Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Copper-catalyzed aerobic double functionalization of benzylic C(sp^3)–H bonds for the synthesis of 3-hydroxyisoindolinones

Kanako Nozawa-Kumada,* Yuta Matsuzawa, Kanako Ono, Masanori Shigeno and Yoshinori Kondo*

Graduate School of Pharmaceutical Sciences, Tohoku University, 6-3, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

*E-mail: kanako.kumada.d1@tohoku.ac.jp, yoshinori.kondo.a7@tohoku.ac.jp

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1. General comments

Unless otherwise noted, reactions were carried out under N_2 atmosphere. Melting points were measured with a Yazawa micro melting point apparatus and uncorrected. IR spectra were recorded on a SHIMADZU IRAffinity. ^{1}H-NMR spectra were recorded on a JEOL JNM-AL400 (400 MHz) spectrometer or a JEOL ECA600 (600 MHz) spectrometer. Chemical shifts are expressed in δ (parts per million, ppm) values and coupling constants are expressed in hertz (Hz). ^{1}H NMR spectra were referenced to tetramethylsilane as an internal standard or to a solvent signal ($CDCl_3$: 7.26 ppm, DMSO-d_6: 2.49 ppm, CD_3OD: 3.30 ppm). ^{13}C NMR spectra were referenced to a solvent signal ($CDCl_3$: 77.0 ppm, DMSO-d_6: 39.5 ppm, CD_3OD: 49.0 ppm, acetone-d_6: 29.8 ppm). ^{19}F NMR spectra were referenced to 4-fluorotoluene as an internal standard (−118.0 ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, dd, = double doublet, dt = double triplet, td = triple doublet, m = multiplet. Low and high resolution mass spectra (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX 303 and JMS-700/JMS-T 100 GC spectrometer. Gel permeation chromatography (GPC) was conducted with a Recycling Preparative HPLC LC-9210 (Japan Analytical Industry, Co. Ltd.).

2. Materials

Materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used as received. Flash column chromatography was performed with Kanto silica gel 60 N (spherical, neutral, 70−230 mesh).

3. Preparation of starting materials

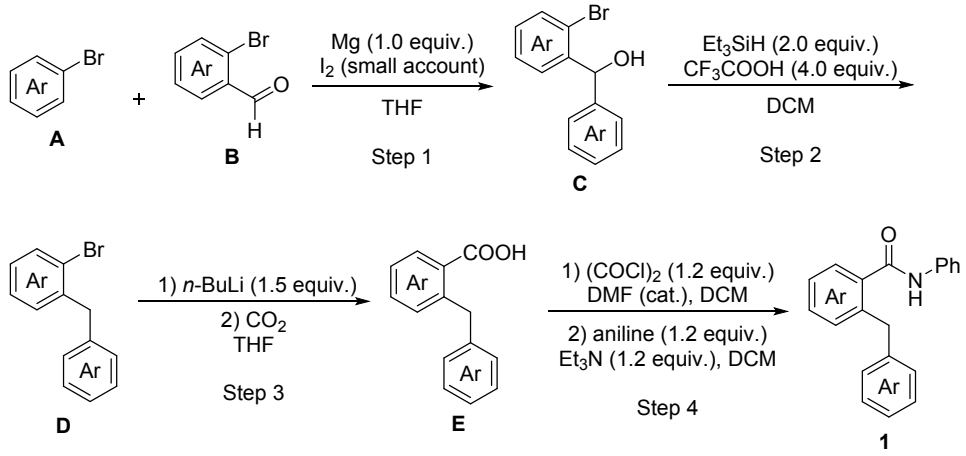
1r[1] was prepared according to the literature procedure. Other starting materials were prepared according to the following methods.

Method A[2]

To a solution of 2-alkylbenzoic acid (1.0 equiv.) in dry DCM (0.25 M) was added $(COCl)_2$ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction mixture was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid chloride. To a solution of acid chloride in dry DCM (0.25 M) were added aniline derivative (1.2 equiv.) and triethylamine (1.2 equiv.) dropwise at 0 °C, and the mixture was stirred at rt overnight. The reaction was diluted with 1M HCl aq. (10 mL) and extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by recrystallization to afford the corresponding amide

compound.

Method B[1,2]



Step 1: A solution of aryl bromide **A** (1.2 equiv.) in THF (0.25 M) was added slowly to the mixture of Mg (1.0 equiv.) with small amount of I_2 (0.01 equiv.), and the mixture was stirred for 1 h. Then, a solution of substrate **B** (1.0 equiv.) in THF (0.10 M) was added to the reaction mixture slowly. The resultant mixture was stirred at rt until the reaction was completed as monitored by TLC. The reaction mixture was slowly diluted with sat. NH_4Cl aq. (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography to give the alcohol **C**.

Step 2: To a solution of the substrate **C** (1.0 equiv.) in DCM (0.20 M) was added CF_3CO_2H (4.0 equiv.) dropwise at 0 °C. After stirred for 10 min, Et_3SiH (2.0 equiv.) was added dropwise, and the resulting mixture was stirred at rt overnight. The solvent was concentrated under reduced pressure, and the residue was purified by SiO_2 column chromatography to give the substrate **D**.

Step 3: To a solution of compound **D** (1.0 equiv.) in THF (0.20 M) was added *n*-BuLi (1.6 M, 1.5 equiv.) dropwise at −78 °C. The reaction mixture was stirred at −78 °C for 1 h. Then anhydrous CO_2 was bubbled through the mixture for 30 min. The reaction mixture was allowed to warm to rt for 30 min. The reaction was quenched with H_2O (10 mL), alkalized with 1M NaOH aq. to pH 12–14, and washed with Et_2O (10 mL). The resulting aqueous layer was acidified with HCl aq. to pH 1–2, and extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), then dried over Na_2SO_4 and concentrated under reduced pressure to give the crude carboxylic acid **E**, which was used in the next step without further purification.

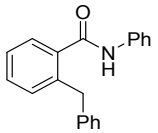
Step 4: To a solution of compound **E** (1.0 equiv.) in dry DCM (0.25 M) was added $(COCl)_2$ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid

chloride. To a solution of acid chloride in dry DCM (0.25 M) were added aniline (1.2 equiv.) and triethylamine (1.2 equiv.) dropwise at 0 °C, and stirred at rt overnight. The reaction was diluted with 1M HCl aq. (10 mL) and extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na_2SO_4 and concentrated under reduced pressure. The crude material was then purified by recrystallization to afford the corresponding amide compound.

Method C[1]

To a solution of 2-benzylbenzoic acid (1.0 equiv.) in dry DCM (0.25 M) was added $(COCl)_2$ (1.2 equiv.) dropwise at 0 °C, followed by a catalytic amount of DMF (3 drops). The reaction was allowed to stir at rt until completion. The solvent was then removed to afford the corresponding crude acid chloride. A solution of the acid chloride in EtOAc (1.0 M) was added dropwise to the mixture of $NH_2OR{\cdot}HCl$ (1.2 equiv.) and K_2CO_3 (2.0 equiv.) in EtOAc (0.25 M) and H_2O (0.50 M) at 0 °C, and stirred at rt overnight. The reaction mixture was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by SiO_2 column chromatography to afford the corresponding amide.

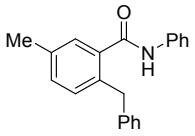
2-Benzyl-*N*-phenylbenzamide (1a)



Prepared according to Method A, 1054.7 mg (74%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 123–125 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.54 (1H, d, J = 7.8 Hz), 7.43–7.37 (3H, m), 7.33–7.29 (4H, m), 7.27–7.23 (3H, m), 7.20–7.16 (3H, m), 7.12 (1H, t, J = 7.3 Hz), 4.24 (2H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.9, 140.5, 138.6, 137.7, 136.8, 131.2, 130.3, 128.9, 128.8, 128.6, 127.4, 126.6, 126.3, 124.4, 119.9, 38.9; LRMS (EI) *m/z*: 287 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{17}NO$: 287.1310, found: 287.1323; IR (neat): 3328, 3026, 1654, 1597, 1525, 1495, 1436, 1320, 744, 722 cm^{-1}.

2-Benzyl-5-methyl-*N*-phenylbenzamide (1b)

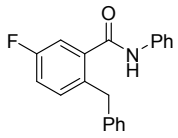


Prepared according to Method B, 843.9 mg (31% over 4 steps, 10.0 mmol scale), recrystallized from

DCM/hexane, colorless needles, mp. 164–165 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.37–7.34 (3H, m), 7.31–7.28 (3H, m), 7.25–7.21 (3H, m), 7.18–7.15 (4H, m), 7.10 (1H, t, J = 7.6 Hz), 4.18 (2H, s), 2.36 (3H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 168.0, 140.8, 137.7, 136.7, 136.4, 135.3, 131.2, 131.1, 128.9, 128.7, 128.6, 128.1, 126.2, 124.4, 119.8, 38.6, 20.9; LRMS (EI) *m/z*: 301 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{19}NO$: 301.1467, found: 301.1470; IR (neat): 3247, 3028, 1652, 1593, 1501, 1436, 1326, 752, 731 cm^{-1}.

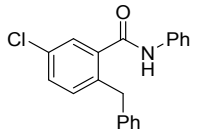
2-Benzyl-5-fluoro-*N*-phenylbenzamide (1c)



Prepared according to Method B, 689.6 mg (23% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 133–135 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.47 (1H, s), 7.34 (2H, d, J = 8.0 Hz), 7.28 (2H, t, J = 7.7 Hz), 7.24–7.16 (5H, m), 7.12–7.05 (4H, m), 4.14 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 166.5, 161.0 (C–F, $^{1}J_{C-F}$ = 247.7 Hz), 140.3, 138.2 (C–F, $^{3}J_{C-F}$ = 5.8 Hz), 137.4, 134.2 (C–F, $^{4}J_{C-F}$ = 2.9 Hz), 132.9, 132.8, 128.9, 128.7 (C–F, $^{3}J_{C-F}$ = 5.8 Hz), 126.4, 124.7, 120.0, 117.2 (C–F, $^{2}J_{C-F}$ = 21.6 Hz), 114.5 (C–F, $^{2}J_{C-F}$ = 23.0 Hz), 38.2; ^{19}F NMR (565 MHz, $CDCl_3$/TMS) δ (ppm): –114.6; LRMS (EI) *m/z*: 305 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{16}FNO$: 305.1216, found: 305.1194; IR (neat): 3239, 3072, 1653, 1595, 1493, 1442, 1328, 751, 731 cm^{-1}.

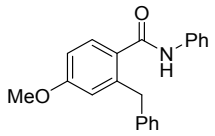
2-Benzyl-5-chloro-*N*-phenylbenzamide (1d)



Prepared according to Method B, 81.4 mg (3% over 4 steps, 7.5 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 145–147 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.49 (1H, s), 7.37–7.35 (3H, m), 7.30 (2H, t, J = 7.8 Hz), 7.25–7.17 (5H, m), 7.14–7.11 (3H, m), 4.17 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 166.4, 140.0, 138.3, 137.4, 137.2, 132.6, 132.5, 130.4, 129.0, 128.8, 128.7, 127.5, 126.5, 124.8, 120.0, 38.5; LRMS (EI) *m/z*: 321 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{16}{}^{35}ClNO$: 321.0920, found: 321.0924; IR (neat): 3247, 2962, 1650, 1595, 1495, 1442, 1327, 749, 731 cm^{-1}.

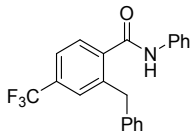
2-Benzyl-4-methoxy-*N*-phenylbenzamide (1e)



Prepared according to Method B, 602.6 mg (19% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 165–167 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.51 (1H, d, J = 8.3 Hz), 7.36–7.25 (7H, m), 7.20–7.18 (3H, m), 7.10 (1H, t, J = 7.3 Hz), 6.81–6.78 (2H, m), 4.23 (2H, s), 3.80 (3H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.6, 161.0, 140.9, 140.4, 137.9, 129.4, 129.3, 128.9, 128.8, 128.7, 126.3, 124.3, 119.8, 117.0, 111.5, 55.3, 39.2; LRMS (EI) *m/z*: 317 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{19}NO_2$: 317.1416, found: 317.1407; IR (neat): 3291, 3030, 1645, 1595, 1521, 1494, 1436, 1244, 753, 721 cm^{-1}.

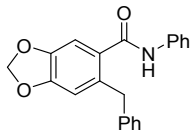
2-Benzyl-*N*-phenyl-4-(trifluoromethyl)benzamide (1f)



Prepared according to Method B, 334.6 mg (9% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 188–192 °C.

^{1}H NMR (600 MHz, CD_3OD) δ (ppm): 7.64–7.60 (2H, m), 7.57–7.53 (3H, m), 7.32 (2H, t, J = 7.9 Hz), 7.21–7.12 (6H, m), 4.24 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, CD_3OD) δ (ppm): 169.6, 142.0, 141.9, 141.0, 139.5, 132.9 (C–F, $^{2}J_{C–F}$ = 32.5 Hz), 130.2, 129.8, 129.6, 129.2, 128.2 (C–F, $^{3}J_{C–F}$ = 3.8 Hz), 127.5, 125.8, 125.3 (C–F, $^{1}J_{C–F}$ = 271.2 Hz), 124.3 (C–F, $^{3}J_{C–F}$ = 3.8 Hz), 121.9, 39.6; ^{19}F NMR (565 MHz, CD_3OD): −61.5; LRMS (EI) *m/z*: 355 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{16}F_3NO$: 355.1184, found: 355.1178; IR (neat): 3290, 3042, 1651, 1598, 1528, 1322, 1152, 1097, 752, 732 cm^{-1}.

6-Benzyl-*N*-phenylbenzo[*d*][1,3]dioxole-5-carboxamide (1g)

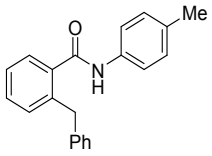


Prepared according to Method B, 666.5 mg (27% over 4 steps, 7.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 180–185 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.34–7.26 (7H, m), 7.21 (1H, t, J = 7.2 Hz), 7.18 (2H, d, J = 6.8 Hz), 7.10 (1H, t, J = 7.2 Hz), 7.04 (1H, s), 6.73 (1H, s), 6.00 (2H, s), 4.15 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.2, 149.3, 146.2, 140.6, 137.7, 133.2, 130.1, 129.0, 128.7,

128.6, 126.4, 124.4, 119.7, 111.2, 107.8, 101.6, 38.8; LRMS (EI) *m/z*: 331 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{17}NO_3$: 331.1208, found: 331.1204; IR (neat): 3236, 3056, 1639, 1594, 1494, 1446, 1035, 751, 731 cm^{-1}.

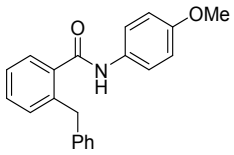
2-Benzyl-*N*-(*p*-tolyl)benzamide (1h)



Prepared according to Method A, 458.0 mg (51%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 149–151 °C.

^1H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.51 (1H, d, *J* = 7.4 Hz), 7.40 (1H, t, *J* = 7.4 Hz), 7.30–7.23 (7H, m), 7.19–7.16 (3H, m), 7.11 (2H, d, *J* = 8.2 Hz), 4.22 (2H, s), 2.31 (3H, s); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.8, 140.6, 138.5, 137.0, 135.1, 134.1, 131.2, 130.3, 129.4, 128.8, 128.6, 127.4, 126.6, 126.3, 119.9, 39.0, 20.9; LRMS (EI) *m/z*: 301 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{19}NO$: 301.1467, found: 301.1476; IR (neat): 3230, 3027, 1643, 1599, 1510, 1325, 1090, 810, 738 cm^{-1}.

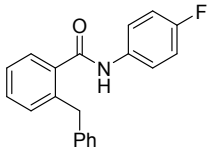
2-Benzyl-*N*-(4-methoxyphenyl)benzamide (1i)



Prepared according to Method A, 782.0 mg (84%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 148–150 °C.

^1H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.52 (1H, d, *J* = 7.3 Hz), 7.40 (1H, t, *J* = 7.3 Hz), 7.31–7.16 (10H, m), 6.85 (2H, d, *J* = 9.2 Hz), 4.23 (2H, s), 3.80 (3H, s); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.7, 156.5, 140.7, 138.6, 136.9, 131.2, 130.8, 130.3, 128.8, 128.6, 127.4, 126.6, 126.3, 121.7, 114.1, 55.5, 39.0; LRMS (EI) *m/z*: 317 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{19}NO_2$: 317.1416, found: 317.1424; IR (neat): 3276, 3025, 1647, 1512, 1248, 823, 734 cm^{-1}.

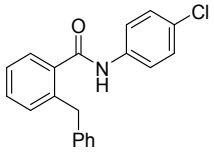
2-Benzyl-*N*-(4-fluorophenyl)benzamide (1j)



Prepared according to Method A, 733.7 mg (87%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 124–126 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.53 (1H, d, J = 7.6 Hz), 7.43 (1H, t, J = 7.6 Hz), 7.33–7.30 (4H, m), 7.26–7.24 (2H, m), 7.20–7.15 (4H, m), 7.00 (2H, t, J = 8.6 Hz), 4.23 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.9, 159.4 (C–F, $^1J_{C-F}$ = 244.8 Hz), 140.5, 138.5, 136.6, 133.7 (C–F, $^4J_{C-F}$ = 2.9 Hz), 131.2, 130.4, 128.8, 128.5, 127.3, 126.5, 126.2, 121.7 (C–F, $^3J_{C-F}$ = 7.2 Hz), 115.5 (C–F, $^2J_{C-F}$ = 23.0 Hz), 38.9; ^{19}F NMR (565 MHz, $CDCl_3$/TMS) δ (ppm): –119.0; LRMS (EI) *m/z*: 305 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{16}FNO$: 305.1216, found: 305.1223; IR (neat): 3286, 1650, 1505, 1403, 1210, 834, 741 cm^{-1}.

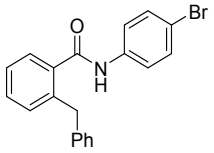
2-Benzyl-*N*-(4-chlorophenyl)benzamide (1k)



Prepared according to Method A, 540.9 mg (55%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 143–145 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.50 (1H, d, J = 6.4 Hz), 7.42 (1H, t, J = 7.4 Hz), 7.30–7.23 (9H, m), 7.18 (1H, t, J = 7.4 Hz), 7.12 (2H, d, J = 7.3 Hz), 4.20 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.8, 140.5, 138.4, 136.6, 136.2, 131.4, 130.6, 129.4, 128.9, 128.8, 128.7, 127.5, 126.7, 126.4, 121.0, 39.0; LRMS (EI) *m/z*: 321 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{16}{}^{35}ClNO$: 321.0920, found: 321.0916; IR (neat): 3301, 1651, 1590, 1505, 1396, 1308, 820, 745 cm^{-1}.

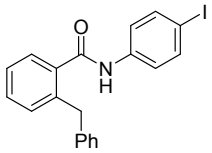
2-Benzyl-*N*-(4-bromophenyl)benzamide (1l)



Prepared according to Method A, 1010.2 mg (90%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 136–138 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.51 (1H, d, J = 6.4 Hz), 7.44–7.39 (3H, m), 7.32–7.24 (7H, m), 7.19–7.17 (1H, m), 7.14 (2H, d, J = 6.4 Hz), 4.21 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.8, 140.5, 138.4, 136.7, 136.6, 131.9, 131.4, 130.6, 128.8, 128.7, 127.5, 126.7, 126.4, 121.3, 117.0, 39.1; LRMS (EI) *m/z*: 365 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{16}{}^{79}BrNO$: 365.0415, found: 365.0423; IR (neat): 3296, 1653, 1586, 1506, 1391, 817, 745, 703 cm^{-1}.

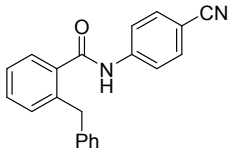
2-Benzyl-*N*-(4-iodophenyl)benzamide (1m)



Prepared according to Method A, 977.2 mg (82%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 163–165 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.59 (2H, d, J = 6.4 Hz), 7.51 (1H, d, J = 7.3 Hz), 7.43 (1H, t, J = 7.3 Hz), 7.31 (2H, t, J = 7.3 Hz), 7.25–7.24 (3H, m), 7.19–7.17 (1H, m), 7.15–7.12 (4H, m), 4.21 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.8, 140.5, 138.4, 137.9, 137.4, 136.6, 131.4, 130.6, 128.74, 128.68, 127.5, 126.7, 126.4, 121.6, 87.6, 39.1; LRMS (EI) *m/z*: 413 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{16}INO$: 413.0277, found: 413.0304; IR (neat): 3296, 3021, 1647, 1584, 1506, 1388, 817, 739 cm^{-1}.

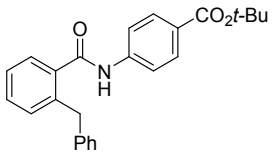
2-Benzyl-*N*-(4-cyanophenyl)benzamide (1n)



Prepared according to Method A, 653.1 mg (70%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 149–152 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.59–7.43 (7H, m), 7.33 (2H, t, J = 6.9 Hz), 7.26–7.17 (3H, m), 7.12 (2H, d, J = 7.3 Hz), 4.20 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 168.1, 141.7, 140.3, 138.4, 136.0, 133.1, 131.5, 130.9, 128.70, 128.68, 127.6, 126.8, 126.5, 119.5, 118.7, 107.2, 39.1; LRMS (EI) *m/z*: 312 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{16}N_2O$: 312.1263, found: 312.1257; IR (neat): 3280, 2226, 1657, 1592, 1508, 1405, 1322, 838, 731 cm^{-1}.

***tert*-Butyl 4-(2-benzylbenzamido)benzoate (1o)**

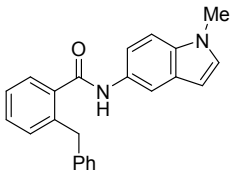


Prepared according to Method A, 555.6 mg (60%, 2.5 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 174–176 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.92 (2H, d, J = 8.3 Hz), 7.54 (1H, d, J = 7.4 Hz), 7.44

–7.32 (6H, m), 7.26–7.14 (5H, m), 4.22 (2H, s), 1.59 (9H, s); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.9, 165.2, 141.3, 140.5, 138.4, 136.6, 131.5, 130.7, 130.5, 128.74, 128.71, 127.7, 127.5, 126.8, 126.4, 118.7, 80.9, 39.1, 28.2; LRMS (EI) *m/z*: 387 (M^+); HRMS (EI-EB) Calcd. for $C_{25}H_{25}NO_3$: 387.1834, found: 387.1846; IR (neat): 3276, 2975, 1702, 1655, 1531, 1295, 1161, 854, 746 cm^{-1}.

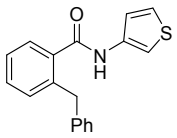
2-Benzyl-*N*-(1-methyl-1*H*-indol-5-yl)benzamide (1p)



Prepared according to Method A, 394.8 mg (35%, 3.3 mmol scale), recrystallized from DCM/hexane, colorless blocks, mp. 205–208 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.78 (1H, s), 7.56 (1H, d, *J* = 7.6 Hz), 7.39 (1H, t, *J* = 7.6 Hz), 7.32–7.17 (9H, m), 7.10 (1H, d, *J* = 8.9 Hz), 7.05 (1H, d, *J* = 2.8 Hz), 6.44 (1H, d, *J* = 3.4 Hz), 4.26 (2H, s), 3.77 (3H, s); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm):167.9, 140.8, 138.7, 137.3, 134.3, 131.1, 130.1, 130.0, 129.7, 128.9, 128.6, 128.5, 127.4, 126.5, 126.2, 115.7, 112.7, 109.2, 101.1, 39.0, 32.9; LRMS (EI) *m/z*: 340 (M^+); HRMS (EI-TOF) Calcd. for $C_{23}H_{20}N_2O$: 340.1576, found: 340.1559; IR (neat): 3065, 1635, 1547, 1484, 1439, 1337, 875, 750, 718, 706 cm^{-1}.

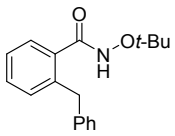
2-Benzyl-*N*-(thiophen-3-yl)benzamide (1q)



Prepared according to Method A, 503.9 mg (84%, 2.0 mmol scale), recrystallized from DCM/hexane, colorless plates, mp. 118–120 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.60 (1H, d, *J* = 2.0 Hz), 7.55–7.51 (2H, m), 7.42 (1H, t, *J* = 7.6 Hz), 7.34–7.25 (4H, m), 7.22–7.16 (4H, m), 6.74 (1H, d, *J* = 3.9 Hz), 4.23 (2H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.0, 140.5, 138.5, 136.3, 135.3, 131.2, 130.4, 128.8, 128.6, 127.6, 126.6, 126.3, 124.4, 121.0, 110.5, 39.0; LRMS (EI) *m/z*: 293 (M^+); HRMS (EI-TOF) Calcd. for $C_{18}H_{15}NOS$: 293.0874, found: 293.0852; IR (neat): 3047, 1641, 1581, 1538, 1307, 967, 835, 779, 738, 701 cm^{-1}.

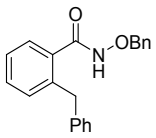
2-Benzyl-*N*-(*tert*-butoxy)benzamide (1s)



Prepared according to Method C, 1015.5 mg (70%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless plates, mp. 96–98 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.90 (1H, s), 7.39–7.33 (2H, m), 7.27–7.15 (7H, m), 4.17 (2H, s), 1.24 (9H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 168.8, 140.4, 139.4, 133.5, 131.0, 130.5, 128.9, 128.5, 127.5, 126.2, 126.1, 82.3, 38.5, 26.2; LRMS (EI) *m/z*: 283 (M^+); HRMS (EI-TOF) Calcd. for $C_{18}H_{21}NO_2$: 283.1572, found: 283.1581; IR (neat): 3222, 2982, 1645, 1510, 901, 738, 702 cm^{-1}.

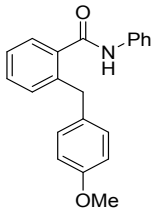
2-Benzyl-*N*-(benzyloxy)benzamide (1t)



Prepared according to Method C, 827.3 mg (86%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 88–89 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 8.50 (1H, br.s), 7.32–7.25 (6H, m), 7.21 (3H, t, *J* = 7.6 Hz), 7.16–7.09 (5H, m), 4.82 (2H, s), 4.10 (2H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.4, 140.3, 139.8, 135.1, 132.7, 130.9, 130.6, 129.1, 129.0, 128.6, 128.4, 128.3, 127.5, 126.1, 126.0, 78.0, 38.4; LRMS (EI) *m/z*: 317 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{19}NO_2$: 317.1416, found: 317.1411; IR (neat): 3194, 1647, 1597, 1496, 1306, 1027, 739, 700 cm^{-1}.

2-(4-Methoxybenzyl)-*N*-phenylbenzamide (1u)

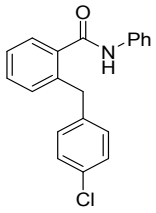


Prepared according to Method B, 516.1 mg (16% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 154–157 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.52 (1H, d, *J* = 7.6 Hz), 7.42–7.39 (3H, m), 7.33–7.27 (5H, m), 7.12 (1H, t, *J* = 7.6 Hz), 7.08 (2H, d, *J* = 8.9 Hz), 6.78 (2H, d, *J* = 8.2 Hz), 4.16 (2H, s), 3.74 (3H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.9, 158.1, 139.0, 137.8, 136.8, 132.6,

131.1, 130.4, 129.8, 128.9, 127.4, 126.5, 124.4, 119.8, 114.0, 55.2, 38.1; LRMS (EI) *m/z*: 317 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{19}NO_2$: 317.1416, found: 317.1428; IR (neat): 3277, 1645, 1595, 1509, 1436, 1245, 1032, 754 cm^{-1}.

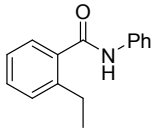
2-(4-Chlorobenzyl)-*N*-phenylbenzamide (1v)



Prepared according to Method B, 435.1 mg (13% over 4 steps, 10.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 170–172 °C.

^1H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.50 (1H, d, *J* = 7.6 Hz), 7.45 (2H, d, *J* = 8.2 Hz), 7.40 (1H, t, *J* = 7.2 Hz), 7.35–7.29 (4H, m), 7.26–7.25 (1H, m), 7.19–7.18 (2H, m), 7.15–7.10 (3H, m), 4.18 (2H, s); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.8, 139.1, 138.8, 137.6, 136.6, 132.0, 131.1, 130.5, 130.3, 129.1, 128.6, 127.1, 126.8, 124.7, 119.9, 38.2; LRMS (EI) *m/z*: 321 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{16}{}^{35}ClNO$: 321.0920, found: 321.0940; IR (neat): 3237, 3072, 1647, 1595, 1490, 1325, 1087, 751, 719 cm^{-1}.

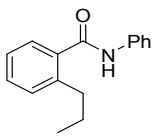
2-Ethyl-*N*-phenylbenzamide (1w)



Prepared according to Method A, 897.0 mg (80%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 140–142 °C.

^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.62 (2H, d, *J* = 7.8 Hz), 7.47–7.24 (7H, m), 7.15 (1H, t, *J* = 7.6 Hz), 2.87 (2H, q, *J* = 7.6 Hz), 1.27 (3H, t, *J* = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 168.2, 142.5, 138.0, 136.2, 130.3, 129.6, 129.1, 126.6, 125.8, 124.5, 119.9, 26.3, 15.9; LRMS (EI) *m/z*: 225 (M^+); HRMS (EI-EB) Calcd. for $C_{15}H_{15}NO$: 225.1154, found: 225.1162; IR (neat): 3270, 2967, 1639, 1596, 1491, 1441, 1324, 892, 758 cm^{-1}.

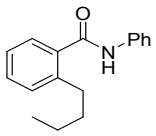
***N*-Phenyl-2-propylbenzamide (1x)**



Prepared according to Method A, 436.6 mg (62%, 3.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 100–102 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.81 (1H, br.s), 7.56 (2H, d, J = 7.3 Hz), 7.35–7.09 (7H, m), 2.74 (2H, t, J = 7.6 Hz), 1.62 (2H, sext, J = 7.6 Hz), 0.91 (3H, t, J = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 168.3, 140.8, 138.0, 136.3, 130.1, 130.0, 128.9, 126.6, 125.7, 124.3, 119.9, 35.1, 24.6, 14.0; LRMS (EI) *m/z*: 239 (M^+); HRMS (EI-TOF) Calcd. for $C_{16}H_{17}NO$: 239.1310, found: 239.1306; IR (neat): 3237, 2966, 1641, 1596, 1539, 1492, 1442, 1325, 760 cm^{-1}.

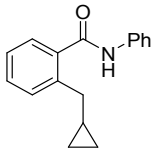
2-Butyl-*N*-phenylbenzamide (1y)



Prepared according to Method A, 485.2 mg (38%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp. 73–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.60–7.58 (3H, m), 7.41–7.32 (4H, m), 7.27 (1H, d, J = 7.8 Hz), 7.24–7.19 (1H, m), 7.14 (1H, t, J = 7.6 Hz), 2.80 (2H, t, J = 7.7 Hz), 1.61 (2H, quin, J = 7.7 Hz), 1.34 (2H, sext, J = 7.7 Hz), 0.89 (3H, t, J = 7.7 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 168.2, 141.2, 138.0, 136.4, 130.2, 130.1, 129.0, 126.6, 125.8, 124.5, 119.9, 33.8, 32.9, 22.6, 13.9; LRMS (EI) *m/z*: 253 (M^+); HRMS (EI-TOF) Calcd. for $C_{17}H_{19}NO$: 253.1467, found: 253.1462; IR (neat): 3306, 2929, 1652, 1597, 1521, 1501, 1436, 1320, 749 cm^{-1}.

2-(Cyclopropylmethyl)-*N*-phenylbenzamide (1z)



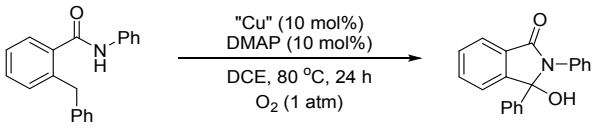
Prepared according to Method A, 170.4 mg (67%, 1.0 mmol scale), recrystallized from DCM/hexane, colorless needles, mp 109–111 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.61 (2H, d, J = 8.3 Hz), 7.49–7.35 (6H, m), 7.30–7.26 (1H, m), 7.15 (1H, t, J = 7.6 Hz), 2.79 (2H, d, J = 6.8 Hz), 1.09–0.99 (1H, m), 0.53–0.49 (2H, m), 0.22 (2H, q, J = 5.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 168.3, 140.4, 137.9, 136.3, 130.2, 130.0, 129.0, 126.5, 126.0, 124.5, 119.8, 37.2, 11.8, 4.8; LRMS (EI) *m/z*: 251 (M^+); HRMS (EI-TOF) Calcd. for $C_{17}H_{17}NO$: 251.1310, found: 251.1304; IR (neat): 3293, 1651, 1598, 1519, 1501, 1438, 1322, 746 cm^{-1}.

4. General procedure for the intramolecular C(sp^3)–H amidation of 1a (Table 1, entry 1)

Under O_2 atmosphere, a mixture of 2-alkylbenzamide (**1a–v**, 0.20 mmol), Cu_2O (0.010 mmol, 1.4 mg) and DMAP (0.020 mmol, 2.4 mg) in 1,2-dichloroethane (1.0 mL) was stirred at 80 °C for 24 h in a sealed tube (Maruemu Corporation, NR-10, φ16.5×105×φ10.0 mm, 12 mL volume). The reaction mixture was diluted with water (10 mL) and extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by SiO_2 column chromatography to give the corresponding desired compound **2a**–**v**.

Table S1. Effect of copper sources

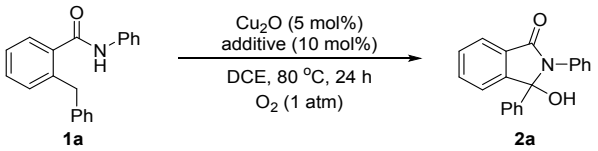


1a **2a**

entry	copper source	yield (%)[a]
1	none	0
2	CuCl	(89)
3	CuBr	(74)
4	CuI	70
5	CuCN	79
6	CuOAc	(91)
7[b]	Cu_2O	(92)
8	$[(MeCN)_4Cu]PF_6$	67
9	$[(MeCN)_4Cu]OTf$	65
10	$CuCl_2$	37
11	$CuBr_2$	59
12	$Cu(OH)_2$	88

[a] Determined by ^{1}H-NMR using 1,1,2-trichloroethane as an internal standard. Isolated yields in parentheses. [b] Cu_2O (5 mol%) was used.

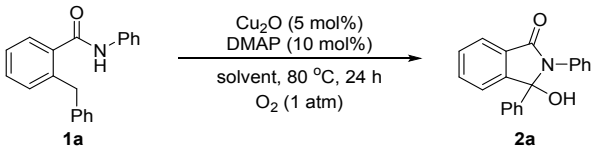
Table S2. Effect of additives



entry	base	yield (%)[a]
1	none	0
2	DMAP	(92)
3	pyridine	(85)
4	4-aminopyridine	48
5	4-methoxypyridine	(80)
6	4-*t*-butylpyridine	(91)
7	3-cyanopyridine	0
8	2,6-di-*t*-butylpyridine	0
9	bipyridine	0
10	1,10-phenanthroline	0
11	NEt_3	66
12	DBU	(81)
13	TBD	40
14	proron sponge	0
15	K_2CO_3	0
16	KO*t*-Bu	0
17	NaH	0
18	LiHMDS	0

[a] Determined by ^{1}H-NMR using 1,1,2-trichloroethane as an internal standard. Isolated yields in parentheses.

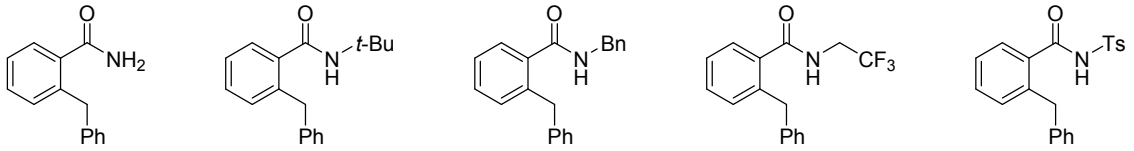
Table S3. Effect of solvents



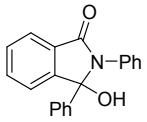
entry	solvent	yield (%)[a]
1	DCE	(92)
2	DCM	28
3	THF	0
4	Et_2O	0
5	DME	trace
6	MeCN	33
7	benzene	5
8	toluene	6
9	PhCl	11
10	DMSO	0
11	DMF	0

[a] Determined by ^{1}H-NMR using 1,1,2-trichloroethane as an internal standard. An isolated yield in parentheses.

Figure S1. Unsuccessful substrates in copper-catalyzed aerobic double C(sp^3)−H functionalization



3-Hydroxy-2,3-diphenylisoindolin-1-one (2a)

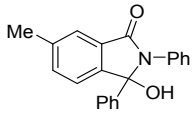


Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 202–204 °C, 52.5 mg (92%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.74 (1H, d, J = 7.3 Hz), 7.51 (1H, t, J = 7.6 Hz), 7.44–7.36 (5H, m), 7.30 (1H, d, J = 7.8 Hz), 7.26–7.17 (5H, m), 7.11 (1H, t, J = 7.6 Hz), 3.87 (1H, br.s); ^{13}C{^{1}H}

NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.4, 148.6, 138.6, 135.8, 133.2, 129.8, 129.7, 128.5, 128.4, 128.3, 126.2, 126.1, 125.4, 123.9, 122.7, 93.0; LRMS (EI) *m/z*: 301 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{15}NO_2$: 301.1103, found: 301.1106; IR (neat): 3193, 1674, 1593, 1495, 1370, 1207, 1045, 939, 861, 756, 707 cm^{-1}.

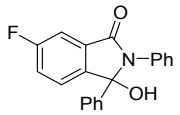
3-Hydroxy-6-methyl-2,3-diphenylisoindolin-1-one (2b)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp 204–207 °C, 52.7 mg (87%).

^1H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.62 (1H, s), 7.58 (1H, s), 7.48 (2H, d, J = 8.2 Hz), 7.41 (1H, d, J = 7.9 Hz), 7.32 (2H, d, J = 7.9 Hz), 7.26–7.09 (7H, m), 2.40 (3H, s); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ (ppm): 166.6, 147.0, 140.2, 139.3, 136.7, 134.0, 129.9, 128.4, 128.3, 127.9, 125.9, 125.7, 125.4, 123.1, 122.6, 92.3, 20.9; LRMS (EI) *m/z*: 315 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{17}NO_2$: 315.1259, found: 315.1288; IR (neat): 3231, 1674, 1498, 1359, 1055, 843 cm^{-1}.

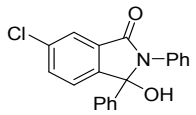
6-Fluoro-3-hydroxy-2,3-diphenylisoindolin-1-one (2c)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 189–191 °C, 61.5 mg (95%).

^1H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.72 (1H, s), 7.62 (1H, d, J = 5.5 Hz), 7.47–7.43 (3H, m), 7.35–7.20 (8H, m), 7.13 (1H, t, J = 7.1 Hz); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ (ppm): 165.3, 162.8 (C–F, $^1J_{C-F}$ = 246.2 Hz), 145.5 (C–F, $^4J_{C-F}$ = 2.9 Hz), 139.6, 136.3, 132.1 (C–F, $^3J_{C-F}$ = 8.6 Hz), 128.5, 128.4, 128.1, 126.1, 126.0, 125.6, 125.2 (C–F, $^3J_{C-F}$ = 8.6 Hz), 120.6 (C–F, $^2J_{C-F}$ = 23.0 Hz), 109.8 (C–F, $^2J_{C-F}$ = 24.5 Hz), 92.1; ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm): −111.5; LRMS (EI) *m/z*: 319 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}FNO_2$: 319.1009, found: 319.0994; IR (neat): 3260, 2929, 1674, 1615, 1496, 1363, 1056, 832 cm^{-1}.

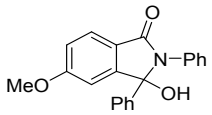
6-Chloro-3-hydroxy-2,3-diphenylisoindolin-1-one (2d)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 207–209 °C, 52.6 mg (87%).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.82 (1H, d, J = 2.1 Hz), 7.71 (1H, s), 7.63 (1H, dd, J = 8.3, 2.1 Hz), 7.45 (2H, d, J = 7.6 Hz), 7.33 (2H, d, J = 7.5 Hz), 7.27–7.23 (5H, m), 7.19 (1H, t, J = 7.6 Hz), 7.11 (1H, t, J = 7.6 Hz); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ (ppm): 164.9, 148.0, 139.3, 136.1, 134.1, 133.1, 131.8, 128.4, 128.3, 128.0, 125.94, 125.89, 125.4, 124.8, 122.7, 92.0; LRMS (EI) *m/z*: 335 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}{}^{35}ClNO_2$: 335.0713, found: 335.0743; IR (neat): 3313, 1687, 1493, 1358, 1048, 824, 767 cm^{-1}.

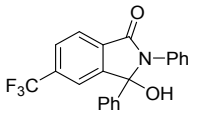
3-Hydroxy-5-methoxy-2,3-diphenylisoindolin-1-one (2e)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 202–203 °C, 63.3 mg (98%).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.75 (1H, d, J = 8.6 Hz), 7.65 (1H, s), 7.47 (2H, d, J = 8.5 Hz), 7.33 (2H, d, J = 7.9 Hz), 7.27–7.19 (5H, m), 7.10–7.07 (2H, m), 6.71 (1H, d, J = 2.2 Hz), 3.75 (3H, s); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ (ppm): 166.2, 163.5, 152.0, 140.1, 136.8, 128.4, 128.3, 128.0, 125.9, 125.5, 125.3, 124.9, 122.2, 115.9, 107.4, 91.9, 55.9; LRMS (EI) *m/z*: 331 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{17}NO_3$: 331.1208, found: 331.1204; IR (neat): 3262, 1669, 1605, 1497, 1359, 1284, 1020, 751, 740 cm^{-1}.

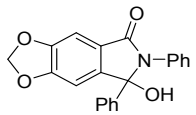
3-Hydroxy-2,3-diphenyl-5-(trifluoromethyl)isoindolin-1-one (2f)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 208–210 °C, 67.7 mg (93%).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 8.07 (1H, d, J = 7.9 Hz), 7.96 (1H, d, J = 7.9 Hz), 7.87 (1H, s), 7.56 (1H, s), 7.49–7.48 (2H, m), 7.40 (2H, d, J = 7.2 Hz), 7.29–7.22 (5H, m), 7.15 (1H, t, J = 7.5 Hz); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ (ppm): 164.9, 150.1, 138.9, 136.0, 133.5, 133.1 (C–F, $^2J_{C–F}$ = 32.2 Hz), 128.5, 128.4, 128.3, 126.8 (C–F, $^3J_{C–F}$ = 3.6 Hz), 126.2, 126.0, 125.6, 124.5, 123.6 (C–F, $^1J_{C–F}$ = 274.3 Hz), 119.6 (C–F, $^3J_{C–F}$ = 3.8 Hz), 92.2; ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm): −60.7; LRMS (EI) *m/z*: 369 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{14}F_3NO_2$: 369.0977, found: 369.0980; IR (neat): 3317, 1691, 1499, 1367, 1321, 1135, 1060, 756, 746 cm^{-1}.

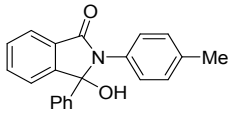
7-Hydroxy-6,7-diphenyl-6,7-dihydro-5*H*-[1,3]dioxolo[4,5-*f*]isoindol-5-one (2g)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 242–243 °C, 64.5 mg (89%).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.59 (1H, s), 7.47 (2H, d, J = 8.2 Hz), 7.32 (2H, d, J = 8.2 Hz), 7.26–7.19 (6H, m), 7.08 (1H, t, J = 7.4 Hz), 6.73 (1H, s), 6.14 (1H, s), 6.09 (1H, s); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ (ppm): 166.1, 152.0, 148.8, 145.5, 140.1, 136.8, 128.4, 128.3, 127.9, 125.9, 125.4, 125.0, 123.5, 103.0, 102.5, 102.4, 91.7; LRMS (EI) *m/z*: 345 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{15}NO_4$: 345.1001, found: 345.0989; IR (neat): 3268, 2901, 1684, 1609, 1498, 1356, 1309, 940, 831, 745 cm^{-1}.

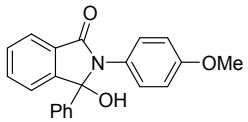
3-Hydroxy-3-phenyl-2-(*p*-tolyl)isoindolin-1-one (2h)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 195–198 °C, 58.9 mg (97%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.81 (1H, d, J = 7.3 Hz), 7.61–7.53 (3H, m), 7.34–7.32 (4H, m), 7.26–7.19 (4H, m), 7.05 (2H, d, J = 8.3 Hz), 2.20 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 166.4, 149.6, 140.0, 135.2, 133.8, 133.2, 129.9, 129.4, 128.9, 128.4, 127.9, 126.0, 125.8, 123.0, 122.9, 92.2, 20.6; LRMS (EI) *m/z*: 315 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{17}NO_2$: 315.1259, found: 315.1255; IR (neat): 3224, 1674, 1614, 1511, 1358, 1205, 940, 813 cm^{-1}.

