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Supplementary information

Efficient synthesis of multicyclic spirooxindoles via a cascade Michael/Michael/oxa-Michael reaction of curcumins and isatylidene malononitriles

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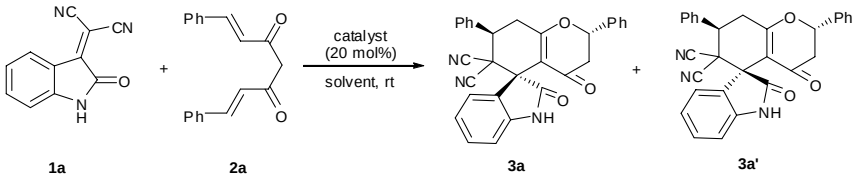
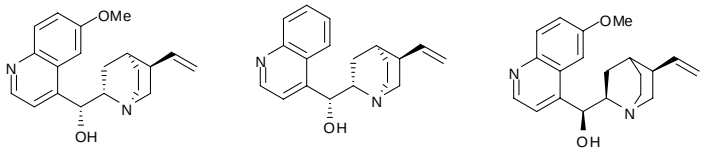
1. Screening of chiral organocatalysts and reaction solvents

Table 1 Screening of chiral organocatalysts and solvents[a]



1a 2a 3a 3a'



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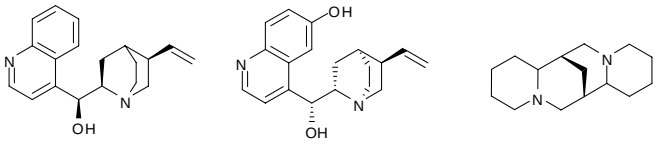

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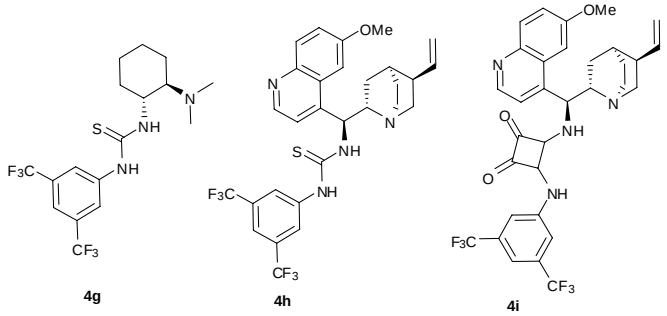


4g 4h 4i

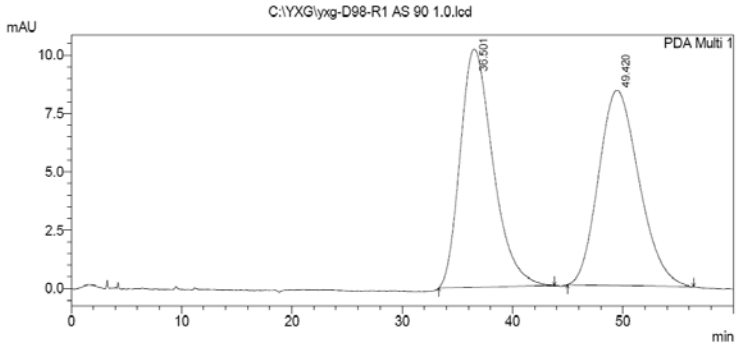
Entry	Catalyst	Solvent	dr [b]	Time (h)	Yield (%)[c]	Ee (%) [d]
1	**4a**	CH_2Cl_2	80/20	24	60	2
2	**4b**	CH_2Cl_2	67/33	24	76	16
3	**4c**	CH_2Cl_2	76/24	24	77	5
4	**4d**	CH_2Cl_2	76/24	24	72	1
5	**4e**	CH_2Cl_2	80/20	24	40	2
6	**4f**	CH_2Cl_2	ND[e]	48	5	ND[e]
7	**4g**	CH_2Cl_2	66/34	48	62	58
8	**4h**	CH_2Cl_2	80/20	48	19	24
9	**4i**	CH_2Cl_2	-	48	NR[f]	-
10	**4g**	Toluene	68/32	48	65	25
11	**4g**	THF	70/30	48	34	20
12	**4g**	Et_2O	63/37	48	17	37
13	**4g**	EtOH	77/23	48	65	38

[a] The reactions were carried out with **1a** (0.05 mmol), **2a** (0.05 mmol) and catalyst (0.01 mmol) in solvent (1 mL) at room temperature. [b] Determined by ^{1}H NMR analysis of the crude product. [c] Isolated yields after column chromatography. [d] Determined by HPLC with a Chiralpak AS-H. [e] Not determined. [f] No reaction.

Chiral HPLC chromatogram

Chiralpak AS-H column (4.6 mm × 25 cm), hexane/2-PrOH = 90: 10, λ = 254 nm, 1.0 mL/min); t_{major}= 36.6 min, t_{minor} = 49.4 min).

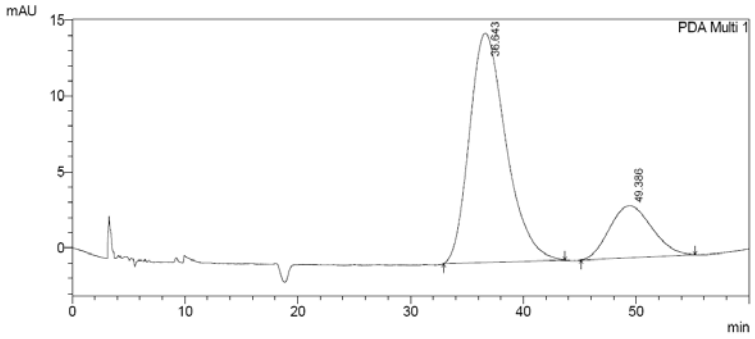
Racemic **3a**



PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.501	2104244	10190	49.722	54.966
2	49.420	2127734	8348	50.278	45.034
Total		4231978	18538	100.000	100.000

3a (58% ee)



PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.643	3406671	15078	79.212	81.486
2	49.386	894042	3426	20.788	18.514
Total		4300713	18504	100.000	100.000

1. General Methods

^{1}H and^{13}C NMR spectra were recorded on a Bruker Advance 400 MHz spectrometer as solutions in $CDCl_3$ or DMSO-d_6. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm, δ) downfield from the internal standard Me_4Si (TMS, δ = 0 ppm). Chemical shifts in ^{13}C NMR spectra are reported relative to the central line of the chloroform signal (δ = 77.0 ppm). The following abbreviations are used to designate chemical shift mutiplicities: s= singlet, d= doublet, m= multiplet. High-resolution mass spectra were obtained with Shimadazu LCMS-IT-TOF mass spectrometer. Optical rotations were measured on a Perkin-Elmer 341 digital polarimeter and are reported as $[\alpha]_D^{20}$ (c in gram per 100 mL of solvent). Infrared (IR) spectra were recorded on a Bruker Tensor 37 spectrophotometer. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak). The crystallographic data were obtained with

Oxford Diffraction Xcalibur Nova diffractometer. Melting points were recorded on an electrothermal digital melting point apparatus and were uncorrected. TLC analysis was performed on precoated silica gel GF254 slides, and visualised by either UV irradiation. The flash column chromatography was carried out over silica gel (230–400 mesh), purchased from Qingdao Haiyang Chemical Co. Ltd. Unless otherwise stated, all reagents were obtained from commercial sources and used as received. The solvents were used as commercial anhydrous grade without further purification. Enantiomeric excesses were determined by HPLC using a Daicel Chiralpak AS-H column (4.6 mm × 25 cm) and eluting with hexane/2-PrOH solution. Curcumins and isatylidene malononitriles were prepared according to the reported procedures.[1,2]

2. Typical procedures

2.1 Typical procedure for the reaction of isatylidene malononitriles and curcumins

A mixture of DMAP (0.01 mmol), isatylidene malononitrile **1a** (0.05 mmol) and curcumin **2a** (0.05 mmol) in ethanol (1 mL) was stirred at room temperature for 18 h. After the solvent was evaporated under vacuum, the residue was purified by flash column chromatography over silica gel (petroleum ether/EtOAc = 2: 1) to provide product **3a** as a yellow solid.

2.2 Asymmetric reaction of isatylidene malononitrile 1a and curcumin 2a

A mixture of Takemoto's catalyst (0.01 mmol), isatylidene malononitrile **1a** (0.05 mmol) and curcumin **2a** (0.05 mmol) in dichloromethane (1 mL) was stirred at room temperature for 48 h. After the solvent was evaporated under vacuum, the residue was purified by flash column chromatography over silica gel (petroleum ether/AcOEt = 2: 1) to provide product **3a** as a yellow solid. The enantiomeric excess of **3a** was determined by HPLC with a Chiralpak AS-H column (4.6 mm × 25 cm) (hexane/2-PrOH = 90: 10, λ = 254 nm, 1.0 mL/min); t_{major}= 27.2 min, t_{minor} = 35.1 min, 58% ee.

3. Spectroscopic data of 3a-3n

3.1 2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile (3a)

Yellow solid, mp 174-176 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.59 – 7.31 (m, 12H), 7.13 (t, J = 7.7 Hz, 1H), 6.93 (d, J = 7.7 Hz, 1H), 5.50 (dd, J = 14.9, 3.0 Hz, 1H), 4.72 (dd, J = 12.4, 4.7 Hz, 1H), 3.41 (dd, J = 19.4, 12.4 Hz, 1H), 3.01 (dd, J = 19.4, 4.7 Hz, 1H), 2.91 (dd, J = 17.9, 15.0 Hz, 1H), 2.61 (dd, J = 17.9, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.45, 174.58, 173.30, 168.48, 141.54, 136.76, 134.62, 130.32, 129.58, 129.38, 129.28, 129.00, 128.75, 127.20, 126.37, 124.52, 123.20, 112.34, 111.44, 111.10, 110.80, 81.10, 53.38, 47.73, 42.75, 39.13, 31.79; IR (KBr) ν/cm^{-1}: 3450, 2350, 1739, 1679; HRMS (ESI) calcd for $C_{30}H_{20}N_3O_3$ $(M-H)^-$: 470.1504, found: 470.1503.

3.2 5'-methoxy-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3b)

Yellow solid. mp 174-176 °C ; ^{1}H NMR (400 MHz, DMSO) δ 11.07 (s, 1H), 7.69 – 7.35 (m, 10H), 7.08 (s, 1H), 6.92 (d, J = 1.2 Hz, 2H), 5.80 (dd, J = 14.6, 2.8 Hz, 1H), 4.60 (dd, J = 12.3, 4.8 Hz, 1H), 3.75 (s, 3H), 3.47 – 3.39 (m, 1H), 3.16 (dd, J = 19.4, 4.8 Hz, 1H), 2.93 (dd, J = 17.6, 14.8 Hz, 1H), 2.59 (dd, J = 17.6, 3.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 188.05, 174.43, 172.55, 154.74, 137.50, 136.07, 135.10, 129.22, 129.00, 128.81, 128.70, 128.56, 126.81, 113.77, 112.20, 112.11, 110.47, 110.07, 80.15, 79.12, 55.40, 53.03, 47.61, 41.93, 30.51; IR (KBr) ν/cm^{-1}: 3490,3035,2961,2250,1729,1677;HRMS (ESI) calcd for $C_{31}H_{22}N_3O_4$ $(M-H)^-$: 500.1610, found: 500.1607.

3.3 5'-chloro-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3c)

White solid. mp 176-178°C ; ^{1}H NMR (400 MHz, DMSO) δ 11.41 (s, 1H), 7.57 (d, J = 7.0 Hz, 2H), 7.53 – 7.38 (m, 10H), 7.04 (d, J = 8.3 Hz, 1H), 5.87 (dd, J = 14.6, 2.7 Hz, 1H), 4.56 (dd, J = 12.2, 4.8 Hz, 1H), 3.50 – 3.41 (m, 1H), 3.23 – 3.13 (m, 1H), 2.95 (dd, J = 17.5, 14.9 Hz, 1H), 2.61 (dd, J = 17.6, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 188.27, 174.35, 173.00, 141.91, 137.44, 134.88, 129.87, 129.46, 129.31, 129.04, 128.84, 128.71, 128.57, 126.83, 125.93, 124.57, 112.10, 111.97, 111.62, 109.49, 80.21, 52.89, 47.33, 41.76, 30.44; IR (KBr) ν/cm^{-1}: 3490, 2366,1721,1675; HRMS (ESI) calcd for $C_{30}H_{19}N_3O_3Cl$ (M-H)$^-$: 504.1115, found: 504.1111.

3.4 7'-bromo-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3d)

Yellow solid. mp 153-155°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.58 – 7.40 (m, 12H), 7.06 (t, J = 7.8 Hz, 1H), 5.52 (d, J = 14.8 Hz, 1H), 4.75 – 4.65 (m, 1H), 3.43 (dd, J = 19.3, 12.5 Hz, 1H), 3.08 – 2.86 (m, 2H), 2.64 (d, J = 17.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.28, 173.63, 173.32, 141.05, 136.65, 134.37, 133.13, 129.70, 129.44, 129.35, 129.04, 128.75, 128.50, 126.37, 124.37, 123.39, 112.17, 111.13, 110.74, 103.75, 81.18, 54.70, 47.48, 42.59, 39.18, 31.72; IR (KBr) ν/cm^{-1}: 3482,2922,2852,2360,1732,1678 ; HRMS (ESI) calcd for $C_{30}H_{20}N_3O_3Br$ (M-H)$^-$: 548.0615, found: 548.0608.

3.5 6'-methoxy-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3e)

Yellow solid. mp 169-171°C ; ^{1}H NMR (400 MHz, DMSO) δ 11.41 (s, 1H), 7.57 (d, J = 7.0 Hz, 2H), 7.53 – 7.38 (m, 10H), 7.04 (d, J = 8.3 Hz, 1H), 5.87 (dd, J = 14.6, 2.7 Hz, 1H), 4.56 (dd, J = 12.2, 4.8 Hz, 1H), 3.50 – 3.41 (m, 1H), 3.23 – 3.13 (m, 1H), 2.95 (dd, J = 17.5, 14.9 Hz, 1H), 2.61 (dd, J = 17.6, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 188.27, 174.35, 173.00, 141.91, 137.44, 134.88, 129.87, 129.46, 129.31, 129.04, 128.84, 128.71, 128.57, 126.83, 125.93, 124.57, 112.10, 111.97, 111.62, 109.49, 80.21, 52.89, 47.33, 41.76, 30.44; IR (KBr) ν/cm^{-1}:3482,1727,1675; HRMS (ESI) calcd for $C_{30}H_{19}N_3O_3Cl$ (M-H)$^-$: 504.1115, found: 504.1111.

3.6 1'-methyl-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3f)

Yellow solid. mp 140-142°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.37 (m, 12H), 7.16 (td, J = 7.7, 0.8 Hz, 1H), 7.00 (d, J = 7.8 Hz, 1H), 5.48 (dd, J = 15.0, 3.1 Hz, 1H), 4.78 (dd, J = 12.5, 4.9 Hz, 1H), 3.41 (dd, J = 19.3, 12.5 Hz, 1H), 3.00 (dd, J = 19.3, 4.9 Hz, 1H), 2.86 (dd, J = 17.8, 15.0 Hz, 1H), 2.56 (dd, J = 17.8, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.04, 173.44, 173.00, 144.43, 136.85, 134.68, 130.36, 129.56, 129.35, 129.25, 129.01, 128.77, 126.75, 126.31, 124.15, 123.27, 112.42, 111.48, 110.93, 109.14, 81.06, 53.11, 47.80, 42.80, 39.17, 31.73, 27.08; IR (KBr) ν/cm^{-1}: 3480,3061,2922,1720,1678; IR (KBr) ν/cm^{-1}: 3480,3061,2922,1720,1678; HRMS (ESI) calcd for $C_{31}H_{22}N_3O_3$ (M-H)$^-$: 484.1661, found:484.1657.

