Supporting Information

Copper-promoted *N*-Cyclopropylation of Anilines and Amines by Cyclopropylboronic acid

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General information

Melting points (m.p.) were recorded using Büchi B-540 melting point apparatus and are uncorrected.

Optical rotations were measured on a Jasco P-1010 polarimeter using 10 cm cells and the sodium D line (589 nm), in the solvent, at concentration and temperature indicated.

Infrared spectra were recorded on a Perkin Elmer Spectrum BX FT-IR spectrometer.

Proton NMR (^{1}H NMR) spectra were recorded at 500 MHz on a Bruker AC-500 spectrometer or at 300 MHz on a Bruker AC-300 spectrometer. Carbon NMR (^{13}C NMR) spectra were similarly recorded at 125 or 75 MHz. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual proton signals in $CDCl_3$ (δ = 7.27, 77.16). Coupling constants (*J*) are reported in Hertz (Hz) and refer to apparent multiplicities. The following abbreviations are used for the multiplicities: s: singlet, bs: broad signal, d: doublet, t: triplet, quint: quintuplet, sept: septuplet, m: multiplet.

Analytical high performance liquid chromatography (HPLC) was performed on Hitachi LaChrom-Elite, equipped with diode array UV detectors. The enantiomeric excesses were determined employing the indicated chiral stationary phase column and by comparing the samples with the appropriate racemic mixtures.

Mass spectra were obtained either from an AEI MS-50 (EI) or an AEI MS-9 using positive or negative electron spray (ES^+ or ES^-) for the high resolution mass spectra (HRMS).

Elemental analyses (EA) were performed on CHN 2400 Perkin-Elmer analysers (carbon, hydrogen, nitrogen).

Flash chromatography was performed using SDS silicagel 60 (35-70 μm). Preparative Thin layer chromatography (TLC) was carried out on 20 x 20 cm plates with a layer thickness of 0.50 mm (SDS Silicagel 60 F254). Visualization was achieved under a UVP mineralight UVGL-58 lamp.

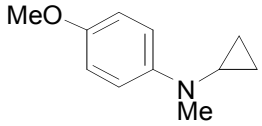
All reagents were obtained from commercial suppliers unless otherwise stated. 1,2-dichloroethane was routinely dried from calcium hydride and distilled prior to use.

General procedure for the *N*-cyclopropylation

To a suspension of cyclopropyl boronic acid (51.6 mg, 0.6 mmol, 2.0 eq), aniline or amine (0.3 mmol) and Na_2CO_3 (63.6 mg, 0.6 mmol, 2.0 eq) in 0.5 ml 1,2-dichloroethane was added a suspension of $Cu(OAc)_2$ (54.5 mg, 0.3 mmol) and bipyridine (46.8 mg, 0.3 mmol, 1.0 eq) in hot dichloroethane (2.5 ml). The mixture was warmed up to 70 °C and stirred for 2-4 h. The resulting mixture was cooled to room temperature and a 25% aqueous NH_4OH solution was added (20 mL). The organic layer was separated and the aqueous layer was extracted 3 times with CH_2Cl_2. The combined organic layers were washed with brine, dried over sodium sulfate and concentrated under reduced pressure. Simple filtration on Celite®, purification by flash column chromatography on silica gel or on preparative TLC afforded the desired pure *N*-cyclopropyl compound.

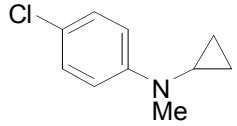
Description of compounds 3a-3q

N-cyclopropyl-*N*-methyl-4-methoxyaniline **3a.**[1]



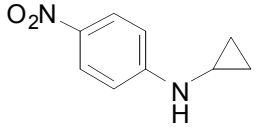
According to the general procedure, filtration on celite® (DCM) afforded the title compound as yellow oil (54 mg, 99 %). R_f = 0.59 (DCM). IR (neat, cm^{-1}) ν 3005, 2923, 1509, 1454, 1360, 1242, 1038, 817; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.97 (d, *J* = 9.3 Hz, 2H), 6.84 (d, *J* = 9.3 Hz, 2H), 3.76 (s, 3H), 2.92 (s, 3H), 2.33-2.28 (m, 1H), 0.82-0.78 (m, 2H), 0.65-0.62 (m, 2H); ^{13}C -NMR ($CDCl_3$, 125 MHz) δ 152.5, 145.7, 115.6, 114.6, 55.9, 40.4, 34.1, 9.1; MS (m/z, ES^+): 178.1 $(M+H)^+$.

N-cyclopropyl-*N*-methyl-4-chloroaniline **3b.**[2]



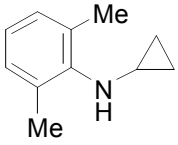
According to the general procedure, purification by preparative TLC (SiO_2, 6:1 heptane/EtOAc) afforded the title compound as pale orange oil (30 mg, 55%). R_f = 0.68 (6:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3086, 3006, 2930, 2816, 1597, 1494, 1454, 1359, 1333, 1236, 811, 733; ^{1}H -NMR ($CDCl_3$, 300 MHz) δ 7.18 (m, 2H), 6.88 (m, 2H), 2.94 (s, 3H), 2.37-2.33 (m, 1H), 0.83-0.78 (m, 2H), 0.61-0.57 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 149.6, 128.8, 122.4, 115.0, 39.3, 33.5, 9.3; MS (m/z, IE): 141, 139, 113, 111.

N-cyclopropyl-4-nitroaniline **3c.**



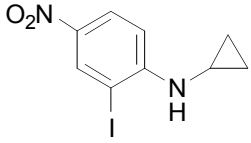
According to the general procedure, purification by preparative TLC (SiO_2, DCM) afforded the title compound as yellow solid (50 mg, 93%). R_f= 0.74 (SiO_2, DCM). M.p. 120-122 ºC; IR (neat, cm^{-1}) ν 3388, 3080, 2986, 1588, 1493, 1294, 1107, 883; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.12 (d, *J* = 9.1 Hz, 2H), 6.75 (d, *J* = 9.1 Hz, 2H), 4.87 (s,1H), 2.59-2.52 (m, 1H), 0,91-0.85 (m, 2H), 0.63-0.58 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 154.4, 139.0, 126.6, 112.1, 25.2, 8.1; HRMS *m/z* (ES^-) calcd for $C_9H_9N_2O_2$ ([M-H]) 177.0664, found 177.0670.

N-cyclopropyl-2,6-dimethylaniline **3d.**



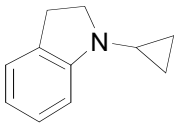
According to the general procedure, filtration on celite® (DCM) afforded the title compound as pale orange oil (48 mg, 98 %). R_f= 0.67 (SiO_2, 4:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3249, 2922, 2852, 1600, 1581, 1471, 1454, 1305, 759 ; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.98 (d, *J* = 7.2 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 2.68-2.662 (m, 1H), 2.30 (s, 6H), 0.68-0.64 (m, 2H), 0.52-0.48 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 146.1, 129.2, 127.9, 121.1, 30.4, 19.8, 9.6; MS (m/z, IE): 161, 146, 144, 132, 117, 105, 91, 77.

N-cyclopropyl-2-iodo-5-nitroaniline **3e.**



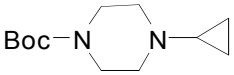
According to the general procedure, filtration on celite® (DCM) afforded the title compound as yellow solid (92 mg, 99 %). R_f= 0.67 (2:1 heptane/EtOAc). M.p. 80-82 ºC; IR (neat, cm^{-1}) ν 3376, 3088, 3003, 1606, 1505, 1340, 1301, 1014, 1008; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 2.5 Hz, 1H), 7.32 (dd, *J* = 8.2-2.5 Hz, 1H), 4.89 (bs, 1H), 2.58-2.54 (m, 1H), 0.96-0.92 (m, 2H), 0.66-0.63 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 149.8, 149.2, 139.5, 113.4, 105.8, 92.2, 25.8, 8.1; Anal. Calcd (%) for $C_9H_9N_2O_2I$: C 35.55, H 2.98, N 9.21; found C 35.51, H 2.68, N 9.05.

N-cyclopropylindoline **3f.**



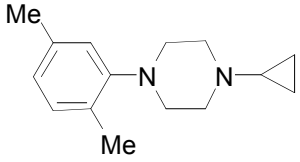
According to the general procedure, purification by flash column chromatography (SiO_2, 4:1 pentane/toluene) afforded the title compound as colorless oil (40 mg, 83%). R_f = 0.27 (SiO_2, 4:1 pentane/toluene). IR (neat, cm^{-1}) ν 3010, 2942, 2820, 1605, 1486, 1451, 1367, 1264, 1220, 744; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.09-7.05 (m, 2H), 6.82 (d, *J* = 7.9 Hz,1H), 6.70 (t, *J* = 7.3 Hz, 1H), 3.36 (t, *J* = 8.1 Hz, 2H), 2.90 (t, *J* = 8.1 Hz, 2H), 2.13-2.09 (m, 1H), 0.69-0.61 (m, 4H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 153.4, 130.7, 127.4, 124.4, 118.7, 108.8, 54.5, 30.4, 28.8, 5.7; HRMS *m/z* (ES^+) calcd for $C_{11}H_{14}N$ ([M+H]) 160.1126, found 160.1119.

N-Boc-*N*-cyclopropylpiperazine **3g.**



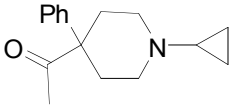
According to the general procedure, filtration on celite® (DCM) afforded the title compound as viscous oil (66 mg, 97%). R_f= 0.58 (SiO_2, 98:2 DCM/MeOH). IR (neat, cm^{-1}) ν 2925, 1693, 1608, 1416, 1363, 1248, 1163, 1003; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.35 (t, *J* = 4.9 Hz, 4H), 2.51 (t, *J* = 4.9 Hz, 4H), 1.60-1.53 (m, 1H), 1.42 (s, 9H), 0.43-0.38 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 155.0, 79.7, 53.3, 43.8, 38.7, 28.6, 6.0; HRMS *m/z* (ES^+) calcd for $C_{12}H_{23}N_2O_2$ ([M+H]) 227.1762, found 227.1760

1-Cyclopropyl-4-(2,5-dimethylphenyl)piperazine **3h.**



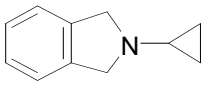
According to the general procedure, purification by preparative TLC (SiO_2, 4:1 heptane/EtOAc) afforded the title compound as colorless oil (53 mg, 75%). R_f = 0.73 (4:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3007, 2936, 2800, 1504, 1450, 1362, 1243, 1143, 993; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.04 (d, *J* = 7.5 Hz, 1H), 6.81 (s, 1H), 6.78 (d, *J* = 7.5 Hz, 1H), 2.91-2.89 (m, 4H), 2.78-2.76 (m, 4H), 2.28 (s, 3H), 2.26 (s, 3H), 1.71-1.67 (m, 1H), 0.49-0.46 (m, 4H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 151.7, 136.3, 131.0, 129.5, 123.9, 120.0, 54.1, 51.8, 38.8, 21.4, 17.7, 5.9; HRMS *m/z* (ES^+) calcd for $C_{15}H_{22}N_2$ ([M+H]) 231.1861, found 231.1864.

N-Cyclopropyl-4-acetyl-4-phenylpiperidine **3i.**



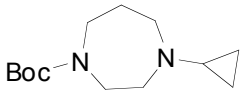
According to the general procedure, purification by flash column chromatography (SiO_2, DCM) afforded the title compound as white solid (67 mg, 92%). R_f = 0.57 (SiO_2, DCM). M.p. 84-86 ºC; IR (neat, cm^{-1}) ν 3086, 3004, 2916, 1697, 1447, 1360, 1348, 1014; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.29-7.17 (m, 5H), 2.84-2.76 (m, 2H), 2.40-2.34 (m, 4H), 2.00-1.91 (m, 2H), 1.85 (s, 3H), 1.51-1.43 (m, 1H), 0.38-0.34 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 209.8, 141.9, 129.1, 127.1, 126.6, 55.0, 51.2, 38.7, 32.9, 25.9, 6.0; HRMS *m/z* (ES^+) calcd for $C_{16}H_{22}NO$ ([M+H]) 244.1701, found 244.1693.

N-cyclopropylisoindoline **3j.**



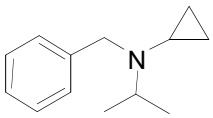
According to the general procedure, purification by flash column chromatography (SiO_2, 4:1 heptane/EtOAc) afforded the title compound as brown oil (34 mg, 71%). R_f = 0.29 (SiO_2, 4:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3007, 2890, 2768, 1720,1462,1454, 1353, 886, 737; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.17 (s, 4H), 4.05 (s, 4H), 2.05-1.99 (m, 1H), 0.53-0.49 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 140.4, 126.9, 122.6, 59.1, 35.8, 6.2; HRMS *m/z* (ES^+) calcd for $C_{11}H_{14}N$ ([M+H]) 160.1126, found 160.1131.

tert-Butyl-4-cyclopropyl-1,4-diazepane-1-carboxylate **3k.**



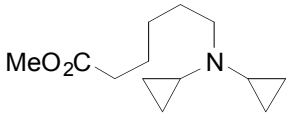
According to the general procedure, purification by flash column chromatography (SiO_2, EtOAc) afforded the title compound as pale orange oil (27 mg, 56%). R_f = 0.48 (SiO_2, EtOAc). IR (neat, cm^{-1}) ν 2930, 1689, 1409, 1364, 1158, 1119, 1014; ^{1}H-NMR ($CDCl_3$, 300 MHz, mixture of rotamers) δ 3.47-3.35 (m, 4H), 2.79-2.69 (m, 4H), 1.83-1.70 (m, 3H), 1.42 (s, 9H), 0.46-0.33 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz, mixture of rotamers) 155.7, 79.4, 56.3, 55.3 and 55.0, 47.0, 46.4 and 46.2, 45.3, 38.0 and 37.9, 28.7, 28.1 and 27.9, 7.4; HRMS *m/z* (ES^+) calcd for $C_{13}H_{25}N_2O_2$ ([M+H]) 241.1916, found 241.1907.

N-benzyl-*N*-isopropylcyclopropylamine **3l.**



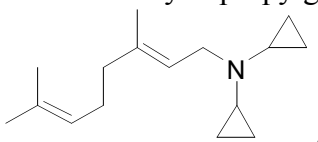
According to the general procedure, purification by flash column chromatography (SiO_2, 9:1 heptane/EtOAc) afforded the title compound as colorless oil (23 mg, 40%). R_f = 0.61 (SiO_2, 4:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3086, 2963, 2926, 1494, 1453, 1345, 1176, 1018, 713, 694; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.30-7.16 (m, 5H), 3.71 (s, 2H), 2.95 (sept, *J* = 6.6 Hz, 1H), 1.92-1.85 (m, 1H), 1.06 (d, *J* = 6.6 Hz, 6H), 0.41-0.23 (m, 4H); ^{13}C -NMR ($CDCl_3$, 75 MHz) 141.4, 129.0, 128.1, 126.6, 55.9, 51.9, 33.2, 19.1, 7.4; HRMS *m/z* (ES^+) calcd for $C_{13}H_{20}N$ ([M+H]) 190.1596, found 190.1596.

Methyl-6-(dicyclopropylamino)hexanoate **3m.**



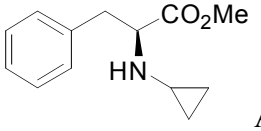
According to the general procedure using 4.0 eq of cyclopropylboronic acid, purification by preparative TLC (SiO_2, 1:1 heptane/EtOAc) afforded the title compound as pale orange oil (40 mg, 60%). R_f = 0.73 (SiO_2, 1:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3091, 2939, 1738, 1436, 1350, 1169, 1012; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.64 (s, 3H), 2.64 (dd, *J* = 7.6-7.8 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.85-1.80 (m, 2H), 1.66-1.55 (m, 4H), 1.30-1.21 (m, 2H), 0.41-0.36 (m, 8H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 174.4, 57.5, 51.6, 37.0, 34.3, 27.6, 26.3, 25.2, 5.8; HRMS *m/z* (ES^+) calcd for $C_{13}H_{24}NO_2$ ([M+H]) 226.1807, found 226.1796.

