Photoredox-Catalyzed Stereoselective Alkylation of Enamides with *N*-Hydroxyphthalimide Esters *via* Decarboxylative Cross-Coupling Reactions

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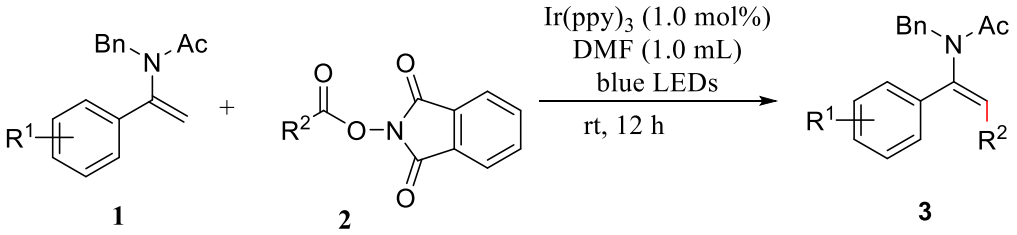
General Information

Unless otherwise noted, all commercially available compounds were used as received. All solvents were purified according to standard procedures. The ^{1}H NMR and spectra was recorded at 400 MHz, ^{13}C NMR was recorded at 100 MHz. ^{1}H and ^{13}C NMR Chemical shifts were calibrated to tetramethylsilane as an external reference. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet); coupling constants (J) are in Hertz (Hz). HRMS were obtained on an IonSpec FT-ICR mass spectrometer with ESI resource. Melting points were measured on a RY-I apparatus and are reported uncorrected.

The starting materials **1** and **2** were readily prepared according to the related literatures.[1-3]

Abbreviations: Bn = benzyl, Ac = acetyl, DMF = *N*,*N*-dimethylformamide, DMAC = *N*,*N*-Dimethylacetamide，DCM= dichloromethane, Ts = *p*-toluenesulfonyl, Boc = *t*-butoxycarbonyl, TEMPO = 2,2,6,6-tetramethylpiperidinooxy.

General Procedure for the Alkylation of Enamides

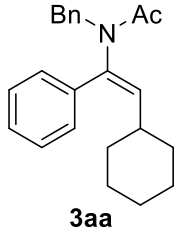


1 **2** **3**

To a Schlenk tube equipped with a magnetic stir bar was charged with enamides **1** (0.30 mmol), alkyl NHP esters **2** (0.36 mmol), and $Ir(ppy)_3$ (2.0 mg, 1.0 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DMF was added *via* syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under blue LEDs for 12 h. The resulting mixture was extracted with ethyl acetate (3×10 mL). The combined organic phase was dried over anhydrous

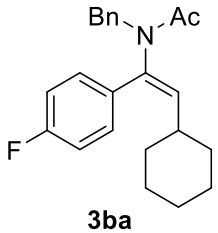
sodium sulfate, and the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10~1:3 *v*/*v*), to give compound **3**.

Analytical Data for the Alkylated Enamides



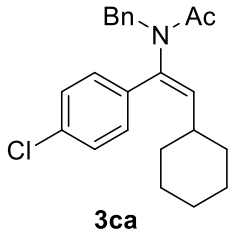
3aa

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-phenylvinyl)acetamide (**3aa**) was obtained in 76% yield (75.9 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.32 (m, 3H), 7.27-7.17 (m, 7H), 5.06 (dd, J = 10.7, 1.5 Hz, 1H), 4.45 (br, s, 2H), 2.37-2.28 (m, 1H), 2.21 (s, 3H), 1.64-1.54 (m, 5H), 1.20-0.95 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 138.6, 137.5, 136.5, 135.4, 129.2, 128.6, 128.5, 128.1, 127.2, 48.8, 37.1, 32.5, 25.8, 25.3, 22.3; HRMS (ESI) calcd for $C_{23}H_{28}NO^+$ $(M + H)^+$ 334.2165, found 334.2162.



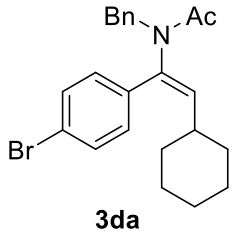
3ba

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(4-fluorophenyl)vinyl)acetamide (**3ba**) was obtained in 89% yield (93.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.07 (m, 7H), 7.00 (t, J = 8.6 Hz, 2H), 4.99 (d, J = 10.7 Hz, 1H), 4.37 (br, s, 2H), 2.22-2.12 (m, 4H), 1.58-1.45 (m, 5H), 1.11-0.87 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.6 (d, J = 248.6 Hz), 138.6, 137.4, 135.6, 131.4 (d, J = 3.4 Hz), 130.2 (d, J = 8.2 Hz), 129.2, 128.2, 127.3, 115.7 (d, J = 21.6 Hz), 48.8, 37.2, 32.5, 25.8, 25.3, 22.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.50; HRMS (ESI) calcd for $C_{23}H_{26}FNNaO^+$ $(M + Na)^+$ 374.1891, found 374.1908.



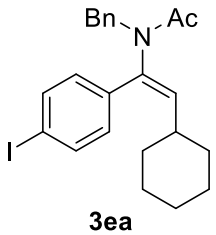
3ca

(*E*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-2-cyclohexylvinyl)acetamide (**3ca**) was obtained in 81% yield (89.7mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 8.6, 1.8 Hz, 2H), 7.29-7.23 (m, 3H), 7.17-7.14 (m, 4H), 5.09 (d, J = 10.8 Hz, 1H), 4.45 (br, s, 2H), 2.30-2.18 (m, 4H), 1.66-1.53 (m, 5H), 1.20-0.96 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 139.3, 137.3, 135.5, 134.4, 133.9, 129.8, 129.3, 129.0, 128.3, 127.4, 48.9, 37.3, 32.5, 25.8, 25.3, 22.4; HRMS (ESI) calcd for $C_{23}H_{27}ClNO^+$ $(M + H)^+$ 368.1776, found 368.1757.



3da

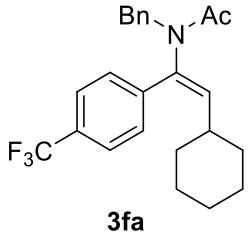
(*E*)-*N*-benzyl-*N*-(1-(4-bromophenyl)-2-cyclohexylvinyl)acetamide (**3da**) was obtained in 78% yield (96.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.4 Hz, 2H), 7.28-7.22 (m, 3H), 7.18-7.15 (m, 2H), 7.11-7.07 (m, 2H), 5.09 (d, J = 10.8 Hz, 1H), 4.45 (br, s, 2H), 2.30-2.18 (m, 4H), 1.66-1.52 (m, 5H), 1.19-0.95 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 139.3, 137.3, 135.5, 134.3, 131.9, 130.1, 129.2, 128.2, 127.3, 122.5, 48.8, 37.2, 32.5, 25.7, 25.3, 22.3; HRMS (ESI) calcd for $C_{23}H_{27}BrNO^+$ $(M + H)^+$ 412.1271, found 412.1270.



3ea

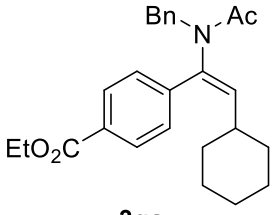
(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(4-iodophenyl)vinyl)acetamide (**3ea**) was obtained in 91% yield (125.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.27-7.14 (m, 5H), 6.98-6.94 (m, 2H), 5.09 (d, J = 10.8 Hz, 1H), 4.45 (br, s, 2H), 2.31-2.21 (m, 1H), 2.18 (s, 3H), 1.65-1.51 (m, 5H), 1.20-0.94 (m, 5H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 139.3, 137.8, 137.3, 135.6, 134.9, 130.2, 129.2, 128.2, 127.3, 94.3, 48.9, 37.2, 32.5, 25.7, 25.2, 22.3; HRMS (ESI) calcd for $C_{23}H_{26}INNaO^+$ $(M + Na)^+$ 482.0951, found 482.0937.



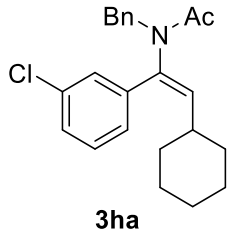
3fa

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(4-(trifluoromethyl)phenyl)vinyl)acetamide (**3fa**) was obtained in 77% yield (93.0 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.28-7.23 (m, 3H), 7.18-7.15 (m, 2H), 5.19 (d, J = 10.9 Hz, 1H), 4.47 (br, s, 2H), 2.32-2.20 (m, 4H), 1.67-1.55 (m, 5H), 1.22-0.97 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 140.4, 139.2, 137.2, 135.4, 130.5 (q, J = 32.6 Hz), 129.3, 128.8, 128.3, 127.4, 125.7 (q, J = 3.7 Hz), 124.0 (q, J = 272.2 Hz), 49.0, 37.3, 32.4, 25.7, 25.2, 22.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.63; HRMS (ESI) calcd for $C_{24}H_{26}F_3NNaO^+$ $(M + Na)^+$ 424.1859, found 424.1844.



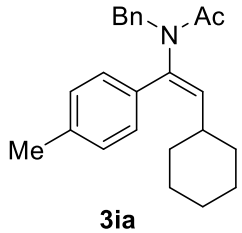
3ga

Ethyl (*E*)-4-(1-(*N*-benzylacetamido)-2-cyclohexylvinyl)benzoate (**3ga**) was obtained in 87% yield (105.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.2 Hz, 2H), 7.31-7.23 (m, 5H), 7.16 (dd, J = 7.5, 1.6 Hz, 2H), 5.17 (d, J = 10.8 Hz, 1H), 4.52-4.37 (m, 4H), 2.35-2.24 (m, 1H), 2.21 (s, 3H), 1.67-1.54 (m, 5H), 1.42 (t, J = 7.1 Hz, 3H), 1.19-0.98 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.1, 140.2, 140.0, 137.3, 135.8, 130.5, 129.9, 129.3, 128.4, 128.2, 127.4, 61.2, 49.0, 37.3, 32.5, 25.7, 25.3, 22.3, 14.4; HRMS (ESI) calcd for $C_{26}H_{31}NNaO_3^+$ $(M + Na)^+$ 428.2196, found 428.2161.



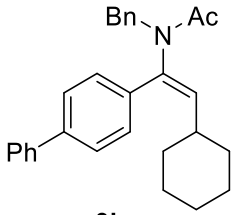
3ha

(*E*)-*N*-benzyl-*N*-(1-(3-chlorophenyl)-2-cyclohexylvinyl)acetamide (**3ha**) was obtained in 88% yield (96.8 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, J = 3.7, 1.5 Hz, 2H), 7.30-7.23 (m, 3H), 7.20-7.16 (m, 3H), 7.13-7.10 (m, 1H), 5.11 (d, J = 10.8 Hz, 1H), 4.46 (br, s, 2H), 2.31-2.19 (m, 4H), 1.67-1.54 (m, 5H), 1.21-0.95 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 139.8, 137.3, 137.3, 135.3, 134.7, 130.0, 129.3, 128.7, 128.4, 128.3, 127.4, 126.8, 49.0, 37.2, 32.5, 25.7, 25.2, 22.3; HRMS (ESI) calcd for $C_{23}H_{27}ClNO^+$ $(M + H)^+$ 368.1776, found 368.1772.



3ia

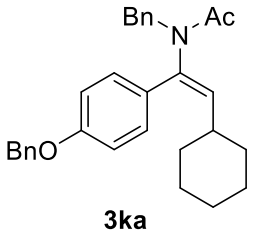
(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(*p*-tolyl)vinyl)acetamide (**3ia**) was obtained in 80% yield (83.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.13 (m, 9H), 5.01 (d, J = 10.7 Hz, 1H), 4.44 (br, s, 2H), 2.40-2.28 (m, 4H), 2.21 (s, 3H), 1.66-1.54 (m, 5H), 1.23-1.08 (m, 3H), 1.02-0.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 138.5, 138.3, 137.6, 136.4, 132.4, 129.4, 129.3, 128.4, 128.2, 127.2, 48.8, 37.2, 32.6, 25.9, 25.4, 22.4, 21.4; HRMS (ESI) calcd for $C_{24}H_{30}NO^+$ $(M + H)^+$ 348.2322, found 348.2328.



3ja

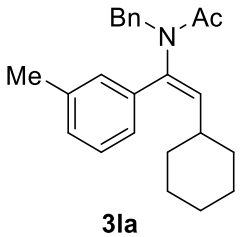
(*E*)-*N*-(1-([1,1'-biphenyl]-4-yl)-2-cyclohexylvinyl)-*N*-benzylacetamide (**3ja**) was obtained in 84% yield (103.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.49-7.44 (m, 2H), 7.40-7.35 (m, 1H), 7.33-7.20 (m, 7H), 5.09 (d, J = 10.8 Hz, 1H), 4.50 (br, s, 2H), 2.45-2.34 (m, 1H), 2.23 (s, 3H), 1.68-1.58 (m, 5H), 1.24-

0.96 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 141.3, 140.4, 139.0, 137.6, 136.2, 134.3, 129.4, 129.0, 128.9, 128.2, 127.7, 127.4, 127.3, 127.1, 48.9, 37.3, 32.6, 25.8, 25.4, 22.4; HRMS (ESI) calcd for $C_{29}H_{31}NNaO^+$ $(M + Na)^+$ 432.2298, found 432.2288.



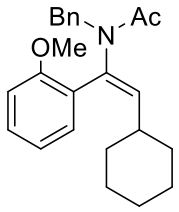
3ka

(*E*)-*N*-benzyl-*N*-(1-(4-(benzyloxy)phenyl)-2-cyclohexylvinyl)acetamide (**3ka**) was obtained in 70% yield (92.3 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.41 (m, 4H), 7.39-7.34 (m, 1H), 7.30-7.23 (m, 3H), 7.22-7.17 (m, 4H), 7.03-6.99 (m, 2H), 5.11 (s, 2H), 5.00 (d, J = 10.7 Hz, 1H), 4.47 (br, s, 2H), 2.38-2.28 (m, 1H), 2.22 (s, 3H), 1.68-1.56 (m, 5H), 1.23-0.96 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 158.9, 137.7, 137.6, 136.8, 136.1, 129.8, 129.3, 128.8, 128.2, 128.2, 127.9, 127.6, 127.2, 114.9, 70.2, 48.8, 37.2, 32.6, 25.9, 25.4, 22.3; HRMS (ESI) calcd for $C_{30}H_{33}NNaO_2^+$ $(M + Na)^+$ 462.2404, found 462.2403.



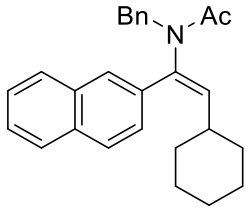
3la

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(*m*-tolyl)vinyl)acetamide (**3la**) was obtained in 54% yield (56.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.15 (m, 7H), 7.07-7.01 (m, 2H), 5.05 (d, J = 10.7 Hz, 1H), 4.45 (br, s, 1H), 2.38-2.29 (m, 4H), 2.21 (s, 3H), 1.66-1.55 (m, 5H), 1.21-0.94 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 138.5, 138.4, 137.7, 136.6, 135.4, 129.3, 128.9, 128.5, 128.2, 127.2, 125.9, 48.9, 37.2, 32.6, 25.9, 25.3, 22.4, 21.7; HRMS (ESI) calcd for $C_{24}H_{30}NO^+$ $(M + H)^+$ 348.2322, found 348.2336.



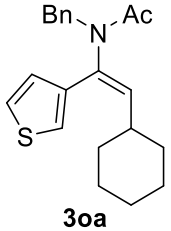
3ma

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(2-methoxyphenyl)vinyl)acetamide (**3ma**) was obtained in 64% yield (69.8 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.22 (m, 1H), 7.17-7.08 (m, 5H), 6.95 (dd, J = 7.5, 1.8 Hz, 1H), 6.85 (td, J = 7.4, 1.0 Hz, 1H), 6.81 (dd, J = 8.3, 0.7 Hz, 1H), 5.09 (d, J = 10.5 Hz, 1H), 4.33 (br, s, 2H), 3.68 (s, 3H), 2.24 (s, 3H), 1.96-1.85 (m, 1H), 1.54-1.44 (m, 5H), 1.04-0.88 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 157.8, 138.8, 138.0, 134.9, 131.9, 130.0, 128.8, 128.0, 126.8, 124.0, 120.3, 111.0, 55.2, 48.2, 37.5, 32.5, 25.9, 25.4, 22.5; HRMS (ESI) calcd for $C_{24}H_{30}NO_2^+$ $(M + H)^+$ 364.2271, found 364.2275.



3na

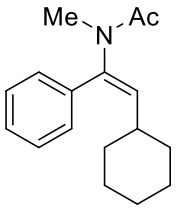
(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(naphthalen-2-yl)vinyl)acetamide (**3na**) was obtained in 76% yield (87.4 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.85 (m, 3H), 7.73 (s, 1H), 7.58-7.53 (m, 2H), 7.39 (dd, J = 8.5, 1.5 Hz, 1H), 7.34-7.24 (m, 5H), 5.20 (d, J = 10.7 Hz, 1H), 4.55 (br, s, 2H), 2.51-2.40 (m, 1H), 2.32 (s, 3H), 1.71-1.60 (m, 5H), 1.24-1.03 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 139.0, 137.6, 136.6, 133.2, 133.2, 132.8, 129.3, 128.4, 128.3, 128.2, 127.8, 127.7, 127.2, 126.7, 126.6, 126.1, 49.0, 37.3, 32.6, 25.8, 25.3, 22.5; HRMS (ESI) calcd for $C_{27}H_{30}NO^+$ $(M + H)^+$ 384.2322, found 384.2336.



3oa

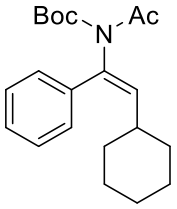
(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(thiophen-3-yl)vinyl)acetamide (**3oa**) was obtained in 72% yield (73.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36

(dd, J = 5.0, 1.2 Hz, 1H), 7.28-7.23 (m, 5H), 7.06 (dd, J = 5.0, 3.6 Hz, 1H), 7.02 (dd, J = 3.6, 1.2 Hz, 1H), 4.95 (d, J = 10.4 Hz, 1H), 4.60 (br, s, 2H), 2.62 (qt, J = 10.7, 3.4 Hz, 1H), 2.13-2.09 (m, 3H), 1.73-1.60 (m, 5H), 1.32-1.10 (m, 3H), 1.00-0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 139.4, 138.8, 137.6, 130.8, 129.7, 128.3, 127.5, 127.3, 126.9, 126.4, 49.5, 37.5, 32.2, 25.8, 25.4, 22.0; HRMS (ESI) calcd for $C_{21}H_{25}NNaOS^+$ $(M + Na)^+$ 362.1549, found 362.1576.



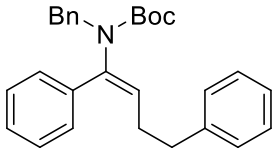
3pa

(*E*)-*N*-(2-cyclohexyl-1-phenylvinyl)-*N*-methylacetamide (**3pa**) was obtained in 65% yield (50.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.33 (m, 3H), 7.29-7.25 (m, 2H), 5.45 (d, J = 10.7 Hz, 1H), 2.91 (s, 3H), 2.45-2.35 (m, 1H), 2.15 (s, 3H), 1.79-1.64 (m, 5H), 1.29-1.13 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 139.5, 135.8, 135.6, 128.7, 128.6, 128.3, 37.2, 35.0, 32.9, 25.9, 25.5, 22.2; HRMS (ESI) calcd for $C_{17}H_{23}NNaO^+$ $(M + Na)^+$ 280.1672, found 280.1672.



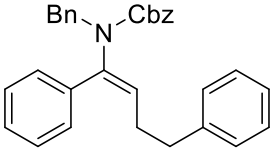
3qa

Tert-butyl (*E*)-acetyl(2-cyclohexyl-1-phenylvinyl)carbamate (**3qa**) was obtained in 53% yield (54.6 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 5H), 5.39 (d, J = 10.6 Hz, 1H), 2.47 (s, 3H), 2.34 (td, J = 10.4, 3.4 Hz, 1H), 1.78m1.61 (m, 5H), 1.37 (s, 9H), 1.23-1.10 (h, J = 11.4, 10.3 Hz, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 153.2, 137.4, 137.2, 134.3, 128.7, 128.1, 127.8, 82.8, 37.2, 32.8, 27.9, 26.4, 26.0, 25.5; HRMS (ESI) calcd for $C_{21}H_{29}NNaO_3^+$ $(M + Na)^+$ 366.2040, found 366.2040.



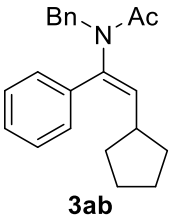
3rs

Tert-butyl (*E*)-benzyl(1,4-diphenylbut-1-en-1-yl)carbamate (**3rs**) was obtained in 65% yield (80.6 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.18 (m, 10H), 7.16-7.11 (m, 1H), 7.10-7.07 (m, 2H), 7.02-6.98 (m, 2H), 5.47 (t, J = 7.5 Hz, 1H), 4.54 (s, 2H), 2.59 (t, J = 7.6 Hz, 2H), 2.42 (q, J = 7.6 Hz, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 141.4, 139.6, 138.9, 137.5, 128.7, 128.5, 128.4, 128.4, 128.3, 128.0, 127.6, 127.2, 126.0, 80.1, 52.8, 36.0, 30.3, 28.2; HRMS (ESI) calcd for $C_{28}H_{31}NNaO_2^+$ $(M + Na)^+$ 436.2247, found 436.2248.



3ss

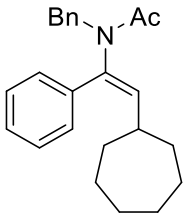
Benzyl (*E*)-benzyl(1,4-diphenylbut-1-en-1-yl)carbamate (**3ss**) was obtained in 73% yield (97.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$ δ 7.32-7.24 (m, 10H), 7.22-7.13 (m, 6H), 7.10-7.06 (m, 2H), 6.99-6.94 (m, 2H), 5.49 (s, 1H), 5.12 (s, 2H), 4.50 (s, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.40 (q, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ156.2, 141.3, 138.3, 138.1, 136.6, 136.4, 129.7, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.4, 126.0, 67.5, 52.4, 35.8, 30.3; HRMS (ESI) calcd for $C_{31}H_{29}NNaO_2^+$ $(M + Na)^+$ 470.2091, found 470.2091.



3ab

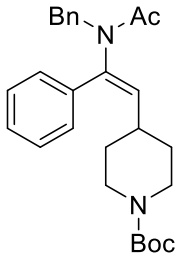
(*E*)-*N*-benzyl-*N*-(2-cyclopentyl-1-phenylvinyl)acetamide (**3ab**) was obtained in 76% yield (72.6 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.33 (m, 3H), 7.29-7.18 (m, 7H), 5.12 (d, J = 10.7 Hz, 1H), 4.46 (br, s, 2H), 2.74-2.62 (m, 1H), 2.21 (s, 3H), 1.78-1.70 (m, 2H), 1.62-1.46 (m, 4H), 1.19-1.10 (m, 2H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 170.9, 138.3, 137.6, 136.7, 135.3, 129.3, 128.7, 128.7, 128.5, 128.2, 127.3, 48.9, 38.9, 33.6, 25.5, 22.3; HRMS (ESI) calcd for $C_{22}H_{25}NNaO^+$ $(M + Na)^+$ 342.1828, found 342.1853.



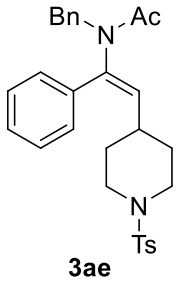
3ac

(*E*)-*N*-benzyl-*N*-(2-cycloheptyl-1-phenylvinyl)acetamide (**3ac**) was obtained in 81% yield (84.1 mg) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.32 (m, 3H), 7.28-7.17 (m, 7H), 5.14 (d, J = 11.1 Hz, 1H), 4.45 (br, s, 2H), 2.53-2.42 (m, 1H), 2.22 (s, 3H), 1.62-1.32 (m, 10H), 1.25-1.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 139.2, 137.5, 135.2, 135.0, 129.2, 128.6, 128.5, 128.4, 128.1, 127.2, 48.7, 38.3, 34.3, 28.2, 26.1, 22.3; HRMS (ESI) calcd for $C_{24}H_{29}NNaO^+$ $(M + Na)^+$ 370.2141, found 370.2163.



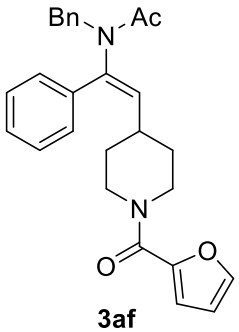
3ad

tert-Butyl (*E*)-4-(2-(*N*-benzylacetamido)-2-phenylvinyl)piperidine-1-carboxylate (**3ad**) was obtained in 74% yield (96.6 mg) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 3H), 7.28-7.22 (m, 5H), 7.18-7.15 (m, 2H), 5.03 (d, J = 10.6 Hz, 1H), 4.46 (br, s, 2H), 3.99 (br, s, 2H), 2.62 (t, J = 11.8 Hz, 2H), 2.50-2.40 (m, 1H), 2.21 (s, 3H), 1.56-1.47 (m, 2H), 1.43 (s, 9H), 1.23-1.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 154.6, 137.7, 137.3, 136.2, 134.9, 129.1, 128.8, 128.8, 128.4, 128.1, 127.2, 79.4, 48.6, 43.3,42.7, 35.3, 31.4, 28.4, 22.2; HRMS (ESI) calcd for $C_{27}H_{35}N_2O_3^+$ $(M + H)^+$ 435.2642, found 435.2642.



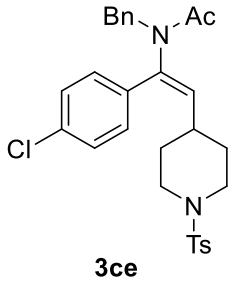
3ae

(*E*)-*N*-benzyl-*N*-(1-phenyl-2-(1-tosylpiperidin-4-yl)vinyl)acetamide (**3ae**) was obtained in 62% yield (90.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.2 Hz, 2H), 7.37-7.33 (m, 3H), 7.30-7.23 (m, 5H), 7.16-7.13 (m, 4H), 5.00 (d, J = 10.5 Hz, 1H), 4.45 (br, s, 2H), 3.65 (d, J = 11.8 Hz, 2H), 2.41 (s, 3H), 2.23-2.12 (m, 6H), 1.61-1.55 (m, 2H), 1.43-1.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 143.6, 138.4, 137.3, 135.4, 134.9, 133.0, 129.7, 129.1, 128.9, 128.8, 128.3, 128.2, 127.7, 127.4, 48.8, 45.4, 34.5, 31.0, 22.3, 21.6; HRMS (ESI) calcd for $C_{29}H_{32}N_2NaO_3S^+$ $(M + Na)^+$ 511.2026, found 511.2036.



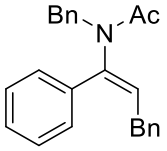
3af

(*E*)-*N*-benzyl-*N*-(2-(1-(furan-2-carbonyl)piperidin-4-yl)-1-phenylvinyl)acetamide(**3af**) was obtained in 64% yield (82.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.37 (m, 4H), 7.26-7.19 (m, 5H), 7.16-7.12 (m, 2H), 6.90 (d, J = 3.5 Hz, 1H), 6.42 (dd, J = 3.4, 1.8 Hz, 1H), 5.02 (d, J = 10.5 Hz, 1H), 4.53-4.35 (m, 4H), 2.84 (br, s, 1H), 2.65-2.55 (m, 1H), 2.20 (s, 3H), 1.61 (d, J = 11.3 Hz, 2H), 1.34-1.22 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 159.2, 148.0, 143.7, 138.2, 137.4, 135.8, 135.0, 129.2, 129.1, 129.0, 128.5, 128.3, 127.4, 116.1, 111.3, 48.8, 45.7, 42.7, 35.6, 31.9, 22.4; HRMS (ESI) calcd for $C_{27}H_{28}N_2NaO_3^+$ $(M + Na)^+$ 451.1992, found 451.2003.



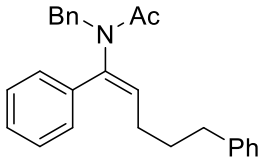
3ce

(*E*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-2-(1-tosylpiperidin-4-yl)vinyl)acetamide (**3ce**) was obtained in 51% yield (80.0 mg) as a white solid. m.p. 145-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.31 (t, J = 7.9 Hz, 4H), 7.25 (dd, J = 5.0, 1.7 Hz, 3H), 7.13-7.10 (m, 2H), 7.05 (d, J = 8.4 Hz, 2H), 5.03 (d, J = 10.5 Hz, 1H), 4.45 (br, s, 2H), 3.66 (d, J = 11.8 Hz, 2H), 2.42 (s, 3H), 2.17-2.09 (m, 6H), 1.56 (dd, J = 13.1, 2.4 Hz, 2H), 1.39 (ddd, J = 15.9, 12.6, 4.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 143.7, 137.5, 137.1, 136.0, 134.8, 133.5, 132.9, 129.8, 129.7, 129.1, 129.1, 128.4, 127.8, 127.5, 48.9, 45.5, 34.7, 31.0, 22.4, 21.6; HRMS (ESI) calcd for $C_{29}H_{31}ClN_2NaO_3S^+$ $(M + Na)^+$ 545.1636, found 545.1630.



3ag

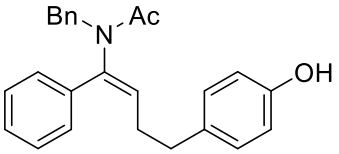
(*E*)-*N*-benzyl-*N*-(1,3-diphenylprop-1-en-1-yl)acetamide (**3ag**) was obtained in 46% yield (47.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (m, 3H), 7.30-7.25 (m, 5H), 7.22-7.17 (m, 5H), 6.84 (d, J = 6.5 Hz, 2H), 5.49 (t, J = 8.1 Hz, 1H), 4.53 (br, s, 2H), 3.50 (d, J = 8.1 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 139.5, 139.3, 137.7, 134.6, 130.2, 129.2, 129.0, 128.9, 128.7, 128.6, 128.5, 128.1, 127.4, 126.4, 48.7, 34.5, 22.5; HRMS (ESI) calcd for $C_{24}H_{23}NNaO^+$ $(M + Na)^+$ 364.1672, found 364.1677.



3ah

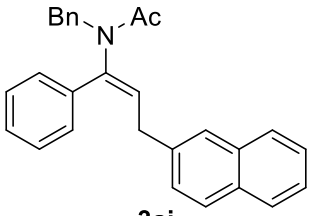
(*E*)-*N*-benzyl-*N*-(1,5-diphenylpent-1-en-1-yl)acetamide (**3ah**) was obtained in 66% yield (73.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.34 (m, 3H),

7.28-7.16 (m, 10H), 7.04 (d, J = 7.6 Hz, 2H), 5.32 (t, J = 7.7 Hz, 1H), 4.48 (br, s, 2H), 2.48 (t, J = 7.7 Hz, 2H), 2.24-2.17 (m, 5H), 1.65-1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 141.8, 138.7, 137.7, 135.0, 132.5, 129.1, 128.7, 128.7, 128.6, 128.4, 128.4, 128.3, 127.3, 126.0, 49.0, 35.4, 31.3, 28.1, 22.4; HRMS (ESI) calcd for $C_{26}H_{27}NNaO^+$ $(M + Na)^+$ 392.1985, found 392.2002.



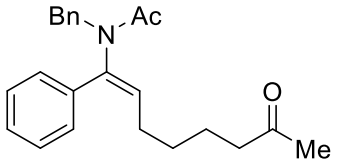
3ai

(*E*)-*N*-benzyl-*N*-(4-(4-hydroxyphenyl)-1-phenylbut-1-en-1-yl)acetamide (**3ai**) was obtained in 72% yield (80.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (br, s, 1H), 7.39-7.34 (m, 3H), 7.29-7.23 (m, 3H), 7.18-7.13 (m, 4H), 6.80-6.72 (m, 4H), 5.29 (t, J = 7.3 Hz, 1H), 4.46 (br, s, 2H), 2.57-2.44 (m, 4H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 155.1, 138.7, 137.3, 134.7, 132.4, 131.8, 129.5, 129.0, 128.8, 128.7, 128.4, 127.4, 115.5, 49.3, 34.5, 30.2, 21.8; HRMS (ESI) calcd for $C_{25}H_{25}NNaO_2^+$ $(M + Na)^+$ 394.1778, found 394.1783.



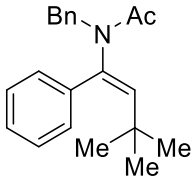
3aj

(*E*)-*N*-benzyl-*N*-(3-(naphthalen-2-yl)-1-phenylprop-1-en-1-yl)acetamide (**3aj**) was obtained in 70% yield (82.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.77 (m, 1H), 7.69 (t, J = 8.0 Hz, 2H), 7.48-7.38 (m, 5H), 7.33-7.29 (m, 5H), 7.26 (s, 1H), 7.24-7.21 (m, 2H), 7.03 (dd, J = 8.4, 1.5 Hz, 1H), 5.61 (t, J = 8.1 Hz, 1H), 4.55 (br, s, 2H), 3.66 (d, J = 8.1 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 139.9, 137.7, 137.0, 134.6, 133.7, 132.2, 129.8, 129.2, 129.0, 128.9, 128.7, 128.6, 128.3, 127.7, 127.6, 127.5, 126.9, 126.2, 126.0, 125.6, 48.8, 34.8, 22.5; HRMS (ESI) calcd for $C_{28}H_{25}NNaO^+$ $(M + Na)^+$ 414.1828, found 414.1837.



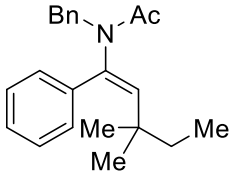
3ak

(*E*)-*N*-benzyl-*N*-(7-oxo-1-phenyloct-1-en-1-yl)acetamide (**3ak**) was obtained in 77% yield (80.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.34 (m, 3H), 7.28-7.18 (m, 7H), 5.28 (t, J = 7.7 Hz, 1H), 4.48 (br, s, 2H), 2.33 (t, J = 7.2 Hz, 2H), 2.22 (s, 3H), 2.17 (dd, J = 15.1, 7.6 Hz, 2H), 2.07 (s, 3H), 1.49-1.41 (m, 2H), 1.33-1.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 170.8, 138.6, 137.7, 135.0, 132.3, 129.0, 128.7, 128.6, 128.6, 128.3, 127.2, 49.0, 43.3, 30.0, 28.9, 28.4, 23.3, 22.3; HRMS (ESI) calcd for $C_{23}H_{27}NNaO_2^+$ $(M + Na)^+$ 372.1934, found 372.1953.



3al

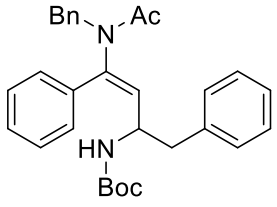
(*E*)-*N*-benzyl-*N*-(3,3-dimethyl-1-phenylbut-1-en-1-yl)acetamide (**3al**) was obtained in 73% yield (67.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 3H), 7.30-7.21 (m, 7H), 5.24 (s, 1H), 4.40 (br, s, 2H), 2.34 (s, 3H), 0.85 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 143.3, 137.7, 136.3, 136.0, 130.0, 129.1, 128.7, 128.2, 128.1, 127.2, 47.9, 32.9, 30.7, 22.6; HRMS (ESI) calcd for $C_{21}H_{25}NNaO^+$ $(M + Na)^+$ 330.1828, found 330.1856.



3am

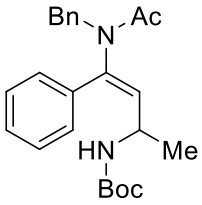
(*E*)-*N*-benzyl-*N*-(3,3-dimethyl-1-phenylpent-1-en-1-yl)acetamide (**3am**) was obtained in 45% yield (43.3 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 3H), 7.28-7.21 (m, 7H), 5.16 (d, J = 13.8 Hz, 1H), 4.42 (br, s, 2H), 2.37 (s, 3H), 1.20 (q, J = 7.5 Hz, 2H), 0.75 (s, 6H), 0.61 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 170.3, 142.6, 137.8, 136.6, 136.5, 129.9, 129.1, 128.7, 128.3, 128.1, 127.2,

47.8, 36.8, 36.3, 28.1, 22.7, 9.1; HRMS (ESI) calcd for $C_{22}H_{28}NO^+$ $(M + H)^+$ 322.2165, found 322.2174.



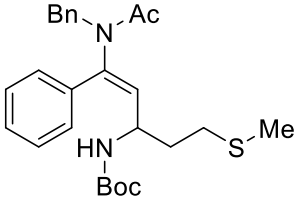
3an

tert-Butyl(*E*)-(4-(*N*-benzylacetamido)-1,4-diphenylbut-3-en-2-yl)carbamate (**3an**) was obtained in 85% yield (120.4 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 6H), 7.20-7.15 (m, 5H), 7.09 (dt, J = 7.4, 3.7 Hz, 2H), 6.84-6.79 (m, 2H), 5.08 (d, J = 9.7 Hz, 1H), 4.80 (d, J = 14.4 Hz, 1H), 4.47 (br, s, 2H), 4.04 (d, J = 14.1 Hz, 1H), 2.85 (d, J = 12.4 Hz, 1H), 2.75-2.68 (m, 1H), 2.08 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 154.6, 140.4, 137.6, 136.4, 134.4, 131.4, 129.7, 129.2, 129.1, 128.8, 128.6, 128.5, 127.4, 126.8, 79.5, 49.8, 48.7, 41.4, 28.3, 22.2; HRMS (ESI) calcd for $C_{30}H_{34}N_2NaO_3^+$ $(M + Na)^+$ 493.2462, found 493.2469.



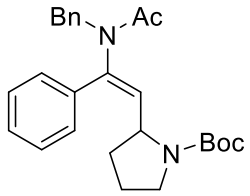
3ao

tert-Butyl(*E*)-(4-(*N*-benzylacetamido)-4-phenylbut-3-en-2-yl)carbamate (**3ao**) was obtained in 50% yield (59.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.18 (m, 10H), 5.04 (d, J = 9.7 Hz, 1H), 4.66 (d, J = 12.5 Hz, 1H), 4.48-4.22 (m, 3H), 2.22 (s, 3H), 1.37 (s, 9H), 1.12 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 154.7, 138.9, 137.5, 134.5, 134.2, 129.3, 129.1, 128.9, 128.7, 128.3, 127.3, 79.3, 48.8, 44.9, 28.4, 22.3, 21.3; HRMS (ESI) calcd for $C_{24}H_{31}N_2O_3^+$ $(M + H)^+$ 395.2329, found 395.2334.



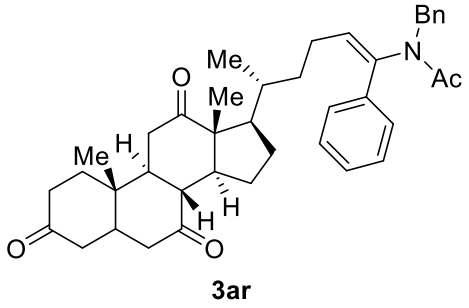
3ap

tert-Butyl(*E*)-(1-(*N*-benzylacetamido)-5-(methylthio)-1-phenylpent-1-en-3-yl)carbamate (**3ap**) was obtained in 57% yield (78.2mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.23 (m, 8H), 7.18 (d, J = 6.8 Hz, 2H), 5.09 (d, J = 9.5 Hz, 1H), 4.95-4.65 (m, 1H), 4.59 (d, J = 8.2 Hz, 1H), 4.38 (s, 1H), 4.27-4.02 (m, 1H), 2.38-2.27 (m, 2H), 2.23 (s, 3H), 2.00 (s, 3H), 1.78-1.59 (m, 2H), 1.40-1.20 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 154.8, 140.0, 137.4, 134.3, 132.2, 129.3, 129.2, 128.9, 128.7, 128.3, 127.4, 79.5, 48.7, 48.5, 34.8, 30.1, 28.3, 22.4, 15.6; HRMS (ESI) calcd for $C_{26}H_{34}N_2NaO_3S^+$ $(M + Na)^+$ 477.2182, found 477.2189.



3aq

tert-Butyl(*E*)-2-(2-(*N*-benzylacetamido)-2-phenylvinyl)pyrrolidine-1-carboxylate (**3aq**) was obtained in 64% yield (81.1 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.16 (m, 10H), 5.13 (s, 2H), 4.48 (s, 1H), 3.82 (d, J = 14.2 Hz, 1H), 3.41-3.26 (m, 2H), 2.28 (s, 3H), 2.12-2.03 (m, 1H), 1.79-1.64 (m, 2H), 1.56-1.48 (m, 1H), 1.41-1.13 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.6, 154.4, 154.1, 138.1, 137.6, 134.7, 134.4, 133.7, 129.4, 129.1, 128.8, 128.6, 128.2, 127.3, 79.6, 79.0, 54.6, 48.7, 46.7, 46.4, 33.4, 33.0, 28.4, 24.2, 23.4, 22.3; HRMS (ESI) calcd for $C_{26}H_{32}N_2NaO_3^+$ $(M + Na)^+$ 443.2305, found 443.2324.



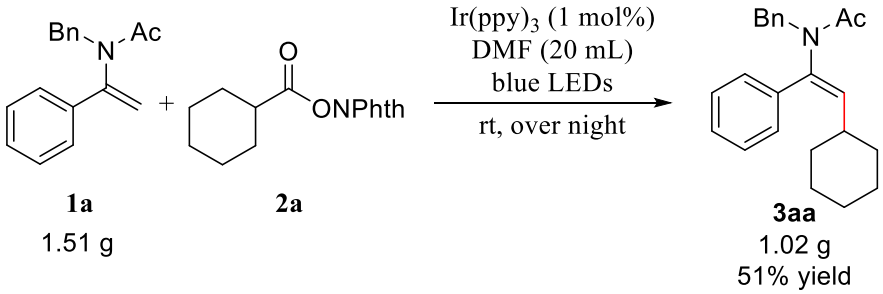
3ar

N-benzyl-*N*-((6*R*,*E*)-6-((8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-3,7,12-trioxohexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)-1-phenylhept-1-en-1-yl)acetamide (**3ar**) was obtained in 82% yield (150.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.33 (m, 3H), 7.28-7.18 (m, 7H), 5.28 (t, J = 7.7 Hz, 1H),

4.61 (d, J = 14.3 Hz, 1H), 4.35 (d, J = 14.3 Hz, 1H), 2.95-2.79 (ddd, J = 36.7, 18.9, 9.3 Hz, 3H), 2.38 -1.76 (m, 19H), 1.61 (td, J = 14.4, 4.7 Hz, 1H), 1.44 -1.37 (m, 4H), 1.19 -1.10 (m, 3H), 1.01 (s, 3H), 0.72 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 209.2, 208.8, 170.8, 138.2, 137.6, 135.0, 132.9, 129.0, 128.6, 128.6, 128.5, 128.2, 127.1, 56.8, 51.8, 49.0, 48.9, 46.8, 45.6, 45.5, 45.0, 42.8, 38.6, 36.5, 36.0, 35.6, 35.2, 35.0, 27.8 25.6, 25.1, 22.3, 21.9, 18.6, 11.8; HRMS (ESI) calcd for $C_{40}H_{49}NNaO_4^+$ (M + Na)$^+$ 630.3554, found 630.3565.

Synthetic Applications of Alkylated Enamides

(1) Gram-scale synthesis of alkylated enamides



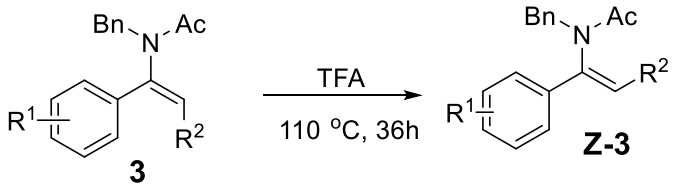
1a
1.51 g

2a

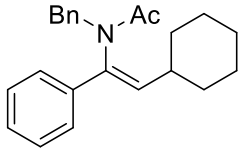
3aa
1.02 g
51% yield

To a Schlenk tube equipped with a magnetic stir bar was charged with enamides **1a** (1.51 g, 6.0 mmol), alkyl NHP esters **2a** (1.97 g, 7.2 mmol), and Ir(ppy_3) (39.3 mg, 1 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 20.0 mL DMF was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under blue LEDs for over night. The resulting mixture was extracted with ethyl acetate. The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10), to give compound **3** in 51% yield (1.02 g).

(2) Conversion of configuration of enamides

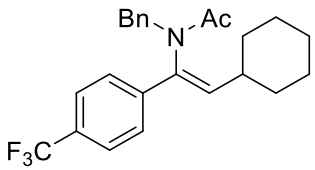


0.3 mmol (1 equiv) of the enamide **3** was dissolved in dry benzene (3.0 mL) in a screw cap vial. 171 mg (1.5 mmol, 5 equiv) of trifluoroacetic acid were added to the solution and the vial was heated at 110 °C for 36 h. The solution was concentrated in vacuum and the product was isolated through flash column chromatography (hexane/ethyl acetate) to furnish ***Z*-3**.



Z-3aa

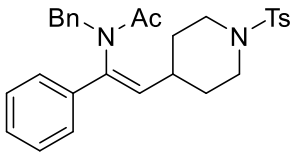
(*Z*)-*N*-benzyl-*N*-(2-cyclohexyl-1-phenylvinyl)acetamide (**Z-3aa**) was obtained in 45% yield (45.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.30 (m, 5H), 7.29-7.20 (m, 5H), 5.77 (d, J = 10.6 Hz, 1H), 5.52 (d, J = 14.0 Hz, 1H), 3.61 (d, J = 14.0 Hz, 1H), 2.12 (s, 3H), 1.90-1.78 (m, 1H), 1.68-1.50 (m, 3H), 1.36-1.31 (m, 1H), 1.20-0.93 (m, 3H), 0.82-0.69 (m, 1H), 0.67-0.55 (m, 1H), 0.12 (dpd, J = 10.4, 3.5, 2.3, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 137.8, 136.5, 136.4, 136.0, 129.9, 129.0, 128.4, 128.3, 127.5, 125.7, 49.4, 37.6, 32.5, 31.5, 25.9, 25.6, 21.4; HRMS (ESI) calcd for $C_{23}H_{28}NO^+$ $(M + H)^+$ 334.2165, found 334.2160.



Z-3fa

(*Z*)-*N*-benzyl-*N*-(2-cyclohexyl-1-(4-(trifluoromethyl)phenyl)vinyl)acetamide (**Z-3fa**) was obtained in 42% yield (50.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.56 (m, 2H), 7.43-7.39 (m, 2H), 7.27-7.22 (m, 5H), 5.89 (d, J = 10.6 Hz, 1H), 5.46 (d, J = 14.0 Hz, 1H), 3.67 (d, J = 14.0 Hz, 1H), 2.10 (s, 3H), 1.89 (dddd, J = 14.2,

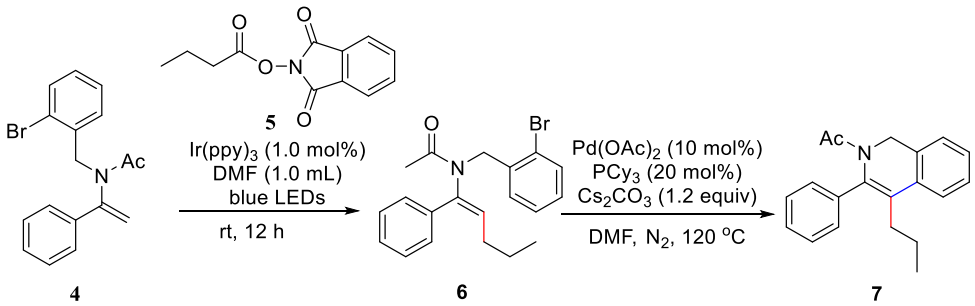
10.9, 7.2, 3.5 Hz, 1H), 1.71-1.54 (m, 3H), 1.42-1.34 (m, 1H), 1.21-0.97 (m, 3H), 0.84-0.61 (m, 2H), 0.19 (dtd, *J* = 10.8, 3.7, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 140.3, 138.3, 137.4, 135.6, 129.9, 128.5, 127.7, 126.0 (q, *J* = 3.7 Hz), 125.9, 124.1 (q, *J* = 272.0 Hz), 49.6, 37.9, 32.4, 31.4, 25.9, 25.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.46; HRMS (ESI) calcd for $C_{24}H_{26}F_3NNaO^+$ $(M + Na)^+$ 424.1859, found 424.1854.



Z-3ae

(*Z*)-*N*-benzyl-*N*-(1-phenyl-2-(1-tosylpiperidin-4-yl)vinyl)acetamide (**Z-3ae**) was obtained in 51% yield (74.8 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.57 (m, 2H), 7.41-7.31 (m, 7H), 7.20-7.11 (m, 5H), 5.72 (d, *J* = 10.3 Hz, 1H), 5.55 (d, *J* = 14.0 Hz, 1H), 3.69 (ddt, *J* = 11.6, 4.3, 2.3 Hz, 1H), 3.45 (d, *J* = 14.0 Hz, 1H), 3.36 (dp, *J* = 13.0, 2.5 Hz, 1H), 2.51 (s, 7H), 2.06-1.95 (s, 4H), 1.70-1.52 (m, 3H), 1.46-1.34 (m, 1H), 1.03-0.92 (m, 1H), -0.14 (dt, *J* = 13.0, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 143.8, 138.2, 137.8, 135.6, 132.9, 132.4, 130.0, 129.8, 129.2, 128.8, 128.4, 127.7, 127.6, 125.8, 49.0, 45.9, 45.8, 35.3, 30.7, 29.9, 21.7, 21.2; HRMS (ESI) calcd for $C_{29}H_{32}N_2NaO_3S^+$ $(M + Na)^+$ 511.2026, found 511.2032.

(3) Preparation of isoquinoline derivative 7



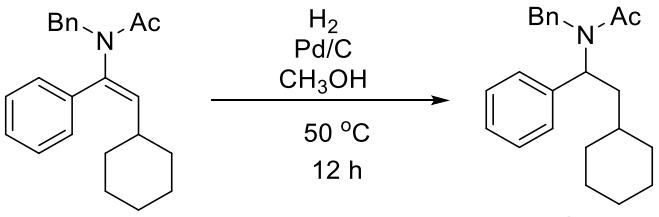
(i) To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **4** (98.7 mg, 0.30 mmol), alkyl NHP ester **5** (139.9 mg, 0.6 mmol), and $Ir(ppy)_3$ (2.0 mg, 1.0 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DMF was added via syringe with gentle stirring under N_2

atmosphere. The tube was sealed and stirred under blue LEDs for 12 h. The resulting mixture was extracted with ethyl acetate. The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 *v*/*v*). (*E*)-*N*-(2-bromobenzyl)-*N*-methyl-1-phenylpent-1-en-1-amine (**6**) was obtained in 65% yield (72.0 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.9 Hz, 1H), 7.40-7.33 (m, 3H), 7.25-7.20 (m, 4H), 7.11-7.06 (m, 1H), 5.50 (t, J = 7.7 Hz, 1H), 4.68 (s, 2H), 2.25 (s, 3H), 2.15 (dd, J = 15.0, 7.5 Hz, 2H), 1.39-1.29 (m, 2H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 138.6, 136.7, 135.0, 133.0, 132.7, 130.9, 128.8, 128.8, 128.6, 128.6, 127.4, 124.1, 49.3, 30.7, 22.7, 22.4, 13.9; HRMS (ESI) calcd for $C_{20}H_{22}BrNNaO^+$ $(M + Na)^+$ 394.0777, found 394.0785.

(ii) To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **6** (74.4 mg, 0.20 mmol), $Pd(OAc)_2$ (4.6 mg, 10 mol%), tricyclohexylphosphane (11.2 mg, 20 mol%), and Cs_2CO_3 (78.3 mg, 1.2 equiv). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 2.0 mL DMF was added *via* syringe with gentle stirring under N_2 atmosphere. And the vial was heated at 120 ^{o}C under the atmosphere of N_2 for 24 h. The solution was diluted by ethyl acetate, washed by ammonium chloride saturated solution. The organic layer was concentrated in vacuum and the product was isolated through flash column chromatography (hexane/ethyl acetate = 8:1) to furnish the related product **7**.

1-(3-phenyl-4-propylisoquinolin-2(1*H*)-yl)ethan-1-one **7** was obtained in 76% yield (44.3 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.23 (m, 9H), 4.98 (s, 2H), 2.73 (t, J = 7.4 Hz, 2H), 1.49-1.35 (m, 5H), 0.69 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 137.9, 135.9, 134.7, 133.5, 130.3, 128.5, 128.1, 127.8, 127.5, 125.4, 124.1, 46.3, 29.8, 24.3, 22.6, 13.5; HRMS (ESI) calcd for $C_{20}H_{21}NNaO^+$ $(M + Na)^+$ 314.1515, found 314.1528.

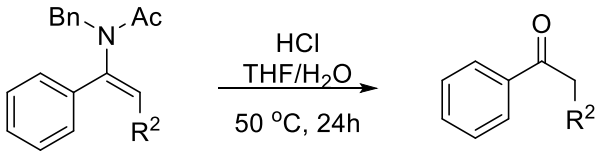
(4) Hydrogenation of enamide 3aa



3aa **8**

(*E*)-*N*-benzyl-*N*-(2-cyclohexyl-1-phenylvinyl)acetamide (**3aa**) (1.0 g) in methanol (15 ml) was hydrogenated at 50 ºC and room pressure in the presence of palladium-charcoal (0.1 g) for 12 h. Upon completion, the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 *v*/*v*). *N*-benzyl-*N*-(2-cyclohexyl-1-phenyl-ethyl)acetamide **8** was obtained in 69% yield (0.69 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) for two conformers: δ 7.37-7.11 (m, 9H), 6.95 (d, J = 6.9 Hz, 1H), 6.13 and 5.07 (2×t, J = 7.7 Hz, 1H), 4.91 and 3.39 (2×d, J = 15.3 Hz, 1H), 4.25 and 3.84 (2×d, J = 17.7 Hz, 1H), 2.36 and 2.02 (2×s, 3H), 1.86-1.51 and 1.23-0.77 (2×m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$) for two conformers: δ 171.9, 171.5, 140.3, 139.8, 139.4, 138.2, 128.8, 128.6, 128.5, 128.1, 127.8, 127.6, 127.6, 127.0, 126.7, 126.1, 59.0, 53.8, 47.9, 45.9, 39.5, 38.4, 34.5, 34.0, 33.5, 33.5, 33.3, 33.2, 26.6, 26.4, 26.3, 26.2, 25.9, 25.6, 22.9, 22.6; HRMS (ESI) calcd for $C_{23}H_{30}NO^+$ $(M + H)^+$ 336.2322, found 336.2333.

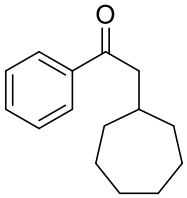
(5) Hydrolysis of enamides



3 **9**

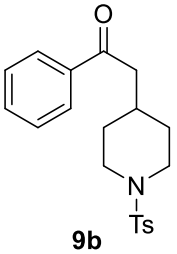
Enamides **3** (0.3 mmol) was added into a tube. Then THF (1 mL) and concentrated hydrochloric acid (1 mL) were added sequentially by syringe. The resulting mixture was stirred at 50 ºC for 24 hours as monitored by TLC. Upon completion, the solvent

was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:100~1:10 *v*/*v*).



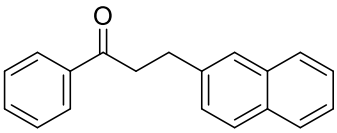
9a

2-Cycloheptyl-1-phenylethan-1-one (**9a**) was obtained in 95% yield (61.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.93 (m, 2H), 7.57-7.52 (m, 1H), 7.48-7.43 (m, 2H), 2.87 (d, J = 6.9 Hz, 2H), 2.27-2.16 (m, 1H), 1.79-1.72 (m, 2H), 1.68-1.44 (m, 8H), 1.32-1.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 137.6, 133.0, 128.7, 128.3, 46.9, 36.1, 35.0, 28.5, 26.4; HRMS (ESI) calcd for $C_{15}H_{21}O^+$ $(M + H)^+$ 217.1587, found 217.1590.



9b

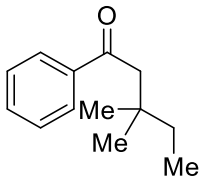
1-Phenyl-2-(1-tosylpiperidin-4-yl)ethan-1-one (**9b**) was obtained in 86% yield (92.2 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.89 (m, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.59-7.53 (m, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 3.78 (d, J = 11.6 Hz, 2H), 2.87 (d, J = 6.6 Hz, 2H), 2.44 (s, 3H), 2.28 (td, J = 12.0, 2.4 Hz, 2H), 1.99-1.88 (m, 1H), 1.82 (d, J = 12.7 Hz, 2H), 1.40 (qd, J = 12.4, 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 143.6, 137.1, 133.4, 133.1, 129.7, 128.8, 128.1, 127.9, 46.5, 44.6, 31.7, 31.5, 21.7; HRMS (ESI) calcd for $C_{20}H_{24}NO_3S^+$ $(M + H)^+$ 358.1471, found 358.1470.



9c

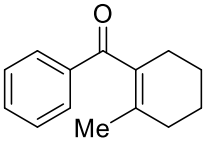
2-(Naphthalen-2-yl)-1-phenylethan-1-one (**9c**) was obtained in 92% yield (71.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.7 Hz, 2H), 7.85-

7.75 (m, 3H), 7.69 (s, 1H), 7.58-7.52 (m, 1H), 7.49-7.37 (m, 5H), 3.44-3.35 (m, 2H), 3.28-3.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 138.9, 136.9, 133.7, 133.2, 132.2, 128.8, 128.3, 128.2, 127.8, 127.6, 127.3, 126.6, 126.2, 125.5, 40.5, 30.4; HRMS (ESI) calcd for $C_{19}H_{17}O^+$ $(M + H)^+$ 261.1274, found 261.1284.



