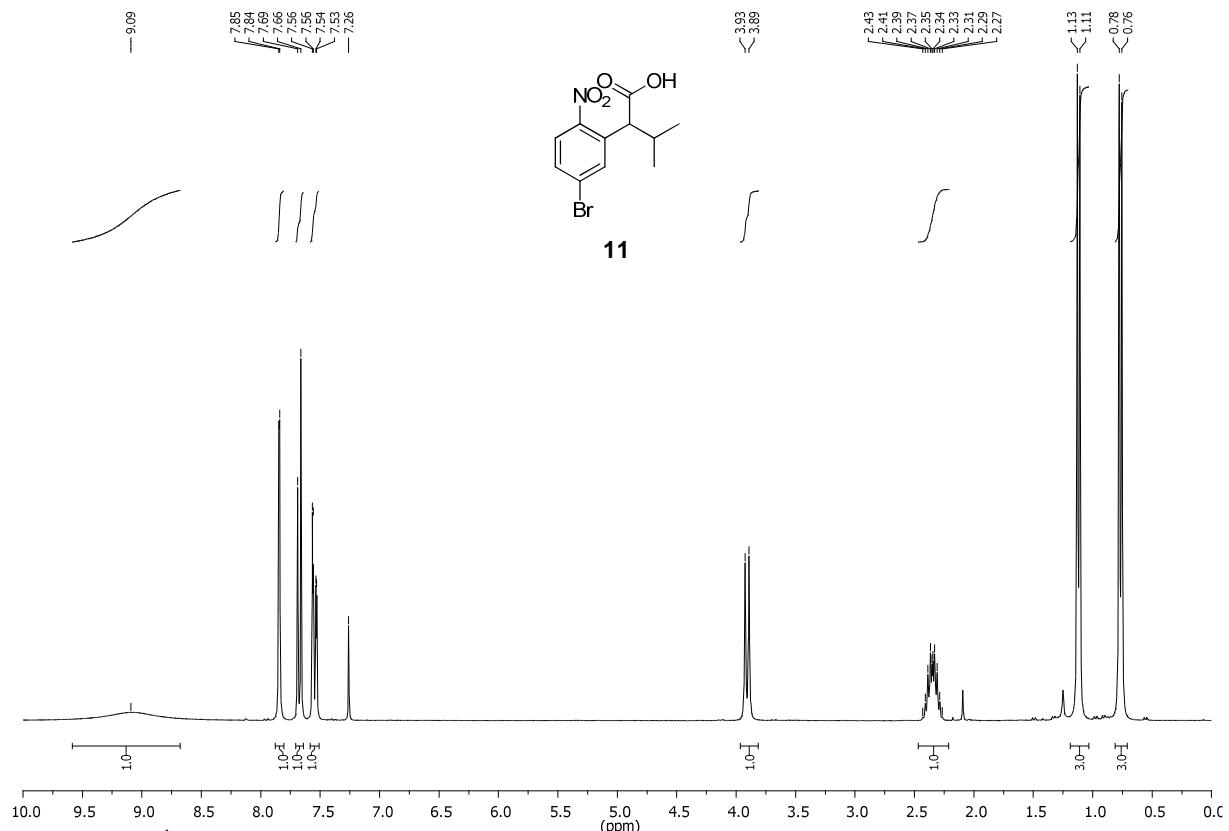
**Figure 73:**  $^1\text{H}$  NMR; ethyl 2-(5-bromo-2-nitrophenyl)-3-methylbutanoate (**10**).



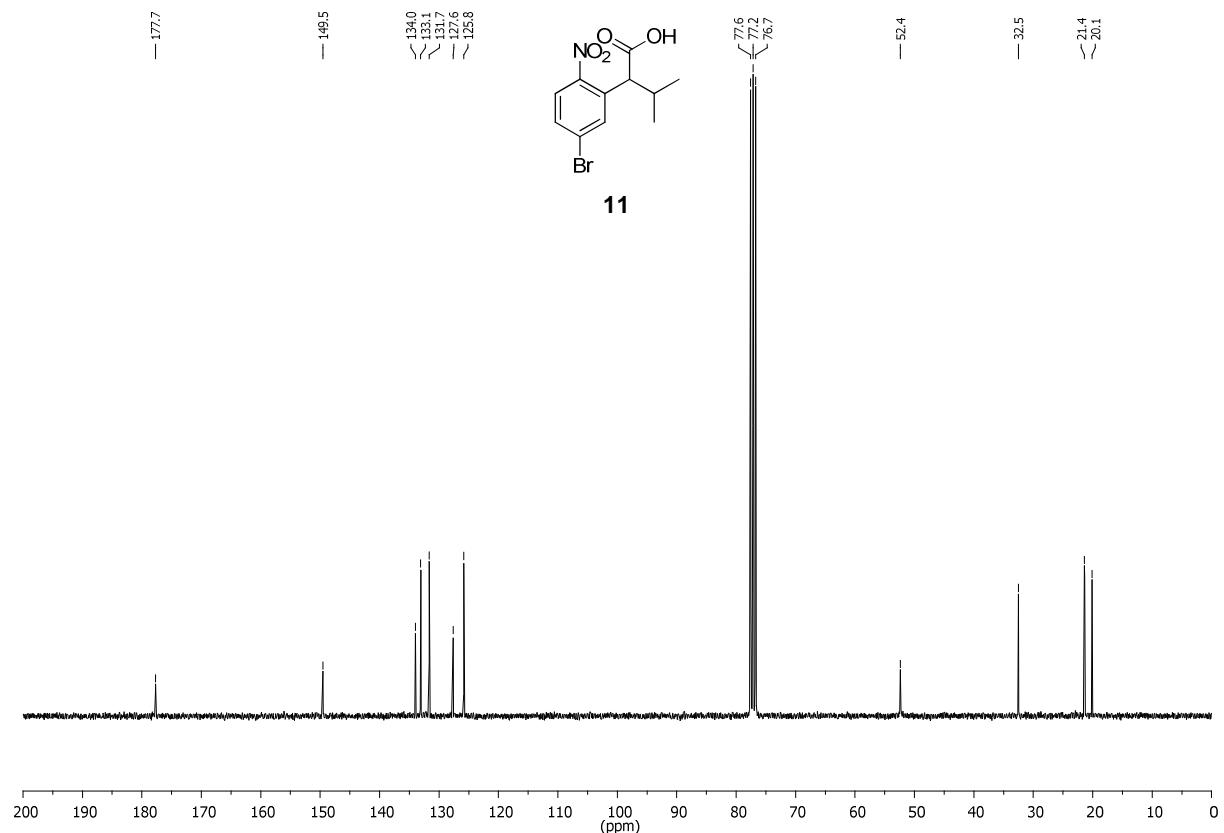
**Figure 74:**  $^{13}\text{C}$  NMR; ethyl 2-(5-bromo-2-nitrophenyl)-3-methylbutanoate (**10**).

## NMR Data

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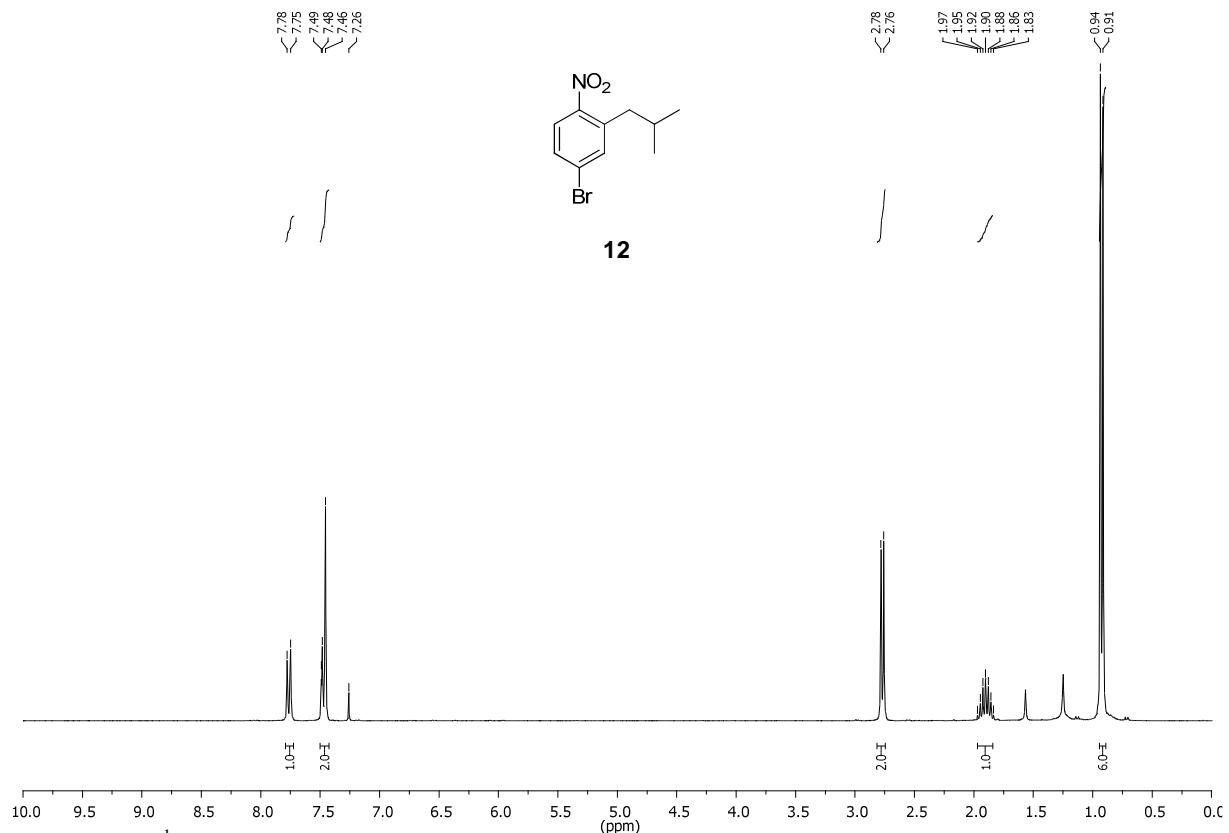
**Figure 75:** <sup>1</sup>H NMR; 2-(5-bromo-2-nitrophenyl)-3-methylbutanoic acid (**11**).



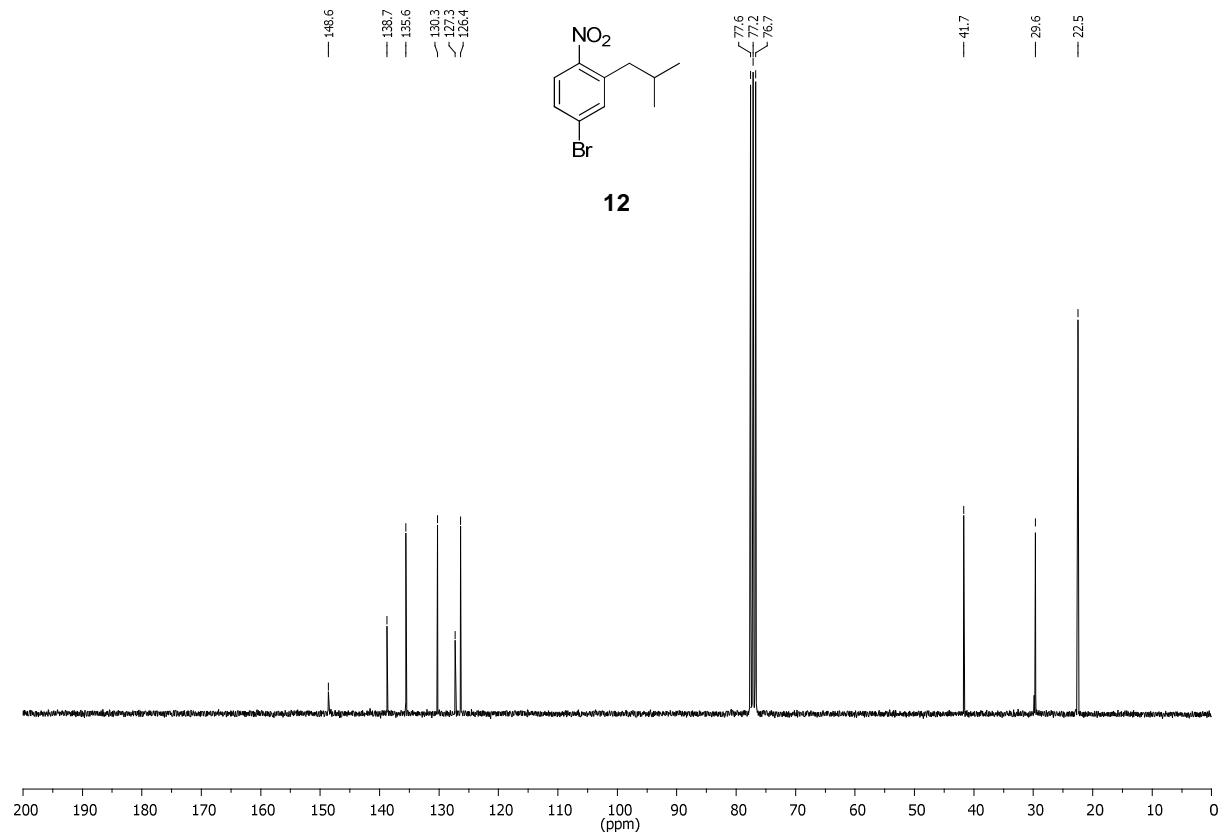
**Figure 76:** <sup>13</sup>C NMR; 2-(5-bromo-2-nitrophenyl)-3-methylbutanoic acid (**11**).

## NMR Data

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**Figure 77:** <sup>1</sup>H NMR; 4-bromo-2-isobutyl-1-nitrobenzene (**12**).



**Figure 78:** <sup>13</sup>C NMR; 4-bromo-2-isobutyl-1-nitrobenzene (**12**).

## NMR Data

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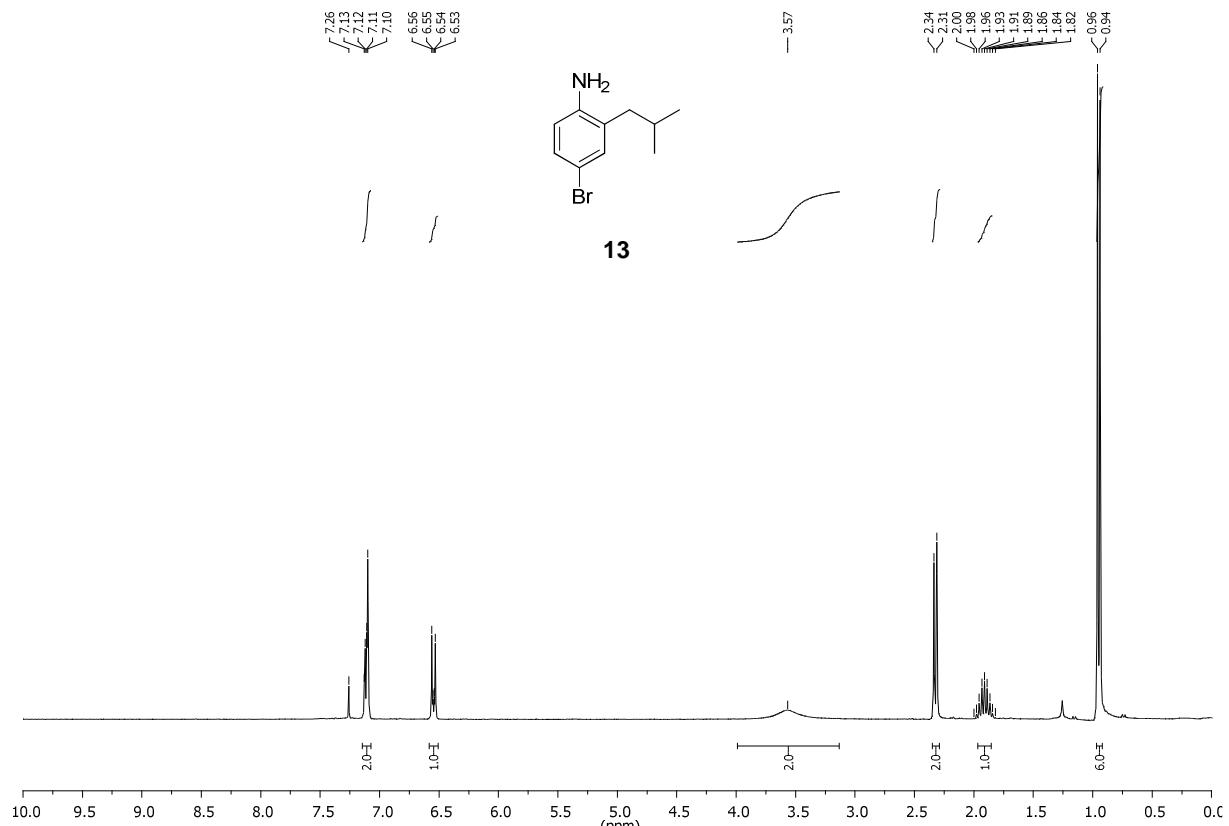


Figure 79: <sup>1</sup>H NMR; 4-bromo-2-isobutylaniline (13).

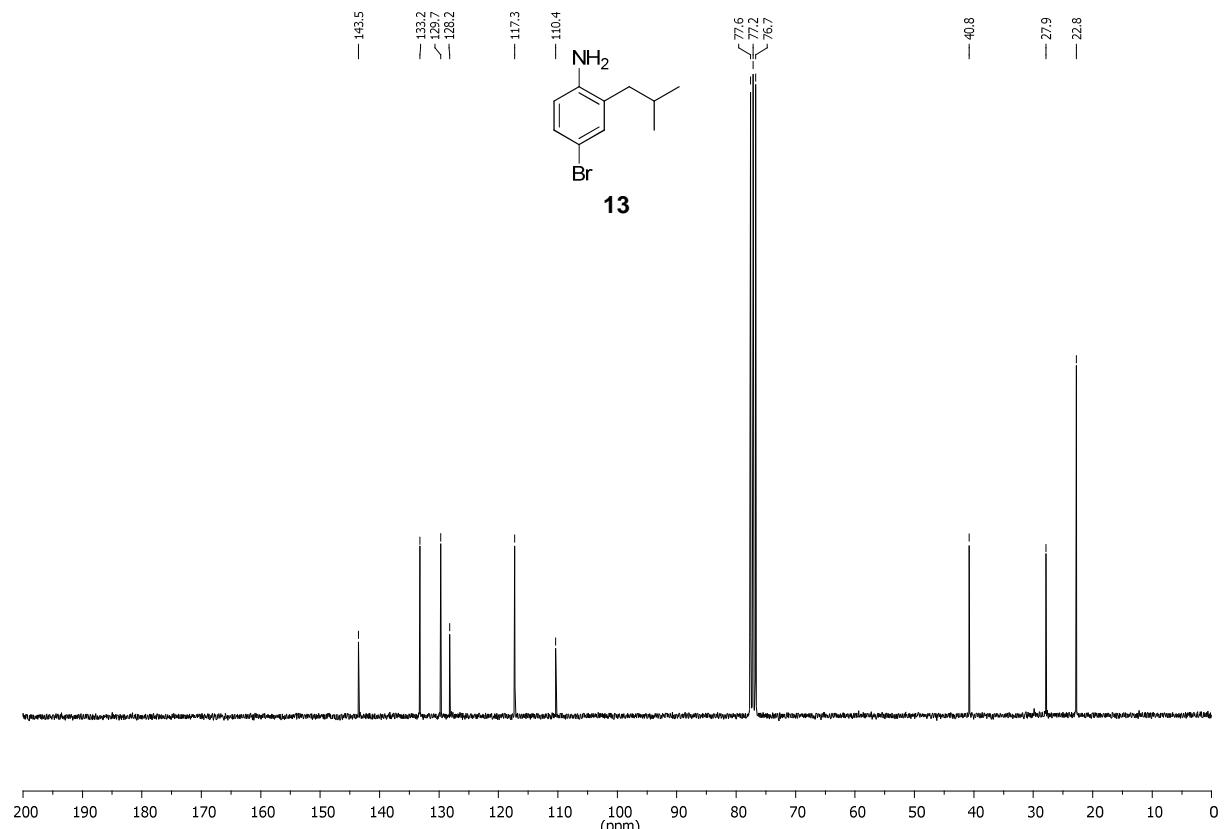
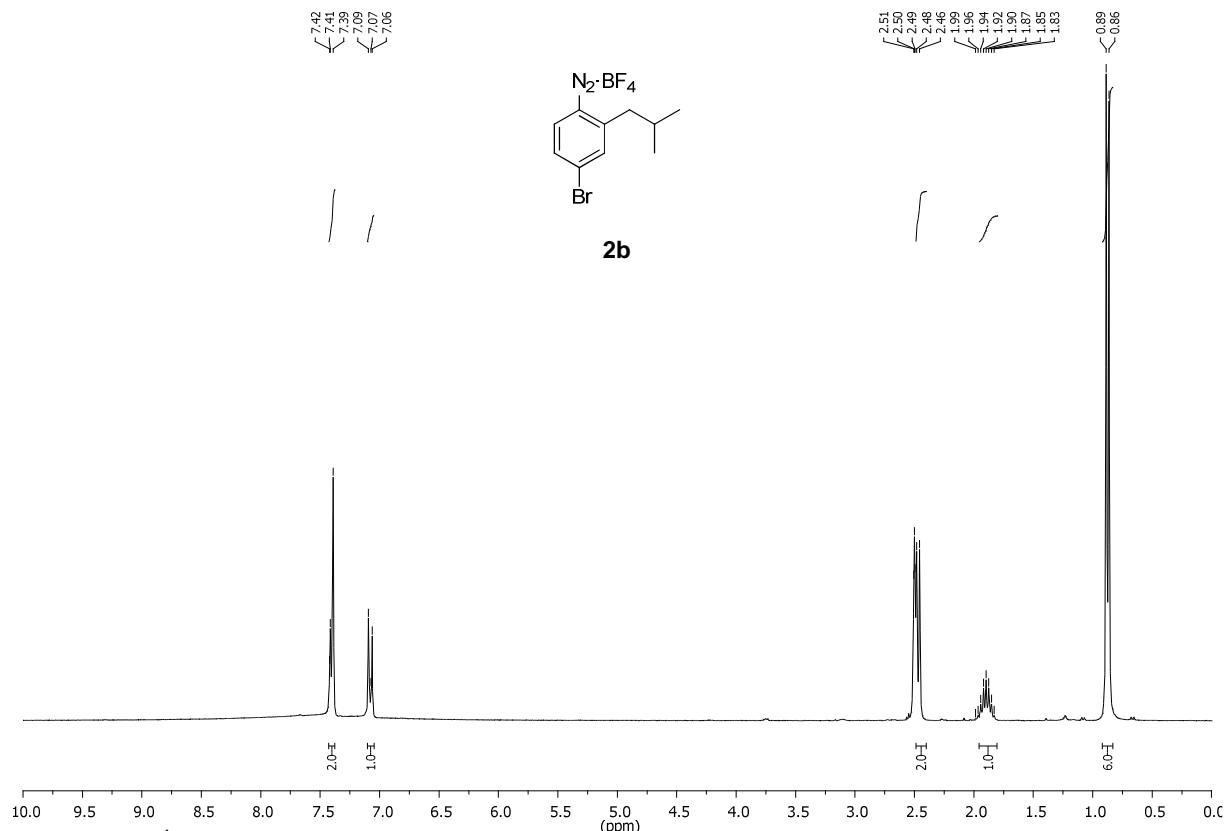


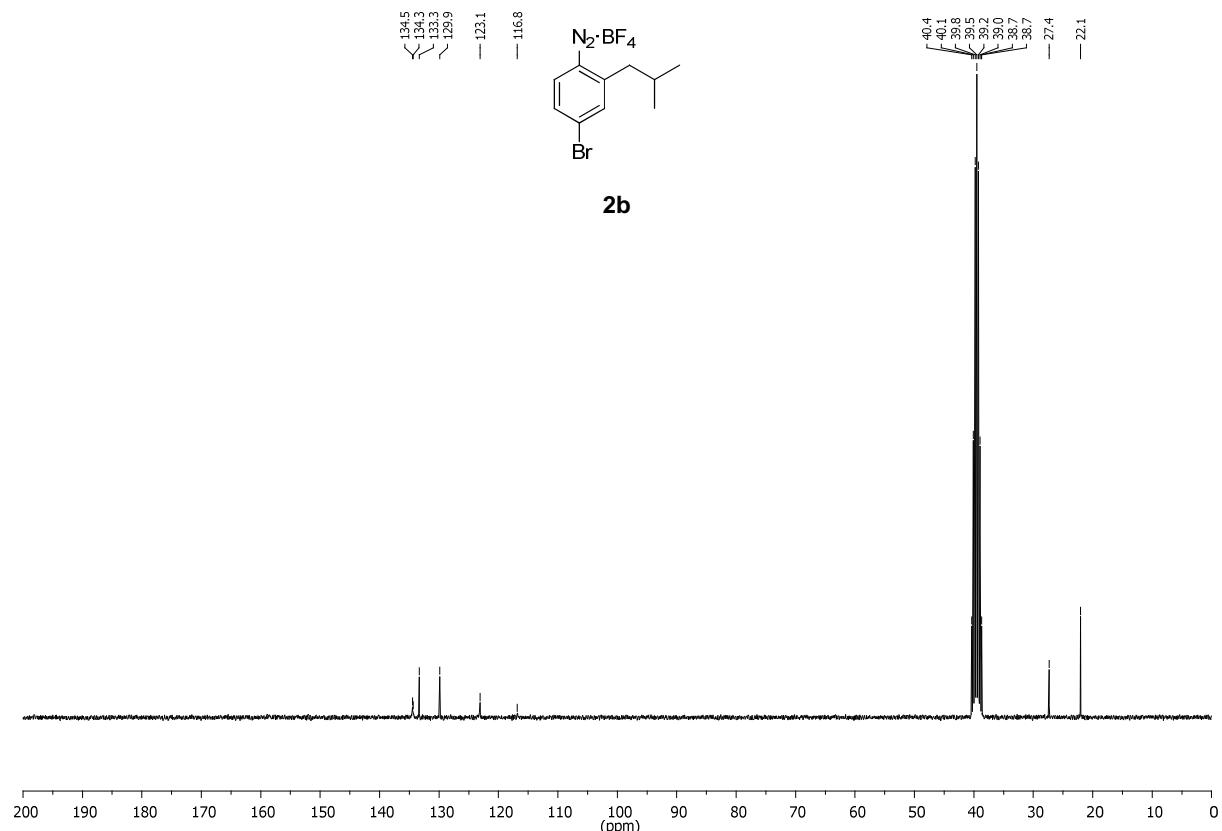
Figure 80: <sup>13</sup>C NMR; 4-bromo-2-isobutylaniline (13).

## NMR Data

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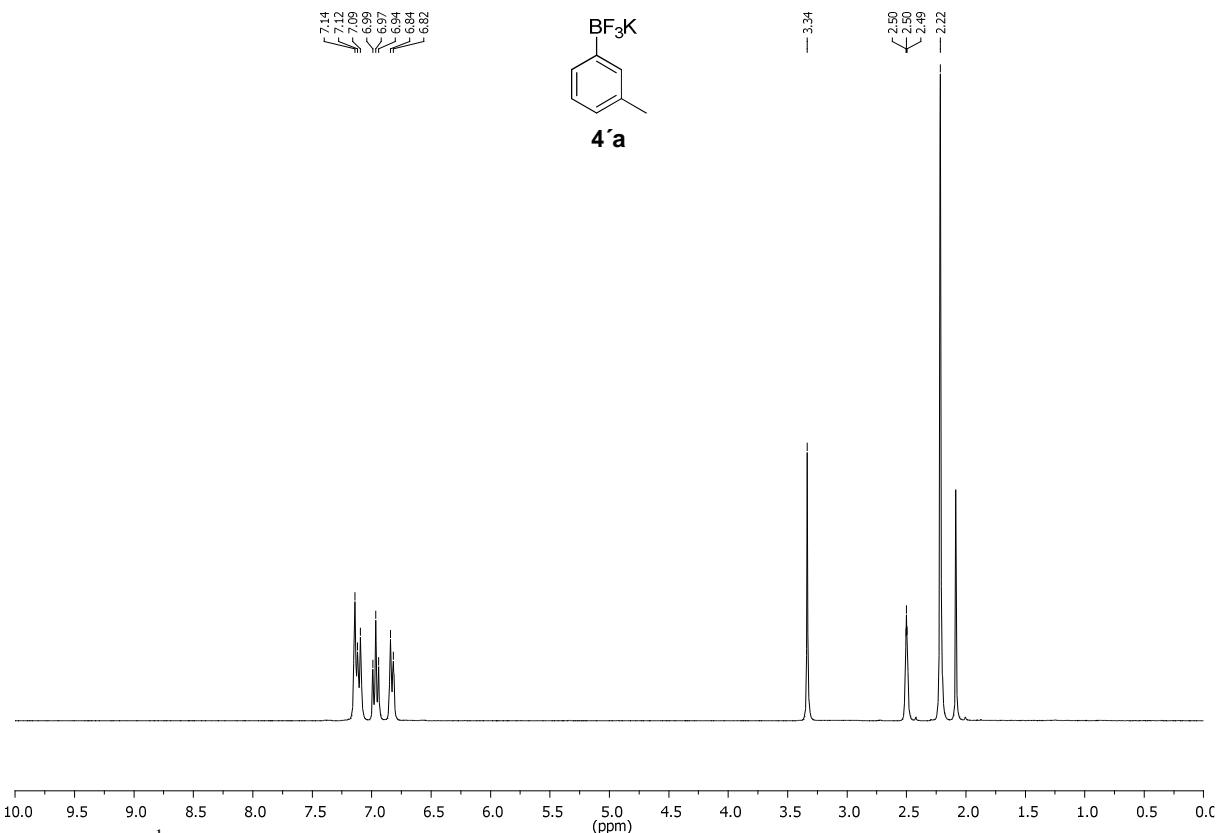
**Figure 81:** <sup>1</sup>H NMR; 4-bromo-2-isobutylbenzenediazonium tetrafluoroborate (**2b**).



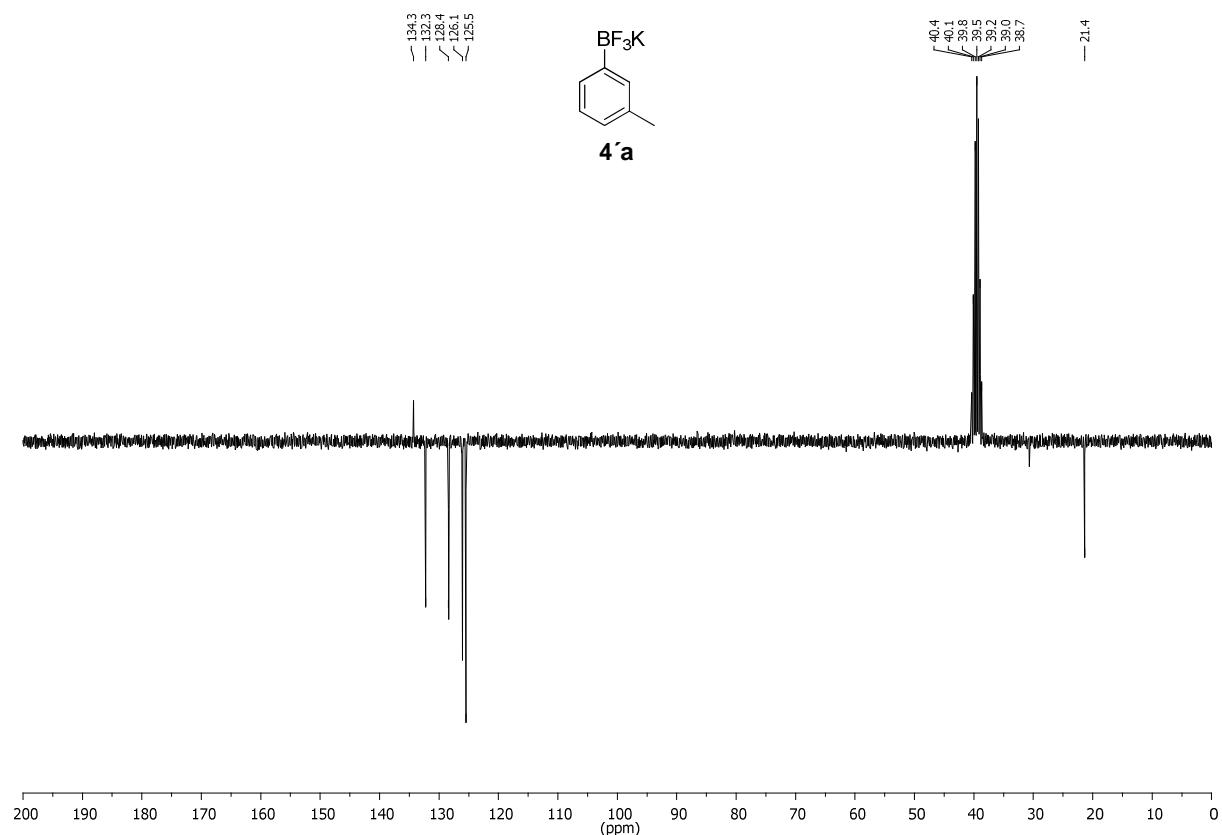
**Figure 82:** <sup>13</sup>C NMR; 4-bromo-2-isobutylbenzenediazonium tetrafluoroborate (**2b**).

