Supporting information

Enzyme-catalyzed domino reaction: Efficient construction of spirocyclic oxindole skeleton using porcine pepsin

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1. General information

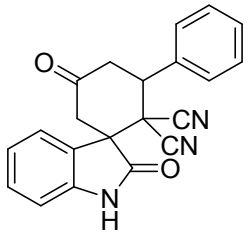
^{1}H NMR spectra and ^{13}C NMR spectra were respectively recorded on 300 MHz or 600 MHz and 75 MHz or 151 MHz NMR spectrometers. Chemical shifts (δ) were expressed in ppm with TMS as internal standard, and coupling constants (*J*) were reported in Hz. Routine monitoring of reaction was performed by TLC using precoated Haiyang GF254 silica gel TLC plates. Flash column chromatography was performed using silica gel (100–200 mesh) from Haiyang Chemical Industry Research Institute, Qingdao, P. R. China. Petroleum ether used was of boiling range 60-80°C. The organic extracts were dried over anhydrous sodium sulfate. Evaporation of solvent was performed at reduced pressure. Relative configurations of the products were determined by comparison with the ^{1}H NMR and ^{13}C NMR analysis of known compounds. Some unknown compounds were further determined by HRMS. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification.

2. Enzymatic assay of pepsin

Unit definition (U mg^{-1}): One unit will produce a ΔA280 of 0.001 per min at pH 2.0 at 37 °C, measured as TCA-soluble products using hemoglobin as substrate. (Final volume = 16 mL. Light path = 1 cm.).

The enzymatic assay was conducted according to the literature.[1]

3. Characterization data of the products

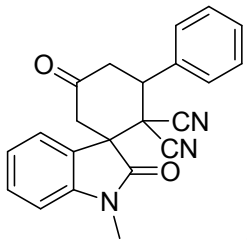


4a

2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 96% yield, 97:3 dr

Mp 247-249 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d6) δ 11.42 (s, 1H), 7.70 – 7.35 (m, 7H), 7.23 – 7.01 (m, 2H), 4.67 (dd, *J* = 13.5, 3.7 Hz, 1H), 3.57 – 3.40 (m, 2H), 2.77 – 2.66 (m, 1H), 2.61 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d6) δ 208.28, 181.20, 148.35, 141.54, 137.36, 135.79, 135.40, 135.31, 132.41, 130.78, 129.28, 119.01, 118.43, 117.30, 59.34, 53.15, 48.92, 48.43, 47.59.

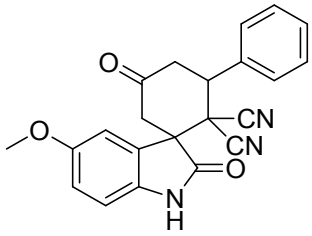


4b

1'-methyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 84% yield, 95:5 dr.

Mp 195-197 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 7.73 (d, *J* = 7.4 Hz, 1H), 7.56 – 7.51 (m, 3H), 7.51 – 7.44 (m, 3H), 7.30 – 7.25 (m , 2H), 4.71 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.56 – 3.44 (m, 2H), 3.26 (s, 3H), 2.79 – 2.62 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.12, 173.47, 143.92, 135.58, 131.53, 129.87, 129.45, 129.38, 125.72, 124.55, 124.00, 112.96, 112.53, 110.48, 53.25, 47.36, 43.20, 42.40, 41.78, 27.22.

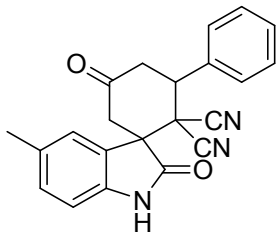


4c

5'-methoxy-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 99% yield, >99:1 dr

Mp 134-136 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.24 (s, 1H), 7.54 – 7.45 (m, 5H), 7.26 (t, *J* = 6.6 Hz, 1H), 7.00 (dt, *J* = 21.0, 5.5 Hz, 2H), 4.70 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.77 (s, 3H), 3.50 – 3.42 (m, 2H), 2.71 (d, *J* = 15.7 Hz, 1H), 2.59 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.13, 175.09, 155.82, 135.65, 135.47, 129.84, 129.43, 129.37, 127.61, 115.69, 113.05, 112.48, 112.26, 111.90, 56.05, 53.71, 47.25, 43.06, 42.68, 41.76.

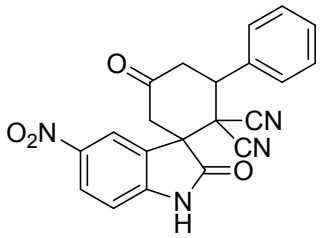


4d

5'-methyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 99% yield, 90:10 dr

Mp 151-153 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.30 (s, 1H), 7.53 – 7.45 (m, 6H), 7.23 (dd, *J* = 8.0, 0.8 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 4.70 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.51 – 3.38 (m, 2H), 2.74 – 2.54 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.16, 175.24, 139.98, 135.67, 132.36, 131.71, 129.83, 129.44, 129.36, 126.59, 125.35, 113.10, 112.51, 111.16, 53.48, 47.25, 43.07, 42.75, 41.80, 21.32.

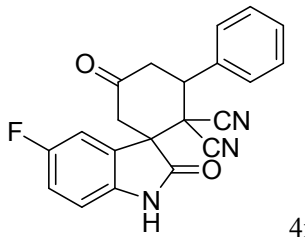


4e

5'-nitro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Yellow solid,75% yield 90:10 dr

Mp 174-176 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.11 (s, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.40 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.57 – 7.46 (m, 5H), 7.28 (d, *J* = 8.7 Hz, 1H), 4.64 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.66 (t, *J* = 12.9 Hz, 1H), 3.53 (dd, *J* = 15.3, 14.1 Hz, 1H), 2.85 – 2.73 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.73, 175.72, 148.93, 143.30, 135.33, 129.98, 129.44, 129.15, 128.44, 127.14, 120.95, 112.73, 112.22, 111.78, 53.49, 46.89, 43.09, 41.87, 41.72.

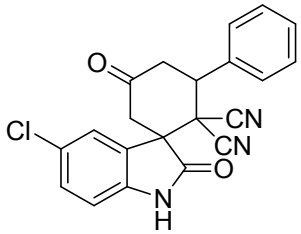


4f

5'-fluoro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 72% yield, >99:1 dr

Mp 220-221 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.44 (s, 1H), 7.55 – 7.44 (m, 6H), 7.29 (td, *J* = 9.1, 2.6 Hz, 1H), 7.07 (dd, *J* = 8.6, 4.4 Hz, 1H), 4.68 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.48 (dt, *J* = 13.8, 6.7 Hz, 2H), 2.77 – 2.64 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.89, 175.21, 159.35, 157.76, 138.83, 135.52, 129.89, 129.44, 129.39, 127.86, 127.80, 118.10, 117.95, 113.01, 112.88, 112.83, 112.54, 112.49, 112.34, 53.78, 47.07, 42.99, 42.26.

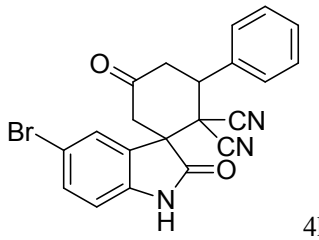


4g

5'-chloro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Yellow solid, 99% yield 88:12 dr

Mp 220-222 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.55 (s, 1H), 7.55 – 7.43 (m, 7H), 7.08 (d, *J* = 8.4 Hz, 1H), 4.66 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.52 – 3.44 (m, 2H), 2.77 – 2.66 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.92, 175.01, 141.54, 135.48, 131.41, 129.92, 129.44, 129.41, 128.25, 127.18, 125.18, 112.94, 112.88, 112.33, 53.61, 47.07, 43.00, 42.18, 41.73.

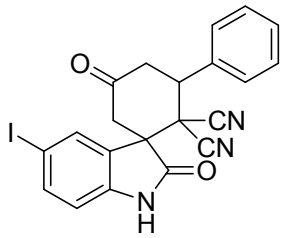


4h

5'-bromo-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 92% yield, 95:5 dr

Mp 146-148 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.55 (s, 1H), 7.81 (d, *J* = 1.5 Hz, 1H), 7.63 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.51 – 7.44 (m, 3H), 7.03 (d, *J* = 8.4 Hz, 1H), 4.67 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.48 (dd, *J* = 27.6, 15.1 Hz, 2H), 2.78 – 2.64 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.86, 174.89, 141.95, 135.49, 134.24, 129.91, 129.40, 128.63, 127.88, 114.77, 113.39, 112.88, 112.35, 53.57, 47.09, 43.02, 42.24, 41.76.

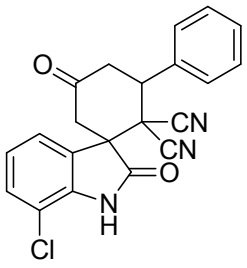


4i

5'-iodo-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 99% yield, 87:13 dr

Mp 190-192 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.55 (s, 1H), 7.97 (d, *J* = 1.2 Hz, 1H), 7.79 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.55 – 7.45 (m, 5H), 6.92 (d, *J* = 8.2 Hz, 1H), 4.67 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.52 – 3.44 (m, 2H), 2.77 – 2.65 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.93, 174.72, 142.34, 139.99, 135.49, 133.34, 132.05, 129.91, 129.43, 129.41, 128.89, 113.75, 112.92, 112.36, 53.34, 47.10, 43.01, 42.26, 41.75.

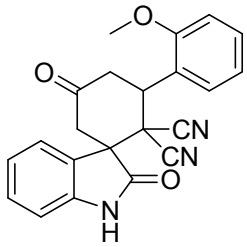


4j

7'-chloro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Brown solid, 73% yield, 88:12 dr.

Mp 238-240 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.88 (s, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.49 (ddd, *J* = 13.7, 10.2, 5.2 Hz, 6H), 7.23 (t, *J* = 8.0 Hz, 1H), 4.66 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.55 – 3.40 (m, 2H), 2.81 – 2.49 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.87, 175.31, 140.40, 135.48, 131.43, 129.91, 129.45, 129.39, 129.16, 128.18, 124.65, 123.56, 115.55, 112.92, 112.33, 54.23, 47.17, 43.04, 42.30, 41.73.

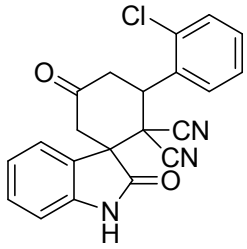


4k

3-(2-methoxyphenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 85% yield, 82:18 dr

Mp 151-153 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.37 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.61 (m, 1H), 7.43 – 7.39 (m, 2H), 7.20 – 7.16 (m, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 7.8 Hz, 1H), 5.49 (dd, *J* = 14.1, 4.0 Hz, 1H), 3.76 (s, 3H), 3.59 – 3.41 (m, 2H), 2.63 – 2.53 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.44, 175.15, 157.46, 142.50, 131.33, 130.85, 128.56, 126.64, 124.76, 123.99, 123.22, 121.17, 113.01, 112.84, 112.01, 111.23, 56.06, 53.30, 46.72, 42.79, 41.83, 33.61.



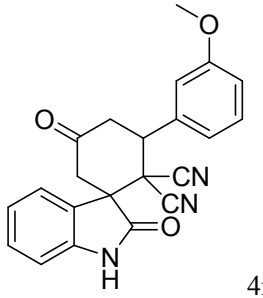
4l

3-(2-chlorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 99% yield, >99:1 dr

Mp 200-202 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.42 (s, 1H), 7.88 – 7.84 (m, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.49 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 5.62 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.46 (t, *J* = 14.8 Hz, 2H), 2.72 – 2.64 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.72,

175.11, 142.49, 134.69, 133.43, 131.48, 131.37, 130.63, 129.77, 128.47, 126.34, 124.82, 123.33, 112.64, 112.33, 111.37, 53.24, 46.25, 42.72, 42.09, 37.27.

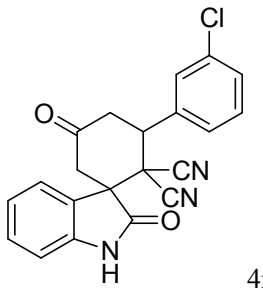


4m

3-(4-methoxyphenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 95% yield, 95:5 dr

Mp 156-158 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.37 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.41 (dt, *J* = 15.4, 7.8 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.09 – 7.01 (m, 4H), 4.65 (dd, *J* = 13.6, 4.1 Hz, 1H), 4.29 (dd, *J* = 13.8, 4.0 Hz, 1H), 3.79 (s, 3H), 3.51 – 3.38 (m, 2H), 2.75 – 2.55 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.06, 175.24, 159.87, 142.46, 137.16, 130.47, 126.51, 124.83, 123.34, 121.50, 115.31, 113.07, 112.63, 111.38, 55.67, 53.48, 47.15, 43.03, 42.66, 41.88.



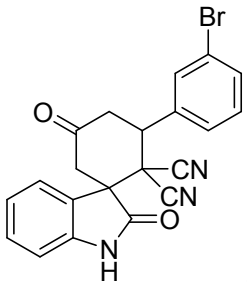
4n

3-(3-chlorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-purple solid, 86% yield, >99:1 dr

Mp 215-217 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.41 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.61 (s,

1H), 7.56 – 7.49 (m, 3H), 7.43 (td, *J* = 7.8, 1.1 Hz, 1H), 7.20 (td, *J* = 7.7, 0.8 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 4.71 (dd, *J* = 13.6, 4.2 Hz, 1H), 3.55 – 3.48 (m, 1H), 3.41 (d, *J* = 16.0 Hz, 1H), 2.75 (dd, *J* = 15.6, 4.1 Hz, 1H), 2.62 (dd, *J* = 16.0, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.88, 175.14, 142.46, 137.98, 133.95, 131.48, 131.21, 129.92, 129.37, 128.41, 126.39, 124.86, 123.39, 112.93, 112.34, 111.42, 53.38, 46.99, 42.65, 42.57, 41.42.

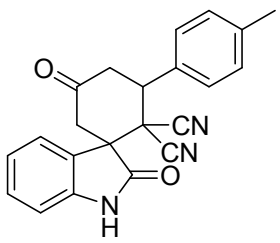


4o

3-(3-bromophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-purple solid, 85% yield, 99:1 dr

Mp 145-147 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.41 (s, 1H), 7.74 (s, 1H), 7.70 – 7.64 (m, 2H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.45 (dt, *J* = 19.2, 7.8 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 4.71 (dd, *J* = 13.6, 3.9 Hz, 1H), 3.51 (t, *J* = 14.7 Hz, 1H), 3.41 (d, *J* = 16.0 Hz, 1H), 2.80 – 2.72 (m, 1H), 2.62 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.82, 175.14, 142.47, 138.21, 132.82, 132.23, 131.48, 131.46, 128.75, 126.39, 124.85, 123.39, 122.46, 112.93, 112.34, 111.43, 53.40, 47.02, 42.62, 41.44.

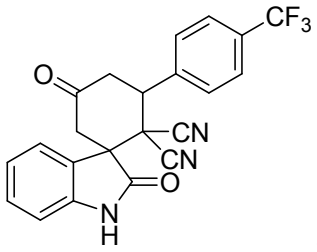


4p

2',5-dioxo-3-(p-tolyl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 97% yield, 87:13 dr

Mp 175-177 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.37 (s, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.37 (m, 3H), 7.27 (dd, *J* = 15.5, 8.1 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 4.64 (dd, *J* = 13.7, 4.1 Hz, 1H), 3.50 – 3.38 (m, 2H), 2.71 – 2.55 (m, 2H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.17, 175.29, 142.45, 139.39, 132.68, 131.38, 129.92, 129.26, 126.56, 124.81, 123.33, 113.13, 112.60, 111.36, 53.45, 47.40, 42.75, 42.67, 41.91, 21.12.

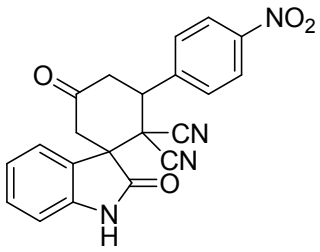


4q

2',5-dioxo-3-(4-(trifluoromethyl)phenyl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 95% yield, 87:13 dr

Mp 200-202 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.44 (s, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 4.82 (dd, *J* = 13.6, 4.1 Hz, 1H) , 3.57 – 3.50 (m, 1H), 3.45 (d, *J* = 16.0 Hz, 1H), 2.82 – 2.76 (m, 1H), 2.64 (dd, *J* = 16.0, 1.3 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.81, 175.18, 142.46, 140.13, 131.51, 130.72, 132.60, 126.36, 126.27, 125.30, 124.86, 123.50, 123.40, 112.86, 112.27, 111.44, 53.42, 46.78, 42.77, 42.58, 41.31.

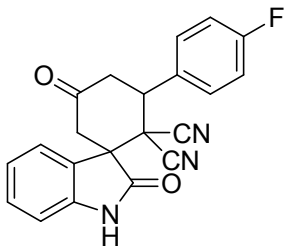


4r

3-(4-nitrophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Yellow solid, 98% yield, 87:13 dr

Mp 203-205 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.45 (s, 1H), 8.35 (d, *J* = 8.8 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 4.88 (dd, *J* = 13.6, 4.1 Hz, 1H), 3.58 – 3.51 (m, 1H), 3.46 (d, *J* = 16.1 Hz, 1H), 2.81 (dd, *J* = 15.7, 2.4 Hz, 1H), 2.66 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.58, 175.14, 148.61, 142.61, 142.47, 131.54, 131.18, 126.31, 124.87, 124.31, 123.42, 112.76, 112.16, 111.46, 53.43, 46.57, 42.68, 42.58, 41.22.



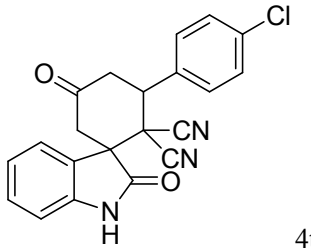
4s

3-(4-fluorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 95% yield, 94:6 dr

Mp 187-189 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.40 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.7 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 4.71 (dd, *J* = 13.6, 4.1 Hz, 1H), 3.51 – 3.45 (m, 1H), 3.42 (d, *J* = 16.0 Hz, 1H), 2.72 (dd, *J* = 15.7, 2.5 Hz, 1H), 2.61 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ

201.98, 175.22, 163.83, 162.19, 142.45, 131.71, 131.65, 131.43, 126.47, 124.83, 123.35, 116.33, 116.19, 113.02, 112.44, 111.39, 53.35, 47.28, 42.60, 42.37, 41.83.

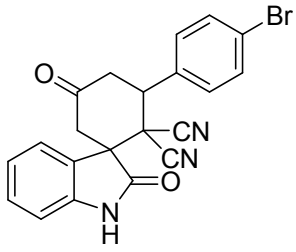


4t

3-(4-chlorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 81% yield, 94:6 dr

Mp 134-136 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.40 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.52 (m, 4H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 4.72 (dd, *J* = 13.6, 4.2 Hz, 1H), 3.52 – 3.39 (m, 2H), 2.78 – 2.57 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.85, 175.20, 142.46, 134.68, 134.60, 131.45, 131.36, 129.38, 126.44, 124.83, 123.37, 112.96, 112.39, 111.41, 53.39, 47.08, 42.63, 42.49, 41.60.



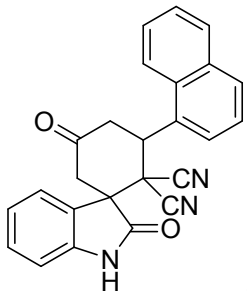
4u

3-(4-bromophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 81% yield, 92:8 dr

Mp 143-145 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.40 (s, 1H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.67 (t, *J* = 6.7 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.06 (t,

J = 8.2 Hz, 1H), 4.71 (dd, *J* = 13.6, 4.1 Hz, 1H), 4.36 (dd, *J* = 13.8, 4.1 Hz, 1H), 3.50 – 3.40 (m, 2H), 2.77 – 2.70 (m, 1H), 2.61 (dd, *J* = 16.0, 1.5 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.83, 175.20, 142.45, 135.01, 132.33, 131.64, 131.45, 126.43, 124.83, 123.38, 123.30, 112.96, 112.38, 111.42, 53.40, 46.99, 42.64, 42.56, 41.54.

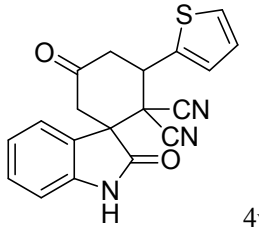


4v

3-(naphthalen-1-yl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

White solid, 82% yield, >99:1 dr

Mp 245-247 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ = 11.56 (s, 1H), 8.12 – 8.01 (m, 3H), 7.98 (d, J=7.3, 1H), 7.76 – 7.68 (m, 2H), 7.65 (t, J=7.2, 1H), 7.60 (t, J=7.4, 1H), 7.44 (t, J=7.7, 1H), 7.22 (t, J=7.6, 1H), 7.08 (d, J=7.8, 1H), 6.05 (dd, J=13.7, 3.5, 1H), 3.70 – 3.61 (m, 1H), 3.54 (d, J=16.1, 1H), 2.83 – 2.72 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ = 202.33, 175.88, 142.36, 134.08, 132.03, 131.84, 131.45, 130.26, 129.57, 127.22, 126.75, 126.55, 126.54, 125.93, 124.87, 123.46, 122.75, 112.90, 112.82, 111.44, 53.58, 47.02, 42.97, 42.91, 35.03.

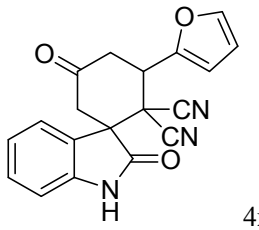


4w

2',5-dioxo-3-(thiophen-2-yl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Yellow solid, 72% yield, >99:1 dr

Mp 230-232 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.44 (s, 1H), 7.66 (t, *J* = 6.6 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 3.2 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.17 – 7.13 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 4.99 (dd, *J* = 13.4, 4.1 Hz, 1H), 3.43 (d, *J* = 16.0 Hz, 1H), 3.37 – 3.29 (m, 1H), 2.88 (dd, *J* = 15.7, 2.5 Hz, 1H), 2.62 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.07, 175.24, 142.45, 138.26, 131.48, 128.78, 127.89, 127.71, 126.45, 124.75, 123.44, 113.17, 112.57, 111.47, 53.24, 47.86, 43.62, 42.55, 39.30.

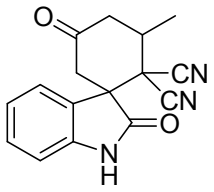


4x

3-(furan-2-yl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 76% yield, 99:1 dr

Mp 237-239 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.42 (s, 1H), 7.79 (d, *J* = 1.1 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.44 (td, *J* = 7.8, 0.8 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.70 (d, *J* = 3.3 Hz, 1H), 6.56 (dd, *J* = 3.2, 1.8 Hz, 1H), 4.84 (dd, *J* = 13.5, 4.3 Hz, 1H), 3.41 (d, *J* = 16.1 Hz, 1H), 3.30 – 3.23 (m, 1H), 2.84 (dd, *J* = 16.0, 2.6 Hz, 1H), 2.61 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 201.28, 175.24, 149.61, 144.67, 142.47, 131.48, 126.35, 124.74, 123.43, 112.98, 112.33, 111.51, 111.45, 110.67, 53.07, 45.46, 42.61, 40.58, 38.03.

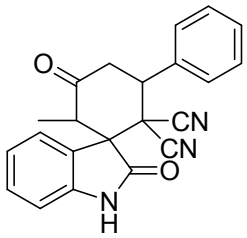


4y

3-methyl-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile[2]

Pale-yellow solid, 32% yield, 99:1 dr

Mp 170-172 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.27 (s, 1H), 7.64 (t, *J* = 6.2 Hz, 1H), 7.43 (d, *J* = 6.9 Hz, 1H), 7.20 (d, *J* = 6.8 Hz, 1H), 7.03 (t, *J* = 6.4 Hz, 1H), 3.51 (dd, *J* = 11.4, 5.7 Hz, 1H), 3.26 (d, *J* = 16.0 Hz, 1H), 2.65 (d, *J* = 15.8 Hz, 1H), 2.56 – 2.47 (m, 2H), 1.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 202.17, 175.12, 142.41, 131.34, 126.63, 124.61, 123.29, 113.63, 112.29, 111.30, 53.05, 46.44, 43.68, 42.54, 33.87, 18.28.



