

Pd-Catalyzed C-3 Functionalization of Indolizines via C-H Bond Cleavage

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Supporting Materials

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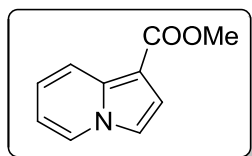
General Unless stated otherwise, all reactions were performed under a purified N₂ atmosphere. All solvents were purified and dried according to standard methods prior to use. ¹H NMR spectra were recorded at 400 MHz using TMS as internal standard. ¹³C NMR spectra were recorded at 100 MHz using TMS as internal standard. The multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), multiplet (m), and broad resonances (br). Mass spectroscopy data were collected on an HRMS-EI and HRMS-ESI instrument.

Preparation and Characterization of Starting Materials:

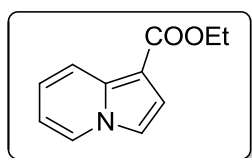
Preparation of 3-unsubstituted indolizines by the method of literature 1: ^[1]

Step 1: To a solution of pyridines (100 mmol) in EtOAc (60 mL) was added the appropriate bromoacetic acid (100 mmol). After the mixture was stirred for 3 h at r.t., the solid was filtered and dried in air to give *N*-(carboxymethyl)pyridinium bromides as white solid.

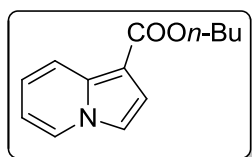
Step 2: A suspension of *N*-(carboxymethyl)pyridinium bromides (10 mmol), alkene (50 mmol), Et₃N (1.5 mL) and MnO₂ (80mmol) in toluene (80 mL) was stirred at 90 °C for 2 h (monitored by TLC). After the mixture was cooled to r.t., the solid was filtered off and washed with acetone. The combined filtrates were evaporated to give a residue, which was purified by chromatography (silica gel, ethyl acetate/petrol ether =1/5) to give the corresponding indolizines.



methyl indolizine-1-carboxylate (CAS#316375-85-6): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a brown oil. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.13 (d, $J = 9.2$ Hz, 1 H), 7.92 (d, $J = 6.8$ Hz, 1 H), 7.20 (d, $J = 2.8$ Hz, 1 H), 7.16 (d, $J = 3.2$ Hz, 1 H), 6.96-7.00 (m, 1 H), 6.62 (dd, $J = 6.8$ Hz, 6.4 Hz, 1 H), 3.86 (s, 3 H).

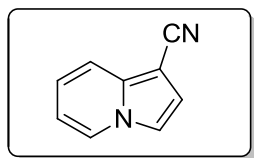


ethyl indolizine-1-carboxylate (CAS#93476-46-1): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a thick, green oil. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.17 (d, $J = 8.8$ Hz, 1 H), 7.98 (d, $J = 6.8$ Hz, 1 H), 7.25 (d, $J = 2.8$ Hz, 1 H), 7.21 (d, $J = 3.2$ Hz, 1 H), 7.00-7.05 (m, 1 H), 6.66-6.70 (m, 1 H), 4.38 (q, $J = 6.8$ Hz, 2 H), 1.41 (t, $J = 7.2$ Hz, 3 H).

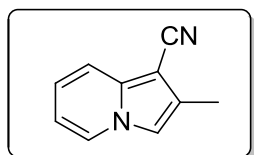


butyl indolizine-1-carboxylate (new compound): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a thick, green oil. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.16 (d, $J = 8.8$ Hz, 1 H), 7.95 (d, $J = 6.8$ Hz, 1 H), 7.24 (d, $J = 2.8$ Hz, 1 H), 7.19 (d, $J = 2.8$ Hz, 1 H), 6.98-7.02 (m, 1 H), 6.63-6.67 (m, 1 H), 4.31 (t, $J = 6.4$ Hz, 2 H), 1.72-1.80 (m, 2 H), 1.44-1.54 (m, 2 H), 0.96 (t, $J = 7.2$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.0, 135.6, 126.0, 122.1, 119.8, 116.1, 113.6, 112.3, 104.0, 63.3, 31.1, 19.4, 13.8.

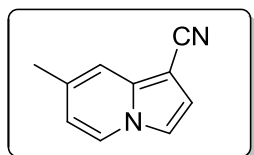
HRMS (ESI) Calcd for $C_{13}H_{15}NO_2$ $[M+Na]^+$ 240.0995, Found 240.0992. Elem. Anal.: C, 71.87; H, 6.96; N, 6.45; O, 14.73.



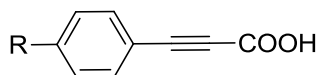
indolizine-1-carbonitrile (CAS#3352-05-4): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a white solid. 1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.00 (d, $J = 6.4$ Hz, 1 H), 7.56 (d, $J = 8.8$ Hz, 1 H), 7.23 (d, $J = 2.4$ Hz, 1 H), 7.03 (d, $J = 6.8$ Hz, 1 H), 6.98-7.00 (m, 1 H), 6.70-6.73 (m, 1 H),



2-methylindolizine-1-carbonitrile (CAS#3243-04-7): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a white solid. 1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.86 (d, $J = 6.4$ Hz, 1 H), 7.43 (d, $J = 8.4$ Hz, 1 H), 7.00 (s, 1 H), 6.91-6.95 (m, 1 H), 6.60-6.63 (m, 1 H), 2.32 (s, 3 H).



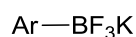
methyl 7-methylindolizine-1-carbonitrile (CAS#890532-35-1): Purification by column chromatography (silica gel, ethyl acetate / petroleum ether = 1/5, v/v) afforded as a black solid. 1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.02 (s, 1 H), 7.44 (d, $J = 7.2$ Hz, 1 H), 7.26 (d, $J = 3.2$ Hz, 1 H), 6.98-7.02 (m, 1 H), 6.65-6.69 (m, 1 H), 2.33 (s, 3 H).



Preparation of phenylpropionic acids:

Step 1: Triphenylphosphine (20 mmol) was added to a well-stirred solution of carbon tetrabromide (10 mmol) in dry dichloromethane (50 mL). Upon addition of aldehyde (5 mmol), the orange colored solution slowly faded away. The reaction mixture was stirred at ambient temperature for 4-6 hours till completion (TLC monitoring). After removal of solvent, the residue was repeatedly triturated with hexane (10 x 25 mL) and hexane solution was concentrated. This cycle was continued three times. Finally the mixture was subjected to column chromatography (silica gel 60-120 mesh, eluent hexane) to afford the (2,2-dibromovinyl)benzene.

Step 2: A solution of (2,2-dibromovinyl)benzene (6 mmol) in 10 mL of dry THF at -78°C was treated with a solution of *n*-BuLi in hexane (1.6 M, 7.5 mL, 12 mmol) under Nitrogen atmosphere. After stirring for 1h at -78°C , the reaction mixture was warmed to 25°C during 1 h, and again cooled to -60°C . Solid carbon dioxide (5 g) was added to the above solution at -60°C and the mixture was allowed to warm gradually to room temperature. The mixture was poured into water, and ethyl acetate was added. The aqueous layer was separated and washed further with ethyl acetate. The aqueous part was acidified with 6(N) HCl and extracted with ethyl acetate (3 x 50 mL). The organic layer was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded pure phenylpropionic acid in 67-70% yield.



Preparation of potassium aryltrifluoroborate salts:

The arylboronic acid (85 mmol) was dissolved in methanol (25 mL), A solution of saturated KHF_2 (60 mL) was added slowly to the mixture with intense stirring in 15 min. The precipitation was washed with cold methanol and using acetonitrile for recrystallization to afford the corresponding aryltrifluoroborate salts.

Typical procedure for the products:

Preparation of C-3 arylation indolizines:

A mixture of indolizines (0.3 mmol), potassium phenyltrifluoroborate salts (0.3 mmol), Pd(OAc)₂ (3 mg, 5 mol%), AgOAc (50 mg, 0.3 mmol), KOAc (59 mg, 0.6 mmol) in DMF (2 mL) was stirred at 90 °C under N₂ for 12 h. Afterward, the mixture was cooled to room temperature, filtered through a pad of celite. The crude product was dissolved in Et₂O (20 mL), washed with water (2×10 mL), brine (10 mL), then dried over MgSO₄. The solvent was evaporated under reduced pressure, and the residue was subjected to flash column chromatography to obtain the desired product.

Preparation of C-3 alkynylation indolizines:

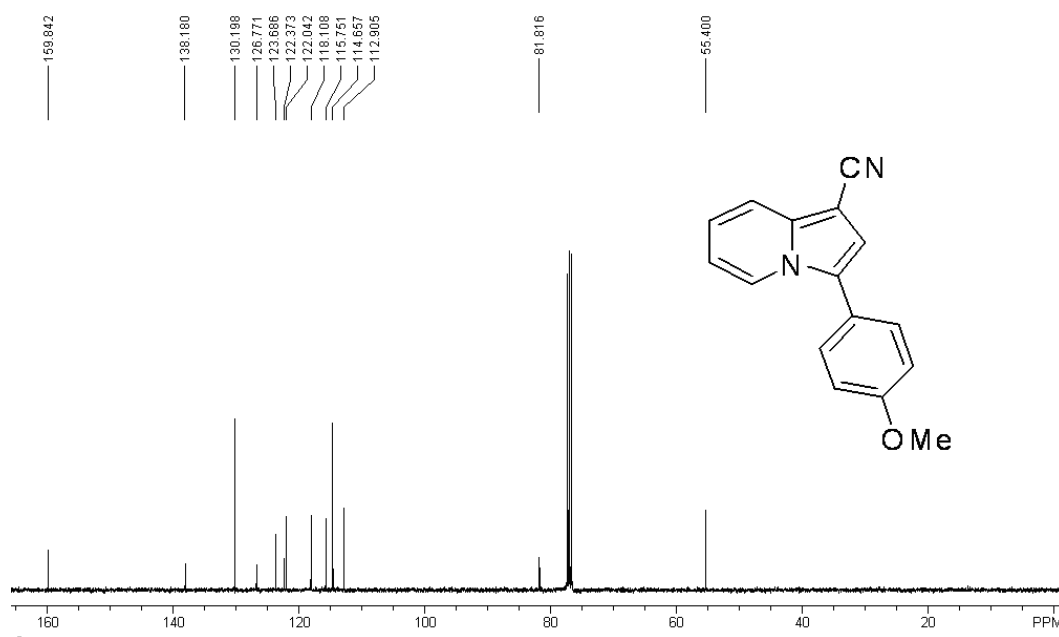
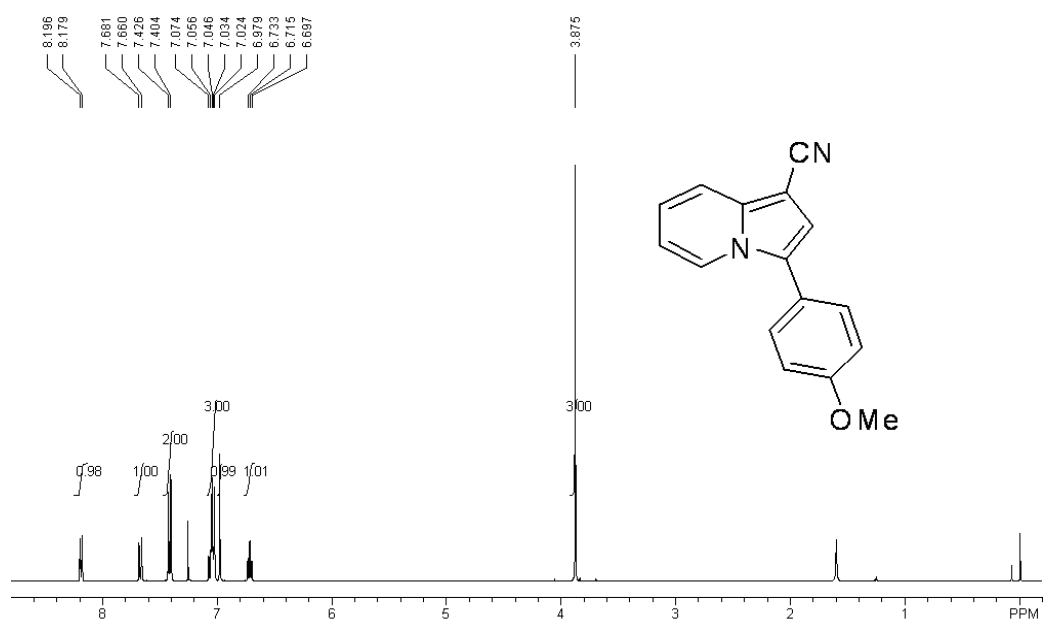
A mixture of indolizines (0.3 mmol), 3-arylpropionic acid (0.3 mmol), Pd(OAc)₂ (3 mg, 5 mol%), Ag₂CO₃ (83 mg, 0.3 mmol) in DMSO/1,4-dioxane (1:1, 2 mL) was stirred at 80 °C under N₂ for 12 h. Afterward, the mixture was cooled to room temperature, filtered through a pad of celite. The crude product was dissolved in Et₂O (10 mL), washed with water (2×10 mL), brine (10 mL), then dried over MgSO₄. The solvent was evaporated under reduced pressure, and the residue was subjected to flash column chromatography to obtain the desired product.

Characterization data of the product

(1) 3-(4-methoxyphenyl)indolizine-1-carbonitrile (T 2-1, new compound)

White solid. m.p. 241-242 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.19 (d, $J = 6.8$ Hz, 1 H), 7.67 (d, $J = 8.4$ Hz, 1 H), 7.41 (d, $J = 8.4$ Hz, 2 H), 7.02-7.08 (m, 3 H), 6.98 (s, 1 H), 6.72 (t, $J = 7.2$ Hz, 1 H), 3.88 (s, 3 H). ^{13}C NMR (100MHz, CDCl_3) δ 159.8, 138.2, 130.2, 126.8, 123.7, 122.4, 122.0, 118.1, 115.6, 114.7, 112.9, 81.8, 55.4. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}$ (M^+) 248.0950, Found 248.0957.

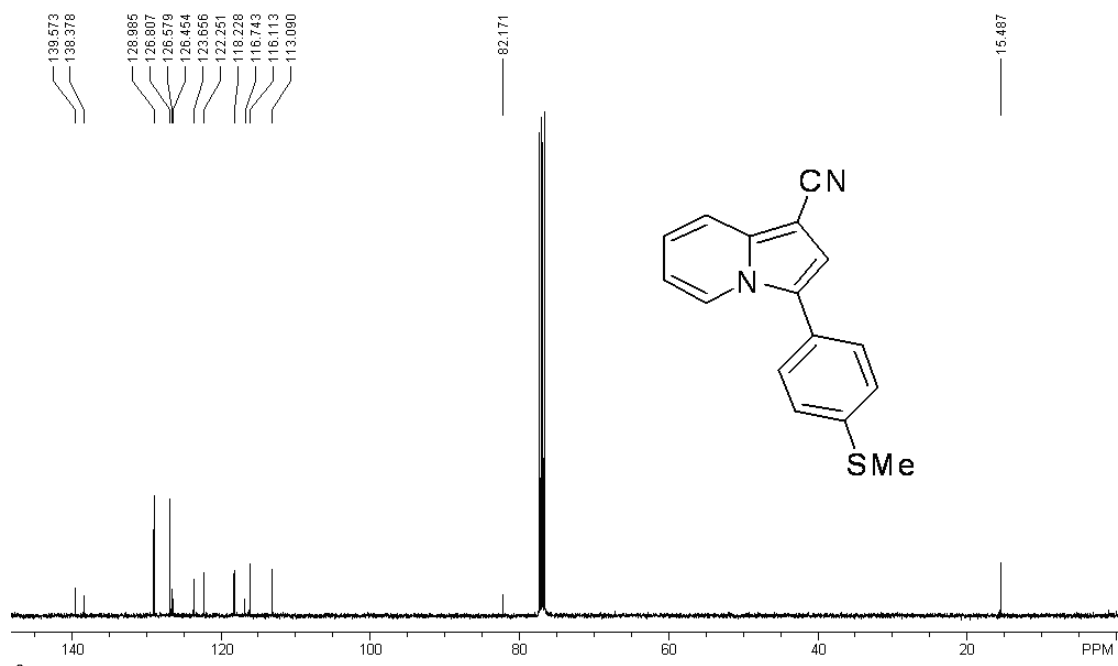
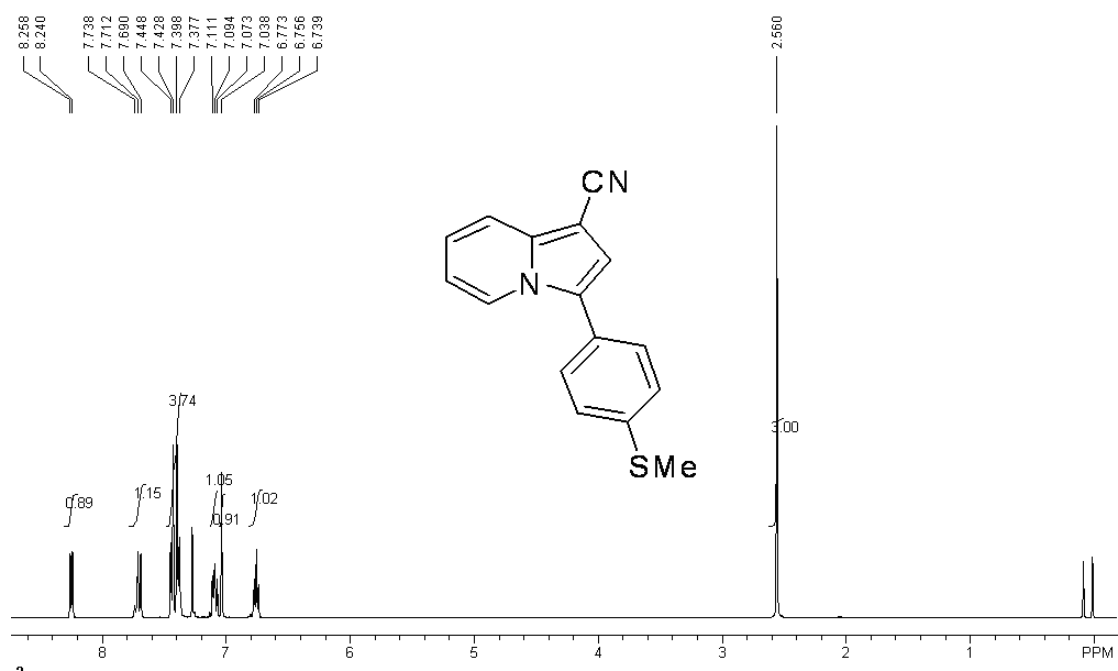
Elem. Anal.: C, 77.40; H, 4.87; N, 11.29; O, 6.44.



