Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Synthesis and biological evaluation of Suffrutines A, B and their N-fused analogues

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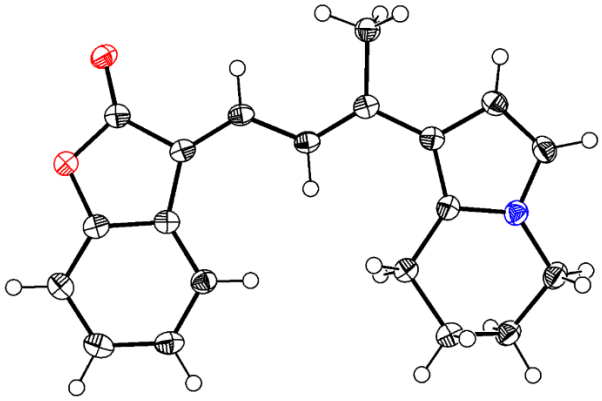
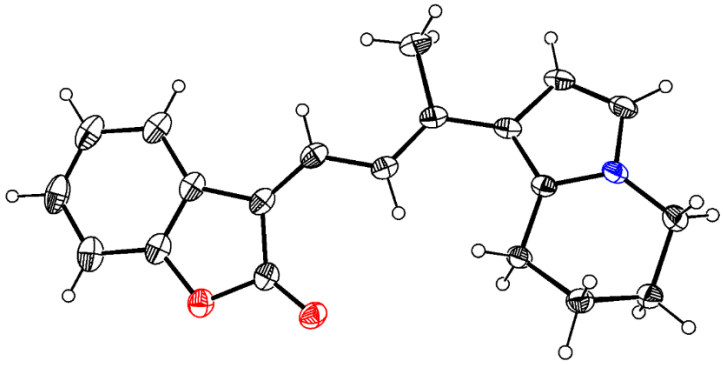
1. single-crystal X-ray crystallography date

Table S1 Crystal data and structure refinement for suffrutines A (**1a**)



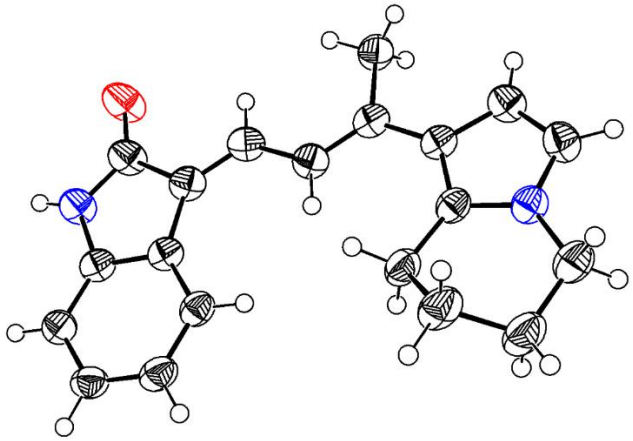
Identification code	**1a**
Empirical formula	$C_{20}H_{19}O_2N$
Formula weight	305.36
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	7.2127(2)
b/Å	8.9207(2)
c/Å	12.7145(2)
α/°	109.478(2)
β/°	95.908(2)
γ/°	96.652(2)
Volume/Å^3	757.27(3)
Z	2
ρ_{calc}g/cm^3	1.339
μ/mm^{-1}	0.684
F(000)	324.0
Crystal size/mm^3	0.3 × 0.2 × 0.05
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.46 to 153.078
Index ranges	-8 ≤ h ≤ 7, -11 ≤ k ≤ 11, -16 ≤ l ≤ 15
Reflections collected	29628
Independent reflections	3069 [R_{int} = 0.0353, R_{sigma} = 0.0158]
Data/restraints/parameters	3069/0/210
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0386, wR_2 = 0.0991
Final R indexes [all data]	R_1 = 0.0408, wR_2 = 0.1008
Largest diff. peak/hole / e Å^{-3}	0.33/-0.20

Table S2. Crystal data and structure refinement for suffrutines B (**1b**)



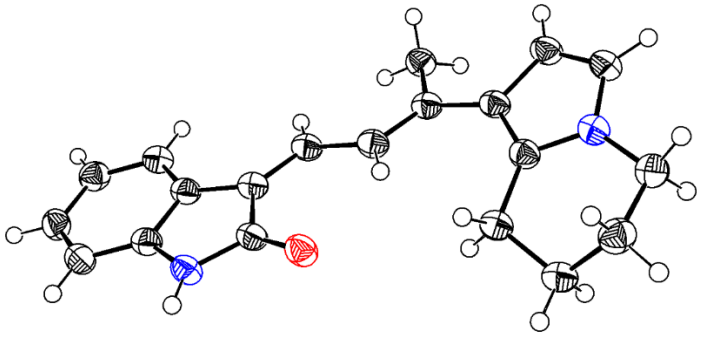
Identification code	**1b**
Empirical formula	$C_{20}H_{19}NO_2$
Formula weight	305.36
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.4864(3)
b/Å	15.2133(8)
c/Å	13.6983(7)
α/°	90
β/°	93.229(4)
γ/°	90
Volume/Å^3	1557.66(13)
Z	4
ρ_{calc}g/cm^3	1.302
μ/mm^{-1}	0.665
F(000)	648.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.694 to 151.822
Index ranges	-9 ≤ h ≤ 9, -16 ≤ k ≤ 18, -16 ≤ l ≤ 16
Reflections collected	9744
Independent reflections	3071 [R_{int} = 0.0624, R_{sigma} = 0.0644]
Data/restraints/parameters	3071/0/209
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0657, wR_2 = 0.1724
Final R indexes [all data]	R_1 = 0.0759, wR_2 = 0.1847
Largest diff. peak/hole / e Å^{-3}	0.38/-0.30

Table S3. Crystal data and structure refinement for 1’-aza-suffrutines A (**2a**)



Identification code	**2a**
Empirical formula	$C_{20}H_{20}N_2O$
Formula weight	304.38
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.4021(3)
b/Å	8.2439(3)
c/Å	20.2269(8)
α/°	90
β/°	94.773(3)
γ/°	90
Volume/Å^3	1562.35(10)
Z	4
ρ_{calc}g/cm^3	1.294
μ/mm^{-1}	0.630
F(000)	648.0
Crystal size/mm^3	0.3 × 0.3 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.774 to 152.738
Index ranges	-11 ≤ h ≤ 8, -9 ≤ k ≤ 9, -25 ≤ l ≤ 25
Reflections collected	9457
Independent reflections	3077 [R_{int} = 0.0423, R_{sigma} = 0.0445]
Data/restraints/parameters	3077/0/228
Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0633, wR_2 = 0.1669
Final R indexes [all data]	R_1 = 0.0759, wR_2 = 0.1787
Largest diff. peak/hole / e Å^{-3}	0.27/-0.26

Table S4. Crystal data and structure refinement for 1'-aza-suffrutines B (**2b**)



Identification code	**2b**
Empirical formula	$C_{20}H_{20}N_2O$
Formula weight	304.38
Temperature/K	99.99(10)
Crystal system	triclinic
Space group	P-1
a/Å	5.16300(10)
b/Å	12.1968(2)
c/Å	13.1905(2)
α/°	103.4930(10)
β/°	100.6160(10)
γ/°	96.617(2)
Volume/Å^3	782.93(2)
Z	2
ρ_{calc}g/cm^3	1.291
μ/mm^{-1}	0.629
F(000)	324.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.062 to 153.974
Index ranges	-6 ≤ h ≤ 6, -15 ≤ k ≤ 13, -16 ≤ l ≤ 16
Reflections collected	30393
Independent reflections	3245 [R_{int} = 0.0639, R_{sigma} = 0.0279]
Data/restraints/parameters	3245/0/209
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0598, wR_2 = 0.1708
Final R indexes [all data]	R_1 = 0.0633, wR_2 = 0.1751
Largest diff. peak/hole / e Å^{-3}	0.39/-0.32

2. The *in-situ* ^{1}HNMR monitoring experiments

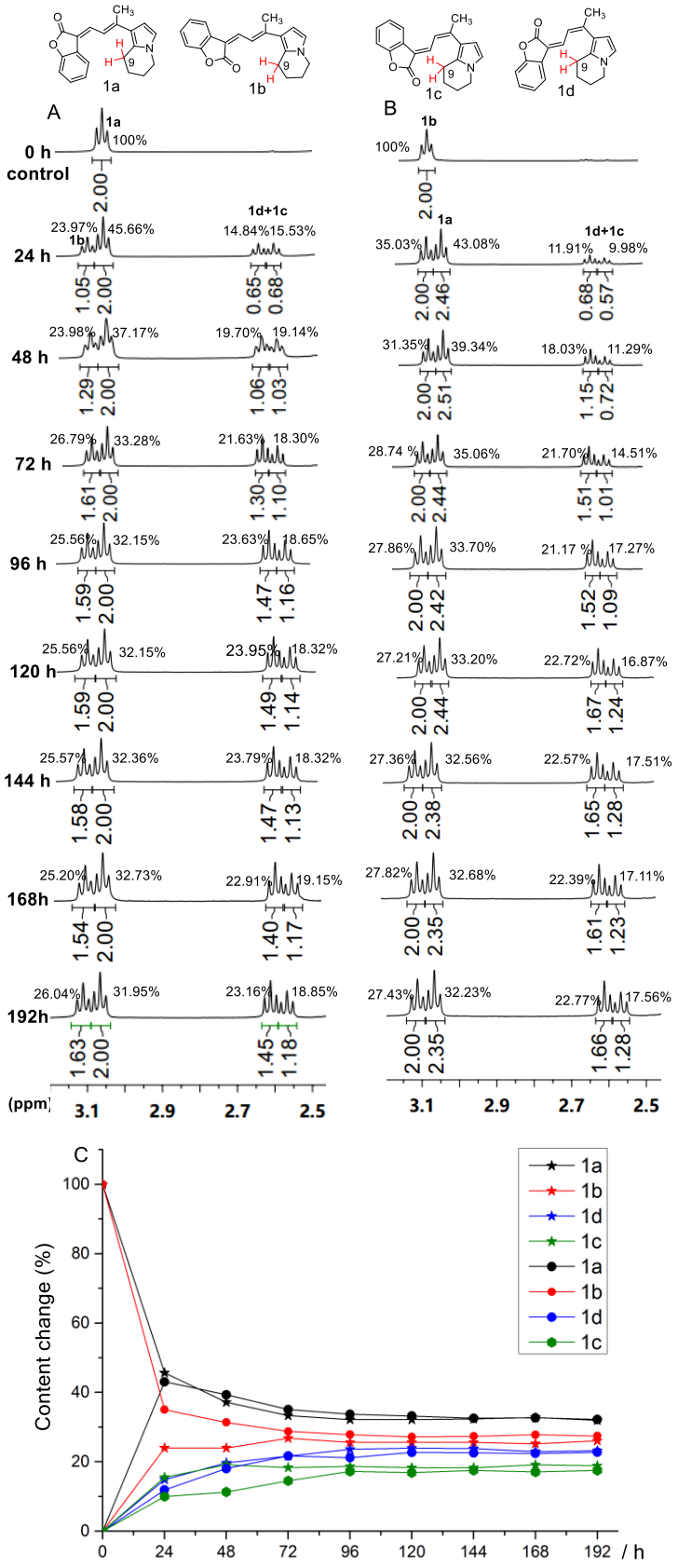
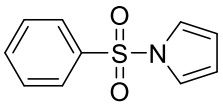


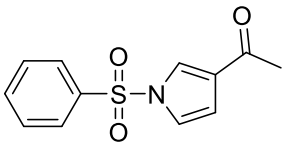
Figure S1. *In-situ* ^{1}HNMR spectra monitoring of 9-H for every isomer in $CDCl_3$ under ambient temperature/light (fluorescent lamp at 25 °C) conditions. (A: conversion of pure **1a** after 0, 24, 48, 72, 96 h. B: conversion of **1b** after 0, 24, 48, 72, 96 h. C: the content change of the isomers starting from pure **1a** and **1b** (★: starting from pure **1a**; ●: starting from pure **1b**. black: **1a**, red: **1b**, green:**1c**, blue:**1d**).

