Supporting Information

Synthesis of Isoindolinones via Palladium-Catalyzed C–H Activation of *N*-Methoxybenzamides

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General Information

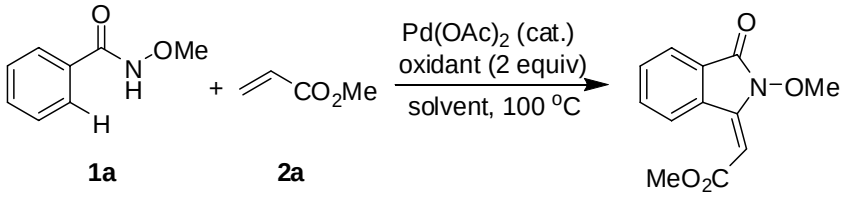
Unless otherwise noted, all commercial materials and solvents were used without further purification. ^{1}H and ^{13}C NMR spectra were referenced to residue $CHCl_3$ at 7.26 ppm and 77.16 ppm, respectively. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (integration, s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, coupling constant(s) in Hz). High-resolution mass spectra (HRMS) were recorded on Bruker VPEXII spectrometer with EI mode and Thermo Scientific LTQ Orbitrap XL with ESI mode.

General Procedure

General Procedure for the Preparation of 1a-1m:[1] *O*-Methylhydroxylamine hydrochloride (1.67 g, 20 mmol) and K_2CO_3 (5.52 g, 40 mmol) were dissolved in a mixture of water (50 mL) and EtOAc (100 mL) in a round-bottomed flask. The solution was cooled to 0 °C in an ice bath. An acyl chloride (20 mmol) was then added via syringe. After stirring at room temperature for 5 h, the aqueous layer was separated out. The organic layer was washed with water and then brine. After drying over $MgSO_4$, evaporation of the solvent gave a sticky residue. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 3/1 as the eluent to give the desired product.

Screening Conditions for the Synthesis of 3aa: To a stirred solution of *N*-methoxybenzamide **1a** (75.6 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), and methyl acrylate **2a** (90.6 μL, 1.0 mmol) in a chosen solvent (5 mL) at 100 °C was added an oxidant (1.0 mmol). The reaction was monitored by TLC and stopped at the desired time. Then the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 6/1 as the eluent to get product **3aa**. Besides the data in Table 1 in the main text, additional results are collected in Table S1

Table S1. Screening Conditions for the Pd-Catalyzed Reaction of *N*-Methoxybenzamide and Methyl Acrylate.[a]



1a **2a** **3aa**

Entry	Oxidant	Solvent	Time (h)	Yield (%)
1	$K_2S_2O_8$	HOAc	24	trace
2	PhIOAc	HOAc	24	0
3	O_2	HOAc	24	trace
4	BQ	1,4-dioxane	24	0
5	BQ	DMF	24	trace
6	BQ	DCE	24	trace
7	BQ	CH_3CN	24	trace

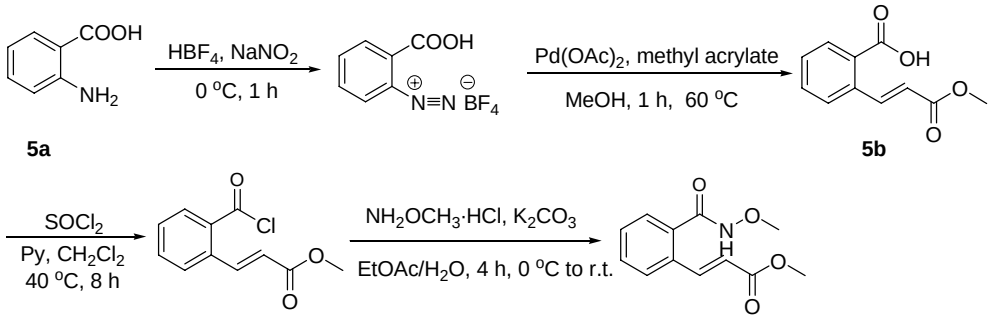
[a]All reactions were carried out with **1a** (0.5 mmol), **2a** (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), oxidant (1.0 mmol), solvent (5 mL), 100 °C.

General Procedure for the Synthesis of 3aa-3ma and 3ab-3kb: To a stirred solution of *N*-methoxybenzamides **1a** (**1b-1m**, 0.5 mmol), $Pd(OAc)_2$ (0.025 mmol, 0.05mmol for **3ja** and **3jb**), and acrylate ester **2a** or **2b** (1.0 mmol) in AcOH (5 mL) at 100 °C (120°C for **3ka**, **3la**, and **3kb**) was added BQ (108.1 mg, 1.0 mmol). The reaction was monitored by TLC. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 6/1 as the eluent to give product **3aa** (**3ba-3ma,** and **3ab-3kb**).

General Procedure for the Synthesis of 3ac, 3cc, and 3dc: To a stirred solution of *N*-methoxybenzamide **1a** (**1c** or **1d**, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), and acrylamide **2c** (1.0 mmol, 1.5 mmol for **3cc**) in AcOH (5 mL) at 100 °C was added BQ (108.1 mg, 1.0 mmol). The reaction was monitored by TLC. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 3/1~1/1 as the eluent to afford product **3ac** (**3cc** and **3dc)**.

Synthesis of 3ad: To a stirred solution of *N*-methoxybenzamide **1a** (75.6 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), and styrene **2d** (1.0 mmol, 114.4 μL) in AcOH (5 mL) at 100 °C was added BQ (108.1 mg, 1.0 mmol). The reaction was monitored by TLC. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 6/1 as the eluent to afford product **3ad** (57.8mg, 46%).

Synthesis of 5aa:[1,2]



A solution of $NaNO_2$ (0.57 g, 8.26 mmol) in water (3 mL) was added dropwise to an ice-cold 2-aminobenzoic acid (1.0 g, 8.13 mmol) in 42% HBF_4 (3.3 mL, 20.62 mmol). Stirring was continued for 1 h at 0 °C after which methanol (0.5 mL), ethyl acrylate (1.11 g, 1.5 mL, 11.13 mmol) and $Pd(OAc)_2$ (35 mg, 0.15 mmol) were added to the mixture, which was then heated in a water bath for 1 h. The mixture was then extracted with diethyl ether, and the extract was washed with saturated aqueous $NaHCO_3$, dried with Na_2SO_4 and evaporated. Chromatography of the residue over silica gel gave (*E*)-2-(3-methoxy-3-oxoprop-1-enyl)benzoic acid **5b** as a white solid.

Reaction of **5b** (1.28 g, 6.2 mmol) with $SOCl_2$ (0.9 mL, 1.24 mmol) and pyridine (0.6 mL) in CH_2Cl_2 (20 mL) for 5 h afforded **5c**.

O-Methylhydroxylamine hydrochloride (0.52 g, 6.2 mmol) and K_2CO_3 (1.71 g, 12.4 mmol) were dissolved in a mixture of water (25 mL) and EtOAc (50 mL) in a round-bottomed flask. The solution was cooled to 0 °C in an ice bath. Compound **5c** was then added via syringe. After stirring at room temperature for 5 h, the aqueous layer was separated out. The organic layer was washed with water and then brine. After drying over $MgSO_4$, evaporation of the solvent gave a sticky residue. Recrystallization from petroleum ether/ethyl acetate gave the (*E*)-methyl 3-(2-(methoxycarbamoyl)phenyl)acrylate **5aa**.

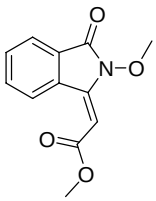
Synthesis of 6aa:[3] To a stirred solution of *N*-methoxybenzamides **1a** (75.6 mg, 0.5 mmol), $PdCl_2(CH_3CN)_2$ (12.8 mg, 0.05 mmol), CuCl (27.3 mg, 0.055 mmol), and methyl acrylate **2a** (90.6 μL, 1 mmol) at 50 °C in Et_2O under a dioxygen atmosphere for 16 h. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with

petroleum ether/ethyl acetate 6/1 as the eluent to get product **6aa**.

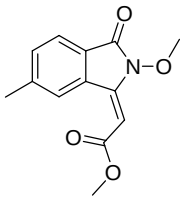
Synthesis of 7aa: To a stirred solution of *N*-methoxybenzamides **1a** (151.2 mg, 1.0 mmol), ^{t}BuOK (28.0 mg, 0.25 mmol) and methyl acrylate **2a** (181.2 μL, 2 mmol) at room temperature in MeOH for 12 h. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 3/1 as the eluent to get product **7aa** (150.4 mg, 63%).

Synthesis of 8aa: To a stirred solution of *N*-methoxybenzamides **1a** (75.6 mg, 0.5 mmol), Pd $(OAc)_2$ (5.6 mg, 0.025 mmol) and methyl acrylate **2a** (90.6 μL, 1 mmol) in AcOH(2.5 mL)/TFA (2.5 mL) at 80 ^{o}C was added $Cu(OTf)_2$ (217.1 mg, 1.0 mmol) for 5h. Upon completion, the solvent was evaporated to dryness in vacuo. The residual was separated on a silica gel column with petroleum ether/ethyl acetate 4/1 as the eluent to give product **8aa** (71.6 mg, 61%).

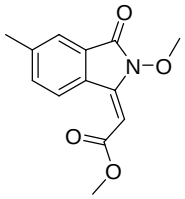
Characterization of Synthesized Compounds



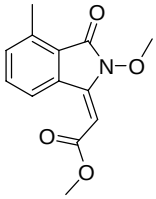
(*E*)-Methyl 2-(2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3aa): white solid. IR (KBr) *v* 1736, 1719, 1641, 1434, 1326, 1188, 1157, 1000, 908, 844, 770, 684 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (1H, d, J = 7.8 Hz), 7.86 (1H, d, J = 7.2 Hz), 7.70 (1H, t, J = 7.8 Hz), 7.61 (1H, t, J = 7.4 Hz), 6.00 (1H, s), 4.04 (3H, s), 3.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 161.7, 143.9, 133.6, 131.6, 130.2, 128.1, 127.4, 123.3, 97.2, 64.3, 51.8; HRMS (EI–TOF): m/z [M^+] calcd for $C_{12}H_{11}NO_4$, 233.0688; found, 233.0685.



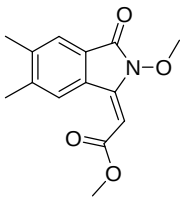
(*E*)-Methyl 2-(2-methoxy-6-methyl-3-oxoisoindolin-1-ylidene)acetate (3ba): white solid. IR (KBr) *v* 1739, 1717, 1645, 1437, 1321, 1157, 1005, 950, 907, 839, 781, 688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (1H, s), 7.74 (1H, d, J = 7.6 Hz), 7.41 (1H, d, J = 7.6 Hz), 5.97 (1H, s), 4.02 (3H, s), 3.84 (3H, s), 2.52 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 162.0, 144.8, 144.4, 132.5, 130.5, 128.8, 124.9, 123.4, 96.9, 64.4, 51.9, 22.5; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{13}NO_4$, 247.0845; found, 247.0844.



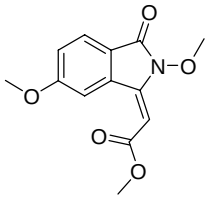
(*E*)-Methyl 2-(2-methoxy-5-methyl-3-oxoisoindolin-1-ylidene)acetate (3ca): white solid. IR (KBr) *v* 1736, 1717, 1639, 1487, 1438, 1394, 1320, 1153, 1135, 1020, 938, 840, 786, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (1H, d, J = 8.0 Hz), 7.66-7.65 (1H, m), 7.50-7.47 (1H, m), 5.95 (1H, s), 4.02 (3H, s), 3.83 (3H, s), 2.48 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 162.0, 144.4, 142.6, 134.4, 128.2, 127.74, 127.67, 123.9, 96.6, 64.5, 51.8, 21.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{13}NO_4$, 247.0845; found, 247.0839.



(*E*)-Methyl 2-(2-methoxy-4-methyl-3-oxoisoindolin-1-ylidene)acetate (3da): white solid. IR (KBr) *v* 1715, 1631, 1429, 1323, 1138, 1007, 879, 845, 803, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (1H, d, J = 8.0 Hz), 7.55 (1H, t, J = 7.8 Hz), 7.35 (1H, d, J = 7.6 Hz), 5.94 (1H, s), 4.02 (3H, s), 3.83 (3H, s), 2.71 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 162.6, 144.1, 138.0, 134.1, 133.2, 130.8, 125.9, 124.3, 96.2, 64.3, 51.8, 17.6; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{13}NO_4$, 247.0845; found, 247.0853.

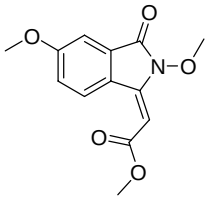


(*E*)-Methyl 2-(2-methoxy-5,6-dimethyl-3-oxoisoindolin-1-ylidene)acetate (3ea): pale yellow solid. IR (KBr) *v* 1728, 1715, 1644, 1471, 1433, 1318, 1155, 998, 906, 846, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (1H, s), 7.60 (1H, s), 5.92 (1H, s), 4.01 (3H, s), 3.83 (3H, s), 2.42 (3H, s), 2.37 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 162.3, 144.7, 143.3, 141.2, 129.2, 128.2, 125.4, 124.4, 96.2, 64.4, 51.8, 20.9, 20.4; HRMS (EI–TOF): m/z [M^+] calcd for $C_{14}H_{15}NO_4$, 261.1001; found, 261.1010.

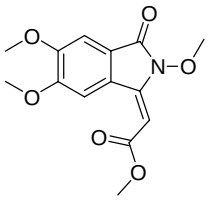


(*E*)-Methyl 2-(2,6-dimethoxy-3-oxoisoindolin-1-ylidene)acetate (3fa): white solid. IR (KBr) *v* 1737, 1720, 1644, 1487, 1322, 1293, 1253, 1147, 1007, 886, 836, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (1H, d, J = 2.4 Hz), 7.75 (1H, d, J = 8.4 Hz), 7.10 (1H, dd, J = 8.4, 2.4 Hz), 5.97 (1H,

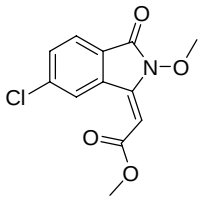
s), 4.02 (3H, s), 3.95 (3H, s), 3.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 164.5, 162.0 144.5, 132.5, 125.0, 119.7, 118.3, 113.1, 97.0, 64.4, 56.0, 51.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{13}NO_5$, 263.0794; found, 263.0796.



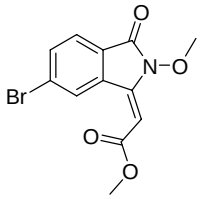
(*E*)-Methyl 2-(2,5-dimethoxy-3-oxoisoindolin-1-ylidene)acetate (3ga): white solid. IR (KBr) ν 1733, 1715, 1639, 1614, 1492, 1436, 1321, 1293, 1264, 1164, 1142, 1014, 868, 839, 791, 706 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H, d, J = 8.4 Hz), 7.34 (1H, d, J = 2.4 Hz), 7.17 (1H, dd, J = 8.8, 2.4 Hz), 5.91 (1H, s), 4.02 (3H, s), 3.91 (3H, s), 3.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 162.6, 161.9, 144.2, 130.1, 129.7, 122.6, 120.1, 107.6, 96.0, 64.5, 56.0, 51.8; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{13}NO_5$, 263.0794; found, 263.0789.



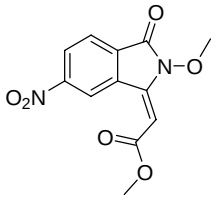
(*E*)-Methyl 2-(2,5,6-trimethoxy-3-oxoisoindolin-1-ylidene)acetate (3ha): white solid. IR (KBr) ν 1741, 1715, 1639, 1606, 1590, 1497, 1475, 1392, 1299, 1222, 1186, 1147, 1139, 1083, 1015, 988, 882, 830, 781 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (1H, s), 7.31 (1H, s), 5.92 (1H, s), 4.04 (3H, s), 4.01 (3H, s), 3.98 (3H, s), 3.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 162.5, 153.4, 152.2, 144.8, 124.2, 120.7, 111.0, 105.4, 96.3, 64.6, 56.6, 56.5, 51.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{14}H_{15}NO_6$, 293.0899; found, 293.0892.



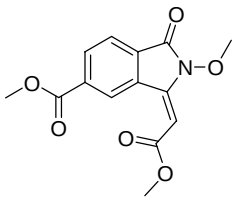
(*E*)-Methyl 2-(6-chloro-2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3ia): white solid. IR (KBr) ν 1723, 1648, 1440, 1324, 1196, 1165, 1147, 1003, 949, 908, 853, 841, 780, 685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (1H, d, J = 2.0 Hz), 7.78 (1H, d, J = 8.0 Hz), 7.59 (1H, dd, J = 8.0, 2.0 Hz), 6.03 (1H, s), 4.03 (3H, s), 3.85 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 160.9, 143.0, 140.3, 132.0, 131.7, 128.7, 125.8, 124.6, 98.4, 64.6, 52.1; HRMS (EI–TOF): m/z [M^+] calcd for $C_{12}H_{10}{}^{35}ClNO_4$, 267.0298; found, 267.0303.



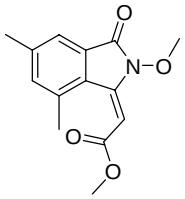
(*E*)-Methyl 2-(6-bromo-2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3ja): white solid. IR (KBr) *v* 1741, 1718, 1649, 1438, 1327, 1198, 1169, 1144, 1006, 948, 911, 851, 839, 780, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.24 (1H, d, J = 1.6 Hz), 7.77 (1H, dd, J = 8.0, 1.6 Hz), 7.71 (1H, d, J = 8.0 Hz), 6.02 (1H, s), 4.04 (3H, s), 3.85 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 161.0, 142.9, 134.9, 131.7, 131.5, 128.6, 126.3, 124.7, 98.4, 64.6, 52.1; HRMS (EI–TOF): m/z [M^+] calcd for $C_{12}H_{10}{}^{79}BrNO_4$, 310.9793; found, 310.9785.



(*E*)-Methyl 2-(2-methoxy-6-nitro-3-oxoisoindolin-1-ylidene)acetate (3ka): brown yellow solid. IR (KBr) *v* 1750, 1707, 1640, 1531, 1440, 1341, 1318, 1193, 1157, 1108, 1006, 955, 869, 825, 735, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.95 (1H, d, J = 2.0 Hz), 8.49 (1H, dd, J = 8.4, 2.0 Hz), 8.03 (1H, d, J = 8.4 Hz), 6.14 (1H, s), 4.08 (3H, s), 3.90 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 159.6, 151.6, 142.0, 132.4, 131.2, 126.8, 124.4, 124.0, 100.1, 64.8, 52.4; HRMS (EI–TOF): m/z [M^+] calcd for $C_{12}H_{10}N_2O_6$, 278.0539; found, 278.0537.

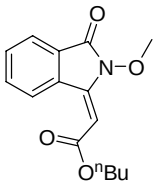


(*E*)-Methyl 2-methoxy-3-(2-methoxy-2-oxoethylidene)-1-oxoisoindoline-5-carboxylate (3la): white solid. IR (KBr) *v* 2957, 1750, 1732, 1646, 1439, 1325, 1294, 1260, 1191, 1169, 1143, 1007, 971, 907, 838, 758, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.64 (1H, d, J = 0.4 Hz), 8.31 (1H, dd, J = 7.8, 1.4 Hz), 7.93 (1H, dd, J = 7.8, 0.6 Hz), 4.06 (3H, s), 4.00 (3H, s), 3.88 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 166.1, 160.8, 143.1, 135.1, 133.0, 131.1, 130.4, 129.4, 123.5, 98.6, 64.6, 52.9, 52.1; HRMS (ESI): *m/z* [M^++H] calcd for $C_{14}H_{14}NO_6$, 292.0816; found, 292.0817.

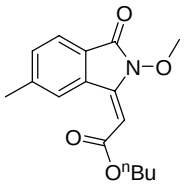


(*E*)-Methyl 2-(2-methoxy-5, 7-dimethyl-3-oxoisoindolin-1-ylidene)acetate (3ma): pale yellow solid. IR (KBr) *v* 2953, 1732, 1716, 1659, 1434, 1367, 1306, 1277, 1206, 1182, 1151, 1120, 1054, 997, 867, 813, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (1H, s), 7.22 (1H, s), 5.89 (1H, s), 4.06

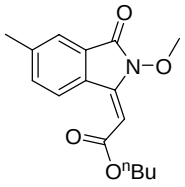
(3H, s), 3.82 (3H, s), 2.51 (3H, s), 2.42 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.4, 141.3, 139.6, 137.2, 134.1, 127.8, 127.6, 122.3, 98.2, 64.8, 52.1, 21.5, 20.7; HRMS (ESI): *m/z* [M^++H] calcd for $C_{14}H_{16}NO_4$, 262.1074; found, 262.1074.



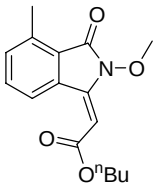
(*E*)-Butyl 2-(2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3ab): white solid. IR (KBr) *v* 2961, 1732, 1712，1644, 1471, 1404, 1320, 1163, 999, 903, 853, 782, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (1H, d, *J* = 8.0 Hz), 7.85 (1H, dd, *J* = 7.2, 0.8 Hz), 7.69 (1H, td, *J* = 7.6, 1.2 Hz), 7.60 (1H, td, *J* = 7.6, 0.8 Hz), 6.00 (1H, s), 4.24 (2H, t, *J* = 6.8 Hz), 4.05 (3H, s), 1.76-1.68 (2H, m), 1.49-1.41 (2H, m), 0.98 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 161.9, 144.0, 133.8, 131.7, 130.5, 128.4, 127.7, 123.5, 98.0, 64.8, 64.6, 31.0, 19.4, 14.0; HRMS (EI–TOF): m/z [M^+] calcd for $C_{15}H_{17}NO_4$, 275.1158; found, 275.1157.



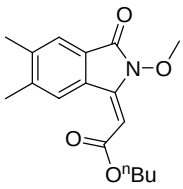
(*E*)-Butyl 2-(2-methoxy-6-methyl-3-oxoisoindolin-1-ylidene)acetate (3bb): pale yellow solid. IR (KBr) *v* 2963, 1740, 1717, 1639, 1462, 1436, 1319, 1158, 1125, 995, 908, 837, 781, 688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (1H, s), 7.73 (1H, d, *J* = 7.6 Hz), 7.40 (1H, d, *J* = 7.6 Hz), 5.96 (1H, s), 4.24 (2H, t, *J* = 6.8 Hz), 4.03 (3H, s), 2.51 (3H, s), 1.74-1.68 (2H, m), 1.49-1.41 (2H, m), 0.98 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 161.8, 144.6, 144.0, 132.2, 130.5, 128.7, 124.8, 123.2, 97.4, 64.6, 64.3, 30.8, 22.4, 19.2, 13.7; HRMS (EI–TOF): m/z [M^+] calcd for $C_{16}H_{19}NO_4$, 289.1314; found, 289.1308.



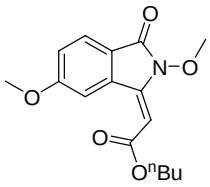
(*E*)-Butyl 2-(2-methoxy-5-methyl-3-oxoisoindolin-1-ylidene)acetate (3cb): white solid. IR (KBr) *v* 2959, 1738, 1719, 1640, 1483, 1318, 1158, 1125, 1020, 839, 802, 711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (1H, d, *J* = 8.0 Hz), 7.65 (1H, t, *J* = 0.8 Hz), 7.47 (1H, dd, *J* = 8.0, 0.8 Hz), 5.94 (1H, s), 4.23 (2H, t, *J* = 6.8 Hz), 4.03 (3H, s), 2.47 (3H, s), 1.75-1.67 (2H, m), 1.50-1.40 (2H, m), 0.98 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 161.9, 144.0, 142.4, 134.2, 128.1, 127.61, 127.58, 123.7, 97.0, 64.5, 64.3, 30.8, 21.7, 19.2, 13.7; HRMS (EI–TOF): m/z [M^+] calcd for $C_{16}H_{19}NO_4$, 289.1314; found, 289.1322.



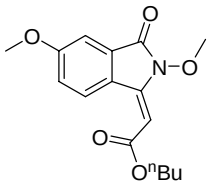
(*E*)-Butyl 2-(2-methoxy-4-methyl-3-oxoisoindolin-1-ylidene)acetate (3db): pale yellow solid. IR (KBr) *v* 2961, 1739, 1708, 1638, 1441, 1329, 1316, 1151, 1011, 879, 844, 804, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (1H, d, J = 7.6 Hz), 7.53 (1H, t, J = 7.6 Hz), 7.34 (1H, d, J = 7.6 Hz), 5.94 (1H, s), 4.23 (2H, t, J = 6.6 Hz), 4.03 (3H, s), 2.70 (3H, s), 1.75-1.67 (2H, m), 1.50-1.41 (2H, m), 0.97 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 162.6, 143.8, 137.9, 134.0, 133.1, 130.8, 125.9, 124.3, 96.8, 64.6, 64.3, 30.9, 19.3, 17.6, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{16}H_{19}NO_4$, 289.1314; found, 289.1305.



(*E*)-Butyl 2-(2-methoxy-5, 6-dimethyl-3-oxoisoindolin-1-ylidene)acetate (3eb): pale yellow solid. IR (KBr) *v* 2961, 1731, 1708, 1635, 1471, 1314, 1157, 1145, 850, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (1H, s), 7.60 (1H, s), 5.92 (1H, s), 4.23 (2H, t, J = 6.8 Hz), 4.01 (3H, s), 2.41 (3H, s), 2.37 (3H, s), 1.75-1.67 (2H, m), 1.50-1.41 (2H, m), 0.98 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 162.2, 144.4, 143.2, 141.1, 129.2, 128.2, 125.3, 124.3, 96.8, 64.6, 64.4, 30.9, 20.9, 20.4, 19.3, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{17}H_{21}NO_4$, 303.1471; found, 303.1466.

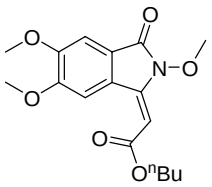


(*E*)-Butyl 2-(2, 6-dimethoxy-3-oxoisoindolin-1-ylidene)acetate (3fb): white solid. IR (KBr) *v* 2958, 1720, 1710, 1642, 1588, 1486, 1439, 1319, 1292, 1243, 1136, 1018, 899, 838, 710, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (1H, d, J = 2.4 Hz), 7.75 (1H, d, J = 8.4 Hz), 7.09 (1H, dd, J = 8.4, 2.4 Hz), 5.96 (1H, s), 4.23 (2H, t, J = 6.8 Hz), 4.02 (3H, s), 3.94 (3H, s), 1.75-1.67 (2H, m), 1.50-1.41 (2H, m), 0.98 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.5, 162.0, 144.2, 132.6, 125.0, 119.7, 118.2, 113.2, 97.6, 64.7, 64.5, 56.0, 30.9, 19.4, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{16}H_{19}NO_5$, 305.1263; found, 305.1262.

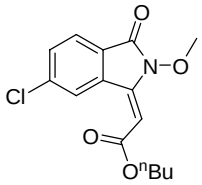


(*E*)-Butyl 2-(2, 5-dimethoxy-3-oxoisoindolin-1-ylidene)acetate (3gb): white solid. IR (KBr) *v*

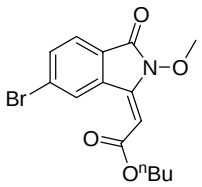
2956, 1735, 1710, 1636, 1615, 1492, 1318, 1294, 1258, 1168, 1137, 1013, 945, 849, 801, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H, d, J = 8.8 Hz), 7.34 (1H, d, J = 2.6 Hz), 7.16 (1H, dd, J = 8.8, 2.6 Hz), 5.91 (1H, s), 4.23 (2H, t, J = 6.6 Hz), 4.03 (3H, s), 3.90 (3H, s), 1.73-1.67 (2H, m), 1.49-1.42 (2H, m), 0.98 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 162.4, 161.8, 143.9, 130.0, 129.6, 122.6, 120.0, 107.4, 96.4, 64.5, 64.4, 55.8, 30.8, 19.2, 13.7; HRMS (EI–TOF): m/z [M^+] calcd for $C_{16}H_{19}NO_5$, 305.1263; found, 305.1255.



(*E*)-Butyl 2-(2, 5, 6-trimethoxy-3-oxoisoindolin-1-ylidene)acetate (3hb): white solid. IR (KBr) ν 2954, 1735, 1710, 1637, 1605, 1500, 1471, 1300, 1222, 1141, 1005, 888, 843, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (1H, s), 7.30 (1H, s), 5.92 (1H, s), 4.22 (2H, t, J = 6.8 Hz), 4.04 (3H, s), 4.02 (3H, s), 3.97 (3H, s), 1.75-1.67 (2H, m), 1.50-1.41 (2H, m), 0.98 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 162.5, 153.4, 152.1, 144.5, 124.2, 120.7, 111.0, 105.3, 96.9, 64.64, 64.58, 56.6, 56.5, 30.9, 19.3, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{17}H_{21}NO_6$, 335.1369; found, 335.1368.

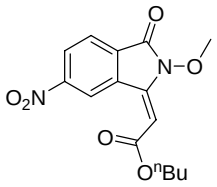


(*E*)-Butyl 2-(6-chloro-2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3ib): pale yellow solid. IR (KBr) ν 2965, 1734, 1714, 1642, 1428, 1319, 1167, 1148, 909, 844, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.08 (1H, d, J = 1.6 Hz), 7.78 (1H, d, J = 8.0 Hz), 7.58 (1H, dd, J = 8.0, 1.6 Hz), 6.02 (1H, s), 4.25 (2H, t, J = 6.8 Hz), 4.04 (3H, s), 1.76-1.68 (2H, m), 1.51-1.41 (2H, m), 0.98 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 160.9, 142.8, 140.2, 131.9, 131.7, 128.7, 125.8, 124.5, 99.0, 65.0, 64.6, 30.9, 19.3, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{15}H_{16}{}^{35}ClNO_4$, 309.0768; found, 309.0761.

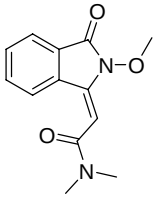


(*E*)-Butyl 2-(6-bromo-2-methoxy-3-oxoisoindolin-1-ylidene)acetate (3jb): white solid. IR (KBr) ν 2965, 1741, 1716, 1644, 1422, 1321, 1162, 1014, 993, 969, 849, 839, 780, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.24 (1H, d, J = 1.6 Hz), 7.76 (1H, dd, J = 8.0, 1.6 Hz), 7.71 (1H, d, J = 8.0 Hz), 6.02 (1H, s), 4.26 (2H, t, J = 6.6 Hz), 4.04 (3H, s), 1.76-1.69 (2H, m), 1.51-1.41 (2H, m), 0.98 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.0, 142.6, 134.8, 131.8, 131.5, 128.6, 126.3, 124.7, 99.1, 65.0, 64.6, 30.9, 19.3, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for

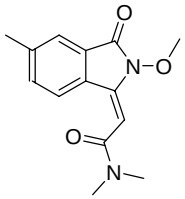
$C_{15}H_{16}{}^{79}BrNO_4$, 353.0263; found, 353.0257.



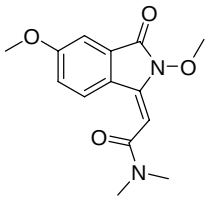
(*E*)-Butyl 2-(2-methoxy-6-nitro-3-oxoisoindolin-1-ylidene)acetate (3kb): brown yellow solid. IR (KBr) *v* 2962, 1742, 1708, 1651, 1537, 1342, 1323, 1177, 1107, 1014, 988, 936, 855, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.95 (1H, d, J = 2.0 Hz), 8.48 (1H, dd, J = 8.2, 2.0 Hz), 8.03 (1H, d, J = 8.2 Hz), 6.14 (1H, s), 4.30 (2H, t, J = 6.6 Hz), 4.09 (3H, s), 1.78-1.71 (2H, m), 1.52-1.42 (2H, m), 0.99 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 159.6, 151.5, 141.7, 132.4, 131.3, 126.7, 124.4, 124.1, 100.7, 65.4, 64.9, 30.8, 19.3, 13.9; HRMS (EI–TOF): m/z [M^+] calcd for $C_{15}H_{16}N_2O_6$, 320.1008; found, 320.1002.



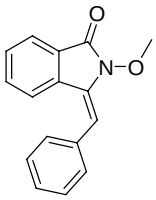
(*E*)-2-(2-Methoxy-3-oxoisoindolin-1-ylidene)-*N*,*N*-dimethylacetamide (3ac): pale yellow solid. IR (KBr) *v* 2944, 1743, 1657, 1633, 1469, 1407, 1371, 1125, 997, 912, 834, 767, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (1H, d, J = 7.6 Hz), 7.82 (1H, d, J = 7.6 Hz), 7.60 (1H, td, J = 7.6, 1.6 Hz), 7.53 (1H, td, J = 7.6, 1.2 Hz), 6.17 (1H, s), 4.04 (3H, s), 3.15 (3H, s), 3.12 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.5, 138.9, 133.2, 130.8, 130.6, 127.6, 126.3, 123.2, 99.7, 64.4, 38.4, 35.5; HRMS (EI–TOF): m/z [M^+] calcd for $C_{13}H_{14}N_2O_3$, 246.1004; found, 246.1000.



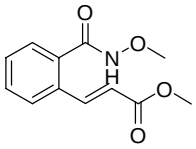
(*E*)-2-(2-Methoxy-5-methyl-3-oxoisoindolin-1-ylidene)-*N*,*N*-dimethylacetamide (3cc): pale yellow solid. IR (KBr) 2928, 1727, 1648, 1626, 1490, 1369, 1140, 1015, 832, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (1H, d, J = 8.0 Hz), 7.62 (1H, s), 7.39 (1H, d, J = 8.0 Hz), 6.12 (1H, s), 4.02 (3H, s), 3.13 (3H, s), 2.44 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 161.8, 141.6, 139.3, 134.0, 128.0, 127.7, 126.3, 123.6, 98.8, 64.4, 38.4, 35.5, 21.8; HRMS (EI–TOF): m/z [M^+] calcd for $C_{14}H_{16}N_2O_3$, 260.1161; found, 260.1168.



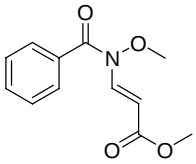
(*E*)-2-(2, 5-Dimethoxy-3-oxoisoindolin-1-ylidene)-*N*,*N*-dimethylacetamide (3dc): pale yellow solid. IR (KBr) *v* 2934, 1726, 1647, 1610, 1518, 1484, 1388, 1293, 1243, 1030, 1179, 834, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (1H, d, J = 8.8 Hz), 7.31 (1H, d, J = 2.6 Hz), 7.11 (1H, dd, J = 8.8, 2.6 Hz), 6.11 (1H, s), 4.03 (3H, s), 3.88 (3H, s), 3.16 (3H, s), 3.11 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 161.9, 161.6, 139.3, 129.4, 128.3, 122.9, 120.1, 106.8, 98.0, 64.3, 55.8, 38.3, 35.4; HRMS (ESI): *m/z* [M^++H] calcd for $C_{14}H_{17}N_2O_4$, 277.1183; found, 277.1183.



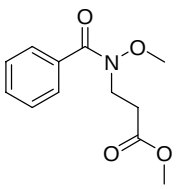
(*E*)-3-Benzylidene-2-methoxyisoindolin-1-one (3ad): pale yellow solid. IR (KBr) *v* 1714, 1651, 1472, 1388, 1229, 1185, 1130, 1000, 909, 839, 775, 764, 720, 696, 680, 606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (1H, d, J = 7.6 Hz), 7.51-7.35 (8H, m), 6.77 (1H, s), 4.11 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 134.5, 132.1, 131.9, 131.4, 129.6, 129.5 (2C), 128.8 (2C), 128.1, 128.0, 123.4, 123.0, 110.1, 64.3; HRMS (ESI): *m/z* [M^++H] calcd for $C_{16}H_{14}NO_2$, 252.1019; found, 252.1022.



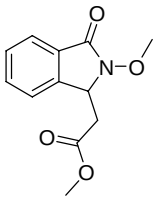
(*E*)-Methyl 3-(2-(methoxycarbamoyl)phenyl)acrylate (5aa): white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (1H, s), 7.98 (1H, d, J = 16.0 Hz), 7.63 (1H, d, J = 7.6 Hz), 7.50-7.46 (2H, m), 7.40 (1H, t, J = 7.6 Hz), 6.39 (1H, J = 16.0 Hz), 3.91 (3H, s), 3.78 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.5, 141.6, 133.4, 131.0, 129.8, 128.1, 127.2, 120.6, 64.6, 51.9; HRMS (ESI): *m/z* [M^++H] calcd for $C_{12}H_{14}NO_4$, 236.0917; found, 236.0915.