(2) 3-(4-(methylthio)phenyl)indolizine-1-carbonitrile (T 2-2, new compound)

Yellow solid. m.p. 250-252 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) 8.25 (d, $J = 7.2$ Hz, 1 H), 7.71 (t, $J = 9.6$ Hz, 1 H), 7.38-7.45 (m, 4 H), 7.09 (t, $J = 7.6$ Hz, 1 H), 7.04 (s, 1 H), 6.76 (t, $J = 6.8$ Hz, 1 H), 2.56 (s, 3 H). ^{13}C NMR (100MHz, CDCl_3) δ 139.6, 138.4, 129.0, 126.8, 126.6, 126.5, 123.7, 122.3, 118.2, 116.7, 116.1, 113.1, 82.2, 15.5. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{S}$ (M^+) 264.0721, Found 264.0725.

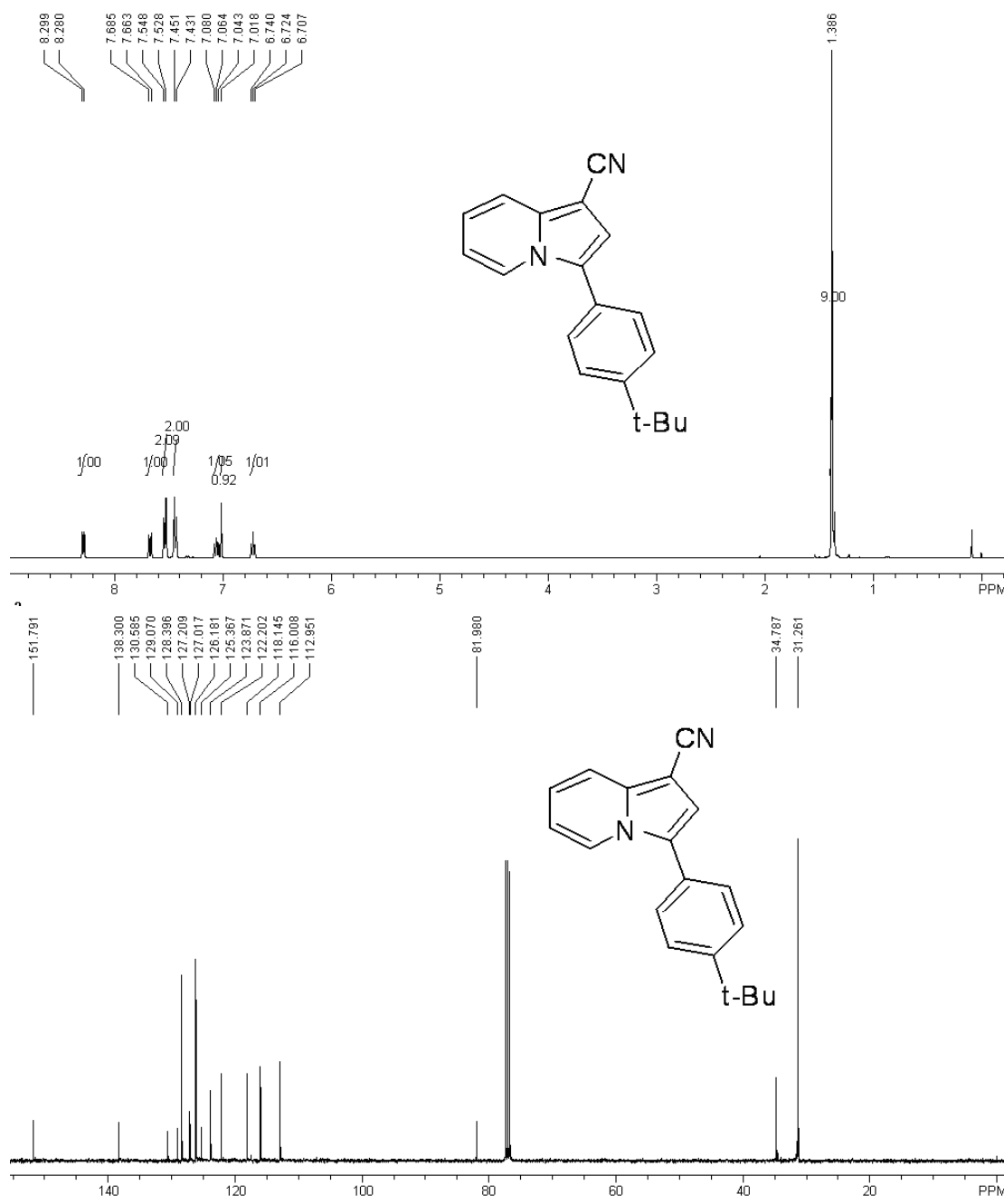
Elem. Anal.: C, 72.70; H, 4.58; N, 10.60; S, 12.12.



(3) 3-(4-tert-butylphenyl)indolizine-1-carbonitrile (T 2-3, new compound)

White solid. m.p. 236-238 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.29 (d, $J = 7.6$ Hz, 1 H), 7.68 (d, $J = 8.8$ Hz, 1 H), 7.54 (d, $J = 8.0$ Hz, 2 H), 7.44 (d, $J = 8.0$ Hz, 2 H), 7.06 (t, $J = 7.6$ Hz, 1 H), 7.02 (s, 1 H), 6.72 (t, $J = 6.8$ Hz, 1 H), 1.39 (s, 9 H). ^{13}C NMR (100 MHz, CDCl_3) δ 151.8, 138.3, 130.6, 129.1, 128.4, 127.2, 127.0, 126.2, 125.4, 123.9, 122.2, 118.1, 116.0, 113.0, 82.0, 34.8, 31.3. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2$ (M^+) 274.1470, Found 274.1479.

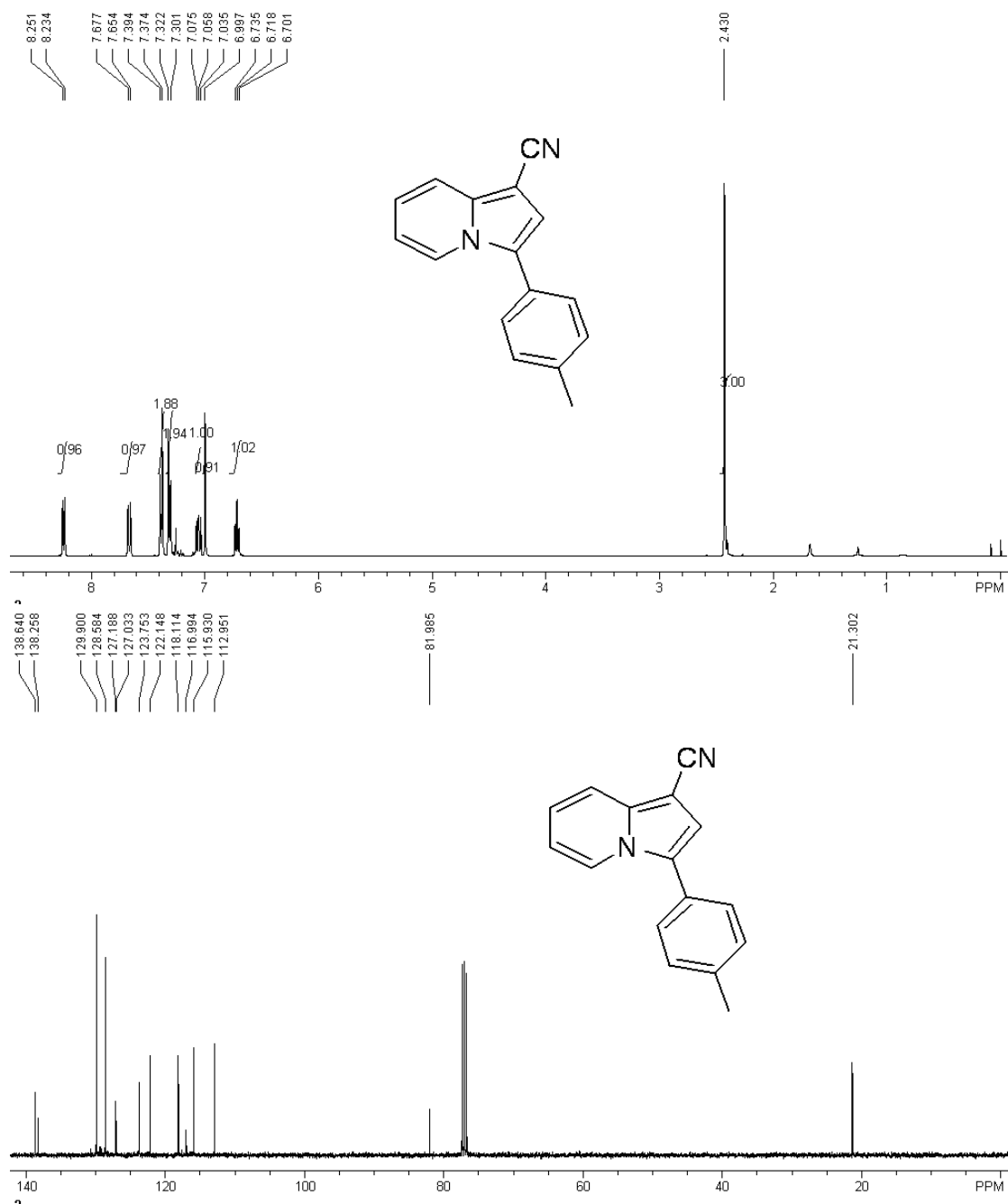
Elem. Anal.: C, 83.18; H, 6.61; N, 10.21.



(4) 3-p-tolyindolizine-1-carbonitrile (T 2-4, CAS#247075-85-0) [2]

White solid. m.p. 232-233 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.24 (d, $J = 6.8$ Hz, 1 H), 7.67 (d, $J = 9.2$ Hz, 1 H), 7.38 (d, $J = 8.0$ Hz, 2 H), 7.31 (d, $J = 8.4$ Hz, 2 H), 7.06 (t, $J = 8.0$ Hz, 1 H), 7.00 (s, 1 H), 6.72 (t, $J = 6.8$ Hz, 1 H), 2.43 (s, 3 H).
 $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 138.6, 138.3, 129.9, 128.6, 127.2, 127.0, 123.8, 122.1, 118.1, 117.0, 115.9, 113.0, 82.0, 21.3. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$ (M^+) 232.1000, Found 232.1001.

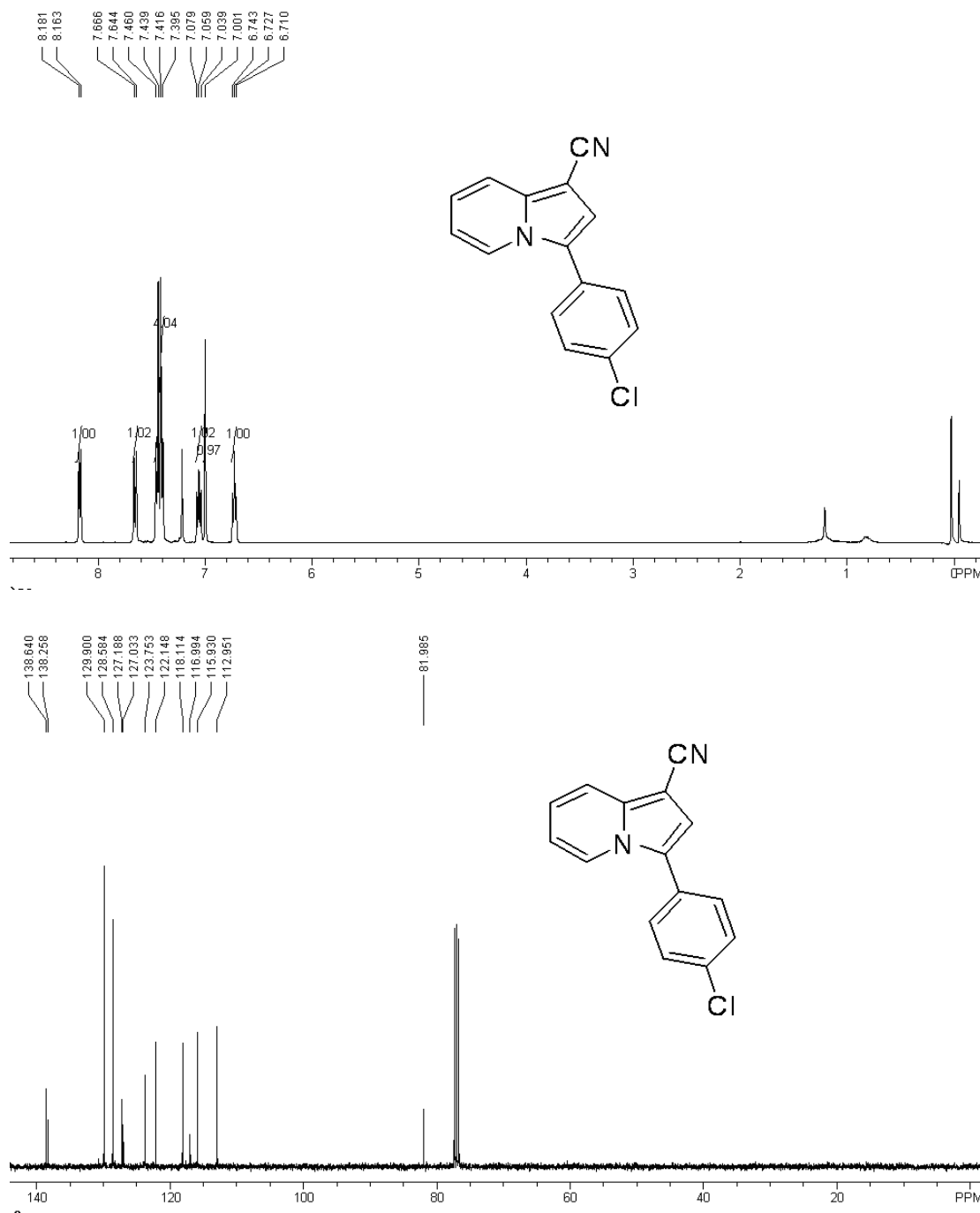
Elem. Anal.: C, 82.73; H, 5.21; N, 12.06.



(5) 3-(4-chlorophenyl)indolizine-1-carbonitrile (T 2-5, new compound)

Light yellow solid. m.p. 244-246 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.17 (d, J = 7.2 Hz, 1 H), 7.65 (d, J = 8.8 Hz, 1 H), 7.40-7.46 (m, 4 H), 7.06 (t, J = 8.0 Hz, 1 H), 7.00 (s, 1 H), 6.73 (t, J = 6.8 Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.6, 138.3, 129.9, 128.6, 127.2, 127.0, 123.8, 122.1, 118.1, 117.0, 115.9, 113.0, 82.0. HRMS (EI) Calcd for $\text{C}_{15}\text{H}_9\text{N}_2\text{Cl}$ (M^+) 252.0454, Found 252.0452.

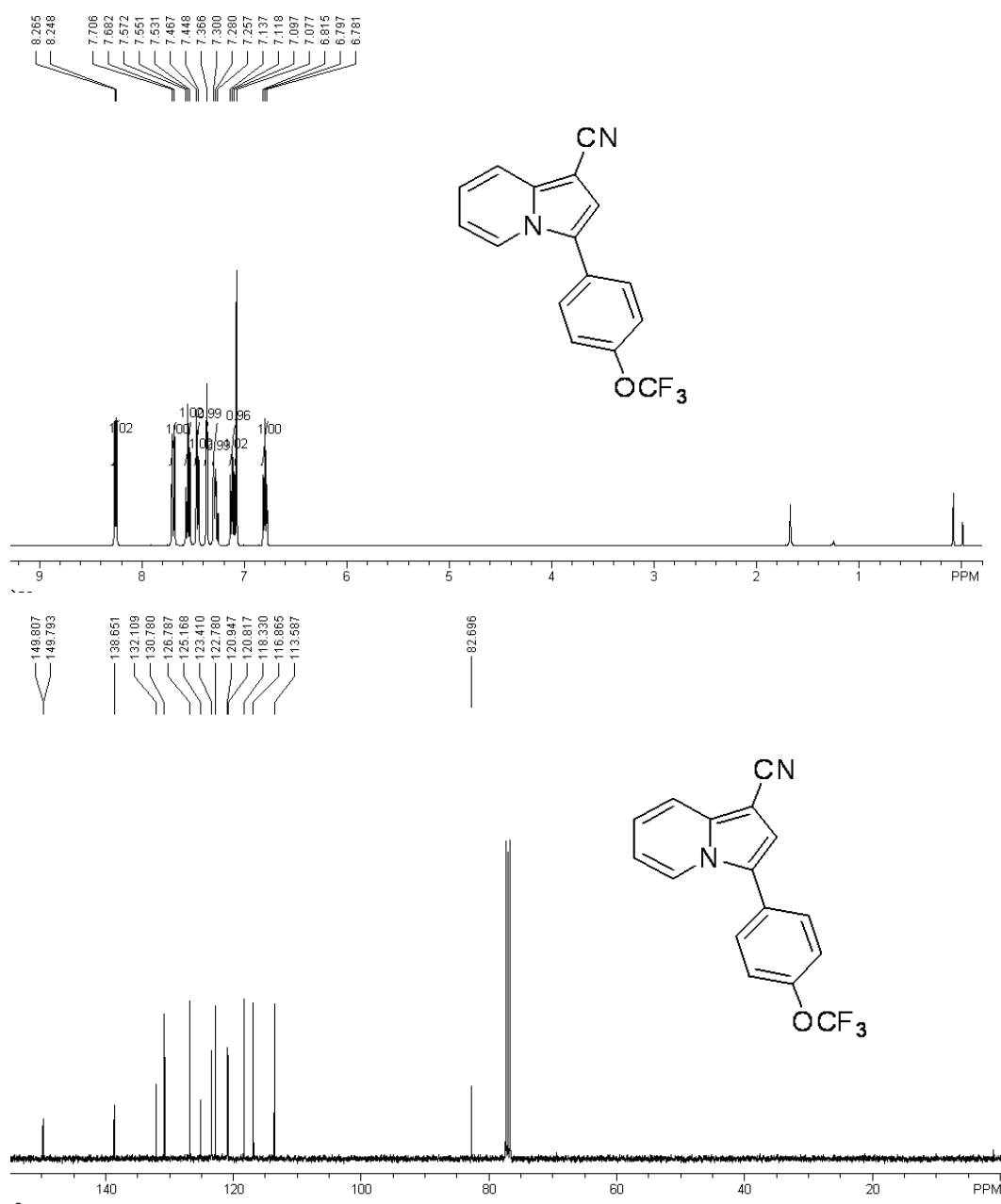
Elem. Anal.: C, 71.29; H, 3.59; Cl, 14.03, N, 11.09.



