Electronic supplementary information (ESI) for

Synthesis of 4-functionalized-1*H*-indoles from 2,3-dihalophenols

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General information

All reactions involving air-sensitive compounds were carried out under a N_2 atmosphere in oven-dried glassware with magnetic stirring. Temperatures are reported as bath temperatures. Solvents used in extraction and purification were distilled prior to use. TLC was performed on alumina-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized by UV light (254 nm) and/or by staining with a Ce/Mo reagent, anisaldehyde or phosphomolybdic acid solution and subsequent heating. R_f values refer to silica gel. Flash column chromatography was carried out on silica gel 60, 230-400 mesh. Melting points were obtained with open capillary tubes and are uncorrected. ^{1}H NMR spectra were recorded at 400 or 300 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the residual solvent resonance as the internal standard ($CHCl_3$: δ 7.26). Data are reported as follows: chemical shift, multiplicity (s: singlet, br s: broad singlet, d: doublet, dd: doublet of doublets, dt: doublet of triplets, ddd: doublet of doublet of doublets, t: triplet, t app: apparent triplet, td: triplet of doublets, tdd: triplet of doublet of doublets, q: quartet, m: multiplet), coupling constants (*J* in Hz) and integration. ^{13}C NMR spectra were recorded at 100.6 or 75.4 MHz using broadband proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as internal standard ($CDCl_3$: δ 77.16). Carbon multiplicities were assigned by DEPT techniques. GC-MS analysis and low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV on a mass spectrometer and only the molecular ions and/or base peaks as well as significant peaks in MS are given. High-resolution mass spectrometry (HRMS) was carried out on a mass spectrometer. Infrared spectra were recorded with a FT-IR spectrophotometer. Melting points were measured on a Gallenkamp apparatous using open capillary rubes and are uncorrected. All commercially available reagents were used without purification unless otherwise indicated and were purchased from standard chemical suppliers.

Experimental procedures and characterization data for synthesized compounds

Synthesis of trifluoroacetamides 1:[1]

2,2,2-Trifluoro-*N*-(3-fluorophenyl)acetamide (1a): purification by crystallization from hexane afforded **1a** (6.37 g, 77%) as a white solid: 67–69 ºC (lit.[1] mp 69–70 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.38 (br s, 1H), 7.48 (dt, *J* = 10.2, 2.1 Hz, 1H), 7.34 (td, *J* = 8.2, 2.1 Hz, 1H), 7.26 (ddd, *J* = 8.2, 2.1, 1.1 Hz, 1H), 6.95 (tdd, *J* = 8.2, 2.5, 1.1 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 162.9 (d, *J* = 246.6 Hz, C), 155.3 (q, *J* = 37.8 Hz, C), 136.5 (d, *J* = 10.6 Hz, C), 130.7 (d, *J* = 9.2 Hz, CH), 116.2 (d, *J* = 3.2 Hz, CH), 115.7 (q, *J* = 288.4 Hz, C), 113.5 (d, *J* = 21.2 Hz, CH), 108.5 (d, *J* = 26.6 Hz, CH); EI-LRMS *m/z* 207 (M^+, 100), 138 (45), 110 (36), 95 (32), 83 (18).

***N*-(3-Chlorophenyl)-2,2,2-trifluoroacetamide (1b):** purification by crystallization from hexane afforded **1b** (7.15 g, 77%) as a white solid: mp 68–70 ºC (lit.[2] mp 66–68 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.24 (br s, 1H), 7.66 (t, *J* = 2.0 Hz, 1H), 7.42 (ddd, *J* = 8.0, 2.0, 1.1 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.22 (ddd, *J* = 8.0, 2.0, 1.1 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 155.3 (d, *J* = 37.8 Hz, 1H), 136.2 (C), 135.2 (C), 130.5 (CH), 126.7 (CH), 121.0 (CH), 118.8 (CH), 115.7 (d, *J* = 288.5 Hz, C); EI-LRMS *m/z* 225 (M^++2, 33), 223 (M^+, 100), 154 (51), 126 (19).

Synthesis of 2,2,2-trifluoro-*N*-(3-fluoro-2-iodophenyl)acetamide (2a):

To a solution of *N,N,N′,N′*-tetramethylethylenediamine (4.54 cm^3, 30.2 mmol) in anhydrous THF (40 cm^3) at –80 ºC was added slowly *t*BuLi (20 cm^3 of a 1.5M solution in pentane, 30 mmol). After 5 min a solution of **1a** (2.48 g, 12 mmol) in THF (10 cm^3) was added dropwise avoiding temperature exceed –70 ºC. After 40 min at –80 ºC, a solution of iodine in THF (10 cm^3) was added dropwise to the reaction mixture. The resulting solution was stirred for 40 min at –80 ºC. Then, the reaction mixture was allowed to reach room temperature and quenched with an aqueous solution of $Na_2S_2O_3$ (10%). The aqueous phase was extracted with Et_2O (3 × 30 cm^3), and the combined organic layers were washed with HCl 1M, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude was purified by column chromatography (hexane/EtOAc, 8/1) on silica gel affording **2a** (2.31 g, 58%) as a white-pale reddish solid: R_f 0.44 (hexane/AcOEt, 6/1); mp 104–106 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.39 (br s, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.40 (td, *J* = 8.3, 2.1 Hz, 1H), 7.01–6.94 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 161.9 (d, *J* = 245.6 Hz, C), 155.0 (q, *J* = 37.7 Hz, C), 137.4 (d, *J* = 3.6 Hz, C), 130.9 (d, *J* = 8.9 Hz, CH), 117.5 (d, *J* = 3.1 Hz, CH), 115.7 (q, *J* = 288.5 Hz, C), 113.3 (d, *J* = 23.8 Hz, CH), 79.0 (d, *J* = 28.8 Hz, C); EI-LRMS *m/z* 333 (M^+, 53), 206 (100), 186 (26), 137 (13), 109 (22); IR (KBr) 3218, 3061, 1717, 1580, 1548, 1463, 1207, 1165, 788, 733 cm^{-1}; HRMS calcd for $C_8H_4F_4INO$, 332.9274; found, 332.9283.

Synthesis of 4-fluoro-2-phenyl-1*H*-indole (3a) from 2a:

A mixture of **2a** (169 mg, 0.5 mmol), phenylacetylene (77 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in anhydrous DMA (4 cm^3) was heated for 4 h at 80 ºC under a nitrogen atmosphere (cyclization was completed as monitored by GC-MS). CH_2Cl_2 (20 cm^3) and

water (20 cm^3) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 20 cm^3). The combined organic layers were washed with water (2 × 60 cm^3). The organic layer was dried over Na_2SO_4 and concentrated at reduced pressure. The remaining residue was purified by column chromatography (hexane/EtOAc, 8/1) on silica gel affording **3a** (92 mg, 87%) as a brown solid: R_f 0.47 (hexane/AcOEt, 4/1); mp 62–64 ºC (lit.[3] mp 65–67 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.45 (br s, 1H), 7.70–7.63 (m, 2H), 7.51–7.43 (m, 2H), 7.41–7.33 (m, 1H), 7.21–7.09 (m, 2H), 6.93 (dd, *J* = 2.2, 0.7 Hz, 1H), 6.84 (ddd, *J* = 10.3, 7.4 1.2 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 156.5 (d, *J* = 246.8 Hz, C), 139.3 (d, *J* = 11.2 Hz, C), 138.0 (C), 131.9 (C), 129.2 (2 × CH), 128.1 (CH), 125.3 (2 × CH), 122.8 (d, *J* = 7.6 Hz, CH), 118.6 (d, *J* = 22.4 Hz, C), 107.1 (d, *J* = 3.6 Hz, CH), 105.1 (d, *J* = 18.9 Hz, CH), 95.8 (CH); HRMS calcd for $C_{14}H_{10}FN$, 211.0797; found, 211.0787.

General procedure for the synthesis of *O*-2,3-dihalophenyl *N,N*-diethylcarbamates 4:[4]

*n*BuLi (8.25 cm^3 of a 1.6M solution in hexane, 13.2 mmol) was added to a solution of *i*Pr_2NH (1.85 cm^3, 13.2 mmol) in THF (40 cm^3) at 0 ºC. After 30 min at 0 ºC, the LDA solution was cooled to −78 ºC, and the corresponding 3-halophenyl *N,N*-diethylcarbamate (12 mmol) was added. The resulting solution was stirred for 30 min at −78 ºC, and then iodine (3.66 g, 14.4 mmol) was added. After 30 min at low temperature, the reaction mixture was allowed to reach room temperature and quenched with saturated aqueous $Na_2S_2O_3$. The aqueous phase was extracted with Et_2O (3 × 30 cm^3), and the combined organic layers were washed with HCl 1M, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude was purified by column chromatography (hexane/EtOAc, 5/1) on silica gel affording the title compounds **4**, whose spectroscopic and characterization data have been previously reported.[4]

Procedure for the synthesis of 2,3-dihalophenyl ethers 5a and 5b:[5]

To a solution of lithium 2,2,6,6-tetramethylpiperidide (20 mmol, generated from *n*BuLi and 2,2,6,6-tetramethylpiperidine) in dry THF (30 cm^3), a solution of *t*Bu_2Zn (22 mmol, generated from *t*BuLi and $ZnCl_2$) in dry THF (30 cm^3) was added at −78 ºC, and the reaction mixture was stirred at 0 ºC for 30 min. Then, the corresponding 3-haloanisole (10 mmol) was added at −78 ºC, the reaction mixture was allowed to reach −45 ºC (for X = Cl) or −30 ºC (for X = Br), and it was stirred at this temperature overnight. Iodine (17.78 g, 70 mmol) in THF (30 cm^3) was added to the reaction mixture and it was stirred at room temperature for 2 h. The reaction was quenched with saturated $Na_2S_2O_3$, and the aqueous solution was extracted with EtOAc (3 × 15 cm^3). The combined organic layers were washed with water (2 × 30 cm^3) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc) to afford the 2,3-dihalophenylethers **5a** and **5b**.

1-Chloro-2-iodo-3-methoxybenzene (5a): purification by column chromatography (hexane/EtOAc, 20/1) on silica gel afforded **5a** (2.23 g, 86%) as a white solid: R_f 0.28 (hexane/AcOEt, 20/1); mp 52–54 ºC (lit.[6] mp 53.5 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.22 (t, *J* = 8.1 Hz, 1H), 7.08 (ddd, *J* = 8.1, 1.3, 0.5 Hz, 1H), 6.67 (dd, *J* = 8.1, 1.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 159.9 (C), 139.8 (C), 129.9 (CH),

121.9 (CH), 108.5 (CH), 91.3 (C), 56.9 (CH_3); EI-LRMS *m/z* 270 (M^++2, 31), 268 (M^+, 100), 253 (23), 225 (12), 126 (24), 111 (11); HRMS calcd for C_7H_6ClIO, 267.9152; found, 267.9166.

1-Bromo-2-iodo-3-methoxybenzene (5b): purification by column chromatography (hexane/EtOAc, 20/1) on silica gel afforded **5b** (2.60 g, 83%) as a white solid: R_f 0.25 (hexane/AcOEt, 20/1); mp 63–65 ºC (lit.[5b] mp 62.5–64 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.26 (td, *J* = 8.0, 1.2 Hz, 1H), 7.18 (dt, *J* = 8.0, 1.2 Hz, 1H), 6.71 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 160.1 (C), 131.2 (C), 130.2 (CH), 125.2 (CH), 108.9 (CH), 94.4 (C), 57.0 (CH_3); EI-LRMS *m/z* 314 (M^++2, 100), 312 (M^+, 100), 299 (21), 297 (20), 172 (42), 170 (40); HRMS calcd for C_7H_6BrIO, 311.8647; found, 311.8635.

General procedure for the synthesis of *N*-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamides 8 from 4:

To a solution of the corresponding 2,3-dihalophenyl *N,N*-diethylcarbamate **4** (1 equiv) in EtOH (10 cm^3/mmol) NaOH (10 equiv) was added, and the mixture was refluxed for 5–8 h (completion of the hydrolysis was monitored by GC-MS). After the mixture was cooled to room temperature, most of the EtOH was removed under reduced pressure and the residue was diluted with Et_2O and water. The organic phase was rejected and then, the aqueous solution was carefully neutralized with a HCl 1M solution. The aqueous phase was extracted with Et_2O (3 × 30 cm^3), and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Without further purification, the crude phenol **6** was dissolved in anhydrous DMF (2 cm^3/mmol) under a nitrogen atmosphere and NaOH (3 equiv) was added to the mixture. After 1 h at room temperature, 2-bromo-2-methylpropanamide (3 equiv) was added and the reaction was stirred for 2 h at room temperature. After complete alkylation of **6** to the corresponding 2-(2,3-dihalophenoxy)-2-methylpropanamide **7** (monitored by GC-MS), NaOH (9 equiv) was added and the mixture was heated at 60 ºC for 2 h. The reaction was quenched with H_2O and the corresponding *N*-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamide **8** was recovered as a solid after filtration.

***N*-(3-Fluoro-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8a):** Reaction of 3-fluoro-2-iodophenyl *N,N*-diethylcarbamate **4a** (674 mg, 2 mmol) according to the general procedure afforded **8a** (536 mg, 83%) as a white solid: mp 95–97 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.31 (br s, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.35–7.26 (m, 1H), 6.83 (t, *J* = 8.3 Hz, 1H), 2.71 (s, 1H), 1.58 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.0 (C), 161.8 (d, *J* = 243.7 Hz, C), 139.8 (d, *J* = 3.5 Hz, C), 130.5 (d, *J* = 9.0 Hz, CH), 116.5 (d, *J* = 2.9 Hz, CH), 111.2 (d, *J* = 23.8 Hz, CH), 78.1 (d, *J* = 27.9 Hz, C), 74.7 (C), 28.1 (2 × CH_3); EI-LRMS *m/z* 323 (M^+, 27), 265 (33), 237 (100), 138 (19), 59 (81); IR (KBr) 3420, 3368, 3289, 1661, 1462, 1416, 776 cm^{-1}; HRMS calcd for $C_{10}H_{11}FINO_2$, 322.9819; found, 322.9812.

***N*-(3-Chloro-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8b):** Reaction of 3-chloro-2-iodophenyl *N,N*-diethylcarbamate **4b** (3.53 g, 10 mmol) according to the general procedure afforded **8b** (2.78 g, 82%) as a white solid: mp 113–115 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.33 (br s, 1H), 8.21 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.31–7.21 (m, 2H), 2.47 (s, 1H), 1.58 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.0 (C), 140.4 (C), 139.1 (C), 129.8 (CH), 125.1 (CH), 118.9 (CH), 95.1 (C), 74.7 (C), 28.0 (2 × CH_3); EI-LRMS *m/z* 341 (M^++2, 3),

339 (M^+, 8), 281 (10), 253 (62), 194 (15), 154 (24), 59 (100); IR (KBr) 3398, 3291, 1662, 1575, 1539, 1444, 1396, 1126, 776 cm^{-1}; HRMS calcd for $C_{10}H_{11}ClINO_2$, 338.9523; found, 338.9514.

***N*-(3-Bromo-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8c):** Reaction of 3-bromo-2-iodophenyl *N,N*-diethylcarbamate **4c** (794 mg, 2 mmol) according to the general procedure afforded **8c** (620 mg, 81%) as a white solid: mp 118–120 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.33 (br s, 1H), 8.23 (dd, J = 8.1, 1.4 Hz, 1H), 7.4 (dd, J = 8.1, 1.4 Hz, 1H), 7.22 (t, J = 8.1 Hz, 1H), 2.55 (s, 1H), 1.57 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 174.9 (C), 140.5 (C), 130.4 (C), 130.1 (CH), 128.5 (CH), 119.4 (CH), 98.2 (C), 74.7 (C), 28.0 (2 × CH_3); EI-LRMS *m/z* 385 (M^++2, 3), 383 (M^+, 3), 325 (4), 299 (24), 297 (25), 240 (10), 238 (10), 200 (15), 198 (15), 59 (100); IR (KBr) 3387, 3285, 1652, 1651, 1525, 1392, 776, 693 cm^{-1}; HRMS calcd for $C_{10}H_{11}BrINO_2$, 382.9018; found, 382.9012.

***N*-(2,3-Diiodophenyl)-2-hydroxy-2-methylpropanamide (8d):** Reaction of 2,3-diiodophenyl *N,N*-diethylcarbamate **4d** (890 mg, 2 mmol) according to the general procedure afforded **8d** (680 mg, 79%) as a white solid: mp 144–146 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.28 (br s, 1H), 8.24 (dd, J = 8.2, 1.4 Hz, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.09 (t app, J = 8.0 Hz, 1H), 2.53 (br s, 1H), 1.57 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 175.1 (C), 140.0 (C), 135.4 (CH), 130.4 (CH), 120.2 (CH), 108.8 (C), 104.5 (C), 74.5 (C), 28.0 (2 × CH_3); EI-LRMS *m/z* 431 (M^+, 21), 372 (8), 345 (85), 286 (62), 246 (44), 218 (14), 91 (15), 59 (100); IR (KBr) 3318, 1651, 1568, 1523, 1386, 773 cm^{-1}; HRMS calcd for $C_{10}H_{11}I_2NO_2$, 430.8879; found, 430.8873.

General procedure for the synthesis of *N*-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamides 8 from 5:

BBr_3 (20 cm^3 of a 1M solution in CH_2Cl_2, 20 mmol) was added dropwise to a solution of the corresponding anisole **7** (4 mmol) in CH_2Cl_2 (120 cm^3) at –78 ºC.[7] The mixture was allowed to reach room temperature overnight, and then $NaHCO_3$ (1.68 g, 20 mmol) was added. The resulting mixture was cooled to 0 ºC, and MeOH (70 cm^3) was added dropwise. After 30 min at 0 ºC, the mixture was warmed to room temperature and stirred for 1 h. Most of the solvent was removed under reduced pressure and the residue was diluted with water and CH_2Cl_2. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 30 cm^3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Whitout further purification, the corresponding crude dihalophenol **6** was dissolved in anhydrous DMF (8 cm^3) under a nitrogen atmosphere and NaOH (480 mg, 12 mmol) was added to the mixture. After 1 h at room temperature, 2-bromo-2-methylpropanamide (1.99 g, 12 mmol) was added and the reaction was stirred for 2 h at room temperature. After complete alkylation of **6** to the corresponding 2-(2,3-dihalophenoxy)-2-methylpropanamide **7** (monitored by GC-MS), NaOH (9 equiv) was added and the mixture was heated at 60 ºC for 2 h. The reaction was quenched with H_2O and the corresponding *N*-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamide **8** was recovered as a solid after filtration.

General procedure for the synthesis of 2-alkynyl-3-haloanilides 9 and 10:

A mixture of the corresponding *N*-(2,3-dihalophenyl)propanamide **8b** or **8c** (1 mmol), alkyne (1.5 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 0.03 mmol), CuI (9.5 mg, 0.05 mmol) and Et_2NH (110 mg, 1.5 mmol) in anhydrous DMF (4 cm^3) was stirred under a nitrogen atmosphere at 40, 50 or 80 ºC for the desired time until complete consumption of starting material as monitored by GC-MS (2–6 h). CH_2Cl_2 (20 cm^3) and aq HCl (20 cm^3 of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 20 cm^3). The combined organic layers were washed with water (2 × 60 cm^3). The organic layer was dried over Na_2SO_4 and concentrated at reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 5/1) to afford the coupled products.

***N*-(3-Chloro-2-(2-phenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9a):** Reaction of **8b** (339 mg, 1 mmol) with phenylacetylene (153 mg, 1.5 mmol) for 2 h at 80 ºC, according to the general procedure, afforded **9a** (268 mg, 86%) as a white solid: R_f 0.36 (hexane/AcOEt, 4/1); mp 139–141 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.83 (br s, 1H), 8.42 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.65–7.57 (m, 2H), 7.40–7.34 (m, 3H), 7.24 (t, *J* = 8.2 Hz, 1H), 7.15 (dd, *J* = 8.2, 1.1 Hz, 1H), 2.35 (br s, 1H), 1.58 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 174.7 (C), 140.2 (C), 135.7 (C), 131.8 (2 × CH), 129.9 (CH), 129.2 (CH), 128.7 (2 × CH), 124.2 (CH), 122.4 (C), 116.8 (CH), 112.9 (C), 101.7 (C), 81.6 (C), 74.8 (C), 28.1 (2 × CH_3) EI-LRMS *m/z* 315 (M^++2, 17), 313 (M^+, 51), 254 (54), 229 (33), 227 (100), 190 (27), 59 (41); IR (KBr) 3365, 3321, 1665, 1571, 1534, 1452, 759, 692 cm^{-1}; HRMS calcd for $C_{18}H_{16}ClNO_2$, 313.0870; found, 313.0857.

***N*-(3-Chloro-2-(hex-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (9b):** Reaction of **8b** (339 mg, 1 mmol) with 1-hexyne (123 mg, 1.5 mmol) for 2.5 h at 80 ºC, according to the general procedure, afforded **9b** (264 mg, 90%) as a pale brown solid: R_f 0.26 (hexane/AcOEt, 5/1); mp 66–68 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.65 (br s, 1H), 8.37 (d, *J* = 8.1 Hz, 1H), 7.24–7.07 (m, 2H), 2.55 (t, *J* = 6.9 Hz, 2H), 2.45 (br s, 1H), 1.70–1.46 (m, 4H), 1.56 (s, 6H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 174.8 (C), 140.2 (C), 135.6 (C), 129.0 (CH), 124.1 (CH), 116.7 (CH), 113.5 (C), 103.7 (C), 74.5 (C), 73.1 (C), 30.7 (CH_2), 28.1 (2 × CH_3), 22.1 (CH_2), 19.6 (CH_2), 13.7 (CH_3); EI-LRMS *m/z* 295 (M^++2, 17), 293 (M^+; 51), 207 (48), 193 (41), 178 (64), 164 (88), 59 (100); IR (KBr) 3419, 3322, 1670, 1572, 1516, 1450, 981 cm^{-1}; HRMS calcd for $C_{16}H_{20}ClNO_2$, 293.1183; found, 293.1184.

***N*-(3-Chloro-2-(hept-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (9c):** Reaction of **8b** (339 mg, 1 mmol) with 1-hetptyne (144 mg, 1.5 mmol) for 2.5 h at 80 ºC, according to the general procedure, afforded **9c** (249 mg, 81%) as a pale brown solid: R_f 0.35 (hexane/AcOEt, 4/1); mp 76–78 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (br s, 1H), 8.32 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.15–7.05 (m, 2H), 3.49 (s, 1H), 2.49 (t, *J* = 7.1 Hz, 2H), 1.68–1.56 (m, 2H), 1.53 (s, 6H), 1.47–1.21 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.3 (C), 140.0 (C), 135.6 (C), 128.8 (CH), 124.0 (CH), 116.6 (CH), 113.6 (C), 103.8 (C), 74.2 (C), 73.0 (C), 31.1 (CH_2), 28.2 (CH_2), 27.9 (2 × CH_3), 22.2 (CH_2), 19.7 (CH_2), 14.0 (CH_3); EI-LRMS *m/z* 309 (M^++2, 7), 307 (M^+, 21), 206 (20), 180 (35), 164 (44), 59 (100); IR (KBr) 3311, 2953, 1662, 1569, 1520, 1453, 1139, 790, 731 cm^{-1}; HRMS calcd for $C_{17}H_{22}ClNO_2$, 307.1339; found, 307.1342.

***N*-(3-Chloro-2-(2-cyclohexenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9d):** Reaction of **8b** (339 mg, 1 mmol) with 1-ethynylcyclohexene (159 mg, 1.5 mmol) for 3 h at 80 ºC, according to the general procedure, afforded **9d** (254 mg, 80%) as a white solid: R_f 0.34 (hexane/AcOEt, 5/1); mp 145–147 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.67 (br s, 1H), 8.36 (dd, J = 8.1, 1.3 Hz, 1H), 7.17 (t, J = 8.1 Hz, 1H), 7.10 (dd, J = 8.1, 1.3 Hz, 1H), 6.36–6.30 (m, 1H), 2.80 (s, 1H), 2.30–2.22 (m, 2H), 2.18–2.10 (m, 2H), 1.72–1.57 (m, 4H), 1.55 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 174.9 (C), 139.7 (C), 137.0 (CH), 135.4 (C), 129.2 (CH), 124.1 (CH), 120.3 (C), 116.6 (CH), 113.4 (C), 103.8 (C), 79.0 (C), 74.5 (C), 29.0 (CH_2), 28.0 (2 × CH_3), 26.0 (CH_2), 22.3 (CH_2), 21.5 (CH_2); EI-LRMS *m/z* 319 (M^++2, 23), 317 (M^+, 72), 281 (25), 231 (57), 207 (100), 180 (26), 59 (55); IR (KBr) 3372, 3320, 1652, 1572, 1532, 1450, 1435, 1197, 1184, 778, 725 cm^{-1}; HRMS calcd for $C_{18}H_{20}ClNO_2$, 317.1183; found, 317.1190.

***N*-(3-Chloro-2-(2-(trimethylsilyl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9e):** Reaction of **8b** (339 mg, 1 mmol) with trimethylsilylacetylene (147 mg, 1.5 mmol) for 5.5 h at 40 ºC, according to the general procedure, afforded **9e** (251 mg, 81%) as a pale brown solid: R_f 0.47 (hexane/AcOEt, 4/1); mp 144–146 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.66 (br s, 1H), 8.37 (dd, J = 8.3, 0.9 Hz, 1H), 7.21 (t, J = 8.3 Hz, 1H), 7.09 (dd, J = 8.3, 0.9 Hz, 1H), 2.60 (br s, 1H), 1.55 (s, 6H), 0.29 (d, J = 0.9 Hz, 9H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.0 (C), 140.8 (C), 135.8 (C), 130.0 (CH), 124.1 (CH), 116.8 (CH), 112.8 (C), 108.1 (C), 96.6 (C), 74.6 (C), 28.1 (2 × CH_3), 0.0 (3 × CH_3); EI-LRMS *m/z* 311 (M^++2, 10), 309 (M^+, 29), 236 (100), 208 (39); HRMS calcd for $C_{15}H_{20}ClNO_2Si$, 309.0952; found, 309.0951.

***N*-(3-Bromo-2-(2-phenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10a):** Reaction of **8c** (383 mg, 1 mmol) with 1-phenylacetylene (153 mg, 1.5 mmol) for 3.5 h at 50 ºC, according to the general procedure, afforded **10a** (286 mg, 80%) as a white solid: R_f 0.32 (hexane/AcOEt, 4/1); mp 131–133 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.86 (br s, 1H), 8.44 (dd, J = 8.2, 1.0 Hz, 1H), 7.63–7.58 (m, 2H), 7.38–7.29 (m, 4H), 7.13 (t, J = 8.2 Hz, 1H), 2.87 (s, 1H), 1.55 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.0 (C), 140.1 (C), 131.7 (2 × CH), 130.1 (CH), 129.2 (CH), 128.6 (2 × CH), 127.3 (CH), 125.0 (C), 122.3 (C), 117.3 (CH), 115.0 (C), 101.1 (C), 83.4 (C), 74.7 (C), 28.0 (2 × CH_3); EI-LRMS *m/z* 359 (M^++2, 62), 357 (M^+, 62), 300 (60), 298 (58), 273 (100), 271 (100), 191 (60), 165 (53), 59 (83); IR (KBr) 3372, 3312, 1661, 1566, 1532, 1446, 1200, 1131, 752, 726, 689 cm^{-1}; HRMS calcd for $C_{18}H_{16}BrNO_2$, 357.0364; found, 357.0368.

***N*-(3-Bromo-2-(hex-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (10b):** Reaction of **8c** (383 mg, 1 mmol) with 1-hexyne (123 mg, 1.5 mmol) for 3.5 h at 50 ºC, according to the general procedure, afforded **10b** (431 mg, 85%) as a pale brown solid: R_f 0.31 (hexane/AcOEt, 4/1); mp 70–72 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.76 (br s, 1H), 8.36 (dd, J = 8.2, 1.0 Hz, 1H), 7.25 (dd, J = 8.2, 1.0 Hz, 1H), 7.05 (t, J = 8.2 Hz, 1H), 3.42 (s, 1H), 2.50 (t, J = 7.0 Hz, 2H), 1.64–1.43 (m, 4H), 1.52 (s, 6H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.3 (C), 140.1 (C), 129.2 (CH), 127.2 (CH), 125.0 (C), 117.1 (CH), 115.6 (C), 103.1 (C), 74.8 (C), 74.2 (C), 30.5 (CH_2), 27.9 (2 × CH_3), 22.1 (CH_2), 19.5 (CH_2), 13.7 (CH_3); EI-LRMS *m/z* 339 (M^++2, 37), 337 (M^+, 36), 253 (29), 251 (30), 226 (50), 210 (51), 157 (25), 129 (26), 59 (100); IR (KBr) 3419, 3319, 1673, 1567, 1520, 1427, 980, 729 cm^{-1}; HRMS calcd for $C_{16}H_{20}BrNO_2$, 337.0677; found, 337.0676.

***N*-(3-Bromo-2-(hept-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (10c):** Reaction of **8c** (383 mg, 1 mmol) with 1-heptyne (144 mg, 1.5 mmol) for 3.5 h at 50 ºC, according to the general procedure, afforded

10c (277 mg, 79%) as a white solid: R_f 0.30 (hexane/AcOEt, 4/1); mp 79–81 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.35 (dd, J = 8.2, 0.8 Hz, 1H), 7.24 (dd, J = 8.2, 0.8 Hz, 1H), 7.03 (t, J = 8.2 Hz, 1H), 3.58 (s, 1H), 2.47 (t, J = 7.2 Hz, 2H), 1.68–1.57 (m, 2H), 1.52 (s, 6H), 1.49–1.24 (m, 4H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.4 (C), 140.1 (C), 129.1 (CH), 127.1 (CH), 125.0 (C), 117.1 (CH), 115.6 (C), 103.2 (C), 74.8 (C), 74.2 (C), 31.1 (CH_2), 28.2 (CH_2), 27.8 (2 × CH_3), 22.2 (CH_2), 19.7 (CH_2), 14.0 (CH_3); EI-LRMS *m/z* 353 (M^++2, 15), 351 (M^+, 15), 226 (28), 210 (30), 157 (21), 59 (100); IR (KBr) 3295, 2930, 1661, 1564, 1520, 1449, 1130, 981, 788, 730 cm^{-1}; HRMS calcd for $C_{17}H_{22}BrNO_2$, 351.0834; found, 351.0822.

***N*-(3-bromo-2-(2-cyclohexenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10d):** Reaction of **8c** (383 mg, 1 mmol) with 1-ethynylcyclohexene (159 mg, 1.5 mmol) for 5 h at 50 ºC, according to the general procedure, afforded **10d** (310 mg, 86%) as a white solid: R_f 0.32 (hexane/AcOEt, 4/1); mp 154–156 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.65 (br s, 1H), 8.42 (dd, J = 8.2, 1.1 Hz, 1H), 7.29 (dd, J = 8.2 Hz, 1.1 Hz, 1H), 7.12 (t, J = 8.2 Hz, 1H), 6.37–6-32 (m, 1H), 2.48 (br s, 1H), 2.32–2.22 (m, 2H), 2.21–2.12 (m, 2H), 1.77–1.58 (m, 4H), 1.56 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 174.8 (C), 139.9 (C), 137.1 (CH), 129.6 (CH), 127.2 (CH), 124.9 (C), 120.4 (C), 117.2 (CH), 115.4 (C), 103.2 (C), 80.9 (C), 74.6 (C), 28.9 (CH_2), 28.1 (2 × CH_3), 26.0 (CH_2), 22.3 (CH_2), 21.5 (CH_2); EI-LRMS *m/z* 363 (M^++2, 100), 361 (M^+, 100), 277 (53), 275 (53), 167 (34), 59 (63); IR (KBr) 3376, 3318, 2929, 1653, 1566, 1530, 1446, 1433, 976, 775, 724 cm^{-1}; HRMS calcd for $C_{18}H_{20}BrNO_2$, 361.0677; found, 361.0677.

***N*-(3-Bromo-2-(2-(trimethylsilyl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10e):** Reaction of **8c** (383 mg, 1 mmol) with trimethylsilylacetylene (147 mg, 1.5 mmol) for 3 h at 40 ºC, according to the general procedure, and afforded **10e** (251 mg, 71%) as a pale brown solid: R_f 0.39 (hexane/AcOEt, 4/1); mp 150–152 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.70 (br s, 1H), 8.40 (dt, J = 8.2, 0.9 Hz, 1H), 7.27 (td, J = 8.2, 0.9 Hz, 1H), 7.12 (t, J = 8.2 Hz, 1H), 2.83 (s, 1H), 1.54 (d, J = 0.6 Hz, 6H), 0.28 (d, J = 0.8 Hz, 9H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 175.1 (C), 140.8 (C), 130.3 (CH), 127.2 (CH), 125.0 (C), 117.3 (CH), 114.8 (C), 107.5 (C), 98.3 (C), 74.4 (C), 28.0 (2 × CH_3), -0.1 (3 × CH_3); EI-LRMS *m/z* 355 (M^++2, 28), 353 (M^+, 27), 282 (100), 280 (100), 254 (37), 252 (37), 238 (19), 236 (18); HRMS calcd for $C_{15}H_{20}BrNO_2Si$, 353.0447; found, 353.0450.

***N*-(3-Bromo-2-(2-(thiophen-3-yl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10f):** Reaction of **8c** (383 mg, 1 mmol) with 3-ethynylthiophene (162 mg, 1.5 mmol) for 3.5 h at 50 ºC, according to the general procedure, afforded **10f** (269 mg, 74%) as a white solid: R_f 0.37 (hexane/AcOEt, 4/1); mp 132–134 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.82 (br s, 1H), 8.41 (d, J = 8.3 Hz, 1H), 7.63 (dd, J = 2.9, 1.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.24 (dd, J = 4.9, 1.1 Hz, 1H), 7.11 (t, J = 8.3 Hz, 1H), 2.90 (s, 1H), 1.53 (s, 6H); ^{13}C NMR (100.8 MHz, $CDCl_3$) δ = 175.0 (C), 140.1 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 127.3 (CH), 125.9 (CH), 124.7 (C), 121.4 (C), 117.3 (CH), 115.1 (C), 96.3 (C), 83.1 (C), 74.7 (C), 28.0 (2 × CH_3); EI-LRMS *m/z* 365 (M^++2, 40), 363 (M^+, 44), 305 (19), 279 (61), 277 (59), 226 (14), 198 (29), 196 (32), 171 (23), 59 (100); HRMS calcd for $C_{16}H_{14}BrNO_2S$, 362.9929; found, 362.9928.

General procedure for the synthesis of 4-halo-1*H*-indoles 11 and 12 from anilides 9 and 10:

To a solution of the corresponding 2-alkynyl-3-haloanilide **9** or **10** (1 equiv) in anhydrous DMF (4 cm^3/mmol) freshly powdered NaOH (3 equiv) was added. The resulting mixture was refluxed under a nitrogen atmosphere at 140 ºC until the cyclization was completed (as monitored by GC-MS). CH_2Cl_2 (10 cm^3) and aq HCl (10 cm^3 of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 10 cm^3). The combined organic layers were washed with water (2 × 30 cm^3), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the corresponding 4-haloindole **11** or **12**.

4-Chloro-2-phenyl-1*H*-indole (11a): From **9a** (94 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (4 h), and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **11a** (54 mg, 79%) as a white solid: R_f 0.32 (hexane/AcOEt, 6/1); mp 73–75 ºC (lit.[8] mp 74–77 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.43 (br s, 1H), 7.70–7.63 (m, 2H), 7.50–7.43 (m, 2H), 7.39–7.33 (m, 1H), 7.31–7.27 (m, 1H), 7.17–7.08 (m, 2H), 6.94 (dd, J = 2.2, 0.8 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 138.6 (C), 137.4 (C), 131.8 (C), 129.2 (2 × CH), 128.3 (CH), 128.2 (C), 125.9 (C), 125.4 (2 × CH), 122.9 (CH), 120.1 (CH), 109.6 (CH), 98.5 (CH); EI-LRMS *m/z* 229 (M^++2, 33), 227 (M^+, 100), 191 (10), 165 (16), 113 (10); IR (KBr) 3449, 2961, 2924, 1452, 1261, 1098, 803, 756, 688 cm^{-1}; HRMS calcd for $C_{14}H_{10}ClN$, 227.0502; found, 227.0501.

2-Butyl-4-chloro-1*H*-indole (11b): From **9b** (88 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (2.5 h), and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11b** (53 mg, 86%) as a colourless oil: R_f 0.46 (hexane/EtOAc, 6/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.90 (br s, 1H), 7.18 (dt, J = 7.7, 1.0 Hz, 1H), 7.12 (dd, J = 7.6, 1.1 Hz, 1H), 7.05 (t, J = 7.7 Hz, 1H), 6.38 (dd, J = 2.2, 0.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.51–1.38 (m, 2H), 0.99 (t, J = 7.3, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 141.0 (C), 136.5 (C), 127.6 (C), 125.0 (C), 121.6 (CH), 119.4 (CH), 109.1 (CH), 98.1 (CH), 31.2 (CH_2), 28.0 (CH_2), 22.5 (CH_2), 14.0 (CH_3); EI-LRMS *m/z* 209 (M^++2, 10), 207 (M^+, 33), 164 (100), 128 (8), 101 (6); IR (KBr) 3417, 2957, 2929, 1575, 1548, 1433, 1330, 1182, 941, 765 cm^{-1}; HRMS calcd for $C_{12}H_{14}ClN$, 207.0815; found, 207.0822.

4-Chloro-2-pentyl-1*H*-indole (11c): From **9c** (154 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (2.5 h) and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **11c** (93 mg, 84%) as a pale brown solid: R_f 0.46 (hexane/AcOEt, 5/1); mp 24–26 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.96 (br s, 1H), 7.19 (dd, J = 7.6, 0.9 Hz, 1H), 7.11–7.00 (m, 2H), 6.36 (d, J = 0.9 Hz, 1H), 2.75 (t, J = 7.6 Hz, 2H), 1.79–1.68 (m, 2H), 1.43–1.25 (m, 4H), 0.93 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 141.0 (C), 136.5 (C), 127.7 (C), 125.0 (C), 121.6 (CH), 119.4 (CH), 109.0 (CH), 98.1 (CH), 31.6 (CH_2), 28.8 (CH_2), 28.3 (CH_2), 22.6 (CH_2), 14.1 (CH_3); EI-LRMS *m/z* 223 (M^++2 11), 221, (M^+, 34), 178 (24), 164 (100), 128 (9), 101 (6); IR (KBr) 3417, 2956, 2928, 1547, 1433, 1329, 1182, 939, 765 cm^{-1}; HRMS calcd for $C_{13}H_{16}ClN$, 221.0971; found, 221.0980.

4-Chloro-2-cyclohexenyl-1*H*-indole (11d): From **9d** (94 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (2.5 h), and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11d** (56 mg, 81%) as a pale brown oil: R_f 0.70 (hexane/EtOAc, 6/1); ^{1}H NMR (300

MHz, $CDCl_3$) δ = 8.21 (br s, 1H), 7.21–7.17 (m,1H), 7.09–7.02 (m, 2H), 6.54 (d, J = 2.0 Hz, 1H), 6.17–6.12 (m, 1H), 2.51–2.44 (m, 2H), 2.29–2.21 (m, 2H), 1.85–1.76 (m, 2H), 1.75–1.65 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 140.1 (C), 136.8 (C), 128.8 (C), 127.8 (C), 125.6 (C), 123.8 (CH), 122.5 (CH), 119.5 (CH), 109.1 (CH), 97.1 (CH), 26.0 (CH_2), 25.6 (CH_2), 22.5 (CH_2), 22.2 (CH_2); EI-LRMS *m/z* 233 (M^++2, 32), 231 (M^+, 100), 203 (35), 164 (34), 151 (29); IR (neat) 3433, 2928, 1569, 1432, 1334, 1184, 947, 764, 731 cm^{-1}; HRMS calcd for $C_{14}H_{14}ClN$, 231.0815; found, 231.0814.

4-Chloro-1*H*-indole (11e):[9] From **9e** (168 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (4 h), and purification by flash column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11e** (55 mg, 73%) as a brown oil: R_f 0.33 (hexane/AcOEt, 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.25 (br s, 1H), 7.31–7.21 (m, 2H), 7.16–7.08 (m, 2H), 6.70–6.62 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 136.6 (C), 126.9 (C), 126.2 (C), 124.9 (CH), 122.7 (CH), 119.7 (CH), 109.8 (CH), 101.4 (CH); EI-LRMS *m/z* 153 (M^++2, 31), 151 (M^+, 100), 116 (18), 89 (27).