(*E*)-Methyl 3-(*N*-methoxybenzamido)acrylate (6aa): white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (1H, d, J = 14 Hz), 7.76 (1H, d, J = 7.2 Hz), 7.57 (1H, tt, J = 7.4, 1.6 Hz), 7.47 (1H, tt, J = 7.4, 1.2 Hz), 5.68 (1H, d, J = 14 Hz), 3.76 (3H, s), 3.66 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 166.7, 137.0, 132.4, 131.9, 129.2 (2C), 128.6 (2C), 99.3, 62.6, 51.7; HRMS (ESI): *m/z* [M^++H] calcd for $C_{12}H_{14}NO_4$, 236.0917; found, 236.0908.



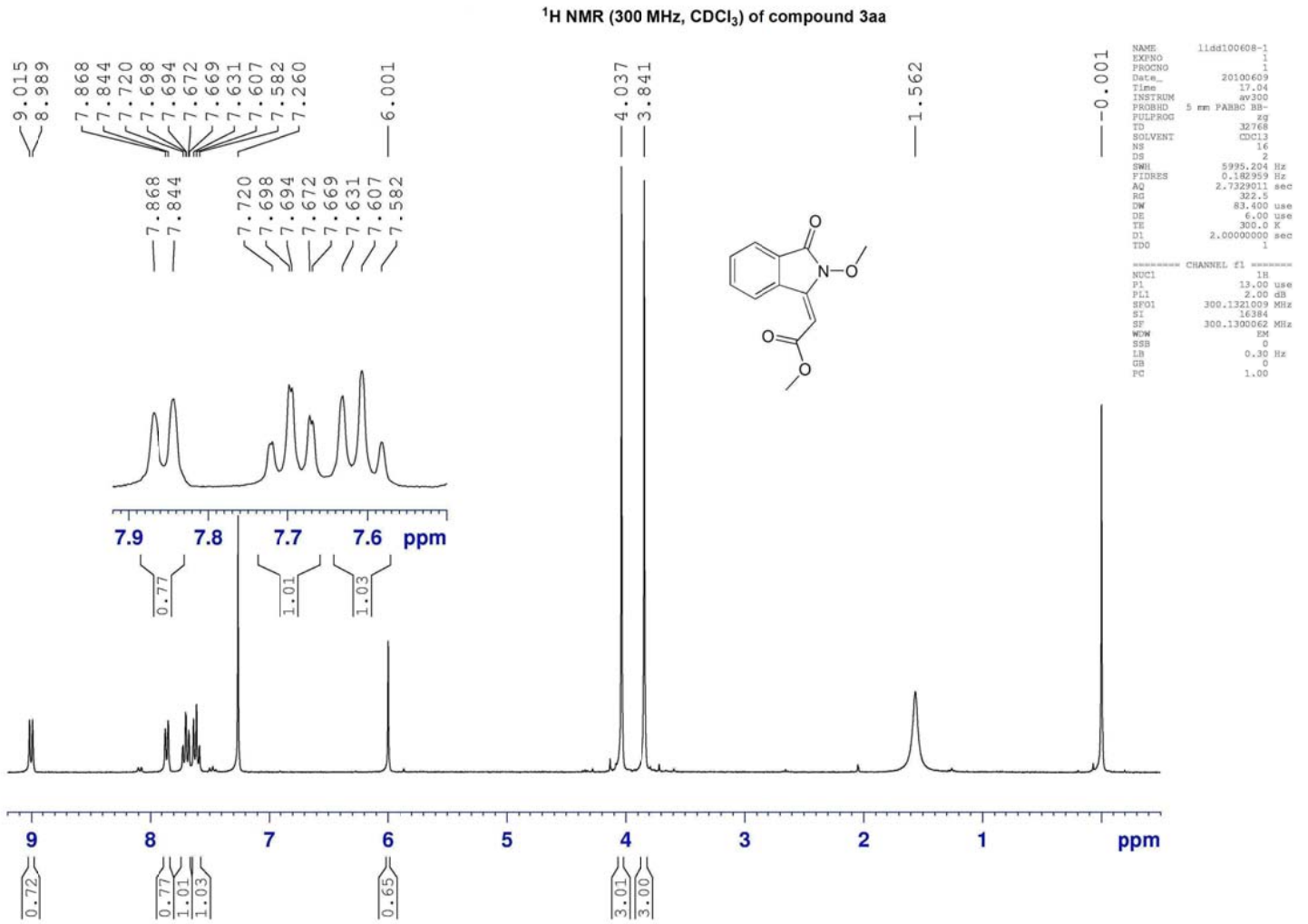
Methyl 3-(*N*-methoxybenzamido)propanoate (7aa): colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (2H, m), 7.47-7.43 (1H, m), 7.41-7.37 (2H, m), 4.04 (1H, t, J = 6.9 Hz), 3.69 (3H, s), 3.53 (3H, s), 2.72 (1H, t, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 170.2, 134.1, 130.7, 128.1 (2C), 128.0 (2C), 61.6, 51.8, 42.3, 32.0.



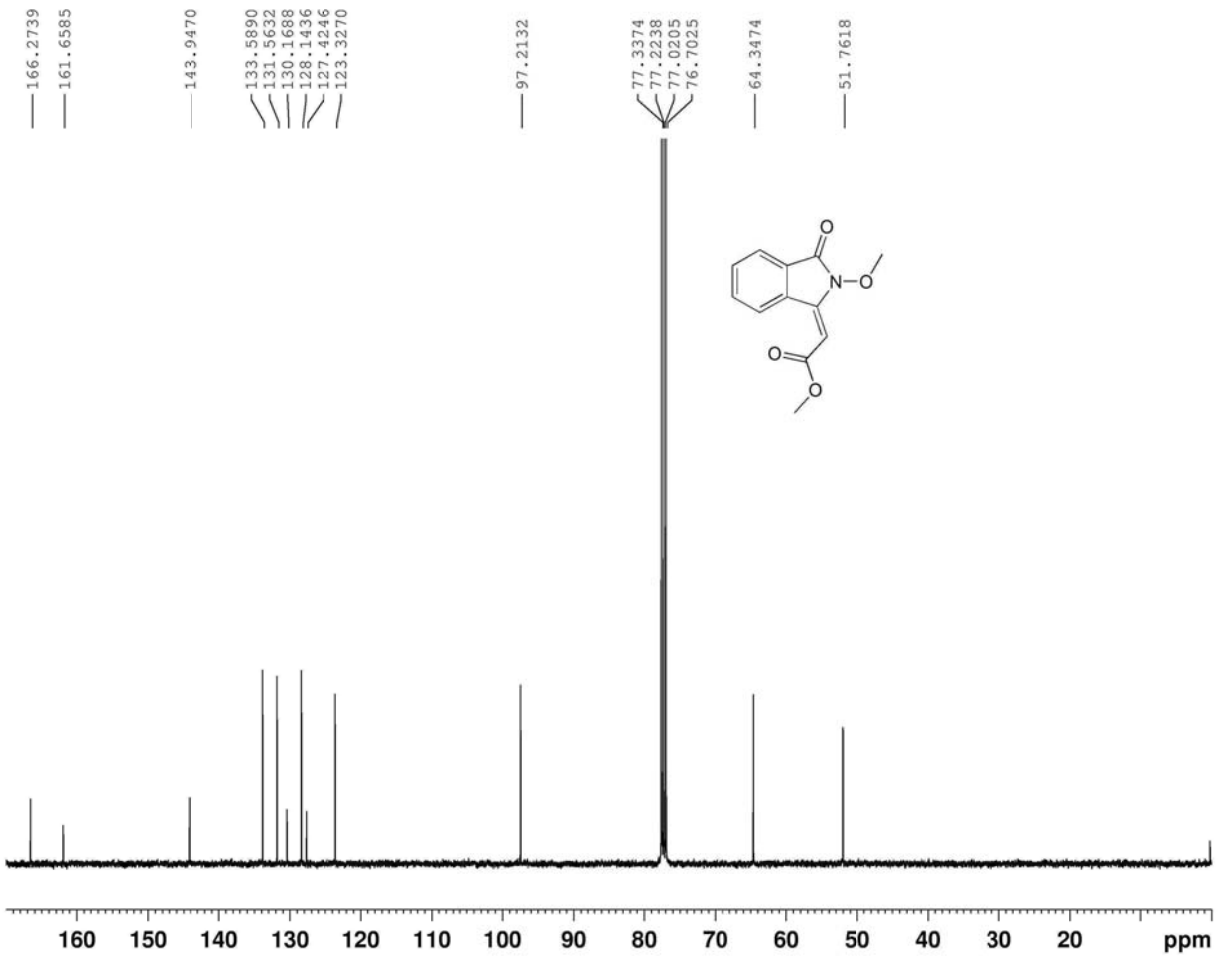
Methyl 2-(2-methoxy-3-oxoisoindolin-1-yl)acetate (8aa): yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (1H, d, J = 7.5 Hz), 7.58 (1H, t, J = 7.5 Hz), 7.51 (1H, d, J = 7.5 Hz), 7.44 (1H, t , J = 7.5 Hz), 5.21 (1H, t, J = 6.5 Hz), 3.94 (3H, s), 3.76 (3H, s), 2.95 (1H, dd, J = 16.2, 6.6 Hz), 2.72 (1H, dd , J = 16.2, 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.5, 141.5, 132.4, 129.6, 128.9, 123.9, 122.6, 63.8, 56.1, 52.0, 36.9.

References

(1) Fisher, L. E.; Caroon, J. M.; Jahangir, Stabler, S. R.; Lundberg, S.; Muchowski, J. M. *J. Org. Chem.* 1993, **58**, 3643.
(2) Sengupta, S.; Bhattacharya, S. *Journal of the Chemical Society, Perkin Transactions 1:* 1993, **17**,1943
(3) Ragaini, F.; Longo, T.; Cenini, S. *J. Mol. Catal. A: Chem.* 1996, **110**, L171.



^{13}C NMR (400 MHz, $CDCl_3$) of compound 3aa



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FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
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PL1	3.00 dB
PL1W	41.92221451 W
SFO1	100.6479773 MHz
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NUC2	1H
PCPD2	90.00 usec
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PL12	15.94 dB
PL13	17.00 dB
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PL12W	0.35825154 W
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SFO2	400.2316009 MHz
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SSB	0
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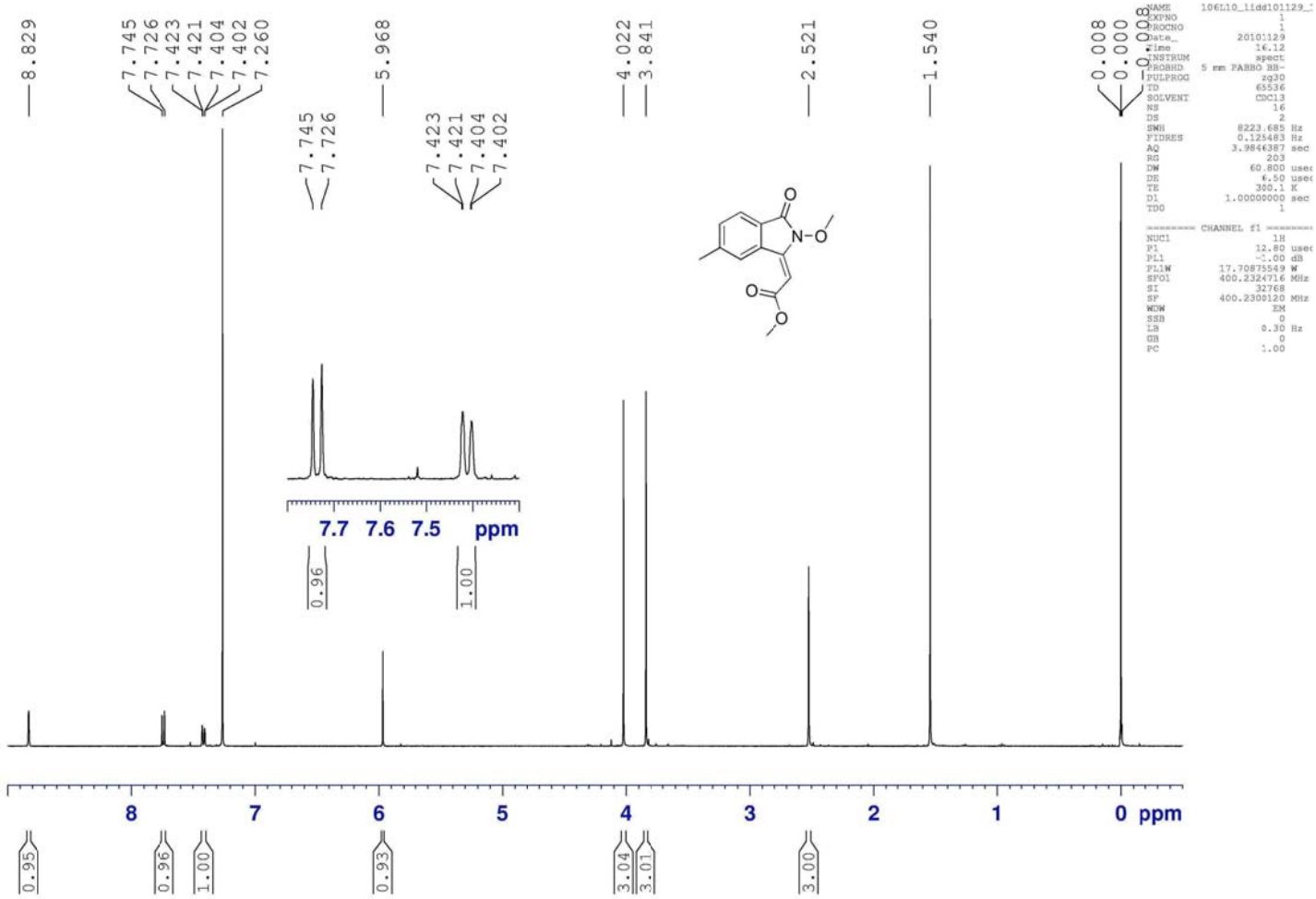
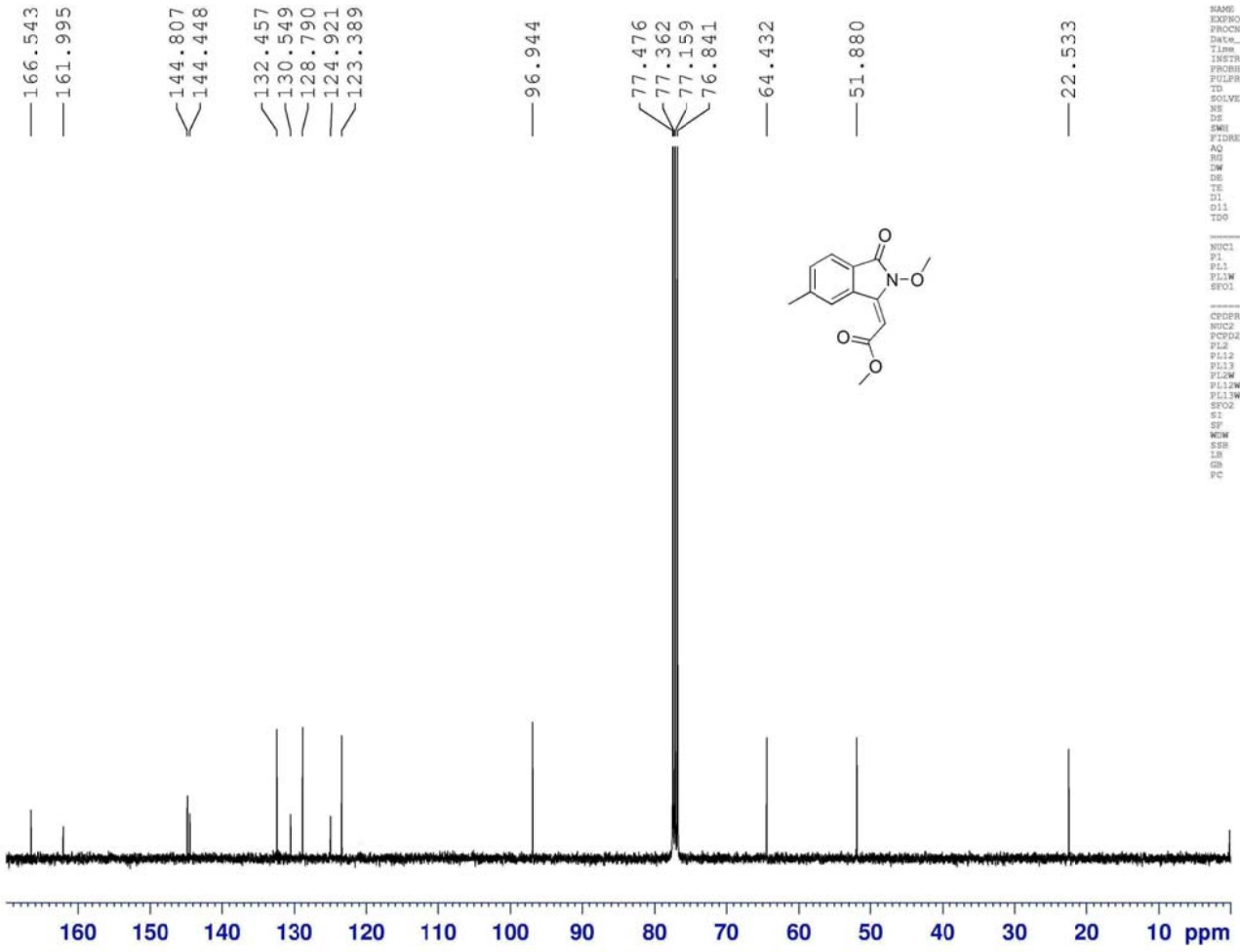
GB	0
PC	1.40

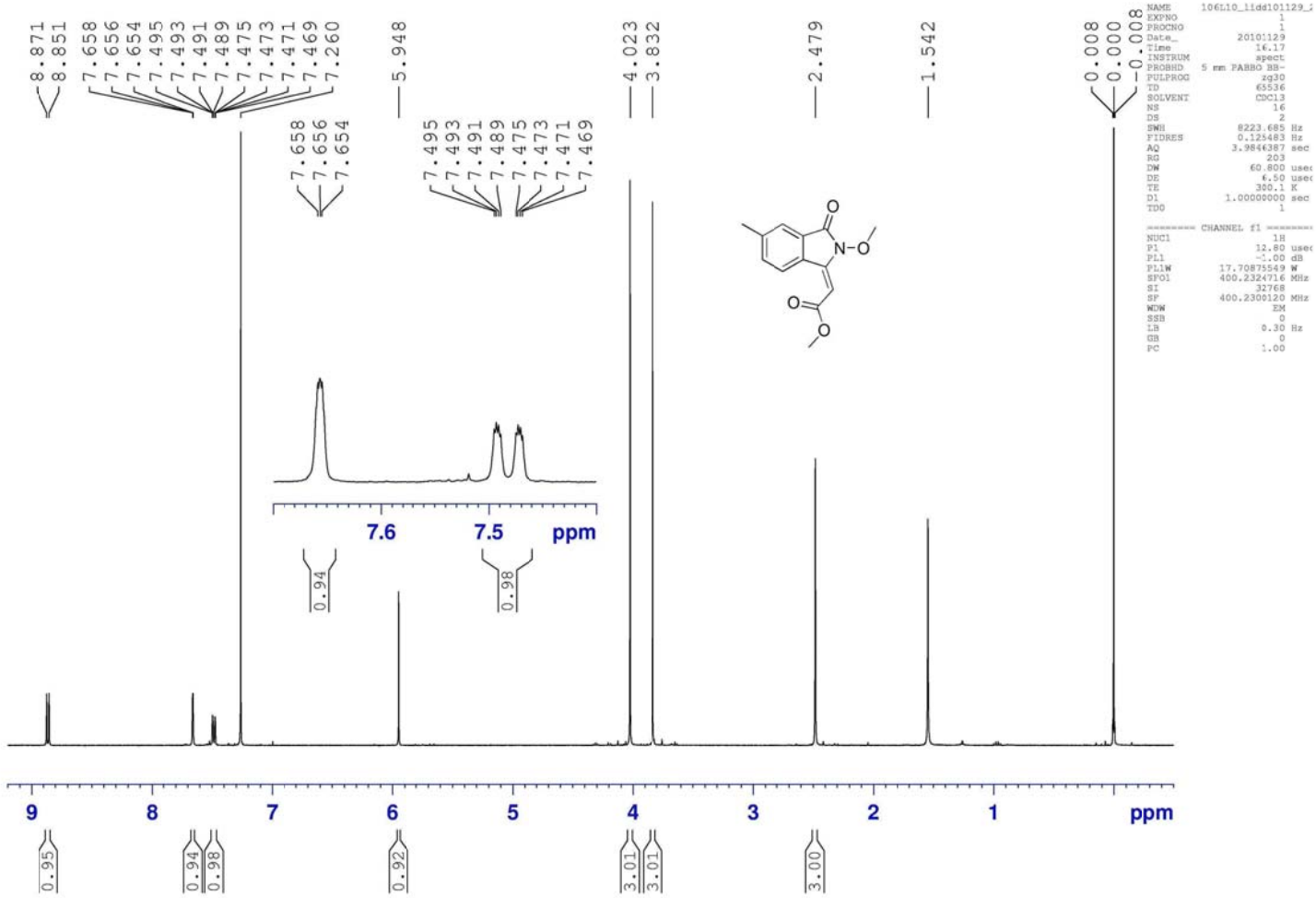
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3ba



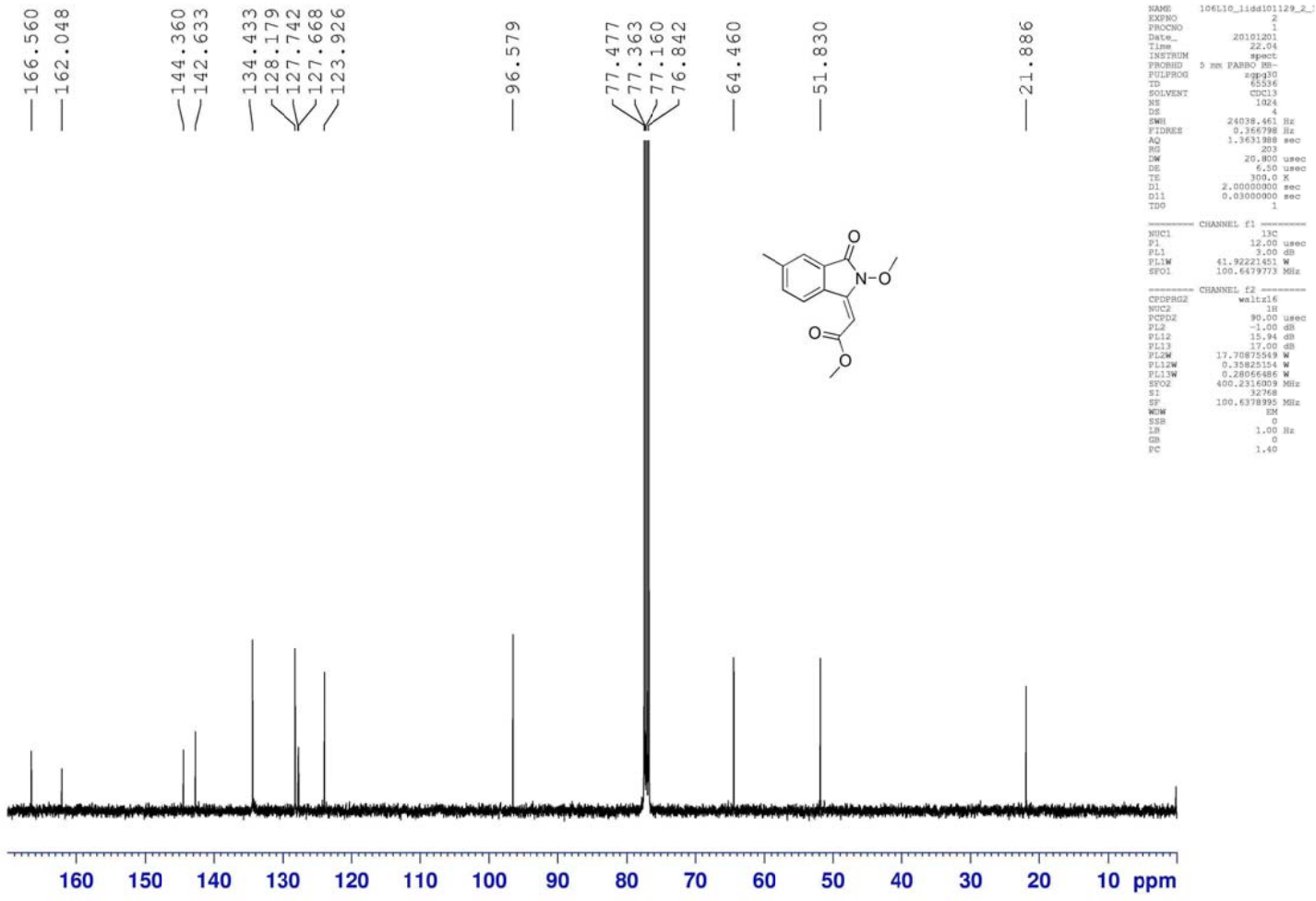
^{13}C NMR (400 MHz, $CDCl_3$) of compound 3ba

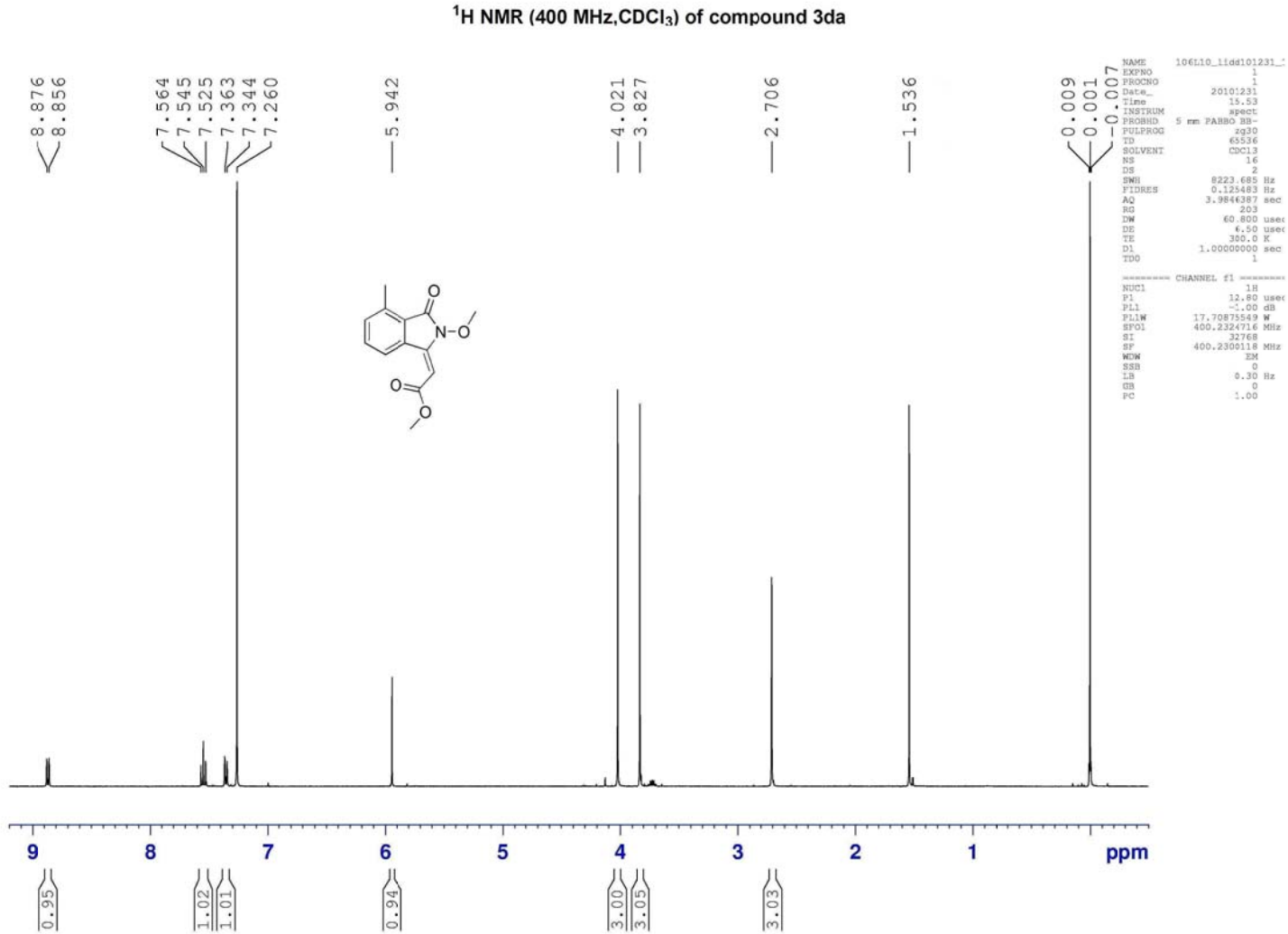


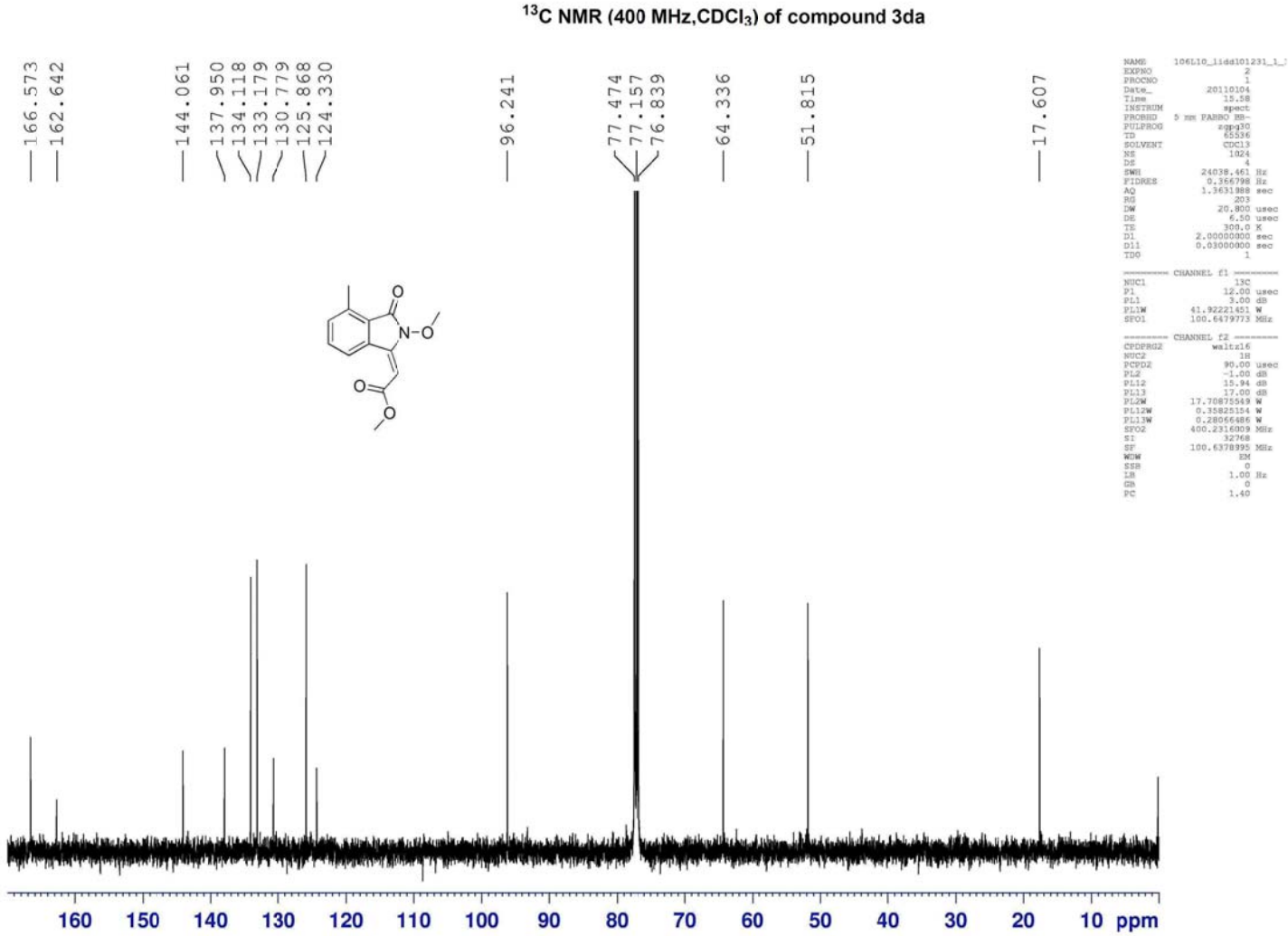
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ca