3. Characterization data of products 5-2b



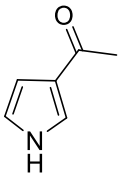
5

N-(Phenylsulfonyl) pyrrole (5). Pyrrole (10.0 g, 149.1 mmol) was added to a well-agitated suspension of NaOH (17.9 g, 447.3 mmol) in 10 mL of dichloromethane. This mixture was then cooled to 0 °C and stirred for 10 min, following which a solution of phenylsulfonyl chloride (31.6 g, 178.9 mmol) in 2 mL of dichloroethane was added dropwise. After the completion of addition, the reaction was allowed to come to room temperature and left stirring overnight. The reaction was quenched by pouring onto 60 mL H_2O. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 60 mL). The combined organic extract was washed with water to neutrality and dried over Na_2SO_4. Removed of the solvent and purified by recrystallization to give **5** as white solid in yield of 76.3 % (23.6 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.82 (m, 2H), 7.62-7.56 (m, 1H), 7.53-7.46 (m, 2H), 7.18-7.14 (m, 2H), 6.34-6.25 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.10, 133.84, 129.39, 126.77, 120.82, 113.71.



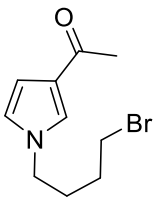
6

3-Acetyl-N-(phenylsulfonyl) pyrrole (6). To a well stirred suspension of anhydrous aluminum chloride (1.9 g, 14.5 mmol) in 5 mL of dry 1,2-dichloromethane, acetyl chloride (0.8 g, 9.7 mmol) was added in portions and the resulting mixture was stirred at 0 °C. After complete solubilization of aluminum chloride, a solution of **5** (1.0 g, 4.8 mmol) in dry 1,2-dichloromethane (5 mL) was added slowly. The mixture was stirred for 12 h at room temperature and poured into ice-cold water (20 mL). The organic layer was separated and the aqueous layer was extracted with 1,2-dichloromethane (3 × 20 mL). After drying over Na_2SO_4, filtration and evaporation of the solvent, crude **6** was obtained and purified by recrystallized as white solid (93.18 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.91 (m, 2H), 7.75 (t, *J* = 2.0 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 2H), 7.16 (dd, *J* = 3.2, 2.4 Hz, 1H), 6.69 (dd, *J* = 3.6, 1.6 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.87, 138.08, 134.66, 129.77, 129.47, 127.16, 124.64, 121.70, 112.52, 27.32.



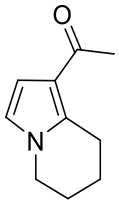
7

1-(1H-pyrrol-3-yl) ethan-1-one (7). A mixture of 3 (2.0 g, 8.0 mmol), NaOH (0.48 g, 12.0 mmol) and methanol (20 mL) was added into a 100 mL round bottom flask equipped with a condenser. The mixture was stirred at 60 °C for 0.5 hours. After which time the reaction mixture was allowed to cool and methanol was removed in vacuo. The aqueous solution was thoroughly extracted with ethyl acetate. Combined organic extracts were washed with water to neutrality and dried over Na_2SO_4. Removal of the solvent in vacuo and purification by flash chromatography on silica gel eluting with EtOAc-PE as the eluent to afford the white solid **7** (831.3 mg, 94.92 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.45 (s, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 6.66 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.64, 126.06, 123.96, 119.82, 108.72, 27.26.



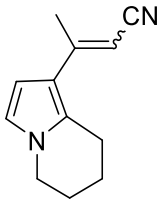
9

1-(1-(4-bromobutyl)-1H-pyrrol-3-yl) ethan-1-one (9). To a solution of **7** (2.3 g, 21.4 mmol) in DMSO (25 mL) was added KOH (1.8 g, 31.0 mmol). The solution was stirring for 10 minutes in ice bath before the addition of 1,4-dibromobutane (9.2 g, 42.7 mmol). The reaction mixture was stirred for 1 hours at room temperature, and was then quenched with H_2O, extracted with ethyl acetate (3 × 40 mL), and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography to provide a colorless soil **9** (68.9 %) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 2.1 Hz, 1H), 6.62 (d, *J* = 2.8 Hz, 1H), 6.59 (d, *J* = 2.8 Hz, 1H), 3.94 (t, *J* = 6.4 Hz, 2H), 3.39 (t, *J* = 6.4 Hz, 2H), 2.39 (3H, s), 2.04-1.91 (2H, m), 1.87-1.79 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.39, 126.13, 125.49, 122.06, 109.53, 49.25, 32.61, 29.63, 29.52, 27.05.



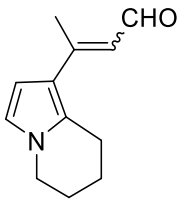
10

1-(5,6,7,8-tetrahydroindolizin-1-yl)ethan-1-one (10) In a silica tube (30 mL) containing a stirring bar was charged with intermediate **9** (0.5 g, 2.1mmol), $Pd(PPh_3)_4$ (473 mg, 0.41 mmol), Cs_2CO_3 (325.8 mg, 4.1 mmol), the tube was then evacuated and back-filled with nitrogen three times, anhydrous Dimethyl sulfoxide was added via syringe. The resulting mixture was carried on the 10 W blue LED at room temperature for 24 h and filtered, the filtrate was extracted with EtOAc, and washed with H_2O (20 mL × 3). The organic layer was dried over Na_2SO_4 and filtered, and the solvent evaporated. The crude product was concentrated and purified by column chromatography over silica gel with EtOAc-PE as the eluent to give the colorless oil **10** in 40.22 % yields. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (d, *J* = 3.0 Hz, 1H), 6.44 (d, *J* = 3.0 Hz, 1H), 3.93 (t, *J* = 5.9 Hz, 2H), 3.09 (t, *J* = 6.4 Hz, 2H), 2.37 (s, 3H), 2.00-1.89 (m, 2H), 1.89-1.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.35, 136.40, 120.03, 119.24, 110.10, 45.65, 28.15, 24.33, 22.85, 20.13.



12

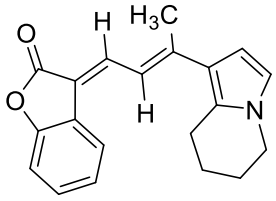
3-(5,6,7,8-Tetrahydroindolizin-1-yl)but-2-enenitrile (12). Diethyl cyanomethylphosphonate (2.5 g, 15 mmol) was added to a stirred suspension of NaH (600 mg, 60% in mineral oil, 15 mmol) in dry toluene (5 mL) under an argon atmosphere. The gel-like solution was heated to 110 °C, and dry DMF (1 mL) was added to obtain a clear solution. 1-(5,6,7,8- Tetrahydroindolizin-1-yl)ethan-1-one **(6)** (245.0 mg, 1.5 mmol) in dry toluene (2 mL) was added dropwise, and the reaction mixture was stirred at 110 °C for 11 h. The reaction mixture was cooled to room temperature, and H_2O (20 mL) was added. The aqueous layer was extracted with EtOAc (20 × 3 mL); the organic layer was separated, washed with brine, dried over Na_2SO_4, and filtered, and all volatiles were removed under reduced pressure. Purification by flash chromatography gave the product **12** as a colorless oil (247.7 mg, 88.7 %). *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (d, *J* = 3.0 Hz, 1H), 6.26 (d, *J* = 3.0 Hz, 1H), 5.12 (s, 1H), 3.95 (t, *J* = 6.4 Hz, 2H), 2.84 (t, *J* = 6.4 Hz, 2H), 2.37 (d, *J* = 0.8 Hz, 3H), 1.98-1.92 (m, 2H), 1.90-1.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.59, 129.69, 120.05, 119.48, 118.36, 107.65, 88.78, 45.88, 24.77, 22.76, 21.34, 20.84.



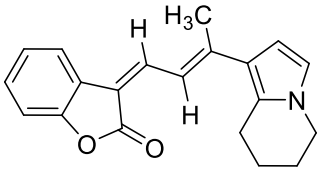
13

3-(5,6,7,8-Tetrahydroindolizin-1-yl)but-2-enal (13). 3-(5,6,7,8-tetrahydroindolizin-1-yl)but-2-enenitrile **12** (313.5 mg, 1.8 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and cooled to 0 °C. DIBAL-H (800 µL, 1 M in hexane, 2.9 mmol) was added, and the reaction mixture was stirred at 0 °C for 2 h. The solution was quenched with aqueous, saturated Rochelle salt solution (5 mL) and vigorously stirred at room temperature overnight. H_2O (10 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and filtered, and the solvent was evaporated under reduced pressure.

Purification by flash chromatography gave the product **13** as a pale-yellow oil (158.0 mg, 45.9 %), which was obtained as a mixture of E/Z isomers (ratio E/Z ≈ 8.1:1.9). E-isomer: ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.99 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 2.8 Hz, 1H), 6.38 (d, *J* = 3.2 Hz, 1H), 5.95 (d, *J* = 8.0 Hz, 1H), 3.93 (t, *J* = 6.0 Hz, 3H), 2.83 (t, *J* = 6.0 Hz, 2H), 2.43 (s, 3H), 1.85-1.86 (m, 3H), 1.77-1.178 (m, 2H). 13C NMR (100 MHz, DMSO-*d*$_6$) δ 191.08, 155.48, 131.14, 125.41, 122.49, 121.16, 108.22, 45.89, 25.29, 22.68, 20.84, 17.37. Z-isomer: ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.38 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 2.8 Hz, 1H) , 6.18 (d, *J* = 2.8 Hz, 1H), 5.85 (d, *J* = 8.0 Hz, 1H), 3.93 (t, *J* = 6.0 Hz, 3H), 2.57 (t, *J* = 6.0 Hz, 1H), 2.17 (s, 3H), 1.85-1.86 (m, 3H), 1.70-1.172 (m, 1H). ^{13}CNMR (100 MHz, DMSO-*d*$_6$) δ 192.77, 158.00, 130.02,121.08, 120.63, 119.76, 109.68, 45.61, 26.37, 23.70, 23.11, 21.10.

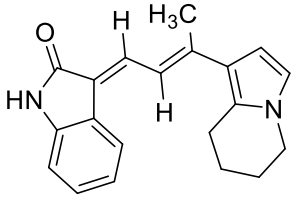


1a

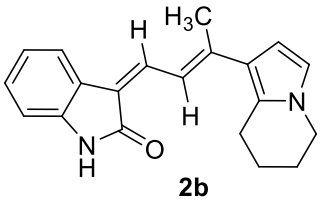


1b

(**E)-3-((E)-3-(5,6,7,8-tetrahydroindolizin-1-yl)but-2-en-1-ylidene)benzofuran-2(3H)-one (suffrutines A (1a)) and (Z)-3-((E)-3-(5,6,7,8-tetrahydroindolizin-1-yl)but-2-en-1-ylidene)benzofuran-2(3H)-one (suffrutines B (1b))** In a 25 mL round-bottom flask, 3-(5,6,7,8-Tetrahydroindolizin-1-yl) but-2-enal (**13**) (300.8 mg, 1.6 mmol), 2-hydroxyphenylacetic acid (**14**) (245.9, 1.6 mmol), $(CH_3CO)_2O$ (434.90 mg, 4.3 mmol, 404.6 μL) and NEt_3 (320.8 mg, 3.2 mmol, 440.7 μL) were stirred at 80 ℃ for 1 h. Water was added to quencher the reaction and the mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue which consisted of 4 isomers was purified by column chromatography on silica gel (EtOAc/PE = 1:5) in dark to provide suffrutines A (**1a**) (215.7 mg, 44.6 %) and B (**1b**) (123.0 mg, 25.4 %) as a red solid. suffrutines A and B are very sensitive toward visible light in a solution and isomerization would readily occur. Suffrutines A (**1a**): mp 152.1–153.9 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 7.75 (d, *J* = 13.2 Hz, 1H), 7.72 (d, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.24 (m, 2H), 6.99 (d, *J* = 13.2 Hz, 1H), 6.77 (d, *J* = 3.2 Hz, 1H), 6.50 (d, *J* = 2.8 Hz, 1H), 3.98 (t, *J* = 6.0 Hz, 2H), 3.04 (t, *J* = 6.0 Hz, 2H), 2.37 (s, 3H), 1.92 (m,,2H), 1.86 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 169.45, 152.49, 152.27, 137.41, 131.87, 128.71, 124.63, 124.18, 122.67 , 121.74, 121.58, 116.97, 113.50, 110.80, 108.73, 46.01, 25.63, 22.60 , 20.97, 17.69. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{20}H_{19}NO_2$, 306.1489, found 306.1483. Suffrutines B (**1b**): mp 139.0-140.7 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.13 (d, *J* = 12.7 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.73 (d, *J* = 12.7 Hz, 1H), 7.27-7.22 (t, *J* = 7.6 Hz 1H), 7.15 (t, *J* = 7.6 Hz, 2H), 6.73 (d, *J* = 2.8 Hz, 1H), 6.39 (d, *J* = 2.8 Hz, 1H), 3.96 (t, *J* = 6.0 Hz, 2H), 2.97 (t, *J* = 6.0 Hz, 2H), 2.39 (s, 3H), 1.88 (m, 4H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 167.48, 151.54, 150.75, 138.71, 131.36, 128.07, 126.14, 123.89 121.85, 121.30, 120.04, 118.10, 112.71, 110.41, 108.58, 46.01, 25.68, 22.67, 20.92, 17.35. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{20}H_{19}NO_2$, 328.1308, found 328.1302.



