

Supporting Information

Synthesis of pyrazolo[5,1-*a*]isoindoles via silver-mediated cascade cyclization of 1,5-enynes with diazo compounds

Jiarong Li,^a He Wang,^{*a} Chunbo Li,^a Jing Sun,^a Xin Wang,^b Ran Sun^b and Lei Li^{*b}

^aSchool of Petrochemical Engineering, Liaoning Petrochemical University, Fushun
113001, P.R. China. E-mail: heliwang123@126.com.

^bFaculty of Science, Liaoning Petrochemical University, Fushun 113
001, P. R. China. E-mail: lilei0814.com@163.com.

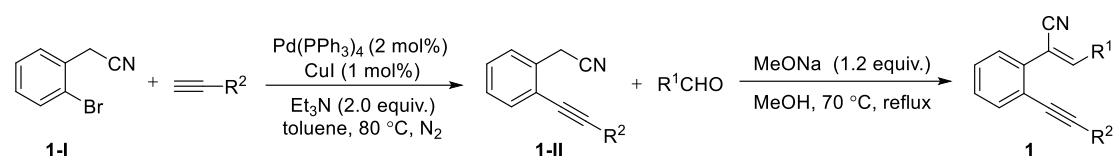
Table of Contents

1. General Information	2
2. Preparation of substrates and analytical data of compounds 1	2
3. Experimental section and analytical data of compound 3	15
4. Derivatization of Product	36
6. Crystal structure of 3aa	43
7. References	44
8. NMR Spectra	45

1. General Information

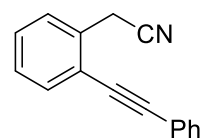
All chemicals were obtained from commercial sources and used as received unless otherwise noted. The ^1H NMR spectra were recorded at 400 MHz in CDCl_3 and the ^{13}C NMR spectra were recorded at 101 MHz in CDCl_3 with TMS as the internal standard. All coupling constants (J values) were reported in Hertz (Hz). High-resolution mass spectra (HRMS) were obtained using a waters UPLC G2-XS focus spectrometer (ESI-TOF). Column chromatography was performed on silica gel (300-400 mesh) with ethyl acetate (EA)/petroleum ether (PE).

2. Preparation of substrates and analytical data of compounds 1

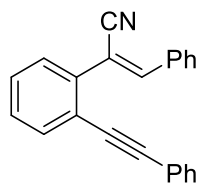


Scheme S1. Synthesis of 1,5-Enynes **1**.

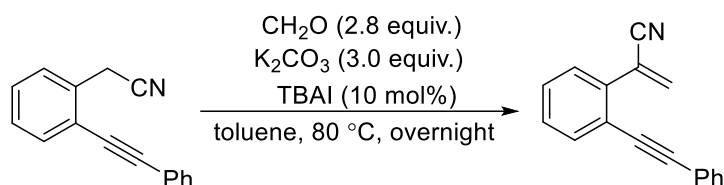
Typical synthetic procedure (with **1a** as an example)



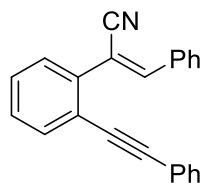
Synthesis of 2-(2-(phenylethynyl)phenyl)acetonitrile^[1]: The 2-(2-bromophenyl)acetonitrile (10.0 mmol), $\text{Pd}(\text{PPh}_3)_4$ (2 mol%, 0.2 mmol, 0.23 g), CuI (1 mol%, 0.1 mmol, 19.1 mg), Et_3N (20.0 mmol) were placed in a nitrogen-filled Schlenk tube. After toluene (50 mL) was added, the mixture was stirred at room temperature for 5 minutes and phenylacetylene (12.0 mmol) was added. The reaction mixture was allowed to stir at $80\text{ }^\circ\text{C}$ for 12 h and the resulting solution was filtered and washed with saturated brine and extracted with ethyl acetate ($3 \times 20\text{ mL}$). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the product. The compound was Purified by column to give 2-(2-(phenylethynyl)phenyl)acetonitrile white solid (1.96 g, 90%).



Synthesis of (Z)-3-phenyl-2-(2-(phenylethynyl)phenyl)acrylonitrile: To a solution of ethyl 2-(2-(phenylethynyl)phenyl)acetonitrile (10.0 mmol, 2.17 g) in 50 mL of methyl alcohol was added benzaldehyde (12.0 mmol, 1.2 equiv.) and sodium methylate (12.0 mmol, 1.2 equiv., 0.65 g). The reaction mixture was stirred in an oil bath at 70 °C. After 12 h, the reaction mixture was cooled to room temperature. The mixture was extracted with CH₂Cl₂ three times, dried over the anhydrous Na₂SO₄ and concentrated in vacuo. The compound was Purified by column to give (Z)-3-phenyl-2-(2-(phenylethynyl)phenyl)acrylonitrile white solid (2.19 g, 72%).



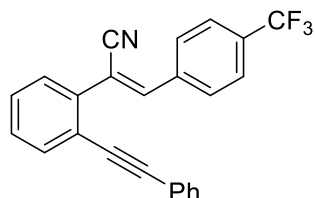
Synthesis of 2-(2-(phenylethynyl)phenyl)acrylonitrile (1p)^[2]: The ethyl 2-(2-(phenylethynyl)phenyl)acetonitrile (10.0 mmol, 2.17 g), K₂CO₃ (30 mmol, 4.14 g) and TBAI (0.1 mmol, 0.37g) were dissolved in toluene (20 mL) and allowed to stir under reflux. The CH₂O (37% in H₂O, 2 mL) was slowly injected into the solution in toluene for the period over 2 h. The reaction mixture was allowed to stir for overnight at 80 °C, then quenched with H₂O and extracted with ethyl acetate for three times. The combined organic layer was collected and dried over anhydrous MgSO₄, purified by column chromatography to afford yellow liquid (0.92 g, 40%).



(Z)-3-phenyl-2-(2-(phenylethynyl)phenyl)acrylonitrile (1a)

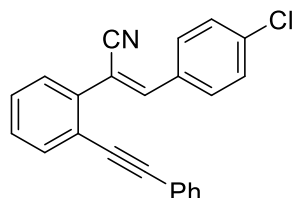
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 100-102 °C; yield: 2.19 g (72%); ¹H NMR (400 MHz, CDCl₃) δ 7.94-7.92 (m, 2H), 7.69 (s, 1H), 7.67-7.65 (m, 1H), 7.57-7.55 (m, 1H),

7.51-7.45 (m, 5H), 7.44-7.37 (m, 2H), 7.33-7.27 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 147.3, 137.0, 133.6, 133.5, 131.5, 130.7, 129.3, 128.9, 128.9, 128.8, 128.7, 128.6, 128.4, 122.8, 121.7, 117.9, 110.2, 95.1, 87.4. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{15}\text{NNa}^+$ 328.1102; Found 328.1107.



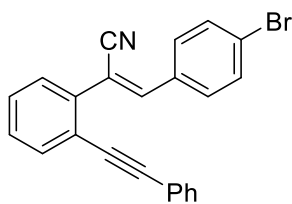
(Z)-2-(2-(phenylethynyl)phenyl)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (1b)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 108-110 °C; yield: 2.53 g (68%); ^1H NMR (400 MHz, CDCl_3) δ 8.01-7.98 (m, 2H), 7.73-7.71 (m, 3H), 7.68-7.64 (m, 1H), 7.58-7.53 (m, 1H), 7.51-7.45 (m, 2H), 7.45-7.39 (m, 2H), 7.36-7.28 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 145.3, 136.8, 136.8, 136.2, 133.6, 132.0 (q, $J = 32.5$ Hz), 131.5, 129.4, 129.2, 128.9, 128.9, 128.8, 128.4, 126.0, 125.9 (q, $J = 3.7$ Hz), 123.7 (q, $J = 270.6$ Hz), 122.6, 121.7, 117.3, 113.0, 95.4, 87.1. ^{19}F NMR (376 MHz, CDCl_3) δ -62. 91. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{24}\text{H}_{14}\text{NNaF}_3^+$ 396.0976; Found 396.0981.



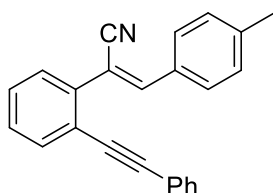
(Z)-3-(4-chlorophenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1c)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 101-103 °C; yield: 2.51 g (74%); ^1H NMR (400 MHz, CDCl_3) δ 7.87-7.84 (m, 2H), 7.67-7.62 (m, 2H), 7.55-7.52 (m, 1H), 7.48-7.36 (m, 6H), 7.33-7.29 (m, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 145.8, 136.7, 136.6, 133.5, 132.0, 131.5, 130.5, 129.2, 128.9, 128.8, 128.8, 128.7, 128.4, 122.7, 121.7, 117.7, 110.7, 95.2, 87.3. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{14}\text{NNaCl}^+$ 361.5480; Found 361.5482.



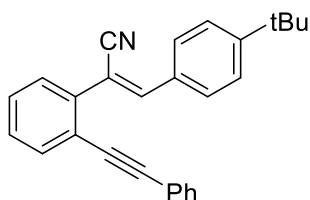
(Z)-3-(4-bromophenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1d)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 91-93 °C; yield: 2.88g (75%); ¹H NMR (400 MHz, CDCl₃) δ 7.80-7.75 (m, 2H), 7.66-7.58 (m, 4H), 7.55-7.52 (m, 1H), 7.48-7.46 (m, 2H), 7.43-7.37 (m, 2H), 7.34-7.28 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 145.8, 136.6, 133.5, 132.4, 132.2, 131.5, 130.6, 128.9, 128.8, 128.7, 128.4, 125.1, 122.6, 121.6, 117.7, 110.9, 95.2, 87.3. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₃H₁₄NNaBr⁺, 406.0207; Found, 406.0199.



(Z)-2-(2-(phenylethynyl)phenyl)-3-(p-tolyl)acrylonitrile (1e)

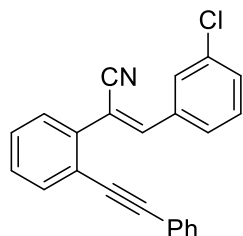
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Purified by column chromatography using petroleum ether/ ethyl acetate (5:1, V/V) as an eluent. Pale yellow solid; m.p.: 108-110 °C; yield: 2.24 g (70%); ¹H NMR (400 MHz, CDCl₃) δ 7.84-7.82 (m, 2H), 7.64-7.62 (m, 2H), 7.54-7.47 (m, 3H), 7.41-7.33 (m, 2H), 7.32-7.26 (m, 5H), 2.41 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 141.3, 137.2, 133.4, 131.5, 130.9, 129.7, 129.4, 128.9, 128.8, 128.6, 128.5, 128.4, 122.8, 121.6, 118.2, 108.9, 95.1, 87.5, 21.6. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₄H₁₇NNa⁺, 342.1259; Found, 342.1262.



(Z)-3-(4-(tert-butyl)phenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1f)

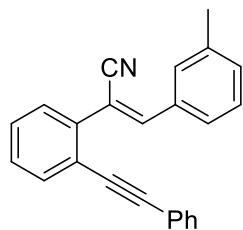
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 74-76 °C; yield: 2.60 g (70%); ¹H NMR (400

MHz, CDCl₃) δ 7.88-7.85 (m, 2H), 7.63-7.61 (m, 2H), 7.52-7.46 (m, 5H), 7.38-7.34 (m, 2H), 7.31-7.27 (m, 3H), 1.34 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 141.3, 137.2, 133.4, 131.5, 130.9, 129.7, 129.4, 128.9, 128.8, 128.6, 128.5, 128.4, 122.8, 121.6, 118.2, 108.9, 95.1, 87.5, 21.6. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₇H₂₃NNa⁺ 384.1728; Found 384.1725.



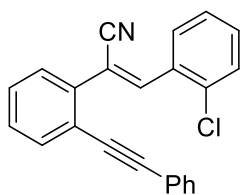
(Z)-3-(3-chlorophenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1g)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 96-98 °C; yield: 2.51 g (74%); ¹H NMR (400 MHz, CDCl₃) δ 7.86-7.81 (m, 2H), 7.67-7.62 (m, 2H), 7.56-7.46 (m, 3H), 7.44-7.37 (m, 4H), 7.36-7.28 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 145.5, 136.4, 135.3, 134.9, 133.5, 131.5, 130.6, 130.2, 129.3, 129.0, 128.9, 128.8, 128.7, 128.4, 127.0, 122.6, 121.7, 117.4, 111.8, 95.3, 87.2. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₃H₁₄NNaCl⁺ 361.5480; Found 361.5482.



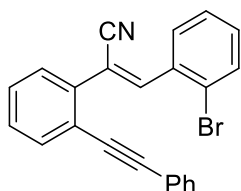
(Z)-2-(2-(phenylethynyl)phenyl)-3-(m-tolyl)acrylonitrile (1h)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 64-66 °C; yield: 2.56 g (80%); ¹H NMR (400 MHz, CDCl₃) δ 7.96-7.89 (m, 2H), 7.69 (s, 1H), 7.65-7.61 (m, 1H), 7.55-7.53 (m, 1H), 7.49-7.43 (m, 3H), 7.42-7.34 (m, 2H), 7.29-7.26 (m, 2H), 7.19-7.15 (m, 1H), 7.13-7.09 (m, 1H), 2.26 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 138.0, 137.0, 133.6, 133.4, 132.8, 130.7, 129.5, 129.4, 128.9, 128.9, 128.7, 128.6, 128.3, 122.6, 121.8, 118.0, 110.0, 95.3, 87.2, 21.2. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₄H₁₇NNa⁺ 342.1259; Found 342.1262.



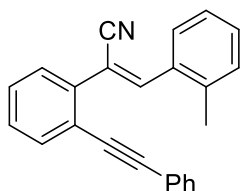
(Z)-3-(2-chlorophenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1i)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 92-94 °C; yield: 2.48 g (73%); ¹H NMR (400 MHz, CDCl₃) δ 8.24-8.19 (m, 1H), 8.04 (s, 1H), 7.69-7.64 (m, 1H), 7.59-7.56 (m, 1H), 7.53-7.49 (m, 2H), 7.47-7.45 (m, 1H), 7.43-7.38 (m, 4H), 7.36-7.27 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 143.7, 136.2, 134.7, 133.6, 132.1, 131.6, 131.4, 129.9, 129.4, 129.0, 128.8, 128.6, 128.3, 127.2, 122.8, 121.8, 117.2, 113.5, 95.4, 87.1. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₃H₁₄NNaCl⁺ 361.5480; Found 361.5482.



(Z)-3-(2-bromophenyl)-2-(2-(phenylethynyl)phenyl)acrylonitrile(1j)

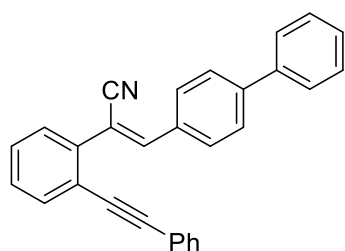
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 103-104 °C; yield: 2.79 g (73%); ¹H NMR (400 MHz, CDCl₃) δ 8.11-8.08 (m, 1H), 7.91 (s, 1H), 7.64-7.58 (m, 2H), 7.55-7.44 (m, 3H), 7.42-7.34 (m, 3H), 7.30-7.21 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 146.2, 136.1, 133.9, 133.6, 133.1, 131.7, 131.6, 131.6, 129.7, 129.1, 129.1, 128.8, 128.6, 128.3, 128.3, 127.8, 124.9, 122.8, 121.9, 117.1, 113.7, 95.5, 87.1. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₃H₁₄NNaBr⁺ 407.2650; Found 407.2652.



(Z)-2-(2-(phenylethynyl)phenyl)-3-(o-tolyl)acrylonitrile (1k)

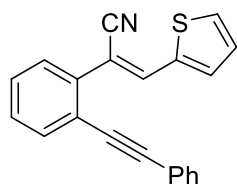
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 119-121 °C; yield: 2.52 g (79%); ¹H NMR (400 MHz, CDCl₃) δ 7.99-7.96 (m, 1H), 7.83 (s, 1H), 7.60-7.56 (m, 1H), 7.50-7.47 (m, 1H),

7.43-7.38 (m, 2H), 7.36-7.28 (m, 2H), 7.28-7.19 (m, 5H), 7.16-7.14 (m, 1H), 2.25 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 146.3, 137.6, 136.8, 133.6, 133.0, 131.5, 130.5, 130.3, 129.0, 128.8, 128.8, 128.6, 128.4, 128.0, 126.4, 122.8, 121.7, 117.7, 112.3, 95.0, 87.5, 20.0. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₄H₁₇NNa⁺ 342.1259; Found 342.1262.



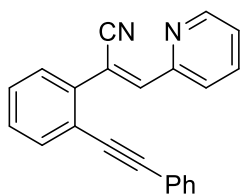
(Z)-3-([1,1'-biphenyl]-4-yl)-2-(2-(phenylethynyl)phenyl)acrylonitrile (1l)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 108-110 °C; yield: 2.67 g (70%); ¹H NMR (400 MHz, CDCl₃) δ 8.01-7.99 (m, 2H), 7.71-7.62 (m, 6H), 7.56-7.55 (m, 1H), 7.52-7.45 (m, 4H), 7.43-7.36 (m, 3H), 7.31-7.29 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 146.8, 143.4, 139.9, 137.0, 133.5, 132.5, 131.5, 129.9, 128.9, 128.9, 128.8, 128.7, 128.6, 128.4, 128.0, 127.7, 127.5, 127.3, 127.1, 122.8, 121.7, 118.1, 109.8, 95.2, 87.5. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₉H₁₉NNa⁺ 404.1415; Found 404.1412.



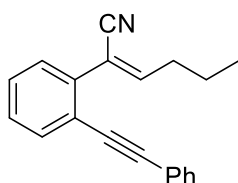
(Z)-2-(2-(phenylethynyl)phenyl)-3-(thiophen-2-yl)acrylonitrile (1m)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 59-61 °C; yield: 2.02 g (65%); ¹H NMR (400 MHz, CDCl₃) δ 7.90 (s, 1H), 7.66-7.61 (m, 2H), 7.56-7.50 (m, 4H), 7.40-7.29 (m, 5H), 7.15-7.12 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 139.3, 137.7, 136.2, 133.6, 132.6, 131.5, 130.4, 128.8, 128.7, 128.5, 128.4, 127.9, 122.8, 121.4, 118.2, 106.8, 95.3, 87.6. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₁H₁₃NNaS⁺ 334.0666; Found 334.0666.



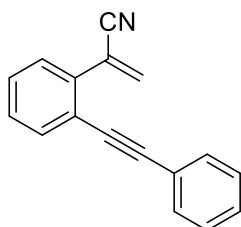
(Z)-2-(2-(phenylethynyl)phenyl)-3-(pyridin-2-yl)acrylonitrile (1n)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 67-69 °C; yield: 2.45 g (80%); ¹H NMR (400 MHz, CDCl₃) δ 8.77-8.76 (m, 1H), 7.93-7.91 (m, 1H), 7.80-7.76 (m, 2H), 7.64-7.58 (m, 2H), 7.53-7.51 (m, 2H), 7.43-7.37 (m, 2H), 7.33-7.27 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 152.1, 150.0, 146.1, 136.8, 136.5, 133.5, 131.6, 129.1, 128.8, 128.6, 128.3, 124.4, 124.2, 122.7, 121.8, 117.4, 113.5, 95.4, 87.3. HRMS (ESI-TOF) m/Z: [M+H]⁺ Calcd for C₂₂H₁₅N₂⁺ 307.1235; Found 307.1240.



(Z)-2-(2-(phenylethynyl)phenyl)hex-2-enenitrile (1o)

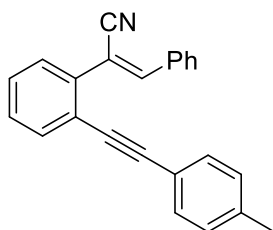
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow oily liquid; yield: 1.79 g (66%); ¹H NMR (400 MHz, CDCl₃) δ 7.60-7.54 (m, 3H), 7.41-7.33 (m, 6H), 6.95 (t, *J* = 7.6 Hz, 1H), 2.60 (q, *J* = 7.6 Hz, 2H), 1.65-1.55 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 152.5, 135.8, 133.3, 131.5, 128.7, 128.6, 128.6, 128.4, 128.4, 122.9, 121.4, 116.6, 114.8, 94.7, 87.4, 34.1, 21.9, 13.6. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₀H₁₇NNa⁺ 294.1259; Found 294.1264.



2-(2-(phenylethynyl)phenyl)acrylonitrile (1p)

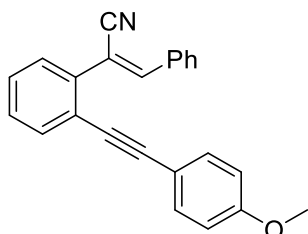
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow liquid; yield: 0.92 g (40%); ¹H NMR (400 MHz, CDCl₃) δ 7.92-

7.54 (m, 3H), 7.46-7.42 (m, 1H), 7.38-7.33 (m, 5H), 6.50 (s, 1H), 6.34 (s, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 134.8, 134.0, 133.4, 131.6, 129.3, 128.8, 128.8, 128.6, 128.5, 122.7, 122.3, 121.3, 117.8, 95.5, 87.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{11}\text{NNa}^+$ 252.0786; Found 252.0781.



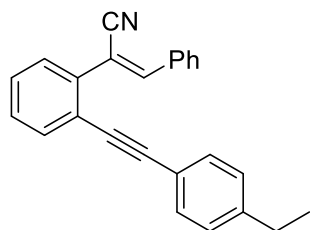
(Z)-3-phenyl-2-(2-(p-tolylethynyl)phenyl)acrylonitrile (1q)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 81-83 °C; yield: 2.39 g (75%); ^1H NMR (400 MHz, CDCl_3) δ 7.93-7.91 (m, 2H), 7.71 (s, 1H), 7.65-7.62 (m, 1H), 7.56-7.53 (m, 1H), 7.50-7.45 (m, 3H), 7.42-7.35 (m, 4H), 7.12 (d, $J = 7.6$ Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 147.3, 138.8, 136.9, 133.6, 133.4, 131.4, 130.7, 129.3, 129.2, 128.9, 128.9, 128.7, 128.6, 121.9, 119.7, 118.0, 110.2, 95.4, 86.8, 21.5. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{24}\text{H}_{17}\text{NNa}^+$ 342.1259; Found 342.1262.



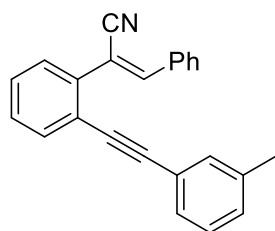
(Z)-2-(2-((4-methoxyphenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1r)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 59-61 °C; yield: 2.68 g (80%); ^1H NMR (400 MHz, CDCl_3) δ 7.94-7.91 (m, 2H), 7.69 (s, 1H), 7.64-7.61 (m, 1H), 7.55-7.35 (m, 8H), 6.84 (d, $J = 8.4$ Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.9, 147.2, 136.7, 133.6, 133.2, 133.0, 130.7, 129.3, 129.0, 128.9, 128.7, 128.4, 122.1, 118.0, 114.9, 114.1, 110.3, 95.4, 86.3, 55.3. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{24}\text{H}_{17}\text{NONa}^+$ 358.1208; Found 358.1211.



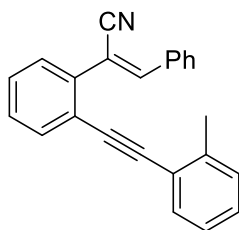
(Z)-2-(2-((4-ethylphenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1s)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 56-57 °C; yield: 2.13 mg (64%); ¹H NMR (400 MHz, CDCl₃) δ 7.73-7.71 (m, 2H), 7.50 (s, 1H), 7.45-7.42 (m, 1H), 7.36-7.33 (m, 1H), 7.30-7.24 (m, 3H), 7.22-7.14 (m, 4H), 6.93 (d, *J* = 8.4 Hz, 2H), 2.43 (q, *J* = 7.6 Hz, 2H), 1.02 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 147.3, 145.1, 136.8, 133.6, 133.4, 131.5, 130.7, 129.9, 129.3, 129.0, 128.9, 128.9, 128.7, 128.6, 128.0, 121.9, 119.9, 118.0, 110.2, 95.4, 86.8, 28.8, 15.3. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₅H₁₉NNa⁺ 356.1410; Found 356.1414.



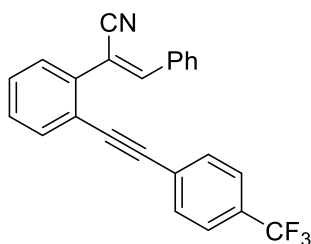
(Z)-3-phenyl-2-(2-(*m*-tolylethynyl)phenyl)acrylonitrile (1t)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 93-95 °C; yield: 54.7 mg (80%); ¹H NMR (400 MHz, CDCl₃) δ 7.95-7.93 (m, 2H), 7.72 (s, 1H), 7.66-7.63 (m, 1H), 7.58-7.2. (m, 1H), 7.51-7.46 (m, 3H), 7.44-7.36 (m, 2H), 7.31-7.28 (m, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.14-7.12 (m, 2H), 2.34 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 138.1, 137.0, 133.6, 133.4, 132.1, 130.7, 129.5, 129.4, 128.9, 128.9, 128.7, 128.6, 128.3, 122.6, 121.8, 118.0, 110.0, 95.3, 87.2, 21.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₄H₁₇NNa⁺ 342.1257; Found 342.1262.



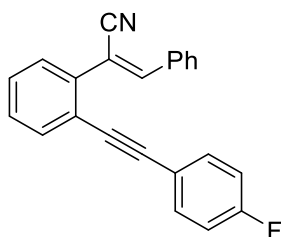
(Z)-3-phenyl-2-(2-(*o*-tolylethynyl)phenyl)acrylonitrile (1u)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 61-62 °C; yield: 56.1 mg (82%); ¹H NMR (400 MHz, CDCl₃) δ 7.94-7.92 (m, 2H), 7.69-7.67 (m, 2H), 7.59-7.57 (m, 1H), 7.51-7.39 (m, 6H), 7.27-7.12 (m, 3H), 2.43 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 147.3, 140.1, 136.8, 133.6, 133.6, 132.0, 130.7, 129.5, 129.3, 128.9, 128.9, 128.7, 128.7, 128.6, 125.6, 122.6, 122.0, 118.0, 110.2, 94.0, 91.2, 20.7. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₄H₁₇NNa⁺ 342.1258; Found 342.1262.



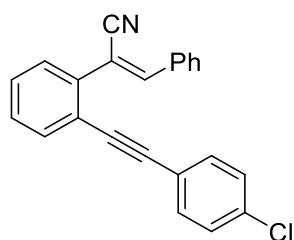
(Z)-3-phenyl-2-(2-(4-(trifluoromethyl)phenyl)ethynyl)phenyl)acrylonitrile(1v)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 73-75 °C; yield: 49.2 mg (68%); ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.91 (m, 2H), 7.66-7.64 (m, 1H), 7.60-7.52 (m, 6H), 7.50-7.37 (m, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 147.6, 137.4, 133.5, 133.4, 131.7, 130.9, 130.3 (q, *J* = 32.5 Hz), 129.4, 129.3, 129.0, 129.0, 128.9, 126.6, 126.6, 125.3 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 270.5 Hz), 122.5, 121.1, 117.8, 110.0, 93.7, 89.6. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.80. HRMS (ESI-TOF) m/Z: [M+Na]⁺ Calcd for C₂₄H₁₄NNaF₃⁺ 396.0976; Found 396.0981.



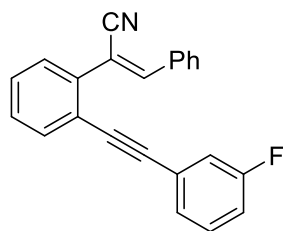
(Z)-2-(2-(4-fluorophenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1w)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 86-88 °C; yield: 53.1 mg (77%); ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.91 (m, 2H), 7.65-7.62 (m, 2H), 7.55-7.45 (m, 6H), 7.44-7.36 (m, 2H), 7.03-6.97 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.7 (d, *J* = 248.5 Hz), 147.4, 137.1, 133.5, 133.5 (d, *J* = 8.4 Hz), 133.3, 130.8, 129.3, 129.0, 128.9, 128.8, 128.8, 121.6, 118.9 (d, *J* = 3.4 Hz), 117.8, 115.7 (d, *J* = 21.9 Hz), 110.2, 94.2, 87.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -110.20. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₃H₁₄NNaF⁺ 345.0962; Found 345.0966.



(Z)-2-(2-((4-chlorophenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1x)

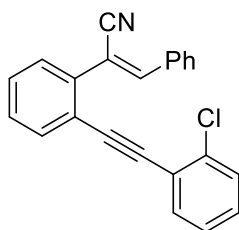
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 103-105 °C; yield: 52.7 mg (73%); ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.91 (m, 2H), 7.65-7.61 (m, 2H), 7.55-7.52 (m, 1H), 7.51-7.46 (m, 3H), 7.45-7.37 (m, 4H), 7.30-7.26 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 137.2, 134.7, 133.5, 133.4, 132.7, 130.8, 129.3, 129.0, 128.9, 128.8, 128.7, 121.5, 121.3, 117.8, 110.6, 94.1, 88.3. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₃H₁₄NNaCl⁺ 361.5489; Found 361.5482.



(Z)-2-(2-((3-fluorophenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1y)

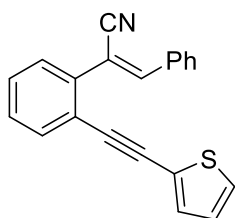
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 68-70 °C; yield: 53.1 mg (77%); ¹H NMR (400 MHz, CDCl₃) δ 7.82-7.77 (m, 2H), 7.53-7.48 (m, 2H), 7.42-7.24 (m, 6H), 7.17-7.06 (m, 3H), 6.92-6.90 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 163.4 (d, *J* = 245.3 Hz), 148.2, 147.5, 137.3, 133.5, 133.5, 130.9, 130.1 (d, *J* = 8.6 Hz), 129.3, 129.3, 129.2, 129.0,

129.02, 128.8, 127.5 (d, $J = 3.0$ Hz), 124.6 (d, $J = 9.4$ Hz), 121.3, 118.3 (d, $J = 22.7$ Hz), 117.9, 116.0 (d, $J = 21.1$ Hz), 110.0, 93.9, 93.9, 88.2. ^{19}F NMR (376 MHz, CDCl_3) δ -112.53. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{14}\text{NNaF}^+$ 345.0962; Found 345.0966.



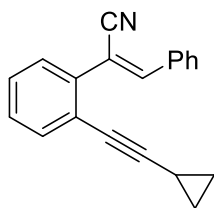
(Z)-2-(2-((2-chlorophenyl)ethynyl)phenyl)-3-phenylacrylonitrile (1z)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 82-84 °C; yield: 52.7 mg (73%); ^1H NMR (400 MHz, CDCl_3) δ 7.93-7.91 (m, 2H), 7.73-7.70 (m, 2H), 7.59-7.58 (m, 1H), 7.54-7.51 (m, 1H), 7.50-7.36 (m, 6H), 7.27-7.17 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 147.6, 137.0, 135.8, 133.9, 133.7, 133.4, 130.7, 129.6, 129.3, 129.2, 129.1, 128.9, 128.9, 128.7, 126.5, 122.8, 121.3, 118.0, 110.0, 92.3, 91.6. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{14}\text{NNaCl}^+$ 361.5489; Found 361.5482.



(Z)-3-phenyl-2-(2-(thiophen-2-ylethynyl)phenyl)acrylonitrile (1aa)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 52-54 °C; yield: 46.8 mg (70%); ^1H NMR (400 MHz, CDCl_3) δ 7.93-7.92 (m, 2H), 7.70 (s, 1H), 7.64-7.61 (m, 1H), 7.58-7.55 (m, 1H), 7.51-7.45 (m, 3H), 7.44-7.35 (m, 2H), 7.29-7.23 (m, 2H), 6.99-6.97 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 147.4, 136.7, 133.5, 133.1, 132.3, 130.7, 129.3, 128.9, 128.9, 128.9, 128.7, 127.9, 127.2, 122.7, 121.3, 117.9, 109.9, 91.2, 88.4. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{13}\text{NNaS}^+$ 334.0670; Found 334.0666.

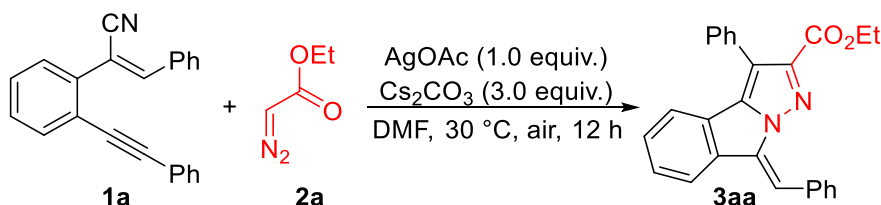


(Z)-2-(2-(cyclopropylethynyl)phenyl)-3-phenylacrylonitrile (**1ab**)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Pale yellow solid; m.p.: 67-69 °C; yield: 46.8 mg (70%); ¹H NMR (400 MHz, CDCl₃) δ 7.91-7.88 (m, 2H), 7.51 (s, 1H), 7.50-7.45 (m, 5H), 7.35-7.27 (m, 2H), 1.49-1.42 (m, 1H), 0.87-0.78 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 146.4, 136.5, 133.2, 133.0, 130.2, 128.8, 128.5, 128.3, 128.1, 127.5, 122.0, 117.4, 109.9, 99.5, 73.4, 8.3. HRMS (ESI-TOF) m/Z: [M+H]⁺ Calcd for C₂₀H₁₆N⁺ 270.1277; Found 270.1283.

3. Experimental section and analytical data of compound 3

3.1 General procedure for the preparation of **3** (**3aa** as example).^[3]

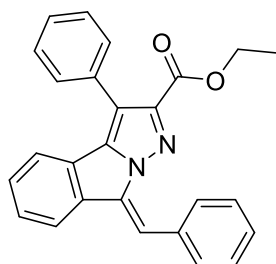


A 35 mL sealed tube equipped with a magnetic stir bar was charged with **1a** (0.2 mmol, 61.1 mg), ethyl diazoacetate (0.4 mmol, 42 μL), AgOAc (0.2 mmol, 33.4 mg), and Cs₂CO₃ (0.6 mmol, 195.5 mg) in DMF (3.0 mL). The reaction mixture was stirred at 30 °C under air for 12 h. Upon completion (monitored by TLC), the solvent was extracted three times with CH₂Cl₂, and then the combined organic layers were washed three times with saturated brine. The aqueous phase was treated with NaClO(aq) to quench the formed cyanide by-products. Then, the combined organic layers were dried with anhydrous MgSO₄, filtered, and evaporated in vacuo. The resulting crude residue was purified by silica gel column chromatography (EtOAc/petroleum ether = 1:10, v/v) to afford the pure product **3aa** (62.0 mg, 79%) as a yellow solid.

3.2 A gram-scale synthesis of compound **3aa**:

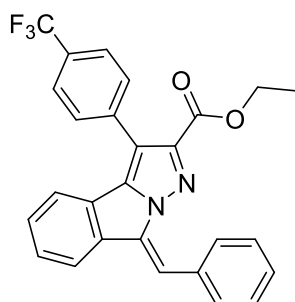
A sealed tube (75 mL) equipped with a magnetic stir bar was charged with **1a** (4 mmol), ethyl diazoacetate (8 mmol), AgOAc (4 mmol), Cs₂CO₃ (12 mmol), and DMF (0.1 M). The resulting mixture was stirred at 30 °C under air for 12 hours. Upon completion, the solvent was extracted three times with CH₂Cl₂, and then the combined organic layers were washed three times with saturated brine. The aqueous phase was treated with NaClO(aq) to quench the formed cyanide by-products. Then, the combined organic layers were dried with anhydrous MgSO₄, filtered, and evaporated in vacuo. The resulting crude residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate and petroleum ether, to afford product **3aa** (1.00 g, 64%) as a yellow solid.

3.3. Characterization Data of Compound **3**.



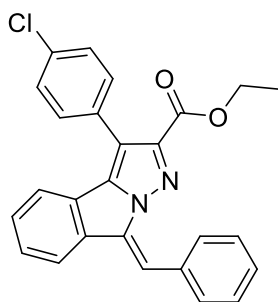
Ethyl(Z)-8-benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aa)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 148-149 °C; yield: 62.0 mg (79%); ¹H NMR (400 MHz, CDCl₃) δ 8.20 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.30-7.12 (m, 8H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.79 (s, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 1.11 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.3, 144.2, 143.6, 137.3, 132.6, 131.2, 131.1, 130.5, 129.9, 129.4, 128.9, 128.3, 128.1, 128.0, 127.8, 127.4, 120.4, 120.2, 118.0, 115.0, 60.8, 14.0. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₆H₂₀N₂O₂Na⁺ 415.1422; found 415.1426.



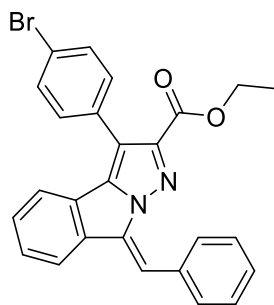
Ethyl(*Z*)-8-benzylidene-3-(4-(trifluoromethyl)phenyl)-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ab)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 189-190 °C; yield: 77.2 mg (84%); ¹H NMR (400 MHz, CDCl₃) δ 8.20 (d, *J* = 7.6 Hz, 2H), 7.55-7.49 (m, 5H), 7.33-7.28 (m, 2H), 7.26-7.22 (m, 1H), 7.19-7.15 (m, 2H), 7.12-7.08 (m, 1H), 6.77 (s, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.1, 143.9, 143.7, 137.3, 135.1, 132.4, 131.3, 130.3, 130.2, 129.7 (q, *J* = 3.6 Hz), 129.6, 128.9, 128.3, 128.3, 126.8, 125.0 (q, *J* = 3.6 Hz), 124.3 (q, *J* = 270.5 Hz), 120.5, 120.0, 116.4, 115.6, 61.0, 14.0. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.47. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₇H₁₉F₃N₂O₂Na⁺ 483.1296; found 483.1299.



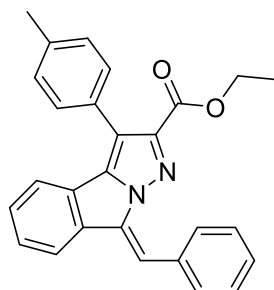
Ethyl(*Z*)-8-benzylidene-3-(4-chlorophenyl)-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ac)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 186-187 °C; yield: 74.1 mg (87%); ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.40-7.19 (m, 9H), 7.15-7.11 (m, 1H), 6.83 (s, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 143.9, 143.6, 137.2, 133.7, 132.5, 131.3, 131.3, 130.4, 129.6, 129.5, 128.9, 128.3, 128.3, 128.1, 127.0, 120.4, 120.1, 116.7, 115.3, 60.9, 14.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₆H₁₉ClN₂O₂Na⁺ 449.1033; found 449.1037.



Ethyl(Z)-8-benzylidene-3-(4-bromophenyl)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ad)

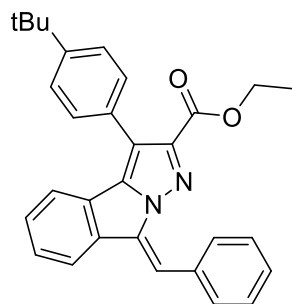
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 172-173 °C; yield: 74.2 mg (79%); ¹H NMR (400 MHz, CDCl₃) δ 8.38 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.62-7.59 (m, 2H), 7.51-7.46 (m, 4H), 7.44-7.43 (m, 3H), 7.30-7.26 (m, 1H), 6.97 (s, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.2, 143.9, 143.6, 137.3, 132.6, 131.7, 131.3, 131.3, 130.4, 130.1, 129.6, 128.9, 128.3, 128.2, 127.0, 121.9, 120.5, 120.1, 116.8, 115.4, 60.9, 14.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₆H₁₉BrN₂O₂Na⁺ 493.0528; found 493.0531.



Ethyl(Z)-8-benzylidene-3-(*p*-tolyl)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ae)

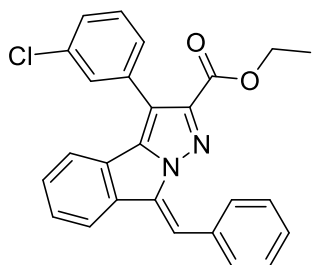
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 155-156 °C; yield: 62.5 mg (77%); ¹H NMR (400 MHz, CDCl₃) δ 8.39 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.49-7.43 (m, 5H), 7.40-7.36 (m, 1H), 7.33-7.22 (m, 4H), 6.95 (s, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.4, 144.2, 143.5, 137.5, 137.3, 132.7, 131.3, 130.6, 129.9, 129.4, 128.9, 128.9, 128.3, 128.0, 127.9, 127.5, 120.4, 120.2, 118.2, 114.9, 60.9, 21.4, 14.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for

C₂₇H₂₂N₂O₂Na⁺ 429.1579; found 429.1582.



Ethyl(Z)-8-benzylidene-3-(4-(*tert*-butyl)phenyl)-8H-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3af)

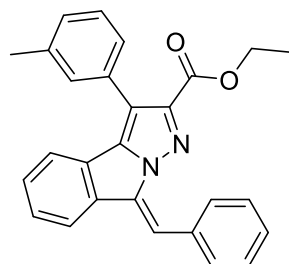
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 165-166 °C; yield: 64.5 mg (72%); ¹H NMR (400 MHz, CDCl₃) δ 8.38 (d, *J* = 7.6 Hz, 2H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.55-7.53 (m, 2H), 7.49-7.44 (m, 5H), 7.40-7.36 (m, 1H), 7.33-7.24 (m, 2H), 6.95 (s, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 1.39 (s, 9H), 1.33 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 150.7, 144.2, 143.5, 137.3, 132.7, 131.3, 130.6, 129.6, 129.4, 128.9, 128.3, 127.9, 127.5, 125.0, 120.3, 120.3, 118.2, 114.8, 60.8, 34.7, 31.4, 14.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₃₀H₂₈N₂O₂Na⁺ 471.2048; found 471.2051.



Ethyl(Z)-8-benzylidene-3-(3-chlorophenyl)-8H-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ag)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 147-148 °C; yield: 71.5 mg (84%); ¹H NMR (400 MHz, CDCl₃) δ 8.31 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.54 (s, 1H), 7.44-7.40 (m, 3H), 7.36-7.31 (m, 4H), 7.30-7.26 (m, 1H), 7.24-7.19 (m, 1H), 6.90 (s, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.1, 144.1, 143.7, 137.3, 133.9, 133.1, 132.5, 131.4, 130.3, 130.1, 129.6, 129.4, 129.0, 128.3, 128.2, 128.2, 127.8, 126.9, 120.5, 120.1, 116.4, 115.5, 61.0, 14.1. HRMS (ESI-TOF) *m/z*:

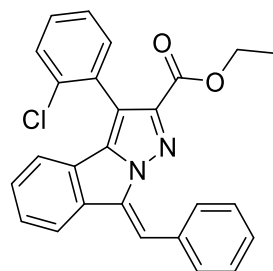
$[M+Na]^+$ calcd for $C_{26}H_{19}ClN_2O_2Na^+$ 449.1033; found 449.1036.



Ethyl(Z)-8-benzylidene-3-(*m*-tolyl)-8H-pyrazolo[5,1-*a*]isoindole-2-carboxylate

(3ah)

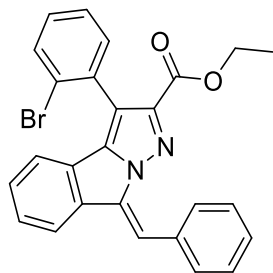
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 120-121 °C; yield: 56.9 mg (70%); 1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, $J = 7.2$ Hz, 2H), 7.64 (d, $J = 7.6$ Hz, 1H), 7.44-7.40 (m, 2H), 7.38-7.29 (m, 5H), 7.28-7.24 (m, 1H), 7.22-7.20 (m, 1H), 7.18-7.14(m, 1H), 6.90 (s, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.37 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 144.3, 143.6, 137.6, 137.3, 132.7, 131.3, 131.0, 130.6, 130.5, 129.4, 128.9, 128.5, 128.3, 128.0, 127.9, 127.4, 127.1, 120.4, 120.2, 118.2, 115.0, 60.8, 21.6, 14.1. HRMS (ESI-TOF) m/Z: $[M+Na]^+$ calcd for $C_{27}H_{22}N_2O_2Na^+$ 429.1579; found 429.1583.



Ethyl(Z)-8-benzylidene-3-(2-chlorophenyl)-8H-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ai)

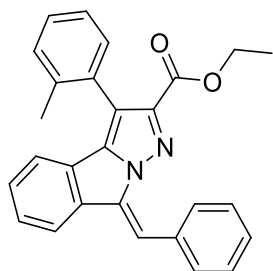
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 138-139 °C; yield: 69.0 mg (81%); 1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, $J = 7.6$ Hz, 2H), 7.73 (d, $J = 8.0$ Hz, 1H), 7.57-7.4 (m, 4H), 7.44-7.33 (m, 4H), 7.30-7.26 (m, 1H), 7.21-7.18 (m, 1H), 7.03 (s, 1H), 4.30 (m, 2H), 1.26 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 145.3, 144.3, 137.3, 134.4, 132.6, 131.9, 131.3, 130.8, 130.6, 129.6, 129.5, 129.3, 128.9, 128.4, 128.2, 127.1,

126.5, 120.6, 120.4, 115.4, 114.2, 60.9, 13.9. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{26}H_{19}ClN_2O_2Na^+$ 449.1033; found 449.1036.



Ethyl(Z)-8-benzylidene-3-(2-bromophenyl)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aj)

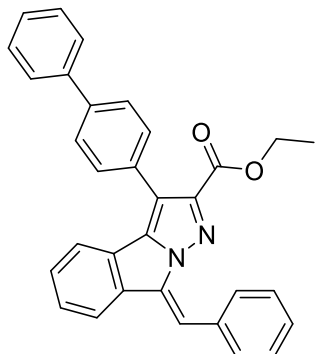
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 163-164 °C; yield: 68.8 mg (73%); 1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, $J = 7.6$ Hz, 2H), 7.65 (d, $J = 8.0$ Hz, 2H), 7.45-7.40 (m, 3H), 7.36-7.31 (m, 2H), 7.30-7.26 (m, 1H), 7.24-7.18 (m, 2H), 7.09 (d, $J = 7.6$ Hz, 1H), 6.96 (s, 1H), 4.21 (m, 2H), 1.16 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 145.2, 144.2, 137.3, 132.9, 132.7, 132.6, 131.8, 131.3, 130.6, 129.5, 129.5, 128.9, 128.4, 128.2, 127.1, 127.0, 124.8, 120.7, 120.4, 116.0, 115.5, 60.9, 13.9. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{26}H_{19}BrN_2O_2Na^+$ 493.0528; found 493.0532.



Ethyl(Z)-8-benzylidene-3-(*o*-tolyl)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ak)

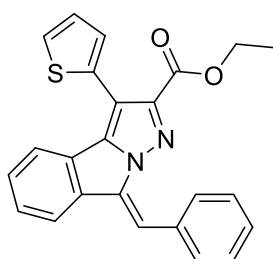
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 109-110 °C; yield: 37.4 mg (46%); 1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, $J = 7.6$ Hz, 2H), 7.76 (d, $J = 7.6$ Hz, 1H), 7.54-7.50 (m, 2H), 7.45-7.41 (m, 1H), 7.39-7.34 (m, 4H), 7.30-7.25 (m, 2H), 7.10 (d, $J = 7.6$ Hz, 1H), 7.05 (s, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.24 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 145.1, 144.0, 137.3, 132.7, 131.2, 130.9, 130.7, 130.3, 129.9,

129.5, 129.0, 128.4, 128.1, 127.9, 127.4, 125.5, 120.4, 120.3, 116.7, 115.1, 60.7, 20.1, 13.9. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{27}H_{22}N_2O_2Na^+$ 429.1579; found 429.1582.



Ethyl(*Z*)-3-([1,1'-biphenyl]-4-yl)-8-benzylidene-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3al)

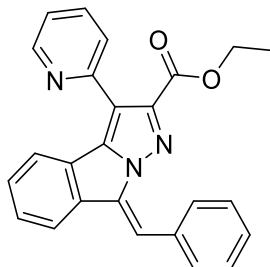
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 172-173 °C; yield: 56.1 mg (60%); 1H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, $J = 7.6$ Hz, 2H), 7.70-7.65 (m, 7H), 7.50-7.43 (m, 5H), 7.41-7.30 (m, 3H), 7.28-7.24 (m, 1H), 6.96 (s, 1H), 4.34 (q, $J = 7.2$ Hz, 2H), 1.34 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 144.2, 143.6, 140.8, 140.5, 137.3, 132.7, 131.3, 130.5, 130.4, 130.1, 129.5, 128.9, 128.9, 128.3, 128.1, 127.4, 127.4, 127.1, 126.8, 120.4, 120.3, 117.8, 115.1, 60.9, 14.2. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{32}H_{24}N_2O_2Na^+$ 491.1735; found 491.1737.



Ethyl(*Z*)-8-benzylidene-3-(thiophen-2-yl)-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3am)

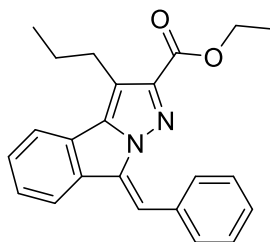
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 142-143 °C; yield: 35.8 mg (45%); 1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, $J = 7.6$ Hz, 2H), 7.69 (t, $J = 7.6$ Hz, 2H), 7.46-7.42 (m, 2H), 7.40-7.27 (m, 5H), 7.13-7.10 (m, 1H), 6.95 (s, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 1.33 (t, J

= 7.2 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.1, 144.6, 144.1, 137.2, 132.6, 131.3, 130.4, 129.5, 128.9, 128.8, 128.3, 128.2, 127.1, 127.0, 126.1, 120.6, 120.4, 115.3, 110.4, 61.0, 14.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{18}\text{SN}_2\text{O}_2\text{Na}^+$ 421.0987; found 421.0991.



Ethyl(Z)-8-benzylidene-3-(pyridin-2-yl)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3an)

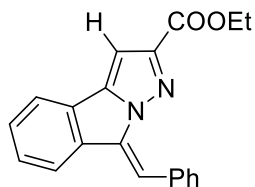
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 147-148 °C; yield: 62.1 mg (79%); ^1H NMR (400 MHz, CDCl_3) δ 8.75 (d, $J = 4.8$ Hz, 1H), 8.37 (d, $J = 7.6$ Hz, 2H), 7.97-7.94 (m, 1H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.75 (td, $J = 8.0, 2.0$ Hz, 1H), 7.70-7.68 (m, 1H), 7.48-7.44 (m, 2H), 7.41-7.33 (m, 3H), 7.27-7.24 (m, 1H), 6.99 (s, 1H), 4.38 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.7, 151.1, 149.0, 145.2, 143.9, 137.4, 135.9, 132.7, 131.4, 130.6, 129.5, 129.0, 128.8, 128.3, 128.3, 127.5, 125.3, 122.5, 122.2, 120.1, 118.1, 115.3, 61.1, 14.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{20}\text{N}_3\text{O}_2^+$ 394.1556; found 394.1559.



Ethyl(Z)-8-benzylidene-3-propyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ao)

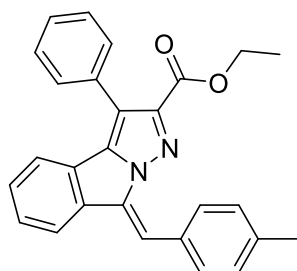
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 84-85 °C; yield: 19.3 mg (27%); ^1H NMR (400 MHz, CDCl_3) δ 8.40 (d, $J = 7.6$ Hz, 2H), 7.75 (d, $J = 7.2$ Hz, 1H), 7.61 (d, $J = 7.6$ Hz, 1H), 7.49-7.36 (m, 5H), 6.94 (s, 1H), 4.42 (q, $J = 7.2$ Hz, 2H), 3.02 (t, $J = 7.2$ Hz, 2H), 1.79-1.69 (m, 2H), 1.45 (t, $J = 7.2$ Hz, 3H), 1.01 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz,

CDCl₃) δ 162.9, 145.1, 143.9, 137.2, 132.8, 131.1, 130.7, 129.3, 129.0, 128.3, 128.0, 127.4, 120.5, 120.1, 118.2, 114.3, 60.7, 25.8, 23.9, 14.2, 13.9. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₂₃H₂₂N₂O₂Na⁺ 381.1579; found 381.1580.



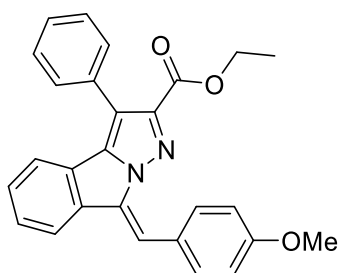
Ethyl (Z)-8-benzylidene-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ap)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. White solid; m.p.: 150-151 °C; yield: 24 mg (38%); ¹H NMR (400 MHz, CDCl₃) δ 8.15-8.12 (m, 1H), 7.97-7.94 (m, 2H), 7.78-7.74 (m, 1H), 7.63-7.47 (m, 6H), 7.19 (s, 1H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.43 (t, $J = 7.2$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.8, 144.1, 140.3, 138.5, 133.0, 129.5, 129.5, 129.0, 128.5, 128.4, 127.9, 127.4, 124.0, 123.5, 115.0, 100.8, 61.2, 14.4. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₂₀H₁₆N₂O₂Na⁺ 339.1115; found 339.1112.



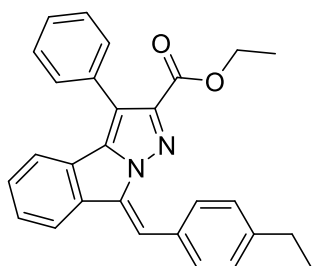
Ethyl (Z)-8-(4-methylbenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aq)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 134-135 °C; yield: 57.7 mg (71%); ¹H NMR (400 MHz, CDCl₃) δ 8.33 (d, $J = 8.0$ Hz, 2H), 7.70 (d, $J = 7.6$ Hz, 1H), 7.62 (6.8 Hz, 2H), 7.51-7.41 (m, 4H), 7.35-7.24 (m, 4H), 6.97 (s, 1H), 4.36 (q, $J = 7.2$ Hz, 2H), 2.44 (s, 3H), 1.35 (s, $J = 7.2$ Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.4, 144.0, 143.5, 139.8, 137.4, 131.4, 131.3, 130.0, 129.9, 129.8, 129.1, 128.7, 128.1, 127.9, 127.7, 127.2, 120.3, 120.1, 117.9, 115.3, 60.8, 21.7, 14.1. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₂₇H₂₂N₂O₂Na⁺ 429.1579; found 429.1582.



Ethyl(Z)-8-(4-methoxybenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ar)

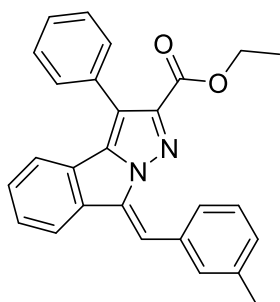
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 152-153 °C; yield: 65.0 mg (77%); ¹H NMR (400 MHz, CDCl₃) δ 8.45 (d, *J* = 9.2 Hz, 2H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.63-7.61 (m, 2H), 7.51-7.46 (m, 2H), 7.45-7.41 (m, 2H), 7.34-7.30 (m, 1H), 7.26-7.22 (m, 1H), 7.02-7.00 (m, 2H), 6.93 (s, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.88 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 160.6, 143.7, 143.3, 137.5, 133.3, 131.3, 130.0, 128.7, 128.4, 128.1, 127.8, 127.7, 126.9, 125.6, 120.1, 120.0, 117.8, 115.2, 113.8, 60.8, 55.4, 14.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₇H₂₂N₂O₃Na⁺ 445.1528; found 445.1530.



Ethyl(Z)-8-(4-ethylbenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3as)

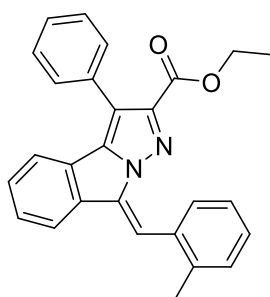
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 125-126 °C; yield: 38.6 mg (46%); ¹H NMR (400 MHz, CDCl₃) δ 8.26 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.52-7.49 (m, 2H), 7.39-7.21 (m, 7H), 7.18-7.14 (m, 1H), 6.89 (s, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.25-1.17 (m, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 162.4, 146.1, 144.0, 143.5, 137.4, 131.4, 131.2, 130.2, 130.0, 129.9, 128.7, 128.1, 127.9, 127.7, 127.2, 120.3,

120.2, 117.9, 115.3, 60.8, 28.9, 15.4, 14.1. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{28}H_{24}N_2O_2Na^+$ 443.1735; found 443.1738.



Ethyl(*Z*)-8-(3-methylbenzylidene)-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3at)

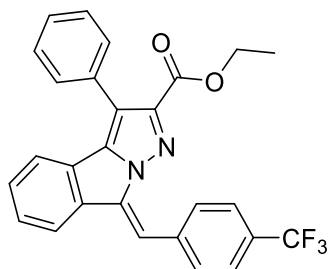
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 129-130 °C; yield: 65.0 mg (80%); 1H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.00 (d, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 7.6$ Hz, 1H), 7.64-7.61 (m, 2H), 7.51-7.31 (m, 6H), 7.28-7.22 (m, 2H), 6.96 (s, 1H), 4.37 (q, $J = 7.2$ Hz, 2H), 2.50 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 143.9, 143.6, 137.9, 137.4, 132.6, 131.8, 131.1, 130.3, 130.0, 128.2, 128.7, 128.2, 128.1, 127.9, 127.8, 127.2, 120.3, 120.1, 118.1, 115.3, 60.9, 21.6, 14.2. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{27}H_{22}N_2O_2Na^+$ 429.1579; found 429.1583.



Ethyl(*Z*)-8-(2-methylbenzylidene)-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3au)

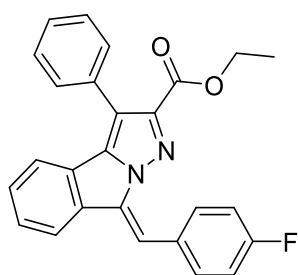
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 123-124 °C; yield: 60.1 mg (74%); 1H NMR (400 MHz, $CDCl_3$) δ 8.35-8.32 (m, 1H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.54-7.52 (m, 2H), 7.43-7.38 (m, 3H), 7.35-7.19 (m, 6H), 7.07 (s, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 2.39 (s, 3H), 1.20 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 144.4, 143.6, 137.4,

136.9, 131.4, 131.3, 131.2, 130.7, 130.0, 129.9, 129.4, 129.1, 128.1, 128.1, 127.7, 127.6, 125.4, 120.6, 120.3, 118.1, 112.6, 60.8, 20.5, 14.0. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{27}H_{22}N_2O_2Na^+$ 429.1579; found 429.1583.



Ethyl(Z)-3-phenyl-8-(4-(trifluoromethyl)benzylidene)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3av)

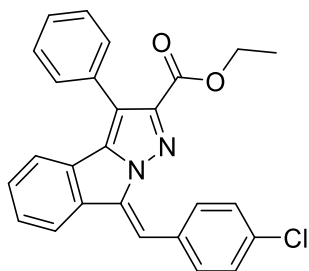
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 171-172 °C; yield: 59.8 mg (65%); 1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, $J = 8.4$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 3H), 7.61-7.58 (m, 2H), 7.50-7.28 (m, 6H), 6.94 (s, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 1.33 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 144.7, 143.8, 136.8, 136.1, 132.1, 131.2, 130.8, 130.0 (q, $J = 32.8$ Hz), 129.9, 129.5, 128.2, 128.1, 127.9, 127.6, 125.1, 125.1 (q, $J = 3.4$ Hz), 124.1 (q, $J = 270.0$ Hz), 120.7, 120.3, 118.4, 112.7, 61.0, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{27}H_{19}F_3N_2O_2Na^+$ 483.1296; found 483.1299.



Ethyl(Z)-8-(4-fluorobenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aw)

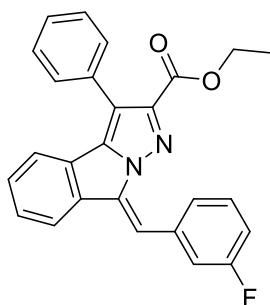
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 177-178 °C; yield: 68.1 mg (83%); 1H NMR (400 MHz, $CDCl_3$) δ 8.42-8.37 (m, 2H), 7.65-7.57 (m, 3H), 7.48-7.44 (m, 2H), 7.41-7.38 (m, 2H), 7.32-7.28 (m, 1H), 7.26-7.22 (m, 1H), 7.15-7.10 (m, 2H), 6.87 (s, 1H), 4.33 (q, $J = 7.2$

Hz, 2H), 1.32 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 163.1 (d, $J = 249.5$ Hz), 162.3, 144.1, 143.5, 137.1, 133.4 (d, $J = 8.2$ Hz), 131.0, 130.1 (d, $J = 2.3$ Hz), 129.9, 128.9, 128.1, 128.0, 127.8, 127.2, 120.2 (d, $J = 6.6$ Hz), 118.0, 115.3 (d, $J = 21.4$ Hz), 113.7, 60.9, 14.1. ^{19}F NMR (376 MHz, CDCl_3) δ -110.30. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{19}\text{FN}_2\text{O}_2\text{Na}^+$ 433.1328; found 433.1330.



Ethyl(Z)-8-(4-chlorobenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ax)

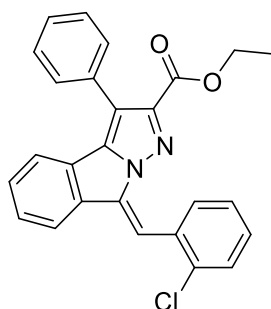
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 163-164 °C; yield: 70.0 mg (82%); ^1H NMR (400 MHz, CDCl_3) δ 8.16 (d, $J = 8.4$ Hz, 2H), 7.48-7.43 (m, 3H), 7.34-7.23 (m, 6H), 7.17-7.07 (m, 2H), 6.66 (s, 1H), 4.19 (q, $J = 7.2$ Hz, 2H), 1.18 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.2, 144.3, 143.6, 137.0, 135.1, 132.5, 131.2, 130.9, 130.7, 129.9, 129.1, 128.5, 128.1, 128.0, 127.8, 127.3, 120.4, 120.2, 118.1, 113.4, 60.9, 14.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{19}\text{ClN}_2\text{O}_2\text{Na}^+$ 449.1033; found 449.1036.



Ethyl(Z)-8-(3-fluorobenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ay)

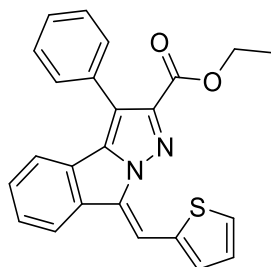
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 143-144 °C; yield: 62.3 mg (76%); ^1H NMR (400 MHz, CDCl_3) δ 8.58 (d, $J = 11.2$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 7.6$ Hz,

1H), 7.58 (d, $J = 7.2$ Hz, 2H), 7.47-7.22 (m, 7H), 7.09-7.04 (m, 1H), 6.86 (s, 1H), 4.32 (q, $J = 7.2$ Hz, 2H), 1.34 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.4 (d, $J = 272.9$ Hz), 162.2, 144.3, 143.6, 137.0, 134.8 (d, $J = 8.8$ Hz), 131.2, 130.8, 129.9, 129.5 (d, $J = 8.2$ Hz), 129.2, 128.1, 128.1, 127.8, 127.5, 127.3, 127.3, 120.4, 120.0, 118.3, 117.7 (d, $J = 23.8$ Hz), 116.2 (d, $J = 21.4$ Hz), 113.5, 113.4, 61.0, 14.0. ^{19}F NMR (376 MHz, CDCl_3) δ -112.71. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{19}\text{FN}_2\text{O}_2\text{Na}^+$ 433.1328; found 433.1329.



Ethyl(Z)-8-(2-chlorobenzylidene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3az)

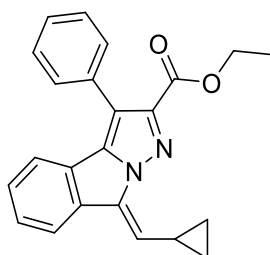
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 185-186 °C; yield: 70.8 mg (83%); ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 7.6$ Hz, 1H), 7.51-7.48 (m, 2H), 7.40-7.20 (m, 10H), 4.20 (q, $J = 7.2$ Hz, 2H), 1.18 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.2, 144.6, 143.8, 136.9, 134.6, 132.3, 132.1, 131.0, 130.6, 130.4, 129.9, 129.4, 129.2, 128.2, 128.1, 127.8, 127.6, 126.1, 120.9, 120.3, 118.3, 110.4, 60.8, 14.0. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{26}\text{H}_{19}\text{ClN}_2\text{O}_2\text{Na}^+$ 449.1033; found 449.1036.



Ethyl(Z)-3-phenyl-8-(thiophen-2-ylmethylene)-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aaa)

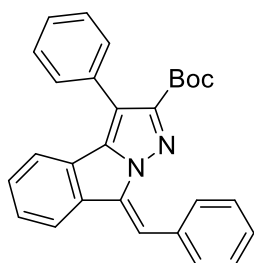
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V)

as an eluent. Yellow solid; m.p.: 170-171 °C; yield: 74.9 mg (94%); ¹H NMR (400 MHz, CDCl₃) δ 8.20 (d, *J* = 3.6 Hz, 1H), 7.60-7.54 (m, 3H), 7.49-7.47 (m, 1H), 7.43-7.34 (m, 4H), 7.26-7.22 (m, 1H), 7.20-7.17 (m, 1H), 7.16-7.13 (m, 1H), 7.08 (s, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 144.1, 142.6, 136.6, 136.5, 133.6, 131.2, 130.2, 130.0, 128.6, 128.2, 128.1, 127.8, 127.7, 127.6, 127.0, 120.2, 120.1, 118.1, 107.1, 60.9, 14.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₄H₁₈SN₂O₂Na⁺ 421.0987; found 421.0990.