3.7 1'-benzyl-2',4-dioxo-2,7-diphenyl-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3g)

White solid. mp 135-137°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.28 (m, 17H), 7.15 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 5.53 (dd, J = 14.9, 2.8 Hz, 1H), 5.20 (d, J = 16.1 Hz, 1H), 5.02 (d, J = 16.1 Hz, 1H), 4.86 (dd, J = 12.4, 4.8 Hz, 1H), 3.47 (dd, J = 19.3, 12.4 Hz, 1H), 3.05 (dd, J = 19.3, 4.9 Hz, 1H), 2.95 (dd, J = 17.7, 15.1 Hz, 1H), 2.63 (dd, J = 17.8, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.97, 173.84, 173.03, 143.85, 136.85, 134.86, 134.68, 130.24, 129.59, 129.38, 129.28, 129.03, 128.82, 127.64, 127.21, 126.74, 126.38, 124.17, 123.33, 112.45, 111.71, 111.18, 110.47, 81.11, 53.08, 47.84, 45.21, 42.82, 39.30, 31.81;IR (KBr) ν/cm^{-1}: 3480,3064,3033,2921,2852,2250,1729,1677;HRMS

(ESI) calcd for $C_{37}H_{26}N_3O_3$ $(M-H)^-$: 560.1974, found: 560.1977.

3.8 2,7-bis(4-methoxyphenyl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline] -6,6(2H)-dicarbonitrile(3h)

Yellow solid. mp 191-194 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (br, 1H), 7.43 (ddd, J = 25.7, 21.0, 7.7 Hz, 6H), 7.14 (t, J = 7.6 Hz, 1H), 7.04 – 6.86 (m, 5H), 5.46 (dd, J = 15.0, 2.7 Hz, 1H), 4.68 (dd, J = 12.3, 4.7 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.37 (dd, J = 19.4, 12.5 Hz, 1H), 3.07 – 2.86 (m, 2H), 2.59 (dd, J = 17.9, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.83, 174.74, 173.55, 160.44, 160.39, 141.62, 130.24, 129.93, 128.73, 128.14, 127.35, 126.54, 124.44, 123.12, 114.63, 114.36, 112.46, 111.65, 110.95, 110.83, 80.90, 55.38, 55.28, 53.39, 48.11, 42.45, 38.52, 31.93; HRMS (ESI) calcd for $C_{32}H_{24}N_3O_5$ $(M-H)^-$: 530.1716, found: 530.1718.

3.9 2,7-bis(4-chlorophenyl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3i)

Yellow solid. mp 191-194°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.49 – 7.27 (m, 9H), 7.13 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.8 Hz, 1H), 5.48 (dd, J = 14.8, 2.9 Hz, 1H), 4.71 (dd, J = 12.4, 4.8 Hz, 1H), 3.35 (dd, J = 19.3, 12.4 Hz, 1H), 2.99 (dd, J = 19.3, 4.9 Hz, 1H), 2.86 (dd, J = 17.8, 15.0 Hz, 1H), 2.59 (dd, J = 17.9, 3.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.12, 174.54, 172.86, 141.57, 135.78, 135.38, 135.14, 132.98, 130.47, 130.07, 129.58, 129.26, 127.74, 126.94, 124.44, 123.29, 112.12, 111.30, 111.20, 110.96, 80.32, 53.28, 47.57, 42.58, 38.58, 31.67; IR(KBr) ν/cm^{-1}: 3450,2926,1729,1678;HRMS (ESI) calcd for $C_{30}H_{18}N_3O_3Cl_2$(M-H)$^-$: 538.0725, found: 538.0722.

3.10 2,7-bis(2-methoxyphenyl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3j)

Yellow solid. mp 244°C, decompose ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.47 (d, J = 7.5 Hz, 1H), 7.35 (dd, J = 13.1, 6.7 Hz, 3H), 7.13 (t, J = 7.7 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.99 – 6.88 (m, 3H), 5.85 (dd, J = 13.7, 4.2 Hz, 1H), 5.47 (dd, J = 12.5, 4.6 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.36 (dd, J = 19.0, 12.6 Hz, 1H), 2.93 (dd, J = 19.2, 4.7 Hz, 1H), 2.71 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ 189.09, 174.45, 173.90, 157.78, 155.89, 141.55, 130.34, 130.11, 129.92, 127.51, 126.51, 125.70, 124.66, 123.27, 123.00, 120.94, 112.68, 111.67, 111.29, 110.99, 110.64, 110.46, 76.22, 55.57, 55.35, 53.51, 47.17, 41.89,31.38; IR (KBr) ν/cm^{-1}: 3479,3414,2357,1732,1637,1618;HRMS (ESI) calcd for $C_{32}H_{24}N_3O_5$ $(M-H)^-$: 530.1716, found: 530.1716.

3.11 2,7-bis(2-chlorophenyl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3k)

Yellow solid. mp 206-209°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.65 – 7.32 (m, 9H), 7.17 (t, J = 7.7 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 5.93 (dd, J = 13.2, 4.7 Hz, 1H), 5.63 (dd, J = 12.3, 4.9 Hz, 1H), 3.34 (dd, J = 19.2, 12.3 Hz, 1H), 3.06 (dd, J = 19.2, 4.9 Hz, 1H), 2.86 – 2.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.95, 174.07, 172.80, 141.63, 135.74, 134.92, 132.62, 131.76, 130.72, 130.49, 130.44, 130.14, 129.88, 127.98, 127.72, 127.58, 127.21, 126.82, 124.61, 123.21, 112.42, 111.38, 110.90, 110.83, 77.91, 53.35, 46.59, 41.65, 34.38, 32.03; HRMS (ESI) calcd for $C_{30}H_{18}N_3O_3Cl_2$ $(M-H)^-$: 538.0725, found: 538.0725.

3.12 2,7-bis(2,6-dimethoxyphenyl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3' -indolin]-6,6(2H)-dicarbonitrile(3l)

Yellow solid. mp 175-177°C ; ^{1}H NMR (400 MHz, DMSO) δ 11.15 (s, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.34 (td, J = 7.7, 1.0 Hz, 1H), 7.17 (dd, J = 11.1, 2.7 Hz, 2H), 7.05 (m, 3H), 6.96 (m, 3H), 5.85 (dd, J = 14.6, 3.1 Hz, 1H), 5.26 (dd, J = 12.5, 4.7 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 3.73 (s, 3H),

3.52 – 3.40 (m, 1H), 3.05 (dd, *J* = 19.4, 4.9 Hz, 1H), 2.92 (dd, *J* = 17.7, 14.7 Hz, 1H), 2.52 – 2.49 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ 188.04, 174.17, 173.11, 153.26, 153.15, 151.46, 150.01, 143.00, 129.77, 127.61, 126.16, 124.31, 124.23, 121.78, 114.62, 114.42, 113.84, 113.19, 112.83, 112.71, 112.54, 112.16, 110.01, 109.90, 79.12, 75.30, 56.10, 55.46, 55.37, 52.74, 46.99, 40.96, 30.28; HRMS (ESI) calcd for $C_{34}H_{28}N_3O_7$ $(M-H)^-$: 590.1927, found: 590.1928.

3.13 2,7-di(furan-2-yl)-2',4-dioxo-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3m)

Yellow solid. mp 155-157°C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.50 (d, *J* = 7.7 Hz, 3H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.1 Hz, 1H), 6.97 (d, *J* = 7.2 Hz, 1H), 6.63 – 6.33 (m, 4H), 5.52 (dd, *J* = 14.9 , 2.1 Hz, 1H), 4.86 (dd, *J* = 11.9, 5.0 Hz, 1H), 3.39 (dd, *J* = 19.4, 12.0 Hz, 1H), 3.14 (dd, *J* = 17.8, 14.9 Hz, 1H), 2.98 (dd, *J* = 19.4, 5.0 Hz, 1H), 2.61 (dd, *J* = 17.8, 2.1, Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.70, 174.29, 172.19, 148.92, 148.14, 144.01, 143.90, 141.42, 130.38, 126.85, 124.45, 123.28, 111.86, 111.28, 110.82, 110.74, 110.49, 110.37, 73.54, 52.85, 46.16, 39.06, 34.03, 30.56; IR (KBr) ν/cm^{-1}: 3419,2924,1728,1618; HRMS (ESI) calcd for $C_{26}H_{16}N_3O_5$ $(M-H)^-$: 450.1090, found: 450.1091.

3.14 2',4-dioxo-2,7-di(thiophen-2-yl)-3,4,7,8-tetrahydrospiro[chromene-5,3'-indoline]-6,6(2H)-dicarbonitrile(3n)

Yellow solid. mp 244°C, decompose; ^{1}H NMR (400 MHz, DMSO) δ 11.25 (s, 1H), 7.72 – 7.56 (m, 2H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.28 (m, 3H), 7.18 – 6.96 (m, 4H), 6.02 (dd, *J* = 14.5, 3.1 Hz, 1H), 4.86 (dd, *J* = 11.7, 5.3 Hz, 1H), 3.32 – 3.16 (m, 2H), 3.01 (dd, *J* = 17.7, 14.6 Hz, 1H), 2.71 (dd, *J* = 17.7, 3.2 Hz, 1H);^{13}C NMR (100 MHz, DMSO) δ 187.53, 174.47, 171.54, 142.92, 139.37, 137.18, 129.95, 128.13, 127.50, 127.44, 127.30, 127.07, 127.04, 124.32, 121.97, 112.15, 112.10, 110.22, 75.56, 52.61, 48.30, 41.98, 34.78, 32.53; IR (KBr) ν/cm^{-1}: 3478,2924,2354,1728,1670,1618; HRMS (ESI) calcd for $C_{26}H_{16}N_3O_3S_2$ $(M-H)^-$: 482.0633, found: 482.0636.

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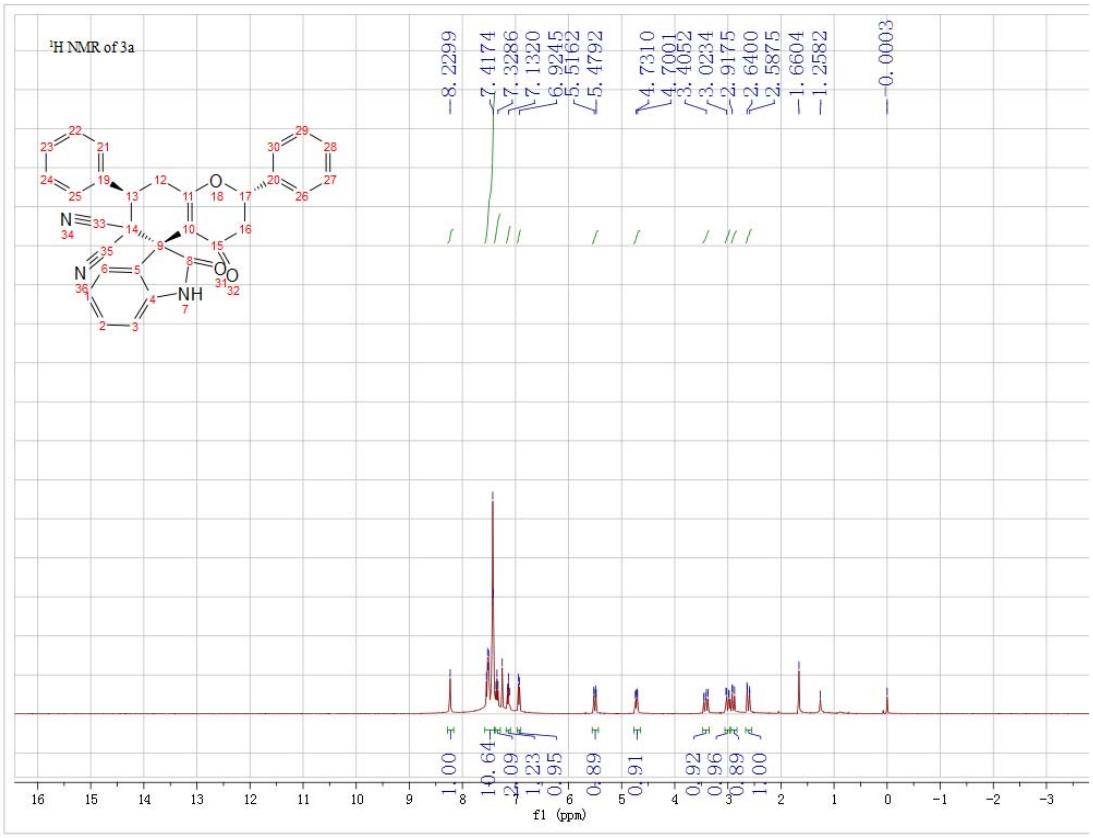