3-Hydroxy-2-(4-methoxyphenyl)-3-phenylisoindolin-1-one (2i)

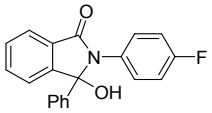


Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 206–209 °C, 66.7 mg (99%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.80 (1H, d, J = 6.8 Hz), 7.61–7.51 (3H, m), 7.32–7.18 (8H, m), 6.82 (2H, d, J = 8.8 Hz), 3.68 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 166.4, 157.4, 149.6, 140.0, 133.1, 130.0, 129.4, 128.9, 128.3, 127.94, 127.85, 126.1, 123.0, 122.9, 113.6, 92.1, 55.2; LRMS (EI) *m/z*: 331 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{17}NO_3$: 331.1208, found: 331.1204; IR

(neat): 3200, 2956, 1669, 1611, 1512, 1368, 1253, 1028, 858, 782 cm^{-1}.

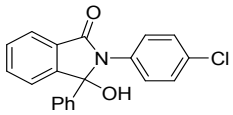
2-(4-Fluorophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2j)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp. 187–189 °C, 60.9 mg (96%).

^1H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.83 (1H, d, J = 7.2 Hz), 7.65 (1H, s), 7.62 (1H, td, J = 7.6, 1.2 Hz), 7.57 (1H, td, J = 7.6, 1.0 Hz), 7.48–7.46 (2H, m), 7.34–7.32 (2H, m), 7.28–7.25 (3H, m), 7.22–7.20 (1H, m), 7.13–7.10 (2H, m); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ (ppm): 166.5, 160.0 (C–F, $^1J_{C–F}$ = 242.1 Hz), 149.5, 139.8, 133.4, 132.7 (C–F, $^4J_{C–F}$ = 2.9 Hz), 129.7, 129.6, 128.5, 128.1, 127.9 (C–F, $^3J_{C–F}$ = 8.6 Hz), 126.0, 123.2, 123.0, 115.2 (C–F, $^2J_{C–F}$ = 22.9 Hz), 92.3; ^{19}F NMR (565 MHz, DMSO-d_6) δ (ppm): −115.8; LRMS (EI) *m/z*: 319 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}FNO_2$: 319.1009, found: 319.0988; IR (neat): 3219, 2363, 1675, 1506, 1363, 1059, 858, 770 cm^{-1}.

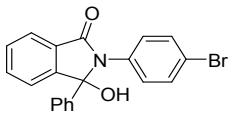
2-(4-Chlorophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2k)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 216–220 °C, 56.0 mg (86%).

^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.84 (1H, d, J = 6.8 Hz), 7.74 (1H, br.s), 7.64–7.55 (4H, m), 7.36–7.32 (4H, m), 7.29–7.19 (4H, m); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ (ppm): 166.4, 149.4, 139.7, 135.6, 133.5, 129.8, 129.6, 129.4, 128.6, 128.4, 128.1, 126.5, 125.9, 123.2, 122.9, 92.4; LRMS (EI) *m/z*: 335 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}{}^{35}ClNO_2$: 335.0713, found: 335.0725; IR (neat): 3205, 1674, 1496, 1359, 1206, 941, 859, 756 cm^{-1}.

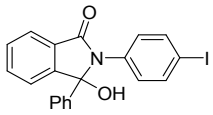
2-(4-Bromophenyl)-3-hydroxy-3-phenylisoindolin-1-one (2l)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 235–238 °C, 67.9 mg (87%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.83 (1H, d, J = 7.3 Hz), 7.74 (1H, s), 7.64–7.53 (4H, m), 7.46 (2H, d, J = 8.8 Hz), 7.35 (2H, d, J = 7.3 Hz), 7.29–7.25 (3H, m), 7.23–7.20 (1H, m); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 166.3, 149.3, 139.7, 136.0, 133.4, 131.2, 129.5, 129.3, 128.5, 128.0, 126.6, 125.8, 123.1, 122.8, 117.9, 92.3; LRMS (EI) *m/z*: 379 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}{}^{79}BrNO_2$: 379.0208, found: 379.0187; IR (neat): 3295, 1674, 1494, 1357, 942, 821, 754 cm^{-1}.

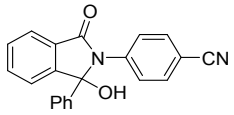
3-Hydroxy-2-(4-iodophenyl)-3-phenylisoindolin-1-one (2m)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless plates, mp. 236–239 °C, 76.0 mg (91%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.84 (1H, d, J = 7.3 Hz), 7.75 (1H, s), 7.63–7.54 (4H, m), 7.42 (2H, d, J = 8.8 Hz), 7.36 (2H, d, J = 7.3 Hz), 7.29–7.19 (4H, m); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 166.4, 149.4, 139.7, 137.2, 136.6, 133.5, 129.6, 129.4, 128.6, 128.1, 126.9, 125.9, 123.2, 122.9, 92.4, 90.6; LRMS (EI) *m/z*: 427 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}INO_2$: 427.0069, found: 427.0055; IR (neat): 3318, 1675, 1607, 1490, 1354, 1057, 943, 818 cm^{-1}.

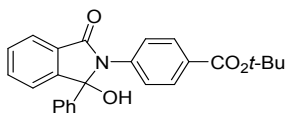
4-(1-Hydroxy-3-oxo-1-phenylisoindolin-2-yl)benzonitrile (2n)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 197–198 °C, 52.9 mg (83%).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 7.96–7.94 (3H, m), 7.87 (1H, d, J = 7.4 Hz), 7.74–7.72 (2H, m), 7.61 (1H, td, J = 7.6, 1.2 Hz), 7.58 (1H, t, J = 7.5 Hz), 7.40 (2H, d, J = 7.4 Hz), 7.31–7.28 (3H, m), 7.23 (1H, t, J = 7.4 Hz); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ (ppm): 166.6, 149.2, 141.2, 139.5, 133.9, 132.5, 129.7, 128.70, 128.67, 128.2, 125.6, 123.4, 123.0, 122.8, 118.7, 106.6, 92.7; LRMS (EI) *m/z*: 326 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{14}N_2O_2$: 326.1055, found: 326.1085; IR (neat): 3247, 2225, 1679, 1602, 1506, 1350, 1062, 940, 844, 773 cm^{-1}.

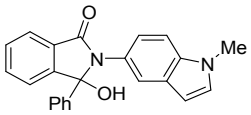
***tert*-Butyl 4-(1-hydroxy-3-oxo-1-phenylisoindolin-2-yl)benzoate (2o)**



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless plates, mp. 219–222 °C, 78.5 mg (96%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.87–7.83 (4H, m), 7.79–7.77 (2H, m), 7.63 (1H, t, J = 7.1 Hz), 7.57 (1H, t, J = 7.6 Hz), 7.38 (2H, d, J = 7.3 Hz), 7.30–7.24 (3H, m), 7.20 (1H, t, J = 7.3 Hz), 1.49 (9H, s); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 166.5, 164.5, 149.3, 141.0, 139.7, 133.6, 129.6, 129.2, 129.1, 128.5, 128.0, 127.4, 125.7, 123.2, 123.0, 122.8, 92.6, 80.5, 27.7; LRMS (EI) *m/z*: 401 (M^+); HRMS (EI-TOF) Calcd. for $C_{25}H_{23}NO_4$: 401.1627, found: 401.1623; IR (neat): 3236, 2974, 1708, 1679, 1605, 1355, 1284, 1114, 942, 856 cm^{-1}.

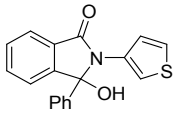
3-Hydroxy-2-(1-methyl-1*H*-indol-5-yl)-3-phenylisoindolin-1-one (2p)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 4/1 to AcOEt), recrystallized from DCM/hexane colorless needles, mp. 205–206 °C, 70.3 mg (>99%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.86 (1H, d, J = 7.3 Hz), 7.55–7.48 (3H, m), 7.38–7.36 (2H, m), 7.33 (1H, d, J = 7.3 Hz), 7.26–7.21 (3H, m), 7.14 (1H, d, J = 8.8 Hz), 7.04 (1H, dd, J = 8.3, 2.0 Hz), 6.98 (1H, d, J = 2.9 Hz), 6.34 (1H, d, J = 2.9 Hz), 3.71 (3H, s), 3.46 (1H, br.s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.7, 148.7, 139.0, 135.6, 132.8, 130.7, 129.6, 129.2, 128.4, 128.22, 128.18, 126.8, 126.3, 123.8, 122.8, 121.5, 120.2, 109.2, 101.5, 92.7, 32.8; LRMS (EI) *m/z*: 354 (M^+); HRMS (EI-TOF) Calcd. for $C_{23}H_{18}N_2O_2$: 354.1368, found: 354.1403; IR (neat): 3263, 1684, 1494, 1451, 1357, 1200, 1050, 768, 755, 745 cm^{-1}.

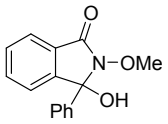
3-Hydroxy-3-phenyl-2-(thiophen-3-yl)isoindolin-1-one (2q)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1 to AcOEt), recrystallized from DCM/hexane, colorless needles, mp. 246–248 °C, 48.9 mg (79%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.81 (1H, d, J = 7.8 Hz), 7.66 (1H, s), 7.60–7.54 (3H, m), 7.39–7.36 (3H, m), 7.34–7.28 (4H, m), 7.25–7.24 (1H, m); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 165.3, 149.2, 140.1, 134.4, 133.2, 129.4, 129.1, 128.6, 128.0, 125.5, 124.0, 123.0, 122.8, 122.6, 112.5, 91.9; LRMS (EI) *m/z*: 307 (M^+); HRMS (EI-TOF) Calcd. for $C_{18}H_{13}NO_2S$: 307.0667, found: 307.0676; IR (neat): 3263, 1682, 1541, 1426, 1356, 1201, 1049, 768, 756, 745 cm^{-1}.

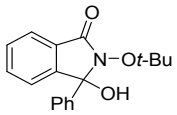
3-Hydroxy-2-methoxy-3-phenylisoindolin-1-one (2r)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp. 162–164 °C, 32.8 mg (61%).

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.76 (1H, d, *J* =7.7 Hz), 7.52 (1H, td, *J* = 7.7, 1.1 Hz), 7.49–7.45 (3H, m), 7.38–7.32 (3H, m), 7.29 (1H, d, *J* = 7.7 Hz), 3.88–3.87 (4H, m); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 164.8, 145.9, 137.7, 133.4, 129.8, 128.8, 128.5, 127.9, 126.2, 123.7, 122.7, 90.8, 65.5; LRMS (EI) *m/z*: 255 (M^+); HRMS (EI-EB) Calcd. for $C_{15}H_{13}NO_3$: 255.0895, found: 255.0897; IR (neat): 3217, 2944, 1711, 1681, 1613, 1469, 1365, 1201, 1048, 1000, 770, 704 cm^{-1}.

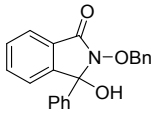
2-(*tert*-Butoxy)-3-hydroxy-3-phenylisoindolin-1-one (2s)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp 157–159 °C, 35.4 mg (62%).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.75 (1H, d, *J* = 7.8 Hz), 7.62 (1H, t, *J* = 7.6 Hz), 7.54 (1H, t, *J* = 7.3 Hz), 7.41 (1H, s), 7.34–7.19 (6H, m), 1.23 (9H, s); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ (ppm): 167.1, 147.5, 139.5, 133.4, 129.4, 128.01, 127.98, 127.7, 126.2, 123.1, 122.6, 90.8, 82.3, 27.7; LRMS (FAB) *m/z*: 298 $(M+H)^+$; HRMS (FAB-EB) Calcd. for $C_{18}H_{20}NO_3$: 298.1443, found: 298.1428; IR (neat): 3327, 2971, 1689, 1468, 1369, 1174, 1062, 959, 772 cm^{-1}.

2-(Benzyloxy)-3-hydroxy-3-phenylisoindolin-1-one (2t)

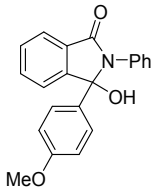


Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless needles, mp. 173–175 °C, 48.7 mg (76%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.79 (1H, d, *J* = 7.3 Hz), 7.51 (1H, td, *J* = 7.6, 1.3 Hz), 7.47–7.43 (3H, m), 7.36–7.25 (9H, m), 5.16 (1H, d, *J* = 10.8 Hz), 4.89 (1H, d, *J* = 10.8 Hz), 3.42 (1H, br.s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 165.1, 146.1, 137.8, 135.3, 133.3, 129.7, 129.4, 128.69, 128.66, 128.5, 128.3, 127.9, 126.3, 123.6, 122.8, 90.8, 79.1; LRMS (EI) *m/z*: 331 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{17}NO_3$: 331.1208, found: 331.1196; IR (neat): 3290, 2889, 1705, 1695,

1468, 1059, 977, 772 cm^{-1}.

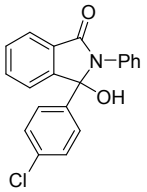
3-Hydroxy-3-(4-methoxyphenyl)-2-phenylisoindolin-1-one (2u)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless needles, mp. 199–200 °C, 56.6 mg (88%).

^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.65 (1H, d, *J* = 7.8 Hz), 7.49 (1H, t, *J* = 7.6 Hz), 7.42 (2H, d, *J* = 7.8 Hz), 7.35 (1H, t, *J* = 7.3 Hz), 7.30–7.25 (3H, m), 7.18 (2H, t, *J* = 7.8 Hz), 7.10 (1H, t, *J* = 7.3 Hz), 6.74 (2H, d, *J* = 8.8 Hz), 4.12 (1H, br.s), 3.72 (3H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.4, 159.4, 148.8, 135.8, 133.1, 130.6, 129.6, 129.5, 128.5, 127.4, 126.1, 125.4, 123.7, 122.6, 113.7, 93.0, 55.1; LRMS (EI) *m/z*: 331 (M^+); HRMS (EI-EB) Calcd. for $C_{21}H_{17}NO_3$: 331.1208, found: 331.1212; IR (neat): 3236, 1674, 1607, 1495, 1363, 1250, 1172, 1028, 828, 758 cm^{-1}.

3-(4-Chlorophenyl)-3-hydroxy-2-phenylisoindolin-1-one (2v)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from ethanol, colorless prisms, mp. 236–238 °C, 59.4 mg (91%).

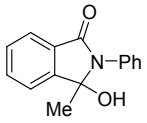
^1H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.80 (1H, d, *J* = 7.6 Hz), 7.54 (1H, t, *J* = 7.3 Hz), 7.47–7.42 (3H, m), 7.31–7.28 (3H, m), 7.25–7.20 (4H, m), 7.13 (1H, t, *J* = 7.6 Hz), 3.57 (1H, s); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 167.0, 148.2, 137.3, 135.7, 134.4, 133.4, 130.1, 130.0, 128.72, 128.70, 127.7, 126.4, 125.5, 124.1, 122.6, 92.5; LRMS (EI) *m/z*: 335 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{14}{}^{35}ClNO_2$: 335.0713, found: 335.0716; IR (neat): 3172, 1679, 1598, 1491, 1366, 1055, 935, 816, 755 cm^{-1}.

5. General procedure for the intramolecular C(sp^3)–H amidation of 2-alkyl-*N*-phenylbenzamide (Scheme 1, 2w–z)

A mixture of 2-alkyl-*N*-phenylbenzamide (**1w**–**z**, 0.40 mmol), Cu_2O (0.020 mmol, 2.9 mg) and DMAP (0.040 mmol, 4.9 mg) in 1,2-dichloroethane (2.0 mL) was placed in a high-pressure vessel (Taiatsu

Glass Industry, Co., Ltd., TVS-1, 50 mL volume) and stirred under 2 atm of O_2 at 80 °C for 24 h. The reaction mixture was diluted with water (10 mL) and extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by SiO_2 column chromatography to give the corresponding desired compound **2w**–**z**.

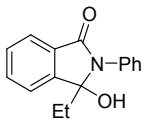
3-Hydroxy-3-methyl-2-phenylisoindolin-1-one (2w)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 190–193 °C, 57.1 mg (62%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.59–7.58 (2H, m), 7.53 (1H, d, *J* = 7.8 Hz), 7.47 (2H, d, *J* = 7.8 Hz), 7.40–7.26 (4H, m), 3.74 (1H, br.s), 1.60 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 166.6, 147.9, 135.4, 132.8, 130.0, 129.6, 128.9, 127.1, 127.0, 123.7, 121.6, 90.4, 24.3; LRMS (EI) *m/z*: 239 (M^+); HRMS (EI-EB) Calcd. for $C_{15}H_{13}NO_2$: 239.0946, found: 239.0936; IR (neat): 3355, 2993, 1674, 1612, 1495, 1466, 1387, 1148, 947, 760, 700 cm^{-1}.

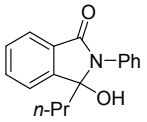
3-Ethyl-3-hydroxy-2-phenylisoindolin-1-one (2x)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1) and GPC (eluent; THF), recrystallized from DCM/hexane, colorless prisms, mp. 166–168 °C, 66.7 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.57–7.50 (4H, m), 7.42 (1H, d, *J* = 7.3 Hz), 7.35–7.24 (4H, m), 4.28 (1H, br.s), 2.09–1.93 (2H, m), 0.41 (3H, t, *J* = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.1, 146.1, 135.4, 132.7, 130.8, 129.5, 128.7, 126.6, 126.1, 123.5, 121.7, 93.9, 28.7, 7.7; LRMS (EI) *m/z*: 253 (M^+); HRMS (EI-TOF) Calcd. for $C_{16}H_{15}NO_2$: 253.1103, found: 253.1105; IR (neat): 3269, 2968, 1680, 1615, 1494, 1370, 1092, 1035, 751, 699 cm^{-1}.

3-Hydroxy-2-phenyl-3-propylisoindolin-1-one (2y)

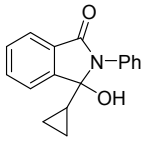


Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1) and GPC (eluent; THF),

recrystallized from DCM/hexane, colorless needles, mp. 151–153 °C, 67.9 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.77 (1H, d, *J* = 7.8 Hz), 7.65–7.56 (4H, m), 7.49 (1H, t, *J* = 7.6 Hz), 7.41 (2H, t, *J* = 7.8 Hz), 7.31 (1H, t, *J* = 7.3 Hz), 3.09 (1H, s), 2.05 (1H, td, *J* = 12.0, 4.7 Hz), 1.96 (1H, td, *J* = 12.0, 4.7 Hz), 1.08–1.05 (1H, m), 0.76–0.66 (4H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.0, 146.4, 135.4, 132.7, 130.8, 129.5, 128.8, 126.7, 126.3, 123.6, 121.7, 93.2, 38.0, 16.7, 13.6; LRMS (EI) *m/z*: 267 (M^+); HRMS (EI-TOF) Calcd. for $C_{17}H_{17}NO_2$: 267.1259, found: 267.1265; IR (neat): 3276, 2964, 1678, 1604, 1494, 1374, 1075, 761, 701 cm^{-1}.

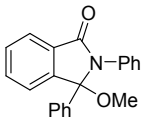
3-Cyclopropyl-3-hydroxy-2-phenylisoindolin-1-one (2z)



Purified by SiO_2 column chromatography (eluent; hexane/AcOEt = 2/1), recrystallized from DCM/hexane, colorless prisms, mp. 132–133 °C, 76.8 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.75 (1H, d, *J* = 7.3 Hz), 7.63–7.58 (2H, m), 7.50–7.45 (3H, m), 7.40 (2H, t, *J* = 7.6 Hz), 7.36–7.34 (1H, m), 2.94 (1H, br.s), 1.09–1.02 (1H, m), 0.60–0.47 (2H, m), 0.46–0.39 (1H, m), 0.34–0.28 (1H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 166.7, 147.3, 135.6, 132.2, 130.5, 129.4, 128.5, 128.2, 127.1, 123.3, 122.4, 91.0, 17.9, 1.7; LRMS (EI) *m/z*: 265 (M^+); HRMS (EI-TOF) Calcd. for $C_{17}H_{15}NO_2$: 265.1103, found: 265.1128; IR (neat): 3300, 3014, 1684, 1595, 1505, 1384, 1146, 1023, 848, 756, 702 cm^{-1}.

3-Methoxy-2,3-diphenylisoindolin-1-one (3)[3]



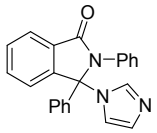
To a solution of **2a** (46.6 mg, 0.15 mmol) in MeOH (5.0 mL) was added 1M HCl aq. (1.0 mL). The reaction mixture was stirred at 40 °C for 4 h, and then diluted with sat. K_2CO_3 aq. (10 mL). The resulting mixture was extracted with DCM (3 × 10 mL), and the combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; hexane/EtOAc = 4/1) to afford **3** (47.9 mg, 98%).

Recrystallized from DCM/hexane, colorless prisms, mp. 151–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.99–7.97 (1H, m), 7.58–7.52 (4H, m), 7.39 (2H, dd, *J* = 7.6, 1.7 Hz), 7.27–7.20 (6H, m), 7.11 (1H, t, *J* = 7.6 Hz), 3.15 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.6, 145.1, 138.9, 136.3, 133.1, 131.4, 129.8, 128.6, 128.3, 128.2, 126.1,

125.7, 124.0, 123.9, 123.0, 97.1, 50.3; LRMS (EI) *m/z*: 315 (M^+); HRMS (EI-TOF) Calcd. for $C_{21}H_{17}NO_2$: 315.1259, found: 315.1251; IR (neat): 2933, 2849, 1715, 1596, 1490, 1349, 1073, 863, 754, 705 cm^{-1}.

3-(1*H*-imidazol-1-yl)-2,3-diphenylisoindolin-1-one (4)[4]

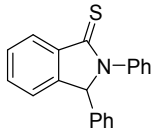


To a solution of imidazole (386.4 mg, 5.6 mmol) in DCM (4.0 mL) was added $SOCl_2$ (120 μL, 1.6 mmol) at 0 °C. After the reaction mixture was stirred for 5 min at 0 °C, **2a** (211.7 mg, 0.70 mmol) was added with stirring. After 10 min, the reaction mixture was diluted with H_2O and extracted with DCM (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; EtOAc) to afford **4** (249.6 mg, >99%).

Recrystallized from MeOH, colorless prisms, mp 165–168 °C.

^1H NMR (400 MHz, CD_3OD) δ (ppm): 8.00–7.98 (1H, m), 7.74–7.67 (2H, m), 7.50–7.44 (7H, m), 7.34–7.26 (3H, m), 6.97 (1H, s), 6.93–6.91 (2H, m), 6.82 (1H, s); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ (ppm): 169.8, 147.7, 139.1, 137.7, 136.1, 135.2, 131.9, 130.9, 130.5, 130.4, 130.3, 129.9, 129.8, 129.4, 128.3, 125.6, 125.0, 120.8, 86.0; LRMS (EI) *m/z*: 351 (M^+); HRMS (EI-EB) Calcd. for $C_{23}H_{17}N_3O$: 351.1372, found: 351.1364; IR (neat): 1711, 1600, 1493, 1344, 1218, 761, 703 cm^{-1}.

2,3-Diphenylisoindoline-1-thione (5)[5]



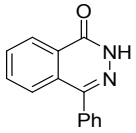
A mixture of **2a** (148.3 mg, 0.50 mmol) and Lawesson's reagent (227.7 mg, 0.55 mmol) in toluene (5.0 mL) was stirred at 120 °C for 10 min and then concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; hexane/EtOAc = 8/1) to afford **5** (141.2 mg, 95%).

Recrystallized from DCM/hexane, yellow needles, mp. 137–140 °C.

^1H NMR (600 MHz, DMSO-d_6) δ (ppm): 8.02 (1H, d, J = 7.6 Hz), 7.64 (1H, t, J = 7.3 Hz), 7.61–7.57 (3H, m), 7.37 (2H, t, J = 7.9 Hz), 7.31 (1H, d, J = 7.6 Hz), 7.26–7.20 (4H, m), 7.12 (2H, d, J = 6.8 Hz), 6.78 (1H, s); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ (ppm): 192.7, 144.9, 138.3, 138.1, 136.1, 132.5, 128.9, 128.8, 128.6, 128.4, 127.5, 127.3, 127.0, 125.3, 122.8, 73.4; LRMS (EI) *m/z*: 301 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{15}NS$: 301.0925, found: 301.0922; IR (neat): 2892, 1597, 1490, 1472,

1455, 1402, 1302, 771, 708 cm^{-1}.

4-Phenylphthalazin-1(2*H*)-one (6)[6]

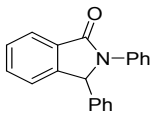


To a solution of **2a** (127.9 mg, 0.42 mmol) in 1-propanol (5.0 mL) was added $N_2H_4 \cdot H_2O$ (300 μL, 6.2 mmol) and the reaction mixture was stirred at 100 °C for 16 h. Then, the mixture was cooled to 0 °C and added H_2O (5.0 mL). The residue was diluted with EtOAc (10 mL), washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; hexane/EtOAc = 2/1) to afford **6** (86.3 mg, 91%).

Recrystallized from DCM/hexane, colorless prisms, mp. 219–222 °C.

^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 10.53 (1H, br.s), 8.55–8.53 (1H, m), 7.84–7.75 (3H, m), 7.61–7.52 (5H, m); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 160.5, 148.2, 135.0, 133.4, 131.5, 129.7, 129.4, 129.2, 128.6, 128.3, 127.0, 126.9; LRMS (EI) *m/z*: 222 (M^+); HRMS (EI-TOF) Calcd. for $C_{14}H_{10}N_2O$: 222.0793, found: 222.0772; IR (neat): 2869, 1665, 1607, 1486, 1337, 1153, 896, 781, 749 cm^{-1}.

2,3-Diphenylisoindolin-1-one (7)[7]

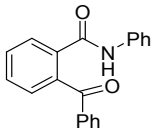


To a solution of 2-benzoyl-*N*-phenylbenzamide (724.8 mg, 2.4 mmol) in CH_3CN (10 mL) was added Et_3SiH (800 μL, 5.0 mmol) and $TiCl_4$ (1.0 M in DCM, 5.0 mL, 5.0 mmol). The reaction mixture was stirred at reflux for 4 h and then concentrated under reduced pressure. The mixture was diluted with EtOAc (10 mL), washed with brine (10 mL), dried over Na_2SO_4, and concentrated reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; hexane/EtOAc = 2/1) to afford **7** (504.3 mg, 73%).

Recrystallized from DCM/hexane, colorless needles, mp. 190–192 °C.

^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.97 (1H, d, J = 6.4 Hz), 7.61 (2H, d, J = 7.8 Hz), 7.52–7.46 (2H, m), 7.31–7.20 (8H, m), 7.08 (1H, t, J = 7.1 Hz), 6.08 (1H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 167.9, 145.6, 137.63, 137.58, 132.4, 131.1, 129.1, 128.8, 128.5, 128.3, 126.9, 124.9, 124.1, 123.0, 122.5, 65.6; LRMS (EI) *m/z*: 285 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{15}NO$: 285.1154, found: 285.1134; IR (neat): 3042, 1684, 1599, 1493, 1368, 1143, 753, 737 cm^{-1}.

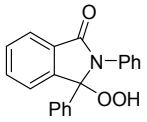
2-Benzoyl-*N*-phenylbenzamide (8)



Prepared according to Method A, 305.7 mg (20%, 5.0 mmol scale), recrystallized from DCM/hexane, colorless prisms, mp. 199–201 °C.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.90 (1H, d, J = 7.3 Hz), 7.70–7.63 (3H, m), 7.57–7.52 (2H, m), 7.38–7.32 (3H, m), 7.07 (2H, t, J = 8.0 Hz) 6.83 (1H, t, J = 7.3 Hz), 6.68 (2H, d, J = 7.8 Hz), 4.96 (1H, br.s); ^{13}C{^{1}H} NMR (150 MHz, acetone-d_6) δ (ppm): 169.6, 152.1, 144.5, 141.0, 135.6, 131.1, 129.9, 129.5, 129.3, 126.6, 126.5, 126.1, 124.3, 120.7, 118.8, 118.7; LRMS (EI) *m/z*: 301 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{15}NO_2$: 301.1103, found: 301.1124; IR (neat): 3347, 3062, 1736, 1599, 1517, 1451, 1271, 1108, 871, 749 cm^{-1}.

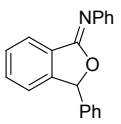
3-Hydroperoxy-2,3-diphenylisoindolin-1-one (9)[8]



To a solution of **2a** (309.4 mg, 1.0 mmol) and H_2SO_4 (200 μL) in DCM (5.0 mL) was added H_2O_2 (30% in H_2O, 250 μL) dropwise at 0 °C. The mixture became homogeneous after 5 min and was gradually warmed to rt. After stirring for 24 h at rt, the solution was washed with sat. Na_2CO_3 aq. (3 × 10 mL) and brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was then purified by recrystallization from DCM/hexane to afford **9** (290.3 mg, 89%) as colorless prisms, mp. 201–204 °C.

^{1}H NMR (600 MHz, $CDCl_3$/TMS) δ (ppm): 7.97 (1H, d, J = 7.3 Hz), 7.89 (1H, s), 7.62–7.56 (2H, m), 7.42 (2H, d, J = 7.3 Hz), 7.37 (1H, d, J = 7.3 Hz), 7.31–7.26 (6H, m), 7.19 (1H, t, J = 6.9 Hz), 5.30 (1H, s); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 168.0, 144.5, 135.6, 135.5, 133.0, 131.8, 130.1, 129.1, 128.9, 128.6, 126.8, 126.2, 126.1, 124.0, 122.7, 100.7; LRMS (EI) *m/z*: 317 (M^+); HRMS (EI-EB) Calcd. for $C_{20}H_{15}NO_3$: 317.1052, found: 317.1067; IR (neat): 3238, 2813, 1738, 1669, 1490, 1366, 870, 756, 701 cm-^{1}.

(*Z*)-*N*,3-diphenylisobenzofuran-1(3H)-imine (10)[9]



To a solution of *N*-phenylthiobenzamide (1.3 g, 6.2 mmol) in THF (40 mL) was added *n*-BuLi (1.6 M in hexane, 8.4 mL, 13.4 mmol) dropwise at −78 °C and the mixture was gradually warmed to 0 °C. After stirring for 1.5 h at the same temperature, the mixture was cooled to −78 °C and treated with benzaldehyde (689.2 mg, 6.7 mmol), then temperature was gradually warmed to 0 °C and H_2O (1.3 mL) was added. After stirring for 2 days at rt, the reaction mixture was diluted with sat. NH_4Cl aq. (30 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), then dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by SiO_2 column chromatography (eluent; hexane/EtOAc = 20/1) to afford **10** (717.3 mg, 41%).

Recrystallized from DCM/hexane, colorless needles, mp. 145–148 °C.

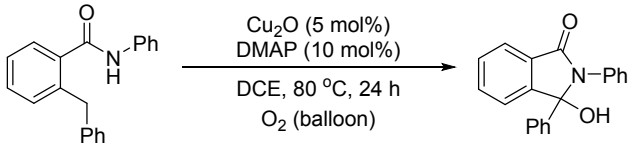
^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 8.04–8.01 (1H, m), 7.53–7.51 (2H, m), 7.37–7.22 (10H, m), 7.08 (1H, t, *J* = 7.1 Hz), 6.46 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 158.3, 146.5, 146.4, 138.0, 132.1, 130.6, 129.02, 128.99, 128.9, 128.6, 126.9, 124.1, 124.0, 123.6, 122.3, 85.8; LRMS (EI) *m/z*: 285 (M^+); HRMS (EI-TOF) Calcd. for $C_{20}H_{15}NO$: 285.1154, found: 285.1151; IR (neat): 3025, 1737, 1683, 1592, 1489, 1201, 1059, 952, 764, 736 cm^{-1}.

Preparation of ethereal H_2O_2[10]

Et_2O (50 mL) was placed in a separatory funnel and washed with four portions (30 mL each) of NaCl-saturated H_2O_2 (prepared by stirring the commercially available 30% aqueous hydrogen peroxide with an excess of powdered NaCl at ambient temperature until the initially cloudy liquid phase became a clear solution; the supernatant was used). The ethereal layer was then dried over $MgSO_4$. The supernatant (*ca.* 1.7 M in H_2O_2 as titrated with 0.1 M $KMnO_4$) was used directly in the transformation from the iminolactone **10** to **2a**.

6. Procedure for gram-scale synthesis of the 3-hydroxyisoindolinone 2a

Scheme S1. Gram-scale synthesis of 3-hydroxyisoindolinone **2a**



1a (1.44 g) → **2a** (1.39 g) 91%

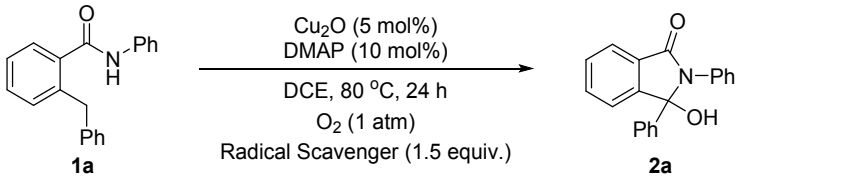
A mixture of 2-benzyl-*N*-phenylbenzamide (**1a**, 5.0 mmol, 1.44 g), Cu_2O (0.25 mmol, 35.3 mg) and DMAP (0.50 mmol, 61.0 mg) in 1,2-dichloroethane (25 mL) was stirred at 80 °C for 24 h in a two-necked flask with a balloon filled with O_2. The reaction mixture was diluted with water (30 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine (30 mL) and

dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by SiO_2 column chromatography to give the corresponding desired compound **2a** (1.39 g, 91%).

7. Mechanistic study

The reaction was carried out in the presence of 1.5 equiv. radical scavenger (BHT or 9,10-dihydroanthracene). The reaction was completely inhibited, indicating that it proceeded *via* a radical process. (**Scheme S2**).

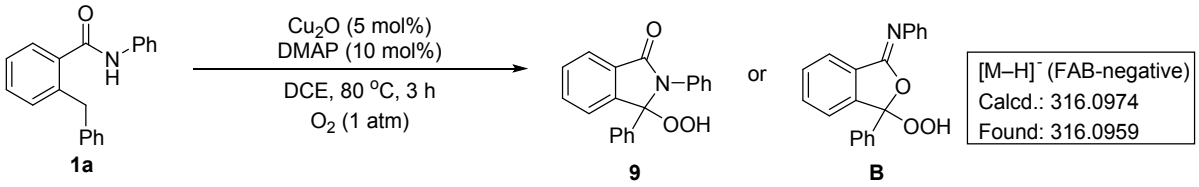
Scheme S2. Radical scavenging experiment of **1a**



None: 92%
BHT: 0%
9,10-Dihydroanthracene: 0%

When the reaction of **1a** was conducted for 3h, the peroxide **9** or **B** was detected by FAB-HRMS of the crude reaction mixture (**Scheme S3**). The result suggests that it is an intermediate in this reaction.

Scheme S3. HRMS experiment on the reaction mixture



$[M–H]^-$ (FAB-negative)
Calcd.: 316.0974
Found: 316.0959

8. References

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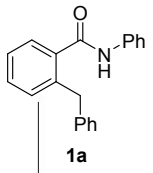
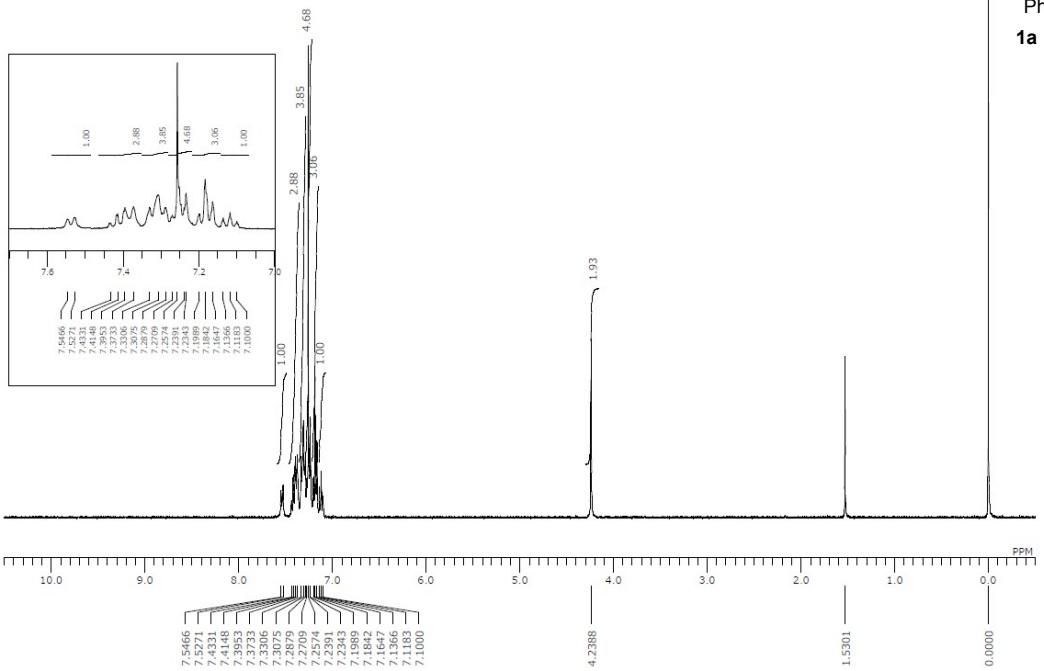
9. ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra

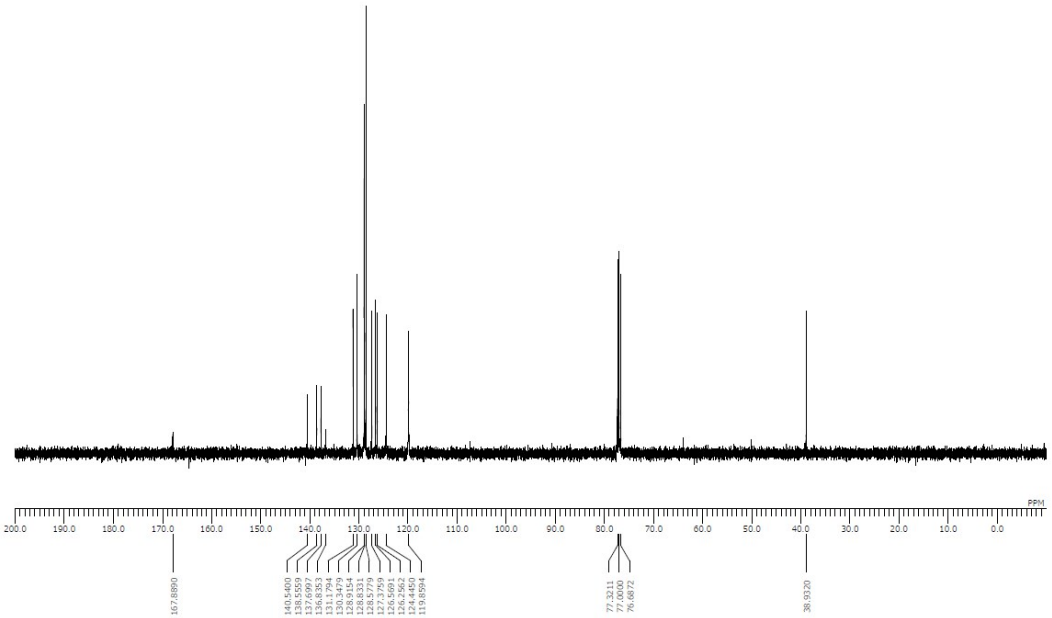
^{1}H-NMR spectrum of **1a** ($CDCl_3$, 400 MHz)

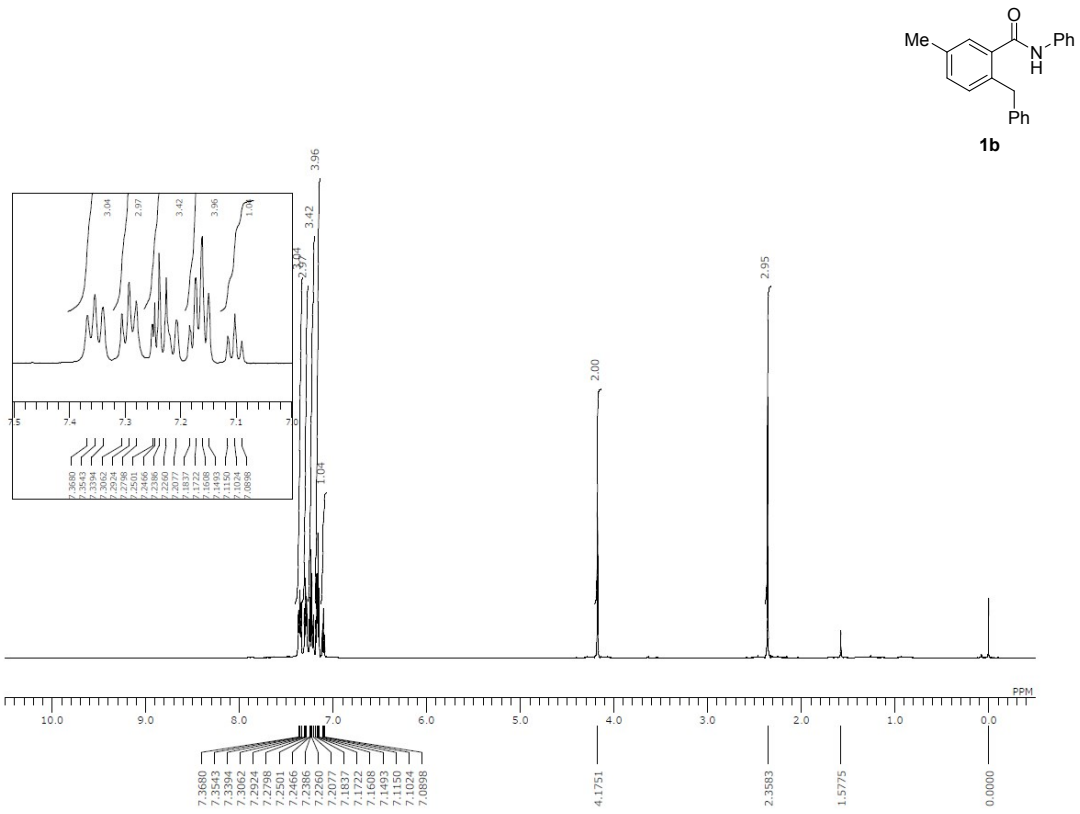


1a



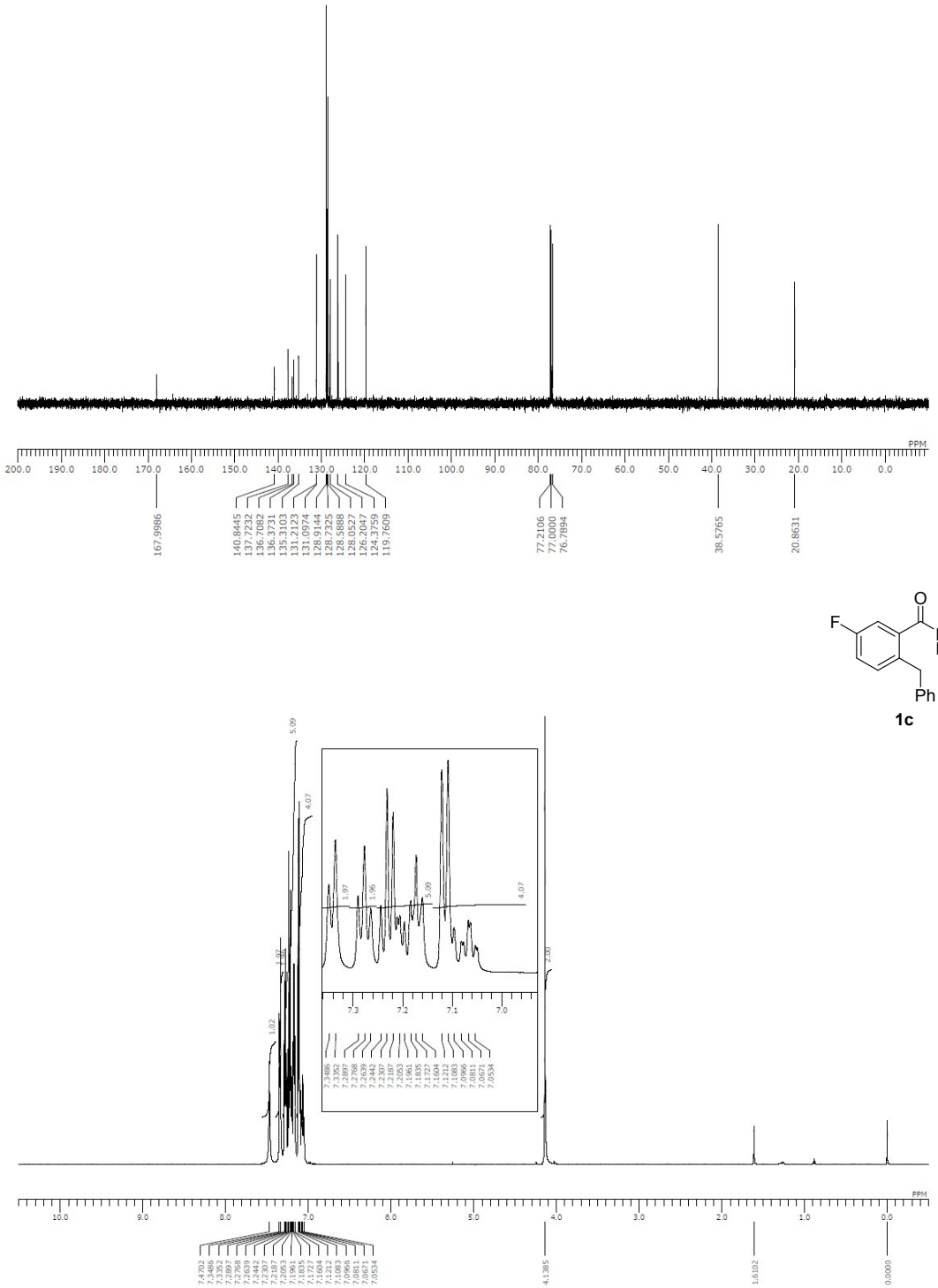
^{13}C-NMR spectrum of **1a** ($CDCl_3$, 100 MHz)