N-dicyclopropylgeranylamine **3n.**



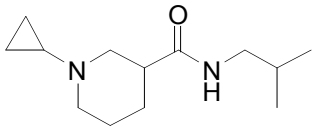
According to the general procedure using 4.0 eq of cyclopropylboronic acid, purification by flash column chromatography (SiO_2, 9:1 heptane/EtOAc) afforded the title compound as colorless oil (38 mg, 55%). R_f = 0.60 (SiO_2, 4:1 heptane/EtOAc). IR (neat, cm^{-1}) ν 3089, 2918, 2852, 1447, 1353, 1214, 1020, 1010, 917, 824; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.41 (d, *J* = 7.4 Hz, 1H), 5.11-5.06 (m, 1H), 3.35 (d, *J* = 7.4 Hz, 2H), 2.12-1.92 (m, 6H), 1.67 (s, 3H), 1.66 (s, 3H), 1.58 (s, 3H), 0.50-0.40 (m, 8H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 138.3, 131.6, 124.6, 120.5, 53.7, 40.2, 36.3, 26.7, 25.9, 17.9, 16.3, 6.05; HRMS *m/z* (ES^+) calcd for $C_{16}H_{28}N$ ([M+H]) 234.2222, found 234.2218.

(S)-Methyl-2-(cyclopropylamino)-3-phenylpropanoate **3o.**



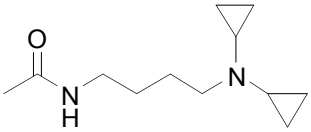
According to the general procedure using $NaHCO_3$ instead of Na_2CO_3 (50.4 mg, 0.6 mmol, 2.0 eq), purification by flash column chromatography (SiO_2, 3:7 Heptane/DCM) afforded the title compound as colorless oil (31 mg, 47%). R_f = 0.23 (SiO_2, 3:7 Heptane/DCM). IR (neat, cm^{-1}) ν 3028, 2950, 1732, 1454, 1434, 1197, 1169, 730, 698; $[\alpha]_D$ = -15.6, (c 1.20, Acetone); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.28-7.21 (m, 3H), 7.19-7.13 (m, 2H), 3.63 (s, 3H), 3.62 (t, *J* = 6.8 Hz, 1H), 2.91 (d, *J* = 6.8 Hz, 2H), 2.15 (bs, 1H), 2.10-2.05 (m, 1H), 0.42-0.25 (m, 4H); ^{13}C -NMR ($CDCl_3$, 75 MHz) 175.3, 137.5, 129.3, 128.6, 126.9, 63.2, 51.8, 39.7, 29.2, 7.0 and 6.2; Chiral HPLC: (*R*)-**3o**, t_R 8.3 min (6.8 %); (*S*)-**3o**, t_S 9.4 min (93.2 %) (Daicel Chiralcel OD-H, hexane/*i*PrOH, 99/1; 0.75 mL/min; HRMS *m/z* (ES^+) calcd for $C_{13}H_{18}NO_2$ ([M+H]) 220.1338, found 220.1342.

1-Cyclopropyl-*N*-isobutylpiperidine-3-carboxamide **3p.**



According to the general procedure, purification by flash column chromatography (SiO_2, 1:1 heptane/EtOAc) afforded the title compound as a white solid (64 mg, 95%). R_f = 0.12 (SiO_2, 1:1 heptane/EtOAc). M.p. 76-78 ºC; IR (neat, cm^{-1}) ν 3289, 2932, 2806, 1639, 1557, 1362, 1218, 1162, 703; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.71 (bs, 1H), 3.07-3.02 (m, 1H), 3.00-2.93 (m, 2H), 2.85 (bs, 1H), 2.46-2.40 (m, 2H), 2.28 (bs, 1H), 1.84 (bs, 1H), 1.67 (sept, *J* = 6.7 Hz, 1H), 1.59-1.46 (m, 4H), 0.85 (d, *J* = 6.8 Hz, 6H), 0.49-0.42 (m, 2H), 0.36-0.27 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 175.3, 55.6, 54.2, 46.6, 41.8, 38.8, 28.6, 27.3, 22.8, 20.4, 6.3 and 6.0; HRMS *m/z* (ES^+) calcd for $C_{14}H_{20}N$ ([M+H]) 225.1967, found 225.1966.

N-(dicyclopropylamino)butyl)acetamide **3q.**



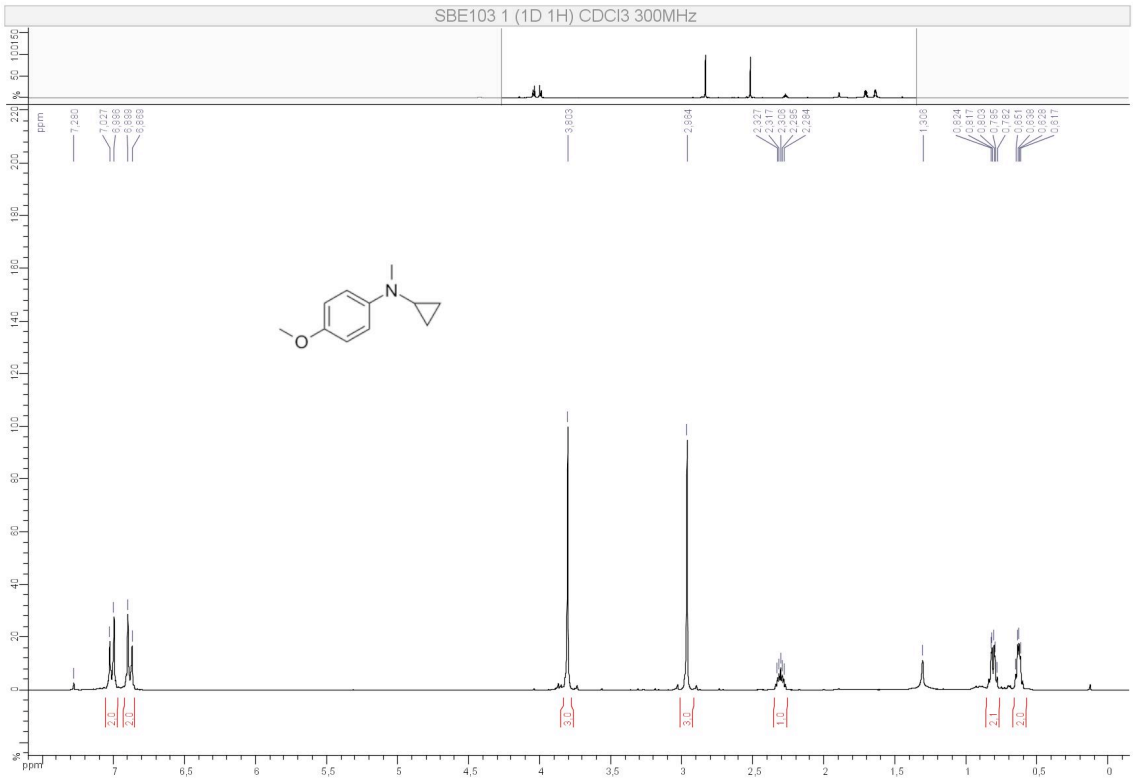
According to the general procedure using 4.0 eq of cyclopropylboronic acid, purification by flash column chromatography (SiO_2, 2% of MeOH in DCM) afforded the title compound as colorless oil (39 mg, 62%). R_f = 0.22 (SiO_2, 2% of MeOH in DCM). IR (neat, cm^{-1}) ν 3284, 3089, 3008, 2931, 1644, 1555, 1446, 1364, 1350, 1021, 1012, 733; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 5.70 (bs, 1H), 3.21 (dd, *J* = 6.8-6.7 Hz, 2H),2,65 (dd, *J* = 7.1-7.3Hz, 2H), 1.93 (s, 3H), 1,83-1,79 (m, 2H), 1,62-1,56 (m, 2H), 1.47-1.41 (m, 2H), 0.42-0.37 (m, 4H), 0.36-0.32 (m, 4H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 170.2, 57.4, 39.8, 37.1, 28.1, 24.3, 23.5, 5.8; HRMS *m/z* (ES^+) calcd for $C_{12}H_{23}N_2O$ ([M+H]) 211.1810, found 211.1801.

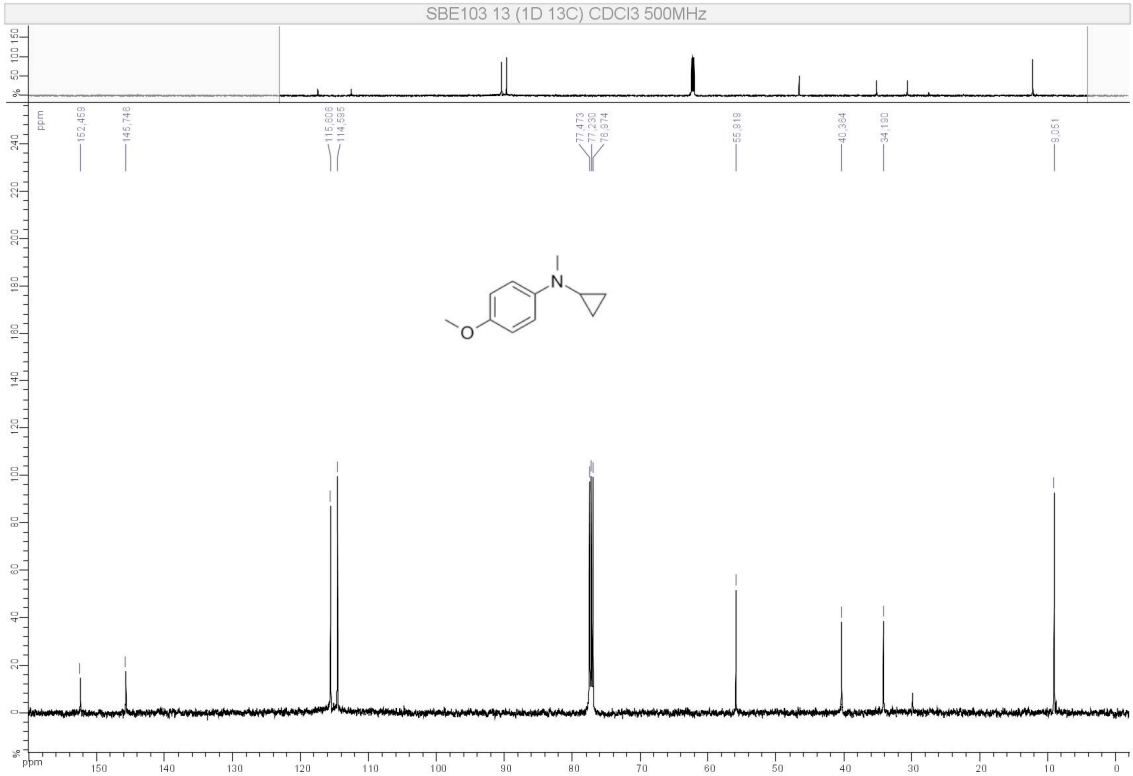
References

(1) Satoh, T.; Miura, M.; Sakai, K.; Yokoyama, Y. *Tetrahedron* **2006**, *62*, 4253-4261.
(2) Loeppky, R. N.; Elomari, S. *J. Org. Chem.* **1999**, *65*, 96-103.

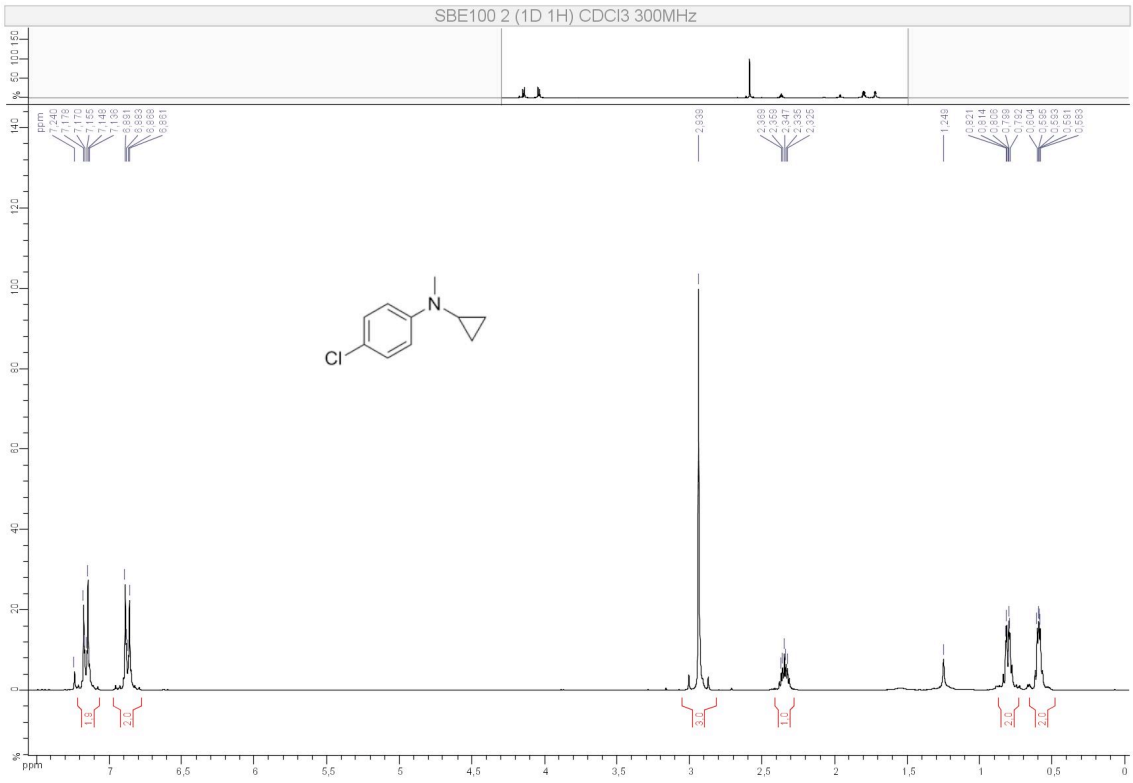
Spectral data

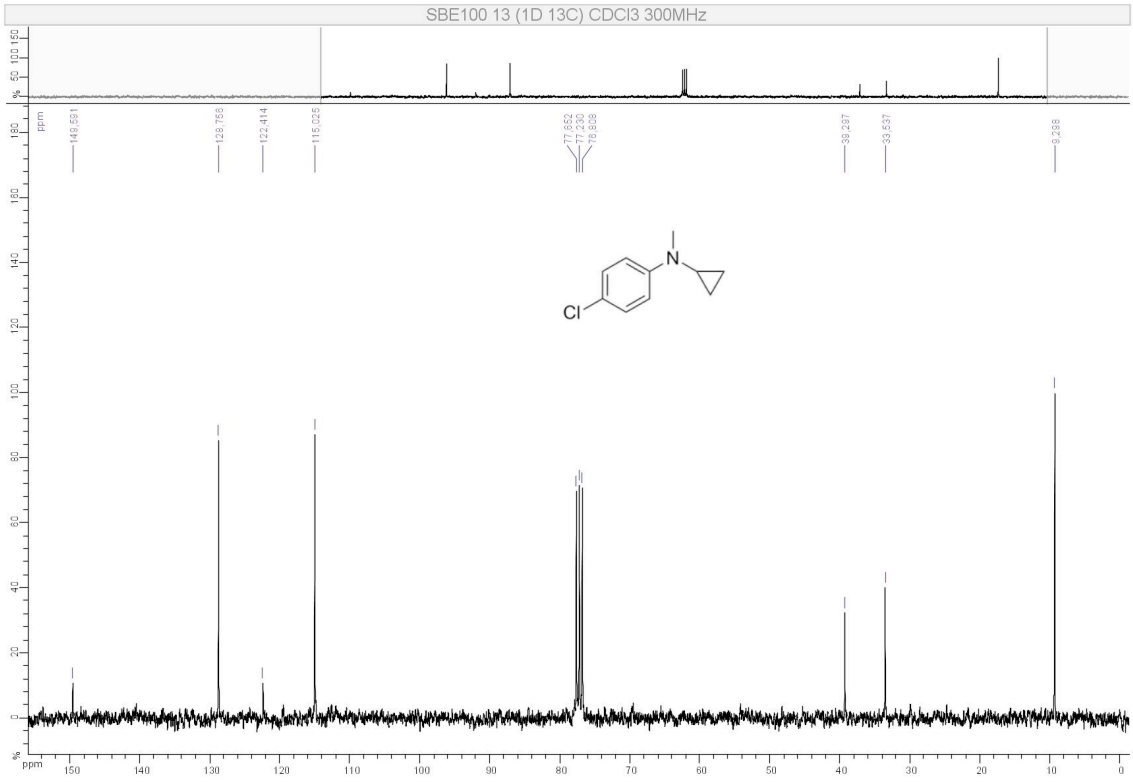
Compound **3a** :



