Photoredox-Catalyzed Regio- & Stereoselective C(sp^2)–H Cyanoalkylation of Enamides with Cycloketone Oximes via Selective C-C Bond Cleavage/Radical Addition Cascade

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Supporting Information

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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. All enamides or enecarbamates were prepared using existing methods.[1] Cycloketone oximes were prepared using reported methods.[2]

^{1}H, ^{19}F, ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker Avance 400 MHz spectrometers. 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). NMR spectra were taken using TMS (^{1}H, δ = 0), $CDCl_3$ (^{1}H, δ = 7.26), and $CDCl_3$ (^{13}C, CPD δ = 77.00) as the internal standards, respectively. HRMS were obtained on an IonSpec FT-ICR mass spectrometer with ESI resource. Column chromatography was generally performed on silica gel (300-400 mesh) and reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of the reactions.

The photoredox-catalyzed transformations were carried out in a customized dark cassette equipped with three 15 W blue LEDs lamp from different directions for irradiation along with an electronic cooling fan for heat dissipation (**Figure S1**). A magnetic hotplate stirrer was placed in the dark cassette for stirring. The reaction vessel was placed in the center of the stirrer so that the average distance from the lamp to the reaction medium was 10 cm. The 15 W blue LEDs were purchased from Ctech Global Pte Ltd (Singapore) with the maximum absorption wavelength of 460-465 nm. The borosilicate made reaction vessels (Schlenk tubes) were all purchased from Synthware Glassware.

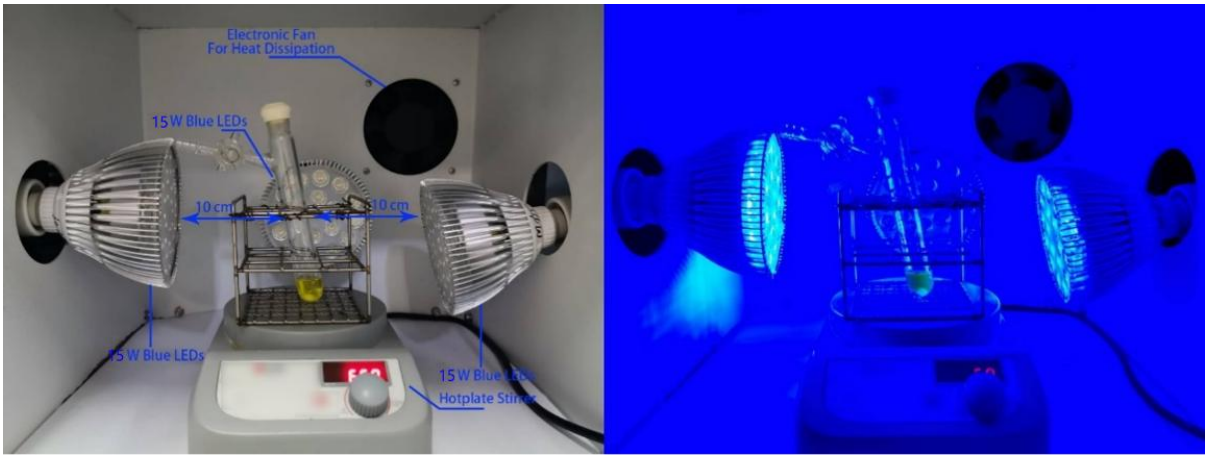
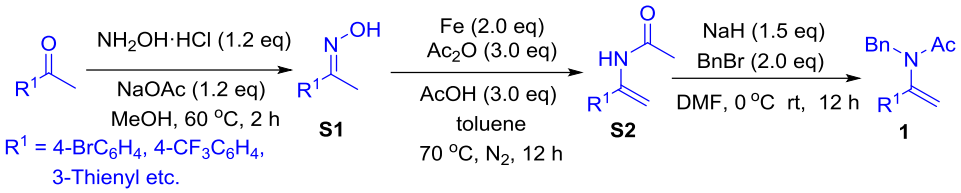


Figure S1 The customized dark cassette equipped with 3×15 W blue LEDs lamps

Abbreviations: Bn = benzyl, Ac = acetyl, ^{t}Bu = *tert*-butyl, Boc = *t*-butoxycarbonyl, Cbz = benzyloxycarbonyl, Cy = cyclohexyl, TEMPO = 2,2,6,6-tetramethylpiperidinooxy.

General Procedure for the Preparation of Enamides[1]



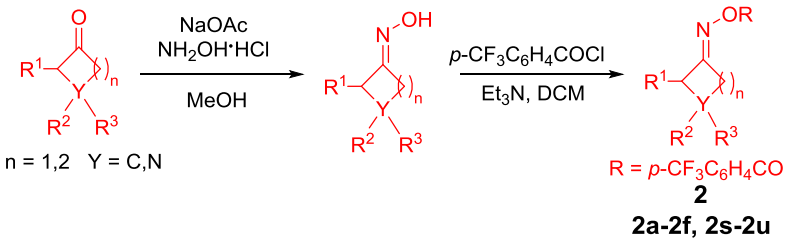
A mixture of ketone (10 mmol), NaOAc (12 mmol) and hydroxylamine hydrochloride (12 mmol) in methanol (5 mL) was stirred for 2 h at 60 ºC. After cooling to room temperature, water was added and the mixture was extracted with ethyl acetate (2×50 mL) dried over $MgSO_4$. The organic solvent was evaporated to afford the ketoxime pure enough for next step.

To an oven-dried 50 mL two-neck RBF assembled with a condenser was added ketoxime. The flask was vacuumed and backfilled with N_2 for three times. Anhydrous toluene (20 mL) was added followed by acetic anhydride (30 mmol), acetic acid (30 mmol) and iron powder (20 mmol). The reaction flask was put into a 70 °C preheated oil bath and allowed to stir for 5 hours under nitrogen atmosphere. After cooling to room temperature, ethyl acetate was added and the mixture was filtered through a short pad of celite. The solution thus obtained was evaporated to product crude enamide, which was directly purified by column chromatography.

1.0 mmol of enamide was dissolved in 3.0 mL of dry DMF. The solution was cooled to 0 °C and 1.5 mmol of sodium hydride (60% dispersion in mineral oil) was added in portions. The resulting suspension was stirred at the same temperature for 10 min. 2.0 mmol of benzyl bromide was then added drop wise and the solution was warmed to room temperature overnight. Upon the completion of the reaction as monitored by TLC, the excess amount of sodium hydride was quenched by adding 1.0 mL of water at 0 °C. The organic layer was extracted with ethyl acetate through stages of extraction with water. The combined organic layer was concentrated under reduced pressure and the pure product was isolated by flash column chromatography eluting with ethyl acetate/petroleum ether (1:3 *v/v*).

General Procedure for the Preparation of cycloketone oximes[2]

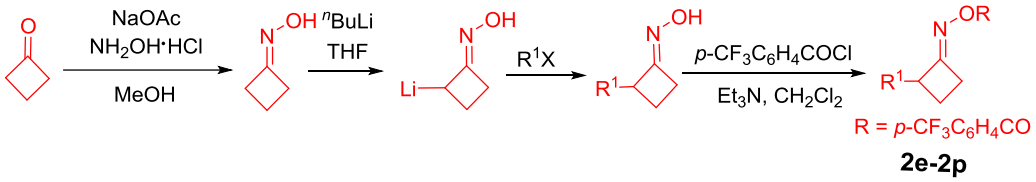
Method A:



To a stirred solution of cyclobutanones (1.0 eq.) in MeOH (0.5 M) was added hydroxylamine hydrochloride (2.0 eq.) at room temperature. After stirring for 2 h, pyridine was removed under reduced pressure. The residue was diluted with water and extracted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude material, which were used in the next step without further purification.

To a mixture of cyclobutanone oxime (1.0 eq), triethylamine (2.0 eq) and CH_2Cl_2 (0.5 M) in a 30 mL two-necked flask was added benzoyl chloride (1.5 eq) at 0 °C. After 6 h, water was added to the above solution, and the mixture was diluted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO_2 with EtOAc–hexane as an eluent to give cyclobutanone *O*-benzoyl oximes.

Method B:



2e-2p

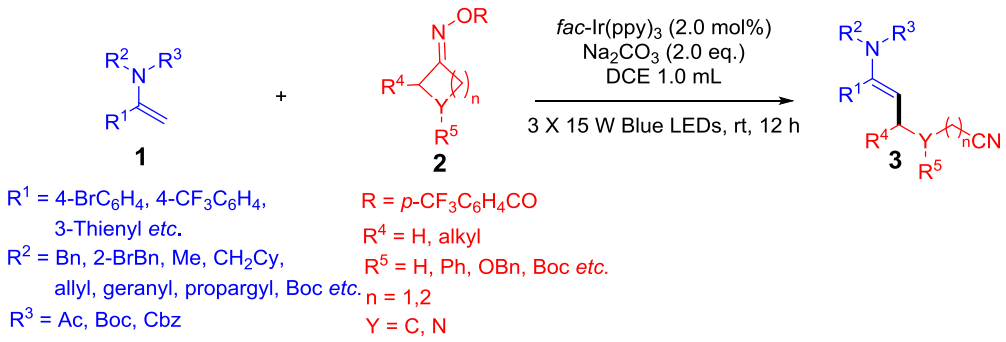
To a stirred solution of cyclobutanones (1.0 eq.) in MeOH (0.5 M) was added hydroxylamine hydrochloride (2.0 eq.) at rt. After stirring for 2 h, MeOH was removed under reduced pressure. The residue was diluted with water and extracted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude material, which were used in the next step without further purification.

To a mixture of hydroxylamine hydrochloride (18.0 mmol), sodium acetate (22.5 mmol), ethanol (10.5 mL) and water (4.5 mL) in a 30 mL two-necked flask was added cyclobutanone (15.0 mmol) and the mixture was stirred at 100 °C for 12 h. The reaction mixture was cooled to room temperature and then ethanol was removed under reduced pressure and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography to give cyclobutanone oxime as a white solid (1.0 g, 78%).

Cyclobutanone oxime (1.0 eq) in absolute THF (0.5 M) was added ^{n}BuLi (2.0 eq) slowly at 0 °C, then continue to stirring for another 15 min at this temperature for the formation of syn dianion. Then

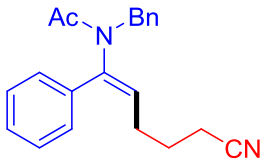
R^1X (1.0 eq) was added dropwise at 0 °C, then the mixture was warmed to room temperature for 2 h. Subsequently, the reaction was quenched by cold water, and the mixture was diluted with ethyl acetate. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO_2 with EtOAc–hexane as an eluent to give desired substituted oximes.

General Procedure for the Synthesis of *β*-cyanoalkylated of Enamides



To a Schlenk tube equipped with a magnetic stir bar was charged with enamides or enecarbamates **1** (0.45 mmol), Cyclobutanone Oximes **2** (0.3 mmol), *fac*-Ir(ppy)$_3$ (3.9 mg, 2.0 mol%), and Na_2CO_3 (63.6 mg, 0.6 mmol). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL 1,2-dichloroethane (DCE) was added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under 3×15 W 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 flash column chromatography, eluting with ethyl acetate/petroleum ether (1:10~1:2 *v/v*), to afford compound **3aa-3za, 3a'a-3e'a**, **3ab-3au**.

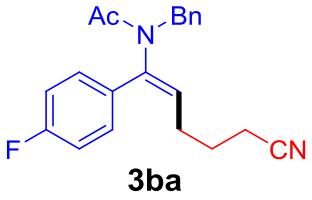
Analytical Data for the *β*-cyanoalkylated Enamides



3aa

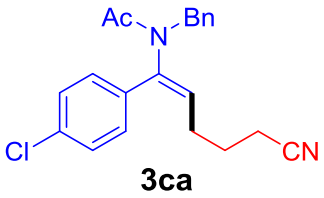
(*E*)-*N*-benzyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (3aa): 74.5 mg, 78% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v/v*). ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.45-7.34 (m, 4H), 7.32-7.21 (m, 7H), 7.20-7.16 (m, 3H), 5.20 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.30 (q, J = 7.6 Hz, 2H), 2.21 (s, 3H), 2.15 (t, J = 7.1 Hz, 2H), 1.67-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.43, 140.08, 137.51, 134.49, 129.70, 128.99, 128.81, 128.52, 128.32, 127.35, 119.05, 48.91, 27.32, 25.19, 22.26, 16.53. HRMS calcd for $C_{21}H_{23}N_2O^+$ $[M+H]^+$ 319.1805, found 319.1793.



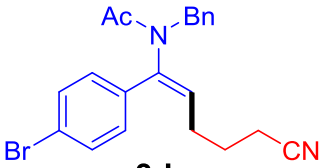
3ba

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-fluorophenyl)pent-1-en-1-yl)acetamide (3ba): 70.6 mg, 70% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.24 (m, 3H), 7.21 (dd, J = 8.4, 5.5 Hz, 2H), 7.17 (d, J = 6.8 Hz, 2H), 7.10 (t, J = 8.4 Hz, 2H), 5.22 (t, J = 7.4 Hz, 1H), 4.50 (s, 2H), 2.28 (q, J = 7.5 Hz, 2H), 2.21 (s, 3H), 2.16 (t, J = 7.0 Hz, 2H), 1.68-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.37, 162.65 (d, J_{C-F} = 248.2 Hz), 138.98, 137.24, 130.43 (d, J_{C-F} = 3.5 Hz), 130.32 (d, J_{C-F} = 8.2 Hz), 129.73, 128.85, 128.28, 127.34, 118.98, 115.81 (d, J = 21.6 Hz), 48.81, 27.20, 24.98, 22.14, 16.43. ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.43. HRMS calcd for $C_{21}H_{22}FN_2O^+$ $[M+H]^+$ 337.1711, found 337.1710.



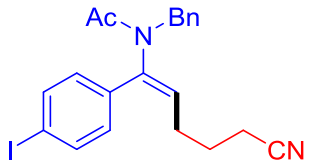
3ca

(*E*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-5-cyanopent-1-en-1-yl)acetamide (3ca): 77.3 mg, 73% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.4 Hz, 2H), 7.30-7.25 (m, 3H), 7.19-7.13 (m, 4H), 5.23 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.29 (q, J = 7.6 Hz, 2H), 2.19 (s, 3H), 2.16 (t, J = 7.1 Hz, 2H), 1.67-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.39, 139.08, 137.30, 134.89, 132.99, 130.30, 129.86, 129.13, 128.98, 128.41, 127.49, 118.99, 48.98, 27.34, 25.10, 22.28, 16.58. HRMS calcd for $C_{21}H_{22}ClN_2O^+$ $[M+H]^+$ 353.1415, found 353.1410.



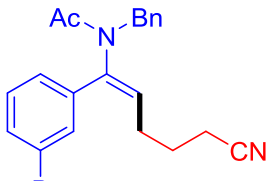
3da

(*E*)-*N*-benzyl-*N*-(1-(4-bromophenyl)-5-cyanopent-1-en-1-yl)acetamide (3da): 93.0 mg, 78% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.4 Hz, 2H), 7.31-7.22 (m, 3H), 7.18-7.14 (m, 2H), 7.12-7.08 (m, 2H), 5.25 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.28 (q, J = 7.6 Hz, 2H), 2.19 (s, 3H), 2.16 (d, J = 14.2 Hz, 2H), 1.66-1.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.31, 138.92, 137.14, 133.34, 131.94, 130.33, 130.02, 128.83, 128.28, 127.36, 122.94, 118.92, 48.87, 27.22, 24.94, 22.15, 16.43. HRMS calcd for $C_{21}H_{22}BrN_2O^+$ $[M+H]^+$ 397.0910, found 397.0906.



3ea

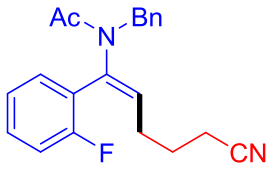
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-iodophenyl)pent-1-en-1-yl)acetamide (3ea): 62.6 mg, 47% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.30-7.25 (m, 3H), 7.18-7.13 (m, 2H), 6.96 (d, J = 8.4 Hz, 2H), 5.23 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.28 (q, J = 7.6 Hz, 2H), 2.17 (d, J = 10.2 Hz, 5H), 1.63 (q, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.37, 139.24, 138.03, 137.28, 134.06, 130.41, 130.23, 128.98, 128.41, 127.49, 118.97, 94.90, 49.00, 27.35, 25.09, 22.28, 16.58. HRMS calcd for $C_{21}H_{22}IN_2O^+$ $[M+H]^+$ 445.0771, found 445.0786.



3fa

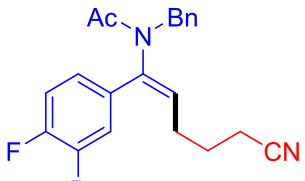
(*E*)-*N*-benzyl-*N*-(1-(3-bromophenyl)-5-cyanopent-1-en-1-yl)acetamide (3fa): 95.4 mg, 80% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.1 Hz, 1H), 7.34 (t, J = 1.8 Hz, 1H), 7.31-7.24 (m, 4H), 7.19-7.14 (m, 3H), 5.27 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 2.29 (q, J = 7.6 Hz, 2H), 2.18 (d, J = 13.7 Hz, 4H),

1.67-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.21, 138.68, 137.15, 136.64, 131.92, 131.11, 130.78, 130.25, 128.83, 128.30, 127.39, 127.22, 122.85, 118.88, 48.97, 27.19, 24.97, 22.18, 16.43. HRMS calcd for $C_{21}H_{22}BrN_2O^+$ $[M+H]^+$ 397.0910, found 397.0914.



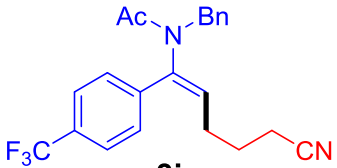
3ga

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(2-fluorophenyl)pent-1-en-1-yl)acetamide (3ga): 82.8 mg, 82% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.31 (m, 1H), 7.31-7.08 (m, 9H), 5.36 (t, J = 7.6 Hz, 1H), 4.49 (s, 2H), 2.25 (s, 3H), 2.18-2.05 (m, 4H), 1.68-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.38, 160.03 (d, $J_{C\text{-}F}$ = 247.6 Hz), 137.30, 134.49, 132.12, 130.94 (d, $J_{C\text{-}F}$ = 8.5 Hz), 130.67 (d, $J_{C\text{-}F}$ = 3.5 Hz), 128.79, 128.22, 127.24, 124.42 (d, $J_{C\text{-}F}$ = 3.8 Hz), 122.25 (d, $J_{C\text{-}F}$ = 15.0 Hz), 119.03, 116.27 (d, $J_{C\text{-}F}$ = 22.6 Hz), 48.69, 27.44, 24.50, 22.11, 16.43. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.23. HRMS calcd for $C_{21}H_{22}FN_2O^+$ $[M+H]^+$ 337.1711, found 337.1731.



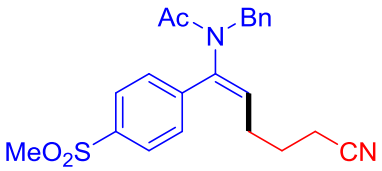
3ha

(*E*)-*N*-benzyl-*N*-(1-(3-bromo-4-fluorophenyl)-5-cyanopent-1-en-1-yl)acetamide (3ha): 90.9 mg, 73% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 1H), 7.31-7.24 (m, 3H), 7.16 (d, J = 6.3 Hz, 4H), 5.28 (t, J = 7.6 Hz, 1H), 4.51 (s, 2H), 2.29 (q, J = 7.5 Hz, 2H), 2.19 (d, J = 3.8 Hz, 5H), 1.69-1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.19, 158.96 (d, $J_{C\text{-}F}$ = 249.3 Hz), 137.95, 137.05, 133.33, 132.12 (d, $J_{C\text{-}F}$ = 4.3 Hz), 130.71, 129.35 (d, $J_{C\text{-}F}$ = 7.9 Hz), 128.82, 128.35, 127.47, 116.74 (d, $J_{C\text{-}F}$ = 22.7 Hz), 109.59 (d, $J_{C\text{-}F}$ = 20.3 Hz), 49.01, 27.19, 24.93, 22.18, 16.47. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.61. HRMS calcd for $C_{21}H_{21}BrFN_2O^+$ $[M+H]^+$ 415.0816, found 415.0814.



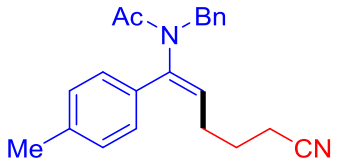
3ia

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(trifluoromethyl)phenyl)pent-1-en-1-yl)acetamide (3ia): 70.7 mg, 61% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 7.3 Hz, 3H), 7.16-7.10 (m, 2H), 5.31 (t, J = 7.6 Hz, 1H), 4.48 (s, 2H), 2.28 (q, J = 7.6 Hz, 2H), 2.18 (s, 3H), 2.14 (t, J = 7.1 Hz, 2H), 1.69-1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.33, 138.89, 138.28, 137.16, 131.52, 130.83 (q, J_{C-F} = 32.5 Hz), 128.96, 128.91, 128.42, 127.52, 125.81 (q, J_{C-F} = 3.6 Hz), 123.80 (q, J_{C-F} = 270.2 Hz), 118.92, 49.08, 27.30, 25.01, 22.22, 16.51. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.60. HRMS calcd for $C_{22}H_{22}F_3N_2O^+$ $[M+H]^+$ 387.1679, found 387.1682.



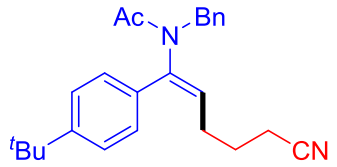
3ja

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(methylsulfonyl)phenyl)pent-1-en-1-yl)acetamide (3ja): 65.5 mg, 55% yield (*E*/*Z* = 92:8). Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.61-7.49 [m, 0.23H of (*Z*)-isomer], 7.43-7.32 [m, 2H + 0.18H of (*Z*)-isomer], 7.29-7.18 [m, 3H + 0.27H of (*Z*)-isomer], 7.14-7.05[m, 2H + 0.18H of (*Z*)-isomer], 6.08 [dd, J = 10.1, 4.6 Hz, 1H of (*Z*)-isomer], 5.54 [d, J = 13.9 Hz, 0.09H one of proton of (*Z*)-isomer], 5.36 (t, J = 7.6 Hz, 1H), 4.47 (s, 2H), 3.46 [d, J = 13.9 Hz, 0.09H one of proton of (*Z*)-isomer], 3.05 (s, 3H), 2.28 (q, J = 7.6 Hz, 2H), 2.16 (d, J = 5.2 Hz, 5H), 2.03-1.94 [m, 0.27H one of proton of (*Z*)-isomer], 1.93-1.80 [m, 0.27H one of proton of (*Z*)-isomer], 1.65-1.57 (m, 2H), 1.49-1.31 [m, 0.09H one of proton of (*Z*)-isomer], 0.92-0.80 [m, 0.09H one of proton of (*Z*)-isomer]. ^{13}C NMR (100 MHz, $CDCl_3$) δ *E*-isomer: 170.36, 140.83, 140.32, 138.64, 137.06, 132.47, 129.52, 129.03, 128.57, 128.05, 127.71, 118.91, 49.31, 44.50, 27.40, 25.03, 22.36, 16.67. *Z*-isomer: 170.49, 141.24, 140.58, 138.23, 136.99, 131.52, 130.07, 128.66, 128.41, 128.10, 126.64, 119.22, 48.73, 44.56, 28.01, 24.15, 21.27. HRMS calcd for $C_{22}H_{25}N_2O_3S^+$ $[M+H]^+$ 397.1580, found 397.1588.



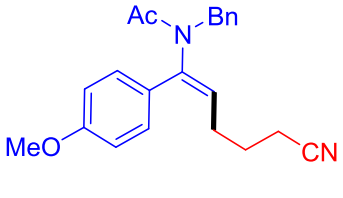
3ka

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(*p*-tolyl)pent-1-en-1-yl)acetamide (3ka): 70.8 mg, 71% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (dd, J = 6.8, 1.8 Hz, 1H), 7.24-7.14 (m, 6H), 7.10 (d, J = 8.1 Hz, 2H), 5.13 (t, J = 7.6 Hz, 1H), 4.47 (s, 2H), 2.36 (s, 3H), 2.27 (q, J = 7.6 Hz, 2H), 2.18 (s, 3H), 2.12 (t, J = 7.1 Hz, 2H), 1.64-1.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.43, 139.96, 138.96, 137.55, 131.46, 129.47, 129.14, 128.95, 128.39, 128.26, 127.28, 119.10, 48.79, 27.31, 25.17, 22.23, 21.26, 16.49. HRMS calcd for $C_{22}H_{25}N_2O^+$ $[M+H]^+$ 333.1961, found 333.1957.

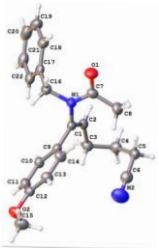


3la

(*E*)-*N*-benzyl-*N*-(1-(4-(*tert*-butyl)phenyl)-5-cyanopent-1-en-1-yl)acetamide (3la): 61.8 mg, 55% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.39 (m, 2H), 7.31-7.23 (m, 3H), 7.21-7.14 (m, 4H), 5.15 (t, J = 7.0 Hz, 1H), 4.51 (s, 2H), 2.33 (q, J = 7.1 Hz, 2H), 2.20 (d, J = 1.5 Hz, 3H), 2.18-2.12 (m, 2H), 1.68-1.58 (m, 2H), 1.35 (d, J = 1.8 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.57, 152.18, 139.97, 137.71, 131.48, 129.43, 129.14, 128.37, 128.30, 127.40, 125.80, 119.26, 48.97, 34.83, 31.35, 27.45, 25.34, 22.33, 16.61. HRMS calcd for $C_{25}H_{31}N_2O^+$ $[M+H]^+$ 375.2431, found 375.2416.



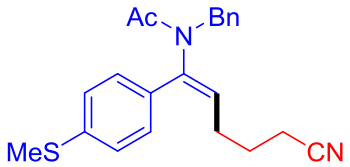
3ma



(CCDC 2068194)

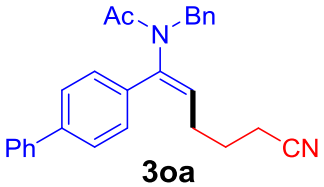
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-methoxyphenyl)pent-1-en-1-yl)acetamide (3ma): 89.9 mg, 86% yield. White solid. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 3H), 7.20-7.14 (m, 4H), 6.93 (d, J = 8.7 Hz, 2H), 5.12 (t, J = 7.6 Hz, 1H), 4.50 (s, 2H), 3.83 (s, 3H), 2.30 (q, J = 7.6 Hz, 2H), 2.20 (s, 3H), 2.15 (t, J = 7.1 Hz, 2H), 1.66-1.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.43, 159.88, 139.66, 137.52, 129.78, 128.92, 128.44, 128.23, 127.24, 126.60, 119.07, 114.13, 55.30, 48.81, 27.28, 25.16, 22.18, 16.46. HRMS calcd for $C_{22}H_{25}N_2O_2^+$ $[M+H]^+$ 349.1911, found 349.1924.



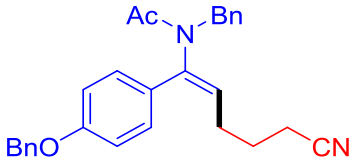
3na

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(methylthio)phenyl)pent-1-en-1-yl)acetamide (3na): 39.4 mg, 36% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 5H), 7.19-7.12 (m, 4H), 5.17 (t, J = 7.6 Hz, 1H), 4.51 (s, 2H), 2.51 (s, 3H), 2.31 (q, J = 7.7 Hz, 2H), 2.20 (s, 3H), 2.16 (t, J = 7.1 Hz, 2H), 1.67-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.55, 140.13, 139.68, 137.51, 130.91, 129.47, 129.06, 128.91, 128.39, 127.44, 126.25, 119.07, 49.03, 27.42, 25.25, 22.30, 16.61, 15.39. HRMS calcd for $C_{22}H_{25}N_2OS^+$ $[M+H]^+$ 365.1682, found 365.1662.



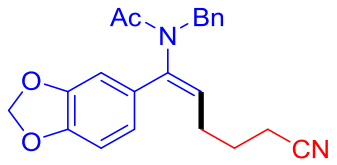
3oa

(*E*)-*N*-(1-([1,1'-biphenyl]-4-yl)-5-cyanopent-1-en-1-yl)-*N*-benzylacetamide (3oa): 44.9 mg, 38% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (t, J = 8.5 Hz, 4H), 7.47 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.33-7.26 (m, 5H), 7.23-7.19 (m, 2H), 5.22 (t, J = 7.6 Hz, 1H), 4.56 (s, 2H), 2.37 (q, J = 7.6 Hz, 2H), 2.24 (s, 3H), 2.17 (t, J = 7.1 Hz, 2H), 1.70-1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.64, 141.84, 140.15, 139.83, 137.56, 133.37, 129.96, 129.13, 129.02, 129.00, 128.43, 127.87, 127.53, 127.47, 127.14, 119.14, 49.10, 27.50, 25.29, 22.36, 16.65. HRMS calcd for $C_{27}H_{27}N_2O^+$ $[M+H]^+$ 395.2118, found 395.2100.



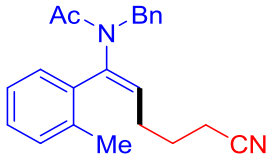
3pa

(*E*)-*N*-benzyl-*N*-(1-(4-(benzyloxy)phenyl)-5-cyanopent-1-en-1-yl)acetamide (3pa): 94.2 mg, 74% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.31-7.25 (m, 2H), 7.23 (dd, *J* = 6.6, 2.0 Hz, 1H), 7.19-7.12 (m, 3H), 7.10-7.03 (m, 4H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.01 (t, *J* = 7.6 Hz, 1H), 4.97 (s, 2H), 4.40 (s, 2H), 2.18 (q, *J* = 7.6 Hz, 2H), 2.09 (s, 3H), 2.01 (t, *J* = 7.1 Hz, 2H), 1.53-1.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.33, 159.04, 139.57, 137.50, 136.51, 129.78, 128.90, 128.55, 128.49, 128.19, 128.02, 127.42, 127.21, 126.86, 119.04, 114.97, 70.00, 48.79, 27.24, 25.11, 22.16, 16.40. HRMS calcd for $C_{28}H_{29}N_2O_2^+$ $[M+H]^+$ 425.2224, found 425.2220.



3qa

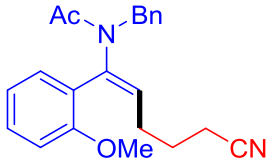
(*E*)-*N*-(1-(benzo[d][1,3]dioxol-5-yl)-5-cyanopent-1-en-1-yl)-*N*-benzylacetamide (3qa): 83.7 mg, 77% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.22 (m, 3H), 7.21-7.16 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.75-6.67 (m, 2H), 6.00 (s, 2H), 5.12 (t, *J* = 7.6 Hz, 1H), 4.50 (s, 2H), 2.29 (q, *J* = 7.6 Hz, 2H), 2.19 (s, 3H), 2.16 (t, *J* = 7.2 Hz, 2H), 1.66-1.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.30, 148.03, 139.56, 137.44, 128.87, 128.81, 128.23, 128.17, 127.26, 122.63, 119.03, 108.42, 101.43, 48.76, 27.30, 25.09, 22.13, 16.47. HRMS calcd for $C_{22}H_{23}N_2O_3^+$ $[M+H]^+$ 363.1703, found 363.1711.



3ra

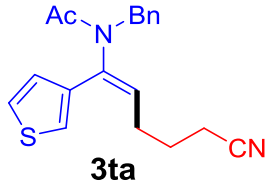
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(o-tolyl)pent-1-en-1-yl)acetamide (3ra): 64.8 mg, 65% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.30-7.17 (m, 6H), 7.12 (d, J = 7.0 Hz, 2H), 7.08-7.04 (m, 1H), 5.42 (s, 1H), 4.42 (s, 2H), 2.36 (s, 3H), 2.20 (s, 2H), 2.13 (s, 3H), 2.02 (q, J = 7.6 Hz, 2H), 1.69-1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.68, 140.02, 137.61, 137.20, 133.66, 131.01, 129.83, 129.03, 128.40, 128.19, 127.18, 126.11, 119.13, 99.98, 48.35, 27.63, 24.96, 22.61, 19.77, 16.81. HRMS calcd for $C_{22}H_{25}N_2O^+$ $[M+H]^+$ 333.1961, found 333.1971.



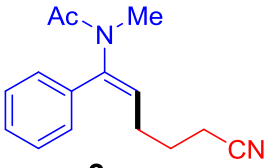
3sa

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(2-methoxyphenyl)pent-1-en-1-yl)acetamide (3sa): 84.7 mg, 81% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.30 (m, 1H), 7.27-7.12 (m, 5H), 7.03-6.87 (m, 3H), 5.30 (t, J = 7.6 Hz, 1H), 4.45 (s, 2H), 3.77 (s, 3H), 2.31 (s, 3H), 2.12 (t, J = 7.2 Hz, 2H), 2.06 (q, J = 7.5 Hz, 2H), 1.64-1.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.89, 157.40, 138.07, 137.80, 131.34, 130.32, 129.98, 128.50, 127.98, 126.85, 122.97, 120.30, 119.11, 111.07, 55.11, 48.21, 27.26, 24.73, 22.20, 16.29. HRMS calcd for $C_{22}H_{25}N_2O_2^+$ $[M+H]^+$ 349.1911, found 349.1910.



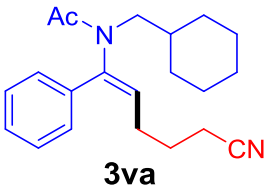
3ta

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(thiophen-3-yl)pent-1-en-1-yl)acetamide (3ta): 64.2 mg, 66% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.35 (m, 1H), 7.31-7.18 (m, 6H), 7.02 (dd, J = 5.0, 1.1 Hz, 1H), 5.12 (t, J = 7.5 Hz, 1H), 4.59 (s, 2H), 2.38 (q, J = 7.5 Hz, 2H), 2.19-2.07 (m, 5H), 1.68-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.31, 137.53, 136.10, 135.52, 129.71, 129.08, 128.28, 127.38, 126.99, 126.52, 125.02, 119.04, 49.37, 27.13, 24.96, 22.05, 16.39. HRMS calcd for $C_{19}H_{21}N_2OS^+$ $[M+H]^+$ 325.1369, found 325.1372.



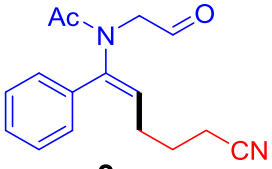
3ua

(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-methylacetamide (3ua): 47.3 mg, 65% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.33 (m, 3H), 7.32-7.23 (m, 2H), 6.09 (t, *J* = 7.2 Hz, 0.1H, minor *Z* isomer), 5.63 (t, *J* = 7.5 Hz, 1H), 3.07 (s, 0.3H, minor *Z* isomer), 2.97 (s, 3H), 2.45 (q, *J* = 7.8 Hz, 2H), 2.38 (t, *J* = 7.1 Hz, 1H), 2.12 (s, 3H), 1.95 (s, 0.3H, minor *Z* isomer), 1.87-1.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ Major *E*-isomer: 170.74, 142.71, 134.66, 128.73, 128.28, 127.06, 125.09, 119.08, 35.20, 27.51, 25.31, 22.06, 16.87. Minor *Z*-isomer: 171.00, 142.65, 135.49, 129.01, 128.87, 127.12, 125.18, 119.14, 34.81, 29.63, 26.93, 24.73, 21.11. HRMS calcd for $C_{15}H_{19}N_2O^+$ $[M+H]^+$ 243.1492, found 243.1510.



3va

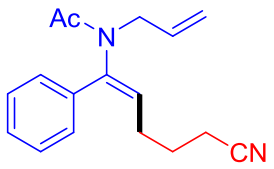
(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(cyclohexylmethyl)acetamide (3a'a): 87.6 mg, 90% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.30 (m, 3H), 7.21 (dd, *J* = 7.8, 1.6 Hz, 2H), 5.53 (t, *J* = 7.5 Hz, 1H), 3.07 (d, *J* = 6.8 Hz, 2H), 2.43 (dt, *J* = 10.6, 7.7 Hz, 2H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.19 (s, 3H), 1.79 (dt, *J* = 14.8, 7.2 Hz, 2H), 1.68-1.50 (m, 6H), 1.18-1.05 (m, 3H), 0.95-0.81 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.80, 141.62, 134.53, 129.01, 128.84, 128.57, 128.32, 119.12, 50.86, 36.62, 30.89, 27.77, 26.50, 25.96, 25.48, 22.53, 17.08. HRMS calcd for $C_{21}H_{29}N_2O^+$ $[M+H]^+$ 325.2274, found 325.2279.



3wa

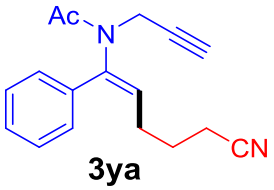
(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(2-oxoethyl)acetamide (3wa): 39.7 mg, 49% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.45-7.37 (m, 3H), 7.35-7.25 (m, 2H), 5.82 (t, J = 7.6 Hz, 1H), 4.07 (s, 2H), 2.46 (q, J = 7.7 Hz, 2H), 2.38 (t, J = 7.1 Hz, 2H), 2.22 (s, 3H), 1.82 (dt, J = 14.7, 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.94, 171.28, 141.22, 134.19, 129.39, 129.02, 128.55, 119.13, 56.95, 27.71, 25.28, 21.72, 17.02. HRMS calcd for $C_{16}H_{19}N_2O_2^+$ $[M+H]^+$ 271.1441, found 271.1442.



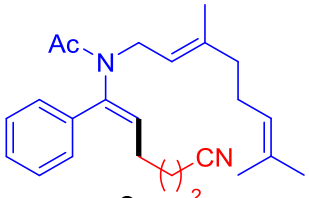
3xa

(*E*)-*N*-allyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (3xa): 50.7 mg, 63% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.36 (m, 3H), 7.28-7.24 (m, 2H), 5.83-5.72 (m, 1H), 5.54 (t, J = 7.5 Hz, 1H), 5.14-4.97 (m, 2H), 3.94 (d, J = 6.3 Hz, 2H), 2.45 (q, J = 7.6 Hz, 2H), 2.37 (t, J = 7.1 Hz, 2H), 2.16 (s, 3H), 1.84-1.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.35, 140.77, 134.80, 133.24, 128.99, 128.83, 128.80, 128.55, 119.14, 117.88, 48.99, 27.67, 25.46, 22.39, 16.96. HRMS calcd for $C_{17}H_{21}N_2O^+$ $[M+H]^+$ 269.1648, found 269.1660.



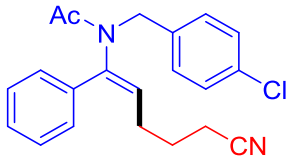
3ya

(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(prop-2-yn-1-yl)acetamide (3ya): 40.7 mg, 51% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.38 (m, 3H), 7.34-7.29 (m, 2H), 5.73 (t, J = 7.5 Hz, 1H), 4.21 (d, J = 2.1 Hz, 2H), 2.49 (q, J = 7.6 Hz, 2H), 2.40 (t, J = 7.1 Hz, 2H), 2.20 (t, J = 2.2 Hz, 1H), 2.13 (s, 3H), 1.88-1.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.30, 140.23, 134.42, 129.35, 129.18, 128.88, 128.62, 119.18, 79.12, 71.86, 35.98, 27.69, 25.45, 22.29, 16.95. HRMS calcd for $C_{17}H_{19}N_2O^+$ $[M+H]^+$ 267.1492, found 267.1487.



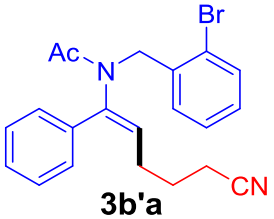
3za

***N*-((*E*)-5-cyano-1-phenylpent-1-en-1-yl)-*N*-((*E*)-3,7-dimethylocta-2,6-dien-1-yl)acetamide (3za)**: 74.4 mg, 68% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.34 (m, 3H), 7.24 (d, J = 7.1 Hz, 2H), 5.50 (t, J = 7.5 Hz, 1H), 5.15 (t, J = 6.8 Hz, 1H), 5.04 (t, J = 6.2 Hz, 1H), 3.94 (d, J = 7.0 Hz, 2H), 2.43 (q, J = 7.6 Hz, 2H), 2.34 (t, J = 7.1 Hz, 2H), 2.12 (s, 3H), 2.06-1.97 (m, 2H), 1.97-1.91 (m, 2H), 1.81-1.73 (m, 2H), 1.66 (s, 3H), 1.58 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.25, 141.06, 139.19, 134.89, 131.66, 128.88, 128.68, 128.62, 128.37, 125.72, 124.02, 119.40, 43.95, 39.62, 27.74, 26.55, 25.80, 25.48, 22.43, 17.78, 16.97, 16.15. HRMS calcd for $C_{24}H_{33}N_2O^+$ $[M+H]^+$ 365.2587, found 365.2574.



3a'a

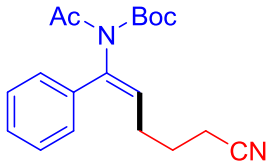
(*E*)-*N*-(4-chlorobenzyl)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (3a'a): 78.3 mg, 74% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.38 (m, 3H), 7.29-7.20 (m, 4H), 7.12 (d, J = 8.5 Hz, 2H), 5.22 (t, J = 7.6 Hz, 1H), 4.44 (s, 2H), 2.35 (q, J = 7.6 Hz, 2H), 2.23 (d, J = 6.1 Hz, 5H), 1.67 (dt, J = 14.7, 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.65, 140.21, 136.09, 134.32, 133.29, 130.49, 129.72, 129.25, 129.02, 128.64, 128.58, 119.06, 48.36, 27.57, 25.29, 22.34, 16.85. HRMS calcd for $C_{21}H_{22}ClN_2O^+$ $[M+H]^+$ 353.1415, found 353.1426.



3b'a

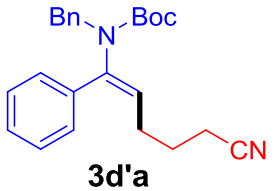
(*E*)-*N*-(2-bromobenzyl)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (3b'a): 78.4 mg, 66% yield. Yellow oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 1H), 7.42-7.35 (m, 3H), 7.24-7.18 (m, 4H), 7.14-7.08 (m, 1H), 5.42 (t, J = 7.6 Hz, 1H), 4.70 (s, 2H), 2.32 (q, J = 7.7 Hz, 2H), 2.21 (d, J = 11.3 Hz, 5H), 1.69-1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.74, 140.28, 136.52, 134.34, 132.71, 131.00, 129.57, 128.97, 128.72, 128.53, 127.41, 124.00, 119.06, 49.18, 27.43, 25.15, 22.25, 16.66. HRMS calcd for $C_{21}H_{22}BrN_2O^+$ $[M+H]^+$ 397.0910, found 397.0912.



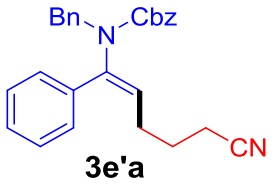
3c'a

***tert*-butyl (*E*)-acetyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (3c'a)**: 78.7 mg, 80% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 3H), 7.26 (d, J = 1.8 Hz, 1H), 7.24 (dd, J = 2.6, 1.1 Hz, 1H), 5.47 (t, J = 7.7 Hz, 1H), 2.53 (s, 3H), 2.40 (q, J = 7.2 Hz, 2H), 2.34 (t, J = 7.4 Hz, 2H), 1.81-1.71 (m, 2H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.65, 152.73, 137.47, 136.28, 129.25, 128.83, 128.28, 119.63, 83.35, 27.86, 27.21, 26.64, 25.40, 16.30. HRMS calcd for $C_{19}H_{25}N_2O_3^+$ $[M+H]^+$ 329.1860, found 329.1851.



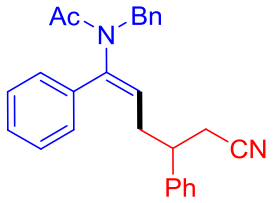
3d'a

***tert*-butyl (*E*)-benzyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (3d'a)**: 90.4 mg, 80% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.23 (m, 8H), 7.20-7.15 (m, 2H), 5.31 (t, J = 7.6 Hz, 1H), 4.53 (s, 2H), 2.21 (q, J = 7.4 Hz, 2H), 2.11 (t, J = 7.3 Hz, 2H), 1.63-1.54 (m, 2H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.04, 140.12, 138.47, 136.58, 128.61, 128.30, 128.16, 127.93, 127.16, 119.33, 80.25, 51.88, 28.18, 26.99, 25.46, 16.17. HRMS calcd for $C_{24}H_{29}N_2O_2^+$ $[M+H]^+$ 377.2224, found 377.2222.



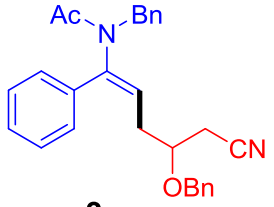
3e'a

benzyl (*E*)-benzyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (3e'a): 103.4 mg, 84% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 10H), 7.25-7.15 (m, 5H), 5.29 (s, 1H), 5.17 (s, 2H), 4.47 (s, 2H), 2.20 (q, J = 7.2 Hz, 2H), 1.98 (s, 2H), 1.52 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.14, 137.79, 136.31, 135.57, 128.95, 128.60, 128.53, 128.47, 128.44, 128.27, 128.20, 127.50, 67.85, 51.51, 26.99, 25.36, 15.93. HRMS calcd for $C_{27}H_{27}N_2O_2^+$ $[M+H]^+$ 411.2067, found 411.2068.



3ab

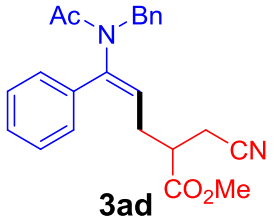
(*E*)-*N*-benzyl-*N*-(5-cyano-1,4-diphenylpent-1-en-1-yl)acetamide (3ab): 92.3 mg, 78% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.38 (m, 3H), 7.30-7.22 (m, 6H), 7.16-7.12 (m, 2H), 7.09 (dd, J = 6.7, 2.7 Hz, 2H), 6.93 (dd, J = 6.4, 2.9 Hz, 2H), 5.08 (dd, J = 8.2, 6.5 Hz, 1H), 4.73 (d, J = 14.4 Hz, 1H), 4.04 (d, J = 14.4 Hz, 1H), 3.04-2.85 (m, 1H), 2.78-2.55 (m, 2H), 2.45 (dd, J = 7.0, 4.0 Hz, 2H), 1.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.72, 140.63, 140.22, 137.51, 134.58, 129.17, 129.09, 128.92, 128.87, 128.71, 128.46, 128.42, 127.95, 127.37, 127.27, 118.14, 48.95, 42.44, 33.55, 25.05, 21.68. HRMS calcd for $C_{27}H_{27}N_2O^+$ $[M+H]^+$ 395.2118, found 395.2132.



3ac

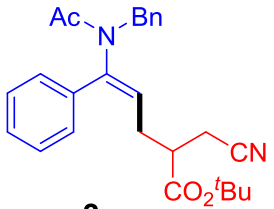
(*E*)-*N*-benzyl-*N*-(4-(benzyloxy)-5-cyano-1-phenylpent-1-en-1-yl)acetamide (3ac): 51.0 mg, 40% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.0 Hz, 3H), 7.32 (d, J = 7.3 Hz, 3H), 7.28-7.19 (m, 7H), 7.19-7.15 (m, 2H), 5.29 (t, J = 7.6 Hz, 1H), 4.60-4.27 (m, 4H), 3.63-3.56 (m, 1H), 2.62-2.42 (m, 2H),

2.30 (d, J = 5.7 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.64, 141.38, 137.63, 137.01, 134.42, 129.19, 129.04, 128.97, 128.71, 128.69, 128.51, 128.32, 127.97, 127.50, 126.17, 117.14, 74.01, 72.06, 48.93, 33.20, 22.82, 22.38. HRMS calcd for $C_{28}H_{29}N_2O_2^+$ $[M+H]^+$ 425.2224, found 425.2219.



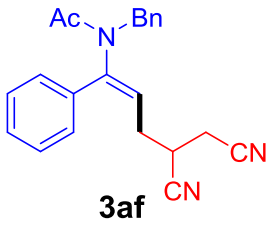
3ad

methyl (*E*)-5-(*N*-benzylacetamido)-2-(cyanomethyl)-5-phenylpent-4-enoate (3ad): 102.8 mg, 91% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.41 (m, 3H), 7.34-7.25 (m, 3H), 7.25-7.21 (m, 2H), 7.20-7.16 (m, 2H), 5.19 (t, J = 7.2 Hz, 1H), 4.64-4.37 (m, 2H), 3.63 (s, 3H), 2.77-2.51 (m, 3H), 2.49-2.25 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.99, 170.44, 141.81, 137.45, 134.22, 129.29, 128.99, 128.93, 128.60, 128.47, 127.48, 126.22, 117.26, 52.65, 49.03, 41.37, 29.82, 22.38, 18.99. HRMS calcd for $C_{23}H_{25}N_2O_3^+$ $[M+H]^+$ 377.1860, found 377.1855.



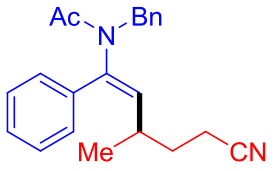
3ae

***tert*-butyl (*E*)-5-(*N*-benzylacetamido)-2-(cyanomethyl)-5-phenylpent-4-enoate (3ae)**: 94.2 mg, 75% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.36 (m, 3H), 7.33-7.23 (m, 1H), 7.20-7.16 (m, 4H), 5.20 (t, J = 7.2 Hz, 1H), 4.51(s, 2H), 2.68-2.24 (m, 4.5H), 2.22 (s, 3H), 2.22-2.18 (m, 0.5H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.58, 170.40, 141.46, 137.46, 134.22, 129.16, 128.90, 128.86, 128.59, 128.42, 127.43, 126.65, 117.38, 82.52, 48.97, 42.27, 29.80, 27.88, 22.39, 18.94. HRMS calcd for $C_{26}H_{31}N_2O_3^+$ $[M+H]^+$ 419.2329, found 419.2325.



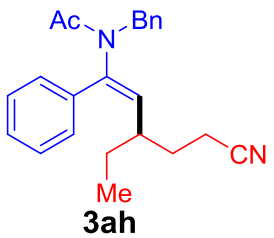
3af

(*E*)-*N*-benzyl-*N*-(4,5-dicyano-1-phenylpent-1-en-1-yl)acetamide (3af): 92.7 mg, 90% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.38 (m, 3H), 7.31-7.24 (m, 3H), 7.24-7.20 (m, 2H), 7.19-7.14 (m, 2H), 5.28 (t, J = 6.8 Hz, 1H), 4.70-4.33 (m, 2H), 2.92-2.73 (m, 1H), 2.65-2.53 (m, 2H), 2.52-2.35 (m, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.32, 143.47, 137.23, 133.84, 129.57, 129.06, 128.85, 128.61, 128.52, 127.52, 123.81, 118.29, 115.32, 49.04, 30.22, 28.27, 22.54, 20.31. HRMS calcd for $C_{22}H_{22}N_3O^+$ $[M+H]^+$ 344.1757, found 344.1749.



3ag

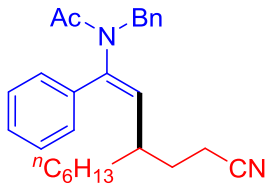
(*E*)-*N*-benzyl-*N*-(5-cyano-3-methyl-1-phenylpent-1-en-1-yl)acetamide (3ag): 69.8 mg, 70% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.37 (m, 3H), 7.34-7.27 (m, 3H), 7.27-7.22 (m, 2H), 7.21-7.16 (m, 2H), 4.89 (t, J = 12.6 Hz, 2H), 4.11 (d, J = 14.3 Hz, 1H), 2.70-2.57 (m, 1H), 2.27 (s, 3H), 2.07-1.84 (m, 2H), 1.59 (td, J = 13.7, 7.7 Hz, 1H), 1.44 (td, J = 14.2, 8.2 Hz, 1H), 0.90 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.07, 138.76, 137.42, 136.18, 134.39, 129.16, 128.99, 128.88, 128.42, 128.34, 127.45, 119.33, 48.19, 32.30, 31.60, 22.34, 19.94, 14.85. HRMS calcd for $C_{22}H_{25}N_2O^+$ $[M+H]^+$ 333.1961, found 333.1973.



3ah

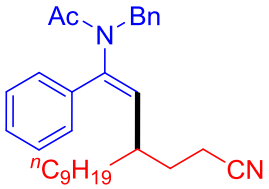
(*E*)-*N*-benzyl-*N*-(5-cyano-3-ethyl-1-phenylpent-1-en-1-yl)acetamide (3ah): 53.0 mg, 51% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.45-7.42 (m, 3H), 7.35-7.28 (m, 3H), 7.28-7.22 (m, 2H), 7.21-7.17 (m, 2H), 4.94-4.80 (m, 2H), 4.14 (d, *J* = 14.4 Hz, 1H), 2.43 (ddd, *J* = 13.9, 9.1, 5.0 Hz, 1H), 2.31 (s, 3H), 1.93 (ddd, *J* = 16.3, 8.2, 5.7 Hz, 1H), 1.78 (dt, *J* = 16.5, 7.8 Hz, 1H), 1.67 (ddd, *J* = 16.5, 8.1, 4.0 Hz, 1H), 1.44-1.29 (m, 2H), 1.20 (dq, *J* = 13.9, 7.6 Hz, 1H), 0.69 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.12, 140.08, 137.60, 135.25, 134.64, 129.21, 129.02, 128.97, 128.62, 128.53, 127.62, 119.51, 77.48, 76.84, 48.20, 38.26, 30.66, 27.85, 22.54, 14.81, 11.44. HRMS calcd for $C_{23}H_{27}N_2O^+$ $[M+H]^+$ 347.2118, found 347.2097.



3ai

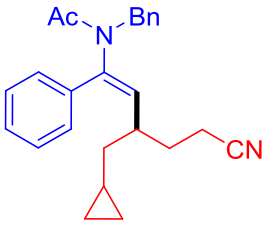
(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylnon-1-en-1-yl)acetamide (3ai): 82.1 mg, 68% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.36 (m, 3H), 7.34-7.28 (m, 3H), 7.24 (d, *J* = 6.8 Hz, 2H), 7.20-7.16 (m, 2H), 4.94-4.80 (m, 2H), 4.12 (d, *J* = 14.4 Hz, 1H), 2.52-2.46 (m, 1H), 2.31 (s, 3H), 1.95-1.88 (m, 1H), 1.82-1.74 (m, 1H), 1.69-1.60 (m, 1H), 1.42-1.32 (m, 1H), 1.21-1.01 (m, 10H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.99, 139.74, 137.50, 135.44, 134.53, 129.10, 128.90, 128.86, 128.49, 127.50, 119.44, 48.04, 36.44, 34.85, 31.59, 30.94, 29.09, 26.70, 22.54, 22.41, 14.70, 14.05. HRMS calcd for $C_{27}H_{35}N_2O^+$ $[M+H]^+$ 403.2744, found 403.2756.



3aj

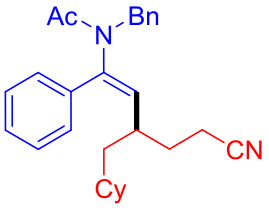
(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenyldodec-1-en-1-yl)acetamide (3aj): 93.4 mg, 70% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.37 (m, 3H), 7.34-7.27 (m, 3H), 7.24 (d, *J* = 7.1 Hz, 2H), 7.19 (d, *J* = 7.0 Hz, 2H), 4.88 (d, *J* = 11.0 Hz, 2H), 4.12 (d, *J* = 14.4 Hz, 1H), 2.55-2.44 (m, 1H), 2.31 (s, 3H), 1.91 (dt, *J* = 14.0, 6.9 Hz, 1H), 1.77 (dt, *J* = 16.5, 7.9 Hz, 1H), 1.69-1.60 (m, 1H), 1.42-1.33 (m, 1H),

1.26-1.02 (m, 16H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.05, 139.81, 137.53, 135.49, 134.56, 129.14, 128.94, 128.89, 128.52, 128.45, 127.55, 119.47, 48.08, 36.48, 34.90, 31.89, 30.98, 29.51, 29.47, 29.44, 29.28, 26.79, 14.74, 14.18. HRMS calcd for $C_{30}H_{41}N_2O^+$ $[M+H]^+$ 445.3213, found 445.3210.



3ak

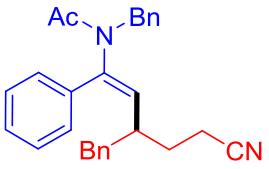
(*E*)-*N*-benzyl-*N*-(5-cyano-3-(cyclopropylmethyl)-1-phenylpent-1-en-1-yl)acetamide (3ak): 59.2 mg, 53% yield. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.35 (m, 3H), 7.33-7.24 (m, 5H), 7.22-7.14 (m, 2H), 4.97 (d, J = 10.9 Hz, 1H), 4.70 (d, J = 14.4 Hz, 1H), 4.33 (d, J = 14.4 Hz, 1H), 2.78-2.56 (m, 1H), 2.31 (s, 3H), 2.01-1.90 (m, 1H), 1.86-1.65 (m, 2H), 1.42-1.26 (m, 2H), 0.92 (dq, J = 12.6, 6.2 Hz, 1H), 0.36-0.29 (m, 2H), 0.27-0.20 (m, 1H), -0.11--0.22 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.10, 139.89, 137.58, 135.14, 134.62, 129.12, 128.97, 128.89, 128.58, 128.45, 127.51, 119.39, 48.22, 39.96, 37.44, 30.69, 22.52, 14.86, 8.54, 5.00, 4.84. HRMS calcd for $C_{25}H_{29}N_2O^+$ $[M+H]^+$ 373.2274, found 373.2261.



3al

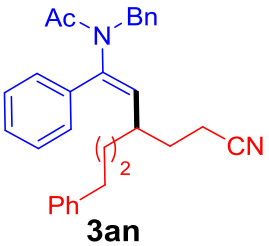
(*E*)-*N*-benzyl-*N*-(5-cyano-3-(cyclohexylmethyl)-1-phenylpent-1-en-1-yl)acetamide (3al): 92.0 mg, 74% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.44-7.38 (m, 3H), 7.36-7.28 (m, 3H), 7.27-7.22 (m, 2H), 7.22-7.17 (m, 2H), 5.11 (d, J = 14.4 Hz, 1H), 4.84 (d, J = 10.7 Hz, 1H), 3.91 (d, J = 14.4 Hz, 1H), 2.59 (dt, J = 9.7, 4.4 Hz, 1H), 2.31 (s, 3H), 1.94-1.83 (m, 1H), 1.79-1.68 (m, 1H), 1.68-1.51 (m, 3H), 1.48-1.27 (m, 3H), 1.14-1.05 (m, 2H), 1.00 (dd, J = 12.4, 4.2 Hz, 4H), 0.90-0.68 (m, 2H), 0.59-0.45 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.05, 139.90, 137.59, 135.71, 134.67, 129.16, 128.97, 128.91,

128.51, 128.46, 127.60, 119.57, 48.09, 42.98, 34.92, 33.83, 33.75, 32.74, 31.28, 26.42, 26.38, 26.05, 22.34, 14.74. HRMS calcd for $C_{28}H_{35}N_2O^+$ $[M+H]^+$ 415.2744, found 415.2744.



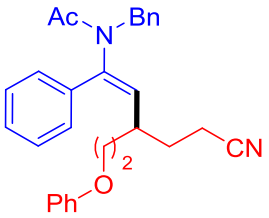
3am

(*E*)-*N*-benzyl-*N*-(3-benzyl-5-cyano-1-phenylpent-1-en-1-yl)acetamide (3am): 73.5 mg, 60% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.30 (m, 6H), 7.21-7.11 (m, 2H), 7.03-6.96 (m, 3H), 6.83-6.76 (m, 2H), 4.96 (d, J = 10.8 Hz, 2H), 4.86 (d, J = 14.5 Hz, 1H), 4.06 (d, J = 14.5 Hz, 1H), 2.90-2.74 (m, 1H), 2.60 (dd, J = 13.8, 6.1 Hz, 1H), 2.47 (dd, J = 13.7, 8.3 Hz, 1H), 2.01 (s, 3H), 1.98-1.88 (m, 1H), 1.87-1.77 (m, 1H), 1.75-1.64 (m, 1H), 1.48-1.35 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.18, 140.64, 138.14, 137.61, 134.49, 134.07, 129.01, 128.97, 128.80, 128.54, 128.51, 128.46, 127.59, 126.58, 119.28, 48.37, 41.17, 38.34, 30.64, 22.23, 14.80. HRMS calcd for $C_{28}H_{29}N_2O^+$ $[M+H]^+$ 409.2274, found 409.2281.



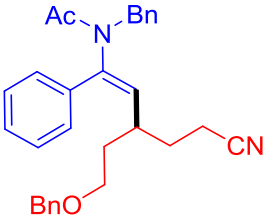
3an

(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1,6-diphenylhex-1-en-1-yl)acetamide (3an): 61.6 mg, 47% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 3H), 7.25 (dd, J = 17.5, 7.4 Hz, 7H), 7.16 (d, J = 6.6 Hz, 3H), 6.98 (d, J = 7.3 Hz, 2H), 4.92-4.75 (m, 2H), 4.12 (d, J = 14.4 Hz, 1H), 2.57-2.45 (m, 1H), 2.38 (q, J = 6.6 Hz, 2H), 2.26 (s, 3H), 1.89 (dt, J = 14.0, 6.6 Hz, 1H), 1.75 (dt, J = 16.5, 7.9 Hz, 1H), 1.63 (td, J = 13.0, 7.8 Hz, 1H), 1.35 (dt, J = 14.6, 7.7 Hz, 4H), 1.17 (dt, J = 12.8, 6.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.03, 141.65, 139.99, 137.51, 135.17, 134.49, 129.16, 129.08, 129.01, 128.57, 128.50, 128.37, 127.60, 125.94, 119.42, 48.10, 36.37, 35.56, 34.26, 30.98, 28.43, 22.49, 14.73. HRMS calcd for $C_{30}H_{33}N_2O^+$ $[M+H]^+$ 437.2587, found 437.2578.



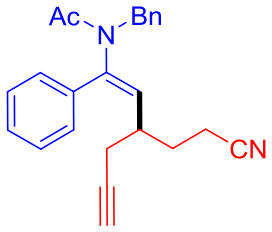
3ao

(*E*)-*N*-benzyl-*N*-(5-cyano-3-(2-phenoxyethyl)-1-phenylpent-1-en-1-yl)acetamide (3ao): 90.8 mg, 69% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 3H), 7.29-7.23 (m, 5H), 7.22-7.18 (m, 2H), 7.14 (d, *J* = 6.9 Hz, 2H), 7.00-6.86 (m, 1H), 6.68 (d, *J* = 8.1 Hz, 2H), 4.93 (d, *J* = 10.9 Hz, 1H), 4.48 (q, *J* = 14.4 Hz, 2H), 3.84-3.69 (m, 1H), 3.51 (td, *J* = 9.1, 4.4 Hz, 1H), 2.86 (dt, *J* = 9.5, 4.9 Hz, 1H), 2.28 (s, 3H), 2.03-1.91 (m, 1H), 1.90-1.76 (m, 2H), 1.75-1.67 (m, 1H), 1.55-1.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.82, 158.21, 140.91, 137.41, 134.09, 133.74, 129.37, 129.01, 128.83, 128.48, 128.40, 127.49, 120.85, 119.17, 114.24, 64.23, 48.08, 34.21, 33.74, 31.07, 22.49, 14.74. HRMS calcd for $C_{29}H_{31}N_2O_2^+$ $[M+H]^+$ 439.2380, found 439.2387.