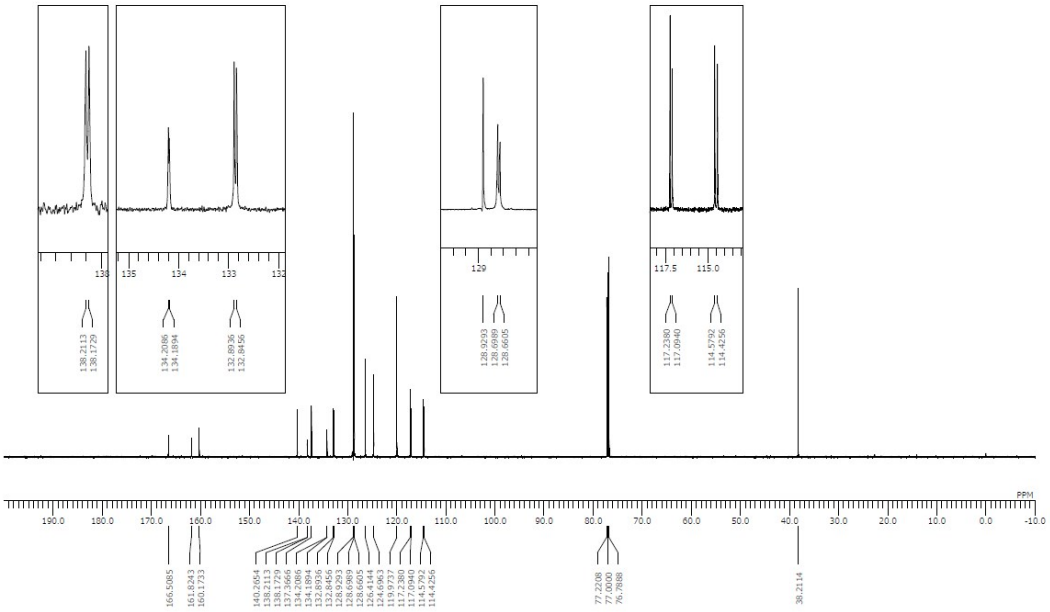
^{1}H-NMR spectrum of **1b** ($CDCl_3$, 600 MHz)

^{13}C-NMR spectrum of **1b** ($CDCl_3$, 150 MHz)

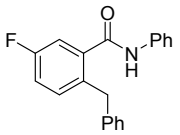


^{1}H-NMR spectrum of **1c** ($CDCl_3$, 600 MHz)

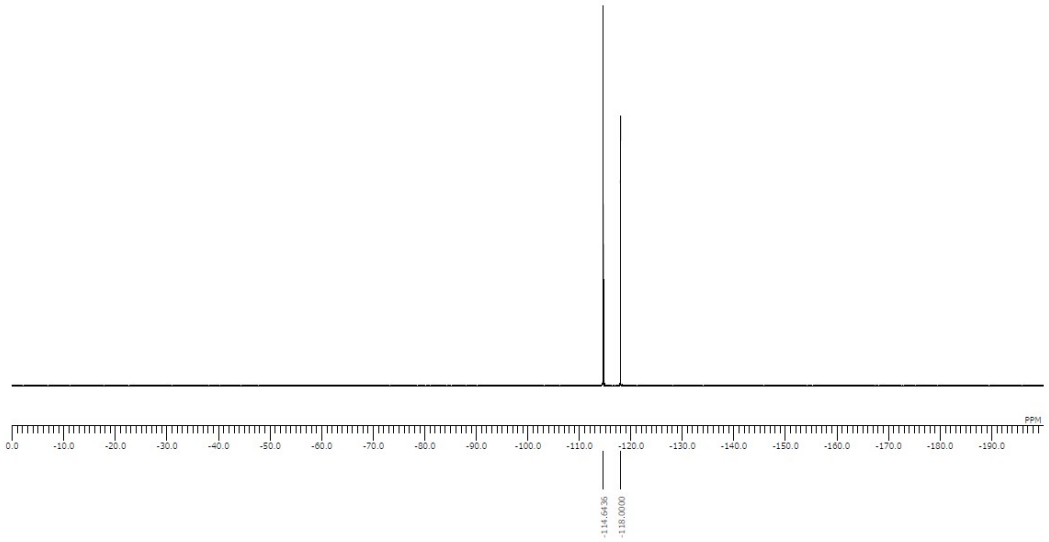
^{13}C-NMR spectrum of **1c** ($CDCl_3$, 150 MHz)



^{19}F-NMR spectrum of **1c** ($CDCl_3$, 565 MHz)



1c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-110.0
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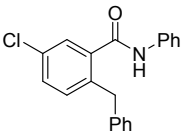
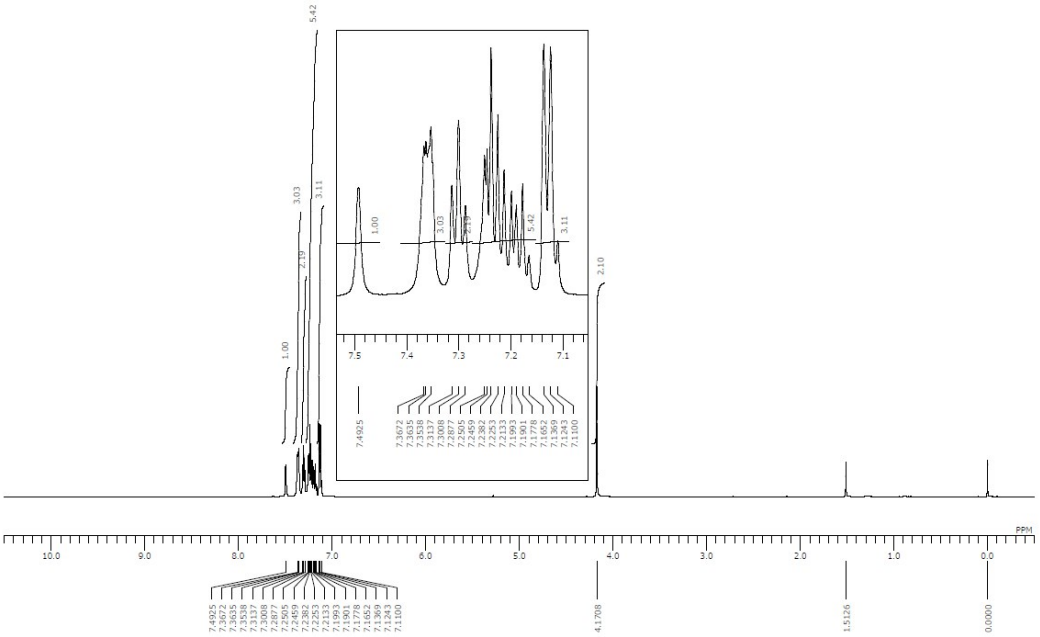
-180.0
-190.0
-114.6436
-118.0000

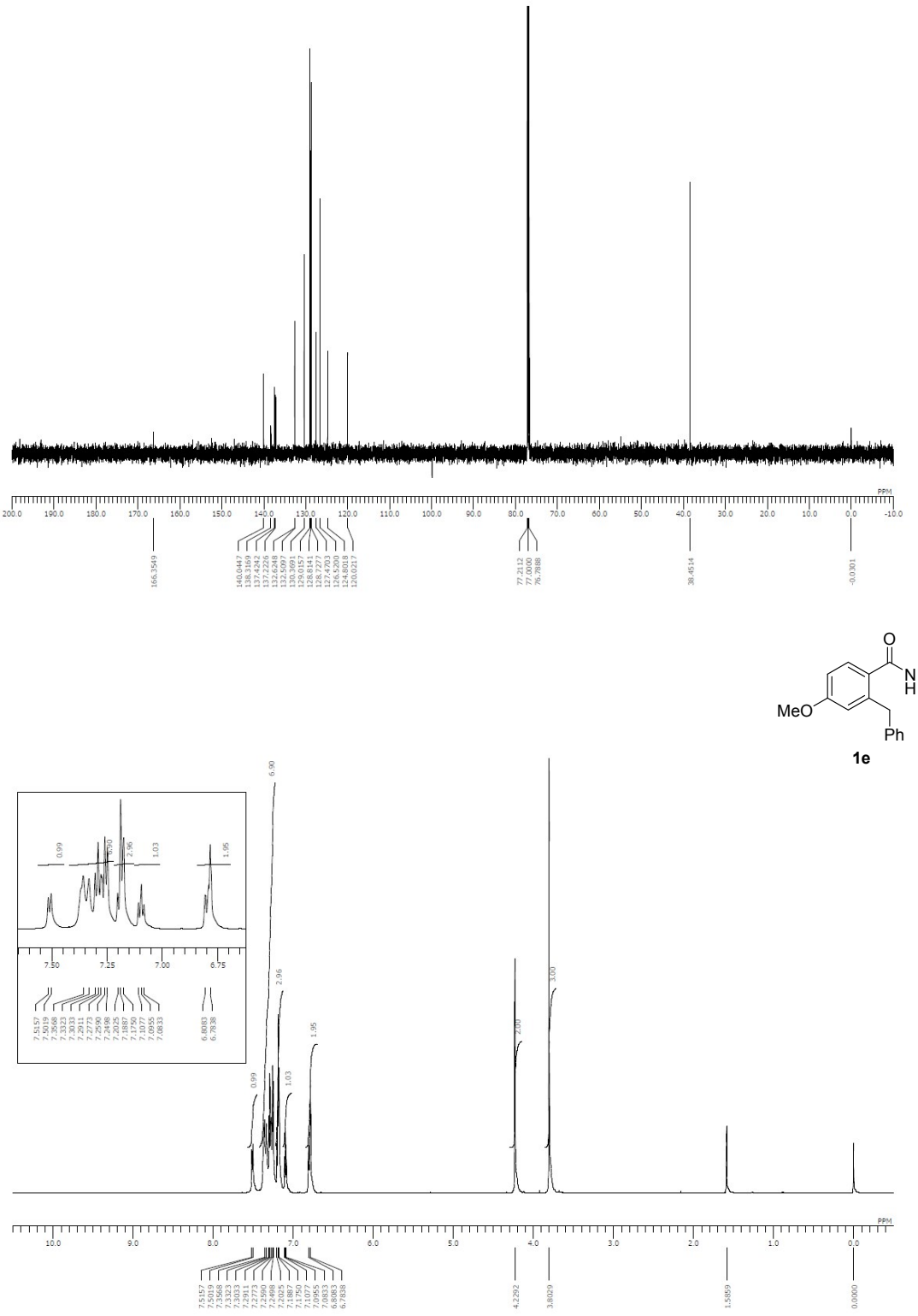


1d



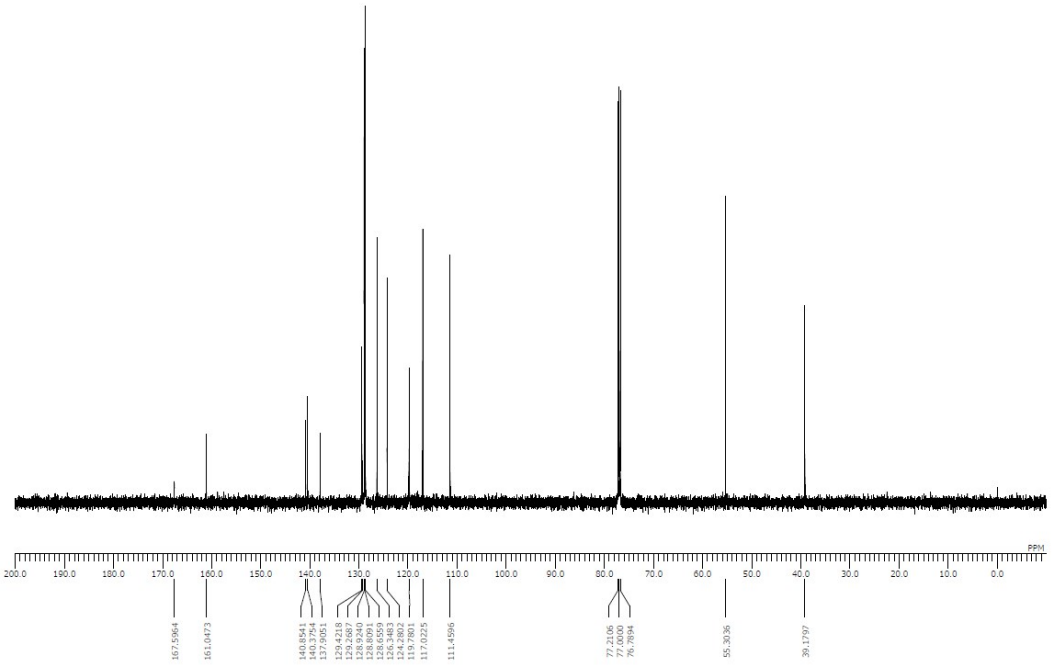
^{1}H-NMR spectrum of **1d** ($CDCl_3$, 600 MHz)

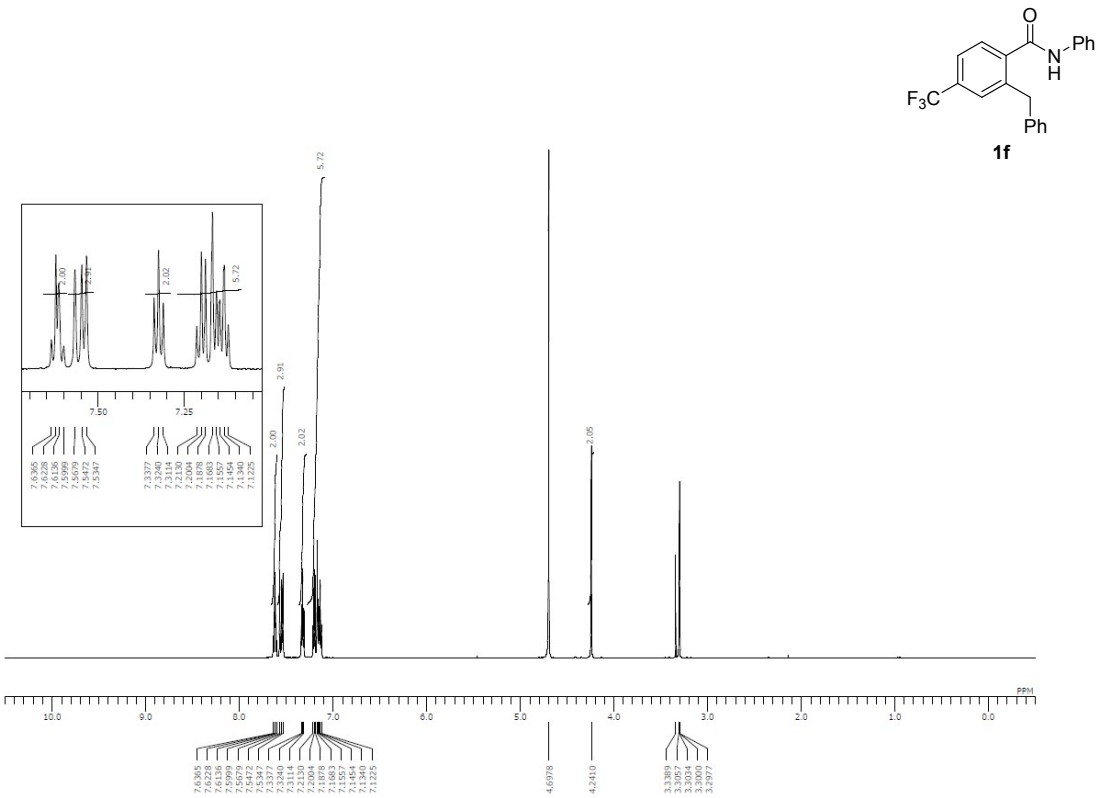
^{13}C-NMR spectrum of **1d** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **1e** ($CDCl_3$, 600 MHz)

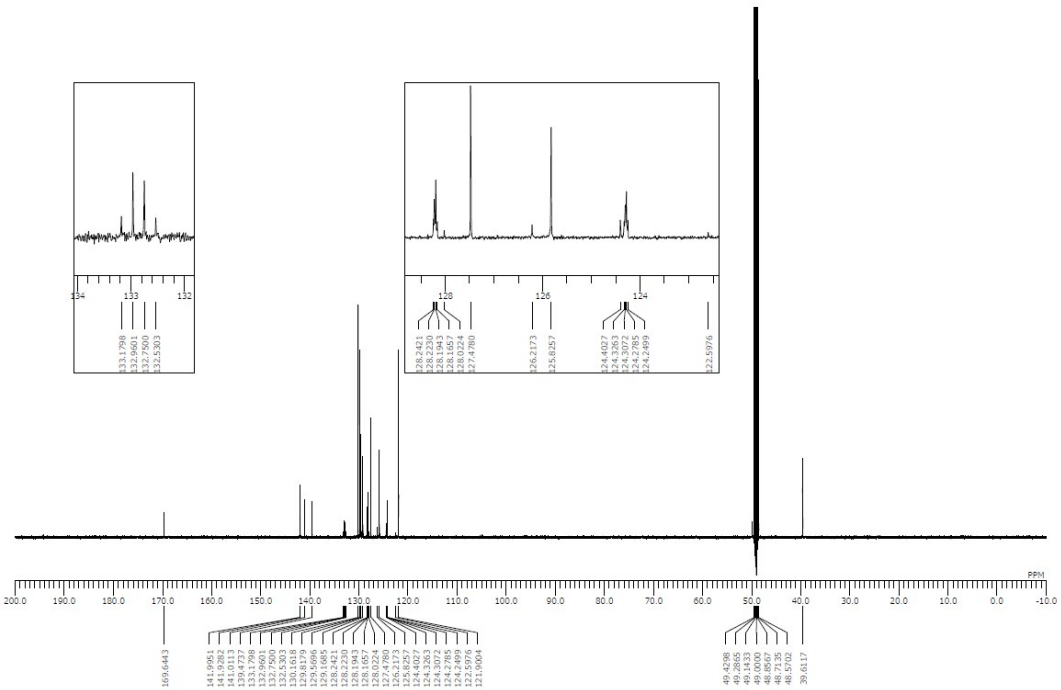
^{13}C-NMR spectrum of **1e** ($CDCl_3$, 150 MHz)



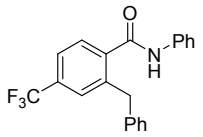


^{1}H-NMR spectrum of **1f** (CD_3OD, 600 MHz)

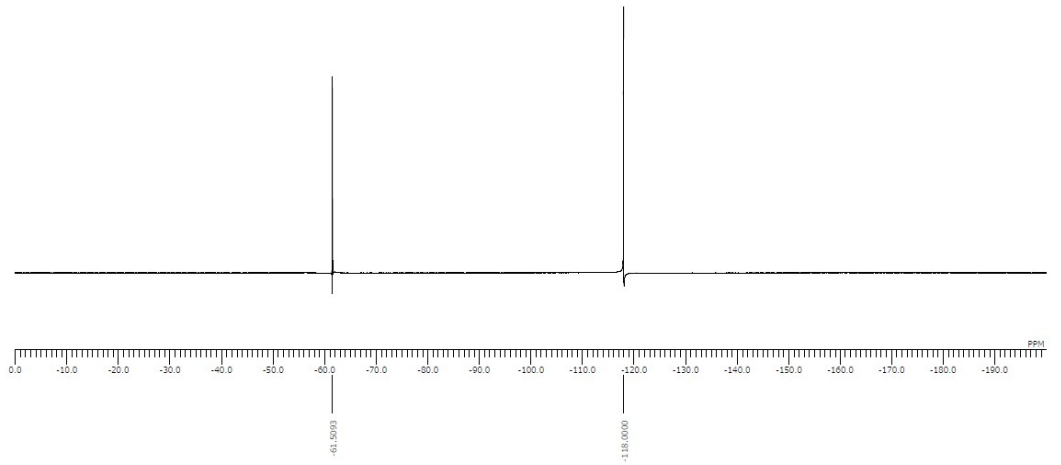
^{13}C-NMR spectrum of **1f** (CD_3OD, 150 MHz)

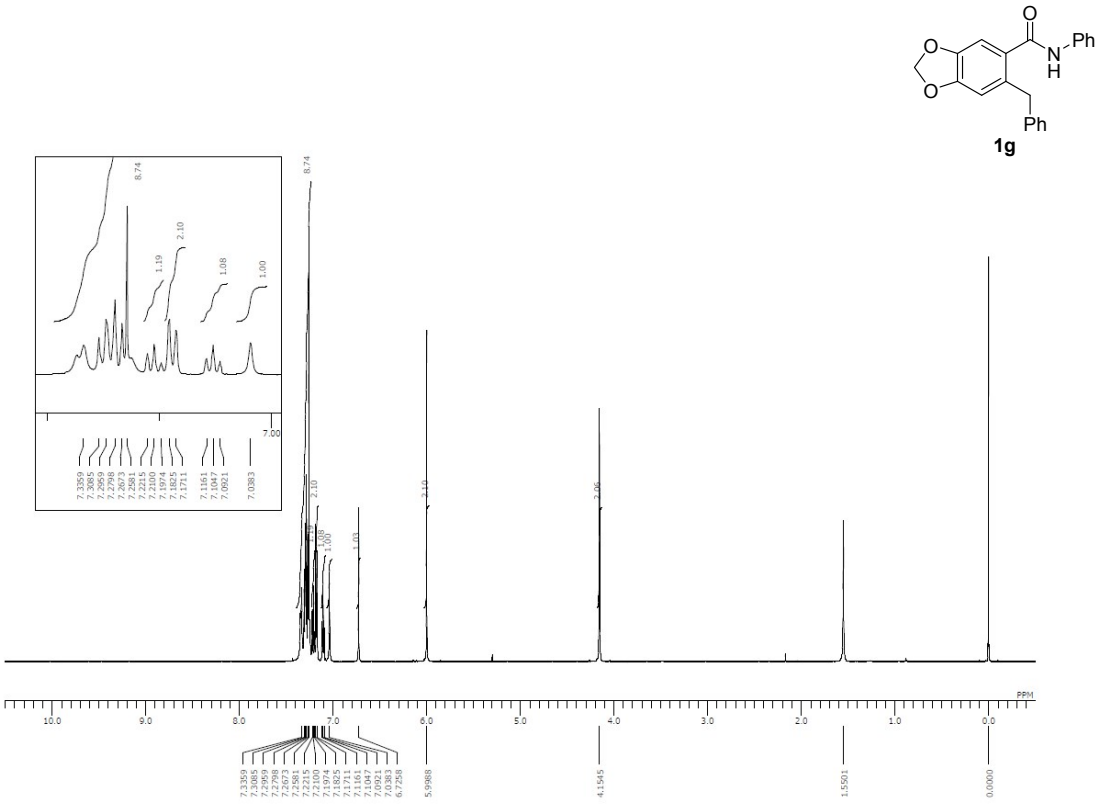


^{19}F-NMR spectrum of **1f** (CD_3OD, 565 MHz)



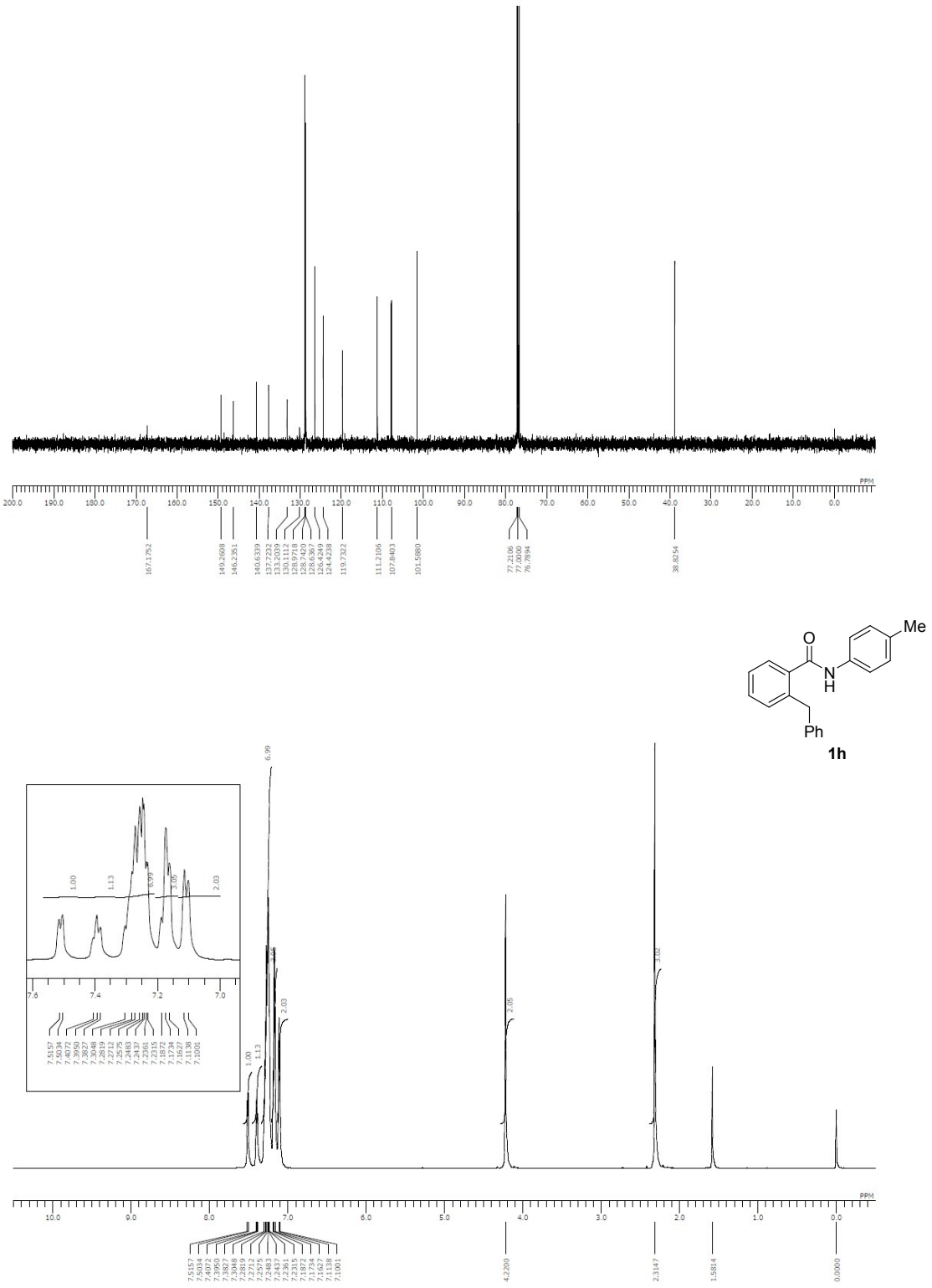
1f





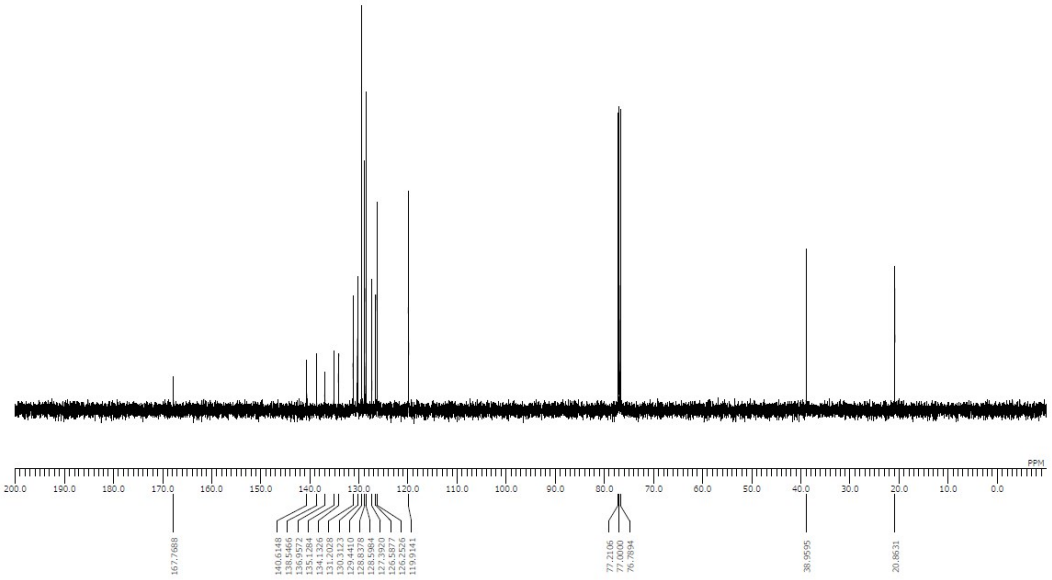
^{1}H-NMR spectrum of **1g** ($CDCl_3$, 600 MHz)

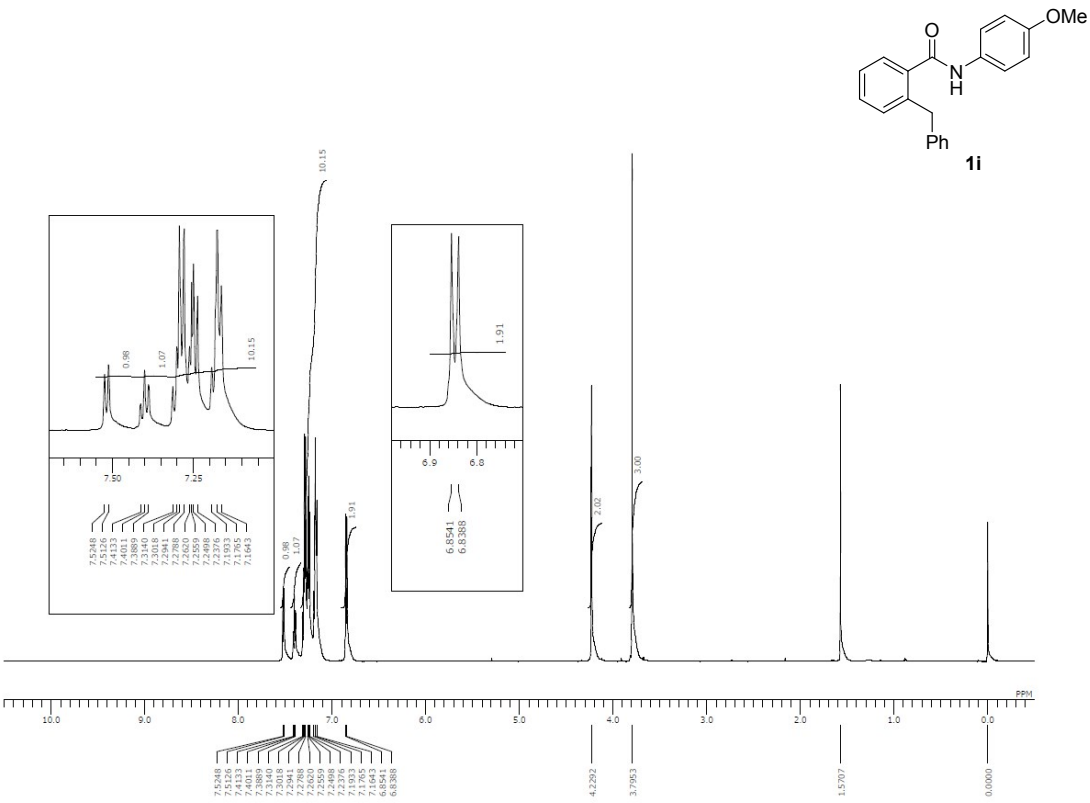
^{13}C-NMR spectrum of **1g** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **1h** ($CDCl_3$, 600 MHz)

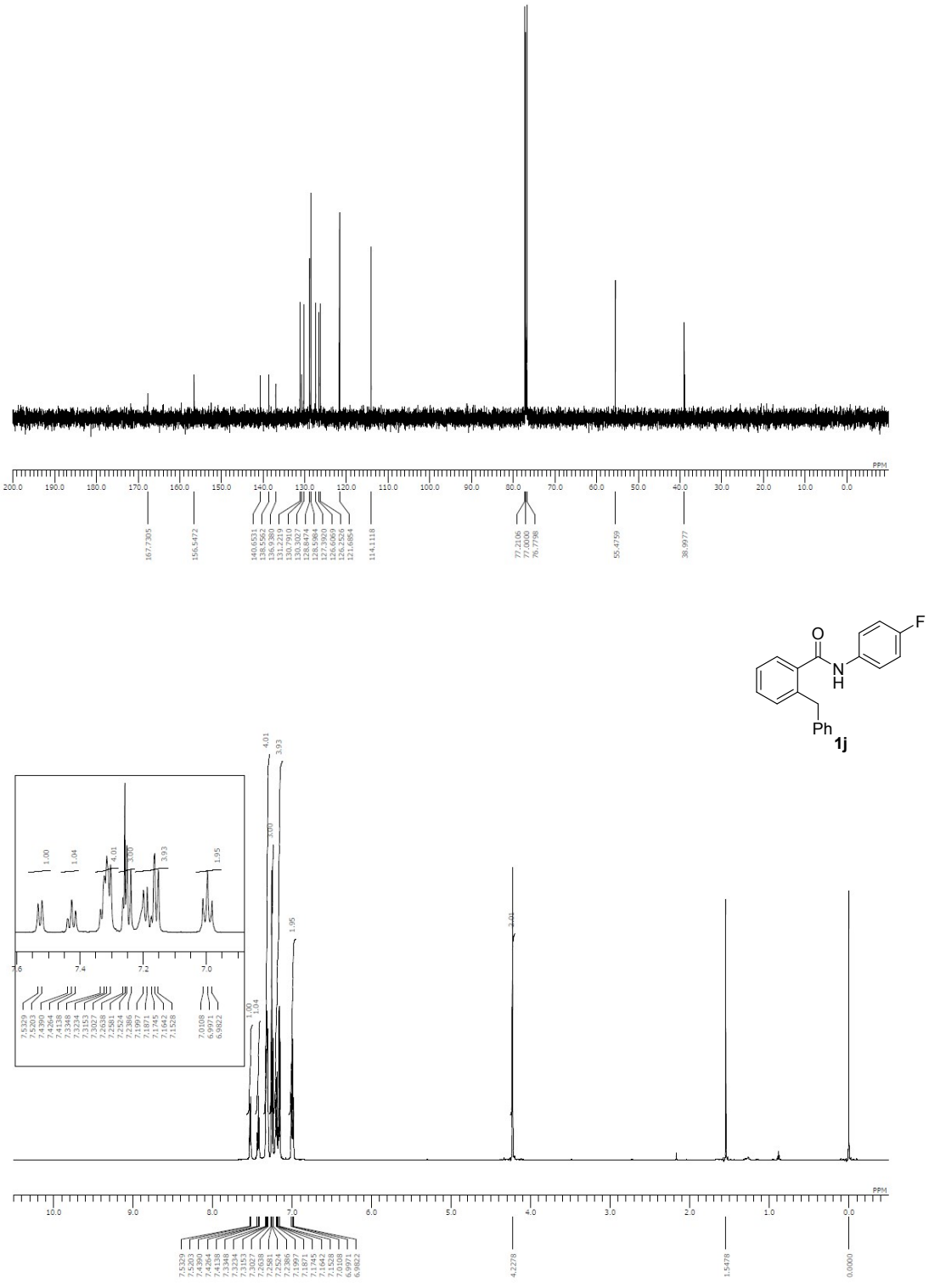
^{13}C-NMR spectrum of **1h** ($CDCl_3$, 150 MHz)





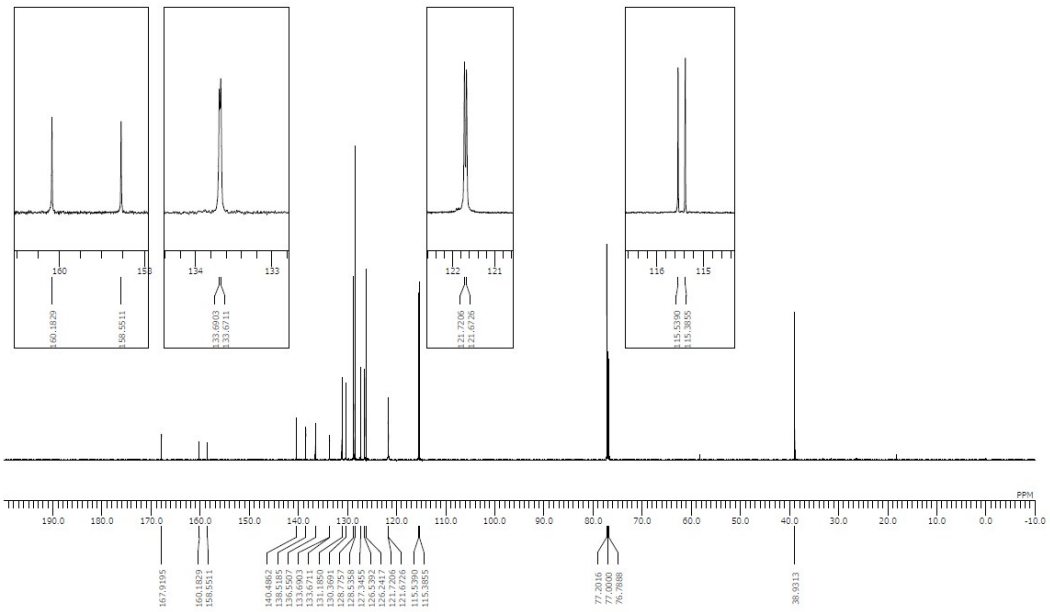
^{1}H-NMR spectrum of **1i** ($CDCl_3$, 600 MHz)

^{13}C-NMR spectrum of **1i** ($CDCl_3$, 150 MHz)

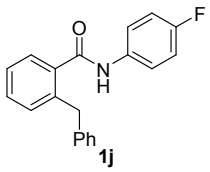


^{1}H-NMR spectrum of **1j** ($CDCl_3$, 600 MHz)

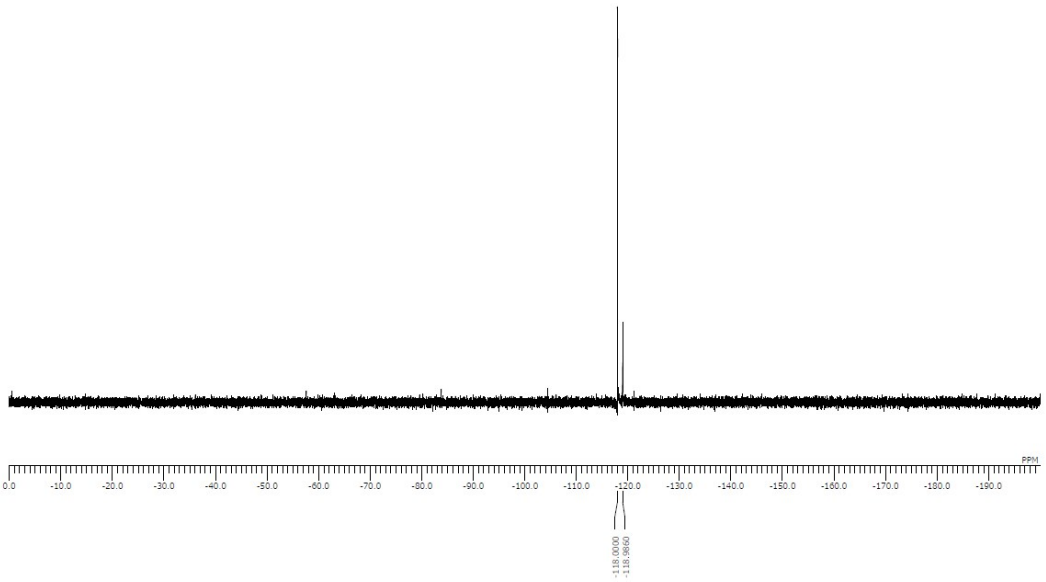
^{13}C-NMR spectrum of **1j** ($CDCl_3$, 150 MHz)



^{19}F-NMR spectrum of **1j** ($CDCl_3$, 565 MHz)



