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Supporting Information

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Palladium-Catalyzed Aryl Amination – Heck Cyclization Reaction Cascade: A One-Flask Approach to 3-Substituted Indoles

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General methods

Spectroscopic data and combustion analyses or HRMS-analyses are reported for all new compounds. Previously reported products were isolated in greater than 95% purity as determined by ^{1}H NMR and if no spectroscopic data were provided combustion analyses or HRMS-analyses are also reported. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR spectra were recorded in $CDCl_3$, d^6- DMSO or C_6D_6 on a Bruker Avance AV-500 instrument. Chemical shifts were measured in ppm and coupling constants in Hertz (Hz). In the cases of ^{1}H NMR and ^{13}C NMR tetramethylsilane and residual protonated solvent were used as internal references, respectively. All ^{13}C NMR spectra were proton decoupled. For ^{19}F NMR $CFCl_3$ was used as external reference. For substrates that could potentially lead to two indole regioisomers a full assignment is provided (based on HMBC and HSQC correlations in the ^{1}H/^{13}C 2D-spectrum). Thin layer chromatography was performed on aluminium plates precoated with silica gel (Merck; 60 F_{254}). Compounds were visualized by illumination using a UV lamp (254 nm) or by charring after dipping in a solution of ammonium molybdate (6.25 g) and cerium(IV)sulfate (2.5 g) in 10% aq. sulphuric acid (250 mL). Chromatographic purifications were performed by flash chromatography using silica gel (Machery-Nagel 60 M; 0.04-0.063 mm, 230-400 mesh). GC-FID for ligand screening reactions was performed on a Shimadzu GC-2010 instrument equipped with a Supelco Equity-1 fused silica capillary column (30mm x 0.25mm x 0.25µm) and a AOC-20i auto injector and a AOC-20s auto sampler using *n*-dodecane as internal standard. Toluene and THF were distilled from sodium/benzophenone and stored over 4 Å molsieves in screw-cap flask. Diethyl ether was predried over 4 Å molsieves and stored in screw-cap flasks. All commercially available reagents and bases were used as received. Elemental analyses were conducted either by dr. Johannes Theiner, the Microanalytical Laboratory, Institute of Physical Chemistry, University of Vienna, Austria or by the Analytical R&D department at Lundbeck A/S.

All ligand screenings were performed with 2-iodobromobenzene (0.33 mmol) and allyl amine (0.33 mmol) in 2 mL toluene in screw-cap vials. The reactions were set up *in air* and analyzed by GC-FID and the yields were estimated relative to an internal standard (*n*-dodecane, 0.33 mmol). The following procedure was followed: The vial was charged with Pd_2dba_3 (2.5%), ligand (5-10%), NaO(*t*-Bu) (0.83 mmol) followed by addition of a stock solution containing 2-iodobromobenzene, allyl amine, and *n*-dodecane. The vials were equipped with stir bars, sealed with PFTE septa screw-caps, and stirred for 15 h at 100 °C (cf. Table 1).

ligand	3-methyl indole	*N*-allyl aniline	2-bromo-*N*-allyl-aniline	PhBr	2-bromoiodobenzene	Sum
A PPh_3	0.0	0.0	0.0	37.8	41.3	79.1
B P(*o*-tol)$_3$	0.0	0.0	0.0	33.8	40.9	74.7
C 1-biphenyl-PCy_2	2.7	4.9	10.7	7.7	0.0	25.9
D X-Phos	4.8	4.1	0.0	0.0	0.0	8.9
E BINAP	0.0	3.0	91.6	0.0	0.0	94.7
F XantPhos	0.0	0.0	86.6	0.0	0.0	86.6
G Di-*i*-Pr-BPF	8.4	0.0	48.6	0.0	0.0	56.9
H DPPF	56.4	6.5	0.0	0.0	6.9	69.8
I DavePhos	26.1	4.3	0.0	0.0	0.0	30.4
J DPEphos	23.7	0.0	0.0	0.0	7.3	31.0
K P(*t*Bu)$_3$ – BF_4	3.7	4.3	20.3	11.4	26.9	66.7
L IPr-DH-imidazole	0.0	3.5	0.0	20.9	42.2	66.6
M 1-biphenyl-P(*t*Bu)$_2$	0.0	0.0	17.5	6.6	46.6	70.7
N IMes-dihydro_imidazole	0.0	0.0	0.0	17.6	62.9	80.6
O IMes-imidazole	0.0	0.0	0.0	14.9	66.7	81.6
P no ligand	0.0	0.0	0.0	8.2	65.6	73.8
Q no Pd/no ligand	0.0	0.0	0.0	0.0	96.6	96.6

Table 1. Results from ligand screening experiments

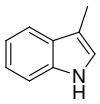
General procedure A: Preparation of 3-methyl indole derivatives

General procedure: To a 7 mL screw-cap vial was added Pd_2dba_3 (1.25 mol%), DPPF (5 mol%), NaO(*t*-Bu) (3.75 mmol), aryl halide (1.5mmol), toluene (4 mL) and allyl amine (1.5 mmol), and the vial was sealed. The mixture was heated from rt to 140 °C (over ~0.5h) and stirred at 140 °C for 5h. The mixture was cooled to rt, adsorbed onto silica gel, and purified by chromatography.

General procedure B: Diazotation of ortho-bromo-anilines[1]

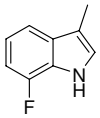
A mixture of *ortho*-bromo-aniline (1.0 equiv), H_2O (200 mL) and 37% aq. HCl (200 mL) was heated to 80 °C while stirring. The mixture was stirred 30 min followed by cooling to 0 °C on an ice/water bath. $NaNO_2$ (1.1 equiv) was added maintaining the internal temperature below 10 °C. The resulting clear, orange solution was stirred at 0 °C for 30 min followed by addition of KI (1.1 equiv) as a solution in H_2O (100 mL) keeping the internal temperature below 10 °C. The black suspension was allowed to reach room temperature and stirred for 12h. The suspension was extracted with 1,2-dichloroethane (200 mL), the organic layer was separated and washed successively with 10% aq. NaOH (200 mL), 1.0 M aq. $Na_2S_2O_3$ (200 mL), 10% aq. HCl (200 mL), sat. aq. $NaHCO_3$ (200 mL) and brine (200 mL). The organic layer was dried over $MgSO_4$, filtered, concentrated *in vacuo*, and finally filtered through a plug of silica gel (eluent: heptanes). The volatiles were removed *in vacuo* to afford the crude product.

3-Methyl-1*H*-indole, scatole (3)



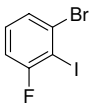
The general procedure A was followed using 1-bromo-2-iodo-benzene (424 mg, 193 µL, 1.5 mmol). After 2 h at 140 °C, the reaction mixture was purified. Yield 166 mg (85%) of the title compound as a colourless solid: mp 91-92 °C, lit.[2] mp 92-93 °C; TLC R_f = 0.47 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[3] δ 7.86 (bs, 1 H), 7.58 (d, *J* = 7.8 Hz, 1 H), 7.34 (d, *J* = 7.8 Hz, 1 H), 7.19 (t, *J* = 7.8 Hz, 1 H), 7.12 (t, *J* = 7.7 Hz, 1 H), 6.97 (s, 1 H), 2.34 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[3] δ 136.2, 128.3, 121.8, 121.5, 119.1, 118.8, 111.7, 110.9, 9.7.

7-Fluoro-3-methyl-1*H*-indole



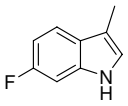
The general procedure A was followed using 1-bromo-3-fluoro-2-iodo-benzene (451 mg, 1.5 mmol). Yield 145 mg (63%) of the title compound as a pale yellow solid: mp 54-55 °C; TLC R_f = 0.51 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (bs, 1 H), 7.33 (d, *J* = 7.9 Hz, 1 H), 7.01 (dt, *J* = 7.8, 4.7 Hz, 1 H), 6.98 (q, *J* = 0.9 Hz, 1 H), 6.89 (dd, *J* = 11.1, 7.8, 1 H) 2.33 (d, *J* = 0.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5 (d, *J* = 243 Hz), 132.1 (d, *J* = 5.2 Hz), 124.5 (d, *J* = 12.1 Hz), 122.2, 119.3 (d, *J* = 6.0 Hz), 114.6 (d, *J* = 3.4 Hz), 112.6, (d, *J* = 2.6 Hz), 106.7 (d, *J* = 15.5 Hz), 9.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.1– -114.2 (m, 1 F); Anal. Calc'd for C_9H_8FN: C, 72.46; H, 5.41; N, 9.39. Found: C, 72.41; H, 5.49; N, 9.10.

Synthesis of 1-bromo-3-fluoro-2-iodo-benzene



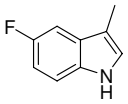
The general procedure B was followed using 2-bromo-6-fluoro-aniline (25.0 g, 0.13 mol). Yield 23.8 g (60%) of the title compound as a pale orange oil: TLC R_f = 0.58 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dt, *J* = 8.1, 1.3 Hz, 1 H), 7.20 (dt, *J* = 8.1, 5.7 Hz, 1 H), 6.99 (dt, *J* = 8.1, 1.3 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4 (d, *J* = 248 Hz), 132.7, 132.4 (d, *J* = 8.6 Hz), 130.1 (d, *J* = 3.4 Hz), 115.6 (d, *J* = 25.0 Hz), 92.3 (d, *J* = 27.6 Hz); ^{19}F NMR (471 MHz, $CDCl_3$) δ -83.0– -83.1 (m, 1 F); Anal. Calc'd for C_6H_3FBrI: C, 23.95; H, 1.00. Found: C, 23.95; H, 1.01.

6-Fluoro-3-methyl-1*H*-indole



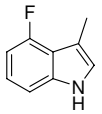
The general procedure A was followed using 1-bromo-4-fluoro-2-iodo-benzene (451 mg, 196 µL, 1.5 mmol). Yield 168 mg (75%) of the title compound as a colourless solid: mp 100-101 °C; TLC R_f = 0.40 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (bs, 1 H), 7.46 (dd, *J* = 8.8, 5.4 Hz, 1 H), 7.02 (dd, *J* = 9.8, 2.4 Hz, 1 H), 6.93 (q, *J* = 1.0 Hz, 1 H), 6.88 (ddd, *J* = 9.8, 8.8, 2.4 Hz, 1 H), 2.31 (d, *J* = 1.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4 (d, *J* = 237 Hz), 136.5, (d, *J* = 12.1 Hz), 125.3, 122.1 (d, *J* = 3.4 Hz), 119.9 (d, *J* = 10.3 Hz), 112.3, 108.1 (d, *J* = 24.1 Hz), 97.6 (d, *J* = 25.9 Hz), 10.1; ^{19}F NMR (471 MHz, $CDCl_3$) δ -122.2 (dt, *J* = 9.9, 5.4 Hz, 1 F); Anal. Calc'd for C_9H_8FN: C, 72.46; H, 5.41; N, 9.39. Found: C, 72.34, H, 5.55; N, 9.22.

5-Fluoro-3-methyl-1*H*-indole



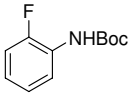
The general procedure A was followed using 2-bromo-4-fluoro-1-iodo-benzene (451 mg, 195 µL, 1.5 mmol). Yield 145 mg (65%) of the title compound as a colourless solid: mp 82-83 °C; TLC R_f = 0.36 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (bs, 1 H), 7.26 (dd, *J* = 9.4, 2.4 Hz, 1 H), 7.25 (dd, *J* = 9.2, 4.4 Hz, 1 H), 7.01 (s, 1 H), 6.93 (dd, *J* = 9.2, 2.4 Hz, 1 H), 2.29 (d, *J* = 1.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7 (d, *J* = 234 Hz), 132.7, 128.7 (d, *J* = 9.5 Hz), 123.4, 111.9 (d, *J* = 5.2 Hz), 111.5 (d, *J* = 9.5 Hz), 110.2 (d, *J* = 26.7 Hz), 103.7 (d, *J* = 23.3 Hz), 9.6; ^{19}F NMR (471 MHz, $CDCl_3$) δ -125.7 (dt, *J* = 9.2, 4.6 Hz, 1 F); Anal. Calc'd for C_9H_8FN: C, 72.46; H, 5.41; N, 9.39. Found: C, 72.40; H, 5.42; N, 9.20.

4-Fluoro-3-methyl-1*H*-indole



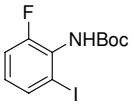
The general procedure A was followed using 2-bromo-1-fluoro-3-iodo-benzene (451 mg, 1,5 mmol). Yield 161 mg (72%) of the title compound as a pale orange oil: TLC R_f = 0.42 (heptanes:EtOAc = 4:1); ^{1}H NMR 7.89 (bs, 1 H), 7.08 (d, *J* = 7.9 Hz, 1 H), 7.04 (dt, *J* = 7.9, 4.6 Hz, 1 H), 6.87 (bs, 1 H), 6.71 (dd, *J* = 10.8, 7.8 Hz, 1 H); 2.45 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2 (d, *J* = 247 Hz), 139.5 (d, *J* = 11.2 Hz), 122.8 (d, *J* = 7.8 Hz), 121.9, 117.4 (d, *J* = 19.8 Hz), 110.9 (d, *J* = 3.0 Hz), 107.4 (d, *J* = 3.4 Hz), 104.7 (d, *J* = 19.8 Hz), 11.8 (d, *J* = 1.7 Hz); ^{19}F NMR (471 MHz, $CDCl_3$) δ -125.6 (dd, *J* = 10.8, 4.6 Hz, 1 F); HRMS calc'd for C_9H_8FN (M+) 149.0635. Found 149.0642.

2-Bromo-1-fluoro-3-iodo-benzene and (2-Fluoro-phenyl)-carbamic acid *tert*-butyl ester[4]



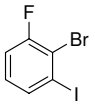
2-Fluoro-aniline (55.6 g, 0.5 mol) and Boc_2O (100.4 g, 0.46 mol) were heated neat to 80 °C while stirring under Ar. The resulting black mixture was stirred 2 h at 80 °C. Subsequently, the mixture was allowed to cool to room temperature. The resulting greyish precipitate was isolated and recrystallized from heptanes. Yield 92.3 g (95%) of the title compound as colourless needles: mp 48-49 °C (heptanes); TLC R_f = 0.58 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10-8.03 (m, 1 H); 7.11-7.02 (m, 2 H), 6.98-6.93 (m, 1 H), 6.69 (bs, 1 H), 1.53 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.8, 151.3 (d, *J* = 241 Hz), 126.3 (d, *J* = 10.3 Hz), 123.9 (d, *J* = 3.4 Hz), 122.2 (d, *J* = 7.8 Hz), 119.4, 114.1 (d, *J* = 19.8 Hz), 80.4, 27.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -133.3 (bs, 1 F); Anal. Calc'd for $C_{11}H_{14}FNO_2$: C, 62.54; H, 6.88; N, 6.63. Found: C, 62.23; H, 6.61; N, 6.85.

(2-Fluoro-6-iodo-phenyl)-carbamic acid *tert*-butyl ester[5]



(2-Fluoro-phenyl)-carbamic acid *tert*-butyl ester (31.7 g, 0.15 mol) was dissolved in THF (750 mL) and the solution was cooled to –78 °C in a CO_2(s)/acetone bath while stirring under Ar. 1.7 M *t*-BuLi (200 mL, 0.34 mol) in pentane was added dropwise while keeping the internal temperature below –50 °C. The resulting intensely orange solution was stirred for an additional 1 h at –78 °C and was then allowed to warm to -20 °C over 30 min. The mixture was cooled to –78 °C and I_2 (50.8 g, 0.20 mol) dissolved in THF (300 mL) was added keeping the internal temperature below –40 °C. The resulting dark purple solution was allowed to warm to room temperature overnight. The reaction mixture was diluted with diethyl ether (250 mL) and quenched with 1 M aq. $Na_2S_2O_3$ (250 mL). The organic layer was separated, washed with brine (250 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford a pale purple precipitate, which was recrystallized from heptanes. Yield 40.1 g (79%) of the title compound as colourless needles: mp 75-76 °C (heptanes); TLC R_f = 0.41 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 1 H); 7.11 (dd, *J* = 9.2, 8.2 Hz, 1 H), 6.95 (ddd, *J* = 8.2, 8.0, 5.3 Hz, 1 H), 5.98 (bs, 1 H), 1.51 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.6 (d, *J* = 254 Hz), 151.0, 132.4 (d, *J* = 3.4 Hz), 127.3 (d, *J* = 7.8 Hz), 126.0 (d, *J* = 13.8 Hz), 114.7 (d, *J* = 21.6 Hz), 97.2, 79.4, 26.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.1 (dd, *J* = 9.2, 5.3 Hz, 1 F); Anal. Calc'd for $C_{11}H_{13}FINO_2$: C, 39.19; H, 3.89; N, 4.16. Found: C, 38.91; H, 3.93; N, 4.27.

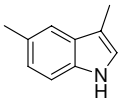
2-Bromo-1-fluoro-3-iodo-benzene



A solution of (2-fluoro-6-iodo-phenyl)-carbamic acid *tert*-butyl ester (22.5 g, 0.067 mol) in EtOH (100 mL) and 48% aq. HBr (100 mL) was stirred at room temperature. After 1 h a pale orange precipitate had formed and the effervescence had ceased. The solvent was removed *in vacuo* and the crude aniline hydrobromide was resuspended in 48% aq. HBr (100 mL). The suspension was heated to 60 °C for 10 min followed by cooling to 0°C in an ice/water bath. A solution of $NaNO_2$ (4.9 g, 70 mmol) in H_2O (25 ml) was added dropwise keeping the internal temperature below 5 °C. The resulting orange suspension of the diazonium salt was stirred for 15 min at 0 °C followed by addition of Cu-powder (1.3 g, 20 mmol). The mixture was heated to 80 °C for 1 h and subsequently cooled to room temperature. The mixture was extracted with 1,2-dichloroethane (250 mL) and the organic layer

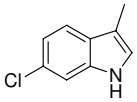
was washed with brine (250 mL), 10% aq. NaOH (250 mL), brine (250 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford an orange oil that crystallized upon standing. The crude product was recrystallized from EtOH. Yield 8.5 g (42% over two steps) of the title compound as colourless needles: mp 35-36 °C (EtOH), lit.[6] mp 31-33 °C; TLC R_f = 0.53 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$)[6] δ 7.68-7.64 (m, 1 H), 7.12-7.08 (m, 1 H), 7.05-7.00 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$)[6] δ 158.0 (d, *J* = 251 Hz), 134.6 (d, *J* = 3.4 Hz), 128.9 (d, *J* = 8.6 Hz), 116.7 (d, *J* = 21.6 Hz), 115.1 (d, *J* = 23.3 Hz), 101.6; ^{19}F NMR (471 MHz, $CDCl_3$) δ -96.4 (dd, *J* = 5.3, 8.2 Hz, 1 F).

3,5-Dimethyl-1*H*-indole



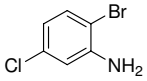
The general procedure A was followed using 2-bromo-1-iodo-4-methyl-benzene (445 mg, 214 µL, 1.5 mmol). Yield 159 mg (73%) of the title compound as a colourless solid: mp 73-74 °C, lit.[7] mp 73-74 °C; TLC R_f = 0.49 (heptanes:EtOAc = 4:1) ^{1}H NMR (500 MHz, $CDCl_3$)[8] δ 7.73 (bs, 1 H), 7.36 (s, 1 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.91 (s, 1 H), 2.46 (s, 3 H), 2.30 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[8] δ 134.6, 128.5, 128.3, 123.4, 121.7, 118.5, 111.2, 110.6, 21.5, 9.7.

6-Chloro-3-methyl-1*H*-indole



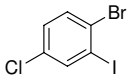
The general procedure A was followed using 1-bromo-4-chloro-2-iodo-benzene (476 mg, 1.5 mmol). Yield 138 mg (56%) of the title compound as a colourless solid: mp 118-119 °C; TLC R_f = 0.38 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (bs, 1 H), 7.47 (d, *J* = 8.4 Hz, 1 H), 7.33 (d, *J* = 1.5 Hz, 1 H), 7.08 (dd, *J* = 8.4, 1.5 Hz, 1 H), 6.96 (q, *J* = 1.0 Hz, 1 H), 2.31 (d, *J* = 1.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.5, 127.8, 126.9, 122.2, 119.8, 119.7, 111.9, 110.8, 9.6; Anal. Calc'd for C_9H_8ClN: C, 65.27; H, 4.87; N, 8.46. Found: C, 65.31; H, 5.04; N, 8.46.

1-bromo-4-chloro-2-iodo-benzene and 2-Bromo-5-chloro-aniline



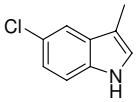
1-Bromo-4-chloro-2-nitrobenzene (30 g, 0.13 mol) was placed in a Parr-flask and dissolved in EtOAc (500 mL). Pt/C (2.48 g, 1.3 mmol, 10% on activated carbon) was added and the mixture was placed in a Parr-shaker. The mixture was flushed with N_2 and then subjected to H_2 (3 bar pressure) at room temperature for 30 min. The mixture was filtered through a plug of celite and the solvent was removed *in vacuo*. This afforded the product as a pale yellow solid. Recrystallization from heptanes gave the pure product. Yield 24.2 g (92%) of the title compound as pale yellow needles: mp 67-68 °C (hexane) lit.[9] mp 59 °C; TLC R_f = 0.36 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[10] δ 7.34 (d, *J* = 8.5 Hz, 1 H), 7.29 (d, *J* = 2.0 Hz, 1 H), 6.81 (dd, *J* = 8.5, 2.0 Hz, 1 H), 5.21 (bs, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.2, 134.9, 133.3, 122.9, 116.2, 106.1.

1-Bromo-4-chloro-2-iodo-benzene



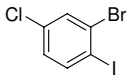
The general procedure B was followed using 2-bromo-5-chloro-aniline (10.0 g, 48 mmol). This afforded the product as a red/brown oil that crystallized upon standing and was recrystallized from EtOH. Yield 7.3 g (48%) of the title compound as colourless needles: mp 32-33 °C (EtOH); TLC R_f = 0.67 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 2.4 Hz, 1 H), 7.52 (d, *J* = 8.5 Hz, 1 H), 7.18 (dd, *J* = 8.5, 2.4 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.0, 133.9, 133.5, 130.1, 128.3, 101.9. Anal. Calc'd for C_6H_3BrClI: C, 22.71; H, 0.95. Found: C, 22.66; H, 0.93.

5-Chloro-3-methyl-1*H*-indole



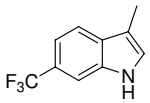
The general procedure A was followed using 2-bromo-4-chloro-1-iodo-benzene (476 mg, 1.5 mmol). Yield 149 mg (60%) of the title compound as a colourless solid: mp 112-113 °C, lit.[8] mp 113-115 °C; TLC R_f = 0.33 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[8] δ 7.89 (bs, 1 H), 7.54 (d, *J* = 1.9 Hz, 1 H), 7.25 (d, *J* = 8.5 Hz, 1 H), 7.13 (dd, *J* = 8.5, 1.9 Hz, 1 H), 6.98 (q, *J* = 1.0 Hz, 1 H), 2.29 (d, *J* = 1.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[8] δ 134.6, 129.4, 124.9, 123.0, 122.1, 118.4, 111.9, 111.6, 9.5.

Synthesis of 2-bromo-4-chloro-1-iodo-benzene



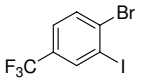
The general procedure B was followed using 2-bromo-4-chloro-aniline (20.0 g, 0.095 mol). The crude product was recrystallized from EtOH. Yield 15.4 g (50%) of the title compound as pale orange needles: mp 31-33 °C (EtOH), lit.[11] mp 33 °C; TLC R_f = 0.70 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1 H), 7.62 (d, *J* = 2.2 Hz, 1 H), 6.99 (dd, *J* = 8.4, 2.2 Hz, 1 H) ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.5, 134.7, 132.2, 130.1, 128.5, 98.3; Anal. Calc'd for C_6H_3BrClI: C, 22.71; H, 0.95. Found: C, 22.47; H, 0.96.

3-Methyl-6-trifluoromethyl-1*H*-indole



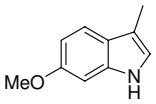
The general procedure A was followed using 1-bromo-2-iodo-4-trifluoromethylbenzene (351 mg, 1,5 mmol), Pd_2dba_3 (34.3 mg, 2.5 mol%) and DPPF (83.2 mg, 10 mol%). Yield 192 mg (64%) of the title compound as a pale yellow solid: mp 128-129 °C; TLC R_f = 0.37 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (bs, 1 H), 7.65 (d, *J* = 8.2 Hz, 1 H), 7.63 (s, 1 H), 7.35 (d, *J* = 8.2 Hz, 1 H), 7.11 (s, 1 H), 2.35 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.9, 130.4, 124.7 (q, *J* = 272 Hz), 124.0, 123.9 (q, *J* = 31.9 Hz), 119.1, 115.7 (q, *J* = 3.4 Hz), 112.0, 108.3 (q, *J* = 4.3 Hz), 9.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -61.0 (s, 3 F); Anal. Calc'd for $C_{10}H_8F_3N$: C, 60.30; H, 4.05; N, 7.03. Found: C, 60.10; H, 4.13; N, 6.80.

Synthesis of 1-bromo-2-iodo-4-trifluoromethylbenzene



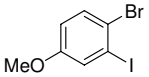
The general procedure B was followed using 2-bromo-5-trifluoromethyl-aniline (25.0 g, 0.10 mol). Yield 29.9 g (82%) of the title compound as a ruby red oil: TLC R_f = 0.67 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 1.9 Hz, 1 H), 7.74 (d, *J* = 8.5 Hz, 1 H), 7.45 (dd, *J* = 8.5, 1.9 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.2 (q, *J* = 4.3 Hz), 133.2 (q, *J* = 1.7 Hz), 132.06, 129.8 (q, *J* = 33.6 Hz), 125.2 (q, *J* = 3.4 Hz), 121.8 (q, *J* = 273 Hz), 100.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -63.3 (s, 3F); Anal. Calc'd for $C_7H_3BrF_3I$: C, 23.96; H, 0.86; Br, 22.77. Found: C, 24.08; H, 1.01; Br, 22.74.

6-Methoxy-3-methyl-1*H*-indole



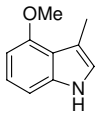
The general procedure A was followed using 1-bromo-2-iodo-4-methoxy-benzene (469 mg, 1.5 mol), Pd_2dba_3 (34.3 mg, 2.5 mol%) and DPPF (83.2 mg, 10 mol%). After 18 h at 140 °C, the reaction mixture was purified. Yield 164 (68%) of the title compound as a colourless solid: mp 125-126 °C, lit.[12] 125 ° (light petroleum); TLC R_f = 0.28 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[12] δ 7.72 (bs, 1 H), 7.44 (d, *J* = 8.5 Hz, 1 H), 6.85 (q, *J* = 1.0 Hz, 1 H), 6.84 (d, *J* = 2.1 Hz, 1 H), 6.79 (dd, *J* = 8.5, 2.1 Hz, 1 H), 3.84 (s, 3 H), 2.30 (d, *J* = 1.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[12] δ 156.6, 136.5, 122.3, 119.8, 118.9, 111.2, 108.5, 94.1, 55.2, 9.2.

Synthesis of 1-bromo-2-iodo-4-methoxy-benzene[13]



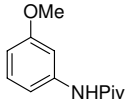
3-Iodo-anisole (23.4 g, 12.0 mL, 0.10 mol) was dissolved in CH_3CN (500 mL) while stirring under Ar. NBS (19.6 g, 0.11 mol) was added, and the resulting yellow solution was refluxed overnight. The mixture was allowed to cool to room temperature, concentrated *in vacuo*, and filtered through a plug of silica (eluent: heptanes. Evaporation afforded a viscous oil that was distilled (91-95 °C, 0.3 mbar, lit.[14] bp 124-126, 2.7 mbar). Yield 25.4 g (81%) of the title compound as a pale yellow oil: TLC R_f = 0.17 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.9 Hz, 1 H), 7.31 (d, *J* = 2.9 Hz, 1 H), 6.69 (dd, *J* = 8.9, 2.9 Hz, 1 H), 3.69 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 133.8, 126.5, 121.4, 117.2, 102.2, 56.8; Anal. Calc'd for C_7H_7BrIO: C, 26.87; H, 1.93. Found: C, 27.00; H, 1.94.

4-Methoxy-3-methyl-1*H*-indole



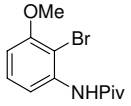
The general procedure A was followed using 2-bromo-1-iodo-3-methoxy-benzene (469 mg, 1.5 mmol), Pd_2dba_3 (34.3 mg, 2.5 mol%) and DPPF (83.2 mg, 10 mol%). After 18 h at 140 °C, the reaction mixture was purified. Yield 171 mg (71%) of the title compound as a pale orange solid: mp 58-59 °C, lit.[12] mp 50 °C; TLC R_f = 0.41 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[12] δ 7.79, (bs, 1 H), 7.05 (t, *J* = 8.0 Hz, 1 H), 6.93 (d, *J* =8.0 Hz, 1 H), 6.80 (s, 1 H), 6.46 (d, *J* = 8.0 Hz, 1 H), 3.91 (s, 3 H), 2.47 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[12] δ 155.7, 138.5, 123.1, 120.6, 118.5, 112.7, 104.8, 99.7, 55.6, 12.6.

2-bromo-1-iodo-3-methoxy-benzene and *N*-(3-Methoxy-phenyl)-2,2-dimethyl-propionamide[15]



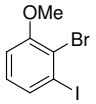
To a vigorously stirred suspension of *m*-anisidine (24.6 g, 0.20 mol) and sat. aq. Na_2CO_3 (250 mL) in 1,2-dichloroethane at room temperature was added trimethylacetyl chloride (24.1 g, 23.5 mL, 0.20 mol) dropwise. After 4 h at room temperature the organic layer was separated. The aqueous layer was extracted with 1,2-dichloroethane (200 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford pale red crystals that were recrystallized from heptanes. Yield 37.5 g (90%) of the title compound as a white solid: mp 124-125 °C (heptanes), lit.[16] mp 124-125 °C; TLC R_f = 0.29 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[17] δ 7.38 (t, *J* = 2.1 Hz, 1 H), 7.32 (bs, 1 H), 7.19 (t, *J* = 8.0 Hz), 6.93 (dd, *J* = 8.0, 2.1 Hz, 1 H), 6.66 (dd, *J* = 8.0, 2.1 Hz, 1 H), 3.80 (s, 3 H), 1.31 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$)[17] δ 177.0, 160.6, 139.7, 129.9, 112.2, 110.8, 105.7, 55.7, 40.1, 28.0.

***N*-(2-Bromo-3-methoxy-phenyl)-2,2-dimethyl-propionamide**[18]



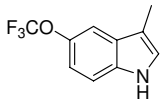
A solution of *N*-(3-methoxy-phenyl)-2,2-dimethyl-propionamide (24.9 g, 0.12 mol) in THF (300 mL) was cooled to 0 °C in an ice/water bath under Ar. To the resulting ruby red solution was added *n*-BuLi (2.0 M in cyclohexane, 150 mL, 0.30 mol) dropwise while stirring. After stirring for 2 h at 0 °C 1,2-dibromoethane (24.8 g, 11.4 mL, 0.13 mol) was added. The mixture was stirred for 1 h at 0 °C and for 1 h at room temperature, quenched with water, washed with brine (200 mL), dried over $MgSO_4$, filtered, and evaporated *in vacuo* to afford dark brown oil. The crude product was purified by silica gel chromatography (eluent: heptanes:EtOAc = 19:1). Yield 26.5 g (77%) of the title compound as a viscous pale yellow oil: TLC R_f = 0.44 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[19] δ 8.14 (bs, 1 H), 8.07 (dd, *J* = 8.2, 1.2 Hz, 1 H), 7.27 (t, *J* = 8.2 Hz, 1 H), 6.67, (dd, *J* = 8.2, 1.2 Hz, 1 H), 3.90 (s, 3 H), 1.36 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.1, 156.3, 137.5, 128.9, 114.2, 107.4, 103.6, 56.8, 40.7, 28.0.

2-Bromo-1-iodo-3-methoxy-benzene



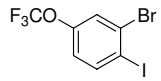
N-(2-Bromo-3-methoxy-phenyl)-2,2-dimethyl-propionamide (17.2 g, 60 mmol) was dissolved in EtOH (200 mL) and 37% aq. HCl (200 mL) was added while stirring. The mixture was refluxed for 6 h followed by cooling to room temperature during which a white precipitate was formed. The solvent was removed *in vacuo* and the resulting white precipitate was converted into 2-bromo-1-iodo-3-methoxy-benzene follwing general procedure B. This afforded a pale orange solid that was recrystallized from EtOH. Yield 10.9 g (58% over two steps) of the title compound as pale orange needles: mp 46-47 °C (EtOH); TLC R_f = 0.24 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$)[19] δ 7.49 (dd, *J* = 8.0, 1.4 Hz, 1 H), 7.00 (t, *J* = 8.0 Hz, 1 H), 6.86 (dd, *J* = 8.0, 1.4 Hz, 1 H), 3.87 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 132.5, 129.8, 119.9, 111.6, 103.5, 57.0.

3-Methyl-5-trifluoromethoxy-1*H*-indole



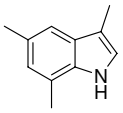
The general procedure A was followed using 2-bromo-1-iodo-4-trifluoromethoxy-benzene (550 mg, 1.5 mmol). Yield 228 mg (71%) of the title compound as a colourless solid: mp 52-53 °C; TLC R_f = 0.33 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (bs, 1 H), 7.41 (bs, 1 H), 7.30 (d, *J* = 8.7 Hz, 1 H), 7.06 (d, *J* = 8.7 Hz, 1 H), 7.04 (bs, 1 H), 2.31 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 134.9, 128.9, 123.9, 121.3 (q, *J* = 255 Hz); 116.2, 112.7, 111.8, 111.7, 9.9; ^{19}F NMR (471 MHz, $CDCl_3$) δ -58.5 (s, 3 F); Anal. Calc'd for $C_{10}H_8F_3NO$: C, 55.82; H, 3.75; N, 6.51. Found: C, 55.76; H, 3.75; N, 6.48.

Synthesis of 2-bromo-1-iodo-4-trifluoromethoxy-benzene



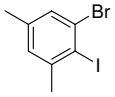
The general procedure B was followed using 2-bromo-4-trifluoromethoxy-aniline (10.0 g, 39 mmol). Yield 9.3 g (65%) of the title compound as a yellow oil; TLC R_f = 0.63 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 1 H), 7.51 (d, *J* = 2.5 Hz, 1 H), 6.91 (dd, *J* = 8.6, 2.5 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.8, 141.4, 130.9, 125.8, 121.5, 120.6 (q, *J* = 259 Hz), 99.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ -58.5 (s, 3 F); Anal. Calc'd for $C_7H_3BrF_3IO$ C, 22.92; H, 0.82; Br, 21.78. Found: C, 22.58; H, 1.03; Br, 21.5.

3,5,7-Trimethyl-1*H*-indole



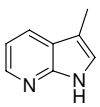
The general procedure A was followed using 1-bromo-2-iodo-3,5-dimethyl-benzene (466 mg, 1,5 mmol). Yield 142 mg (64%) of the title compound as pale orange needles: mp 68-69 °C, lit.[8] mp 68-70°C; TLC R_f = 0.47 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[8] δ 7.68 (bs, 1 H), 7.25 (s, 1 H), 6.93 (s, 1 H), 6.83 (s, 1 H), 2.44 (s, 6 H), 2.30 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$)[8] δ 134.6, 129.0, 128.5, 124.6, 121.8, 120.1, 116.5, 112.2, 21.8, 16.9, 10.2.

Synthesis of 1-bromo-2-iodo-3,5-dimethyl-benzene



The general procedure B was followed using 2-bromo-4,6-dimethyl-aniline (20.0 g, 0.10 mol). The crude product was purified by distillation (bp 74-82 °C, 0.04 mbar, lit.[20] bp 140-142 °C, 13 mbar). Yield 26.3 g (85%) of the title compound as a dark red oil: TLC R_f = 0.61 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$)[20] δ 7.29 (d, *J* = 1.9 Hz, 1 H), 6.96 (d, *J* = 1.9 Hz, 1 H), 2.50 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.8, 138.6, 130.1, 129.8, 128.4, 103.1, 30.3, 19.9.

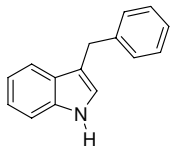
3-Methyl-1*H*-pyrrolo[2,3-b]pyridine



The general procedure A was followed using 2,3-dichloro-pyridine (222 mg, 1.5 mmol). After 20 h at 140 °C, the reaction mixture was purified by silica gel chromatography (eluent: heptanes:EtOAc = 2:1). Yield 121 mg (61%) of

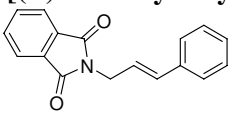
the title compound as a colourless solid: 130-131 °C; TLC R_f = 0.24 (heptanes:EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.59 (bs, 1 H), 8.31 (dd, *J* = 4.4, 1.3 Hz, 1 H), 7.89 (dd, *J* = 7.9, 1.3 Hz, 1 H), 7.07 (s, 1 H), 7.12 (dd, *J* = 7.9, 4.4 Hz, 1 H), 2.33 (d, *J* = 0.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.8, 142.5, 127.2, 122.1, 120.9, 115.2, 110.1, 9.8; HRMS calc'd for $C_8H_8N_2$ ($M+H^+$) 133.0706. Found 133.0765.

3-Benzyl-1*H*-indole



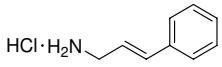
A 7 mL screw-cap vial was charged with (*E*)-3-phenyl-allyl-ammonium chloride (254 mg, 1.5 mmol), NaO(*t*-Bu) (505 mg, 5.25 mmol) and suspended in toluene (4 mL) *in air*. The vial was sealed with a screw-cap fitted with a PTFE septum and stirred 10 min at room temperature. Another vial was charged with Pd_2dba_3 (17.2 mg, 1.25 mol%), DPPF (41.6 mg, 5 mol%) and 1-bromo-2-iodo-benzene (424 mg, 193 µL, 1.5 mmol) *in air*. The vial was placed in an aluminium block, charged with the toluene suspension and sealed with a screw-cap fitted with a PTFE septum. The resulting suspension was heated from room temperature to 140 °C (over 30 min) while stirring and the mixture was kept at that temperature for 12 h. The reaction mixture was subsequently cooled to room temperature, adsorbed onto silica gel and purified by silica gel chromatography (eluent: heptanes:EtOAc = 19:1). Yield 183 mg (59%) of the title compound: mp 95-98 °C.[21] mp 104-106 °C; TLC R_f = 0.38 (heptanes:EtOAc = 4:1) ^{1}H NMR (500 MHz, $CDCl_3$)[21] δ 7.92 (bs, 1 H), 7.52 (d, *J* = 8.0 Hz, 1 H), 7.34 (d, *J* = 7.9 Hz, 1 H), 7.30-7.27 (m, 5 H), 7.18 (t, *J* = 7.9 Hz, 1 H), 7.07 (t, *J* = 7.9 Hz, 1 H), 6.90 (s, 1 H), 4.11 (s, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$)[21] δ 141.6, 136.8, 129.4, 129.1, 128.7, 126.3, 122.7, 122.5, 119.8, 119.6, 116.2, 111.5, 32.0.