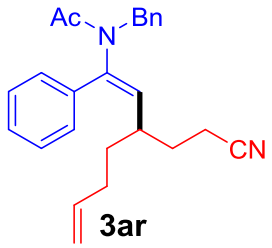
3ap

(*E*)-*N*-benzyl-*N*-(5-(benzyloxy)-3-(2-cyanoethyl)-1-phenylpent-1-en-1-yl)acetamide (3ap): 57.0 mg, 42% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 11H), 7.21-7.15 (m, 4H), 4.89 (d, *J* = 10.9 Hz, 1H), 4.69 (d, *J* = 14.4 Hz, 1H), 4.39-4.11 (m, 3H), 3.28 (dt, *J* = 10.3, 5.4 Hz, 1H), 3.07 (td, *J* = 8.9, 5.1 Hz, 1H), 2.84-2.73 (m, 1H), 2.24 (s, 3H), 1.93-1.88 (m, 1H), 1.79 (dt, *J* = 16.3, 8.0 Hz, 2H), 1.72-1.59 (m, 2H), 1.46-1.33 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.12, 140.50, 138.02, 137.59, 134.50, 134.35, 129.18, 129.11, 129.02, 128.59, 128.49, 127.81, 127.64, 119.37, 73.07, 67.22, 48.25, 34.95, 33.90, 31.21, 22.51, 14.80. HRMS calcd for $C_{30}H_{33}N_2O_2^+$ $[M+H]^+$ 453.2537, found 453.2534.



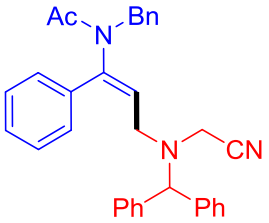
3aq

(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylhex-1-en-5-yn-1-yl)acetamide (3aq): 48.1 mg, 45% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, *J* = 7.3 Hz, 3H), 7.31 (tdd, *J* = 8.0, 3.7, 2.1 Hz, 3H), 7.28-7.24 (m, 2H), 7.21-7.17 (m, 2H), 5.13-4.99 (m, 2H), 3.96 (d, *J* = 14.3 Hz, 1H), 2.84-2.66 (m, 1H), 2.32 (s, 3H), 2.19-2.11 (m, 2H), 1.95 (t, *J* = 2.7 Hz, 2H), 1.90-1.73 (m, 2H), 1.63-1.49 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.24, 141.03, 137.45, 134.27, 132.77, 129.26, 129.18, 129.00, 128.61, 128.49, 127.58, 119.13, 80.20, 71.44, 48.19, 35.20, 29.70, 24.03, 22.59, 14.71. HRMS calcd for $C_{24}H_{25}N_2O^+$ $[M+H]^+$ 357.1961, found 357.1963.



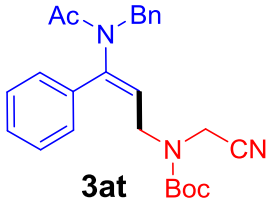
3ar

(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylhepta-1,6-dien-1-yl)acetamide (3ar): 58.1 mg, 52% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (q, *J* = 9.0, 7.7 Hz, 3H), 7.35-7.28 (m, 3H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 6.9 Hz, 2H), 5.54 (td, *J* = 16.8, 6.6 Hz, 1H), 4.95-4.80 (m, 3H), 4.73 (d, *J* = 17.1 Hz, 1H), 4.15 (d, *J* = 14.3 Hz, 1H), 2.59-2.48 (m, 1H), 2.31 (s, 3H), 1.91 (dt, *J* = 14.2, 6.9 Hz, 1H), 1.79 (ddt, *J* = 24.3, 15.6, 8.1 Hz, 3H), 1.66 (ddt, *J* = 16.0, 8.0, 4.7 Hz, 1H), 1.44-1.31 (m, 2H), 1.24 (dt, *J* = 10.1, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.99, 140.17, 137.51, 137.42, 135.01, 134.44, 129.15, 129.04, 128.96, 128.55, 128.49, 127.60, 119.36, 115.26, 48.12, 36.05, 34.19, 30.94, 30.90, 22.47, 14.72. HRMS calcd for $C_{25}H_{29}N_2O^+$ $[M+H]^+$ 373.2274, found 373.2294.



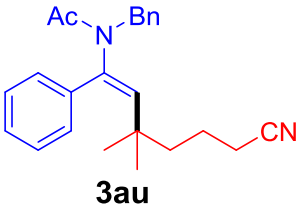
3as

(*E*)-*N*-(3-(benzhydryl(cyanomethyl)amino)-1-phenylprop-1-en-1-yl)-*N*- benzylacetamide (3as): 75.7 mg, 52% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 5.4 Hz, 3H), 7.35 (d, J = 7.3 Hz, 3H), 7.32-7.28 (m, 2H), 7.27-7.15 (m, 12H), 5.31 (t, J = 6.8 Hz, 1H), 4.54 (s, 2H), 4.49 (s, 1H), 3.24 (d, J = 7.1 Hz, 2H), 3.07 (s, 2H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.30, 164.27, 159.88, 142.25, 140.89, 137.58, 134.00, 129.36, 129.15, 129.06, 128.90, 128.64, 128.57, 128.00, 127.85, 127.66, 127.55, 114.75, 72.73, 49.57, 48.75, 39.62, 22.46. HRMS calcd for $C_{33}H_{32}N_3O^+$ $[M+H]^+$ 486.2540, found 486.2559.



3at

***tert*-butyl (*E*)-(3-(*N*-benzylacetamido)-3-phenylallyl)(cyanomethyl)carbamate (3at)**: 100.7 mg, 80% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.41 (m, 3H), 7.32-7.24 (m, 3H), 7.23-7.16 (m, 4H), 5.32 (t, J = 5.2 Hz, 1H), 4.55 (s, 2H), 4.04 (d, J = 5.4 Hz, 2H), 3.91-3.74 (m, 2H), 2.23 (s, 3H), 1.48-1.30 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.50, 153.65, 142.59, 137.34, 133.84, 129.58, 129.01, 128.85, 128.67, 128.52, 127.49, 125.43, 115.74, 82.30, 49.17, 45.36, 34.71, 28.12, 22.48. HRMS calcd for $C_{25}H_{30}N_3O_3^+$ $[M+H]^+$ 420.2282, found 420.2298.



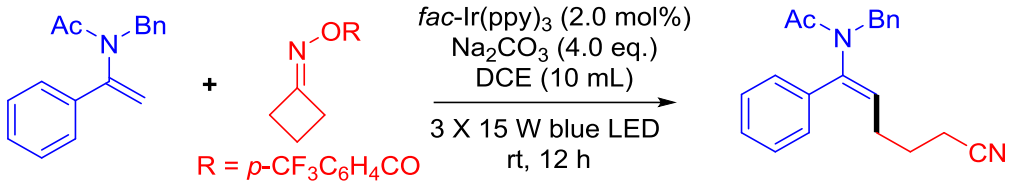
3au

(*E*)-*N*-benzyl-*N*-(6-cyano-3,3-dimethyl-1-phenylhex-1-en-1-yl)acetamide (3au): 50.8 mg, 47% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (10:1 *v*/*v*).

^{1}H NMR (400 MHz, $CDCl_3$) δ7.40-7.37 (m, 3H), 7.36-7.28 (m, 3H), 7.25-7.20 (m, 4H), 5.10 (s, 1H), 4.44 (s, 2H), 2.37 (s, 3H), 2.01 (t, J = 6.8 Hz, 2H), 1.27-1.21 (m, 2H), 1.20-1.12 (m, 2H), 0.79 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ169.94, 141.43, 137.66, 136.81, 135.83, 129.65, 129.15, 128.94, 128.43, 128.25, 127.32, 119.50, 47.36, 42.88, 35.88, 28.58, 22.50, 20.86, 17.58. HRMS calcd for $C_{24}H_{29}N_2O^+$ $[M+H]^+$ 361.2274, found 361.2294.

Synthetic Applications of *β*-cyanoalkylated Enamides

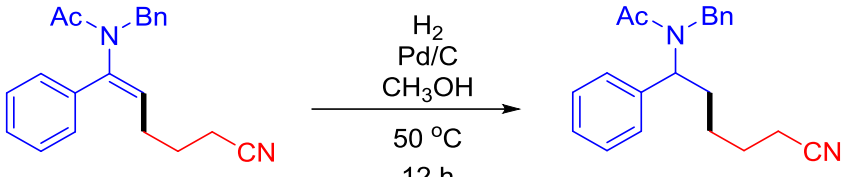
(a) Large-Scale Synthesis of *β*-Cyanoalkylated Enamides



1a 4.5 mmol　　**2a** 3.0 mmol　　**3aa** 0.77 g, 81% yield

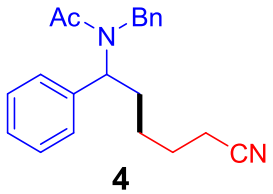
To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **1a** (1.13 g, 4.5 mmol), Cyclobutanone Oximes **2a** (771.6 mg 3.0 mmol), *fac*-Ir(ppy)$_3$ (39.0 mg, 2.0 mol%), and Na_2CO_3 (636.0 mg, 6.0 mmol). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 10.0 mL DCE was then added via syringe with gentle stirring under N_2 atmosphere. The tube was sealed and stirred under blue LEDs for 12 hours. The solvent was then removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:4 *v*/*v*), to give compound **3a** in 81% yield (0.77 g).

(b) Hydrogenation of *β*-cyanoalkylated Enamide 3aa



3aa　　**4**

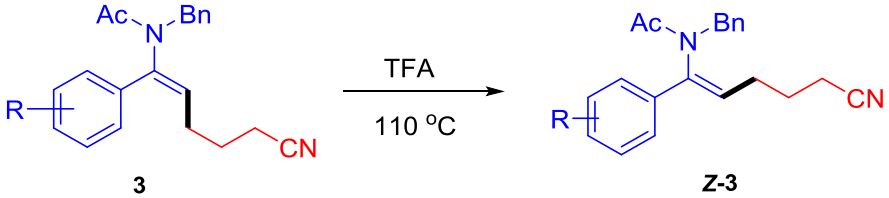
To a 10 mL round bottom flask (RBF) was added (*E*)-*N*-benzyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3aa**) (159.2 mg, 0.5 mmol), palladium-charcoal (0.02 g) and methanol (2.0 mL). The tube was sealed with a rubber stopper, evacuated and backfilled with hydrogen gas filled in a hydrogen balloon (1.0 atm). The resulting mixture was stirred at 50 °C for 12 h. Upon completion of the reaction as monitored by TLC, the solvent was removed under vacuum. The residue was purified directly by column chromatography, eluting with ethyl acetate/petroleum ether (1:10 *v*/*v*) to give **4** as colorless oil.



4

***N*-benzyl-*N*-(5-cyano-1-phenylpentyl)acetamide (4)**: 115.4 mg, 72% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:10 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) for two rotamers: δ 7.40-7.17 (m, 9H), 6.97 (d, J = 7.0 Hz, 1H), 5.94 and 4.96 (2×t, J = 7.8 Hz, 1H), 5.04 and 4.41 (2×d, J = 17.6 Hz, 1H), 4.23 and 3.73 (2×d, J = 17.6 Hz, 1H), 2.26 and 2.05 (t, J = 7.1 Hz, 2H), 2.37 and 2.08 (s, 3H), 1.96-1.74 (m, 2H), 1.73-1.49 (m, 2H), 1.47-1.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) for two conformers: δ 172.04, 139.16, 137.84, 128.66, 128.63, 128.56, 127.91, 127.23, 126.13, 119.67, 56.16, 48.05, 29.96, 25.79, 25.09, 22.82, 17.02.. HRMS calcd for $C_{21}H_{25}N_2O^+$ $[M+H]^+$ 321.1961, found 321.1944.

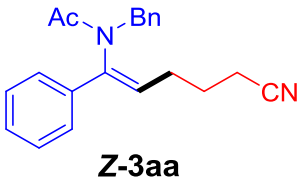
(c) Conversion of Stereochemistry of *β*-cyanoalkylated Enamides



3 R = H, 4-Cl, 4-OMe

***Z*-3**

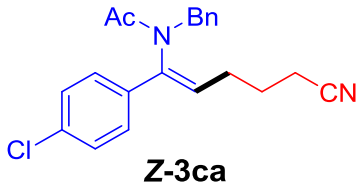
0.3 mmol (1.0 eq) of enamide **3** was dissolved in dry benzene (2.0 mL) in a screw cap vial. 102.6 mg (1.5 mmol, 5.0 eq) of trifluoroacetic acid was then added to the solution and the vial was heated at 110 °C. Upon the completion of the reaction, the mixture was concentrated in vacuum and the product was isolated through flash column chromatography (ethyl acetate/petroleum ether) to furnish ***Z*-3**.



***Z*-3aa**

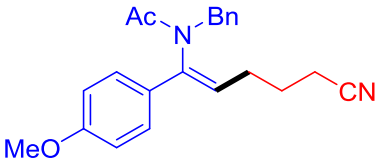
(*Z*)-*N*-benzyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (*Z*-3aa): 52.5 mg, 55% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (m, 5H), 7.31-7.25 (m, 5H), 5.90 (dd, J = 10.2, 4.5 Hz, 1H),

5.62 (d, J = 13.8 Hz, 1H), 3.49 (d, J = 13.8 Hz, 1H), 2.07 (s, 3H), 1.96-1.86 (m, 1H), 1.81 (t, J = 7.3 Hz, 2H), 1.69-1.57 (m, 1H), 1.46-1.32 (m, 1H), 0.86-0.75 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.76, 139.57, 137.47, 135.60, 130.14, 129.22, 128.92, 128.51, 127.86, 127.75, 125.88, 119.35, 48.51, 27.79, 24.41, 21.29, 16.63. HRMS calcd for $C_{21}H_{23}N_2O^+$ $[M+H]^+$ 319.1805, found 319.1804.



***Z*-3ca**

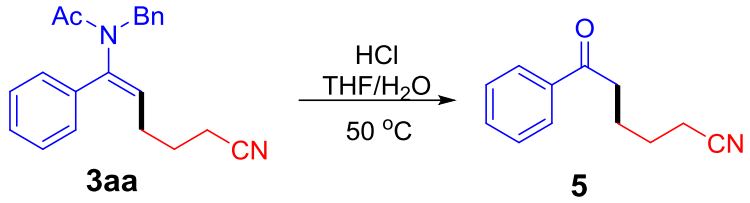
(*Z*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-5-cyanopent-1-en-1-yl)acetamide (*Z*-3ca): 57.2 mg, 54% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.36 (m, 2H), 7.32 (d, J = 2.1 Hz, 1H), 7.31-7.24 (m, 6H), 5.91 (dd, J = 10.2, 4.5 Hz, 1H), 5.59 (d, J = 13.9 Hz, 1H), 3.49 (d, J = 13.9 Hz, 1H), 2.05 (s, 3H), 1.97-1.86 (m, 1H), 1.82 (td, J = 7.2, 2.3 Hz, 2H), 1.69-1.57 (m, 1H), 1.44-1.32 (m, 1H), 0.86-0.75 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.49, 138.61, 137.21, 134.72, 134.17, 130.02, 129.34, 128.49, 128.26, 127.87, 127.10, 119.22, 48.50, 27.75, 24.27, 21.19, 16.57. HRMS calcd for $C_{21}H_{22}ClN_2O^+$ $[M+H]^+$ 353.1415, found 353.1428.



***Z*-3ma**

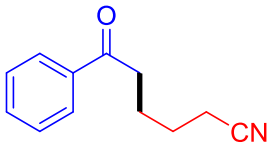
(*Z*)-*N*-benzyl-*N*-(5-cyano-1-(4-methoxyphenyl)pent-1-en-1-yl)acetamide (*Z*-3ma): 66.9 mg, 64% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.26 (m, 7H), 6.97-6.91 (m, 2H), 5.77 (dd, J = 10.2, 4.5 Hz, 1H), 5.60 (d, J = 13.8 Hz, 1H), 3.85 (s, 3H), 3.50 (d, J = 13.8 Hz, 1H), 2.06 (s, 3H), 1.94-1.84 (m, 1H), 1.80 (t, J = 7.3 Hz, 2H), 1.65-1.53 (m, 1H), 1.42-1.32 (m, 1H), 0.78 (m, J = 13.3, 10.1, 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ170.70, 160.17, 139.18, 137.53, 130.13, 128.47, 128.02, 127.80, 127.19, 125.78, 119.41, 114.51, 55.50, 48.45, 27.72, 24.50, 21.28, 16.60. HRMS calcd for $C_{22}H_{25}N_2O_2^+$ $[M+H]^+$ 349.3911, found 349.3900.

(d) Hydrolysis of *β*-cyanoalkylated Enamides 3aa



3aa **5**

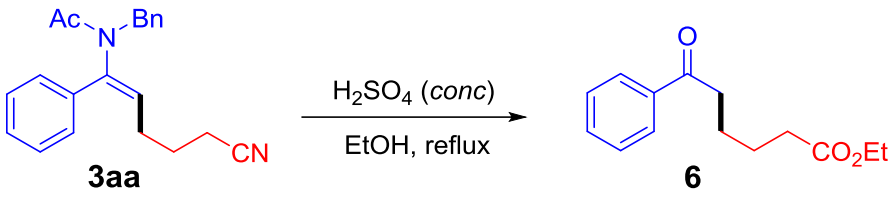
Enamides **3aa** (0.3 mmol) was added into a reaction tube. THF (1.0 mL) and concentrated hydrochloric acid (1.0 mL) were then added sequentially by syringe. The resulting mixture was stirred at 50 °C. Upon completion of the reaction as monitored by TLC, the solvent was removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:10 *v/v*) to give **5** as colorless oil.



5

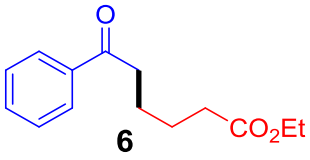
6-oxo-6-phenylhexanenitrile (5): 39.3 mg, 70% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:10 *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 3.05 (t, J = 6.9 Hz, 2H), 2.41 (t, J = 7.1 Hz, 2H), 1.91 (dt, J = 15.1, 7.0 Hz, 2H), 1.83-1.67 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.22, 136.74, 133.35, 128.78, 128.08, 119.66, 37.46, 25.10, 23.18, 17.32. HRMS calcd for $C_{12}H_{14}NO^+$ $[M+H]^+$ 188.1070, found 188.1055.

(e) Hydrolysis-Esterification of *β*-cyanoalkylated Enamide 3aa



3aa **6**

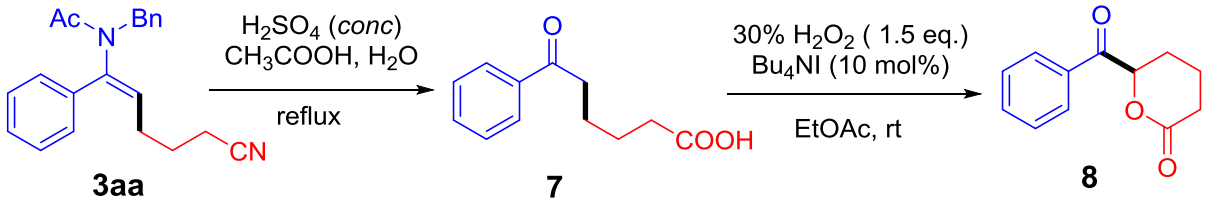
Enamides **3aa** (0.2 mmol) was added into a 10 mL RBF. Concentrated H_2SO_4 (0.4 mL) and EtOH (2.0 mL) were then added sequentially via syringe. The resulting mixture was heat to reflux for 24 hours. Upon completion, the solvent was removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:4 *v/v*) to give **6** as colorless oil.



6

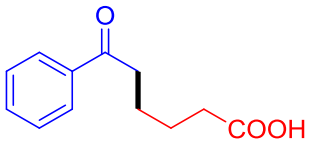
ethyl 6-oxo-6-phenylhexanoate (6): 24.4 mg, 52% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.93 (m, 2H), 7.60-7.53 (m, 1H), 7.50-7.42 (m, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.06-2.89 (m, 2H), 2.37 (t, J = 7.2 Hz, 2H), 1.82-1.70 (m, 4H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.02, 173.62, 136.99, 133.13, 128.70, 128.13, 60.45, 38.27, 34.29, 24.72, 23.75, 14.36. HRMS calcd for $C_{14}H_{19}O_3^+$ $[M+H]^+$ 235.1329, found 235.1333.

(f) Hydrolysis-Oxylactonization of *β*-cyanoalkylated Enamides 3aa[3]



3aa 7 8

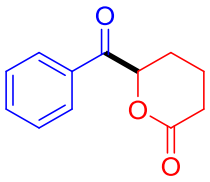
(i) Enamides **3aa** (318.4 mg, 1.0 mmol) was added into 10 mL RBF. H_2SO_4 (0.6 mL), CH_3COOH (1.0 mL) and H_2O (1.0 mL) were then added sequentially via syringe. The resulting mixture was heated to reflux. Upon completion of the reaction as monitored by TLC, the solvent was removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:4 *v*/*v*) to give **7** as colorless oil.



7

6-oxo-6-phenylhexanoic acid (7): 144.3 mg, 70% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.3, 1.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 3.01 (t, J = 7.0 Hz, 2H), 2.43 (t, J = 7.1 Hz, 2H), 1.90-1.64 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.05, 179.81, 136.92, 133.18, 128.71, 128.13, 38.17, 33.99, 24.37, 23.60. HRMS calcd for $C_{12}H_{15}O_3^+$ $[M+H]^+$ 207.1016, found 207.1016.

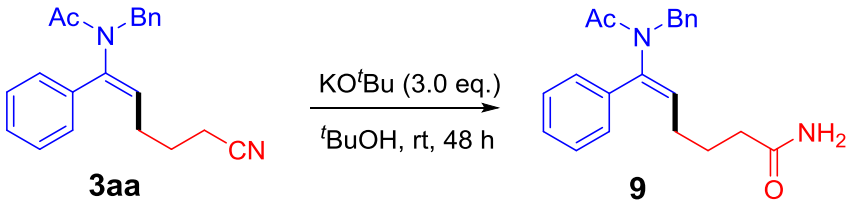
(ii) To a stirring mixture of **7** (123.7 mg, 0.6 mmol) and tetrabutylammonium iodide (22.1 mg, 0.06 mmol, 10 mol%) in EtOAc (3.0 mL) was added 30% H_2O_2 (92 μL, 0.9 mmol, 1.5 eq) at room temperature. Upon completion of the reaction as monitored by TLC, the resulting mixture poured into saturated $Na_2S_2O_3$ aq. (18 mL) and saturated $NaHCO_3$ aq. (18 mL). The mixture was extracted with EtOAc (2 × 20 ml). The organic layer was combined and dried over anhydrous Na_2SO_4 and the solvents were removed under vacuum. The residue was purified by flash column chromatography using eluents ethyl acetate/hexane (1:10-1:2 *v*/*v*) to give **8**.



8

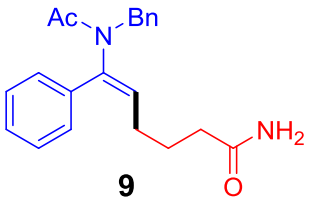
6-benzoyltetrahydro-2H-pyran-2-one (8): 44.1 mg, 36% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/hexane (1:10-1:2 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.90 (m, 2H), 7.71-7.60 (m, 1H), 7.56-7.45 (m, 2H), 5.92 (t, J = 5.2 Hz, 1H), 2.78-2.54 (m, 2H), 2.25 (ddd, J = 19.9, 10.4, 5.3 Hz, 1H), 2.13-2.03 (m, 1H), 1.94-1.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.33, 170.21, 134.31, 133.53, 129.12, 128.72, 79.34, 29.56, 24.62, 17.12. HRMS calcd for $C_{12}H_{13}O_3^+$ $[M+H]^+$ 205.0859, found 205.0857.

(g) The Synthesis of Amide



3aa **9**

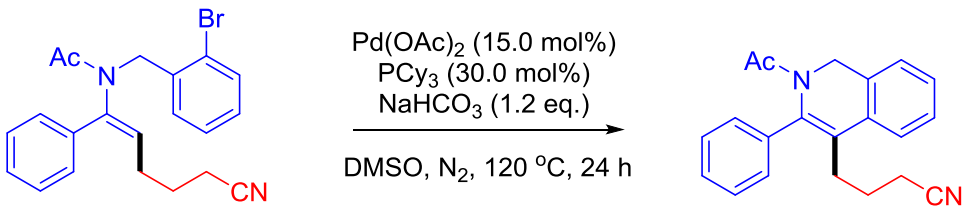
Enamides **3aa** (95.5 mg, 0.3 mmol) and KO^{t}Bu (100.9 mg, 0.9 mmol) were added into a Schlenk tube. The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. ^{t}BuOH (1.0 mL) was then added via syringe with gentle stirring under N_2 atmosphere. The resulting mixture was stirred at room temperature for 48 hours as monitored by TLC. Upon completion, the solvent was removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:1 *v*/*v*) to give **9** as colorless oil.



9

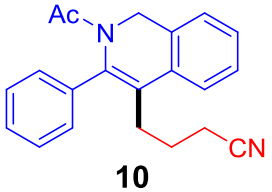
(*E*)-6-(*N*-benzylacetamido)-6-phenylhex-5-enamide (9): 57.5 mg, 57% yield. Colorless oil. Eluents for flash column chromatography petroleum ether/ethyl acetate (1:1 *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.33 (m, 3H), 7.30-7.22 (m, 5H), 7.20-7.16 (m, 2H), 5.87 (s, 1H), 5.54 (s, 1H), 5.28 (t, J = 7.7 Hz, 1H), 4.48 (s, 2H), 2.27-2.15 (m, 5H), 2.10-1.99 (m, 2H), 1.68-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.03, 128.75, 128.65, 128.34, 127.28, 49.00, 34.94, 27.92, 25.07, 22.34. HRMS calcd for $C_{21}H_{25}N_2O_2^+$ $[M+H]^+$ 337.1911, found 337.1909.

(h) Intramolecular Palladium-Catalyzed Heck Coupling Reaction[4]



3b'a **10**

To a Schlenk tube equipped with a magnetic stir bar was charged with enamide **3b'a** (119.2 mg, 0.30 mmol), $Pd(OAc)_2$ (10.5 mg, 15 mol%), tricyclohexylphosphane (25.2 mg, 30 mol%), and $NaHCO_3$ (30.3 mg, 1.2 eq.). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 2.0 mL DMSO was then added via syringe with gentle stirring under N_2 atmosphere. And the vial was heated at 120 °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 eluting with ethyl acetate/petroleum ether (1:8 *v*/*v*) to furnish the give **10**.

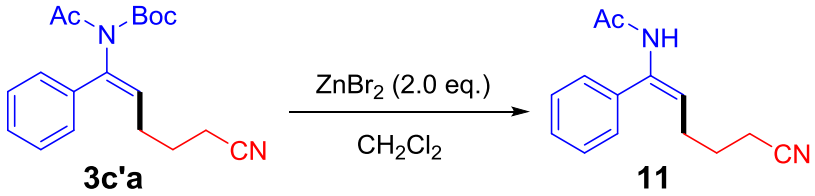


10

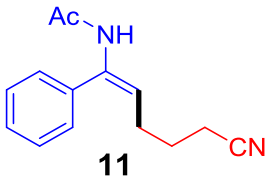
4-(2-acetyl-3-phenyl-1,2-dihydroisoquinolin-4-yl)butanenitrile (10): 70.2 mg, 74% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:8 *v*/*v*). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.46-7.31 (m, 7H), 7.30-7.24 (m, 2H), 4.97 (s, 2H), 2.94 (t, J = 7.1 Hz, 2H), 2.05 (t, J = 7.2 Hz, 2H), 1.71-1.62 (m, 2H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.17, 137.29, 136.98, 134.58, 132.39, 130.28, 128.85, 128.70, 127.95, 127.79, 125.75, 125.07, 123.60, 119.20, 46.18, 26.52, 24.68, 24.42, 16.40. HRMS calcd for $C_{21}H_{21}N_2O^+$ $[M+H]^+$ 317.1648, found 317.1632.

(i) Cleavage of *N*-Boc Protecting Group[5]

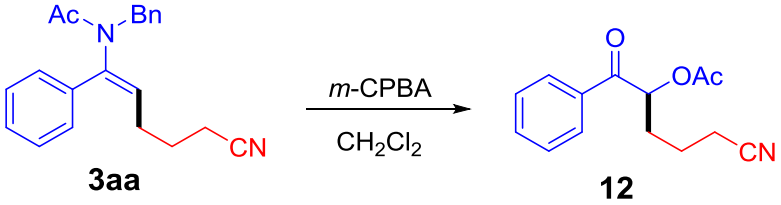


Enamides **3c'a** (65.7 mg, 0.2 mmol) was added into a 5 mL reaction tube. $ZnBr_2$ (90.1 mg, 0.4 mmol) and DCM (1.0 mL) were then added sequentially. The resulting mixture was stirred at room temperature for 4 hours. Upon completion of the reaction as monitored by TLC, the solvent was then removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:4 *v/v*).

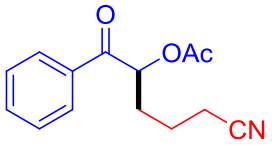


(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (11): 25.6 mg, 56% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (m, 3H), 7.28 (d, J = 7.7 Hz, 2H), 6.54 (s, 1H), 6.32 (t, J = 7.6 Hz, 1H), 2.31 (t, J = 7.2 Hz, 2H), 2.21 (q, J = 7.4 Hz, 2H), 2.07 (s, 3H), 1.78-1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.78, 136.54, 135.44, 128.77, 128.73, 119.74, 116.36, 27.20, 25.92, 24.74, 16.52. HRMS calcd for $C_{14}H_{17}N_2O^+$ $[M+H]^+$ 229.1335, found 229.1340.

(j) The Synthesis of *α*-acyloxyketone



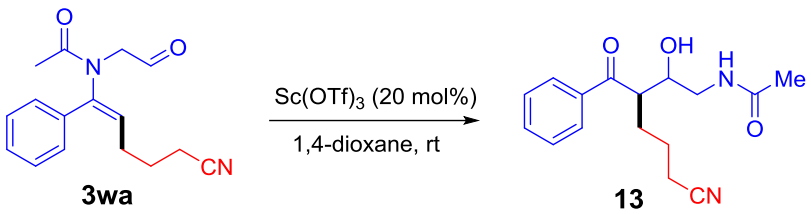
Enamide **3aa** (0.2 mmol) was added into a 10 mL reaction tube. *m*-CPBA (3.0 eq.) was then added to the stirred solution of the enamide in CH_2Cl_2 at 0 °C and the resulting suspension was stirred for 30 min before warming to rt. The mixture was stirred at rt for 24 hours. Upon completion of the reaction as monitored by TLC, the solvent was removed under vacuum. The residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:50 *v/v*) to give **12** as a yellow oil.



12

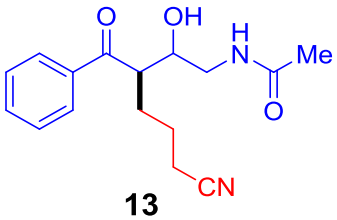
5-cyano-1-oxo-1-phenylpentan-2-yl acetate (12): 30.4 mg, 62% yield. Yellow oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:50 *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.90 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 5.93 (dd, J = 8.0, 4.1 Hz, 1H), 2.50-2.35 (m, 2H), 2.18 (s, 3H), 2.15-2.04 (m, 1H), 1.99 (dt, J = 14.5, 7.8 Hz, 1H), 1.88-1.78 (m, 2H). 13C NMR (100 MHz, $CDCl_3$) δ 195.79, 170.53, 134.39, 134.09, 129.11, 128.50, 119.10, 74.10, 30.05, 21.48, 20.79, 17.05. HRMS calcd for $C_{14}H_{16}NO_3^+$ $[M+H]^+$ 246.1125, found 246.1119.

(k) The Synthesis of Vicinal Amino Alcohols[6]



3wa **13**

To a solution of Enamides **3wa** (81.1 mg, 0.3 mmol) in 1,4-dioxane (4.0 mL) was added $Sc(OTf)_3$ (30 mg, 0.06 mmol). The reaction mixture was stirred at room temperature. Upon completion of the reaction as monitored by TLC, the reaction was quenched with saturated aqueous $NaHCO_3$ (5.0 mL), and extracted with CH_2Cl_2 (3×5.0 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$. The solvent was removed under vacuum, the residue was purified directly by flash column chromatography, eluting with ethyl acetate/petroleum ether (1:4 *v/v*) to give **13** as colorless oil.

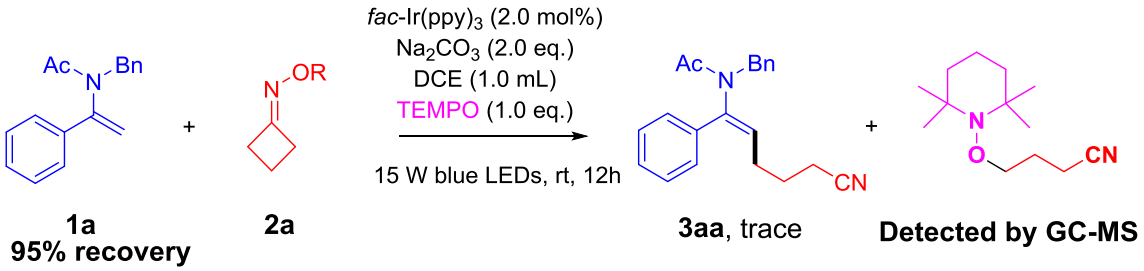


13

***N*-(3-benzoyl-6-cyano-2-hydroxyhexyl)acetamide (13)**: 45.8 mg, 53% yield. Colorless oil. Eluents for flash column chromatography ethyl acetate/petroleum ether (1:4 *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 8.5, 1.6 Hz, 2H), 7.67-7.59 (m, 1H), 7.54-7.48 (m, 2H), 5.96 (t, J = 4.8 Hz, 1H), 4.10-3.98 (m, 2H), 3.63 (ddd, J = 8.8, 6.0, 4.2 Hz, 1H), 3.46 (ddd, J = 14.2, 6.4, 2.6 Hz, 1H), 3.24 (ddd, J = 14.2, 7.4, 5.3 Hz, 1H), 2.31 (t, J = 7.3 Hz, 2H), 2.09-1.99 (m, 1H), 1.97 (s, 3H), 1.96-1.86 (m, 1H), 1.67-1.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.36, 172.38, 136.81, 134.16, 129.18, 128.54, 119.38, 72.47, 48.97, 44.83, 27.99, 23.34, 23.15, 17.57. HRMS calcd for $C_{16}H_{21}N_2O_3^+$ $[M+H]^+$ 289.1547, found 289.1549.

Preliminary Mechanistic Studies

(a) Radical-Trapping Experiment



1a
95% recovery

2a

3aa, trace

Detected by GC-MS

To a Schlenk tube equipped with a magnetic stir bar was charged with enamides **1a** (113.01 mg 0.45 mmol), Cyclobutanone Oximes **2a** (77.12 mg 0.3 mmol), *fac*-Ir(ppy)$_3$ (3.9 mg, 2.0 mol%), Na_2CO_3 (63.6 mg, 0.6 mmol) and TEMPO (51.4 mg, 0.3 mmol). The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DCE was added via syringe with gentle stirring under N_2 atmosphere. It was observed that the transformation was completely inhibited by TEMPO, along with the interception of the cyanoalkyl radical species as detected by GC-MS (**Figure S2**) and 95% of enamide **1a** was recovered, implying the involvement of a radical species.

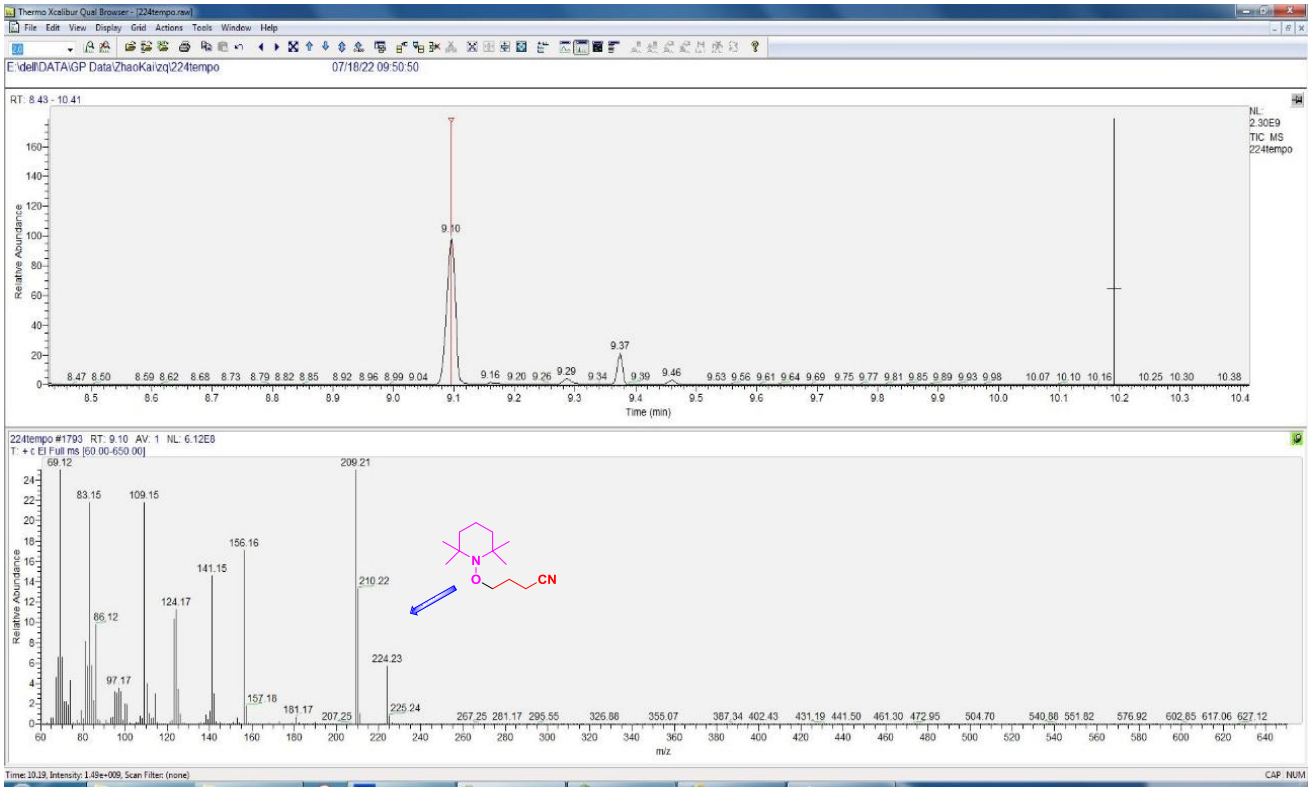
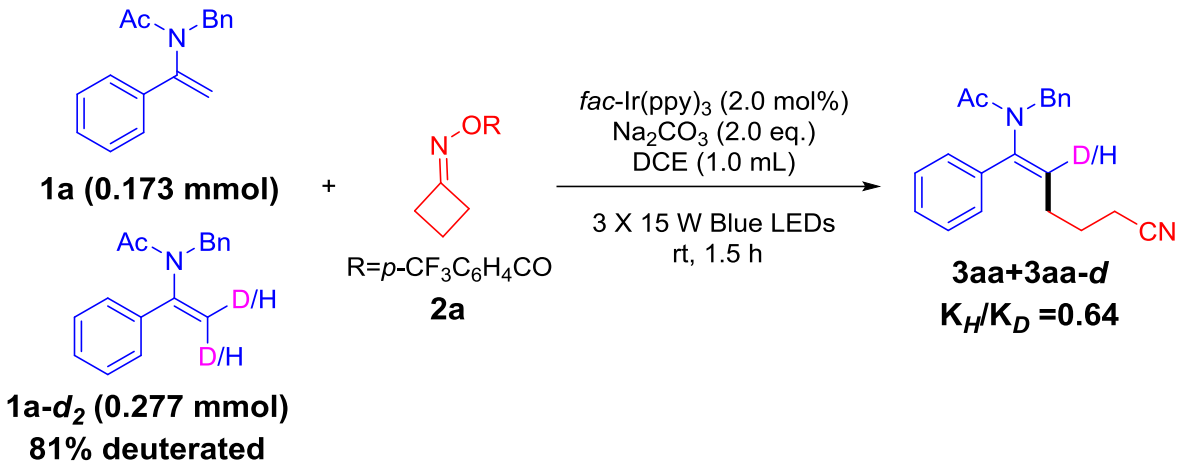


Figure S2 The interception of the cyanoalkyl radical species

(b) Intermolecular Kinetic Isotopic Effect (KIE) Study

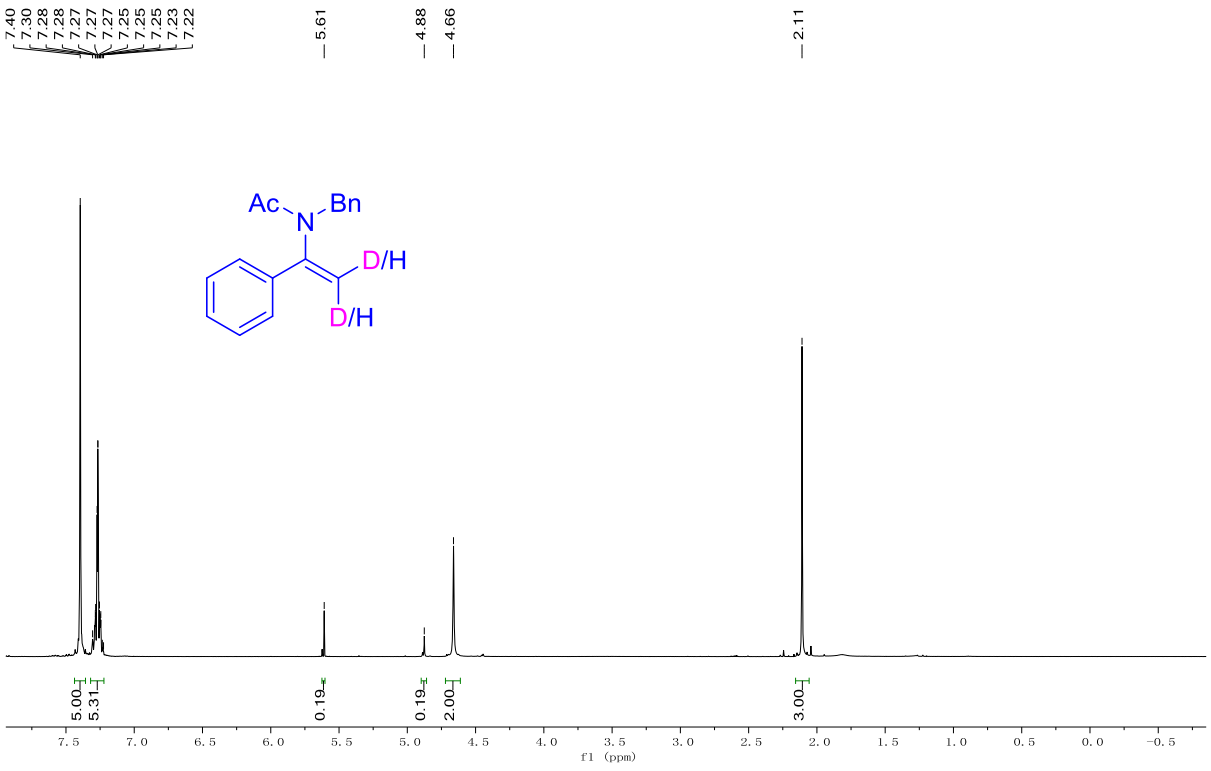


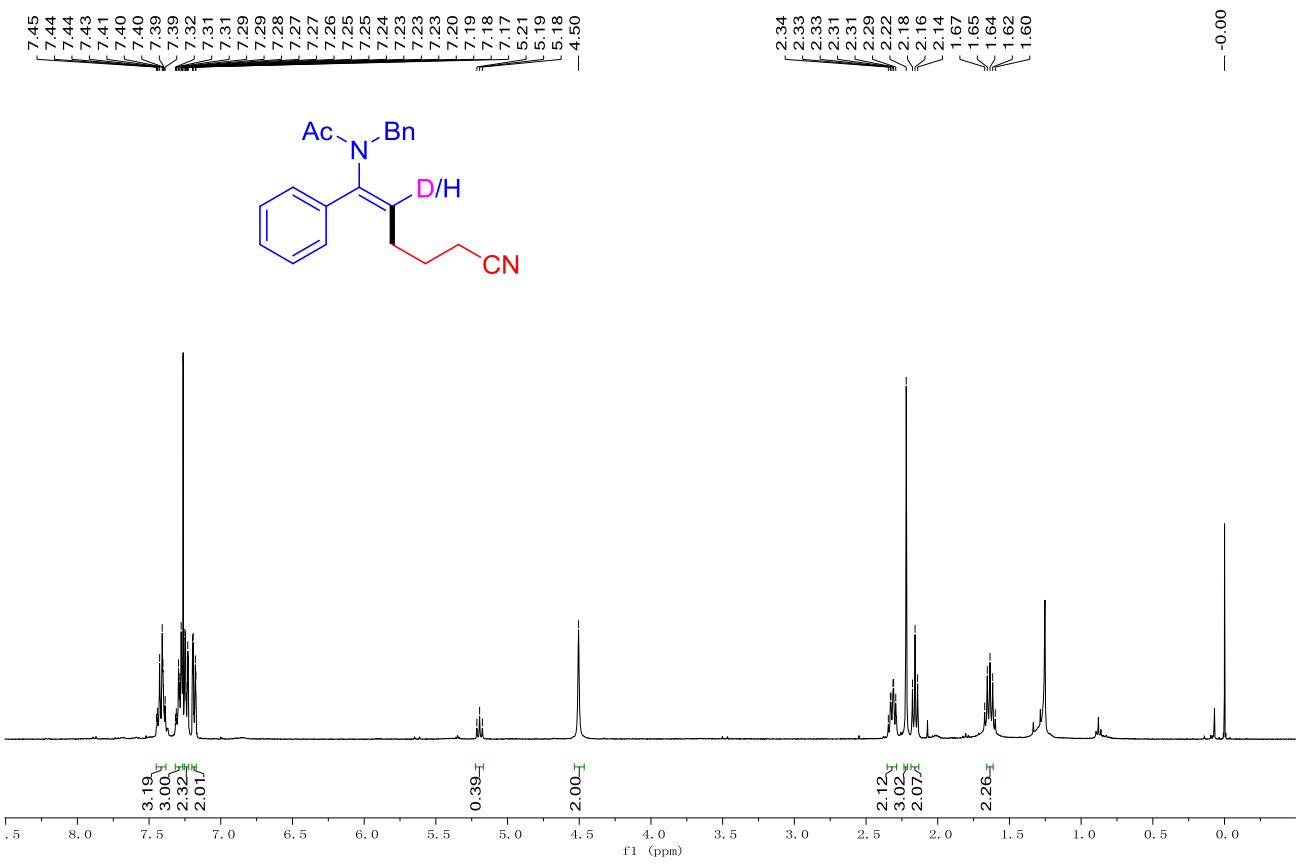
Enamide **1a-*d*$_2$** was prepared according to the literatures[1b,7] as a light yellow oil with 81% deuterium. Enamide **1a** (43.4 mg, 0.173 mmol), **1a-*d*$_2$** (70.3 mg, 0.277 mmol), cyclobutanone oximes **2a** (77.12 mg 0.3 mmol), *fac*-Ir(ppy)$_3$ (3.9 mg, 2.0 mol%), and Na_2CO_3 (63.6 mg, 0.6 mmol) were added into a Schlenk tube. The tube was sealed with a septum, evacuated and backfilled with nitrogen three times. 1.0 mL DCE was then added via syringe with gentle stirring under N_2 atmosphere. The resulting mixture was allowed to stir at room temperature under 3×15 W blue LEDs irradiation for 1.5 h. The product was isolated through thin-layer chromatography using ethyl acetate/petroleum ether

(1:4 *v/v*) as the eluent to afford crude mixture (8% yield). The KIE value (K_H/K_D = 0.64) was determined from the ^{1}H NMR.

In consideration of the 81% deuterated ratio of **1a-*d*$_2$**, 0.277 mmol of **1a-*d*$_2$** (a H-D mixture containing 81% deuterated enamide and 19% undeuterated one) was added along with 0.173 mmol of undeuterated enamide **1a** in the same reaction vessel, so that the real amount of pure deuterated enamide (and its undeuterated competitor) was calculated to be 0.225 mmol approximately. The ratio of deuterated enamide **3aa-*d*** *vs* **3a** in the isolated mixture was 61:39 as determined by ^{1}H NMR, thus giving a calculated K_H/K_D = 0.39/0.61 = 0.64.

Notably, an inverse secondary KIE (KIE<1) is observed, which might be attributed to the change of the hybridization state of the olefinic carbon of the substrate. Based on the mechanism as depicted in Scheme 4, the addition of the cyanoalkyl radical species to the double bonds of enamides to form intermediate **A** changes the hybridization state of the *β*-olefinic carbon from sp^2 to sp^3, leading to an increase of the force constant of the C-H or C-D bonds bending vibrations (which means the C-H bending vibrations became more rigid and difficult). In this pattern, the difference between the zero-point energy in the transition state (ΔG_{TS}) (between the H-containing compound and a D-containing one) is greater than the difference between the starting enamide substrates (ΔG_s), implying that the reaction rate of a deuterium-labelled substrate would surpass the rate of the non-deuterium one at a relatively low conversion, resulting to an inverse KIE of 0.64.





(c) Quantum Yield Measurement

The actinometry measurements were done as follows based on previous literature[8]:

(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, 1.0 mL) were irradiated with 3×15 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 (**Figure S3a**). 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 (**Figure S3b**) between the number of moles of products (y axis) and time (x axis).

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

$$= \frac{\triangle A\ (510\ nm)}{44400} = 1.5152 \times 10^{-8}$$

The quantum yield for Fe^{2+} ($\Phi_{Fe}^{2+} = 1.13$), F = mol Fe^{2+}/Φ_{Fe}^{2+}.Then, the irradiated light intensity was estimated to 1.33 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 3×15 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 dodecane 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) (**Figure S3c**). The slope gives the quantum yield (Φ) of the photoreaction, 0.63.

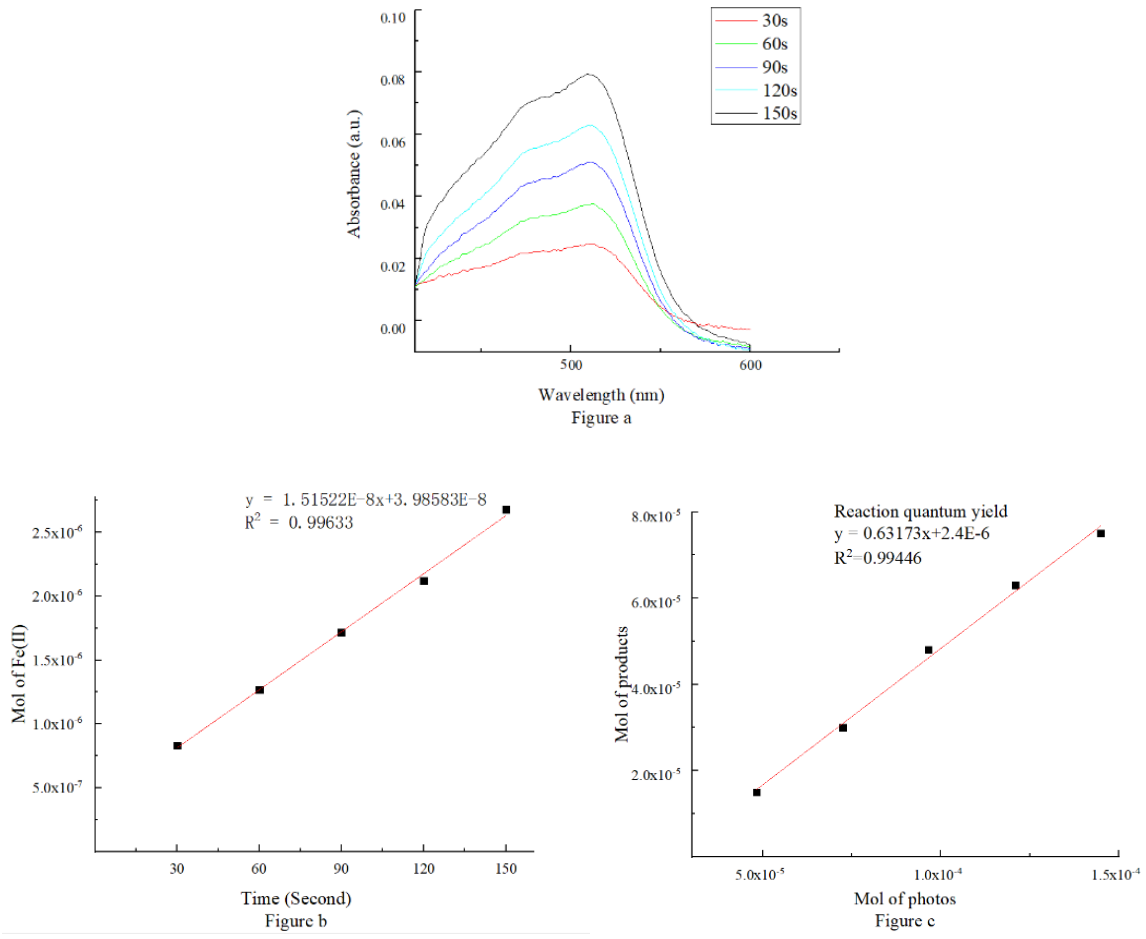


Figure S3 The UV-Vis spectra and data of quantum yield measurement

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 0.63, implying that the reaction is highly possible to proceed in a photoredox catalytic pathway rather than a radical-chain mechanism.

Determination of Stereochemistry by 2D NOESY NMR

2D NOESY NMR experiments of **3al** (**Figure S4**) and **3am** (**Figure S5**) were performed to further testify the stereochemistry. NOE effects between the olefinic hydrogen and the methyl of acetyl group were observed, indicating the *E*-configuration of those compounds. The other products in Table 3 exhibited similar ^{1}H NMR as compared to **3al** and **3am**, which should also be *E*-configured.

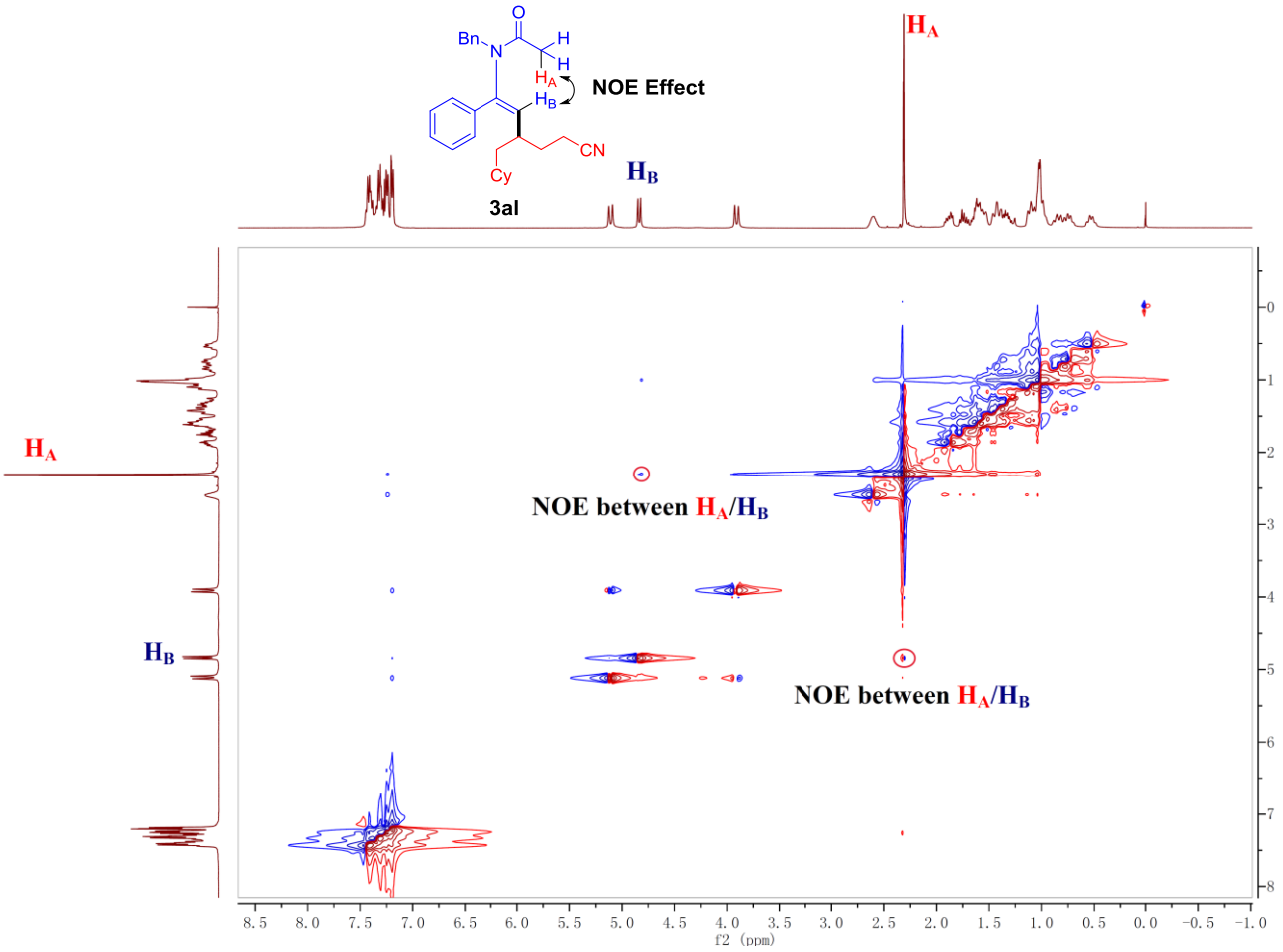


Figure S4 The 2D NOESY NMR of **3al**

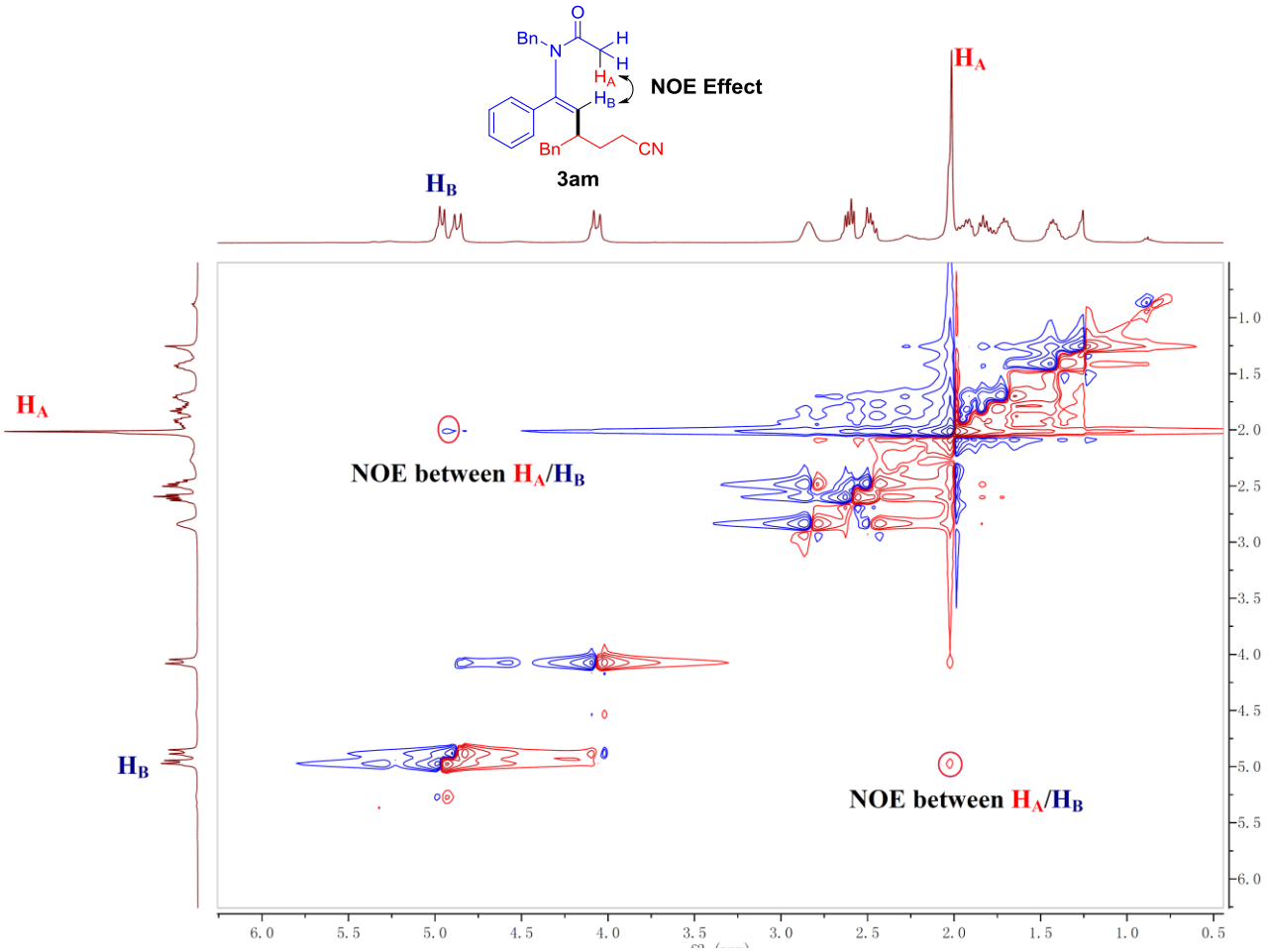


Figure S5 The 2D NOESY NMR of **3am**

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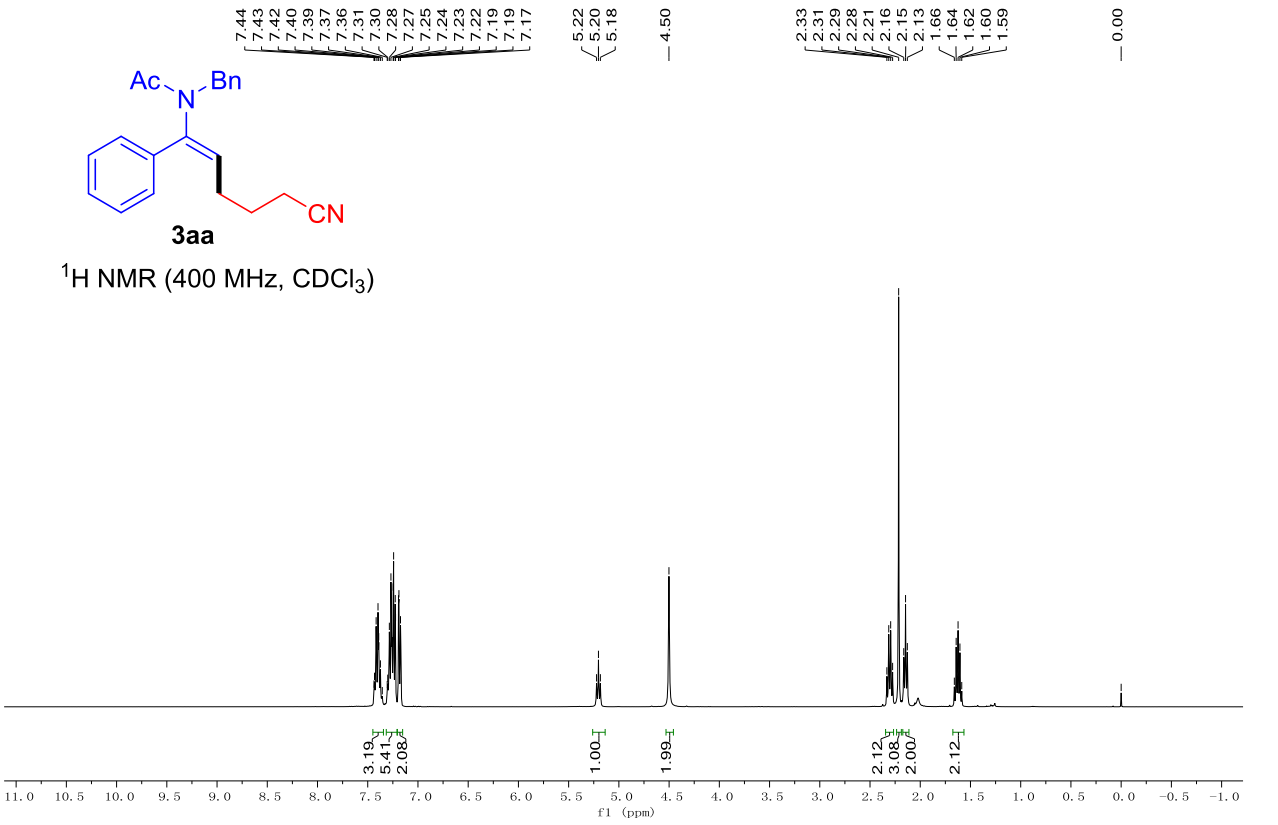
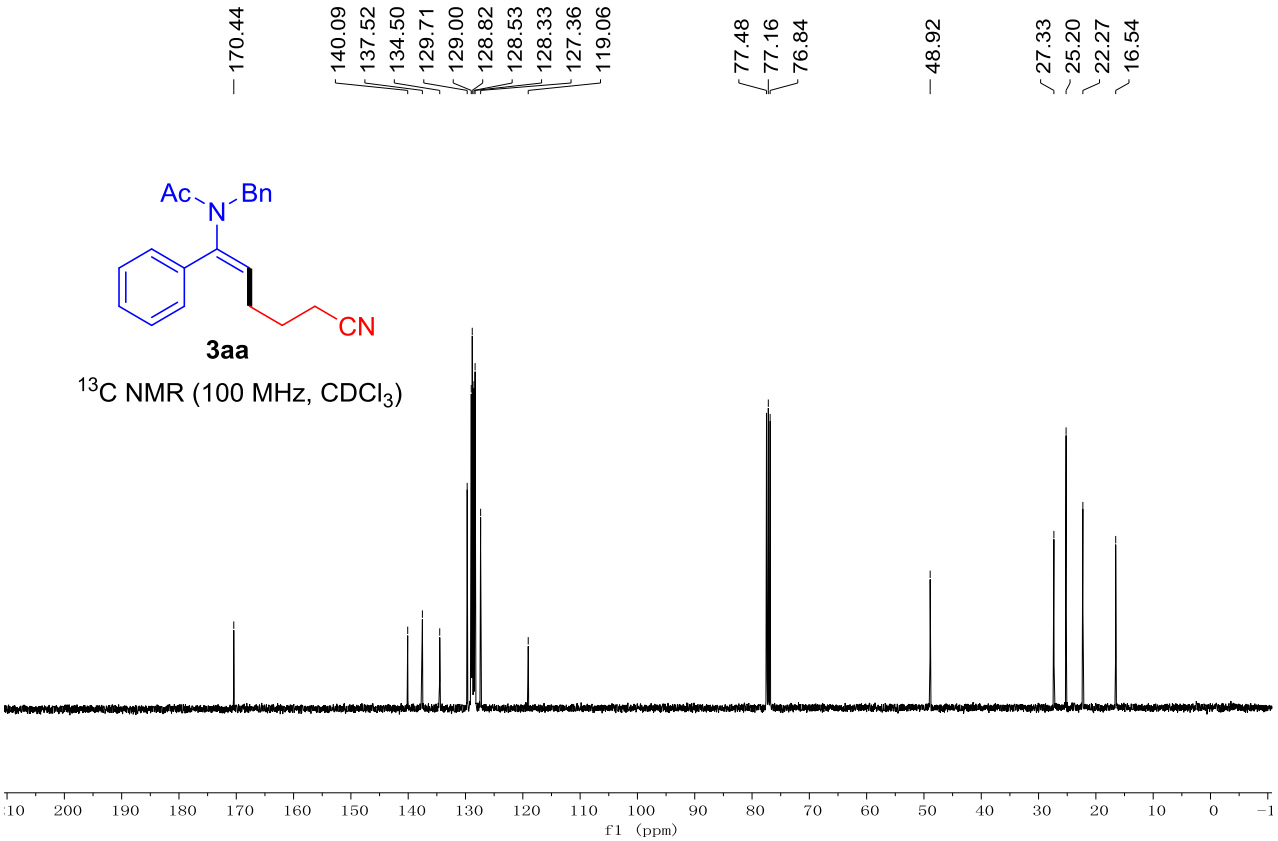
Copies of ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR Spectra