4-Bromo-2-phenyl-1*H*-indole (12a): From **10a** (178 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (5 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded **12a** (113 mg, 83%) as a white solid: R_f 0.38 (hexane/AcOEt, 5/1); mp 100–102 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.42 (br s, 1H), 7.65 (dd, J = 8.4, 1.0 Hz, 2H), 7.49–7.42 (m, 2H), 7.40–7.29 (m, 3H), 7.06 (t, J = 7.9 Hz, 1H), 6.91–6.89 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 138.5 (C), 137.0 (C), 131.7 (C), 130.1 (C), 129.2 (2 × CH), 128.3 (CH), 125.3 (2 × CH), 123.2 (CH), 114.6 (C), 110.2 (CH), 100.2 (CH); EI-LRMS *m/z* 273 (M^++2, 98), 271 (M^+, 100), 191 (27), 165 (34), 136 (11); IR (KBr) 3445, 1475, 1452, 1352, 1289, 1181, 916, 758, 691 cm^{-1}; HRMS calcd for $C_{14}H_{10}BrN$, 270.9997; found, 270.9995.

4-Bromo-2-butyl-1*H*-indole (12b): From **10b** (101 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (3 h), and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **12b** (61 mg, 80%) as a white solid: R_f 0.45 (hexane/AcOEt, 5/1); mp 29–31 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.95 (br s, 1H), 7.26 (dd, J = 7.6, 0.8 Hz, 1H), 7.22 (dt, J = 8.0, 0.8 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.32 (dd, J = 2.2, 0.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.50–1.37 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 141.0 (C), 136.0 (C), 129.6 (C), 122.5 (CH), 121.9 (CH), 113.7 (C), 109.6 (CH), 99.8 (CH), 31.2 (CH_2), 28.0 (CH_2), 22.5 (CH_2), 14.0 (CH_3); EI-LRMS *m/z* 253 (M^++2, 37), 251 (M^+, 37), 210 (100), 208 (98), 129 (32); IR (KBr) 3407, 2958, 2929, 1539, 1430, 1329, 1178, 917, 763, 729 cm^{-1}; HRMS calcd for $C_{12}H_{14}BrN$, 251.0310; found, 251.0309.

4-Bromo-2-pentyl-1*H*-indole (12c): From **10c** (123 mg, 0.35 mmol) and NaOH (42 mg, 1.05 mmol) according to the general procedure (2.5 h) and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **12c** (76 mg, 82%) as a pale brown oil: R_f 0.42 (hexane/EtOAc, 6/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97 (br s, 1H), 7.28–7.20 (m, 2H), 6.98 (t, J = 8.0 Hz, 1H), 6.31 (dd, J = 2.2, 0.8 Hz, 1H), 2.74 (t, J = 7.7, Hz, 2H), 1.79–1.68 (m, 2H), 1.43–1.34 (m, 4H), 0.93 (t, J= 7.0 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 141.0 (C), 136.1 (C), 129.6 (C), 122.5 (CH), 121.9 (CH), 113.7 (C), 109.6 (CH), 99.9 (CH), 31.6 (CH_2), 28.9 (CH_2), 28.3 (CH_2), 22.6 (CH_2), 14.1 (CH_3); EI-LRMS *m/z* 267 (M^++2, 41), 265 (M^+, 42), 224

(19), 210 (100), 208 (98), 129 (32); IR (KBr) 3411, 2956, 2928, 1548, 1430, 1327, 1178, 917, 763 cm^{-1}; HRMS calcd for $C_{13}H_{16}BrN$, 265.0466; found, 265.0467

4-Bromo-2-cyclohexenyl-1*H*-indole (12d): From **10d** (180 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (4 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded afforded **12d** (105 mg, 76%) as a colourless oil: R_f 0.50 (hexane/EtOAc, 6/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.27 (br s, 1H), 7.27–7.20 (m, 2H), 6.99 (t, J = 7.8 Hz, 1H), 6.48 (d, J = 1.9 Hz, 1H), 6.17–6.12 (m, 1H), 2.51–2.43 (m, 2H), 2.28–2.20 (m, 2H), 1.84–1.75 (m, 2H), 1.75–1.65 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 140.2 (C), 136.4 (C), 129.7 (C), 128.9 (C), 123.8 (CH), 122.8 (CH), 122.7 (CH), 114.3 (C), 109.7 (CH), 98.9 (CH), 26.1 (CH_2), 25.6 (CH_2), 22.6 (CH_2), 22.2 (CH_2); EI-LRMS *m/z* 277 (M^++2, 98), 275 (M^+, 100), 247 (24), 195 (23), 167 (38); IR (KBr) 3427, 2927, 1568, 1524, 1429, 1332, 1179, 917, 762, 730 cm^{-1}; HRMS calcd for $C_{14}H_{14}BrN$, 275.0310; found, 275.0314.

4-Bromo-1*H*-indole (12e):[9] From **10e** (176 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (5 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded **12e** (73 mg, 75%) as a colourless oil: R_f 0.29 (hexane/EtOAc, 6/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.28 (br s, 1H), 7.37–7.23 (m, 3H), 7.06 (t, J = 7.9 Hz, 1H), 6.64–6.60 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 136.1 (C), 128.8 (C), 124.8 (CH), 123.0 (CH), 122.9 (CH), 114.9 (C), 110.4 (CH), 103.2 (CH); EI-LRMS *m/z* 197 (M^++2, 100), 195 (M^+, 100), 184 (7), 116 (77), 89 (44); HRMS calcd for C_8H_6BrN, 194.9684; found, 194.9679.

4-Bromo-2-(thiophen-3-yl)-1*H*-indole (12f): From **10f** (181 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (3 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded afforded **12f** (99 mg, 71%) as a pale brown solid: R_f 0.48 (hexane/AcOEt, 4/1); mp 44–46 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.35 (br s, 1H), 7.47–7.38 (m, 3H), 7.29 (d, J = 7.7 Hz, 2H), 7.07–7.00 (m, 1H), 6.75 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 136.6 (C), 134.6 (C), 133.5 (C), 129.9 (C), 127.0 (CH), 125.7 (CH), 123.25 (CH), 123.19 (CH), 119.9 (CH), 114.5 (C), 110.0 (CH), 100.2 (CH); EI-LRMS *m/z* 281 (M^++2, 100), 279 (M^+, 96), 198 (38), 171 (61), 154 (27), 126 (32); HRMS calcd for $C_{12}H_8BrNS$, 276.9561; found, 276.9576.

General procedure for the synthesis of 4-halo-1*H*-indoles 3, 11 and 12 from 2,3-dihaloanilides 8 (one pot procedure):

A mixture of the corresponding *N*-(3-halo-2-iodophenyl)-2-hydroxy-2-methylpropanamide **8** (1 equiv), alkyne (1.5 equiv), $PdCl_2(PPh_3)_2$ (3 mol%), CuI (5 mol%) and Et_2NH (1.5 equiv) in anhydrous DMA (4 cm^3/mol) was stirred under a nitrogen atmosphere at 80 ºC (for **8a** and **8b**), at 50 ºC (for **8c**), or at 40 ºC (when trimetylsilylacetylene is used as alkyne) until complete consumption of starting material **8** as monitored by GC-MS (2–5 h). Then, freshly powdered NaOH (10 equiv) was added to the reaction mixture and it was refluxed under a nitrogen atmosphere at 140 ºC until the cyclization was completed (3–4 h, as monitored by GC-MS). After cooling of the reaction mixture, CH_2Cl_2 (20 cm^3) and aq HCl (20 cm^3 of a 0.5M solution) were added. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 20 cm^3) and the combined organic layers were washed with water (2 × 60 cm^3). The organic layer was dried over anhydrous Na_2SO_4 and concentrated

under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the corresponding 4-halo-1*H*-indoles **3**, **11** and **12**.

4-Fluoro-2-phenyl-1*H*-indole (3a): Treatment of **8a** (161 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **3a** (90 mg, 85%), whose spectroscopic data have been reported above.

2-Butyl-4-fluoro-1*H*-indole (3b): Treatment of **8a** (161 mg, 0.5 mmol) with 1-hexyne (62 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **3b** (74 mg, 77%) as a pale brown oil: R_f 0.50 (hexane/EtOAc, 4/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.92 (br s, 1H), 7.11–7.00 (m, 2H), 6.78 (ddd, J = 10.4, 6.9, 1.7 Hz, 1H), 6.35 (dd, J = 2.2, 0.8 Hz, 1H), 2.75 (t, J = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.51–1.38 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 155.9 (d, J = 245.2 Hz, C), 140.1 (C), 138.6 (d, J = 11.8 Hz, C), 121.4 (d, J = 7.6 Hz, CH), 117.8 (d, J = 22.4 Hz, C), 106.5 (d, J = 3.4 Hz, CH), 104.5 (d, J = 19.1 Hz, CH), 95.4 (CH), 31.3 (CH_2), 27.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3); HRMS calcd for $C_{12}H_{14}FN$, 191.1110; found, 191.1106.

4-Chloro-2-phenyl-1*H*-indole (11a): Treatment of **8b** (170 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **11a** (92 mg, 81%), whose spectroscopic data have been reported above.

2-Butyl-4-chloro-1*H*-indole (11b): Treatment of **8b** (339 mg, 1 mmol) with 1-hexyne (123 mg, 1.5 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 3 mol%), CuI (9 mg, 5 mol%) and Et_2NH (109 mg, 1.5 mmol) in DMA (4 mL) for 2.5 h and then, with NaOH (400 mg, 10 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11b** (147 mg, 71%), whose spectroscopic data have been reported above.

4-Chloro-2-cyclohexenyl-1*H*-indole (11d): Treatment of **8b** (679 mg, 2 mmol) with 1-ethynylcyclohexene (320 mg, 3 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 3 mol%), CuI (19 mg, 5 mol%) and Et_2NH (220 mg, 3 mmol) in DMA (6 mL) for 2 h and then, with NaOH (800 mg, 20 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11d** (379 mg, 82%), whose spectroscopic data have been reported above.

4-Chloro-1*H*-indole (11e):[9] Treatment of **8b** (170 mg, 0.5 mmol) with trimethylsilylacetylene (73 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 5.5 h and then, with NaOH (200 mg, 5 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **11e** (46 mg, 61%), whose spectroscopic data have been reported above.

4-Chloro-2-(3-chlorophenyl)-1*H*-indole (11f): Treatment of **8b** (170 mg, 0.5 mmol) with 1-chloro-3-ethynylbenzene (102 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 2 h and then, with NaOH (200 mg, 5 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **11f** (98 mg, 75%) as a brown solid: R_f 0.63 (hexane/AcOEt, 3/1); mp 80–82 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.44 (br s, 1H), 7.62 (t, J = 1.7 Hz, 1H), 7.50 (dt, J = 7.5, 1.6 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.32–7.24 (m, 2H), 7.17–7.08 (m, 2H), 6.92 (dd, J = 2.2, 0.7 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 137.5 (C), 136.9 (C), 135.1 (C), 133.5 (C), 130.4 (CH), 128.1 (CH), 128.0 (C), 126.1 (C), 125.3 (CH), 123.39 (CH), 123.38 (CH), 120.3 (CH), 109.7 (CH), 99.4 (CH); EI-LRMS *m/z* 265 (M^++4, 13), 263 (M^++2, 62), 261 (M^+, 100), 226 (13), 199 (30), 190 (35), 164 (30), 89 (49); HRMS calcd for $C_{14}H_9Cl_2N$, 261.0112; found, 261.0112.

4-Bromo-2-phenyl-1*H*-indole (12a): Treatment of **8c** (192 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **12a** (66 mg, 49%), whose spectroscopic data have been reported above.

4-Bromo-2-butyl-1*H*-indole (12b): Treatment of **8c** (576 mg, 1.5 mmol) with 1-hexyne (182 mg, 2.25 mmol), $PdCl_2(PPh_3)_2$ (31 mg, 3 mol%), CuI (14 mg, 5 mol%) and Et_2NH (164 mg, 2.25 mmol) in DMA (6 mL) for 2 h and then, with NaOH (600 mg, 15 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded **12b** (207 mg, 55%), whose spectroscopic data have been reported above.

4-Bromo-2-(3-chlorophenyl)-1*H*-indole (12g): Treatment of **8c** (192 mg, 0.5 mmol) with 1-chloro-3-ethynylbenzene (102 mg, 0.75 mmol), $PdCl_2(PPh_3)_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et_2NH (54 mg, 0.75 mmol) in DMA (2 mL) for 2 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded **12g** (73 mg, 48%) as a brown solid: R_f 0.38 (hexane/AcOEt, 4/1); mp 89–91 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47 (br s, 1H), 7.67–7.64 (m, 1H), 7.55 (ddd, J = 7.6, 2.8, 1.3 Hz, 1H), 7.43–7.27 (m, 4H), 7.06 (td, J = 8.1, 1.2 Hz, 1H), 6.90–6.87 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 137.1 (C), 137.0 (C), 135.2 (C), 133.6 (C), 130.5 (CH), 129.9 (C), 128.2 (CH), 125.4 (CH), 123.8 (CH), 123.5 (CH), 123.4 (CH), 114.9 (C), 110.3 (CH), 101.2 (CH); EI-LRMS *m/z* 309 (M^++4, 23), 307 (M^++2, 100), 305 (M^+, 80), 226 (16), 199 (34), 190 (74), 163 (60); HRMS calcd for $C_{14}H_9BrClN$, 304.9607; found, 304.9620.

Synthesis of 2-butyl-4-(furan-2-yl)-1*H*-indole (13):

Pre-milled $Pd(OAc)_2$ (2 mol%)/XPhos (4 mol%) and CsF (100 mg, 0.66 mmol) were added to a Schlenk tube under a nitrogen atmosphere, and the tube was evacuated and backfilled with nitrogen.[10] Then, 4-chloroindole derivative **11b** (62 mg, 0.3 mmol), tributyl(furan-2-yl)stannane (118 mg, 0.33 mmol) and DME (0.8 cm^3) were added to the tube. The reaction was heated to 80 ºC with stirring for 3 h (the consumption of the starting material was monitored by GC-MS). After cooling to room temperature of the reaction vessel, the crude was filtered through zelite and washed with EtOAc (20 cm^3). The solvent was concentrated under

reduced pressure and the residue was purified by column chromatography on silica gel (hexane/EtOAc, 7/1) to afford **13** (66 mg, 92%) as a white solid: R_f 0.43 (hexane/AcOEt, 6/1); mp 50–52 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85 (br s, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.56–7.52 (m, 1H), 7.23–7.20 (m, 2H), 6.85 (d, J = 3.3 Hz, 1H), 6.75 (s, 1H), 6.60 (ddd, J = 3.3 Hz, 1.8, 0.6 Hz, 1H), 2.76 (t, J = 7.6 Hz, 2H), 1.79–1.68 (m, 2H), 1.52–1.39 (m, 2H), 1.01 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 154.8 (C), 141.5 (CH), 141.0 (C), 136.6 (C), 124.4 (C), 122.1 (C), 121.0 (CH), 116.4 (CH), 111.6 (CH), 110.0 (CH), 106.2 (CH), 99.6 (CH), 31.4 (CH_2), 28.1 (CH_2), 22.5 (CH_2), 14.0 (CH_3); EI-LRMS *m/z* 239 (M^+, 56), 196 (100), 167 (14), 154 (4); HRMS calcd for $C_{16}H_{17}NO$, 239.1310; found, 239.1319.

Synthesis of 2,4-Diphenyl-1*H*-indole (14):

4-Bromo-1*H*-indole derivative **12a** (81 mg, 0.3 mmol), phenylboronic acid (55 mg, 0.45 mmol) and [$Pd(PPh_3)_4$] (10 mg, 3 mol%) were introduced in a Schlenk tube under a nitrogen atmosphere. Then, DME (5 cm^3) was added followed by the addition of Na_2CO_3 (48 mg, 0.45 mmol) in H_2O (2 cm^3). The reaction mixture was vigorously stirred and heated at 80 ºC overnight (the progress of the reaction was monitored by GC-MS).[11,12] Then, CH_2Cl_2 (10 cm^3) and H_2O were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 8/1) on silica gel to afford **14** (74 mg, 93%) as a white solid: R_f 0.48 (hexane/AcOEt, 4/1); mp 205–207 ºC (lit.[13] mp 209 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.42 (br s, 1H), 7.89–7.82 (m, 2H), 7.67 (d, J = 8.1 Hz, 2H), 7.61 (t, J = 7.7 Hz, 2H), 7.53–7.44 (m, 3H), 7.43–7.25 (m, 4H), 7.12 (d, J = 2.2 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 141.3 (C), 138.3 (C), 137.3 (C), 134.5 (C), 132.2 (C), 129.1 (2 × CH), 128.9 (2 × CH), 128.7 (2 × CH), 127.8 (CH), 127.6 (C), 127.1 (CH), 125.2 (2 × CH), 122.7 (CH), 120.2 (CH), 110.2 (CH), 99.6 (CH); EI-LRMS *m/z* 269 (M^+, 100), 190 (10), 165 (53), 133 (11), 77 (28); HRMS calcd for $C_{20}H_{15}N$, 269.1204; found, 269.1204.

Synthesis of 4-(hex-1-ynyl)-2-phenyl-1*H*-indole (15):

A mixture of 4-bromo-1*H*-indole derivative **12a** (81 mg, 0.3 mmol), 1-hexyne (37 mg, 0.45 mmol), $PdCl_2(PPh_3)_2$ (12 mg, 6 mol%), CuI (6 mg, 10 mol%) and Et_2NH (33 mg, 0.45 mmol) in anhydrous DMF (3 cm^3) was stirred under a nitrogen atmosphere at 80 ºC for 17 h (complete consumption of the starting material was monitored by GC-MS). Then, CH_2Cl_2 (20 cm^3) and aq HCl (20 cm^3 of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 15 cm^3). The combined organic layers were washed with water (2 × 40 cm^3), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 8/1) to afford **15** (63 mg, 77%) as a brown solid: R_f 0.42 (hexane/AcOEt, 5/1); mp 33–35 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.39 (br s, 1H), 7.69 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 7.3 Hz, 2H), 7.21 (d, J = 7.3 Hz, 1H), 7.11 (t, J = 7.7 Hz, 1H), 6.99–6.97 (m, 1H), 2.55 (t, J = 6.9 Hz, 2H), 1.75–1.63 (m, 2H), 1.62–1.50 (m, 2H), 1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 138.2 (C), 136.5 (C), 132.3 (C), 131.1 (C), 129.2 (2 × CH), 128.0 (CH), 125.3 (2 × CH), 123.9 (CH), 122.3 (CH), 115.8 (C), 110.7 (CH), 99.9 (CH), 93.2 (C), 79.3 (C), 31.2 (CH_2), 22.2 (CH_2), 19.6 (CH_2), 13.9 (CH_3); EI-LRMS *m/z*

273 (M^+, 89), 258 (16), 244 (38), 230 (100), 202 (29), 127 (23); HRMS calcd for $C_{20}H_{19}N$, 273.1517; found, 273.1511.

Synthesis of 4-Bromo-3-((*Z*)-4-methyl-1,3-diphenylpenta-1,3-dienyl)-2-phenyl-*1H*-indole (16):

To a solution of 4-bromo-1*H*-indole derivative **12a** (42 mg, 0.155 mmol) and 4-methyl-1,3-diphenylpent-1-yn-3-ol (42 mg, 0.17 mmol) in MeCN (2 cm^3) was added *p*-toluenesulfonic acid monohydrate (13 mg, 10 mol%).[14] The resulting mixture was heated at 80 ºC for 5.5 h and monitored by GC-MS. The solvent was evaporated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 10/1) to afford **16** (62 mg, 80%) as a white solid: R_f 0.36 (hexane/AcOEt, 5/1); mp 72–74 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.98 (br s, 1H), 7.55–7.48 (m, 4H), 7.39–7.23 (m, 7H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.82 (t, *J* = 7.8 Hz, 1H), 6.77–6.64 (m, 4H), 6.50 (t, *J* = 7.1 Hz, 1H), 1.43 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 144.2 (C), 141.3 (C), 136.91 (C), 136.86 (C), 134.9 (C), 134.5 (C), 134.1 (C), 133.3 (CH), 132.8 (C), 128.55 (2 × CH), 128.53 (2 × CH), 128.4 (2 × CH), 127.8 (CH), 127.2 (2 × CH), 126.94 (2 × CH), 126.87 (C), 126.8 (CH), 126.2 (2 × CH), 124.3 (CH), 124.0 (CH), 122.7 (CH), 115.1 (C), 113.3 (C), 109.4 (CH), 22.2 (CH_3), 21.0 (CH_3); EI-LRMS *m/z* 505 (M^++2, 37), 503 (M^+, 36), 424 (41), 409 (72), 207 (100); HRMS calcd for $C_{32}H_{26}BrN$, 503.1249; found, 503.1255.

Synthesis of 4-chloro-2-phenyl-3-(phenylthio)-1*H*-indole (17):

Freshly powdered NaOH (48 mg, 1.2 mmol) was added to a solution of **9a** (125 mg, 0.4 mmol) in anhydrous DMA (3 cm^3). The resulting mixture was heated under a nitrogen atmosphere for 5 h at 140 ºC (until the cyclization was completed as monitored by GC-MS). Then, Ph_2S_2 (104 mg, 0.48 mmol) was added to the mixture and the reaction was stirred overnight at 140 ºC. Then, CH_2Cl_2 (10 cm^3) and aq HCl (10 cm^3 of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic layers were washed with water (2 × 30 cm^3), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 5/1) to afford **17** (105 mg, 78%) as a white solid: R_f 0.40 (hexane/AcOEt, 5/1); mp 131–133 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.70 (br s, 1H), 7.66 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.43–7.38 (m, 3H), 7.36–7.29 (m, 1H), 7.26–7.05 (m, 7H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ = 144.3 (C), 141.4 (C), 137.3 (C), 131.0 (C), 129.2 (CH), 128.9 (2 × CH), 128.7 (4 × CH), 127.0 (C), 126.8 (C), 125.3 (2 × CH), 124.6 (CH), 123.7 (CH), 122.8 (CH), 110.2 (CH), 98.8 (C); EI-LRMS *m/z* 337 (M^++2, 22), 335 (M^+, 51), 299 (16), 267 (15), 223 (100), 190 (12), 121 (22), 119 (23), 77 (86), 51 (67); HRMS calcd for $C_{20}H_{14}ClNS$, 335.0535; found, 335.0534.

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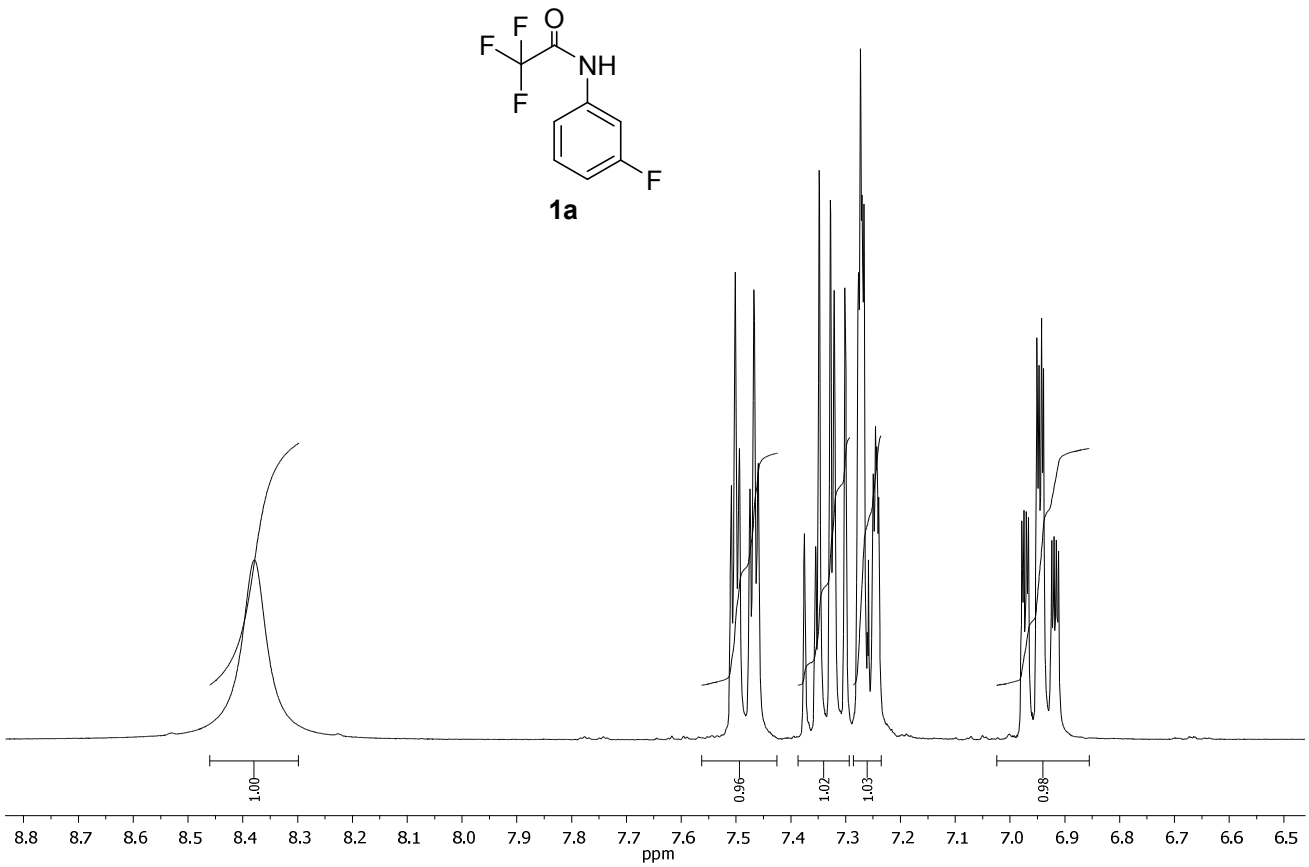
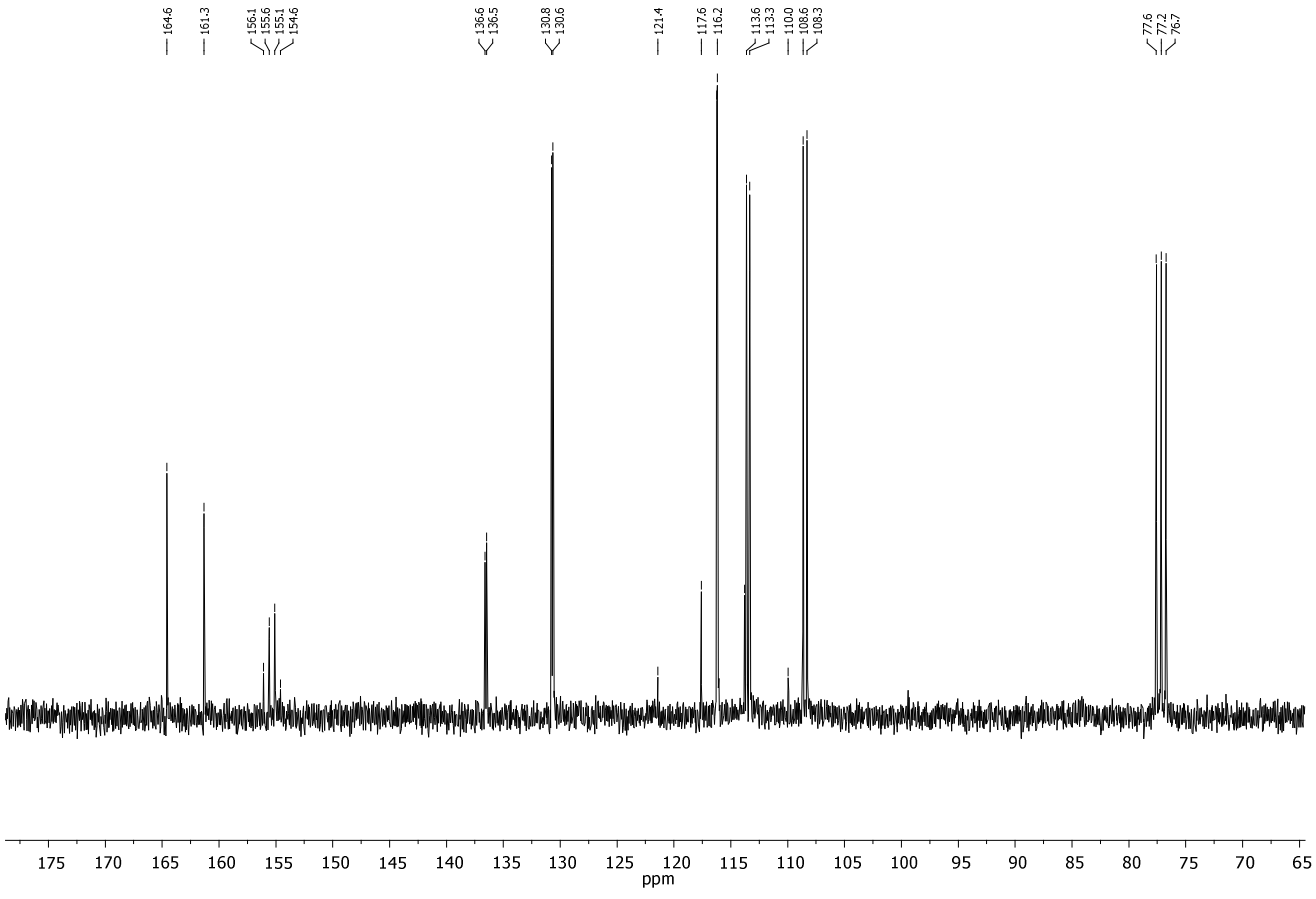
^{1}H-NMR (300 MHz, $CDCl_3$):



^{13}C-NMR (75.4 MHz, $CDCl_3$):



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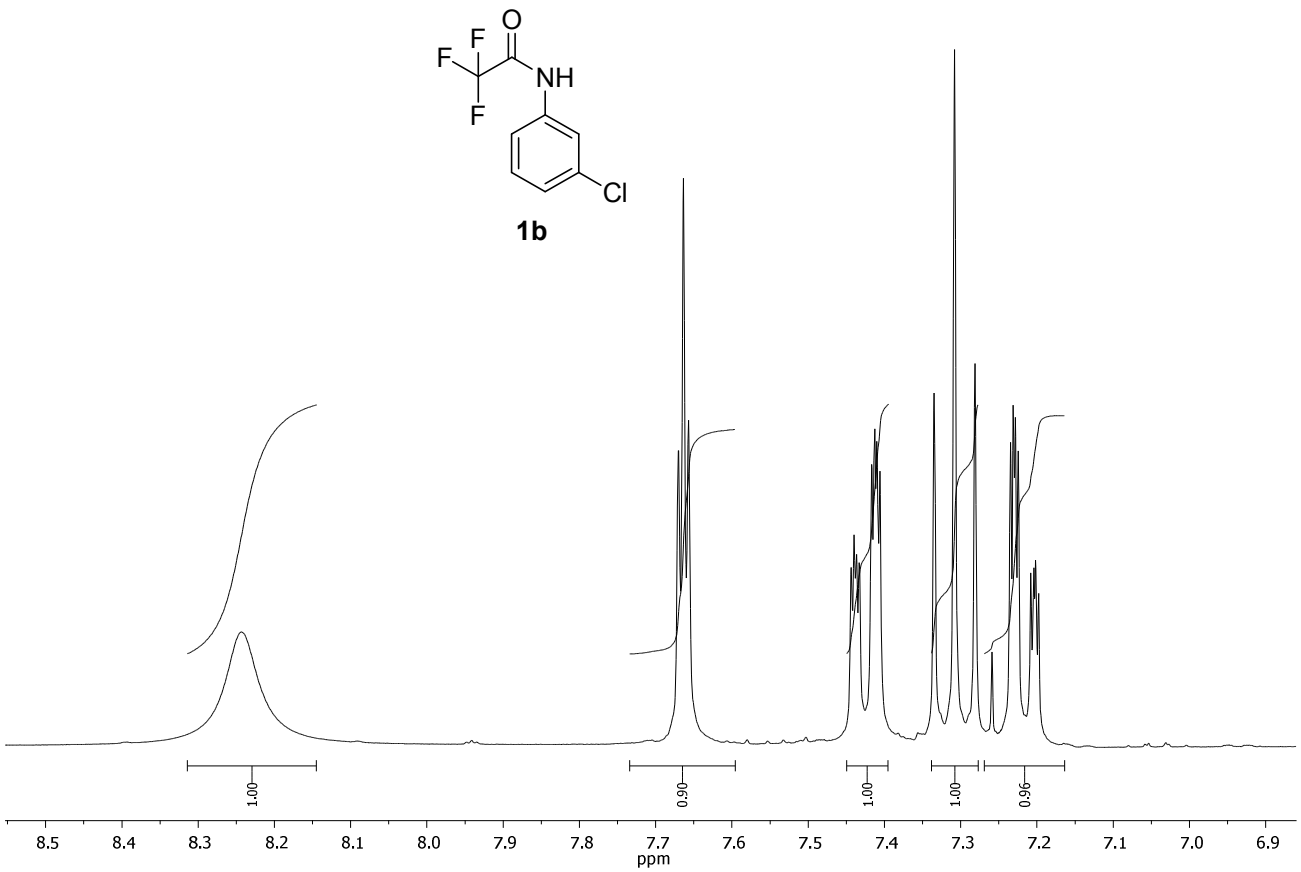

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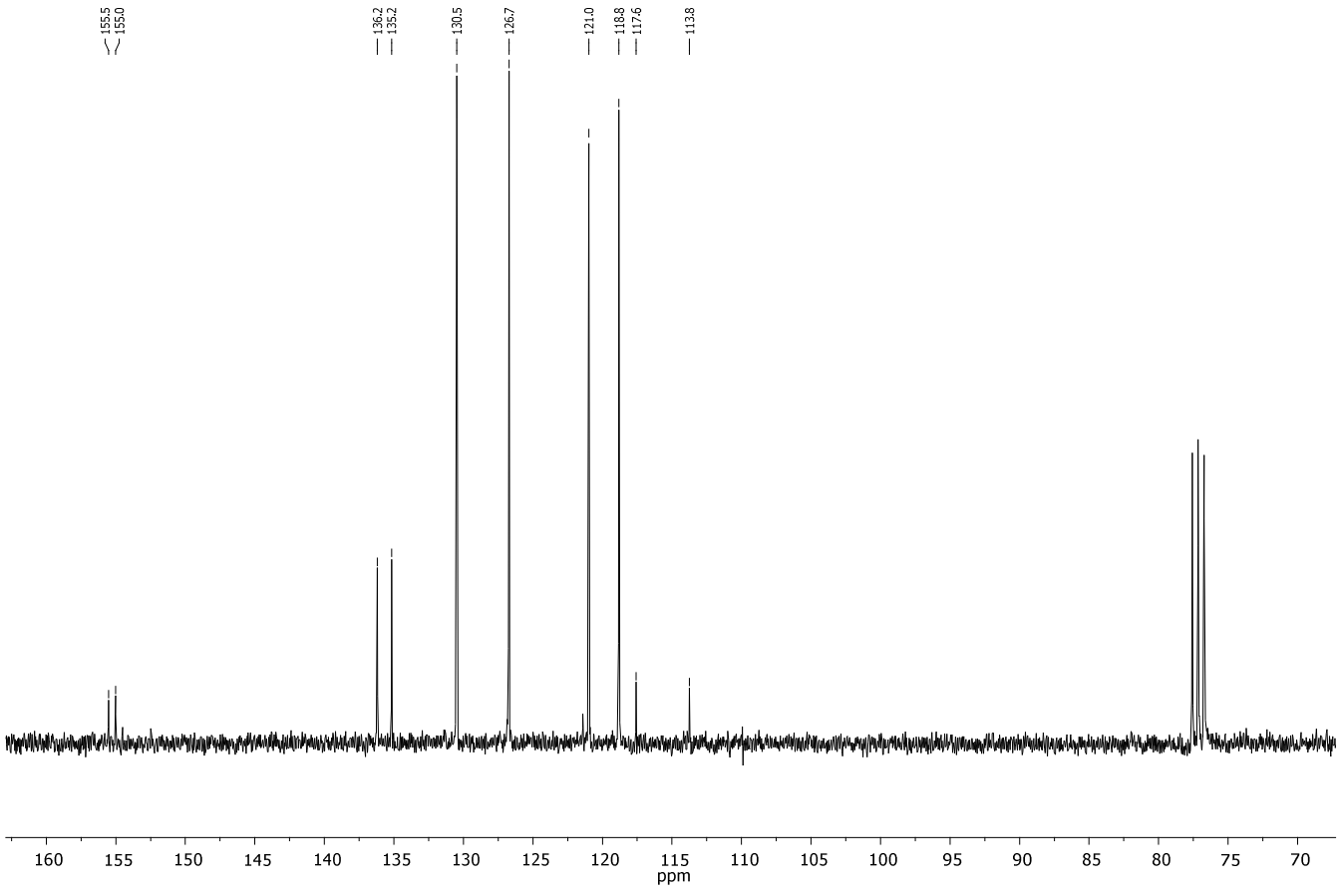

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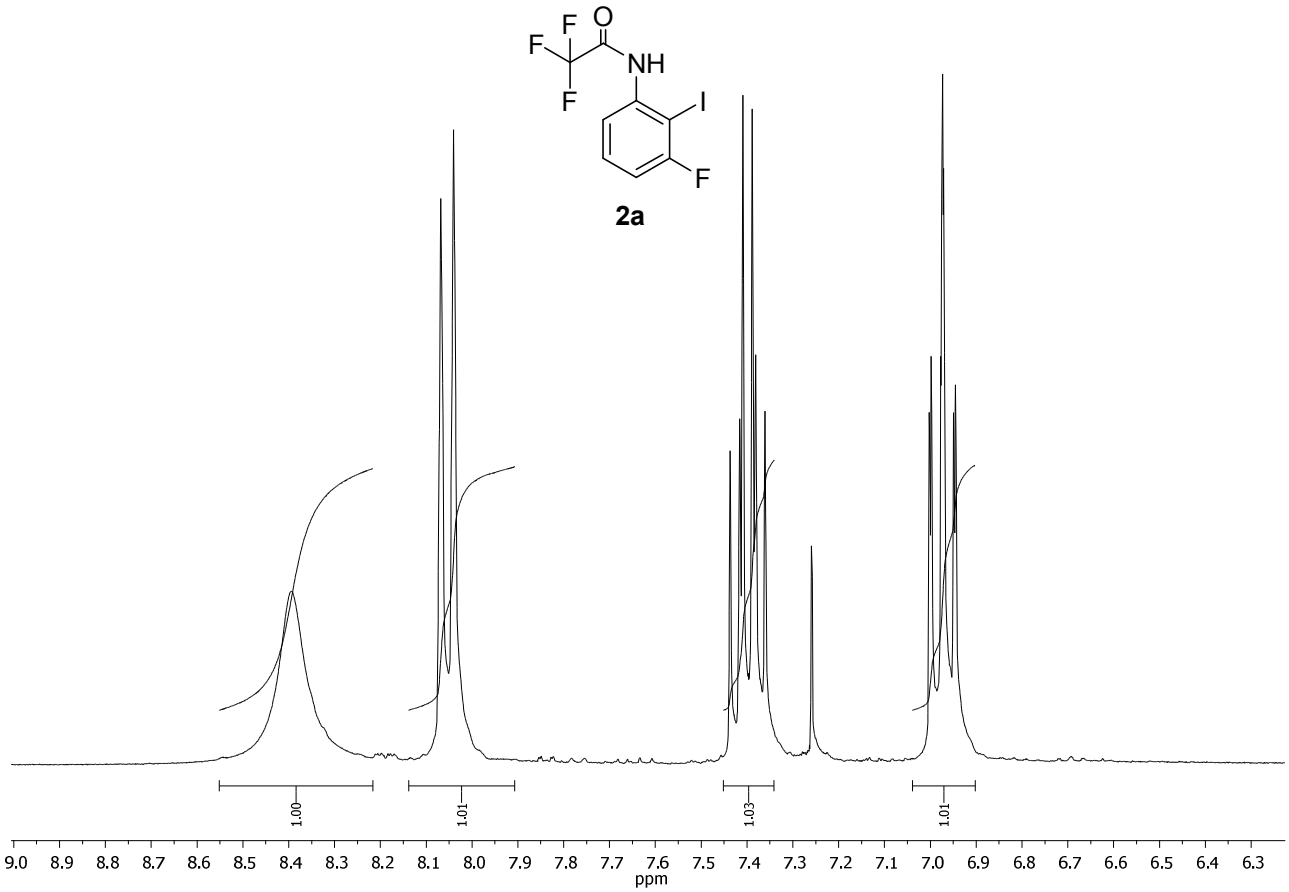