2a

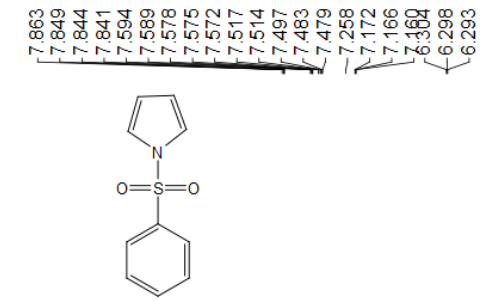


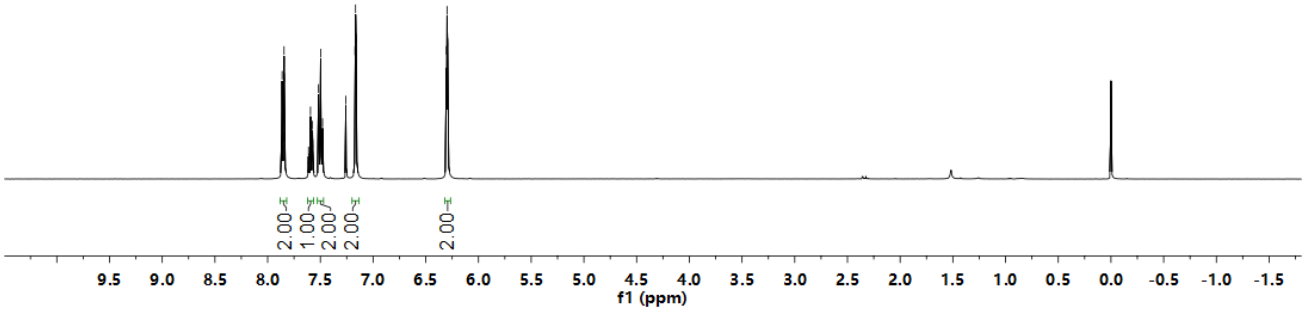
2b

(E)-3-((E)-3-(5,6,7,8-tetrahydroindolizin-1-yl)but-2-en-1-ylidene)indolin-2-one (1'-aza-suffrutines A (2a)) and (Z)-3-((E)-3-(5,6,7,8-tetrahydroindolizin-1-yl)but-2-en-1-ylidene)indolin-2-one (1'-aza-suffrutines B (2b)) In a 25 mL round-bottom flask, 3-(5,6,7,8-Tetrahydroindolizin-1-yl) but-2-enal (**13**) (203.9 mg, 1.08 mmol), indolin-2-one (**15**) (143.4, 1.1 mmol), and piperidine (55.2 mg, 0.65 mmol, 60 μL) were dissolved in ethanol (2.0 mL), The yellow solution was heated to 80 °C for 1 h. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography to give the product as a red solid (312.9 mg, 90.3 %) which consists of 4 isomers. The mainly isomers can be separated by flash chromatography in the dark to give 1'-aza-suffrutines A (**2a**) (255.9 mg, 73.9 %) and 1'-aza-suffrutines B (**2b**) (57 mg, 16.5 %). 1'-aza-suffrutines A (**2a**): mp 207.6-209.8 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.35 (s, 1H), 7.62-7.54 (m, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.98 m, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 2.4 Hz, 1H), 6.40 (d, *J* = 2.8 Hz, 1H), 3.96 (s, 2H), 3.00 (s, 2H), 2.31 (s, 3H), 1.91 (d, J = 3.6 Hz, 2H), 1.85 (d, *J* = 4.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 169.34, 147.58, 141.28, 131.79, 129.45, 127.63, 122.90, 122.34, 121.21, 121.19, 120.42, 116.80, 109.45, 107.73, 45.41, 24.97, 22.25, 20.65, 16.95. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{20}H_{19}N_2O$, 305.1648, found 305.1641. 1'-aza-suffrutines B (**2b**): mp 197.7-199.2 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 10.26 (s, 1H), 7.94 (d, *J* = 12.4 Hz, 1H), 7.81 (d, *J* = 12.4 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.31 (d, *J* = 2.4 Hz, 1H), 3.94 (t, *J* = 6.0 Hz, 2H), 2.94 (t, *J* = 6.0 Hz, 2H), 2.31 (s, 3H), 1.89 (m, 2H), 1.82 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 169.17, 146.13, 140.23, 133.80, 129.56, 127.56, 125.31, 121.90, 120.98, 120.64, 120.56, 119.54, 118.50, 109.45, 108.09, 45.91, 25.43, 22.88, 21.10, 16.93. HRMS-ESI (m/z): $[M + H]^+$ calculated for $C_{20}H_{20}N_2O$, 305.1648, found 305.1641.

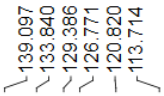
4. Copies of NMR spectra for 5-2b.

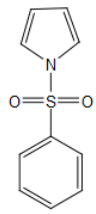
^{1}H NMR spectrum of **5** in $CDCl_3$

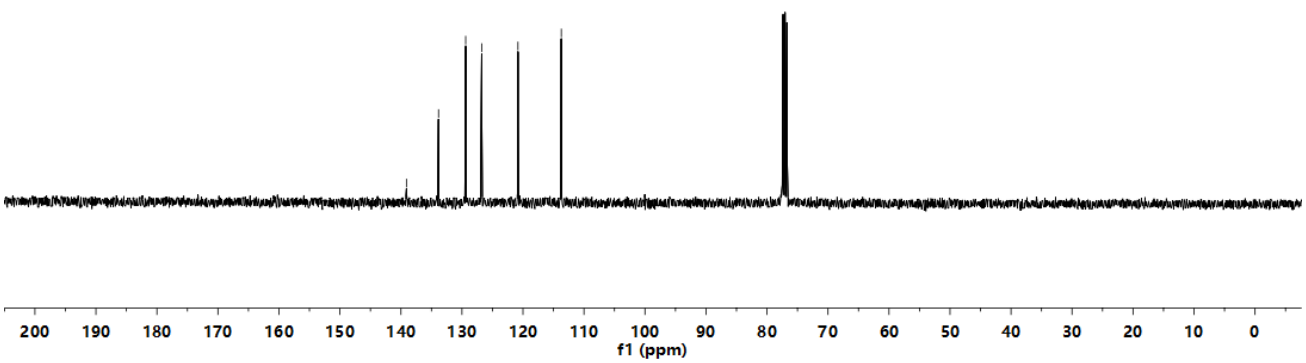




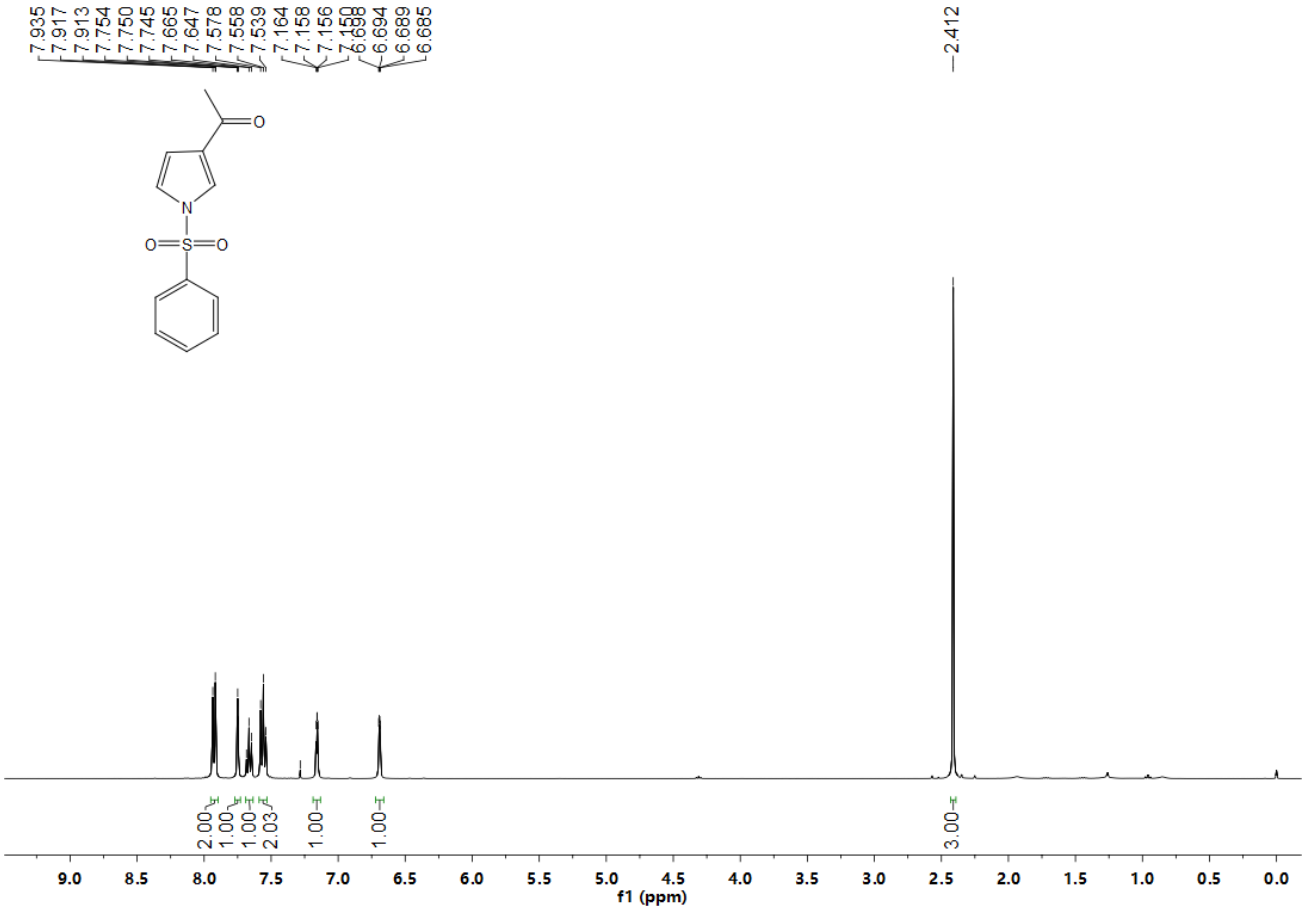
^{13}C NMR spectrum of **5** in $CDCl_3$