(E)-3-phenyl-allyl-ammonium chloride and 2-[(*E*)-3-Phenyl-allyl]-isoindole-1,3-dione[22,23]



Cinnamyl bromide (39.4 g, 0.20 mol) was dissolved in DMF (500 mL, dried over molsieves 4 Å) and potassium phthalimide (44.5 g, 0.24 mol) was added in one portion while stirring under Ar. The mixture was stirred for 10 h at room temperature, diluted with diethyl ether (1.5 L), washed with brine (4 x 500 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting pale orange crystals were recrystallized from toluene. Yield 37.2 g, (70%) as colourless needles: mp 154-155 °C (toluene), lit.[24] mp 155-156 °C (toluene); TLC R_f = 0.29 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[24] δ 7.86 (dd, *J* = 5.3, 2.9 Hz, 2 H), 7.72 (dd, *J* = 5.3, 2.9 Hz, 2 H), 7.36-7.33 (m, 2 H), 7.30-7.26 (m, 2 H), 7.22 (tt, *J* = 7.2, 1.2 Hz, 1 H), 6.66 (bd, *J* = 15.8 Hz, 1 H), 6.26 (dt, *J* = 15.8, 6.5 Hz, 1 H), 4.45 (dd, *J* = 6.5, 1.1 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$)[24] δ 168.3, 136.7, 134.4, 134.2, 132.6, 128.9, 128.3, 126.9, 123.7, 123.1, 40.1.

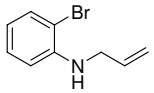
(*E*)-3-Phenyl-allyl-ammonium chloride[25]



A solution of 2-[(*E*)-3-phenyl-allyl]-isoindole-1,3-dione (30 g, 0.11 mol) and hydrazine monohydrate (16.3 g, 15.8 mL, 0.33 mol) in methanol (500 mL) was heated to reflux with vigorous stirring under Ar. The solution was heated at reflux for 1 h. Copious amounts of a flaky white precipitate was generated during that time. The mixture was cooled to 0 °C in an ice/water bath and the precipitate was filtered off. The filtrate was concentrated *in vacuo*

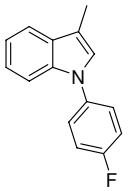
resulting in a heterogenous mixture, which was resuspended in diethyl ether (500 mL), filtered and, and the filtrate was concentrated *in vacuo*. This resulted in a pale yellow oil that was dissolved in EtOH (100 mL) and converted into the hydrocloride using 2.0 M HCl (300 mL) in diethyl ether. The mixture was concentrated *in vacuo*, filtered and recrystallized from EtOH. Yield 12.9 g (69%) of the title compound as colourless needles: mp 235-237 °C lit.[26] mp 233 °C; TLC R_f = 0.21 (EtOAc:EtOH:AcOH = 17:2:1); ^{1}H NMR (500 MHz, DMSO) δ 8.32 (bs, 3 H), 7.45-7.41 (m, 2 H), 7.40-7.35 (m, 2 H), 7.30 (tt, *J* = 7.2, 1.3 Hz, 1 H), 6.75 (d, *J* = 16.1 Hz, 1 H), 6.31 (dt, *J* = 16.1, 6.5 Hz, 1 H), 3.60 (d, *J* = 6.5 Hz, 2 H); ^{13}C NMR (126 MHz, DMSO) δ 134.9, 133.5, 128.0, 127.4, 125.5, 121.3, 39.6; Anal. Calc'd for $C_9H_{12}ClN$: C, 63.72; H, 7.13; N, 8.26. Found: C, 63.45; H, 7.17; N, 8.30.

_N_-Allyl-(2-bromo-phenyl)-amine (2)



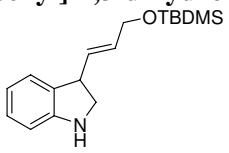
The general procedure A was followed using 1-bromo-2-iodo-benzene (424 mg, 193 µL, 1.5 mmol). The mixture was stirred until the aluminium block had reached 140 ° (30 min) and cooled in an ice/water bath. The reaction mixture was adsorbed onto silica gel and purified by silica gel chromatography (eluent:pentane). Yield 286 mg (91%) of the title compound as a colourless oil: TLC R_f = 0.56 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[27] δ 7.42 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.18-7.13 (m, 1 H), 6.62 (dd, *J* = 8.1, 1.2 Hz, 1 H), 6.58-6.54 (m, 1 H), 5.95 (ddt, *J* = 17.2, 10.4, 5.2 Hz, 1 H), 5.29 (dm, *J* = 17.2 Hz, 1 H), 5.11 (dm, *J* = 10.4 Hz, 1 H), 4.47 (bs, 1 H), 3.83 (d, *J* = 5.2 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$)[27] δ 144.6, 134.5, 132.2, 128.3, 117.7, 116.3, 111.5, 109.6, 46.1.

1-(4-Fluoro-phenyl)-3-methylindole (4)



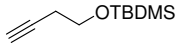
A 7 mL screw-cap vial was charged with Pd_2dba_3 (17.2 mg, 1.25 mol%), DPPF (41.6 mg, 5 mol%), NaO(*t*-Bu) (505 mg, 5.25 mmol) and 1-bromo-2-iodo-benzene (424 mg, 193 µL, 1.5 mmol) *in air*. The vial was placed in an aluminium block, charged with toluene (4.0 mL) and allyl amine (85.7 mg, 113 µL, 1.5 mmol) and sealed with a screw-cap fitted with a PTFE septum. The resulting suspension was heated from room temperature to 140 °C (over 30 min). The mixture was stirred at 140 °C for 2 h followed by addition of Pd_2dba_3 (17.2 mg, 1.25 mol%), DPPF (41.6 mg, 5 mol%) and 1-bromo-4-fluoro-benzene (315 mg, 198 µL) as a suspension in toluene (1.0 mL). The mixture was stirred at 140 °C for 18 h, cooled to room temperature, adsorbed onto silica gel, and purified by silica gel chromatography (eluent: pentane). Yield 68 mg (30%) of the title compound as a pale yellow oil: TLC R_f = 0.20 (pentane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.5 Hz, 1 H), 7.46-7.39 (m, 3 H), 7.24-7.14 (m, 4 H), 7.06 (s, 1 H), 2.38 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2 (d, *J* = 245 Hz), 136.6, 136.5 (d, *J* = 2.8 Hz), 130.0, 126.2 (d, *J* = 7.8 Hz), 126.0, 122.9, 120.2, 119.7, 116.8 (d, *J* = 22.4 Hz), 113.2, 110.5, 10.0; ^{19}F NMR (471 MHz, $CDCl_3$) δ -116.4– -116.5 (m, 1 F); Anal. Calc'd for $C_{15}H_{12}FN$: C, 79.98; H, 5.37; N, 6.22. Found: C, 80.11; H, 5.07; N, 6.25.

3-[(*E*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-propenyl]-2,3-dihydro-1*H*-indole



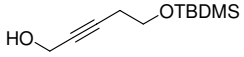
The general procedure A was followed using 1-bromo-2-iodo-benzene (424 mg, 193 µL, 1.5 mmol), (*E*)-5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-enylamine (323 mg, 1.5 mmol), Pd_2dba_3 (34.3 mg, 2.5 mol%), DPPF (83.2 mg, 10 mol%) and Cs_2CO_3 (1222 mg, 3.75 mmol). After 18 h at 140 °C, the reaction mixture was purified by silica gel chromatography (eluent: heptanes:EtOAc = 19:1). Yield 142 mg (33%) of the title compound as a pale yellow oil: TLC R_f = 0.21 (heptanes:EtOAc = 9 :1); ^{1}H NMR (500 MHz, C_6D_6) δ 7.11 (d, *J* = 7.5 Hz, 1 H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.77 (t, *J* = 7.6 Hz, 1 H), 6.44 (d, *J* = 7.6 Hz, 1 H), 5.74 (ddt, *J* = 15.4, 8.8, 1.5 Hz, 1 H), 5.58 (dt, *J* = 15.4, 4.9 Hz, 1 H), 4.05 (d, *J* = 4.9 Hz, 2 H), 3.75 (q, *J* = 8.8 Hz, 1 H), 3.27 (t, *J* = 8.8 Hz, 1 H), 2.90 (t, *J* = 8.8 Hz), 2.83 (bs, 1 H), 0.97 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.6, 132.6, 131.6, 131.0, 128.1, 124.9, 119.3, 110.1, 64.0, 54.2, 46.0, 26.4, 18.9, -4.7; HRMS calc'd for $C_{17}H_{28}NOSi$ ($M+H^+$) 290.1935. Found 290.1930.

(*E*)-5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-enylamine and 1-(*tert*-butyl-dimethyl-silanyloxy)-but-3-yne[28]



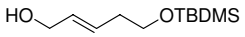
tert-Butyldimethylsilyl chloride (72.4 g, 0.48, mol) was added to a solution of but-3-yn-1-ol (28.0 g, 30.3 mL, 0.40 mol) and imidazole (59.9 g, 0.88 mol) in THF (500 mL) while stirring under Ar. The mixture was stirred 1 h at room temperature, which resulted in the formation of a colourless precipitate. The mixture was filtered through a plug of silica gel (eluent: heptanes), and concentrated *in vacuo* to afford a pale yellow oil. The oil was distilled (bp 31-32 °C, 0.2 mbar, lit.[29] bp 45-46 °C, 3.3 mbar). Yield 66.4 g (90%) of the title compound as a colourless oil: TLC R_f = 0.83 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[29] δ 3.76 (t, *J* = 7.1 Hz, 2 H), 2.41 (dt, *J* = 7.1, 2.4 Hz, 2 H), 1.97 (t, *J* = 2.4 Hz, 1 H), 0.91 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$)[30] δ 81.9, 69.6, 62.1, 26.3, 23.2, 18.7, -4.9.

5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-yn-1-ol[31]



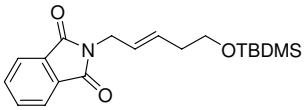
1-(*tert*-Butyl-dimethyl-silanyloxy)-but-3-yne (36.8g, 0.20 mmol) was dissolved in THF (500 mL). The solution was cooled to –78 °C in a CO_2(s)/acetone bath while stirring under Ar. 2.0 M *n*-BuLi (100 mL, 0.20 mmol) in cyclohexane was added dropwise keeping the internal temperature below –50 °C. The resulting pale yellow solution was stirred at –78 °C for 1 h. Paraformaldehyde (30.0 g, 1.0 mol) was added in one portion and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with sat. aq. NH_4Cl (250 mL) and the aqueous layer was extracted with diethyl ether (2 x 250 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to furnish the crude propargylic alcohol as an oil. The product was purified by distillation (bp 103-105 °C, 0.5 mbar, lit.[32] bp 110 °C, 0.3 mbar).Yield 26.2 g (61%) of the title compound as a colourless oil: TLC R_f = 0.45 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[32] δ 4.24 (bs, 2 H), 3.73 (t, *J* = 7.2 Hz, 2 H), 2.44 (tt, *J* = 7.2, 2.0 Hz, 2 H), 1.56 (bs, 1 H), 0.90 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$)[33] δ 83.8, 79.9, 62.2, 51.7, 26.3, 23.5, 18.7, -4.9.

(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-en-1-ol[34]



A solution of Red-Al (68.3 mL, 0.22 mol, 65% in toluene) in diethyl ether (250 mL) was cooled to 0 °C in an ice/water bath while stirring under Ar. 5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-yn-1-ol (30.0 g, 0.14 mol) as a solution in diethyl ether (250 mL) was added dropwise while keeping the internal temperature below 5 °C. Following complete addition, the mixture was stirred 10 min at 0 °C and then allowed to warm to room temperature. The mixture was stirred at room temperature for 16 h, quenched with sat. aq. NH_4Cl (250 mL), and diluted with diethyl ether (500 mL). The aqueous layer was extracted with diethyl ether (500 mL). The combined organic phases were washed with brine (500 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude oil was purified by silica gel chromatography (eluent: heptanes:EtOAc = 9:1 → 4:1). Yield 23.6 g (78%) of the title compound as a colourless oil: TLC R_f = 0.27 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[35] δ 5.74-5.66 (m, 2 H), 4.11-4.07 (m, 2 H), 3.65 (t, *J* = 7.1 Hz, 2 H), 2.31-2.24 (m, 2 H), 1.34 (t, *J* = 5.8 Hz, 1 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 129.4, 127.9, 62.3, 61.1, 34.2, 24.3, 16.7, -6.9.

2-[(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-enyl]-isoindole-1,3-dione[22,23]



Mesyl chloride (12.6 g, 8.5 mL, 0.11 mol) was added dropwise to a solution of (*E*)-5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-en-1-ol (21.6 g, 0.10 mol) and triethylamine (11.2 g, 15.3 mL, 0.11 mol) in 1,2-dichloroethane (250 mL) cooled to 0 °C in an ice/water bath while stirring under Ar. The mixture was stirred 1 h at 0 °C during which time a colourless precipitate was generated. Subsequently the mixture was diluted with diethyl ether (500 mL), washed with brine (3 x 500 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product as a pale yellow oil. Yield 34.6 g (quantitative). The crude product was carried on directly since the allylic mesylate decomposes upon standing

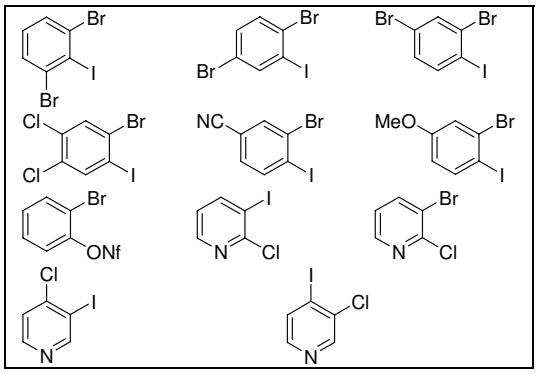
The crude mesylate (34.6 g, 0.10 mol) was dissolved in DMF (250 mL, dried over molsieves 4 Å) and potassium phthalimide (22.3 g, 0.12 mol) was added in one portion while stirring under Ar. The mixture was stirred for 10 h at room temperature, diluted with diethyl ether (500 mL), washed with brine (4 x 250 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude pale yellow oil was purified using silica gel chromatography (eluent: heptanes → heptanes:EtOAc = 9:1). Yield 22.4 g (65% over two steps) of the title compound as a colourless oil that crystallized upon standing: mp 30-31 °C; TLC R_f = 0.26 (heptanes:EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2 H), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2 H), 5.73 (dtt, *J* = 15.4, 6.8, 1.1 Hz, 1 H), 5.59 (dtt, *J* = 15.4, 6.1, 1.3 Hz, 1 H), 4.24 (dd, *J* = 6.1, 1.1 Hz, 2 H), 3.61 (t, *J* = 6.6 Hz, 2 H), 2.23 (q, *J* = 6.7 Hz, 2 H), 0.84 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 135.7, 134.1, 133.2, 127.0, 125.1, 64.4, 41.3, 37.6, 27.7, 20.1, -3.5; Anal. Calc'd for $C_{19}H_{27}NO_3Si$: C, 66.05; H, 7.88; N, 4.05. Found: C, 65.82; H, 7.89; N, 4.35.

(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-enylamine[25]

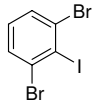
A solution of 2-[(*E*)-5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-enyl]-isoindole-1,3-dione (17.3 g, 0.050 mol) and hydrazine monohydrate (7.4 g, 7.2 mL, 0.15 mol) in methanol (250 mL) was heated to reflux with vigorous stirring under Ar. The solution was heated at reflux for 1 h. Copious amounts of a flaky white precipitate was generated during that time. The mixture was cooled to 0 °C in an ice/water bath and the precipitate was filtered off. The filtrate was concentrated *in vacuo* resulting in a heterogenous mixture, which was resuspended in diethyl ether (250

mL), filtered and the filtrate was concentrated *in vacuo*. This resulted in a pale yellow oil that was purified by distillation (bp 52-53 °C, 0.1 mbar). Yield 8.6 g (80%) of the title compound as a colourless oil: TLC R_f = 0.25 (EtOAc:Et_3N = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.62 (dtt, *J* = 15.5, 5.5, 1.2 Hz, 1 H), 5.55 (dtt, *J* = 15.5, 6.6, 1.3 Hz, 1 H), 3.63 (t, *J* = 6.7 Hz, 2 H), 3.25 (dd, *J* = 5.5, 1.3 Hz, 2 H), 2.24 (q, *J* = 6.7 Hz, 2 H), 1.12 (bs, 2 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.9, 127.1, 63.4, 44.6, 36.3, 26.3, 18.7, -4.9; Anal. Calc'd for $C_{11}H_{25}NO_3Si$: C, 61.33; H, 11.70; N, 6.50. Found: C, 61.05; H, 11.40; N, 6.25.

Substrates tested in the reaction cascade leading to complex product mixtures

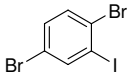


1,3-Dibromo-2-iodo-benzene



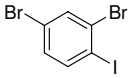
The general procedure B was followed using 2,6-dibromo-aniline (25.0 g, 0.10 mol). The product was isolated as a colourless oil that crystallized upon standing. Yield 16.6 g (46%) of the title compound as colourless needles: mp 99-100 °C, lit.[36] mp 99-100 °C (EtOH); TLC R_f = 0.61 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$)[37] δ 7.57 (d, *J* = 8.0 Hz, 2 H), 7.08 (t, *J* = 8.0 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 131.3, 131.1, 130.3, 109.4.

1,4-Dibromo-2-iodo-benzene



The general procedure B was followed using 2,5-dibromo-aniline (25.0 g, 0.10 mol). The crude product was recrystallized from EtOH. Yield 21.1 g (58%) of the title compound as white needles: mp 36-37 °C (EtOH), lit.[38] mp 38-39 °C; TLC R_f = 0.67 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$)[38] δ 7.99 (d, *J* = 2.1 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1 H), 7.32 (dd, *J* = 8.5, 2.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$)[38] δ 142.6, 133.9, 133.0, 129.0, 121.6, 102.4.

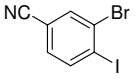
2,4-Dibromo-1-iodo-benzene



The general procedure B was followed using 2,4-dibromo-aniline (25.0 g, 0.10 mol). The crude product was recrystallized from EtOH. Yield 27.8 g (77%) of the title compound as pale pink needles: mp 44-45 °C (EtOH), lit.[39] mp 45-46 °C (EtOH); TLC R_f = 0.67 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.0 Hz, 1 H), 7.69

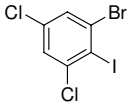
(d, J = 8.4 Hz, 1 H), 7.13 (dd, J = 8.4, 2.0 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 135.5, 132.1, 131.2, 123.1, 99.8; Anal. Calc'd for $C_6H_3Br_2I$: C, 19.92; H, 0.84. Found: C, 19.94; H, 0.77.

3-Bromo-4-iodo-benzonitrile



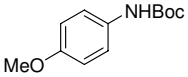
The general procedure B was followed using 4-amino-3-bromo-benzonitrile (20.0 g, 0.10 mol).The crude product was recrystallized from EtOH. Yield (24.5 g, 80%) as pale red needles: mp 139-140 °C (EtOH); TLC R_f = 0.18 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.1 Hz, 1 H), 7.87 (d, J = 1.8 Hz, 1 H), 7.26 (dd, J = 8.1, 1.8 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.5, 135.6, 131.4, 131.3, 117.2, 114.0, 108.4; Anal. Calc'd for C_7H_3BrIN: C, 27.31; H, 0.98; N, 4.55. Found: C, 27.43; H, 0.98; N, 4.57.

1-Bromo-3,5-dichloro-2-iodo-benzene



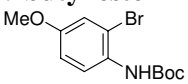
The general procedure B was followed using 2-bromo-4,6-dichloro-aniline (12.0 g, 50 mmol). The crude product was recrystallized from EtOH. Yield 12.9 g (73%) of the title compound as colourless needles: mp 78-79 °C (EtOH), lit.[40] mp 81 °C; TLC R_f = 0.72 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 2.4 Hz, 1 H), 7.41 (d, J = 2.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.9, 135.3, 131.9, 130.5, 127.7, 104.5; Anal. Calc'd for $C_6H_2BrCl_2I$: C, 20.48; H, 0.57. Found: C, 20.84; H, 0.59.

2-Bromo-1-iodo-4-methoxy-benzene and (4-methoxy-phenyl)-carbamic acid *tert*-butyl ester[4]



p-Anisidine (36.9 g, 0.30 mol) and Boc_2O (98.2 g, 0.45 mol) were heated neat to 50 °C while stirring. The mixture was stirred 30 min at 50 °C followed by 2 h stirring at 80 °C. Upon cooling to room temperature, a white precipitate was formed from the black mixture. The solid was isolated and recrystallized from heptanes. Yield 63.5 g (95%) of the title compound as pale grey needles: mp 94-96 °C (heptanes); lit.[41] mp 92-94 °C (hexane-diethyl ether); TLC R_f = 0.38 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[42] δ 7.26 (bd, J = 8.5 Hz, 2 H), 6.85-6.82 (m, 2 H), 6.32 (bs, 1 H), 3.78 (s, 3 H), 1.51 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$)[42] δ 156.1, 153.6, 131.8, 121.0, 114.6, 80.6, 55.9, 28.8.

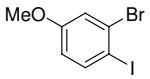
(2-Bromo-4-methoxy-phenyl)-carbamic acid *tert*-butyl ester[43]



A solution of (4-methoxy-phenyl)-carbamic acid *tert*-butyl ester (37.96 g, 0.17 mol) in 750 mL diethyl ether (predried over 4 Å molsieves) was cooled to –78 °C in a CO_2(s)/acetone bath while stirring under Ar. 1.7 M *t*-BuLi (200 mL, 0.34 mol) in pentane was added keeping the internal temperature below -60 °C. The resulting pale yellow mixture was stirred 2 h at –20 °C followed by dropwise addition of 1,2-dibromoethane (14.7 mL, 0.17 mol). The clear, pale orange solution was stirred 12 h at room temperature. The reaction was quenched by addition of sat. aq. NH_4Cl (400 mL), and the organic layer was washed with brine (400 mL), dried over $MgSO_4$, filtered, and

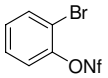
concentrated *in vacuo* to afford a viscous, colourless oil. The crude product was purified by silica gel chromatography (eluent: heptanes:EtOAc = 19:1). Yield 33.8 g (67%) of the title compound as a colourless oil that crystallized upon standing: mp 35-36 °C; TLC R_f = 0.38 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[44] δ 7.95 (bd, *J* = 8.2 Hz, 1 H), 7.07 (d, *J* = 2.8 Hz 1 H), 6.85 (dd, *J* = 8.2, 2.8 Hz, 1 H), 6.72 (bs, 1 H), 3.77 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$)[44] δ 156.1, 153.2, 130.1, 122.2, 117.9, 114.4, 114.0, 81.2, 56.1, 28.7.

2-Bromo-1-iodo-4-methoxy-benzene



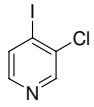
(2-Bromo-4-methoxy-phenyl)-carbamic acid *tert*-butyl ester (33.2 g, 0.11 mol) was dissolved in MeOH (300 mL) and 2.0 M HCl (300 mL) in diethyl ether was added while stirring at room temperature. The mixture was stirred 30 min (until the effervescence had ceased) during which a white precipitate was formed. The solvent was removed *in vacuo* and the resulting white solid was converted into 2-bromo-1-iodo-4-methoxy-benzene following general procedure B. Yield 20.5 g (60%, over two steps) of the title compound as a pale orange oil: TLC R_f = 0.24 (heptanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.7 Hz, 1 H), 7.19 (d, *J* = 2.8 Hz, 1 H), 6.60 (dd, *J* = 8.7, 2.8 Hz, 1 H), 3.78 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.7, 140.7, 130.4, 118.8, 115.8, 89.9, 56.0; Anal. Calc'd for C_7H_7BrIO: C, 26.87; H, 1.93; Br, 25.53. Found: C, 26.96; H, 2.09; Br, 25.49.

2-Bromophenyl nonaflate[45]



A solution of 2-bromo-phenol (8.7 g, 5.8 mL, 50 mmol) in DMF (100 mL, predried over 4 Å molsieves) was stirred at room temperature under Ar. NaH (2.4 g, 60 mmol, 60% dispersion in mineral oil) was added in one portion. The mixture was stirred until the effervescence had ceased (approx. 20 min). Perfluorobutane-1-sulfonyl fluoride (18.1 g, 10.8 mL, 60 mmol) was added and the mixture was stirred for 14 h at room temperature. The solvent was removed *in vacuo* and the resulting oil was filtered through a plug of celite (eluent: heptanes). Yield 21.4 g (94%) of the title compound as a colourless oil: TLC R_f = 0.31 (heptanes:EtOAc = 19:1); ^{1}H NMR (500 MHz, $CDCl_3$)[45] δ 7.69 (dd, *J* = 8.0, 1.3 Hz, 1 H), 7.45-7.34 (m, 2 H), 7.30-7.23 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$)[45] δ 145.4, 132.6, 127.5, 127.2, 121.0, 118.6-105.8 (m, 4 C), 114; ^{19}F NMR (471 MHz, $CDCl_3$) δ -81.1 (t, *J* = 10.7 Hz, 3 F), -109.6 (t, *J* = 13.7 Hz, 2 F), -121.0– -121.1 (m, 2 F).

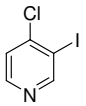
3-Chloro-4-iodopyridine[46]



To a stirred solution of dry diisopropylamine (16.9 g, 0.16 mol, predried over KOH) in THF (250 mL) cooled to -78 ° in a CO_2(s)/acetone bath under Ar was added 1.60 M *n*-BuLi (100 mL, 0.16 mol) in hexane. The solution was stirred 20 min at –78 °C and subsequently treated with 3-chloropyridine (18.2 g, 15.2 mL, 0.16 mol) in THF (50 mL) keeping the internal temperature below –70 °C. This resulted in precipitation of the corresponding lithiated species as a colourless solid from a pale yellow solution. The mixture was stirred 30 min at –78 °C, before it was quenched with a solution of I_2 (40.6 g, 0.16 mol) in THF (150 mL) keeping the internal temperature below –65 °C. The mixture was allowed to warm to room temperature overnight, poured into 1 M aq. $Na_2S_2O_3$ (200 mL), and extracted with Et_2O (3 x 200 mL). The combined organic extracts were washed with 1 M aq. $Na_2S_2O_3$ (200 mL), sat. aq. $NaHCO_3$ (200 mL), H_2O (200 mL), and brine (2 x 200 mL), dried over Na_2SO_4, and evaporated *in vacuo* to

afford a crude brown solid that was recrystallized from hexane. Yield 24.9 g (65%) of the title compound as a pale brown solid: mp 105-106 °C (*n*-hexane), lit.[46] mp 105-106 °C; TLC R_f = 0.27 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1 H), 8.07 (d, *J* = 5.2 Hz, 1 H), 7.80 (d, *J* = 5.2 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$)[47] δ 148.3, 147.2, 137.0, 134.7, 109.0.

4-Chloro-3-iodo-pyridine[46]



The procedure for synthesis of 3-Chloro-4-iodopyridine was followed using 4-chloropyridine hydrochloride (24.0 g, 0.16 mol) and two equivalents of LDA. This gave the crude product as a white solid that was purified using silica gel chromatography (eluent: heptanes:EtOAc = 19:1 → heptanes:EtOAc = 9:1). Yield 18.2 g (48%) of the title compound as white needles: mp 77-79 °C lit.[48] mp 78-80 °C; TLC R_f = 0.26 (heptanes:EtOAc = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$)[49] δ 8.94 (s, 1 H), 8.43 (d, *J* = 5.2 Hz, 1 H), 7.42 (d, *J* = 5.2 Hz, 1 H); ^{13}C NMR[49] δ 158.8, 150.0, 148.3, 125.3, 98.3.

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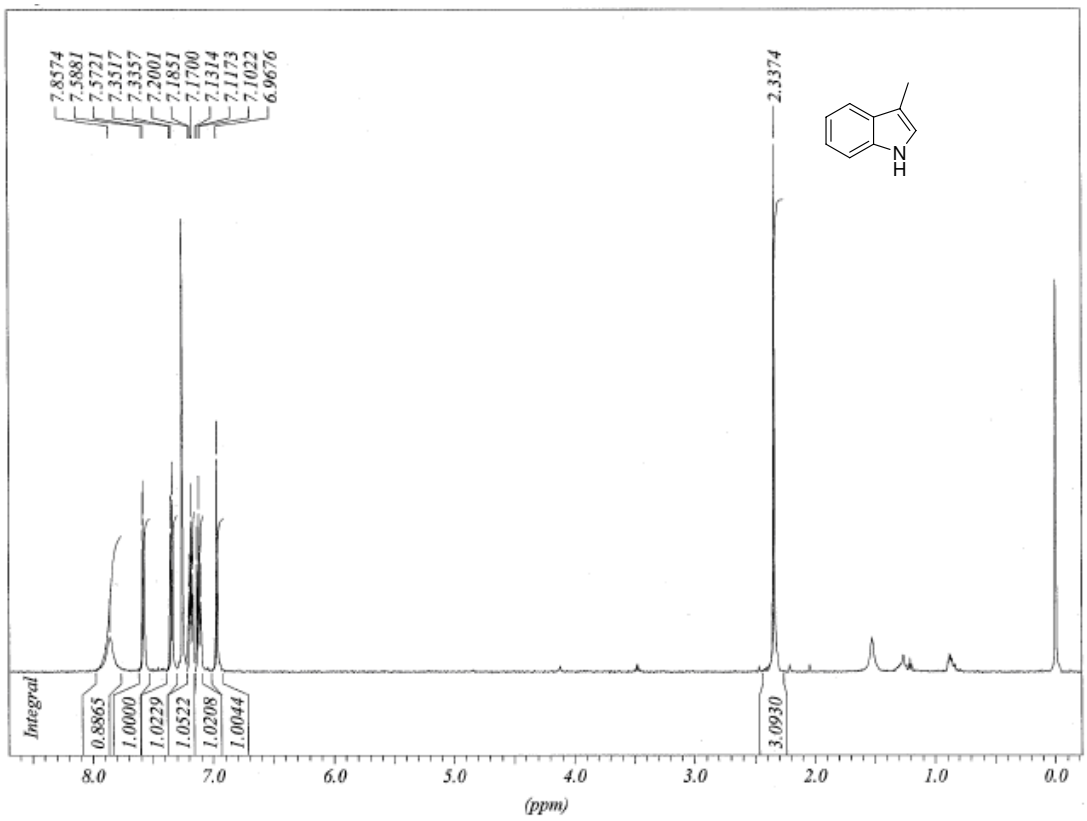
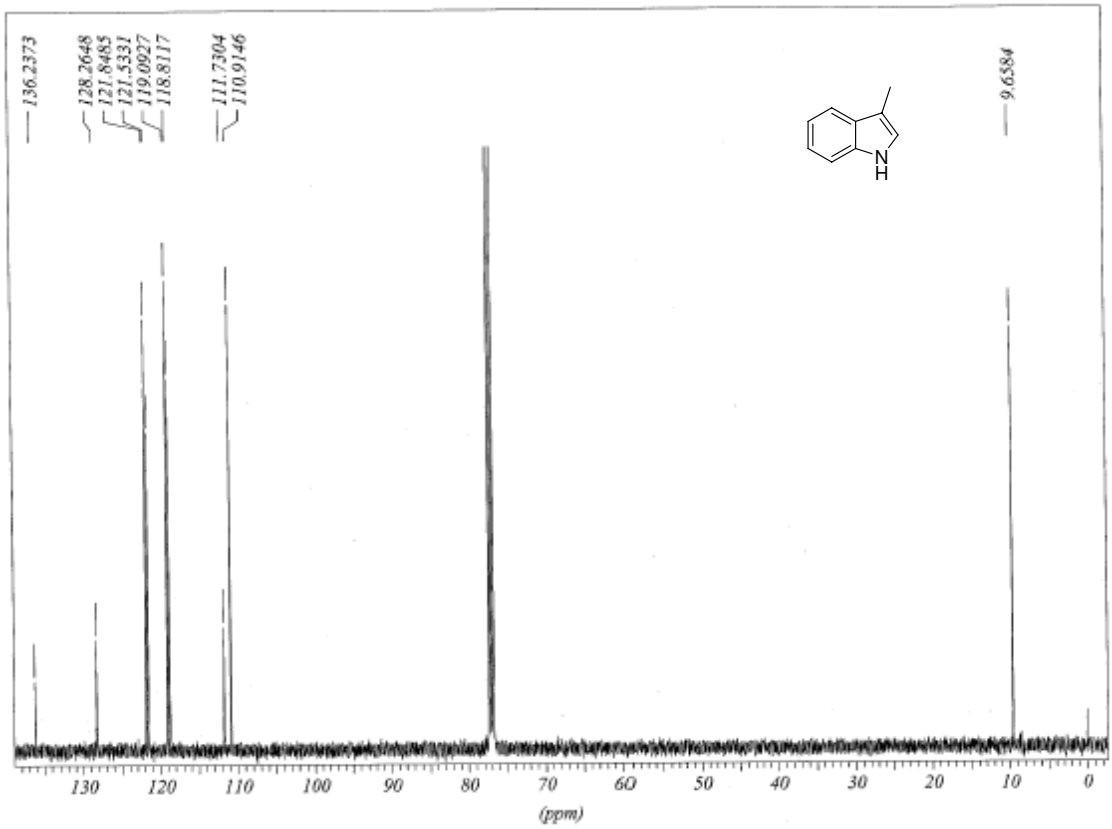
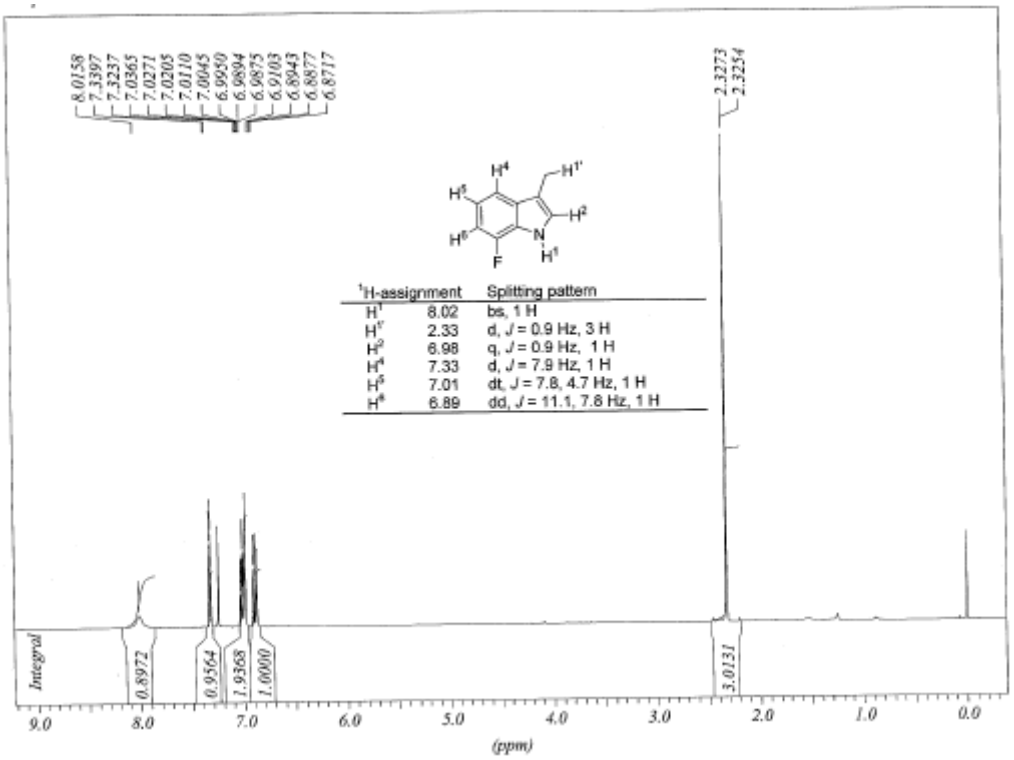
NMR-spectra

3-Methyl-1*H*-indole, scatole (3)