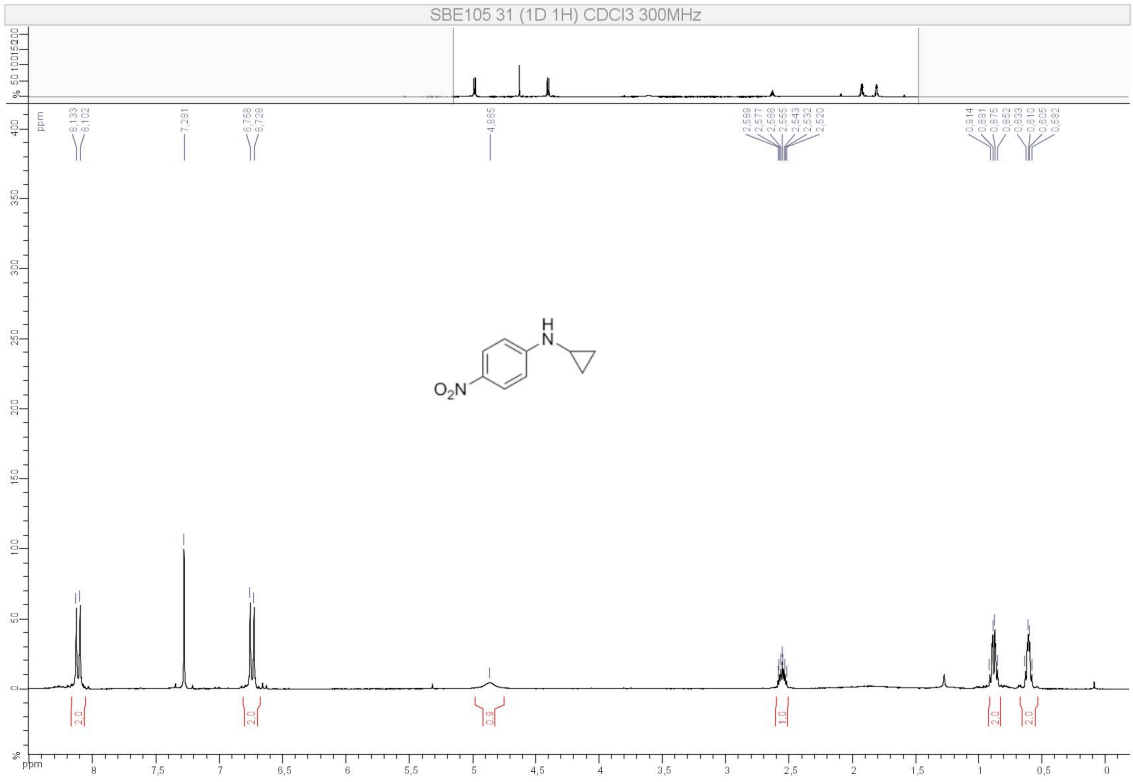


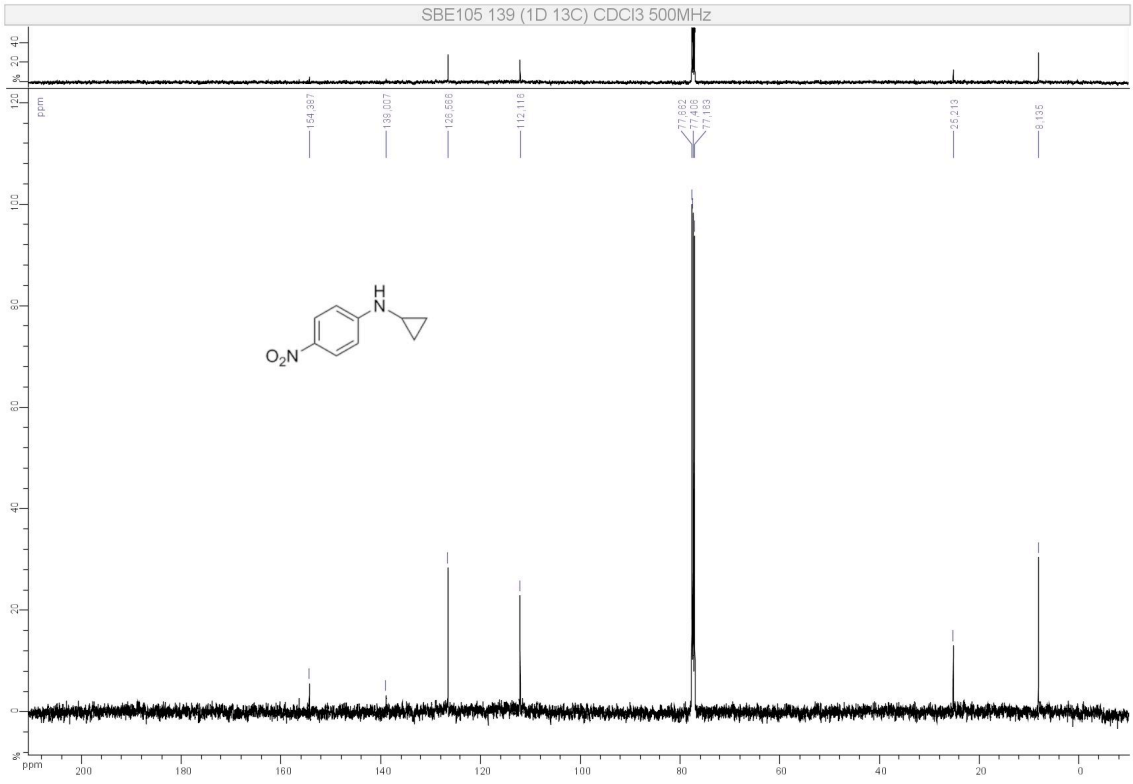
Compound **3b** :


SBE100 2 (1D 1H) CDCl3 300MHz
Cl
N

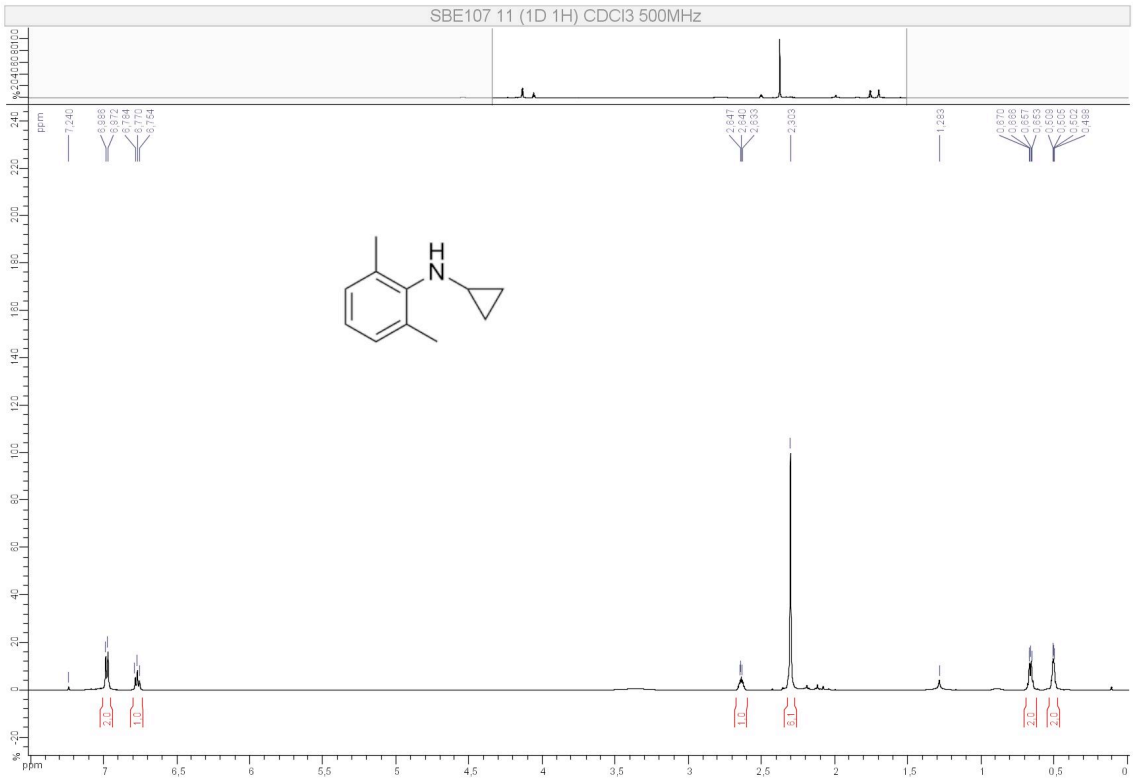

SBE100 13 (1D 13C) CDCl3 300MHz
Cl
N

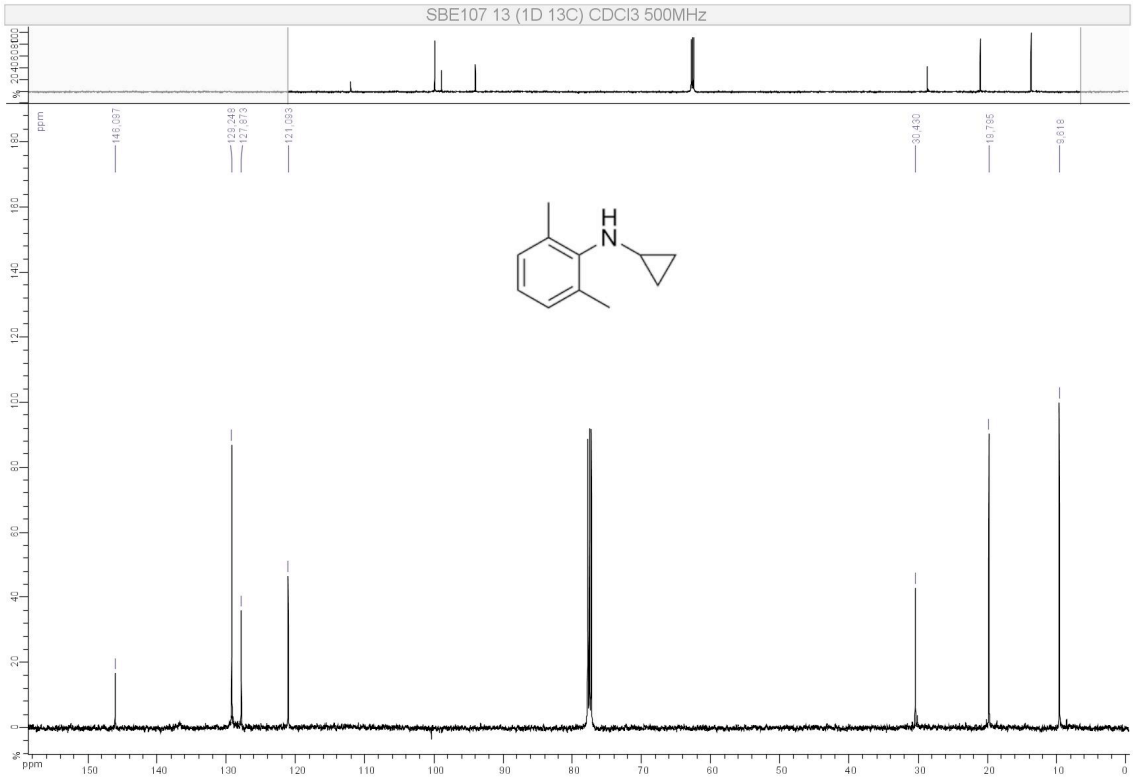
Compound **3c** :


SBE105 31 (1D 1H) CDCl3 300MHz
8.133
8.102
7.281
6.768
6.728
4.865
2.588
2.577
2.568
2.555
2.545
2.532
2.520
0.814
0.801
0.795
0.783
0.633
0.610
0.605
0.582
H
N
O2N
2.0
2.6
3.6
1.6
2.0
2.0