9d

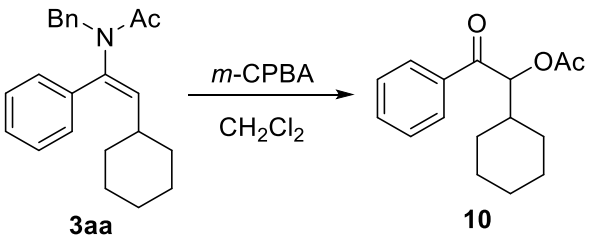
3,3-Dimethyl-1-phenylpentan-1-one (**9d**) was obtained in 89% yield (50.8 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.92 (m, 2H), 7.57-7.52 (m, 1H), 7.48-7.43 (m, 2H), 2.85 (s, 2H), 1.44 (q, J = 7.5 Hz, 2H), 1.01 (s, 6H), 0.87 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 138.9, 132.8, 128.6, 128.3, 47.8, 35.1, 34.3, 27.3, 8.7； HRMS (ESI) calcd for $C_{13}H_{19}O^+$ $(M + H)^+$ 191.1430, found 191.1410.



9e

(2-Methylcyclohex-1-en-1-yl)(phenyl)methanone (**9e**) was obtained in 65% yield (38.8 mg) as a colorless oil.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.81 (m, 2H), 7.55 (ddd, J = 6.7, 3.9, 1.3 Hz, 1H), 7.49-7.43 (m, 2H), 2.26-2.19 (m, 2H), 2.13-2.08 (m, 2H), 1.77-1.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7, 137.1, 134.9, 133.1, 132.5, 129.4, 128.8, 31.3, 27.6, 22.7, 22.4, 21.3; HRMS (ESI) calcd for $C_{14}H_{17}O^+$ $(M + H)^+$ 201.1274, found 201.1285.

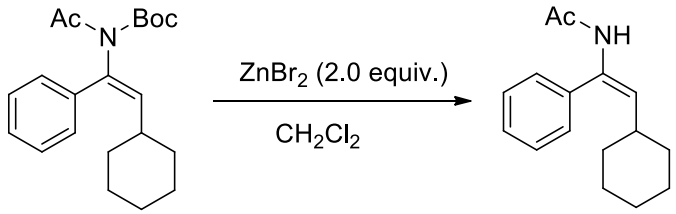
(6) The synthesis of *α*-acyloxyketone



3aa **10**

Enamide **3aa** (0.2 mmol) was added into a tube. Then *m*-CPBA (3.0 equiv) was added to the stirred solution of the enamide in CH_2Cl_2 at 0 ºC and the resultant suspension stirred for 30 min before warming to rt. The resulting mixture was stirred at rt for 24 hours as monitored by TLC. Upon completion, the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:50 *v*/*v*). 1-cyclohexyl-2-oxo-2-phenylethyl acetate (**10**) was obtained in 75% yield (39.0 mg) as a colorless oil.[5] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.4 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 5.72 (d, J = 5.2 Hz, 1H), 2.16 (s, 3H), 1.97-1.88 (m, 1H), 1.74-1.61 (m, 5H), 1.26-1.10 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 171.0, 135.9, 133.6, 128.9, 128.6, 79.1, 39.8, 29.9, 27.7, 26.2, 26.1, 26.0, 20.8; HRMS (ESI) calcd for $C_{16}H_{21}O_3^+$ $(M + H)^+$ 261.1485, found 261.1482.

(7) Cleavage of *N*-Boc Protecting Group[6]

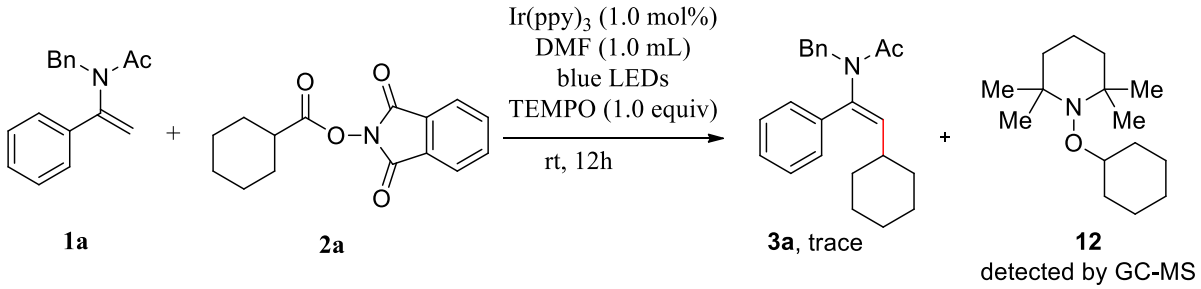


3qa **11**, 88%

Enamides **3qa** (68.7 mg, 0.2 mmol) was added into a reaction tube. Then, $ZnBr_2$ (90.1 mg, 0.4 mmol) and DCM (1 mL) were added sequentially. The resulting mixture was stirred at room temperature for 2 hours as monitored by TLC. Upon completion, the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:4 v/v). (*E*)-*N*-(2-cyclohexyl-1-phenylvinyl)acetamide **11** was obtained in 88% yield (42.8 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H,), 6.56 (s, br, 1H), 6.17 (d, J = 10.5 Hz, 1H), 2.06-1.97 (m, 4H), 1.71-1.53 (m, 5H), 1.23-1.09 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 137.6, 132.4, 128.7, 128.6, 128.2 125.8, 37.2, 33.8, 26.0, 25.8, 24.6. HRMS (ESI) calcd for $C_{16}H_{22}NO^+$ $(M + H)^+$ 244.1696, found 244.1696.

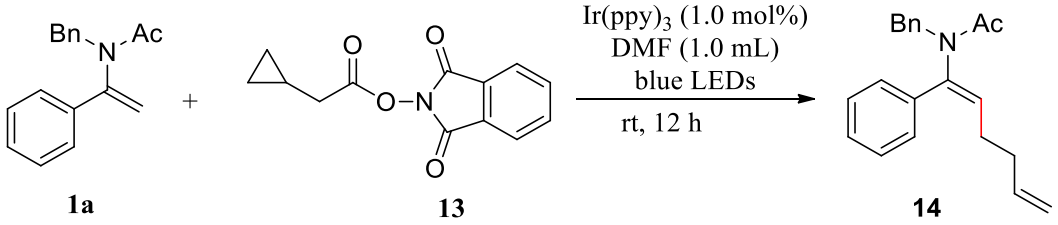
Preliminary Mechanistic Studies

(1) Radical-trapping experiment



1a **2a** **3a**, trace **12** detected by GC-MS

To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **1a** (75.4 mg, 0.30 mmol), alkyl NHP ester **2a** (98.3 mg, 0.36 mmol), TEMPO (46.9 mg, 0.3 mmol), and $Ir(ppy)_3$ (2.0 mg, 1.0 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DMF was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under blue LEDs for 12 h. The adduct **12** of TEMPO and alkyl radical from decarboxylation of NHP ester **2a** was detected by GC-MS: 239.22. There was trace corresponding **3a** detected.



1a **13** **14**

To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **1a** (75.4 mg, 0.30 mmol), alkyl NHP ester **13** (147.1 mg, 0.6 mmol), and $Ir(ppy)_3$ (2.0 mg, 1.0 mol%). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DMF was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under blue LEDs for 12 h. The resulting mixture was extracted with ethyl acetate. The combined organic phase was dried over anhydrous sodium sulfate, and the solvent was then removed under vacuum. The residue was purified directly by silica gel chromatography, eluting with ethyl acetate/petroleum ether (1:10 *v*/*v*). (*E*)-*N*-benzyl-*N*-(1-phenylhexa-1,5-dien-1-yl)

acetamide **14** was obtained in 54% yield (49.5 mg) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 3H), 7.21-7.10 (m, 7H), 5.61-5.50 (m, 1H), 5.23 (t, J = 7.6 Hz, 1H), 4.86-4.80 (dd, J = 11.9, 6.0 Hz, 2H), 4.40 (br, s, 2H), 2.21 (q, J = 7.3 Hz, 2H), 2.14 (s, 3H), 1.97 (q, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 138.7, 137.7, 137.4, 135.0, 132.1, 129.1, 128.7, 128.7, 128.6, 128.3, 127.2, 115.7, 49.1, 33.4, 27.9, 22.5; HRMS (ESI) calcd for $C_{21}H_{23}NNaO^{+}$ $(M + Na)^{+}$ 328.1672, found 328.1693. No cyclopropylmethyl substituted enamide was detected in this reaction.

(2) Quantum yield measurement

In order to determine whether a radical-chain reaction is involved, the quantum yield measurement was conducted, which gives the quantum yield (Φ) of the photoreaction of 0.71, implying that the reaction is highly possible to proceed in a photoredox catalytic pathway rather than a radical-chain mechanism.

The actinometry measurements were done as follows based on previous literature[7]:

(i) The actinometry measurements were determined by standard ferrioxalate actinometry. A solution of ferrioxalate was prepared by dissolving 73.7 mg of potassium ferrioxalate hydrate and 67 μL of concentrated sulfuric acid in a 25 mL volumetric flask and filled to the mark with water (HPLC grade). A buffered solution of phenanthroline was prepared by dissolving 25.0 mg of phenanthroline, 5.2 g of sodium acetate and 0.56 mL of concentrated sulfuric acid in a 50 mL volumetric flask and filled to the mark with water (HPLC grade). Both solutions were stored in the dark.

(ii) The actinometry solutions (V_1, 1mL) were irradiated with 15 W blue LEDs for specified time intervals (30 s, 60 s, 90 s, 120 s, and 150 s). After irradiation, 40 μL (V_2) of the actionmeter solutions were removed and placed in 10 mL (V_3) volumetric flasks. 1.5 mL of buffered solutions were added to these flasks and filled to the mark with water (HPLC grade). The UV-Vis spectra of actinometry samples were recorded for each time interval. The absorbance of the actinometry solutions were monitored at 510 nm. A non-irradiated sample was also prepared and the absorbance at 510 nm measured

in cuvette (l = 1 cm). ε is the molar absorptivity at 510 nm (11,100 L mol^{-1} cm^{-1}). Based on the data, we got the graph (**Fig.1b**) between the number of moles of products (y axis) and time (x axis).

$$\text{mol } Fe^{2+} = \frac{V_1 \times V_3 \times \triangle A\ (510\ nm)}{10^3 \times V_2 \times l \times \varepsilon\ (510\ nm)} = \frac{1\ mL \times 10\ \ mL \times \triangle A\ (510\ nm)}{10^3 \times (40 \times 10^{-3}\ mL) \times 1\ cm \times 11100}$$

$$= \frac{\triangle A\ (510\ nm)}{44400} = 2.1997 \times 10^{-8}$$

The quantum yield for Fe^{2+} ($\Phi_{Fe^{2+}} = 1.13$), F = mol $Fe^{2+}/\Phi_{Fe^{2+}}$.Then, the irradiated light intensity was estimated to 1.95 x 10^{-8} einstein S^{-1} by using $K_3[Fe(C_2O_4)_3]$ as an actinometer.

(iii) For five clean tubes, according to the general procedure, the 0.3 mmol scale model reaction solution was irradiated with 15 W blue LEDs for specified time intervals (30 min, 60 min, 90 min, 120 min and 150 min). The moles of products formed were determined by ^1H NMR yield with mesitylene as reference standard. The number of moles of products (y axis) per unit time is related to the number of photons (x axis, calculated from the light intensity) (**Fig.1c**). The slope gives the quantum yield (Φ) of the photoreaction, 0.71.

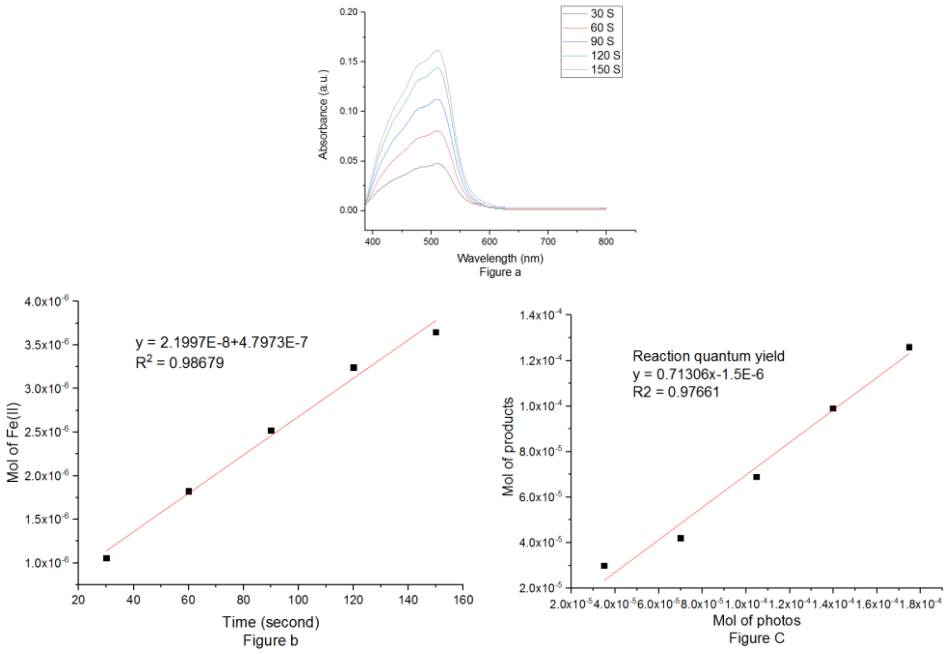
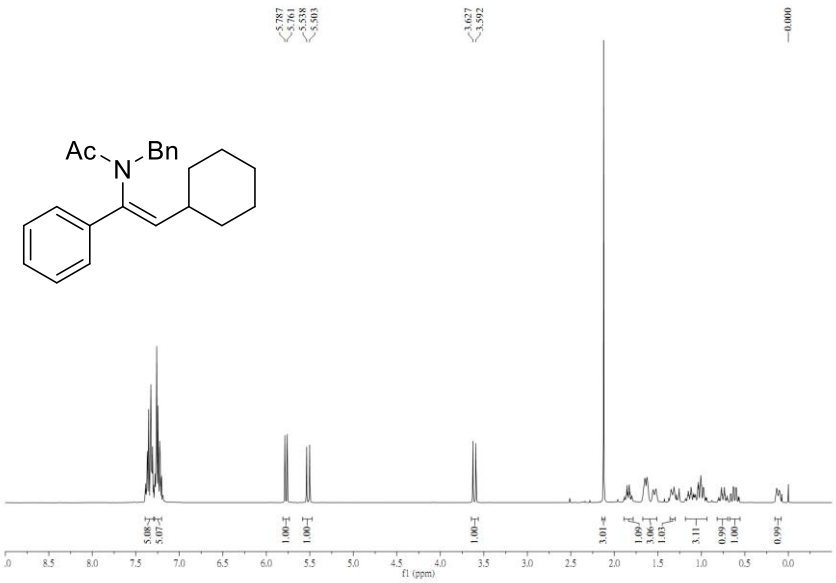


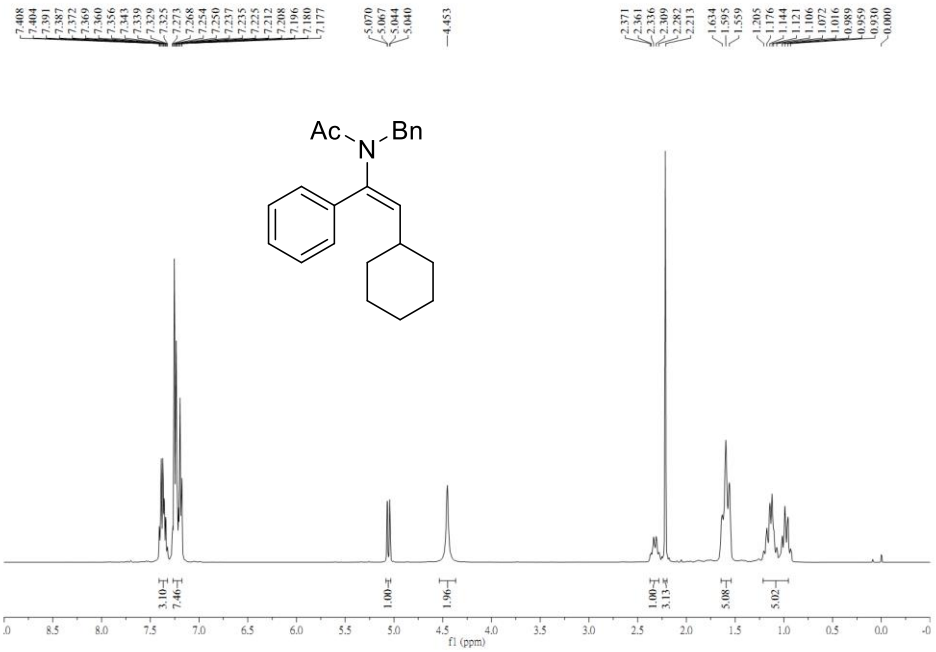
Figure 1. The UV-Vis spectra and data of quantum yield measurement.

(3) ^{1}H NMR evidence for the stereoselectivity of the model reaction

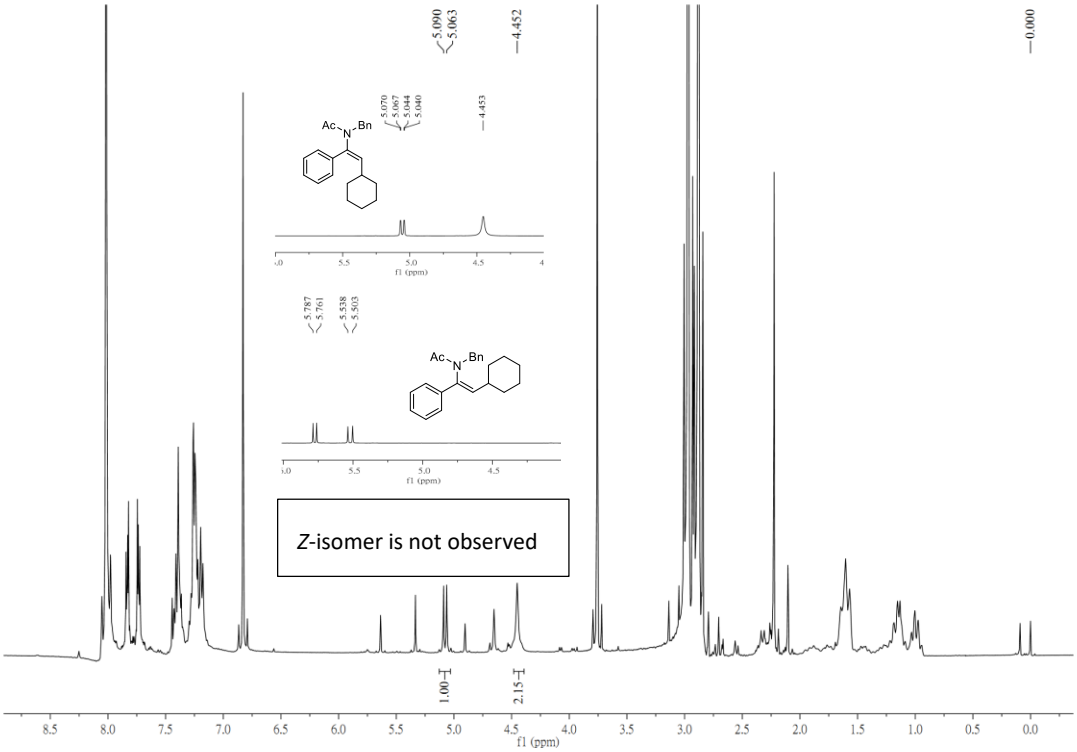
^{1}H NMR of the *Z*-configured enamides:



^{1}H NMR of the *E*-configured enamides:



Crude ^{1}H NMR spectrum of reaction system:



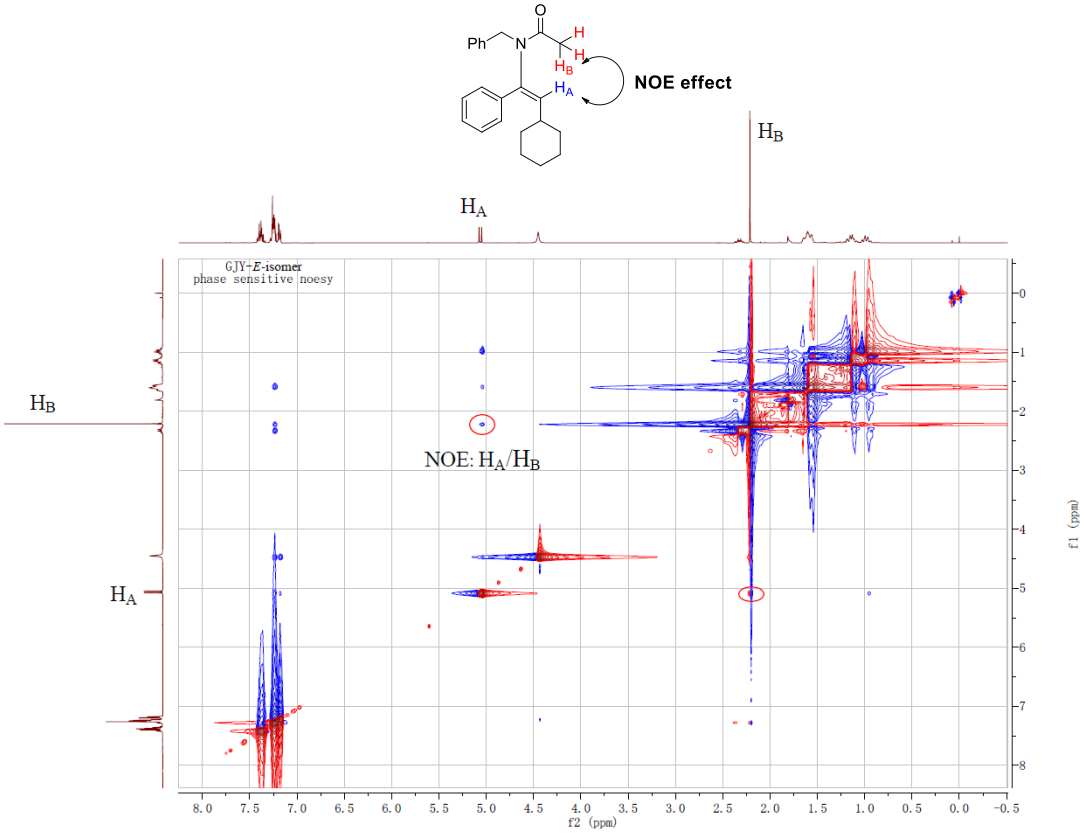
No *Z*-isomer was observed in Crude ^{1}H NMR spectrum of reaction system.

Determination of stereochemisty-NOESY experiment of *E*-3aa and *Z*-3aa

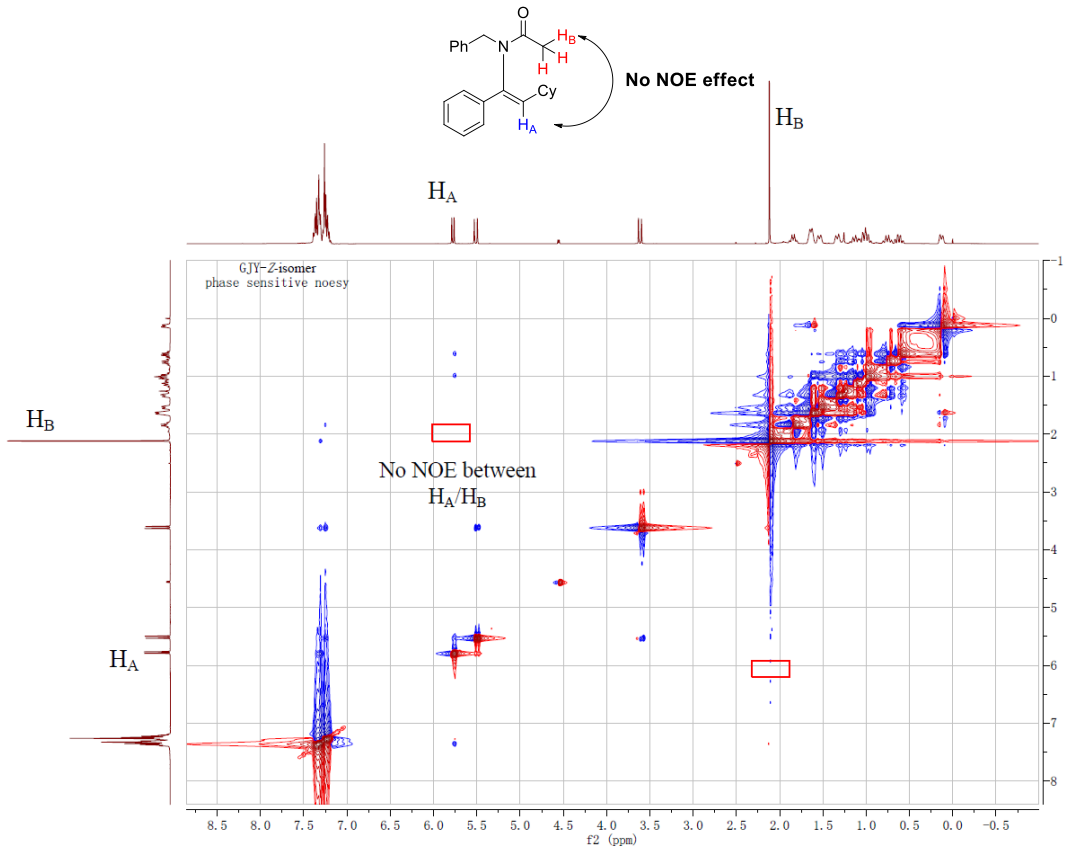
(i) The *E*-stereochemistry of **3ce** was unambiguously confirmed through X-ray analysis. All other E-adducts **3aa-3ss**, **3ab-3ar** exhibit similar signals to **3ce** for their alkene and benzylic hydrogens in ^{1}H NMR. Thus, the stereochemistry of the compounds in Table 2 and Table 3 were assigned as *E*-configuration. For ***Z*-3aa**, ***Z*-3fa** and ***Z*-3ae**, the chemical shift of the olefinic hydrogen (about 0.7 ppm shifts to the low fields) and the spin splitting of benzylic hydrogens (two doublets for *Z*-isomers vs one br s singlet for *E*-isomers).

(ii) NOESY-experiments of ***E*-3aa** and ***Z*-3aa** was performed as well to further testify the stereochemistry. It was shown that for ***E*-3aa**, a NOE effect between the olefinic hydrogen and the methyl of acetyl group was observed, while no NOE effect between the olefinic hydrogen and the methyl of acetyl group was observed for ***Z*-3aa.**

NOESY experiment of *E*-3aa:



NOESY experiment of *Z*-3aa:



References

(1) Van den Berg, M.; Haak, R. M.; Minnaard, A. J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. Rhodium/MonoPhos-Catalysed Asymmetric Hydrogenation of Enamides. *Adv. Synth. Catal.* **2002**, *344*, 1003-1007.

(2) Pankajakshan, S.; Xu, Y.-H.; Cheng, J. K.; Low, M. T.; Loh, T.-P. Palladium-Catalyzed Direct C-H Arylation of Enamides with Simple Arenes. *Angew. Chem. Int. Ed.* **2012**, *51*, 5701-5705.

(3) Lu, X.; Xiao, B.; Liu, L.; Fu, Y. Formation of $C(sp^3)$-$C(sp^3)$Bonds through Nickel-Catalyzed Decarboxylative Olefin Hydroalkylation Reactions. *Chem. Eur. J.* **2016**, *22*, 11161-11164.

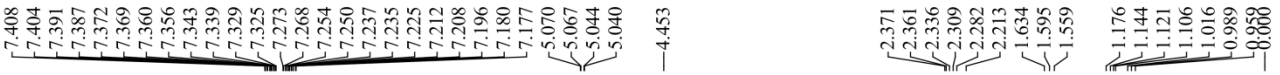
(4) Ryan, S. J.; Candish, L.; Lupton, D. W. *N*-Heterocyclic Carbene-Catalyzed (4 + 2) Cycloaddition/Decarboxylation of Silyl Dienol Ethers with *α*,*β*-Unsaturated Acid Fluorides. *J. Am. Chem. Soc.* **2011**, *133*, 4694-4697.

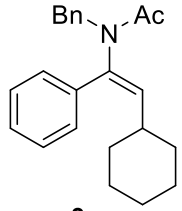
(5) Trost, B. M.; Xu, J.; Schmidt, T. Ligand Controlled Highly Regio- and Enantioselective Synthesis of *α*-Acyloxyketones by Palladium-Catalyzed Allylic Alkylation of 1,2-Enediol Carbonates. *J. Am. Chem. Soc.* **2008**, *130*, 11852-11853.

(6) Nigama, S. C.; Mann, A.; Taddei, M.; Wermutha, C.-G. Selective Removal of the Tert-Butoxycarbonyl Group from Secondary Amines: $ZnBr_2$ as the Deprotecting Reagent. *Synth. Commun.* **1989**, *19*, 3139-3142.

(7) Cismesiaa, M. A.; Yoon, T. P. Characterizing Chain Processes in Visible Light Photoredox Catalysis. *Chem. Sci.* **2015**, *6*, 5426-5434.

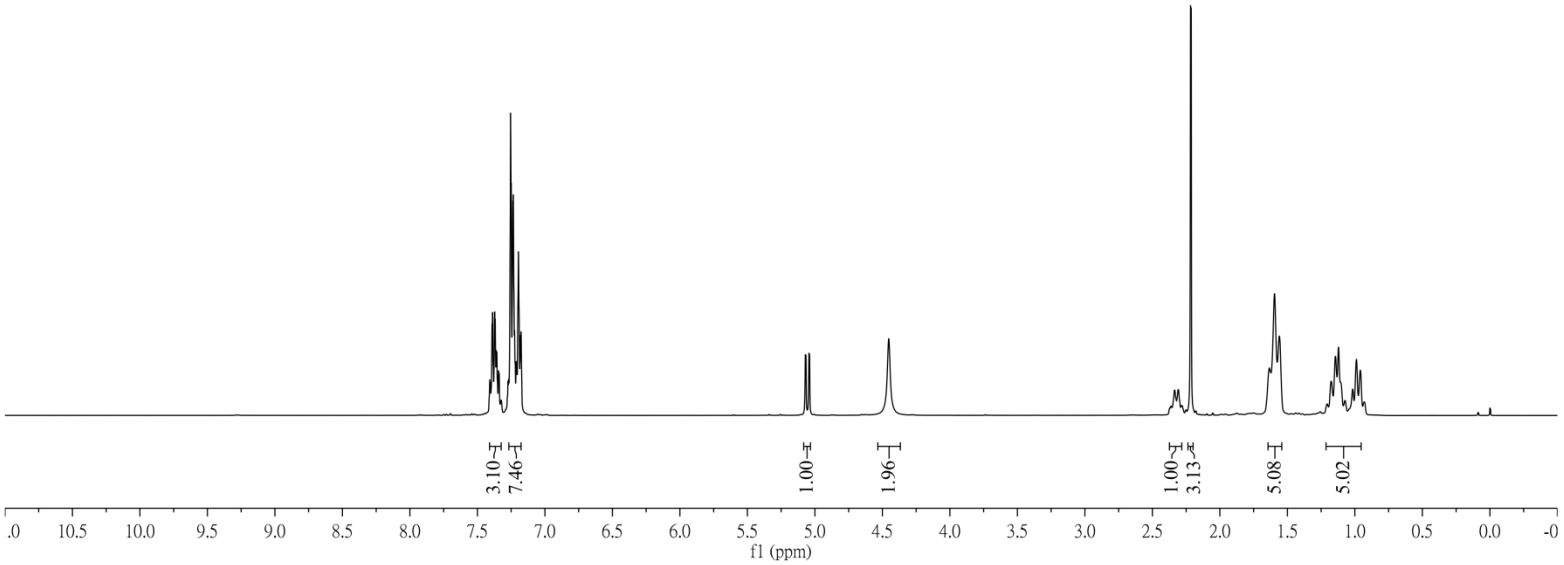
Copies of ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR Spectra

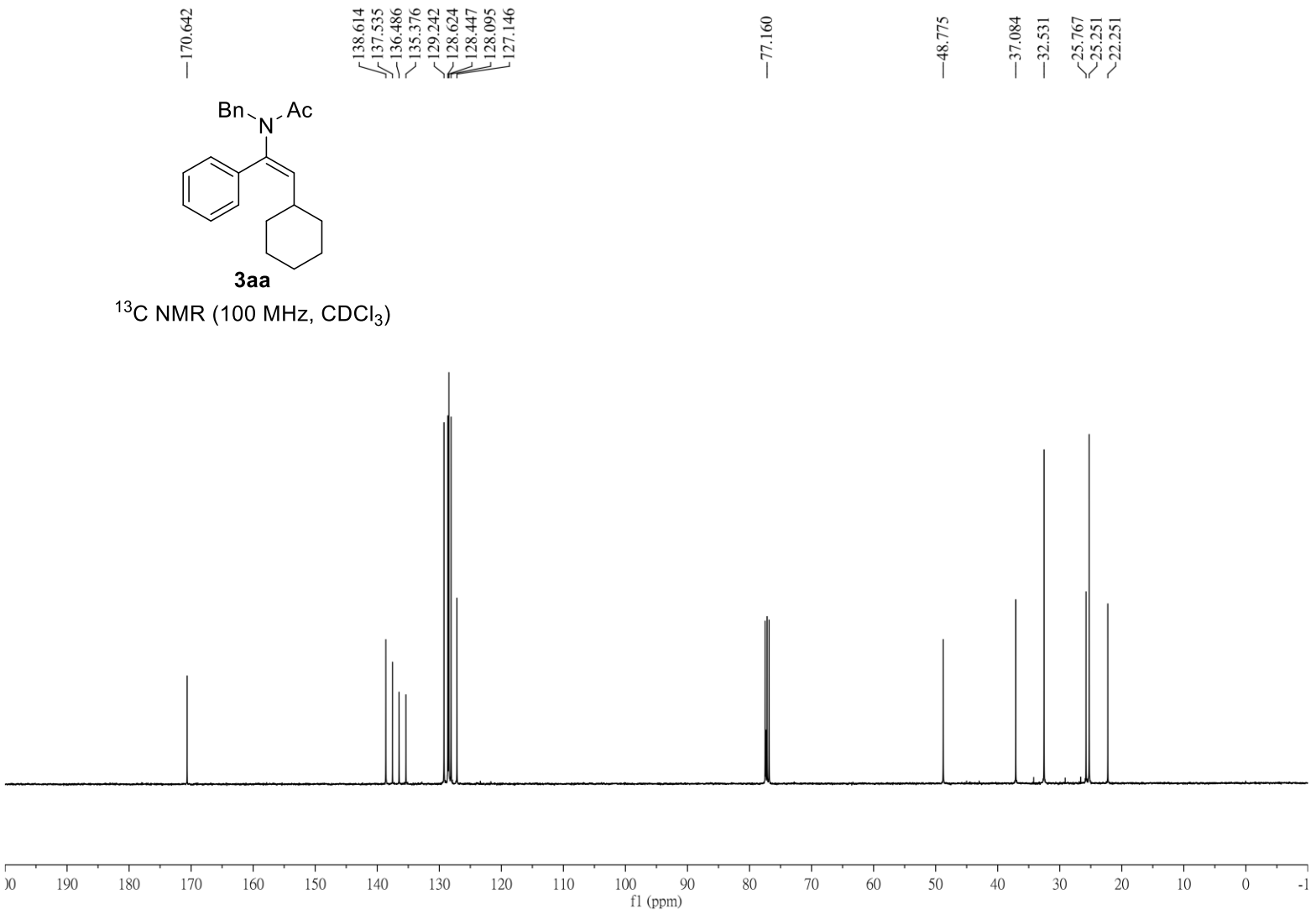




3aa

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

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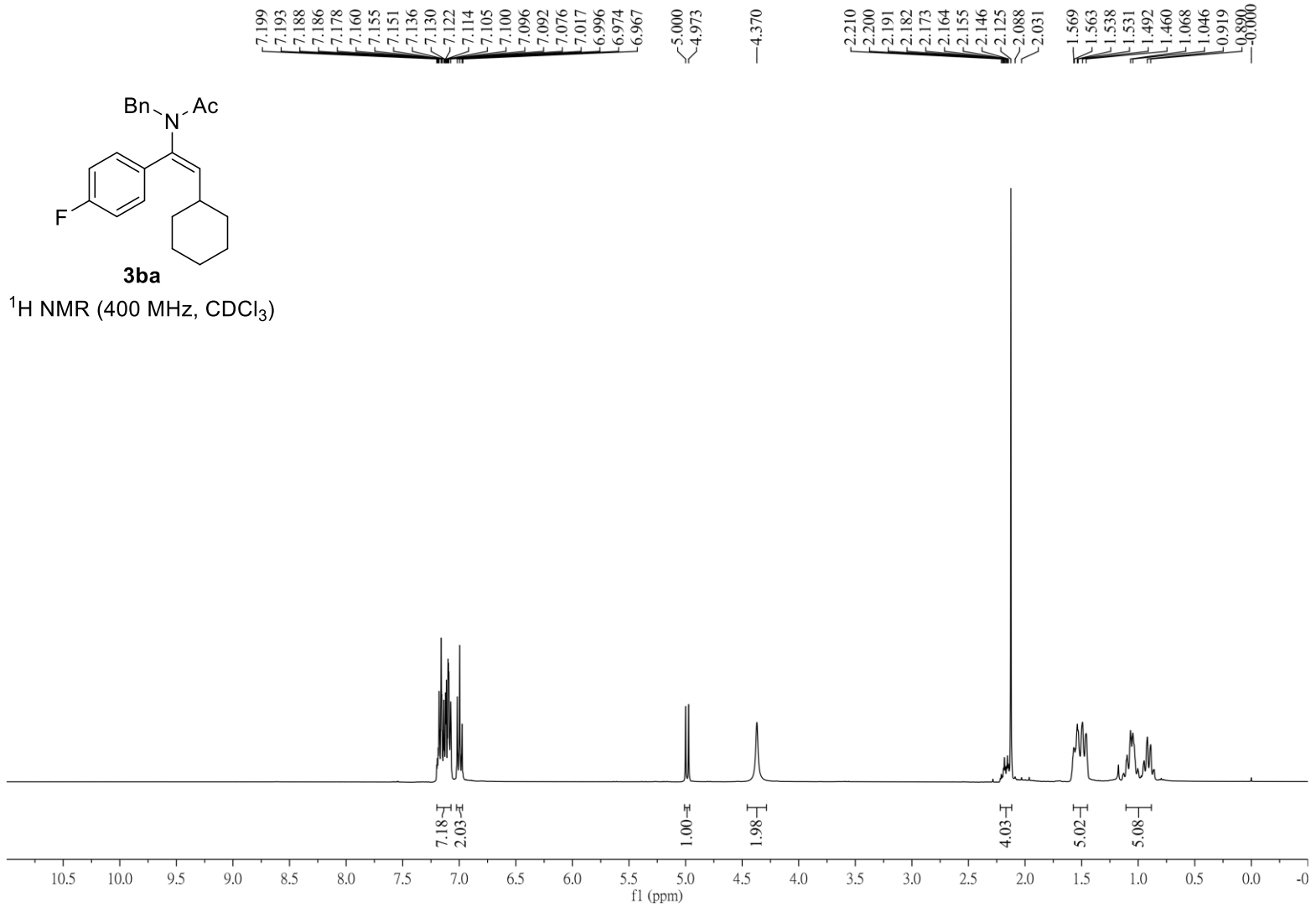
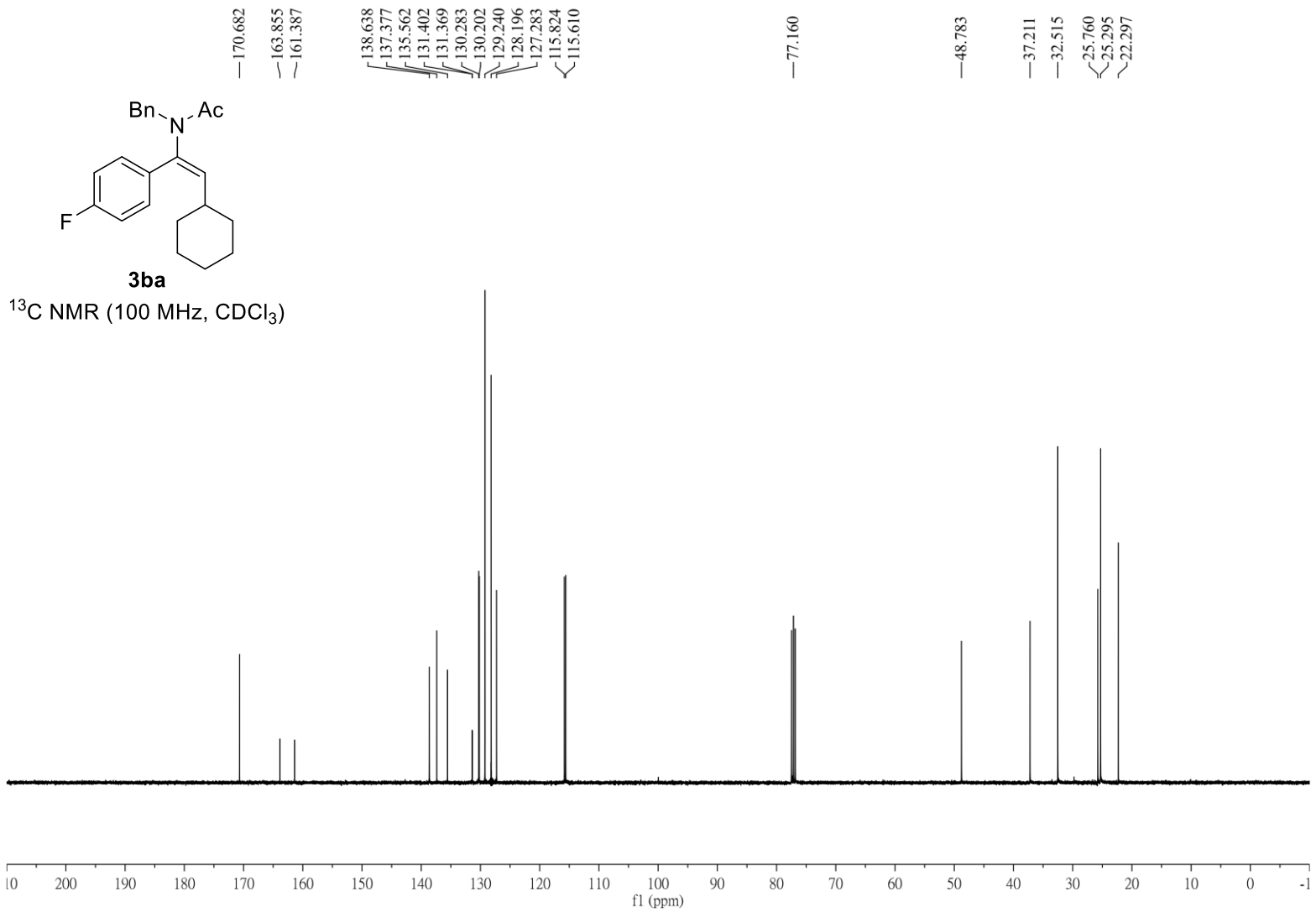
138.614
137.535
136.486
135.376
129.242
128.624
128.447
128.095
127.146
77.160
48.775
37.084
32.531
25.767
25.251
22.251
Bn
N
Ac
3aa
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ba

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


170.682
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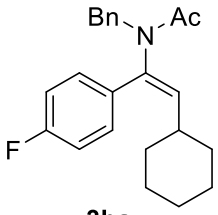
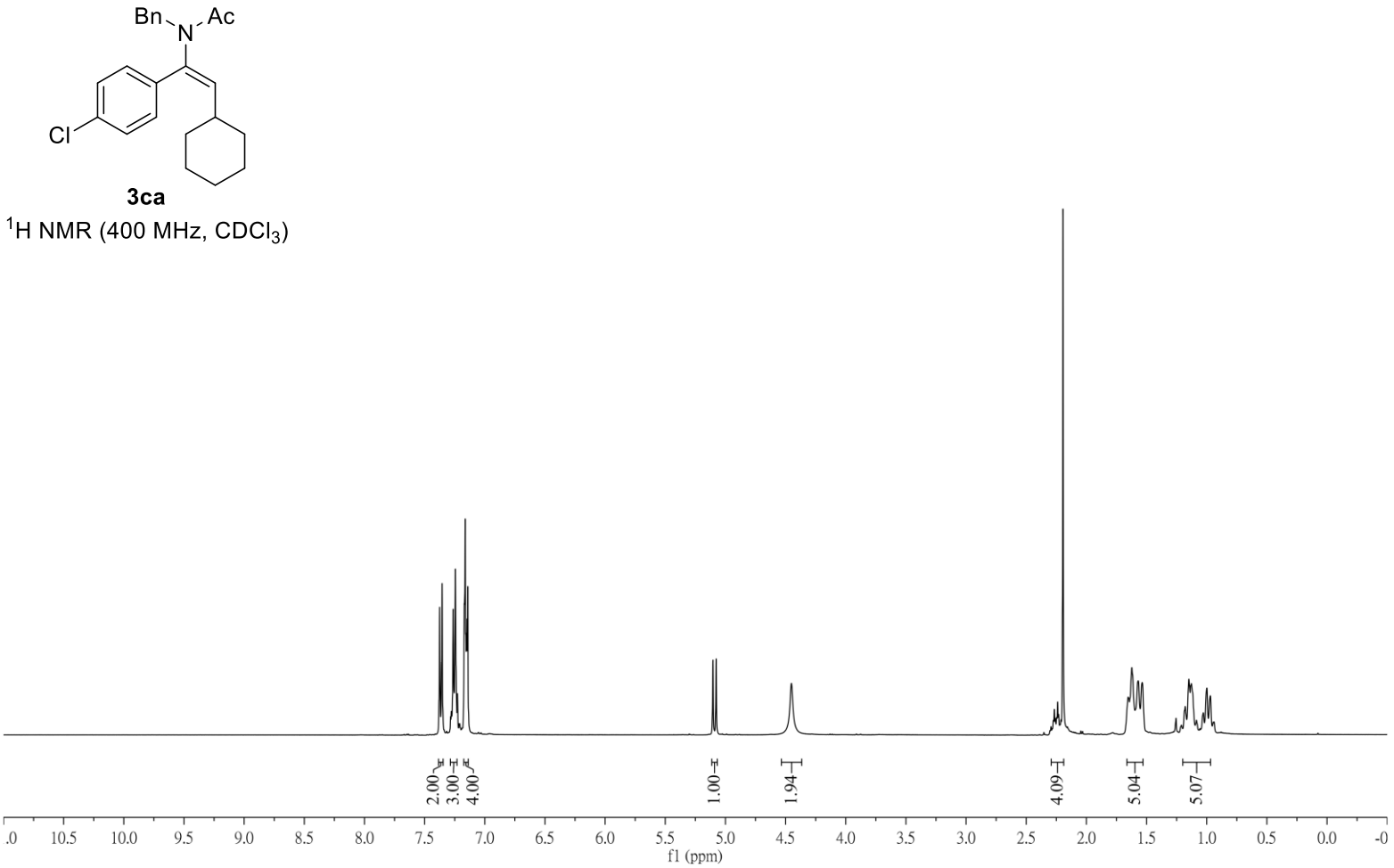
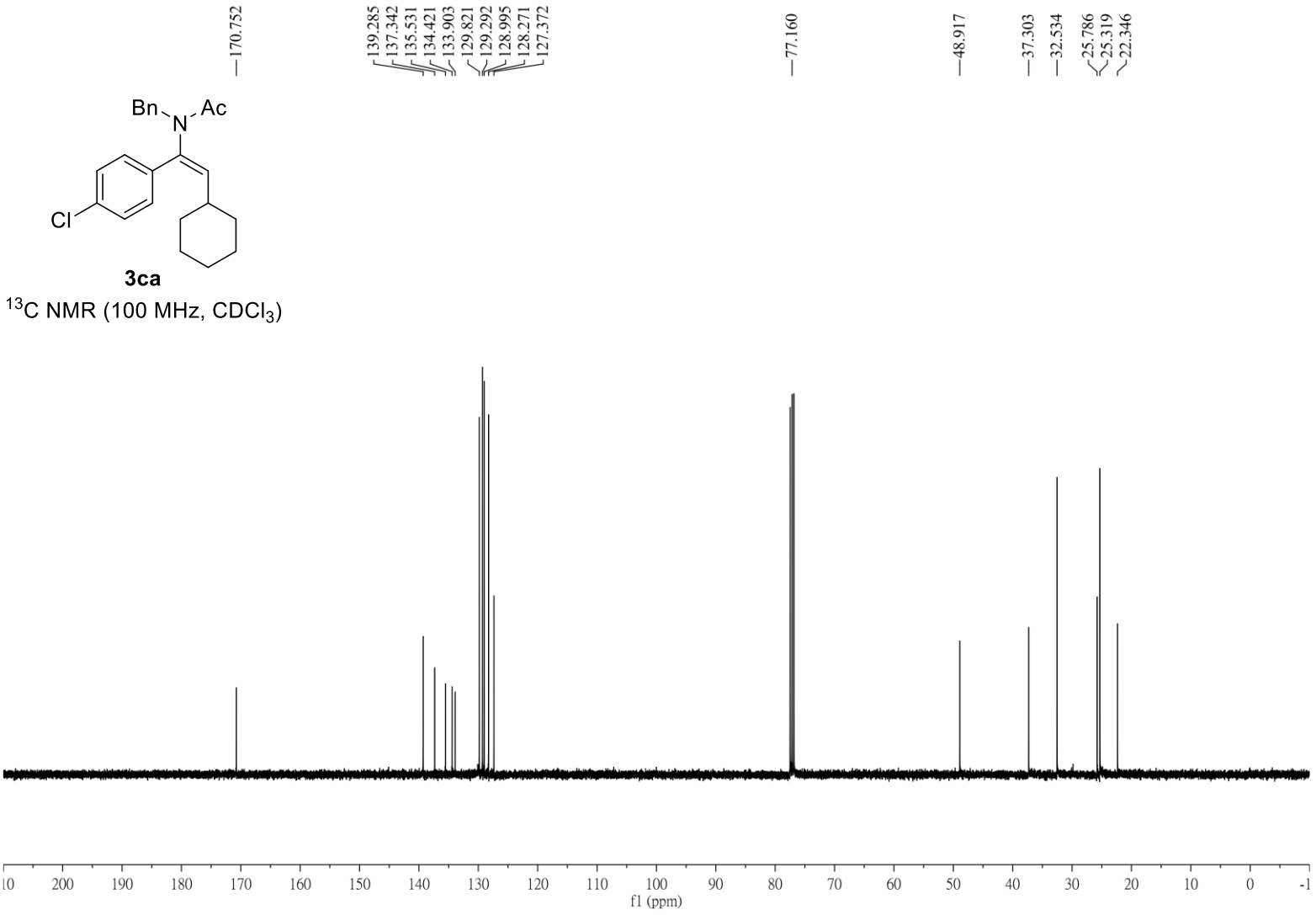
161.387
138.638
137.377
135.562
131.402
131.369
130.283
130.202
129.240
128.196
127.283
115.824
115.610
77.160
48.783
37.211
32.515
25.760
25.295
22.297
Bn
N
Ac
F
3ba
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ba

^{19}F NMR (376 MHz, $CDCl_3$)


7.381
7.376
7.359
7.355
7.284
7.278
7.264
7.244
7.227
7.170
7.162
7.151
7.147
7.141
5.104
5.077
4.452
2.275
2.267
2.258
2.248
2.239
2.231
2.212
2.194
1.653
1.622
1.570
1.536
1.255
1.179
1.148
1.133
1.128
1.085
1.028
0.999
0.970
Bn
N
Ac
Cl
3ca
1H NMR (400 MHz, CDCl3)
2.00
3.00
4.00
1.00
1.94
4.09
5.04
5.07
f1 (ppm)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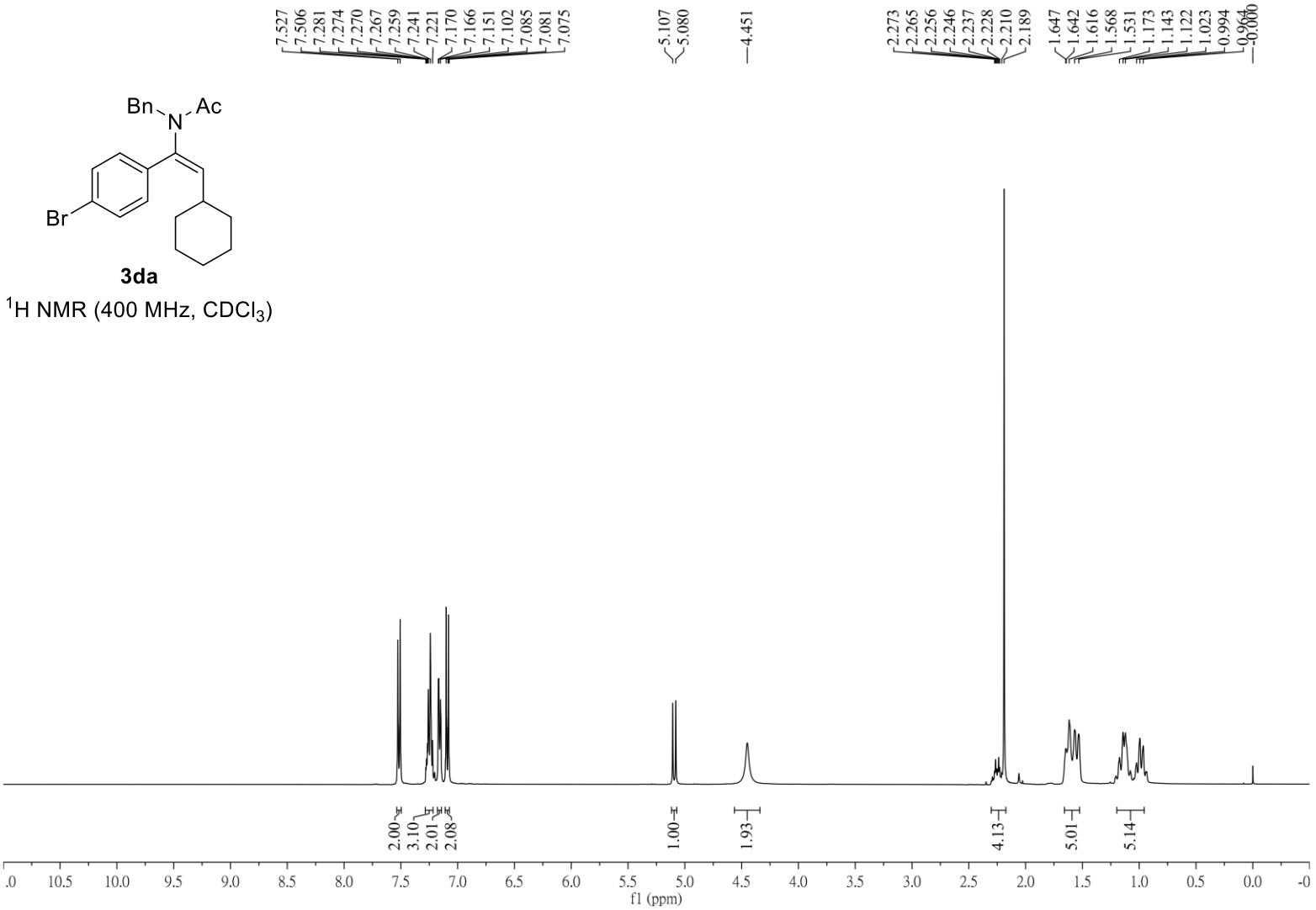
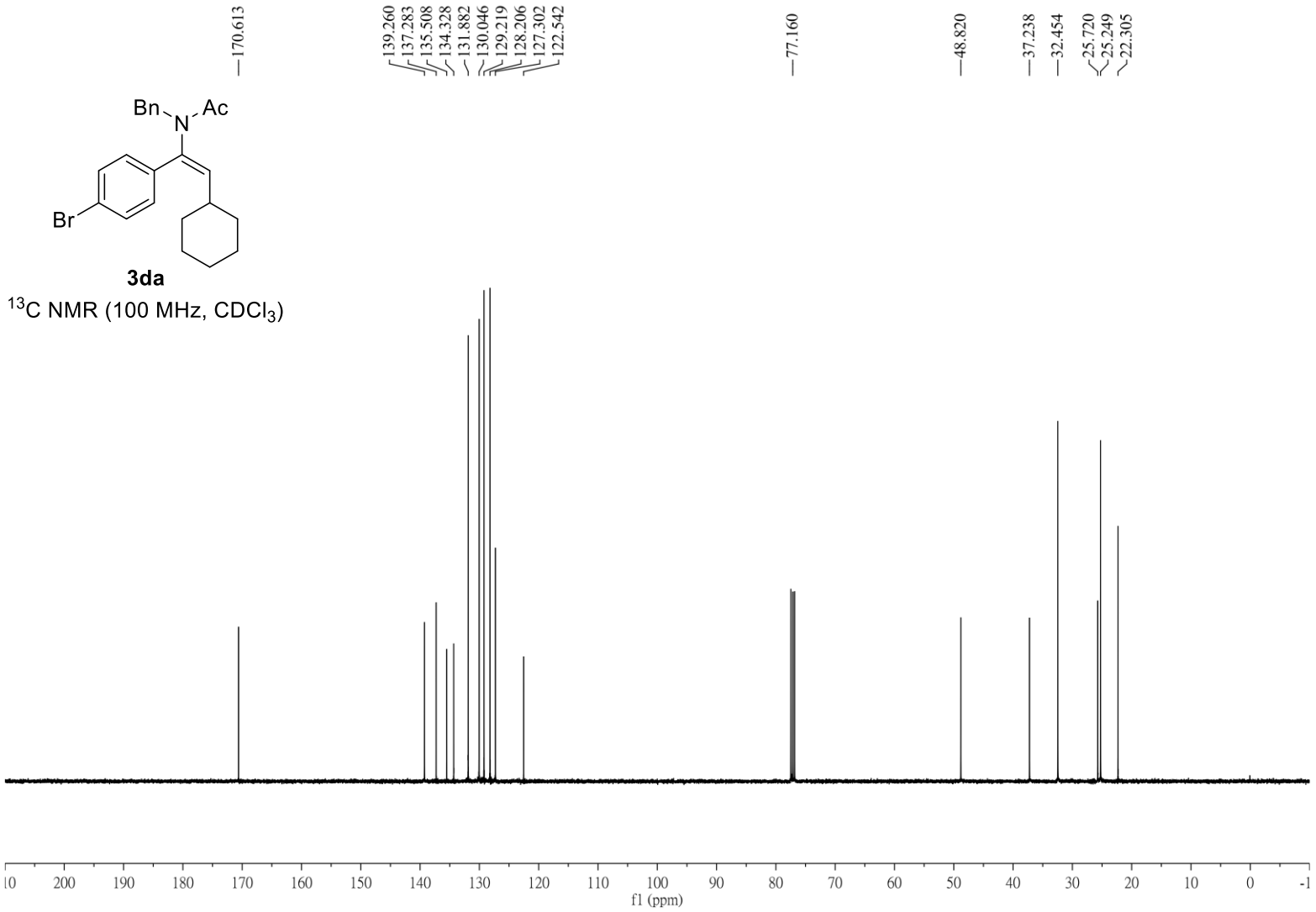
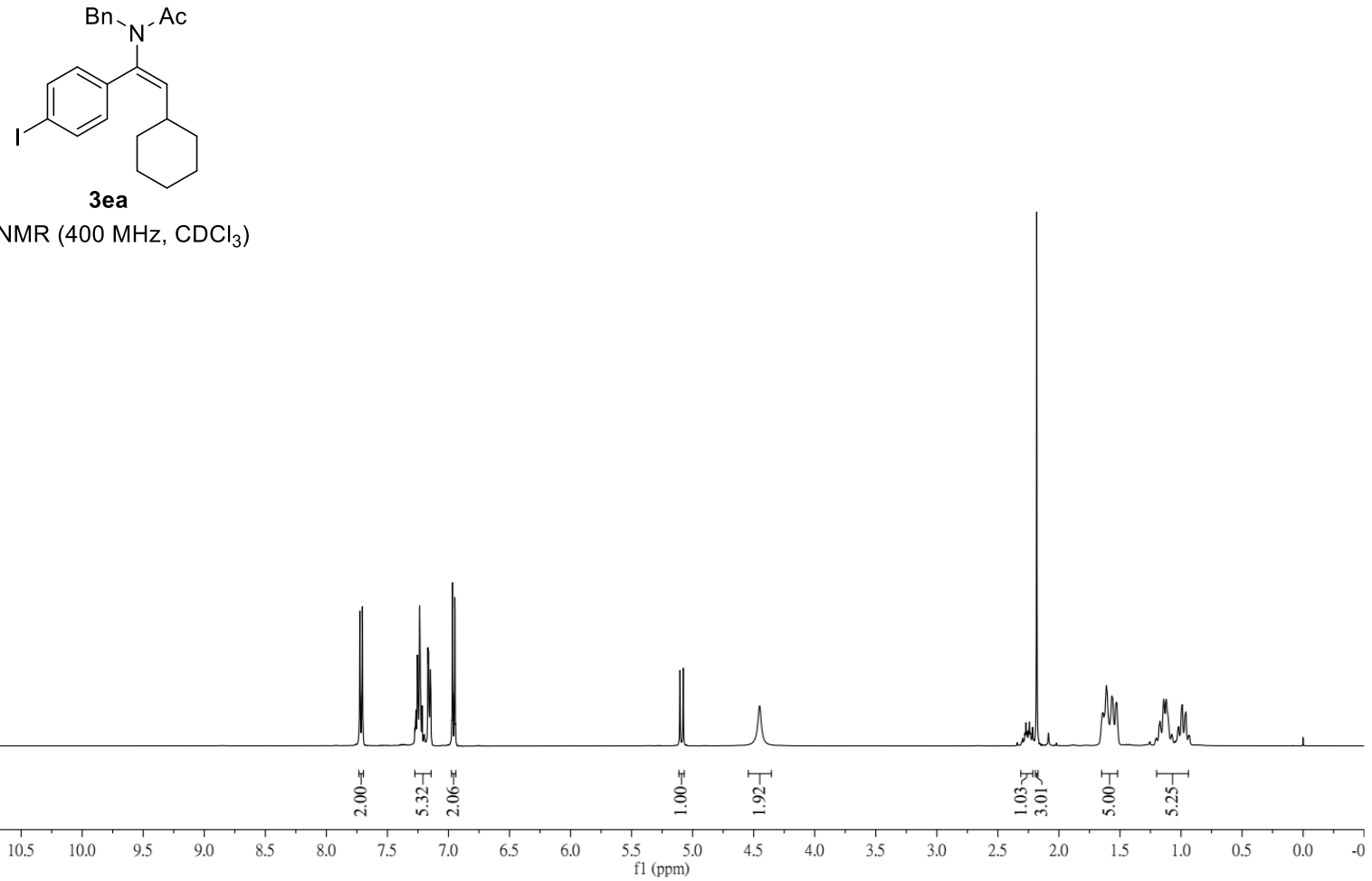
133.903
129.821
129.292
128.995
128.271
127.372
77.160
48.917
37.303
32.534
25.786
25.319
22.346
Bn
N
Ac
Cl
3ca
13C NMR (100 MHz, CDCl3)
f1 (ppm)