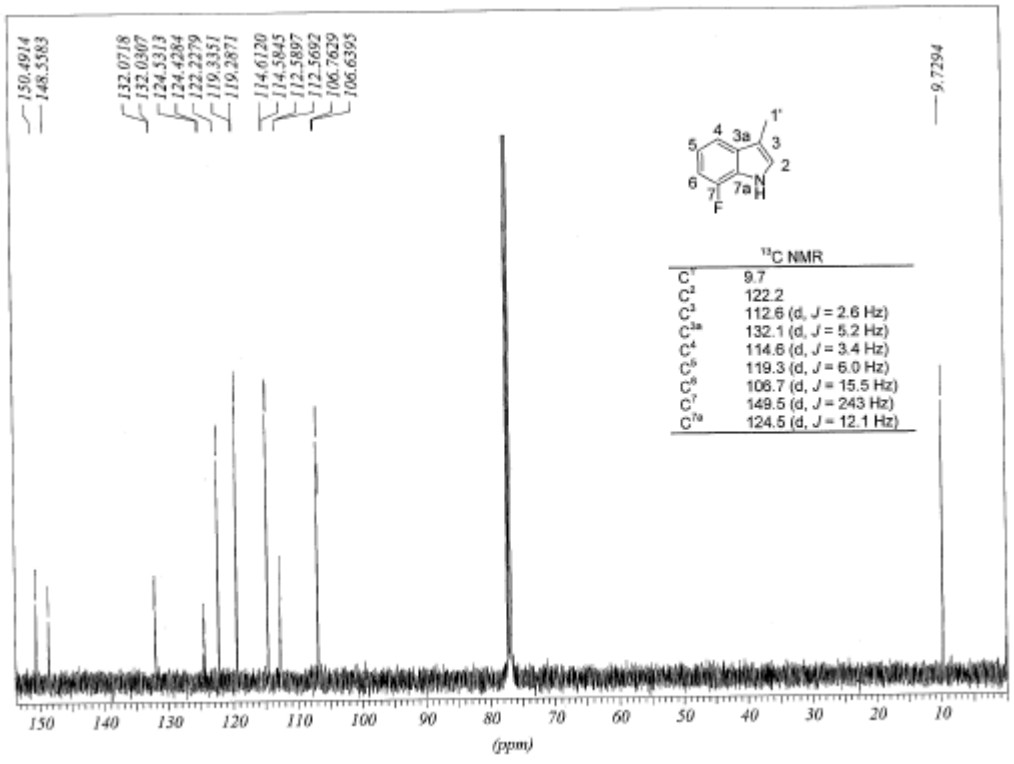




7-Fluoro-3-methyl-1*H*-indole

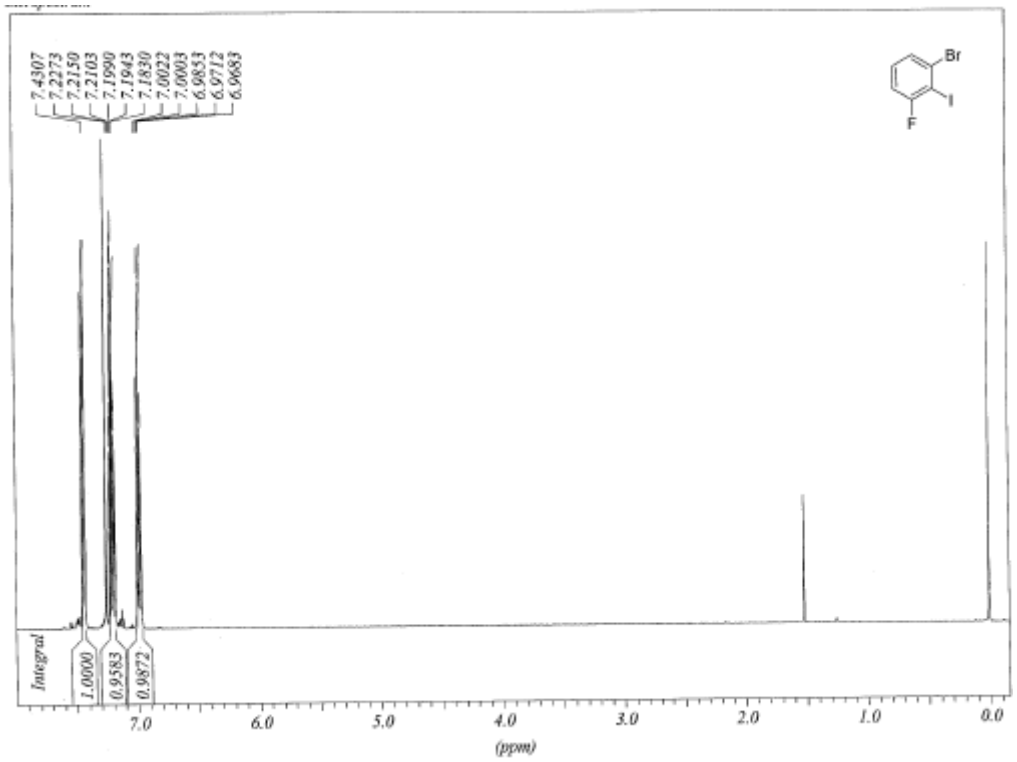


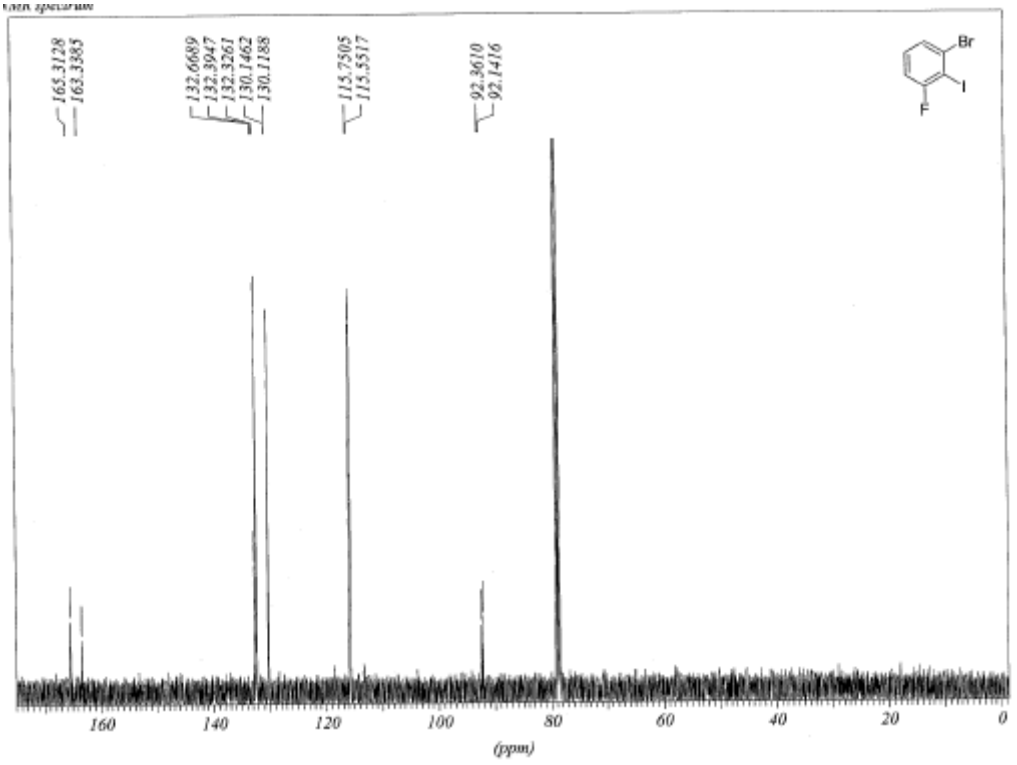
^{1}H-assignment		Splitting pattern
H^1	8.02	bs, 1 H
$H^{1'}$	2.33	d, *J* = 0.9 Hz, 3 H
H^2	6.98	q, *J* = 0.9 Hz, 1 H
H^4	7.33	d, *J* = 7.9 Hz, 1 H
H^5	7.01	dt, *J* = 7.8, 4.7 Hz, 1 H
H^6	6.89	dd, *J* = 11.1, 7.8 Hz, 1 H



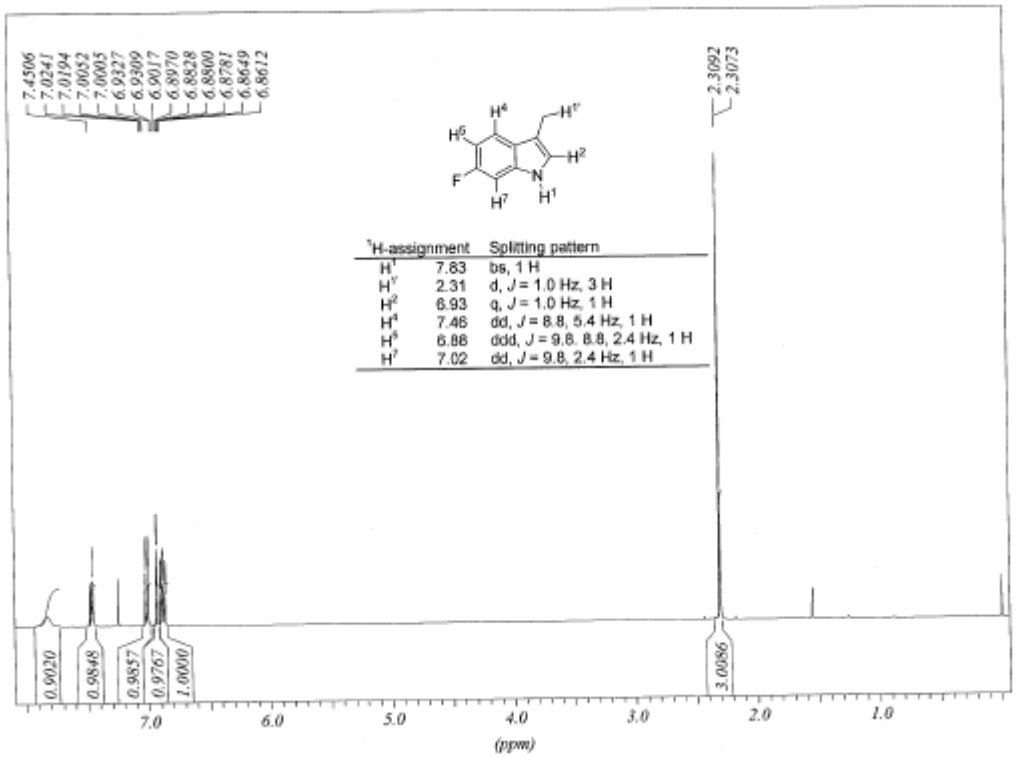
^{13}C NMR	
$C^{1'}$	9.7
C^2	122.2
C^3	112.6 (d, *J* = 2.6 Hz)
C^{3a}	132.1 (d, *J* = 5.2 Hz)
C^4	114.6 (d, *J* = 3.4 Hz)
C^5	119.3 (d, *J* = 6.0 Hz)
C^6	106.7 (d, *J* = 15.5 Hz)
C^7	149.5 (d, *J* = 243 Hz)
C^{7a}	124.5 (d, *J* = 12.1 Hz)

1-Bromo-3-fluoro-2-iodo-benzene

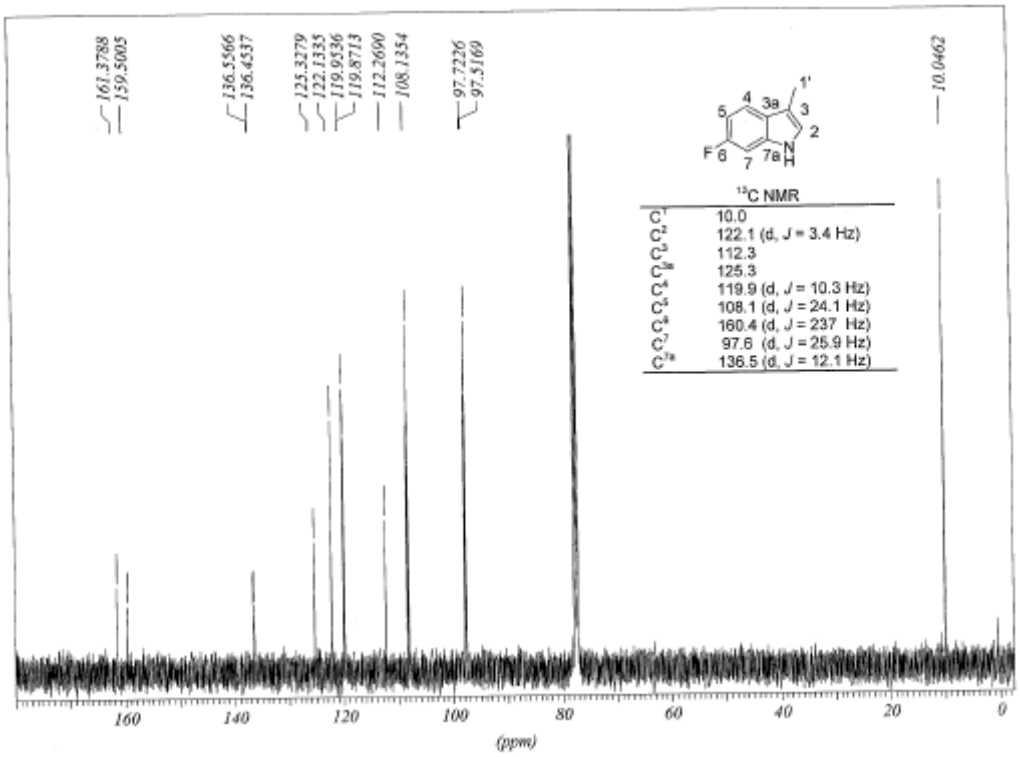




6-Fluoro-3-methyl-1*H*-indole

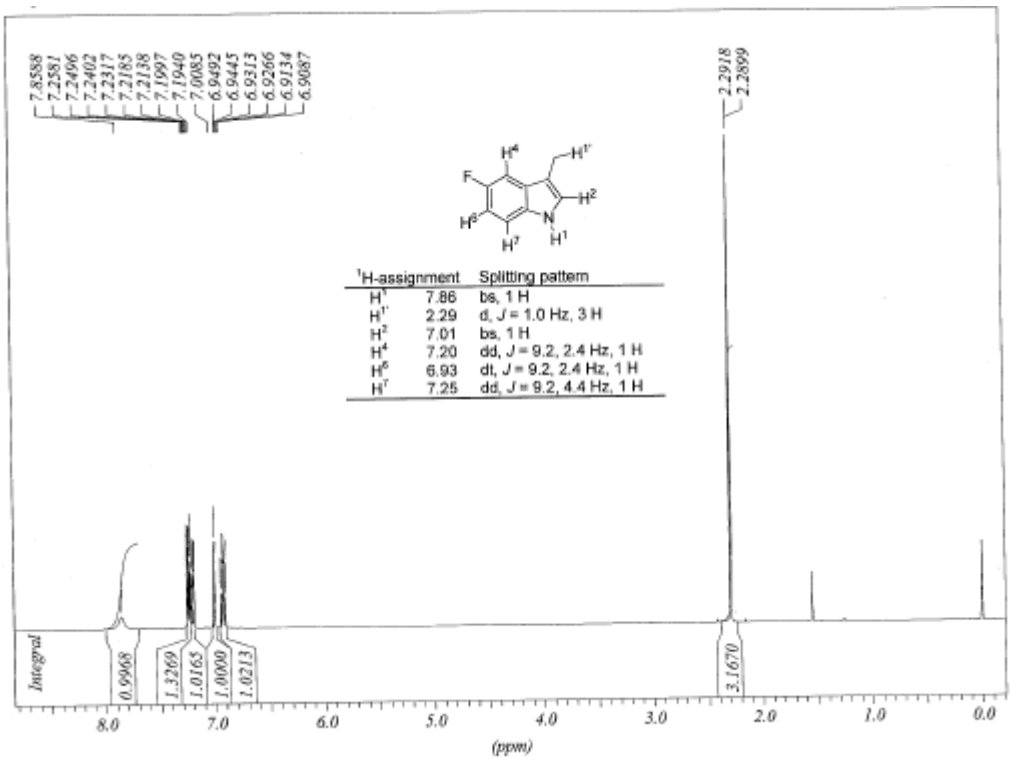


^{1}H-assignment		Splitting pattern
H^1	7.83	bs, 1 H
$H^{1'}$	2.31	d, J = 1.0 Hz, 3 H
H^2	6.93	q, J = 1.0 Hz, 1 H
H^4	7.46	dd, J = 8.8, 5.4 Hz, 1 H
H^5	6.88	ddd, J = 9.8, 8.8, 2.4 Hz, 1 H
H^7	7.02	dd, J = 9.8, 2.4 Hz, 1 H

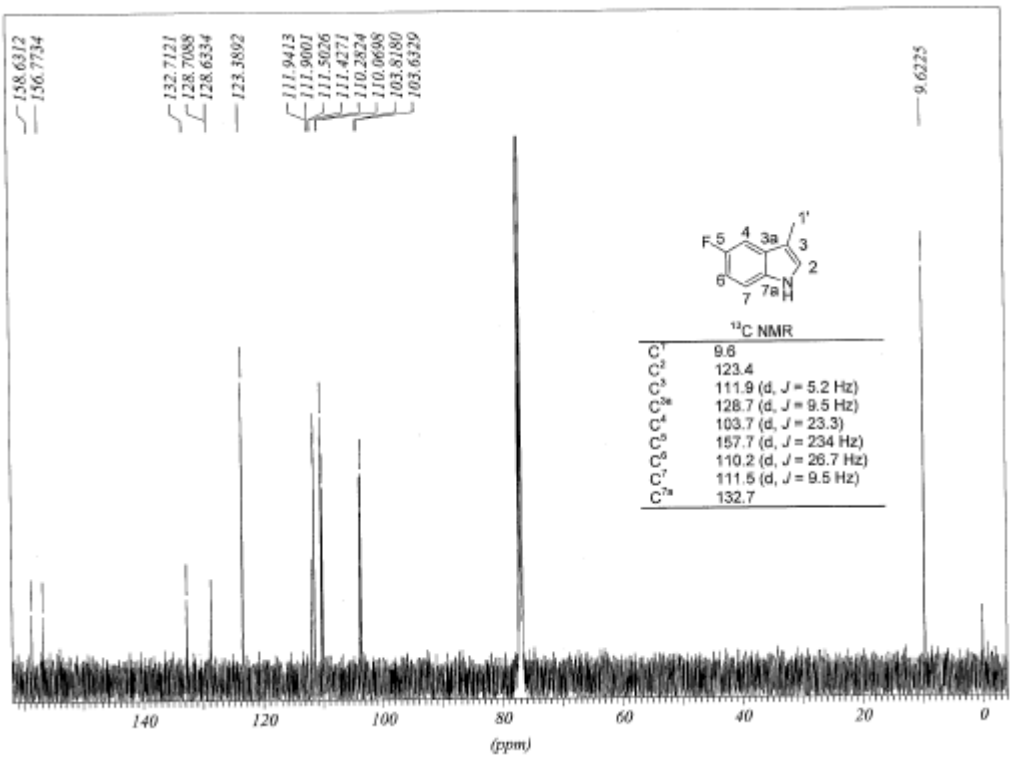


^{13}C NMR	
$C^{1'}$	10.0
C^2	122.1 (d, J = 3.4 Hz)
C^3	112.3
C^{3a}	125.3
C^4	119.9 (d, J = 10.3 Hz)
C^5	108.1 (d, J = 24.1 Hz)
C^6	160.4 (d, J = 237 Hz)
C^7	97.6 (d, J = 25.9 Hz)
C^{7a}	136.5 (d, J = 12.1 Hz)

5-Fluoro-3-methyl-1*H*-indole

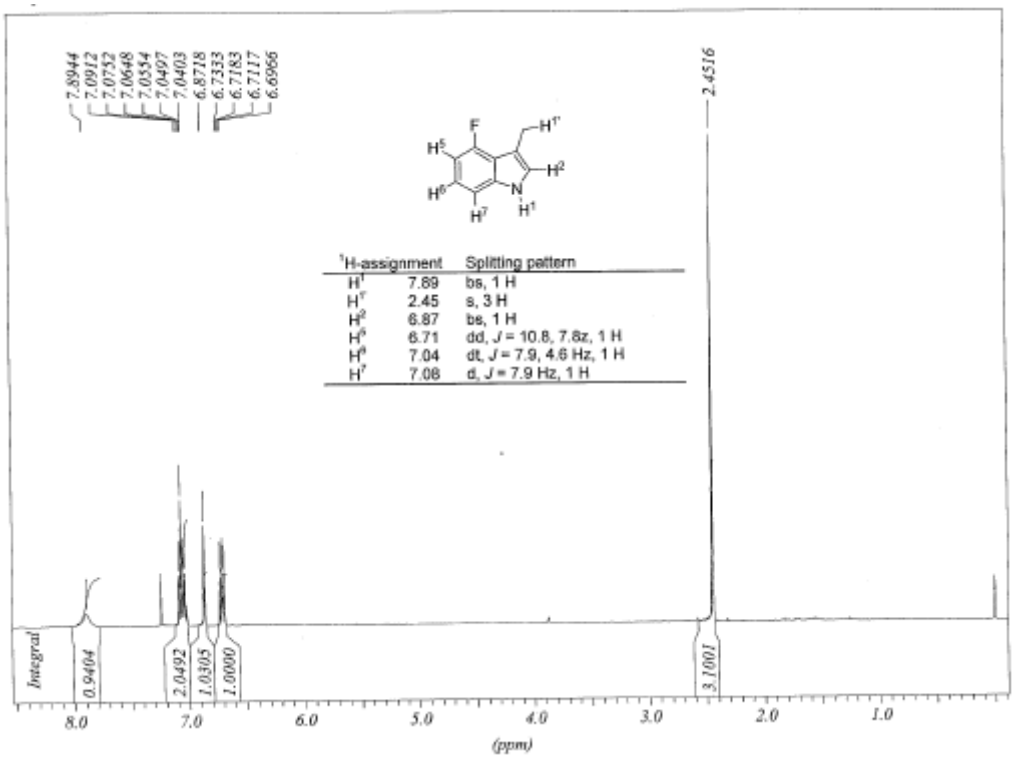


^{1}H-assignment		Splitting pattern
H^1	7.86	bs, 1 H
$H^{1'}$	2.29	d, J = 1.0 Hz, 3 H
H^2	7.01	bs, 1 H
H^4	7.20	dd, J = 9.2, 2.4 Hz, 1 H
H^6	6.93	dt, J = 9.2, 2.4 Hz, 1 H
H^7	7.25	dd, J = 9.2, 4.4 Hz, 1 H

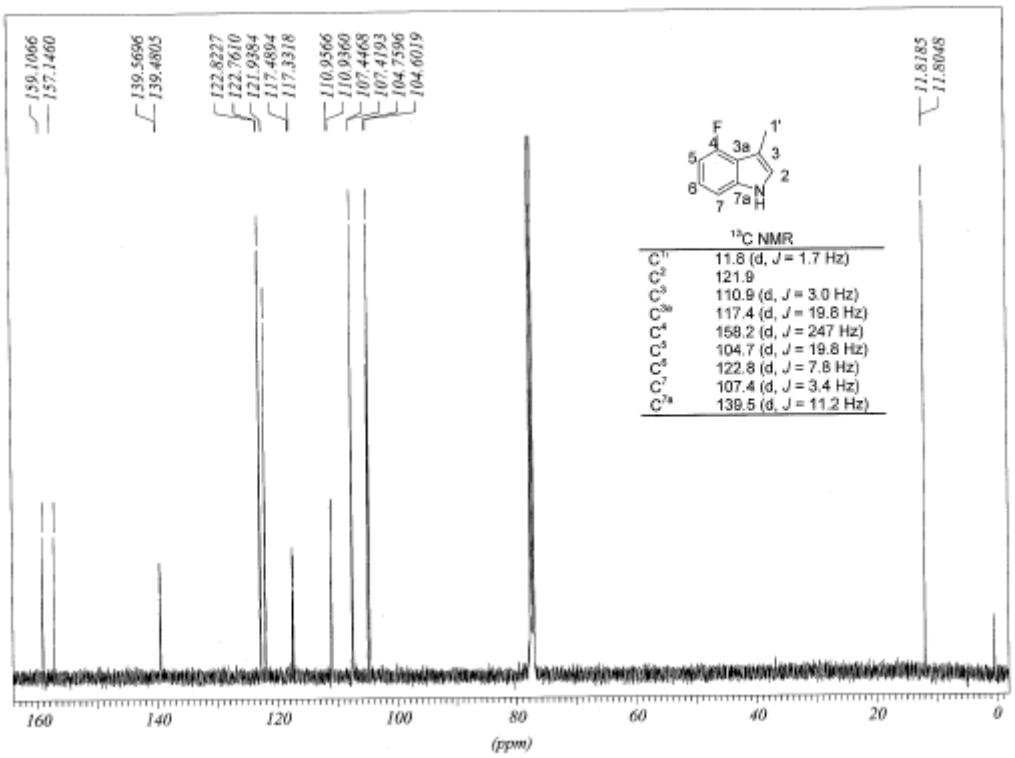


^{13}C NMR	
$C^{1'}$	9.6
C^2	123.4
C^5	111.9 (d, J = 5.2 Hz)
C^{3a}	128.7 (d, J = 9.5 Hz)
C^4	103.7 (d, J = 23.3)
C^5	157.7 (d, J = 234 Hz)
C^6	110.2 (d, J = 26.7 Hz)
C^7	111.5 (d, J = 9.5 Hz)
C^{7a}	132.7

4-Fluoro-3-methyl-1*H*-indole

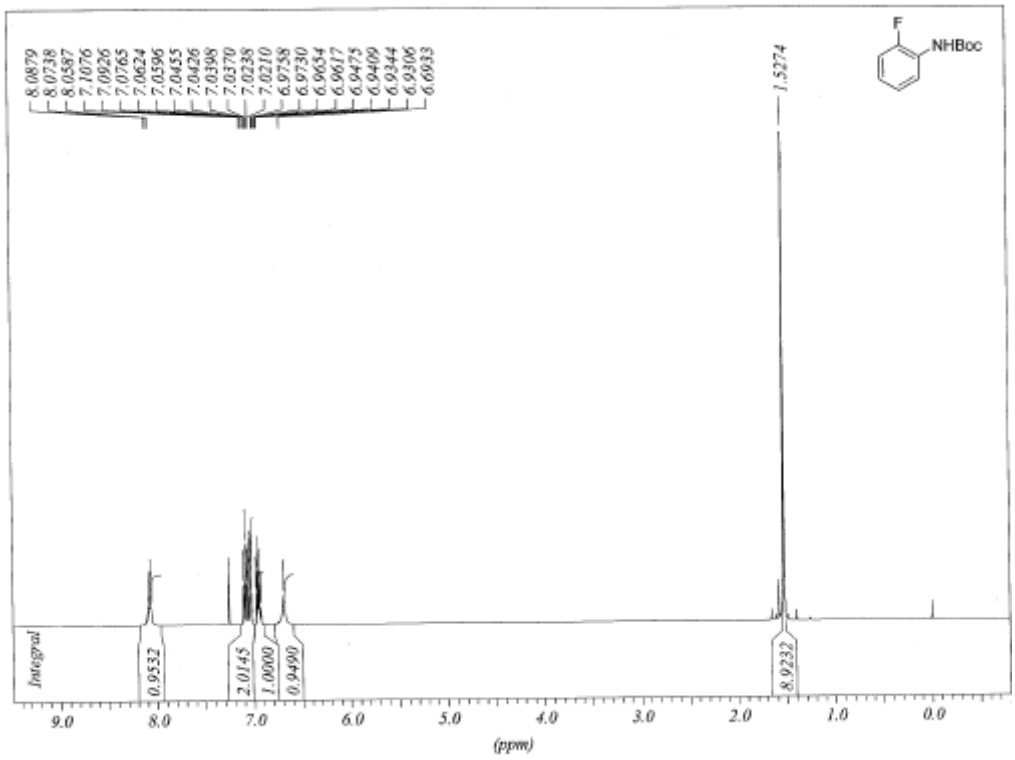


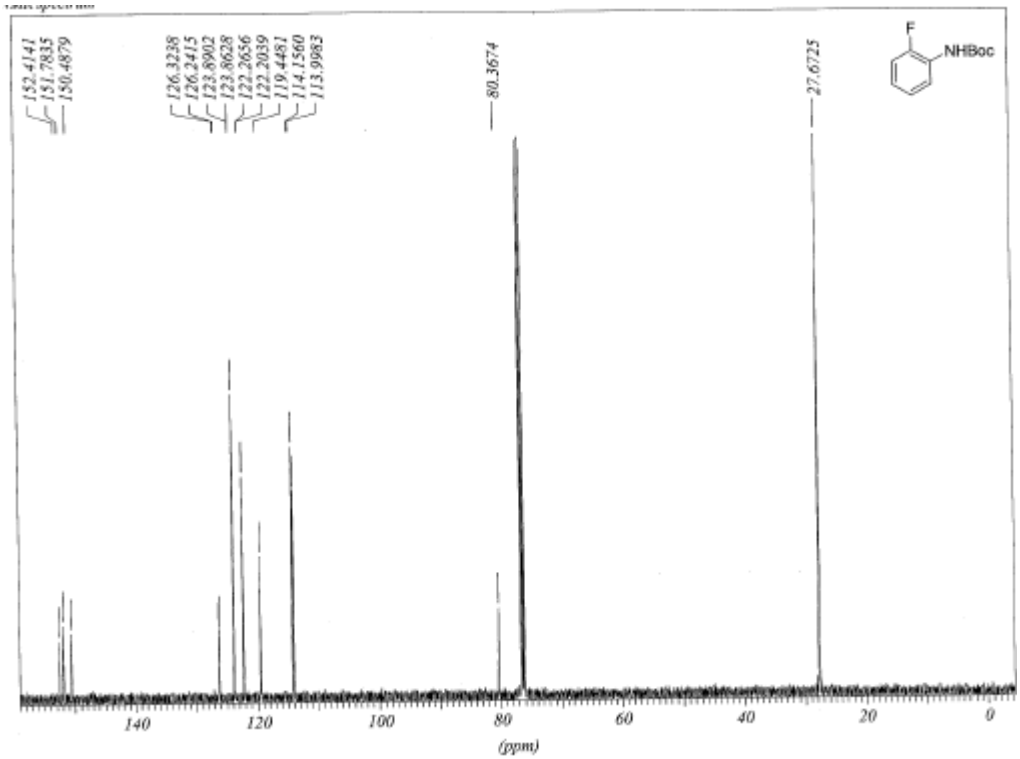
^{1}H-assignment		Splitting pattern
H^1	7.89	bs, 1 H
$H^{1'}$	2.45	s, 3 H
H^2	6.87	bs, 1 H
H^6	6.71	dd, *J* = 10.8, 7.8z, 1 H
H^5	7.04	dt, *J* = 7.9, 4.6 Hz, 1 H
H^7	7.08	d, *J* = 7.9 Hz, 1 H



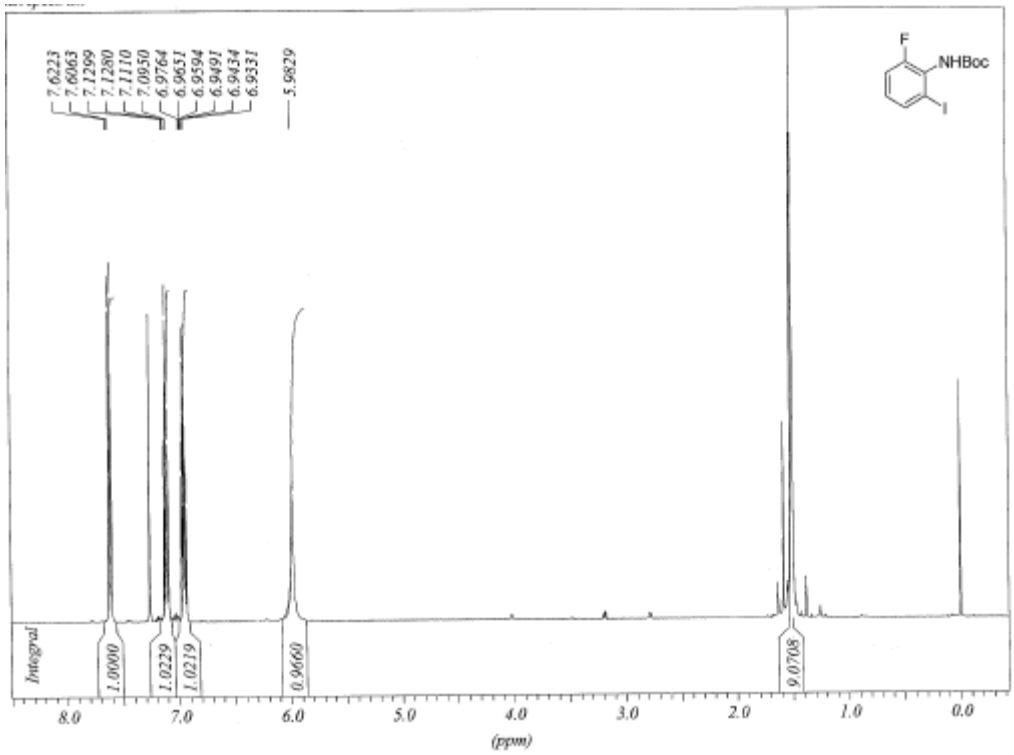
^{13}C NMR	
$C^{1'}$	11.8 (d, *J* = 1.7 Hz)
C^5	121.9
C^{3a}	110.9 (d, *J* = 3.0 Hz)
C^{3a}	117.4 (d, *J* = 19.8 Hz)
C^4	158.2 (d, *J* = 247 Hz)
C^6	104.7 (d, *J* = 19.8 Hz)
C^3	122.8 (d, *J* = 7.8 Hz)
C^7	107.4 (d, *J* = 3.4 Hz)
C^{7a}	139.5 (d, *J* = 11.2 Hz)

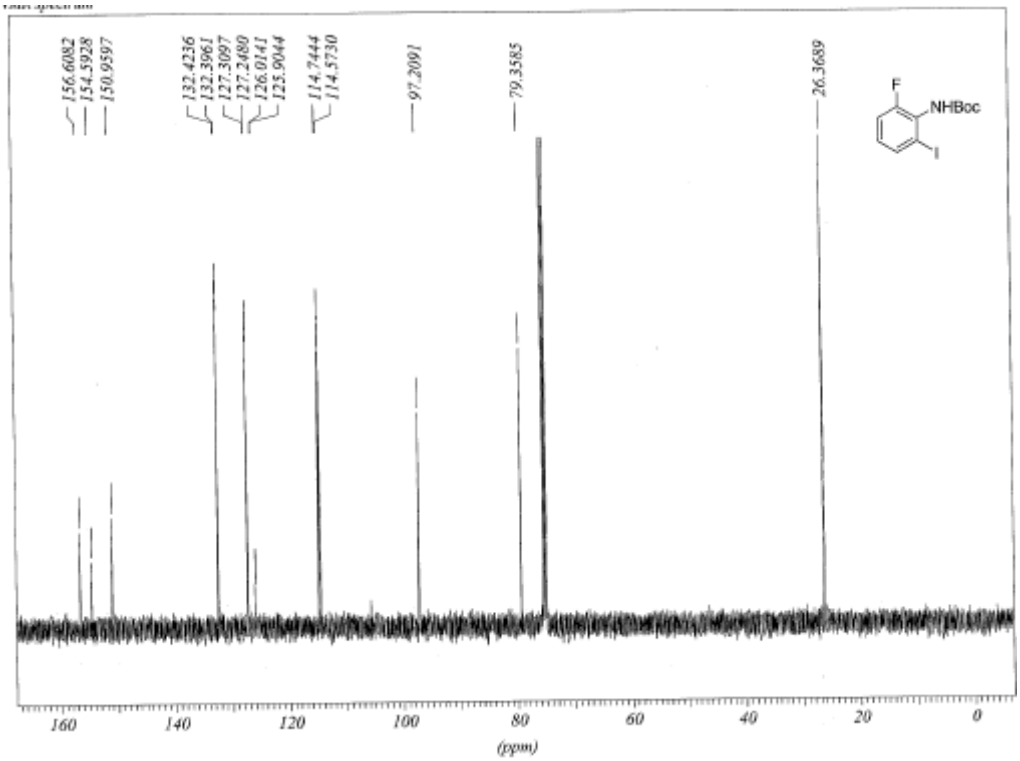
(2-Fluoro-phenyl)-carbamic acid *tert*-butyl ester



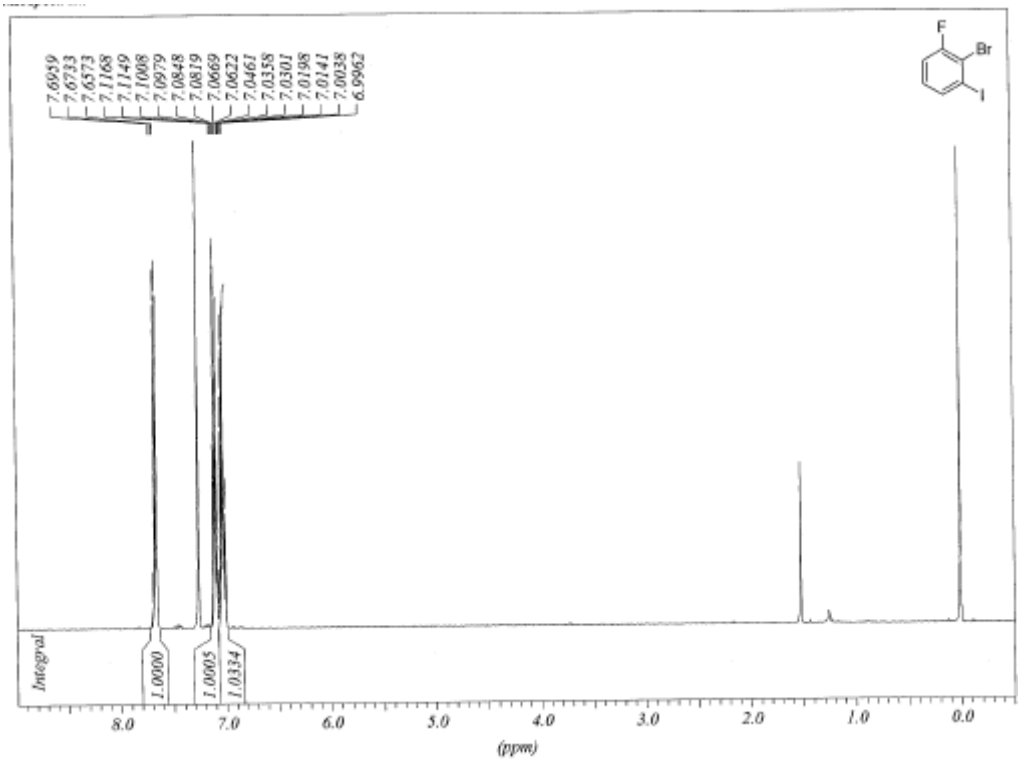


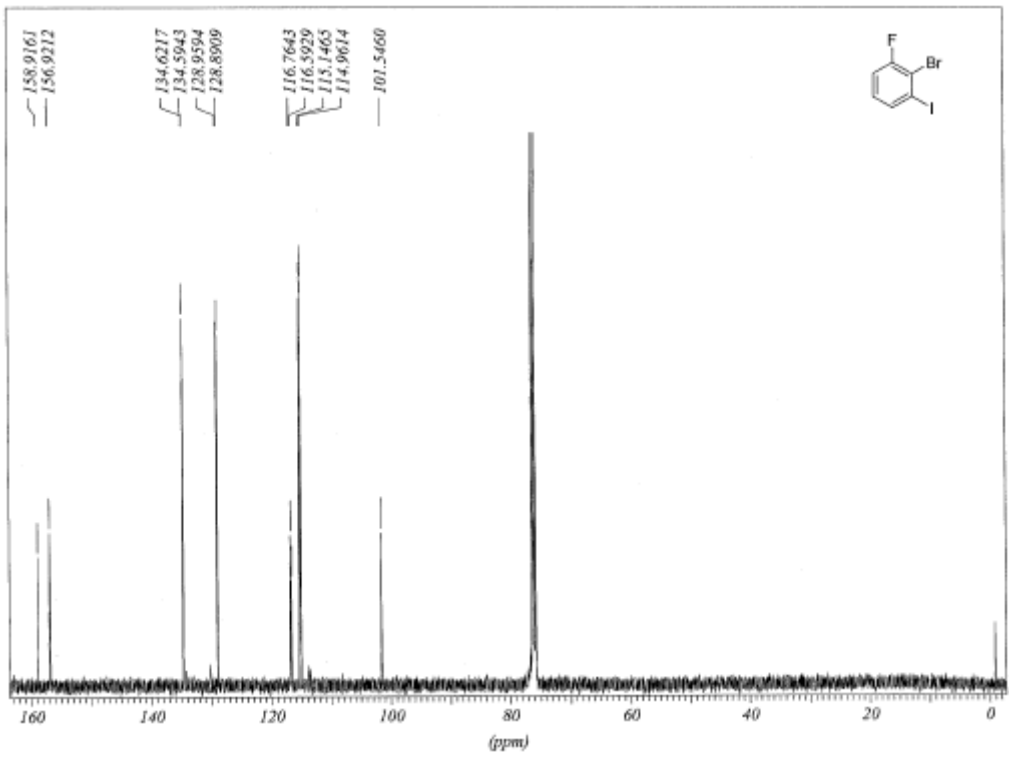
(2-Fluoro-6-iodo-phenyl)-carbamic acid *tert*-butyl ester