1j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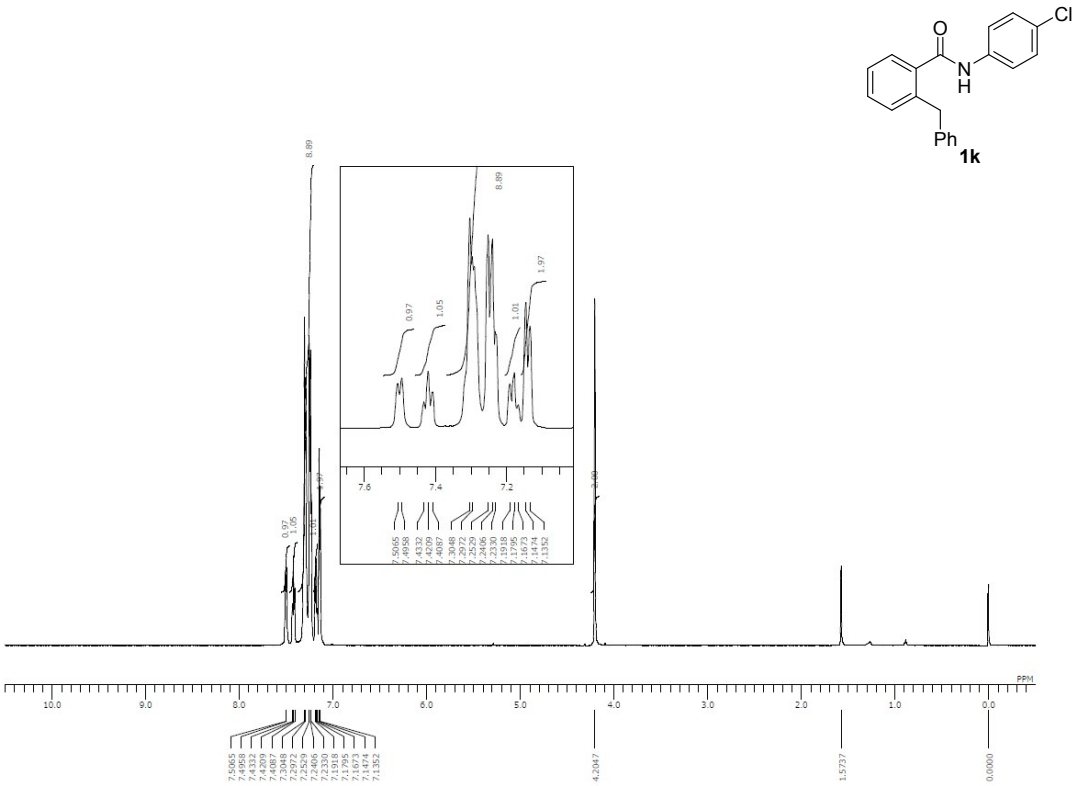
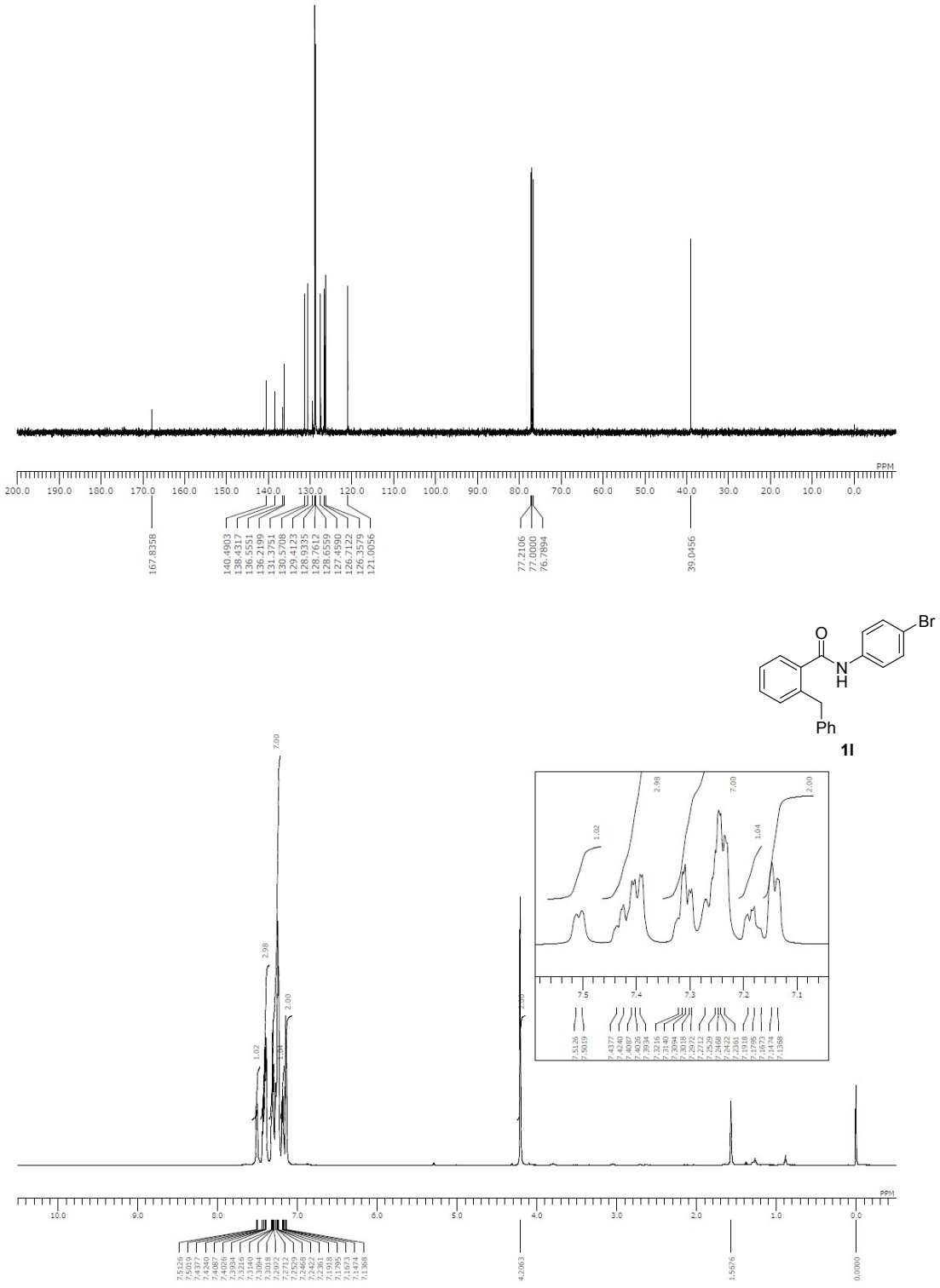


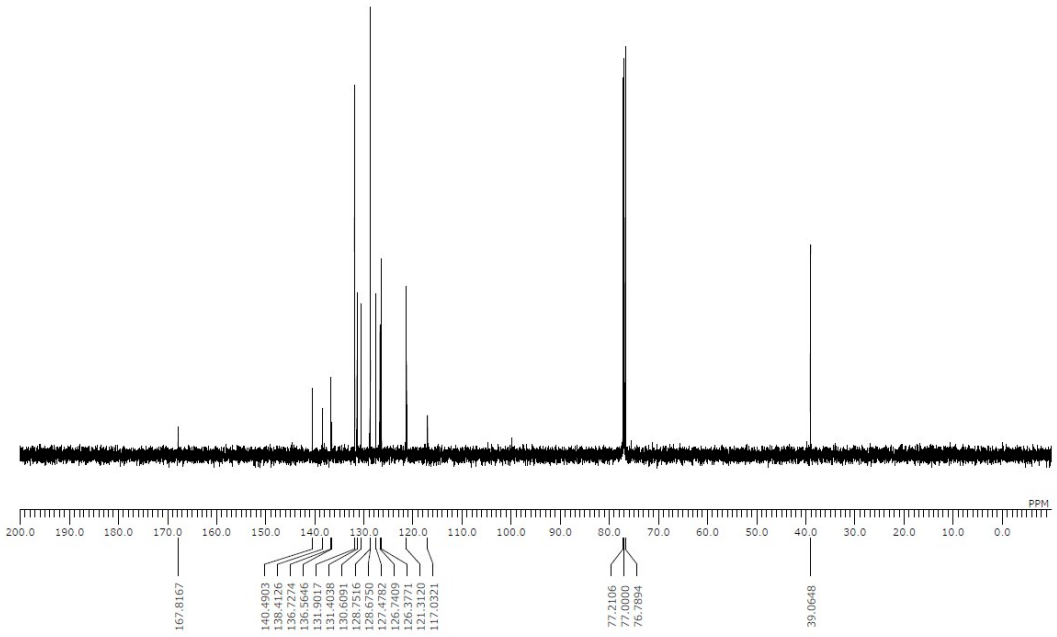
^{1}H-NMR spectrum of **1k** ($CDCl_3$, 600 MHz)

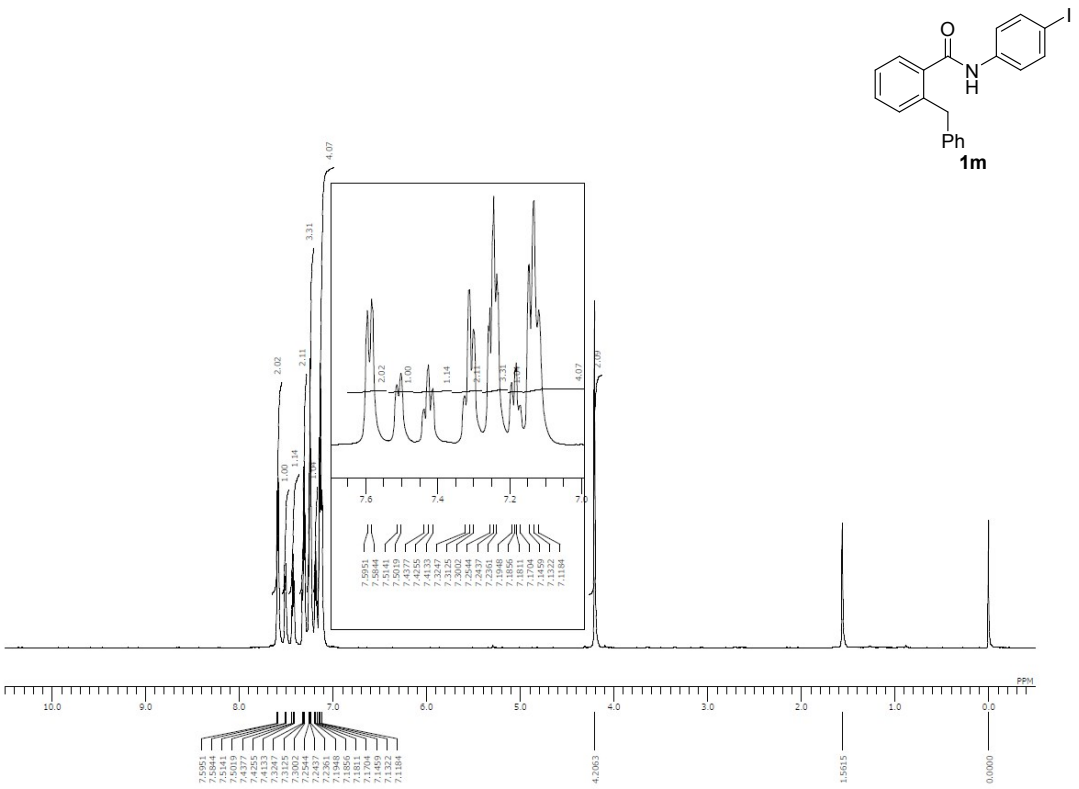
^{13}C-NMR spectrum of **1k** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **1l** ($CDCl_3$, 600 MHz)

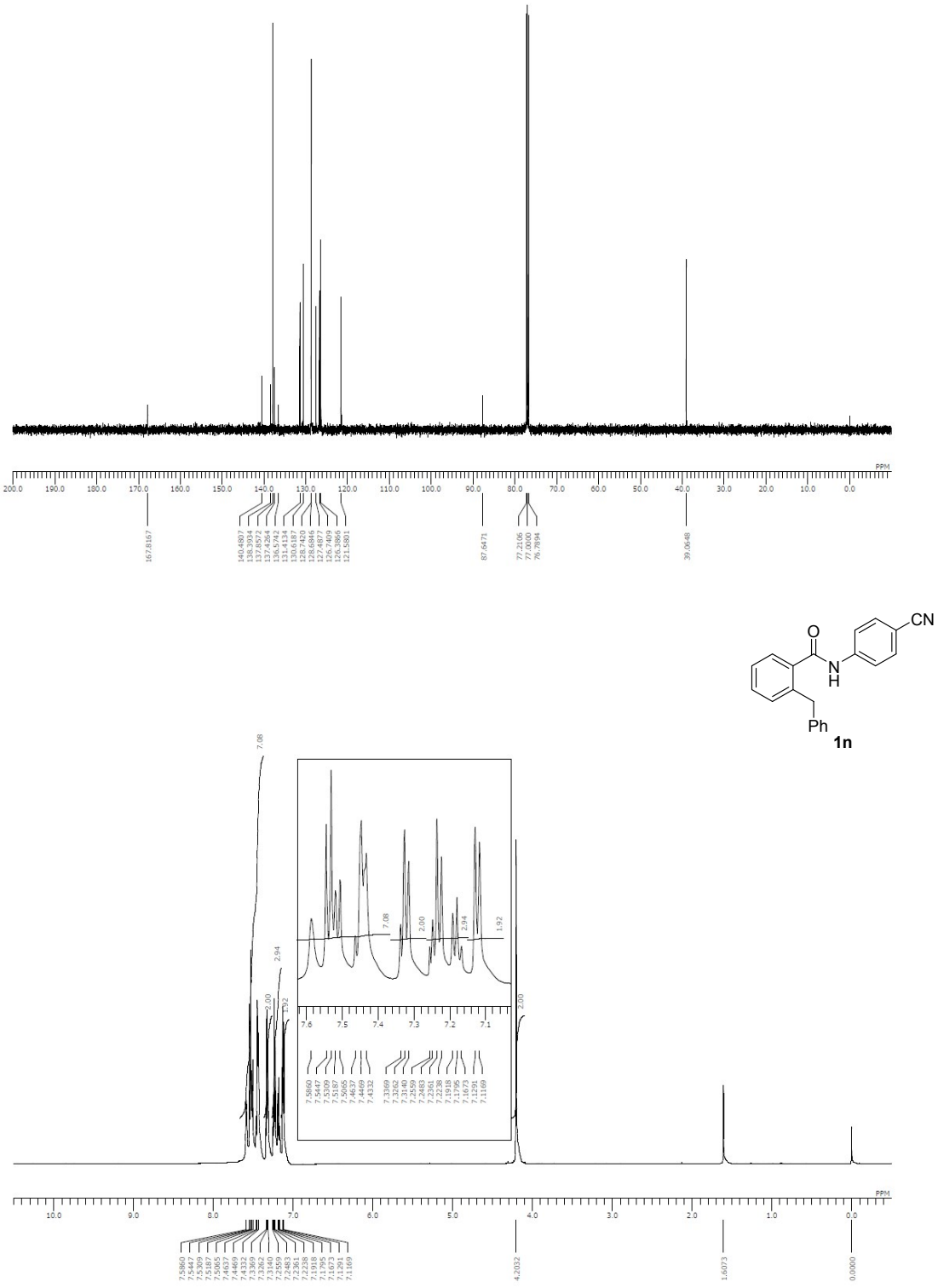
^{13}C-NMR spectrum of **11** ($CDCl_3$, 150 MHz)





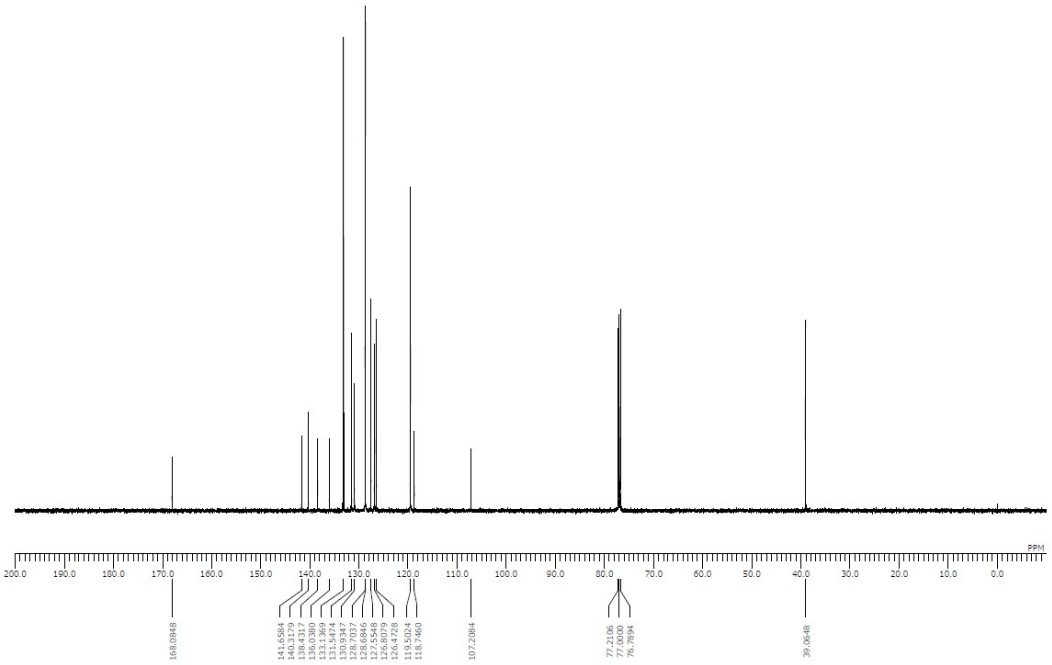
^{1}H-NMR spectrum of **1m** ($CDCl_3$, 600 MHz)

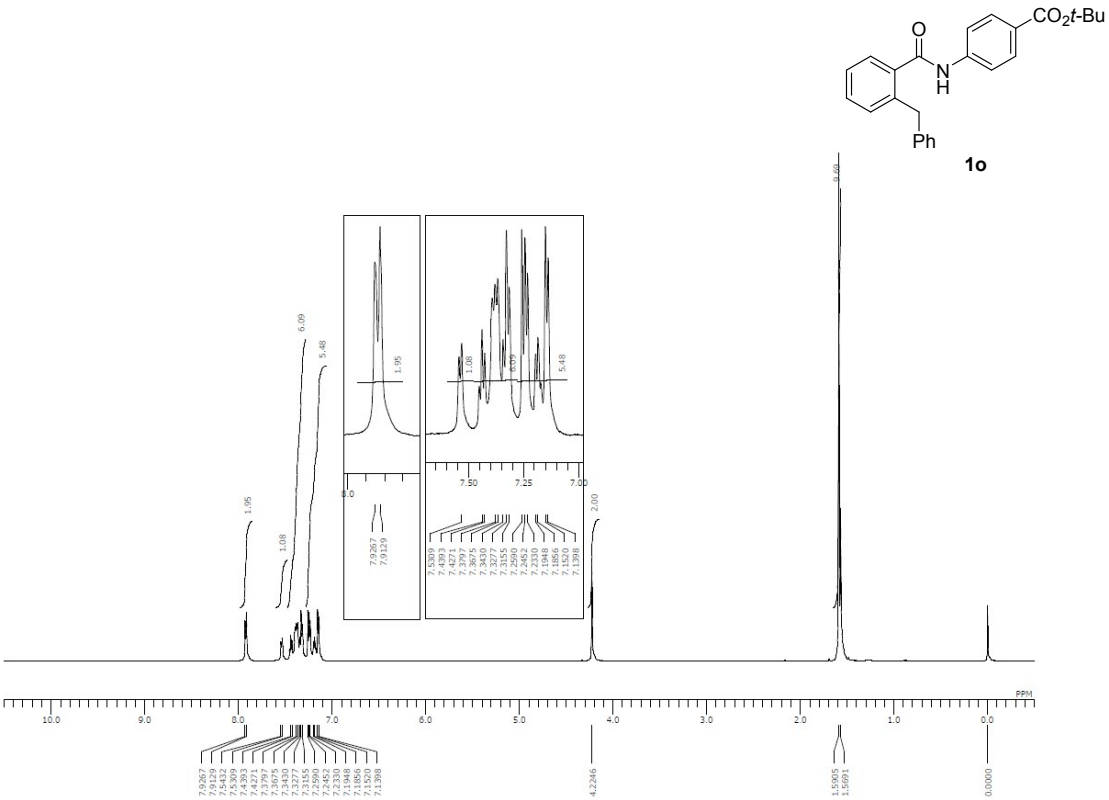
^{13}C-NMR spectrum of **1m** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **1n** ($CDCl_3$, 600 MHz)

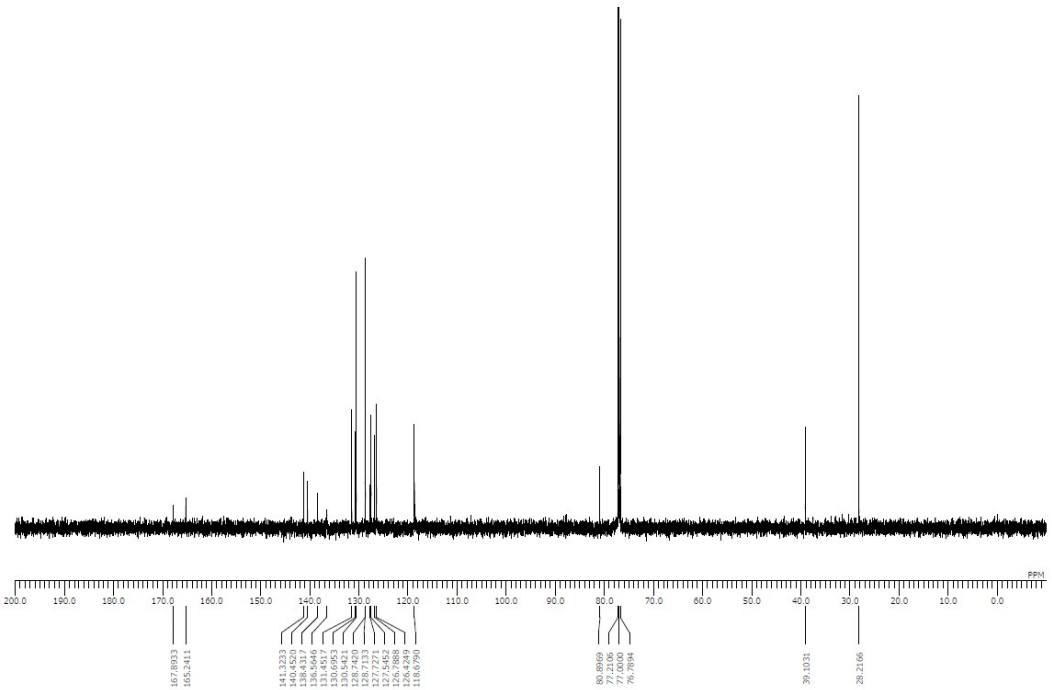
^{13}C-NMR spectrum of **1n** ($CDCl_3$, 150 MHz)



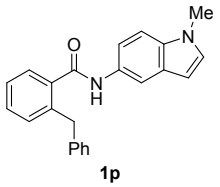


^{1}H-NMR spectrum of **1o** ($CDCl_3$, 600 MHz)

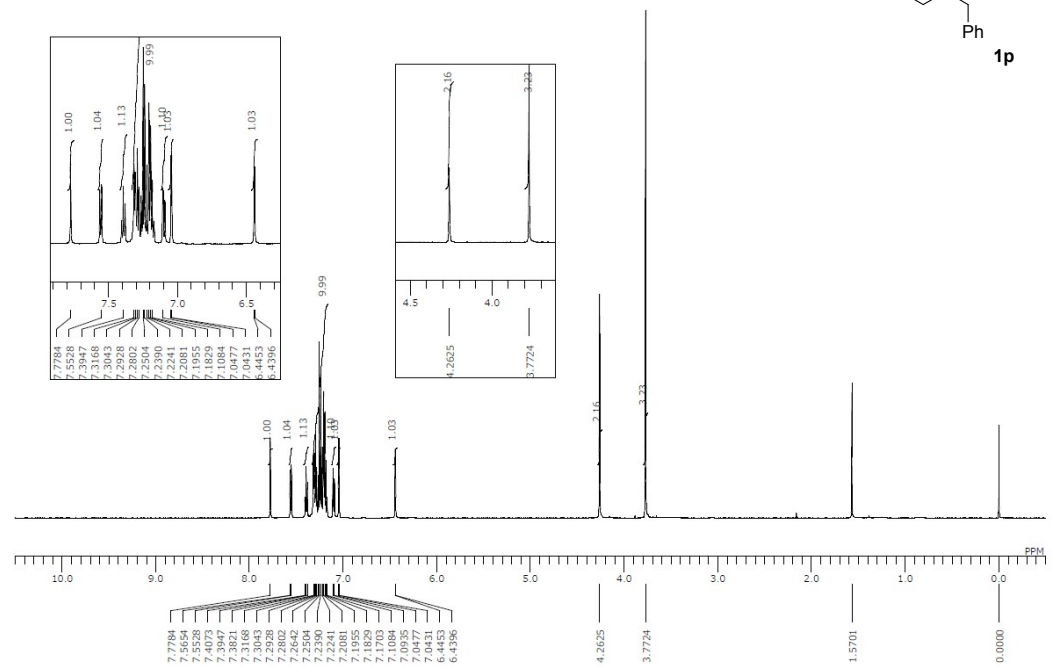
^{13}C-NMR spectrum of **1o** ($CDCl_3$, 150 MHz)



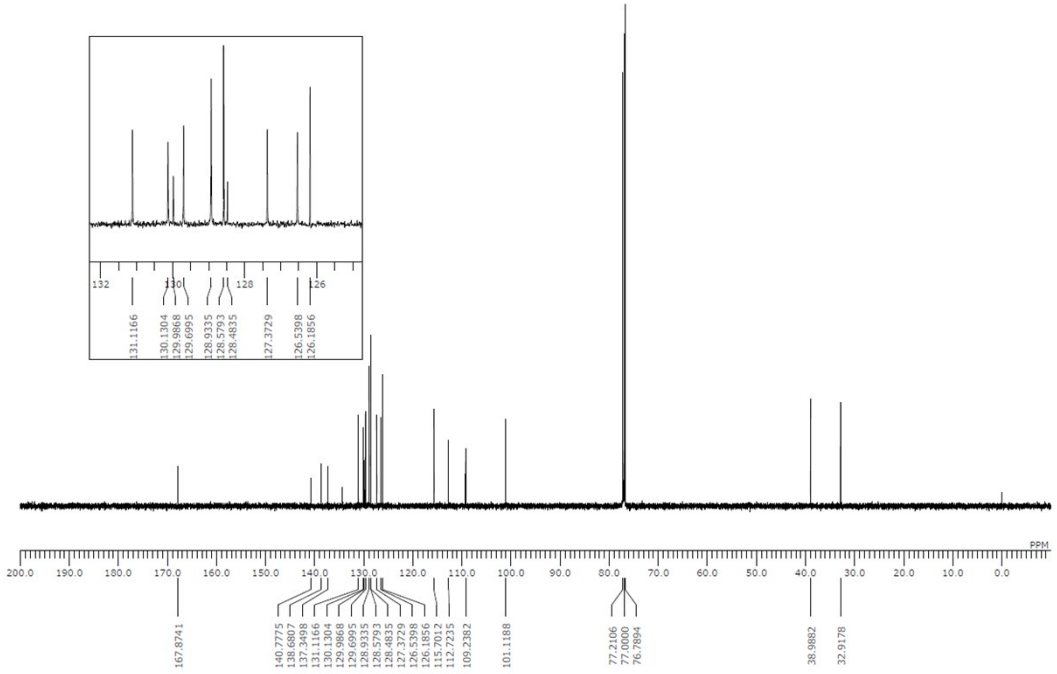
^{1}H-NMR spectrum of **1p** ($CDCl_3$, 600 MHz)



1p



^{13}C-NMR spectrum of **1p** ($CDCl_3$, 150 MHz)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126.5398
126.1856
115.7012
112.7235
109.2382
101.1188
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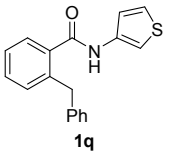
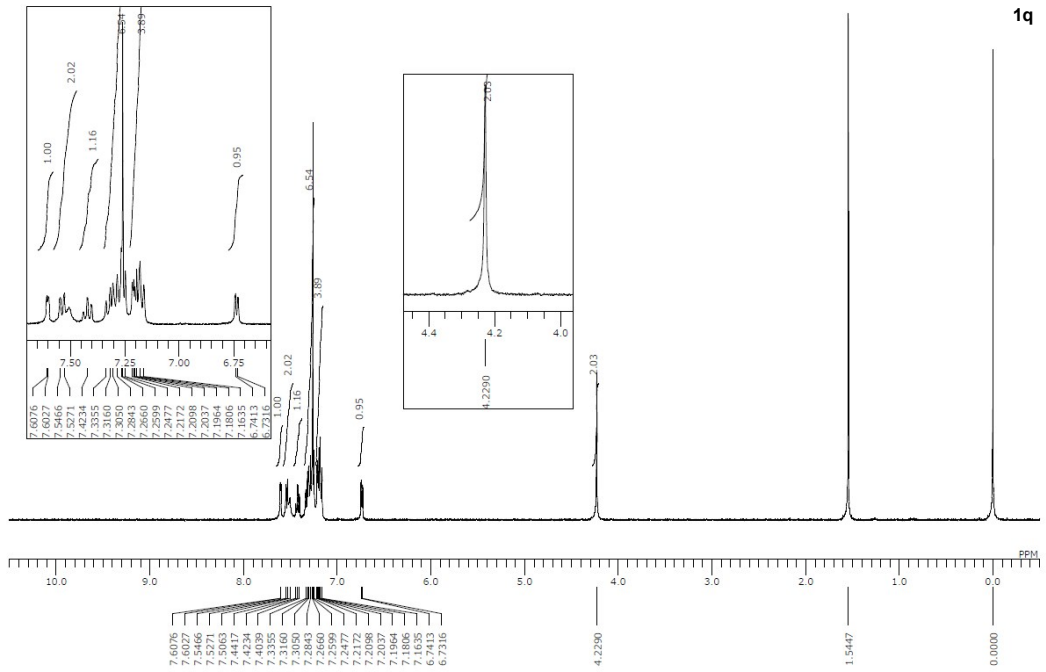
77.0000
76.7894
38.9882
32.9178

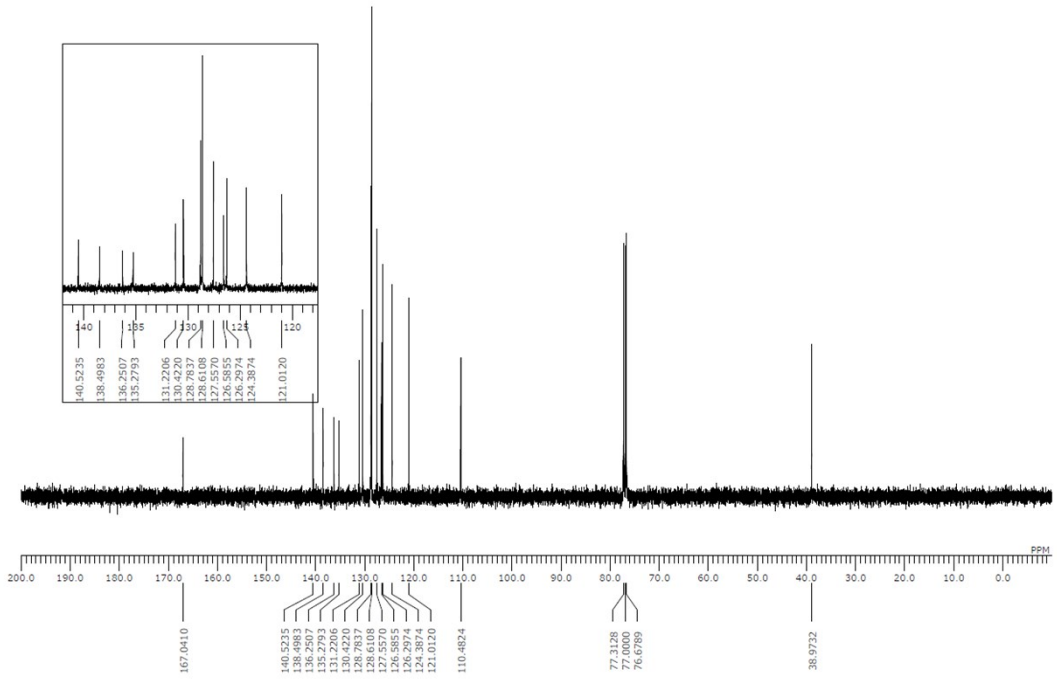
^{1}H-NMR spectrum of **1q** ($CDCl_3$, 400 MHz)

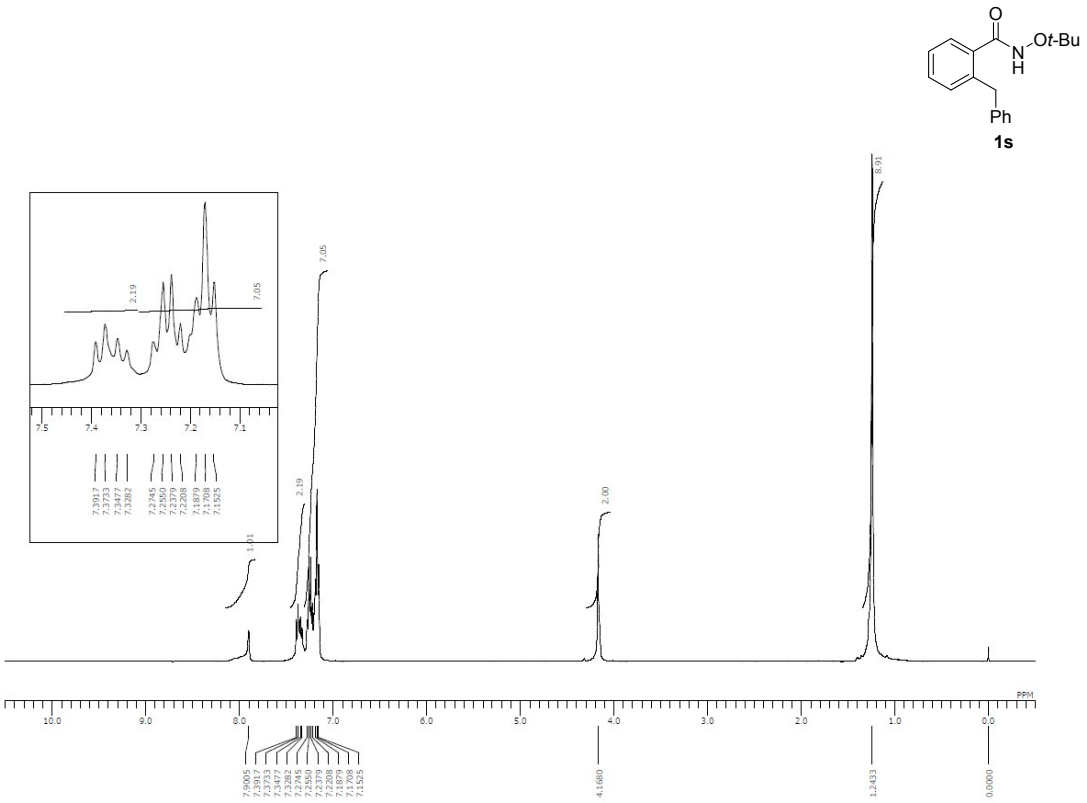


1q



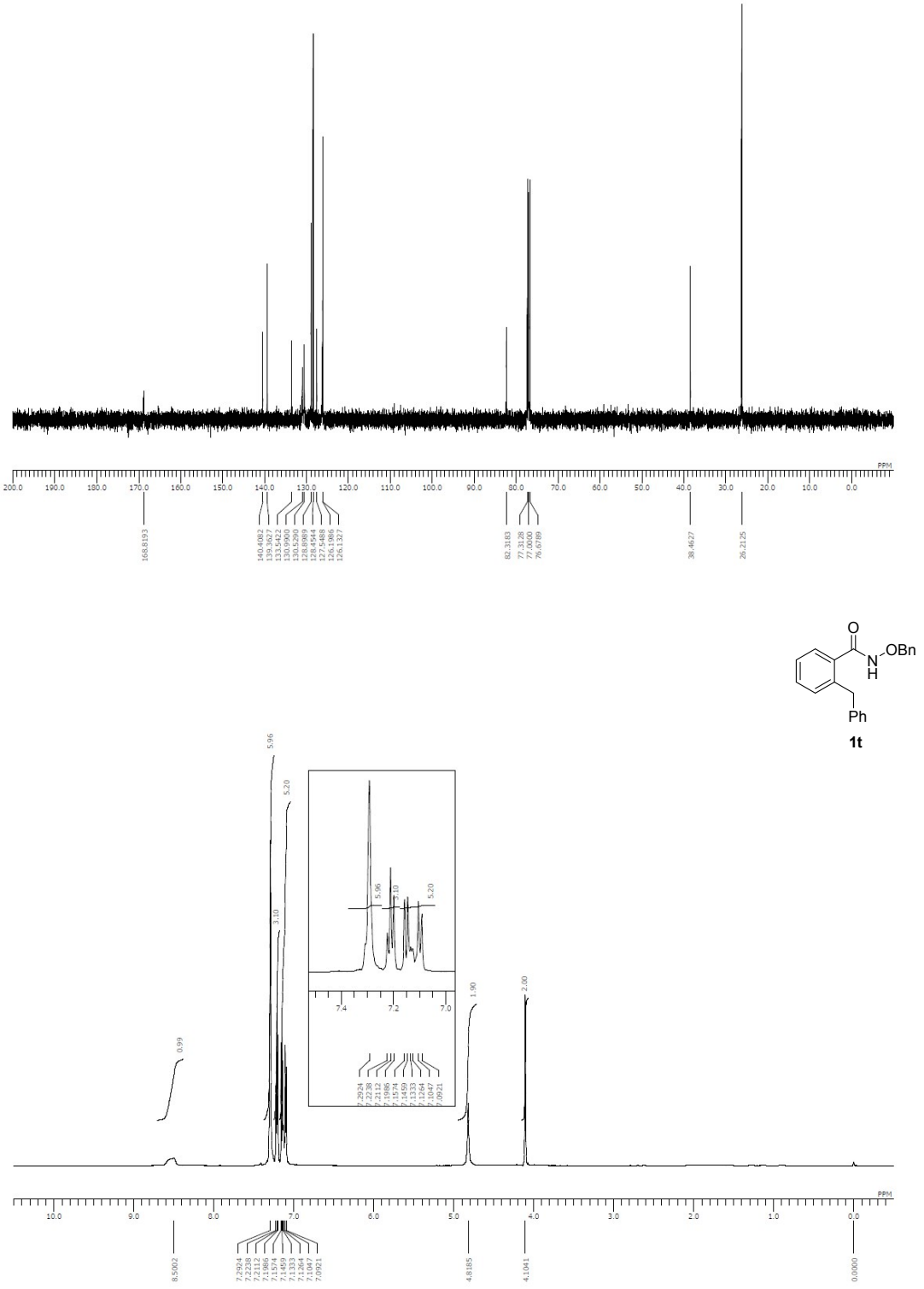
^{13}C-NMR spectrum of **1q** ($CDCl_3$, 100 MHz)





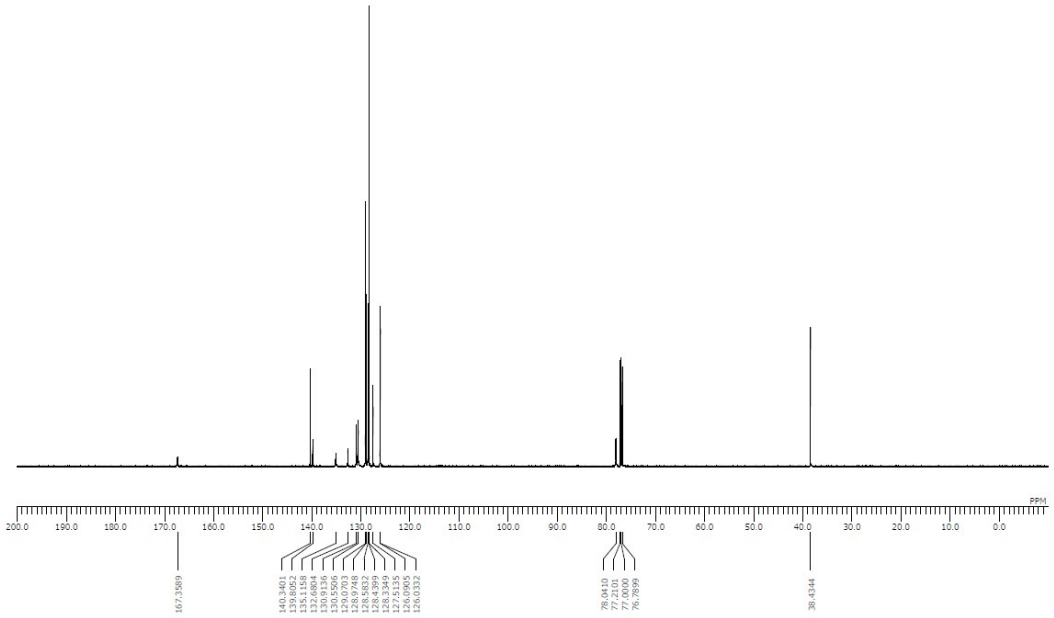
^{1}H-NMR spectrum of **1s** ($CDCl_3$, 400 MHz)

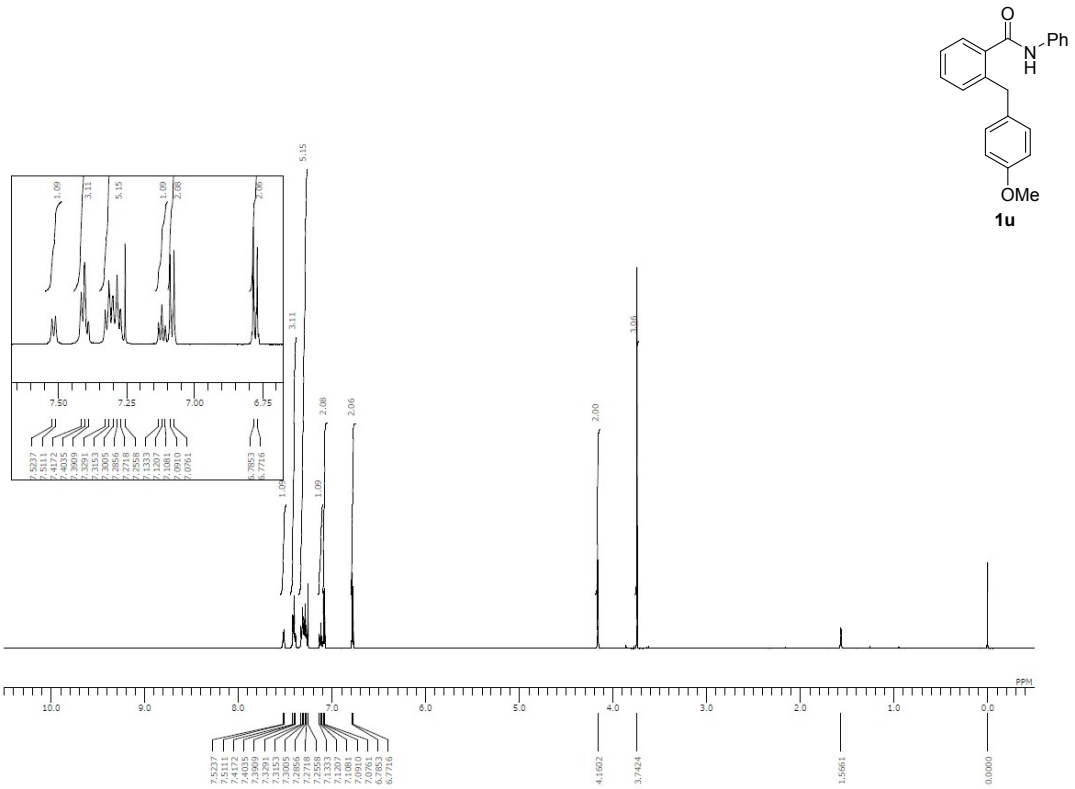
^{13}C-NMR spectrum of **1s** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **1t** ($CDCl_3$, 600 MHz)

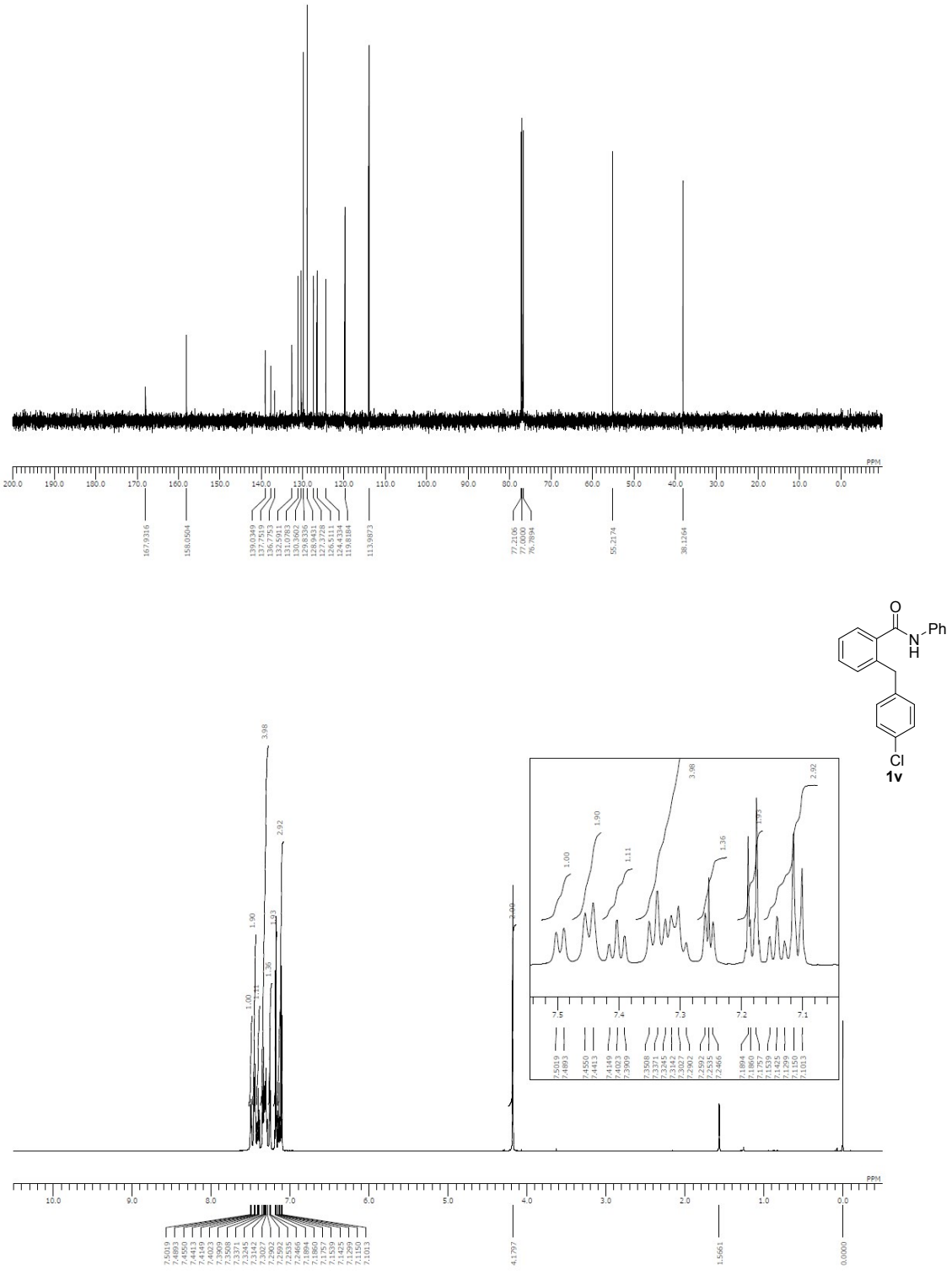
^{13}C-NMR spectrum of **1t** ($CDCl_3$, 150 MHz)