## NMR Data

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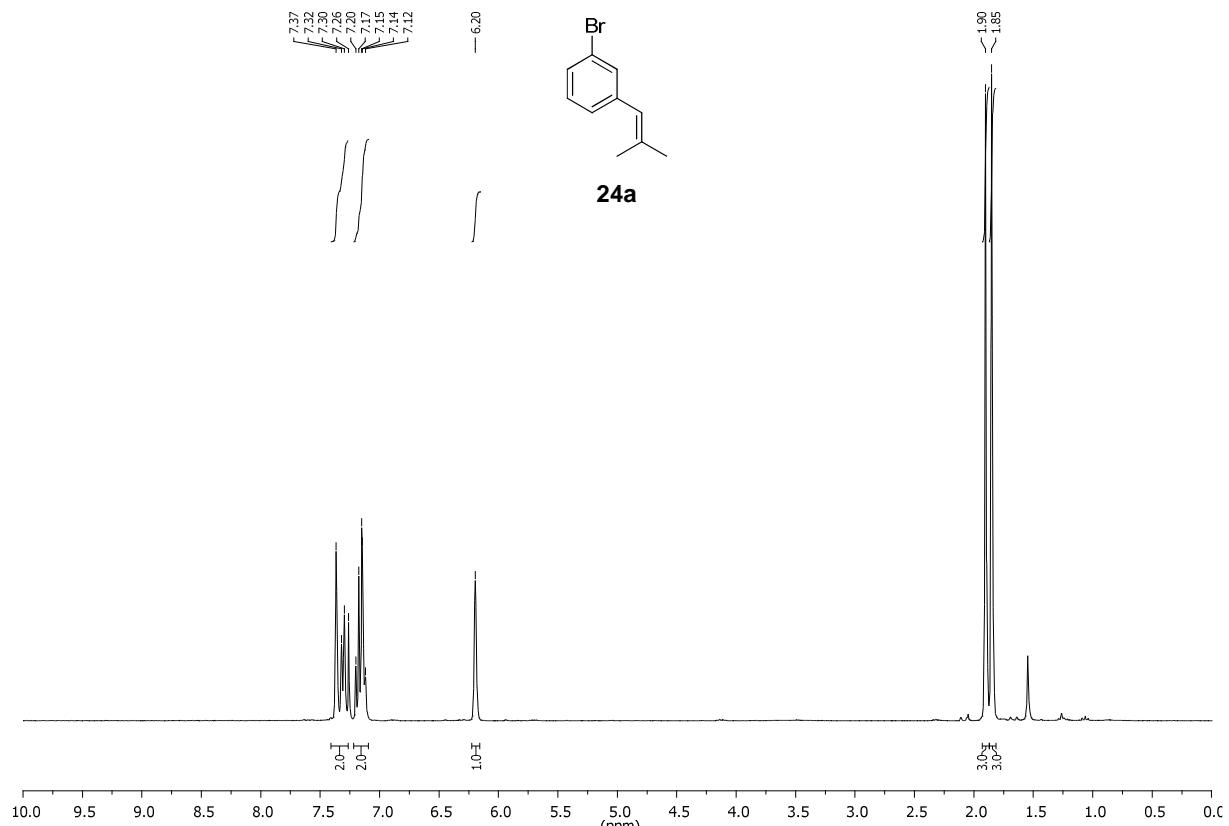
**Figure 83:** <sup>1</sup>H NMR; potassium trifluoro(*m*-tolyl)borate (**4'a**).



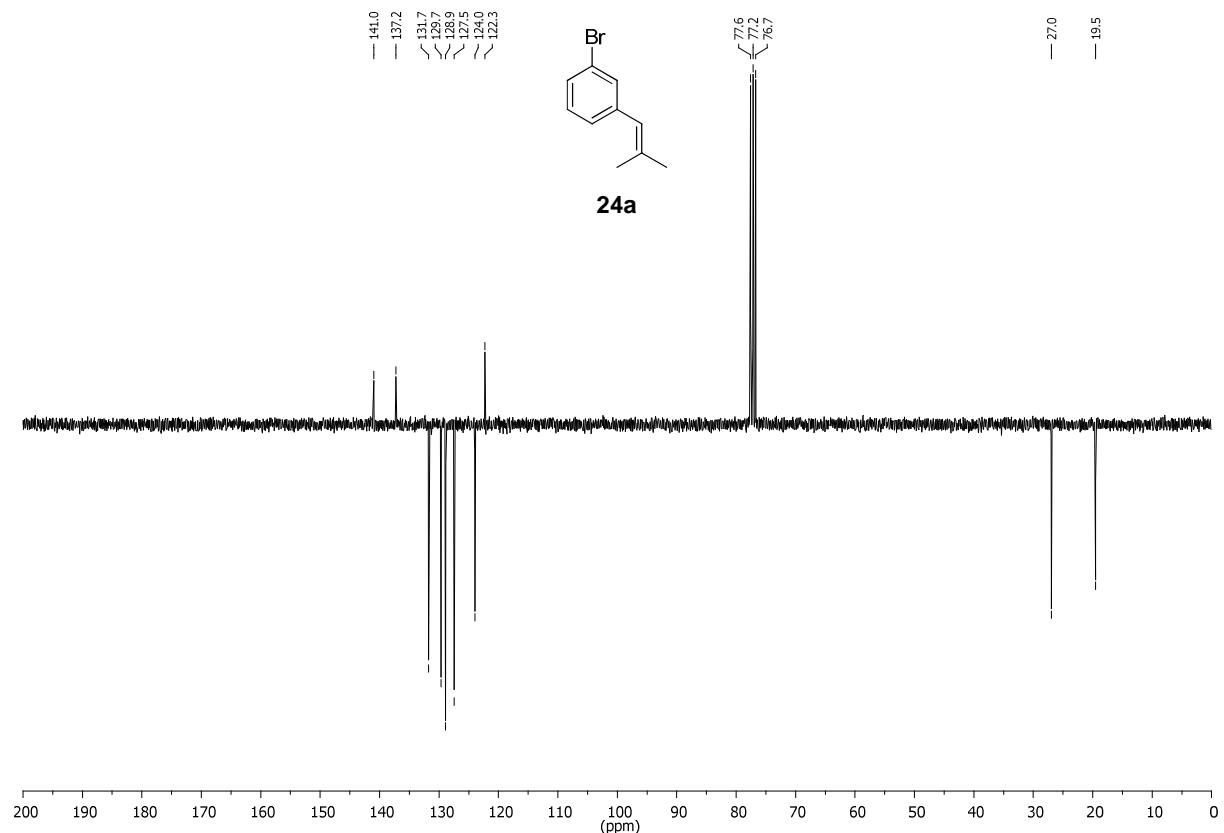
**Figure 84:** <sup>13</sup>C NMR, APT; potassium trifluoro(*m*-tolyl)borate (**4'a**).

## NMR Data

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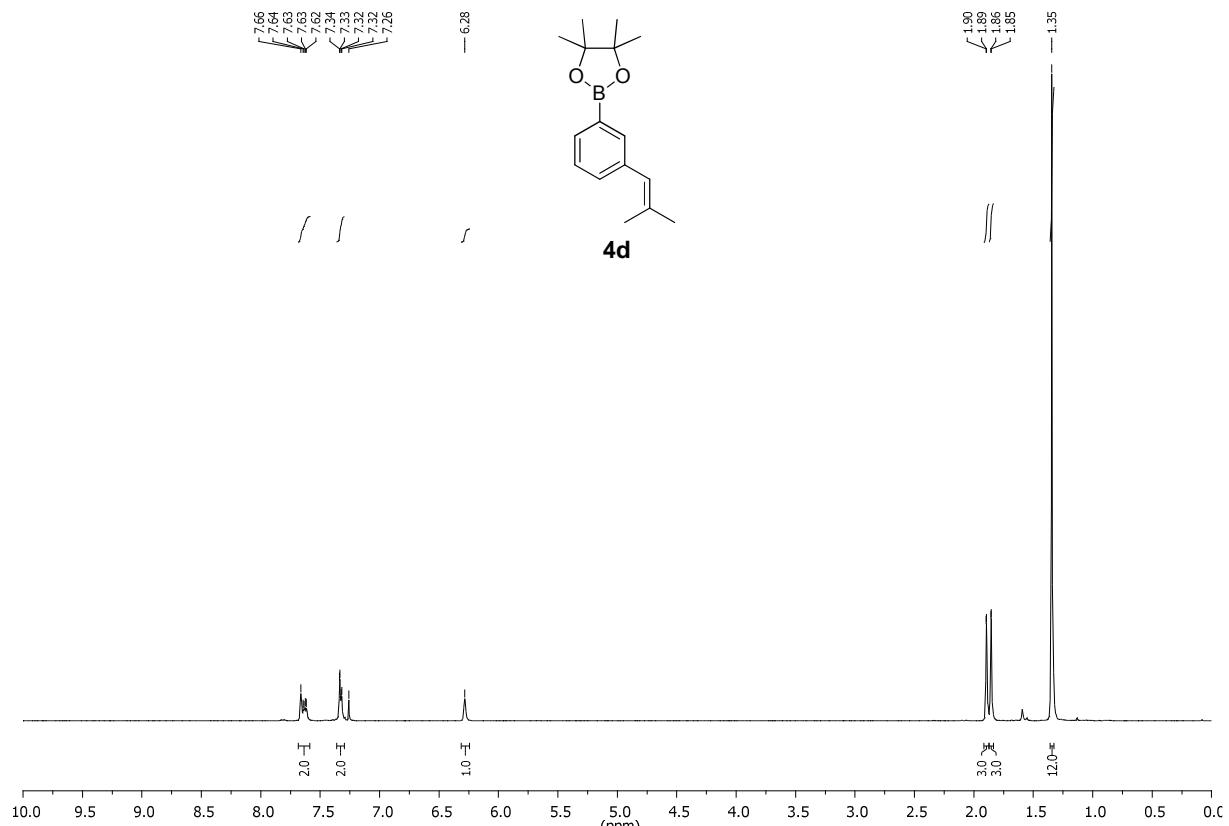
**Figure 85:** <sup>1</sup>H NMR; 1-bromo-3-(2-methylprop-1-en-1-yl)benzene (**24a**).



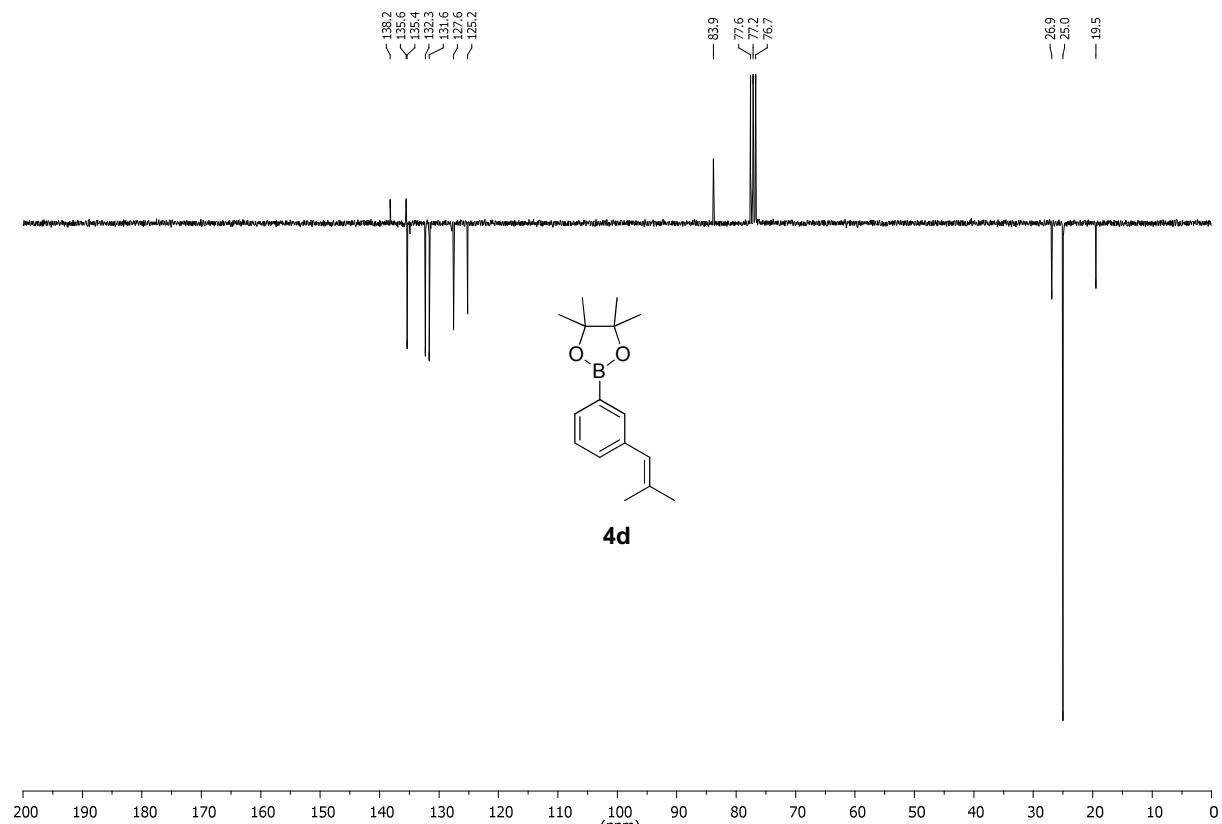
**Figure 86:** <sup>13</sup>C NMR, APT; 1-bromo-3-(2-methylprop-1-en-1-yl)benzene (**24a**).

## NMR Data

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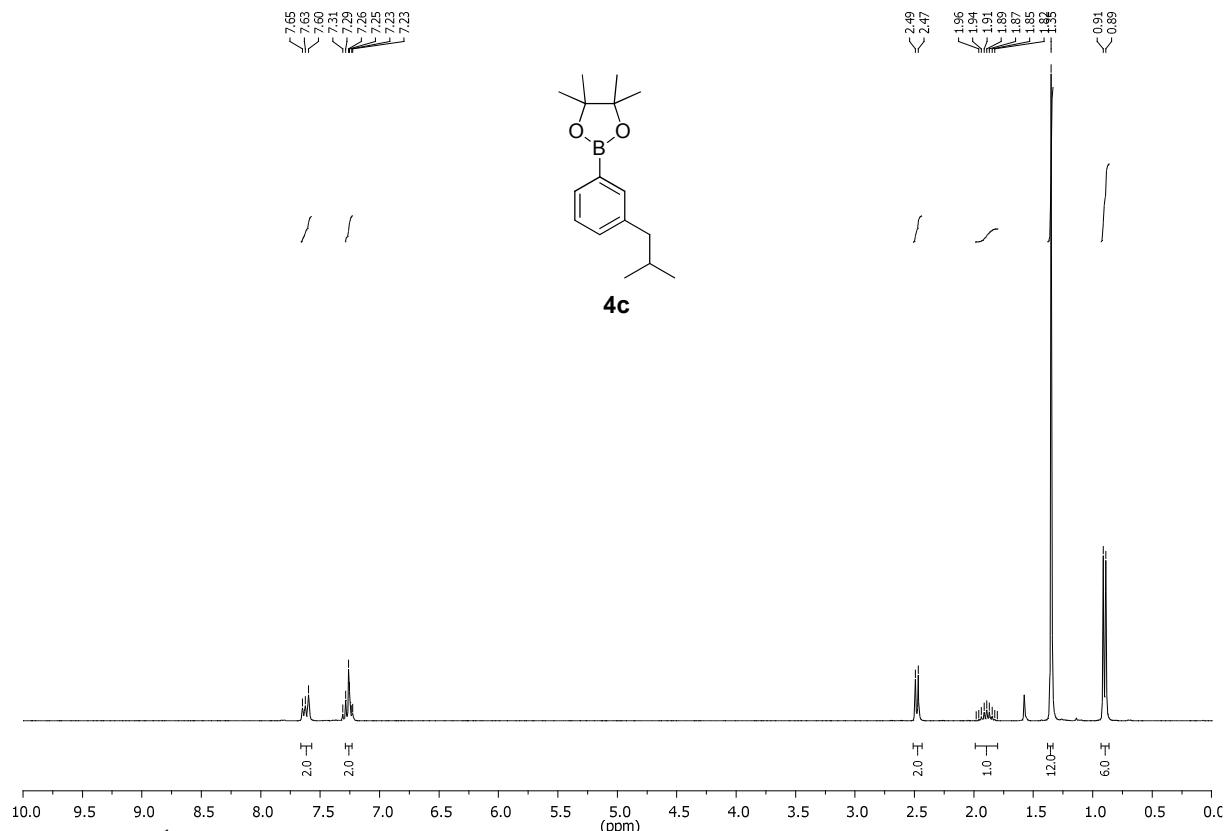
**Figure 87:** <sup>1</sup>H NMR; 4,4,5,5-tetramethyl-2-(3-(2-methylprop-1-en-1-yl)phenyl)-1,3,2-dioxaborolane (**4d**).



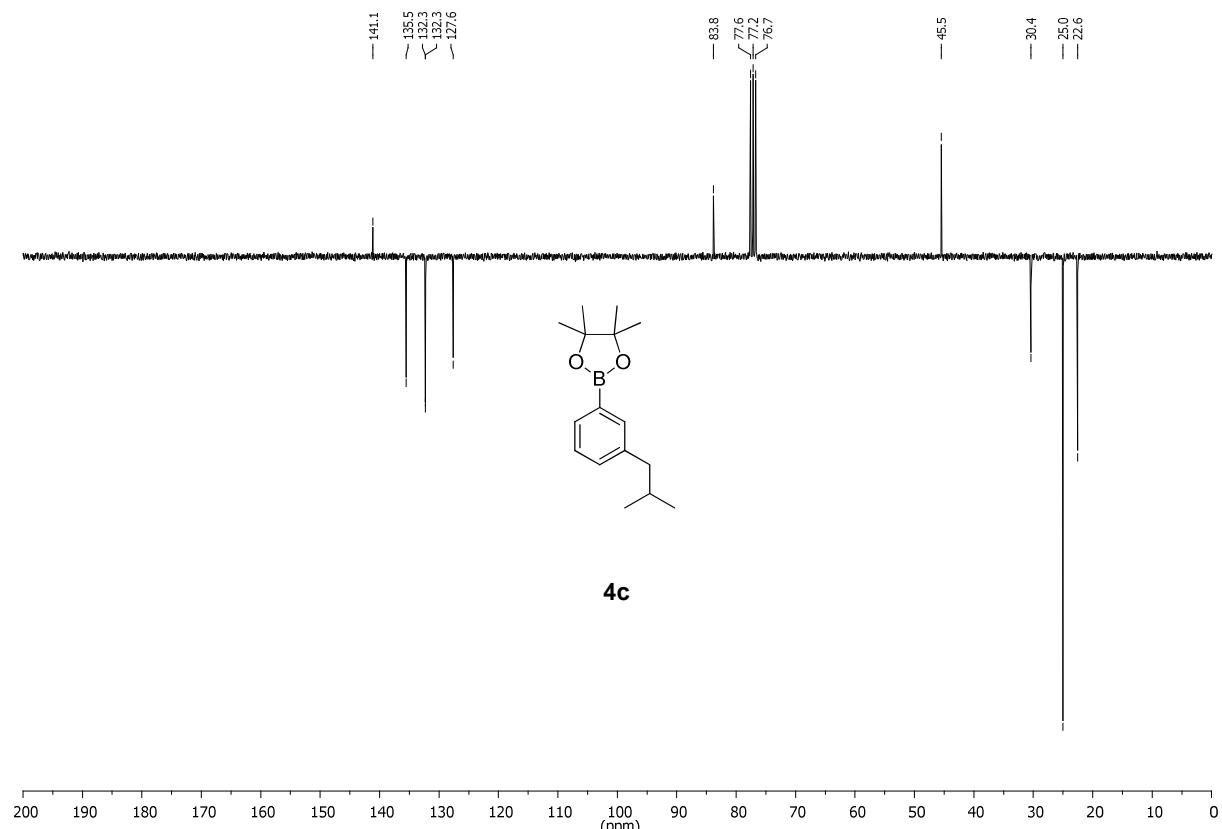
**Figure 88:** <sup>13</sup>C NMR, APT; 4,4,5,5-tetramethyl-2-(3-(2-methylprop-1-en-1-yl)phenyl)-1,3,2-dioxa-borolane (**4d**).

## NMR Data

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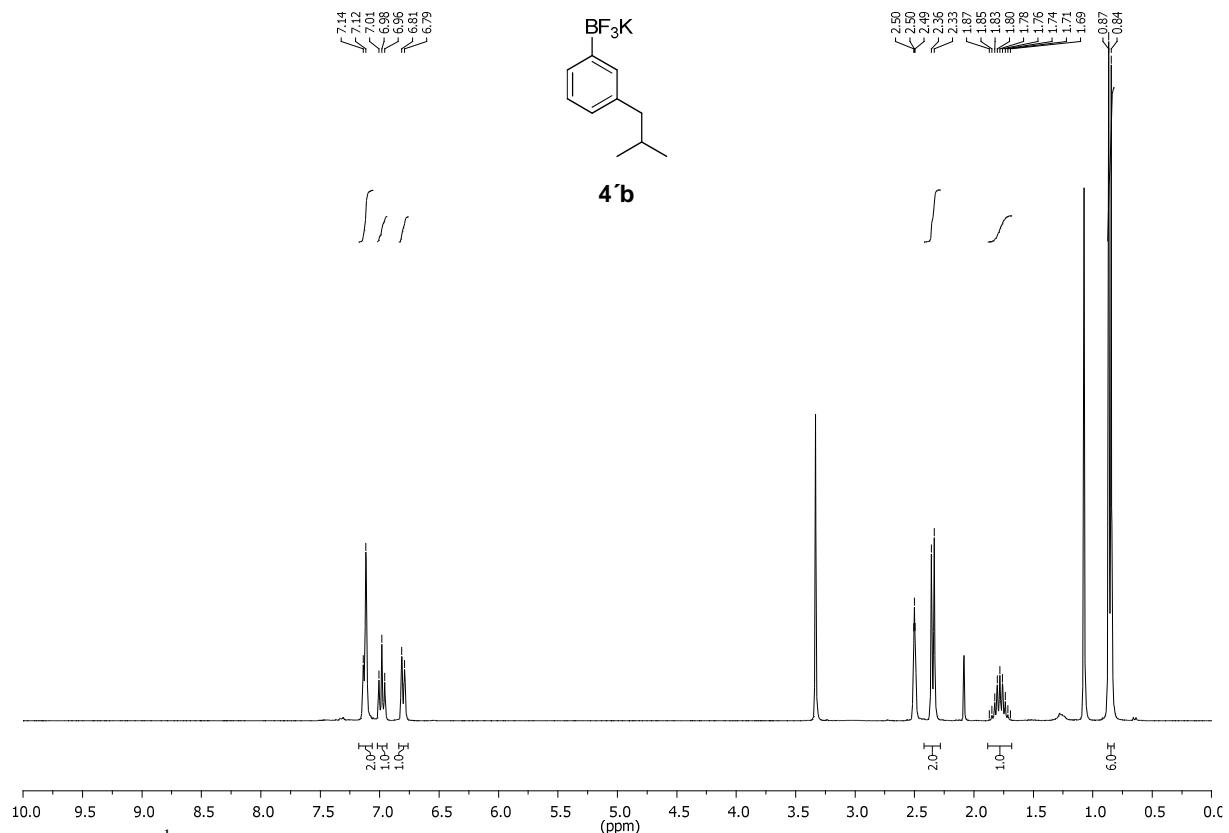
**Figure 89:**  $^1\text{H}$  NMR; 2-(3-isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**).



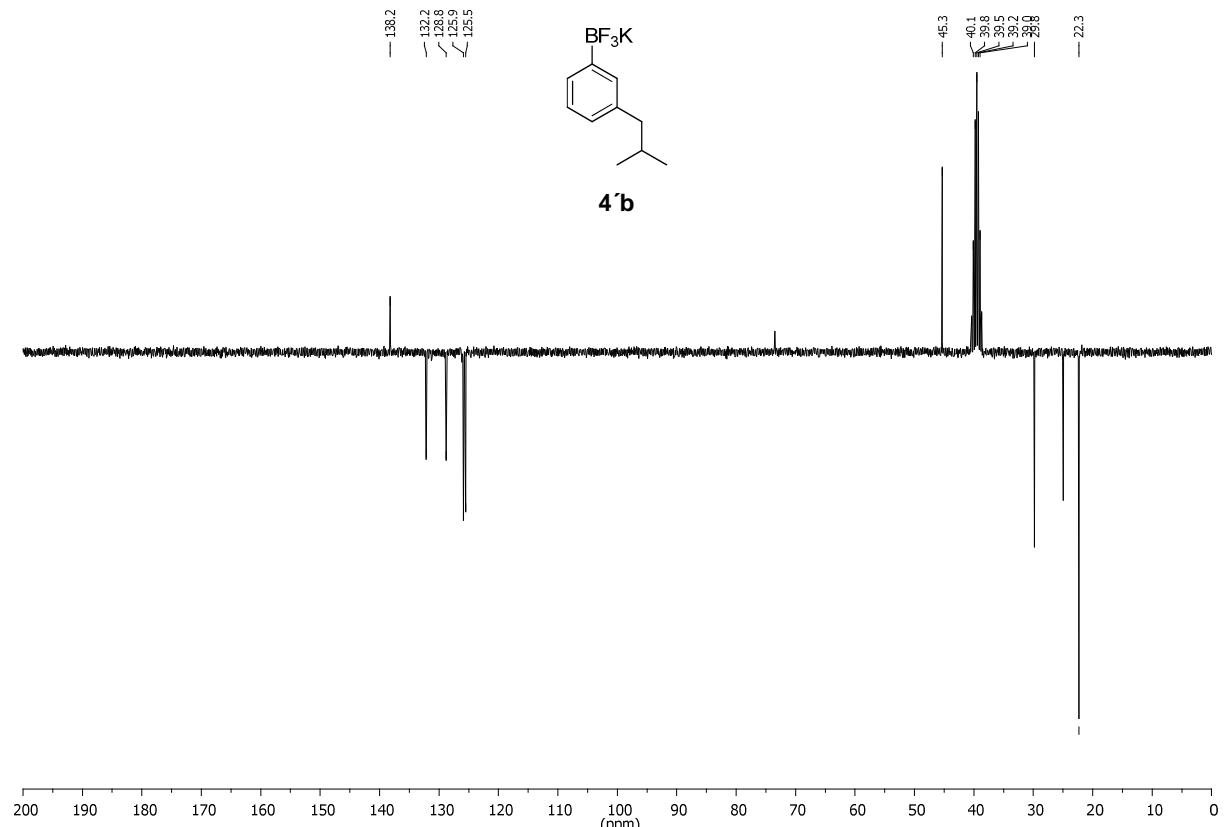
**Figure 90:**  $^{13}\text{C}$  NMR, APT; 2-(3-isobutylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4c**).

## NMR Data

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**Figure 91:** <sup>1</sup>H NMR; potassium trifluoro(3-isobutylphenyl)borate (**4'b**).



**Figure 92:** <sup>13</sup>C NMR, APT; potassium trifluoro(3-isobutylphenyl)borate (**4'b**).

## NMR Data

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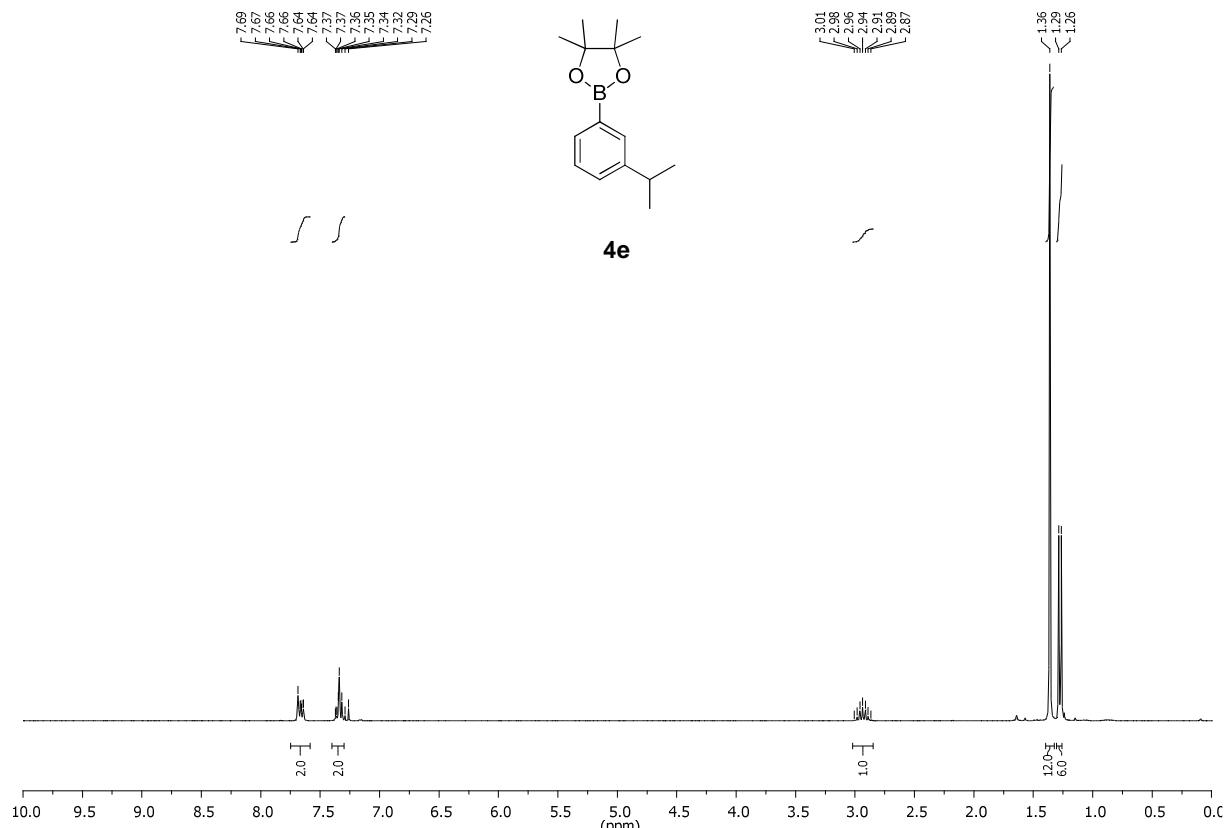


Figure 93: <sup>1</sup>H NMR; 2-(3-isopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4e).