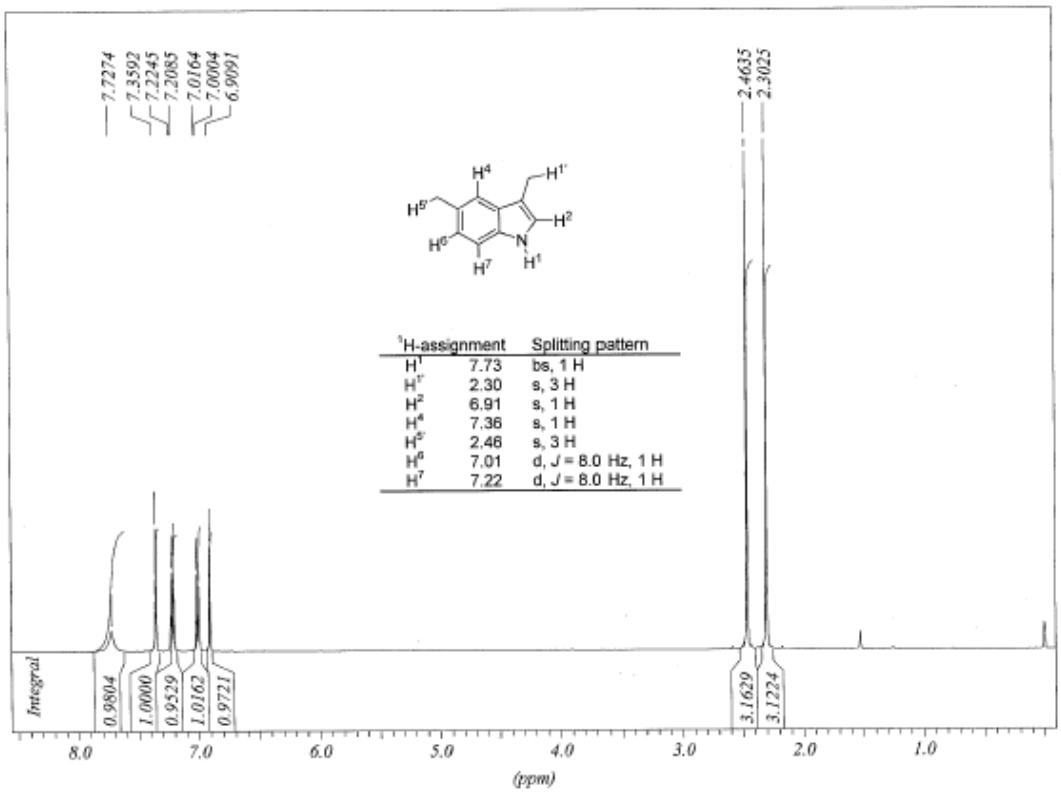


2-Bromo-1-fluoro-3-iodo-benzene

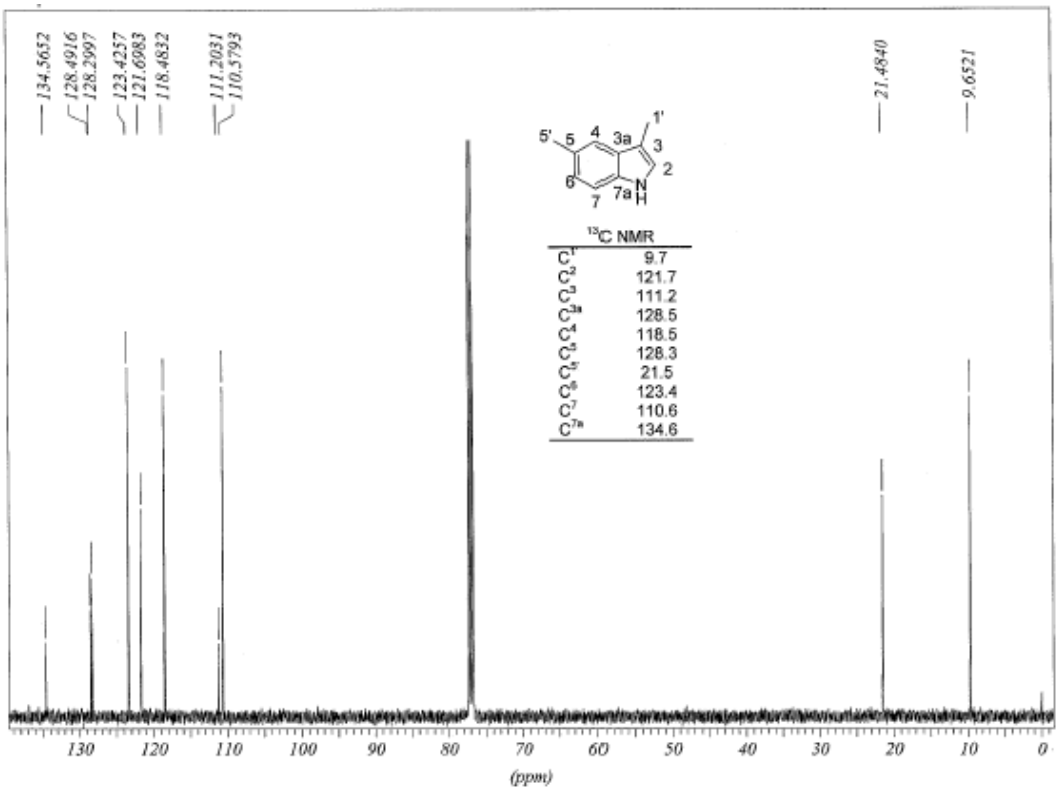




3,5-Dimethyl-1*H*-indole

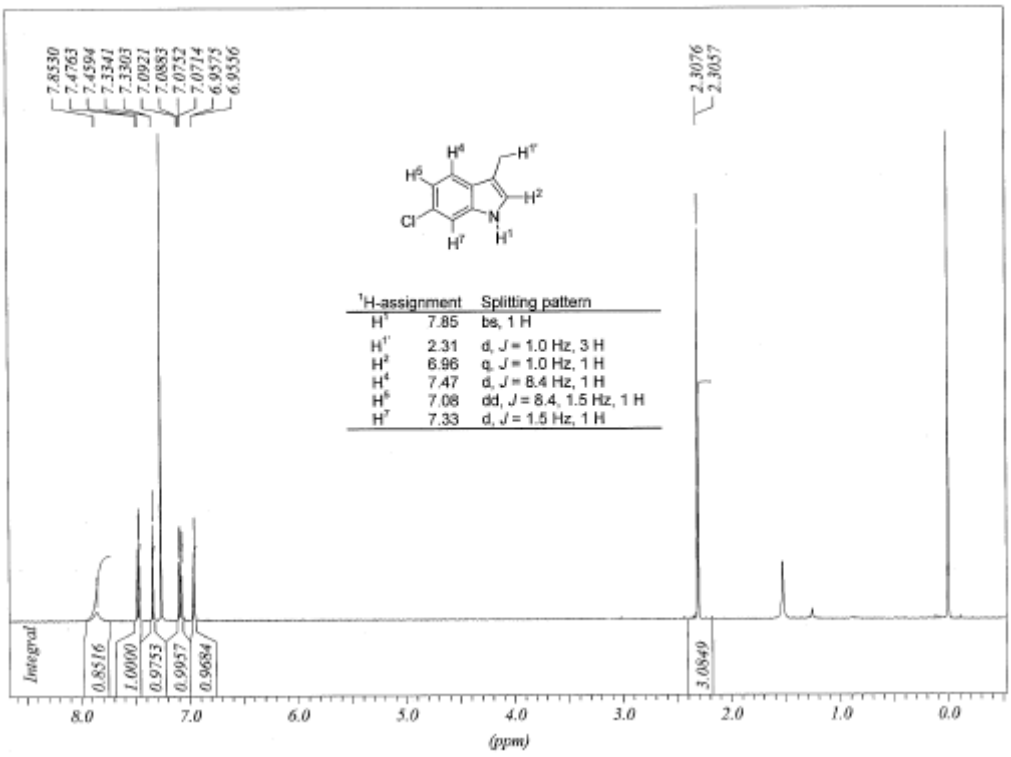


^{1}H-assignment		Splitting pattern
H^1	7.73	bs, 1 H
$H^{1'}$	2.30	s, 3 H
H^2	6.91	s, 1 H
H^4	7.36	s, 1 H
$H^{5'}$	2.46	s, 3 H
H^6	7.01	d, *J* = 8.0 Hz, 1 H
H^7	7.22	d, *J* = 8.0 Hz, 1 H

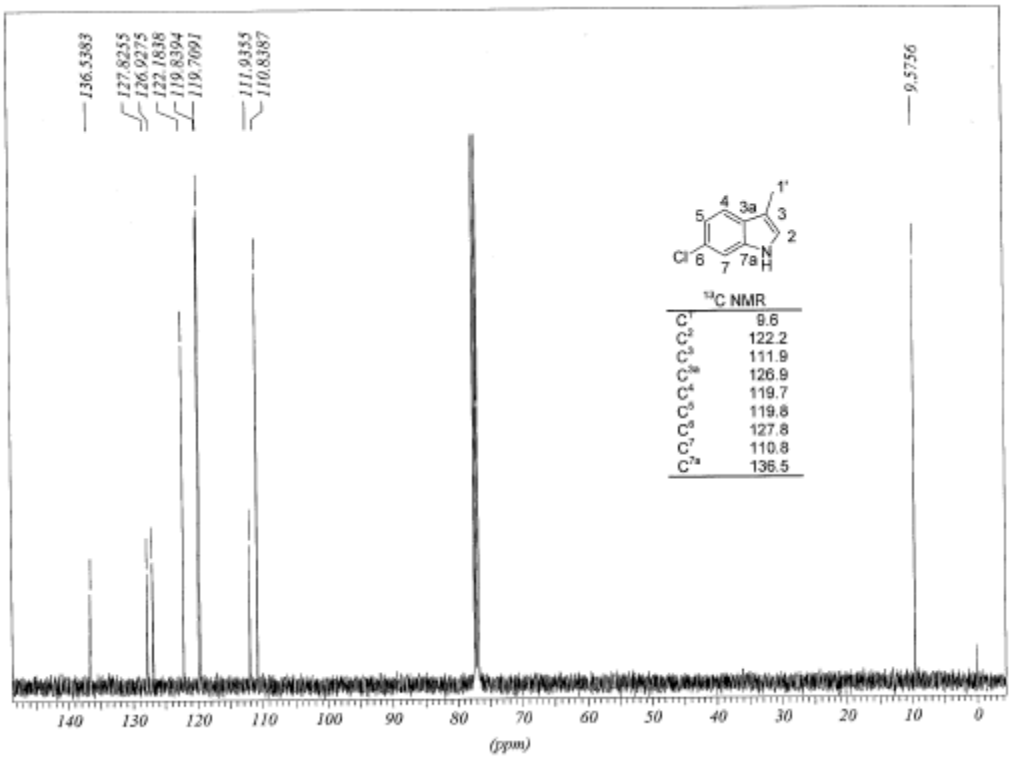


^{13}C NMR	
$C^{1'}$	9.7
C^2	121.7
C^3	111.2
C^{3a}	128.5
C^4	118.5
C^5	128.3
$C^{5'}$	21.5
C^6	123.4
C^7	110.6
C^{7a}	134.6

6-Chloro-3-methyl-1*H*-indole

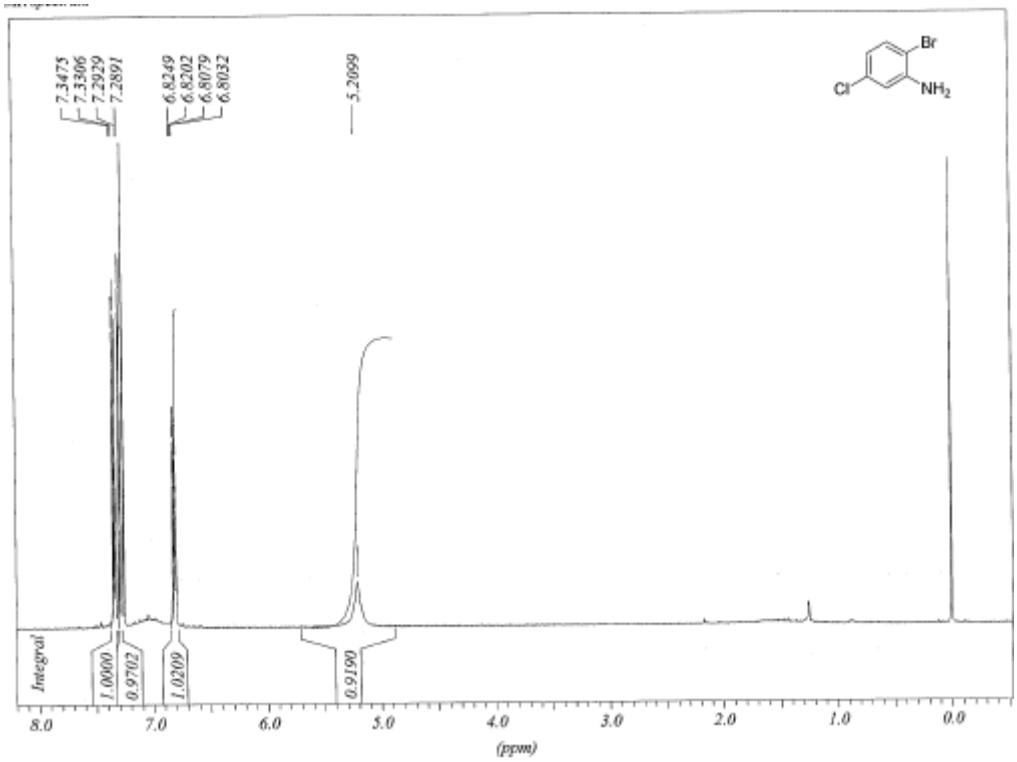


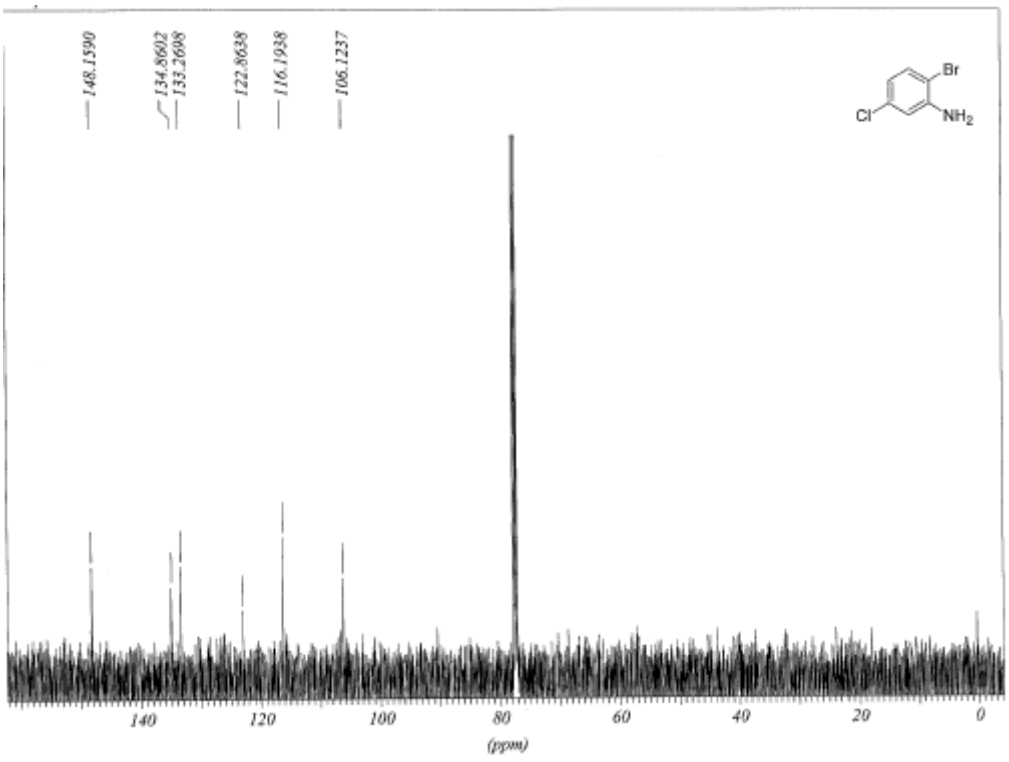
^{1}H-assignment		Splitting pattern
H^1	7.85	bs, 1 H
$H^{1'}$	2.31	d, *J* = 1.0 Hz, 3 H
H^2	6.96	q, *J* = 1.0 Hz, 1 H
H^4	7.47	d, *J* = 8.4 Hz, 1 H
H^5	7.08	dd, *J* = 8.4, 1.5 Hz, 1 H
H^7	7.33	d, *J* = 1.5 Hz, 1 H



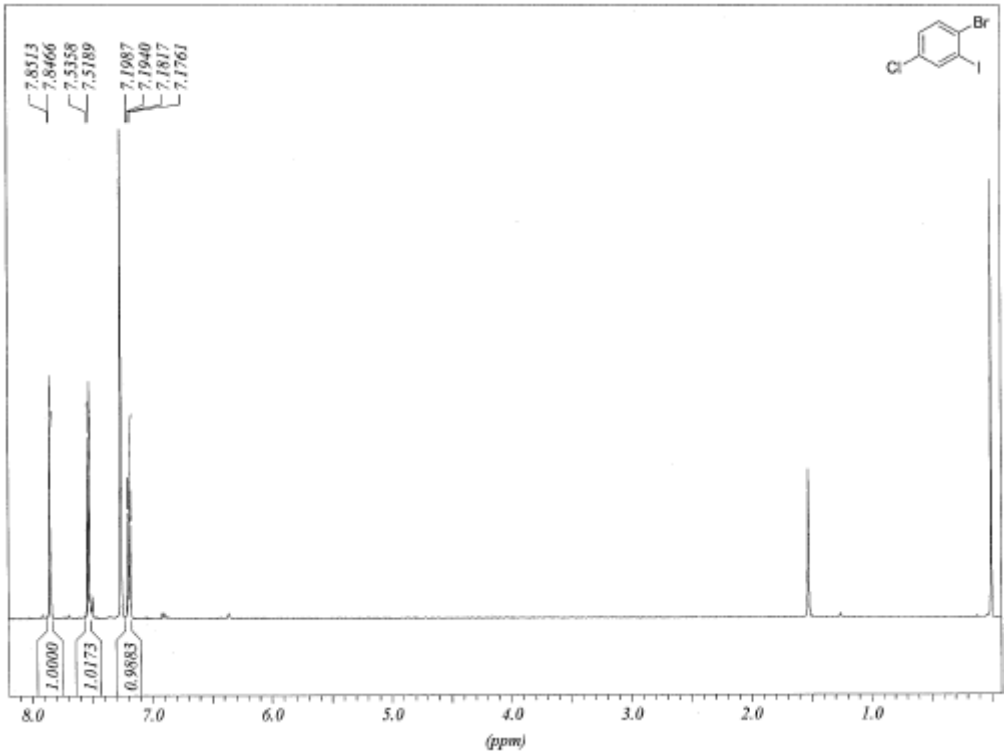
^{13}C NMR	
$C^{1'}$	9.6
C^2	122.2
C^3	111.9
C^{3a}	126.9
C^4	119.7
C^5	119.8
C^6	127.8
C^7	110.8
C^{7a}	136.5

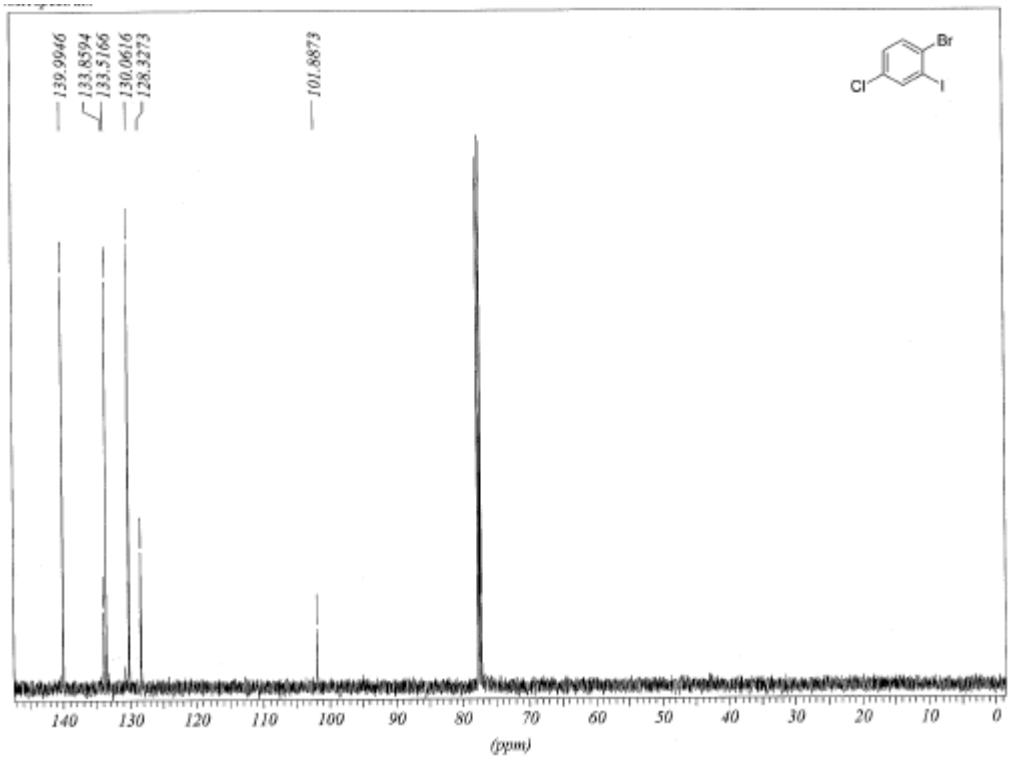
2-Bromo-5-chloro-aniline



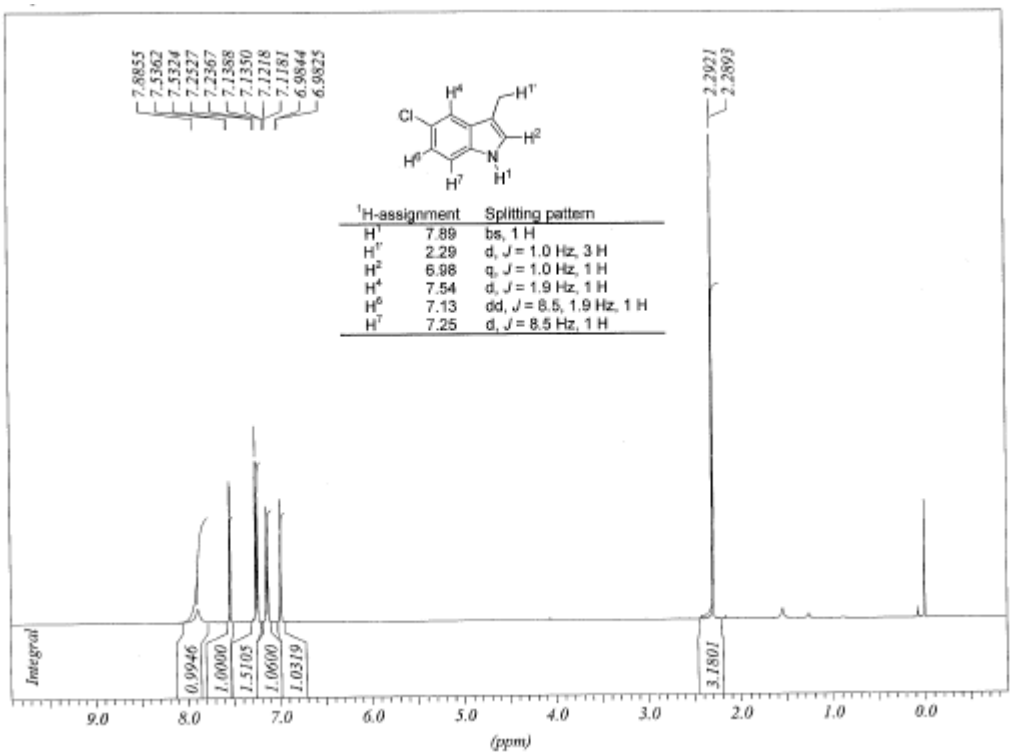


1-Bromo-4-chloro-2-iodo-benzene

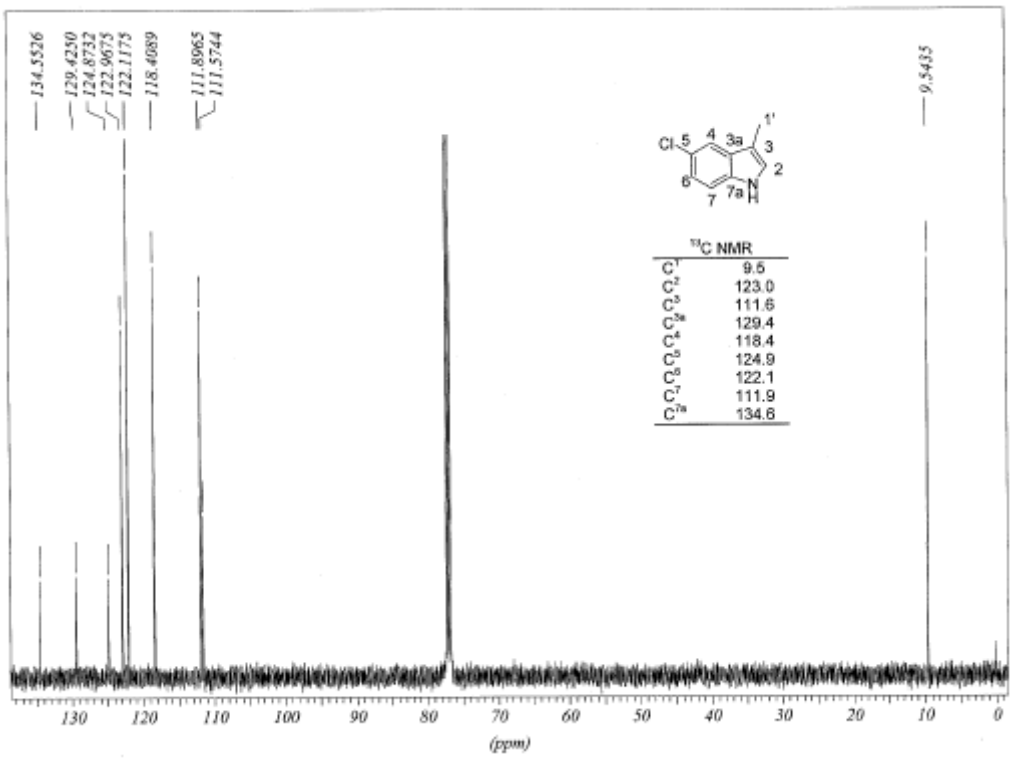




5-Chloro-3-methyl-1*H*-indole

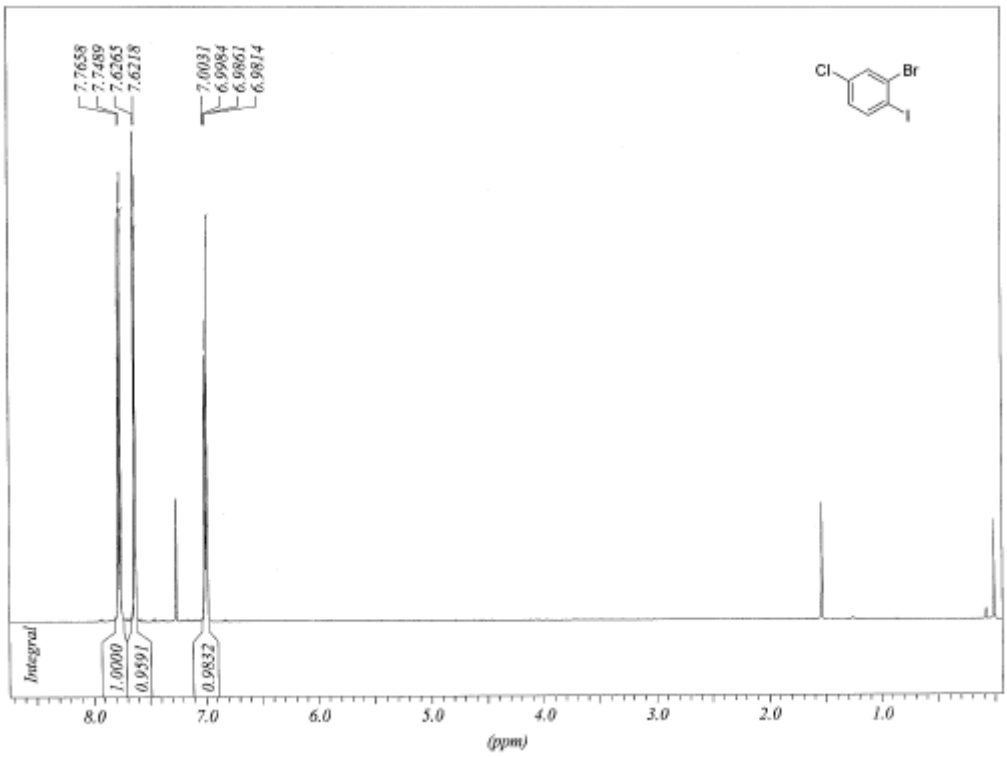


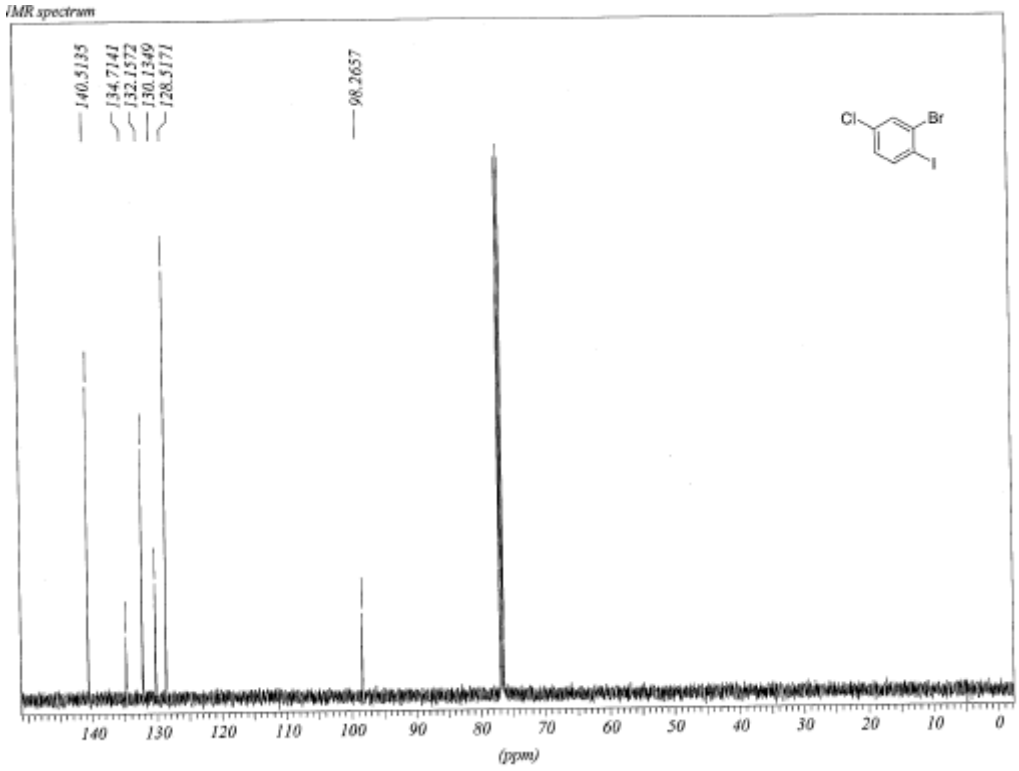
^{1}H-assignment		Splitting pattern
H^1	7.89	bs, 1 H
$H^{1'}$	2.29	d, J = 1.0 Hz, 3 H
H^2	6.98	q, J = 1.0 Hz, 1 H
H^4	7.54	d, J = 1.9 Hz, 1 H
H^6	7.13	dd, J = 8.5, 1.9 Hz, 1 H
H^7	7.25	d, J = 8.5 Hz, 1 H



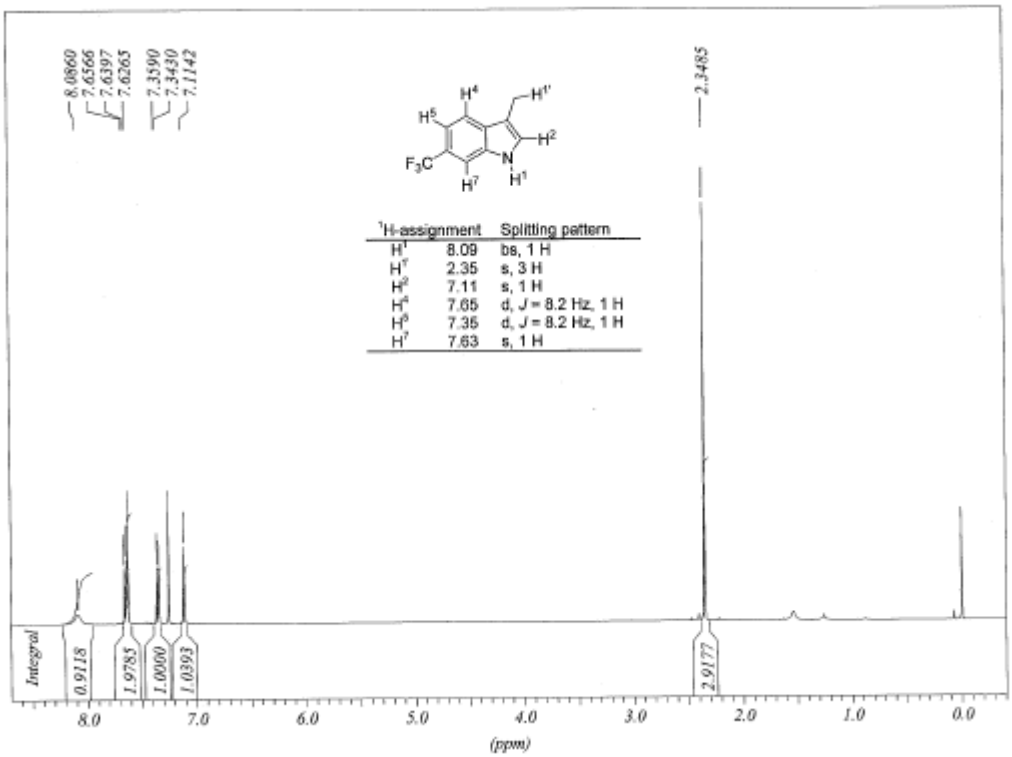
^{13}C NMR	
$C^{1'}$	9.5
C^2	123.0
C^3	111.6
C^{3a}	129.4
C^4	118.4
C^5	124.9
C^6	122.1
C^7	111.9
C^{7a}	134.6

2-Bromo-4-chloro-1-iodo-benzene

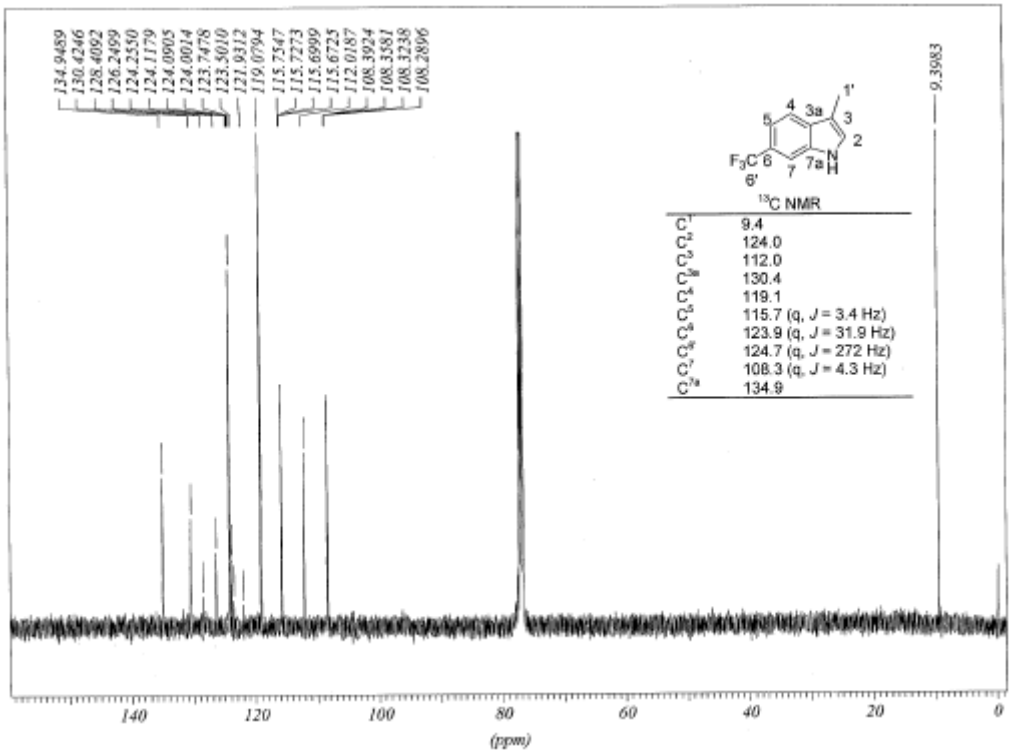




3-Methyl-6-trifluoromethyl-1*H*-indole



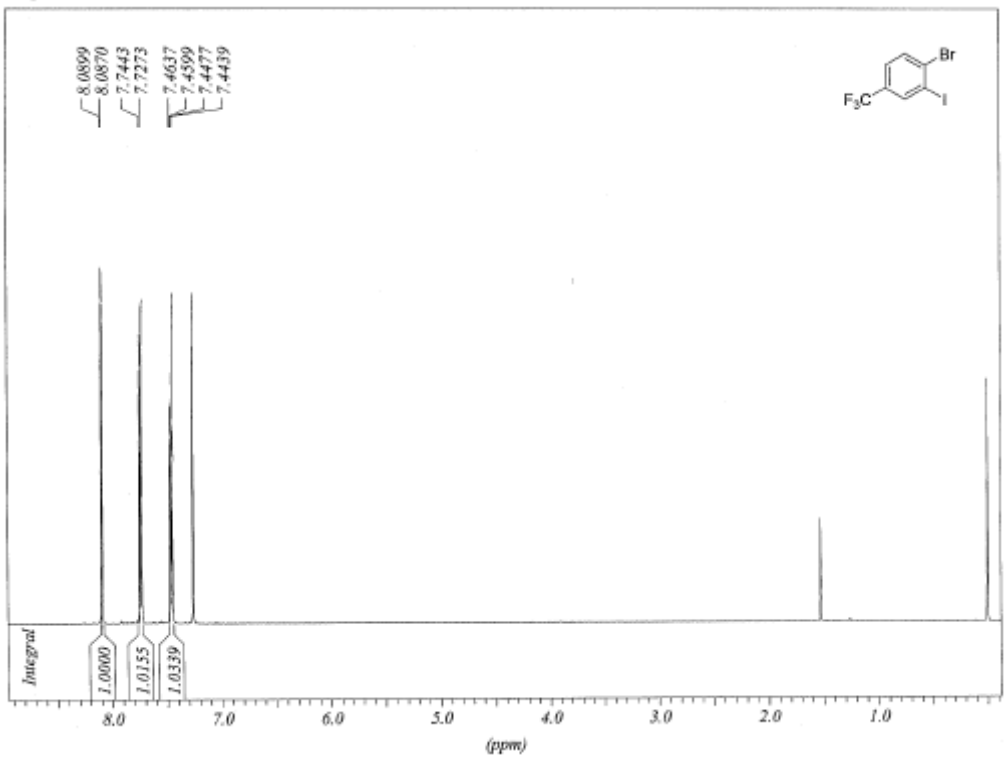
^{1}H-assignment		Splitting pattern
H^1	8.09	bs, 1 H
$H^{1'}$	2.35	s, 3 H
H^2	7.11	s, 1 H
H^5	7.65	d, J = 8.2 Hz, 1 H
H^6	7.35	d, J = 8.2 Hz, 1 H
H^7	7.63	s, 1 H