(*E*)-*N*-benzyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3aa**)

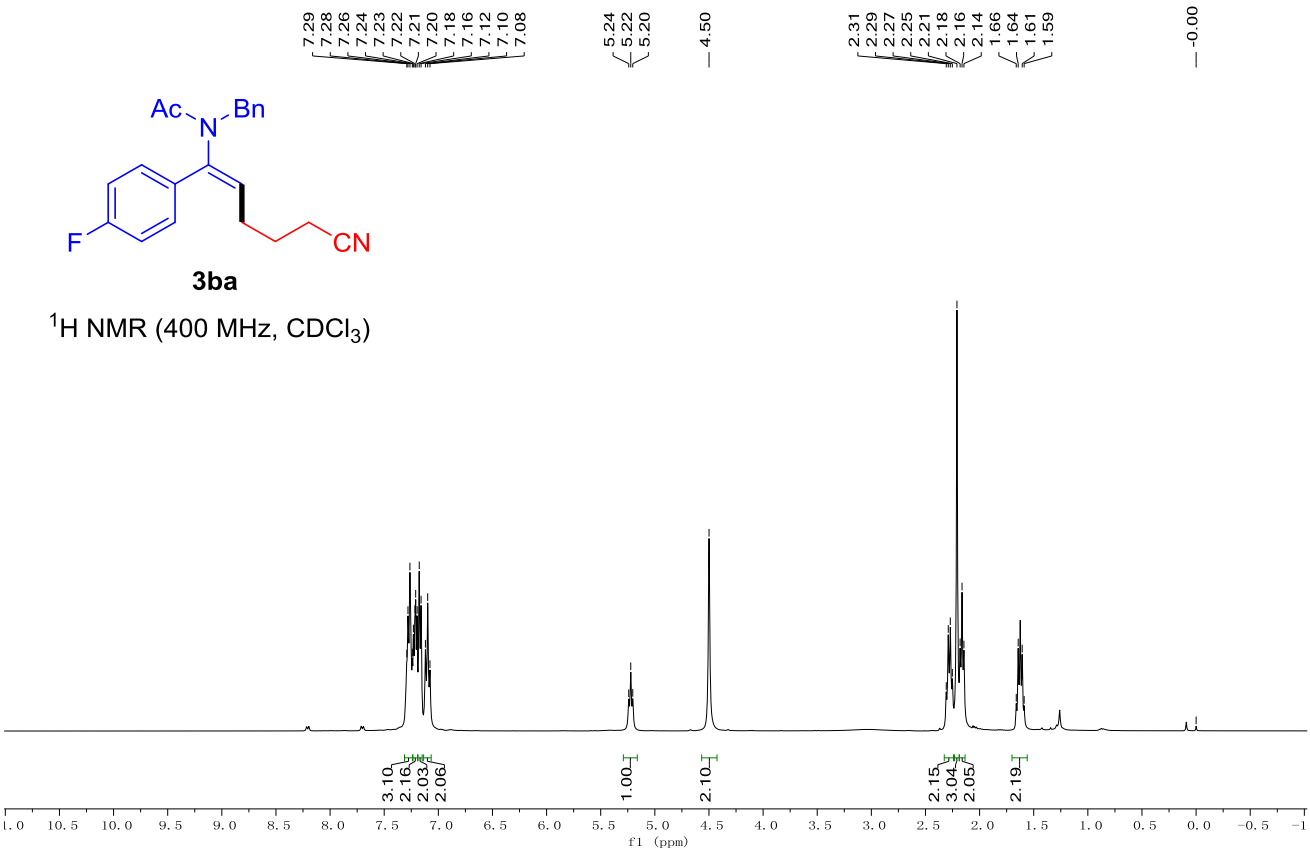


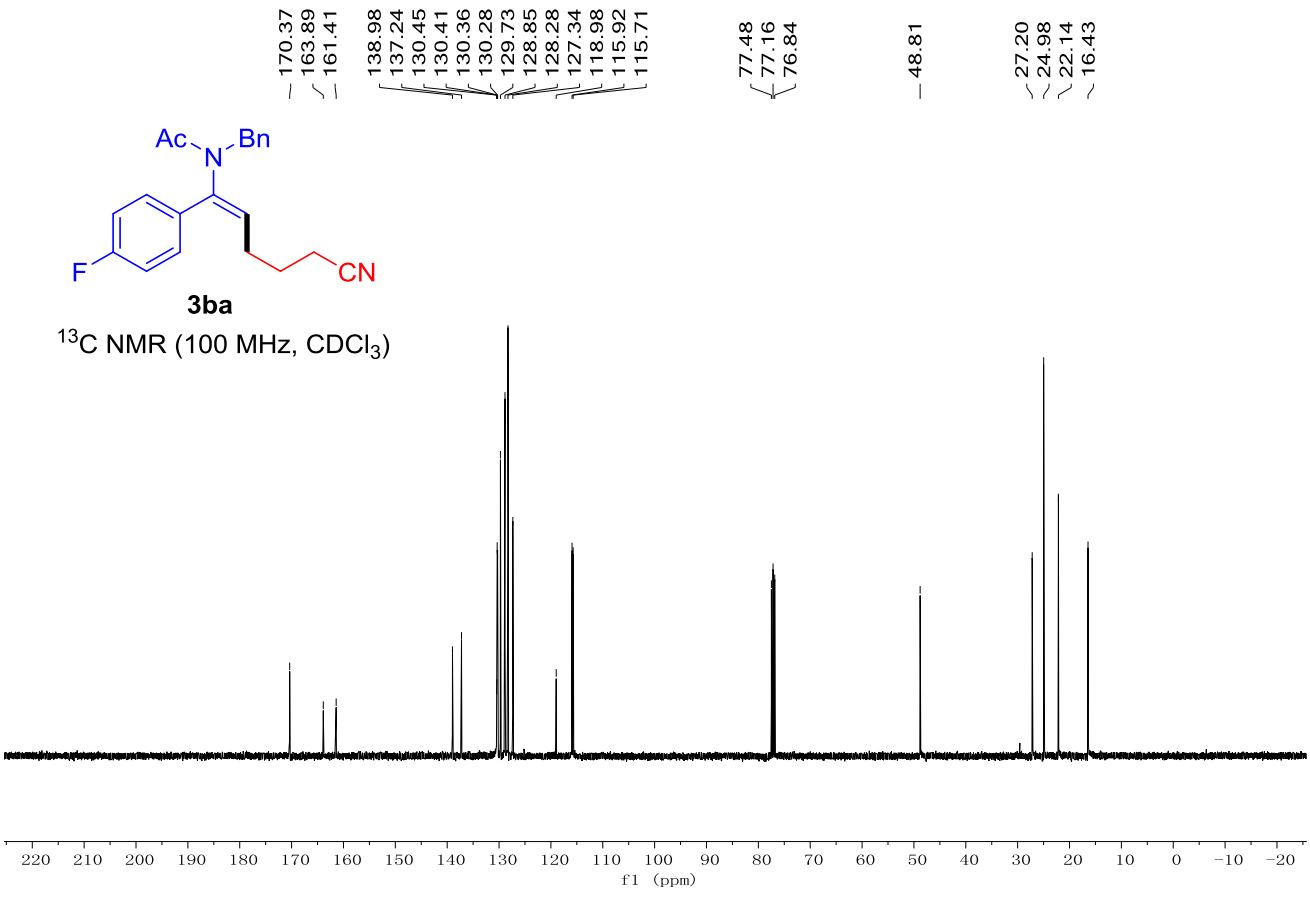
^{1}H NMR (400 MHz, $CDCl_3$)

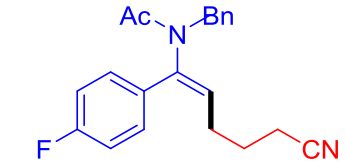


^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-fluorophenyl)pent-1-en-1-yl)acetamide (**3ba**)



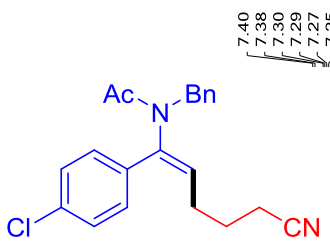




3ba

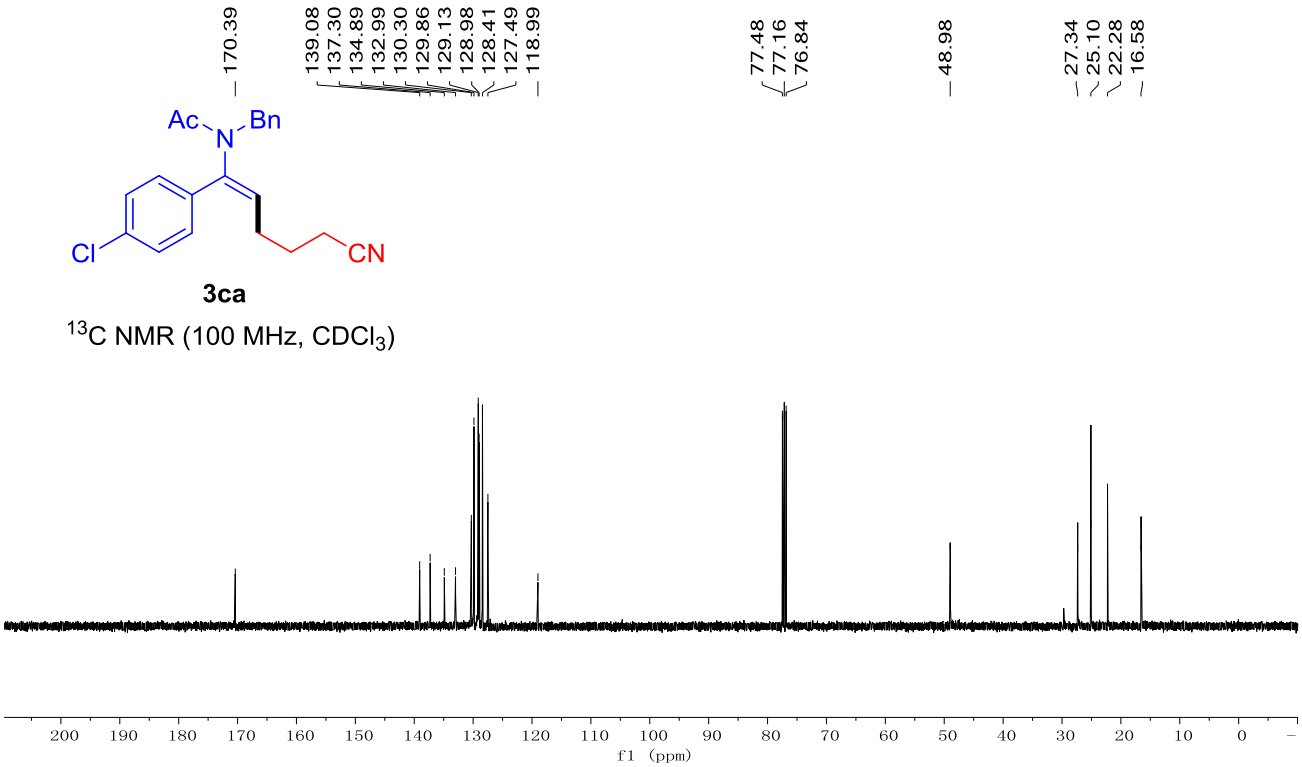
^{19}F NMR (376 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-5-cyanopent-1-en-1-yl)acetamide (**3ca**)

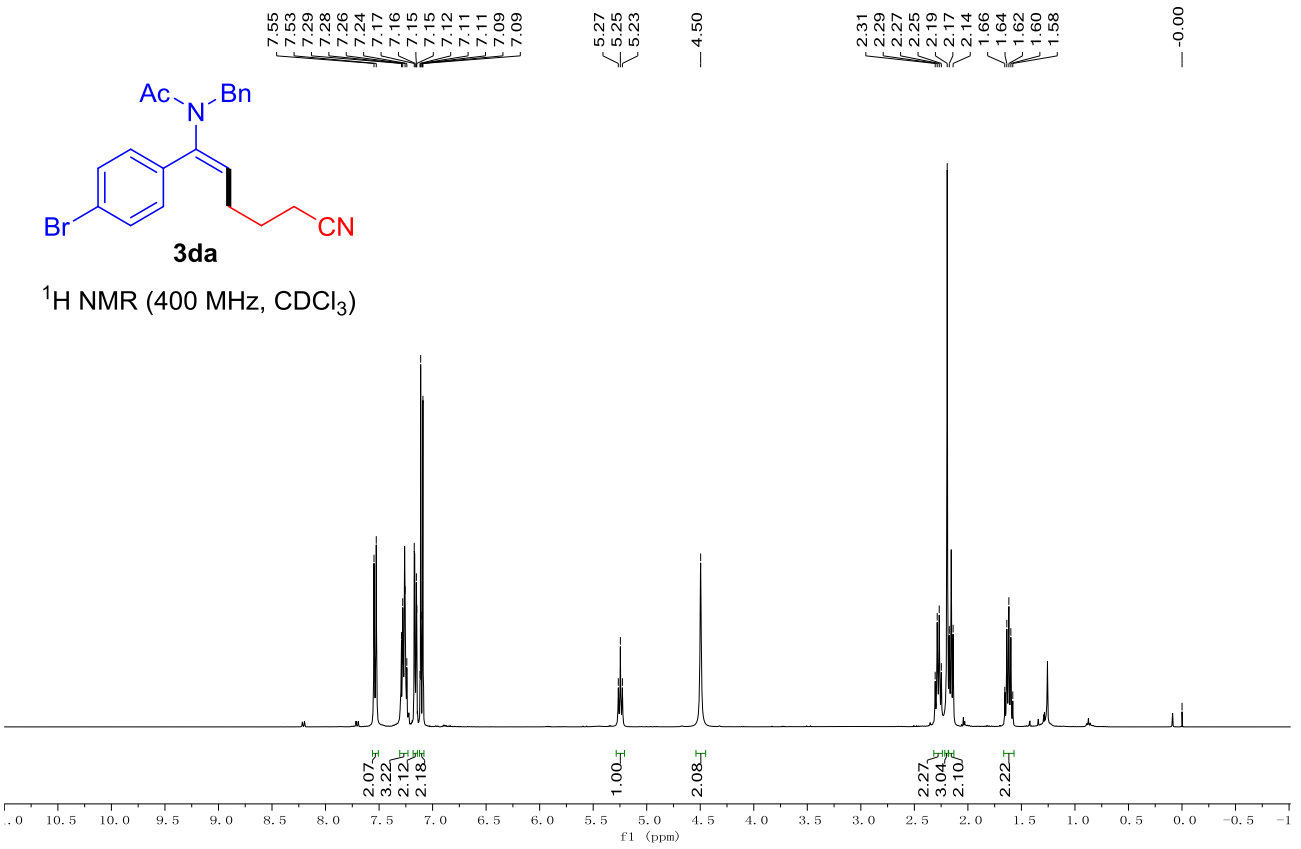


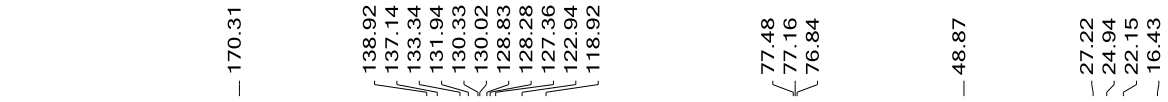
3ca

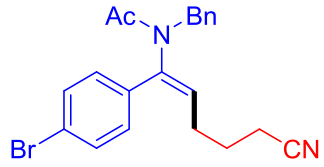
^{1}H NMR (400 MHz, $CDCl_3$)



(*E*)-*N*-benzyl-*N*-(1-(4-bromophenyl)-5-cyanopent-1-en-1-yl)acetamide (**3da**)

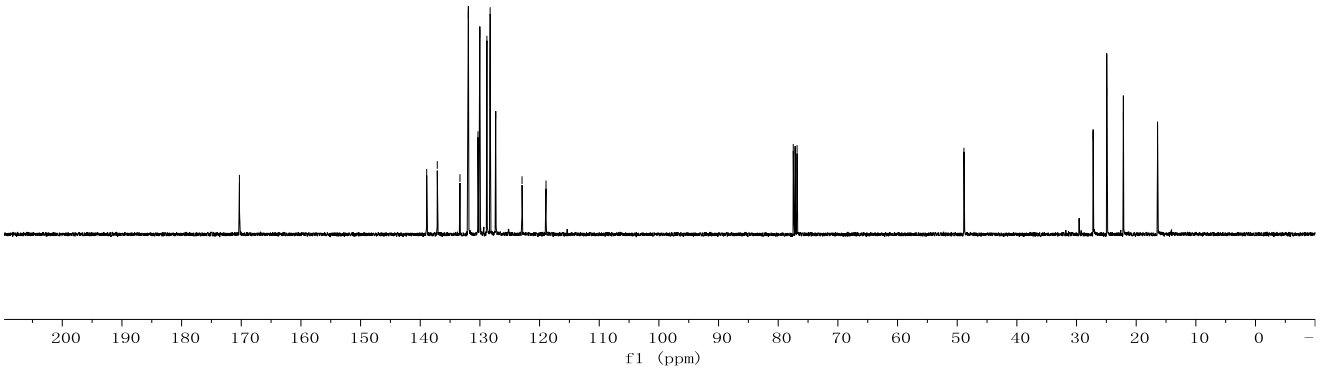




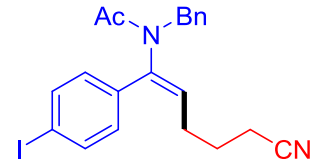


3da

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

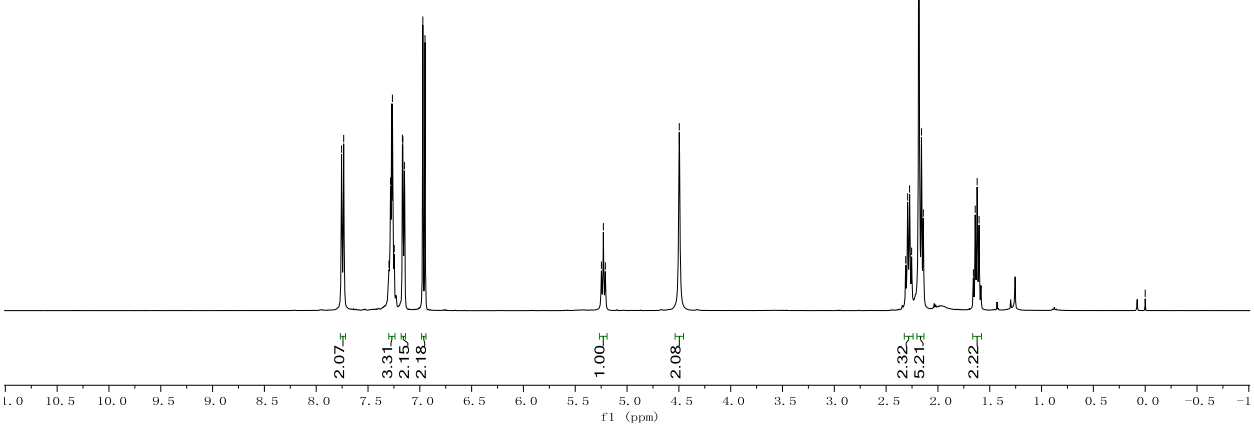


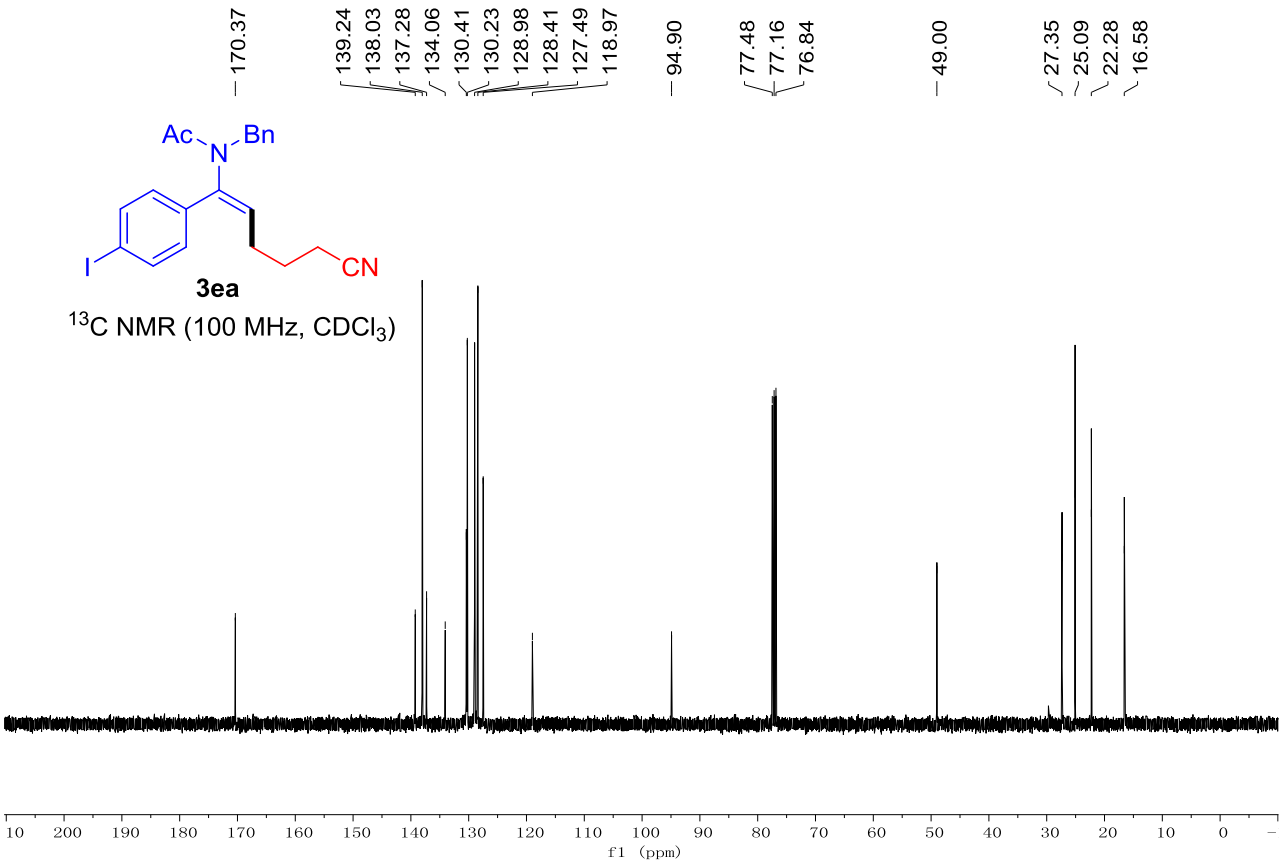
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-iodophenyl)pent-1-en-1-yl)acetamide (**3ea**)



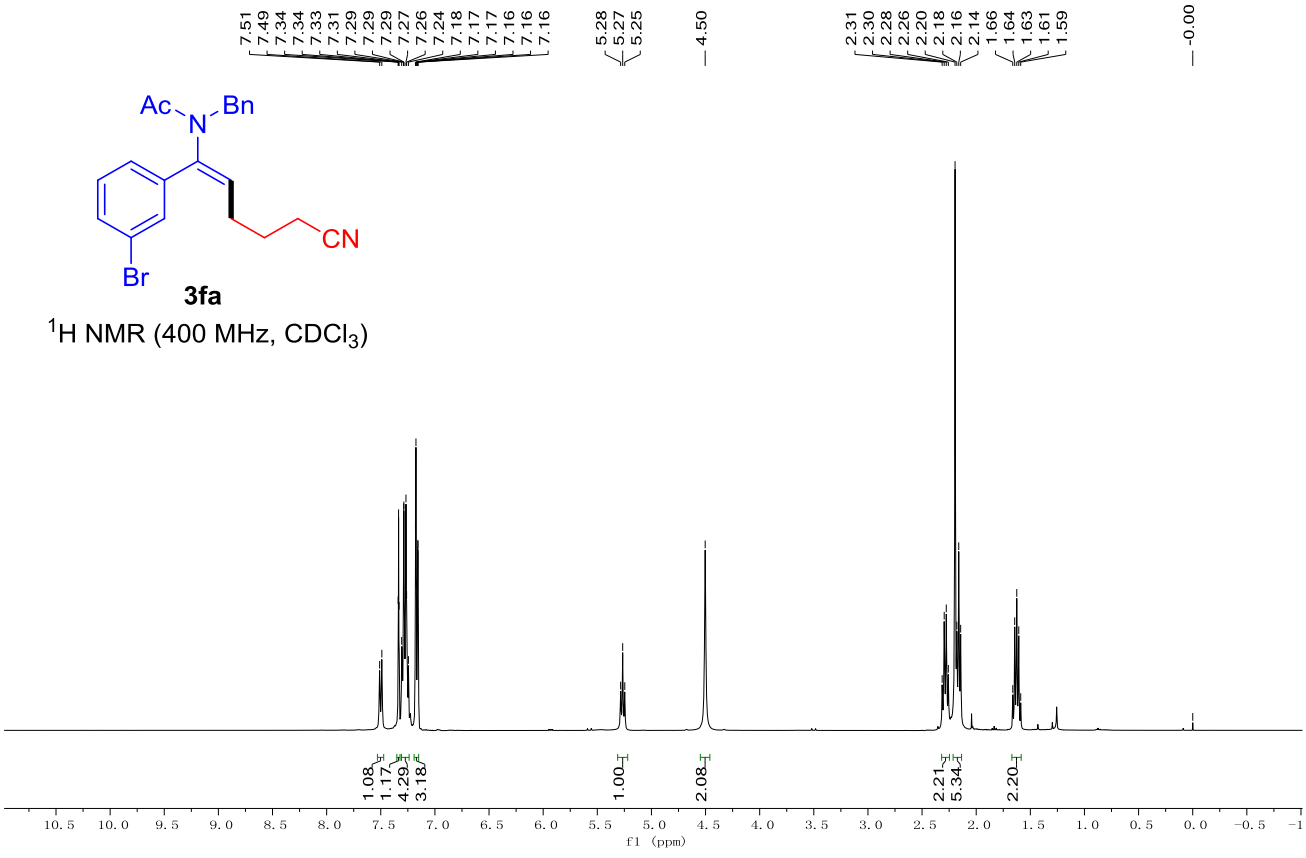
3ea

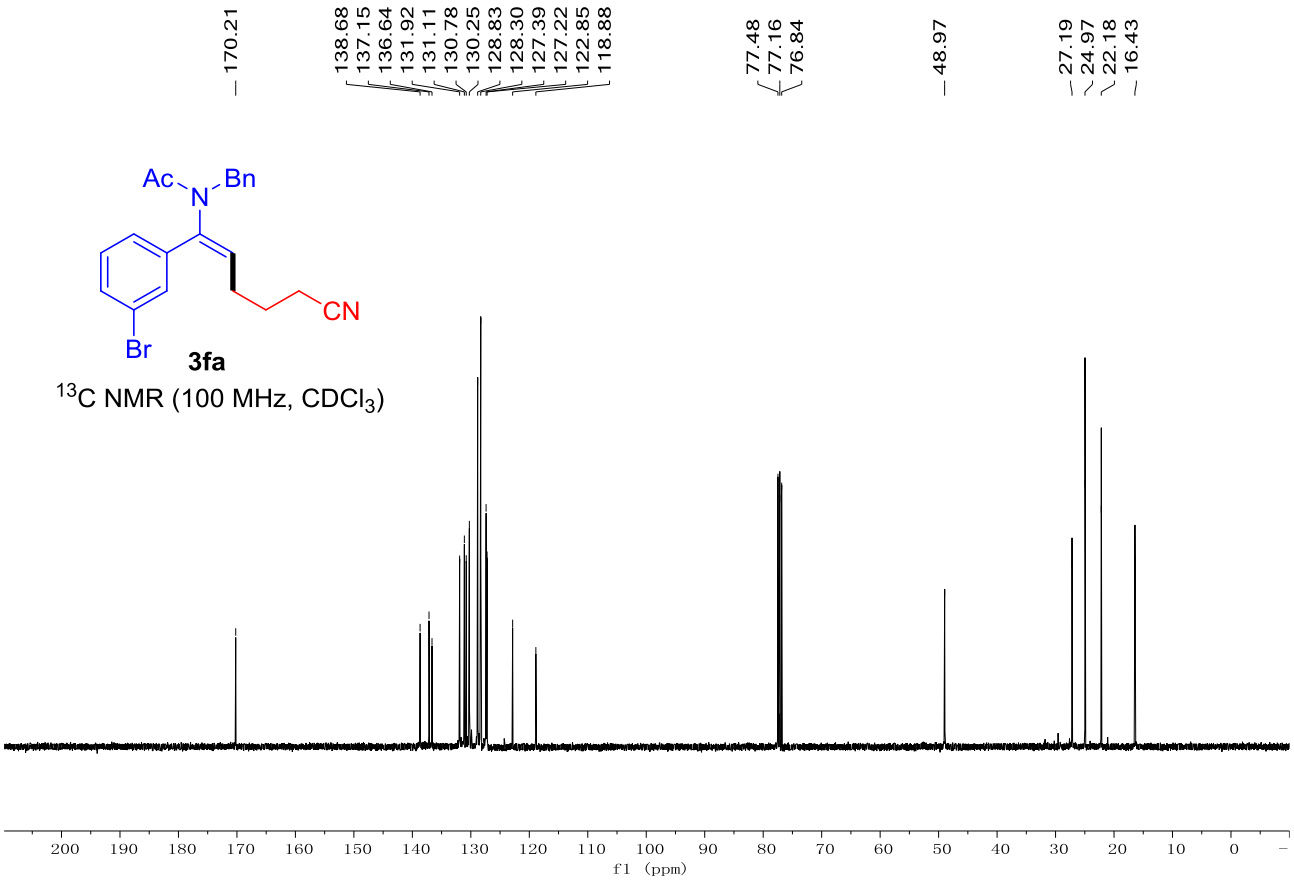
^{1}H NMR (400 MHz, $CDCl_3$)



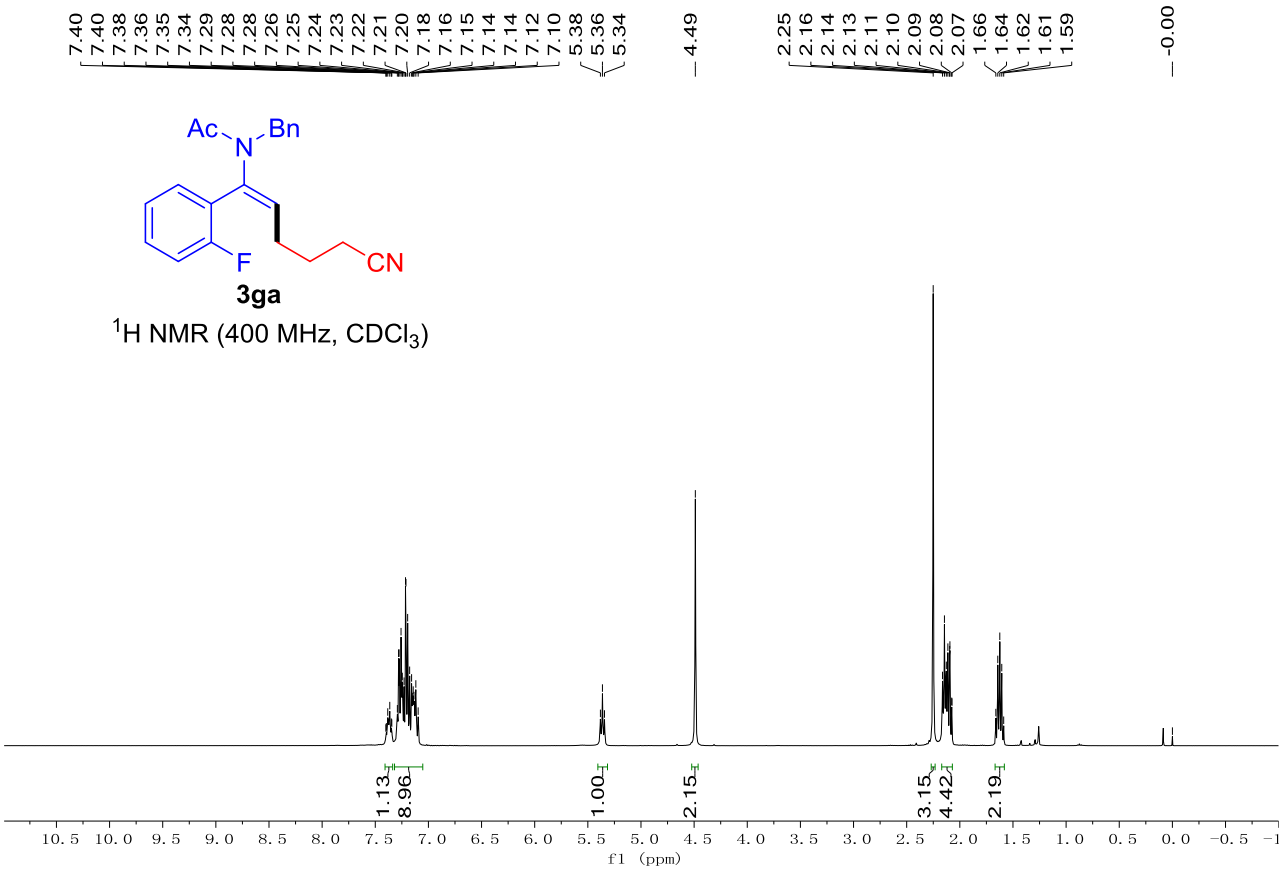


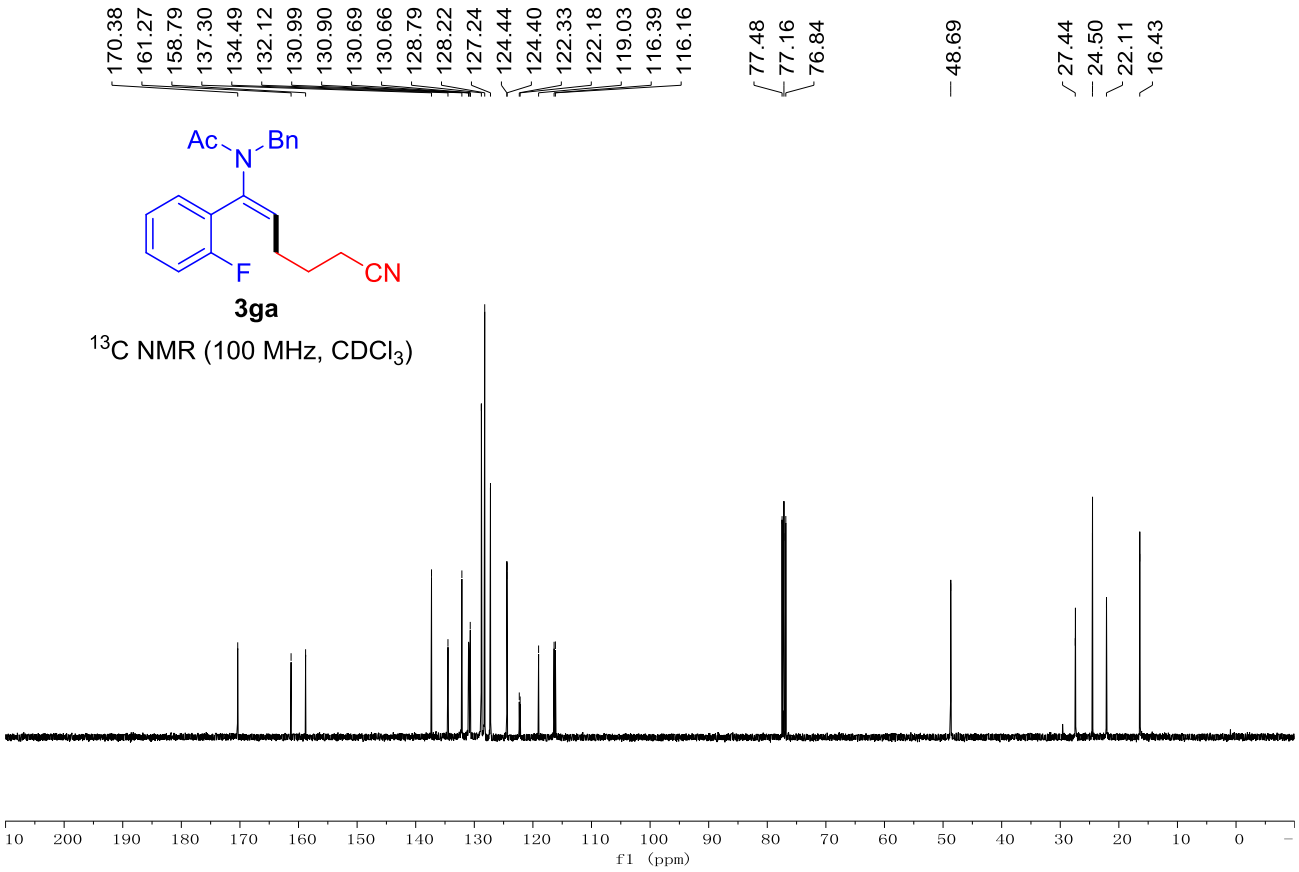
(*E*)-*N*-benzyl-*N*-(1-(3-bromophenyl)-5-cyanopent-1-en-1-yl)acetamide (**3fa**)





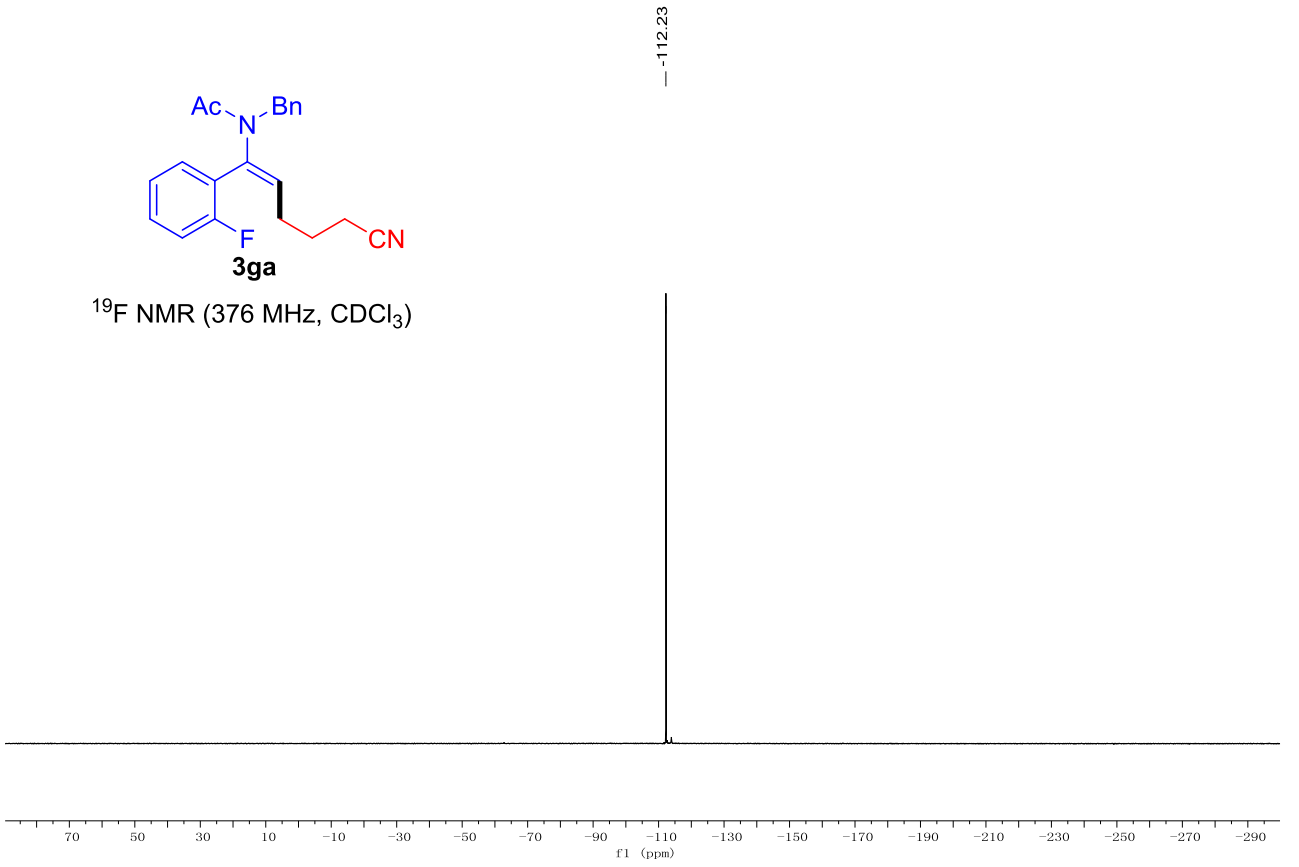
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(2-fluorophenyl)pent-1-en-1-yl)acetamide (**3ga**)





3ga

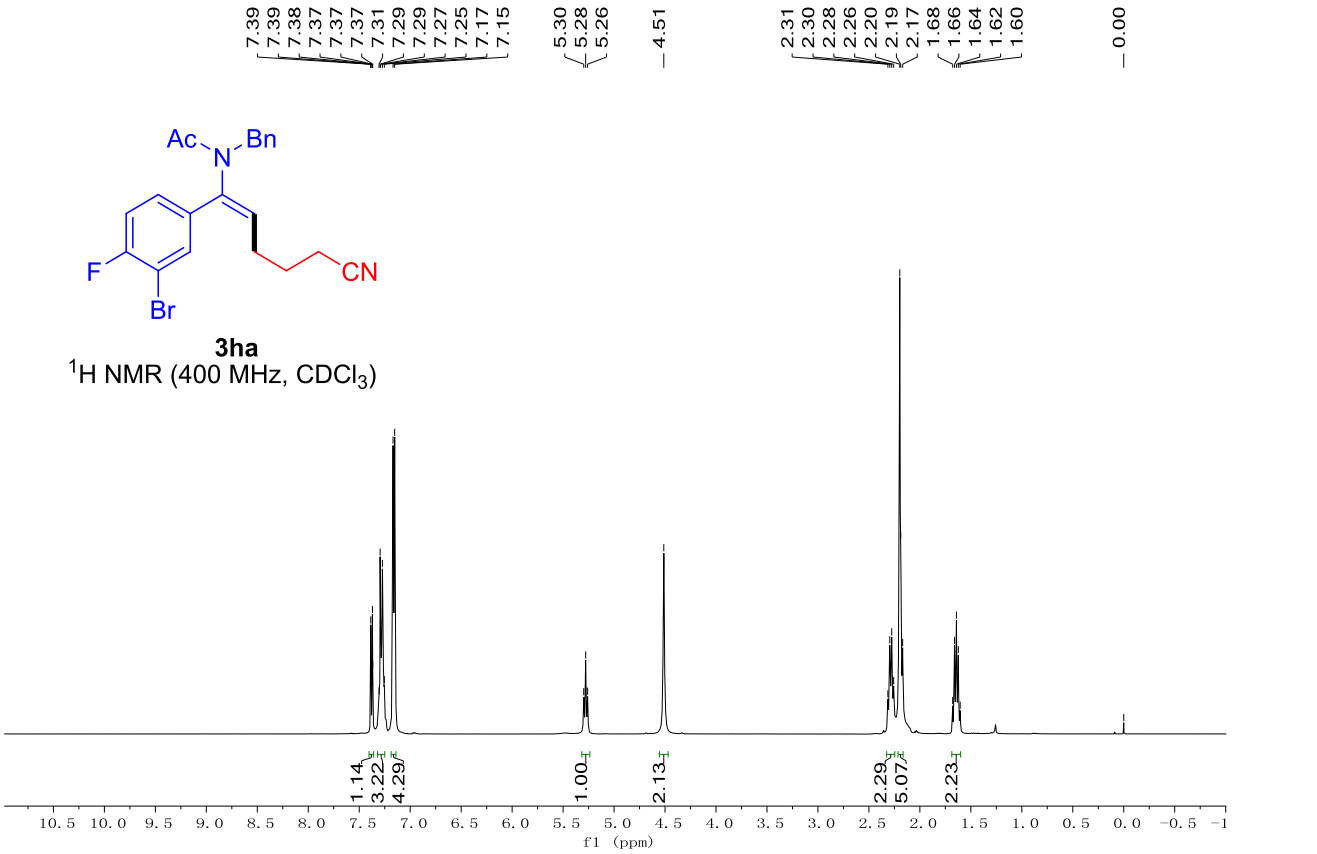
^{13}C NMR (100 MHz, $CDCl_3$)

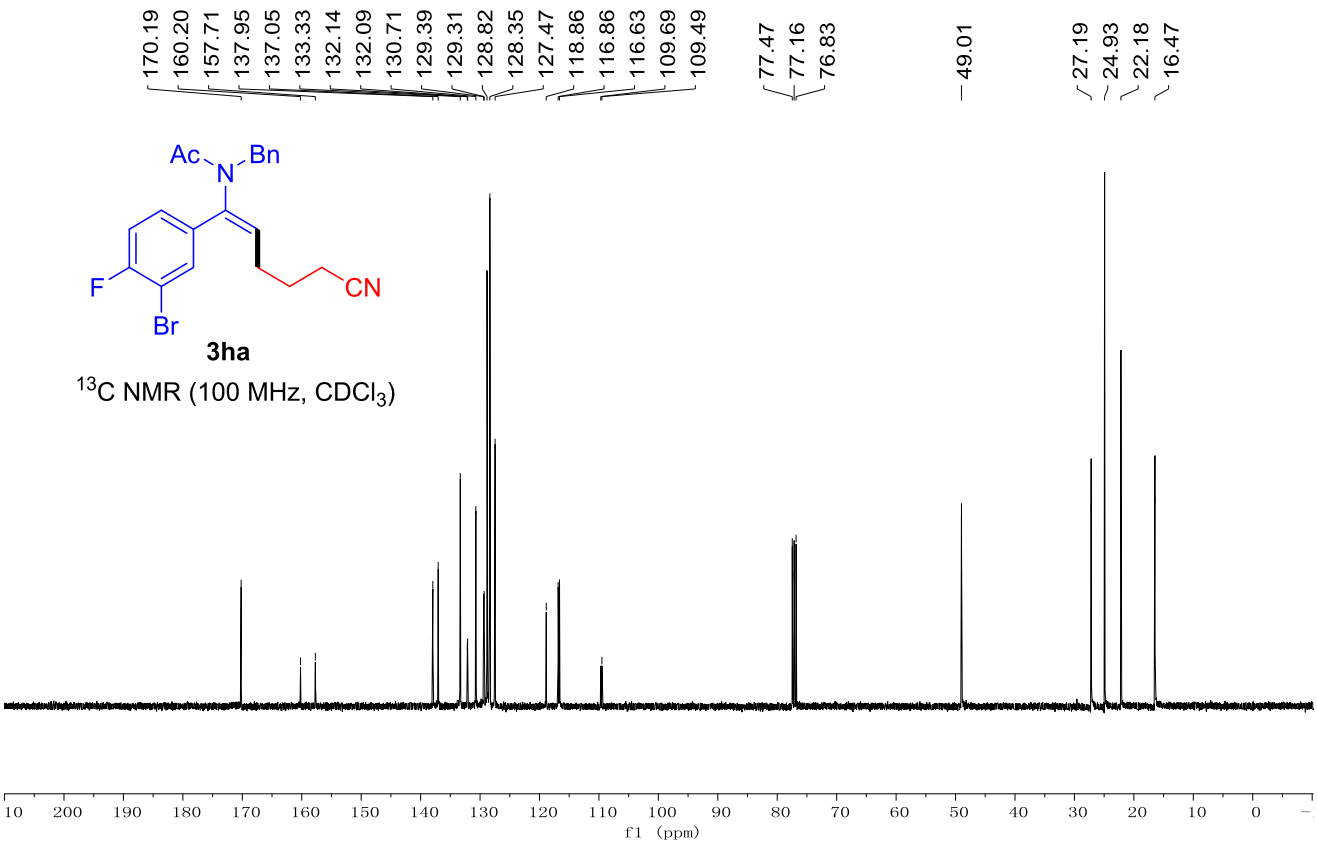


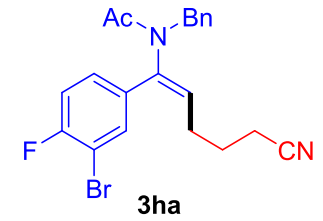
3ga

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

(*E*)-*N*-benzyl-*N*-(1-(3-bromo-4-fluorophenyl)-5-cyanopent-1-en-1-yl)acetamide (**3ha**)



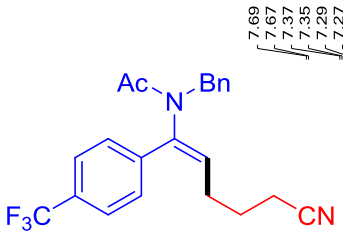




3ha

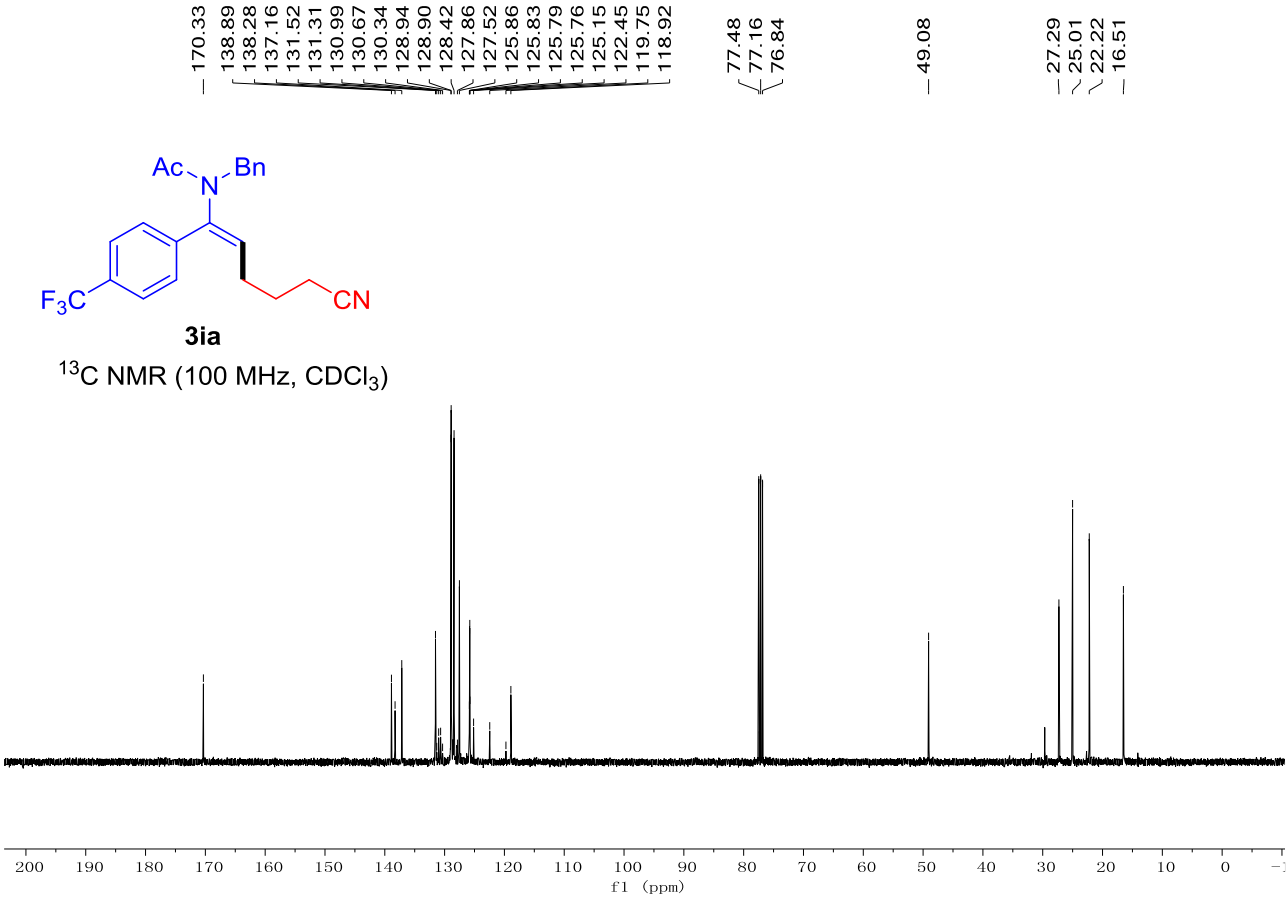
^{19}F NMR (376 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(trifluoromethyl)phenyl)pent-1-en-1-yl)acetamide (**3ia**)



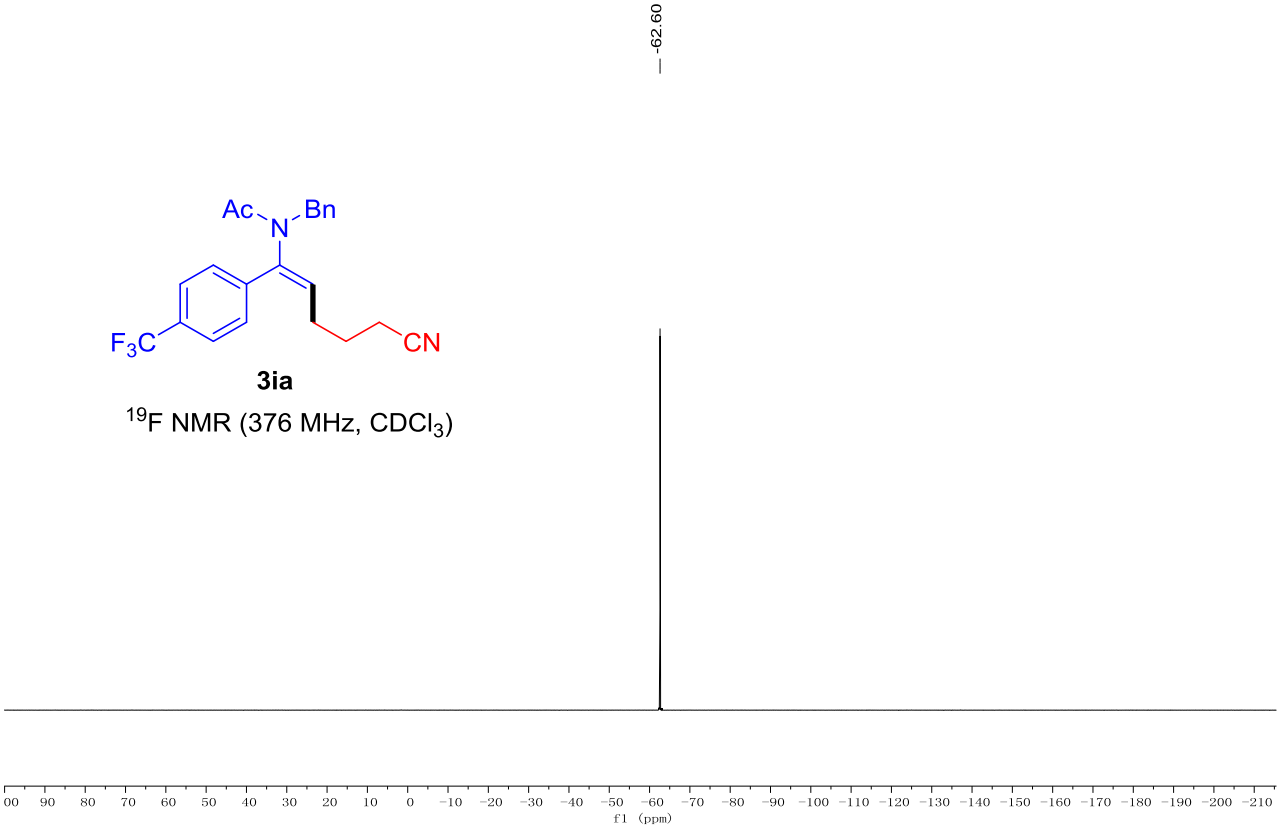
3ia

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



3ia

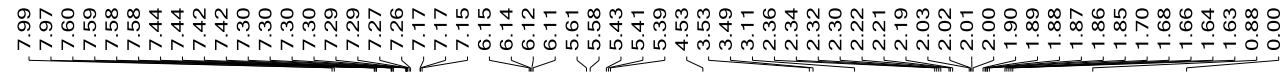
^{13}C NMR (100 MHz, $CDCl_3$)

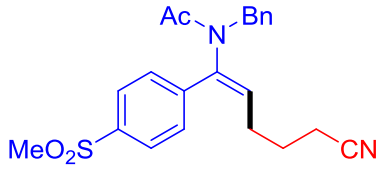


3ia

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

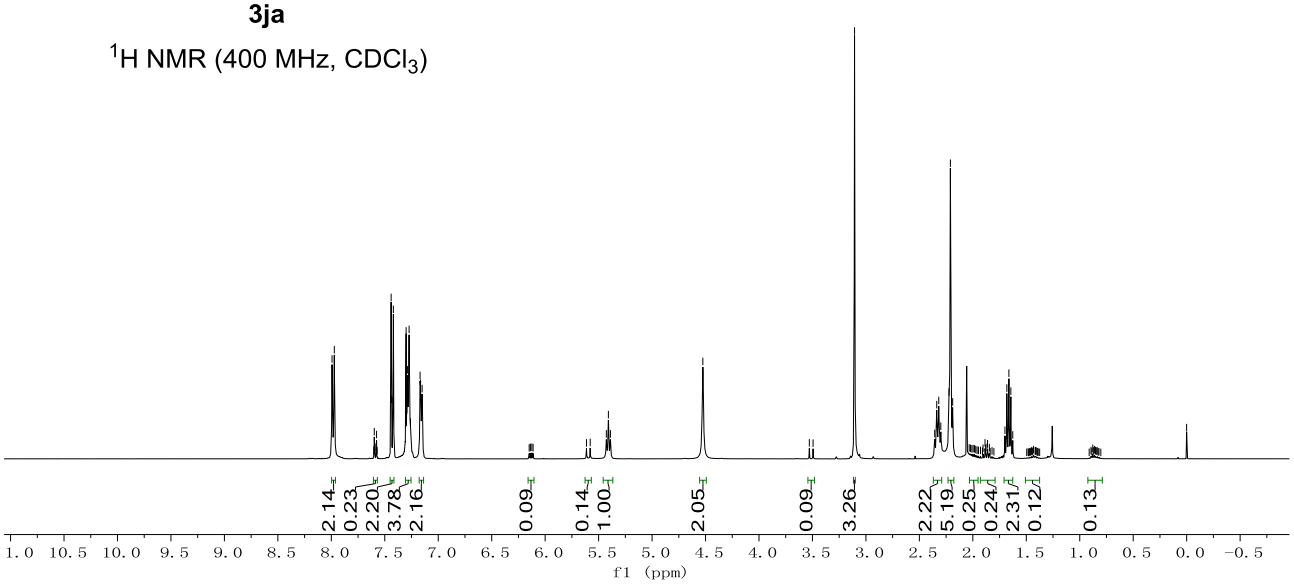
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(methylsulfonyl)phenyl)pent-1-en-1-yl)acetamide (**3ja**)