Ethyl(Z)-8-(cyclopropylmethylene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3aab)

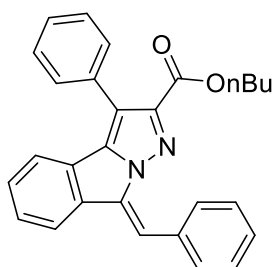
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. White solid; m.p.: 160-161 °C; yield: 48.4 mg (68%); ¹H NMR (400 MHz, CDCl₃) δ 7.59-7.57 (m, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.48-7.39 (m, 4H), 7.32-7.28 (m, 1H), 7.26-7.21 (m, 1H), 5.60 (d, *J* = 10.8 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.37-3.33 (m, 1H), 1.29-1.21 (m, 5H), 0.80-0.76 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.7, 143.9, 142.8, 135.6, 131.6, 131.5, 130.0, 128.1, 128.0, 127.8, 127.5, 126.5, 123.9, 120.1, 119.7, 117.3, 60.9, 14.1, 10.8, 9.8. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₃H₂₀N₂O₂Na⁺ 379.1422; found 379.1426.



tert-Butyl(Z)-8-benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ba)

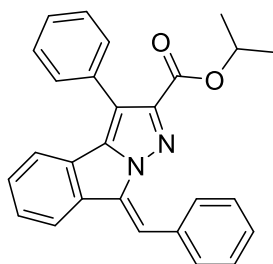
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V)

as an eluent. Yellow solid; m.p.: 149-150 °C; yield: 63.0 mg (75%); ¹H NMR (400 MHz, CDCl₃) δ 8.47-8.44 (m, 2H), 7.73 (d, *J*=8.0 Hz, 1H), 7.59-7.56 (m, 2H), 7.52-7.45 (m, 4H), 7.43-7.38 (m, 3H), 7.37-7.33 (m, 1H), 7.30-7.25 (m, 1H), 6.99 (s, 1H), 1.50 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 161.4, 145.6, 143.5, 137.3, 132.8, 131.6, 131.3, 130.5, 129.9, 129.4, 128.9, 128.3, 128.1, 127.9, 127.6, 127.5, 120.4, 120.1, 117.7, 114.8, 81.5, 28.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₈H₂₄N₂O₂Na⁺ 443.1735; found 443.1735.



Butyl(*Z*)-8-benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ca)

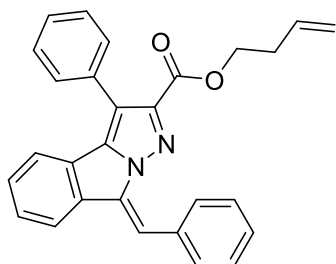
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 125-126 °C; yield: 57.1 mg (68%); ¹H NMR (400 MHz, CDCl₃) δ 8.44-8.41 (m, 2H), 7.72 (d, *J*= 7.6 Hz, 1H), 7.63-7.60 (m, 2H), 7.51-7.40 (m, 7H), 7.37-7.32 (m, 1H), 7.30-7.25 (m, 1H), 6.99 (s, 1H), 4.30 (t, *J*= 6.4 Hz, 2H), 1.73-1.65 (m, 2H), 1.49-1.39 (m, 2H), 0.97 (t, *J*= 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 144.2, 143.6, 137.3, 132.7, 131.3, 131.1, 130.5, 129.9, 129.4, 128.9, 128.3, 128.1, 128.0, 127.7, 127.3, 120.4, 120.2, 118.0, 115.0, 64.6, 30.6, 19.2, 13.8. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₈H₂₄N₂O₂Na⁺ 443.1735; found 443.1738.



(*Z*)-1-(8-Benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindol-2-yl)-2-methylpropan-1-one (3da)

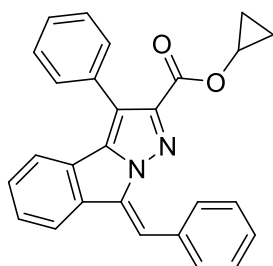
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 97-98 °C; yield: 71.5 mg (88%); ¹H NMR (400 MHz,

CDCl₃) δ 8.43-8.41 (m, 2H), 7.70-7.67 (m, 1H), 7.59-7.57 (m, 2H), 7.49-7.36 (m, 7H), 7.33-7.29 (m, 1H), 7.26-7.22 (m, 1H), 6.96 (s, 1H), 5.24-5.14 (m, 1H), 1.30-1.27 (m, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 161.9, 144.7, 143.5, 137.3, 132.7, 131.4, 131.3, 130.5, 130.0, 129.4, 128.9, 128.3, 128.1, 128.0, 127.7, 127.4, 120.4, 120.2, 117.9, 115.0, 68.5, 21.8. HRMS (ESI-TOF) m/Z: [M+Na]⁺ calcd for C₂₇H₂₂N₂O₂Na⁺ 429.1579; found 429.1582.



But-3-en-1-yl(*Z*)-8-benzylidene-3-phenyl-8H-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ea)

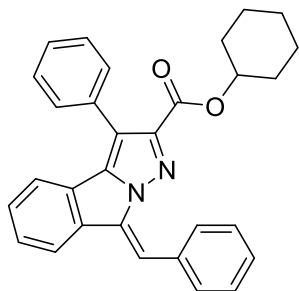
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 96-97 °C; yield: 43.5 mg (52%); ¹H NMR (400 MHz, CDCl₃) δ 8.41-8.38 (m, 2H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.61-7.57 (m, 2H), 7.50-7.38 (m, 7H), 7.35-7.31 (m, 1H), 7.28-7.23 (m, 1H), 6.98 (s, 1H), 5.87-5.76 (m, 1H), 5.16-5.06 (m, 2H), 4.32 (t, *J* = 6.4 Hz, 2H), 2.47-2.42 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.3, 144.0, 143.6, 137.3, 134.1, 132.7, 131.3, 131.1, 130.5, 129.9, 129.4, 128.9, 128.3, 128.1, 128.0, 127.8, 127.3, 120.4, 120.2, 118.1, 117.2, 115.1, 64.1, 32.9. HRMS (ESI-TOF) m/Z: [M+Na]⁺ calcd for C₂₈H₂₂N₂O₂Na⁺ 441.1579; found 441.1582.



(*Z*)-(8-Benzylidene-3-phenyl-8H-pyrazolo[5,1-*a*]isoindol-2-yl)(cyclopropyl)methanone (3fa)

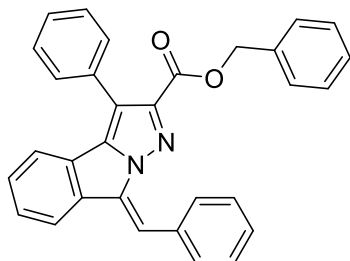
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 155-156 °C; yield: 63.1 mg (78%); ¹H NMR (400 MHz,

CDCl₃) δ 8.18-8.16 (m, 2H), 7.48 (d, J = 7.6 Hz, 1H), 7.38-7.35 (m, 2H), 7.29-7.24 (m, 4H), 7.22-7.17 (m, 3H), 7.14-7.09 (m, 1H), 7.07-7.02 (m, 1H), 6.75 (s, 1H), 4.15-4.10 (m, 1H), 0.56-0.54 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 143.7, 143.6, 137.2, 132.6, 131.3, 131.0, 130.5, 130.0, 129.5, 128.9, 128.3, 128.1, 128.0, 127.8, 127.3, 120.4, 120.2, 118.1, 115.2, 49.3, 5.2. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₂₇H₂₀N₂O₂Na⁺ 427.1422; found 427.1426.



Cyclohexyl(Z)-8-benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ga)

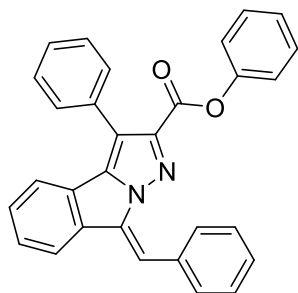
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 214-215 °C; yield: 66.0 mg (74%); ¹H NMR (400 MHz, CDCl₃) δ 8.46-8.44 (m, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.61-7.58 (m, 2H), 7.50-7.38 (m, 7H), 7.35-7.31 (m, 1H), 7.28-7.23 (m, 1H), 6.97 (s, 1H), 5.07-5.01 (m, 1H), 1.89-1.83 (m, 2H), 1.74-1.67 (m, 2H), 1.60-1.34 (m, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 161.8, 144.7, 143.5, 137.3, 132.7, 131.4, 131.3, 130.5, 130.0, 129.4, 128.9, 128.3, 128.1, 127.9, 127.7, 127.4, 120.4, 120.2, 117.9, 115.0, 72.9, 31.3, 25.5, 23.2. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₃₀H₂₆N₂O₂Na⁺ 469.1892; found 469.1896.



Benzyl(Z)-8-benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (3ha)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 159-160 °C; yield: 66.3 mg (73%); ¹H NMR (400 MHz,

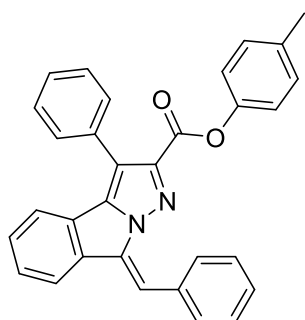
CDCl₃) δ 8.27-8.24 (m, 2H), 7.55 (d, $J = 8.0$ Hz, 1H), 7.47-7.44 (m, 2H), 7.34-7.16 (m, 13H), 7.14-7.09 (m, 1H), 6.83 (s, 1H), 5.20 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.1, 143.8, 143.6, 137.3, 135.9, 132.7, 131.4, 130.1, 130.5, 130.0, 129.5, 128.9, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.8, 127.3, 120.4, 120.2, 118.3, 115.2, 66.3. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for C₃₁H₂₂N₂O₂Na⁺ 477.1579; found 477.1580.



Phenyl(*Z*)-8-benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate

(3ia)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 158-159 °C; yield: 32.5 mg (37%); ¹H NMR (400 MHz, CDCl₃) δ 8.47 (d, $J = 8.0$ Hz, 2H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.69-7.66 (m, 2H), 7.53-7.46 (m, 5H), 7.43-7.38 (m, 5H), 7.35-7.31 (m, 1H), 7.26-7.22 (m, 3H), 7.08 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 150.7, 143.8, 143.2, 137.3, 132.5, 131.3, 130.8, 130.5, 130.0, 129.6, 129.3, 129.0, 128.4, 128.2, 127.9, 127.2, 125.7, 121.6, 120.4, 120.3, 118.8, 115.6. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for C₃₀H₂₀N₂O₂Na⁺ 463.1422; found 463.1425.

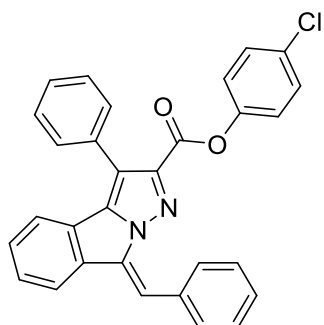


***p*-Tolyl(*Z*)-8-benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate**

(3ja)

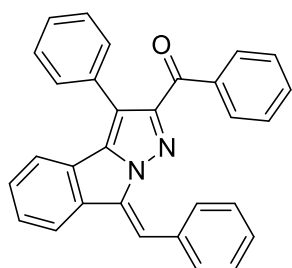
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 117-118 °C; yield: 25.4 mg (28%); ¹H NMR (400 MHz,

CDCl₃) δ 8.46 (d, J = 7.6 Hz, 2H), 7.80 (d, J = 7.6 Hz, 1H), 7.67-7.65 (m, 2H), 7.52-7.31 (m, 9H), 7.20-7.17 (m, 2H), 7.11-7.08 (m, 3H), 2.34 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.8, 148.5, 143.8, 143.3, 137.3, 135.3, 132.5, 131.3, 130.8, 130.5, 130.0, 129.8, 129.6, 129.0, 128.4, 128.2, 127.9, 127.3, 121.3, 120.4, 120.3, 118.7, 115.5, 20.9. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₃₁H₂₂N₂O₂Na⁺ 477.1579; found 477.1581.



4-Chlorophenyl(*Z*)-8-benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindole-2-carboxylate (3ka)

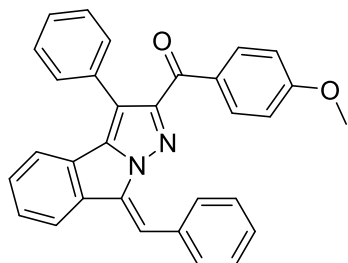
Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 167-168 °C; yield: 25.1 mg (26%); ¹H NMR (400 MHz, CDCl₃) δ 8.45-8.43 (m, 2H), 7.77-7.75 (m, 1H), 7.67-7.66 (m, 2H), 7.52-7.47 (m, 5H), 7.44-7.30 (m, 6H), 7.19-7.15 (m, 2H), 7.06 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 160.4, 149.2, 143.9, 142.8, 137.2, 132.4, 131.3, 131.0, 130.7, 130.5, 130.0, 129.7, 129.4, 129.1, 128.4, 128.3, 128.0, 127.1, 123.0, 120.5, 120.3, 118.9, 115.7. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₃₀H₁₉ClN₂O₂Na⁺ 497.1033; found 497.1034.



(*Z*)-(8-Benzylidene-3-phenyl-8*H*-pyrazolo[5,1-*a*]isoindol-2-yl)(phenyl)methanone (3la)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 180-181 °C; yield: 25.4 mg (30%); ¹H NMR (400 MHz, CDCl₃) δ 8.33-8.22 (m, 4H), 7.78 (d, J = 7.6 Hz, 1H), 7.66-7.31 (m, 14H), 7.04 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 150.7, 143.8, 143.2, 137.3, 132.5, 131.3,

130.8, 130.5, 130.0, 129.6, 129.3, 129.0, 128.4, 128.2, 127.9, 127.2, 125.7, 121.69, 120.4, 120.3, 118.8, 115.6. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{30}H_{20}N_2ONa^+$ 447.1473; found 447.1476.

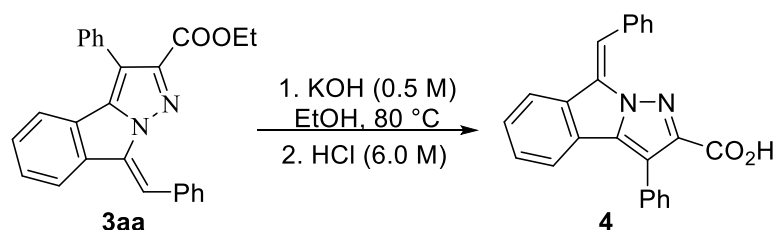


(Z)-(8-Benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindol-2-yl)(4-methoxyphenyl)methanone (3ma)

Purified by column chromatography using petroleum ether/ ethyl acetate (10:1, V/V) as an eluent. Yellow solid; m.p.: 202-203 °C; yield: 25.4 mg (28%); 1H NMR (400 MHz, $CDCl_3$) δ 8.34-8.30 (m, 4H), 7.78-7.76 (m, 1H), 7.64-7.62 (m, 2H), 7.56-7.54 (m, 1H), 7.49-7.45 (m, 2H), 7.41-7.37 (m, 5H), 7.34-7.31 (m, 1H), 7.02 (s, 1H), 6.97-6.95 (m, 2H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.7, 163.3, 150.7, 143.3, 137.4, 133.2, 132.8, 131.5, 131.1, 130.8, 130.5, 129.7, 129.1, 129.0, 128.3, 128.3, 128.1, 127.6, 127.4, 120.4, 118.5, 114.3, 113.2, 55.5. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{31}H_{22}N_2O_2Na^+$ 477.1579; found 477.1582.

4. Derivatization of Product

Synthetic transformation of **3aa** to **4**^[4]



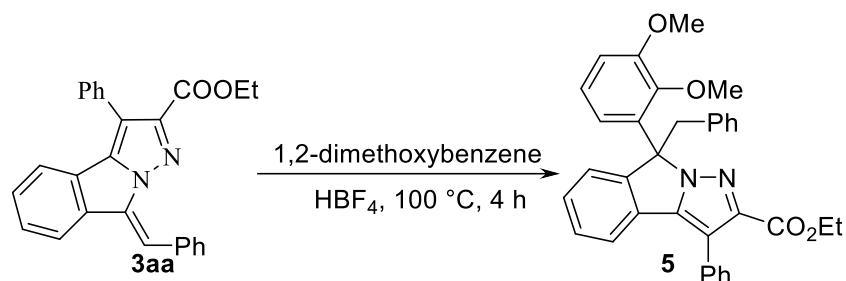
To a solution of **3aa** (0.2 mmol, 78.4 mg) in ethanol (1 mL) was added aqueous KOH (0.5 M, 1 mL). The resulting mixture was heated under reflux at 80 °C for 12 h. After cooling to room temperature, the reaction was quenched with aqueous HCl (6.0 M, 1 mL). The mixture was extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced

pressure to afford product **4** (58.3 mg, 80%) as a yellow solid.

(Z)-8-Benzylidene-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylic acid (4)

Purified by column chromatography using petroleum ether/ ethyl acetate (1:1, V/V) as an eluent. Yellow solid; m.p.: 217-218 °C; yield: 58.3 mg (80%); ¹H NMR (400 MHz, DMSO-d₆) δ 12.97 (s, 1H), 8.46 (d, *J* = 7.6 Hz, 2H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.61-7.58 (m, 2H), 7.54-7.38 (m, 10H). ¹³C NMR (101 MHz, DMSO-d₆) δ 163.6, 145.5, 143.4, 137.4, 133.1, 131.6, 131.3, 130.2, 130.1, 130.1, 129.8, 129.7, 128.8, 128.7, 128.6, 128.0, 126.8, 121.9, 119.9, 117.5, 115.4. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₄H₁₆N₂O₂Na⁺ 387.1109; found 387.1111.

Synthetic transformation of **3aa** to **5**^[5]



To a solution of **3aa** (0.2 mmol, 78.4 mg) and 1,2-dimethoxybenzene (0.3 mmol, 78 μL) in HBF₄ (1 mL) was heated to 100 °C for 2 h. After cooling to room temperature, the reaction mixture was diluted with CH₂Cl₂ and washed repeatedly with distilled water. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to yield the corresponding product **5** (47.7 mg, 45%) as a white solid.

Ethyl 8-benzyl-8-(2,3-dimethoxyphenyl)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (5)

Purified by column chromatography using petroleum ether/ ethyl acetate (5:1, V/V) as an eluent. White solid; m.p.: 86-87 °C; yield: 47.7 mg (45%); ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.27 (m, 7H), 7.16-7.16 (m, 2H), 7.09-7.06 (m, 1H), 7.02-6.97 (m, 1H), 6.93-6.86 (m, 4H), 6.54 (d, *J* = 7.2 Hz, 2H), 4.34 (q, *J* = 7.2 Hz, 2H), 4.15-4.11 (m, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 1.27 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 162.6, 149.2, 149.0, 147.8, 144.0, 143.5, 133.9, 132.1, 131.7, 129.9, 129.8, 129.0, 128.2, 127.8, 127.7, 127.4, 127.3, 126.6, 124.0, 120.1, 119.2, 117.8, 111.1, 110.3, 74.8, 60.7, 56.0, 55.9,

44.7, 26.9, 14.2. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{34}H_{30}N_2O_4Na^+$ 553.2103; found 553.2106.

Synthetic transformation of **3aa** to **6**^[6]

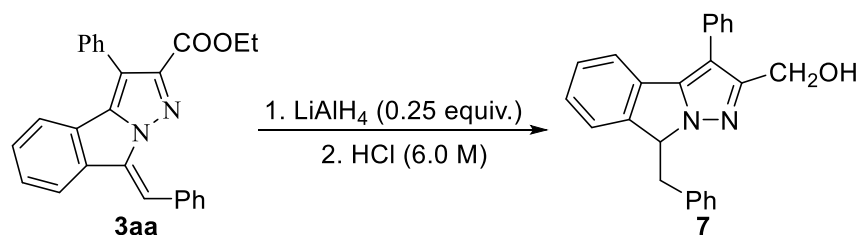


To a solution of **3aa** (0.2 mmol, 78.4 mg) in DMF (2 mL) in a sealed pressure tube was added NBS (1.2 mmol, 213.6 mg). The mixture was stirred under air at 50 °C for 2 h. After completion, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was diluted with ethyl acetate (3 × 15 mL), washed with brine, and dried over anhydrous Na_2SO_4 . The crude product was purified by silica gel column chromatography to afford product **6** (45.2 mg, 48%) as a yellow solid.

Ethyl(E)-8-(bromo(phenyl)methylene)-3-phenyl-8H-pyrazolo[5,1-a]isoindole-2-carboxylate (**6**)

Purified by column chromatography using petroleum ether/ ethyl acetate (5:1, V/V) as an eluent. Yellow solid; m.p.: 227-228 °C; yield: 45.2 mg (48%); 1H NMR (400 MHz, $CDCl_3$) δ 7.58-7.45 (m, 9H), 7.43-7.37 (m, 2H), 7.21-7.17 (m, 1H), 6.97-6.93 (m, 1H), 6.33 (d, $J = 8.0$ Hz, 1H), 4.35 (q, $J = 7.2$ Hz, 2H), 1.32 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 144.5, 143.3, 139.0, 135.1, 132.5, 131.0, 130.0, 129.9, 129.4, 129.3, 129.2, 128.1, 128.0, 127.8, 127.5, 124.2, 120.0, 118.2, 111.8, 61.1, 14.1. HRMS (ESI-TOF) m/z : $[M+Na]^+$ calcd for $C_{26}H_{19}N_2O_2BrNa^+$ 493.0528, found 493.0532.

Synthetic Transformation of **3aa** to **7**

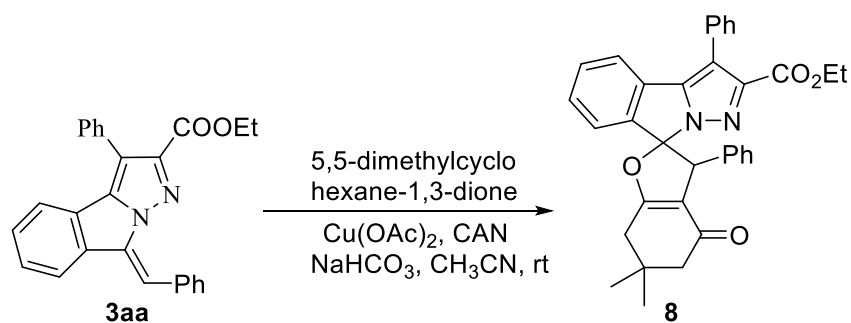


To a solution of **3aa** (0.2 mmol, 78.4 mg) in THF (1 mL) under N₂ was added LiAlH₄ (0.25 equiv.). After the reaction was complete (monitored by TLC), the mixture was quenched with aqueous HCl (6.0 M, 1 mL). The resulting mixture was extracted with CH₂Cl₂ (3 × 10 mL), and the combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to afford product **7** (38.0 mg, 54%) as a white solid.

(8-Benzyl-3-phenyl-8H-pyrazolo[5,1-a]isoindol-2-yl)methanol (7)

Purified by column chromatography using petroleum ether/ ethyl acetate (1:1, V/V) as an eluent. White solid; m.p.: 209-210 °C; yield: 38.0 mg (54%); ¹H NMR (400 MHz, DMSO-d₆) δ 7.63-7.61 (m, 2H), 7.50-7.45 (m, 3H), 7.35-7.26 (m, 4H), 7.15-7.11 (m, 3H), 6.99-6.96 (m, 2H), 5.68-5.65 (m, 1H), 5.25 (t, *J* = 5.2 Hz, 1H), 4.55-4.47 (m, 2H), 3.65-3.60 (m, 1H), 3.34-3.29 (m, 1H). ¹³C NMR (101 MHz, DMSO-d₆) δ 153.8, 144.4, 142.3, 135.9, 133.0, 130.4, 130.0, 129.1, 128.9, 128.6, 128.3, 127.5, 126.9, 124.5, 119.6, 113.9, 63.0, 56.4, 39.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ calcd for C₂₄H₂₀N₂ONa⁺ 375.1576; found 375.1579.

Synthetic Transformation of **3aa** to **8**^[7]

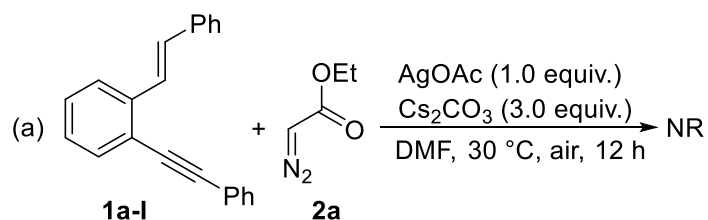


To a solution of **3aa** (0.2 mmol, 78.4 mg) in CH₃CN (2.0 mL) were added dimedone (0.4 mmol, 56.0 mg), Cu(OAc)₂ (0.04 mmol, 7.3 mg), CAN (0.5 mmol, 265.0 mg), and Na₂CO₃ (0.6 mmol, 63.6 mg). The resulting mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure, and the crude residue was Purified by silica gel column chromatography to afford product **8** (46.2 mg, 44%, dr = 2.5:1) as a white solid.

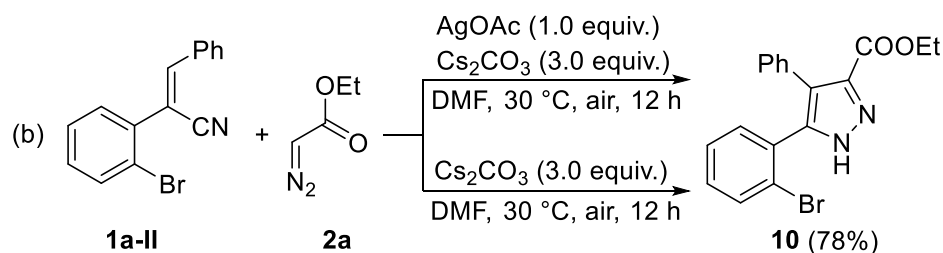
Ethyl 6,6-dimethyl-4-oxo-3,3'-diphenyl-4,5,6,7-tetrahydro-3H-spiro[benzofuran-2,8'-pyrazolo[5,1-a]isoindole]-2'-carboxylate (8)

7.2 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 161.7, 161.4, 134.2, 133.5, 131.9, 131.5, 130.7, 130.3, 130.0, 129.8, 128.7, 127.3, 127.0, 126.9, 126.8, 126.6, 124.8, 123.2, 121.6, 118.7, 60.8, 60.3, 14.1, 14.0. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{27}\text{N}_3\text{O}_4\text{Na}^+$ 528.1894; found 528.1899.

5. Mechanism Experiments



To a solution of **1a-I** (0.2 mmol, 56.0 mg) in DMF (3.0 mL) were added ethyl diazoacetate (0.4 mmol, 42 μL), AgOAc (0.2 mmol, 33.4 mg), and Cs_2CO_3 (0.6 mmol, 195.5 mg). The resulting mixture was stirred at 30 $^\circ\text{C}$ under air for 12 h. The reaction did not proceed, underscoring the essential role of the cyano group in the reaction mechanism.

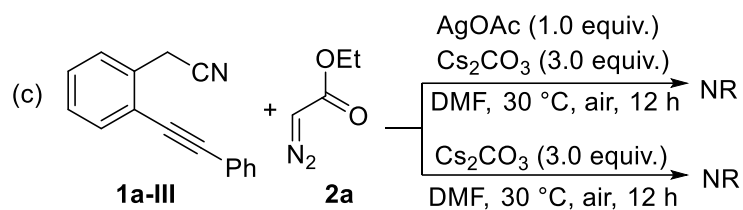


To two solution of **1a-II** (0.2 mmol, 56.8 mg) in DMF (3.0 mL) were added ethyl diazoacetate (0.4 mmol, 42 μL) and Cs_2CO_3 (0.6 mmol, 195.5 mg) among them, one was added with AgOAc (0.2 mmol, 33.4 mg) while the other was not. The resulting mixtures were stirred at 30 $^\circ\text{C}$ for 12 h. After completion of the reaction (monitored by TLC), the mixtures were subjected to extraction, drying, and vacuum distillation to remove the solvent. Purification by flash column chromatography on silica gel (eluting with ethyl acetate/petroleum ether), the conclusion indicates that the non-target [3+2]cycloadduct **10** in 78% yield under both standard and silver-free conditions.

Ethyl 5-(2-bromophenyl)-4-phenyl-1H-pyrazole-3-carboxylate (**10**)

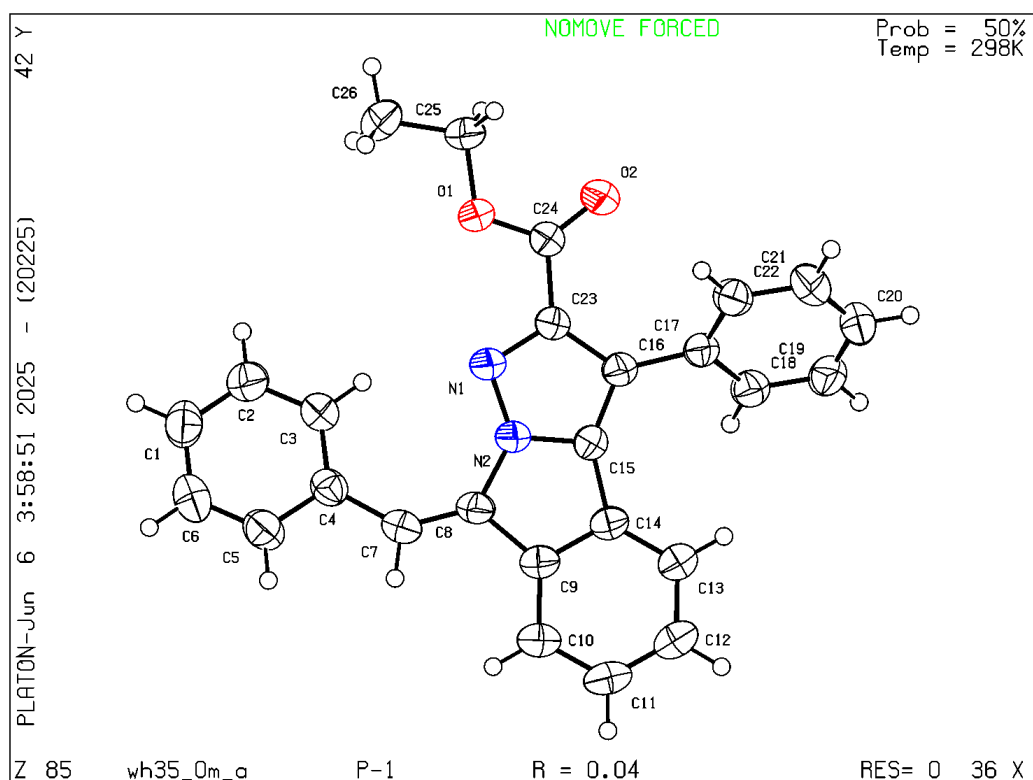
Purified by column chromatography using petroleum ether/ ethyl acetate (3:1, V/V) as an eluent. White solid; m.p.: 60-61 $^\circ\text{C}$; yield: 57.9 mg (78 %); ^1H NMR (400 MHz,

CDCl₃) δ 8.11 (s, 1H), 7.57-7.54 (m, 1H), 7.25-7.17 (m, 8H), 4.33 (d, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 133.0, 132.5, 131.0, 130.3, 130.2, 127.6, 127.3, 127.1, 124.0, 61.2, 14.0. HRMS (ESI-TOF) m/z : [M+Na]⁺ calcd for C₁₈H₁₅N₂O₂BrNa⁺ 393.0206.2; found 393.0209.



To two solutions of **1a-III** (0.2 mmol, 43.4 mg) in DMF (3.0 mL) were added ethyl diazoacetate (0.4 mmol, 42 μ L) and Cs₂CO₃ (0.6 mmol, 195.5 mg), among them, one was added with AgOAc (0.2 mmol, 33.4 mg) while the other was not. The resulting mixtures were stirred at 30 $^\circ$ C for 12 h. Notably, a control experiment conducted under identical conditions failed to yield any product, indicating that a prior [3+2] cycloaddition step is essential for this transformation.

6. Crystal structure of 3aa



Bond precision: C-C = 0.0030 Å

Wavelength=0.71073

Cell: a=10.8575(7)

b=10.8827(7)

c=11.0362(7)

alpha=114.911(2)

beta=98.835(3)

gamma=113.122(2)

Temperature: 298 K

	Calculated	Reported
Volume	1005.01(12)	1005.01(11)
Space group	P -1	P-1
Hall group	-P 1	-P 1
Moiety formula	C ₂₆ H ₂₀ N ₂ O ₂	C ₂₆ H ₂₀ N ₂ O ₂
Sum formula	C ₂₆ H ₂₀ N ₂ O ₂	C ₂₆ H ₂₀ N ₂ O ₂
Mr	392.44	392.44
D_x, g cm⁻³	1.297	1.297
Z	2	2
Mu (mm⁻¹)	0.083	0.083
F₀₀₀	412.0	412.0

F000'	412.17	
h,k,lmax	12,12,13	12,12,13
Nref	3550	3541
Tmin,Tmax	0.987, 0.988	
Tmin'	0.987	

Correction method= Not given

Data completeness= 0.997 Theta(max)= 25.060

R(reflections)= 0.0436(2717) wR2(reflections)= 0.1127(3541)

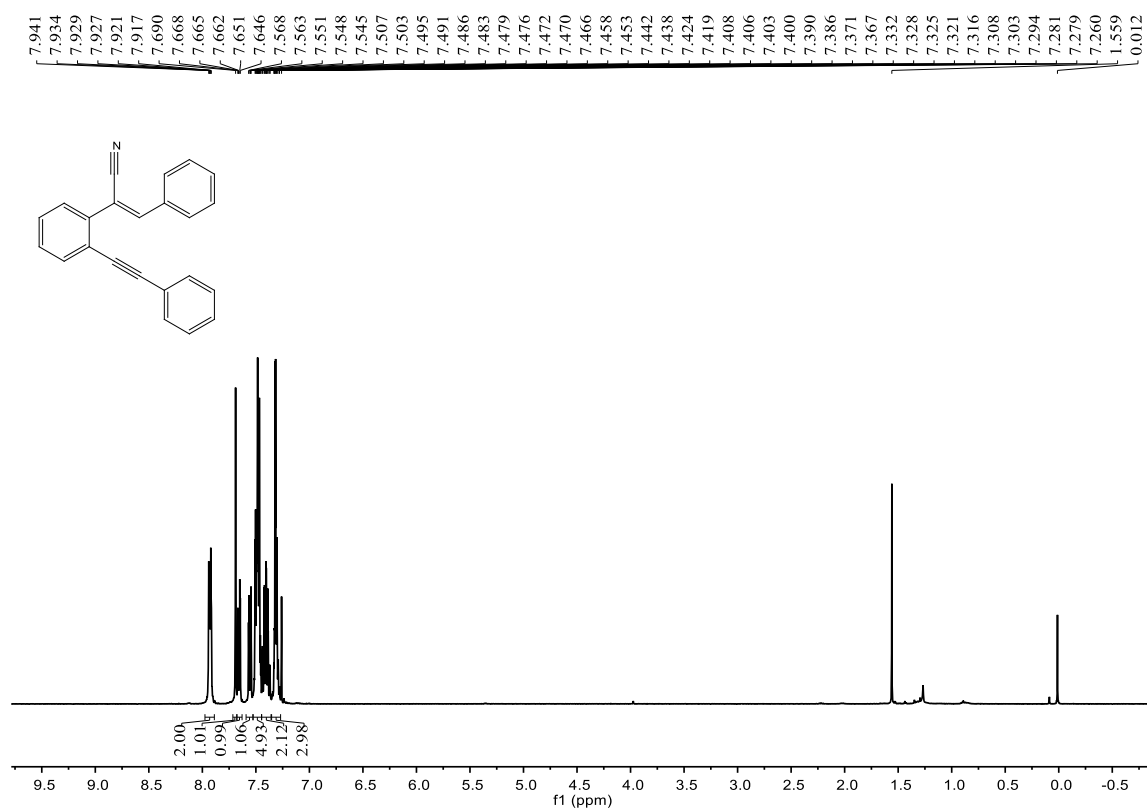
S = 1.042 Npar= 272

7. References

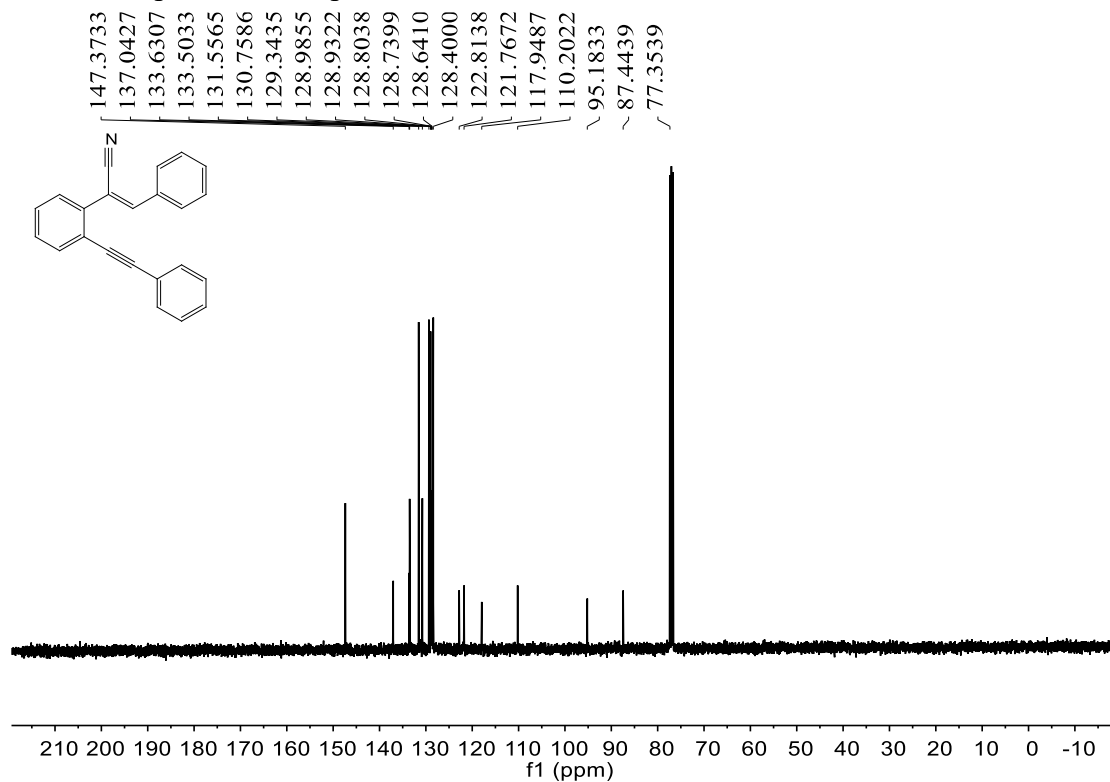
- [1] J. Li, X. Tan, H. Jiang and W. Wu, *Org. Lett.* 2024, **26**, 5409–5414.
- [2] J.-C. Hsieh, A.-Y. Cheng, J.-H. Fu and T.-W. Kang, *Org. Biomol. Chem.*, 2012, **10**, 6404–6409.
- [3] (a) C.-F., Gao, Y. Zhou, H. Ma, Y. Zhang, J. Nie, F.-G. Zhang and J.-A. Ma, *CCS Chem.*, 2022, **4**, 3693–3704; (b) Y. Zhou, C.-F. Gao, H. Ma, J. Nie, J.A. Ma and F.-G. Zhang, *Chem. Asian J.* 2022, **17**, e202200436.
- [4] L. Liu, L. Li, S. Mao, X. Wang, M.-D. Zhou, Y.-L. Zhao and H. Wang, *Chem. Commun.*, 2020, **56**, 7665–7668.
- [5] K. Alam, S. W. Hong, K. H. Oh and J. K. Park, *Angew. Chem. Int. Ed.*, 2017, **56**, 13387–13391.
- [6] H. Chen, Y. Ran, H. Wang, J. Sun, Y. Wang, R. Sun, L. Li and M.-D. Zhou, *Adv. Synth. Catal.*, 2025, **367**, e70080.
- [7] G. Savitha, S. K. Niveditha, D. Muralidharan and P. T. Perumal, *Tetrahedron lett.*, 2007, **48**, 2943–2947.
- [8] D. Zheng, S. Li, Y. Luo and J. Wu, *Org. Lett.*, 2011, **13**, 6402–6405.

8. NMR Spectra

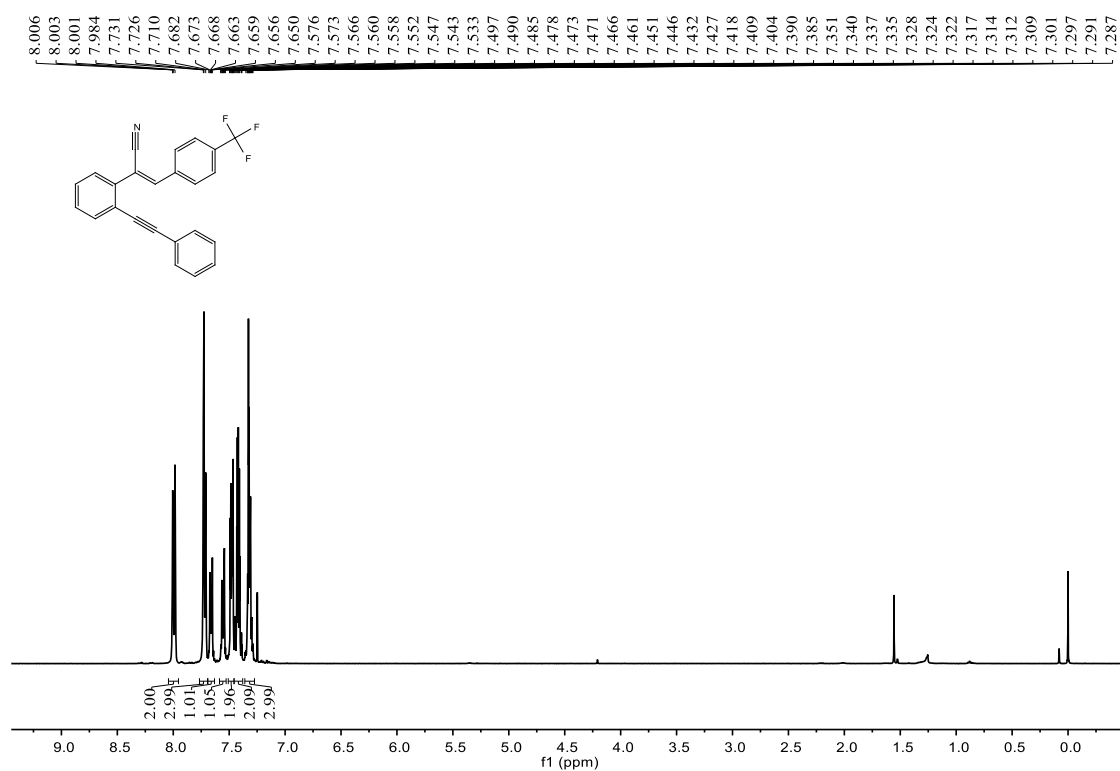
^1H NMR spectra of compound **1a**.



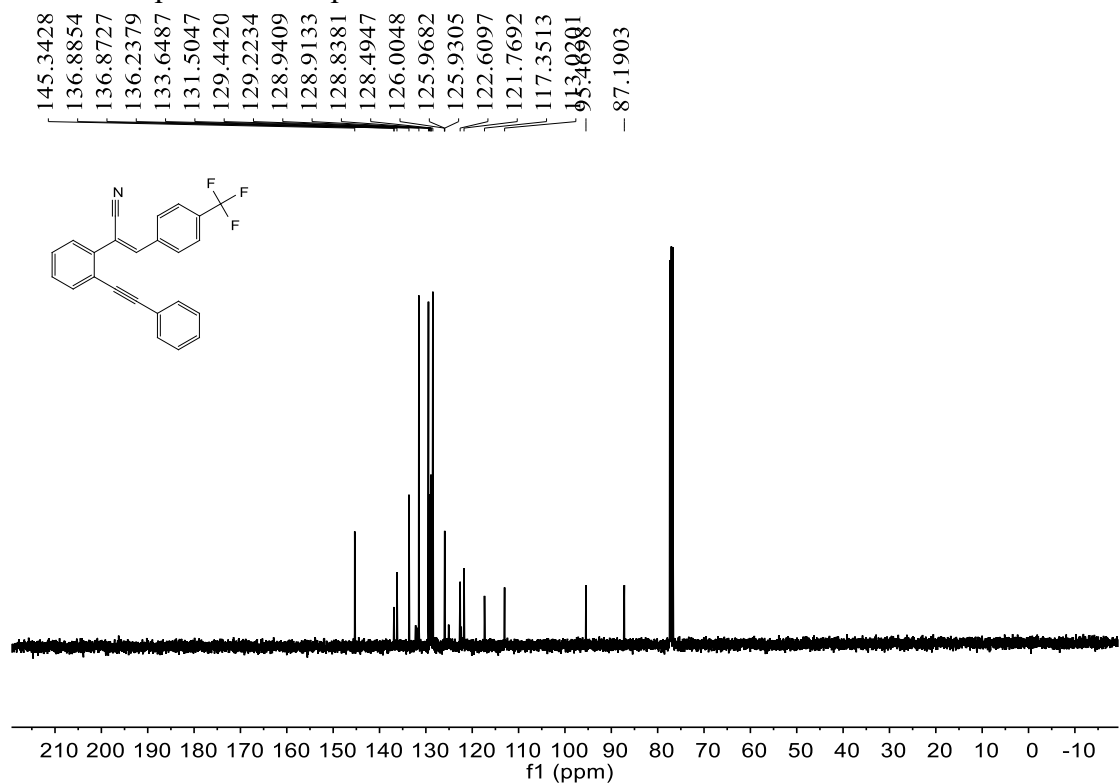
^{13}C NMR spectra of compound **1a**.



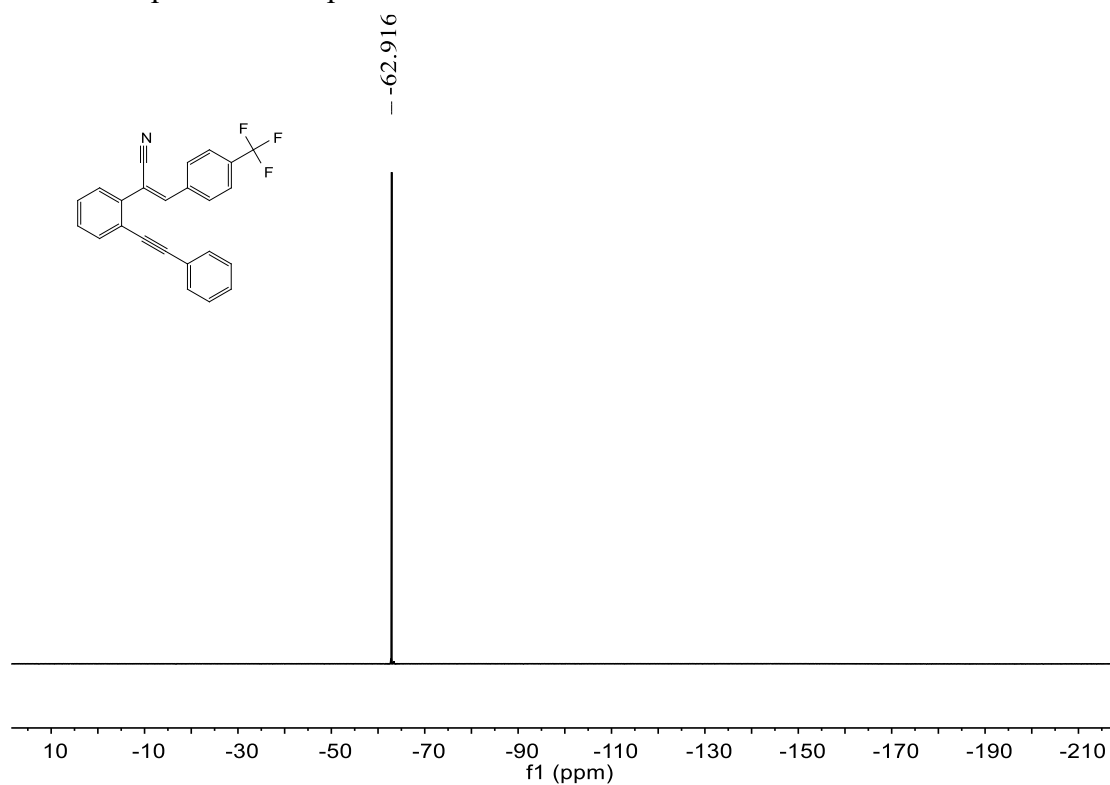
¹H NMR spectra of compound **1b**.



¹³C NMR spectra of compound **1b**.



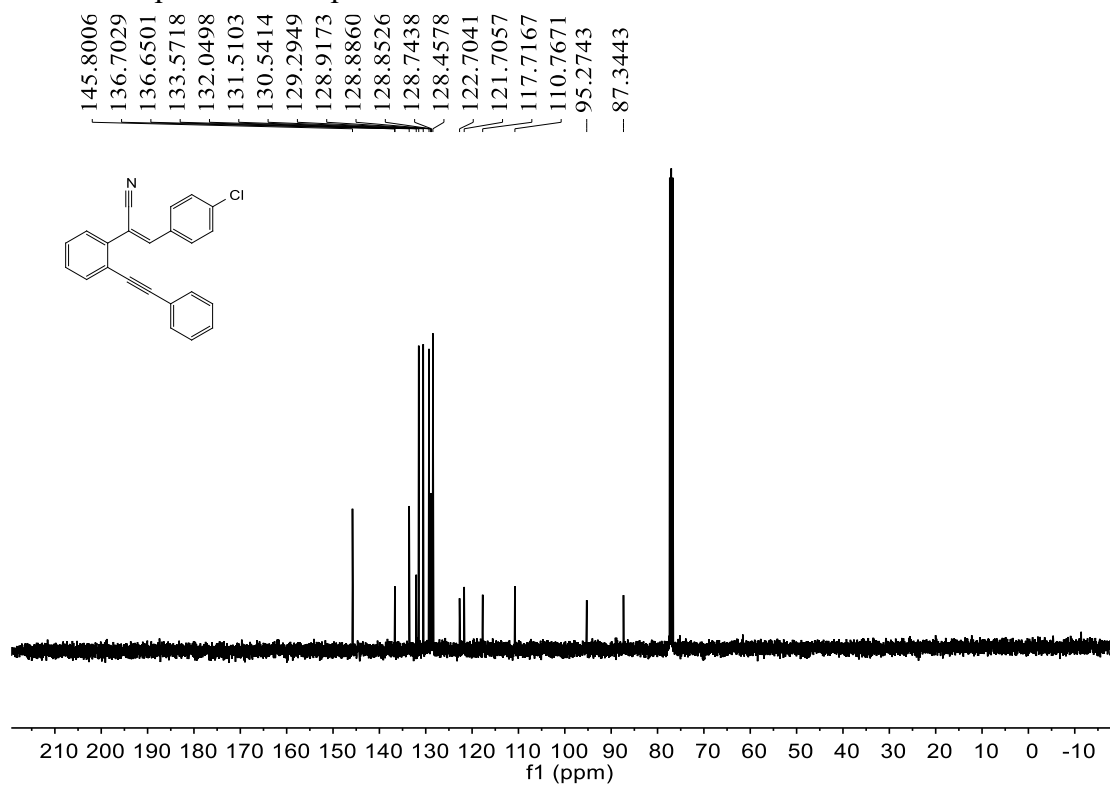
¹⁹F NMR spectra of compound **1b**.



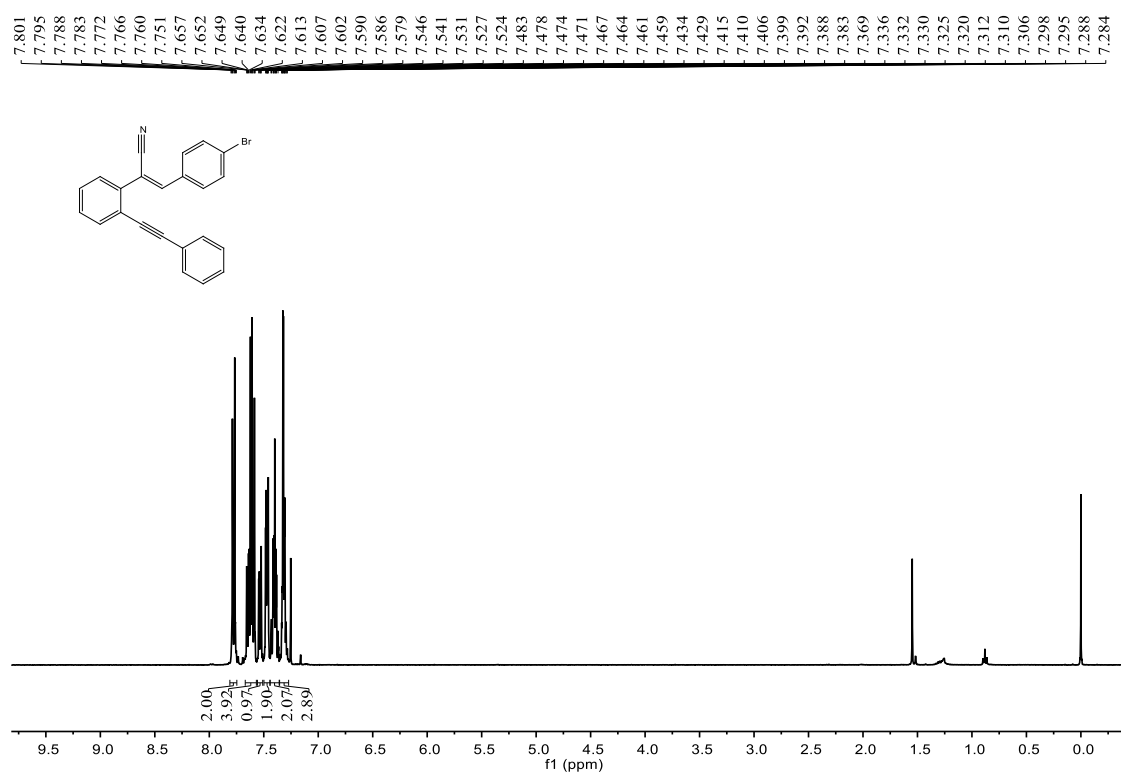
¹H NMR spectra of compound **1c**.



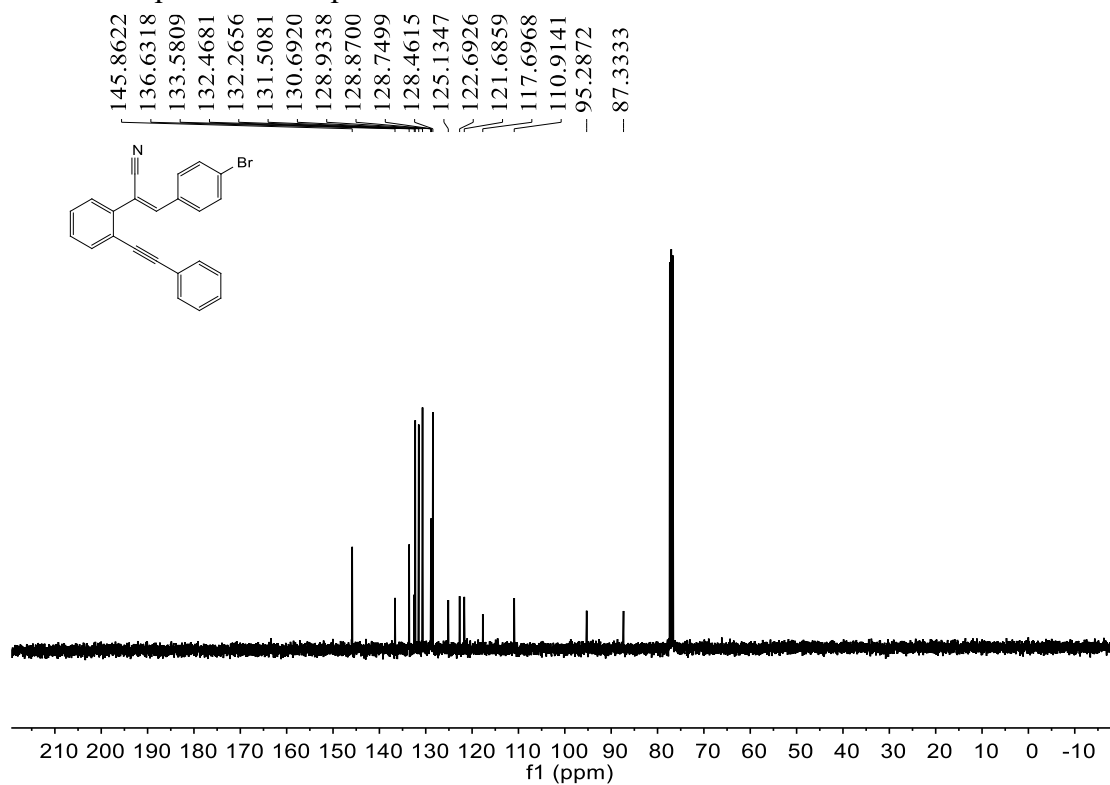
¹³C NMR spectra of compound **1c**.



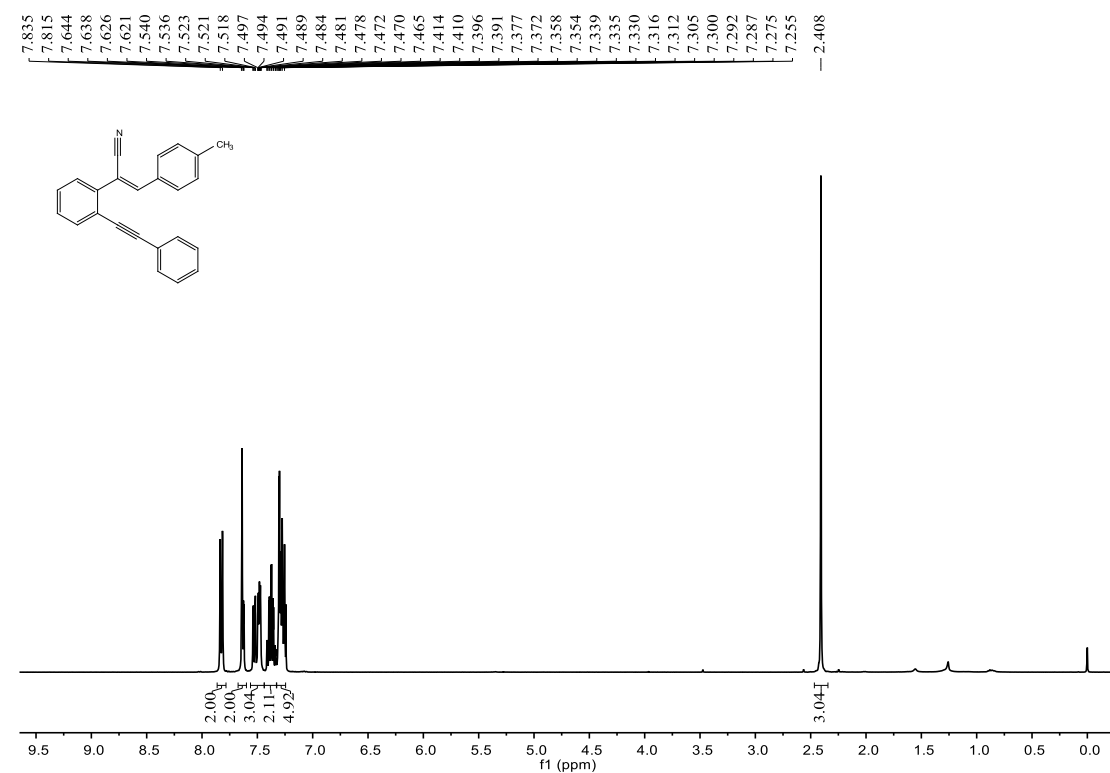
¹H NMR spectra of compound **1d**.



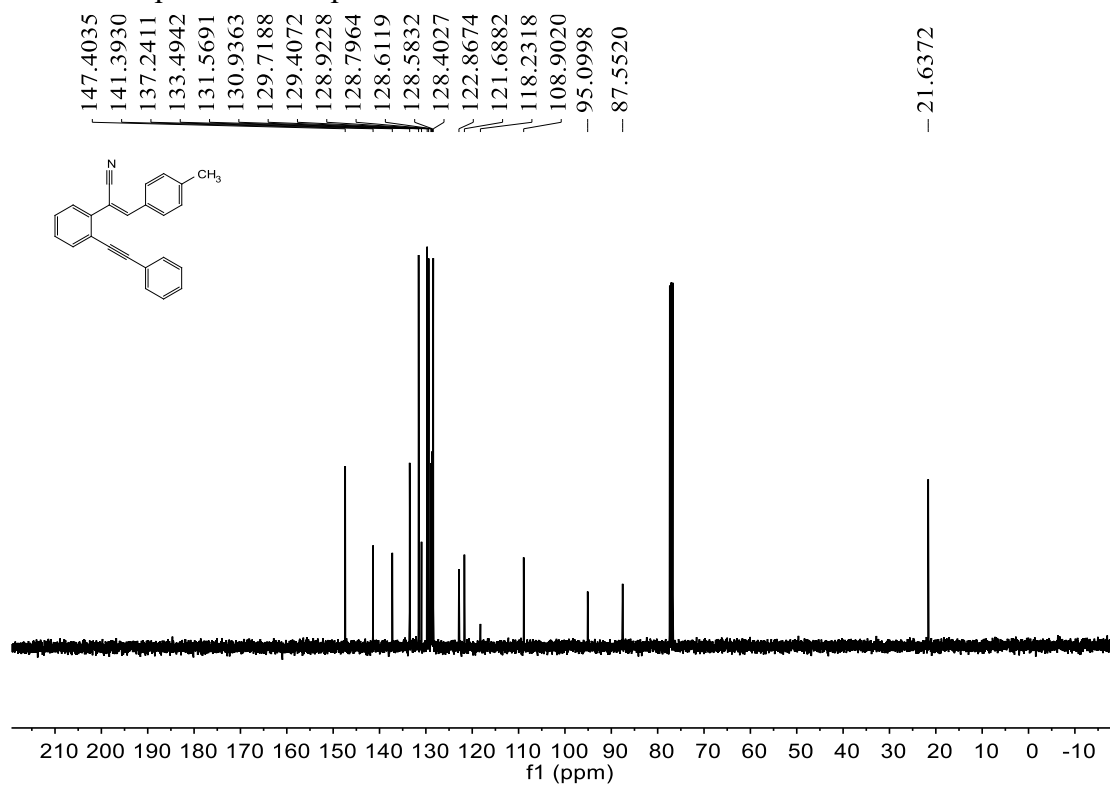
¹³C NMR spectra of compound **1d**.



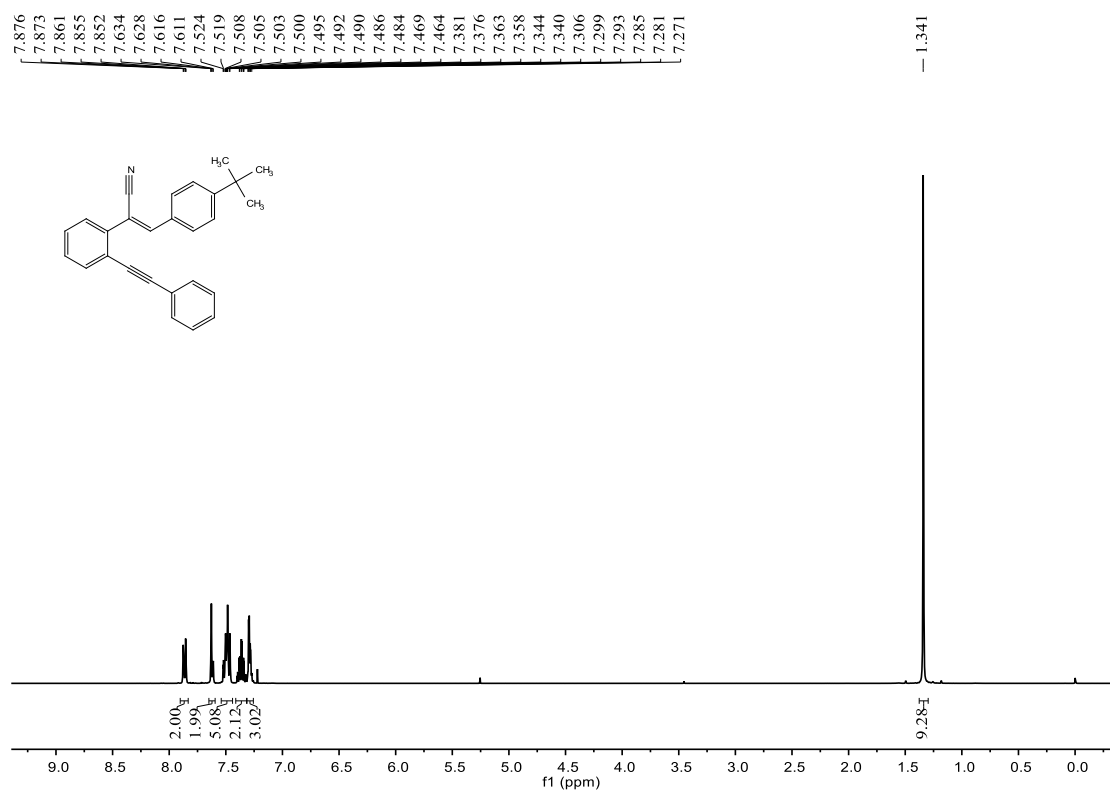
¹H NMR spectra of compound **1e**.