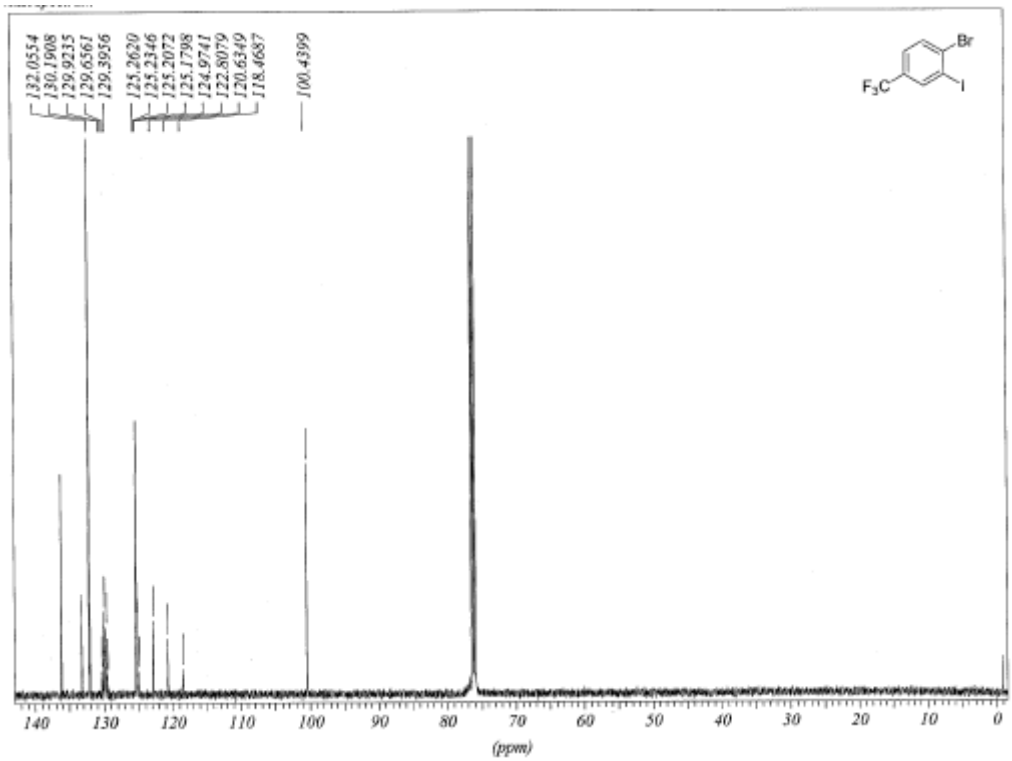


^{13}C NMR

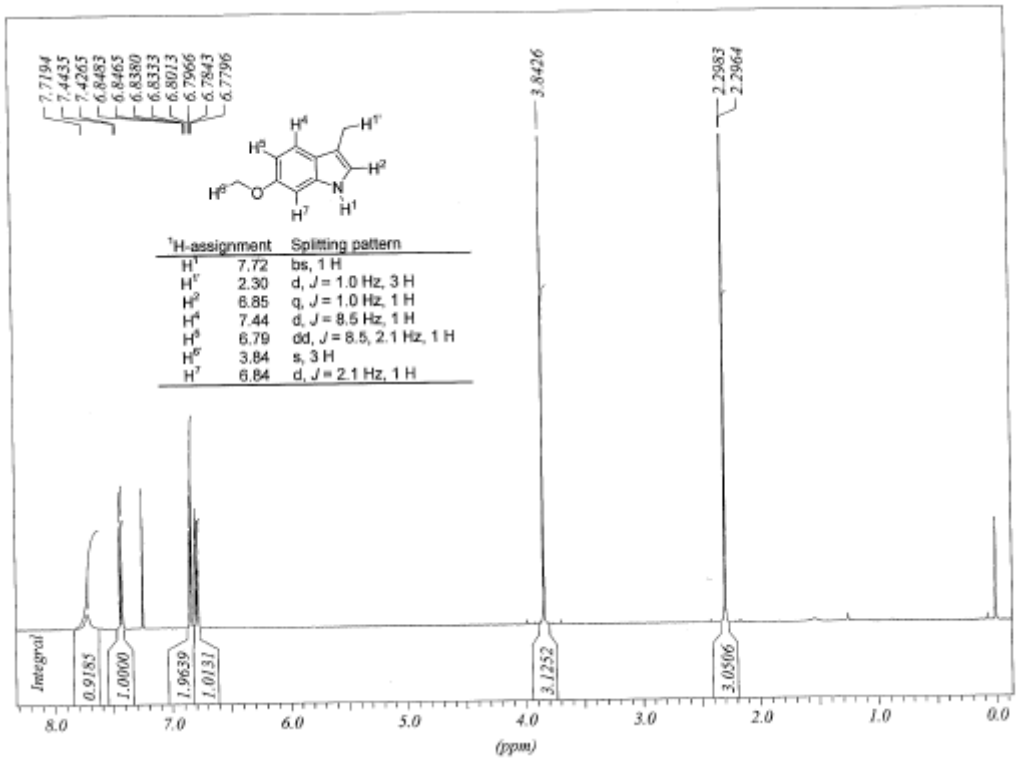
$C^{1'}$	9.4
C^{2}	124.0
C^{3}	112.0
C^{3a}	130.4
C^{5}	119.1
C^{6}	115.7 (q, J = 3.4 Hz)
$C^{6'}$	123.9 (q, J = 31.9 Hz)
C^{7}	124.7 (q, J = 272 Hz)
C^{7a}	108.3 (q, J = 4.3 Hz)
	134.9

1-Bromo-2-iodo-4-trifluoromethylbenzene

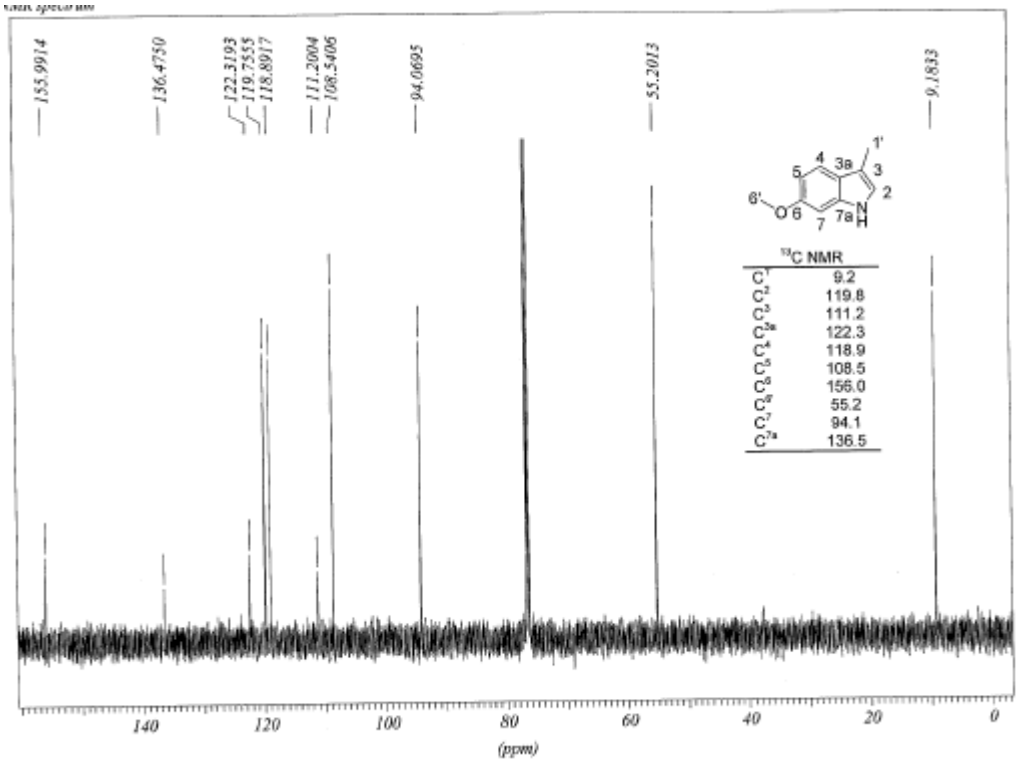




6-Methoxy-3-methyl-1*H*-indole

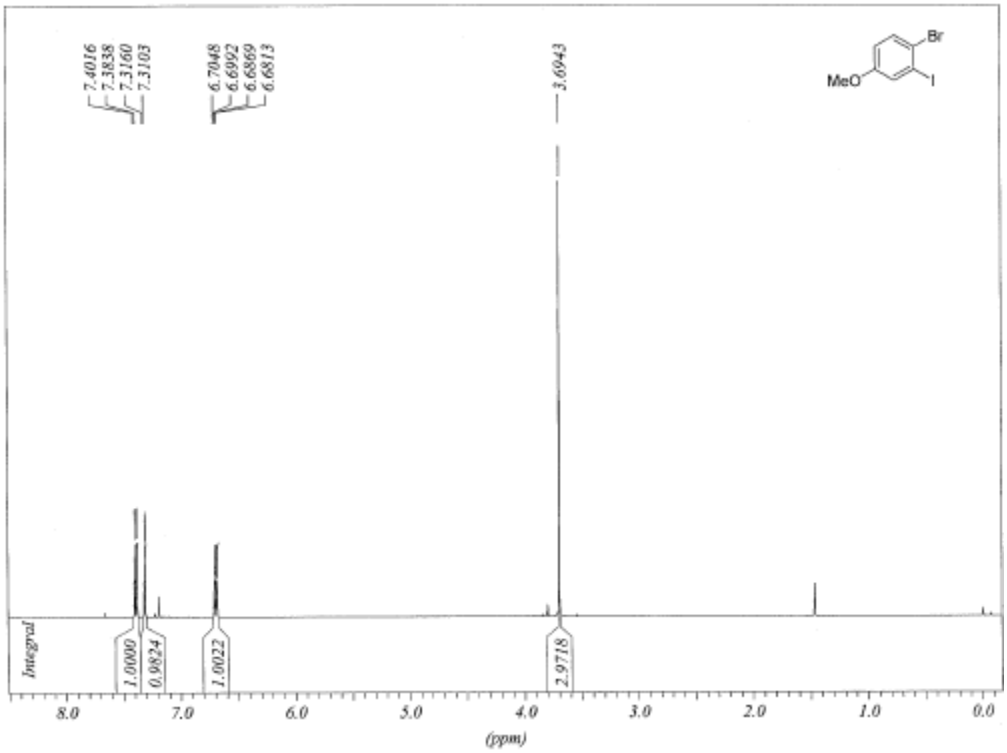


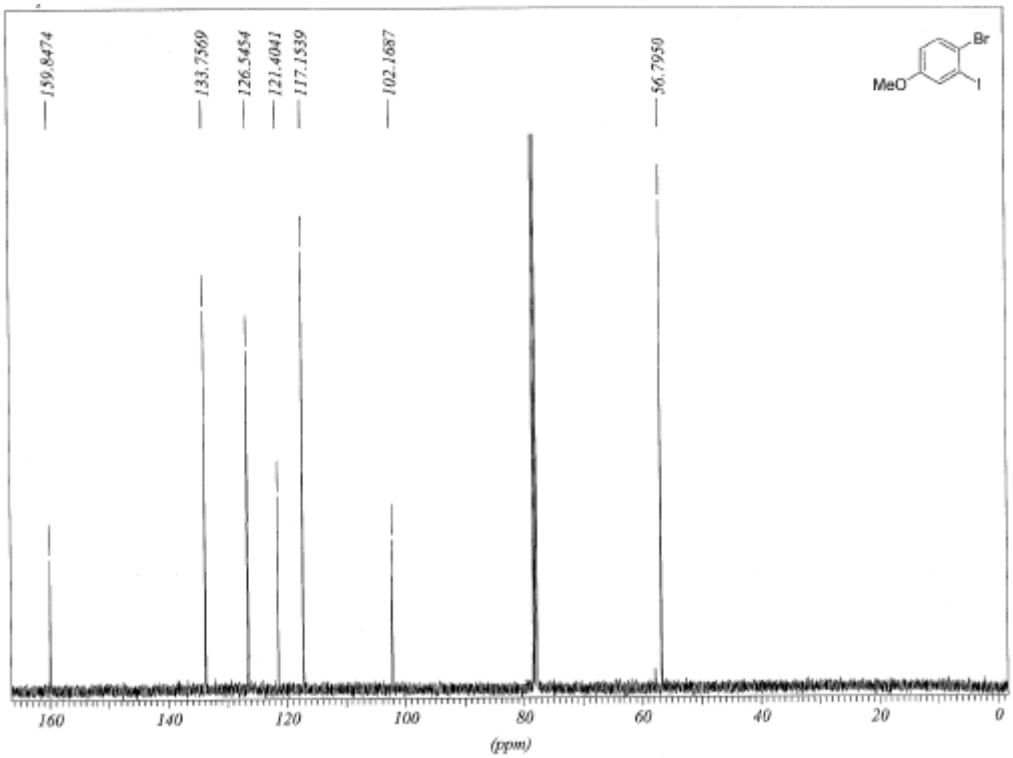
^{1}H-assignment		Splitting pattern
H^1	7.72	bs, 1 H
$H^{1'}$	2.30	d, *J* = 1.0 Hz, 3 H
H^2	6.85	q, *J* = 1.0 Hz, 1 H
H^4	7.44	d, *J* = 8.5 Hz, 1 H
H^5	6.79	dd, *J* = 8.5, 2.1 Hz, 1 H
H^6	3.84	s, 3 H
H^7	6.84	d, *J* = 2.1 Hz, 1 H



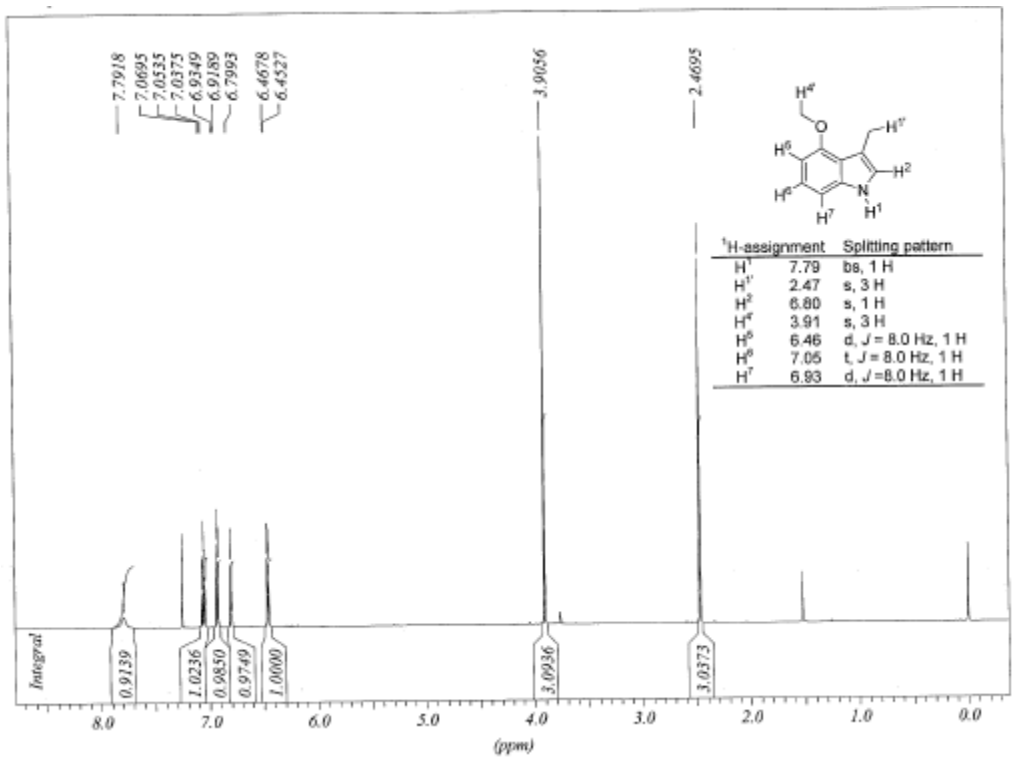
^{13}C NMR	
$C^{1'}$	9.2
C^3	119.8
C^2	111.2
C^{3a}	122.3
C^4	118.9
C^5	108.5
C^6	156.0
$C^{6'}$	55.2
C^7	94.1
C^{7a}	136.5

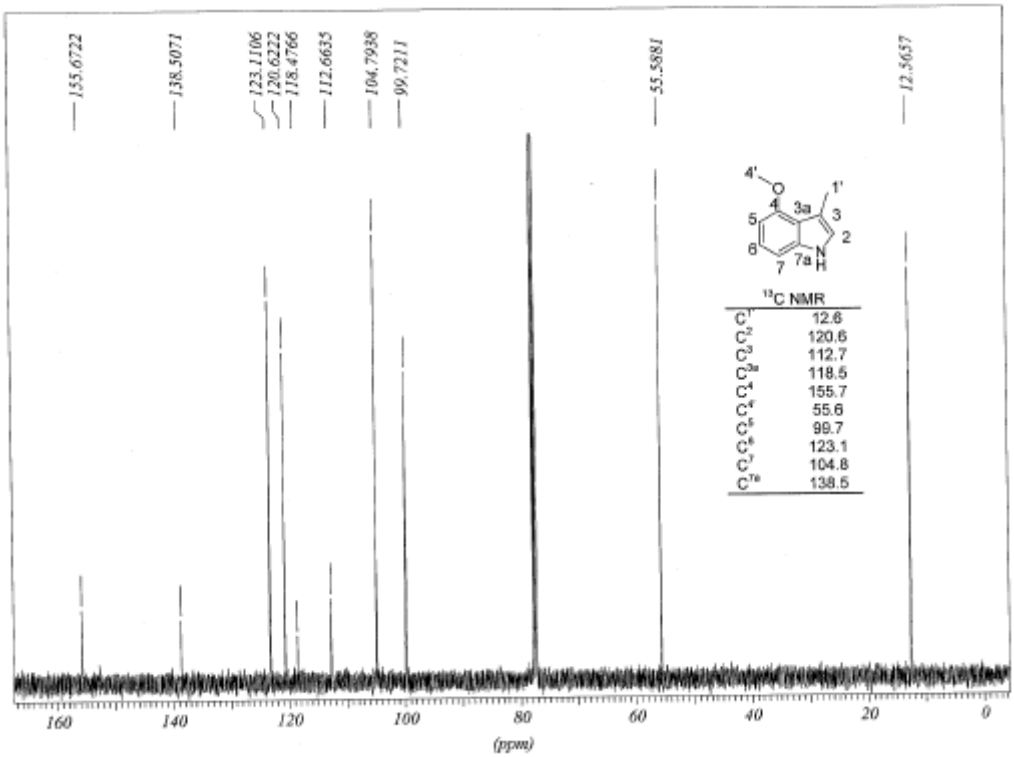
1-Bromo-2-iodo-4-methoxy-benzene



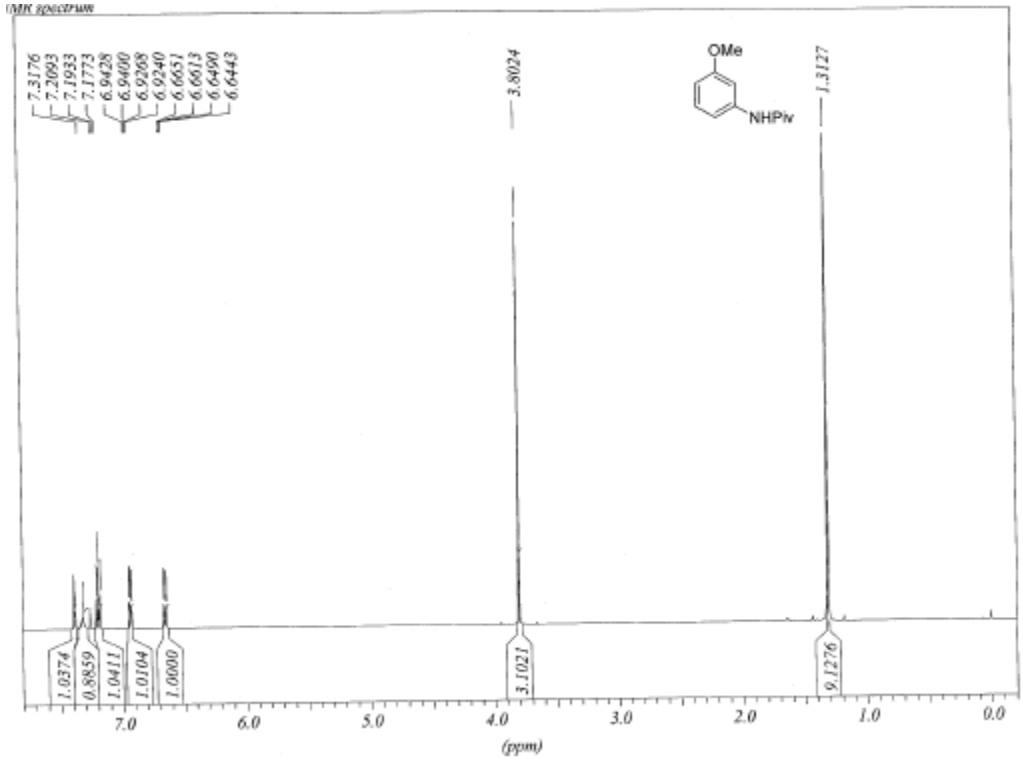


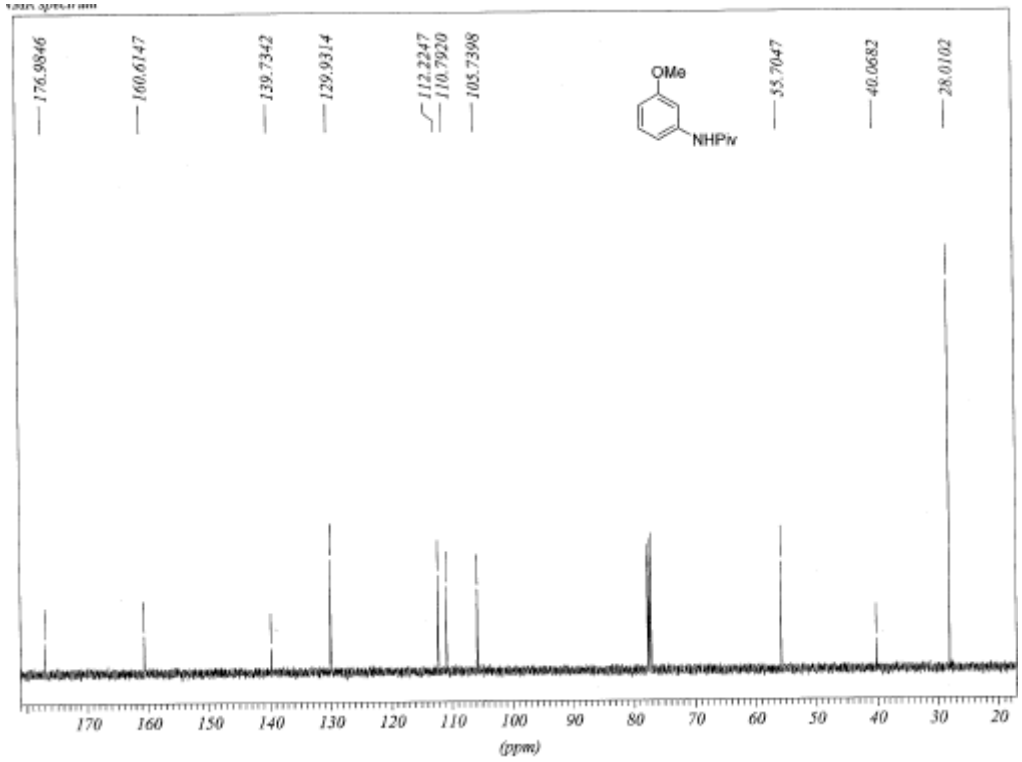
4-Methoxy-3-methyl-1*H*-indole



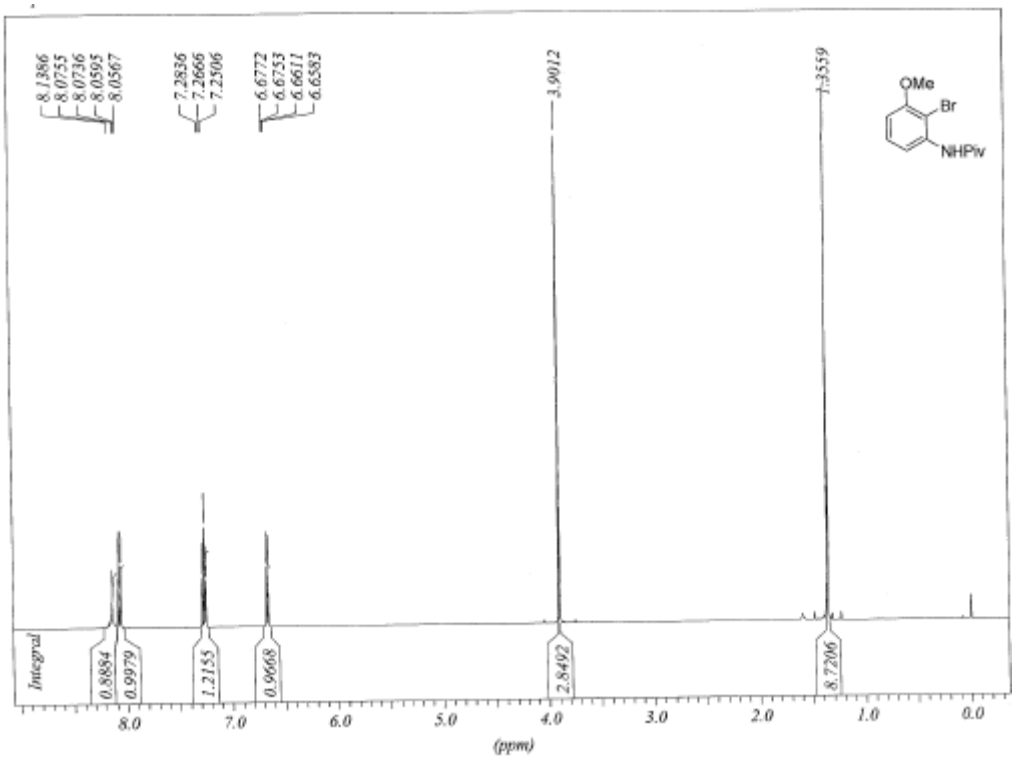


_N_-(3-Methoxy-phenyl)-2,2-dimethyl-propionamide





_N_-(2-Bromo-3-methoxy-phenyl)-2,2-dimethyl-propionamide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OMe
Br
NHPiv
Integral
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1.2155
0.9668
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7.0
6.0
5.0
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3.0
2.0
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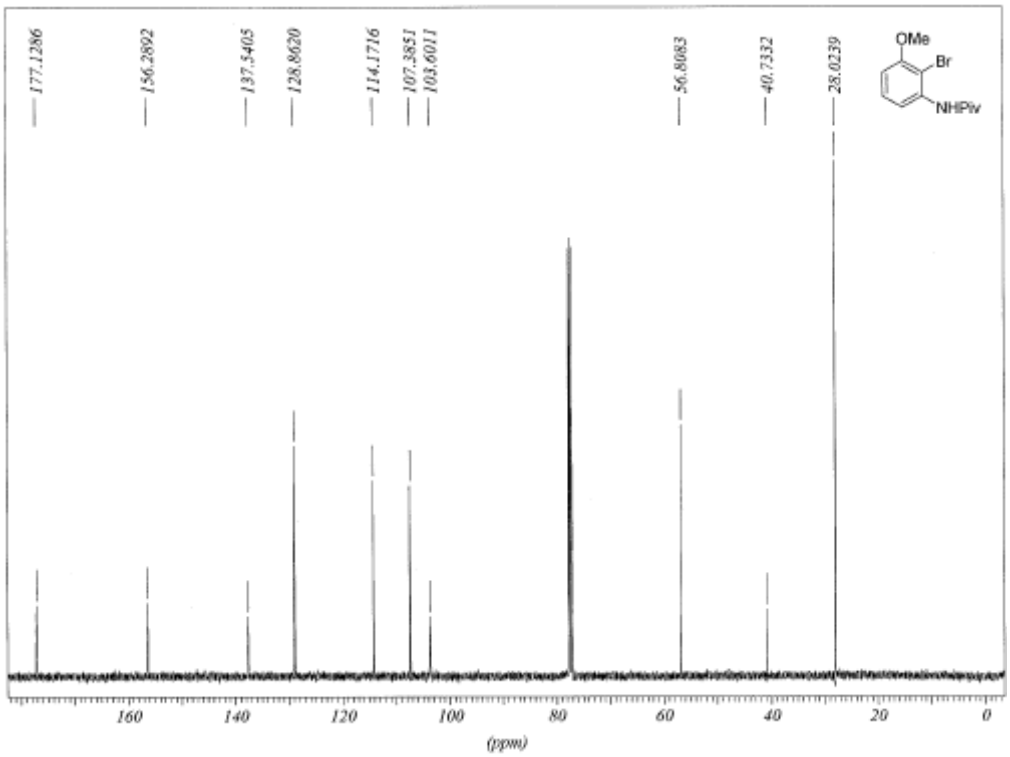
(ppm)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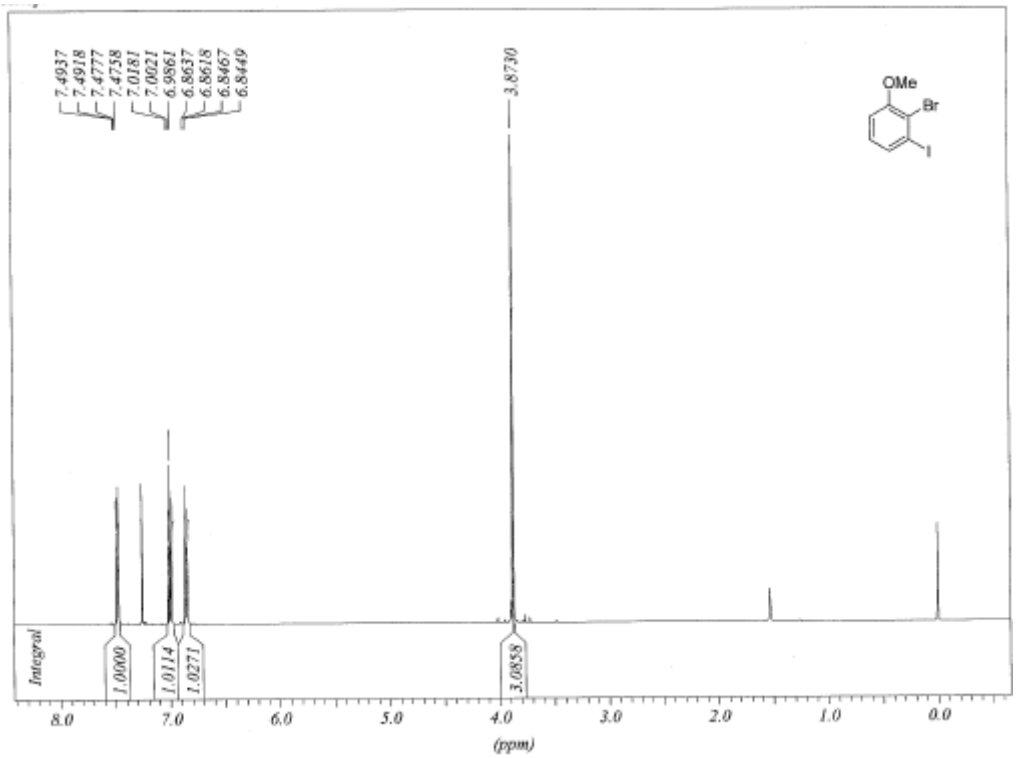
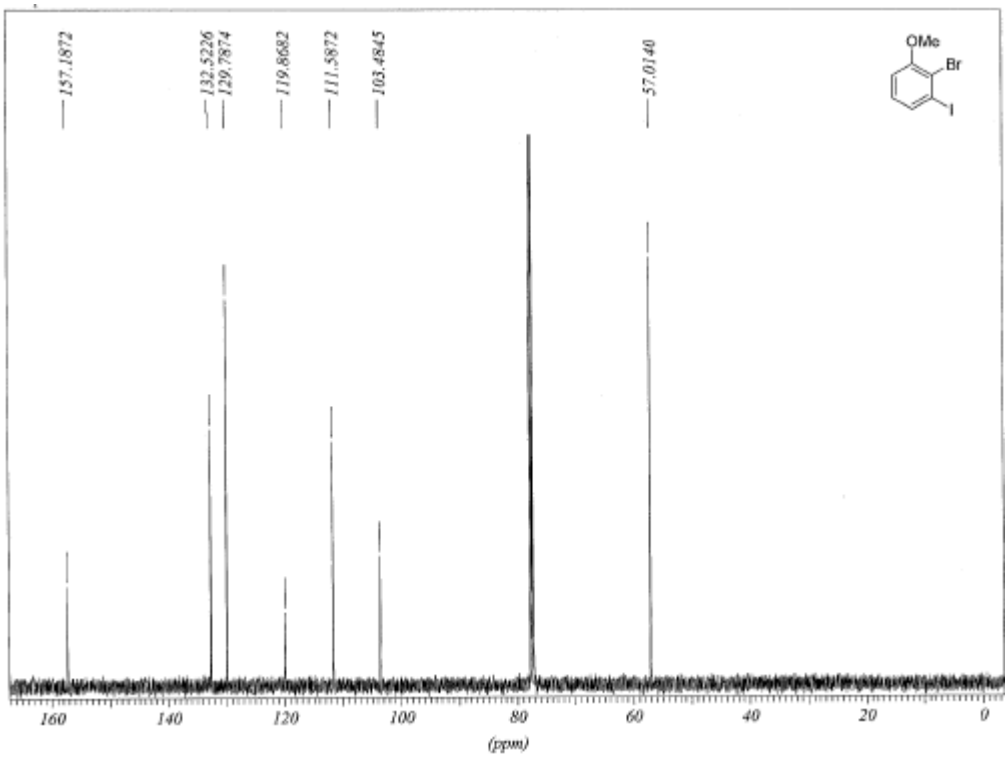
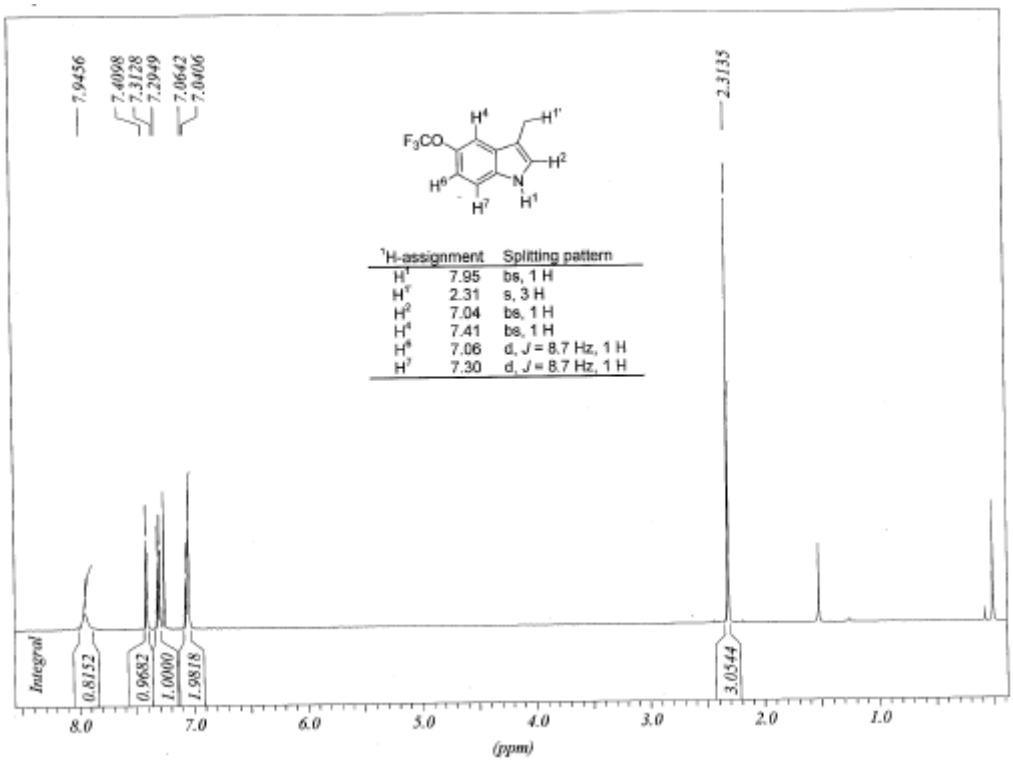
(ppm)