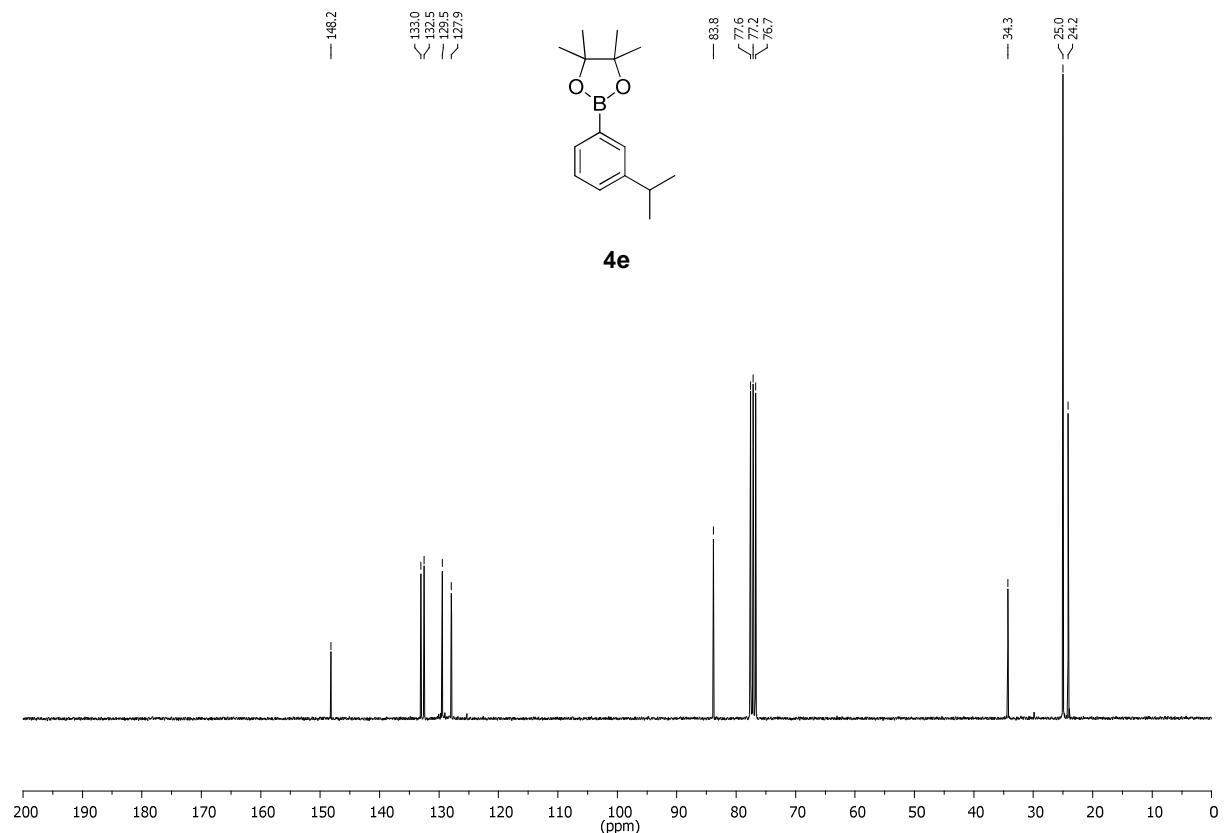
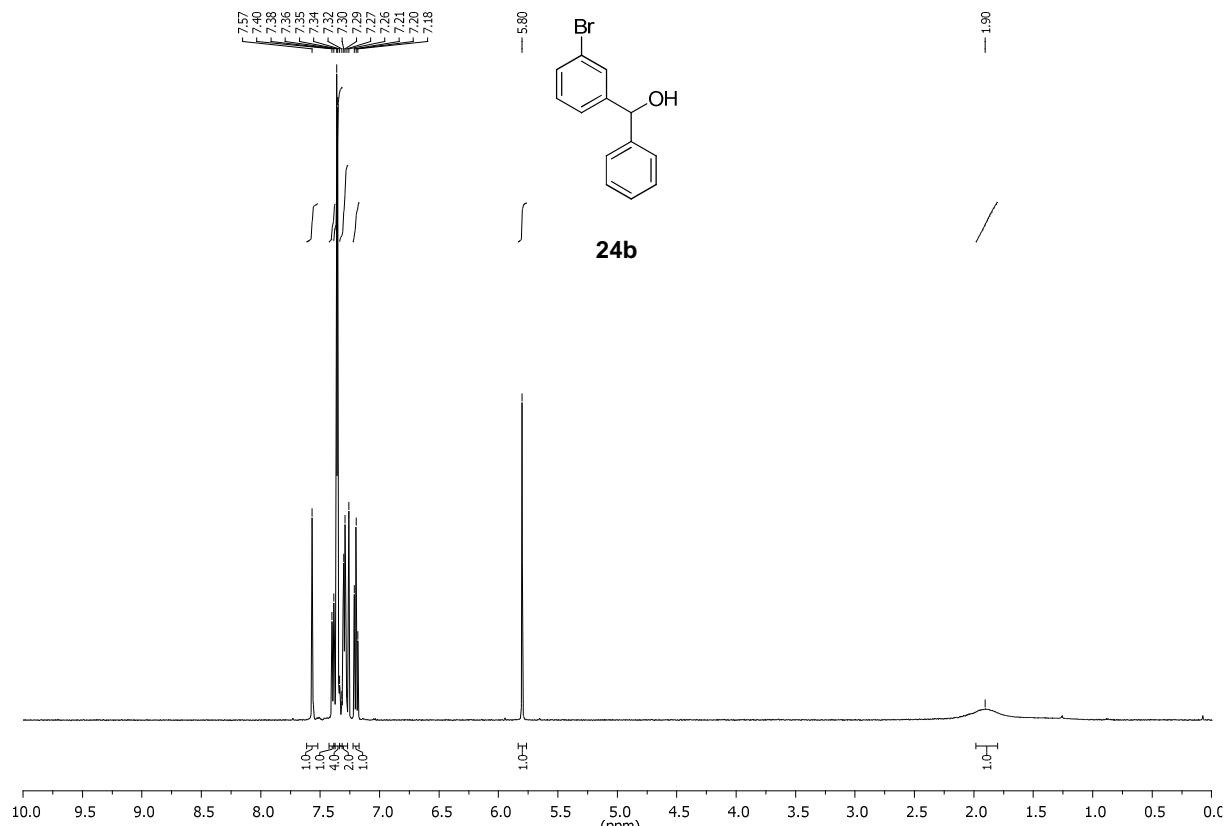


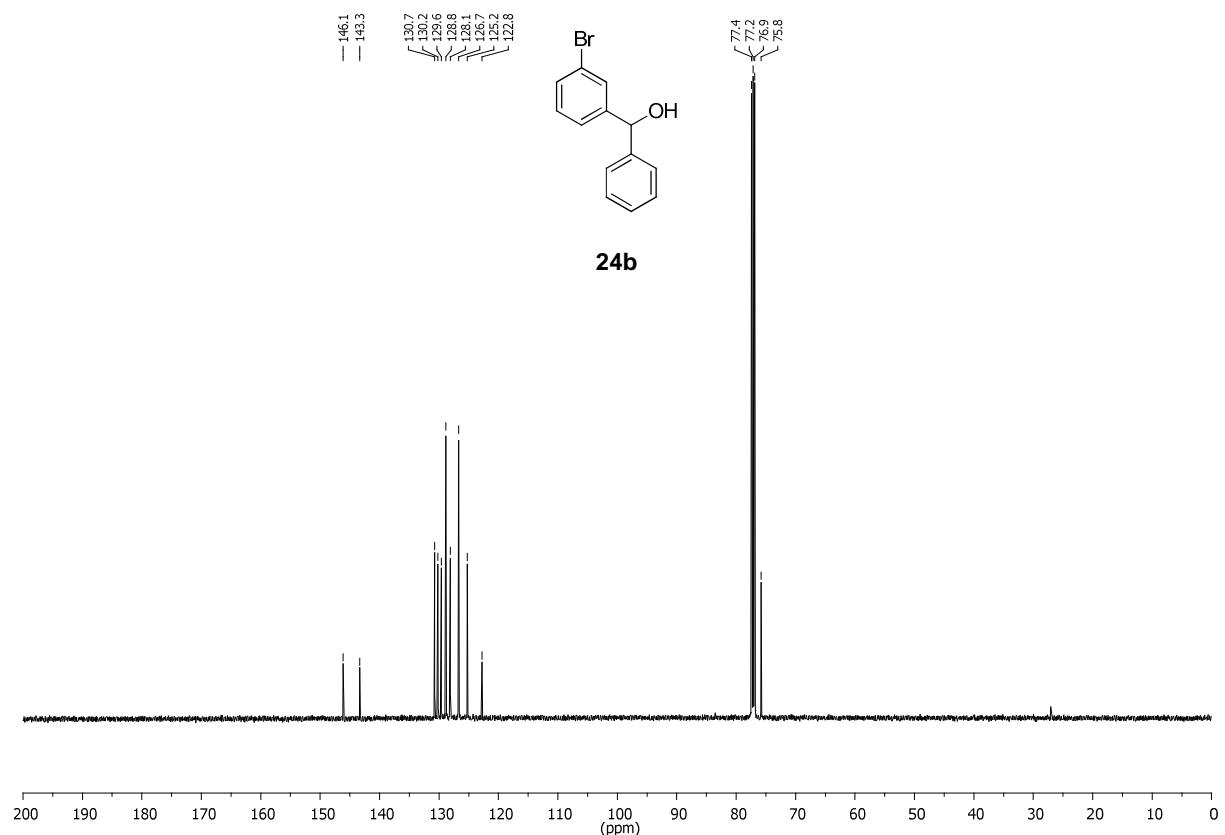
Figure 94: <sup>13</sup>C NMR; 2-(3-isopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4e).

## NMR Data

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**Figure 95:**  $^1\text{H}$  NMR; (3-bromophenyl)(phenyl)methanol (**24b**).



**Figure 96:**  $^{13}\text{C}$  NMR; (3-bromophenyl)(phenyl)methanol (**24b**).

## NMR Data

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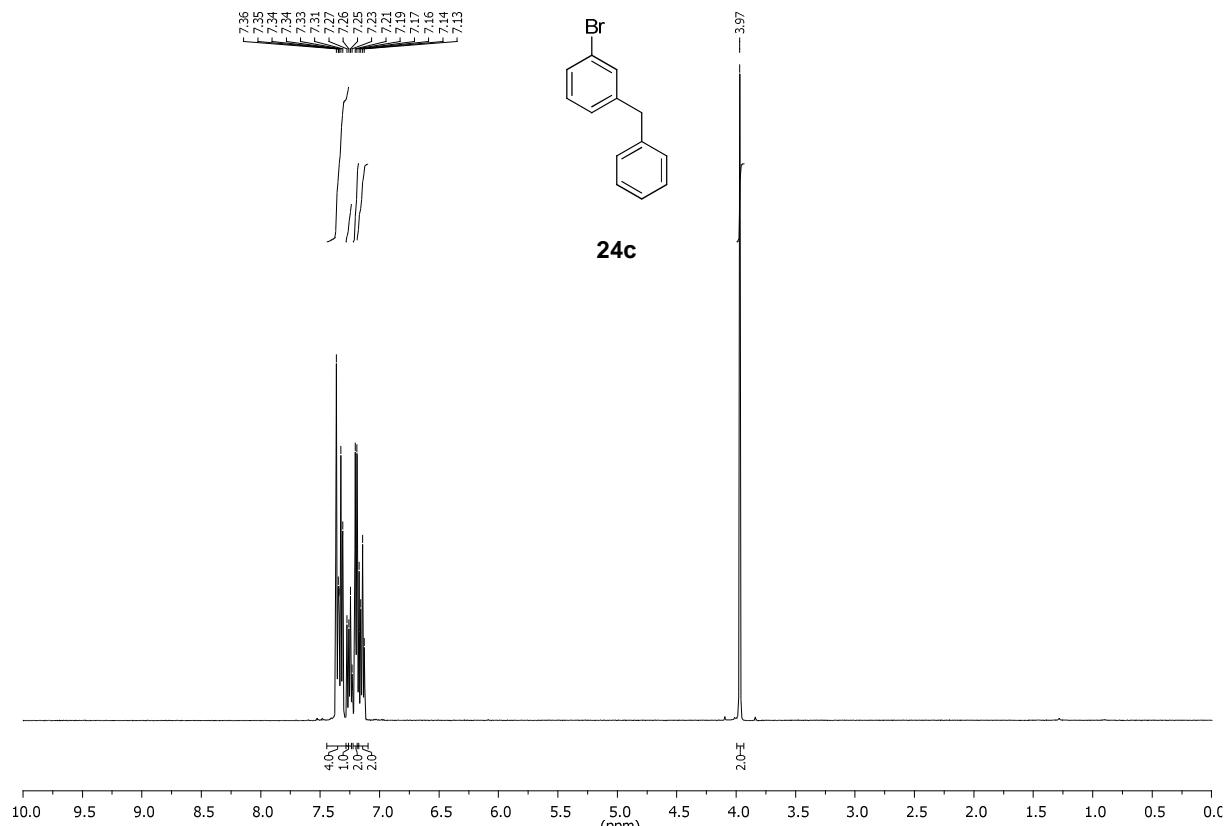


Figure 97: <sup>1</sup>H NMR; 1-benzyl-3-bromobenzene (24c).

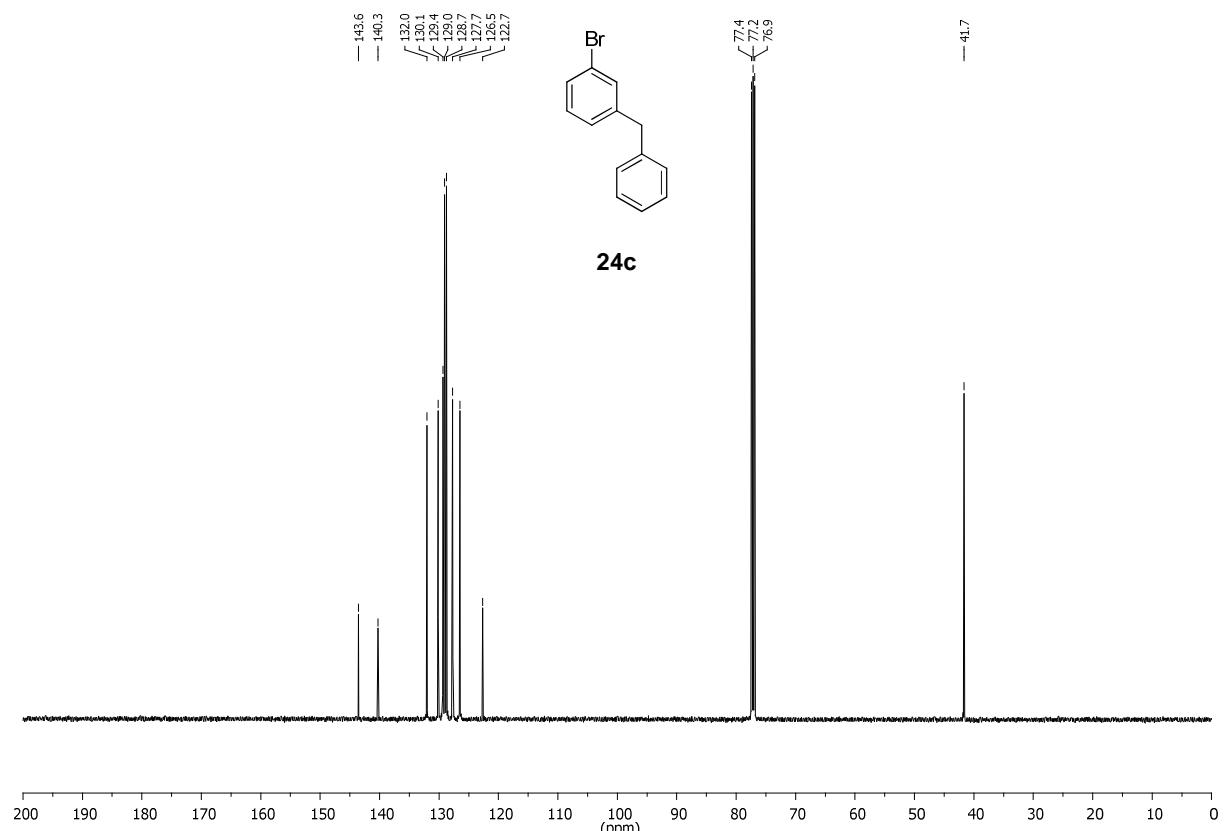


Figure 98: <sup>13</sup>C NMR; 1-benzyl-3-bromobenzene (24c).

## NMR Data

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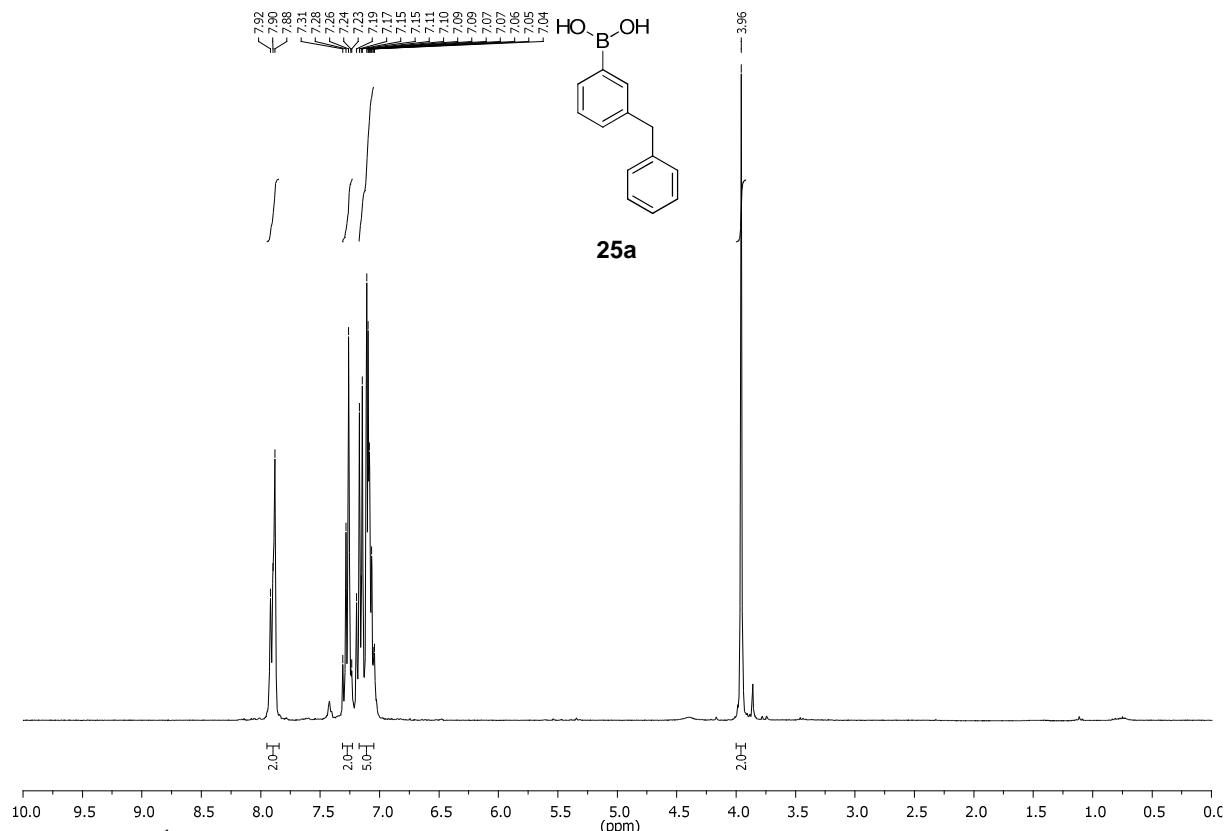


Figure 99: <sup>1</sup>H NMR; (3-benzylphenyl)boronic acid (25a).

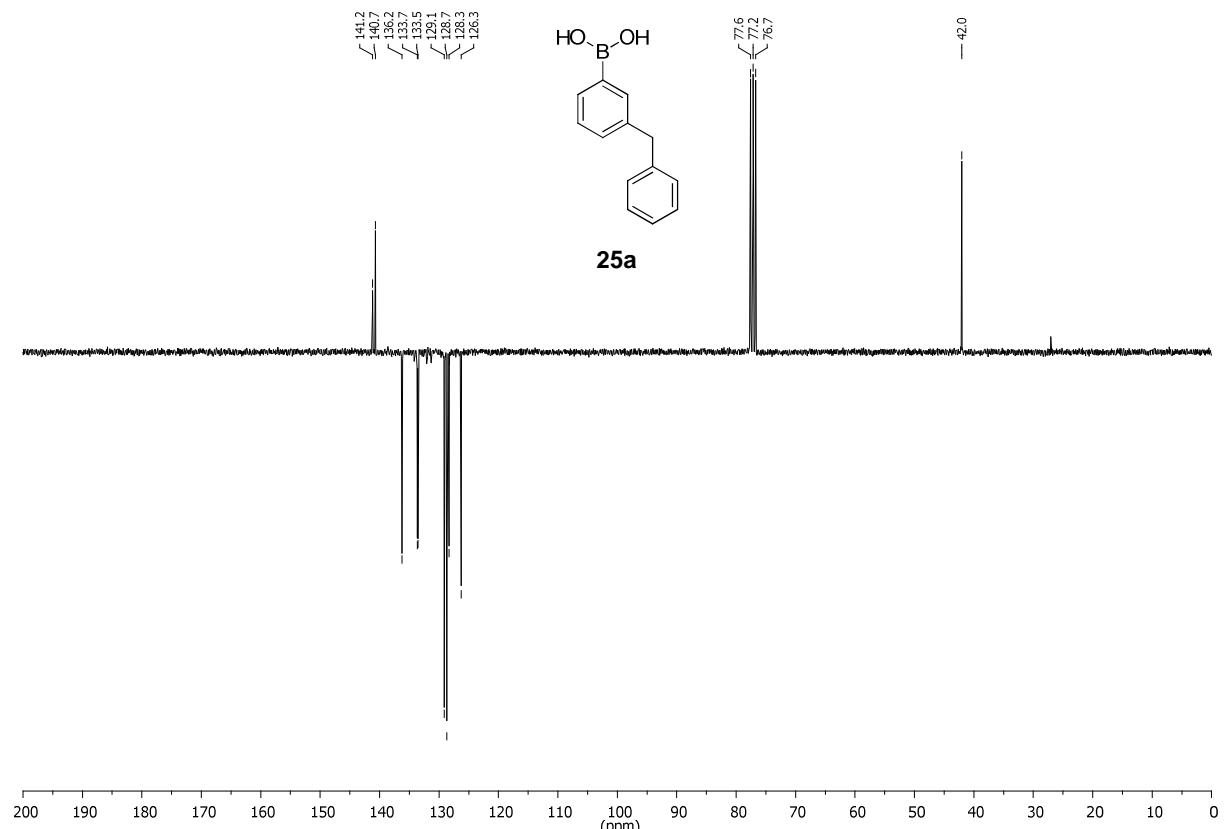
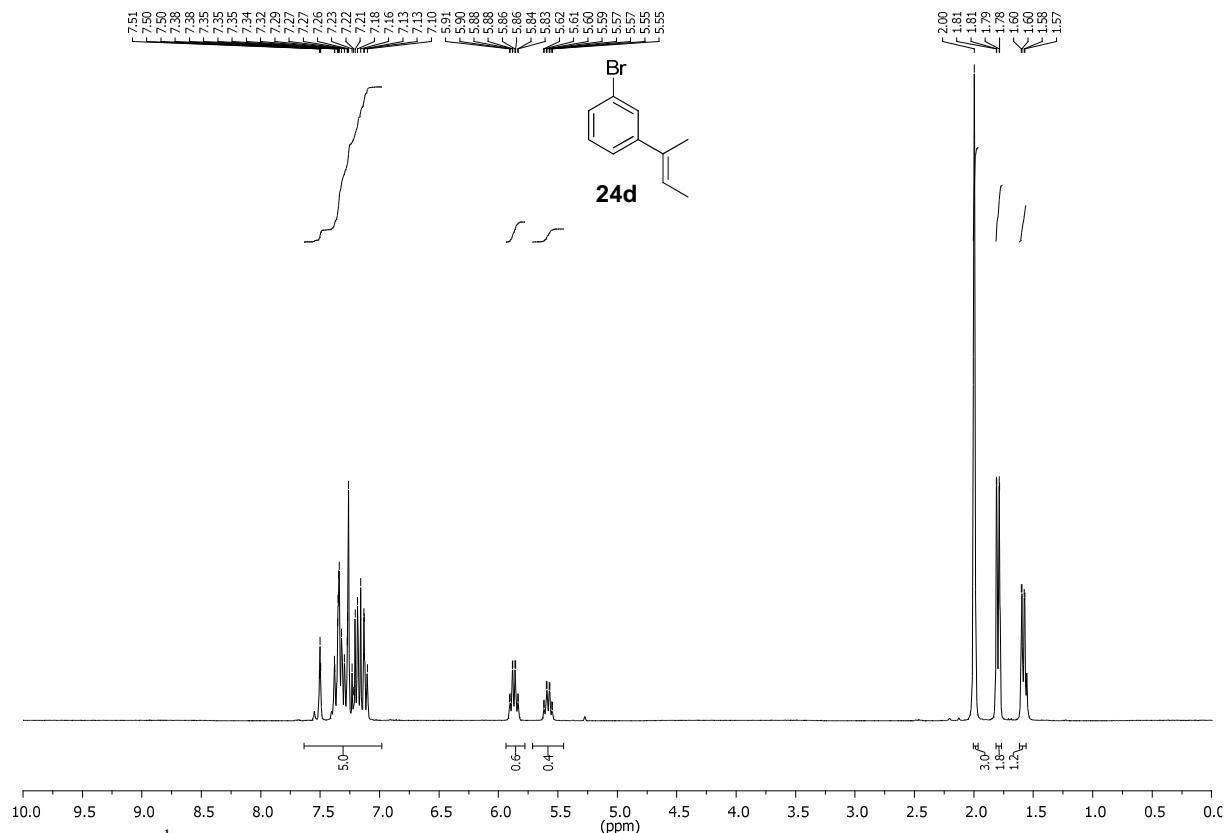


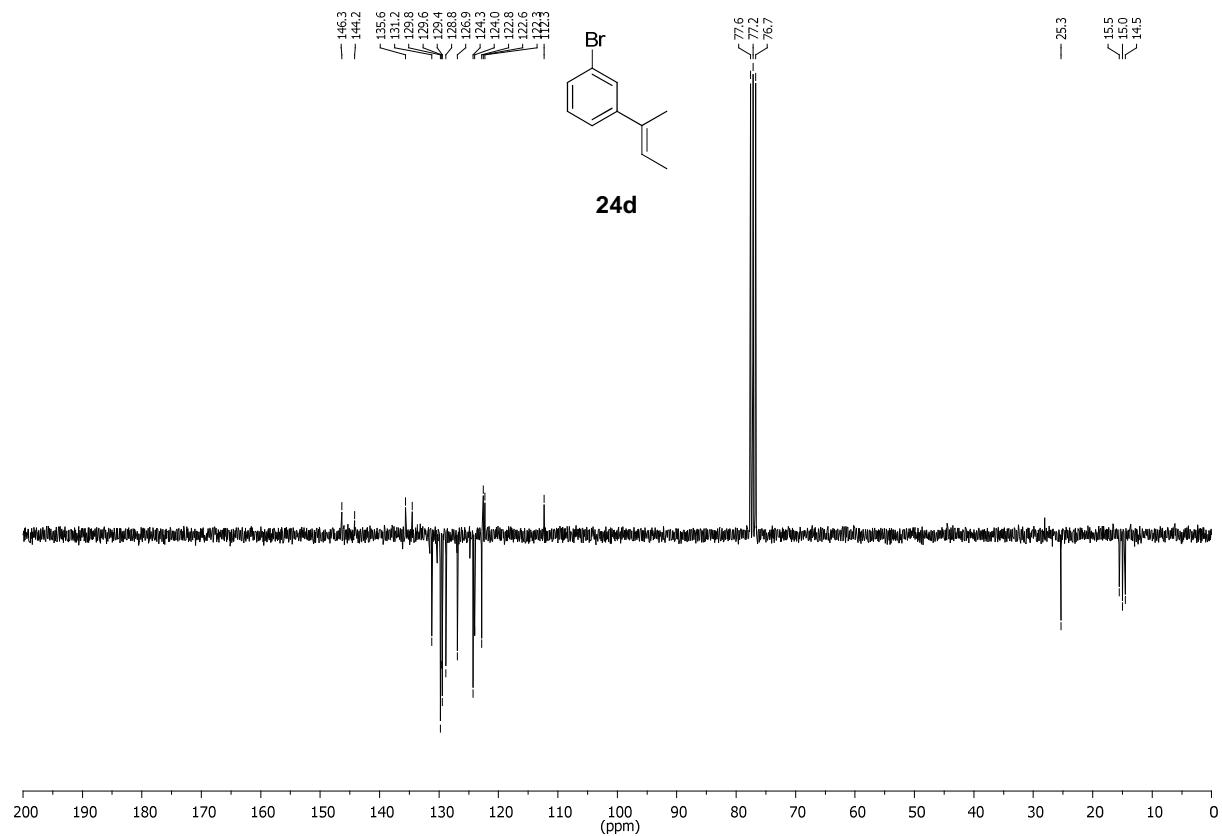
Figure 100: <sup>13</sup>C NMR, APT; (3-benzylphenyl)boronic acid (25a).

## NMR Data

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**Figure 101:** <sup>1</sup>H NMR; 1-bromo-3-(but-2-en-2-yl)benzene (**24d**).



**Figure 102:** <sup>13</sup>C NMR, APT; 1-bromo-3-(but-2-en-2-yl)benzene (**24d**).

## NMR Data

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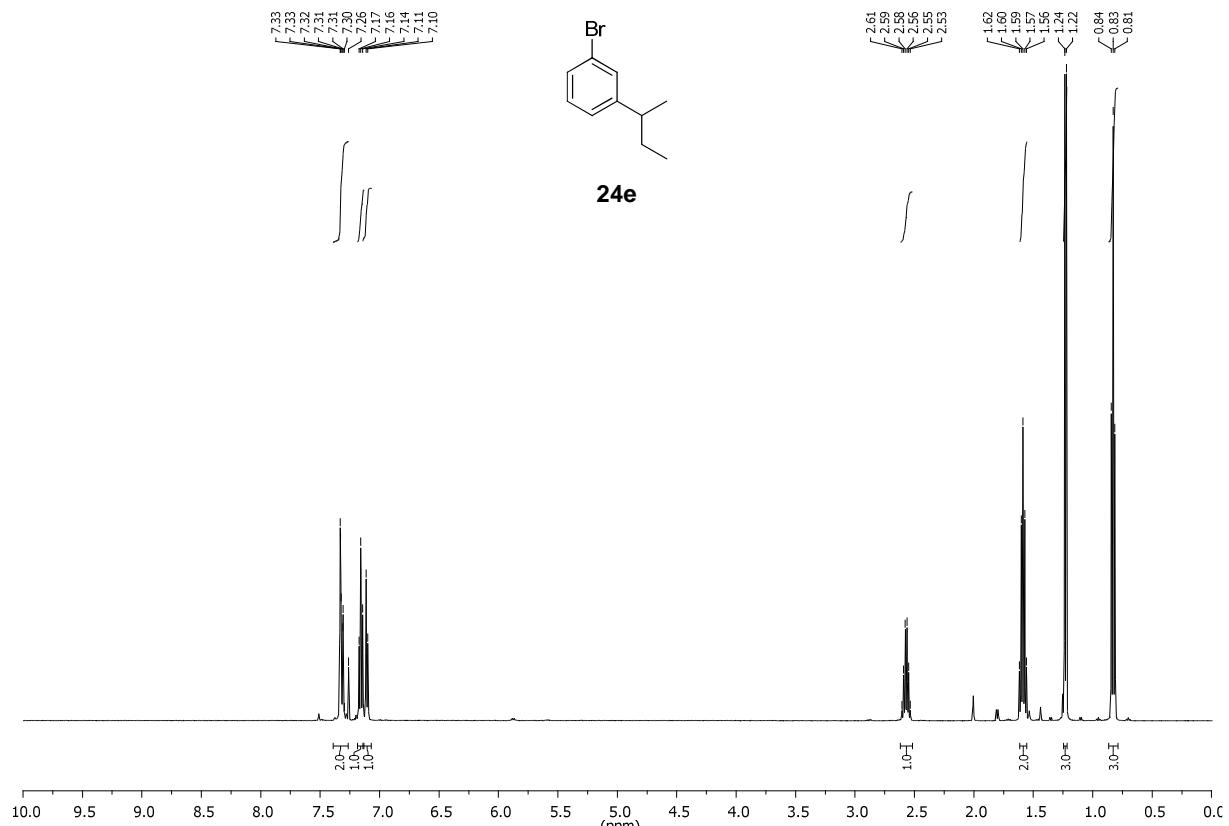


Figure 103: <sup>1</sup>H NMR; 1-bromo-3-(*sec*-butyl)benzene (**24e**).