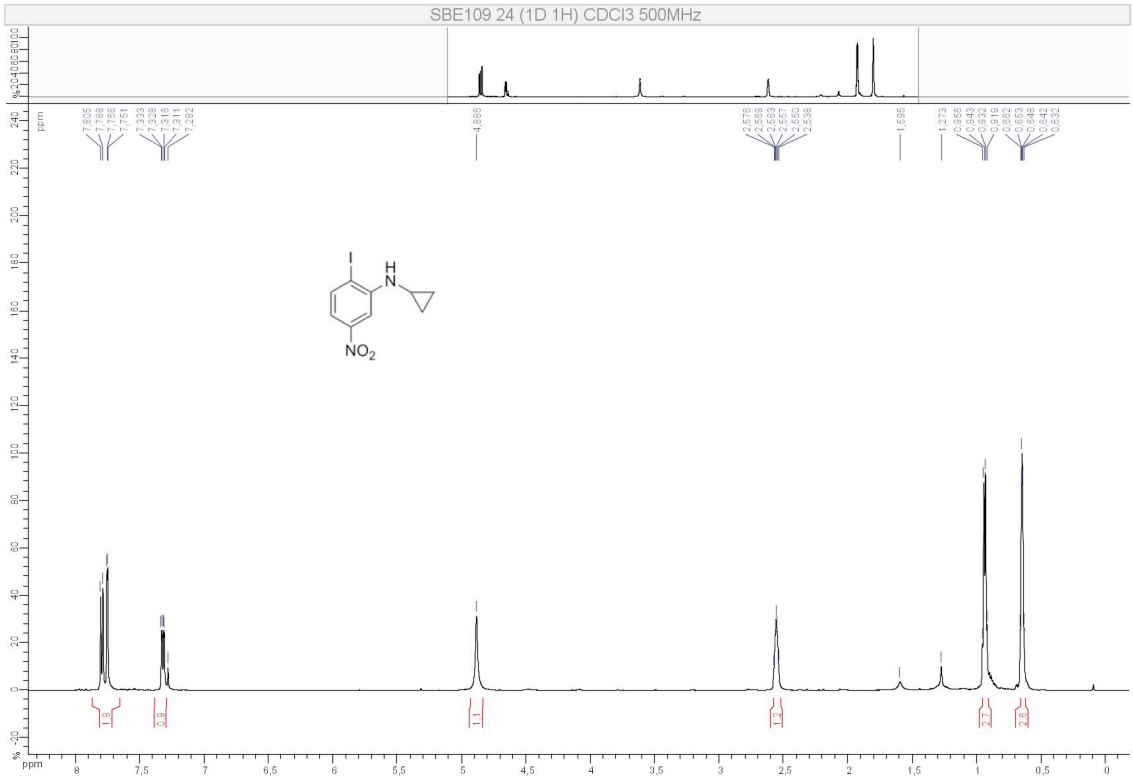

SBE105 139 (1D 13C) CDCl3 500MHz
154.397
139.007
126.656
112.116
77.682
77.406
77.183
26.213
8.135
H
N
O2N

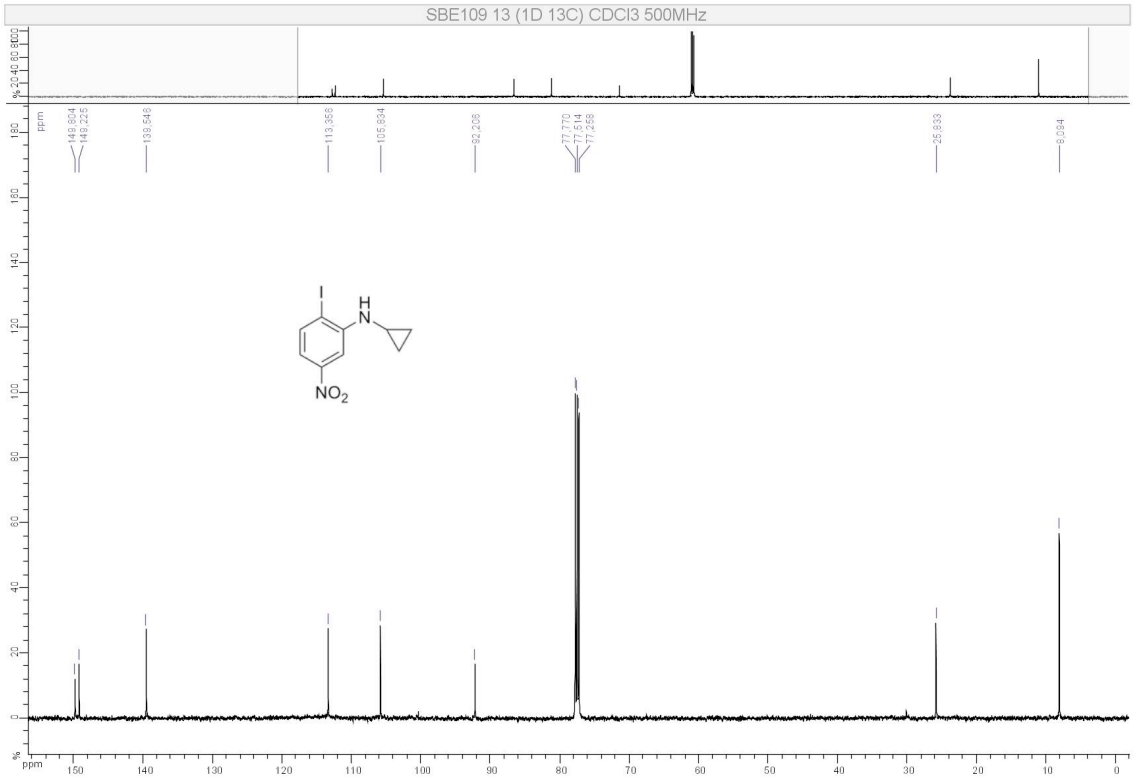
Compound **3d** :


SBE107 11 (1D 1H) CDCl3 500MHz
7.240
6.886
6.872
6.784
6.770
6.754
2.647
2.640
2.583
2.303
1.263
0.870
0.866
0.657
0.653
0.638
0.630
0.502
0.488
ppm

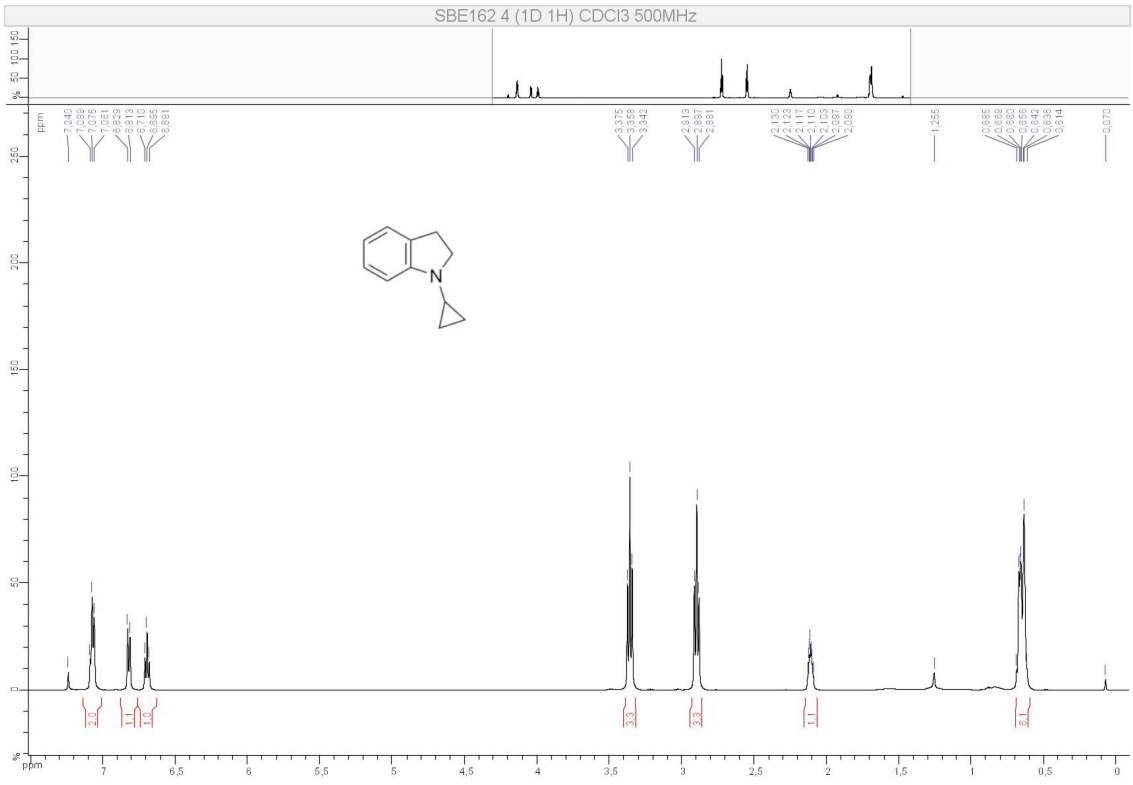

SBE107 13 (1D 13C) CDCl3 500MHz
146.037
129.248
127.873
121.039
30.430
18.796
8.618
ppm

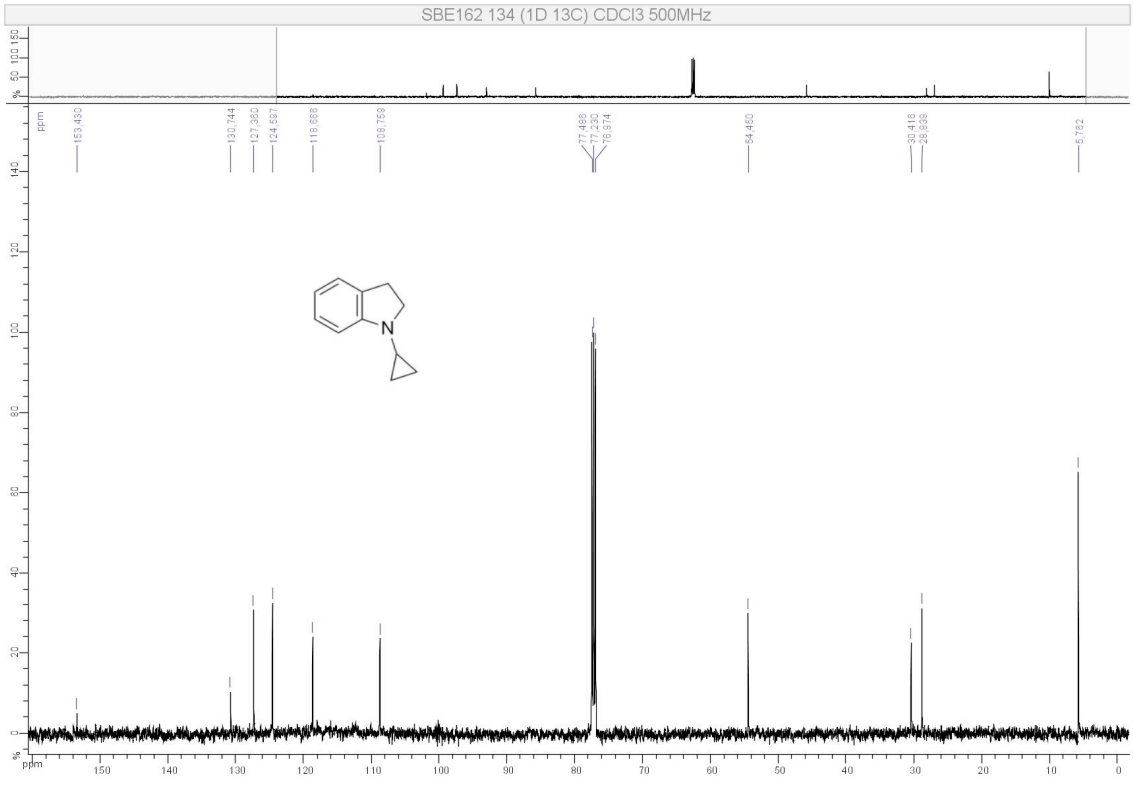
Compound **3e** :


SBE109 24 (1D 1H) CDCl3 500MHz
ppm
I
H
N
NO2

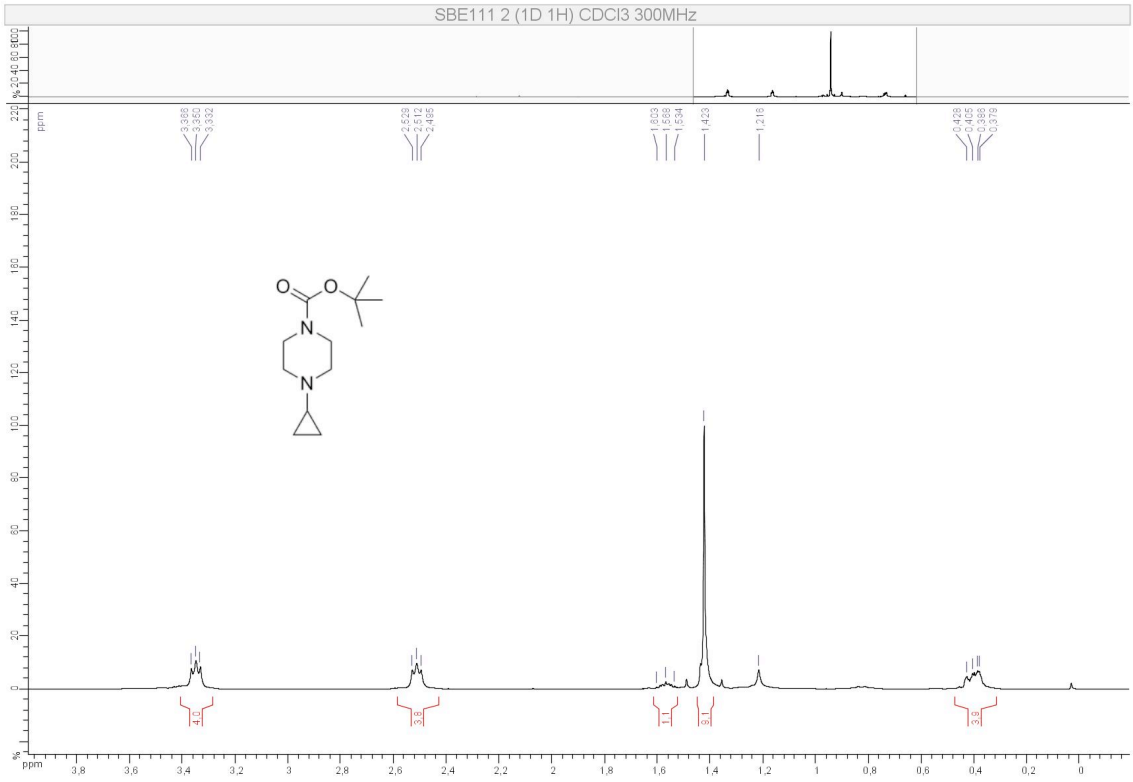

SBE109 13 (1D 13C) CDCl3 500MHz
ppm
I
H
N
NO2

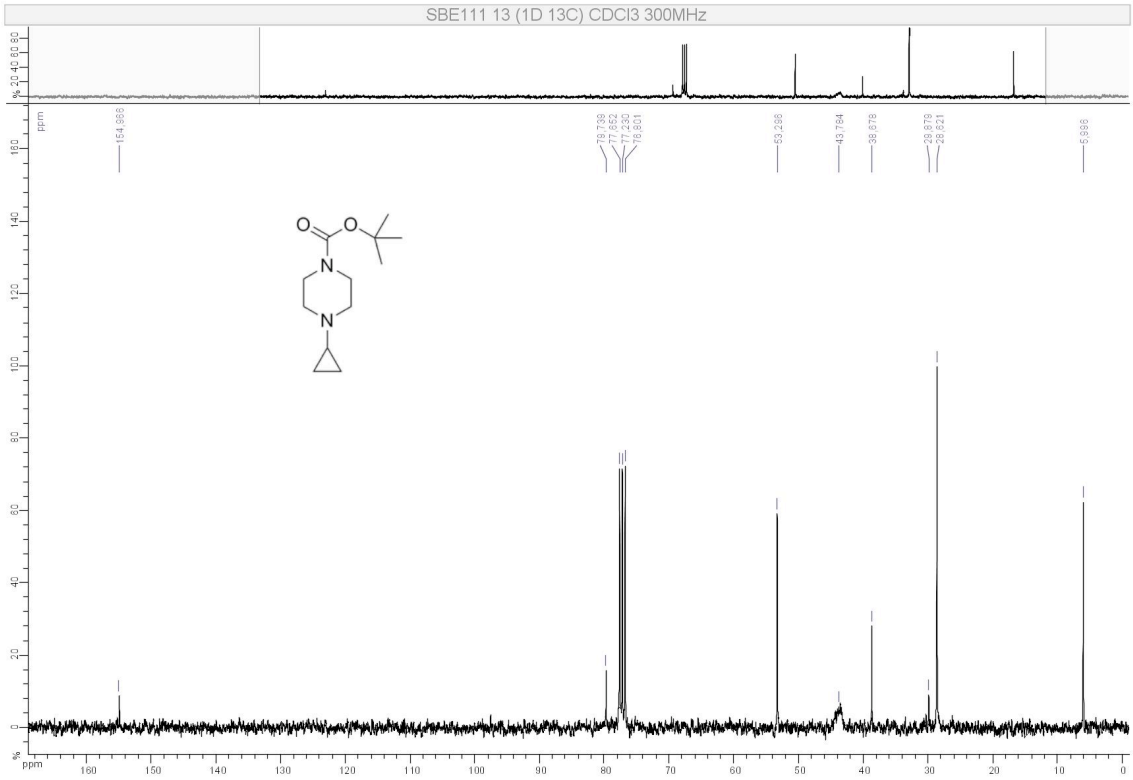
Compound **3f** :