(6) 3-(4-(trifluoromethoxy)phenyl)indolizine-1-carbonitrile (T 2-6, new compound)

White solid. m.p. 276-277 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.26 (d, $J = 6.8$ Hz, 1 H), 7.69 (d, $J = 9.6$ Hz, 1 H), 7.55 (t, $J = 8.4$ Hz, 1 H), 7.46 (d, $J = 7.6$ Hz, 1 H), 7.37 (s, 1 H), 7.28 (t, $J = 8.8$ Hz, 1 H), 7.12 (t, $J = 8.0$ Hz, 1 H), 7.08 (s, 1 H), 7.80 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 149.81, 149.79, 138.7, 132.1, 131.8, 126.8, 125.2, 123.4, 122.8, 120.9, 120.8, 118.3, 116.9, 113.6, 82.7. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_9\text{N}_2\text{OF}_3$ (M^+) 302.0667, Found 302.0664.

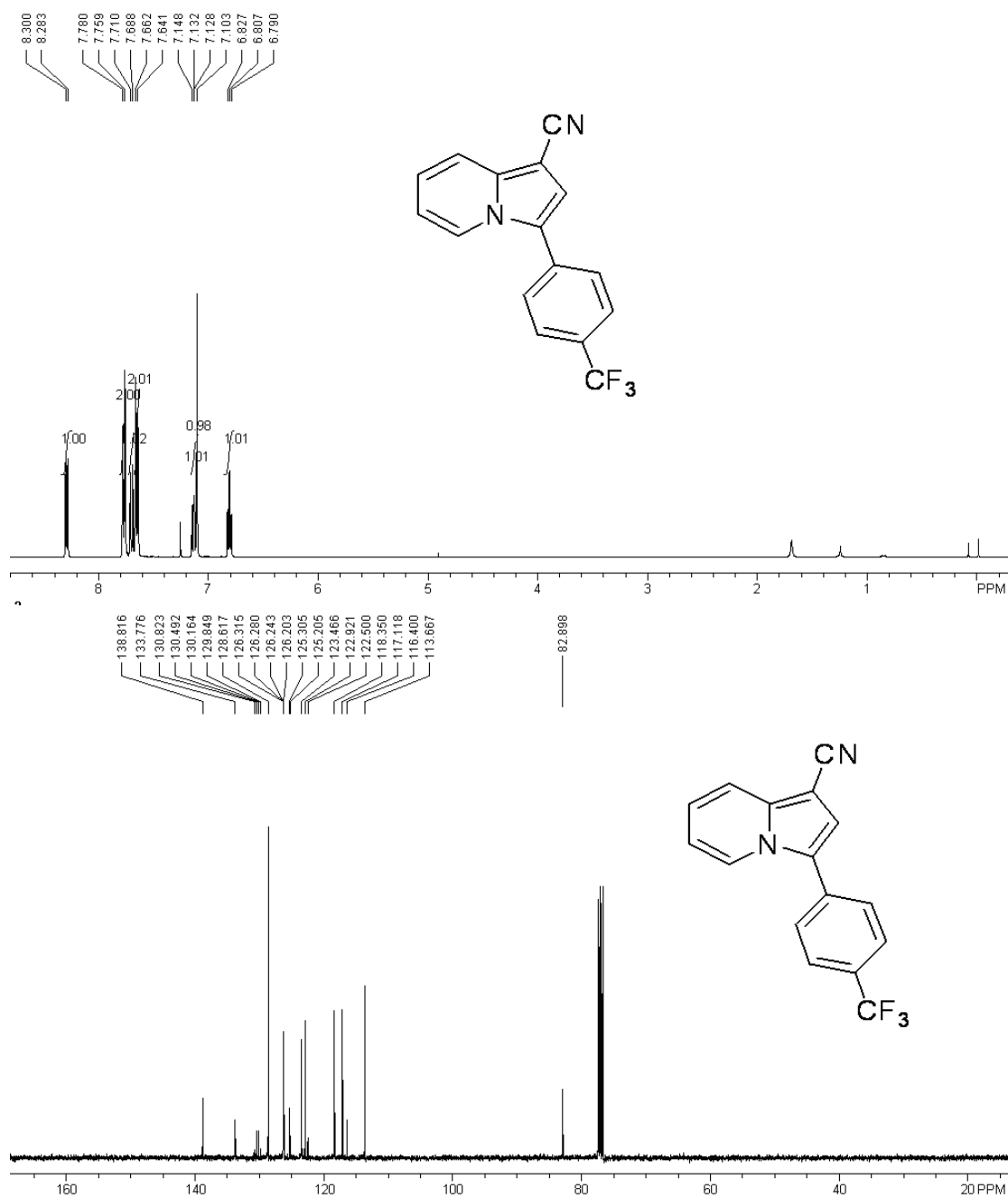
Elem. Anal.: C, 63.58; H, 3.00; F, 18.86, N, 9.27, O, 5.29.



(7) 3-(4-(trifluoromethyl)phenyl)indolizine-1-carbonitrile (T 2-7, new compound)

White solid. m.p. 269-270 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.29 (d, $J = 6.8$ Hz, 1 H), 7.77 (d, $J = 8.4$ Hz, 2 H), 7.68 (d, $J = 8.8$ Hz, 1 H), 7.65 (d, $J = 8.4$ Hz, 2 H), 7.13 (t, $J = 6.4$ Hz, 1 H), 7.10 (s, 1 H), 6.81 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.8, 133.8, 130.3 (q, $J = 32$ Hz), 128.6, 126.3 (q, $J = 4.0$ Hz), 125.3, 125.2, 123.5, 122.9, 122.5, 118.4, 117.1, 116.4, 113.7, 82.9. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_9\text{N}_2\text{F}_3$ (M^+) 286.0718, Found 286.0713.

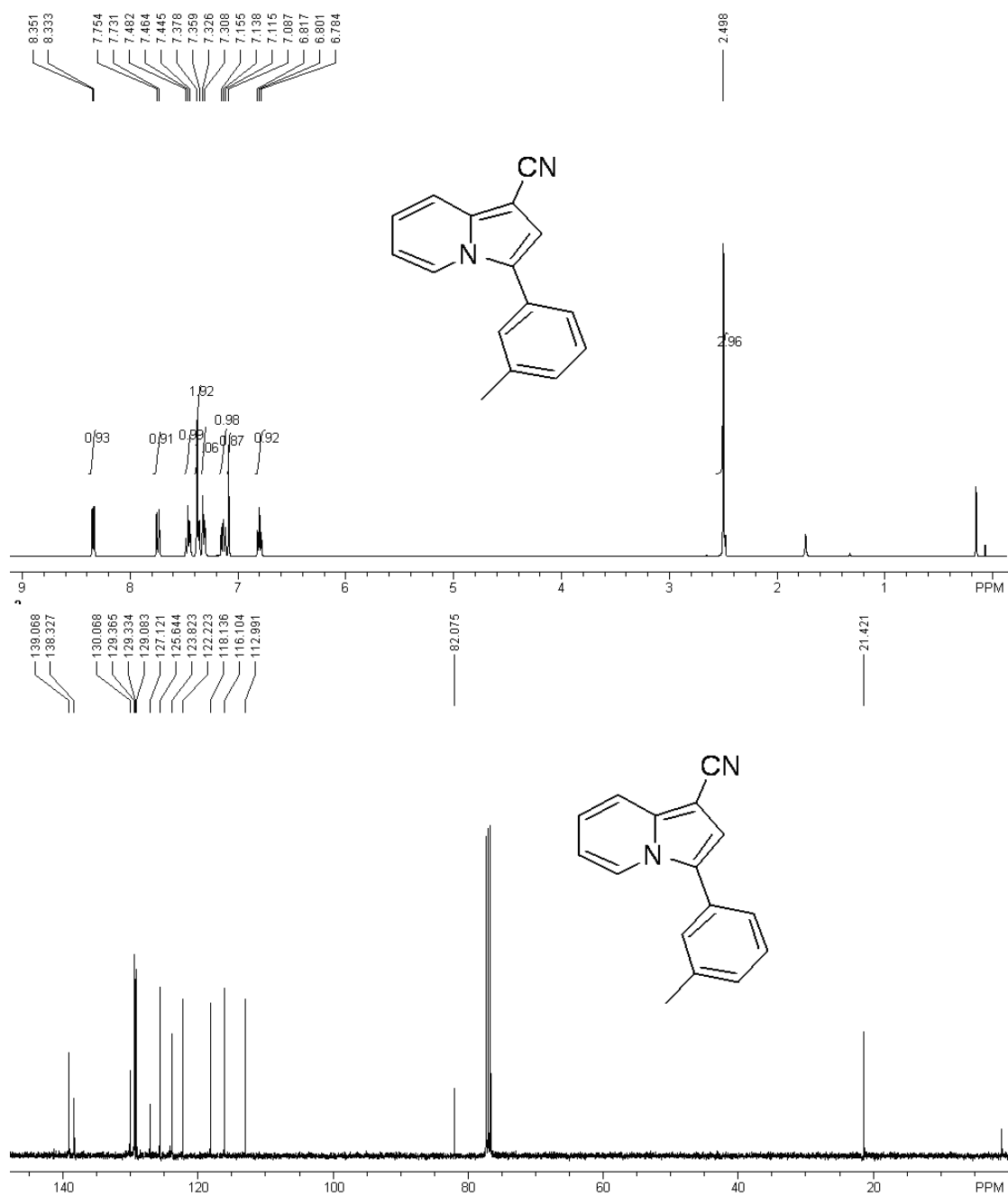
Elem. Anal.: C, 67.13; H, 3.17; F, 19.91, N, 9.79.



(8) 3-m-tolylindolizine-1-carbonitrile (T 2-8, new compound)

White solid. m.p. 239-241 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.34 (d, $J = 7.2$ Hz, 1 H), 7.74 (d, $J = 9.2$ Hz, 1 H), 7.46 (d, $J = 7.6$ Hz, 1 H), 7.31-7.38 (m, 3 H), 7.14 (t, $J = 8.0$ Hz, 1 H), 7.09 (s, 1 H), 6.80 (d, $J = 6.8$ Hz, 1 H), 2.50 (s, 3 H). ^{13}C NMR (100MHz, CDCl_3) δ 139.1, 138.3, 130.1, 129.4, 129.3, 129.1, 127.1, 125.6, 123.8, 118.1, 116.1, 113.0, 82.1, 21.4. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$ (M^+) 232.1000, Found 232.0998.

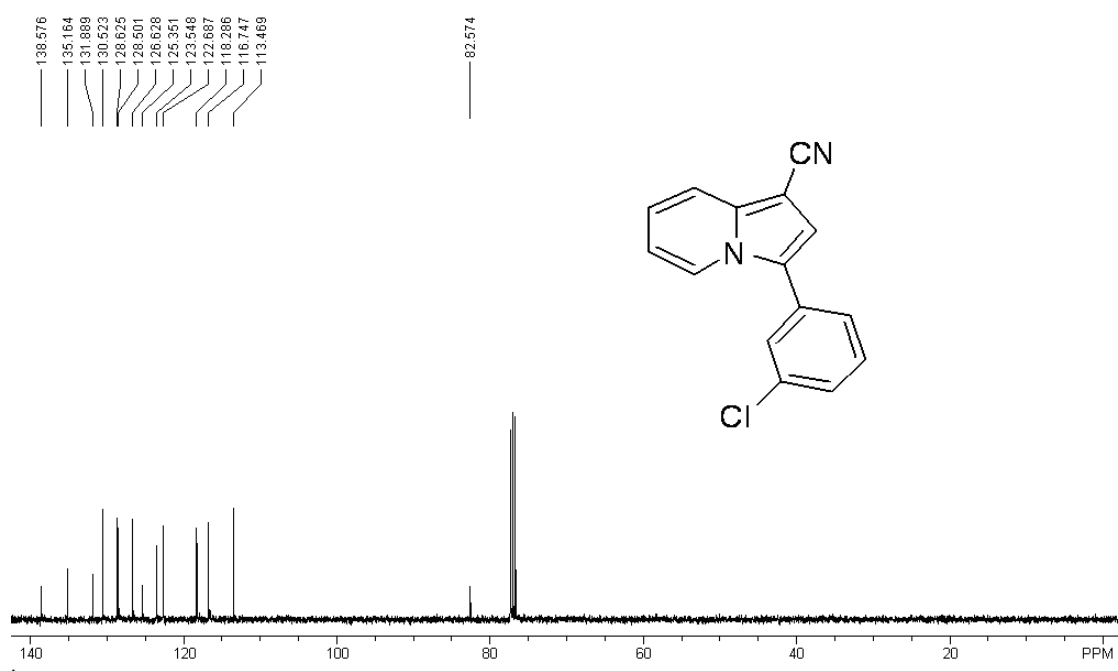
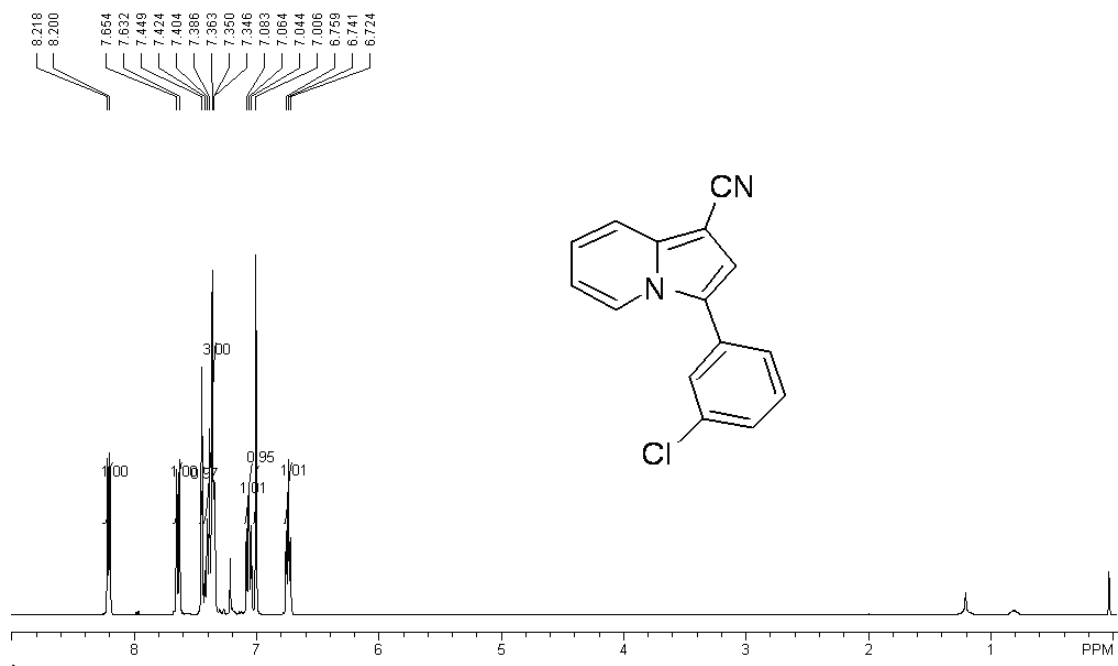
Elem. Anal.: C, 82.73; H, 5.21; N, 12.06.



(9) 3-(3-chlorophenyl)indolizine-1-carbonitrile (T 2-9, new compound)

Yellow solid. m.p. 245-246 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.21 (d, $J = 7.2$ Hz, 1 H), 7.64 (d, $J = 8.8$ Hz, 1 H), 7.15 (s, 1 H), 7.06 (t, $J = 8.0$ Hz, 1 H), 7.01 (s, 1 H), 6.74 (t, $J = 7.2$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.6, 135.2, 131.9, 130.5, 128.6, 128.5, 126.6, 125.4, 123.5, 122.7, 118.3, 116.7, 113.5, 82.6. HRMS (EI) Calcd for $\text{C}_{15}\text{H}_9\text{N}_2\text{Cl}$ (M^+) 252.0454, Found 252.0448.

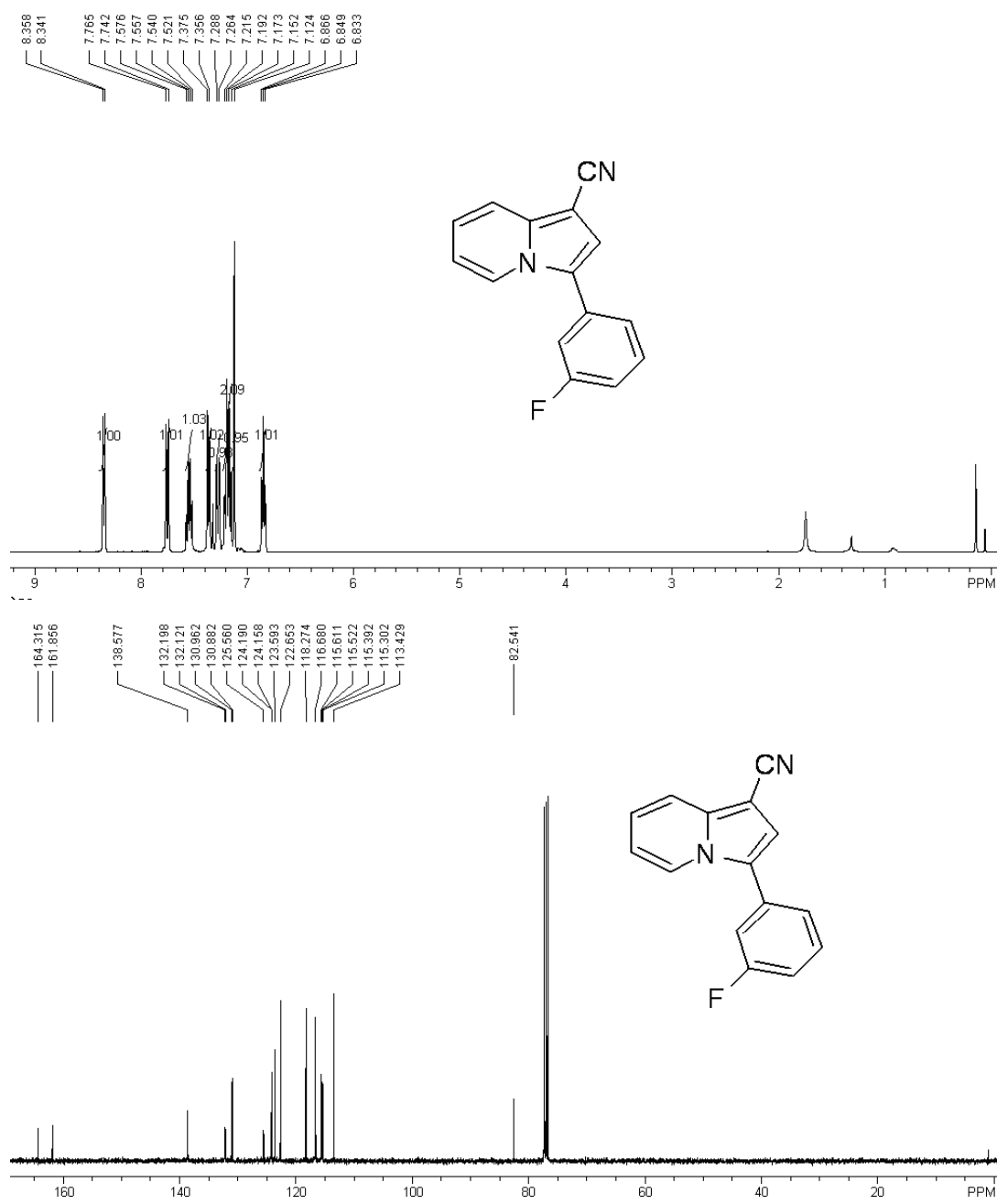
Elem. Anal.: C, 71.29; H, 3.59; Cl, 14.03, N, 11.09.