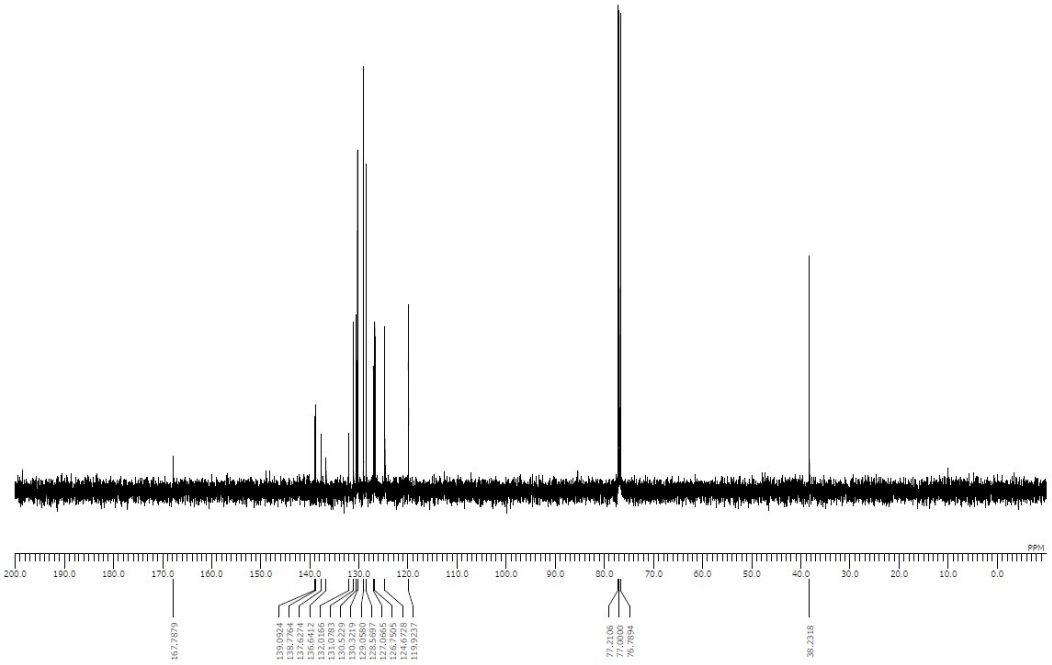
^{1}H-NMR spectrum of **1u** ($CDCl_3$, 600 MHz)

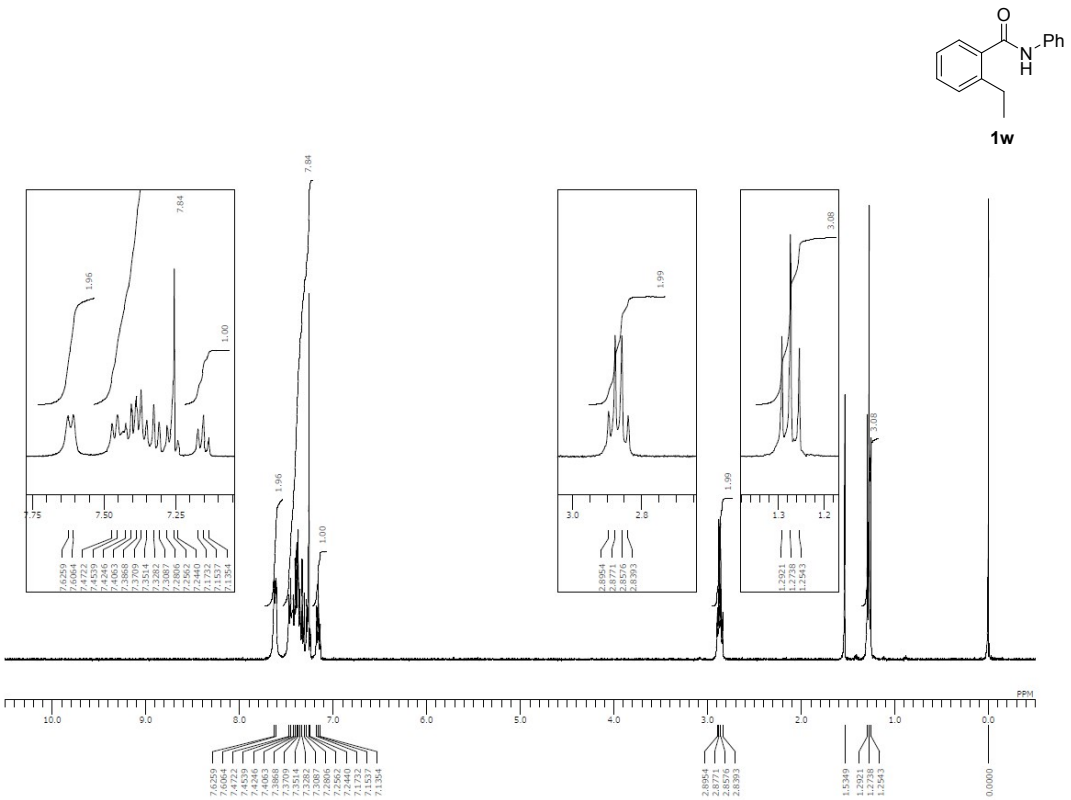
^{13}C-NMR spectrum of **1u** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **1v** ($CDCl_3$, 600 MHz)

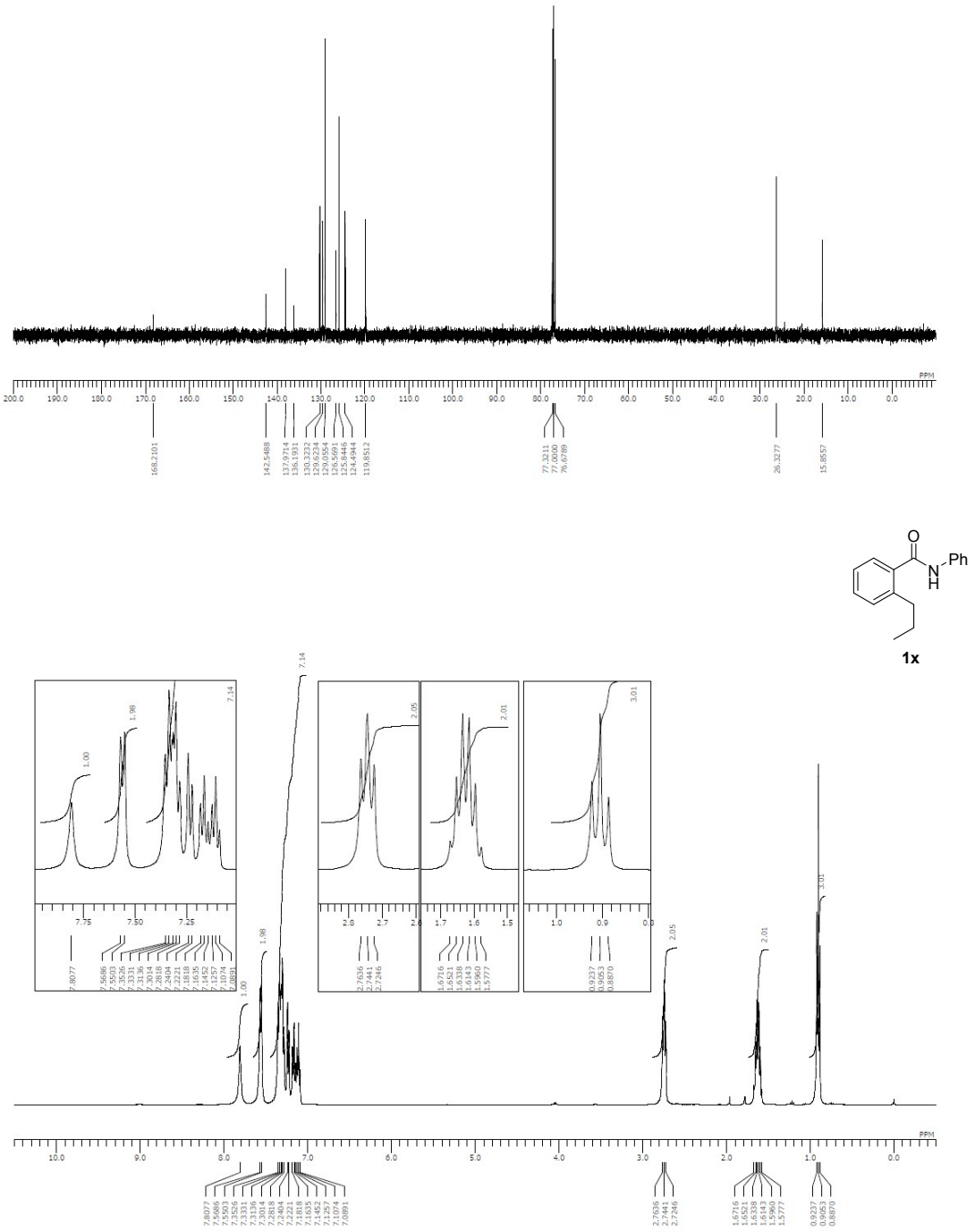
^{13}C-NMR spectrum of **1v** ($CDCl_3$, 150 MHz)





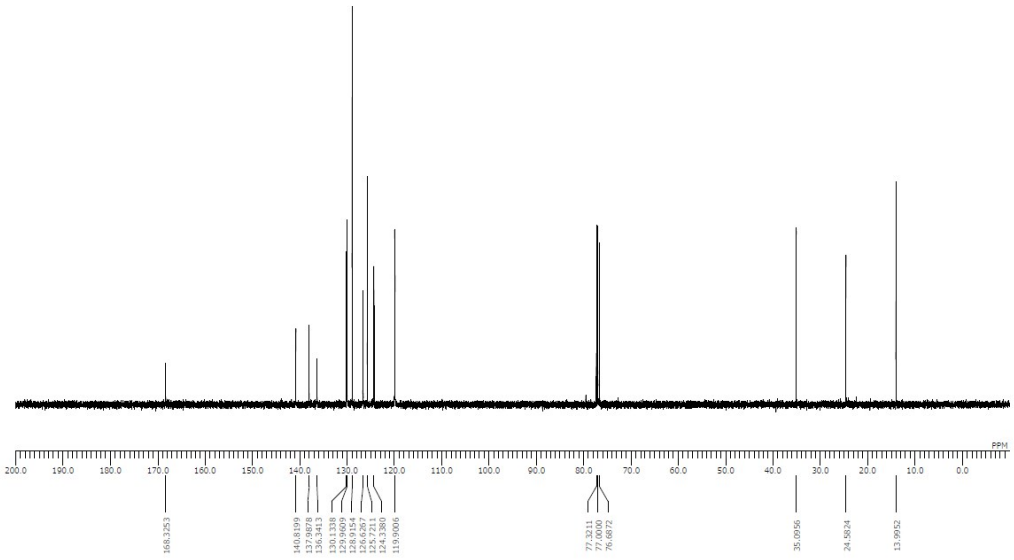
^{1}H-NMR spectrum of **1w** ($CDCl_3$, 400 MHz)

^{13}C-NMR spectrum of **1w** ($CDCl_3$, 100 MHz)

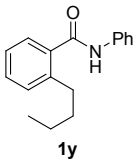


^{1}H-NMR spectrum of **1x** ($CDCl_3$, 400 MHz)

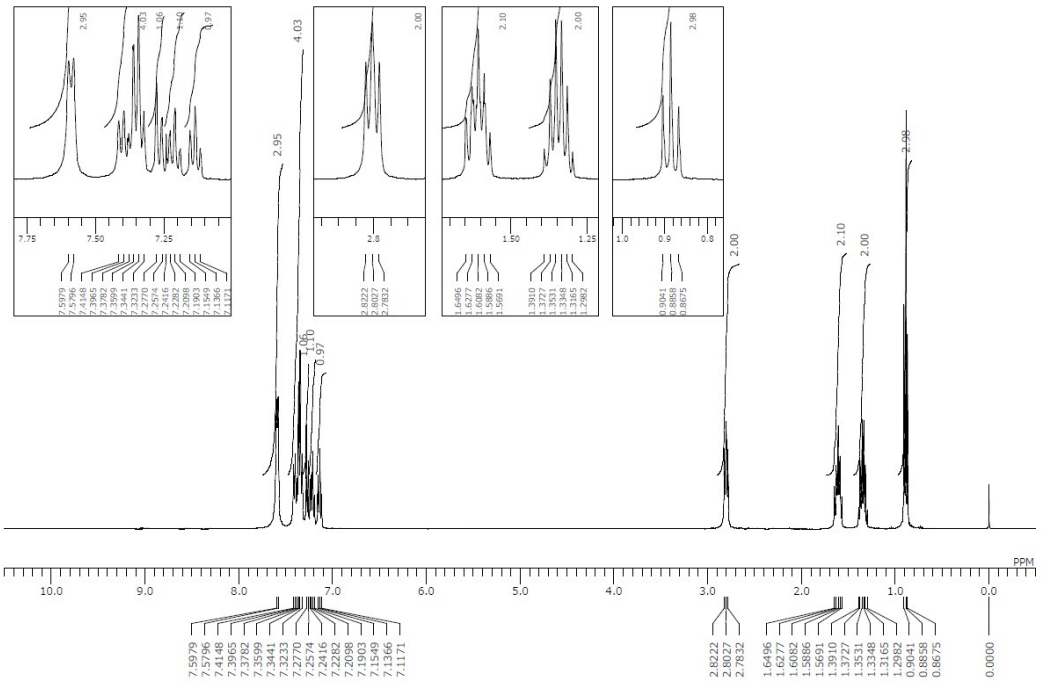
^{13}C-NMR spectrum of **1x** ($CDCl_3$, 100 MHz)



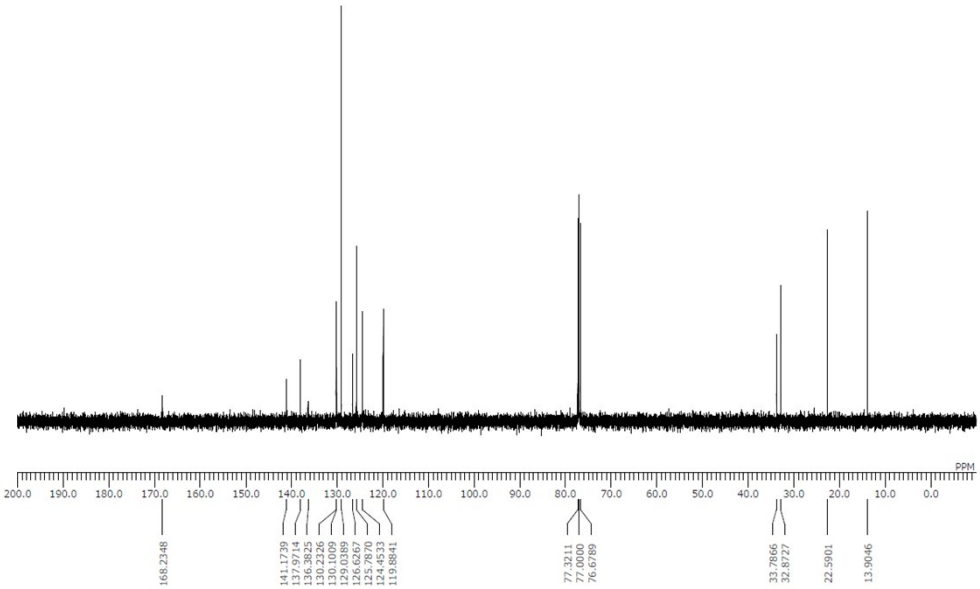
^{1}H-NMR spectrum of **1y** ($CDCl_3$, 400 MHz)

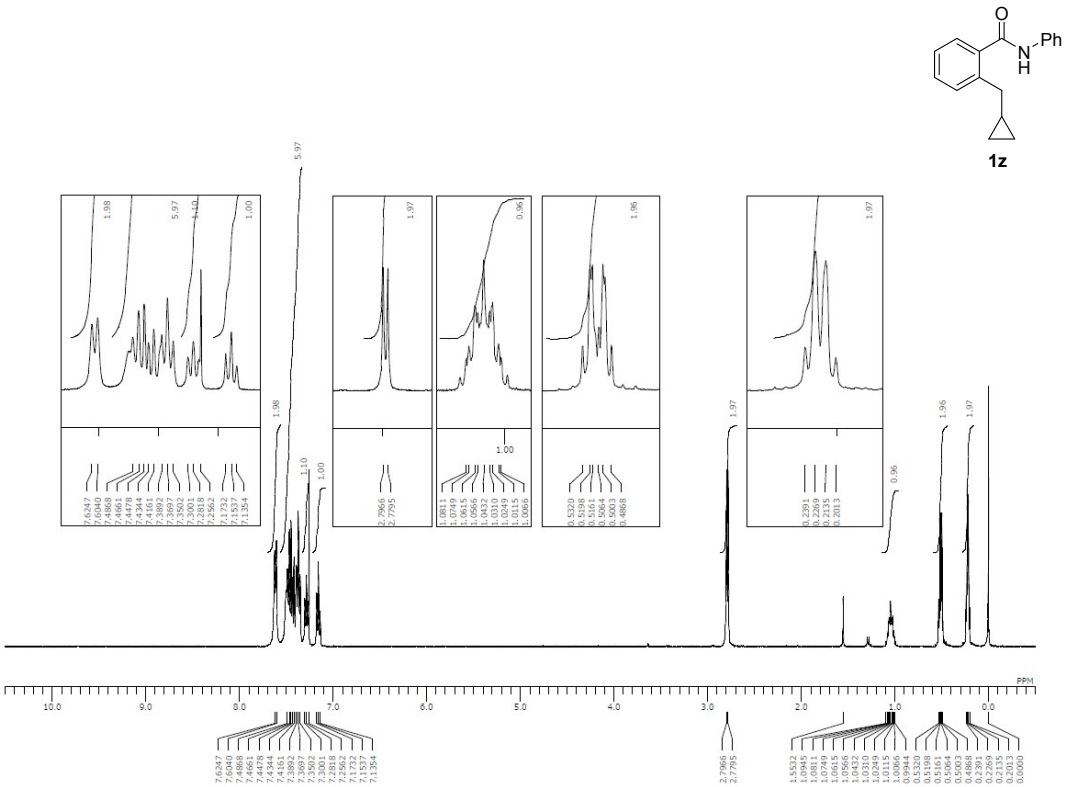


1y



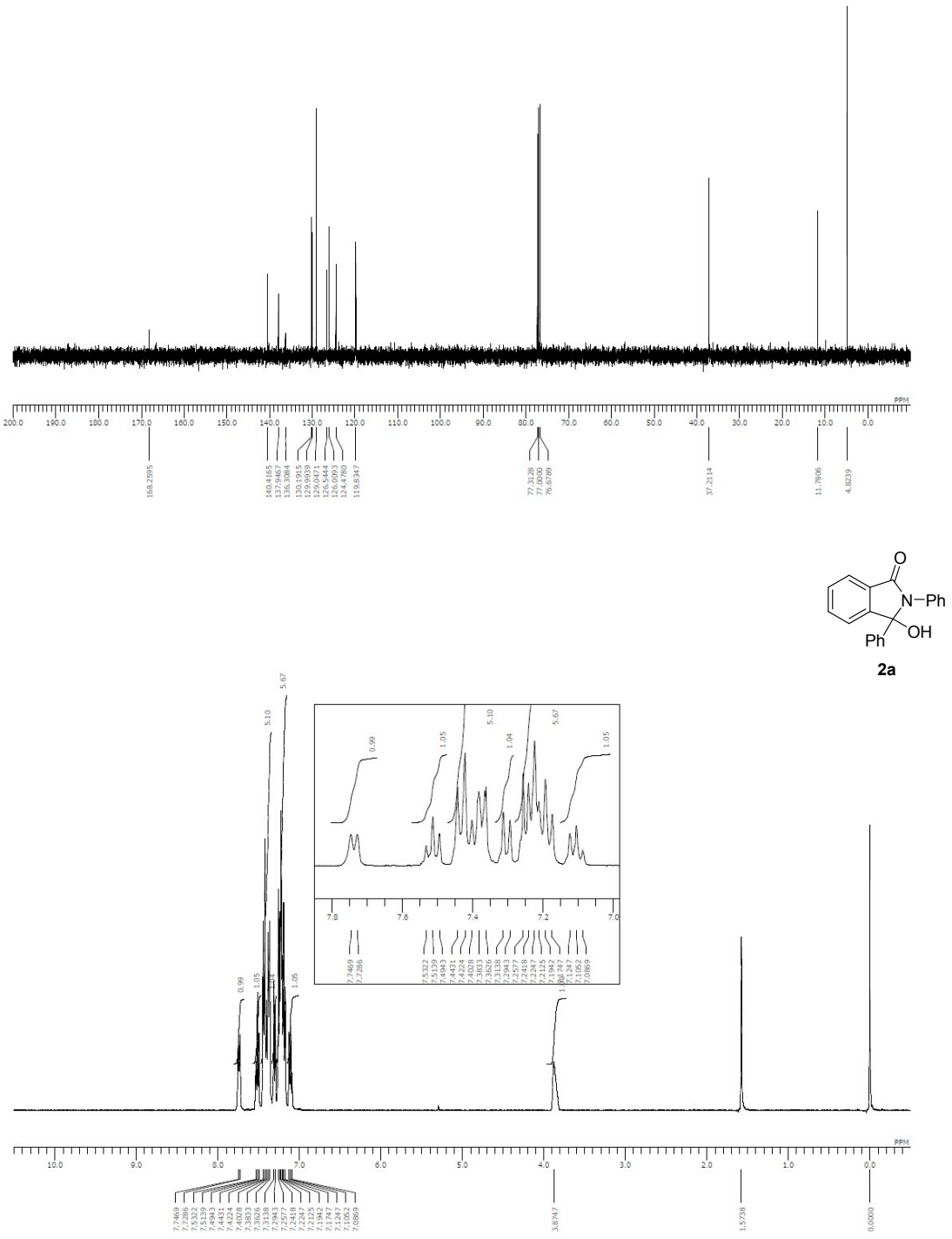
^{13}C-NMR spectrum of **1y** ($CDCl_3$, 100 MHz)





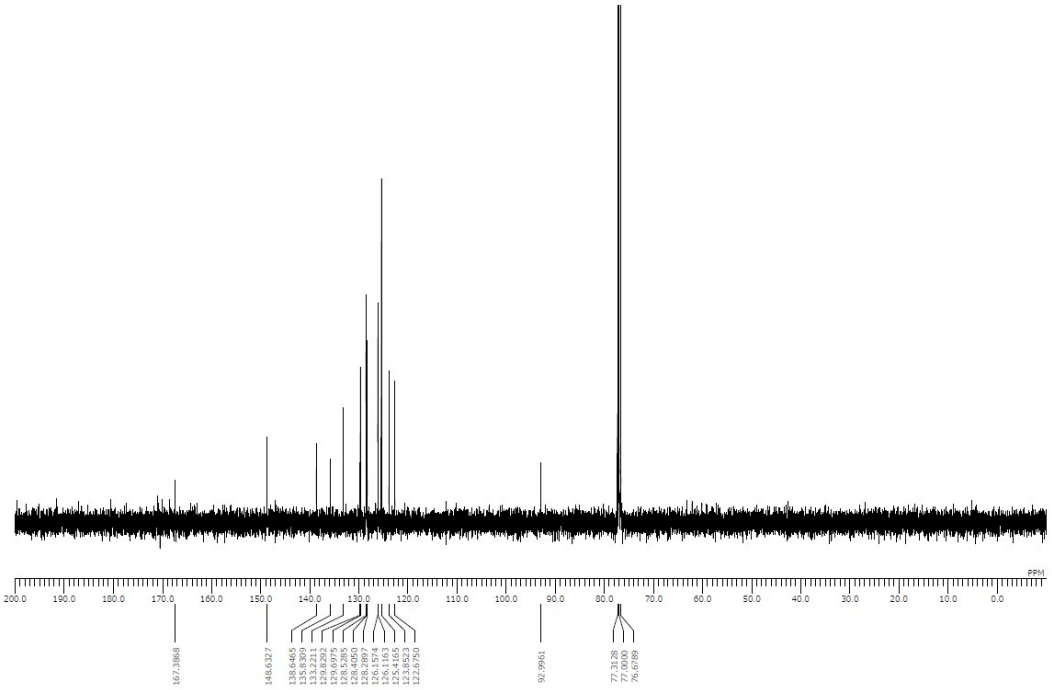
^{1}H-NMR spectrum of **1z** ($CDCl_3$, 400 MHz)

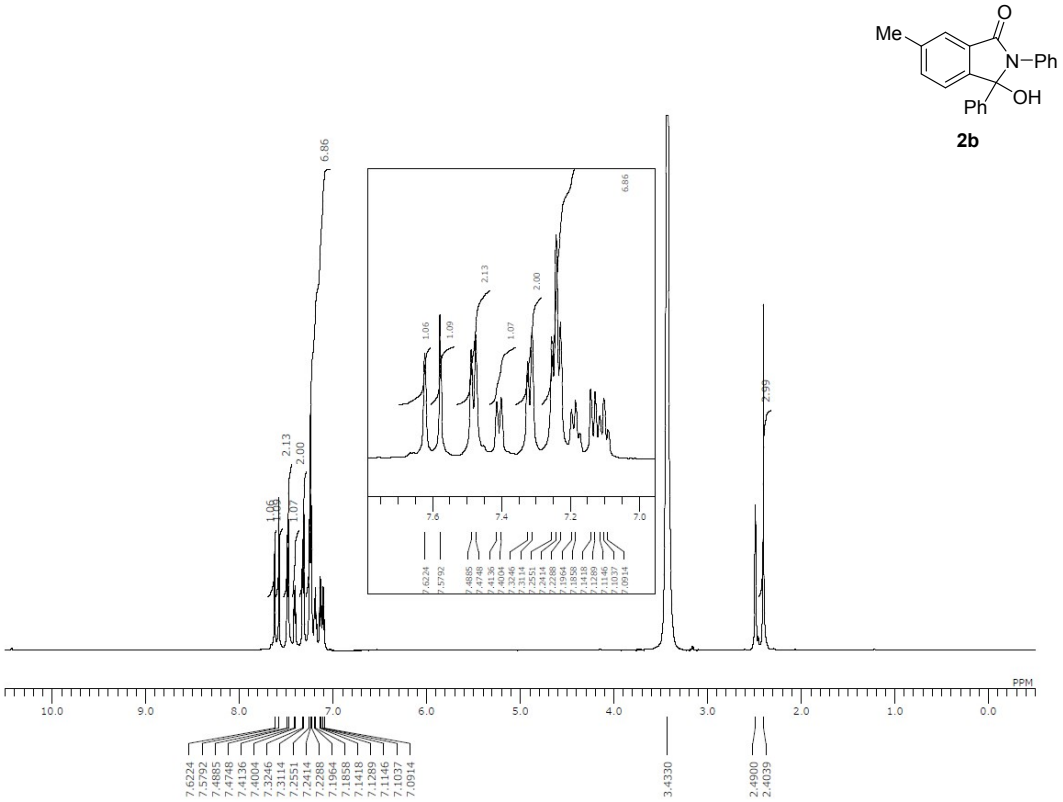
^{13}C-NMR spectrum of **1z** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **2a** ($CDCl_3$, 400 MHz)

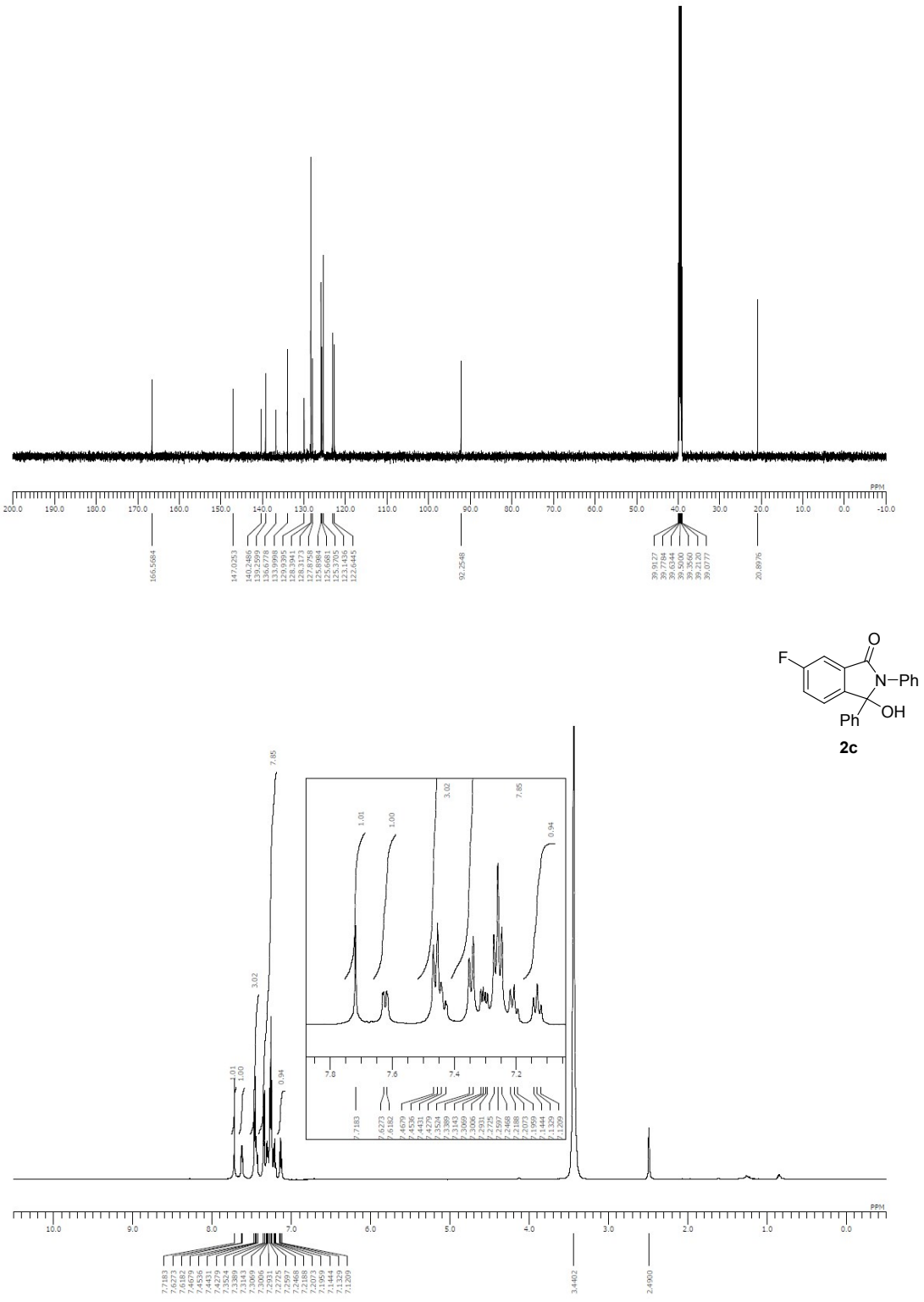
^{13}C-NMR spectrum of **2a** ($CDCl_3$, 100 MHz)





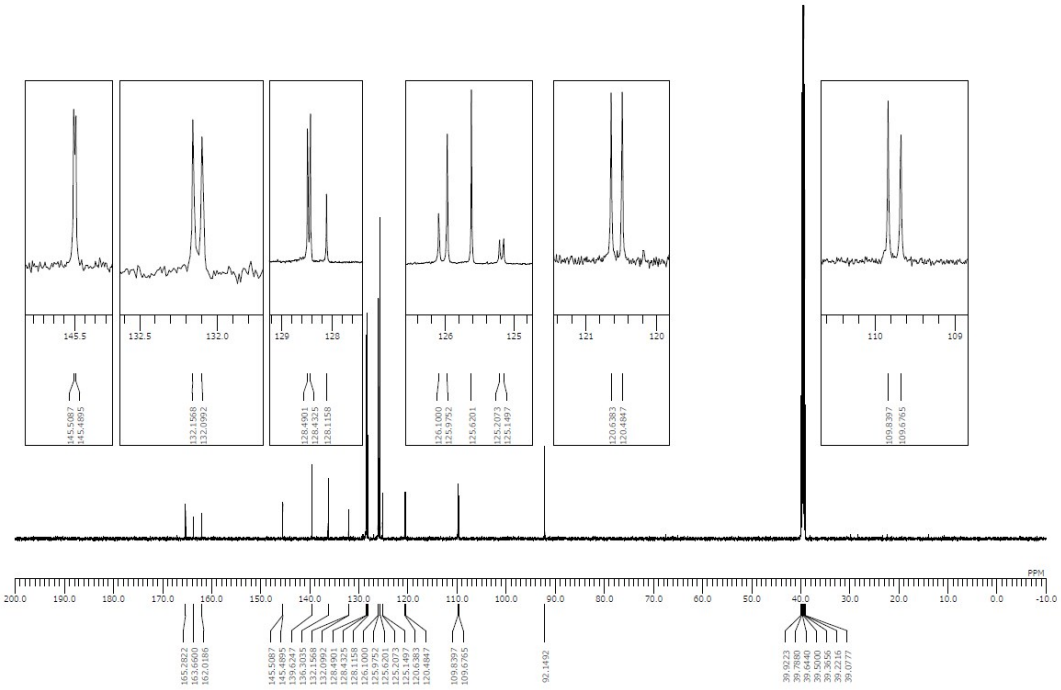
^{1}H-NMR spectrum of **2b** (DMSO-d_6, 600 MHz)

^{13}C-NMR spectrum of **2b** (DMSO-d_6, 150 MHz)

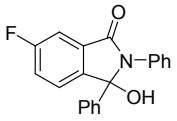


^{1}H-NMR spectrum of **2c** (DMSO-d_6, 600 MHz)

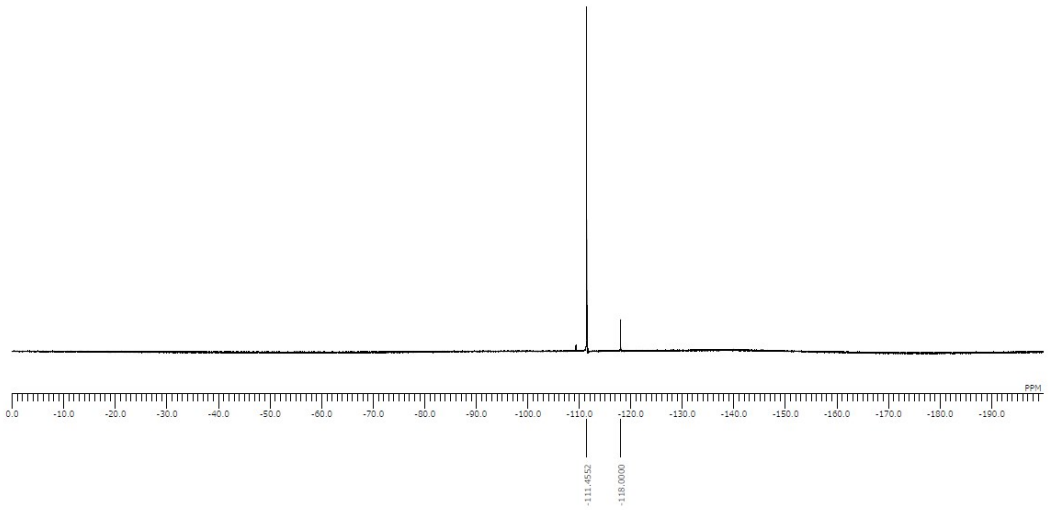
^{13}C-NMR spectrum of **2c** (DMSO-d_6, 150 MHz)



^{19}F-NMR spectrum of **2c** (DMSO-d_6, 565 MHz)



2c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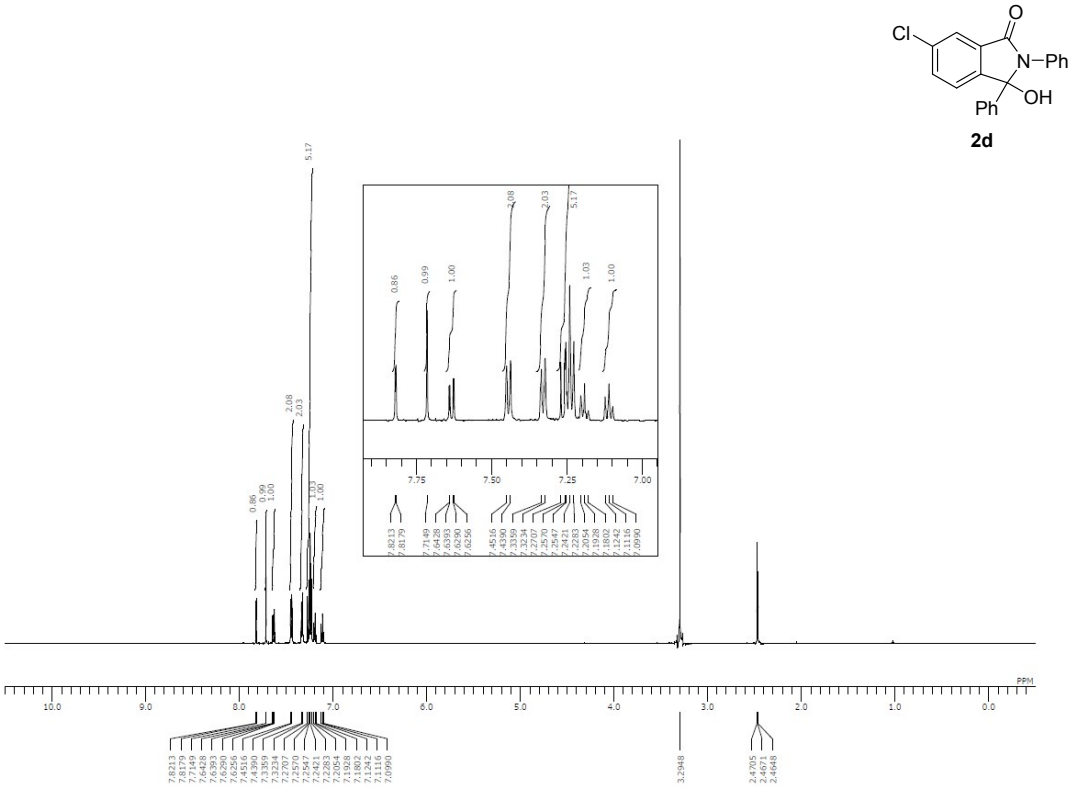
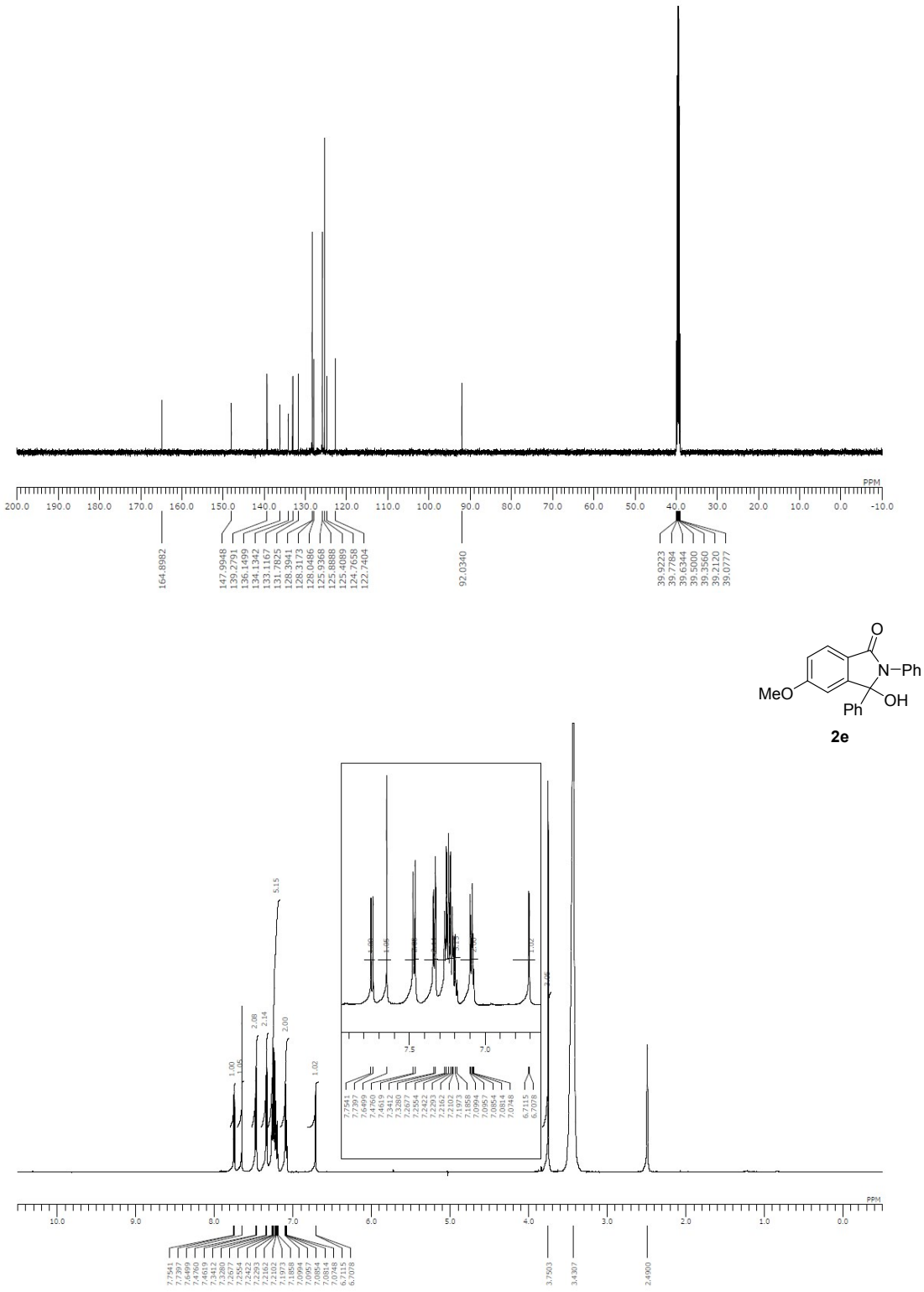


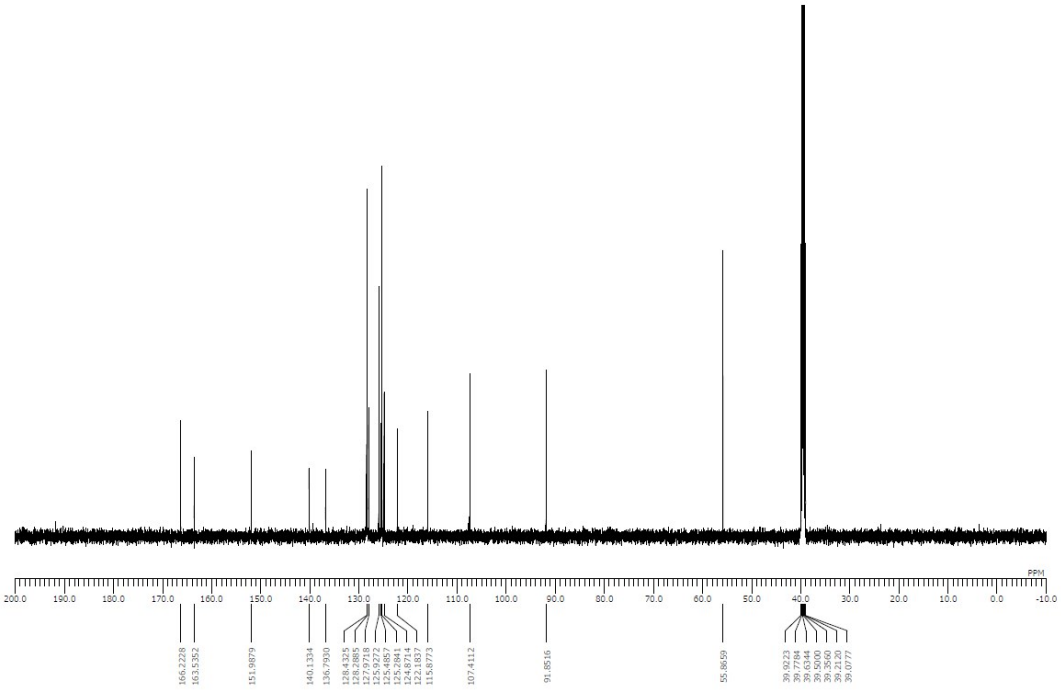
^{1}H-NMR spectrum of **2d** (DMSO-d_6, 600 MHz)