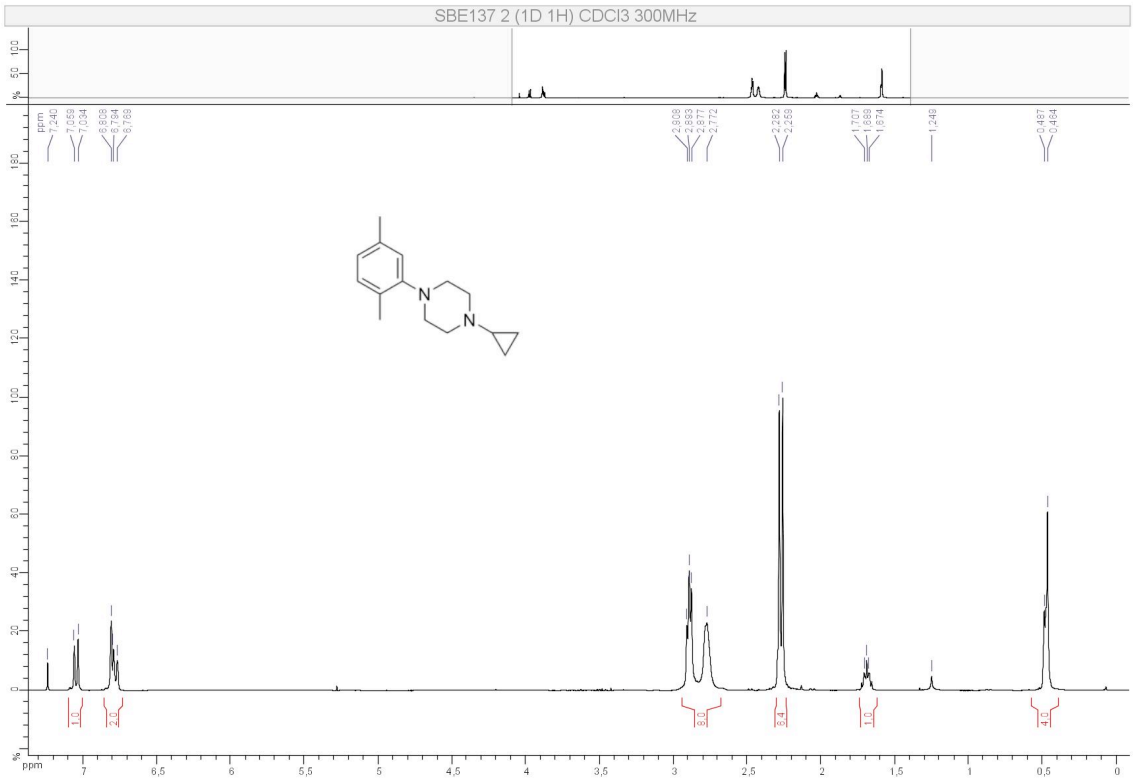


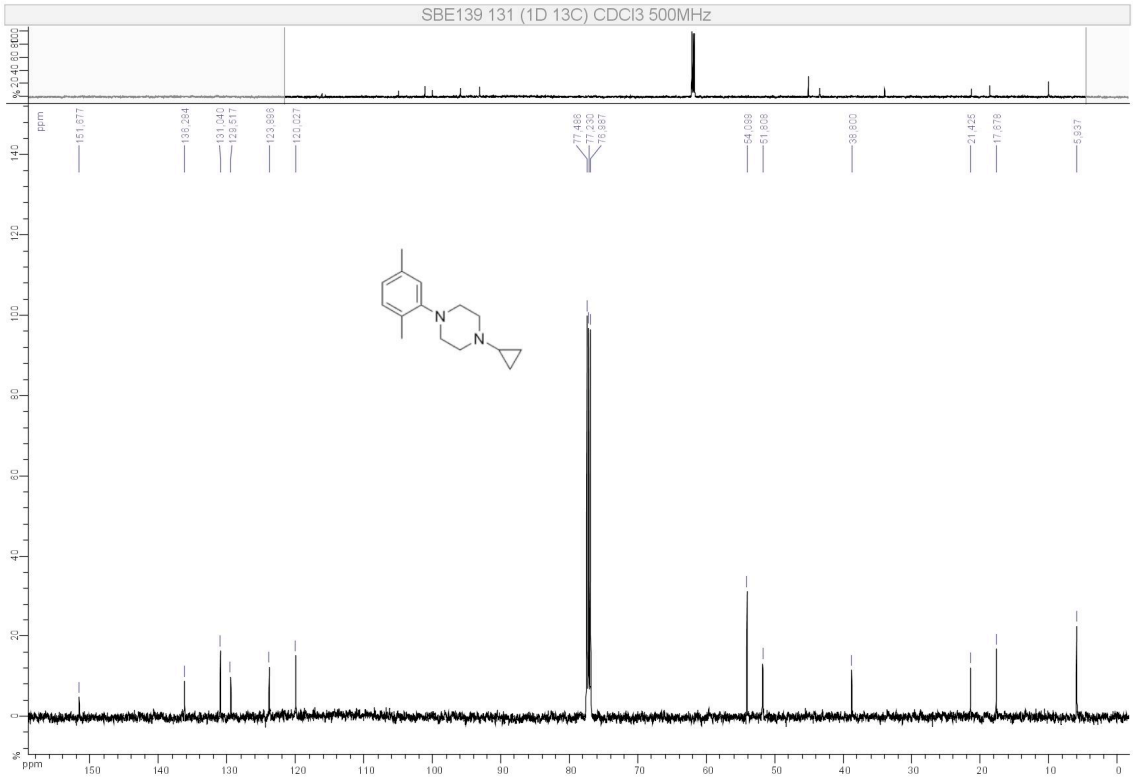
Compound **3g** :



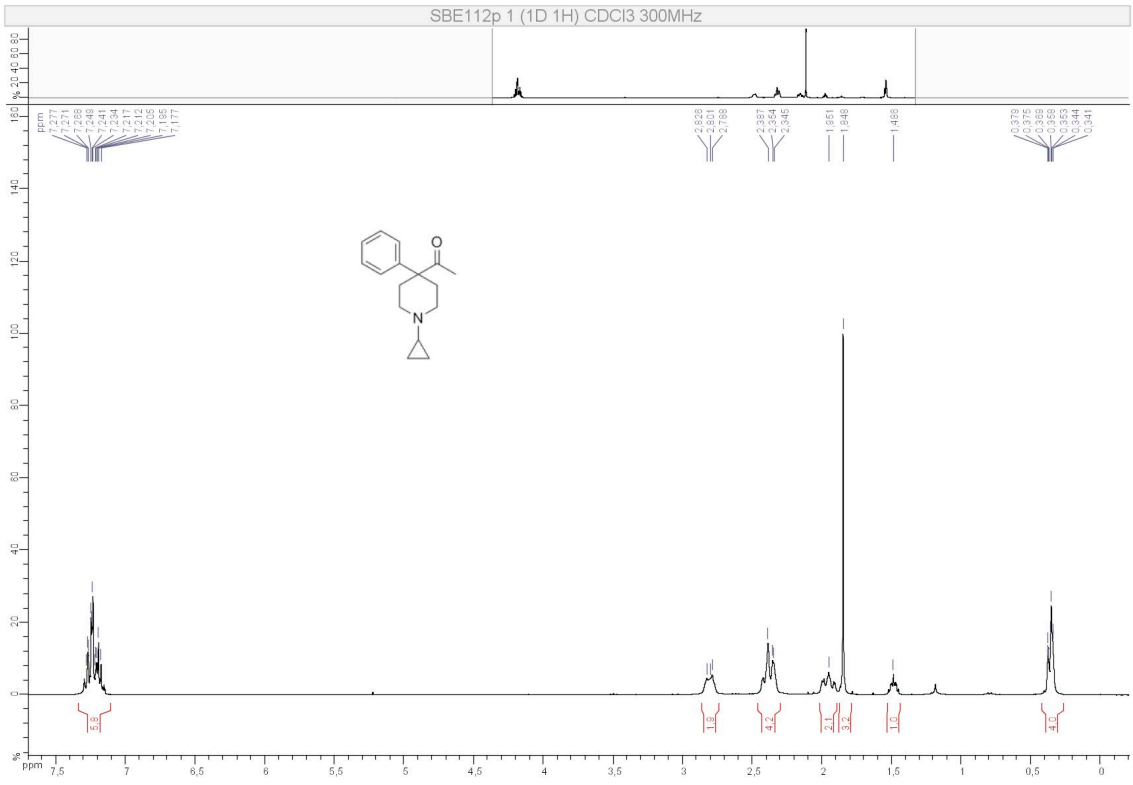


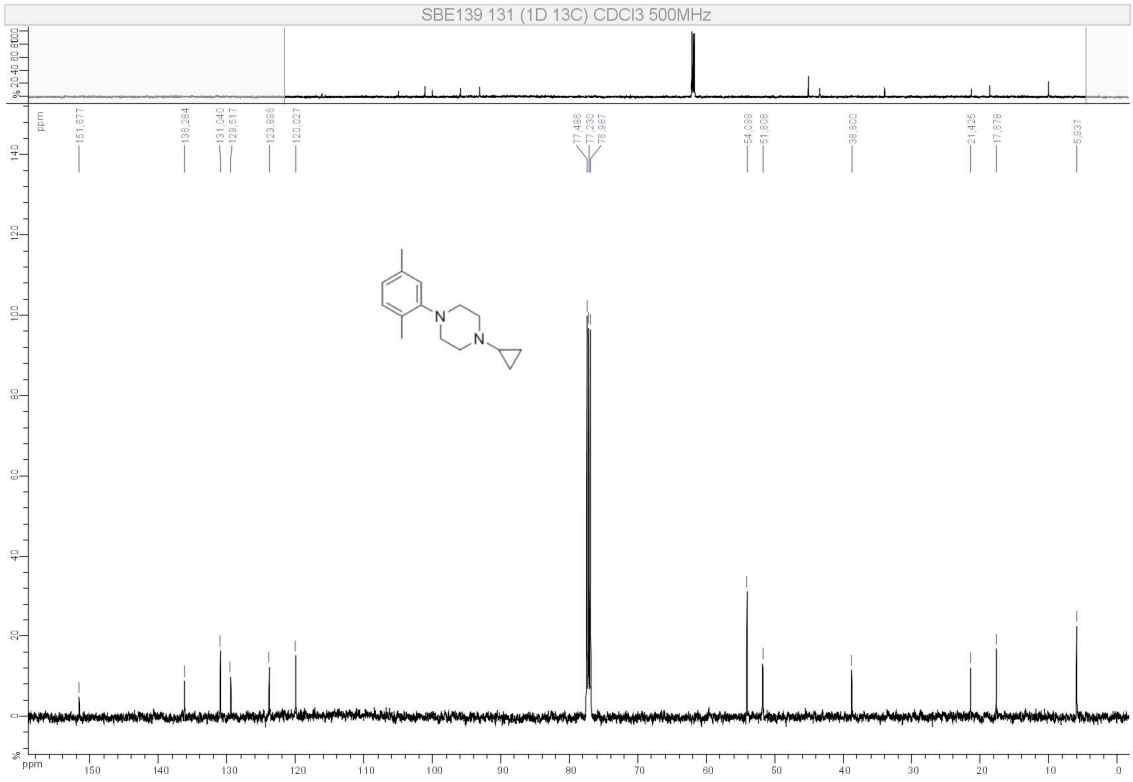
Compound **3h** :



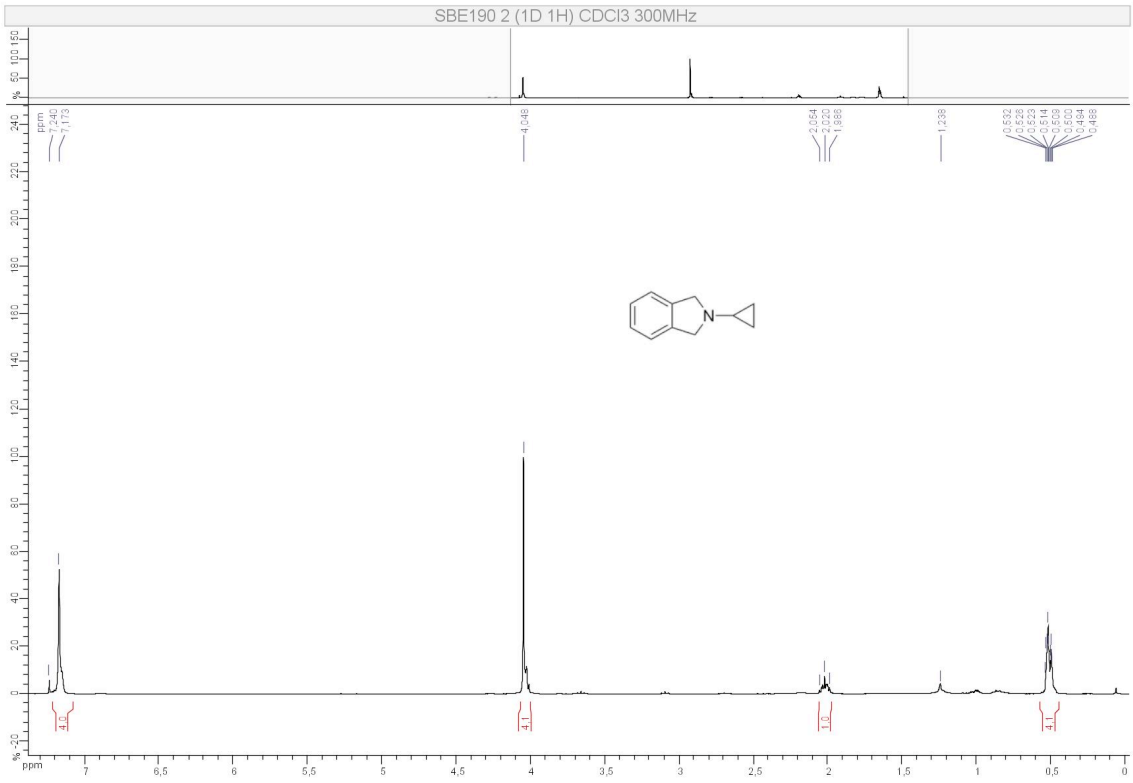


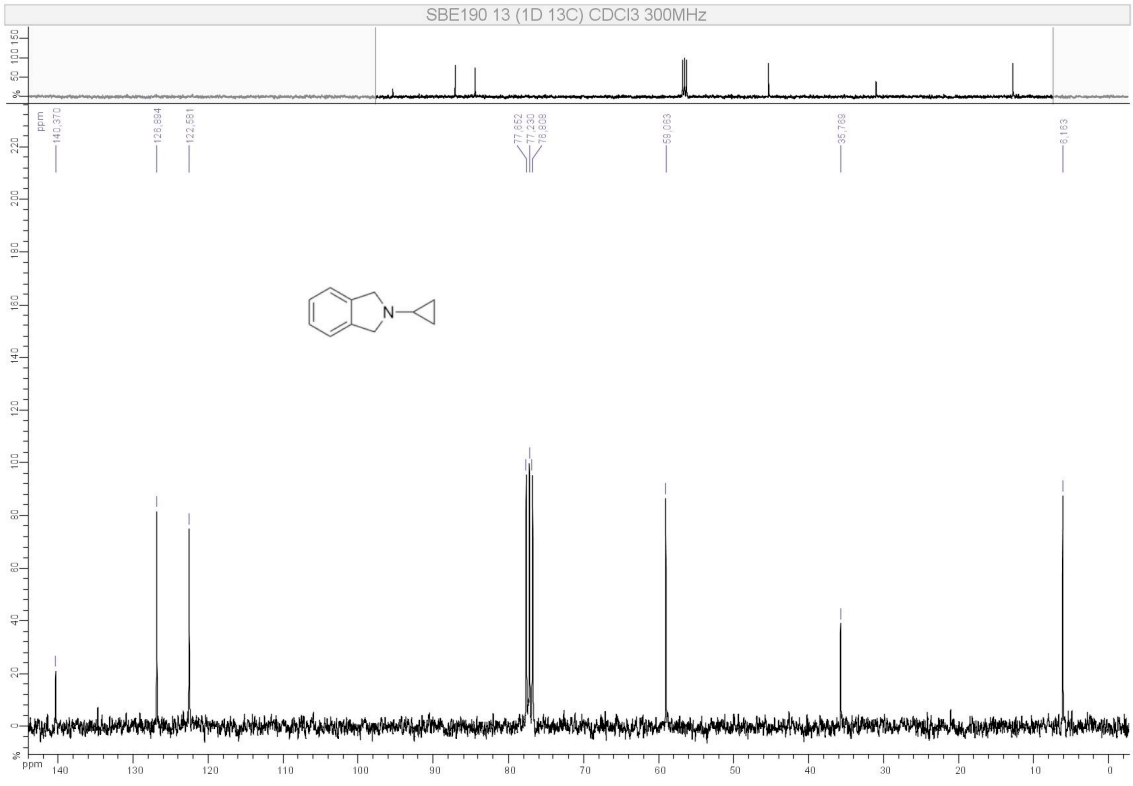
Compound **3i** :