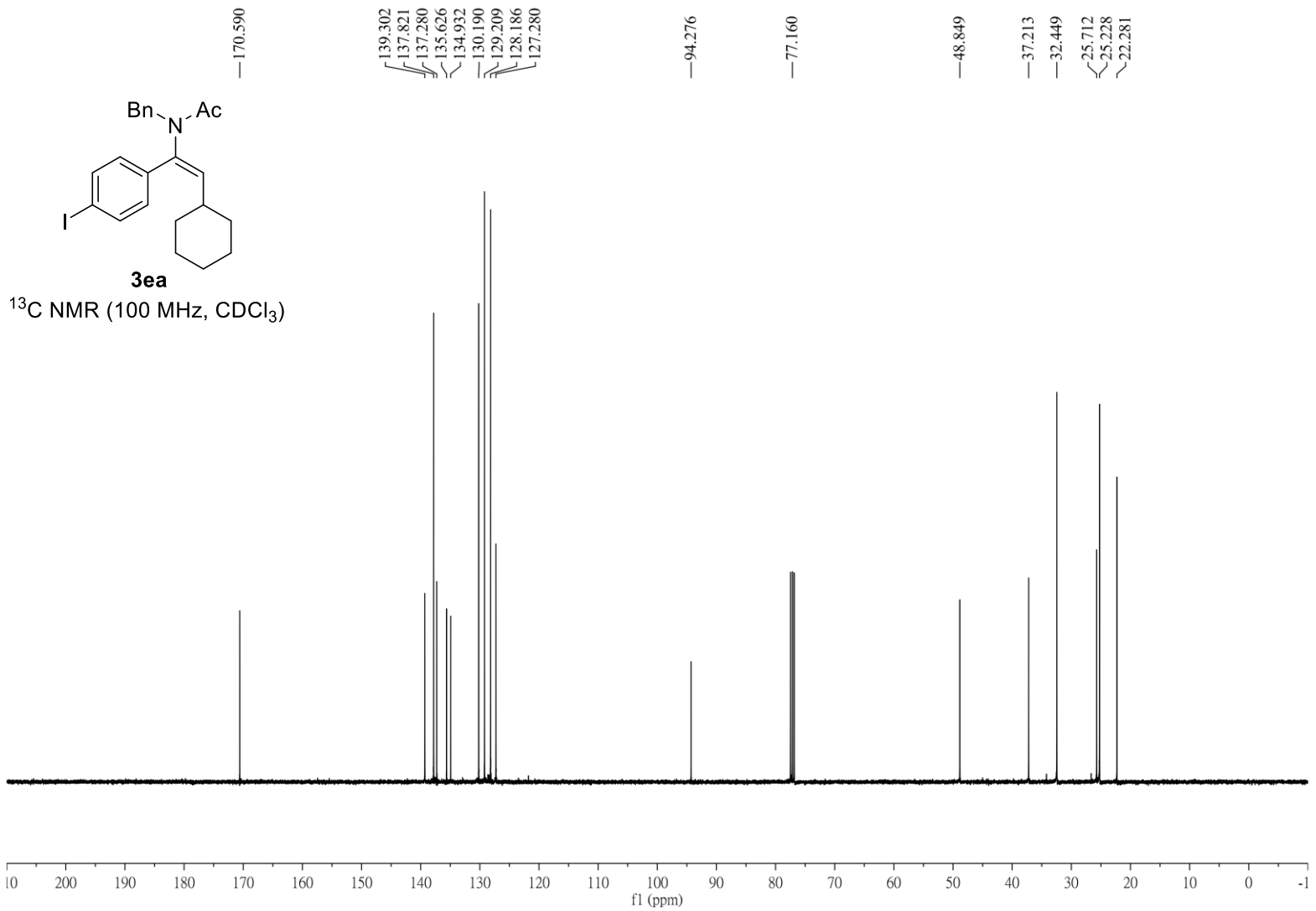

Bn
N
Ac
Br
3da
1H NMR (400 MHz, CDCl3)
7.527
7.506
7.281
7.274
7.270
7.267
7.259
7.241
7.221
7.170
7.166
7.151
7.102
7.085
7.081
7.075
5.107
5.080
4.451
2.273
2.265
2.256
2.246
2.237
2.228
2.210
2.189
1.647
1.642
1.616
1.568
1.531
1.173
1.143
1.122
1.023
0.994
0.964
0.000
2.00
3.10
2.01
2.08
1.00
1.93
4.13
5.01
5.14
f1 (ppm)

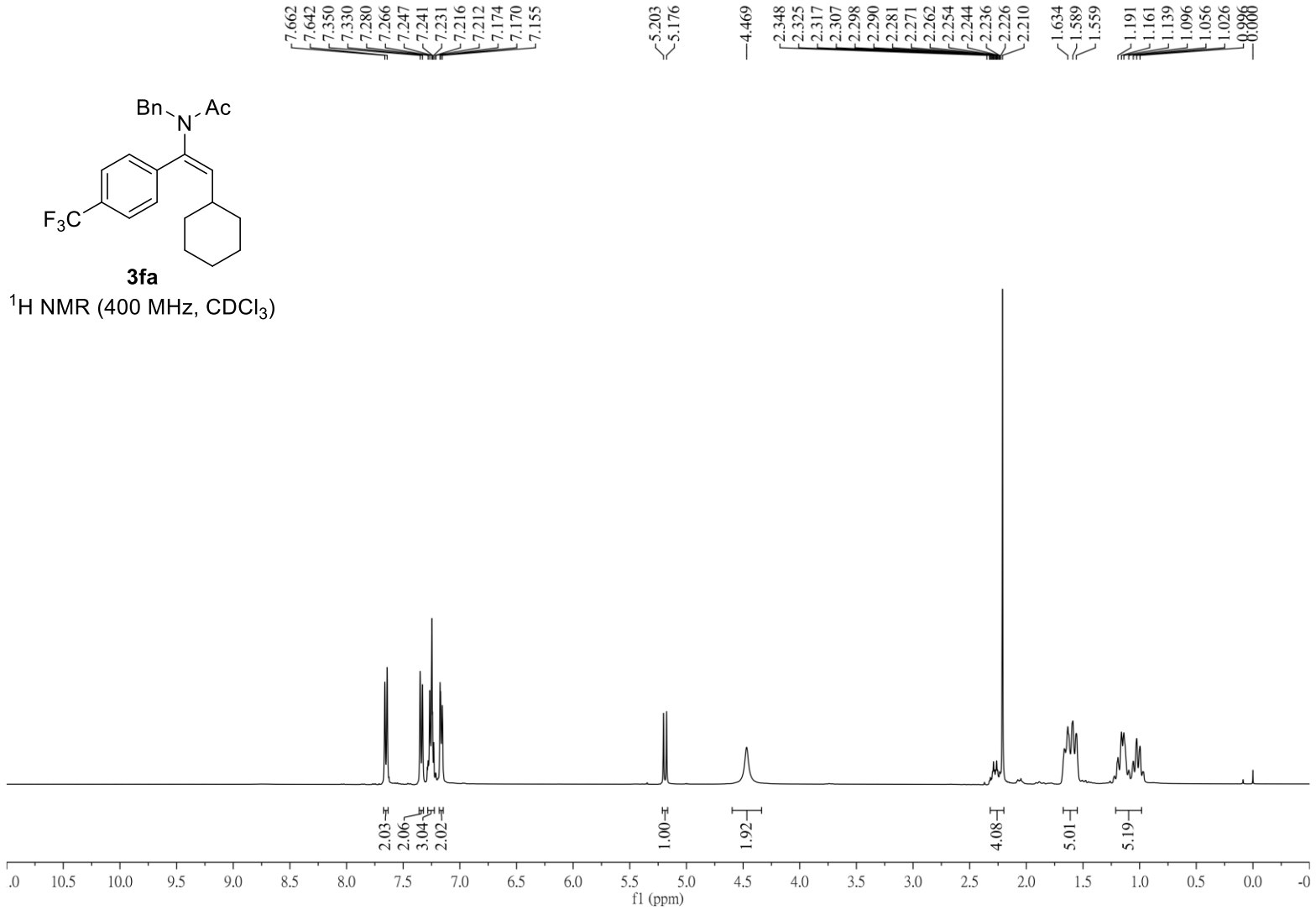

170.613
139.260
137.283
135.508
134.328
131.882
130.046
129.219
128.206
127.302
122.542
77.160
48.820
37.238
32.454
25.720
25.249
22.305
Bn
N
Ac
Br
3da
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ea

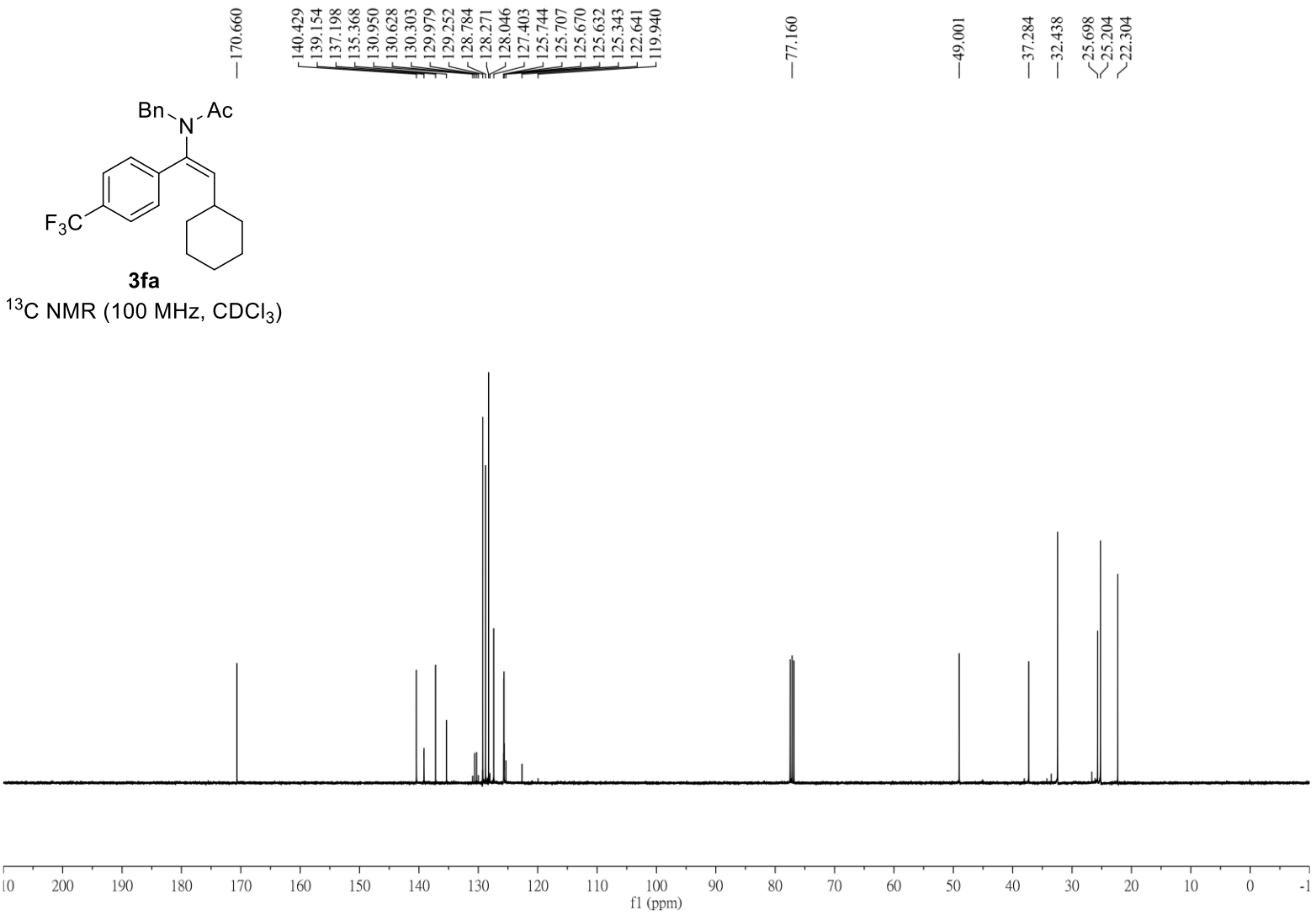
^{1}H NMR (400 MHz, $CDCl_3$)

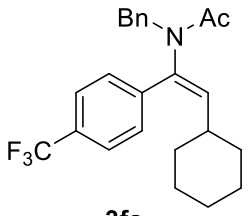

170.590
139.302
137.821
137.280
135.626
134.932
130.190
129.209
128.186
127.280
94.276
77.160
48.849
37.213
32.449
25.712
25.228
22.281
Bn
N
Ac
I
3ea
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3fa

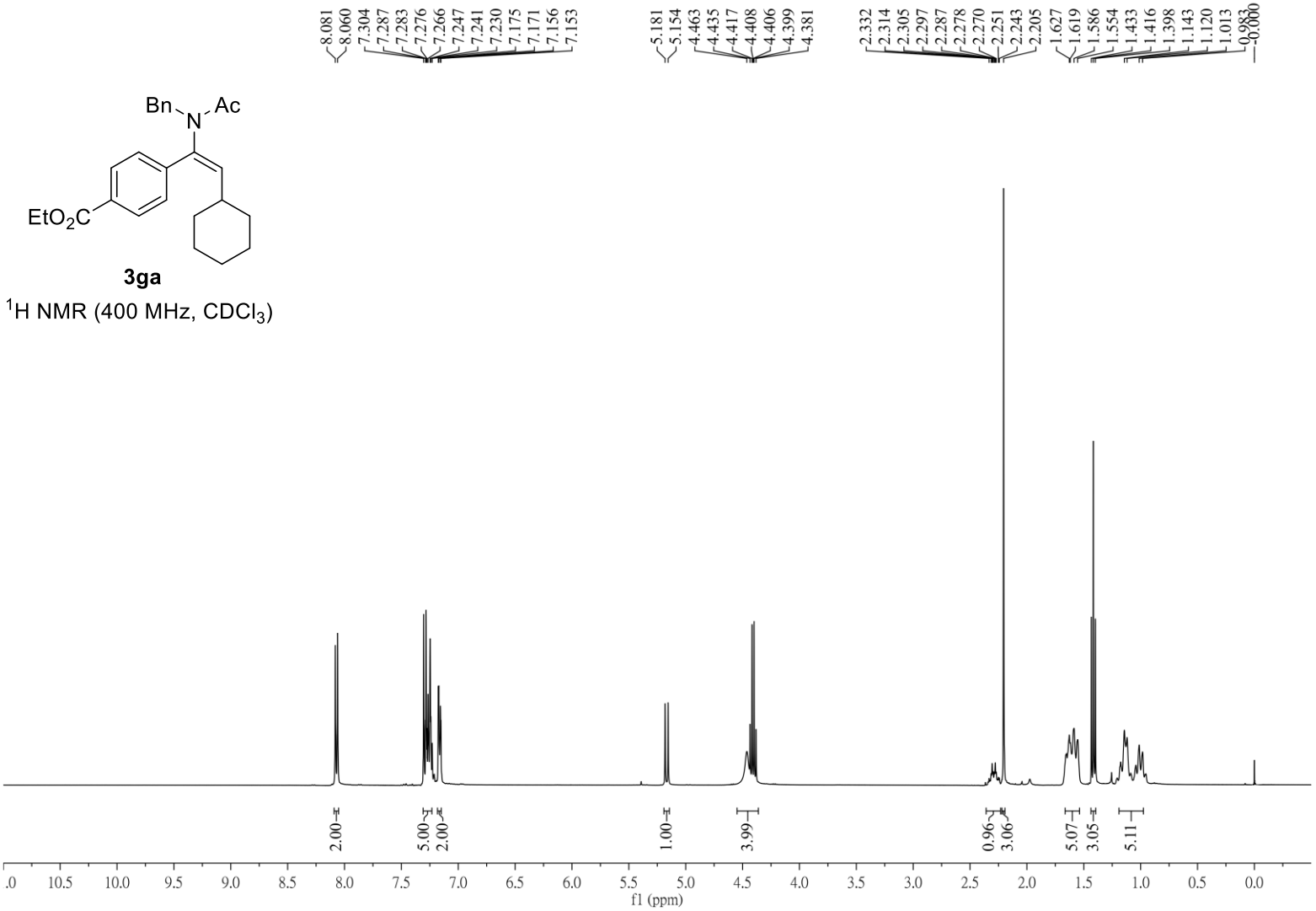
^{1}H NMR (400 MHz, $CDCl_3$)

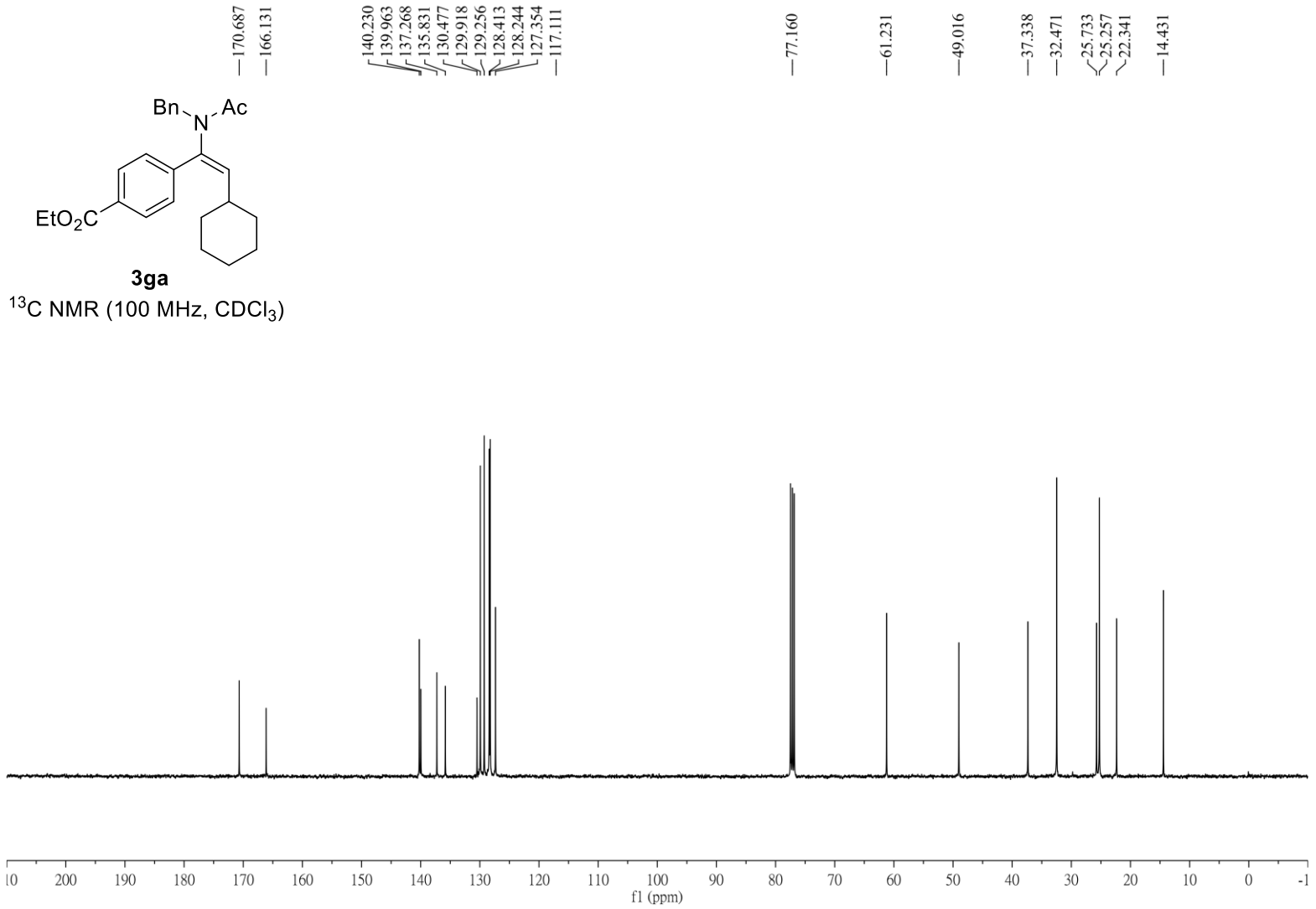

170.660
140.429
139.154
137.198
135.368
130.950
130.628
130.303
129.979
129.252
128.784
128.271
128.046
127.403
125.744
125.707
125.670
125.632
125.343
122.641
119.940
77.160
49.001
37.284
32.438
25.698
25.204
22.304
Bn
N
Ac
F3C
3fa
13C NMR (100 MHz, CDCl3)
f1 (ppm)

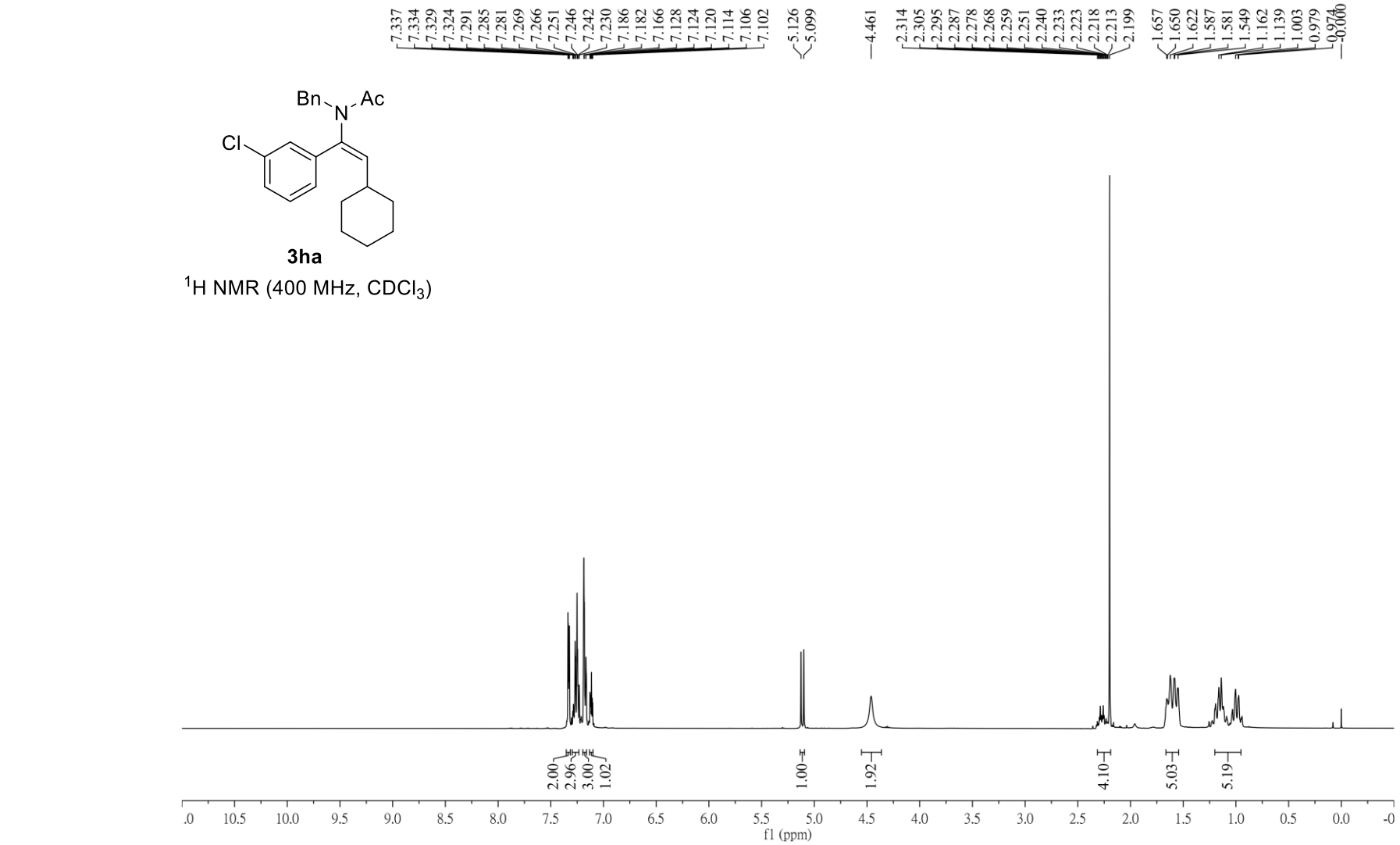


3fa

^{19}F NMR (376 MHz, $CDCl_3$)

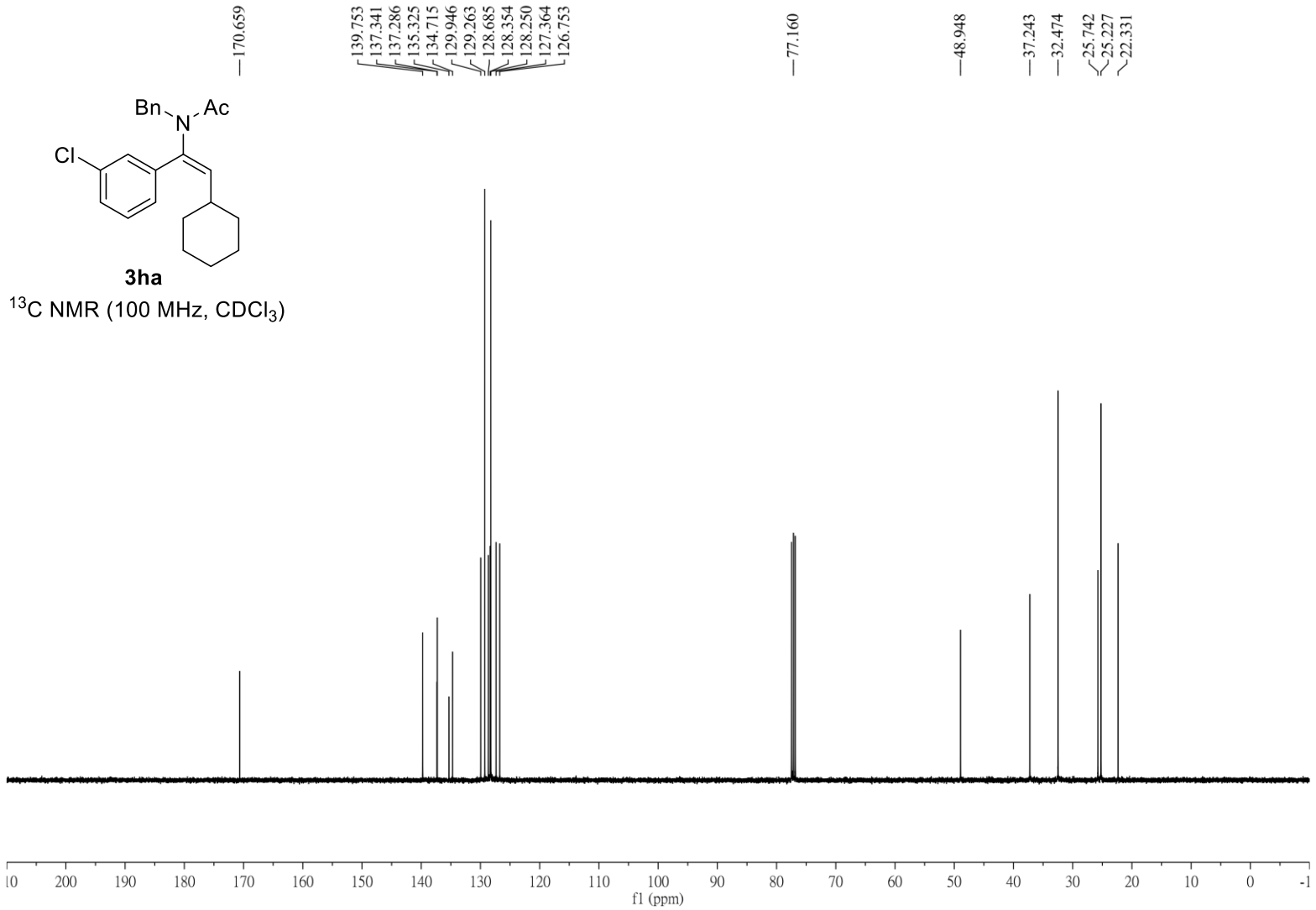

Bn
N
Ac
EtO2C
3ga
1H NMR (400 MHz, CDCl3)
8.081
8.060
7.304
7.287
7.283
7.276
7.266
7.247
7.241
7.230
7.175
7.171
7.156
7.153
5.181
5.154
4.463
4.435
4.417
4.408
4.406
4.399
4.381
2.332
2.314
2.305
2.297
2.287
2.278
2.270
2.251
2.243
2.205
1.627
1.619
1.586
1.554
1.433
1.416
1.398
1.143
1.120
1.013
0.983
0.000
2.00
5.00
2.00
1.00
3.99
0.96
3.06
5.07
3.05
5.11
f1 (ppm)

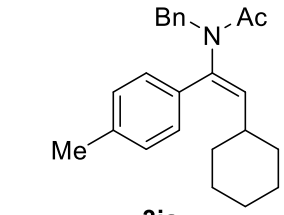

170.687
166.131
140.230
139.963
137.268
135.831
130.477
129.918
129.256
128.413
128.244
127.354
117.111
77.160
61.231
49.016
37.338
32.471
25.733
25.257
22.341
14.431
Bn
N
Ac
EtO2C
3ga
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ha

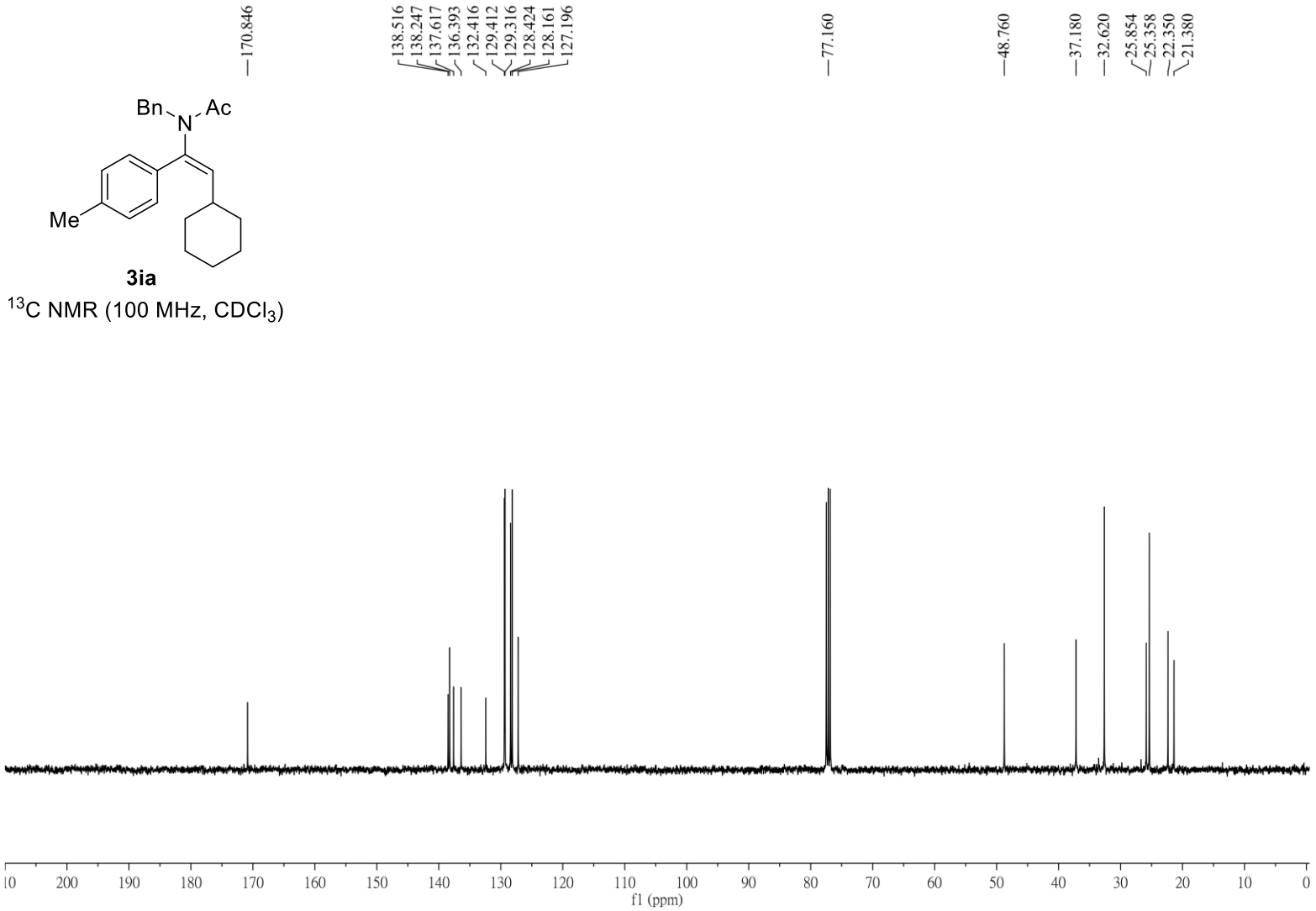
^{1}H NMR (400 MHz, $CDCl_3$)


170.659
139.753
137.341
137.286
135.325
134.715
129.946
129.263
128.685
128.354
128.250
127.364
126.753
77.160
48.948
37.243
32.474
25.742
25.227
22.331
Bn
N
Ac
Cl
3ha
13C NMR (100 MHz, CDCl3)
f1 (ppm)



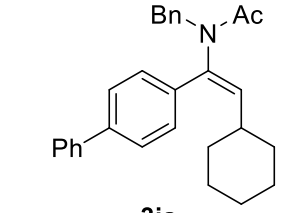
3ia

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



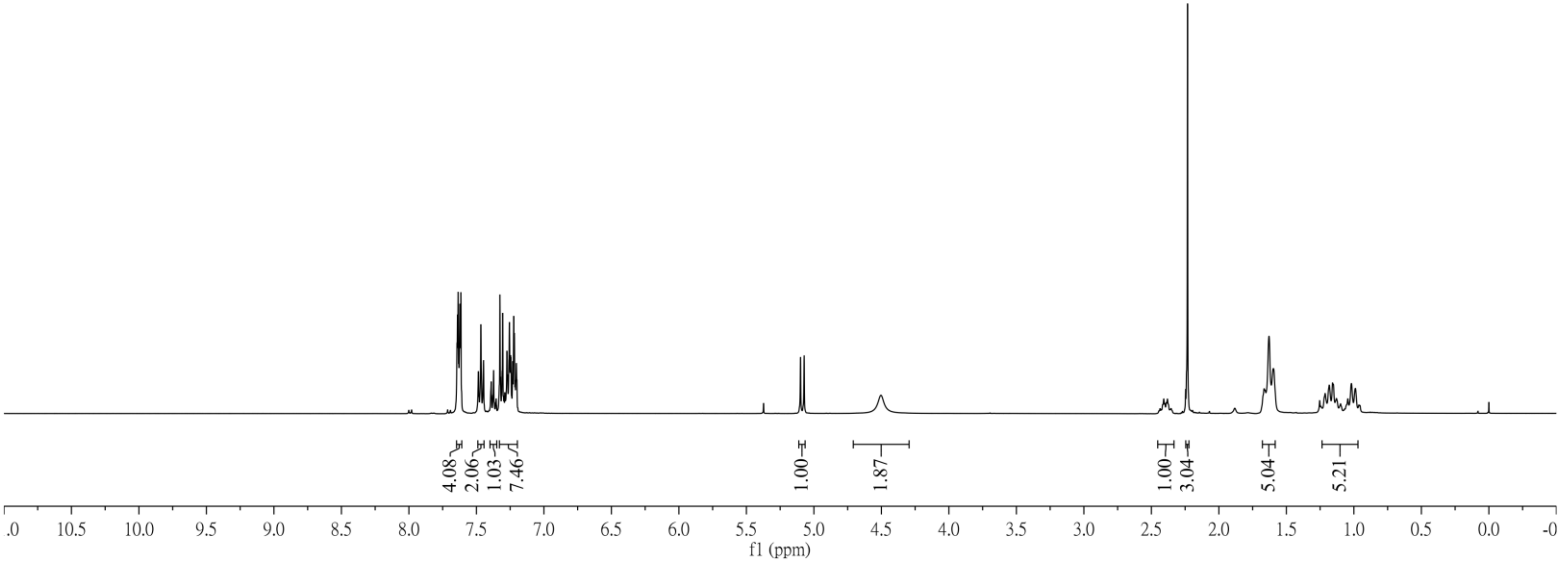
3ia

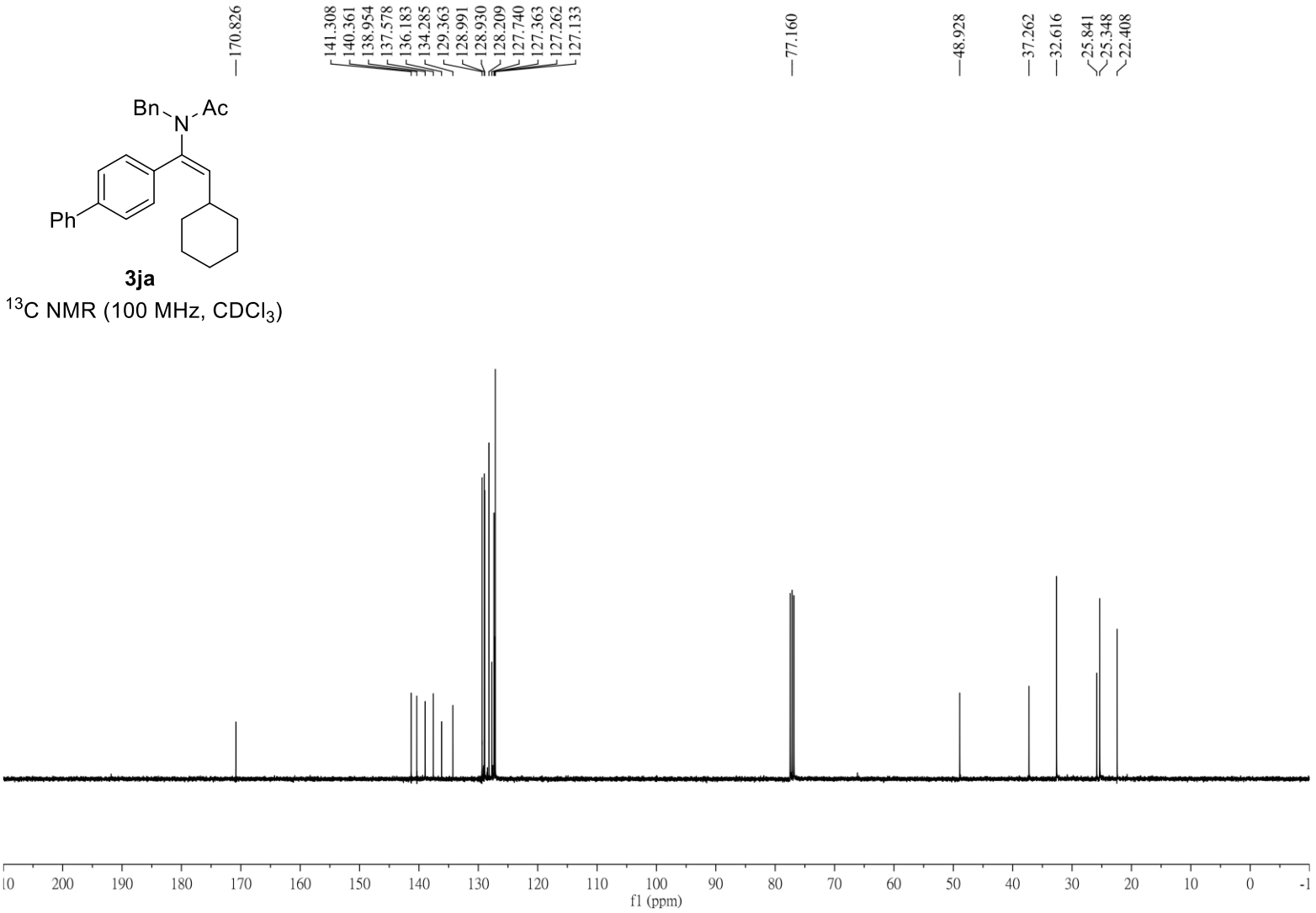
^{13}C NMR (100 MHz, $CDCl_3$)

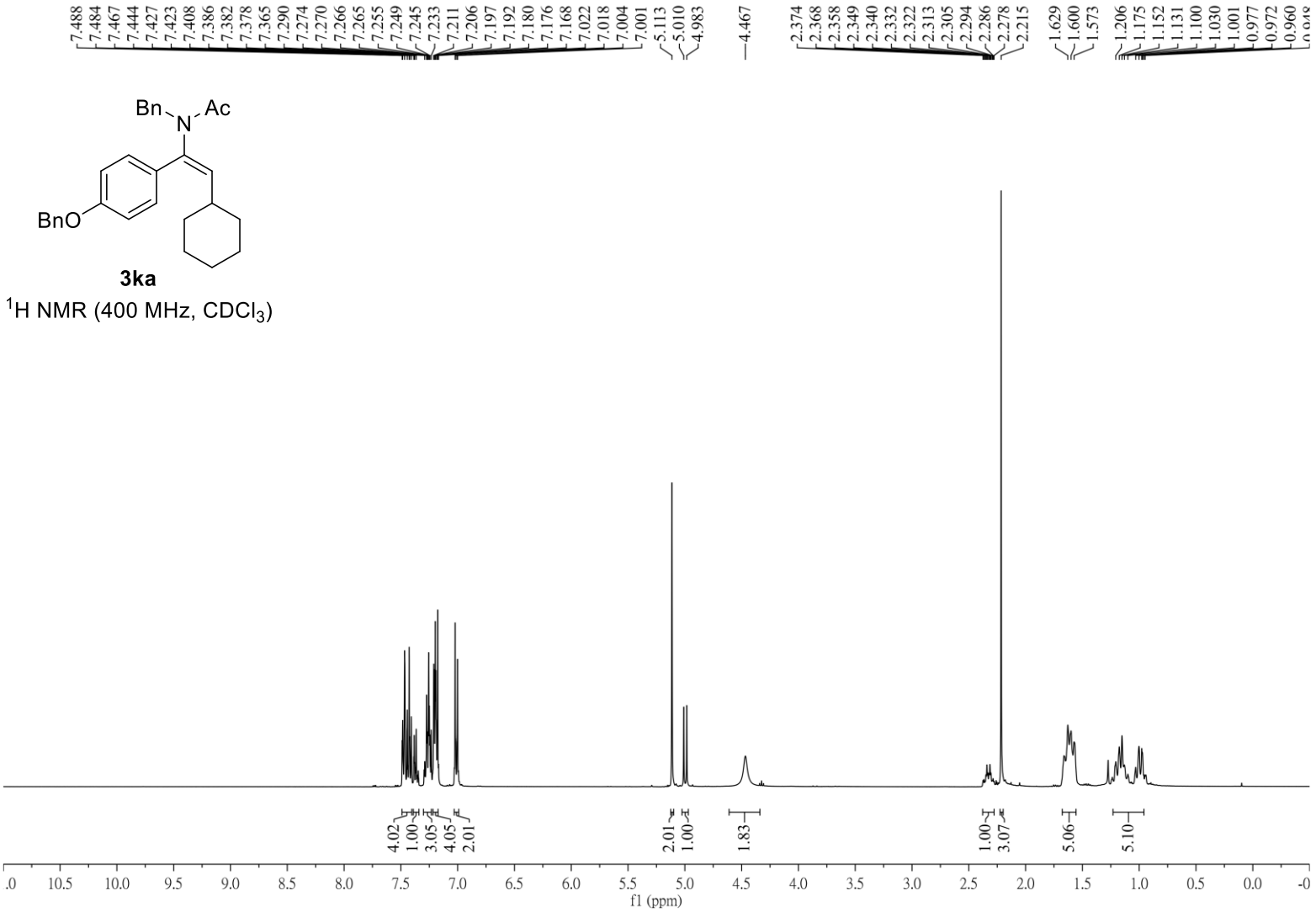


3ja

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

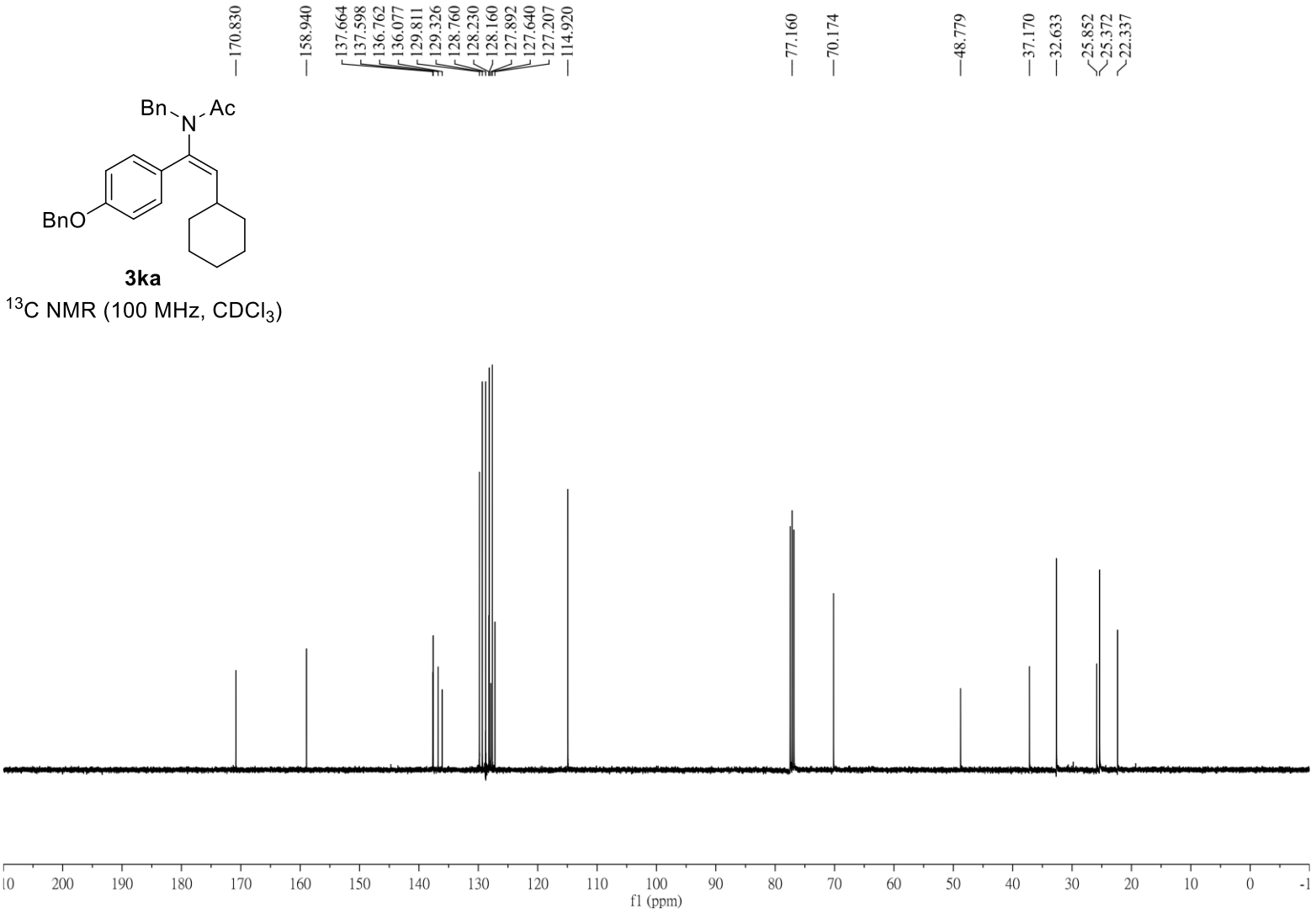


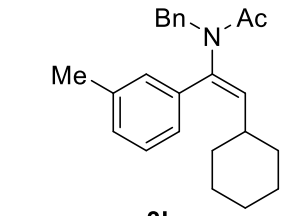

170.826
141.308
140.361
138.954
137.578
136.183
134.285
129.363
128.991
128.930
128.209
127.740
127.363
127.262
127.133
77.160
48.928
37.262
32.616
25.841
25.348
22.408
Bn
N
Ac
Ph
3ja
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ka

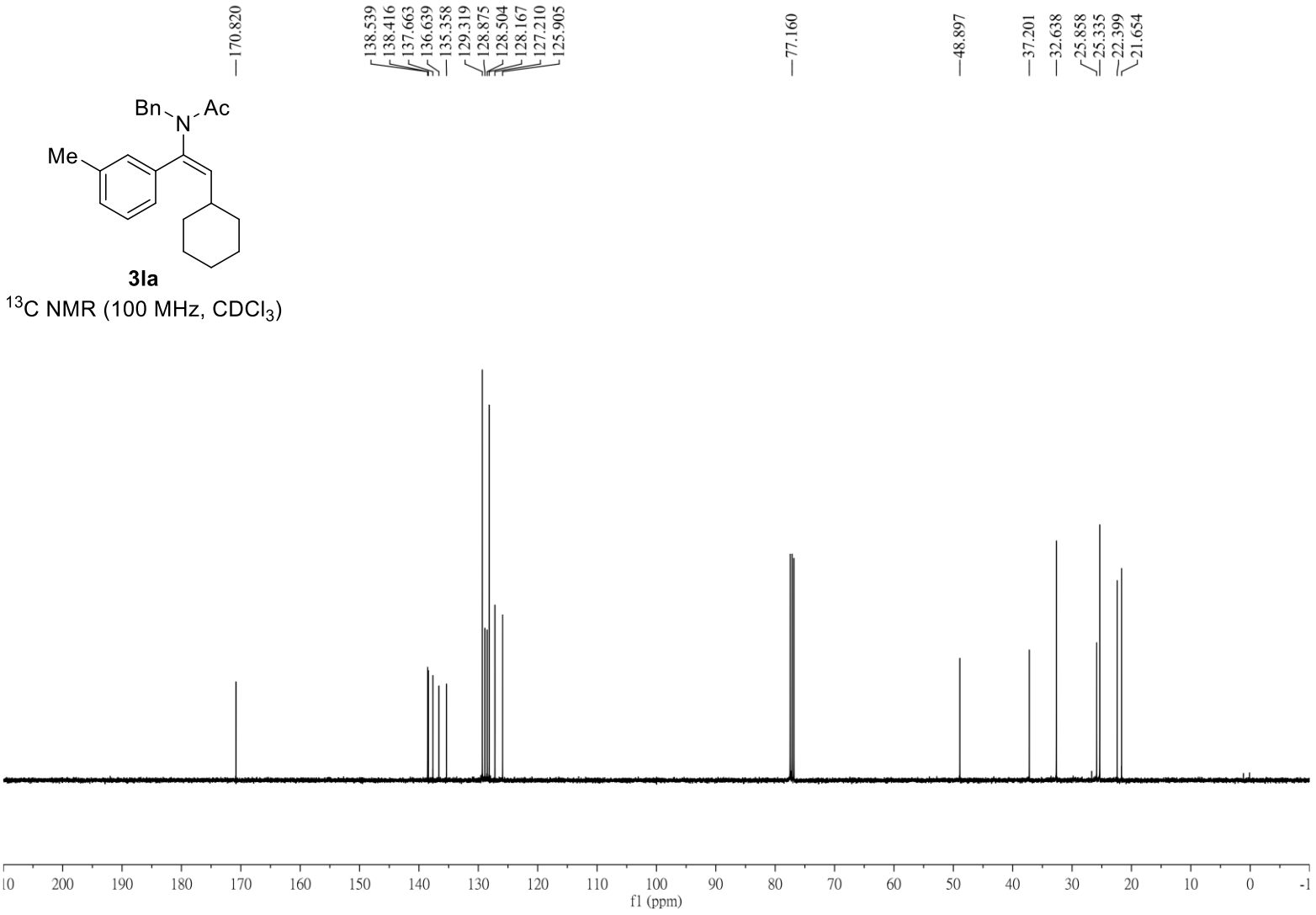
^{1}H NMR (400 MHz, $CDCl_3$)


170.830
158.940
137.664
137.598
136.762
136.077
129.811
129.326
128.760
128.230
128.160
127.892
127.640
127.207
114.920
77.160
70.174
48.779
37.170
32.633
25.852
25.372
22.337
Bn
N
Ac
BnO
3ka
13C NMR (100 MHz, CDCl3)
f1 (ppm)