(10) 3-(3-fluorophenyl)indolizine-1-carbonitrile (T 2-10, new compound)

White solid. m.p. 261-262 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.35 (d, $J = 6.8$ Hz, 1 H), 7.75 (d, $J = 9.2$ Hz, 1 H), 7.52-7.58 (m, 1 H), 7.37 (d, $J = 7.6$ Hz, 1 H), 7.28 (d, $J = 9.6$ Hz, 1 H), 7.15-7.22 (m, 2 H), 7.12 (s, 1 H), 6.85 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 164.3, 161.9, 138.6, 132.2 (d, $J = 7.7$ Hz), 130.9 (d, $J = 8.0$ Hz), 125.6, 124.2 (d, $J = 3.2$ Hz), 123.6, 122.7, 118.3, 116.7, 115.6 (d, $J = 8.9$ Hz), 115.3 (d, $J = 9.0$ Hz), 113.4, 82.5. HRMS (EI) Calcd for $\text{C}_{15}\text{H}_9\text{N}_2\text{F}$ (M^+) 236.0750, Found 236.0745.

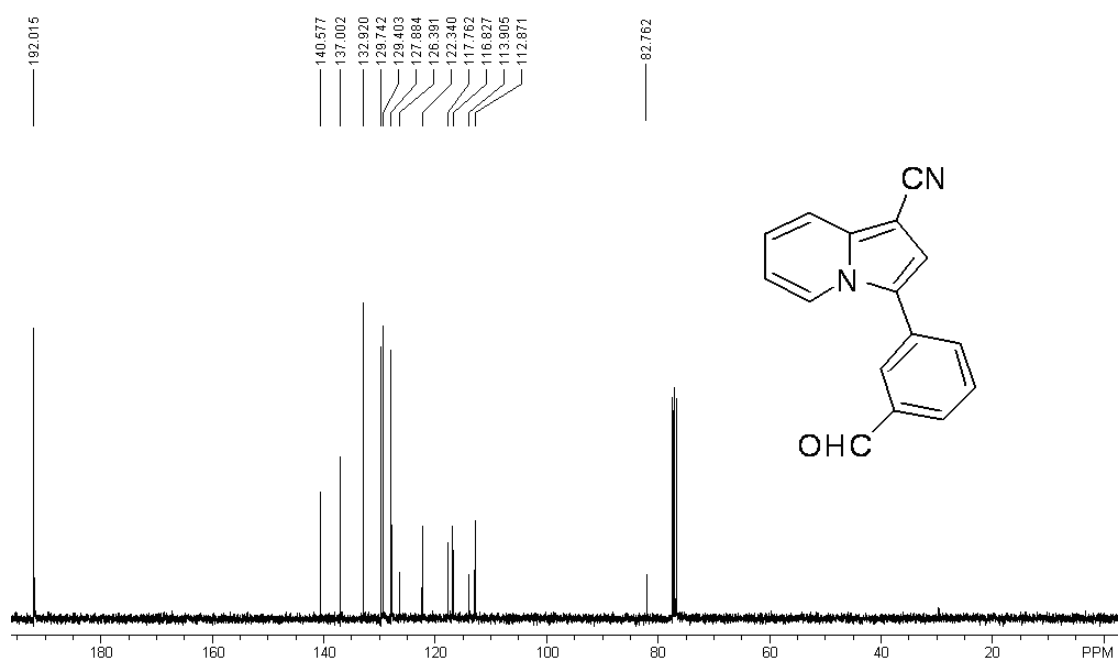
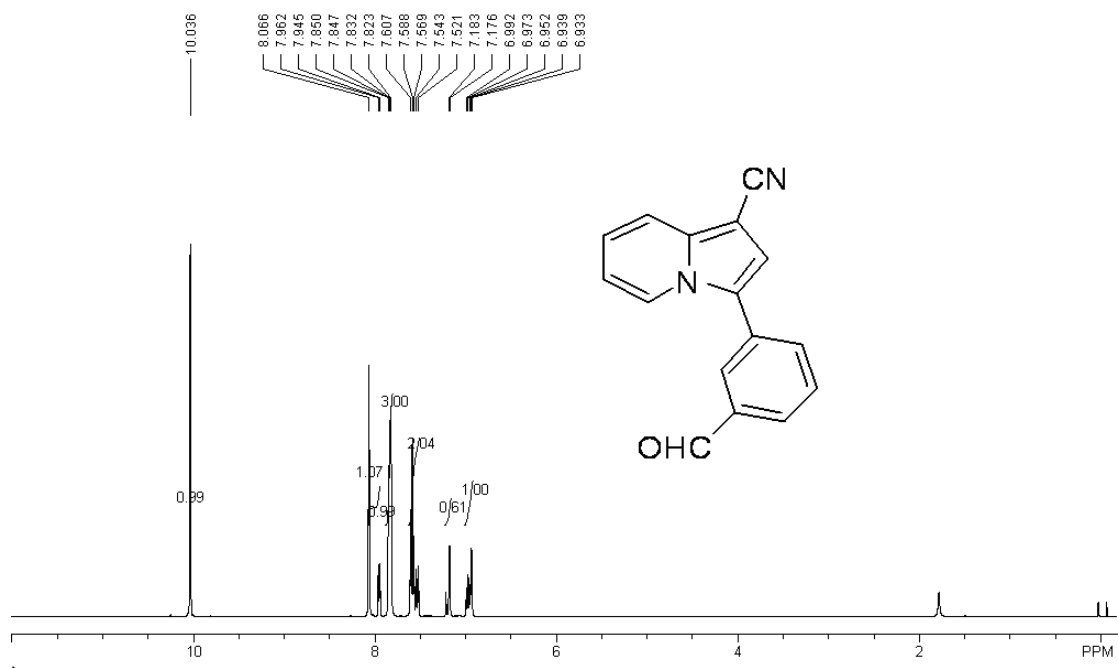
Elem. Anal.: C, 76.26; H, 3.84; Cl, 8.04, N, 11.86.



(11) 3-(3-formylphenyl)indolizine-1-carbonitrile (T 2-11, new compound)

White solid. m.p. 183-186 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 10.04 (s, 1 H), 8.01 (s, 1 H), 7.95 (d, $J = 6.8$ Hz, 1 H), 7.82-7.85 (m, 3 H), 7.26-7.29 (m, 2 H), 7.52-7.61 (m, 2 H), 7.18 (d, $J = 6.8$ Hz, 1 H), 6.93-6.99 (m, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 192.0, 140.6, 137.0, 132.9, 129.7, 129.4, 127.9, 126.4, 122.3, 117.8, 116.8, **113.9**, **112.9**, **82.8**. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}$ (M^+) 246.0793, Found 246.0796.

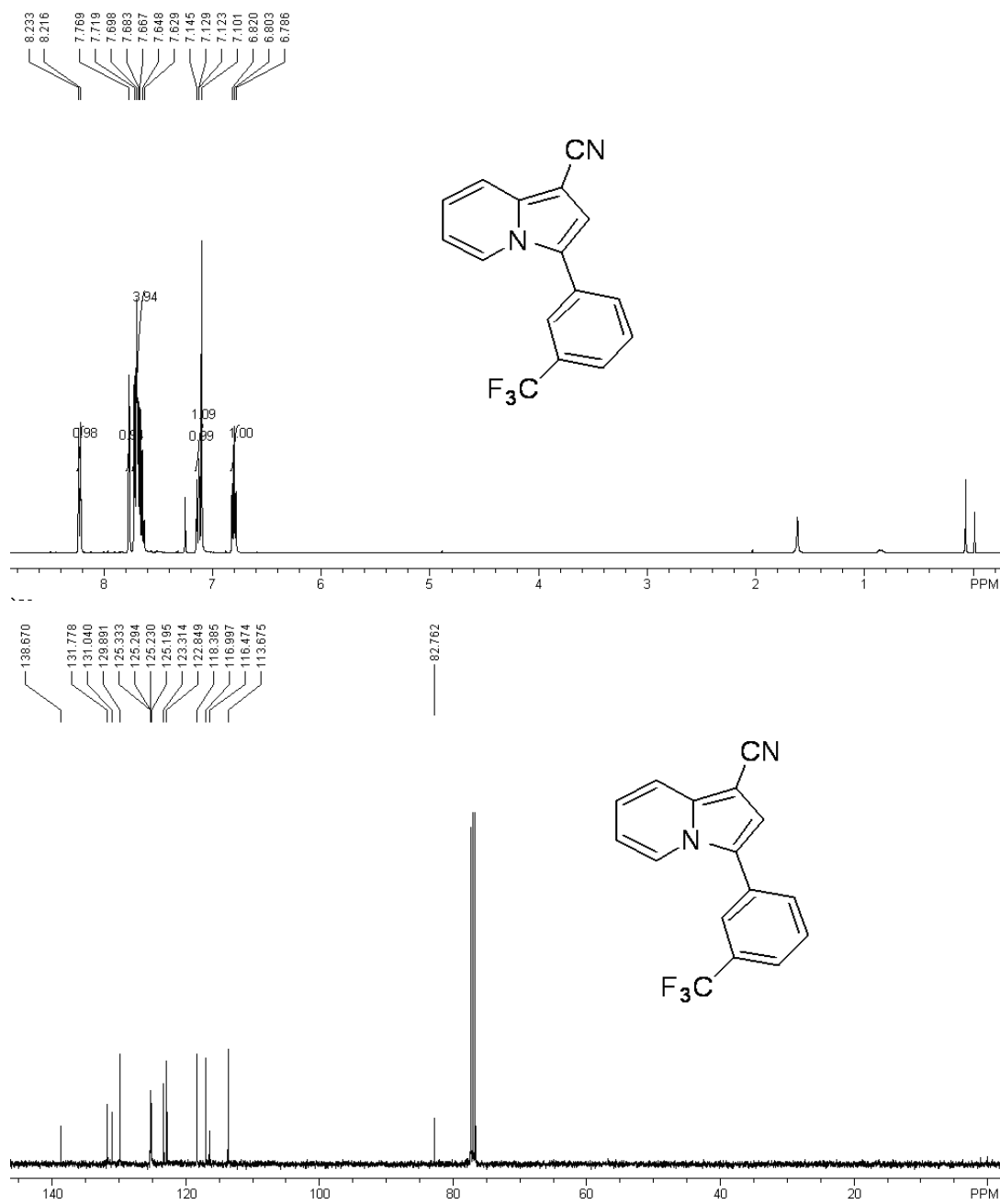
Elem. Anal.: C, 78. 03; H, 4.09; N, 11.38; O, 6.50.



(12) 3-(3-(trifluoromethyl)phenyl)indolizine-1-carbonitrile (T 2-12, new compound)

White solid. m.p. 262-264 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.22 (d, $J = 6.8$ Hz, 1 H), 7.72 (s, 1 H), 7.63-7.72 (m, 4 H), 7.13 (t, $J = 6.4$ Hz, 1 H), 7.10 (s, 1 H), 6.80 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.7, 131.8, 131.0, 129.9, 125.3 (q, $J = 4.6$ Hz), 123.3, 122.8, 118.4, 117.0, 116.5, 113.7, 82.8. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_9\text{N}_2\text{F}_3$ (M^+) 286.0718, Found 286.0721.

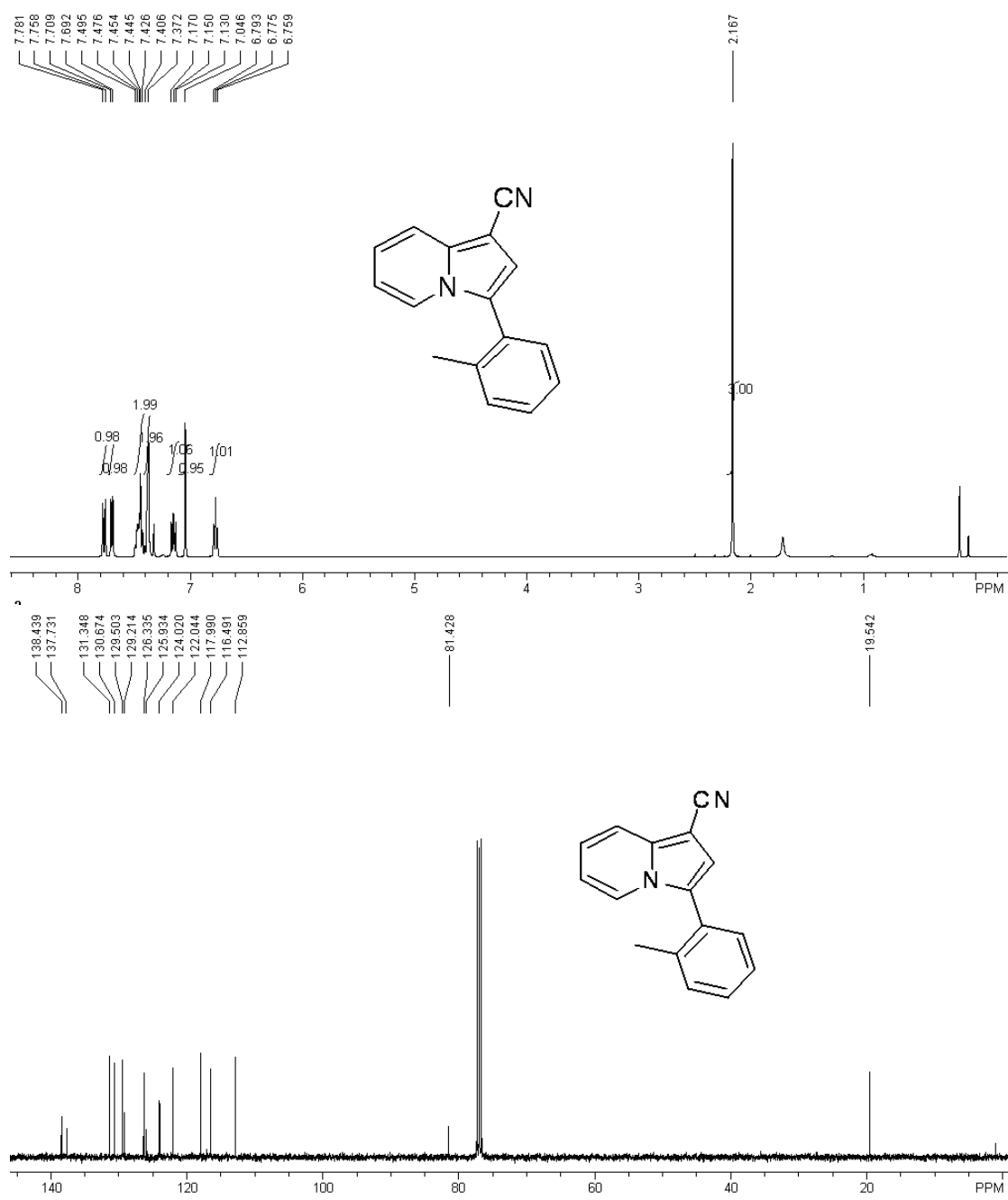
Elem. Anal.: C, 67.13; H, 3.17; F, 19.91, N, 9.79.



(13) 3-o-tolyindolizine-1-carbonitrile (T 2-13, new compound)

White solid. m.p. 209-210 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 7.77 (d, $J = 9.2$ Hz, 1 H), 7.70 (d, $J = 6.8$ Hz, 1 H), 7.37-7.50 (m, 4 H), 7.15 (t, $J = 8.0$ Hz, 1 H), 7.05 (s, 1 H), 6.78 (t, $J = 6.8$ Hz, 1 H), 2.17 (s, 3 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.4, 137.4, 131.3, 130.7, 129.5, 129.2, 126.3, 125.9, 124.0, 122.0, 118.0, 116.5, 112.9, 81.4, 19.5. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$ (M^+) 232.1000, Found 232.0999.