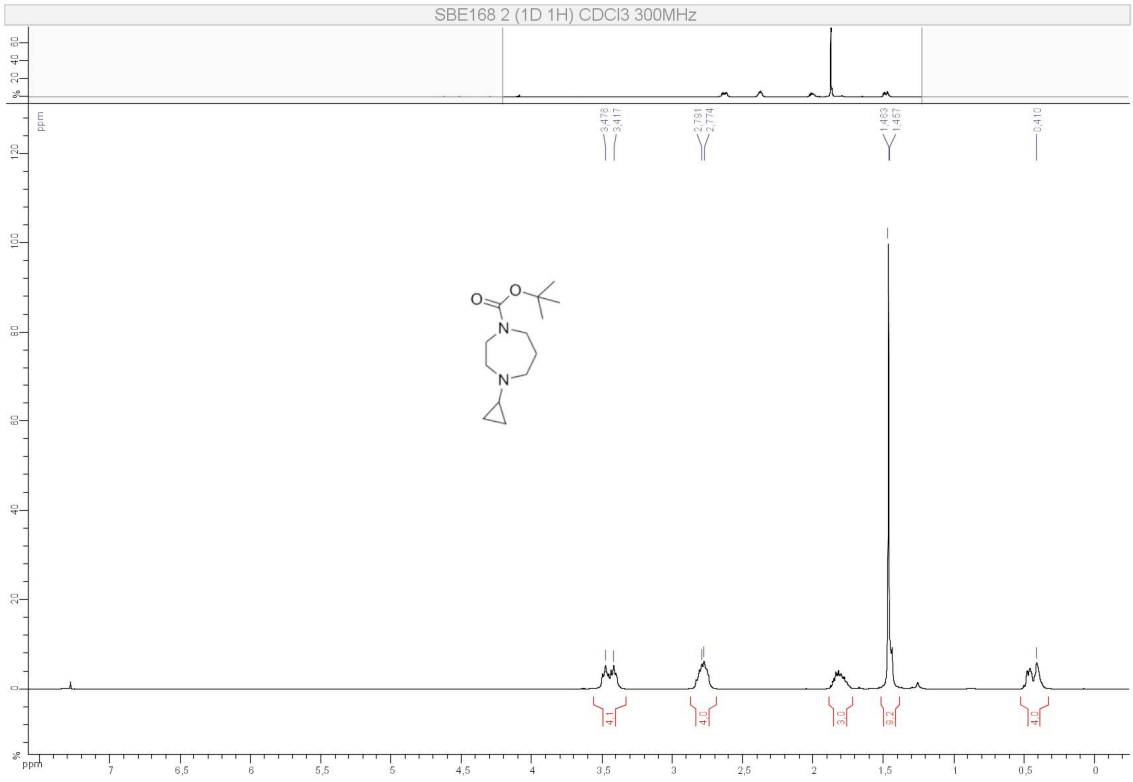


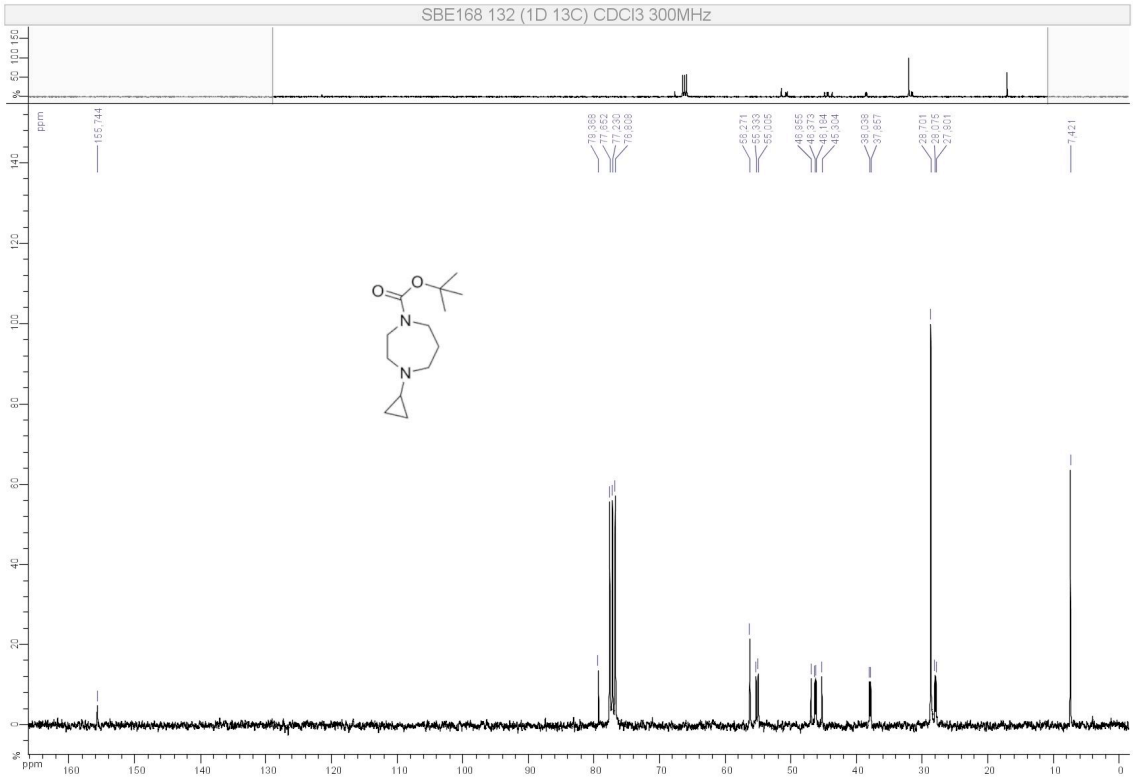
Compound **3j** :


SBE190 2 (1D 1H) CDCl3 300MHz
ppm
7,240
7,179
4,046
2,064
2,023
1,985
1,238
0,532
0,523
0,514
0,509
0,500
0,494
0,488
4,0
4,1
1,0
4,1
ppm

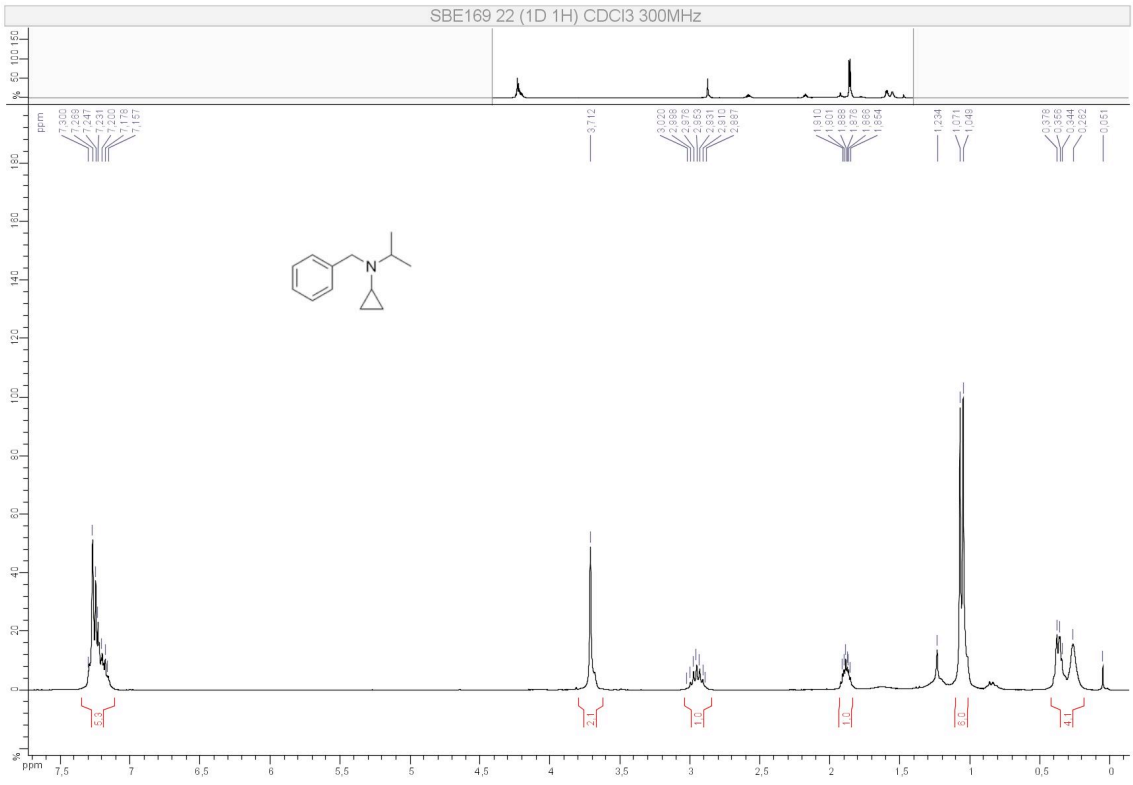

SBE190 13 (1D 13C) CDCl3 300MHz
ppm
140,370
128,894
122,581
77,652
77,230
76,808
69,063
36,769
6,163
ppm

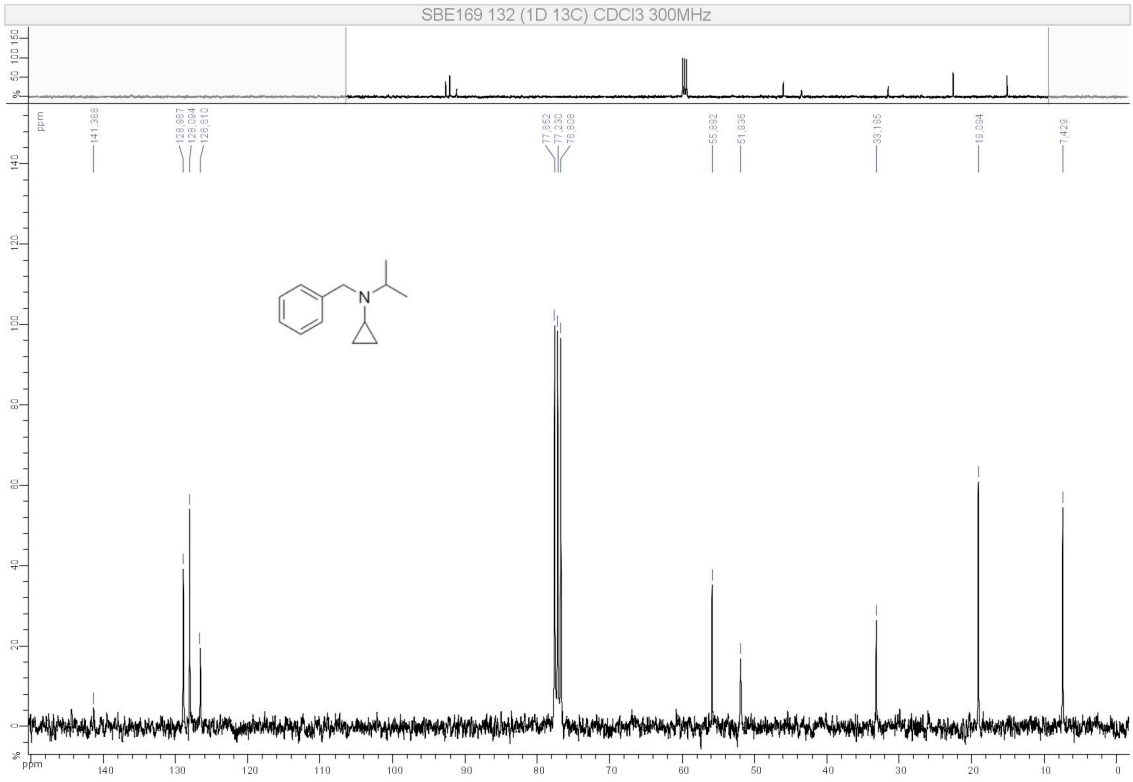
Compound **3k** :


SBE168 2 (1D 1H) CDCl3 300MHz
ppm
3.479
3.417
2.791
2.774
1.463
1.457
0.410
4.1
4.6
5.6
9.2
4.6

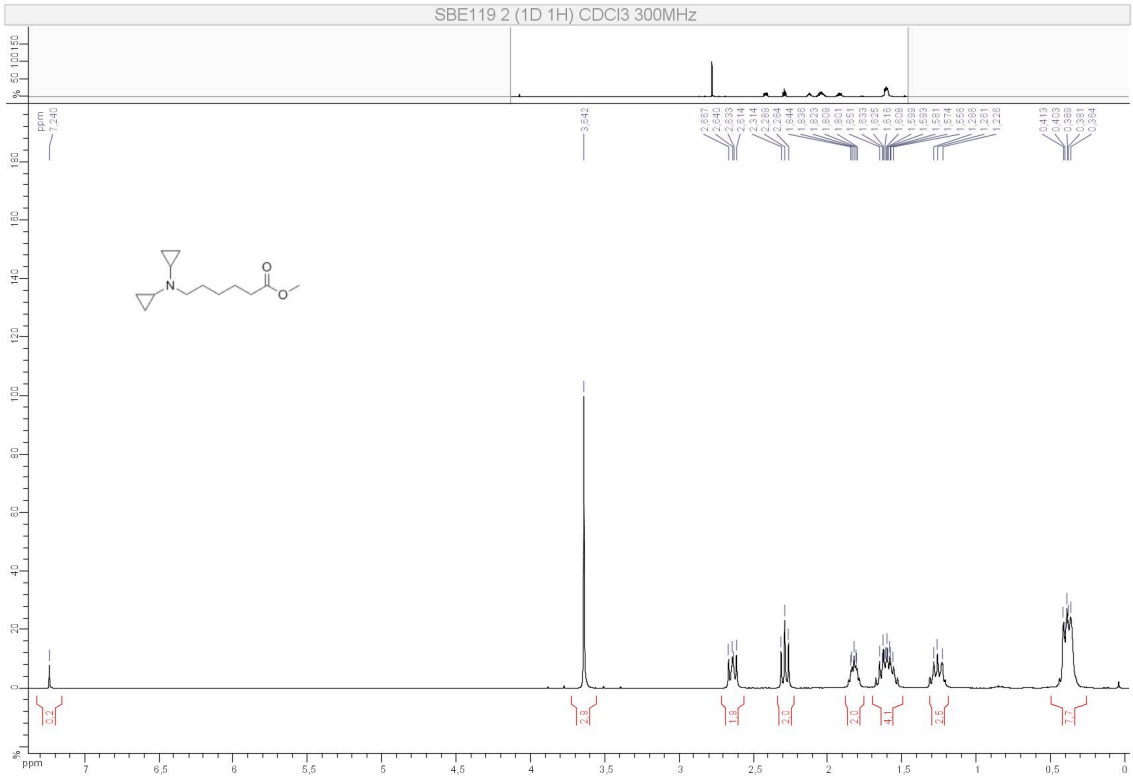

SBE168 132 (1D 13C) CDCl3 300MHz
ppm
155.744
79.369
77.652
77.230
76.809
56.271
55.933
55.605
48.955
48.733
48.184
45.364
28.038
27.857
28.751
28.075
27.901
7.421