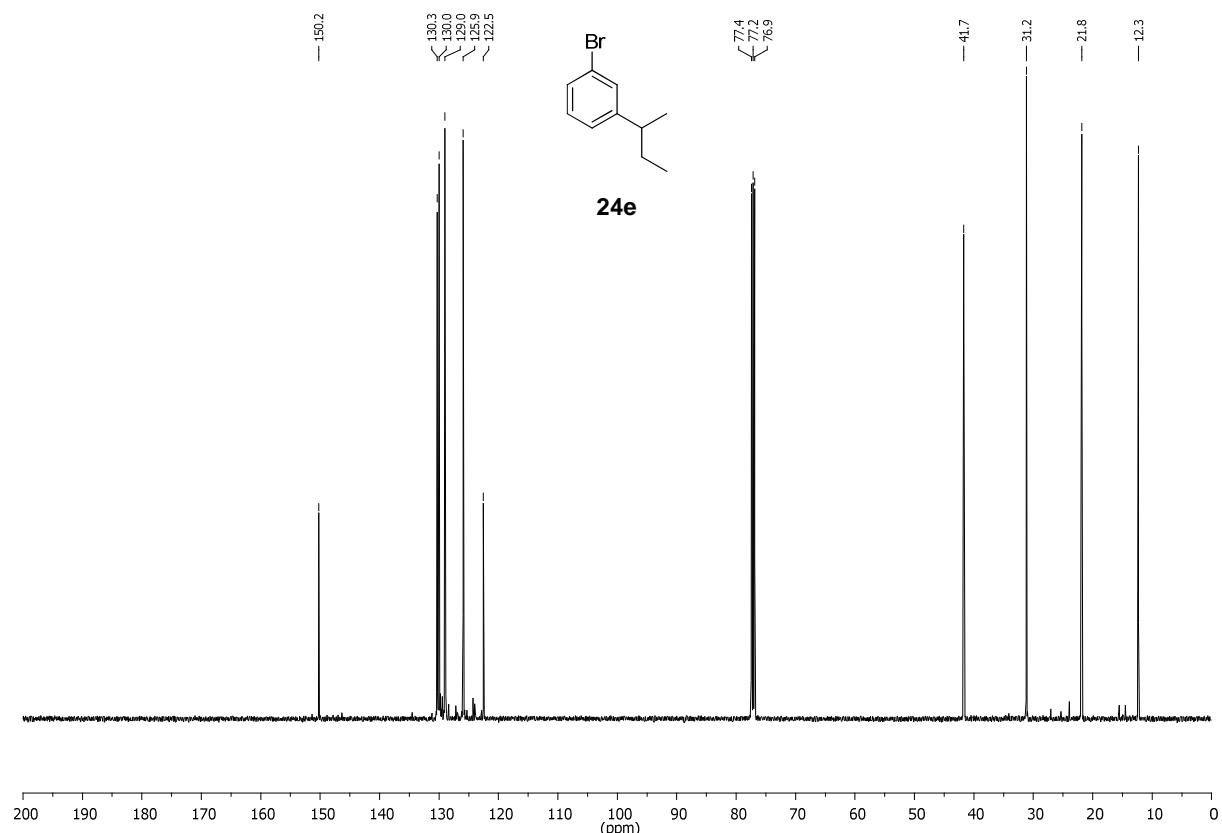


Figure 104: <sup>13</sup>C NMR; 1-bromo-3-(*sec*-butyl)benzene (**24e**).

## NMR Data

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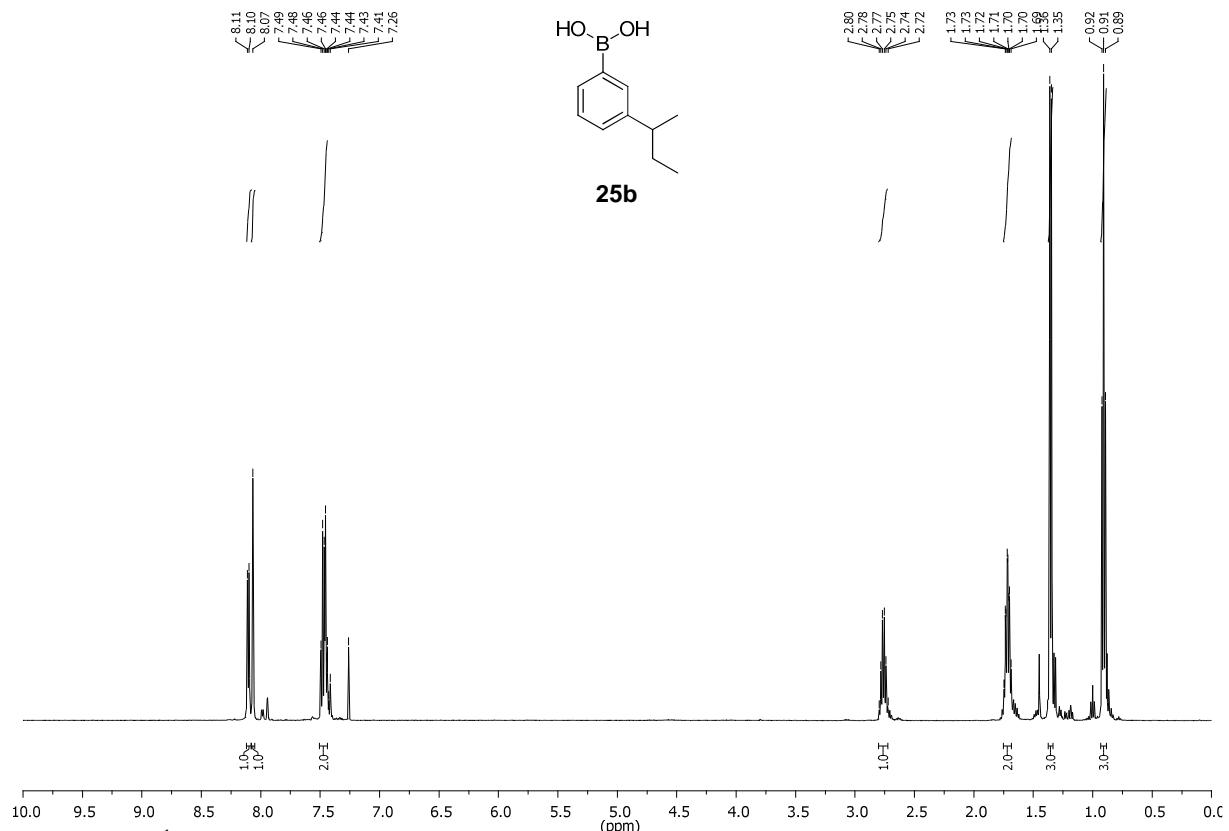


Figure 105: <sup>1</sup>H NMR; (3-(sec-butyl)phenyl)boronic acid (**25b**).

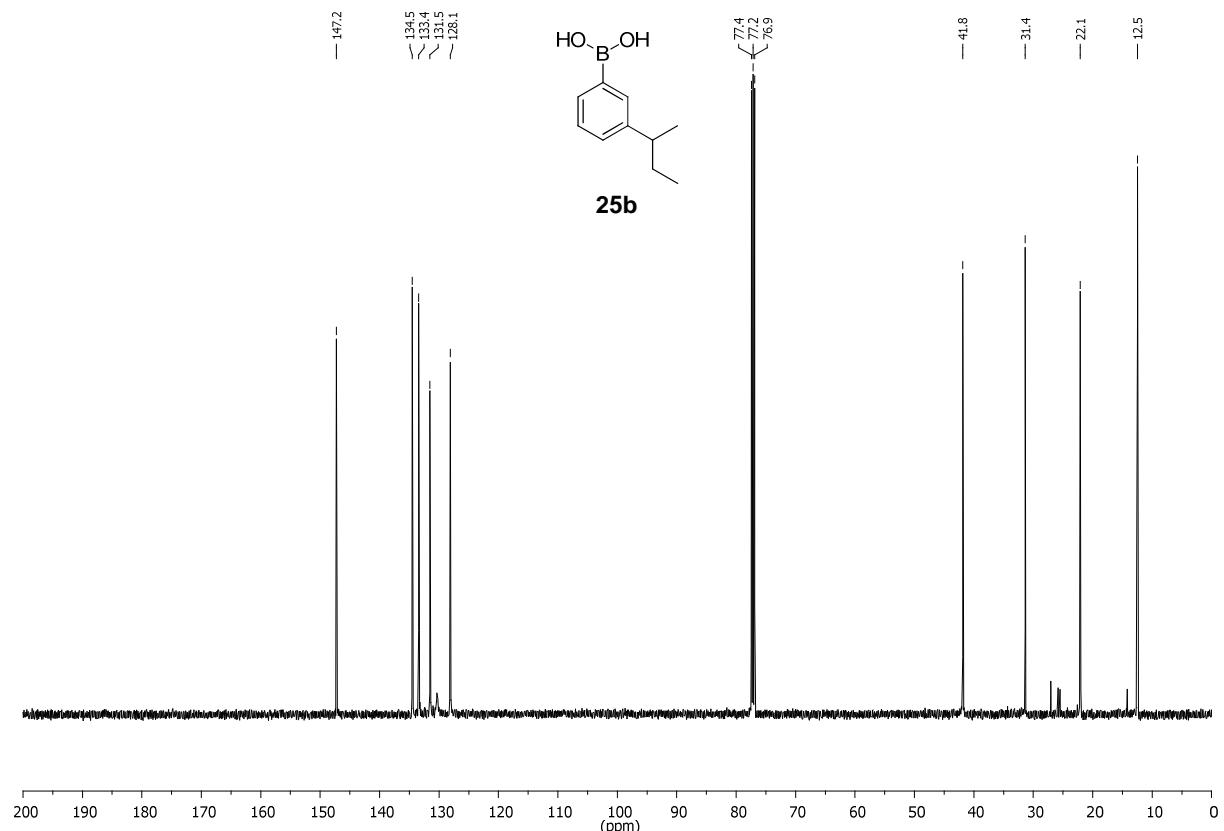
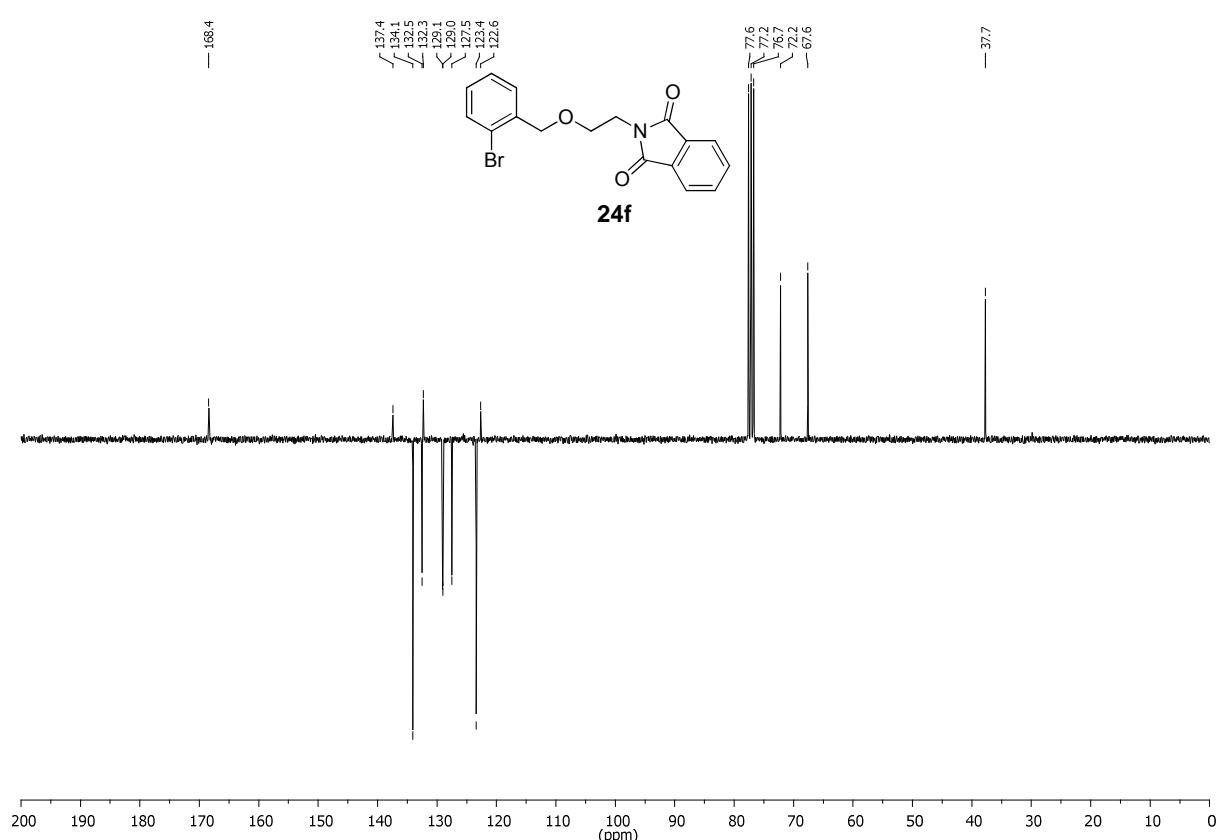
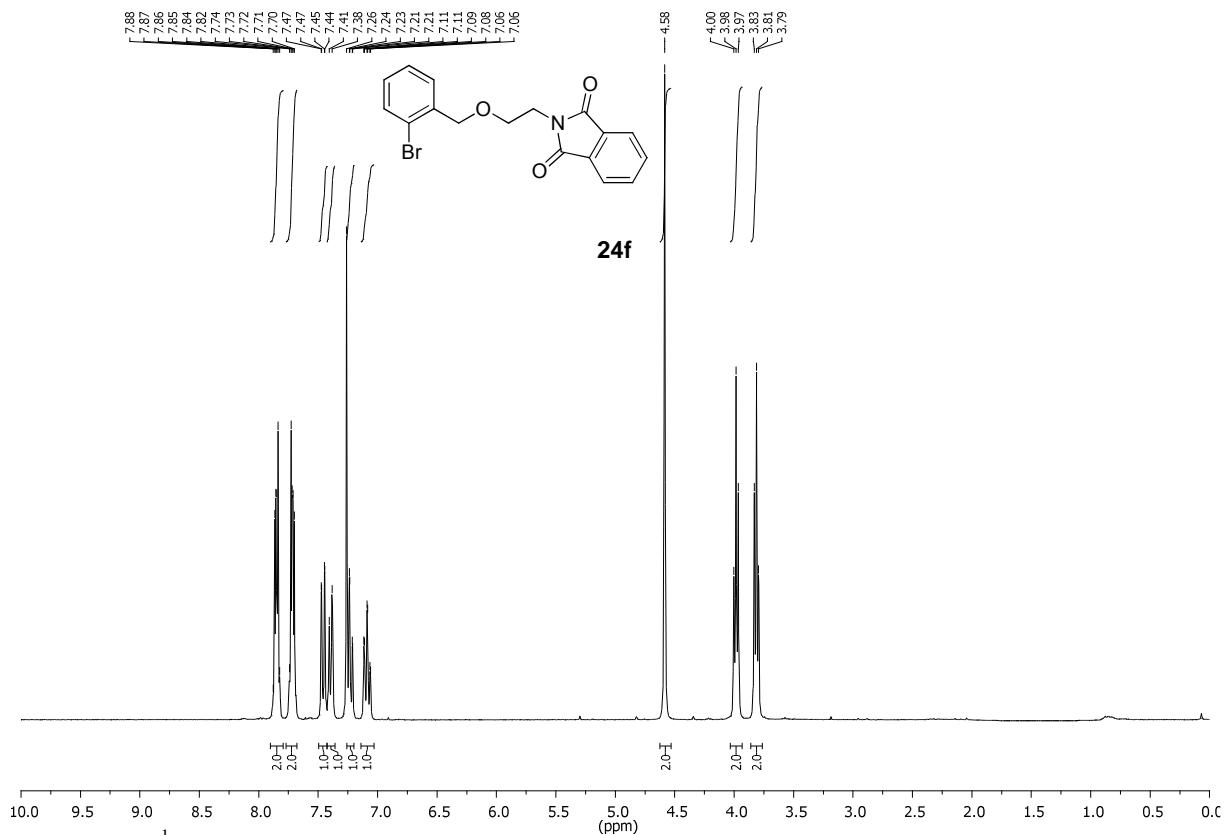


Figure 106: <sup>13</sup>C NMR; (3-(sec-butyl)phenyl)boronic acid (**25b**).

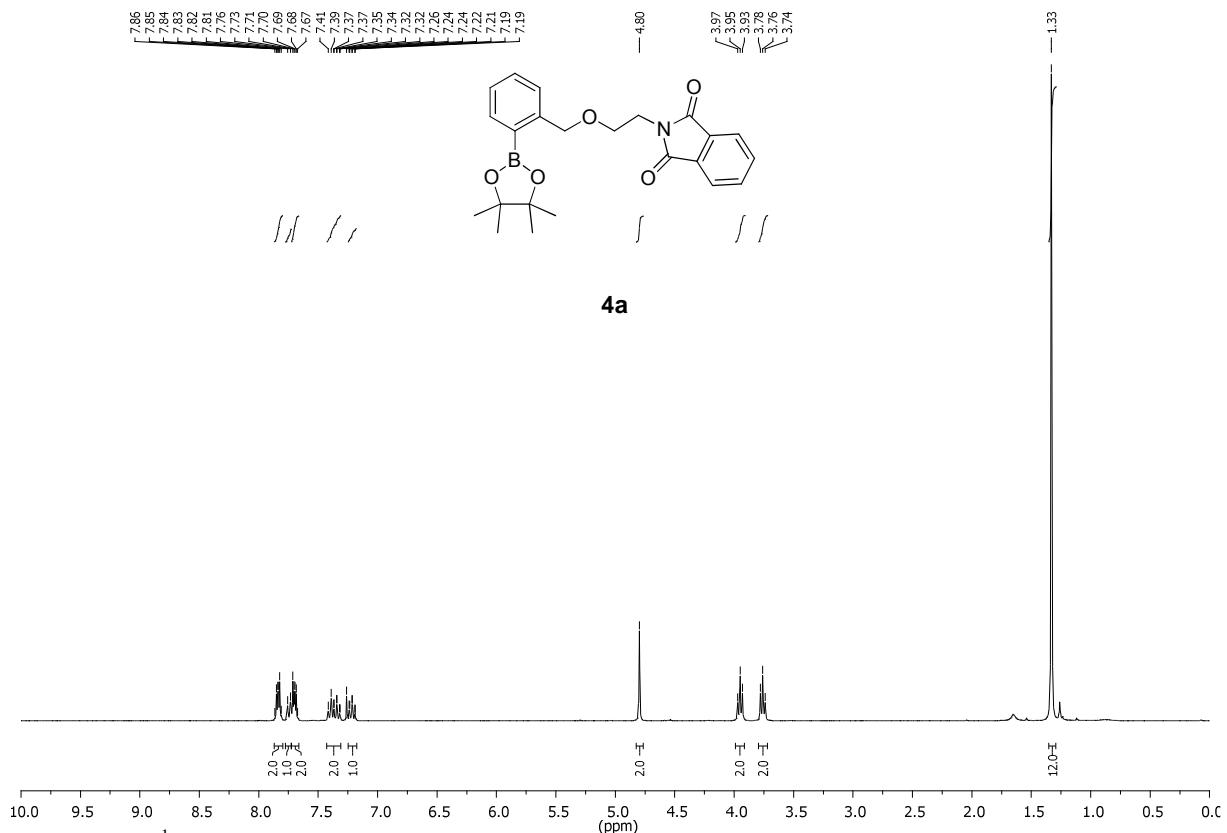
## NMR Data

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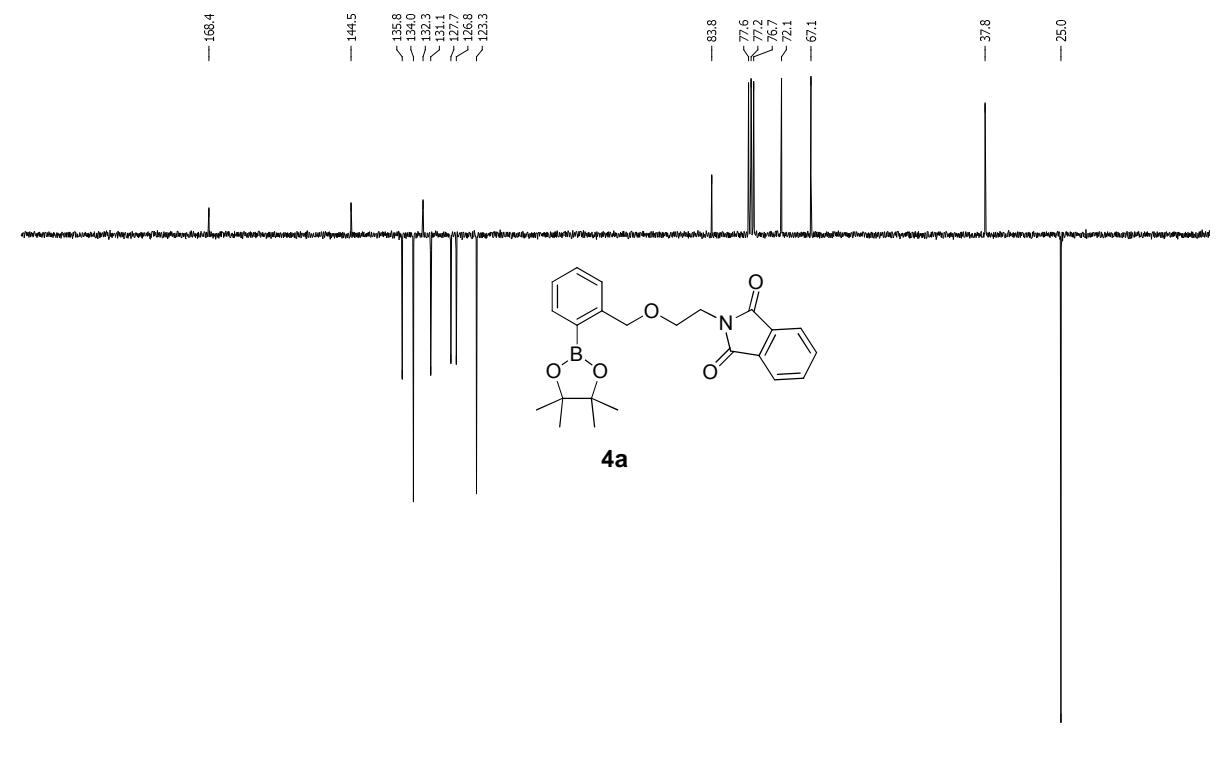


## NMR Data

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**Figure 109:** <sup>1</sup>H NMR; 2-((2-((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)oxy)ethyl)isoindoline-1,3-dione (**4a**).



**Figure 110:** <sup>13</sup>C NMR, APT; 2-((2-((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)oxy)ethyl)isoindoline-1,3-dione (**4a**).

## NMR Data

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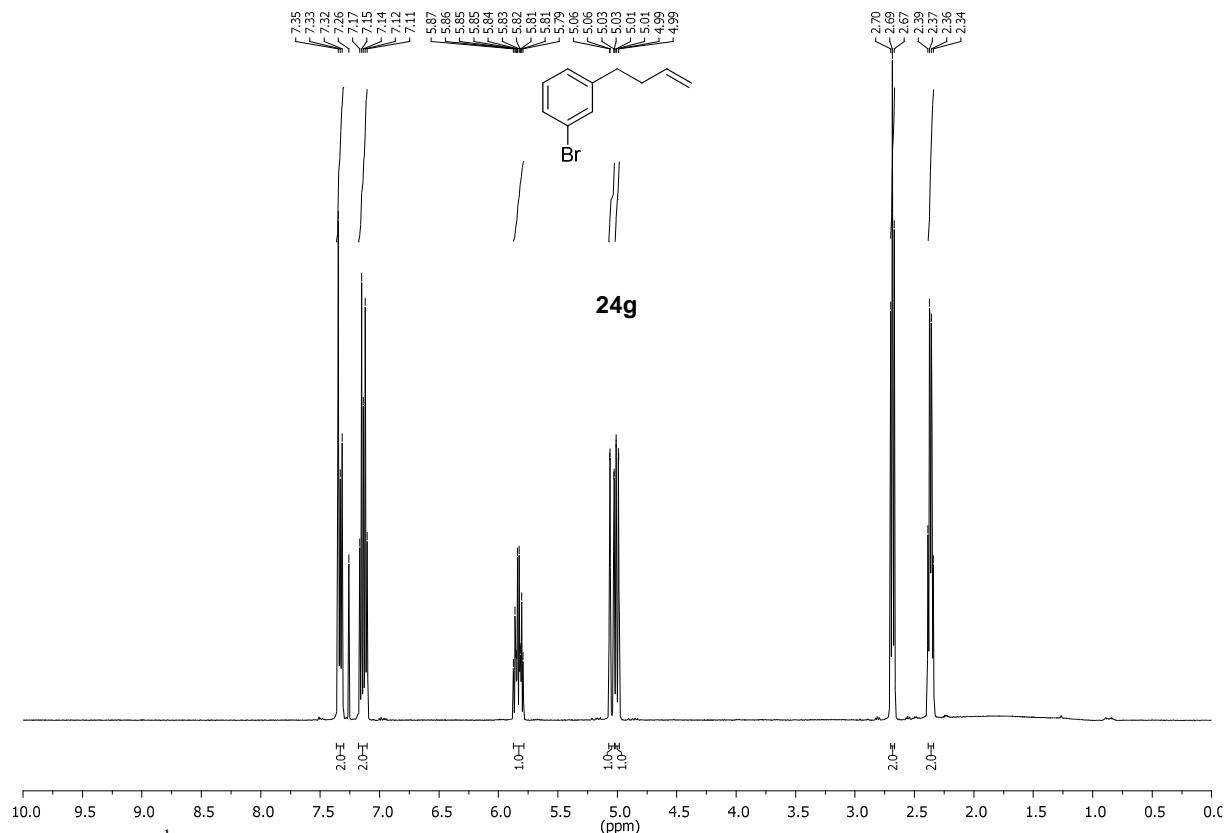


Figure 111: <sup>1</sup>H NMR; 1-bromo-3-(but-3-en-1-yl)benzene (24g).

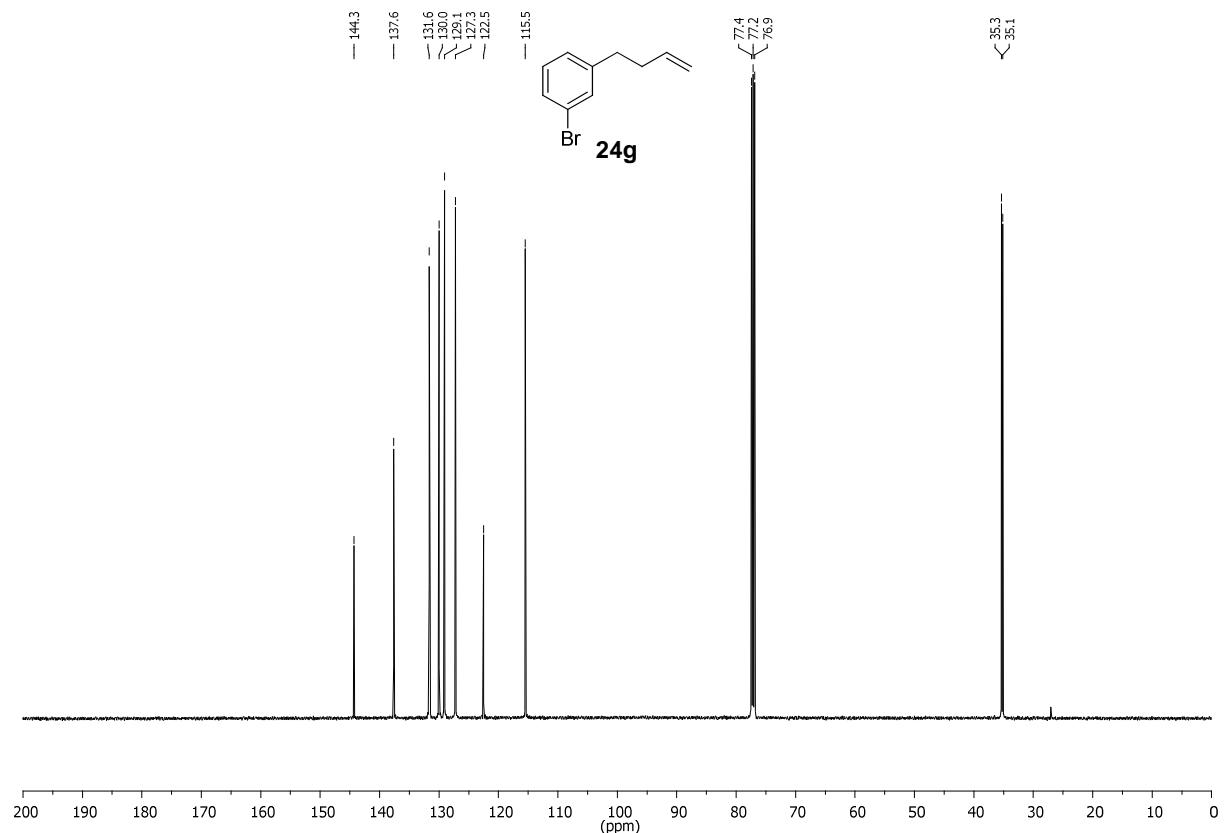


Figure 112: <sup>13</sup>C NMR; 1-bromo-3-(but-3-en-1-yl)benzene (24g).

## NMR Data

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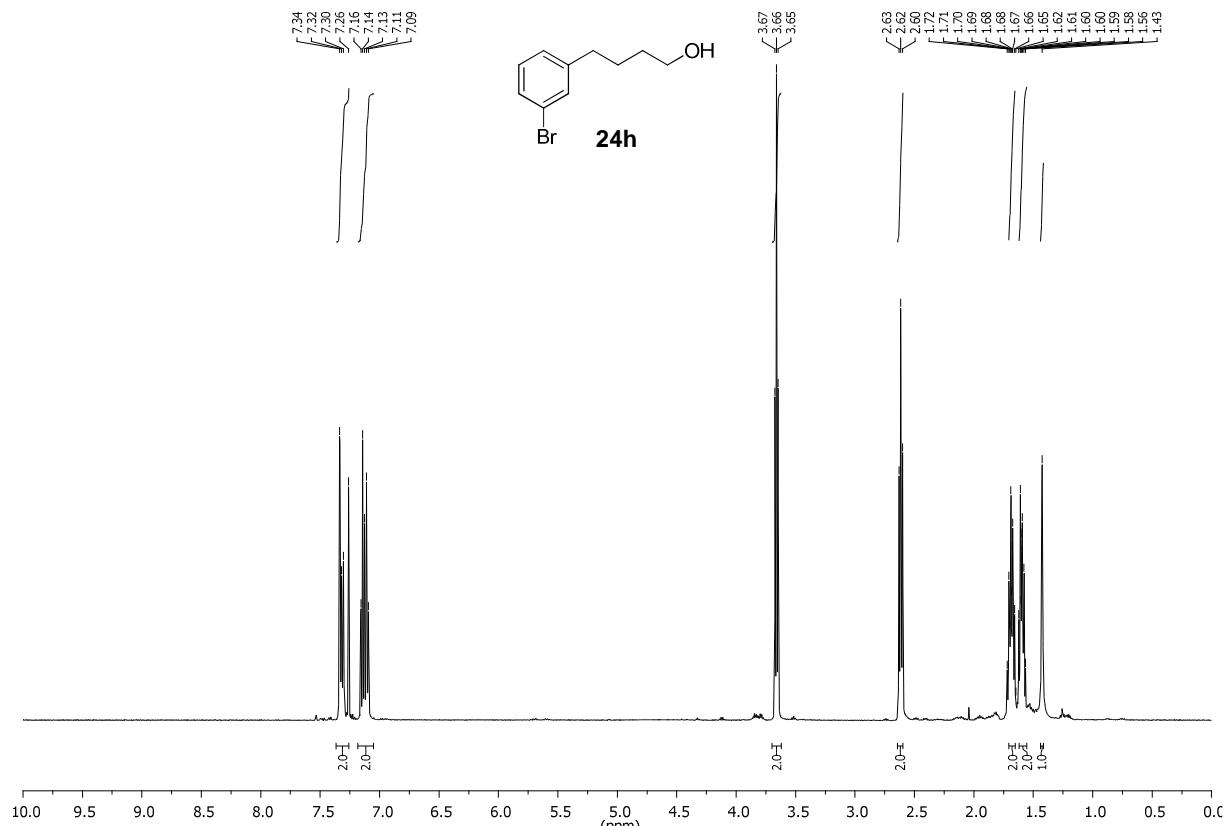


Figure 113: <sup>1</sup>H NMR; 4-(3-bromophenyl)butan-1-ol (**24h**).