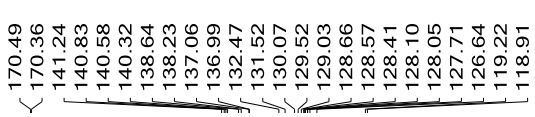


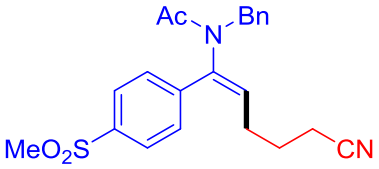


3ja

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

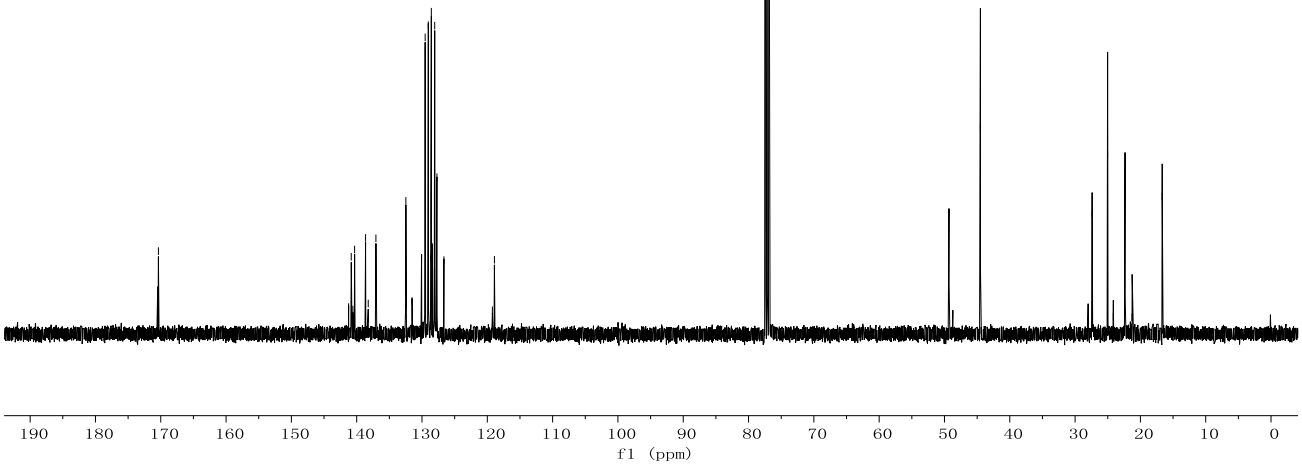




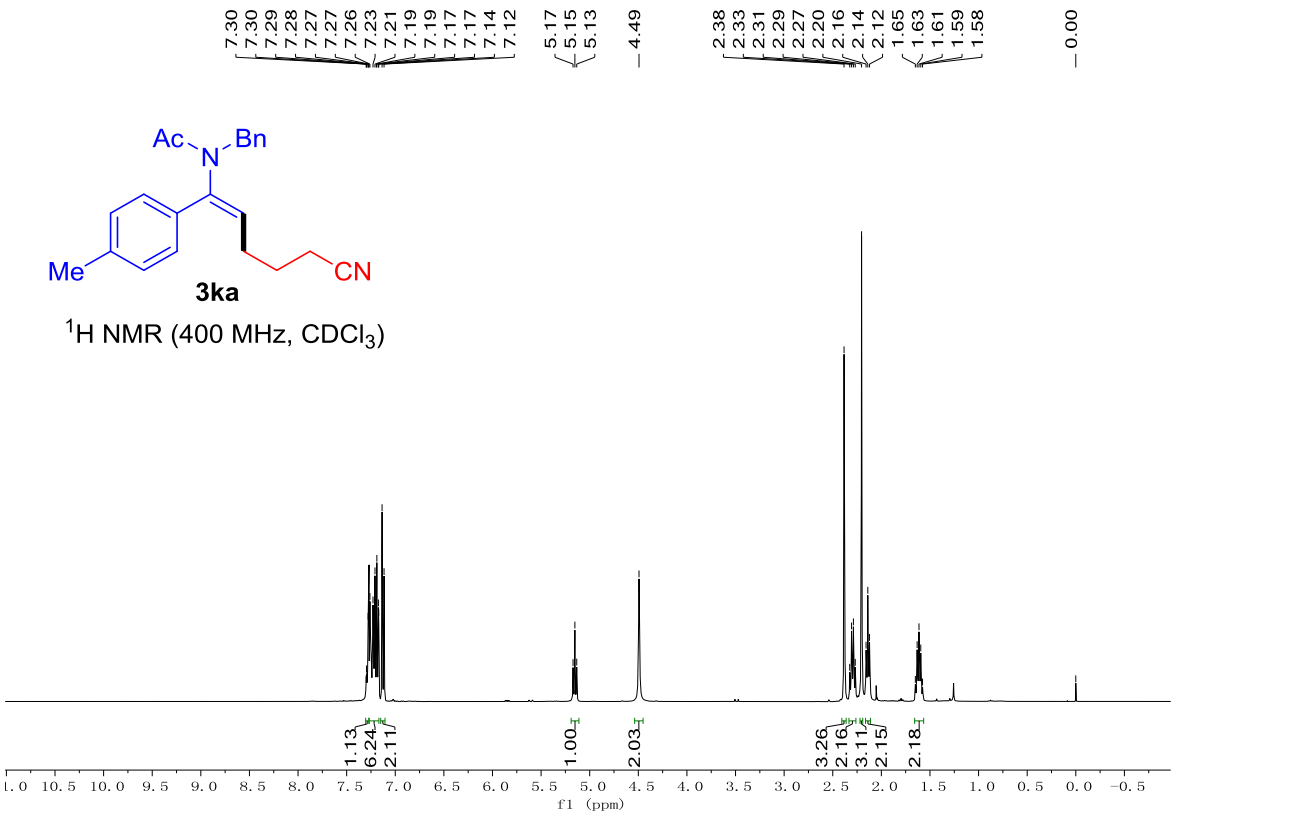


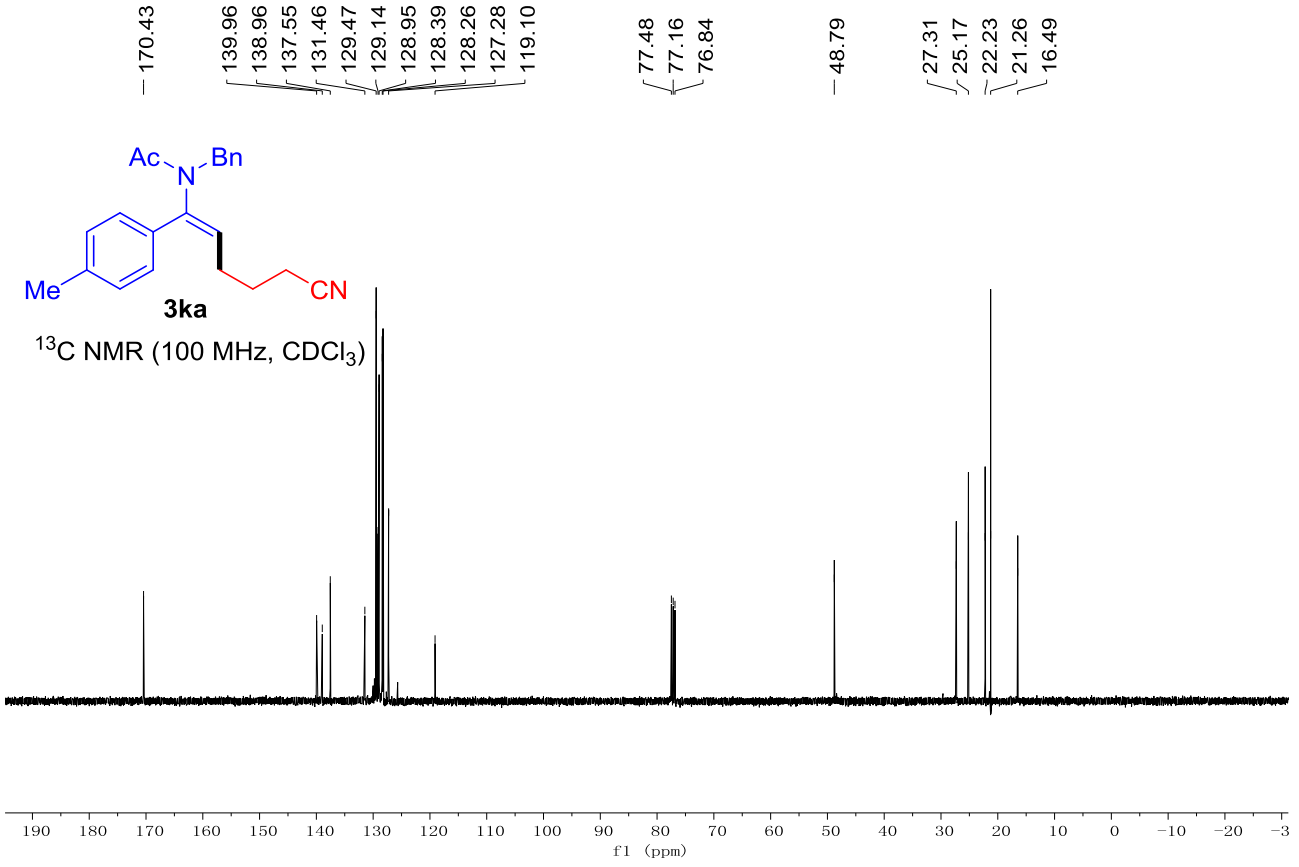
3ja

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

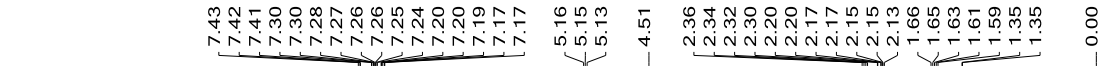


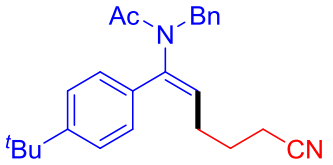
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(*p*-tolyl)pent-1-en-1-yl)acetamide (**3ka**)





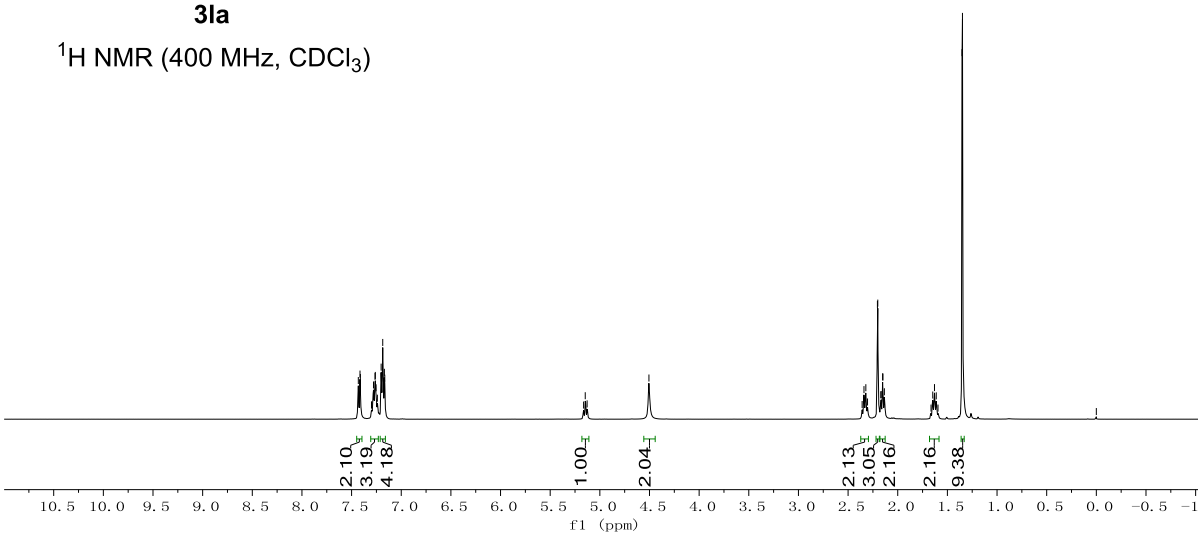
(*E*)-*N*-benzyl-*N*-(1-(4-(tert-butyl)phenyl)-5-cyanopent-1-en-1-yl)acetamide (**3la**)

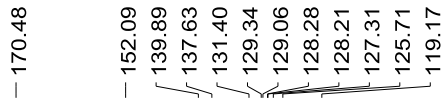


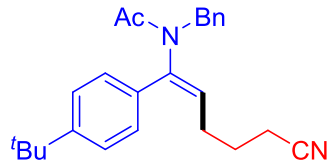


3la

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



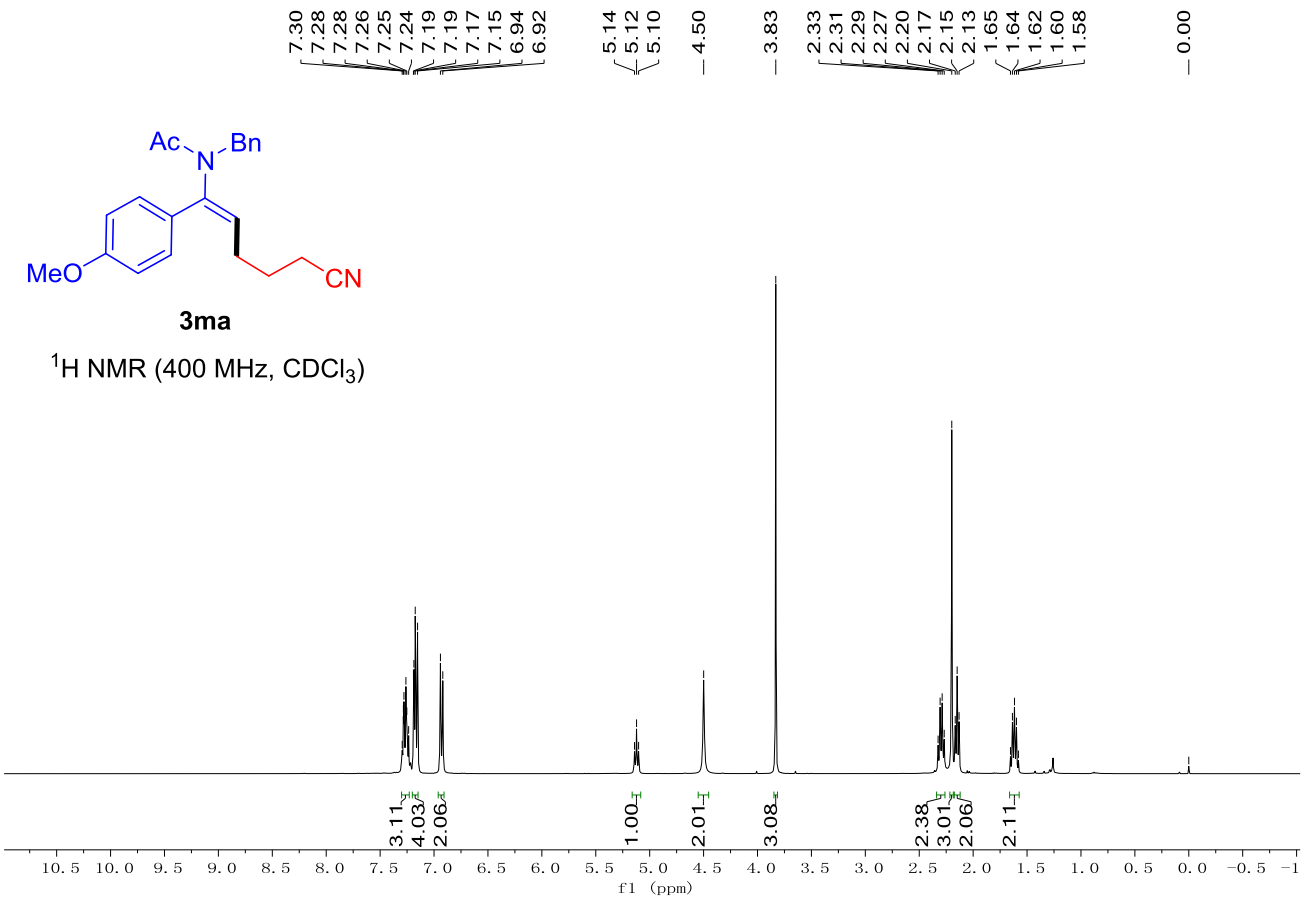


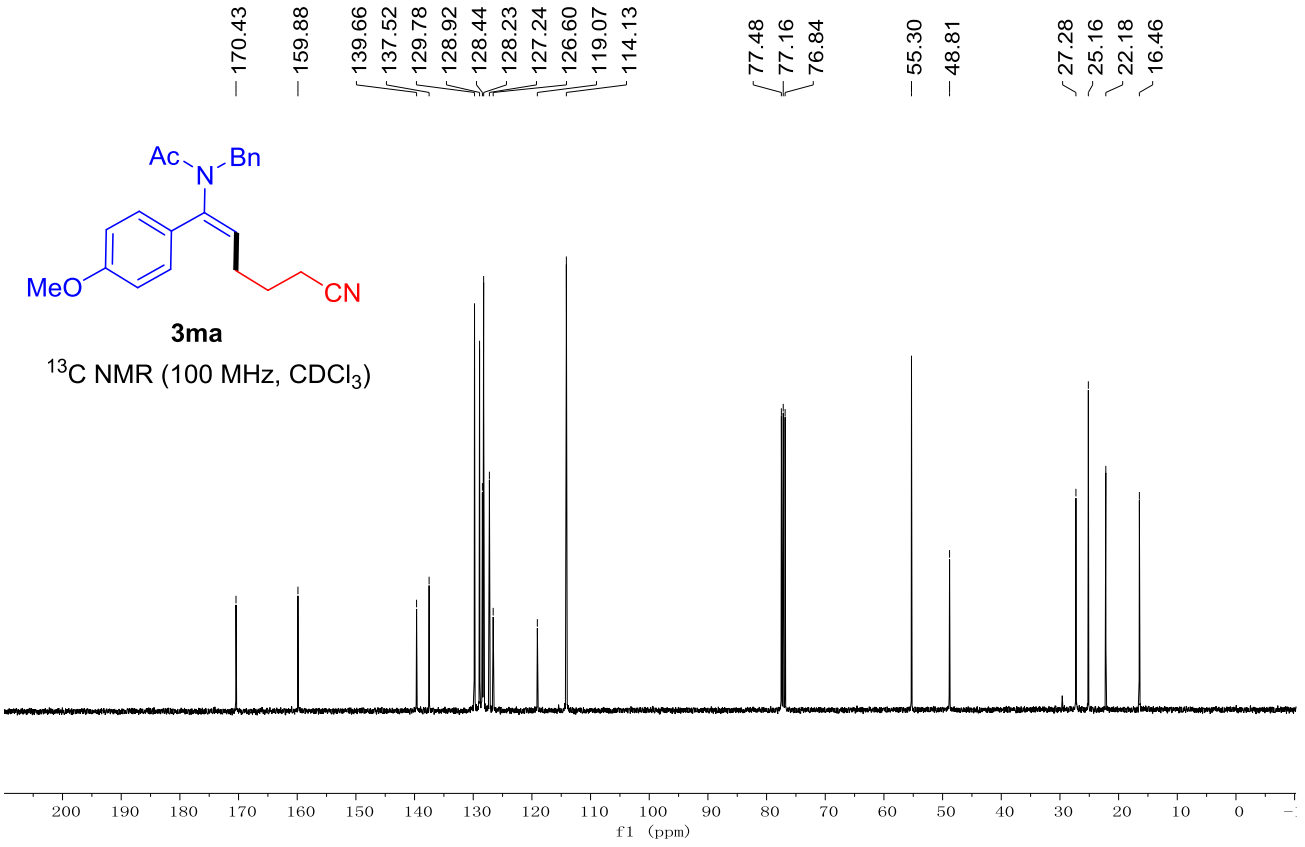


3la

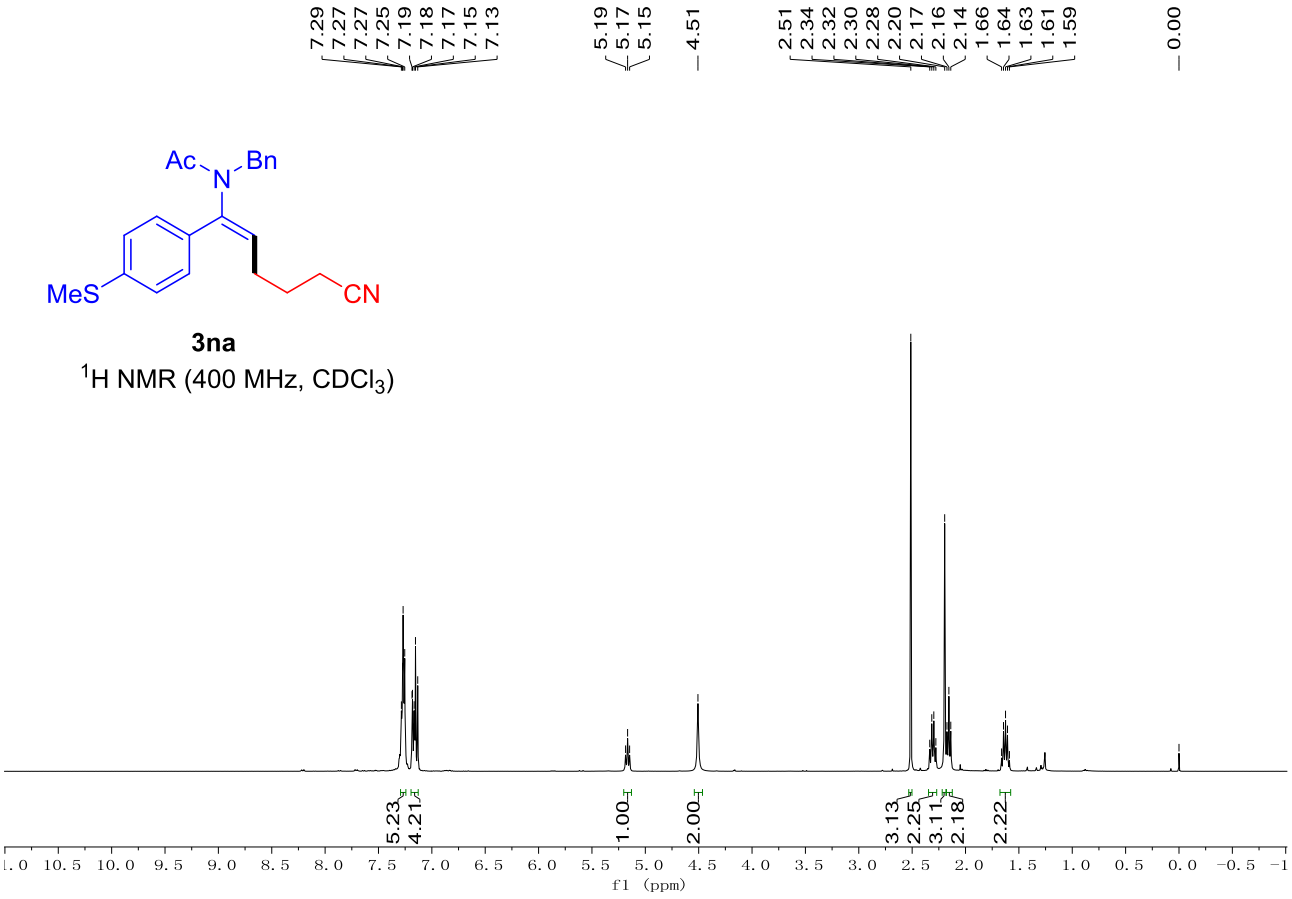
^{13}C NMR (100 MHz, $CDCl_3$)

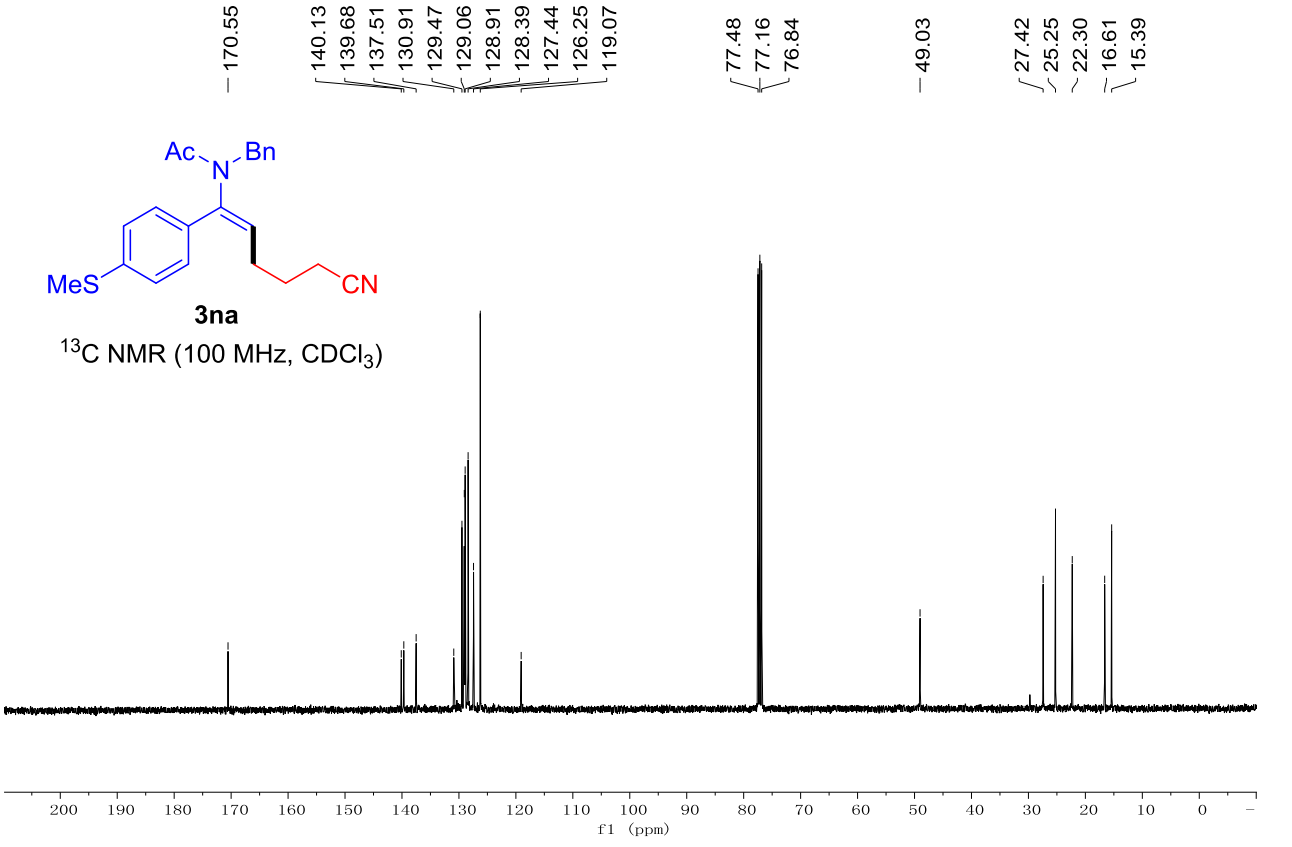
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-methoxyphenyl)pent-1-en-1-yl)acetamide (**3ma**)



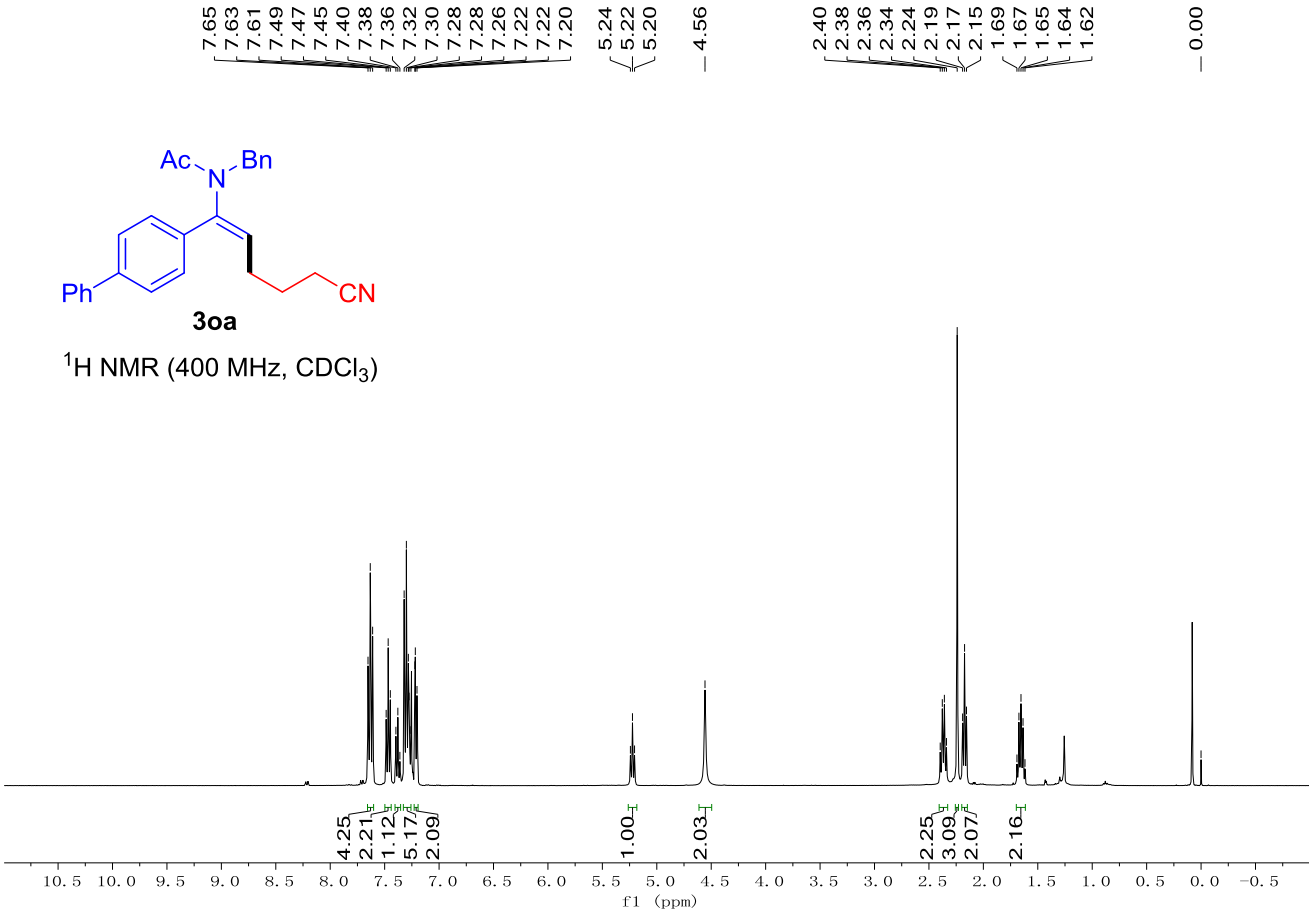


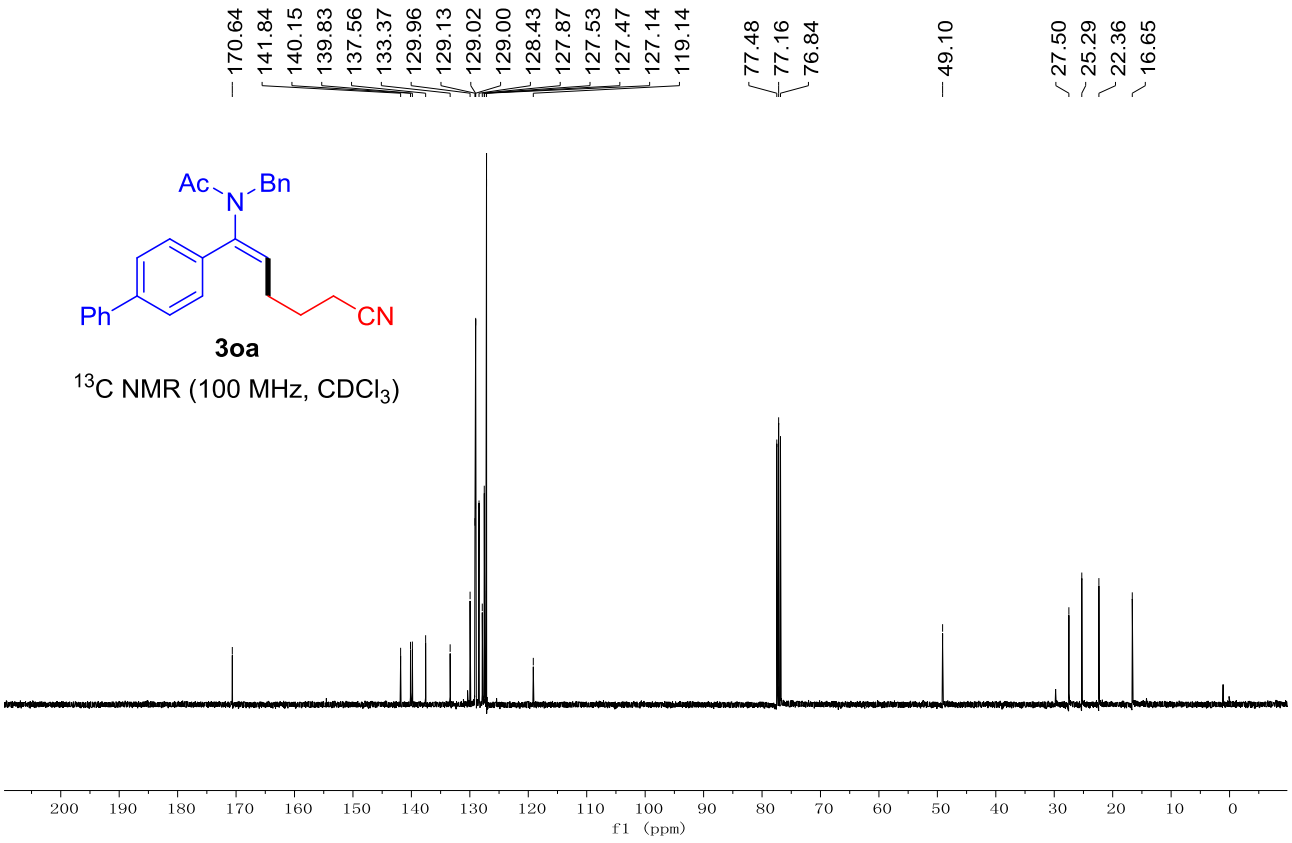
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(4-(methylthio)phenyl)pent-1-en-1-yl)acetamide (**3na**)



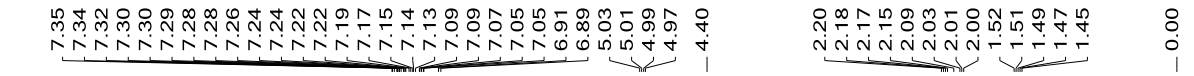


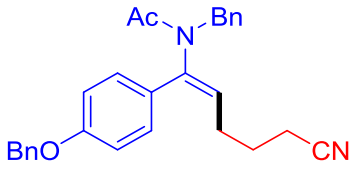
(*E*)-*N*-(1-([1,1'-biphenyl]-4-yl)-5-cyanopent-1-en-1-yl)-*N*-benzylacetamide (**3oa**)





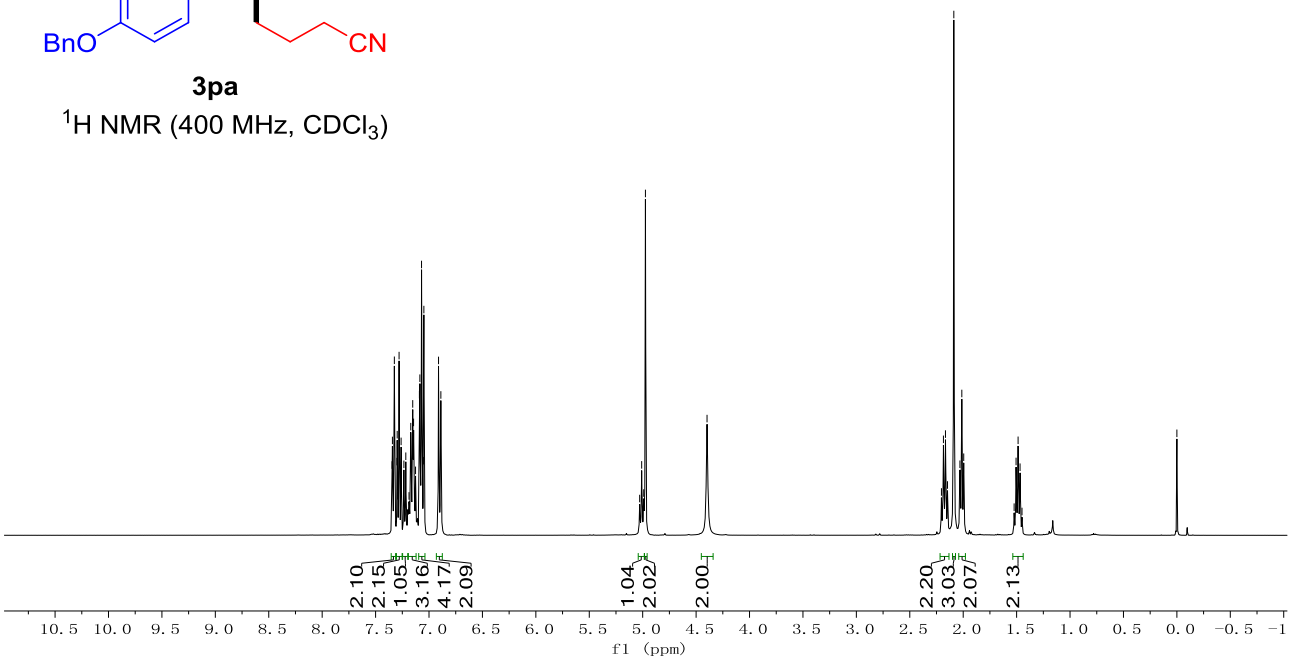
(*E*)-*N*-benzyl-*N*-(1-(4-(benzyloxy)phenyl)-5-cyanopent-1-en-1-yl)acetamide (**3pa**)

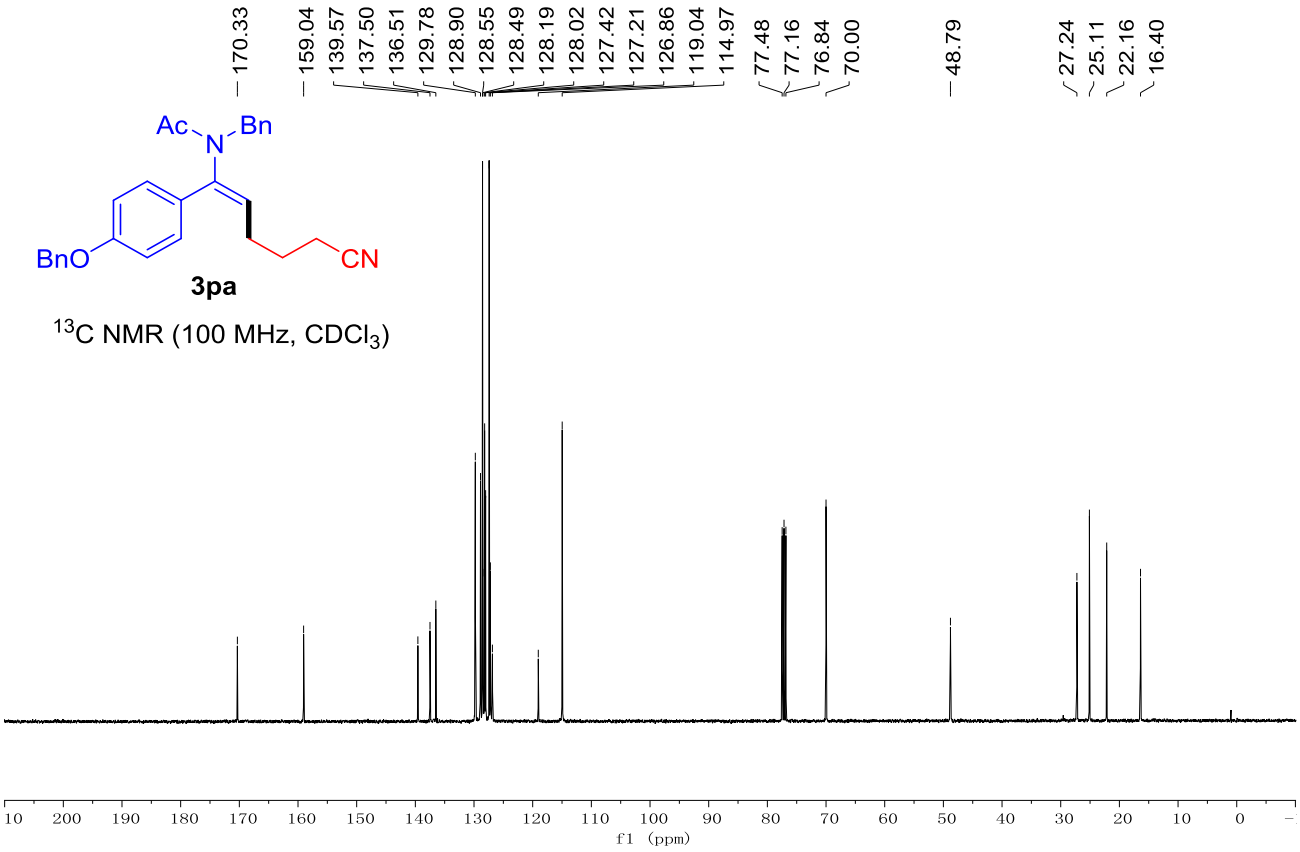




3pa

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

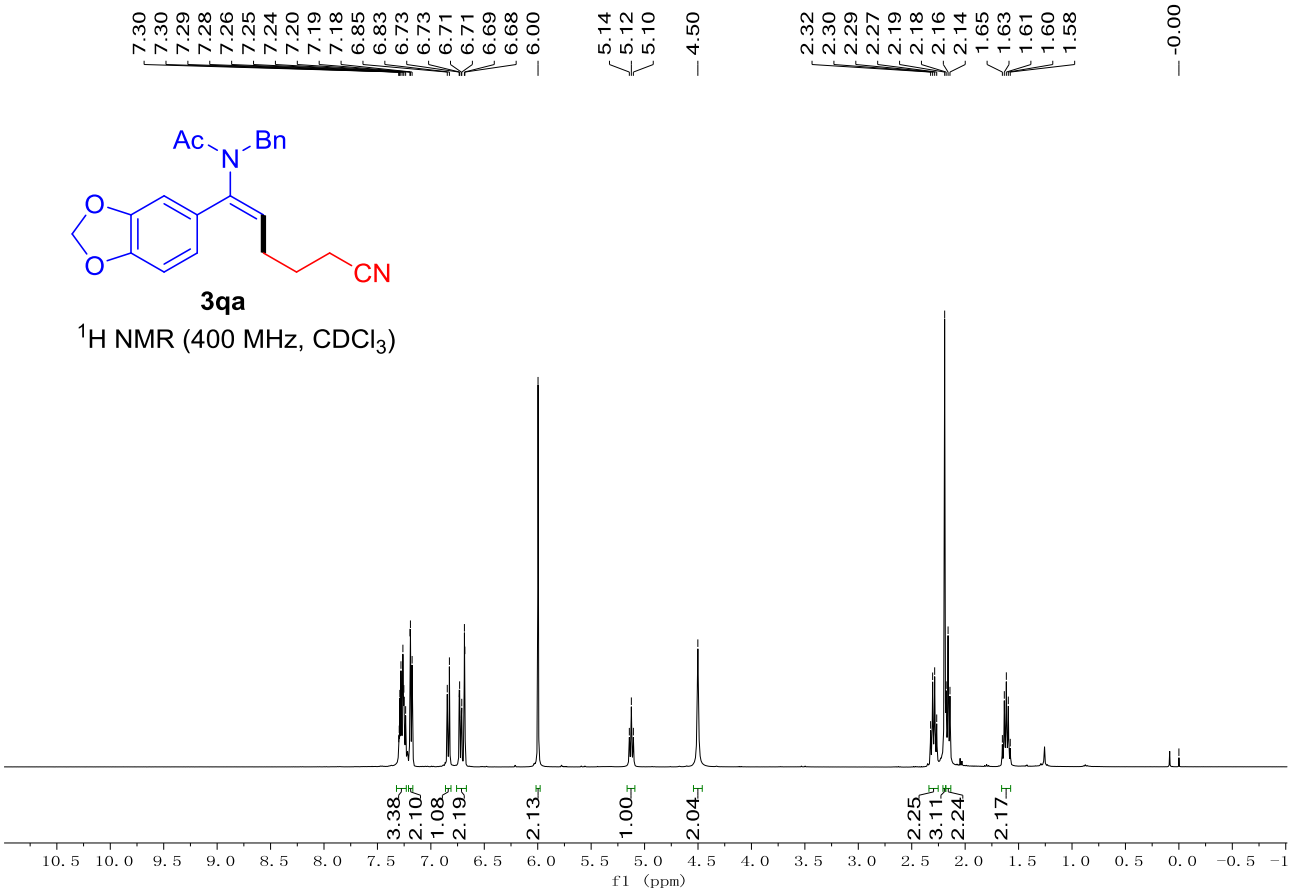


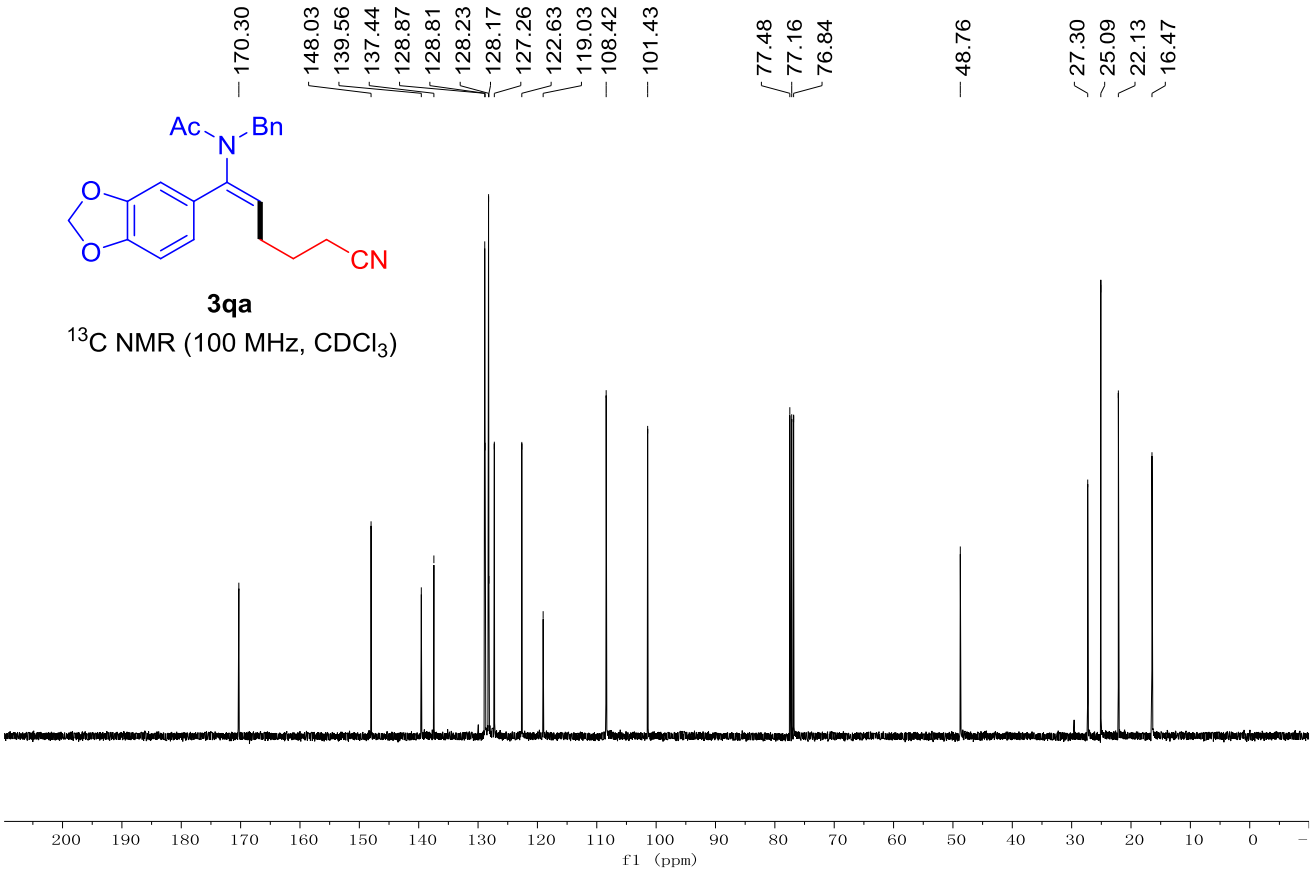


3pa

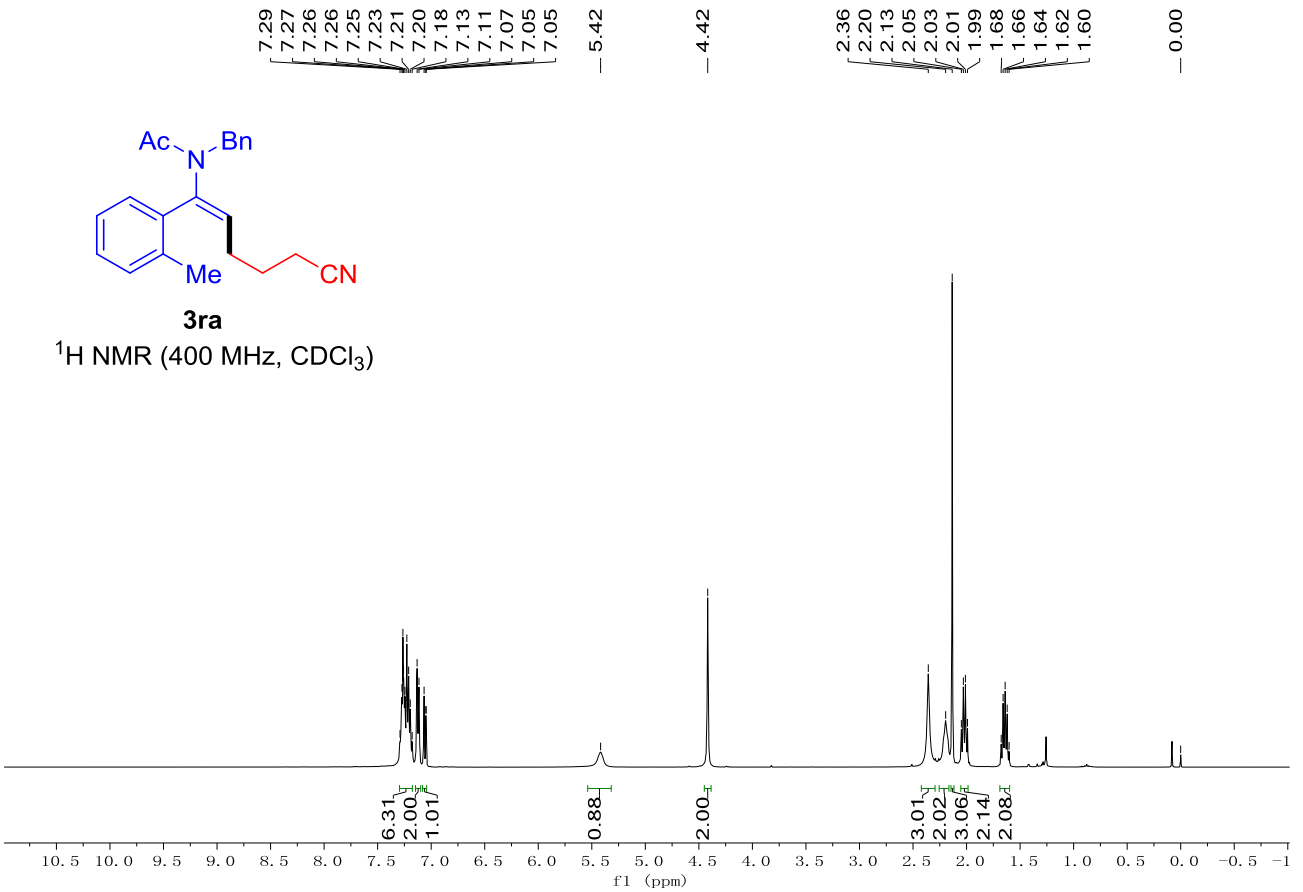
^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-(1-(benzo[d][1,3]dioxol-5-yl)-5-cyanopent-1-en-1-yl)-*N*-benzylacetamide (**3qa**)



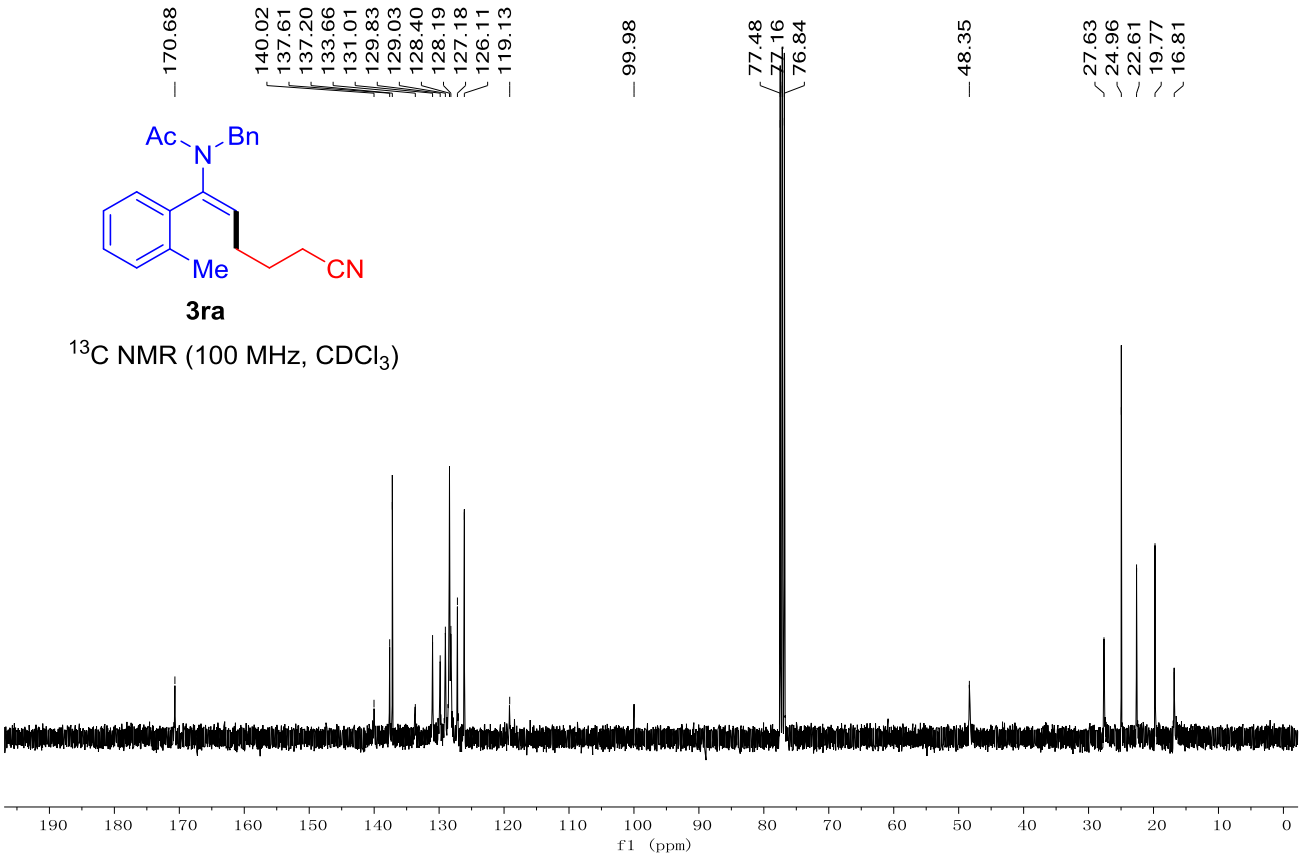


(*E*)-*N*-benzyl-*N*-(5-cyano-1-(o-tolyl)pent-1-en-1-yl)acetamide (**3ra**)



3ra

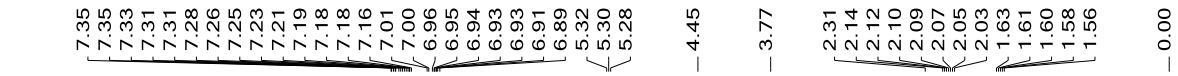
^{1}H NMR (400 MHz, $CDCl_3$)

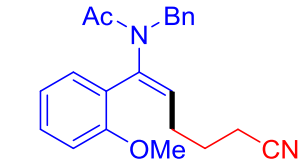


3ra

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

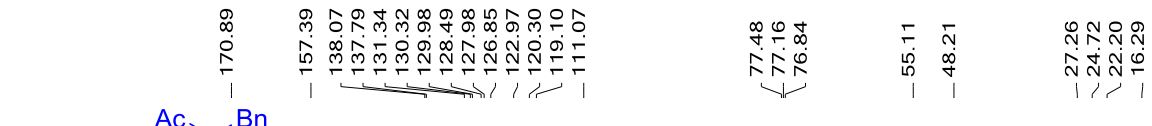
(*E*)-*N*-benzyl-*N*-(5-cyano-1-(2-methoxyphenyl)pent-1-en-1-yl)acetamide (**3sa**)

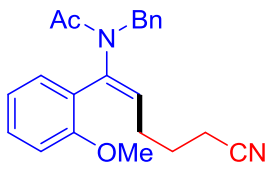




3sa

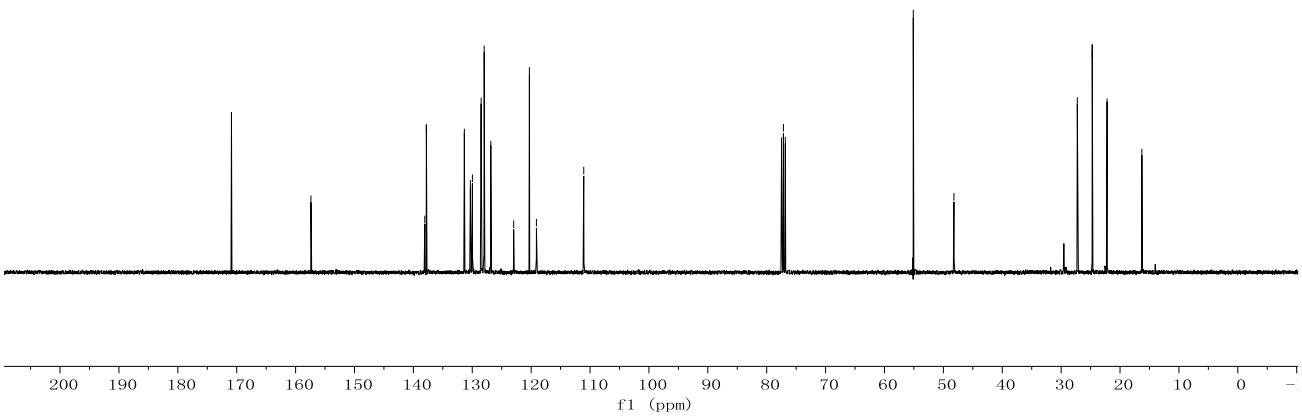
^{1}H NMR (400 MHz, $CDCl_3$)



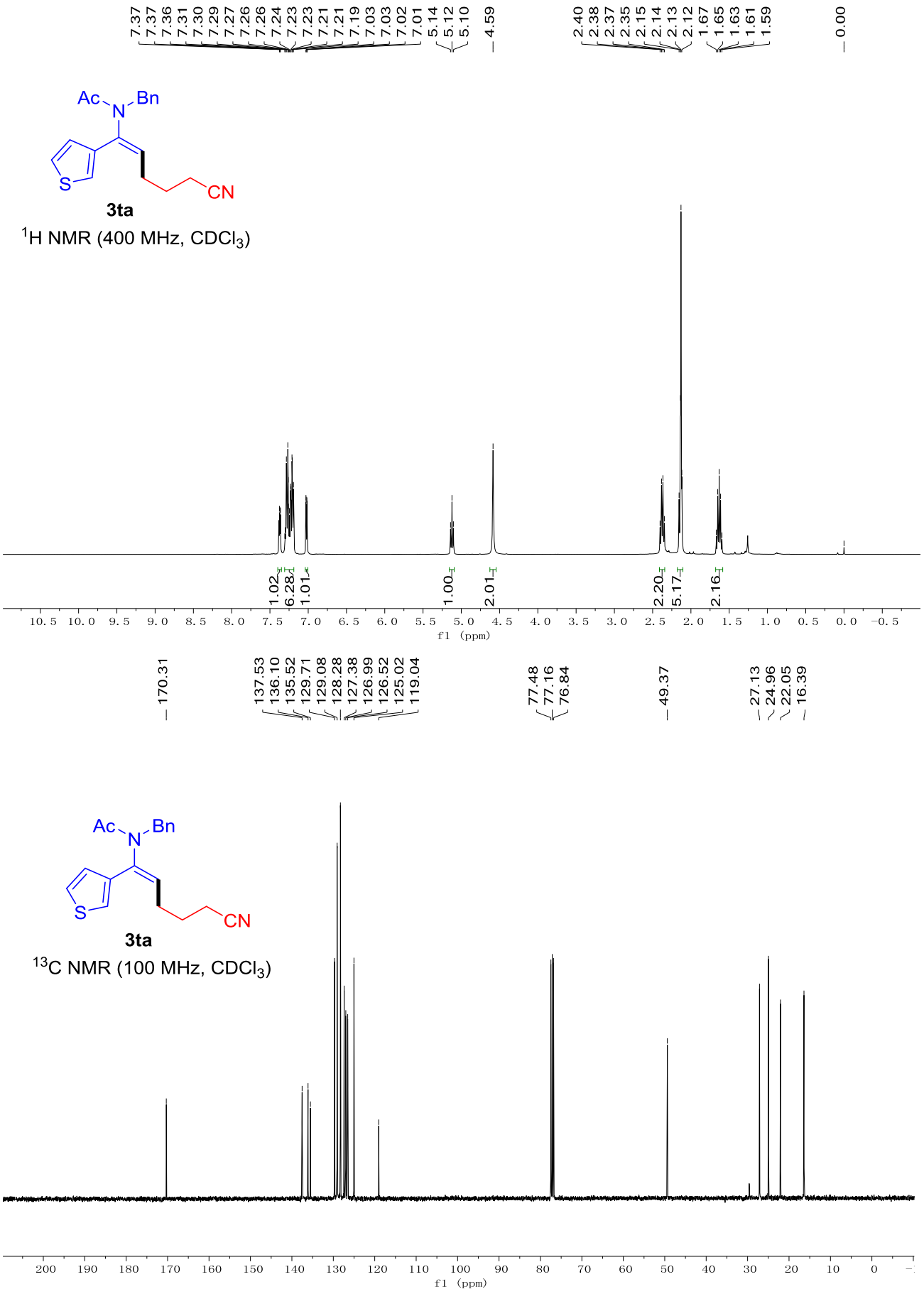


3sa

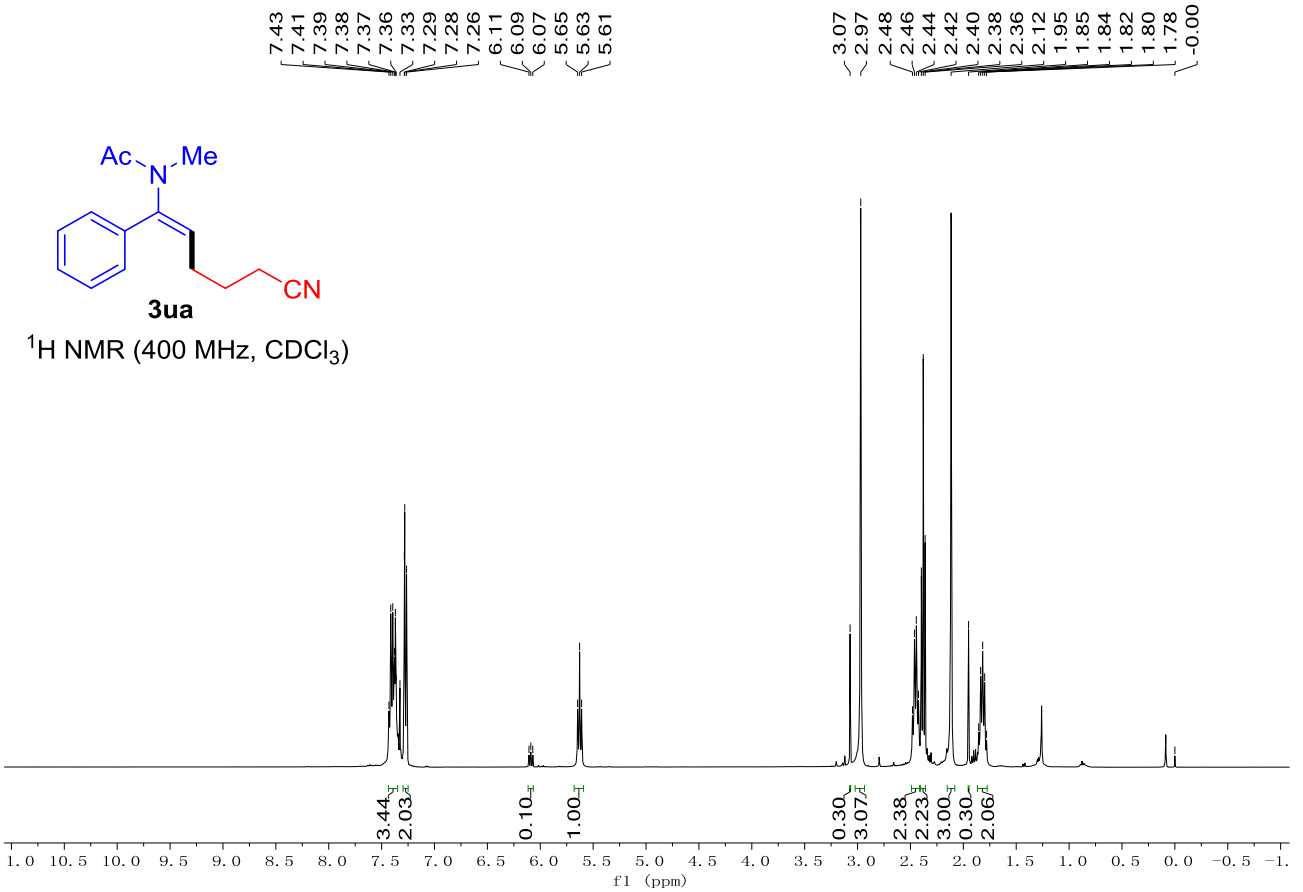
^{13}C NMR (100 MHz, $CDCl_3$)