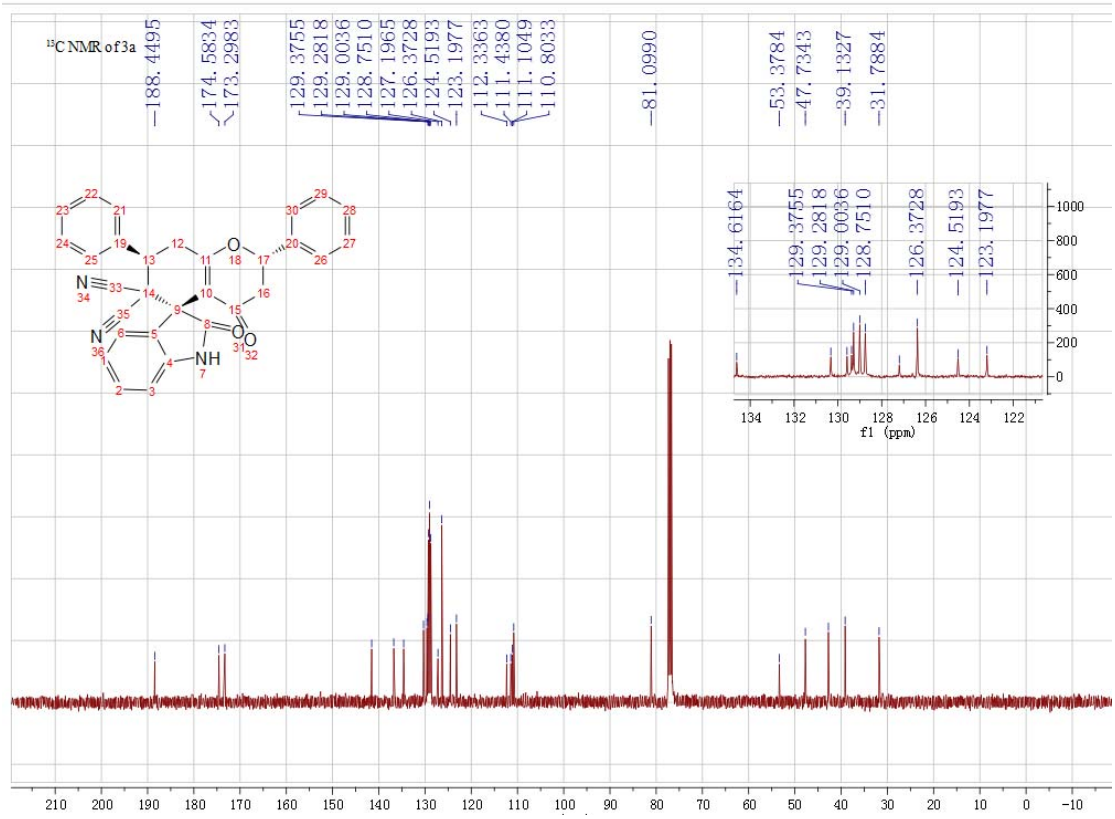

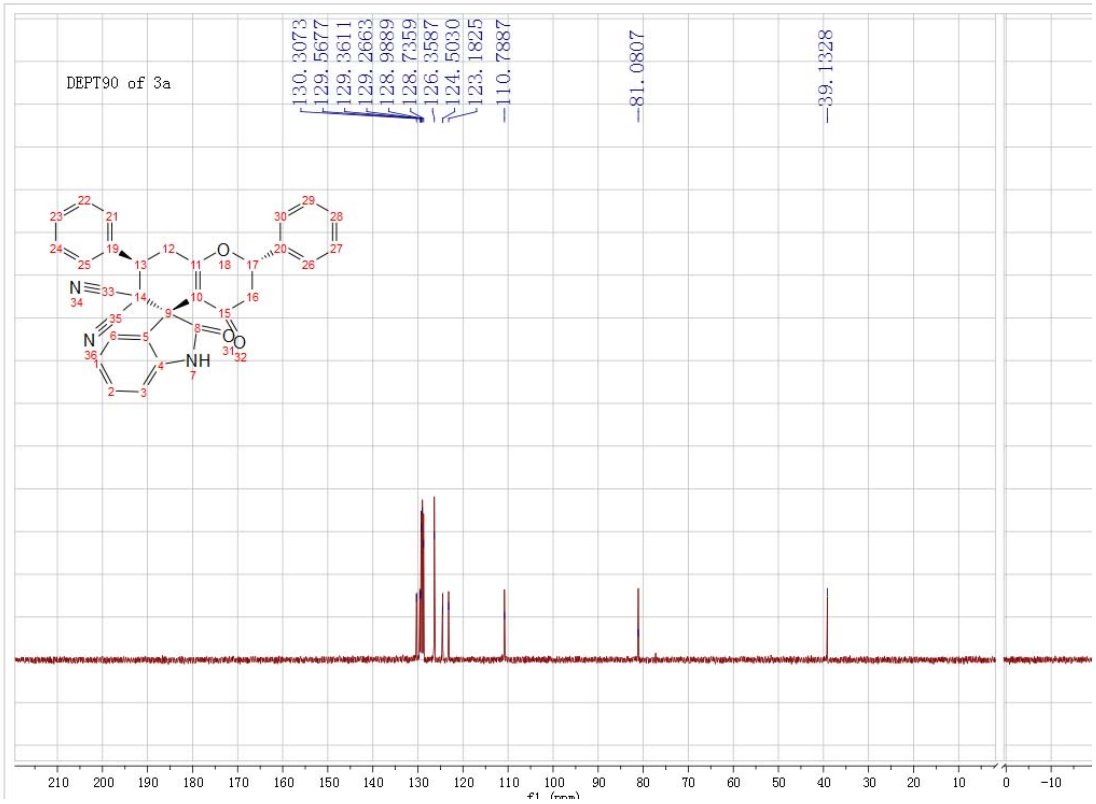
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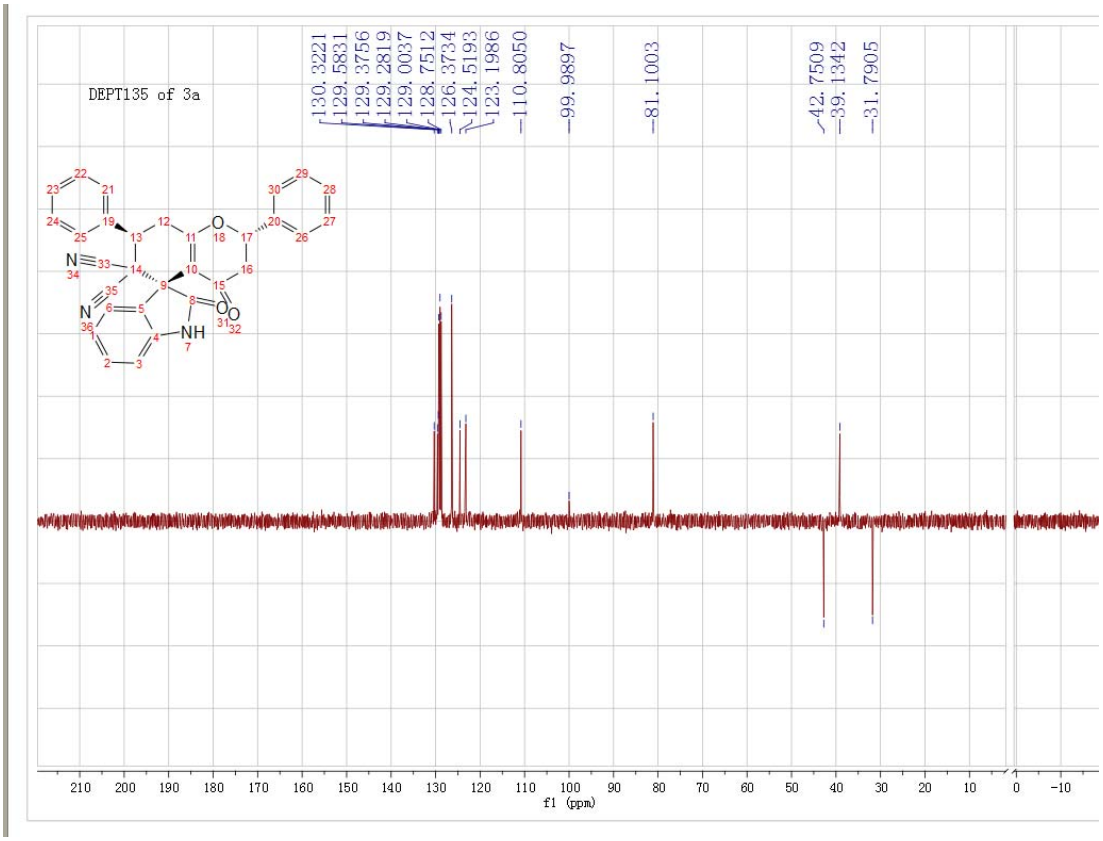
81.0807
39.1328
f1 (ppm)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129.5831
129.3756
129.2819
129.0037
128.7512
126.3734
124.5193
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99.9897
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39.1342
31.7905
f1 (ppm)

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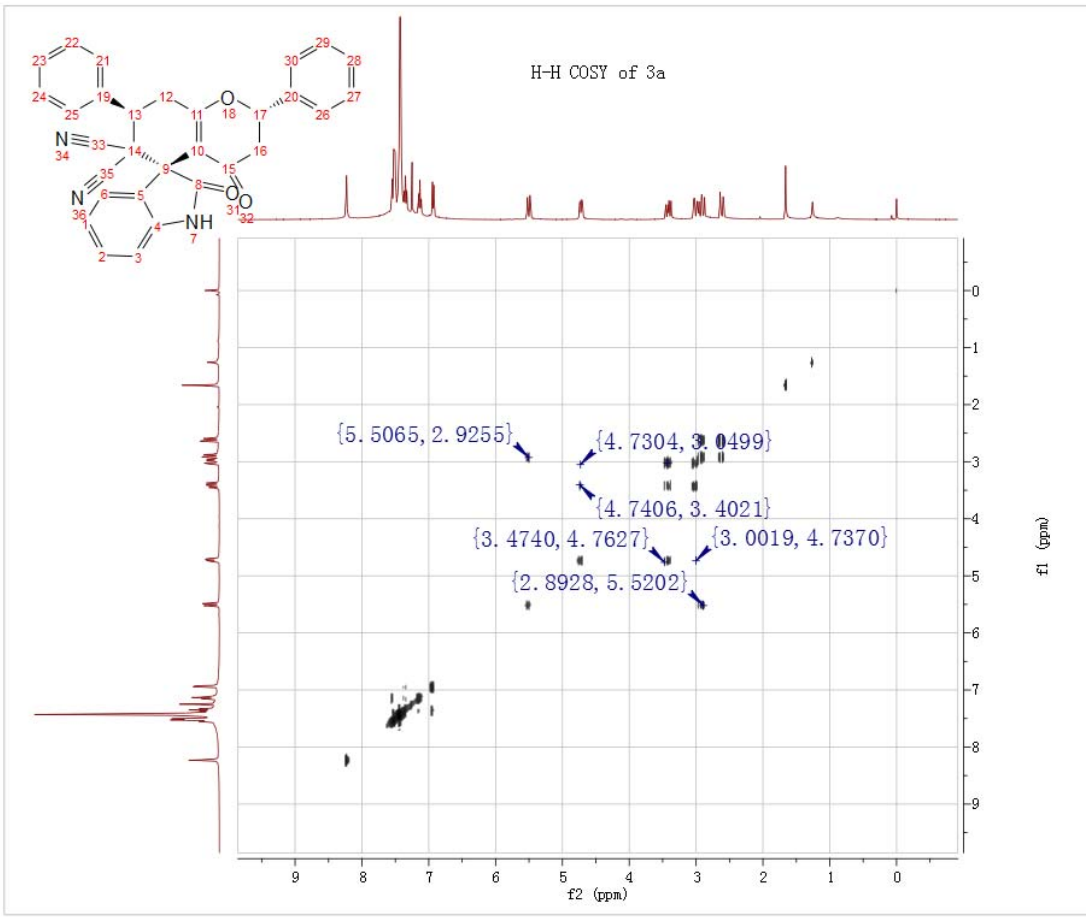

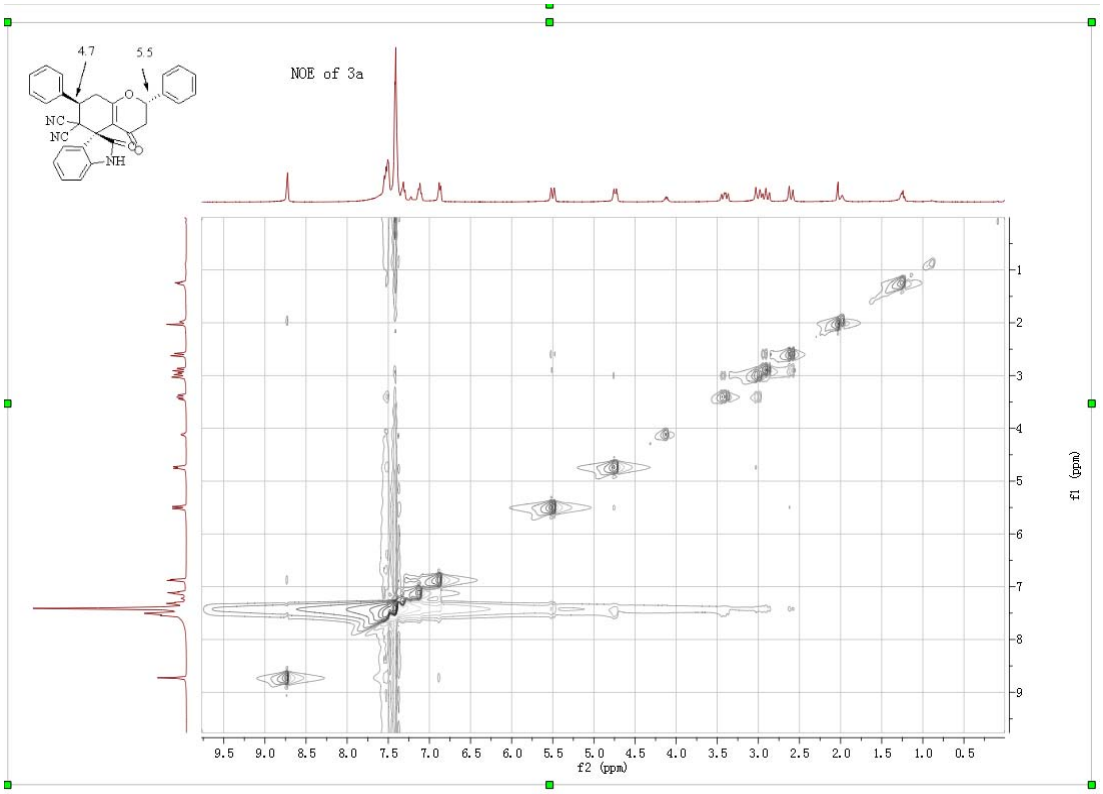

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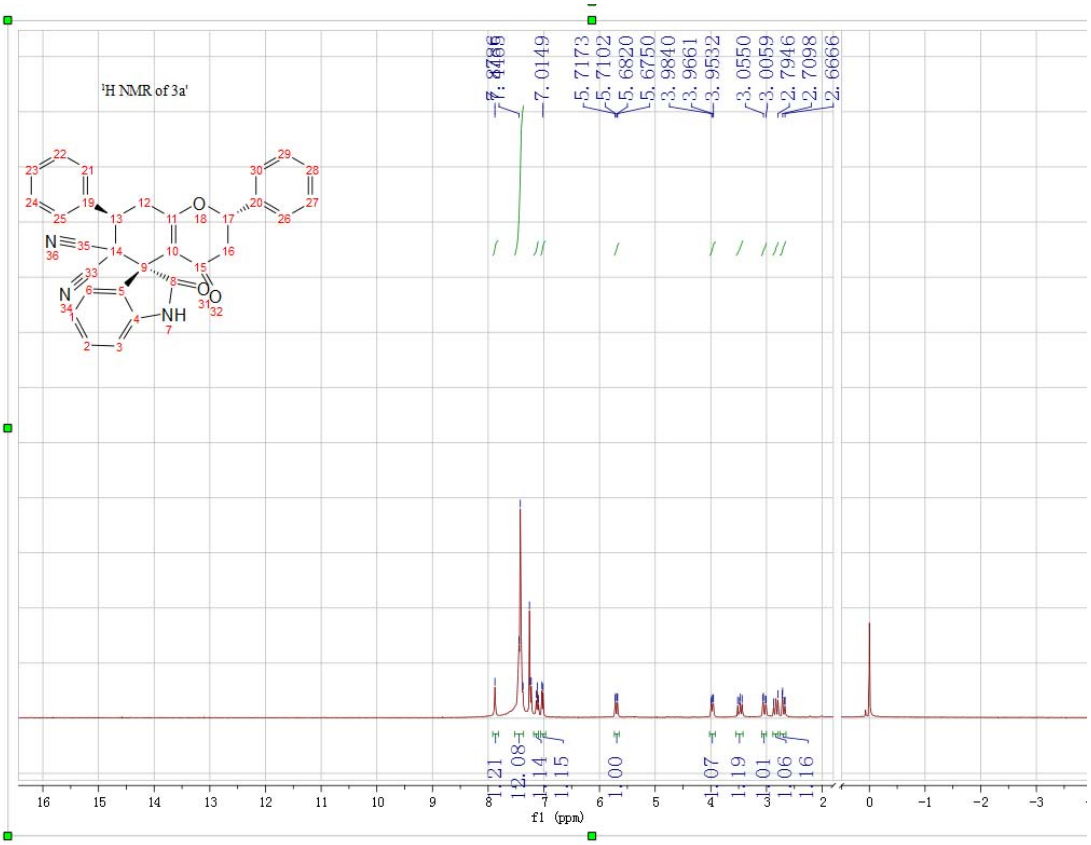