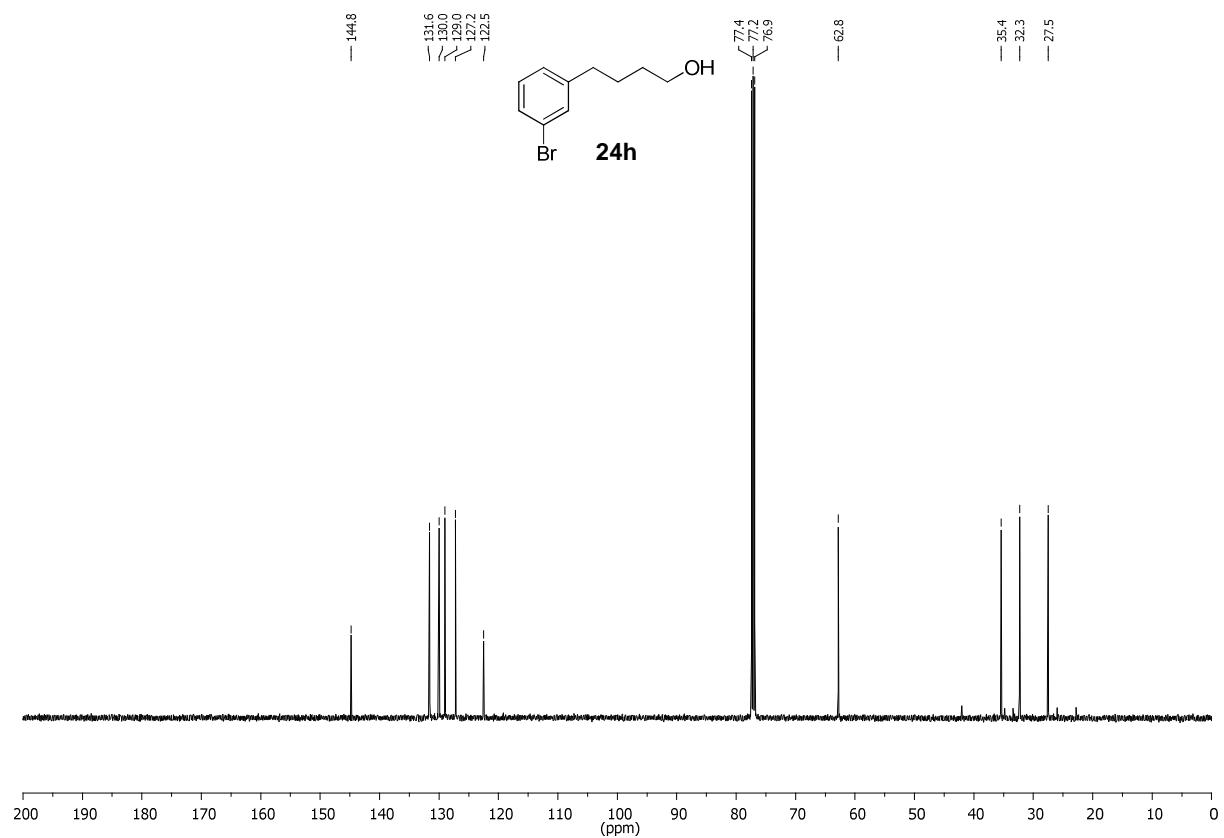


Figure 114: <sup>13</sup>C NMR; 4-(3-bromophenyl)butan-1-ol (**24h**).

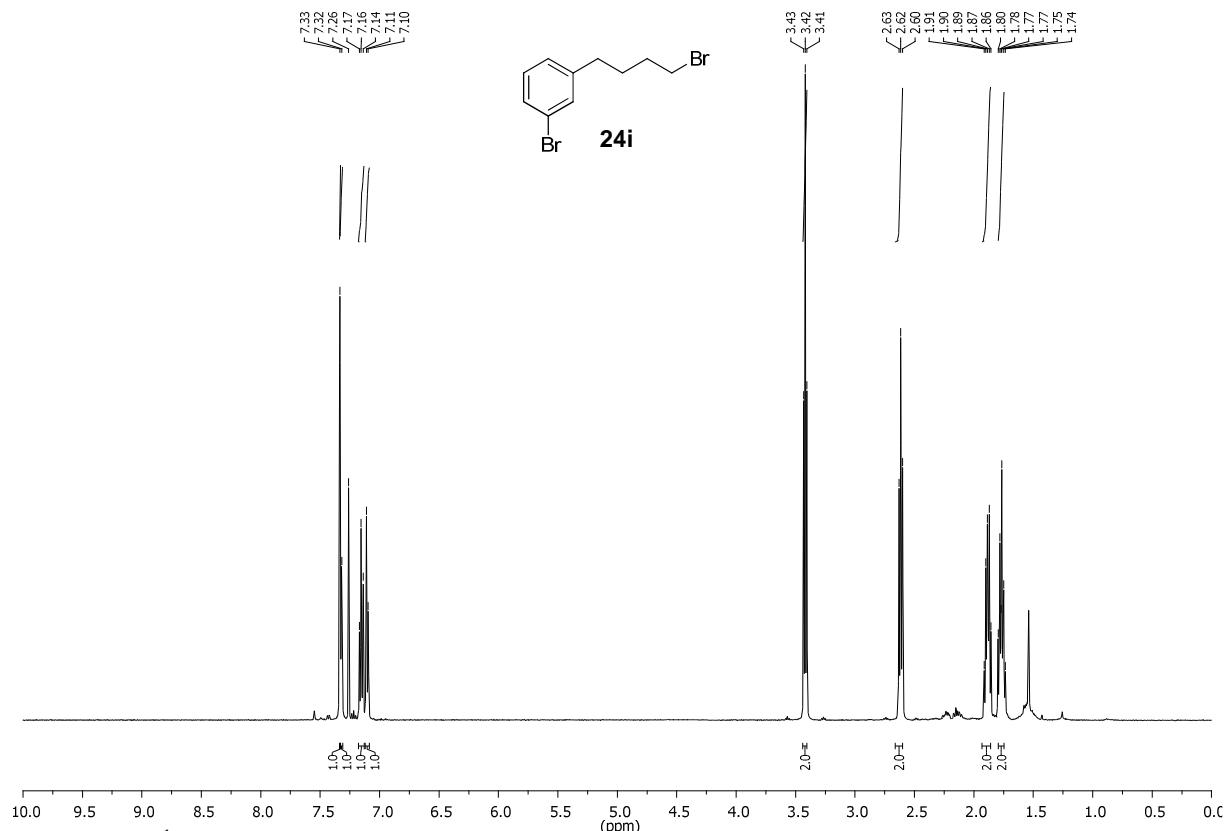


Figure 115: <sup>1</sup>H NMR; 1-bromo-3-(4-bromobutyl)benzene (24i).

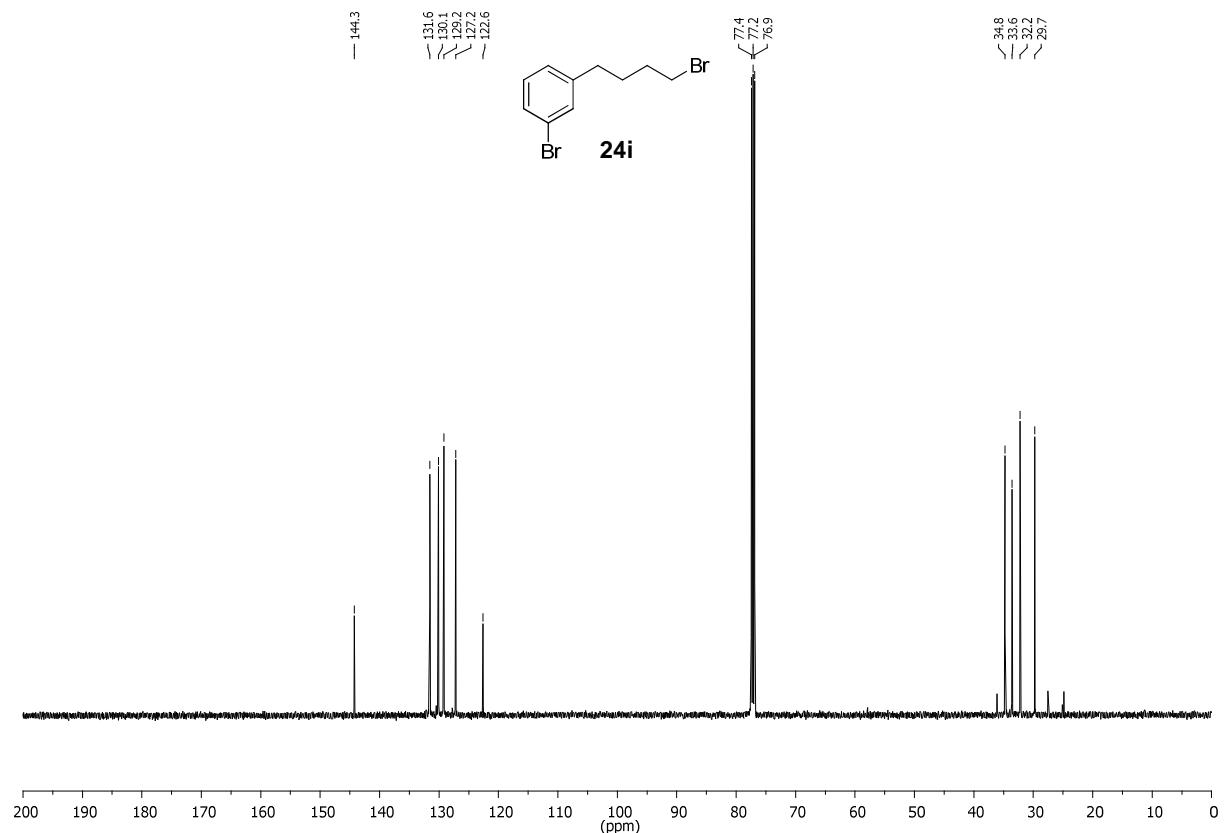


Figure 116: <sup>13</sup>C NMR; 1-bromo-3-(4-bromobutyl)benzene (24i).

## NMR Data

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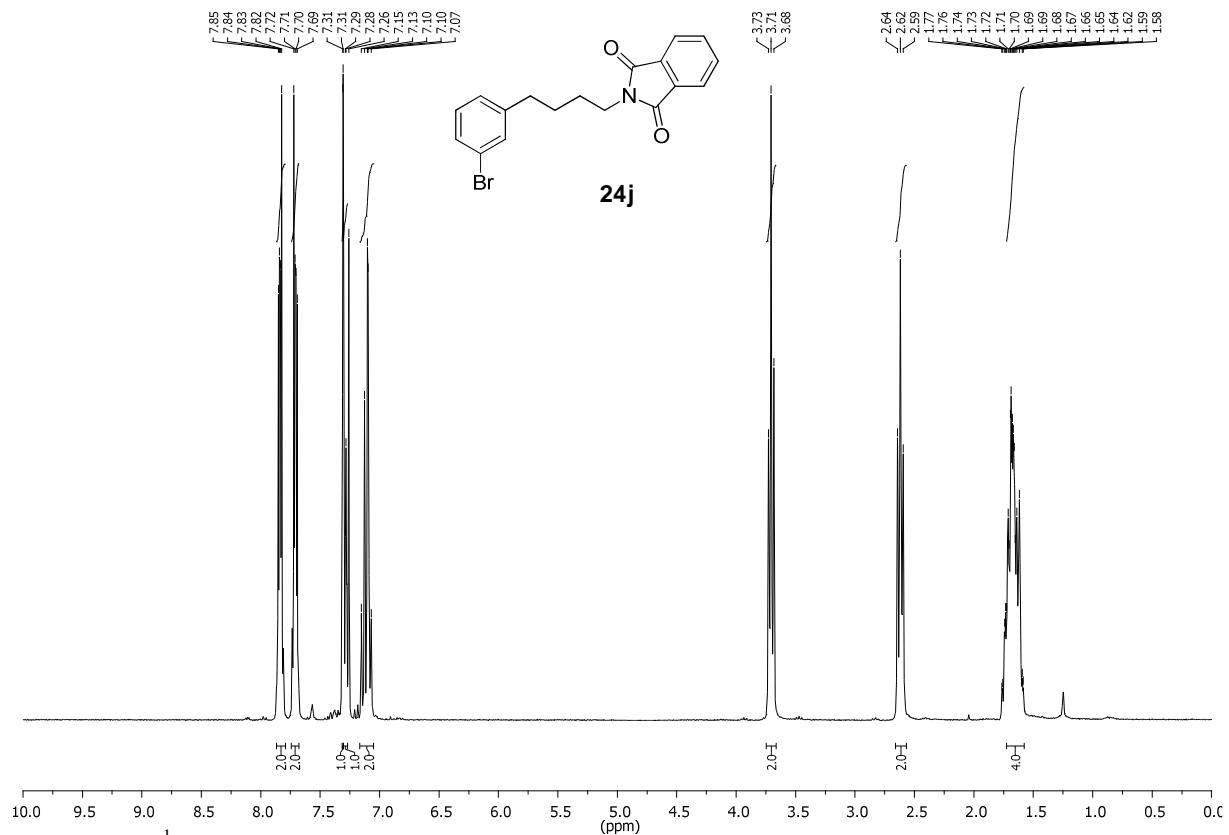


Figure 117: <sup>1</sup>H NMR; 2-(4-(3-bromophenyl)butyl)isoindoline-1,3-dione (24j).

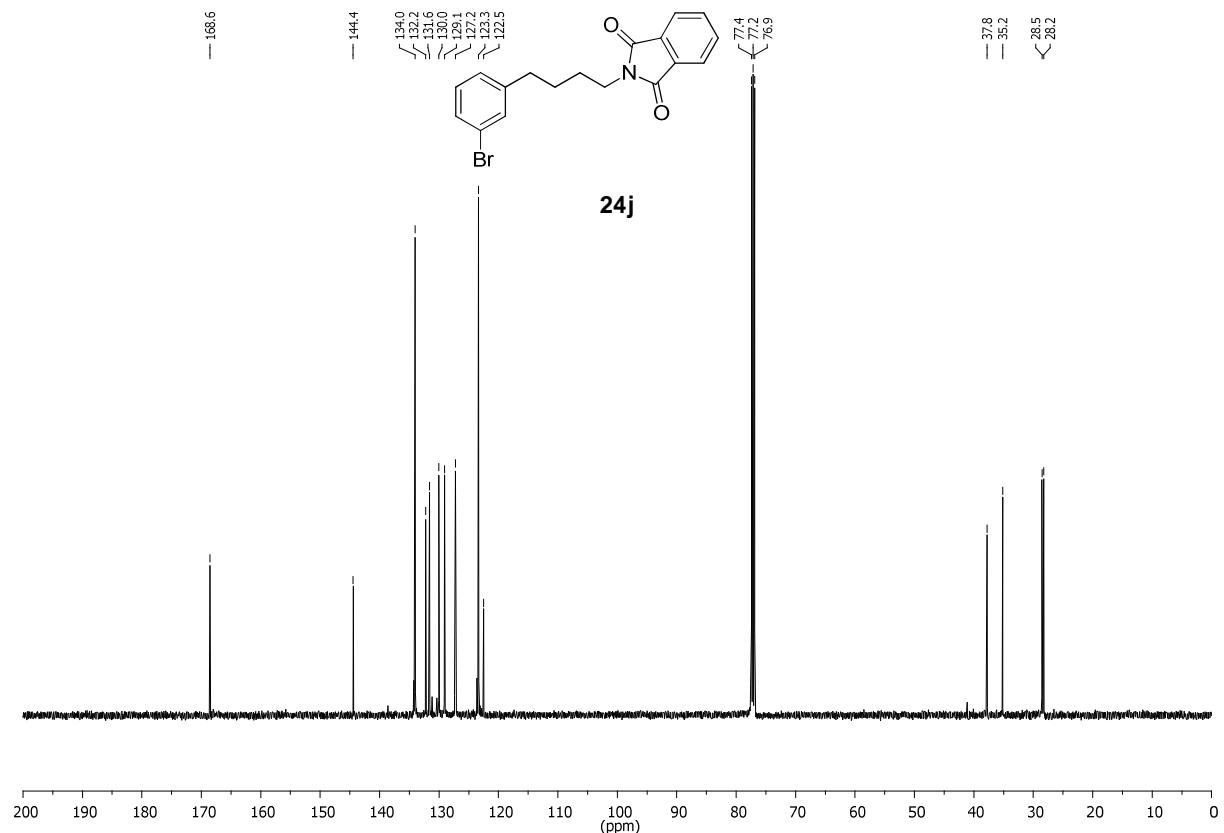
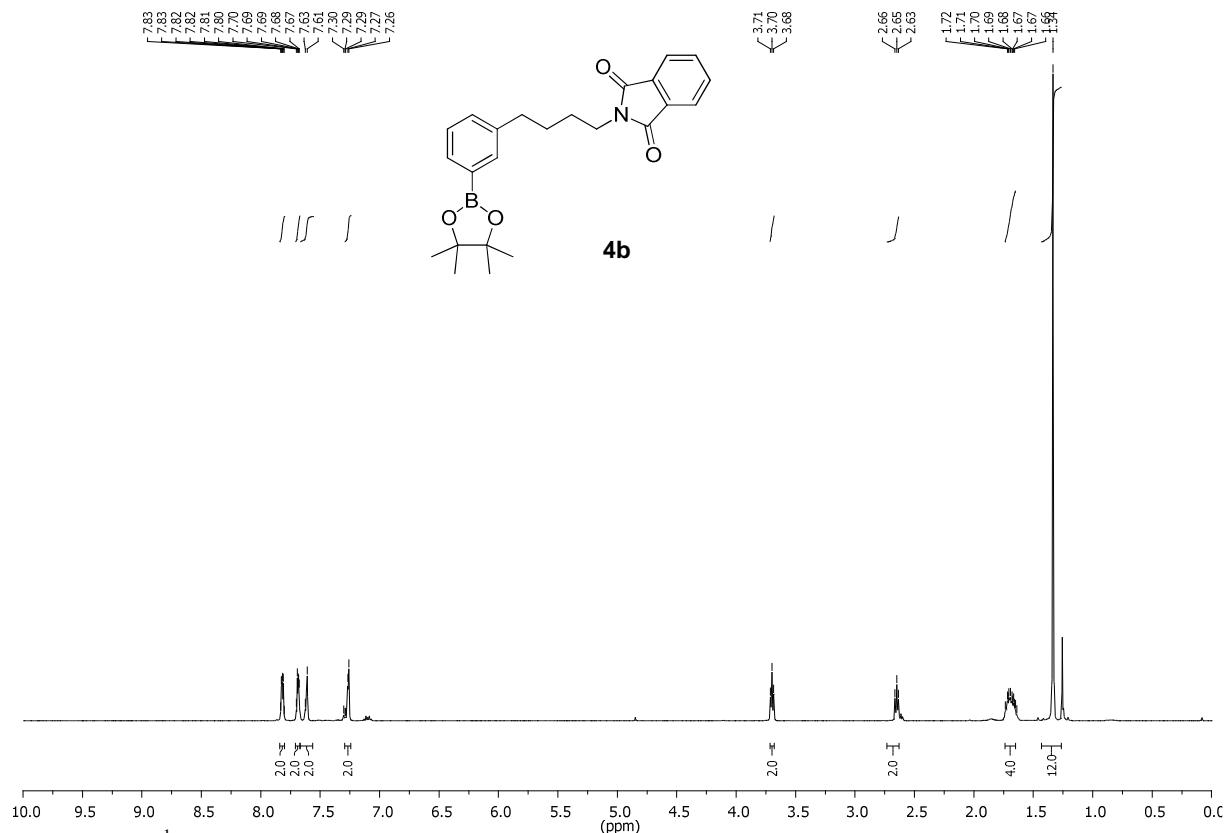


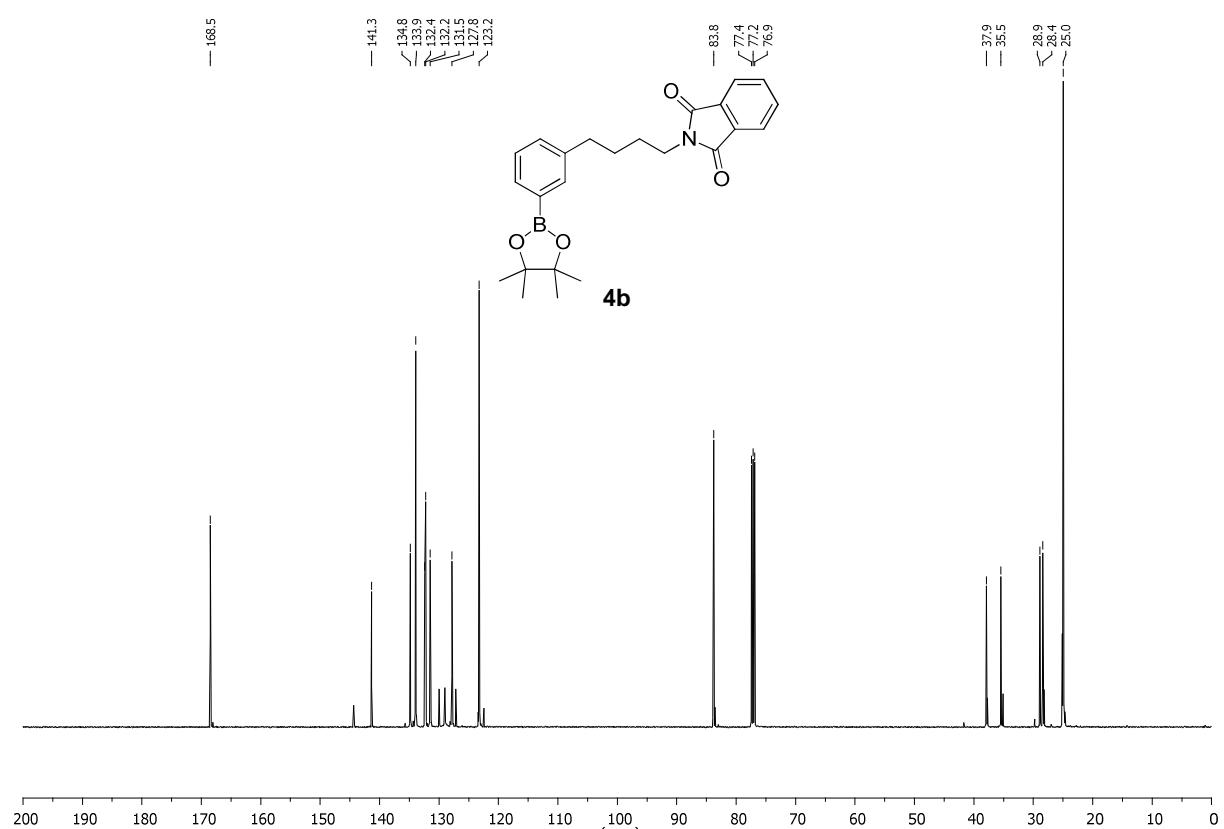
Figure 118: <sup>13</sup>C NMR; 2-(4-(3-bromophenyl)butyl)isoindoline-1,3-dione (24j).

## NMR Data

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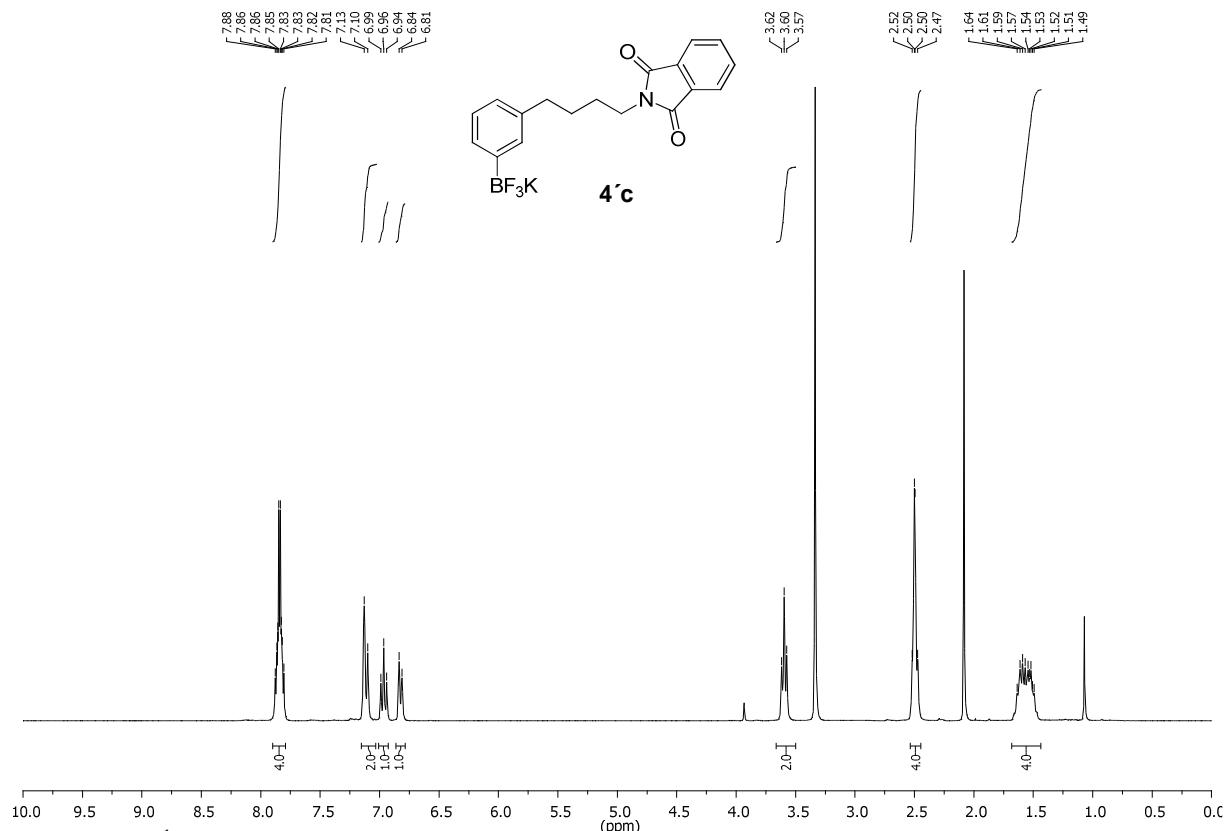
**Figure 119:**  $^1\text{H}$  NMR; 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**4b**).



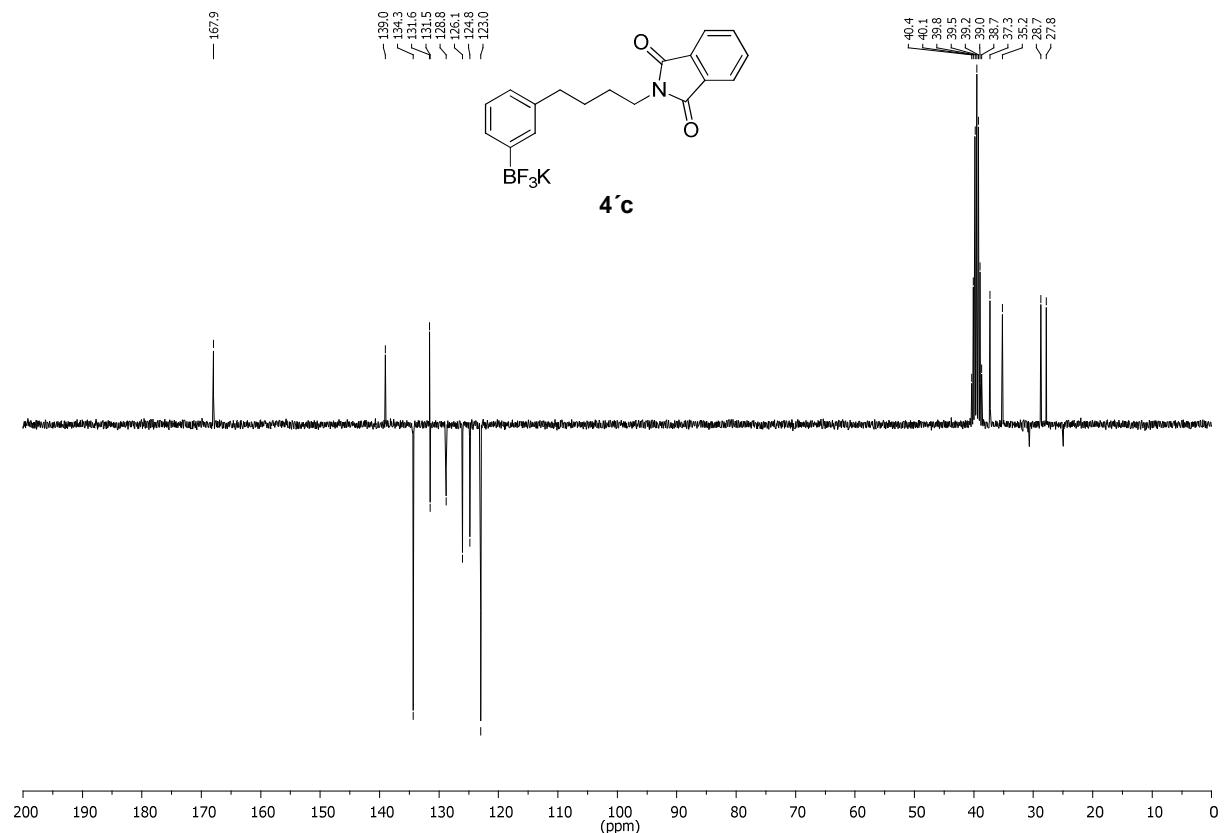
**Figure 120:**  $^{13}\text{C}$  NMR; 2-(4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)isoindoline-1,3-dione (**4b**).