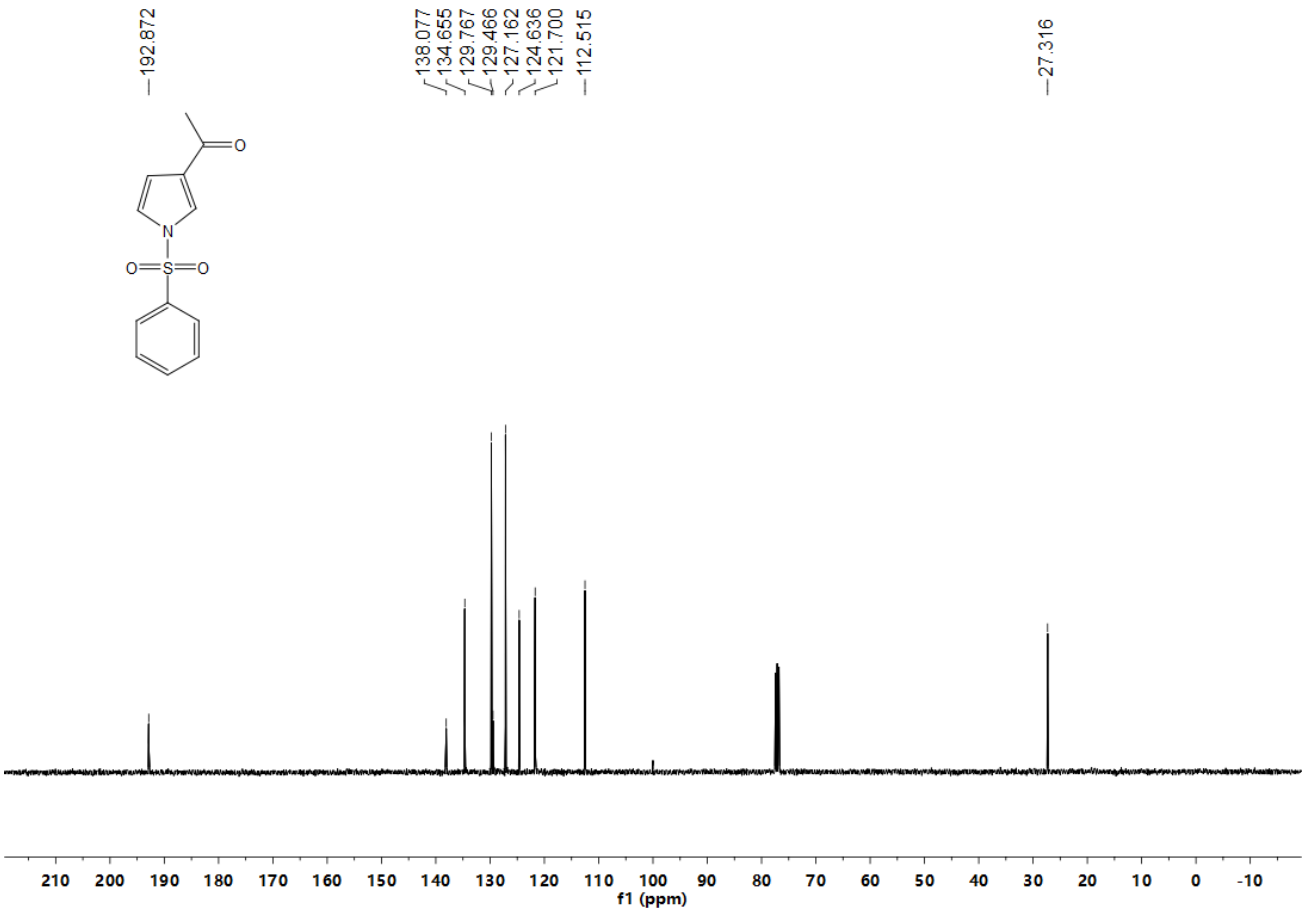




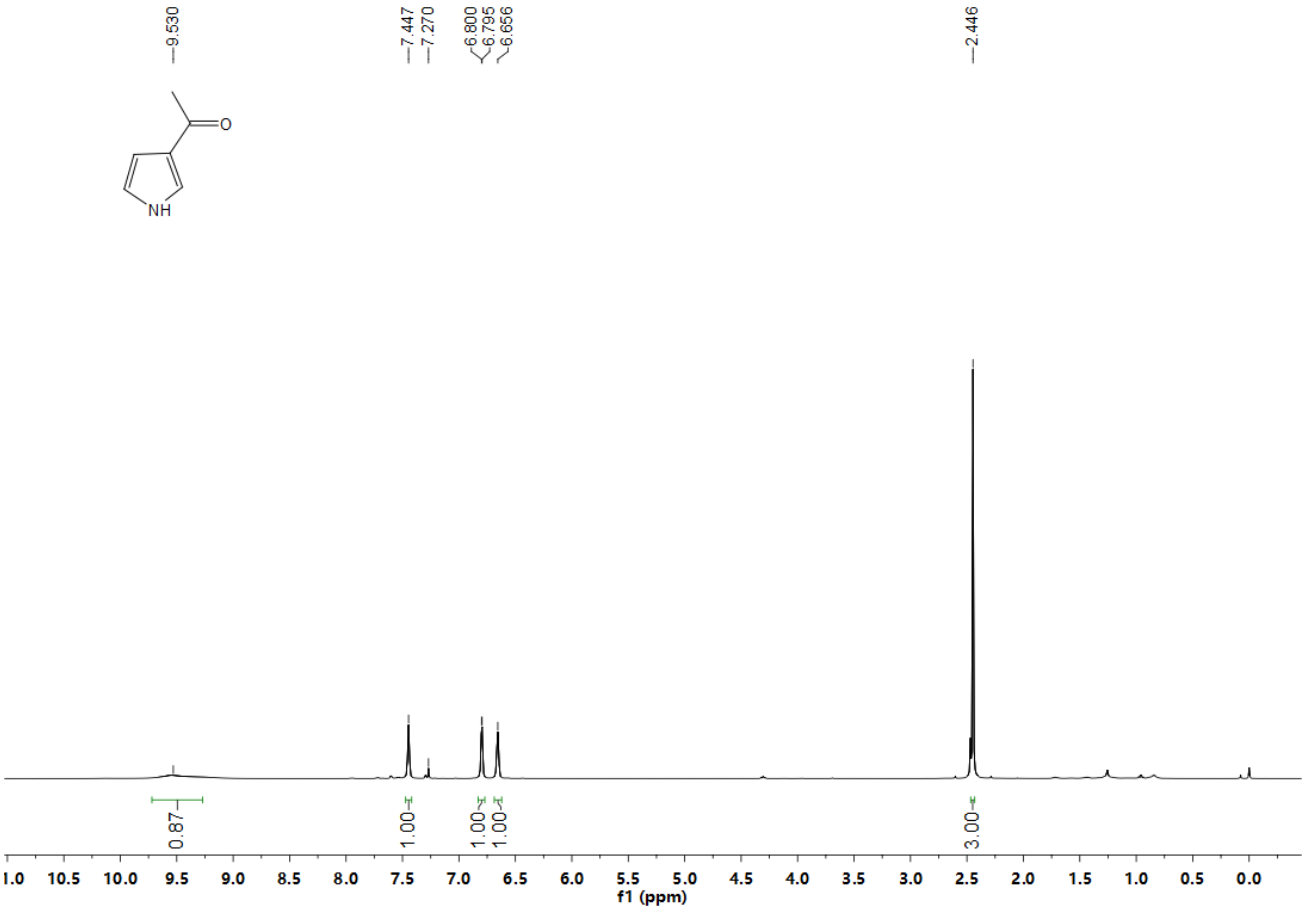
^{1}H NMR spectrum of **6** in $CDCl_3$



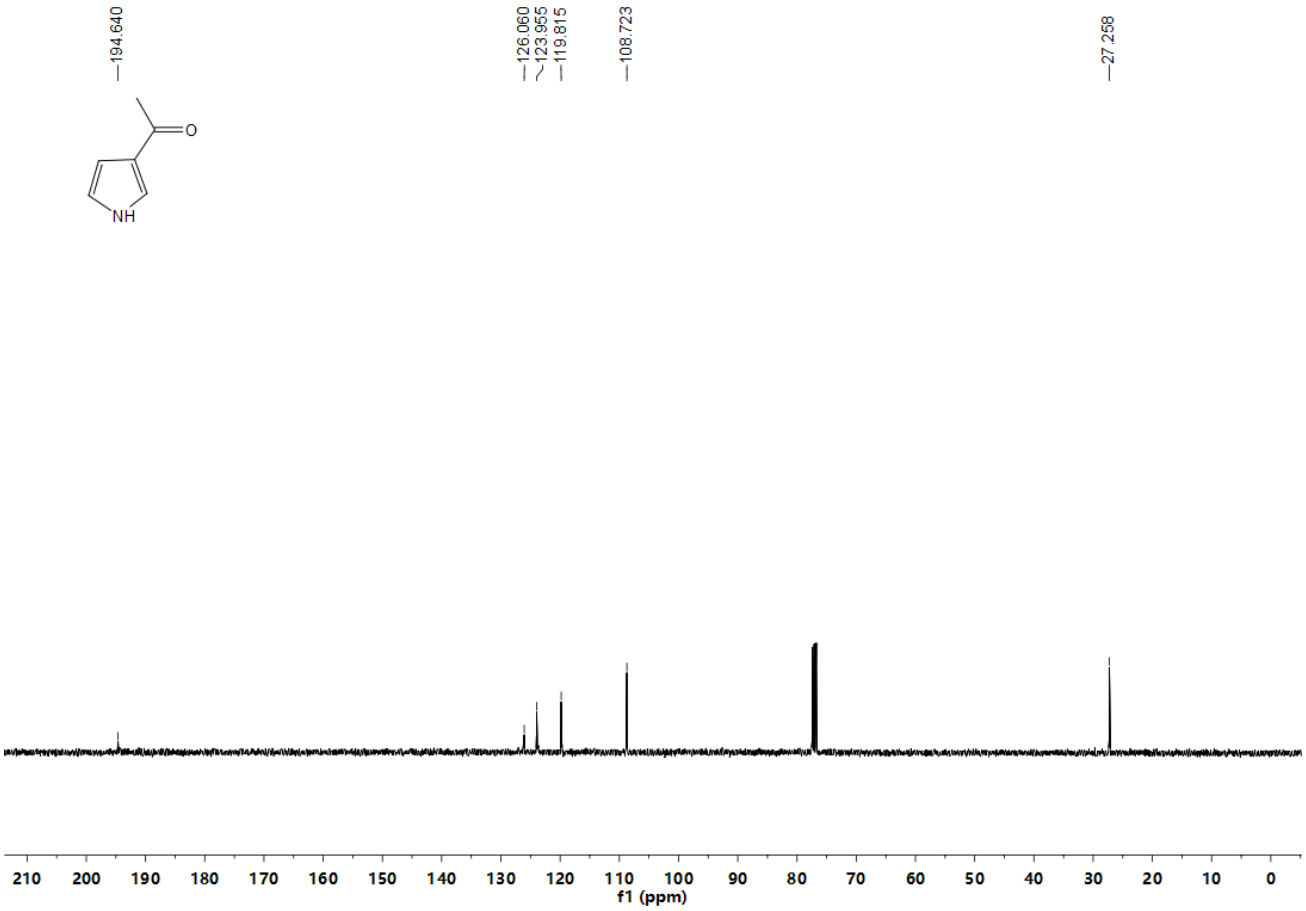
^{13}C NMR spectrum of **6** in $CDCl_3$