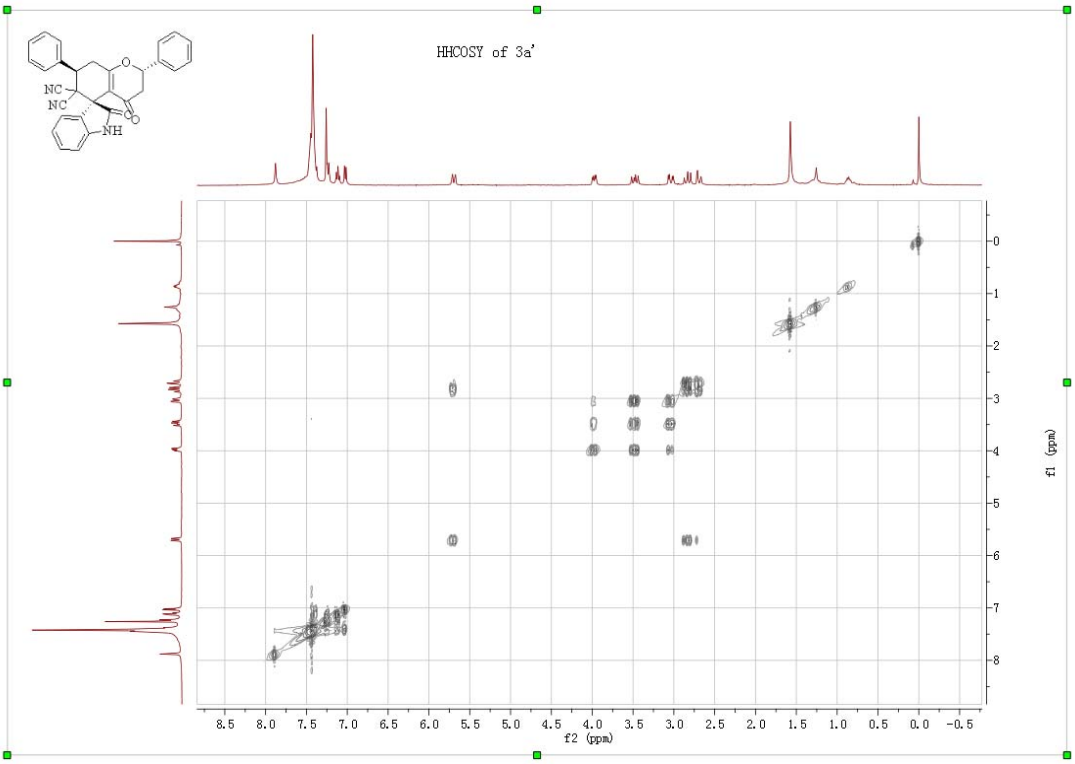

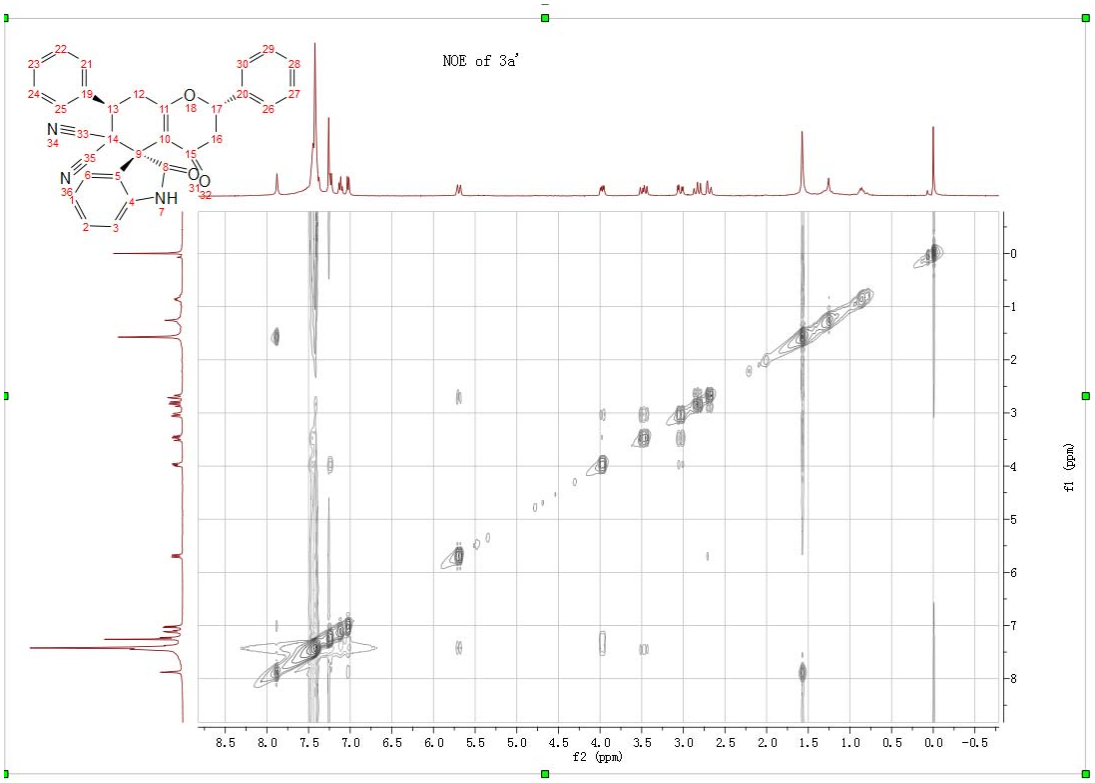
NOE of 3a'
f2 (ppm)
f1 (ppm)

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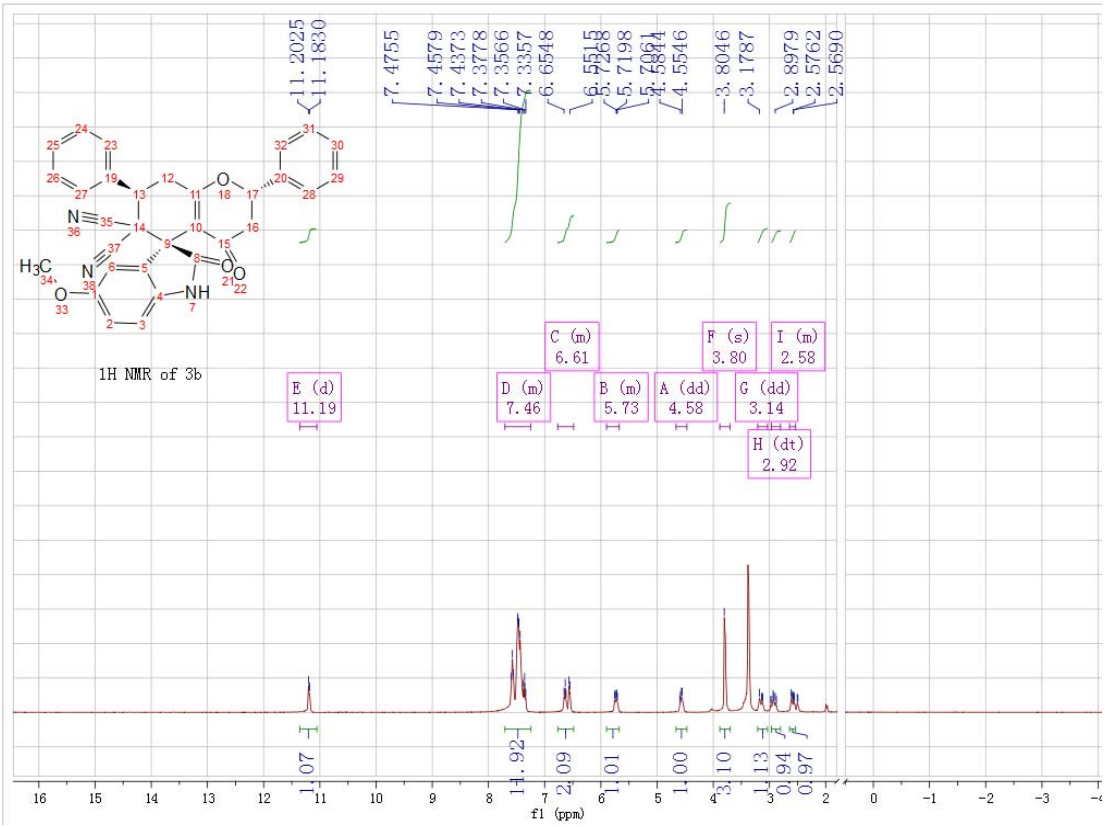
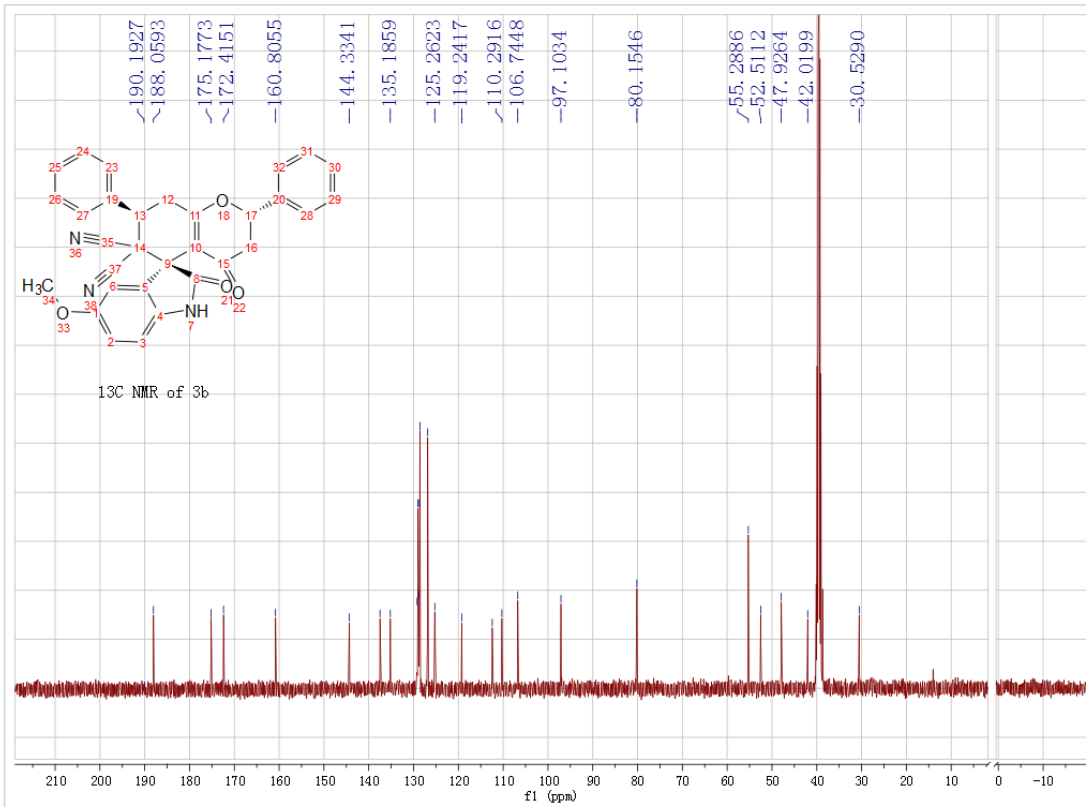


1H NMR of 3b



13C NMR of 3b

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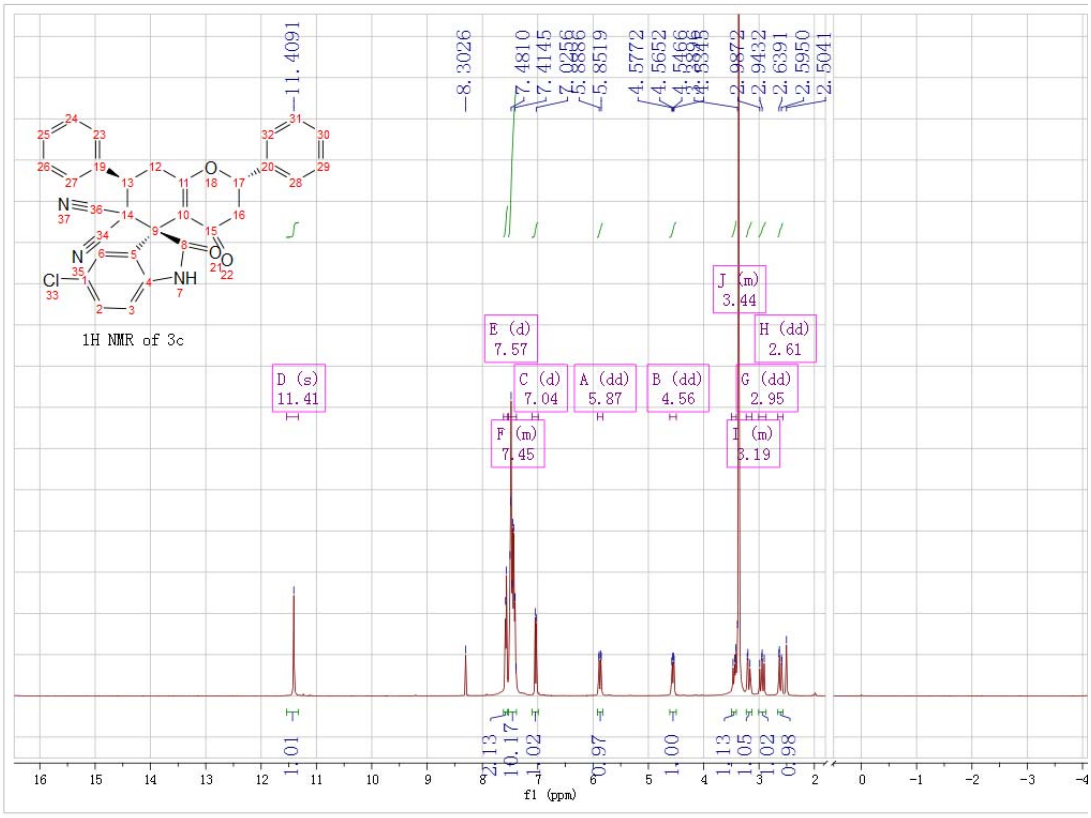