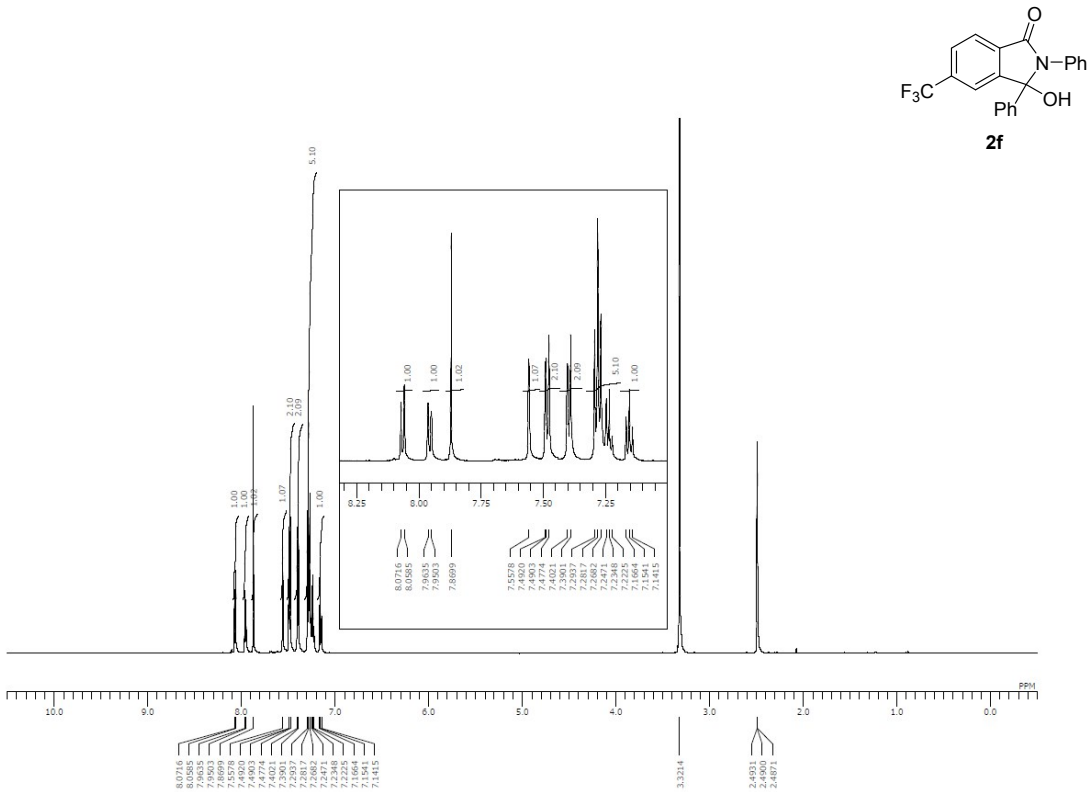
^{13}C-NMR spectrum of **2d** (DMSO-d_6, 150 MHz)



^{1}H-NMR spectrum of **2e** (DMSO-d_6, 600 MHz)

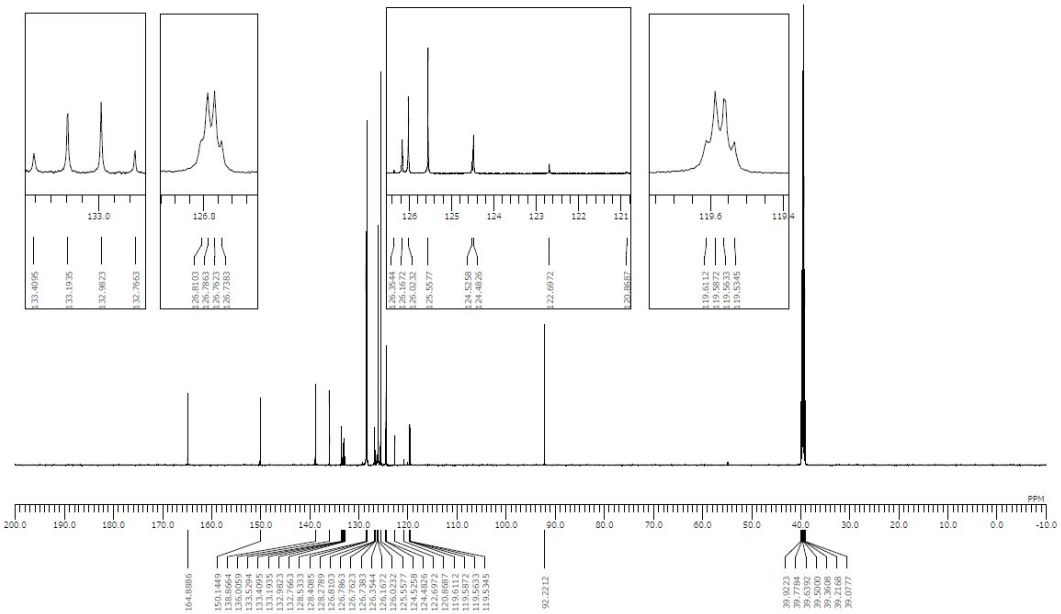
^{13}C-NMR spectrum of **2e** (DMSO-d_6, 150 MHz)



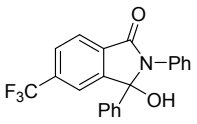


^{1}H-NMR spectrum of **2f** (DMSO-d_6, 600 MHz)

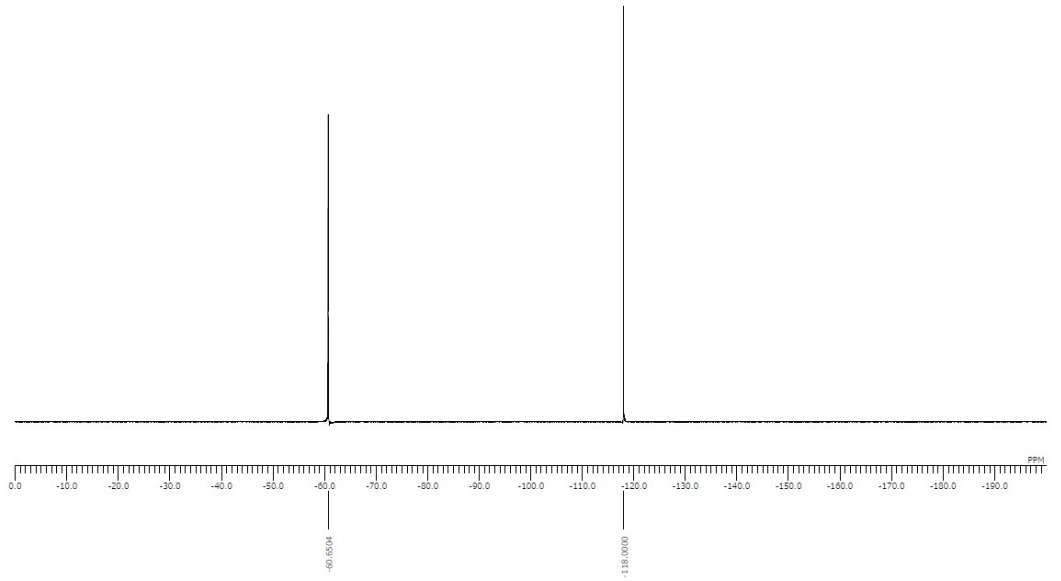
^{13}C-NMR spectrum of **2f** (DMSO-d_6, 150 MHz)

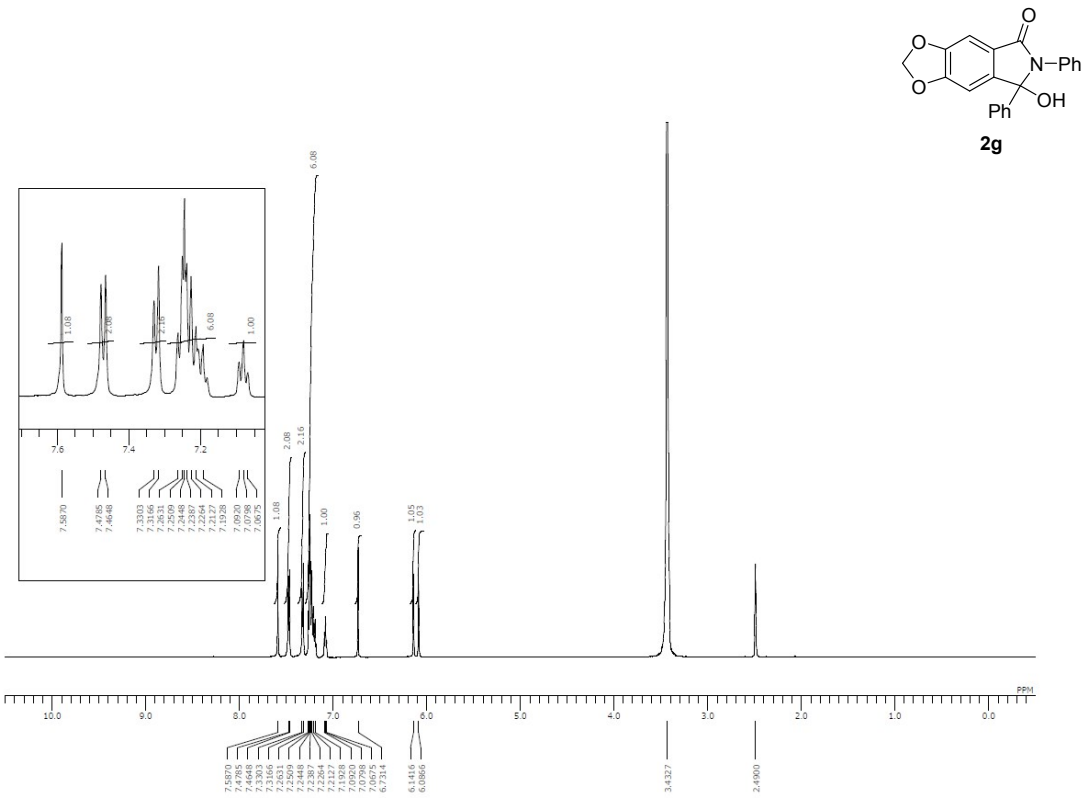


^{19}F-NMR spectrum of **2f** (DMSO-d_6, 565 MHz)



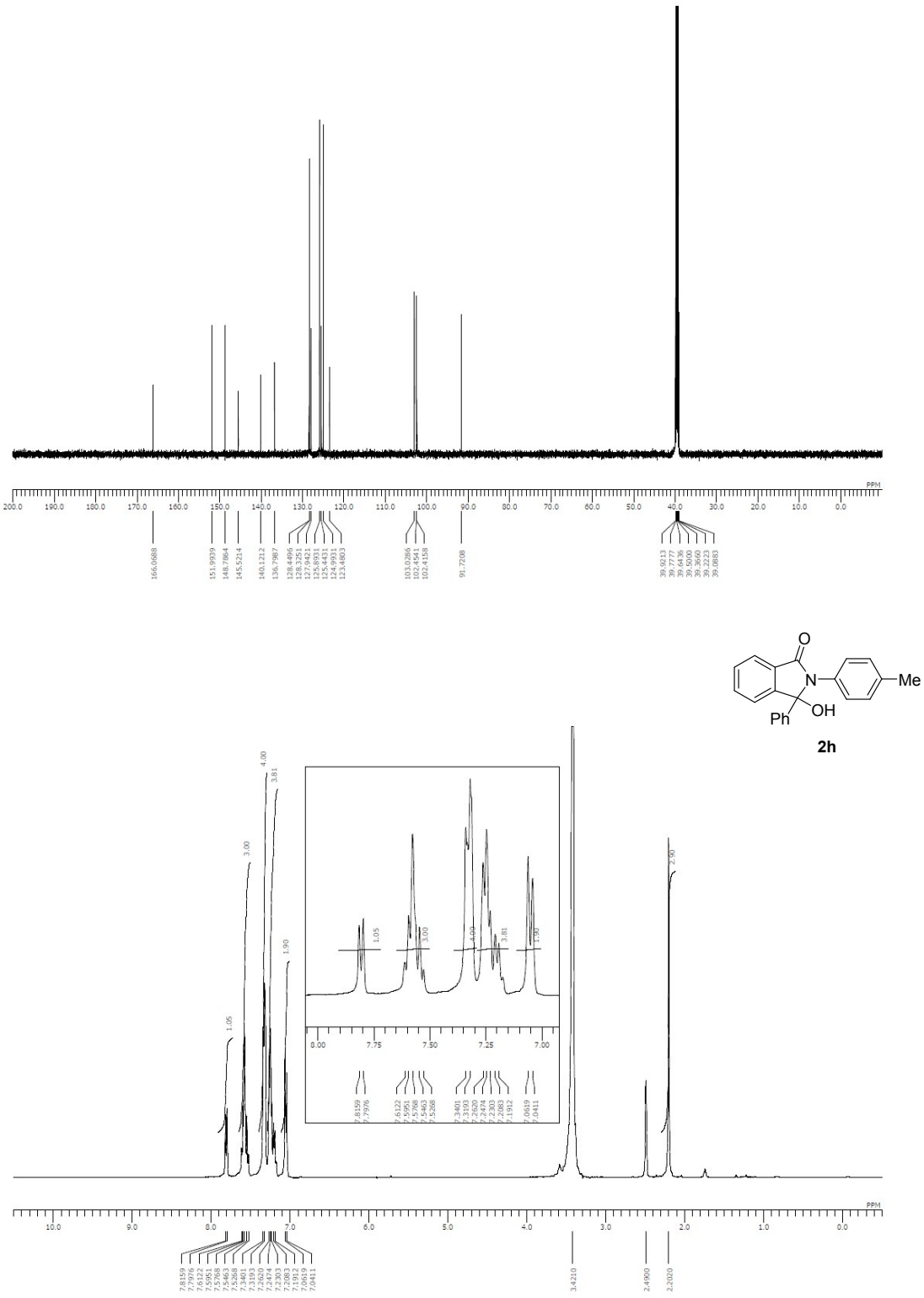
2f





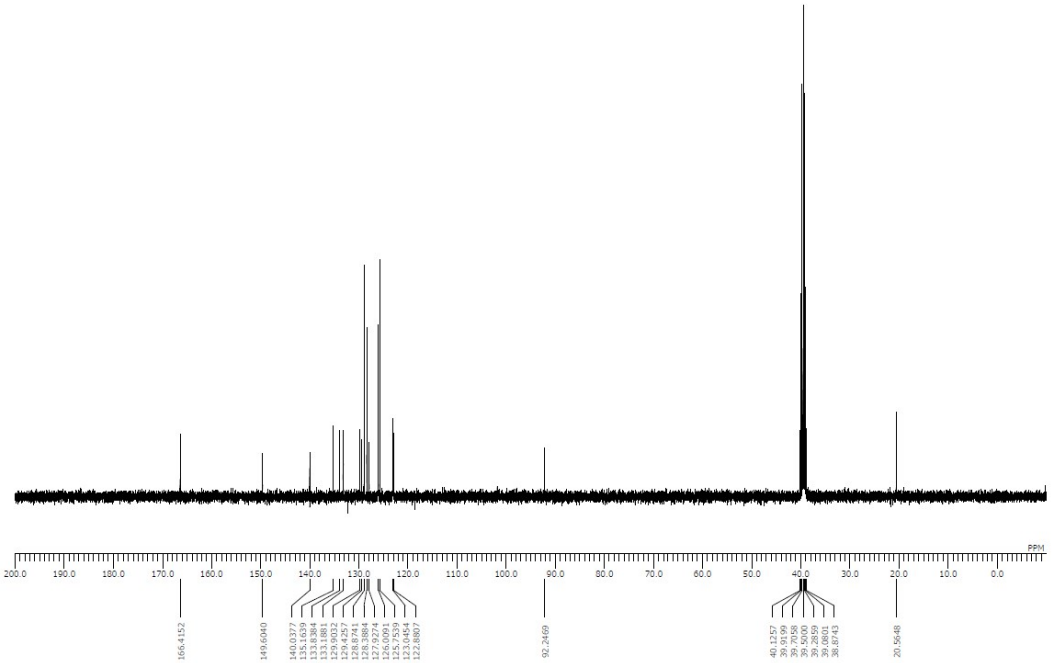
^{1}H-NMR spectrum of **2g** (DMSO-d_6, 600 MHz)

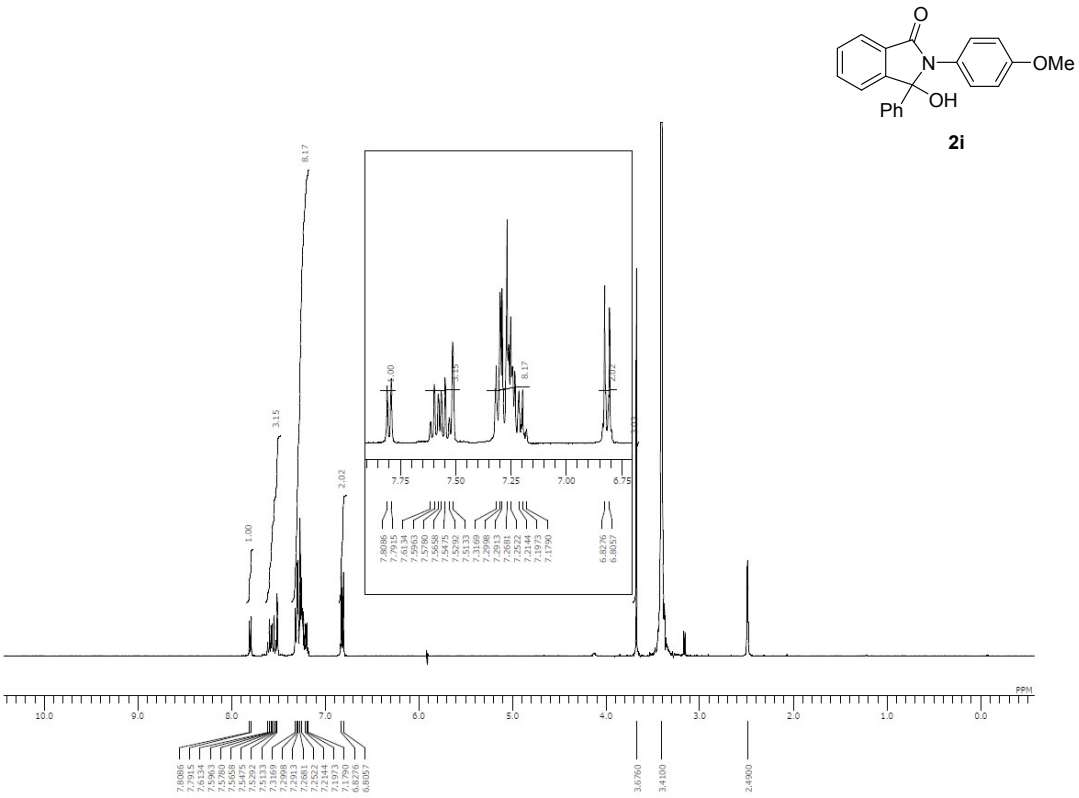
^{13}C-NMR spectrum of **2g** (DMSO-d_6, 150 MHz)



^{1}H-NMR spectrum of **2h** (DMSO-d_6, 400 MHz)

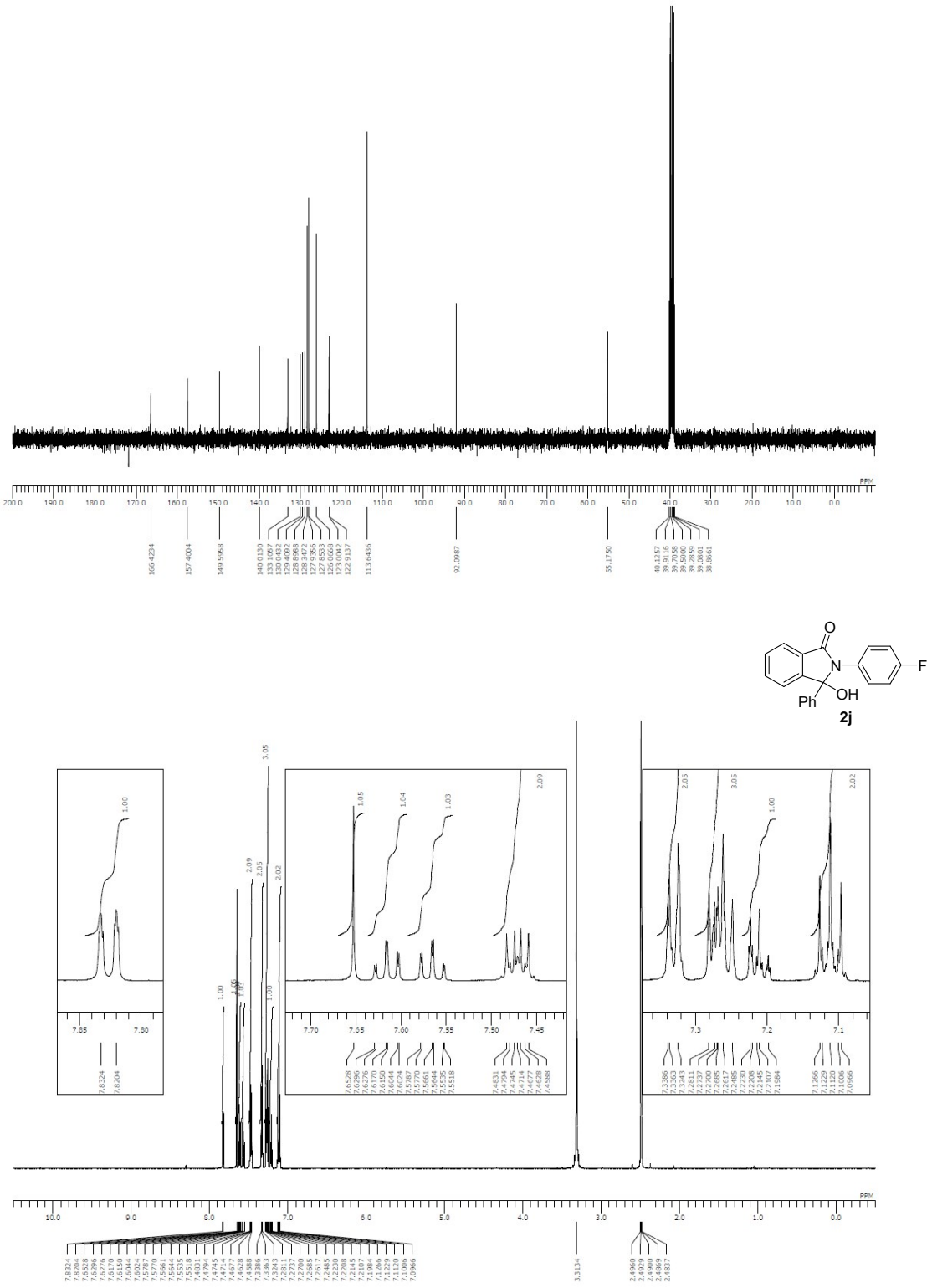
^{13}C-NMR spectrum of **2h** (DMSO-d_6, 100 MHz)





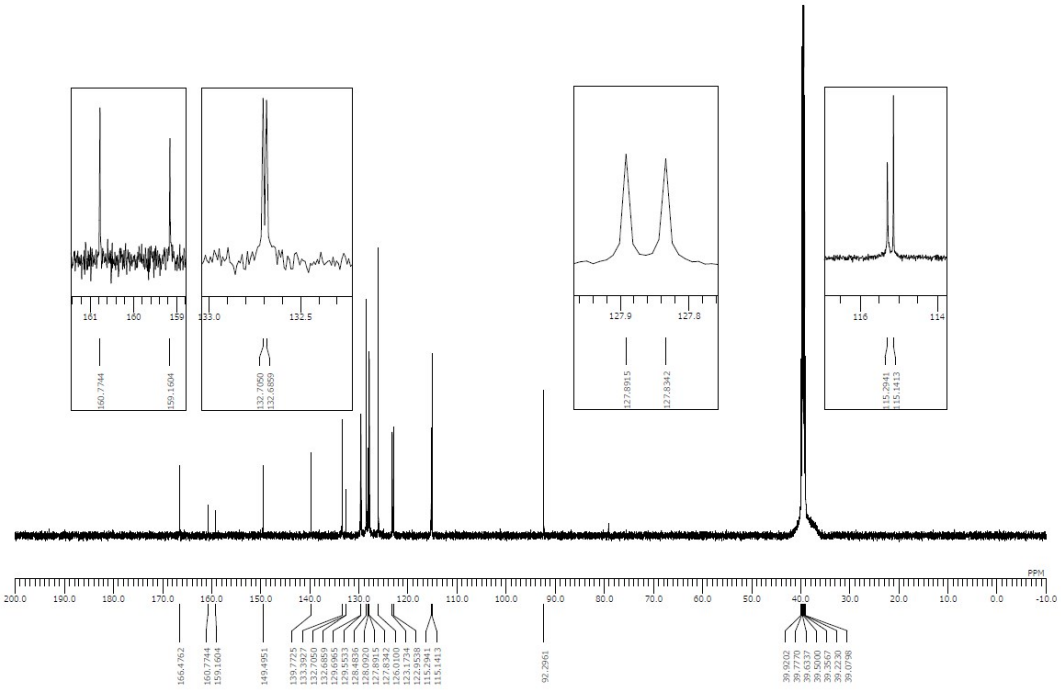
^{1}H-NMR spectrum of **2i** (DMSO-d_6, 400 MHz)

^{13}C-NMR spectrum of **2i** (DMSO-d_6, 100 MHz)

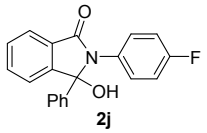


^{1}H-NMR spectrum of **2j** (DMSO-d_6, 600 MHz)

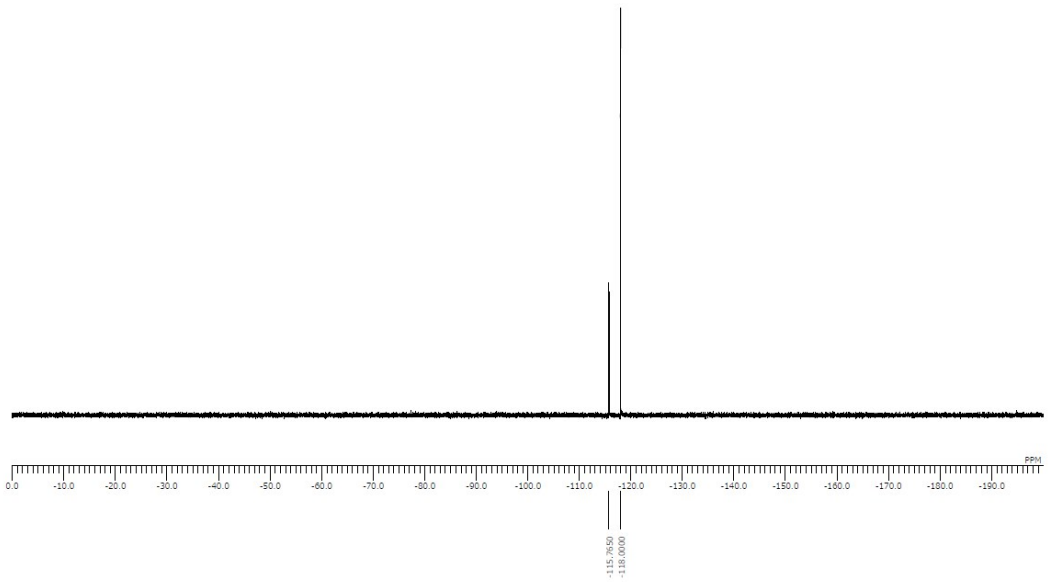
^{13}C-NMR spectrum of **2j** (DMSO-d_6, 150 MHz)



^{19}F-NMR spectrum of **2j** (DMSO-d_6, 565 MHz)



2j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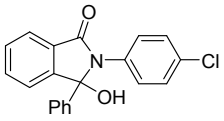
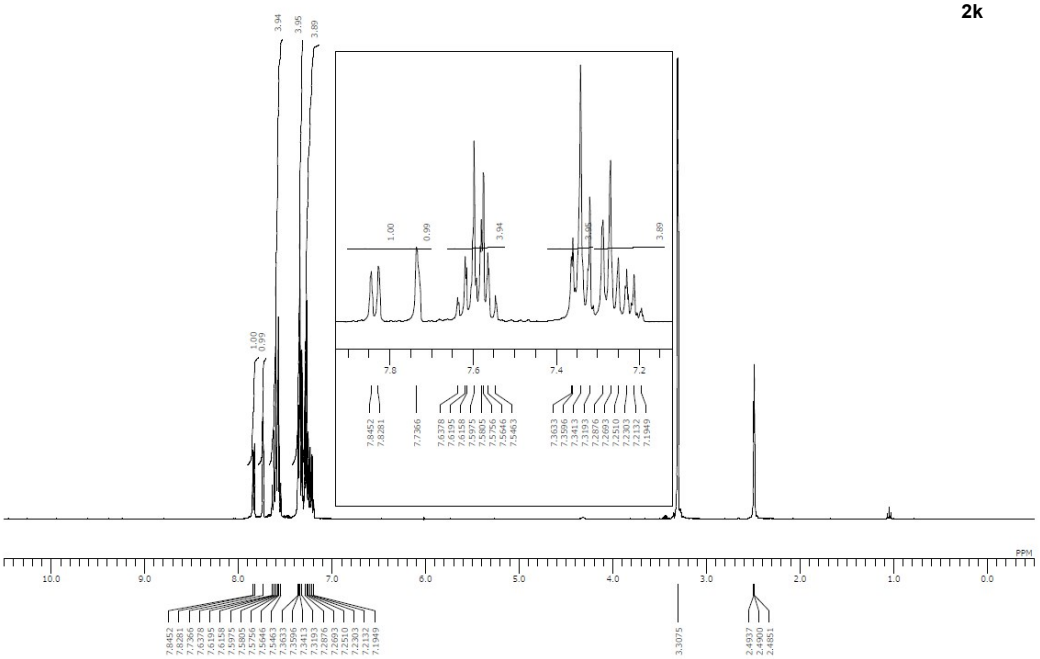
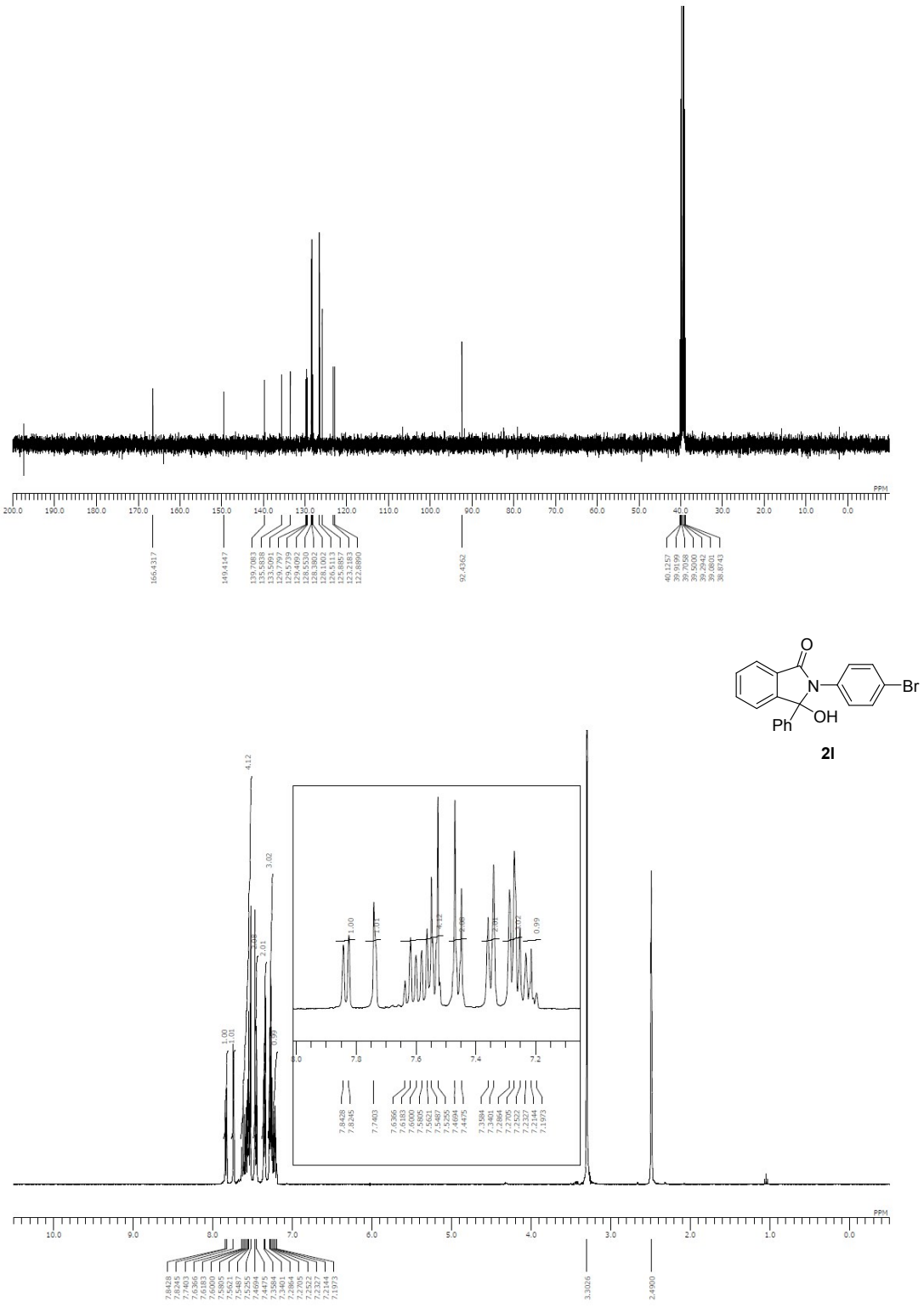


2k



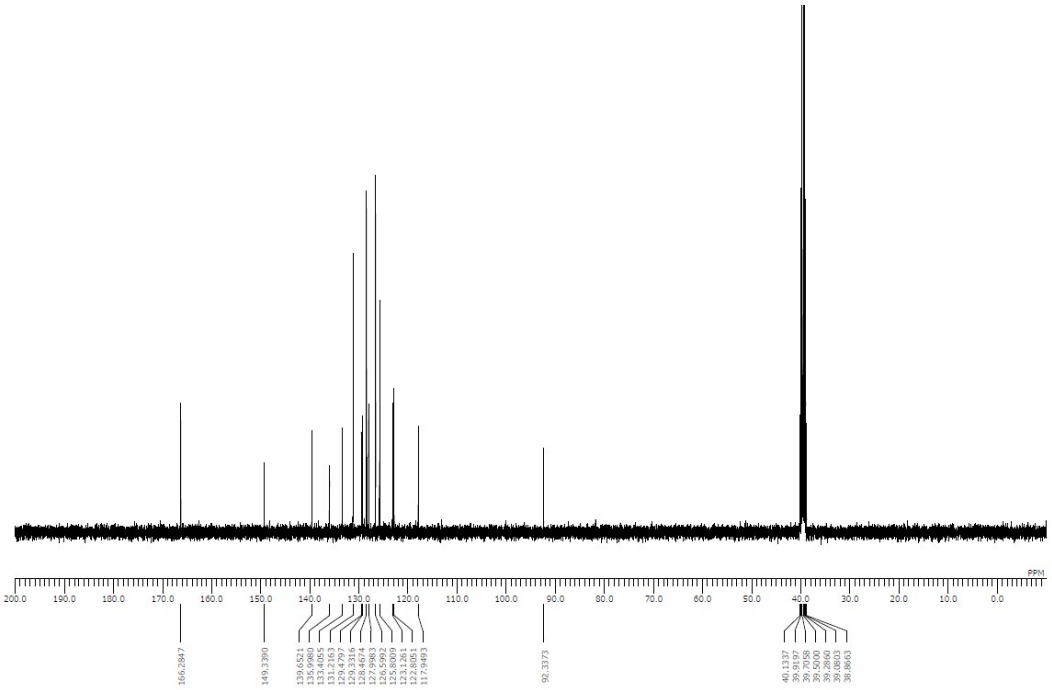
^{1}H-NMR spectrum of **2k** (DMSO-d_6, 400 MHz)

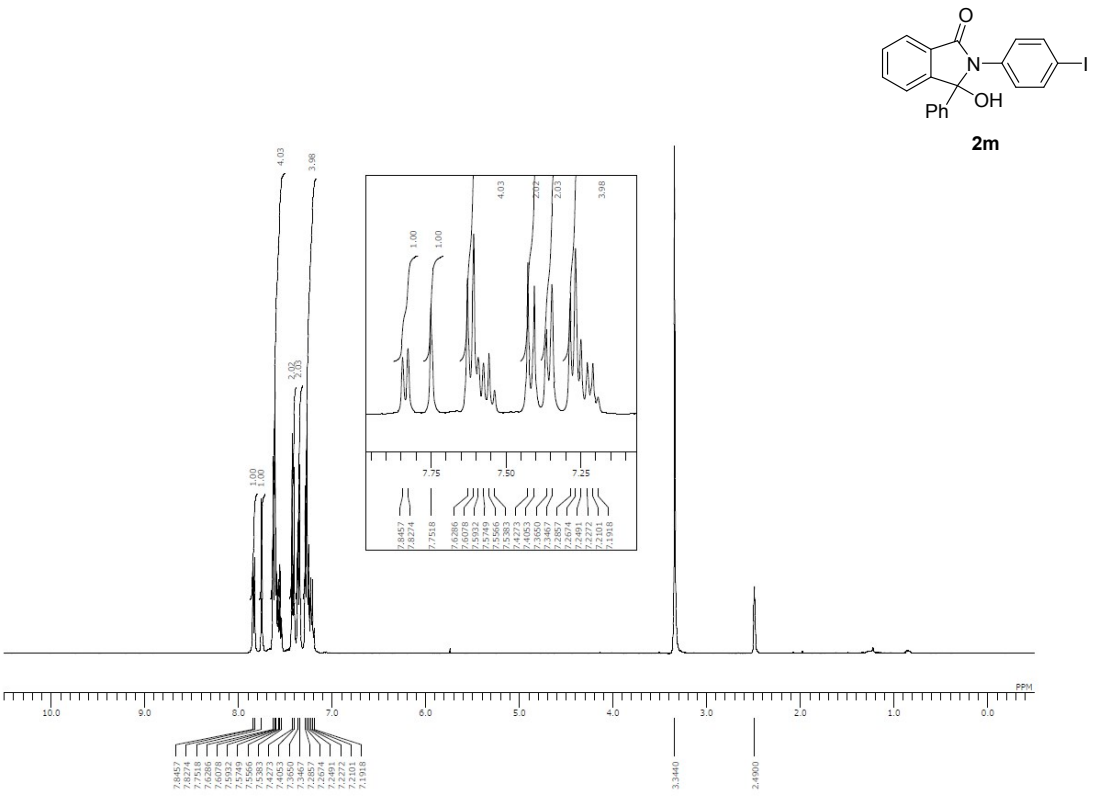
^{13}C-NMR spectrum of **2k** (DMSO-d_6, 100 MHz)



^{1}H-NMR spectrum of **2l** (DMSO-d_6, 400 MHz)

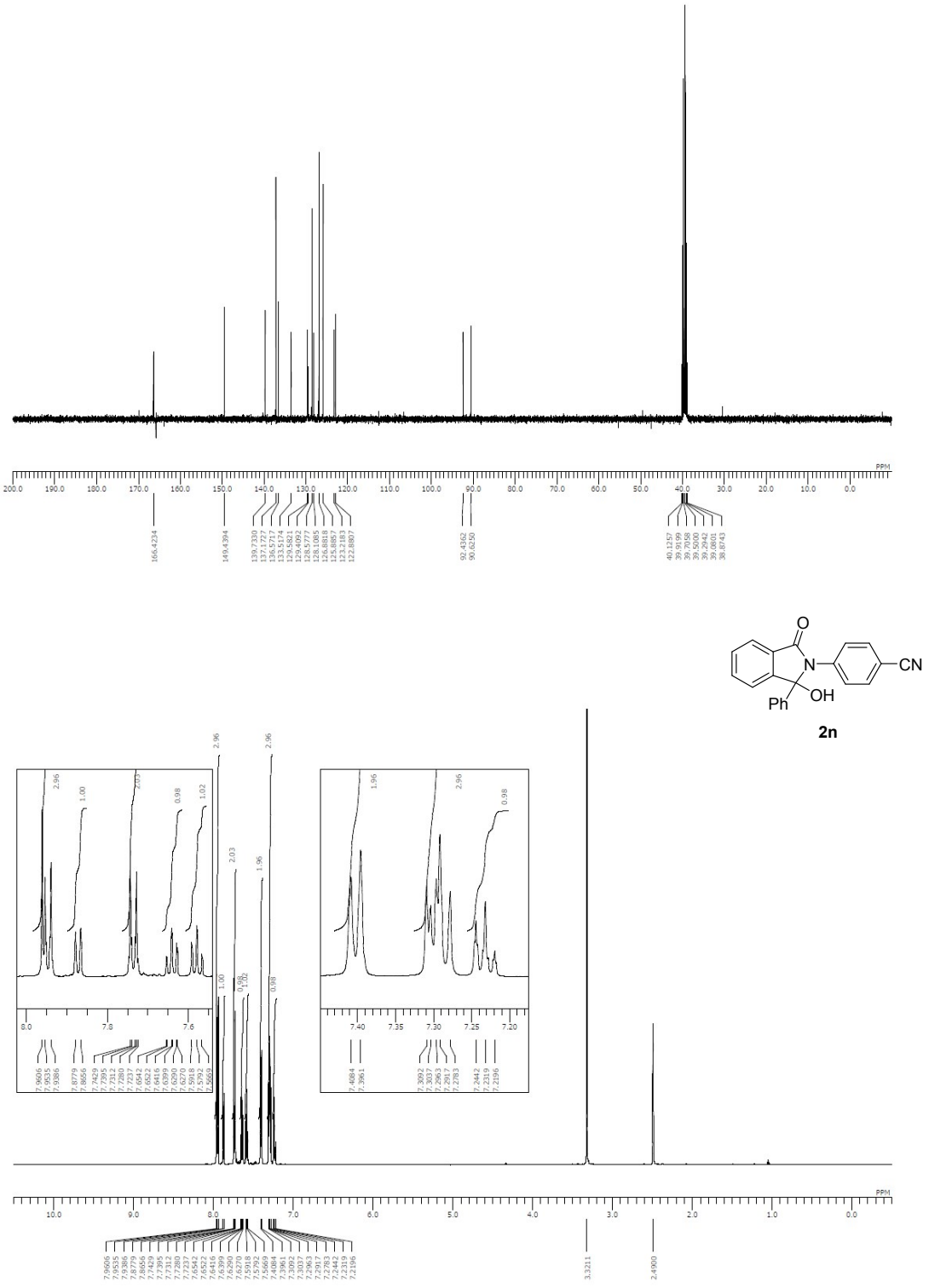
^{13}C-NMR spectrum of **2l** (DMSO-d_6, 100 MHz)





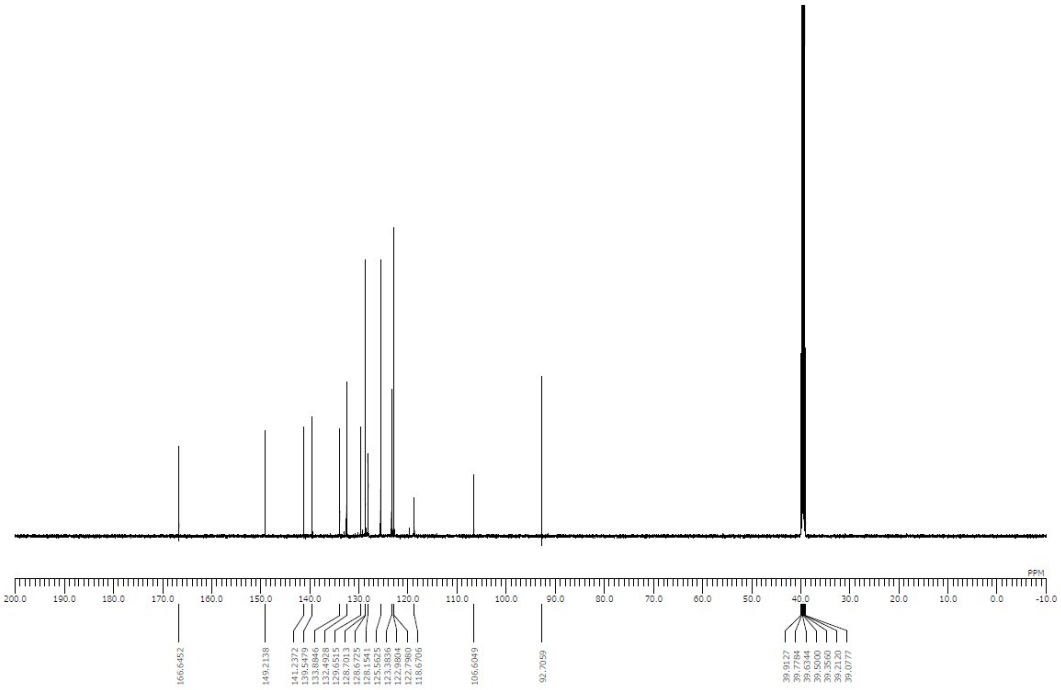
^{1}H-NMR spectrum of **2m** (DMSO-d_6, 400 MHz)