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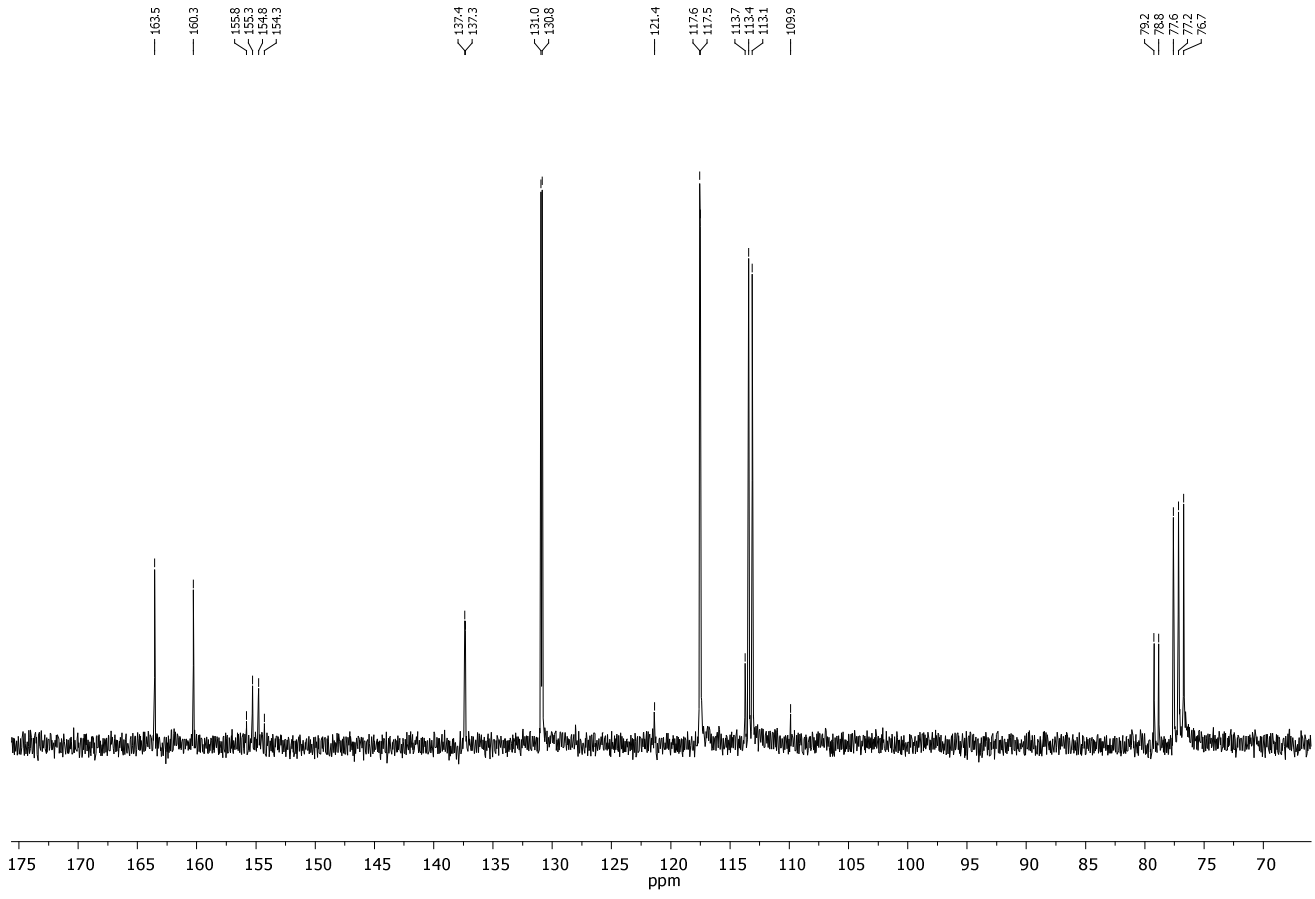

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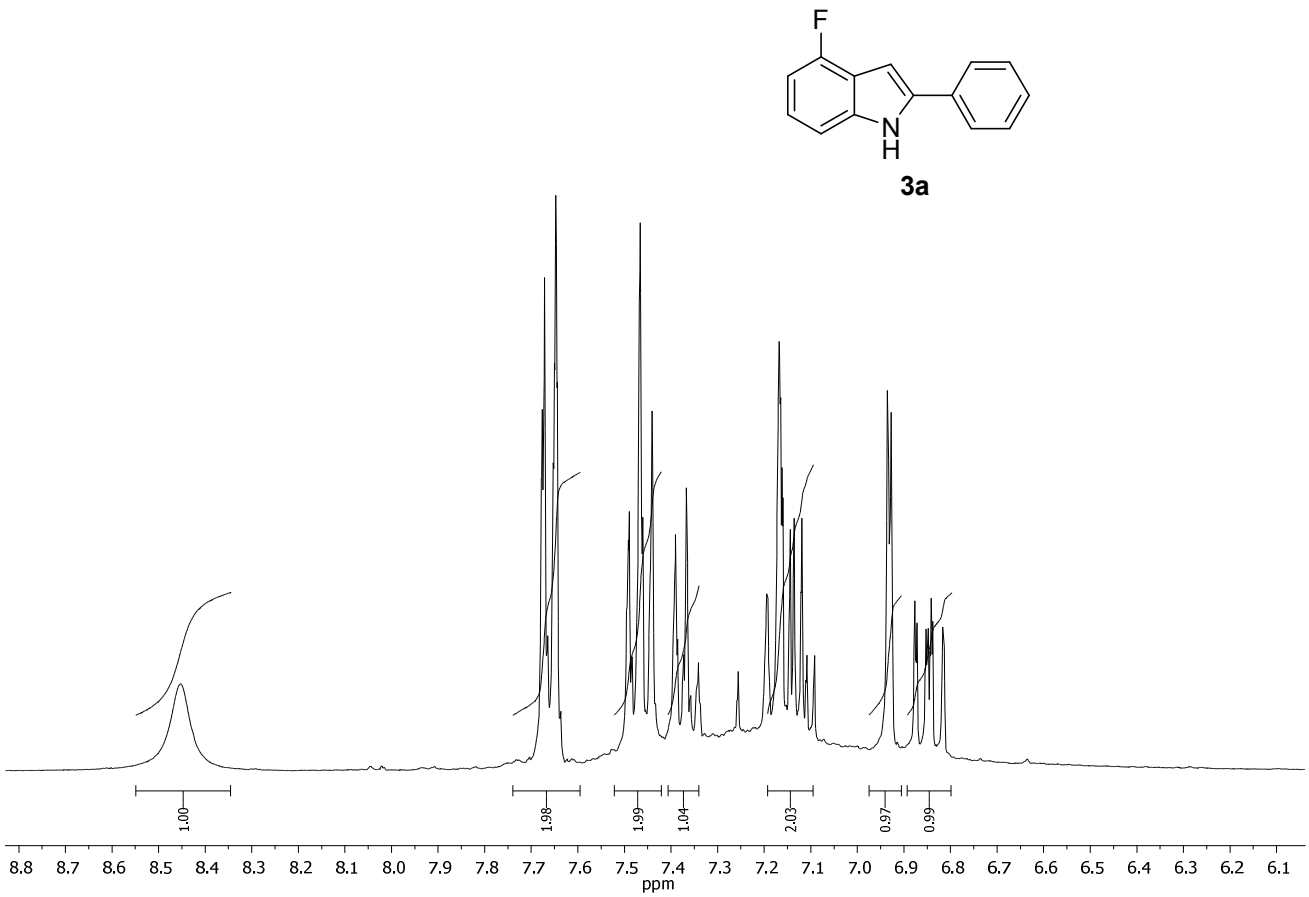

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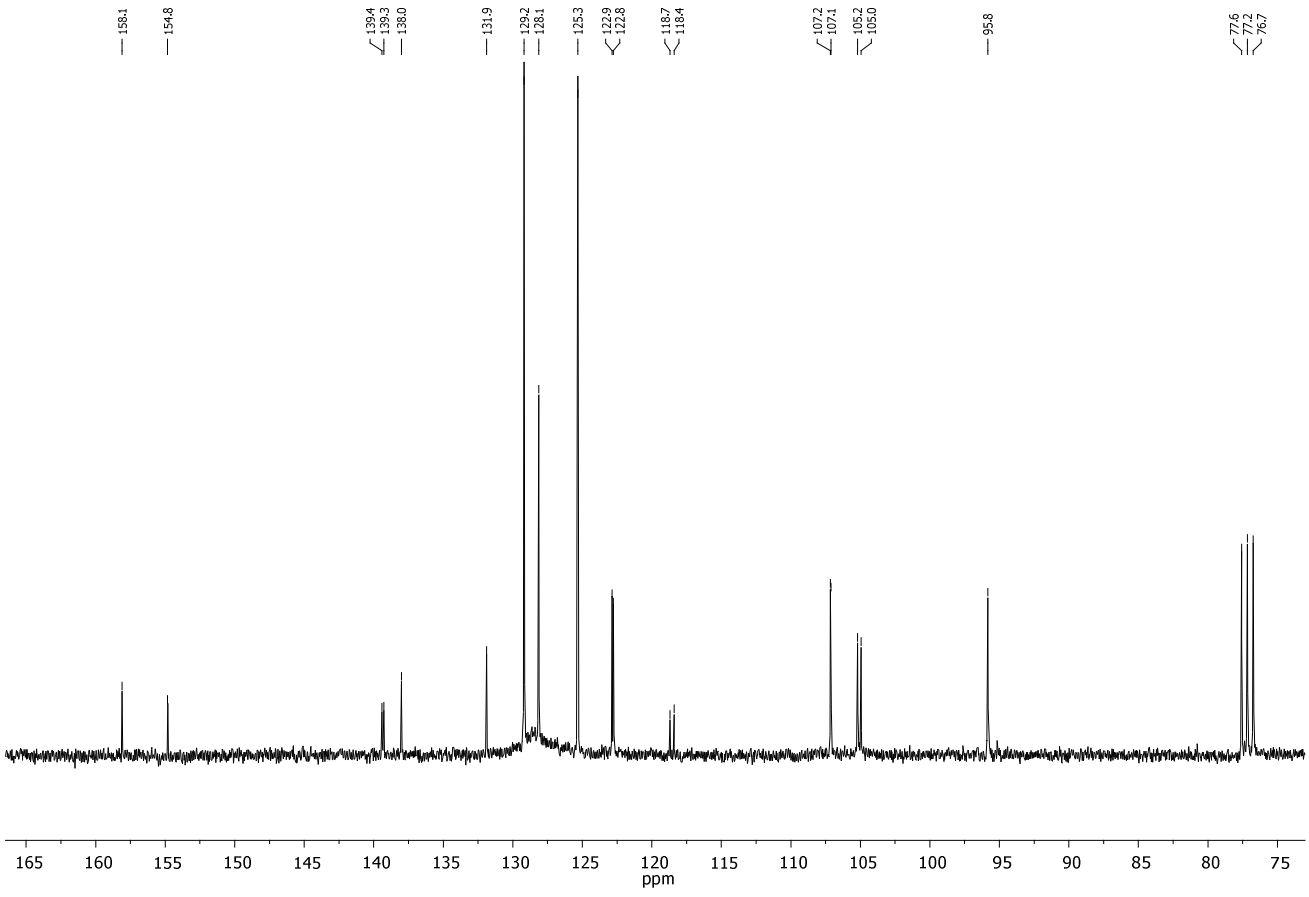

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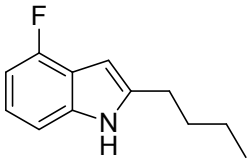

3b

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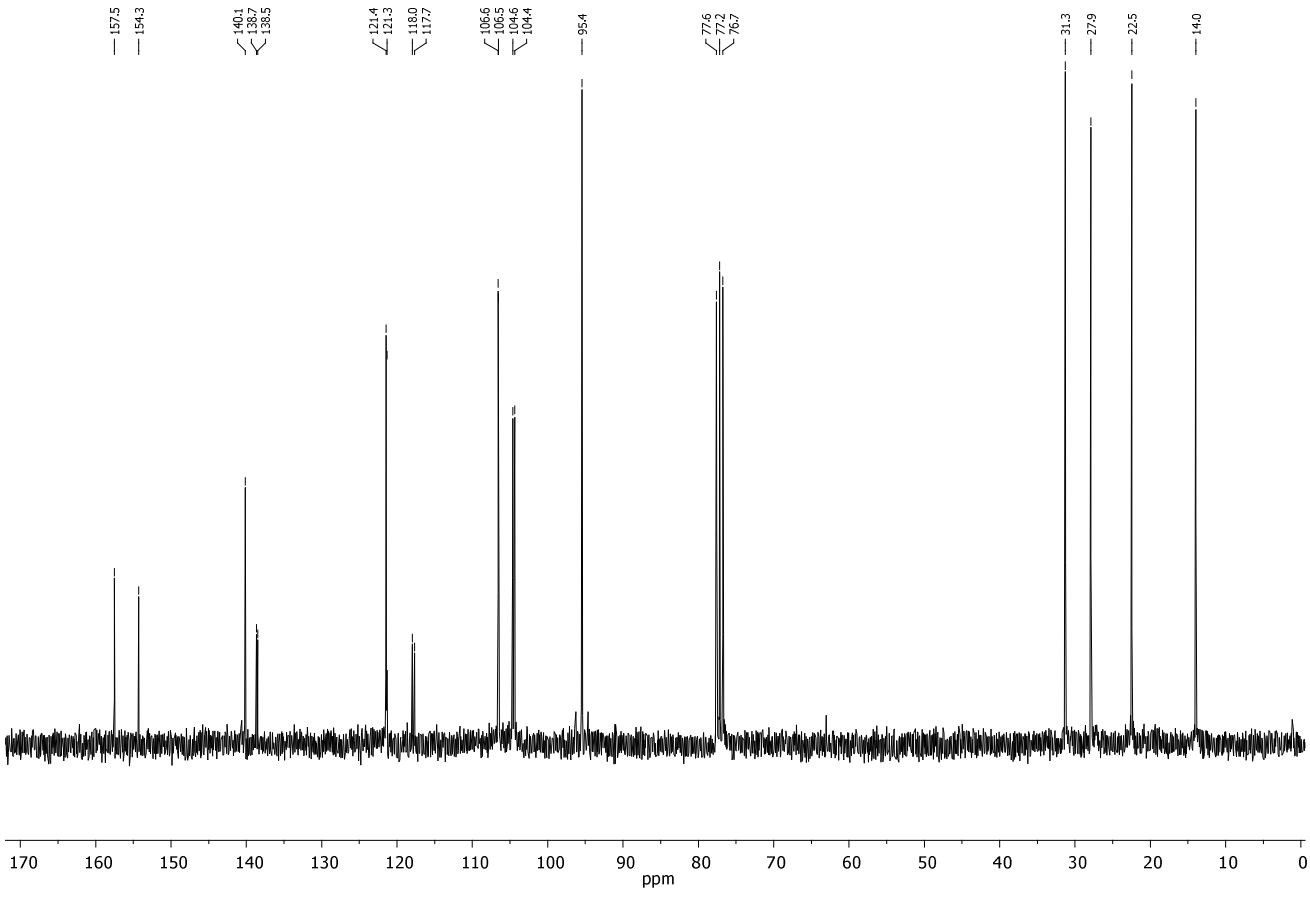

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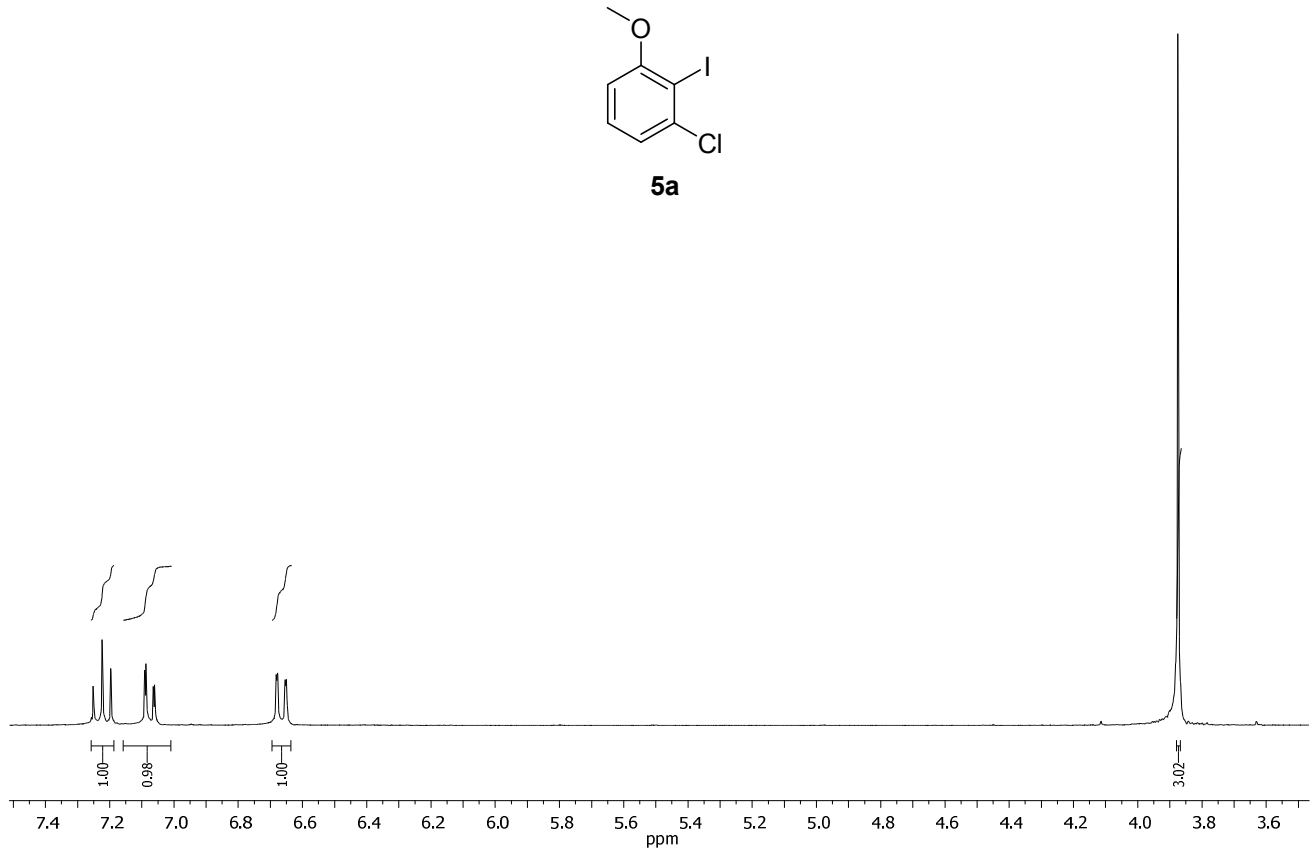

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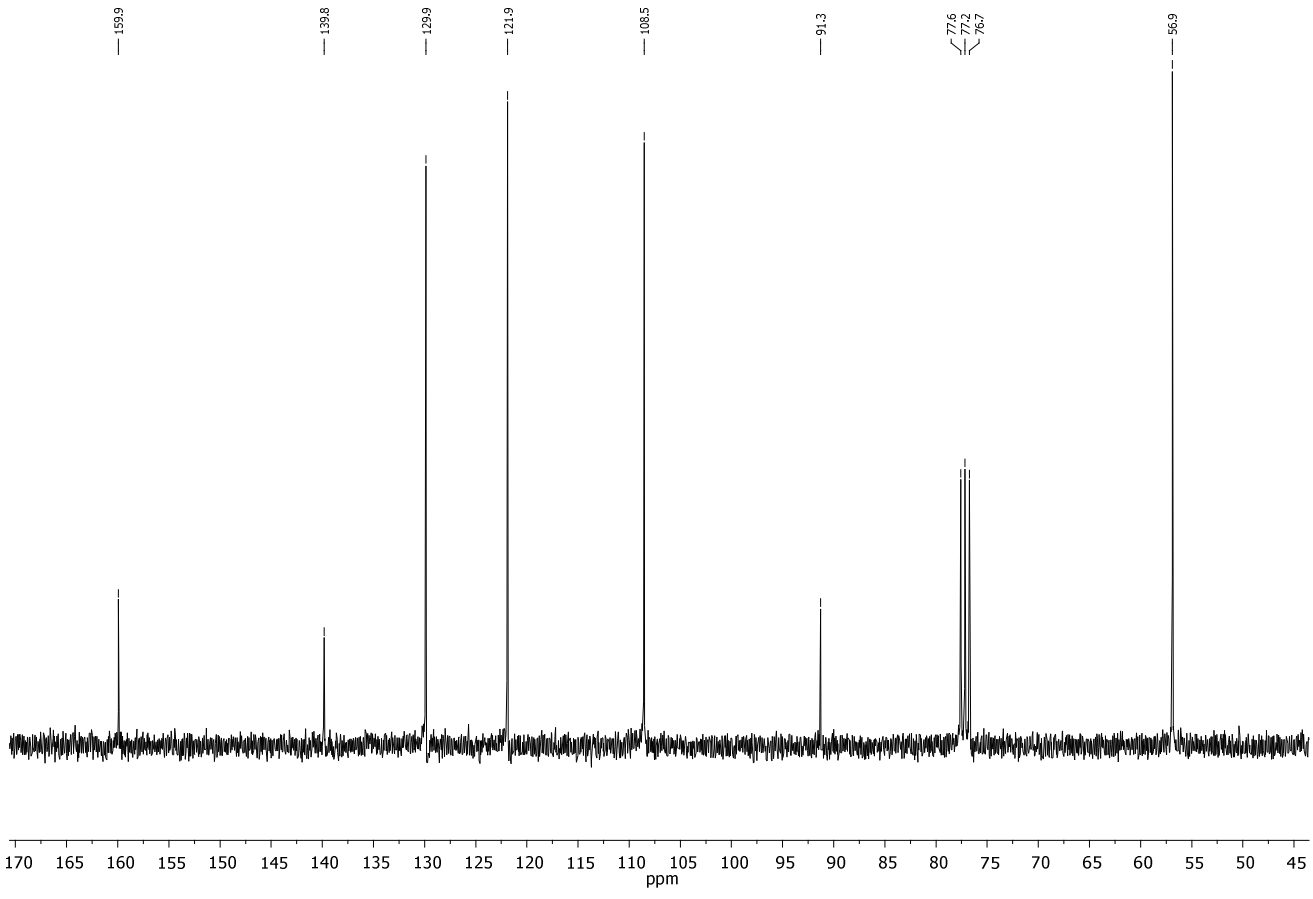

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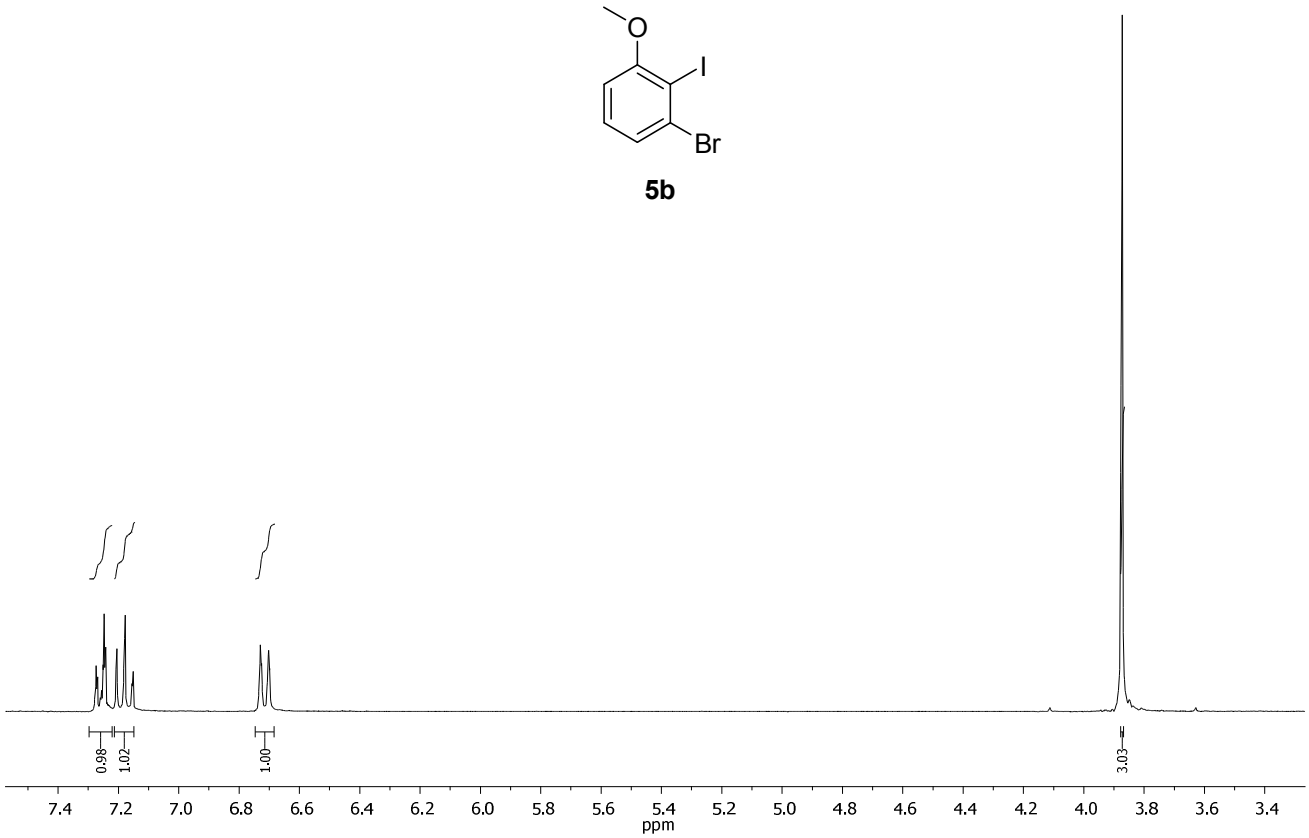

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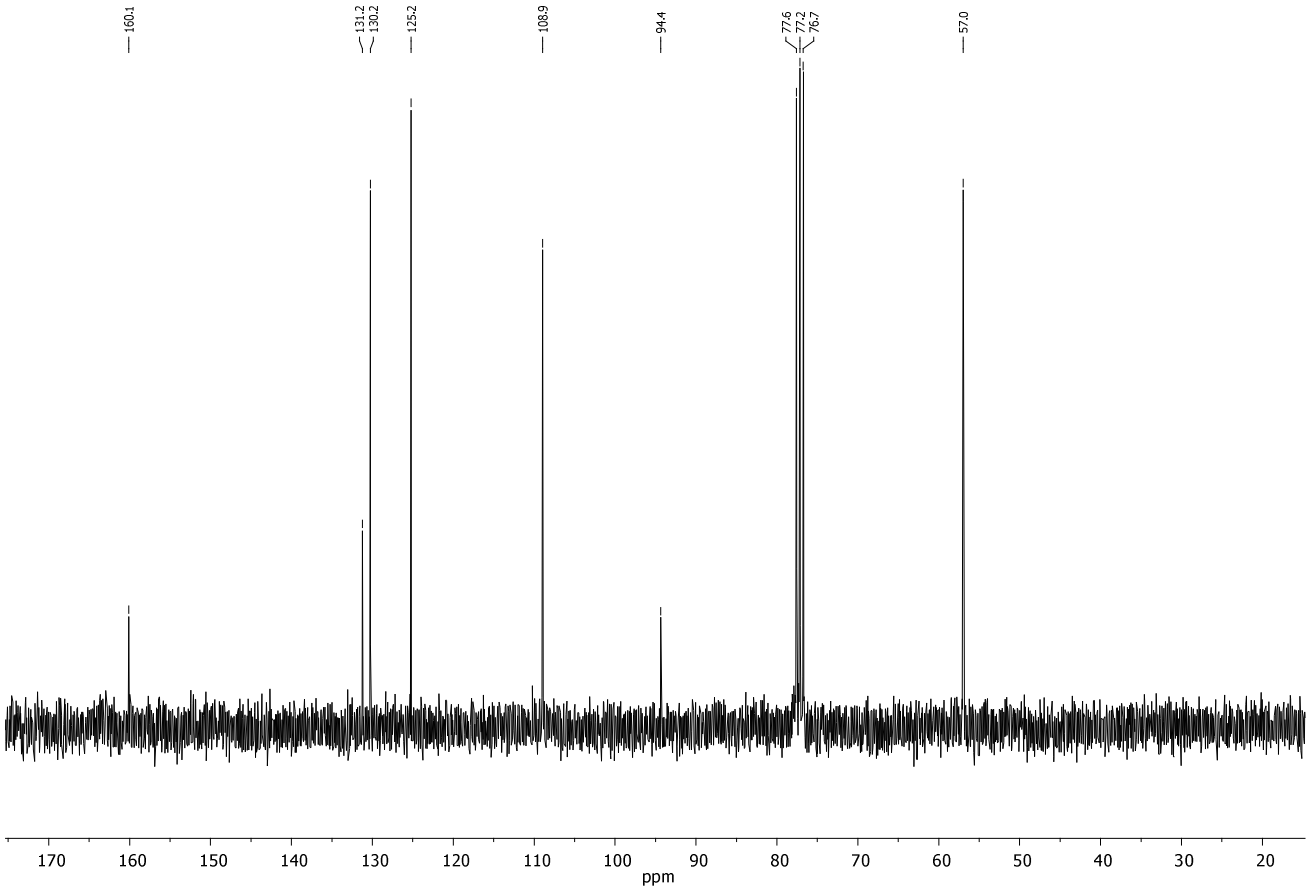

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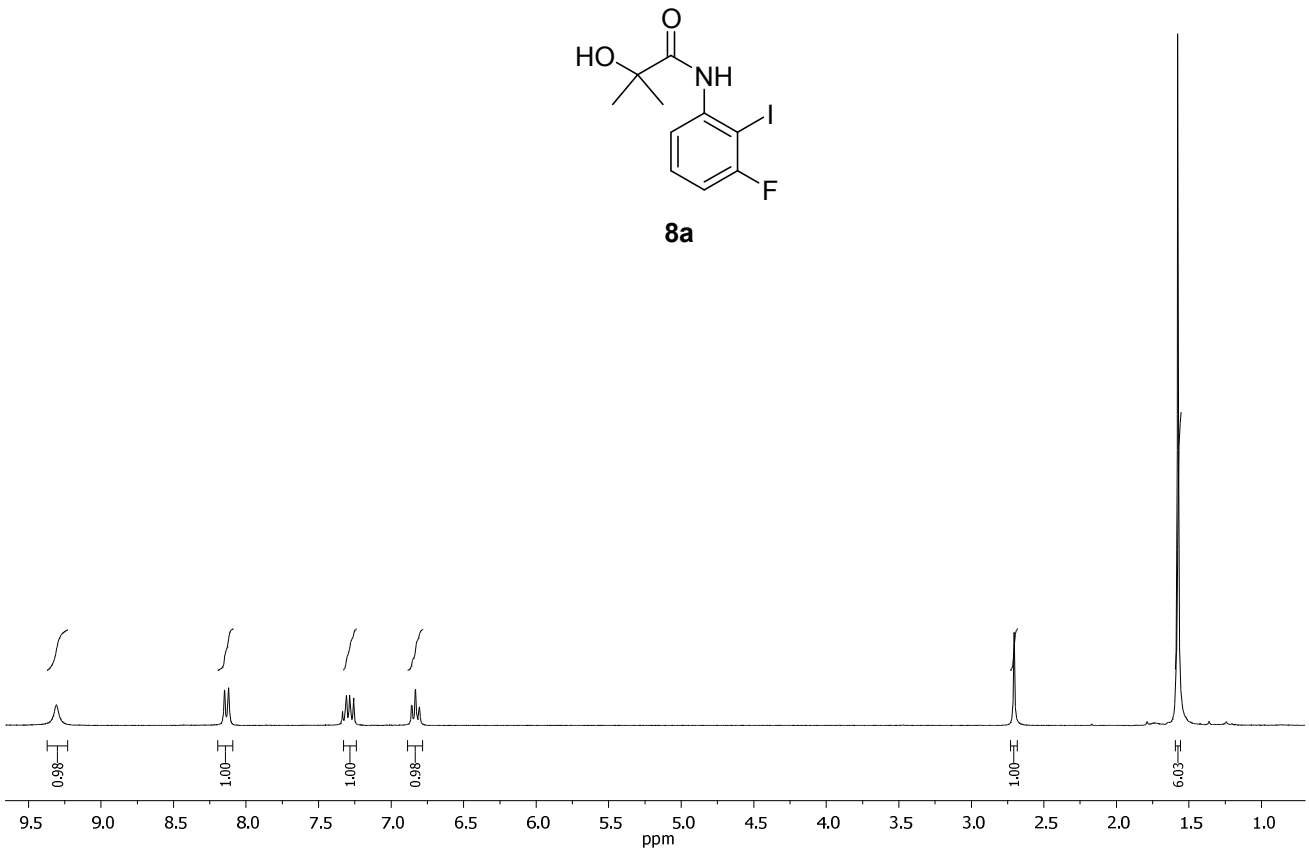

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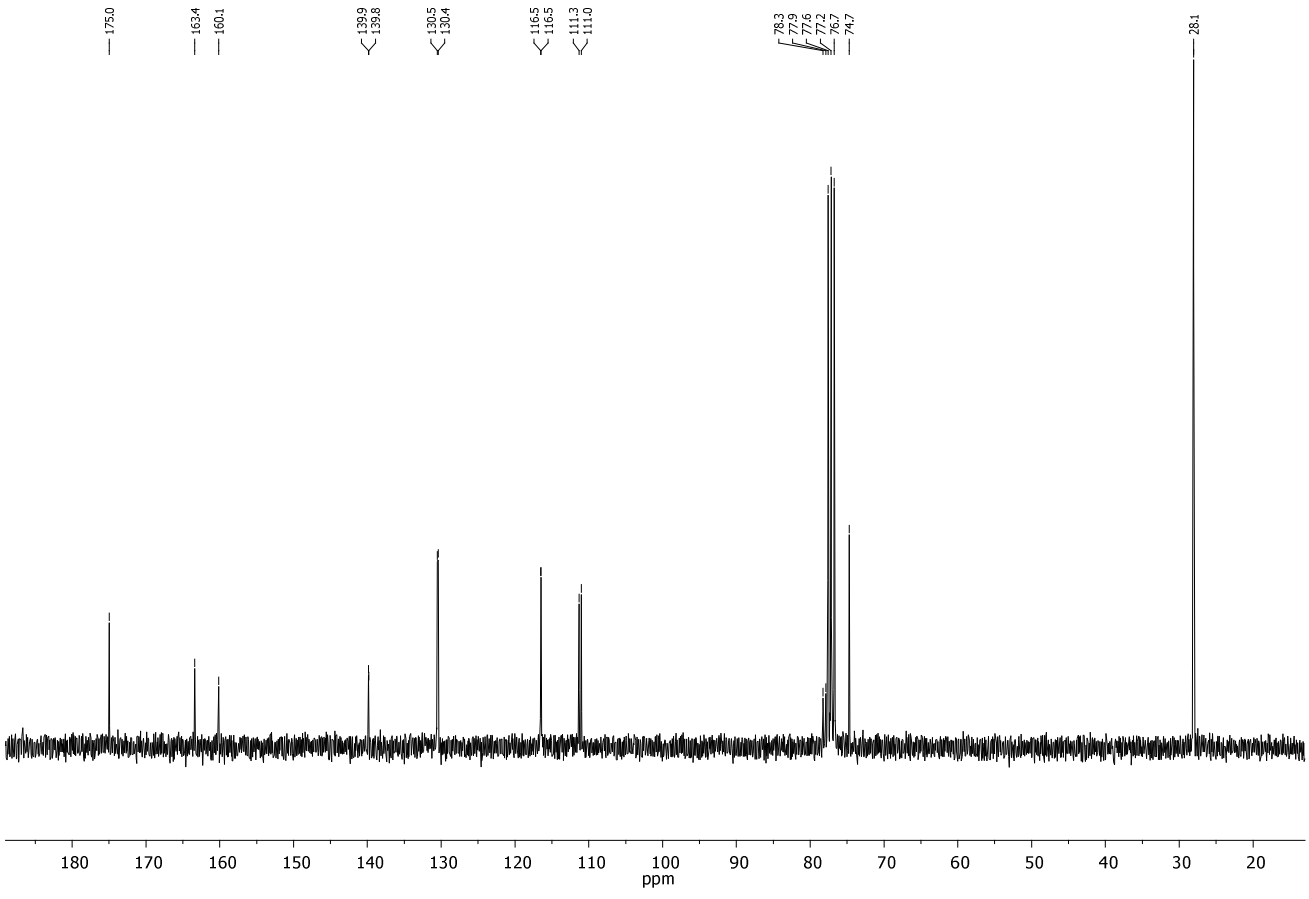

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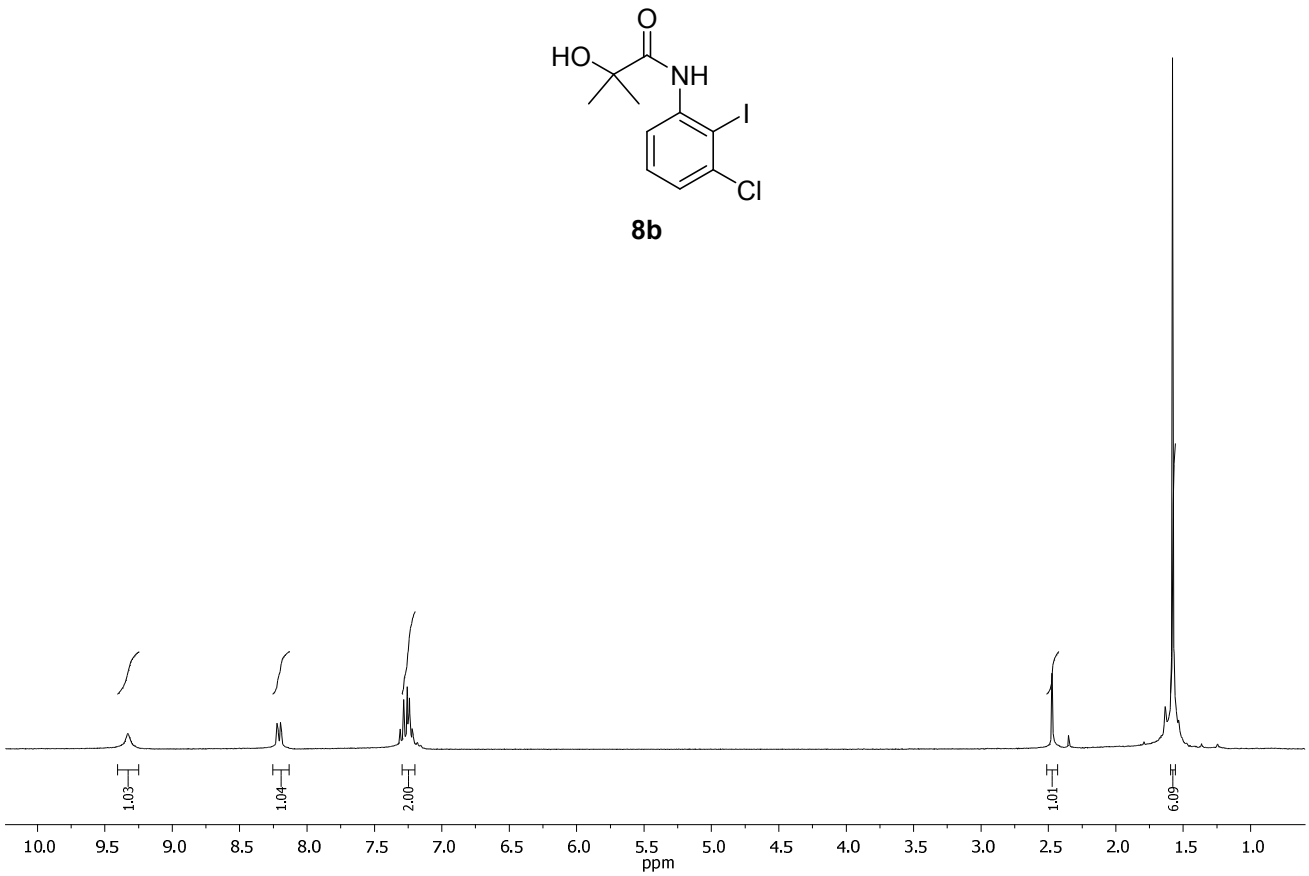