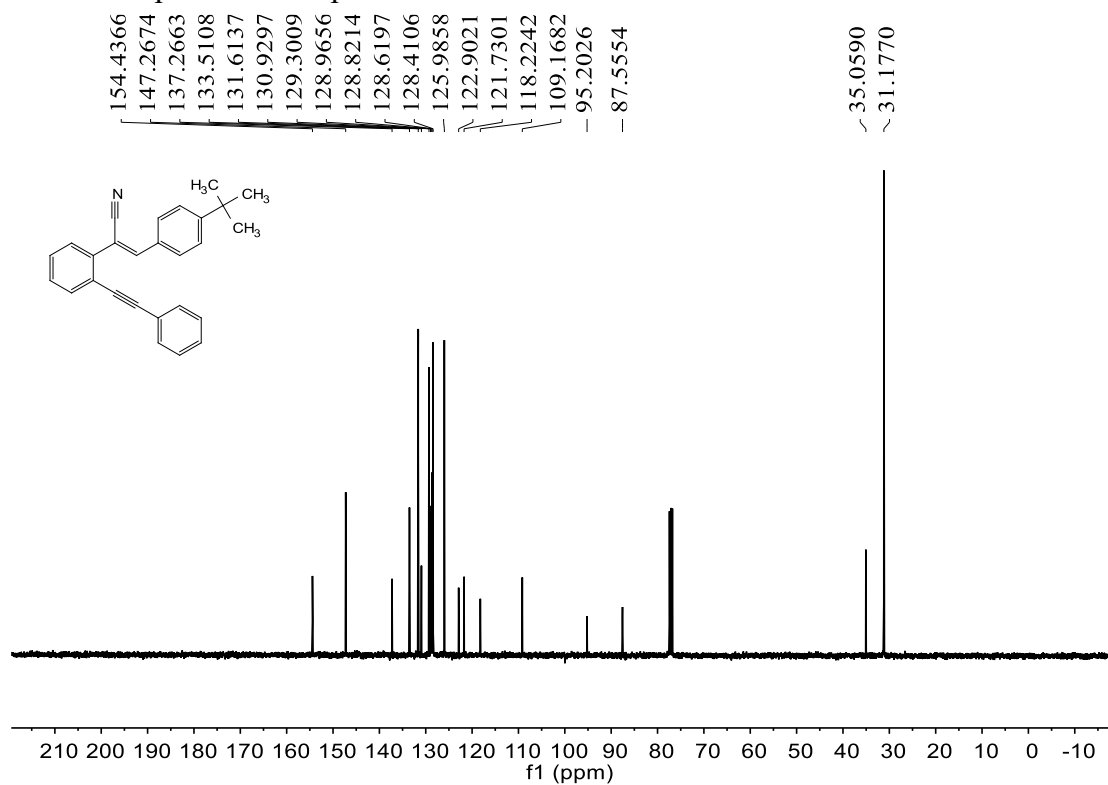
¹³C NMR spectra of compound **1e**.



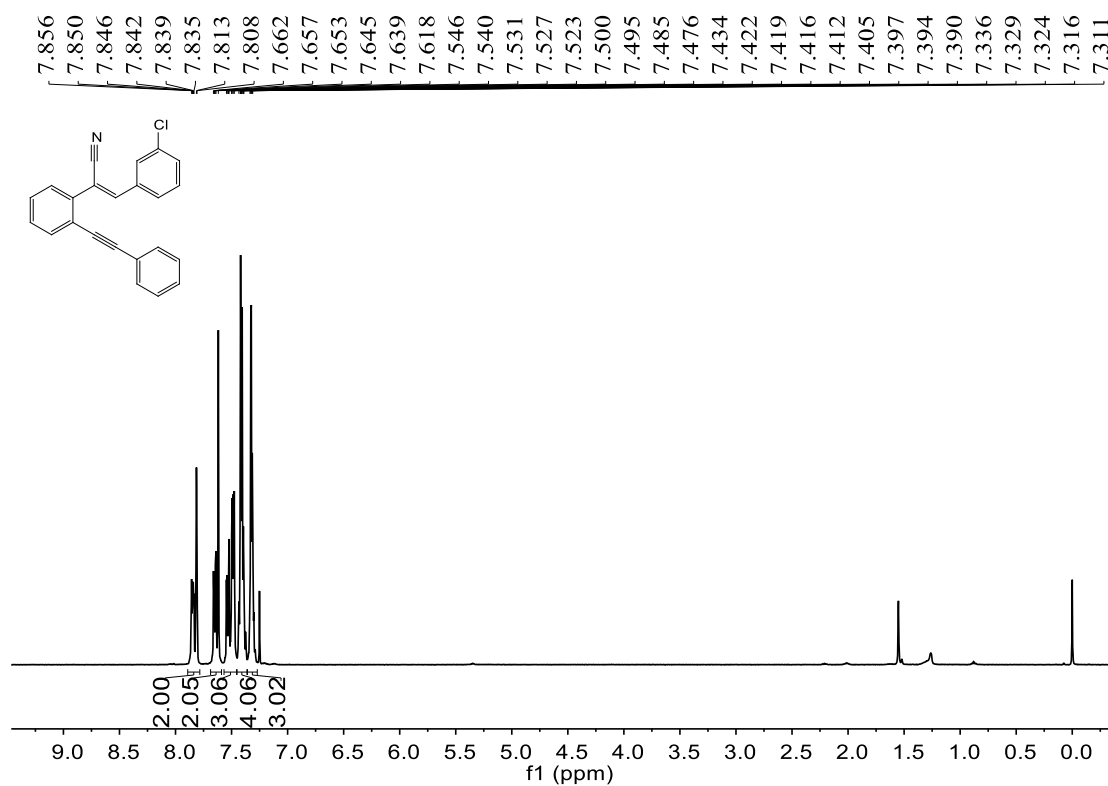
¹H NMR spectra of compound **1f**.



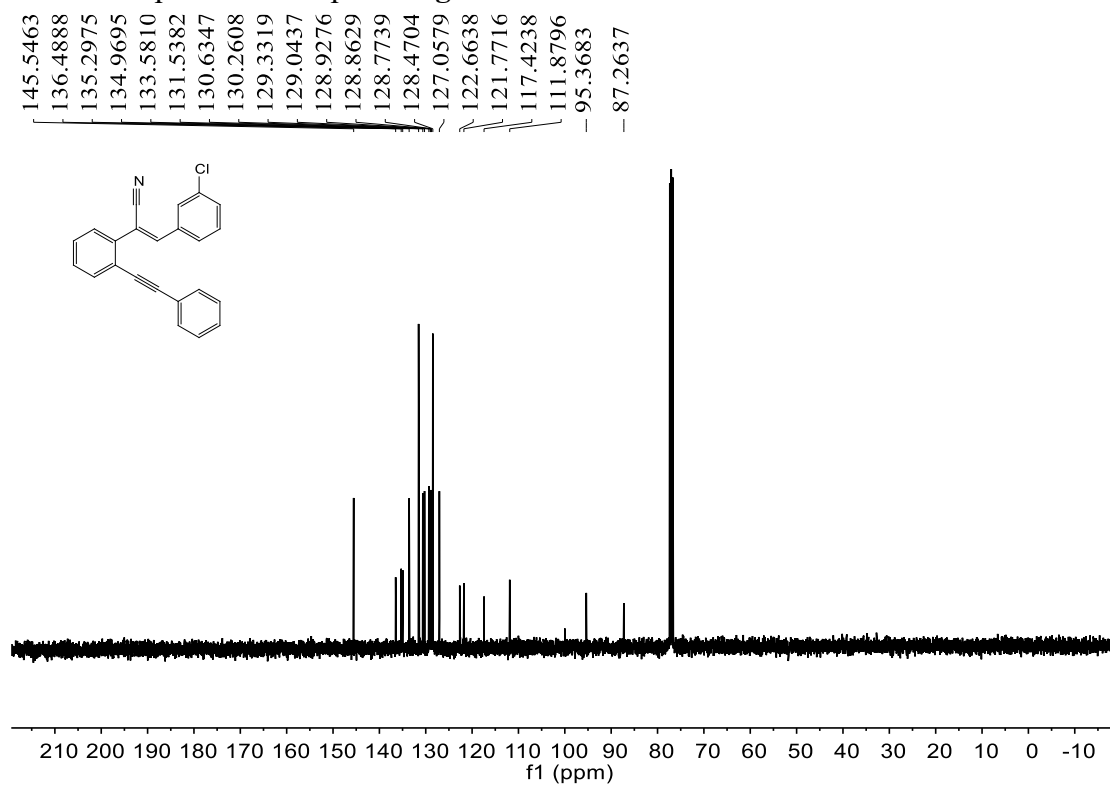
¹³C NMR spectra of compound **1f**.



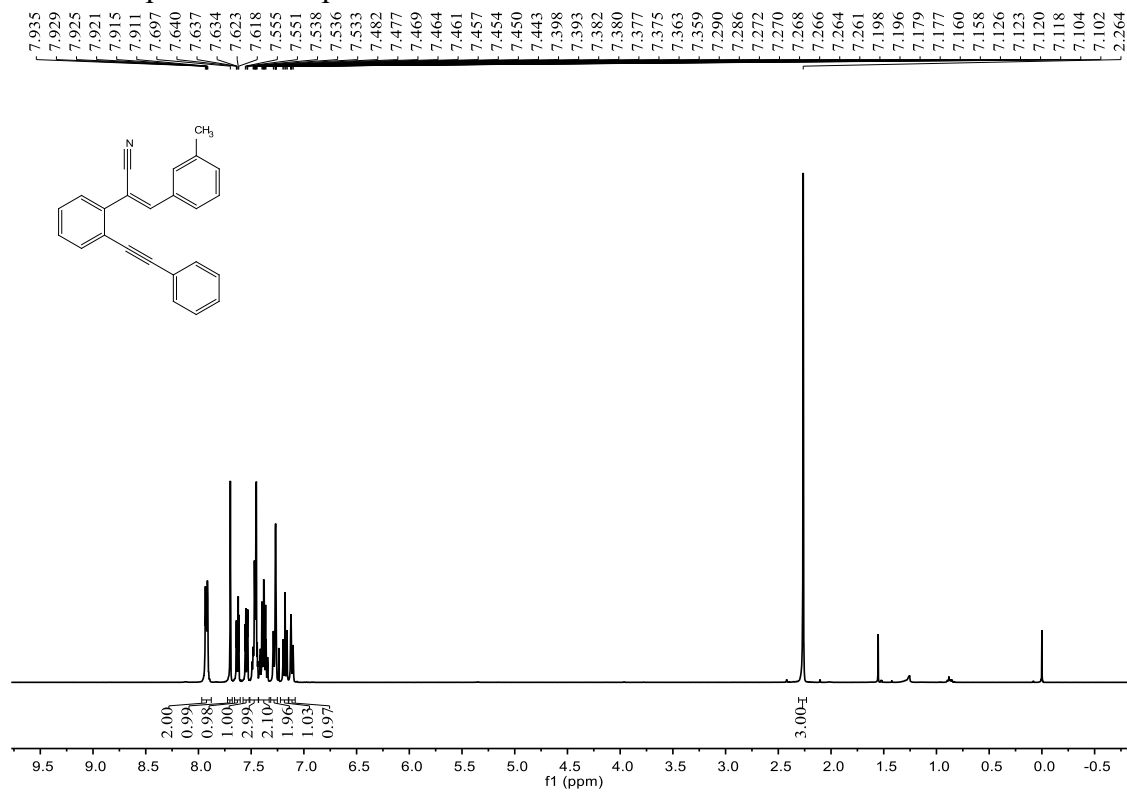
¹H NMR spectra of compound **1g**.



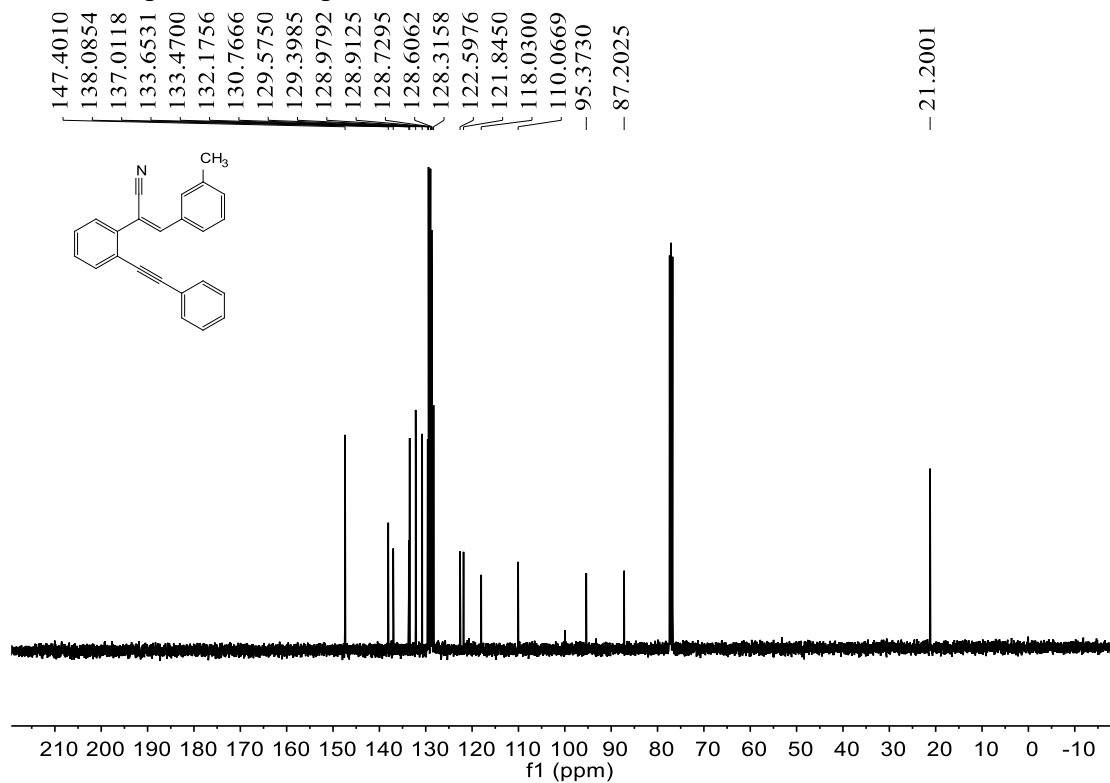
¹³C NMR spectra of compound **1g**.



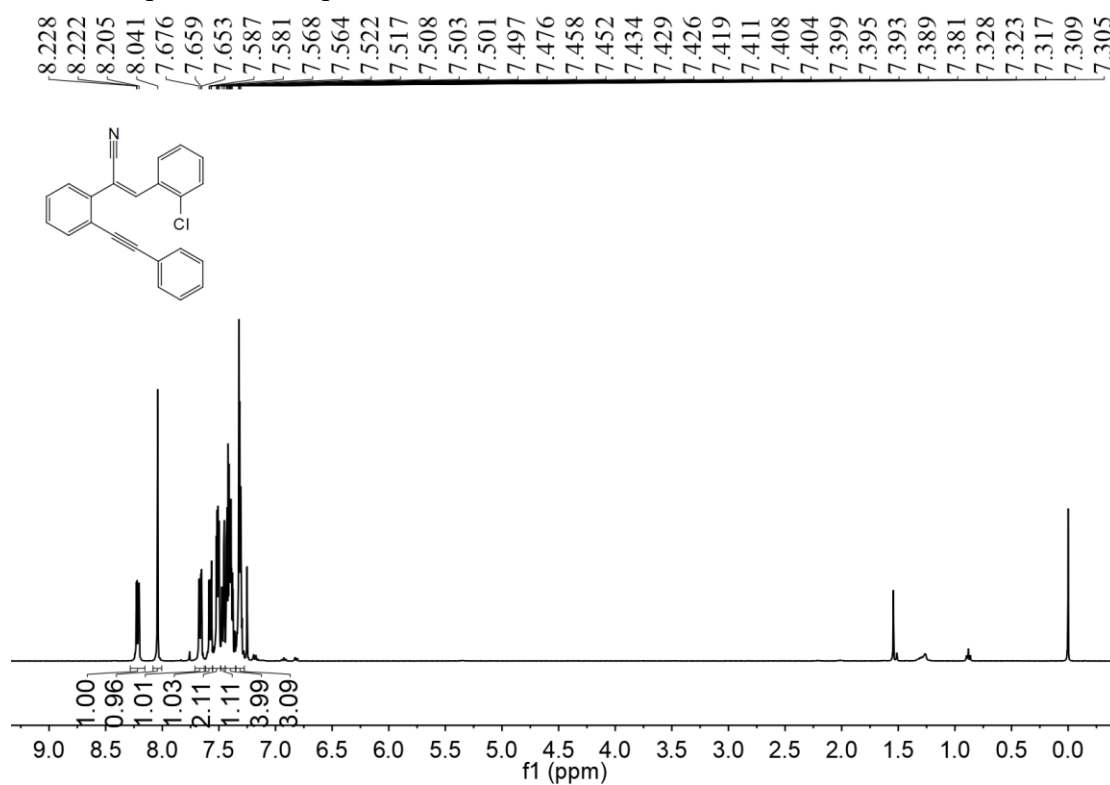
¹H NMR spectra of compound **1h**.



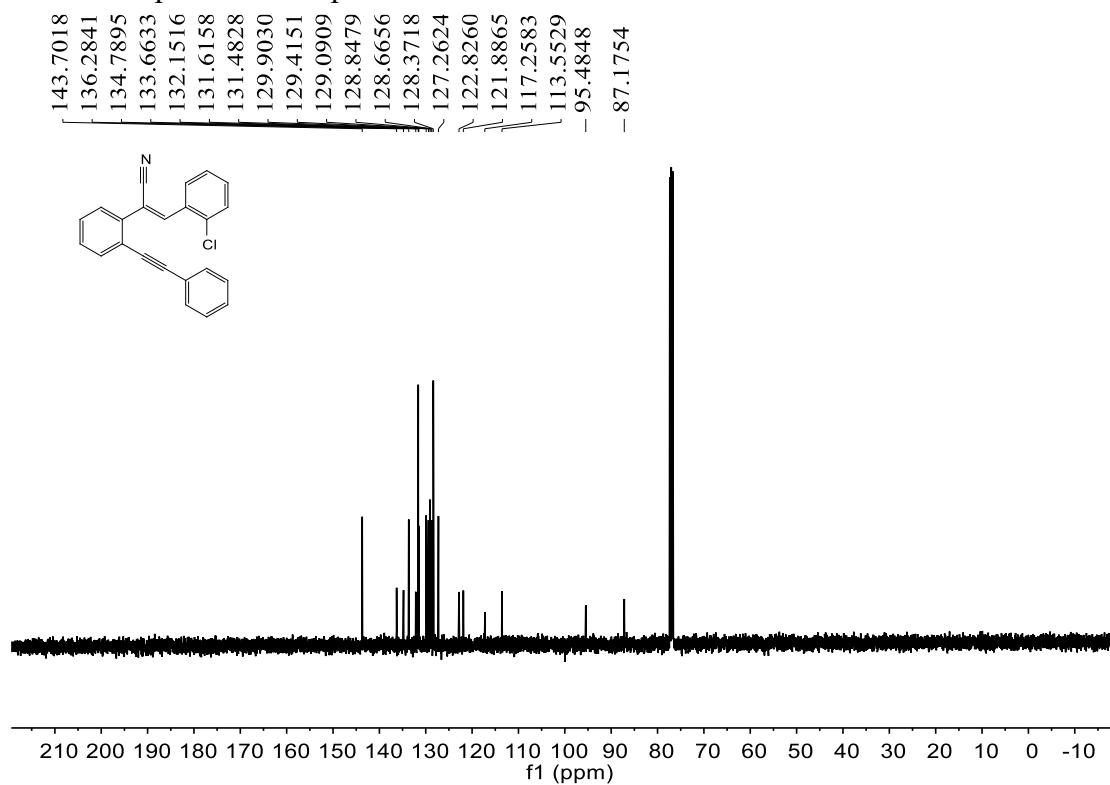
¹H NMR spectra of compound **1h**.



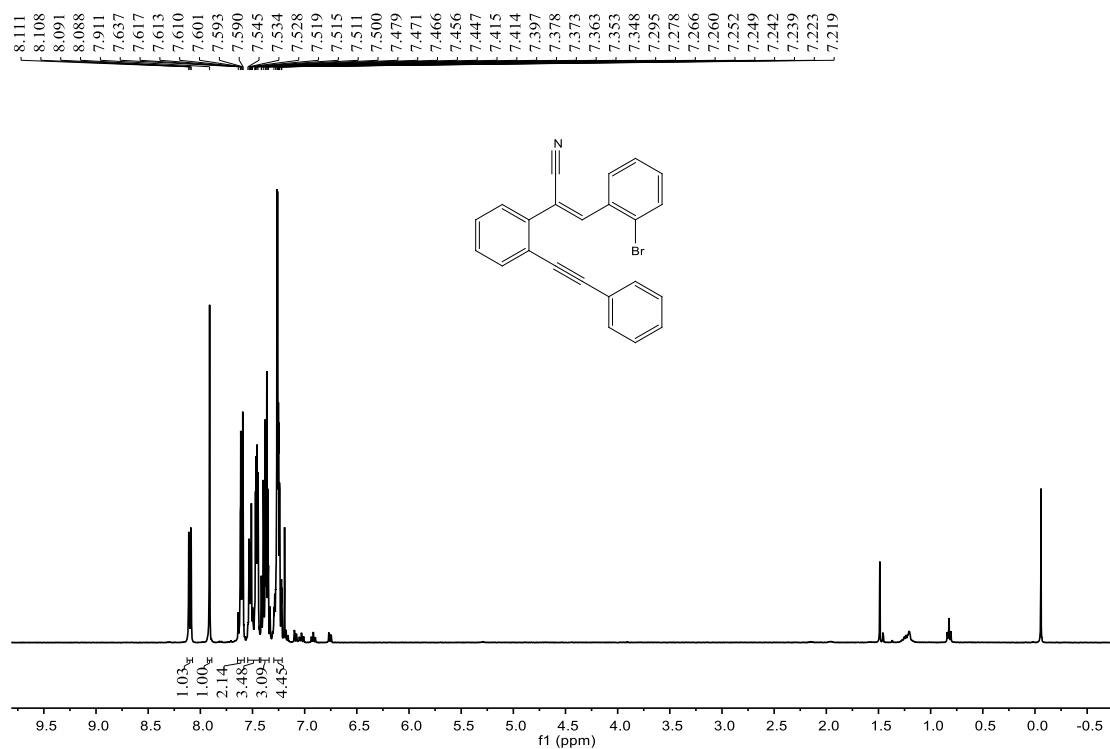
¹H NMR spectra of compound **1i**.



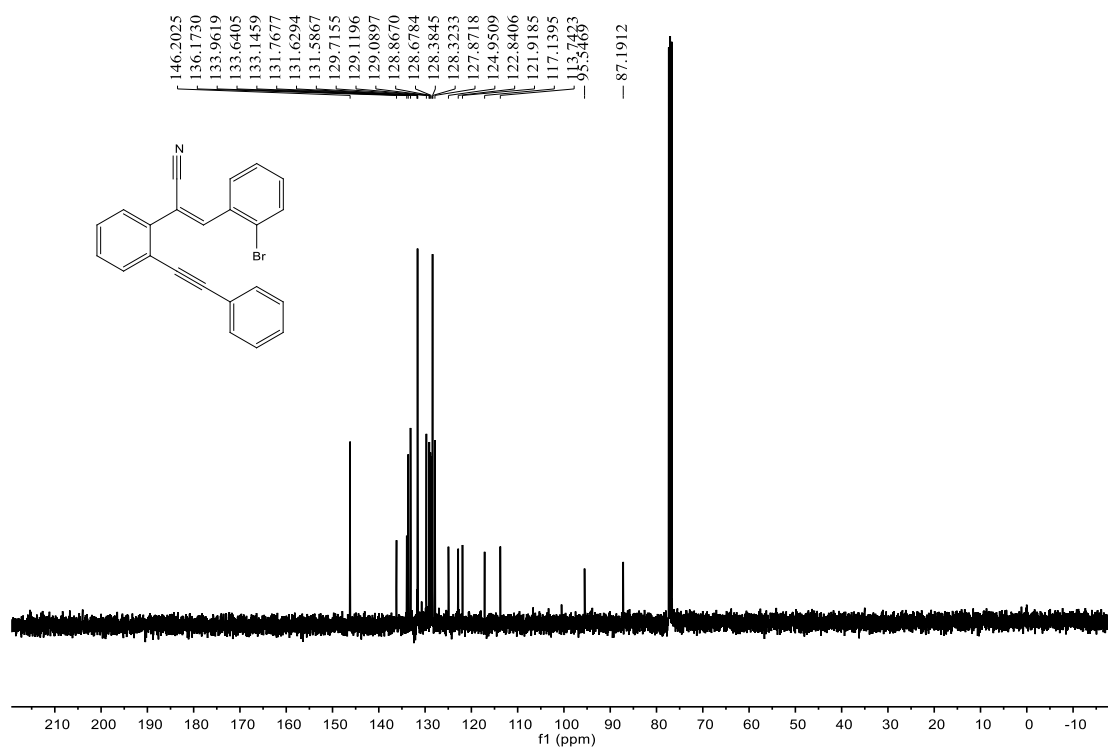
¹³C NMR spectra of compound **1i**.



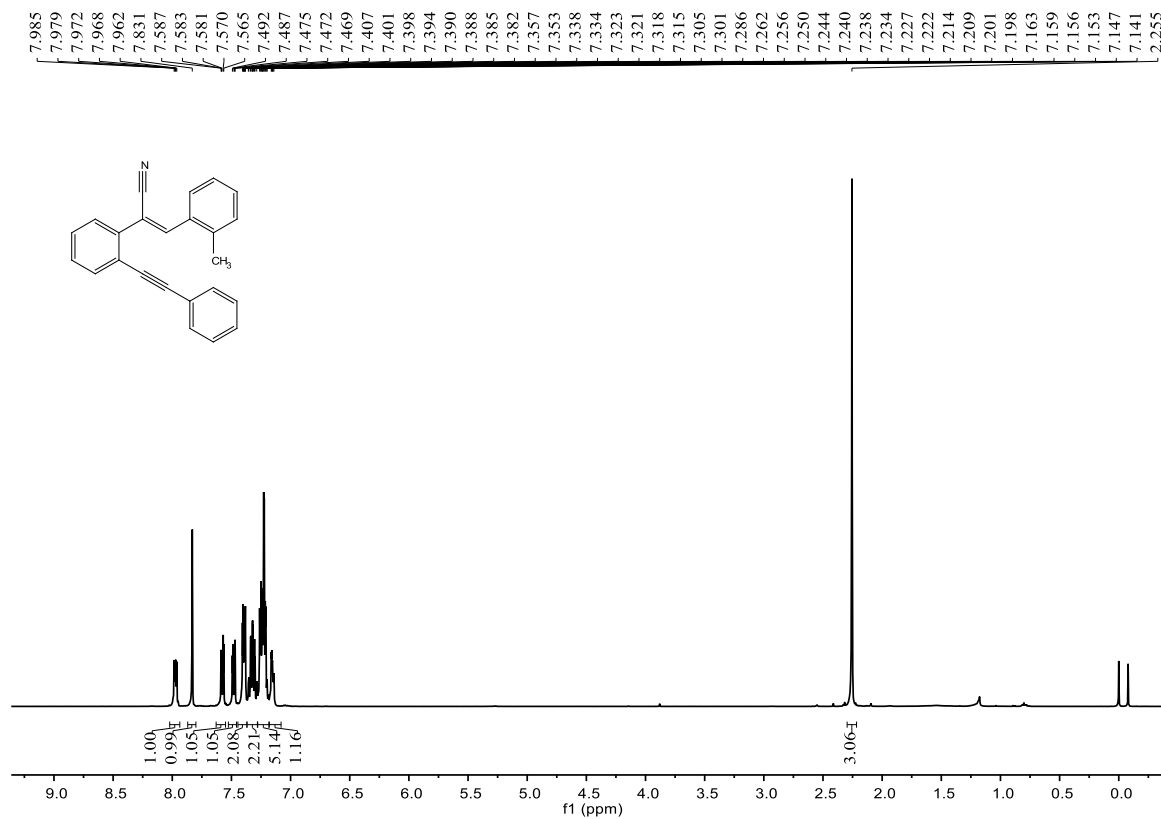
¹H NMR spectra of compound **1j**.



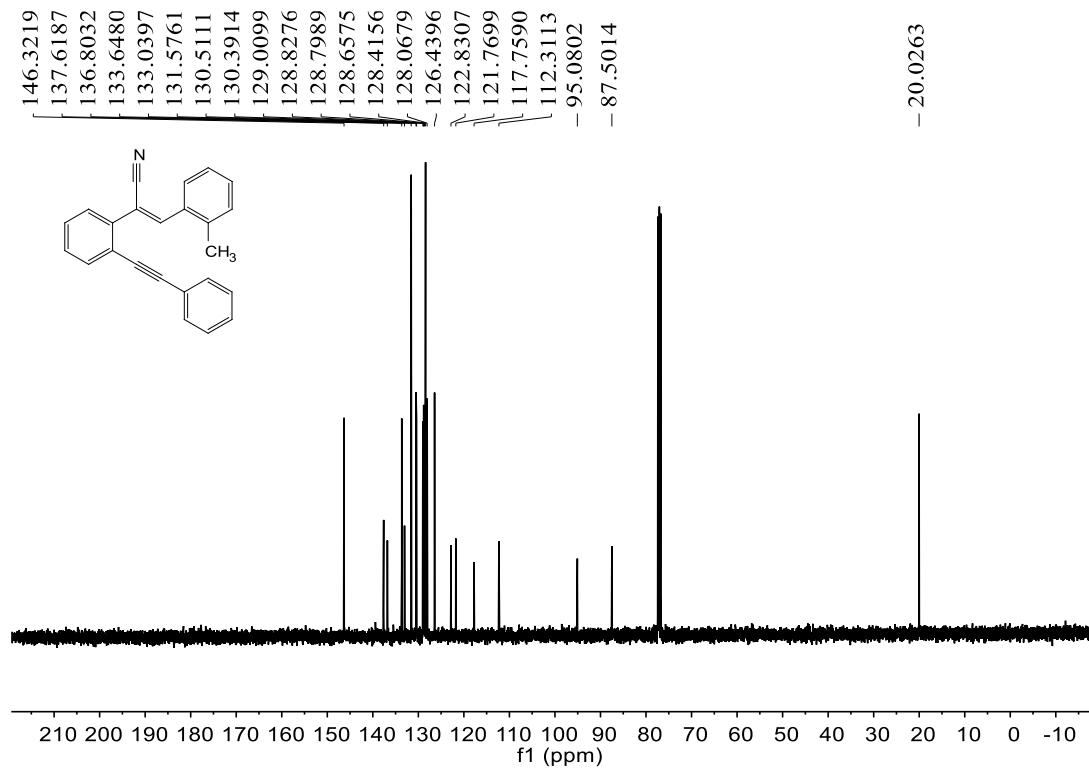
¹³C NMR spectra of compound **1j**.



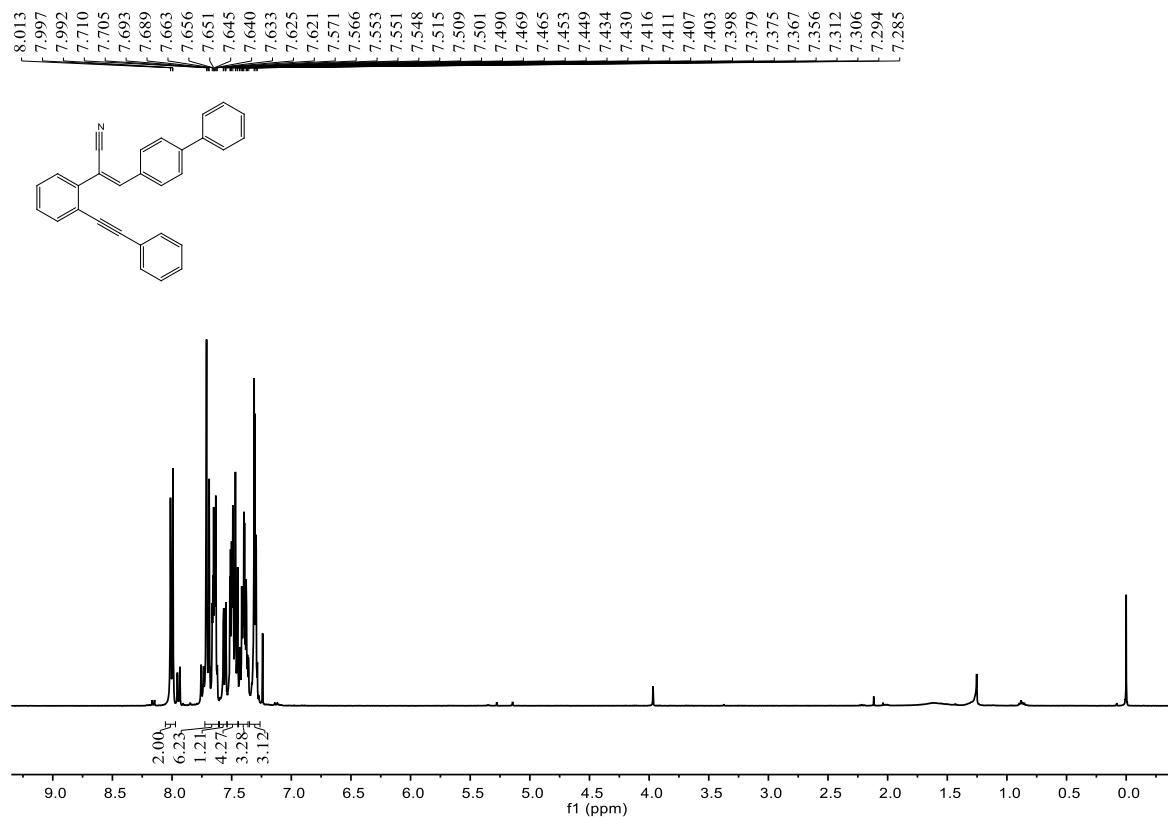
¹H NMR spectra of compound **1k**.



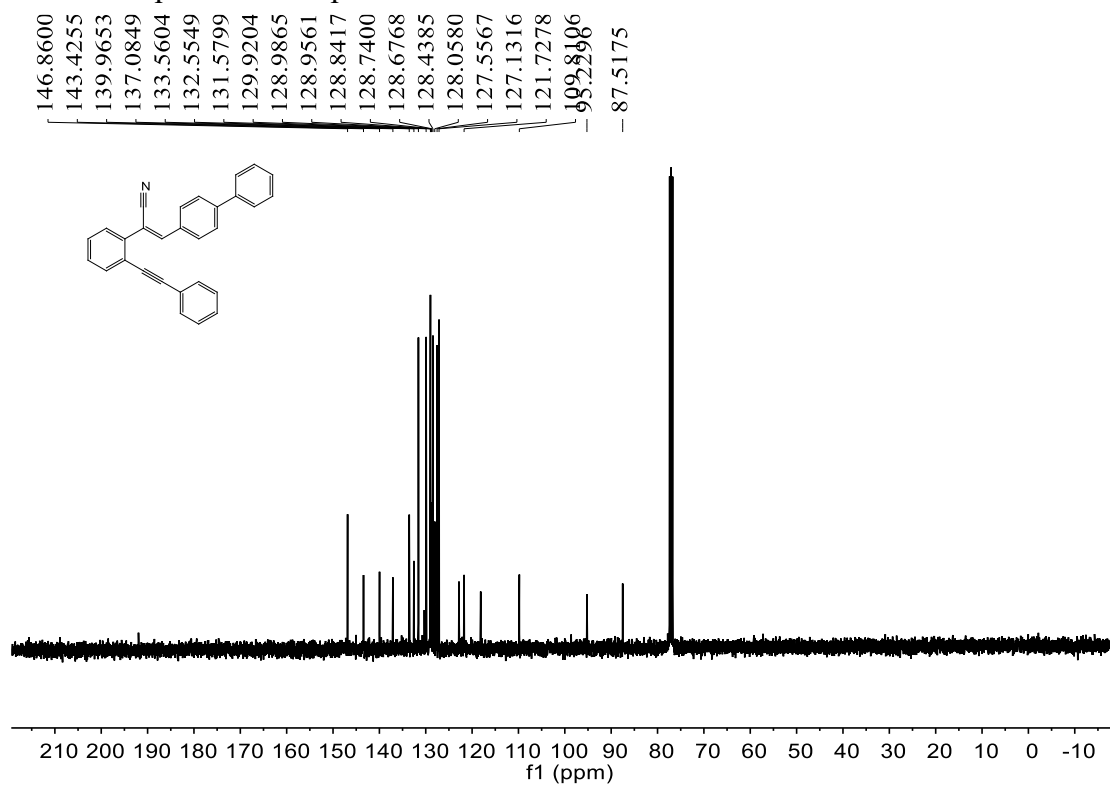
¹³C NMR spectra of compound **1k**.



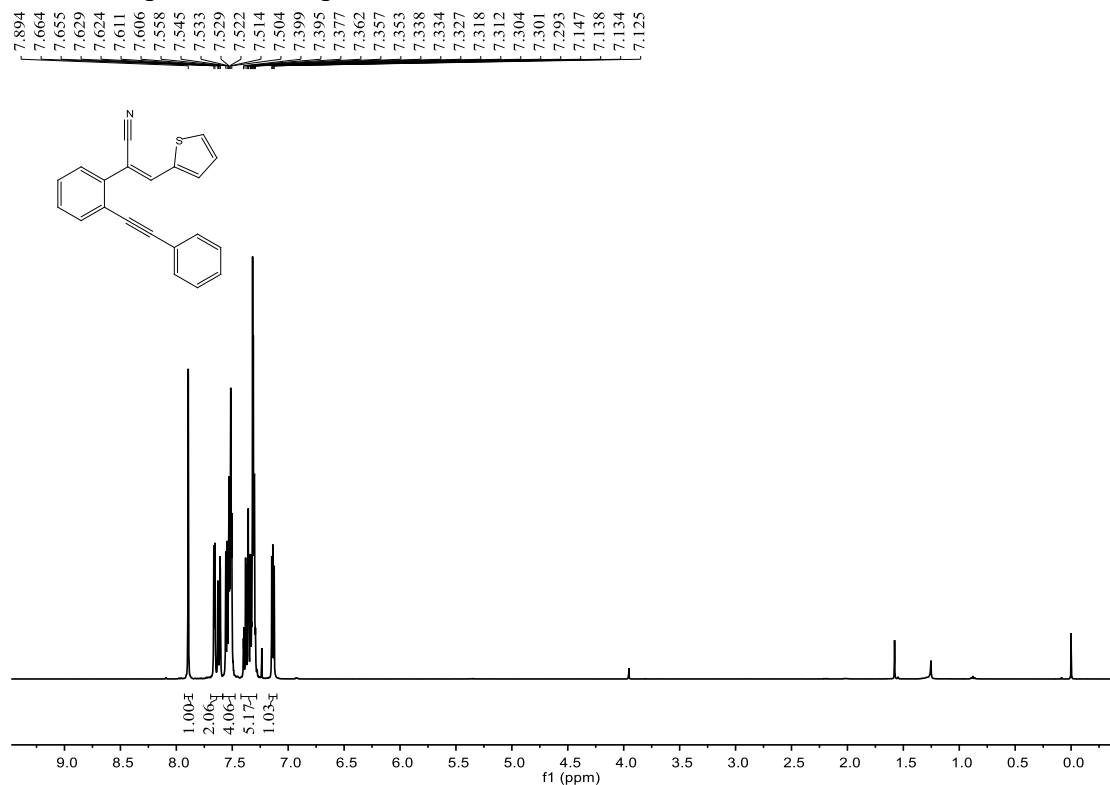
¹H NMR spectra of compound **1l**.



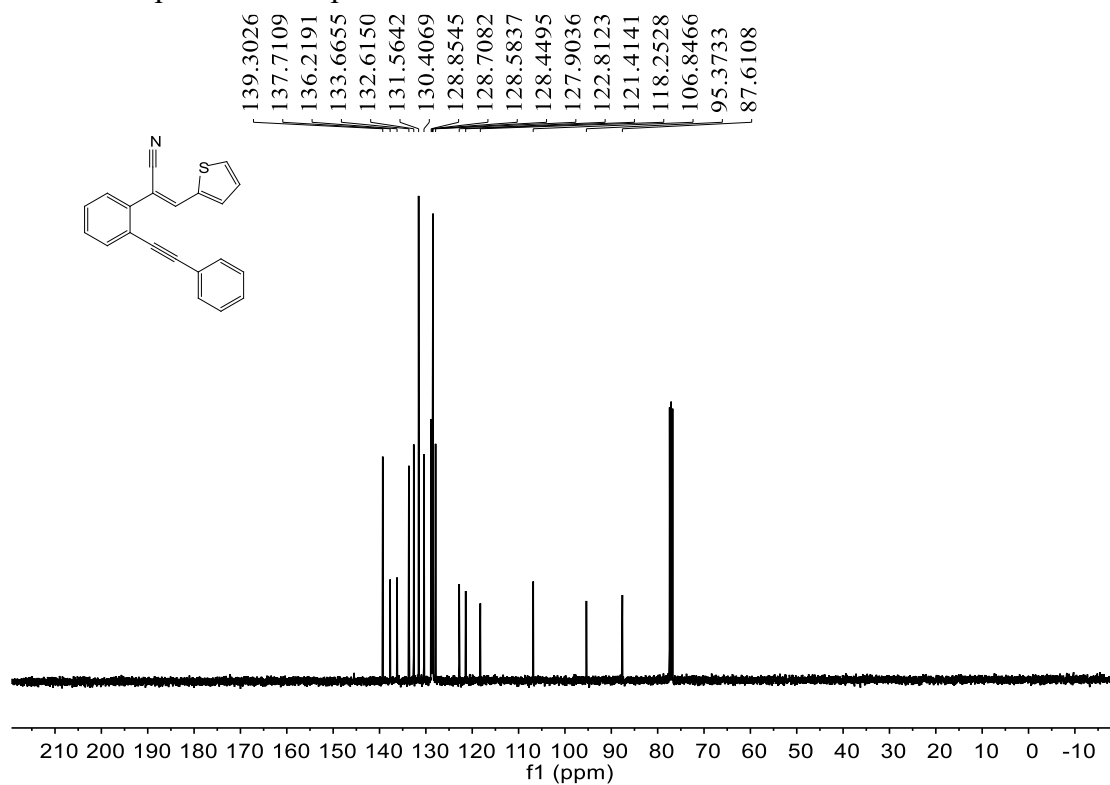
¹³C NMR spectra of compound **1l**.



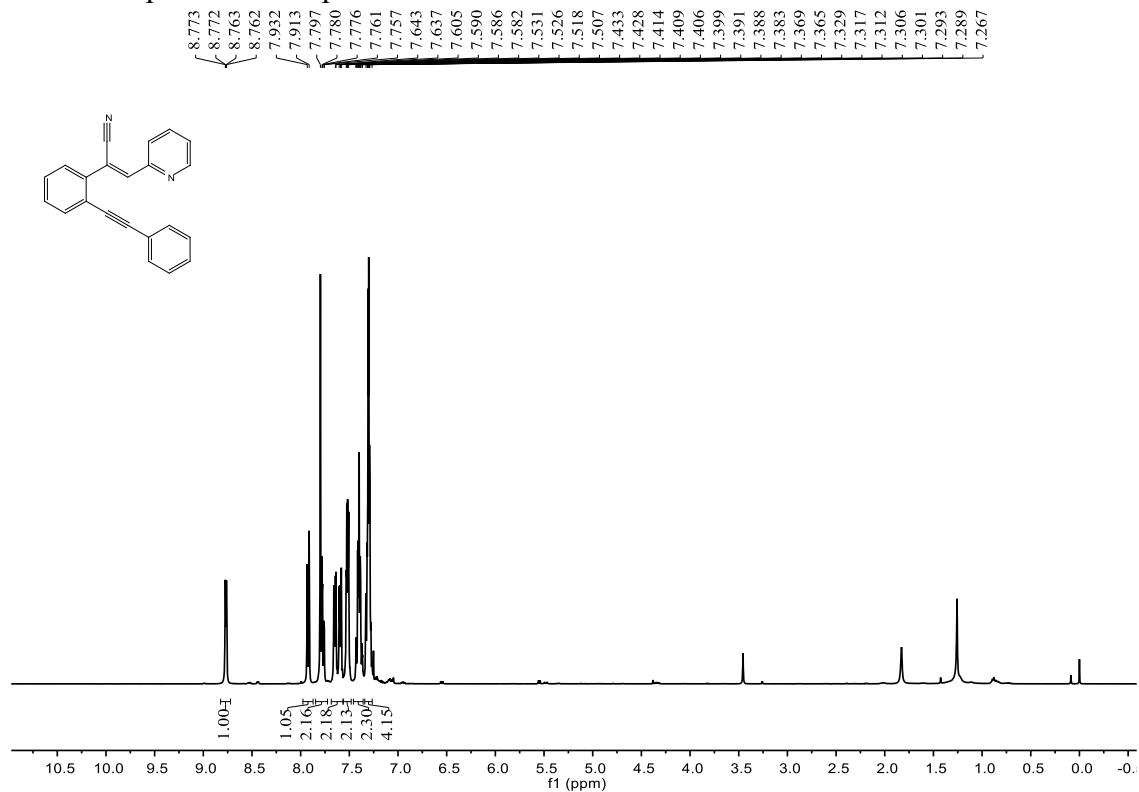
¹H NMR spectra of compound **1m**.



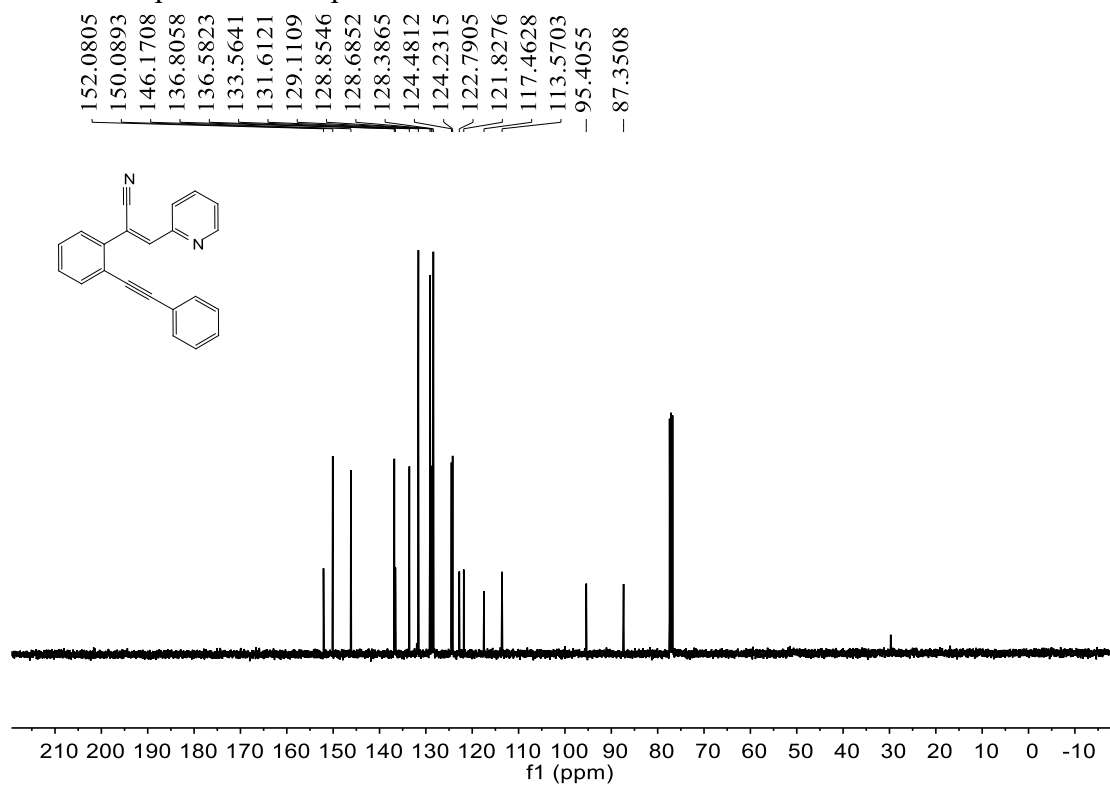
¹³C NMR spectra of compound **1m**.



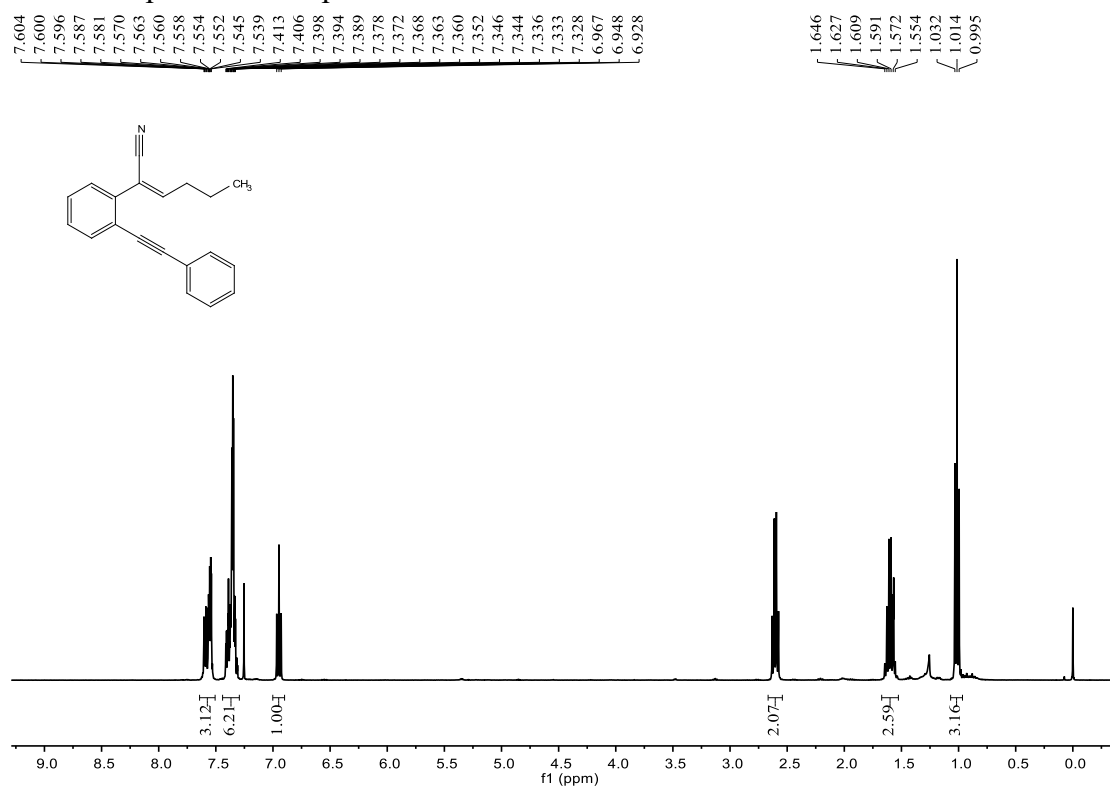
¹H NMR spectra of compound **1n**.



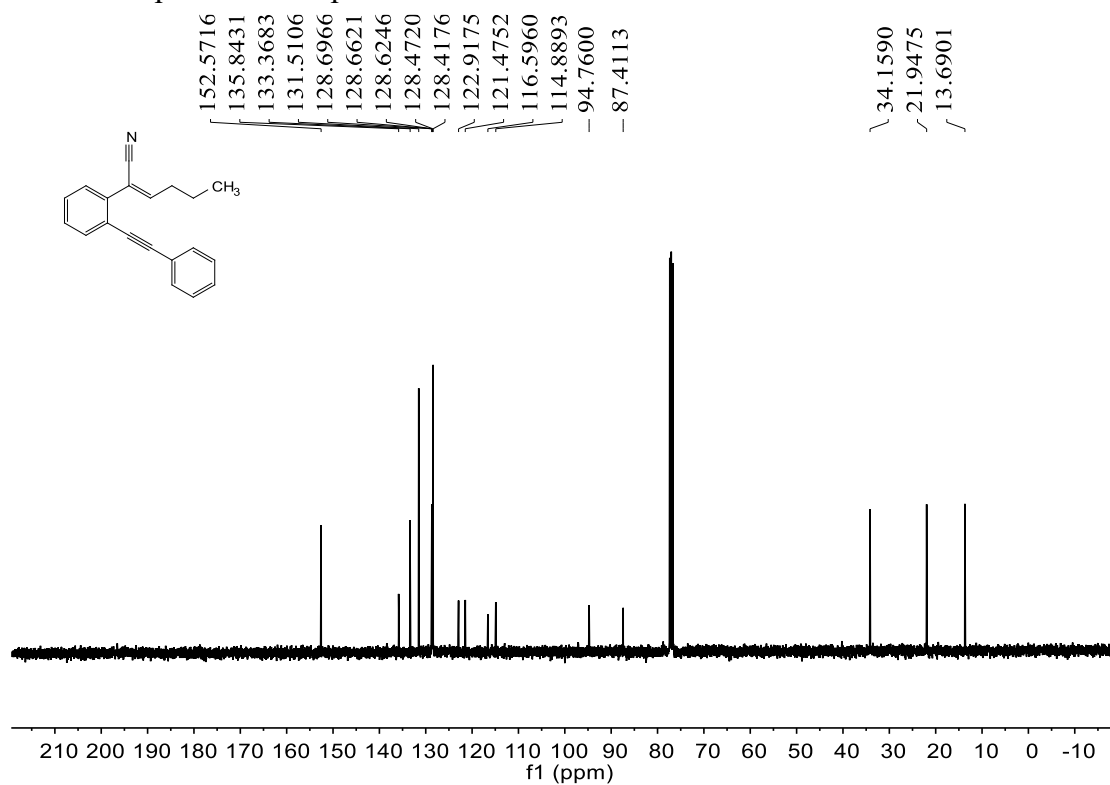
¹³C NMR spectra of compound **1n**.



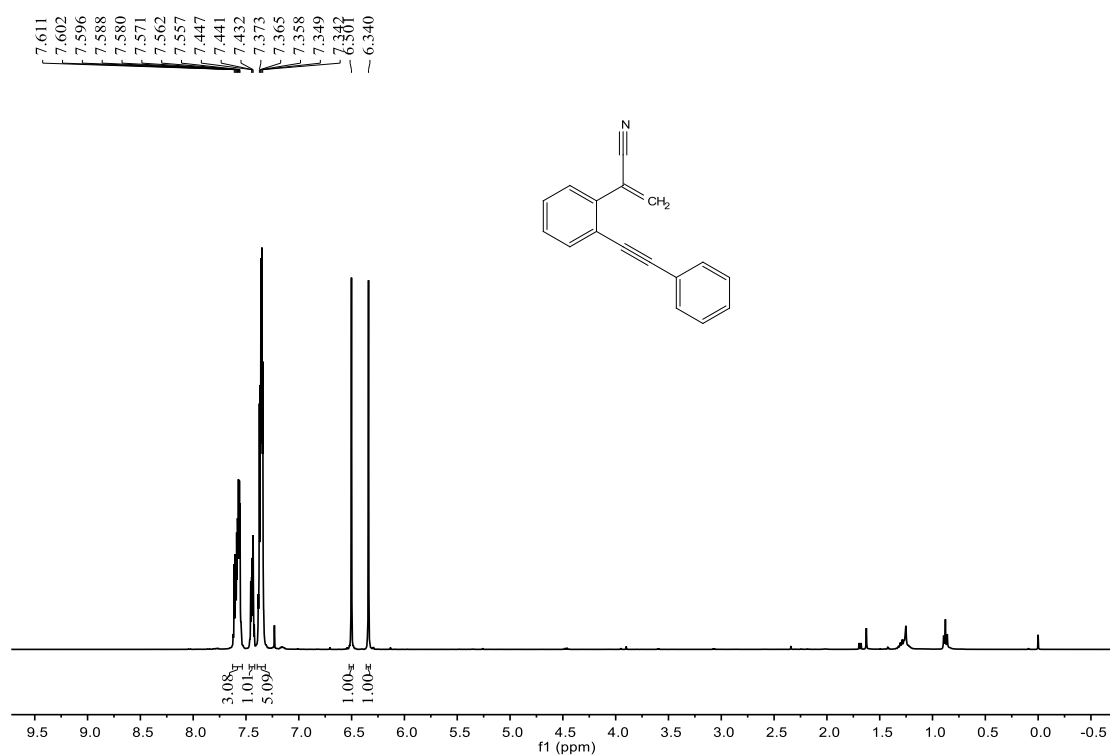
¹H NMR spectra of compound **1o**.



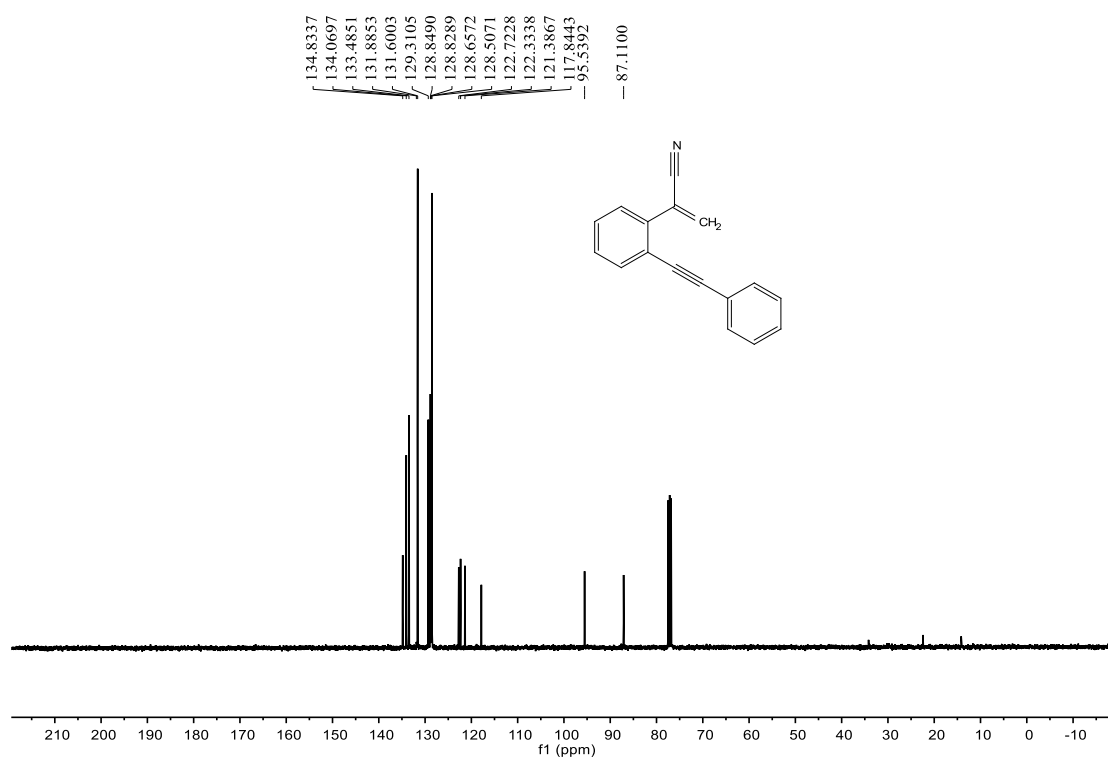
¹³C NMR spectra of compound **1o**.



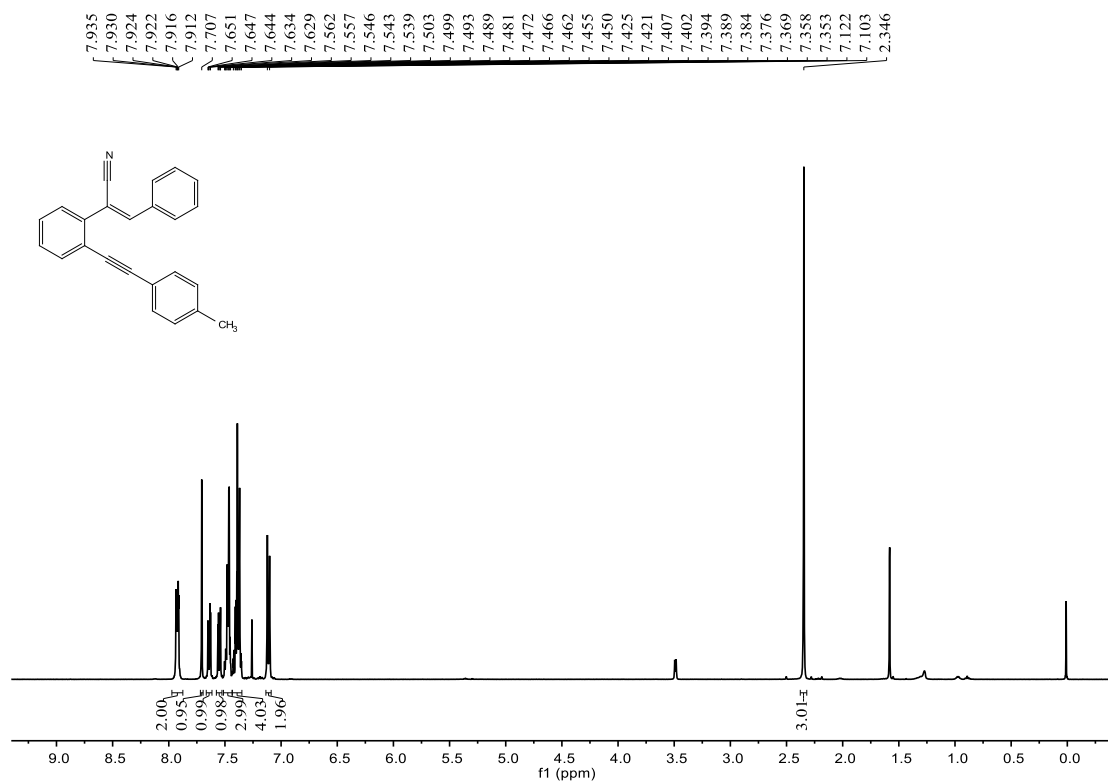
¹H NMR spectra of compound **1p**.



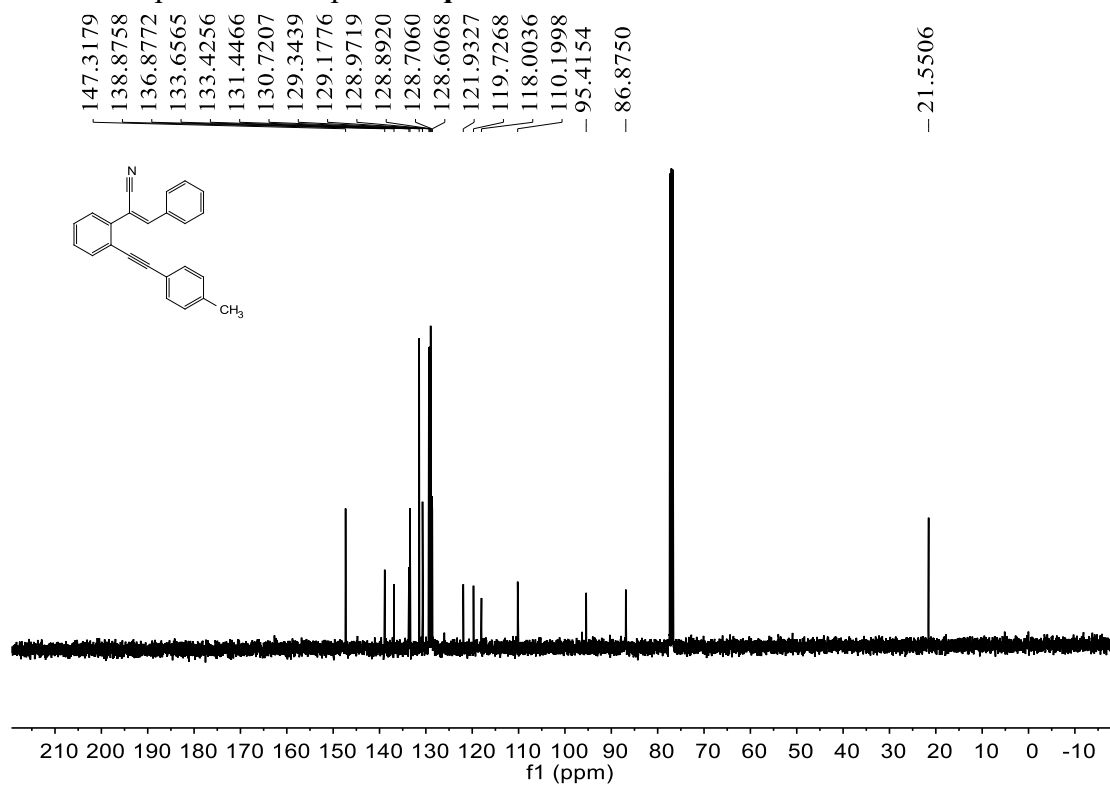
¹³C NMR spectra of compound **1p**.



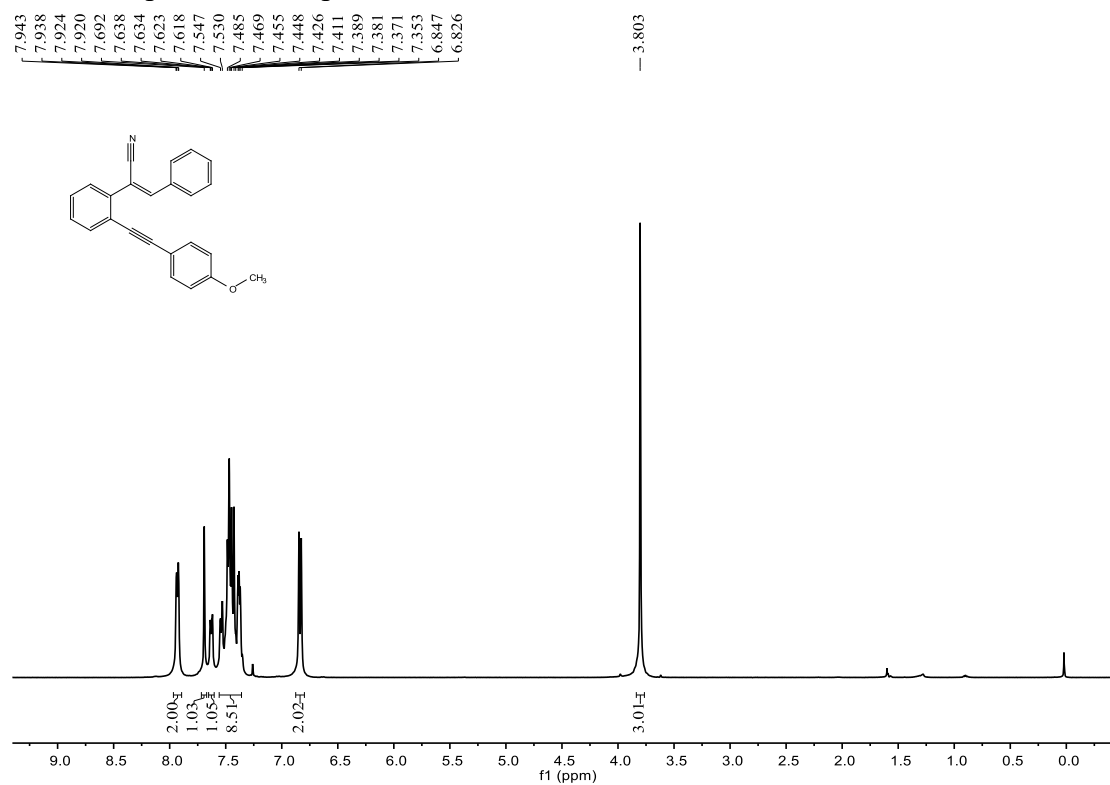
¹H NMR spectra of compound **1q**.