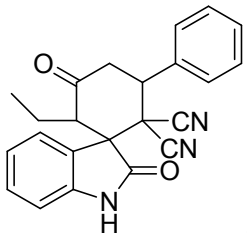
4z

6-methyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile

White solid, 89% yield, 58:42 dr

Mp 155-157 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 11.47 (s, 1H), 7.69 – 7.37 (m, 7H), 7.25 – 7.04 (m, 2H), 4.64-4.31 (m, 1H), 3.67 – 3.43 (m, 2H), 2.86-2.74 (m, 1H), 0.63 (dd, J = 48.6, 6.5 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 203.18, 174.11, 142.98, 135.59, 131.42, 129.84, 129.58, 129.38, 129.07, 124.68, 123.62, 113.07, 111.37, 58.62, 48.15, 45.12, 42.95, 41.91, 9.33.

MS(ESI) m/z:calcd for $C_{22}H_{17}N_3O_2$ $[M+Na]^-$ 378.1213, found 378.1221.



4aa

6-ethyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile

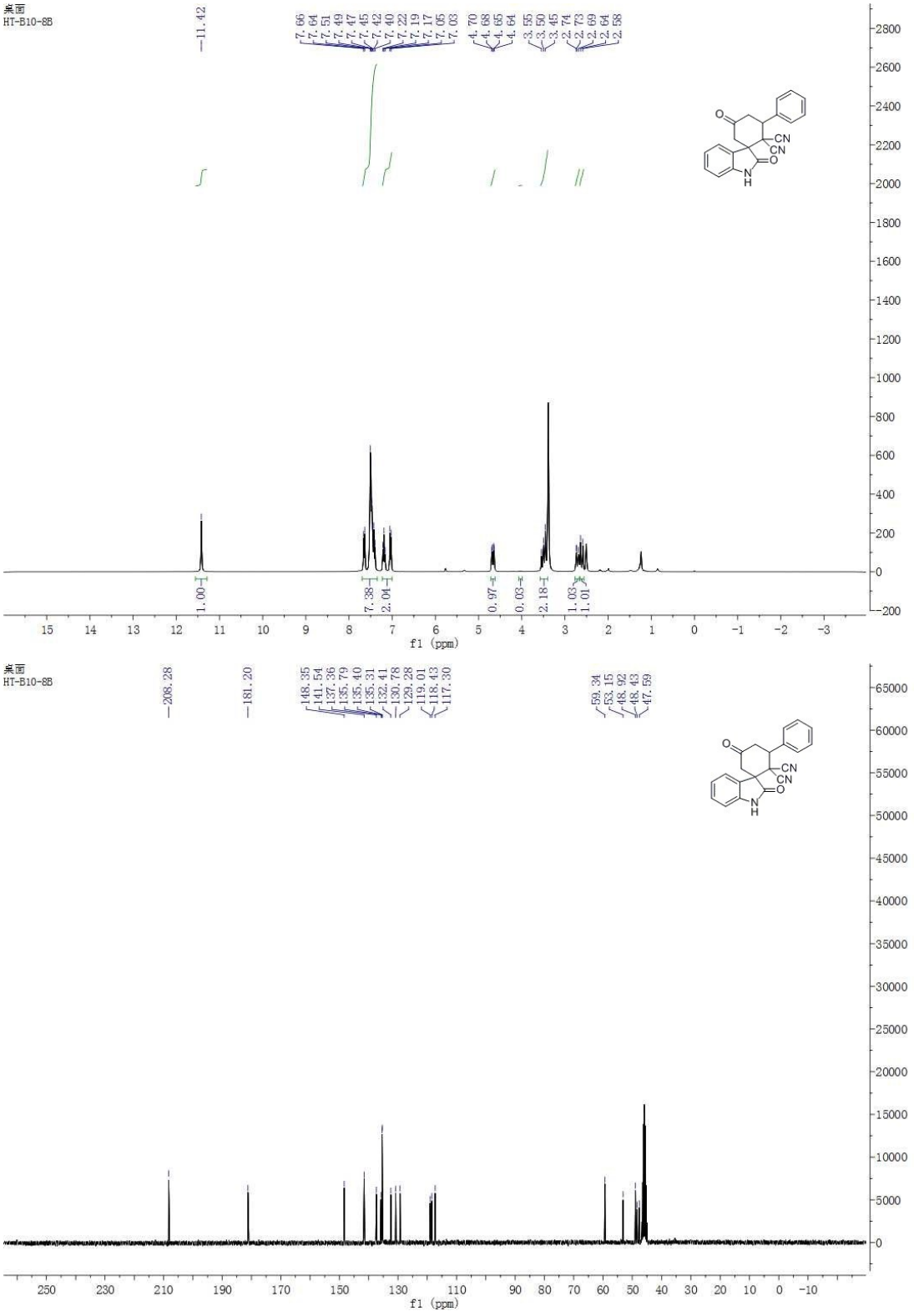
White solid, 71% yield, 73:27 dr

Mp 140-142 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.47 (s, 1H), 7.74 – 7.33 (m, 7H), 7.26 – 7.03 (m, 2H), 4.60-4.27 (m, 1H), 3.67 (dt, J = 64.2, 14.4 Hz, 1H), 3.20 (dd, J = 14.5, 5.5 Hz, 1H), 2.83-2.71 (m, 1H), 1.33 – 1.18 (m, 2H), 0.79 (dd, J = 22.7, 15.3 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 202.63, 174.08, 143.09, 131.47, 129.8, 129.56, 129.34, 129.05, 126.01, 124.70, 123.59, 112.99, 111.35, 58.43, 51.55, 48.43, 43.18, 42.53, 17.74, 13.40.

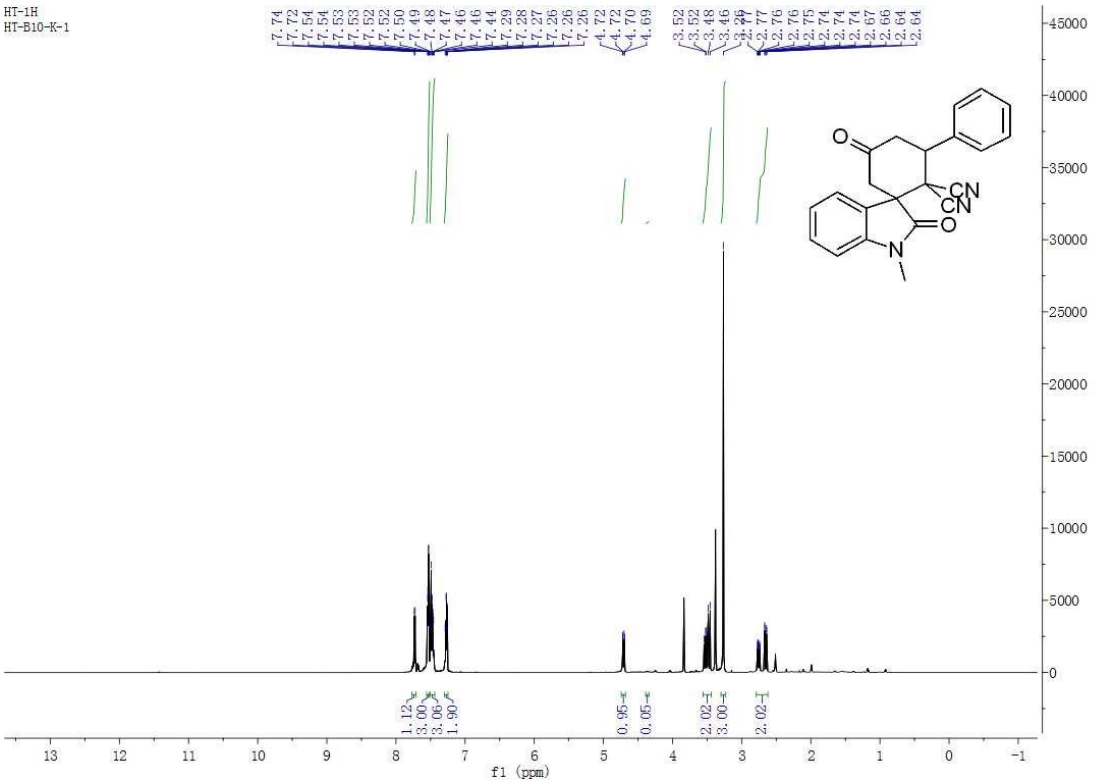
MS(ESI) m/z:calcd for $C_{23}H_{19}N_3O_2$ $[M+Na]^-$ 392.1369, found 392.1380.

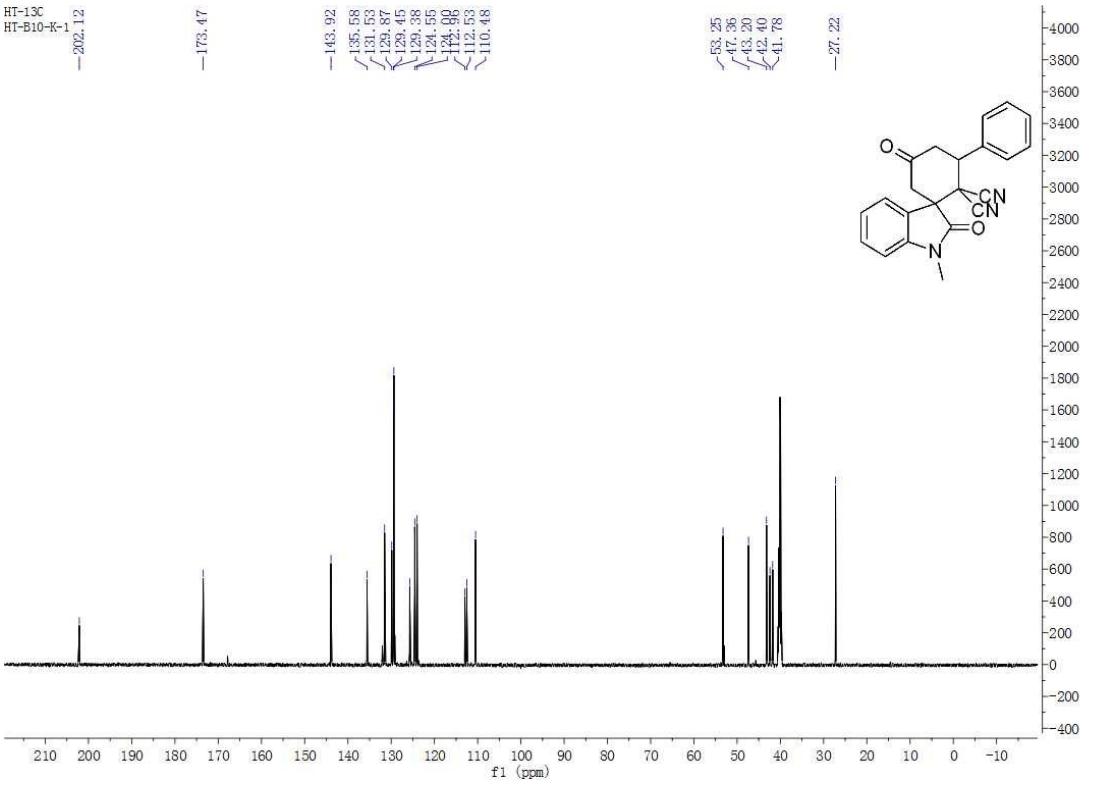
4. ^{1}H NMR, ^{13}C NMR and HRMS spectra copies of the products

4a

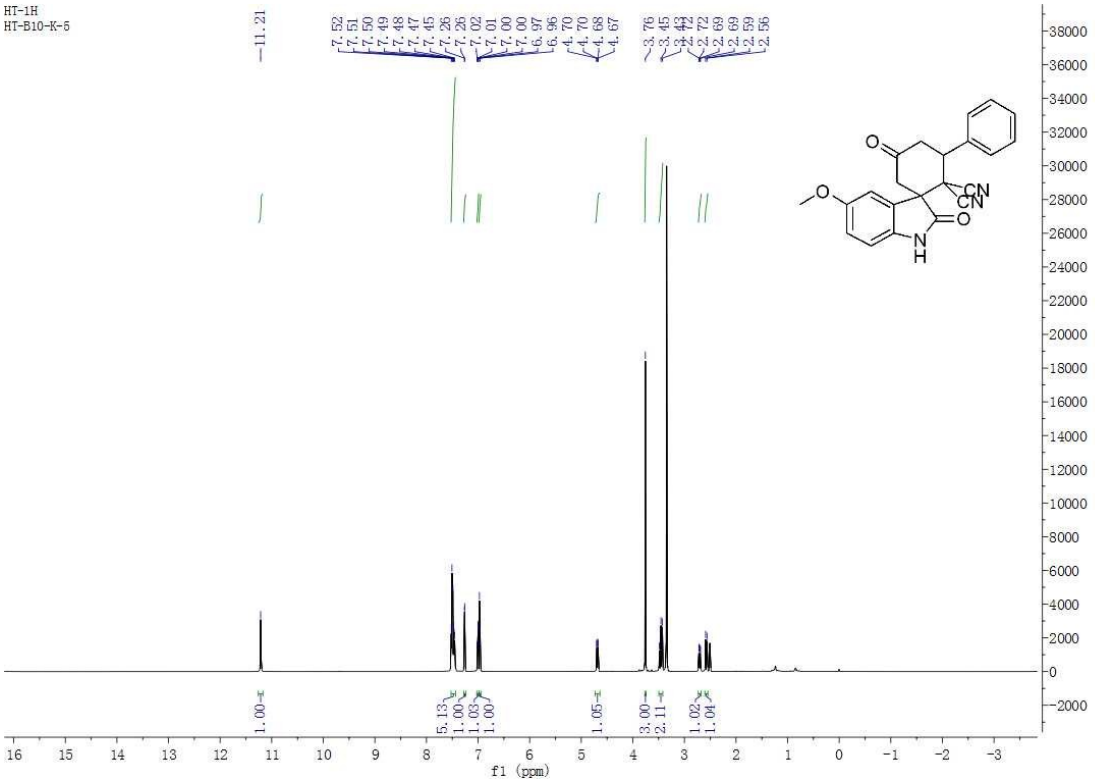


4b





4c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7.52
7.51
7.50
7.49
7.48
7.47
7.45
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7.02
7.01
7.00
7.00
6.97
6.96
4.70
4.70
4.68
4.67
3.76
3.45
3.43
2.72
2.69
2.69
2.59
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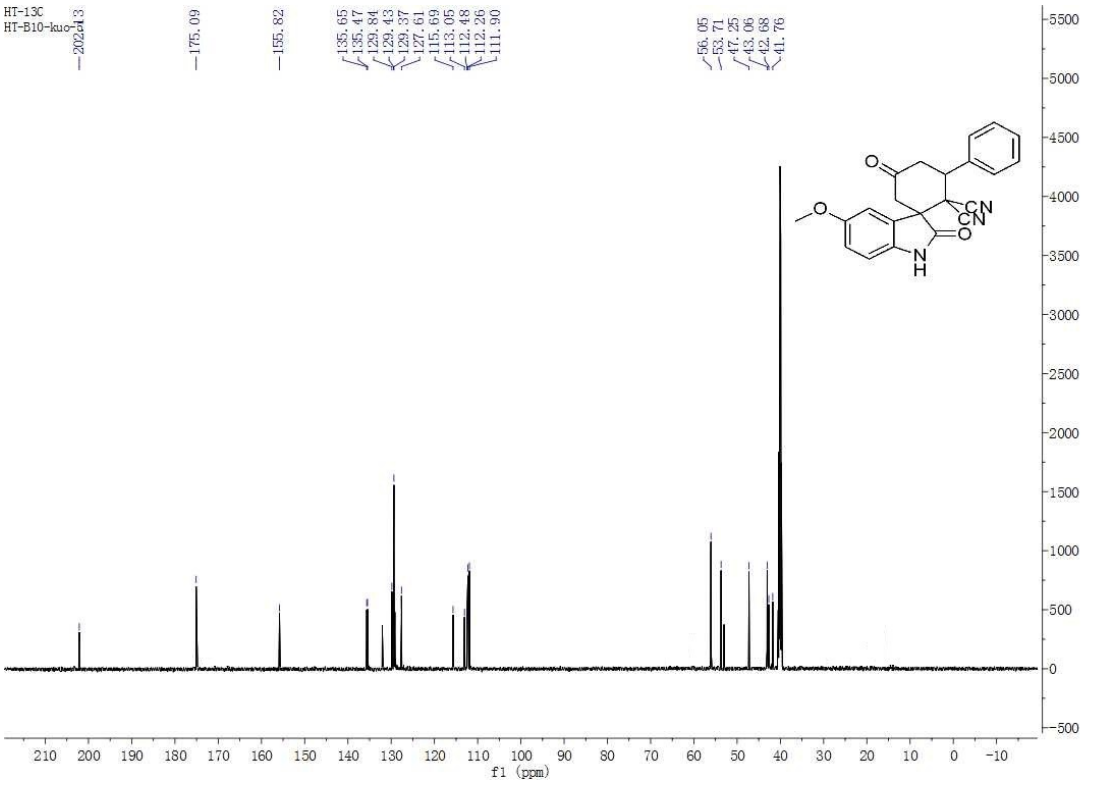
3.00
2.11
1.02
1.04
f1 (ppm)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HT-B10-kuo-
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135.65
135.47
129.84
129.43
129.37
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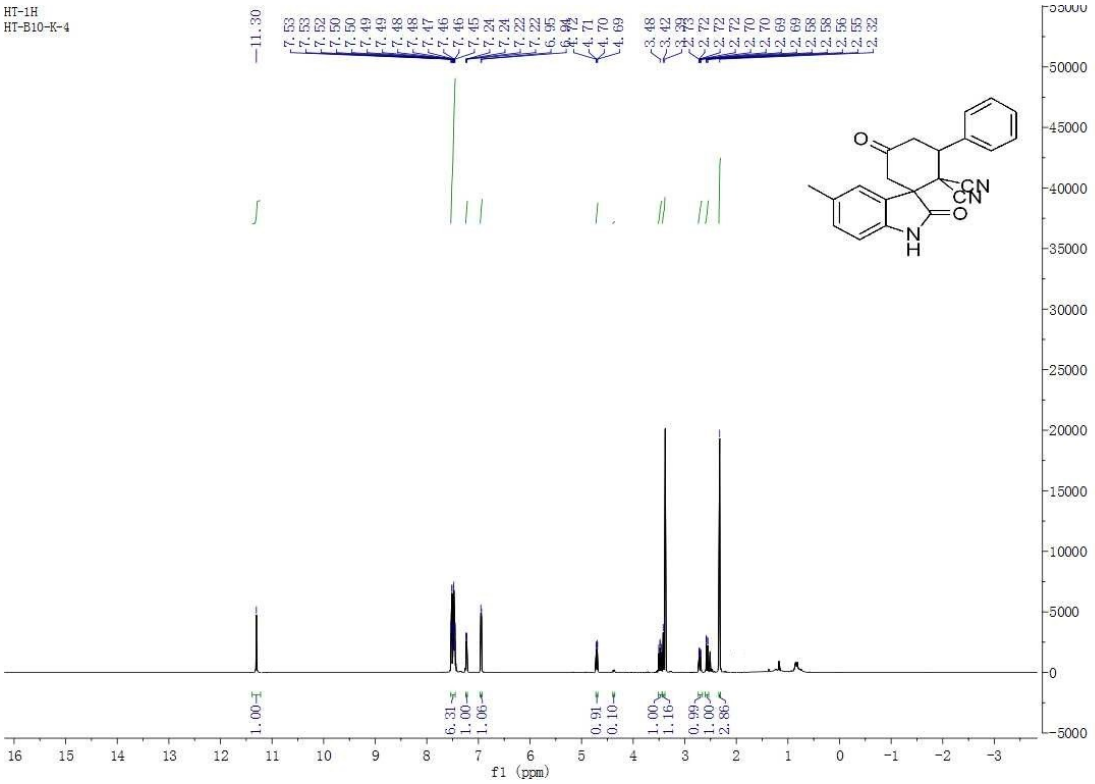
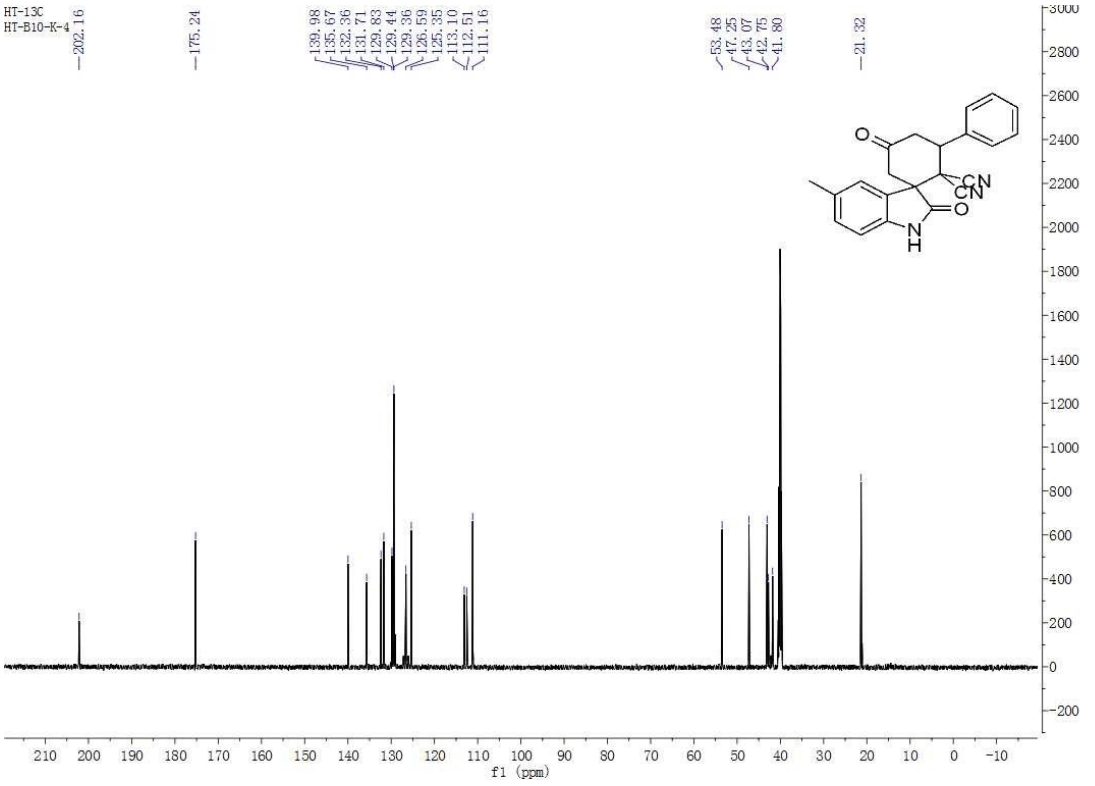
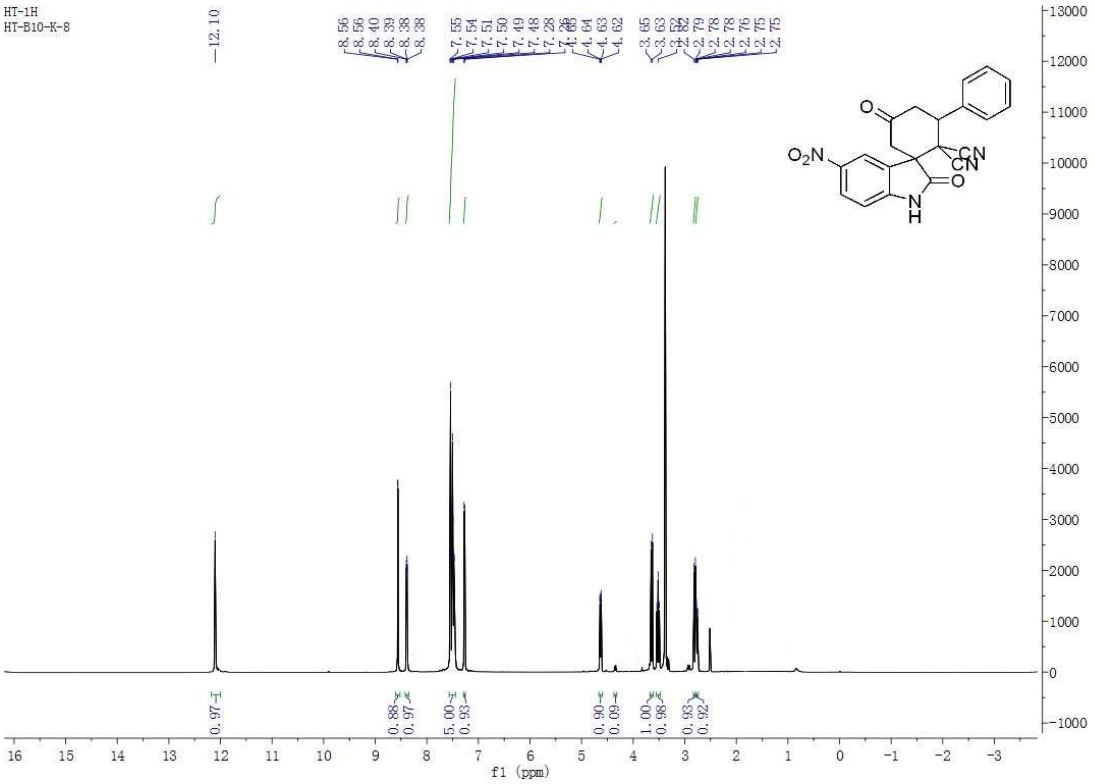
43.06
42.68
41.76
f1 (ppm)