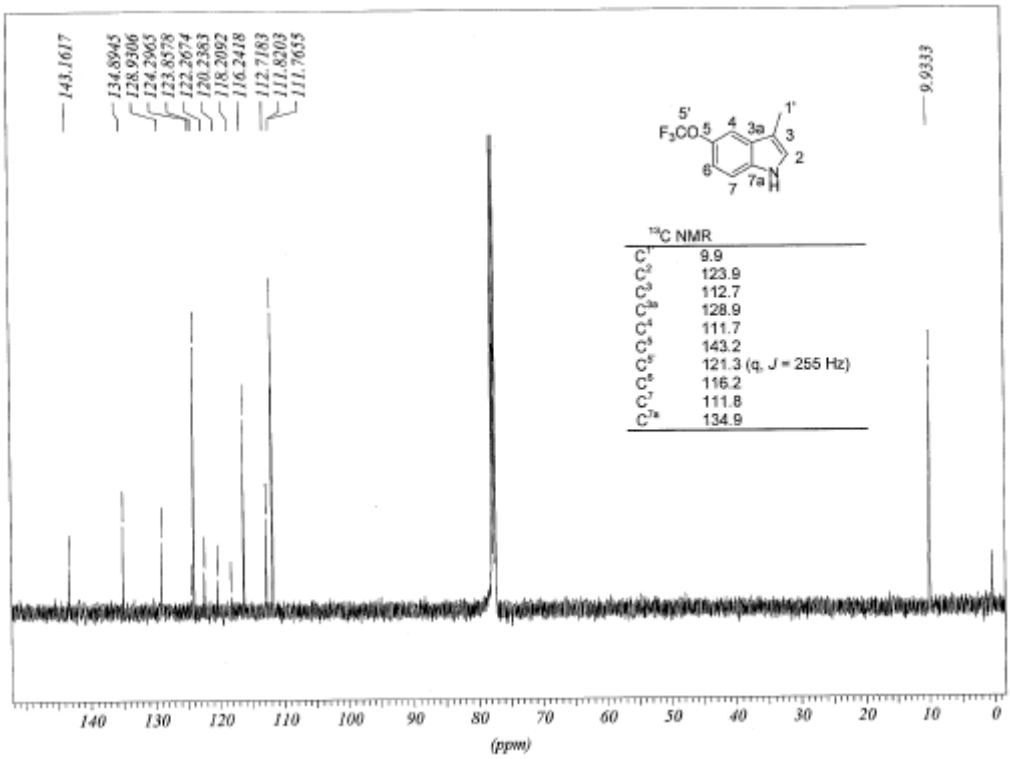
2-Bromo-1-iodo-3-methoxy-benzene



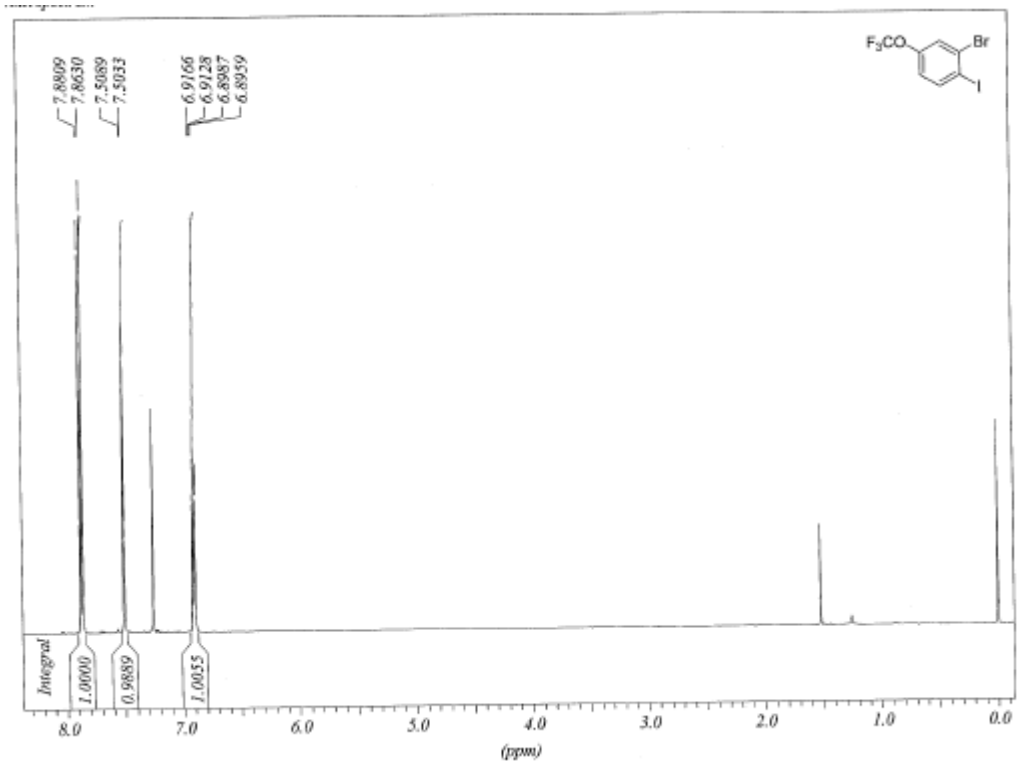


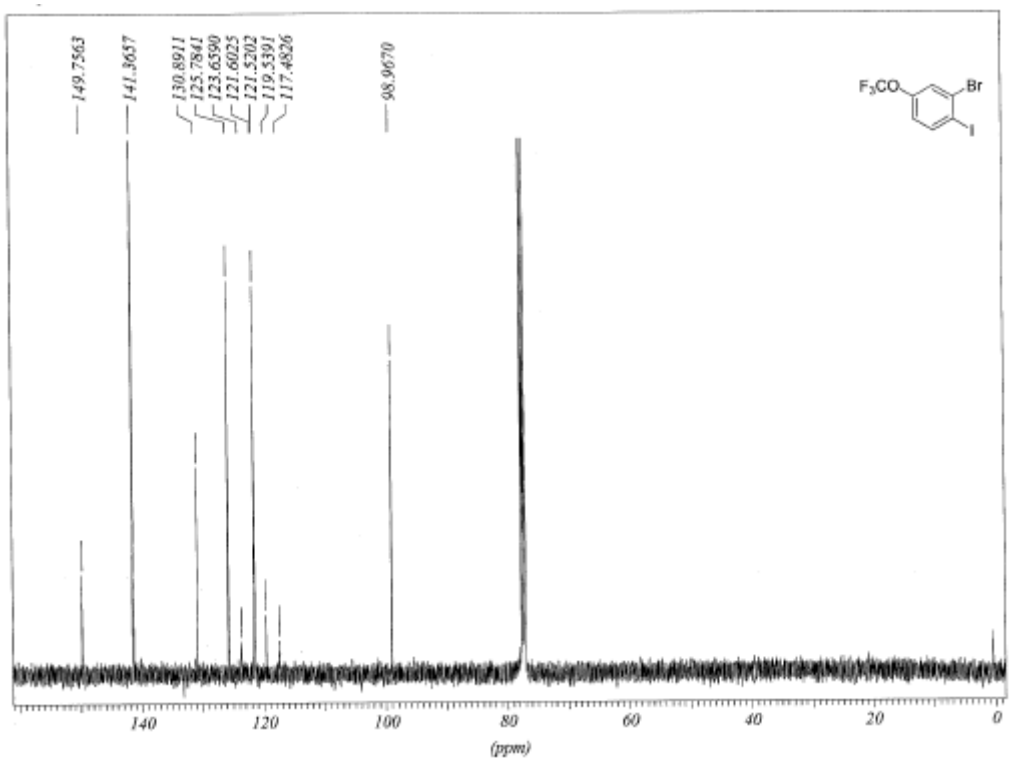
3-Methyl-5-trifluoromethoxy-1*H*-indole



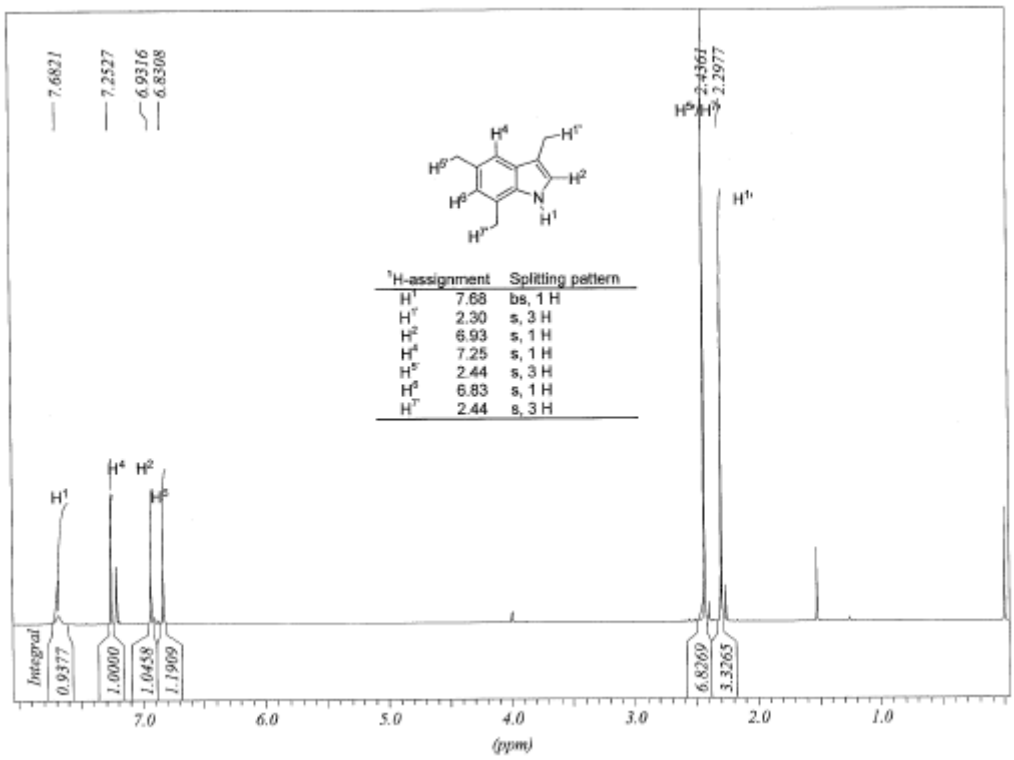


2-Bromo-1-iodo-4-trifluoromethoxy-benzene

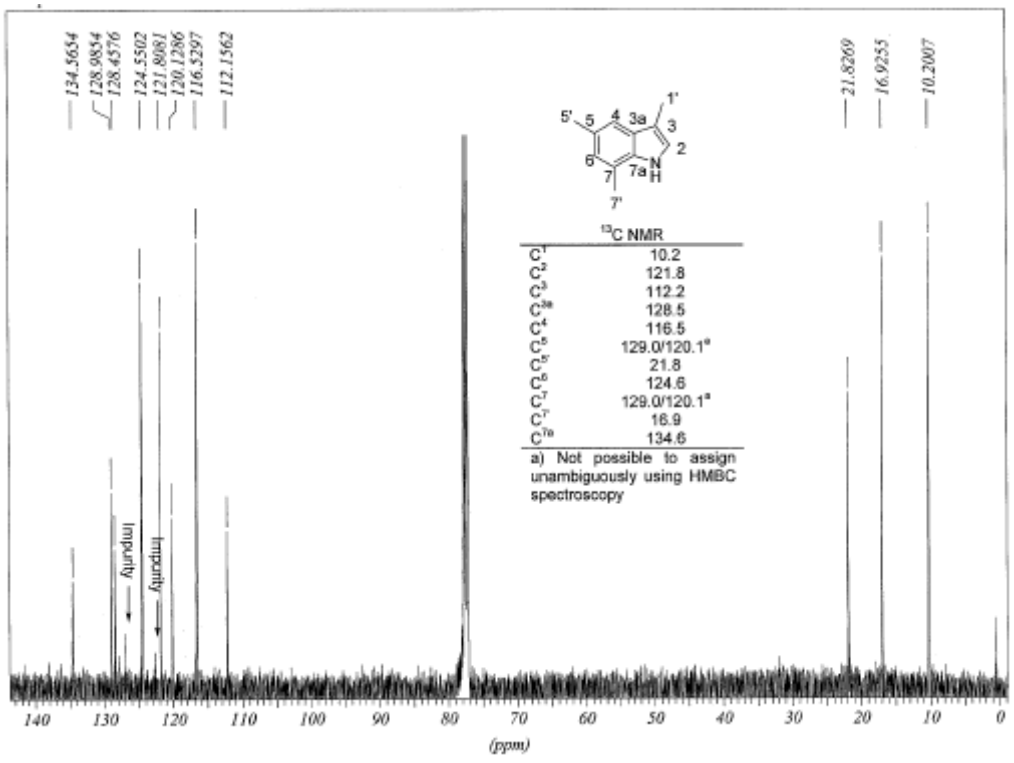




3,5,7-Trimethyl-1*H*-indole



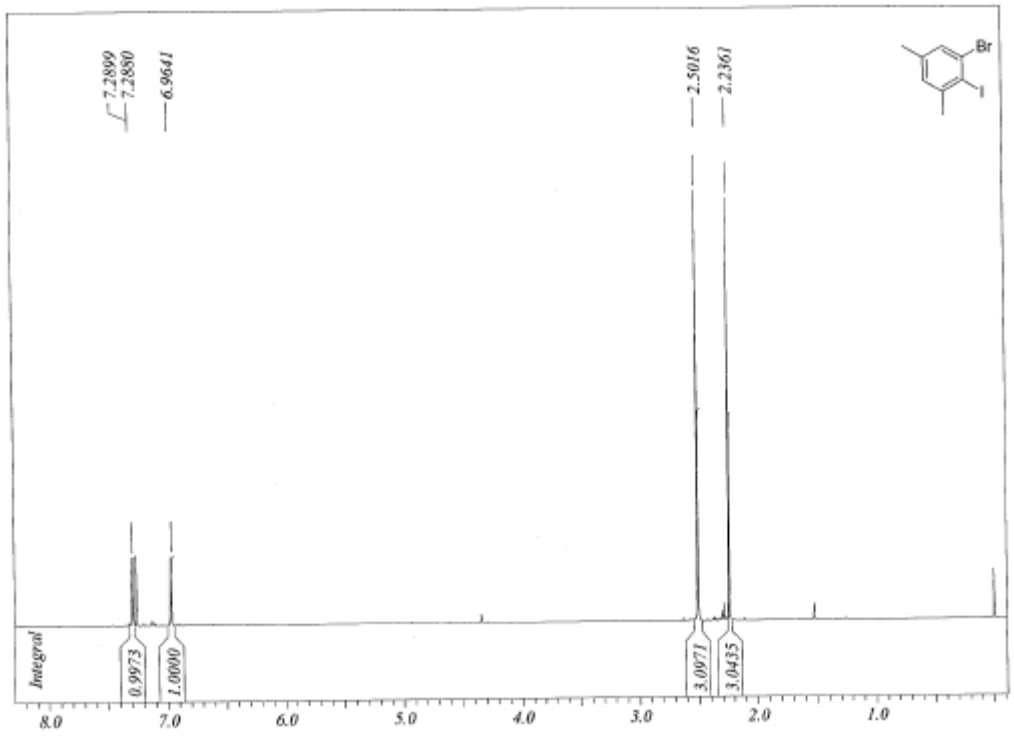
^{1}H-assignment		Splitting pattern
H^1	7.68	bs, 1 H
$H^{7'}$	2.30	s, 3 H
H^2	6.93	s, 1 H
H^4	7.25	s, 1 H
$H^{5'}$	2.44	s, 3 H
H^3	6.83	s, 1 H
$H^{7'}$	2.44	s, 3 H

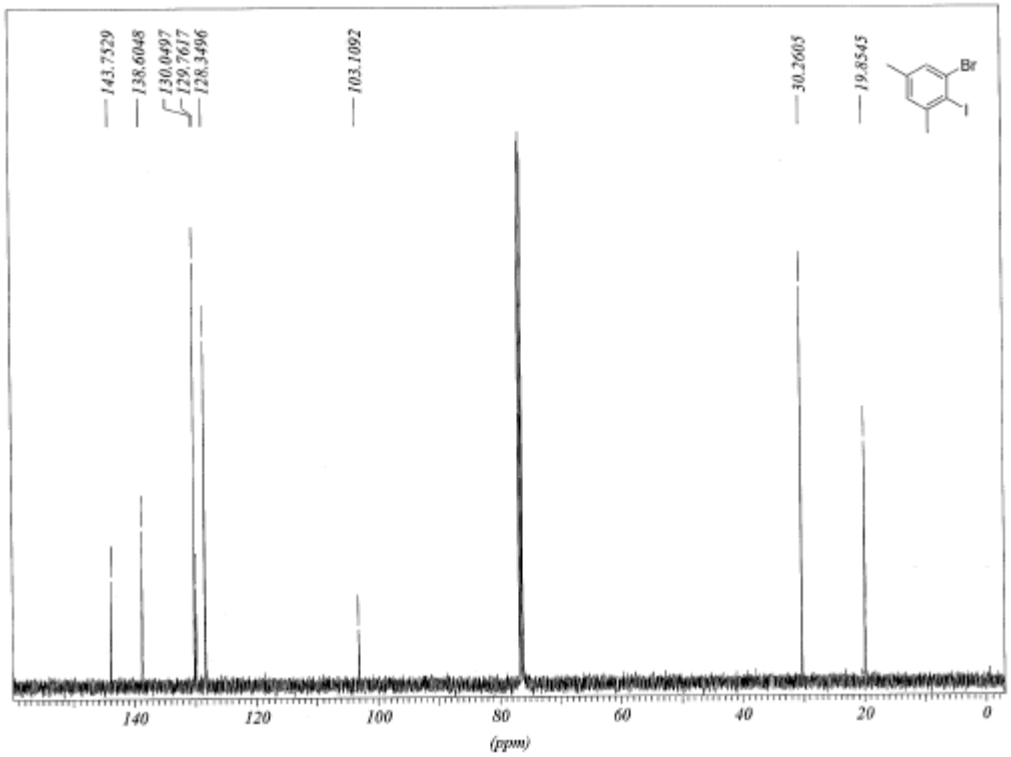


^{13}C NMR	
C^1	10.2
C^2	121.8
C^3	112.2
C^{3a}	128.5
C^4	116.5
C^5	129.0/120.1[a]
$C^{5'}$	21.8
C^6	124.6
C^7	129.0/120.1[a]
$C^{7'}$	16.9
C^{7a}	134.6

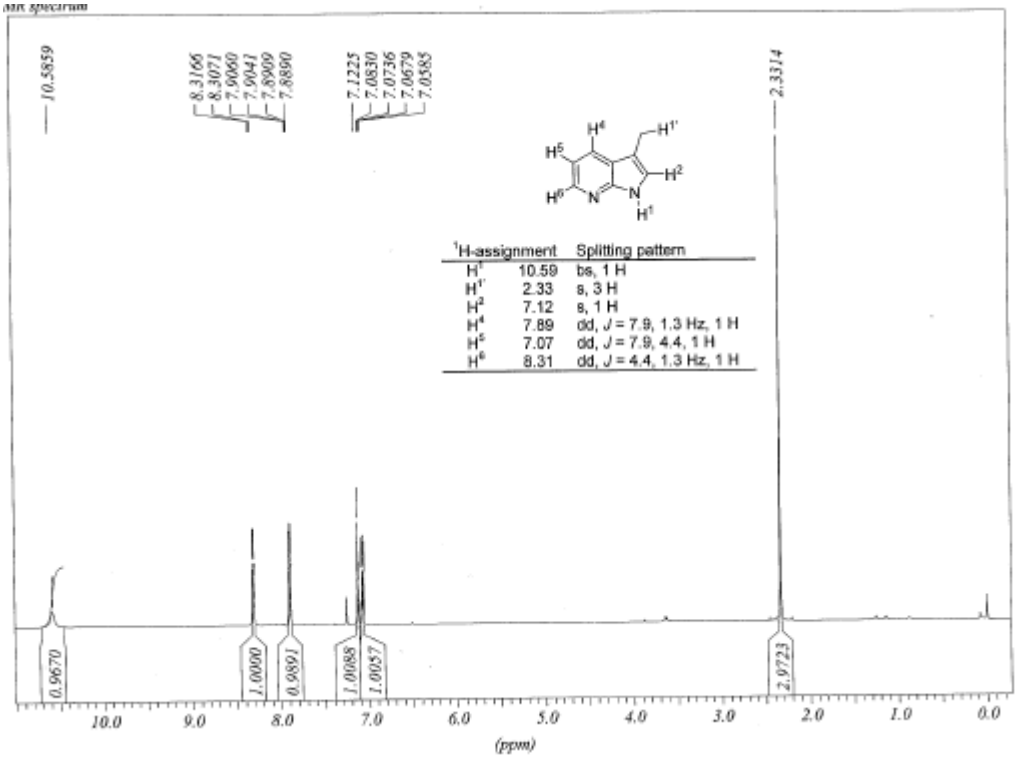
a) Not possible to assign unambiguously using HMBC spectroscopy

1-Bromo-2-iodo-3,5-dimethyl-benzene

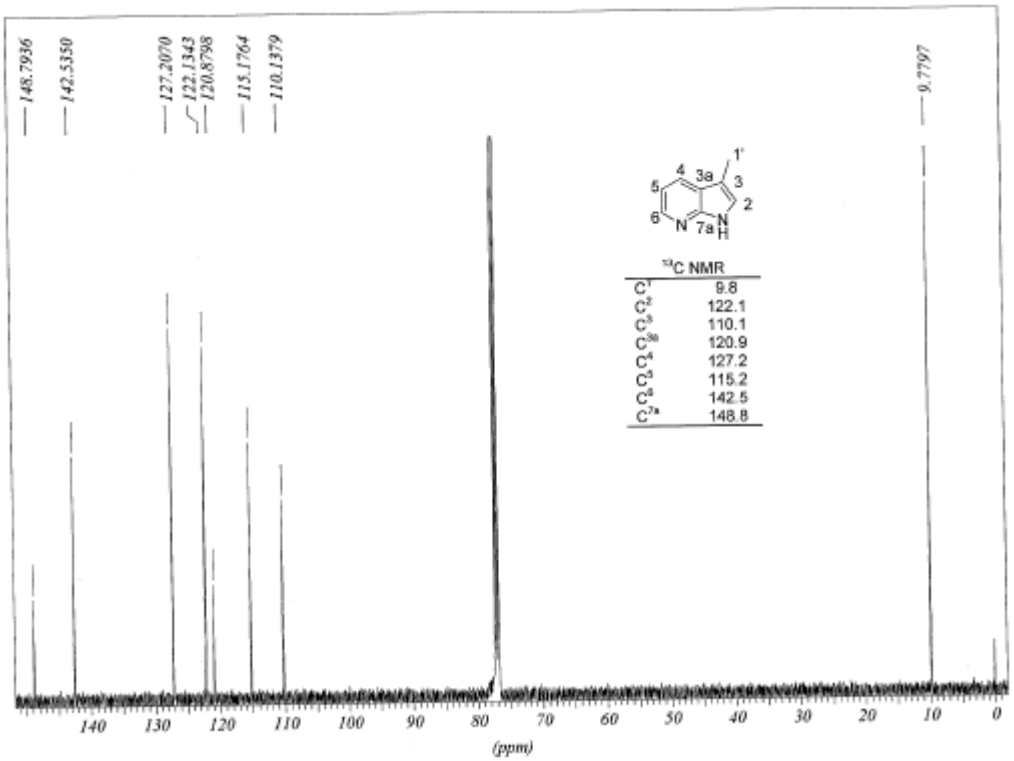




3-Methyl-1*H*-pyrrolo[2,3-b]pyridine

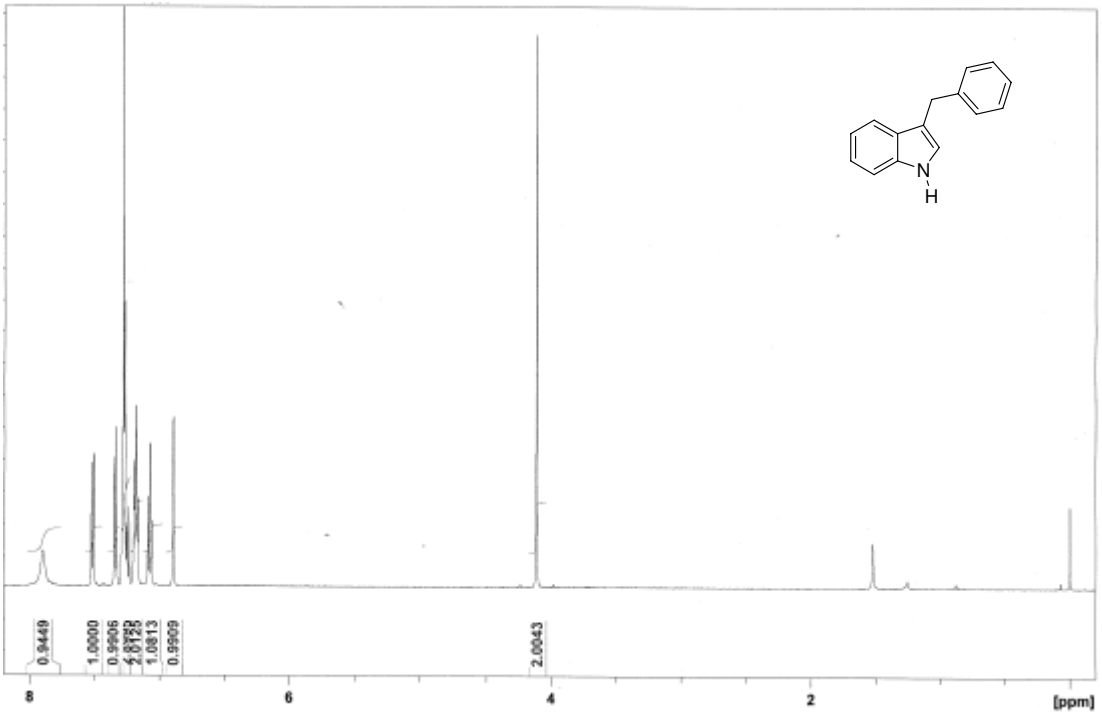


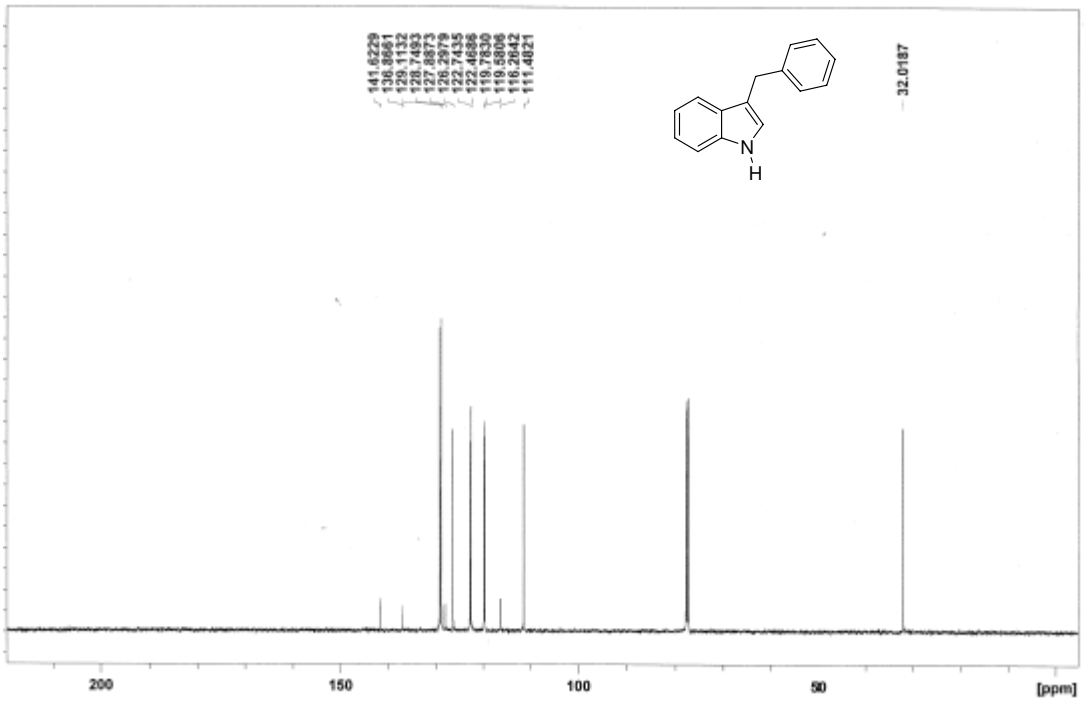
^{1}H-assignment		Splitting pattern
H^1	10.59	bs, 1 H
$H^{1'}$	2.33	s, 3 H
H^2	7.12	s, 1 H
H^4	7.89	dd, *J* = 7.9, 1.3 Hz, 1 H
H^5	7.07	dd, *J* = 7.9, 4.4, 1 H
H^6	8.31	dd, *J* = 4.4, 1.3 Hz, 1 H



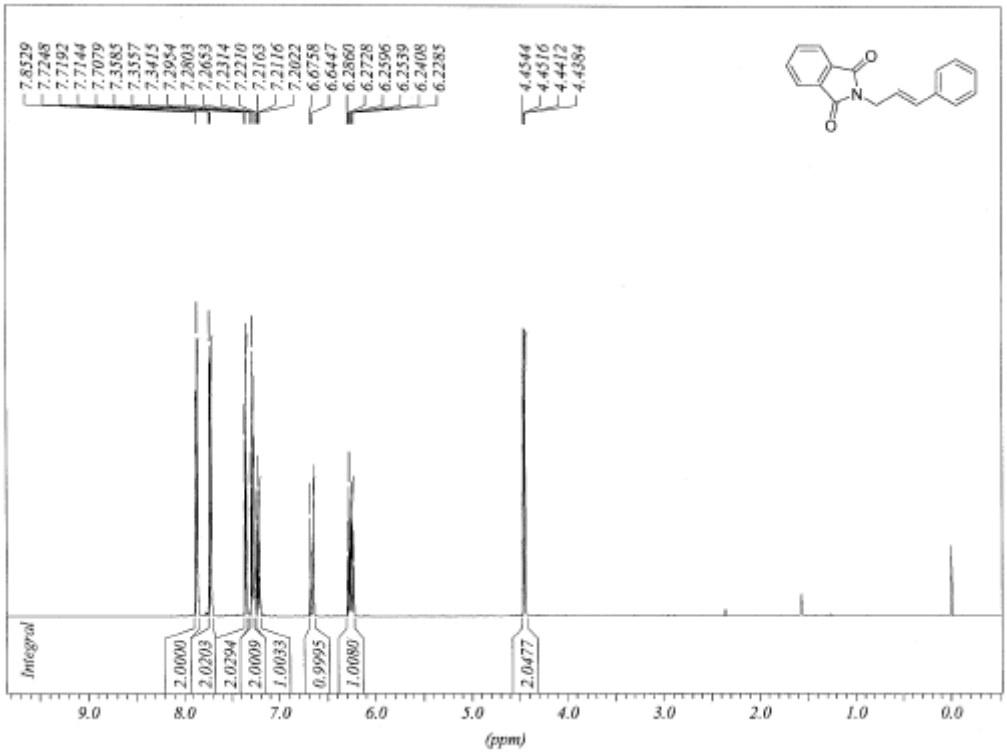
^{13}C NMR	
C^1	9.8
C^2	122.1
C^3	110.1
C^{3a}	120.9
C^4	127.2
C^5	115.2
C^6	142.5
C^{7a}	148.8

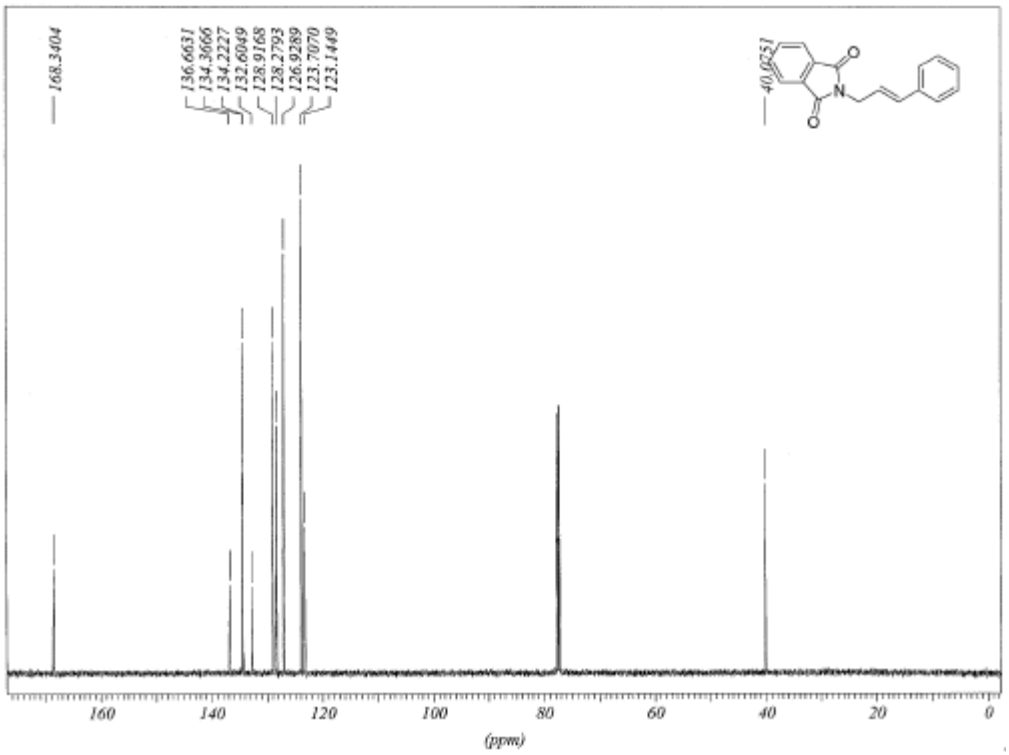
3-Benzyl-1*H*-indole



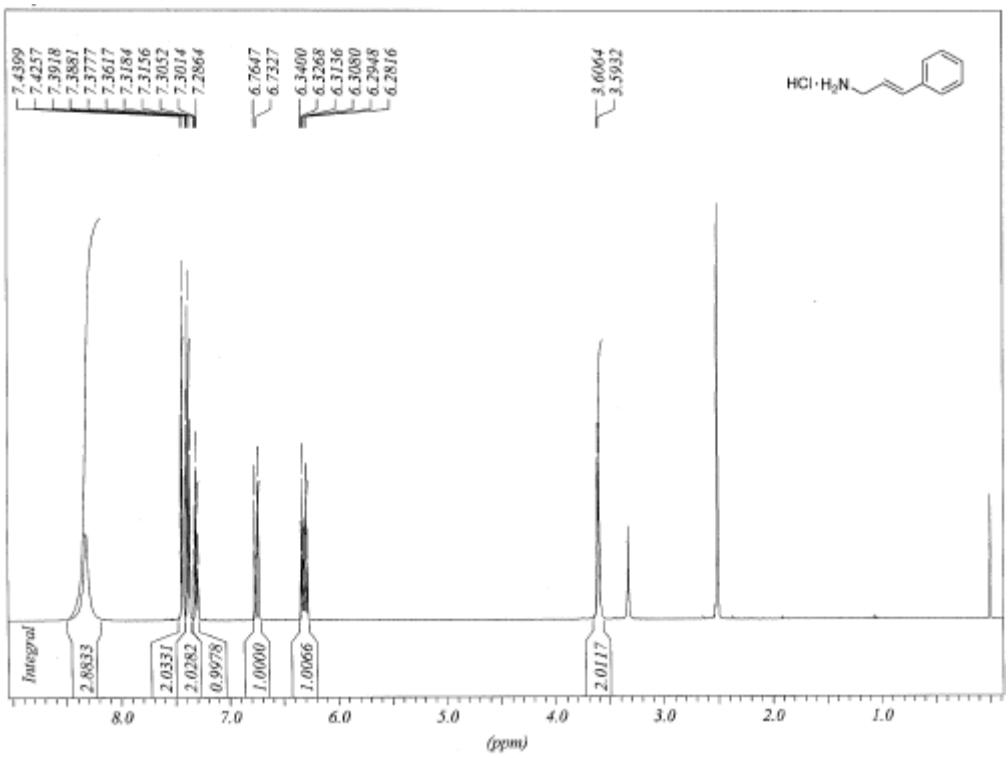


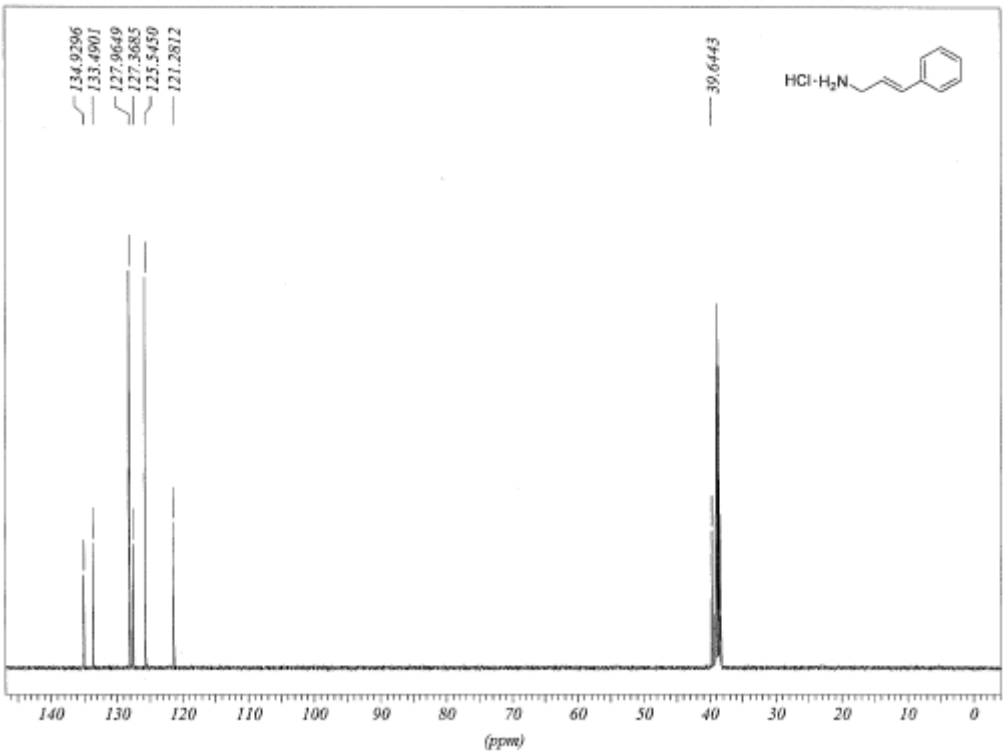
2-[(*E*)-3-Phenyl-allyl]-isoindole-1,3-dione