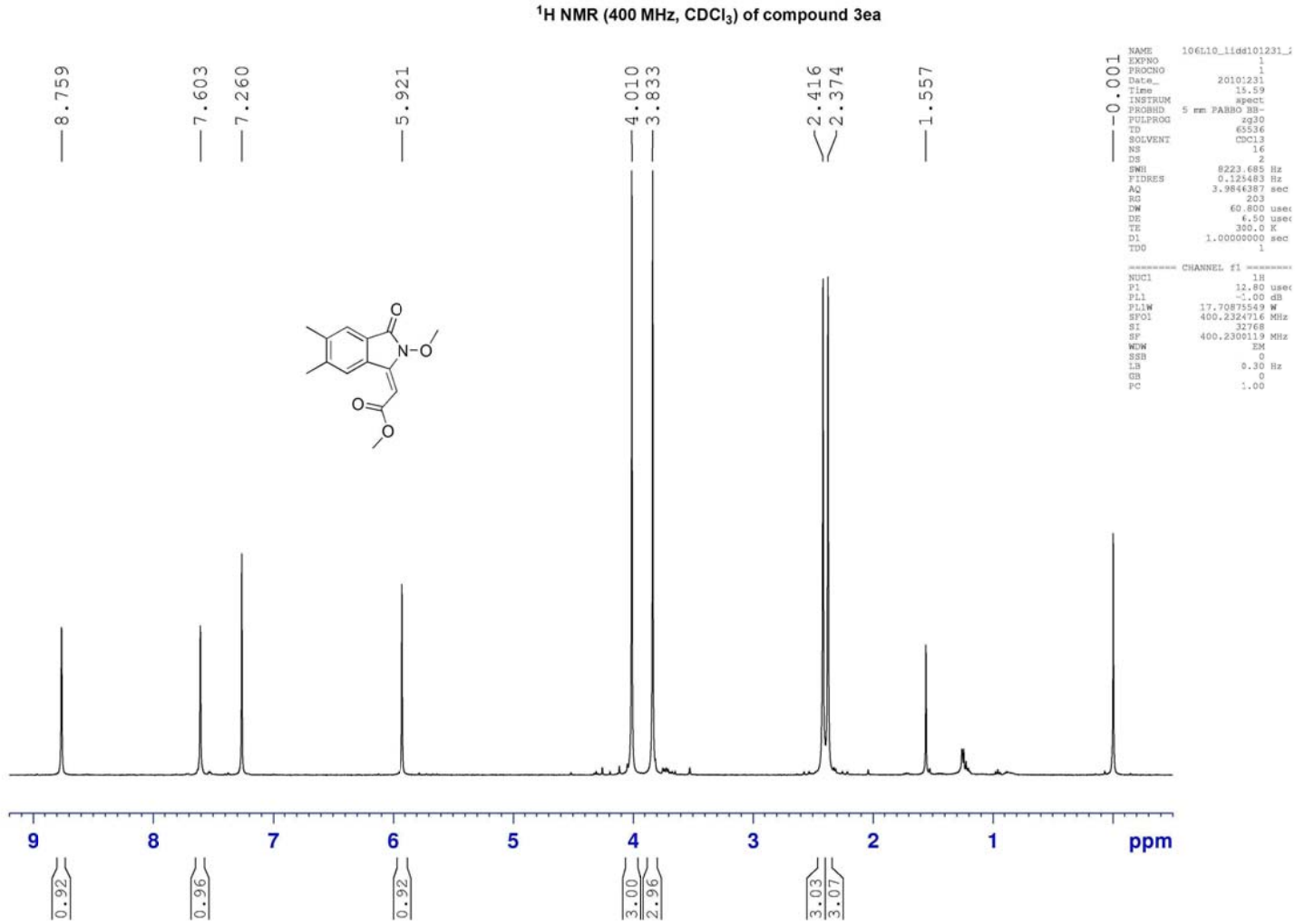


^{13}C NMR (400 MHz, $CDCl_3$) of compound 3ca

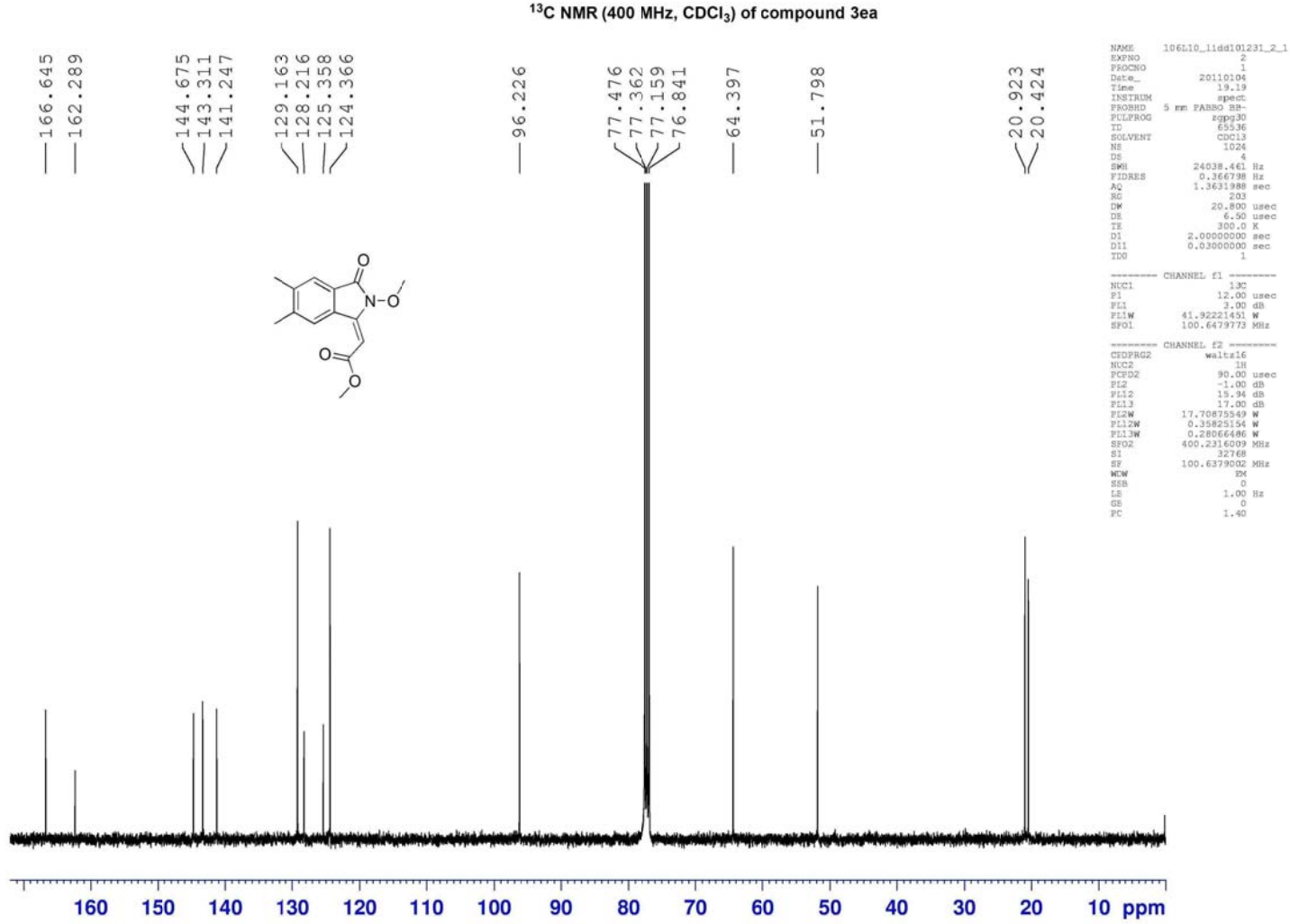


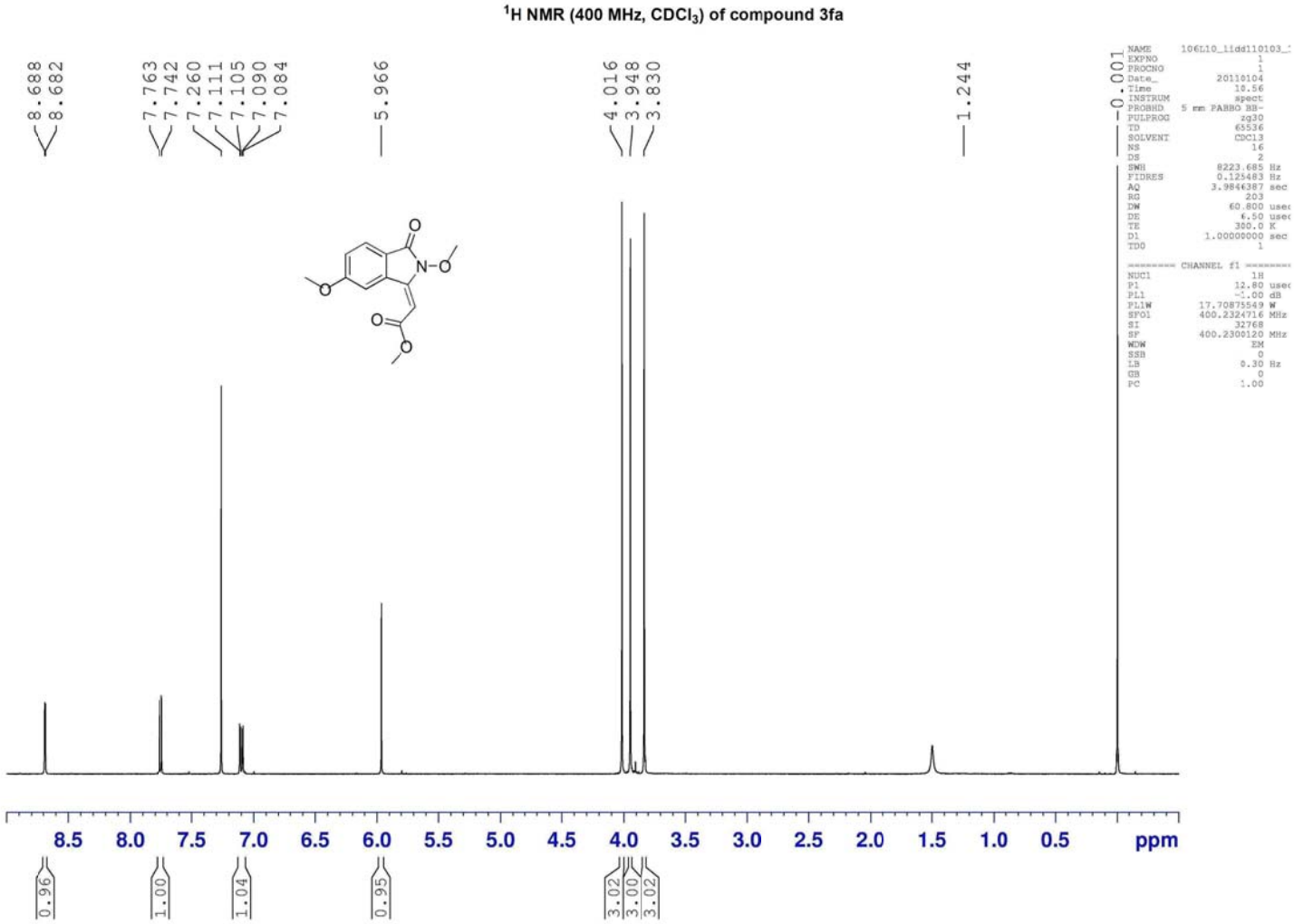


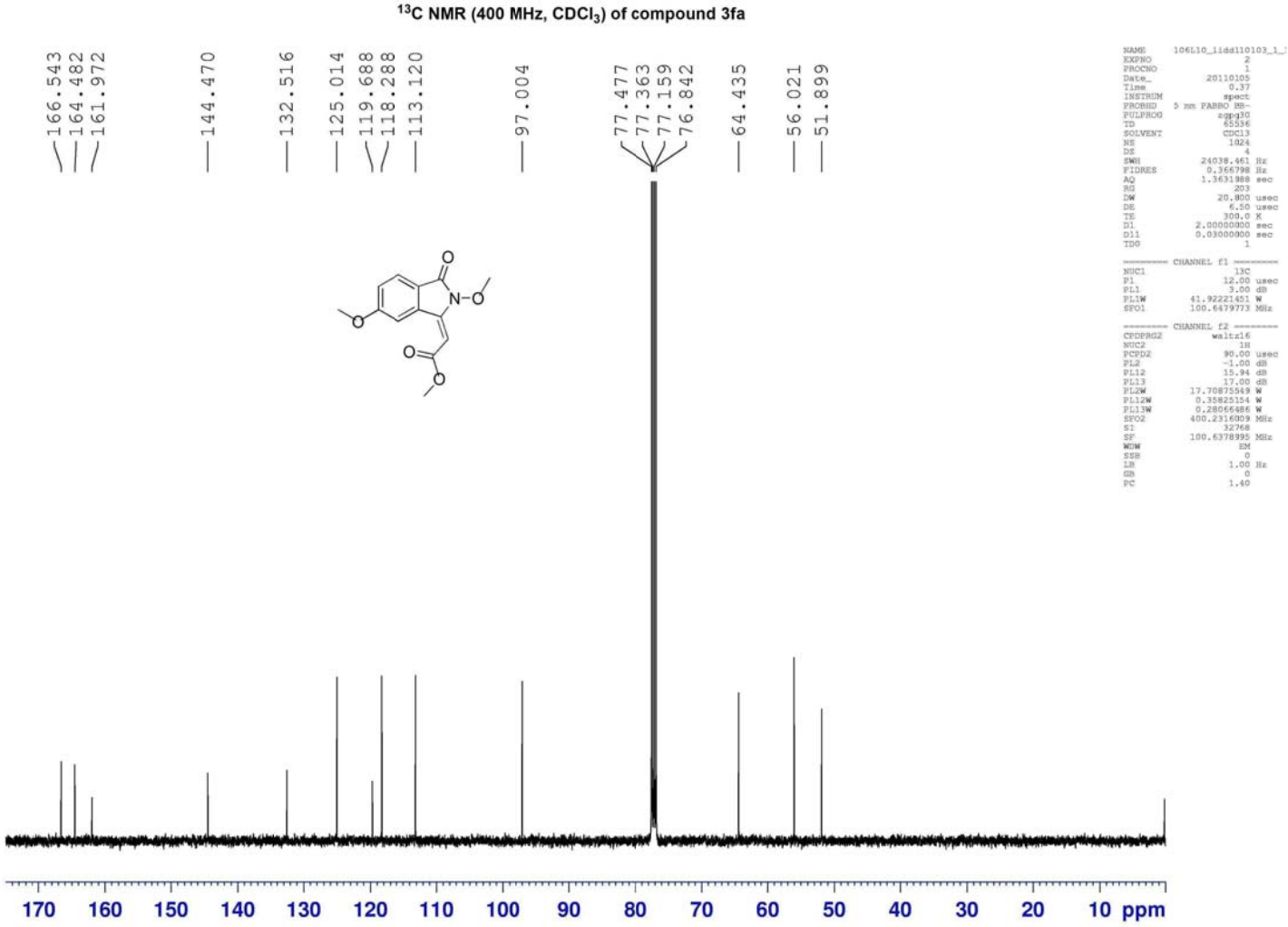




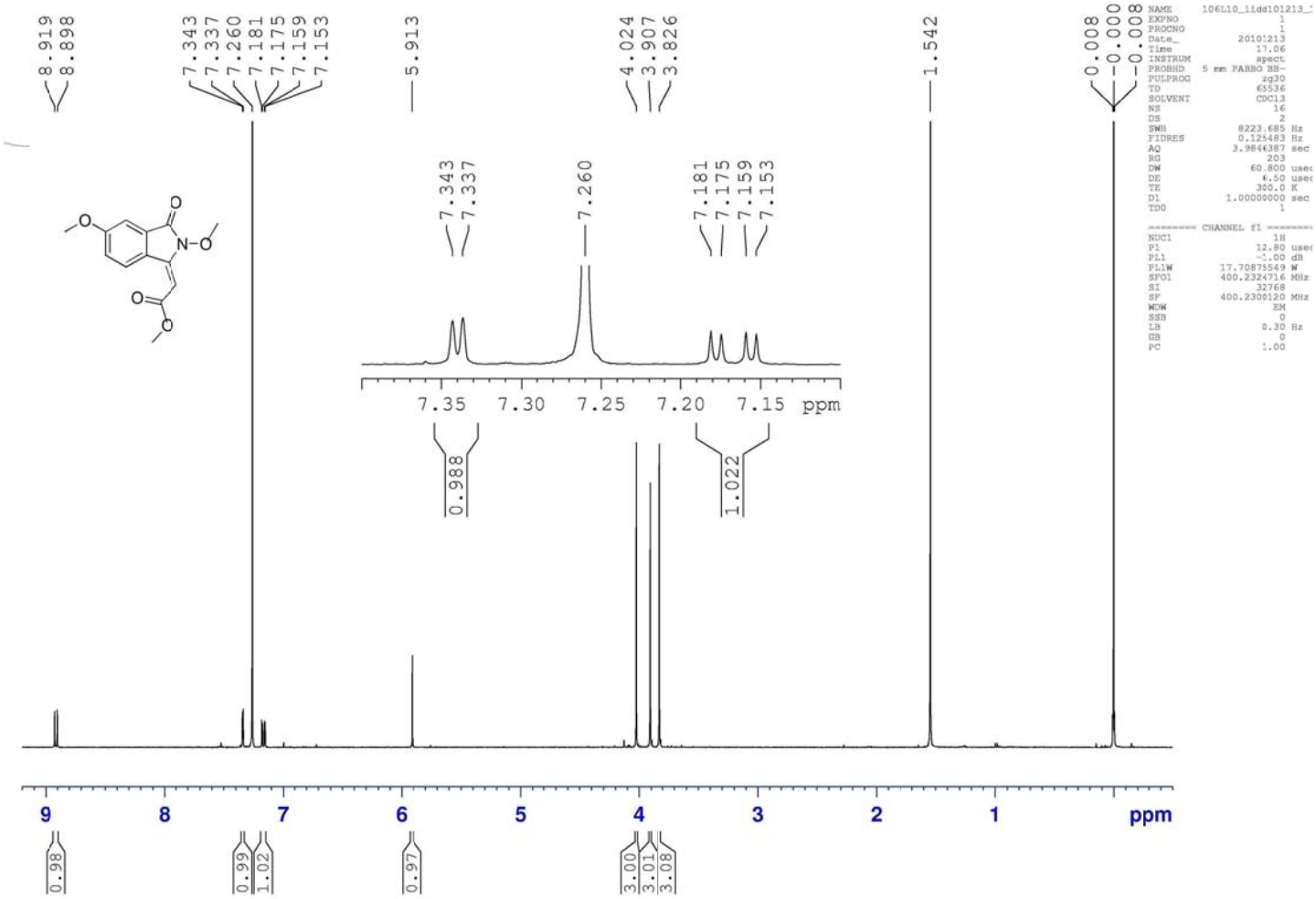
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ea

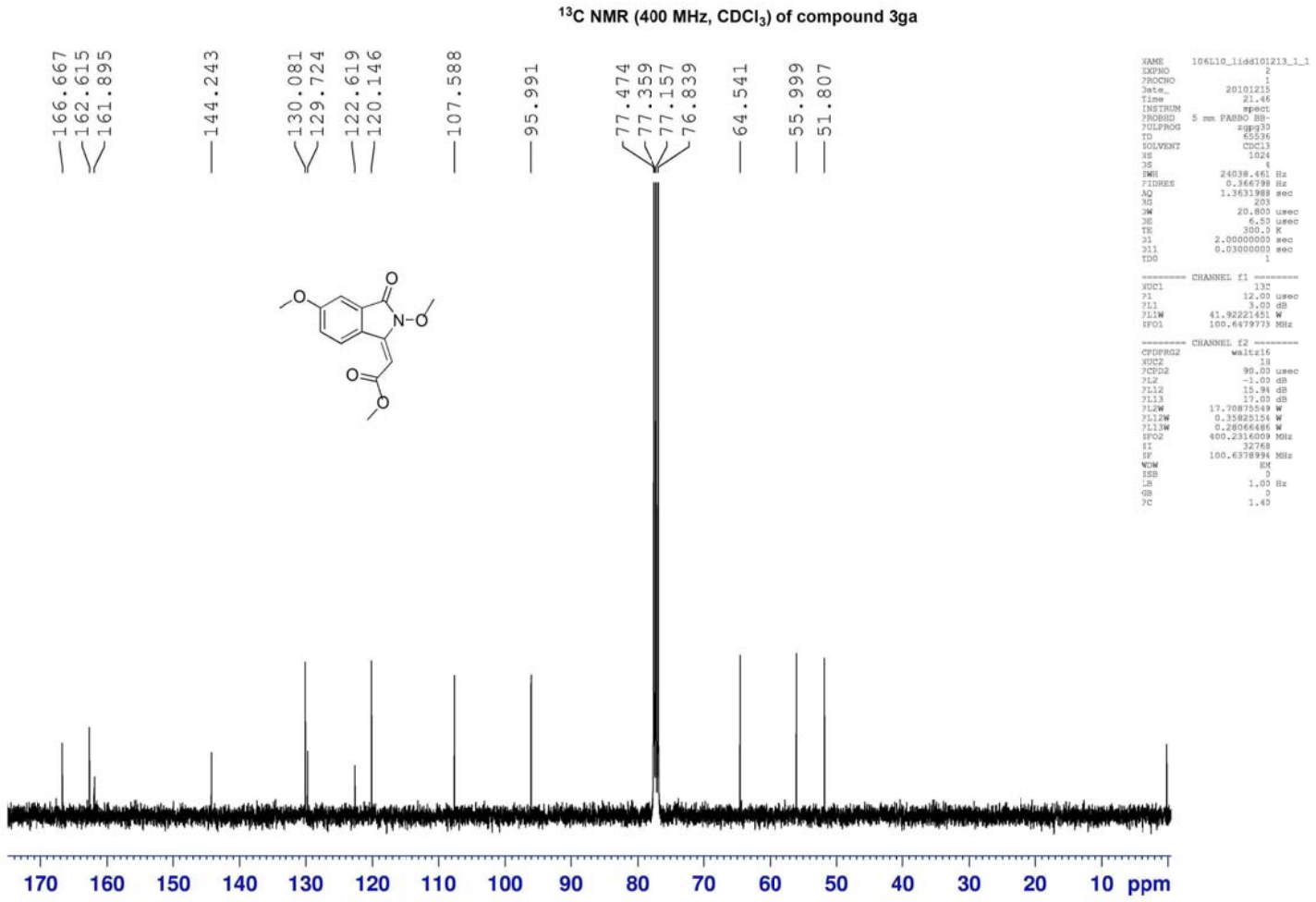


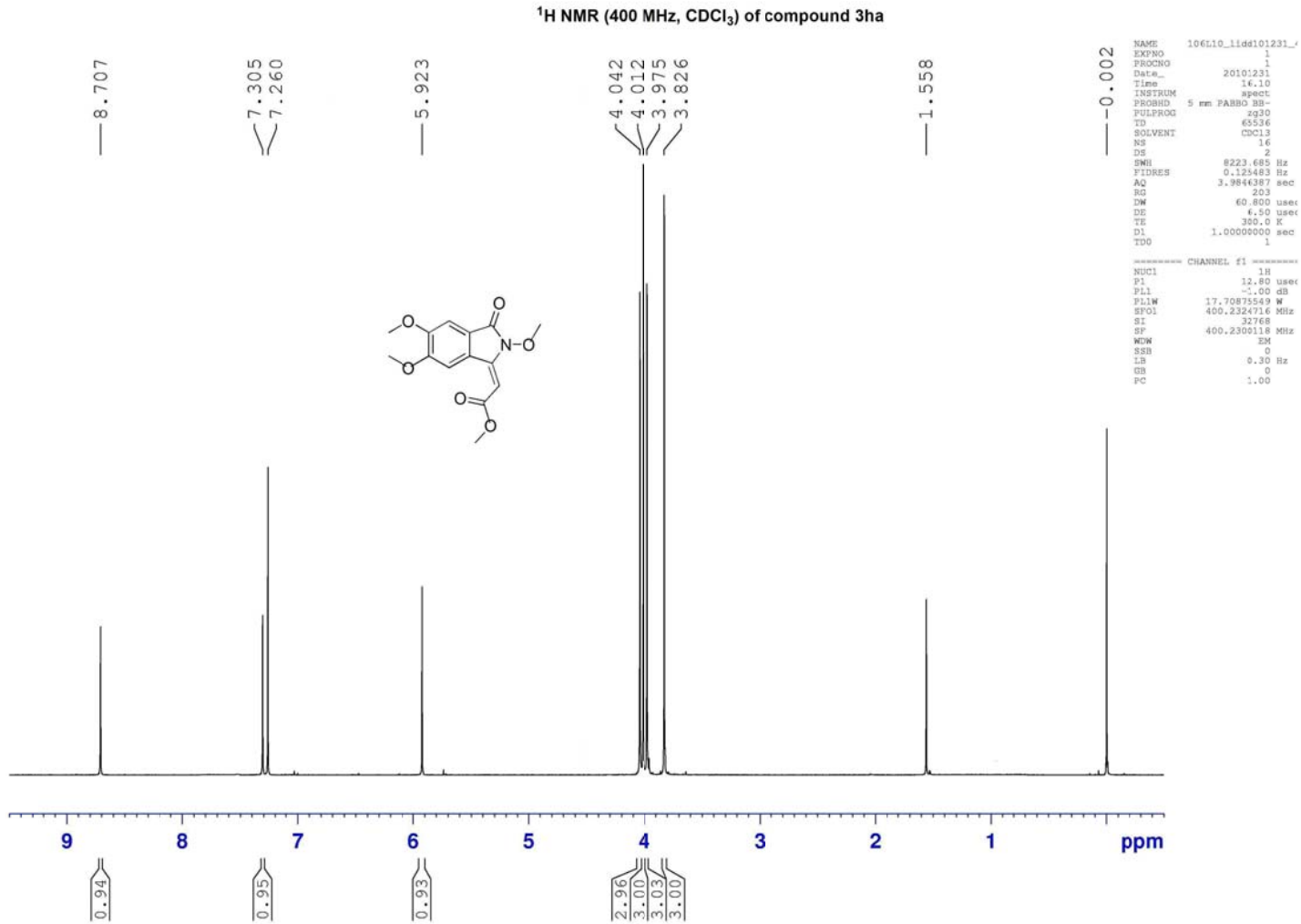




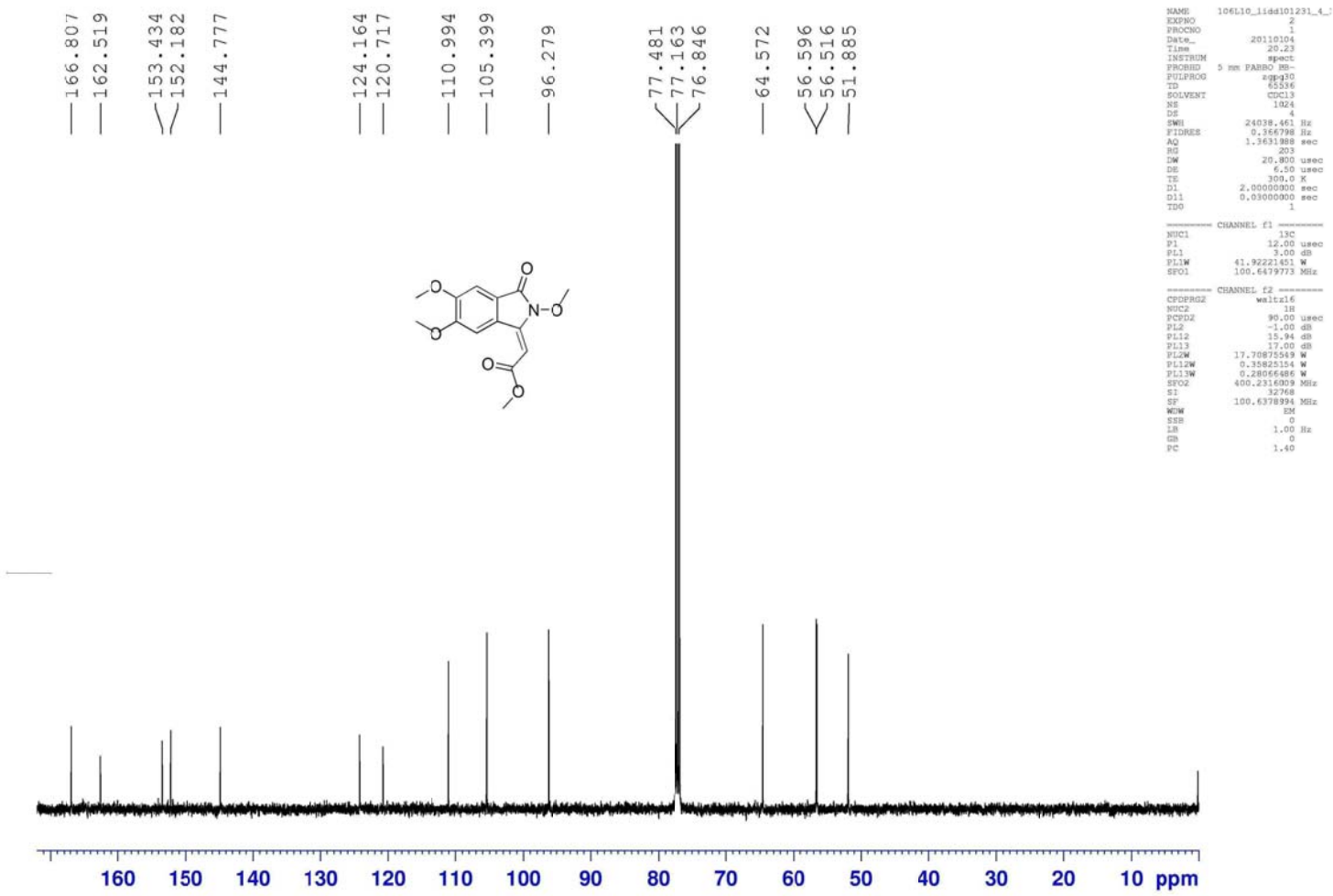
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ga