## NMR Data

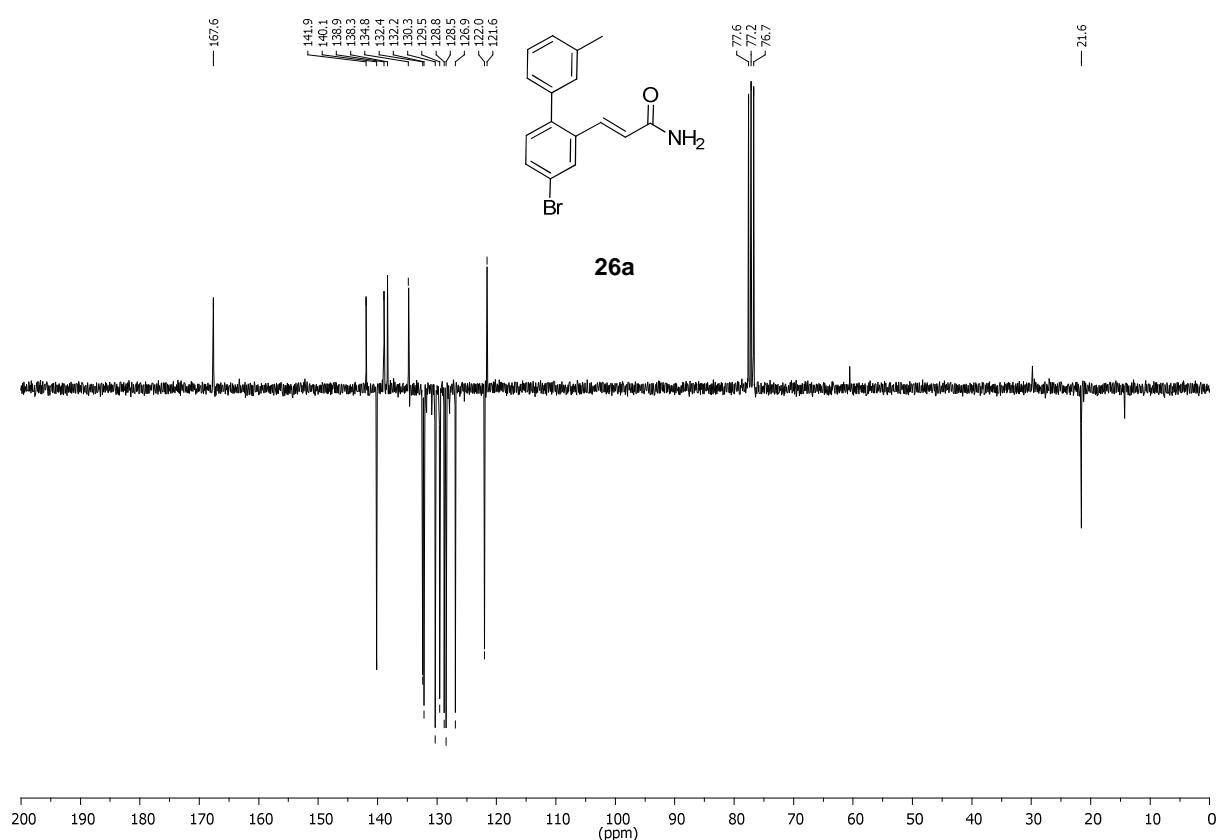
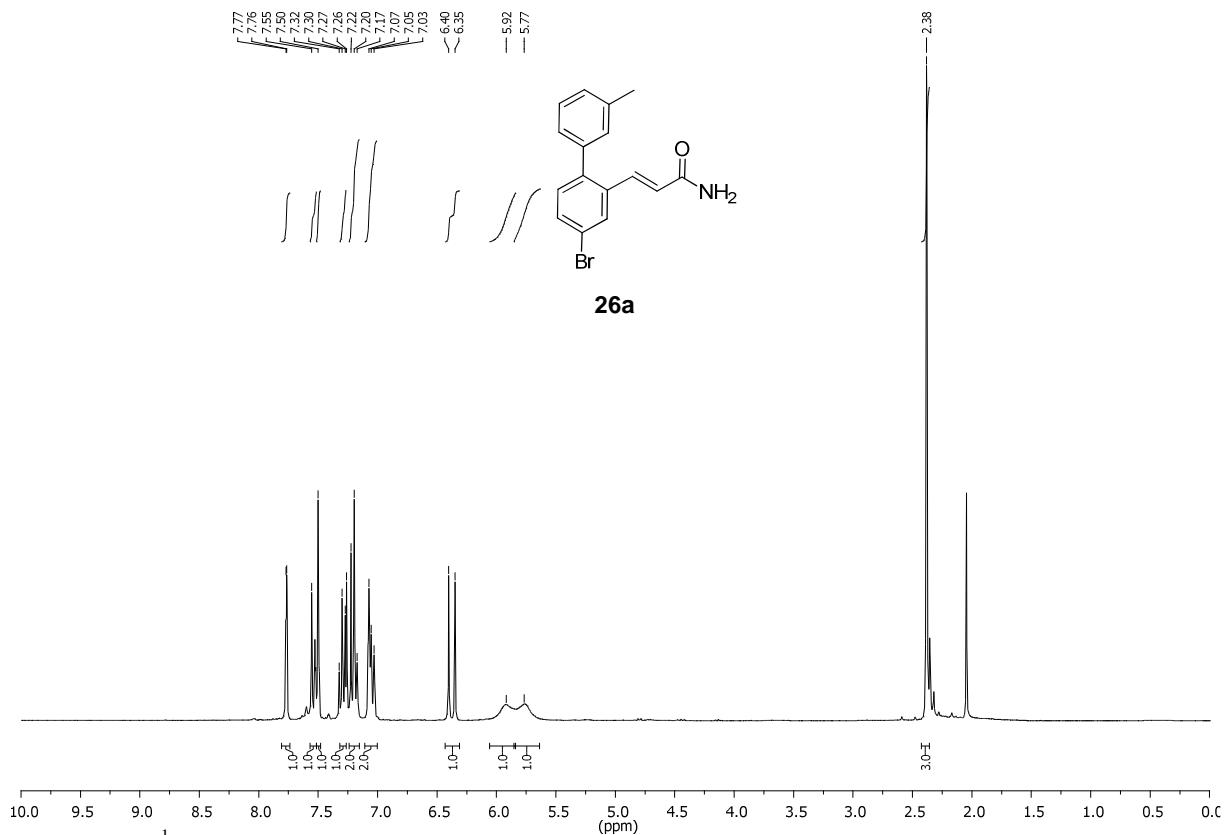
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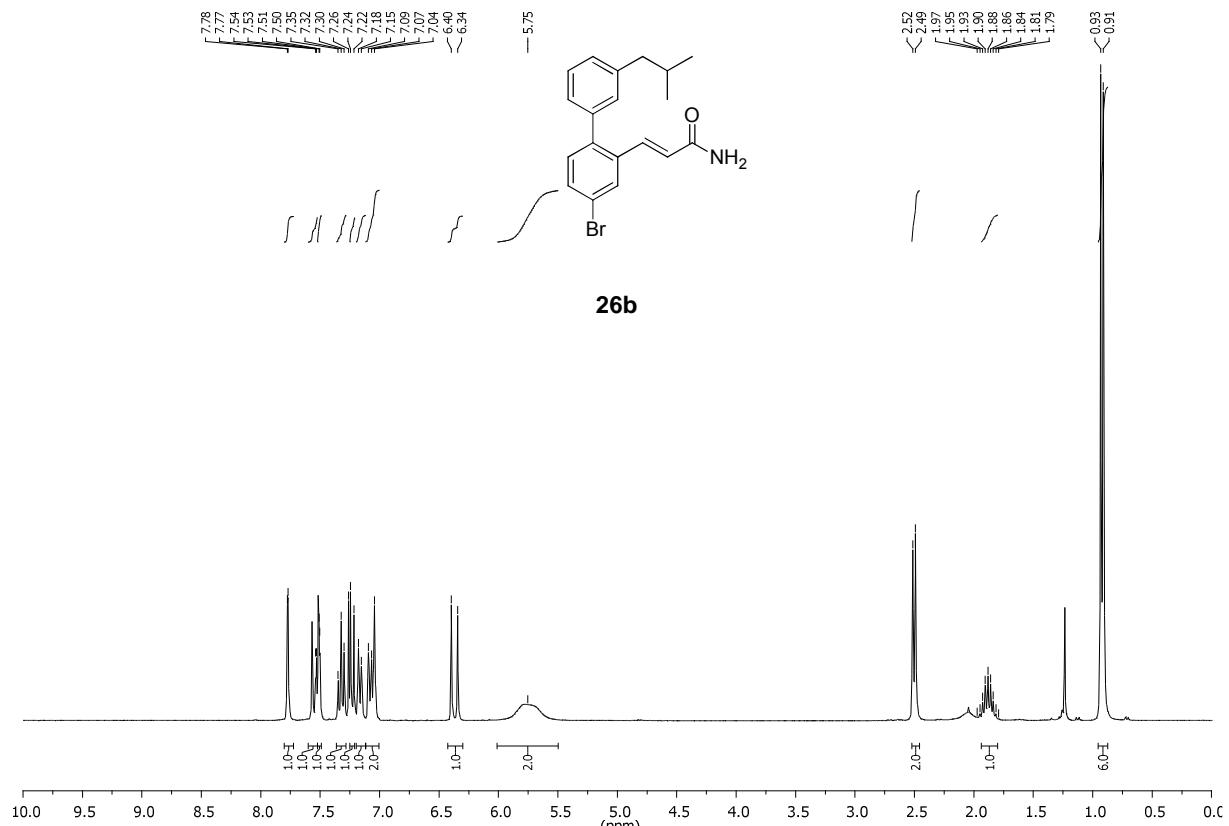


**Figure 121:** <sup>1</sup>H NMR; potassium (3-(4-(1,3-dioxoisoindolin-2-yl)butyl)phenyl)trifluoroborate (**4'c**).

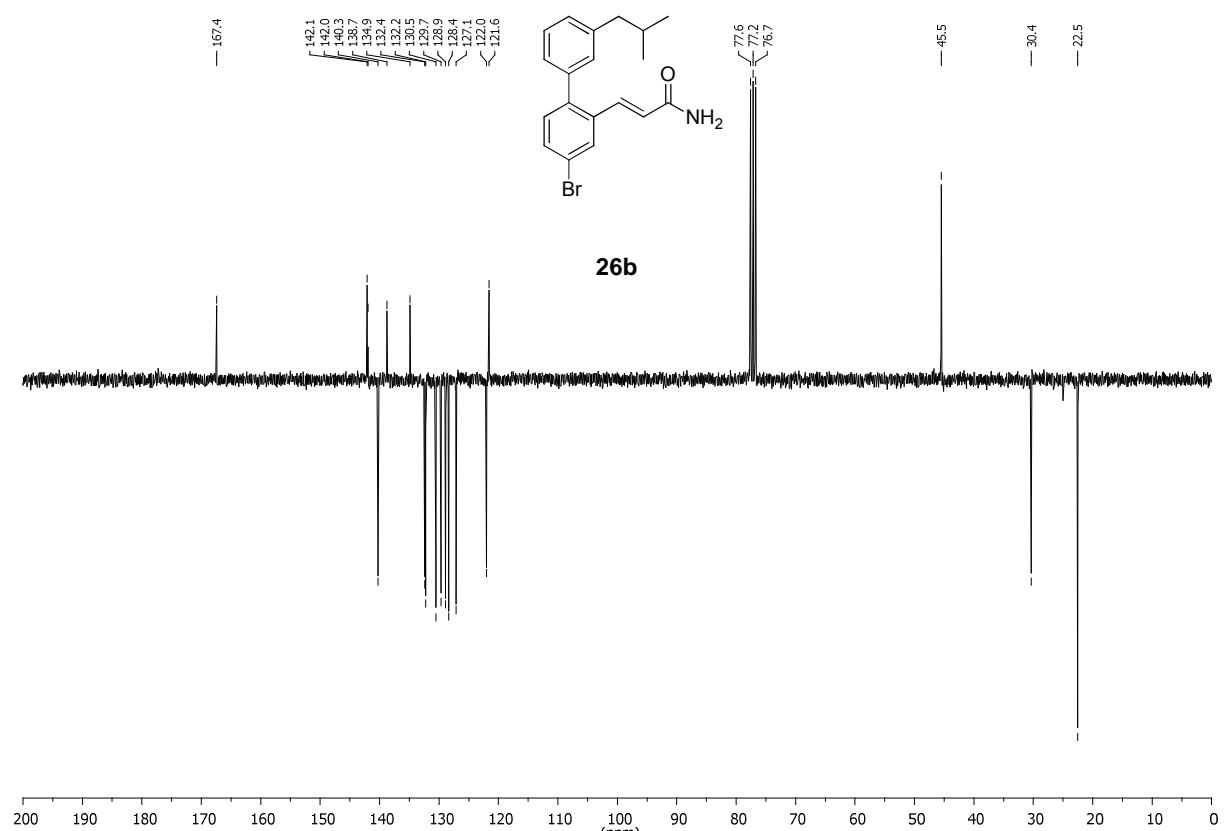


**Figure 122:** <sup>13</sup>C NMR, APT; potassium (3-(4-(1,3-dioxoisoindolin-2-yl)butyl)phenyl)trifluoroborate (**4'c**).

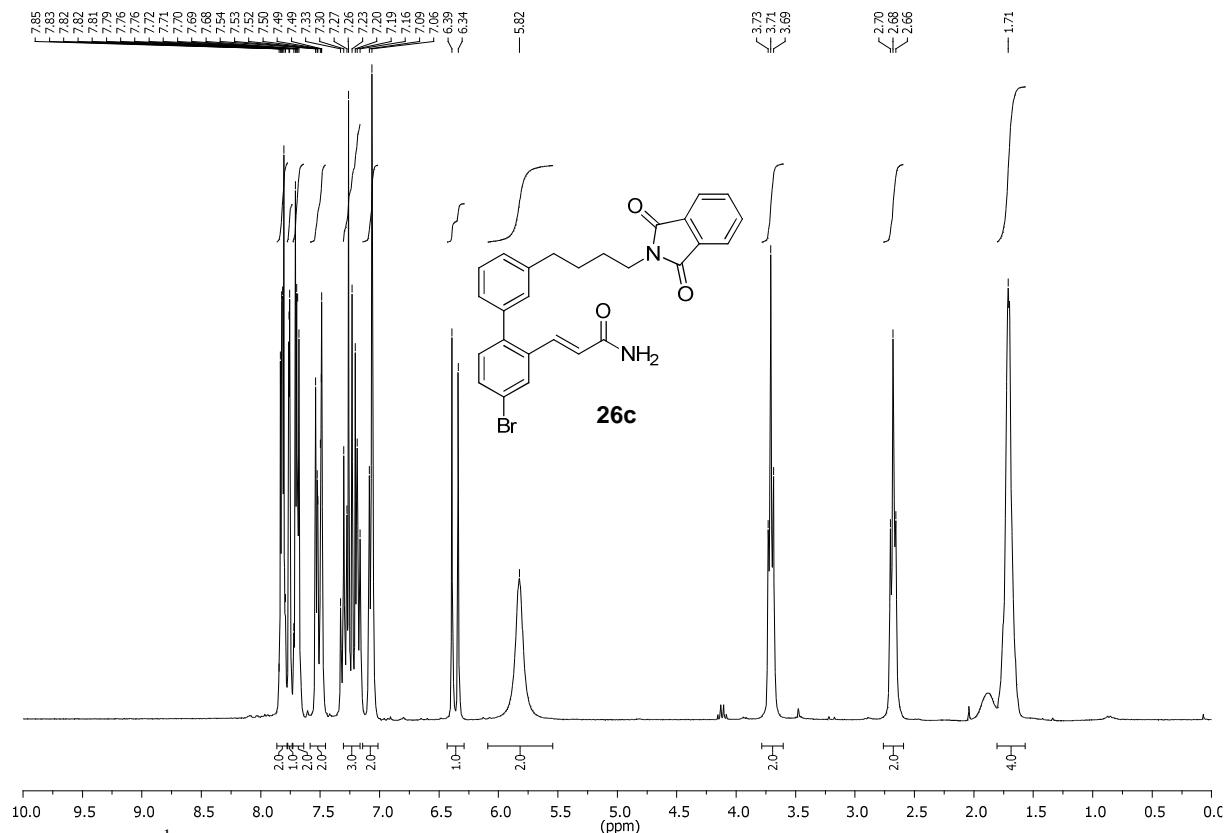




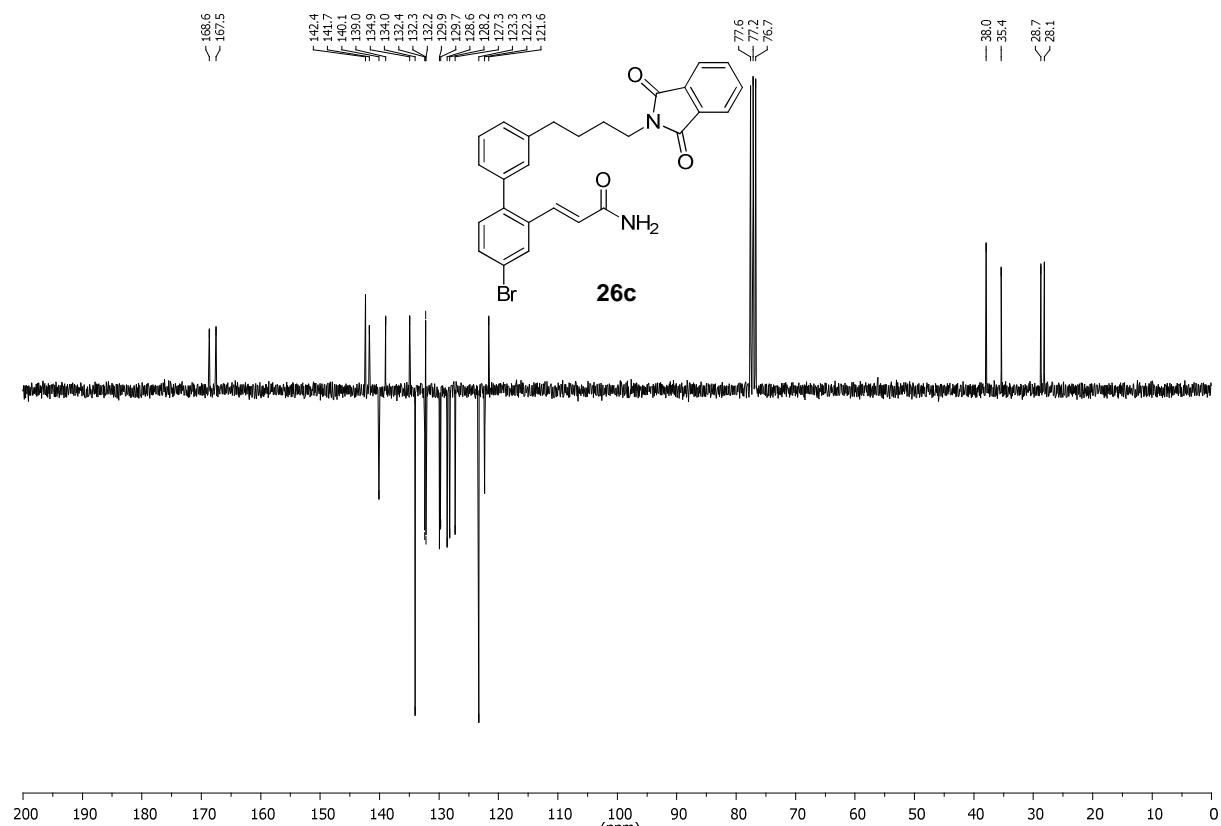
**Figure 125:** <sup>1</sup>H NMR; (*E*)-3-(4-bromo-3'-isobutyl-[1,1'-biphenyl]-2-yl)acrylamide (**26b**).



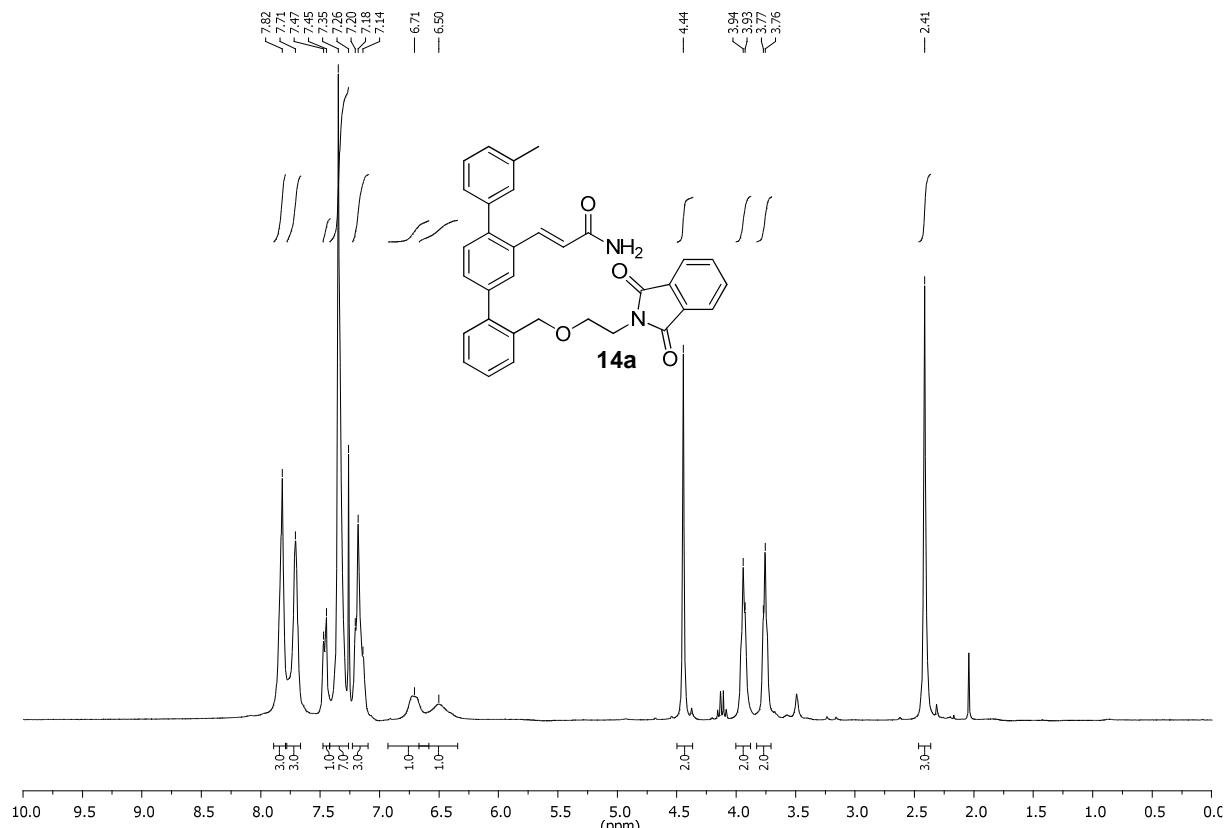
**Figure 126:** <sup>13</sup>C NMR, APT; (*E*-3-(4-bromo-3'-isobutyl-[1,1'-biphenyl]-2-yl)acrylamide (**26b**).



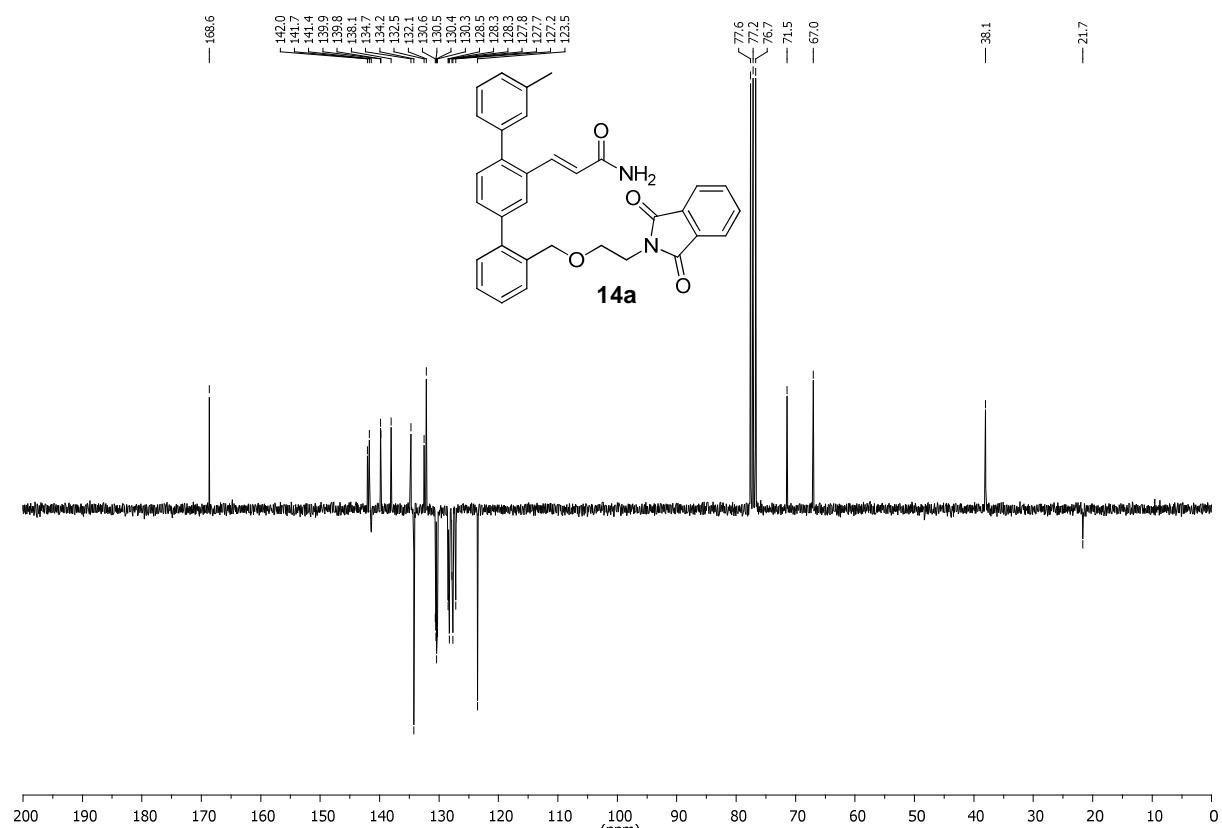
**Figure 127:**  $^1\text{H}$  NMR; (*E*)-3-(4-bromo-3'-(4-(1,3-dioxoisindolin-2-yl)butyl)-[1,1'-biphenyl]-2-yl)acrylamide (**26c**).



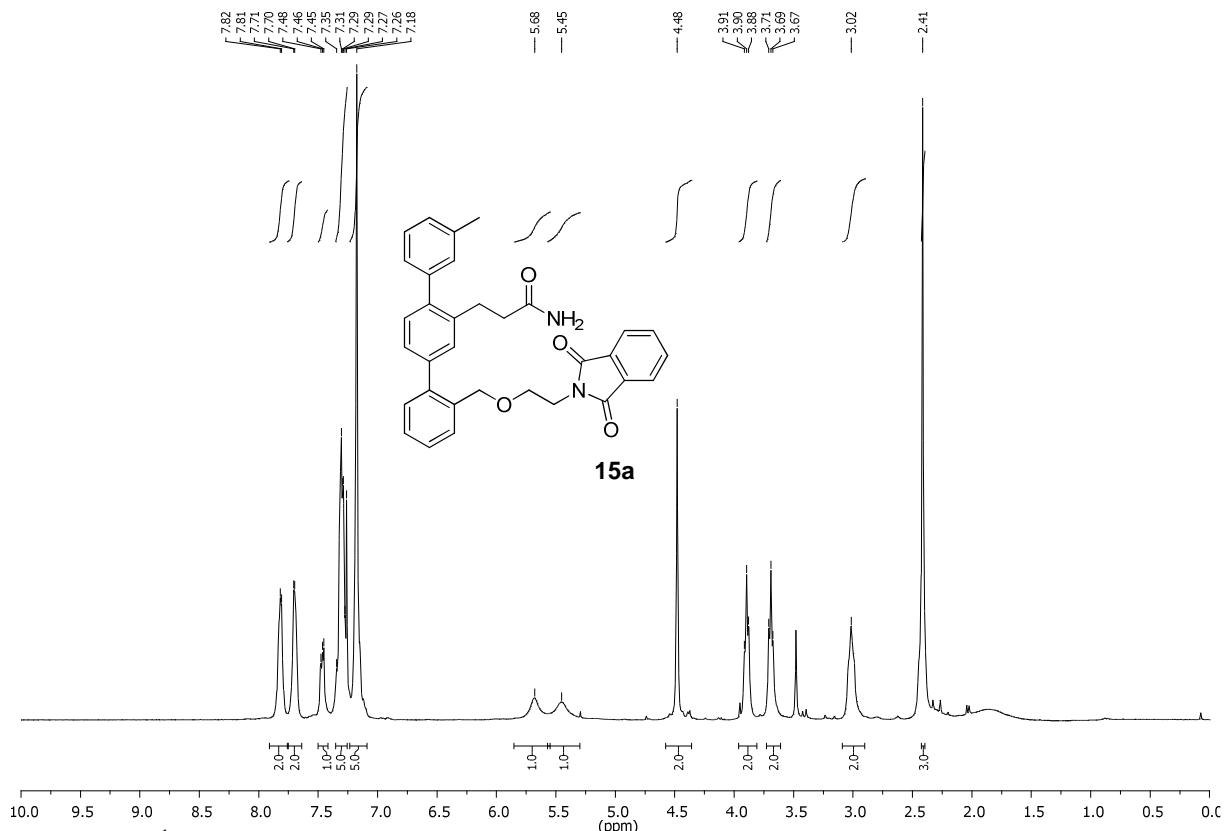
**Figure 128:**  $^{13}\text{C}$  NMR, APT; (*E*)-3-(4-bromo-3'-(4-(1,3-dioxoisindolin-2-yl)butyl)-[1,1'-biphenyl]-2-yl)acrylamide (**26c**).



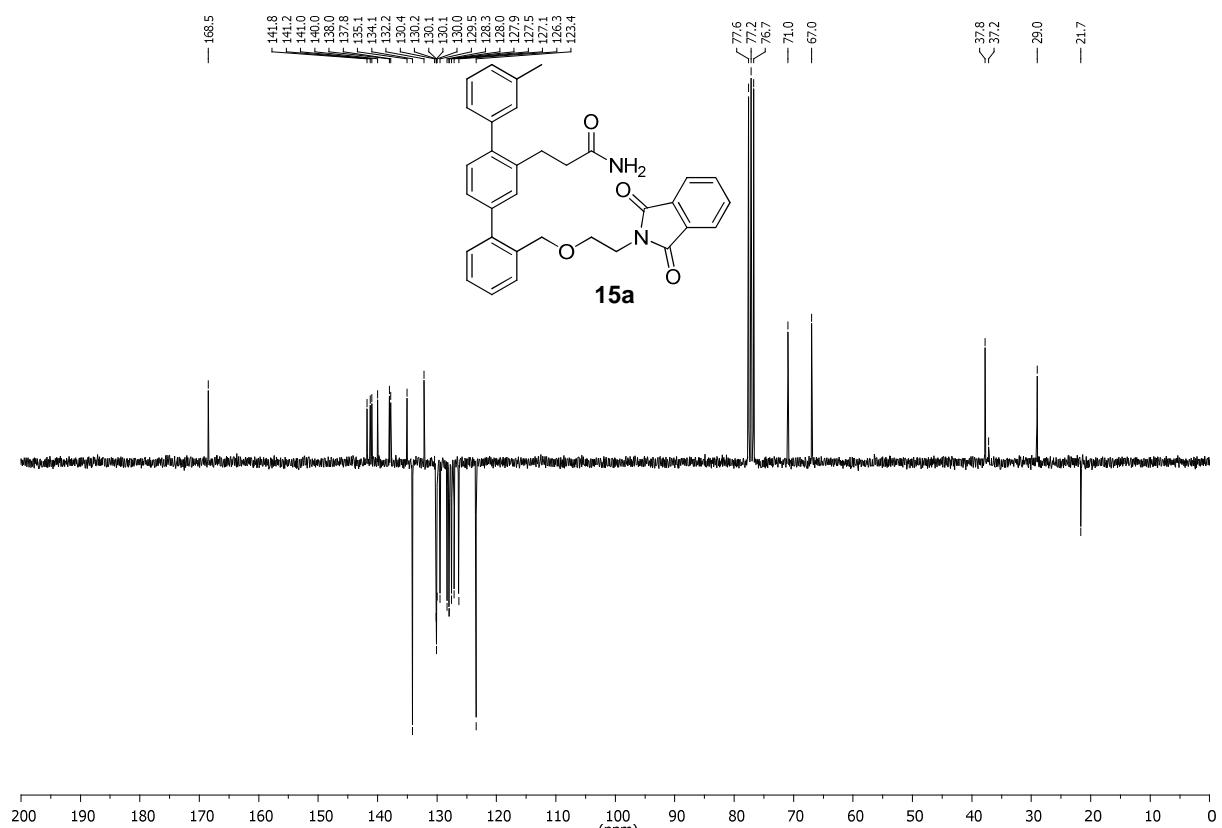
**Figure 129:** <sup>1</sup>H NMR; (*E*)-3-(2"-((2-(1,3-dioxoisoindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14a**).



**Figure 130:** <sup>13</sup>C NMR, APT; (*E*)-3-(2"-((2-(1,3-dioxoisoindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14a**).