4d





4e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HT-B10-K-8
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8.56
8.56
8.40
8.39
8.38
8.38
7.55
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7.50
7.49
7.48
7.28
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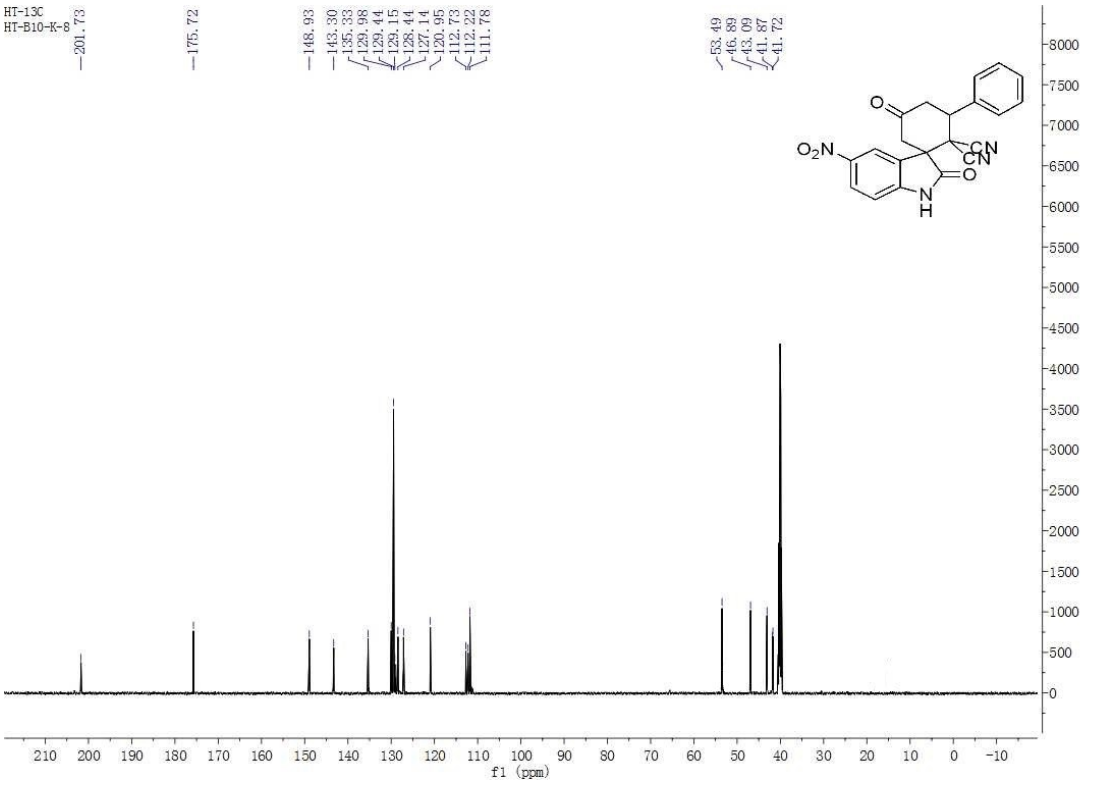
3.63
3.62
2.79
2.78
2.78
2.76
2.75
2.75
0.97
0.88
0.97
5.00
0.93
0.90
0.09
1.00
0.98
0.93
0.92
f1 (ppm)


HT-13C
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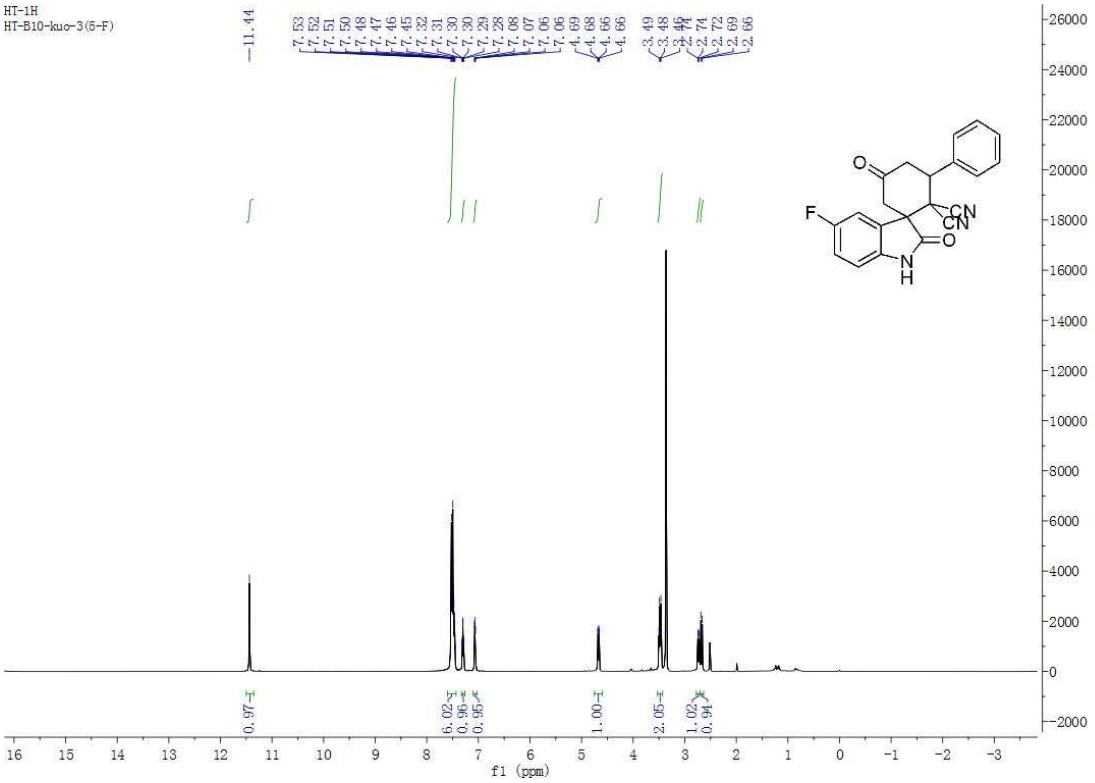
175.72
148.93
143.30
135.33
129.98
129.44
129.15
128.44
127.14
120.95
112.73
112.22
111.78
53.49
46.89
43.09
41.87
41.72
f1 (ppm)

4f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HT-B10-kuo-3(5-F)
11.44
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7.52
7.51
7.50
7.48
7.47
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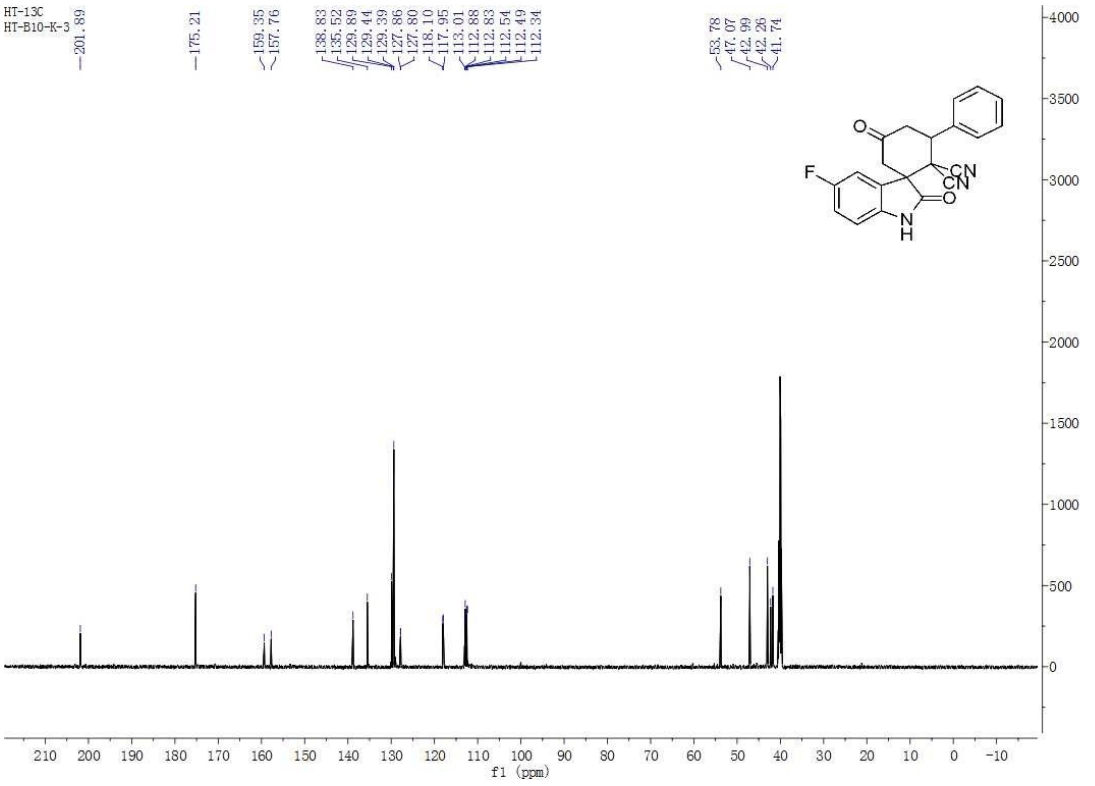
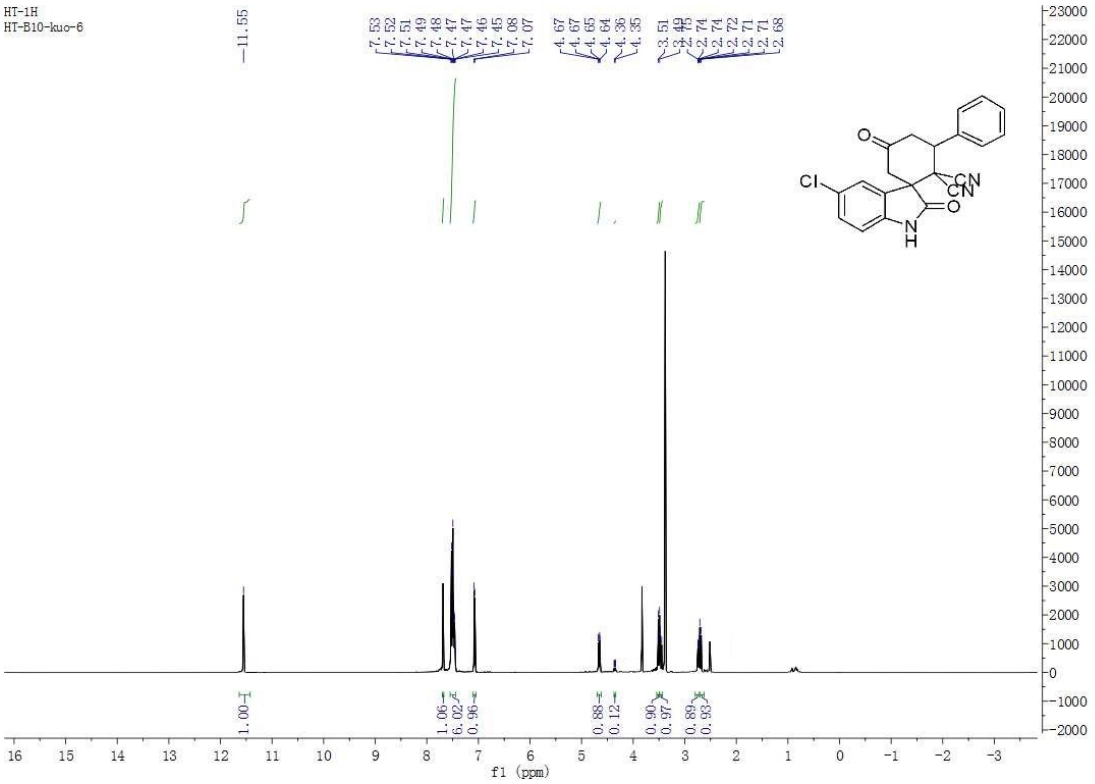
7.45
7.32
7.31
7.30
7.30
7.29
7.28
7.08
7.07
7.06
7.06
7.05
4.69
4.68
4.66
4.66
3.49
3.48
2.74
2.72
2.69
2.66
0.97
6.02
0.96
0.95
1.00
2.05
1.02
0.94
f1 (ppm)


HT-13C
HT-B10-K-3
201.89
175.21
159.35
157.76
138.83
135.52
129.89
129.44
129.39
127.86
127.80
118.10
117.95
113.01
112.88
112.83
112.54
112.49
112.34
53.78
47.07
42.99
42.26
41.74
f1 (ppm)

4g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7.52
7.51
7.49
7.48
7.47
7.47
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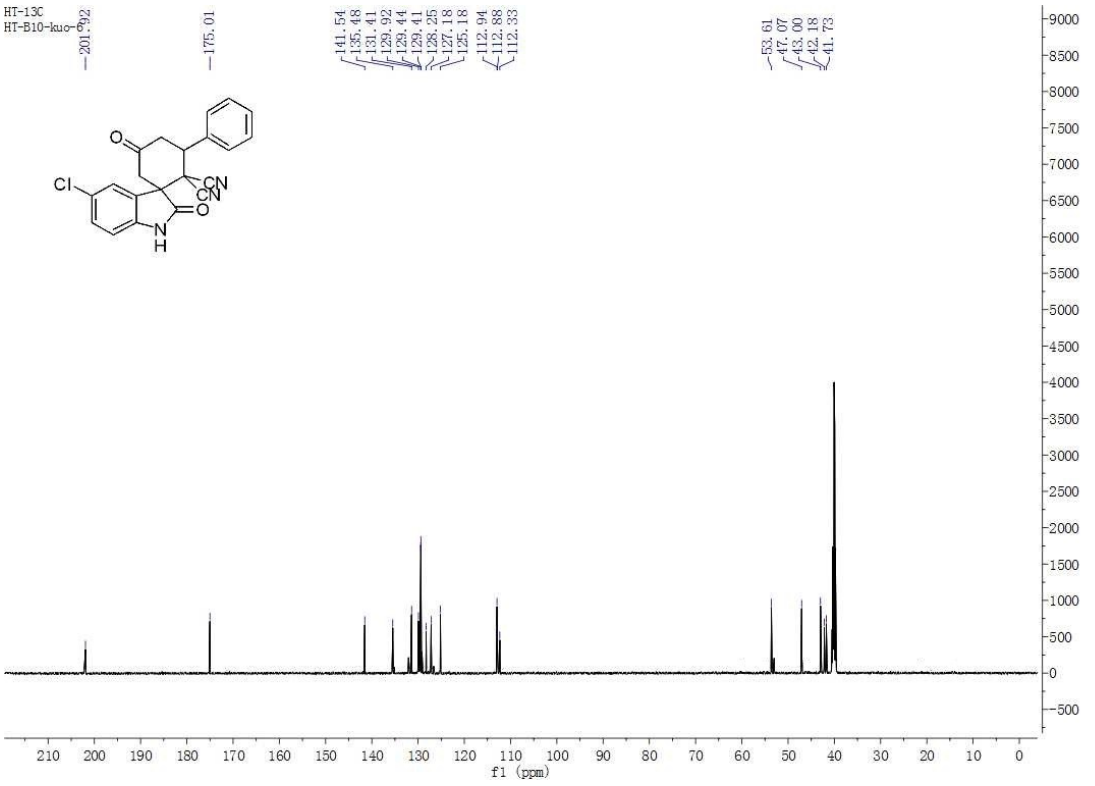
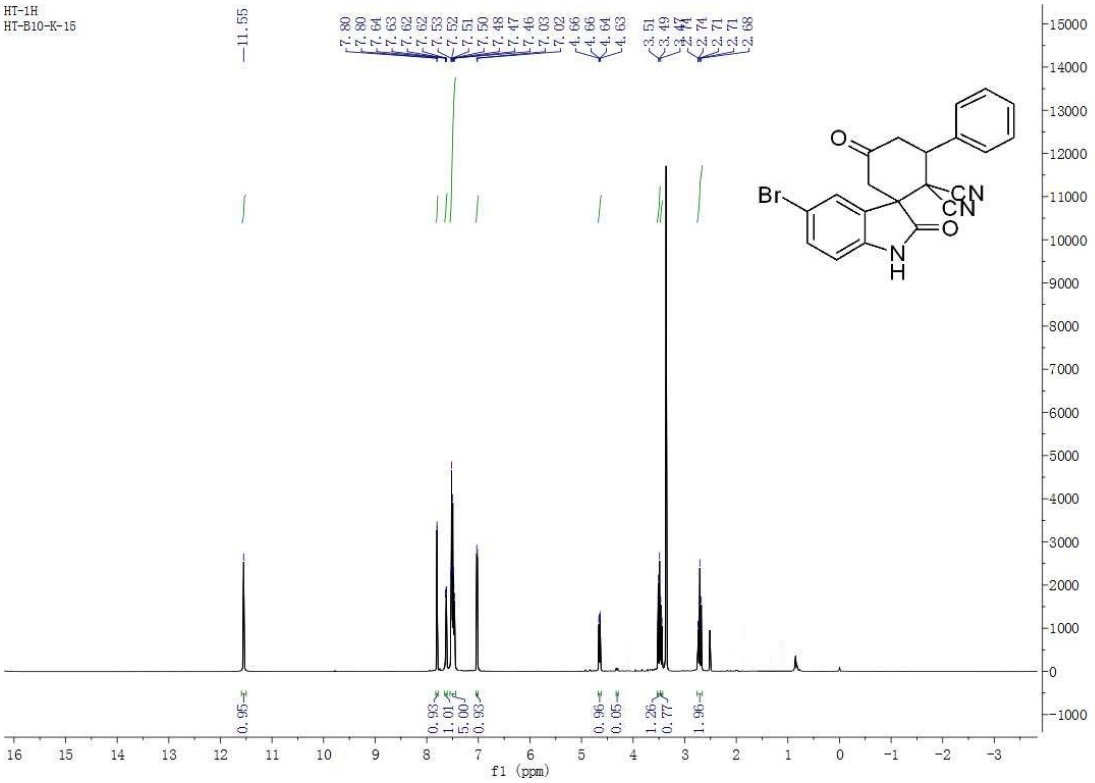
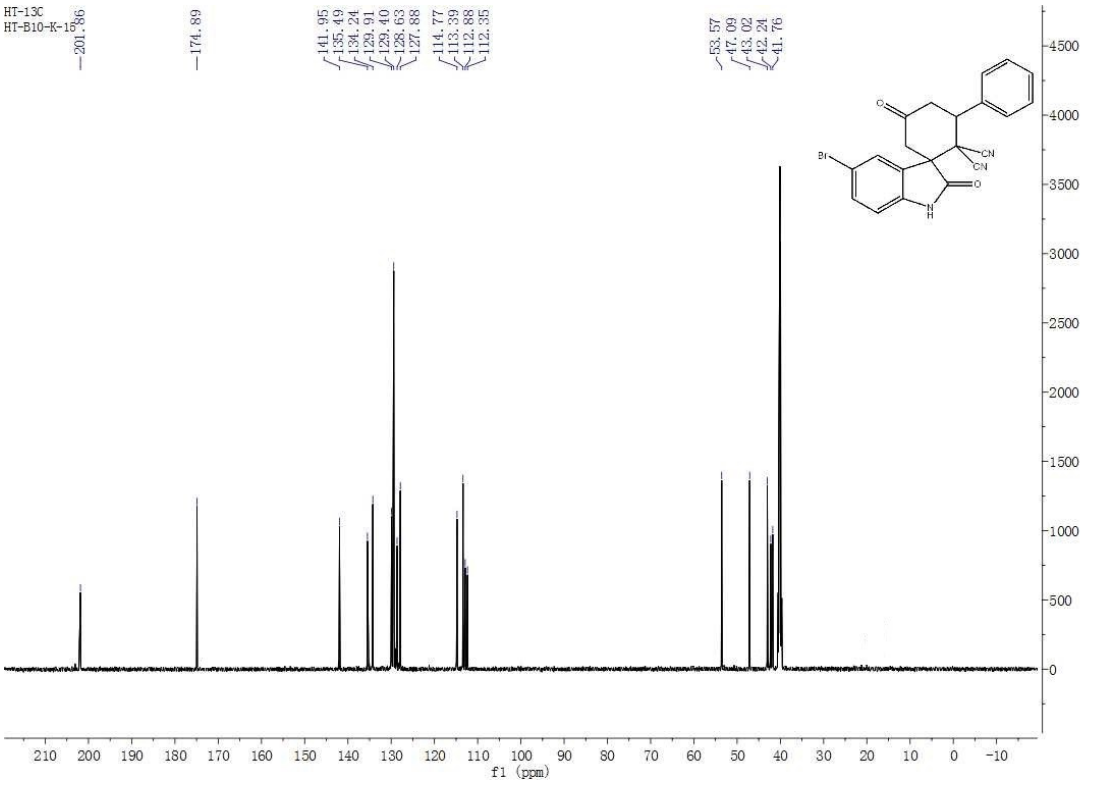
7.45
7.08
7.07
4.67
4.67
4.65
4.64
4.36
4.35
3.51
2.74
2.74
2.72
2.71
2.71
2.68
1.00
1.06
6.02
0.96
0.88
0.12
0.90
0.97
0.89
0.93
f1 (ppm)