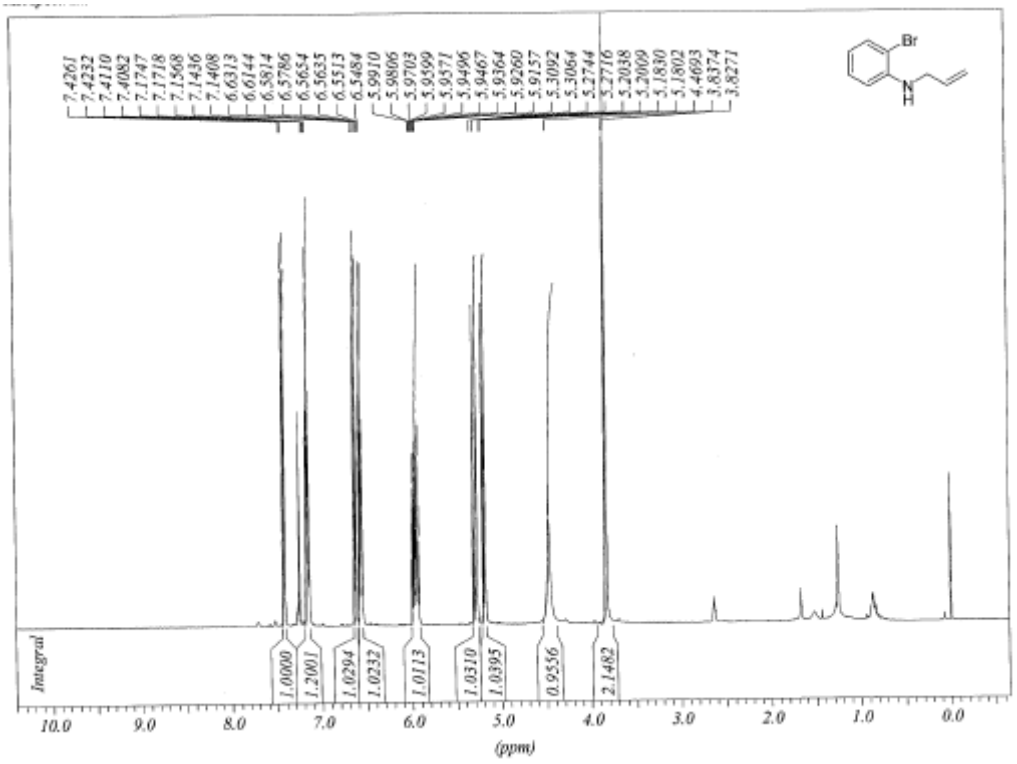


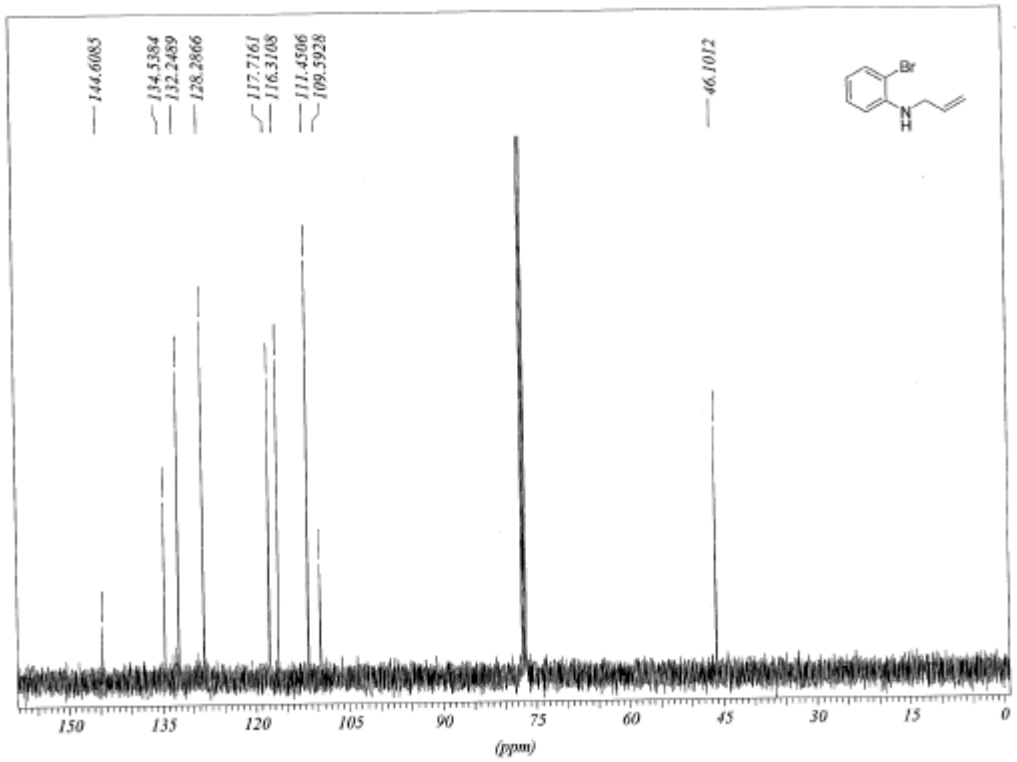
(*E*)-3-Phenyl-allyl-ammonium chloride



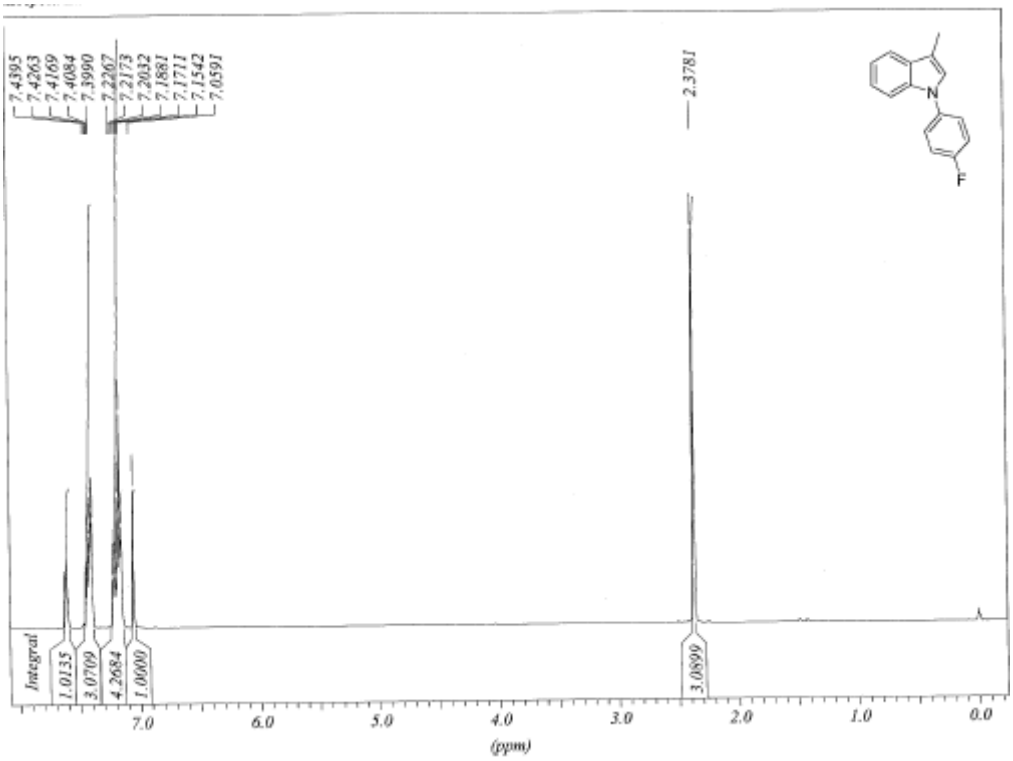


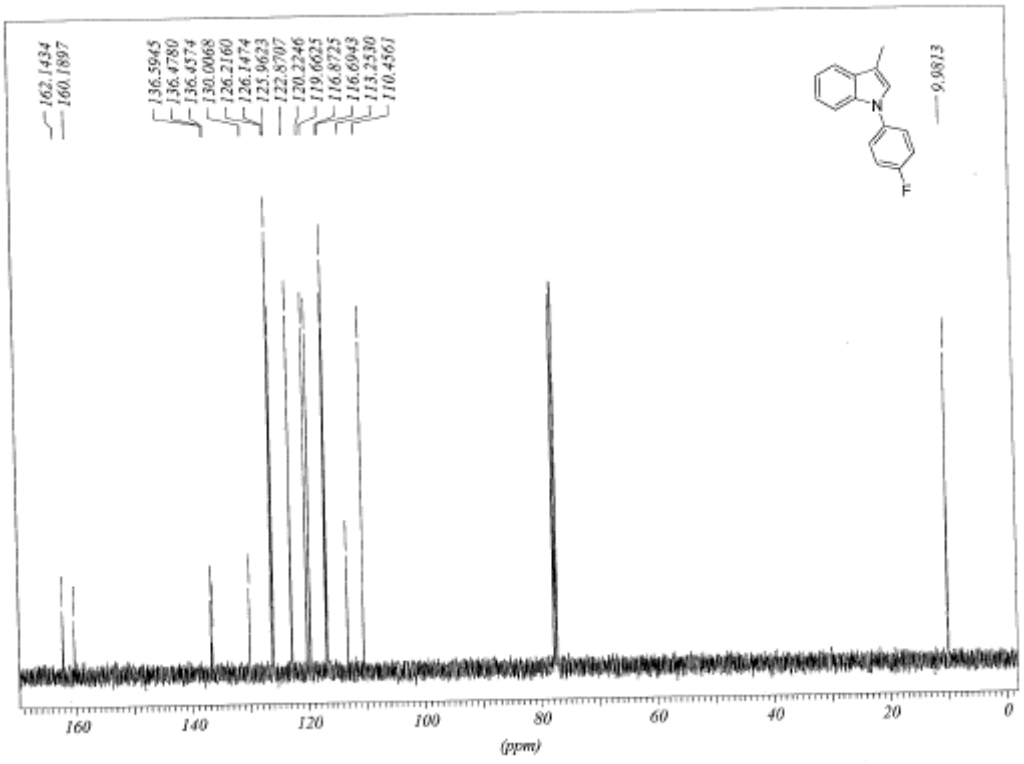
_N_-Allyl-(2-bromo-phenyl)-amine (2)



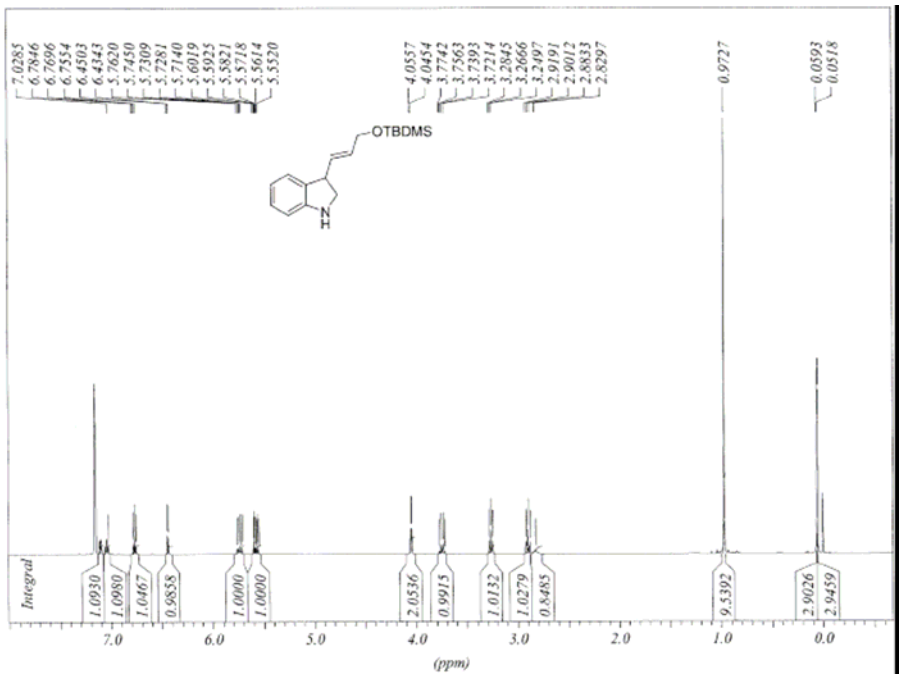


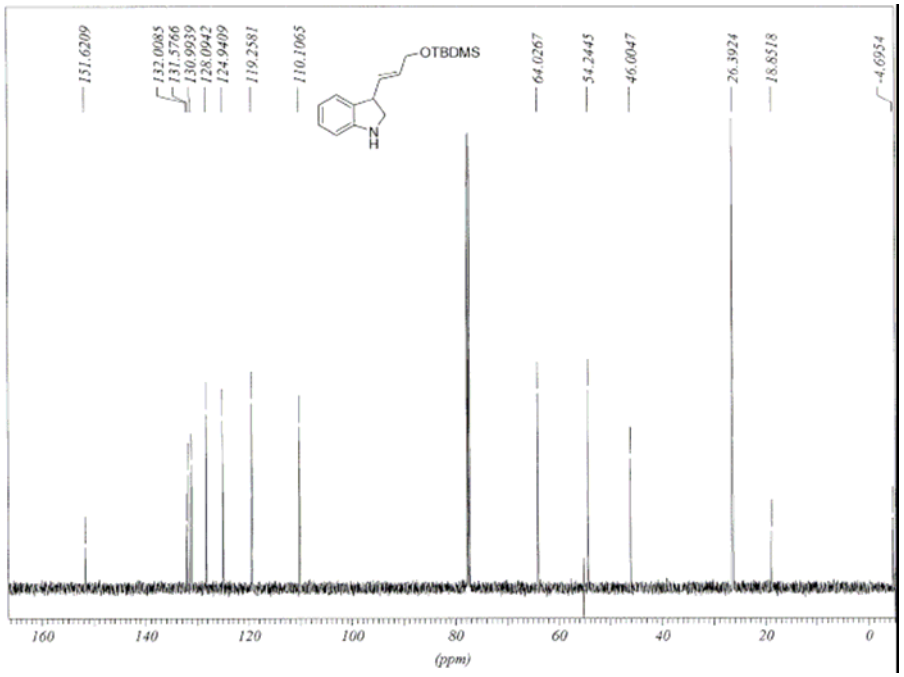
1-(4-Fluoro-phenyl)-3-methyl-1*H*-indole



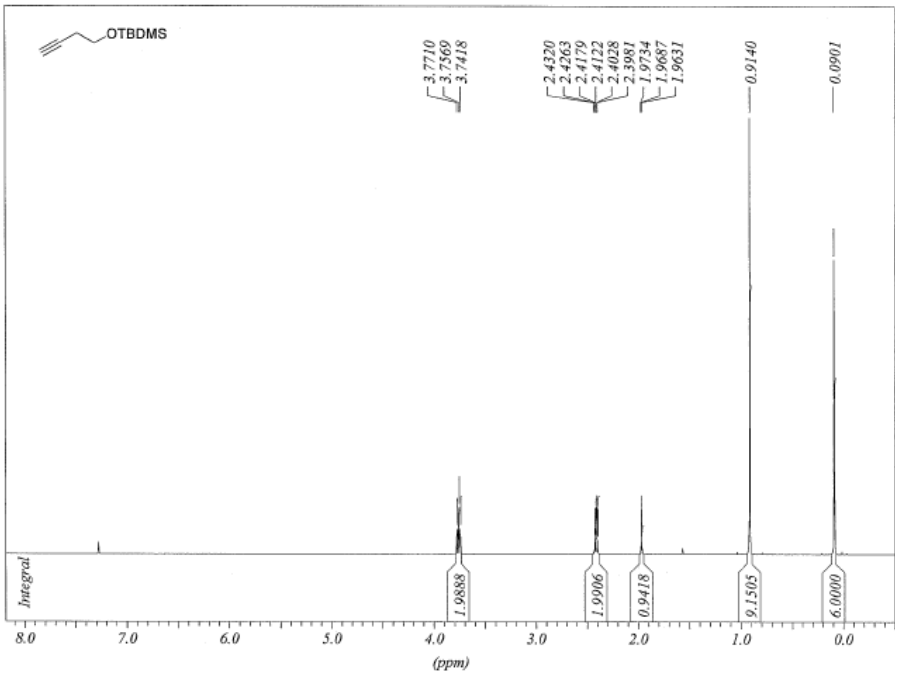


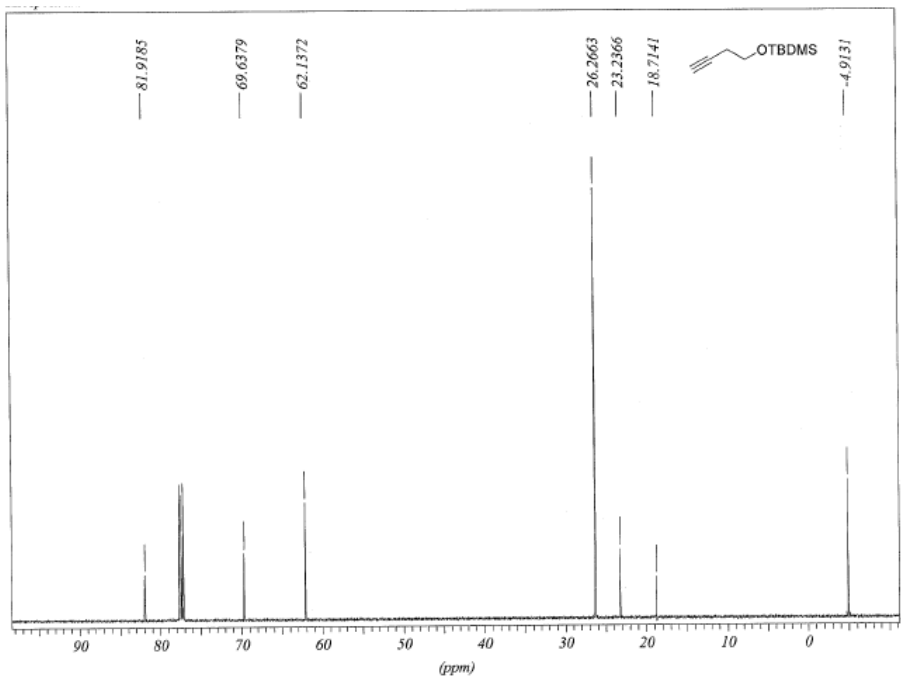
3-[(*E*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-propenyl]-2,3-dihydro-1*H*-indole



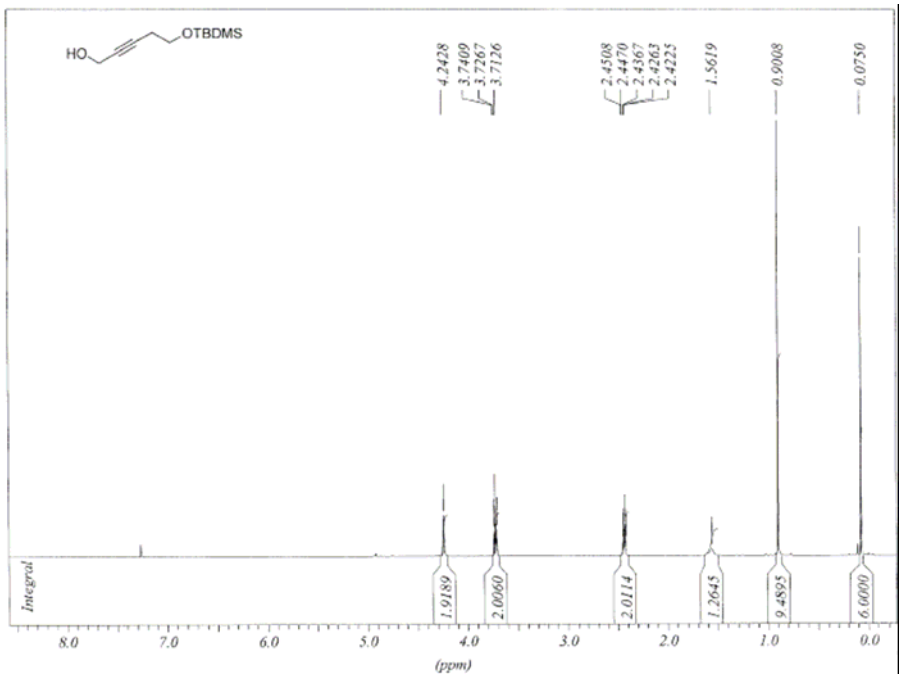


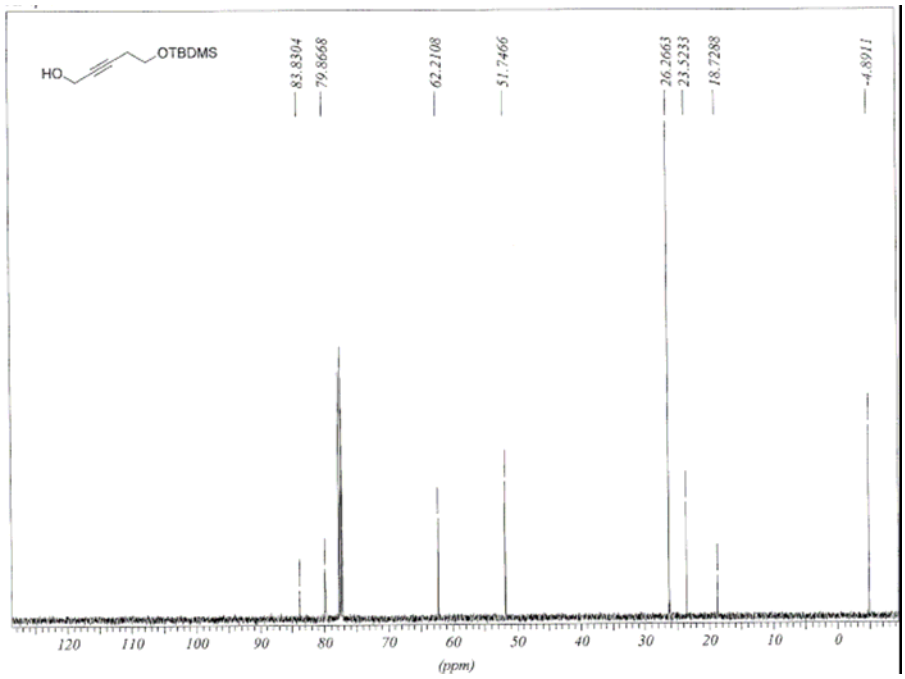
1-(*tert*-Butyl-dimethyl-silanyloxy)-but-3-yne



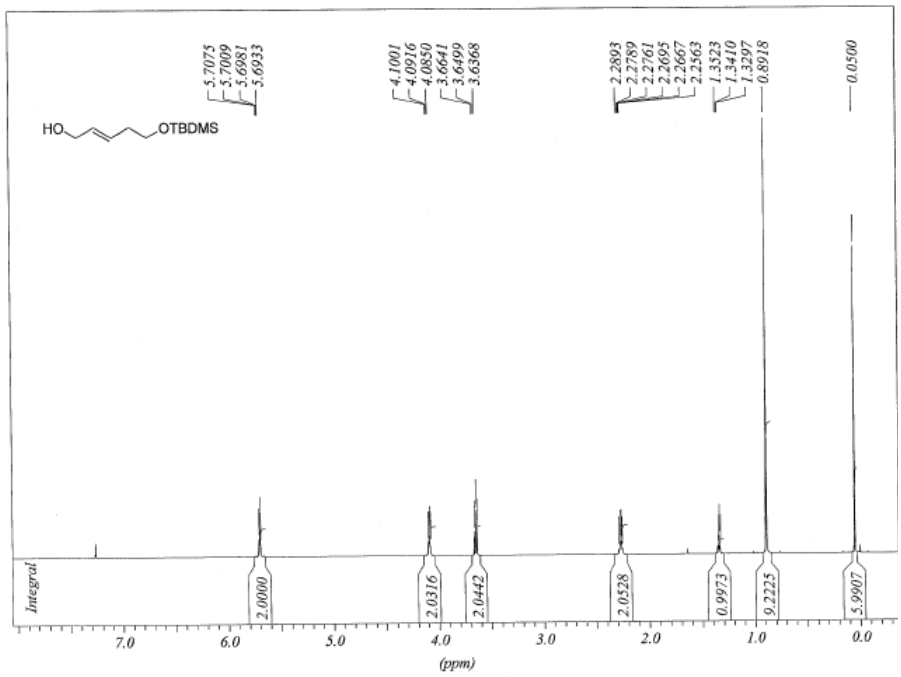


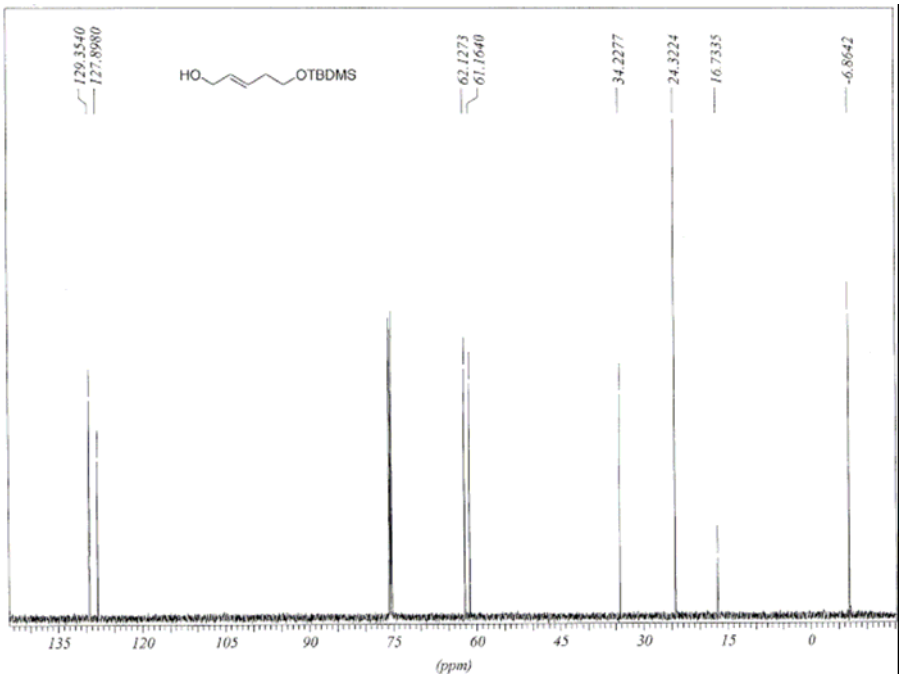
5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-yn-1-ol



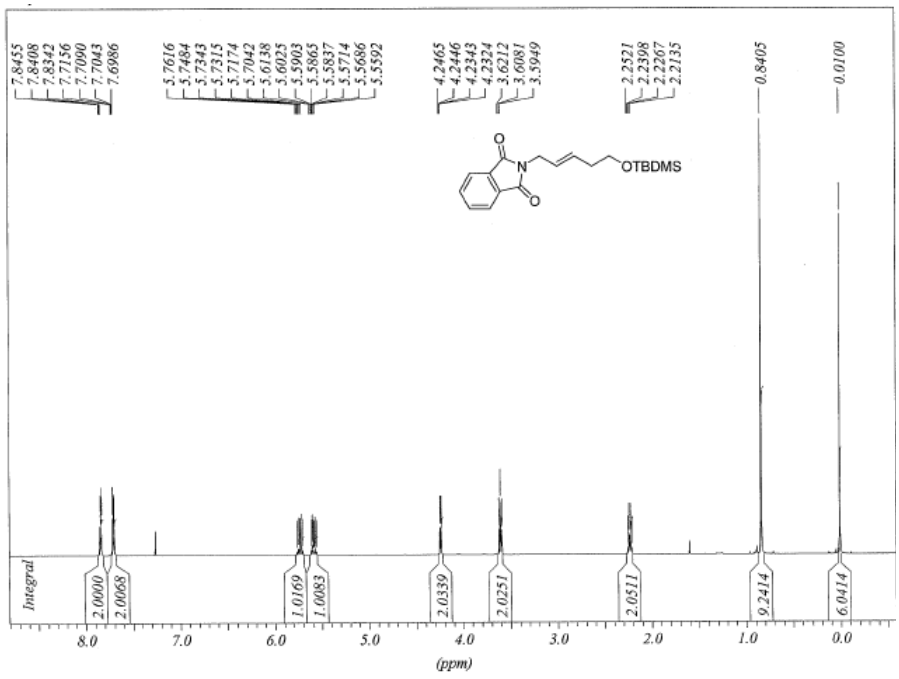


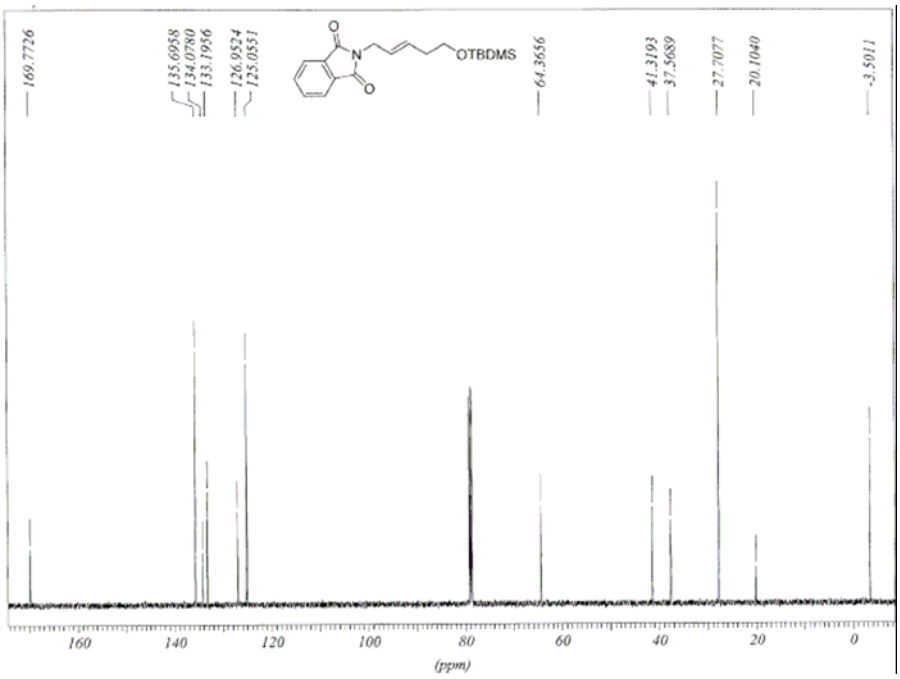
(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-en-1-ol



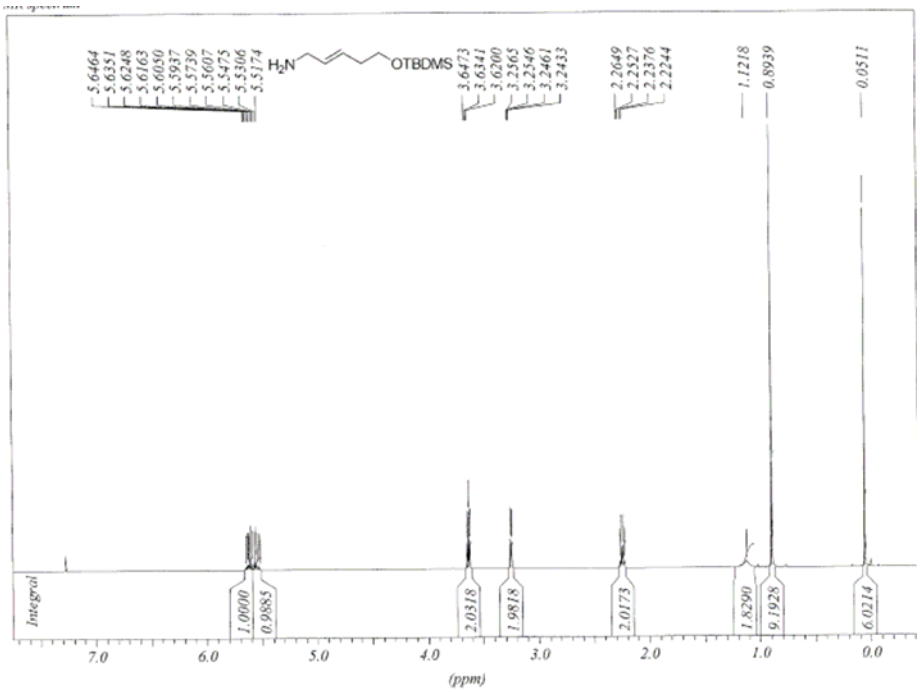


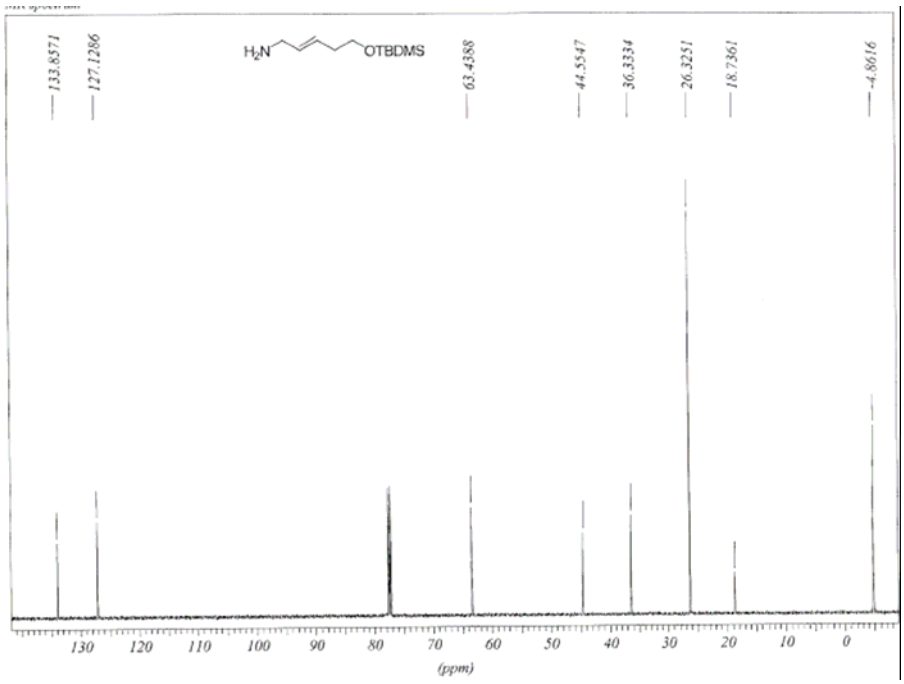
2-[(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-enyl]-isoindole-1,3-dione



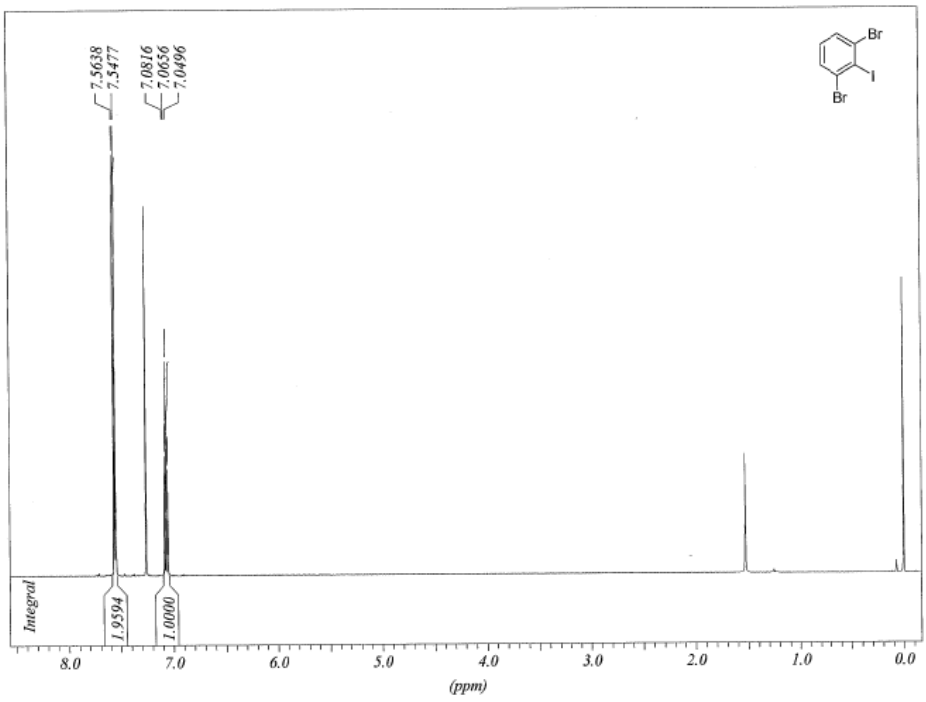


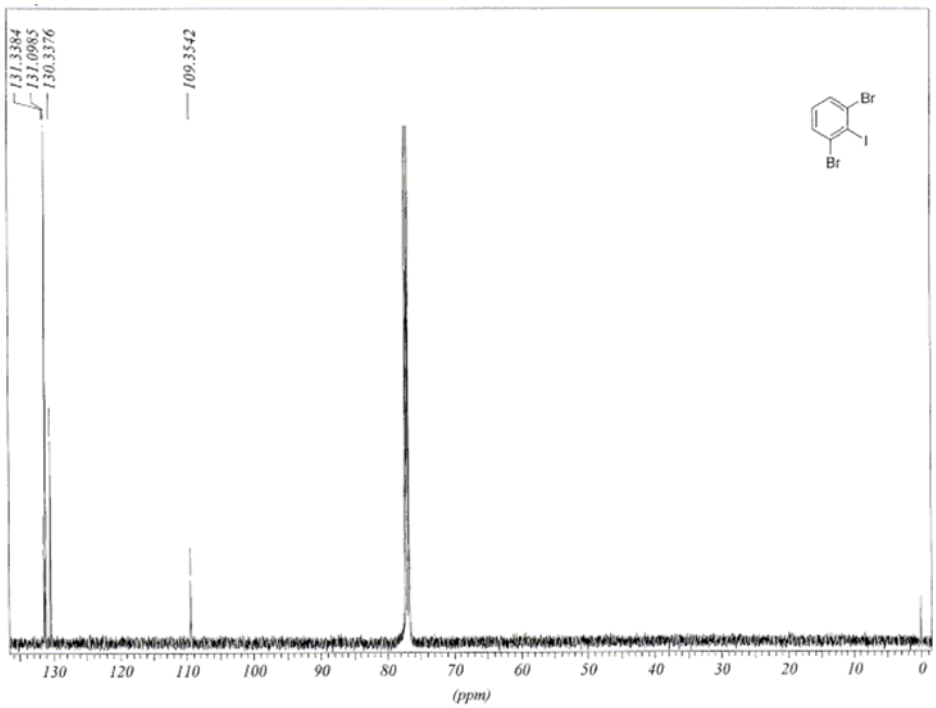
(*E*)-5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-enylamine