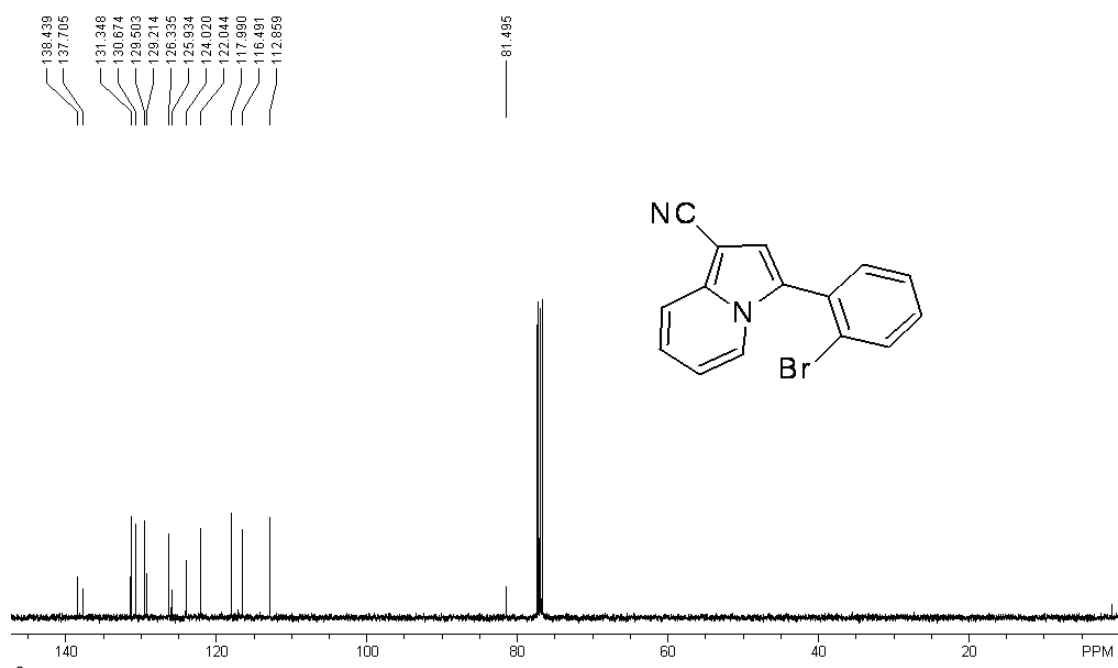
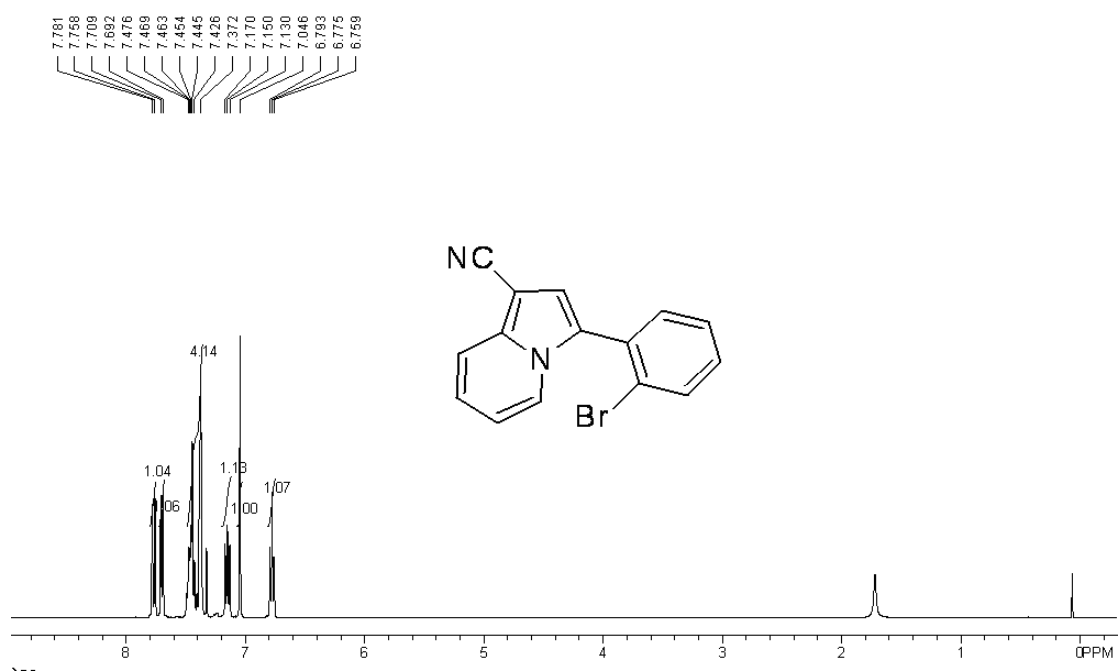
Elem. Anal.: C, 82.73; H, 5.21; N, 12.06.



(14) 3-(2-bromophenyl)indolizine-1-carbonitrile (T 2-14, new compound)

Yellow solid. m.p. 278-279 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 7.77 (d, $J = 9.2$ Hz, 1 H), 7.70 (d, $J = 6.8$ Hz, 1 H), 7.37-7.50 (m, 4 H), 7.15 (t, $J = 8.0$ Hz, 1 H), 7.05 (s, 1 H), 6.78 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.4, 137.4, 131.3, 130.7, 129.5, 129.2, 126.3, 125.9, 124.0, 122.0, 118.0, 116.5, 112.9, 120.0, 81.4. HRMS (EI) Calcd for $\text{C}_{15}\text{H}_9\text{N}_2\text{Br}$ (M^+) 295.9949, Found 295.9944.

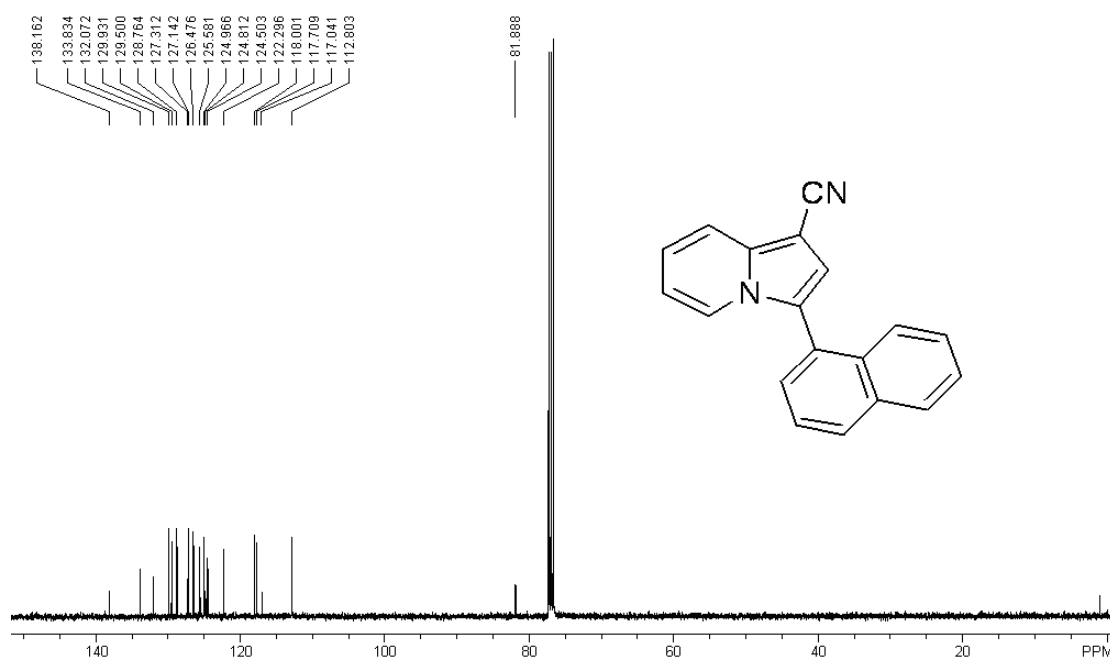
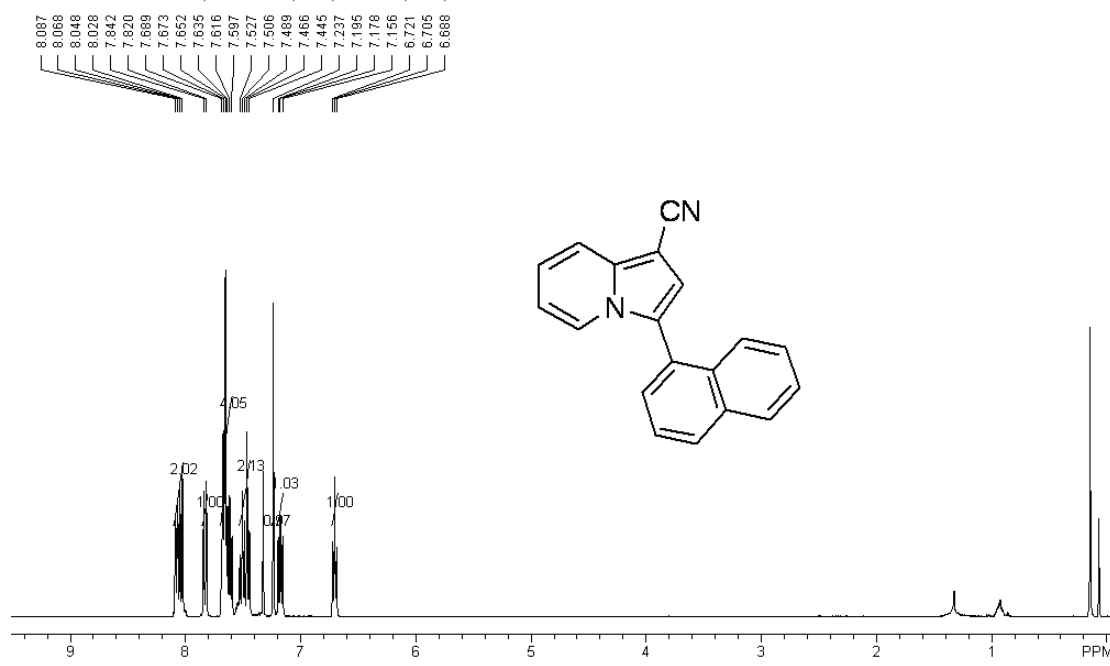
Elem. Anal.: C, 60.63; H, 3.05; Br, 26.89; N, 9.43.



(15) 3-(naphthalen-1-yl)indolizine-1-carbonitrile (T 2-15, new compound)

White solid. m.p. 303-305 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.03-8.09 (m, 2 H), 7.83 (d, $J = 8.8$ Hz, 1 H), 7.60-7.69 (m, 4 H), 7.45-7.53 (m, 2 H), 7.24 (s, 1 H), 7.18 (t, $J = 8.0$ Hz, 1 H), 6.71 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.2, 133.8, 132.1, 129.9, 129.5, 128.8, 127.3, 127.1, 126.5, 125.6, 125.0, 124.8, 124.5, 122.3, 118.0, 117.7, 112.8, 81.9. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{12}\text{N}_2$ (M^+) 268.1000, Found 268.0992.

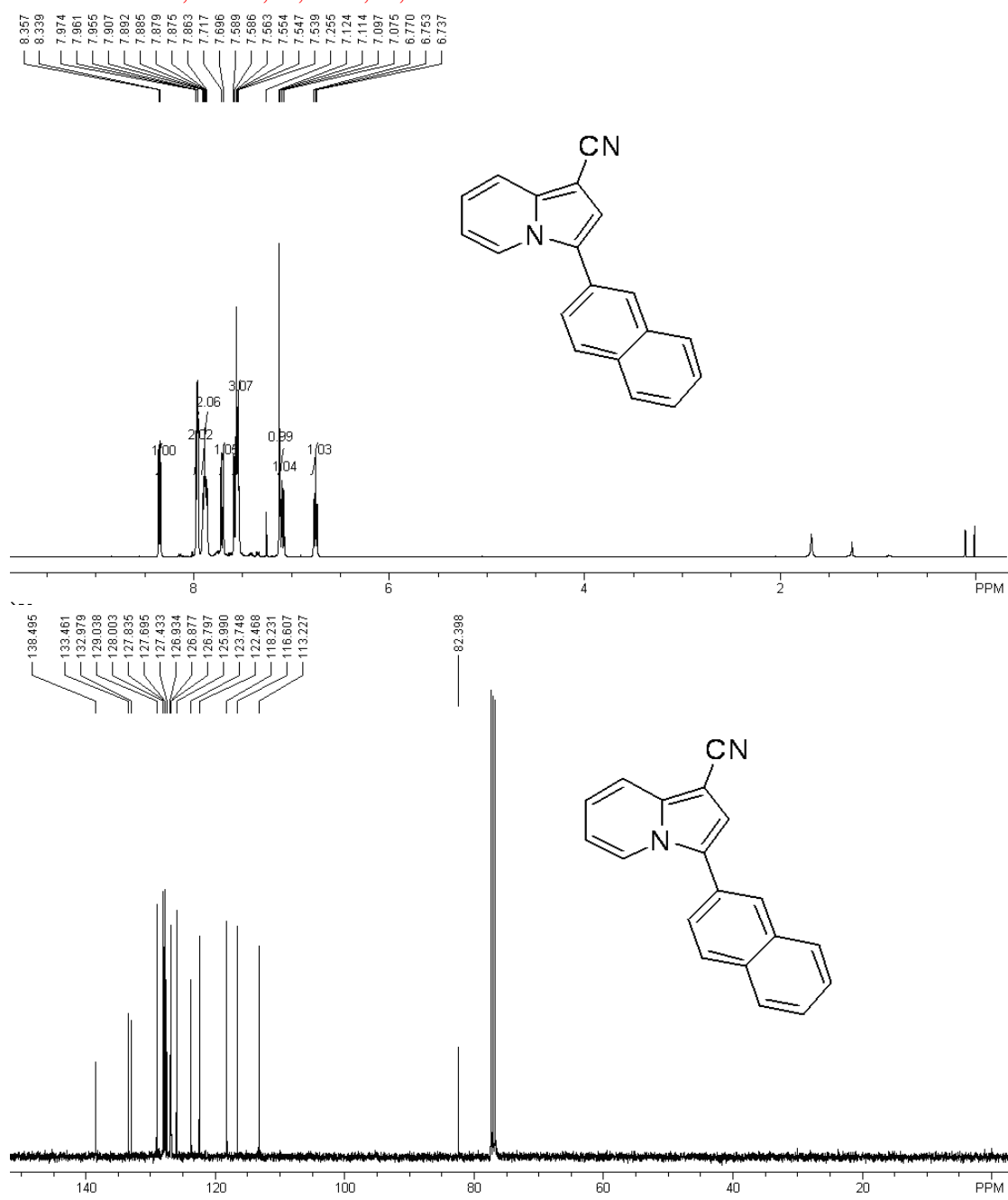
Elem. Anal.: C, 85.05; H, 4.51; N, 10.44.



(16) 3-(naphthalen-2-yl)indolizine-1-carbonitrile (T 2-16, new compound)

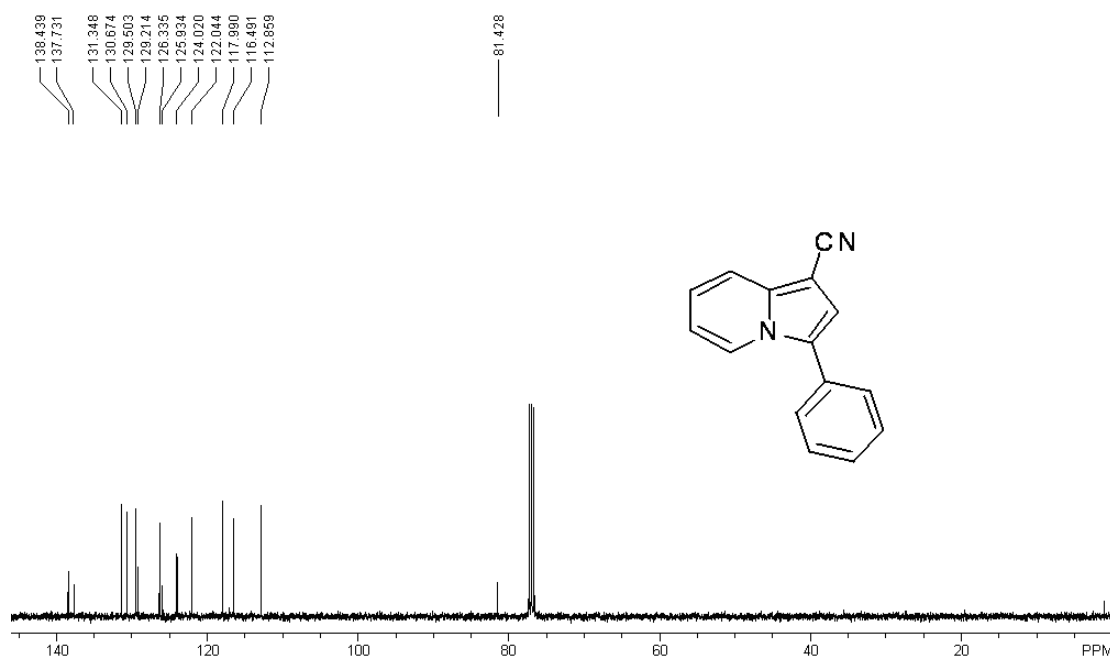
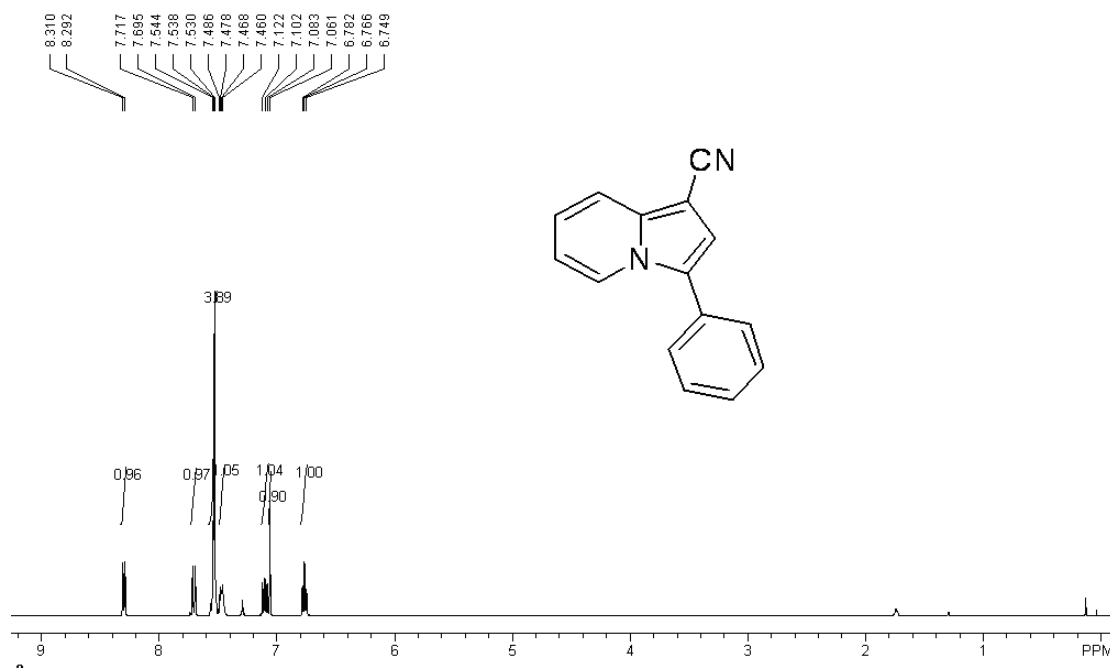
White solid. m.p. 311-312 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.35 (d, $J = 7.2$ Hz, 1 H), 7.95-7.98 (m, 2 H), 7.86-7.91 (m, 2 H), 7.71 (d, $J = 8.4$ Hz, 1 H), 7.54-7.59 (m, 3 H), 7.12 (s, 1 H), 7.10 (t, $J = 8.0$ Hz, 1 H), 6.75 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100MHz, CDCl_3) δ 138.5, 133.5, 133.0, 129.0, 128.0, 127.8, 127.7, 126.9, 126.8, 126.0, 123.7, 122.5, 118.2, 116.6, 113.2, 82.4. HRMS (ESI) Calcd for $\text{C}_{19}\text{H}_{12}\text{N}_2$ (M^+) 268.1000, Found 268.1002.

Elem. Anal.: C, 85.05; H, 4.51; N, 10.44.