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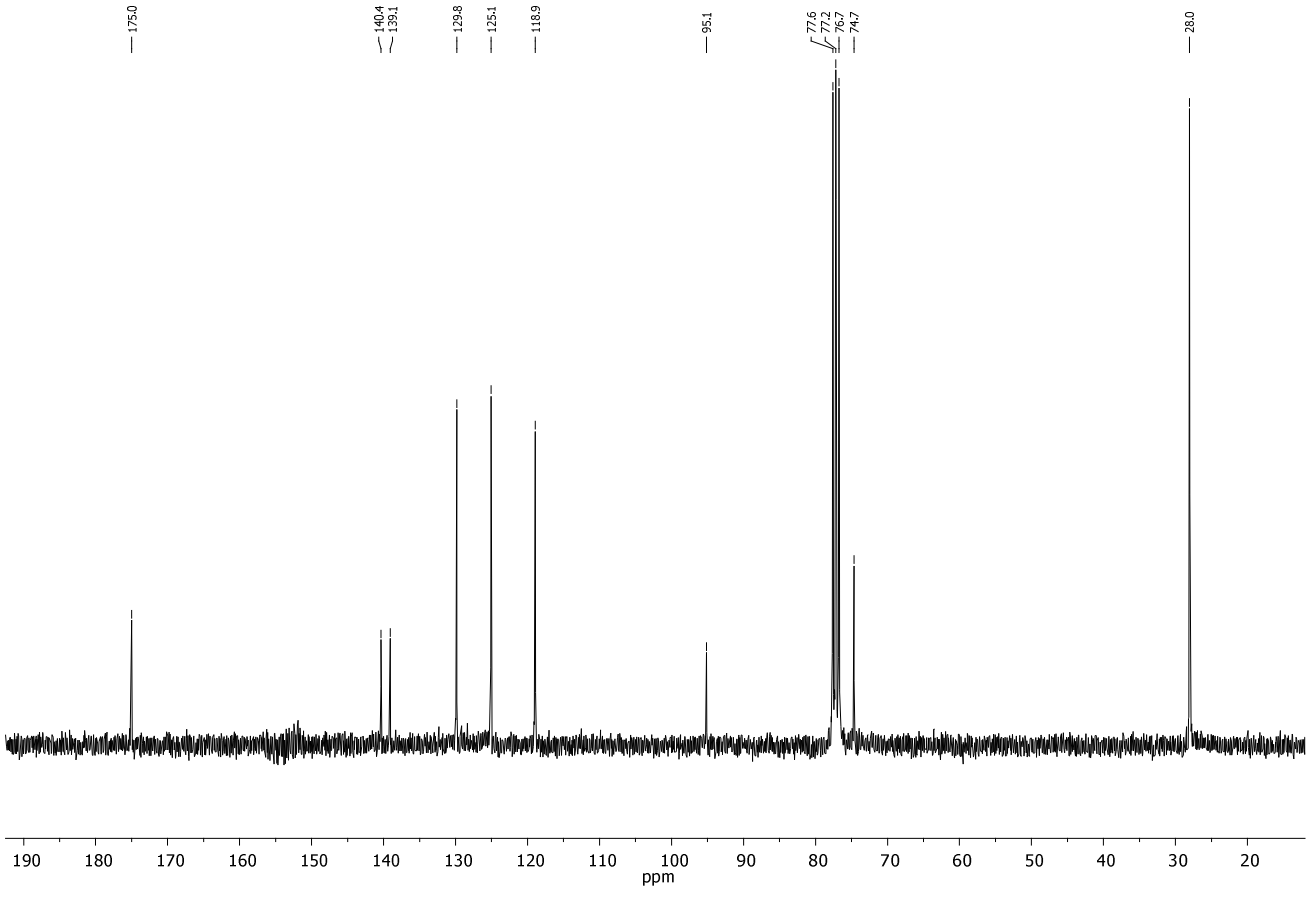

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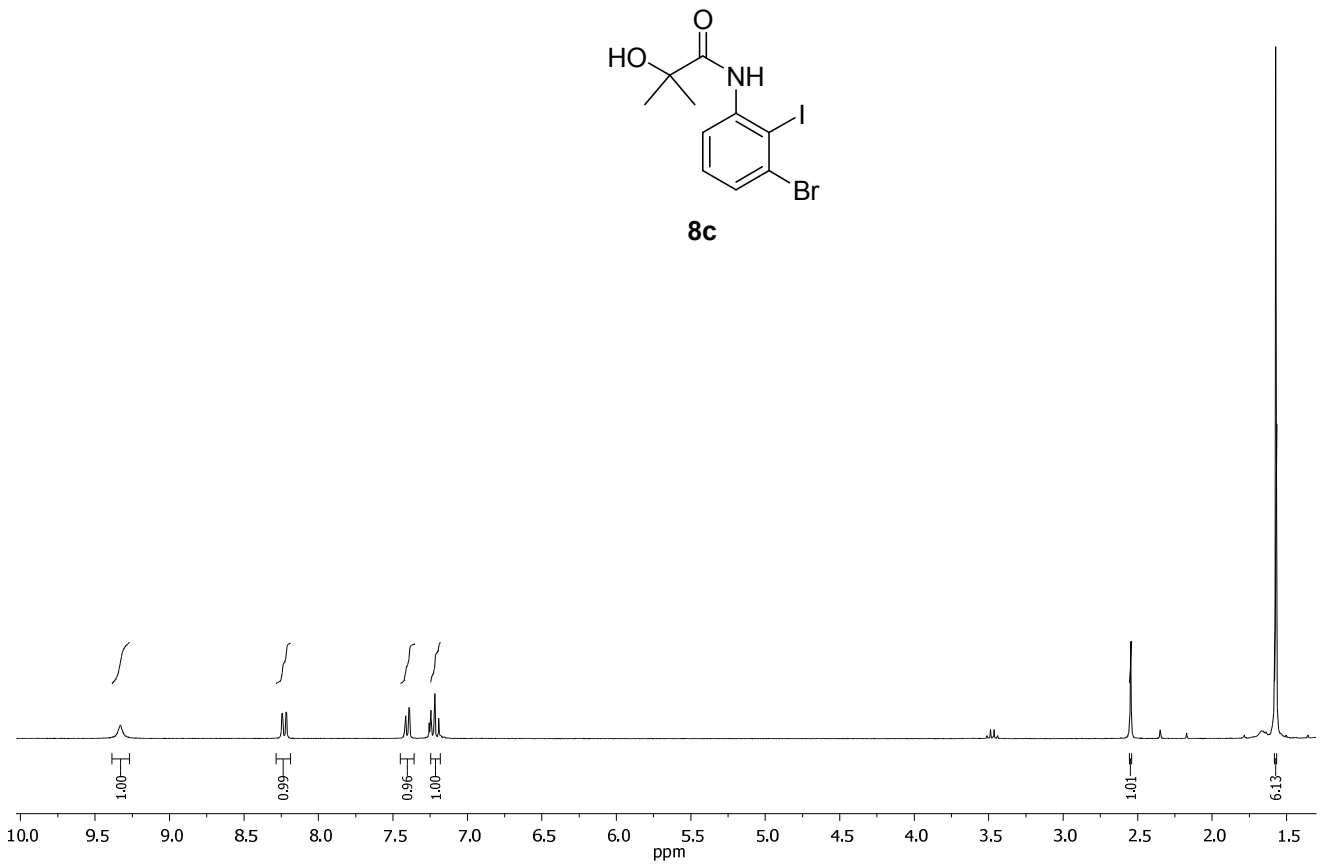

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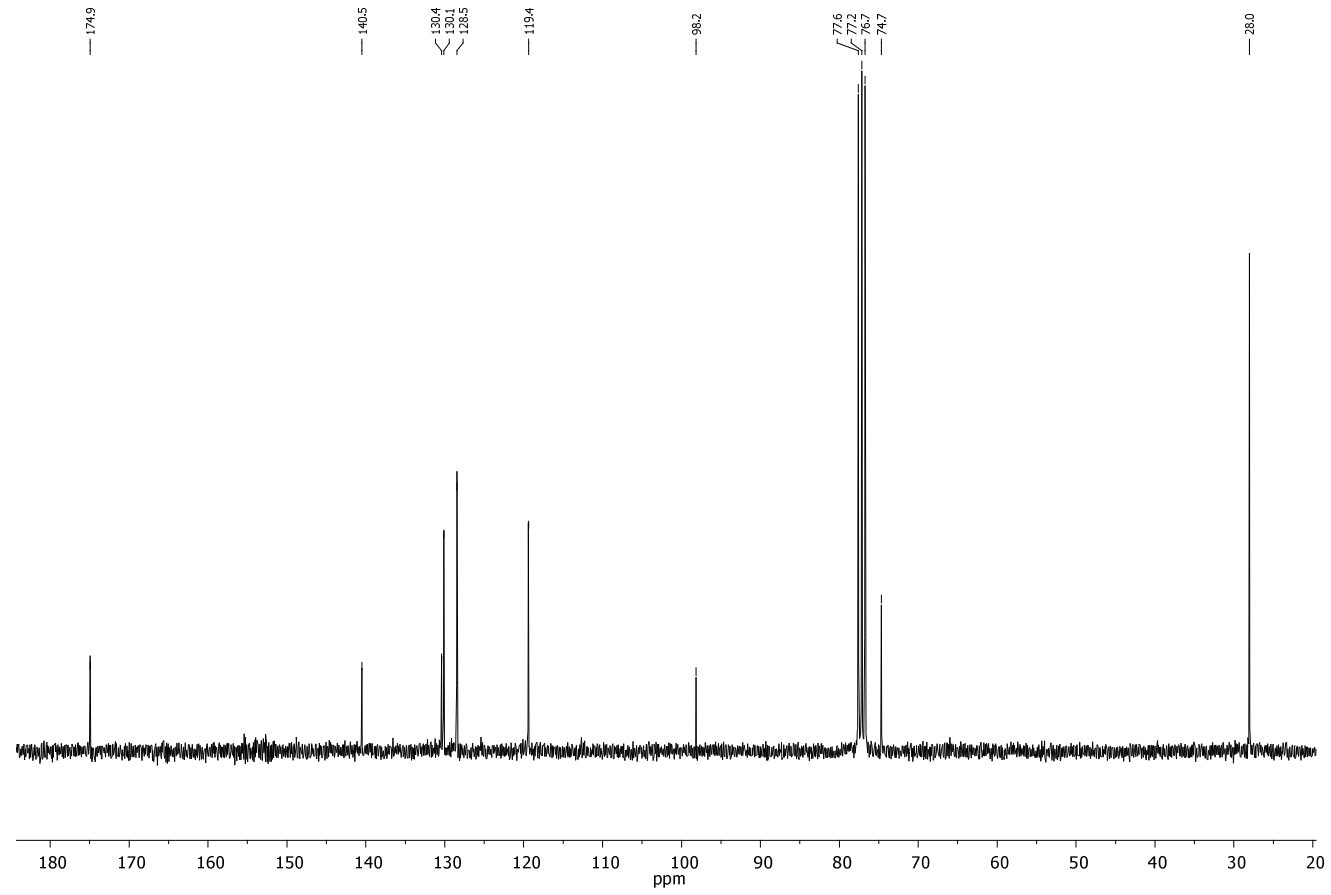

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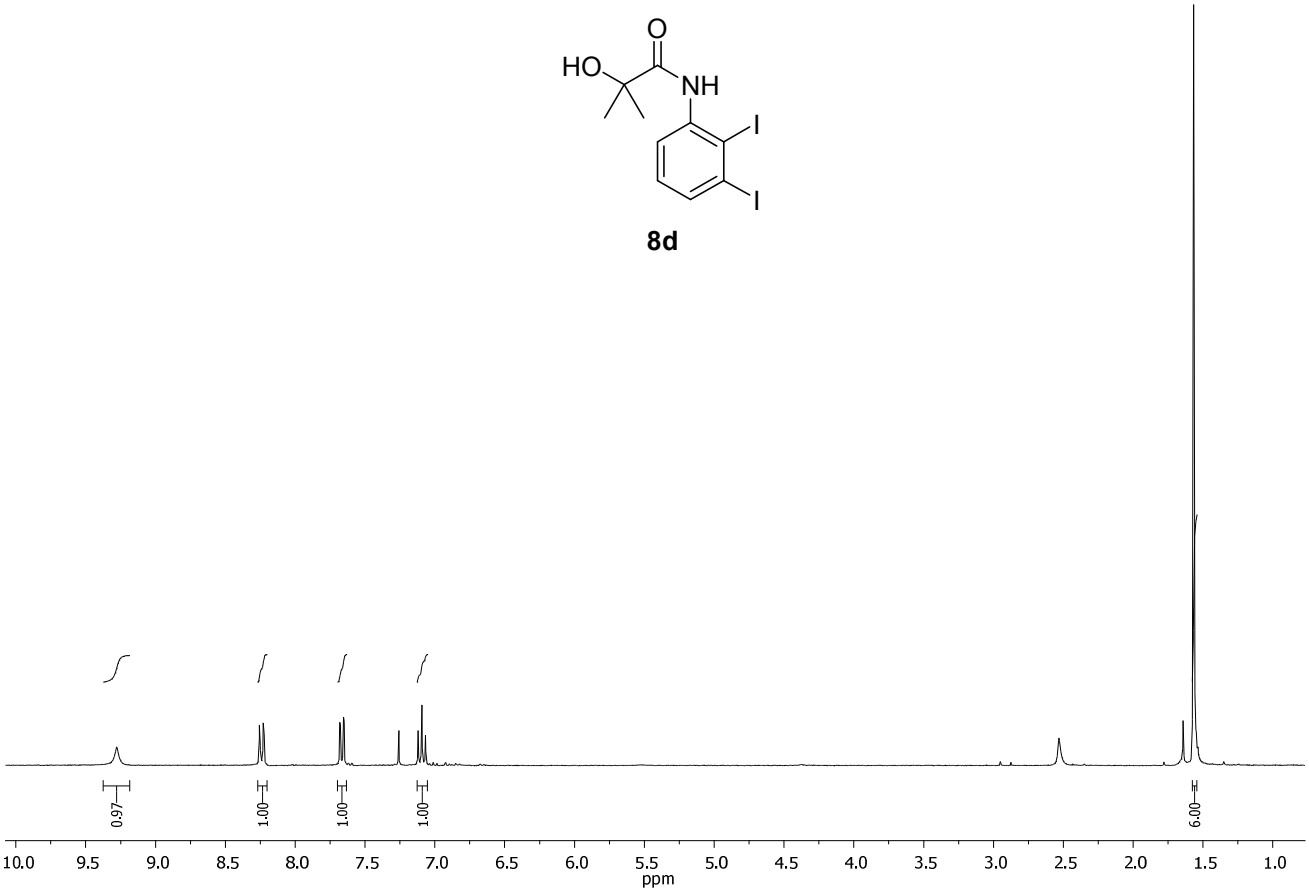

8d

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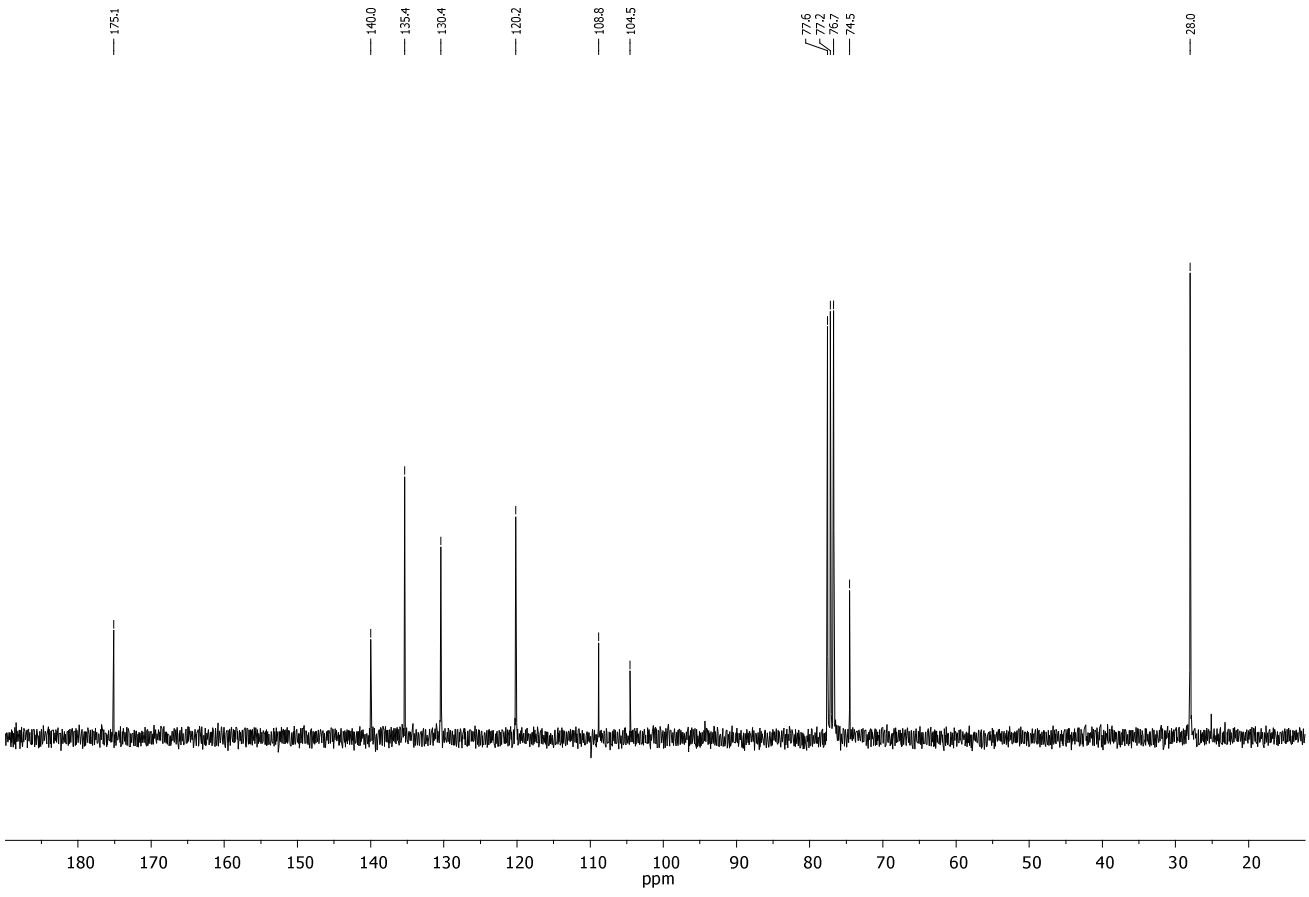

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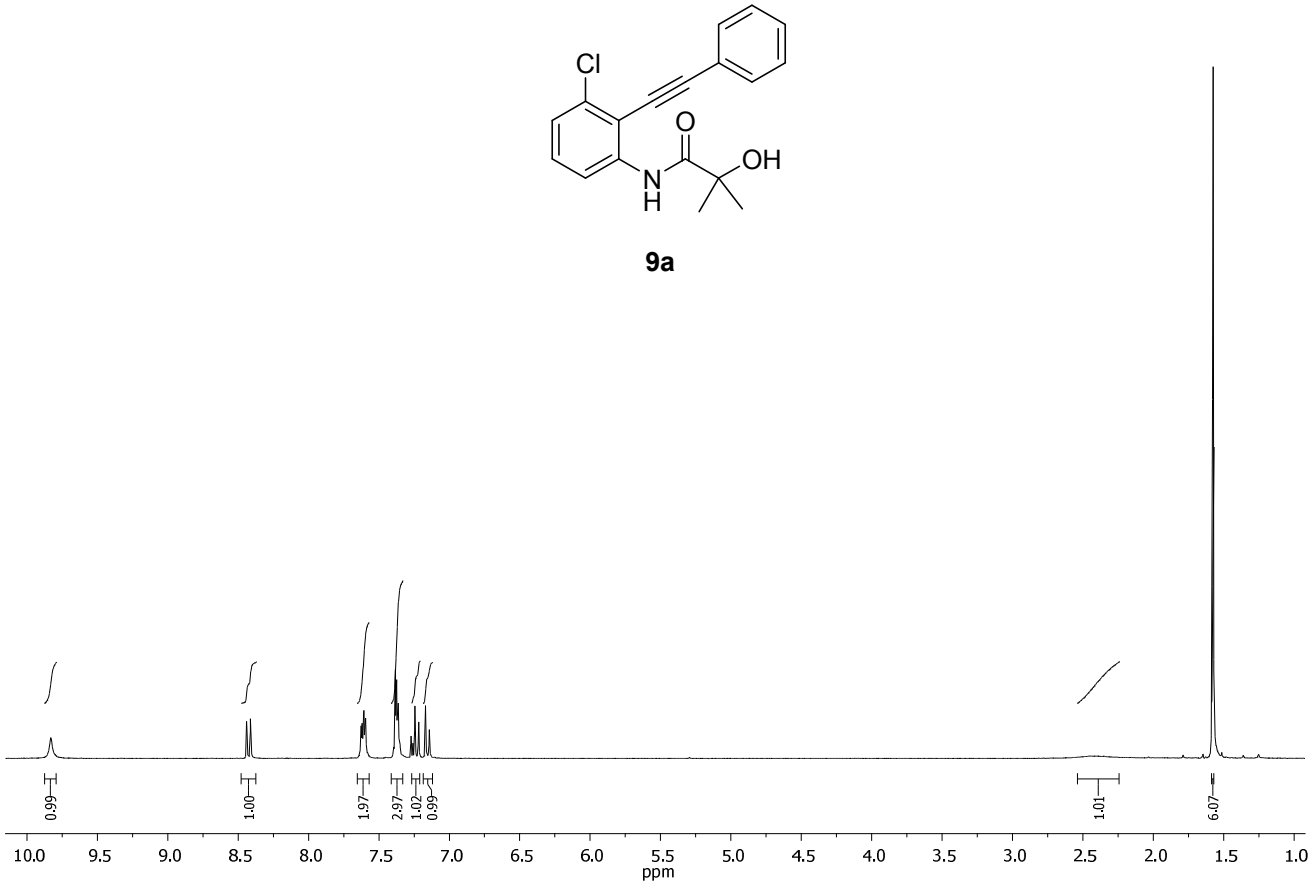

9a

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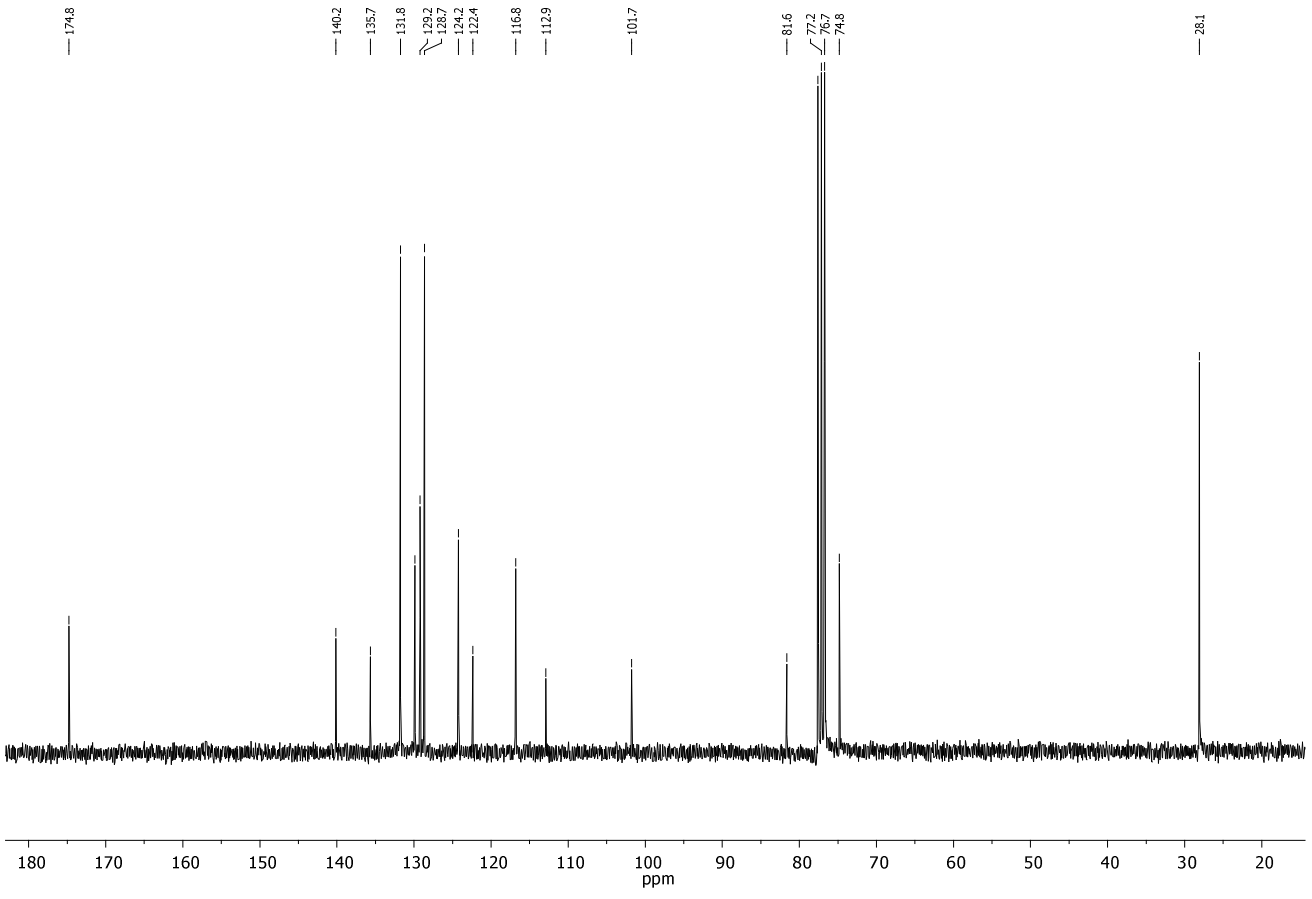

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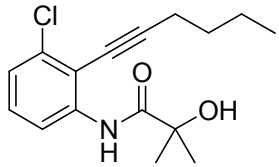

9b

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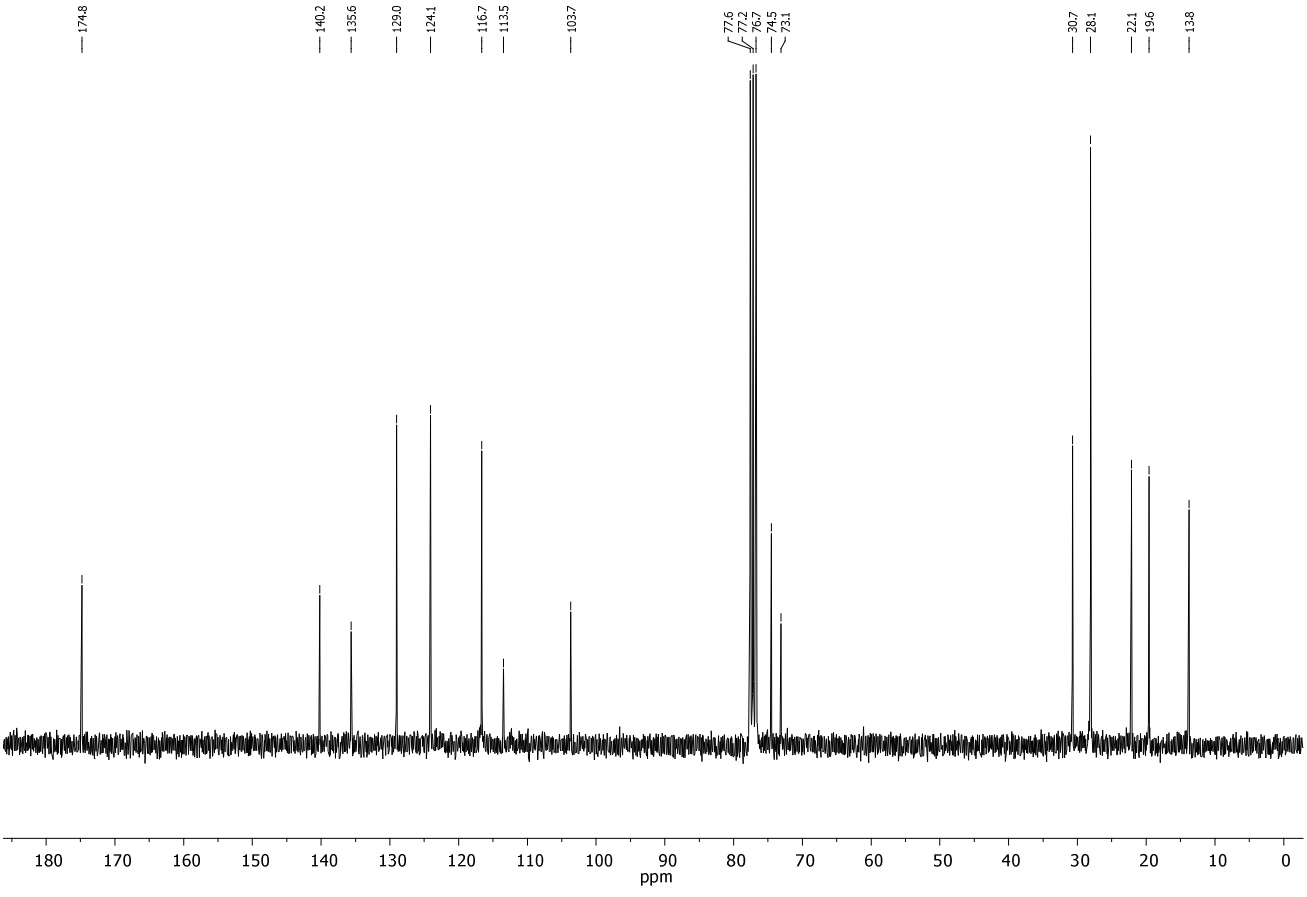

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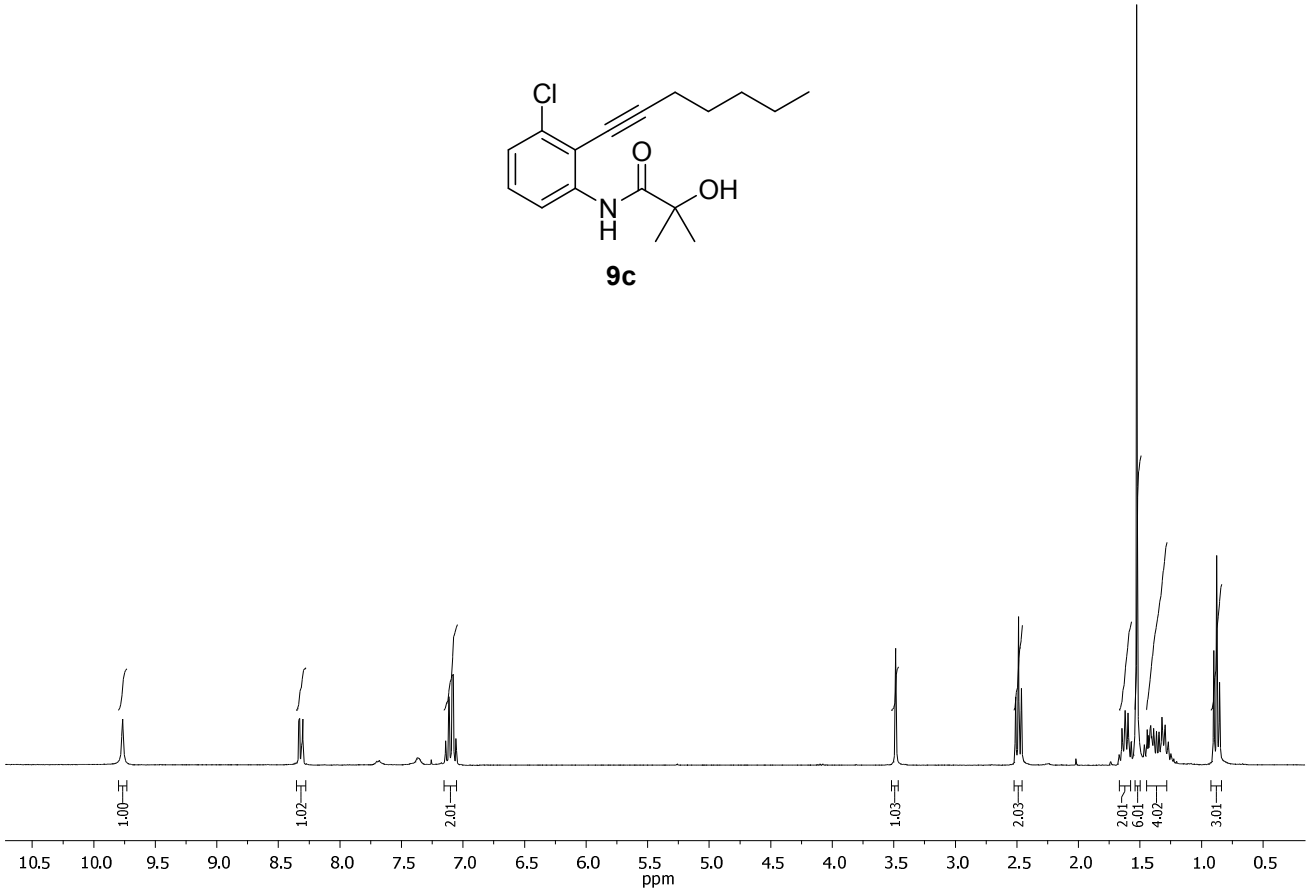

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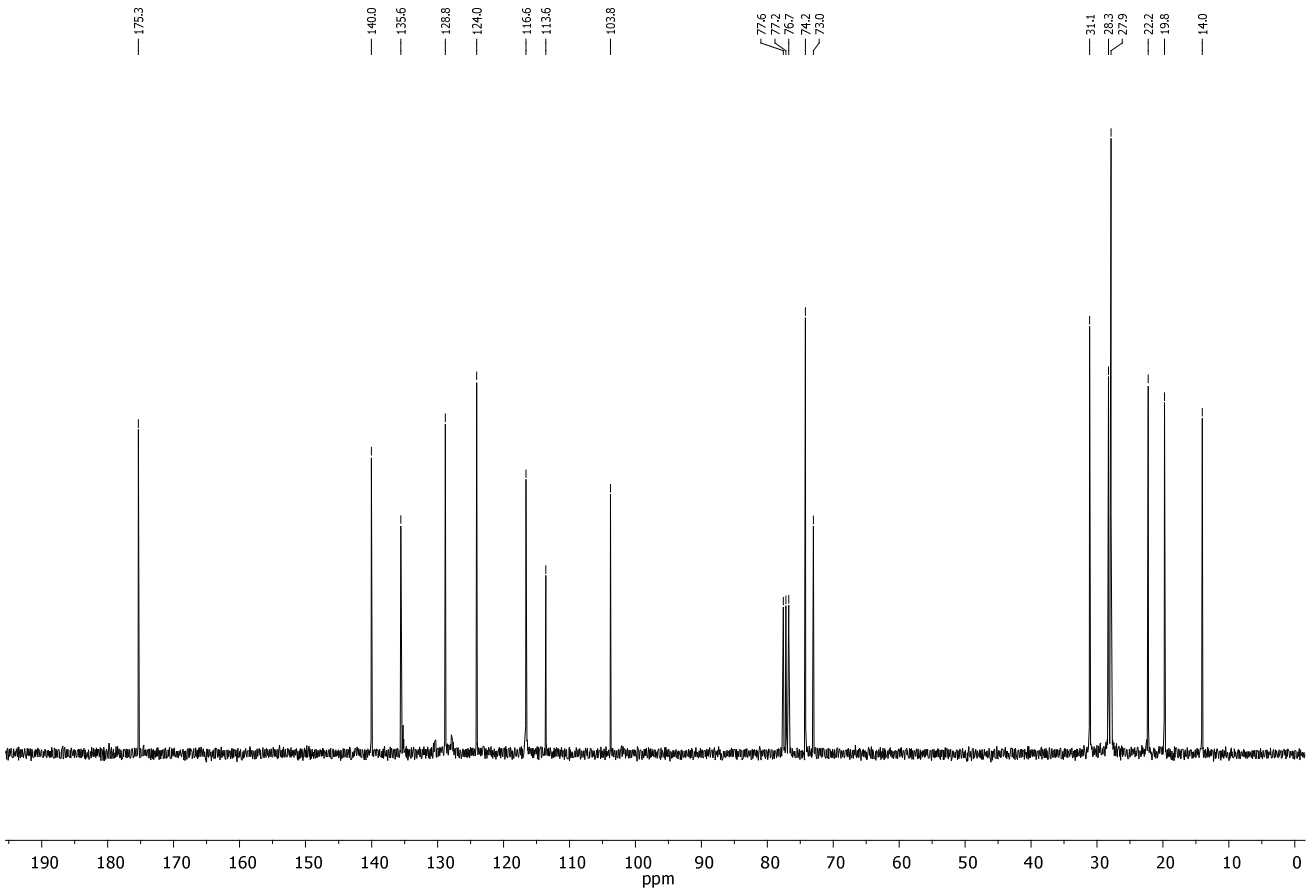

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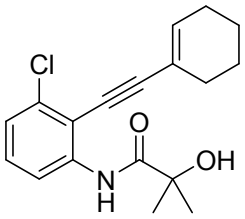

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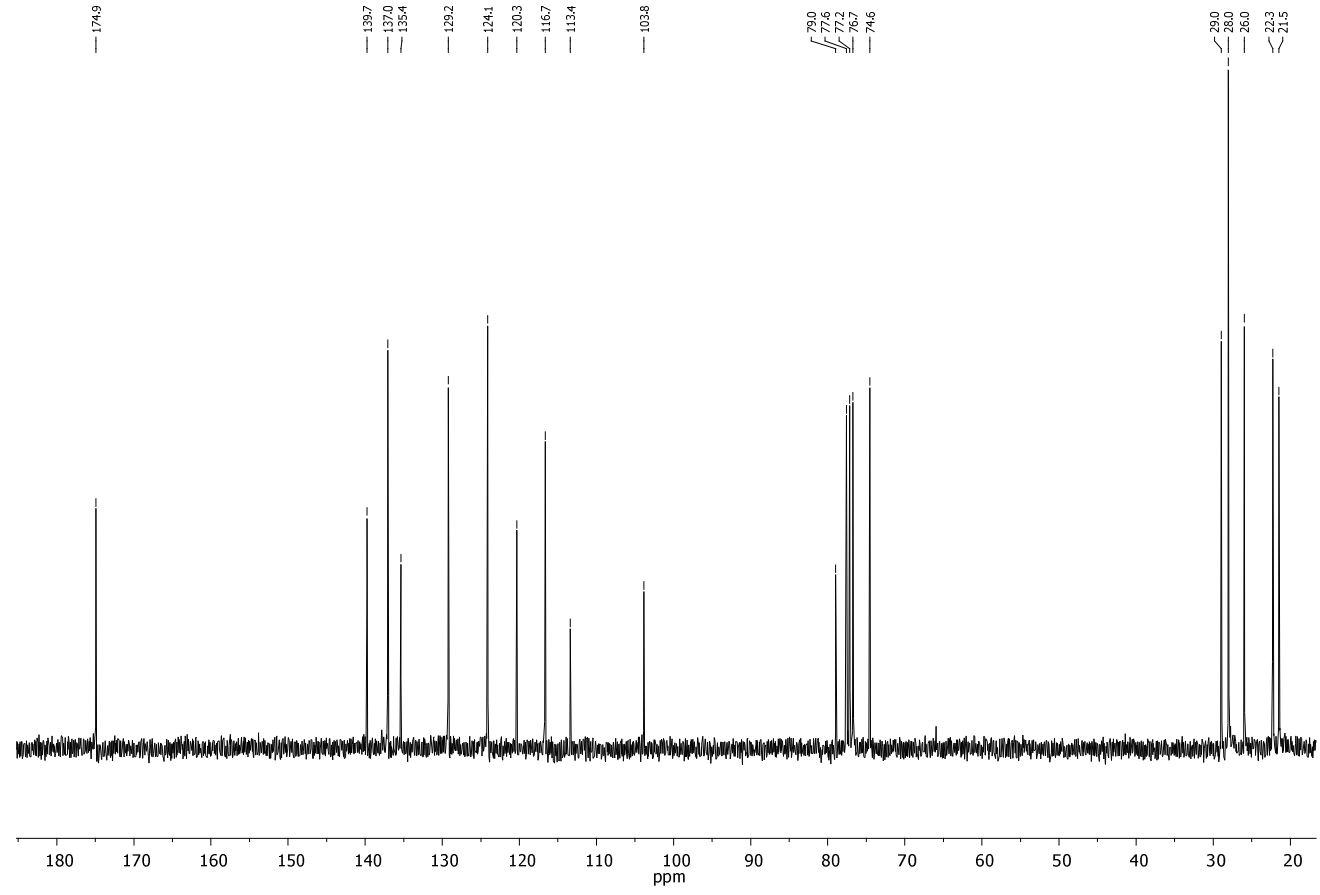