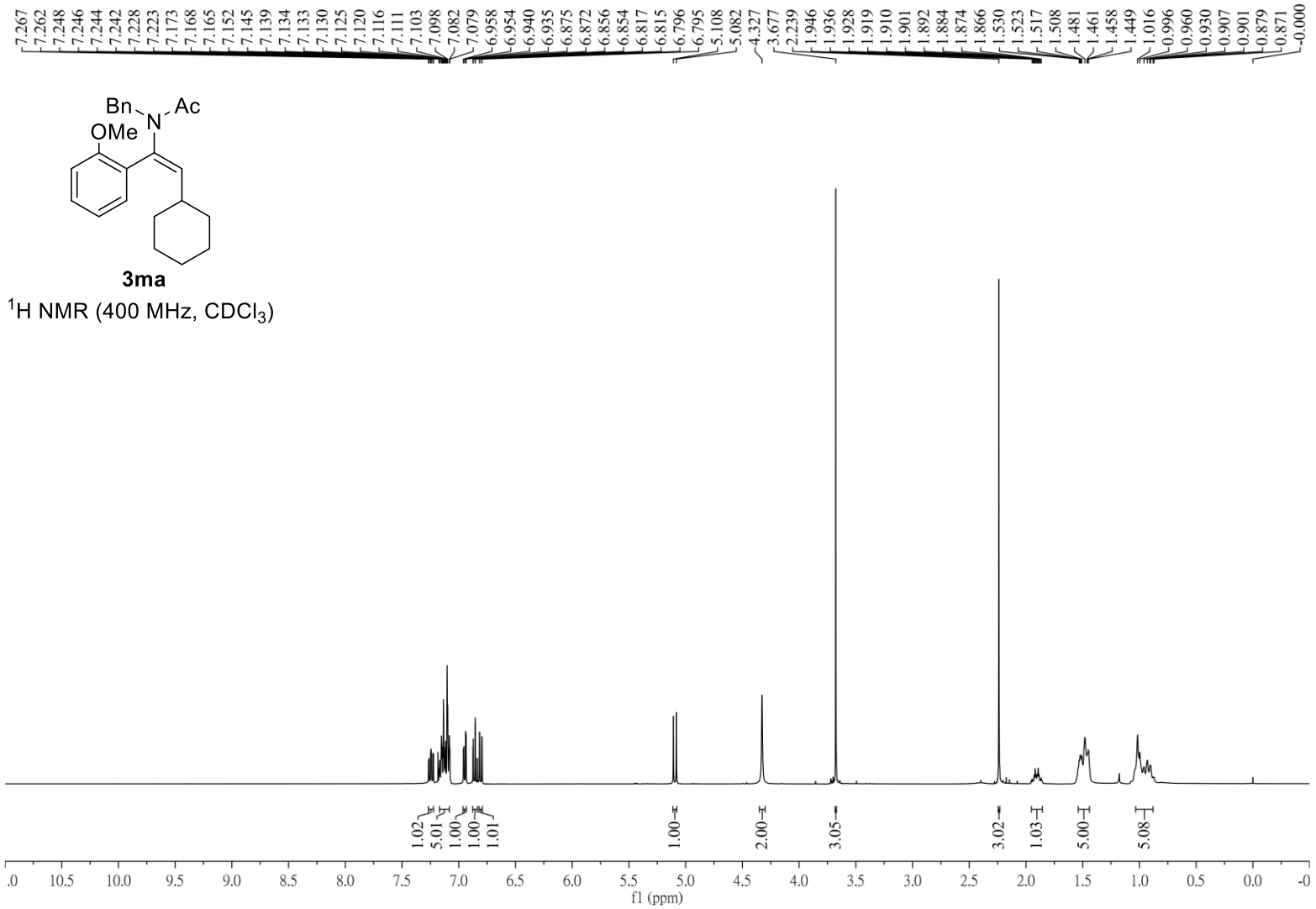
3la

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



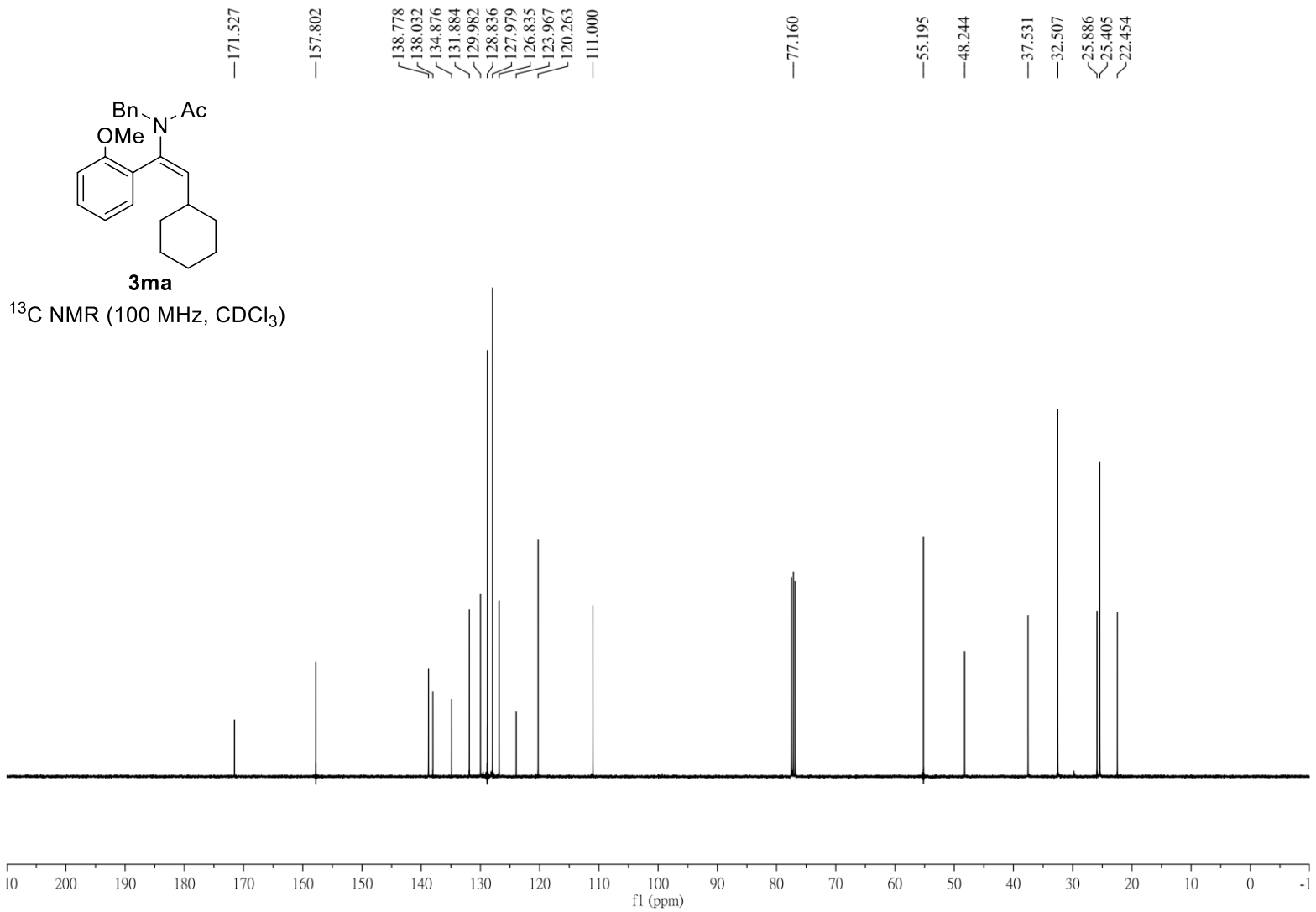
3la

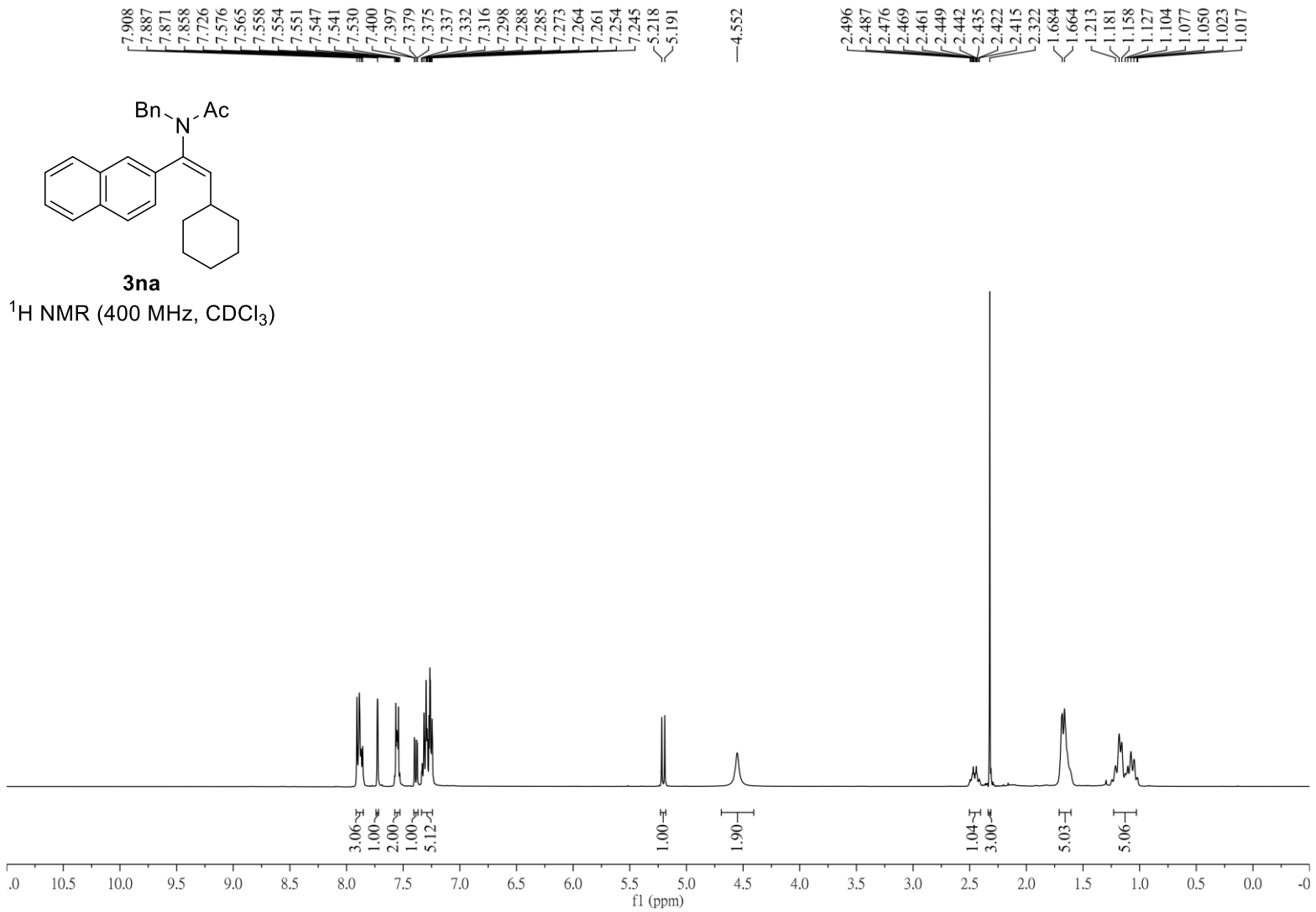
^{13}C NMR (100 MHz, $CDCl_3$)



3ma

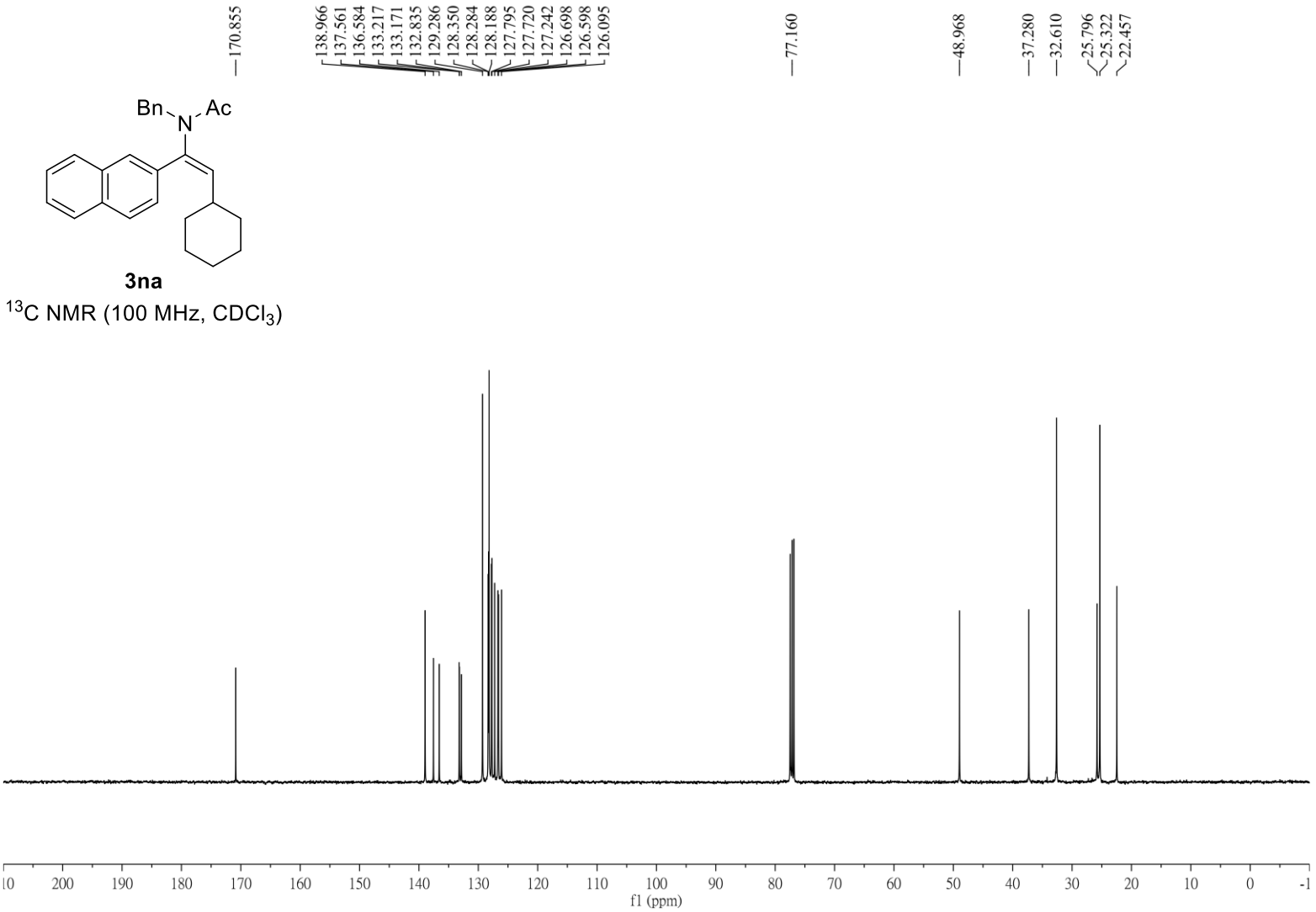
^{1}H NMR (400 MHz, $CDCl_3$)

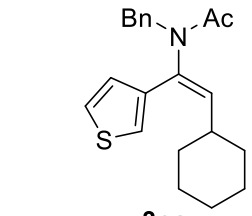

171.527
157.802
138.778
138.032
134.876
131.884
129.982
128.836
127.979
126.835
123.967
120.263
111.000
77.160
55.195
48.244
37.531
32.507
25.886
25.405
22.454
Bn
N
Ac
OMe
3ma
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3na

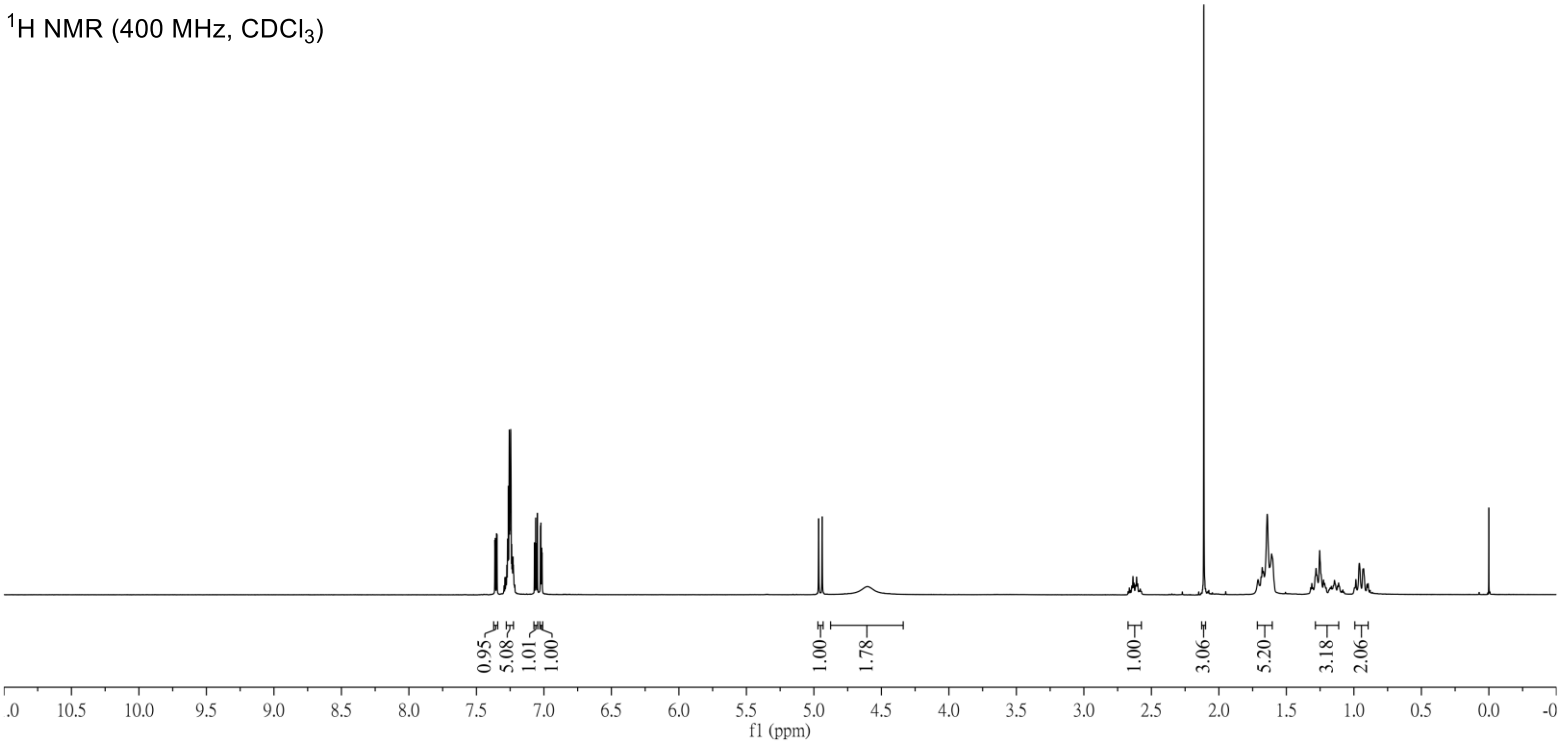
^{1}H NMR (400 MHz, $CDCl_3$)

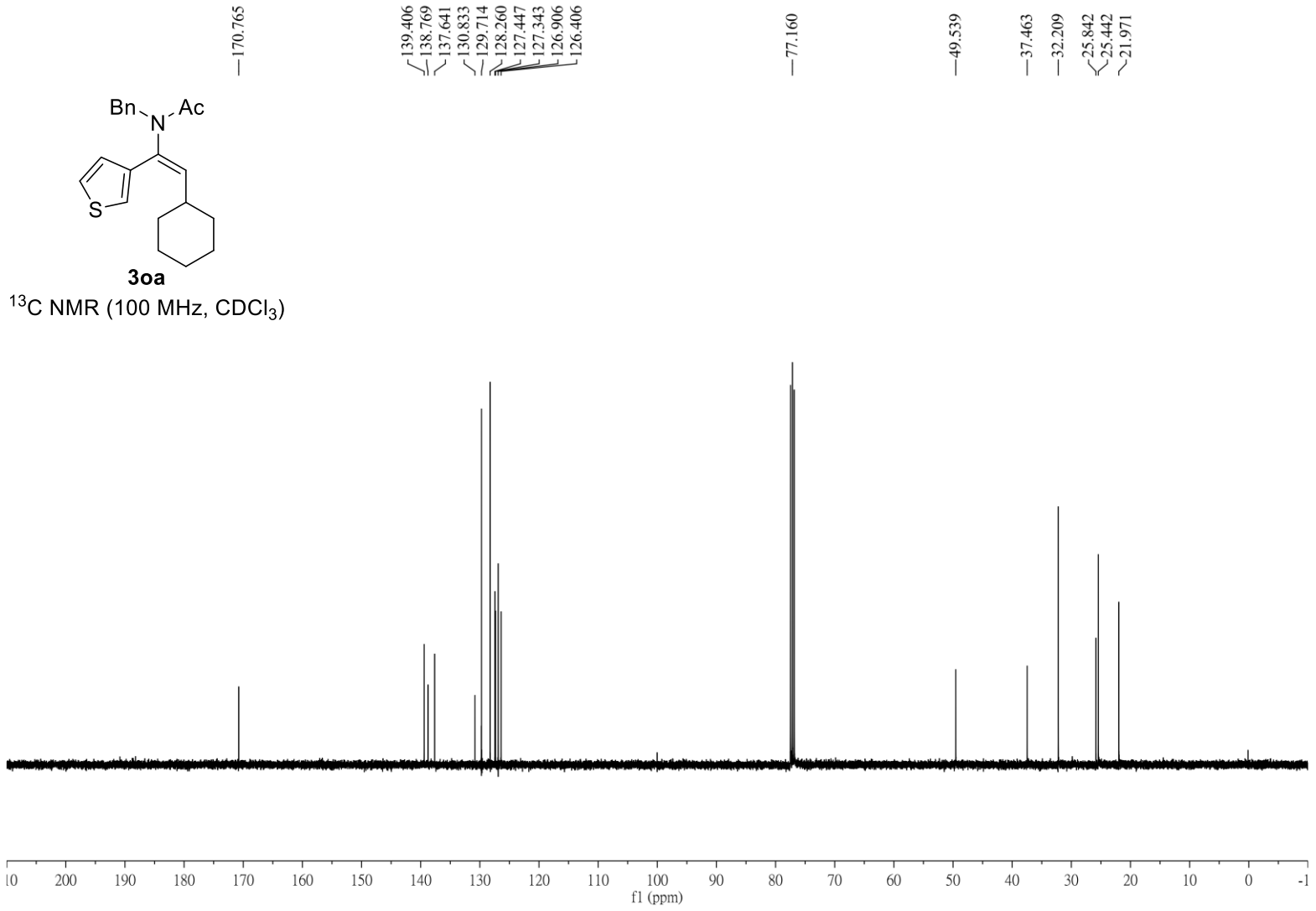

170.855
138.966
137.561
136.584
133.217
133.171
132.835
129.286
128.350
128.284
128.188
127.795
127.720
127.242
126.698
126.598
126.095
77.160
48.968
37.280
32.610
25.796
25.322
22.457
Bn
N
Ac
3na
13C NMR (100 MHz, CDCl3)
f1 (ppm)

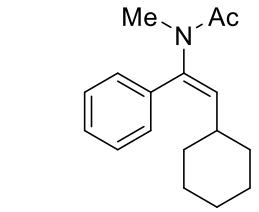


3oa

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

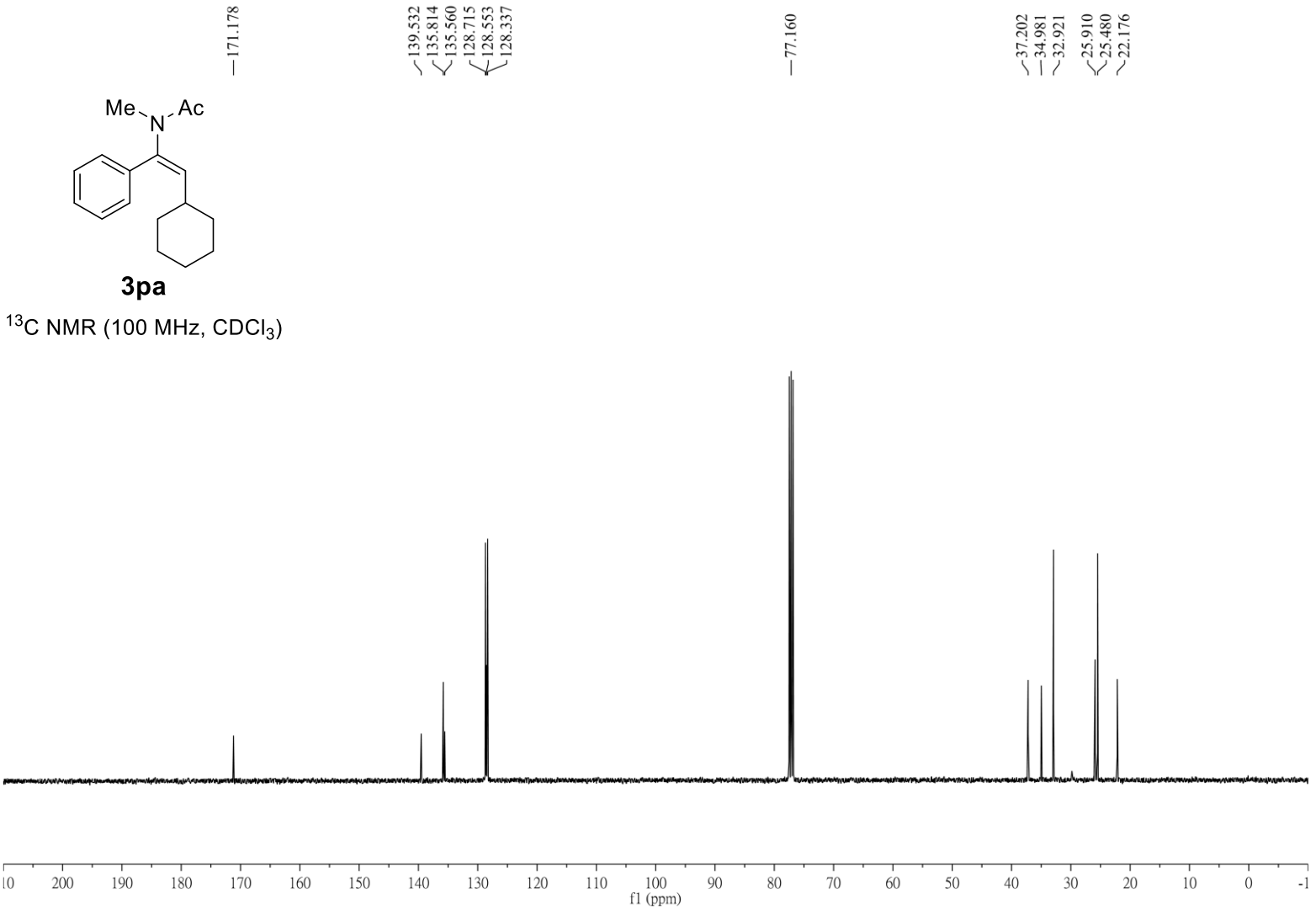


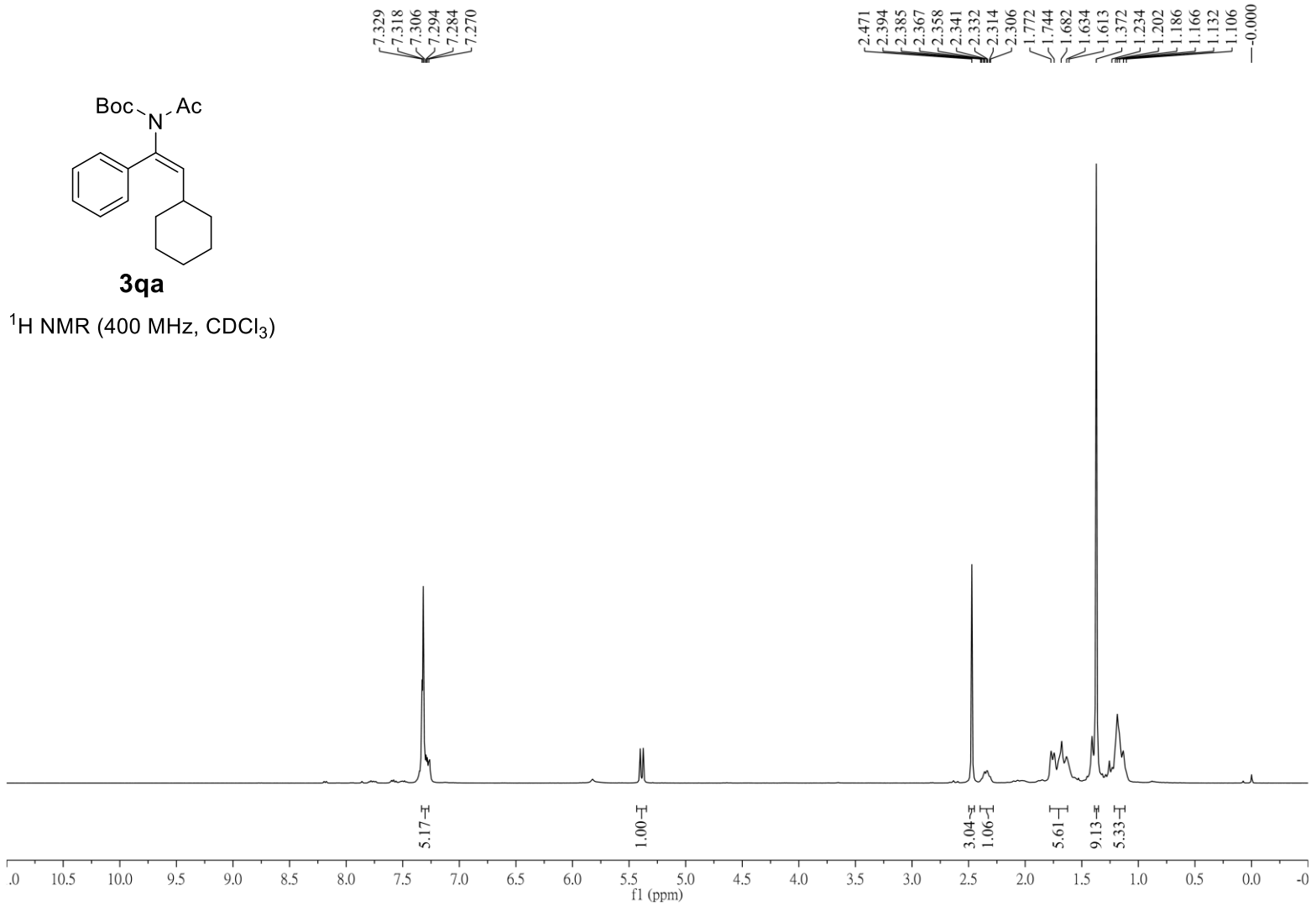

170.765
139.406
138.769
137.641
130.833
129.714
128.260
127.447
127.343
126.906
126.406
77.160
49.539
37.463
32.209
25.842
25.442
21.971
Bn
N
Ac
S
3oa
13C NMR (100 MHz, CDCl3)
f1 (ppm)

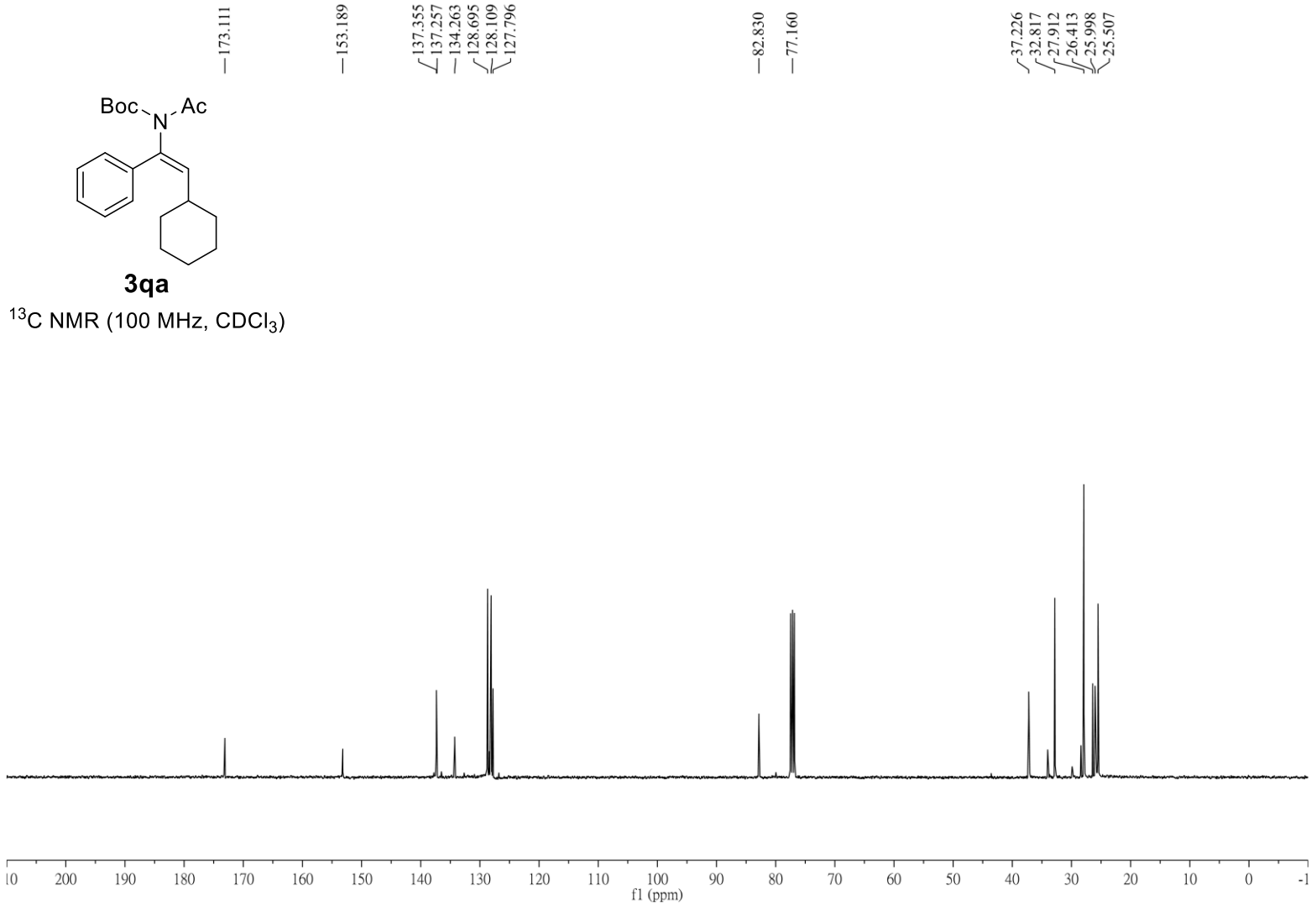


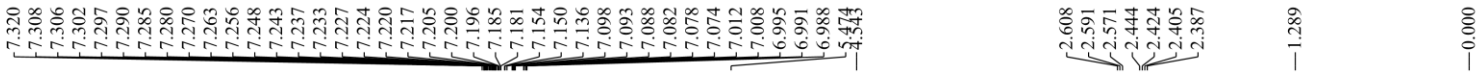
3pa

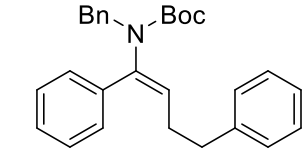
^{1}H NMR (400 MHz, $CDCl_3$)


171.178
139.532
135.814
135.560
128.715
128.553
128.337
77.160
37.202
34.981
32.921
25.910
25.480
22.176
Me
N
Ac
3pa
13C NMR (100 MHz, CDCl3)
f1 (ppm)


Boc
N
Ac
3qa
1H NMR (400 MHz, CDCl3)
7.329
7.318
7.306
7.294
7.284
7.270
2.471
2.394
2.385
2.367
2.358
2.341
2.332
2.314
2.306
1.772
1.744
1.682
1.634
1.613
1.372
1.234
1.202
1.186
1.166
1.132
1.106
-0.000
5.17
1.00
3.04
1.06
5.61
9.13
5.33
f1 (ppm)

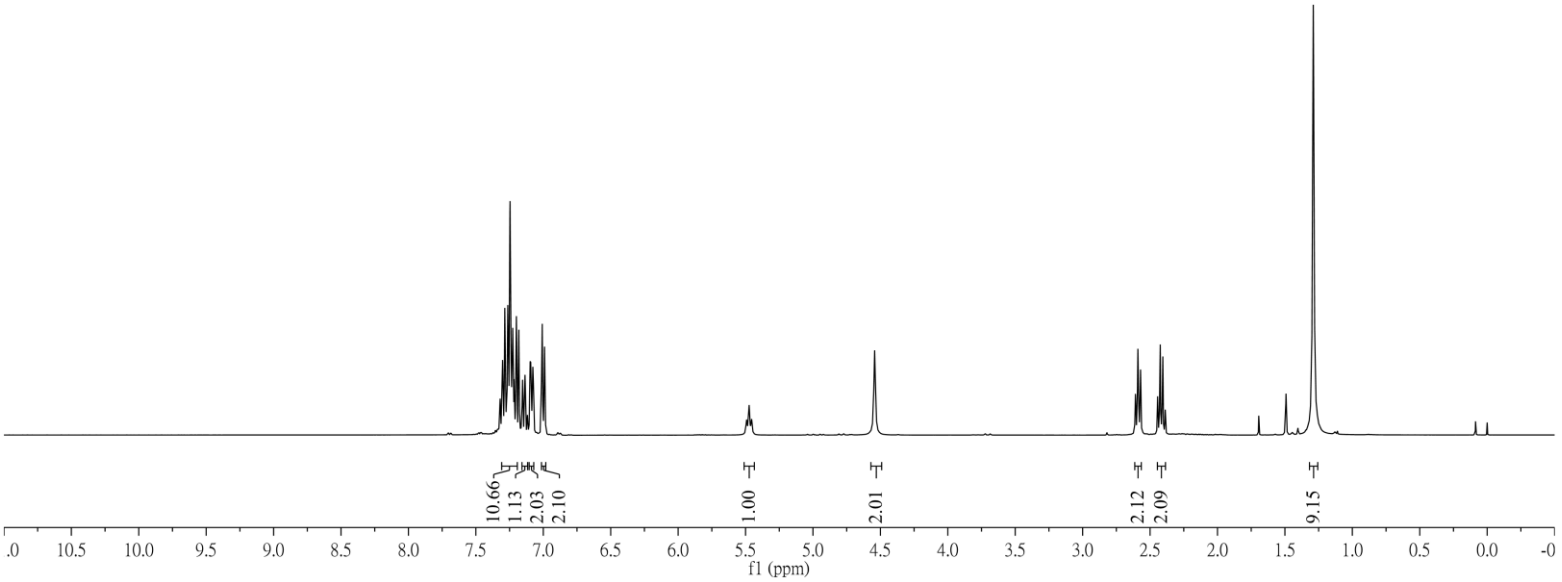

173.111
153.189
137.355
137.257
134.263
128.695
128.109
127.796
82.830
77.160
37.226
32.817
27.912
26.413
25.998
25.507
Boc
N
Ac
3qa
13C NMR (100 MHz, CDCl3)
f1 (ppm)

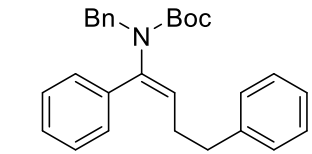




3rs

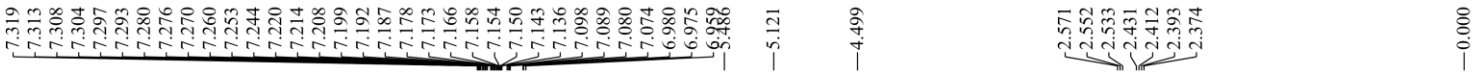
^{1}H NMR (400 MHz, $CDCl_3$)

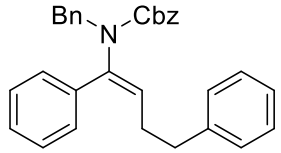




3rs

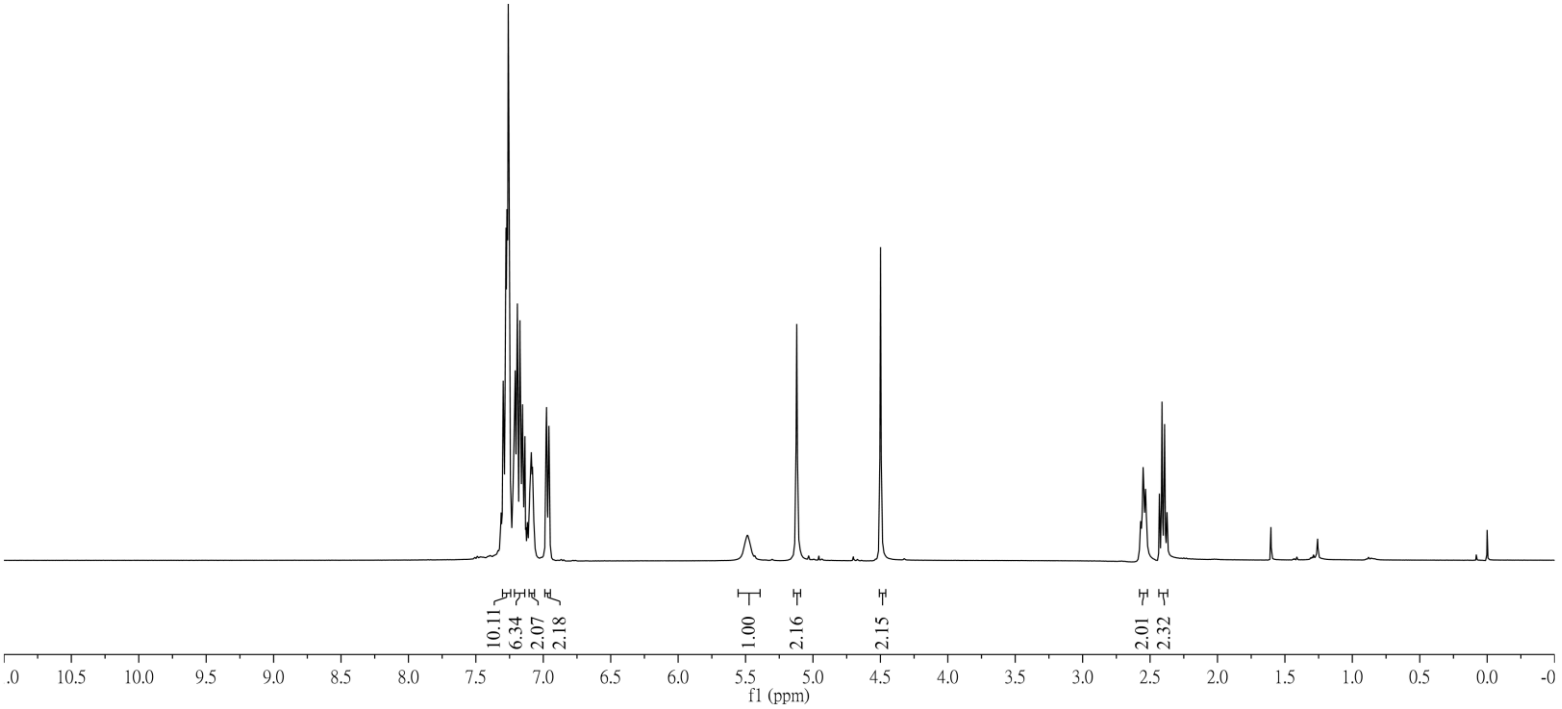
^{13}C NMR (100 MHz, $CDCl_3$)

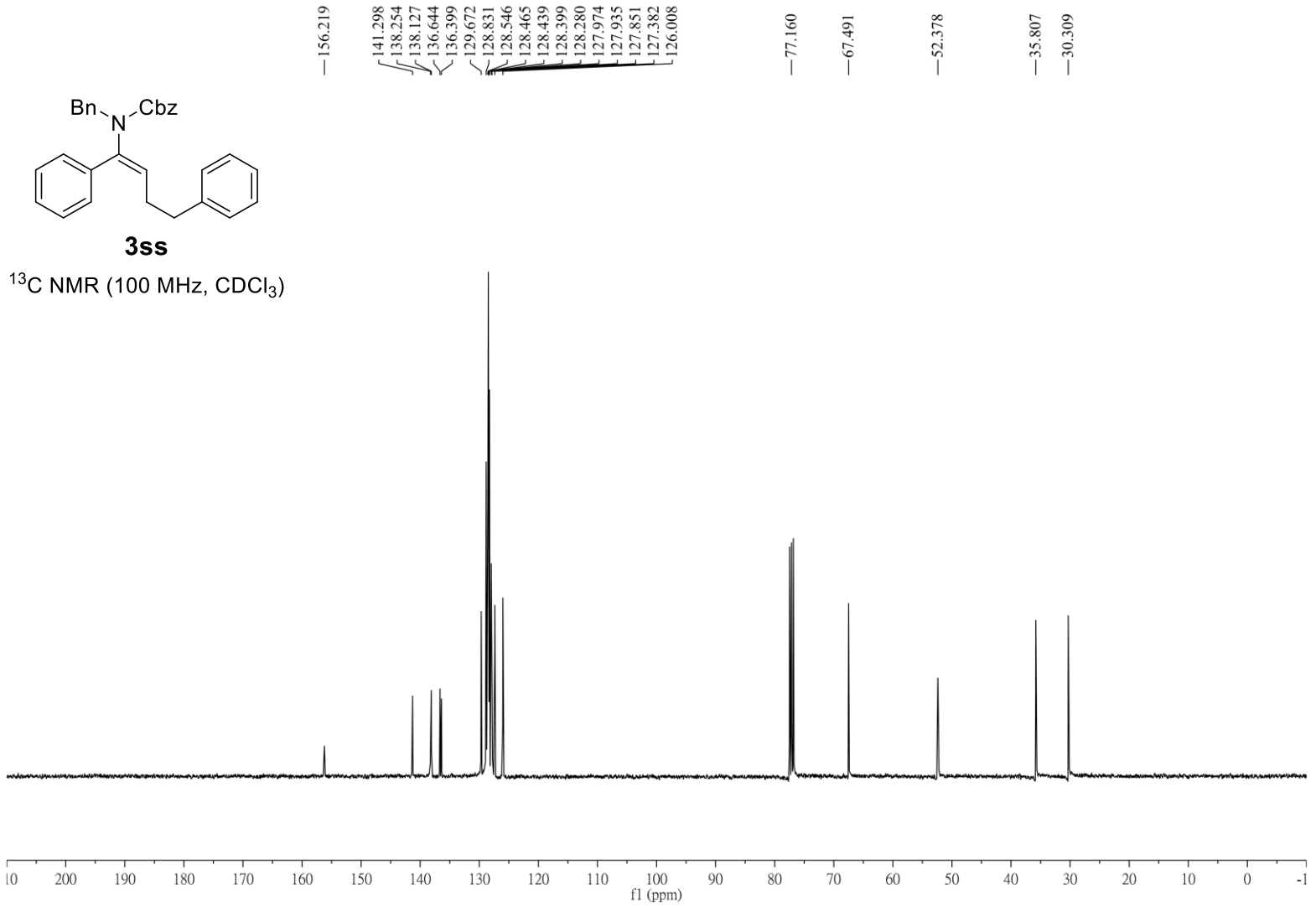


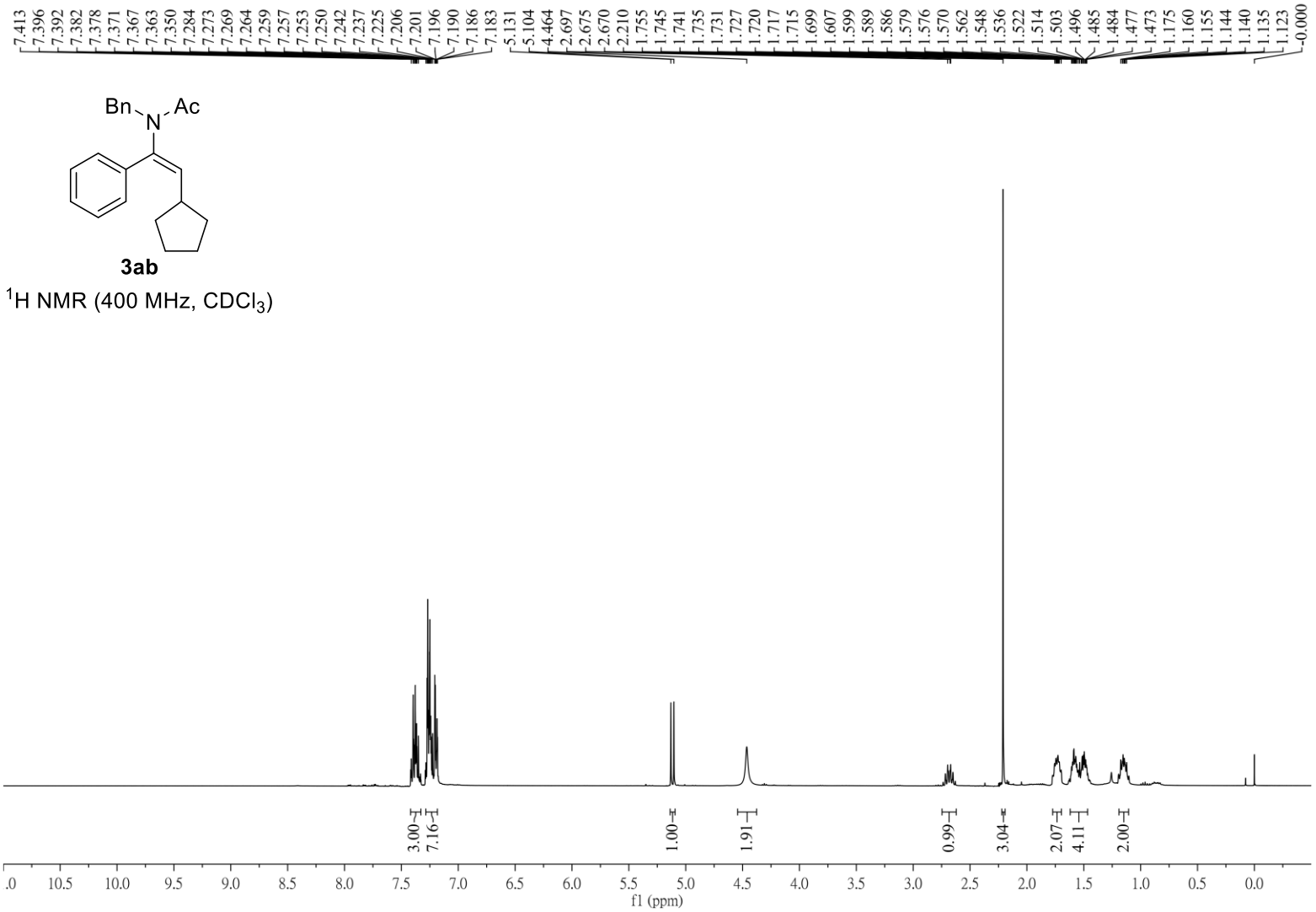


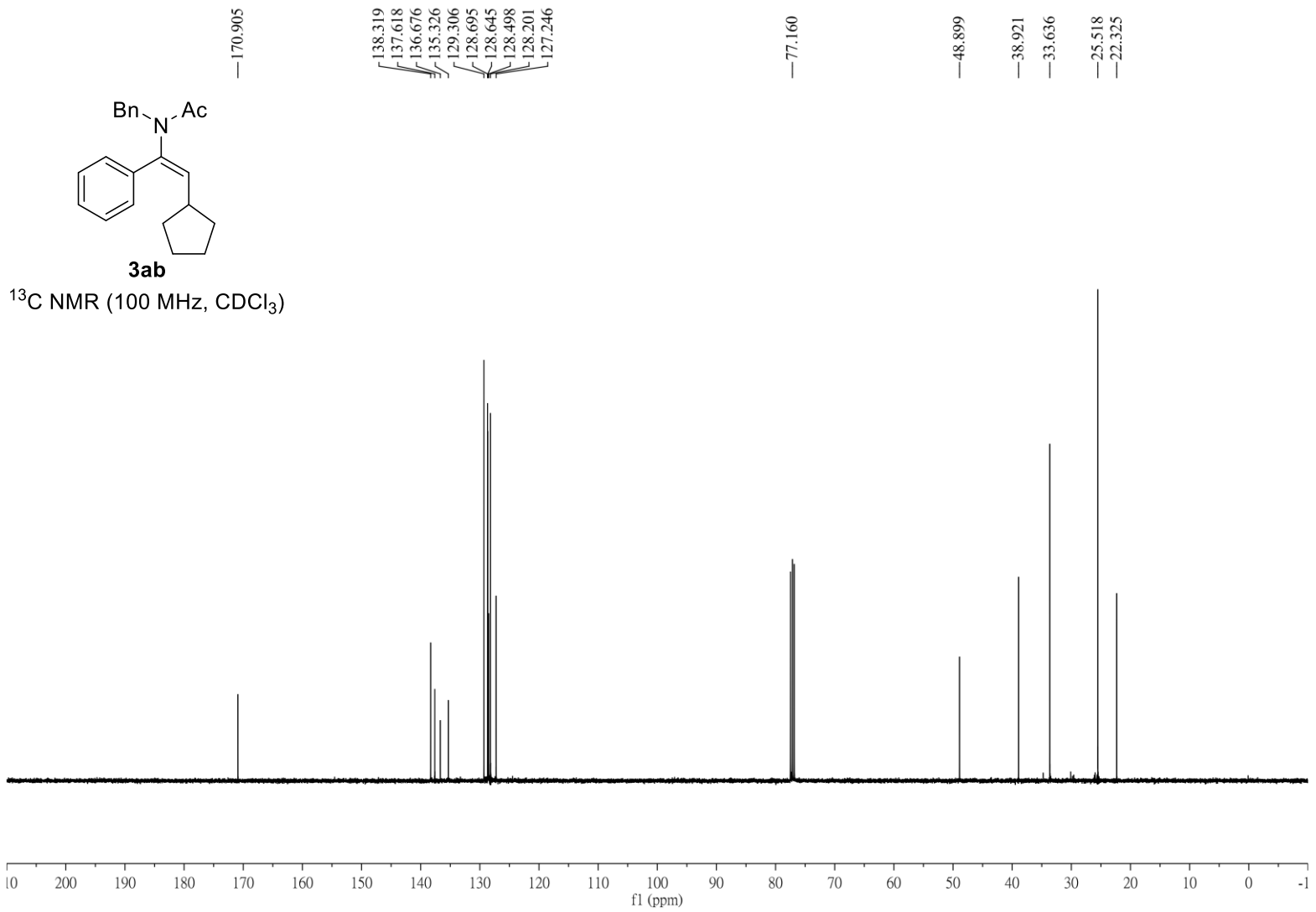
3ss

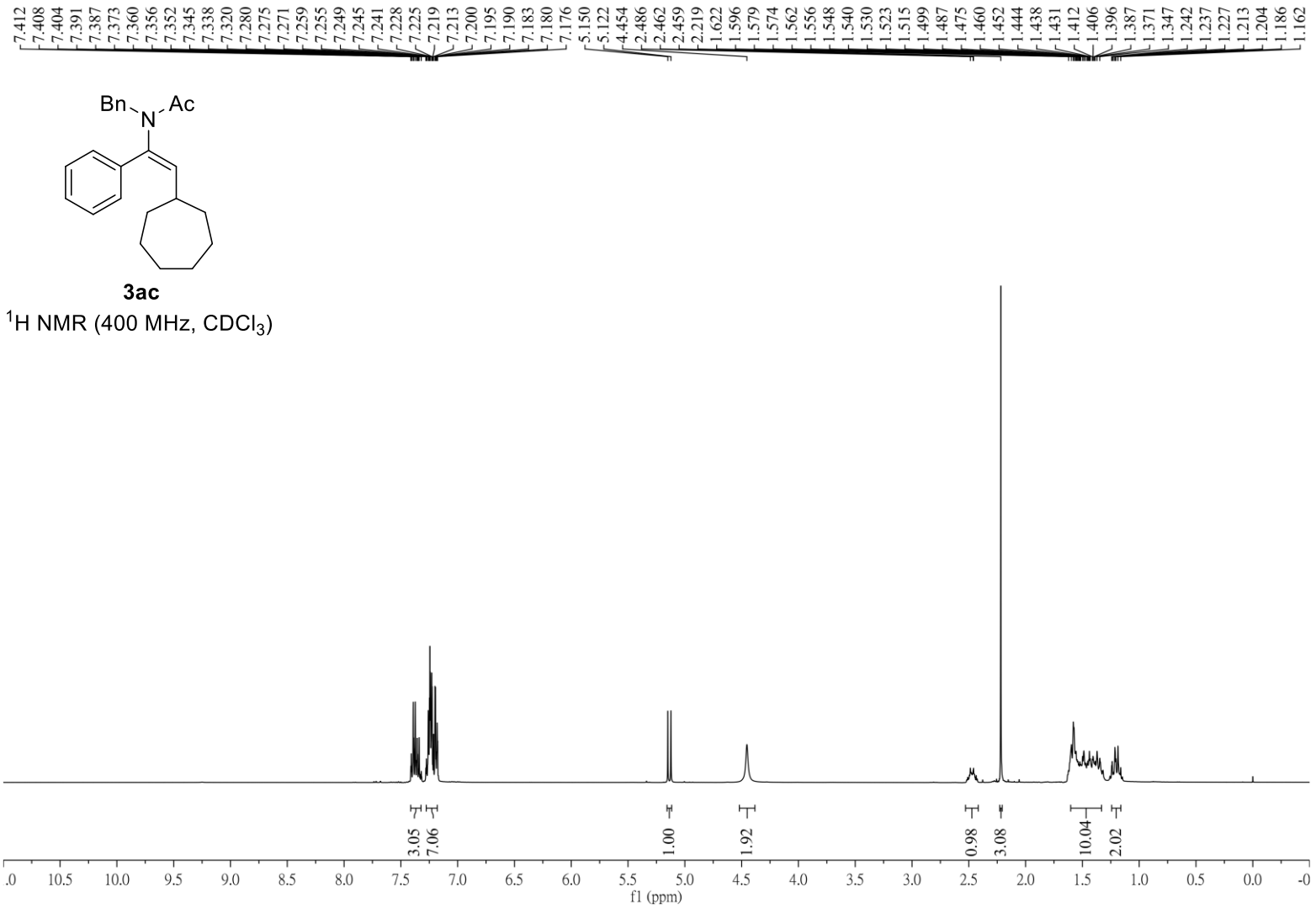
^{1}H NMR (400 MHz, $CDCl_3$)