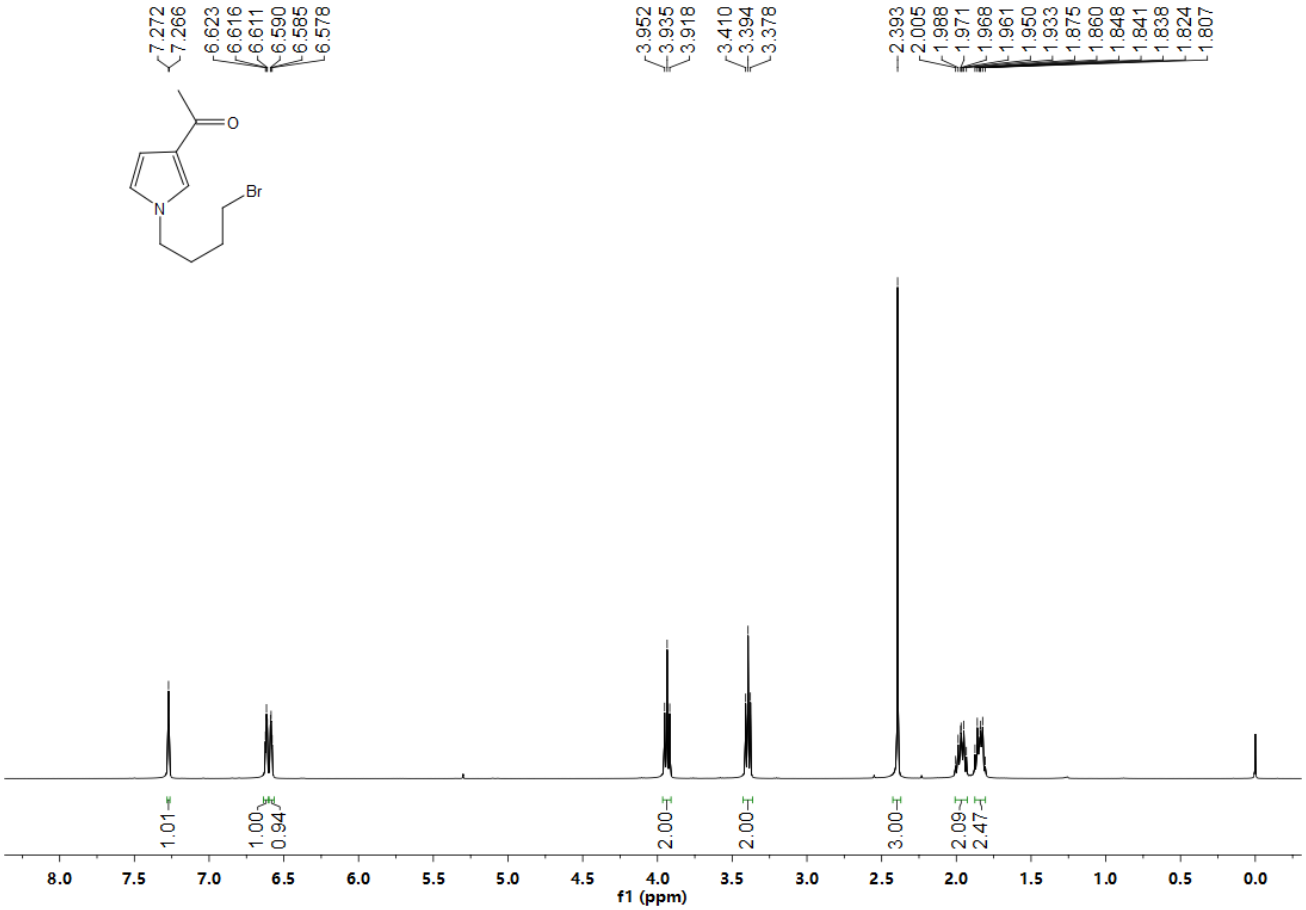
^{1}H NMR spectrum of **7** in $CDCl_3$



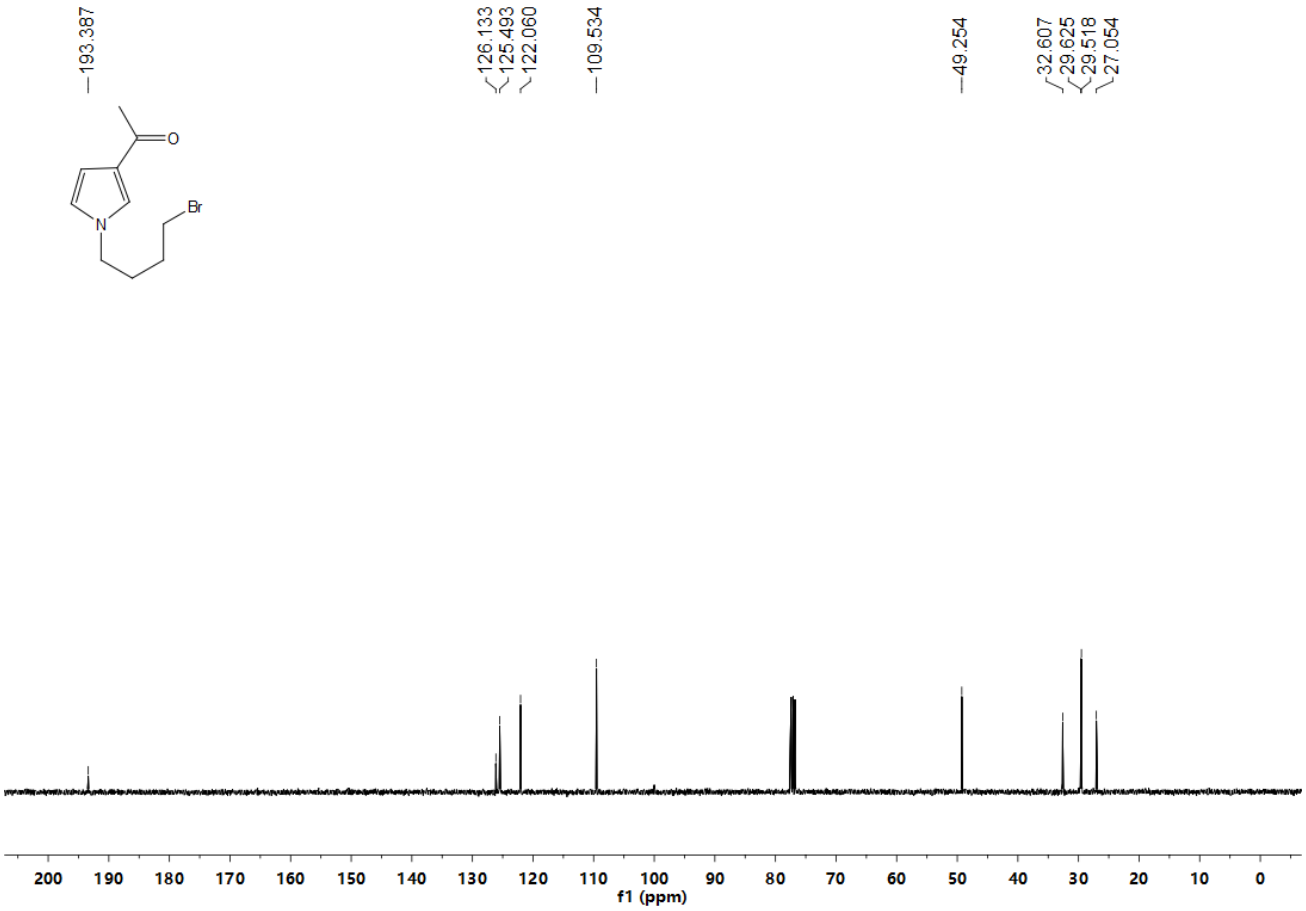
^{13}C NMR spectrum of **7** in $CDCl_3$



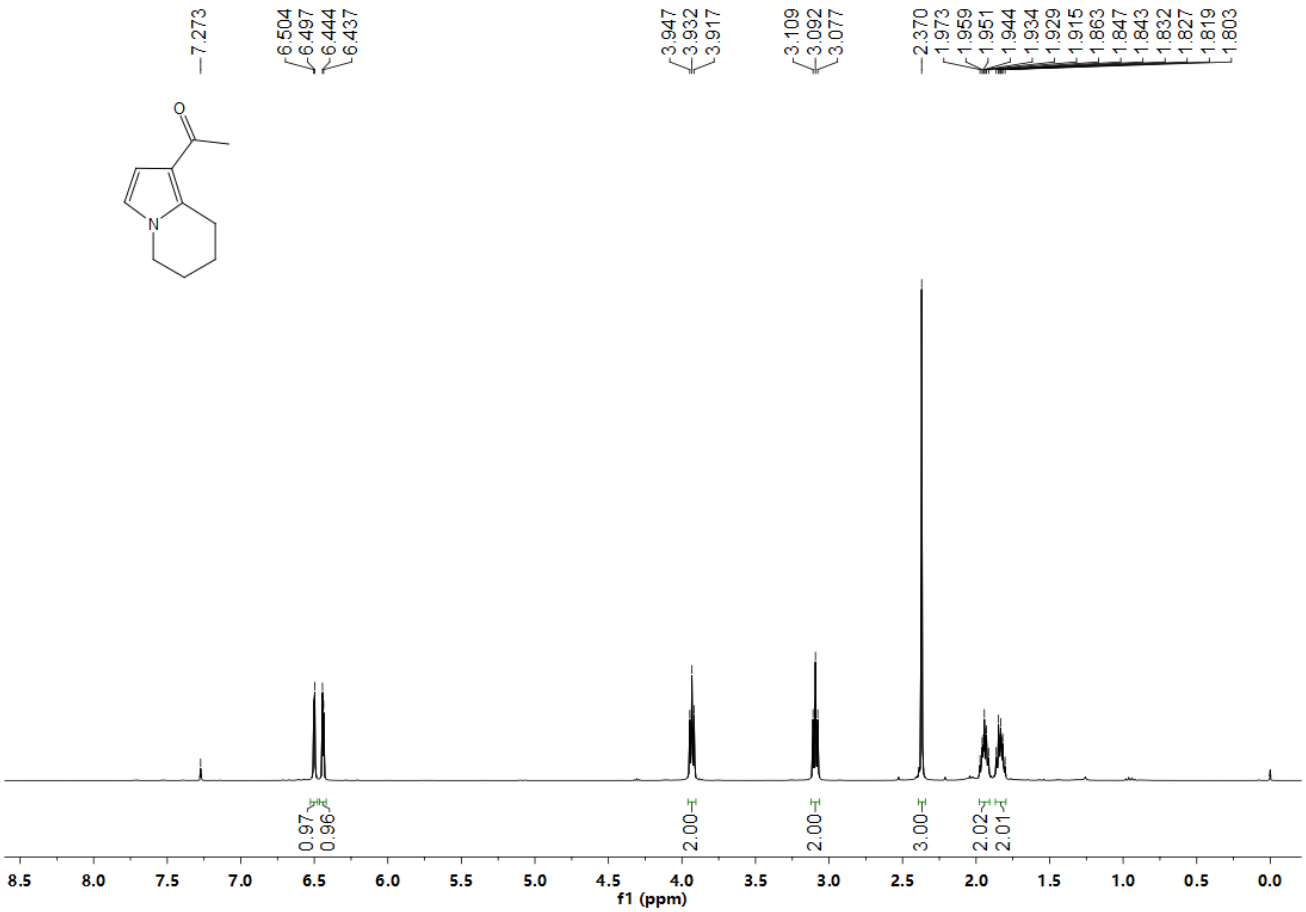
^{1}H NMR spectrum of **9** in $CDCl_3$



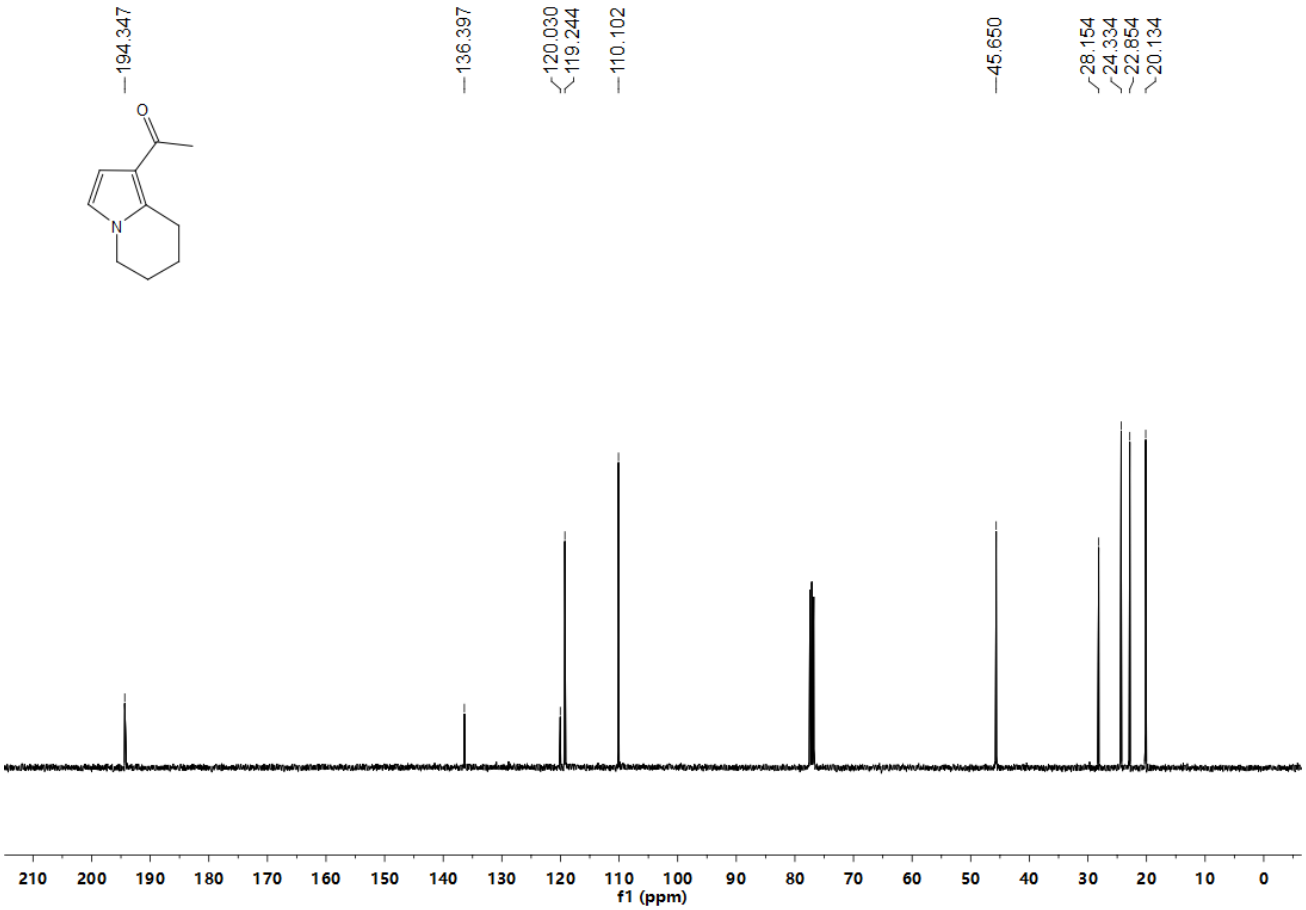
^{13}C NMR spectrum of **9** in $CDCl_3$