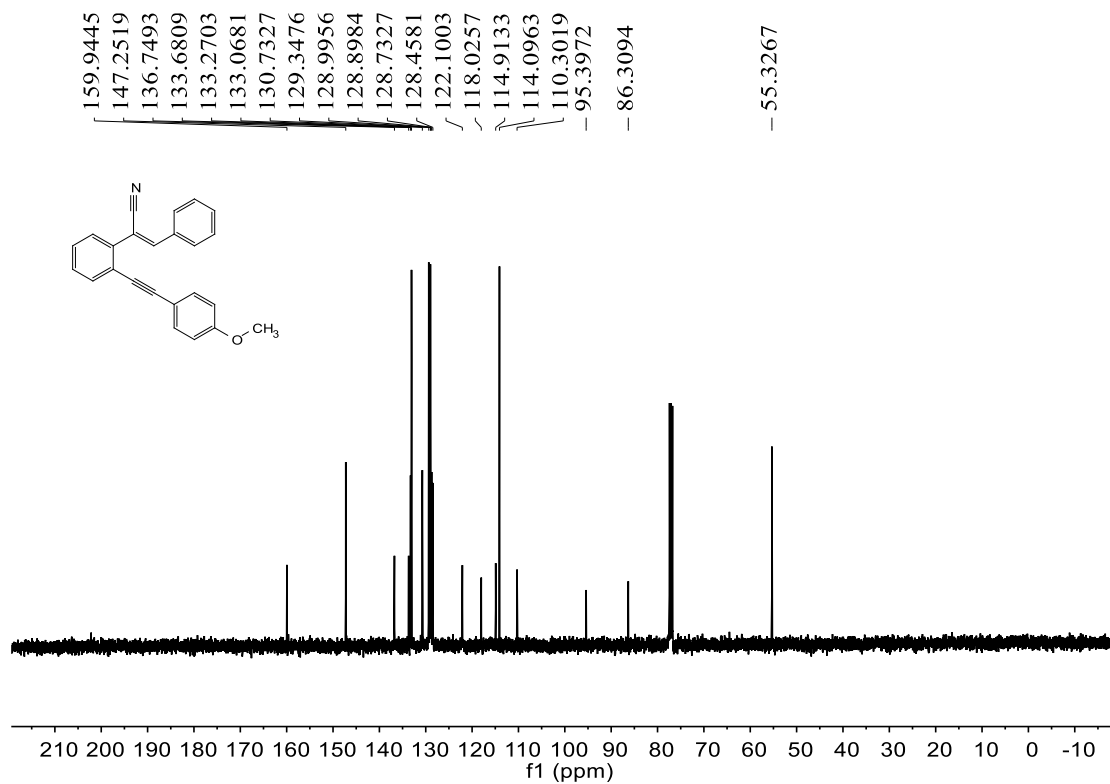
¹³C NMR spectra of compound **1q**.



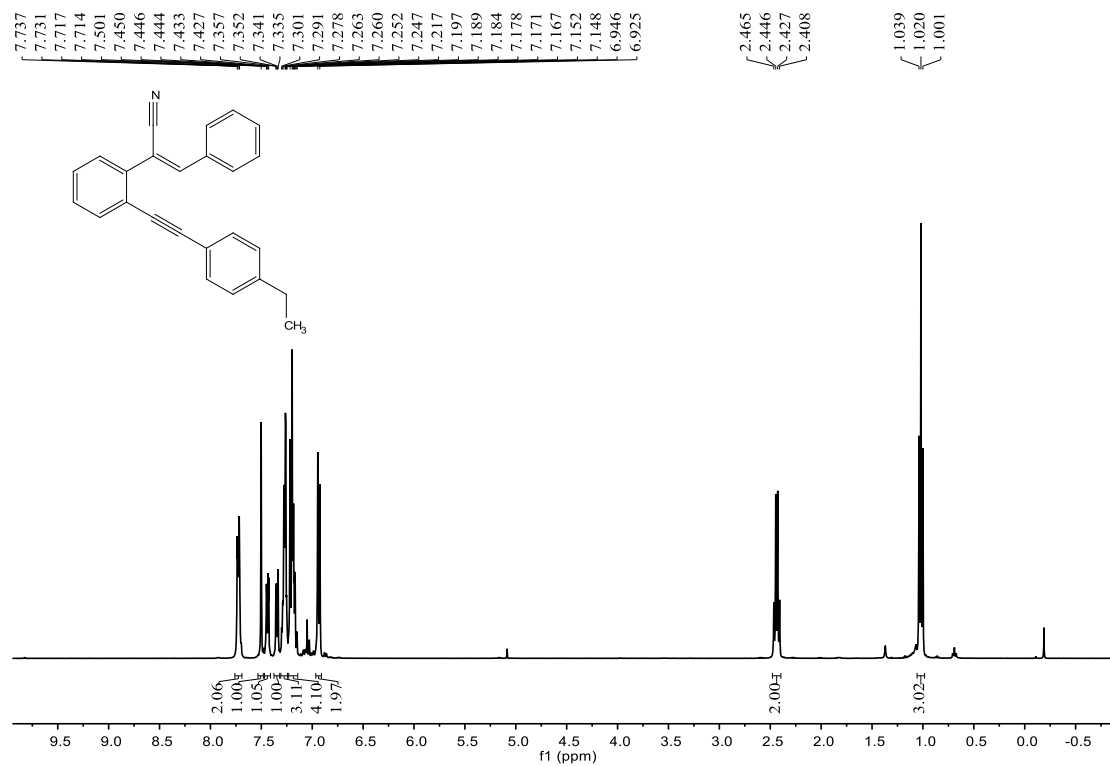
¹H NMR spectra of compound **1r**.



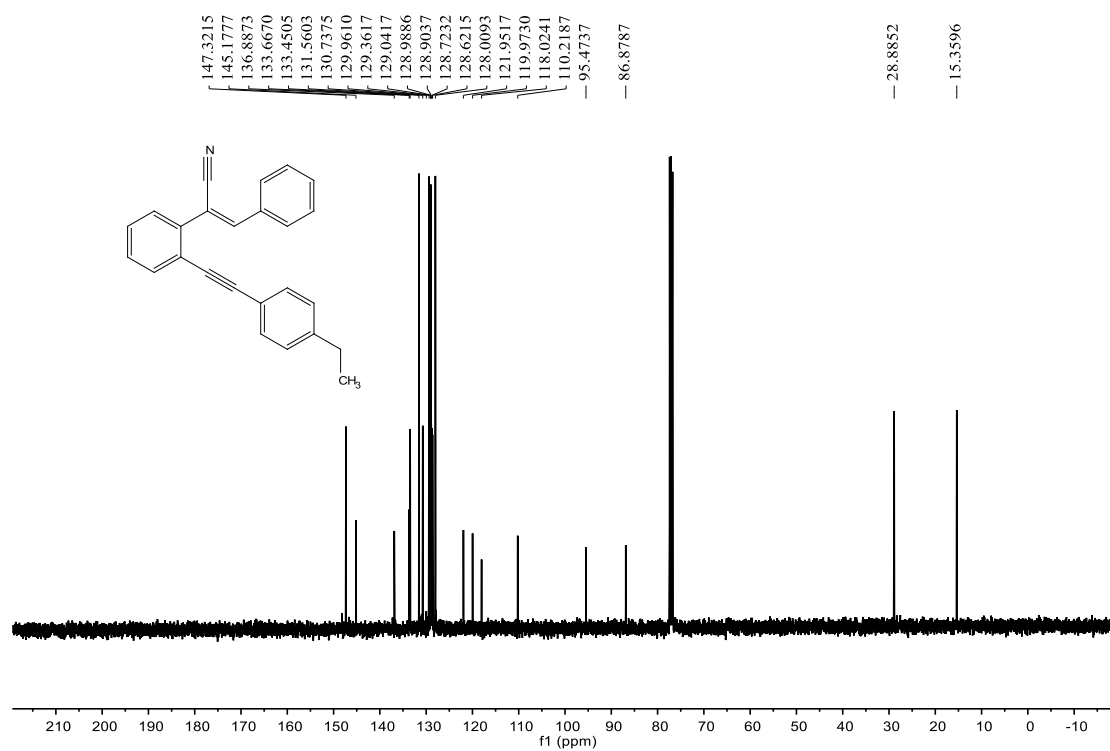
¹³C NMR spectra of compound **1r**.



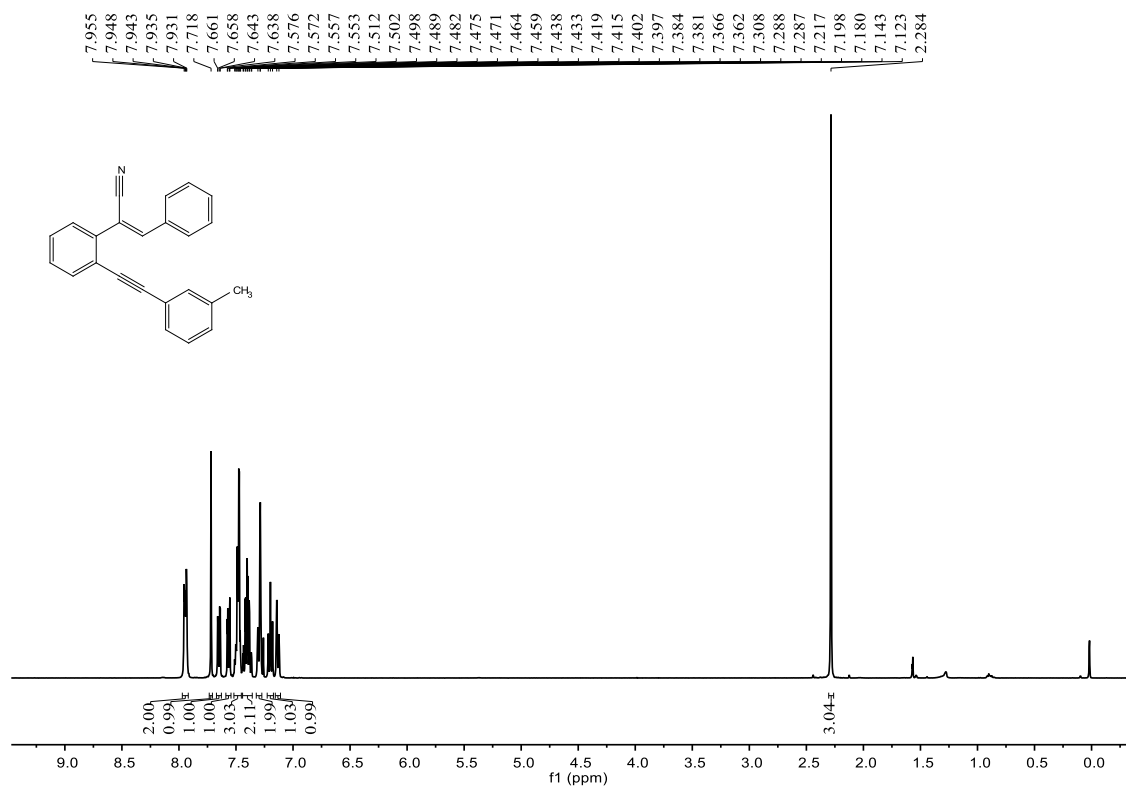
¹H NMR spectra of compound **1s**.



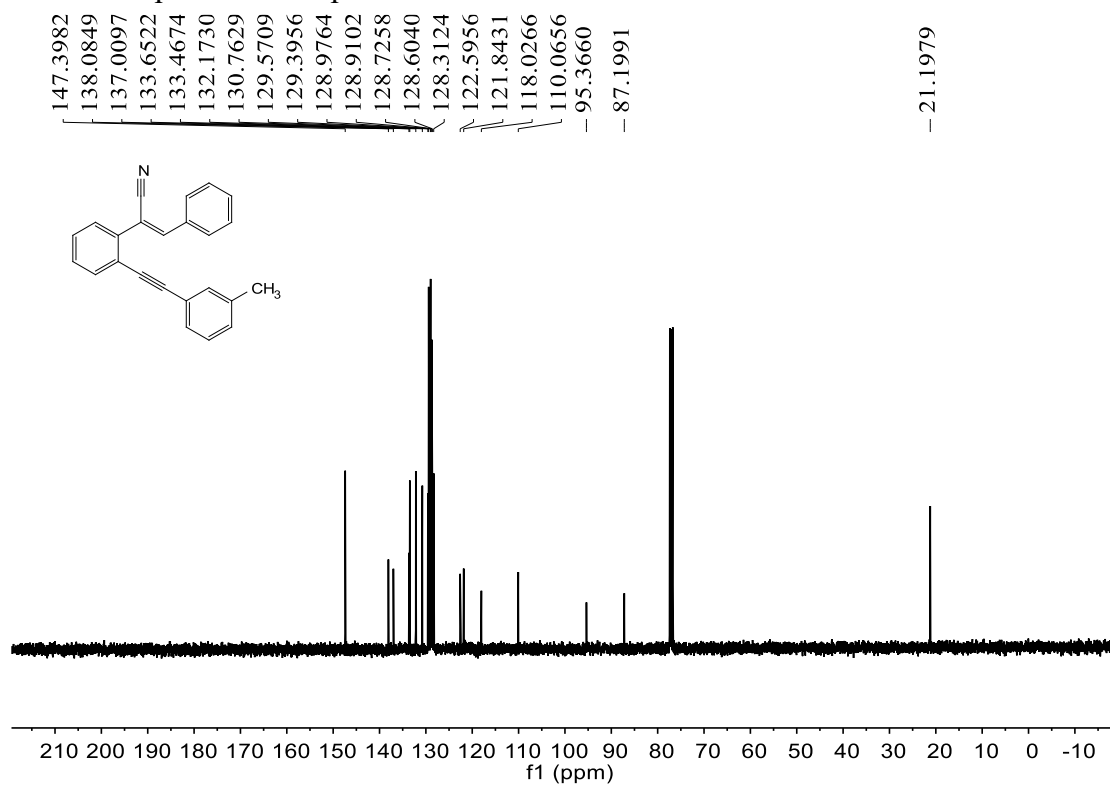
¹³C NMR spectra of compound **1s**.



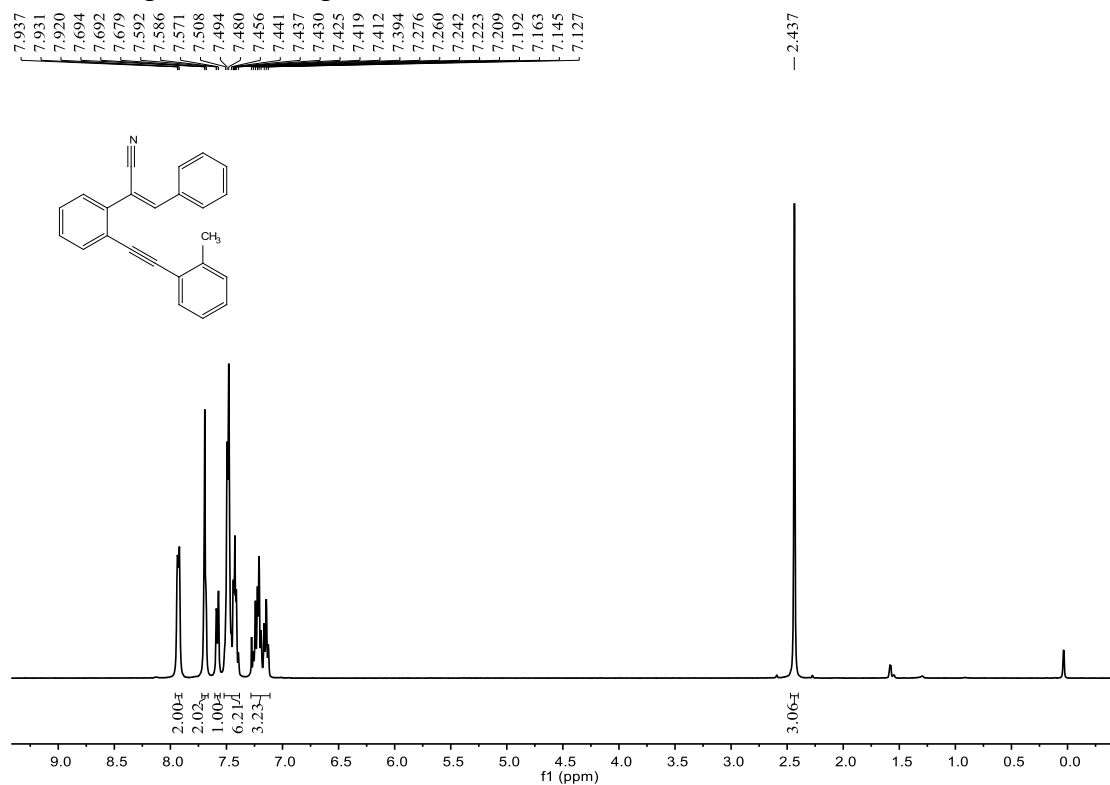
¹H NMR spectra of compound **1t**.



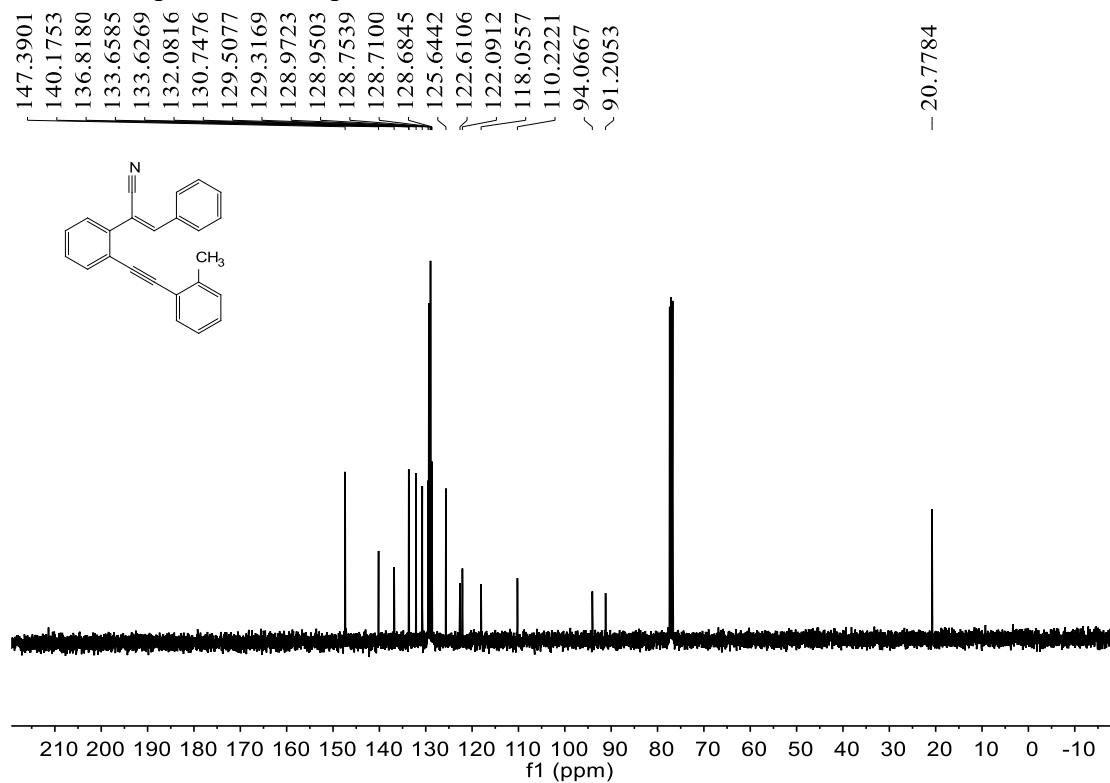
¹³C NMR spectra of compound **1t**.



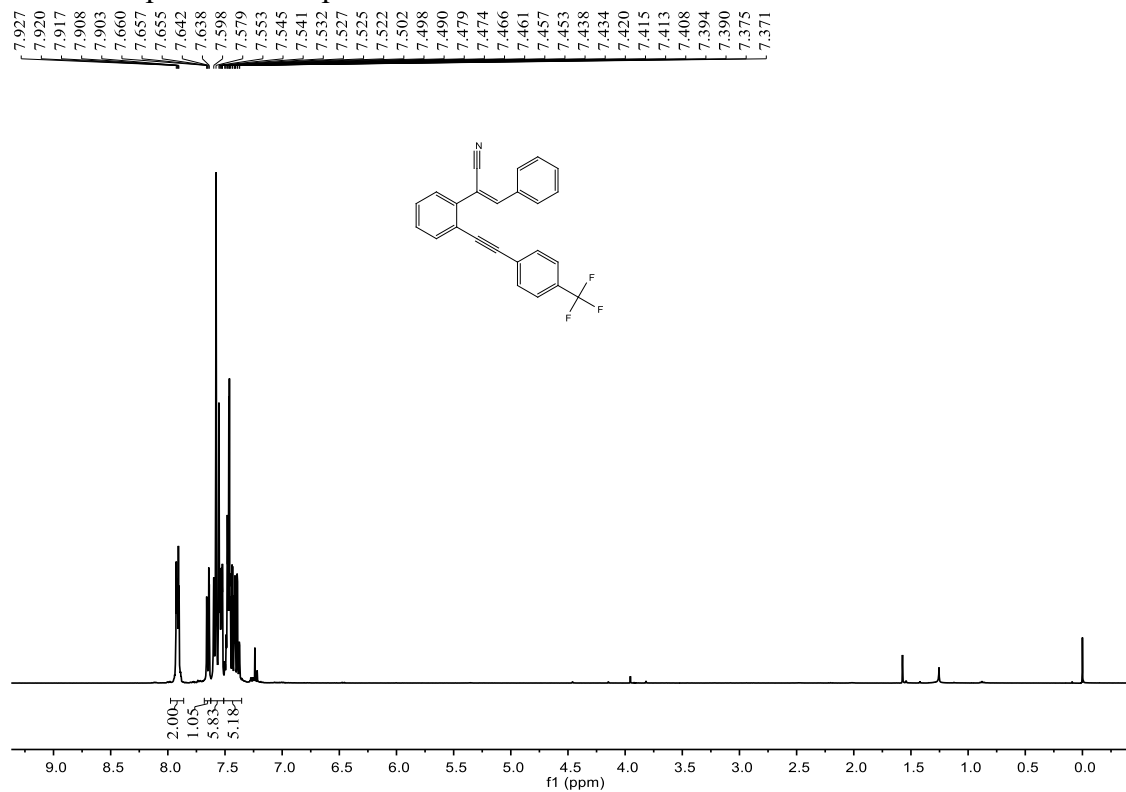
¹H NMR spectra of compound **1u**.



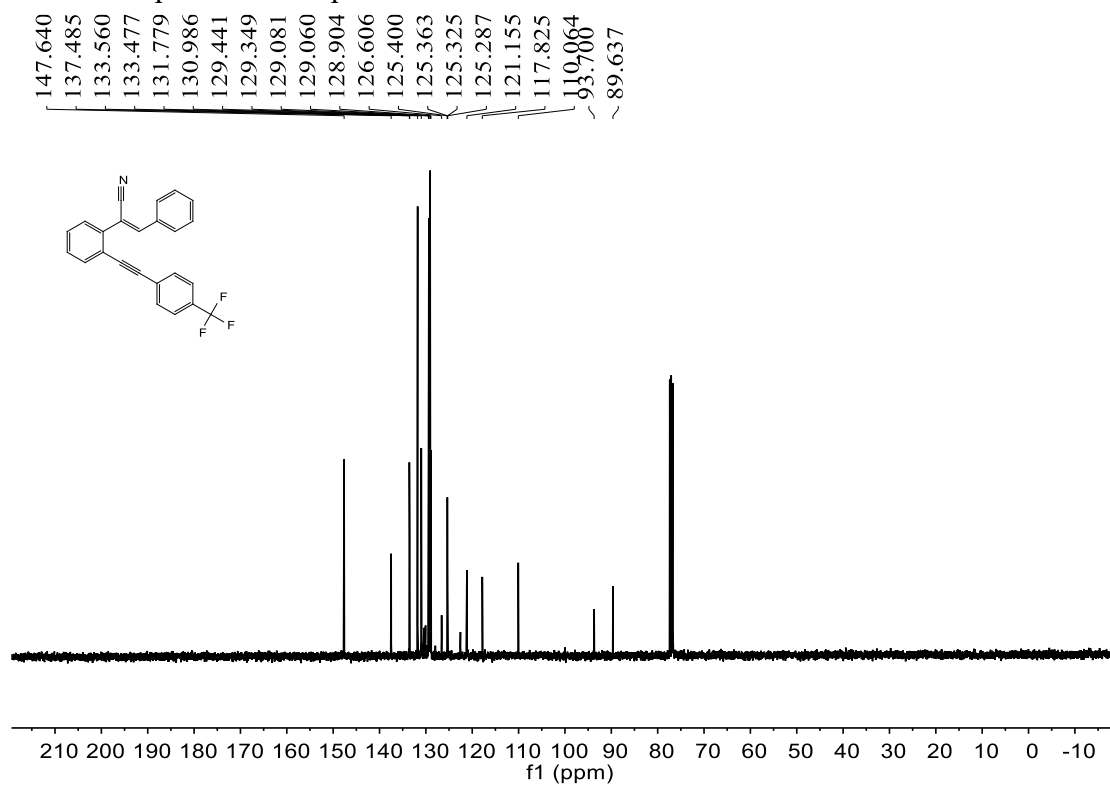
¹³C NMR spectra of compound **1u**.



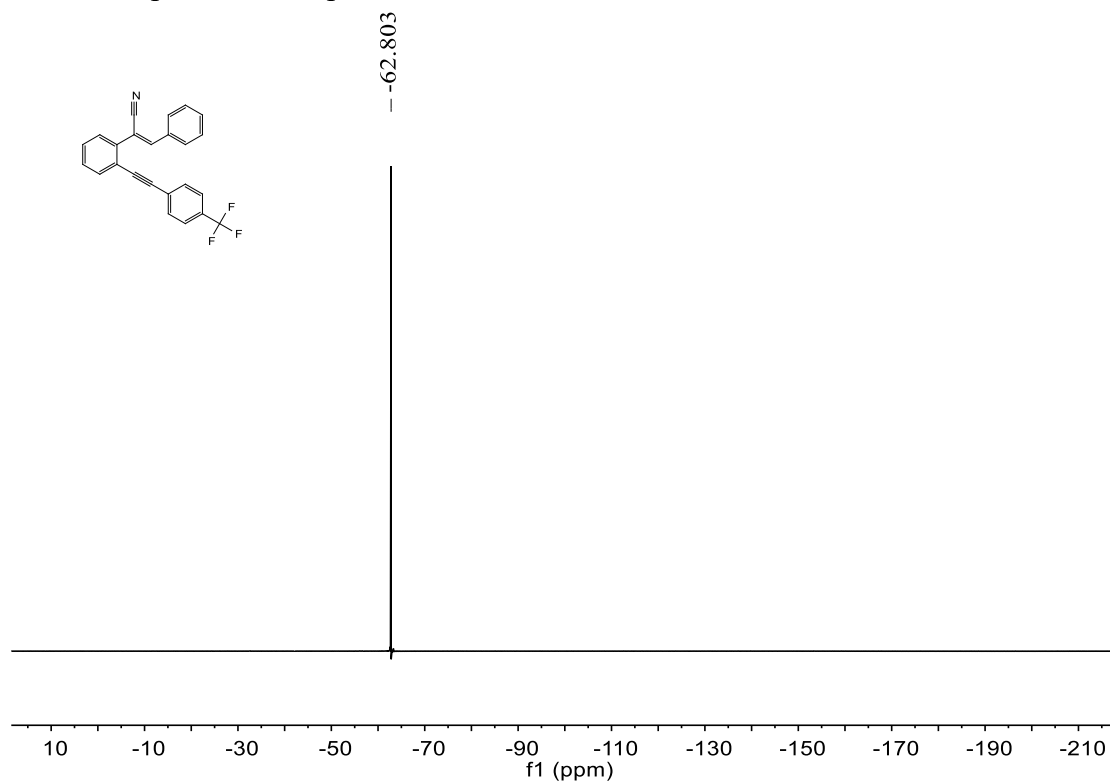
¹H NMR spectra of compound **1v**.



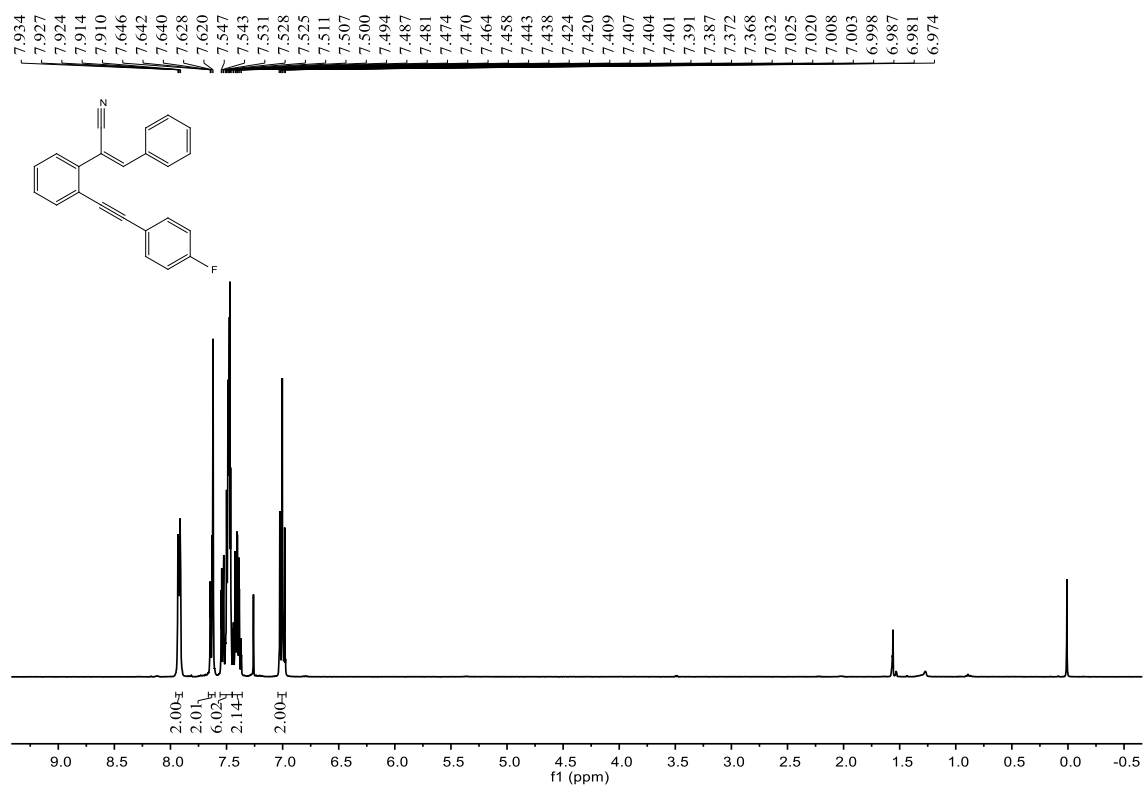
¹³C NMR spectra of compound **1v**.



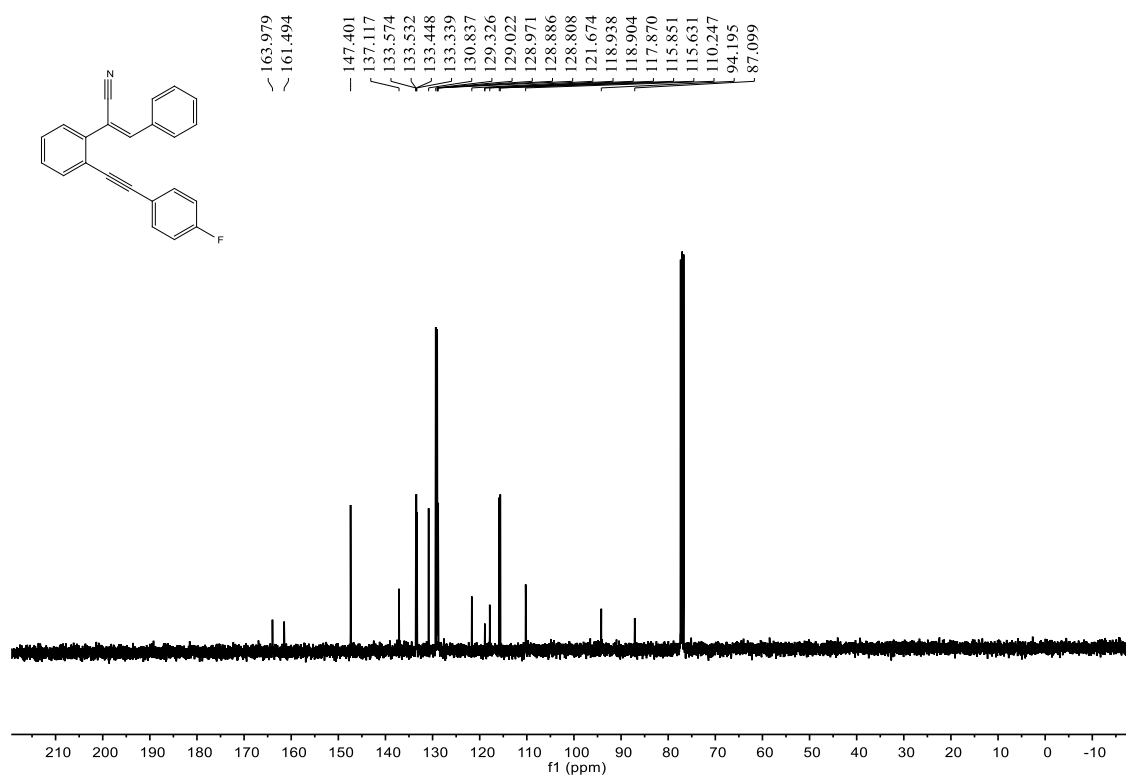
¹⁹F NMR spectra of compound **1v**.



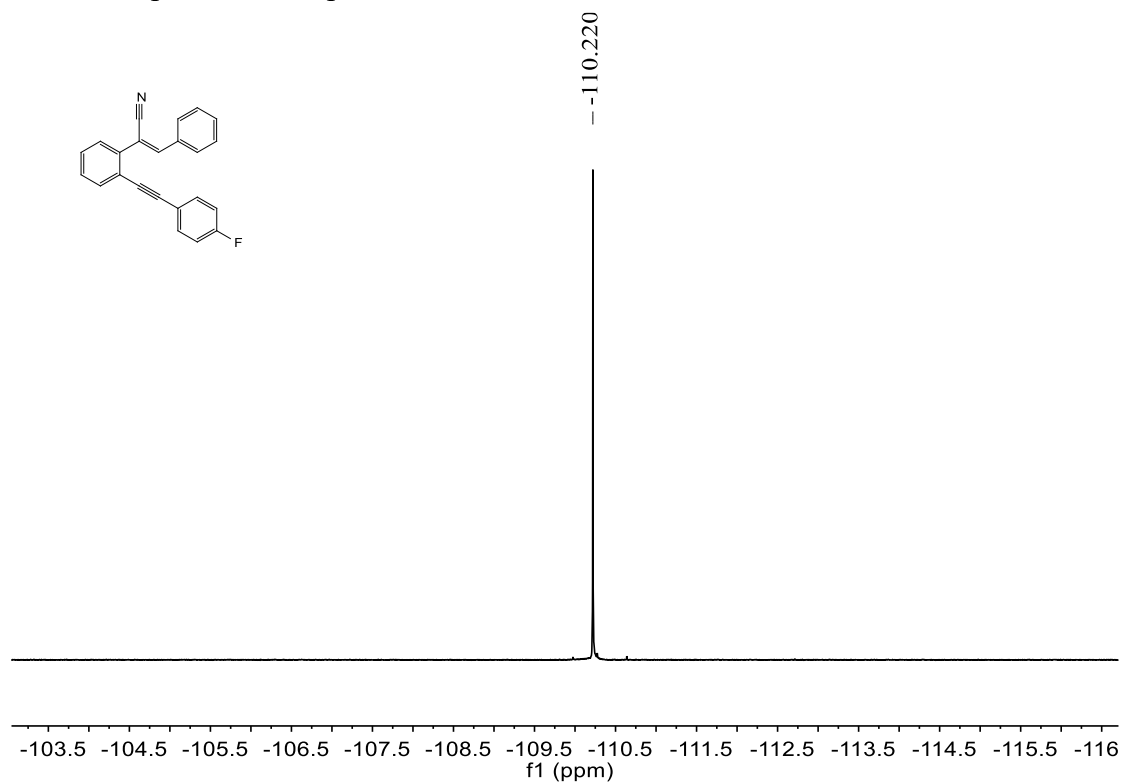
¹H NMR spectra of compound 1w.



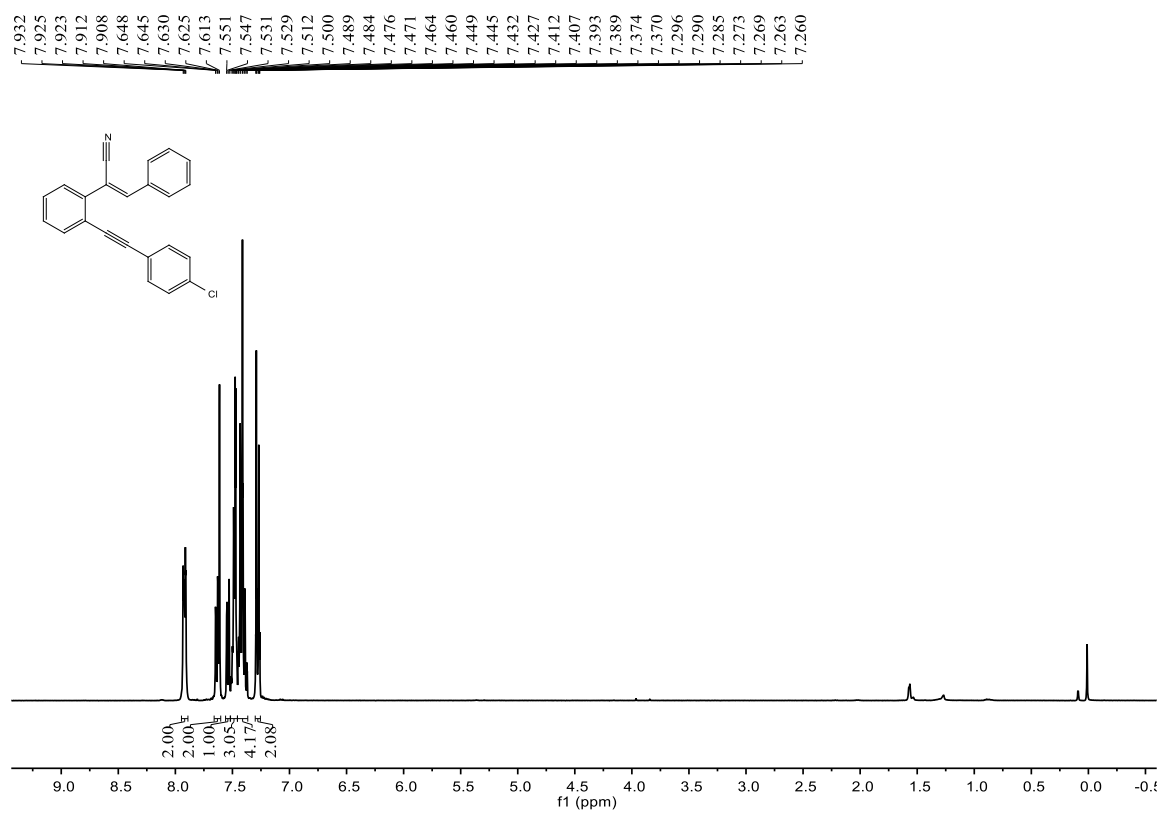
¹³C NMR spectra of compound 1w.



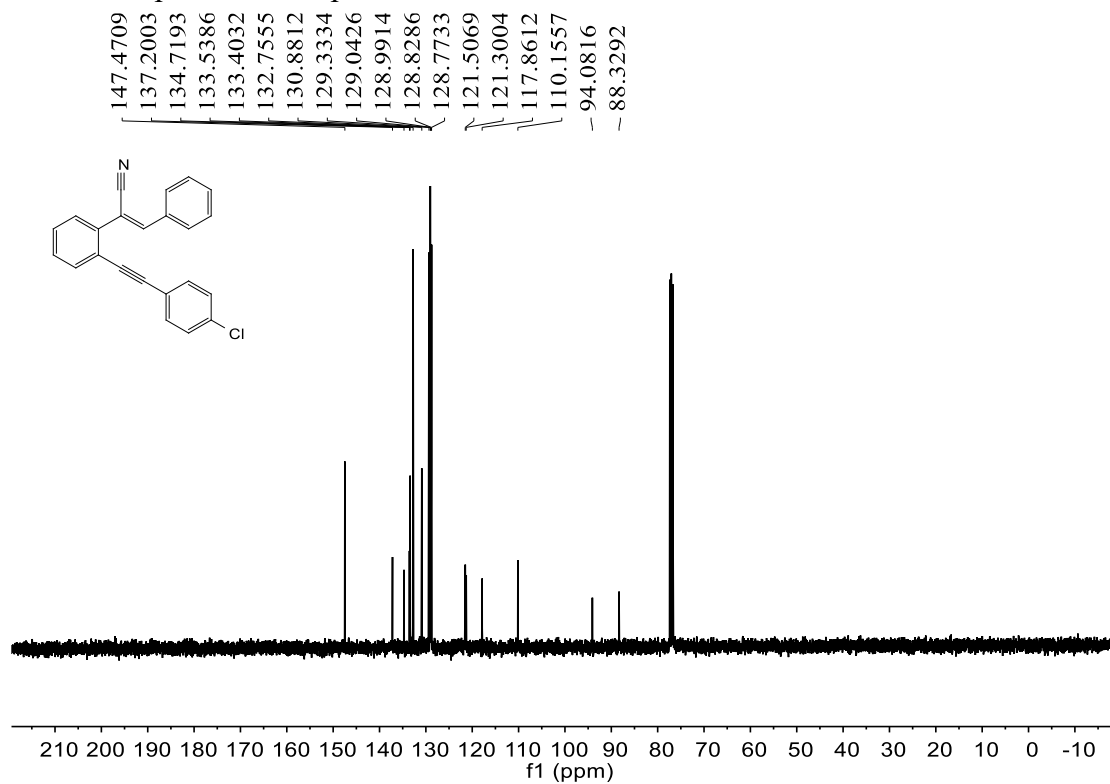
¹⁹F NMR spectra of compound **1w**.



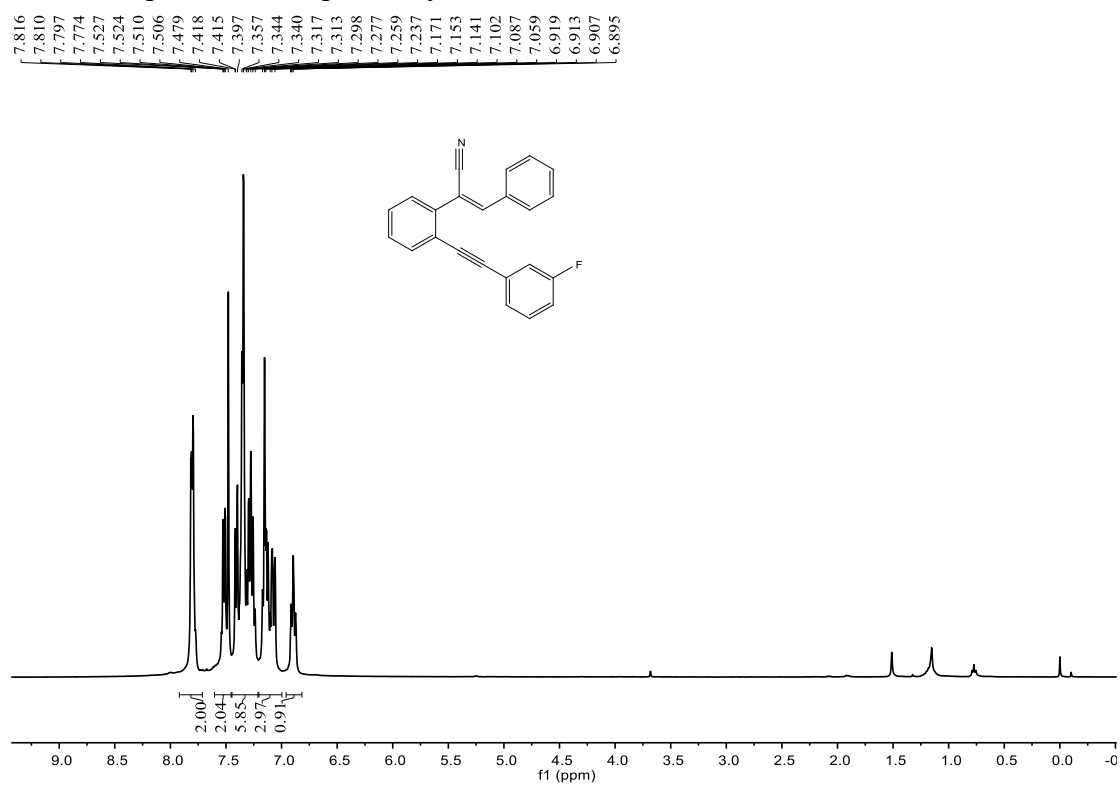
¹H NMR spectra of compound **1x**.



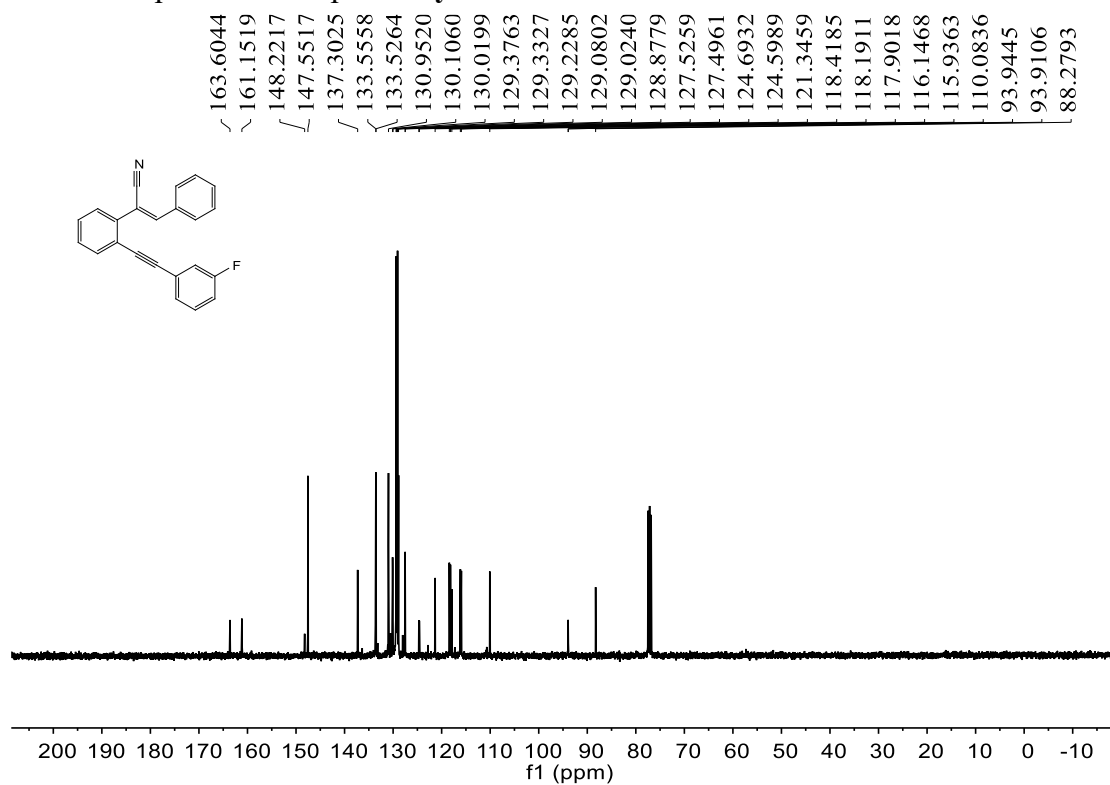
¹³C NMR spectra of compound **1x**.



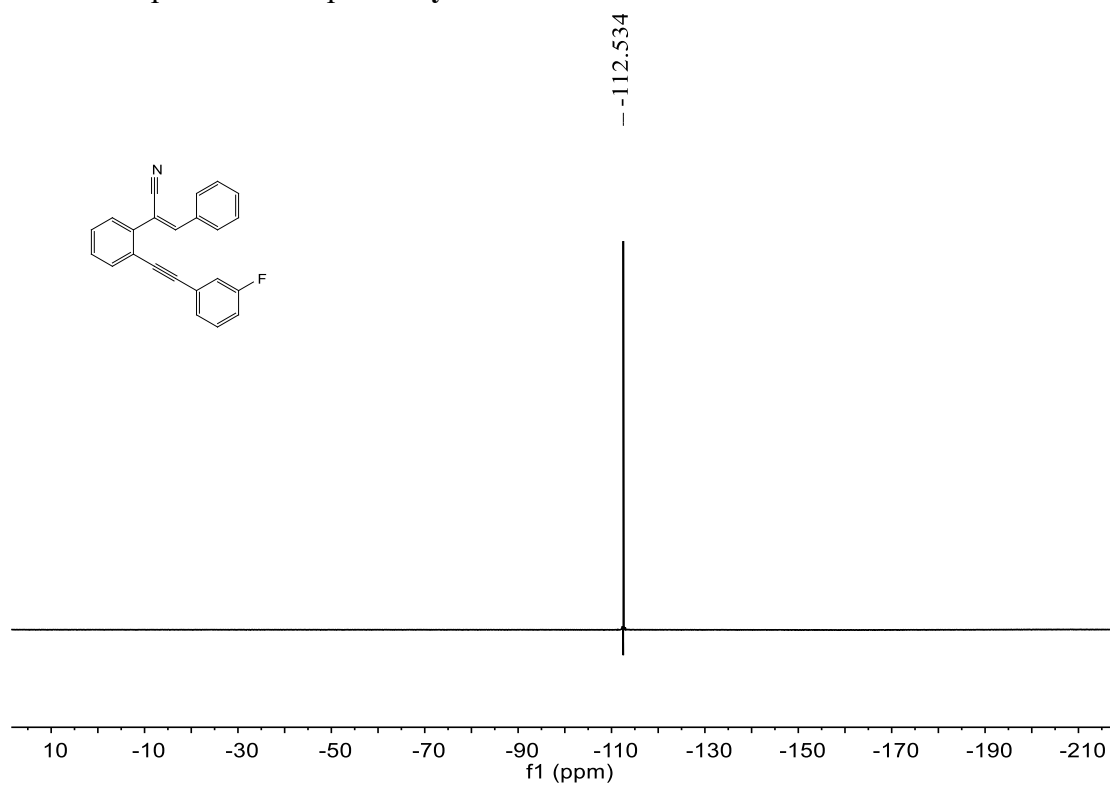
¹H NMR spectra of compound **1y**.



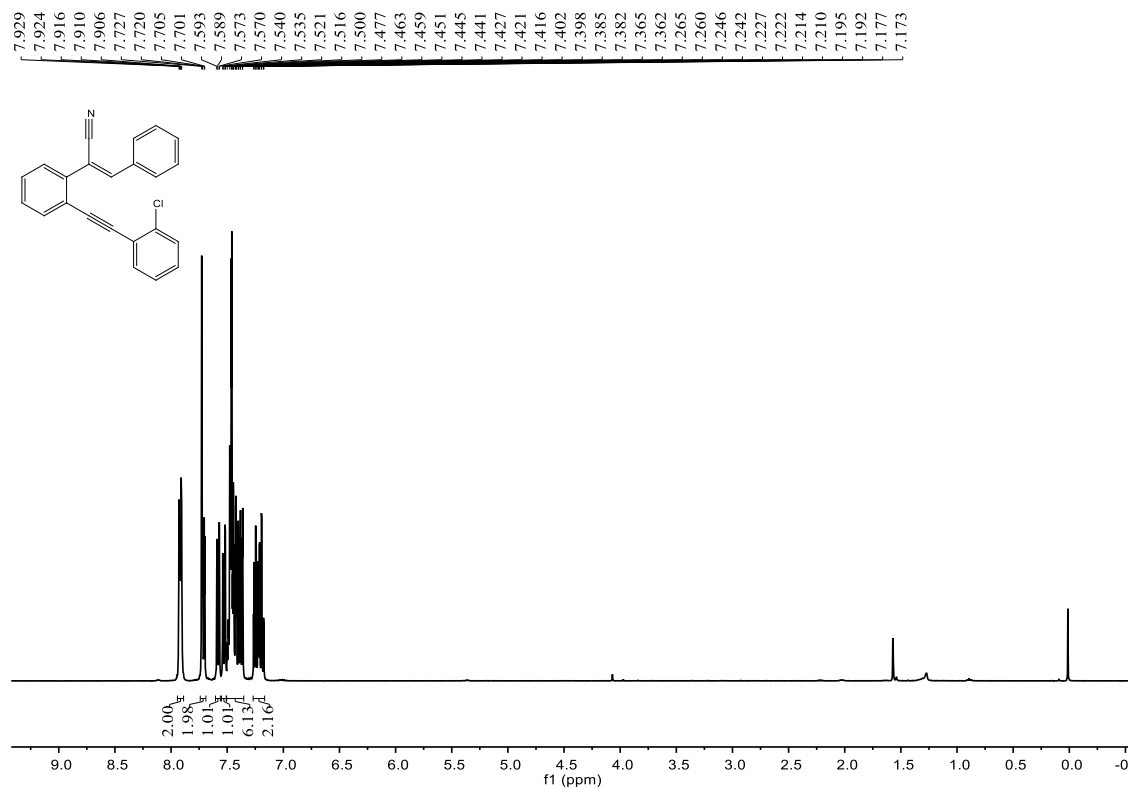
¹³C NMR spectra of compound **1y**.



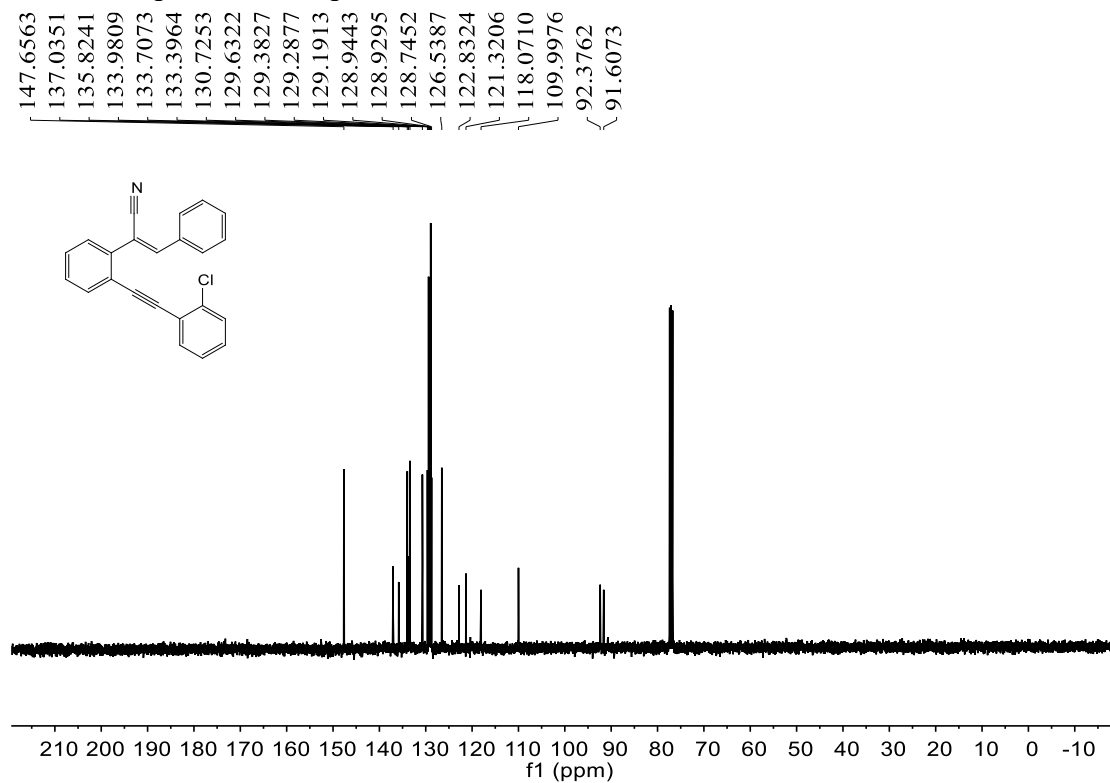
¹⁹F NMR spectra of compound **1y**.



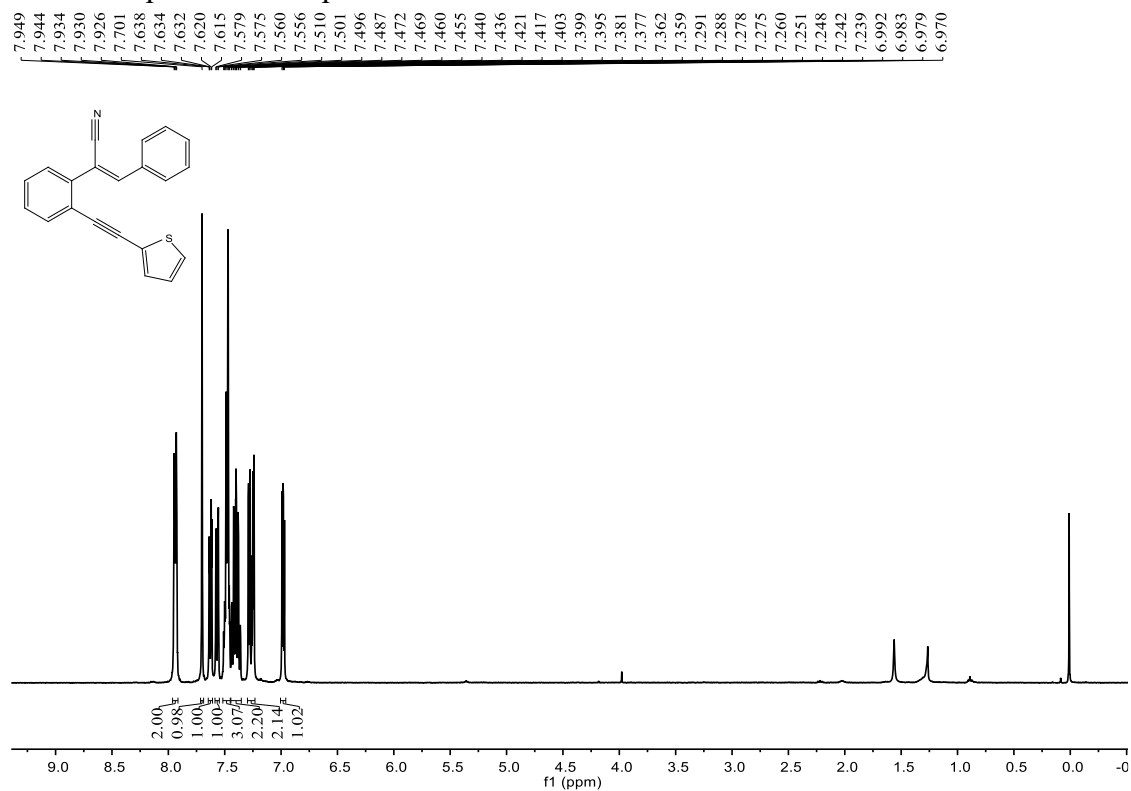
¹H NMR spectra of compound **1z**.



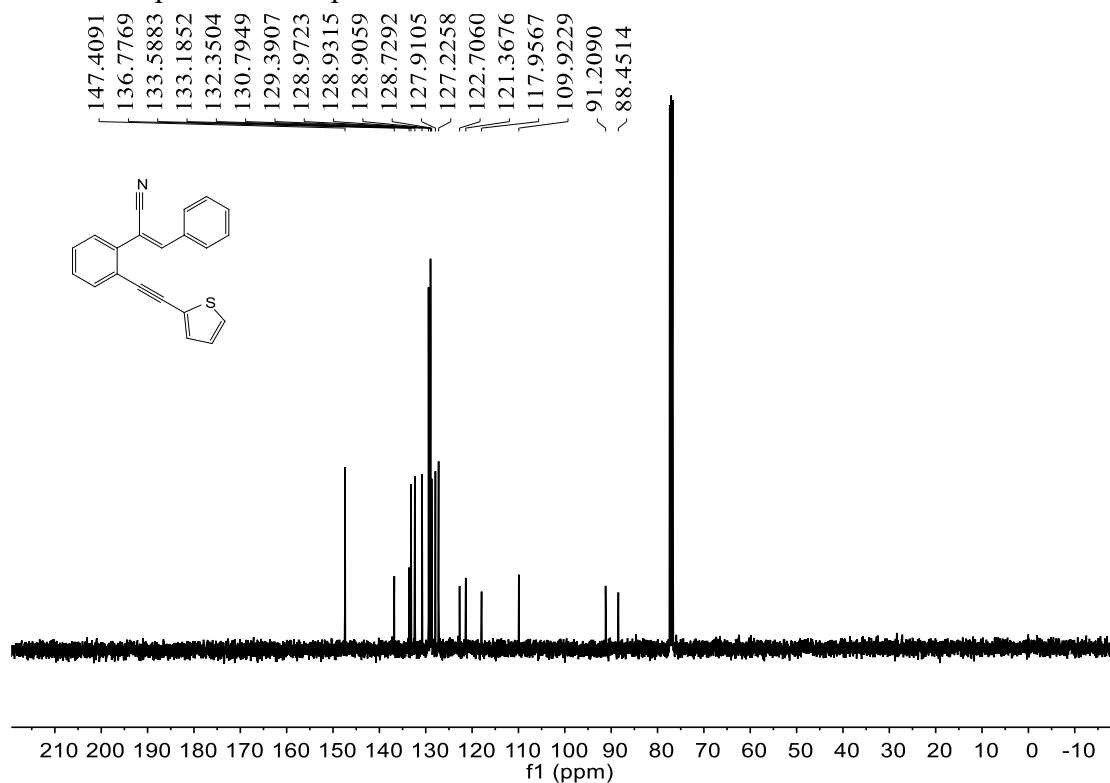
¹³C NMR spectra of compound **1z**.



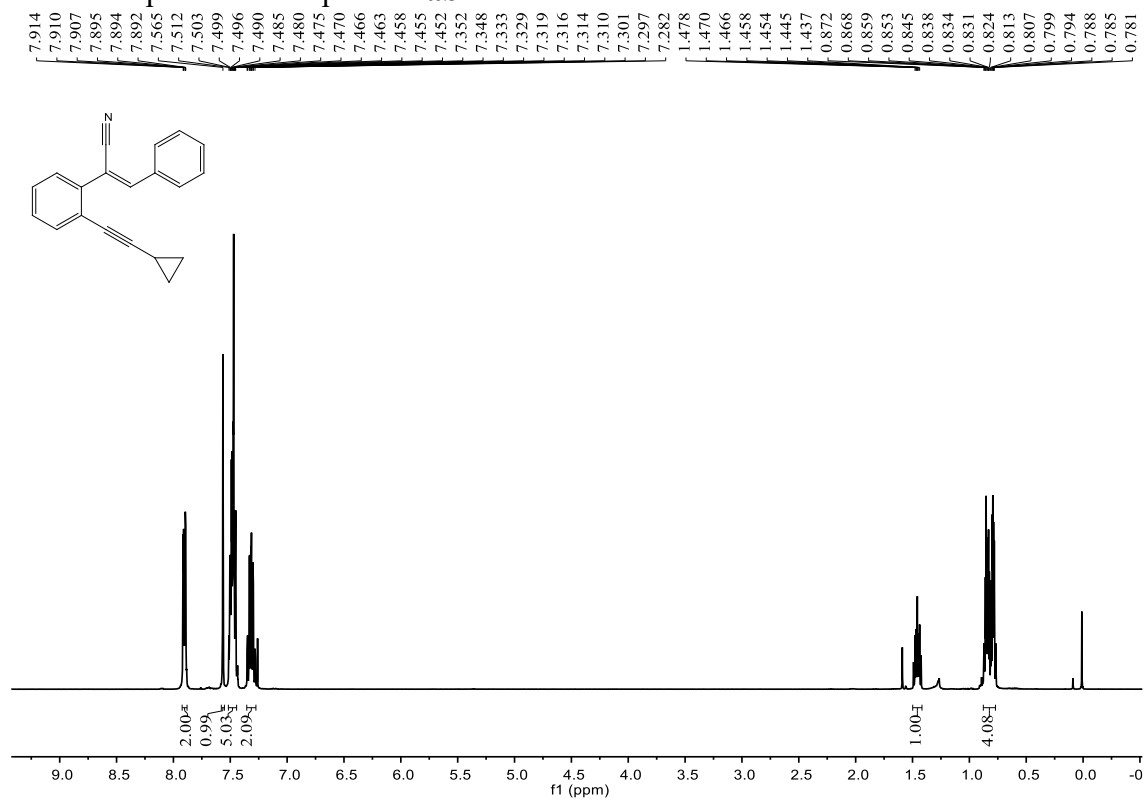
¹H NMR spectra of compound **1aa**.