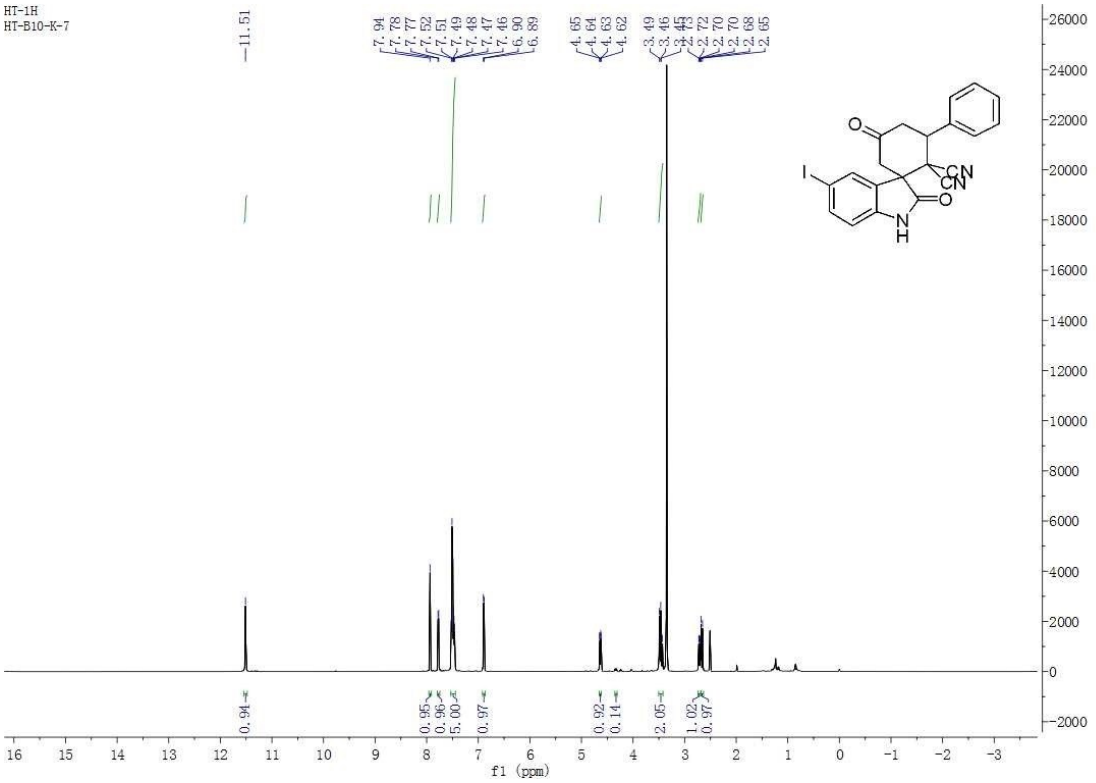

HT-13C
HT-B10-kuo-6
201.92
175.01
141.54
135.48
131.41
129.92
129.44
129.41
128.25
127.18
125.18
112.94
112.88
112.33
53.61
47.07
43.00
42.18
41.73
f1 (ppm)

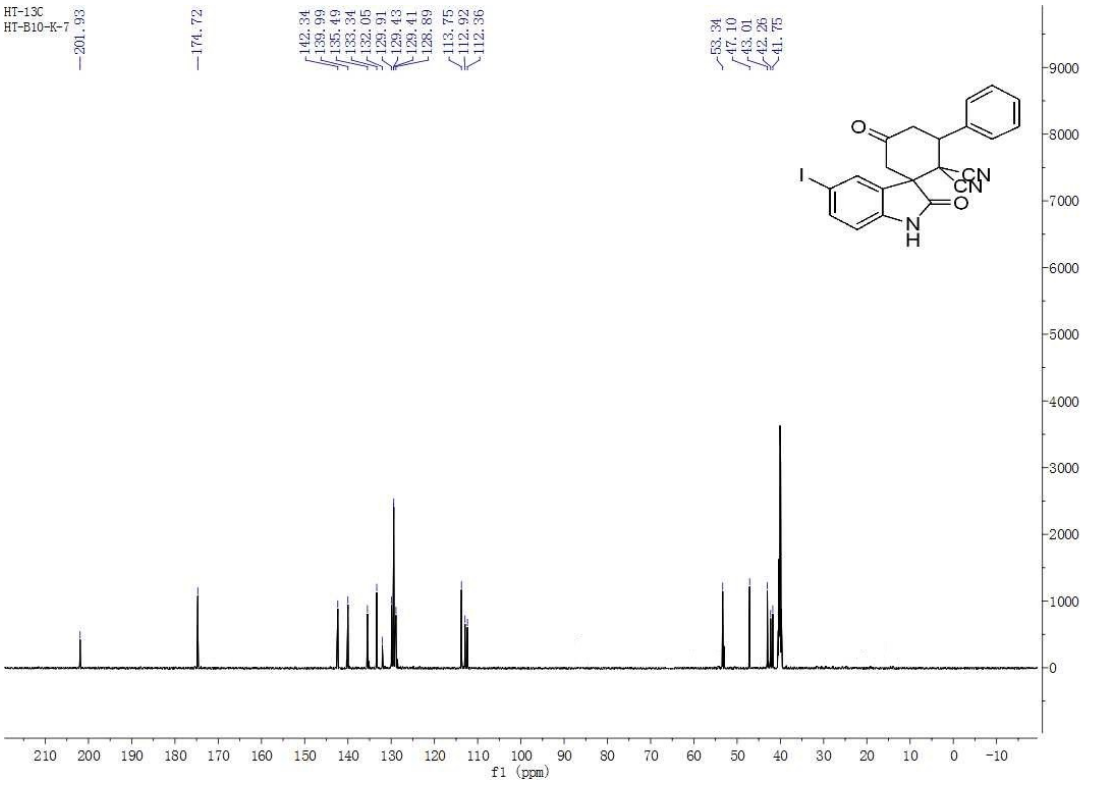
4h


HT-1H
HT-B10-K-15
11.55
7.80
7.80
7.64
7.63
7.62
7.62
7.53
7.52
7.51
7.50
7.48
7.47
7.46
7.03
7.02
4.66
4.66
4.64
4.63
3.51
3.49
2.74
2.71
2.71
2.68
0.95
0.93
1.01
5.00
0.93
0.96
0.05
1.26
0.77
1.96
f1 (ppm)

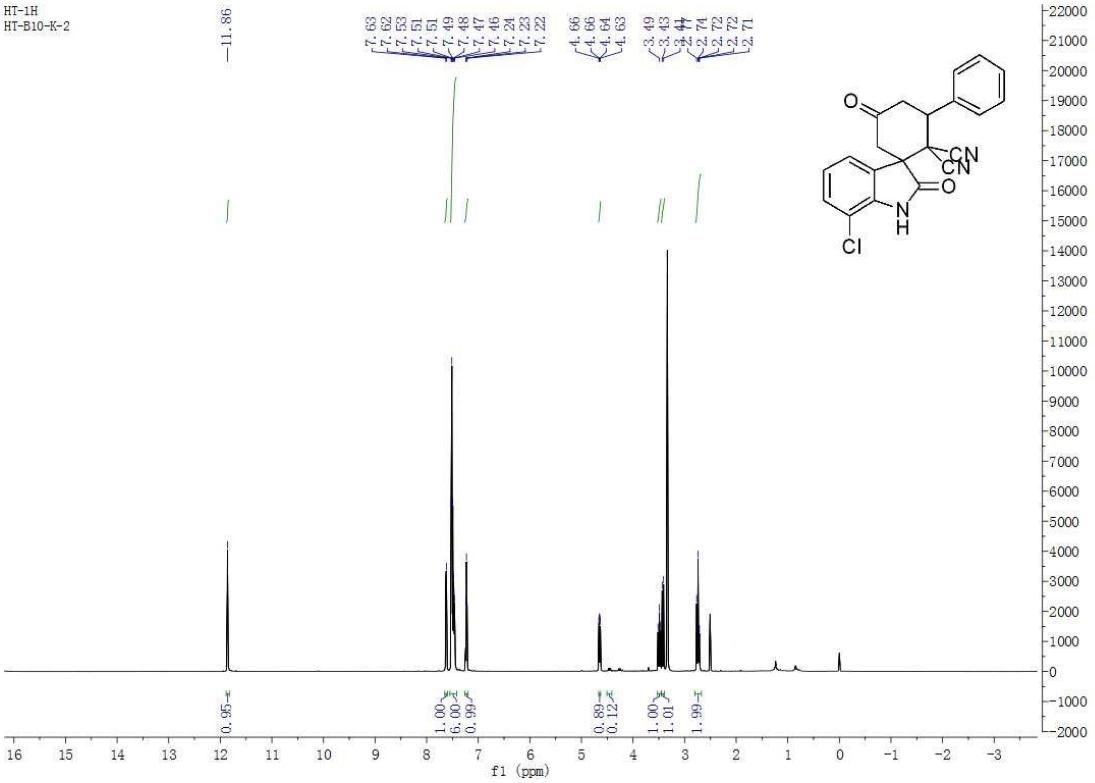

HT-13C
HT-B10-K-15
201.86
174.89
141.95
135.49
134.24
129.91
129.40
128.63
127.88
114.77
113.39
112.88
112.35
53.57
47.09
43.02
42.24
41.76
f1 (ppm)

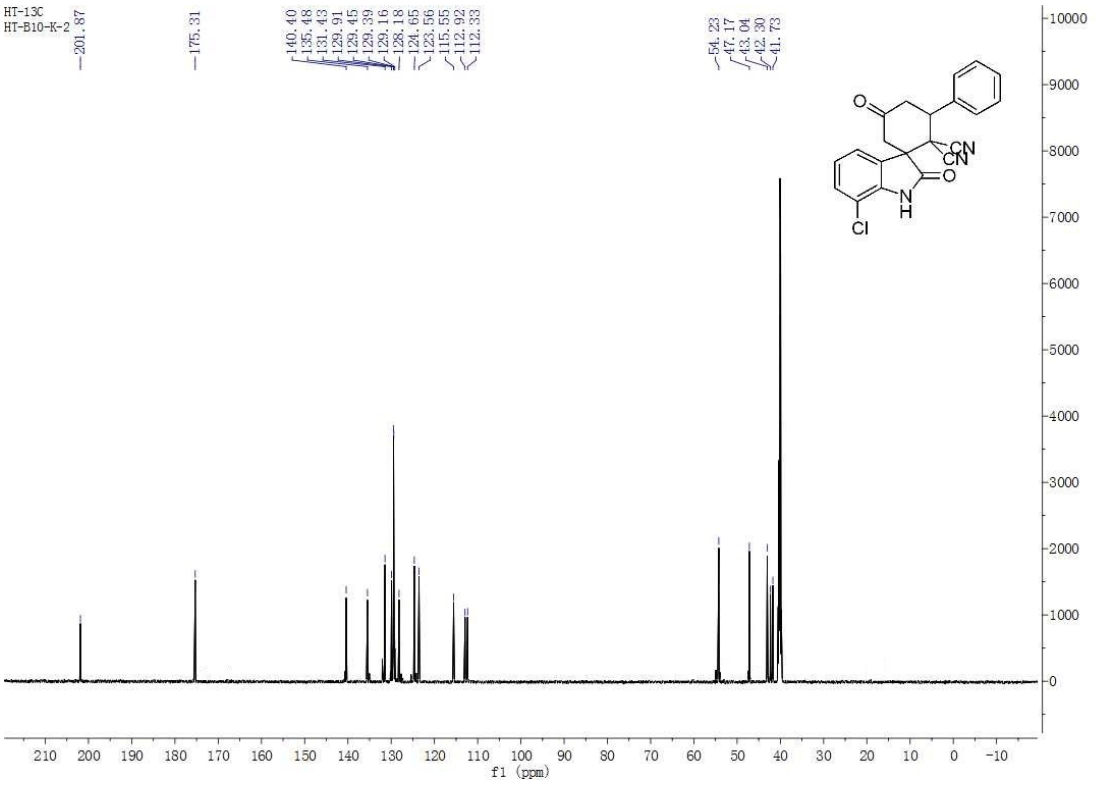
4i


HT-1H
HT-B10-K-7
11.51
7.94
7.78
7.77
7.52
7.51
7.49
7.48
7.47
7.46
6.90
6.89
4.65
4.64
4.63
4.62
3.49
3.46
3.45
2.72
2.70
2.70
2.68
2.65
0.94
0.95
0.96
5.00
0.97
0.92
0.14
2.05
1.02
0.97
f1 (ppm)

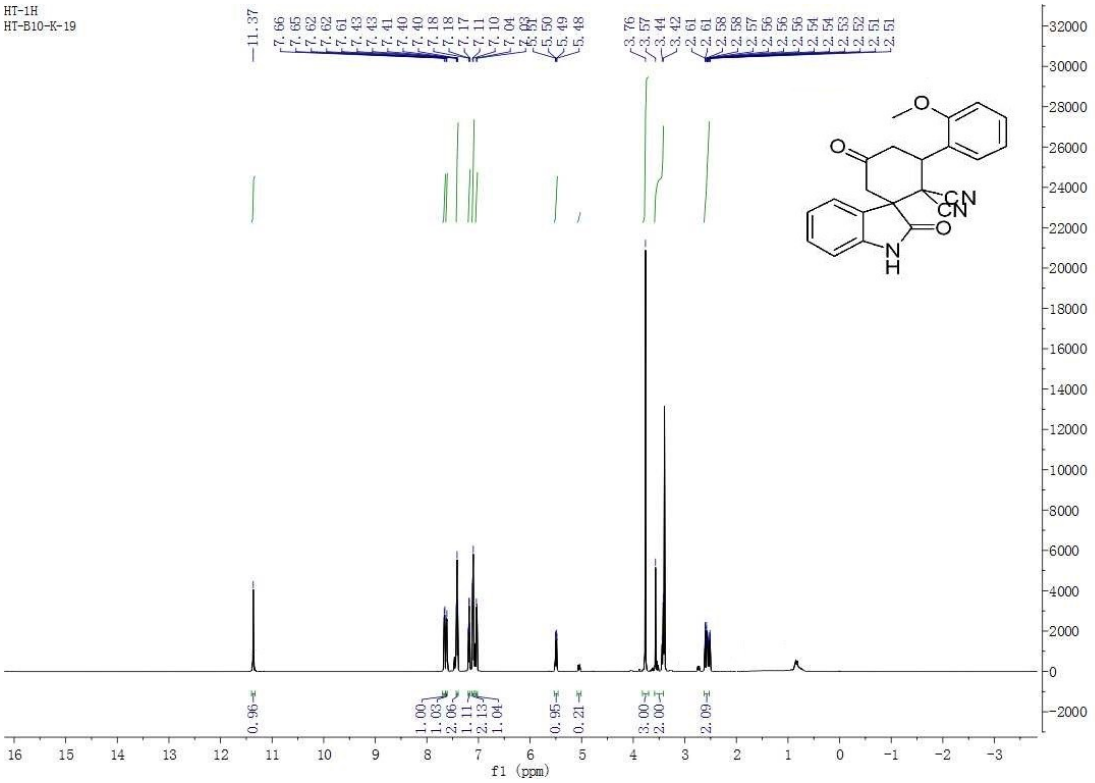

HT-13C
HT-B10-K-7
201.93
174.72
142.34
139.99
135.49
133.34
132.05
129.91
129.43
129.41
128.89
113.75
112.92
112.36
53.34
47.10
43.01
42.26
41.75
f1 (ppm)

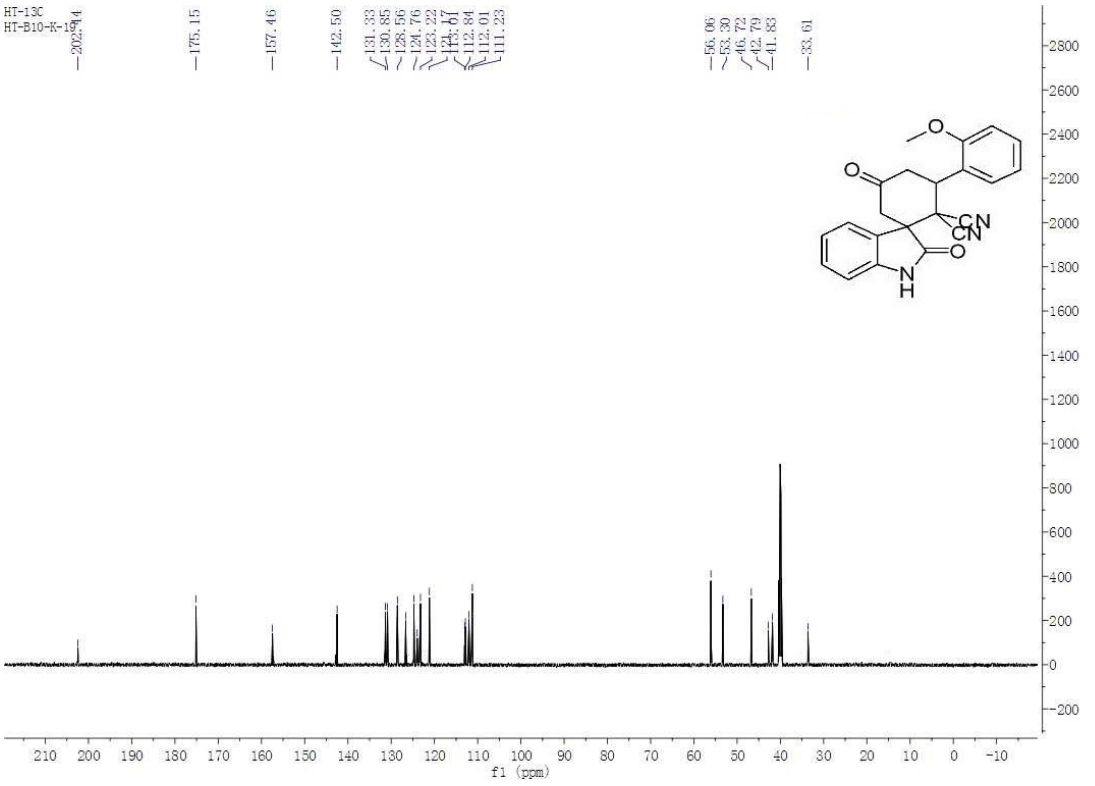
4j


HT-1H
HT-B10-K-2
11.86
7.63
7.62
7.53
7.51
7.51
7.49
7.48
7.47
7.46
7.24
7.23
7.22
4.66
4.66
4.64
4.63
3.49
3.43
2.74
2.72
2.72
2.71
0.95
1.00
6.00
0.99
0.89
0.12
1.00
1.01
1.99
f1 (ppm)

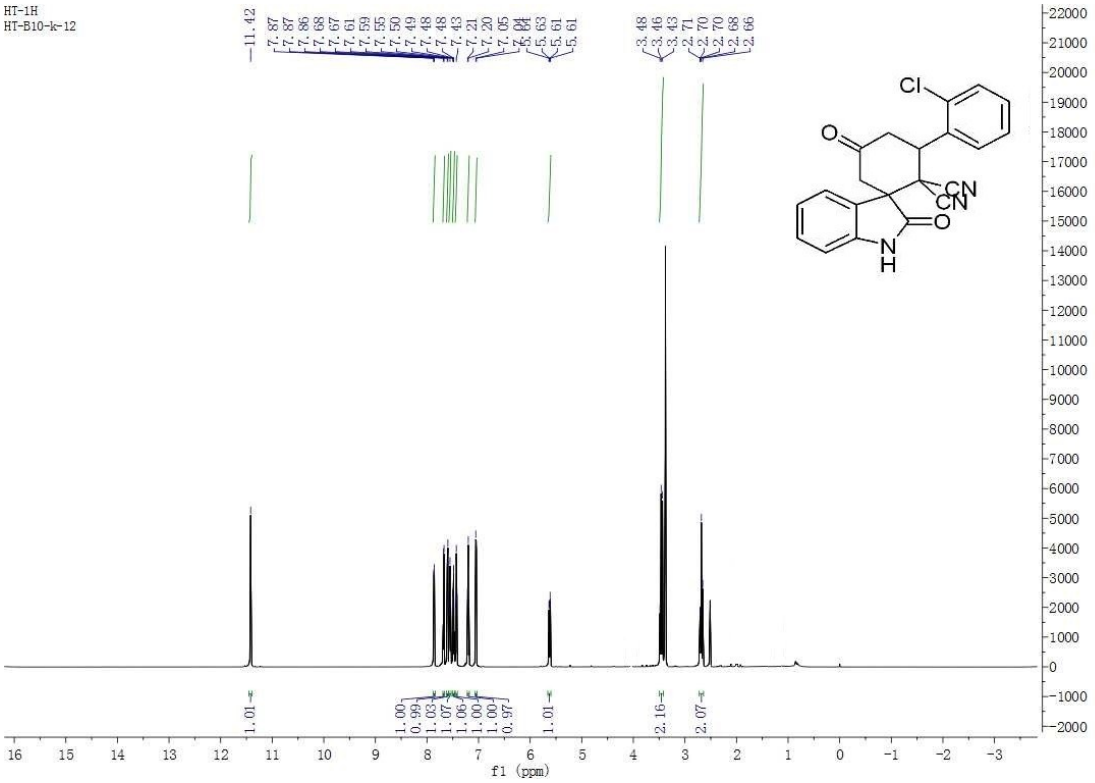

HT-13C
HT-B10-K-2
201.87
175.31
140.40
135.48
131.43
129.91
129.45
129.39
129.16
128.18
124.65
123.56
115.55
112.92
112.33
54.23
47.17
43.04
42.30
41.73
f1 (ppm)