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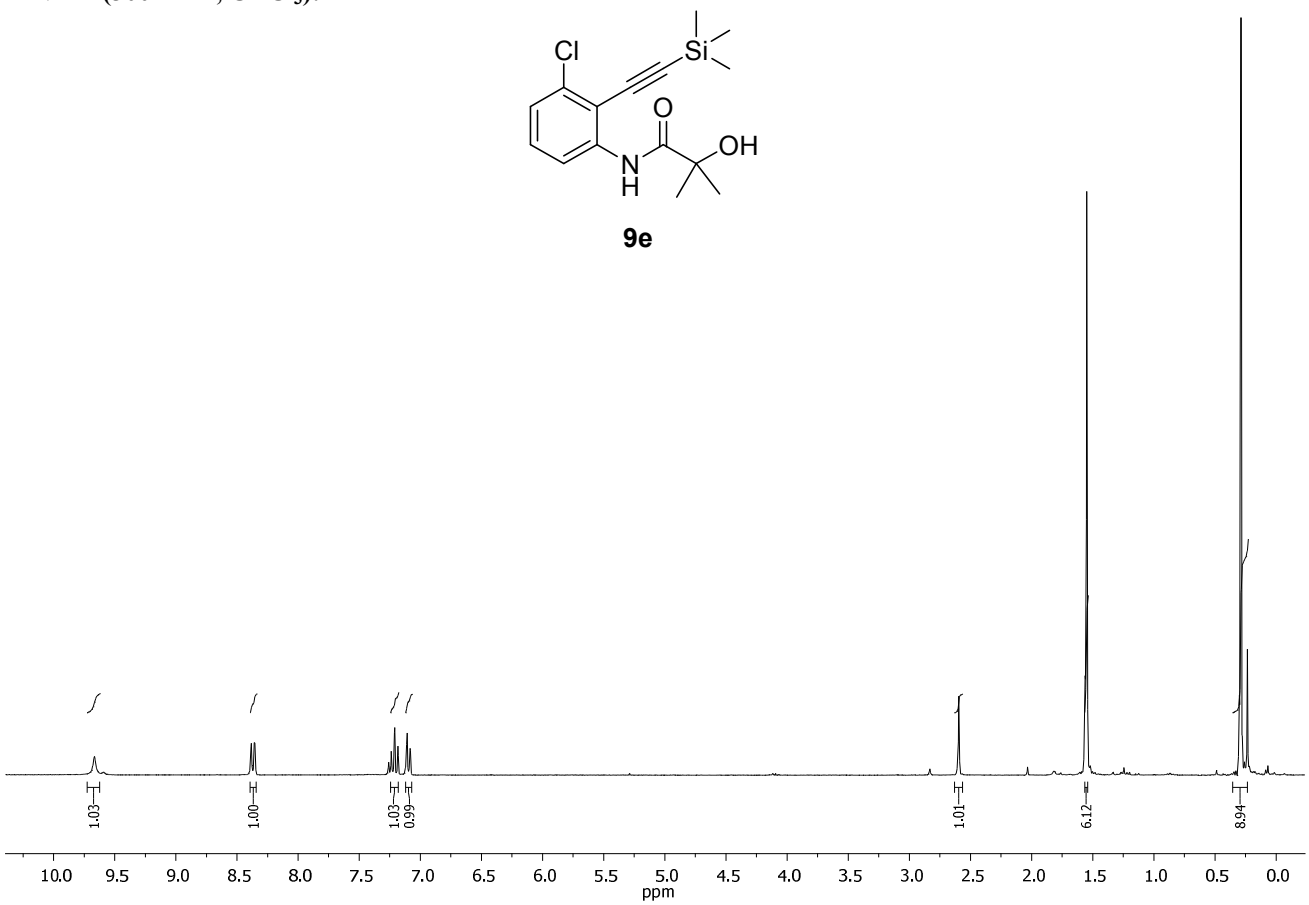

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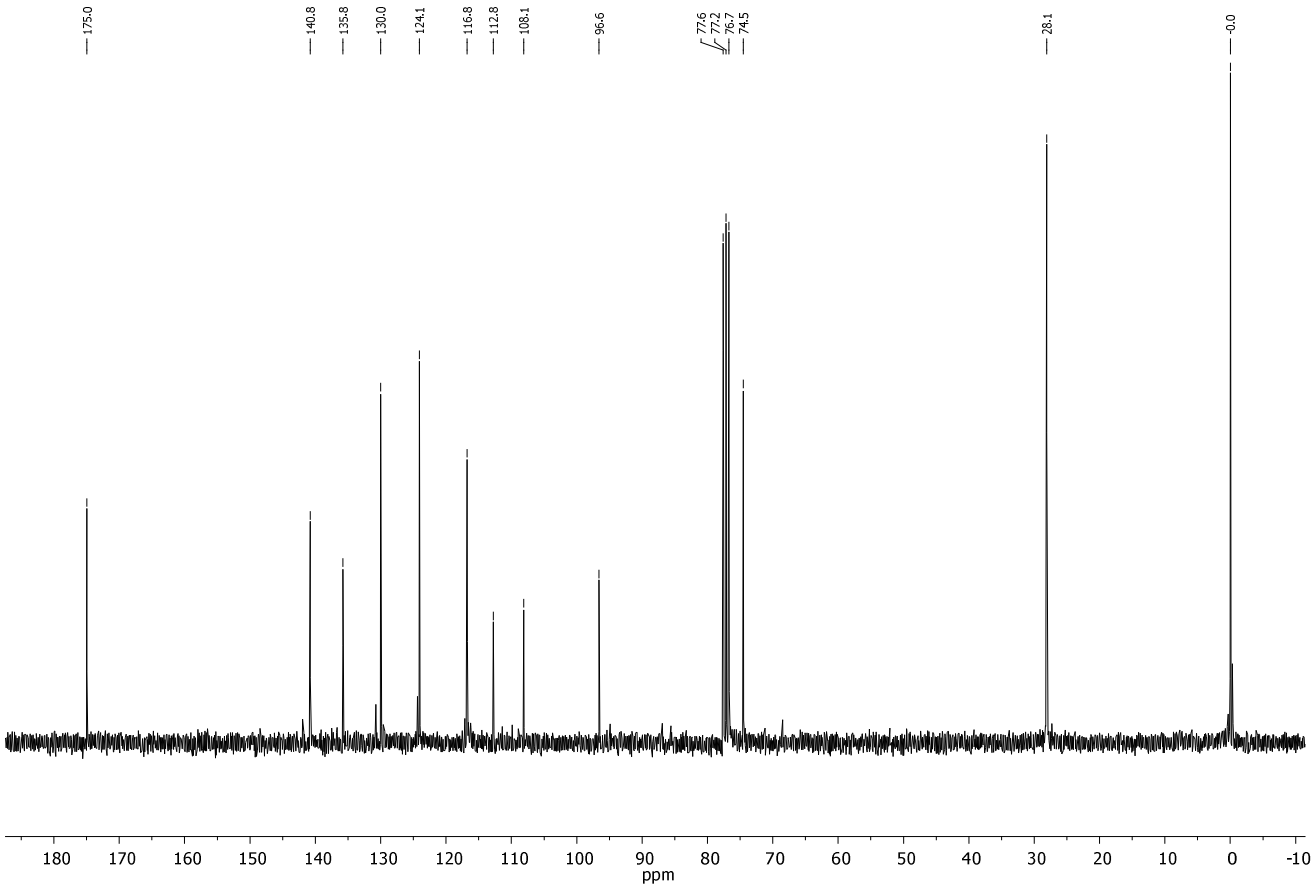

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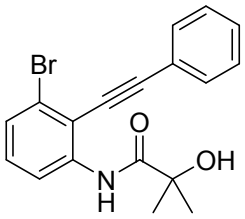

10a

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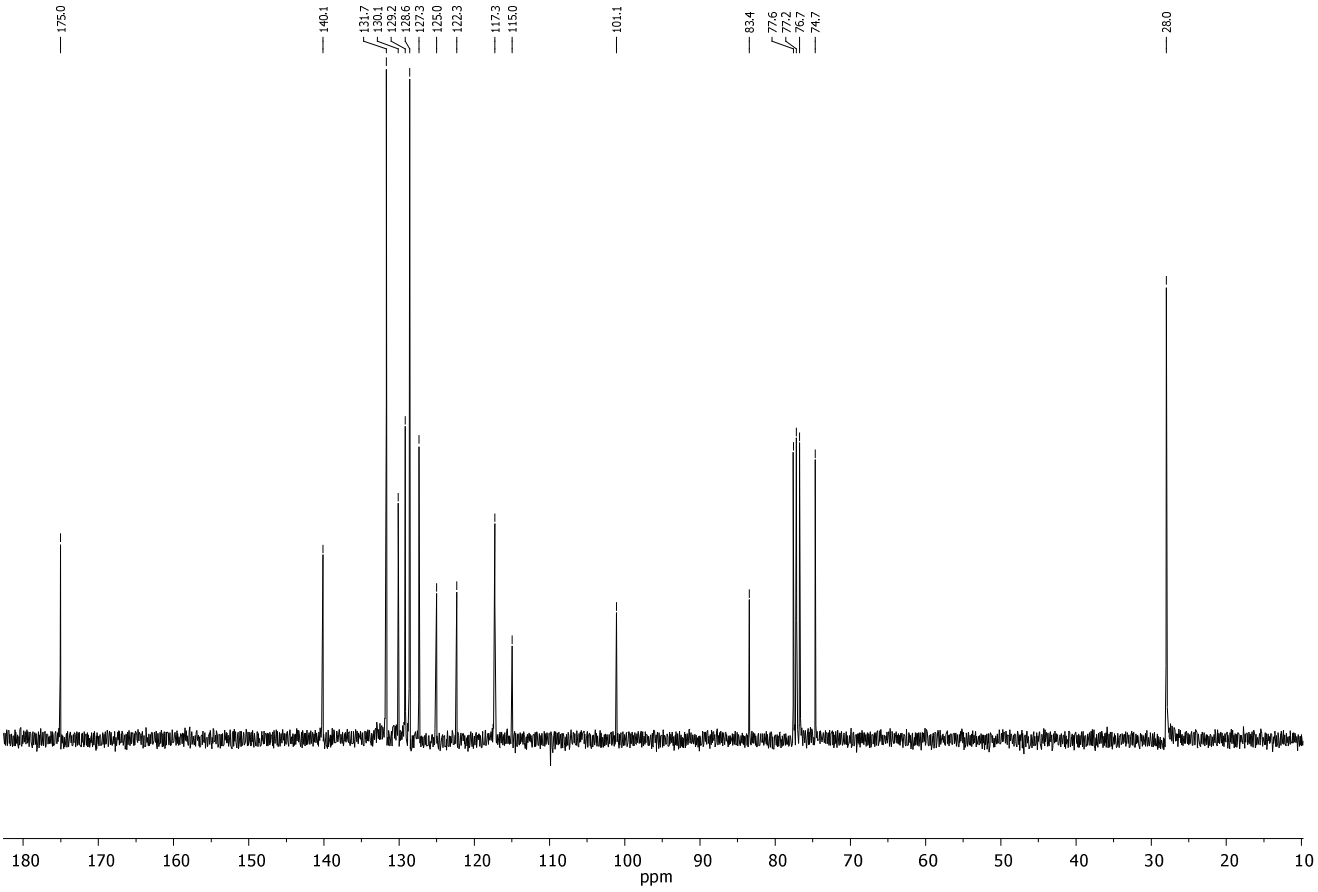

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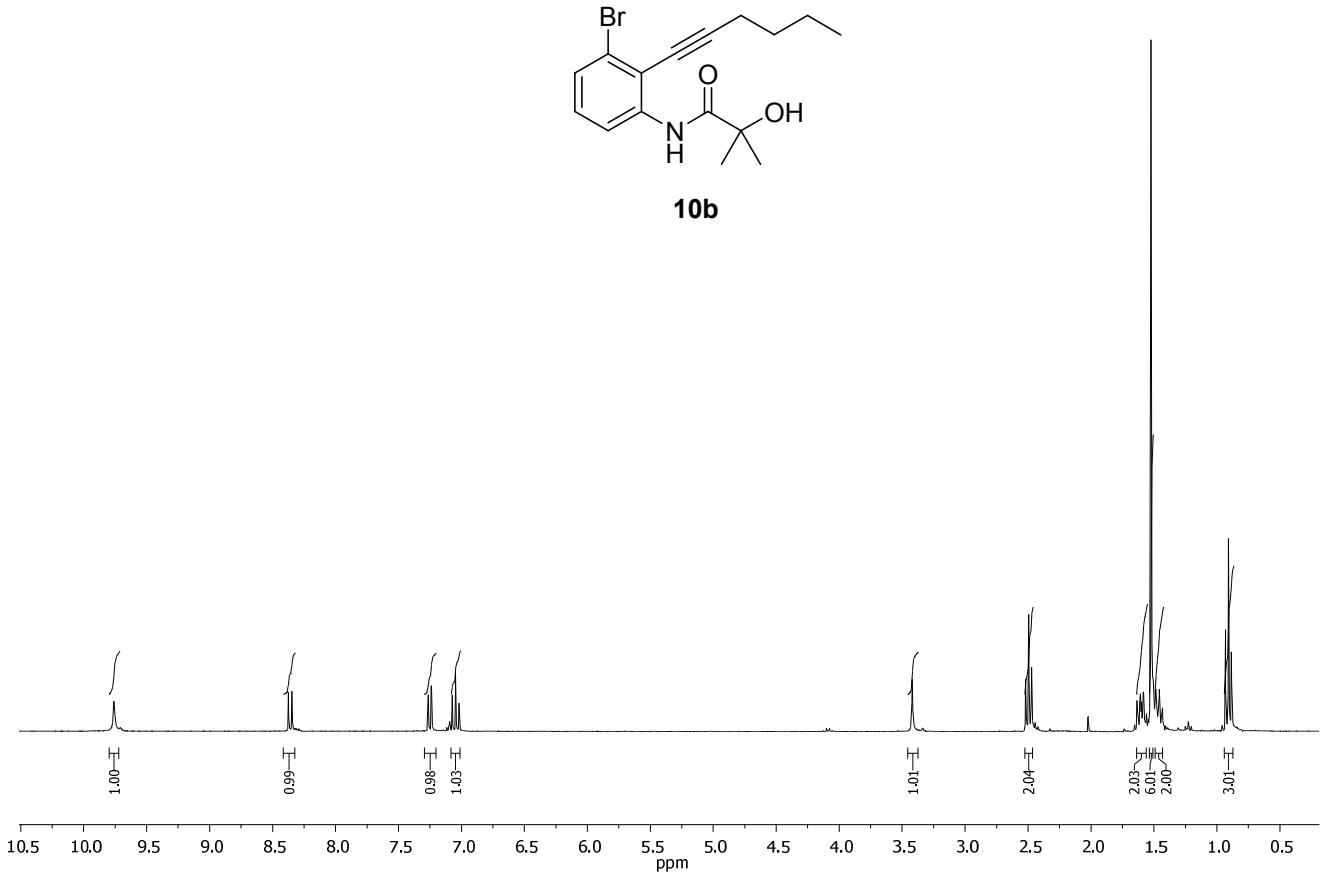

10b

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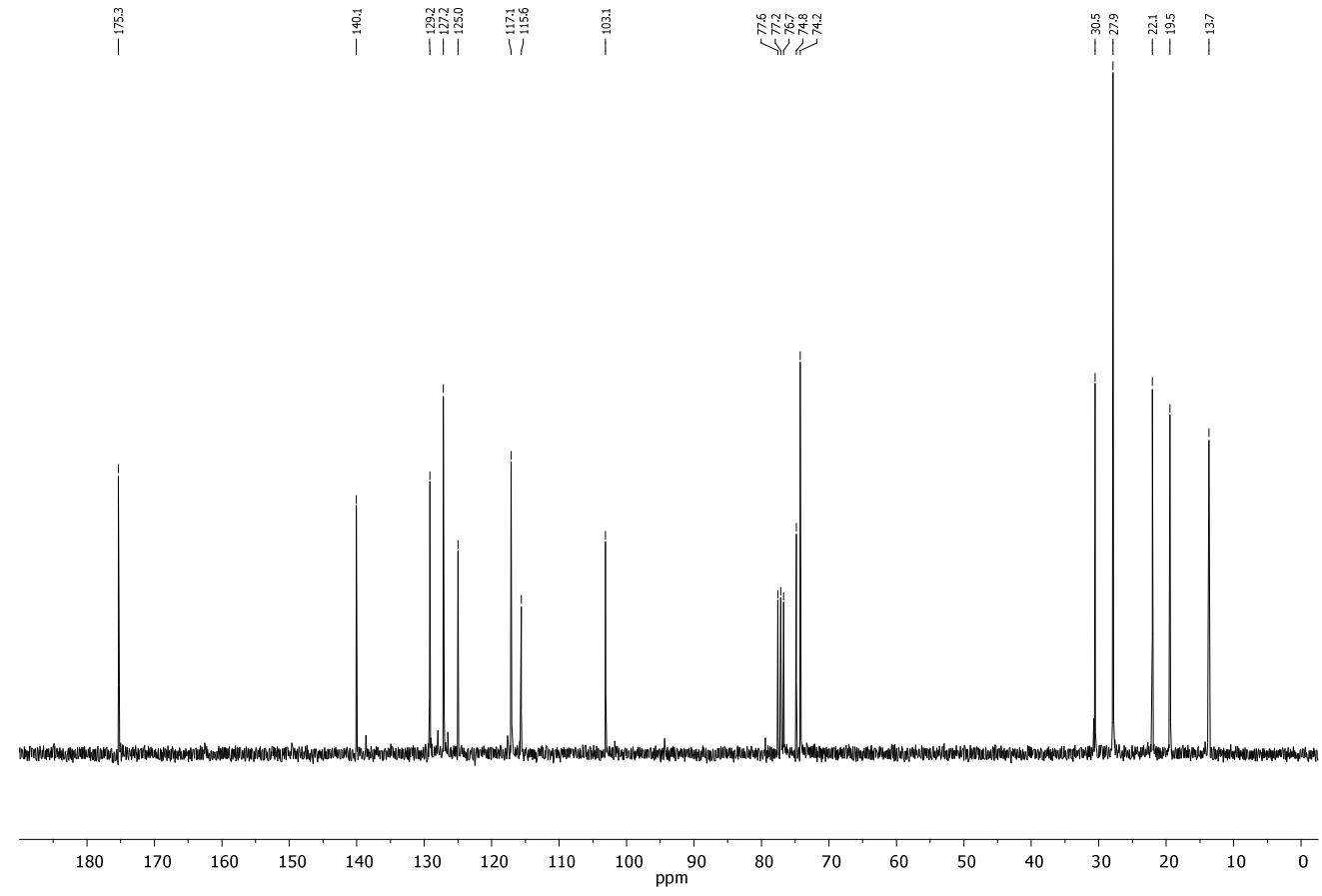

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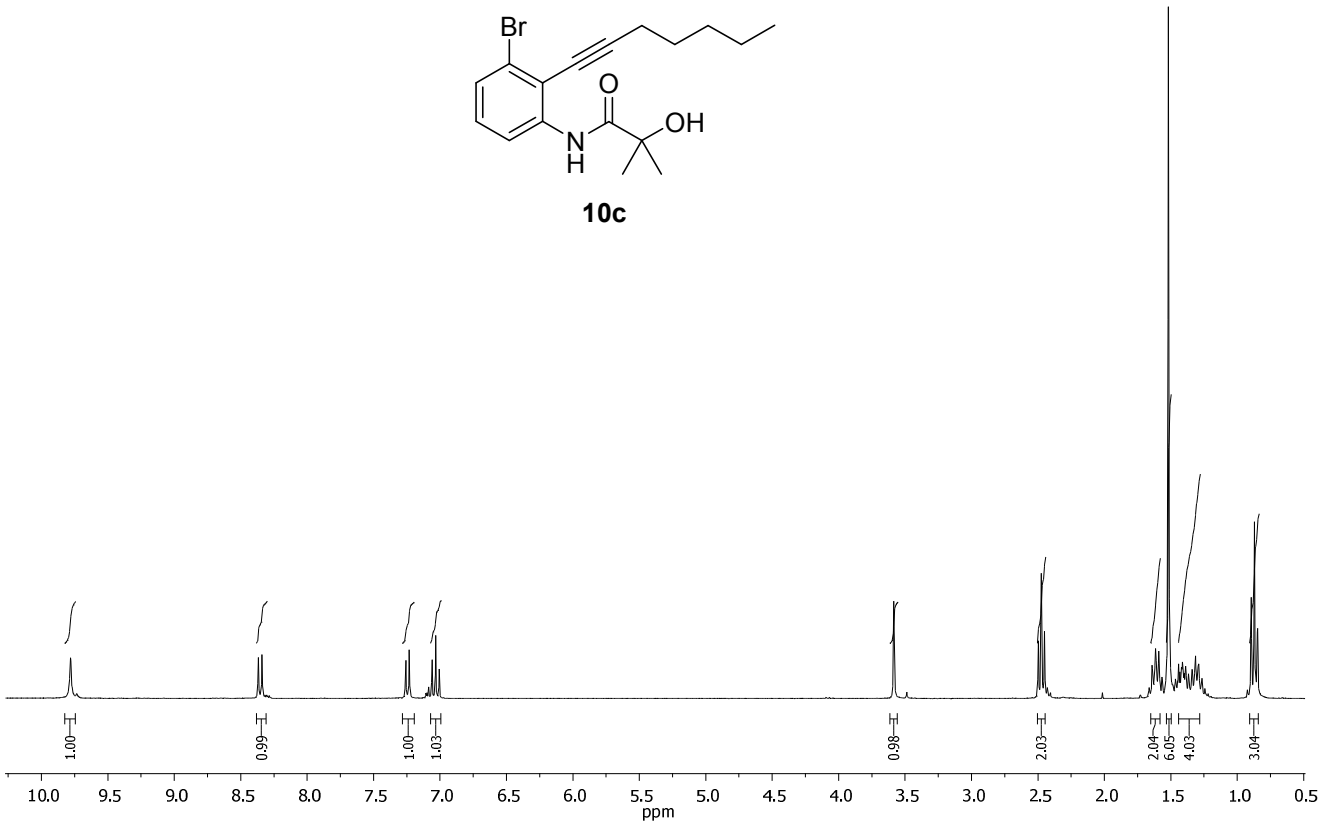

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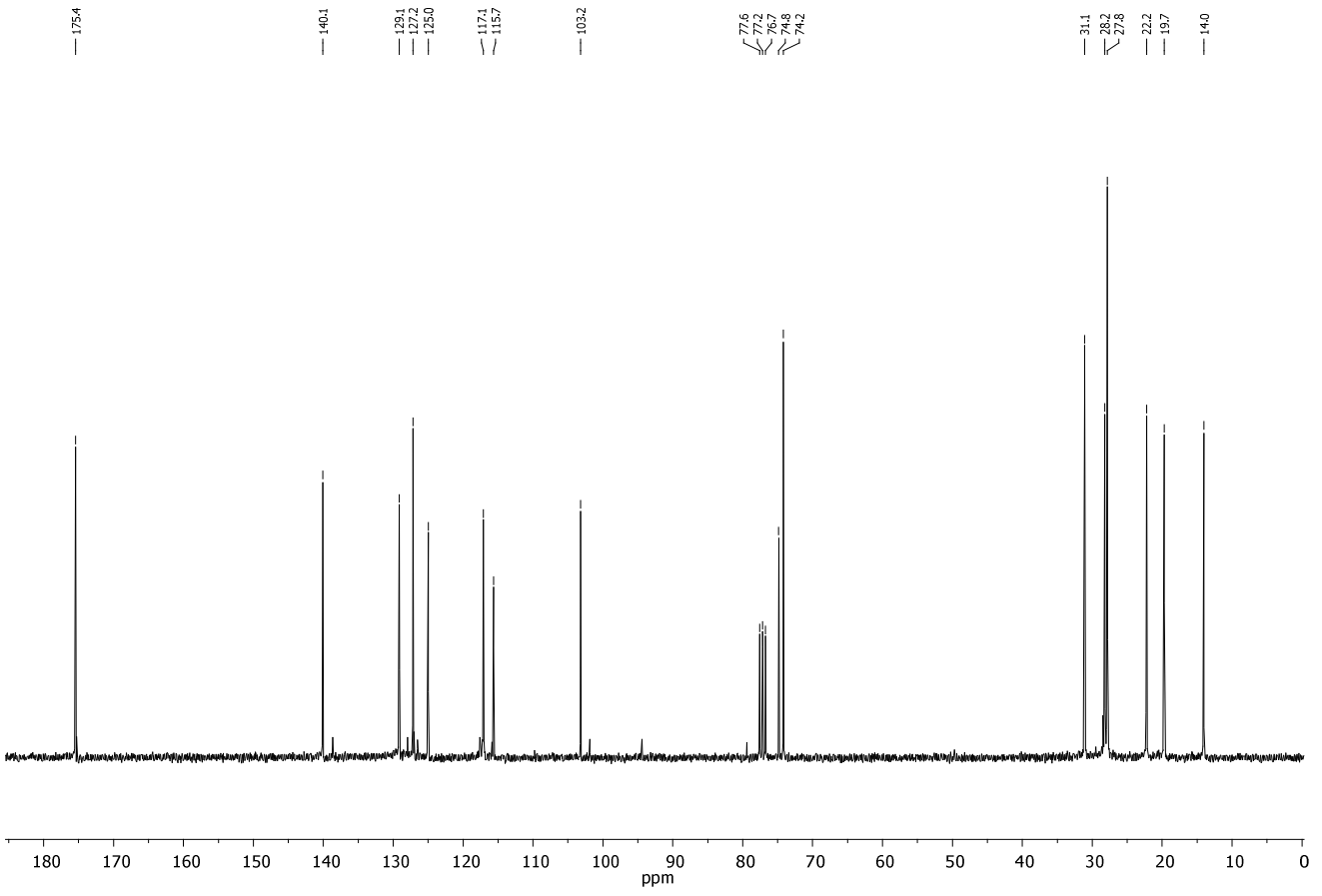

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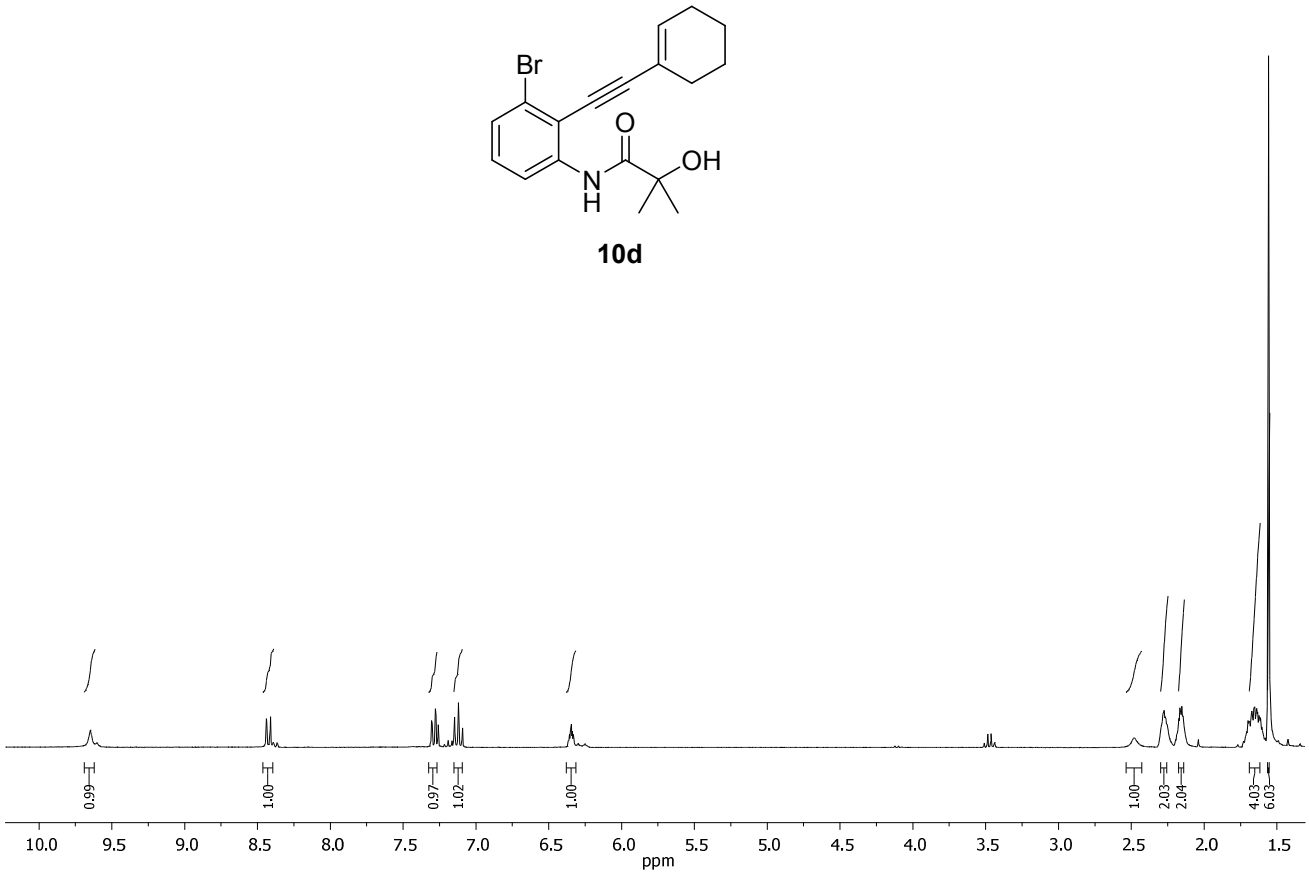
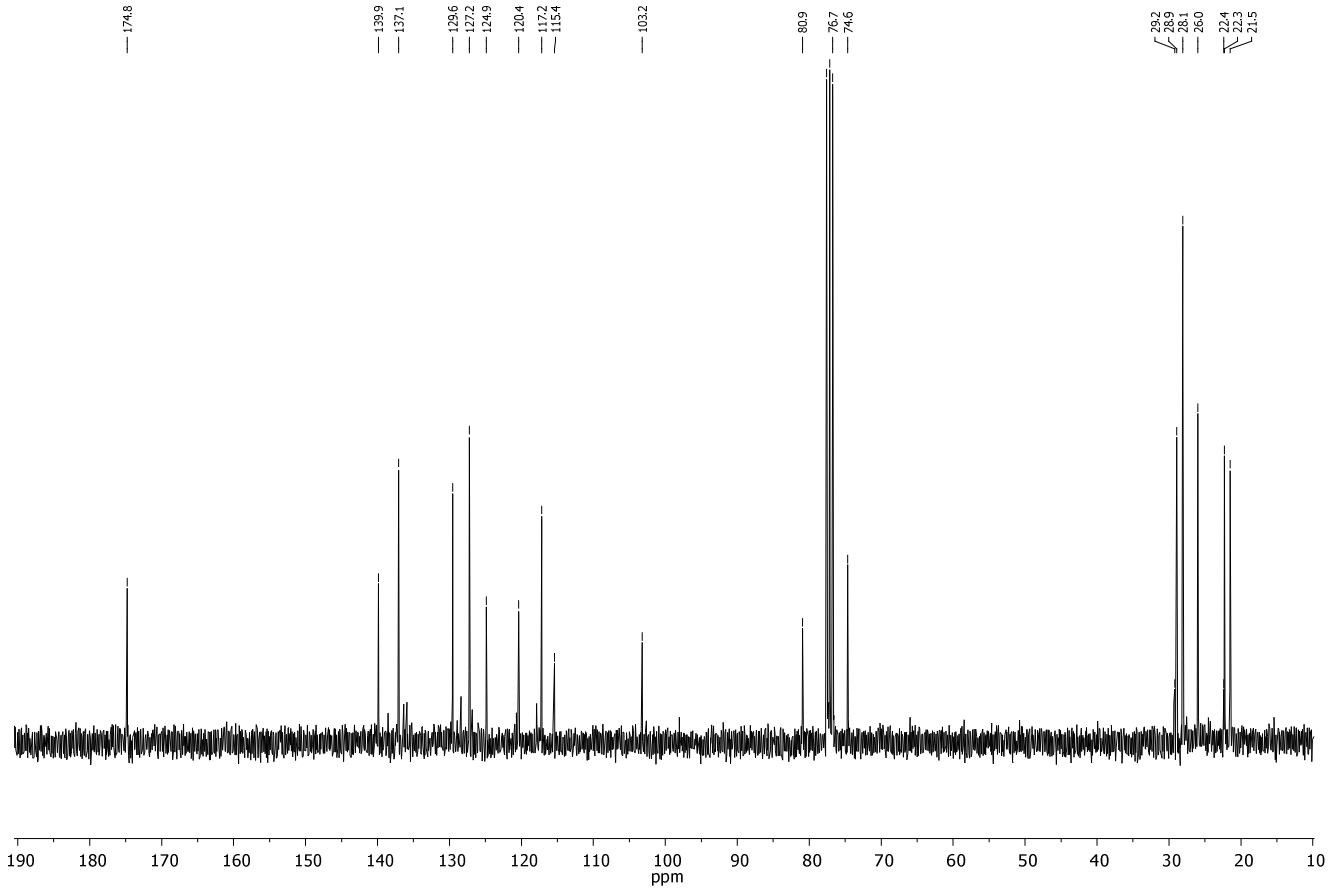
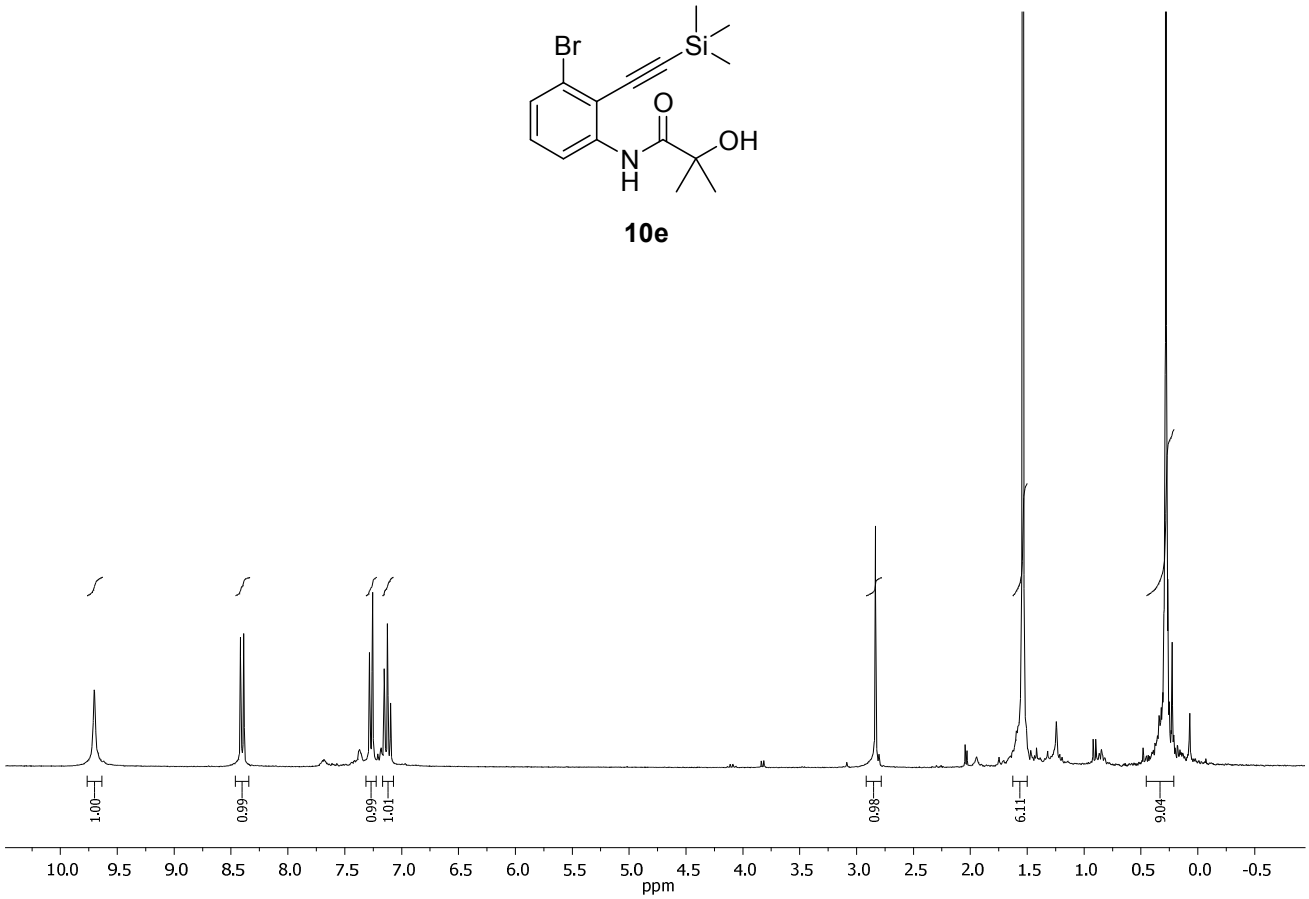


^{13}C-NMR (75.4 MHz, $CDCl_3$):

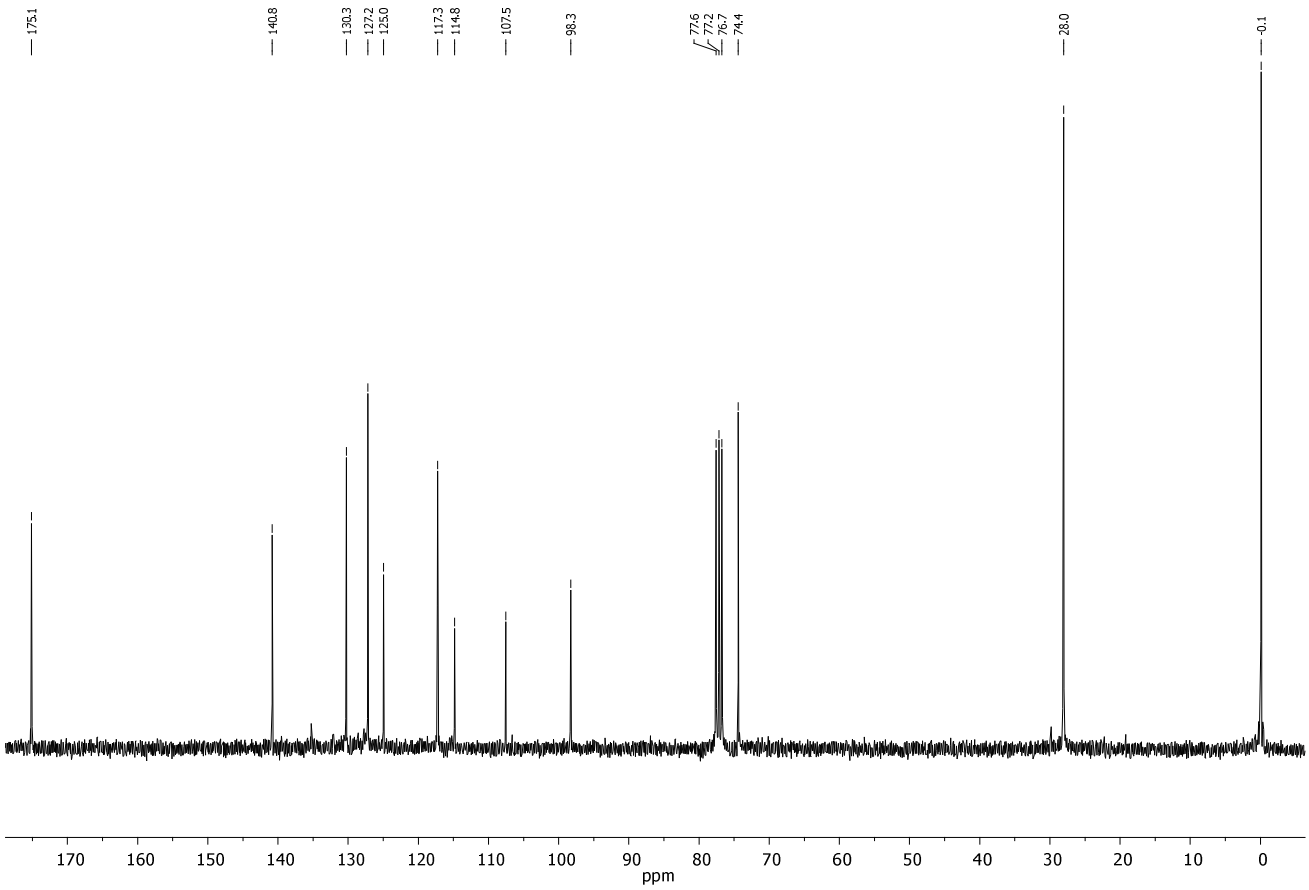


^{1}H-NMR (300 MHz, $CDCl_3$):