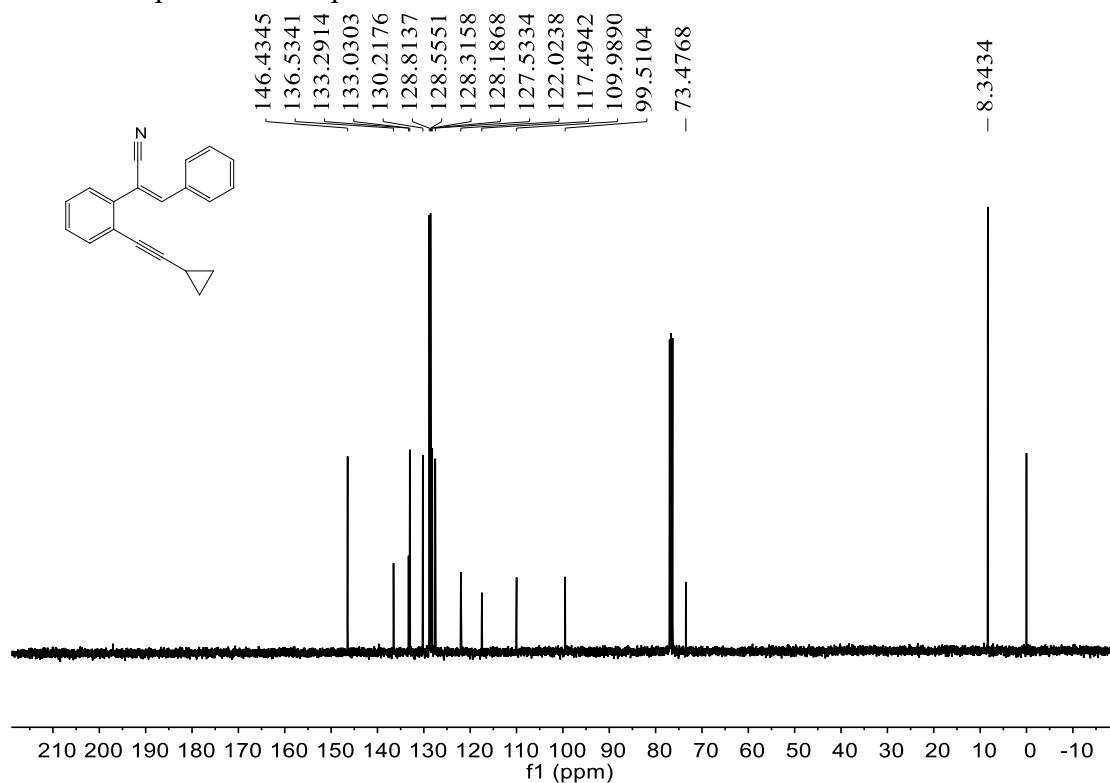
¹³C NMR spectra of compound **1aa**.



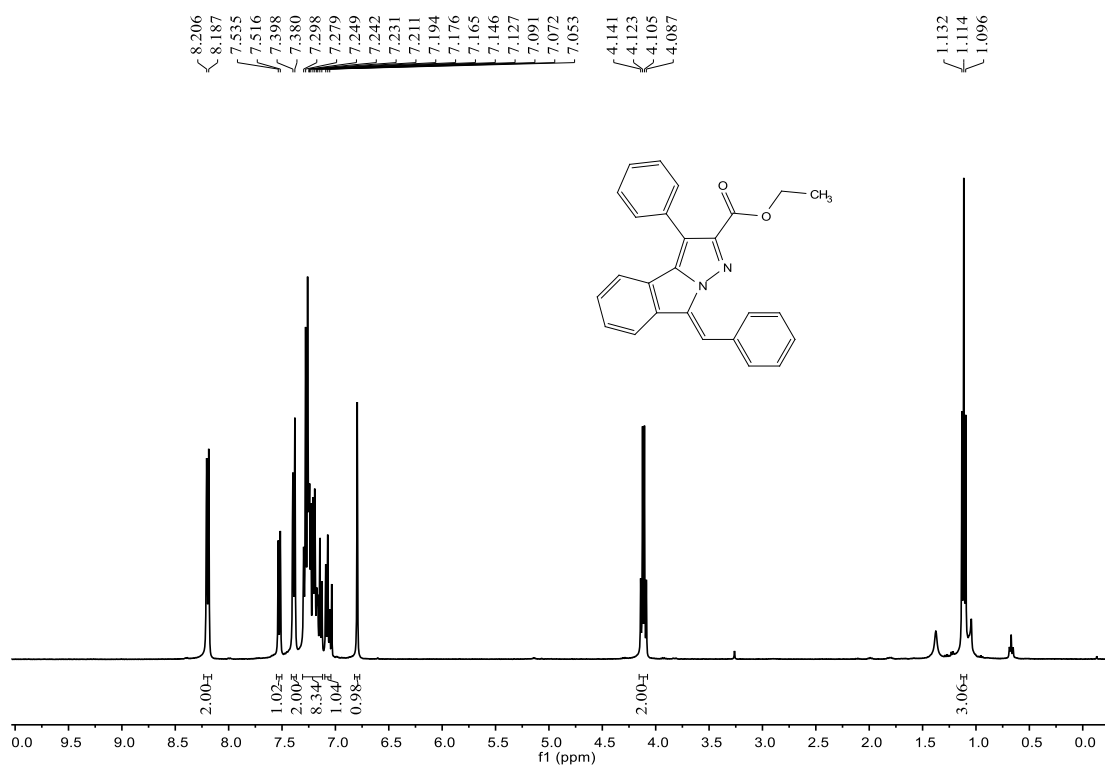
¹H NMR spectra of compound **1ab**.



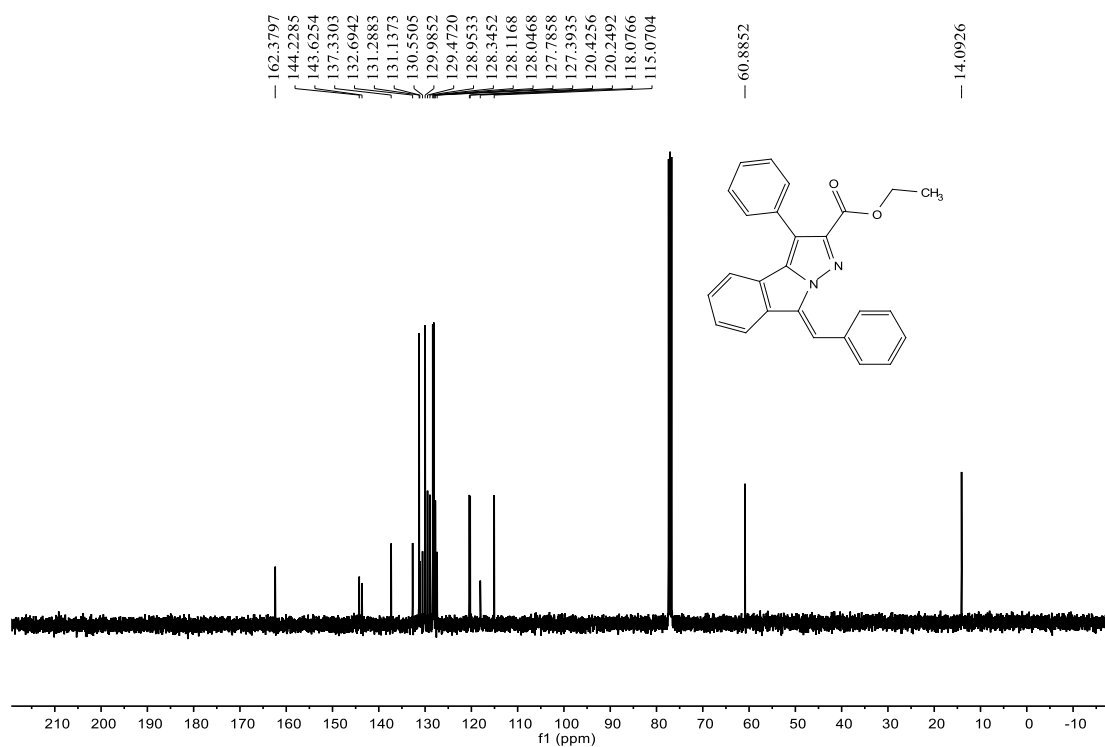
¹³C NMR spectra of compound **1ab**.



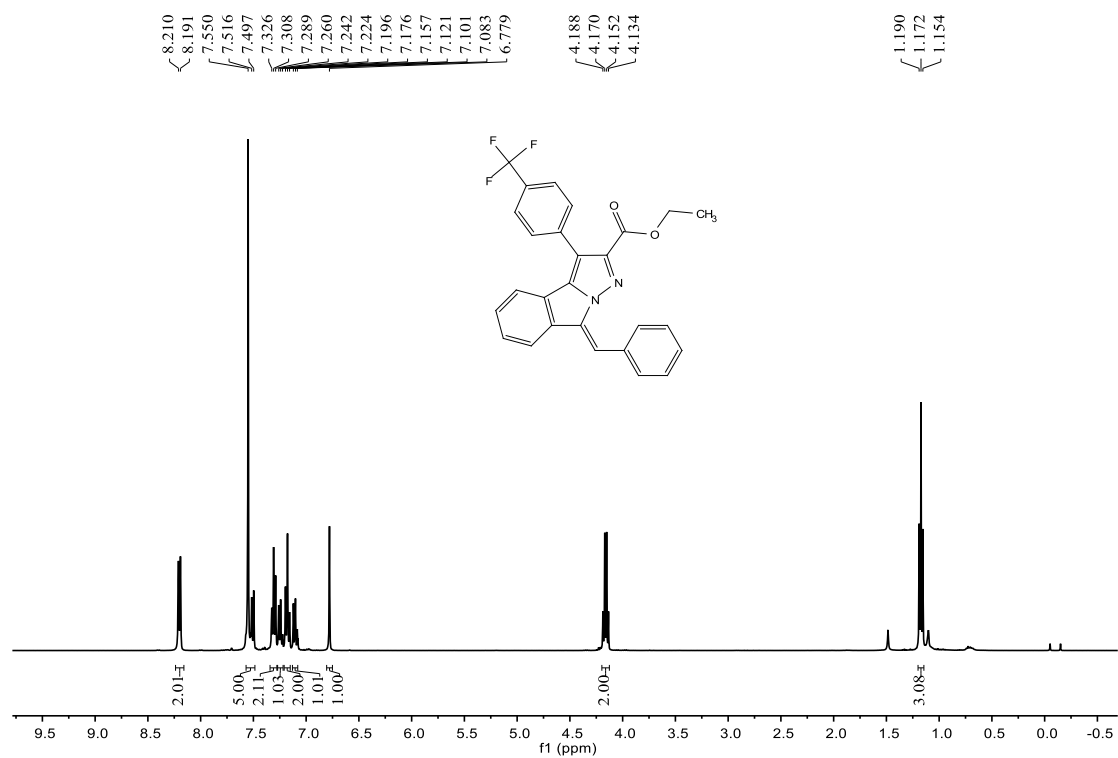
^1H NMR spectra of compound **3aa**.



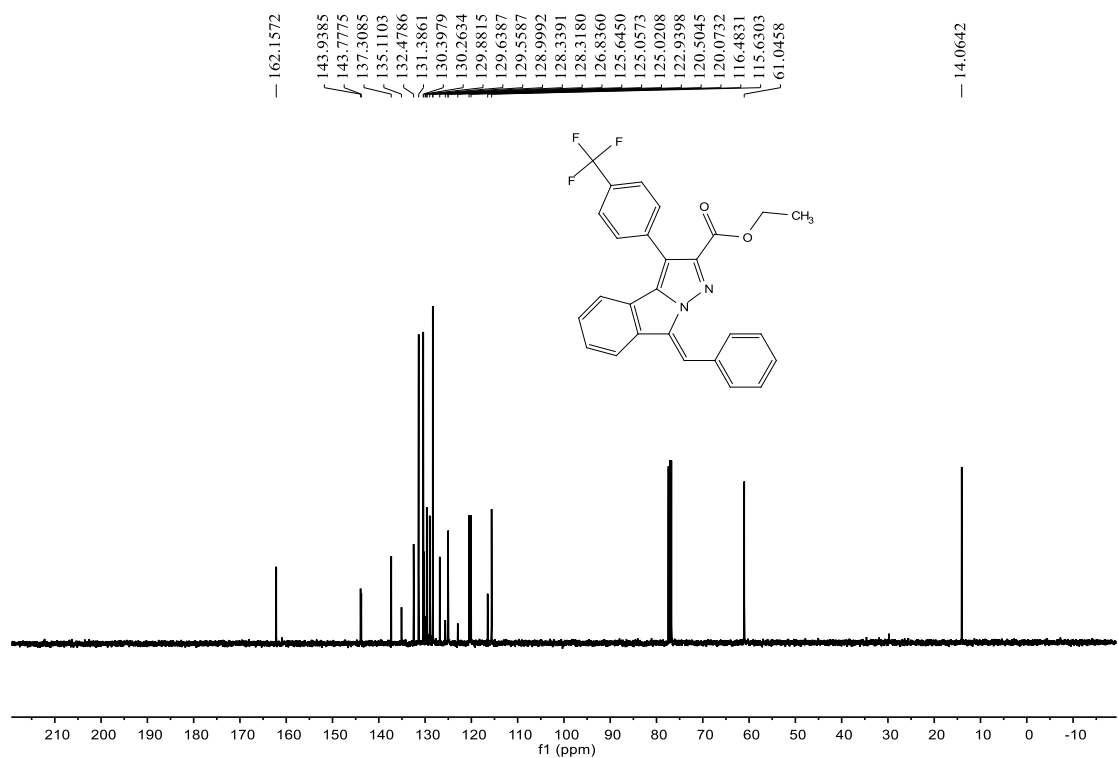
^{13}C NMR spectra of compound **3aa**.



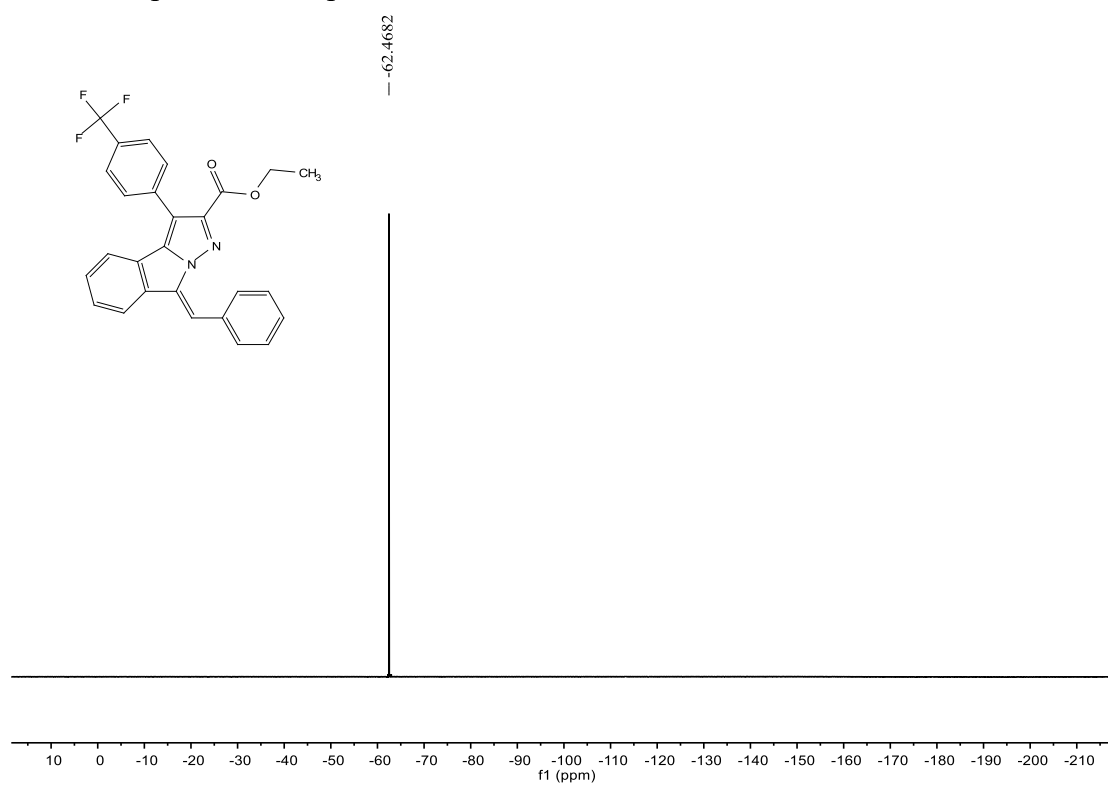
¹H NMR spectra of compound **3ab**.



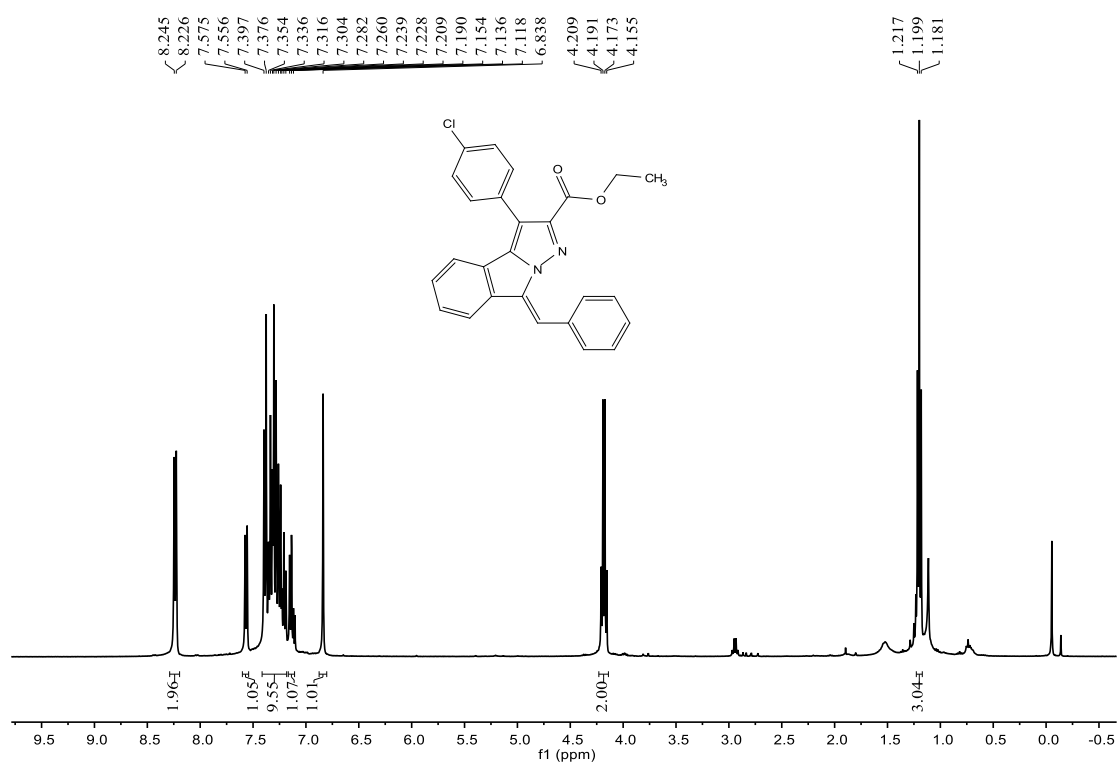
¹³C NMR spectra of compound **3ab**.



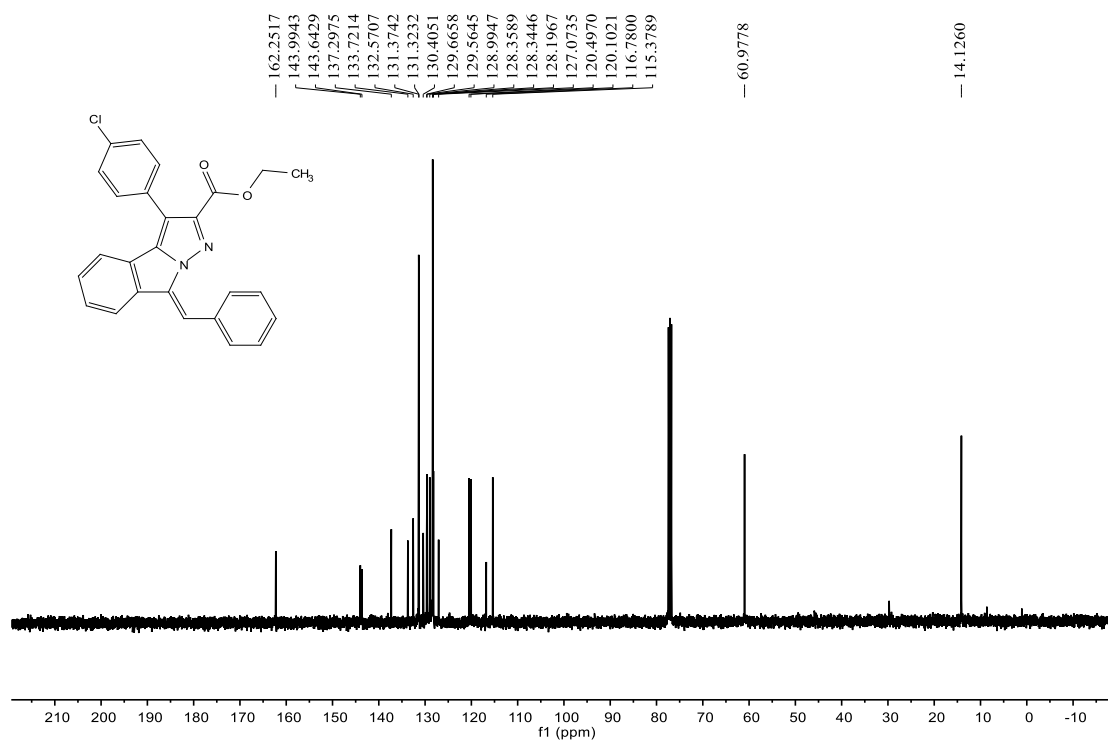
¹⁹F NMR spectra of compound **3ab**.



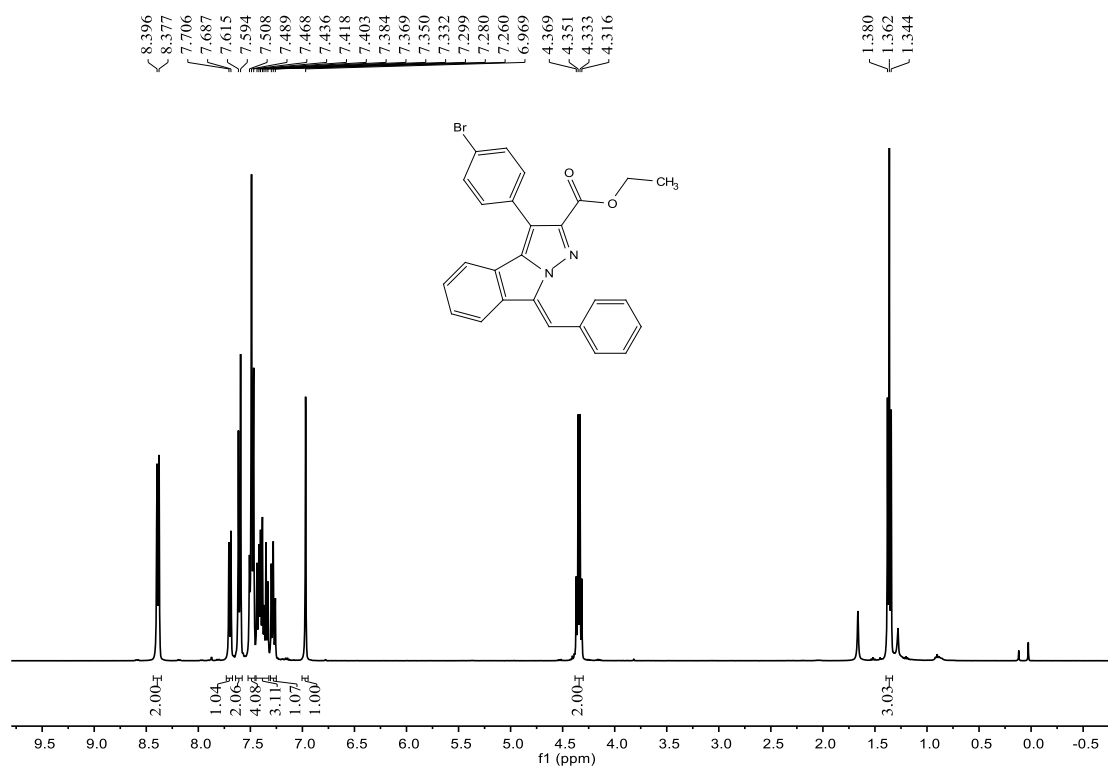
¹H NMR spectra of compound **3ac**.



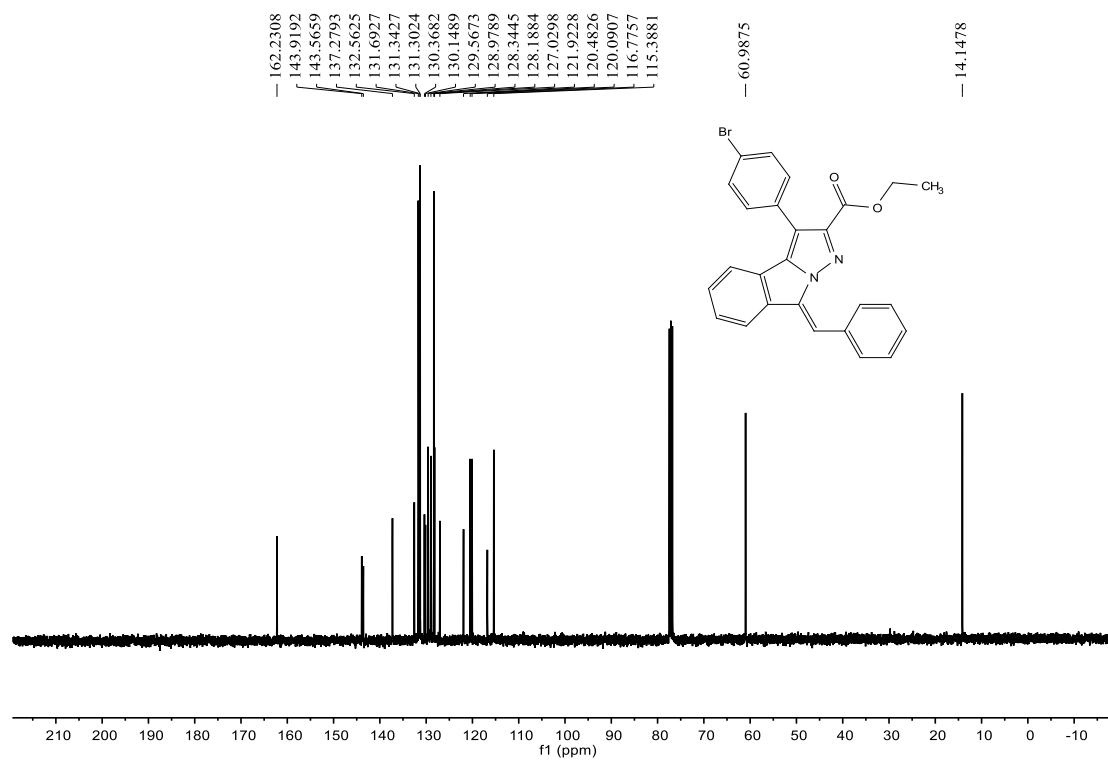
¹³C NMR spectra of compound **3ac**.



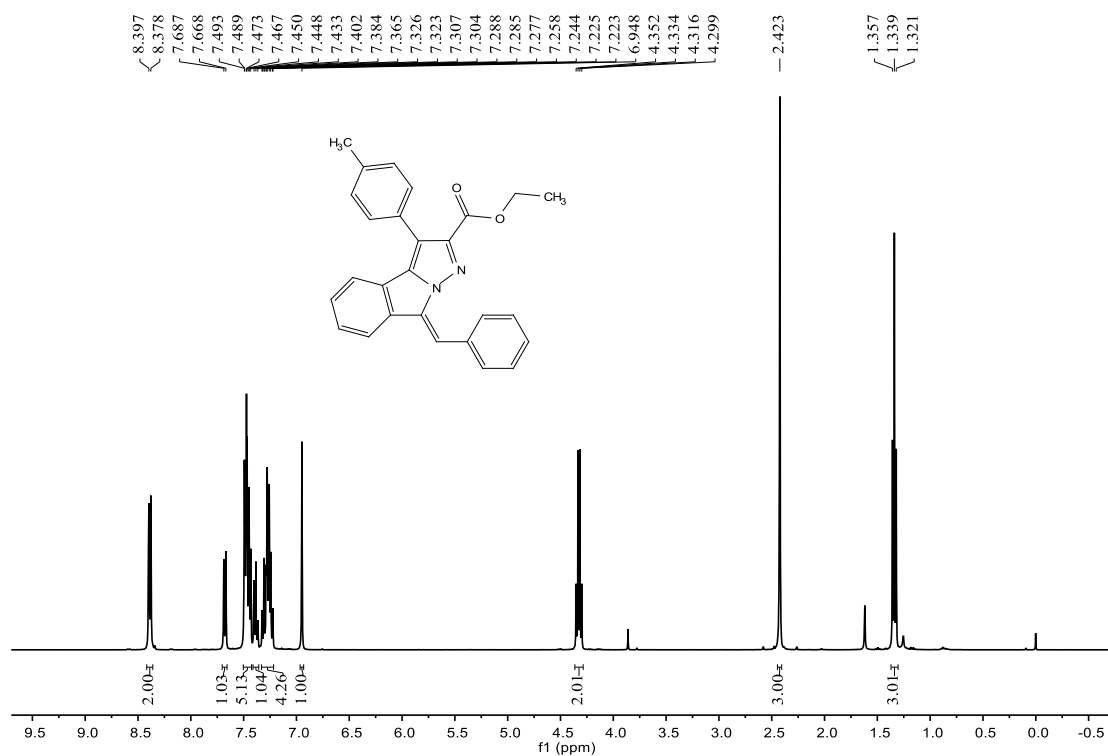
¹H NMR spectra of compound **3ad**.



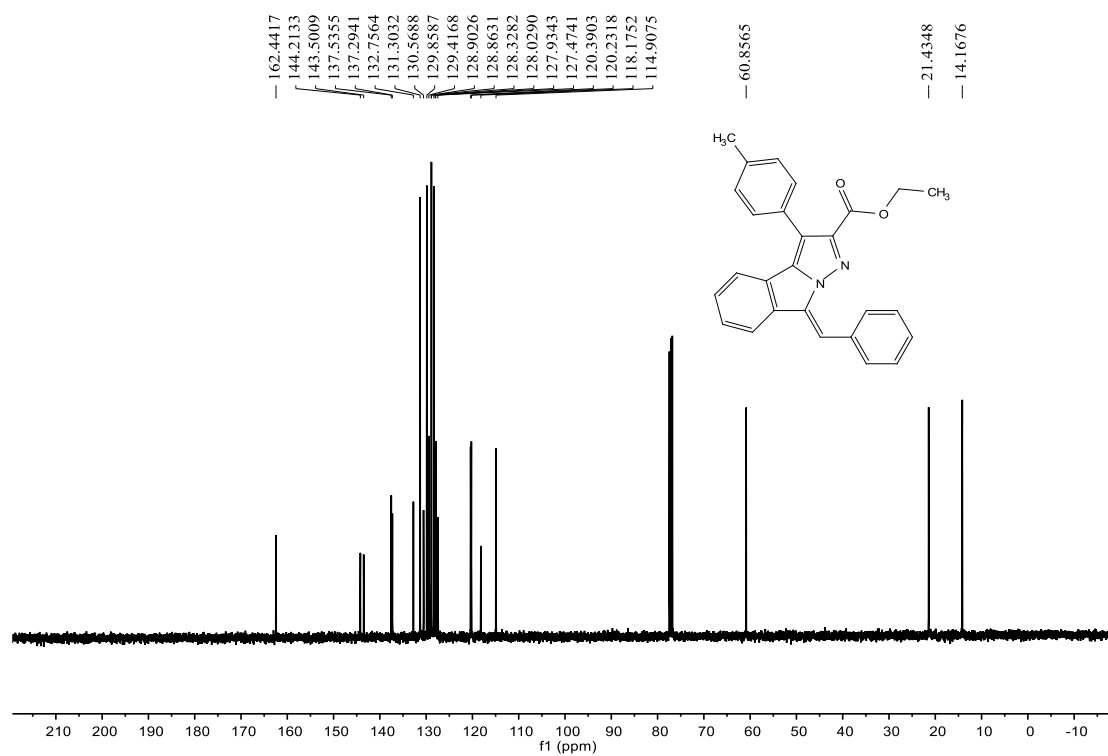
^{13}C NMR spectra of compound **3ad**.



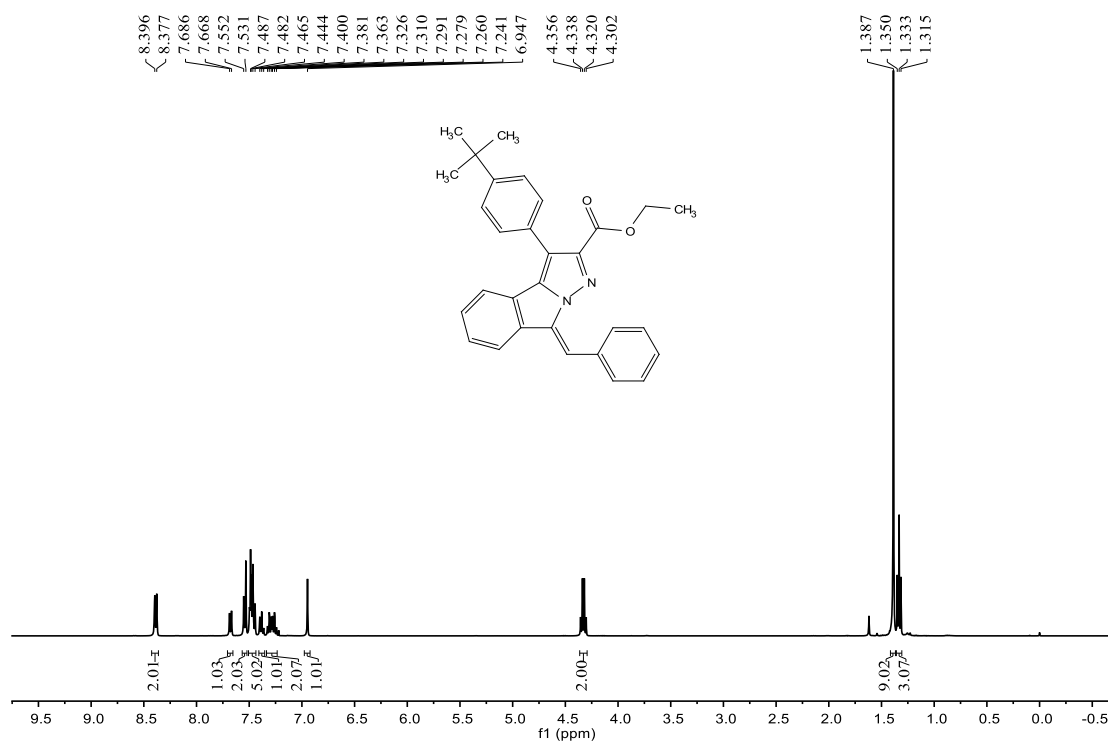
^1H NMR spectra of compound **3ae**.



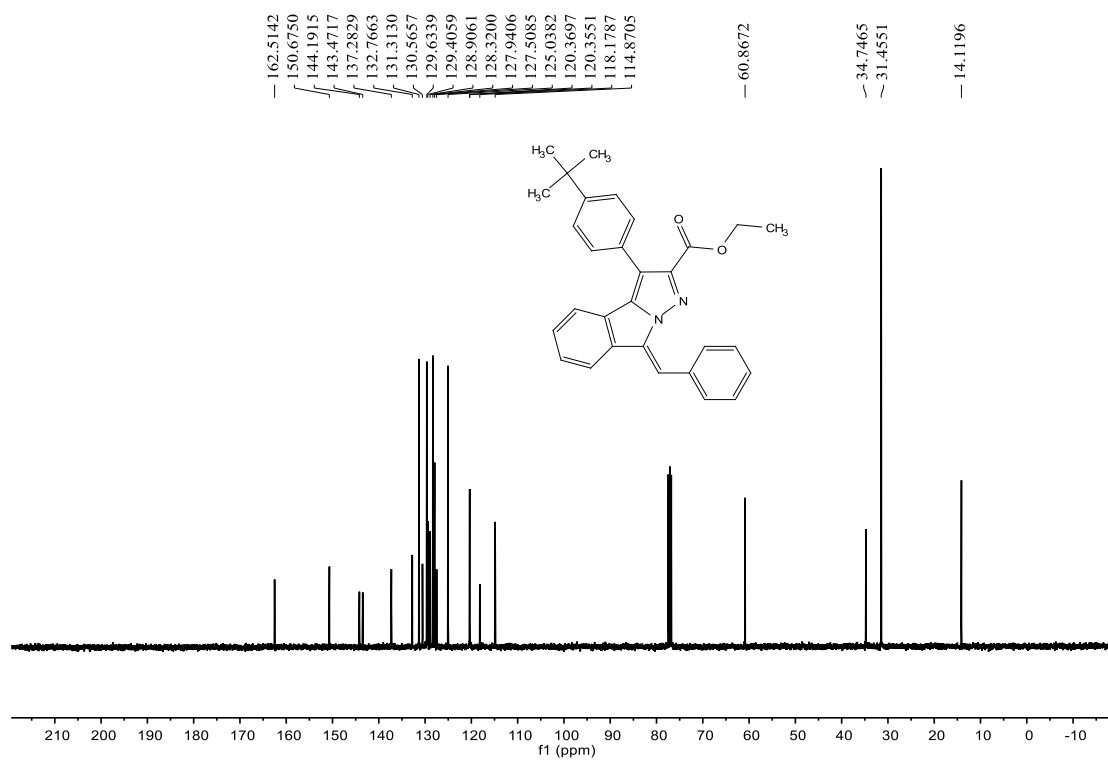
¹³C NMR spectra of compound **3ae**.



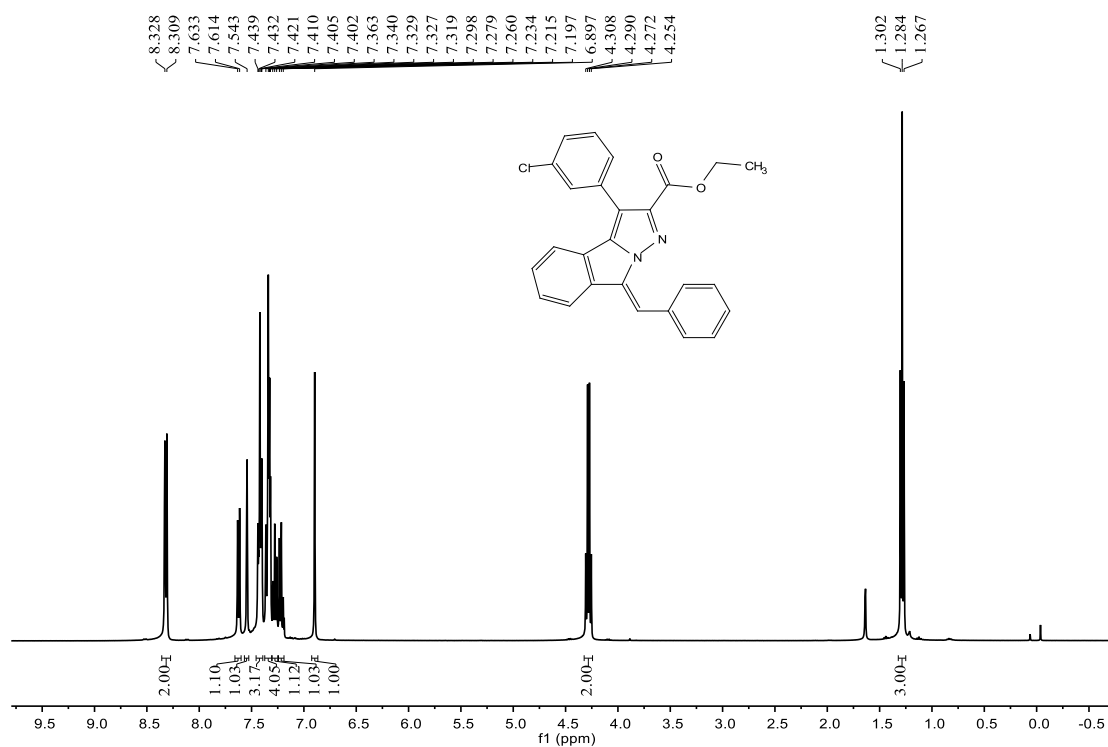
¹H NMR spectra of compound **3af**.



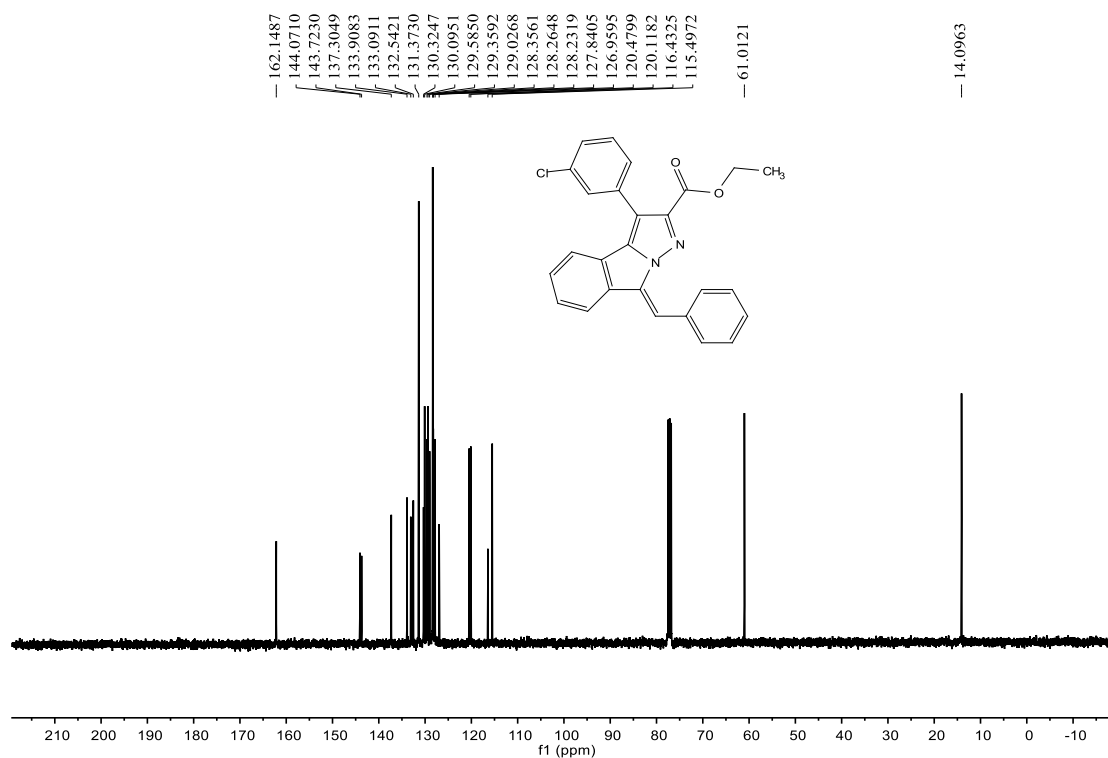
¹H NMR spectra of compound **3af**.



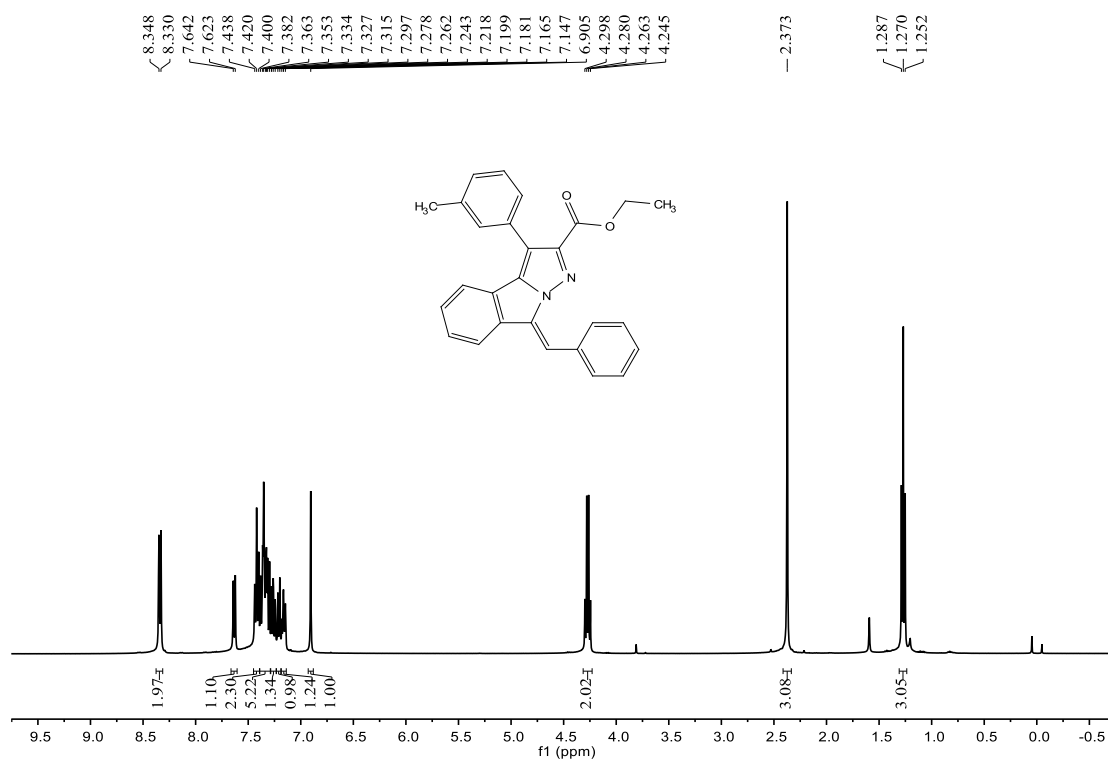
¹H NMR spectra of compound **3ag**.



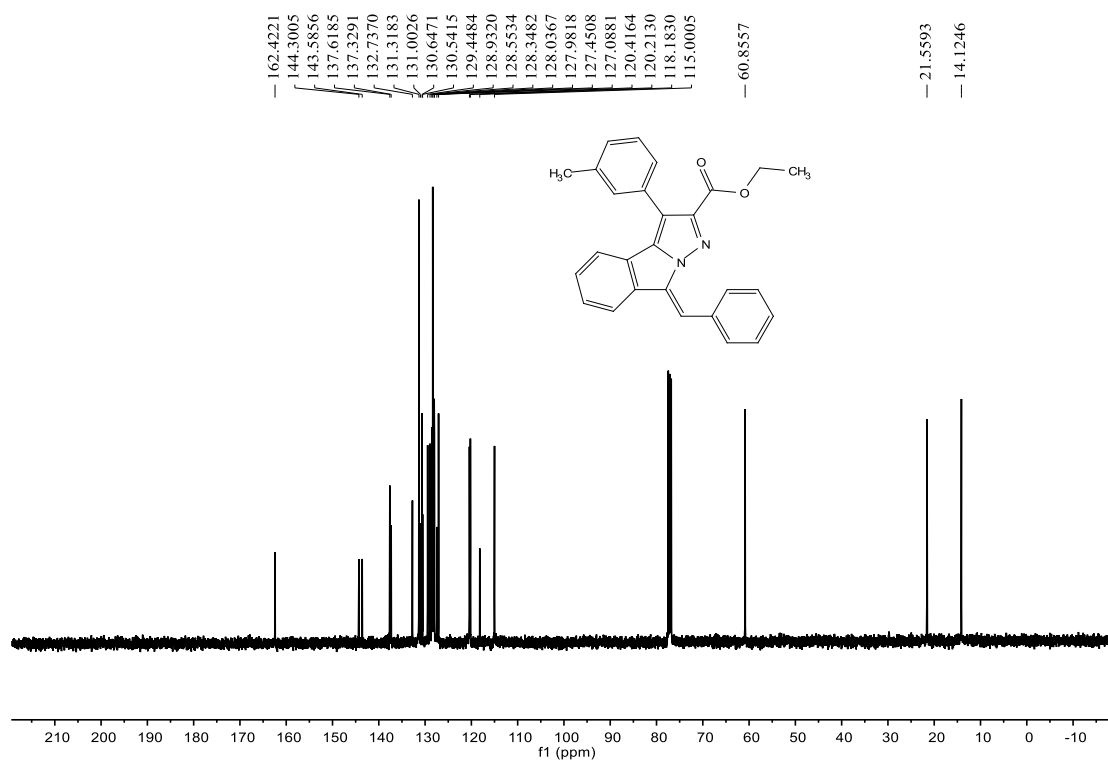
¹³C NMR spectra of compound **3ag**.



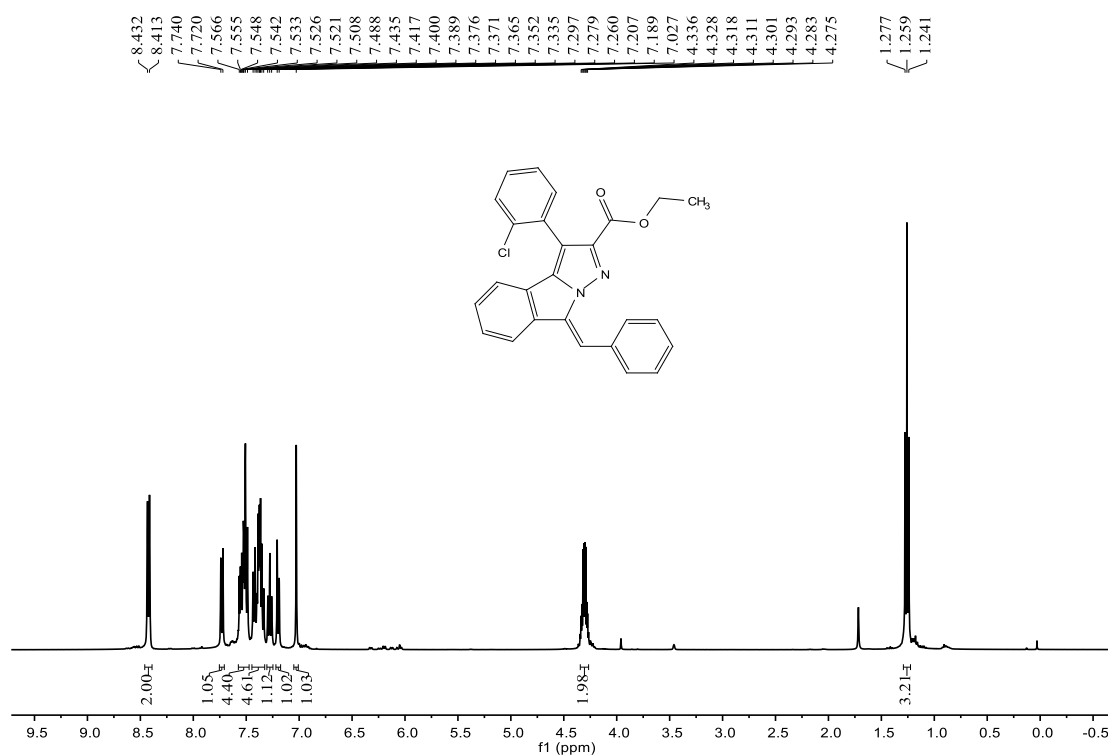
¹H NMR spectra of compound **3ah**.



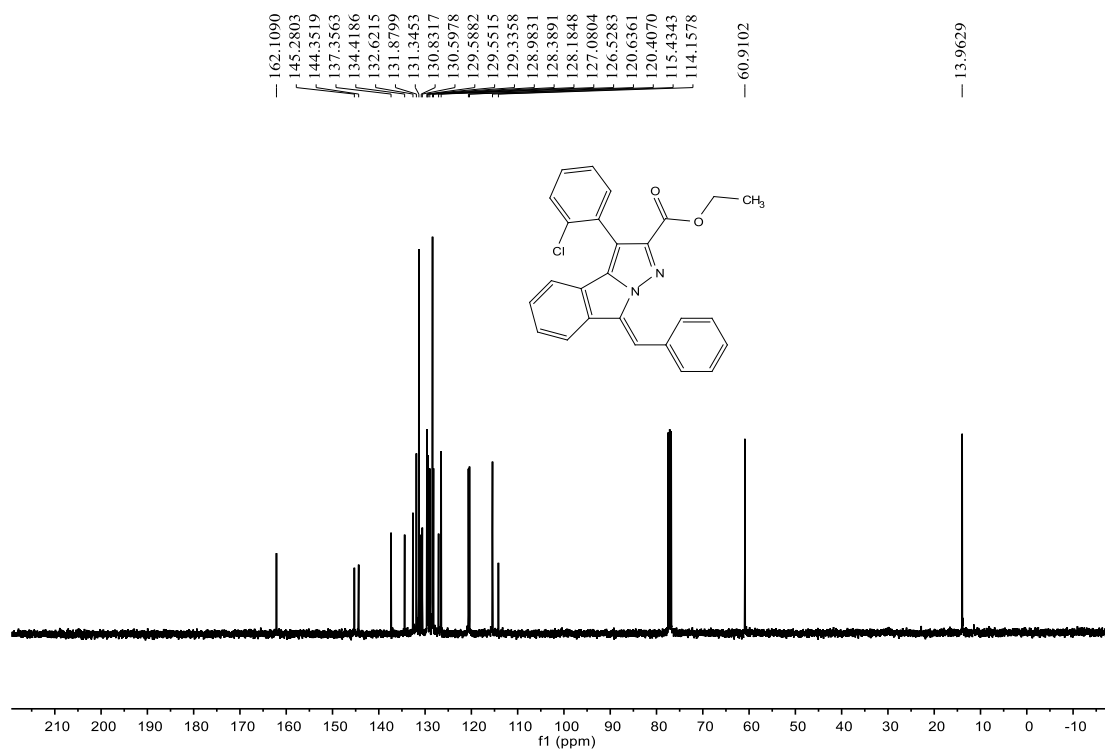
¹³C NMR spectra of compound **3ah**.



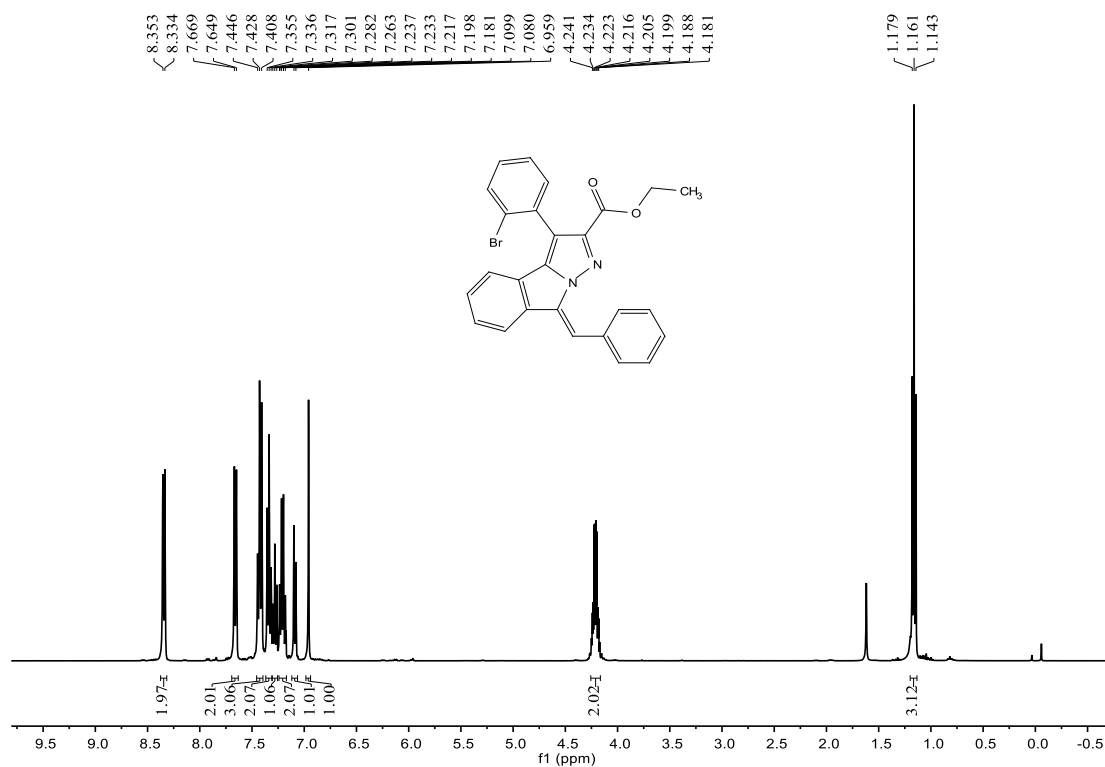
¹H NMR spectra of compound **3ai**.



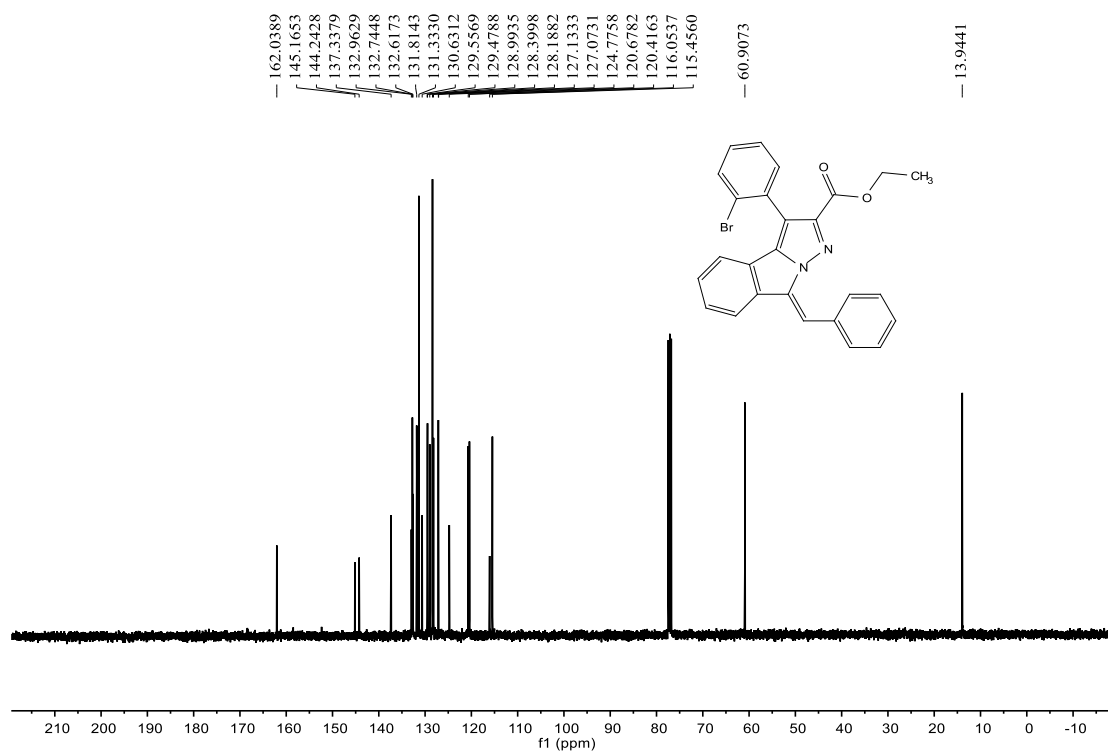
¹³C NMR spectra of compound **3ai**.



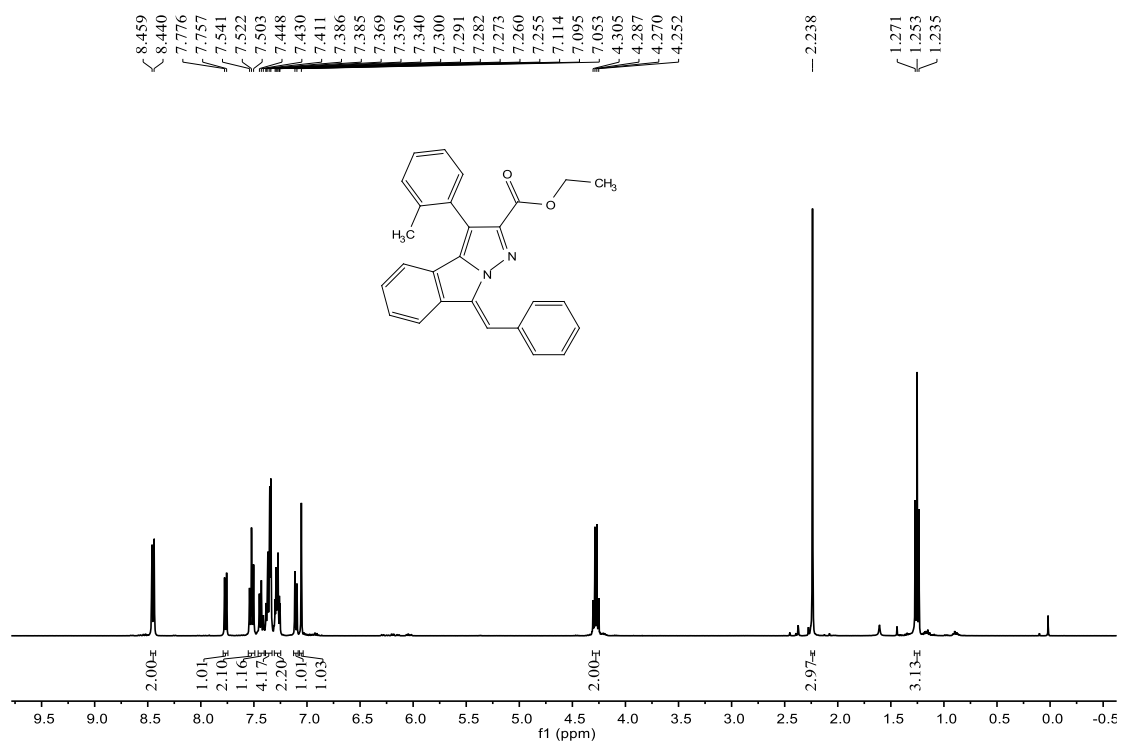
¹H NMR spectra of compound **3aj**.



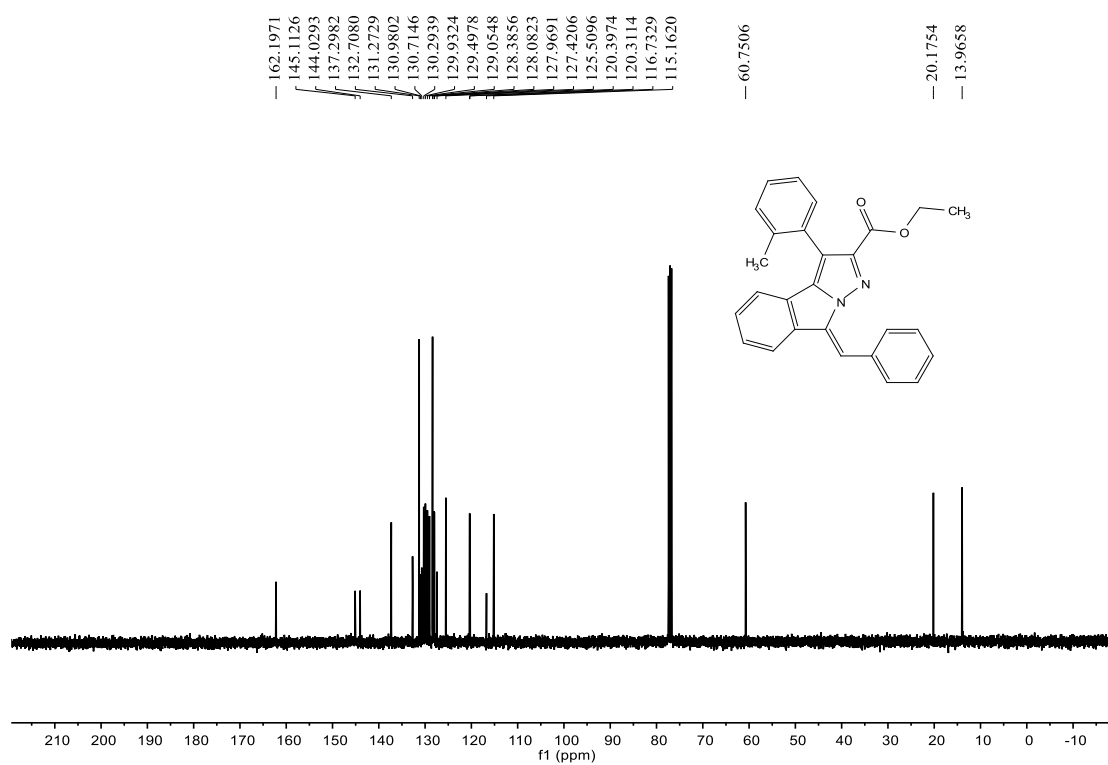
¹³C NMR spectra of compound **3aj**.