156.219
141.298
138.254
138.127
136.644
136.399
129.672
128.831
128.546
128.465
128.439
128.399
128.280
127.974
127.935
127.851
127.382
126.008
77.160
67.491
52.378
35.807
30.309
Bn
N
Cbz
3ss
13C NMR (100 MHz, CDCl3)
f1 (ppm)

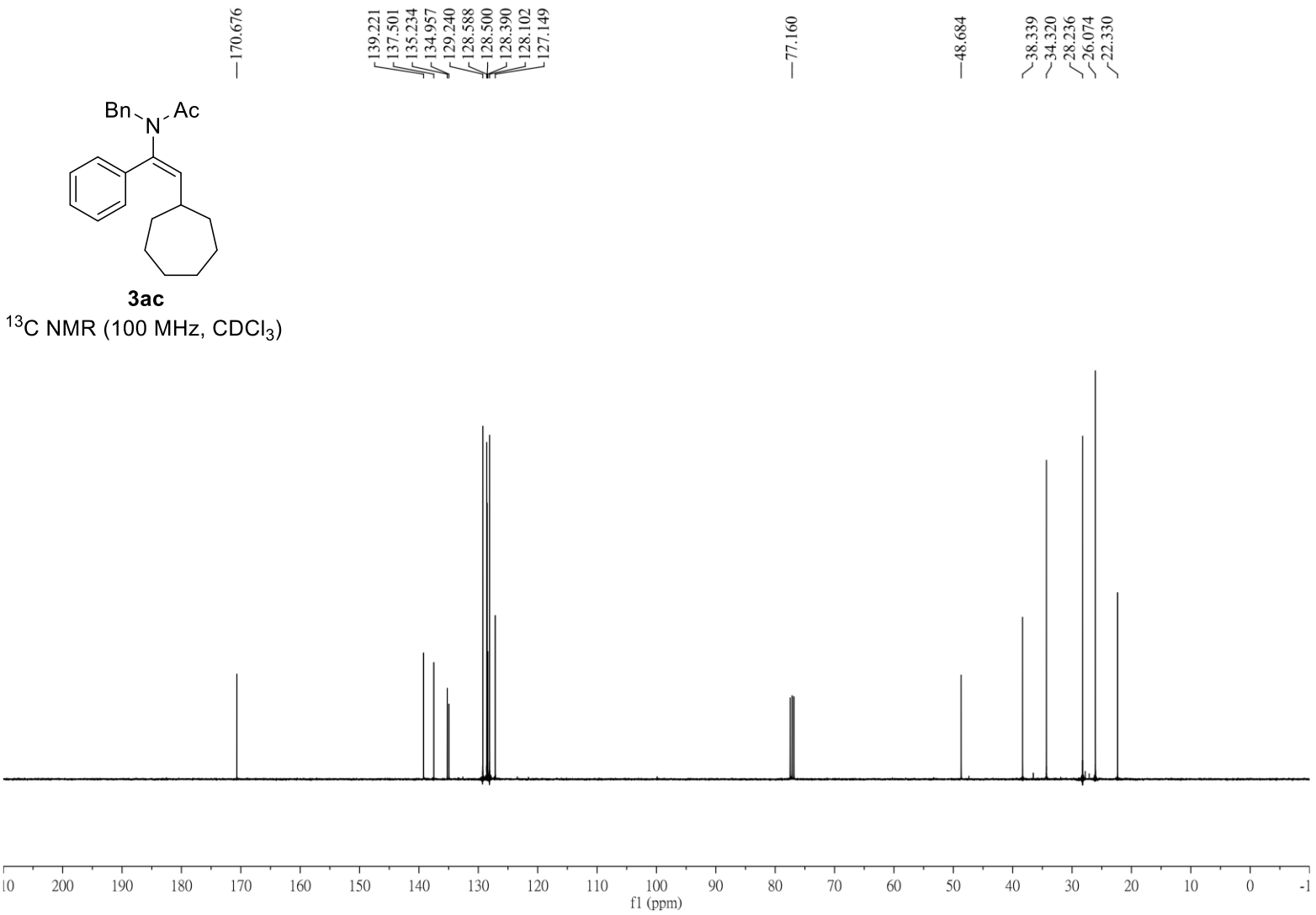

7.413
7.396
7.392
7.382
7.378
7.371
7.367
7.363
7.350
7.284
7.273
7.269
7.264
7.259
7.257
7.253
7.250
7.242
7.237
7.225
7.206
7.201
7.196
7.190
7.186
7.183
5.131
5.104
4.464
2.697
2.675
2.670
2.210
1.755
1.745
1.741
1.735
1.731
1.727
1.720
1.717
1.715
1.699
1.607
1.599
1.589
1.586
1.579
1.576
1.570
1.562
1.548
1.536
1.522
1.514
1.503
1.496
1.485
1.484
1.477
1.473
1.175
1.160
1.155
1.144
1.140
1.135
1.123
-0.000
Bn
N
Ac
3ab
^{1}H NMR (400 MHz, $CDCl_3$)
3.00
7.16
1.00
1.91
0.99
3.04
2.07
4.11
2.00
f1 (ppm)


170.905
138.319
137.618
136.676
135.326
129.306
128.695
128.645
128.498
128.201
127.246
77.160
48.899
38.921
33.636
25.518
22.325
Bn
N
Ac
3ab
13C NMR (100 MHz, CDCl3)
f1 (ppm)



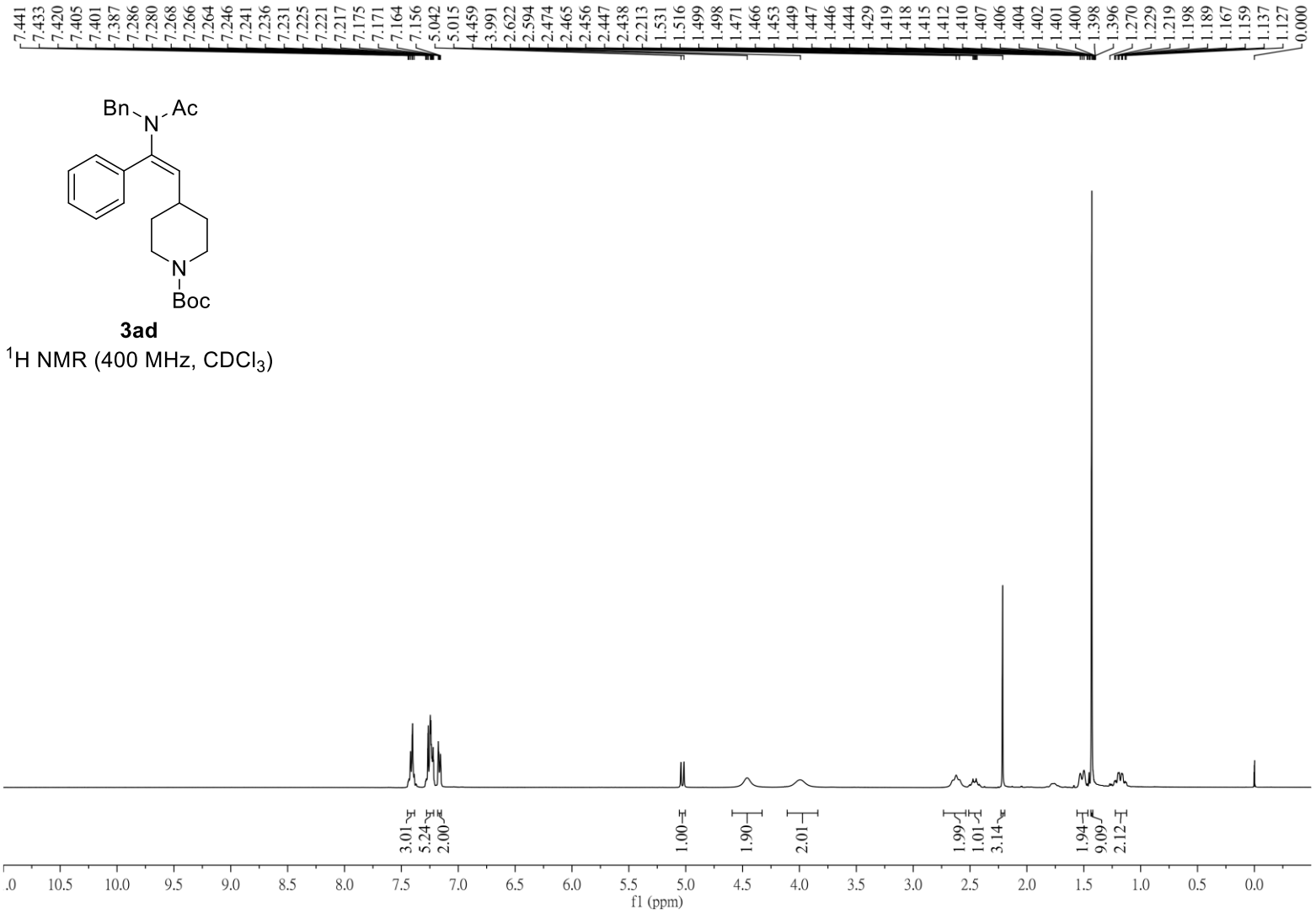
3ac

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



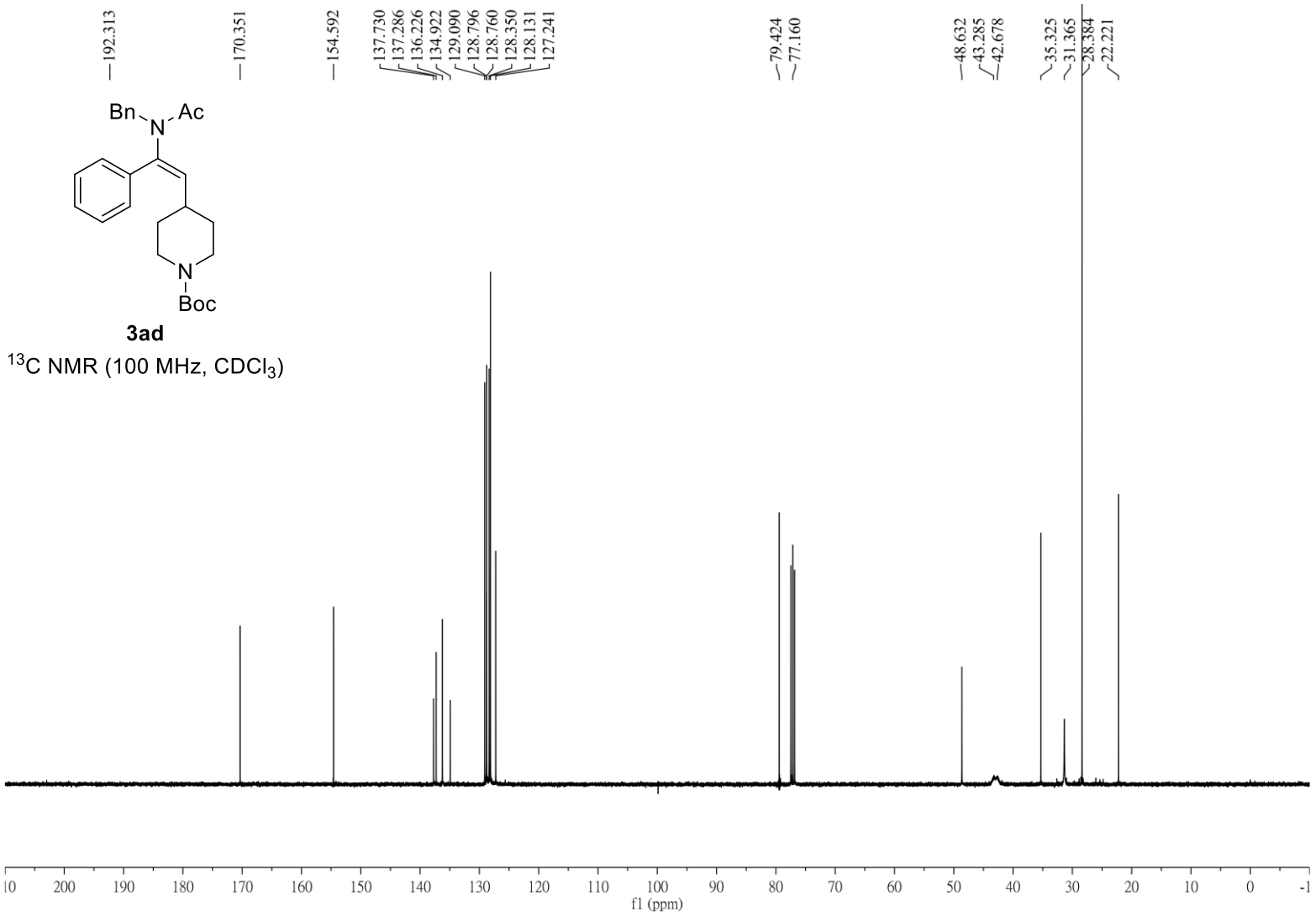
3ac

^{13}C NMR (100 MHz, $CDCl_3$)



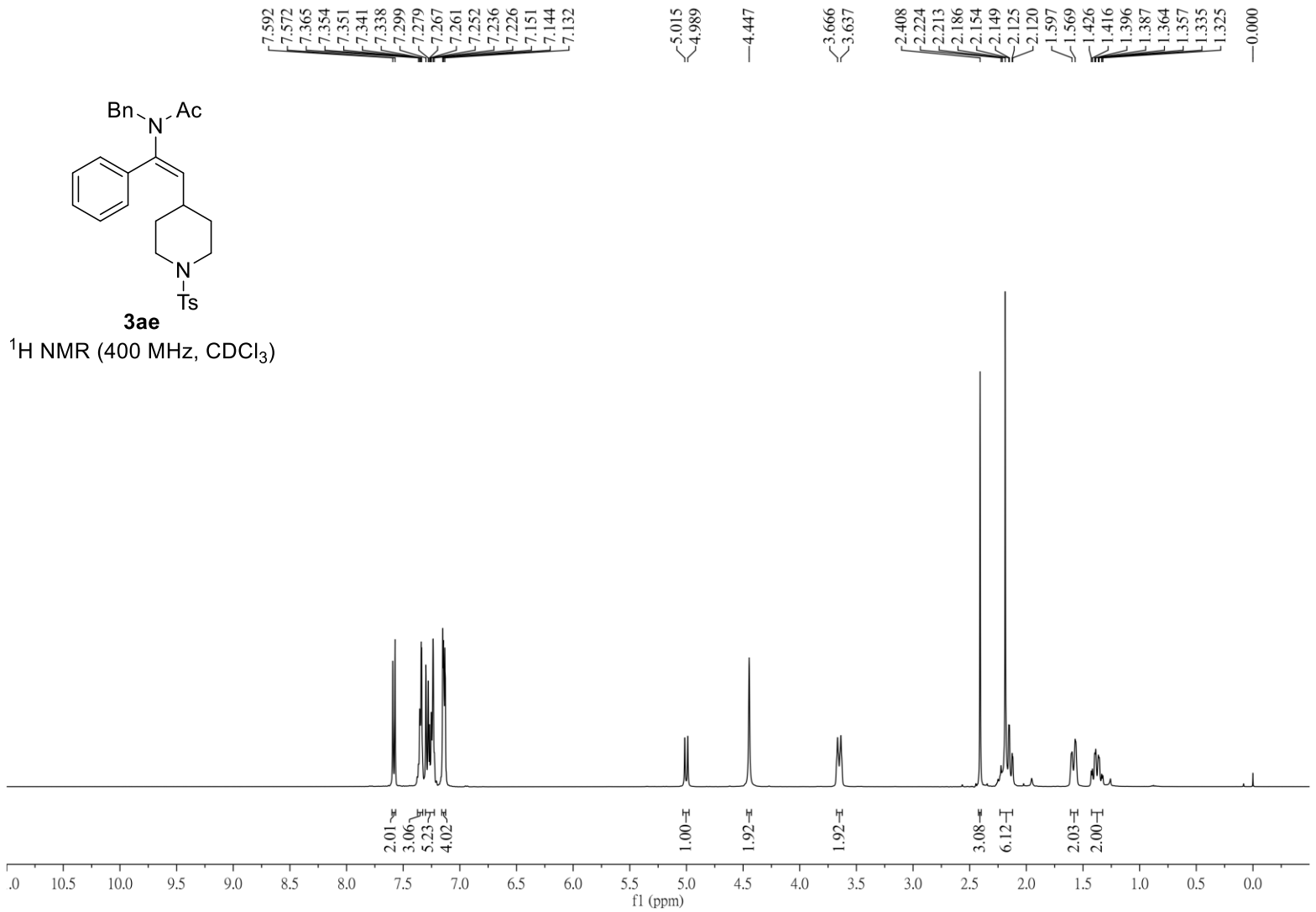
3ad

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



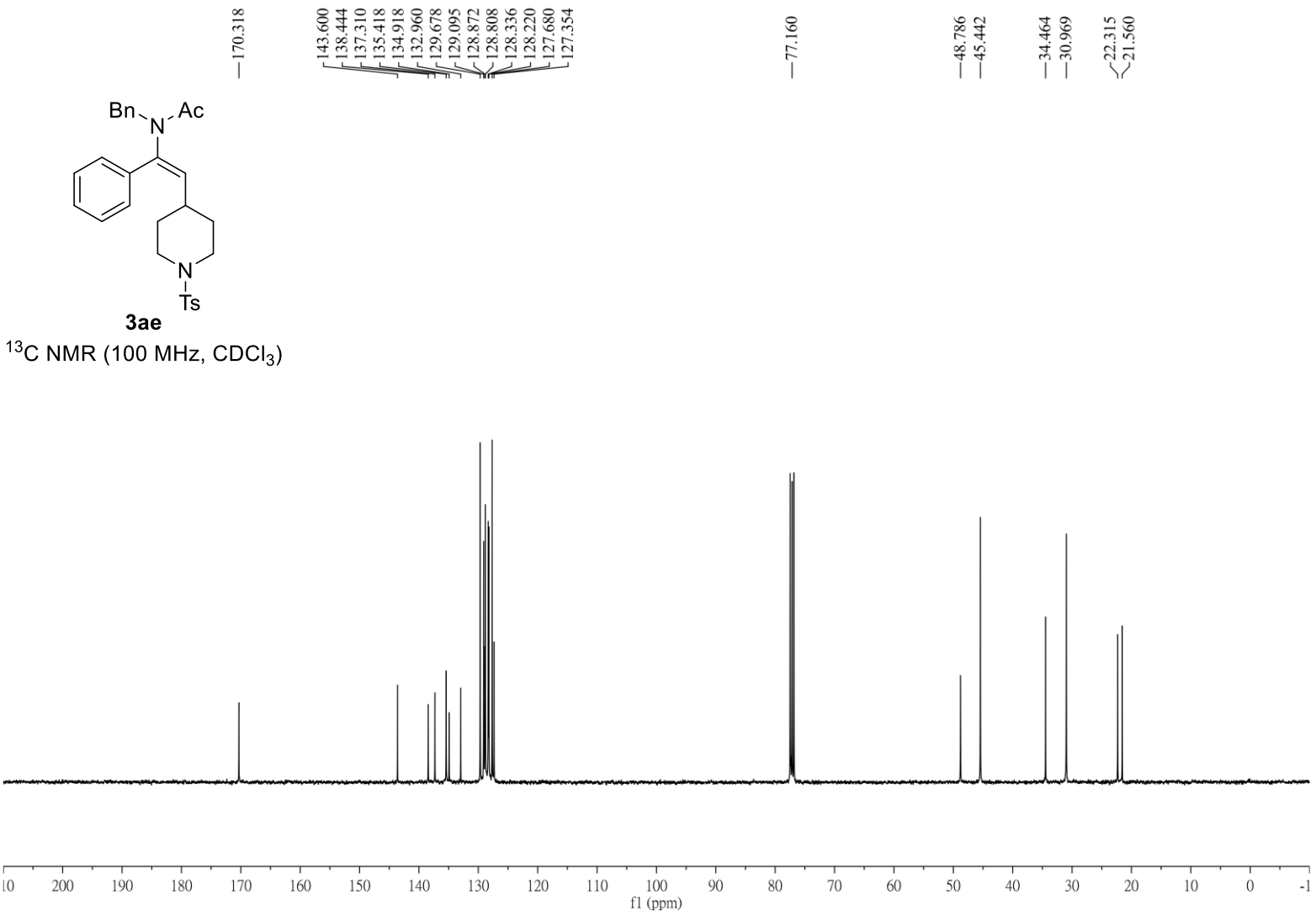
3ad

^{13}C NMR (100 MHz, $CDCl_3$)



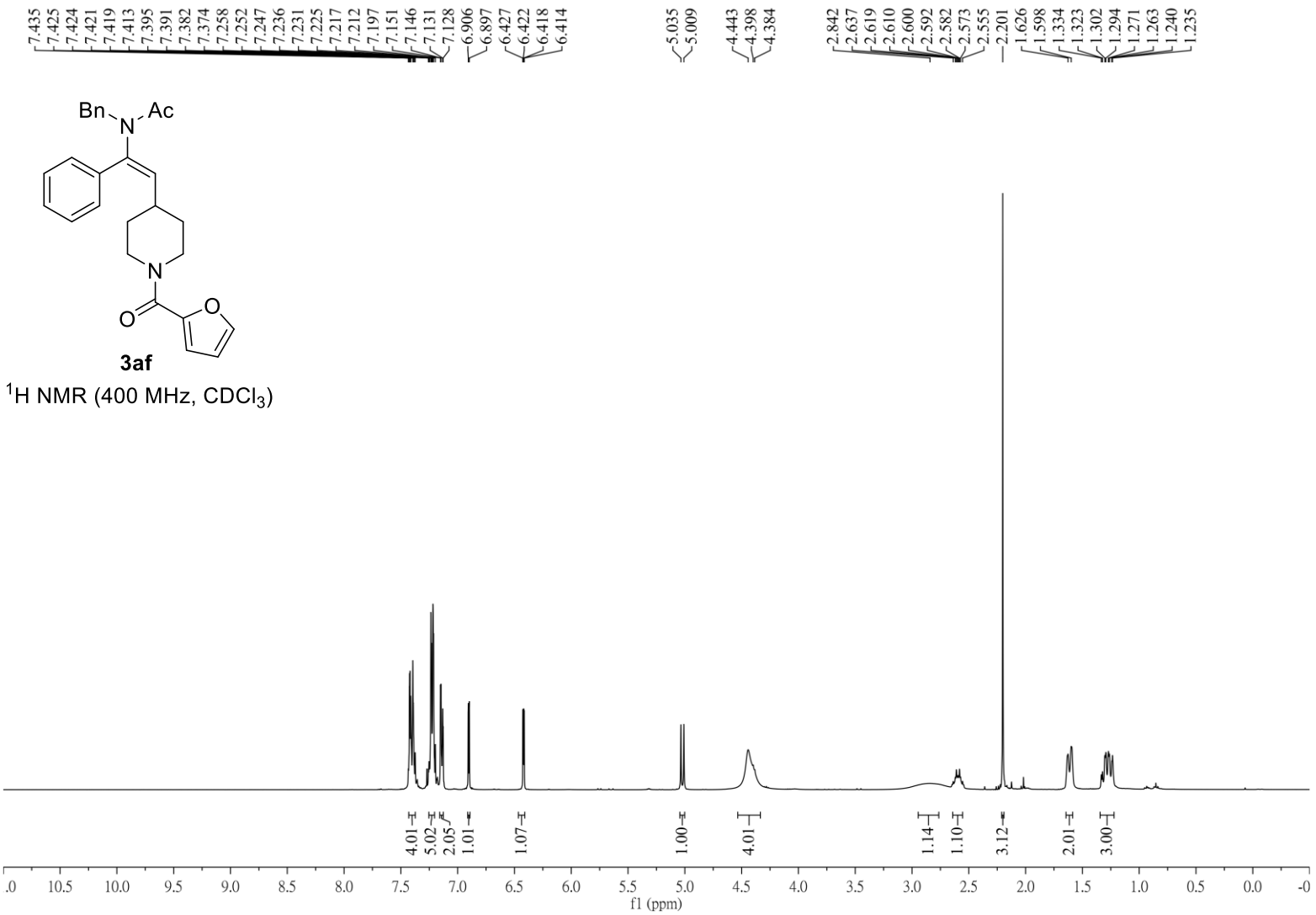
3ae

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



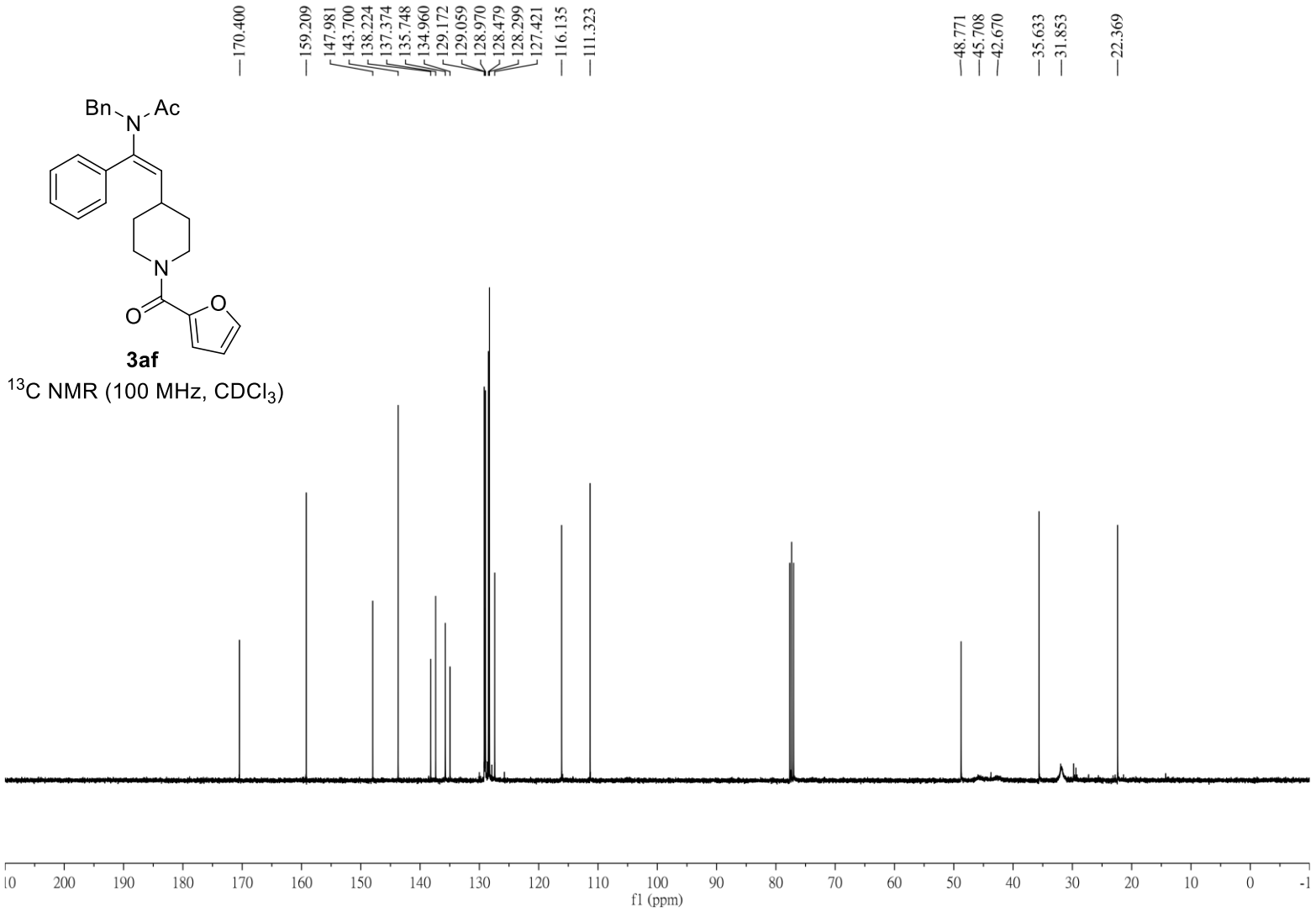
3ae

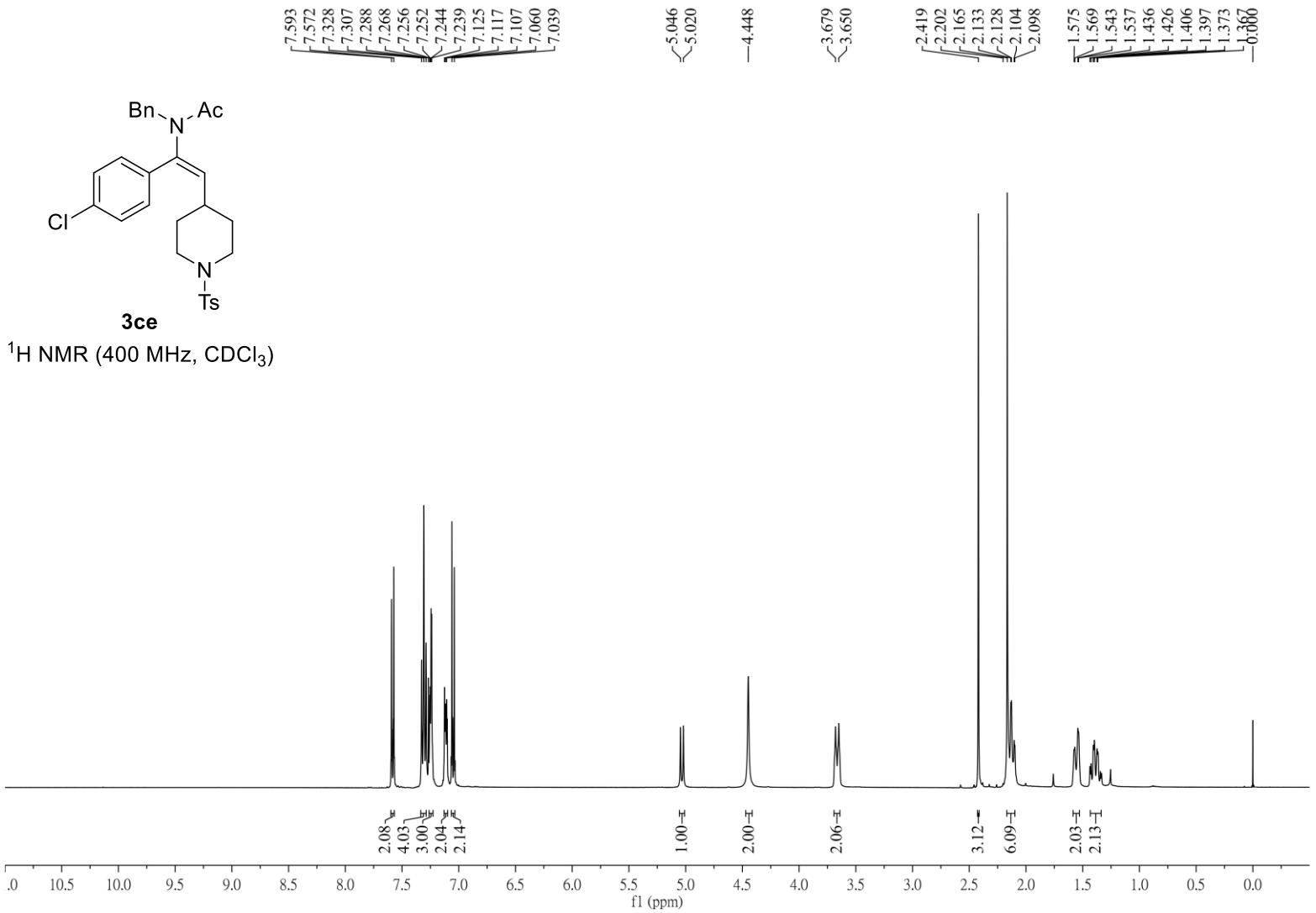
^{13}C NMR (100 MHz, $CDCl_3$)



3af

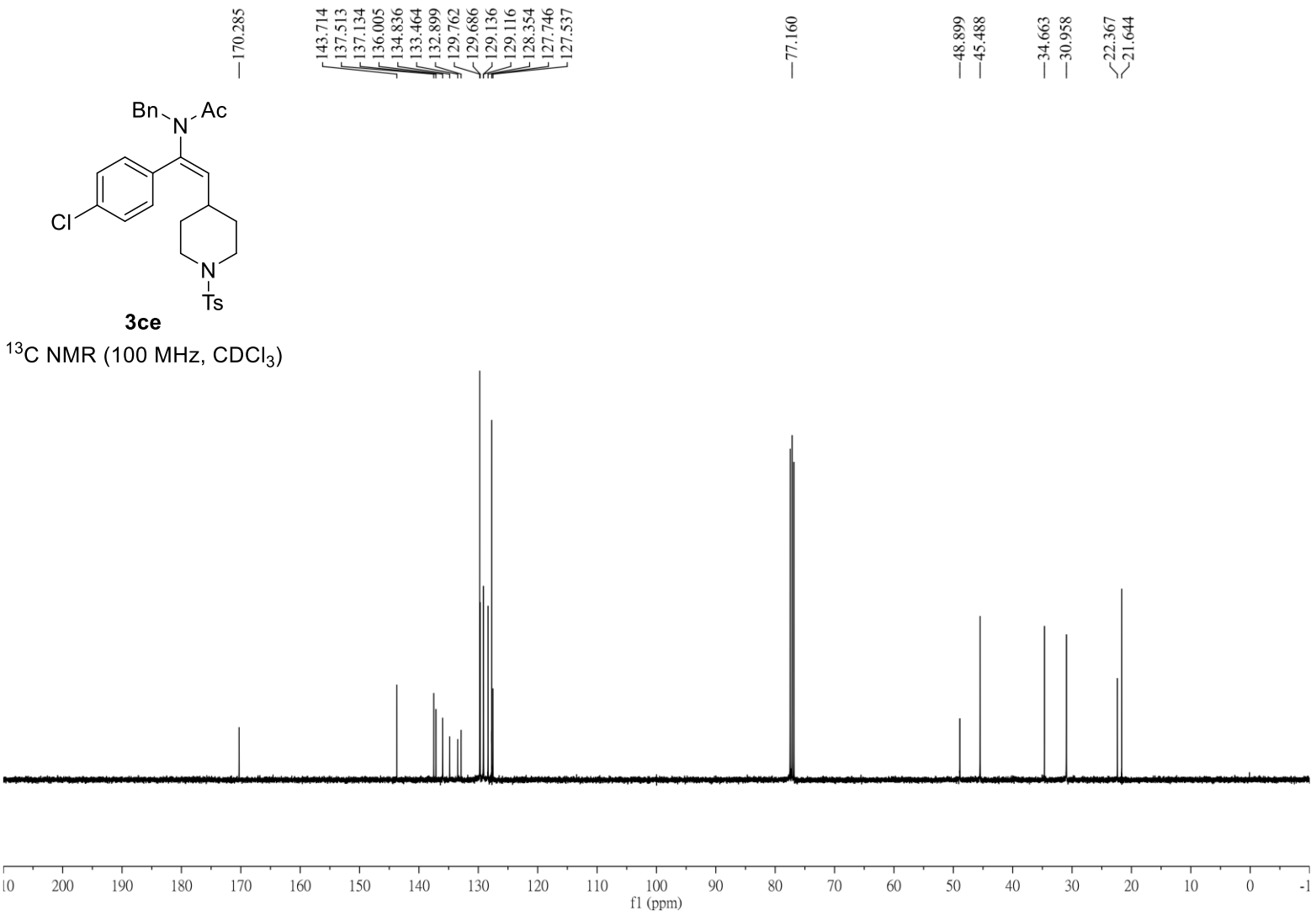
^{1}H NMR (400 MHz, $CDCl_3$)

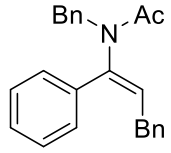

170.400
159.209
147.981
143.700
138.224
137.374
135.748
134.960
129.172
129.059
128.970
128.479
128.299
127.421
116.135
111.323
48.771
45.708
42.670
35.633
31.853
22.369
Bn
N
Ac
N
O
O
3af
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ce

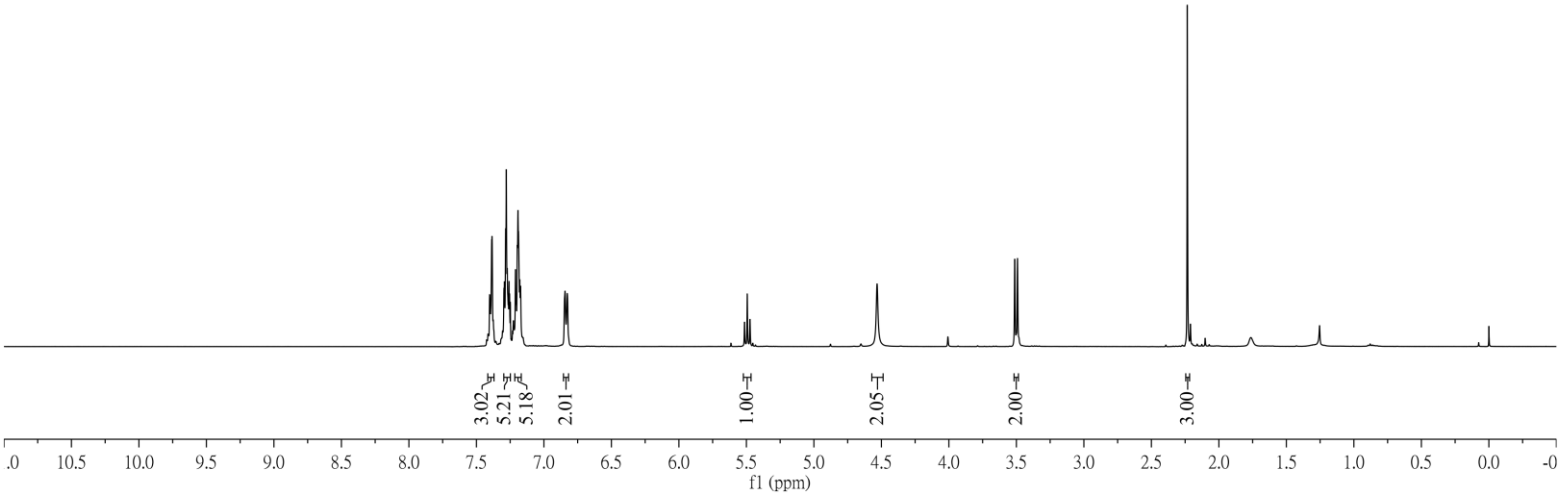
^{1}H NMR (400 MHz, $CDCl_3$)

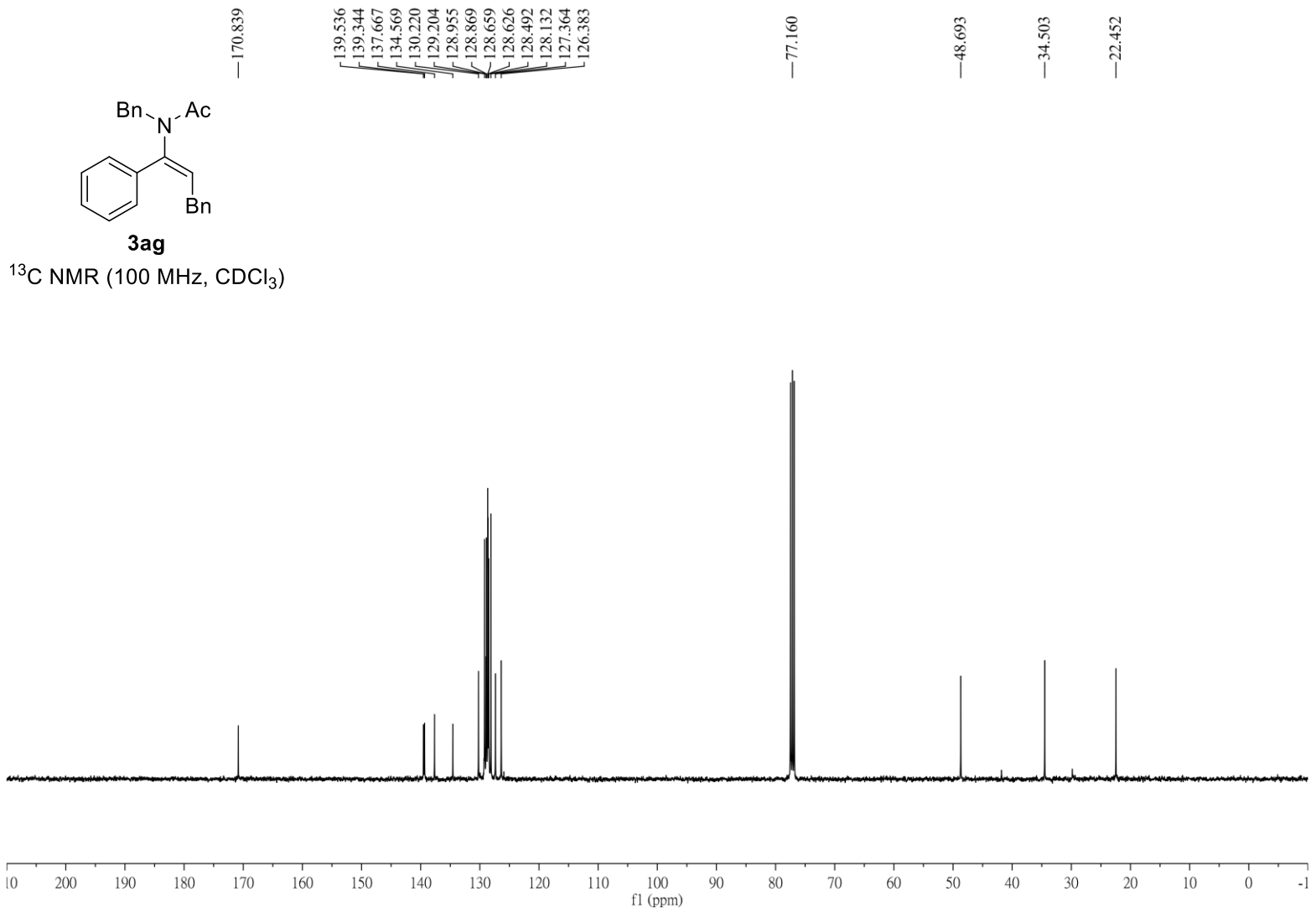

170.285
143.714
137.513
137.134
136.005
134.836
133.464
132.899
129.762
129.686
129.136
129.116
128.354
127.746
127.537
77.160
48.899
45.488
34.663
30.958
22.367
21.644
Bn
N
Ac
Cl
N
Ts
3ce
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3ag

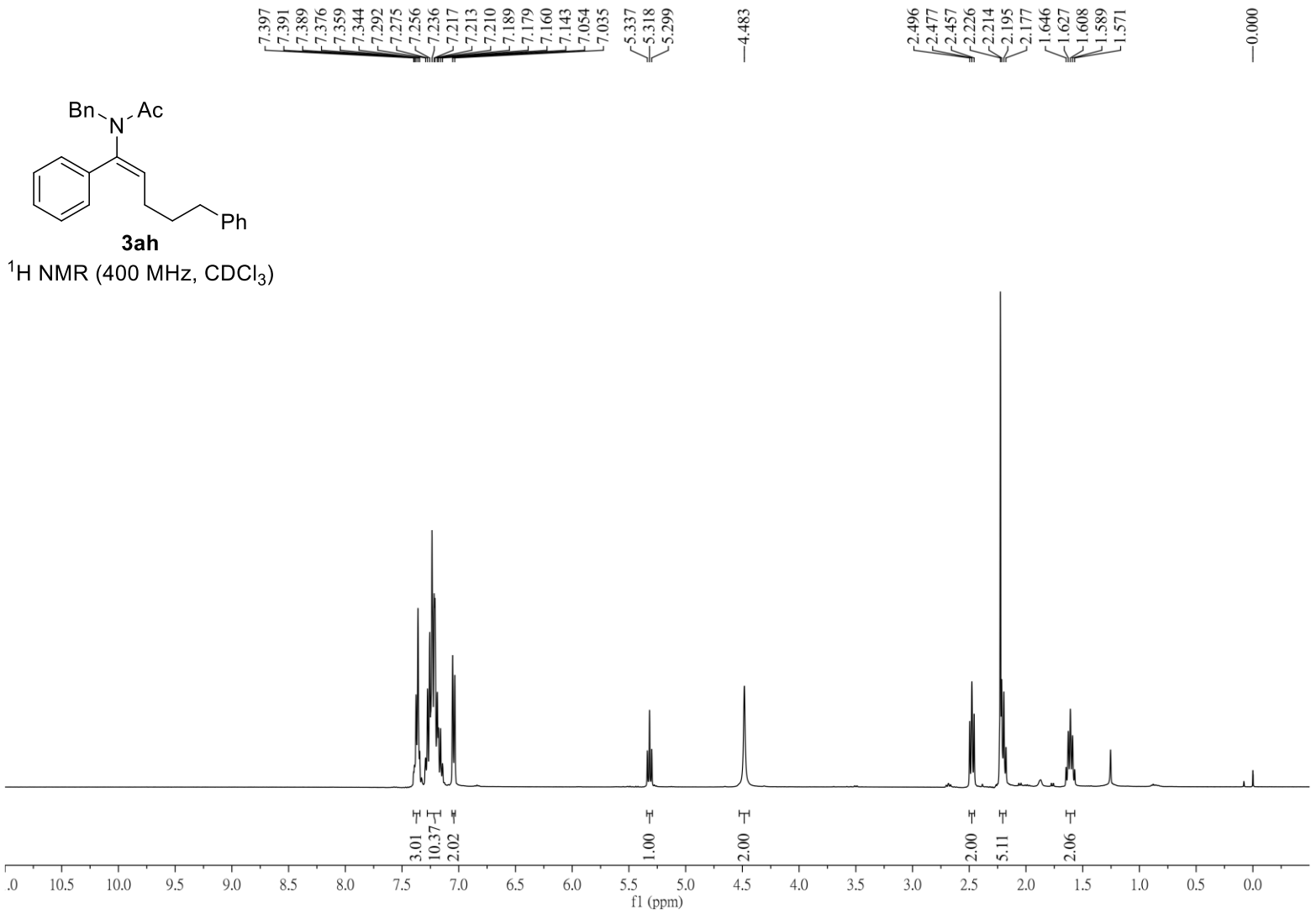
^{1}H NMR (400 MHz, $CDCl_3$)





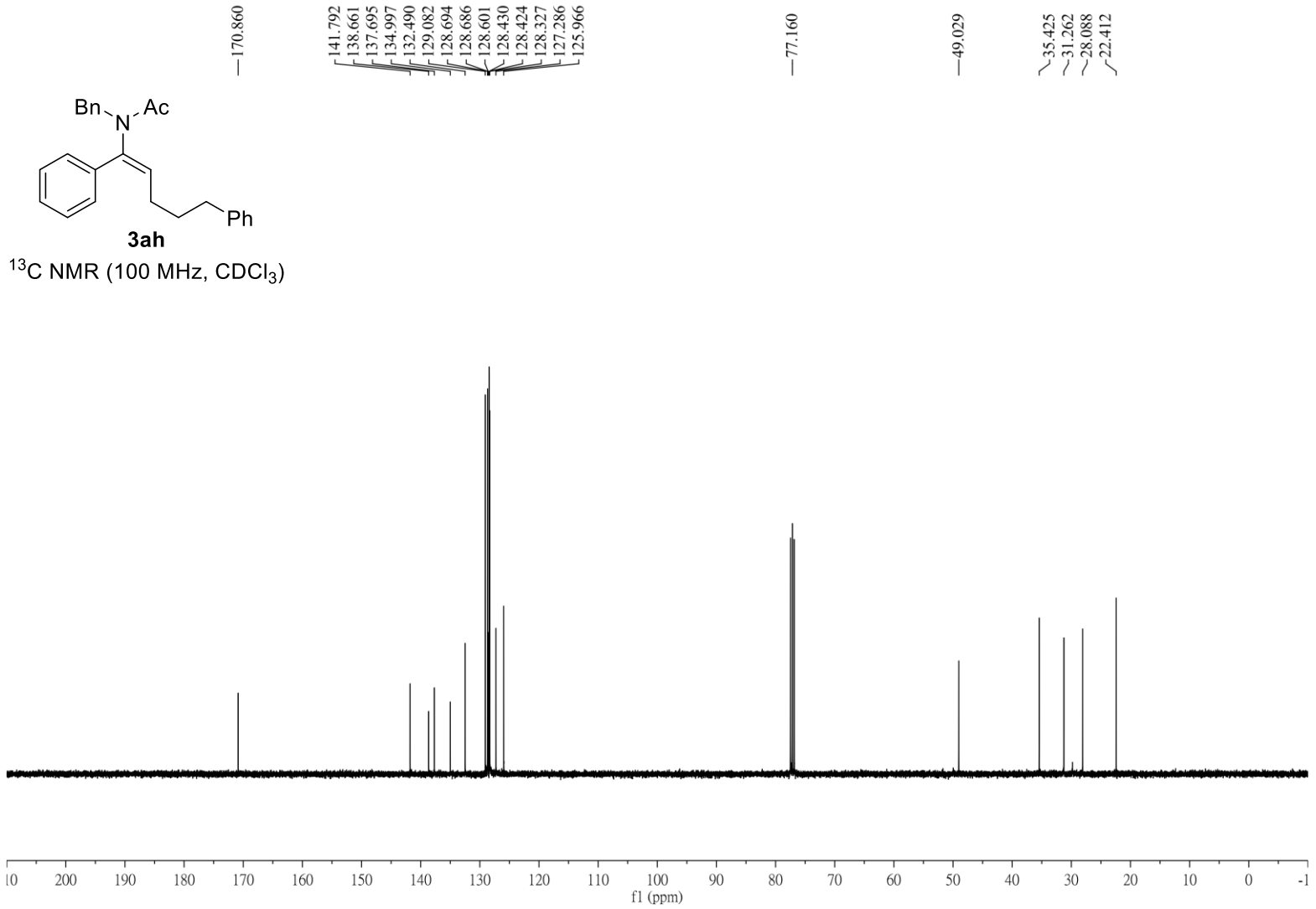
3ag

^{13}C NMR (100 MHz, $CDCl_3$)



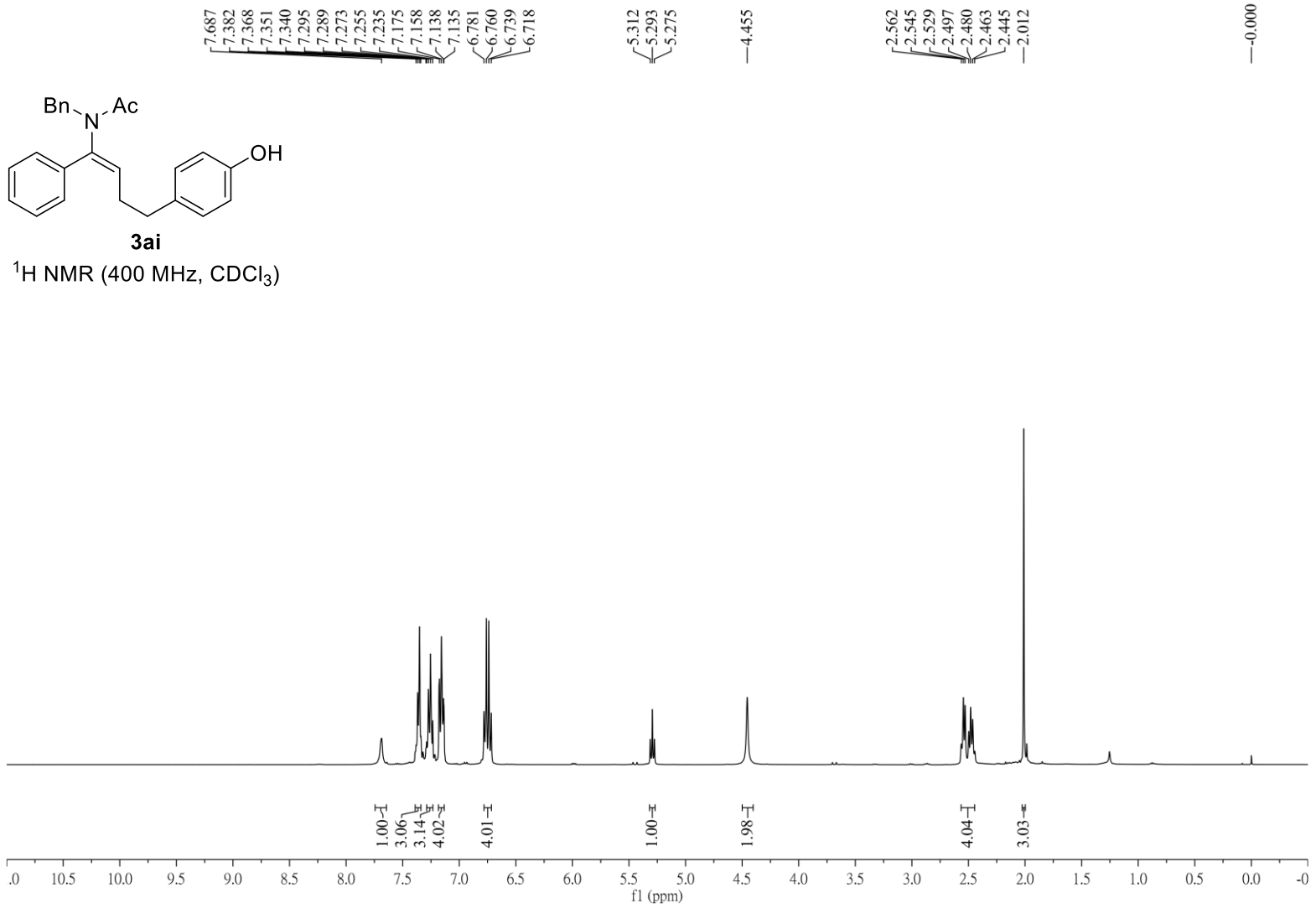
3ah

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



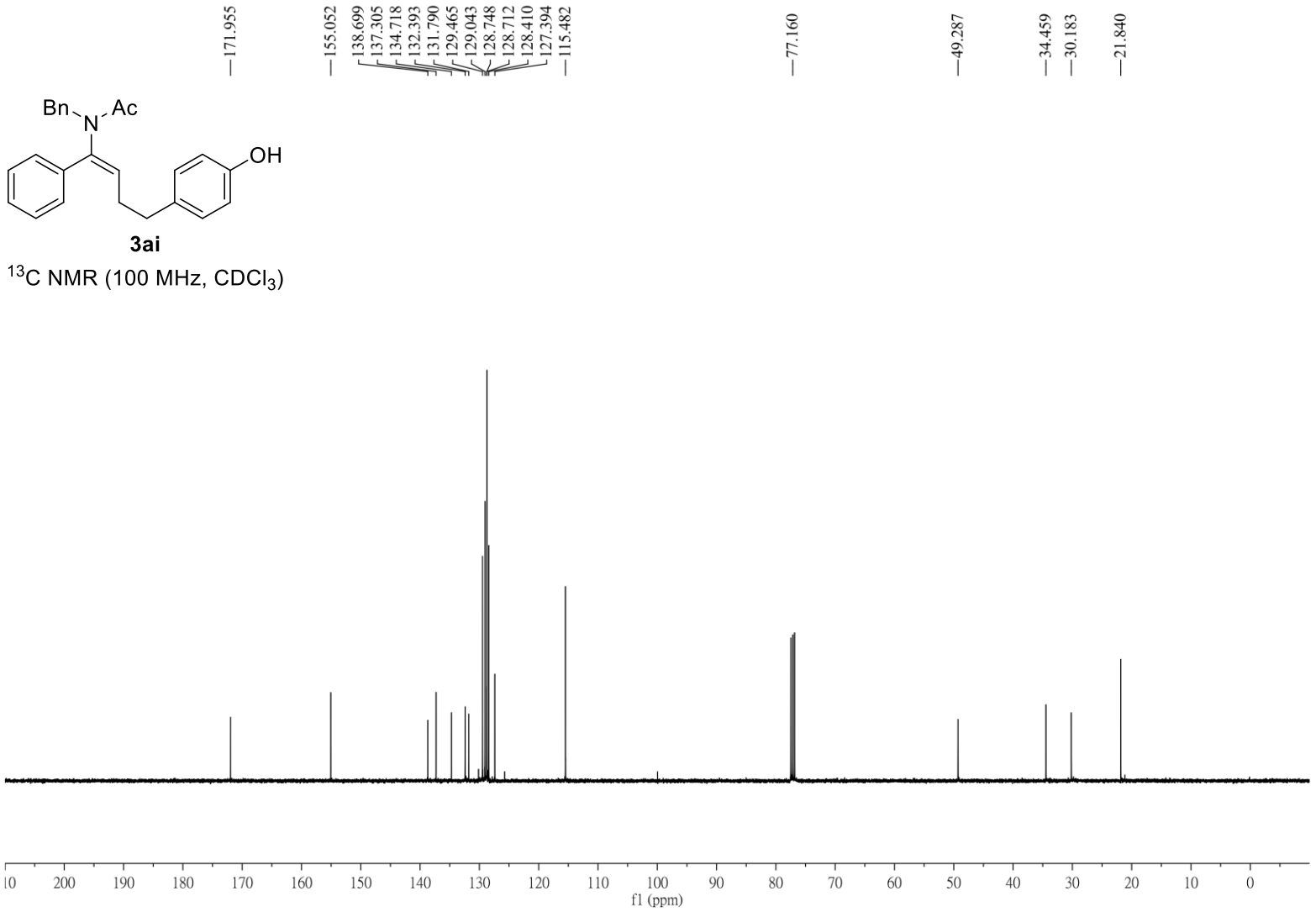
3ah

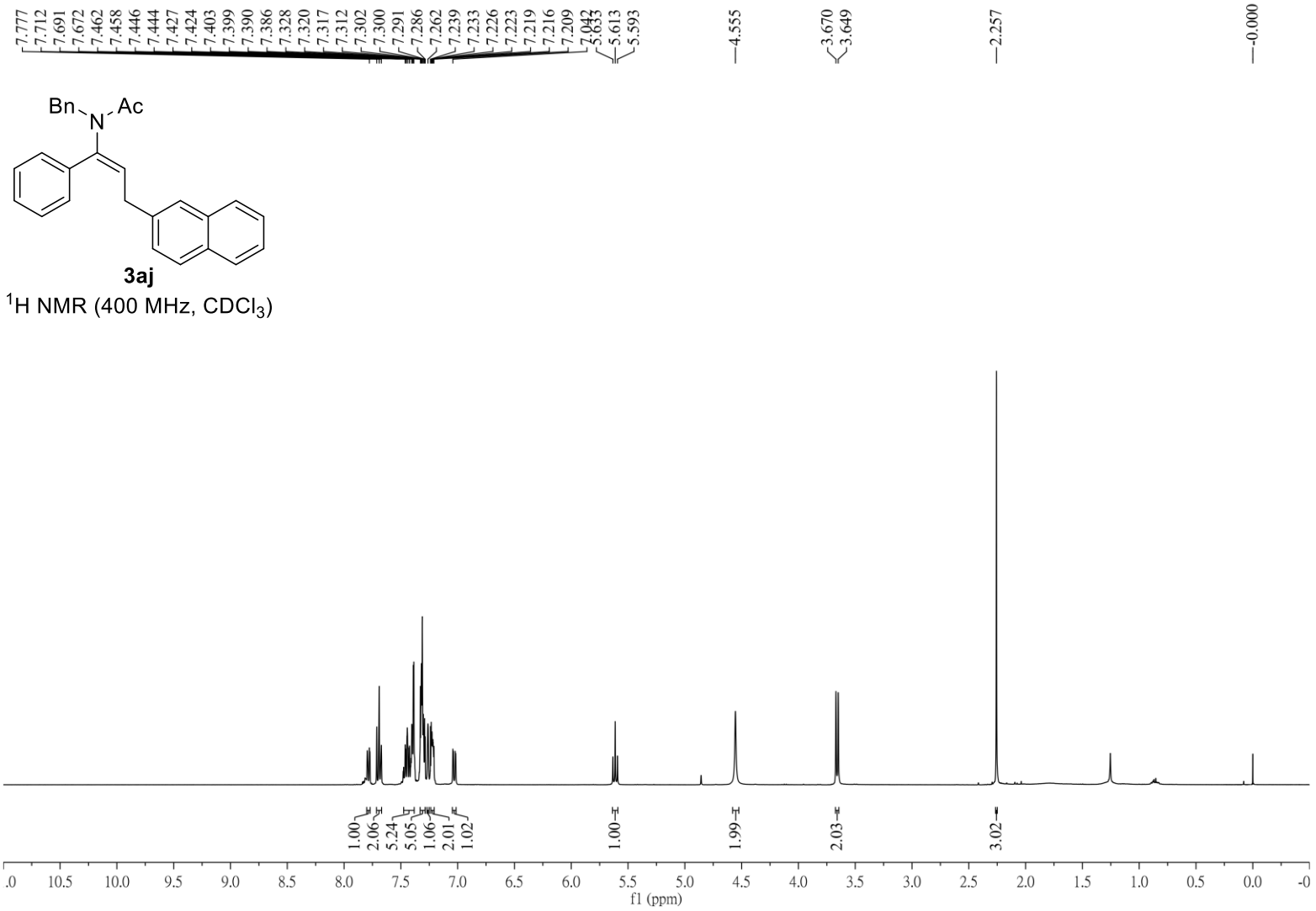
^{13}C NMR (100 MHz, $CDCl_3$)