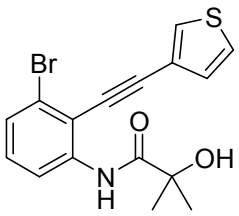


10e

^{13}C-NMR (75.4 MHz, $CDCl_3$):

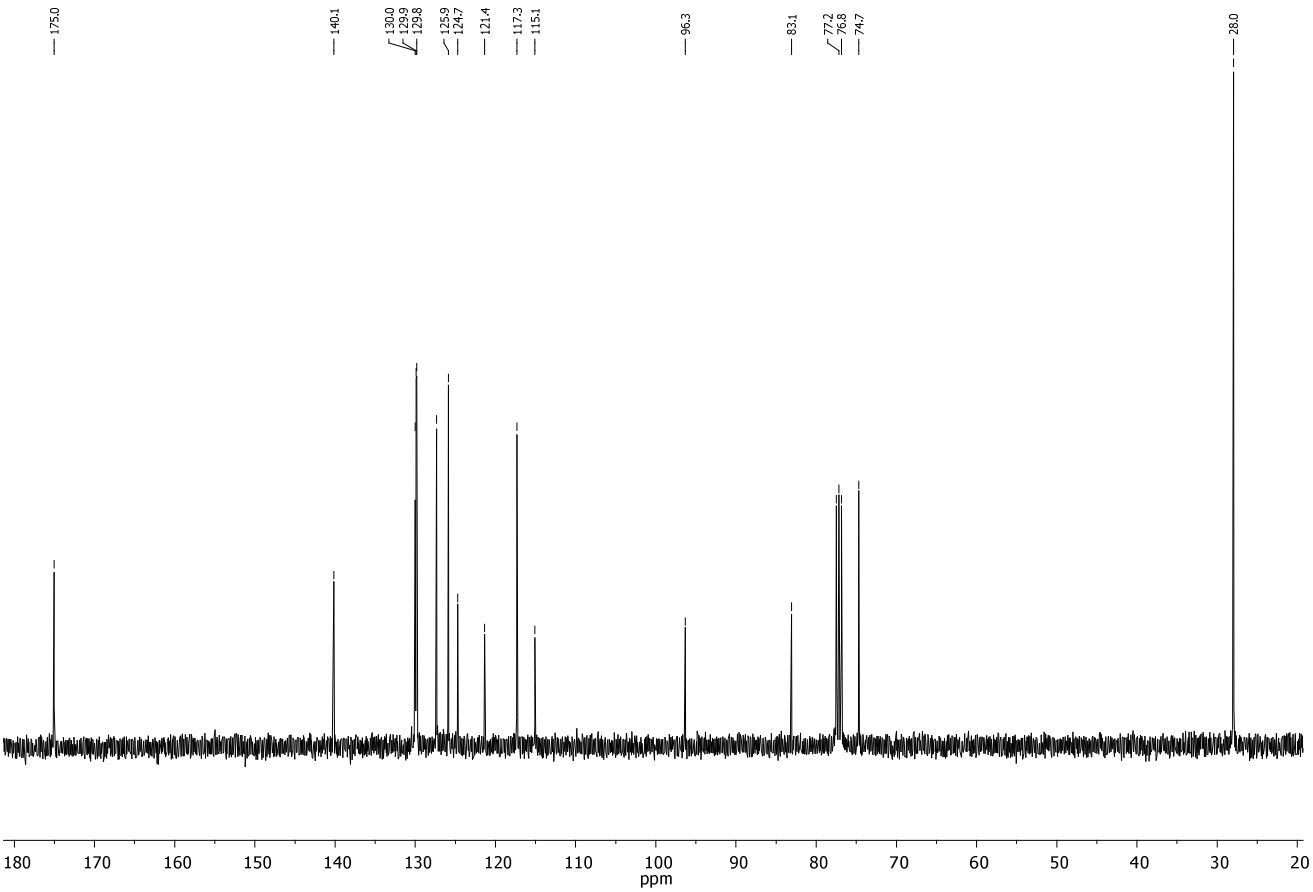


^{1}H-NMR (400 MHz, $CDCl_3$):

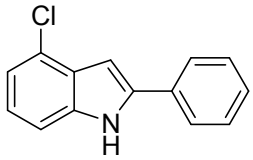


10f

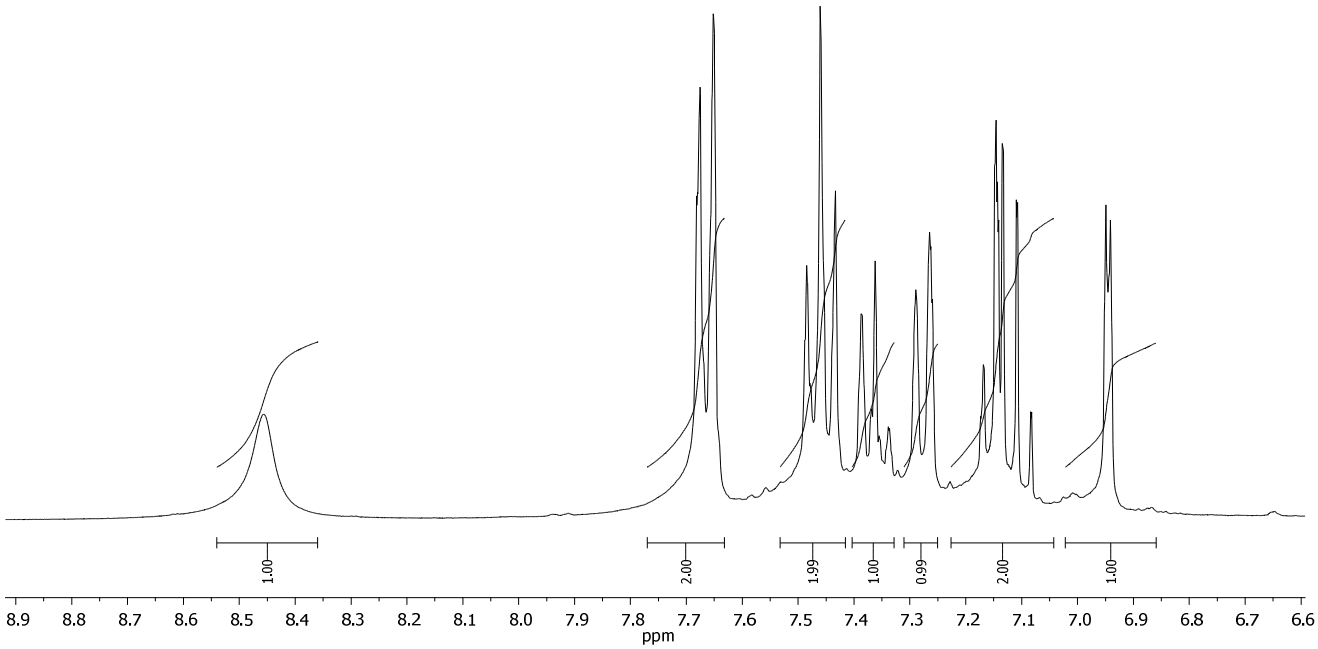
^{13}C-NMR (100.6 MHz, $CDCl_3$):



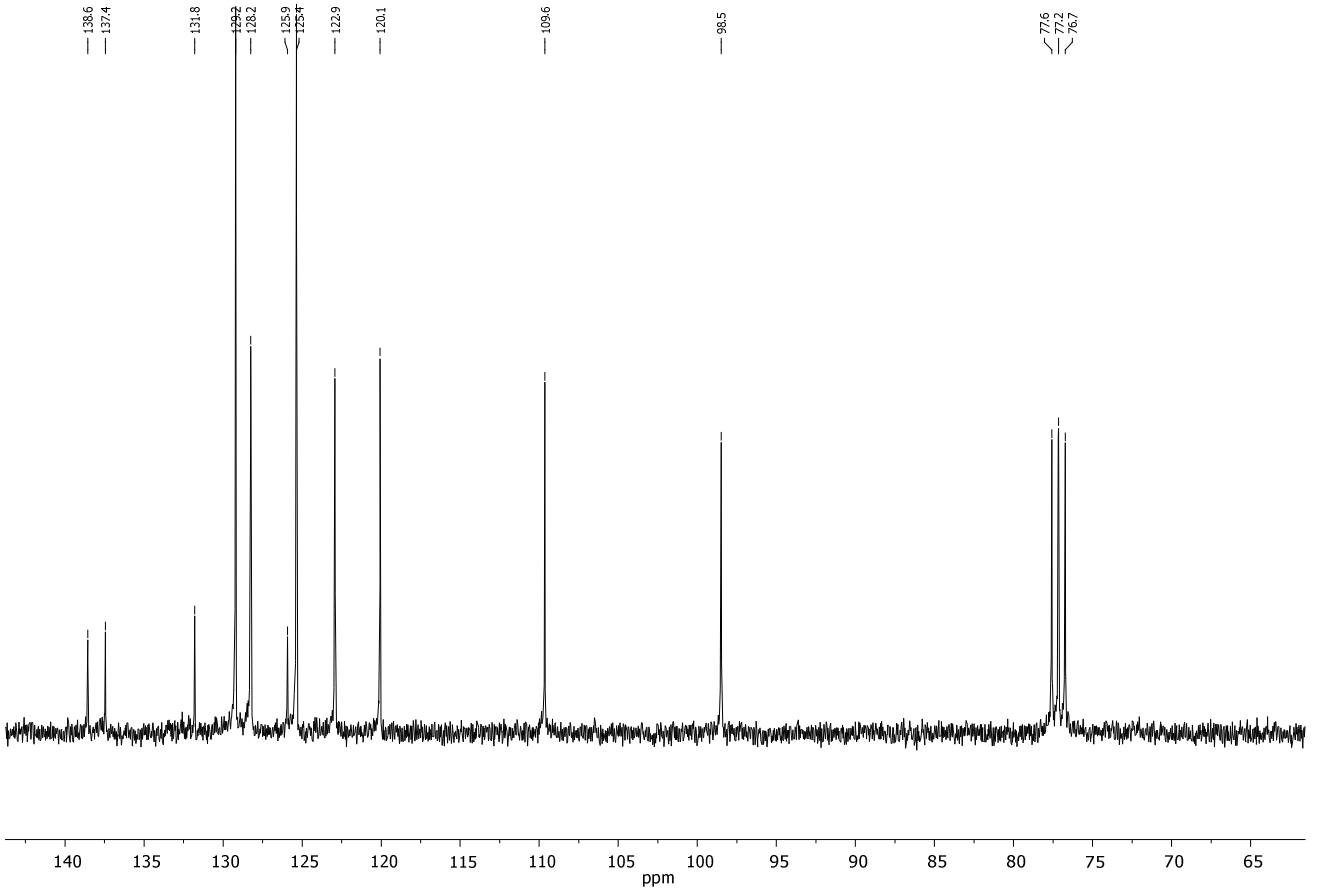
^{1}H-NMR (300 MHz, $CDCl_3$):



11a



^{13}C-NMR (75.4 MHz, $CDCl_3$):



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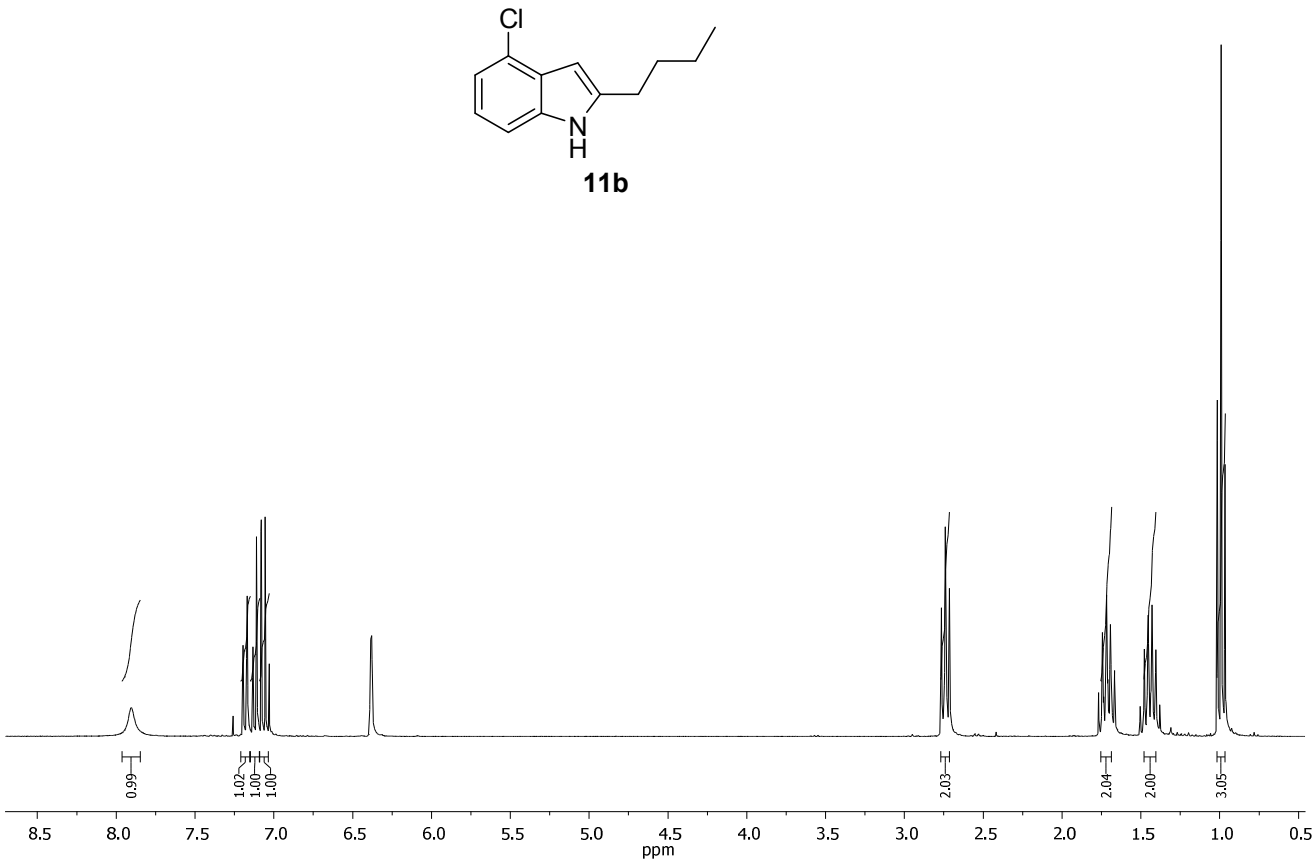

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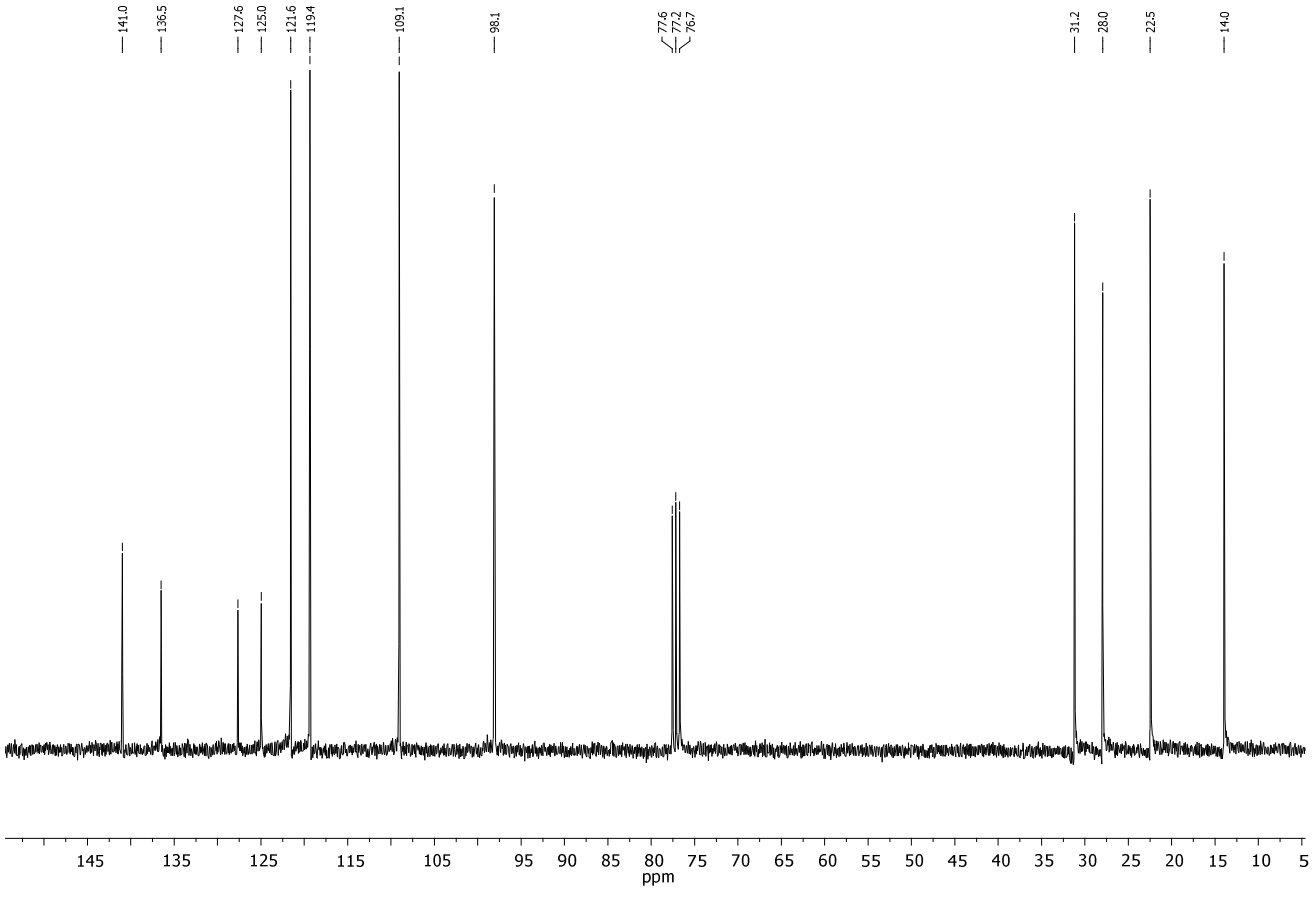

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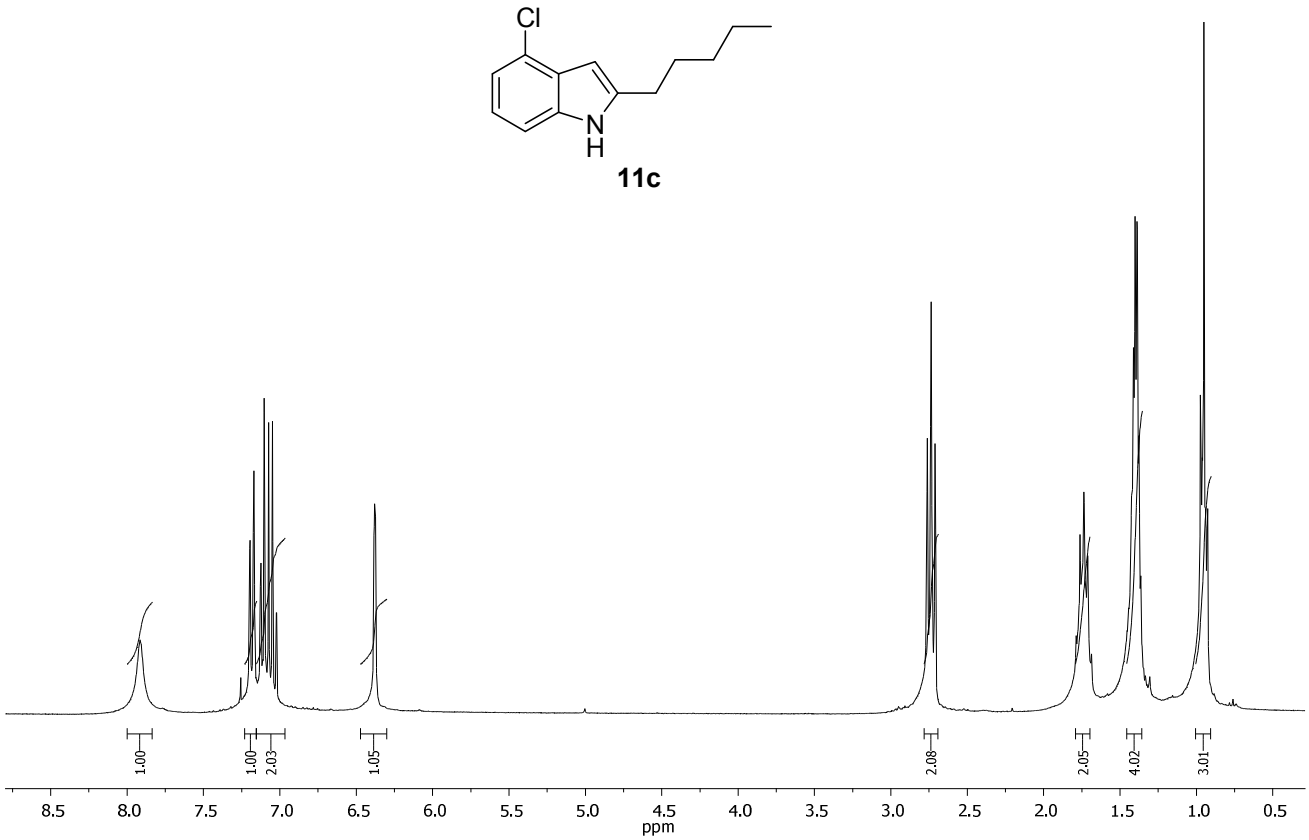

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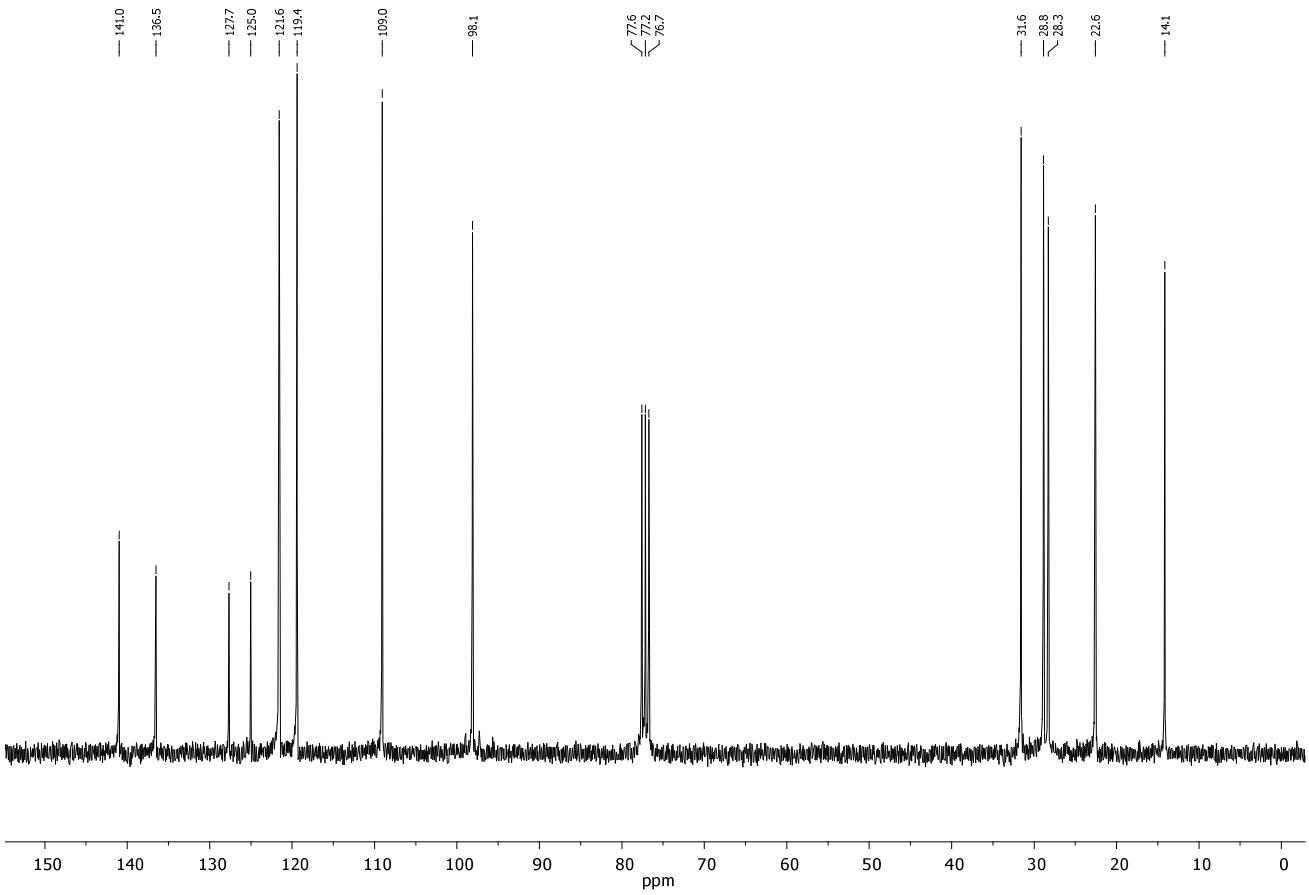

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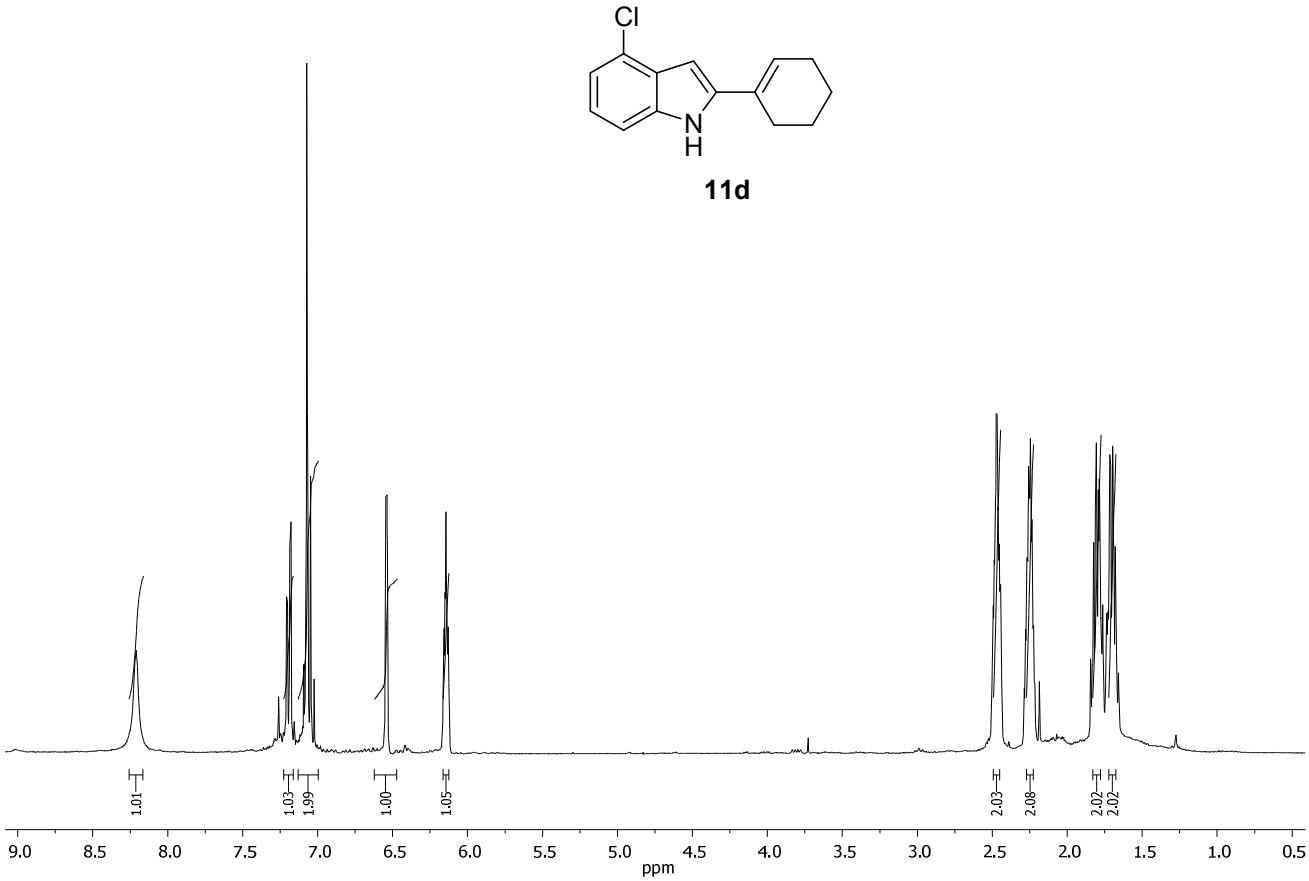

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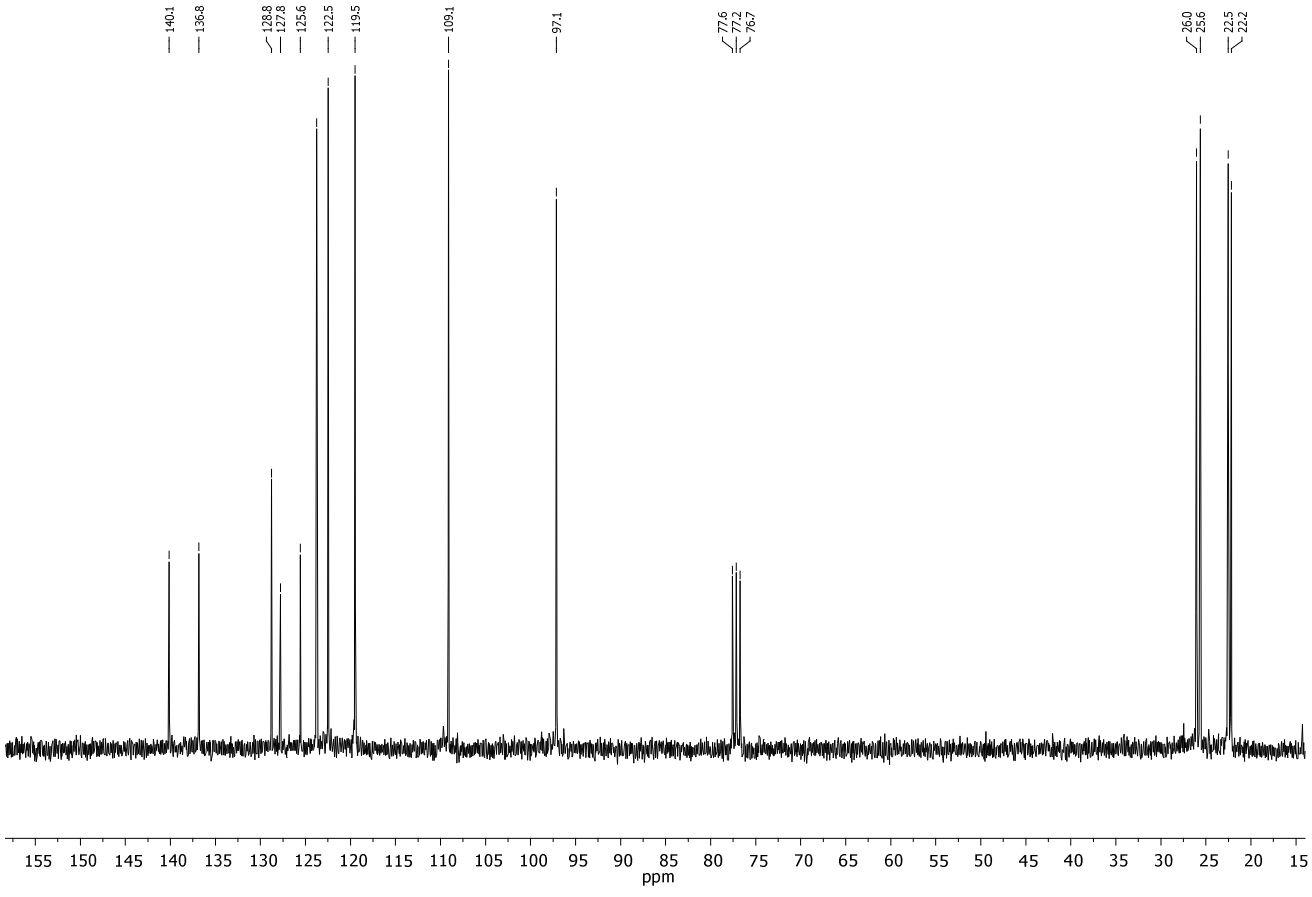

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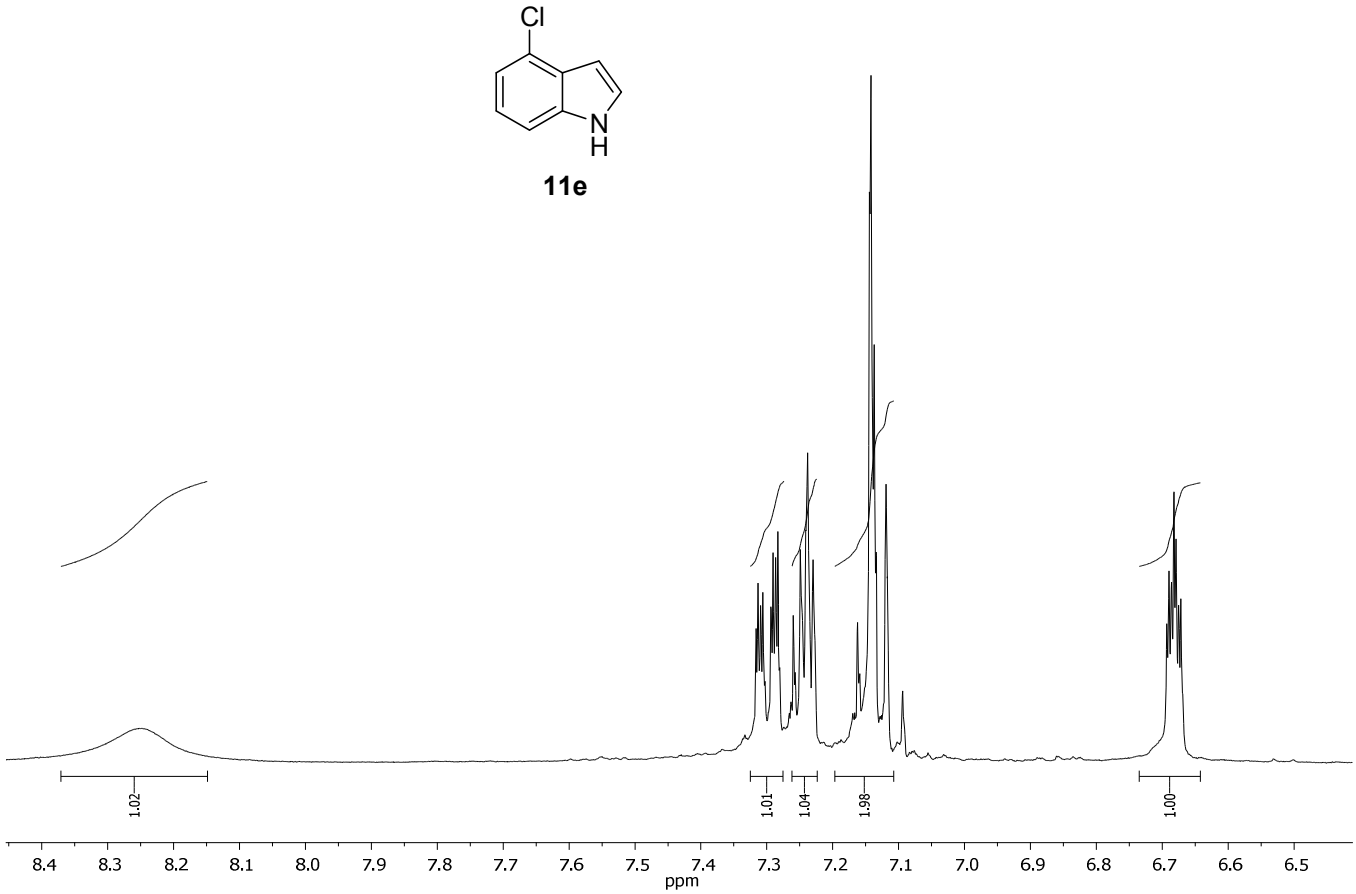

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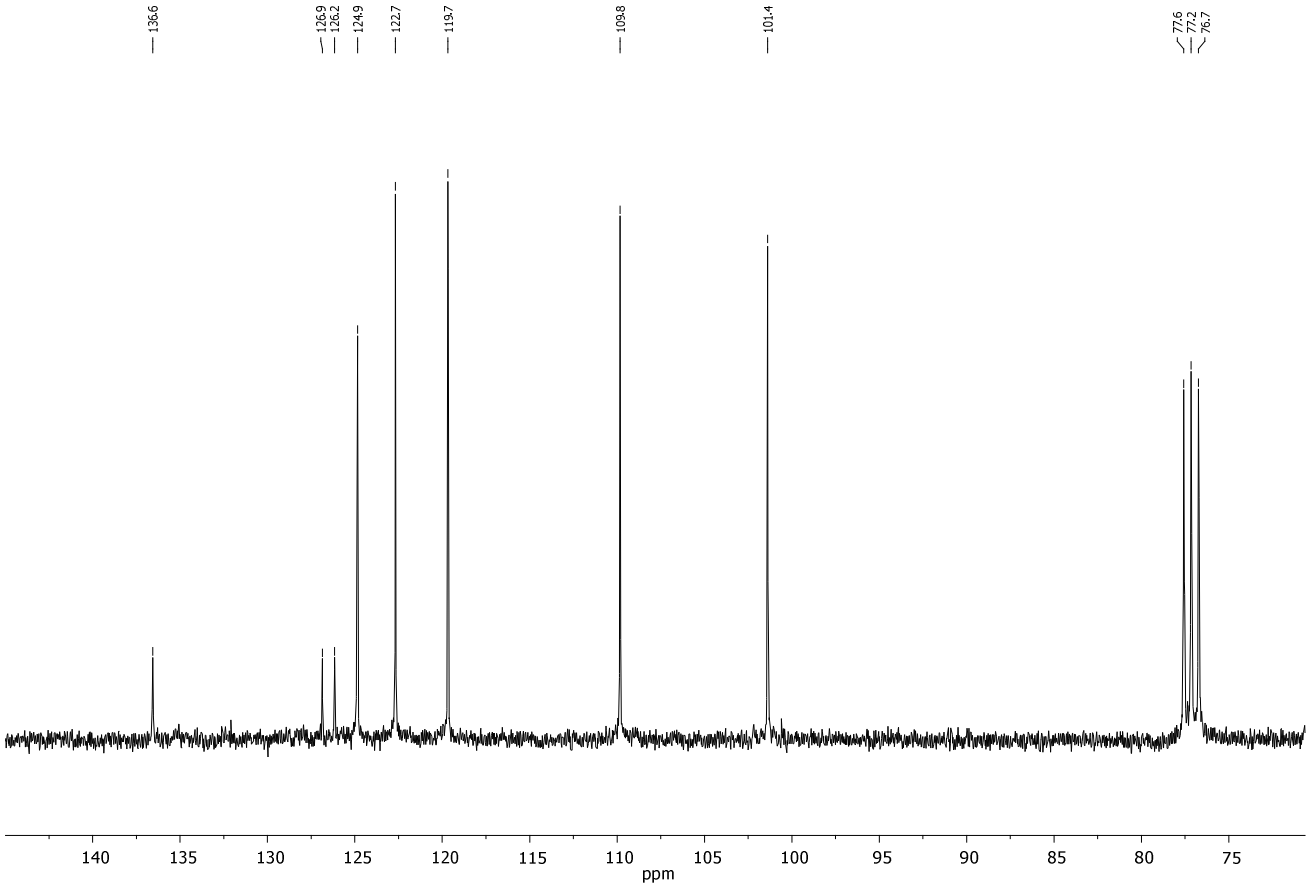

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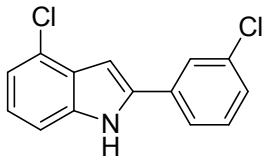