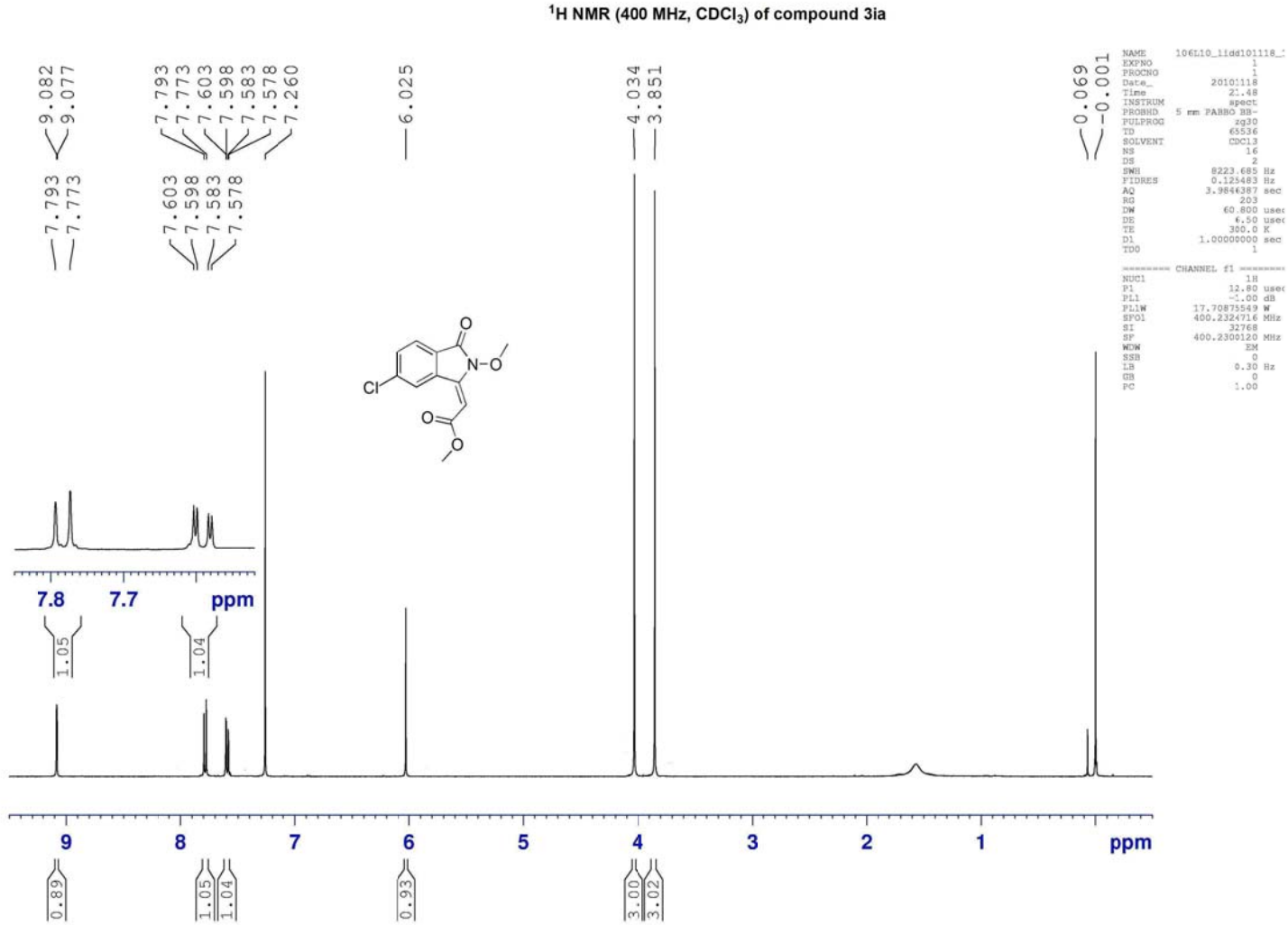






^{13}C NMR (400 MHz, $CDCl_3$) of compound 3ha




^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ia
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7.793
7.773
7.603
7.598
7.583
7.578
7.260
6.025
4.034
3.851
0.069
-0.001
Cl
N-O
O
O
O
7.8
7.7
ppm
1.05
1.04
9
8
7
6
5
4
3
2
1
ppm
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1.05
1.04
0.93
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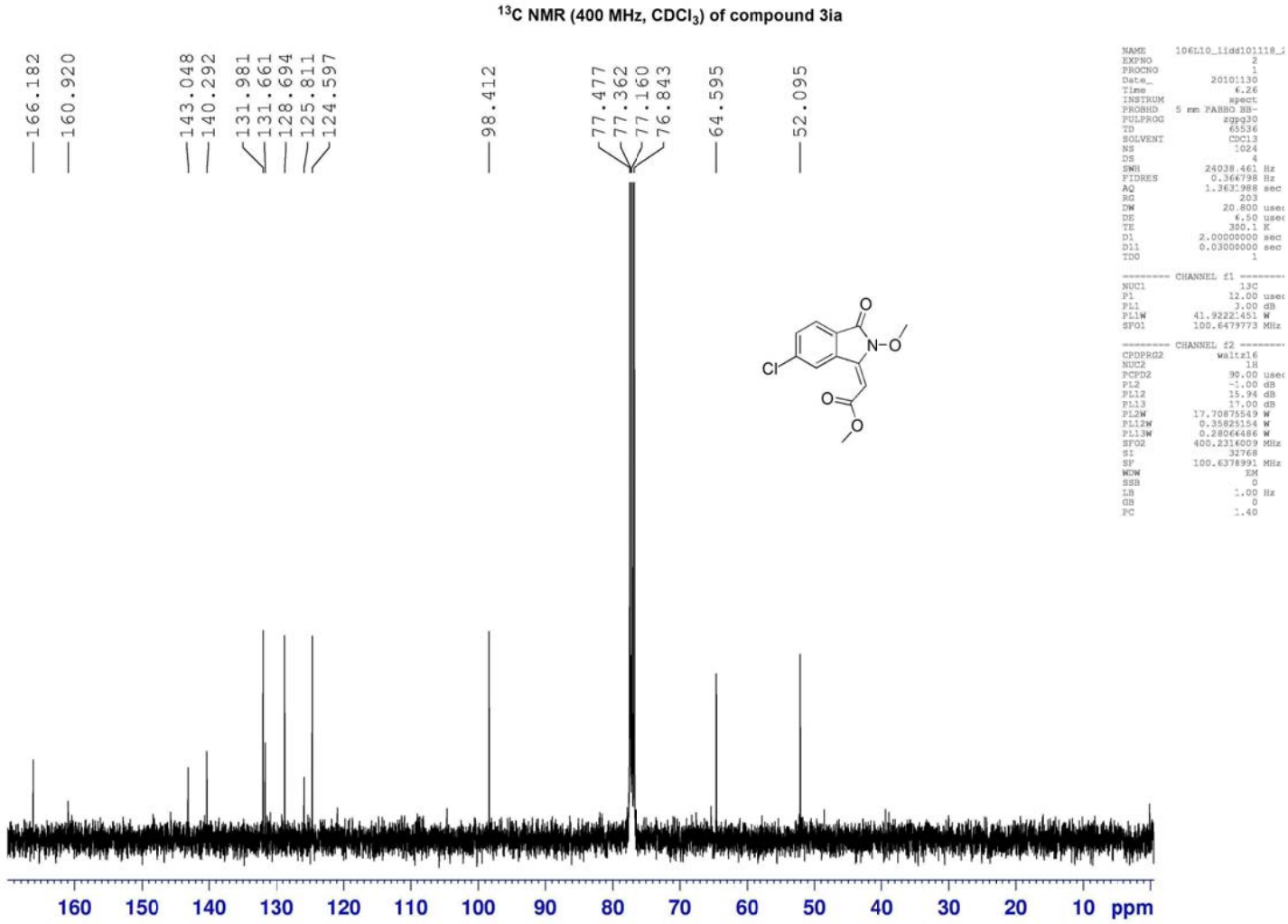
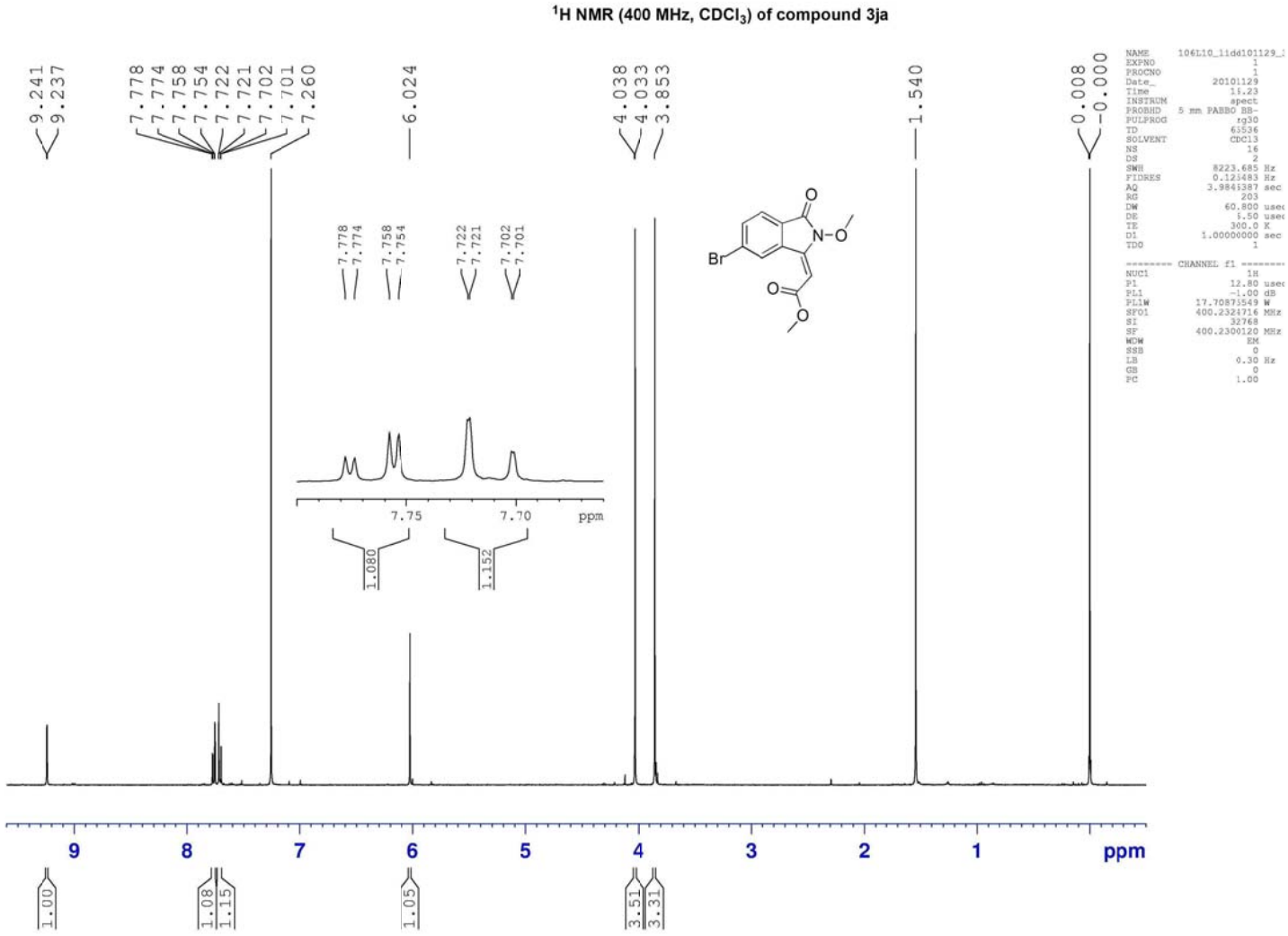
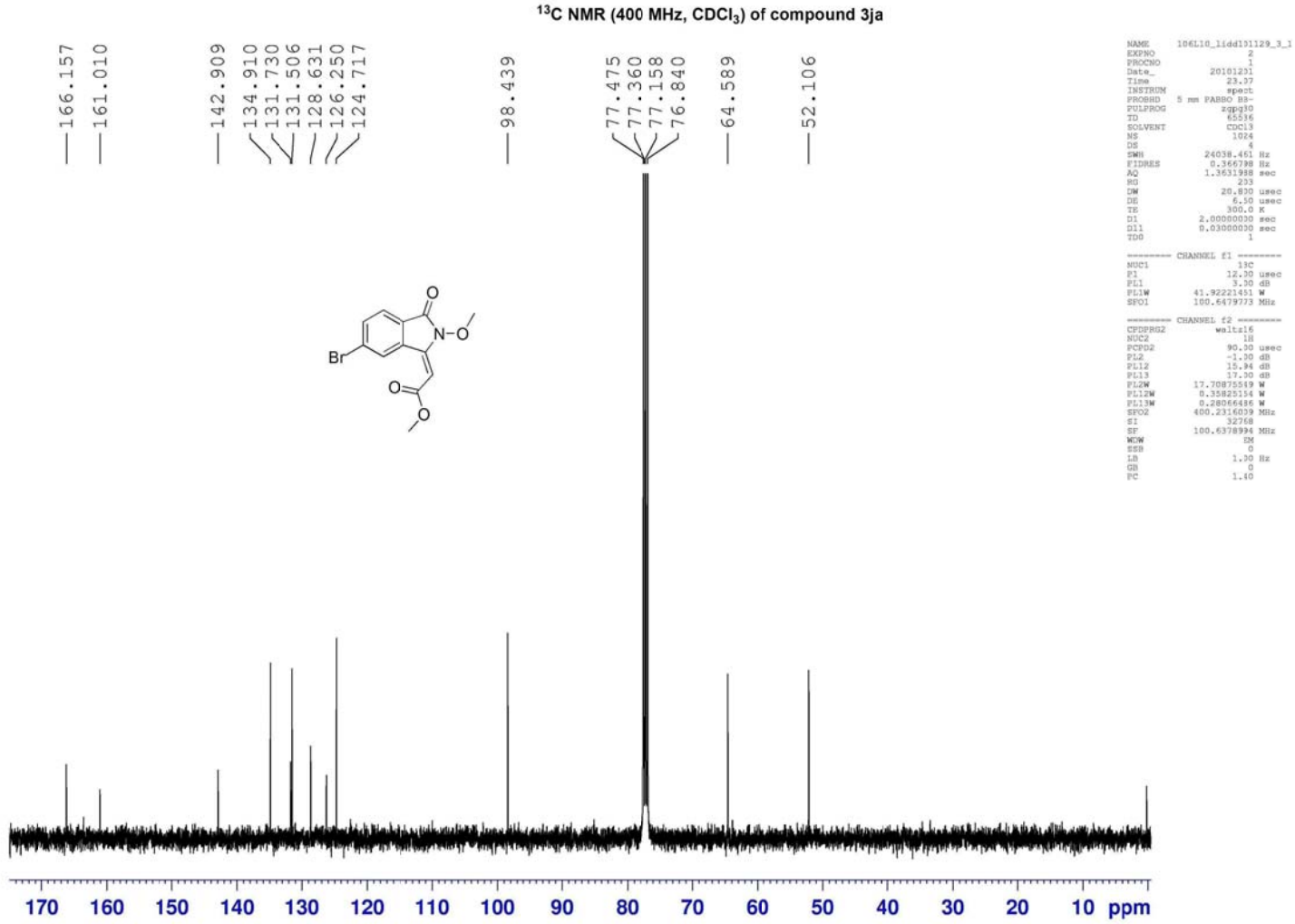
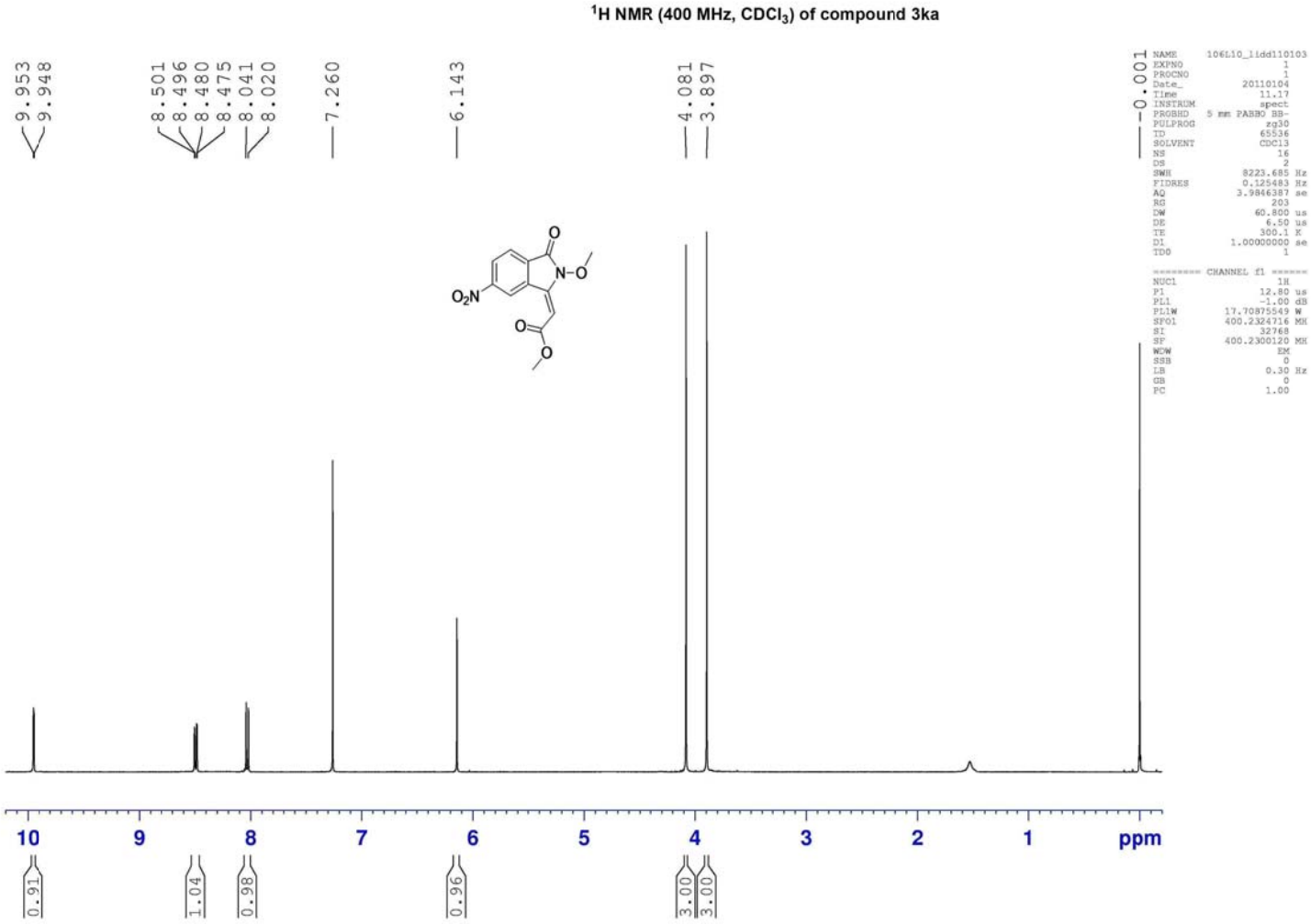
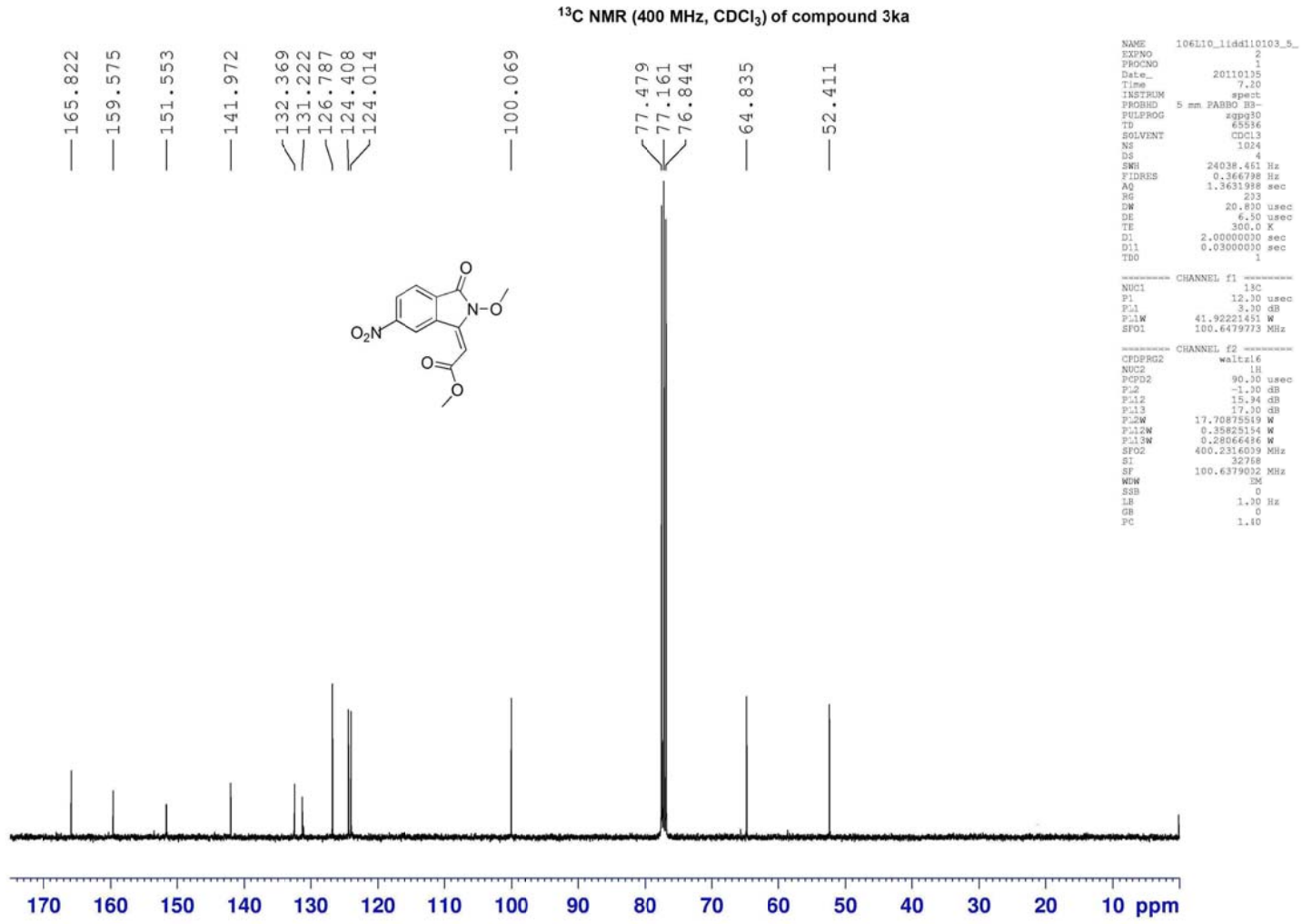
3.02









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SOLVENT                      CDCl3
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DS                                 4
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FIDRES                  0.366798 Hz
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RG                            233
DW                           20.800 usec
DE                            6.50 usec
TE                          300.0 K
D1                     2.00000000 sec
D11                    0.03000000 sec
TD0                              1

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P1                          12.00 usec
PL1                           3.00 dB
PL1W                 41.92221451 W
SFO1                100.6479773 MHz

======== CHANNEL f2 ========
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NUC2                          1H
PCPD2                       90.00 usec
PL2                          -1.00 dB
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PL13                         17.00 dB
PL2W                 17.70875549 W
PL12W                 0.35825154 W
PL13W                 0.28066486 W
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GB                              0
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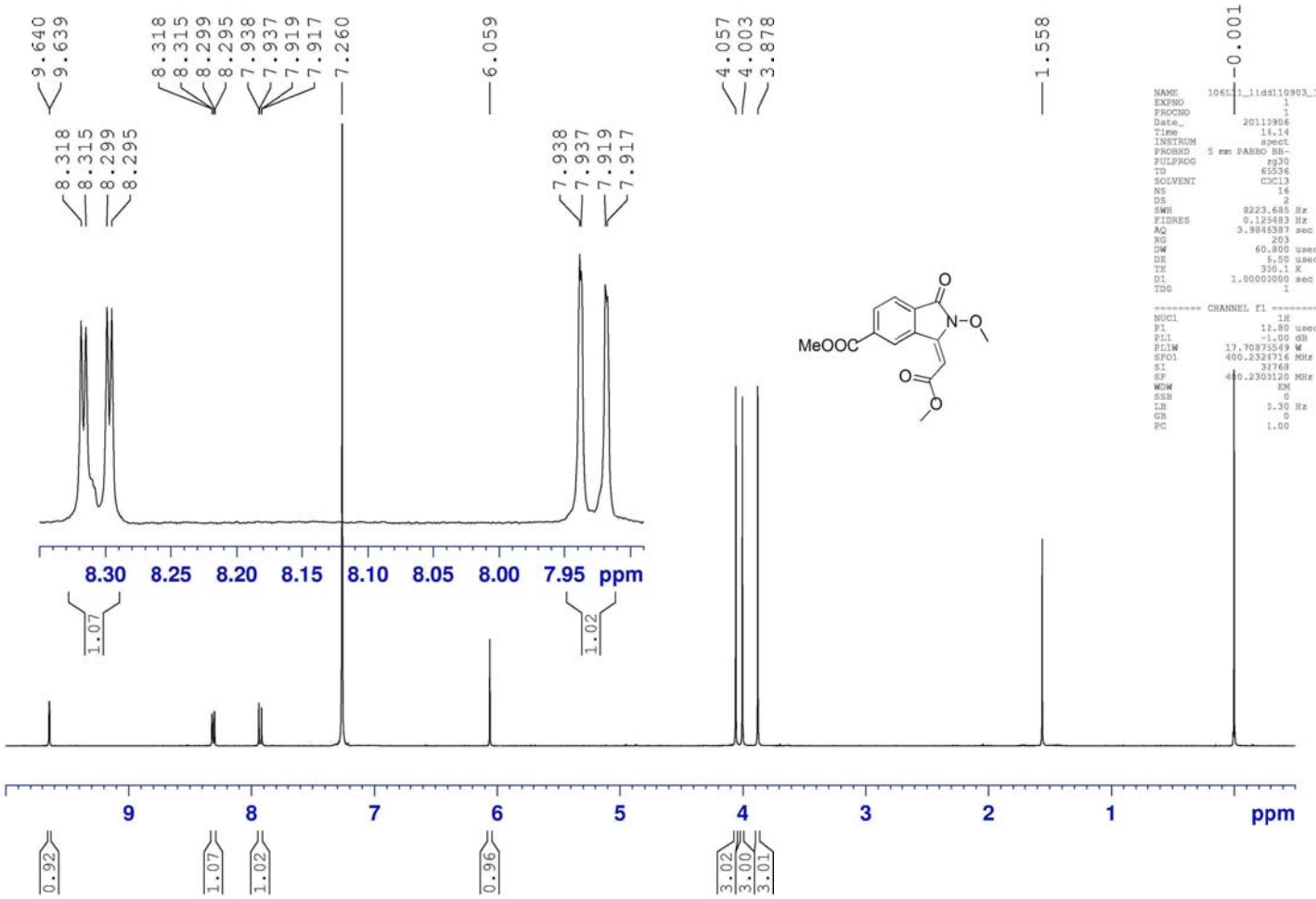
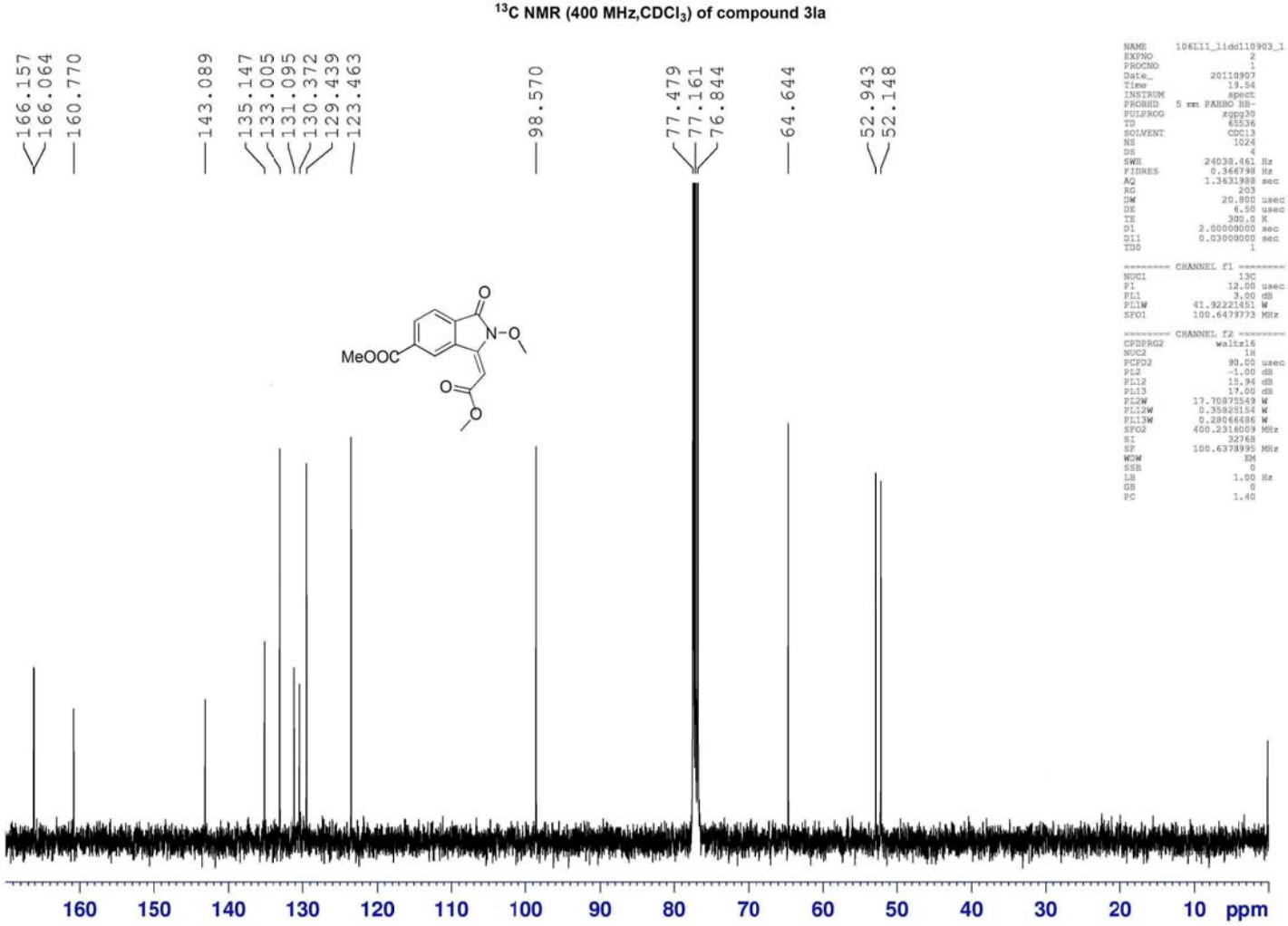
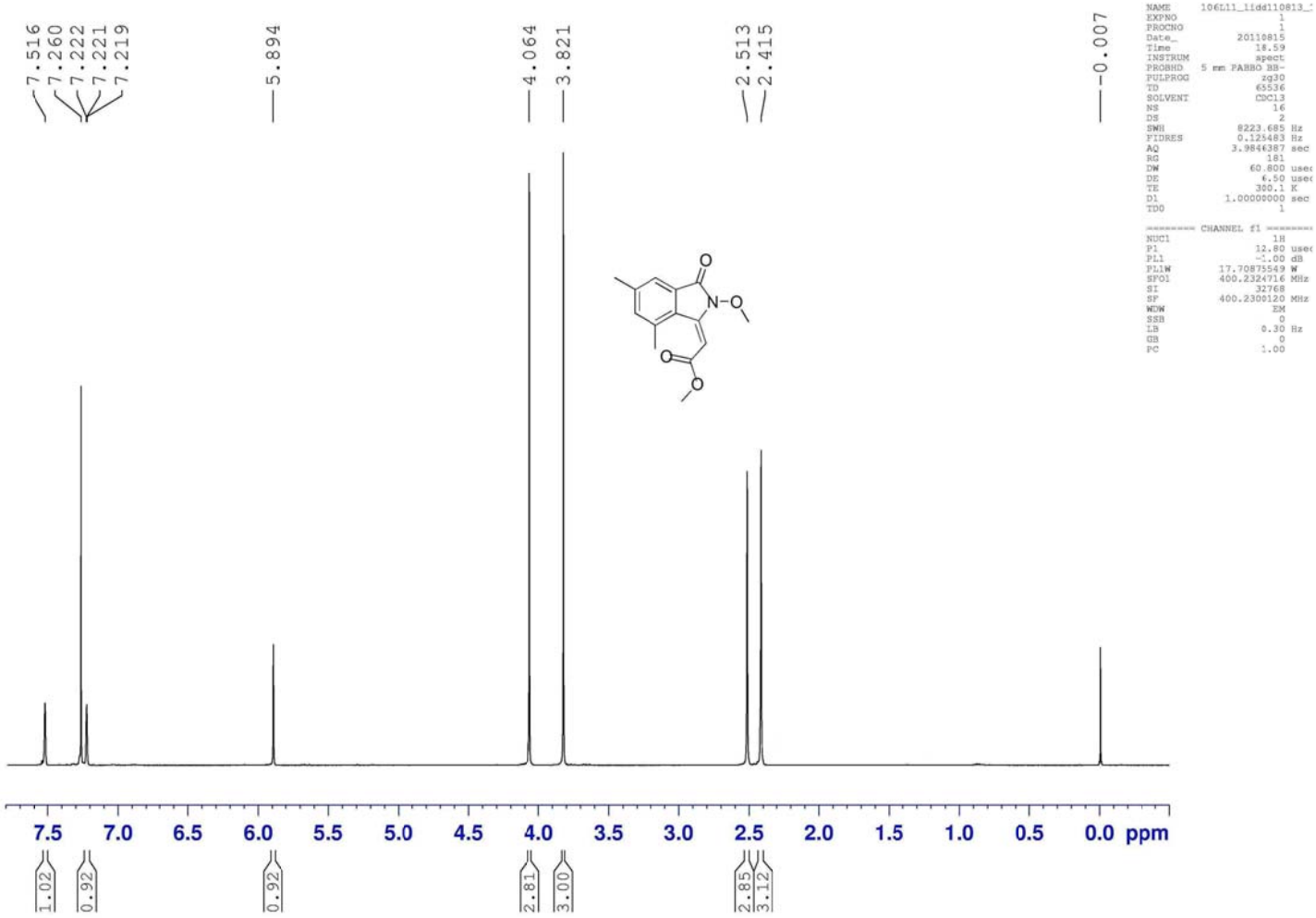
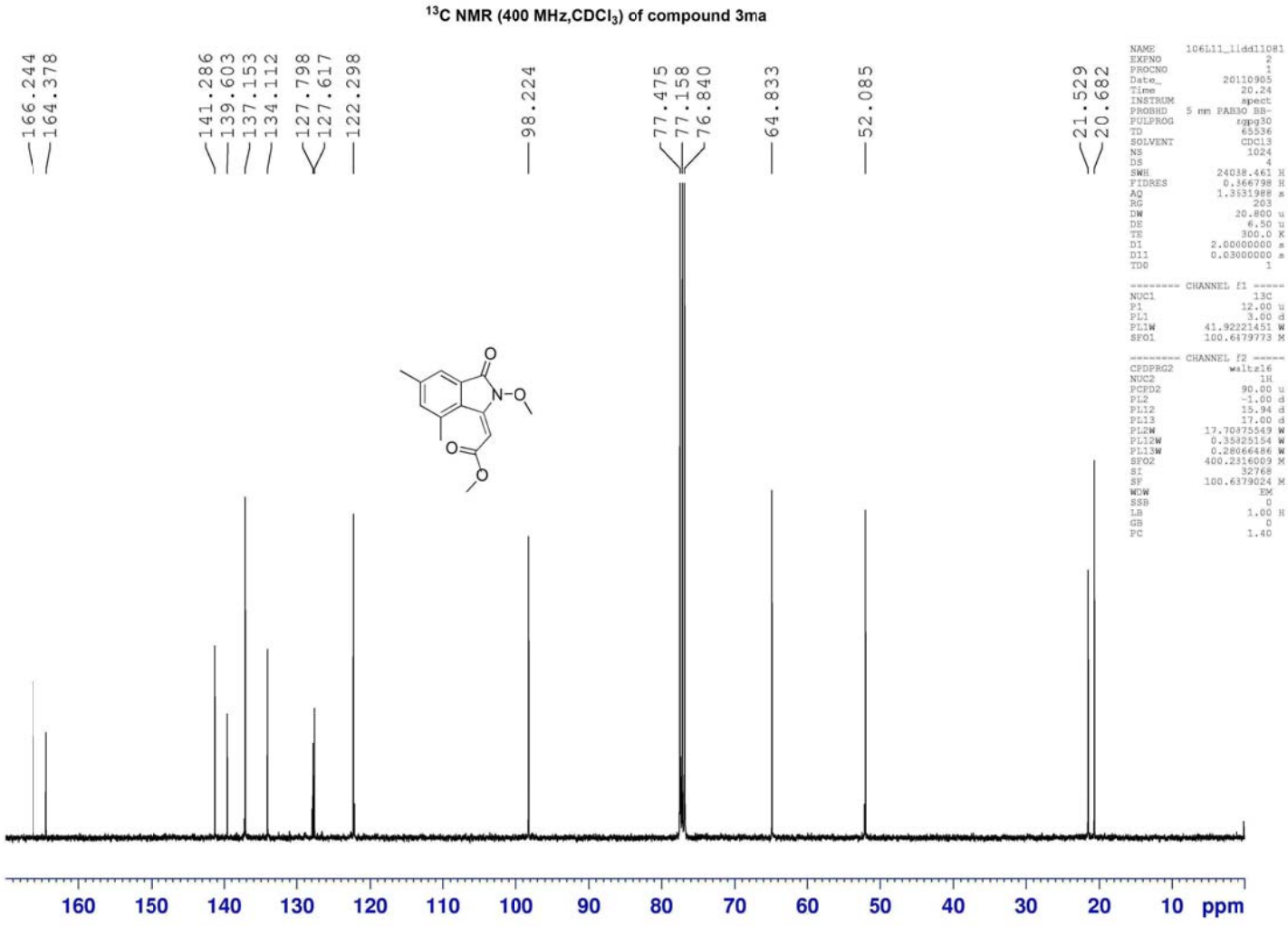
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3la



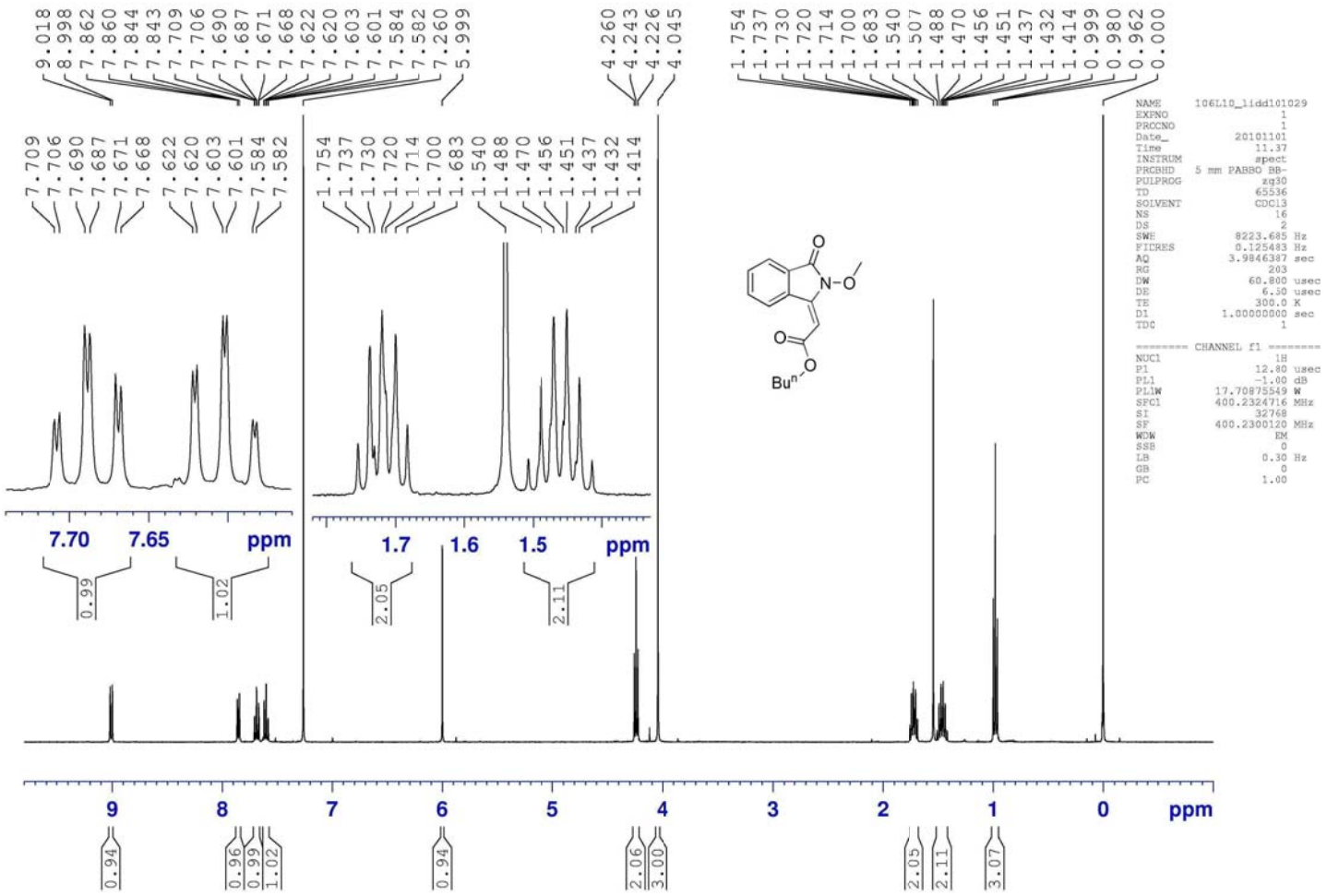


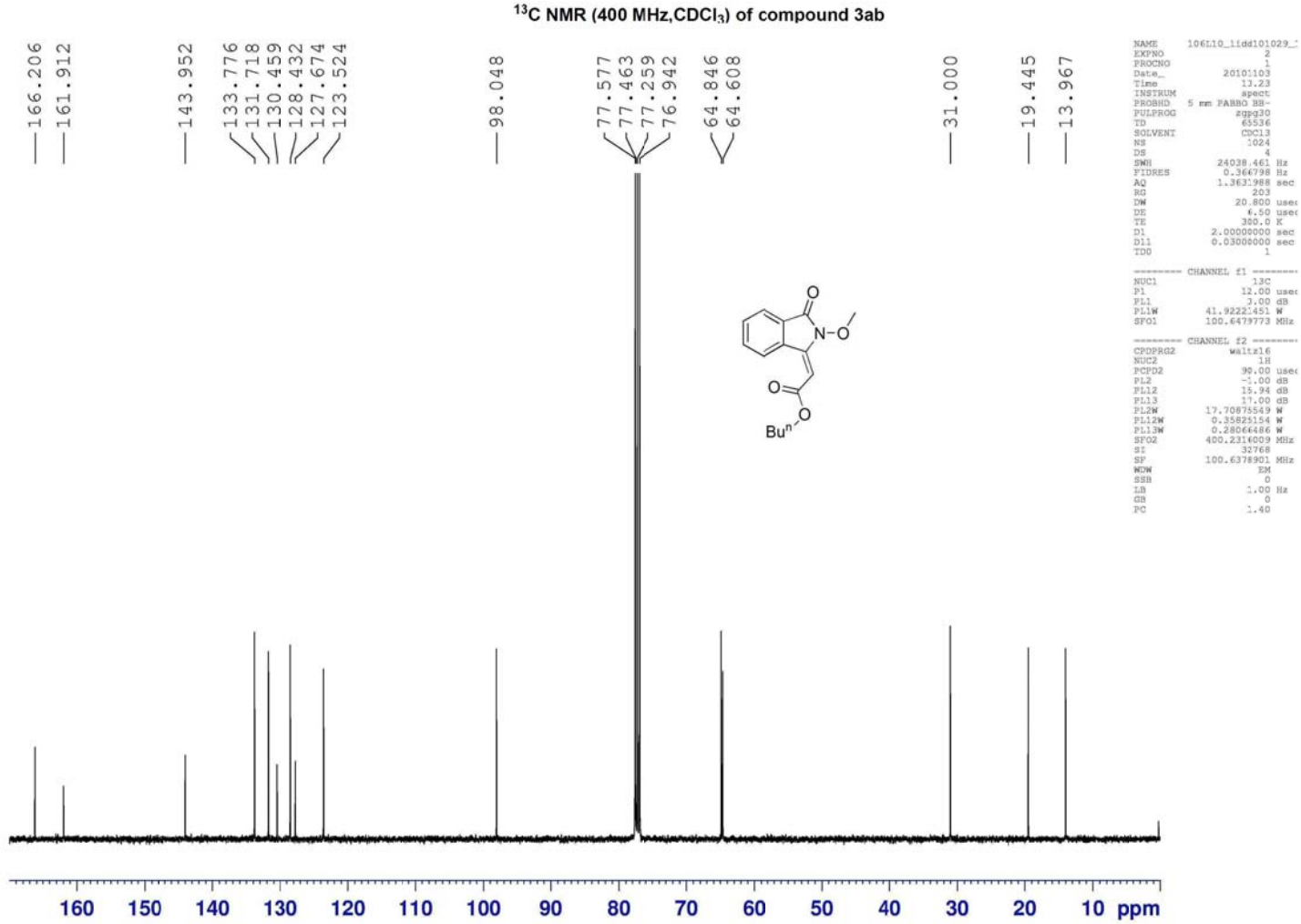
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3ma