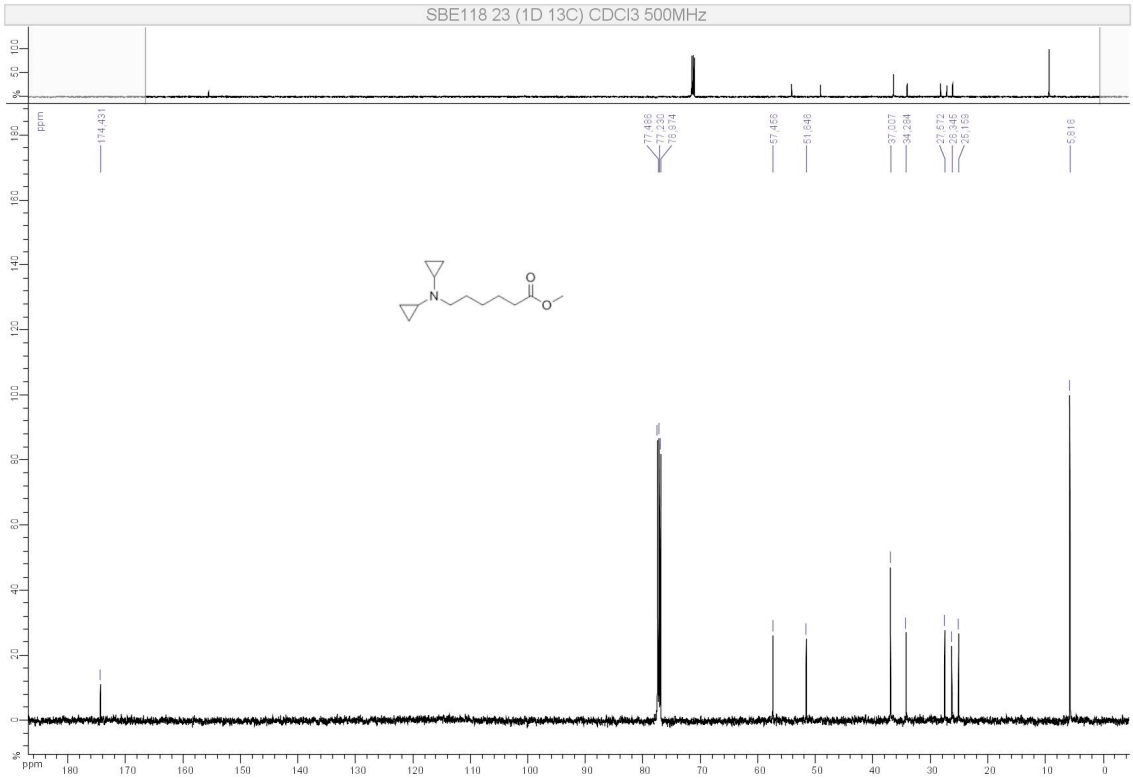
Compounds **3l** :



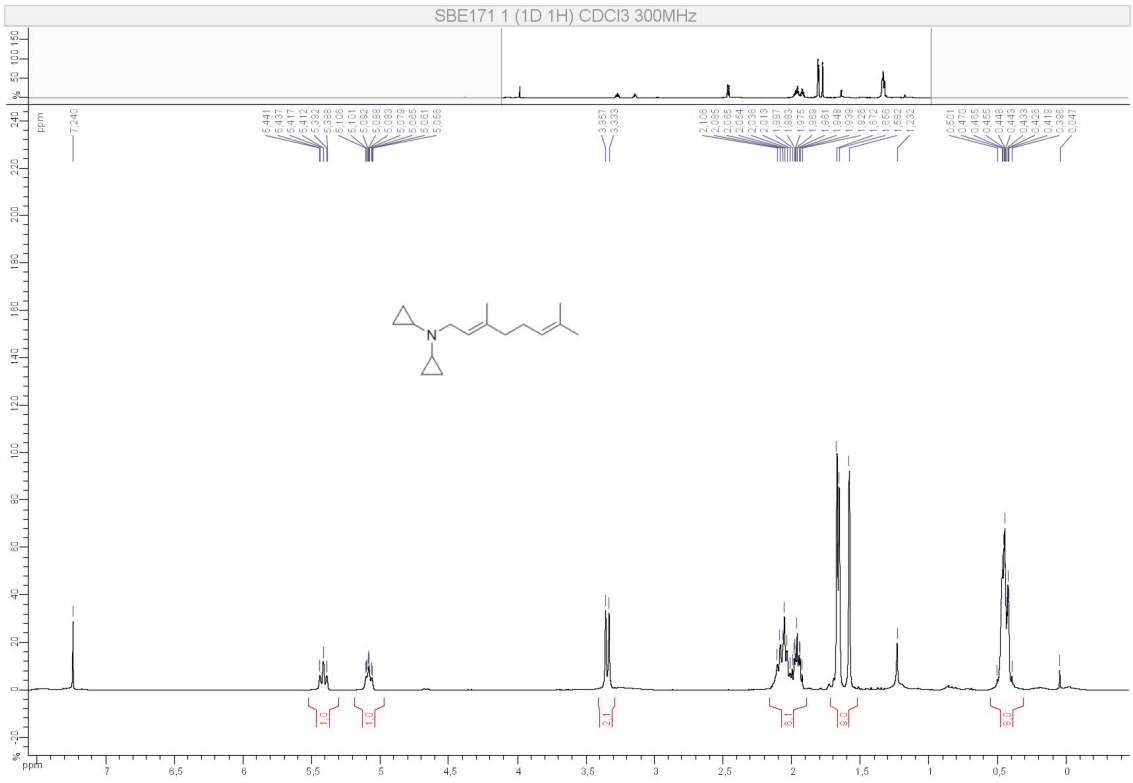


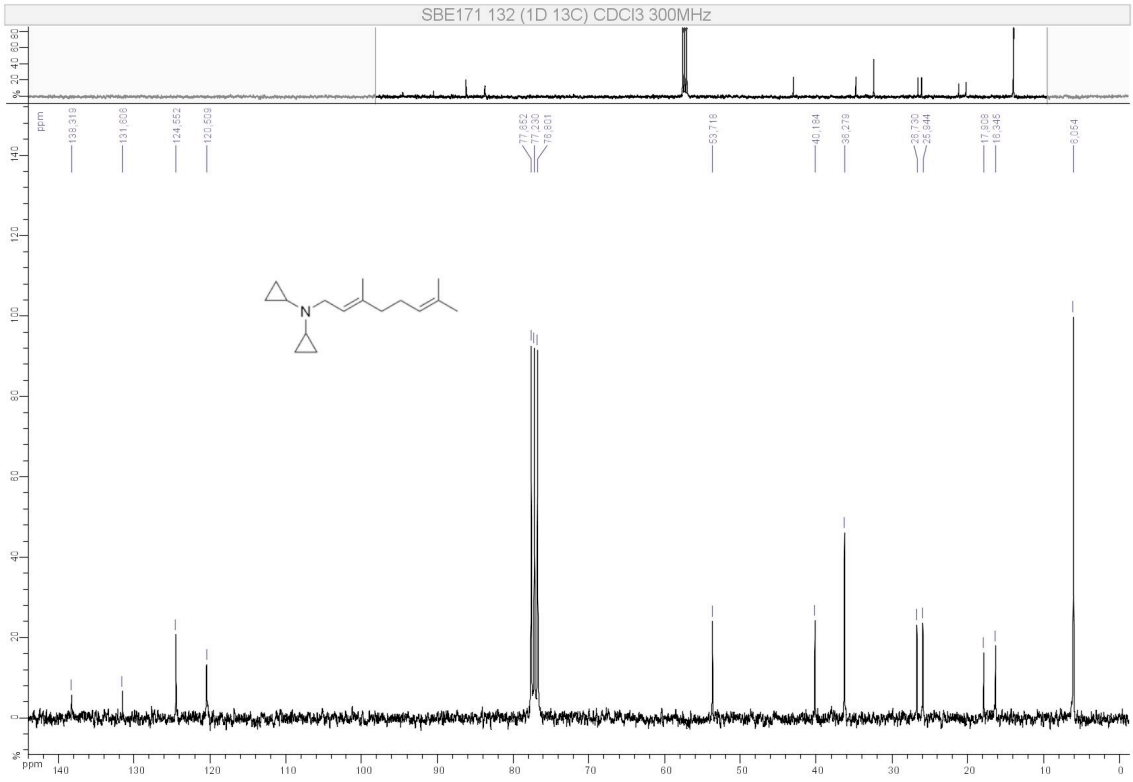
Compound **3m** :


SBE119 2 (1D 1H) CDCl3 300MHz
ppm
7.240
3.642
2.667
2.640
2.633
2.614
2.288
2.264
1.844
1.836
1.823
1.808
1.651
1.633
1.625
1.616
1.608
1.588
1.583
1.574
1.556
1.286
1.261
1.226
0.413
0.403
0.388
0.381
0.364
0.2
2.8
1.8
2.0
2.0
4.1
2.6
7.7

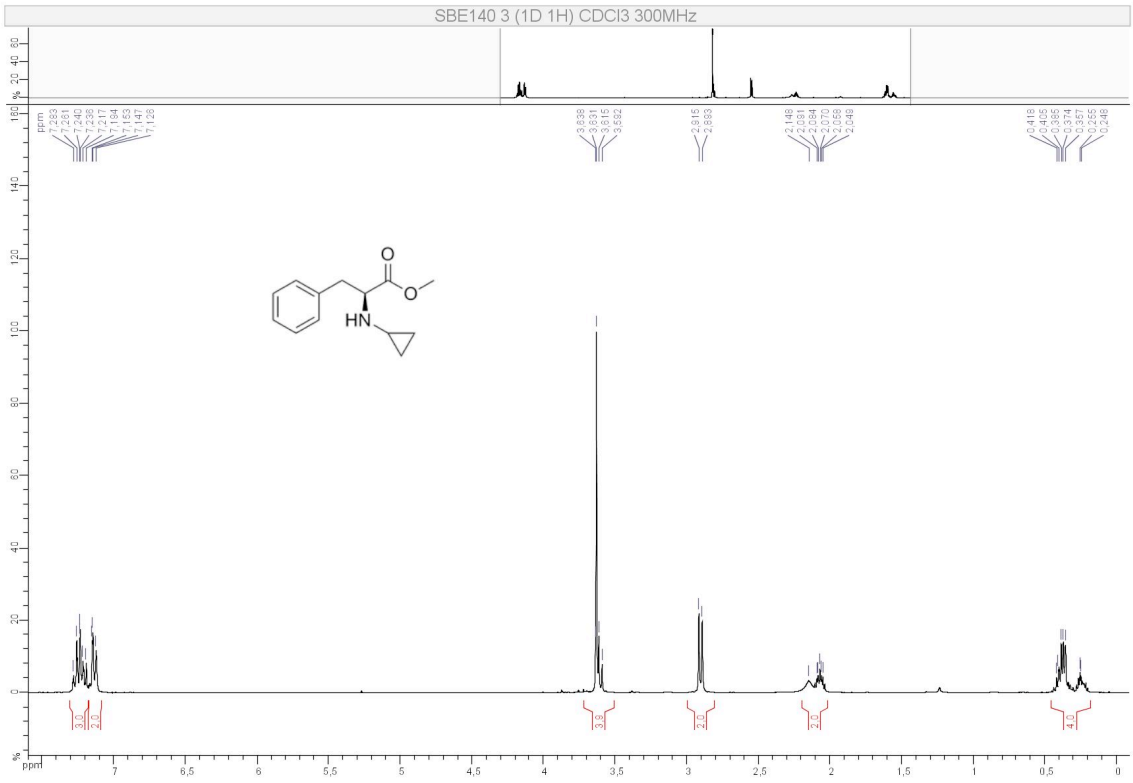

SBE118 23 (1D 13C) CDCl3 500MHz
ppm
174.431
77.486
77.230
76.974
57.453
51.848
37.007
34.284
25.572
25.345
25.159
5.816

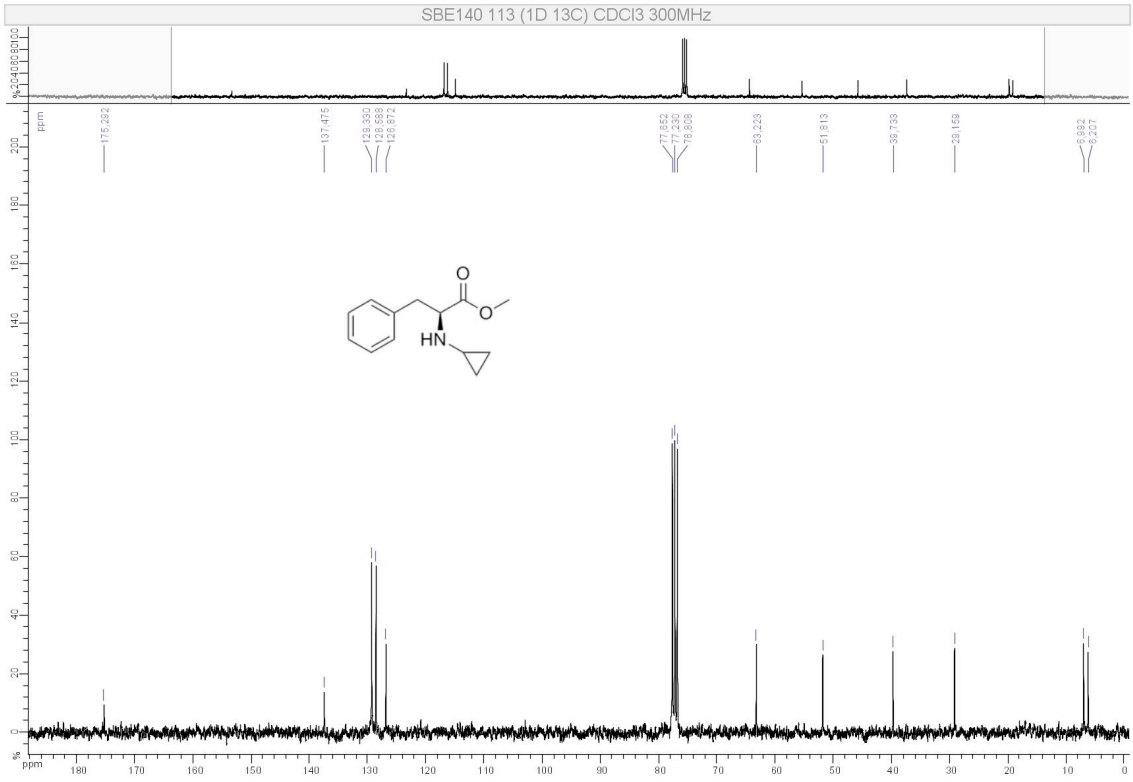
Compound **3n** :