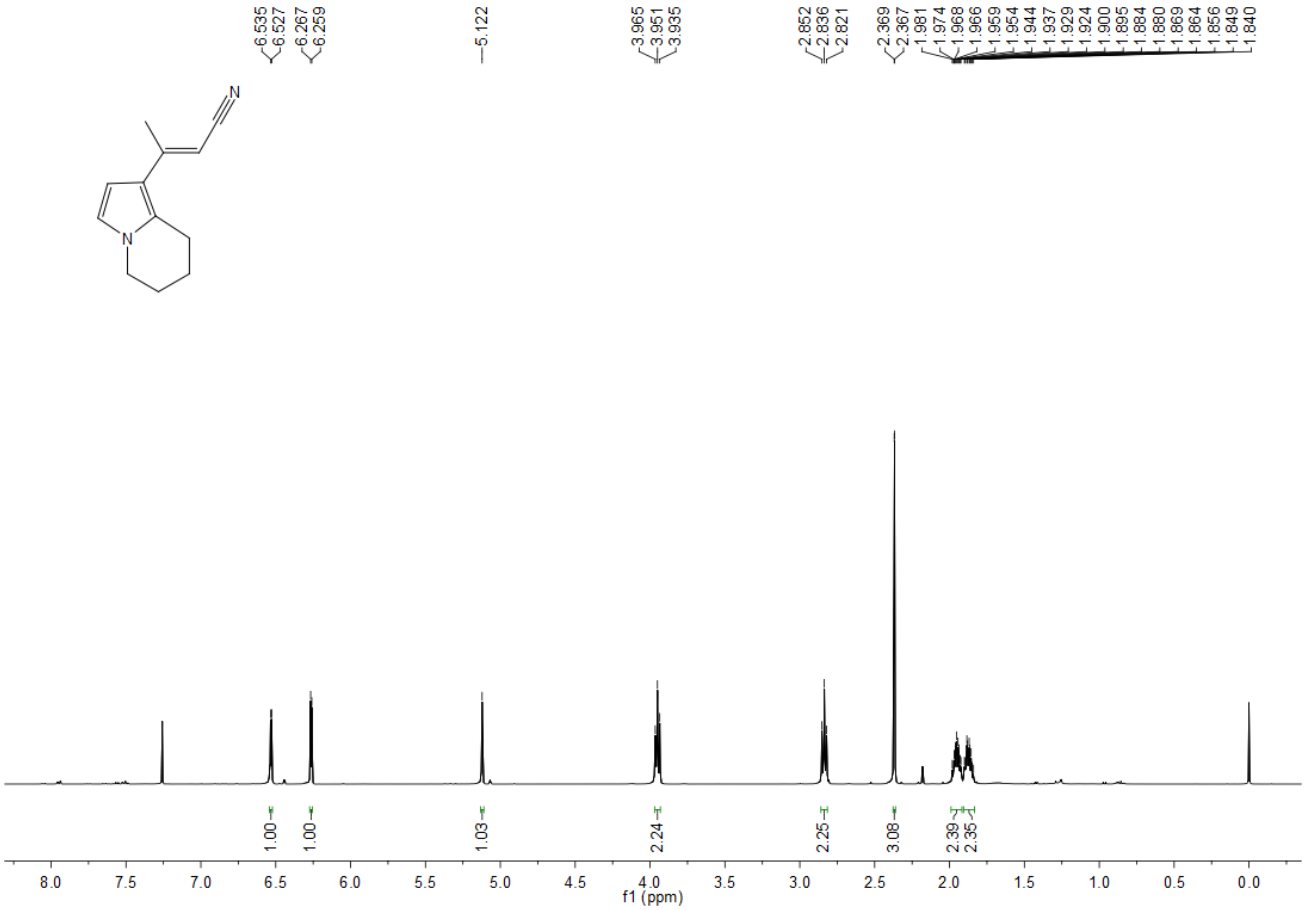
^{1}H NMR spectrum of **10** in $CDCl_3$



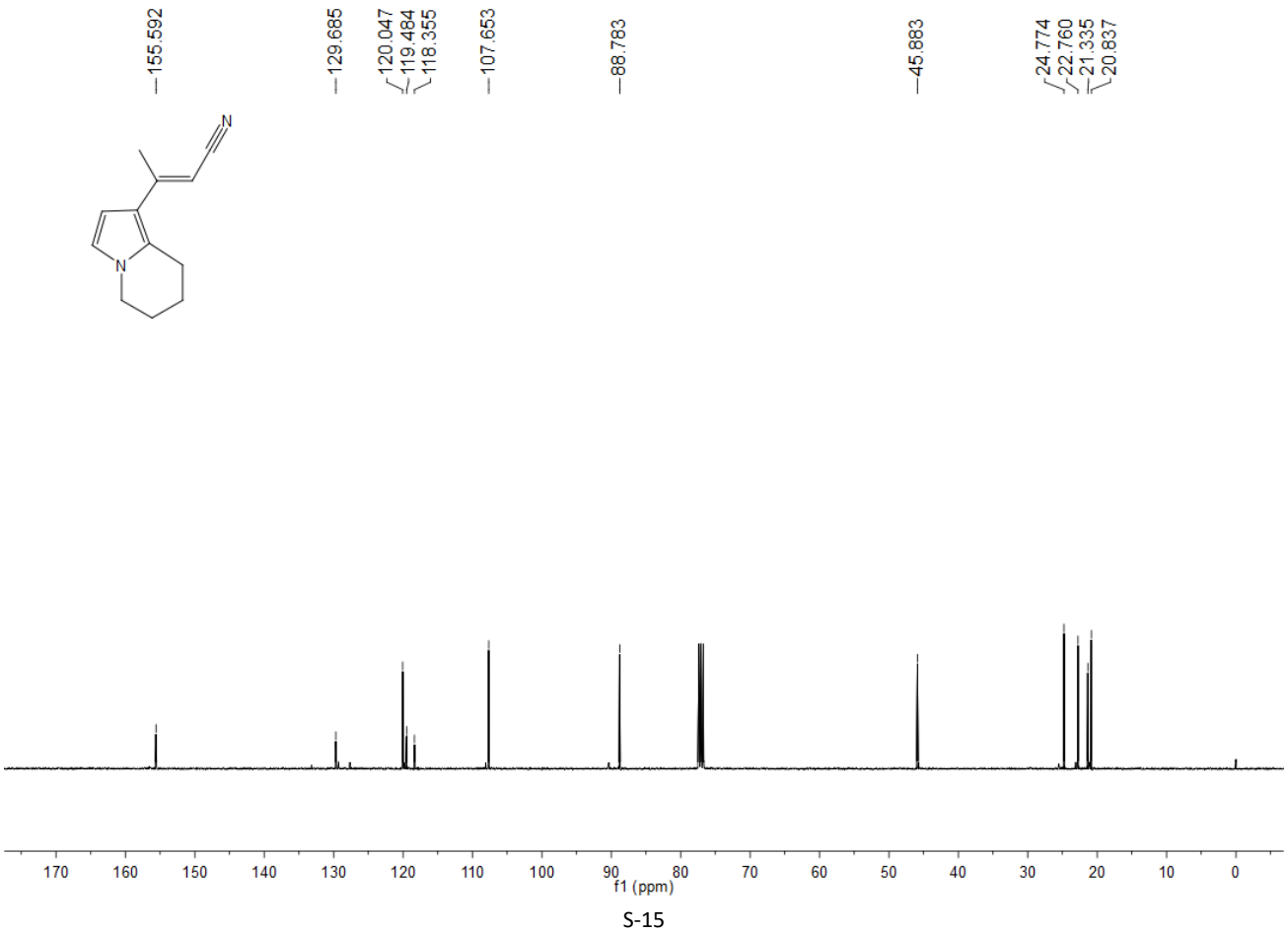
^{13}C NMR spectrum of **10** in $CDCl_3$



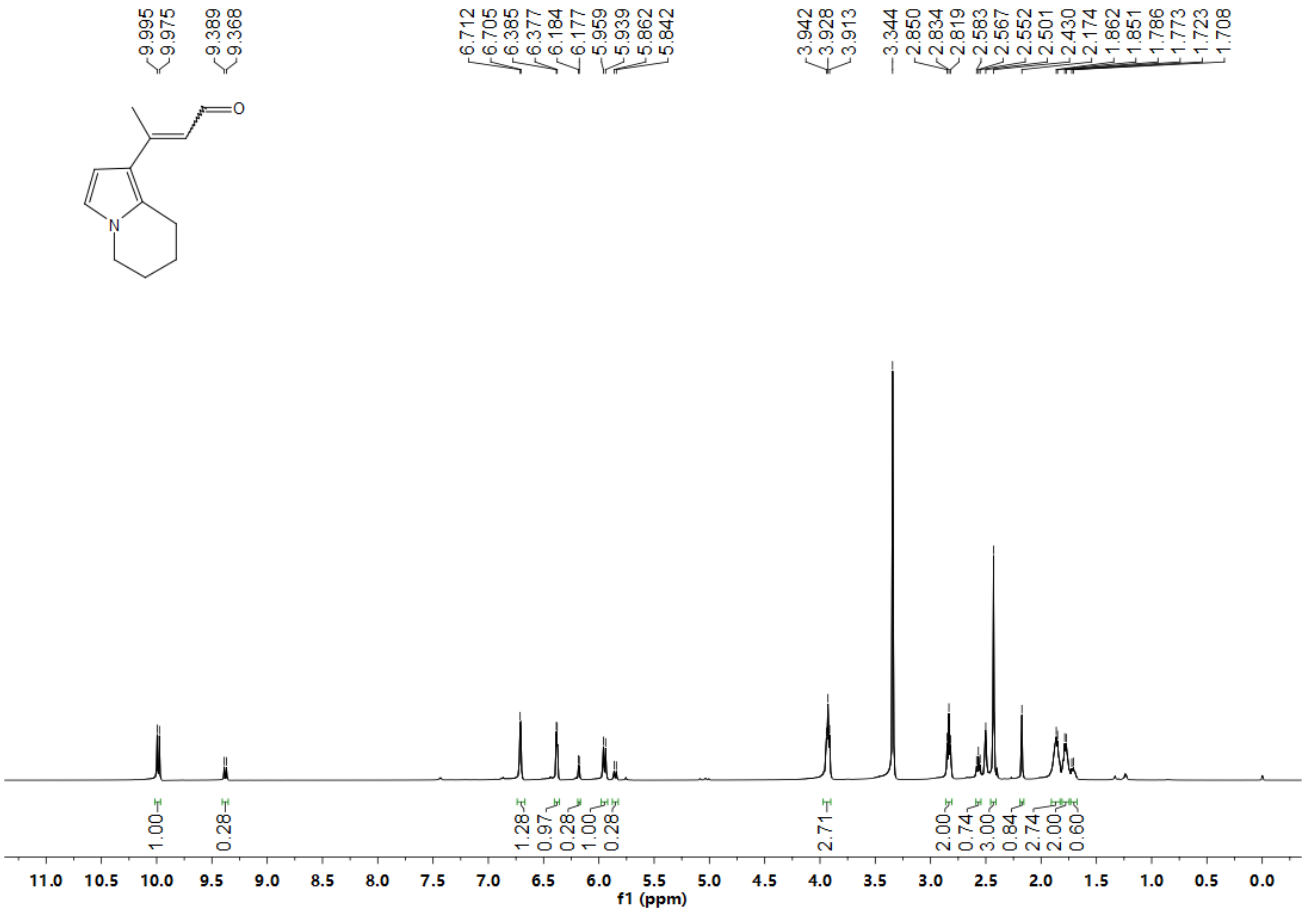
^{1}H NMR spectrum of **12** in $CDCl_3$