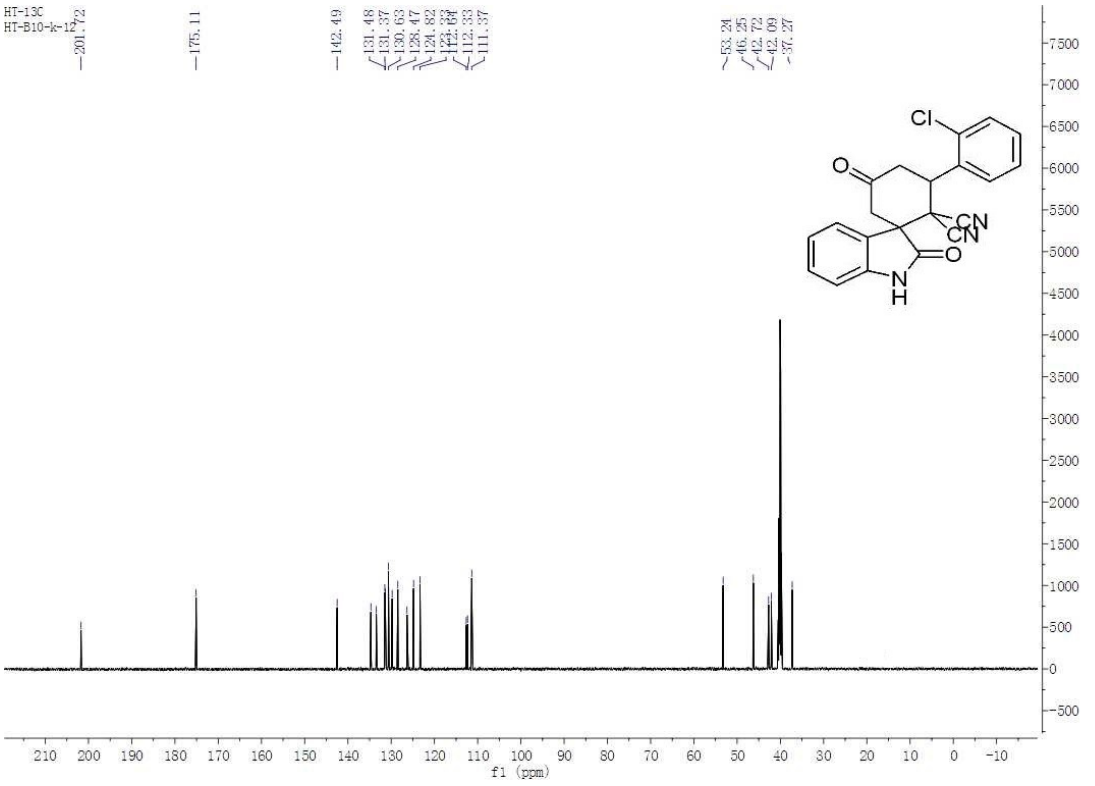
4k



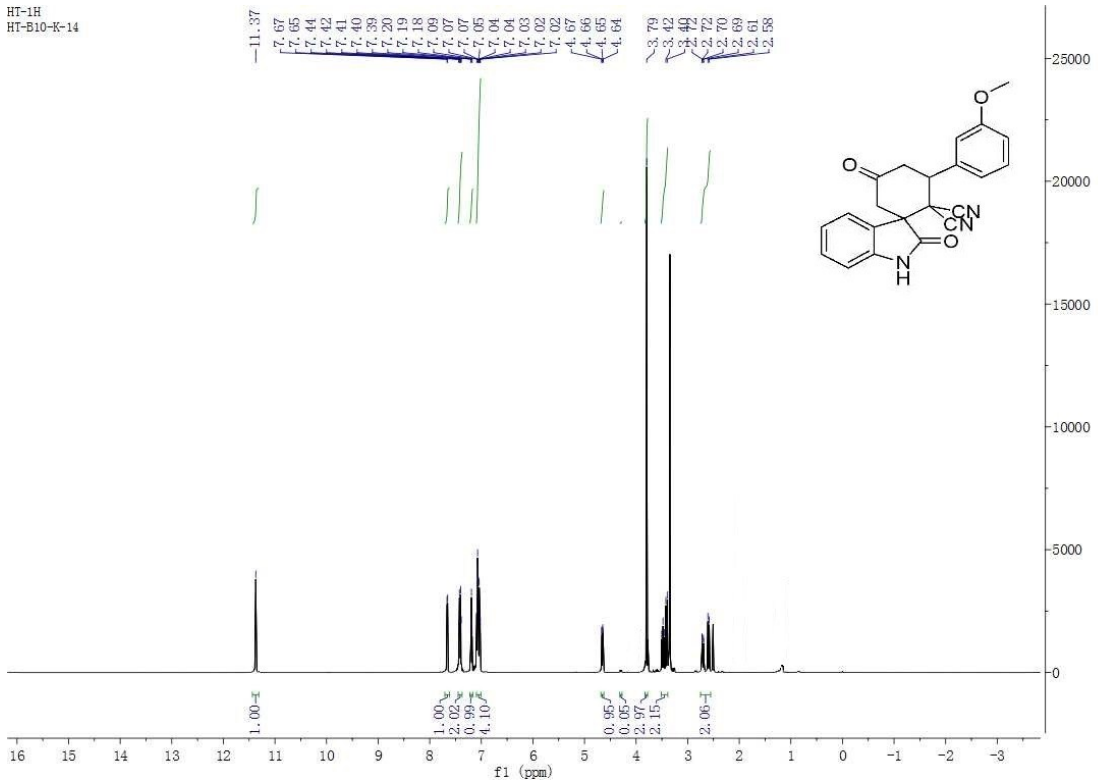


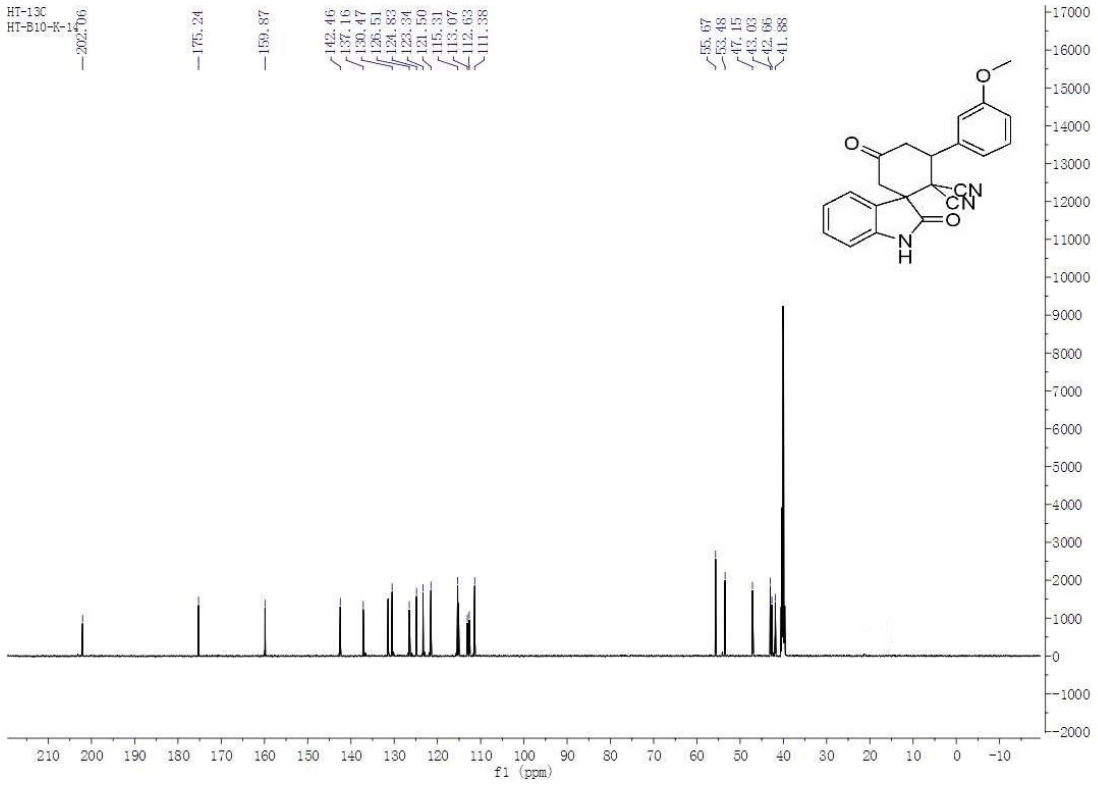
4l


HT-1H
HT-B10-k-12
11.42
7.87
7.87
7.86
7.68
7.67
7.61
7.59
7.55
7.50
7.49
7.48
7.48
7.43
7.21
7.20
7.05
5.63
5.61
5.61
3.48
3.46
3.43
2.71
2.70
2.70
2.68
2.66
1.01
1.00
0.99
1.03
1.07
1.06
1.00
1.00
0.97
1.01
2.16
2.07
Cl
O
CN
CN
O
N
H
f1 (ppm)

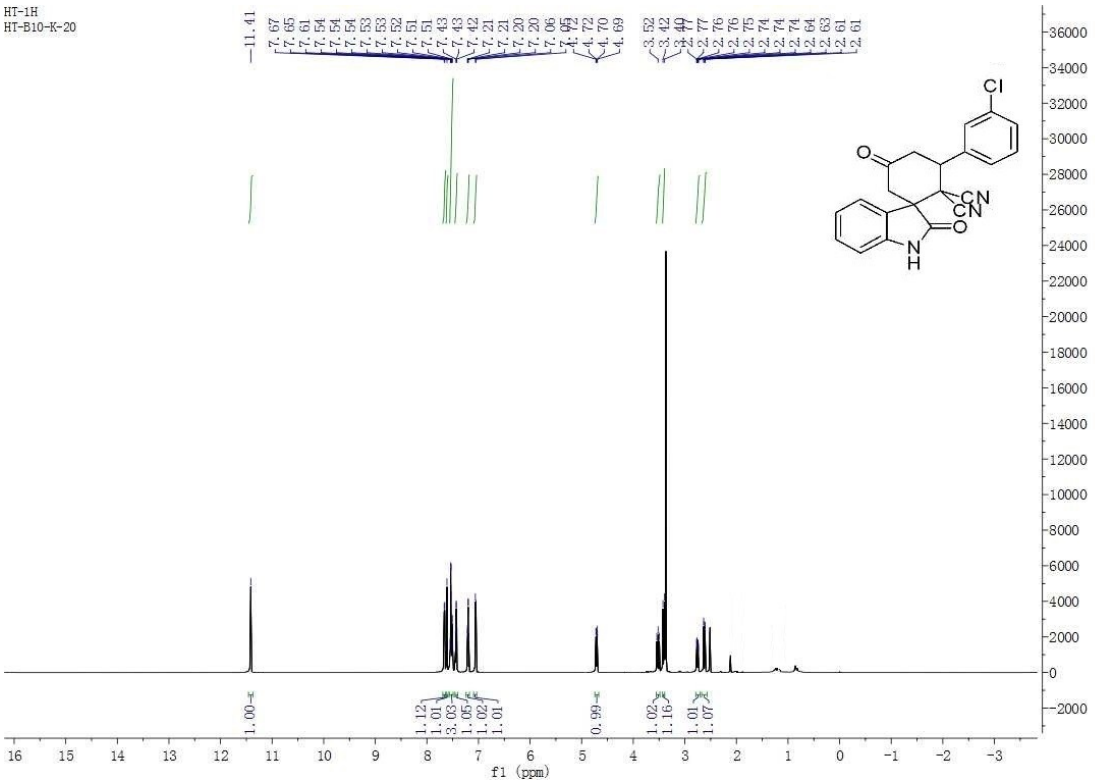

HT-13C
HT-B10-k-12
201.72
175.11
142.49
131.48
131.37
130.63
128.47
124.82
123.33
122.64
112.33
111.37
53.24
46.25
42.72
42.09
37.27
Cl
O
CN
CN
O
N
H
f1 (ppm)

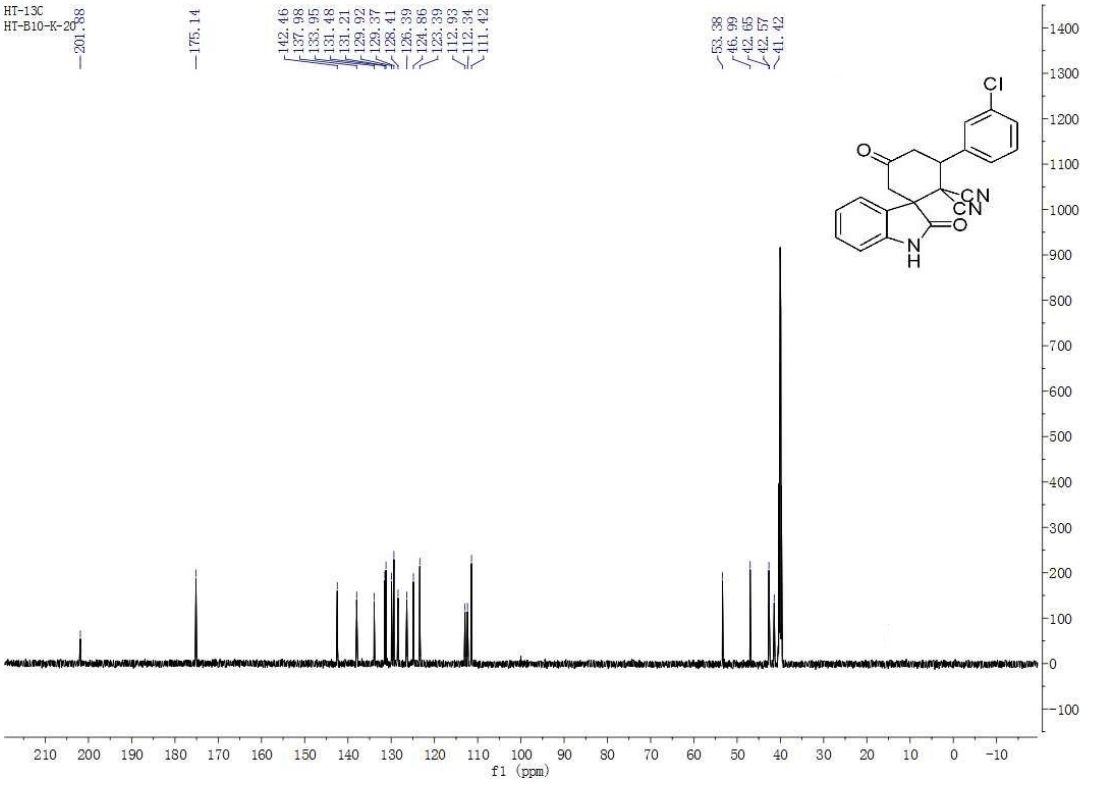
4m


HT-1H
HT-B10-K-14
11.37
7.67
7.65
7.44
7.42
7.41
7.40
7.39
7.20
7.19
7.18
7.09
7.07
7.07
7.05
7.04
7.04
7.03
7.02
7.02
4.67
4.66
4.65
4.64
3.79
3.42
3.40
2.72
2.70
2.69
2.61
2.58
1.00
1.00
2.02
0.99
4.10
0.95
0.05
2.97
2.15
2.06
f1 (ppm)

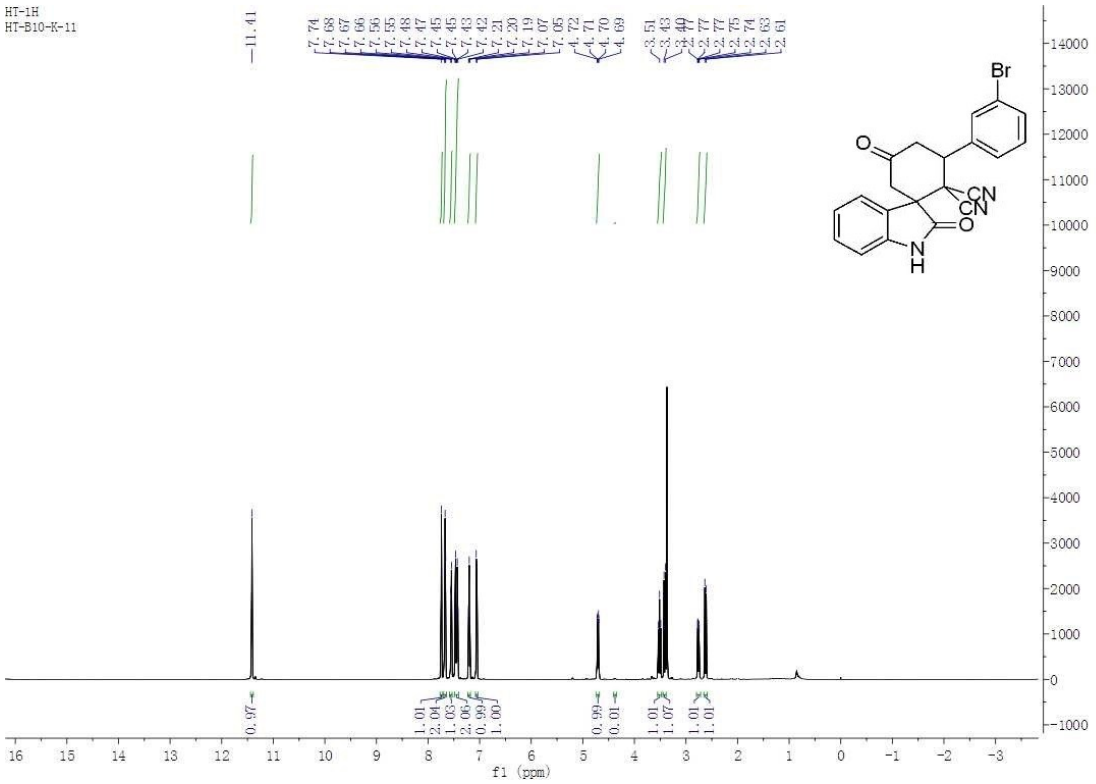

HT-13C
HT-B10-K-14
202.06
175.24
159.87
142.46
137.16
130.47
126.51
124.83
123.34
121.50
115.31
113.07
112.63
111.38
55.67
53.48
47.15
43.03
42.66
41.88
f1 (ppm)

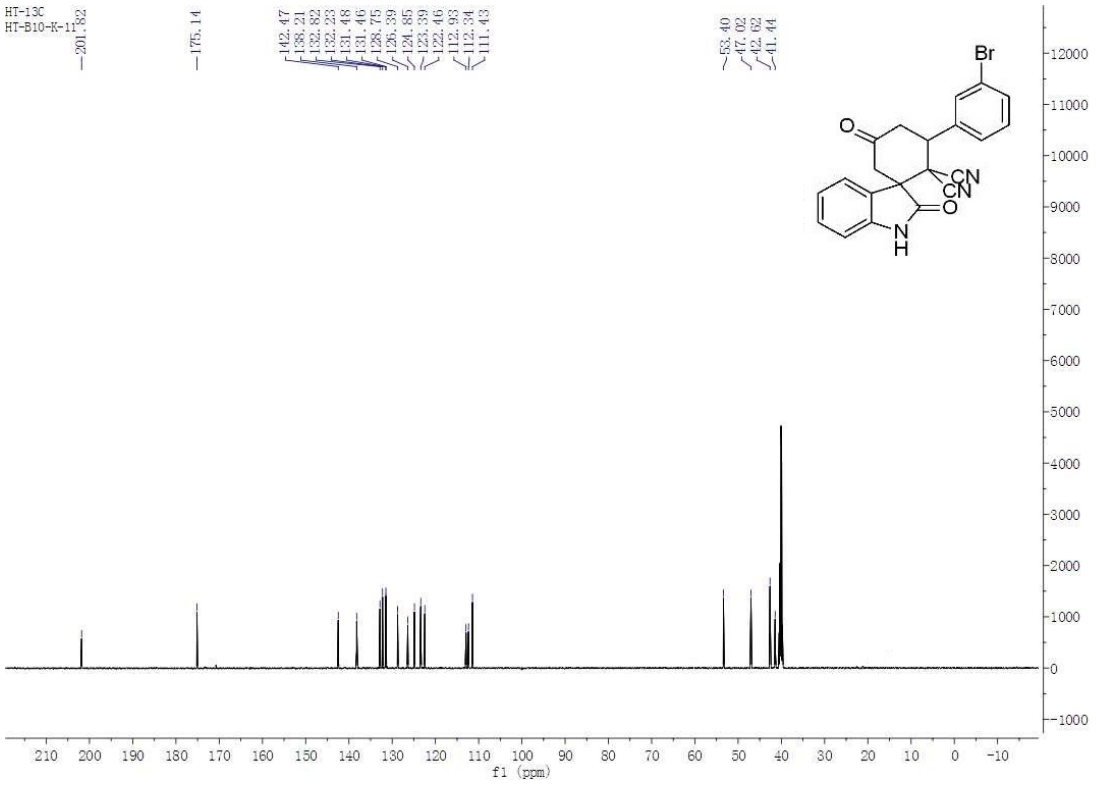
4n


HT-1H
HT-B10-K-20
11.41
7.67
7.65
7.61
7.54
7.54
7.53
7.52
7.51
7.51
7.43
7.43
7.42
7.21
7.21
7.20
7.20
7.06
4.72
4.70
4.69
3.52
3.42
3.40
2.77
2.76
2.76
2.75
2.74
2.74
2.74
2.64
2.63
2.61
2.61
1.00
1.12
1.01
3.03
1.05
1.02
1.01
0.99
1.02
1.16
1.01
1.07
f1 (ppm)

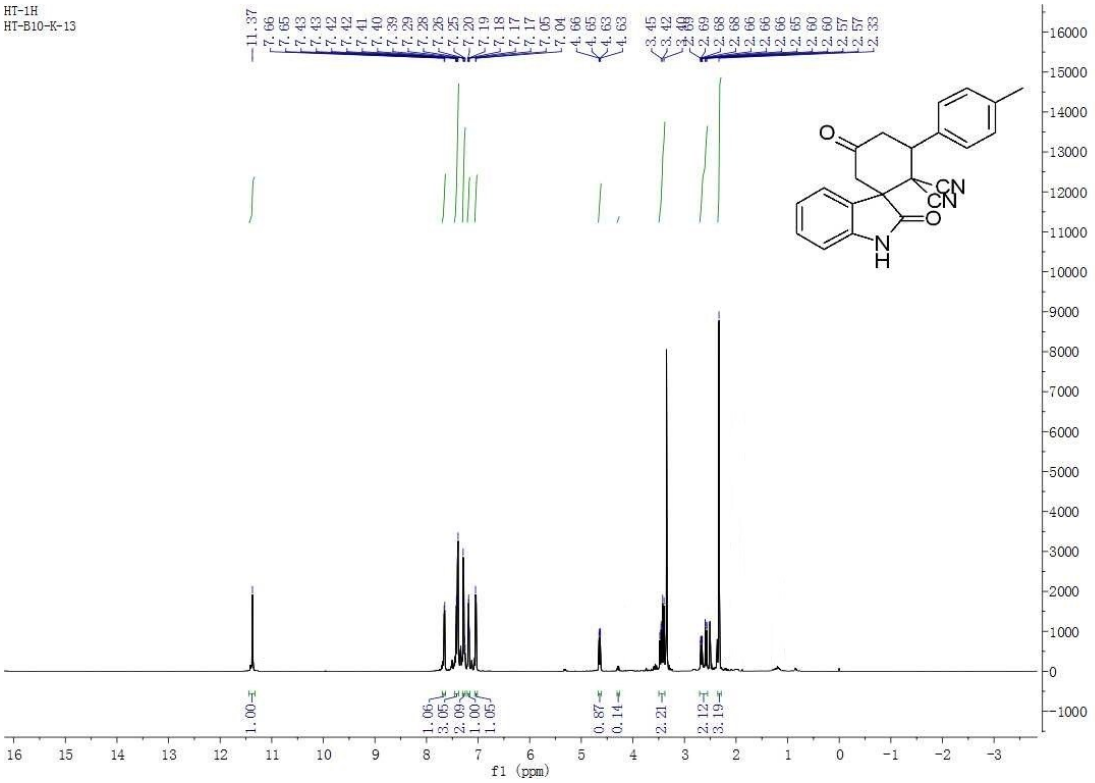

HT-13C
HT-B10-K-20
201.88
175.14
142.46
137.98
133.95
131.48
131.21
129.92
129.37
128.41
126.39
124.86
123.39
112.93
112.34
111.42
53.38
46.99
42.65
42.57
41.42
f1 (ppm)

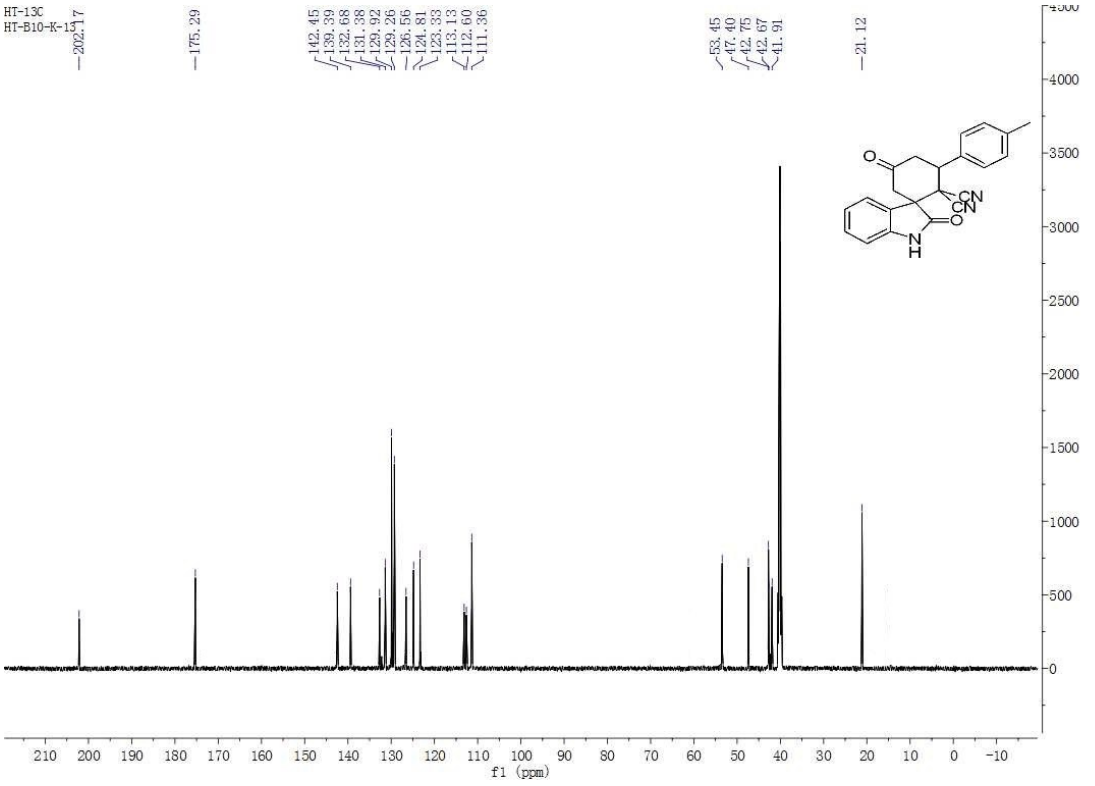
4o


HT-1H
HT-B10-K-11
11.41
7.74
7.68
7.67
7.66
7.56
7.55
7.48
7.47
7.45
7.45
7.43
7.42
7.21
7.20
7.19
7.07
7.05
4.72
4.71
4.70
4.69
3.51
3.43
3.40
2.77
2.77
2.75
2.74
2.63
2.61
Br
O
CN
CN
O
N
H
0.97
1.01
2.04
1.03
2.06
0.99
1.00
0.99
0.01
1.01
1.07
1.01
1.01
f1 (ppm)