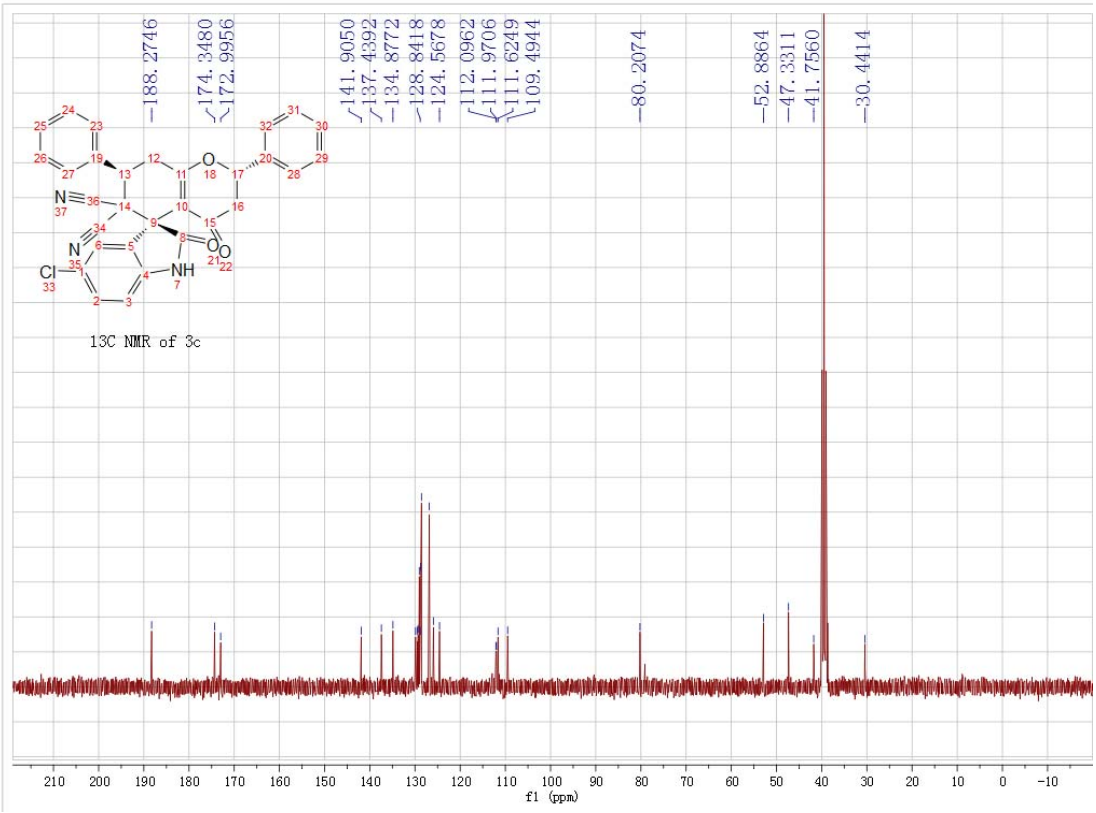

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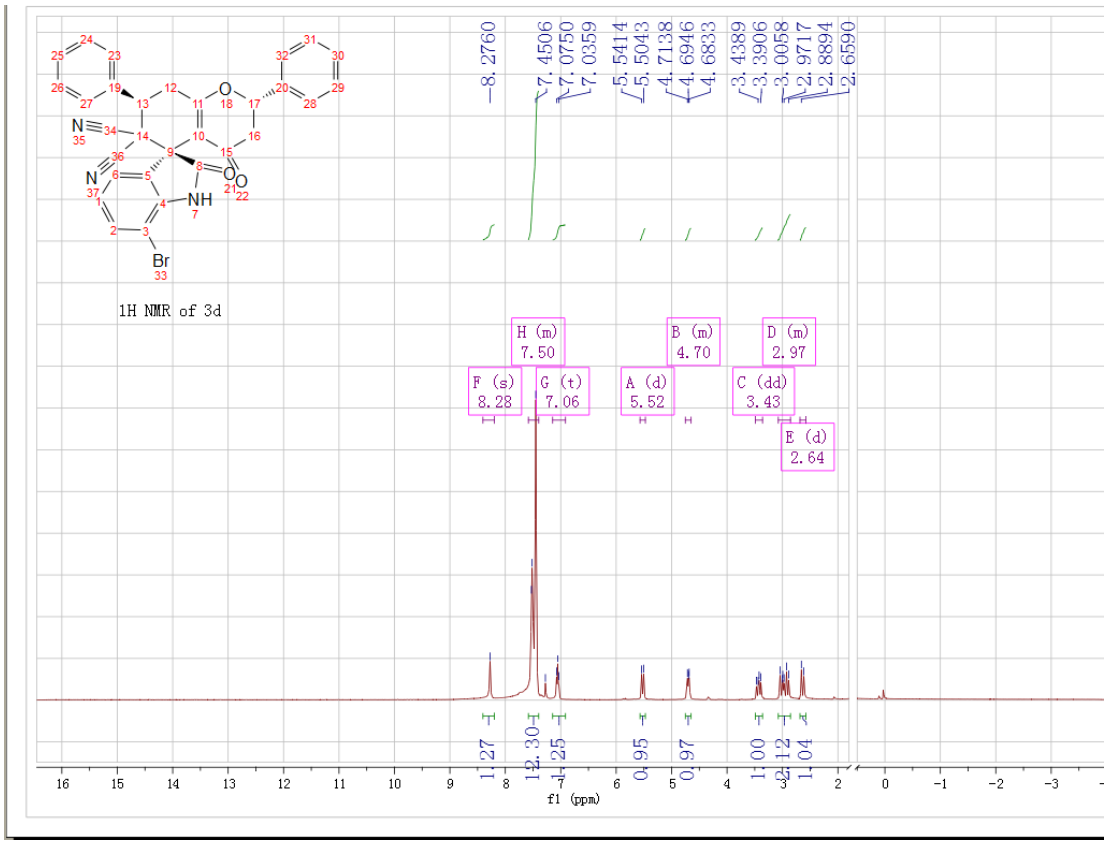

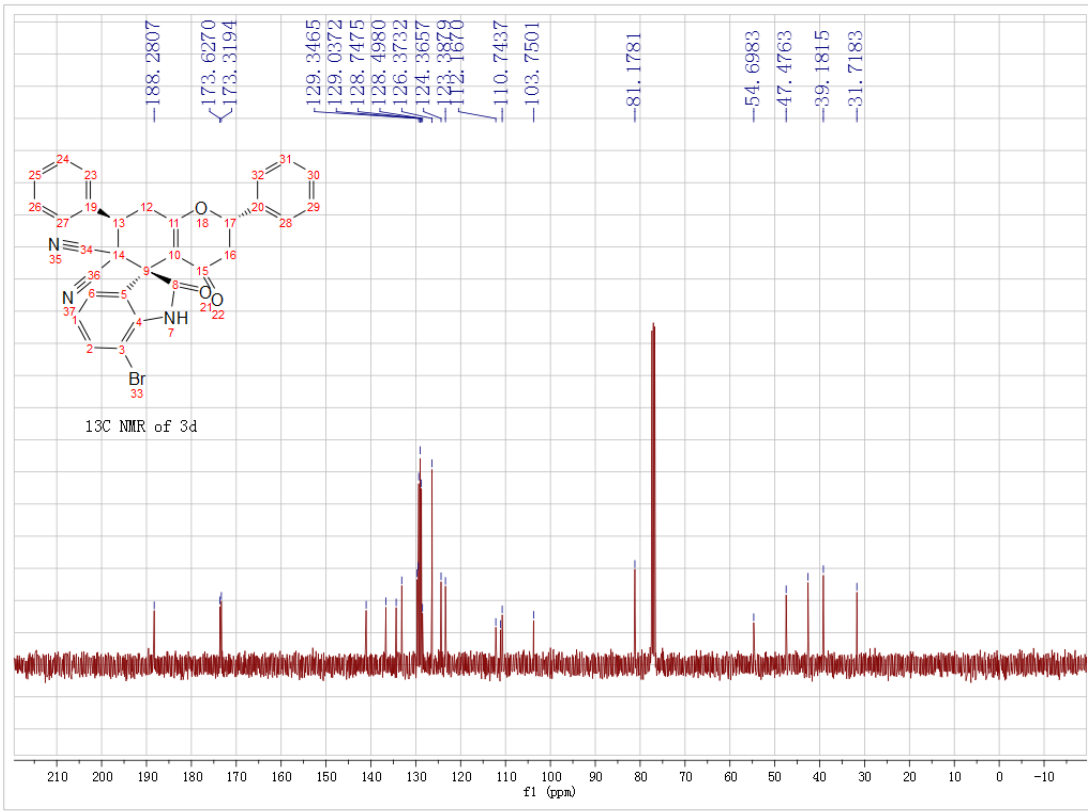

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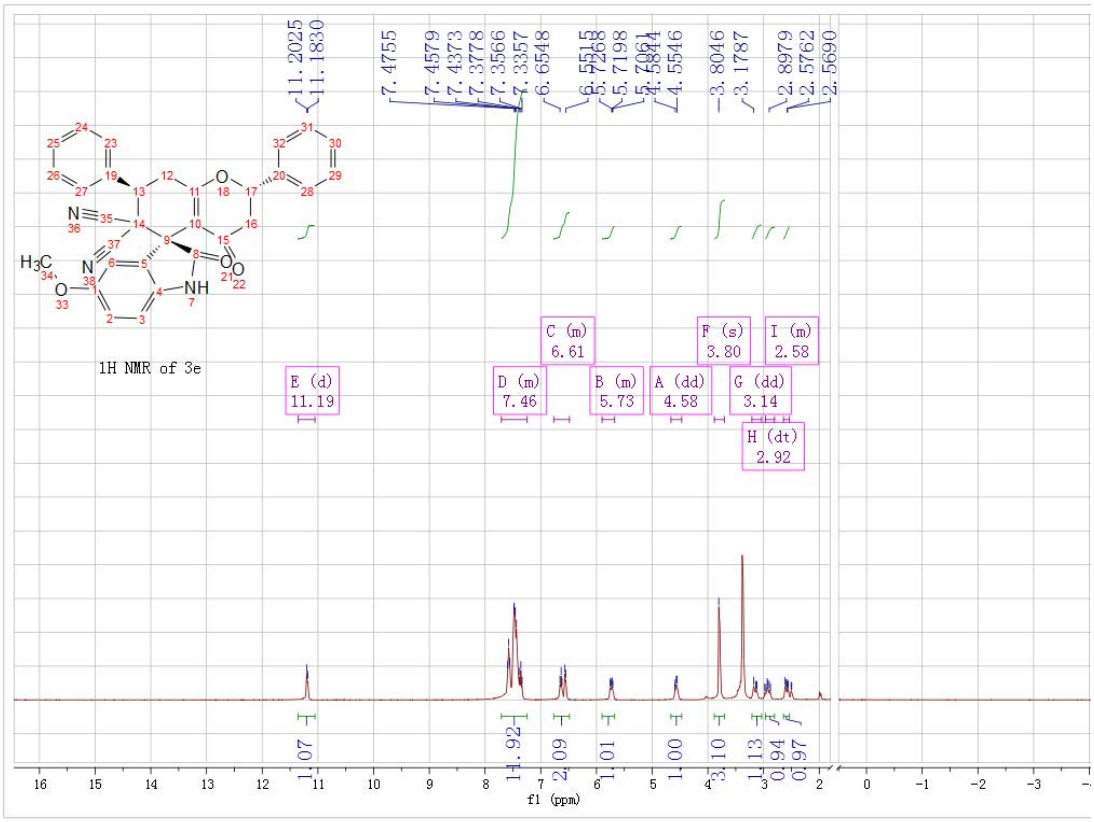

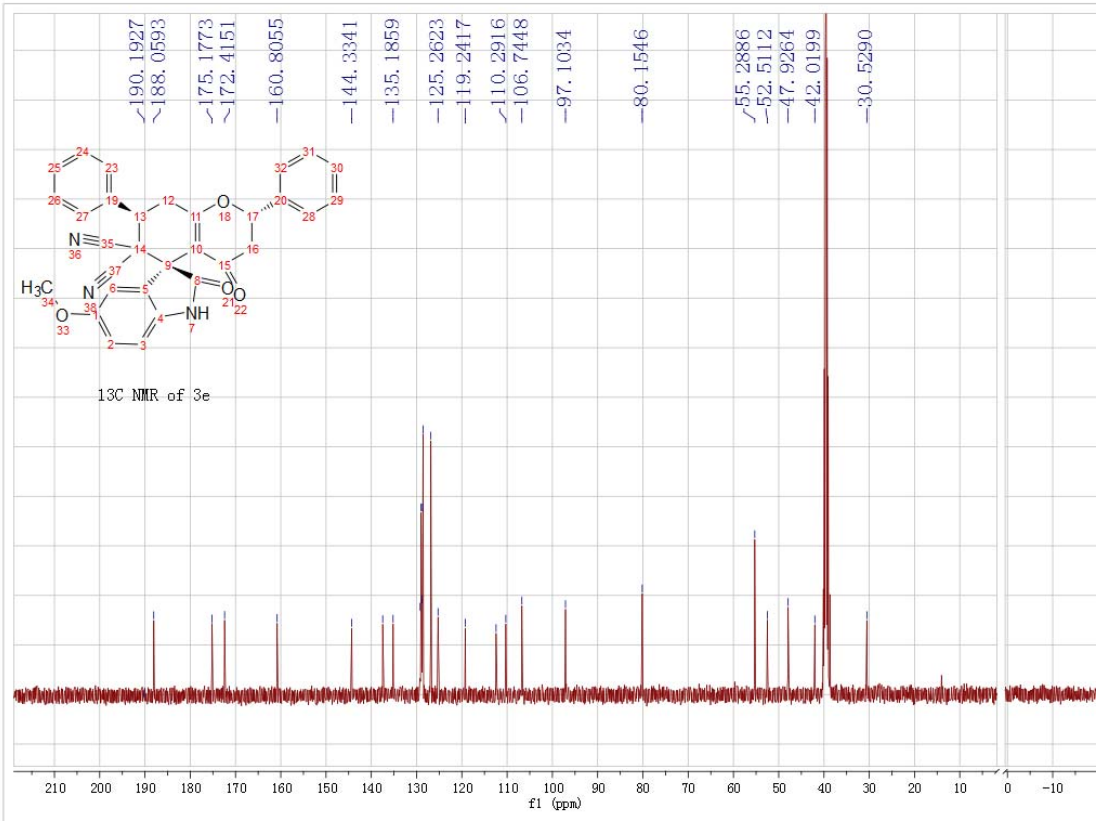

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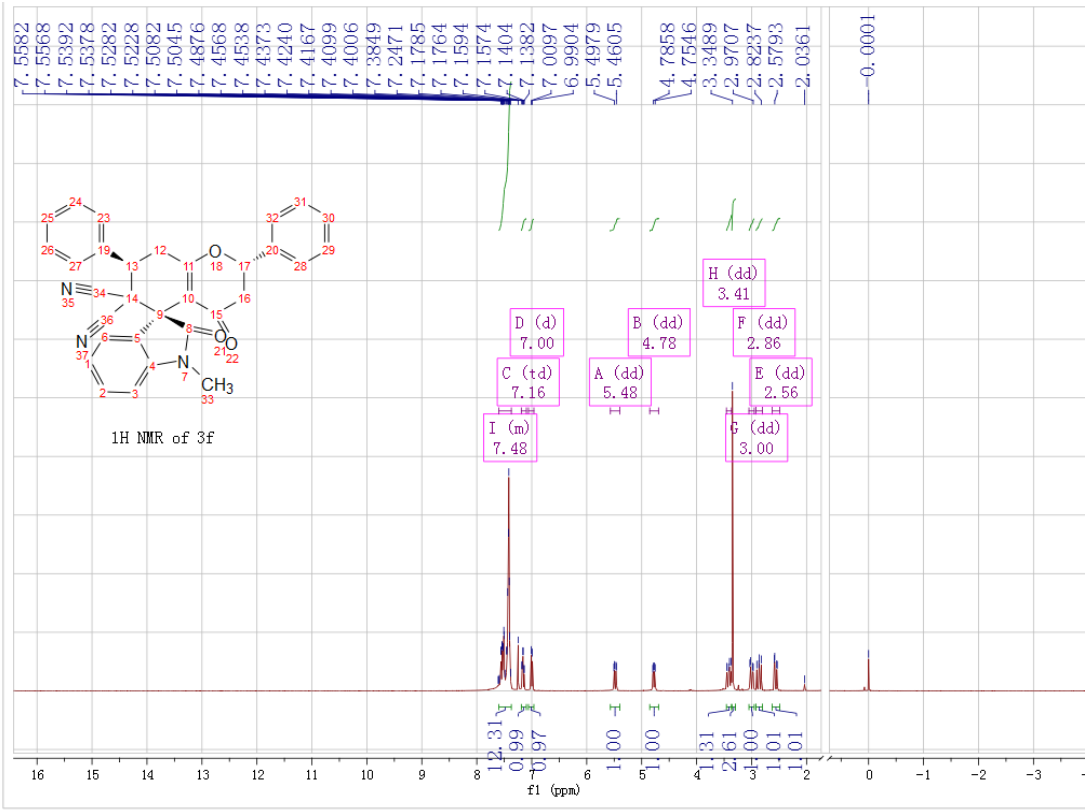