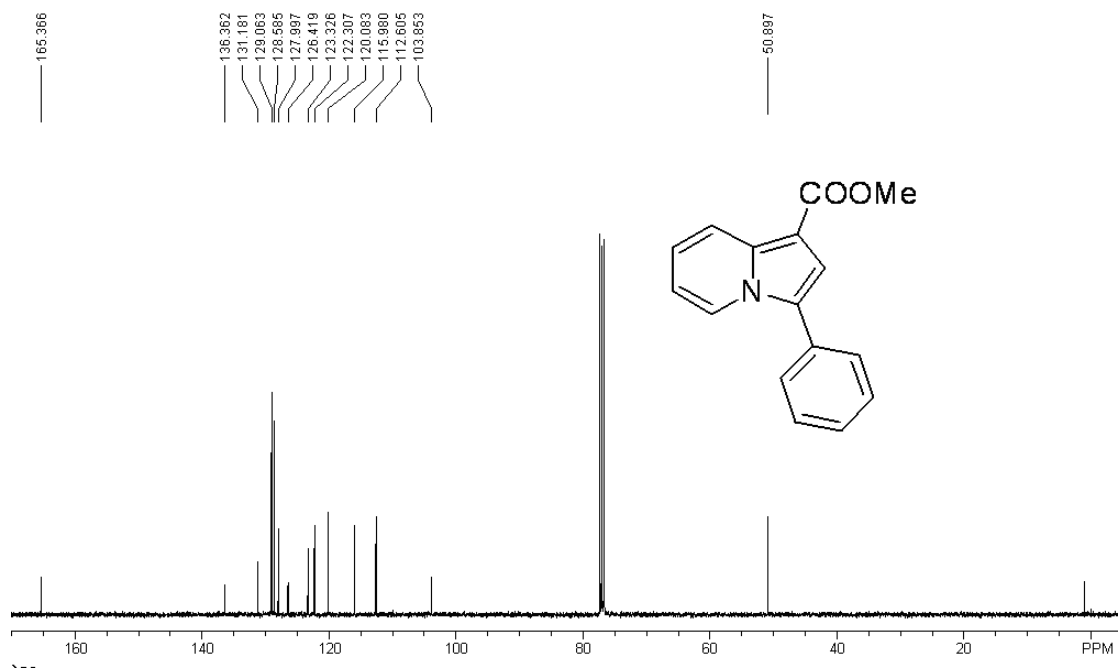
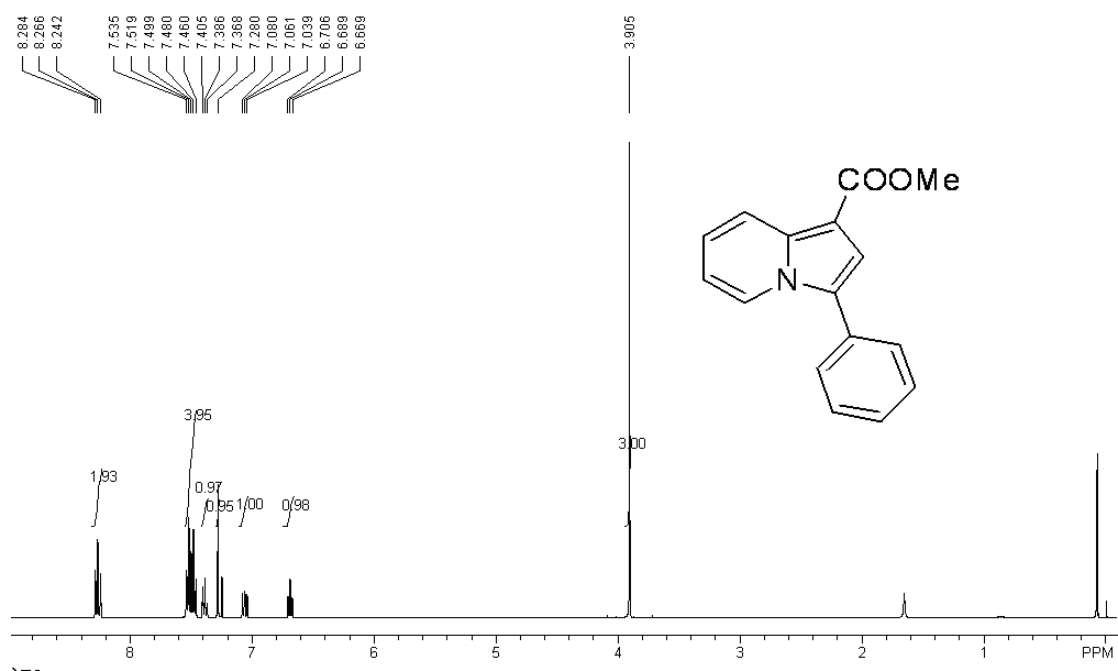
(17) 3-phenylindolizine-1-carbonitrile (T 3-1, CAS#189569-52-6) ^[3]

¹H NMR (400 MHz, CDCl₃, TMS) δ 8.30 (d, *J* = 7.2 Hz, 1 H), 7.71 (d, *J* = 8.8 Hz, 1 H), 7.53-7.55 (m, 4 H), 7.46-7.49 (m, 1 H), 7.10 (t, *J* = 8.0 Hz, 1 H), 7.06 (s, 1 H), 6.77 (t, *J* = 6.8 Hz, 1 H). ¹³C NMR (100MHz, CDCl₃) δ 138.4, 137.7, 131.4, 130.7, 129.5, 129.2, 126.3, 125.9, 124.0, 122.0, 117.9, 116.5, 112.8, 81.4. HRMS (EI) Calcd for C₁₅H₁₀N₂ (M⁺) 218.0844, Found 218.0839.



(18) methyl 3-phenylindolizine-1-carboxylate (T 3-2, CAS#947381-33-1) ^[3]

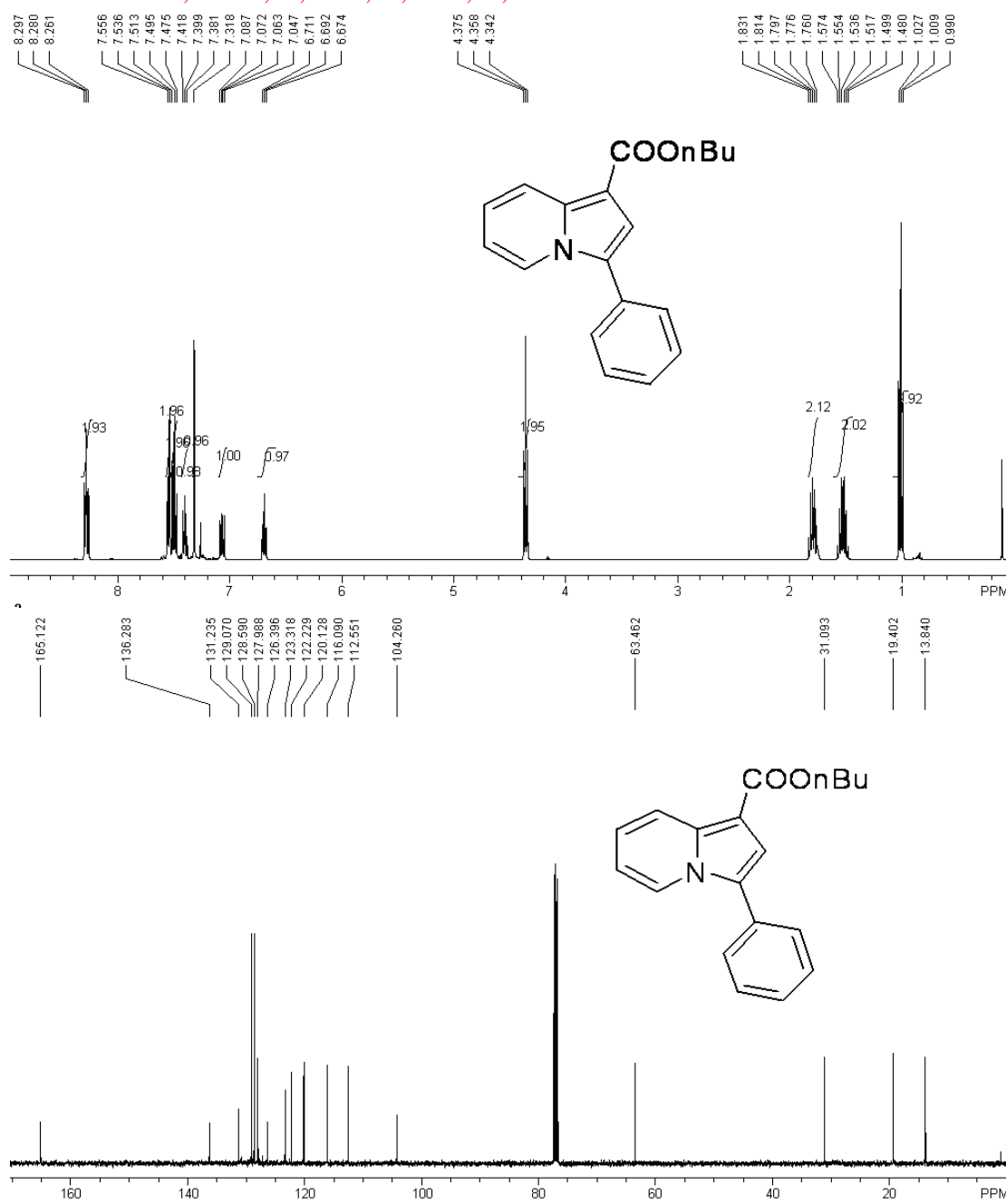
¹H NMR (400 MHz, CDCl₃, TMS) δ 8.27 (t, *J* = 8.8 Hz, 2 H), 7.50 (m, 4 H), 7.39 (t, *J* = 7.2 Hz, 1 H), 7.28 (s, 1 H), 7.06 (t, *J* = 8.0 Hz, 1 H), 6.69 (t, *J* = 7.6 Hz, 1 H), 3.91 (s, 3 H),. ¹³C NMR (100 MHz, CDCl₃) δ 165.4, 136.4, 131.2, 129.1, 128.6, 128.0, 126.4, 123.3, 122.3, 120.7, 112.6, 103.9, 50.9. HRMS (EI) Calcd for C₁₆H₁₃NO₂ (M⁺) 251.0946, Found 251.0951.



(20) butyl 3-phenylindolizine-1-carboxylate (T 3-4, new compound)

Brown oil. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.28 (t, $J = 7.2$ Hz, 2 H), 7.55 (d, $J = 8.0$ Hz, 2 H), 7.50 (t, $J = 7.6$ Hz, 2 H), 7.40 (t, $J = 7.2$ Hz, 1 H), 7.32 (s, 1 H), 7.07 (m, 1 H), 6.70 (t, $J = 7.6$ Hz, 1 H), 4.36 (t, $J = 6.8$ Hz, 2 H), 1.80 (m, 2 H), 1.53 (m, 2 H), 1.01 (t, $J = 7.6$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.1, 136.3, 131.2, 129.1, 128.6, 128.0, 126.4, 123.3, 122.2, 120.1, 116.1, 114.9, 112.6, 104.3, 63.5, 31.1, 19.4, 13.8. HRMS (EI) Calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_2$ (M^+) 293.1416, Found 293.1424.

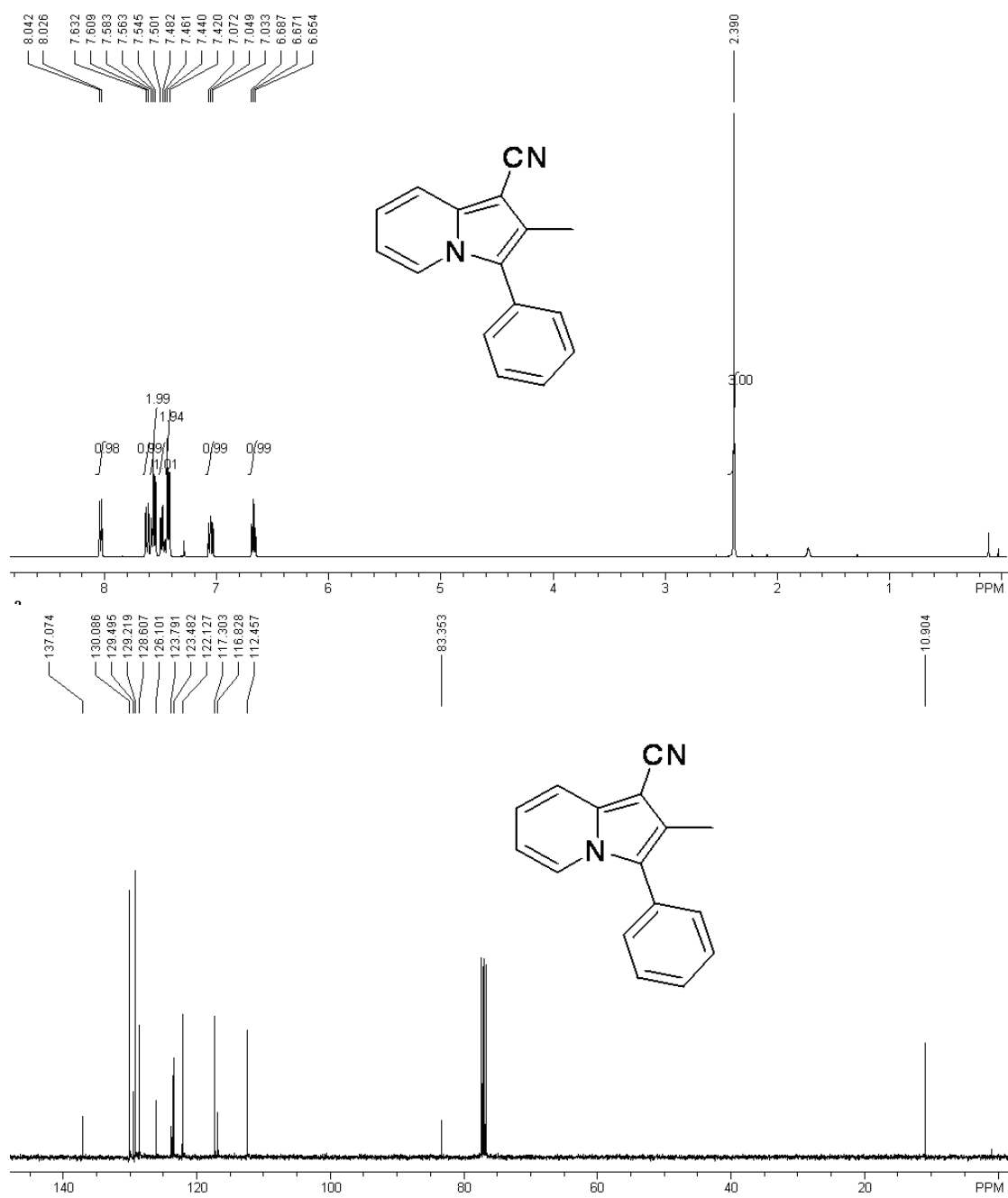
Elem. Anal.: C, 77.79; H, 6.53; N, 4.77, O, 10.91.



(21) 2-methyl-3-phenylindolizine-1-carbonitrile (T 3-5, new compound)

White solid. m.p. 253-254 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.03 (d, $J = 7.2$ Hz, 1 H), 7.62 (d, $J = 9.2$ Hz, 1 H), 7.56 (t, $J = 7.6$ Hz, 2 H), 7.48 (t, $J = 8.0$ Hz, 1 H), 7.43 (d, $J = 8.0$ Hz, 2 H), 7.05 (t, $J = 8.0$ Hz, 1 H), 6.67 (t, $J = 6.8$ Hz, 1 H), 2.39 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.1, 130.1, 129.5, 129.2, 128.6, 126.1, 123.8, 122.1, 117.3, 116.8, 112.5, 83.4, 10.9. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$ (M^+) 232.1000, Found 232.0998.

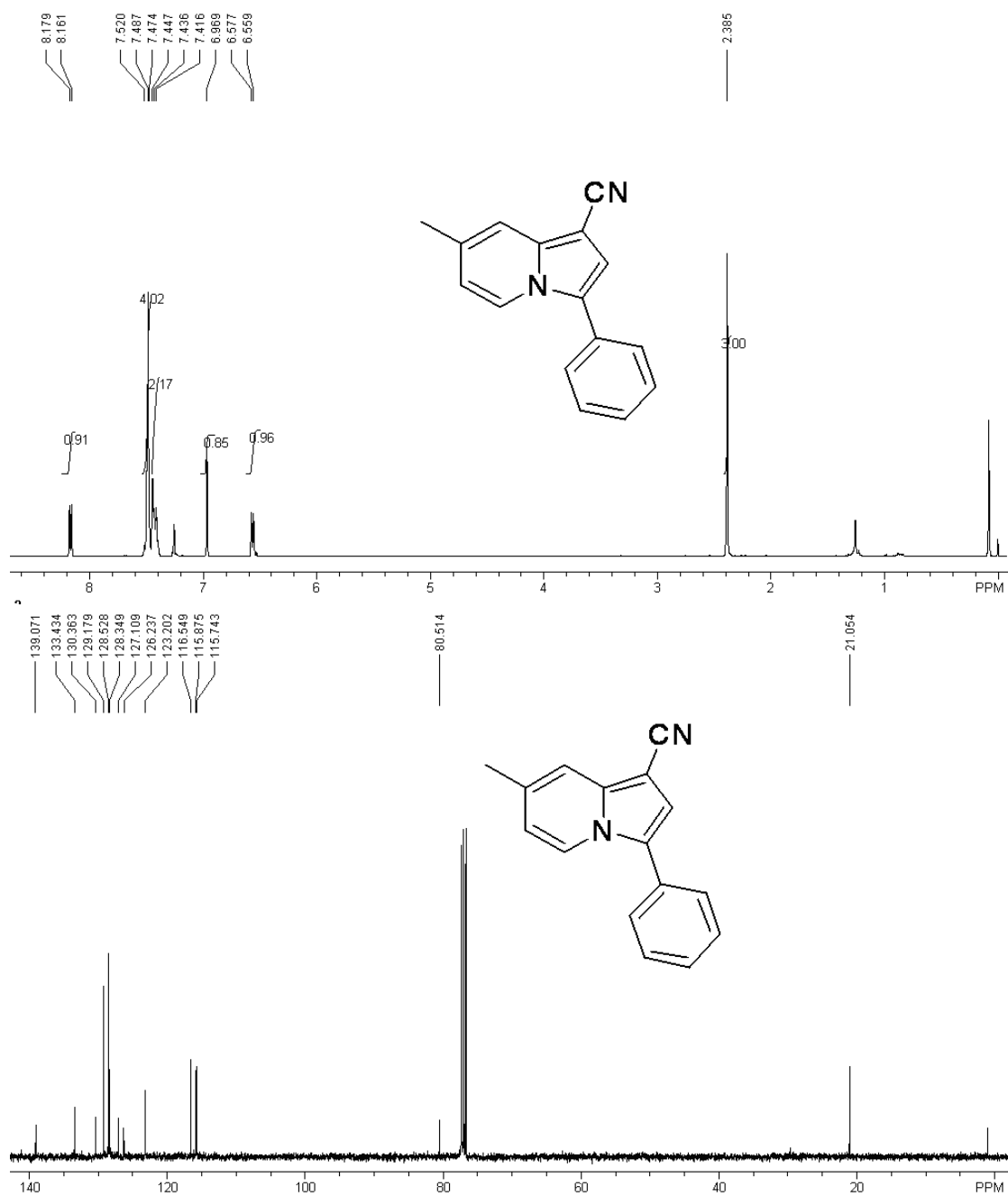
Elem. Anal.: C, 82.73; H, 5.21; N, 12.06.