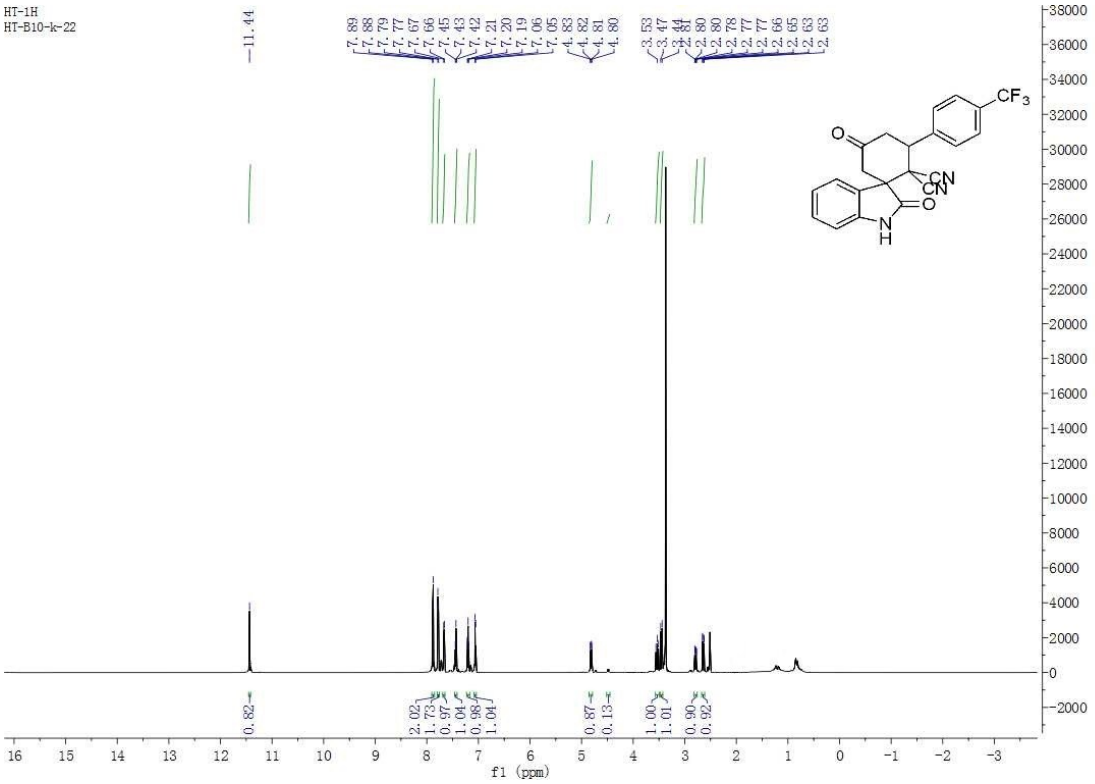

HT-13C
HT-B10-K-11
201.82
175.14
142.47
138.21
132.82
132.23
131.48
131.46
128.75
126.39
124.85
123.39
122.46
112.93
112.34
111.43
53.40
47.02
42.62
41.44
Br
O
CN
CN
O
N
H
f1 (ppm)

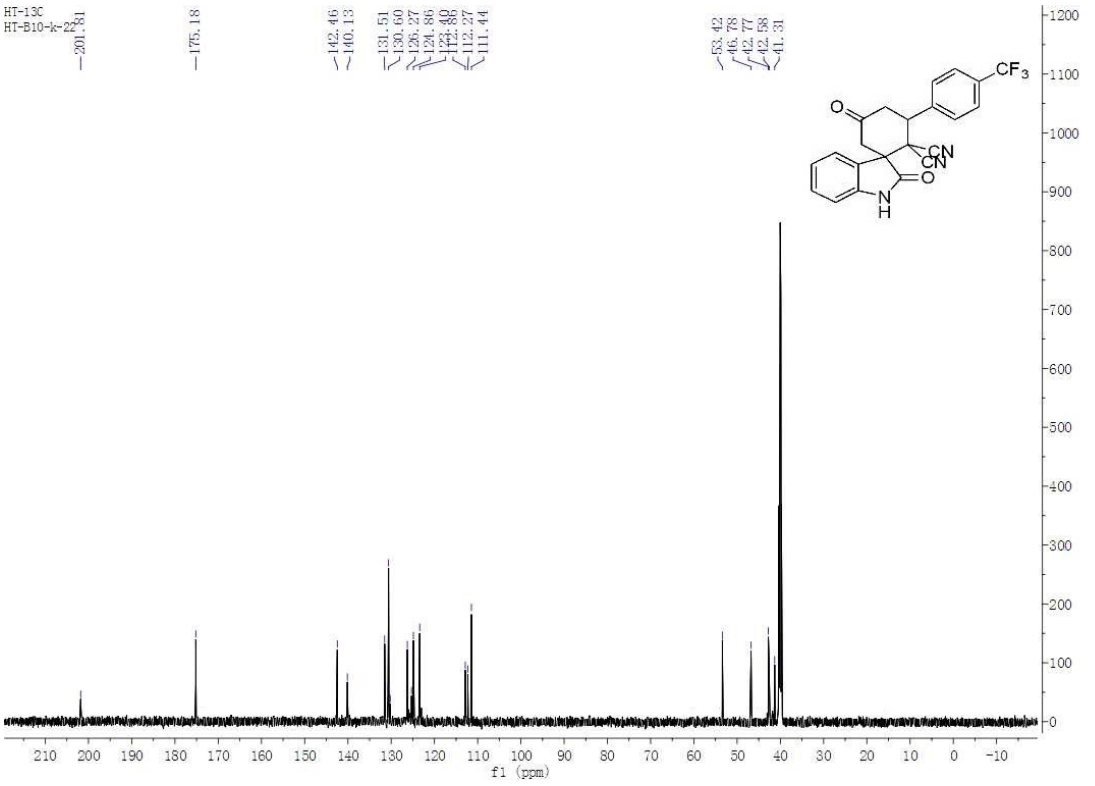
4p



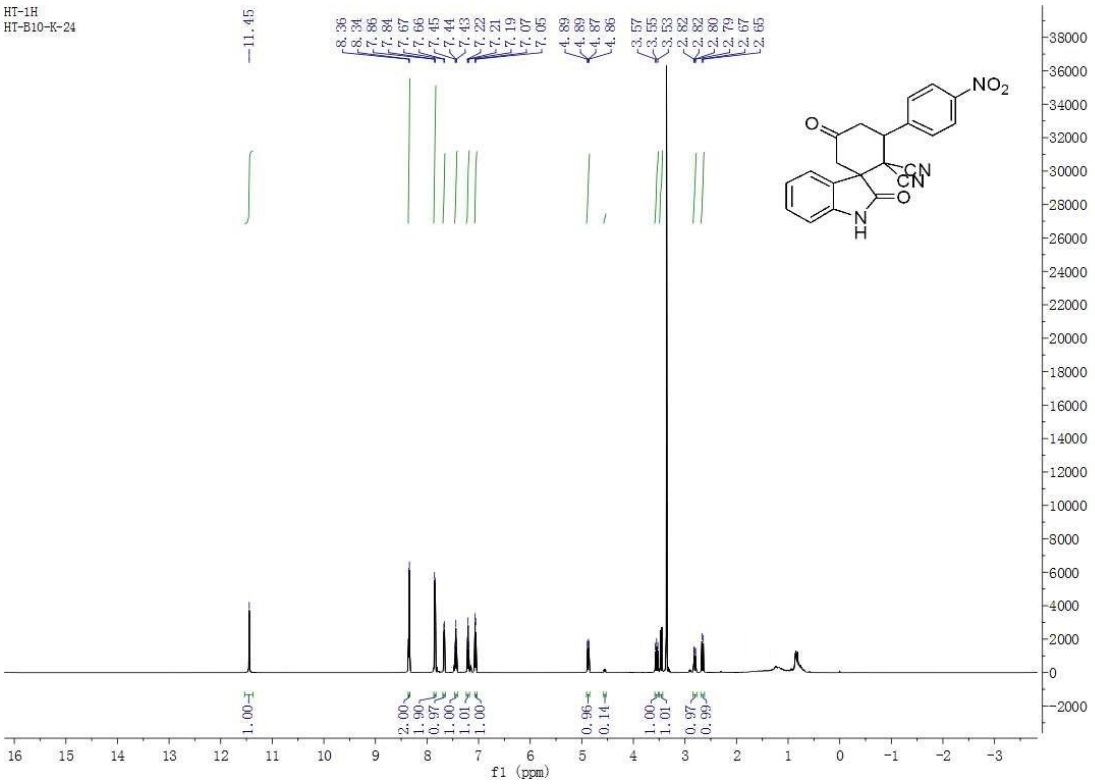


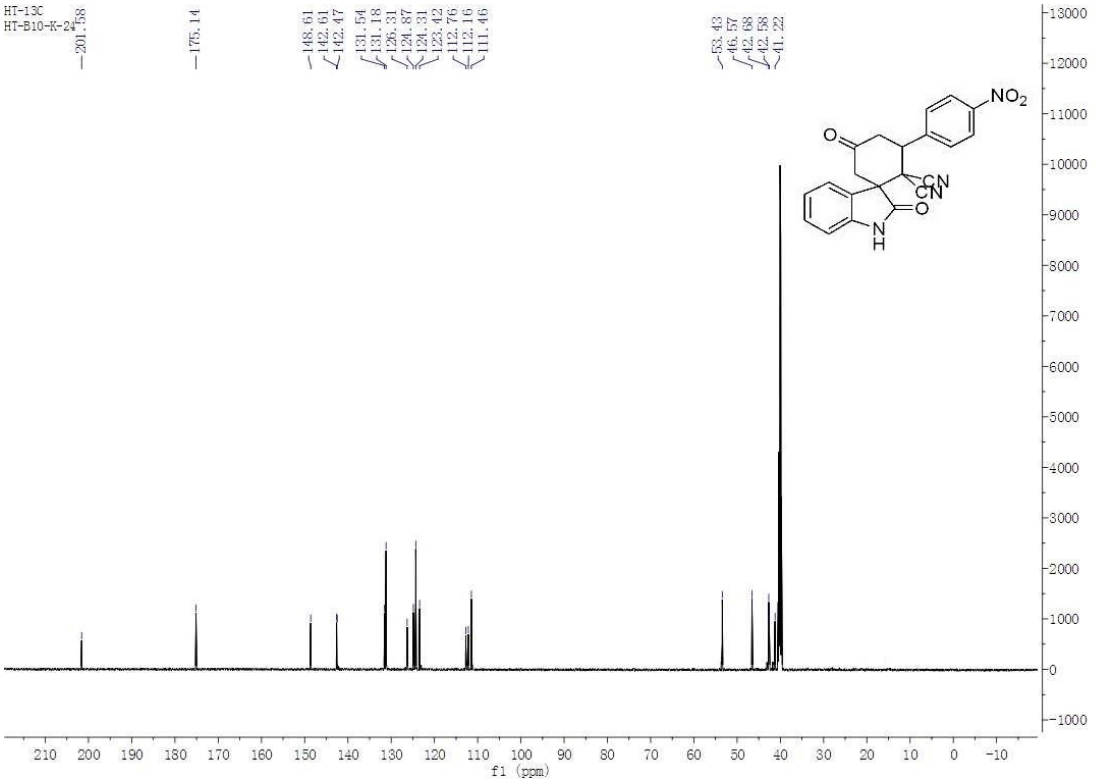
4q


HT-1H
HT-B10-k-22
11.44
7.89
7.88
7.79
7.77
7.67
7.66
7.45
7.43
7.42
7.21
7.20
7.19
7.06
7.05
4.83
4.82
4.81
4.80
3.53
3.47
3.44
2.80
2.78
2.77
2.66
2.65
2.63
2.63
0.82
2.02
1.73
0.97
1.04
0.98
1.04
0.87
0.13
1.00
1.01
0.90
0.92
f1 (ppm)
CF3
CN
CN
O
O
N
H

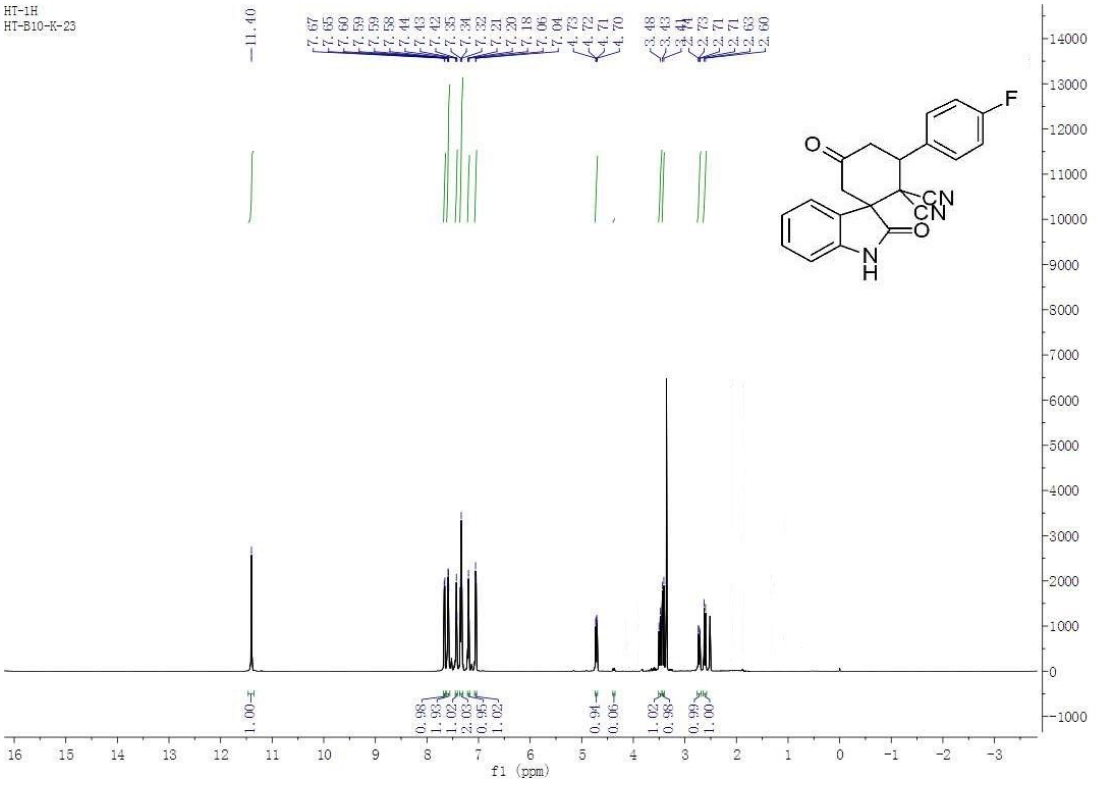

HT-13C
HT-B10-k-22
201.81
175.18
142.46
140.13
131.51
130.60
126.27
124.86
123.49
122.86
112.27
111.44
53.42
46.78
42.77
42.58
41.31
f1 (ppm)
CF3
CN
CN
O
O
N
H

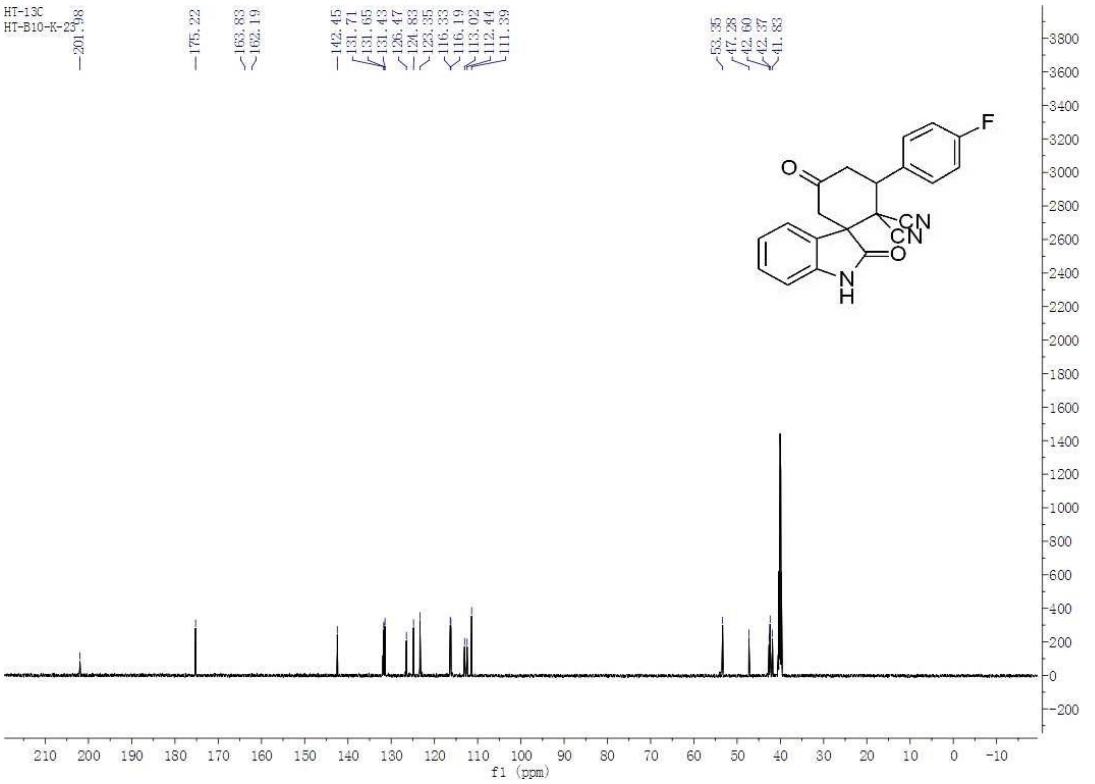
4r


HT-1H
HT-B10-K-24
11.45
8.36
8.34
7.86
7.84
7.67
7.66
7.45
7.44
7.43
7.22
7.21
7.19
7.07
7.05
4.89
4.89
4.87
4.86
3.57
3.55
3.53
2.82
2.82
2.80
2.79
2.67
2.65
1.00
2.00
1.90
0.97
1.00
1.01
1.00
0.96
0.14
1.00
1.01
0.97
0.99
f1 (ppm)

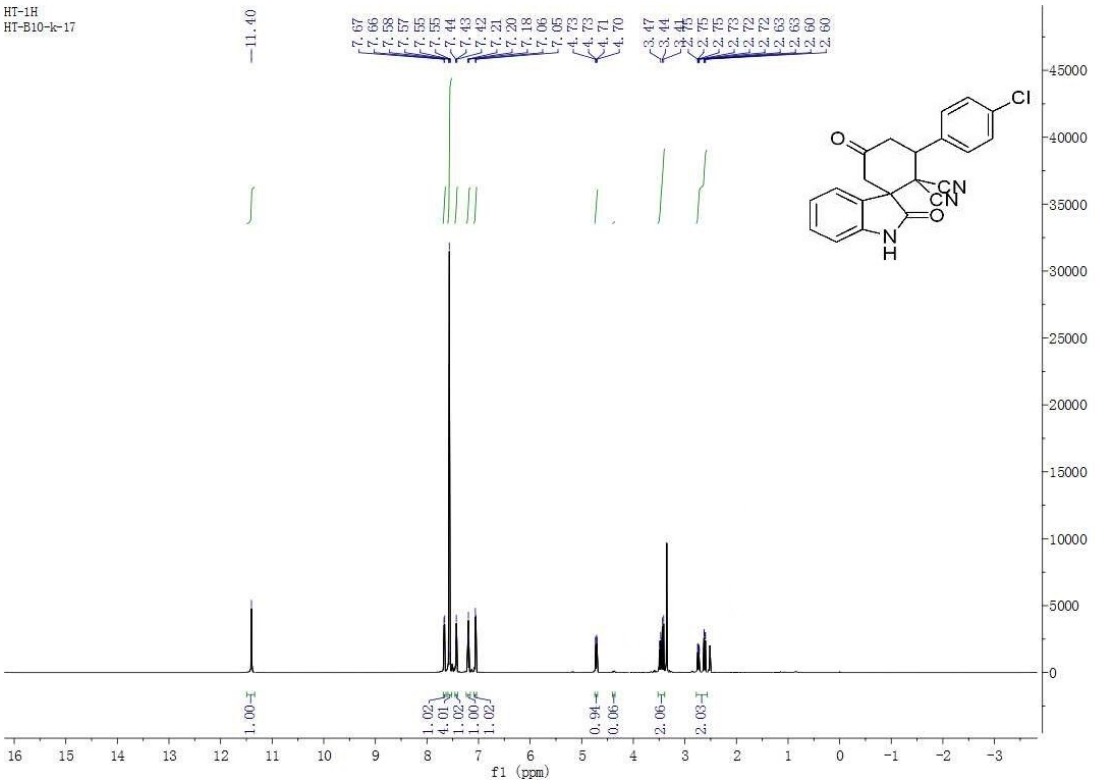

HT-13C
HT-B10-K-24
201.58
175.14
148.61
142.61
142.47
131.54
131.18
126.31
124.87
124.31
123.42
112.76
112.16
111.46
53.43
46.57
42.68
42.58
41.22
f1 (ppm)

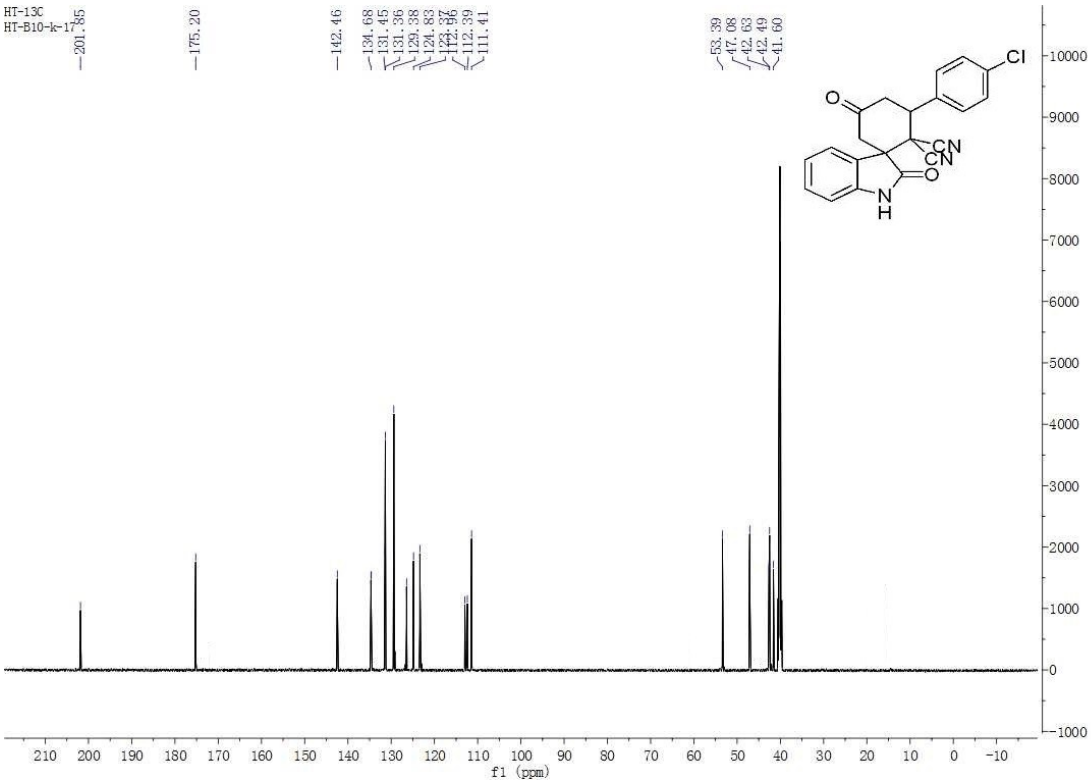
4s


HT-1H
HT-B10-K-23
11.40
7.67
7.65
7.60
7.59
7.59
7.58
7.44
7.43
7.42
7.35
7.34
7.32
7.21
7.20
7.18
7.06
7.04
4.73
4.72
4.71
4.70
3.48
3.43
3.44
2.73
2.71
2.71
2.63
2.60
F
O
CN
CN
O
N
H
1.00
0.98
1.93
1.02
2.03
0.95
1.02
0.94
0.06
1.02
0.98
0.99
1.00
f1 (ppm)