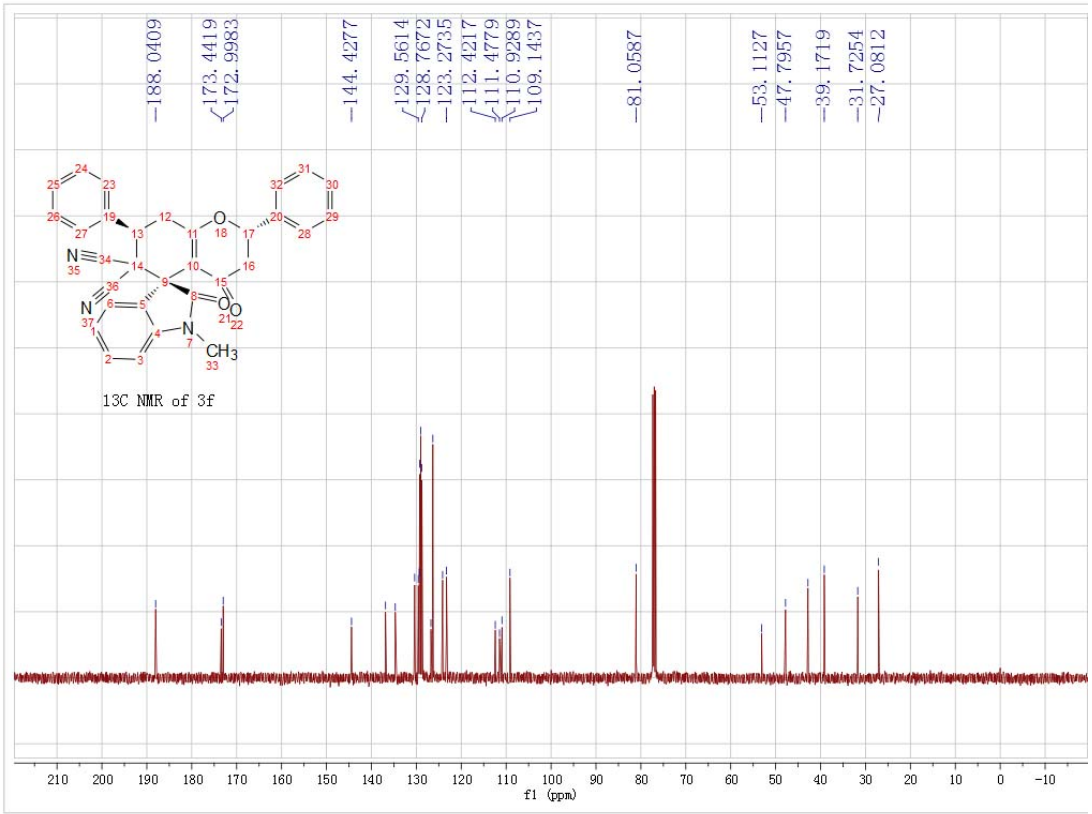

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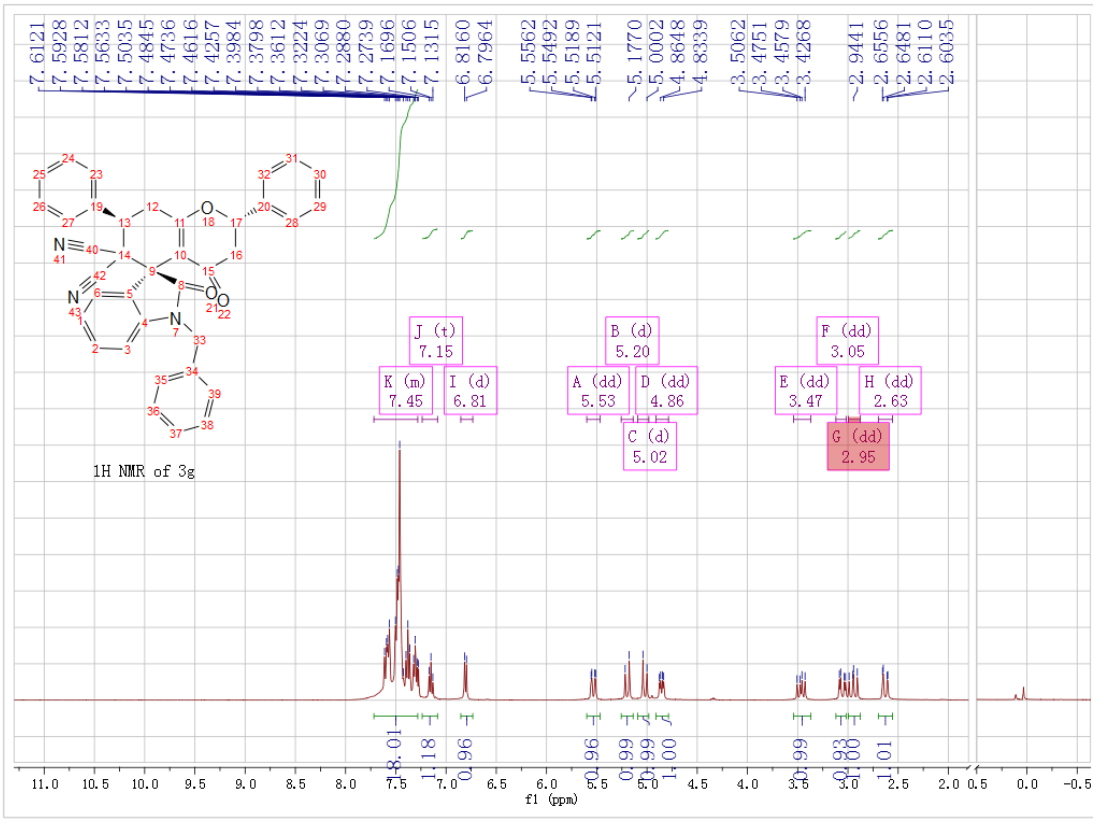

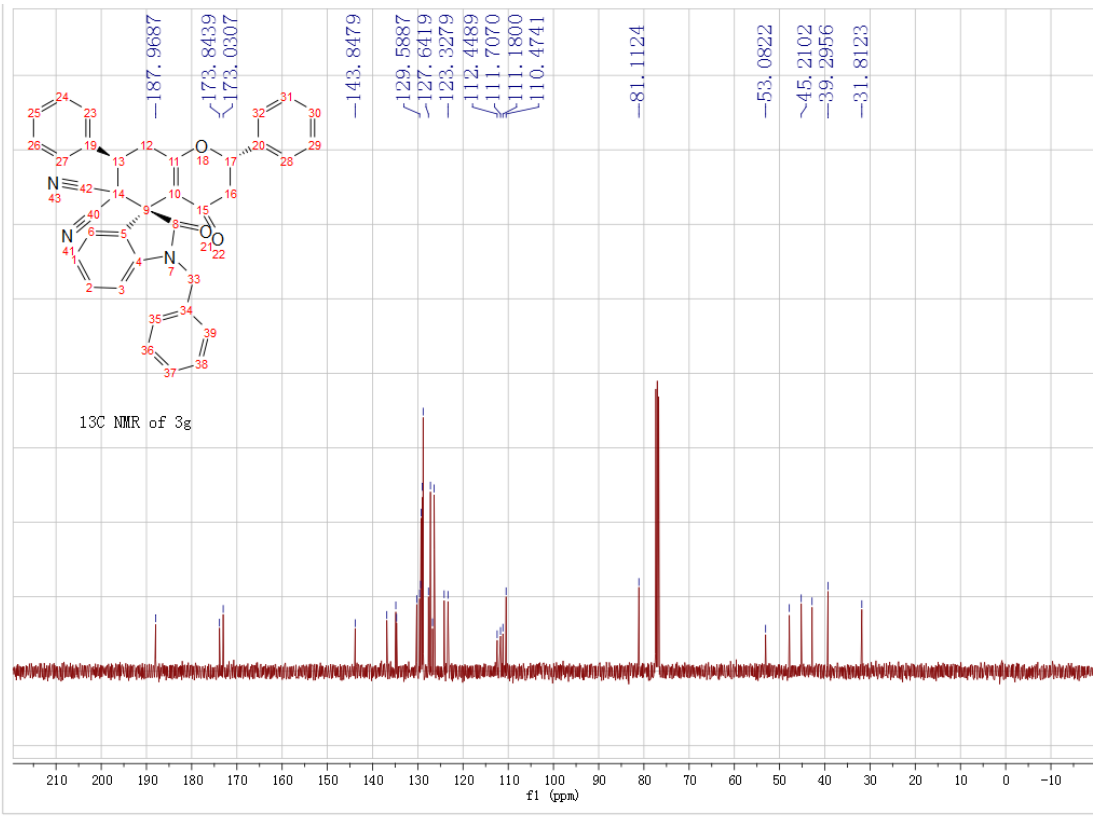

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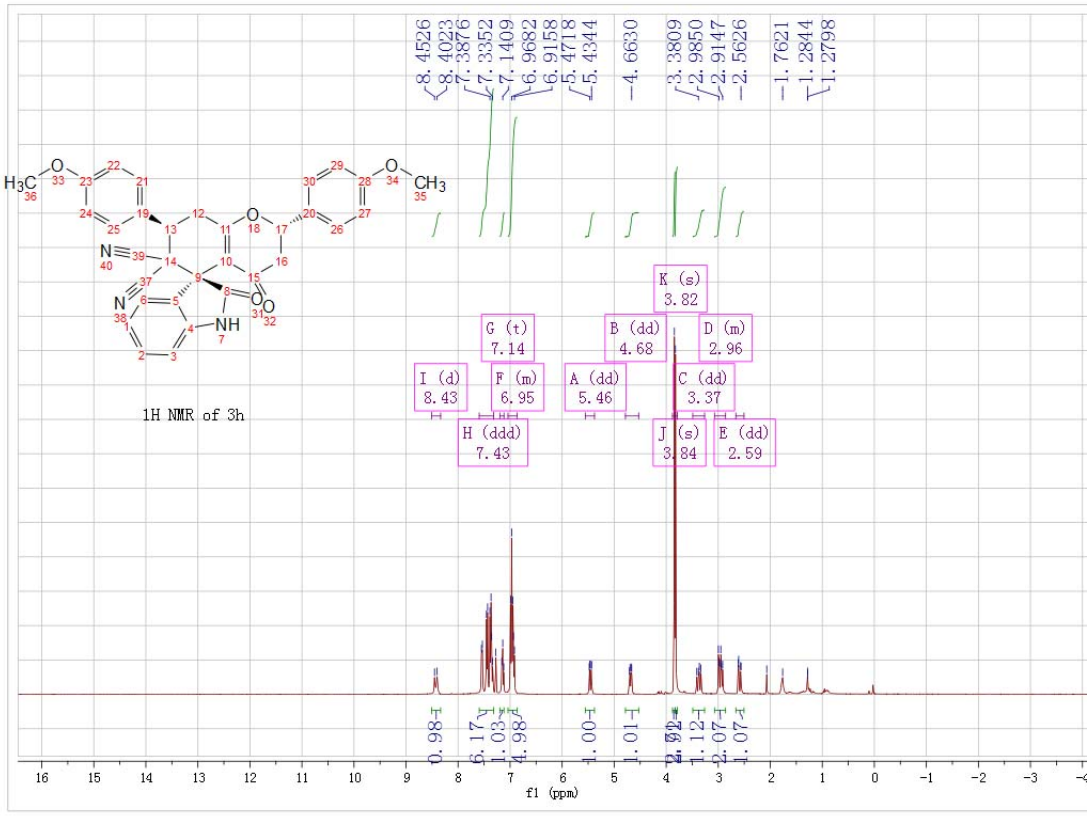

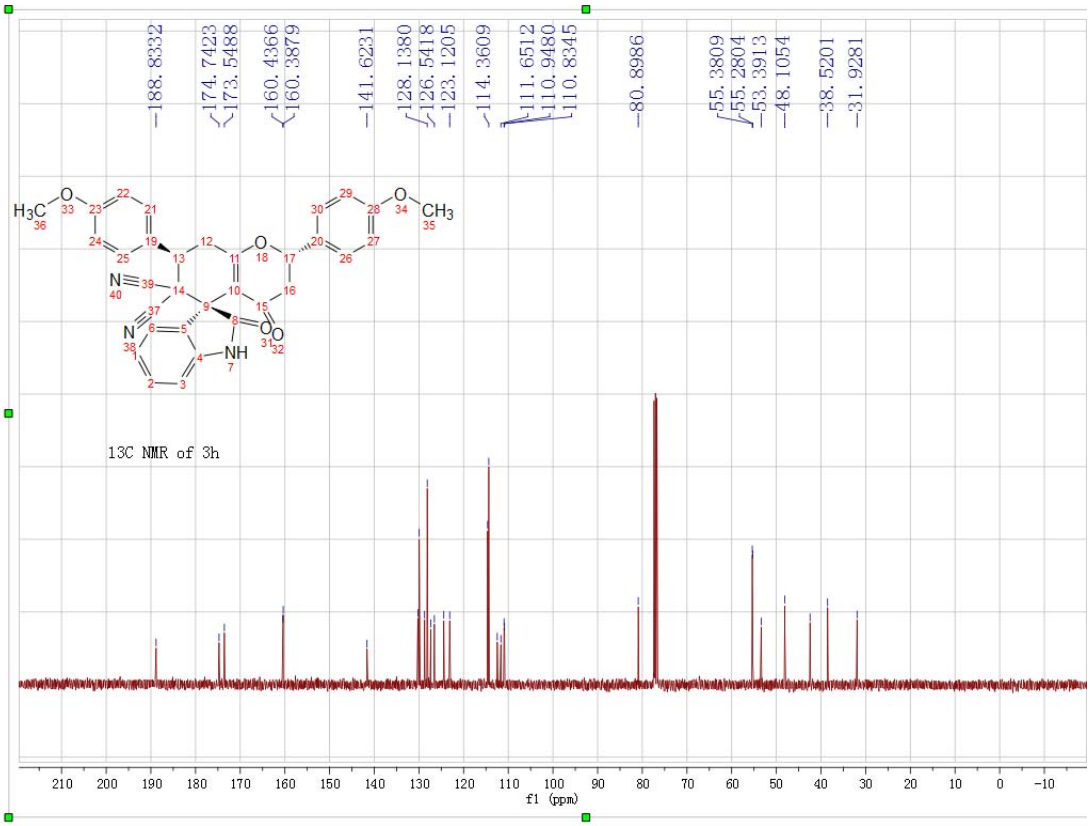

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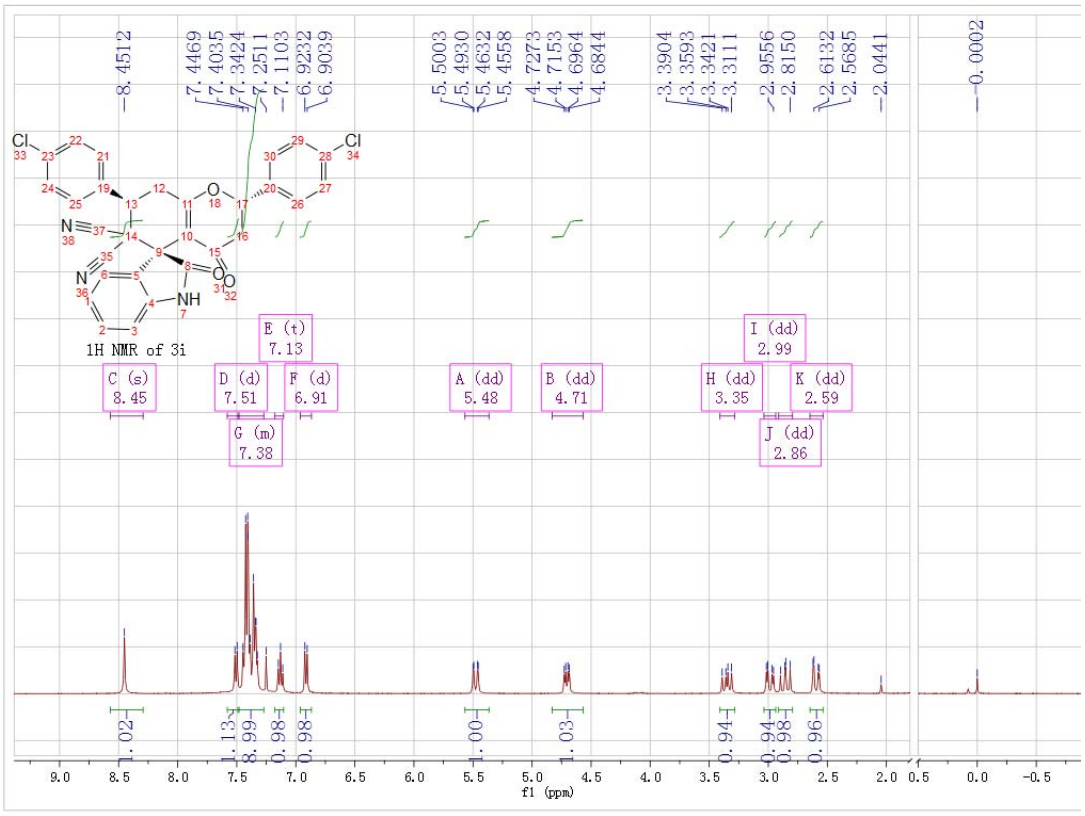