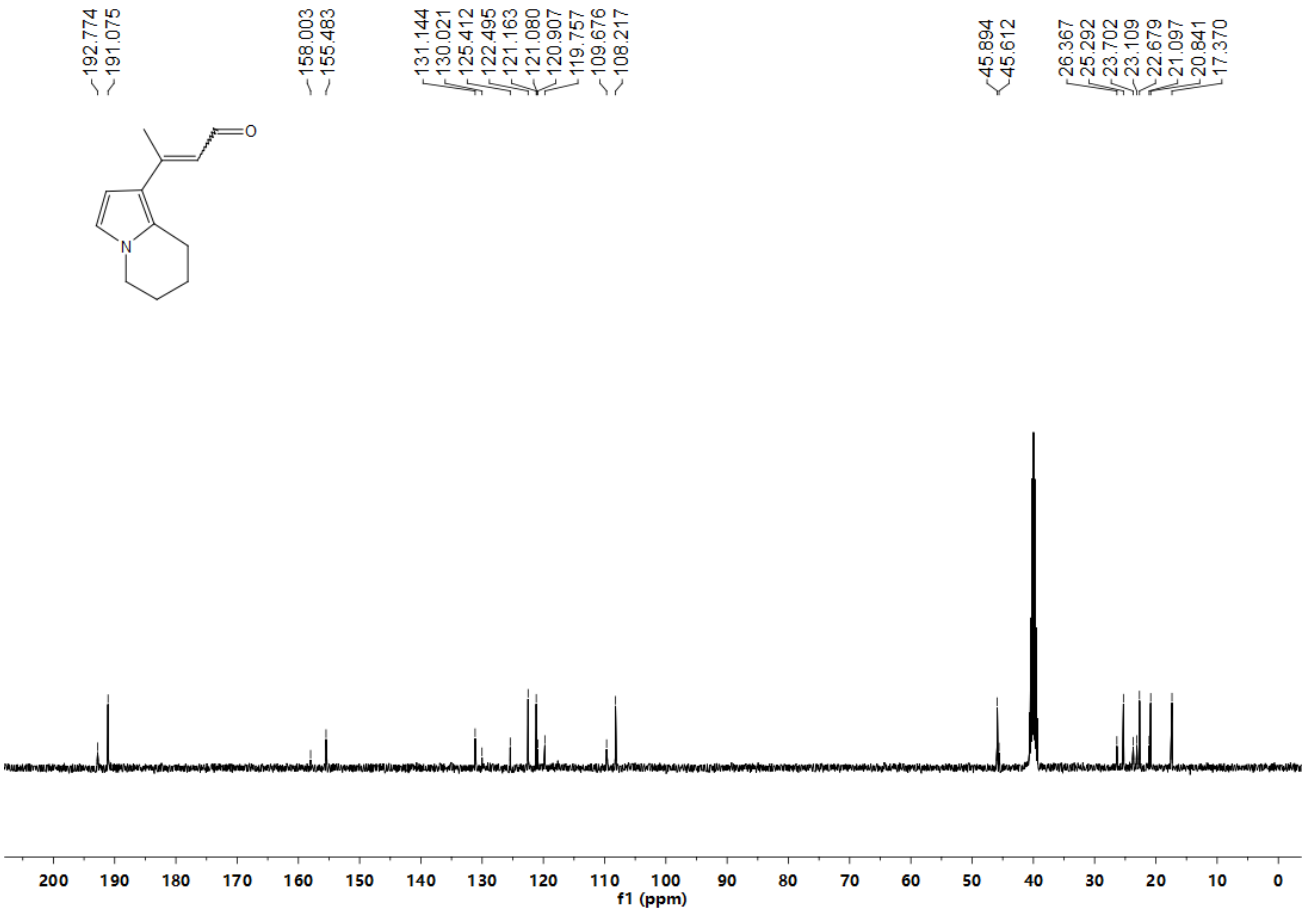
^{13}C NMR spectrum of **12** in $CDCl_3$



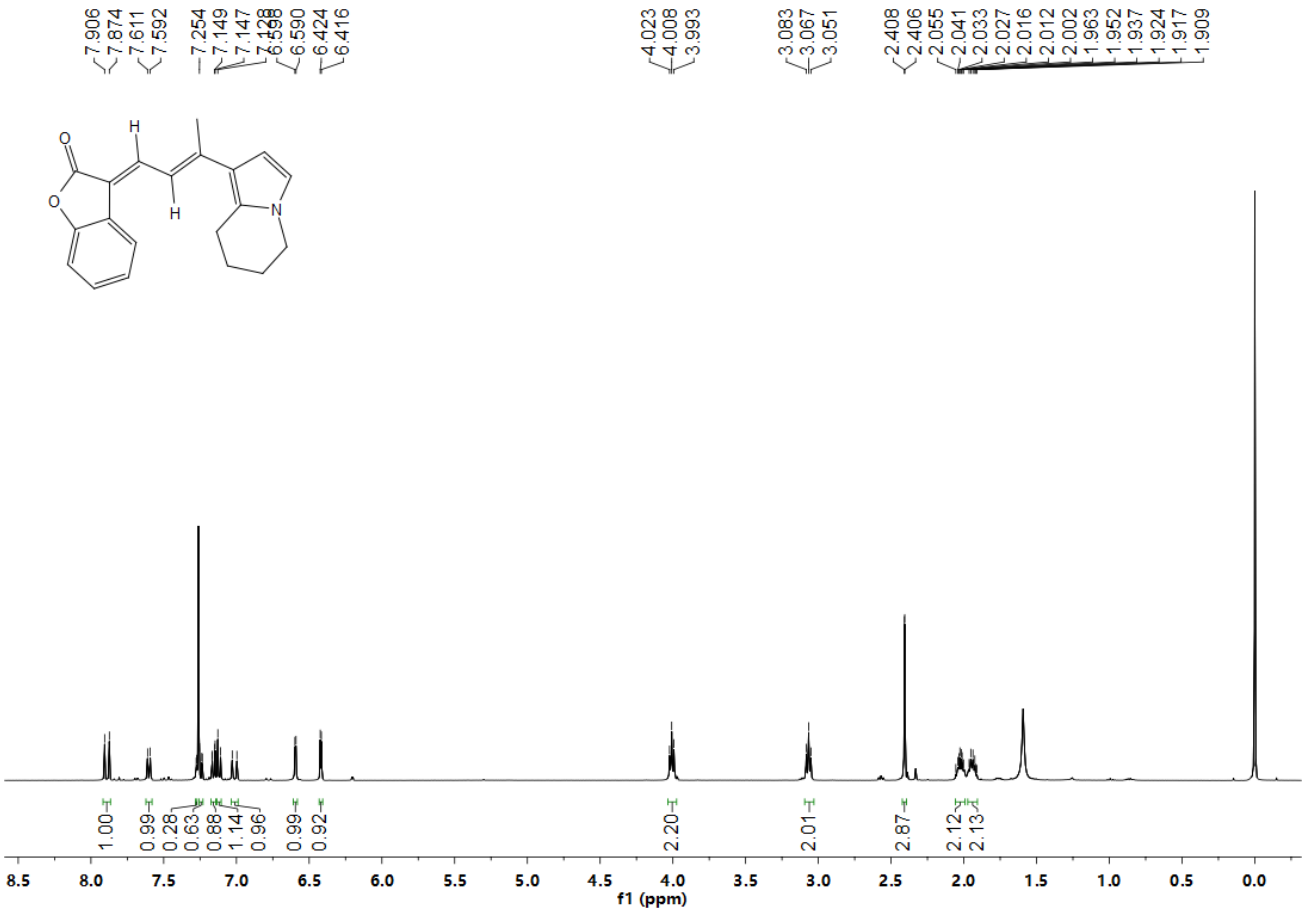
^{1}H NMR spectrum of **13** in DMSO-*d*$_6$



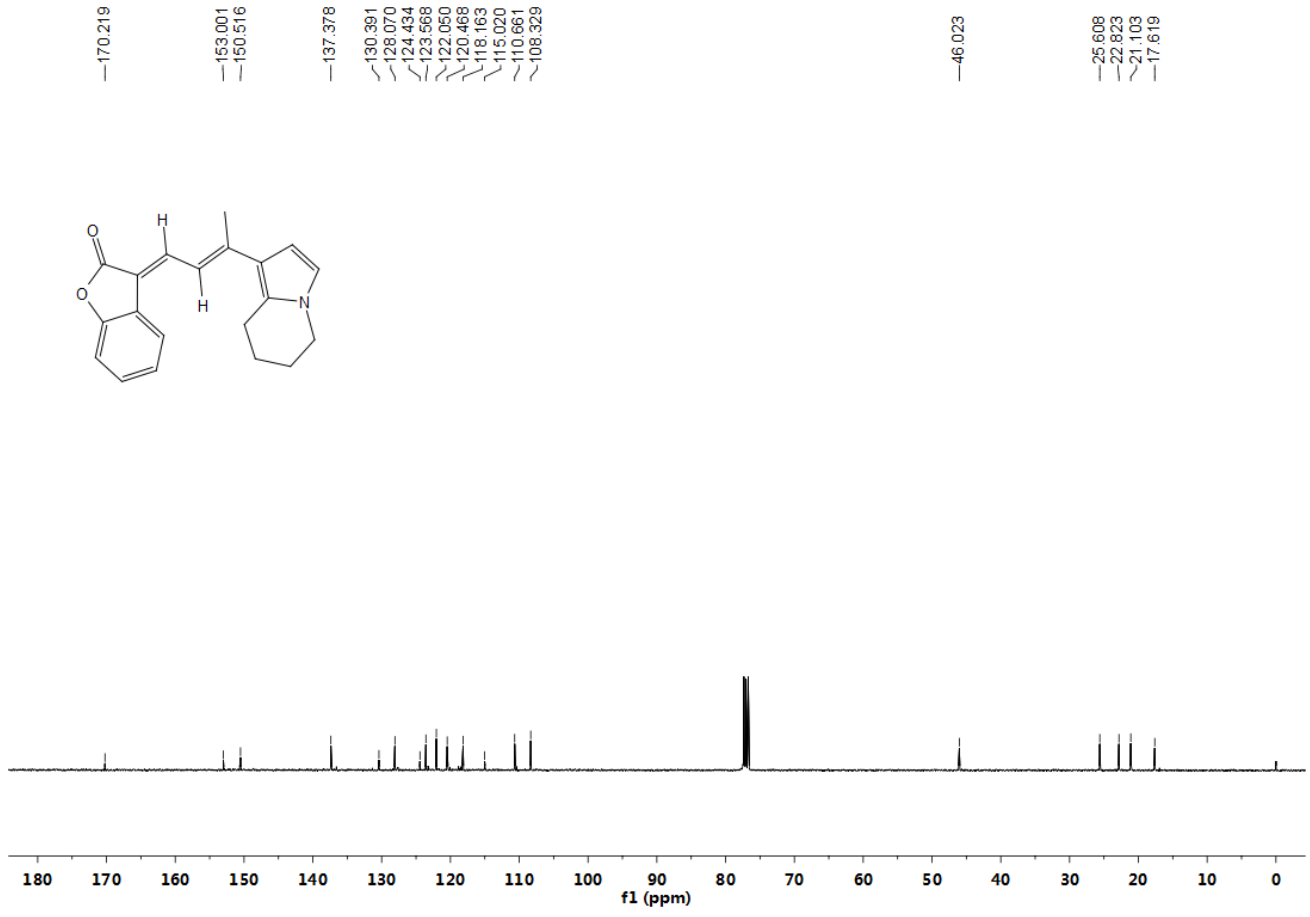
^{13}C NMR spectrum of **13** in DMSO-*d*$_6$