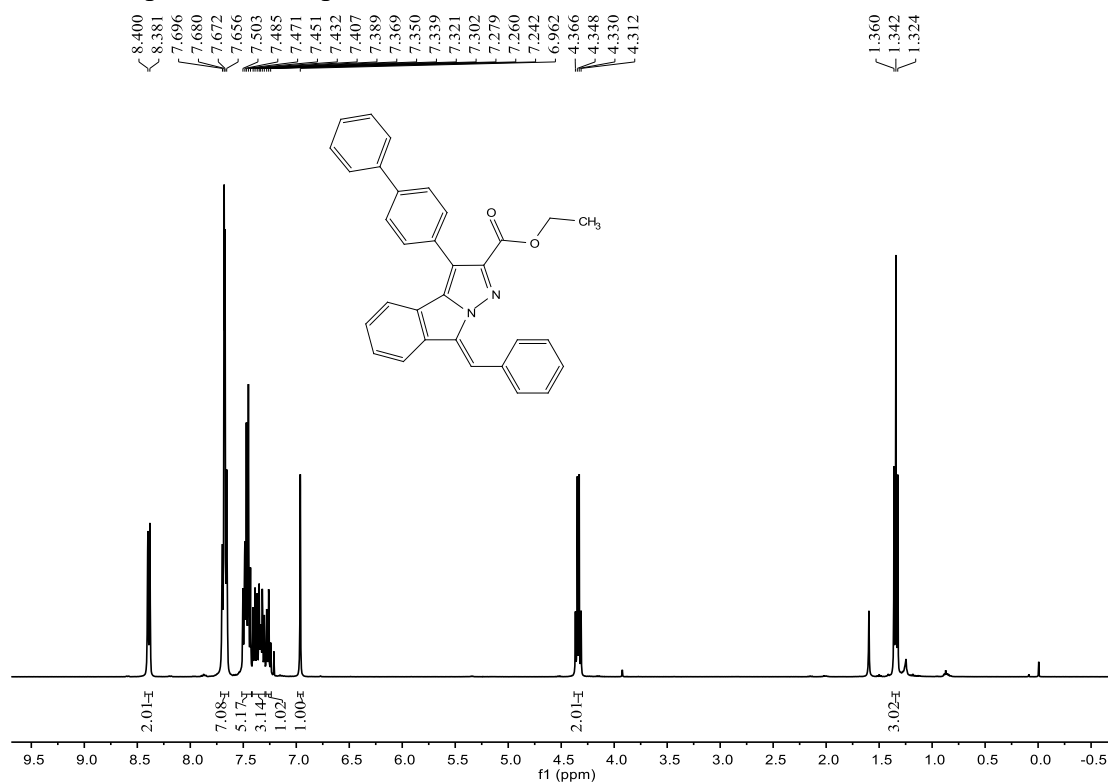
¹H NMR spectra of compound **3ak**.



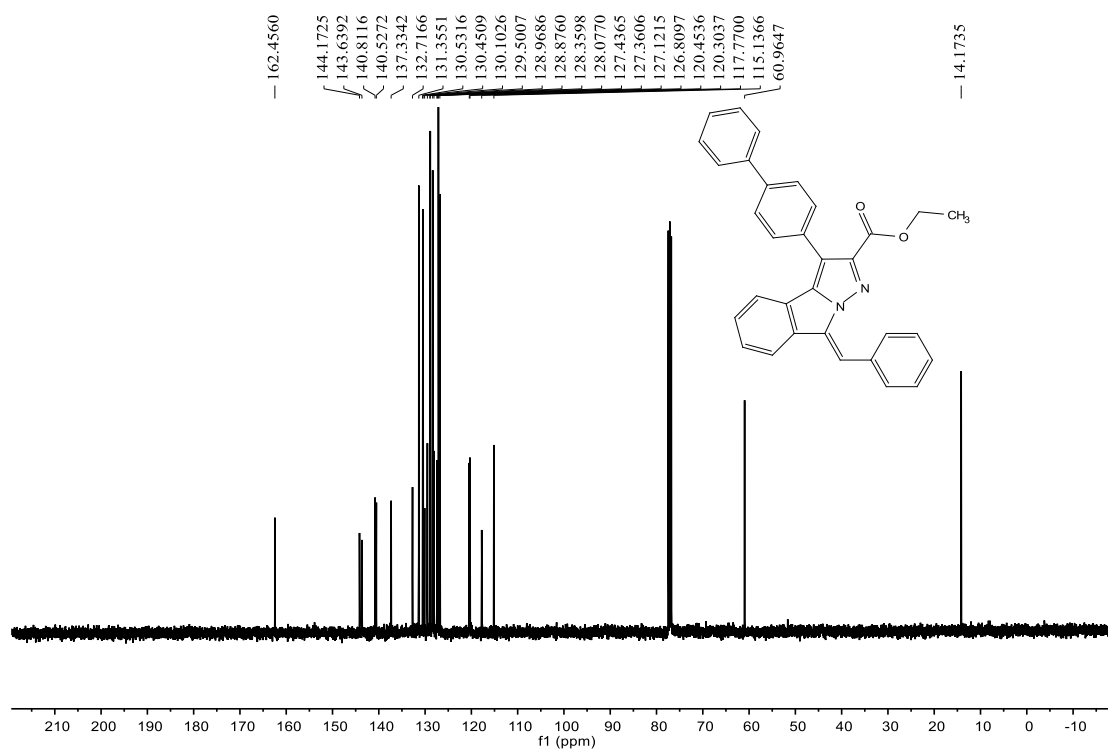
¹³C NMR spectra of compound **3ak**.



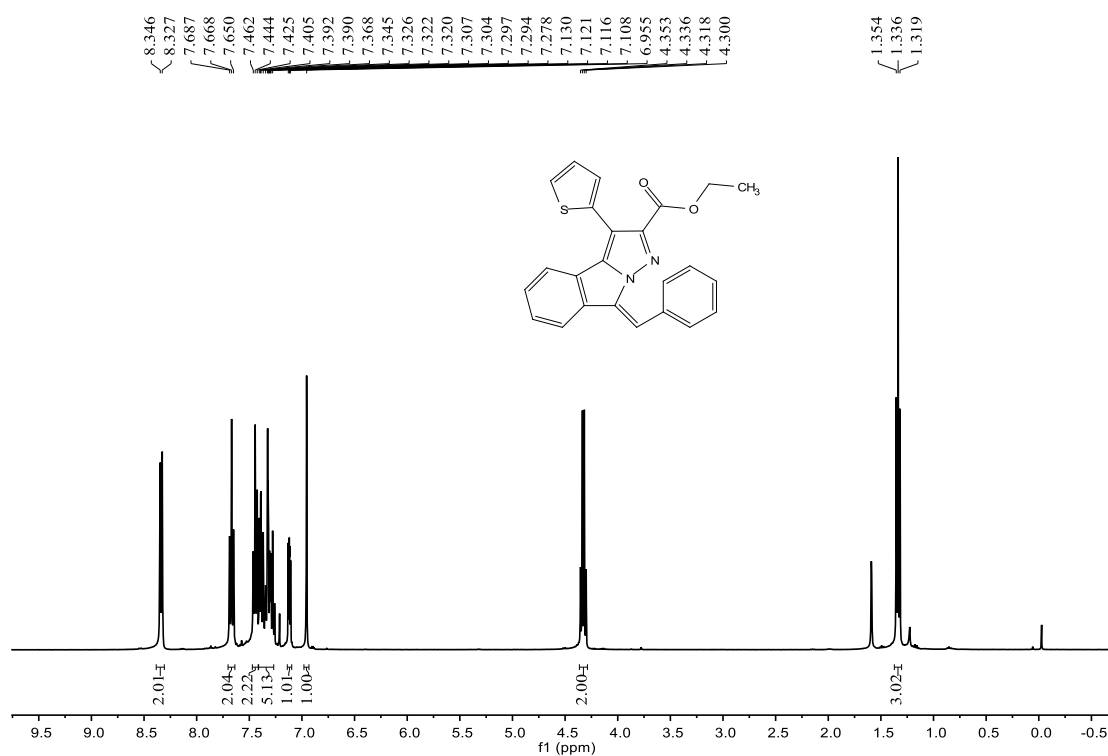
¹H NMR spectra of compound **3al**.



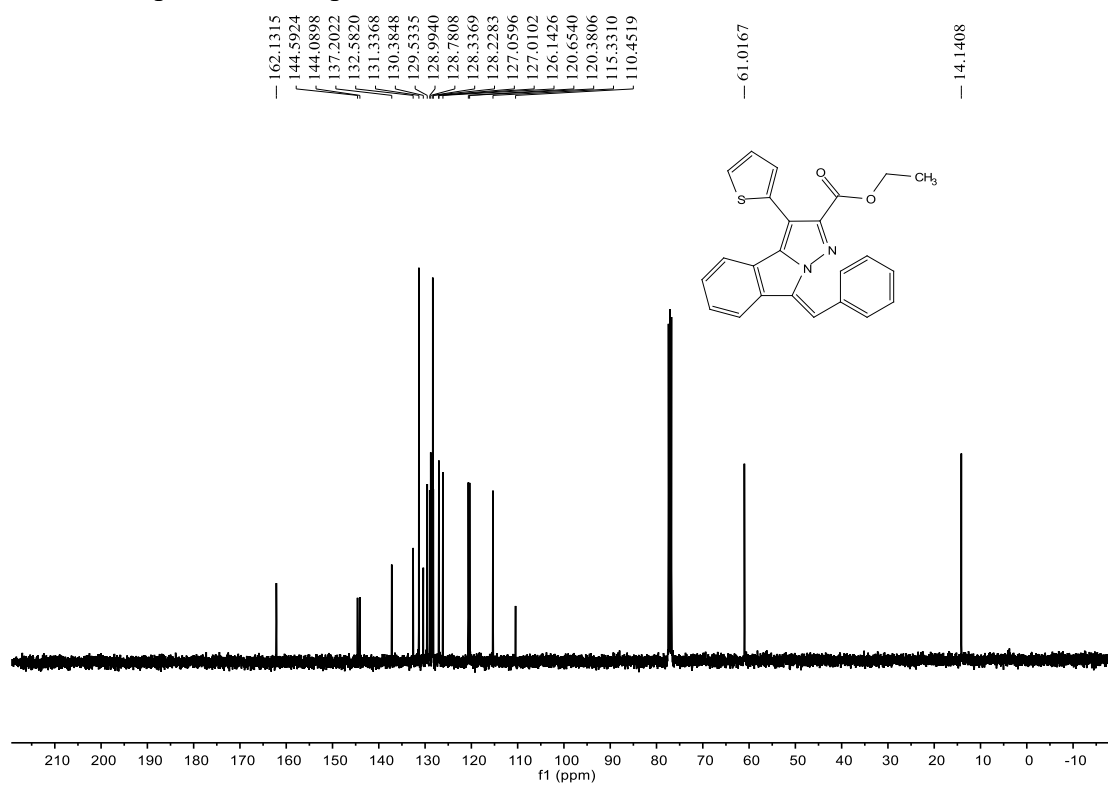
¹³C NMR spectra of compound **3al**.



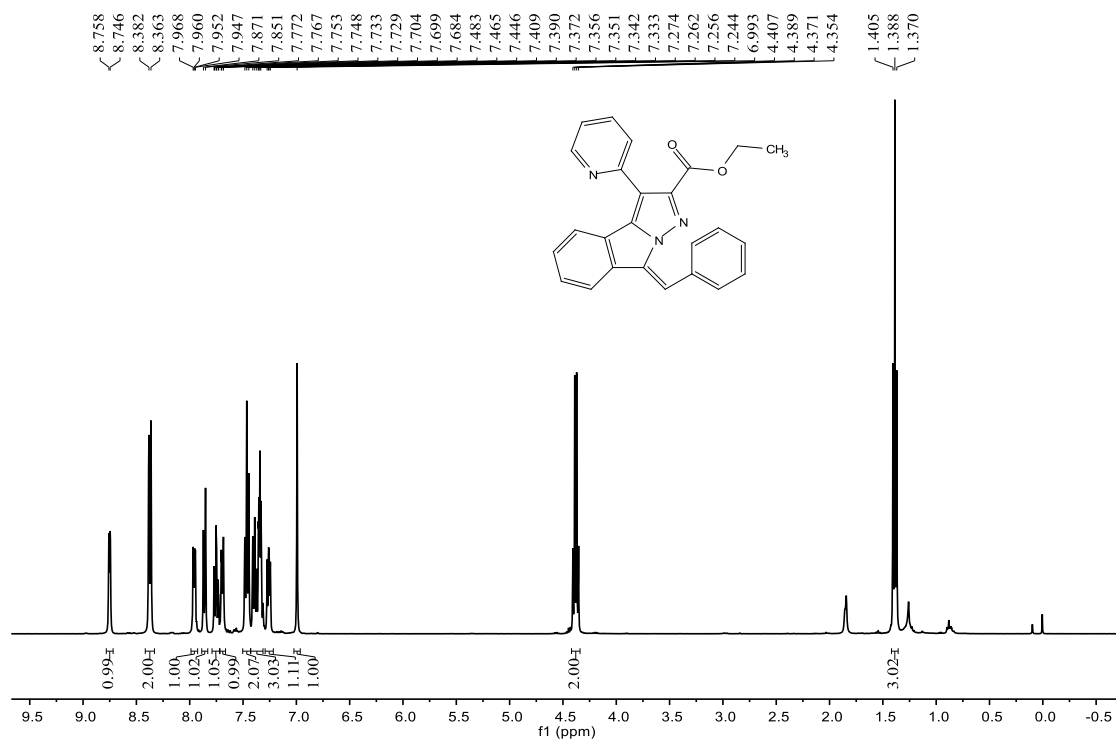
¹H NMR spectra of compound **3am**.



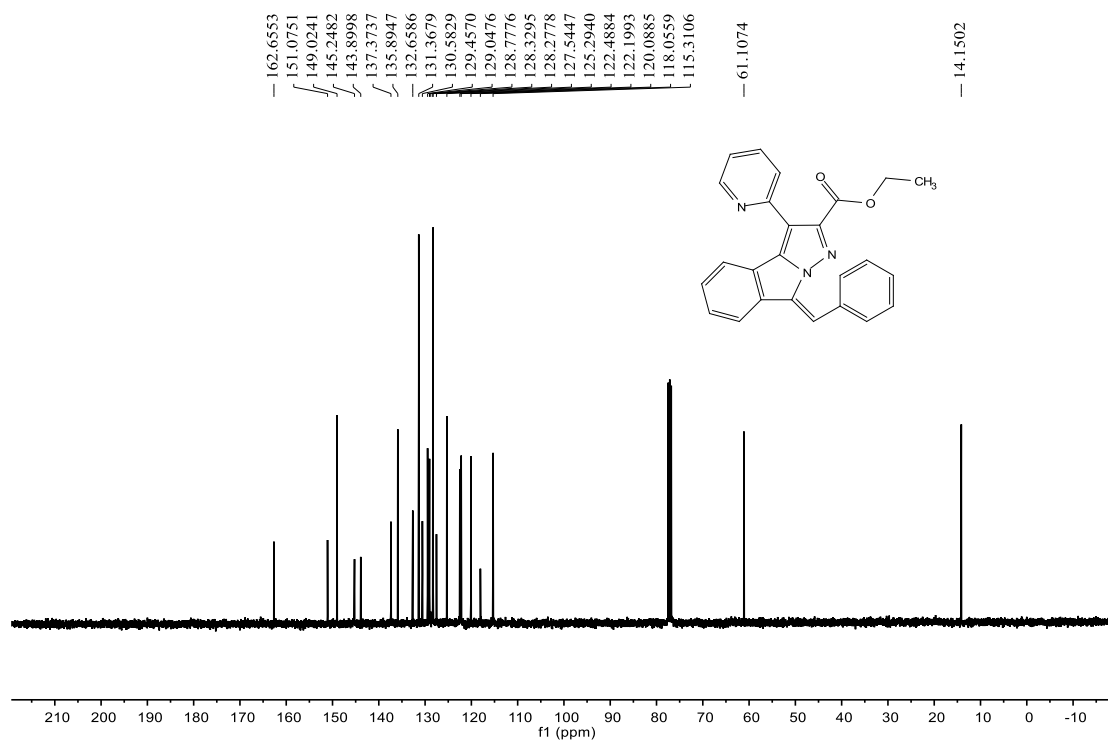
¹³C NMR spectra of compound **3am**.



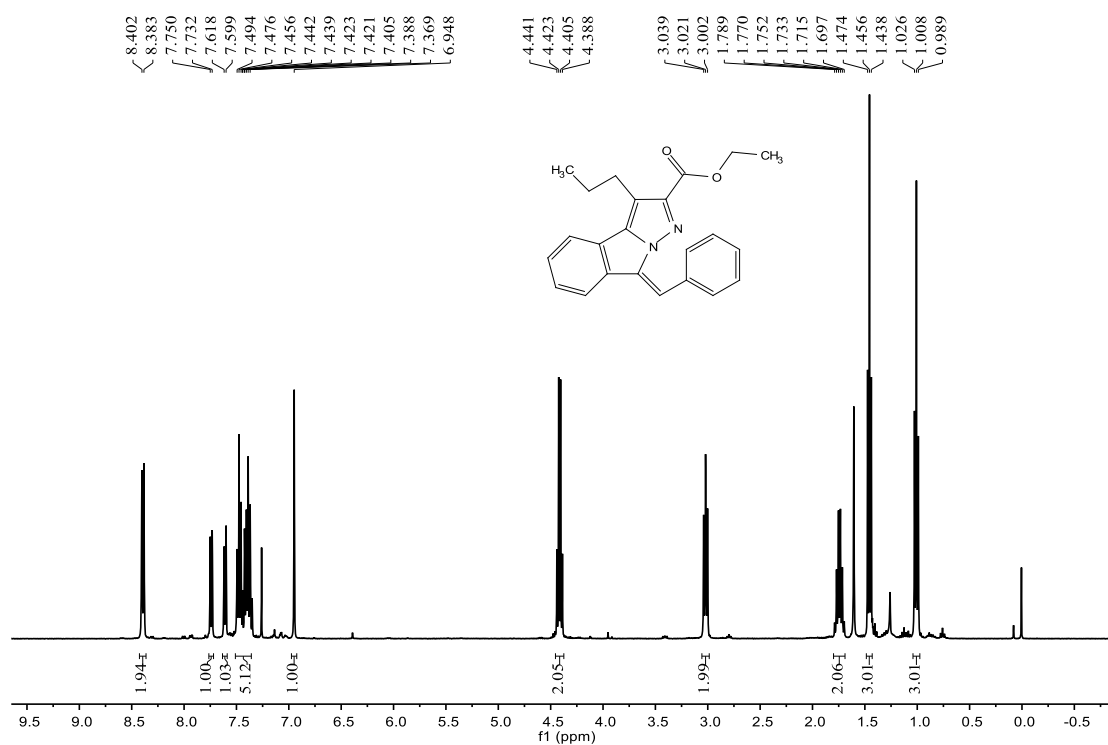
¹H NMR spectra of compound **3am**.



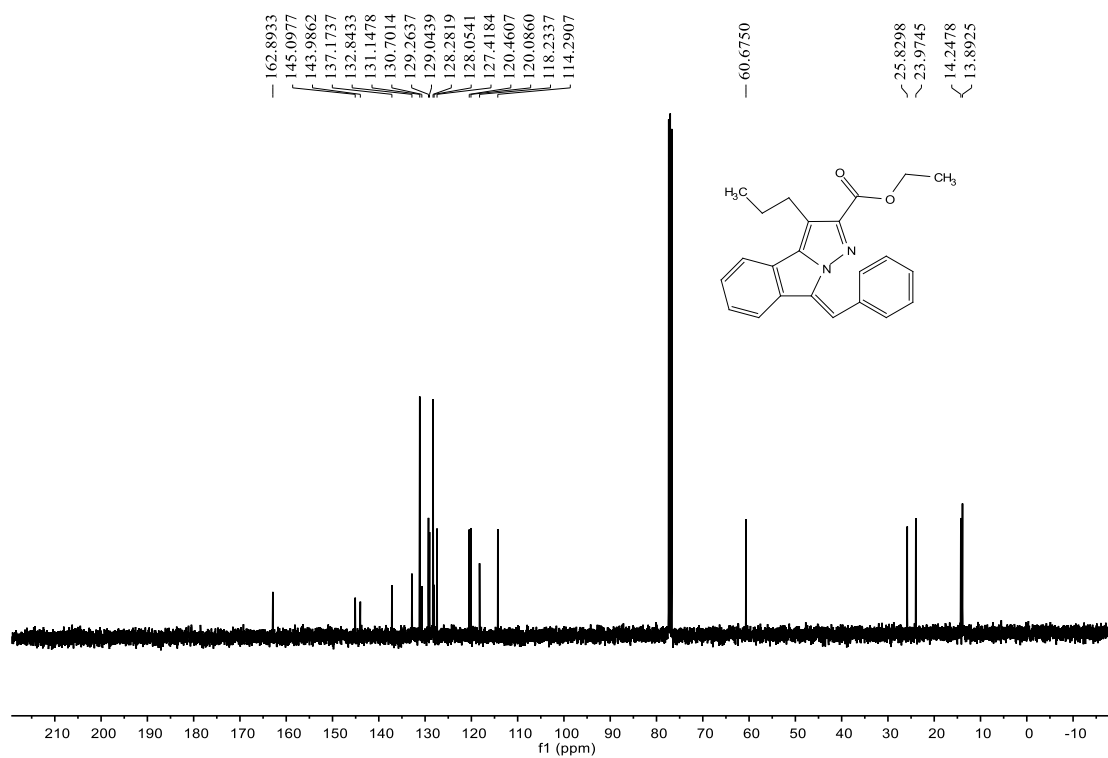
^{13}C NMR spectra of compound **3an**.



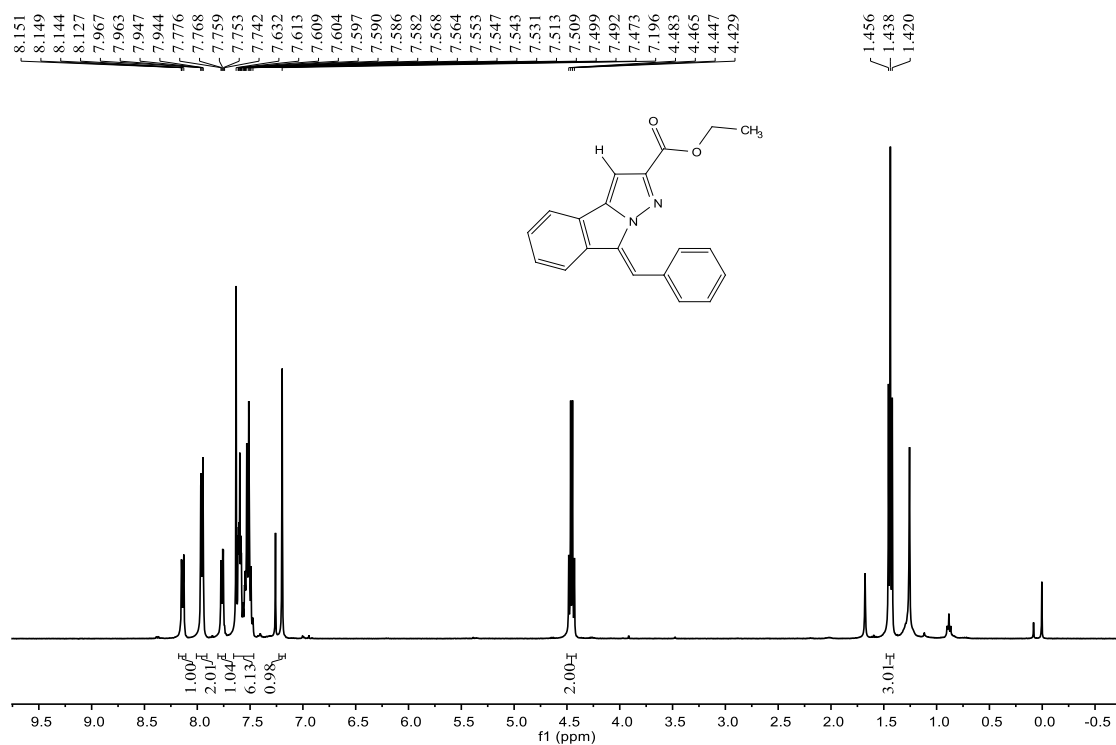
^1H NMR spectra of compound **3ao**.



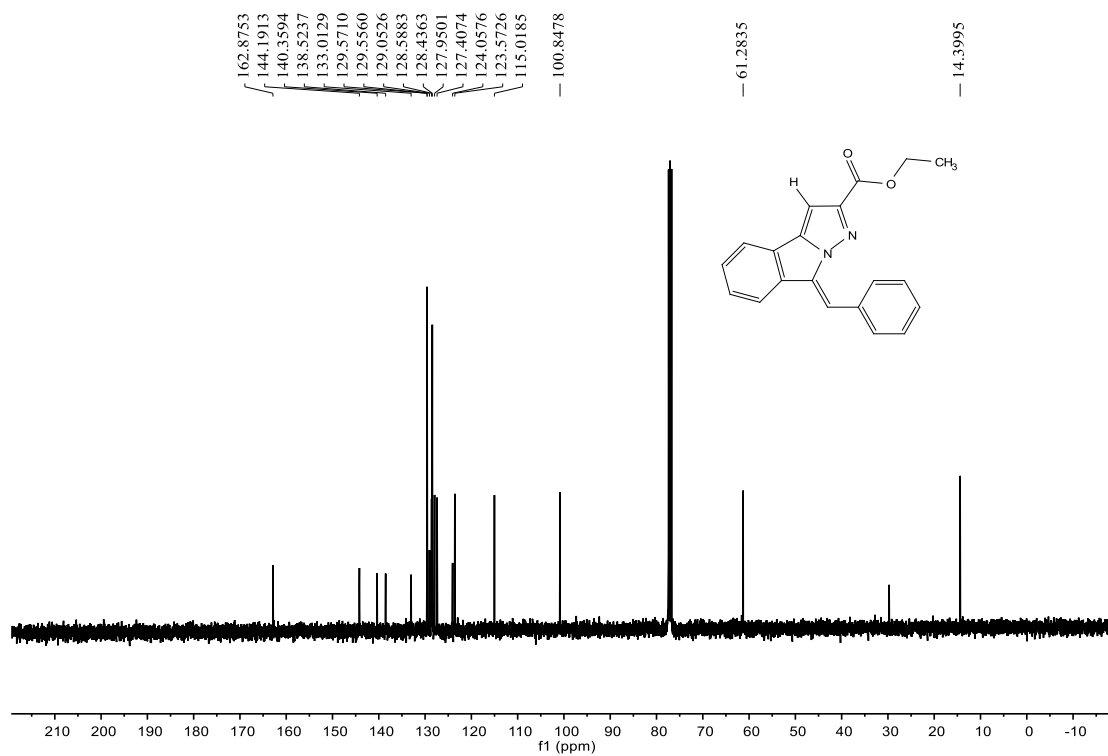
¹³C NMR spectra of compound **3ao**.



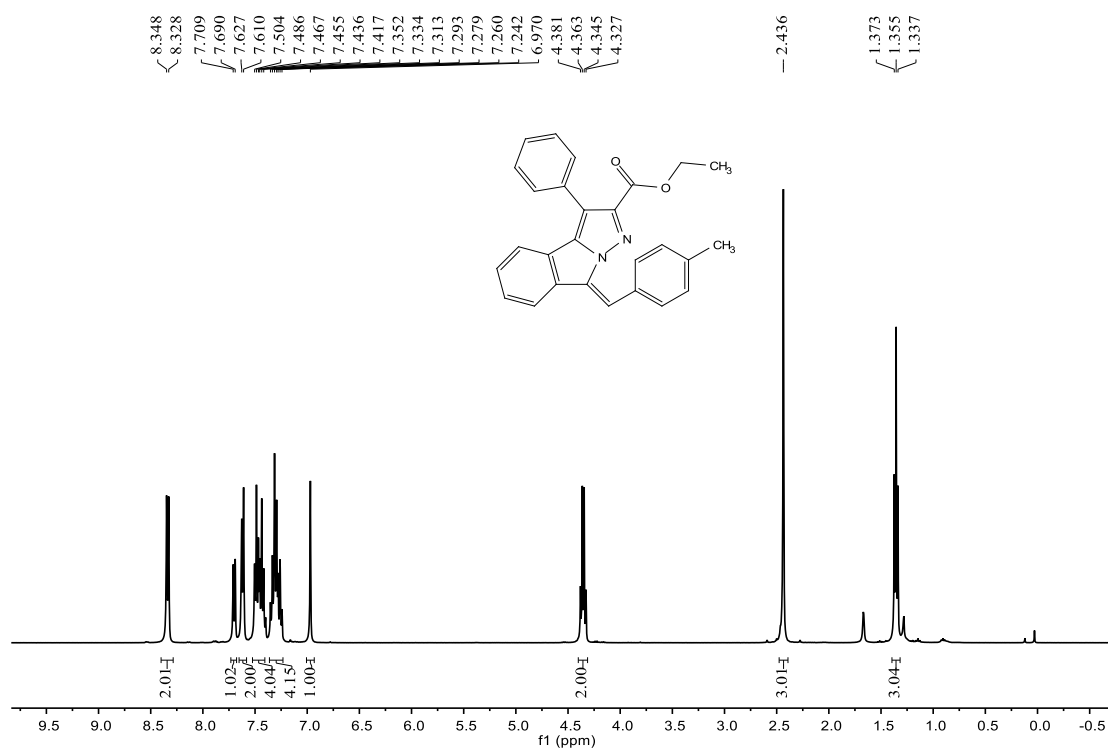
¹H NMR spectra of compound **3ap**.



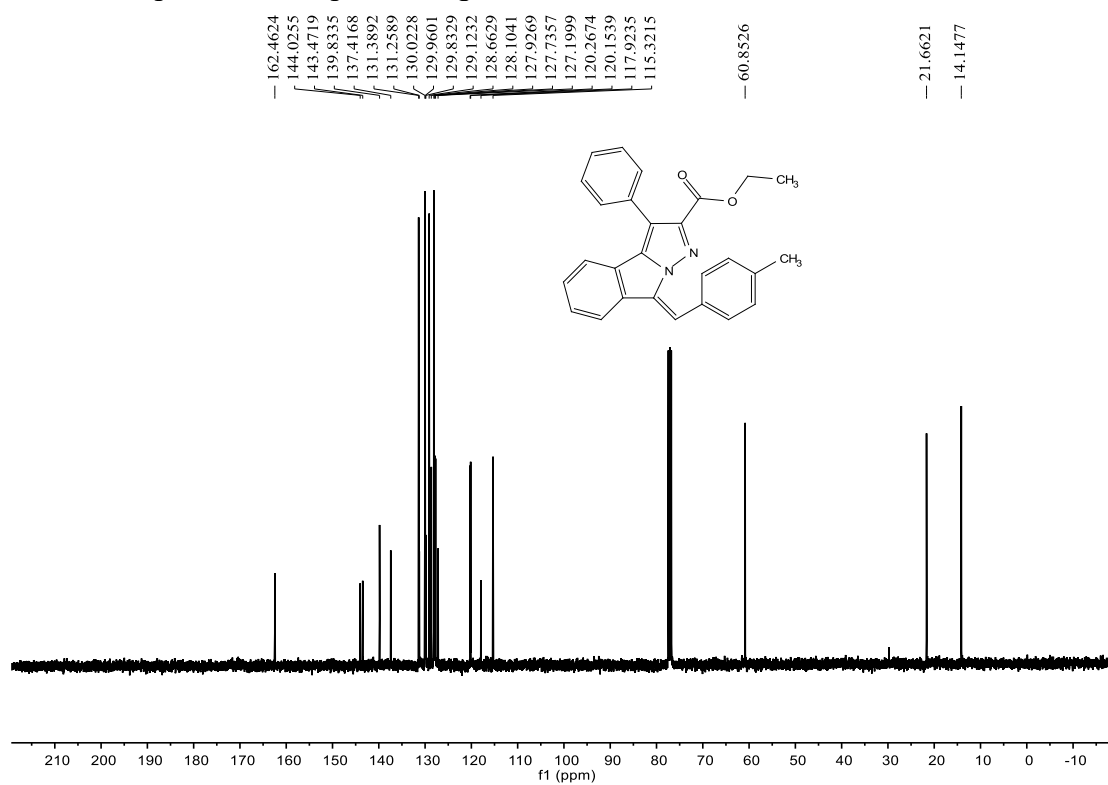
¹H NMR spectra of compound **3ap**.



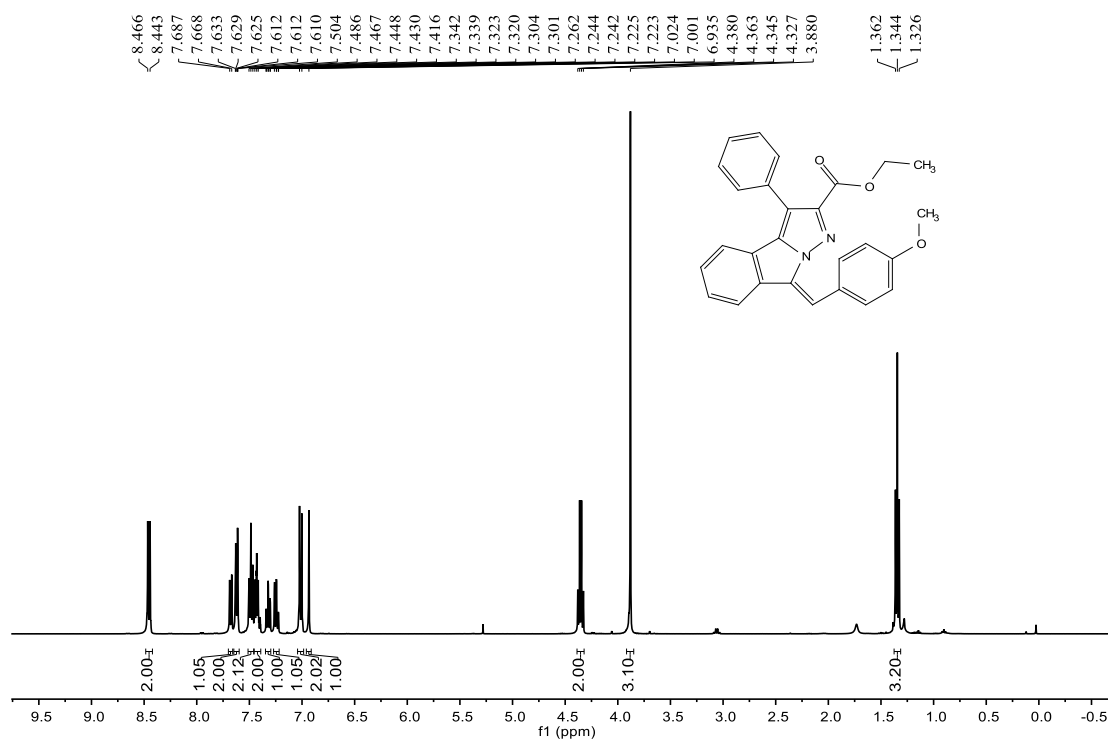
¹H NMR spectra of compound **3aq**.



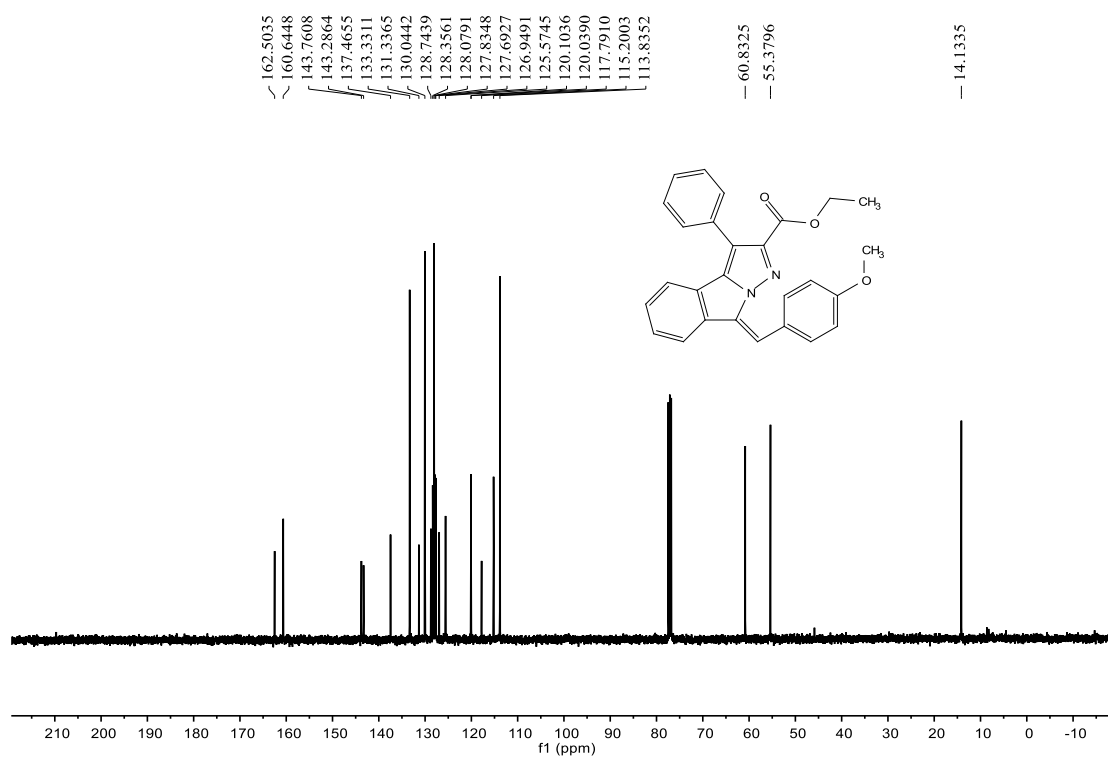
¹³C NMR spectra of compound **3aq**.



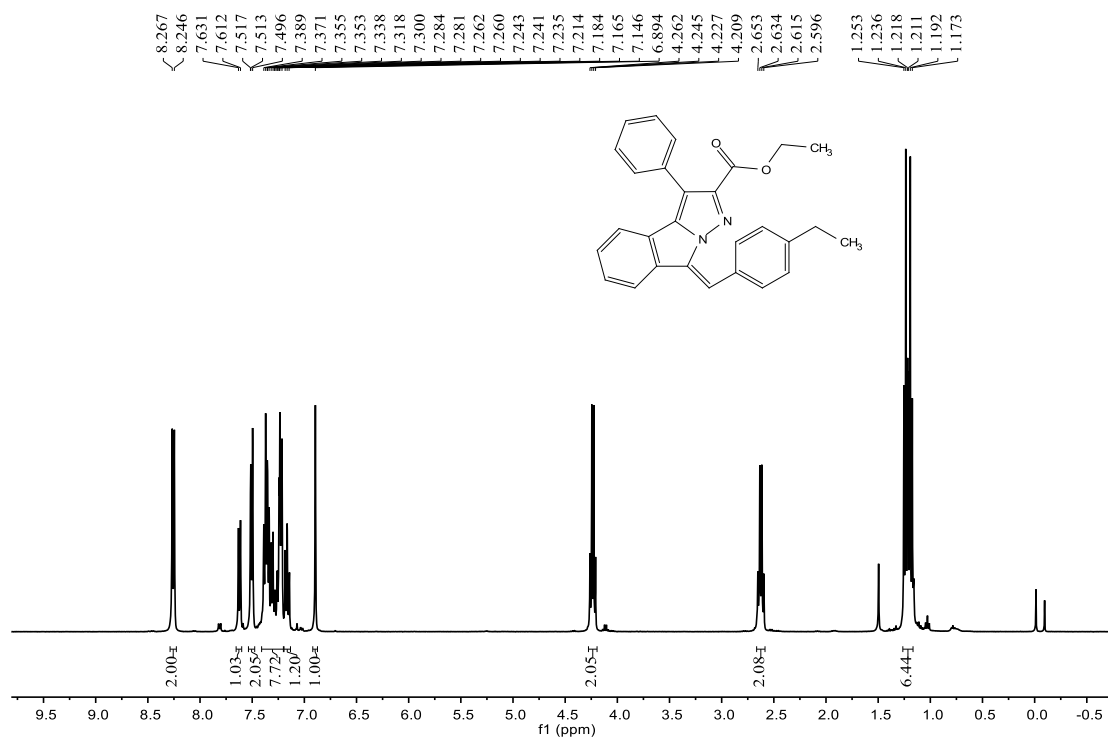
¹H NMR spectra of compound **3ar**.



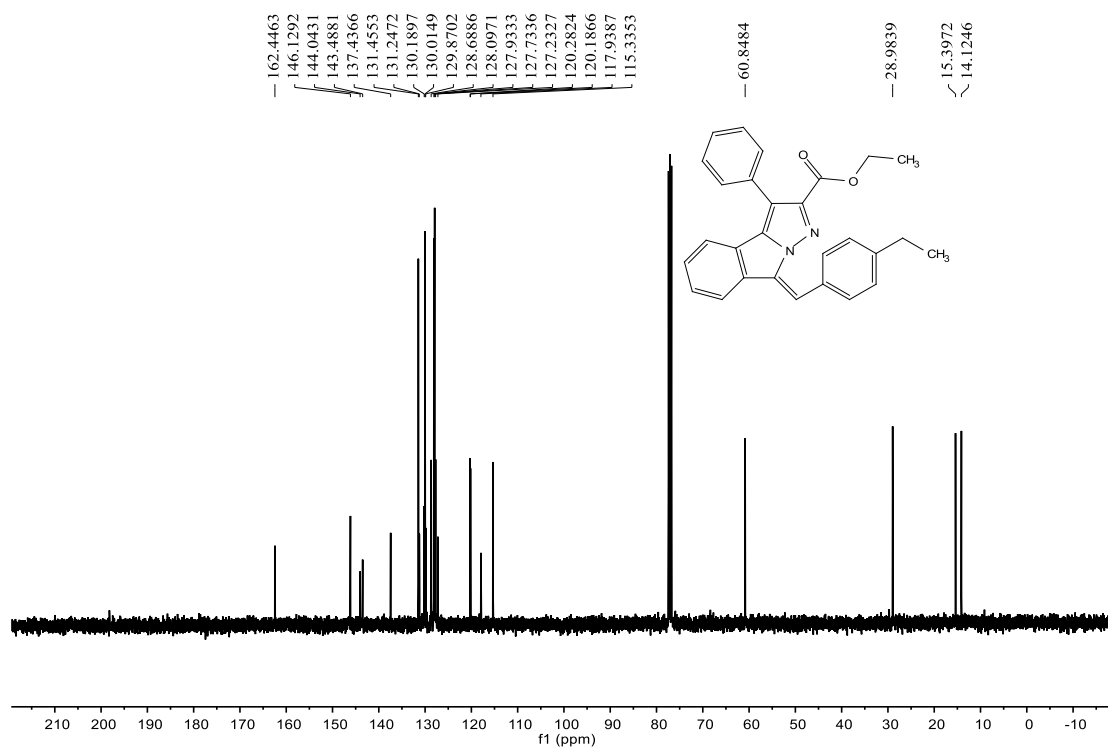
¹³C NMR spectra of compound **3ar**.



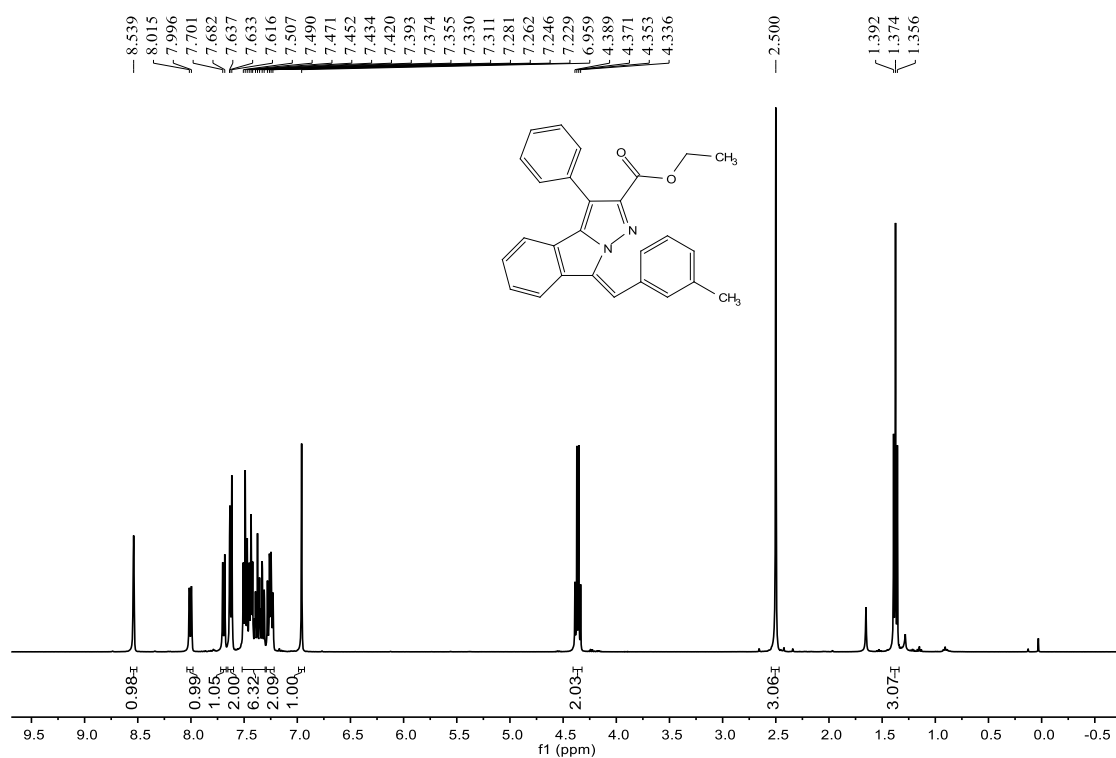
¹H NMR spectra of compound **3as**.



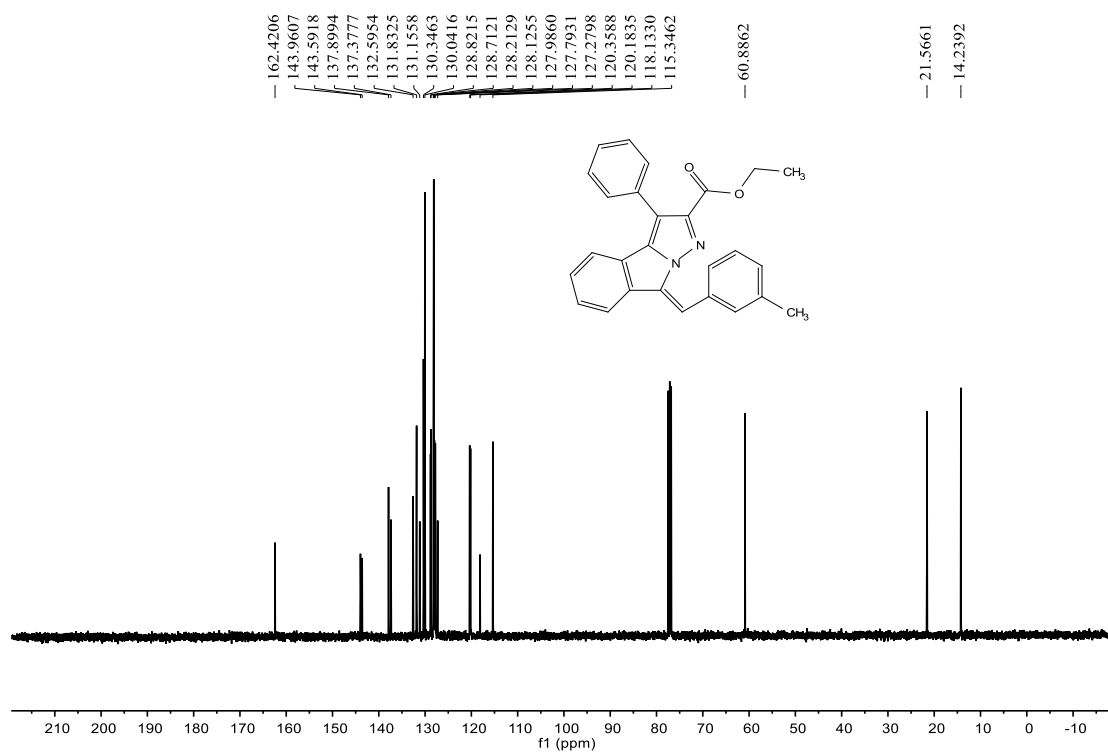
¹³C NMR spectra of compound **3as**.



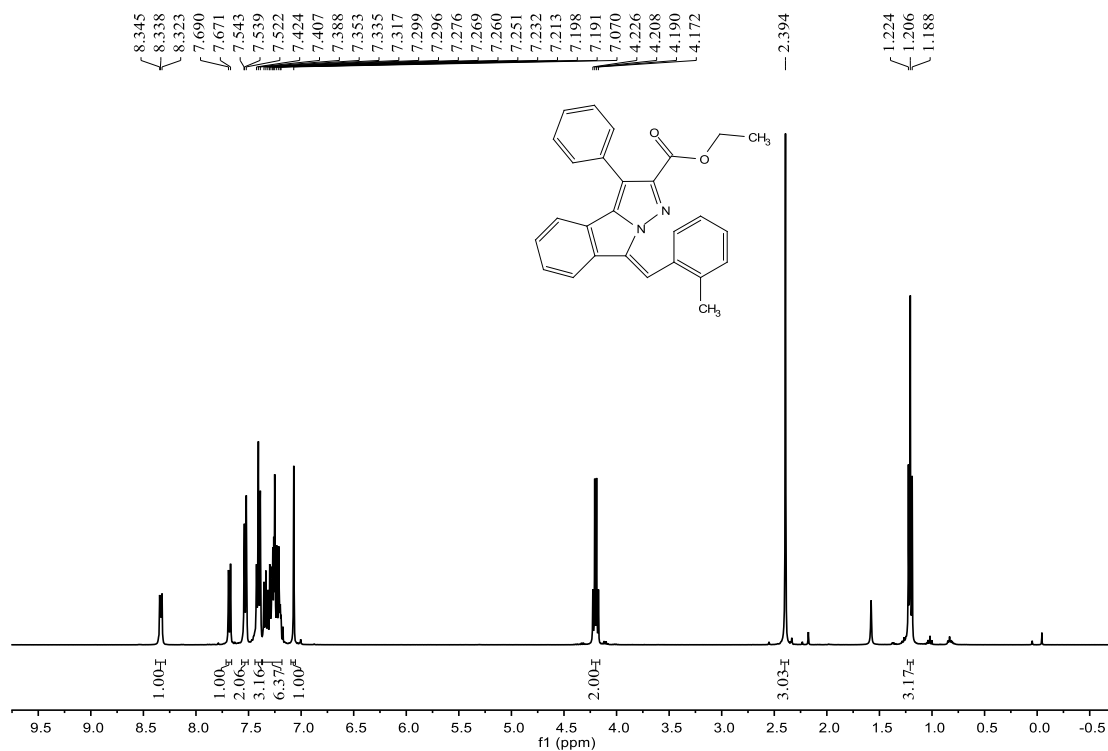
¹H NMR spectra of compound **3at**.



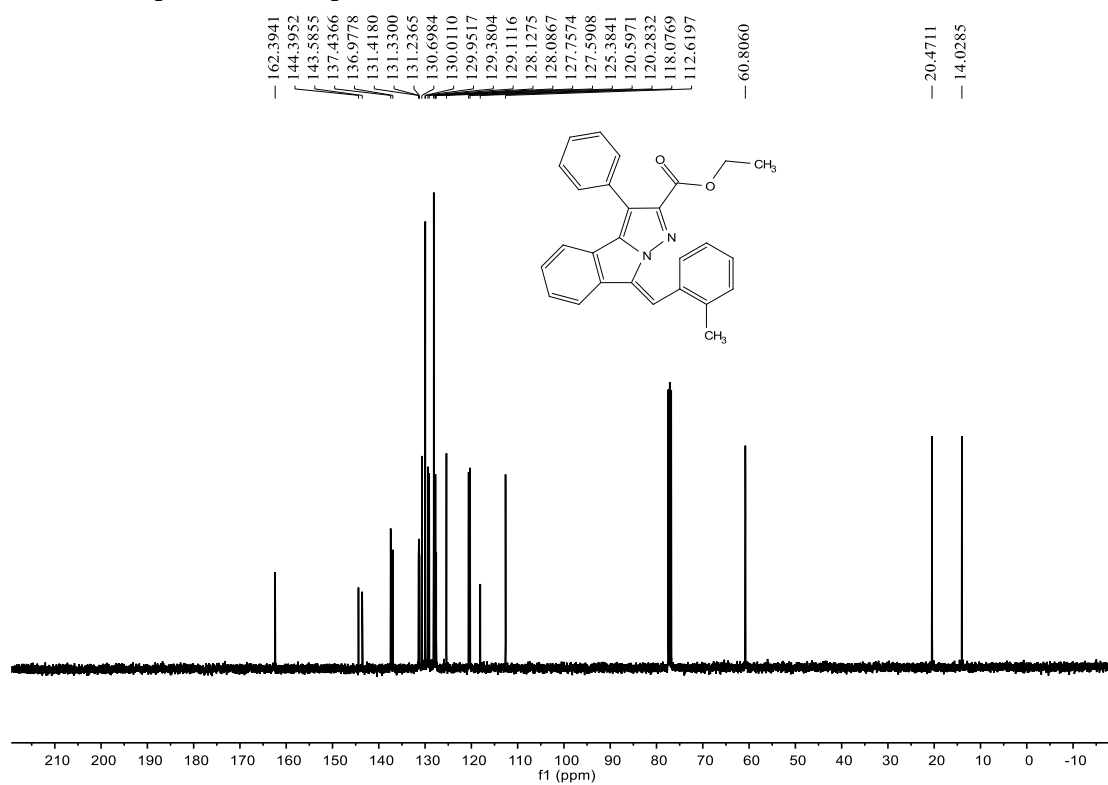
¹³C NMR spectra of compound **3at**.



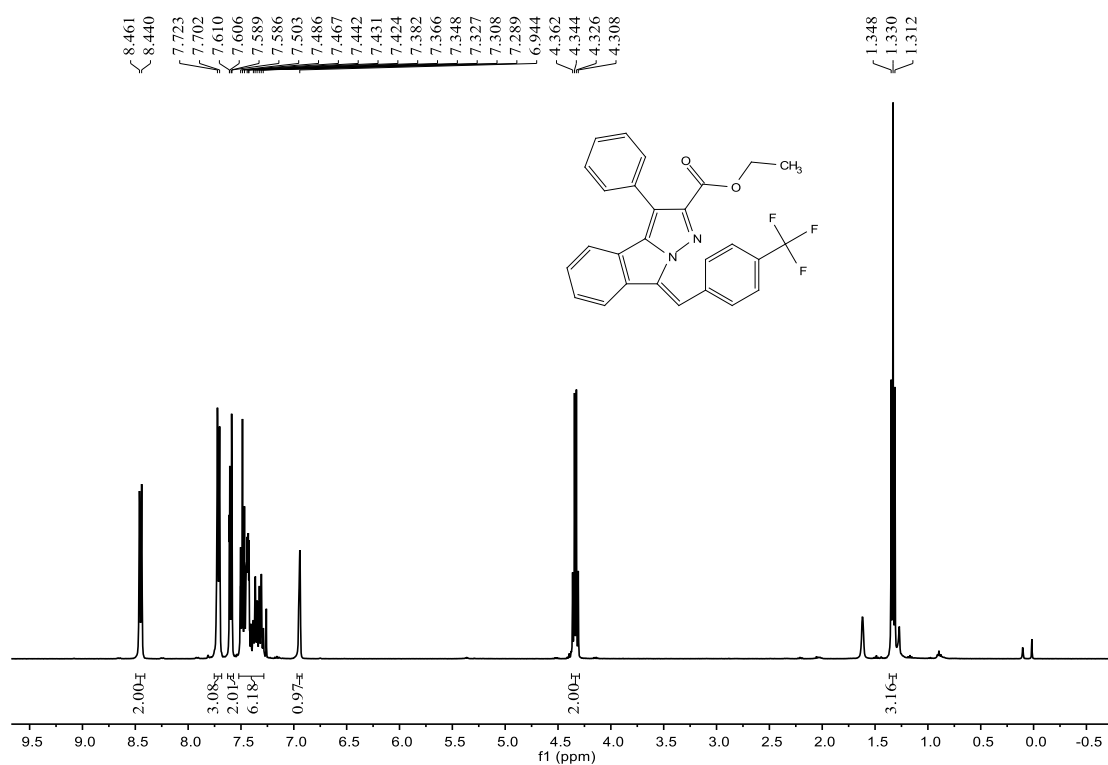
¹H NMR spectra of compound **3au**.



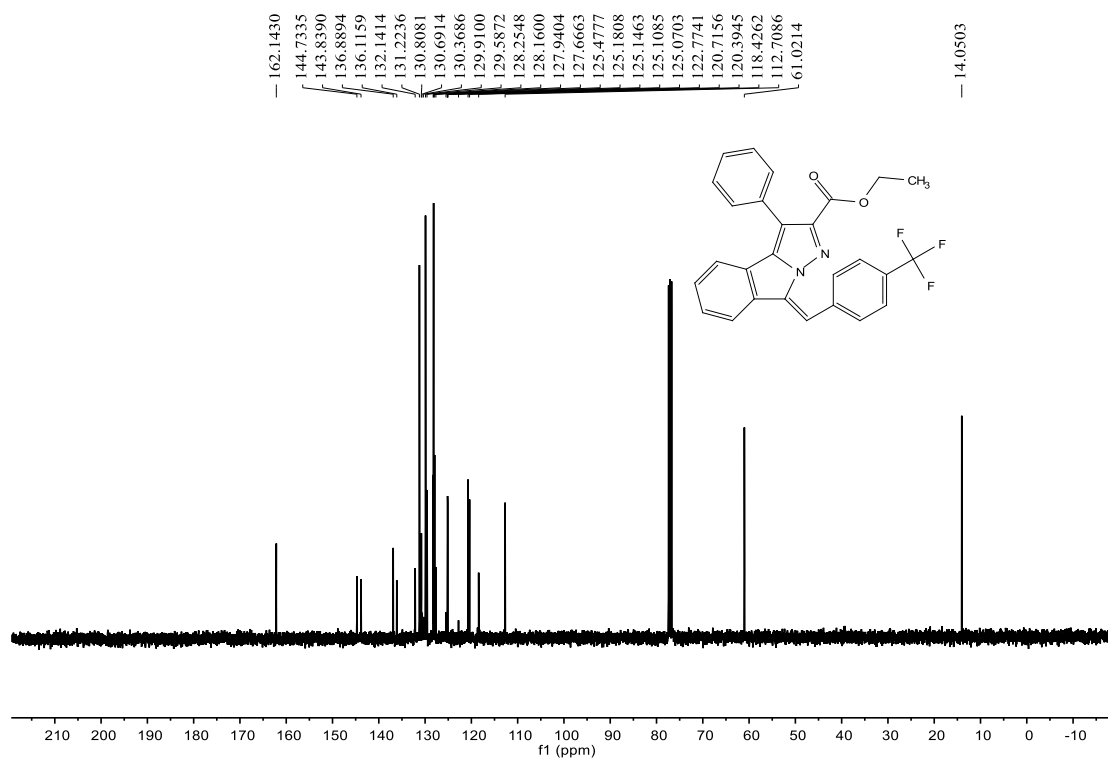
¹³C NMR spectra of compound **3au**.



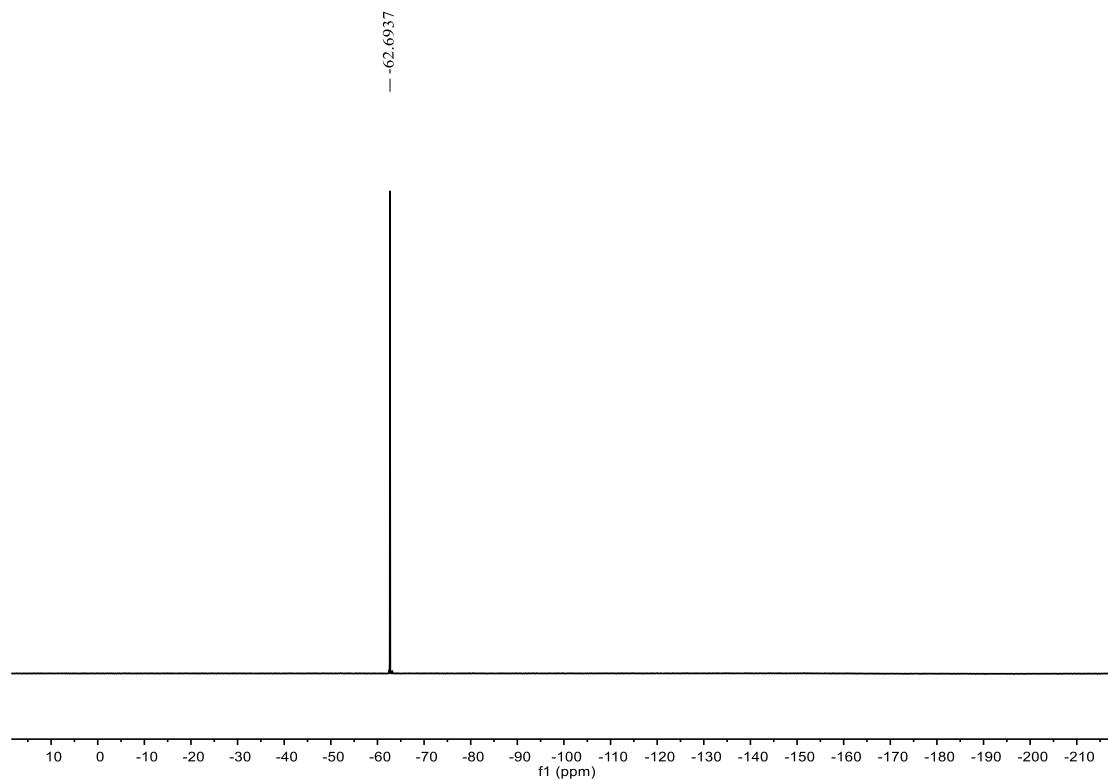
¹H NMR spectra of compound **3av**.



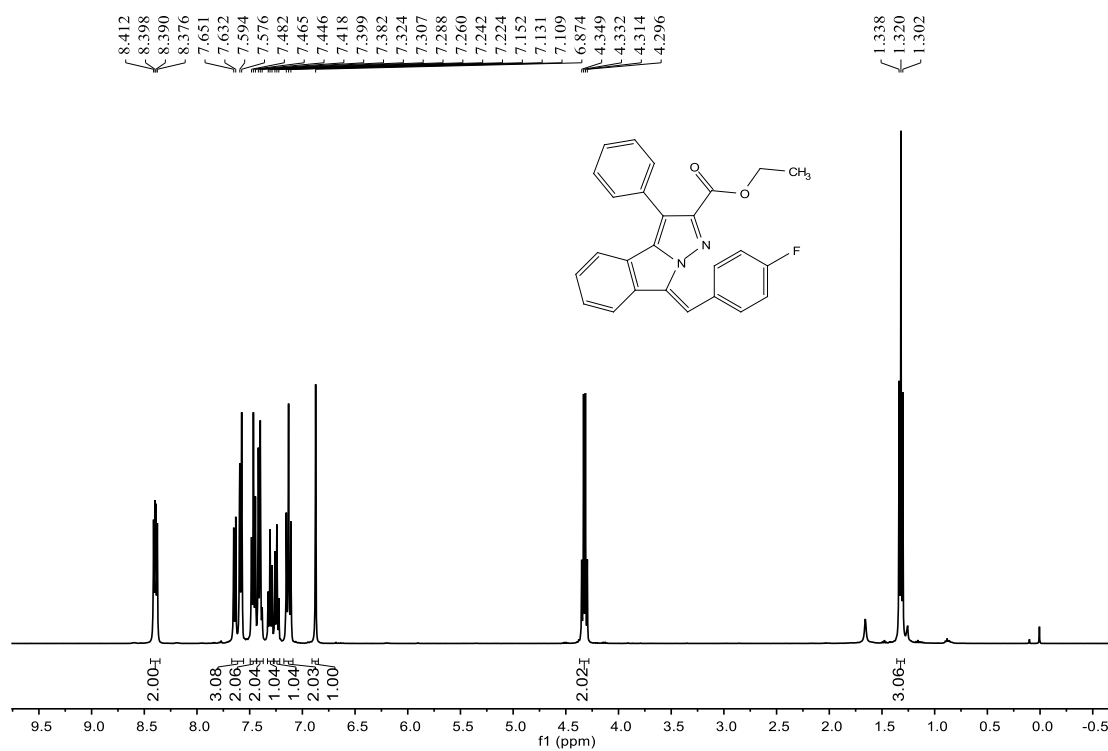
¹³C NMR spectra of compound **3av**.



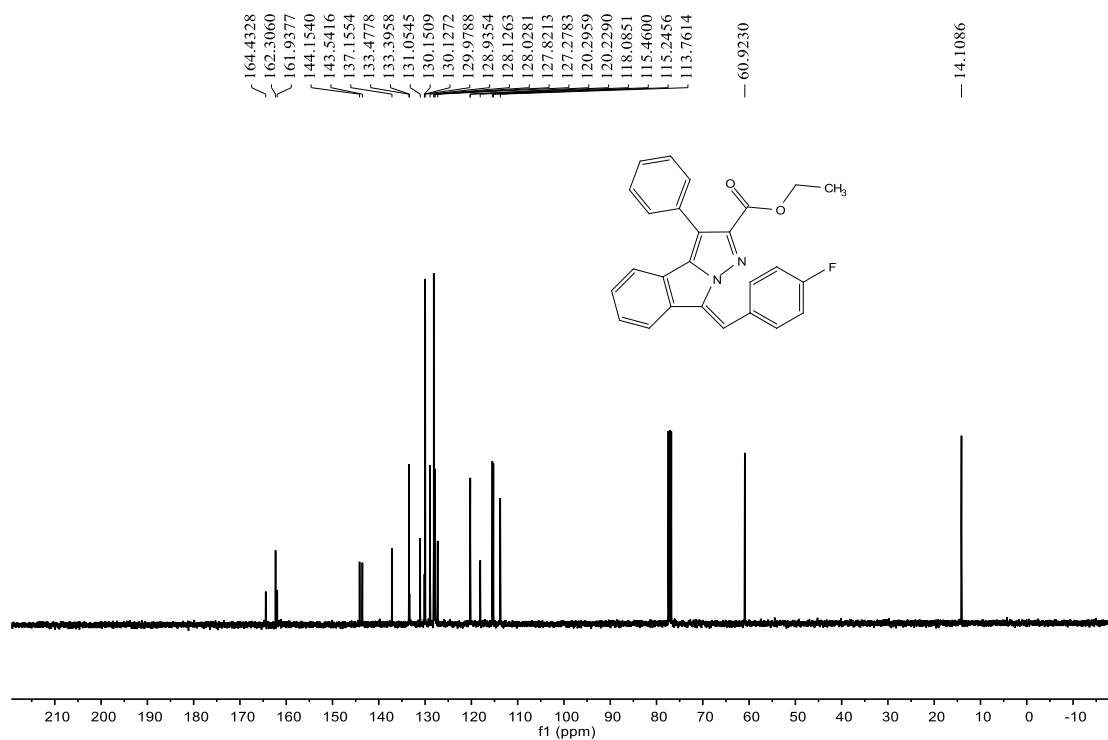
¹⁹F NMR spectra of compound **3av**.