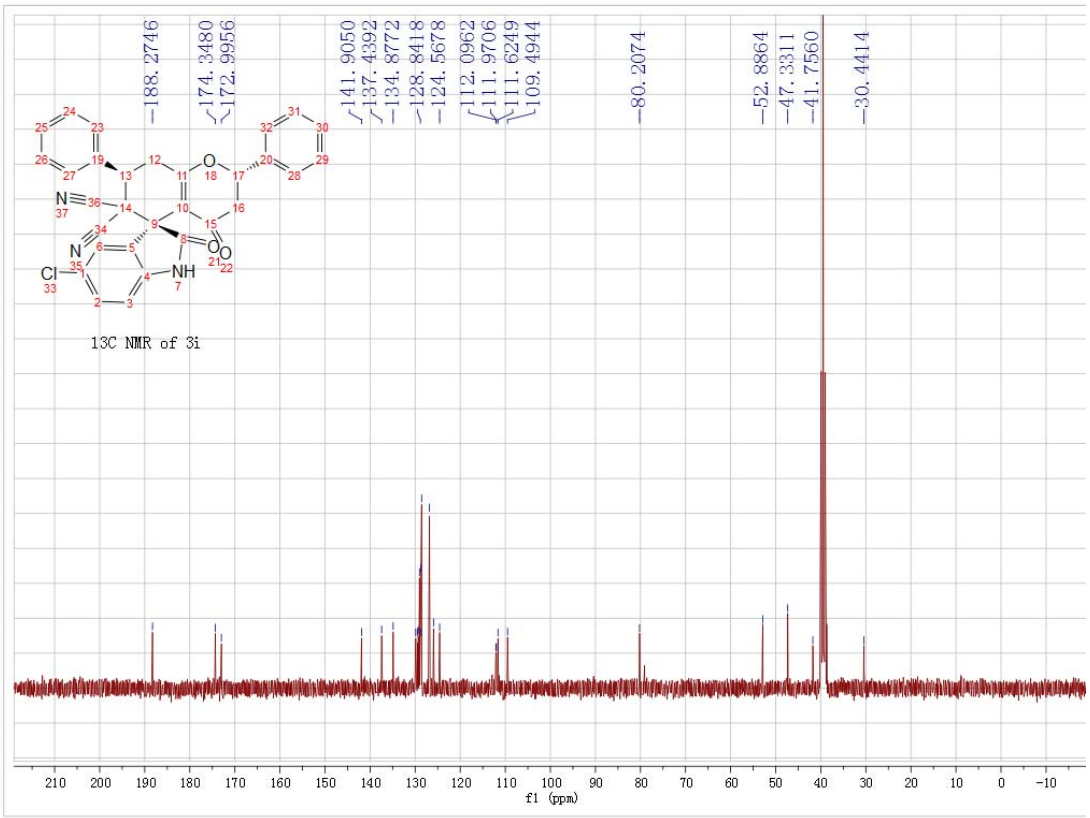

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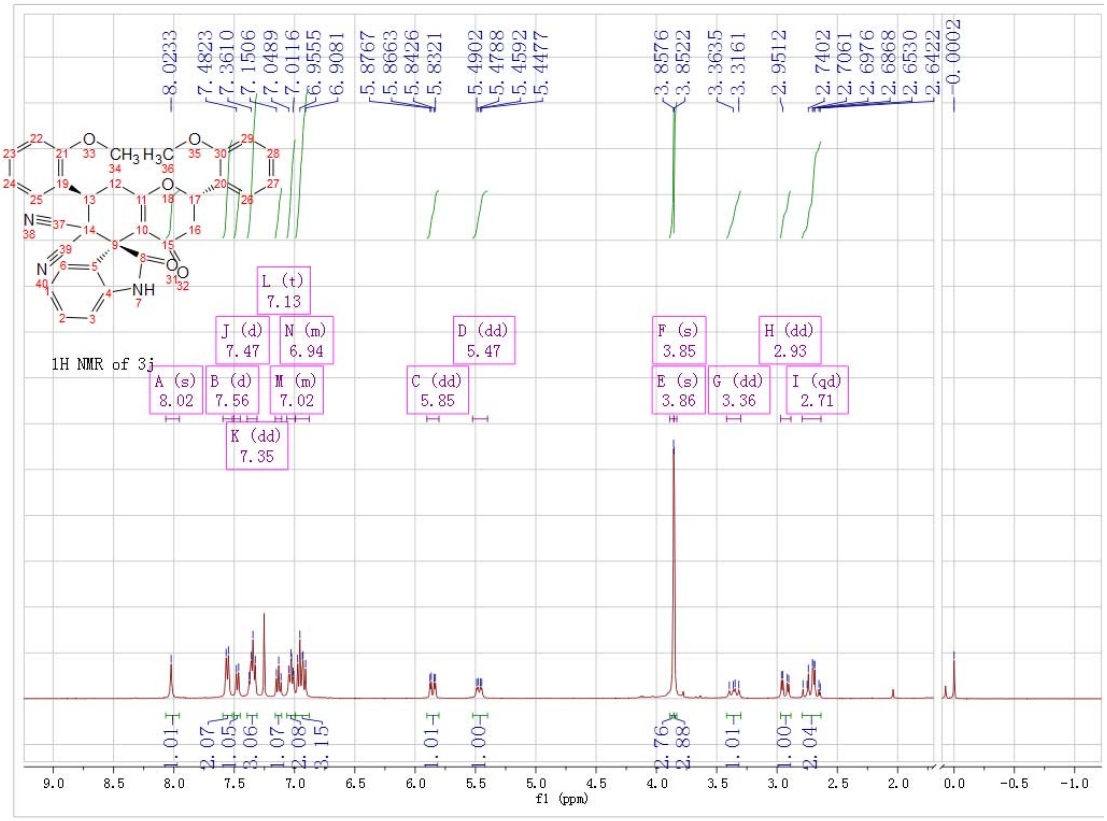

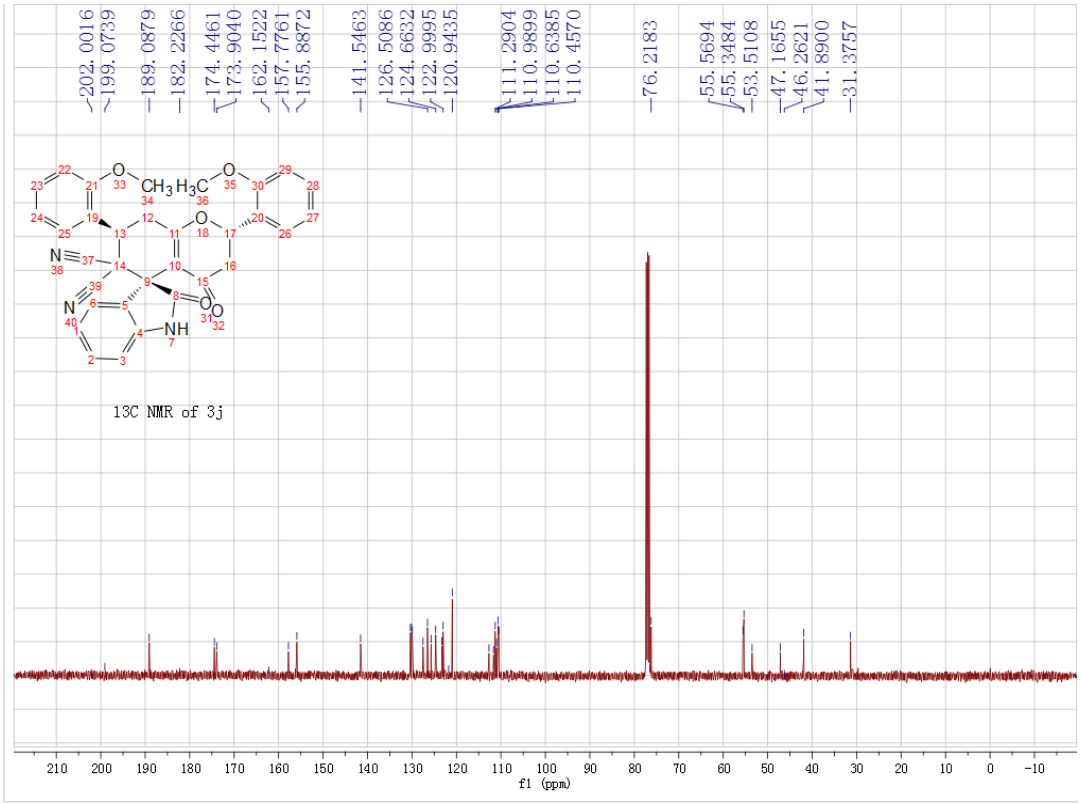

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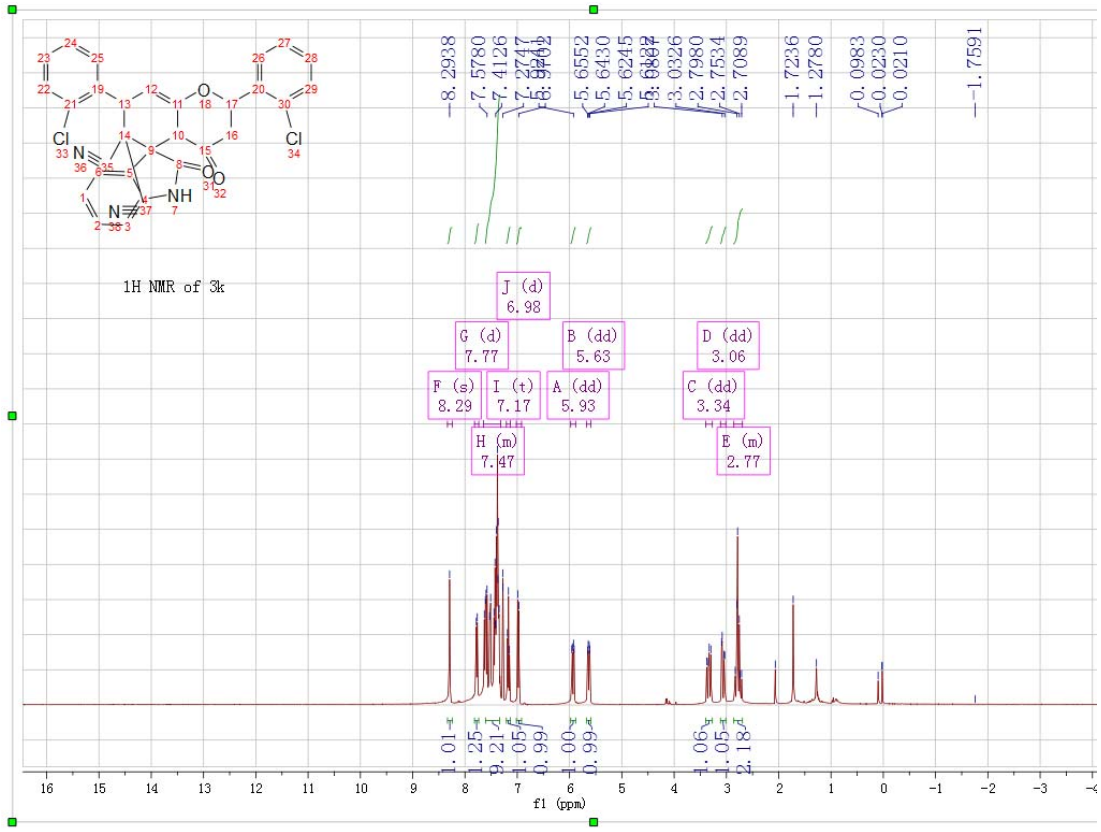
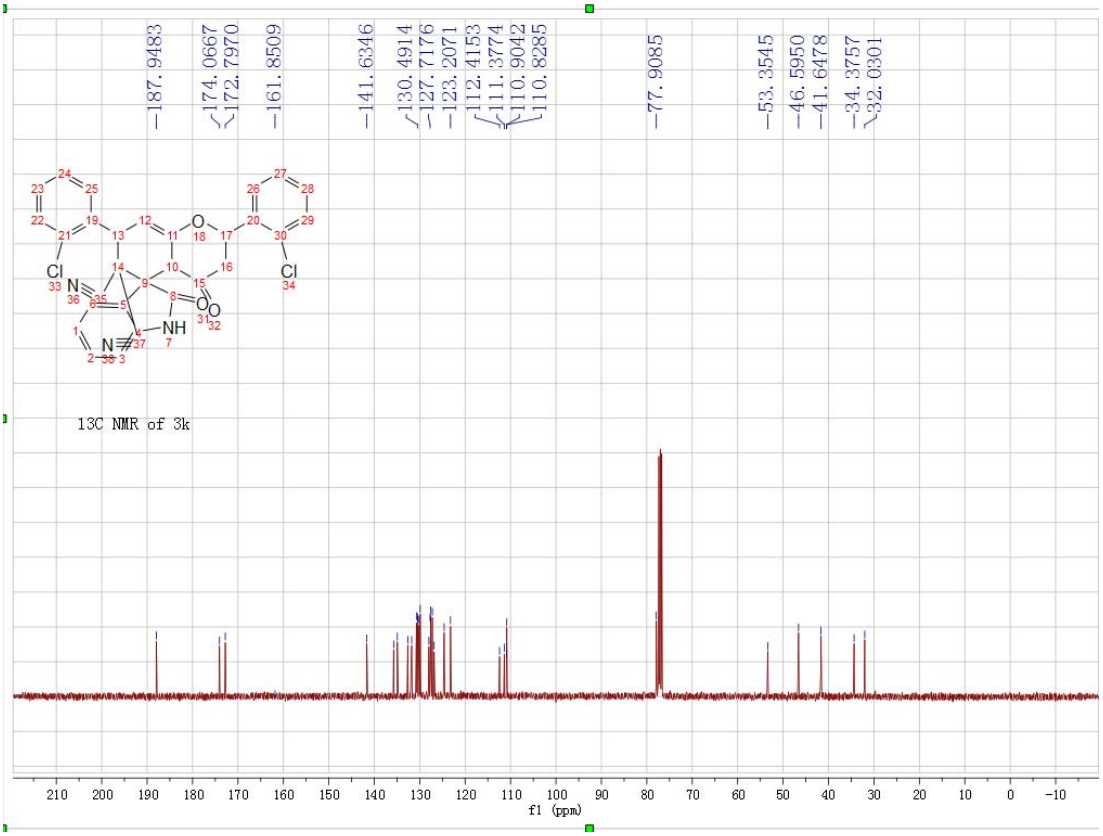
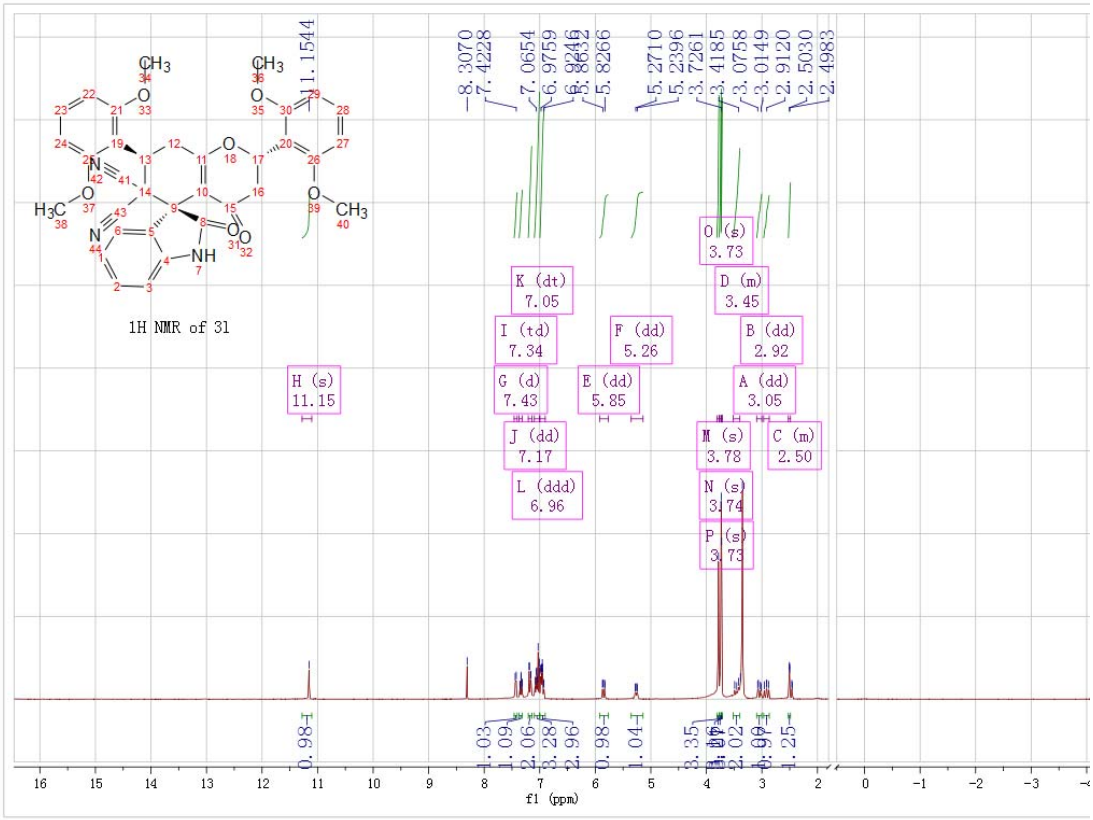
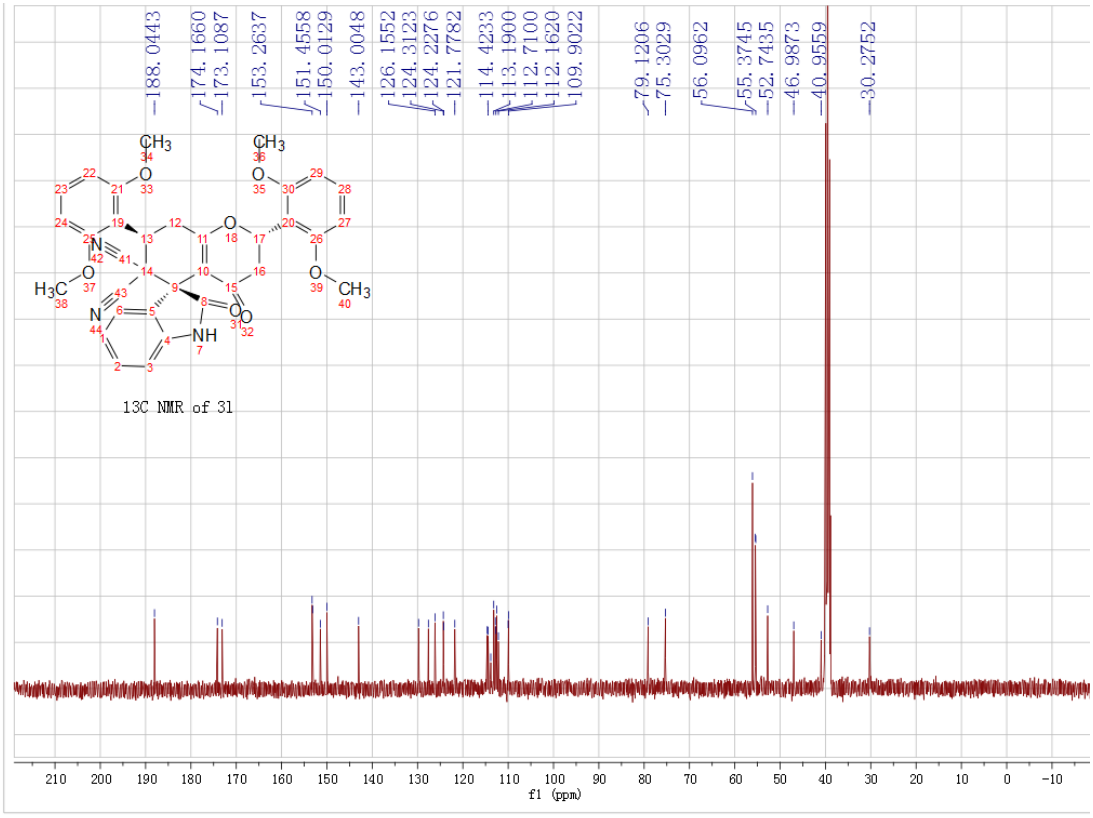