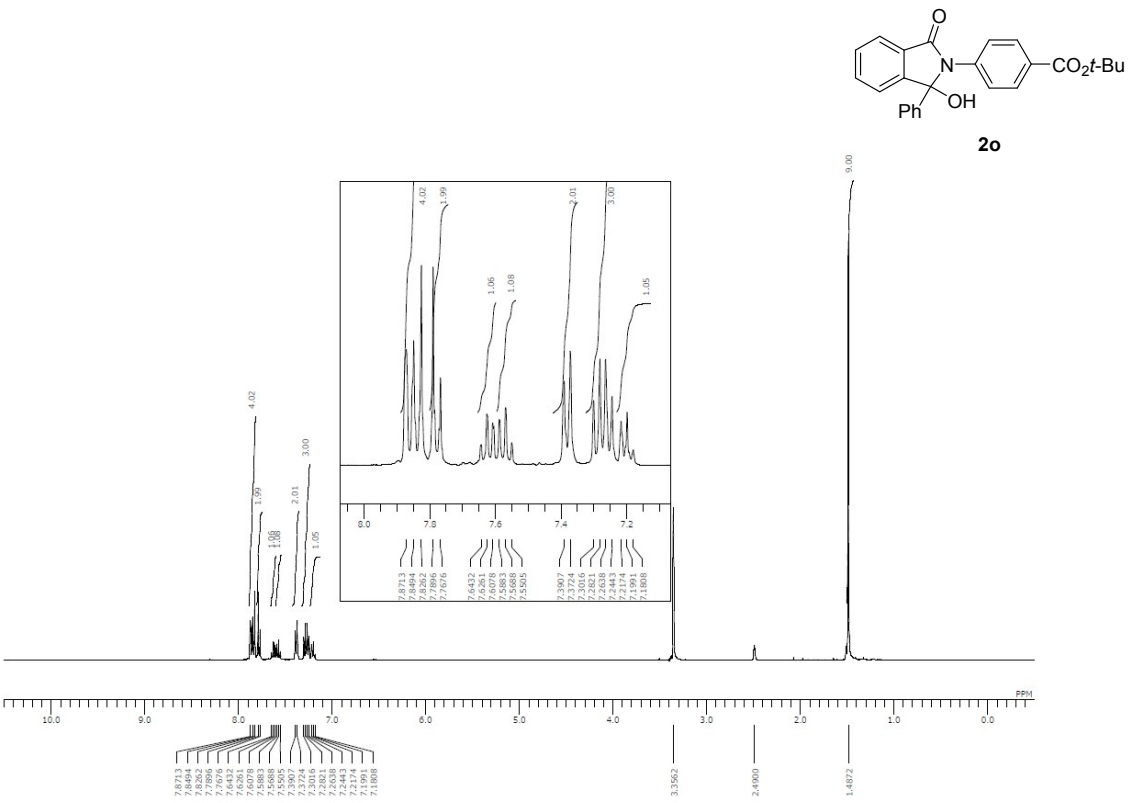
^{13}C-NMR spectrum of **2m** (DMSO-d_6, 100 MHz)



^{1}H-NMR spectrum of **2n** (DMSO-d_6, 600 MHz)

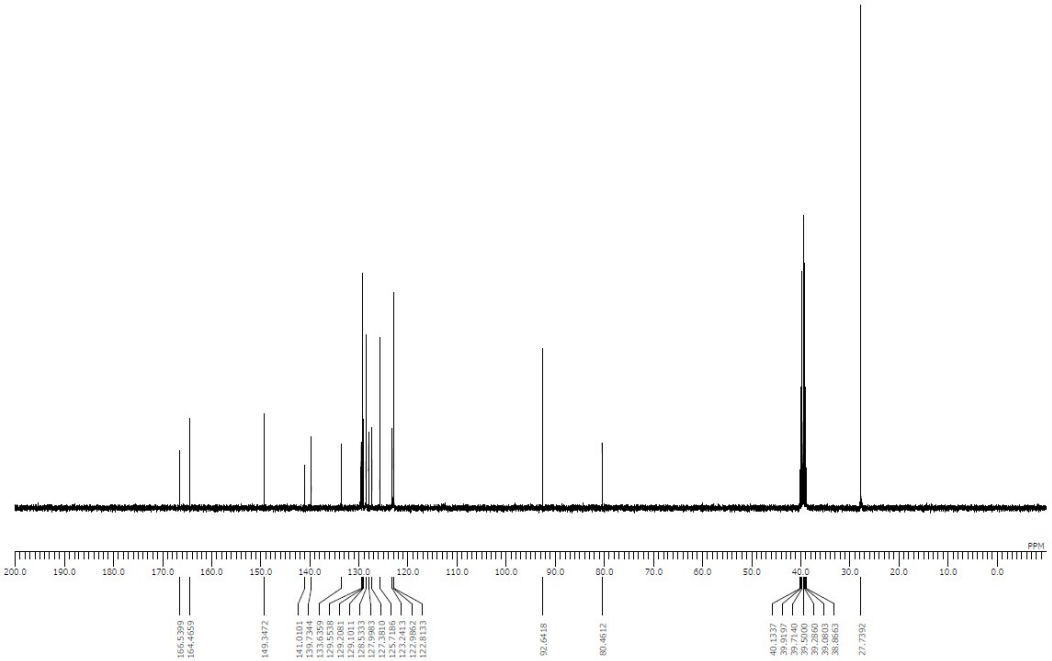
^{13}C-NMR spectrum of **2n** (DMSO-d_6, 150 MHz)



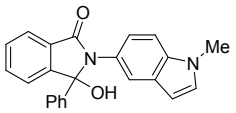


^{1}H-NMR spectrum of **2o** (DMSO-d_6, 400 MHz)

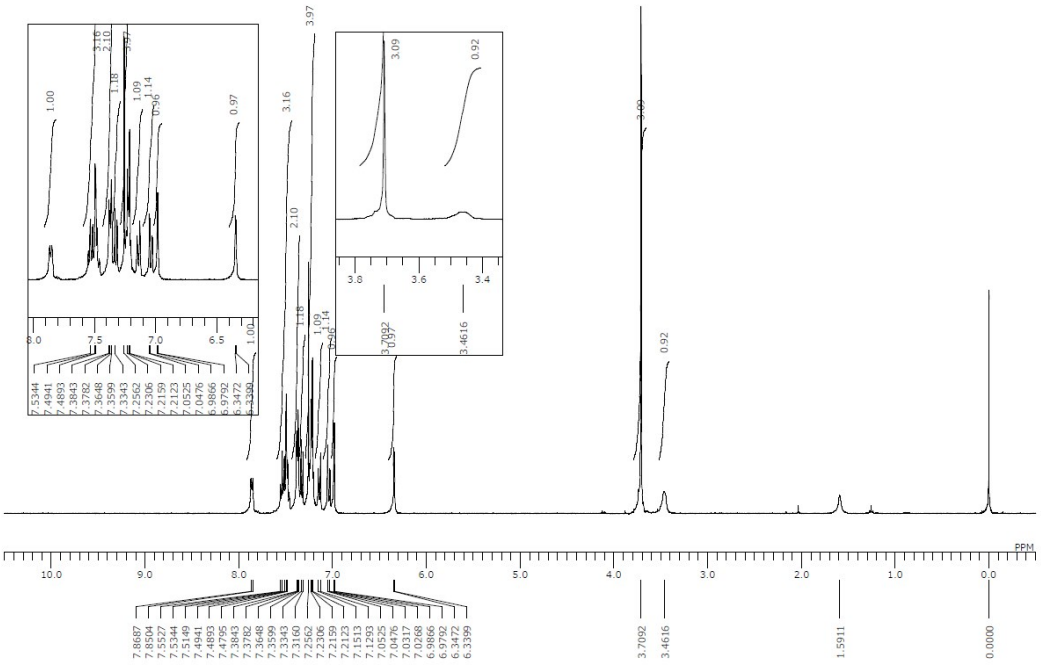
^{13}C-NMR spectrum of **2o** (DMSO-d_6, 100 MHz)



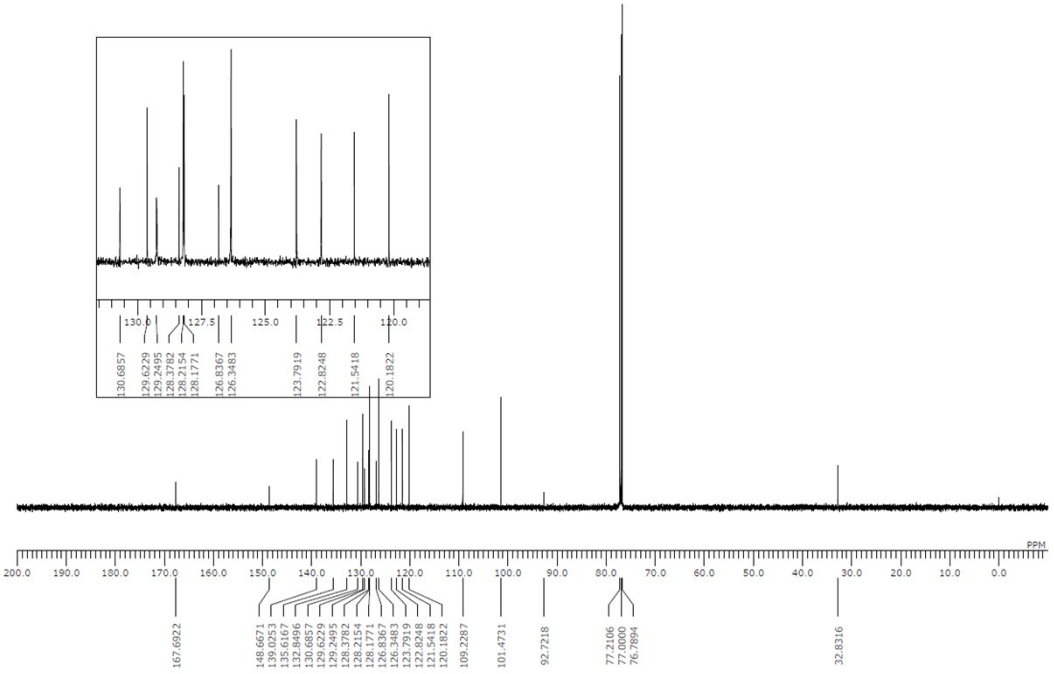
^{1}H-NMR spectrum of **2p** ($CDCl_3$, 400 MHz)



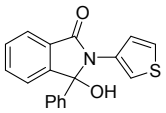
2p



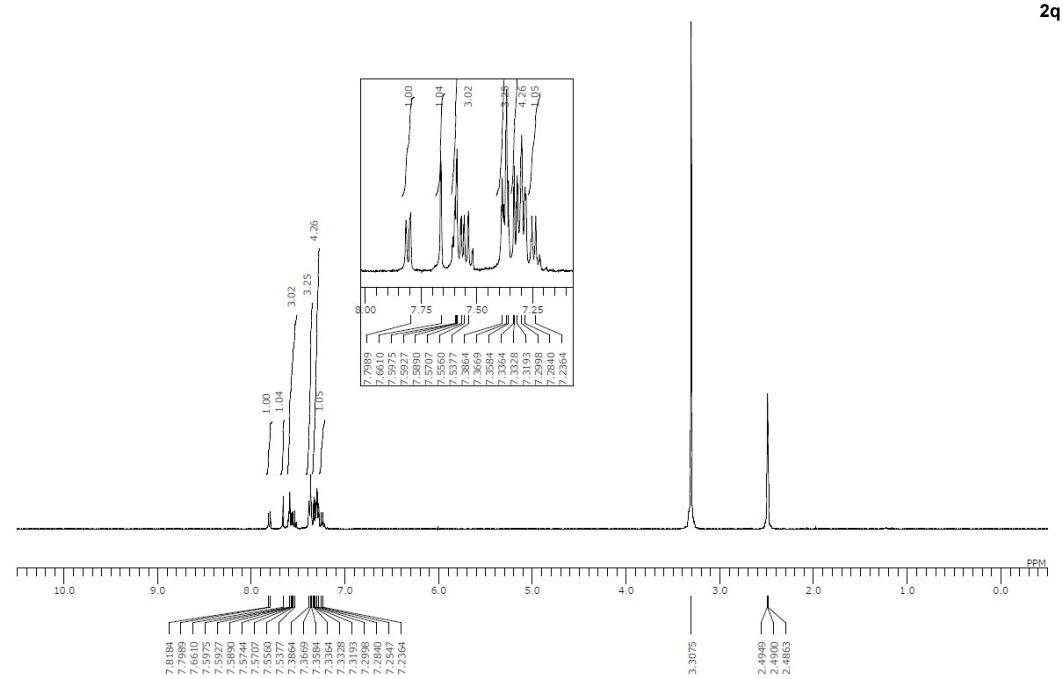
^{13}C-NMR spectrum of **2p** ($CDCl_3$, 150 MHz)



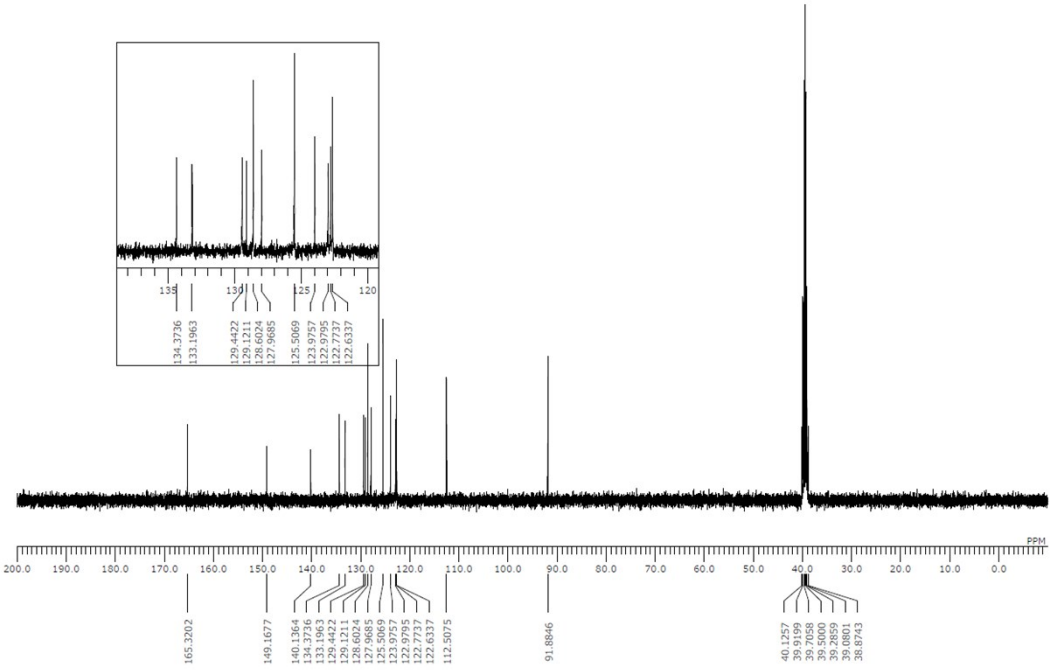
^{1}H-NMR spectrum of **2q** (DMSO-d_6, 400 MHz)

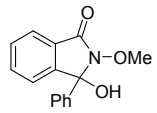


2q

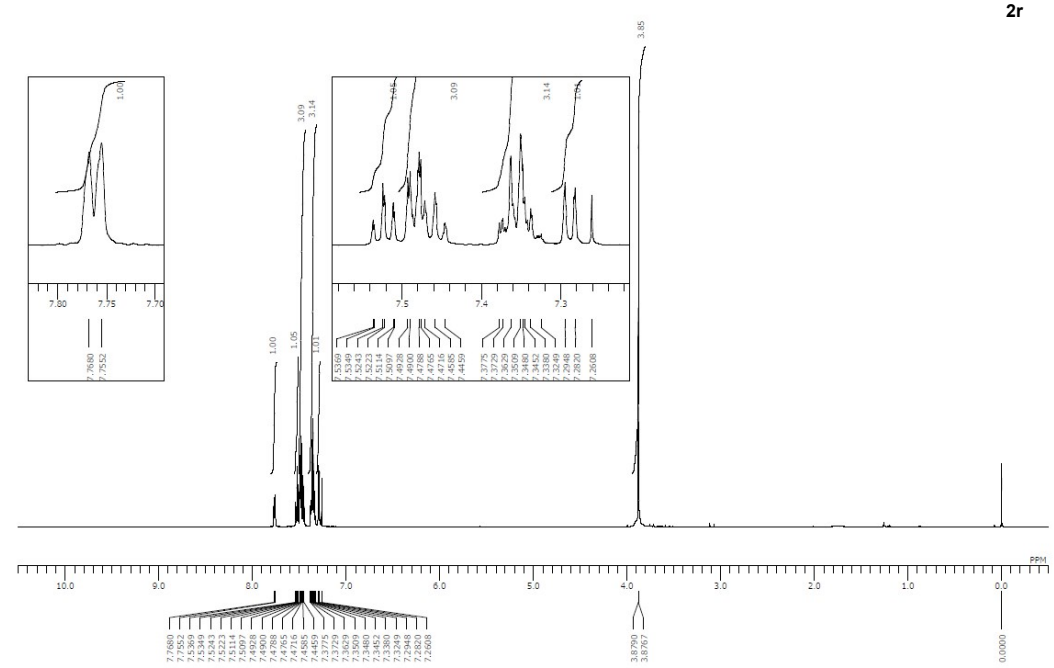


^{13}C-NMR spectrum of **2q** (DMSO-d_6, 100 MHz)



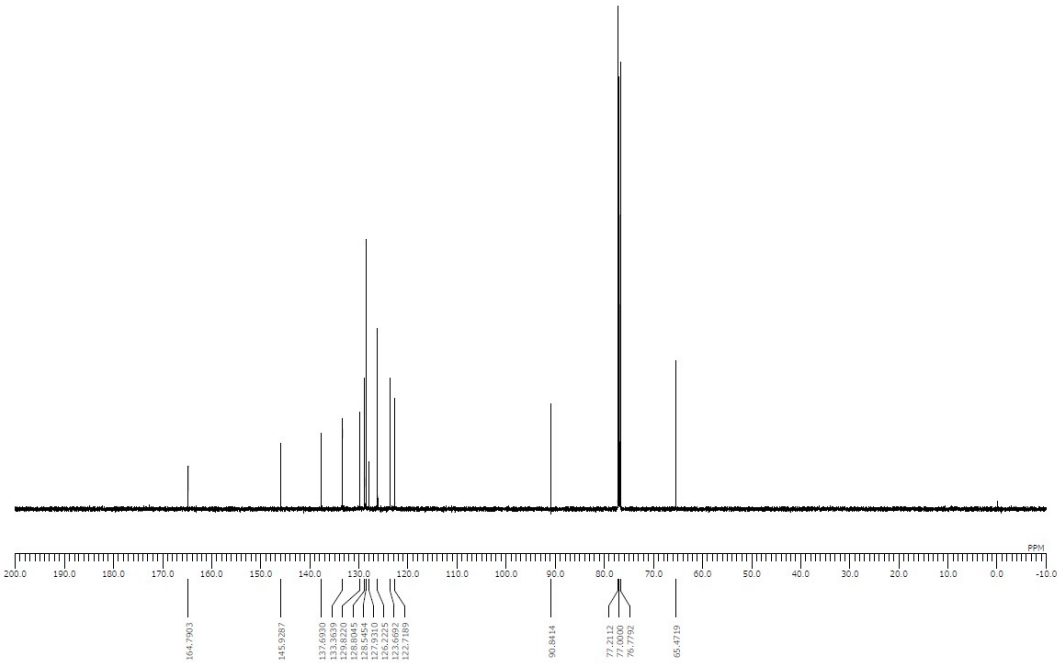


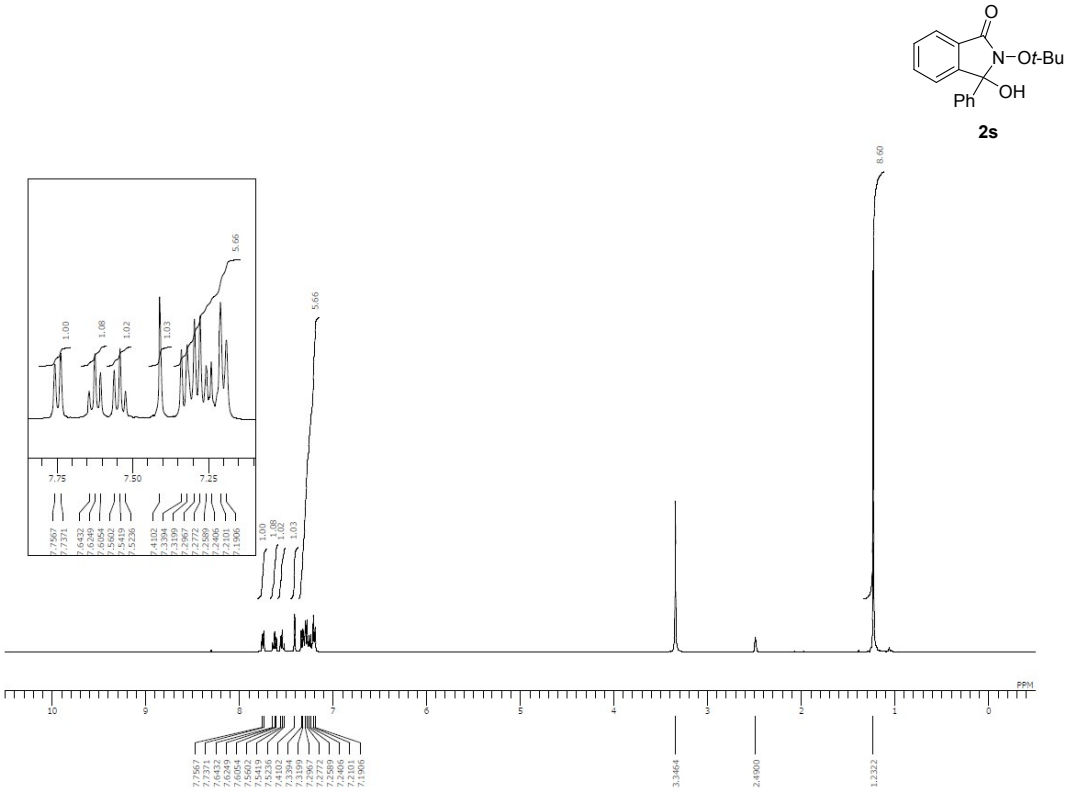
2r



^{1}H-NMR spectrum of **2r** ($CDCl_3$, 600 MHz)

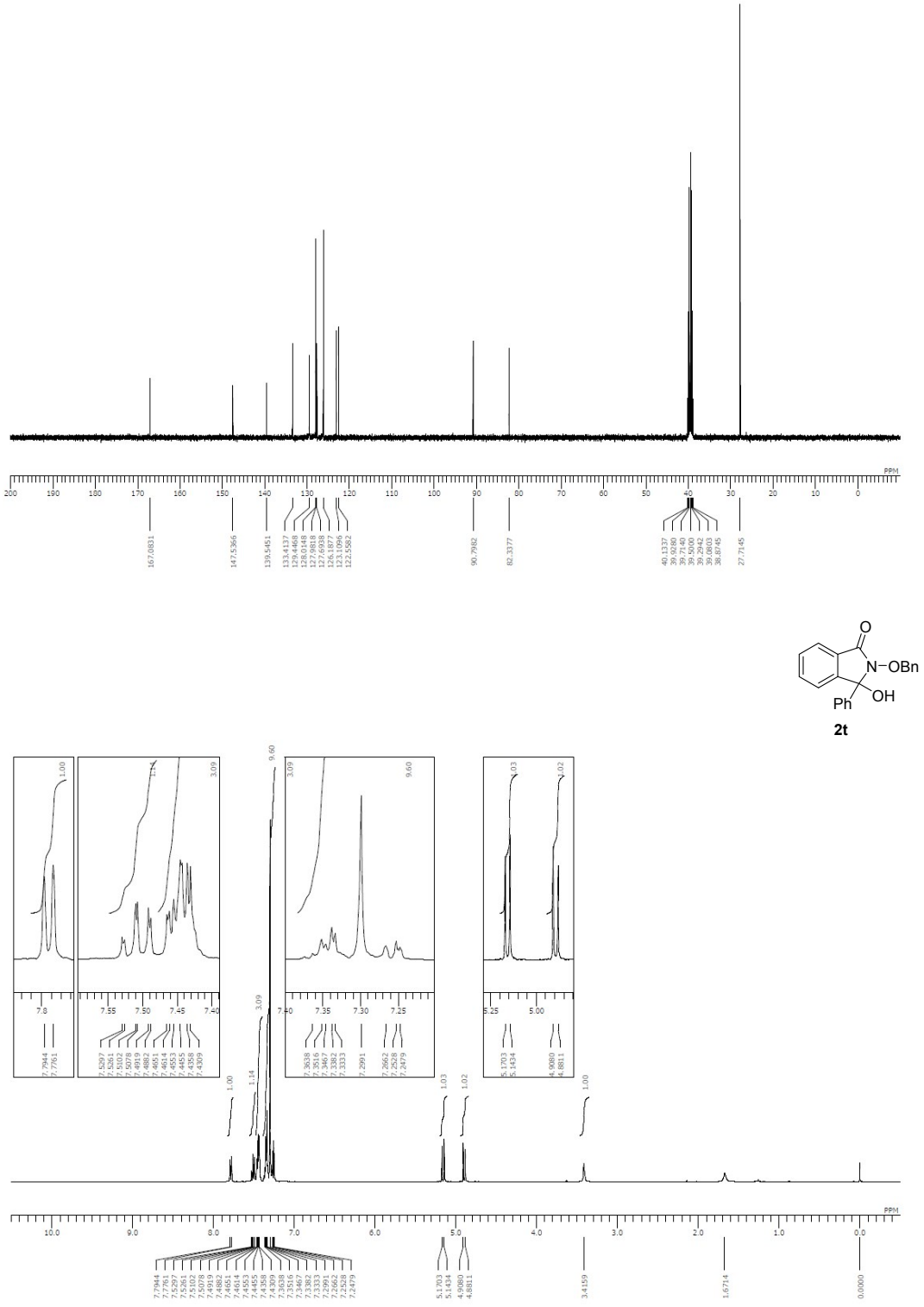
^{13}C-NMR spectrum of **2r** ($CDCl_3$, 150 MHz)





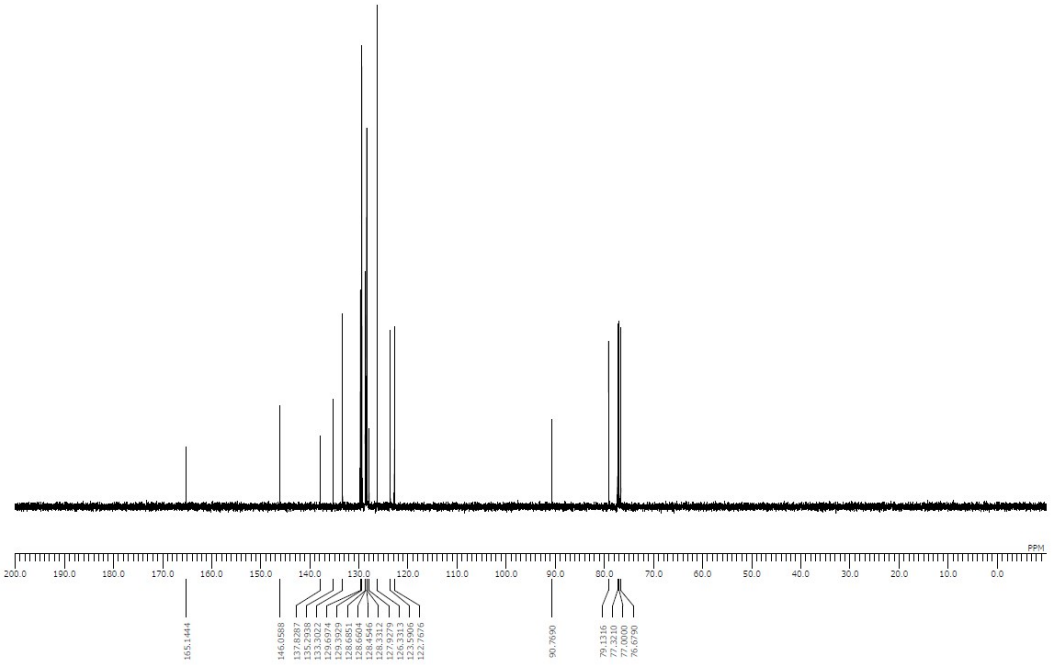
^{1}H-NMR spectrum of **2s** (DMSO-d_6, 400 MHz)

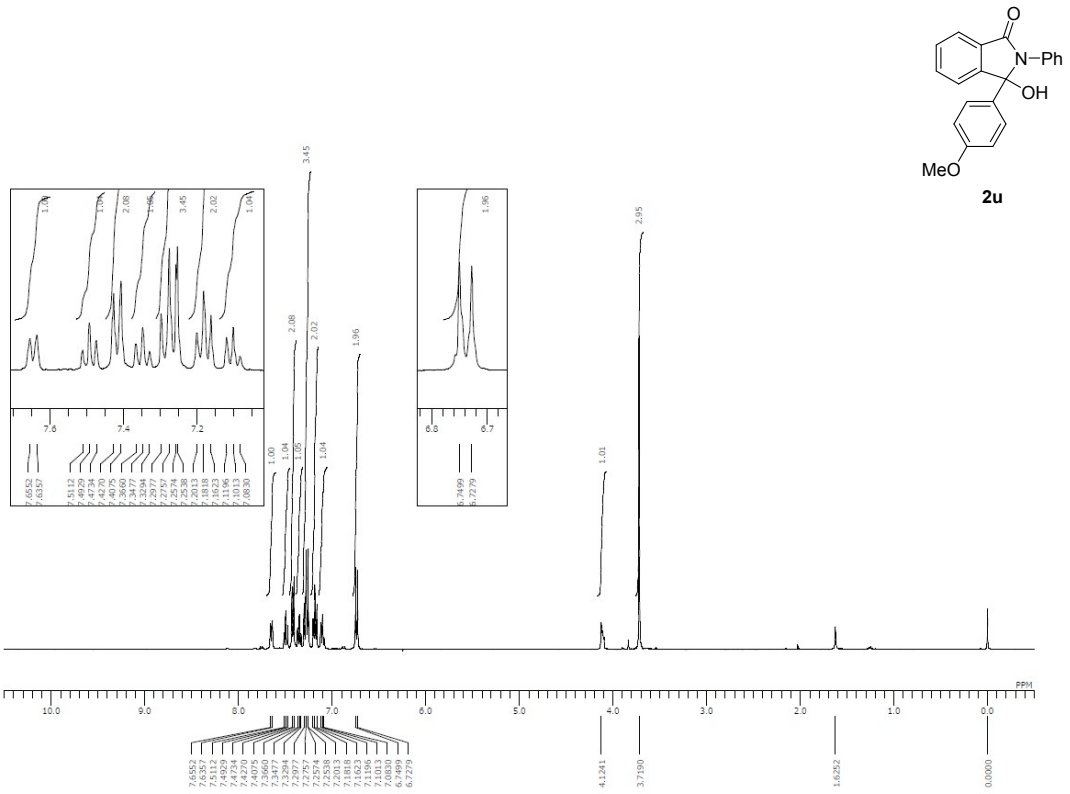
^{13}C-NMR spectrum of **2s** (DMSO-d_6, 100 MHz)



^{1}H-NMR spectrum of **2t** ($CDCl_3$, 400 MHz)

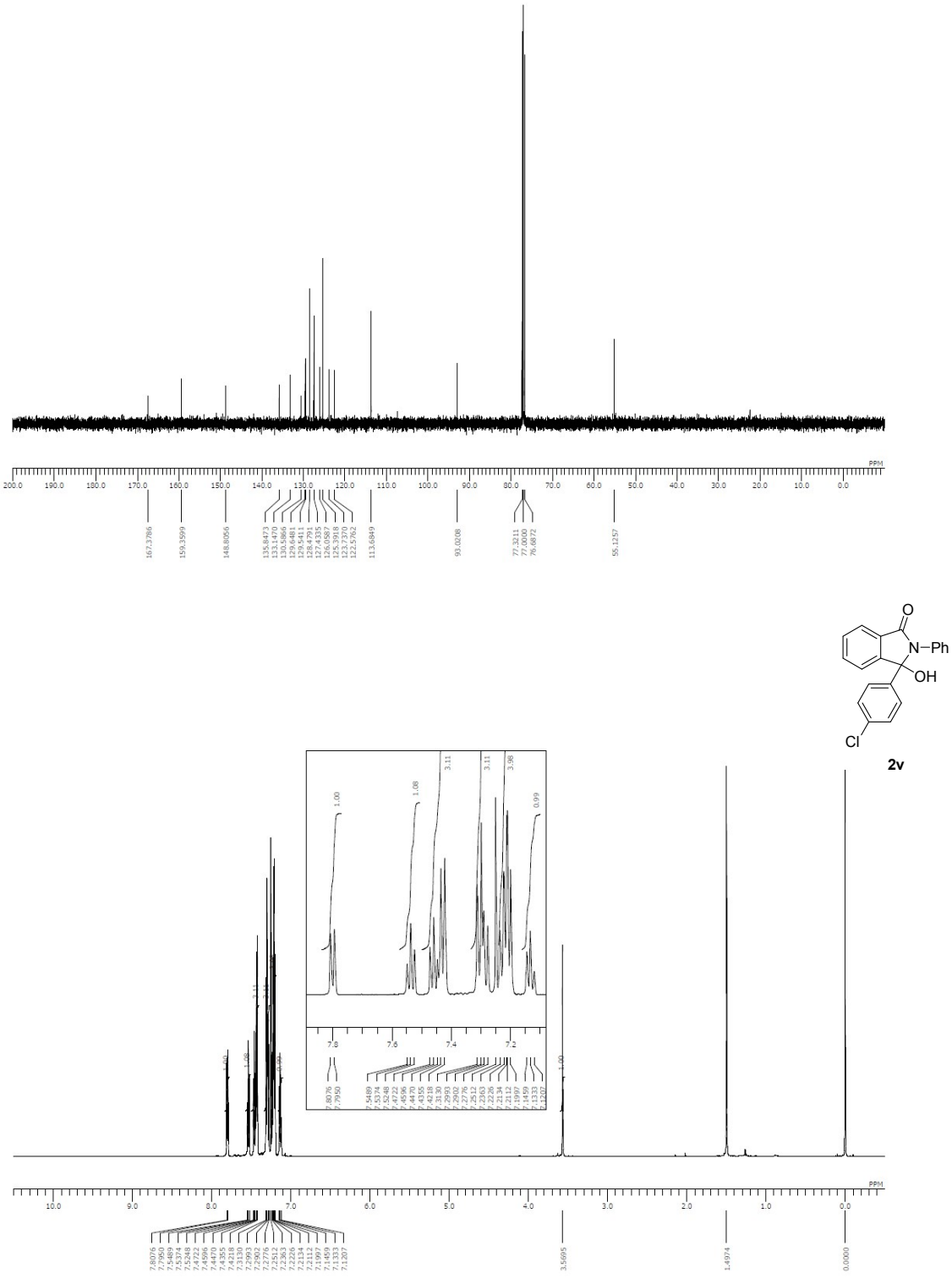
^{13}C-NMR spectrum of **2t** ($CDCl_3$, 100 MHz)





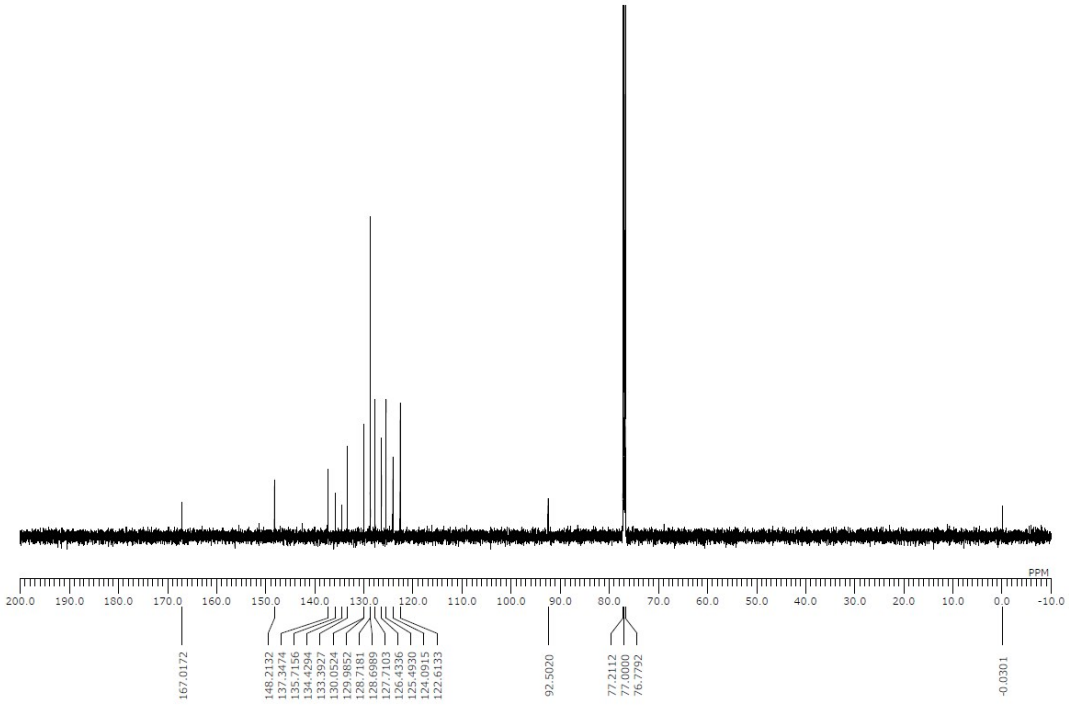
^{1}H-NMR spectrum of **2u** ($CDCl_3$, 400 MHz)

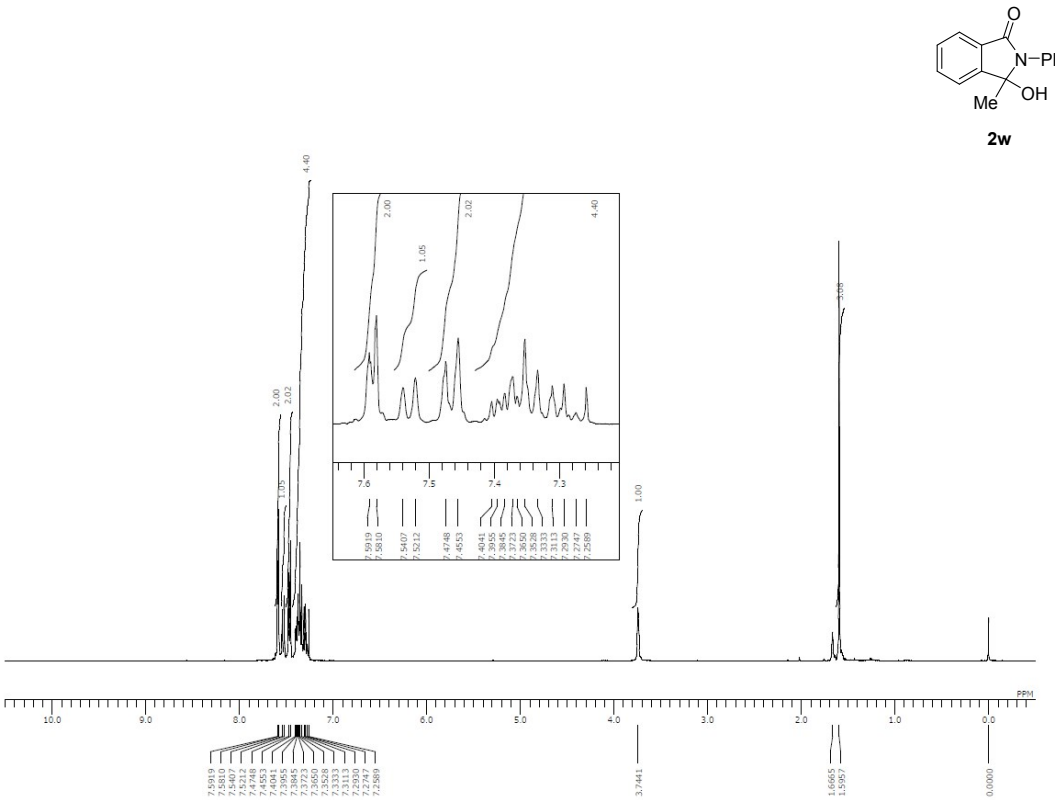
^{13}C-NMR spectrum of **2u** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **2v** ($CDCl_3$, 600 MHz)

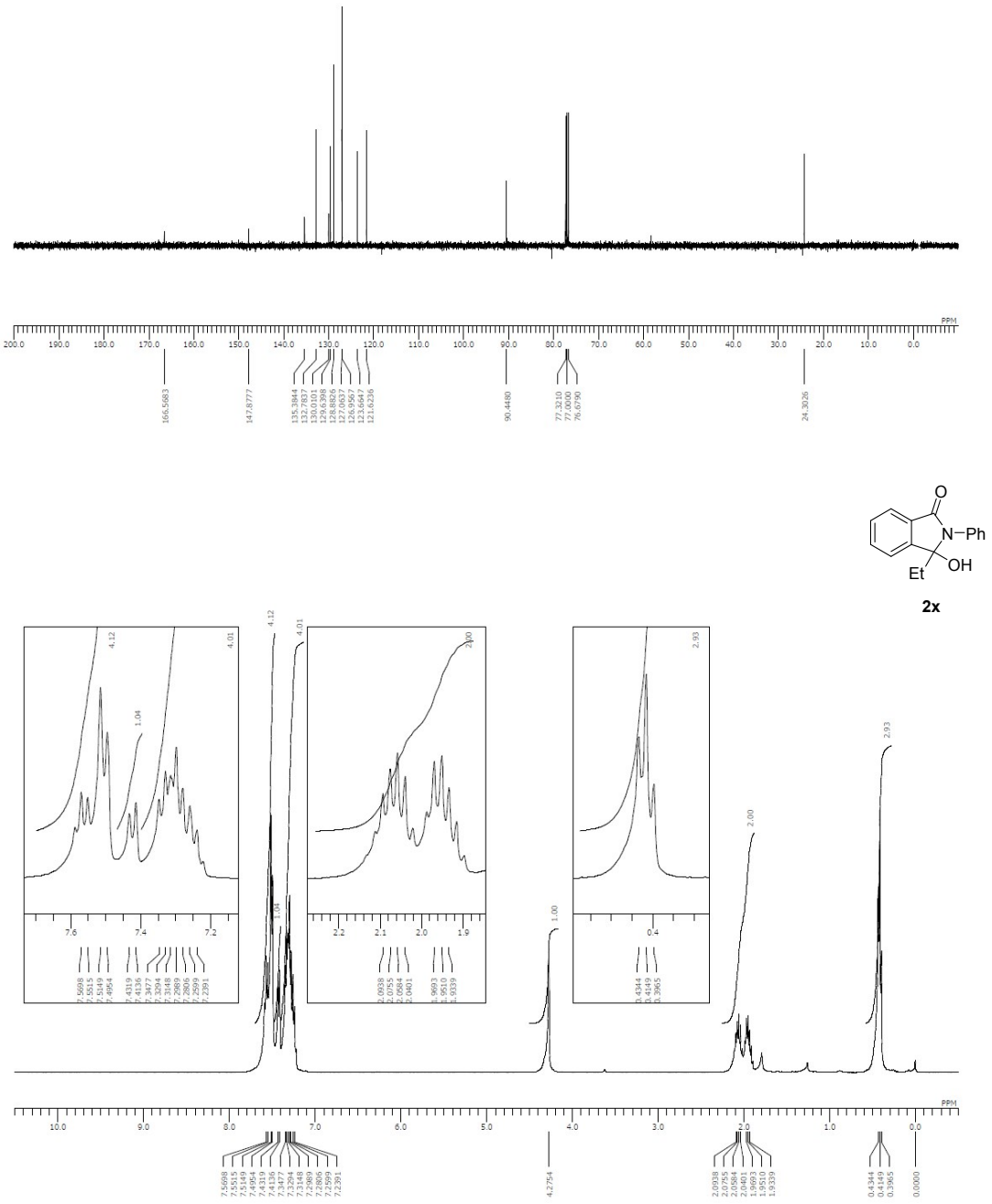
^{13}C-NMR spectrum of **2v** ($CDCl_3$, 150 MHz)