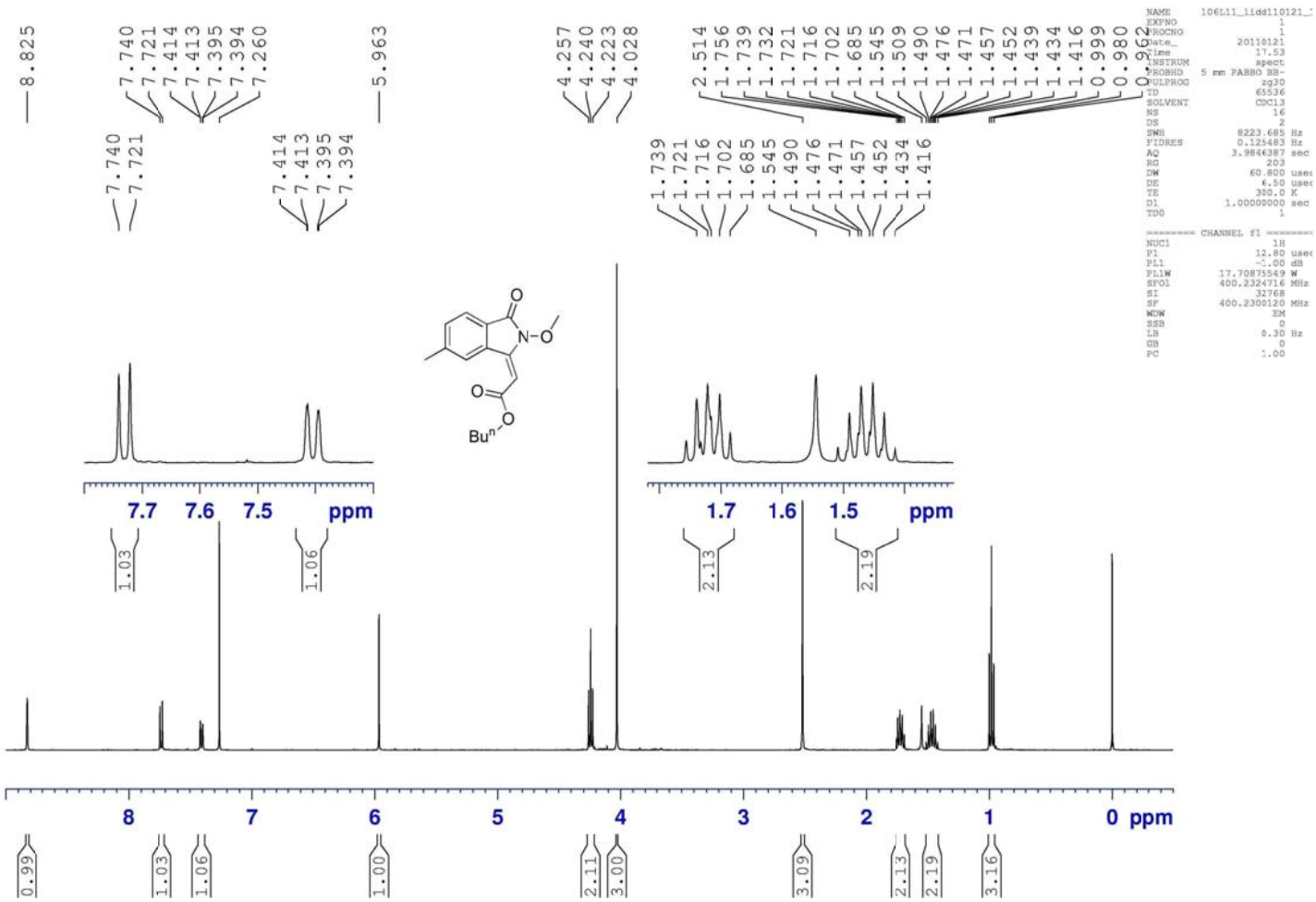


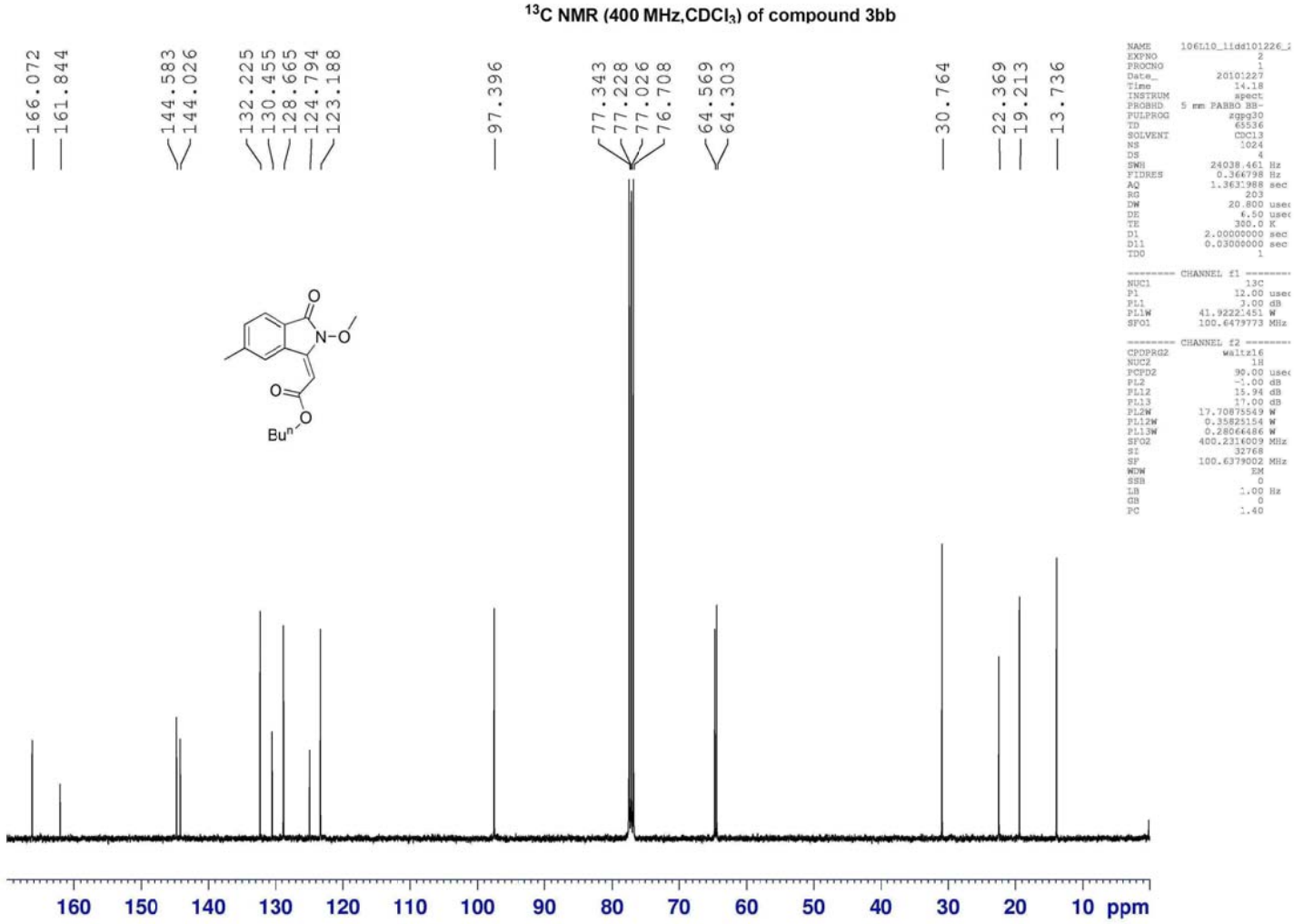
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3ab



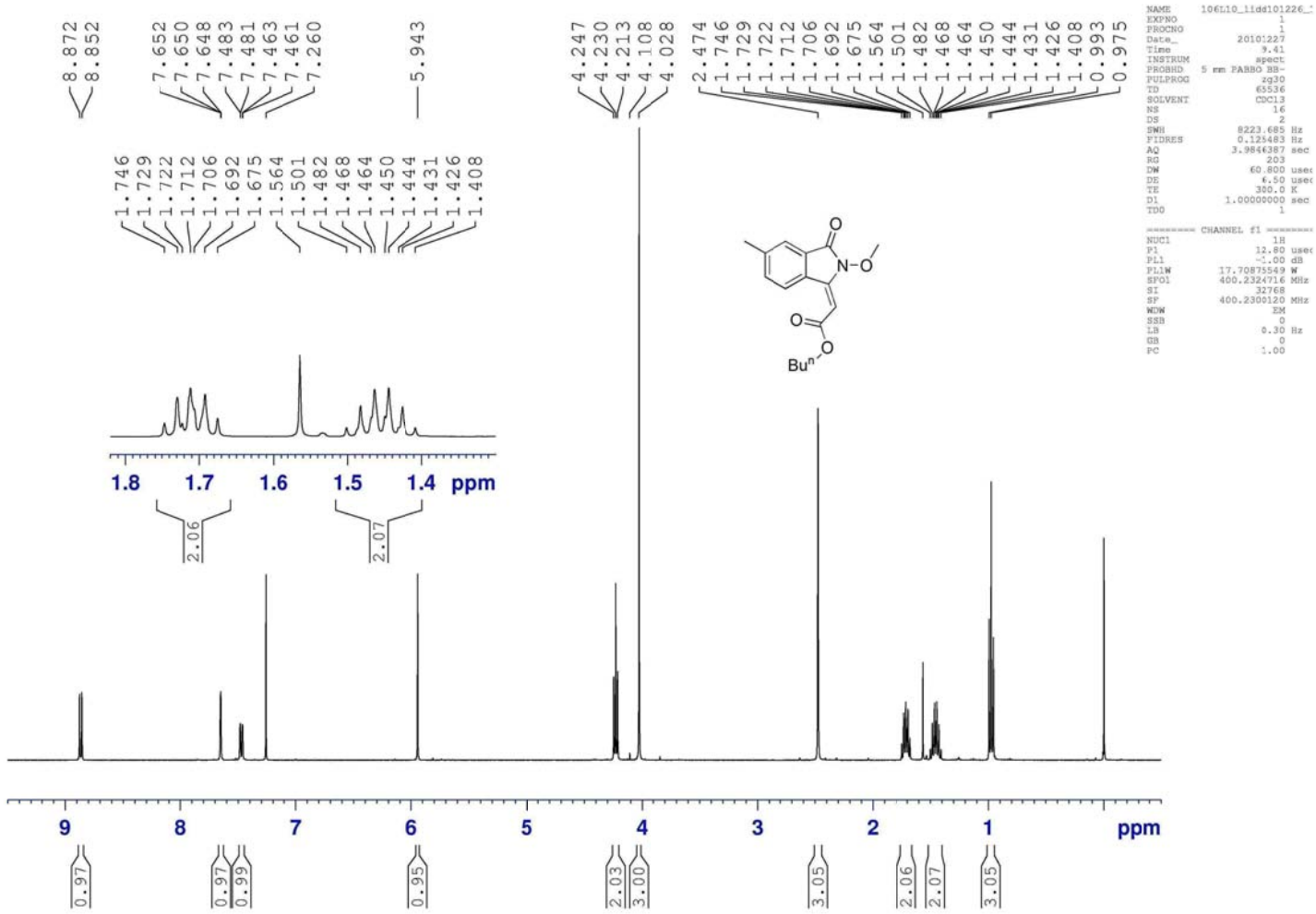


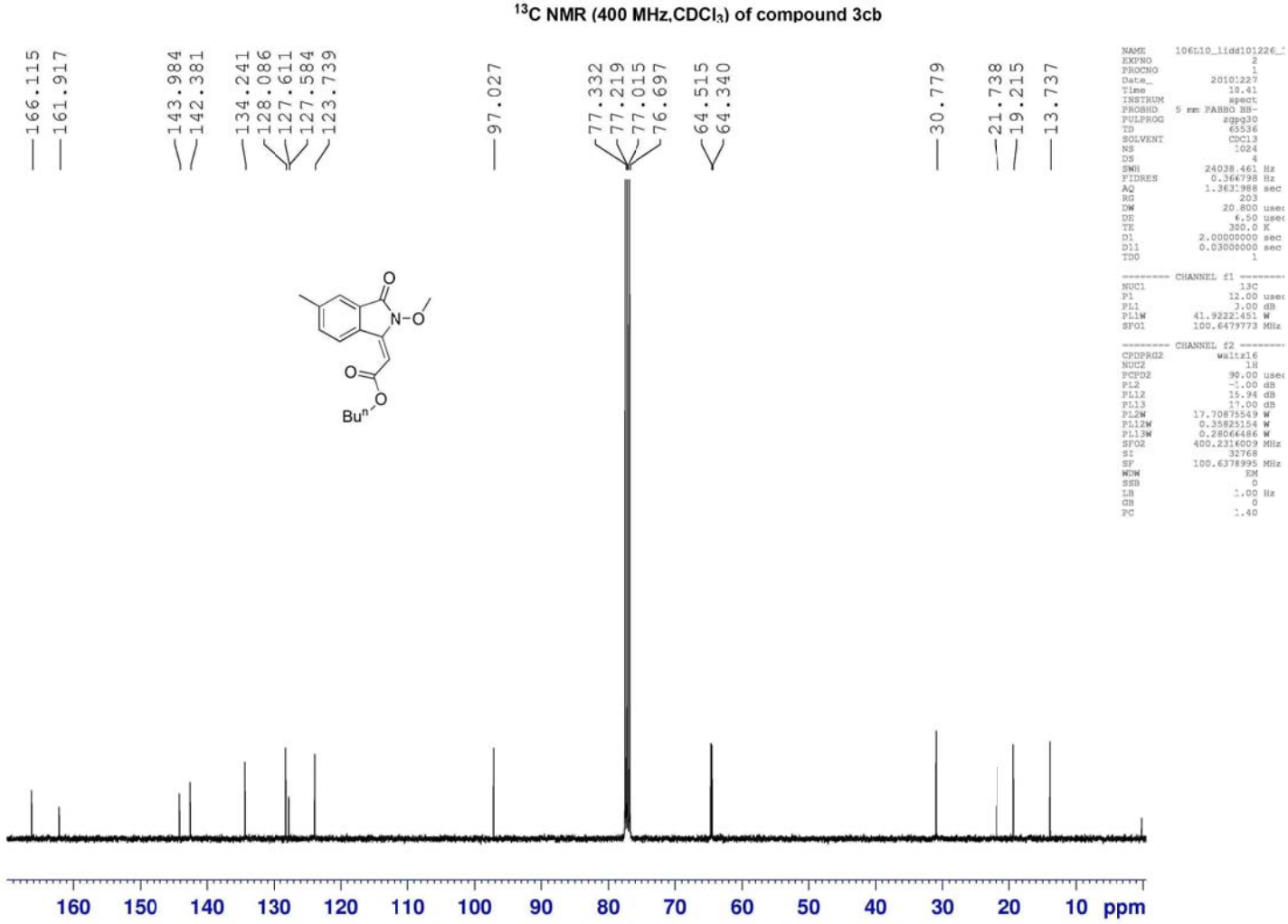
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3bb



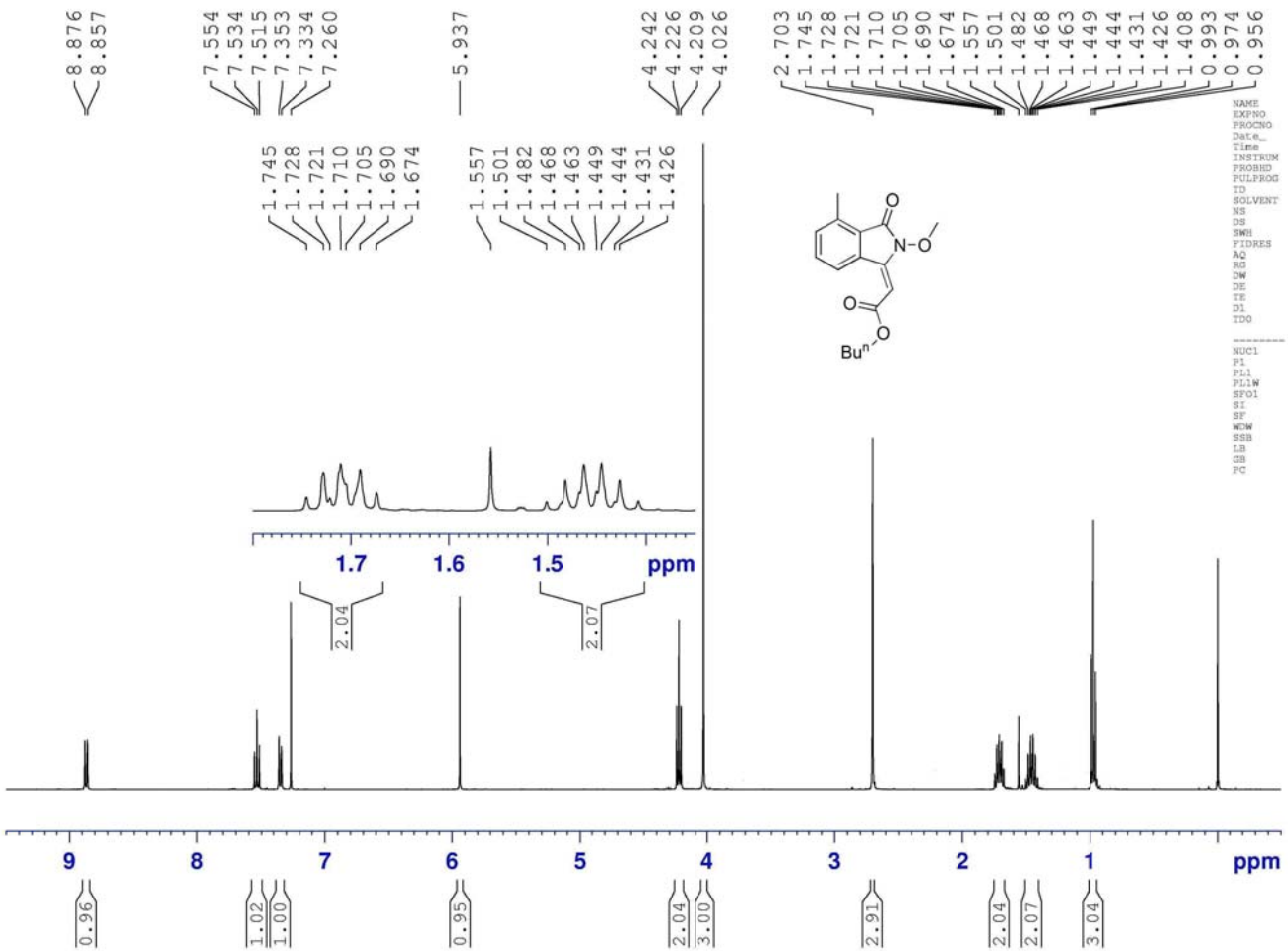


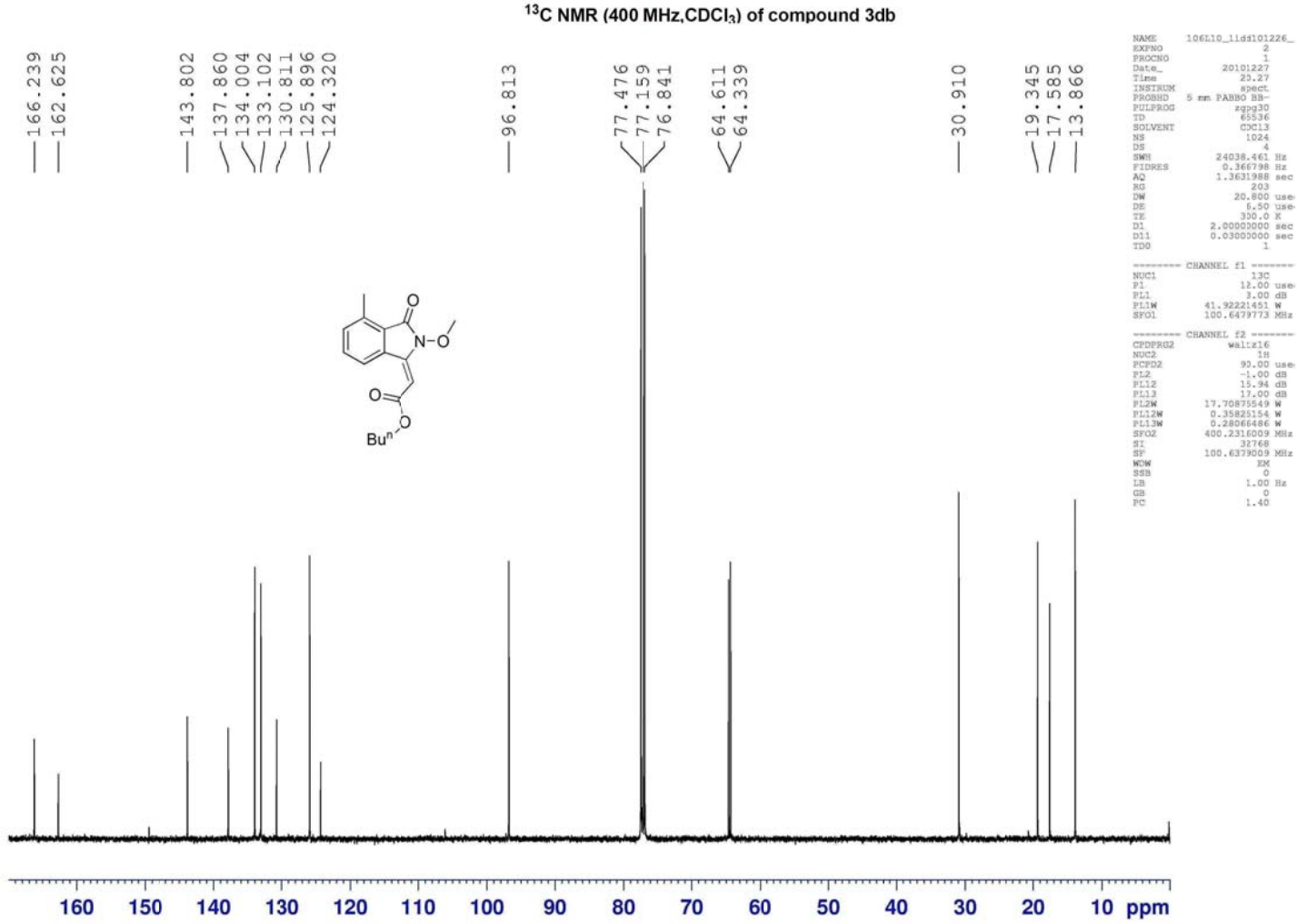
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3cb



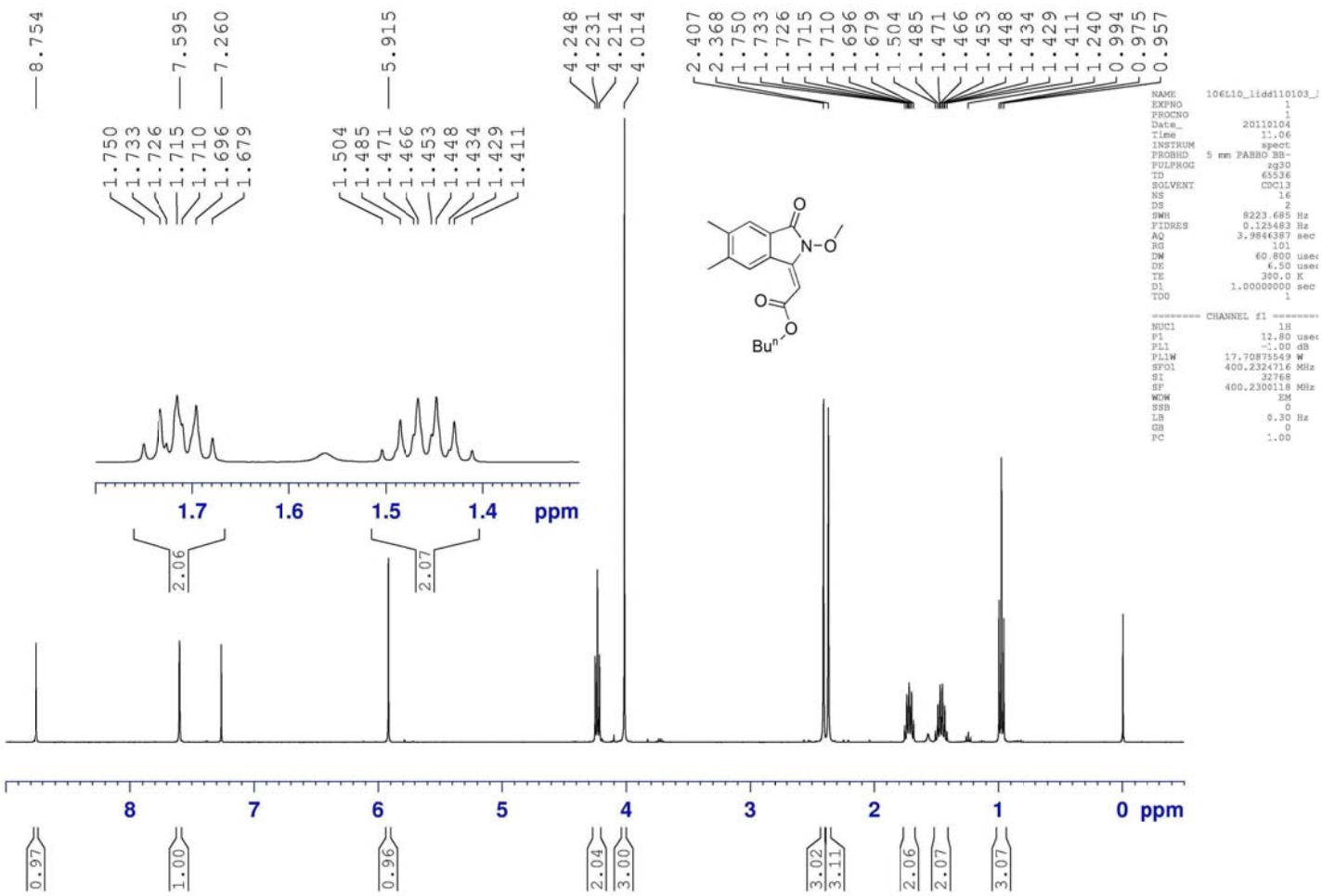


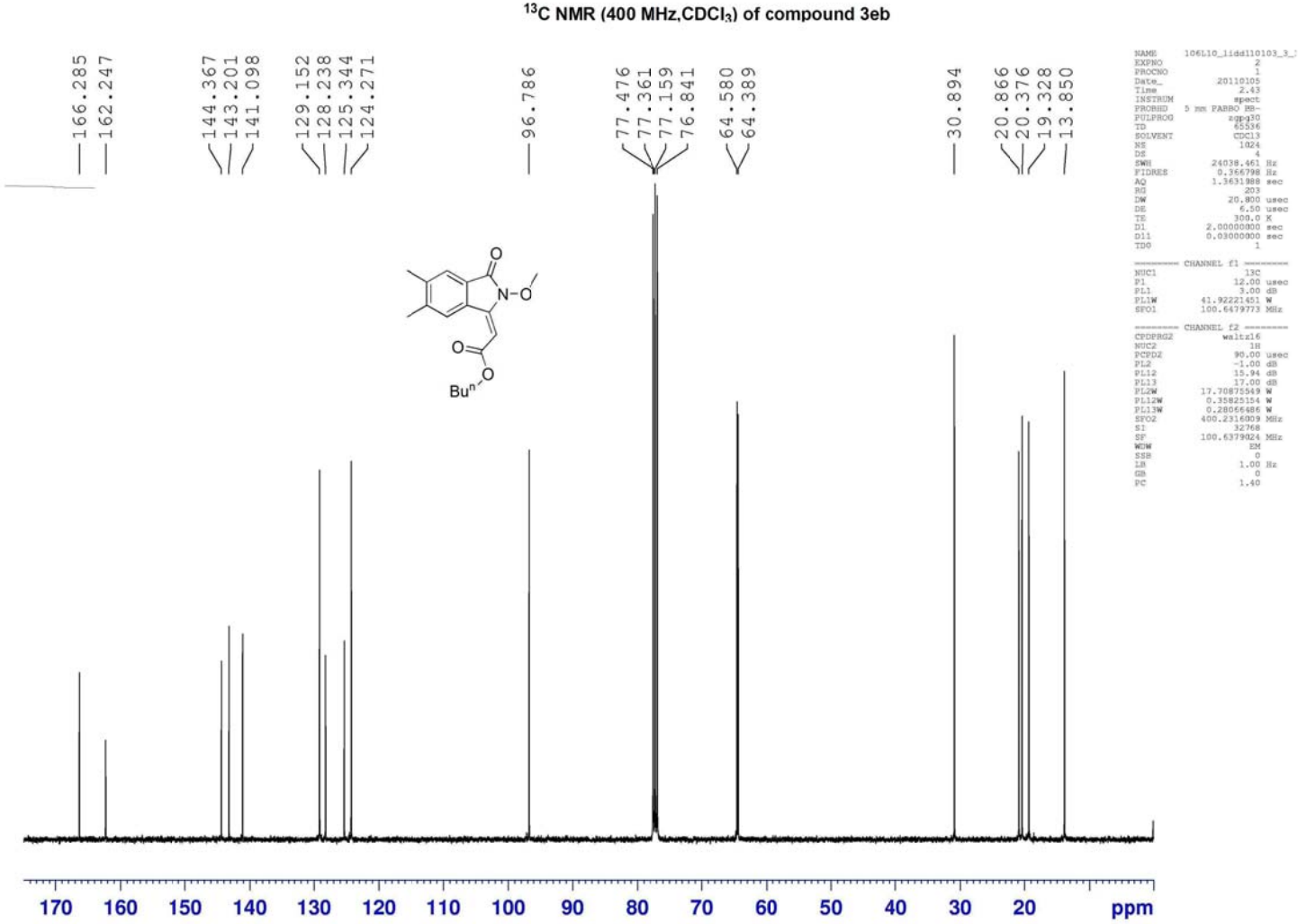
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3db



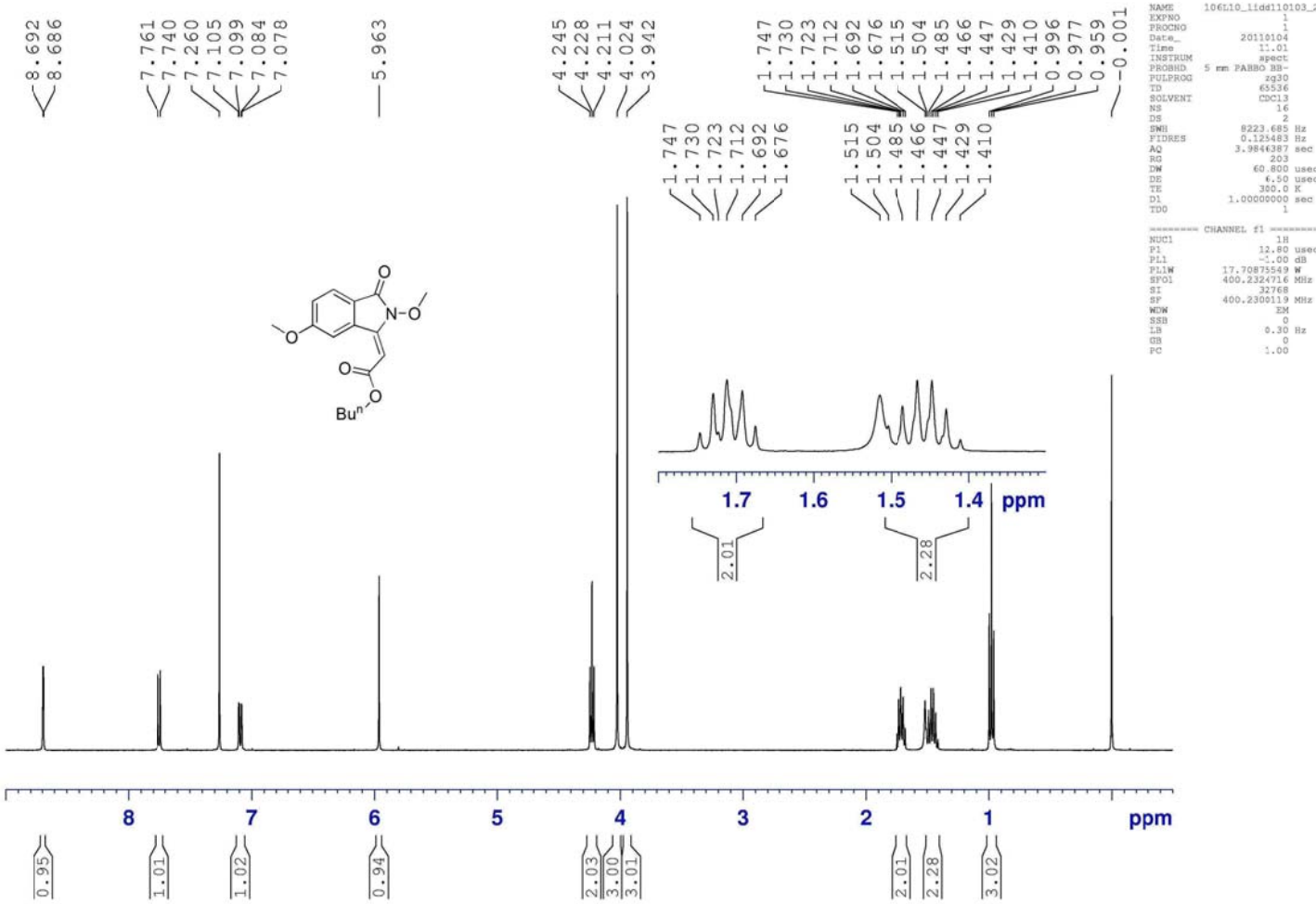

13C NMR (400 MHz,CDCl3) of compound 3db
166.239
162.625
143.802
137.860
134.004
133.102
130.811
125.896
124.320
96.813
77.476
77.159
76.841
64.611
64.339
30.910
19.345
17.585
13.866
Bu
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

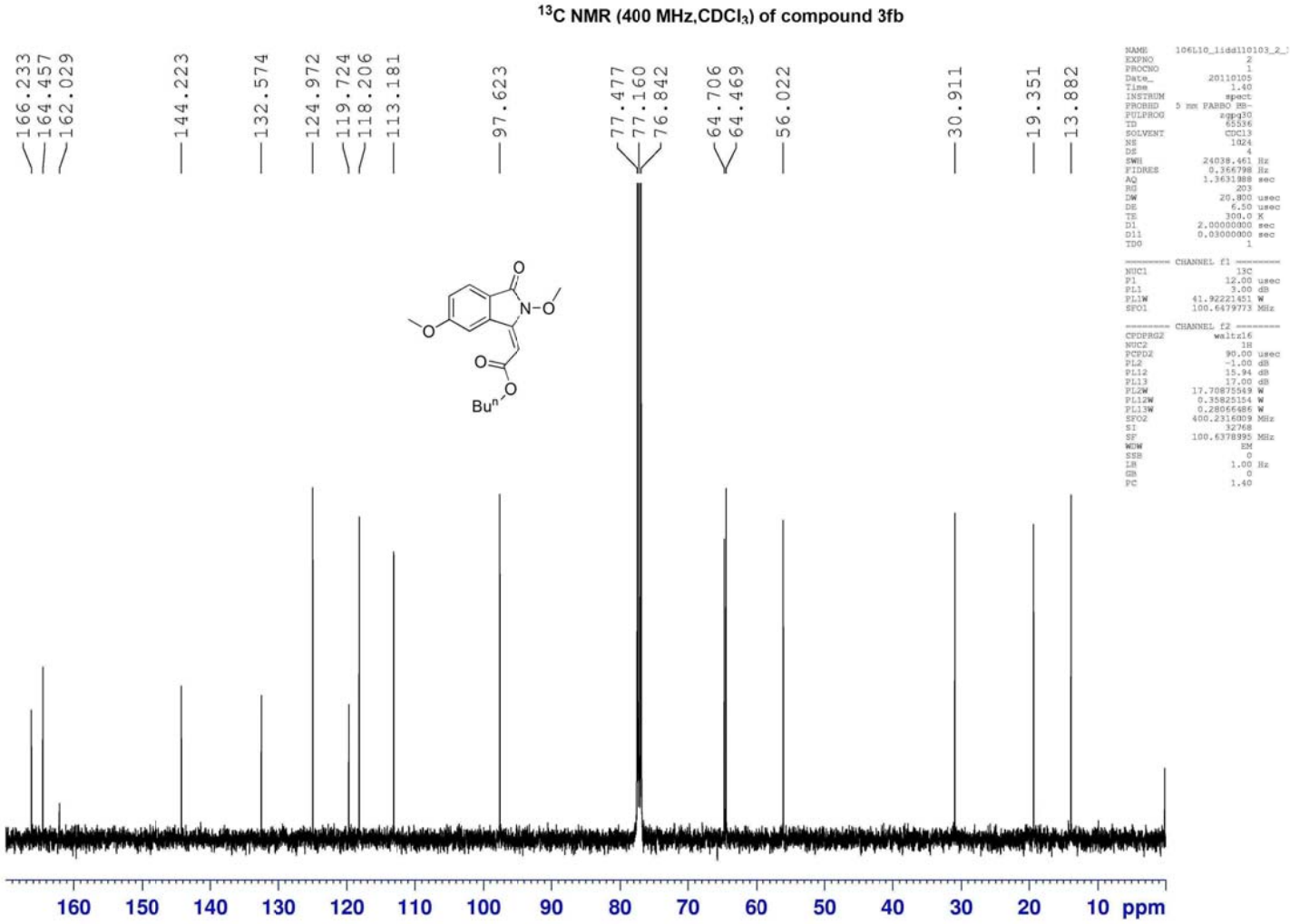
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3eb