1H NMR of 31
H (s) 11.15
K (dt) 7.05
I (td) 7.34
G (d) 7.43
J (dd) 7.17
L (ddd) 6.96
F (dd) 5.26
E (dd) 5.85
O (s) 3.73
D (m) 3.45
B (dd) 2.92
A (dd) 3.05
M (s) 3.78
C (m) 2.50
N (s) 3.74
P (s) 3.73
f1 (ppm)


13C NMR of 31
f1 (ppm)

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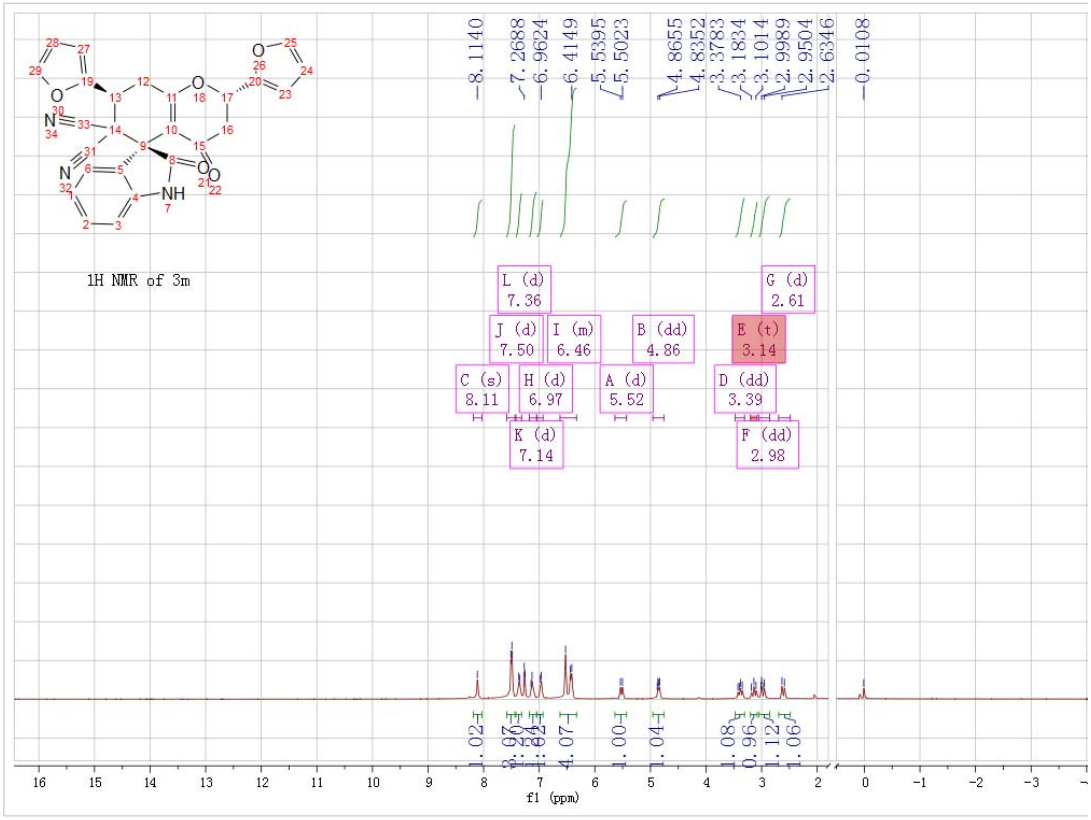

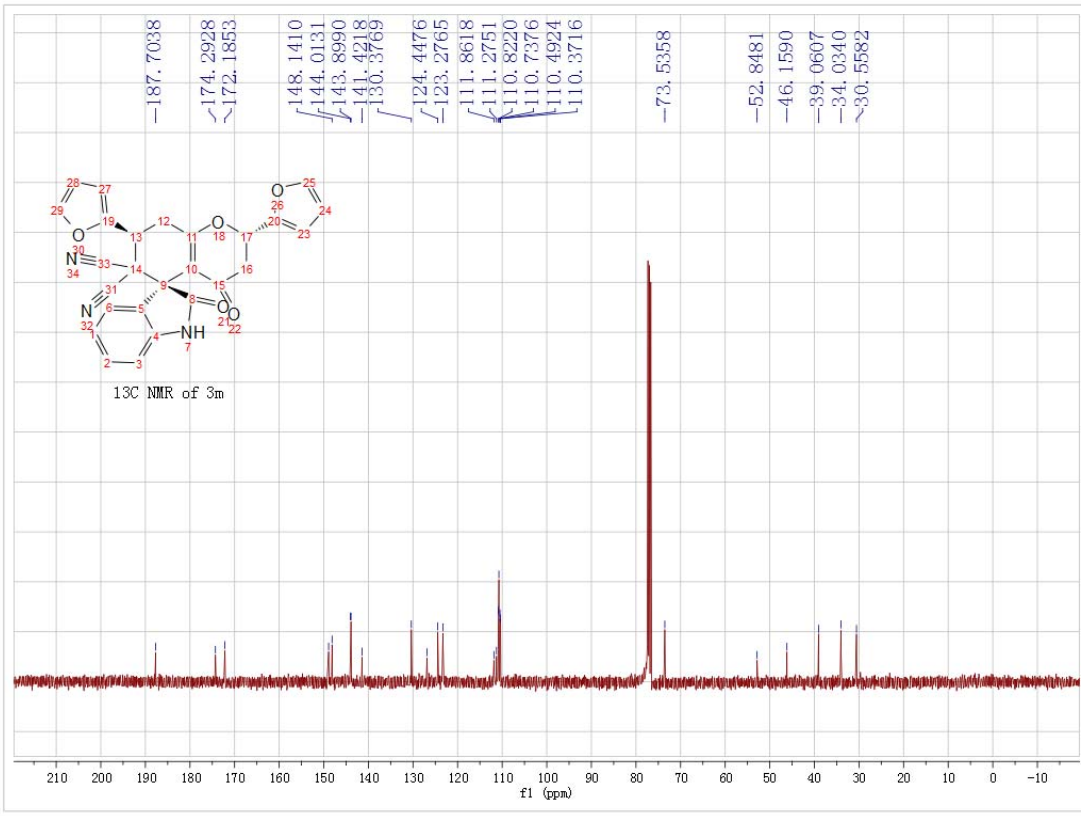

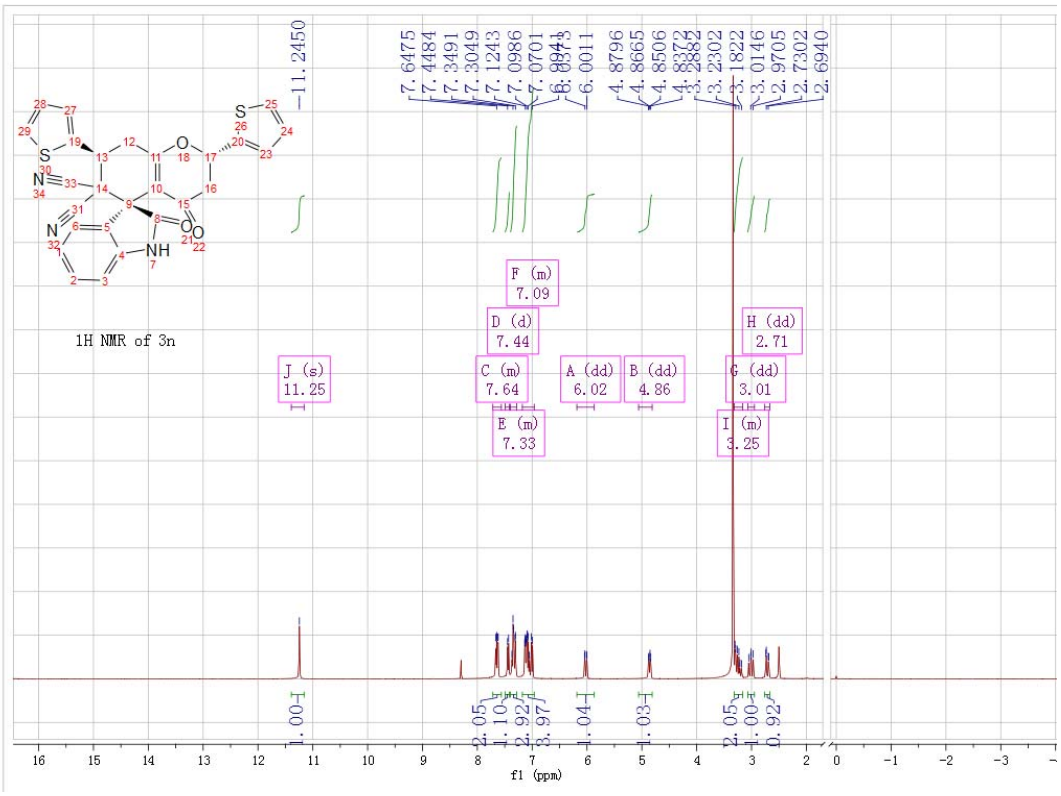

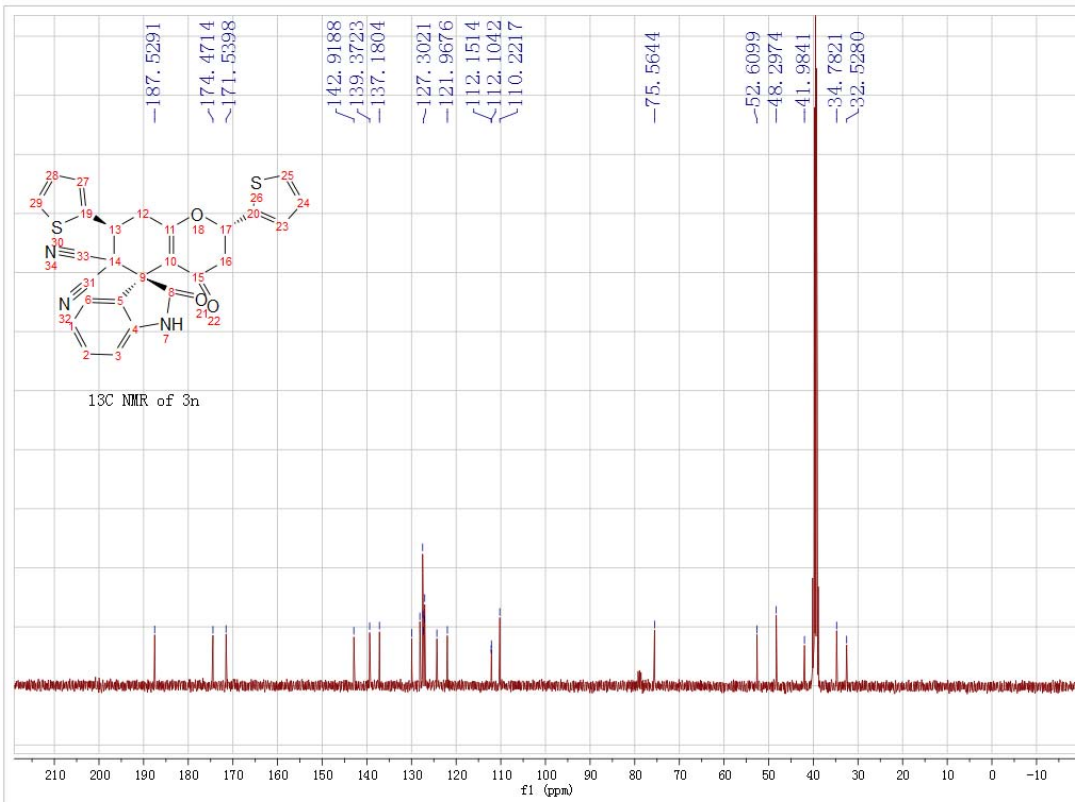

References of supplementary information

1 For the synthesis of curcumin derivatives, see: A. Mazumder, N. Neamati, S. Sunder, J. Schulz, H. Pertz, E. Eich and Y. Pommier, *J. Med. Chem.*, 1997, **40**, 3057.

2 For the synthesis of isatylidene malononitriles, see: H. Liu, G. L. Dou and D. Q. Shi, *J. Comb. Chem.*, 2010, **12**, 292.