(22) 7-methyl-3-phenylindolizine-1-carbonitrile (T 3-6, new compound)

White solid. m.p. 237-238 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.17 (d, $J = 7.2$ Hz, 1 H), 7.85 (d, $J = 7.2$ Hz, 1 H), 7.22 (d, $J = 8.0$ Hz, 2 H), 7.47-7.52 (m, 4 H), 7.41-7.45 (m, 2 H), 6.97 (s, 1 H), 6.57 (d, $J = 7.2$ Hz, 1 H), 2.39 (s, 3 H),. ^{13}C NMR (100 MHz, CDCl_3) δ 139.1, 133.4, 130.4, 129.2, 128.5, 128.3, 127.1, 126.2, 123.2, 116.5, 115.9, 115.7, 80.5, 21.1. HRMS (EI) Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2$ (M^+) 232.1000, Found 232.0996.

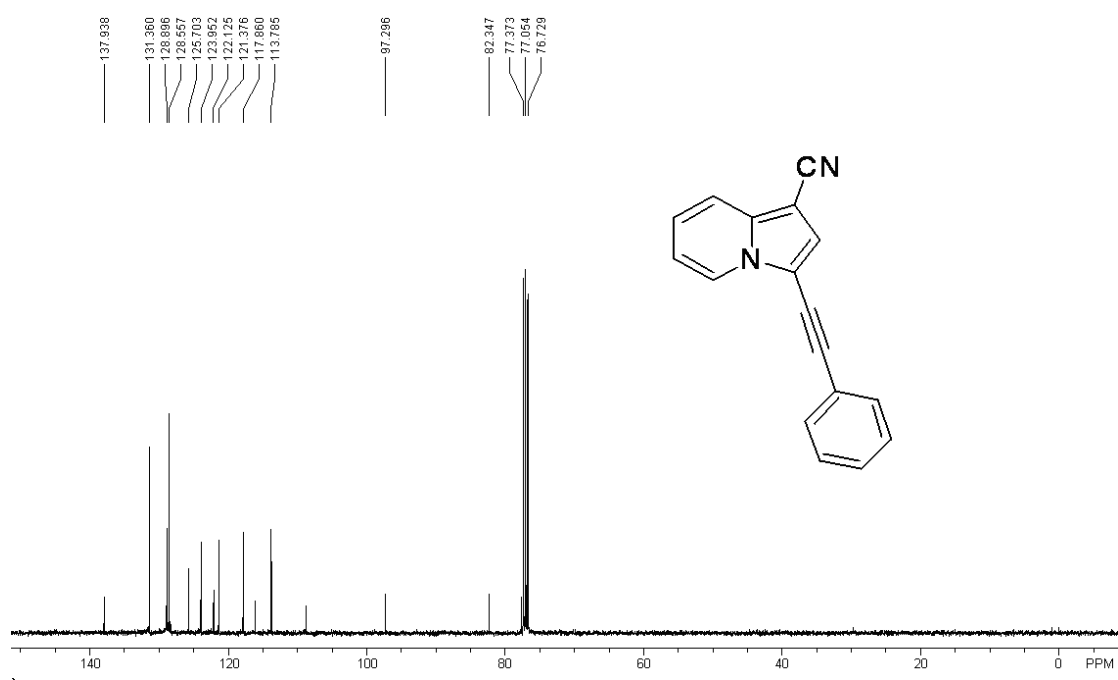
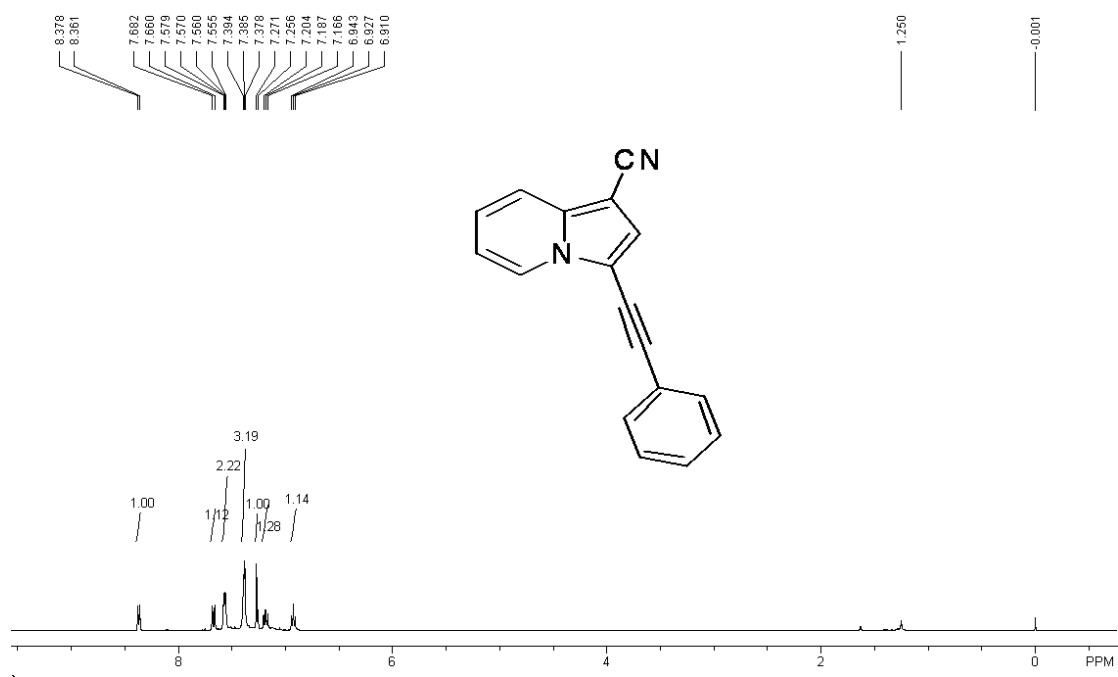
Elem. Anal.: C, 82.73; H, 5.21; N, 12.06.



(23) 3-(phenylethynyl)indolizine-1-carbonitrile (T 5-1, new compound)

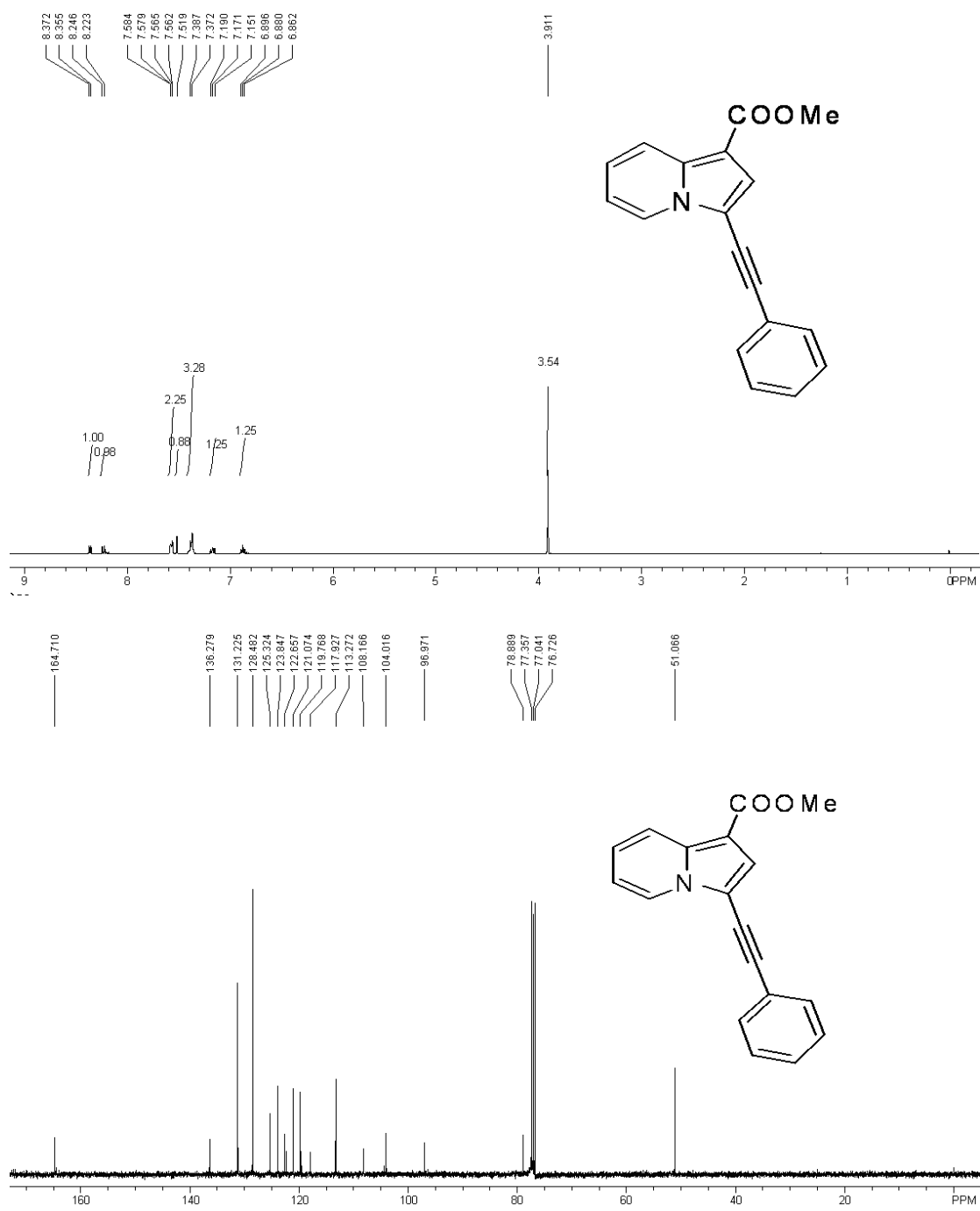
White solid. m.p. 276-278 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.37 (d, $J = 6.8$ Hz, 1 H), 7.67 (d, $J = 8.8$ Hz, 1 H), 7.56-7.58 (m, 2 H), 7.38-7.39 (m, 3 H), 7.28 (s, 1 H), 7.19 (t, $J = 7.6$ Hz, 1 H), 6.92 (t, $J = 6.4$ Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.0, 131.4, 128.9, 128.5, 125.7, 124.0, 122.1, 121.4, 117.9, 113.8, 97.2, 82.3. HRMS (EI) Calcd for $\text{C}_{17}\text{H}_{10}\text{N}_2$ (M^+) 242.0844, Found 242.0851.

Elem. Anal.: C, 84.28; H, 4.16; N, 11.56.



(24) methyl 3-(phenylethynyl)indolizine-1-carboxylate (T 5-2, CAS# 944405-43-0) [4]

^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.36 (d, $J = 6.8$ Hz, 1 H), 8.23 (d, $J = 9.2$ Hz, 1 H), 7.56-7.58 (m, 2 H), 7.52 (s, 1 H), 7.37-7.39 (m, 3 H), 7.17 (t, $J = 8.0$ Hz, 1 H), 6.88 (t, $J = 6.8$ Hz, 1 H), 3.91 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 136.3, 131.2, 128.5, 125.4, 123.8, 122.7, 121.1, 119.8, 117.9, 113.3, 108.2, 104.0, 97.0, 78.9, 51.1. HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{13}\text{NO}_2$ (M^+) 275.0946, Found 275.0941.



(25) ethyl 3-(phenylethynyl)indolizine-1-carboxylate (T 5-3, new compound)

White solid. m.p. 247-248 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.37 (d, $J = 6.8$ Hz, 1 H), 8.24 (d, $J = 8.8$ Hz, 1 H), 7.56-7.58 (m, 2 H), 7.55 (s, 1 H), 7.36-7.39 (m, 3 H), 7.17 (t, $J = 8.0$ Hz, 1 H), 6.88 (t, $J = 7.2$ Hz, 1 H), 4.36-4.41 (m, 2 H), 1.42 (t, $J = 7.2$ Hz, 3 H). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 136.2, 131.2, 128.5, 128.4, 125.3, 123.8, 122.7, 121.2, 119.8, 113.3, 108.1, 104.4, 97.0, 79.0, 59.7, 14.6. HRMS (EI) Calcd for $\text{C}_{19}\text{H}_{15}\text{NO}_2$ (M^+) 289.1103, Found 289.1106.

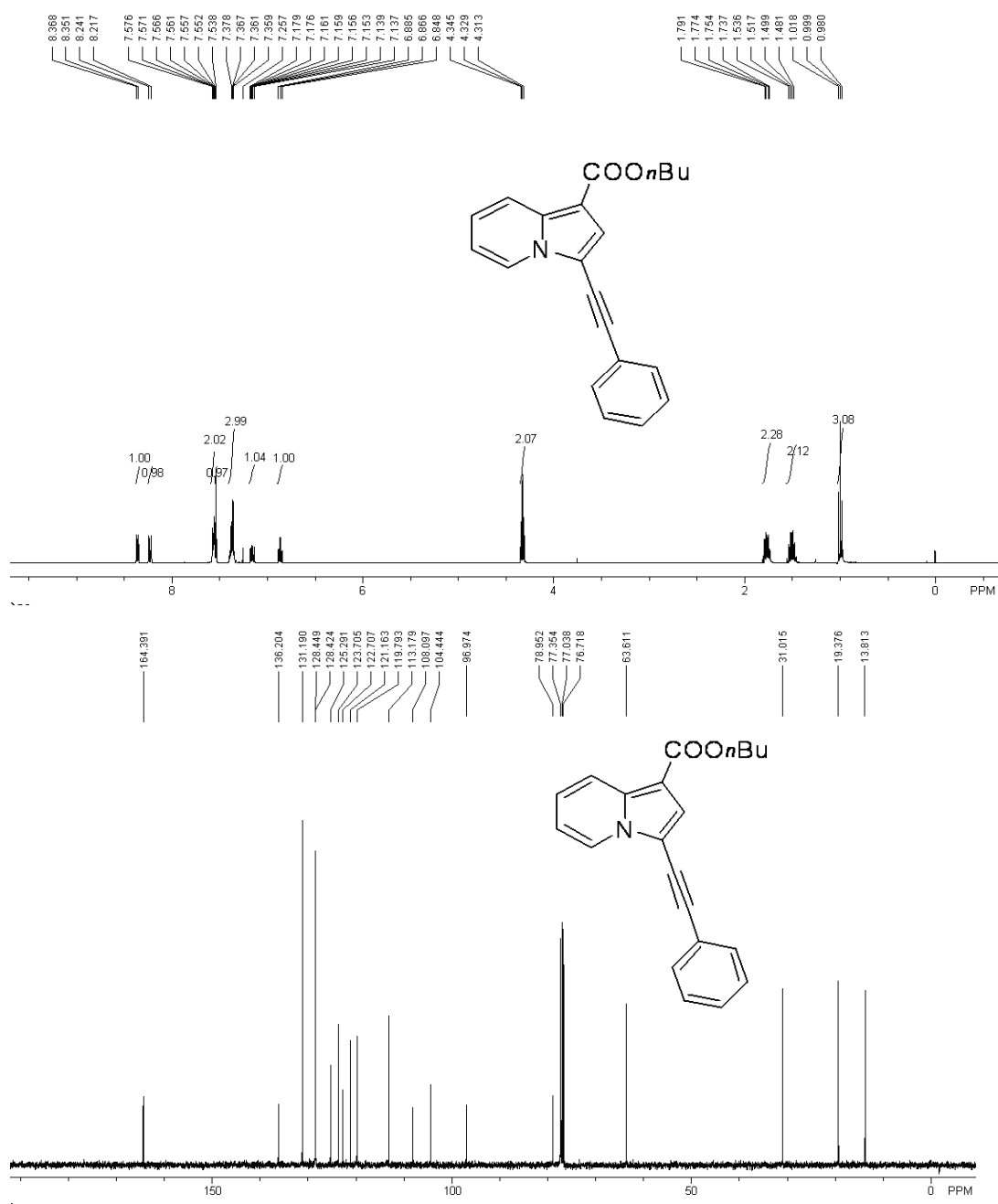
Elem. Anal.: C, 78.87; H, 5.23; N, 4.84; O, 11.06.



(26) butyl 3-(phenylethynyl)indolizine-1-carboxylate (T 5-4, new compound)

Brown solid. m.p. 260-262 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3 , TMS) δ 8.36 (d, $J = 6.8$ Hz, 1 H), 8.23 (d, $J = 9.6$ Hz, 1 H), 7.55-7.58 (m, 2 H), 7.54 (s, 1 H), 7.36-7.38 (m, 3 H), 7.14-7.18 (m, 1 H), 6.87 (t, $J = 7.6$ Hz, 1 H), 4.33 (t, $J = 6.4$ Hz, 2 H), 1.74-1.79 (m, 2 H), 1.48-1.54 (m, 2 H), 1.00 (t, $J = 7.6$ Hz, 3 H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 164.4, 136.2, 131.2, 128.5, 128.4, 125.3, 123.7, 122.7, 121.2, 119.8, 113.2, 108.1, 104.4, 97.0, 78.9, 63.6, 31.0, 19.4, 13.8. HRMS (EI) Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}_2$ (M^+) 317.1416, Found 317.1422.