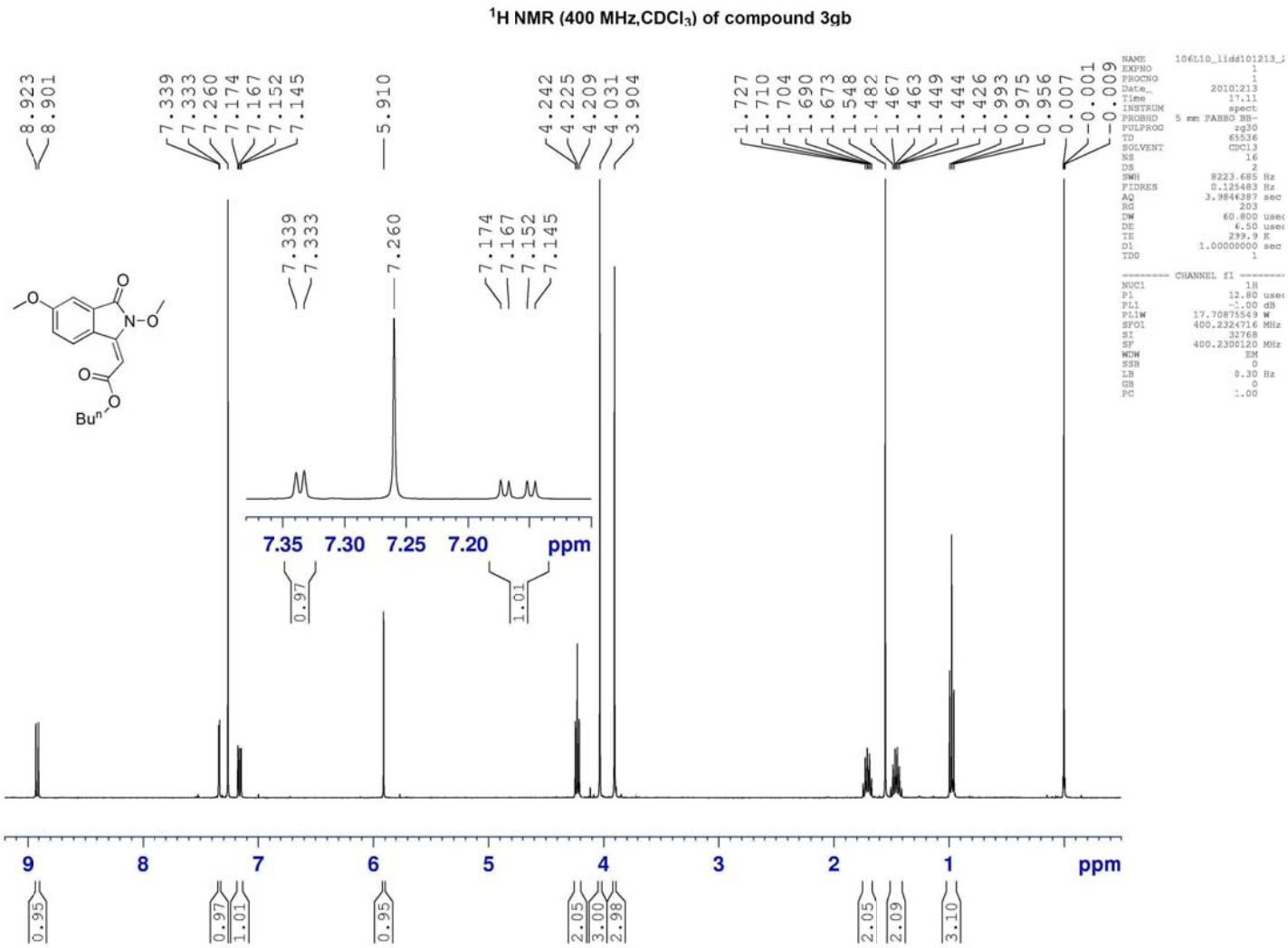


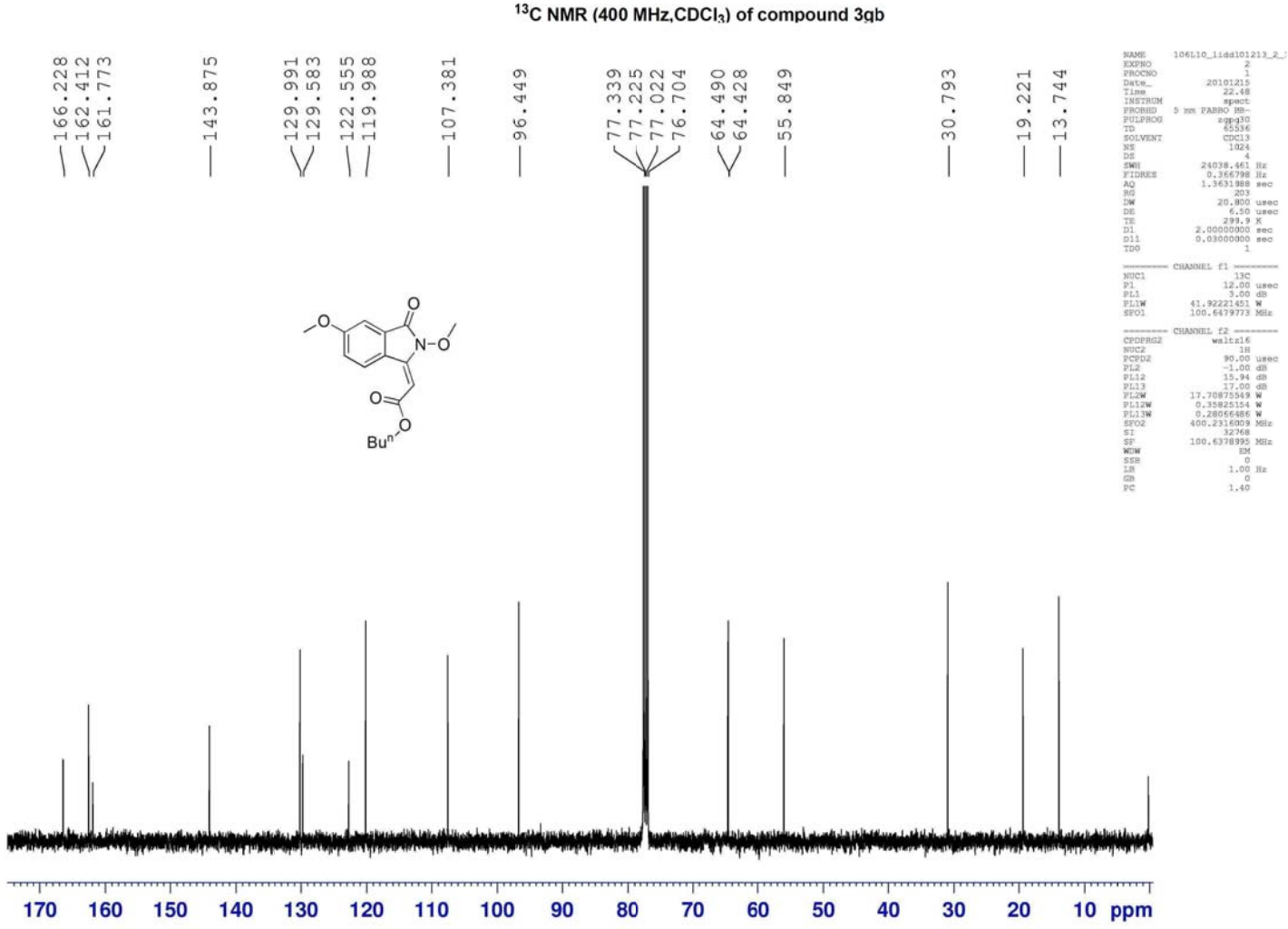

13C NMR (400 MHz,CDCl3) of compound 3eb
166.285
162.247
144.367
143.201
141.098
129.152
128.238
125.344
124.271
96.786
77.476
77.361
77.159
76.841
64.580
64.389
30.894
20.866
20.376
19.328
13.850
Bu^n
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

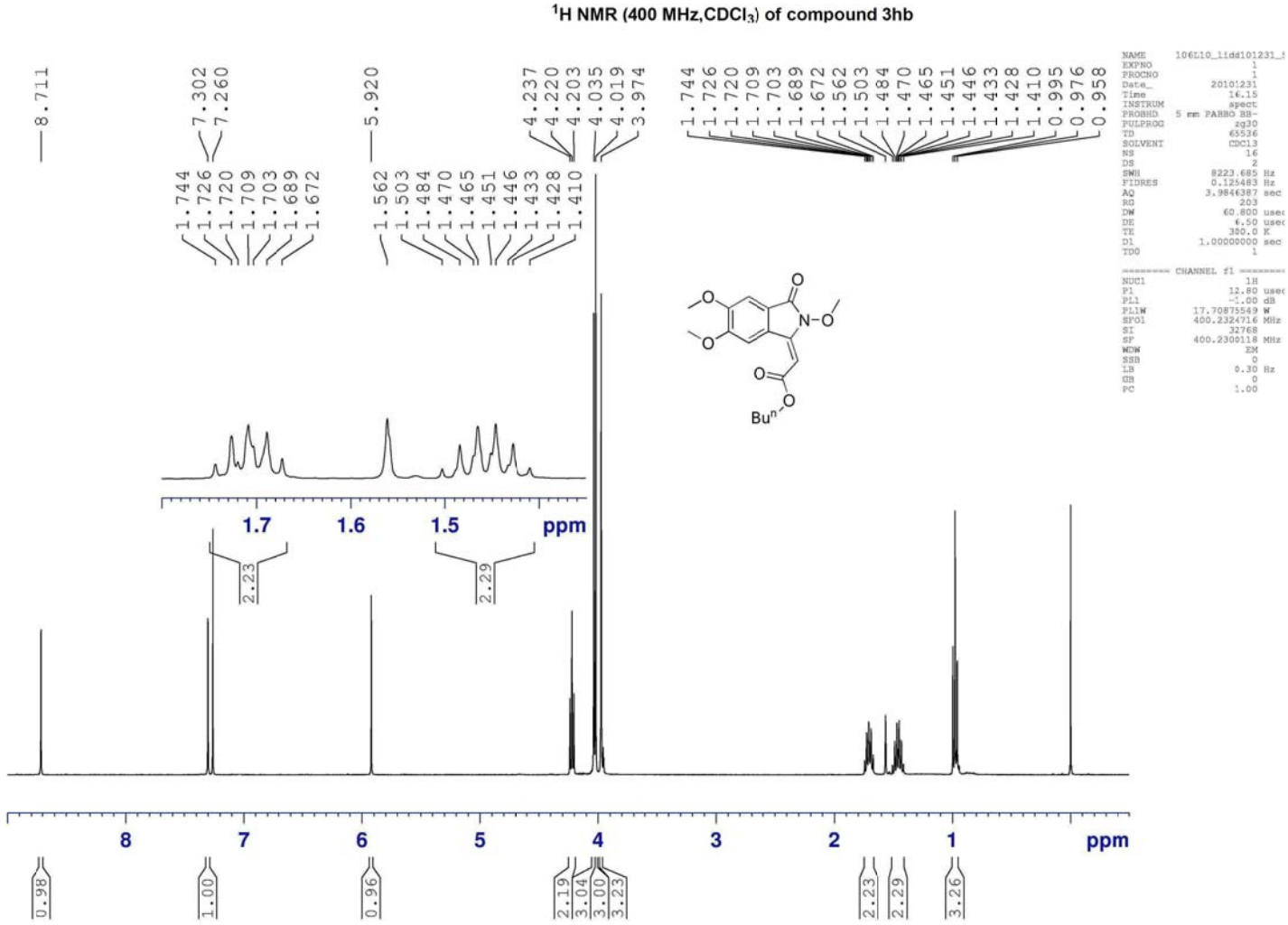
^{1}H NMR (400 MHz,$CDCl_3$) of compound 3fb

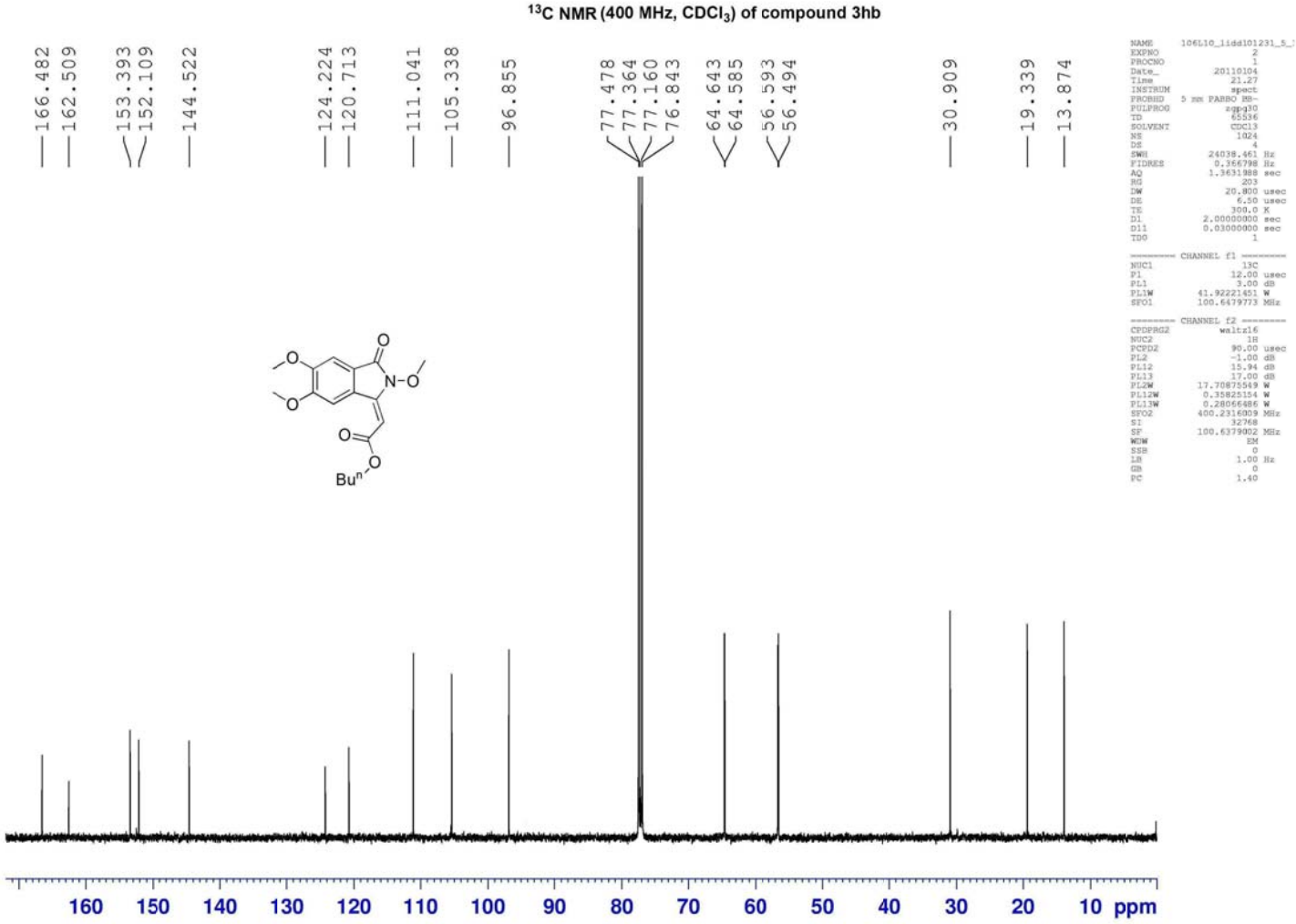




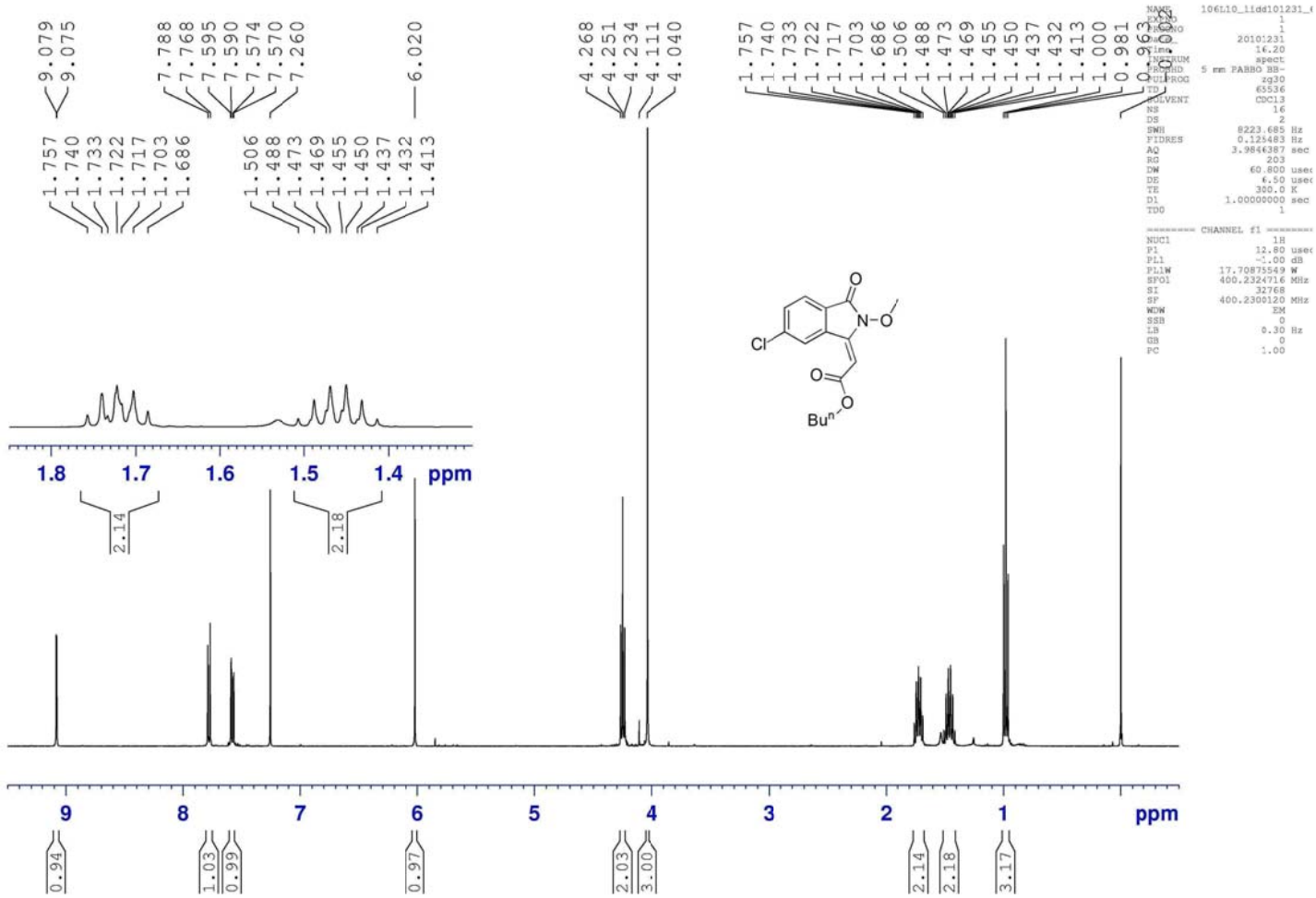


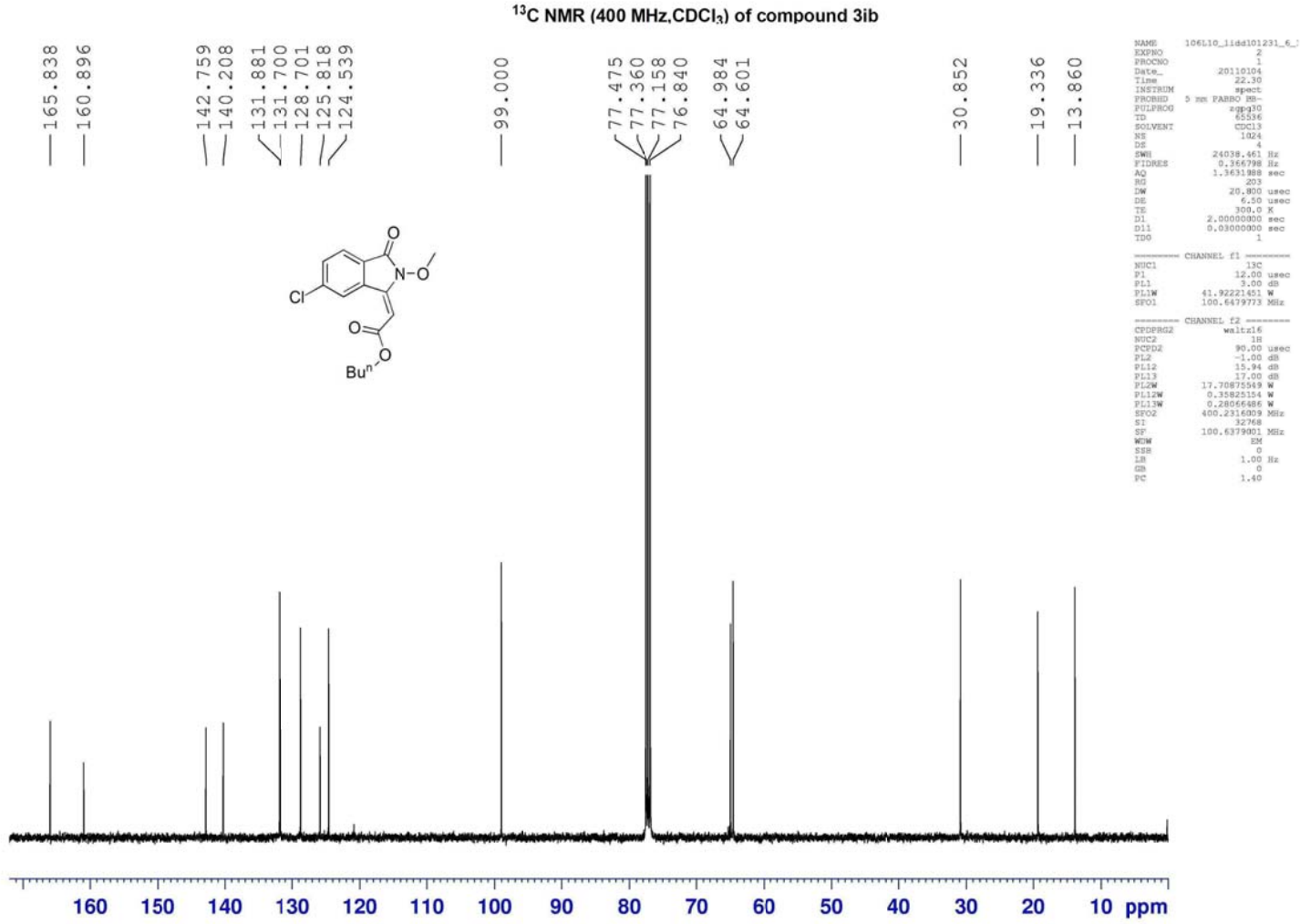


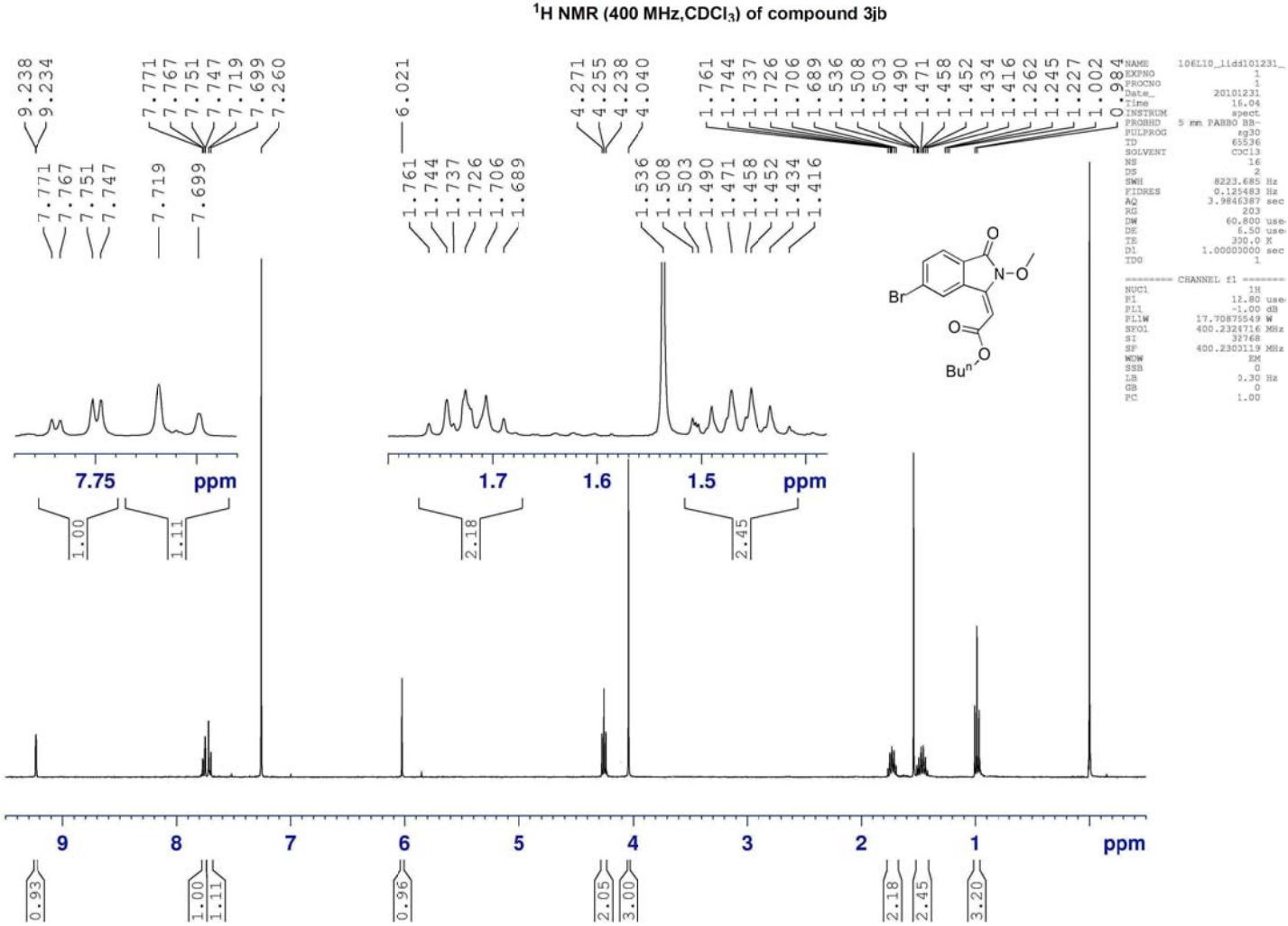

^{1}H NMR (400 MHz,CDCl$_3$) of compound 3hb
8.711
7.302
7.260
5.920
4.237
4.220
4.203
4.035
4.019
3.974
1.744
1.726
1.720
1.709
1.703
1.689
1.672
1.562
1.503
1.484
1.470
1.465
1.451
1.446
1.433
1.428
1.410
0.995
0.976
0.958
Bu^n
1.7
1.6
1.5
ppm
2.23
2.29
8
7
6
5
4
3
2
1
ppm
0.98
1.00
0.96
2.19
3.04
3.00
3.23
2.23
2.29
3.26

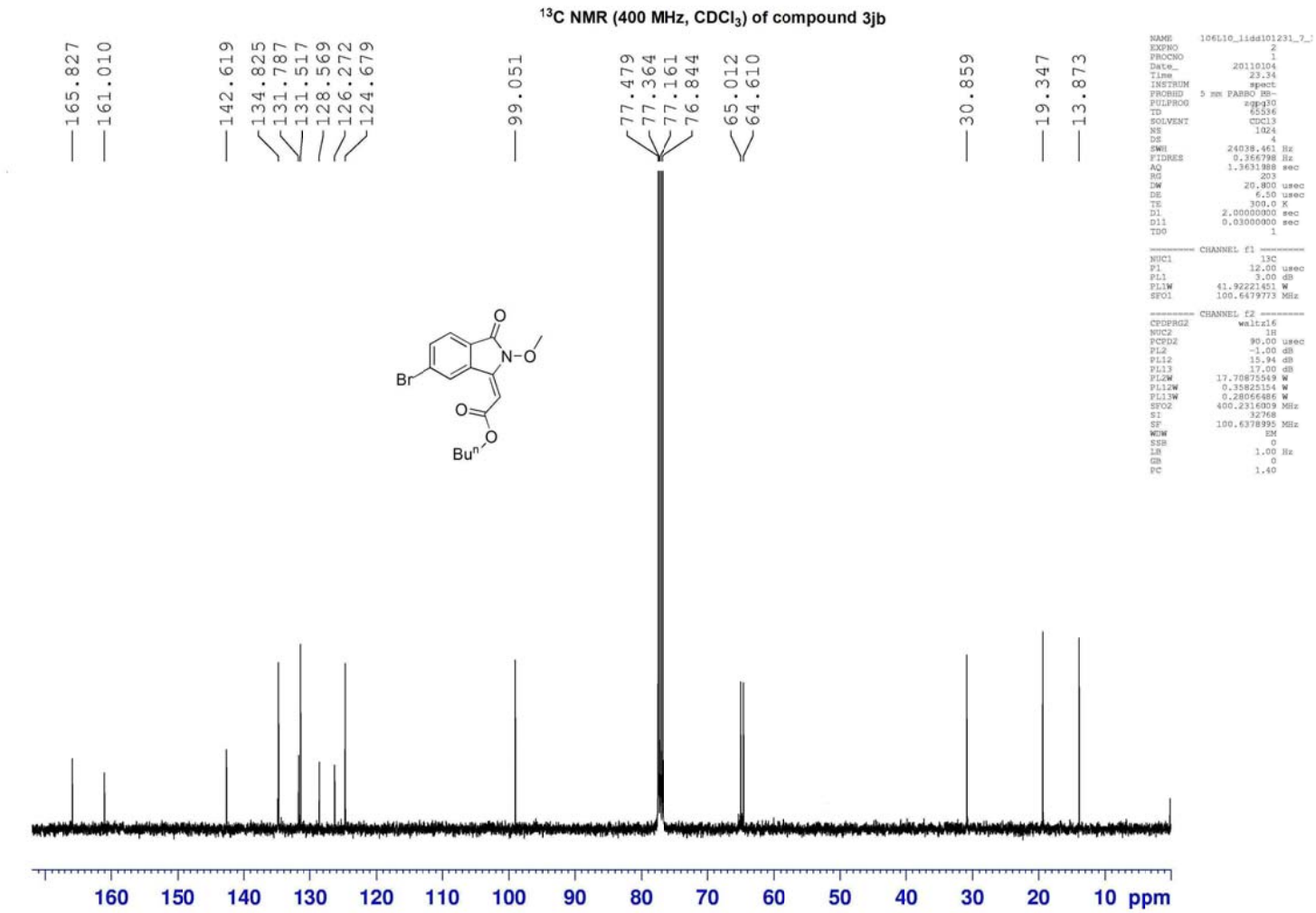

13C NMR (400 MHz, CDCl3) of compound 3hb
166.482
162.509
153.393
152.109
144.522
124.224
120.713
111.041
105.338
96.855
77.478
77.364
77.160
76.843
64.643
64.585
56.593
56.494
30.909
19.339
13.874
Bu^n
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