3ai

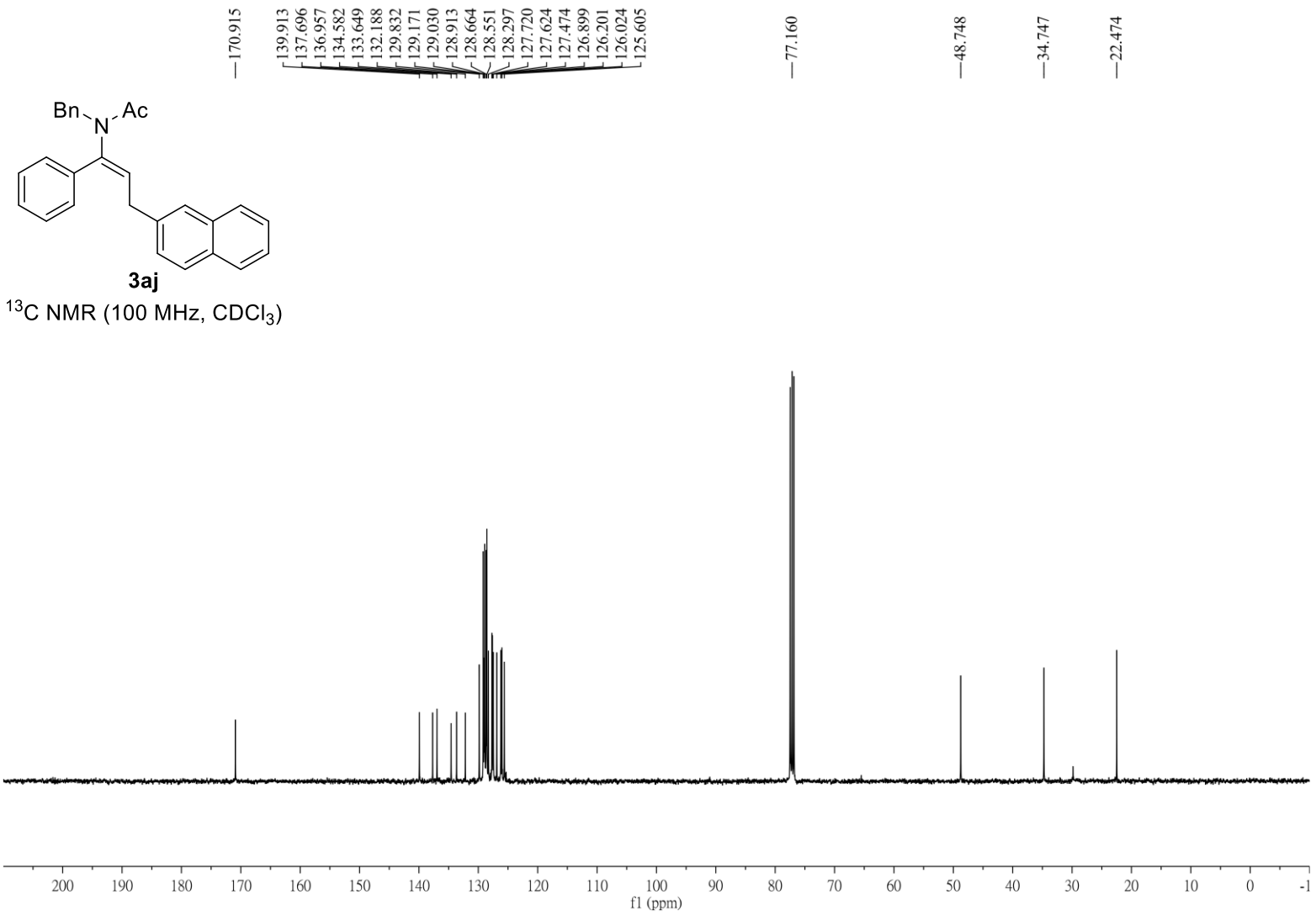
^{1}H NMR (400 MHz, $CDCl_3$)

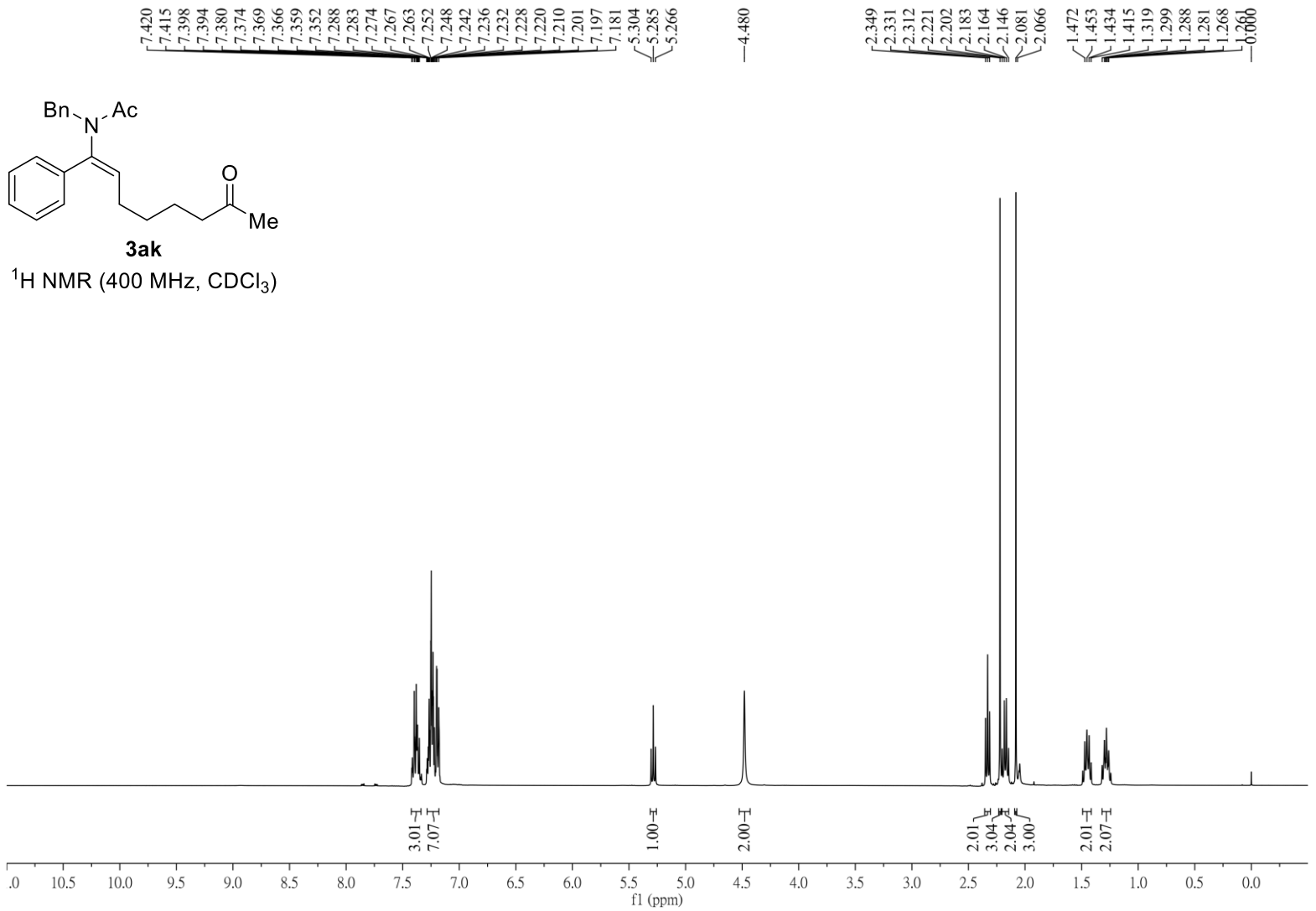

171.955
155.052
138.699
137.305
134.718
132.393
131.790
129.465
129.043
128.748
128.712
128.410
127.394
115.482
77.160
49.287
34.459
30.183
21.840
Bn
N
Ac
OH
3ai
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3aj

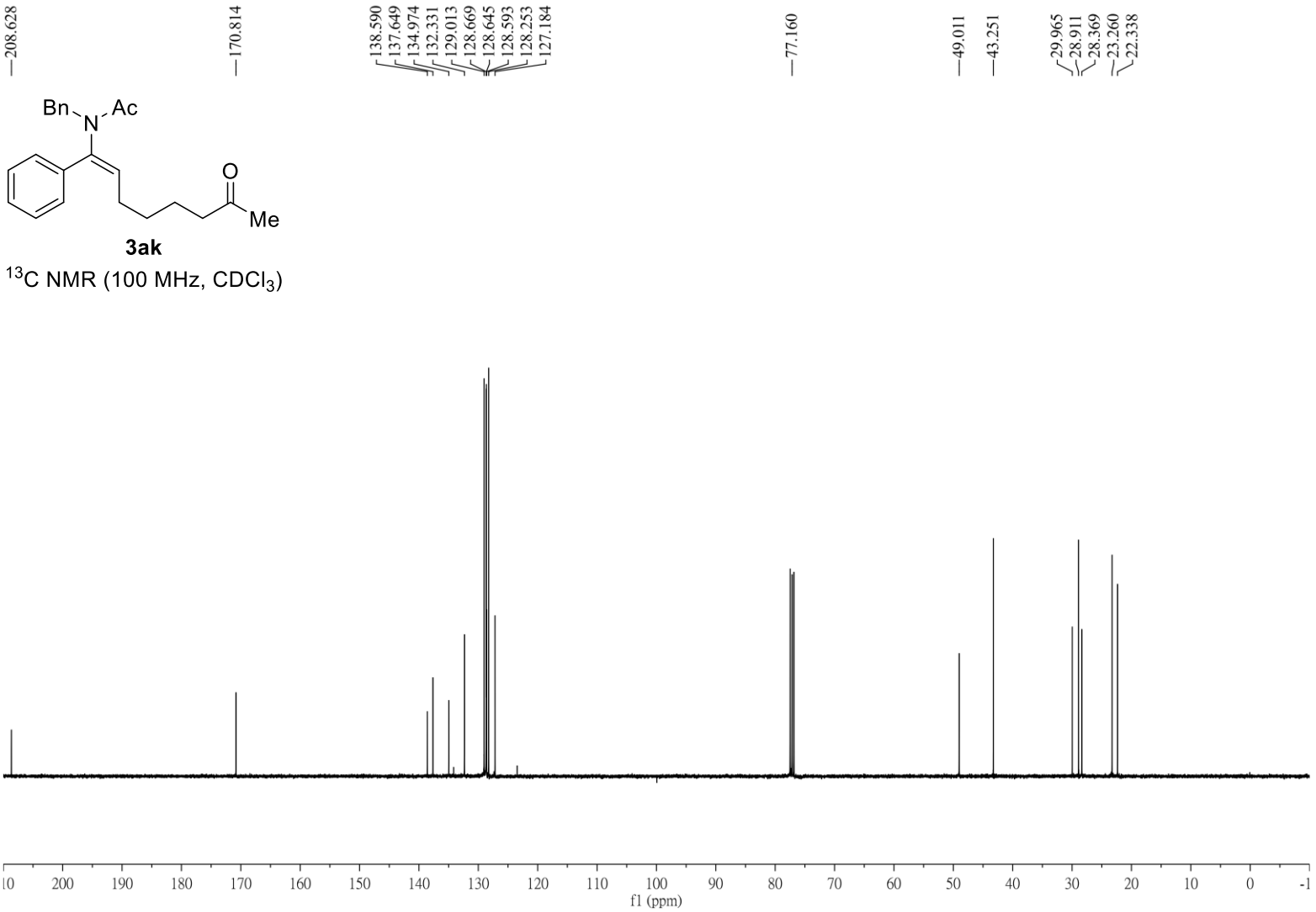
^{1}H NMR (400 MHz, $CDCl_3$)


170.915
139.913
137.696
136.957
134.582
133.649
132.188
129.832
129.171
129.030
128.913
128.664
128.551
128.297
127.720
127.624
127.474
126.899
126.201
126.024
125.605
77.160
48.748
34.747
22.474
Bn
N
Ac
3aj
13C NMR (100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



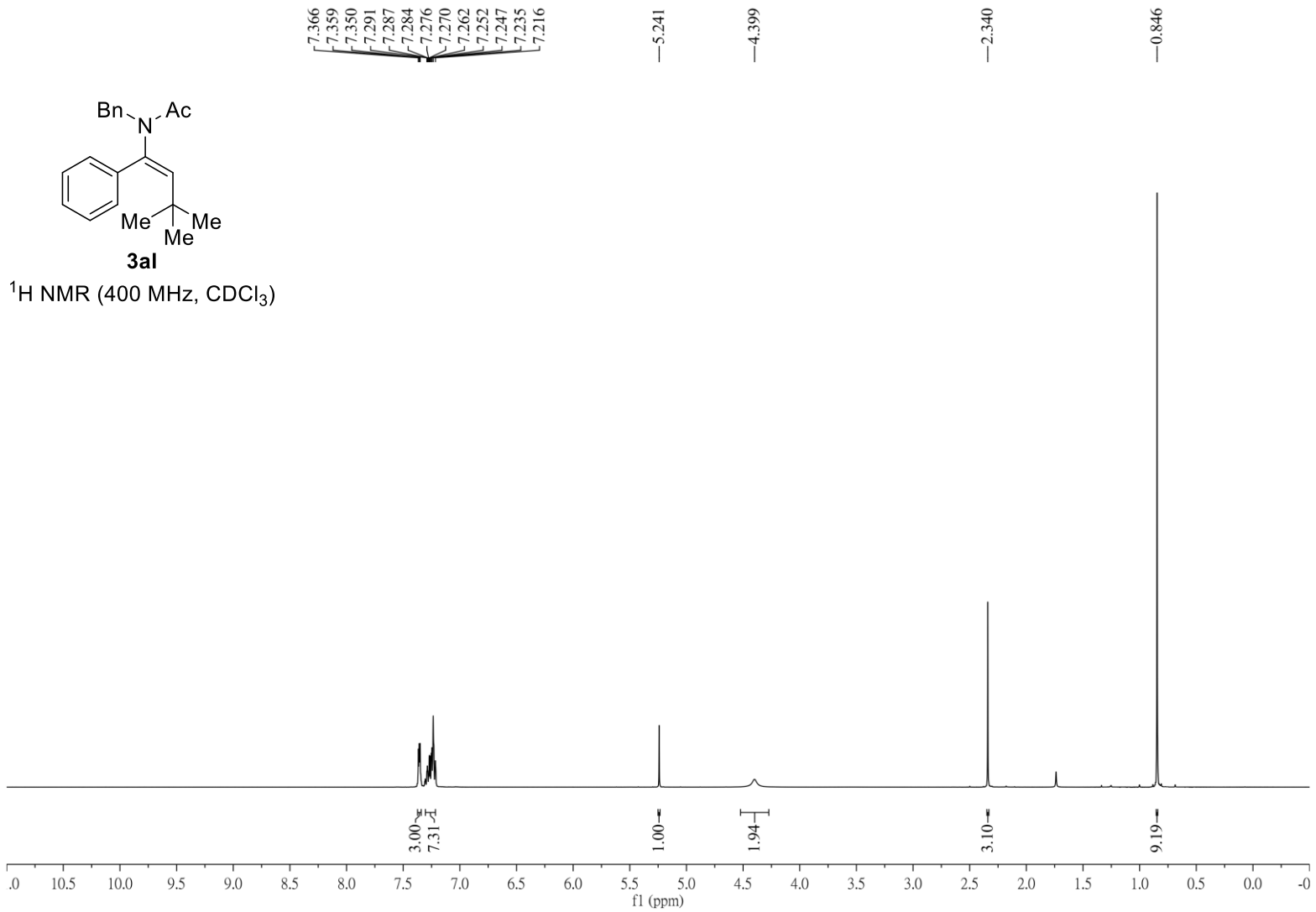
3ak

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



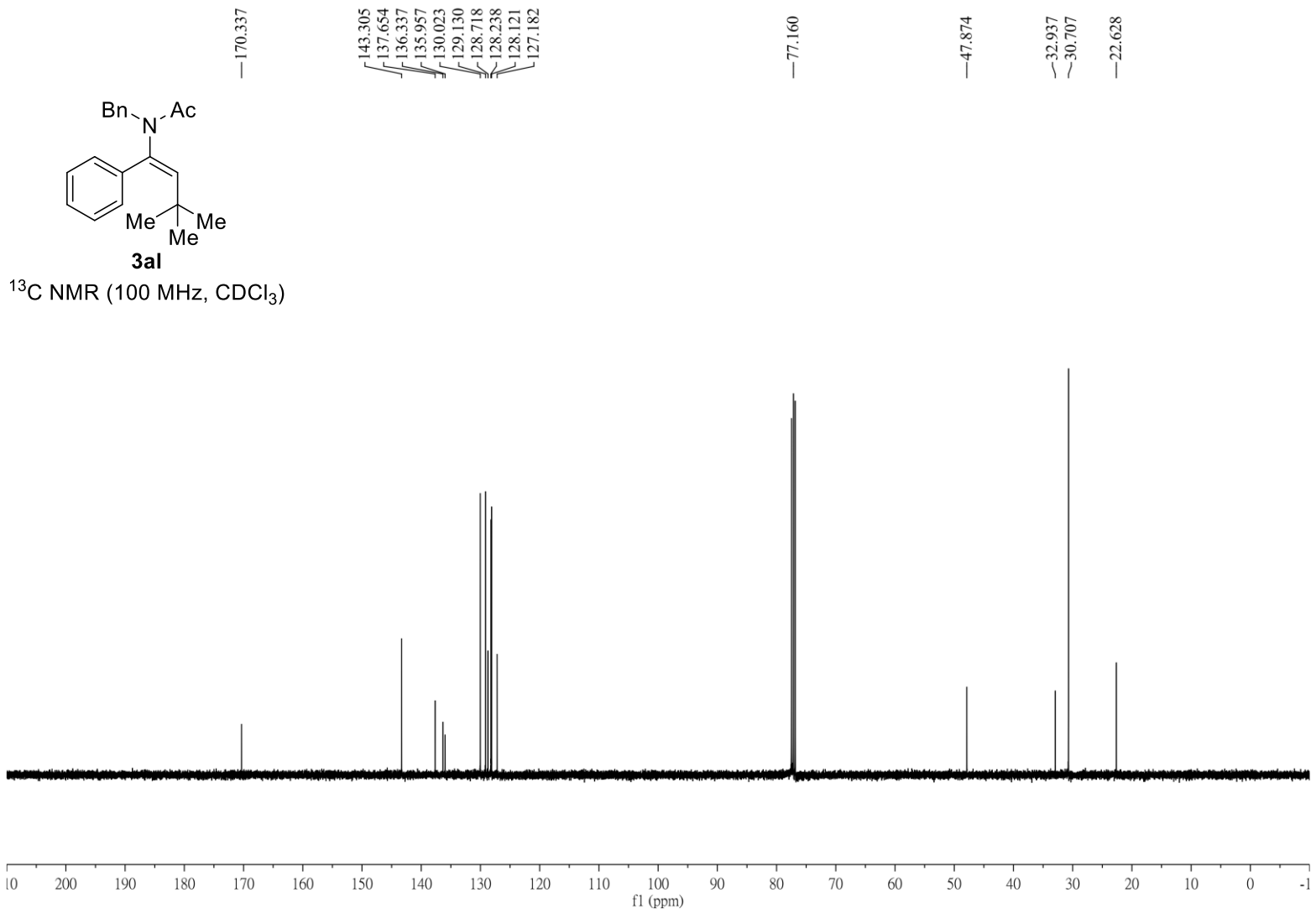
3ak

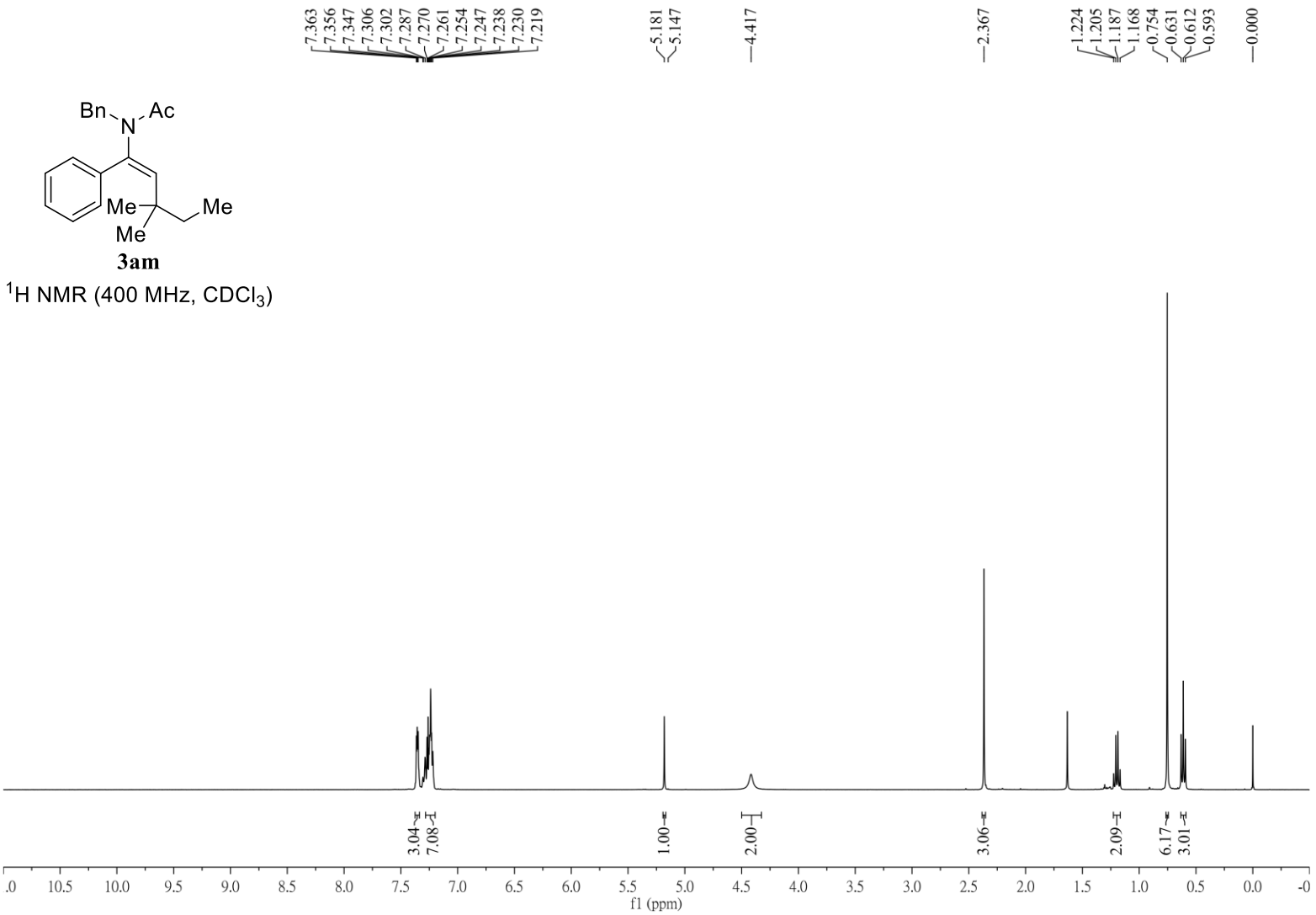
^{13}C NMR (100 MHz, $CDCl_3$)



3al

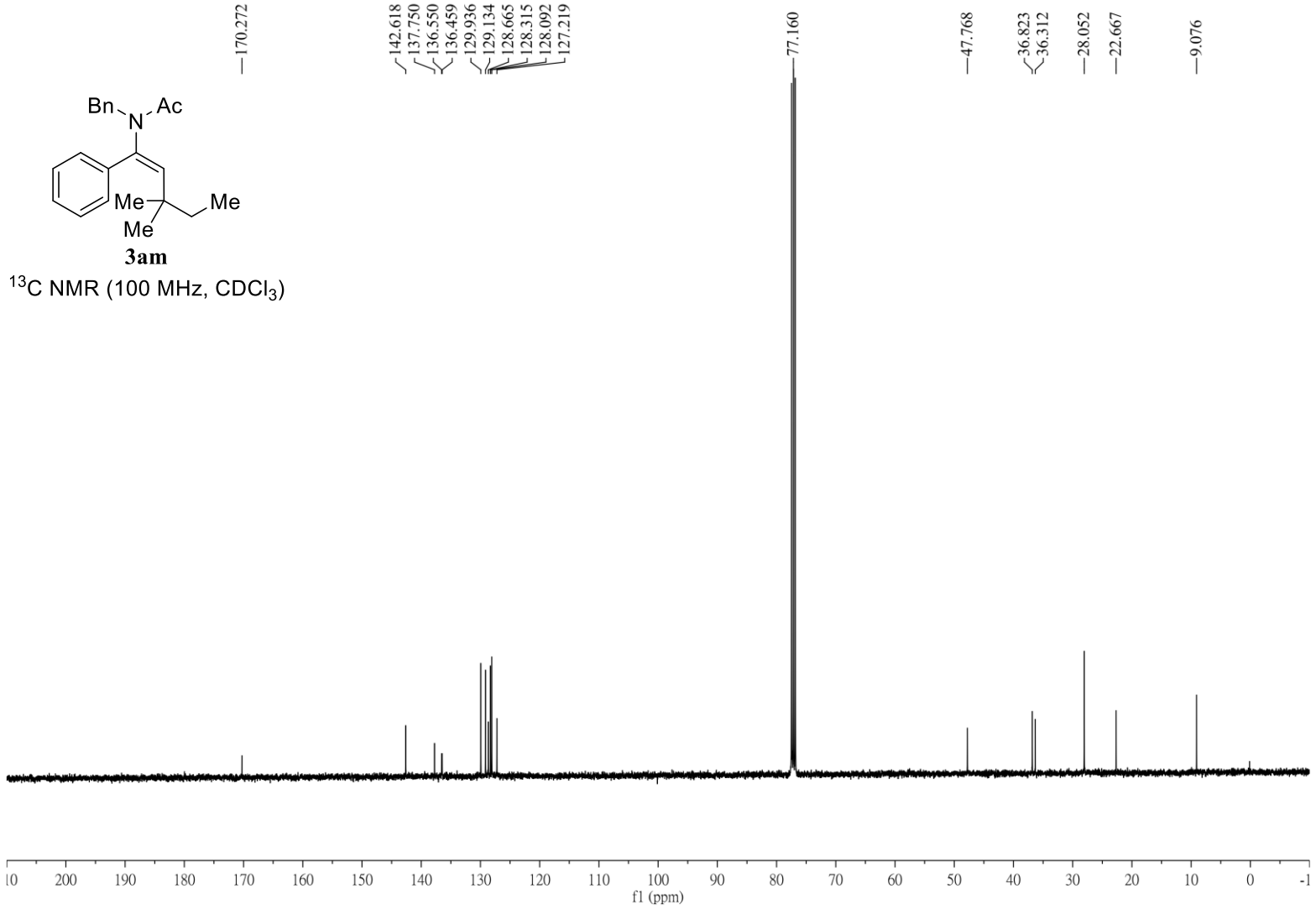
^{1}H NMR (400 MHz, $CDCl_3$)


170.337
143.305
137.654
136.337
135.957
130.023
129.130
128.718
128.238
128.121
127.182
77.160
47.874
32.937
30.707
22.628
Bn
N
Ac
Me
Me
Me
3aI
13C NMR (100 MHz, CDCl3)
f1 (ppm)



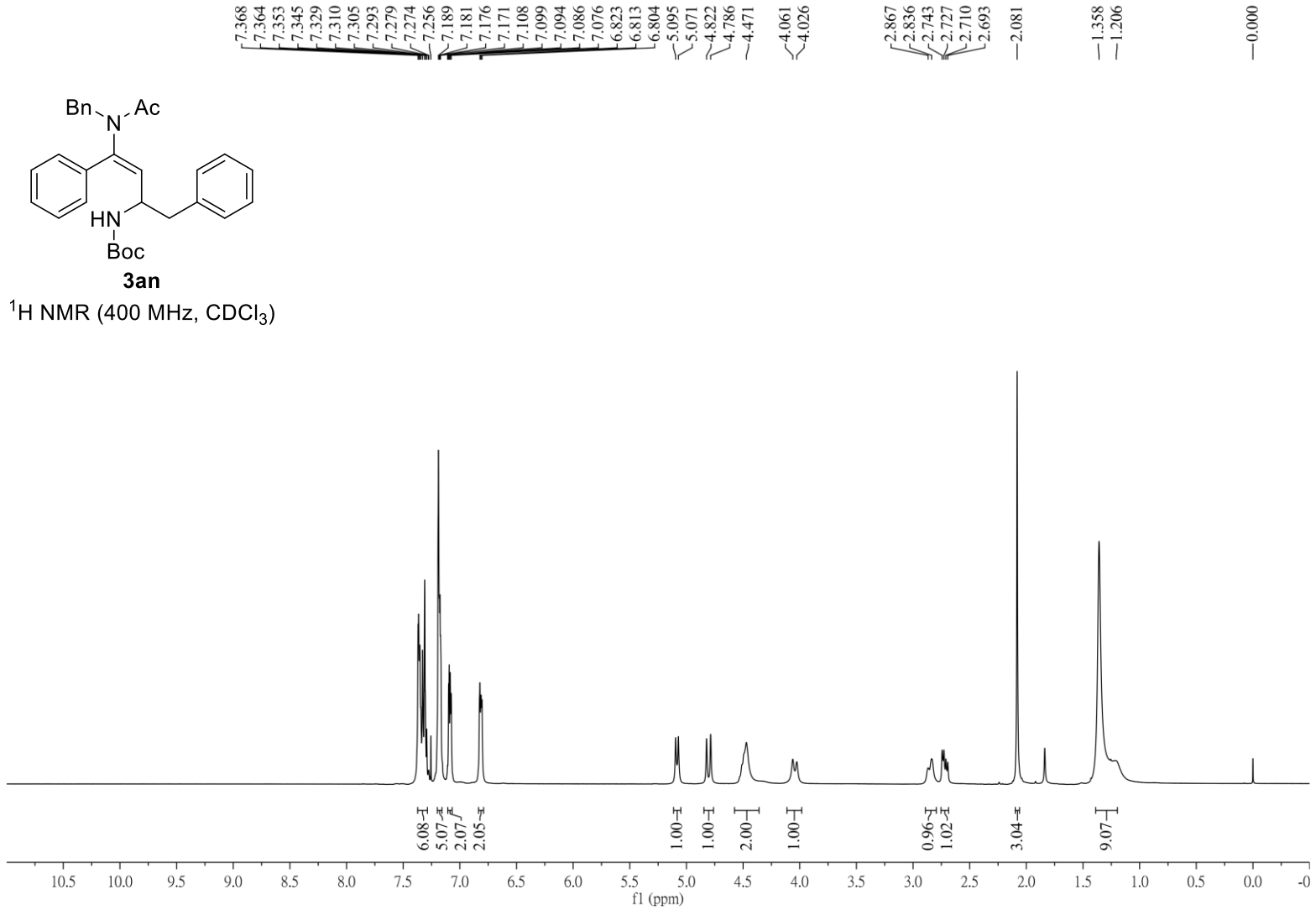
3am

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



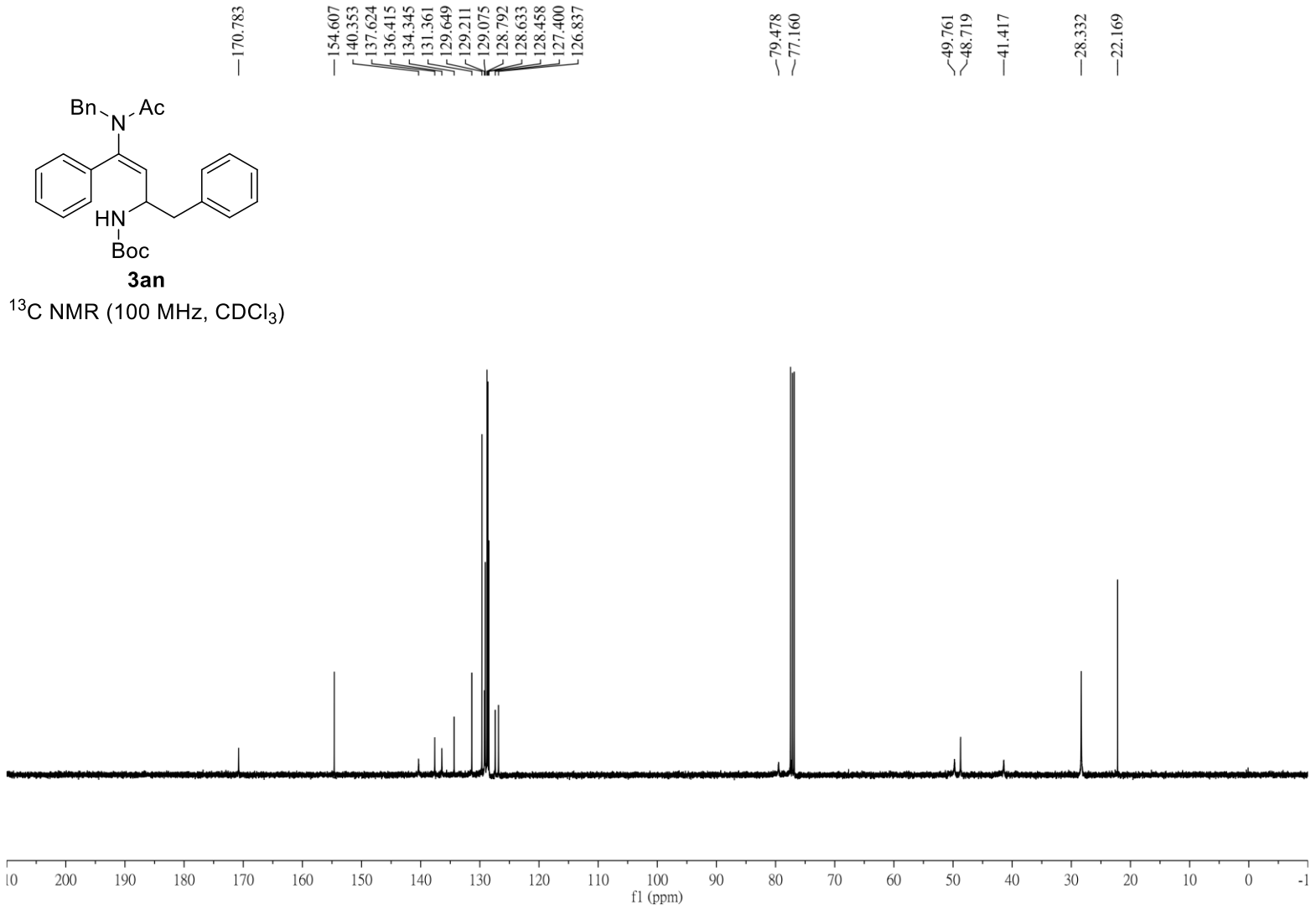
3am

^{13}C NMR (100 MHz, $CDCl_3$)



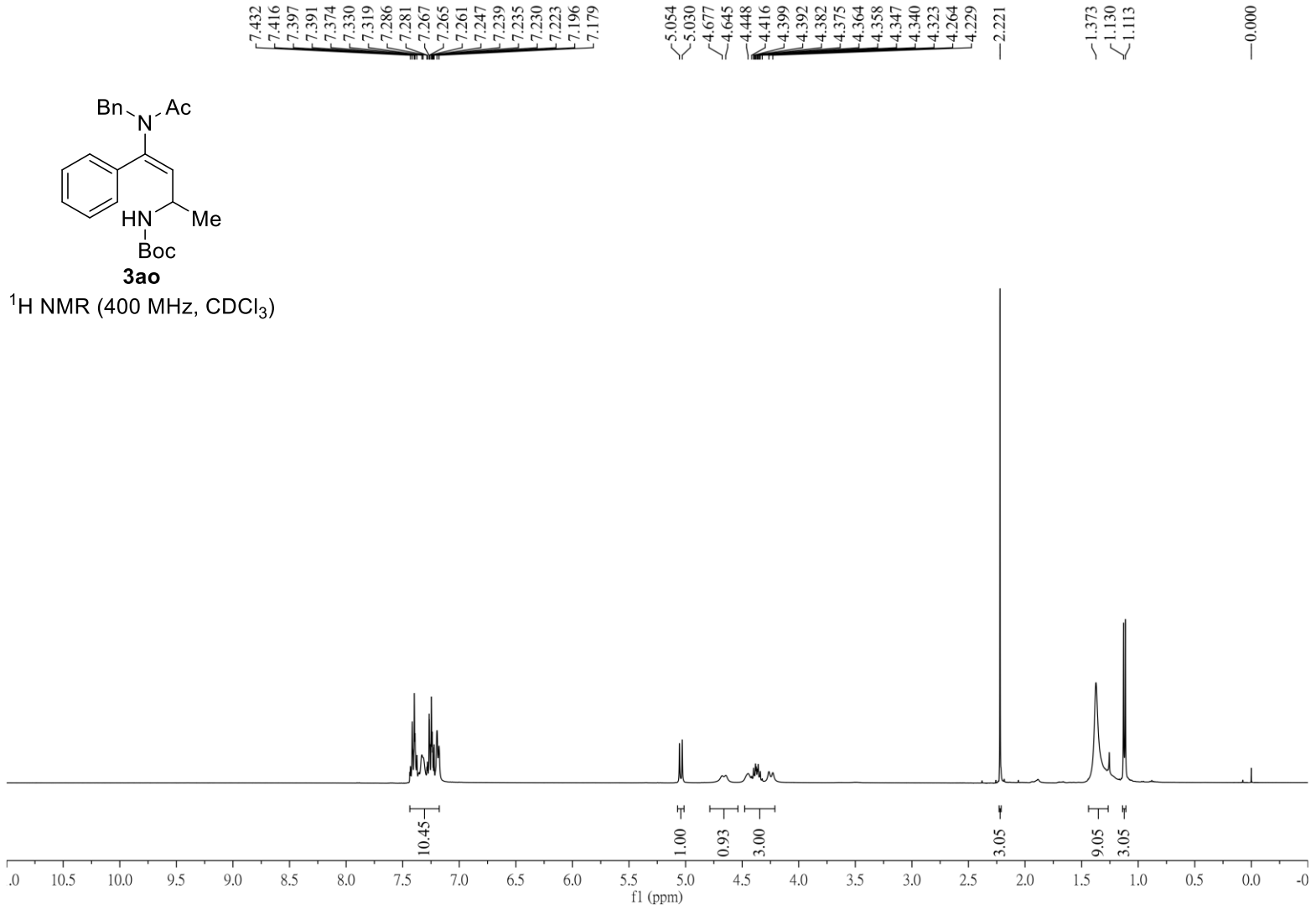
3an

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



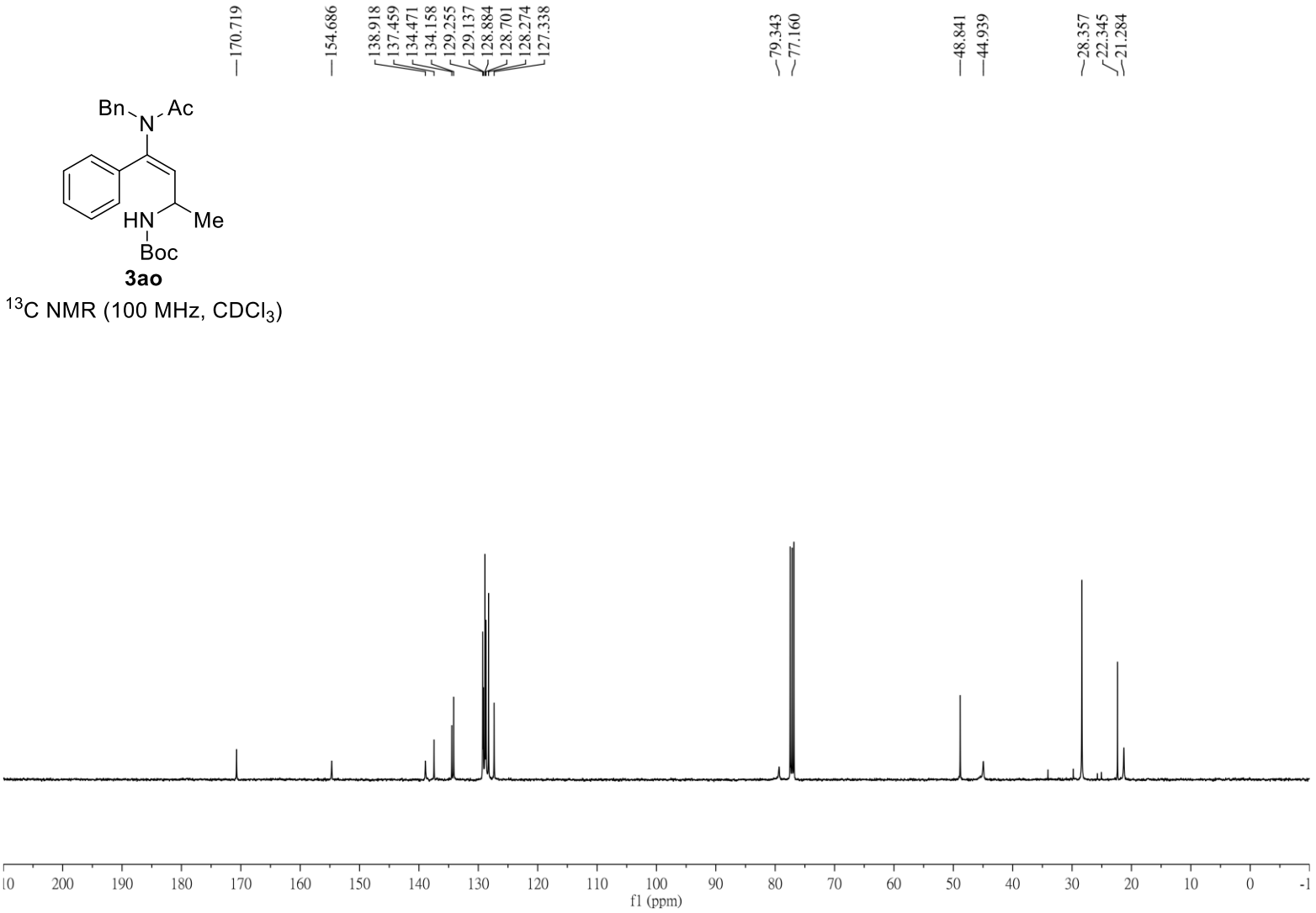
3an

^{13}C NMR (100 MHz, $CDCl_3$)



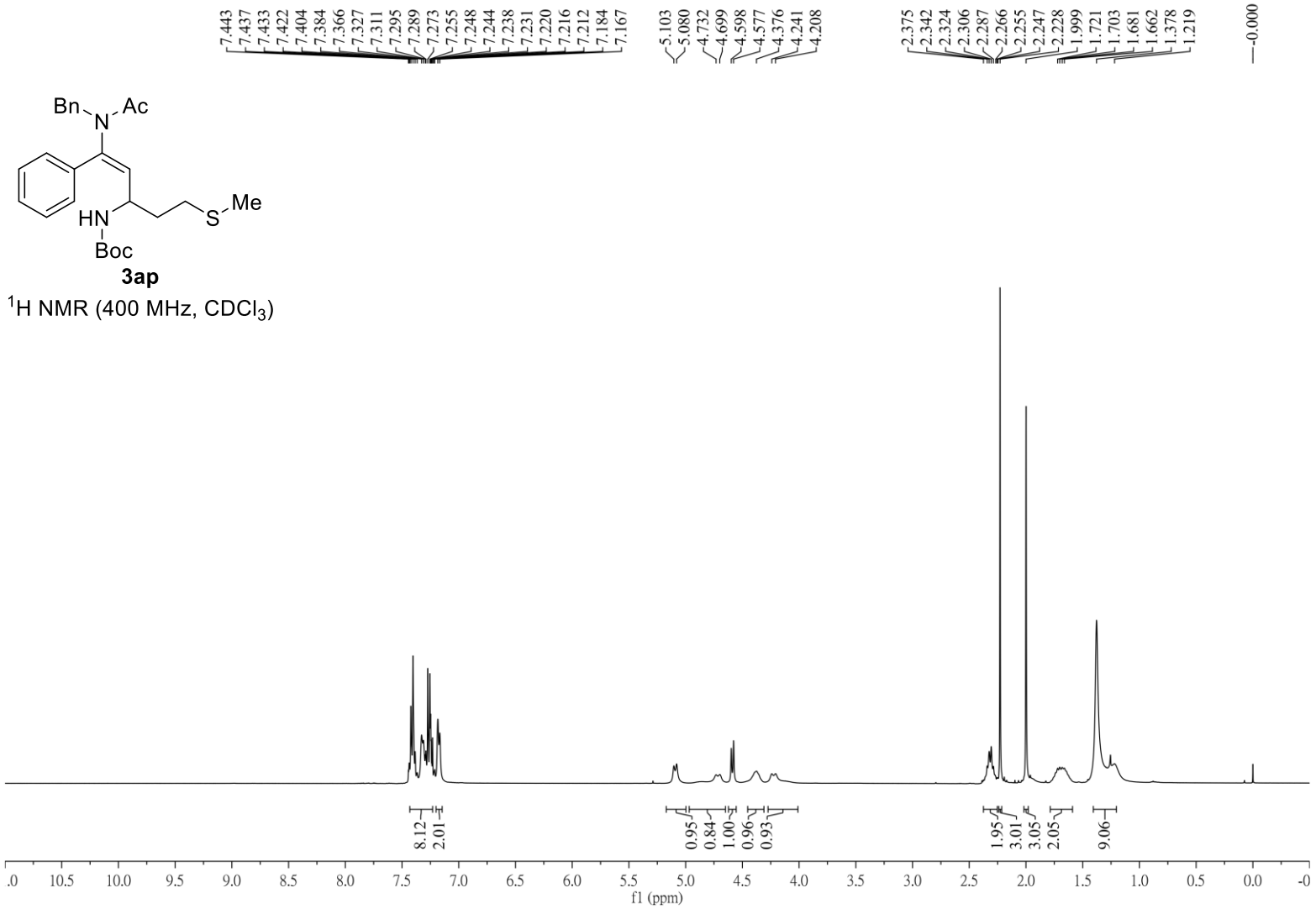
3ao

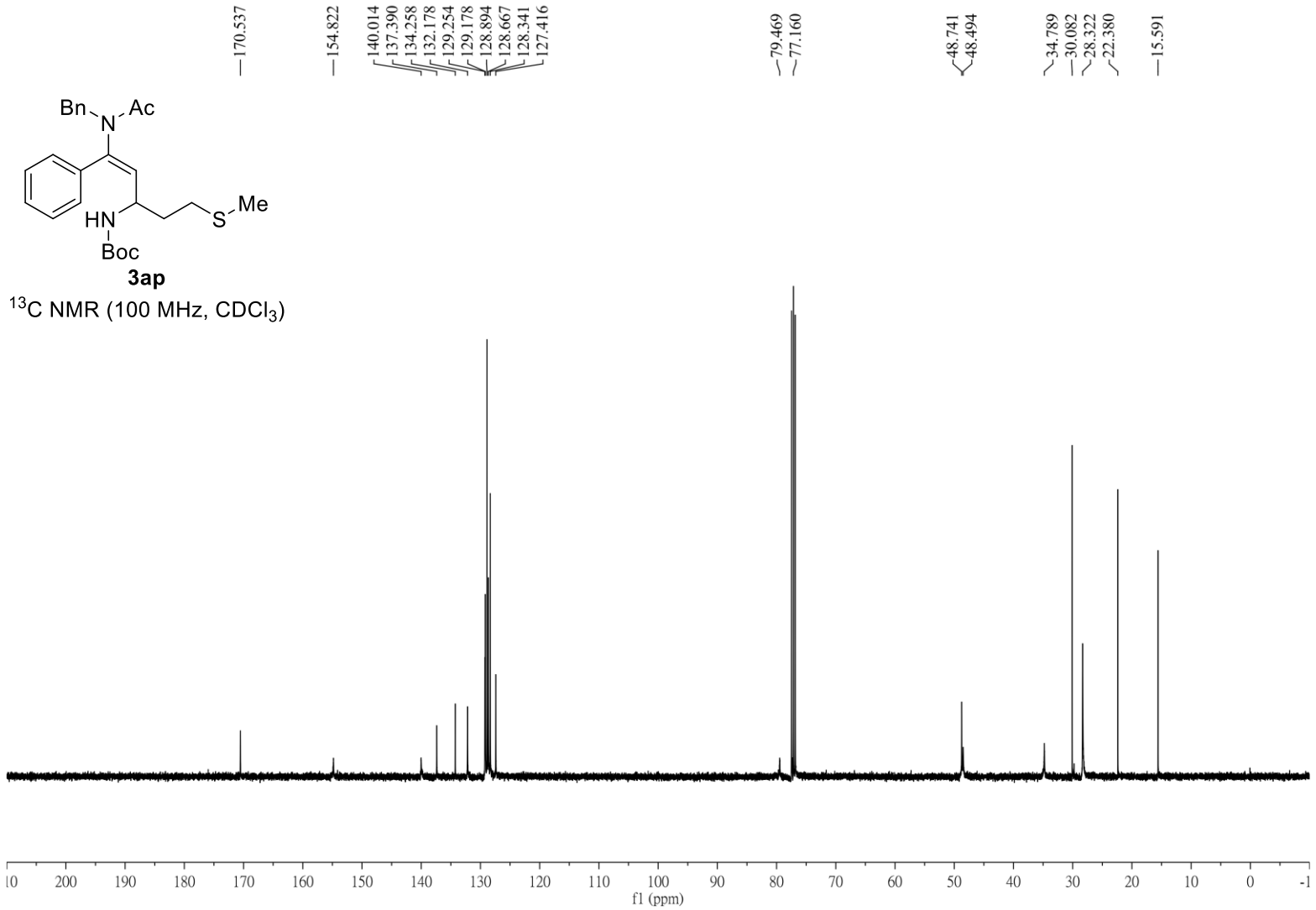
^{1}H NMR (400 MHz, $CDCl_3$)

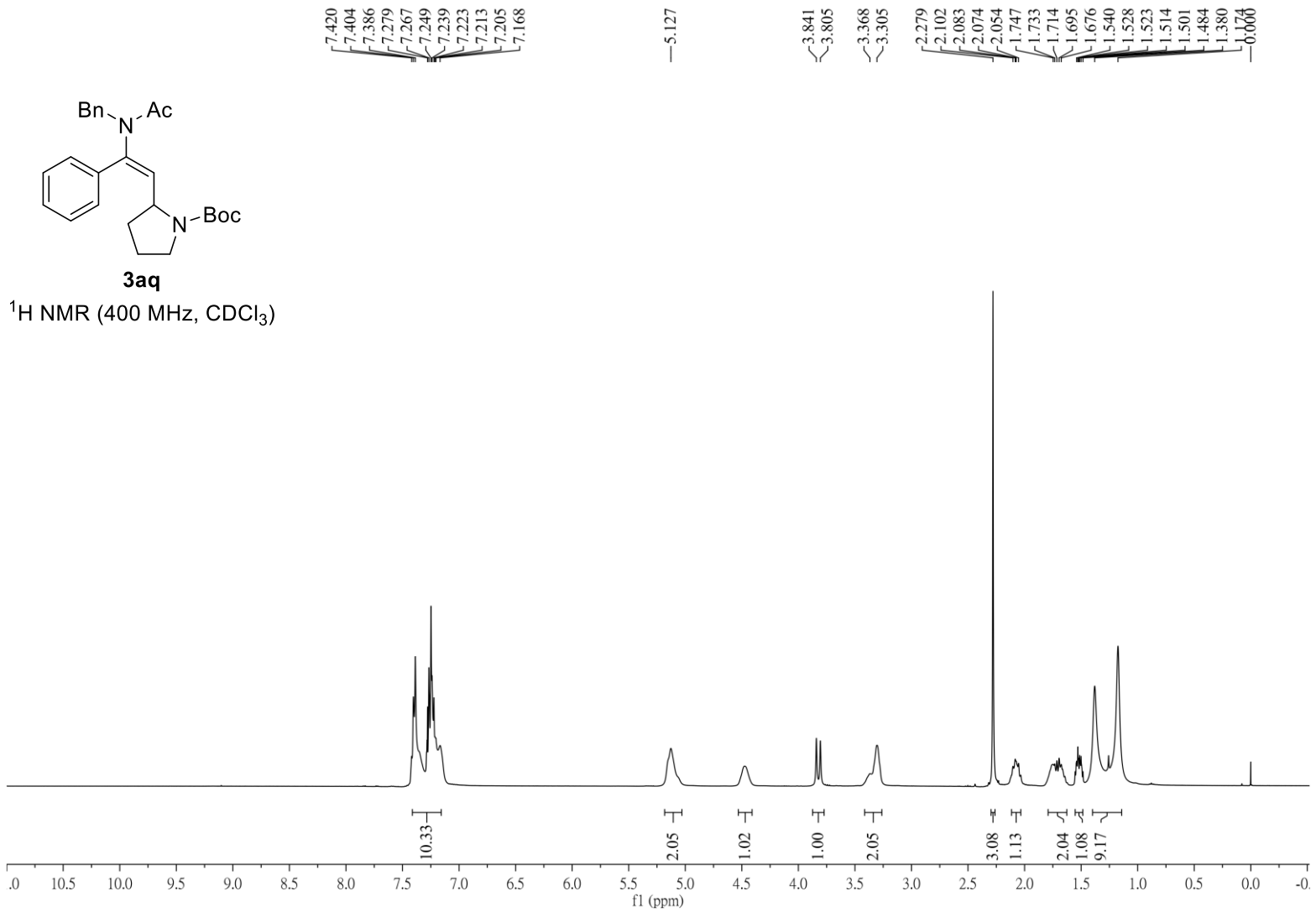


3ao

^{13}C NMR (100 MHz, $CDCl_3$)