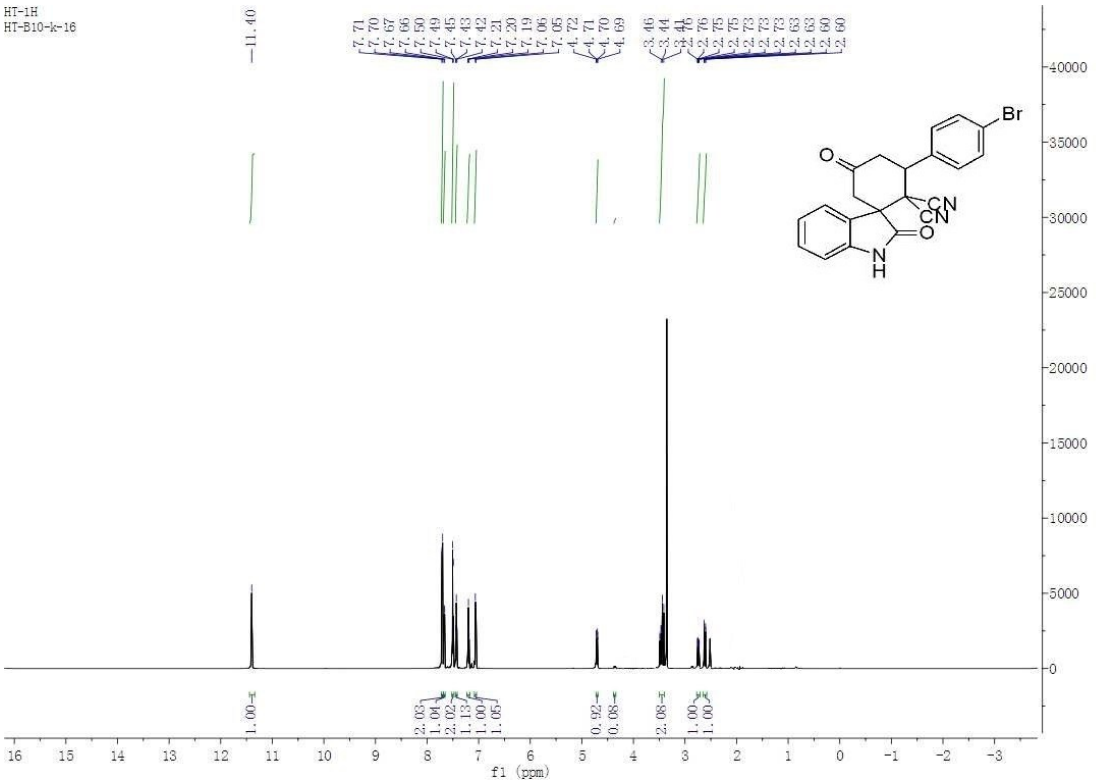

HT-13C
HT-B10-K-23
201.98
175.22
163.83
162.19
142.45
131.71
131.65
131.43
126.47
124.83
123.35
116.33
116.19
113.02
112.44
111.39
53.35
47.28
42.60
42.37
41.83
F
O
CN
CN
O
N
H
f1 (ppm)

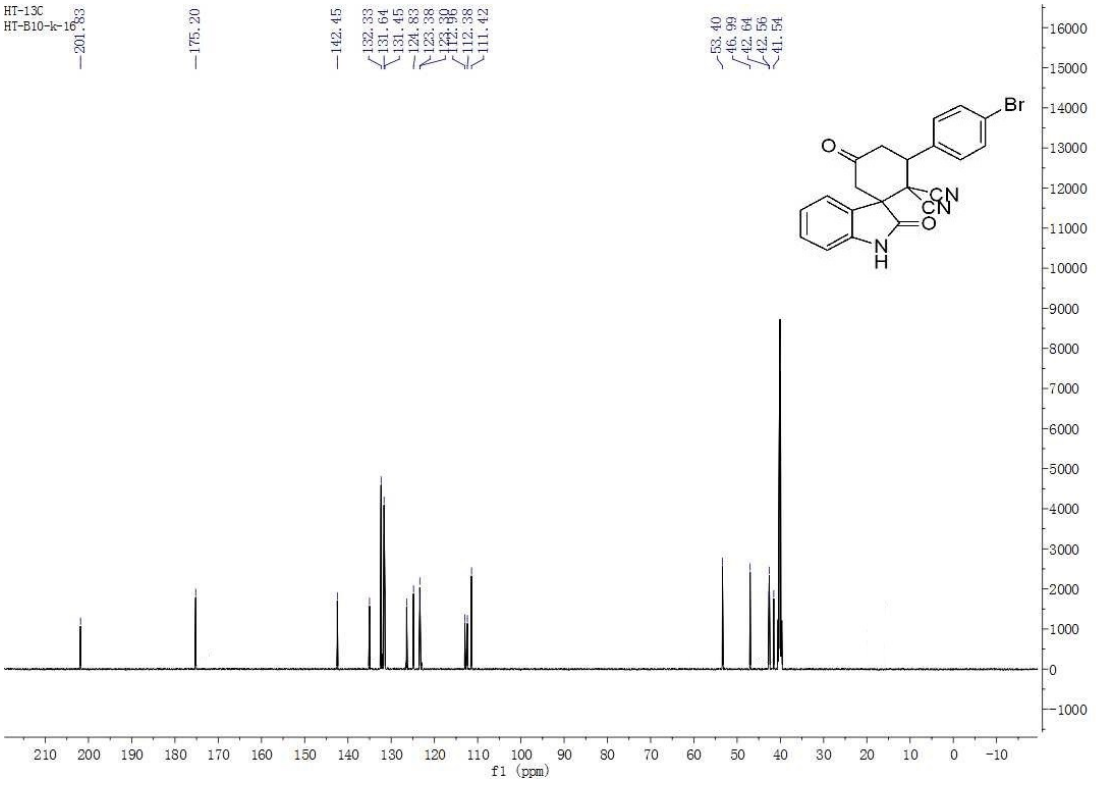
4t


HT-1H
HT-B10-k-17
11.40
7.67
7.66
7.58
7.57
7.55
7.55
7.44
7.43
7.42
7.21
7.20
7.18
7.06
7.05
4.73
4.73
4.71
4.70
3.47
3.44
3.41
2.75
2.73
2.72
2.72
2.63
2.63
2.60
2.60
Cl
O
CN
CN
O
N
H
1.00
1.02
4.01
1.02
1.00
1.02
0.94
0.06
2.06
2.03
f1 (ppm)

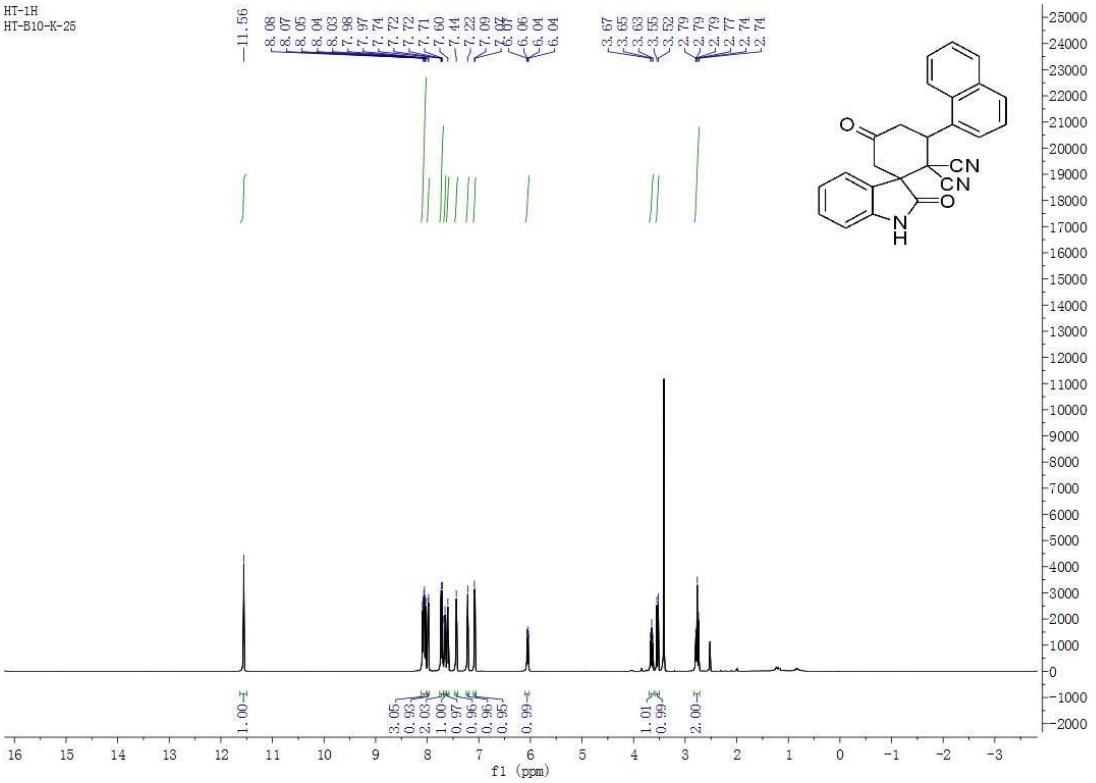

HT-13C
HT-B10-k-17
201.85
175.20
142.46
134.68
131.45
131.36
129.38
124.83
123.37
122.96
112.39
111.41
53.39
47.08
42.63
42.49
41.60
Cl
O
CN
CN
O
N
H
f1 (ppm)

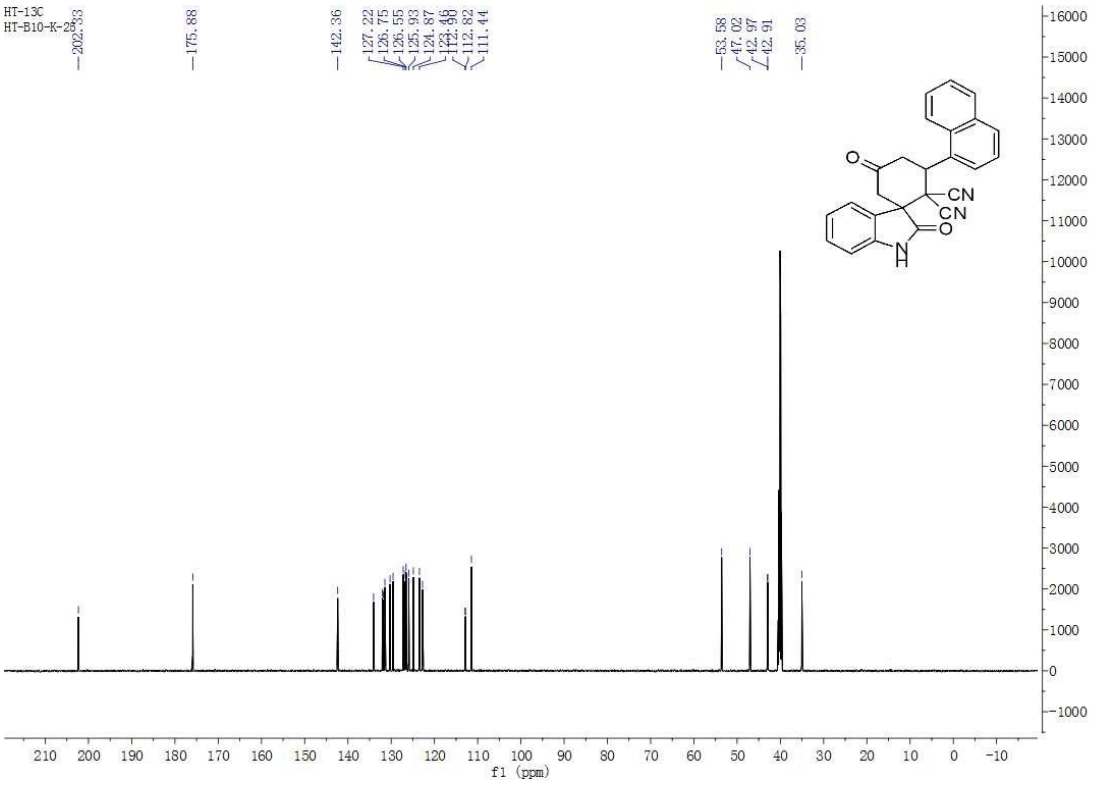
4u


HT-1H
HT-B10-k-16
11.40
7.71
7.70
7.67
7.66
7.50
7.49
7.45
7.43
7.42
7.21
7.20
7.19
7.06
7.05
4.72
4.71
4.70
4.69
3.46
3.44
3.41
3.16
2.76
2.75
2.73
2.73
2.73
2.63
2.63
2.60
2.60
Br
O
CN
CN
O
N
H
1.00
2.03
2.04
2.02
1.13
1.00
1.05
0.92
0.08
2.08
1.00
1.00
f1 (ppm)

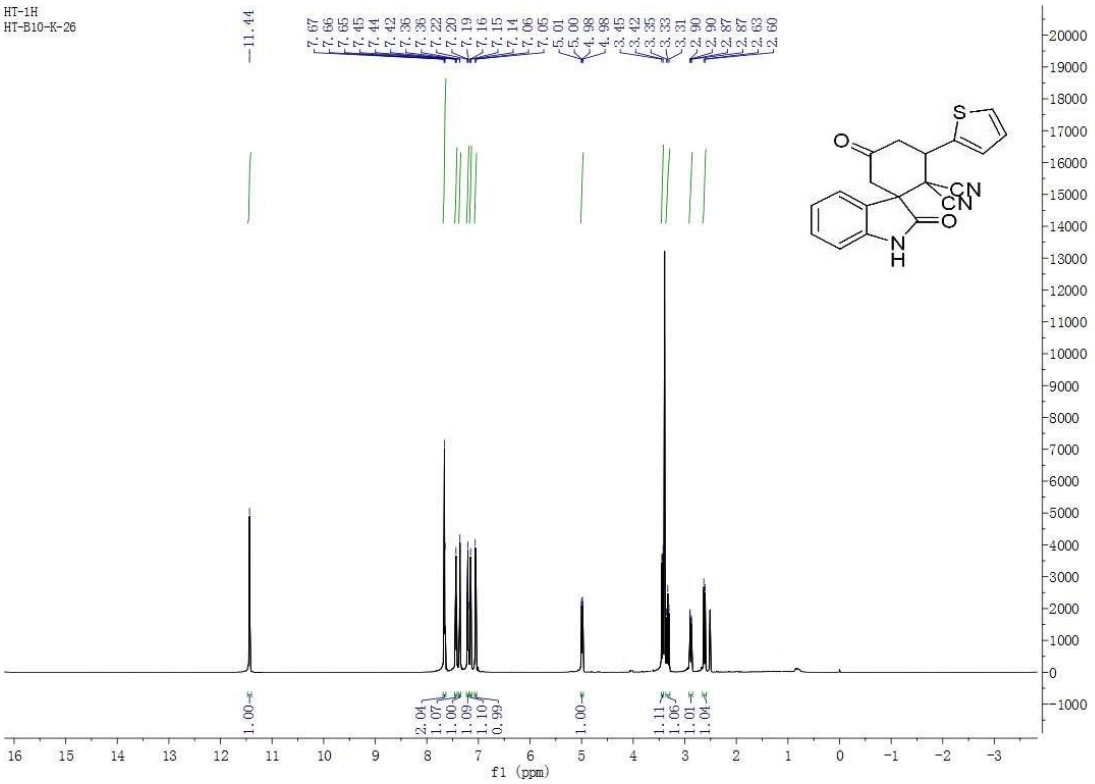

HT-13C
HT-B10-k-16
201.83
175.20
142.45
132.33
131.64
131.45
124.83
123.38
123.30
112.96
112.38
111.42
53.40
46.99
42.64
42.56
41.54
Br
O
CN
CN
O
N
H
f1 (ppm)

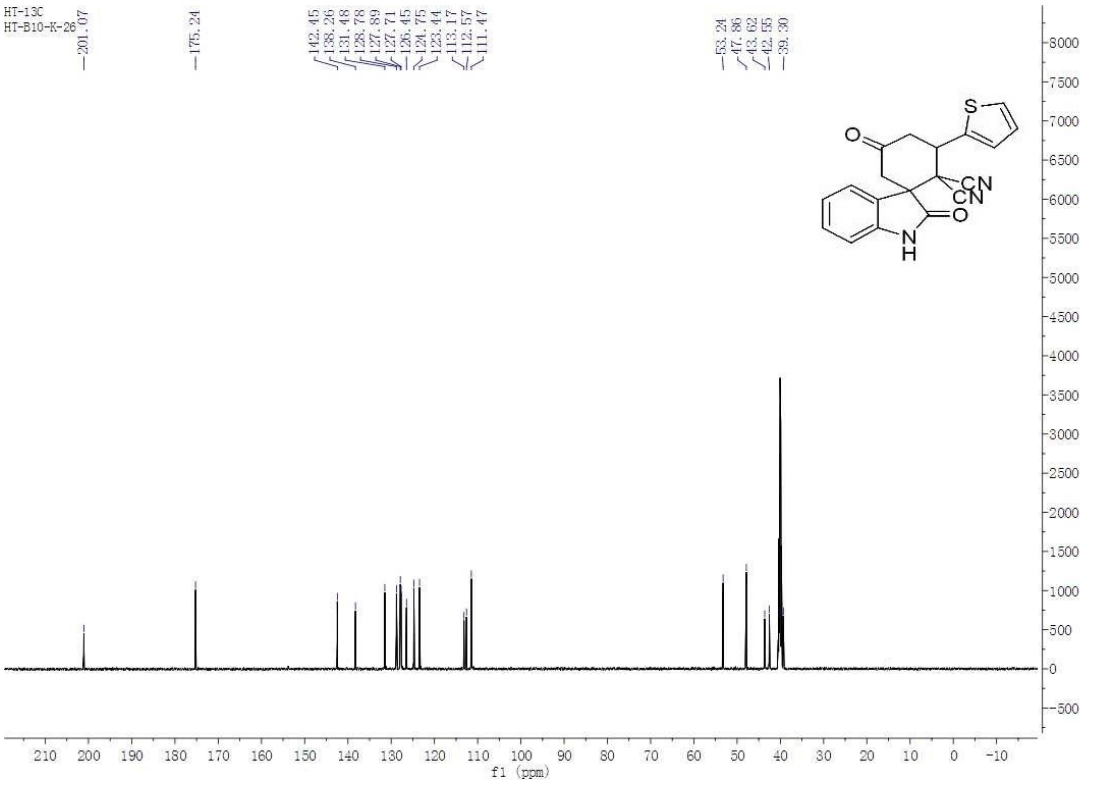
4v



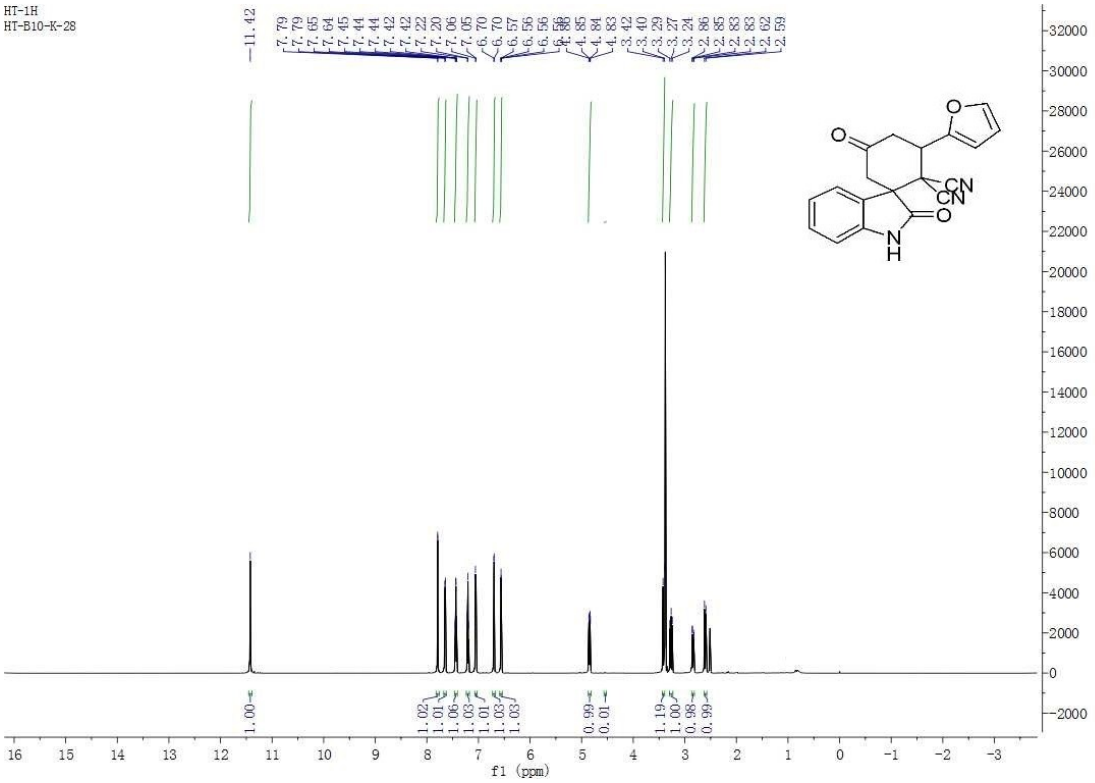


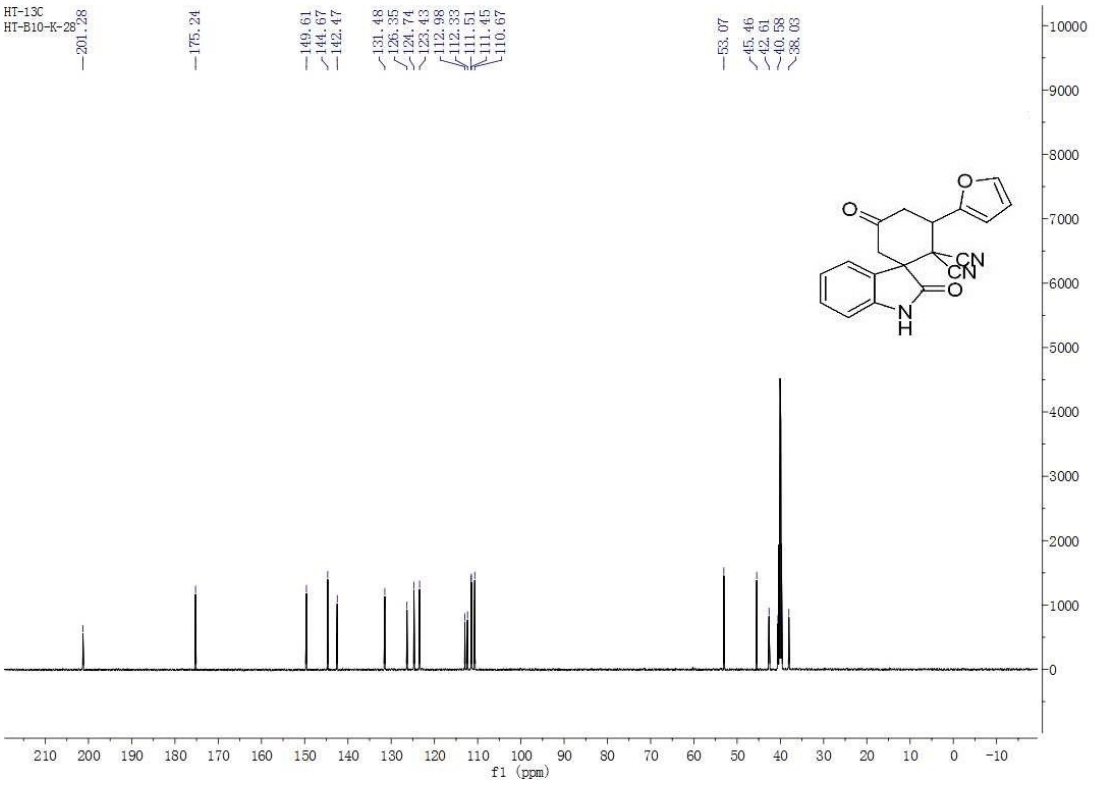
4w


HT-1H
HT-B10-K-26
11.44
7.67
7.66
7.65
7.45
7.44
7.42
7.36
7.36
7.22
7.20
7.19
7.16
7.15
7.14
7.06
7.05
5.01
5.00
4.98
4.98
3.45
3.42
3.35
3.33
3.31
2.90
2.90
2.87
2.63
2.60
1.00
2.04
1.07
1.00
1.09
1.10
0.99
1.00
1.11
1.06
1.01
1.04
f1 (ppm)