^{1}H NMR (400 MHz,$CDCl_3$) of compound 3ib

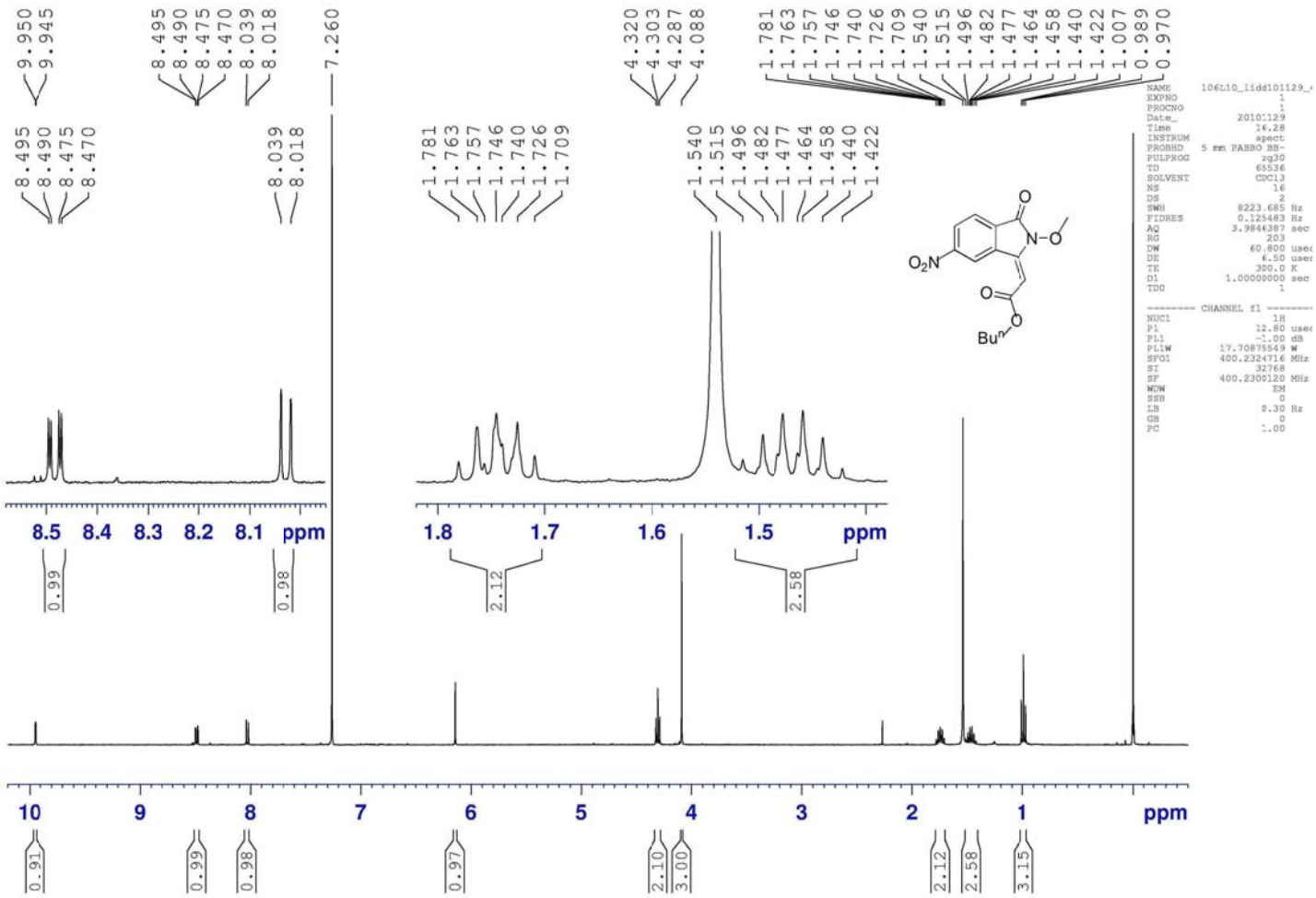




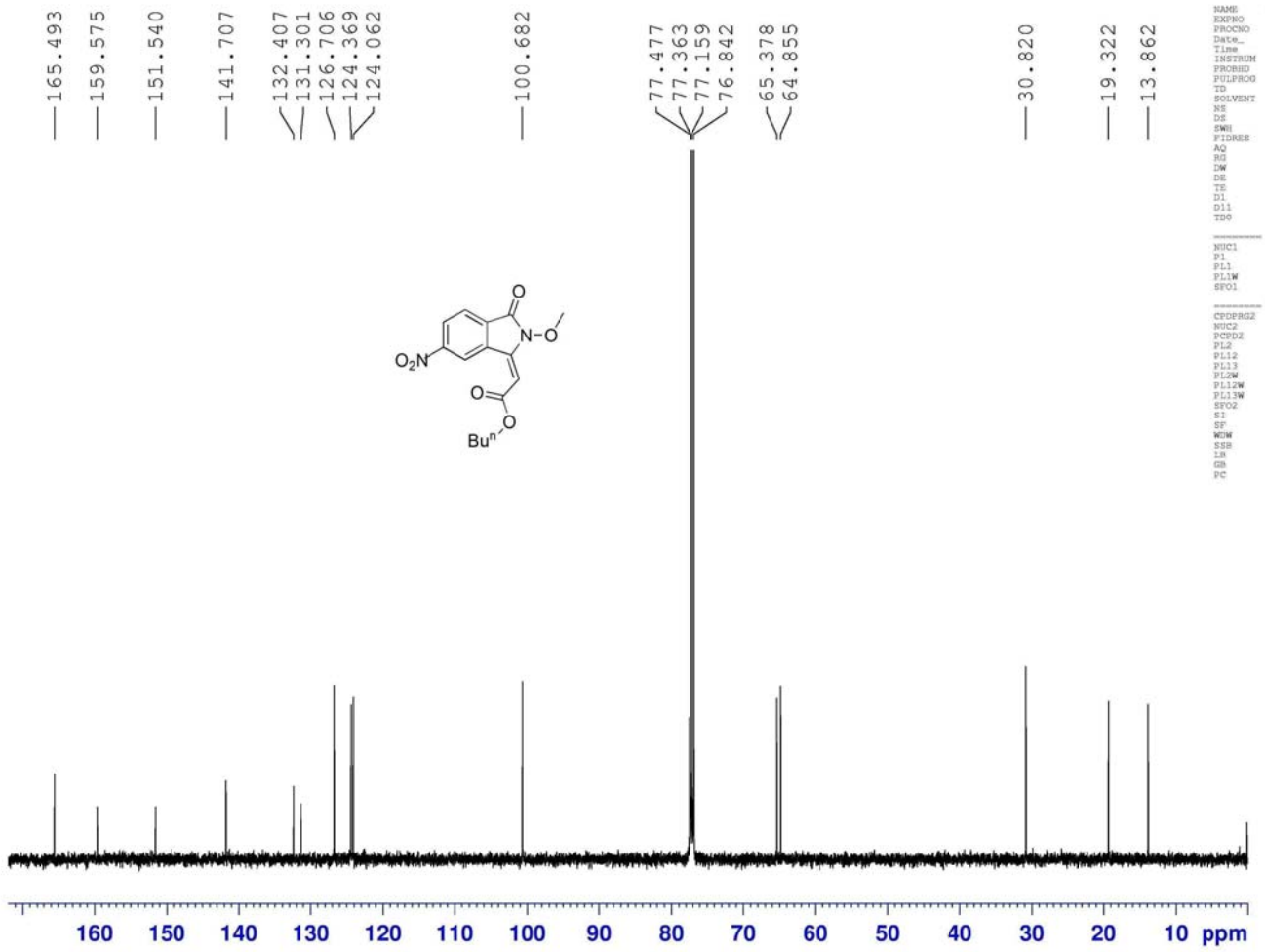


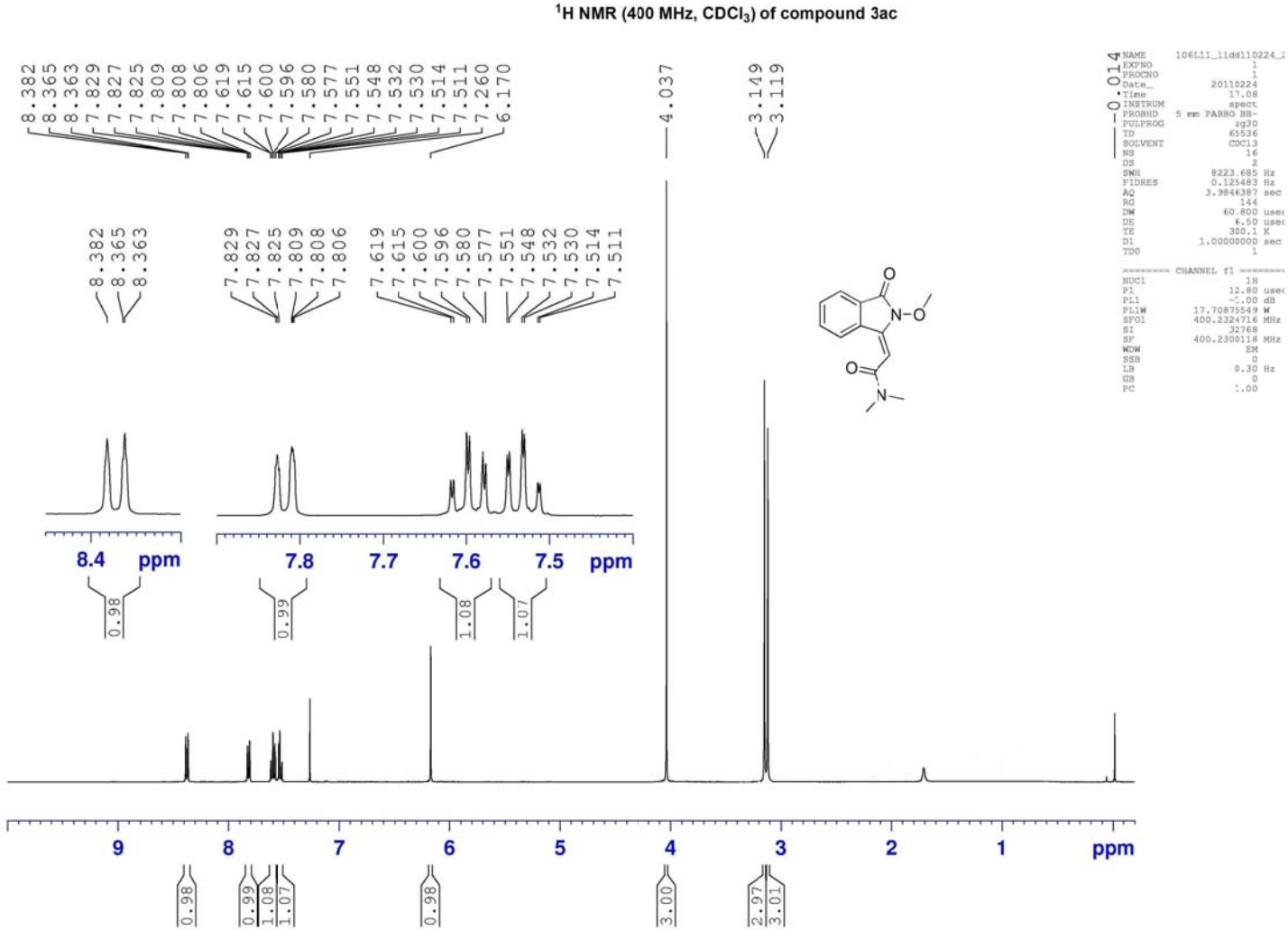


^{1}H NMR (400 MHz,$CDCl_3$) of compound 3kb

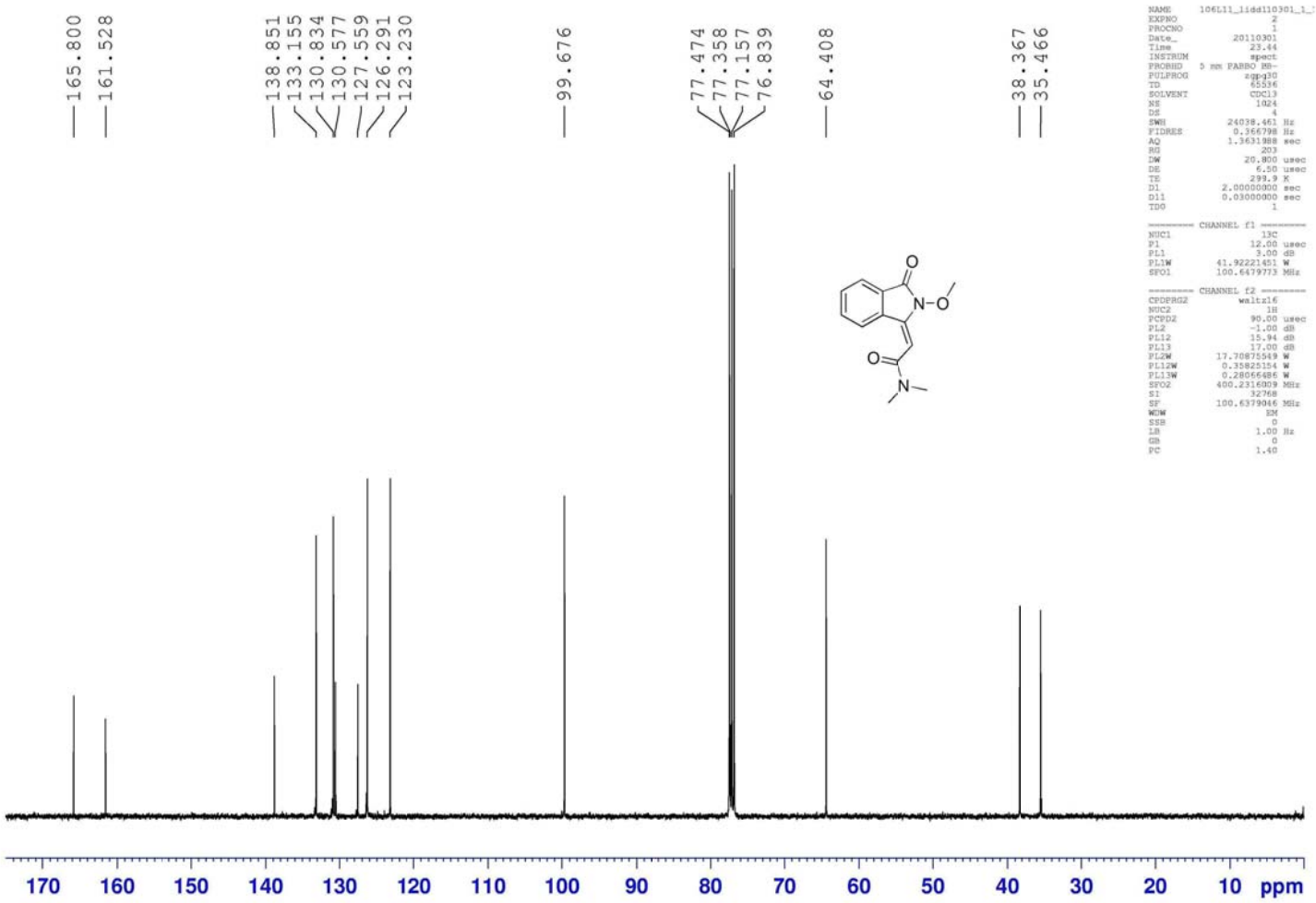


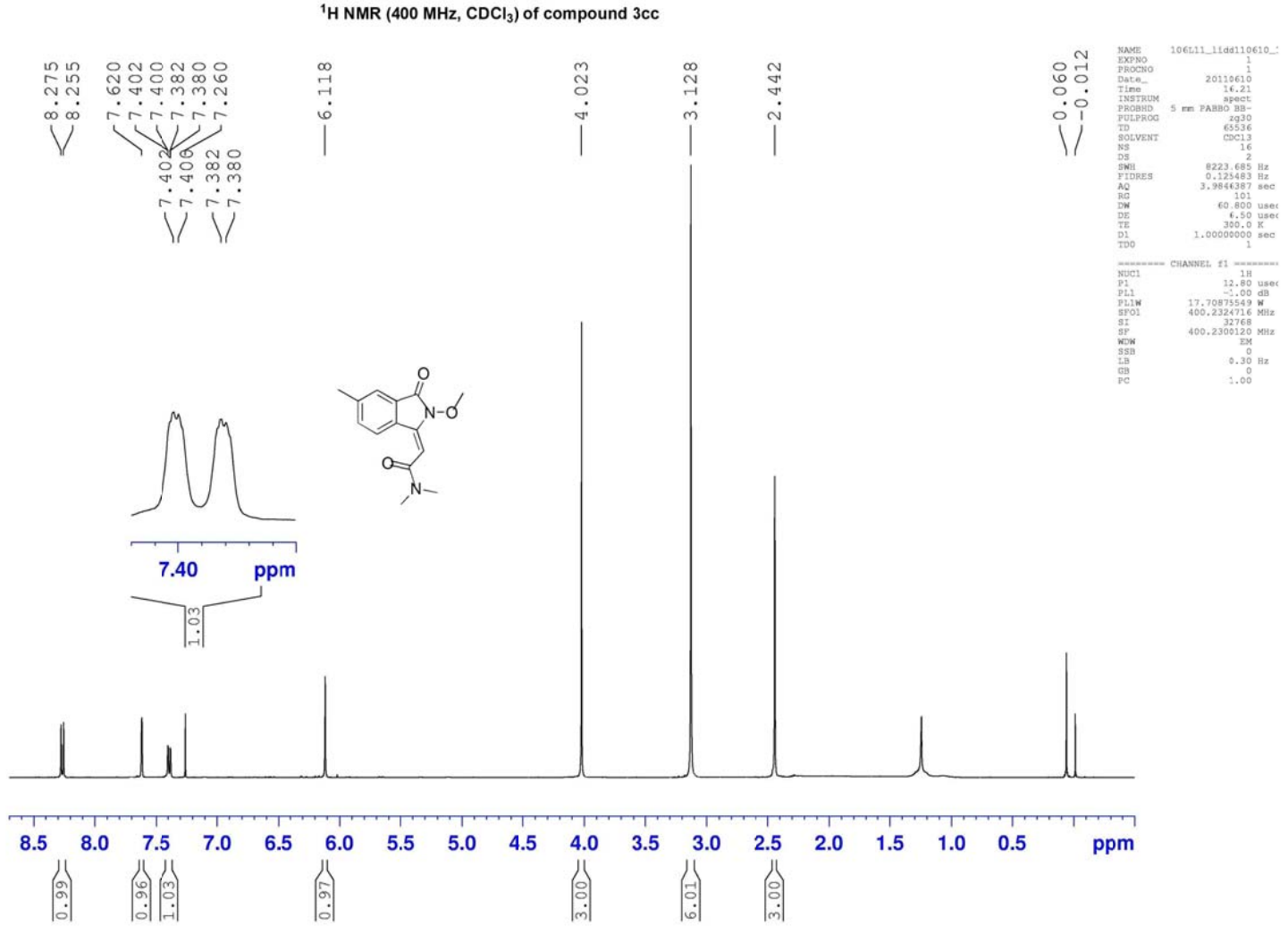
^{13}C NMR (400 MHz,$CDCl_3$) of compound 3kb



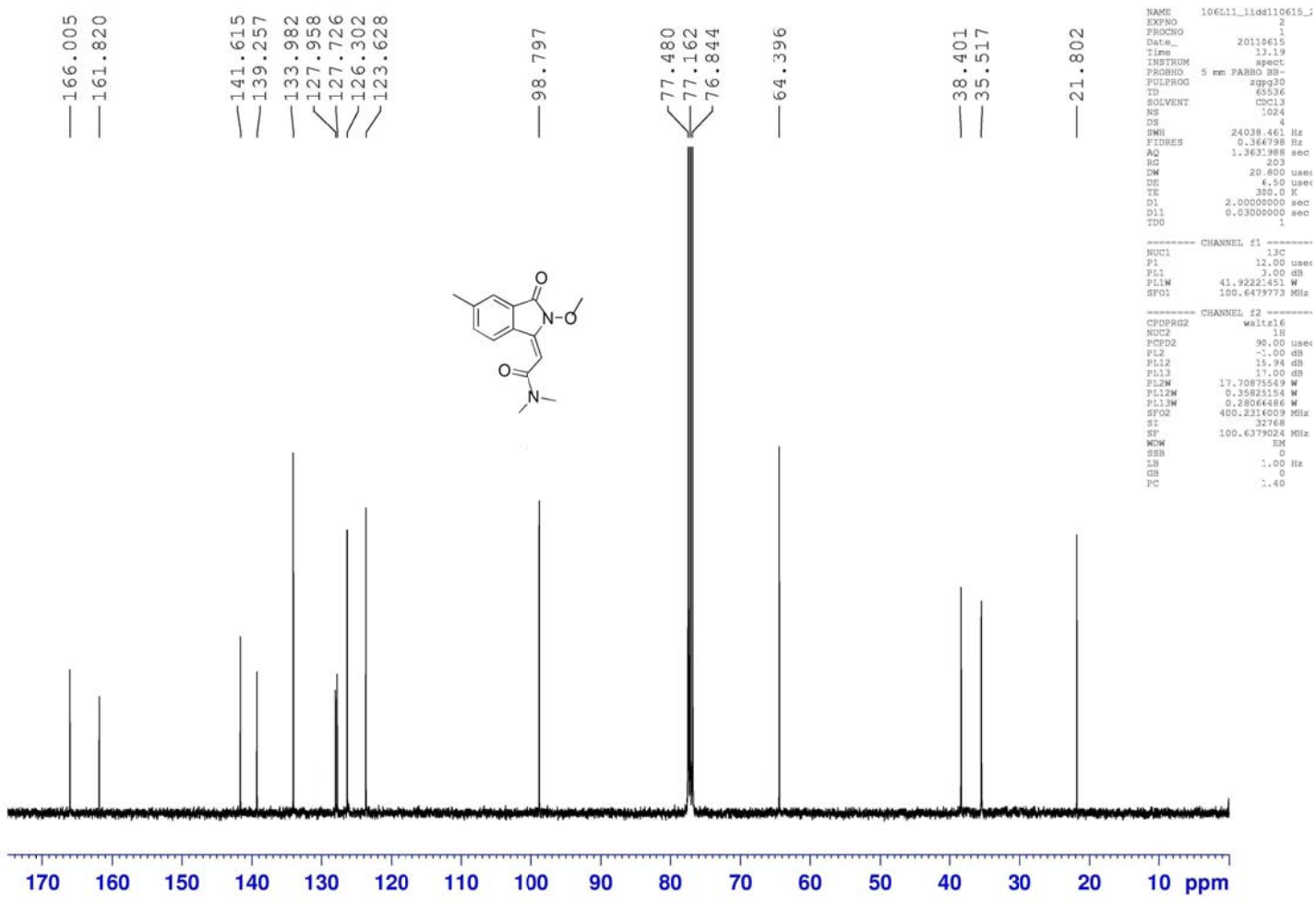

^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ac
8.382
8.365
8.363
7.829
7.827
7.825
7.809
7.808
7.806
7.619
7.615
7.600
7.596
7.580
7.577
7.551
7.548
7.532
7.530
7.514
7.511
7.260
6.170
4.037
3.149
3.119
8.4 ppm
7.8 7.7 7.6 7.5 ppm
0.98
0.99
1.08
1.07
9 8 7 6 5 4 3 2 1 ppm
0.98
0.99
1.08
1.07
0.98
3.00
2.97
3.01

^{13}C NMR (400 MHz, $CDCl_3$) of compound 3ac

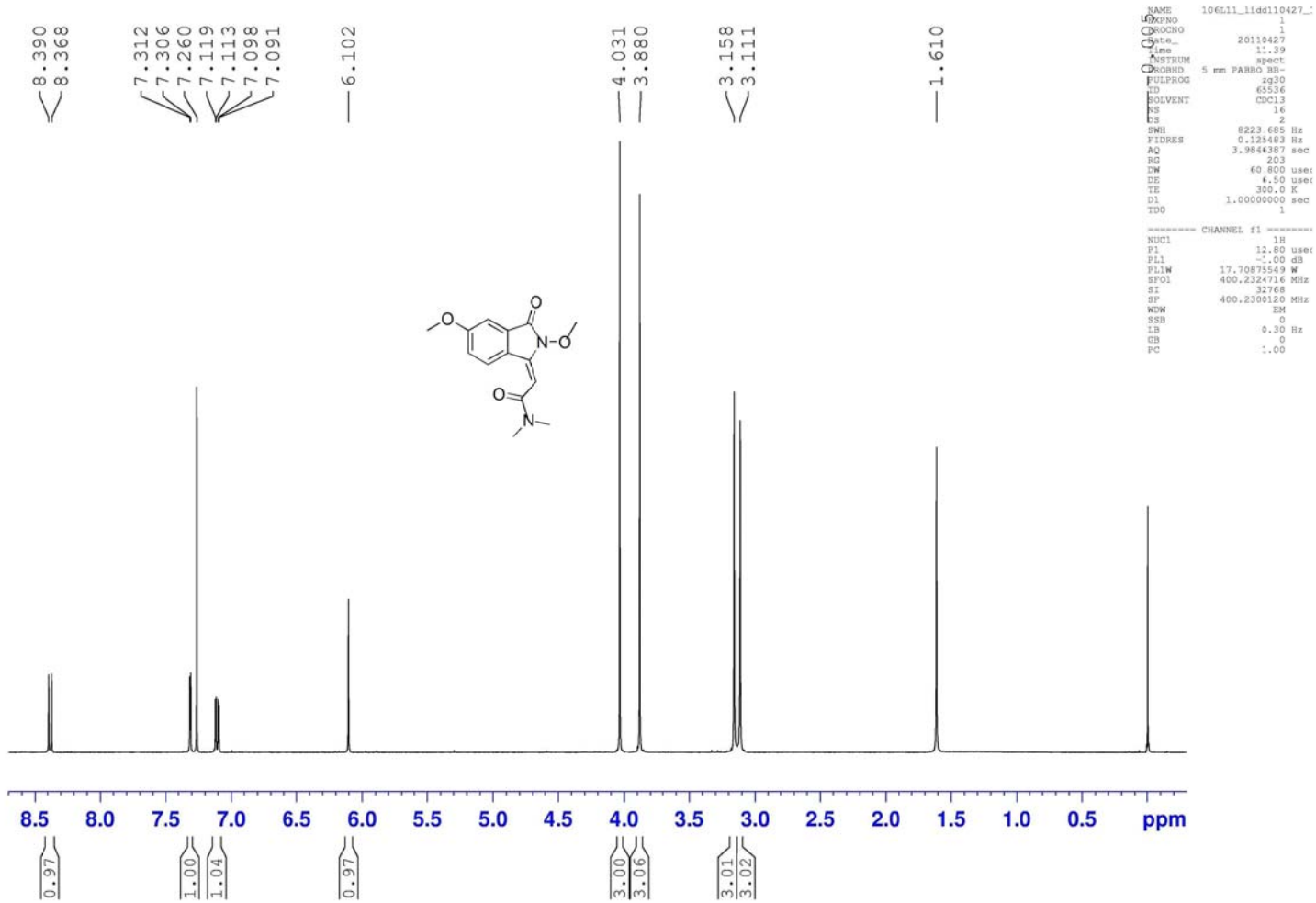



¹H NMR (400 MHz, CDCl₃) of compound 3cc
8.275
8.255
7.620
7.402
7.400
7.382
7.380
7.260
7.402
7.400
7.382
7.380
6.118
4.023
3.128
2.442
0.060
-0.012
7.40
ppm
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.99
0.96
1.03
0.97
3.00
6.01
3.00

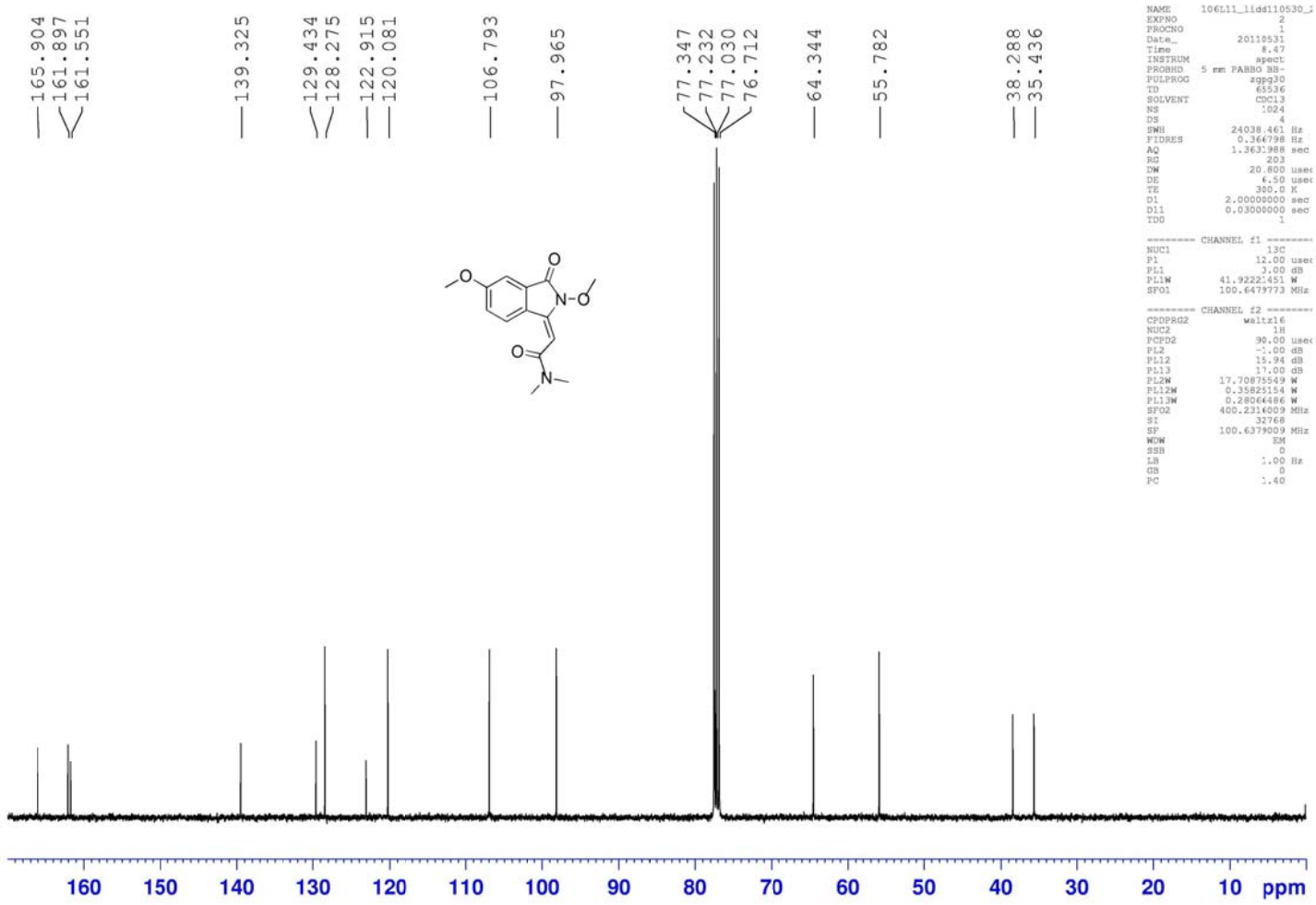
^{13}C NMR (400 MHz, $CDCl_3$) of compound 3cc



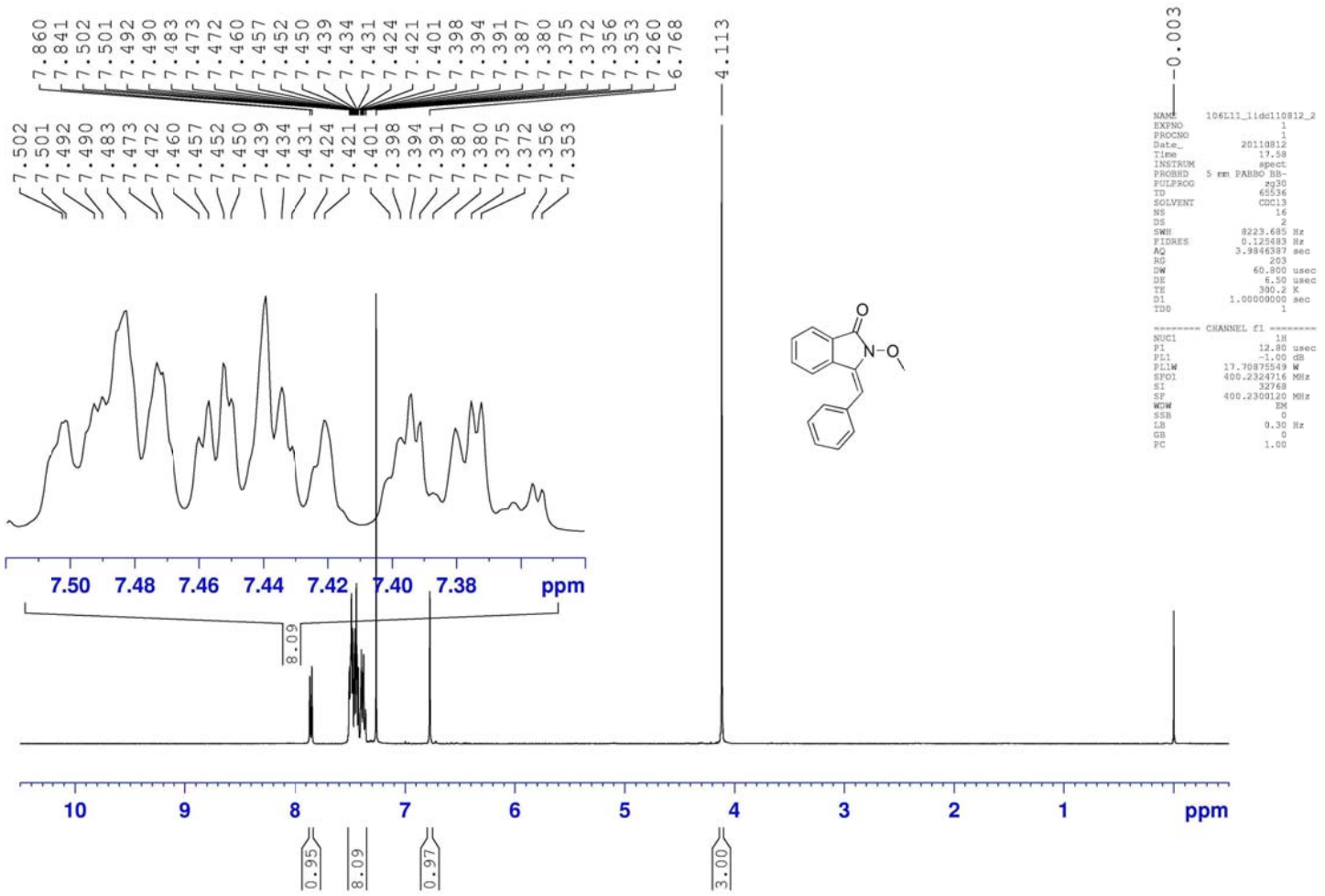
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3dc



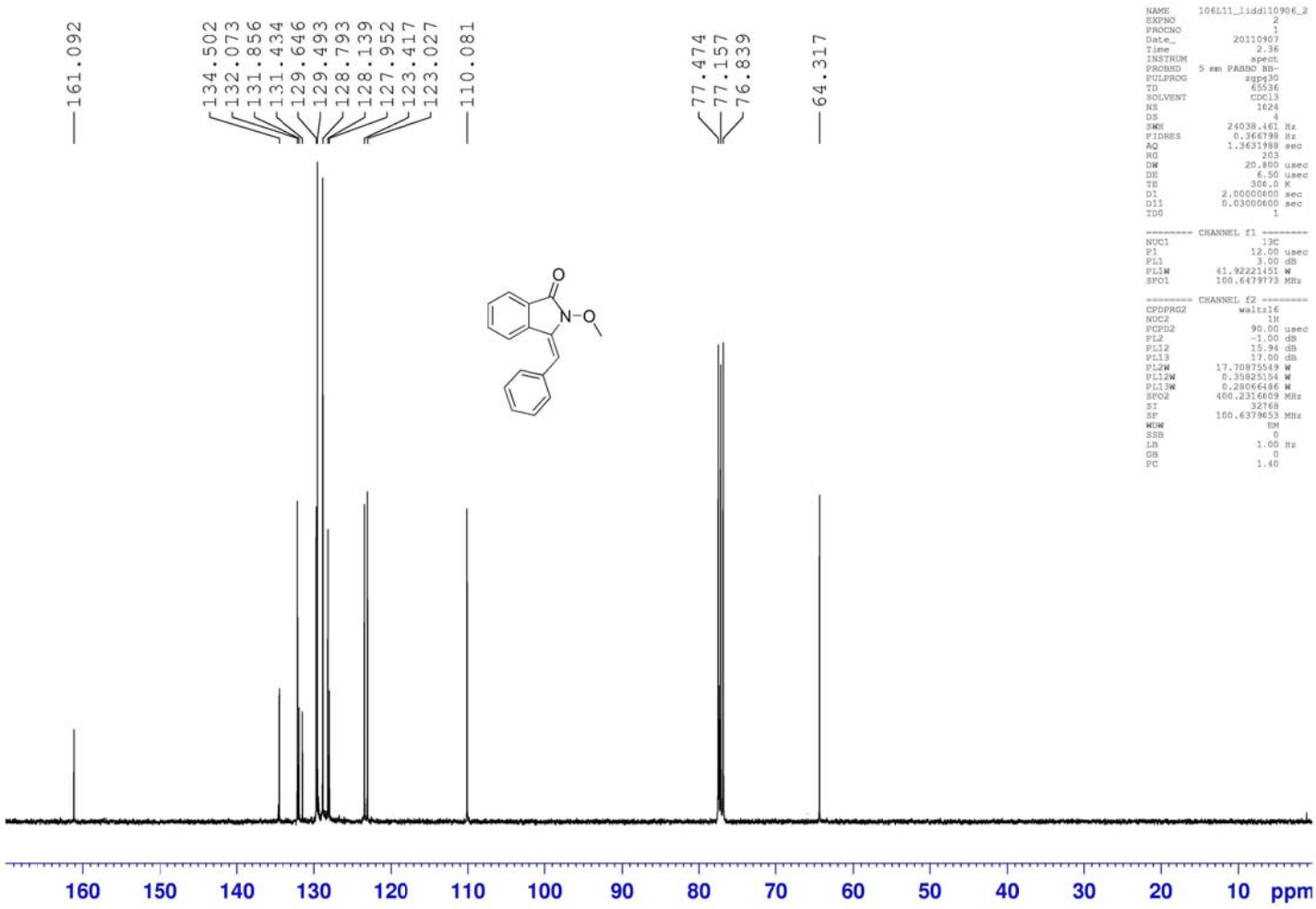
^{13}C NMR (400 MHz, $CDCl_3$) of compound 3dc



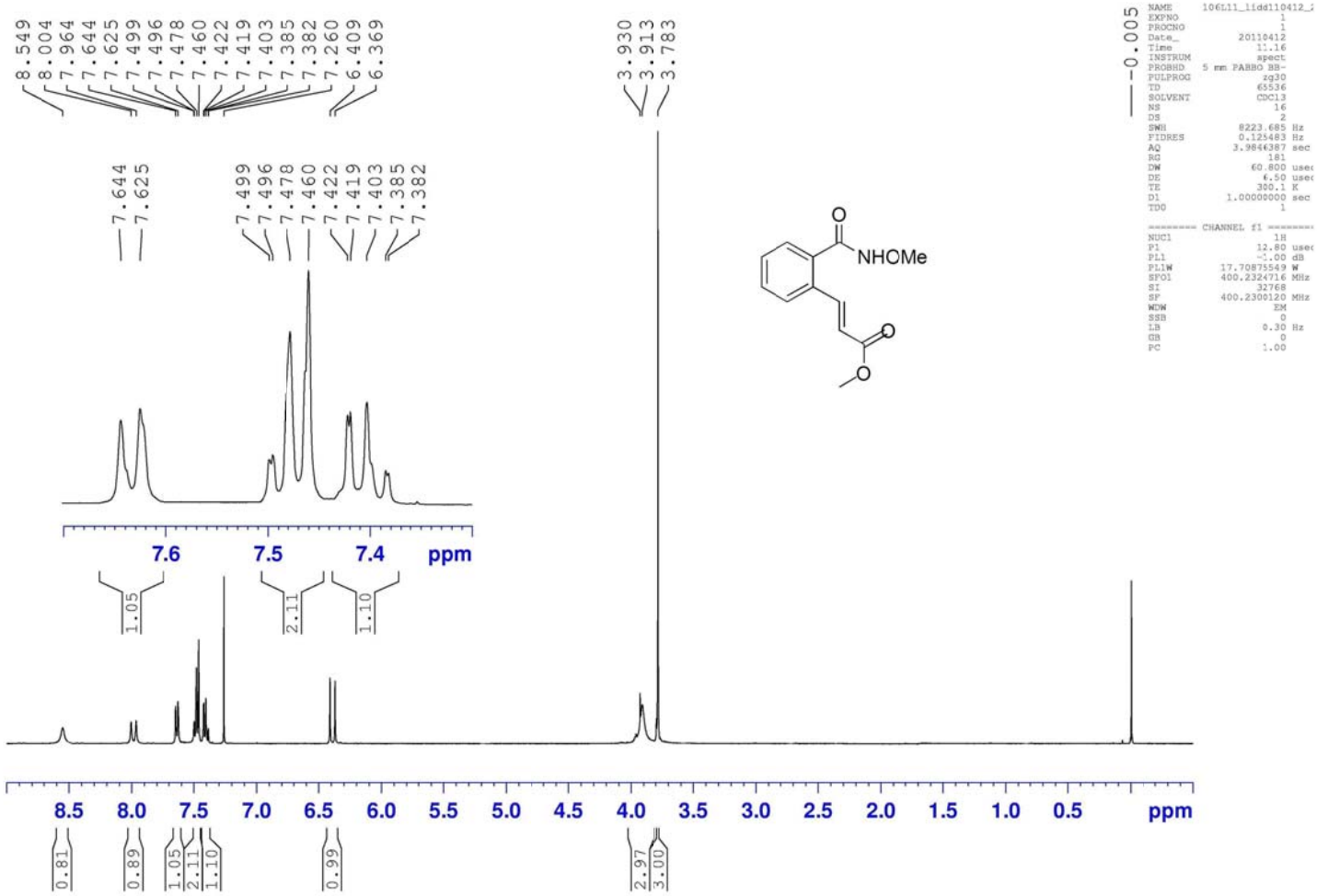
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3ad