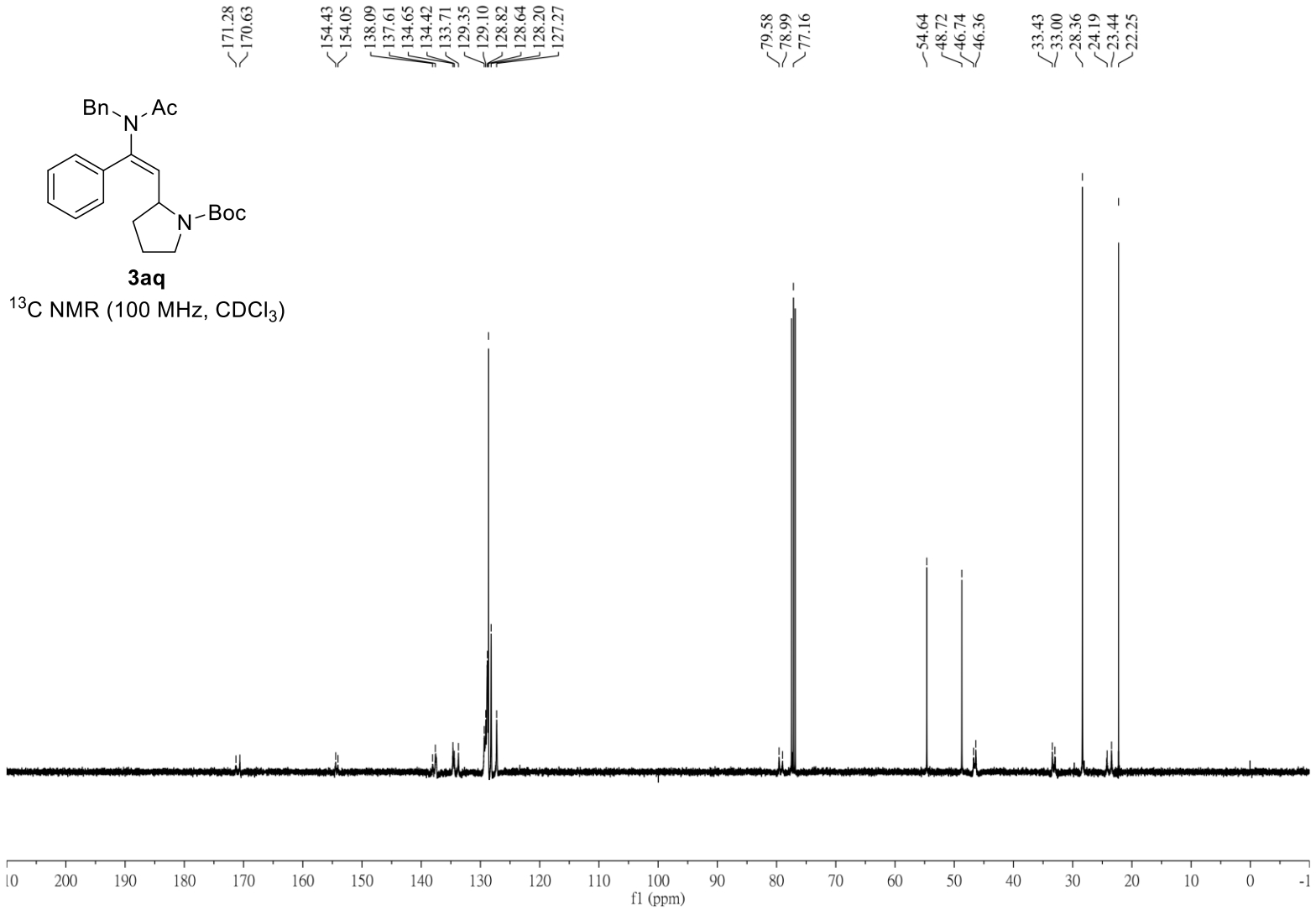

7.443
7.437
7.433
7.422
7.404
7.384
7.366
7.327
7.311
7.295
7.289
7.273
7.255
7.248
7.244
7.238
7.231
7.220
7.216
7.212
7.184
7.167
5.103
5.080
4.732
4.699
4.598
4.577
4.376
4.241
4.208
2.375
2.342
2.324
2.306
2.287
2.266
2.255
2.247
2.228
1.999
1.721
1.703
1.681
1.662
1.378
1.219
-0.000
Bn
N
Ac
HN
Boc
S
Me
3ap
1H NMR (400 MHz, CDCl3)
8.12
2.01
0.95
0.84
1.00
0.96
0.93
1.95
3.01
3.05
2.05
9.06
f1 (ppm)

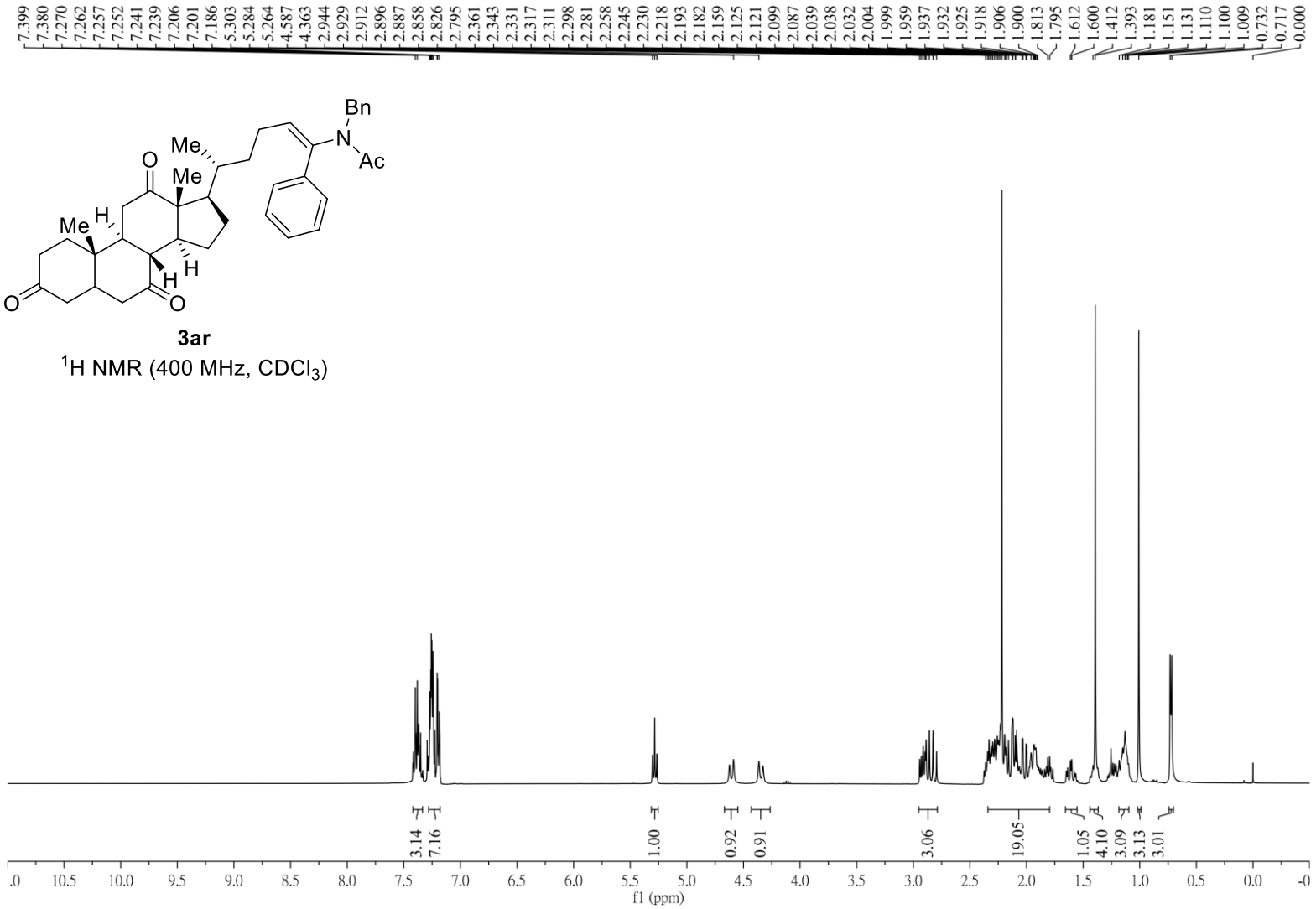

170.537
154.822
140.014
137.390
134.258
132.178
129.254
129.178
128.894
128.667
128.341
127.416
79.469
77.160
48.741
48.494
34.789
30.082
28.322
22.380
15.591
Bn
N
Ac
HN
Boc
S
Me
3ap
13C NMR (100 MHz, CDCl3)
f1 (ppm)



3aq

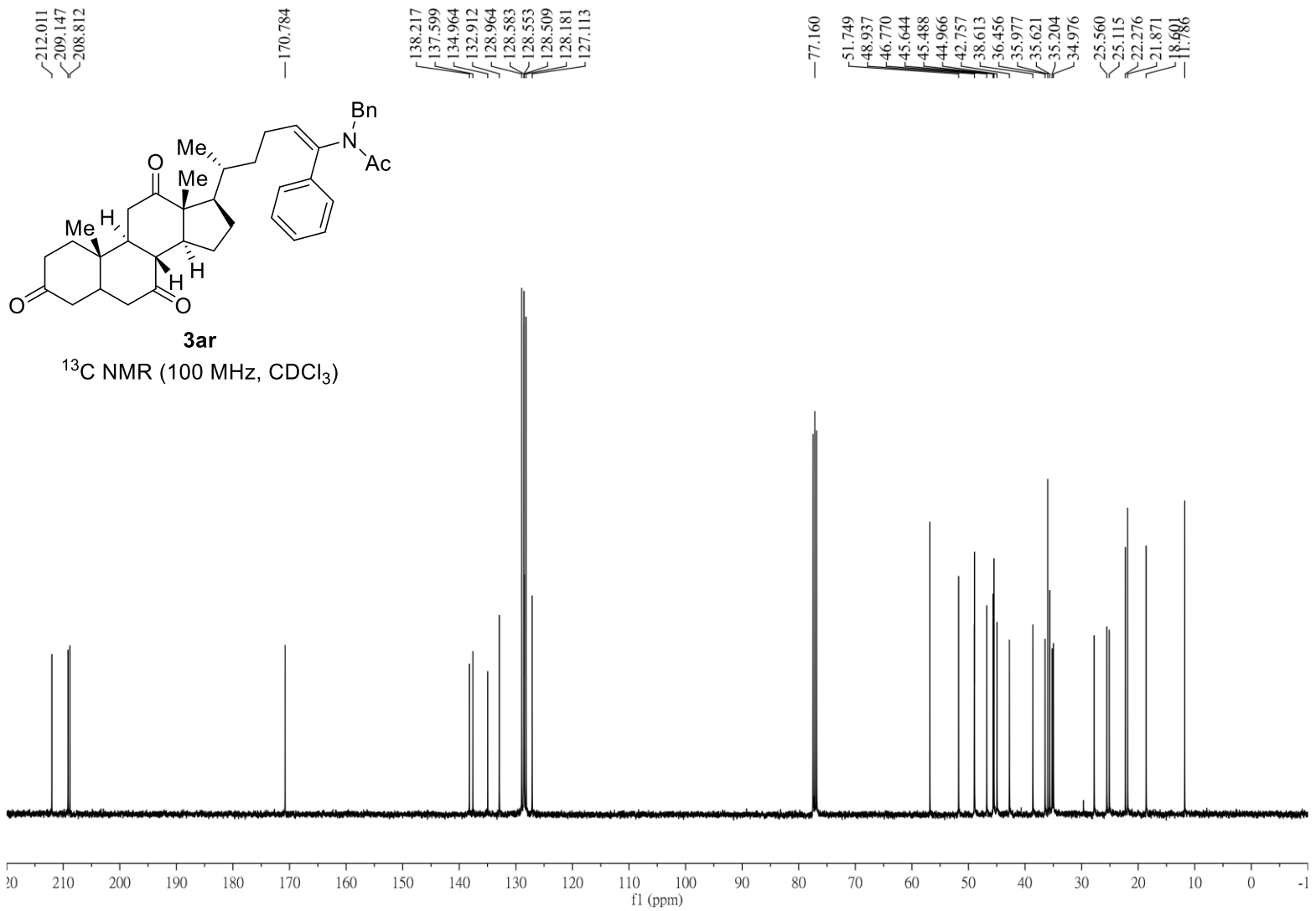
^{1}H NMR (400 MHz, $CDCl_3$)


171.28
170.63
154.43
154.05
138.09
137.61
134.65
134.42
133.71
129.35
129.10
128.82
128.64
128.20
127.27
79.58
78.99
77.16
54.64
48.72
46.74
46.36
33.43
33.00
28.36
24.19
23.44
22.25
Bn
N
Ac
N
Boc
3aq
^{13}C NMR (100 MHz, $CDCl_3$)
f1 (ppm)



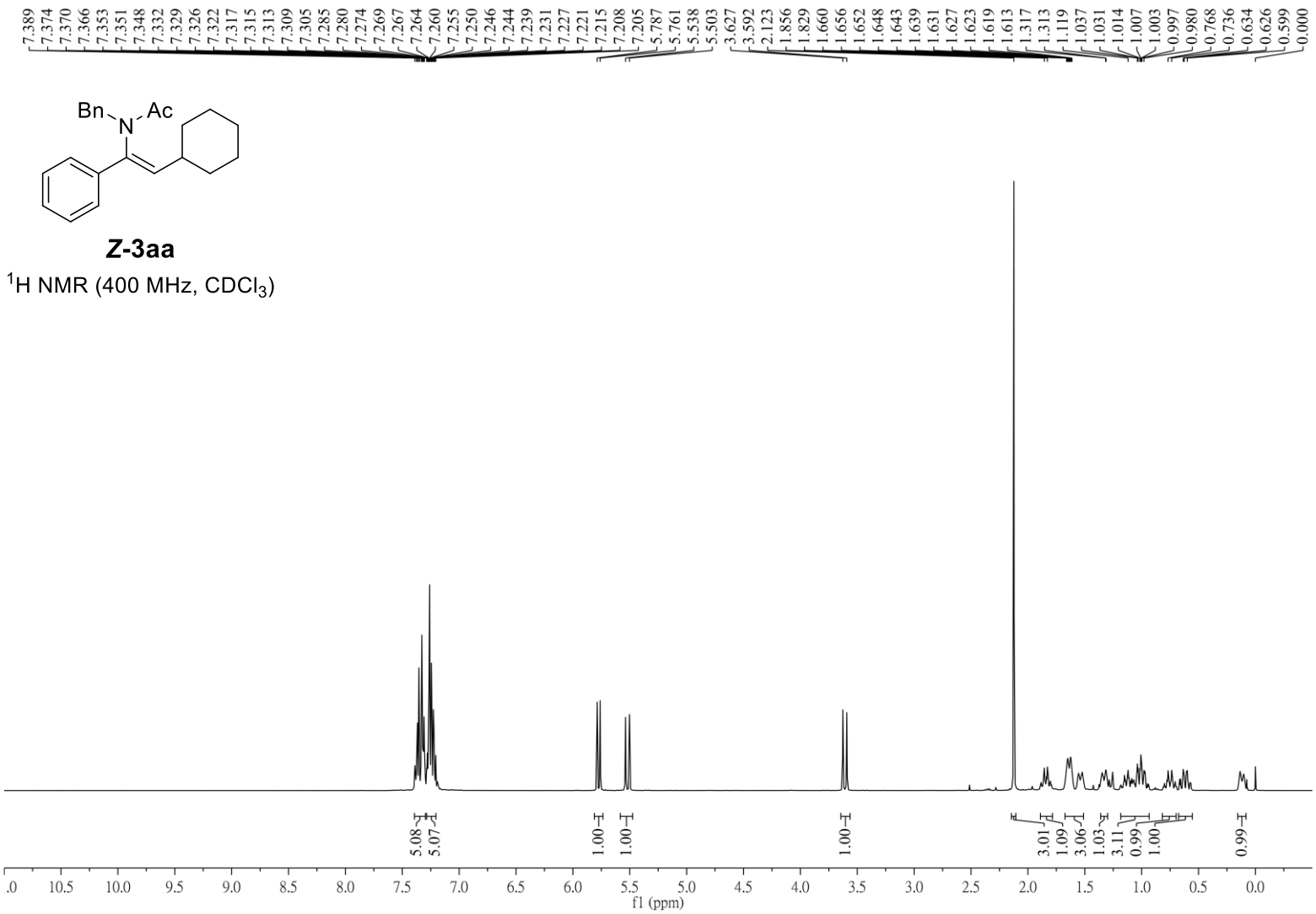
3ar

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



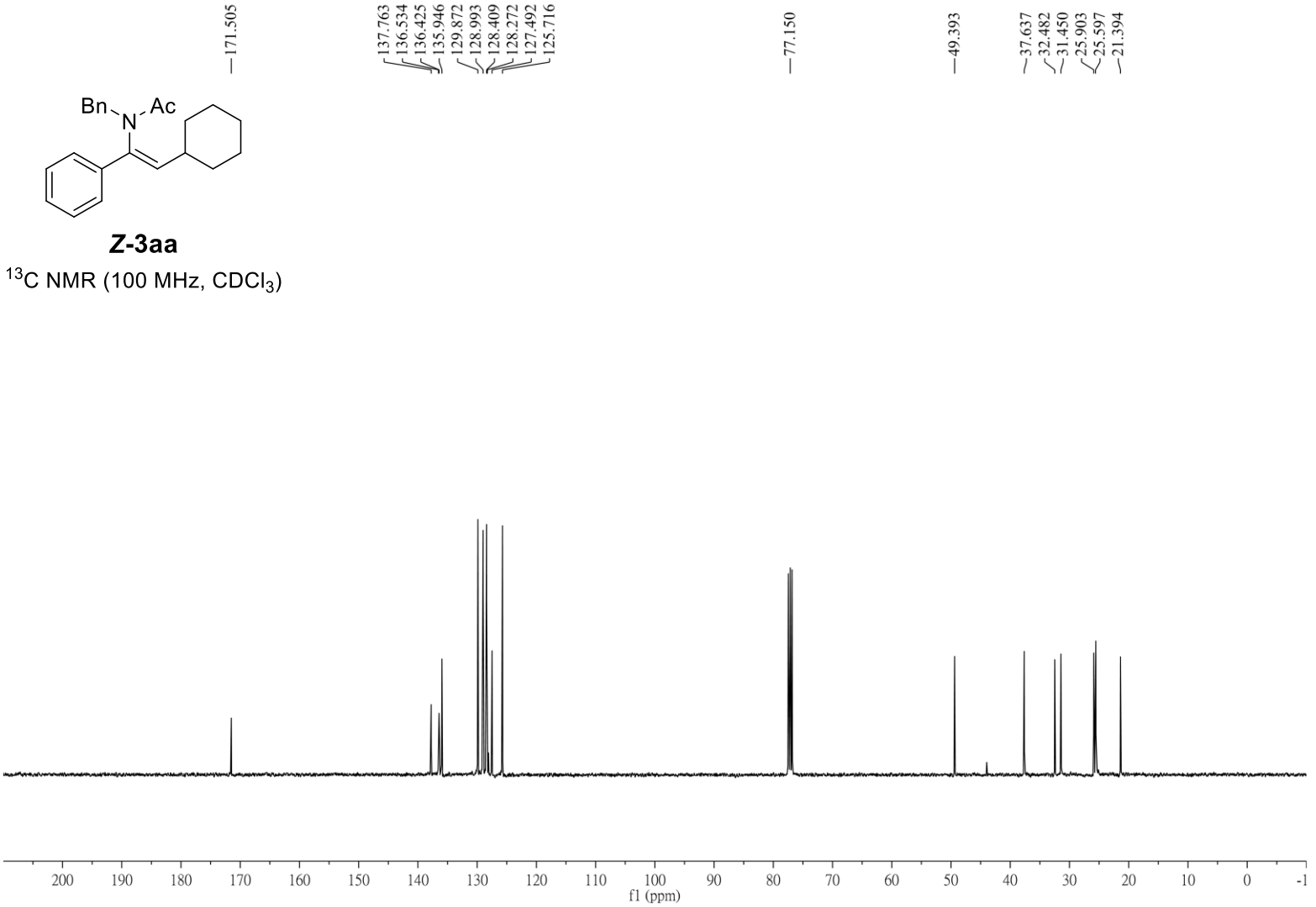
3ar

^{13}C NMR (100 MHz, $CDCl_3$)



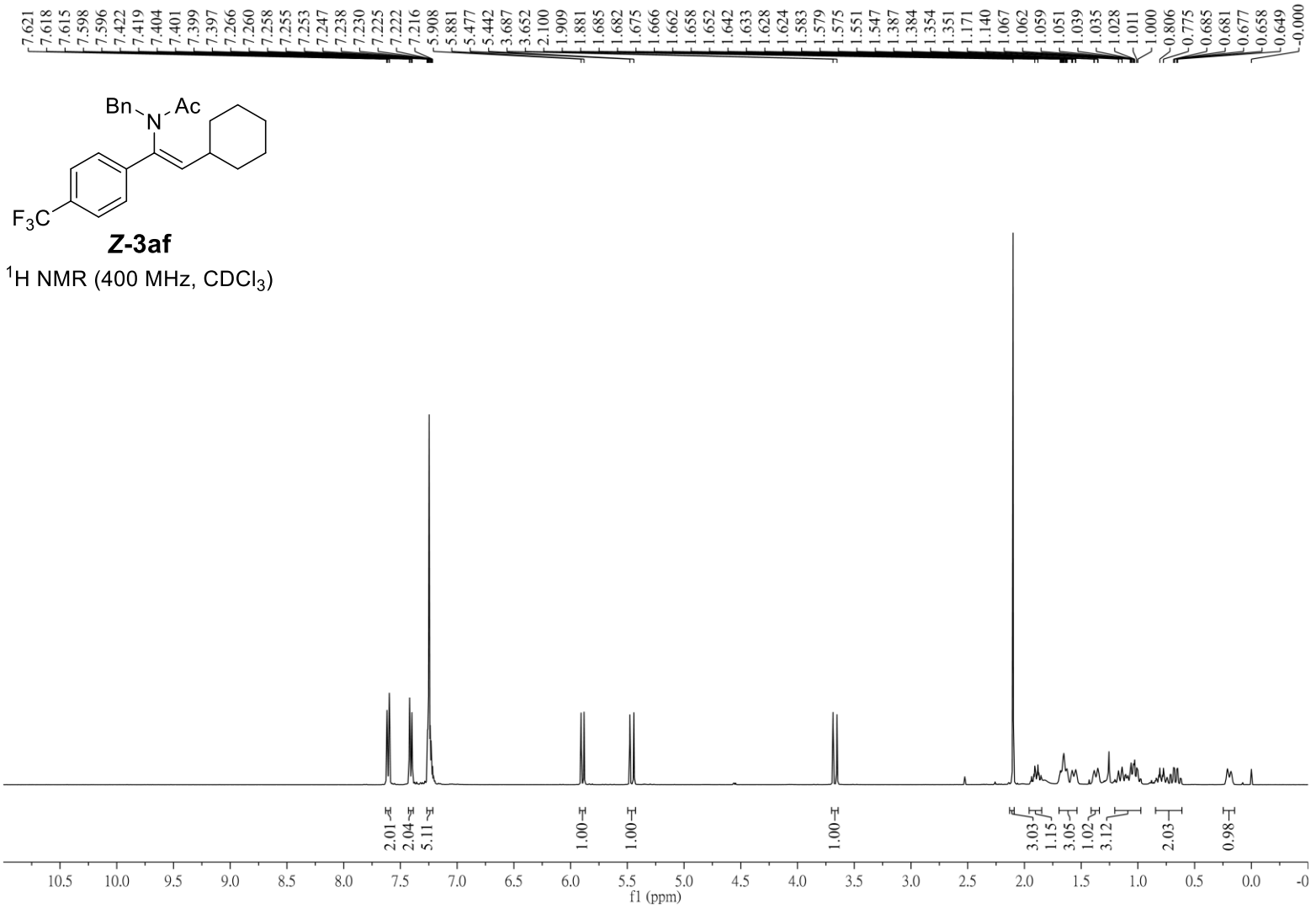
***Z*-3aa**

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



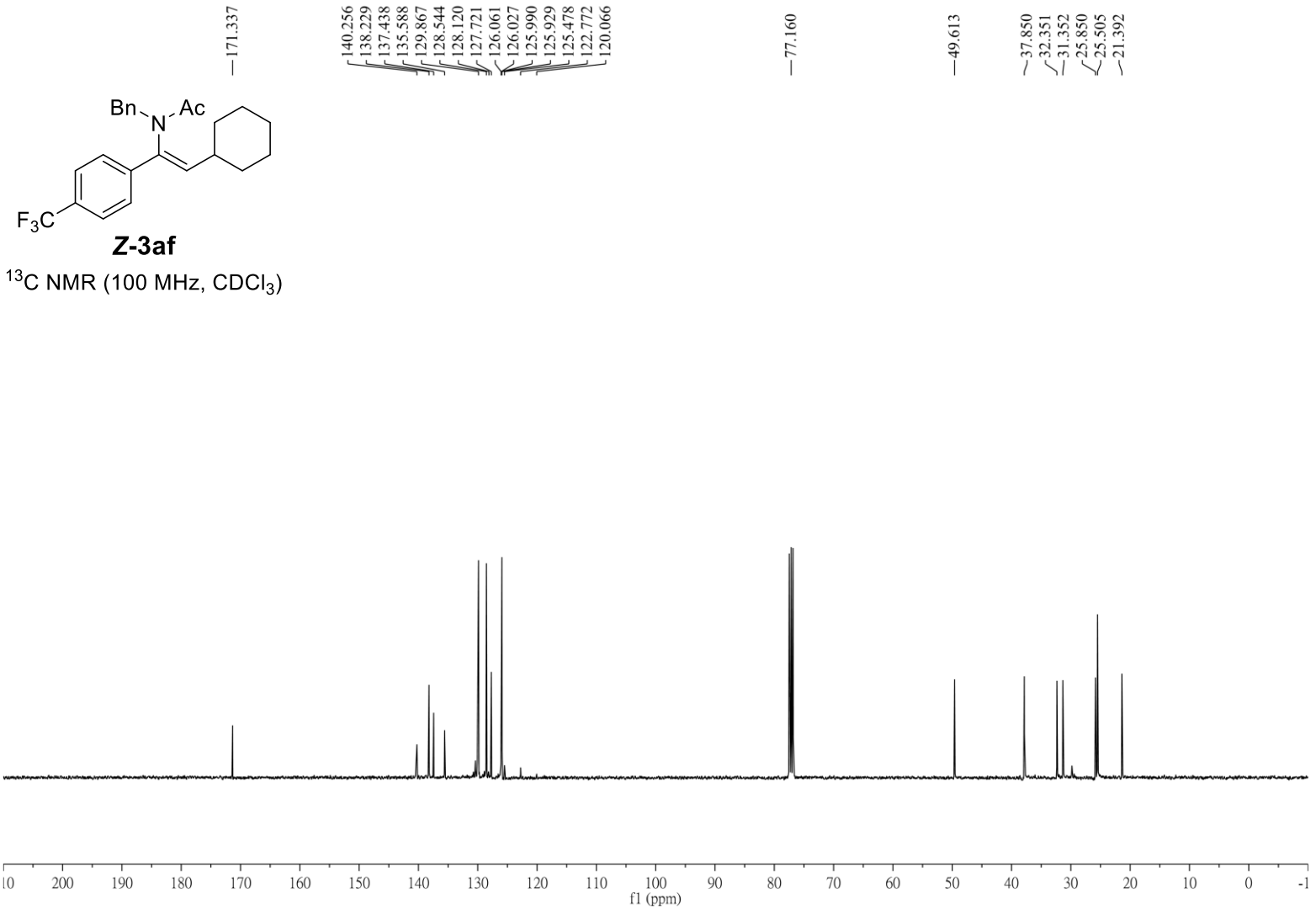
***Z*-3aa**

^{13}C NMR (100 MHz, $CDCl_3$)



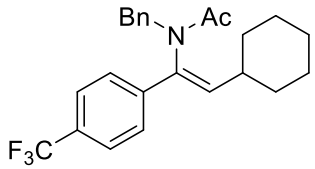
***Z*-3af**

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



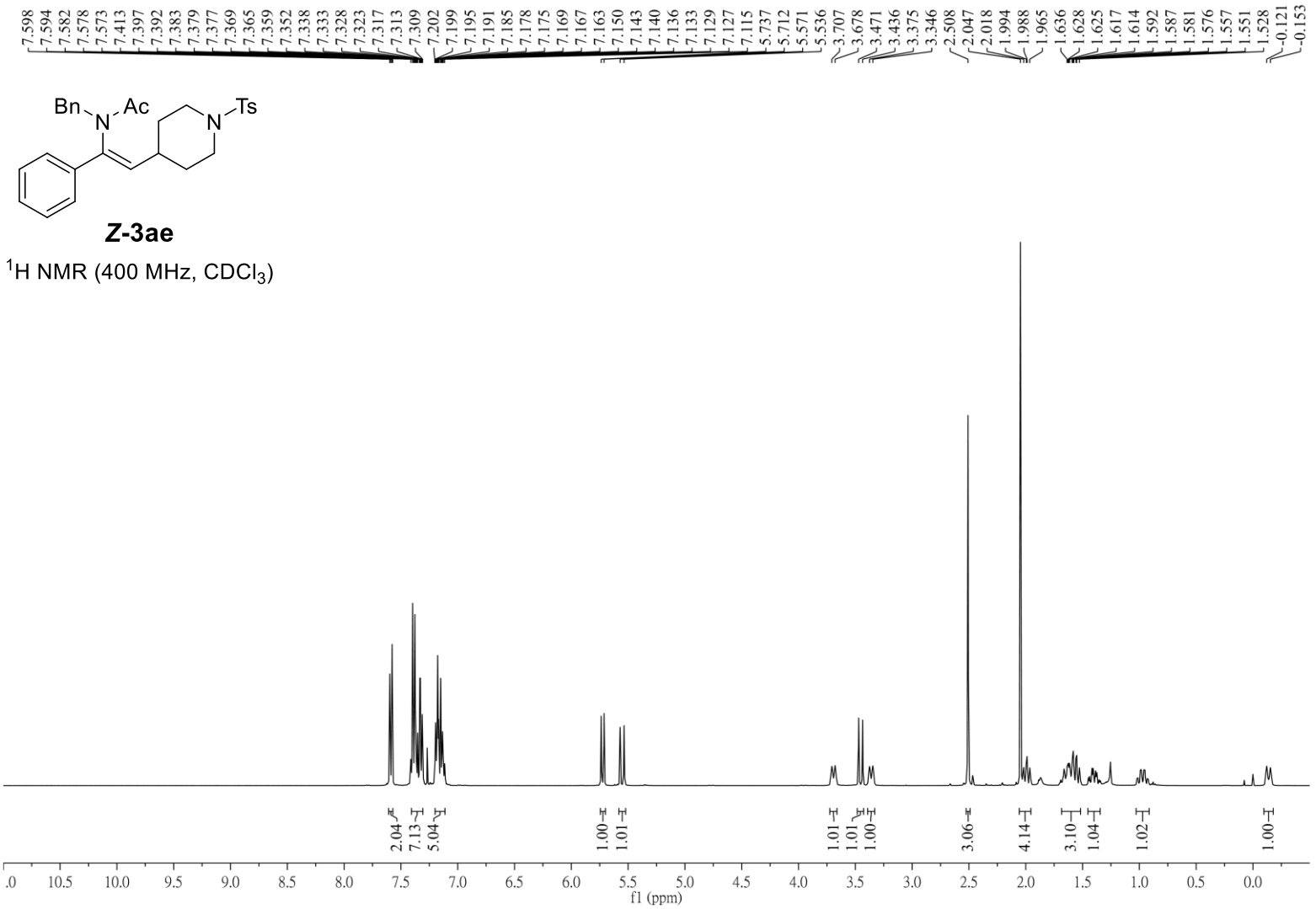
***Z*-3af**

^{13}C NMR (100 MHz, $CDCl_3$)



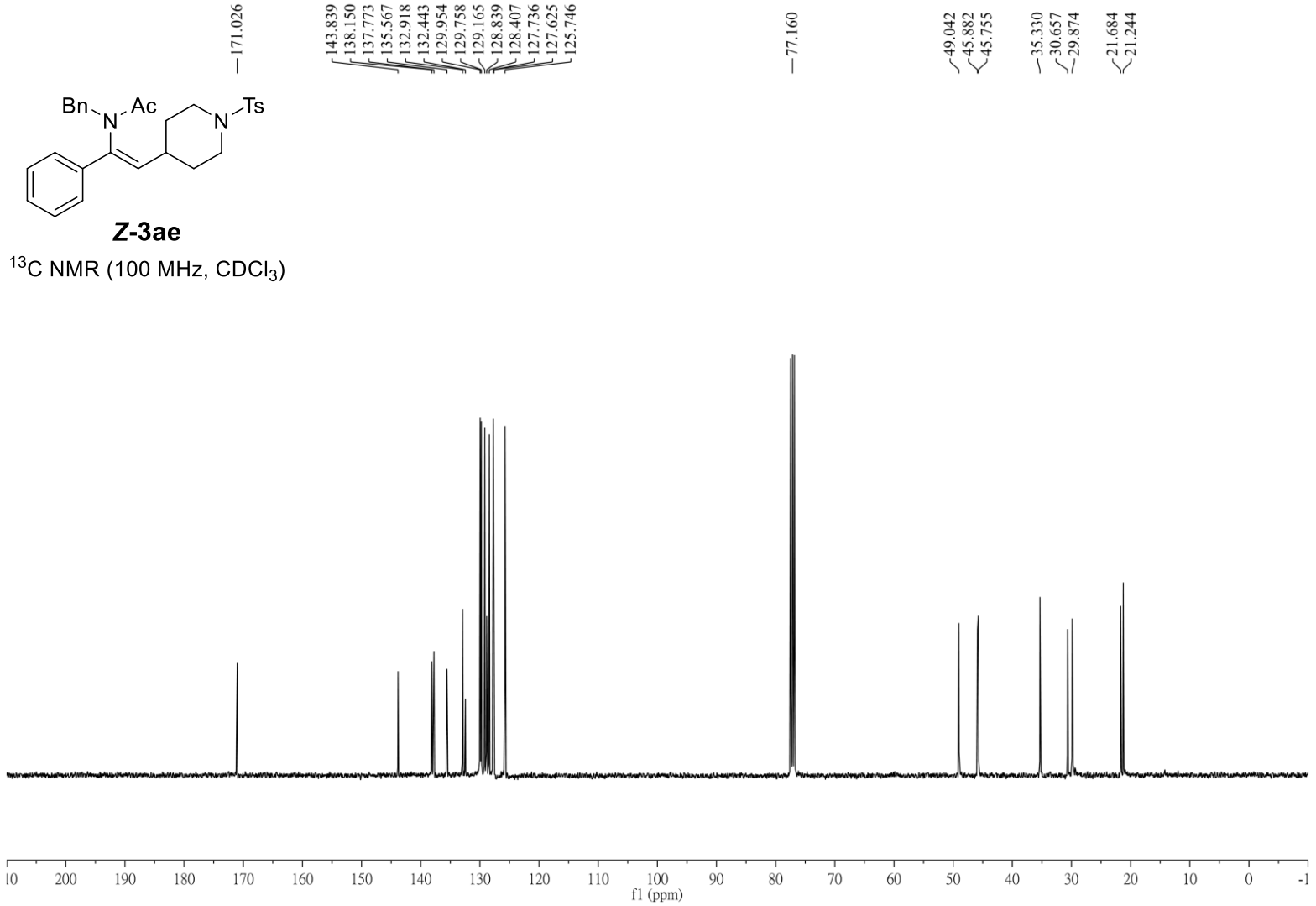
***Z*-3af**

^{19}F NMR (376 MHz, $CDCl_3$)



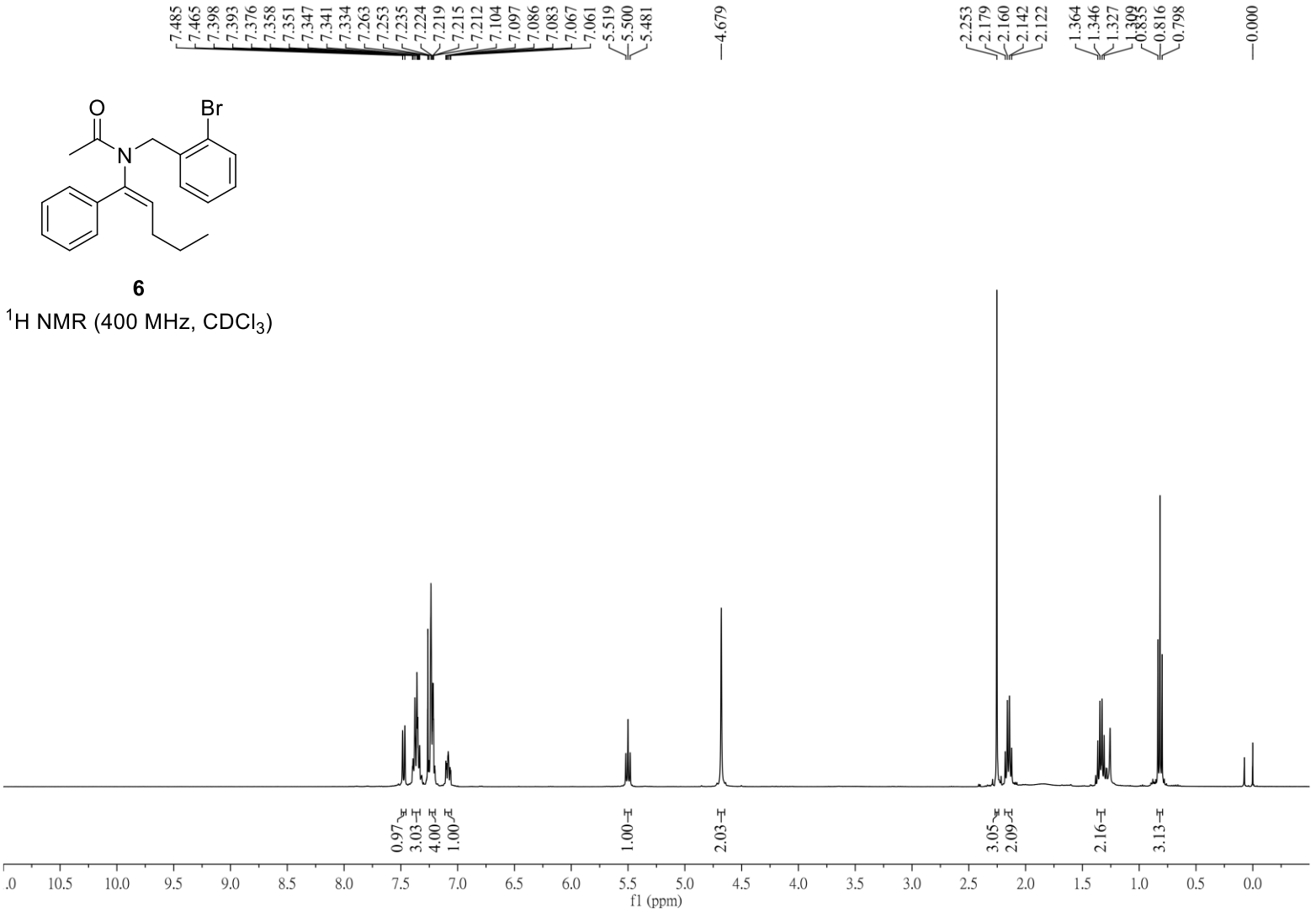
***Z*-3ae**

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



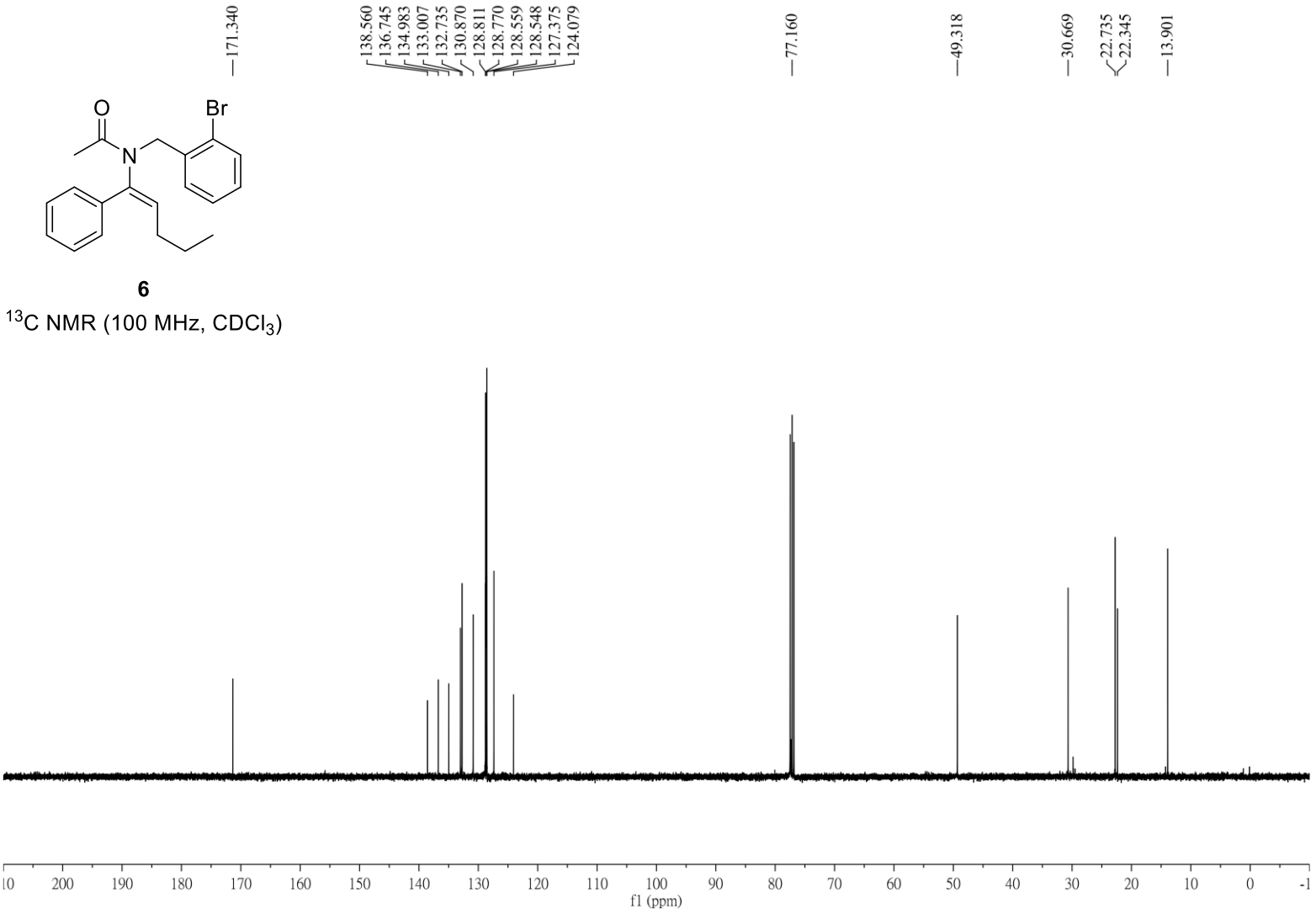
***Z*-3ae**

^{13}C NMR (100 MHz, $CDCl_3$)



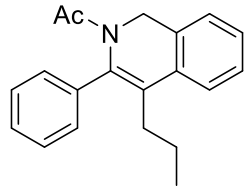
6

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



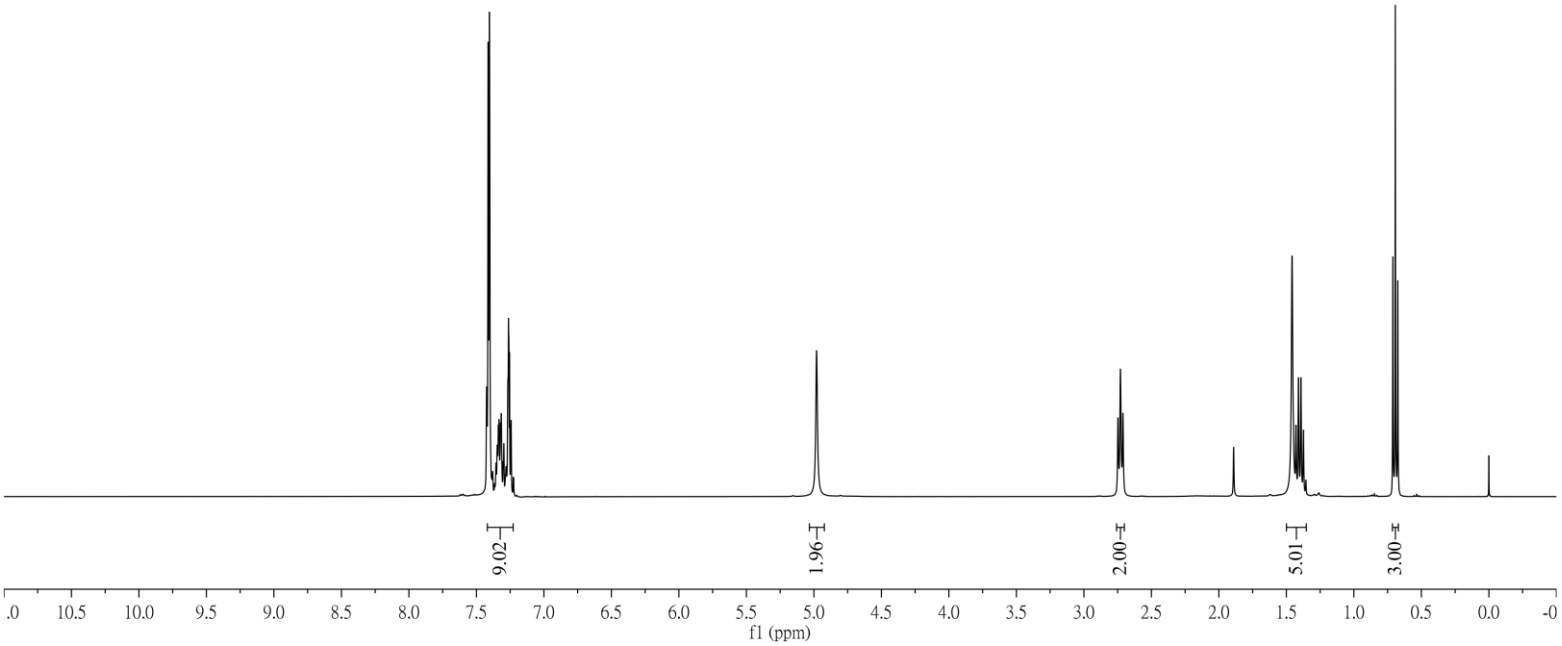
6

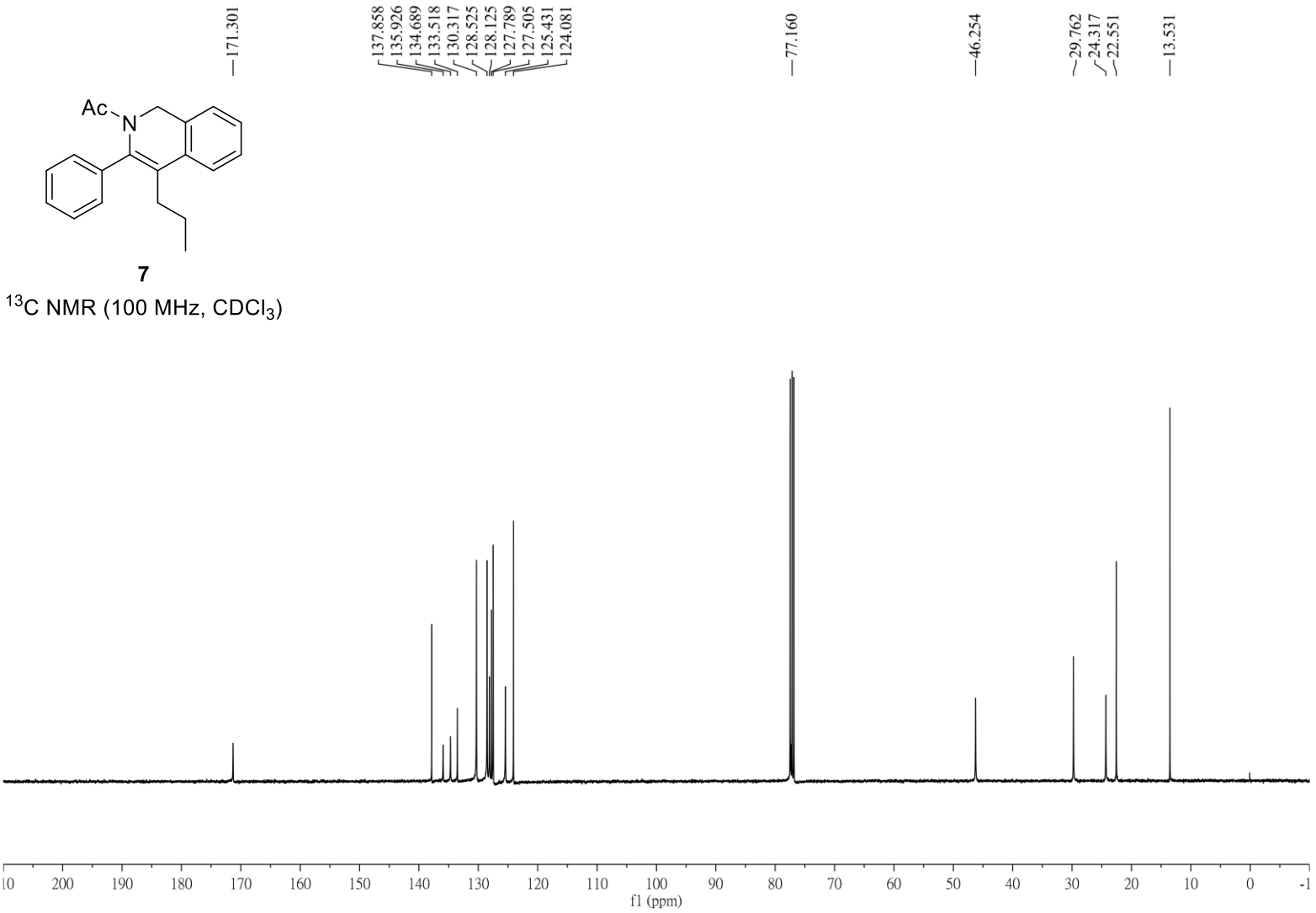
^{13}C NMR (100 MHz, $CDCl_3$)



7

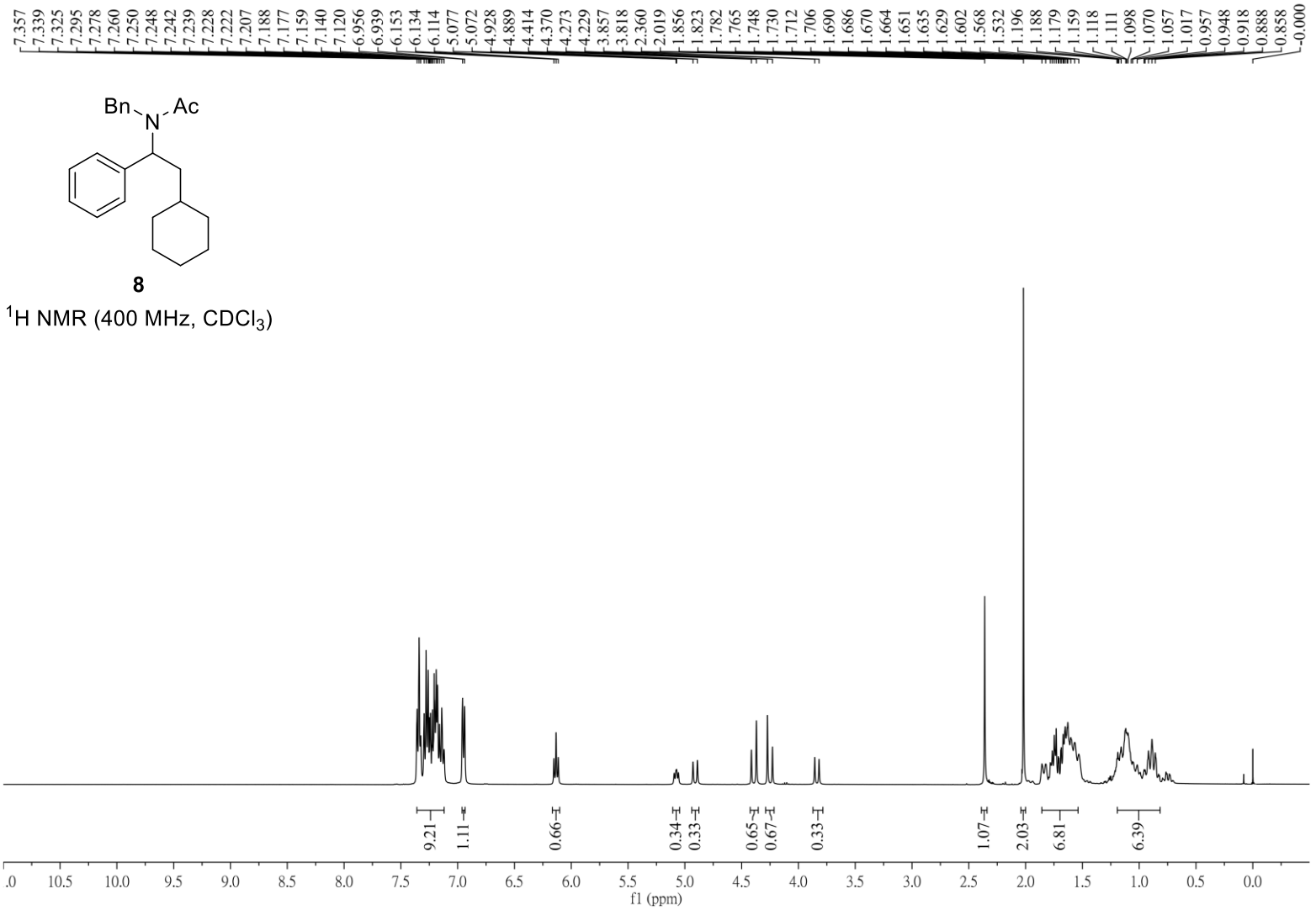
^{1}H NMR (400 MHz, $CDCl_3$)

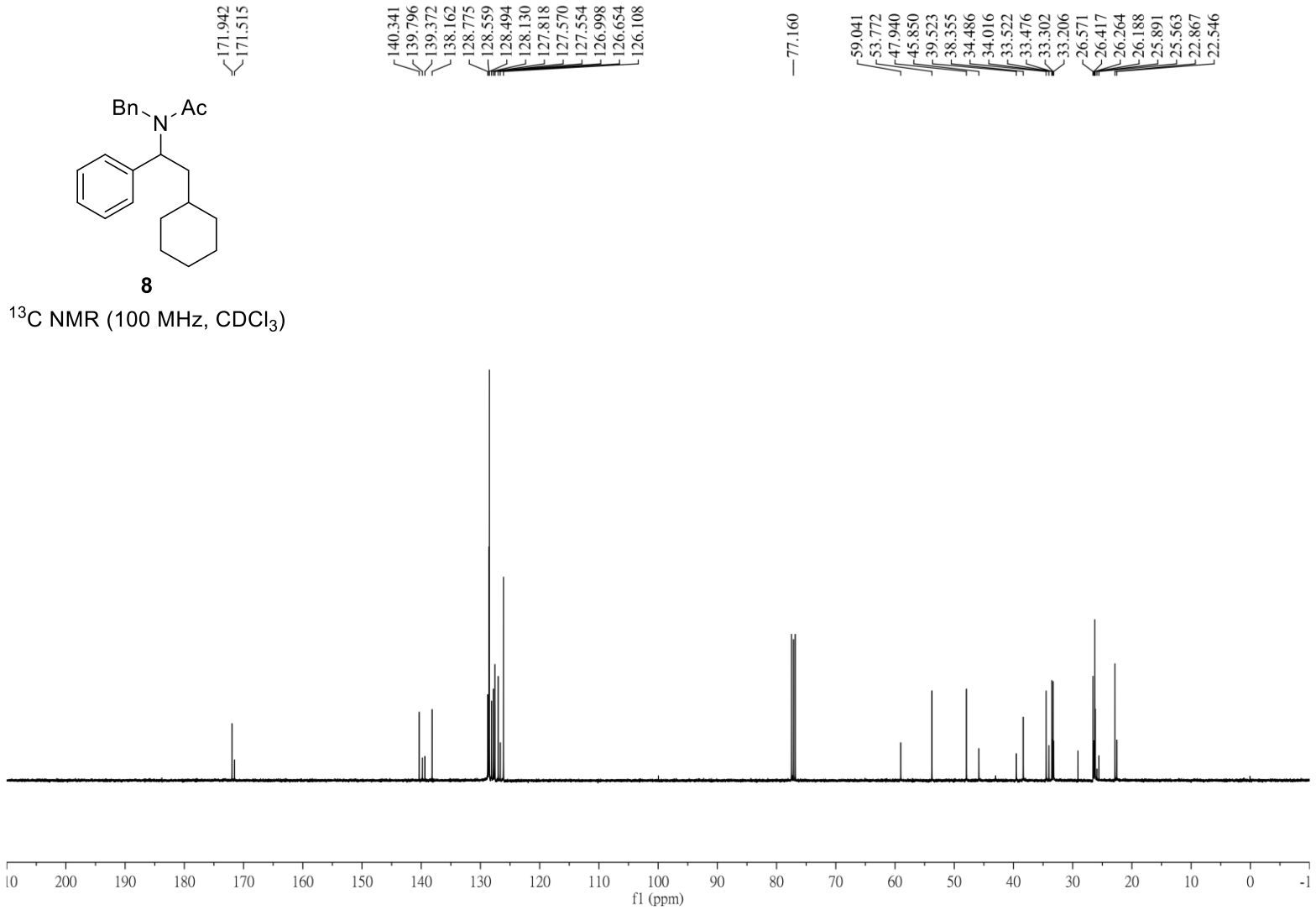


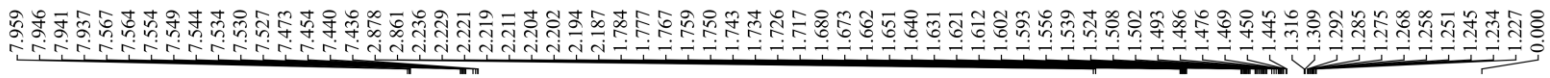


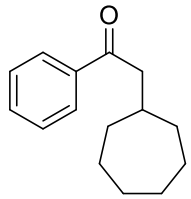
7

^{13}C NMR (100 MHz, $CDCl_3$)