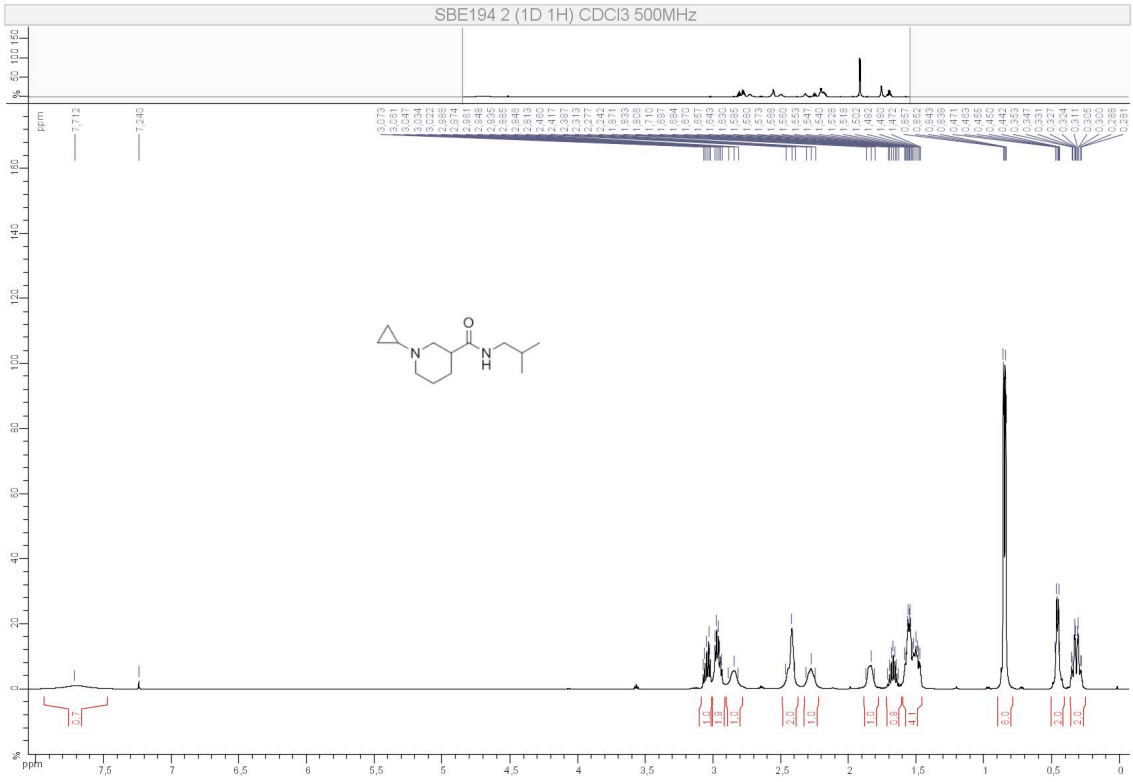


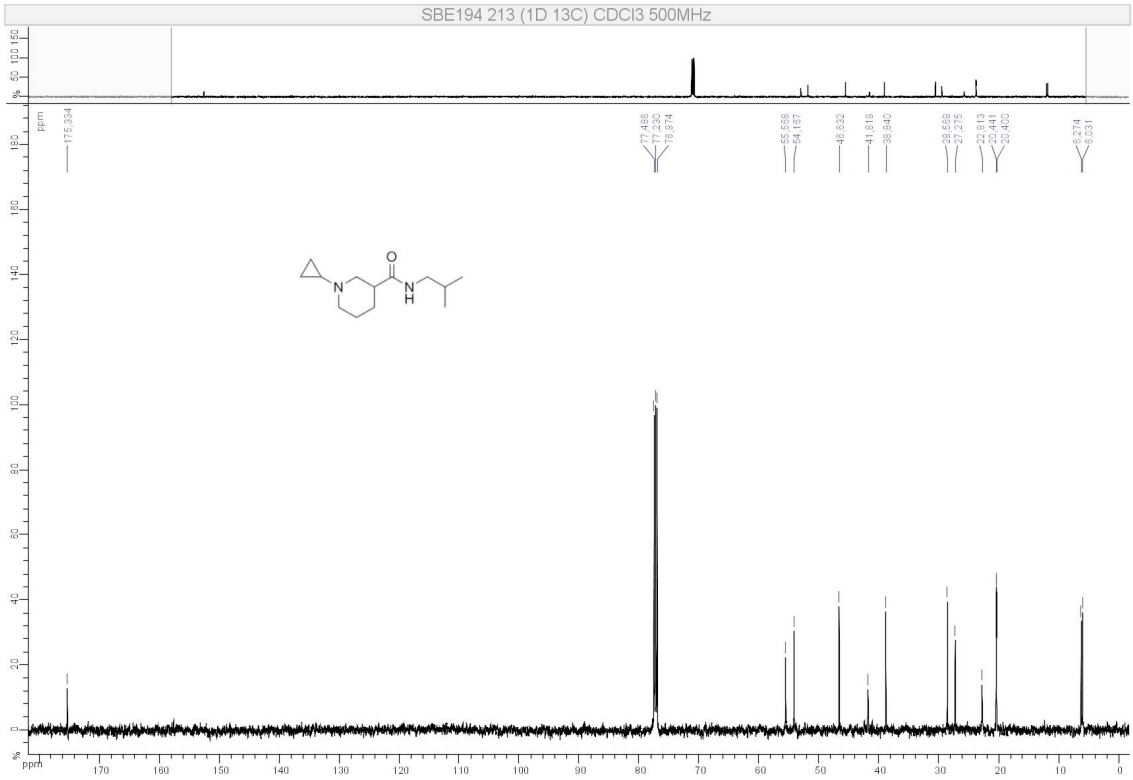
Compound **3o** :


SBE140 3 (1D 1H) CDCl3 300MHz
O
O
HN

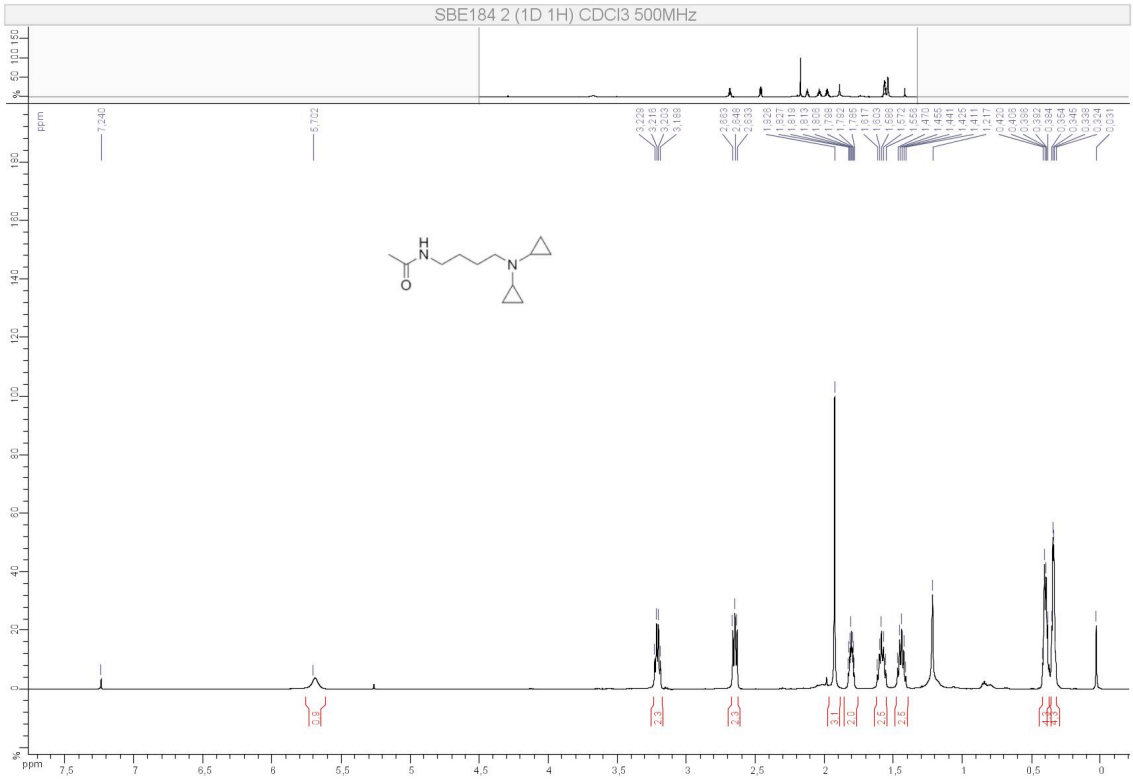

SBE140 113 (1D 13C) CDCl3 300MHz
O
O
HN

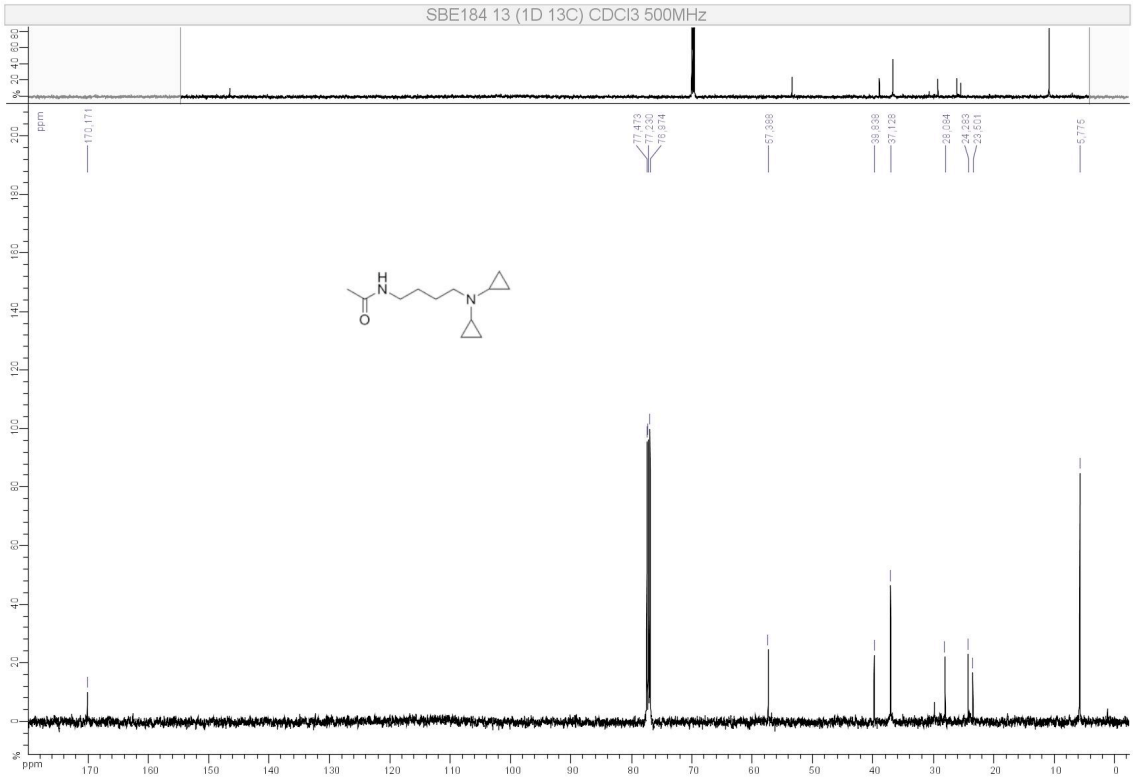
Compound **3p** :





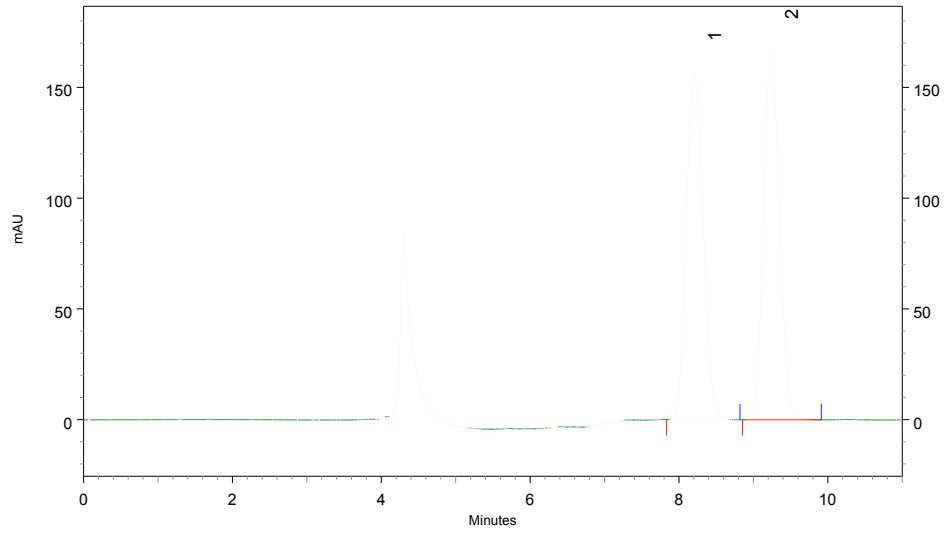
Compound **3q** :





HPLC data for compound **3o**

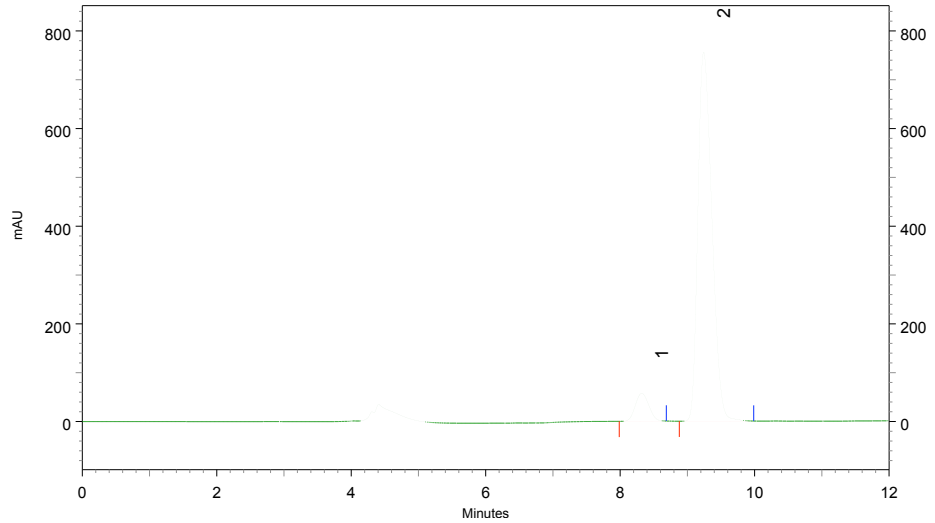
Racemate.



DAD-CH1 (224 nm)
Results

Pk #	Retention Time	Area	Area %
1	8.21	9940015	49.93
2	9.24	9966173	50.07

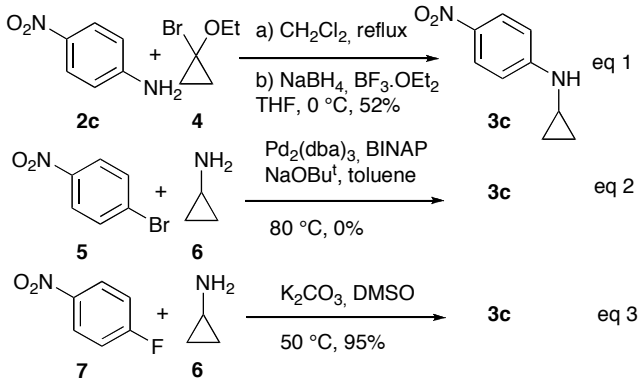
Compound **(*S*)-3o**.



DAD-CH1 (224 nm)
Results

Pk #	Retention Time	Area	Area %
1	8.32	3187658	6.78
2	9.24	43820656	93.22

Synthesis of *N*-cyclopropyl-4-nitroaniline 3c: a comparison with literature procedures.



Scheme 1

In scheme 1 were summarized other methods used for the synthesis of *N*-cyclopropyl-4-nitroaniline **3c** (*cf* entry 3, table 1). Condensation of 4-nitroaniline (**2c**) with 1-bromo-1-ethoxycyclopropane (**4**) followed by reduction afforded **3c** in 52% overall yield (eq 1).[1] On the other hand, reaction between 4-nitro-bromobenzene (**5**) and cyclopropylamine (**6**) failed to give **3c** (eq 2**)**.[2] Finally, the S_NAr reaction between 4-nitro-fluorobenzene with **6** under literature conditions (neat in the presence of Et_3N) afforded **3c** in less than 10% yield.[3] However, stirring a DMSO solution of **6** and **7** in the presence of potassium carbonate afforded **3c** in excellent yield (95%, eq 3).[4] Nevertheless, this last method is applicable only to electron-deficient aromatic fluorides. Overall, these results illustrated well the power of the present synthetic method.

---

1 J. Kang, K. S. Kim, *J. Chem. Soc. Chem. Commun*. **1987**, 897-898.

2 W. Cui, R. N. Loeppky, *Tetrahedron* **2001**, *57*, 2953-2956.

3 C. Hubschwerlen, P. Pflieger, J.-L. Specklin, K. Gubernator, H. Gmünder, P. Angehrn, I. Kompis, *J. Med. Chem*. **1992**, *35*, 1385-1392.

4 L. Neuville, J. Zhu, *Tetrahedron Lett.* **1997**, *38*, 4091-4094.