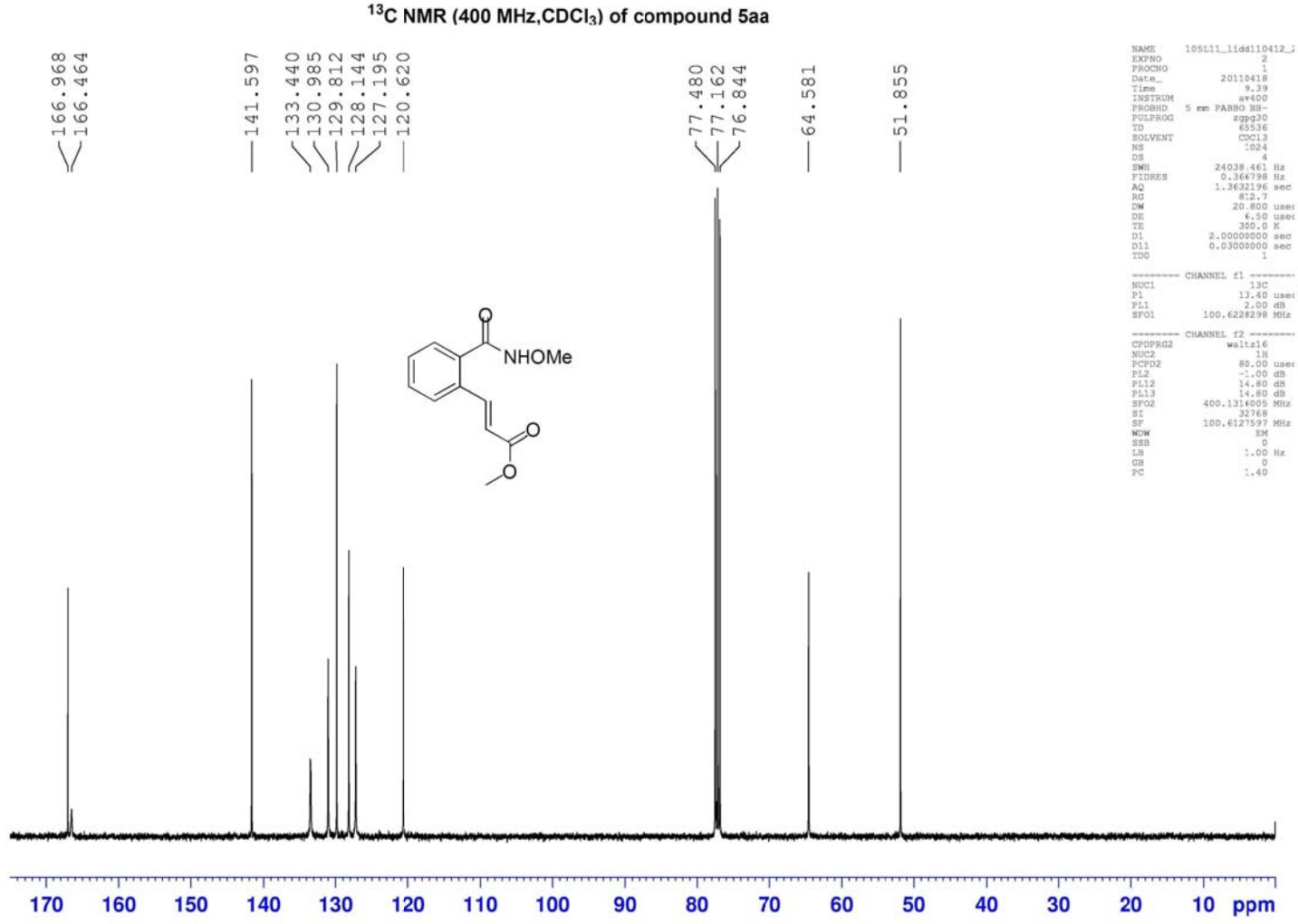


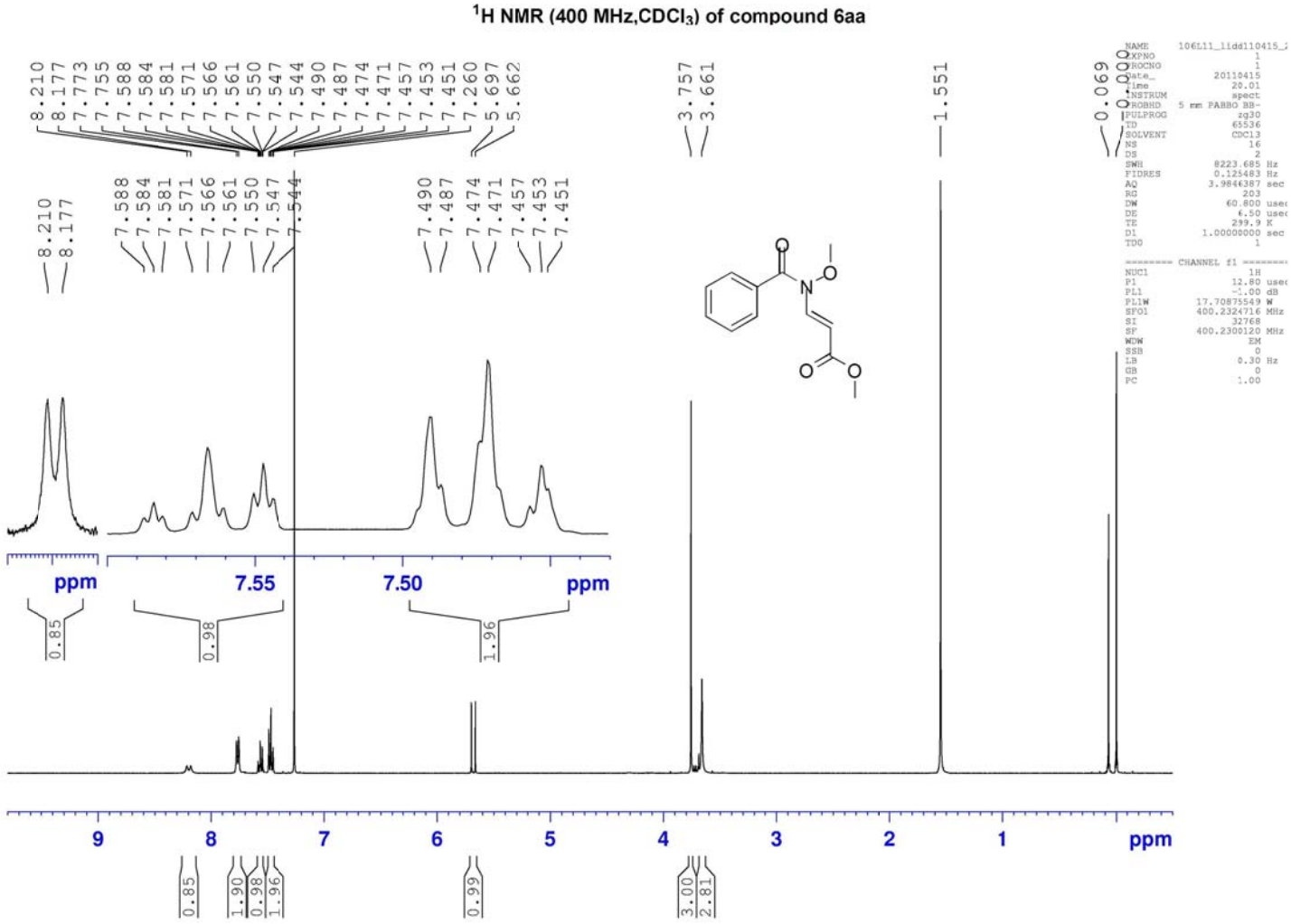
^{13}C NMR (400 MHz, $CDCl_3$) of compound 3ad



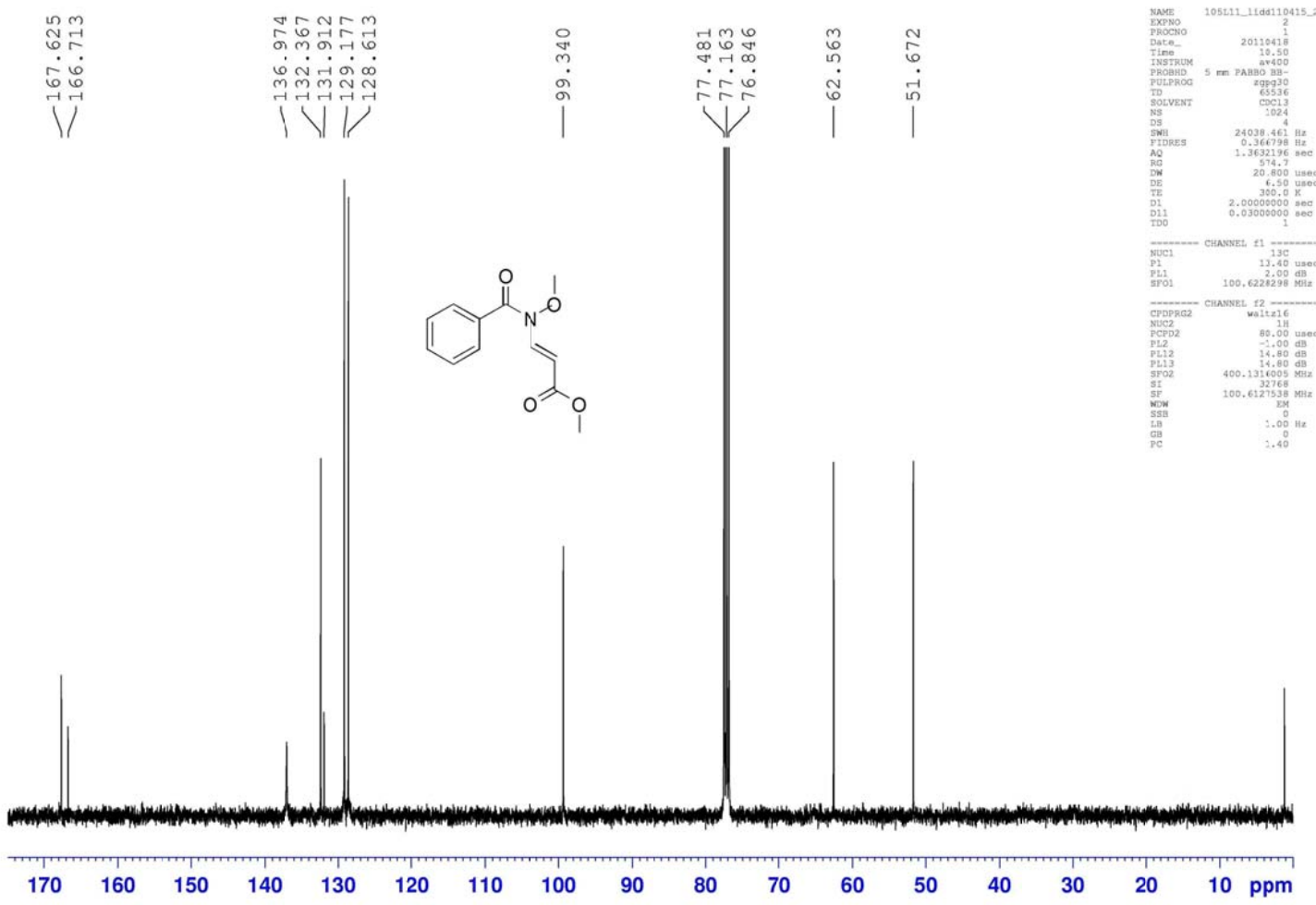
^{1}H NMR (400 MHz,$CDCl_3$) of compound 5aa

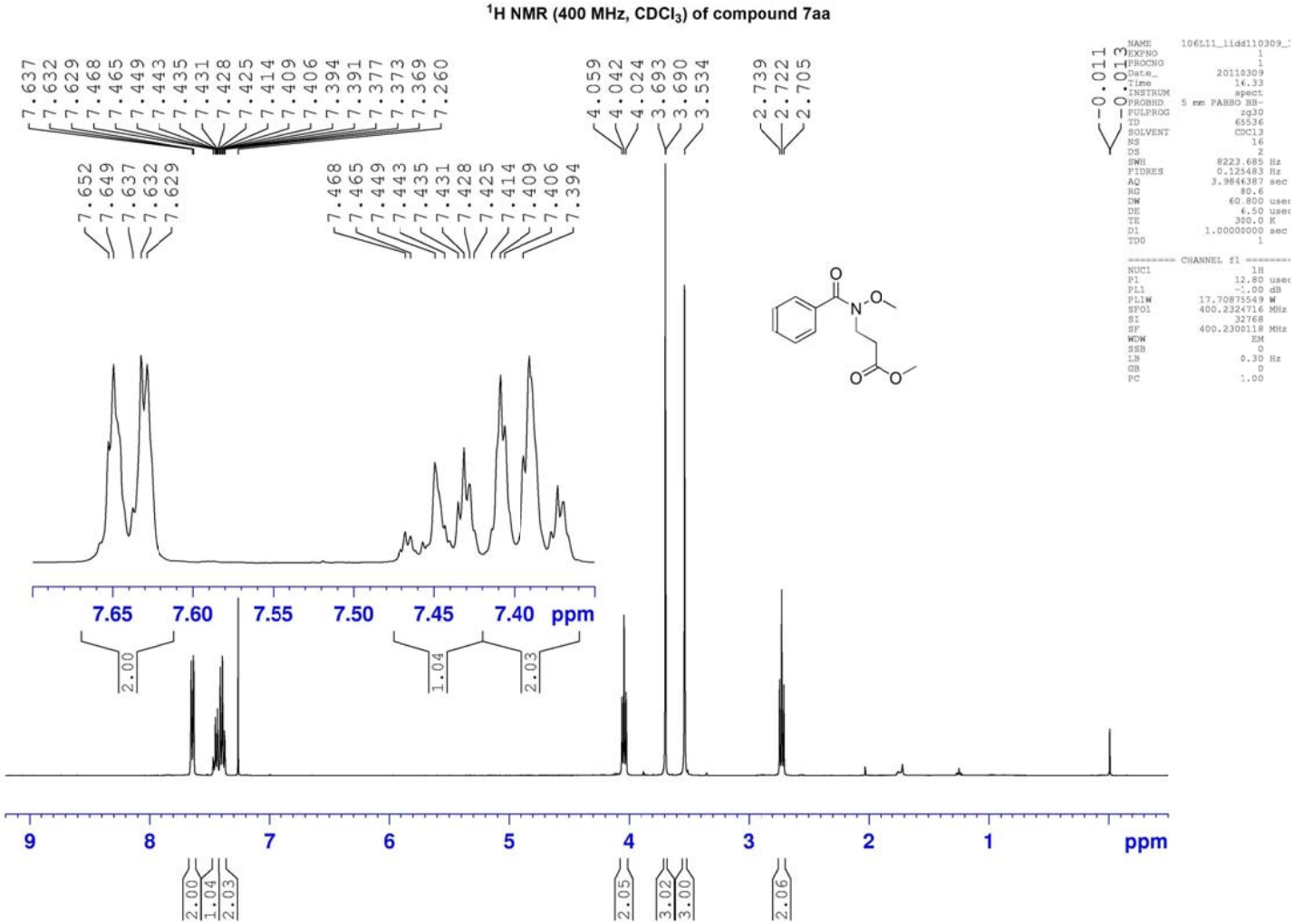




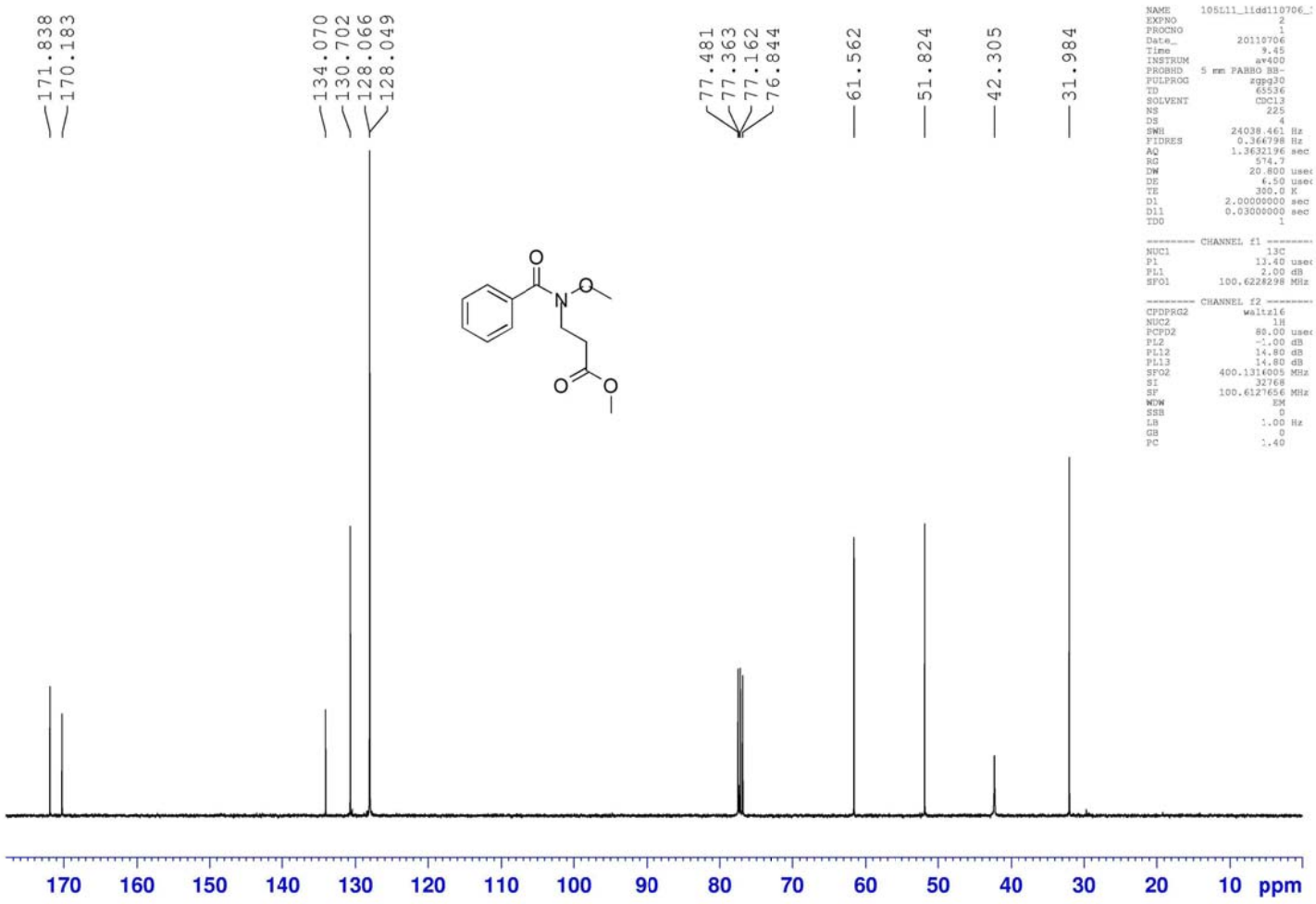


^{13}C NMR (400 MHz,$CDCl_3$) of compound 6aa

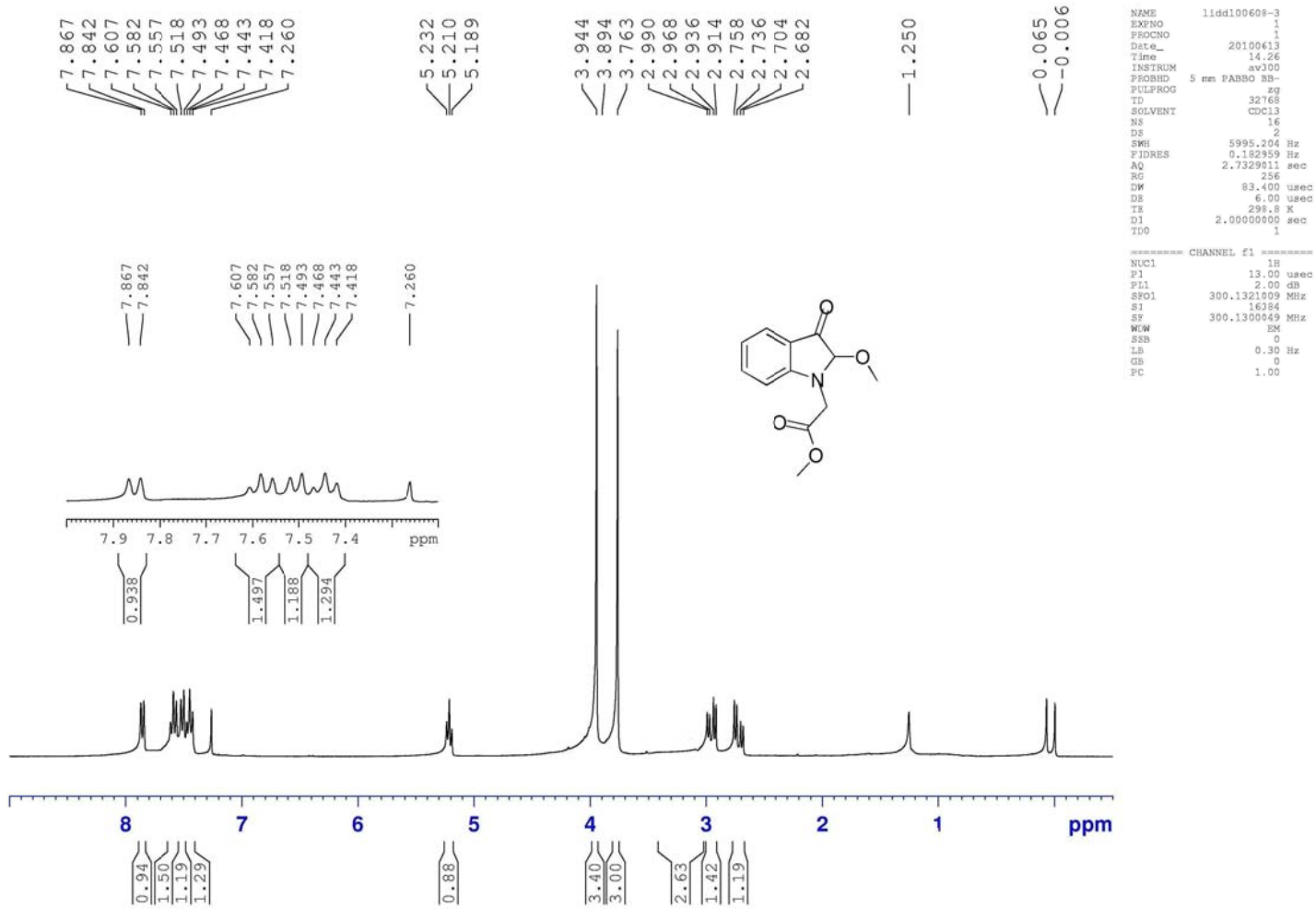




^{13}C NMR (400 MHz,$CDCl_3$) of compound 7aa



^{1}H NMR (300 MHz,$CDCl_3$) of compound 8aa

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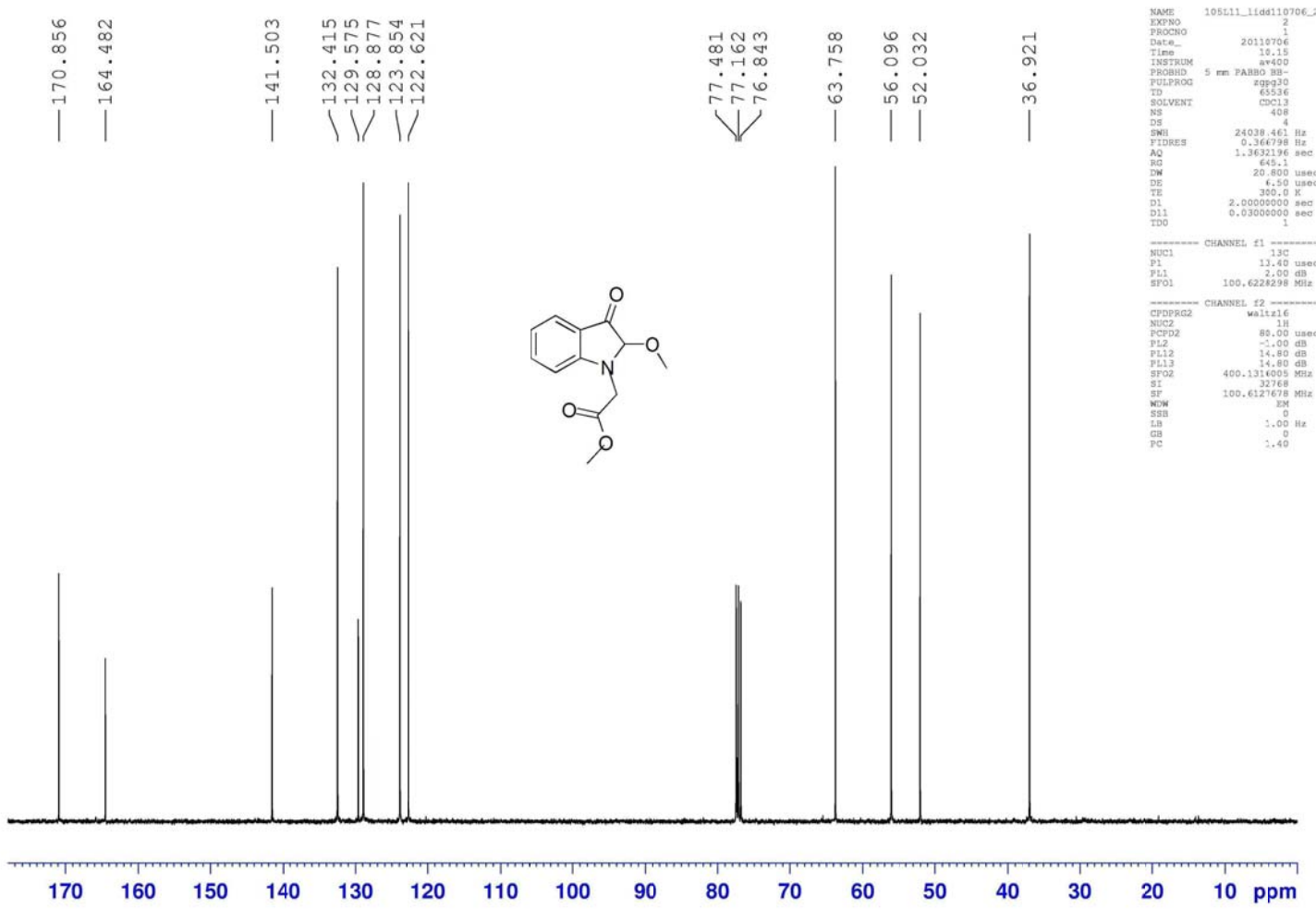
EXPNO                    1
PROCNO                   1
Date_             20100613
Time                 14.26
INSTRUM              av300
PROBHD   5 mm PABBO BB-
PULPROG                 zg
TD                   32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              5995.204 Hz
FIDRES           0.182959 Hz
AQ               2.7329011 sec
RG                     256
DW                83.400 usec
DE                 6.00 usec
TE                298.8 K
D1           2.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 13.00 usec
PL1                 2.00 dB
SFO1        300.1321009 MHz
SI                   16384
SF          300.1300049 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

^{13}C NMR (400 MHz,$CDCl_3$) of compound 8aa

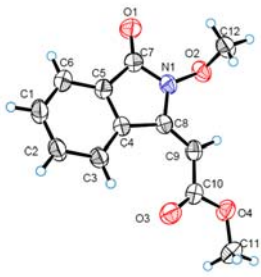


X-ray Single Crystallography

Selected crystals were centered on an Oxford Diffraction Xcalibur diffractometer equipped with a Sapphire 3 CCD detector and a graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The data collection routine, unit cell refinement, and data processing were carried out with the program CrysAlis.[1] Structures were solved by the direct method and refined by full-matrix least-squares methods with SHELXL-97 programs.[2]

[1] CrysAlis V1.171.34.44, Oxford Diffraction Ltd., Poland, 2010.
[2] G. M. Sheldrick, SHELXL-97, Program for Crystal StructureRefinement; Göttingen University, Göttingen, Germany, 1997.

Compound **3aa** was crystallized as needles from MeOH at room temperature for 3 days.



3aa

Table S1. Crystallographic data and refinement details for compound 3aa.

	3aa
CCDC number[a]	832992
Empirical formula	$C_{12}H_{11}O_4N$
Formula weight	233.22
Temperature	291(2)
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	8.0492 (6)
b/Å	19.9116(11)
c/Å	7.3009(5)
α/°	90.00
β/°	107.729 (8)
γ/°	90.00

Volume/Å^3	1114.56(13)
Z	4
ρ_{calc} mg/mm^3	1.390
Mu/mm^{-1}	0.888
F(000)	488
Crystal size	0.30 × 0.20 × 0.20
Theta range for data collection	4.44 to 67.37°
Index ranges	-9 ≤ h ≤ 9, -23 ≤ k ≤ 23, -8 ≤ l ≤ 6
Reflections collected	3702
Independent reflections	1950[R(int) = 0.0224]
Data/restraints/parameters	1950/0/157
Goodness-of-fit on F^2	1.087
Final R indexes [I>2σ (I)]	R_1 = 0.0380, wR_2 = 0.0931
Final R indexes [all data]	R_1 = 0.0464, wR_2 = 0.1052
Largest diff. peak/hole	0.201/-0.198

[a] The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and the deposition numbers are shown here. These data can be obtained free of charge from CCDC via www.ccdc.cam.ac.uk/data_request/cif.

Table S2 Atomic Coordinates (Å×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 3aa. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O4	8810.8(17)	3800.2(6)	11297.7(17)	56.8(4)
O1	8170.3(18)	326.4(6)	10906.9(19)	65.8(4)
O2	10319.4(16)	1460.4(6)	12209.7(16)	56(4)
O3	6534.3(19)	3470.3(6)	8830.9(18)	64.5(4)
C9	8560(2)	2665.8(8)	10737(2)	46.5(4)
N1	8692.1(18)	1466.9(7)	10866.3(19)	48.5(4)
C10	7817(2)	3330.2(9)	10145(2)	48(4)
C3	4707(2)	2175.5(9)	7625(2)	49.9(4)

C4	6104(2)	1837.4(8)	8875(2)	42.1(4)
C5	6026(2)	1138.9(8)	9039(2)	47.3(4)
C2	3270(2)	1804.3(10)	6602(3)	57.6(5)
C1	3192(2)	1115(10)	6809(3)	62.9(5)
C11	8283(3)	4486.6(9)	10834(3)	65.7(5)
C8	7819(2)	2066.8(8)	10151(2)	42.8(4)
C12	11611(2)	1282.7(11)	11290(3)	66.2(5)
C6	4584(2)	771.2(10)	8038(3)	57.8(5)
C7	7701(2)	892.7(8)	10363(2)	49(4)

Table S3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 3aa. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka×b×U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O4	57.6(8)	51.2(7)	56.3(7)	-6.6(5)	9.6(6)	-10.8(6)
O1	65.9(9)	52.5(7)	72.6(8)	11(6)	11.3(7)	2.4(6)
O2	43.2(7)	70.4(8)	44.6(6)	0(5)	-1.4(5)	4.9(6)
O3	63.6(8)	54.2(7)	60.8(8)	2.8(6)	-3(7)	-5.1(6)
C9	40.6(8)	54.6(10)	41(8)	-2.2(7)	7.6(7)	-5.9(7)
N1	38.4(7)	54(8)	45.9(7)	1.5(6)	2.1(6)	0.2(6)
C10	46.9(9)	54.2(9)	43.8(8)	-4.2(7)	14.9(8)	-10.7(8)
C3	41.6(9)	53.7(9)	51.2(9)	-4(7)	9.1(8)	1.2(7)
C4	37.5(8)	49.9(9)	39.1(7)	-2.3(6)	11.8(6)	-2.4(7)
C5	45(9)	50.1(9)	46.5(8)	1(7)	13.3(7)	-4.3(7)
C2	36.3(8)	67.6(12)	62(10)	-6(9)	4.7(8)	0.9(8)
C1	40.7(9)	71.1(12)	70.2(12)	-10(10)	6.8(9)	-11.3(9)
C11	77.9(13)	50.9(10)	69.3(12)	-4.8(9)	23.8(11)	-12.7(10)
C8	39.8(8)	52(9)	35.8(7)	0.1(6)	10.3(7)	-1.1(7)
C12	44.6(10)	72.5(12)	77.3(13)	-4.4(10)	12.3(10)	3.8(9)

C6	50.7(10)	54.8(10)	65.8(11)	-3.3(8)	14.5(9)	-11.2(8)
C7	48.4(9)	51(9)	47(9)	2.7(7)	13.6(8)	-1.1(8)

Table S4 Bond Lengths for 3aa.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O4	C10	1.347(2)	N1	C8	1.404(2)
O4	C11	1.441(2)	C3	C2	1.385(2)
O1	C7	1.217(2)	C3	C4	1.387(2)
O2	N1	1.3768(17)	C4	C5	1.399(2)
O2	C12	1.443(2)	C4	C8	1.483(2)
O3	C10	1.209(2)	C5	C6	1.378(2)
C9	C8	1.344(2)	C5	C7	1.483(2)
C9	C10	1.462(2)	C2	C1	1.384(3)
N1	C7	1.379(2)	C1	C6	1.385(3)

Table S5 Bond Angles for 3aa.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	O4	C11	115.84(14)	C6	C5	C4	122.36(16)
N1	O2	C12	109.55(12)	C6	C5	C7	128.41(16)
C8	C9	C10	127.39(16)	C4	C5	C7	109.21(14)
O2	N1	C7	122.02(13)	C1	C2	C3	121.90(17)
O2	N1	C8	122.20(13)	C2	C1	C6	120.43(16)
C7	N1	C8	115.03(14)	C9	C8	N1	120.91(15)
O3	C10	O4	122.47(16)	C9	C8	C4	135.34(16)
O3	C10	C9	128.11(16)	N1	C8	C4	103.67(13)
O4	C10	C9	109.42(14)	C5	C6	C1	117.73(18)
C2	C3	C4	118.20(17)	O1	C7	N1	125.76(17)
C3	C4	C5	119.36(15)	O1	C7	C5	130.52(17)
C3	C4	C8	132.57(15)	N1	C7	C5	103.72(14)

C5	C4	C8	108.05(13)

Table S6 Torsion Angles for 3aa.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C12	O2	N1	C7	85.36(19)	O2	N1	C8	C4	-176.26(13)
C12	O2	N1	C8	-105.06(17)	C7	N1	C8	C4	-6.01(18)
C11	O4	C10	O3	-1.8(2)	C3	C4	C8	C9	9.5(3)
C11	O4	C10	C9	177.33(14)	C5	C4	C8	C9	-172.03(18)
C8	C9	C10	O3	-12.0(3)	C3	C4	C8	N1	-173.83(16)
C8	C9	C10	O4	168.90(16)	C5	C4	C8	N1	4.64(17)
C2	C3	C4	C5	0.9(2)	C4	C5	C6	C1	1.2(3)
C2	C3	C4	C8	179.18(16)	C7	C5	C6	C1	-176.97(17)
C3	C4	C5	C6	-1.8(2)	C2	C1	C6	C5	0.3(3)
C8	C4	C5	C6	179.52(16)	O2	N1	C7	O1	-5.7(3)
C3	C4	C5	C7	176.67(14)	C8	N1	C7	O1	-175.97(16)
C8	C4	C5	C7	-2.03(17)	O2	N1	C7	C5	175.08(13)
C4	C3	C2	C1	0.6(3)	C8	N1	C7	C5	4.81(19)
C3	C2	C1	C6	-1.2(3)	C6	C5	C7	O1	-2.3(3)
C10	C9	C8	N1	-179.34(15)	C4	C5	C7	O1	179.37(18)
C10	C9	C8	C4	-3.1(3)	C6	C5	C7	N1	176.87(17)
O2	N1	C8	C9	1.0(2)	C4	C5	C7	N1	-1.46(18)
C7	N1	C8	C9	171.26(14)					

Table S7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 3aa.

Atom	*x*	*y*	*z*	U(eq)
H9	9671	2657	11619	56

H3	4736	2639	7479	60
H2	2329	2024	5750	69
H1	2198	881	6118	76
H11A	8331	4590	9567	99
H11C	9053	4781	11750	99
H11B	7112	4547	10878	99
H12B	11550	1592	10263	99
H12A	11390	836	10781	99
H12C	12751	1302	12213	99
H6	4548	308	8183	69