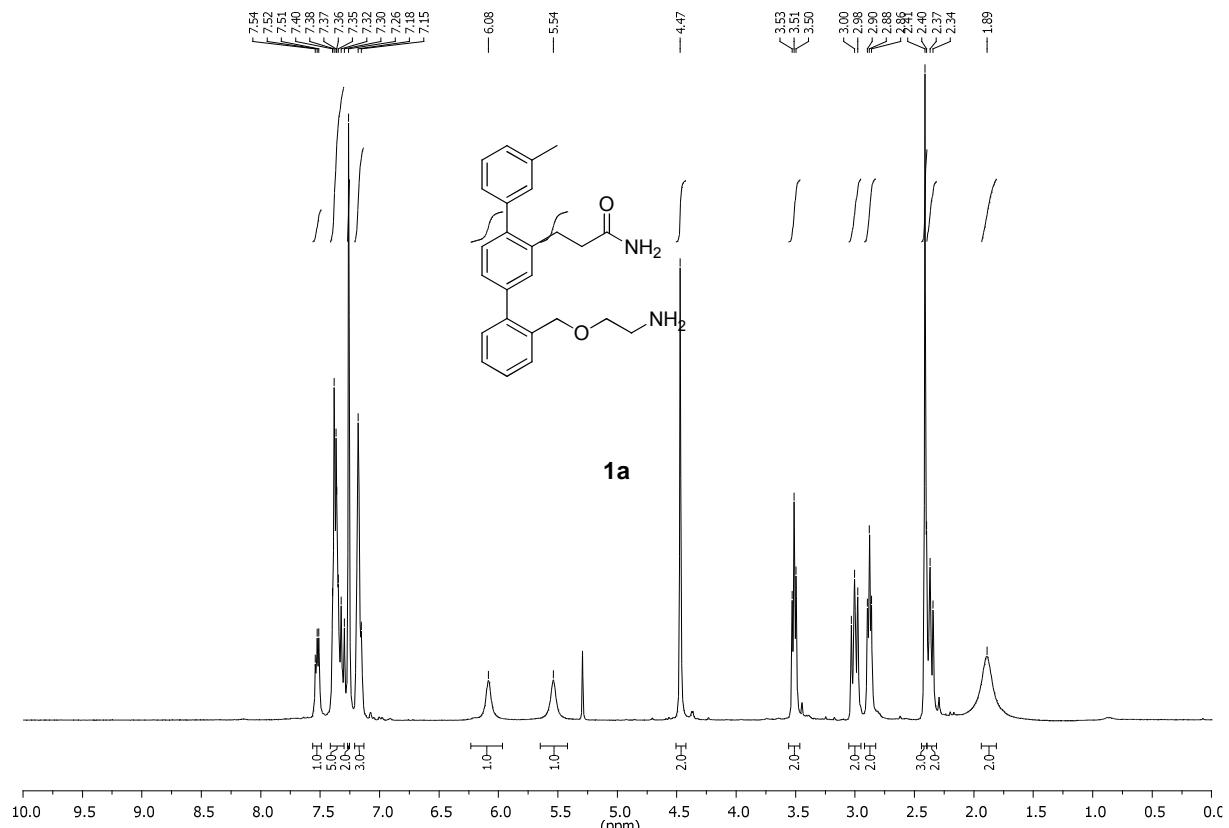
**Figure 131:**  $^1\text{H}$  NMR; 3-(2''-((2-(1,3-dioxoisindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (**15a**).



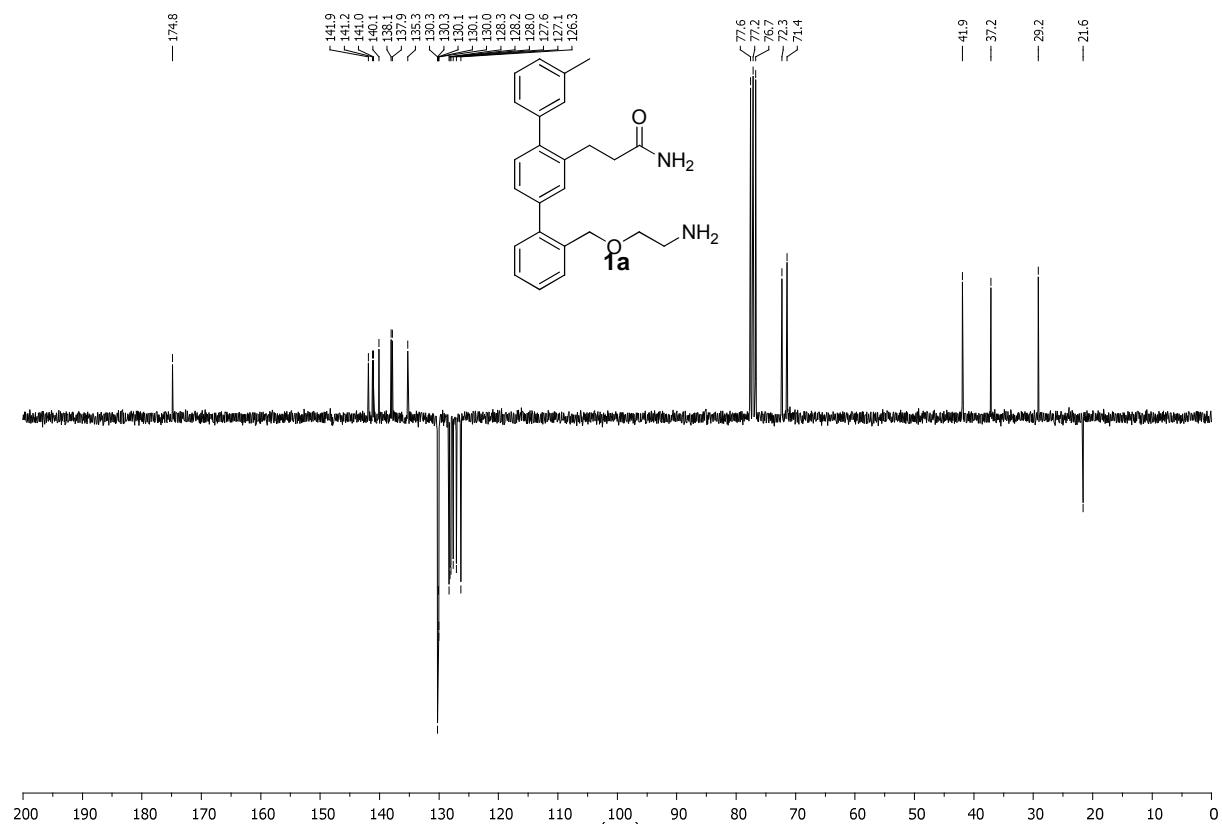
**Figure 132:**  $^{13}\text{C}$  NMR, APT; 3-(2''-((2-(1,3-dioxoisindolin-2-yl)ethoxy)methyl)-3-methyl-[1,1':4',1''-terphenyl]-2'-yl)propanamide (**15a**).

## NMR Data

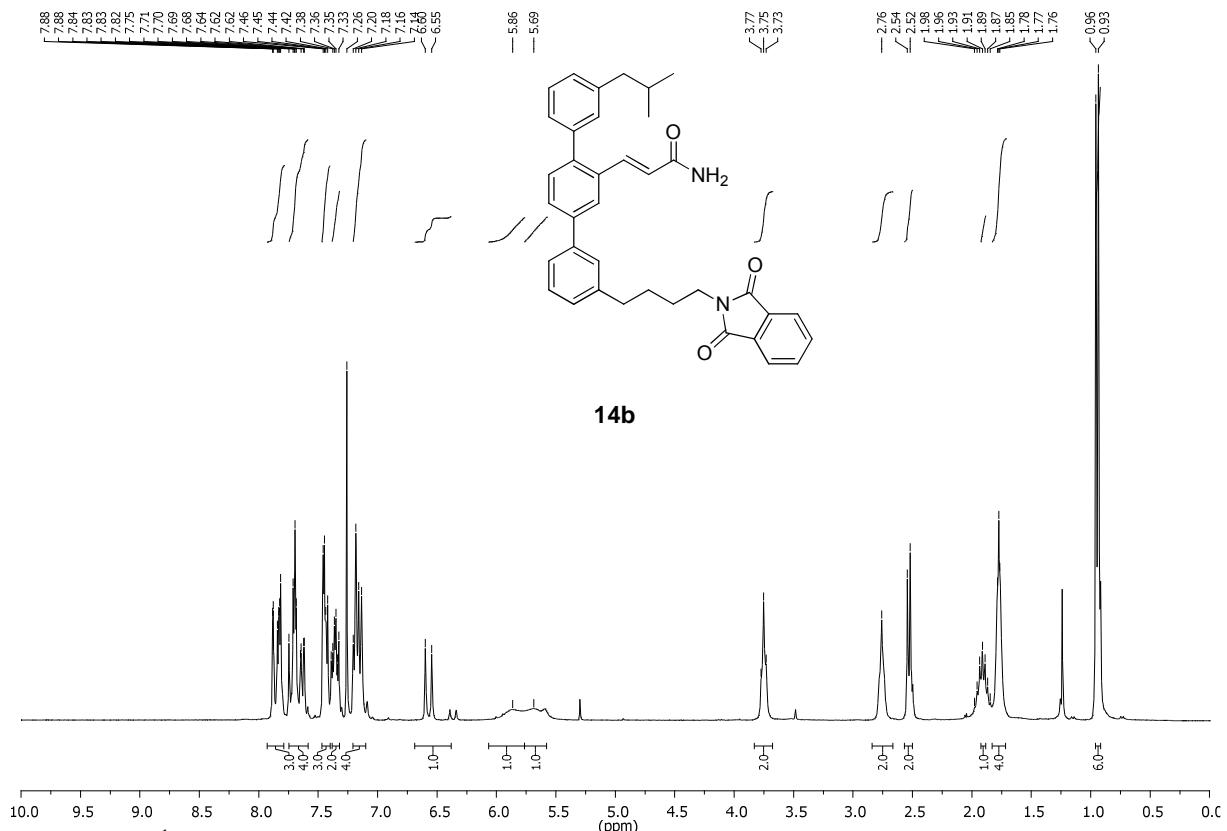
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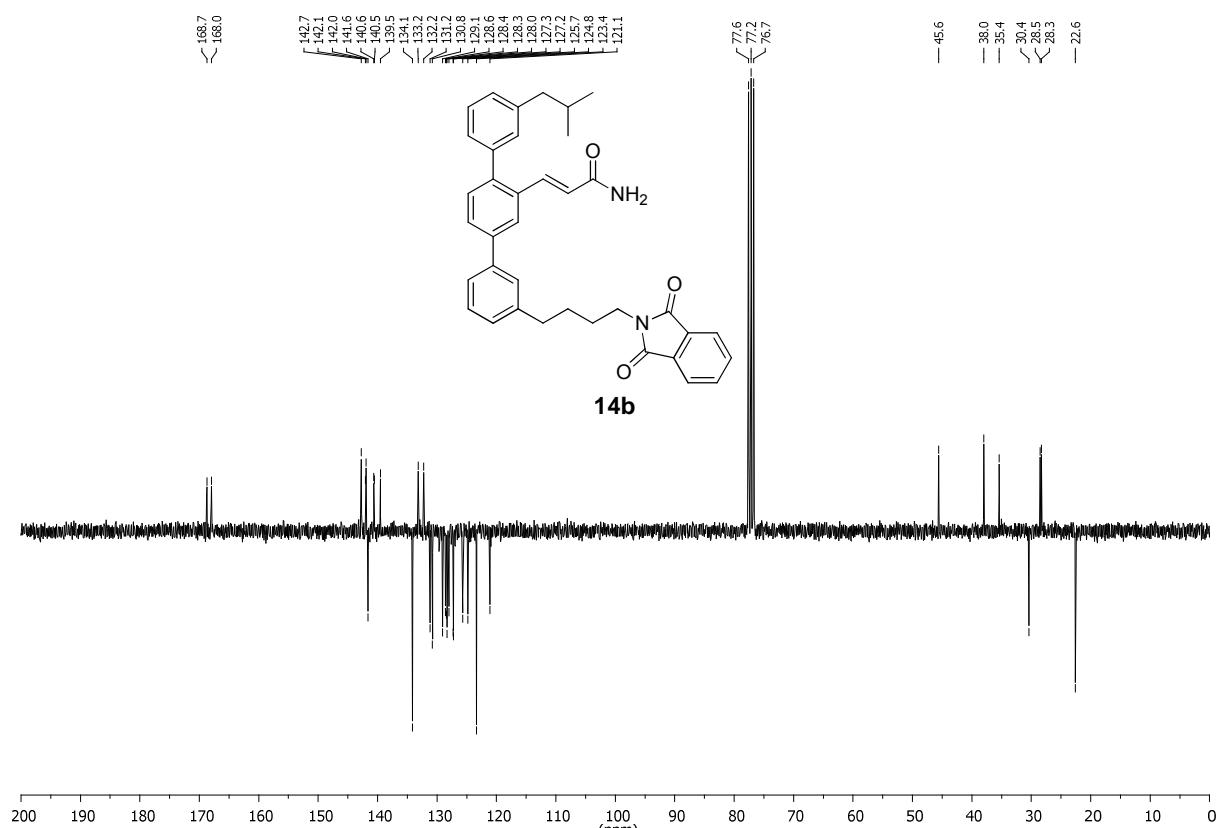
**Figure 133:** <sup>1</sup>H NMR; 3-(2"-((2-aminoethoxy)methyl)-3-methyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**1a**).



**Figure 134:** <sup>13</sup>C NMR, APT; 3-(2"-((2-aminoethoxy)methyl)-3-methyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**1a**).



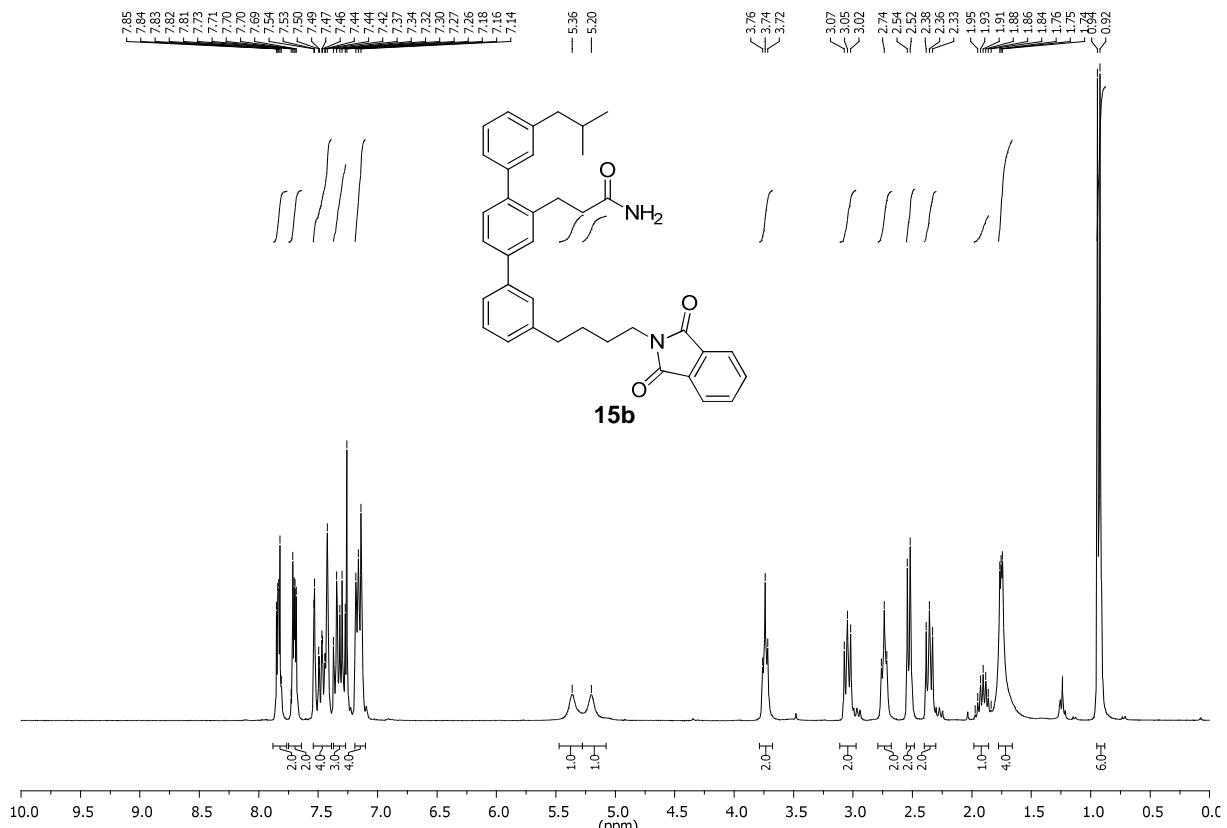
**Figure 135:** <sup>1</sup>H NMR; (*E*)-3-(3''-(4-(1,3-dioxoisindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)-acrylamide (**14b**).



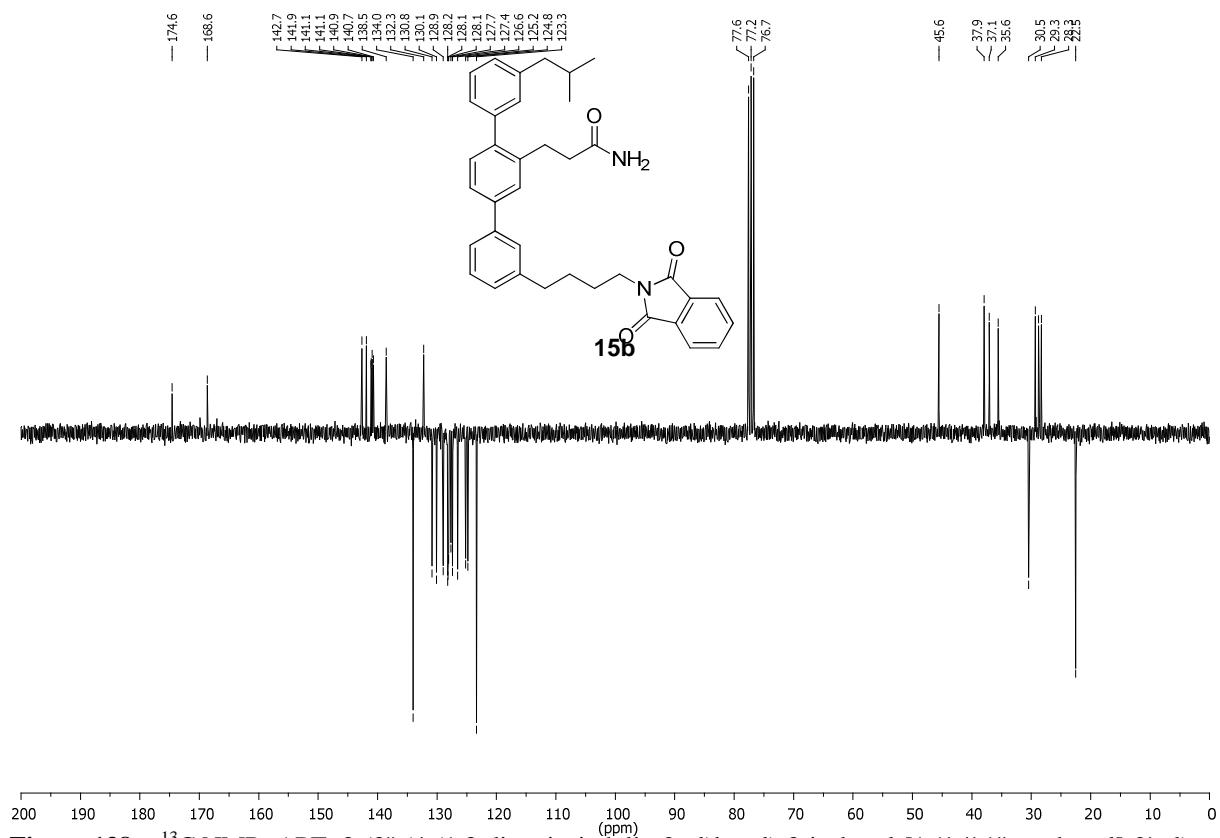
**Figure 136:** <sup>13</sup>C NMR, APT; (*E*)-3-(3''-(4-(1,3-dioxoisindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14b**).

## NMR Data

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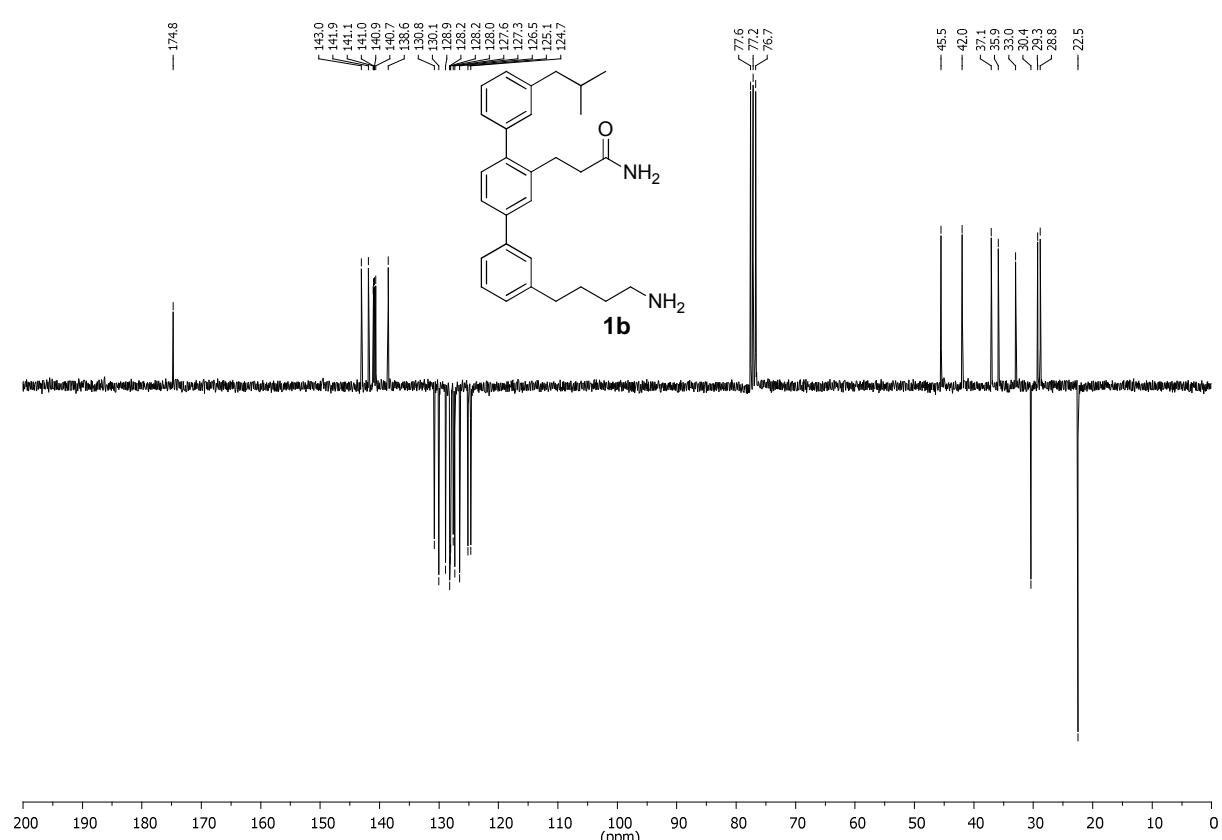
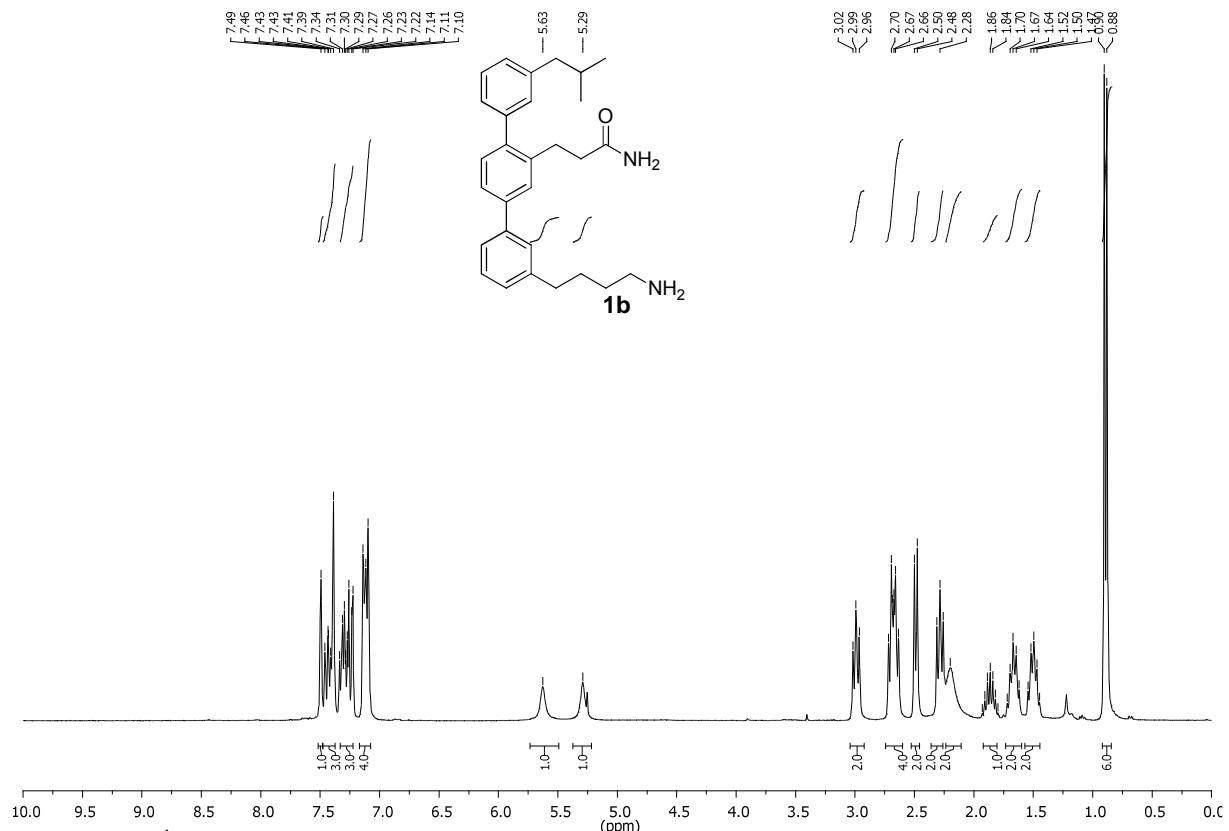
**Figure 137:**  $^1\text{H}$  NMR; 3-(3''-(4-(1,3-dioxoisindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**15b**).



**Figure 138:**  $^{13}\text{C}$  NMR, APT; 3-(3''-(4-(1,3-dioxoisindolin-2-yl)butyl)-3-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**15b**).

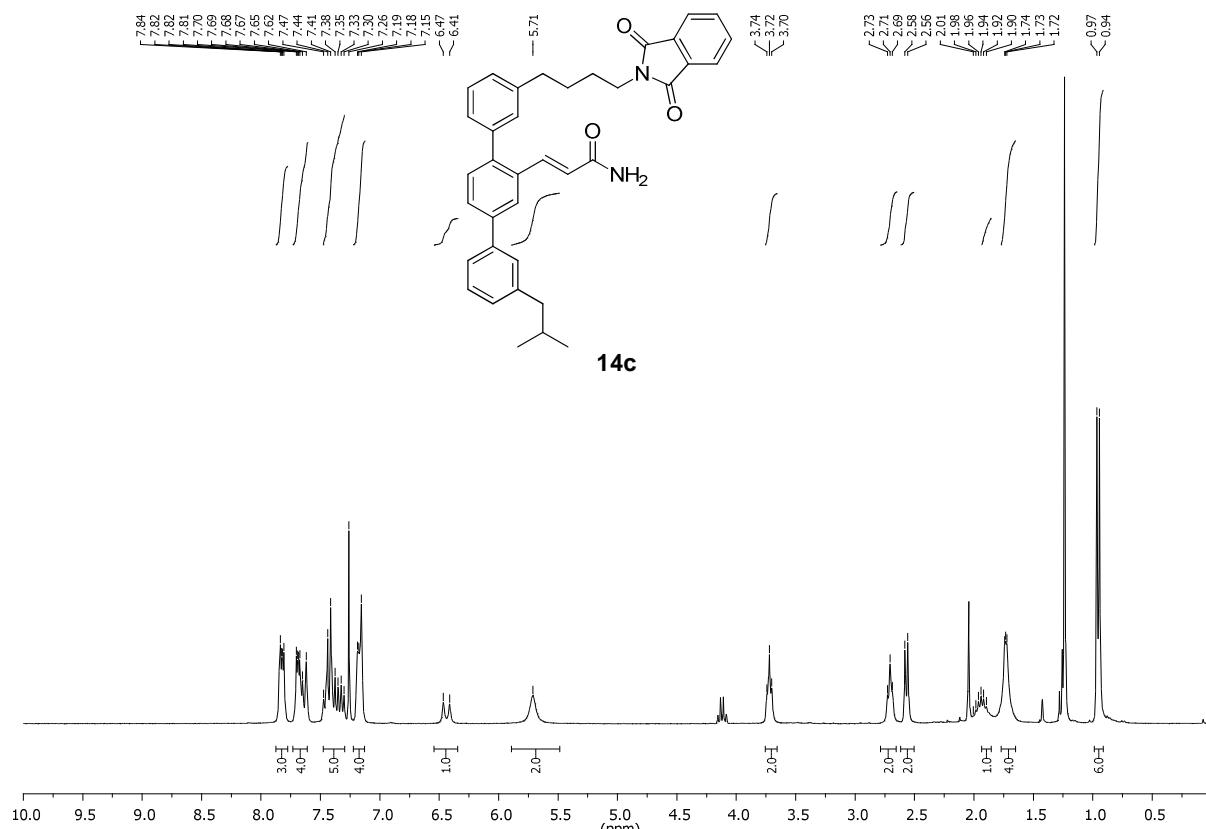
## NMR Data

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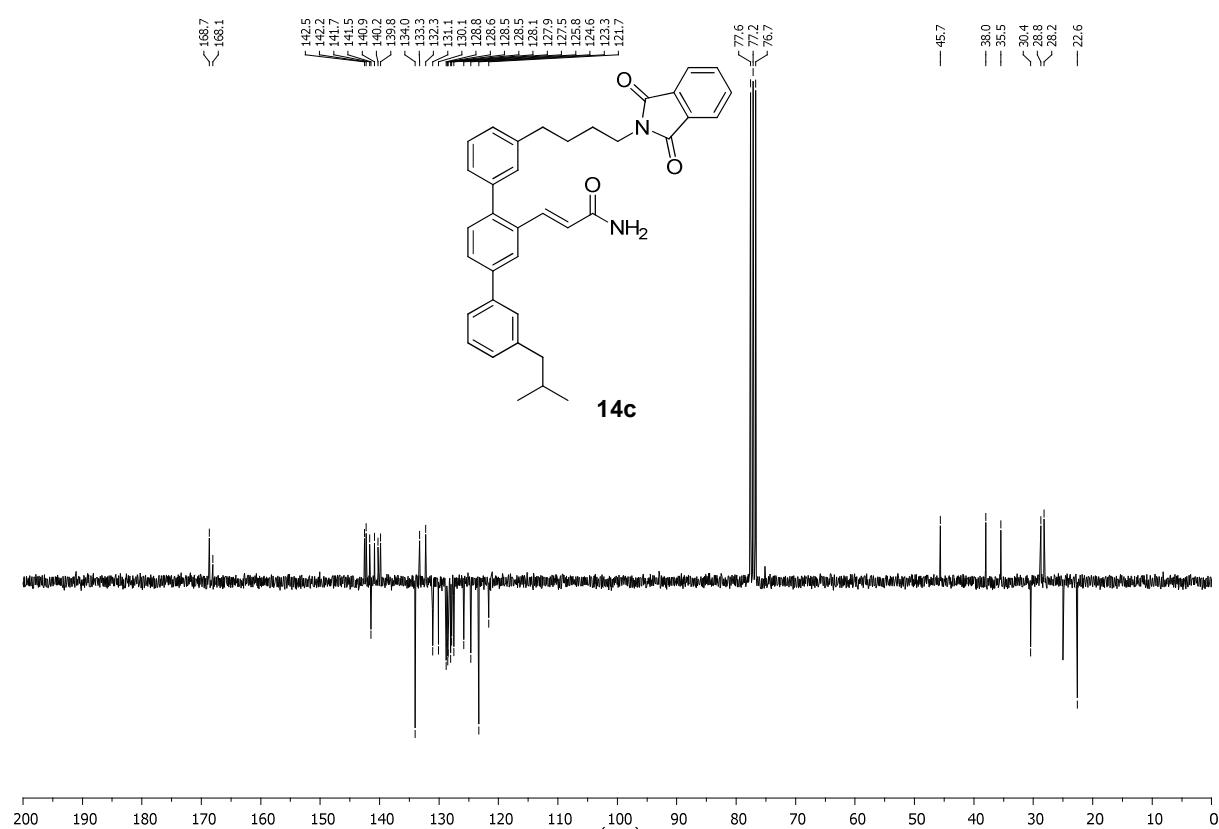