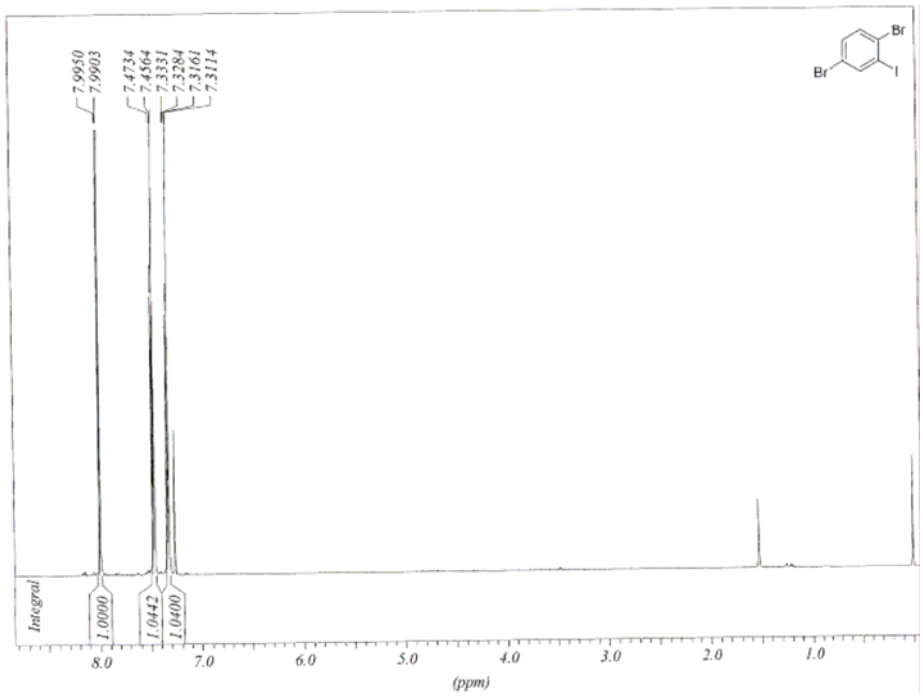


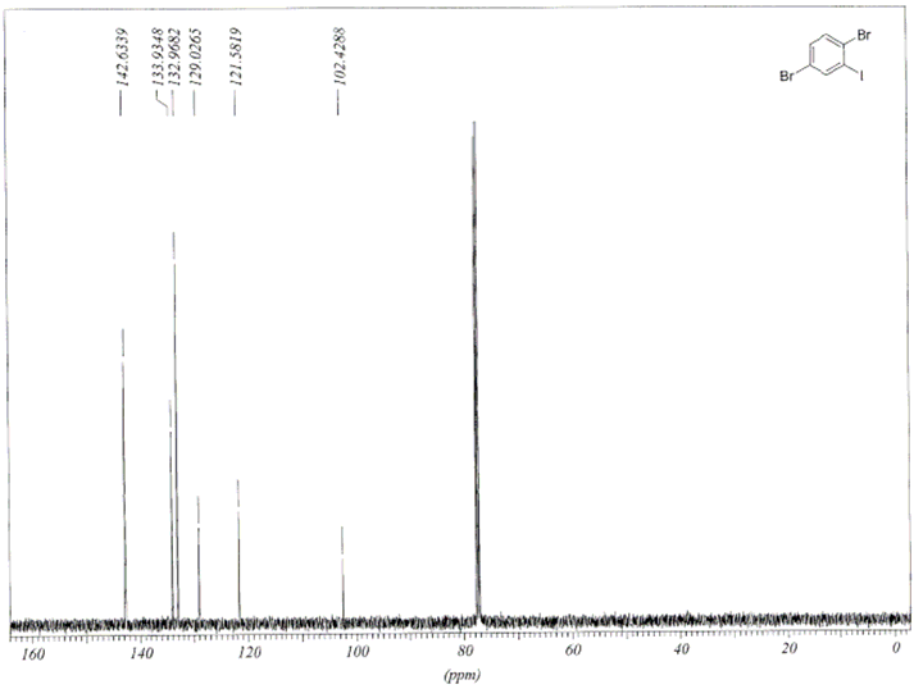
1,3-Dibromo-2-iodo-benzene



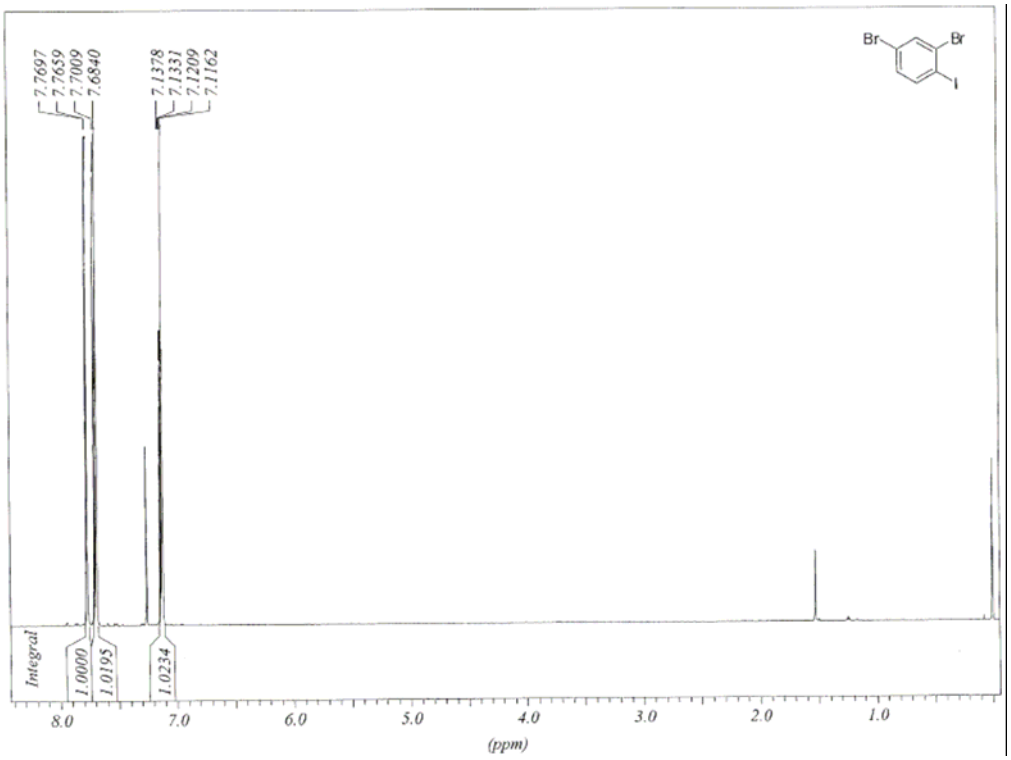


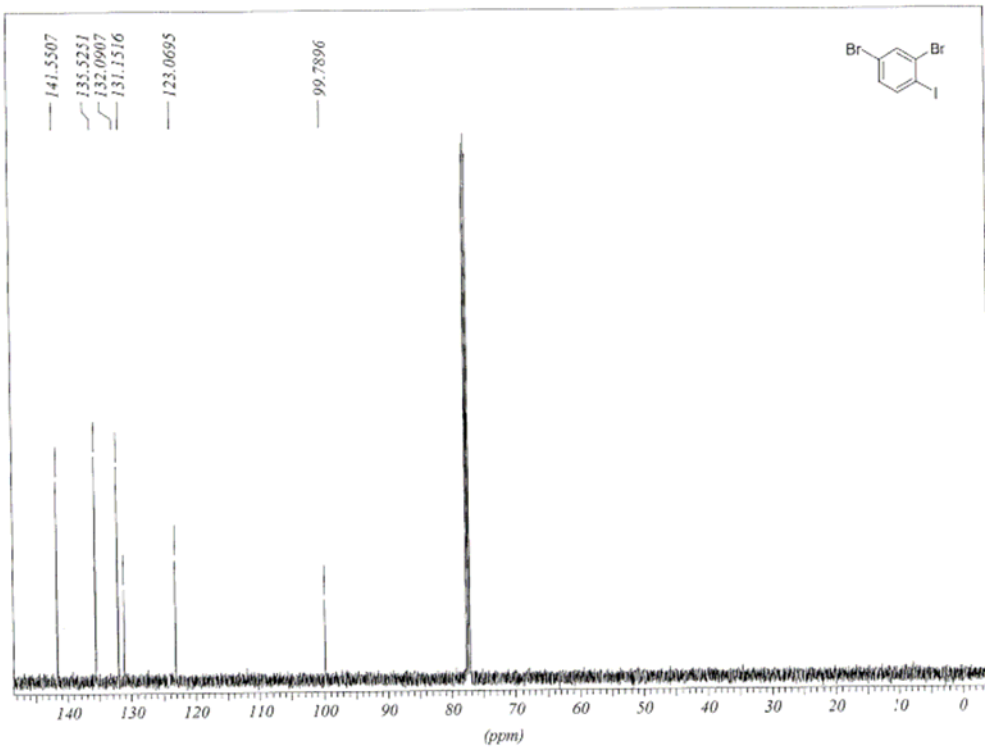
1,4-Dibromo-2-iodo-benzene



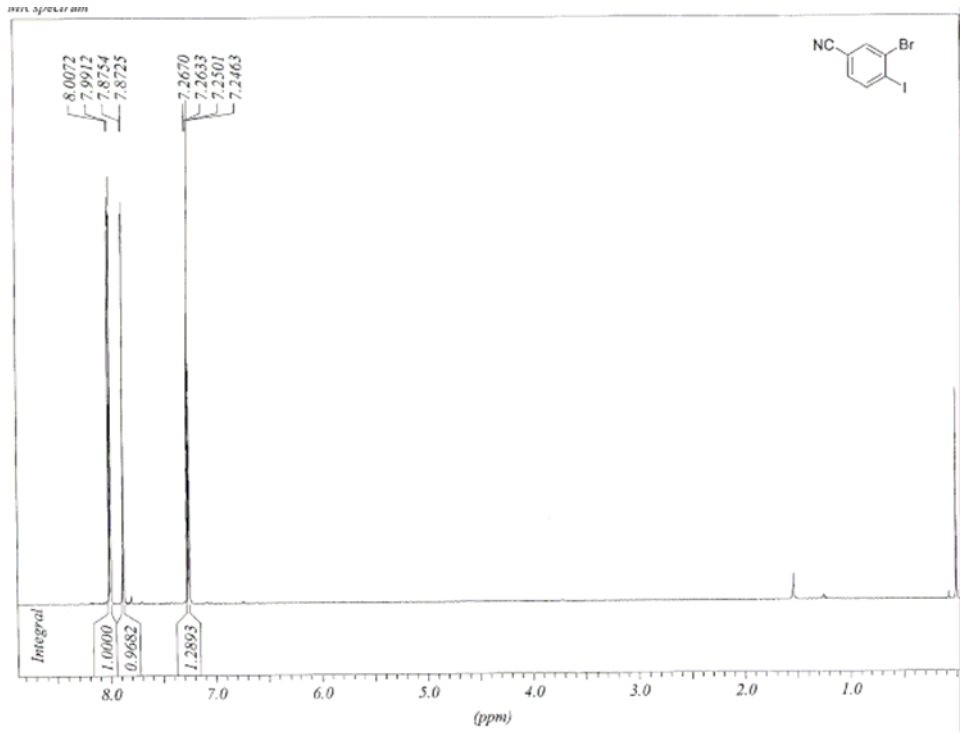


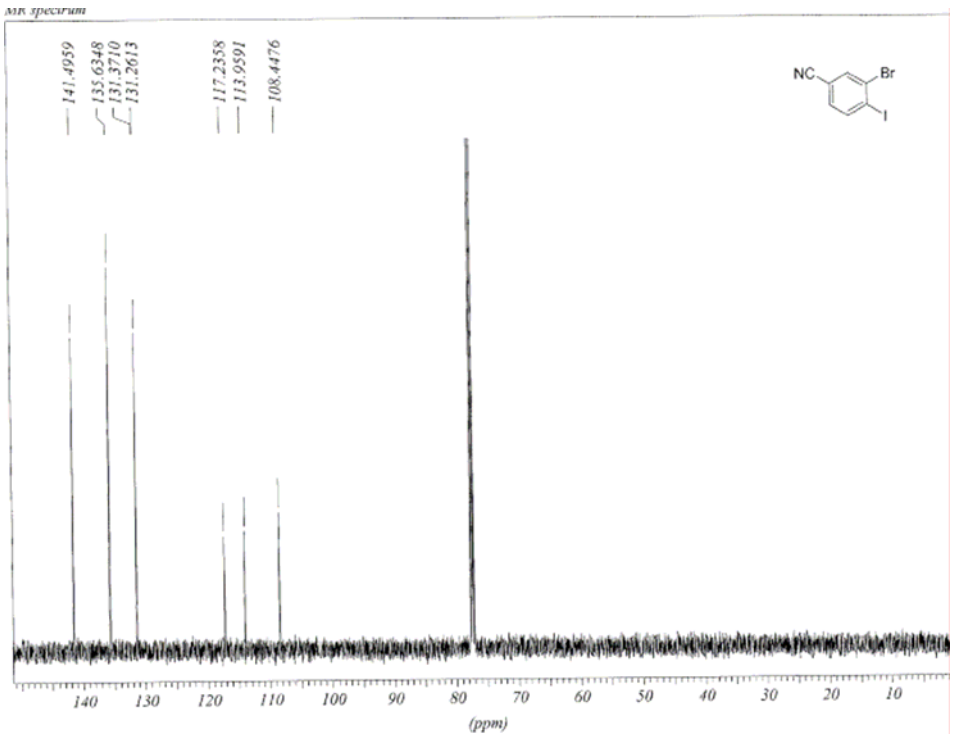
2,4-Dibromo-1-iodo-benzene



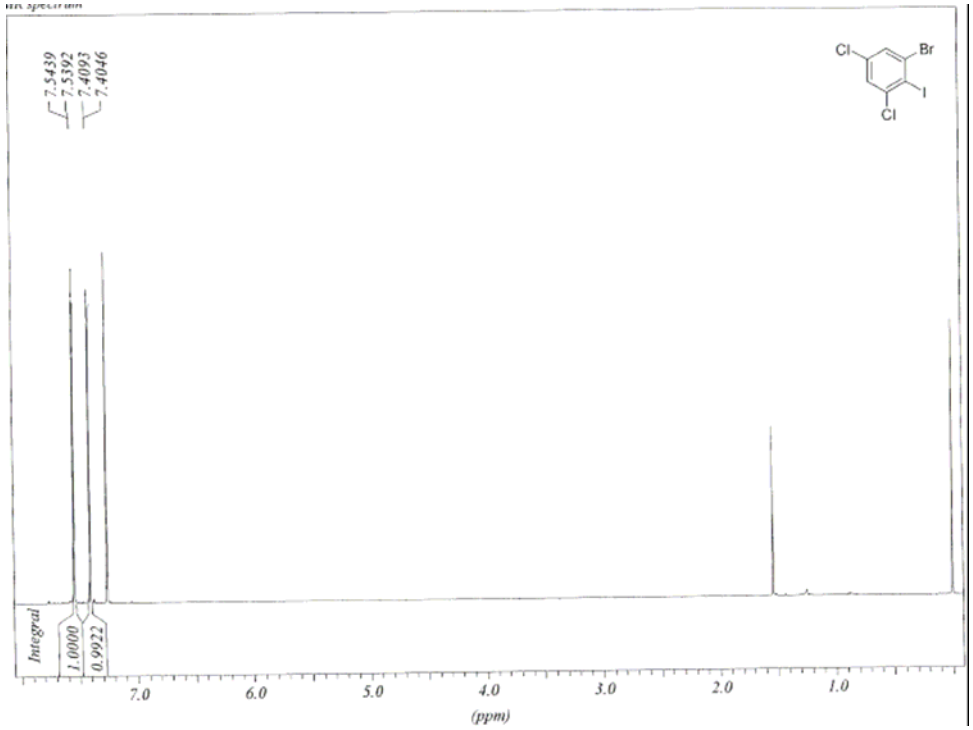


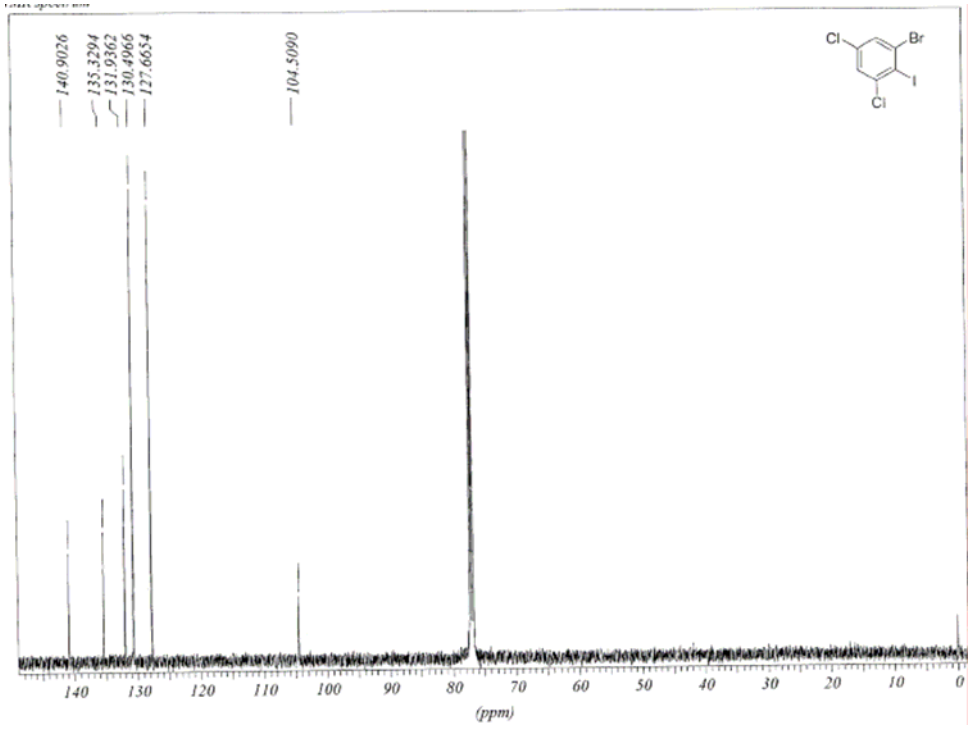
3-Bromo-4-iodo-benzonitrile



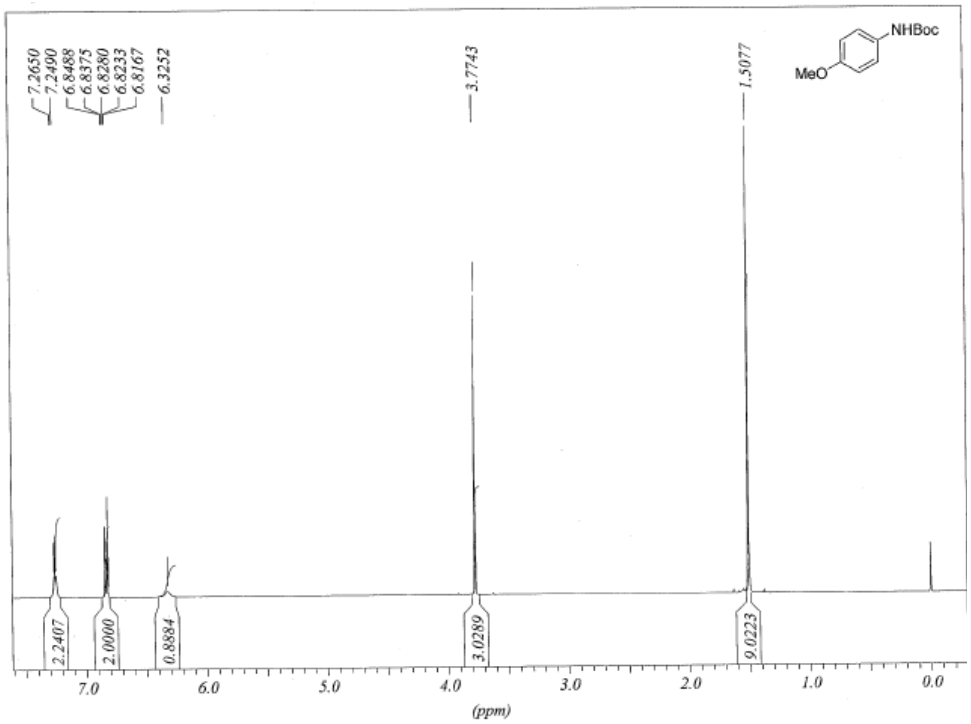


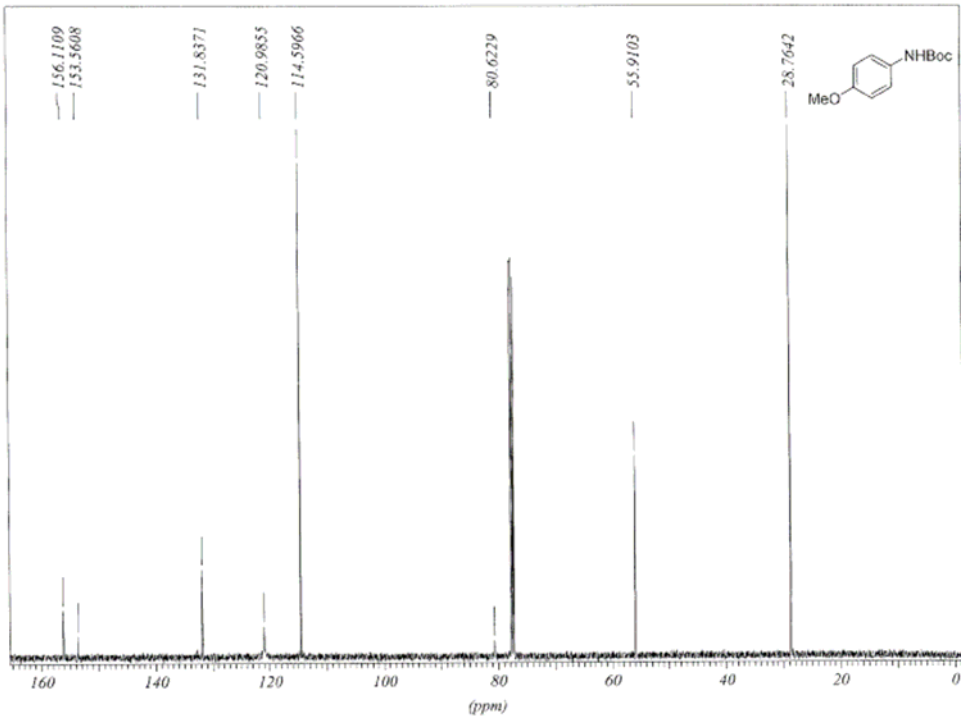
1-Bromo-3,5-dichloro-2-iodo-benzene



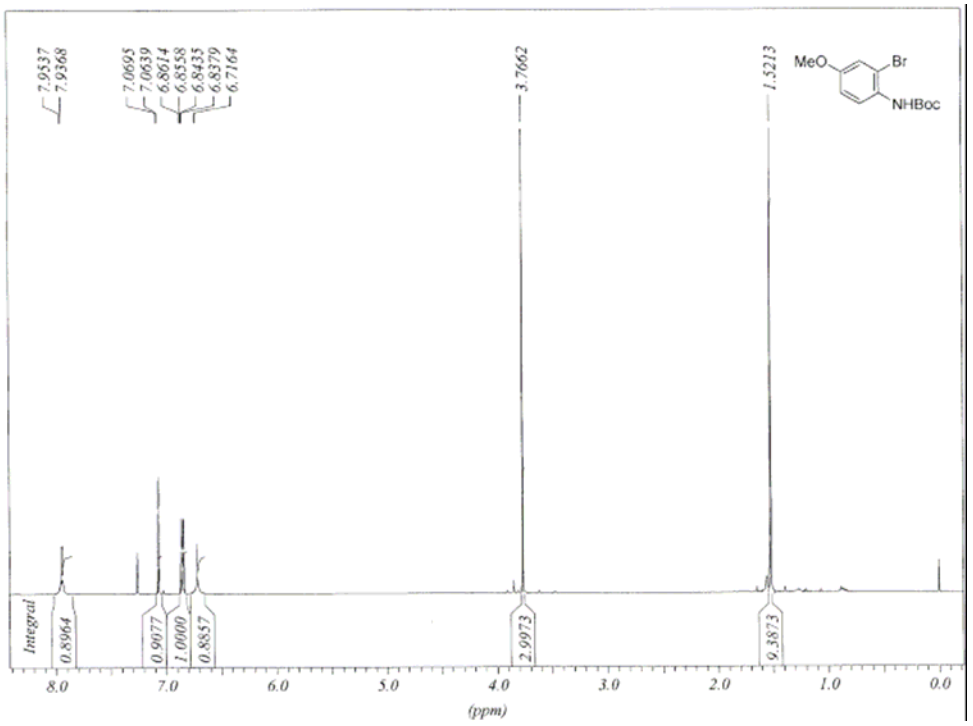


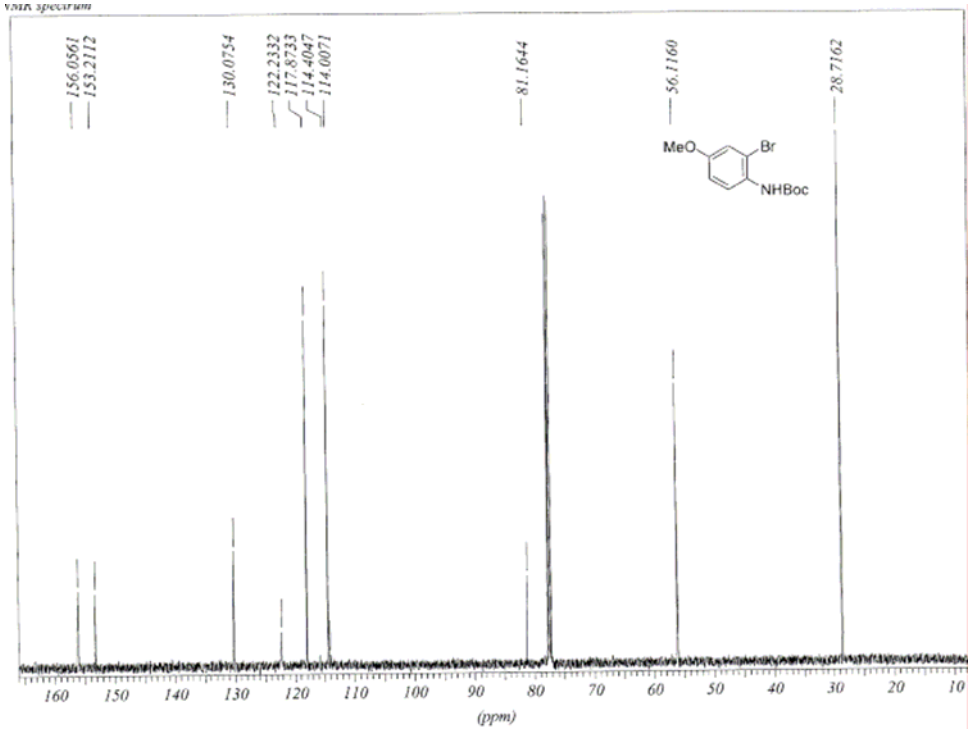
(4-Methoxy-phenyl)-carbamic acid *tert*-butyl ester



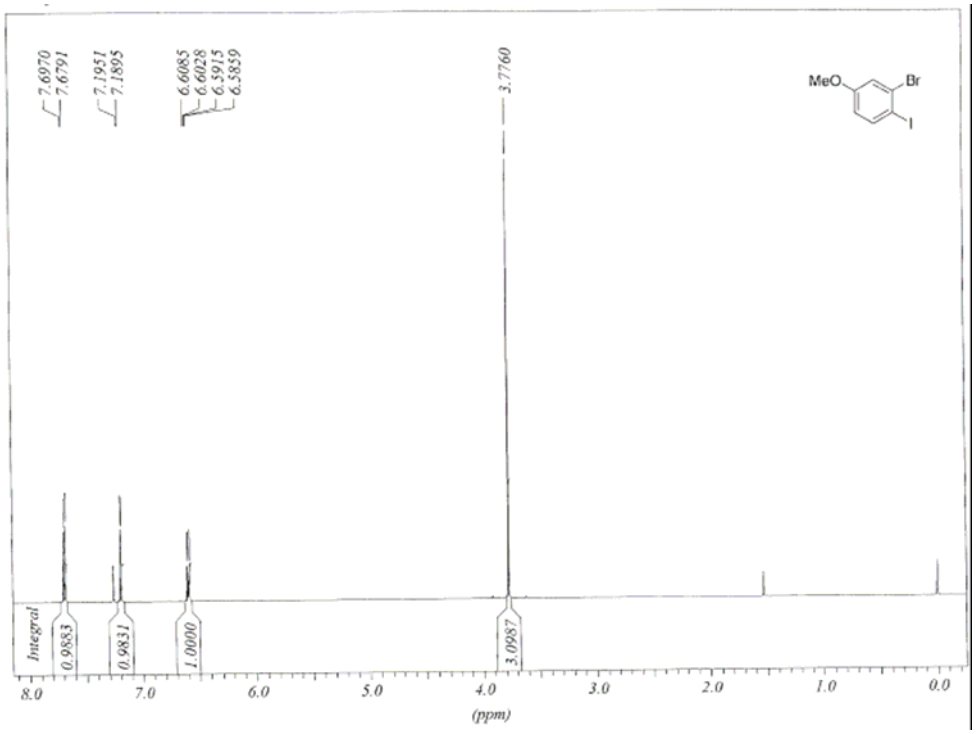


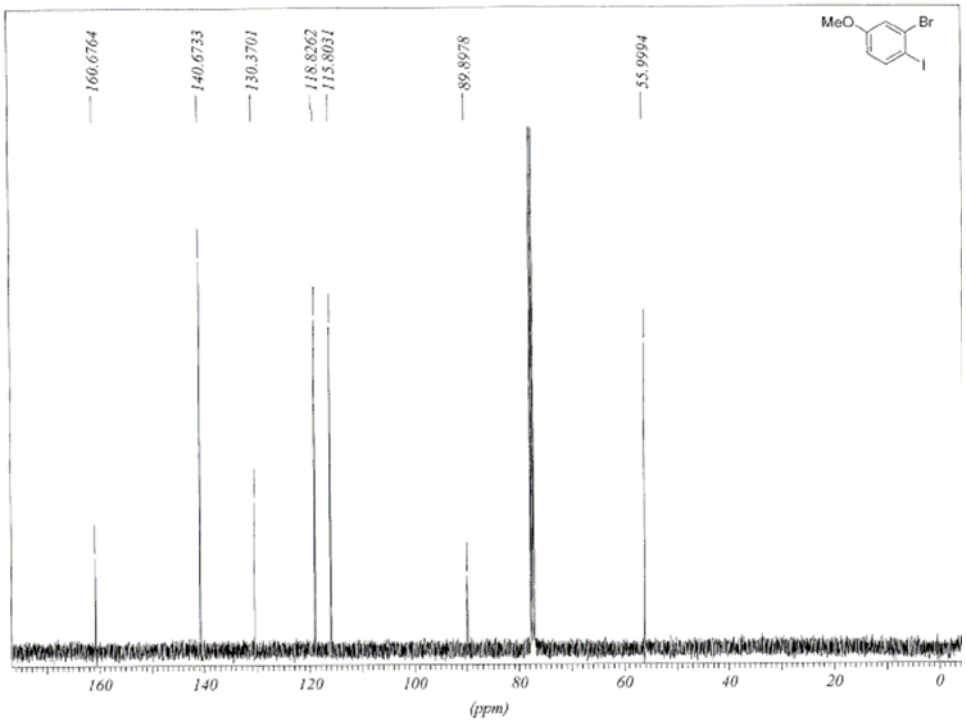
(2-Bromo-4-methoxy-phenyl)-carbamic acid *tert*-butyl ester



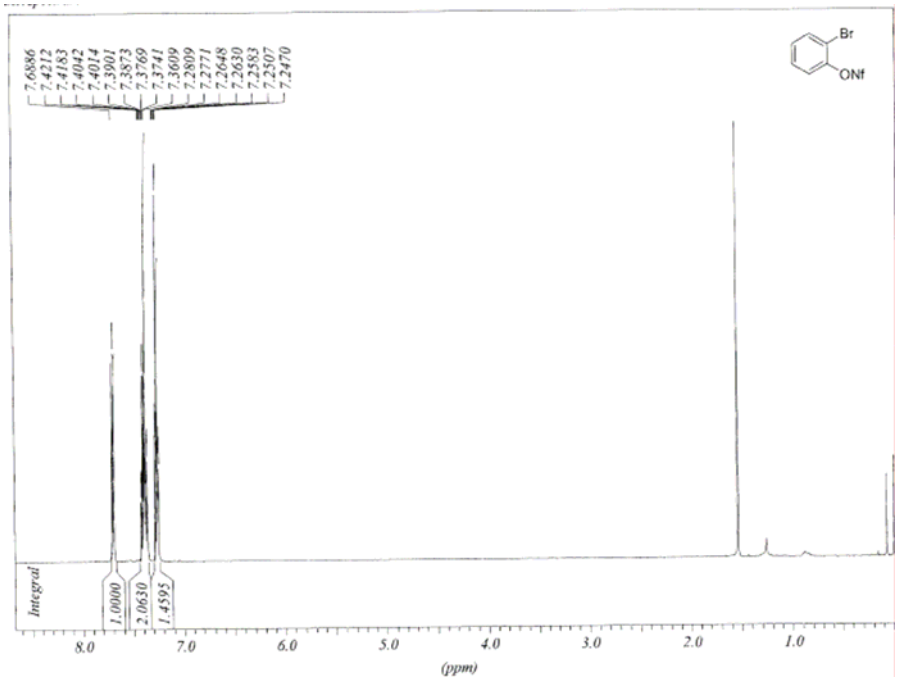


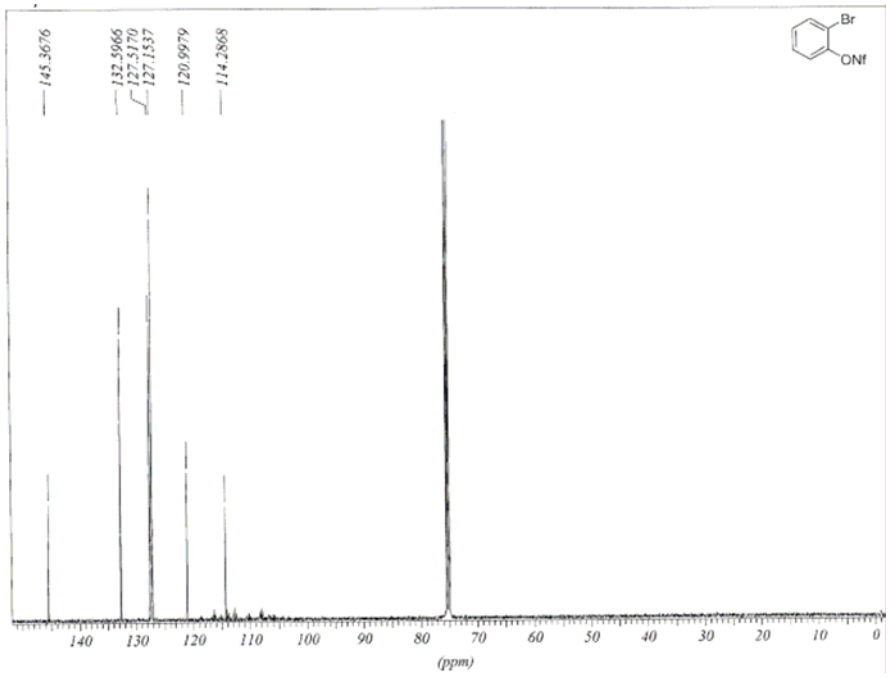
2-Bromo-1-iodo-4-methoxy-benzene



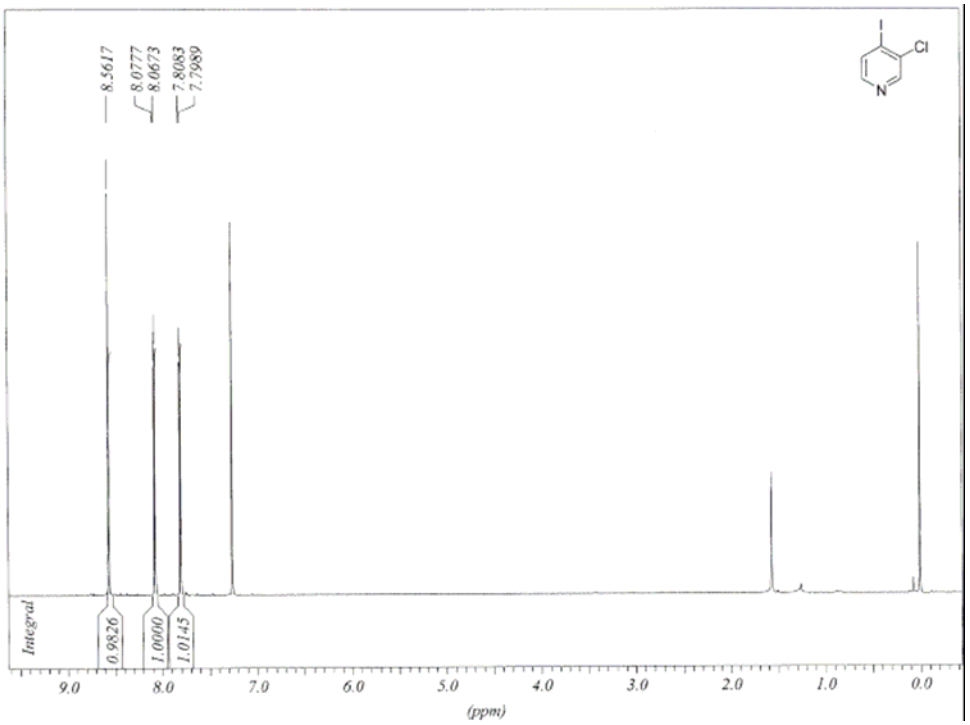


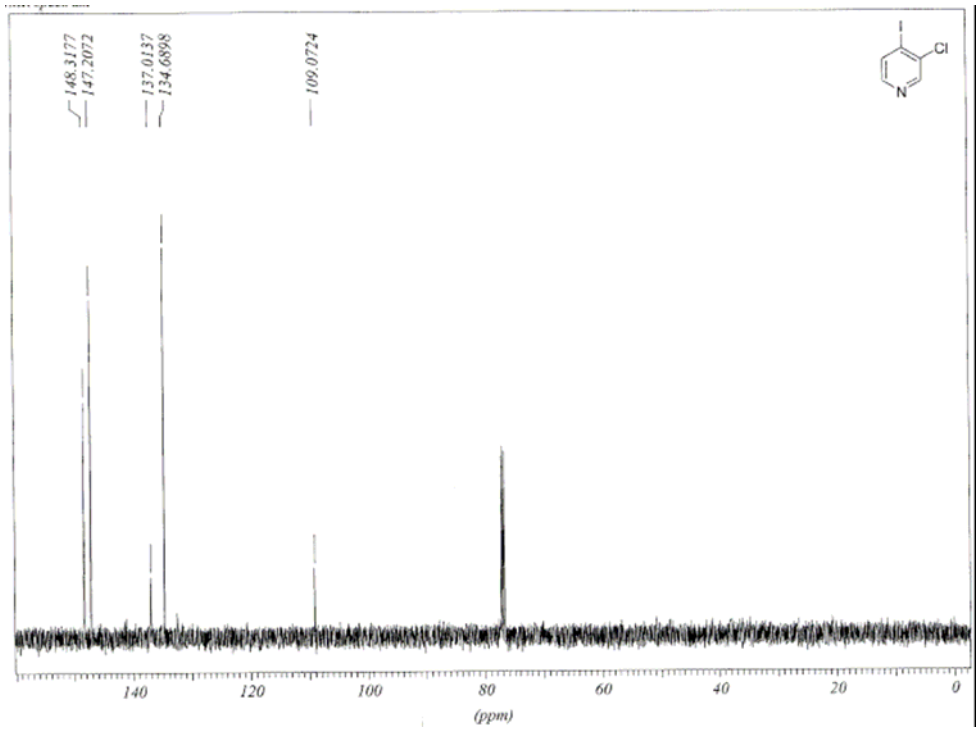
2-Bromophenyl nonaflate





3-Chloro-4-iodopyridine





4-Chloro-3-iodo-pyridine