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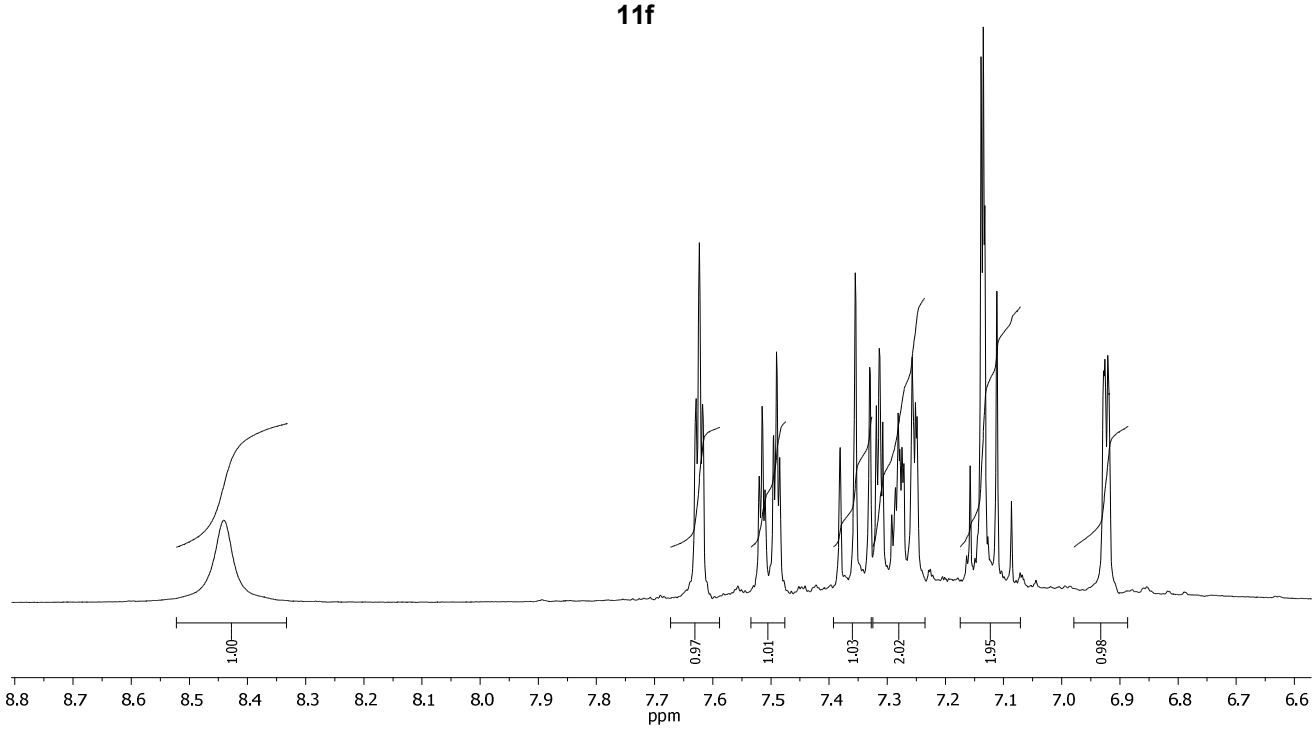

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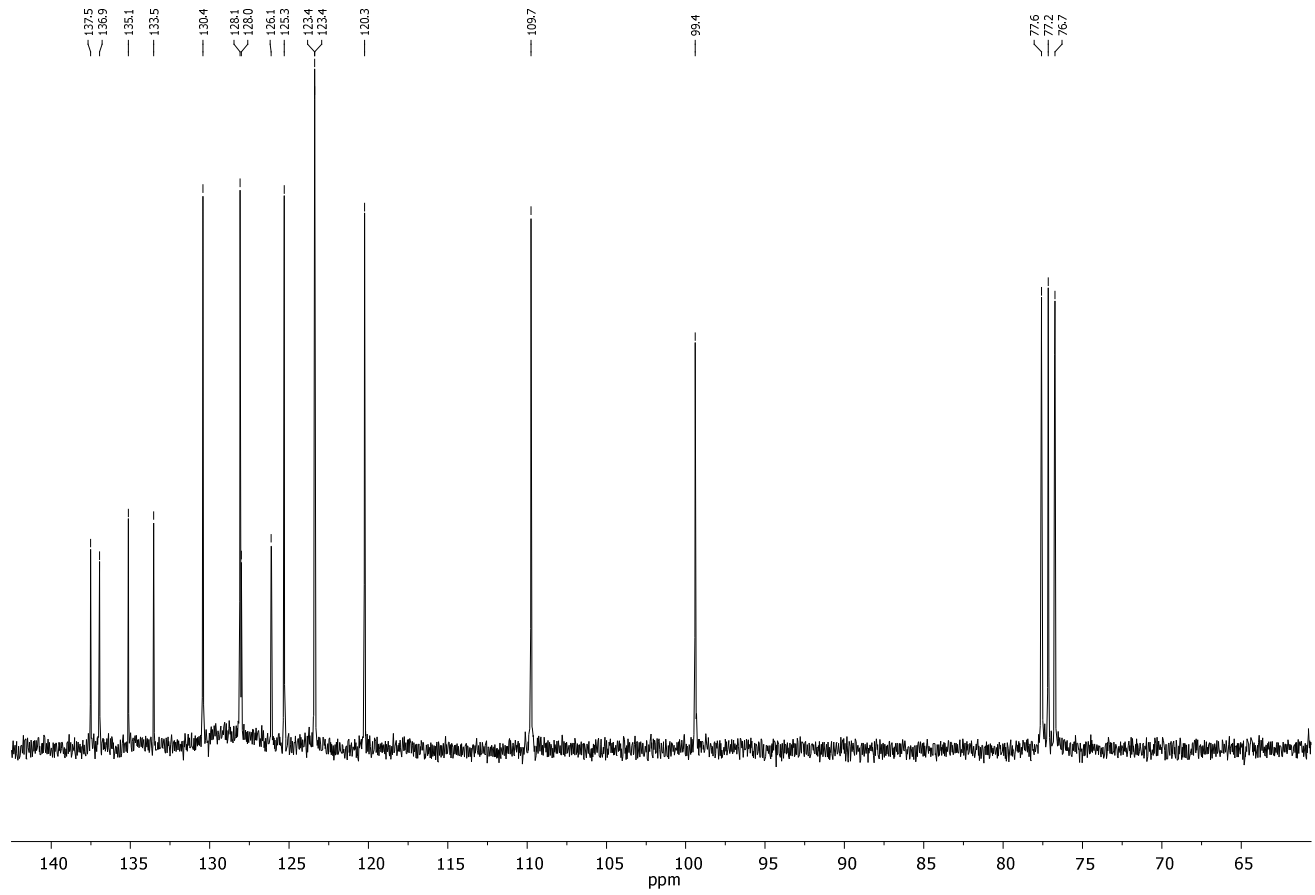

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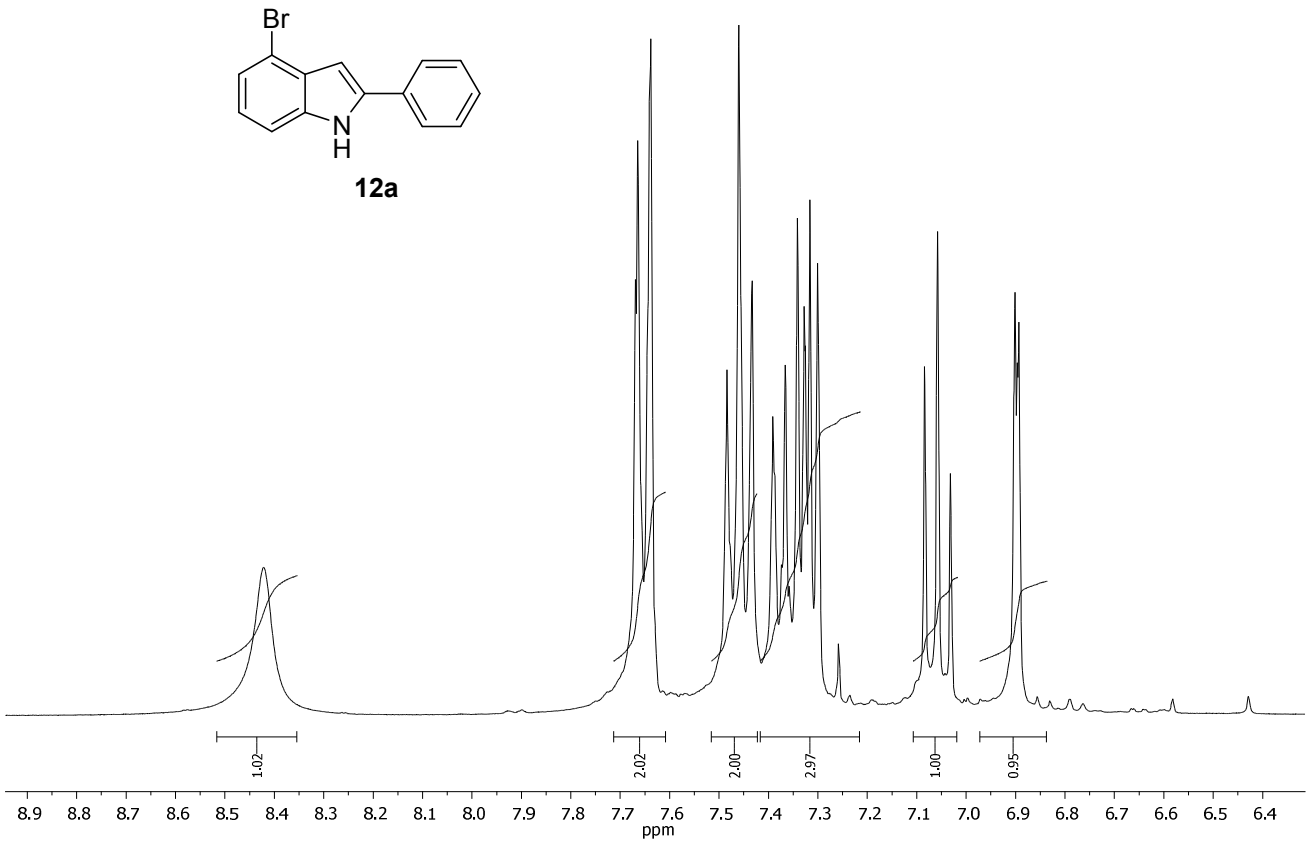

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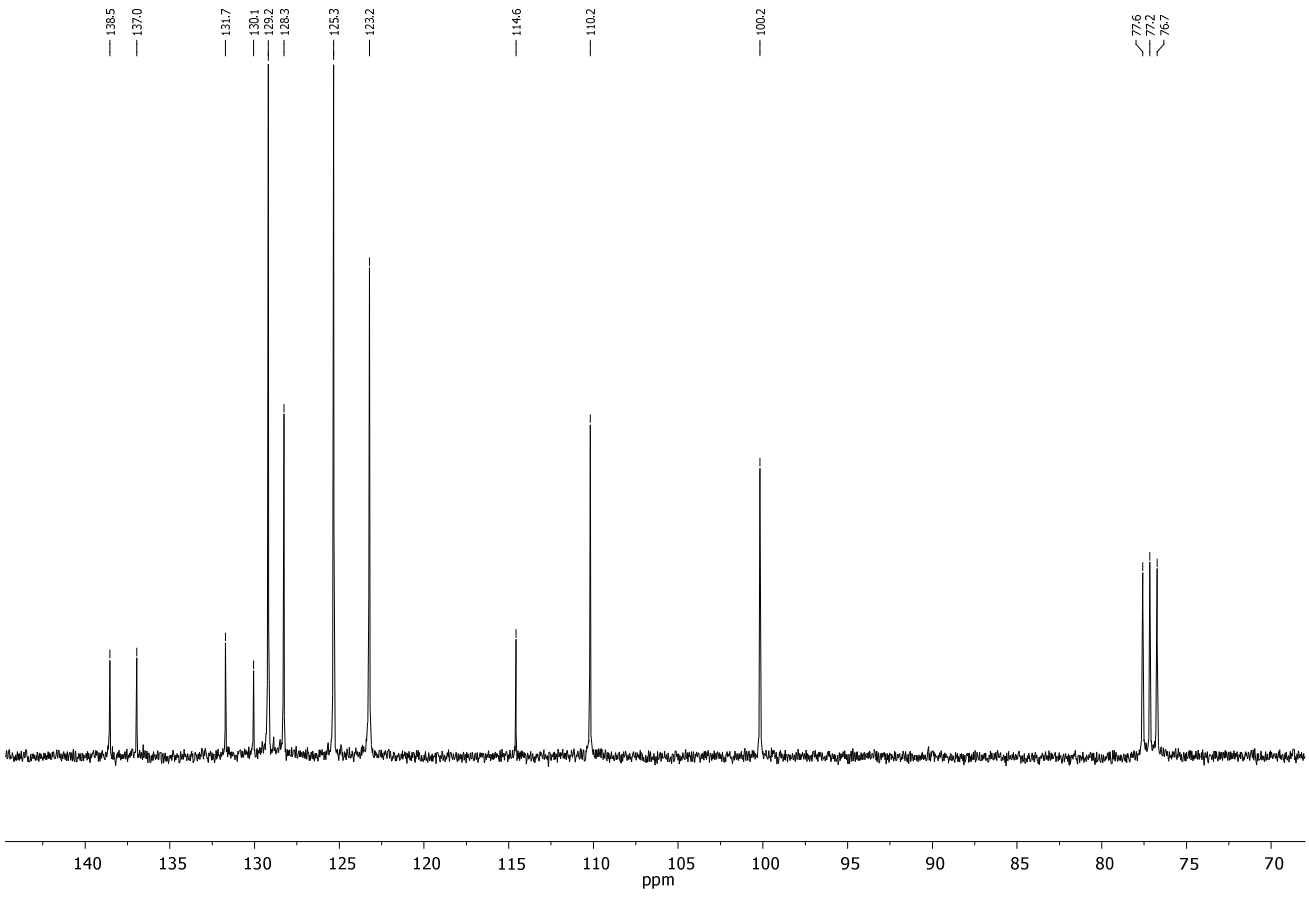

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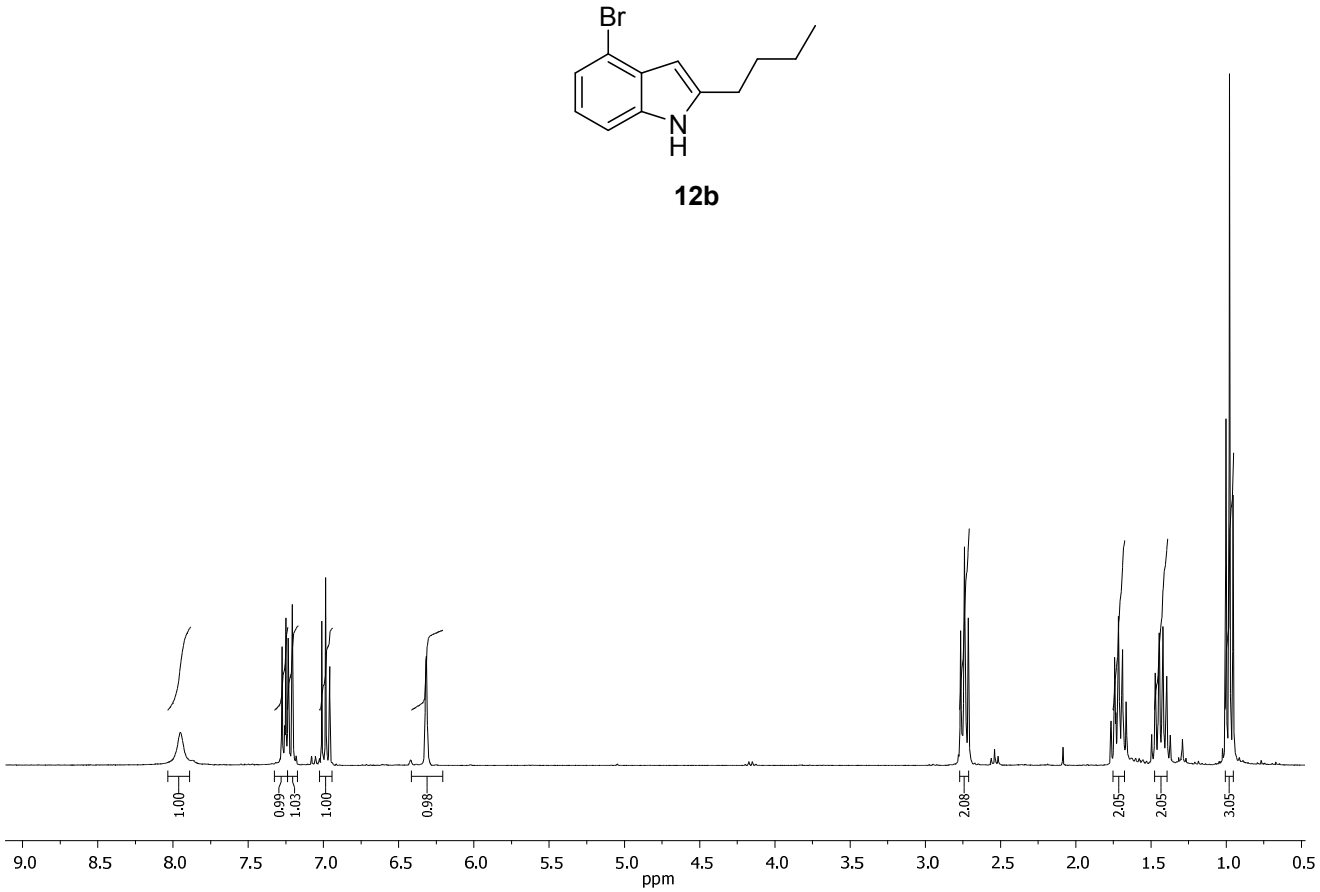

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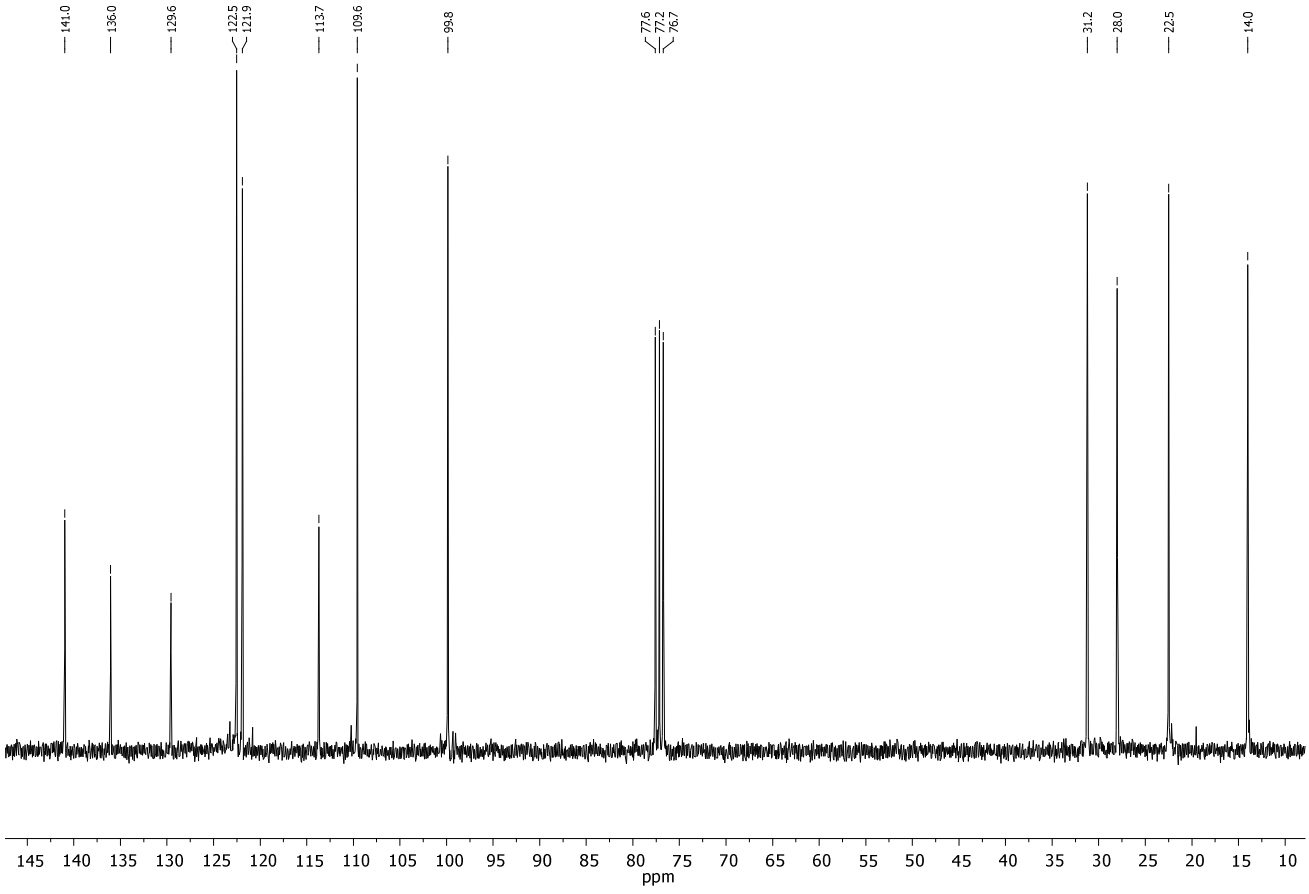

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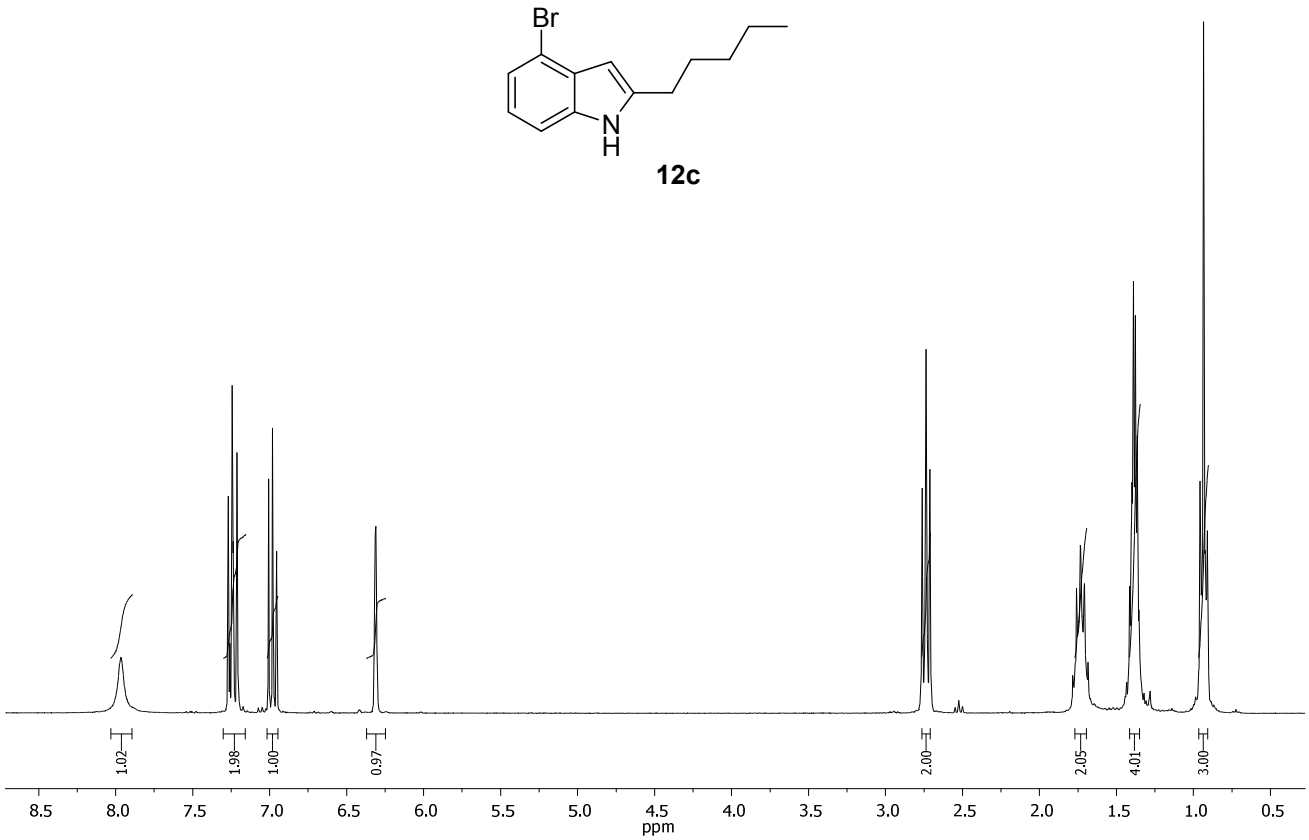

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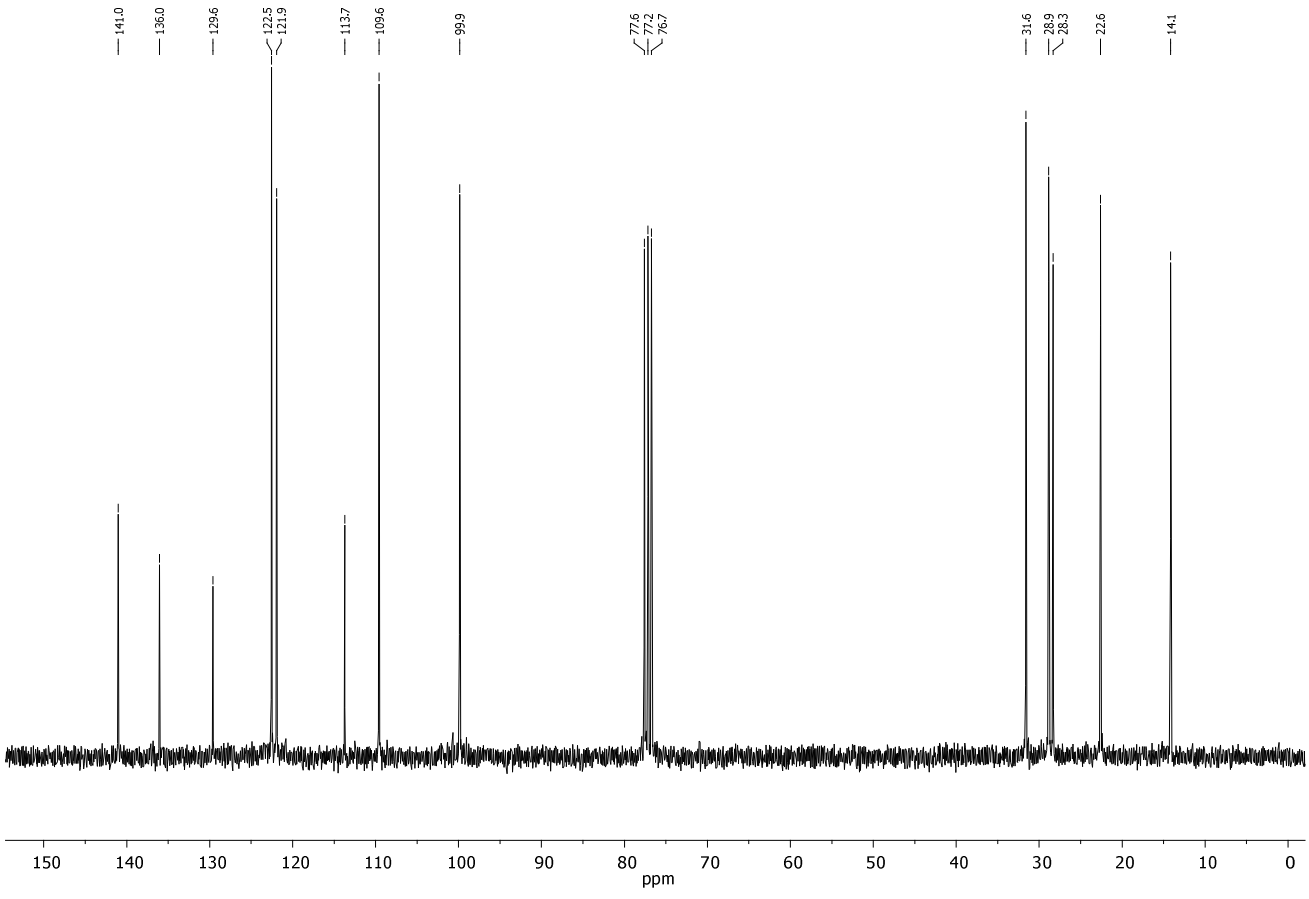

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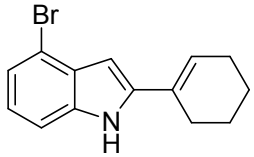
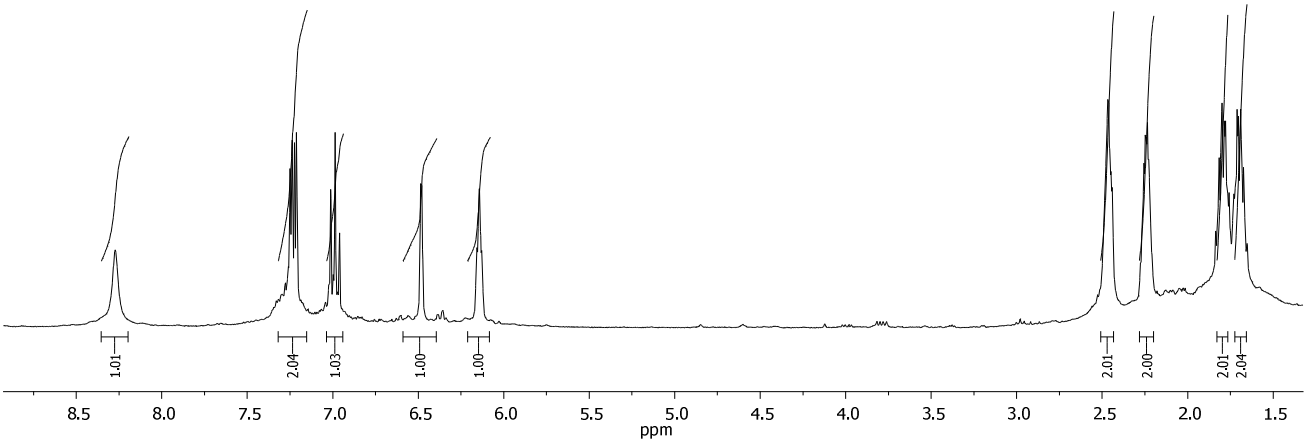
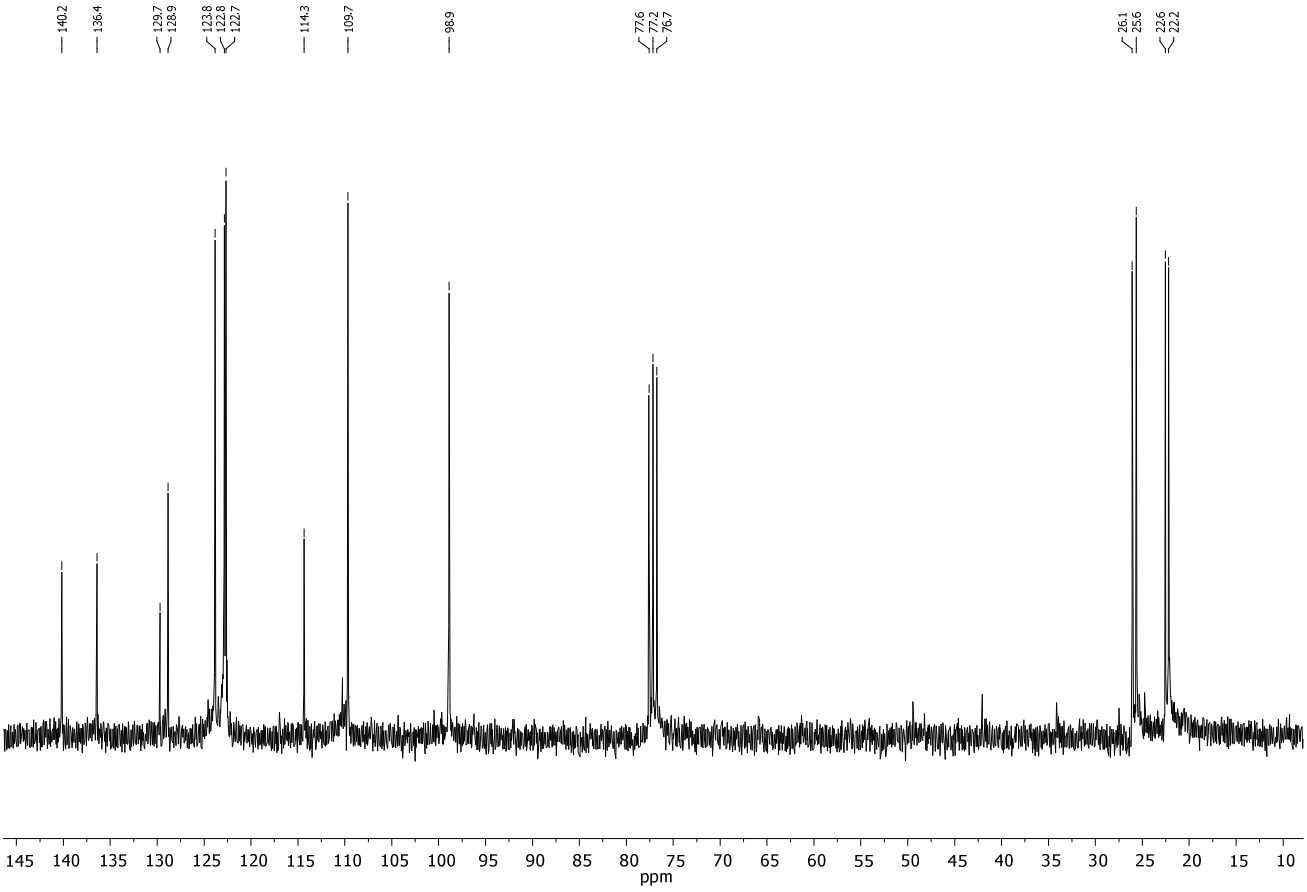


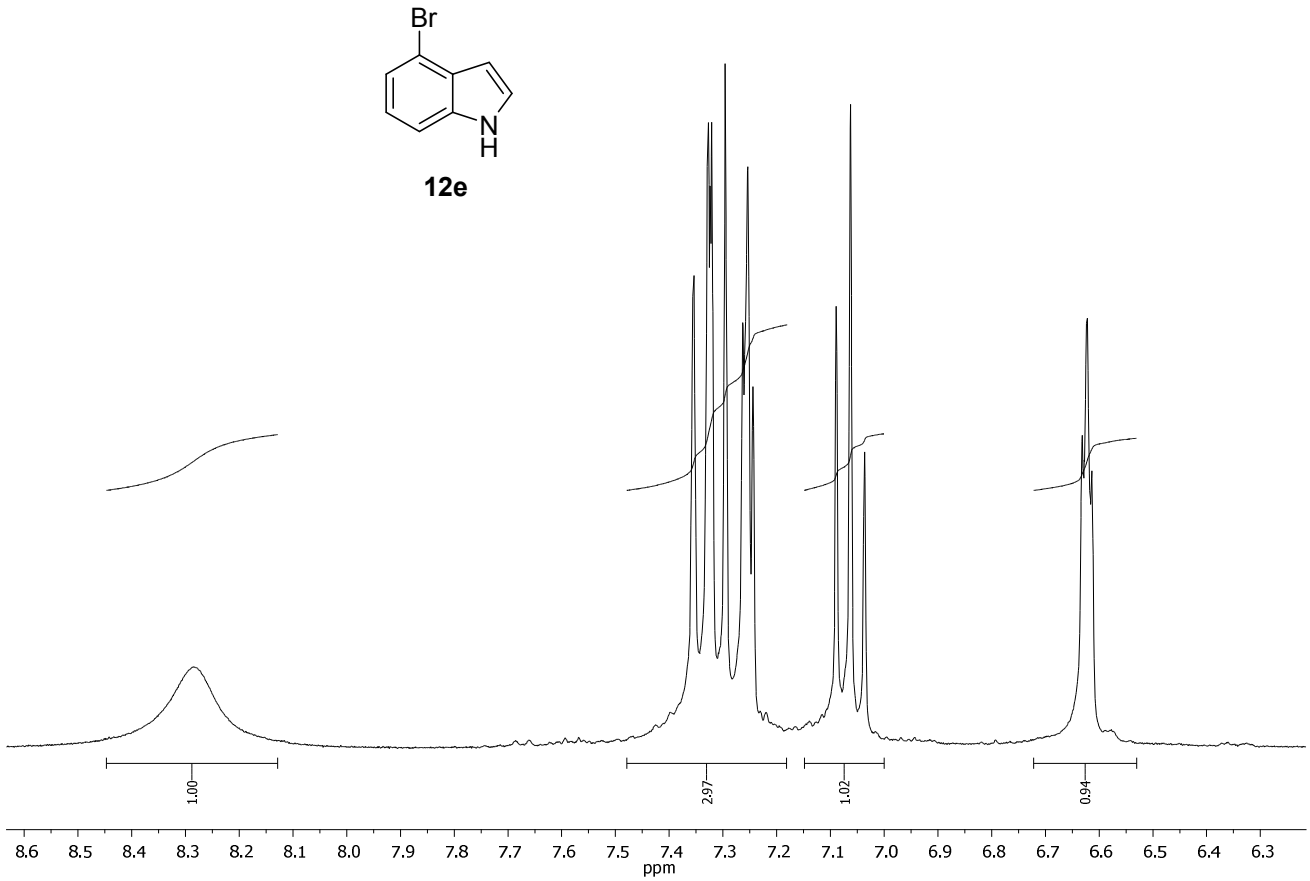
12d



^{13}C-NMR (75.4 MHz, $CDCl_3$):



^{1}H-NMR (300 MHz, $CDCl_3$):



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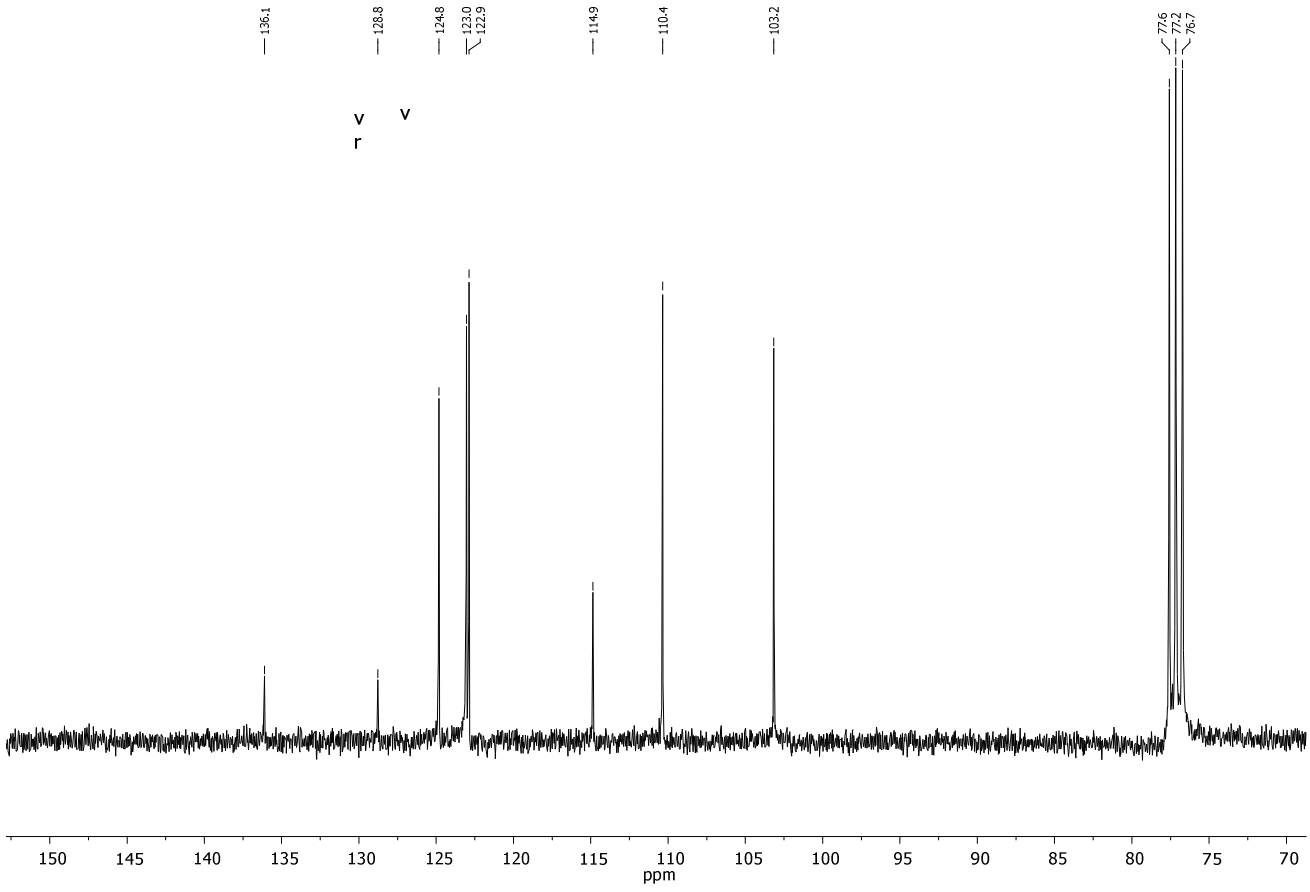