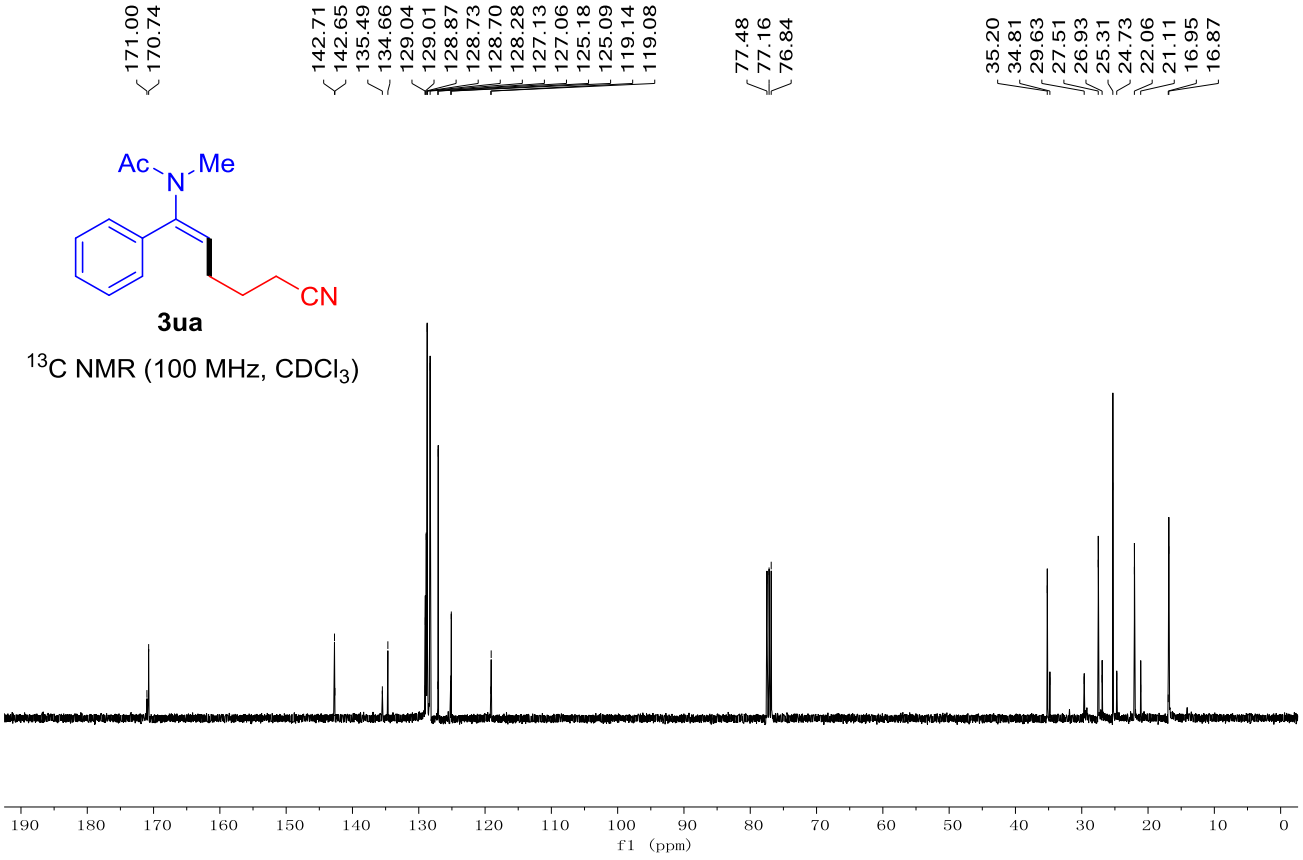


(*E*)-*N*-benzyl-*N*-(5-cyano-1-(thiophen-3-yl)pent-1-en-1-yl)acetamide (**3ta**)

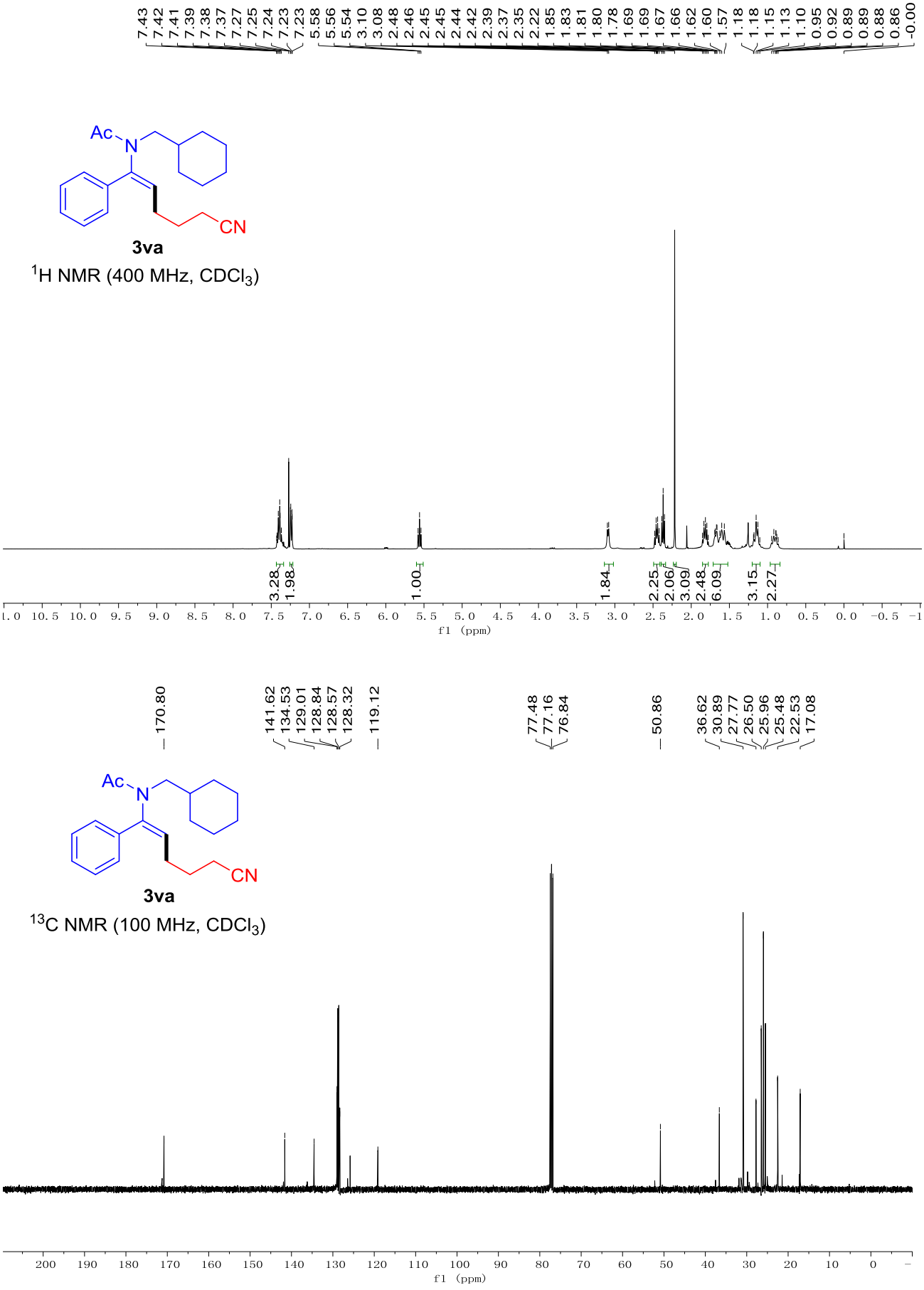


(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-methylacetamide (**3ua**)

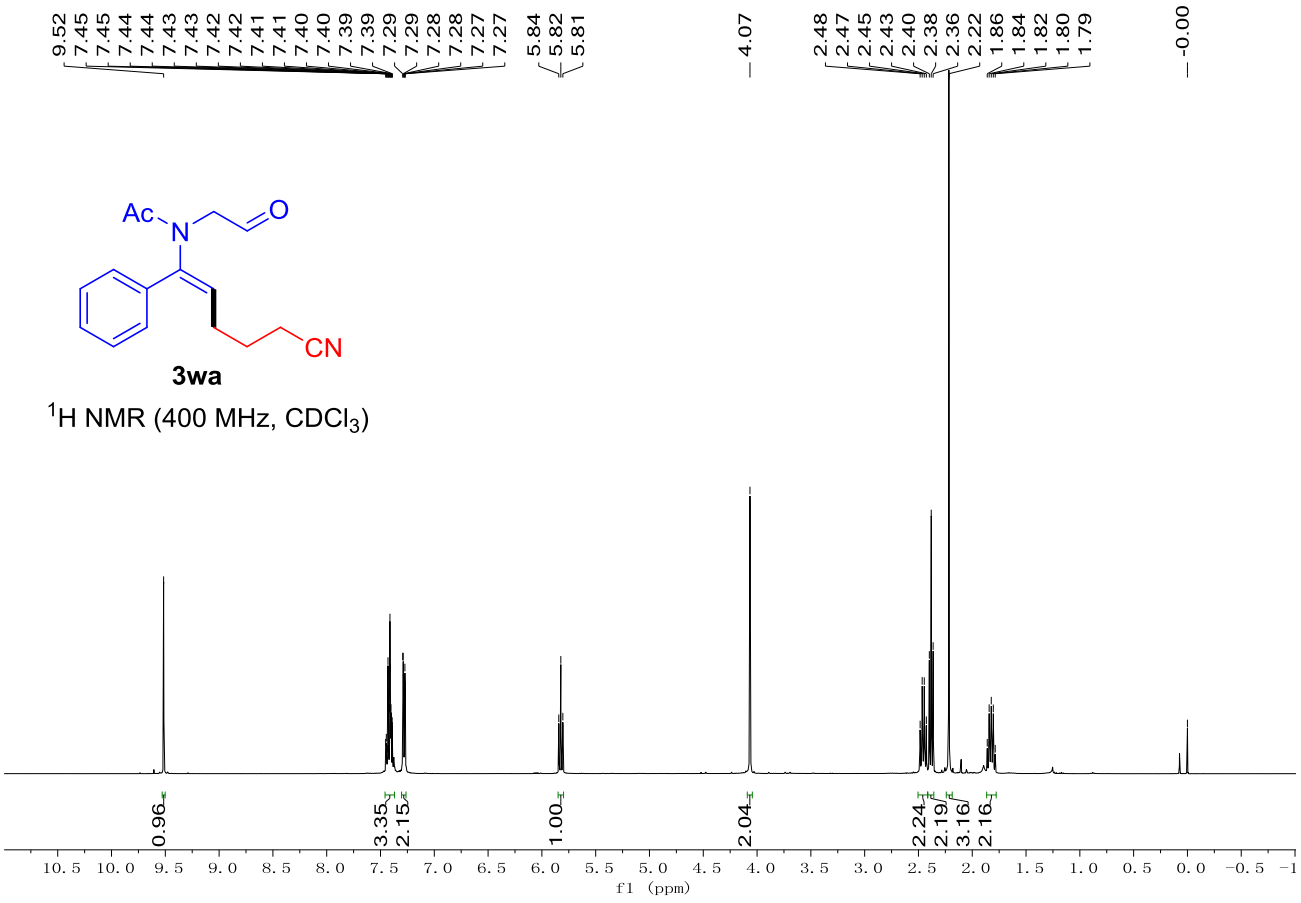




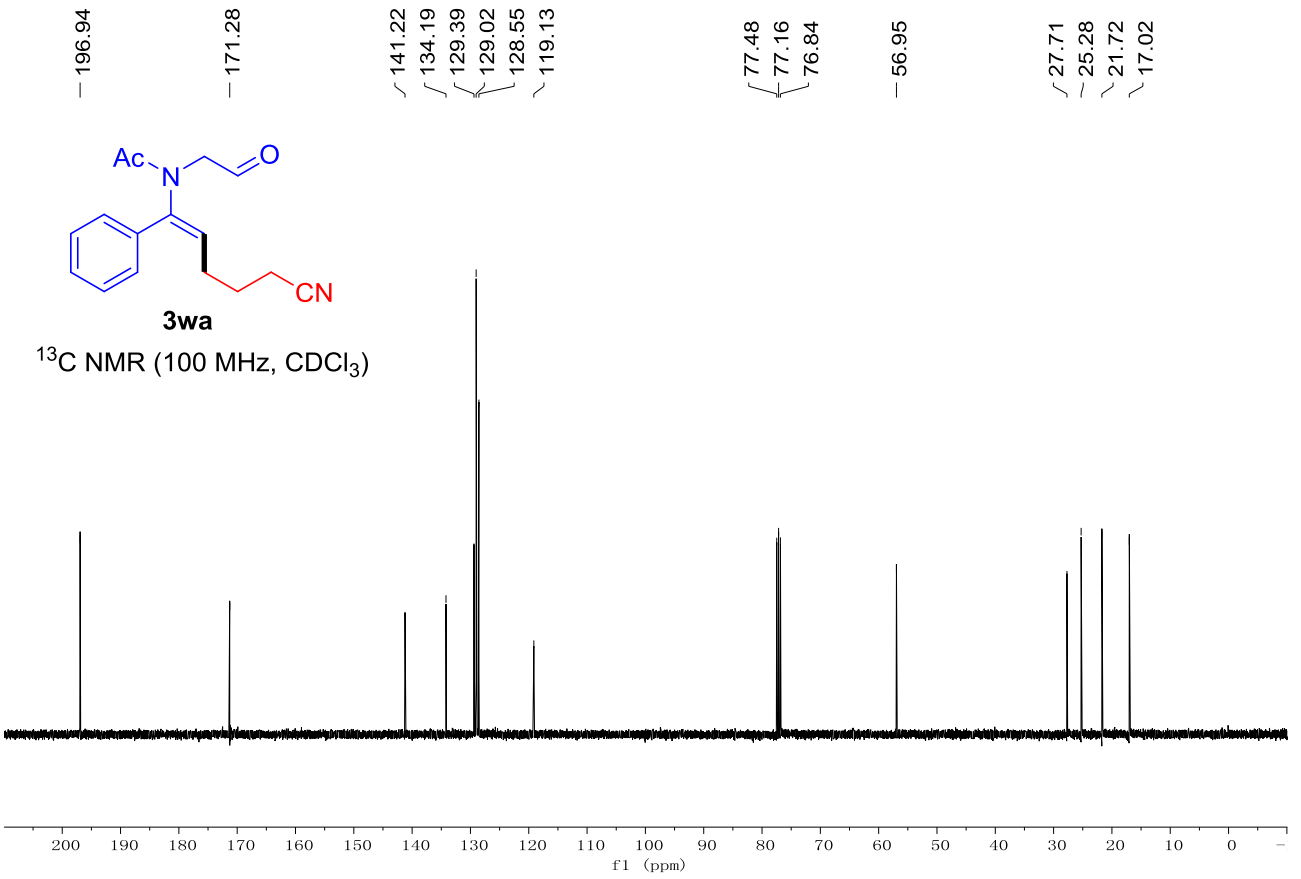
(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(cyclohexylmethyl)acetamide (**3va**)



(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(2-oxoethyl)acetamide (**3wa**)

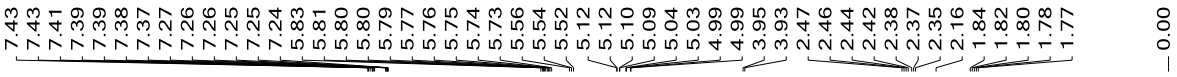


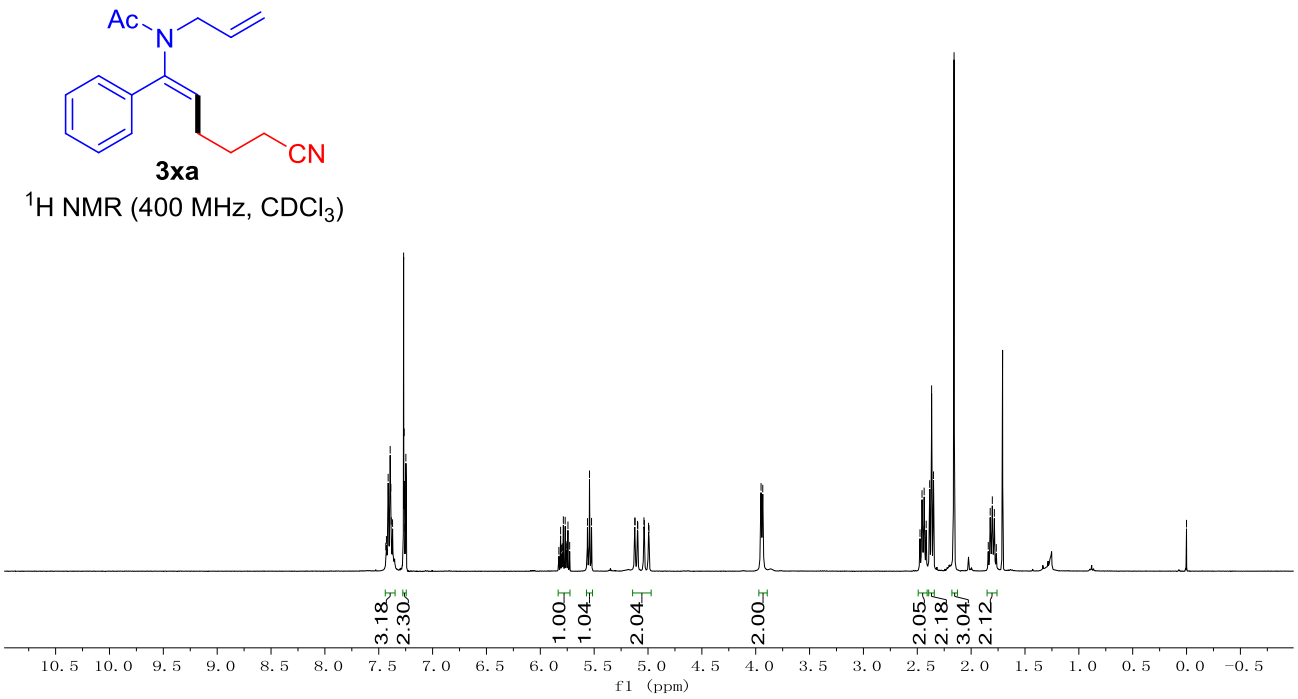
^{1}H NMR (400 MHz, $CDCl_3$)

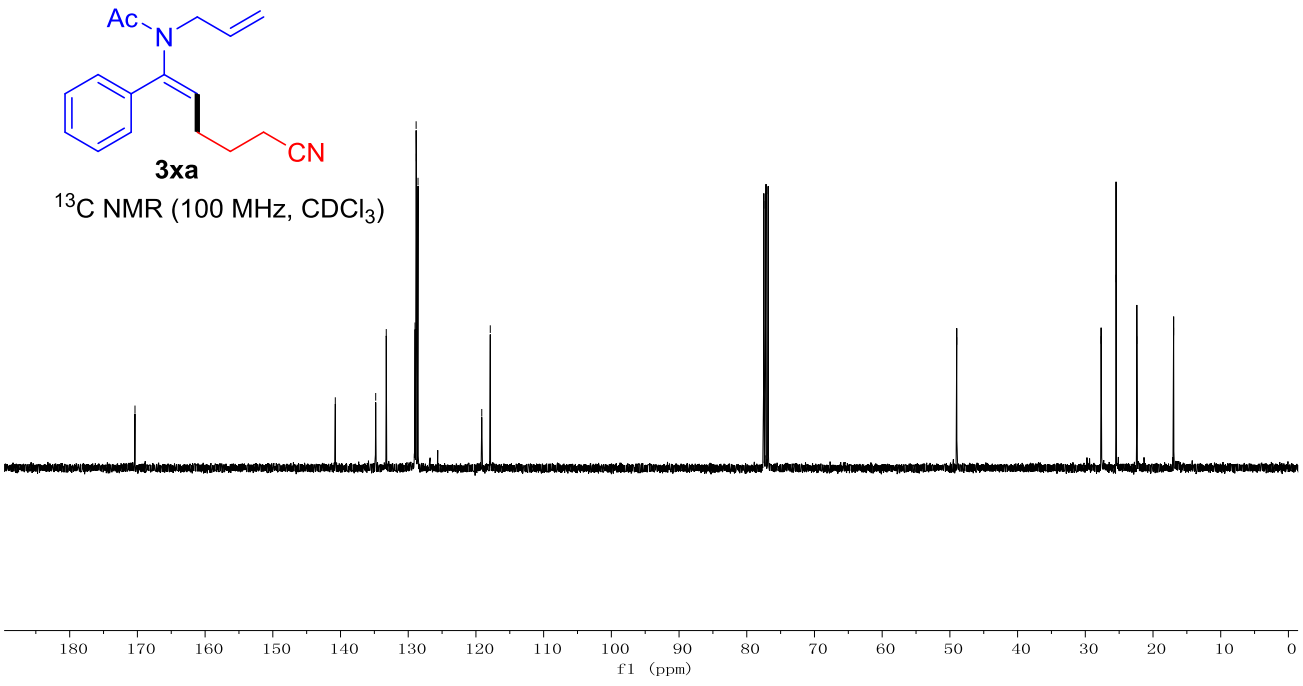


^{13}C NMR (100 MHz, $CDCl_3$)

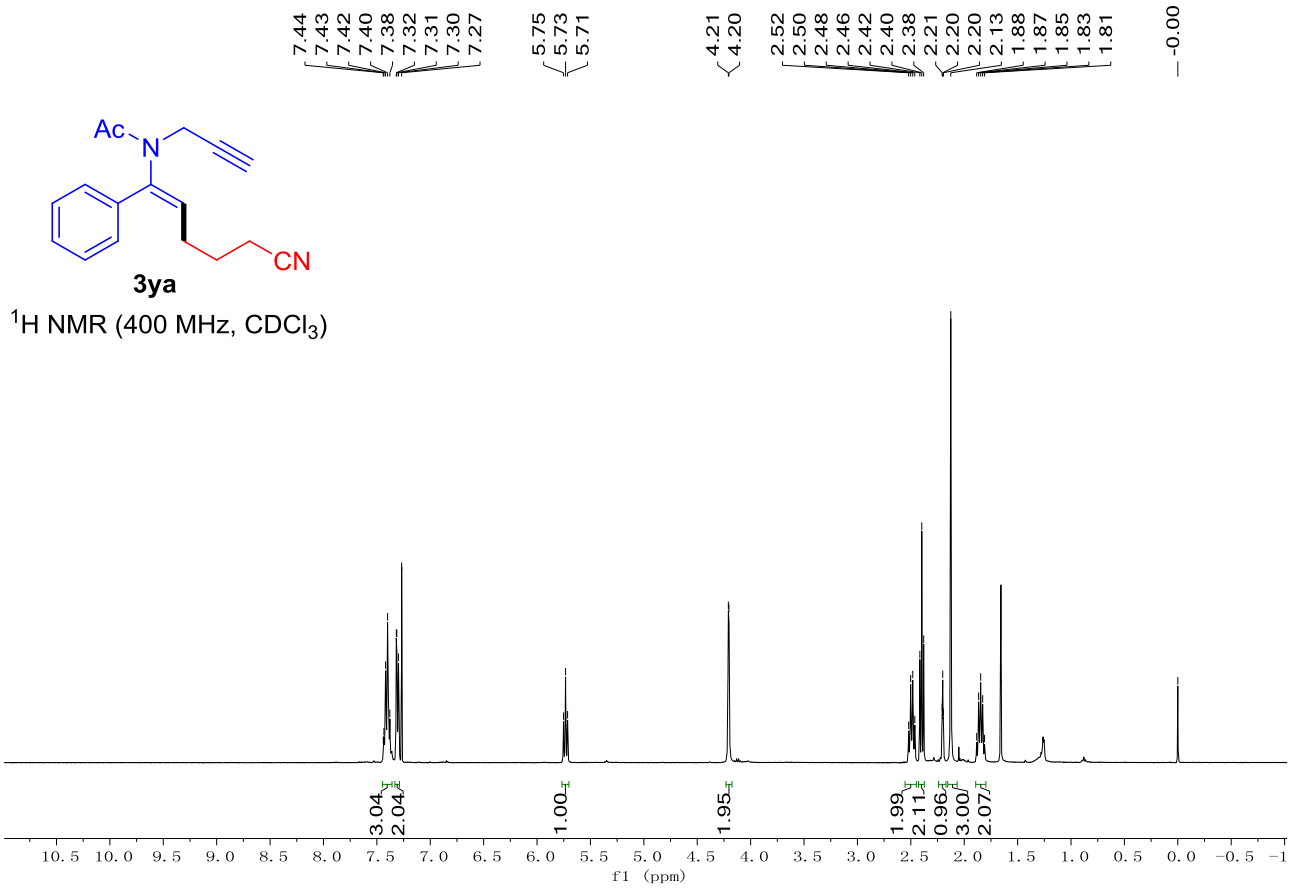
(*E*)-*N*-allyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3xa**)

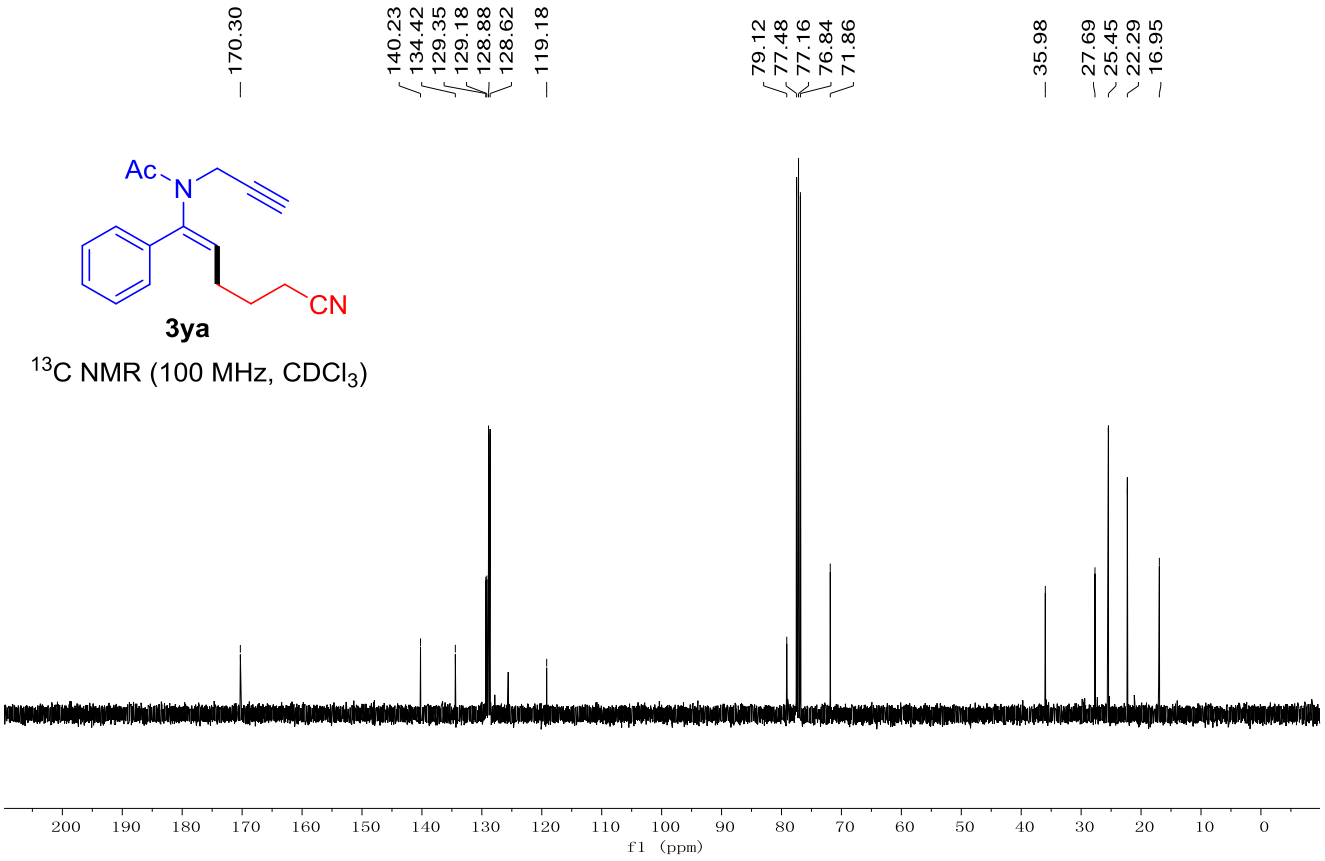




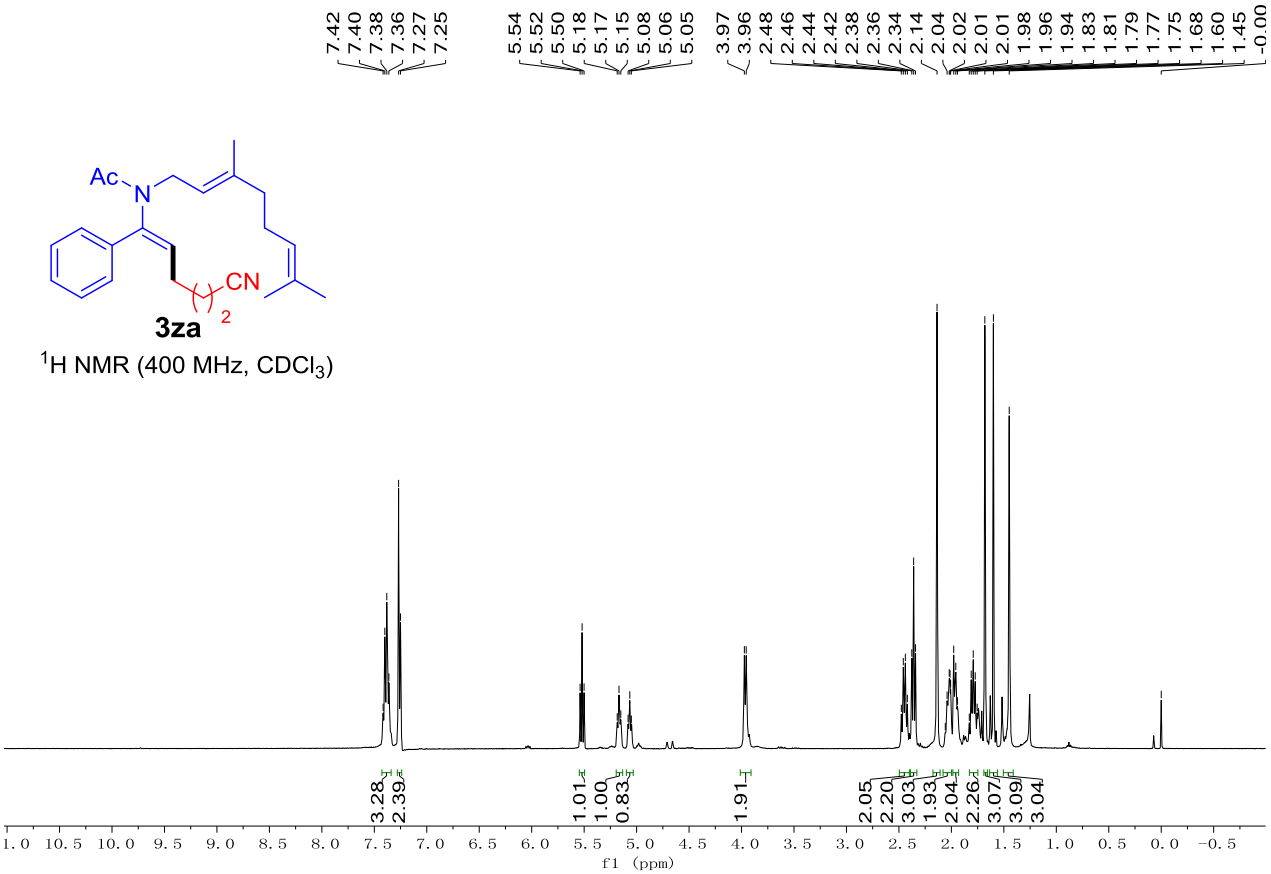


(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)-*N*-(prop-2-yn-1-yl)acetamide (**3ya**)

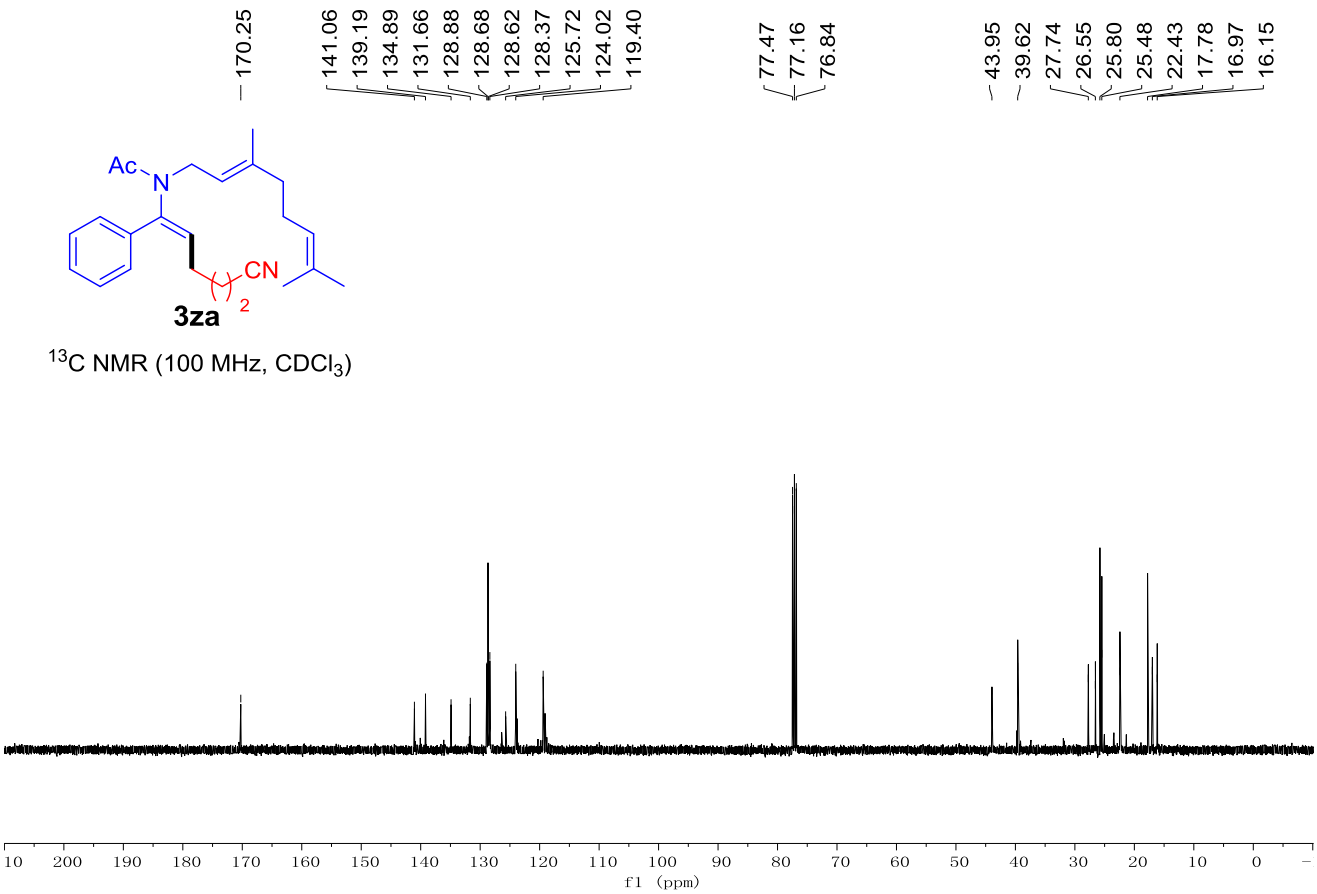




N-((*E*)-5-cyano-1-phenylpent-1-en-1-yl)-*N*-((*E*)-3,7-dimethylocta-2,6-dien-1-yl)acetamide (**3za**)

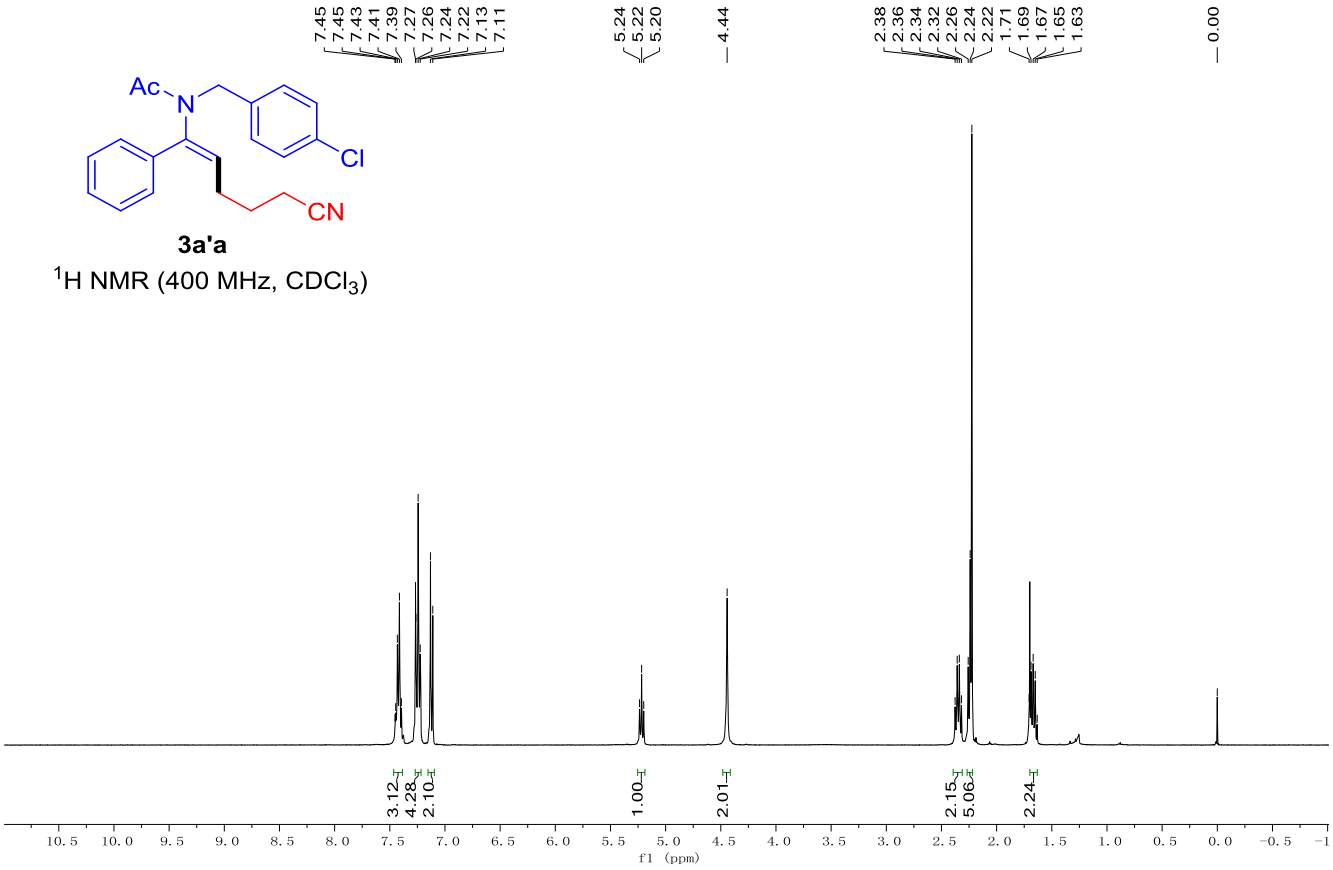


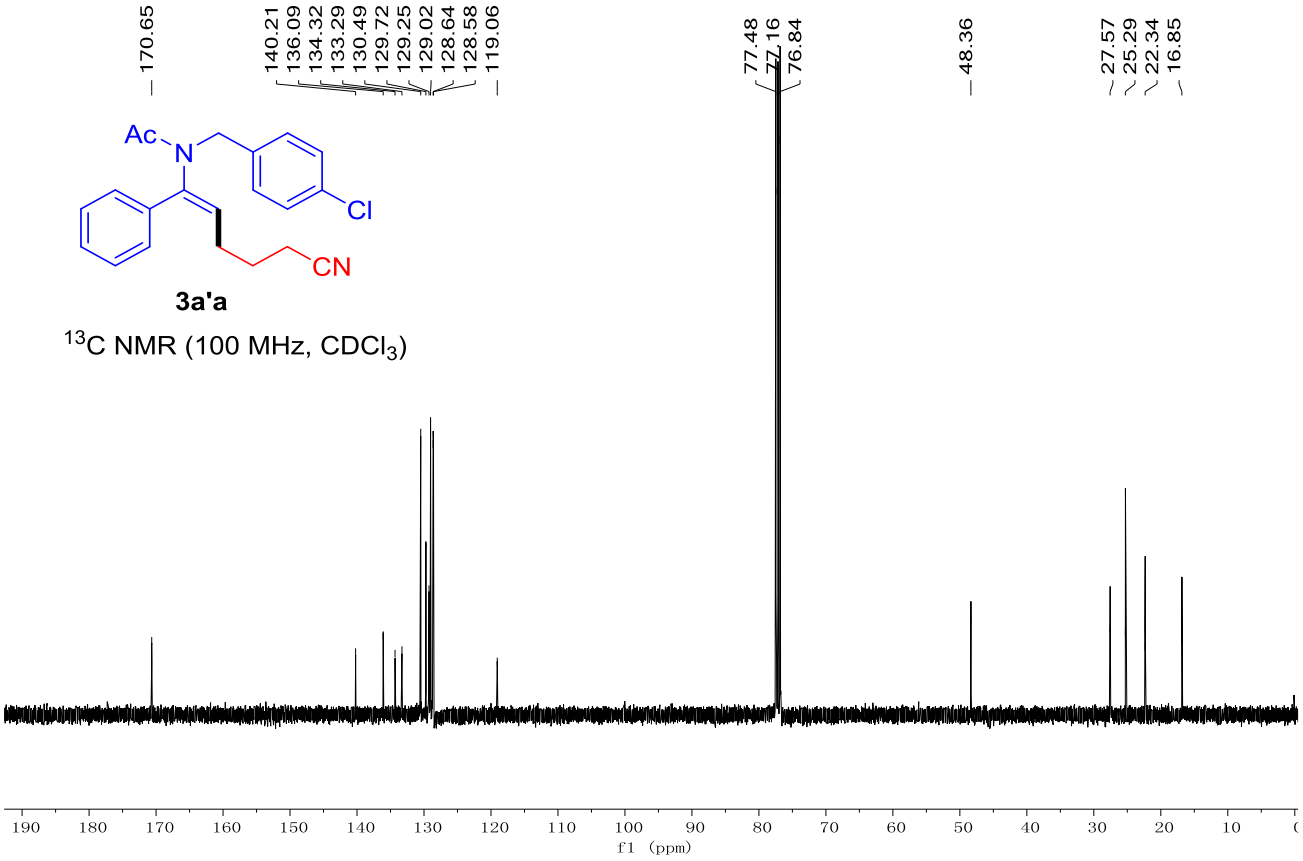
^{1}H NMR (400 MHz, $CDCl_3$)



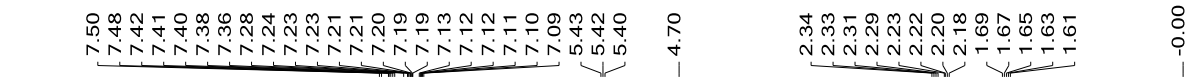
^{13}C NMR (100 MHz, $CDCl_3$)

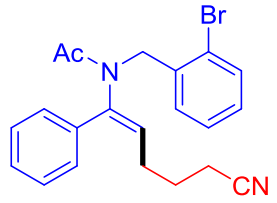
(*E*)-*N*-(4-chlorobenzyl)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3a'a**)





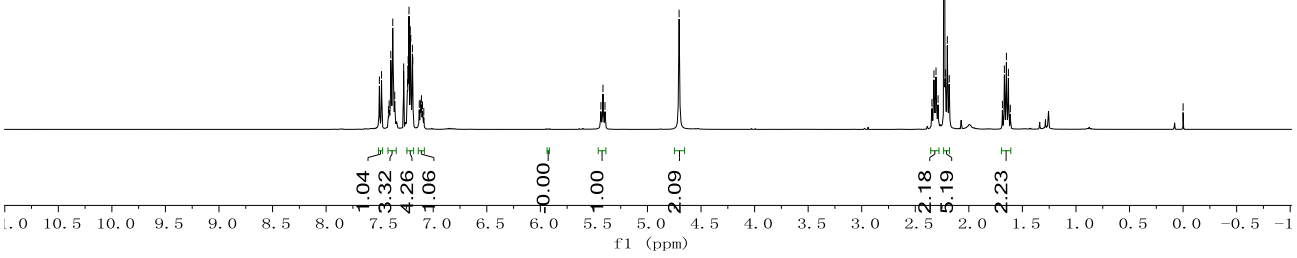
(*E*)-*N*-(2-bromobenzyl)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3b'a**)

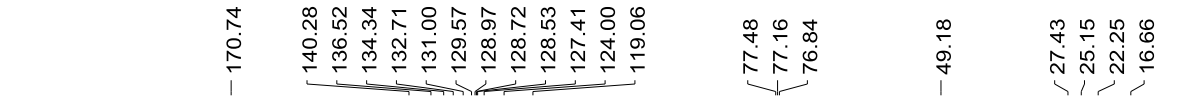


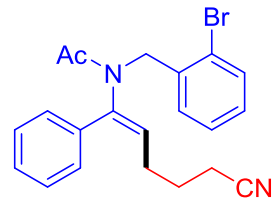


3b'a

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

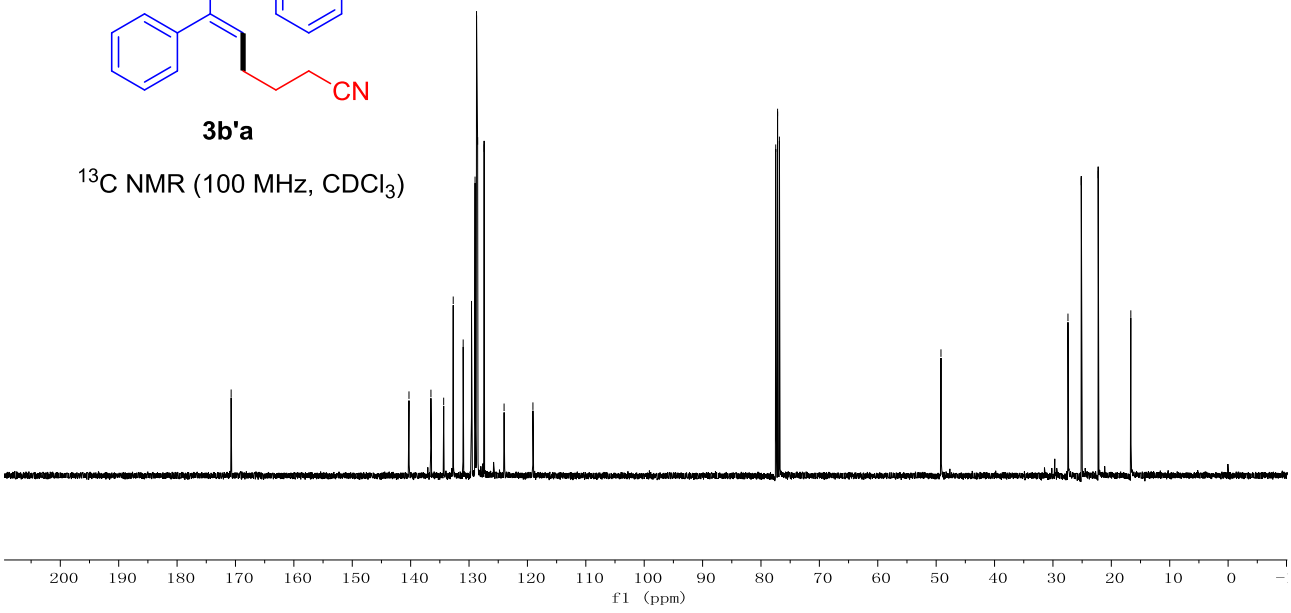




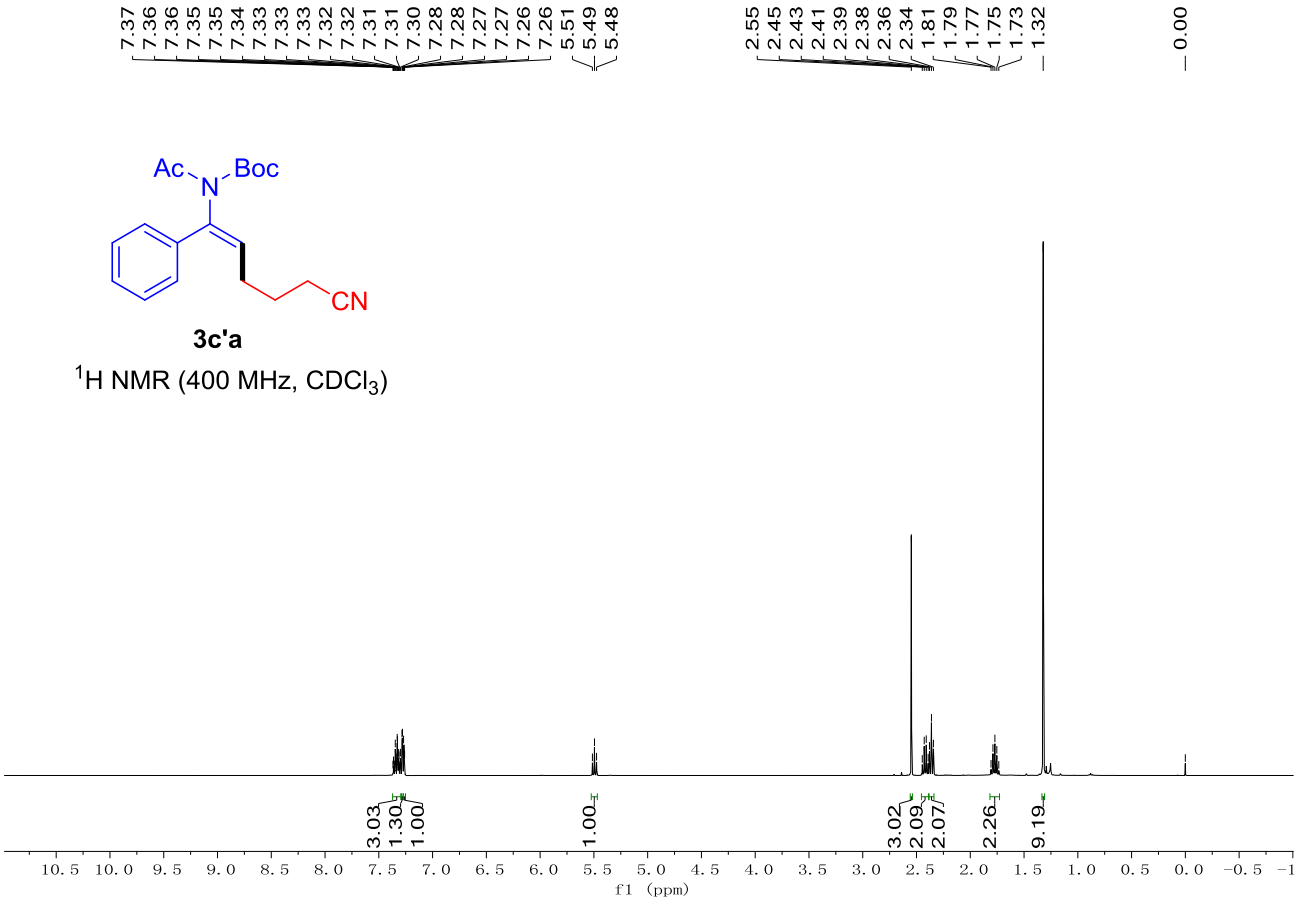


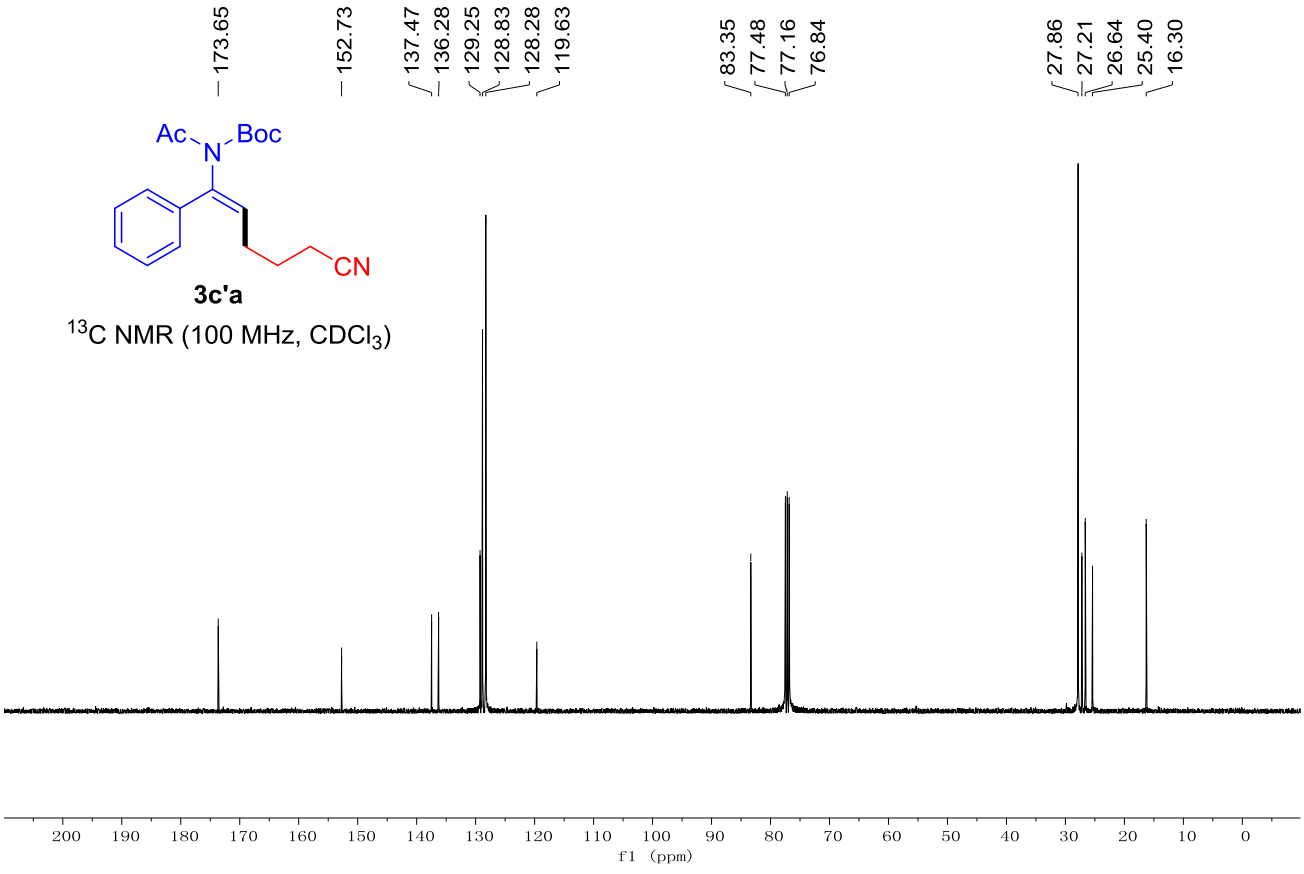
3b'a

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

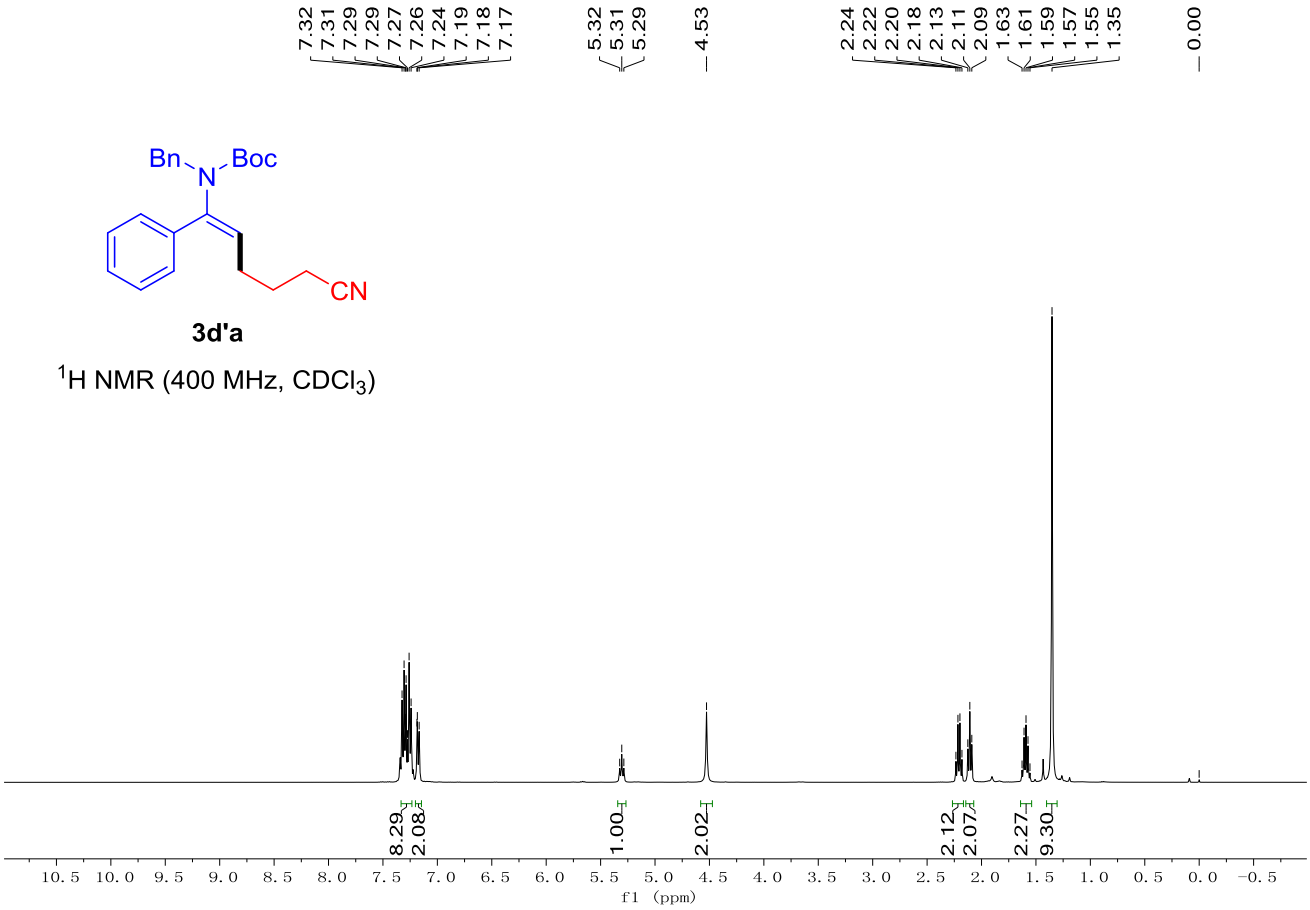


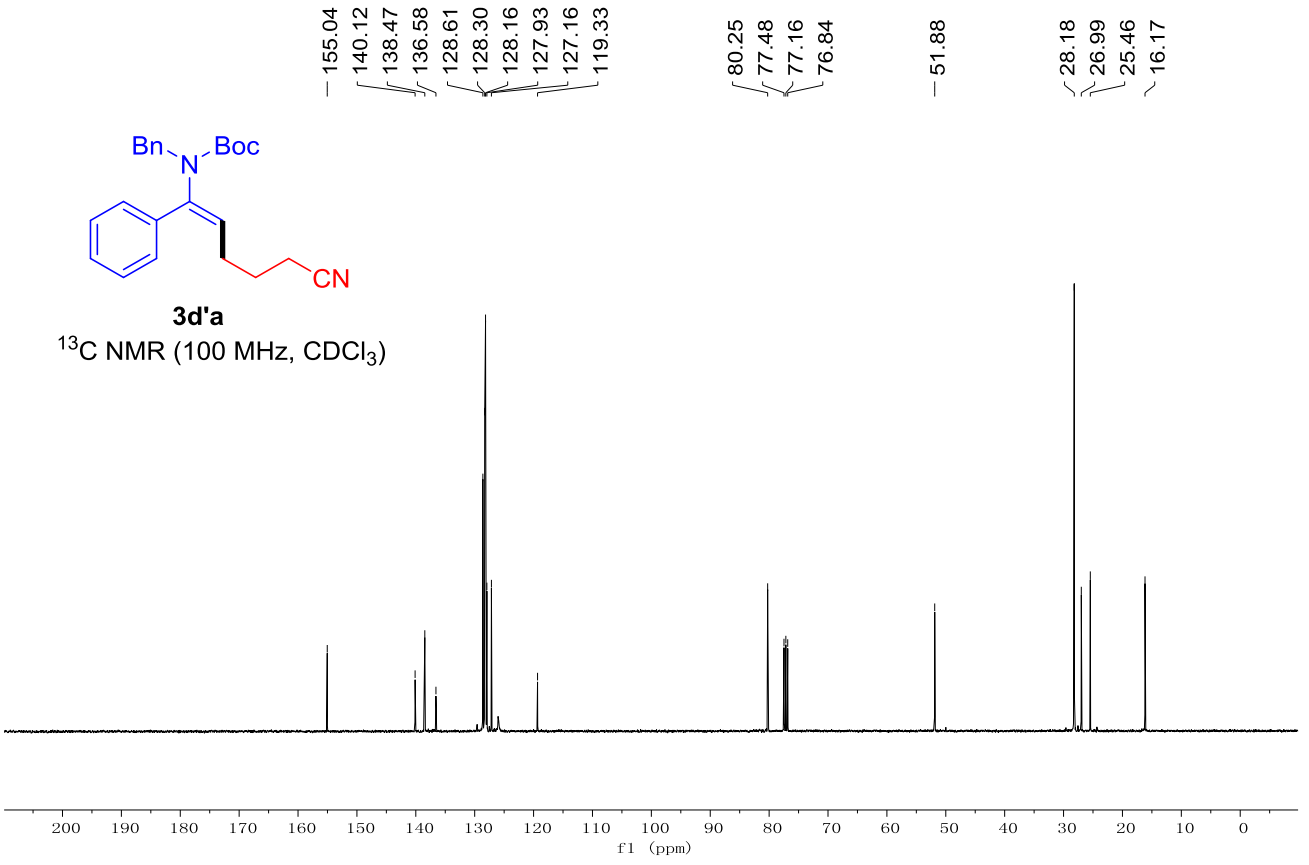
tert-butyl (*E*)-acetyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (**3c'a**)