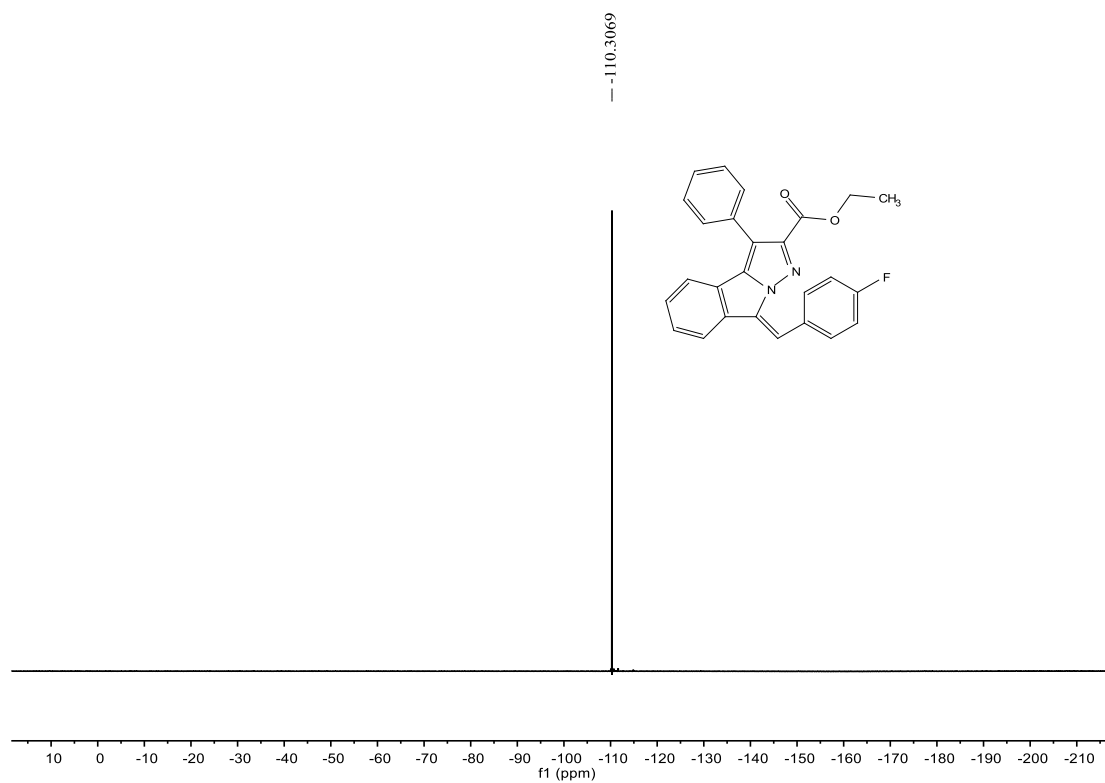
¹H NMR spectra of compound **3aw**.



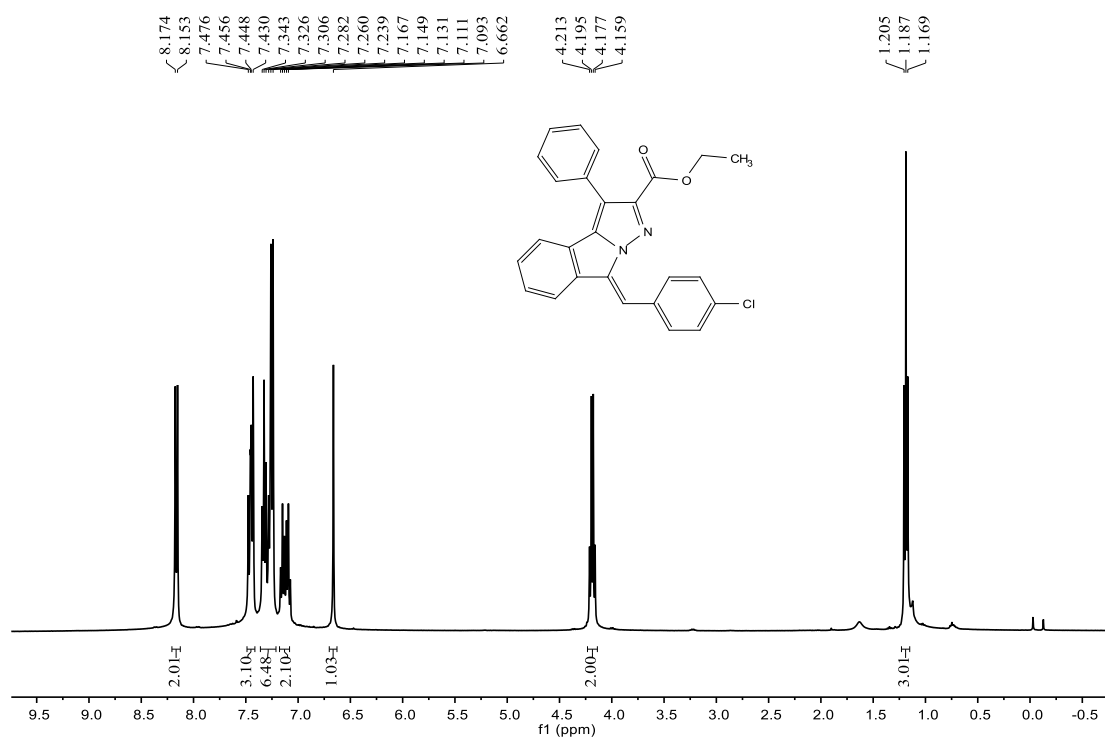
¹³C NMR spectra of compound **3aw**.



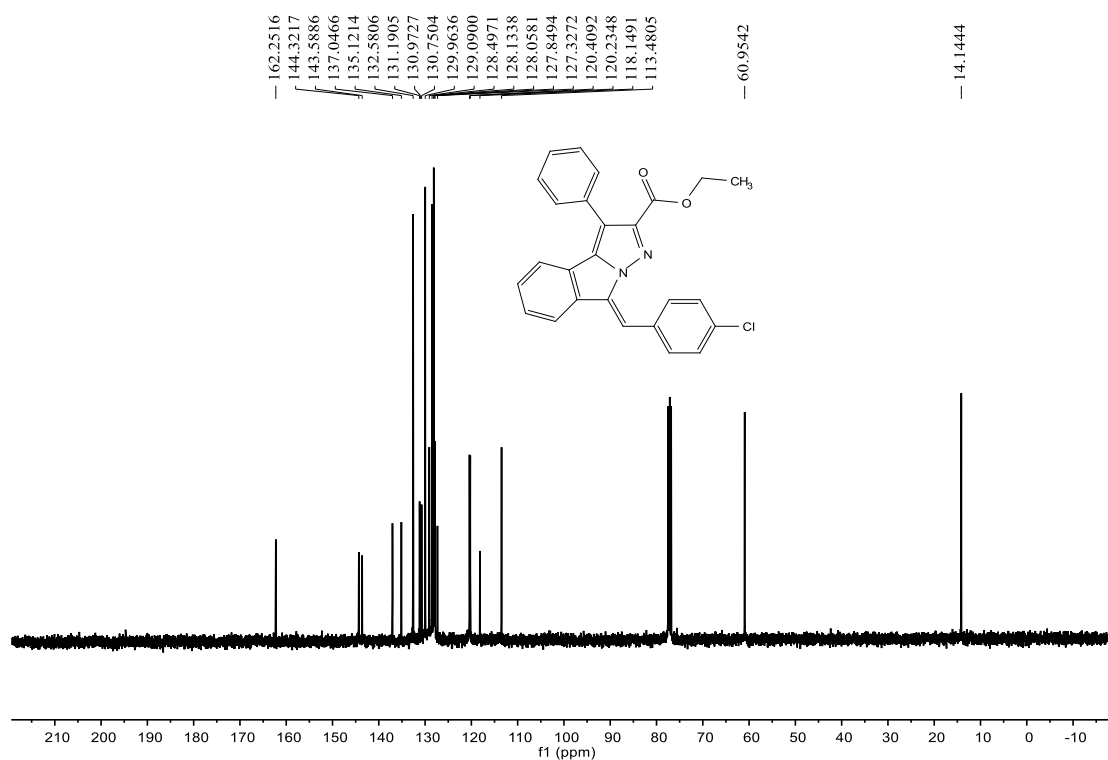
^{19}F NMR spectra of compound **3aw**.



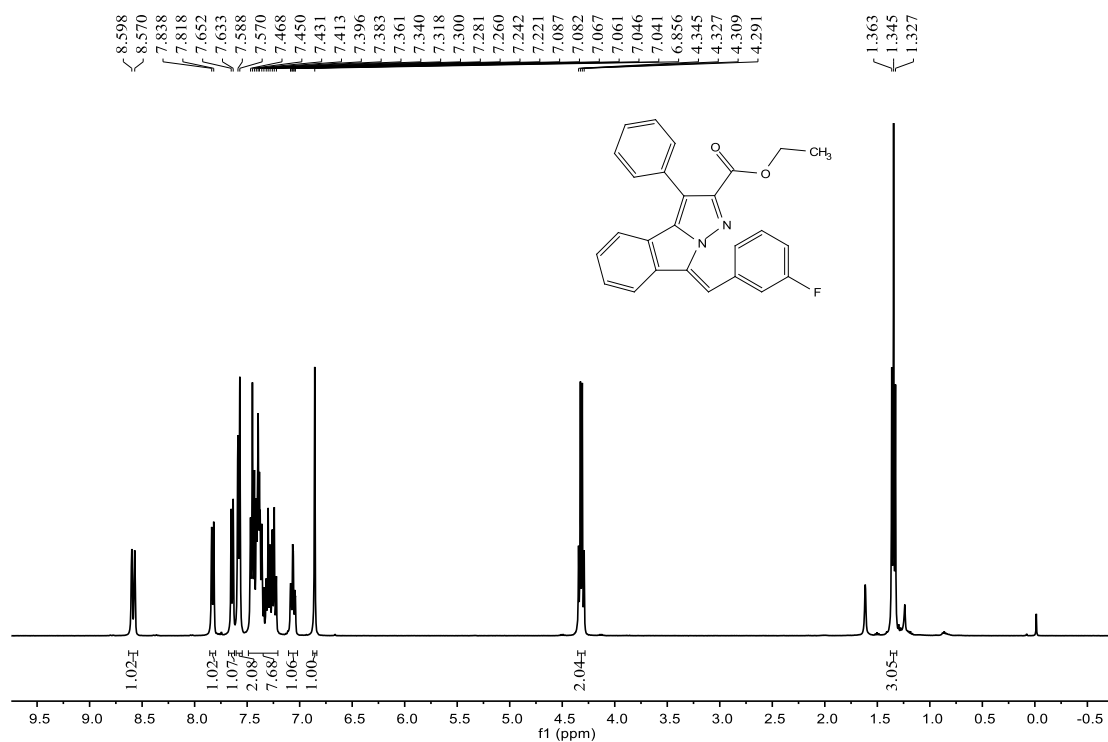
^1H NMR spectra of compound **3ax**.



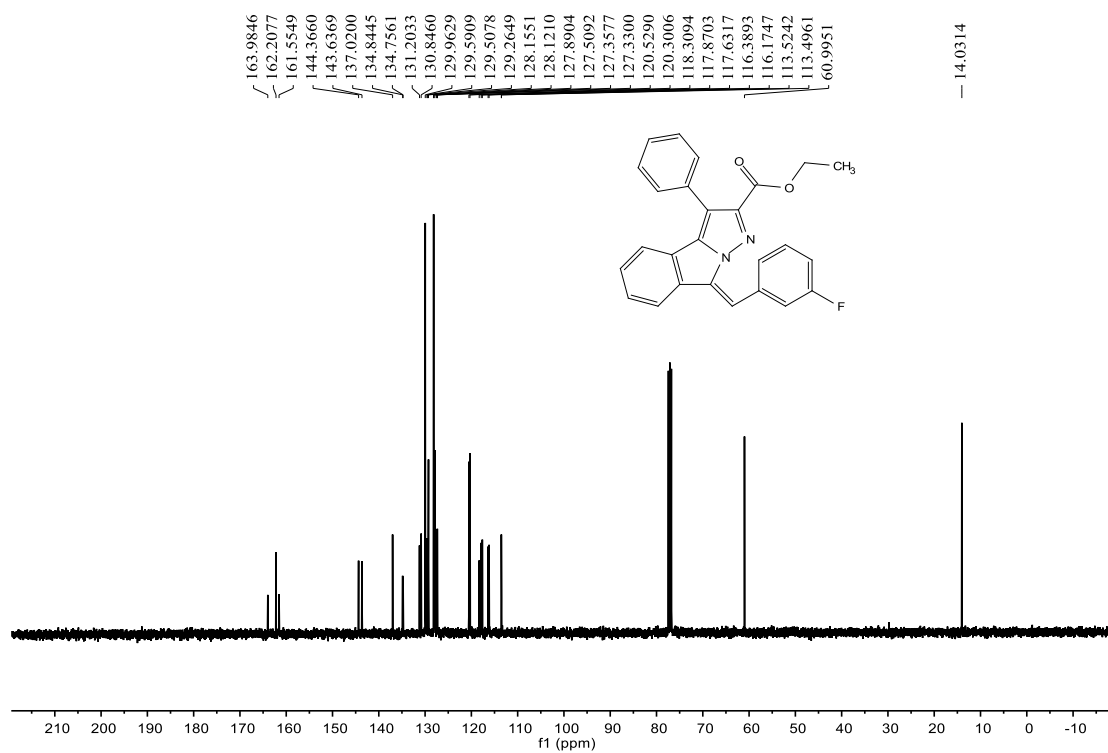
¹³C NMR spectra of compound **3ax**.



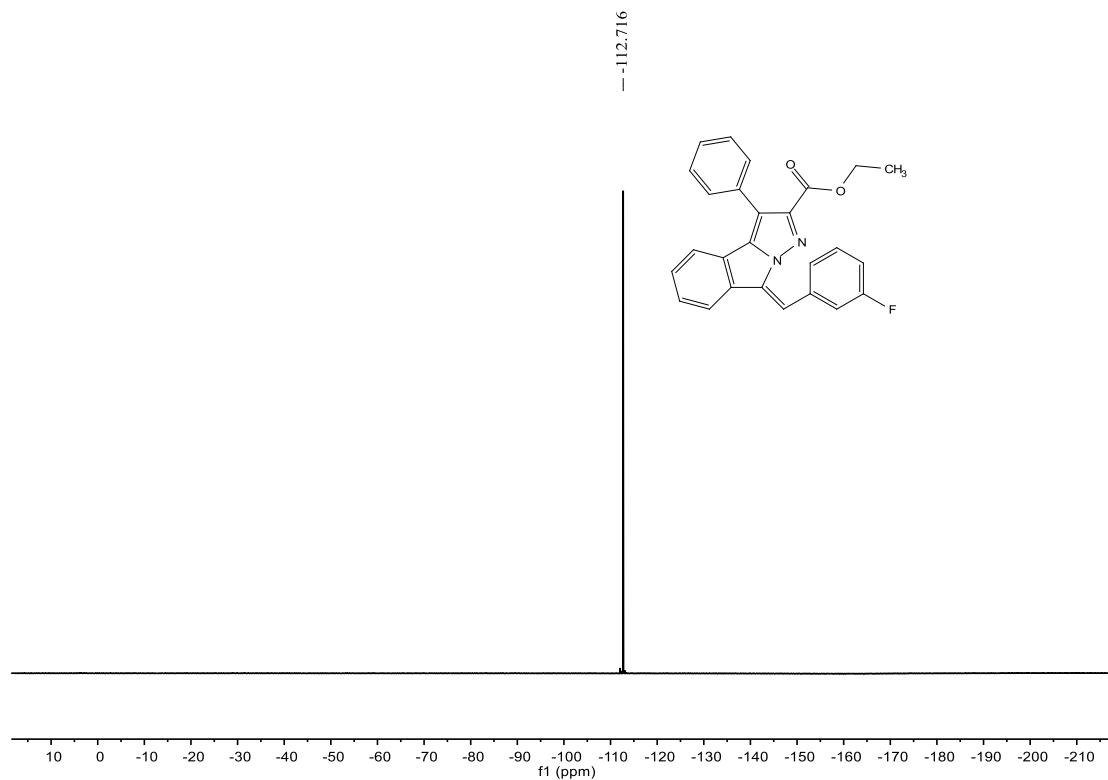
¹H NMR spectra of compound **3ay**.



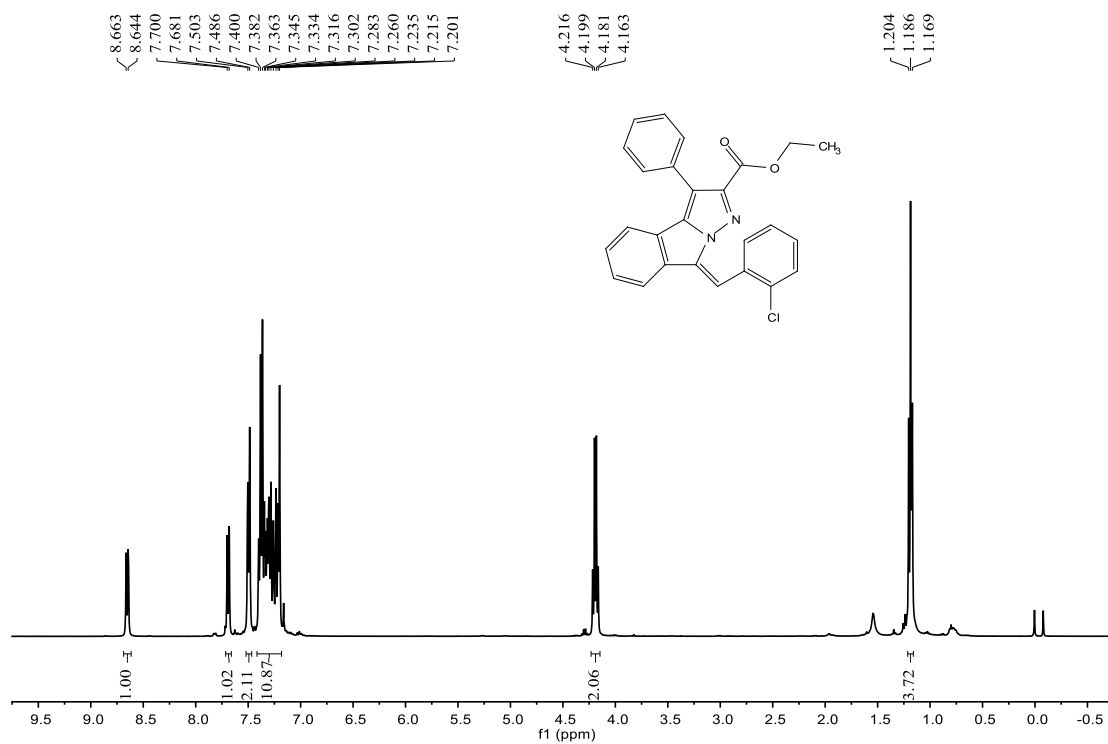
¹³C NMR spectra of compound **3ay**.



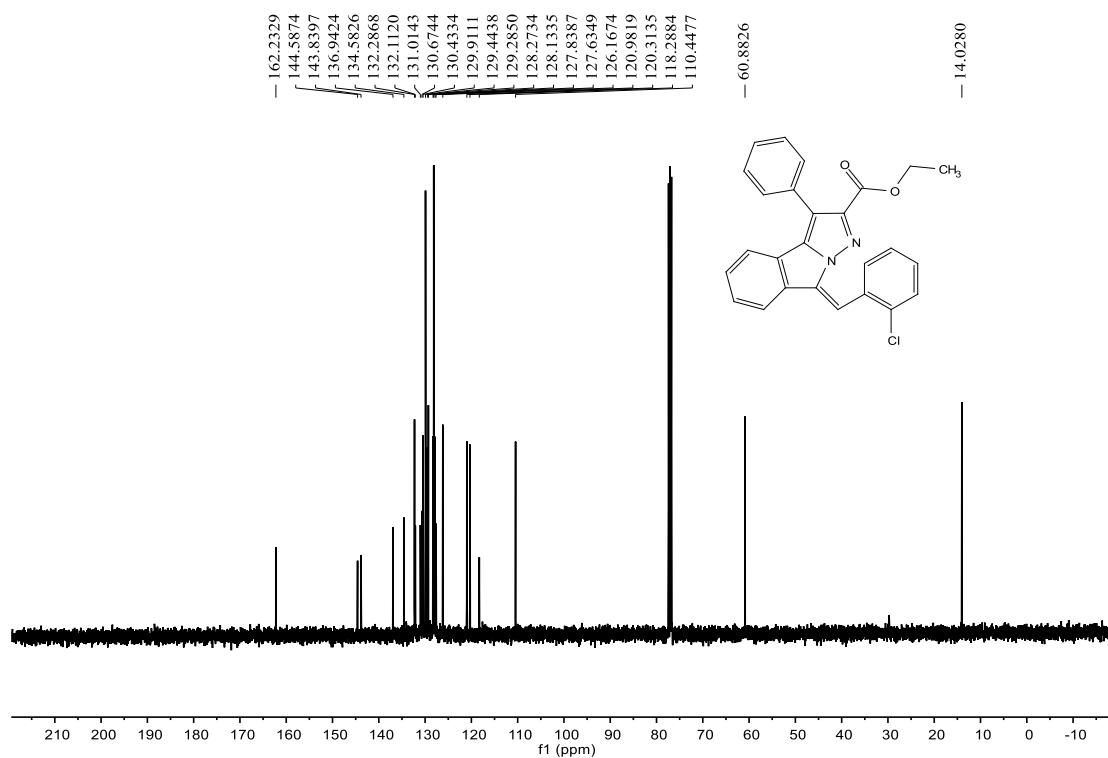
¹⁹F NMR spectra of compound **3ay**.



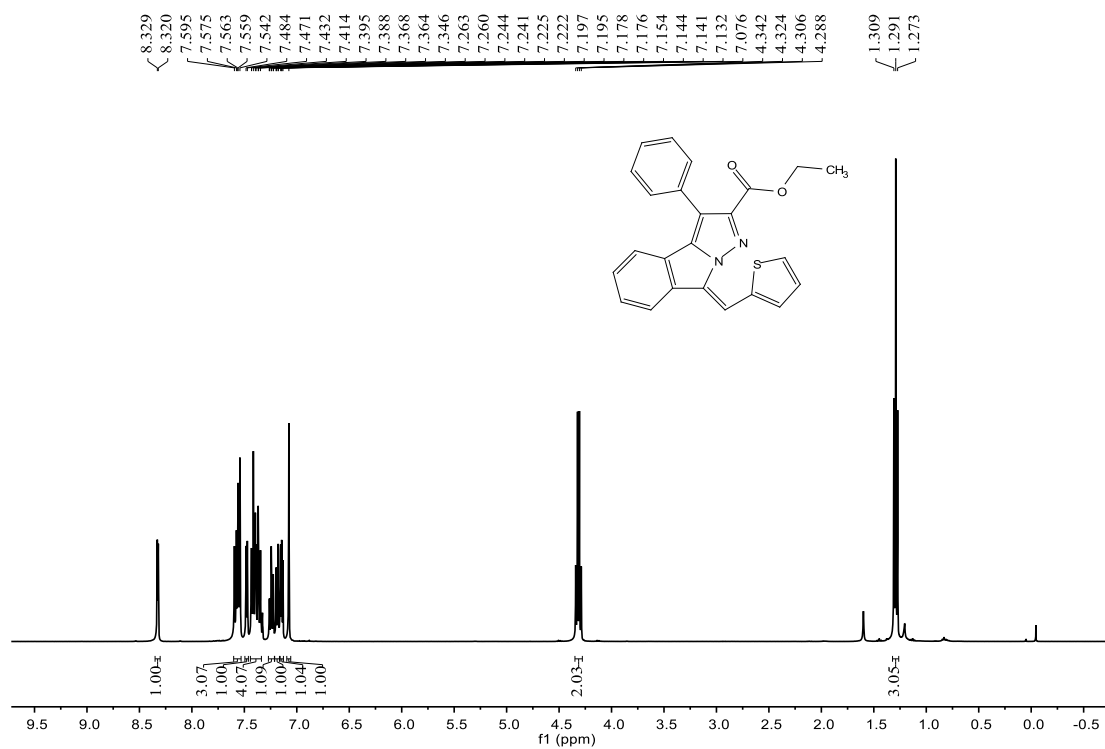
¹H NMR spectra of compound **3az**.



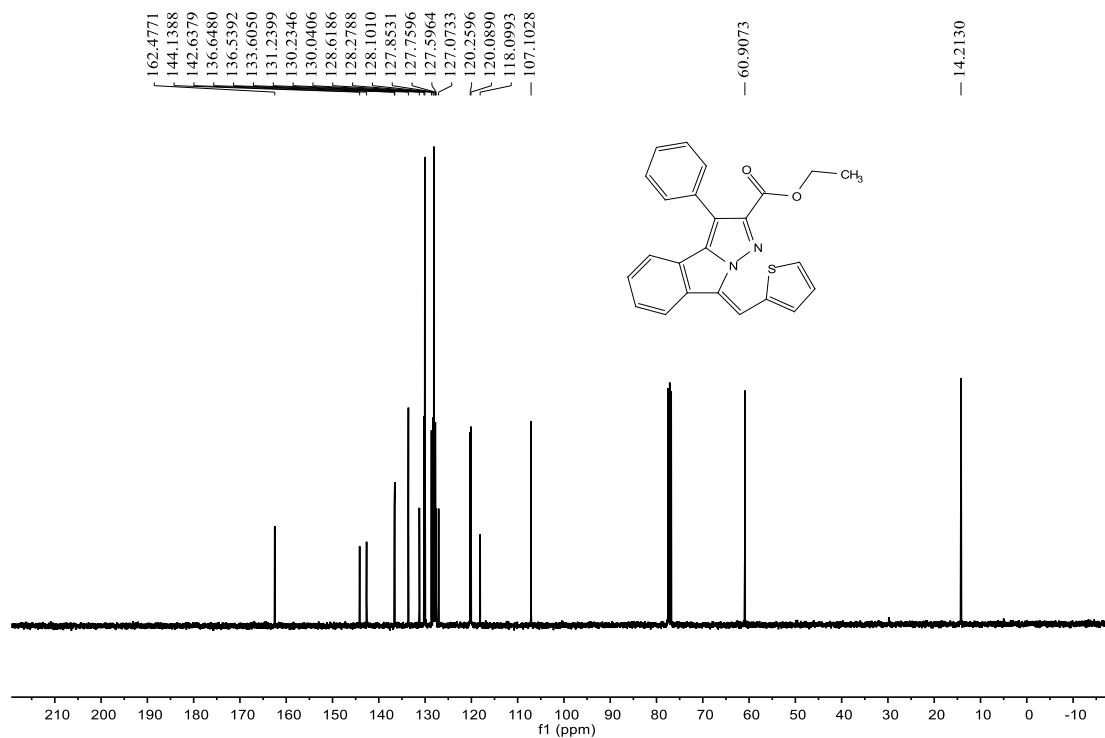
¹³C NMR spectra of compound **3az**.



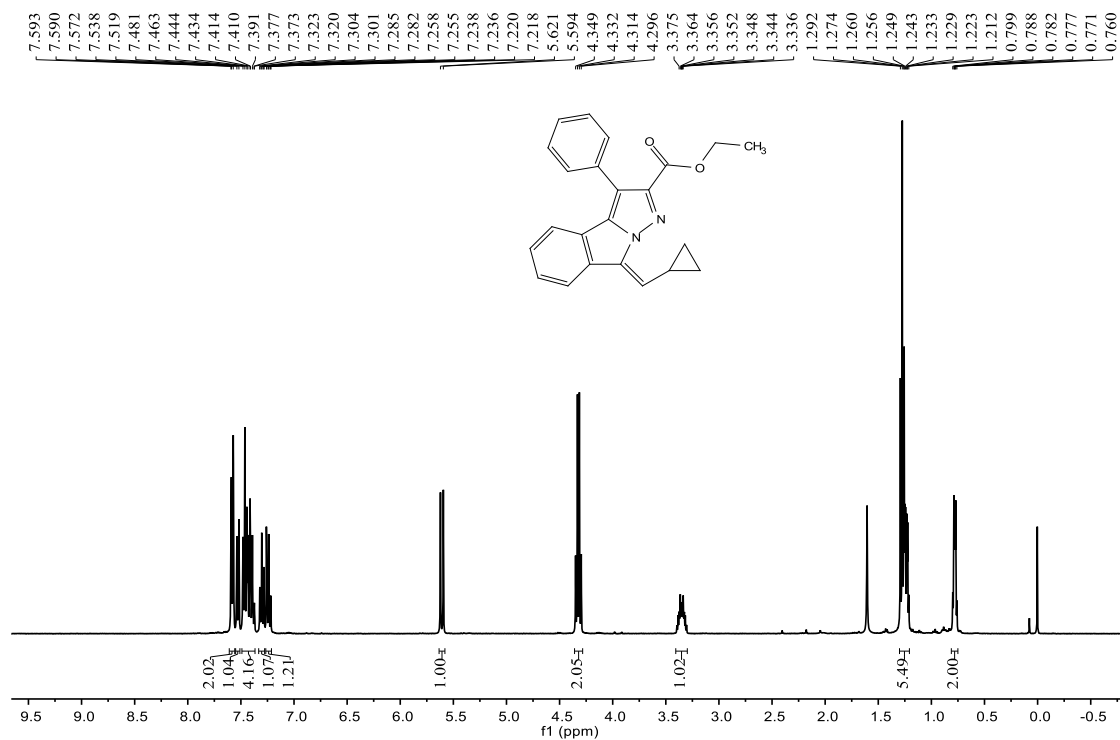
¹H NMR spectra of compound **3aaa**.



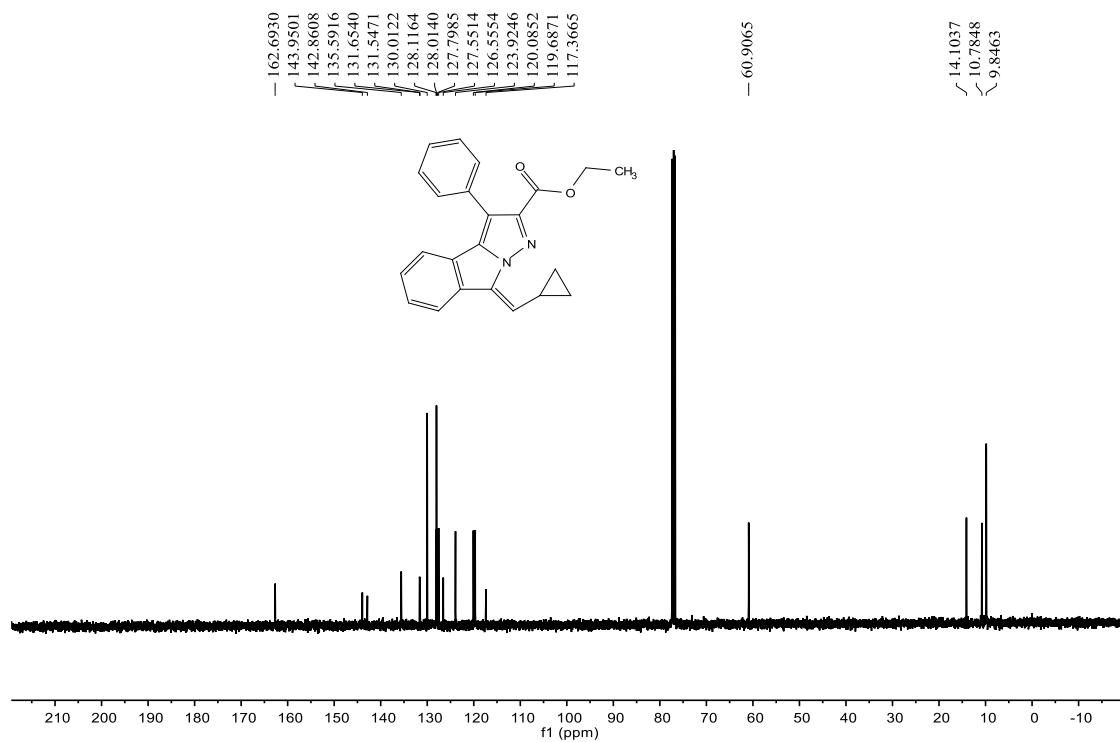
¹³C NMR spectra of compound **3aaa**.



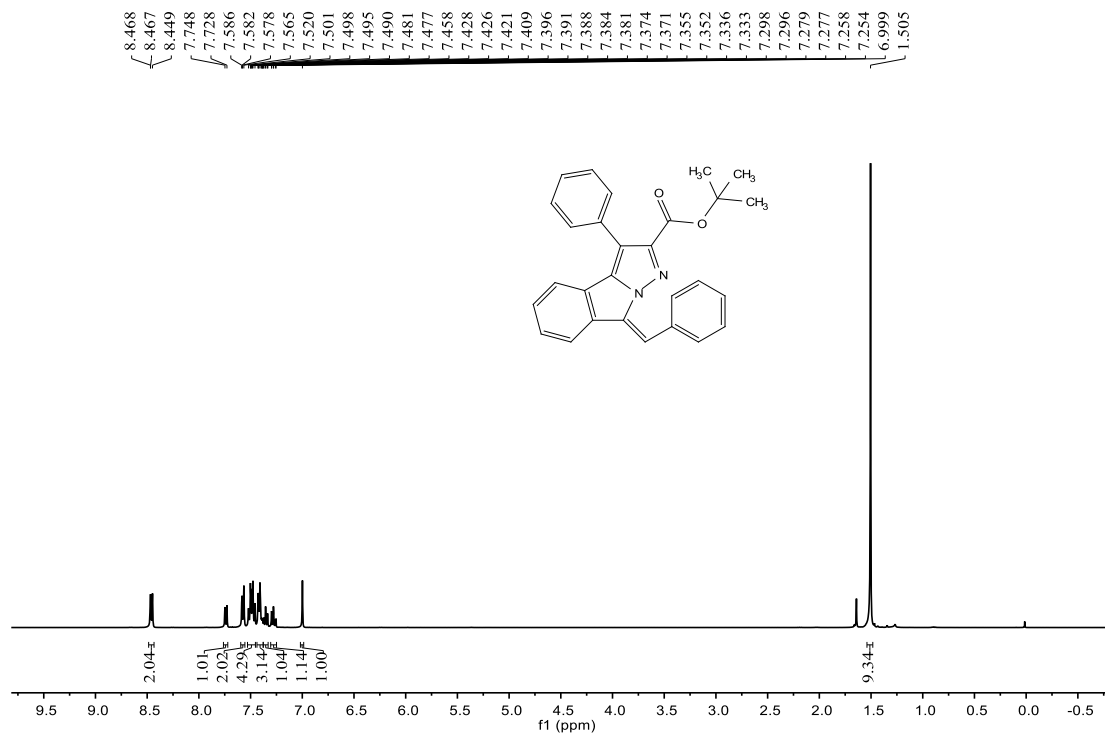
¹H NMR spectra of compound **3aab**.



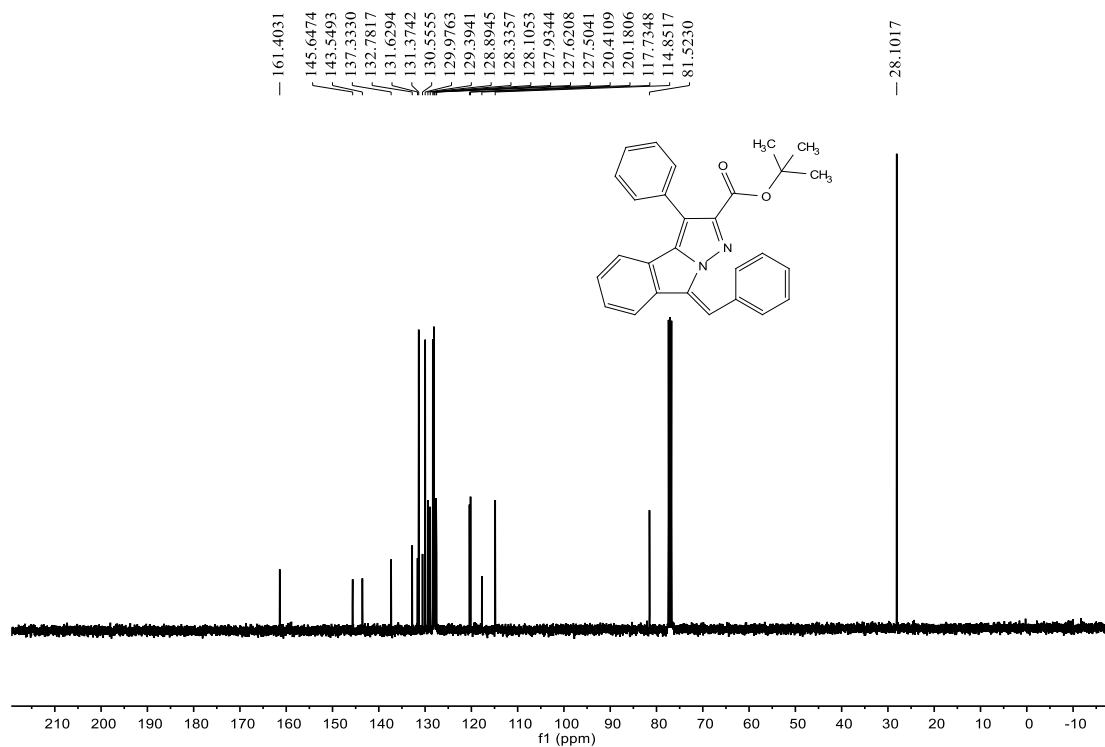
¹³C NMR spectra of compound **3aab**.



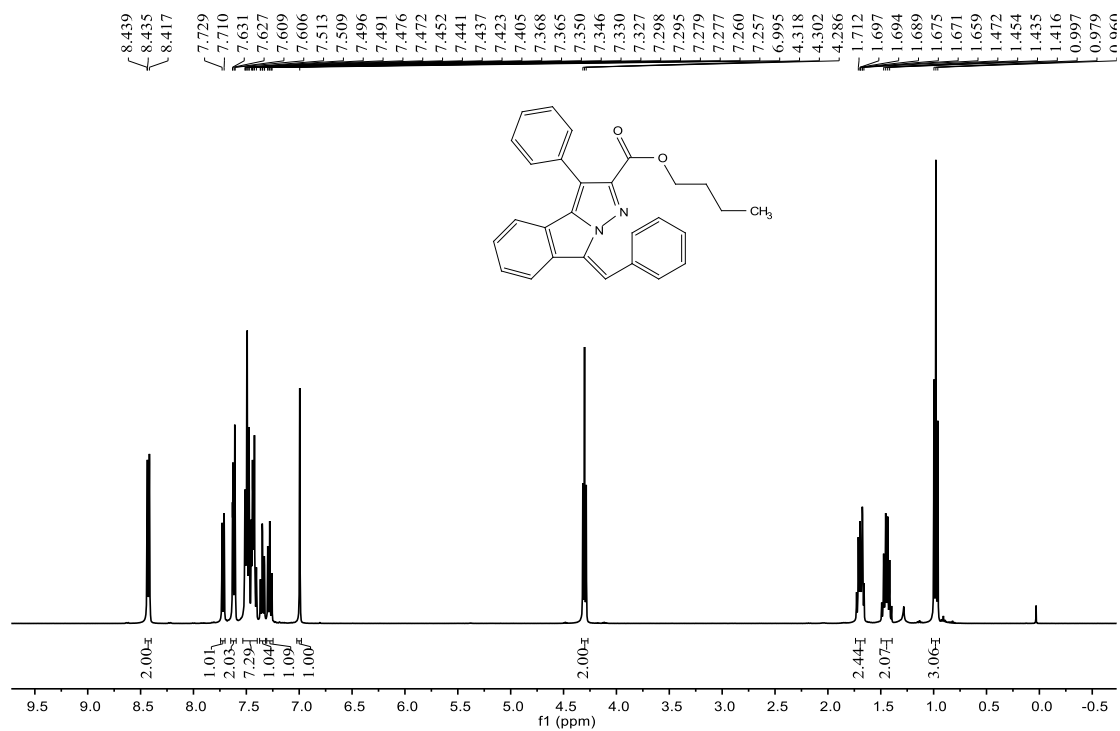
^1H NMR spectra of compound **3ba**.



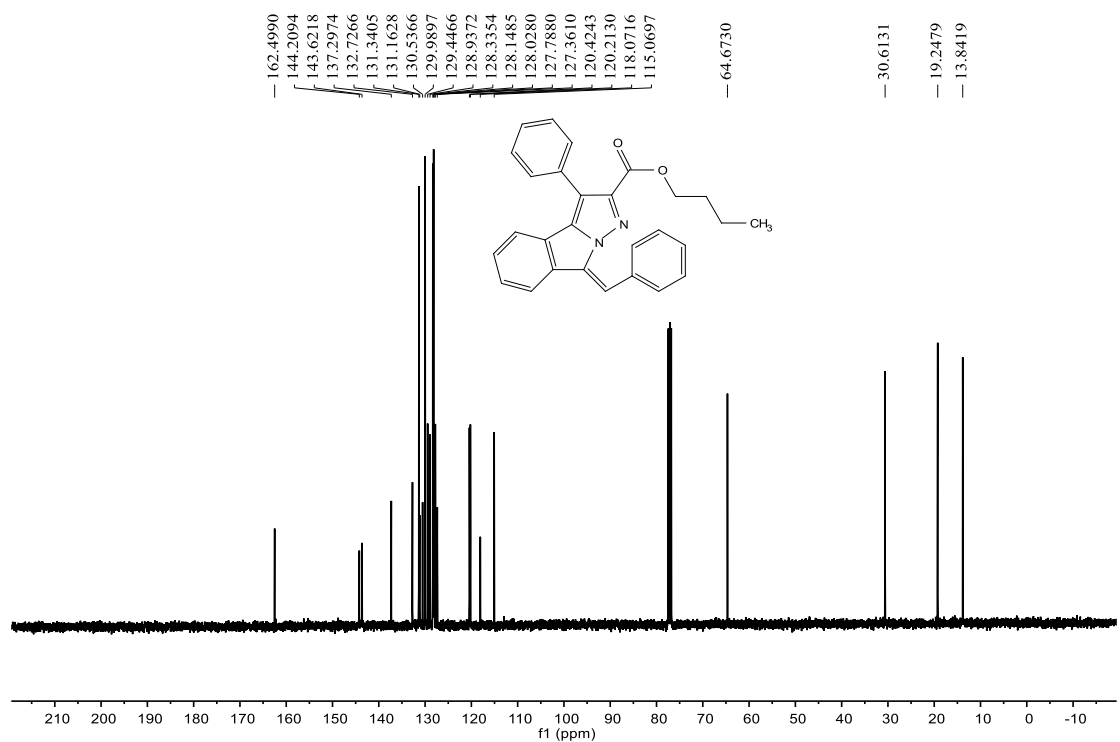
^{13}C NMR spectra of compound **3ba**.



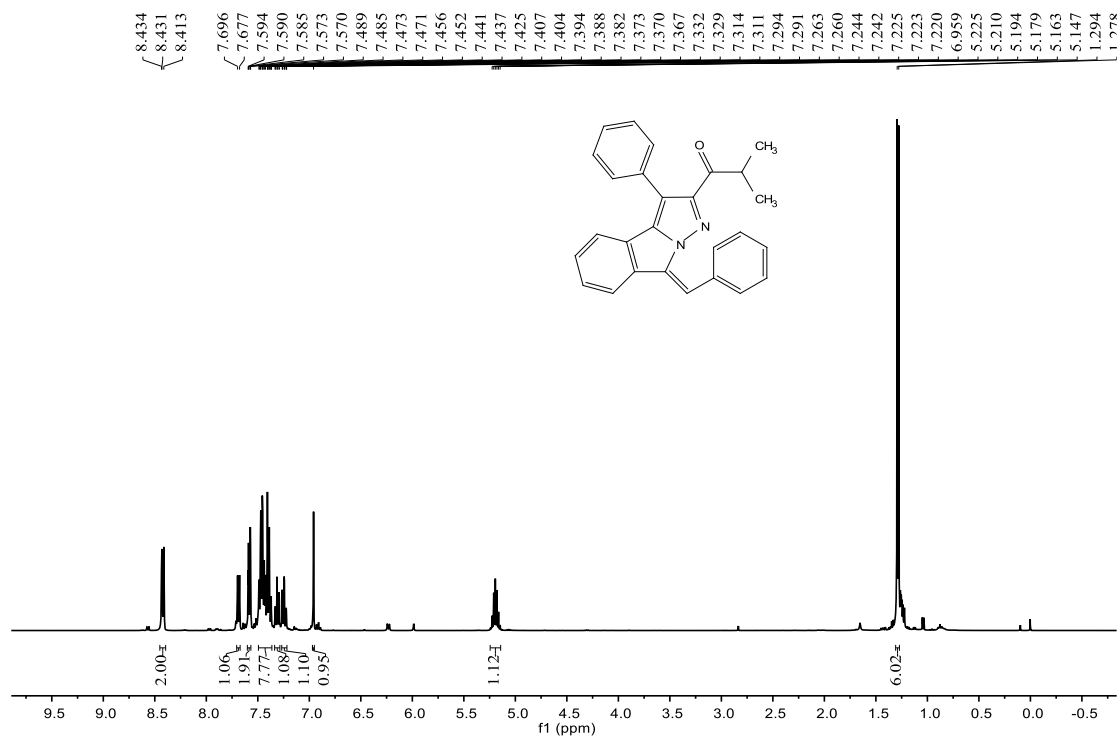
¹H NMR spectra of compound **3ca**.



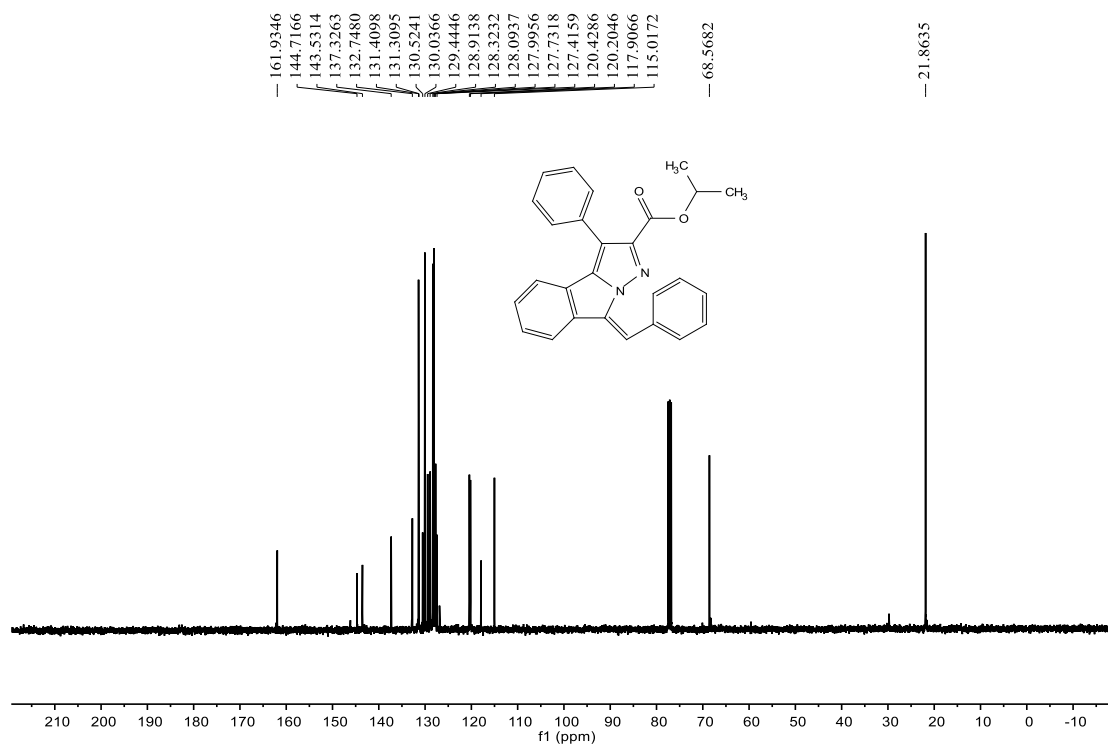
¹³C NMR spectra of compound **3ca**.



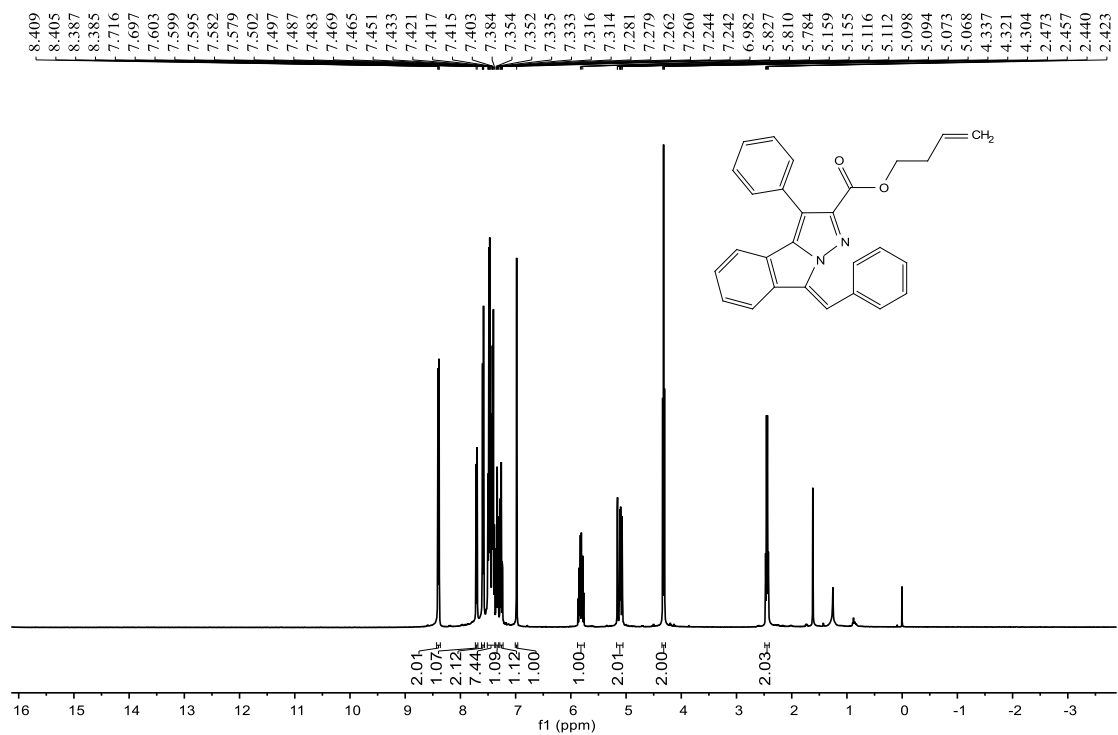
¹H NMR spectra of compound **3da**.



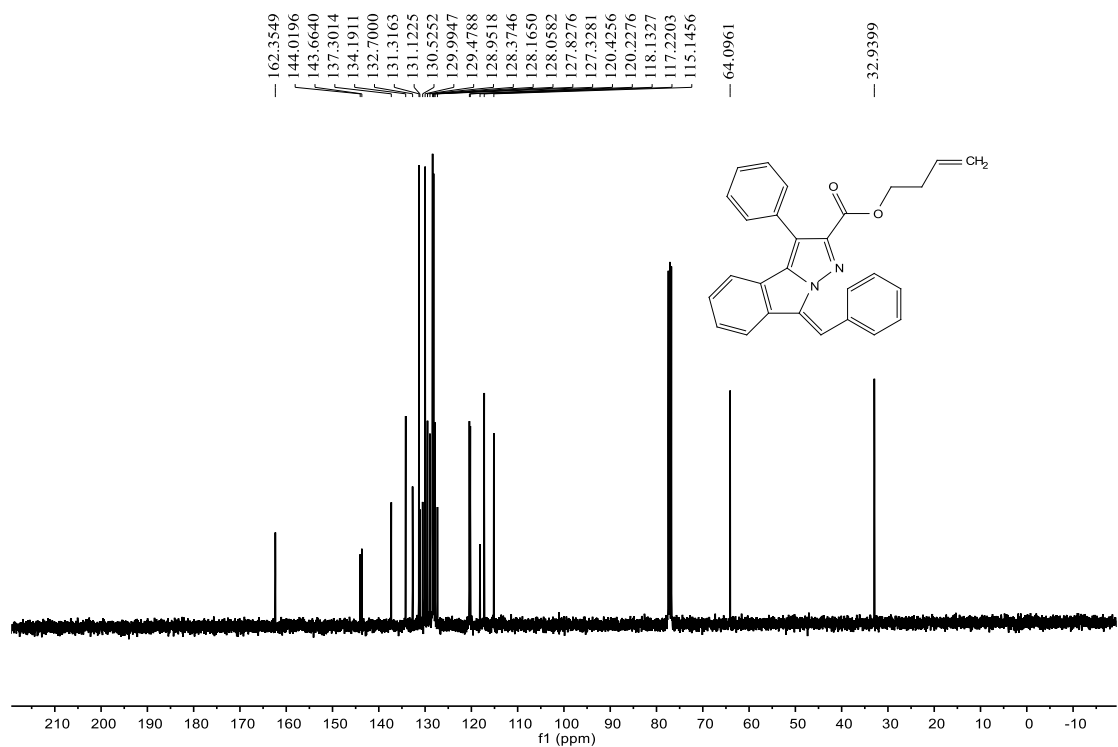
¹³C NMR spectra of compound **3da**.



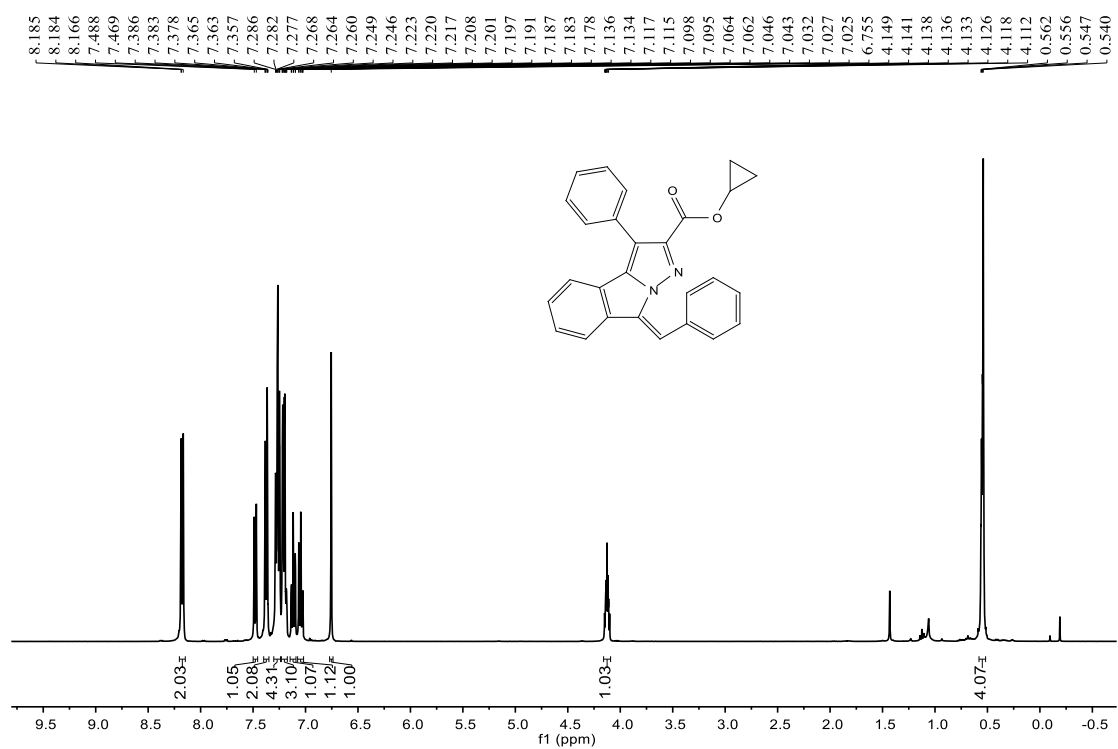
^1H NMR spectra of compound **3ea**.



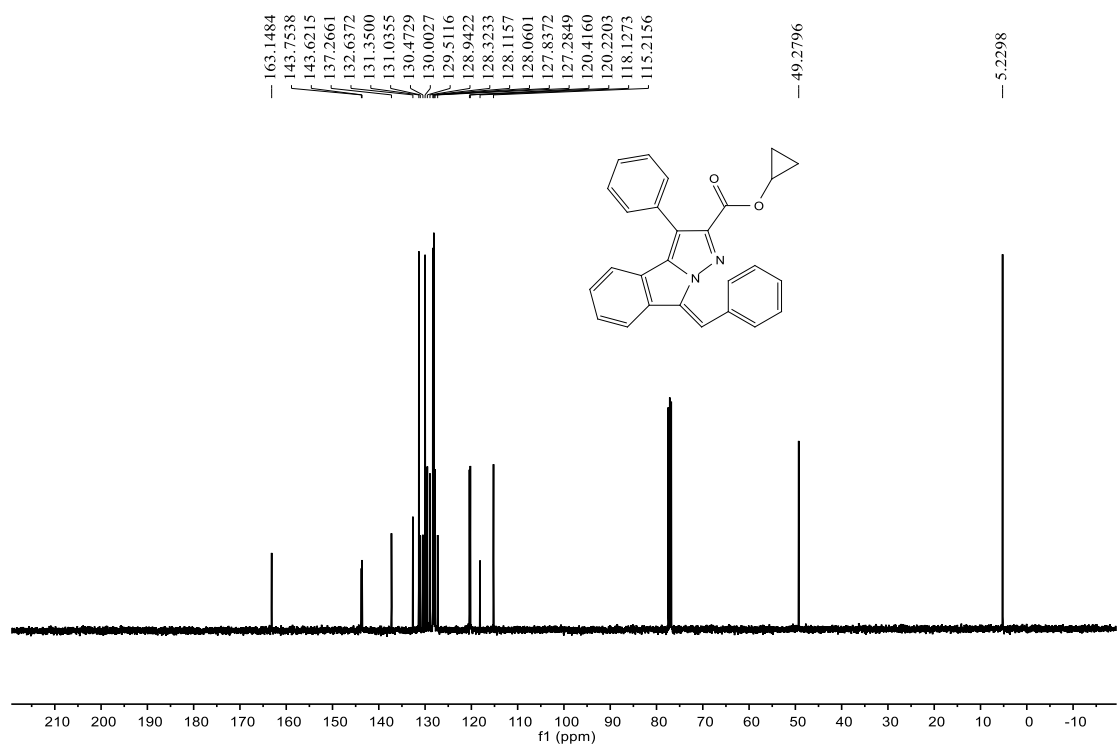
^{13}C NMR spectra of compound **3ea**.



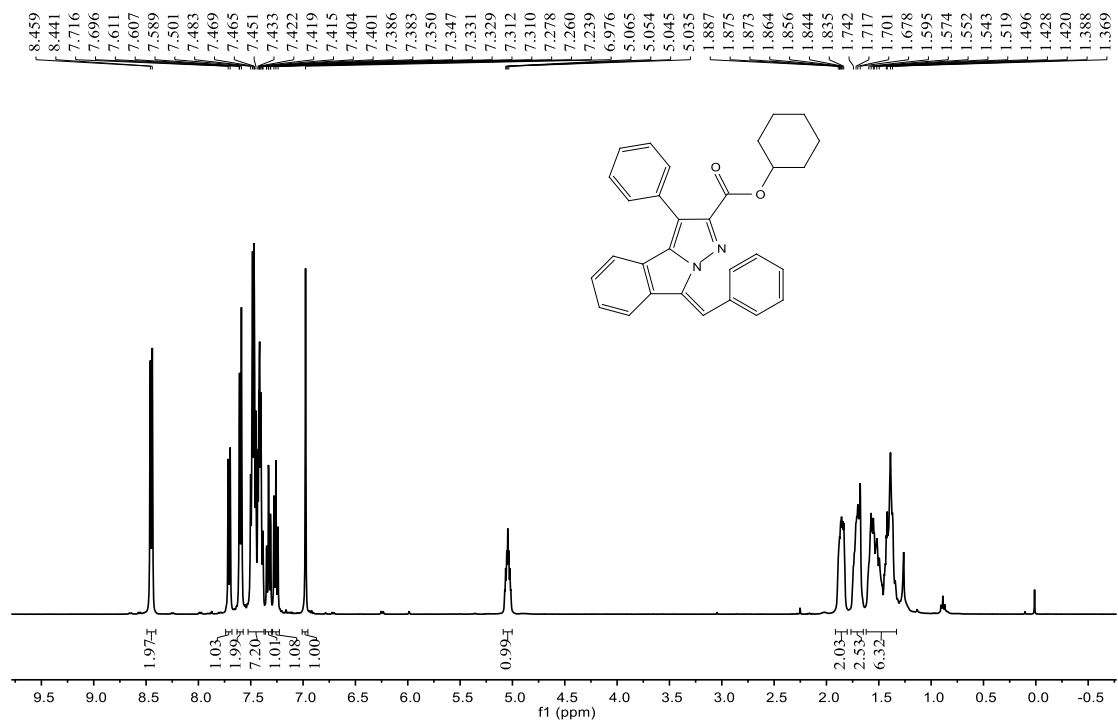
¹H NMR spectra of compound **3fa**.



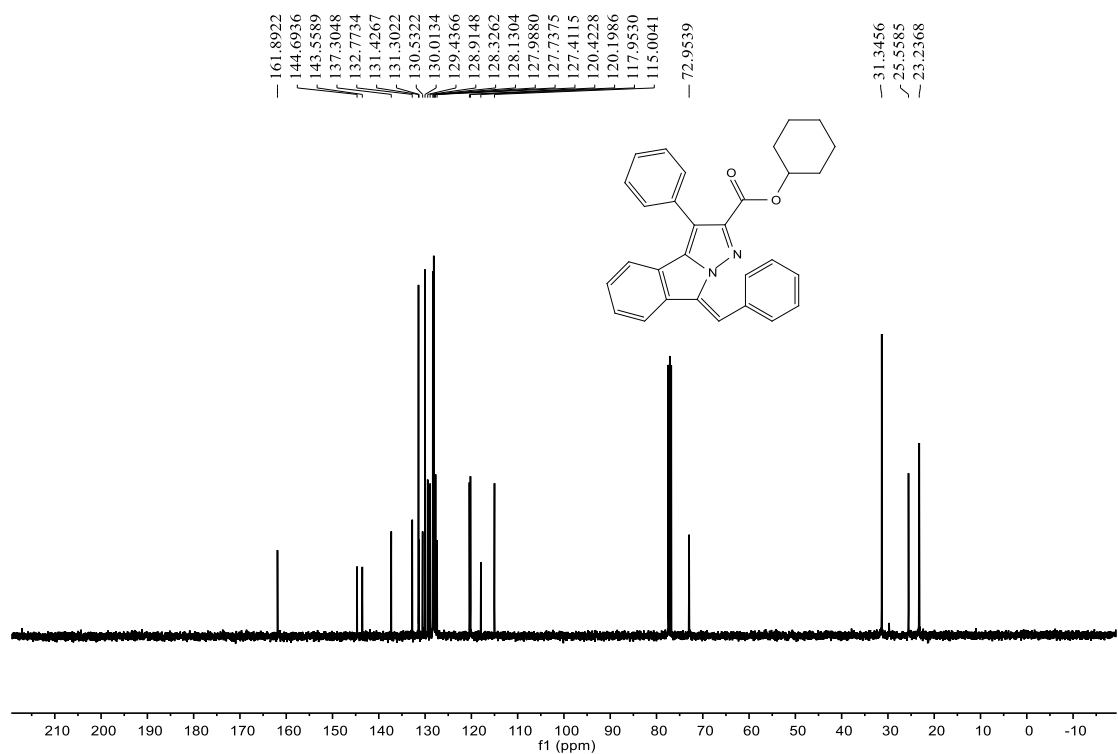
¹³C NMR spectra of compound **3fa**.