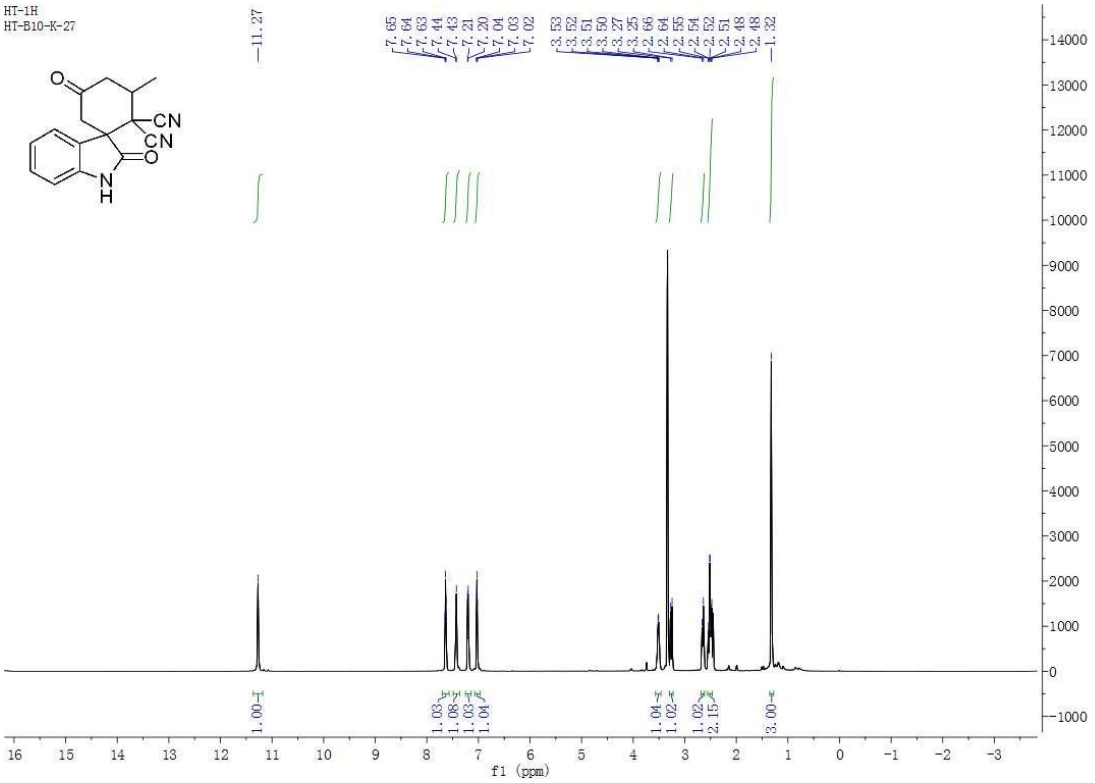

HT-13C
HT-B10-K-26
201.07
175.24
142.45
138.26
131.48
128.78
127.89
127.71
126.45
124.75
123.44
113.17
112.57
111.47
53.24
47.86
43.62
42.55
39.30
f1 (ppm)

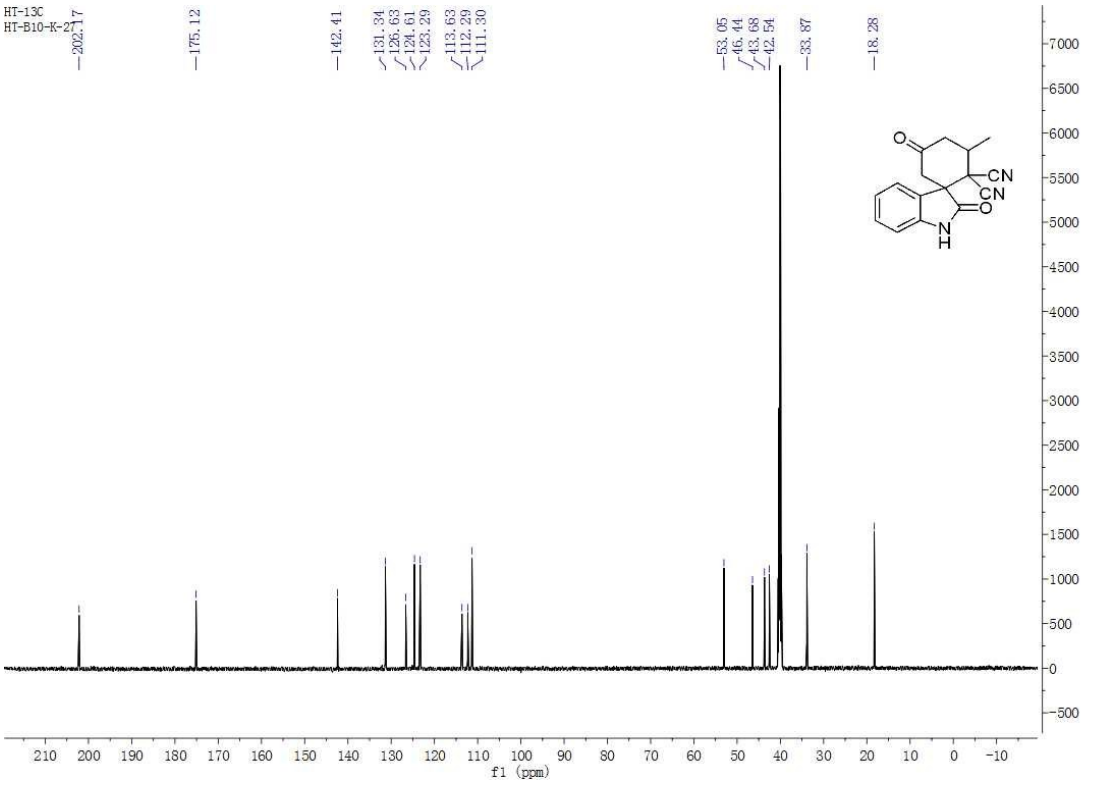
4x


HT-1H
HT-B10-K-28
11.42
7.79
7.79
7.65
7.64
7.45
7.44
7.44
7.42
7.42
7.22
7.20
7.06
7.05
6.70
6.70
6.57
6.56
6.56
4.85
4.84
4.83
3.42
3.40
3.29
3.27
3.24
2.86
2.85
2.83
2.83
2.62
2.59
1.00
1.02
1.01
1.06
1.03
1.01
1.03
1.03
0.99
0.01
1.19
1.00
0.98
0.99
f1 (ppm)

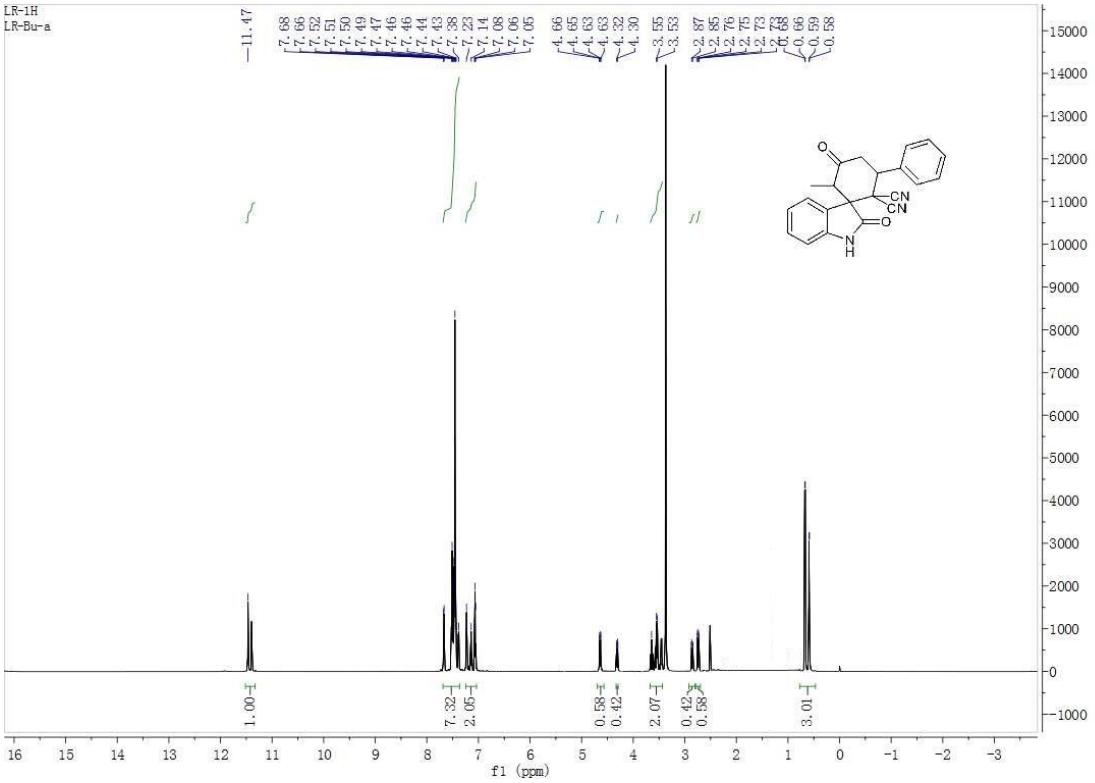

HT-13C
HT-B10-K-28
201.28
175.24
149.61
144.67
142.47
131.48
126.35
124.74
123.43
112.98
112.33
111.51
111.45
110.67
53.07
45.46
42.61
40.58
38.03
f1 (ppm)

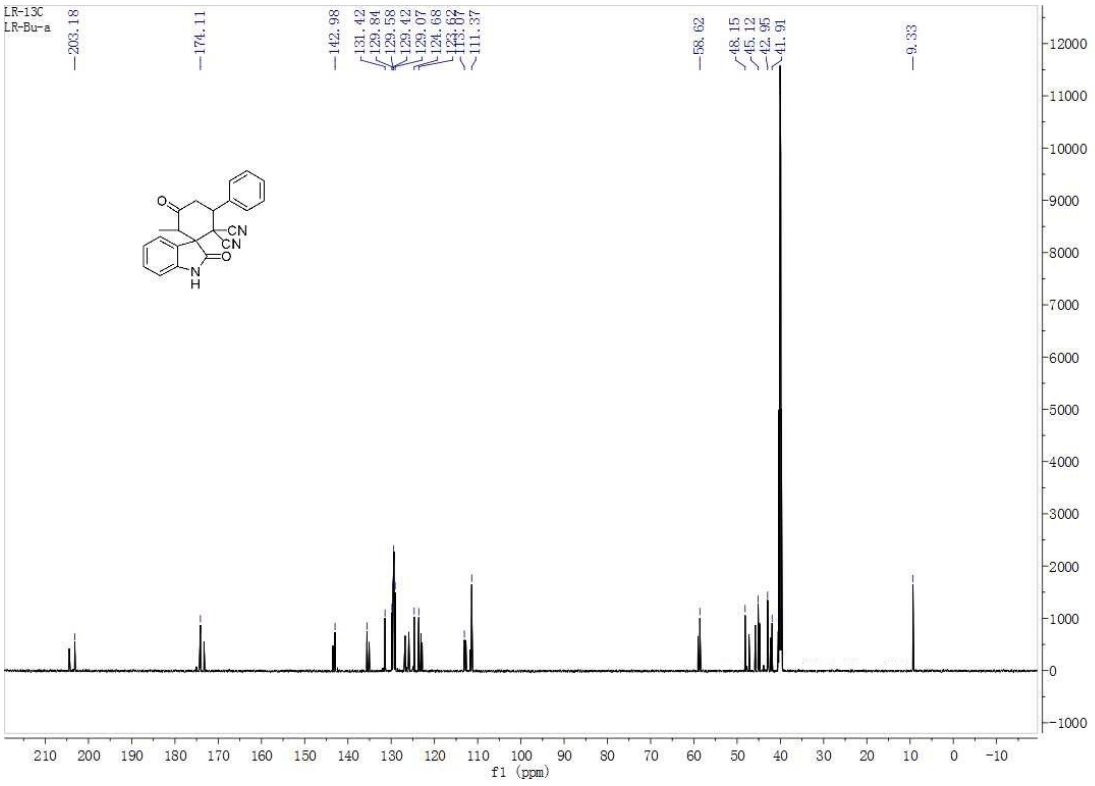
4y


HT-1H
HT-B10-K-27
11.27
7.65
7.64
7.63
7.44
7.43
7.21
7.20
7.04
7.03
7.02
3.53
3.52
3.51
3.50
3.27
3.25
2.66
2.64
2.55
2.54
2.52
2.51
2.48
1.32
1.00
1.03
1.08
1.03
1.04
1.04
1.02
1.02
2.15
3.00
f1 (ppm)

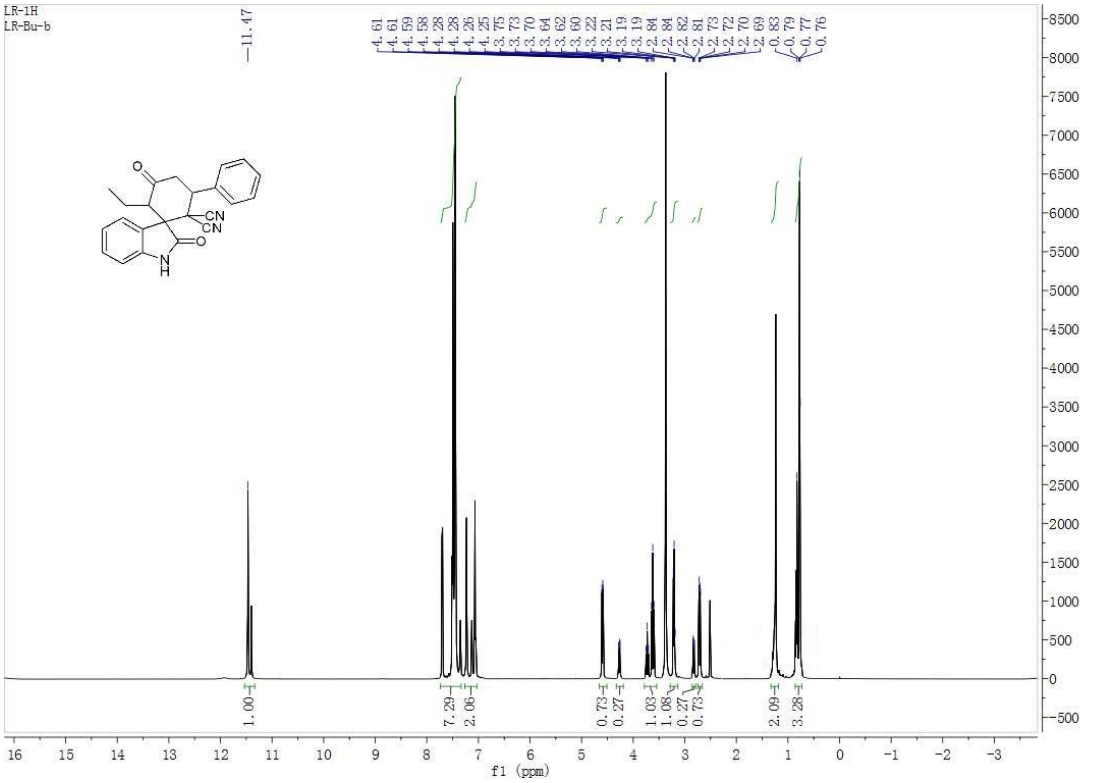

HT-13C
HT-B10-K-27
202.17
175.12
142.41
131.34
126.63
124.61
123.29
113.63
112.29
111.30
53.05
46.44
43.68
42.54
33.87
18.28
f1 (ppm)

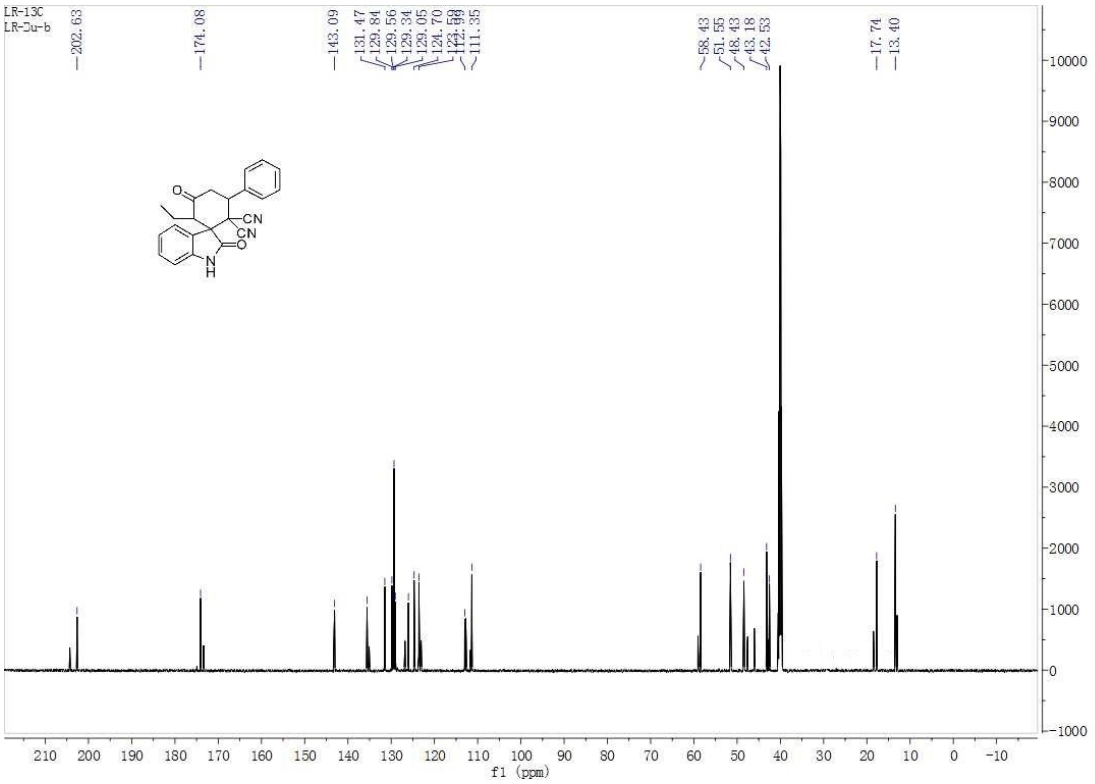
4z


LR-1H
LR-Bu-a
11.47
7.68
7.66
7.52
7.51
7.50
7.49
7.47
7.46
7.46
7.44
7.43
7.38
7.23
7.14
7.08
7.06
7.05
4.66
4.65
4.63
4.63
4.32
4.30
3.55
3.53
2.87
2.85
2.76
2.75
2.73
2.68
0.66
0.59
0.58
1.00
7.32
2.05
0.58
0.42
2.07
0.42
0.58
3.01
f1 (ppm)

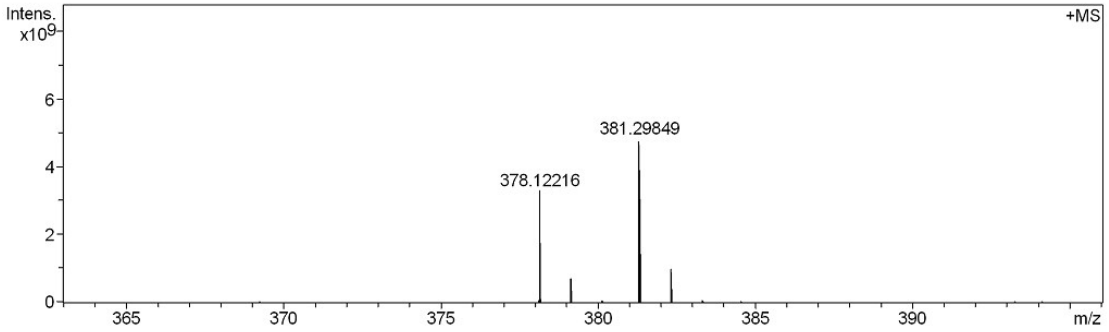

LR-13C
LR-Bu-a
203.18
174.11
142.98
131.42
129.84
129.58
129.42
129.07
124.68
123.82
123.67
111.37
58.62
48.15
45.12
42.95
41.91
9.33
f1 (ppm)

4aa

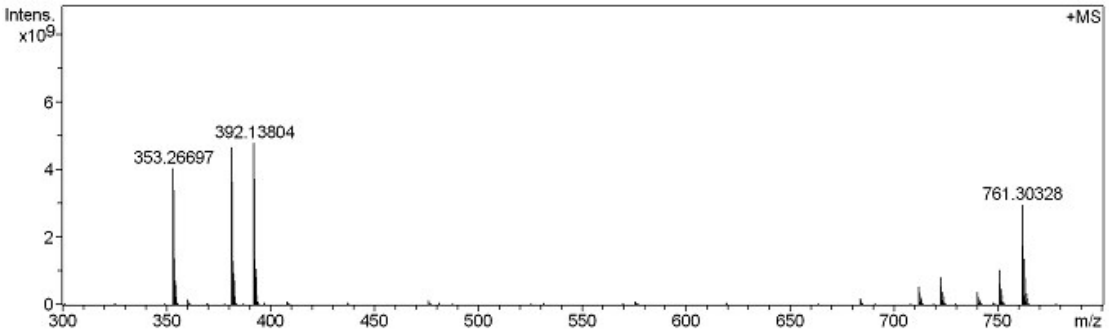

LR-1H
LR-Bu-b
11.47
4.61
4.59
4.38
4.28
4.26
4.25
3.75
3.73
3.70
3.64
3.62
3.60
3.22
3.21
3.19
2.84
2.82
2.81
2.73
2.72
2.70
2.69
0.83
0.79
0.77
0.76
1.00
7.29
2.06
0.73
0.27
1.03
1.08
0.27
0.73
2.09
3.28
f1 (ppm)


LR-13C
LR-Bu-b
202.63
174.08
143.09
131.47
129.84
129.56
129.34
129.05
124.70
111.35
58.43
51.55
48.43
43.18
42.53
17.74
13.40
f1 (ppm)

4z-HRMS



4aa- HRMS



5. References

1. M. L. Anson, *The Journal of General Physiology*, 1938, **22**, 79-89.
2. Y.-B. Lan, H. Zhao, Z.-M. Liu, G.-G. Liu, J.-C. Tao and X.-W. Wang, *Org. Lett.*, 2011, **13**, 4866-4869.