## NMR Data

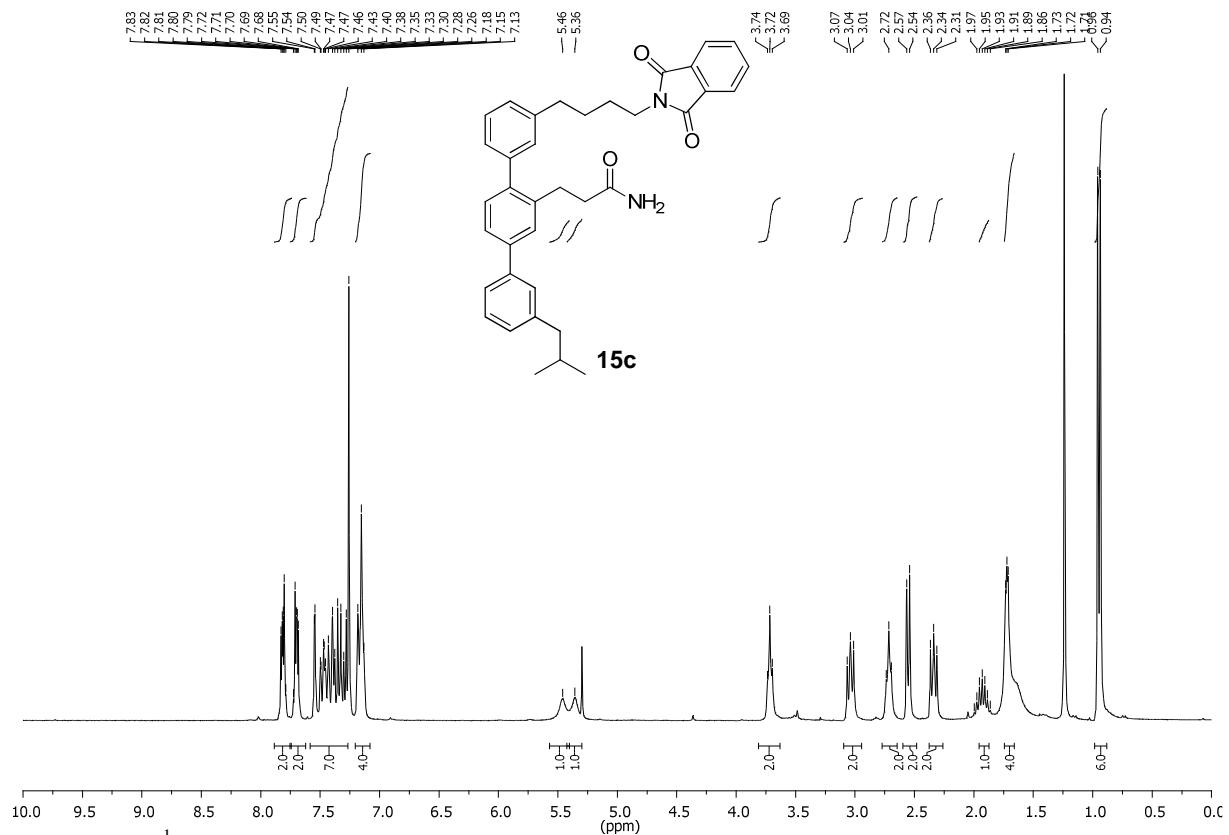
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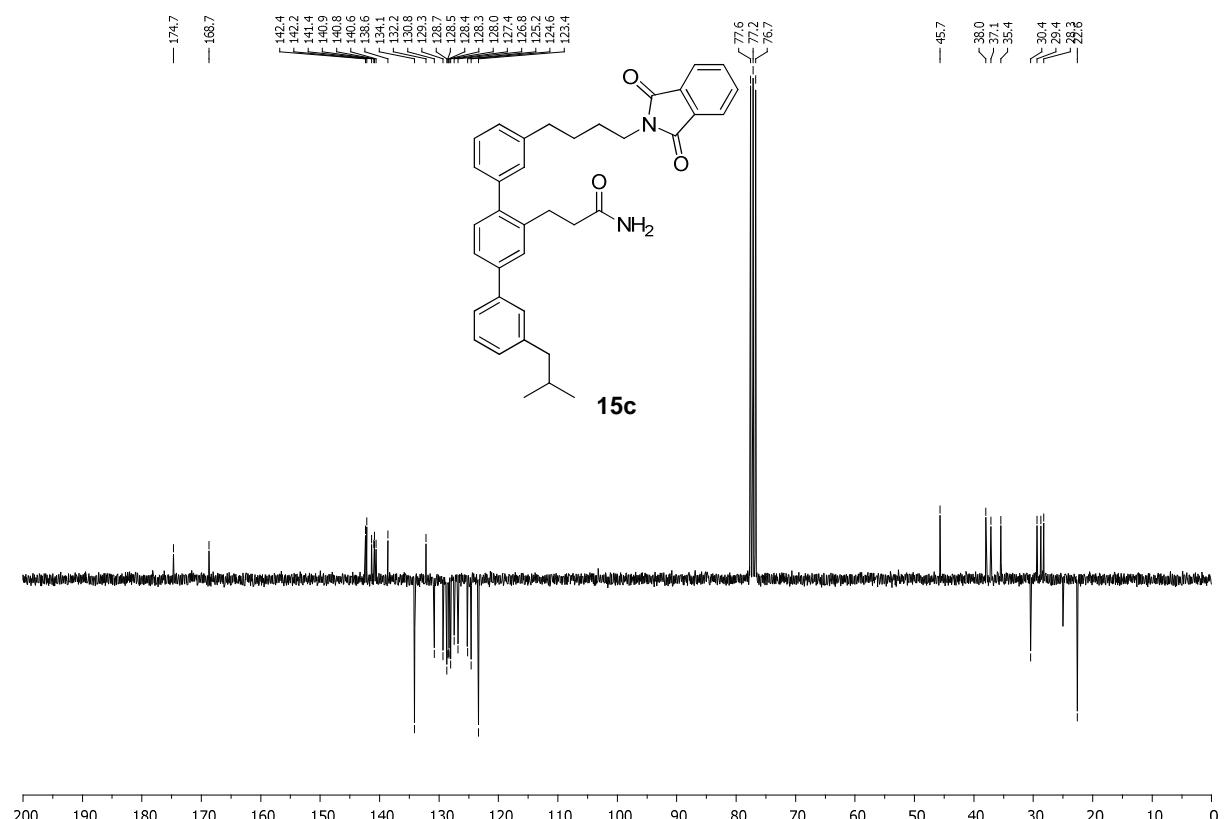
**Figure 141:**  $^1\text{H}$  NMR; (*E*)-3-(3-(4-(1,3-dioxoisindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)-acrylamide (**14c**).



**Figure 142:**  $^{13}\text{C}$  NMR, APT; (*E*)-3-(3-(4-(1,3-dioxoisindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)acrylamide (**14c**).



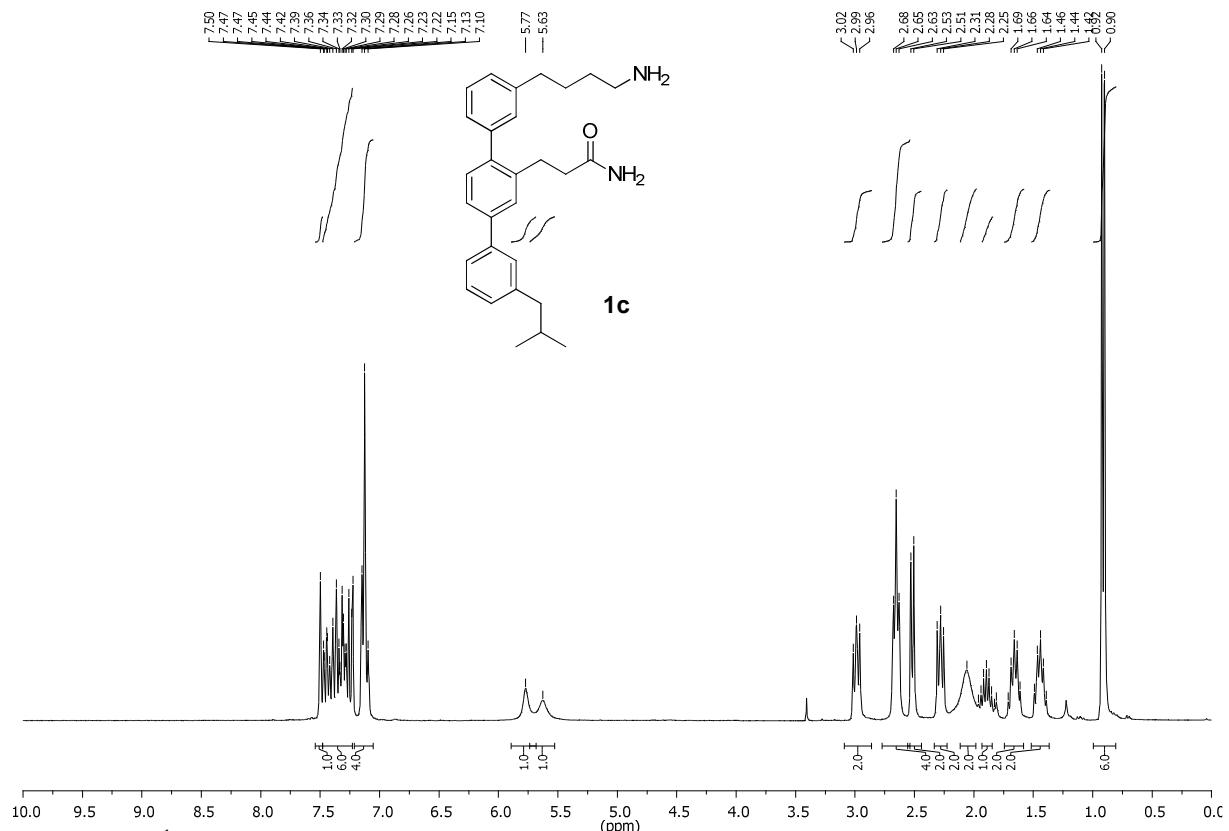
**Figure 143:**  $^1\text{H}$  NMR; 3-(3-(4-(1,3-dioxoisindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**15c**).



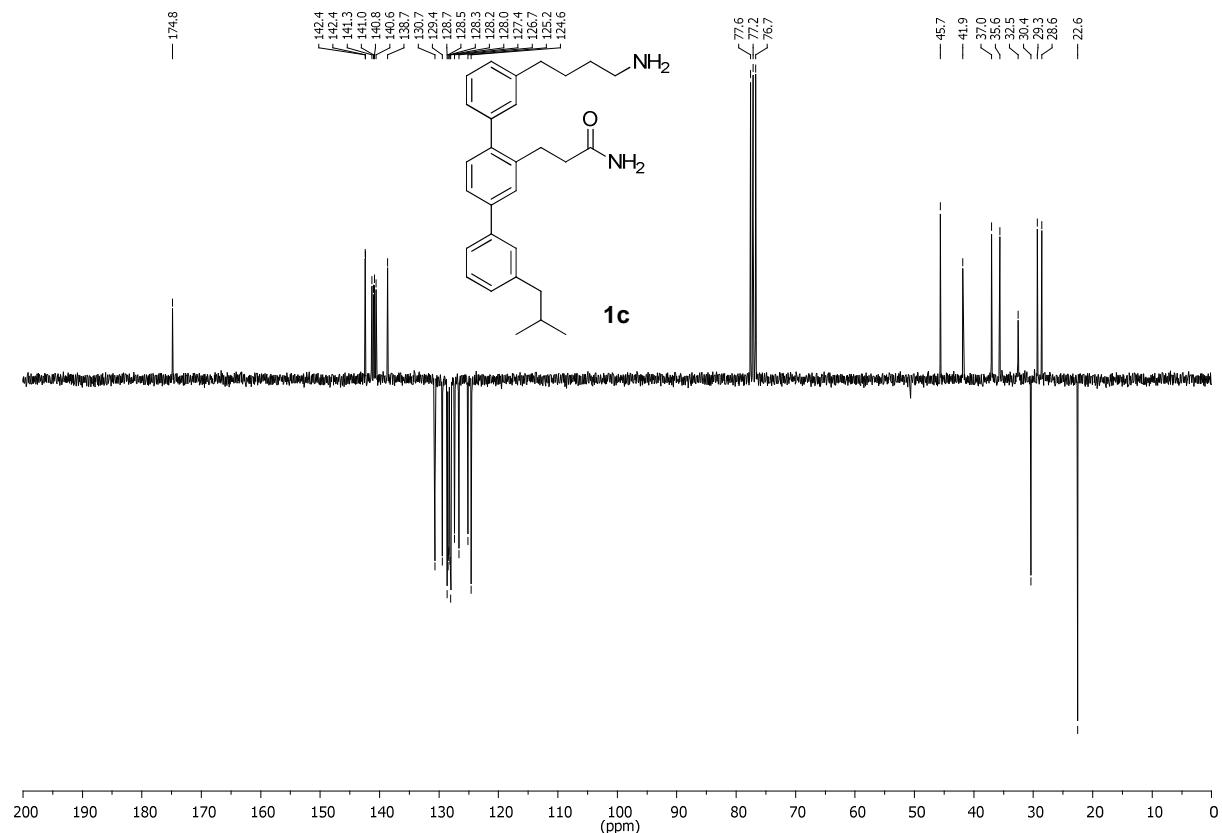
**Figure 144:**  $^{13}\text{C}$  NMR, APT; 3-(3-(4-(1,3-dioxoisindolin-2-yl)butyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**15c**).

## NMR Data

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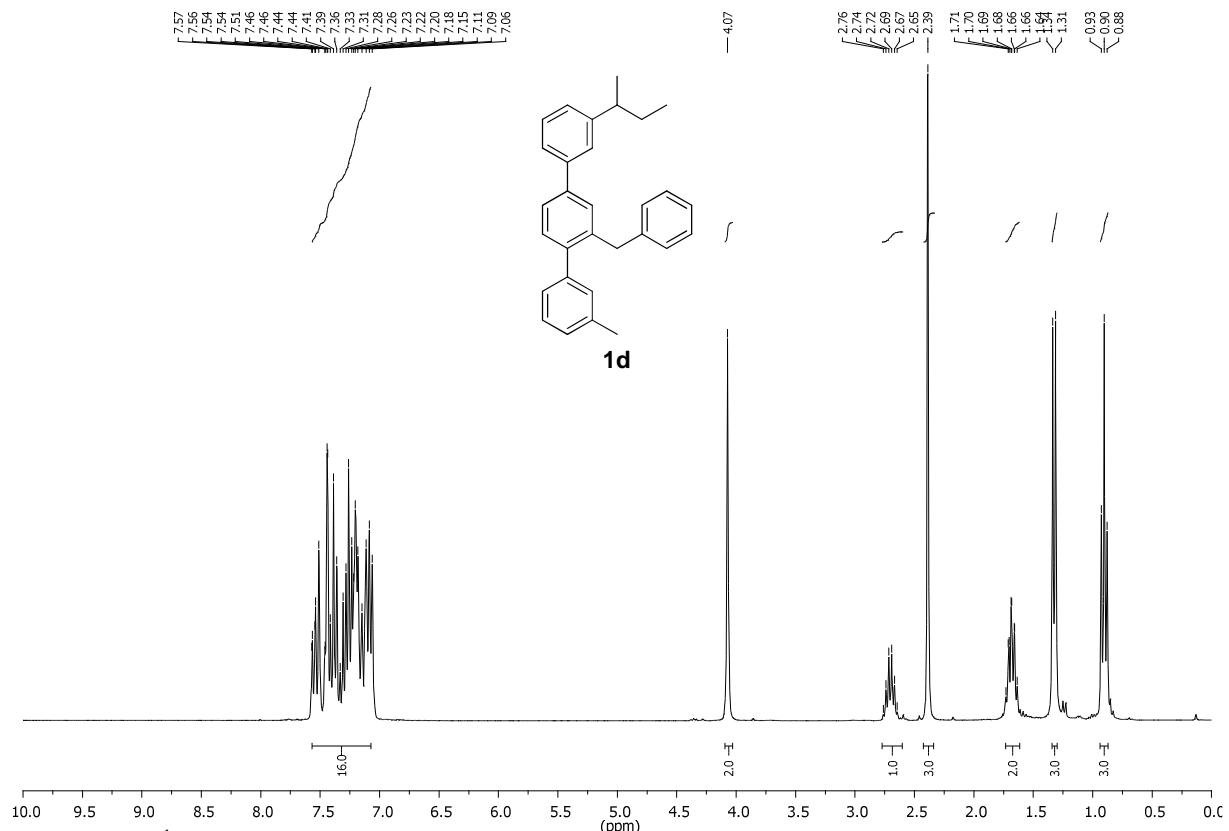
**Figure 145:**  $^1\text{H}$  NMR; 3-(3-(4-aminobutyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**1c**).



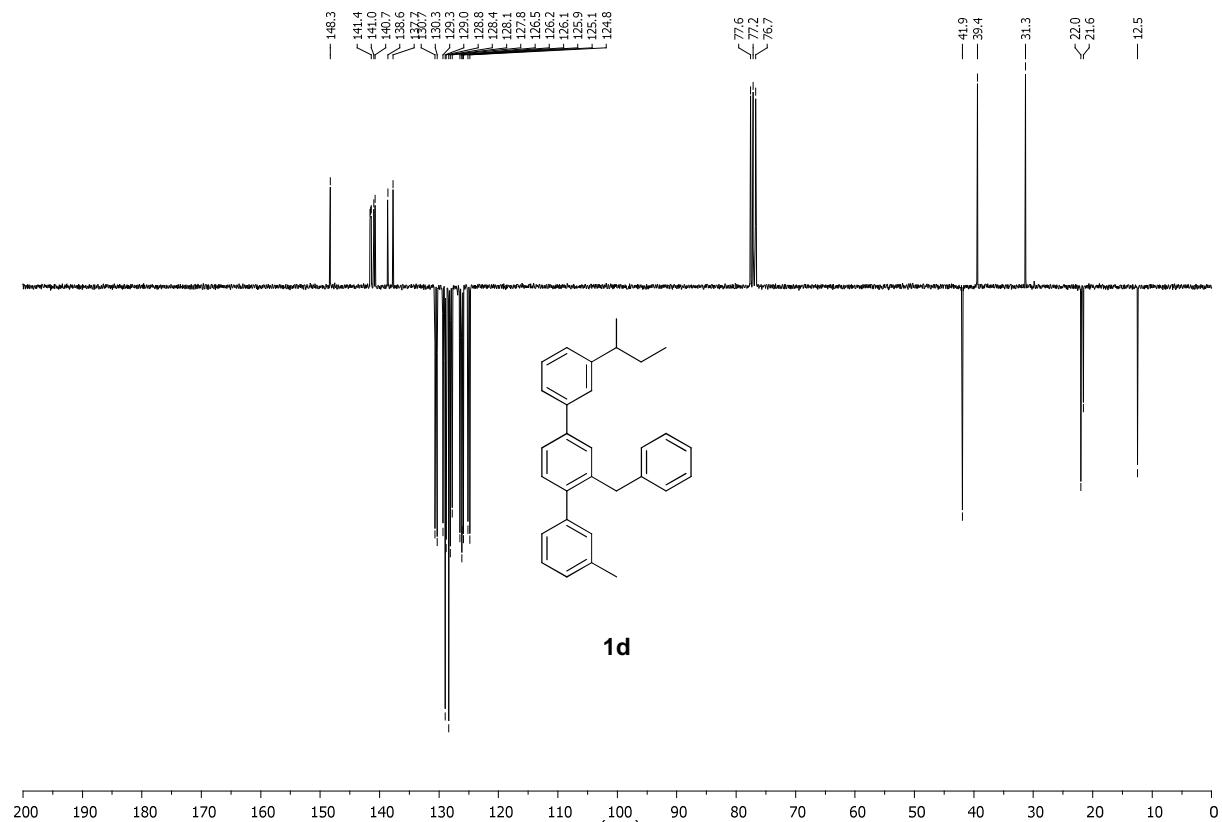
**Figure 146:**  $^{13}\text{C}$  NMR, APT; 3-(3-(4-aminobutyl)-3"-isobutyl-[1,1':4',1"-terphenyl]-2'-yl)propanamide (**1c**).

## NMR Data

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**Figure 147:**  $^1\text{H}$  NMR; 2'-benzyl-3''-(sec-butyl)-3-methyl-1,1':4',1''-terphenyl (**1d**).



**Figure 148:**  $^{13}\text{C}$  NMR, APT; 2'-benzyl-3''-(sec-butyl)-3-methyl-1,1':4',1''-terphenyl (**1d**).

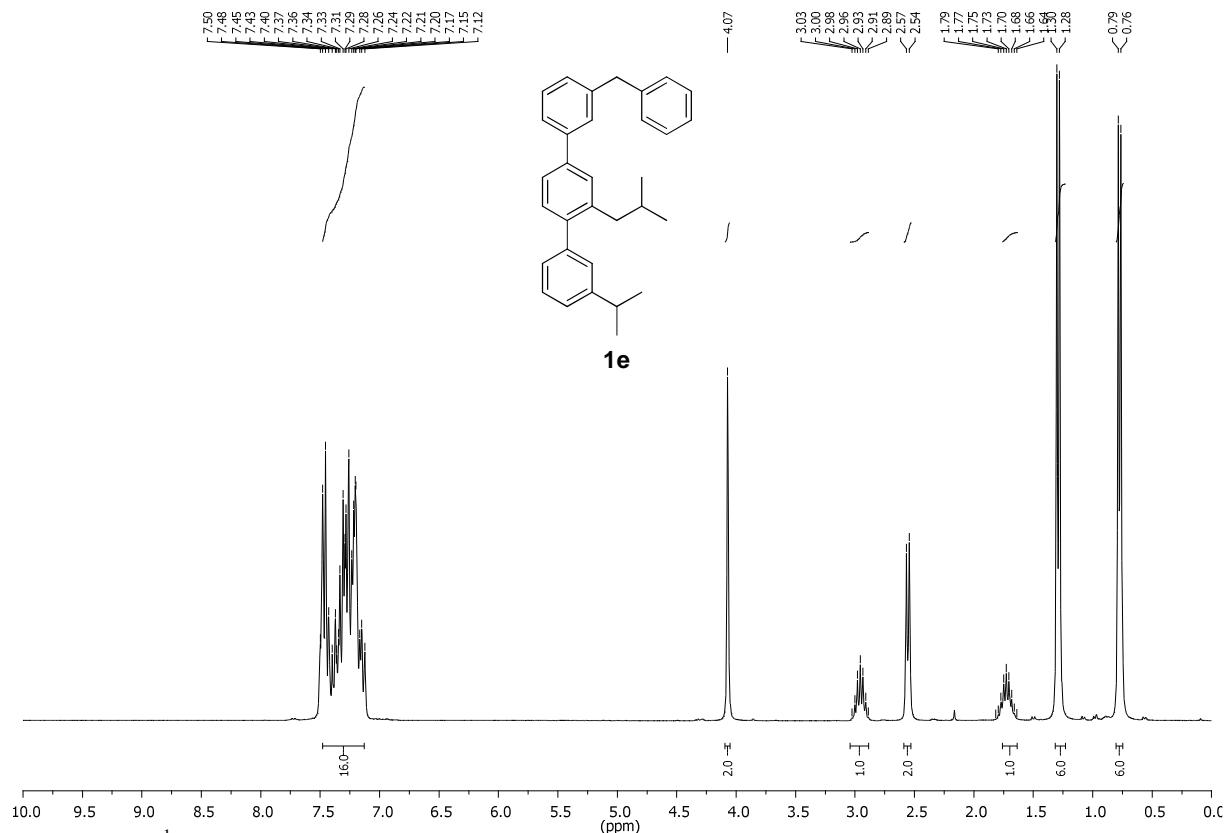


Figure 149:  $^1\text{H}$  NMR; 3''-benzyl-2'-isobutyl-3-isopropyl-1,1':4',1''-terphenyl (**1e**).

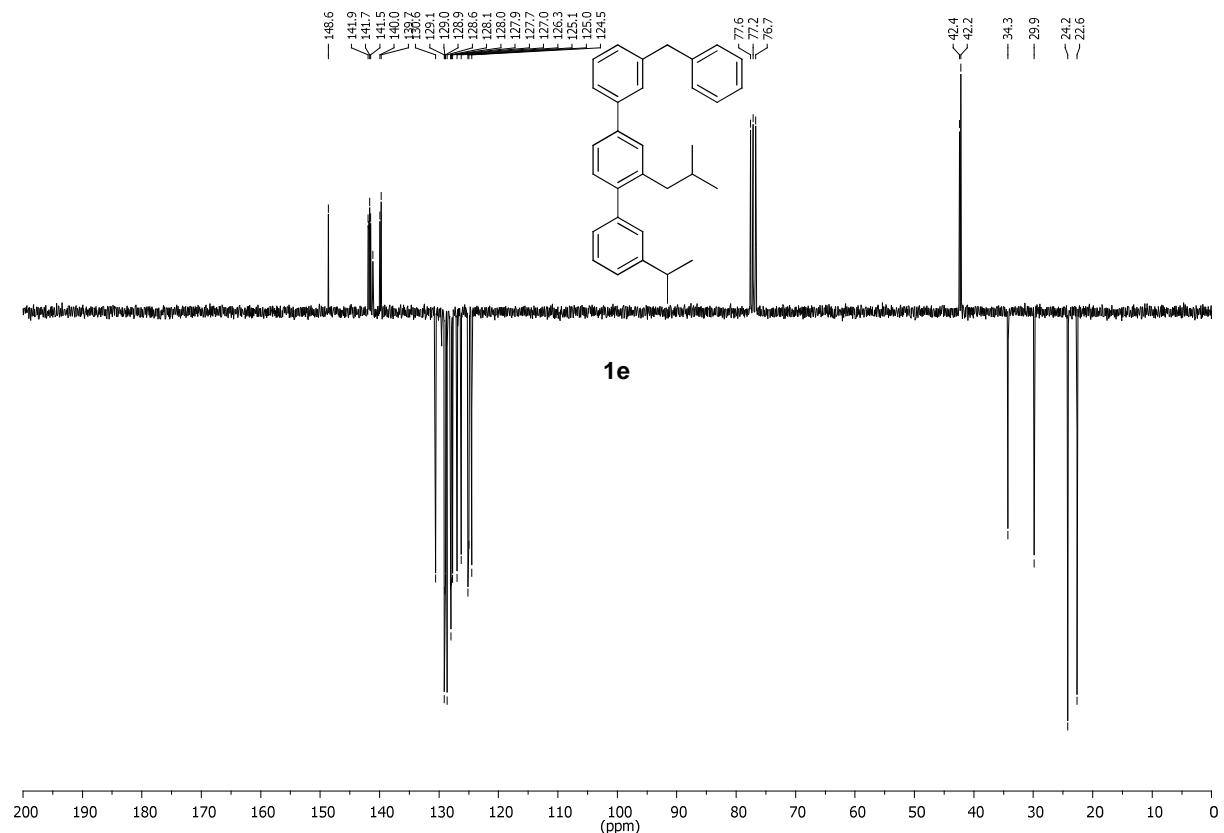


Figure 150:  $^{13}\text{C}$  NMR, APT; 3''-benzyl-2'-isobutyl-3-isopropyl-1,1':4',1''-terphenyl (**1e**).

## 4 References

- [1] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512-7515.
- [2] B. M. Trost, F. D. Toste, K. Greenman, *J. Am. Chem. Soc.* **2003**, *125*, 4518-4526.
- [3] W. G. Kofron, L. M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879-1880.
- [4] G. G. Bianco, H. M. C. Ferraz, A. M. Costa, L. V. Costa-Lotufo, C. Pessoa, M. O. de Moraes, M. G. Schrems, A. Pfaltz, L. F. Silva, *J. Org. Chem.* **2009**, *74*, 2561-2566.
- [5] G. Vassilikogiannakis, M. Hatzimarinaki, M. Orfanopoulos, *J. Org. Chem.* **2000**, *65*, 8180-8187.
- [6] Y. Zhang, M. S. Sigman, *J. Am. Chem. Soc.* **2007**, *129*, 3076-3077.
- [7] A. Arduini, A. Pochini, R. Ungaro, *Synthesis* **1984**, 950-953.
- [8] G. Casnati, A. Pochini, M. G. Terenghi, R. Ungaro, *J. Org. Chem.* **1983**, *48*, 3783-3787.
- [9] U. Azzena, G. Dettori, R. Pireddu, L. Pisano, *Tetrahedron* **2004**, *60*, 1617-1623.
- [10] C. D. Selassie, A. J. Shusterman, S. Kapur, R. P. Verma, L. Zhang, C. Hansch, *J. Chem. Soc., Perkin Trans. 2* **1999**.
- [11] J. M. Rodriguez, N. T. Ross, W. P. Katt, D. Dhar, G.-i. Lee, A. D. Hamilton, *J. Med. Chem.* **2009**, *4*, 649-656.
- [12] P. Bovonsombat, J. Leykajarakul, C. Khan, K. Pla-on, M. M. Krause, P. Khanthapura, R. Ali, N. Doowa, *Tetrahedron Lett.* **2009**, *50*, 2664-2667.
- [13] P. Yates, T. S. Macas, *Can. J. Chem.* **1988**, *66*, 1-10.
- [14] M. Toumi, F. Couty, G. Evano, *Angew. Chem., Int. Ed.* **2007**, *46*, 572-575.
- [15] R. F. Martínez, M. Ávalos, R. Babiano, P. Cintas, J. L. Jiménez, M. E. Light, J. C. Palacios, *Eur. J. Org. Chem.* **2011**, *2011*, 3137-3145.
- [16] K. Fuji, T. Morimoto, K. Tsutsumi, K. Kakiuchi, *Angew. Chem., Int. Ed.* **2003**, *42*, 2409-2411.
- [17] R. A. Abramovitch, B. W. Cue, *J. Org. Chem.* **1980**, *45*, 5316-5319.
- [18] X. M. Zhang, F. G. Bordwell, *J. Am. Chem. Soc.* **1994**, *116*, 968-972.
- [19] W. E. Truce, C.-I. M. Lin, *J. Am. Chem. Soc.* **1973**, *95*, 4426-4428.
- [20] J. Wu, C. Yue, *Synth. Commun.* **2006**, *36*, 2939-2947.
- [21] K. Nanjo, K. Suzuki, M. Sekiya, *Chem. Pharm. Bull.* **1977**, *25*, 2396-2400.
- [22] D. Guiney, C. L. Gibson, C. J. Suckling, *Org. Biomol. Chem.* **2003**, *1*, 664-675.
- [23] S. Trippett, D. M. Walker, *J. Chem. Soc.* **1959**, 3874-3876.
- [24] Y.-Z. Hu, G. Zhang, R. P. Thummel, *Org. Lett.* **2003**, *5*, 2251-2253.

## References

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- [25] J. L. Kenwright, W. R. J. D. Galloway, D. T. Blackwell, A. Isidro-Llobet, J. Hodgkinson, L. Wortmann, S. D. Bowden, M. Welch, D. R. Spring, *Chem. Eur. J.* **2011**, *17*, 2981-2986.
- [26] B. Koppenhoefer, V. Schurig, *Org. Synth.* **1988**, *66*, 151-159.
- [27] M. Tanasova, Q. Yang, C. C. Olmsted, C. Vasileiou, X. Li, M. Anyika, B. Borhan, *Eur. J. Org. Chem.* **2009**, *2009*, 4242-4253.
- [28] Potassium *m*-tolyltrifluoroborate; Sigma Aldrich 738468; www.sigmaaldrich.com.
- [29] Y. Gan, T. A. Spencer, *J. Org. Chem.* **2006**, *71*, 5870-5875.
- [30] J.-Y. Cho, C. N. Iverson, M. R. Smith, *J. Am. Chem. Soc.* **2000**, *122*, 12868-12869.
- [31] K. Matsuda, N. Nakamura, K. Takahashi, K. Inoue, N. Koga, H. Iwamura, *J. Am. Chem. Soc.* **1995**, *117*, 5550-5560.
- [32] Y.-X. Liao, C.-H. Xing, M. Israel, Q.-S. Hu, *Tetrahedron Lett.* **2011**, *52*, 3324-3328.
- [33] S. Nishida, *J. Org. Chem.* **1967**, *32*, 2692-2695.
- [34] a) F. C. Montgomery, W. H. Saunders, *J. Org. Chem.* **1976**, *41*, 2368-2372; b) G. Martelli, P. Spagnolo, M. Tiecco, *J. Chem. Soc. B* **1968**, 901-905.
- [35] C. S. Marvel, R. E. Allen, C. G. Overberger, *J. Am. Chem. Soc.* **1946**, *68*, 1088-1091.
- [36] S. McIntyre, E. Hörmann, F. Menges, S. P. Smidt, A. Pfaltz, *Adv. Synth. Catal.* **2005**, *347*, 282-288.
- [37] R. K. Thalji, K. A. Ahrendt, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2001**, *123*, 9692-9693.
- [38] M. S. Malamas, A. J. Robichaud, A. M. Porte, K. M. Morris, W. R. Solvibile, K. Ji-In, Wyeth Corp., US 2009/48320 A1, **2009**.