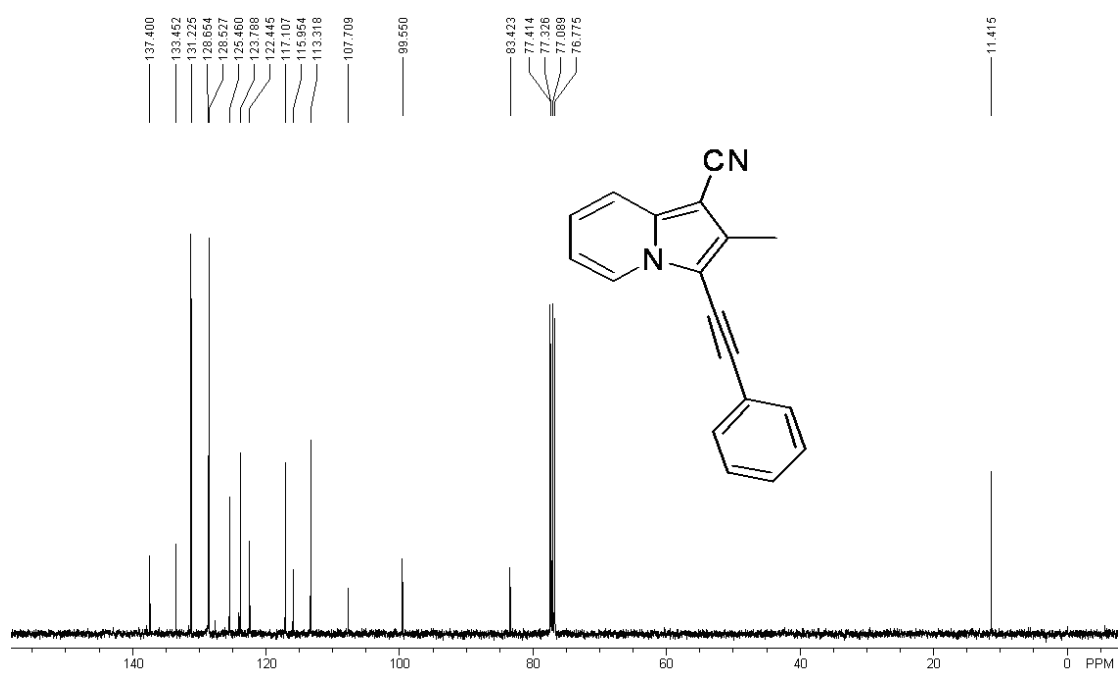
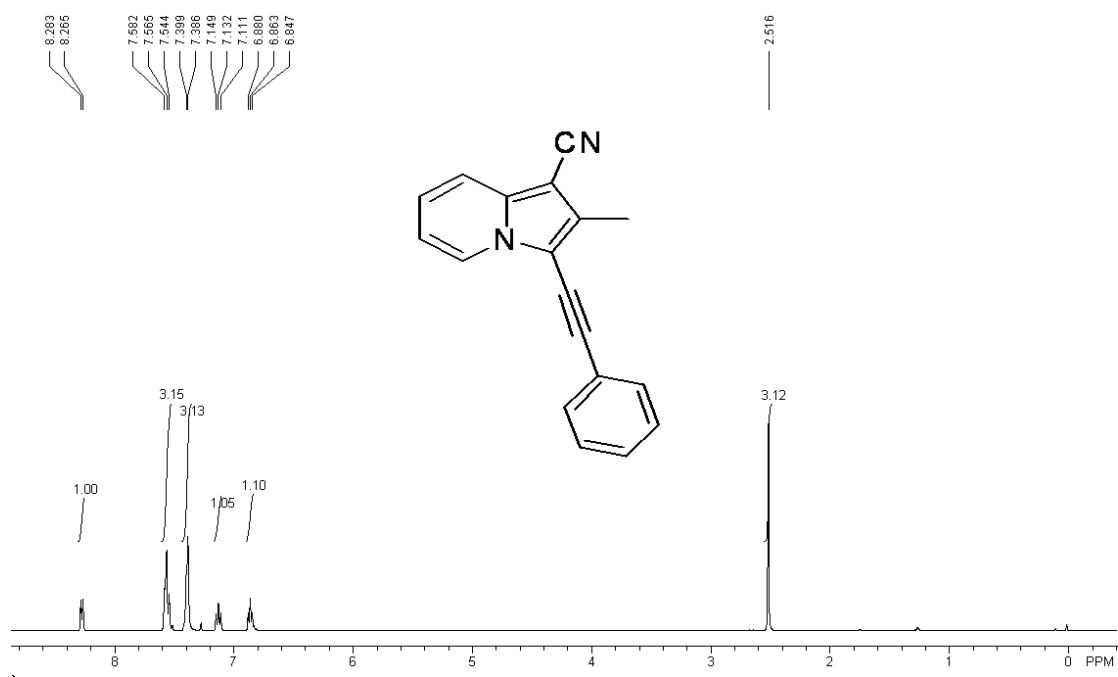
Elem. Anal.: C, 79.47; H, 6.03; N, 4.41; O, 10.08.



(27) 2-methyl-3-(phenylethynyl)indolizine-1-carbonitrile (T 5-5, new compound)

White solid. m.p. 293-294 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.27 (d, $J = 7.2$ Hz, 1 H), 7.54-7.58 (m, 3 H), 7.39-7.40 (m, 3 H), 7.13 (t, $J = 7.6$ Hz, 1 H), 6.86 (t, $J = 7.6$ Hz, 1 H), 2.52 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.4, 133.5, 131.2, 128.7, 128.5, 125.5, 123.8, 122.4, 117.1, 116.0, 113.3, 107.7, 99.6, 83.4, 77.3, 11.4. HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2$ (M^+) 256.1000, Found 256.1001.

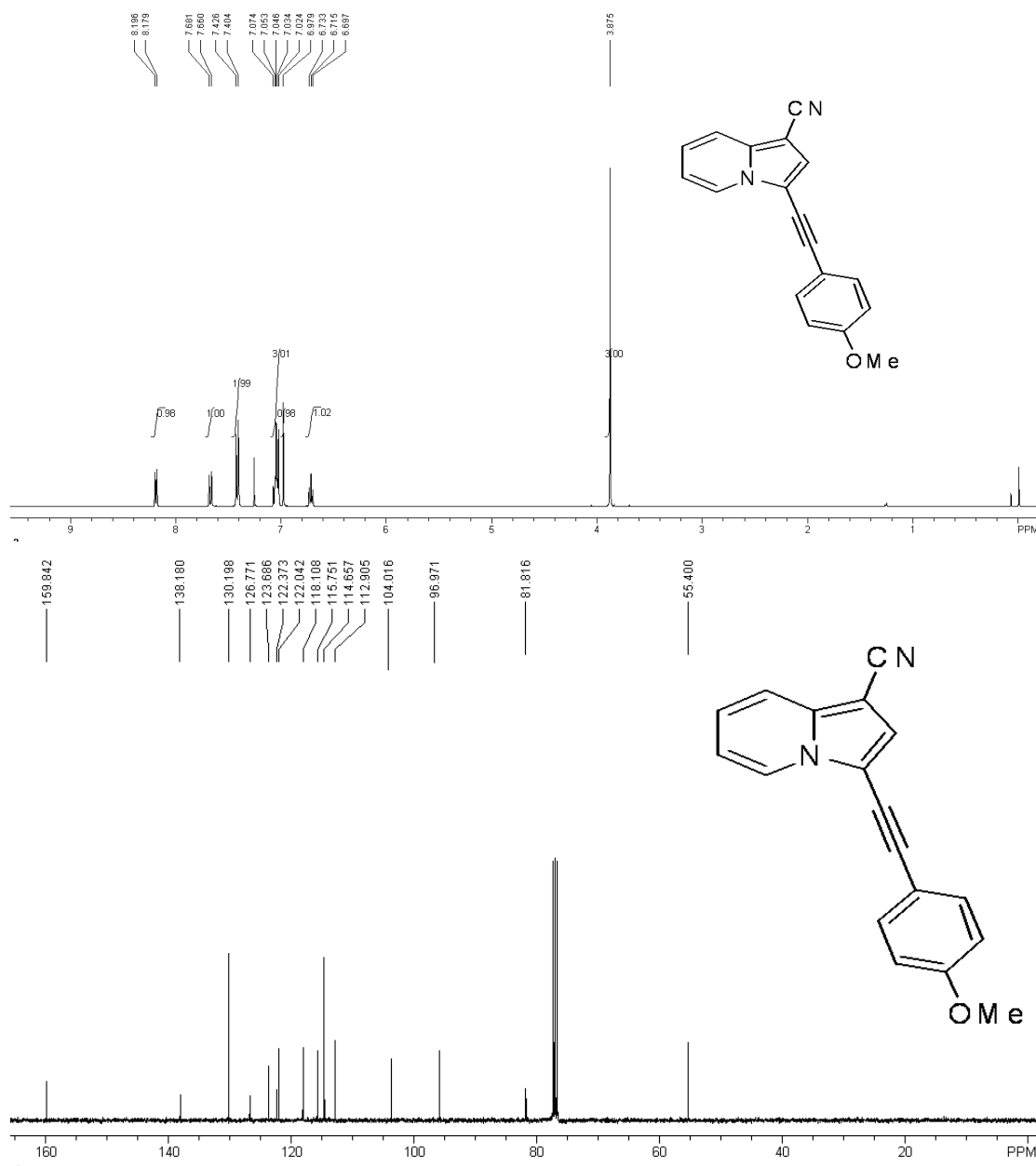
Elem. Anal.: C, 84.35; H, 4.72; N, 10.93.



(28) 3-((4-methoxyphenyl)ethynyl)indolizine-1-carbonitrile (T 5-6, new compound)

White solid. m.p. 296-297 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.18 (d, $J = 6.8$ Hz, 1 H), 7.67 (d, $J = 8.4$ Hz, 1 H), 7.42 (d, $J = 8.8$ Hz, 2 H), 7.02-7.07 (m, 3 H), 6.98 (s, 1 H), 6.71 (t, $J = 7.2$ Hz, 1 H), 3.87 (s, 3 H). ^{13}C NMR (100MHz, CDCl_3) δ 159.9, 138.2, 130.2, 126.8, 123.7, 122.4, 122.0, 118.1, 115.8, 114.6, 112.9, 104.0, 97.0, 81.8, 55.4. HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}$ (M^+) 272.0950, Found 272.0952.

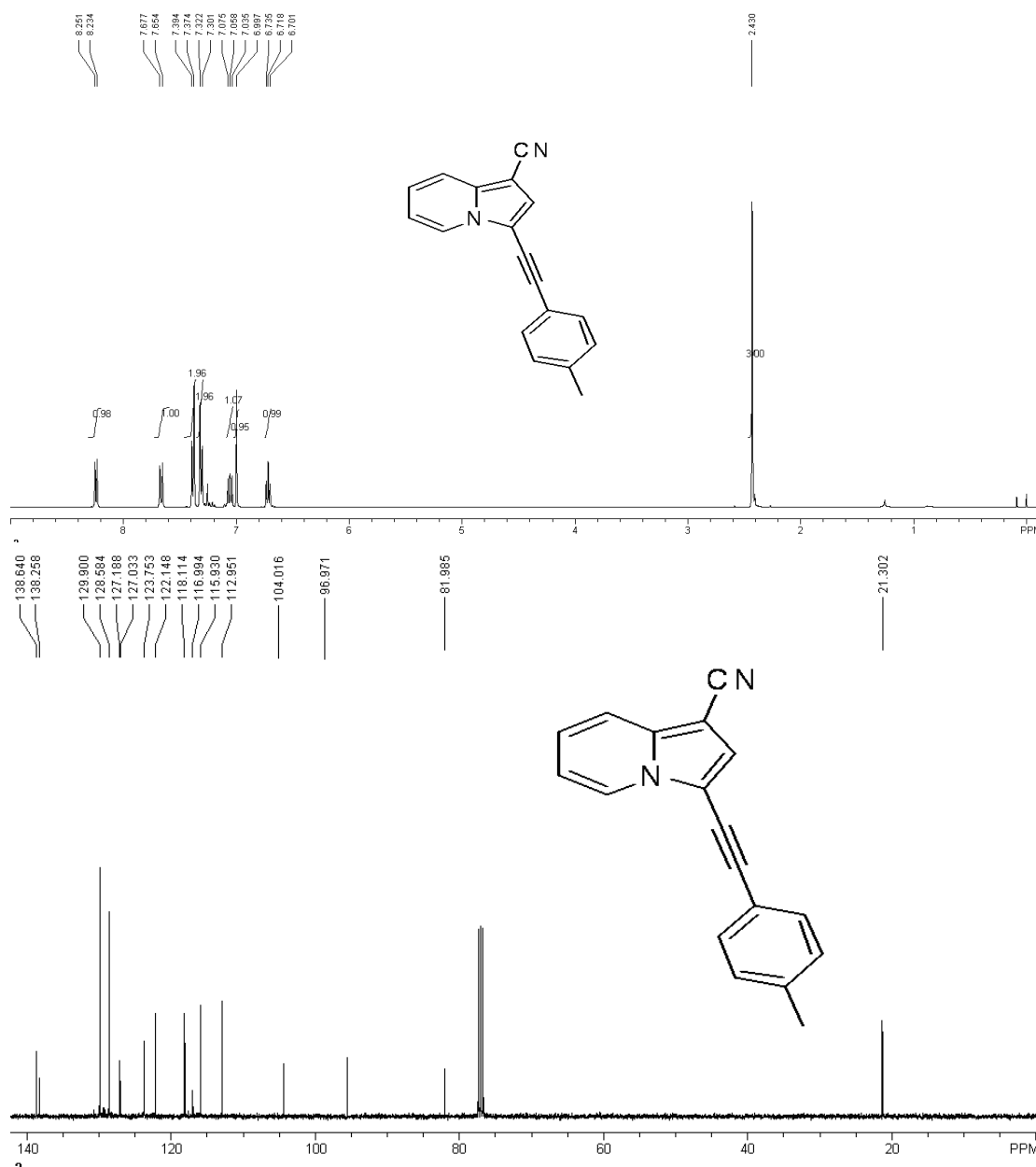
Elem. Anal.: C, 79.39; H, 4.44; N, 10.29; O, 5.88.



(29) 3-(p-tolyethynyl)indolizine-1-carbonitrile (T 5-7, new compound)

White solid. m.p. 279-280 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.24 (d, $J = 6.8$ Hz, 1 H), 7.67 (d, $J = 8.8$ Hz, 1 H), 7.39 (d, $J = 8.0$ Hz, 2 H), 7.31 (d, $J = 8.4$ Hz, 2 H), 7.07 (t, $J = 7.6$ Hz, 1 H), 7.00 (s, 1 H), 6.73 (t, $J = 6.8$ Hz, 1 H), 2.43 (s, 3 H).
 ^{13}C NMR (100 MHz, CDCl_3) δ 138.6, 138.2, 129.9, 128.6, 127.2, 127.0, 123.7, 122.2, 118.1, 117.0, 115.9, 112.9, 104.0, 96.9, 82.0, 21.3. HRMS (EI) Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2$ (M^+) 256.1000, Found 256.0999.

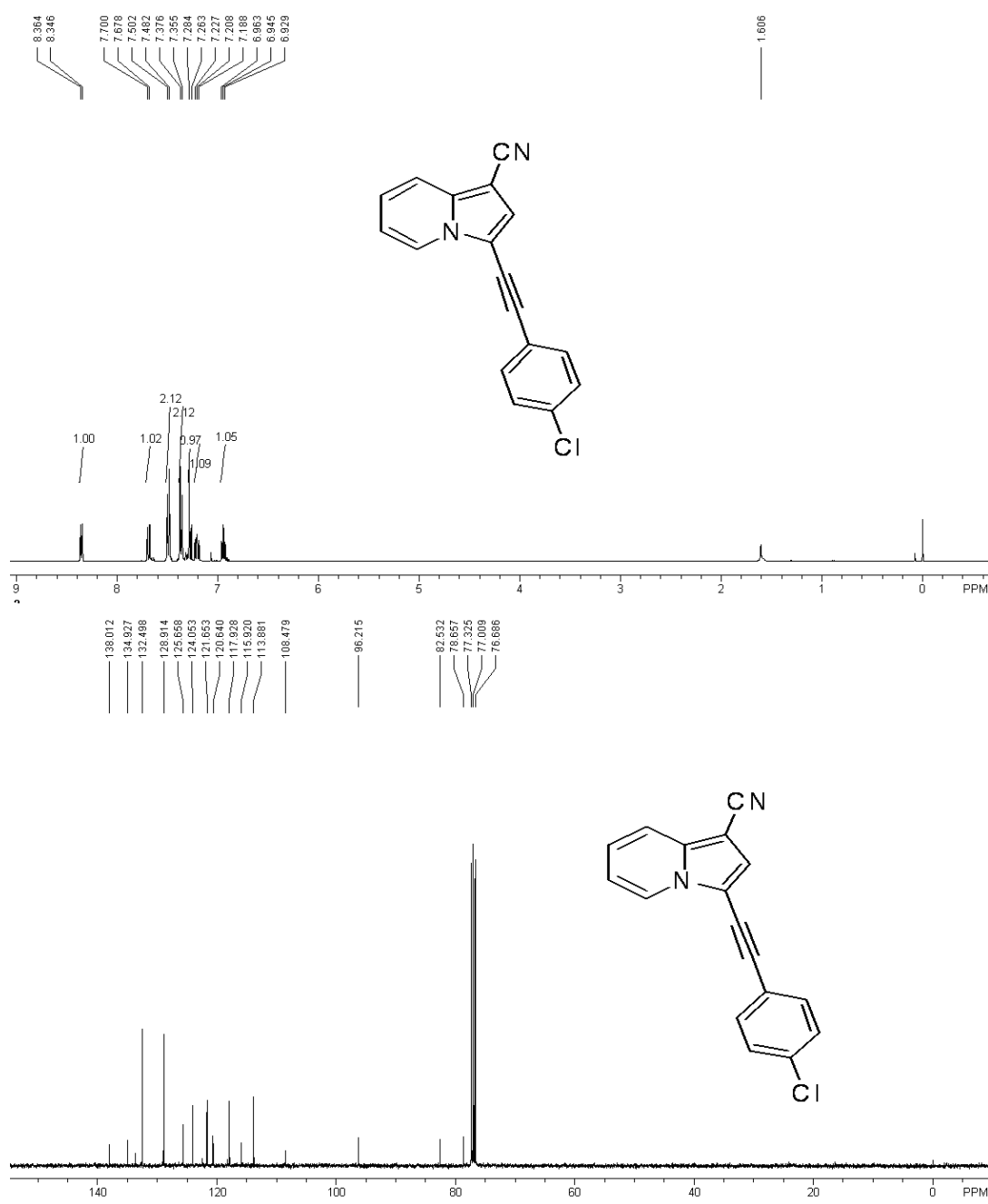
Elem. Anal.: C, 84.35; H, 4.72; N, 10.93.



(30) 3-((4-chlorophenyl)ethynyl)indolizine-1-carbonitrile (T 5-8, new compound)

Yellow solid. m.p. 317-318 °C. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 8.36 (d, $J = 7.2$ Hz, 1 H), 7.69 (d, $J = 8.8$ Hz, 1 H), 7.49 (d, $J = 8.0$ Hz, 2 H), 7.36 (d, $J = 8.4$ Hz, 2 H), 7.28 (s, 1 H), 7.21 (t, $J = 8.0$ Hz, 1 H), 6.95 (t, $J = 6.8$ Hz, 1 H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.0, 134.9, 132.5, 128.9, 125.7, 124.1, 121.7, 120.6, 117.9, 115.9, 113.9, 108.5, 96.2, 82.5, 78.7. HRMS (EI) Calcd for $\text{C}_{17}\text{H}_9\text{ClN}_2$ (M^+) 276.0454, Found 276.0457.

Elem. Anal.: C, 73.79; H, 3.28; Cl, 12.81, N, 10.12.



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- [1] Zhang, L.; Liang, F.; Sun, L.; Hu, Y.; Hu, H. *Synthesis* **2000**, 1733–1737.
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