7.357
7.339
7.325
7.295
7.278
7.260
7.250
7.248
7.242
7.239
7.228
7.222
7.207
7.188
7.177
7.159
7.140
7.120
6.956
6.939
6.153
6.134
6.114
5.077
5.072
4.928
4.889
4.414
4.370
4.273
4.229
3.857
3.818
2.360
2.019
1.856
1.823
1.782
1.765
1.748
1.730
1.712
1.706
1.690
1.686
1.670
1.664
1.651
1.635
1.629
1.602
1.568
1.532
1.196
1.188
1.179
1.159
1.118
1.111
1.098
1.070
1.057
1.017
0.957
0.948
0.918
0.888
0.858
-0.000
Bn
N
Ac
8
1H NMR (400 MHz, CDCl3)
9.21
1.11
0.66
0.34
0.33
0.65
0.67
0.33
1.07
2.03
6.81
6.39
f1 (ppm)

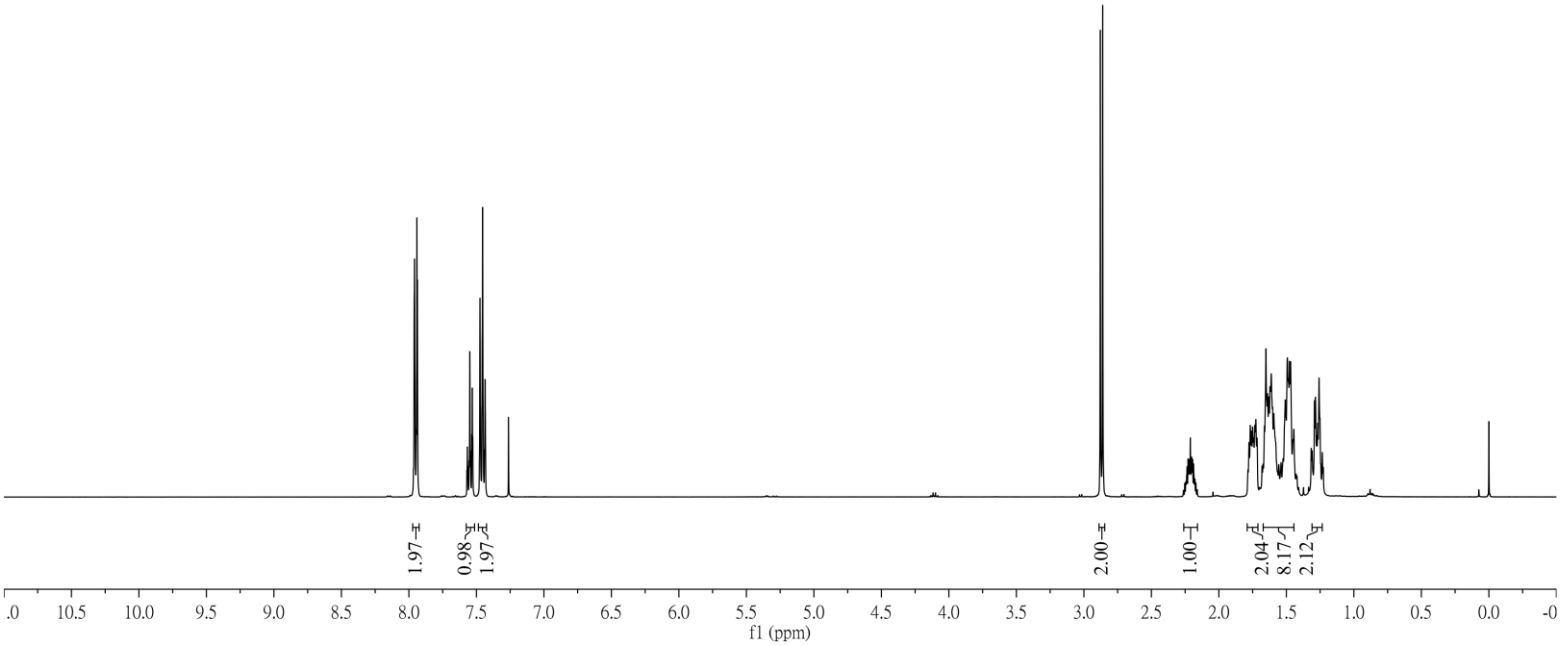

171.942
171.515
140.341
139.796
139.372
138.162
128.775
128.559
128.494
128.130
127.818
127.570
127.554
126.998
126.654
126.108
77.160
59.041
53.772
47.940
45.850
39.523
38.355
34.486
34.016
33.522
33.476
33.302
33.206
26.571
26.417
26.264
26.188
25.891
25.563
22.867
22.546
Bn
N
Ac
8
13C NMR (100 MHz, CDCl3)
f1 (ppm)

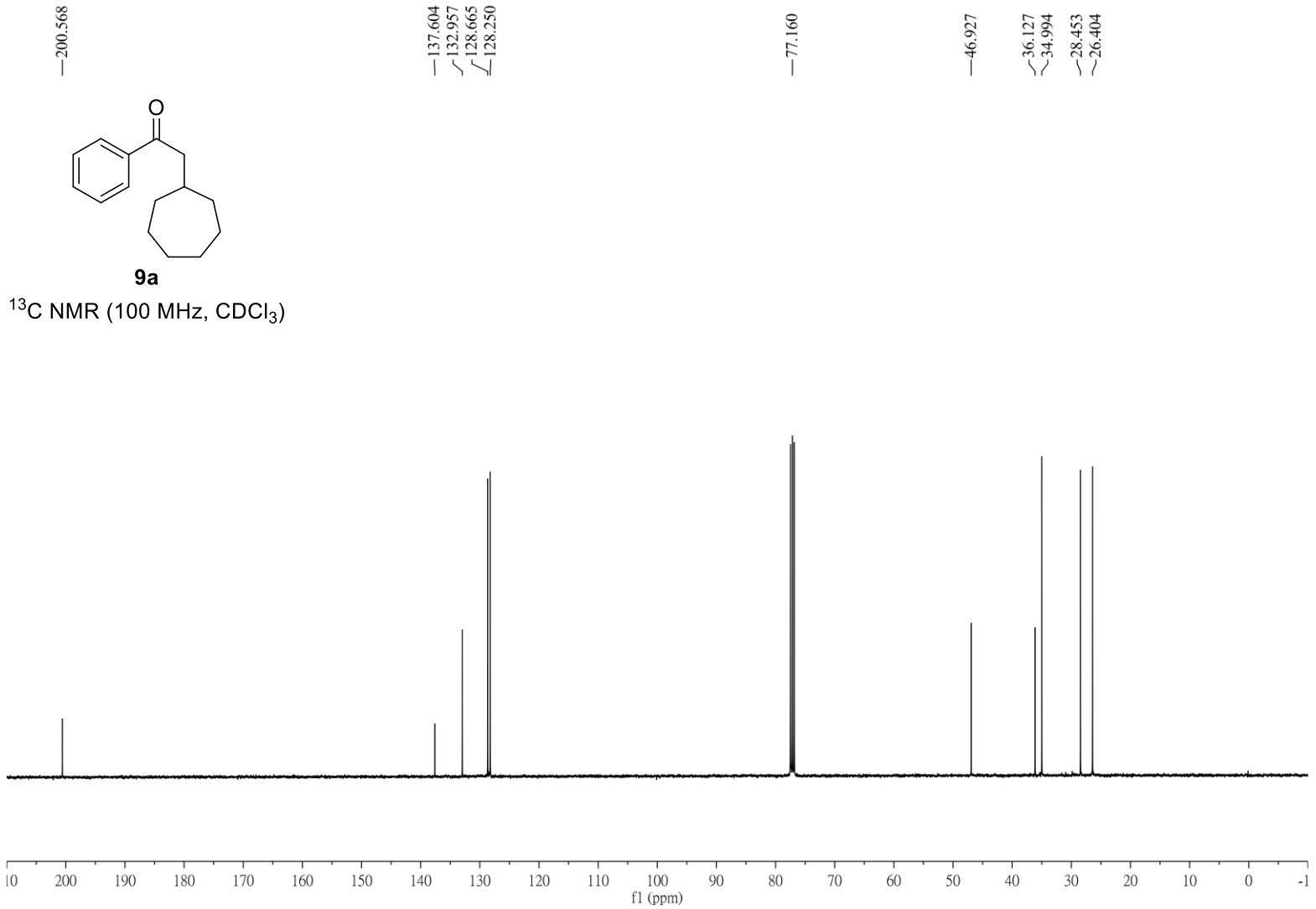


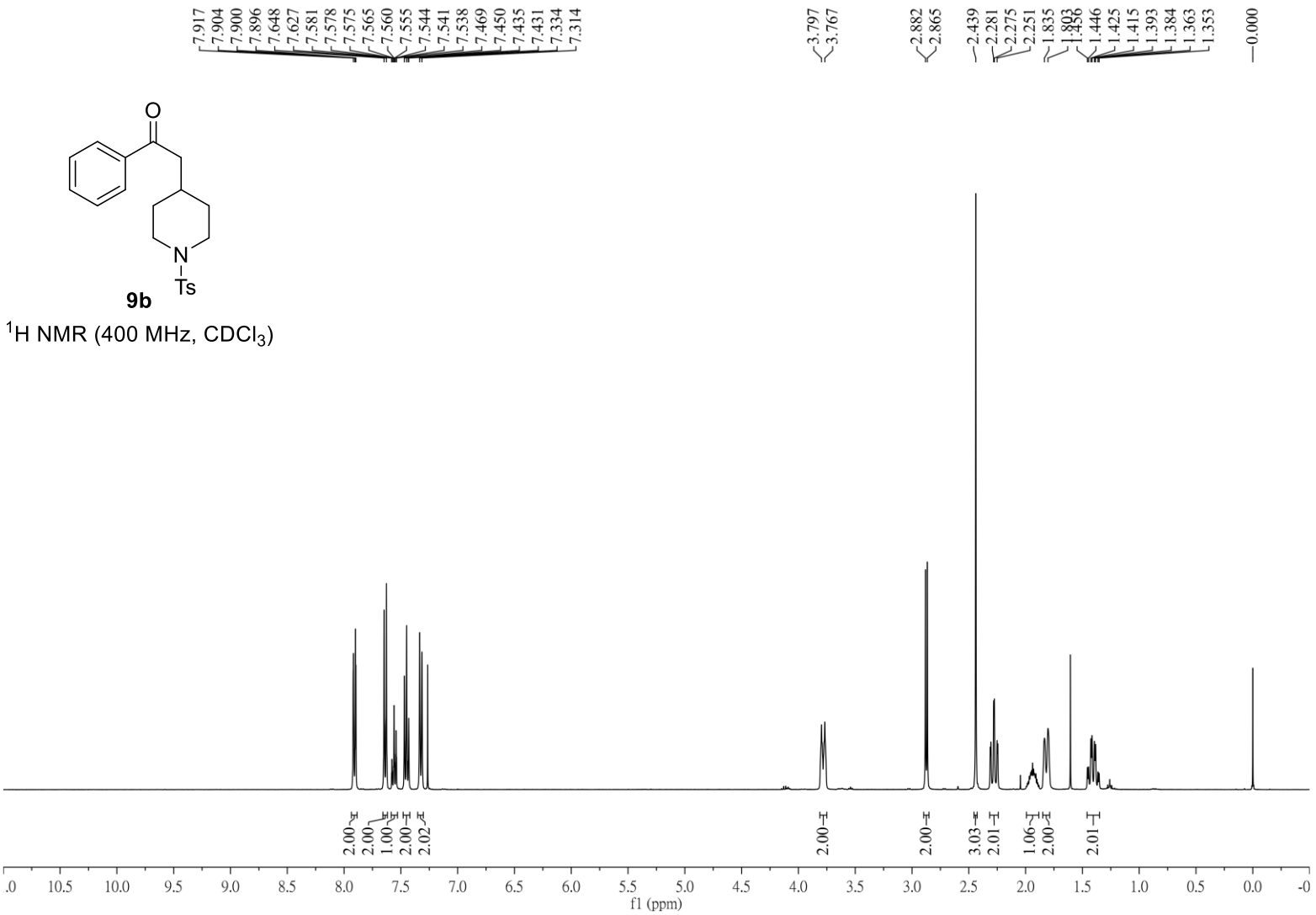


9a

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

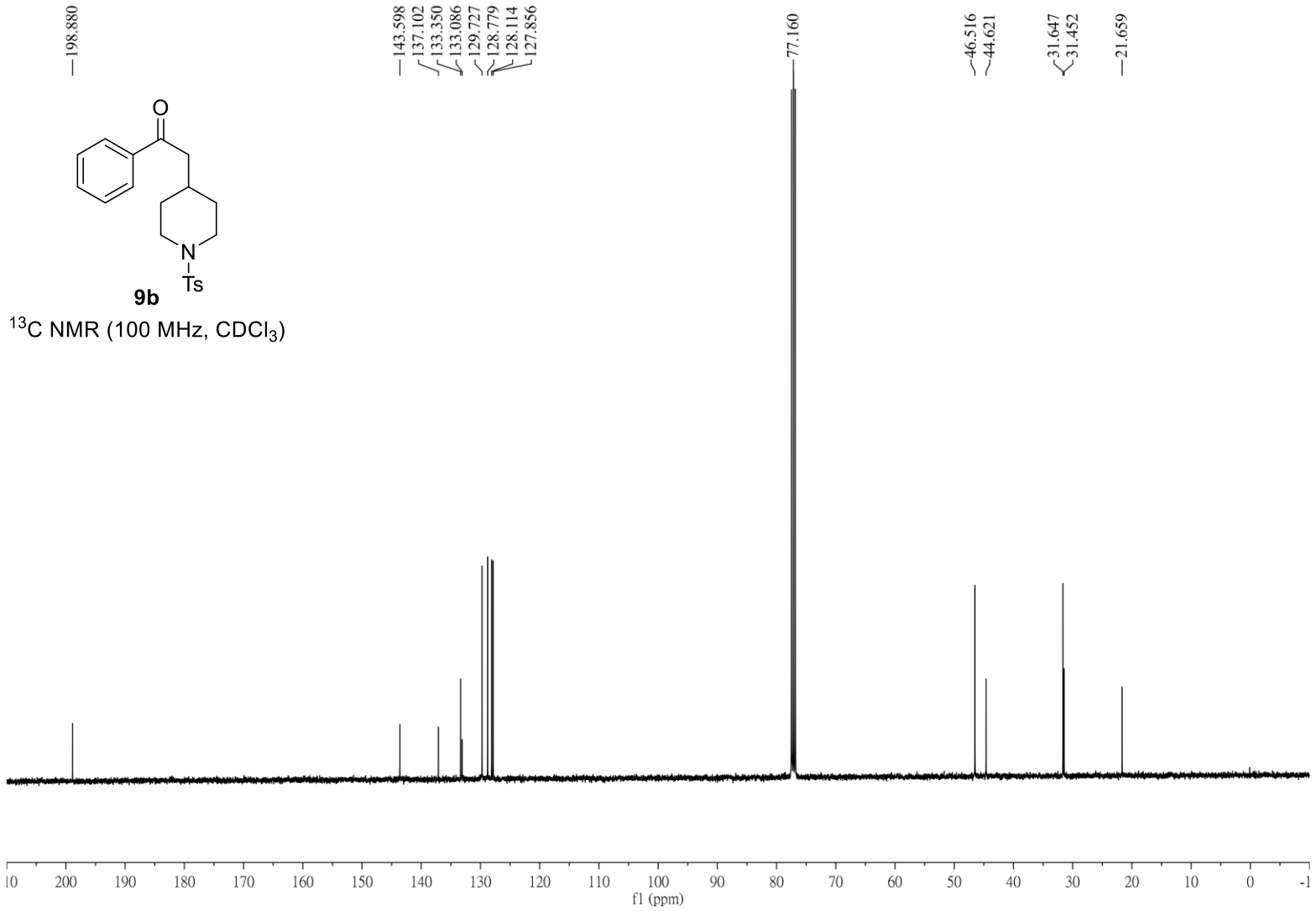


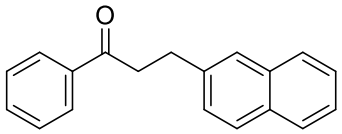

200.568
137.604
132.957
128.665
128.250
77.160
46.927
36.127
34.994
28.453
26.404
O
9a
13C NMR (100 MHz, CDCl3)
f1 (ppm)



9b

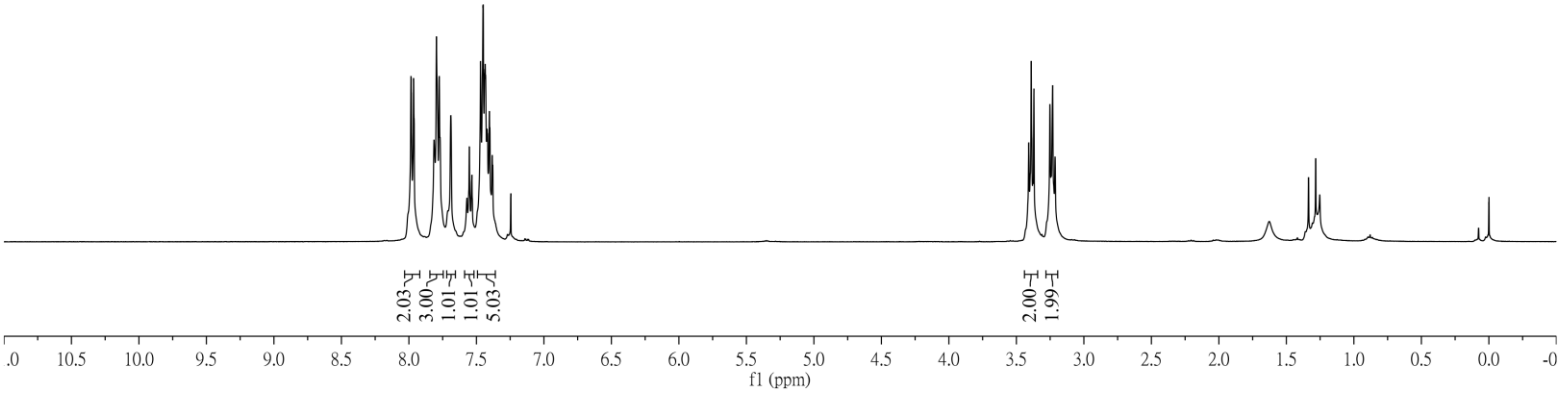
^{1}H NMR (400 MHz, $CDCl_3$)

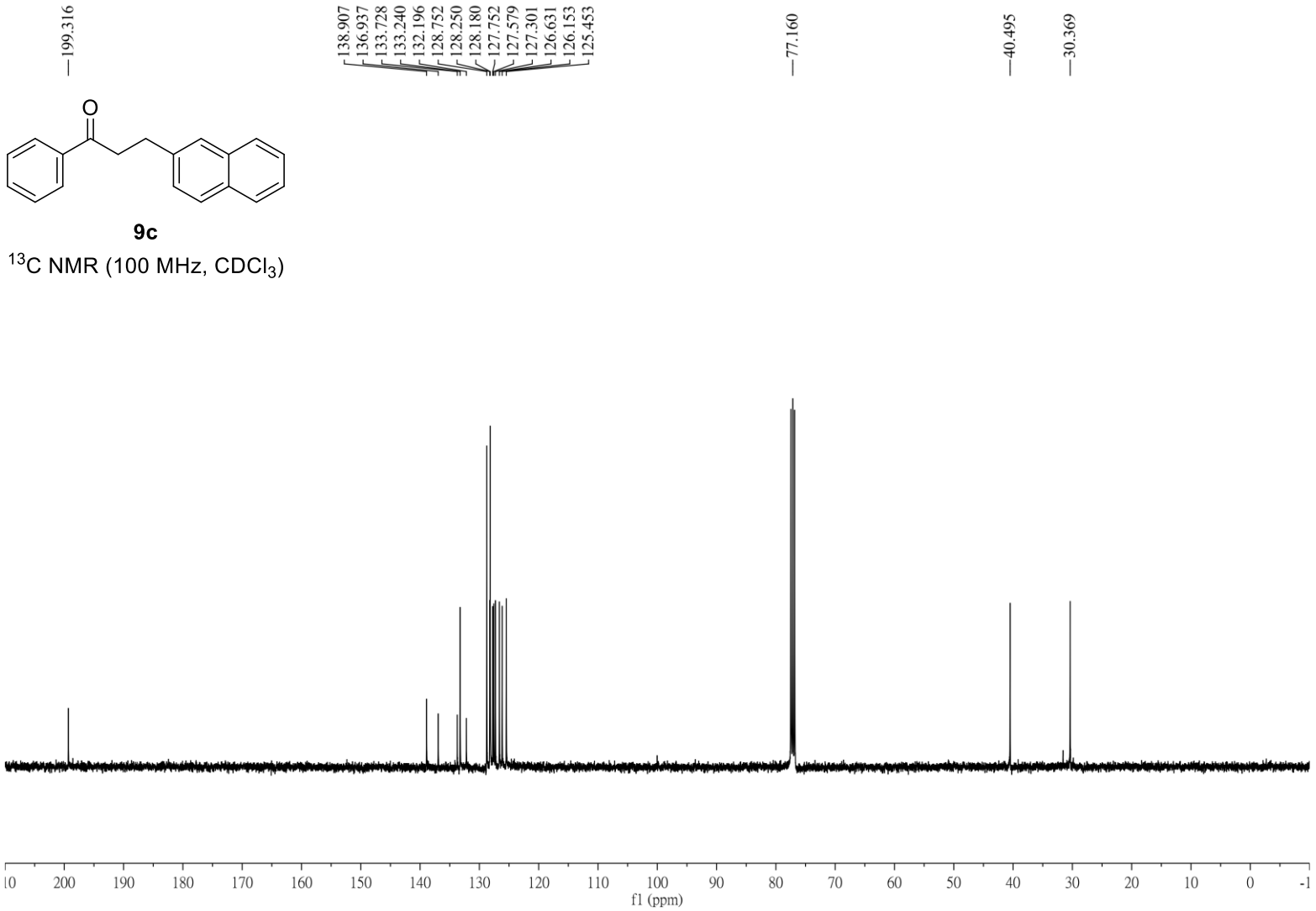

198.880
143.598
137.102
133.350
133.086
129.727
128.779
128.114
127.856
77.160
46.516
44.621
31.647
31.452
21.659
O
N
Ts
9b
13C NMR (100 MHz, CDCl3)
f1 (ppm)



9c

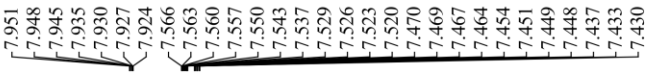
^{1}H NMR (400 MHz, $CDCl_3$)

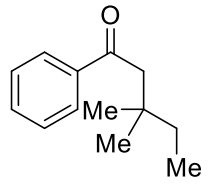




9c

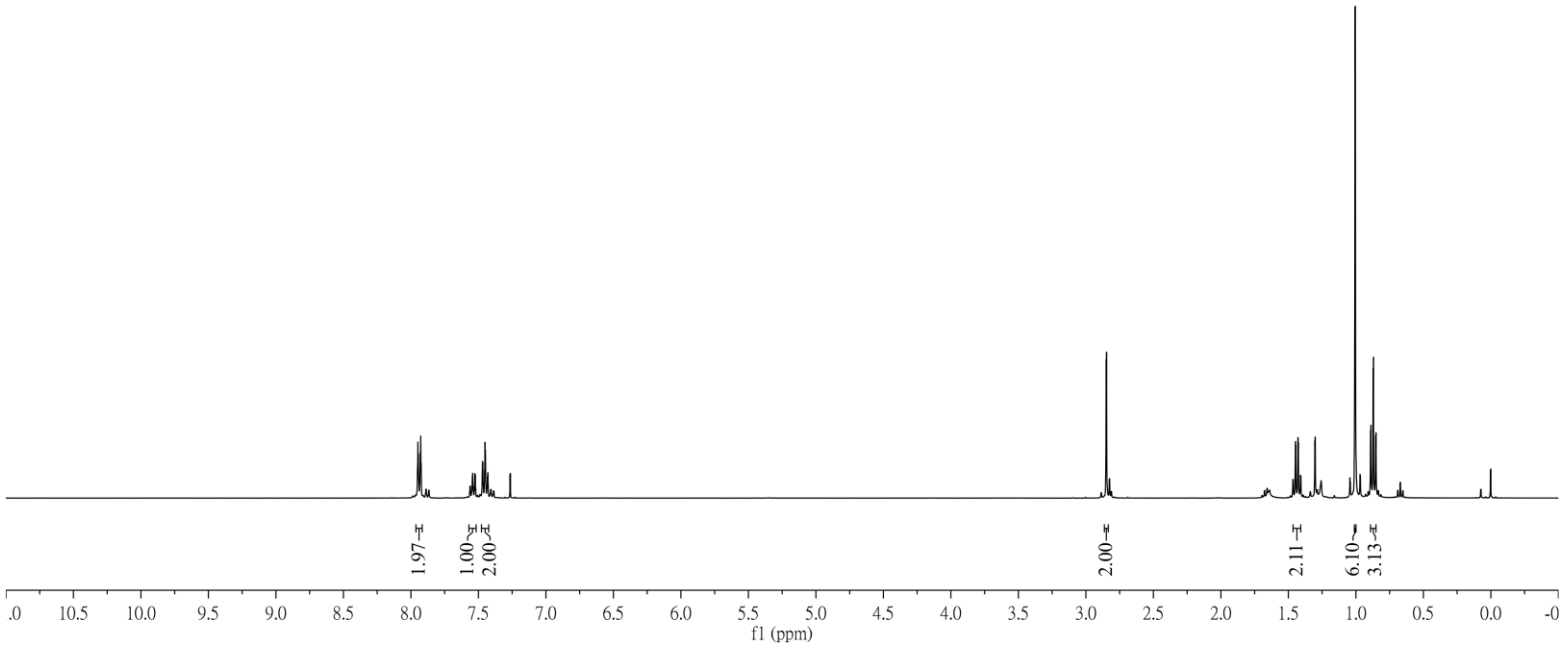
^{13}C NMR (100 MHz, $CDCl_3$)

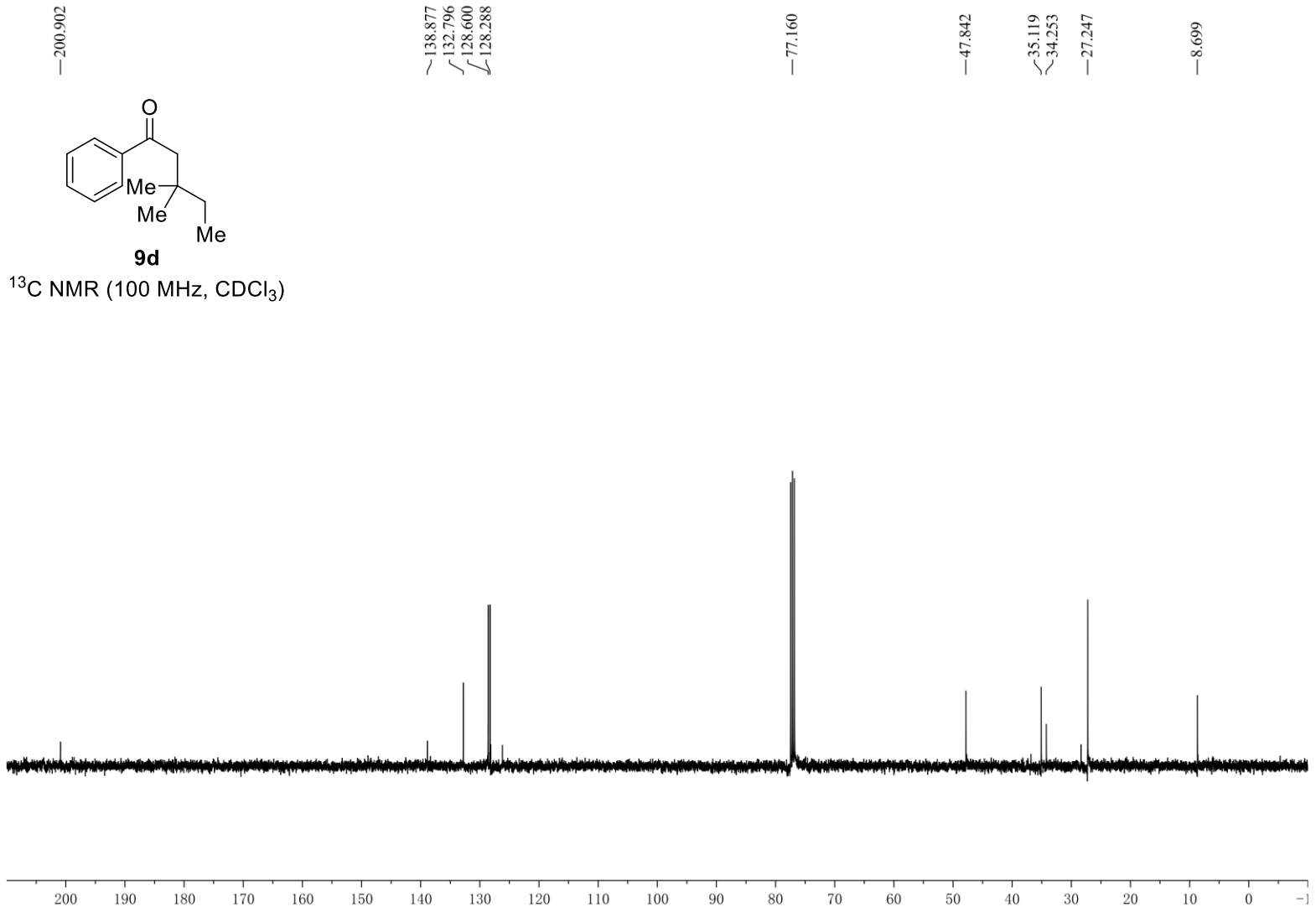




9d

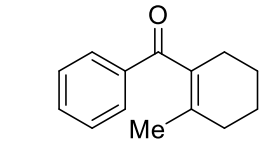
^{1}H NMR (400 MHz, $CDCl_3$)





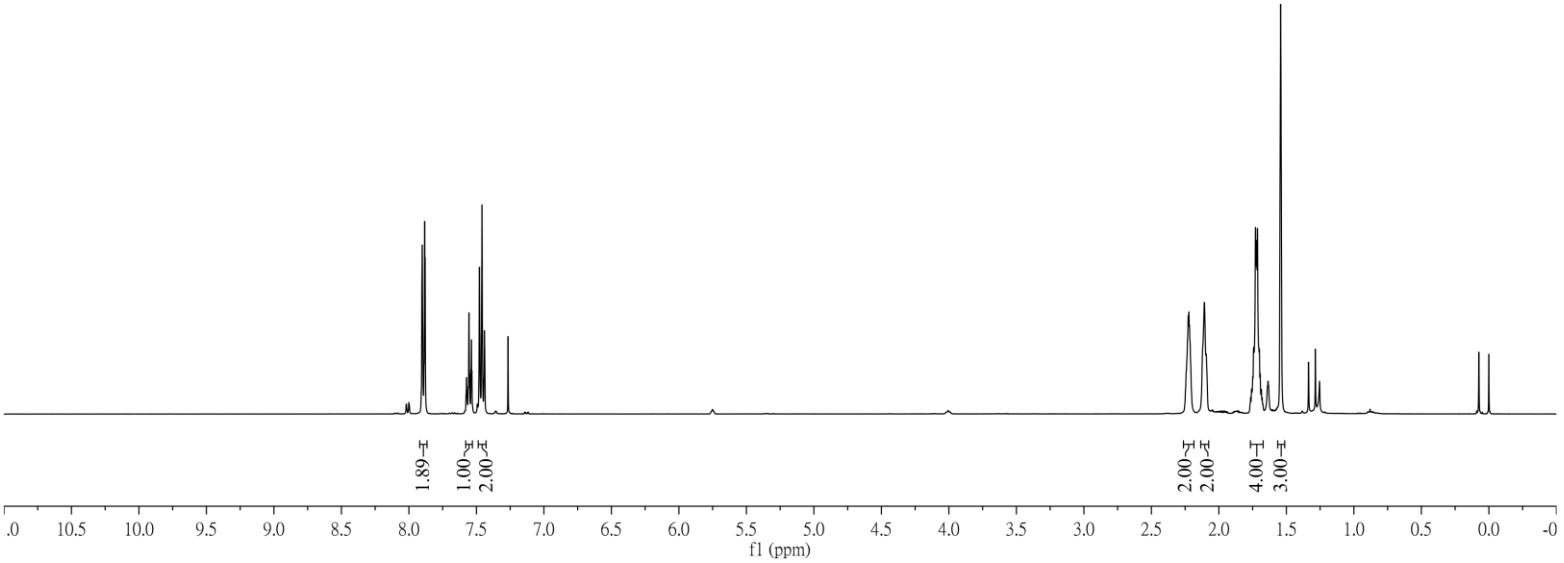
9d

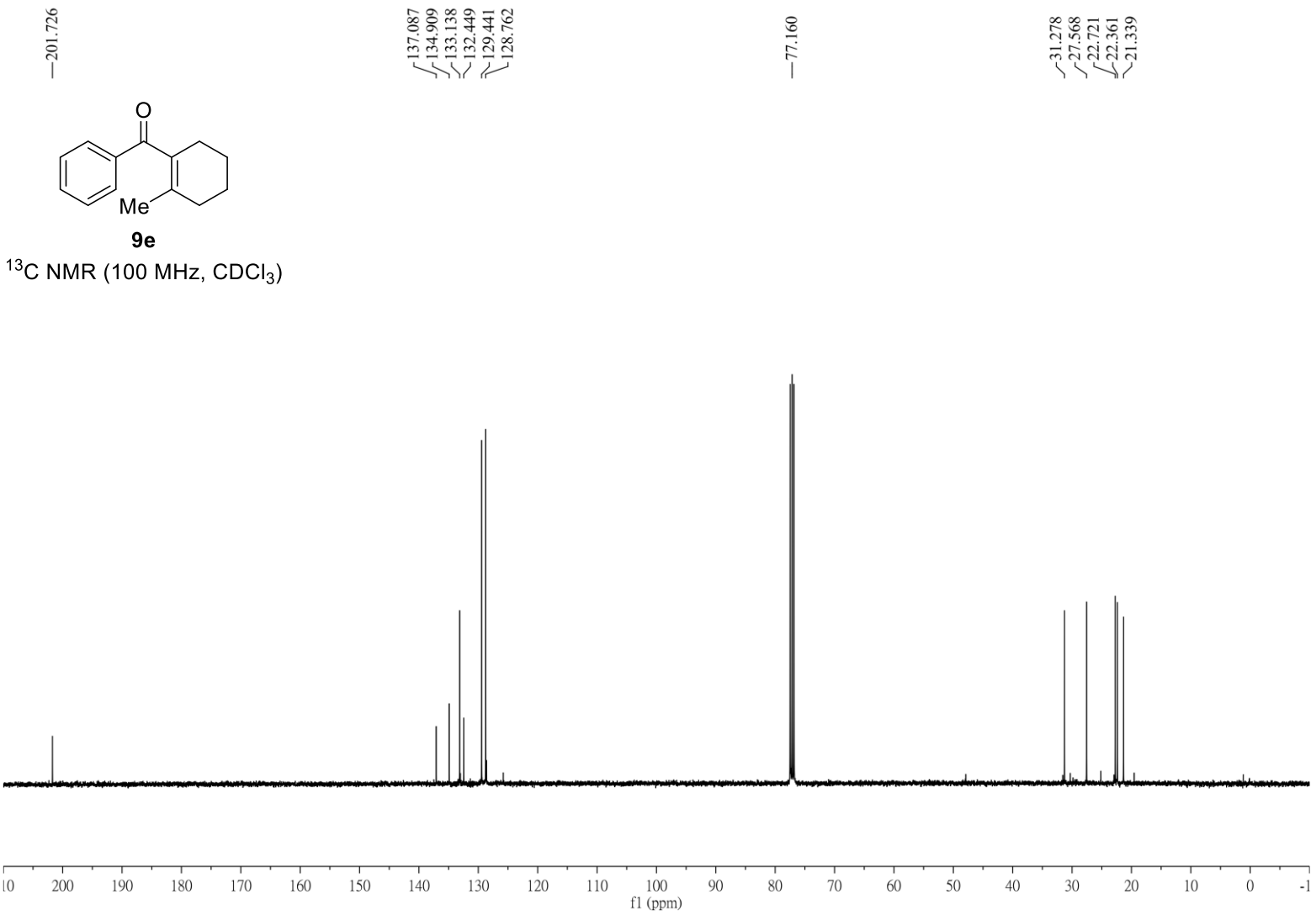
^{13}C NMR (100 MHz, $CDCl_3$)



9e

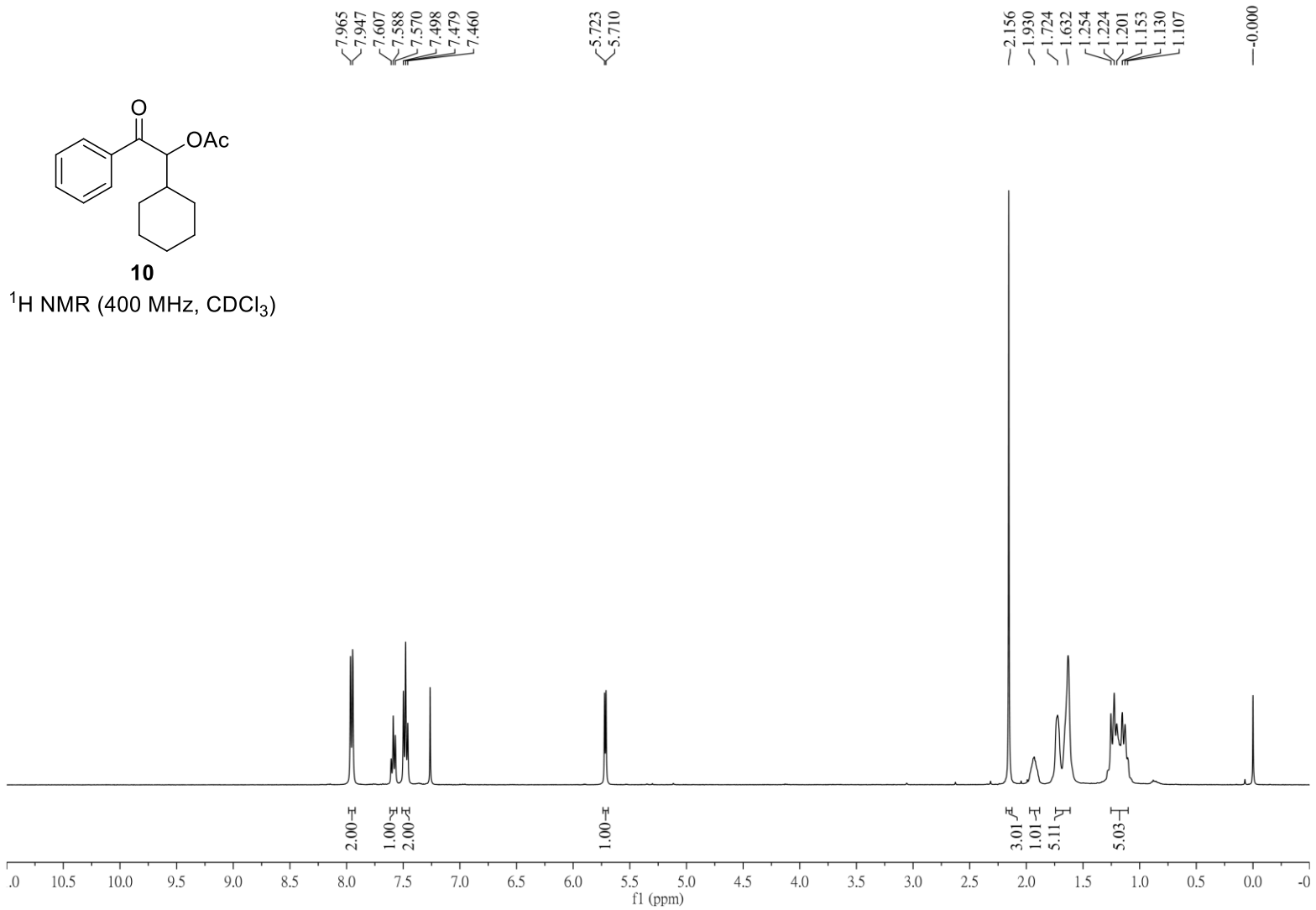
^{1}H NMR (400 MHz, $CDCl_3$)





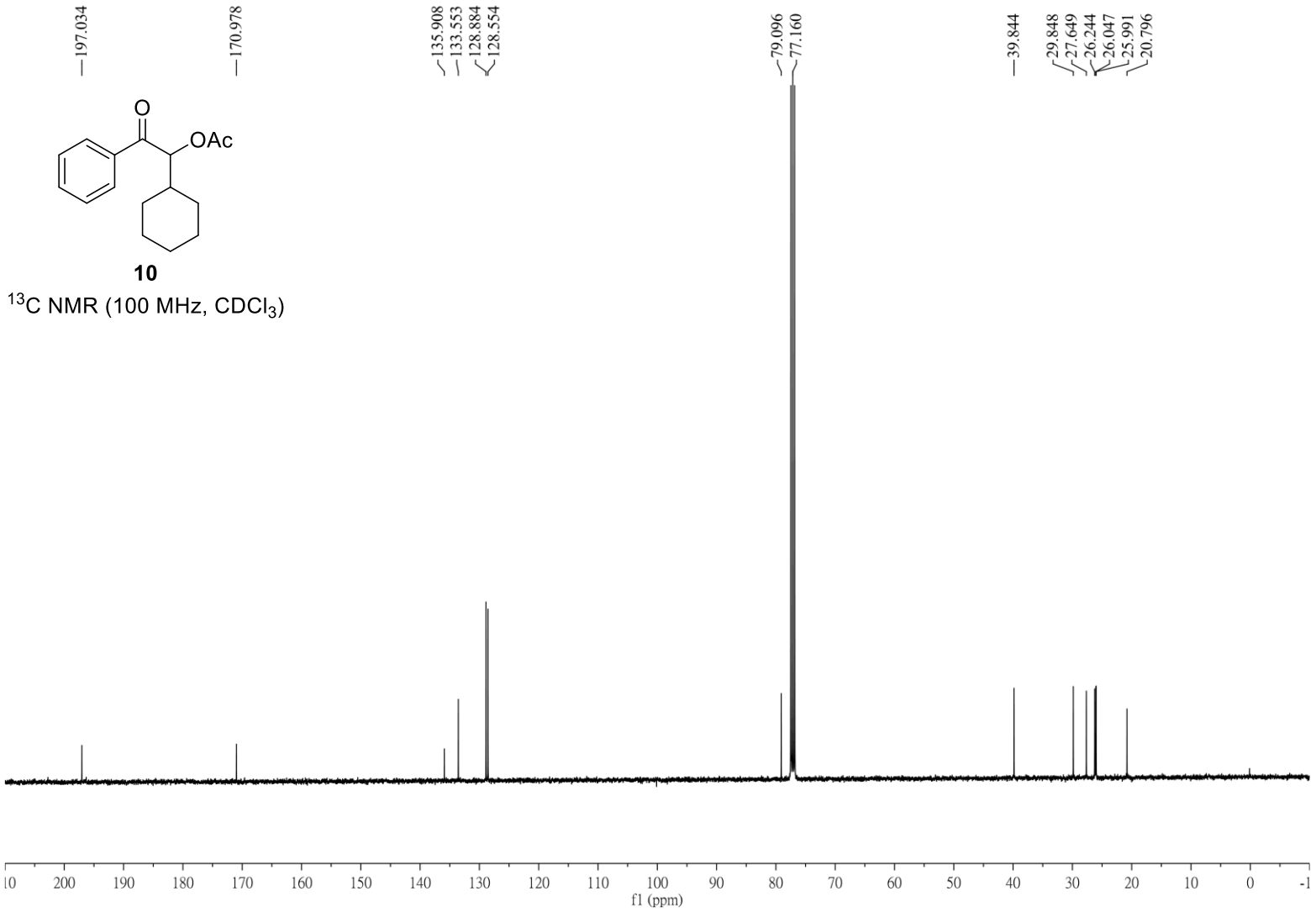
9e

^{13}C NMR (100 MHz, $CDCl_3$)



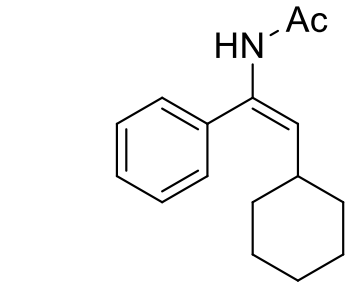
10

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



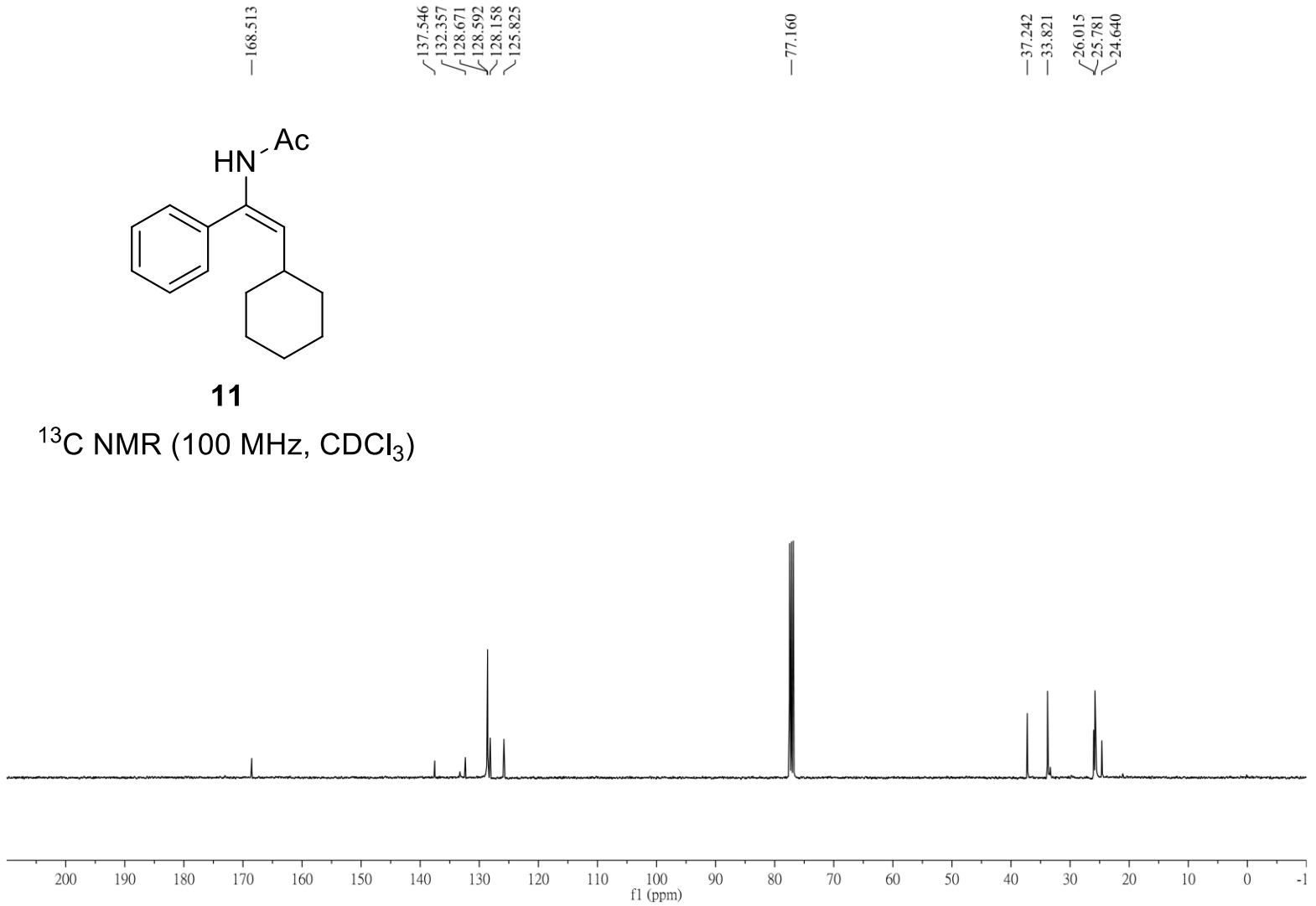
10

^{13}C NMR (100 MHz, $CDCl_3$)



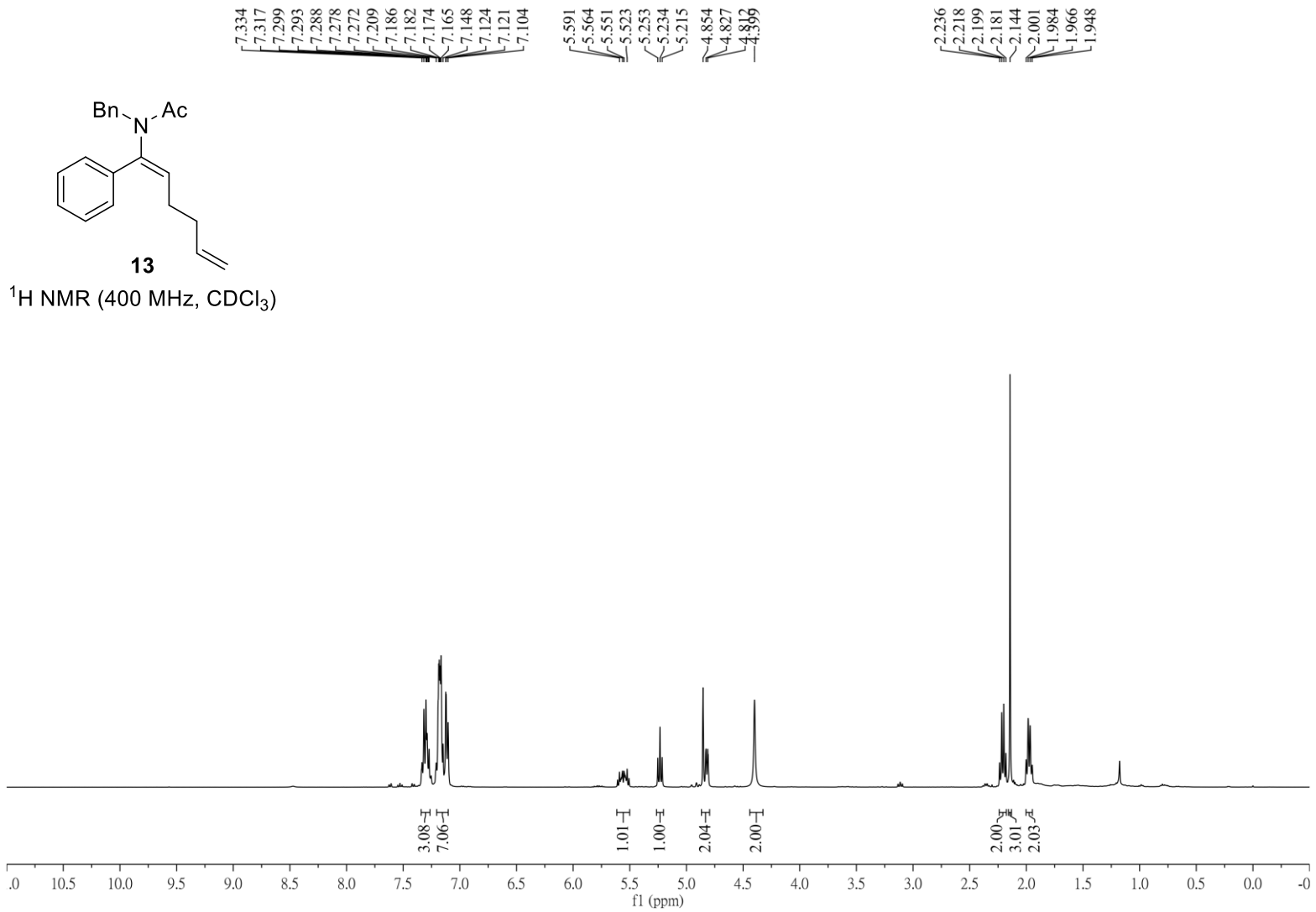
11

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



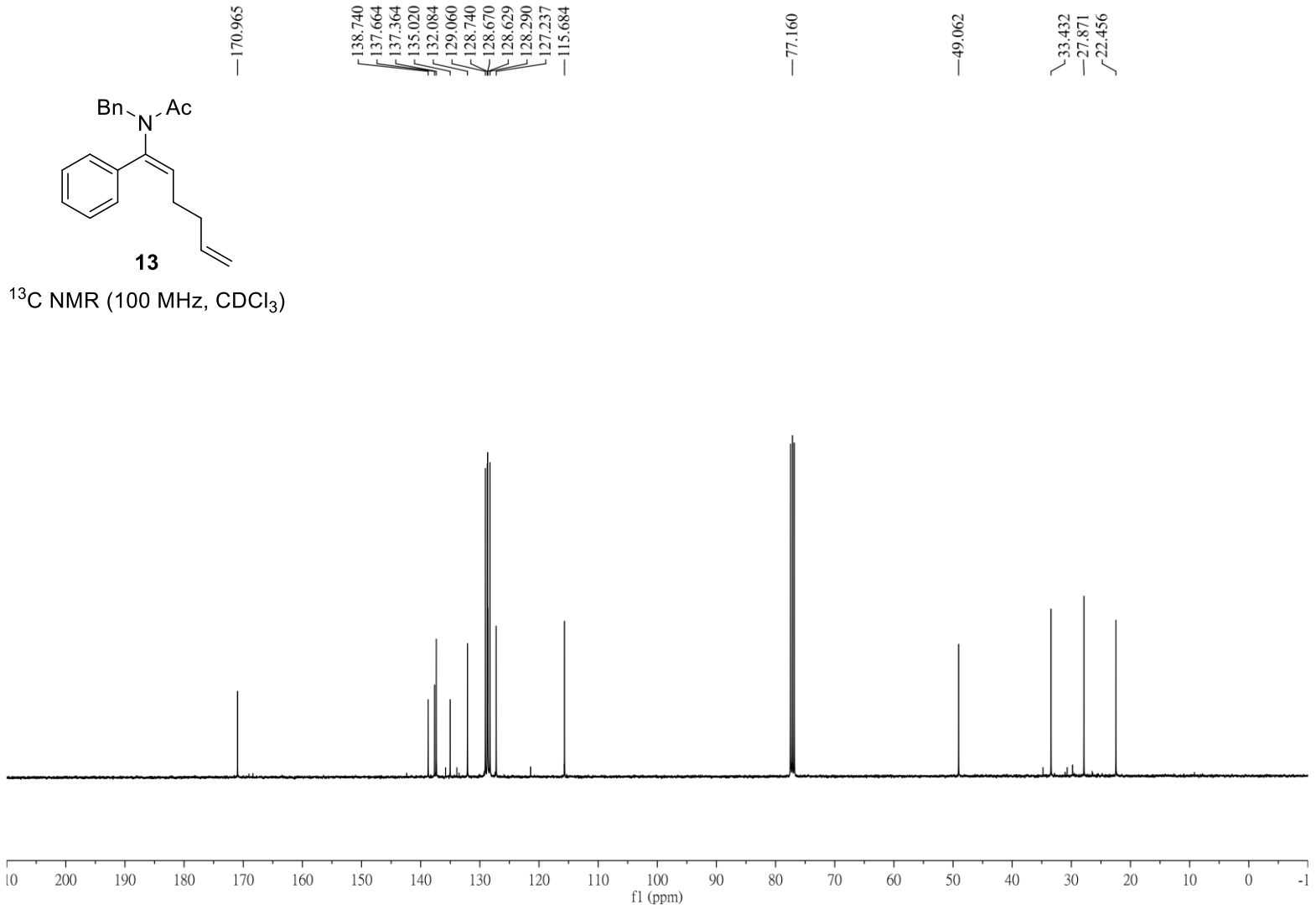
11

^{13}C NMR (100 MHz, $CDCl_3$)



13

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


170.965
138.740
137.664
137.364
135.020
132.084
129.060
128.740
128.670
128.629
128.290
127.237
115.684
77.160
49.062
33.432
27.871
22.456
Bn
N
Ac
13
13C NMR (100 MHz, CDCl3)
f1 (ppm)