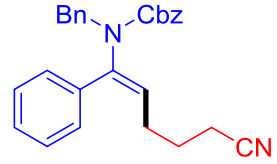


tert-butyl (*E*)-benzyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (**3d'a**)



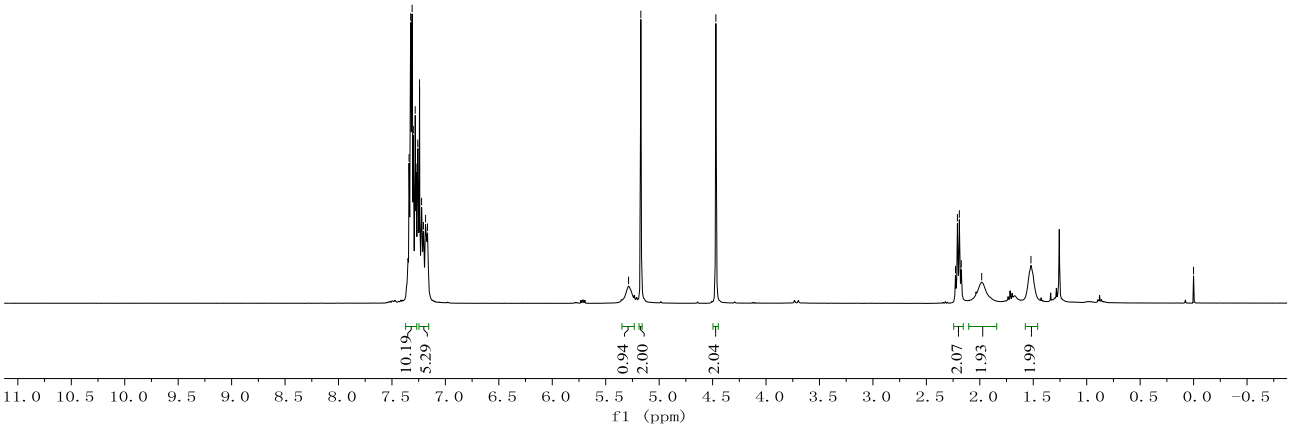


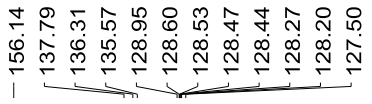
benzyl (*E*)-benzyl(5-cyano-1-phenylpent-1-en-1-yl)carbamate (**3e'a**)

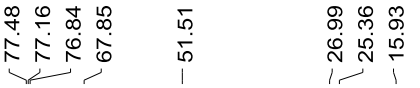


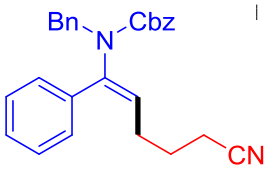
3e'a

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



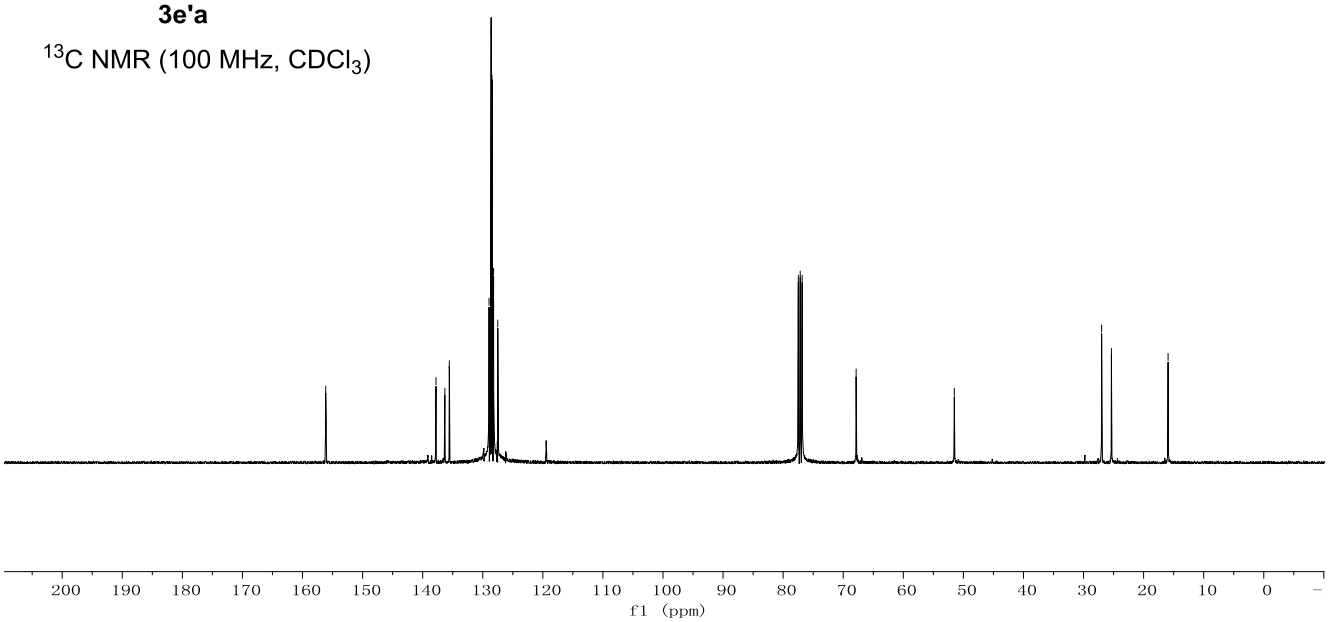




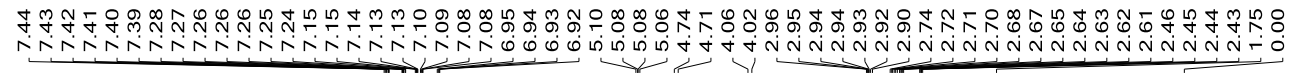


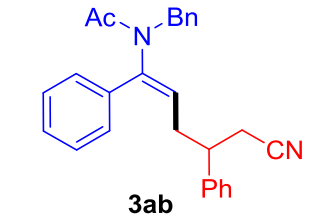
3e'a

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



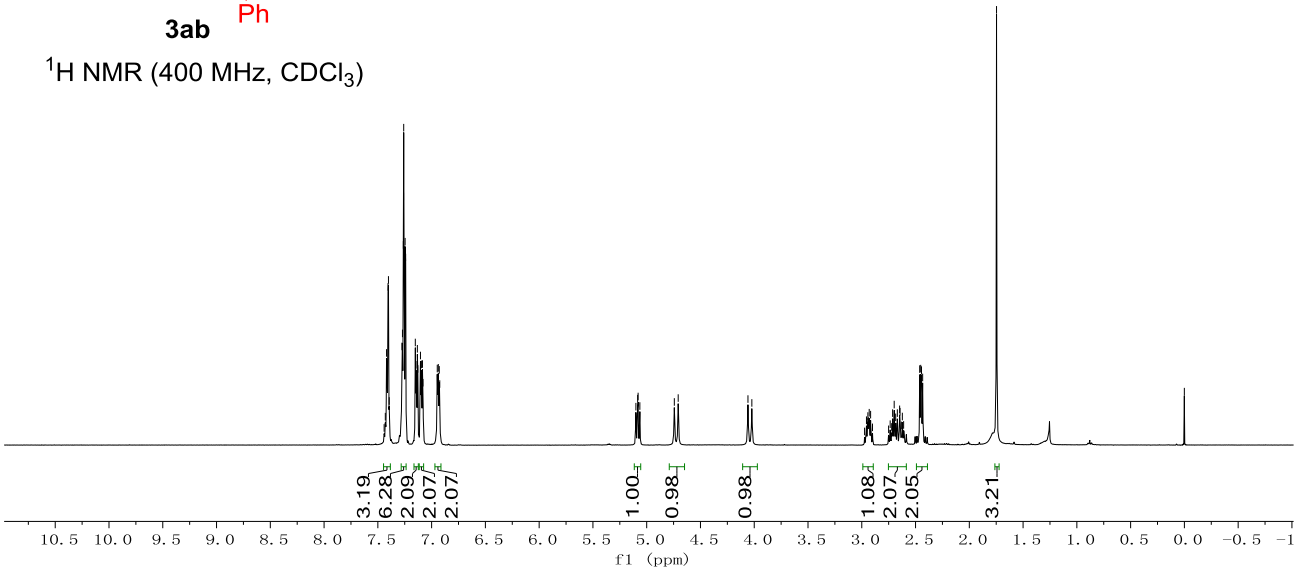
(*E*)-*N*-benzyl-*N*-(5-cyano-1,4-diphenylpent-1-en-1-yl)acetamide (**3ab**)

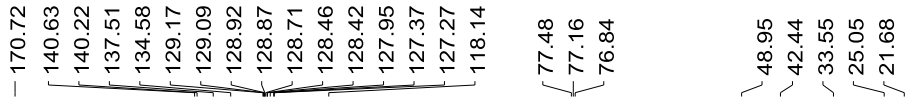


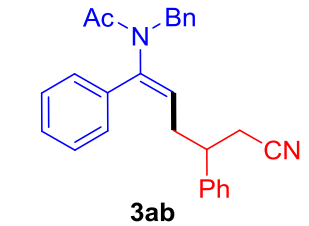


3ab

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

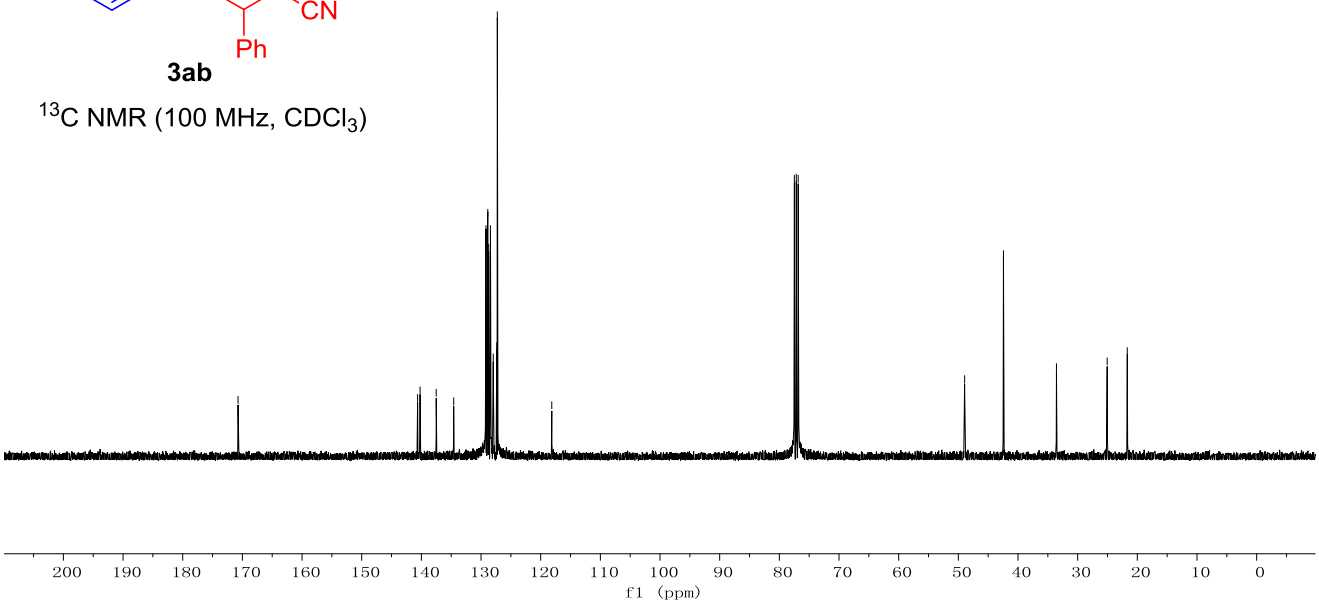




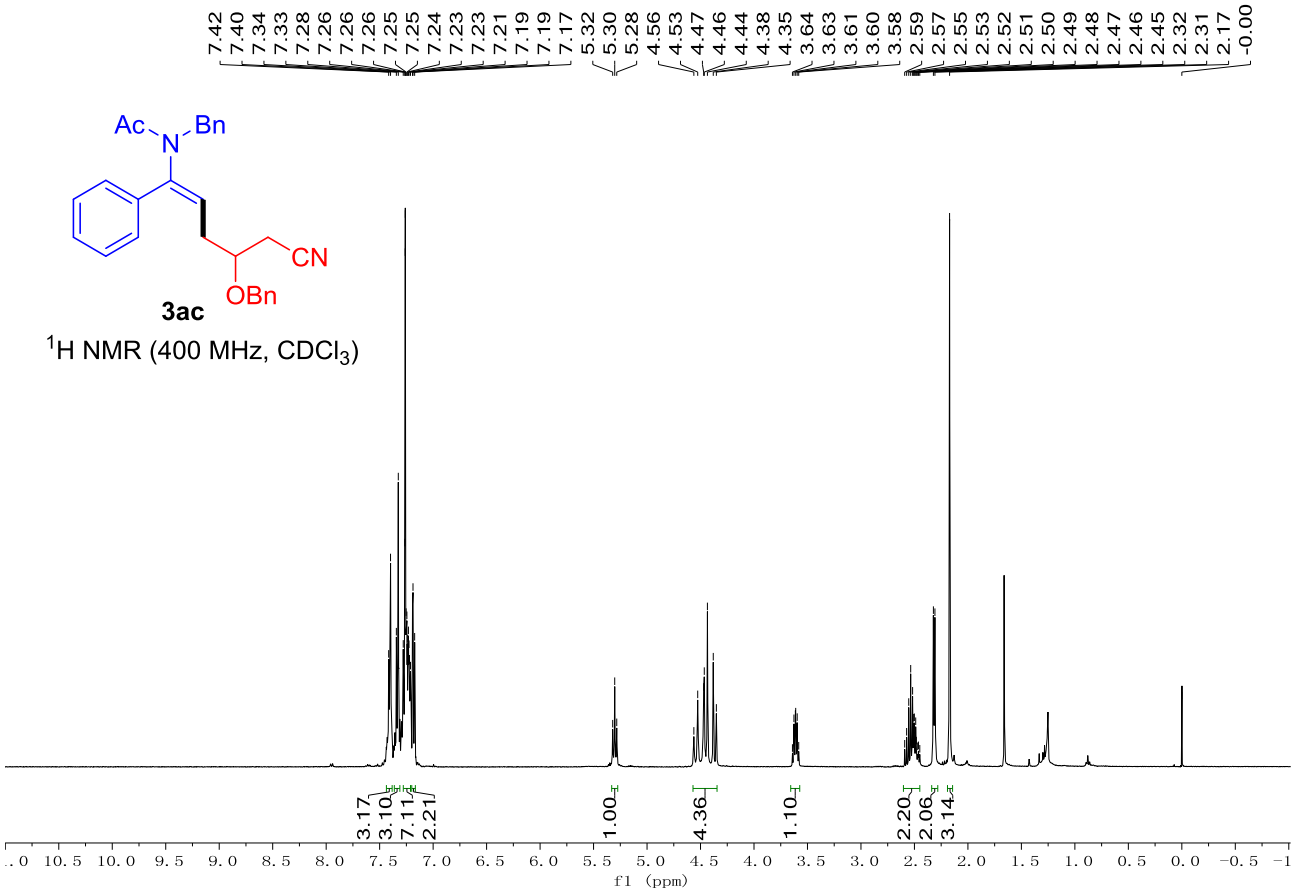


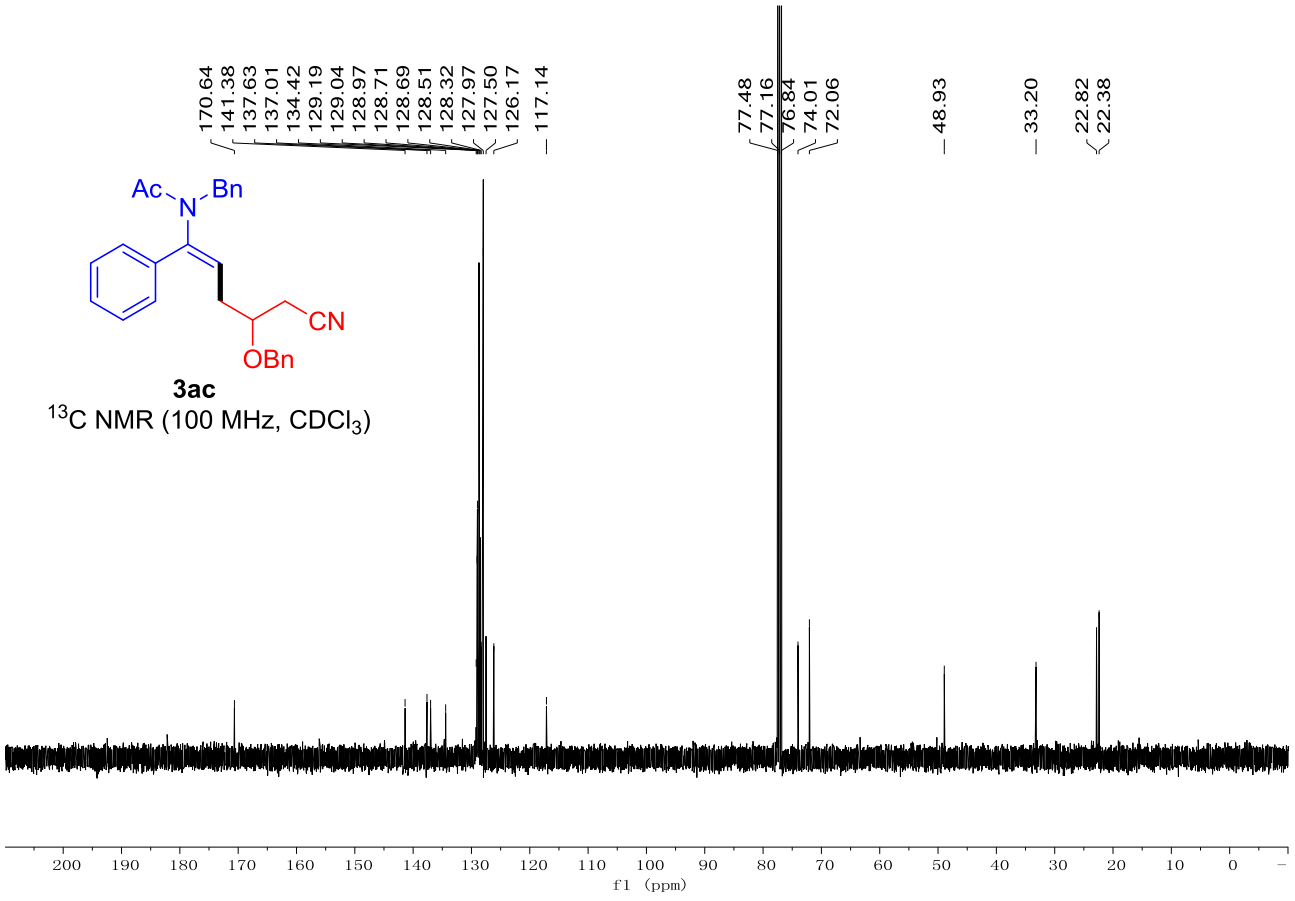
3ab

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

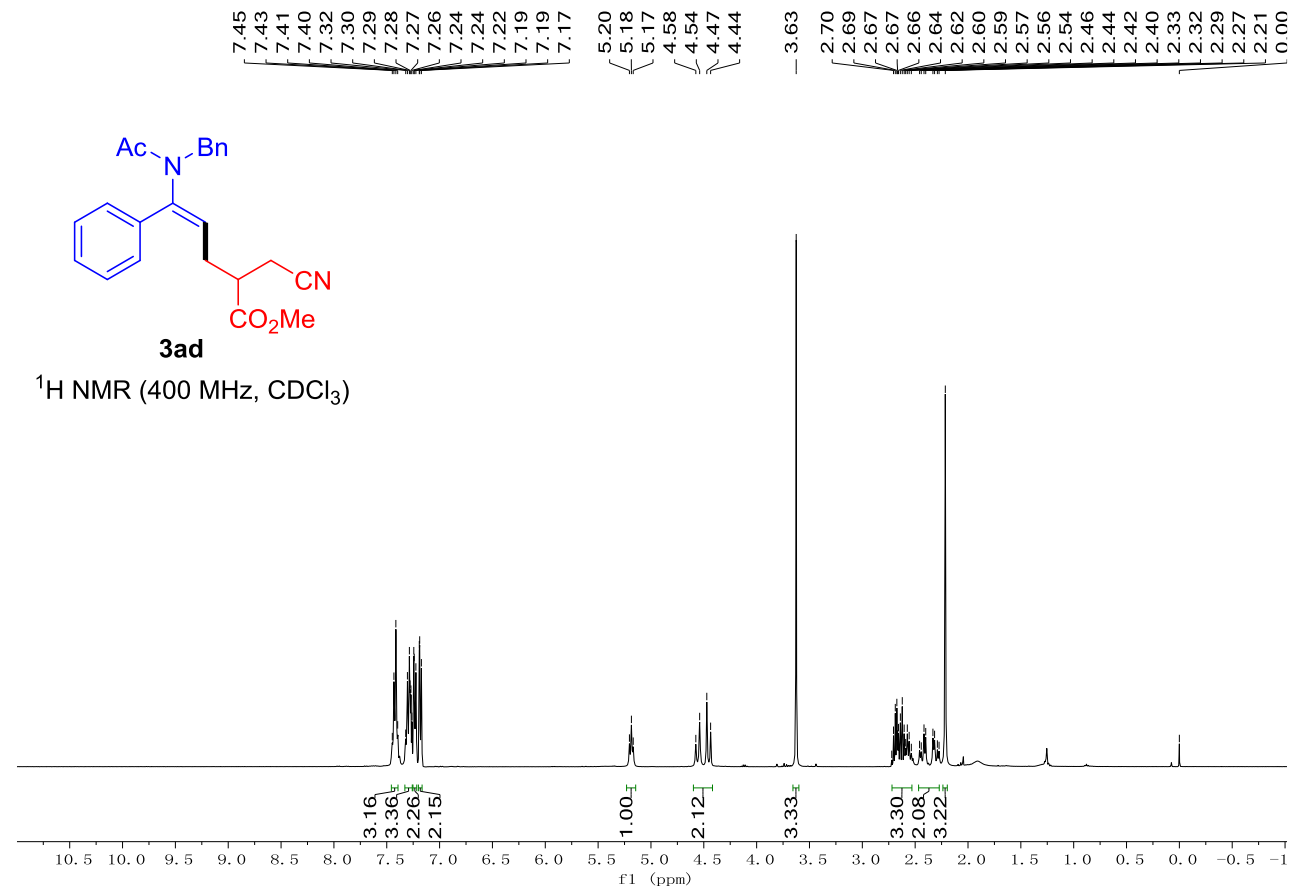


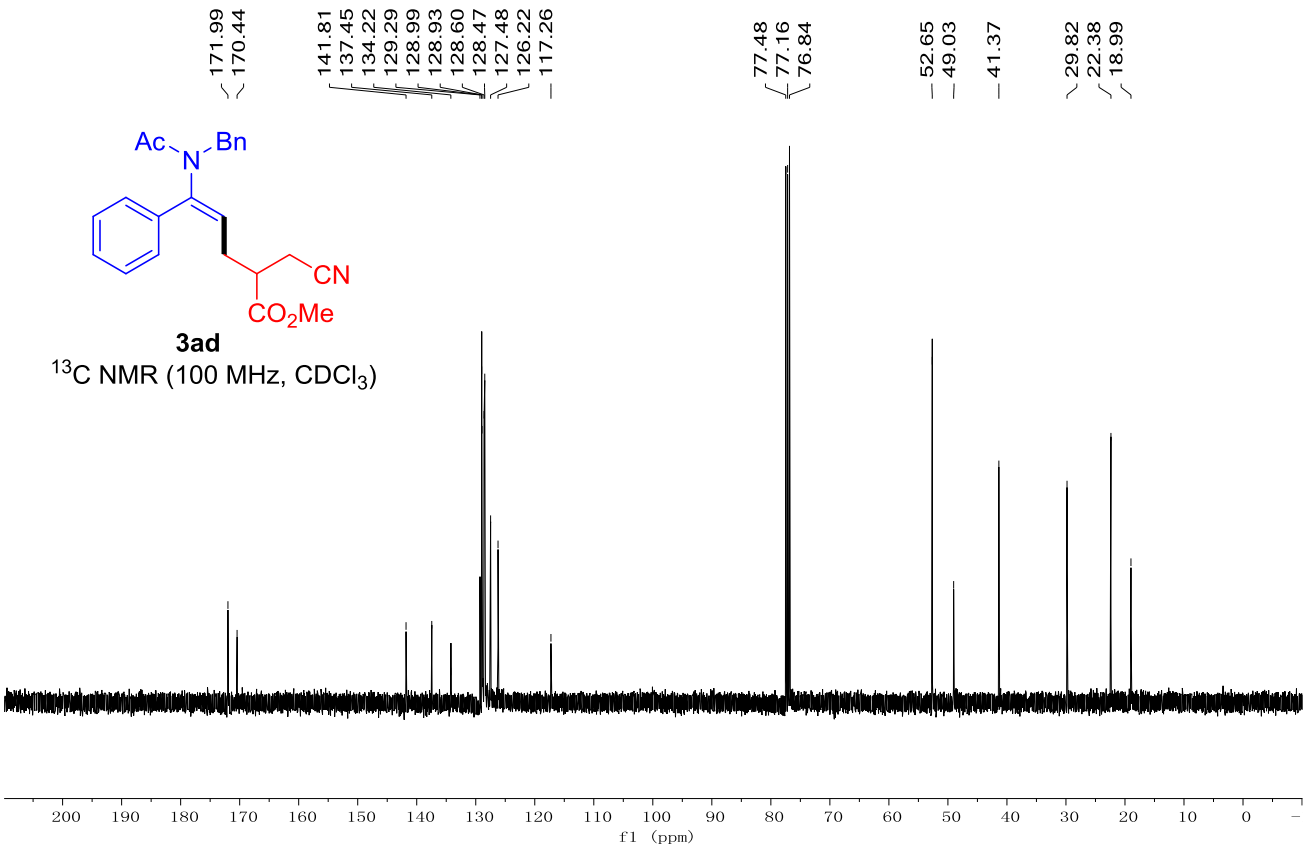
(*E*)-*N*-benzyl-*N*-(4-(benzyloxy)-5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3ac**)



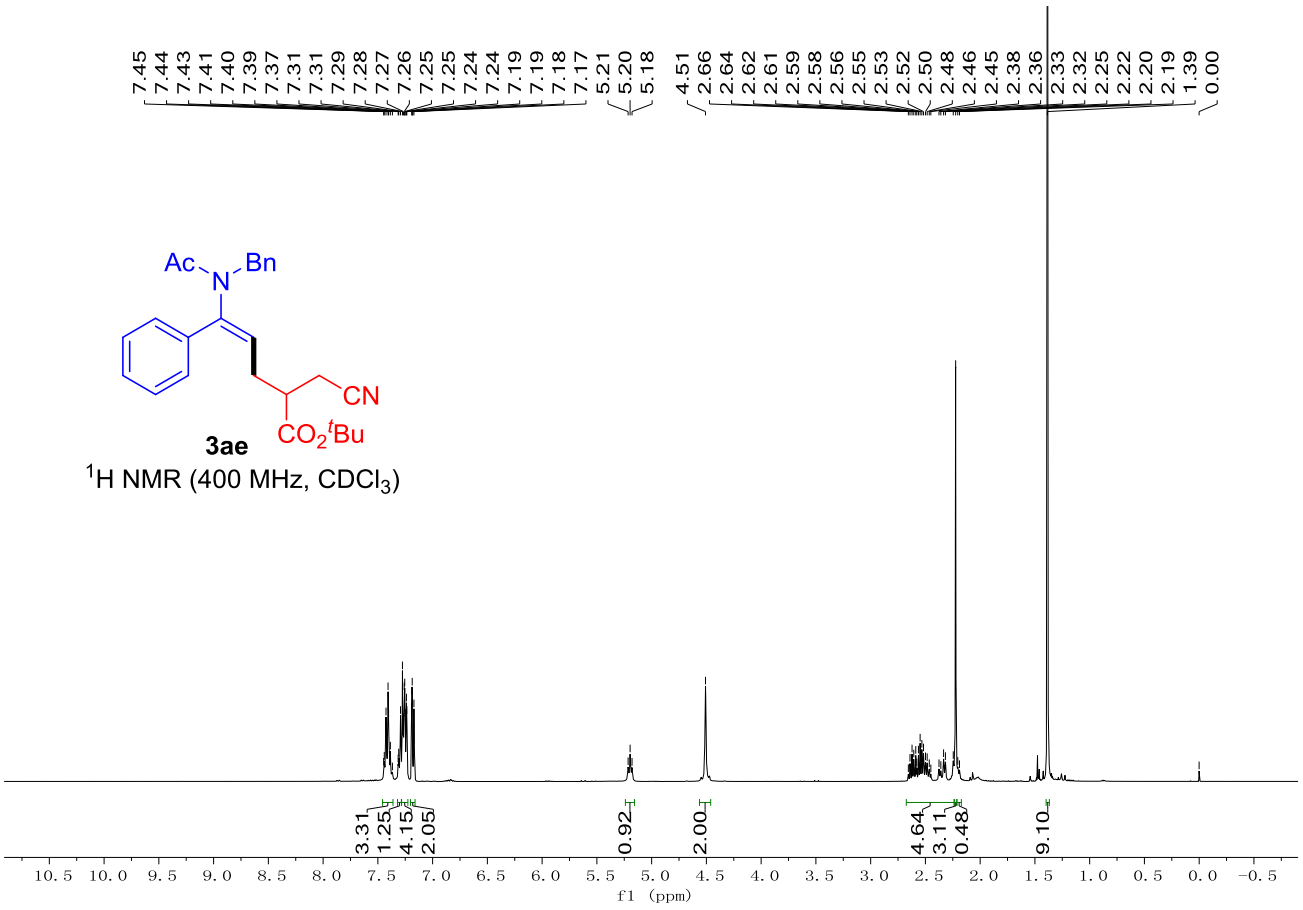


methyl (*E*)-5-(*N*-benzylacetamido)-2-(cyanomethyl)-5-phenylpent-4-enoate(**3ad**)

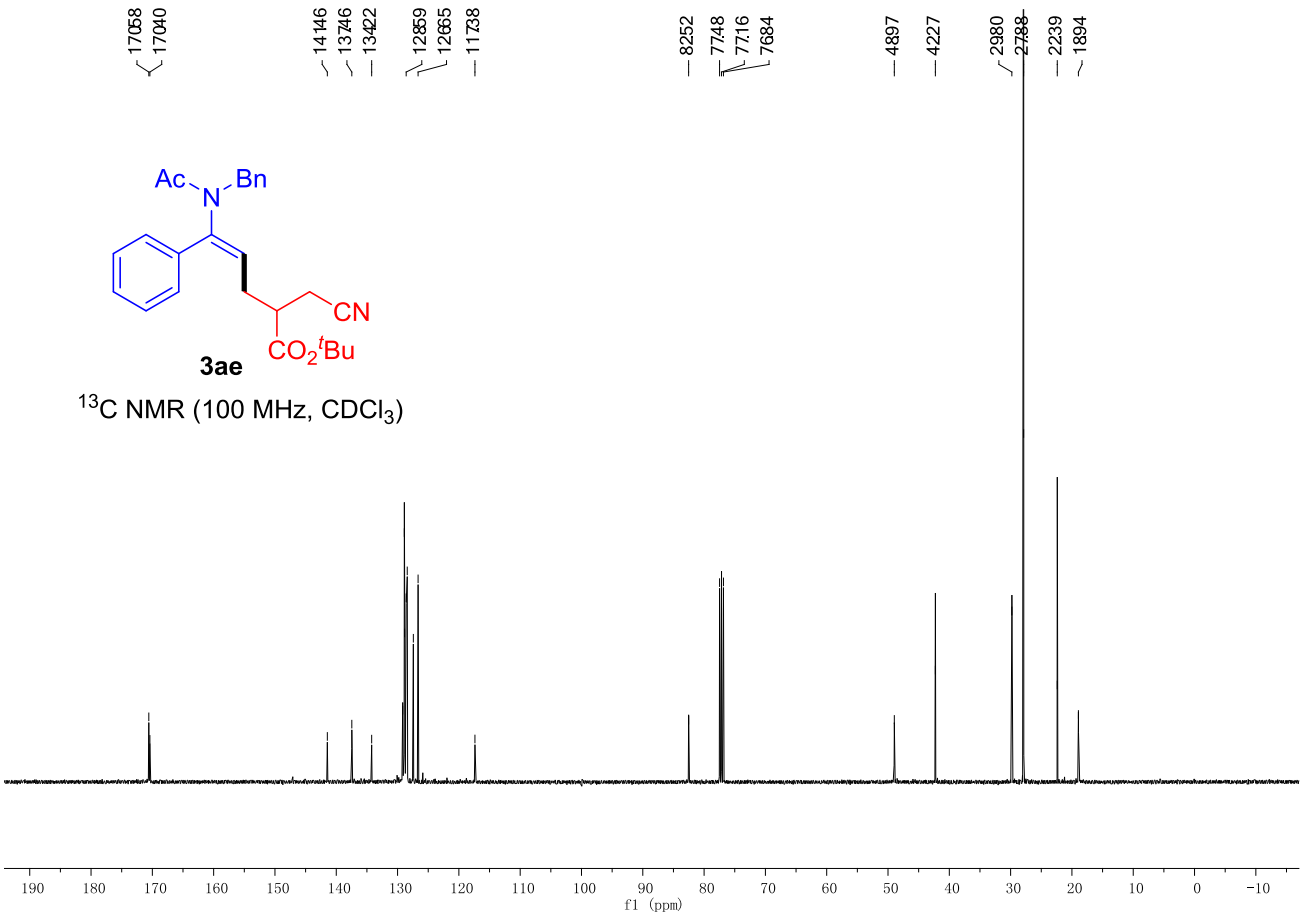




***tert*-butyl (*E*)-5-(*N*-benzylacetamido)-2-(cyanomethyl)-5-phenylpent-4-enoate (3ae)**

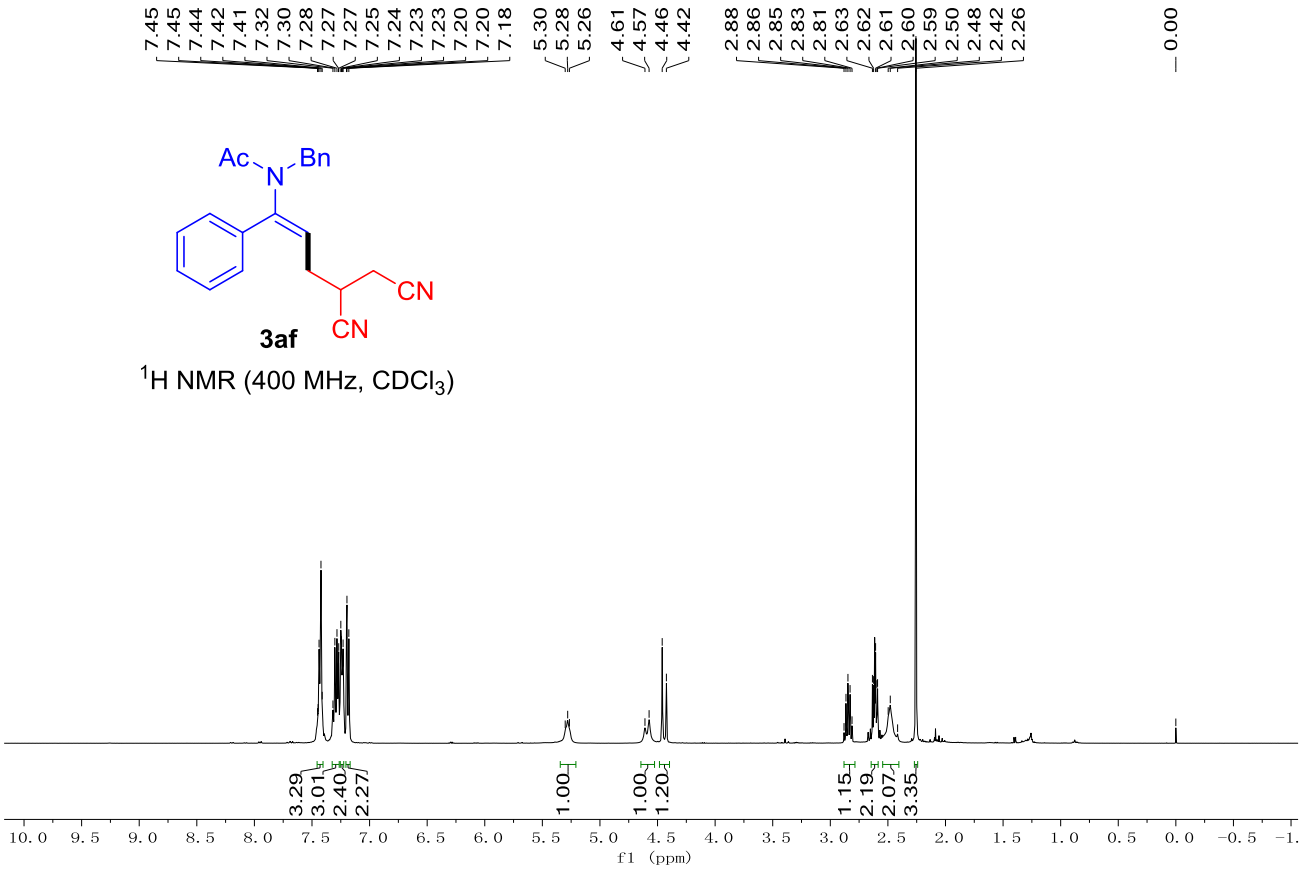


^{1}H NMR (400 MHz, $CDCl_3$)

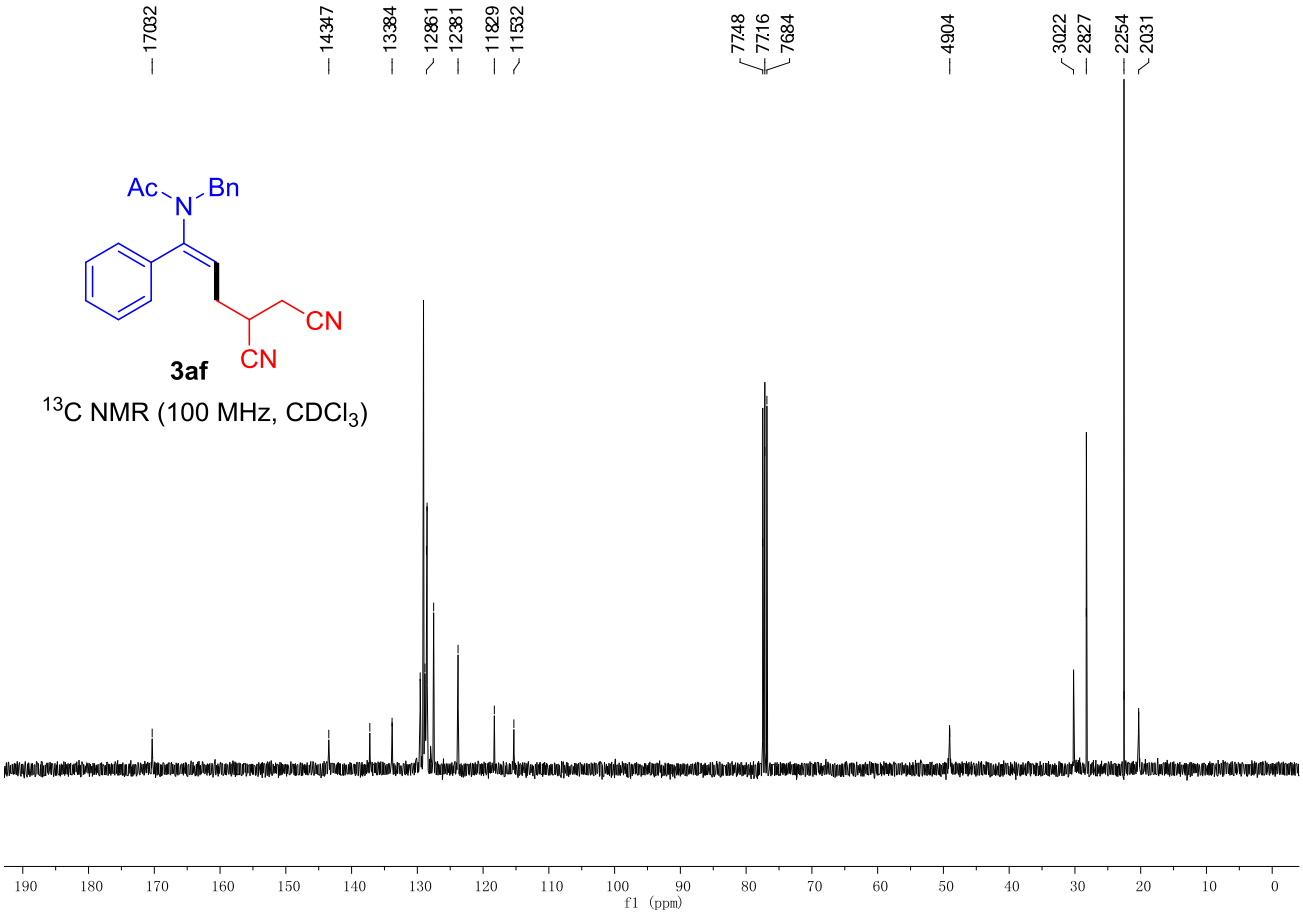


^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(4,5-dicyano-1-phenylpent-1-en-1-yl)acetamide (3af)

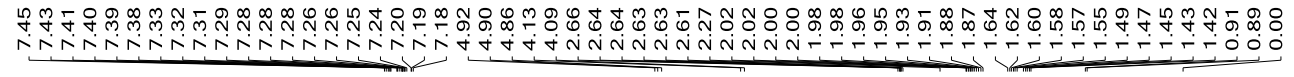


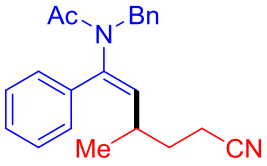
^{1}H NMR (400 MHz, $CDCl_3$)



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

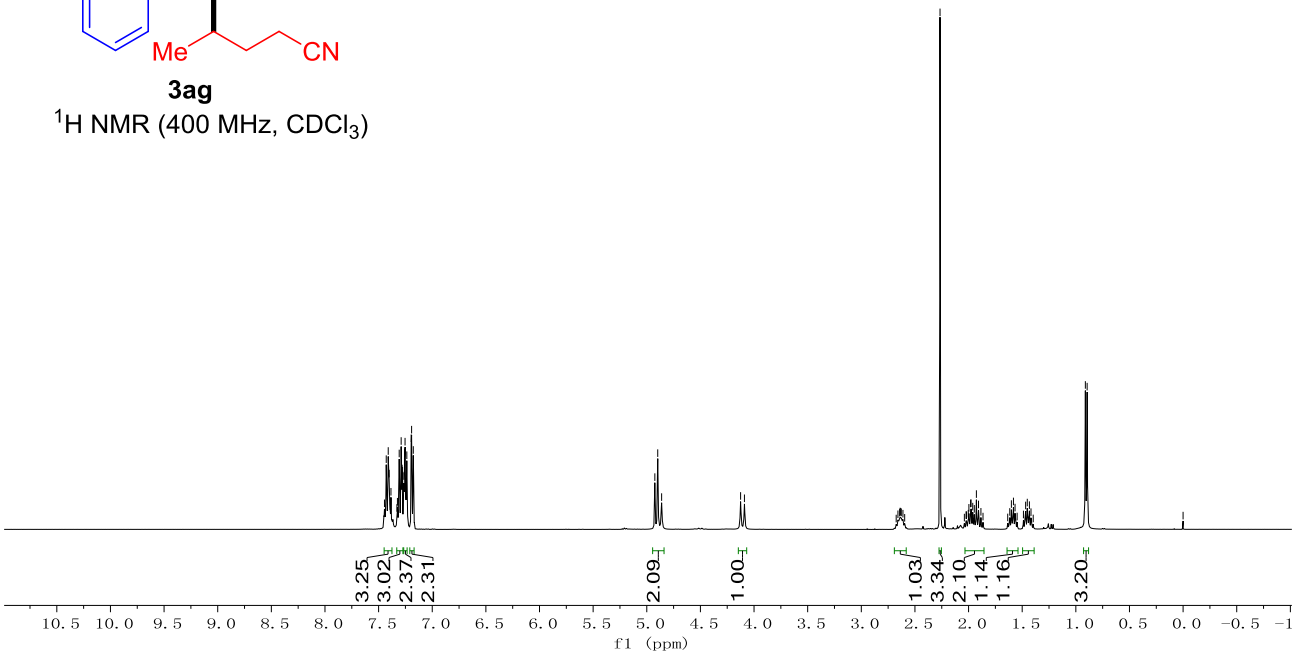
(*E*)-*N*-benzyl-*N*-(5-cyano-3-methyl-1-phenylpent-1-en-1-yl)acetamide (**3ag**)

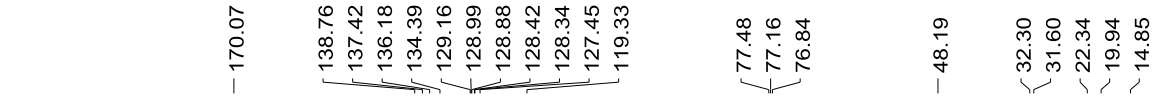


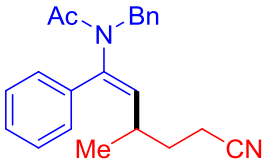


3ag

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

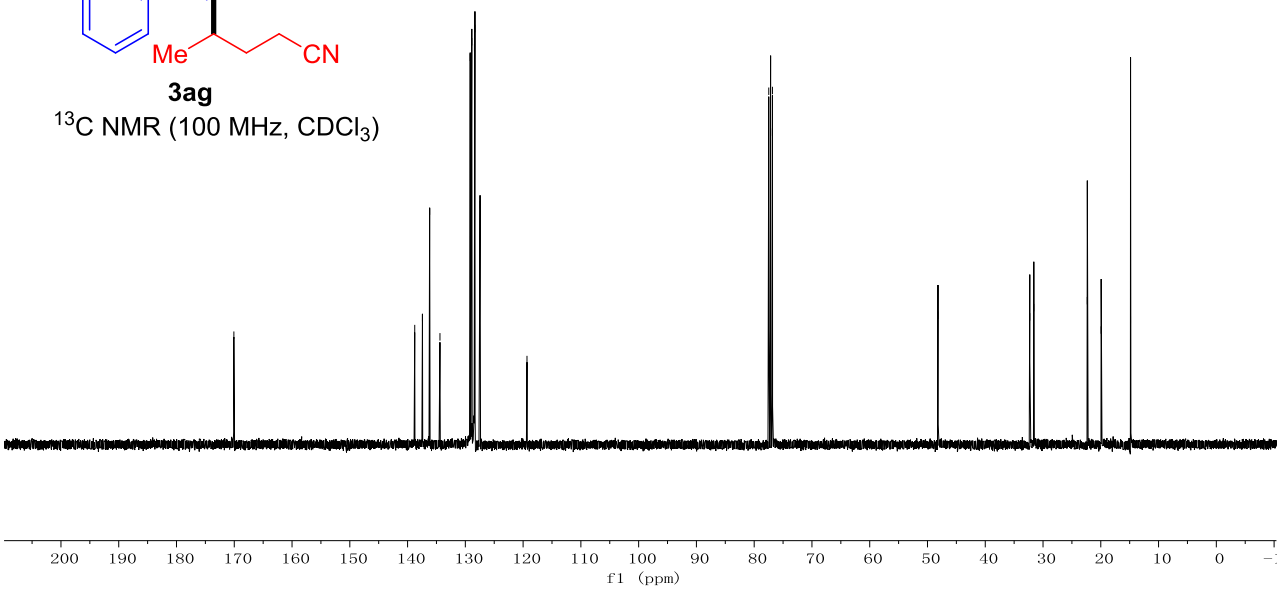




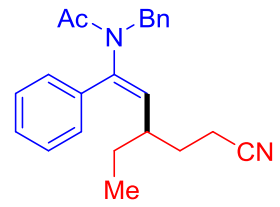


3ag

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

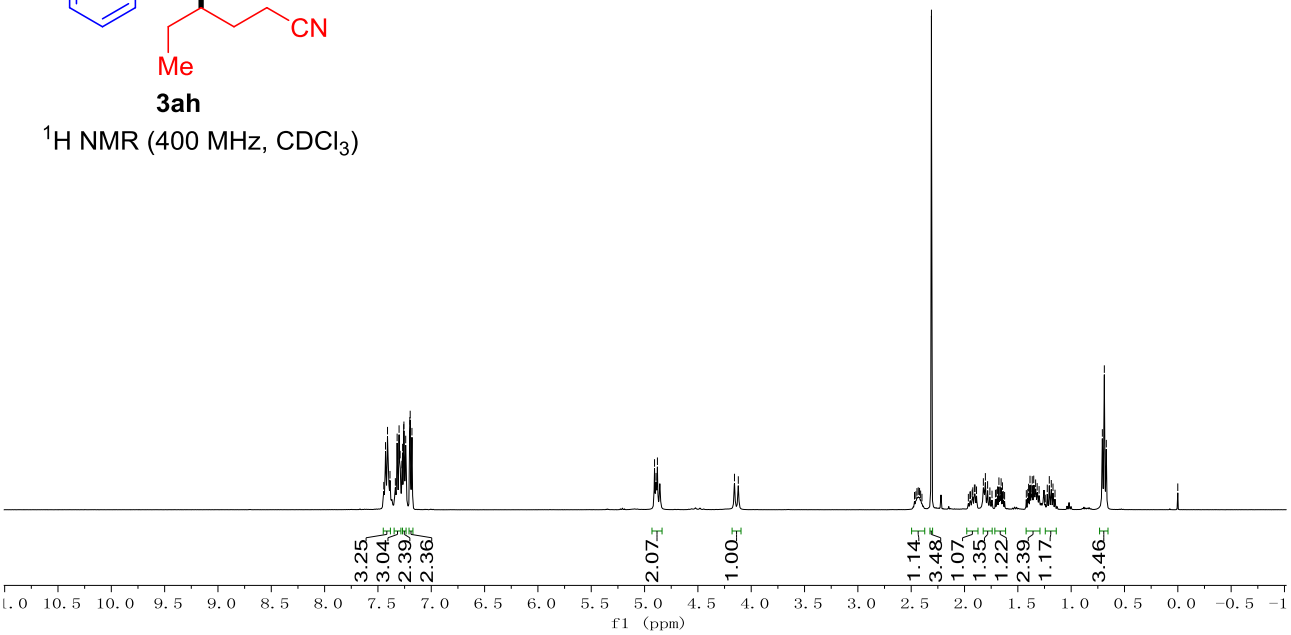


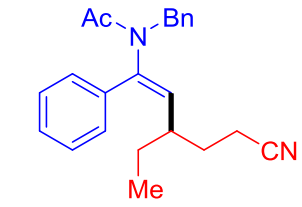
(*E*)-*N*-benzyl-*N*-(5-cyano-3-ethyl-1-phenylpent-1-en-1-yl)acetamide (**3ah**)



3ah

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

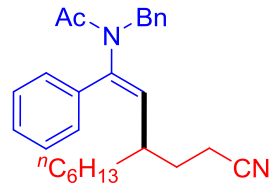




3ah

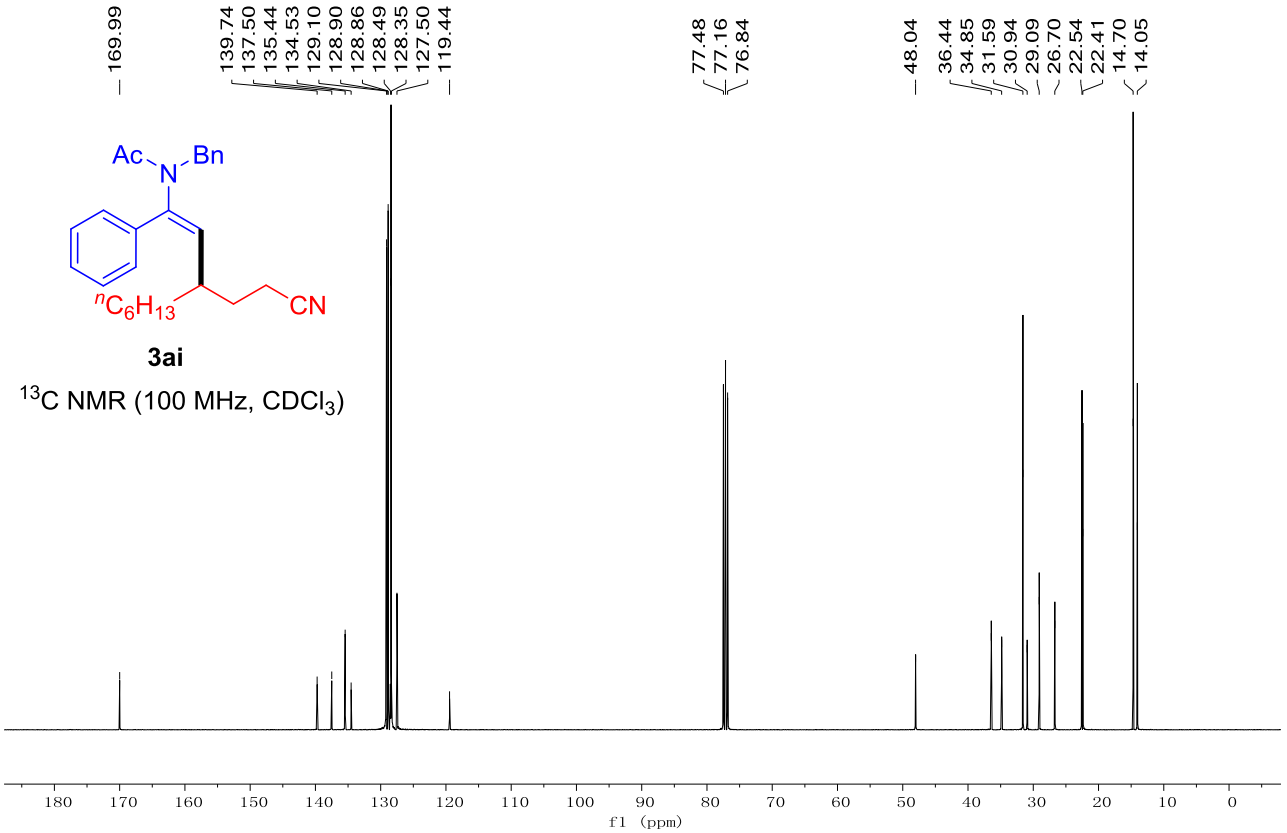
^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylnon-1-en-1-yl)acetamide (**3ai**)



3ai

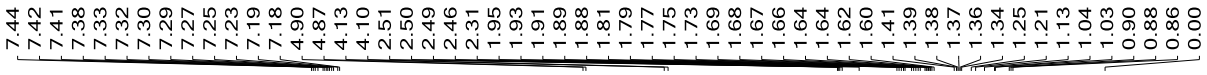
^{1}H NMR (400 MHz, $CDCl_3$)

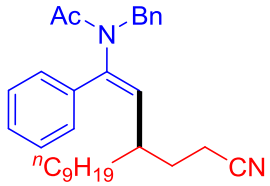


3ai

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

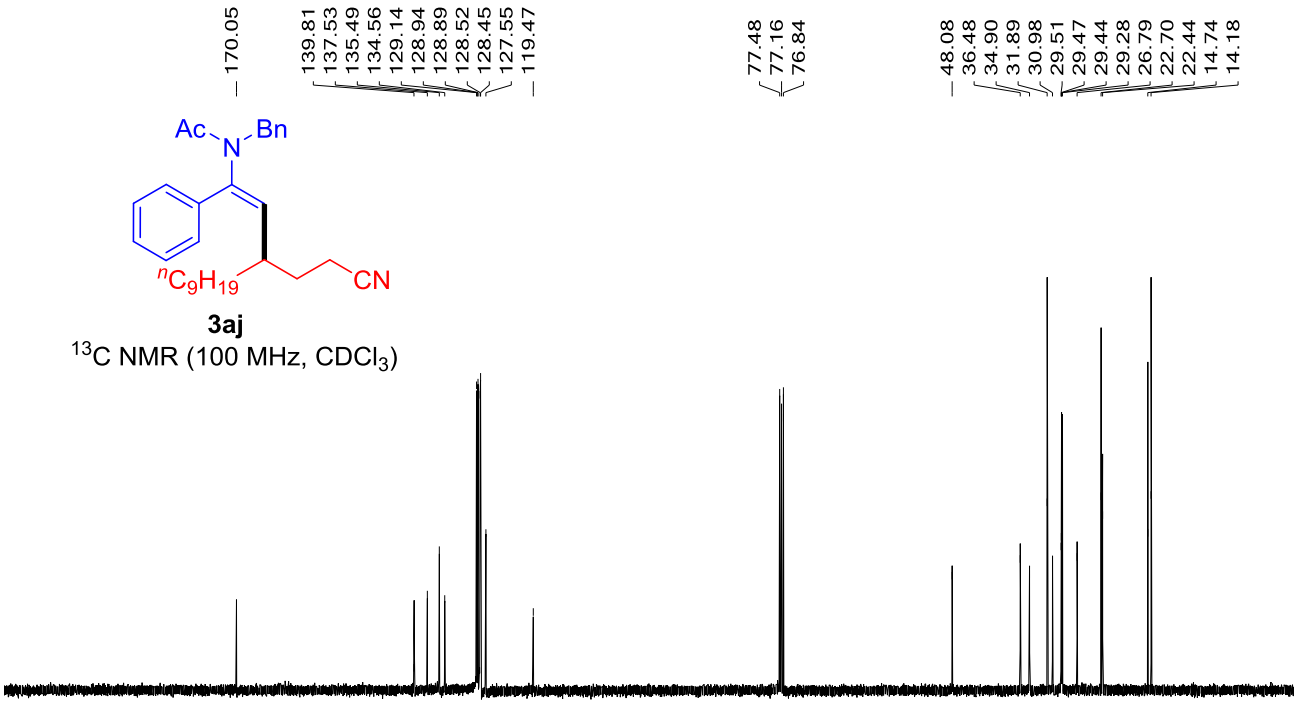
(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenyldodec-1-en-1-yl)acetamide (**3aj**)





3aj

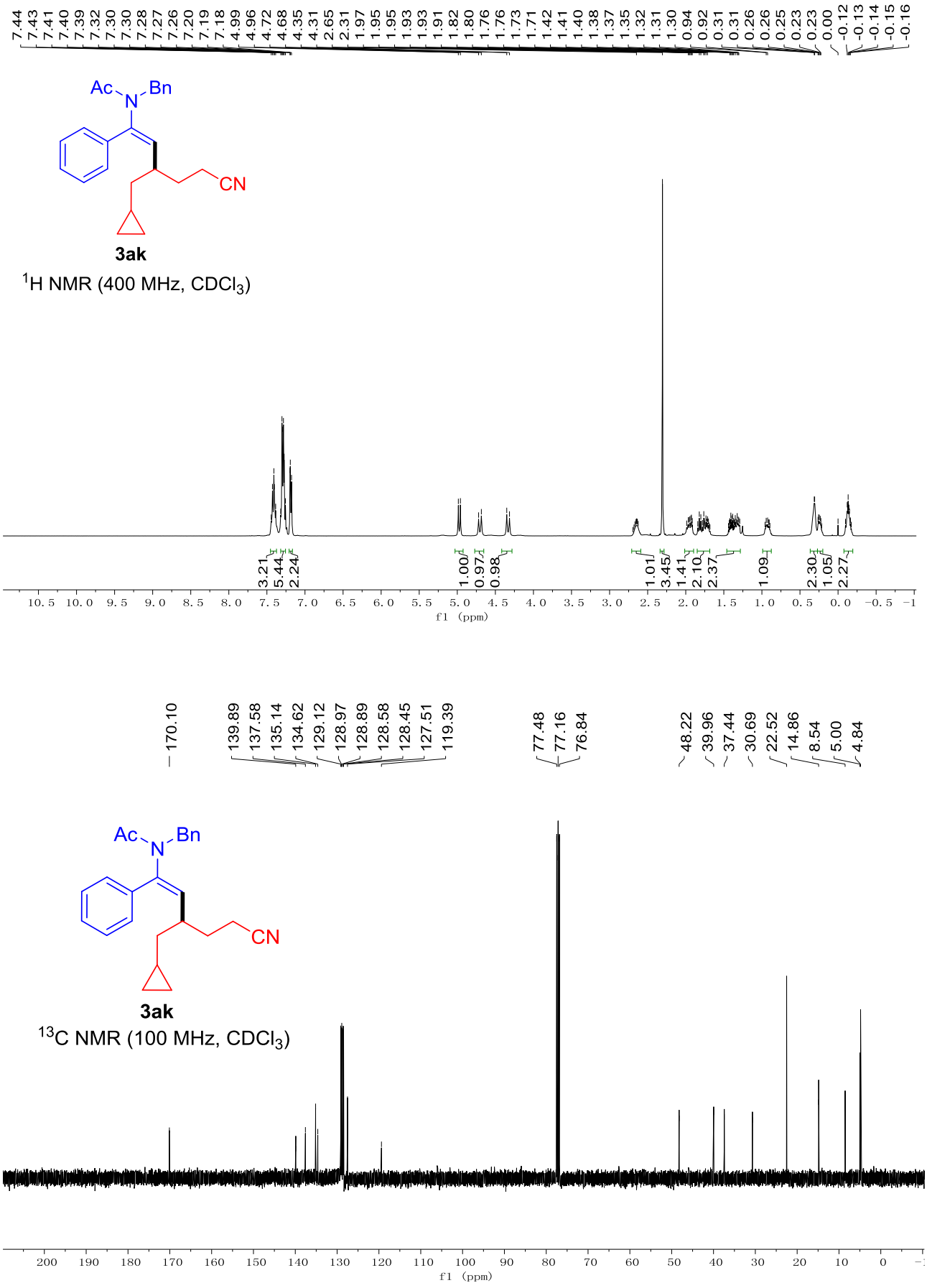
^{1}H NMR (400 MHz, $CDCl_3$)



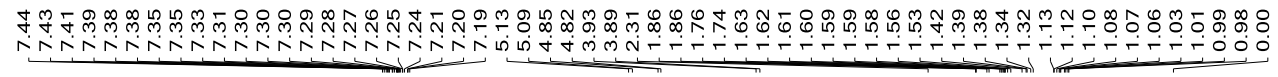
3aj

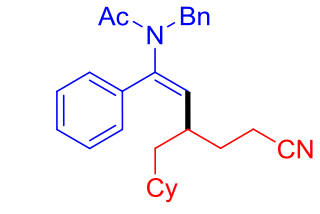
^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(5-cyano-3-(cyclopropylmethyl)-1-phenylpent-1-en-1-yl)acetamide (**3ak**)