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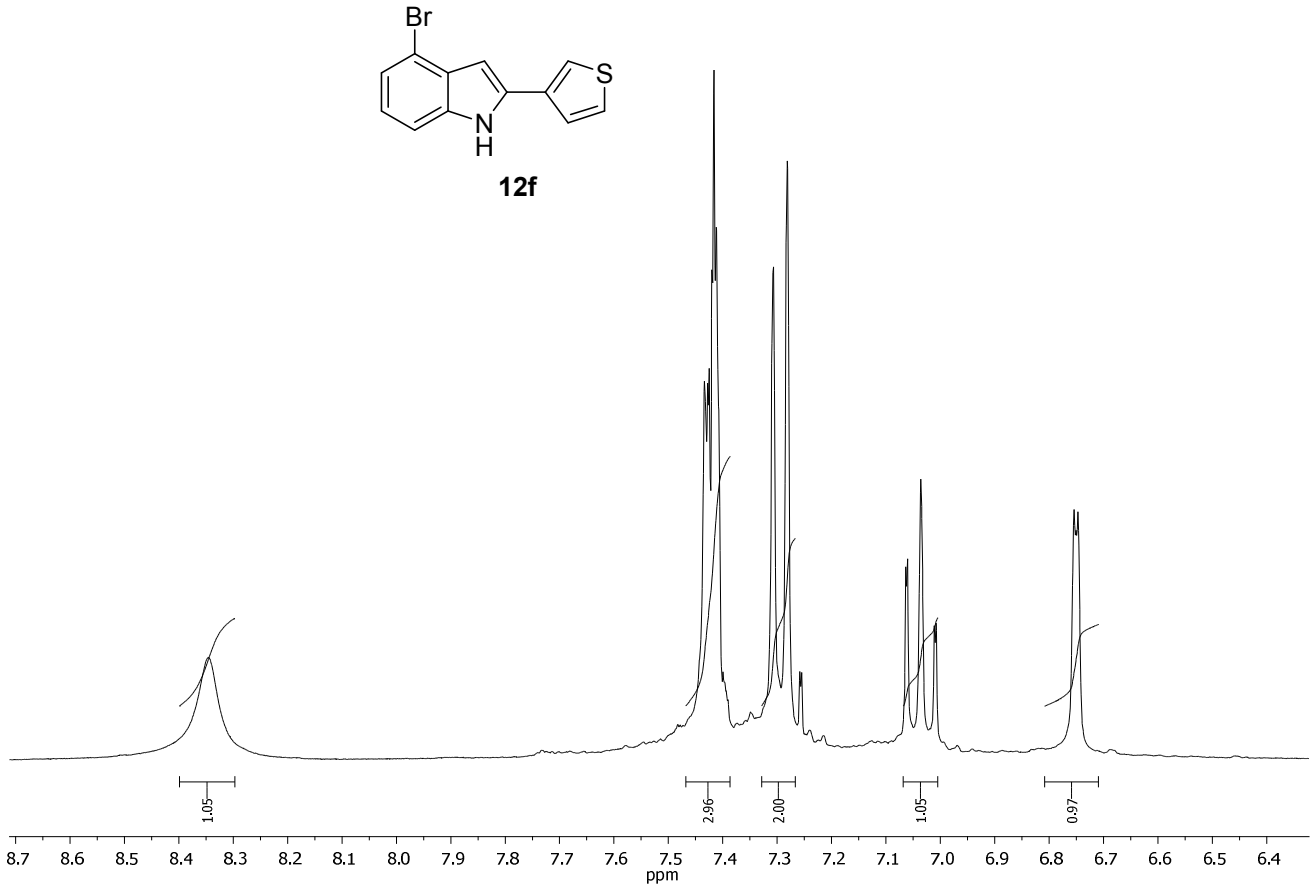

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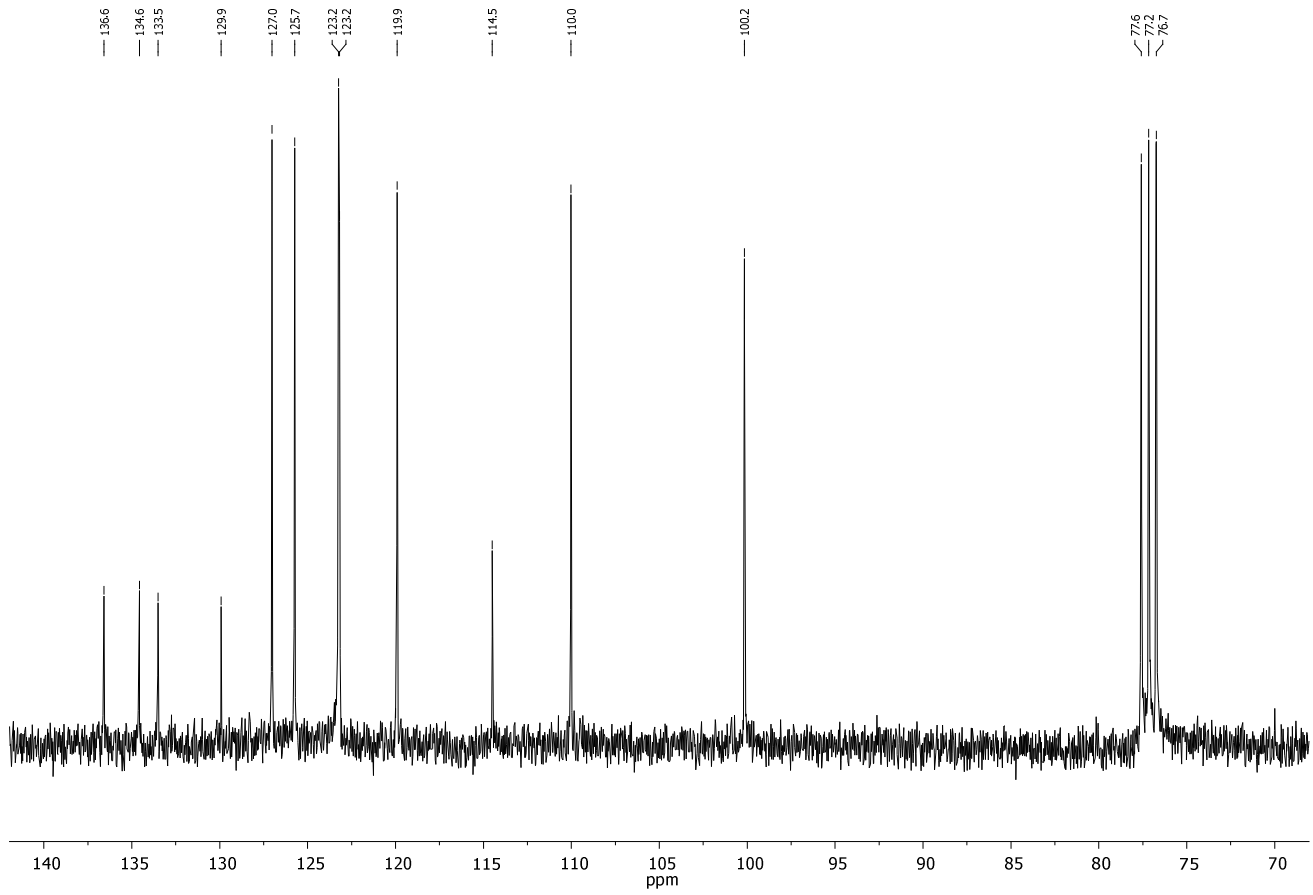

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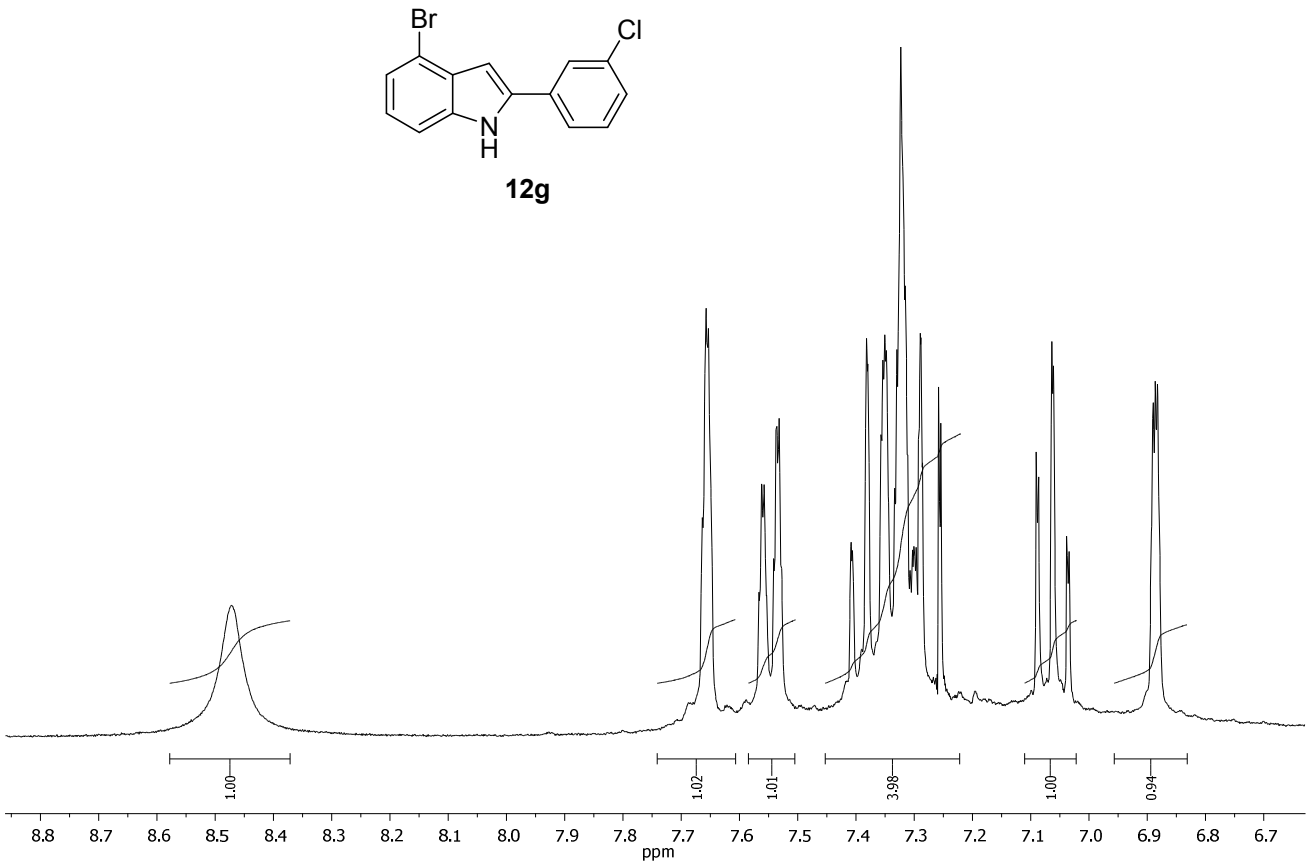

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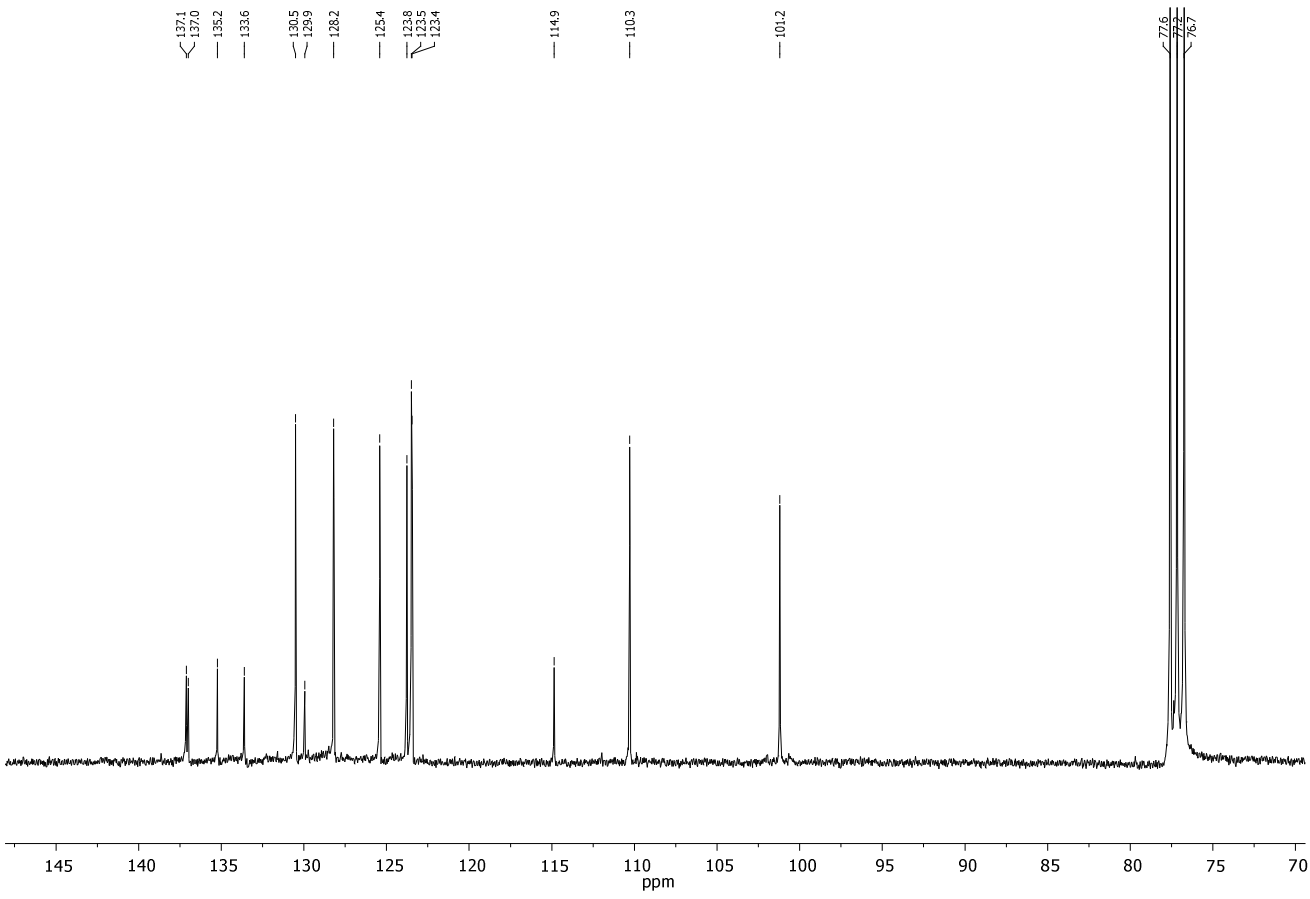

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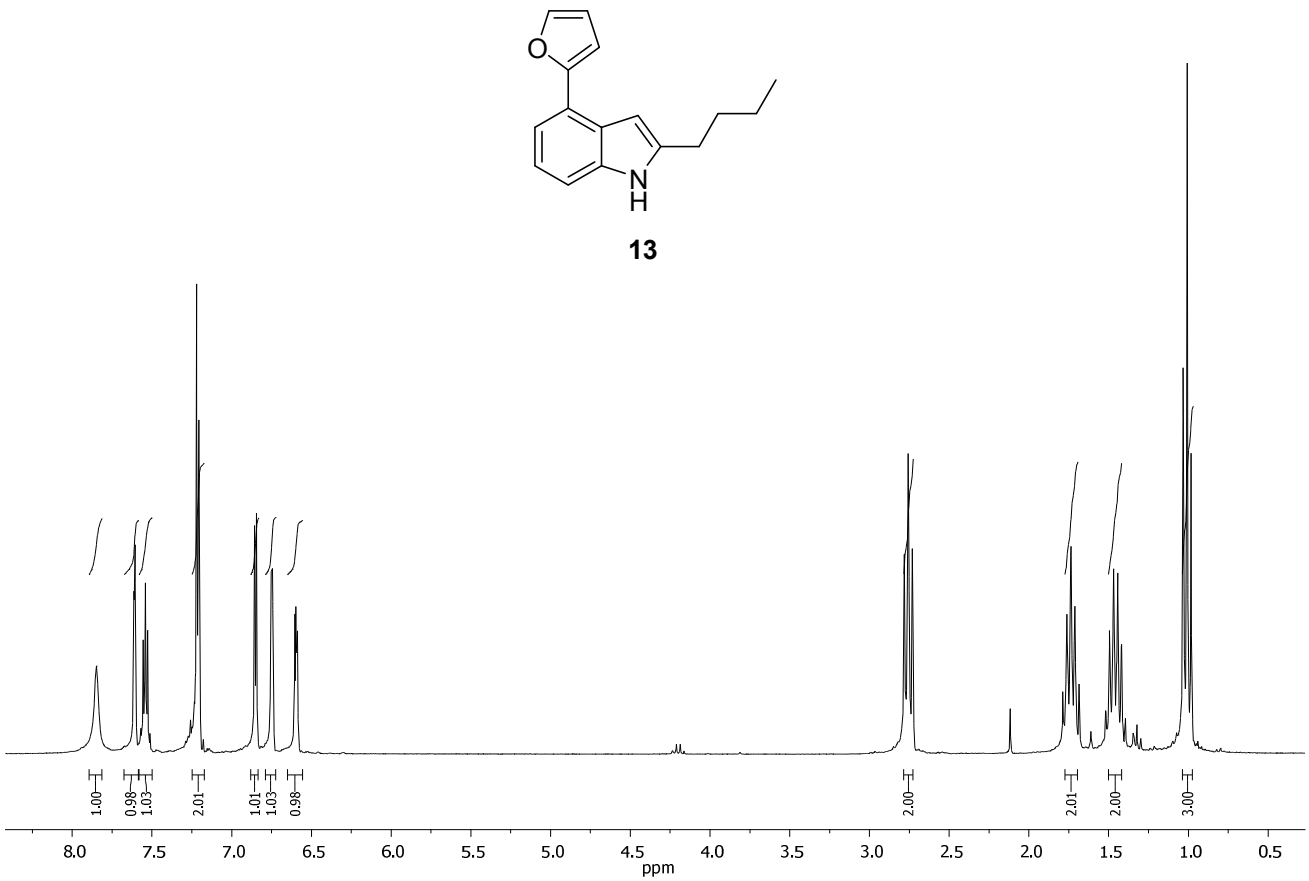

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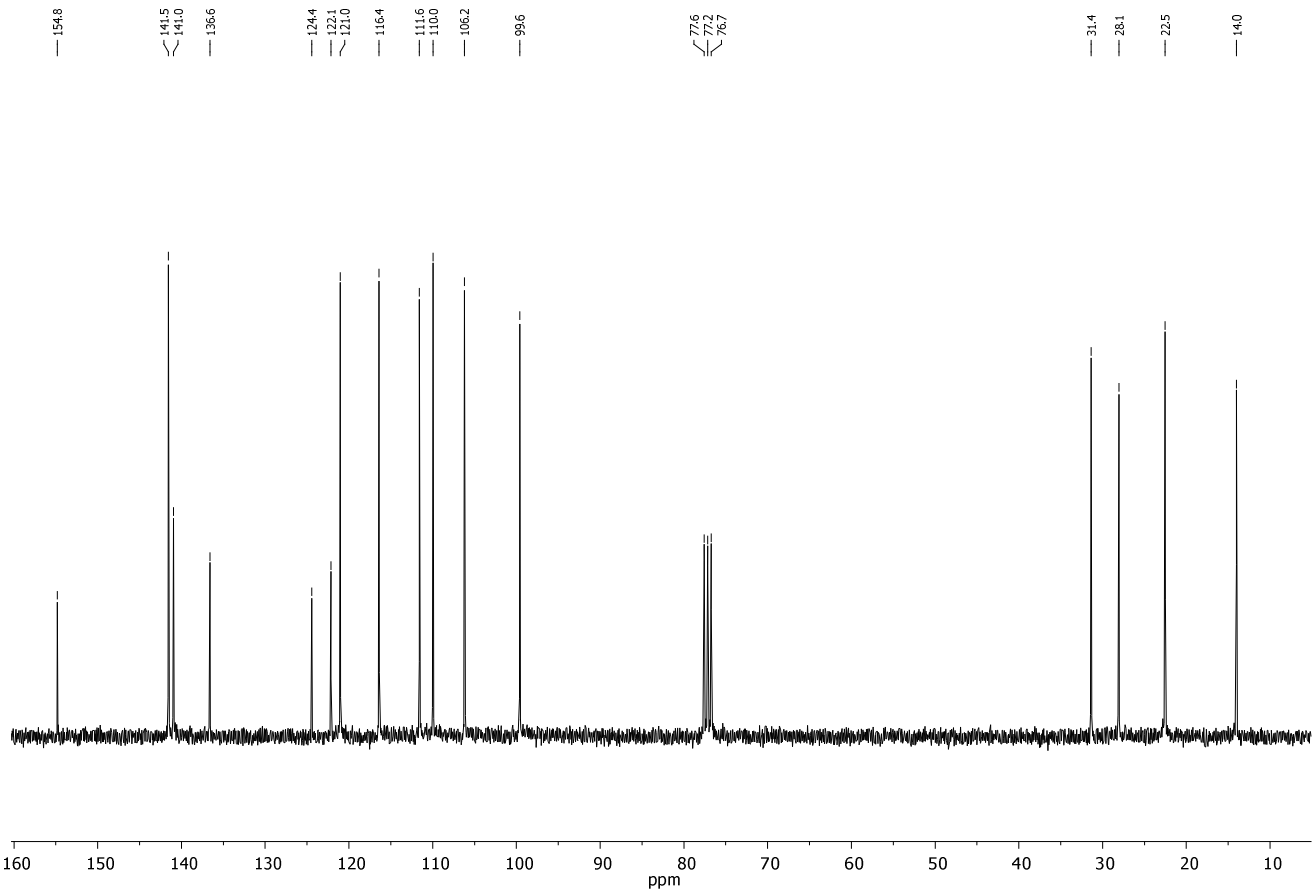

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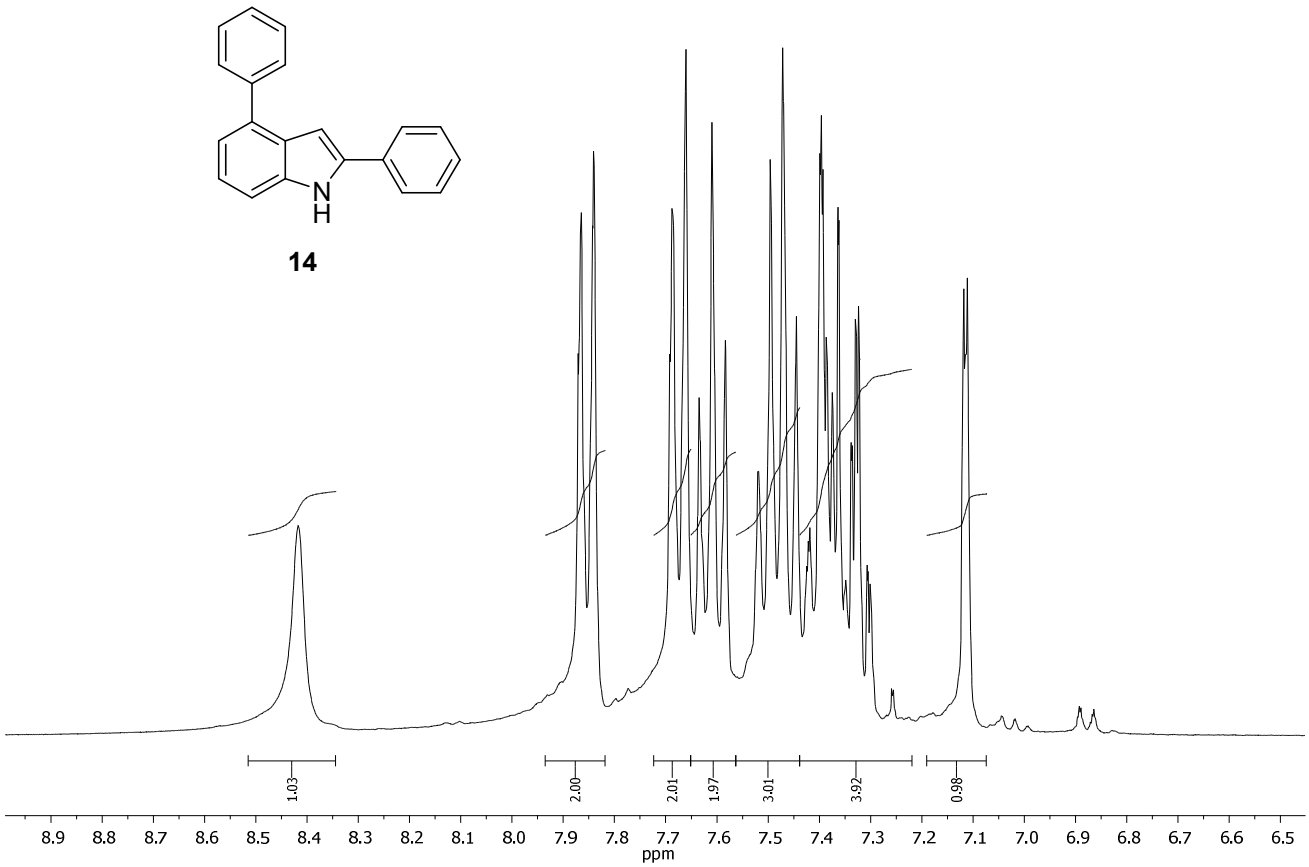

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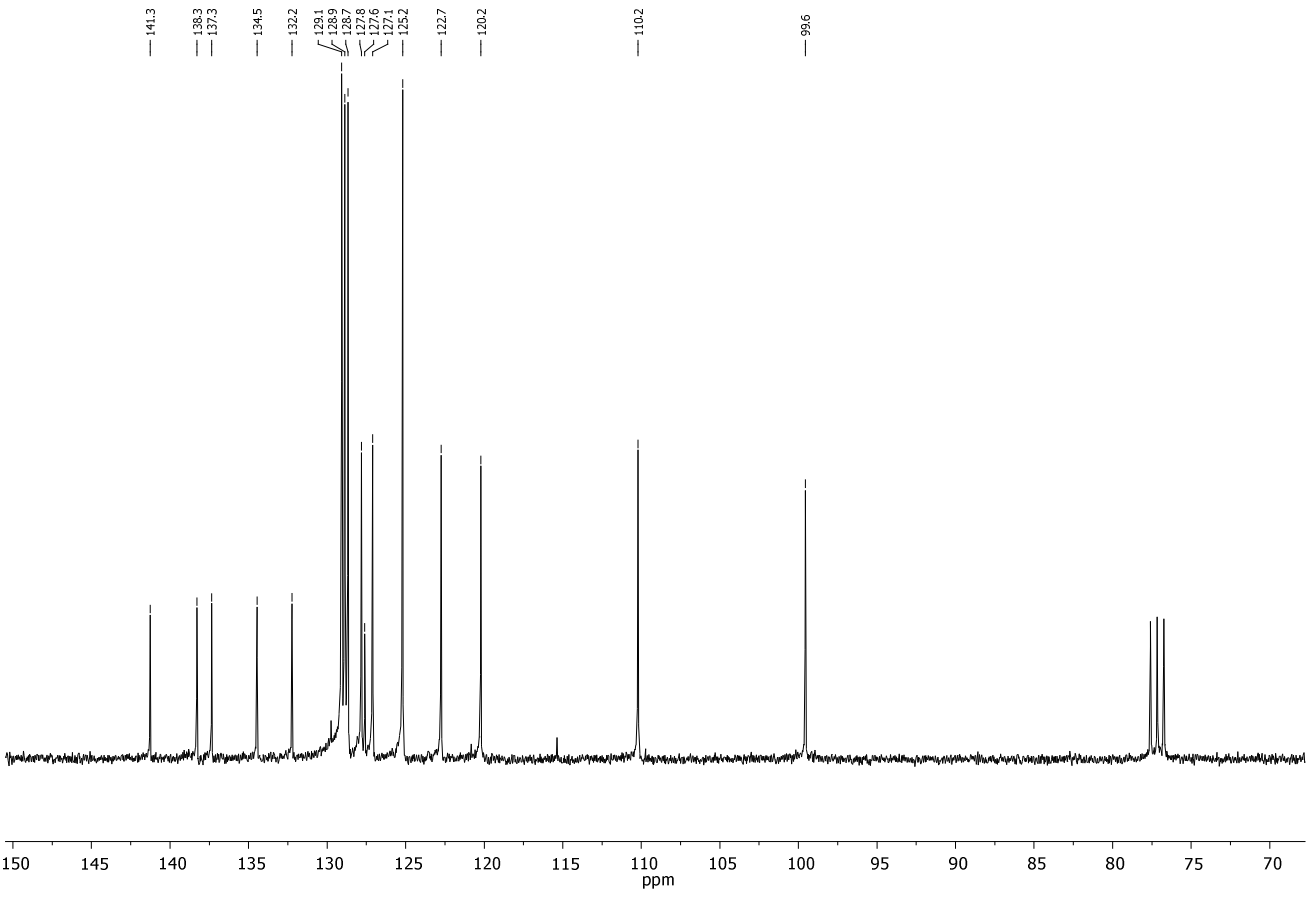

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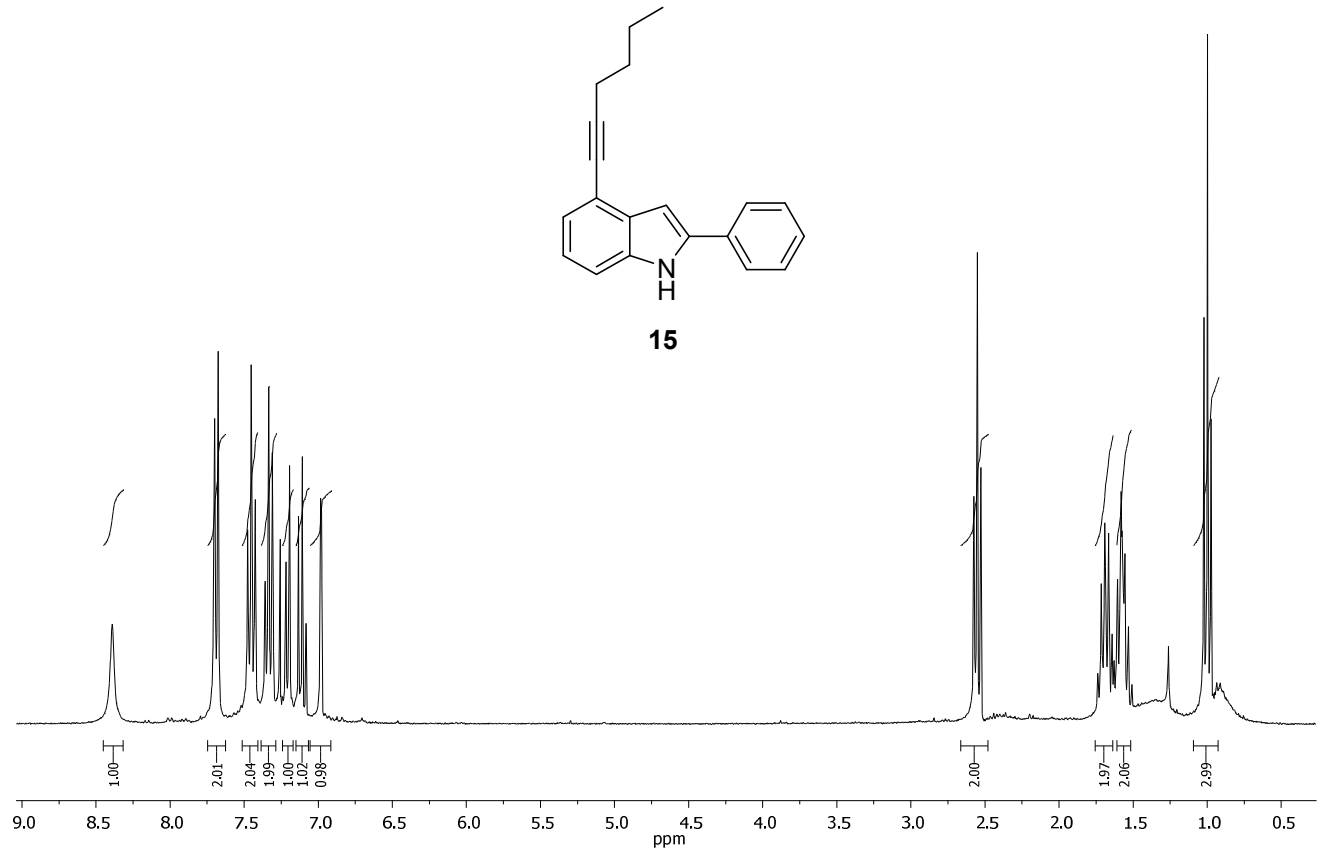

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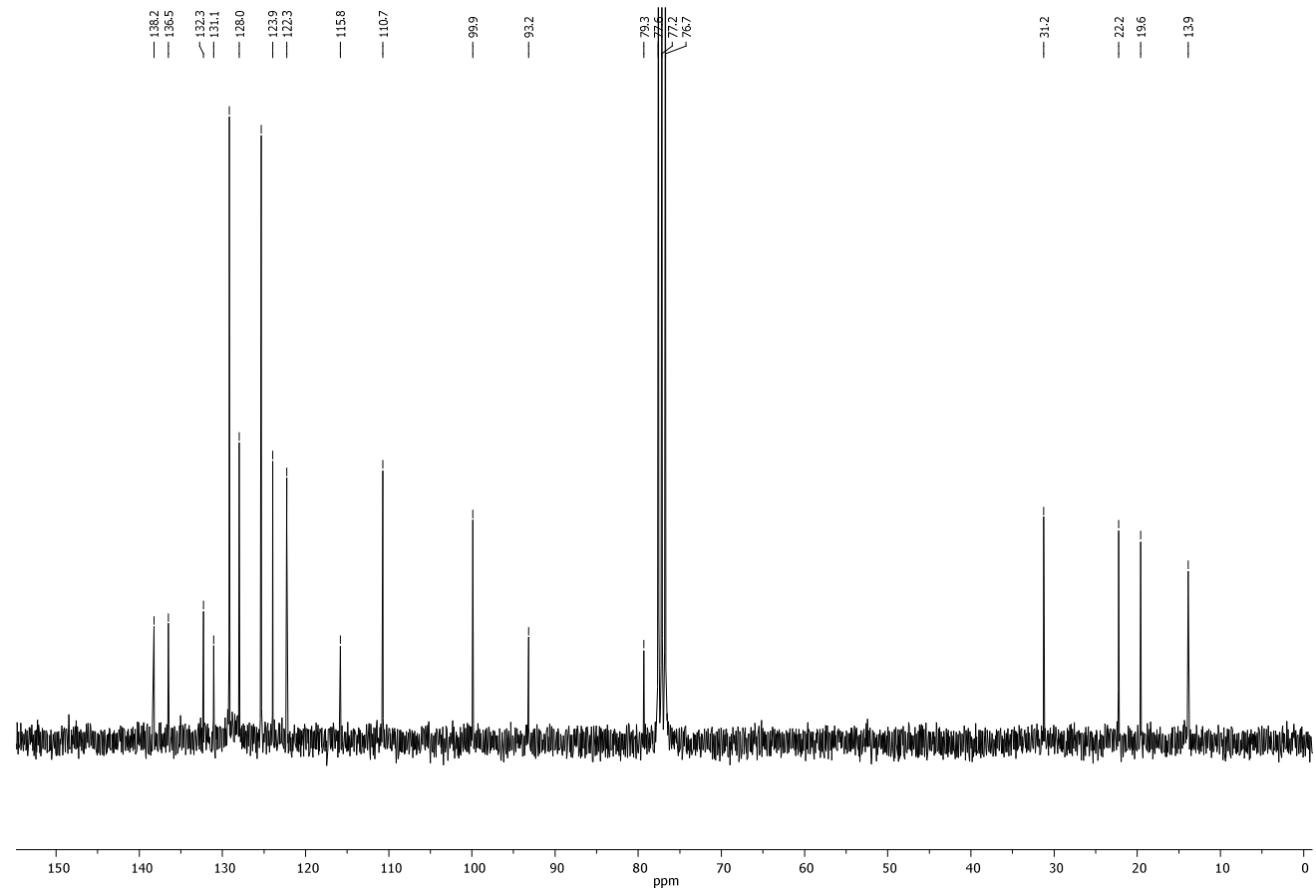

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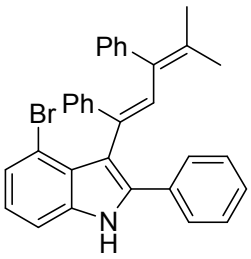

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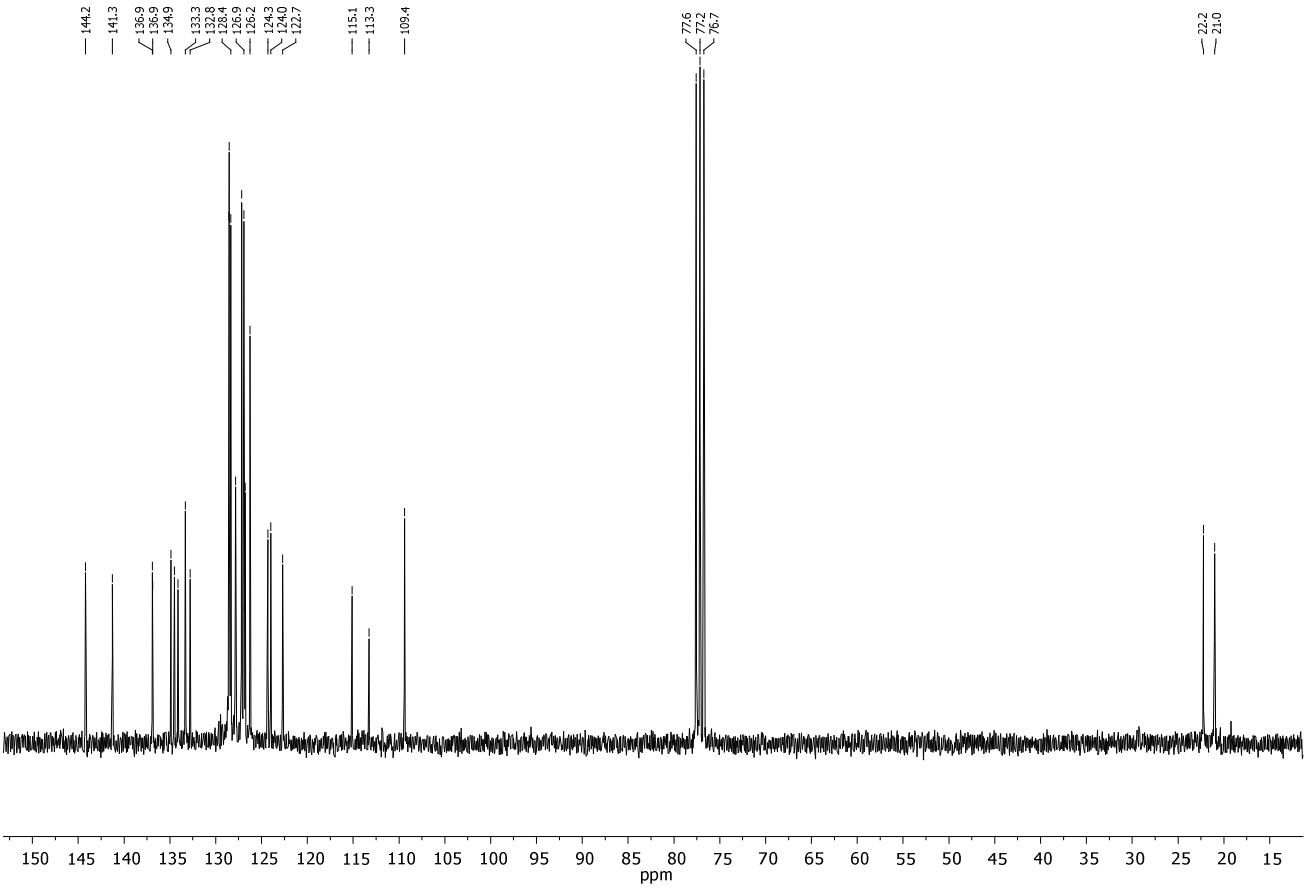

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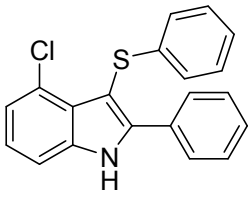

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^{13}C-NMR (75.4 MHz, $CDCl_3$):