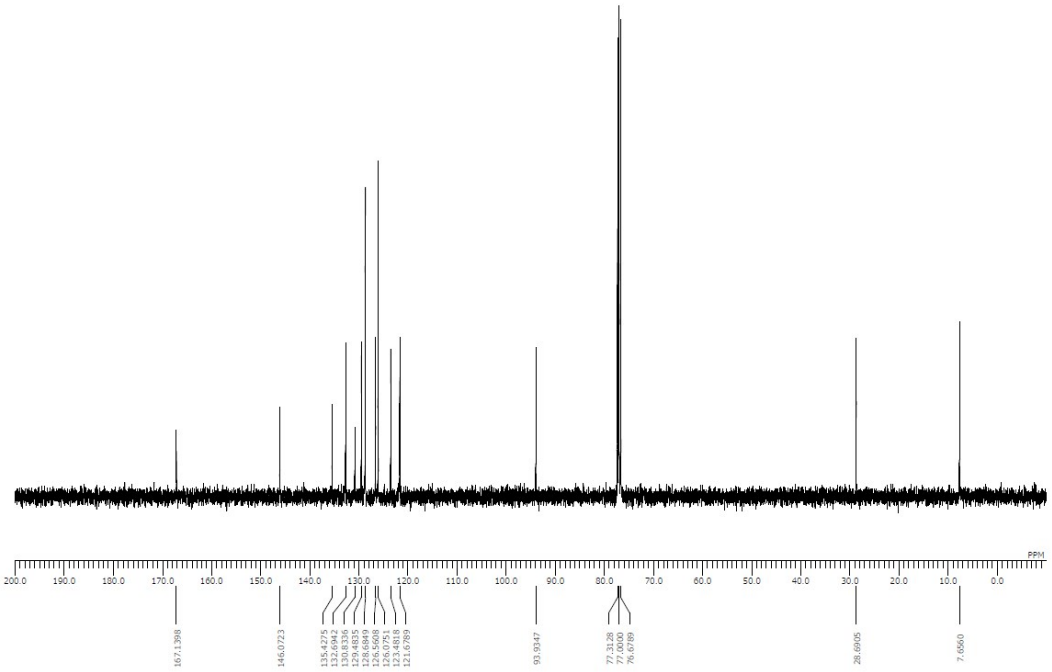
^{1}H-NMR spectrum of **2w** ($CDCl_3$, 400 MHz)

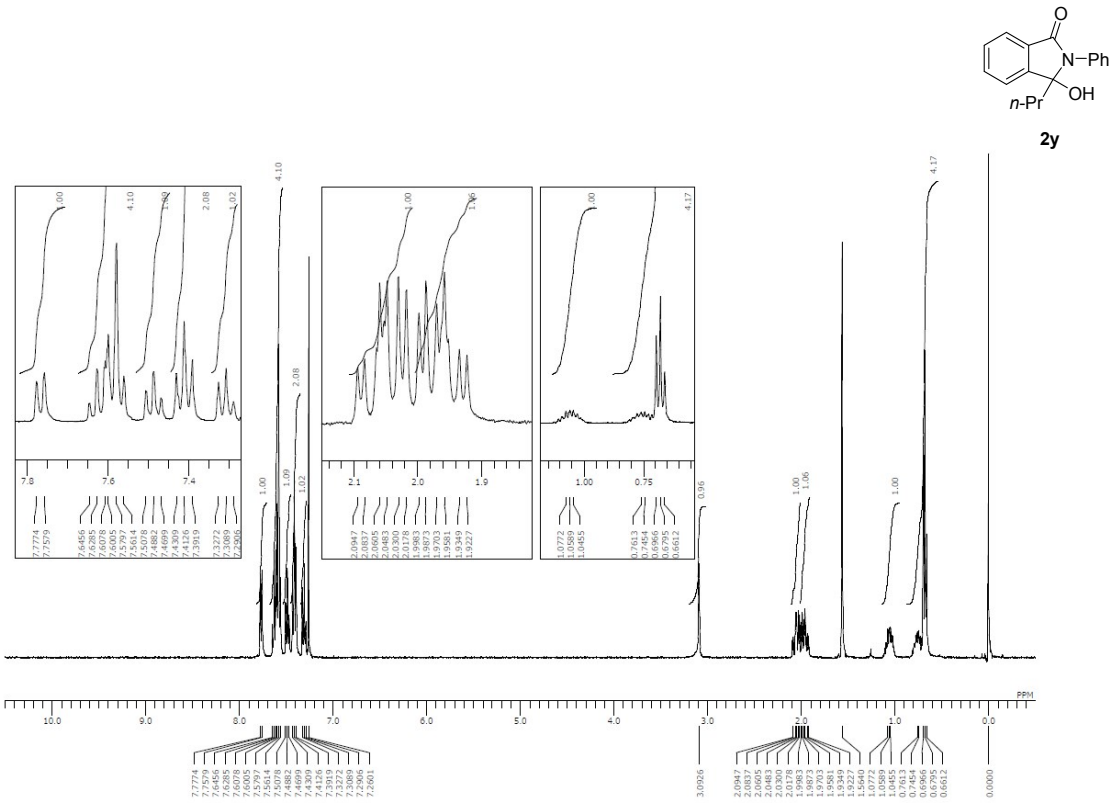
^{13}C-NMR spectrum of **2w** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **2x** ($CDCl_3$, 400 MHz)

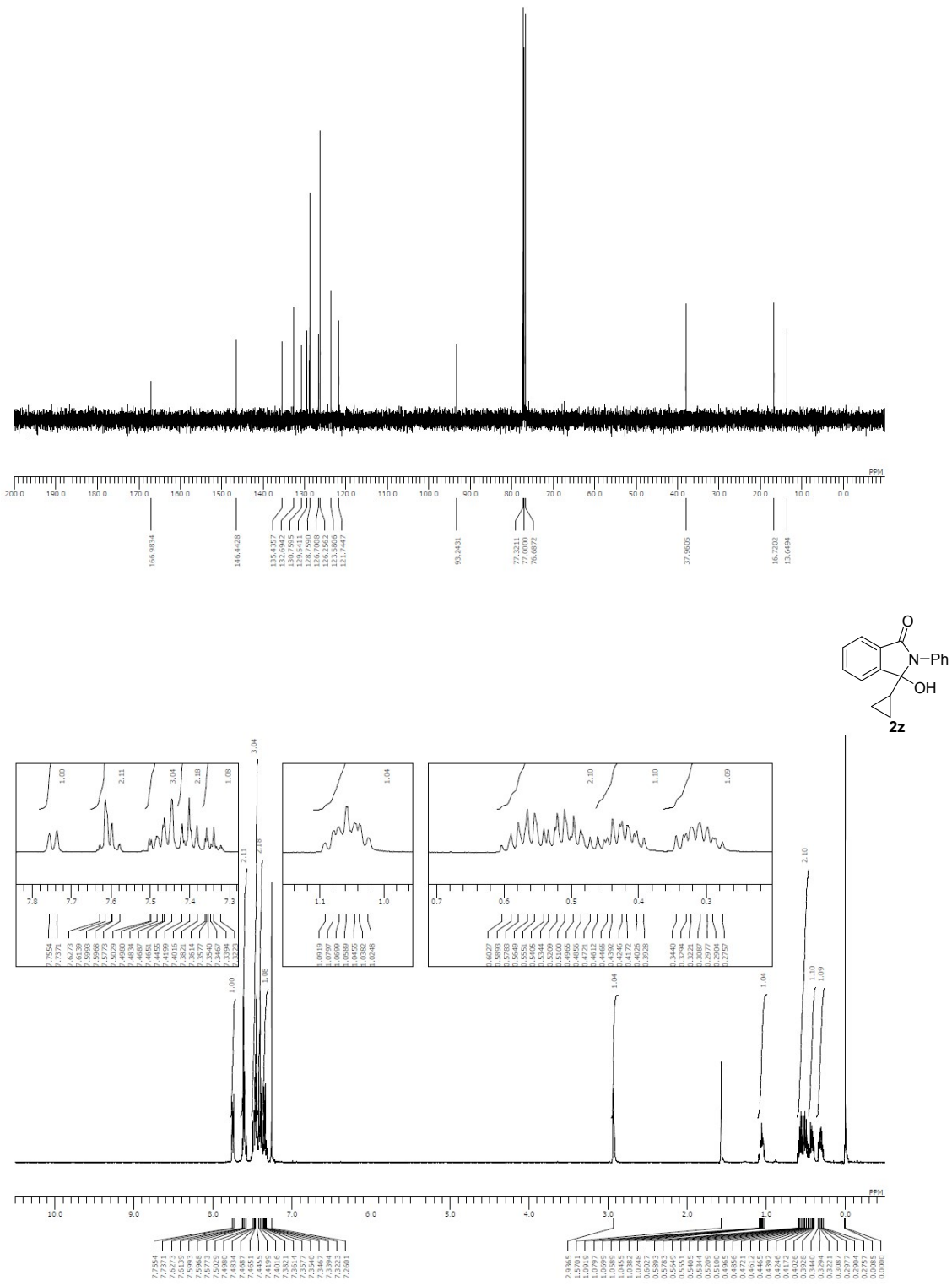
^{13}C-NMR spectrum of **2x** ($CDCl_3$, 100 MHz)





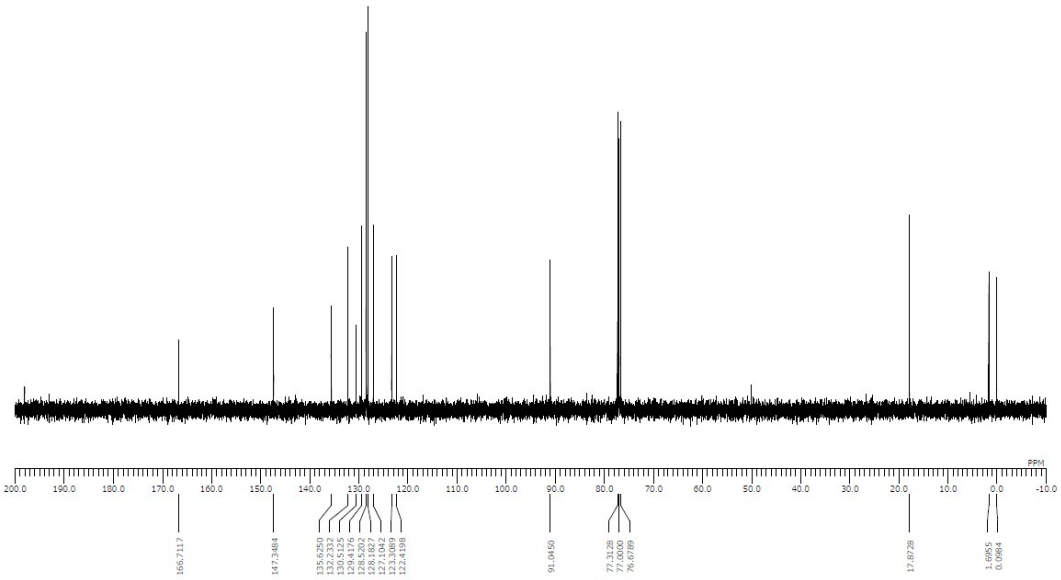
^{1}H-NMR spectrum of **2y** ($CDCl_3$, 400 MHz)

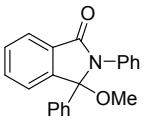
^{13}C-NMR spectrum of **2y** ($CDCl_3$, 100 MHz)



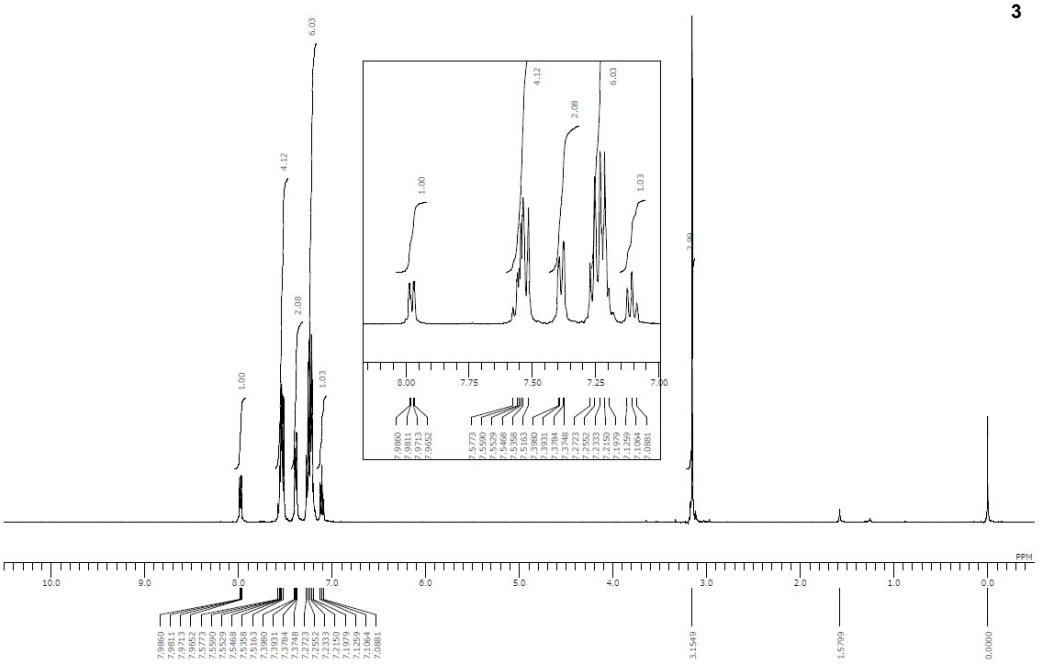
^{1}H-NMR spectrum of **2z** ($CDCl_3$, 400 MHz)

^{13}C-NMR spectrum of **2z** ($CDCl_3$, 100 MHz)



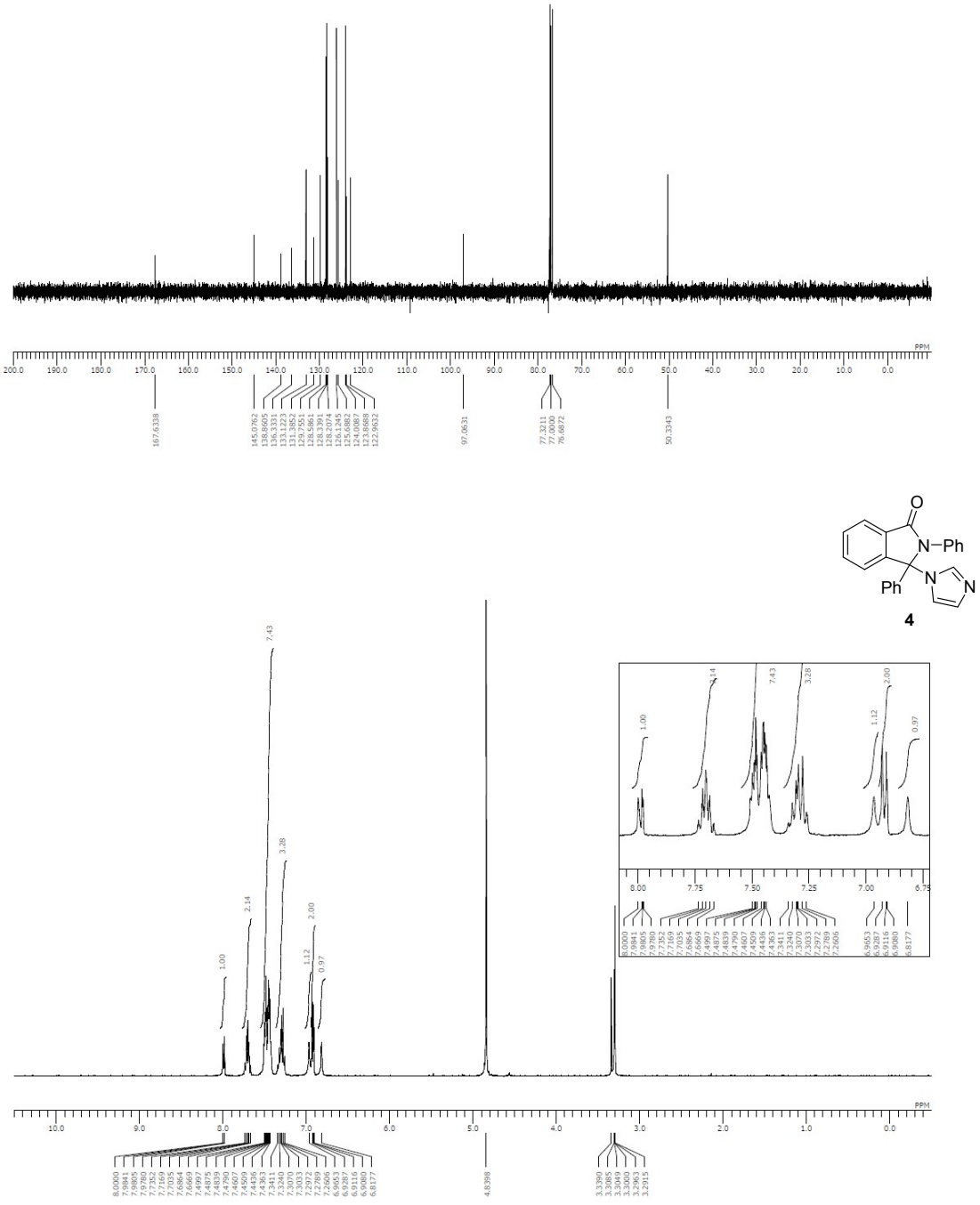


3



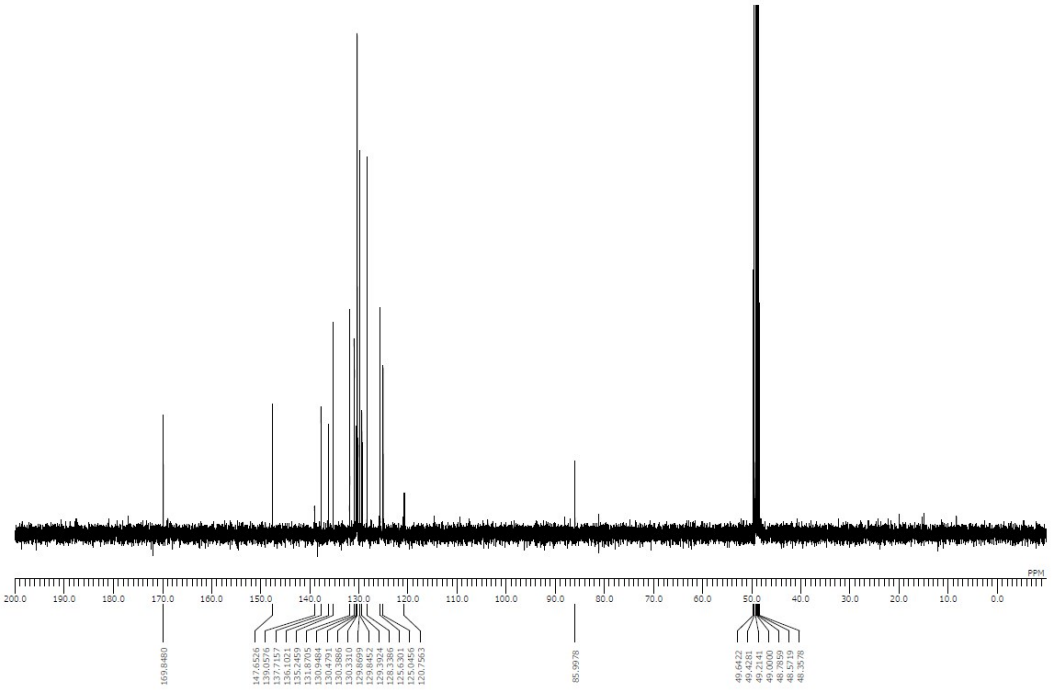
^{1}H-NMR spectrum of **3** ($CDCl_3$, 400 MHz)

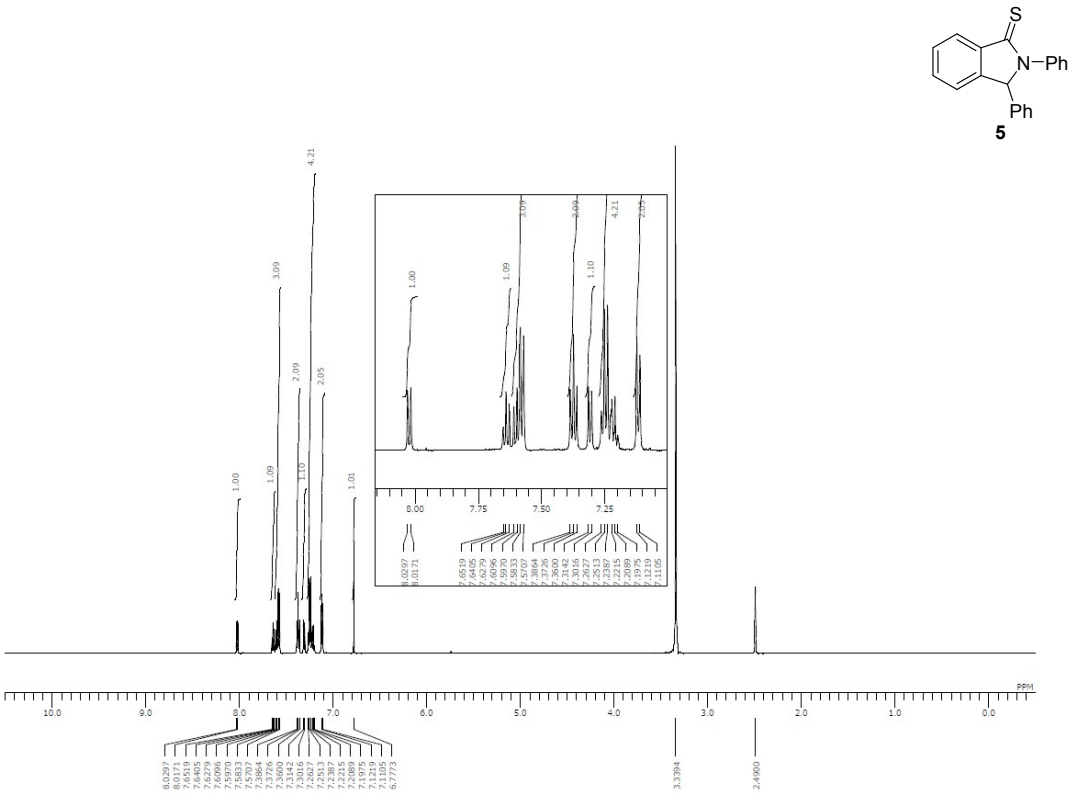
^{13}C-NMR spectrum of **3** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **4** (CD_3OD, 400 MHz)

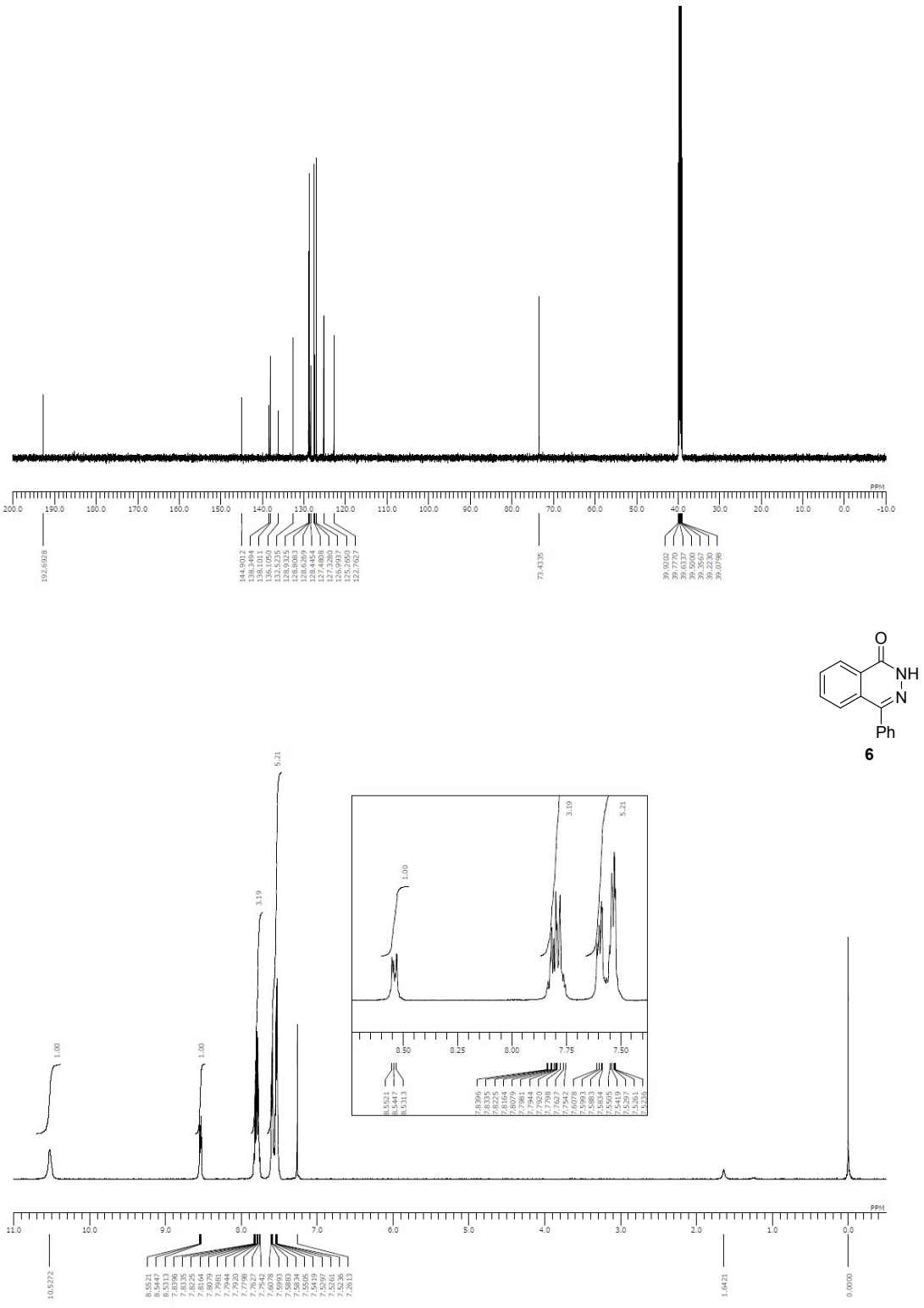
^{13}C-NMR spectrum of **4** (CD_3OD, 100 MHz)





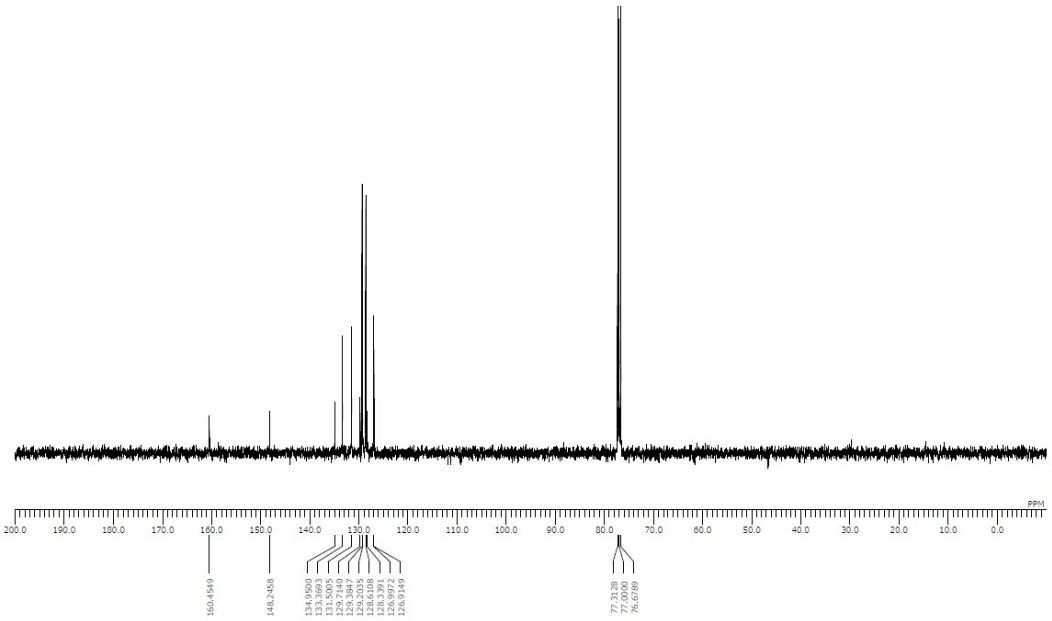
^{1}H-NMR spectrum of **5** (DMSO-d_6, 600 MHz)

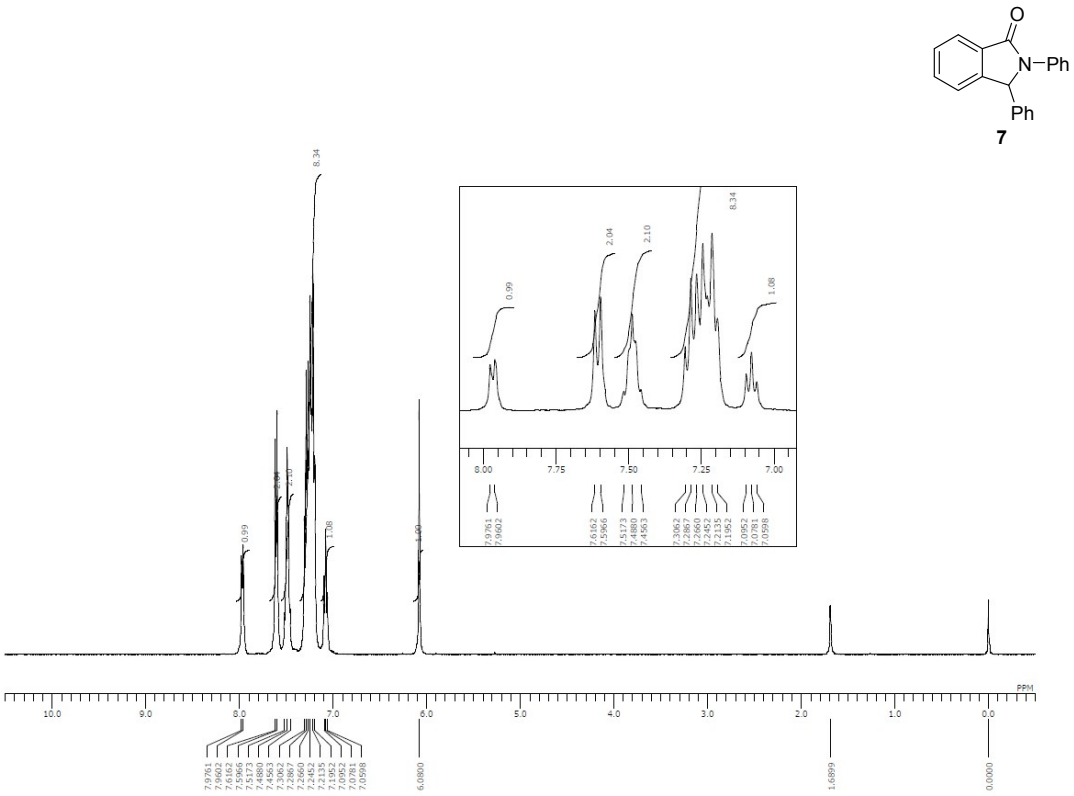
^{13}C-NMR spectrum of **5** (DMSO-d_6, 150 MHz)



^{1}H-NMR spectrum of **6** ($CDCl_3$, 400 MHz)

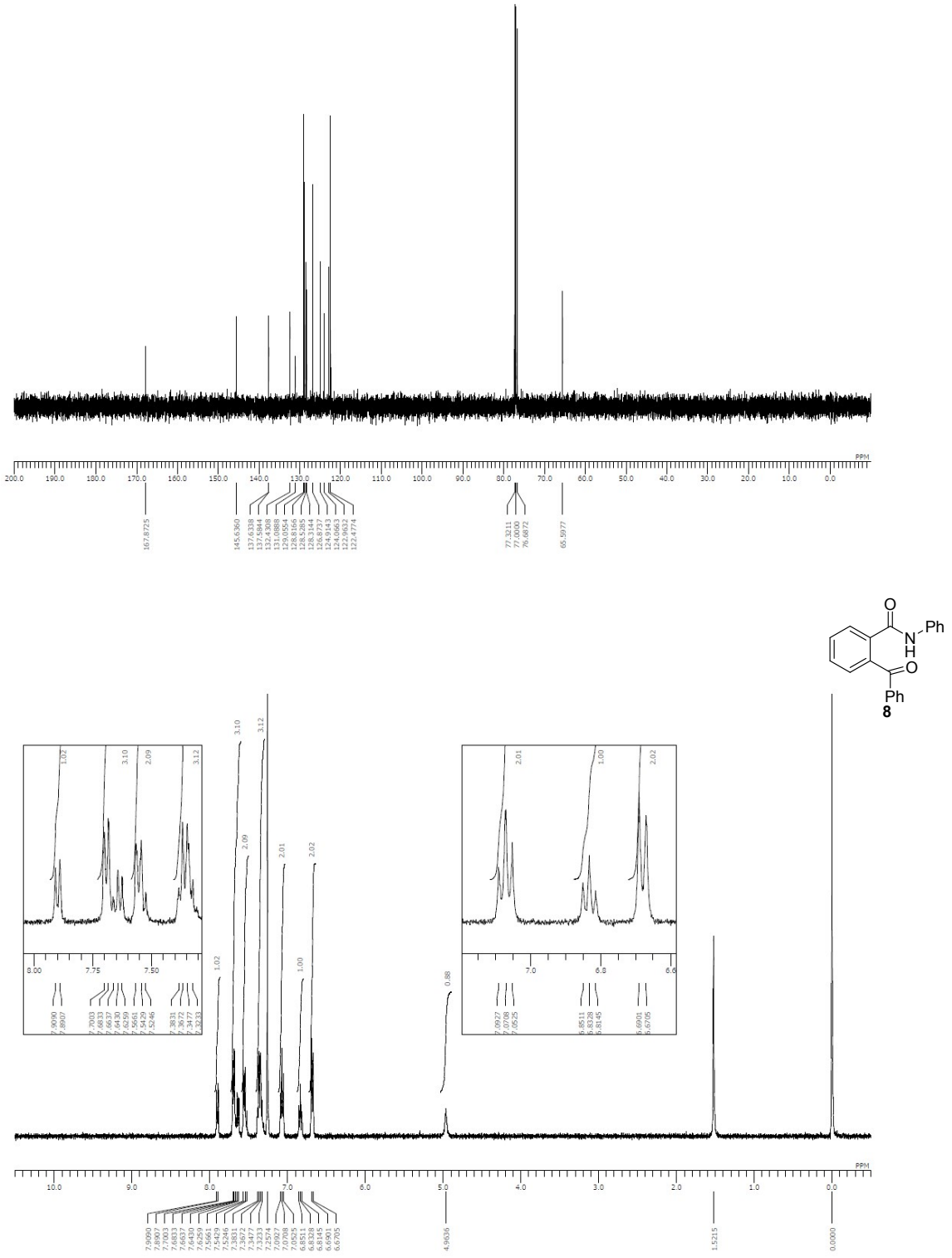
^{13}C-NMR spectrum of **6** ($CDCl_3$, 100 MHz)





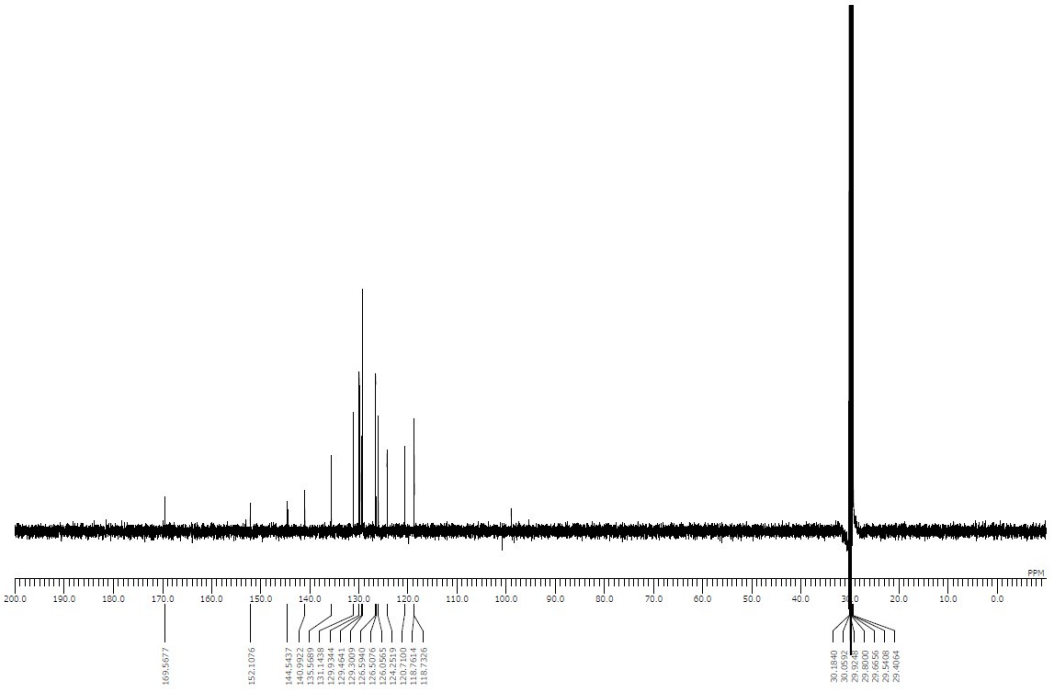
^{1}H-NMR spectrum of **7** ($CDCl_3$, 400 MHz)

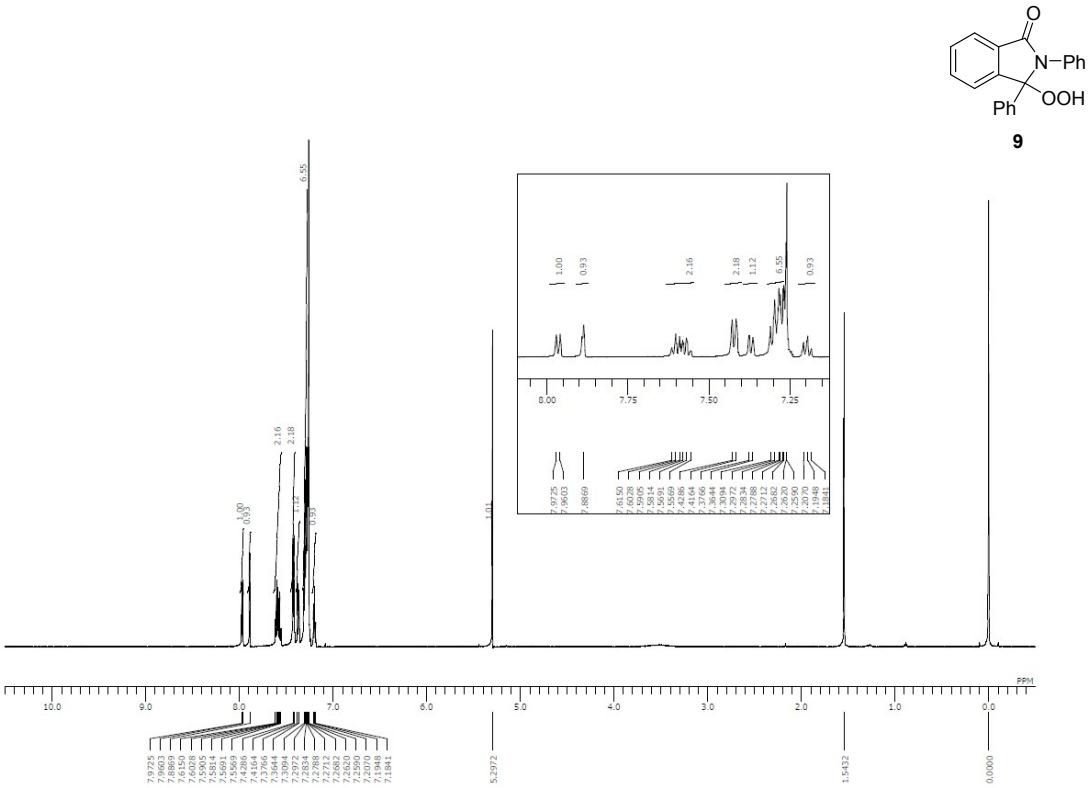
^{13}C-NMR spectrum of **7** ($CDCl_3$, 100 MHz)



^{1}H-NMR spectrum of **8** ($CDCl_3$, 400 MHz)

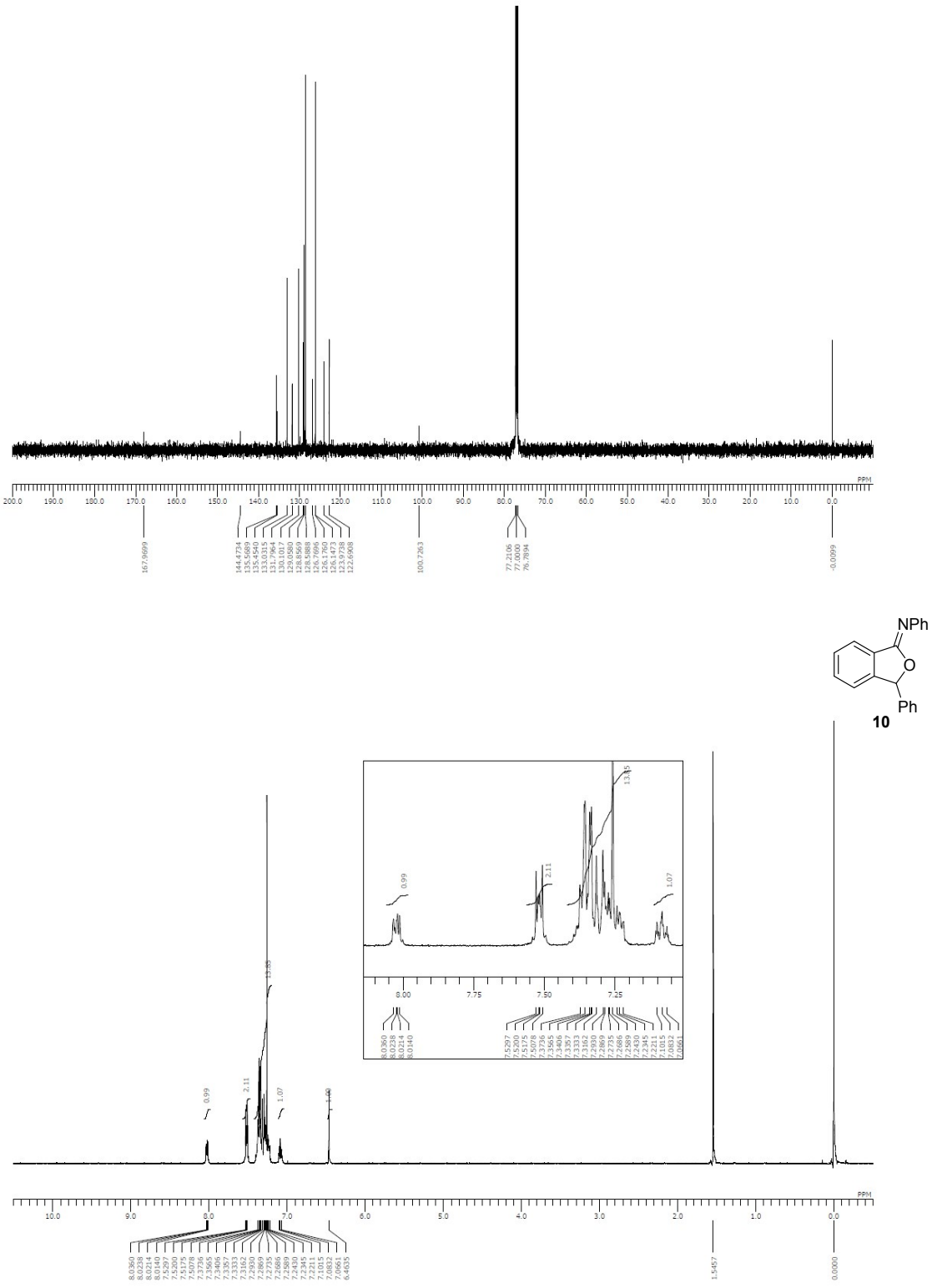
^{13}C-NMR spectrum of **8** (acetone-d_6, 150 MHz)





^{1}H-NMR spectrum of **9** ($CDCl_3$, 600 MHz)

^{13}C-NMR spectrum of **9** ($CDCl_3$, 150 MHz)



^{1}H-NMR spectrum of **10** ($CDCl_3$, 400 MHz)

^{13}C-NMR spectrum of **10** ($CDCl_3$, 100 MHz)