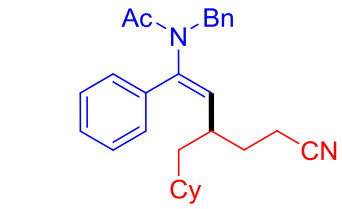
(*E*)-*N*-benzyl-*N*-(5-cyano-3-(cyclohexylmethyl)-1-phenylpent-1-en-1-yl)acetamide (**3al**)





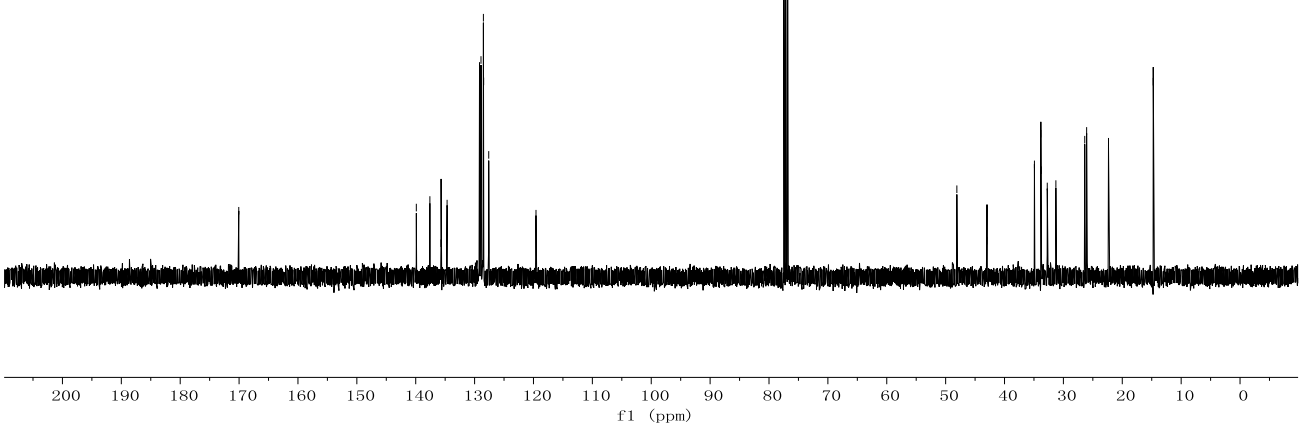
3al

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

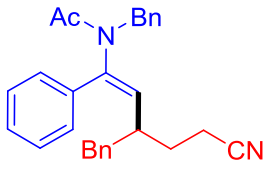


3al

^{13}C NMR (400 MHz, $CDCl_3$)

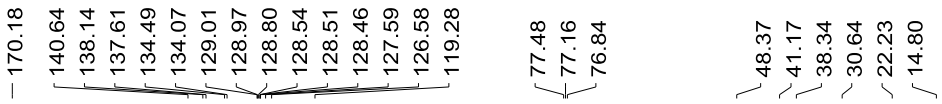


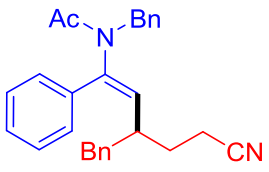
(*E*)-*N*-benzyl-*N*-(3-benzyl-5-cyano-1-phenylpent-1-en-1-yl)acetamide (**3am**)



3am

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

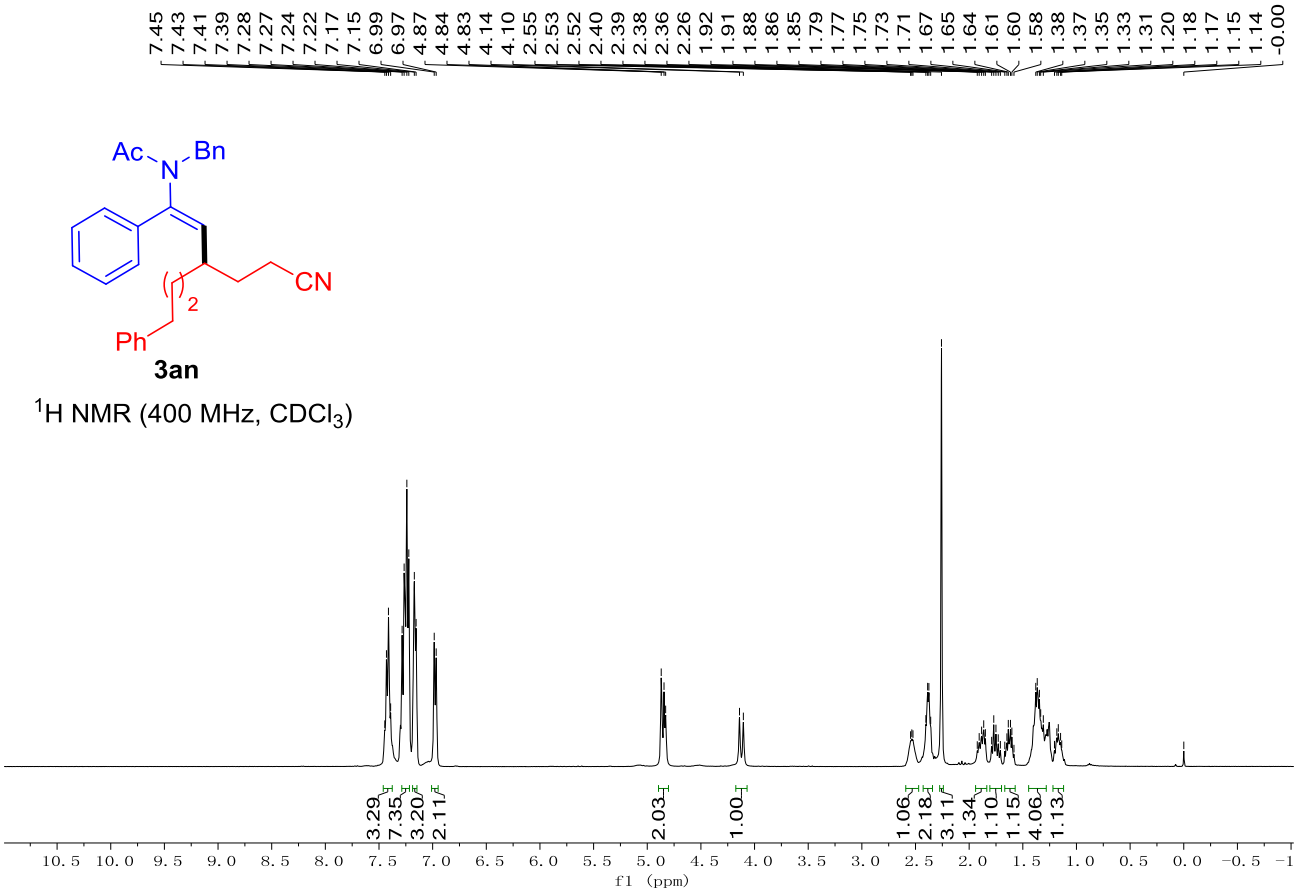


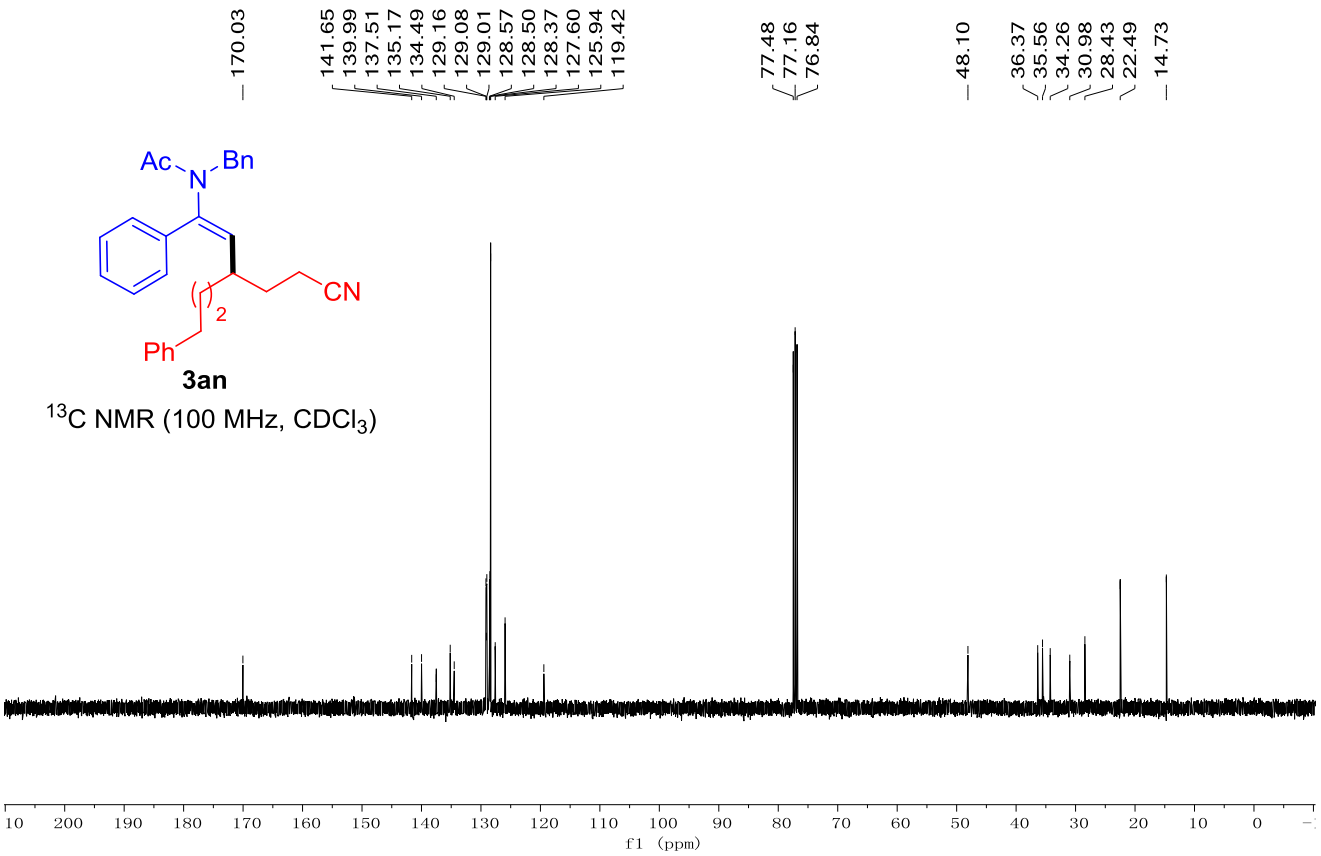


3am

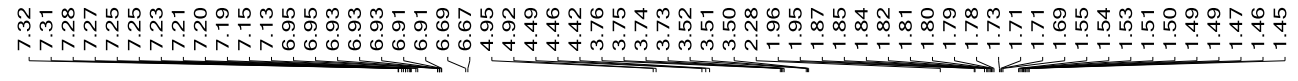
^{13}C NMR (100 MHz, $CDCl_3$)

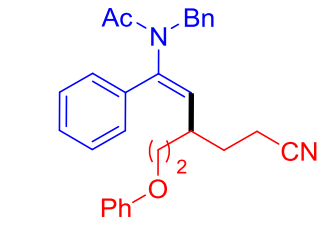
(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1,6-diphenylhex-1-en-1-yl)acetamide (**3an**)





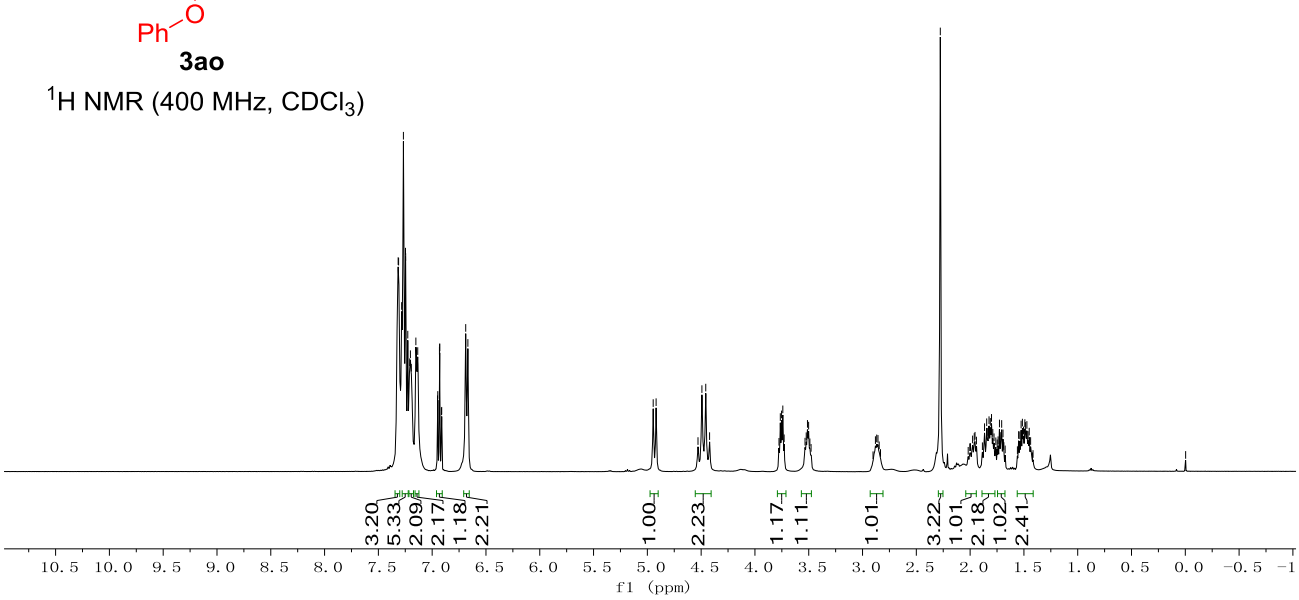
(*E*)-*N*-benzyl-*N*-(5-cyano-3-(2-phenoxyethyl)-1-phenylpent-1-en-1-yl)acetamide (**3ao**)

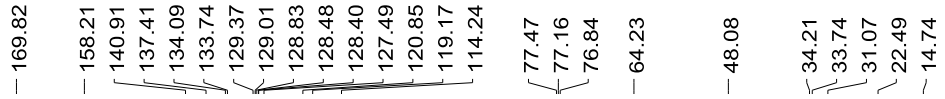


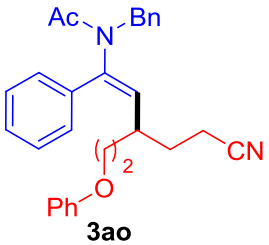


3ao

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



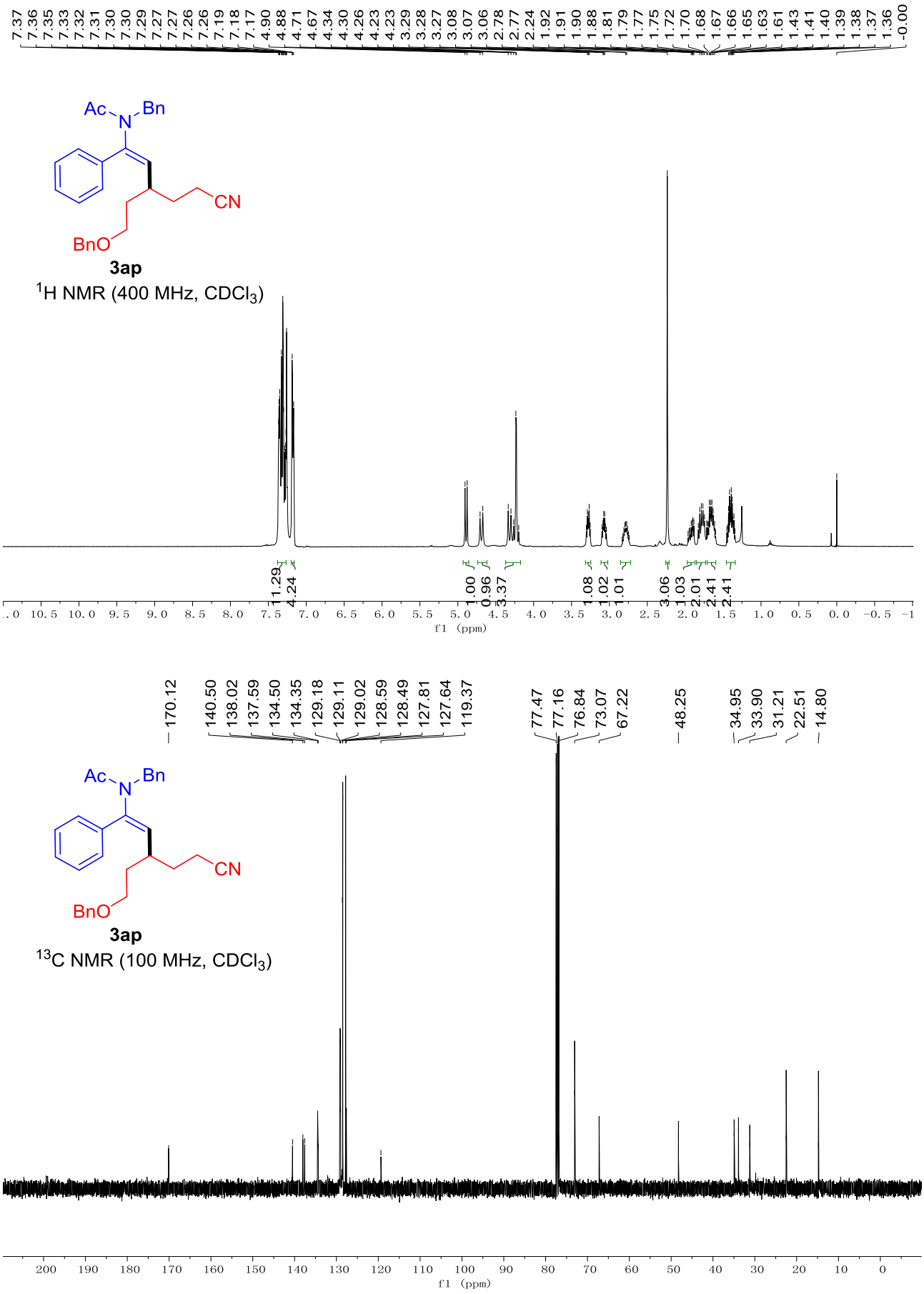




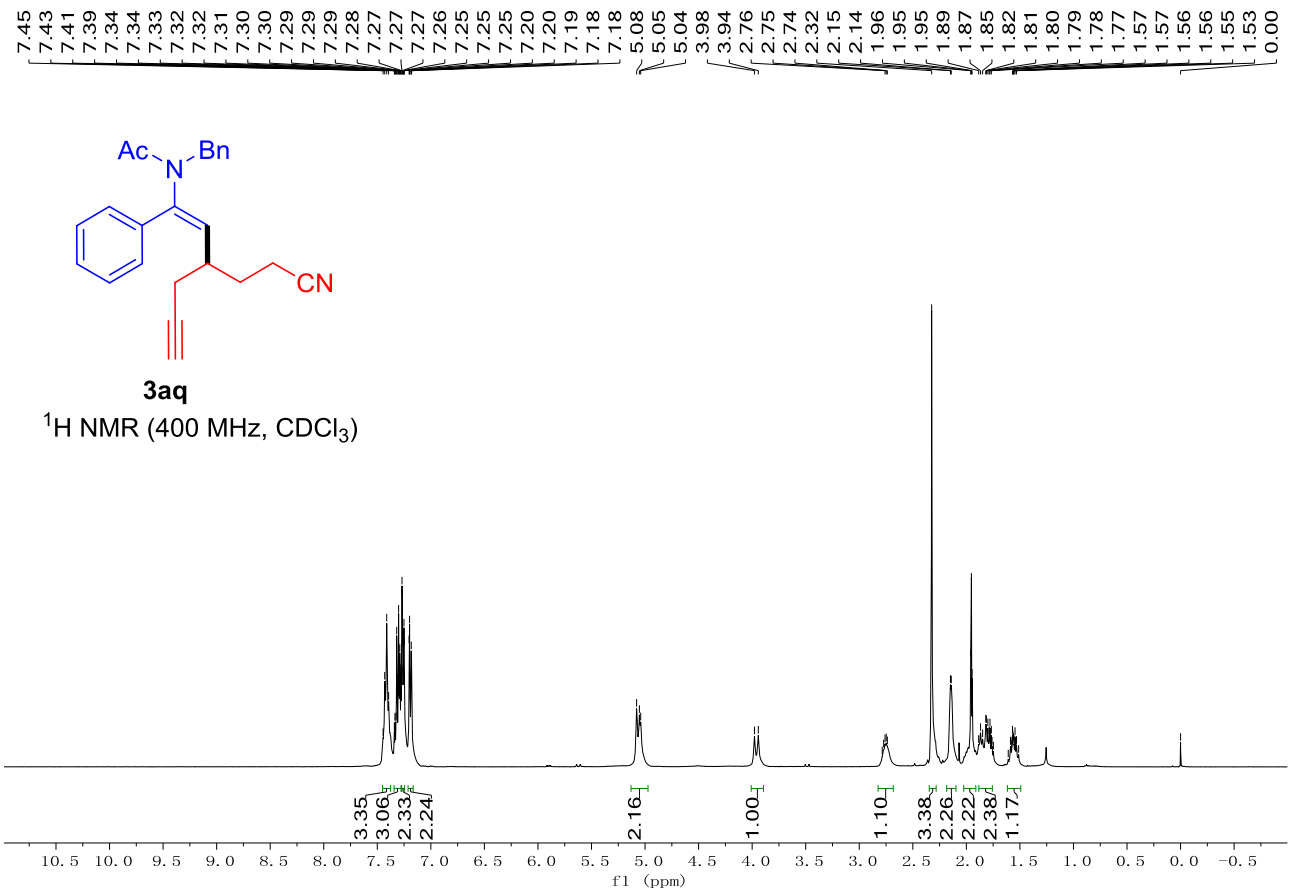
3ao

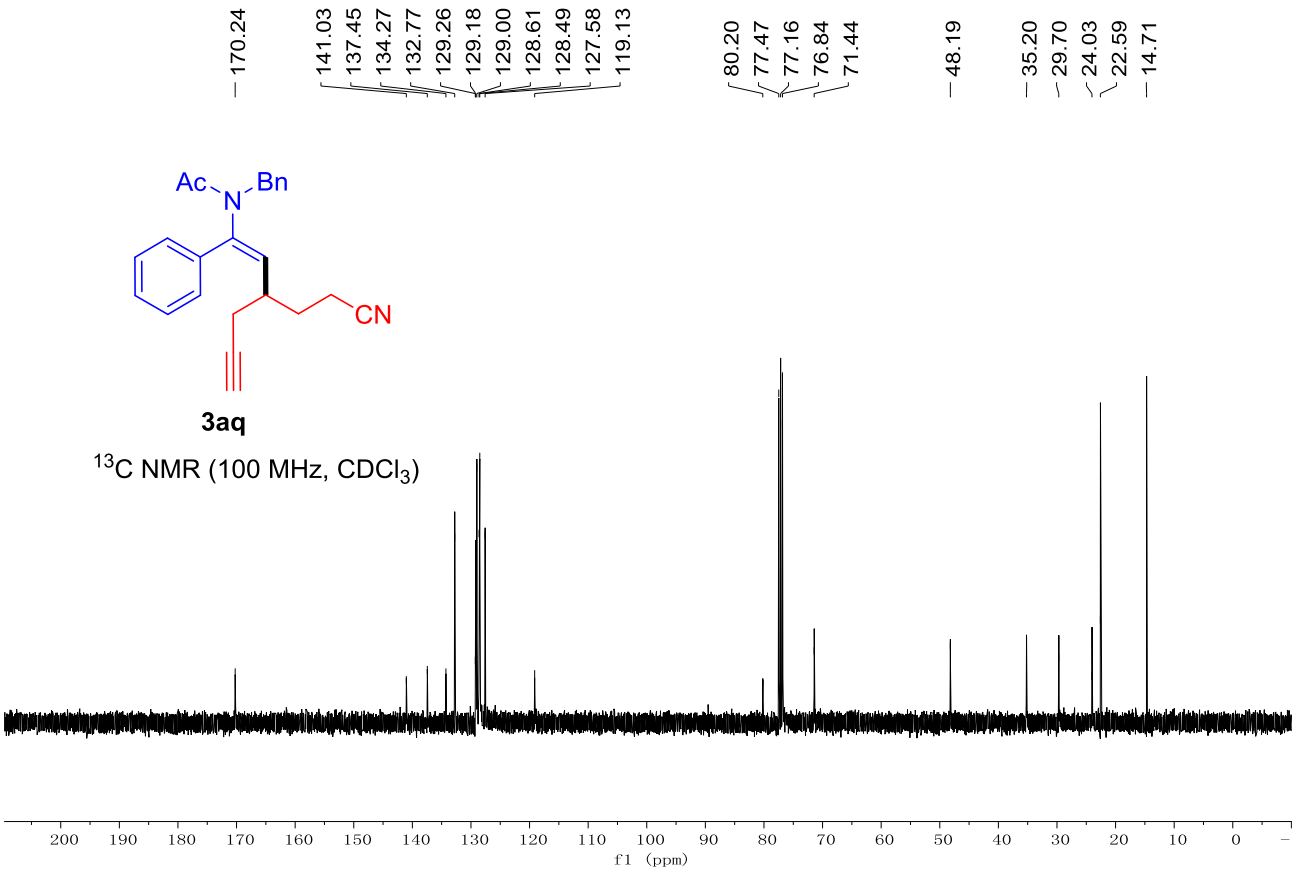
^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(5-(benzyloxy)-3-(2-cyanoethyl)-1-phenylpent-1-en-1-yl)acetamide (**3ap**)

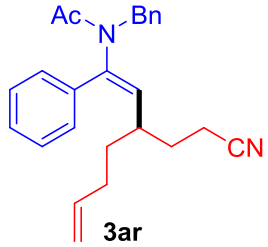


(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylhex-1-en-5-yn-1-yl)acetamide (**3aq**)



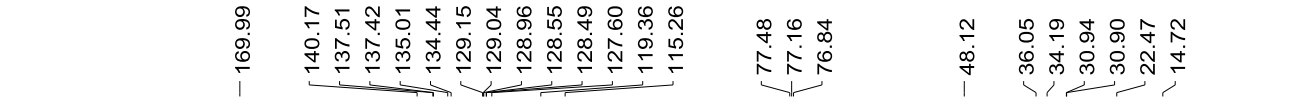


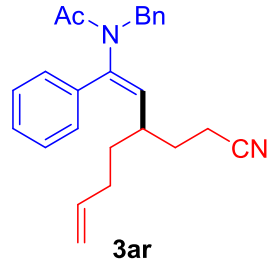
(*E*)-*N*-benzyl-*N*-(3-(2-cyanoethyl)-1-phenylhepta-1,6-dien-1-yl)acetamide (**3ar**)



3ar

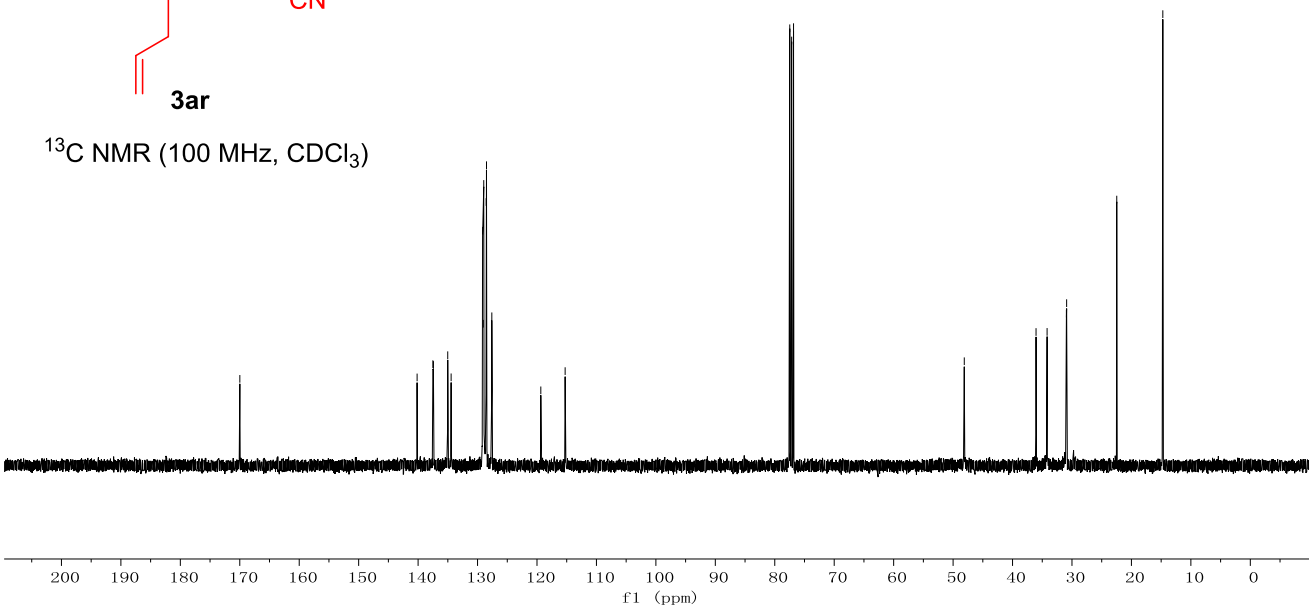
^{1}H NMR (400 MHz, $CDCl_3$)



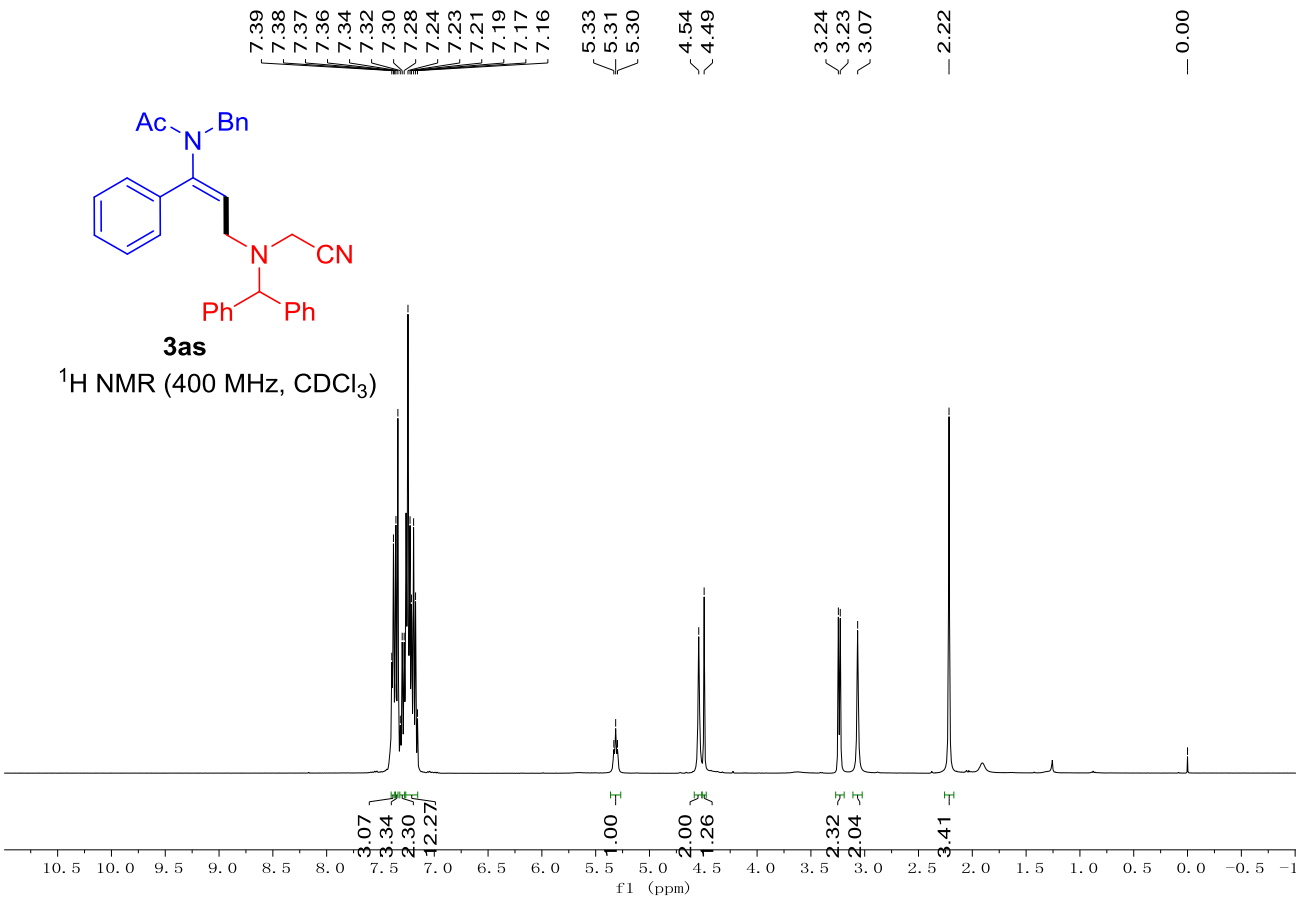


3ar

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

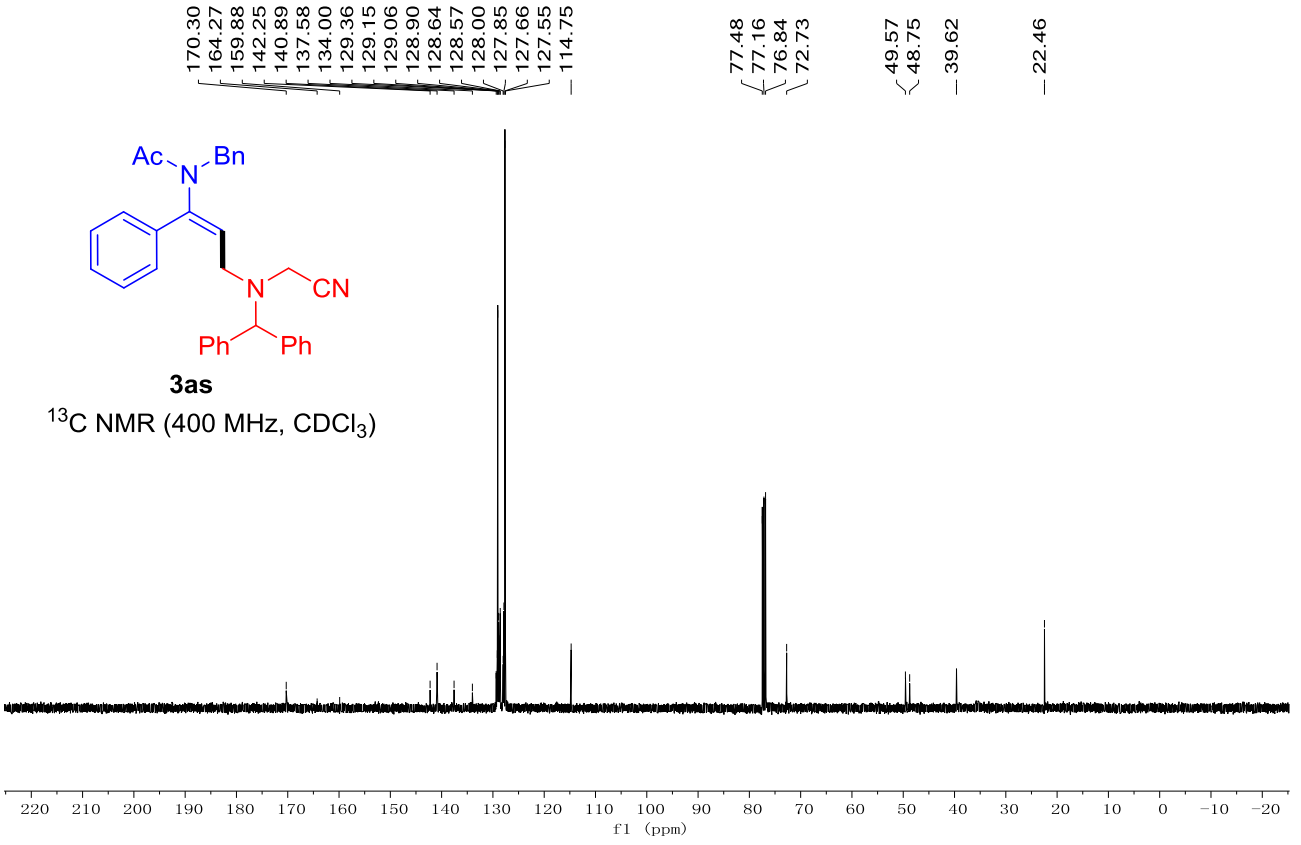


(*E*)-*N*-(3-(benzhydryl(cyanomethyl)amino)-1-phenylprop-1-en-1-yl)-*N*- benzylacetamide (**3as**)



3as

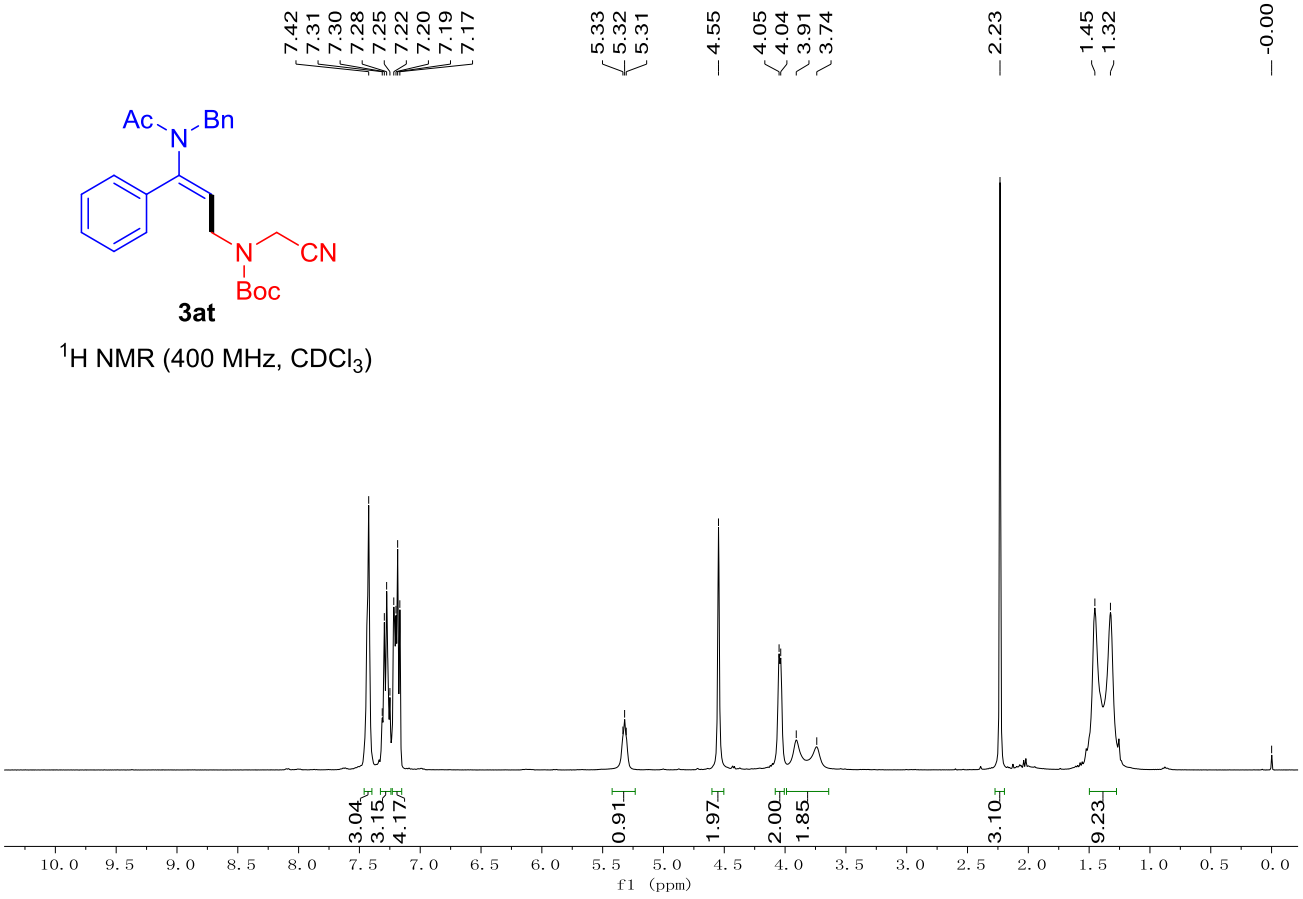
^{1}H NMR (400 MHz, $CDCl_3$)



3as

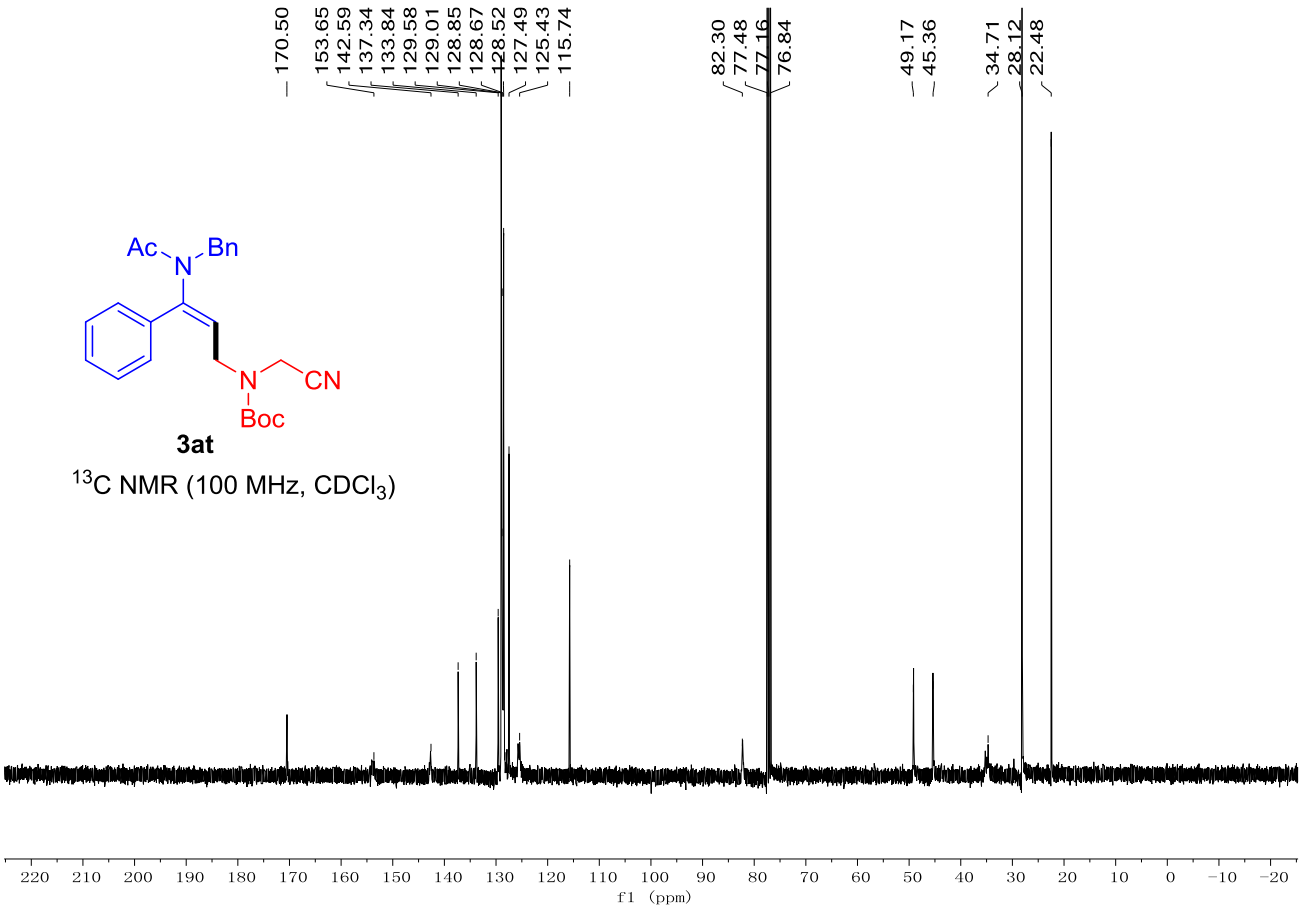
^{13}C NMR (400 MHz, $CDCl_3$)

tert-butyl (*E*)-(3-(*N*-benzylacetamido)-3-phenylallyl)(cyanomethyl)carbamate (**3at**)



3at

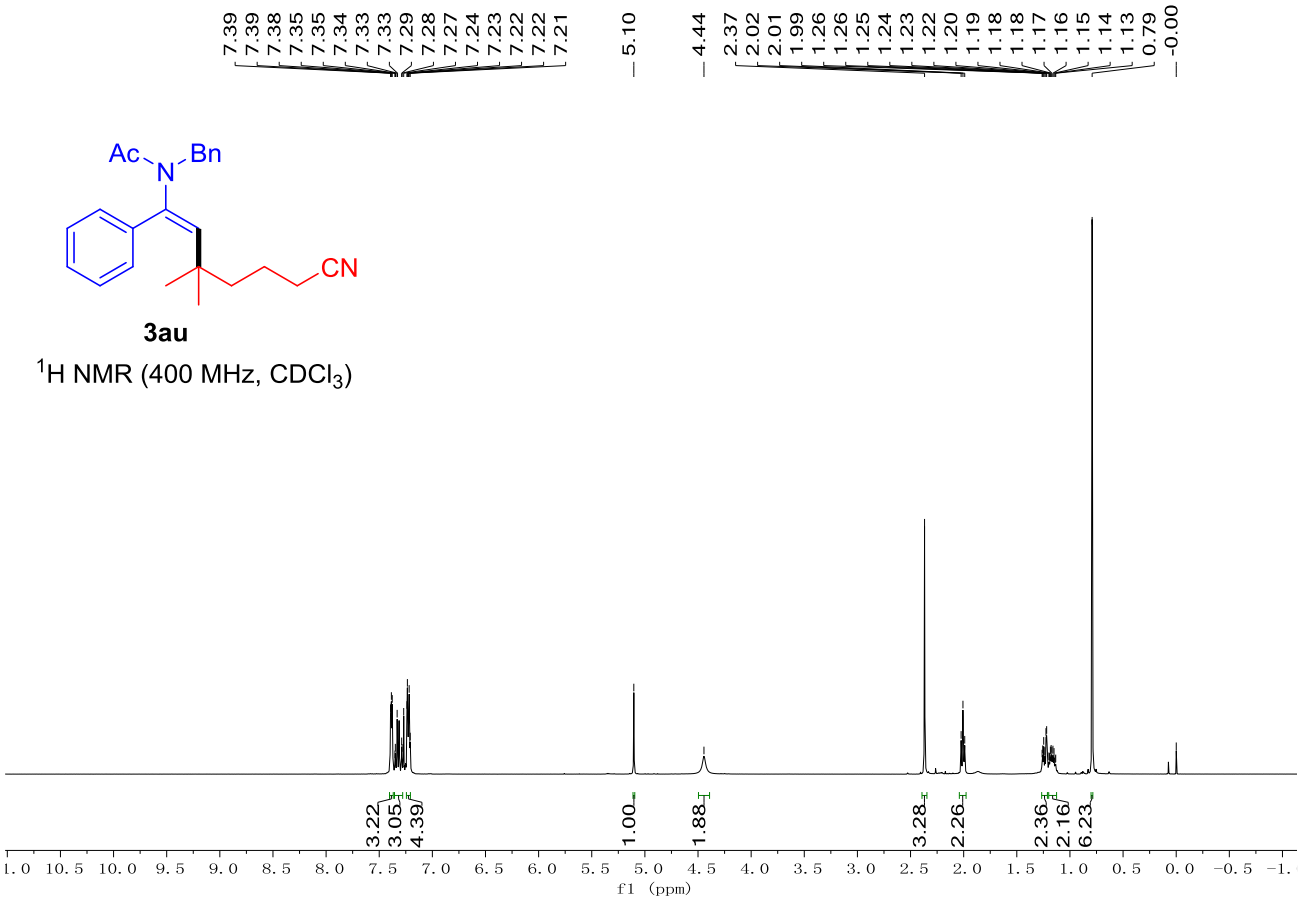
^{1}H NMR (400 MHz, $CDCl_3$)



3at

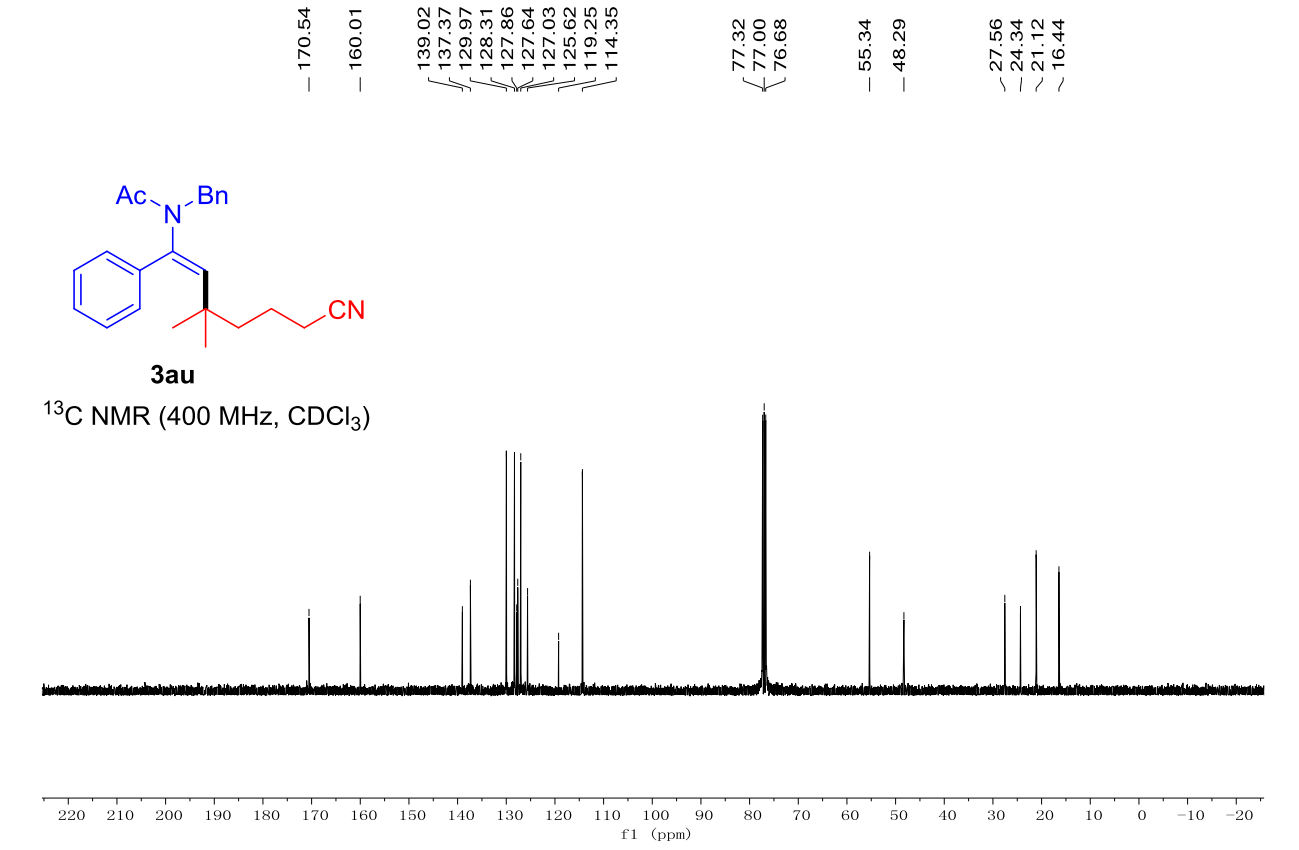
^{13}C NMR (100 MHz, $CDCl_3$)

(*E*)-*N*-benzyl-*N*-(6-cyano-3,3-dimethyl-1-phenylhex-1-en-1-yl)acetamide (**3au**)



3au

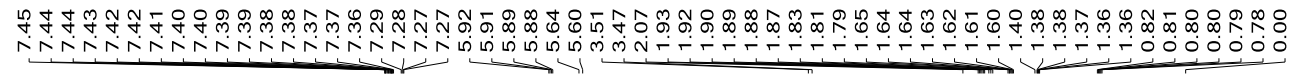
^{1}H NMR (400 MHz, $CDCl_3$)

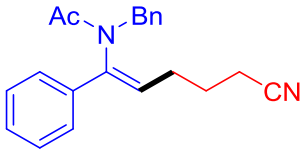


3au

^{13}C NMR (400 MHz, $CDCl_3$)

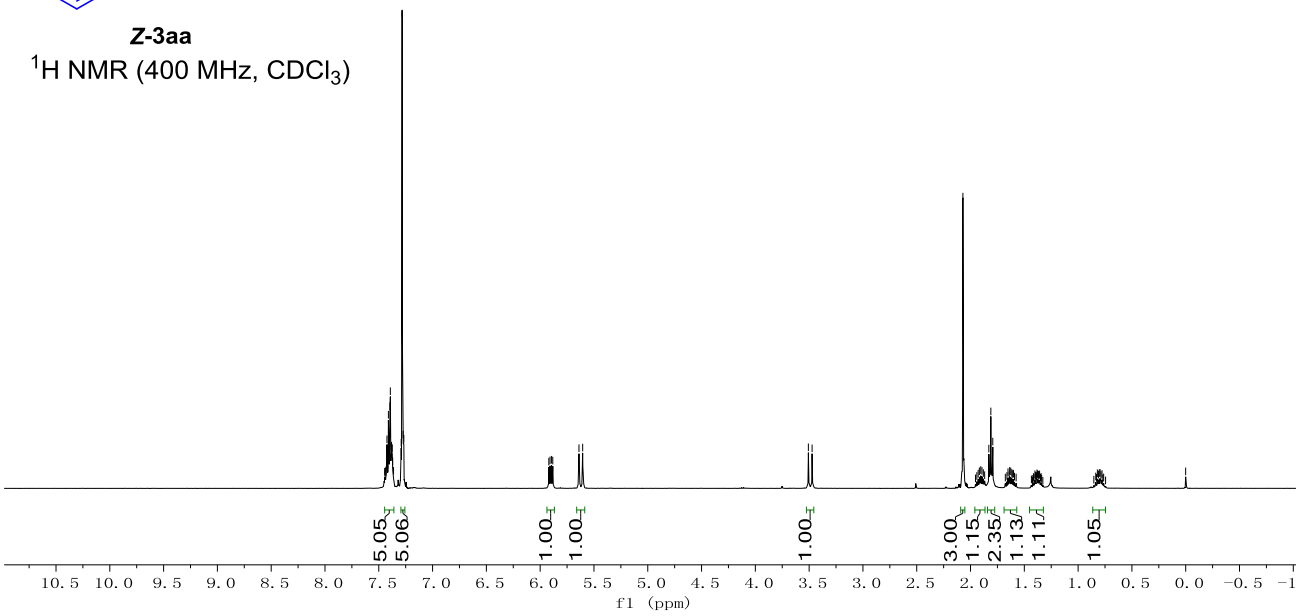
(*Z*)-*N*-benzyl-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (***Z*-3aa**)

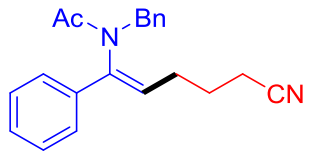




***Z*-3aa**

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

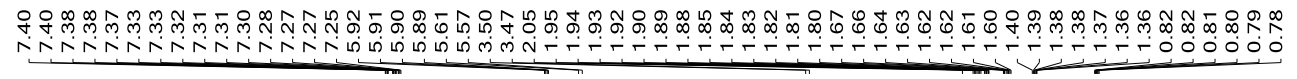


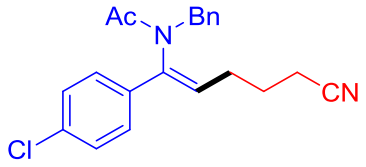


***Z*-3aa**

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

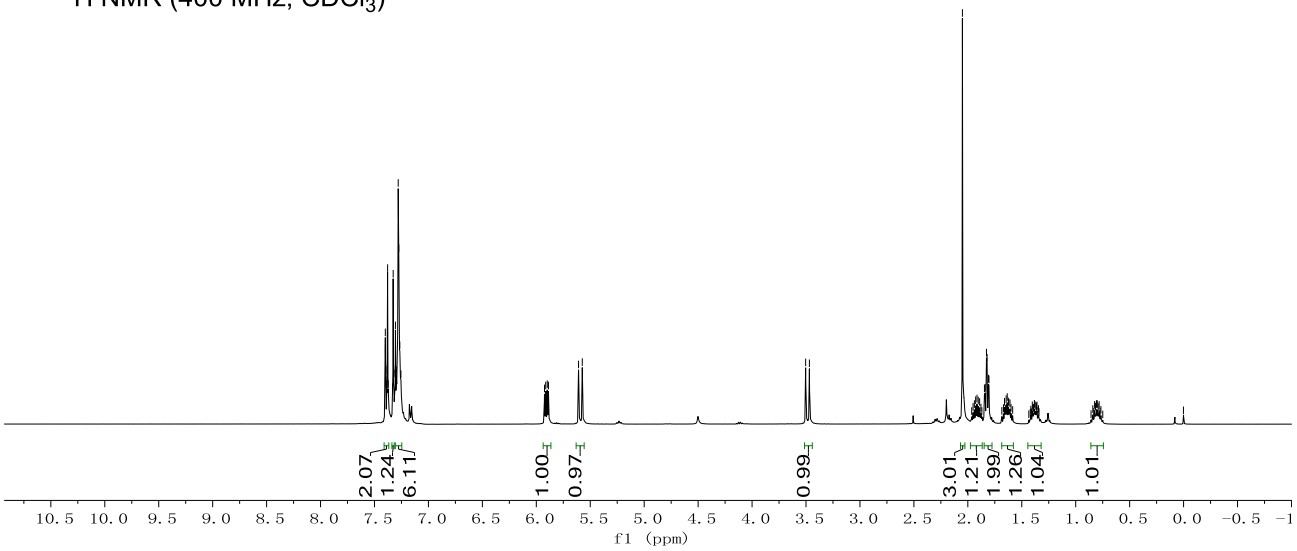
(*Z*)-*N*-benzyl-*N*-(1-(4-chlorophenyl)-5-cyanopent-1-en-1-yl)acetamide (***Z*-3ca**)

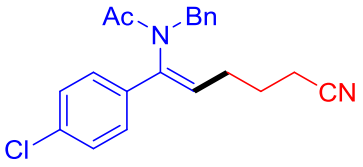




***Z*-3ca**

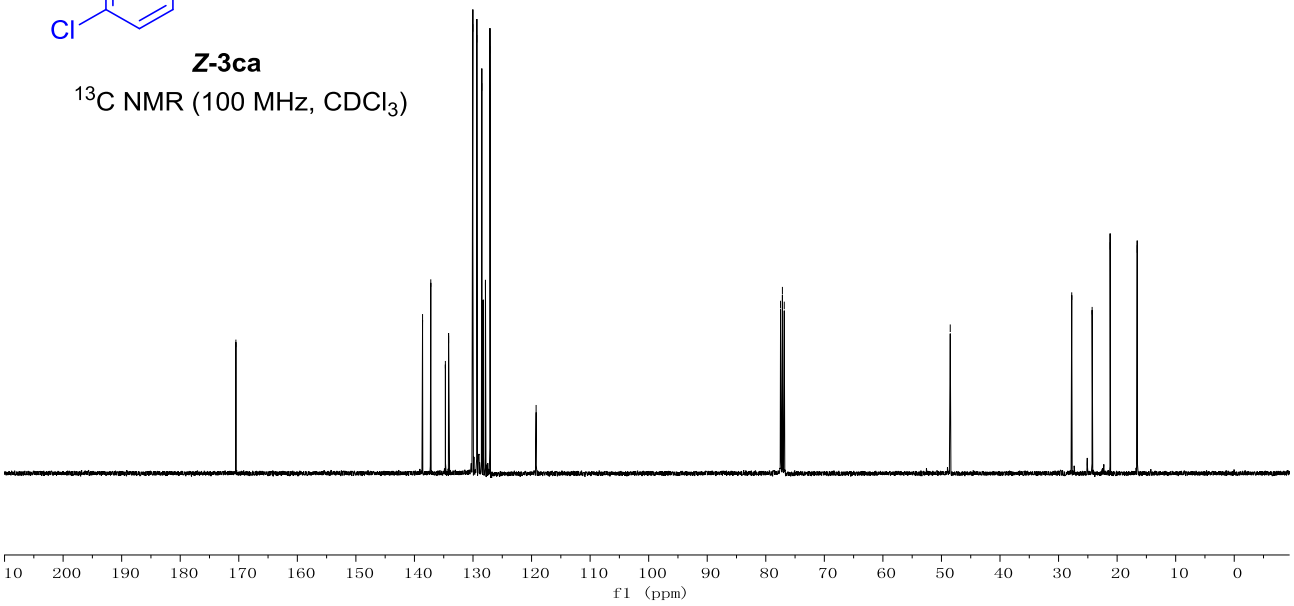
^{1}H NMR (400 MHz, $CDCl_3$)



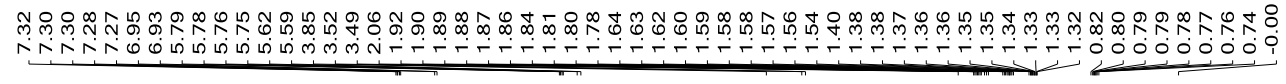


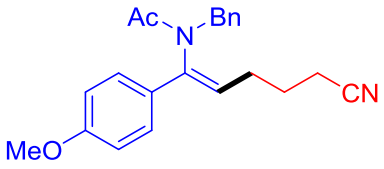
***Z*-3ca**

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



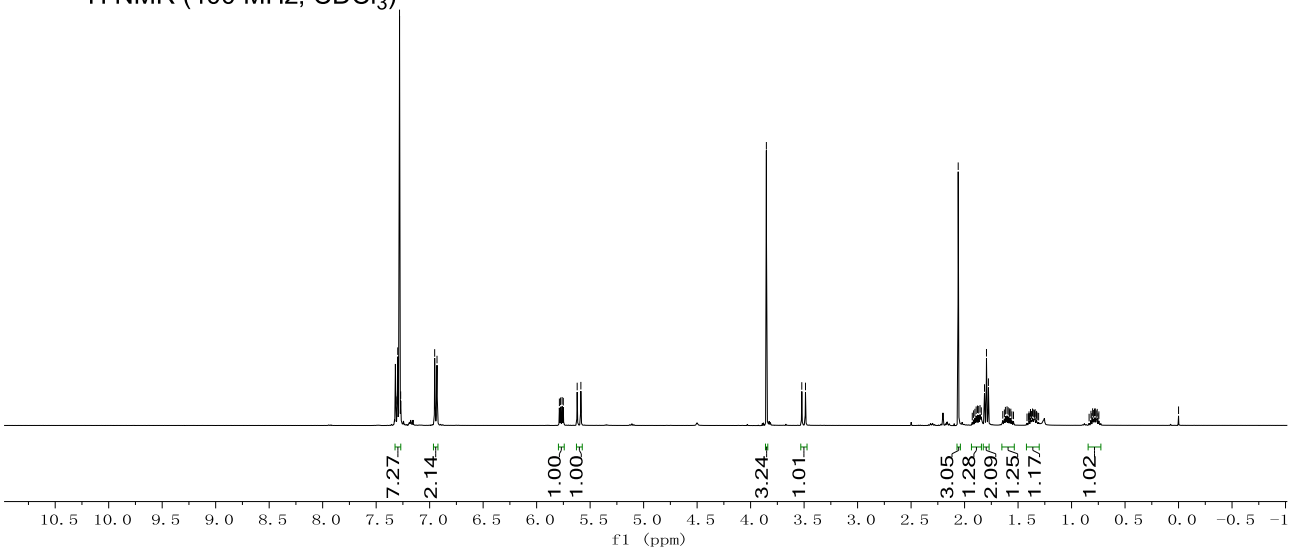
(*Z*)-*N*-benzyl-*N*-(5-cyano-1-(4-methoxyphenyl)pent-1-en-1-yl)acetamide (***Z*-3ma**)