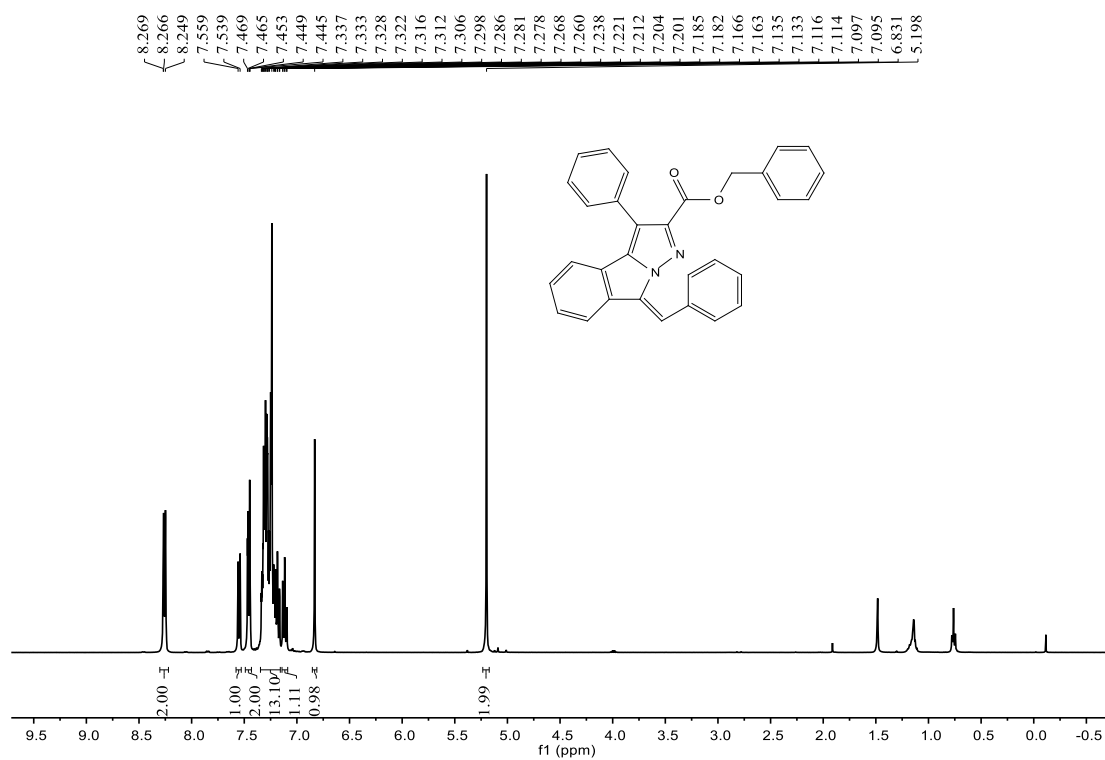
¹H NMR spectra of compound **3ga**.



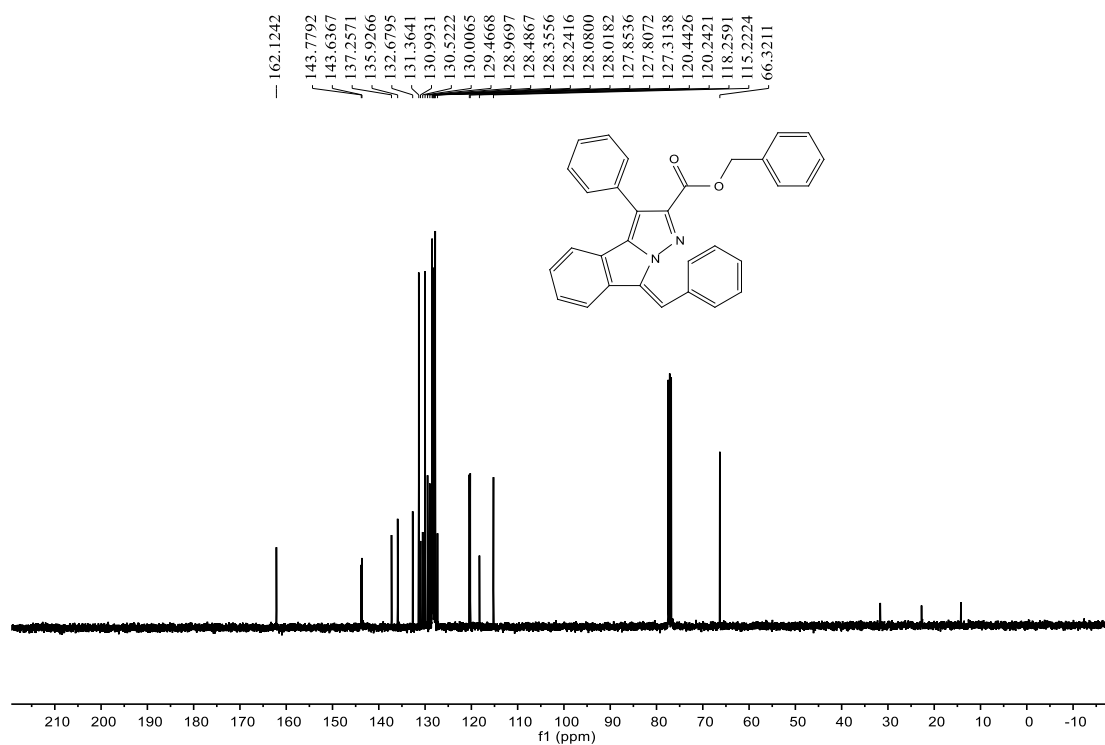
¹³C NMR spectra of compound **3ga**.



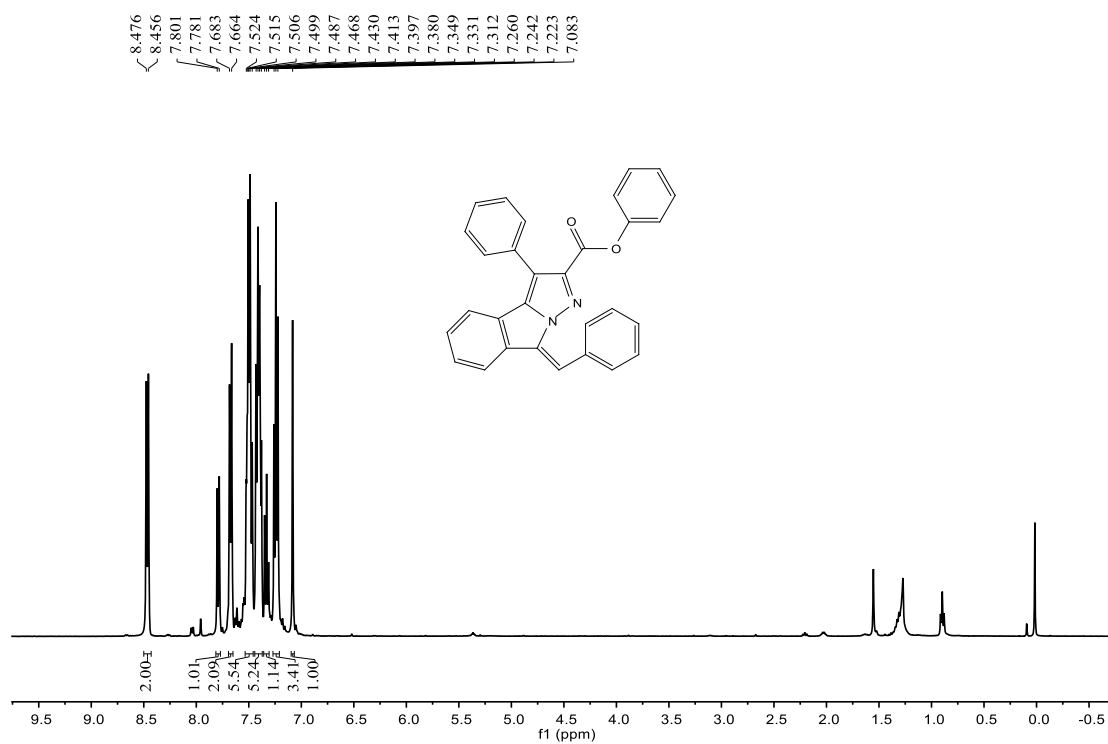
¹H NMR spectra of compound **3ha**.



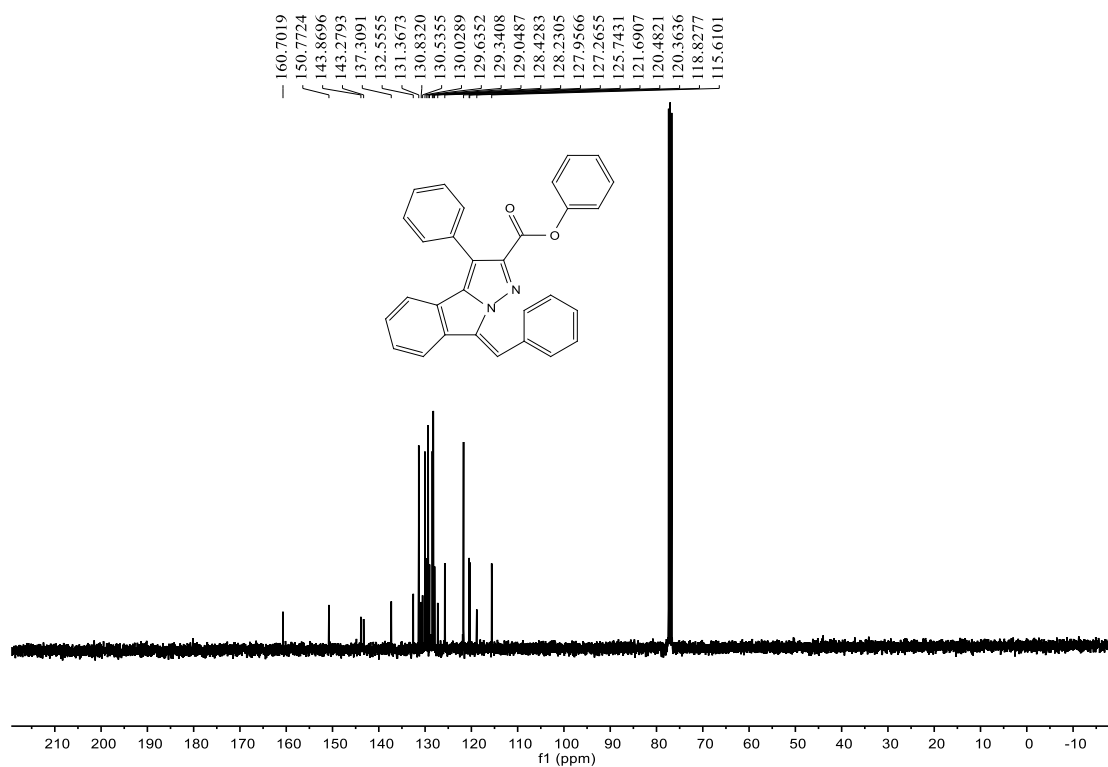
¹³C NMR spectra of compound **3ha**.



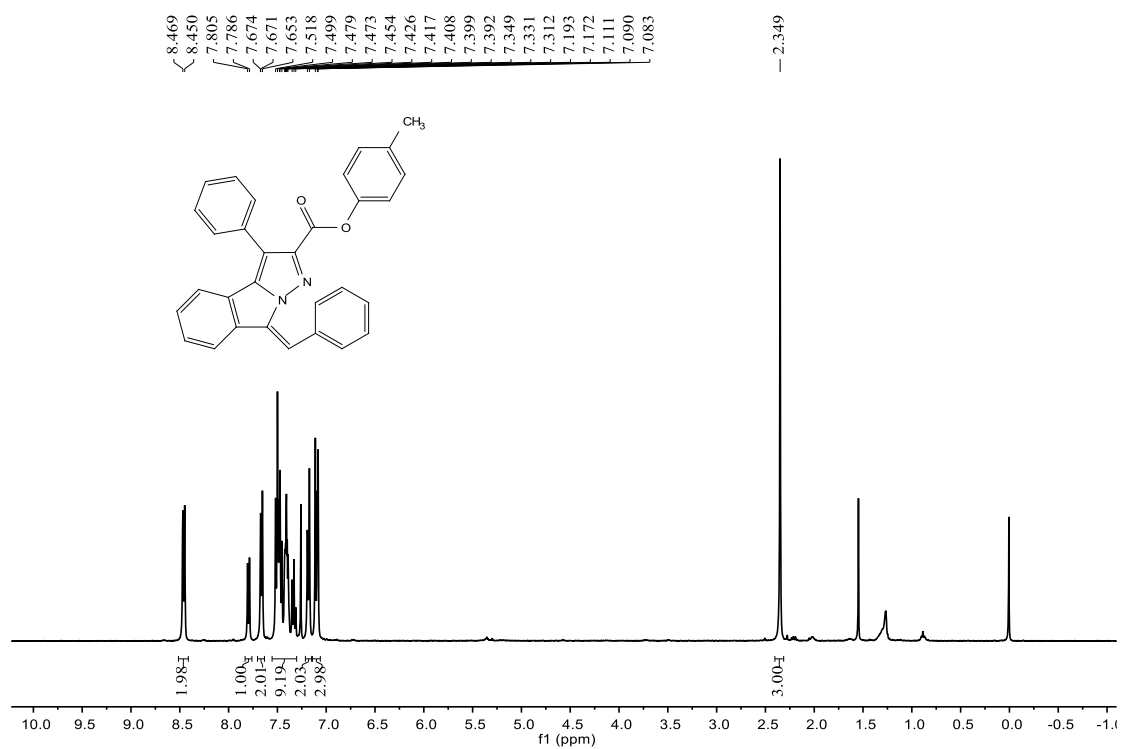
¹H NMR spectra of compound **3ia**.



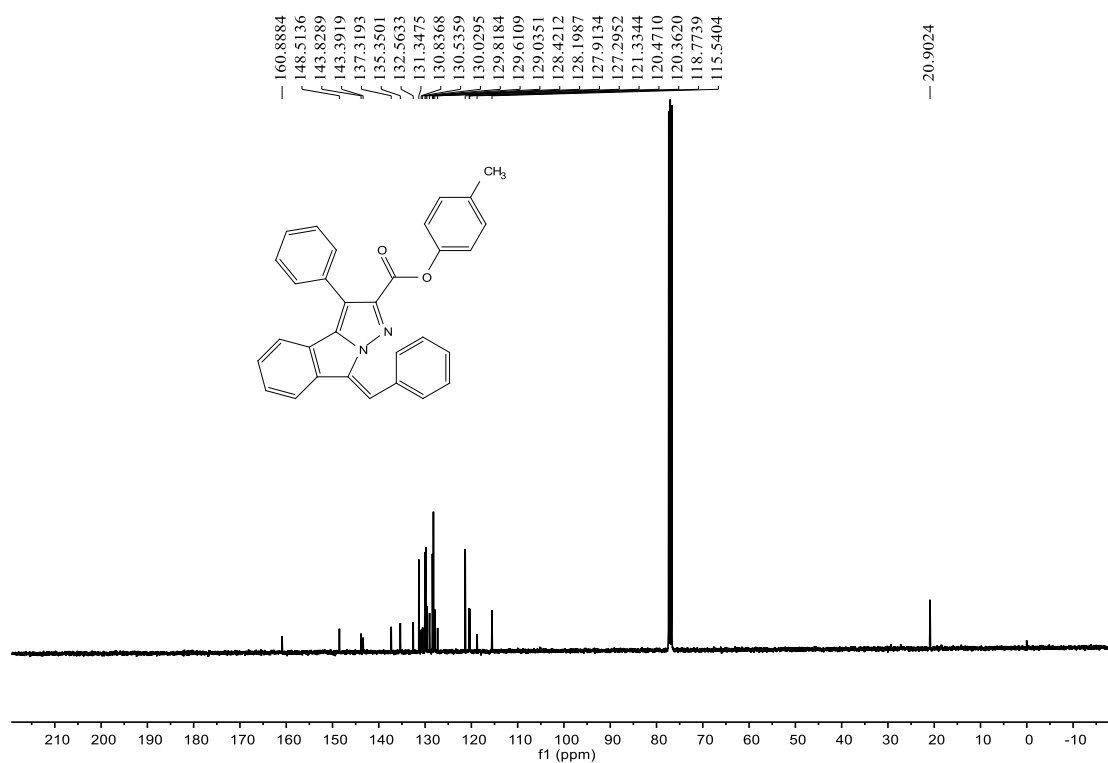
¹³C NMR spectra of compound **3ia**.



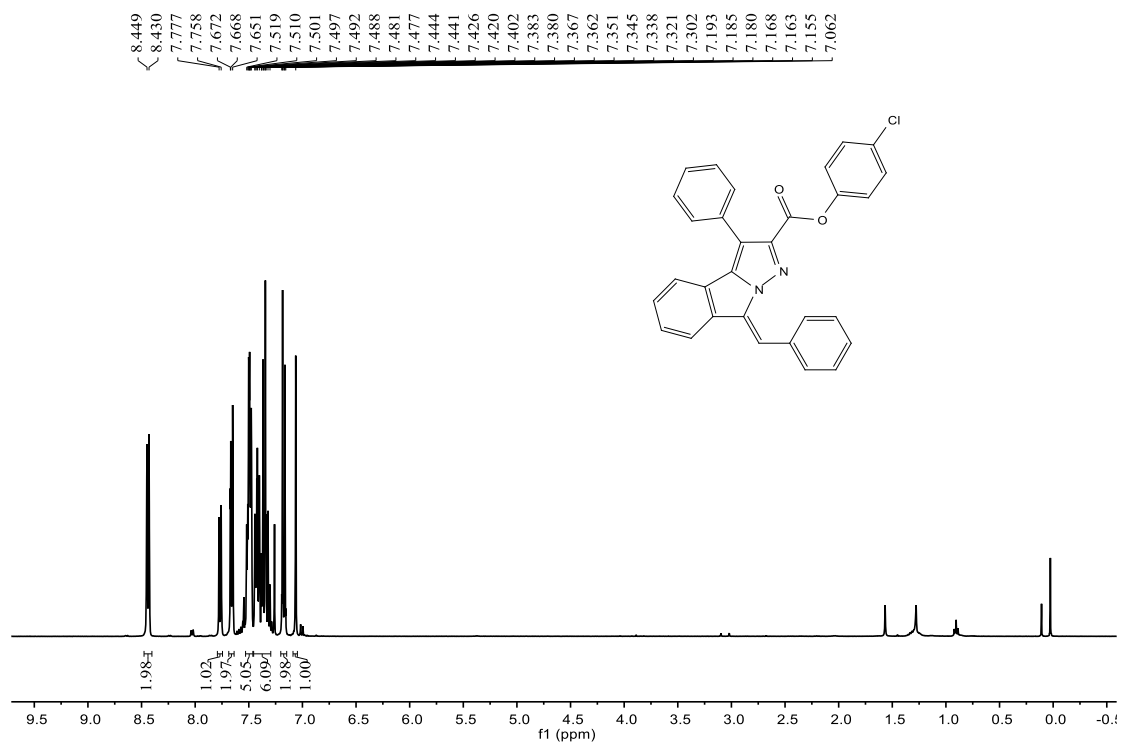
¹H NMR spectra of compound **3ja**.



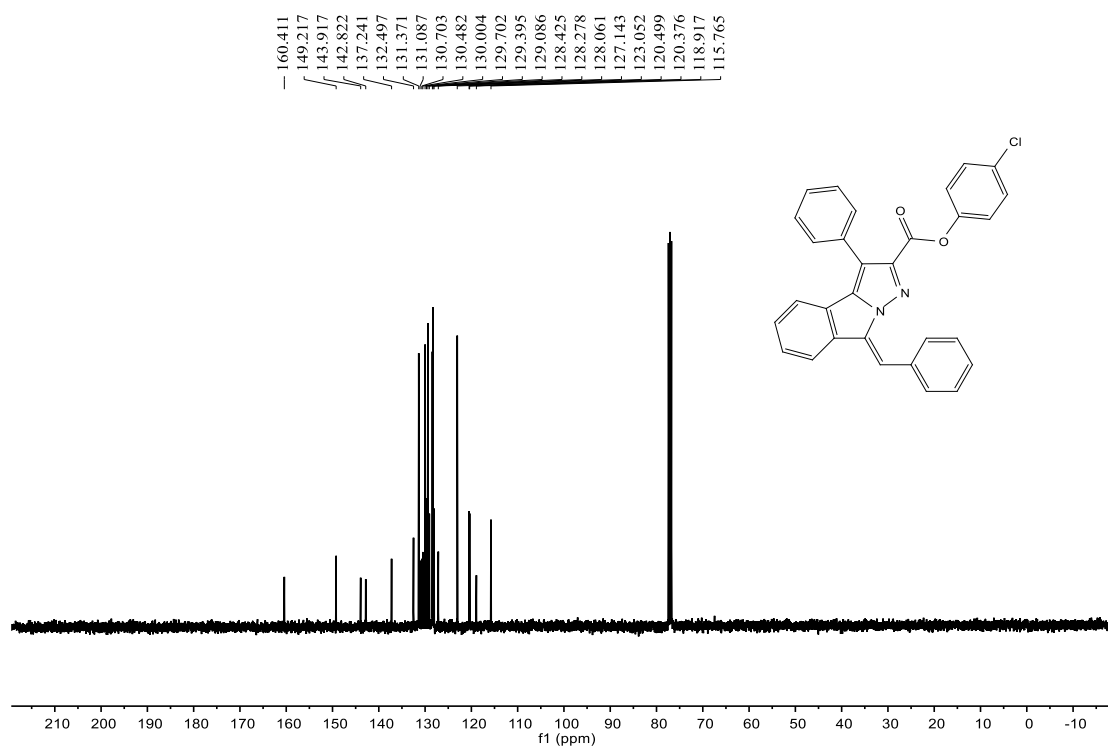
¹³C NMR spectra of compound **3ja**.



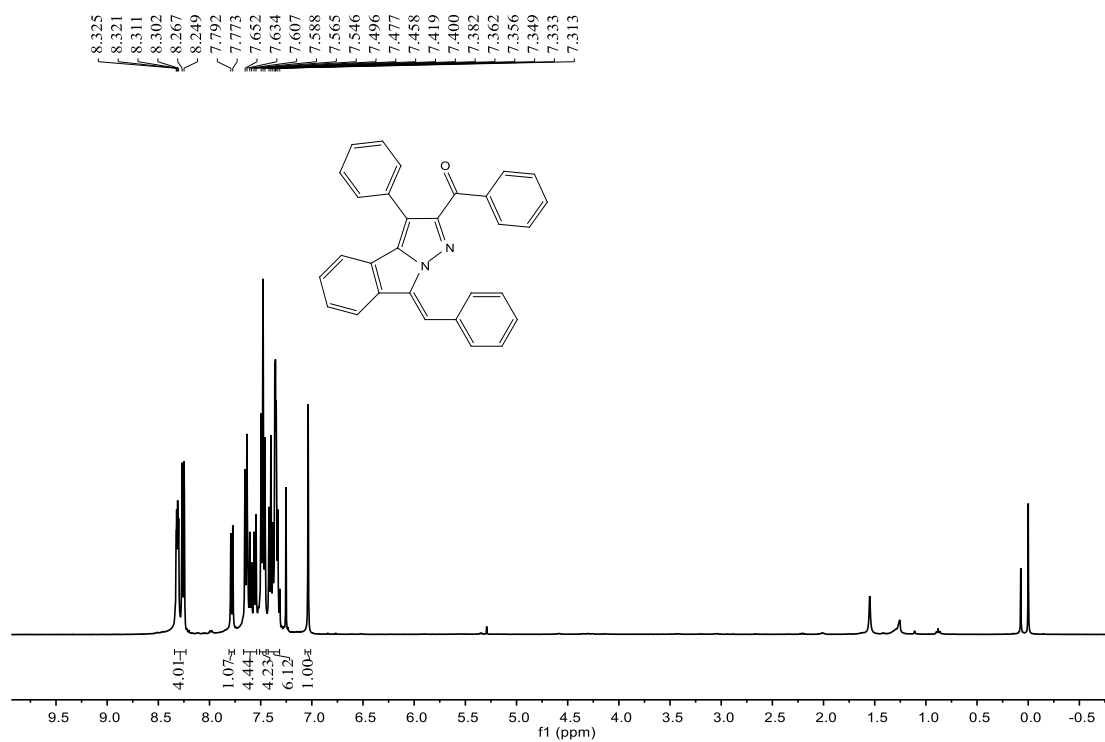
¹H NMR spectra of compound **3ka**.



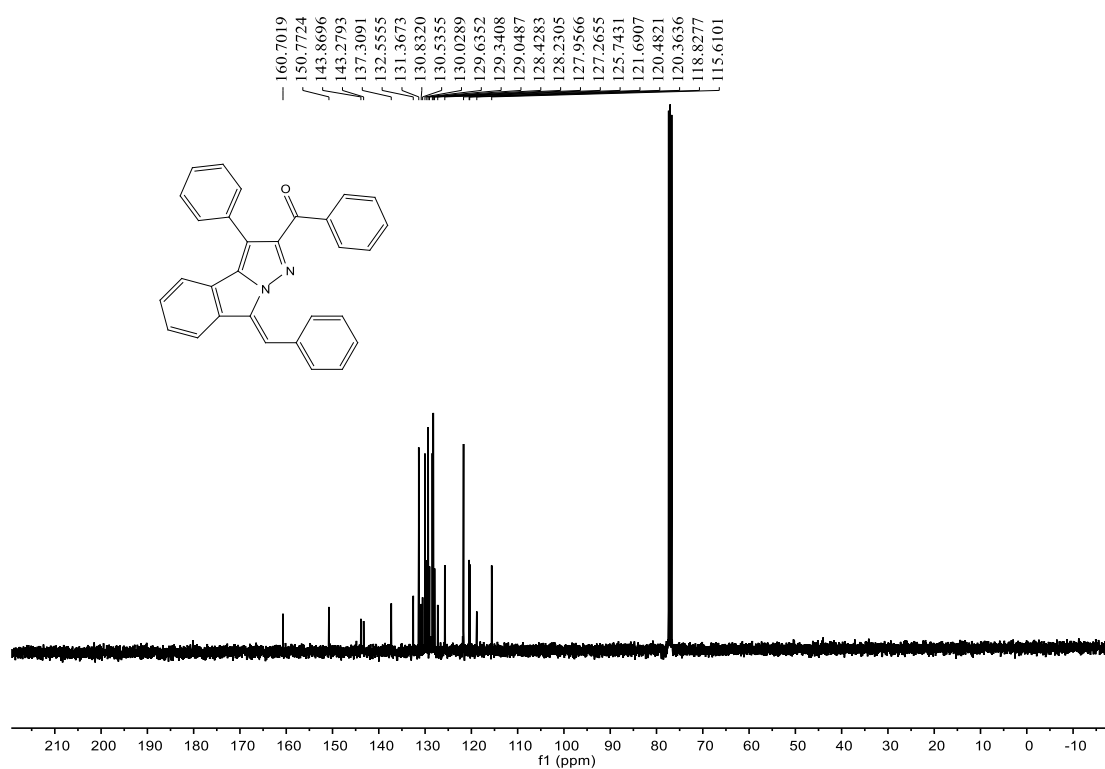
¹³C NMR spectra of compound **3ka**.



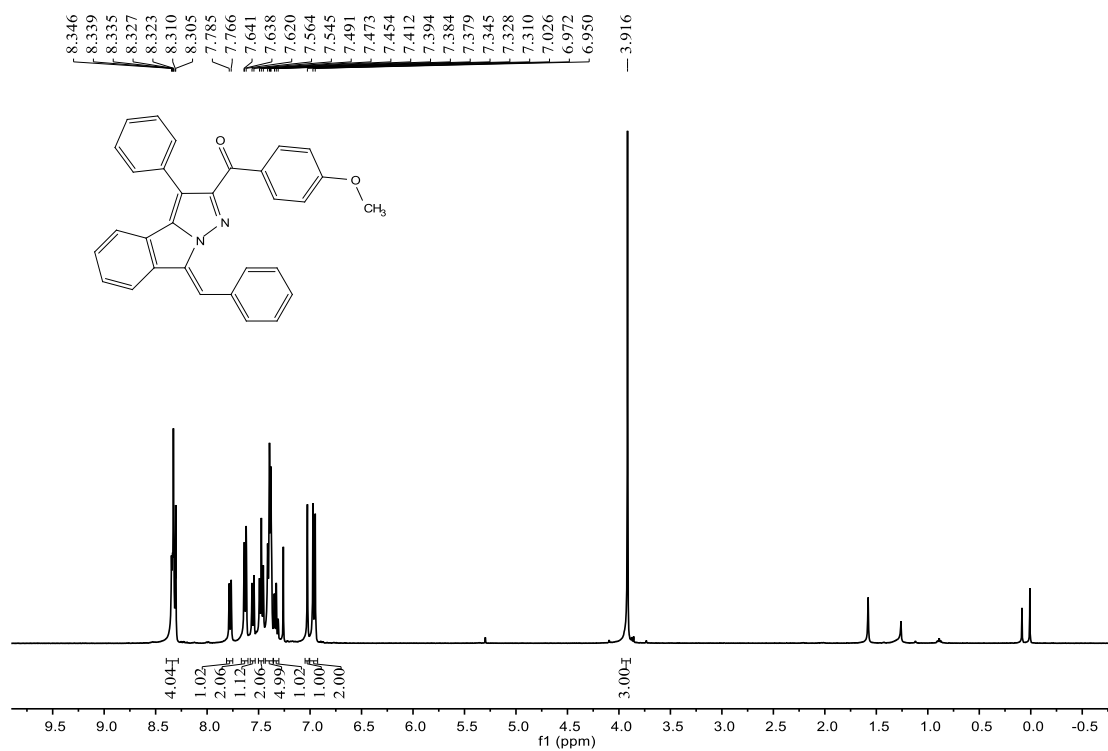
¹H NMR spectra of compound **3la**.



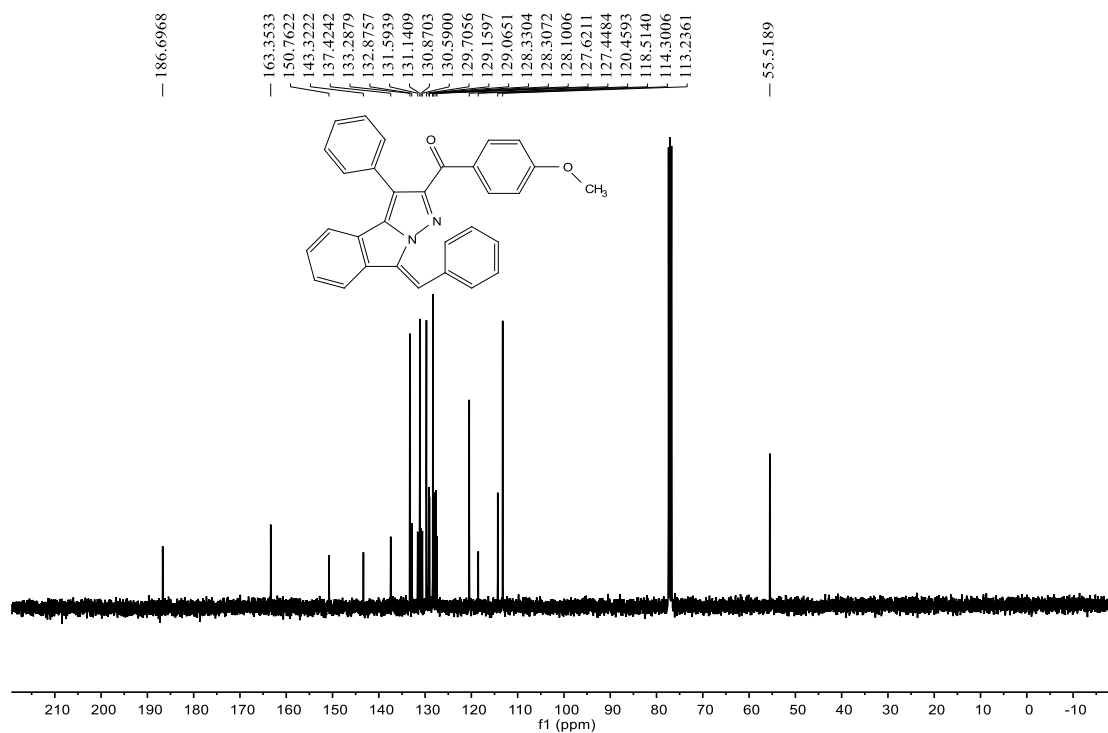
¹³C NMR spectra of compound **3la**.



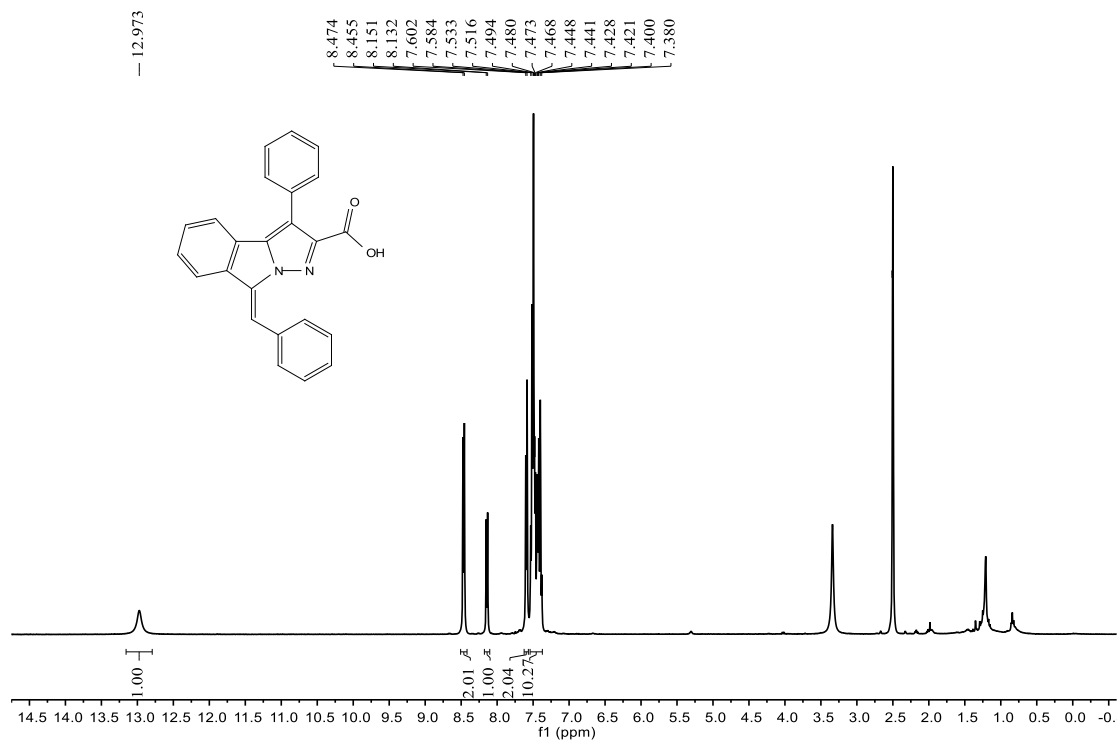
¹H NMR spectra of compound **3ma**.



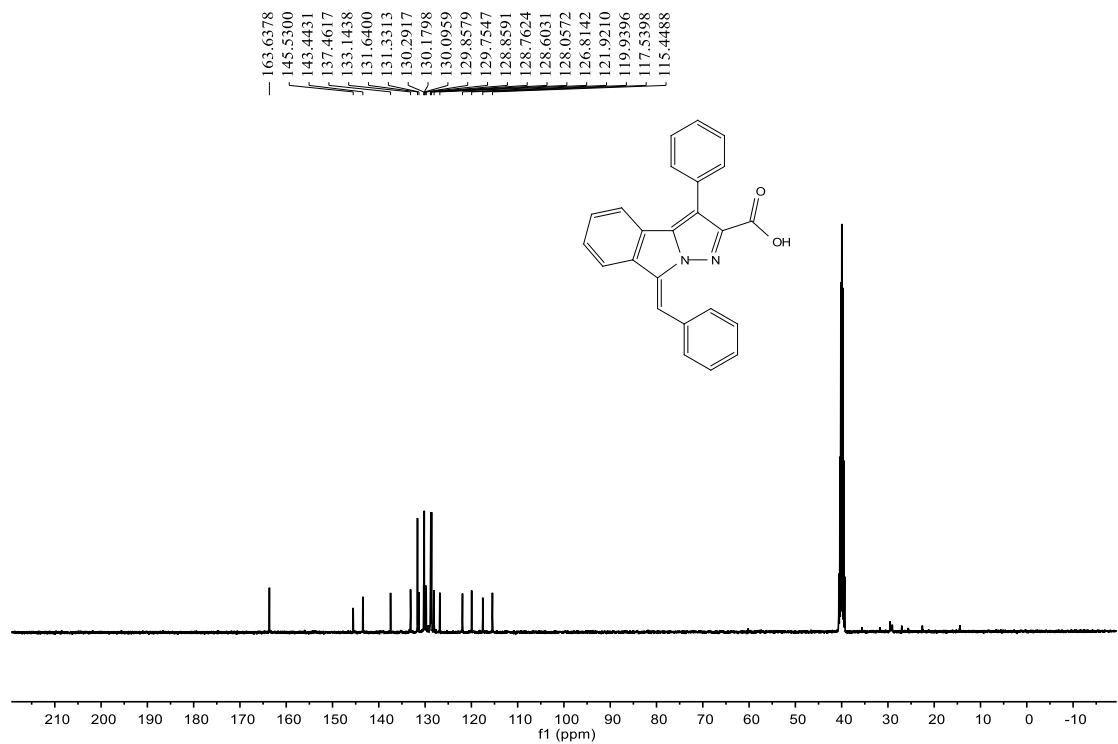
¹³C NMR spectra of compound **3ma**.



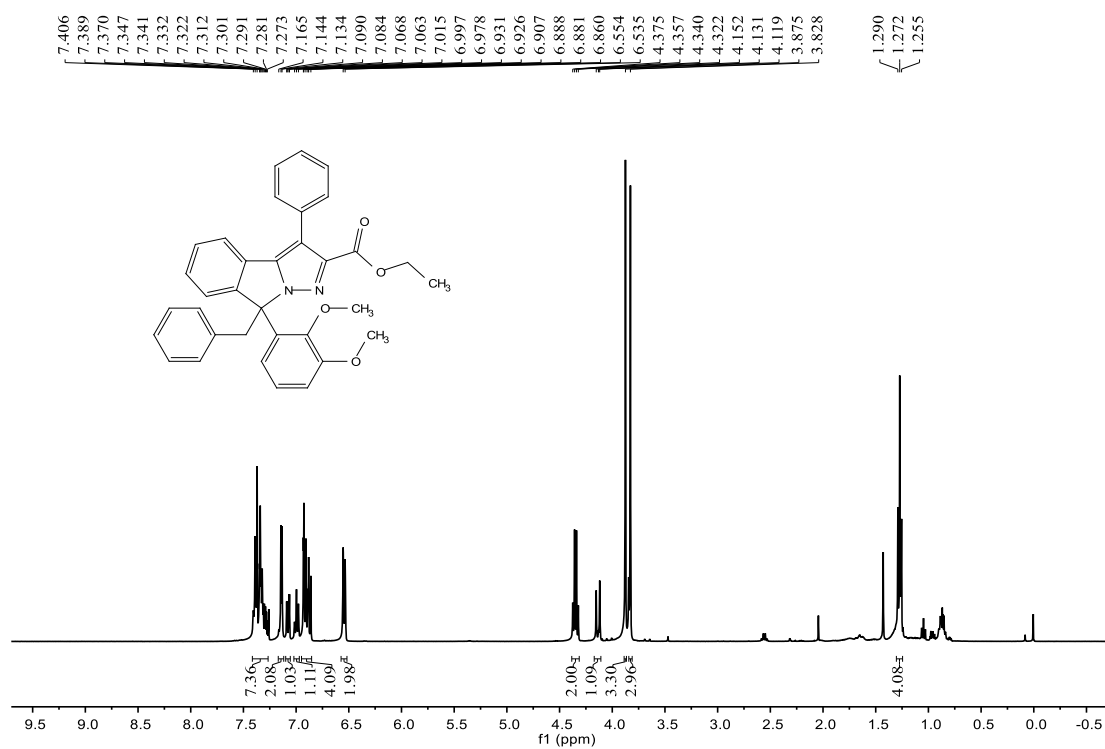
^1H NMR spectra of compound 4.



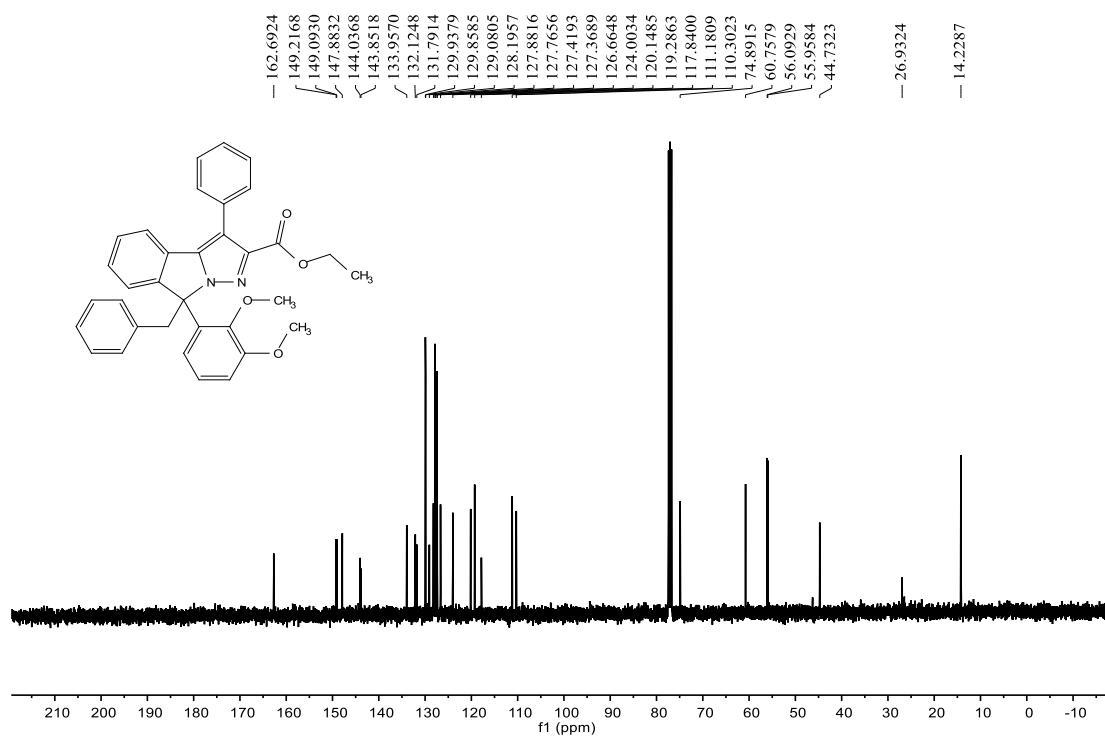
^{13}C NMR spectra of compound 4.



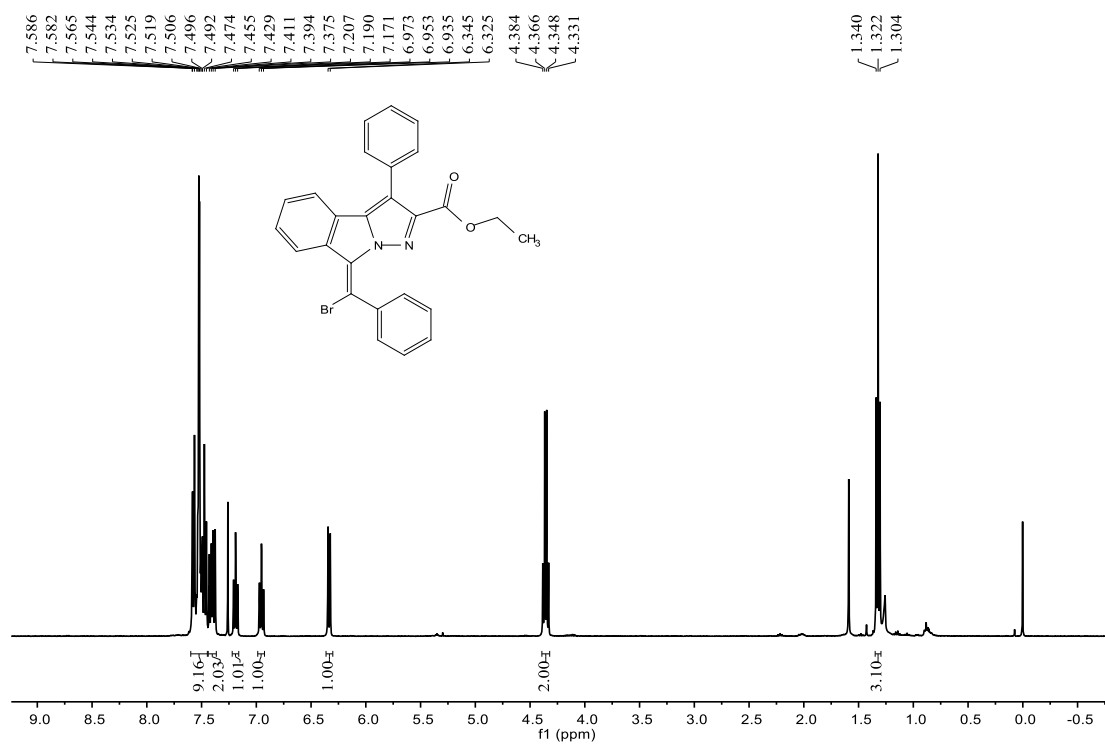
¹H NMR spectra of compound 5.



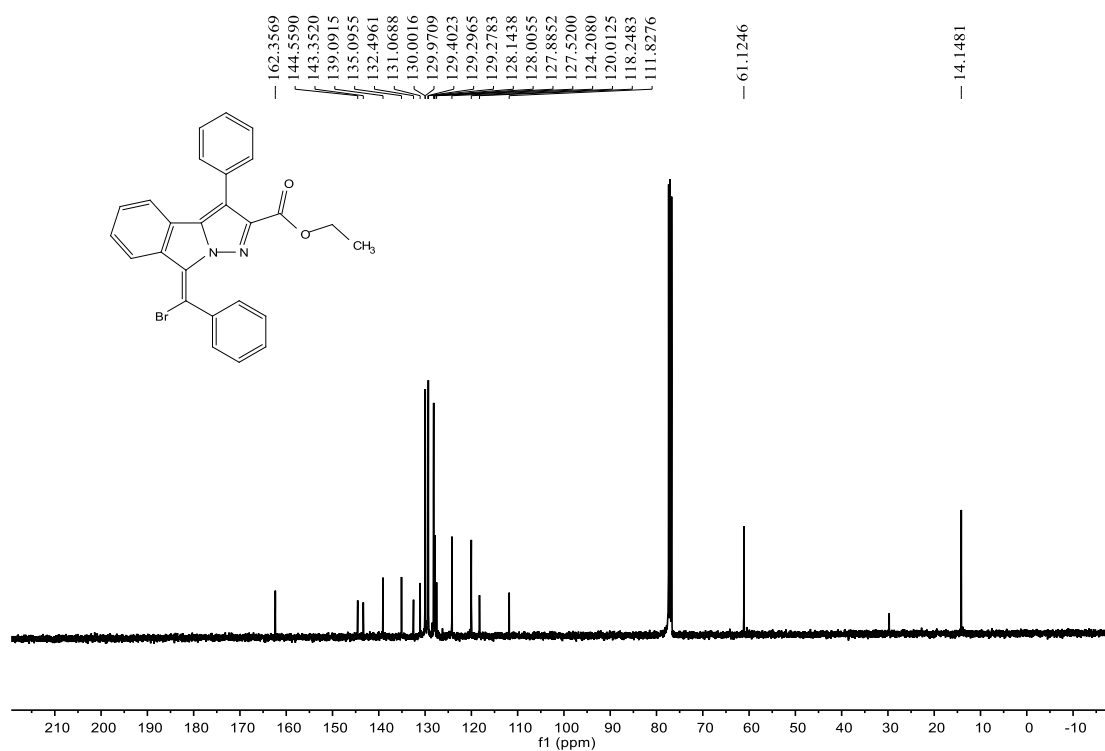
¹³C NMR spectra of compound 5.



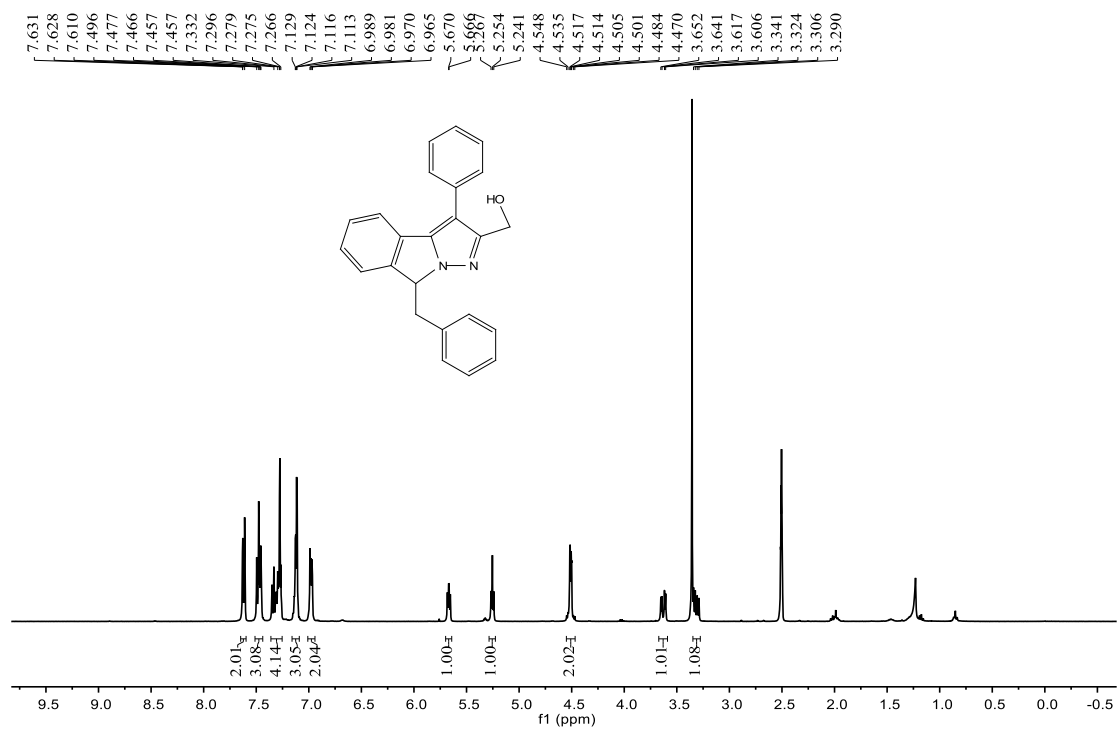
^1H NMR spectra of compound 6.



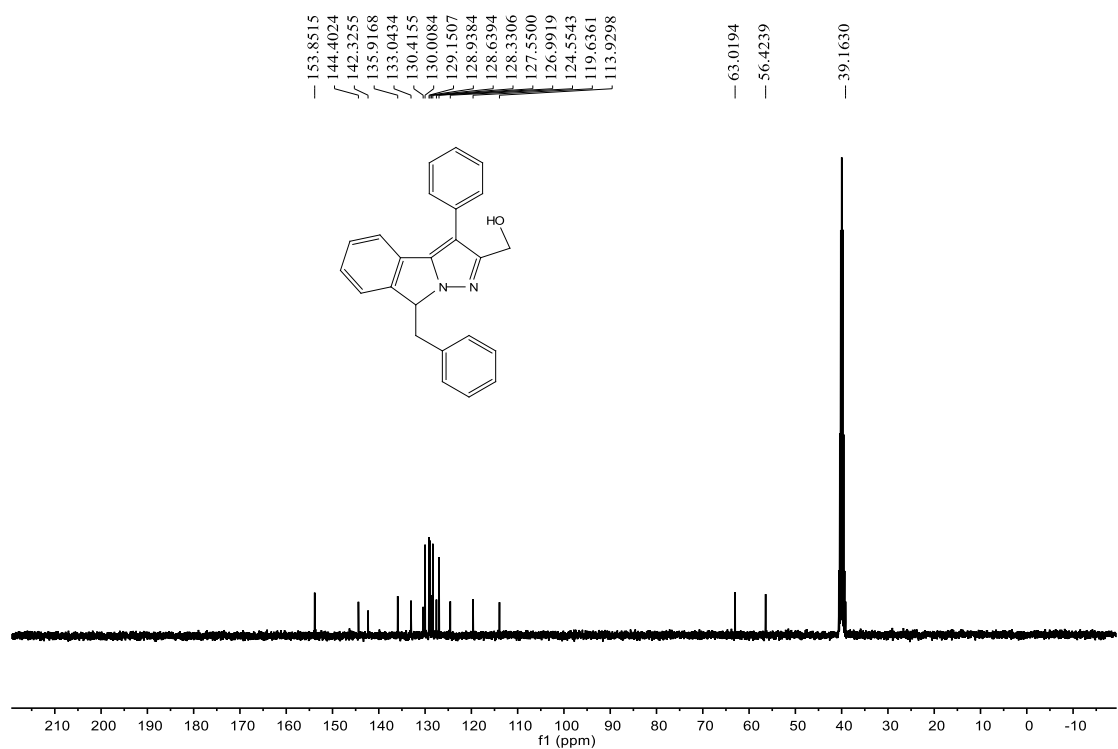
^{13}C NMR spectra of compound 6.



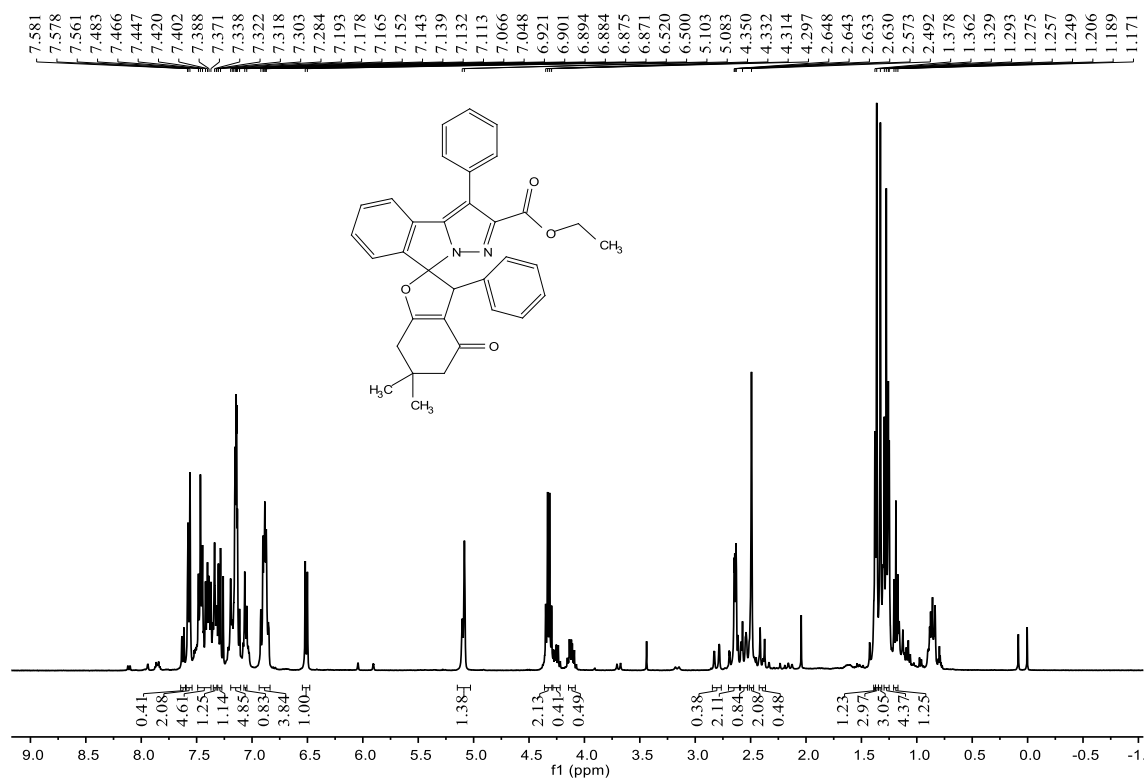
^1H NMR spectra of compound 7.



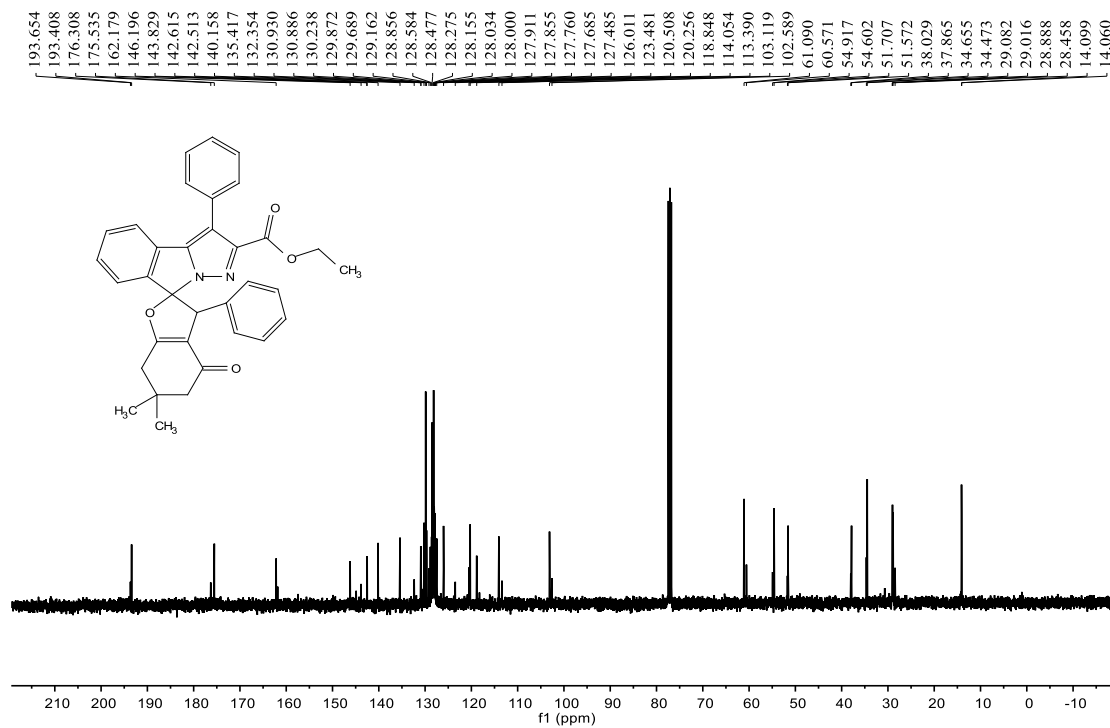
^{13}C NMR spectra of compound 7.



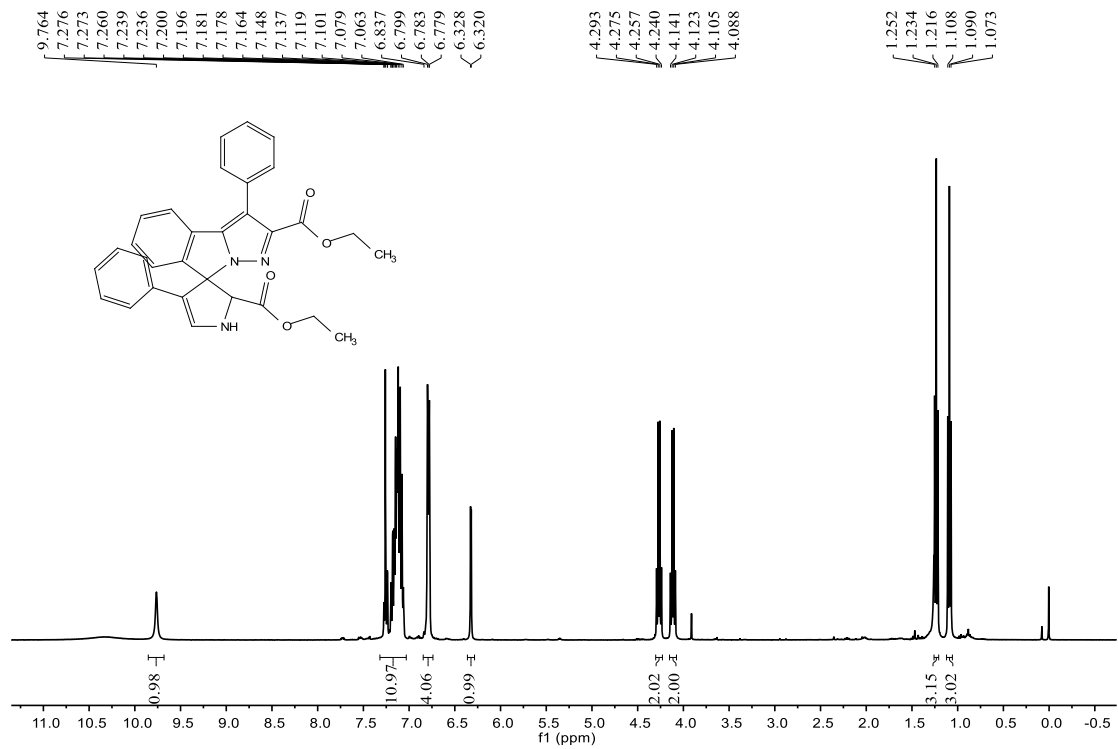
¹H NMR spectra of compound **8**.



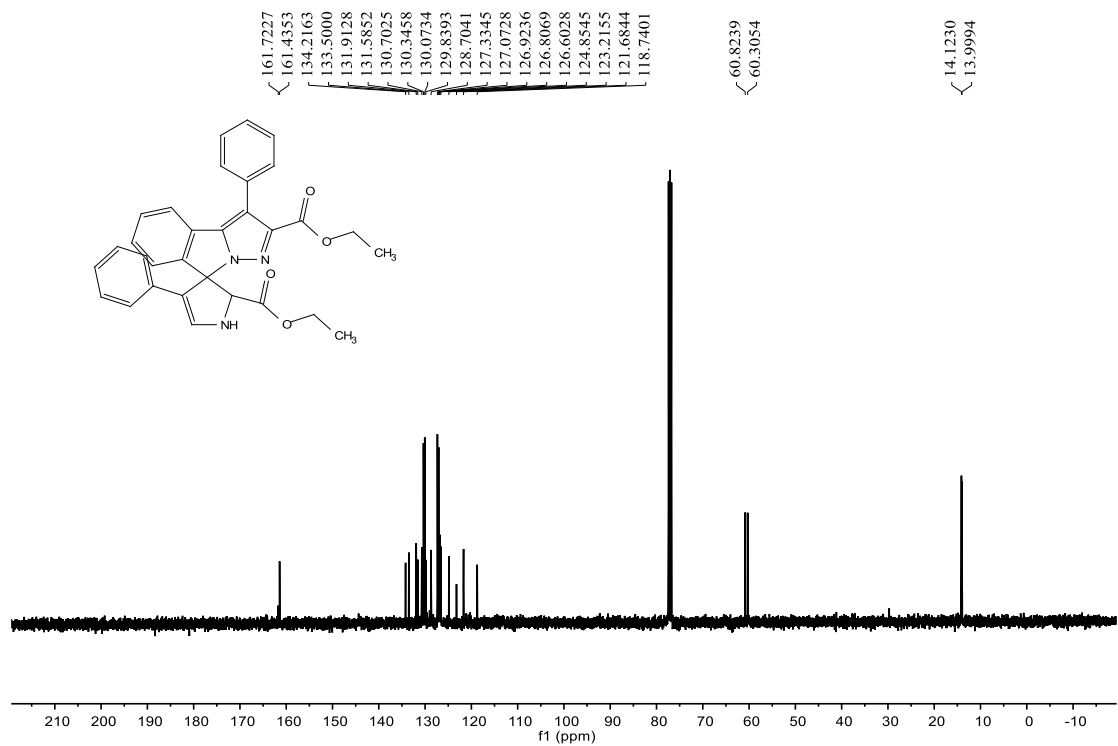
¹³C NMR spectra of compound **8**.



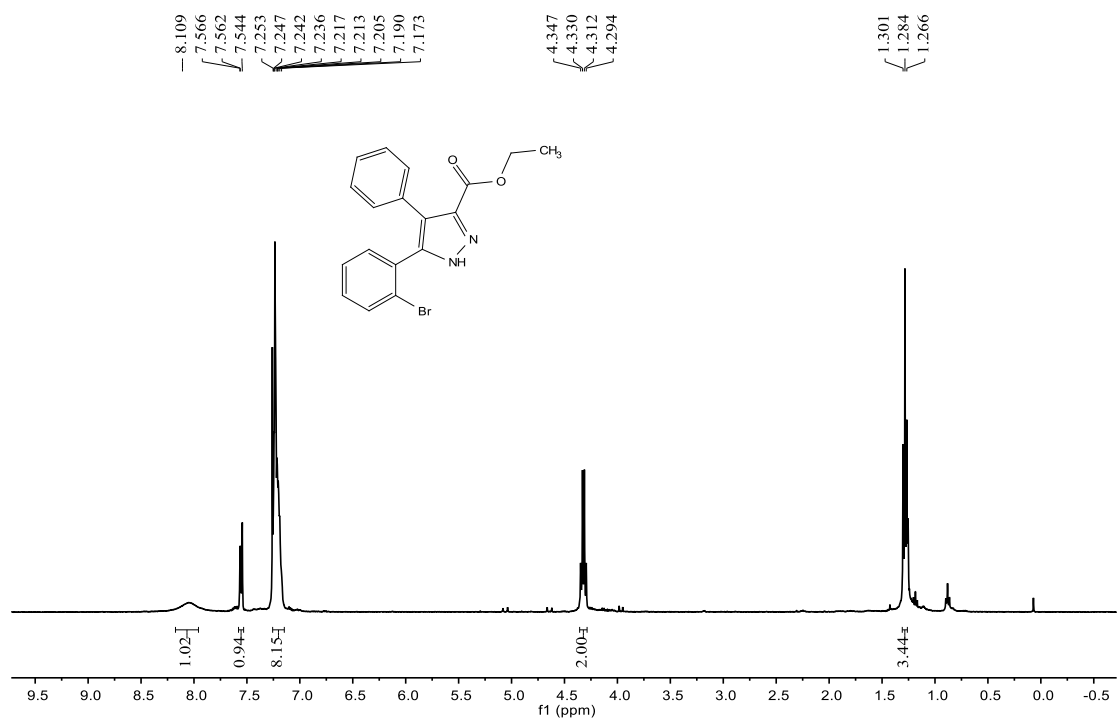
^1H NMR spectra of compound **9**.



^{13}C NMR spectra of compound **9**.



¹H NMR spectra of compound **10**.



¹³C NMR spectra of compound **10**.