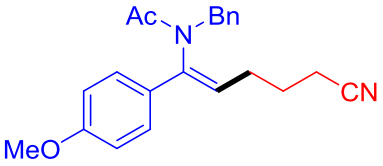




***Z*-3ma**

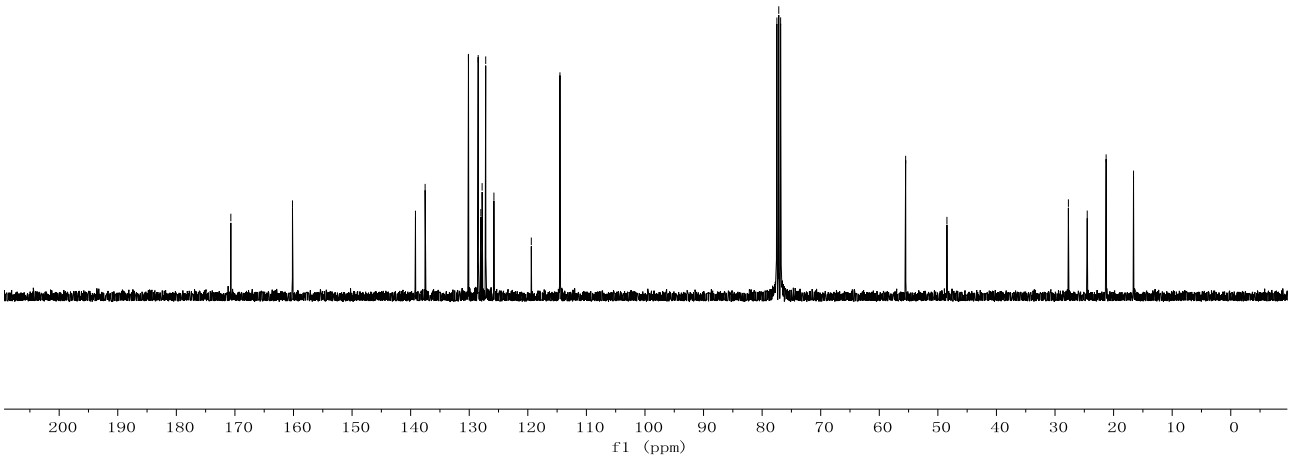
^{1}H NMR (400 MHz, $CDCl_3$)



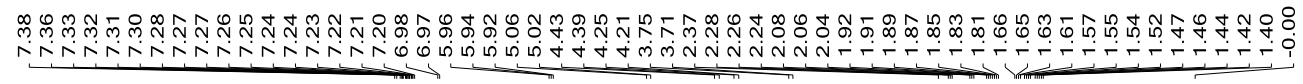


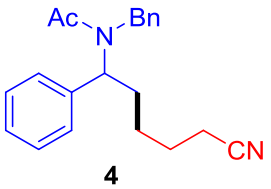
***Z*-3ma**

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



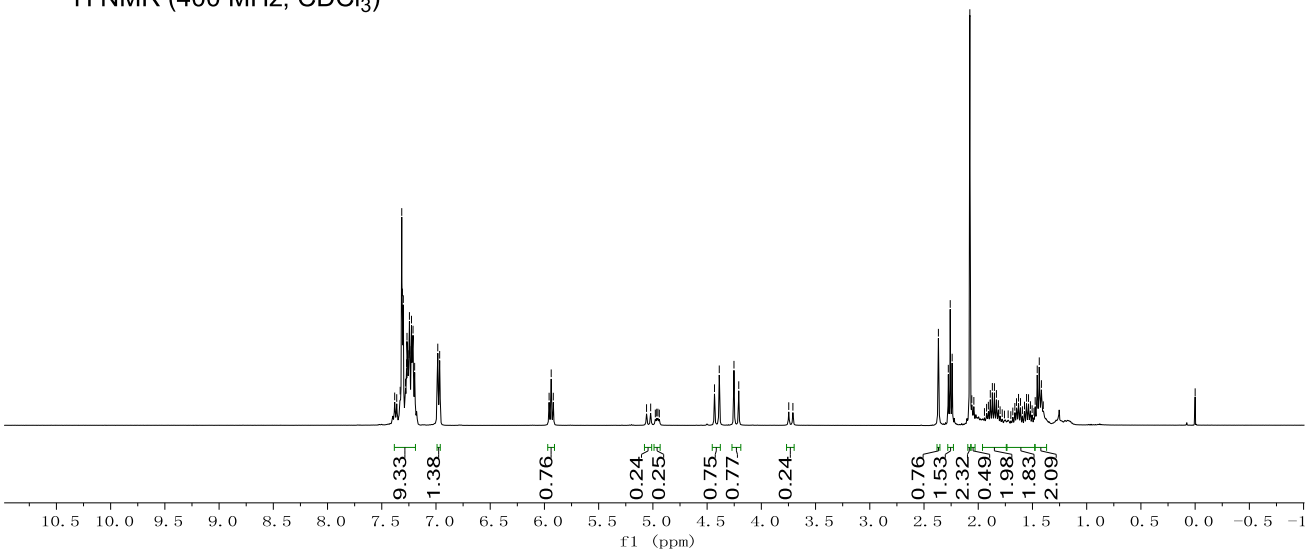
N-benzyl-*N*-(5-cyano-1-phenylpentyl)acetamide (**4**)

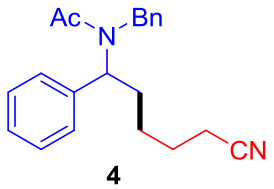




4

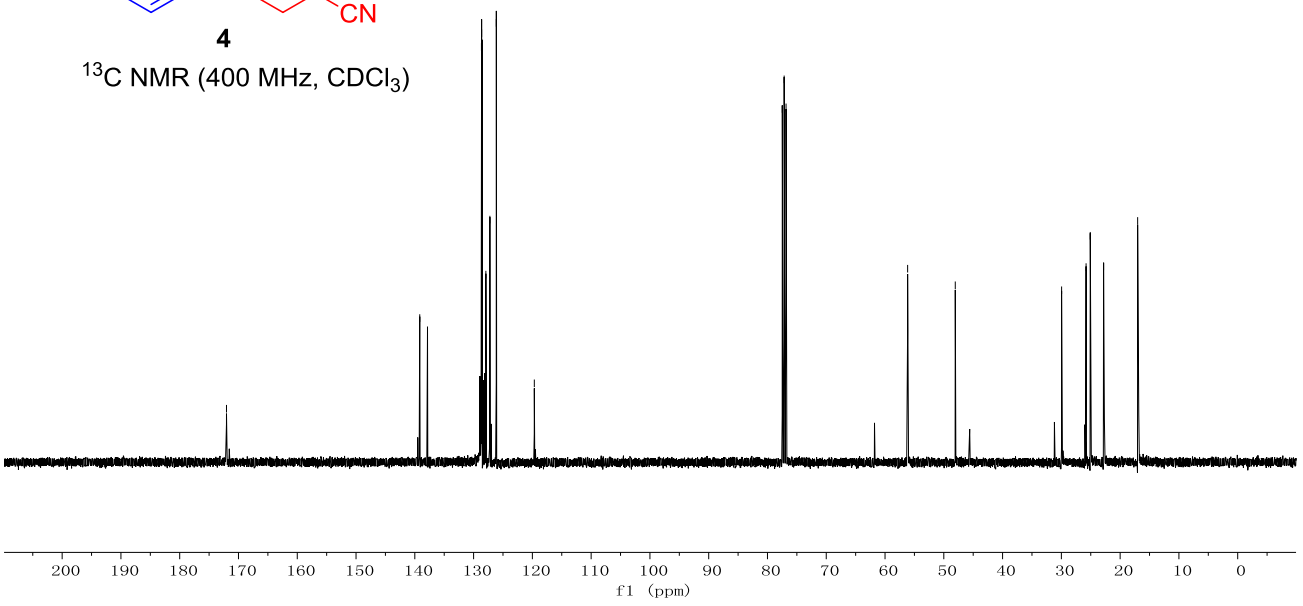
^{1}H NMR (400 MHz, $CDCl_3$)



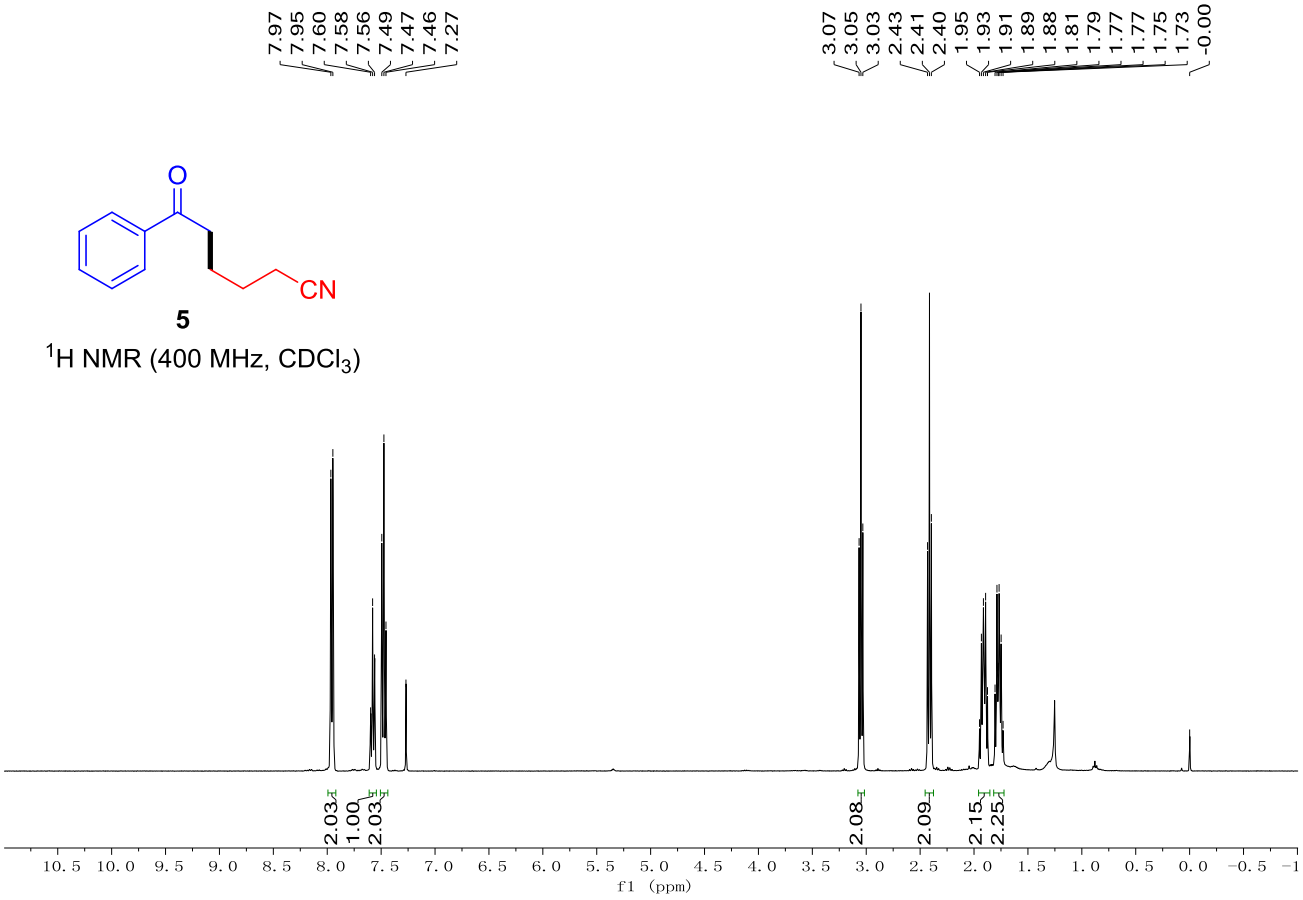


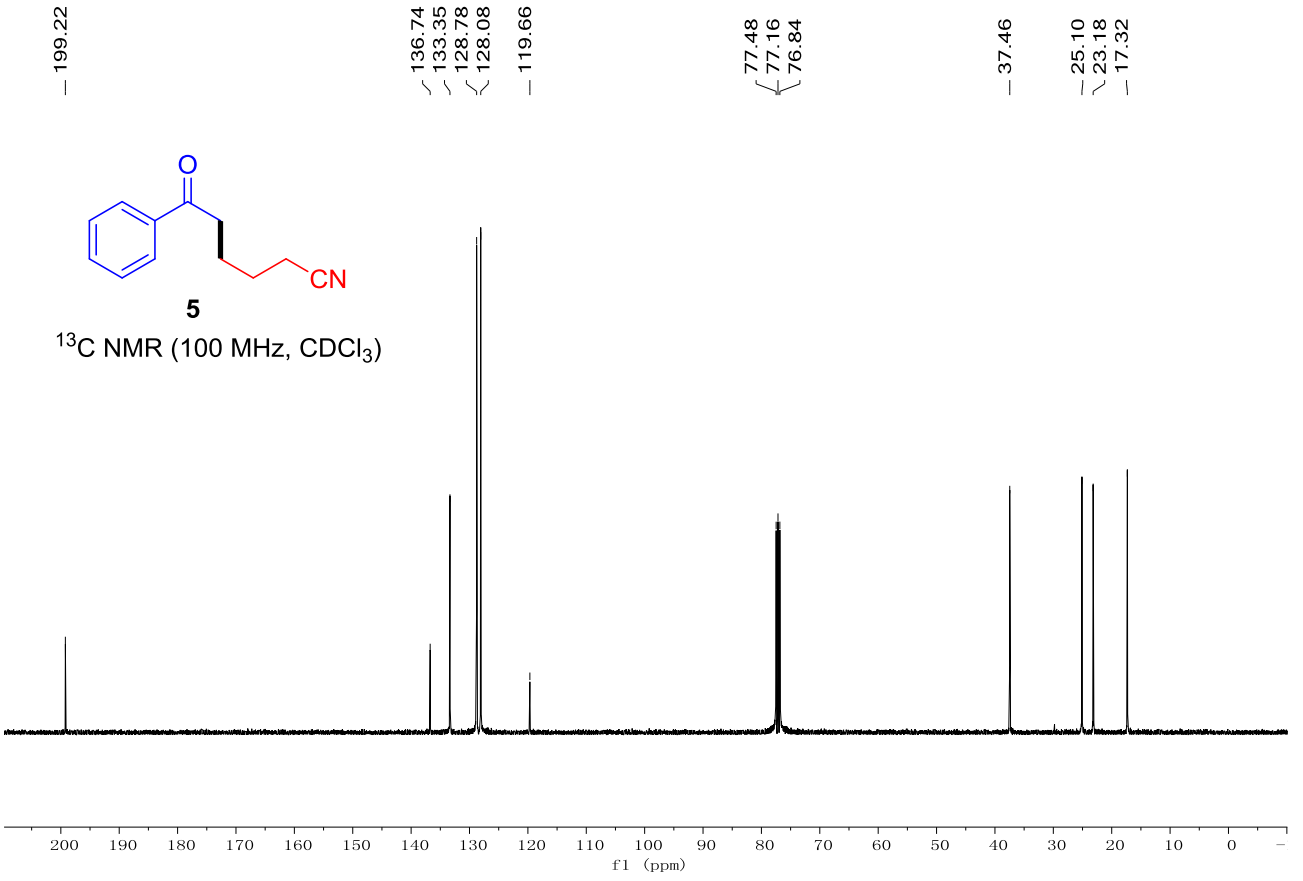
4

^{13}C NMR (400 MHz, $CDCl_3$)

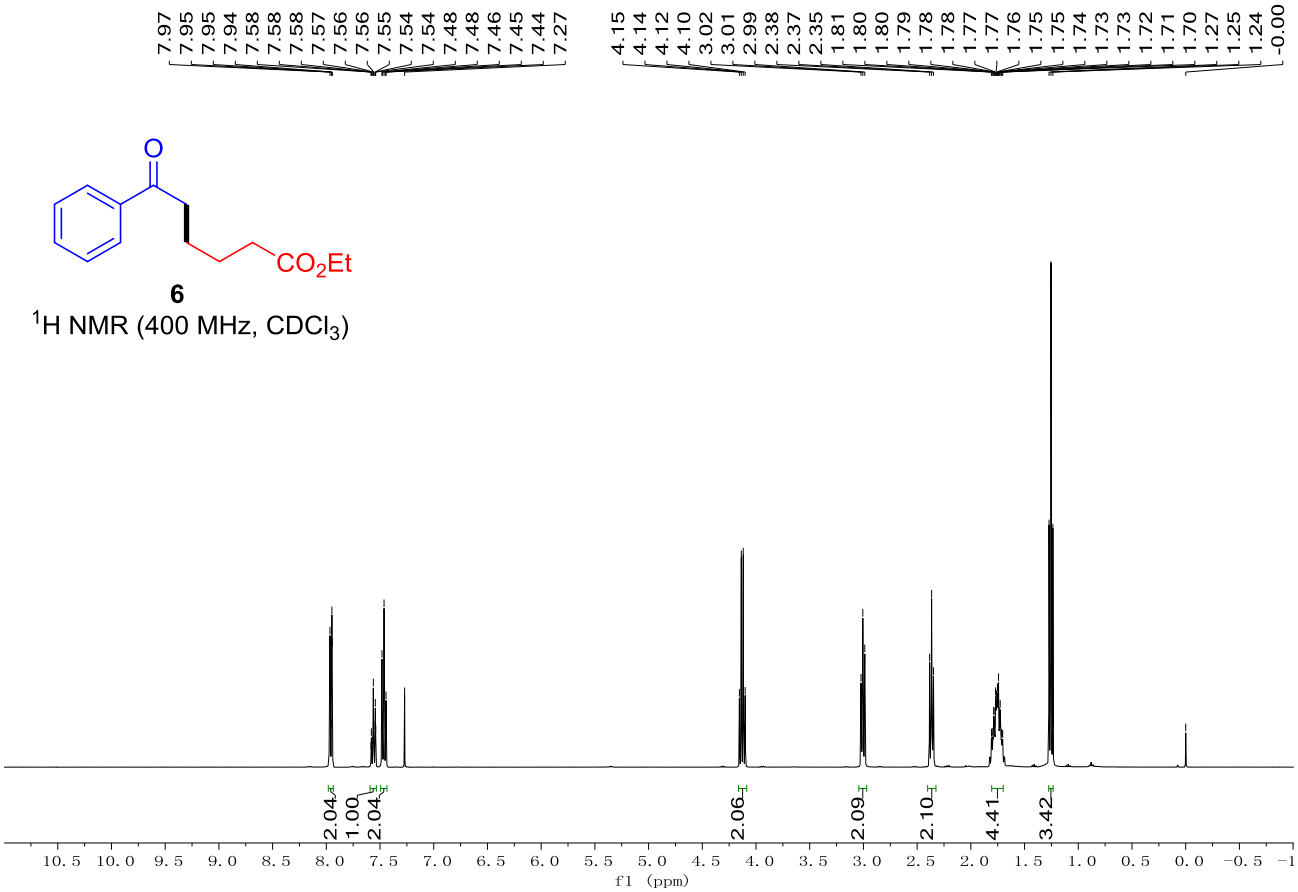


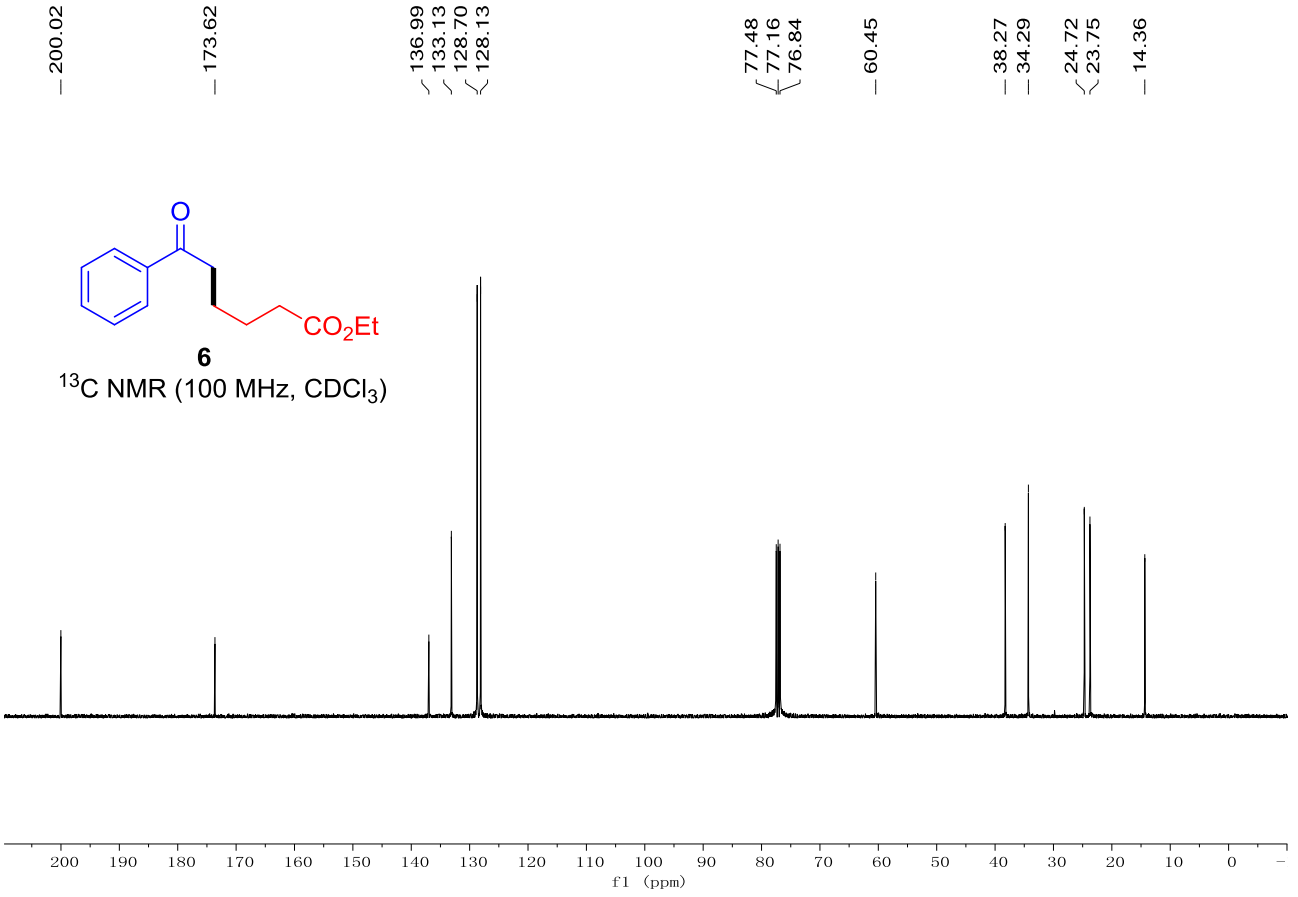
6-oxo-6-phenylhexanenitrile (**5**)



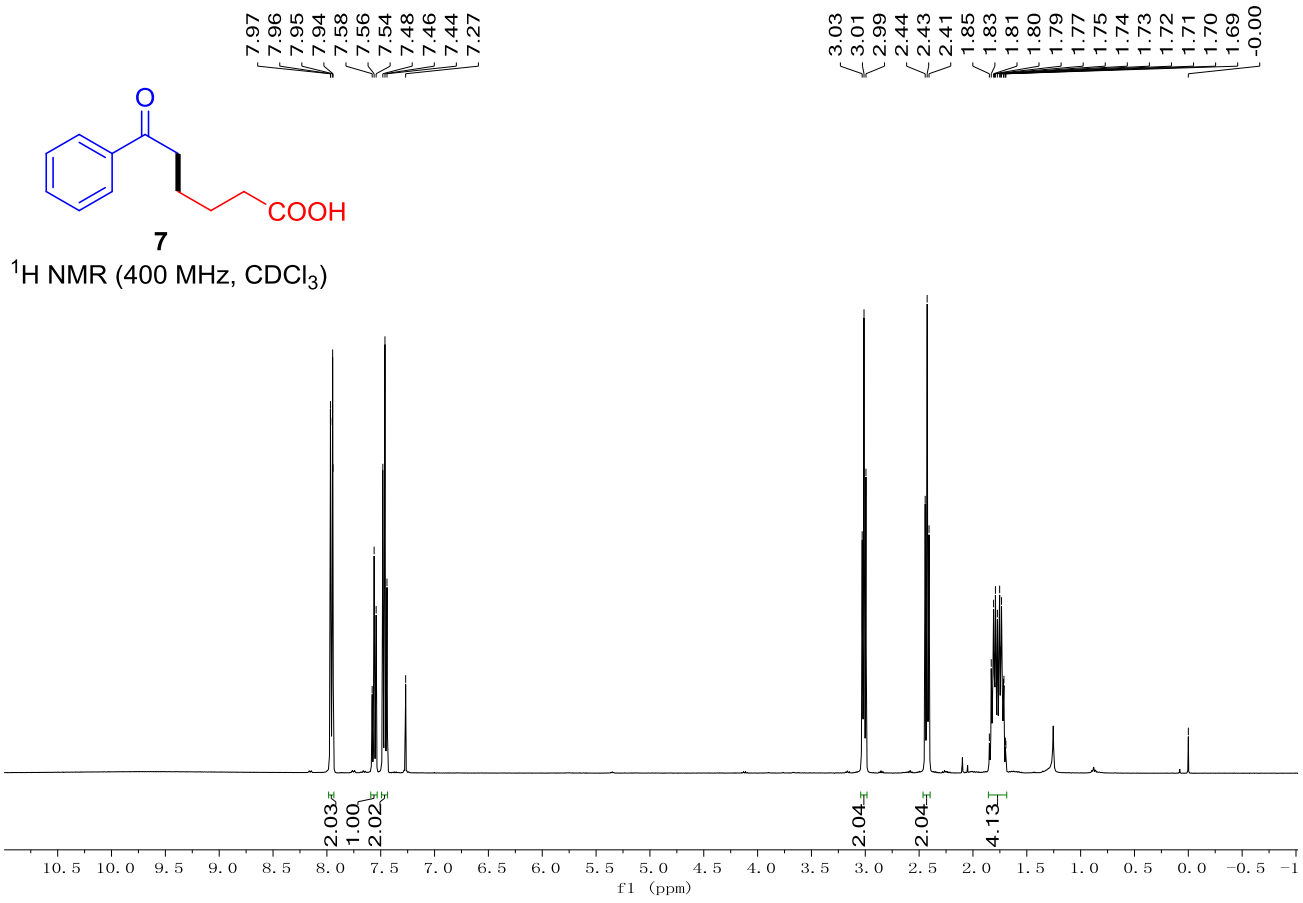


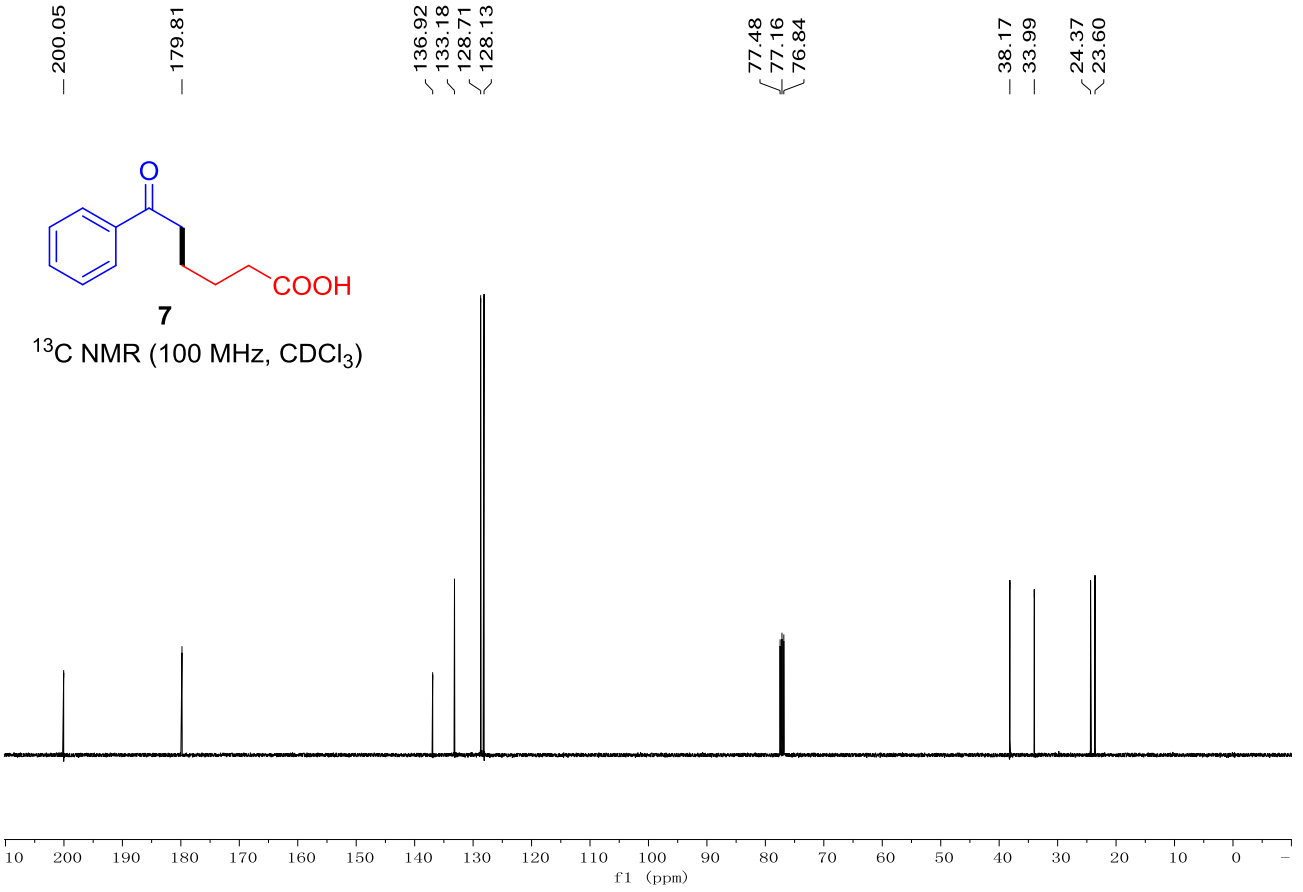
ethyl 6-oxo-6-phenylhexanoate (**6**)



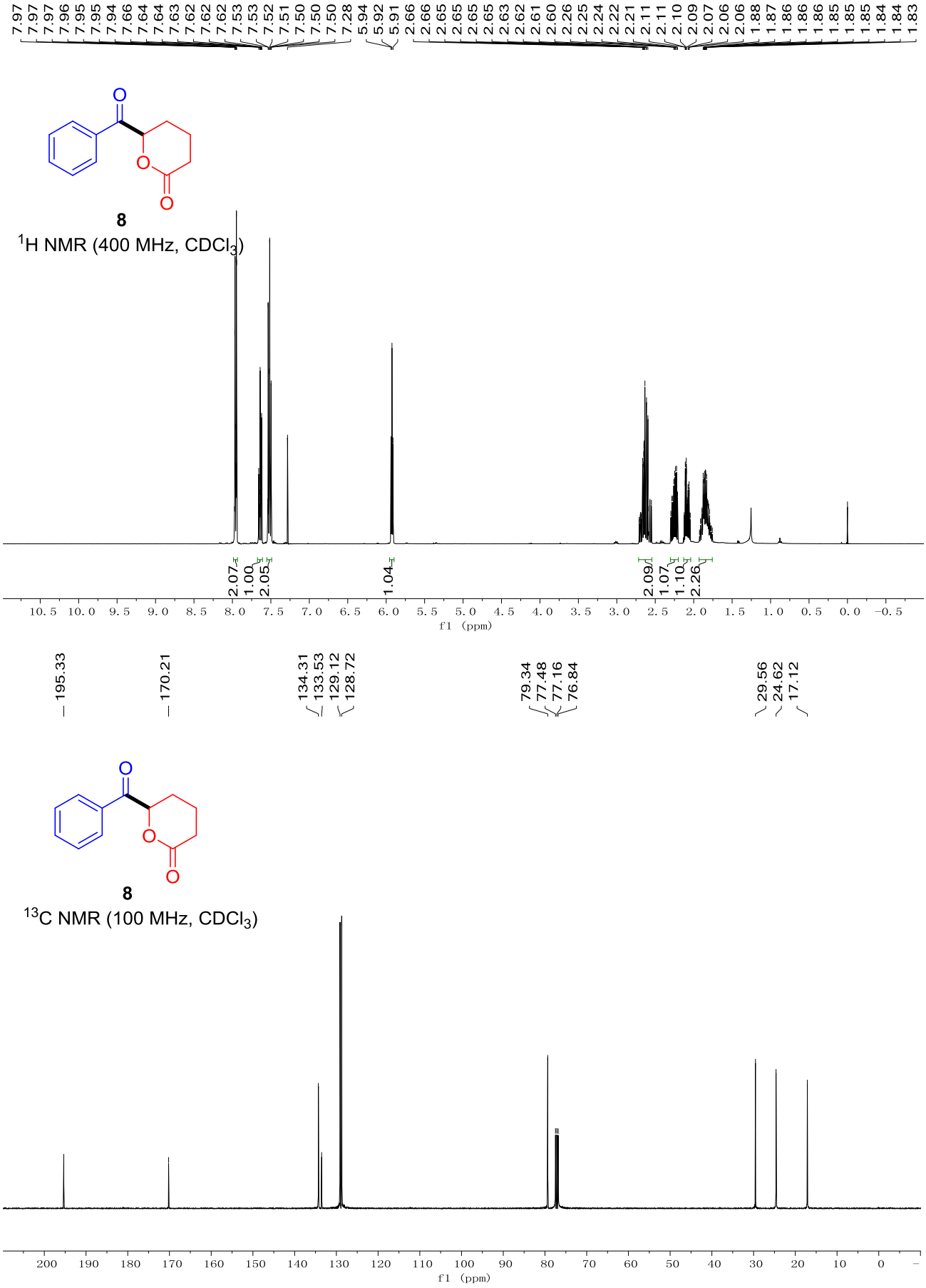


6-oxo-6-phenylhexanoic acid (**7**)

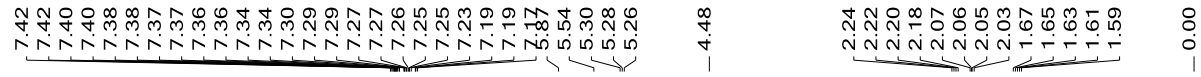


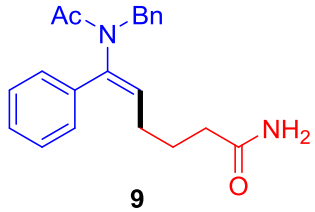


6-benzoyltetrahydro-2H-pyran-2-one (**8**)



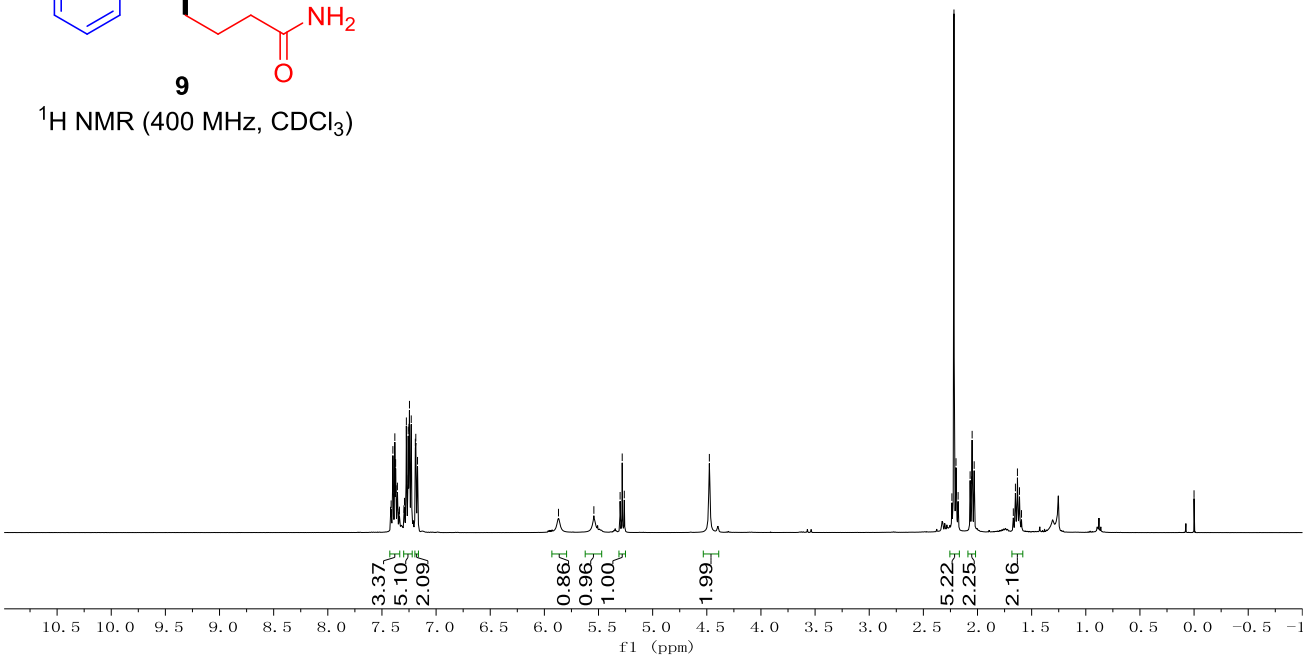
(*E*)-6-(*N*-benzylacetamido)-6-phenylhex-5-enamide (**9**)

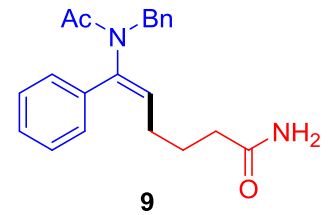




9

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

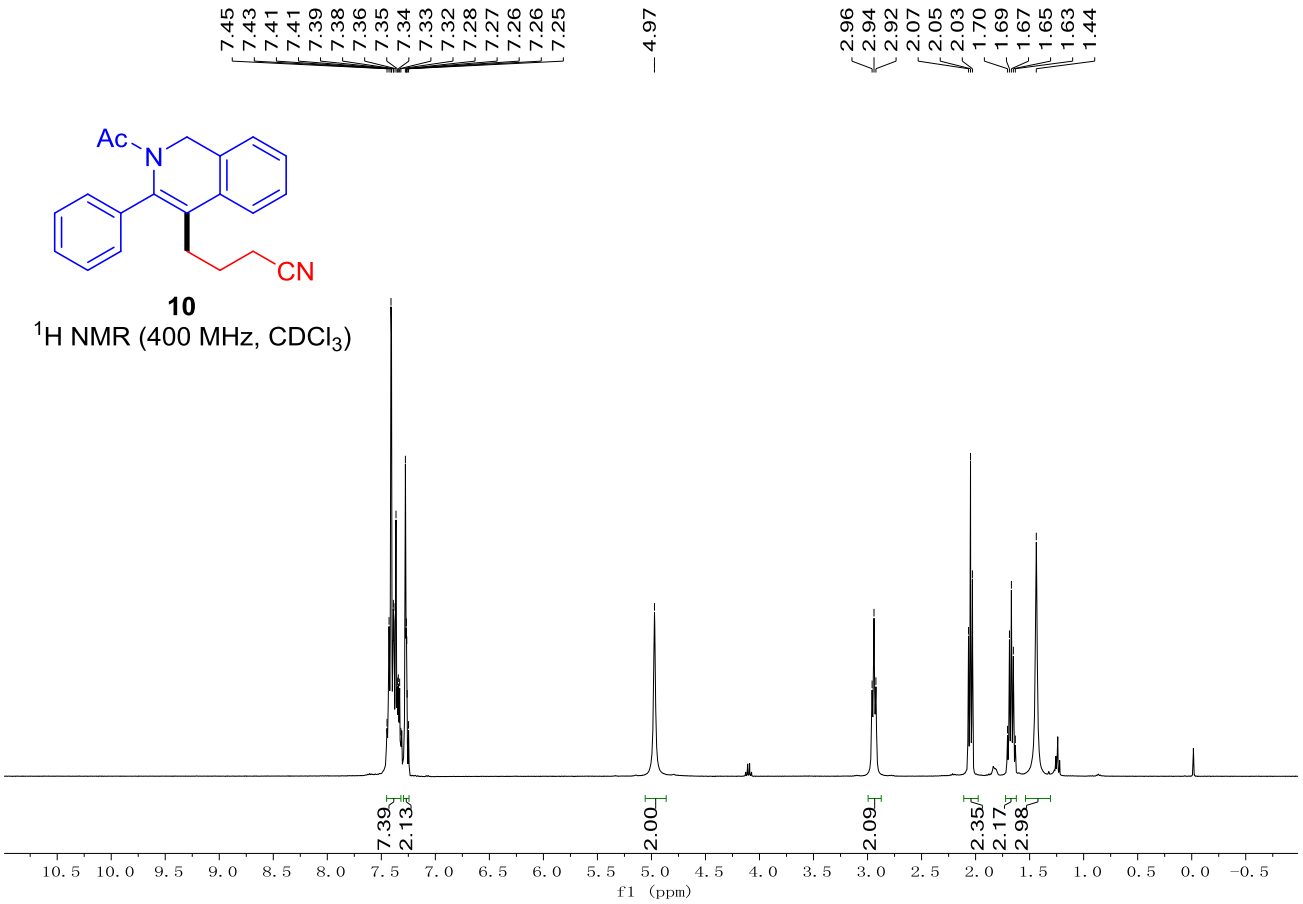


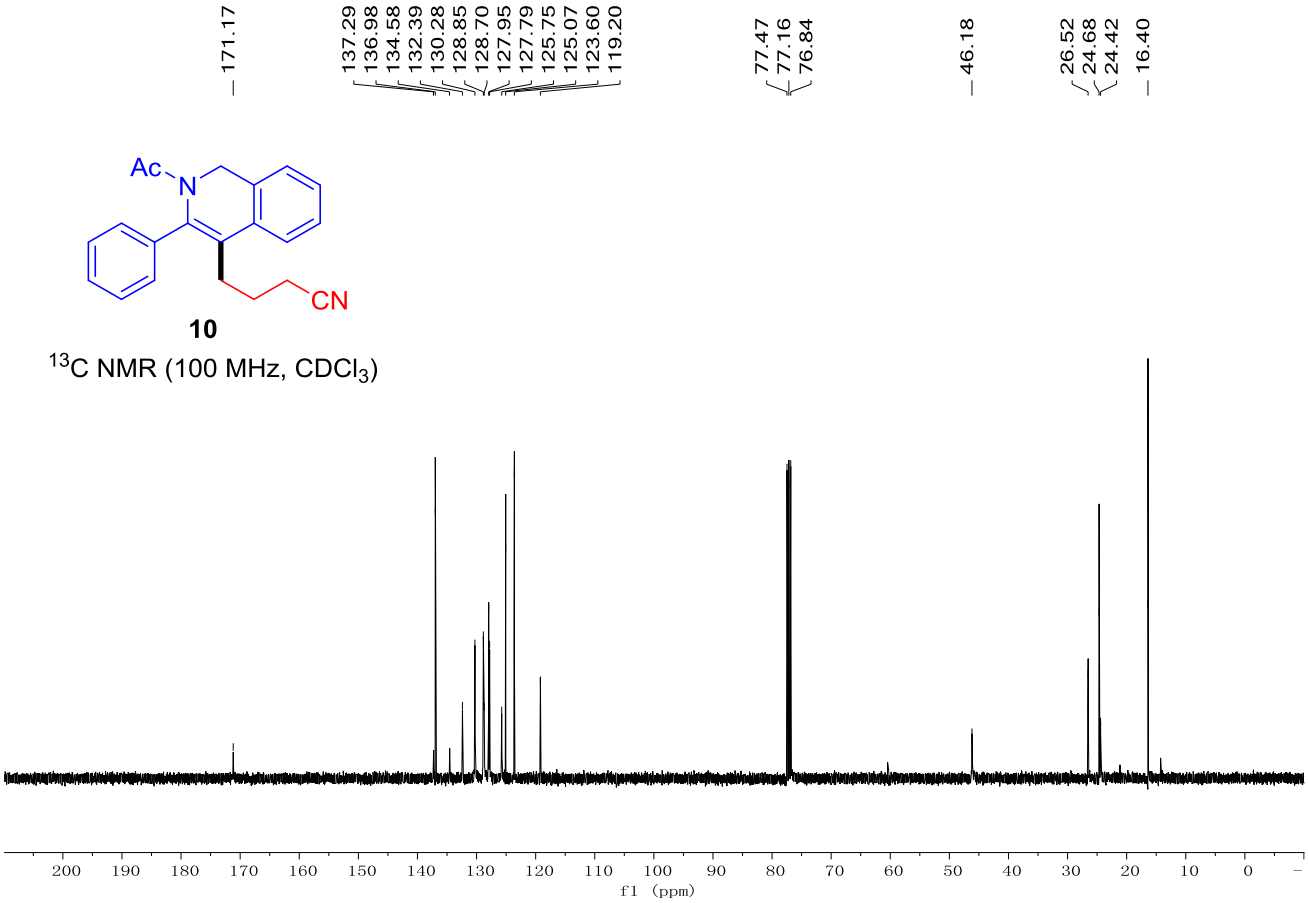


9

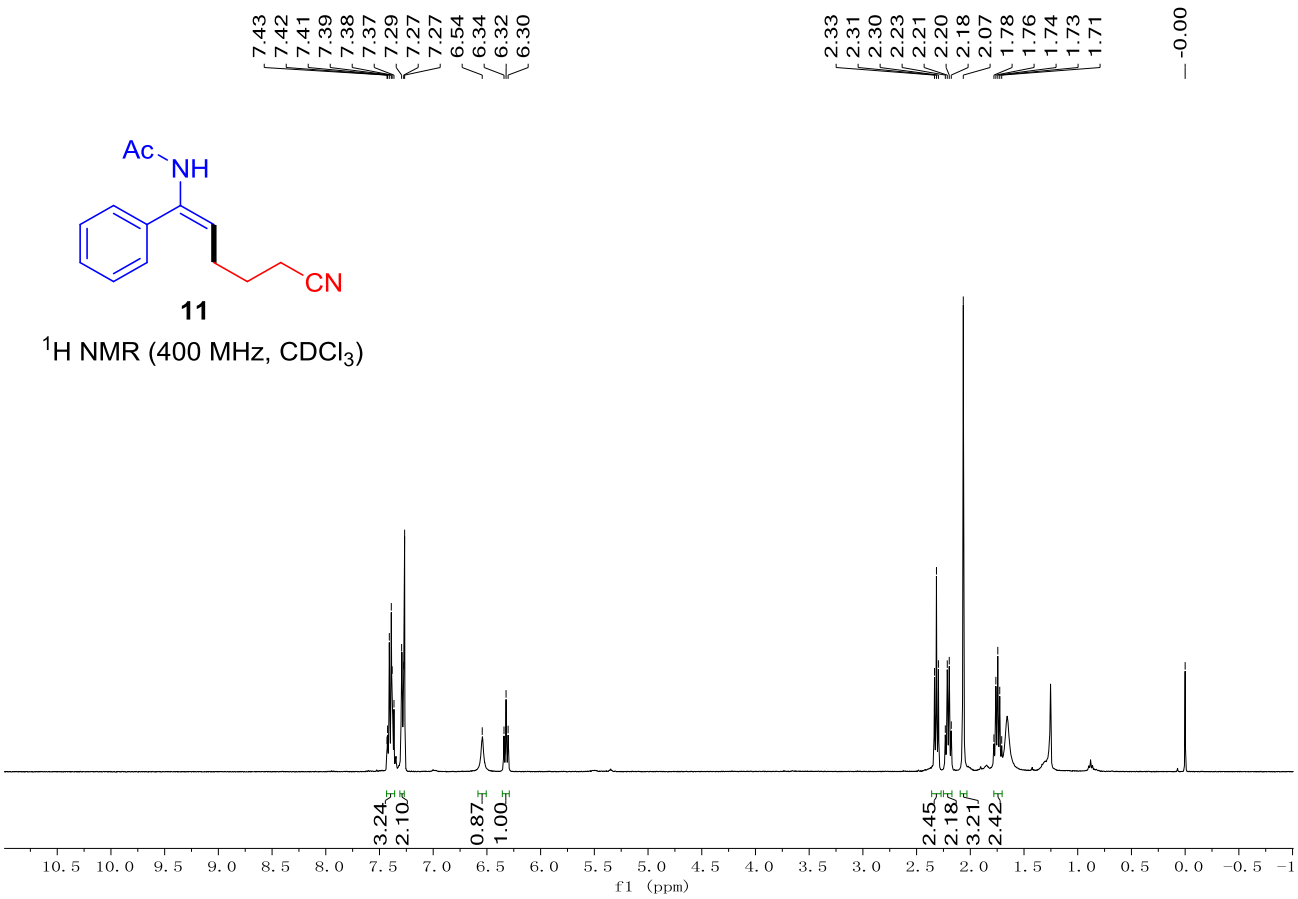
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2-acetyl-3-phenyl-1,2-dihydroisoquinolin-4-yl)butanenitrile (**10**)

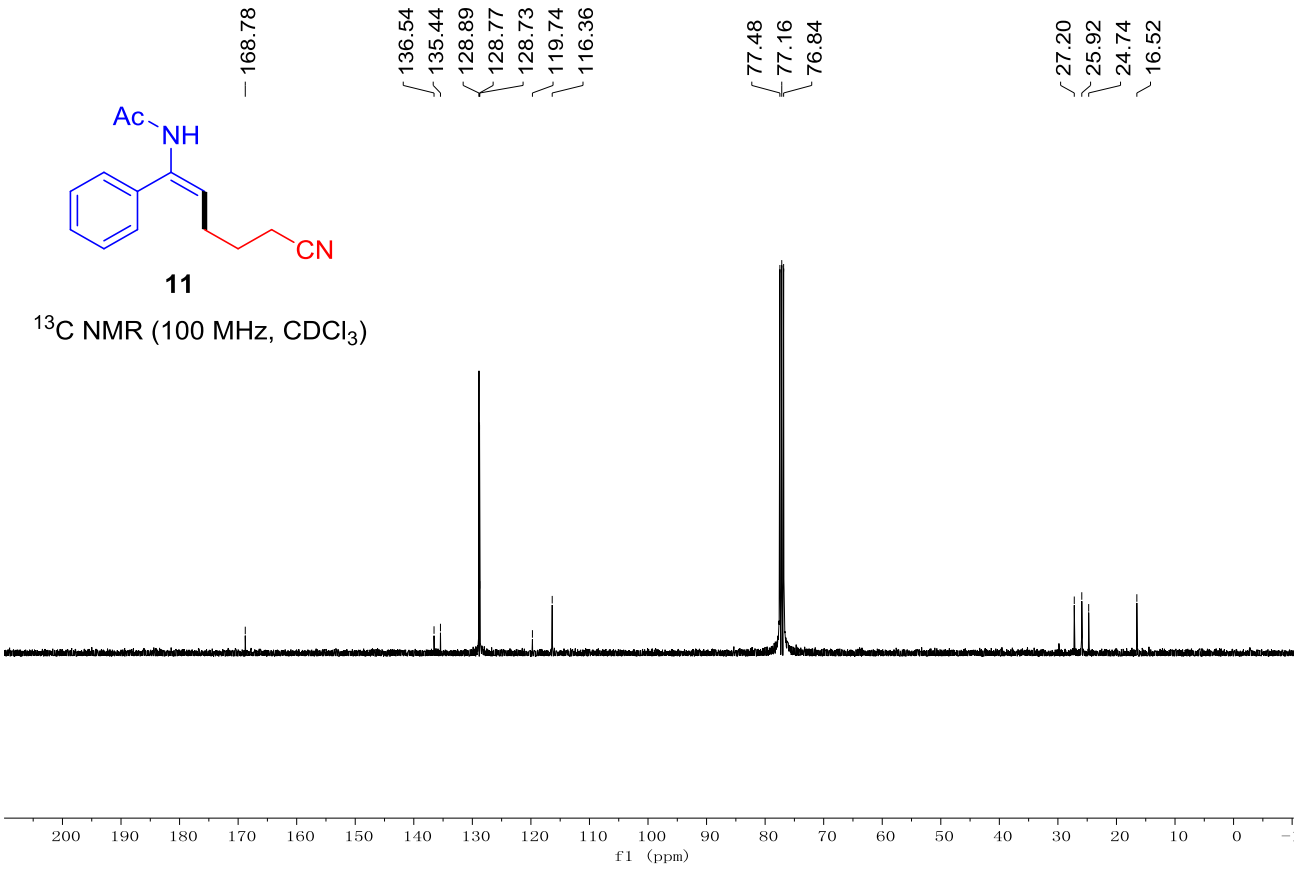




(*E*)-*N*-(5-cyano-1-phenylpent-1-en-1-yl)acetamide (**11**)

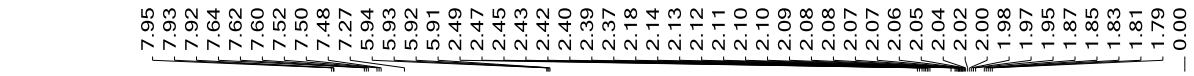


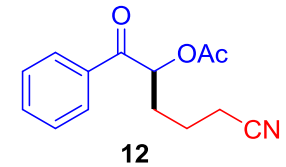
^{1}H NMR (400 MHz, $CDCl_3$)



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

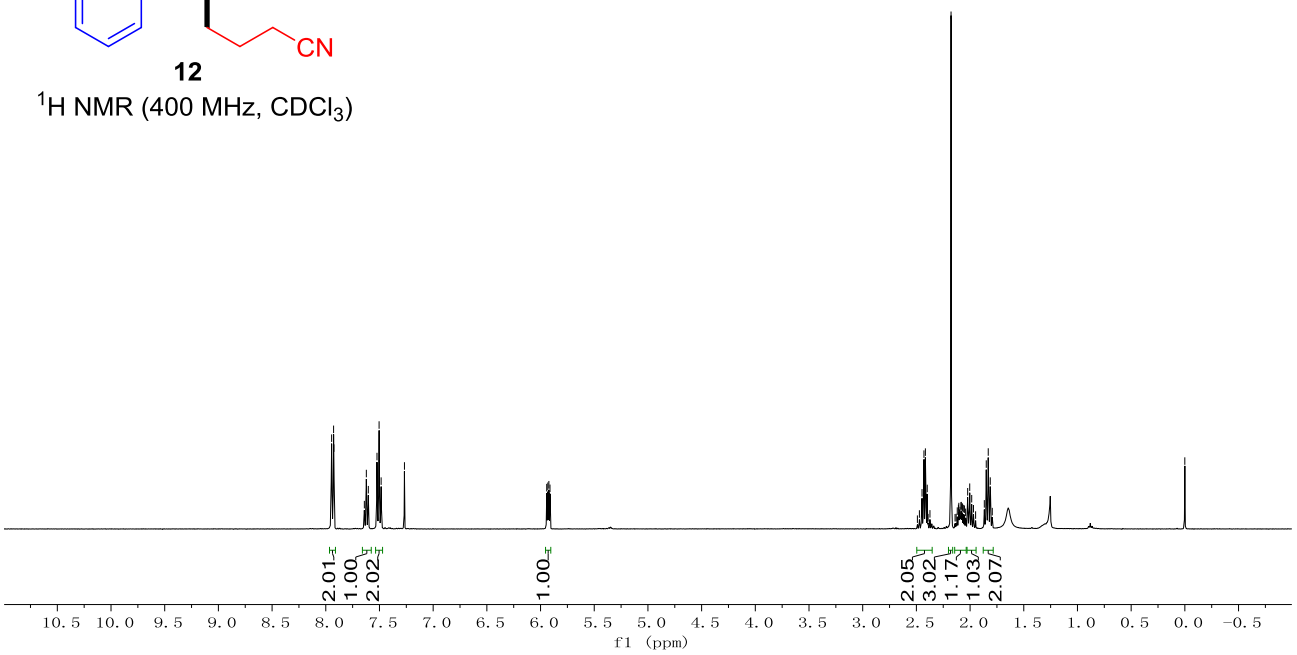
5-cyano-1-oxo-1-phenylpentan-2-yl acetate (**12**)

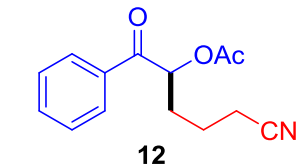




12

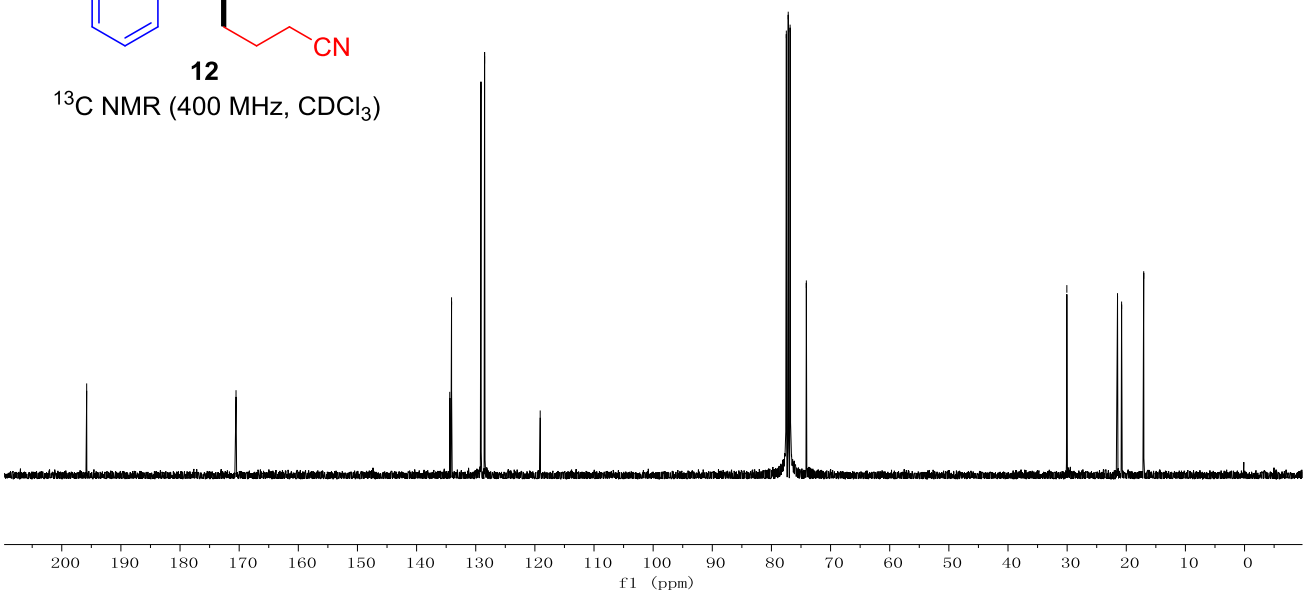
^{1}H NMR (400 MHz, $CDCl_3$)



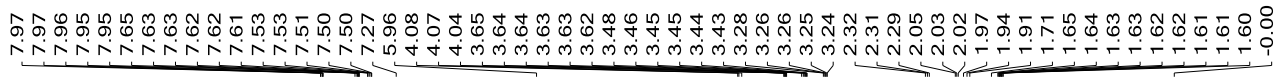


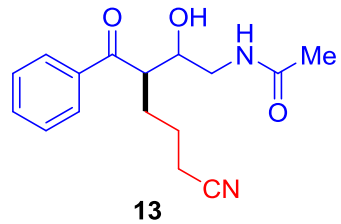
12

^{13}C NMR (400 MHz, $CDCl_3$)



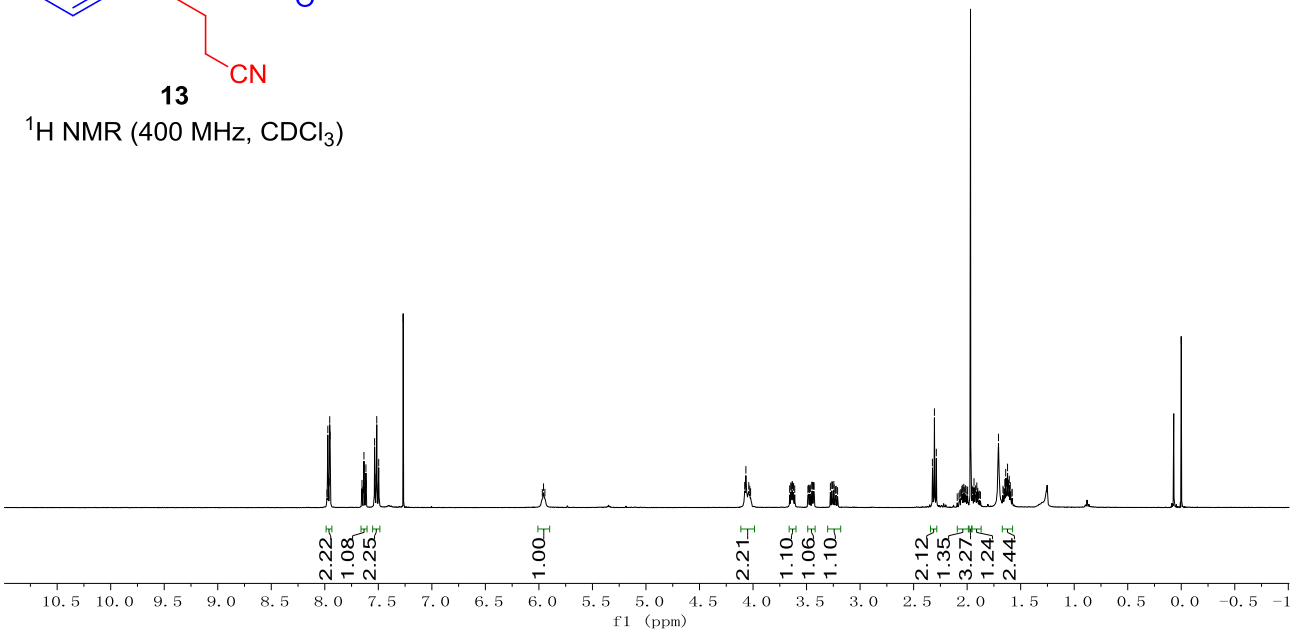
N-(3-benzoyl-6-cyano-2-hydroxyhexyl)acetamide (**13**)

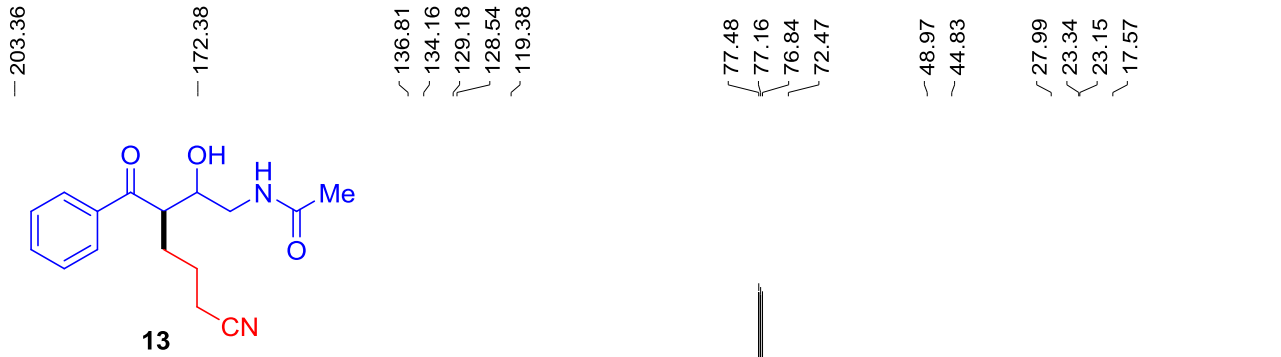




13

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





13

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