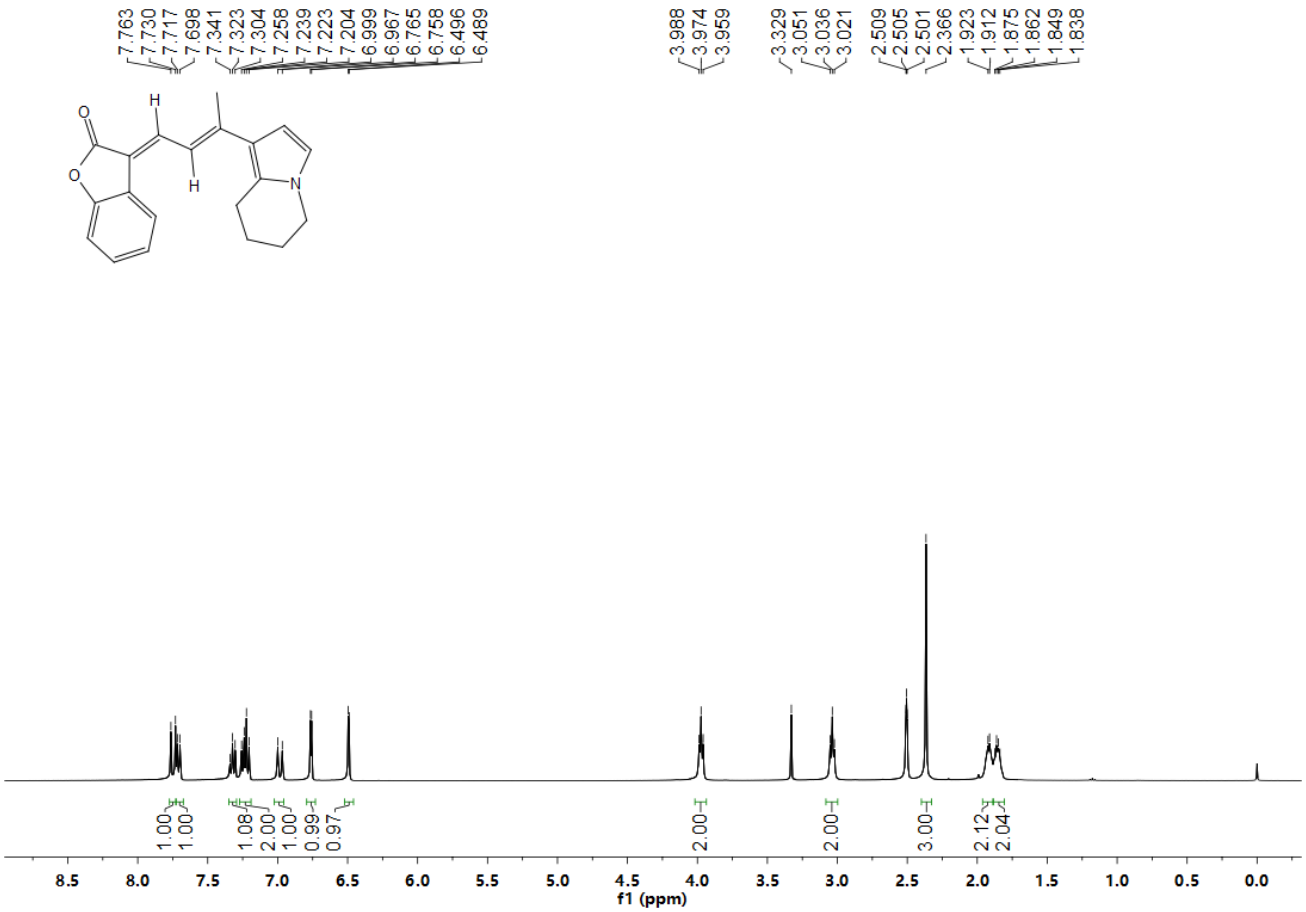
^{1}H NMR spectrum of **1a** in $CDCl_3$



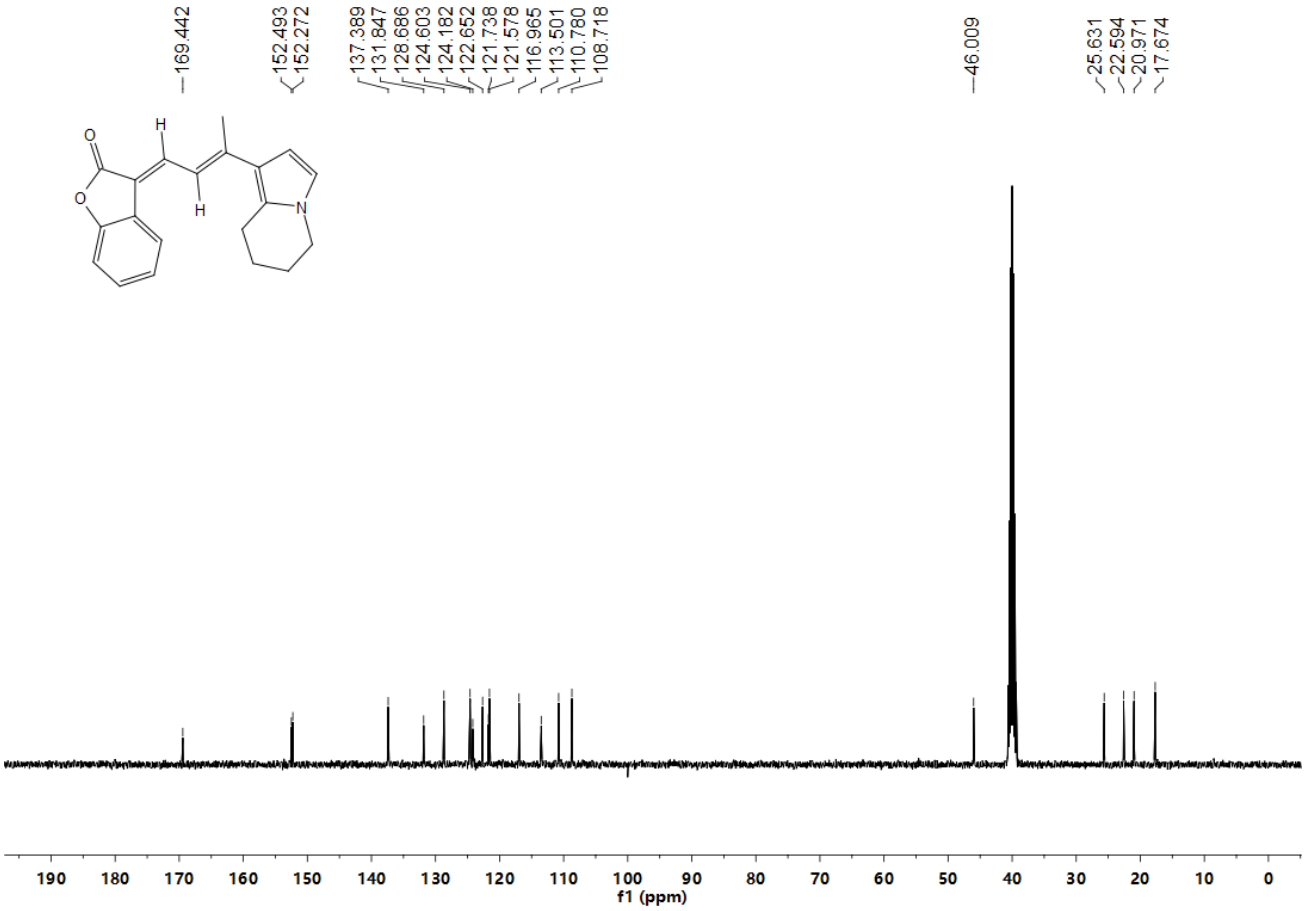
^{13}C NMR spectrum of **1a** in $CDCl_3$



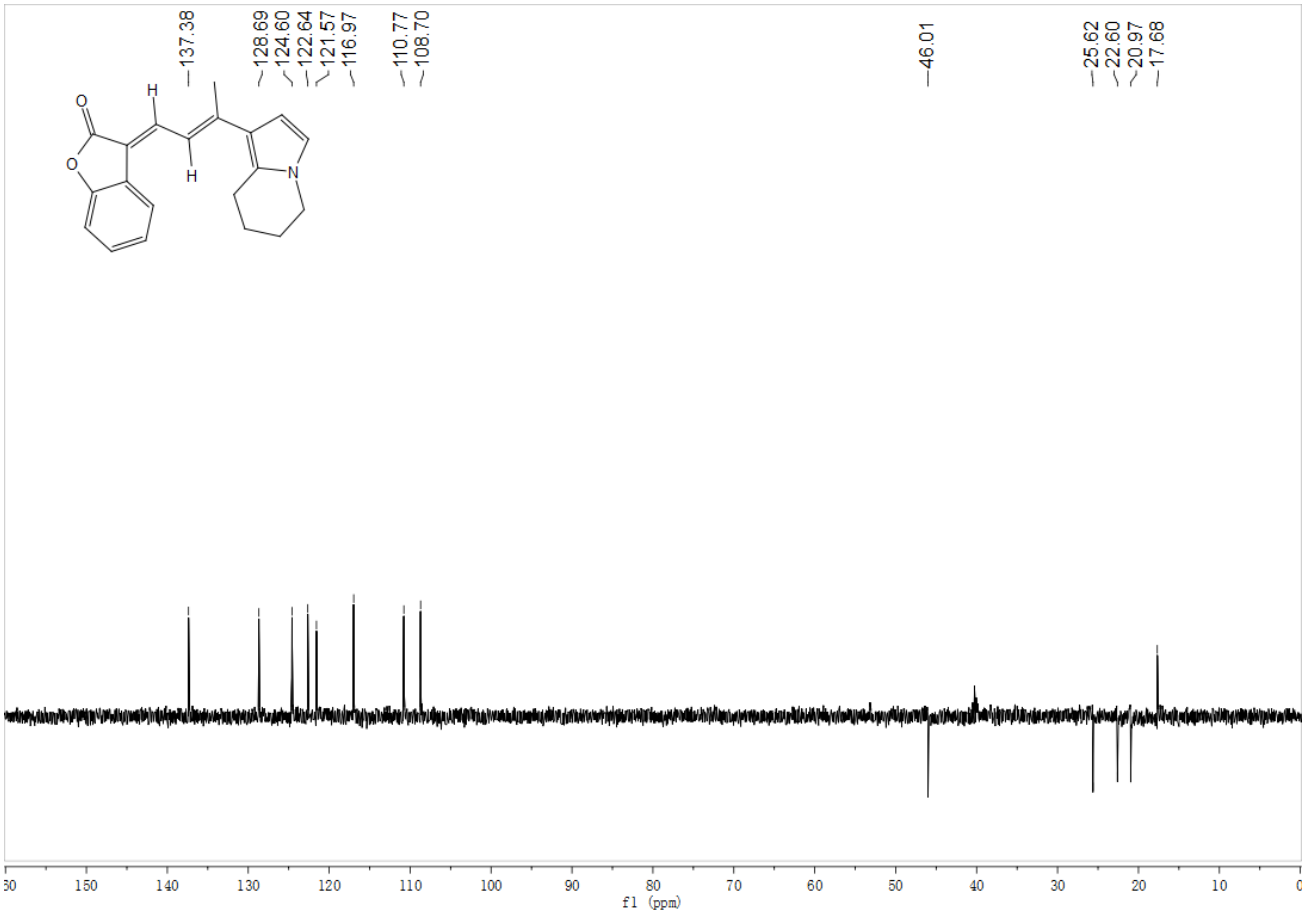
^{1}H NMR spectrum of **1a** in DMSO-d_6



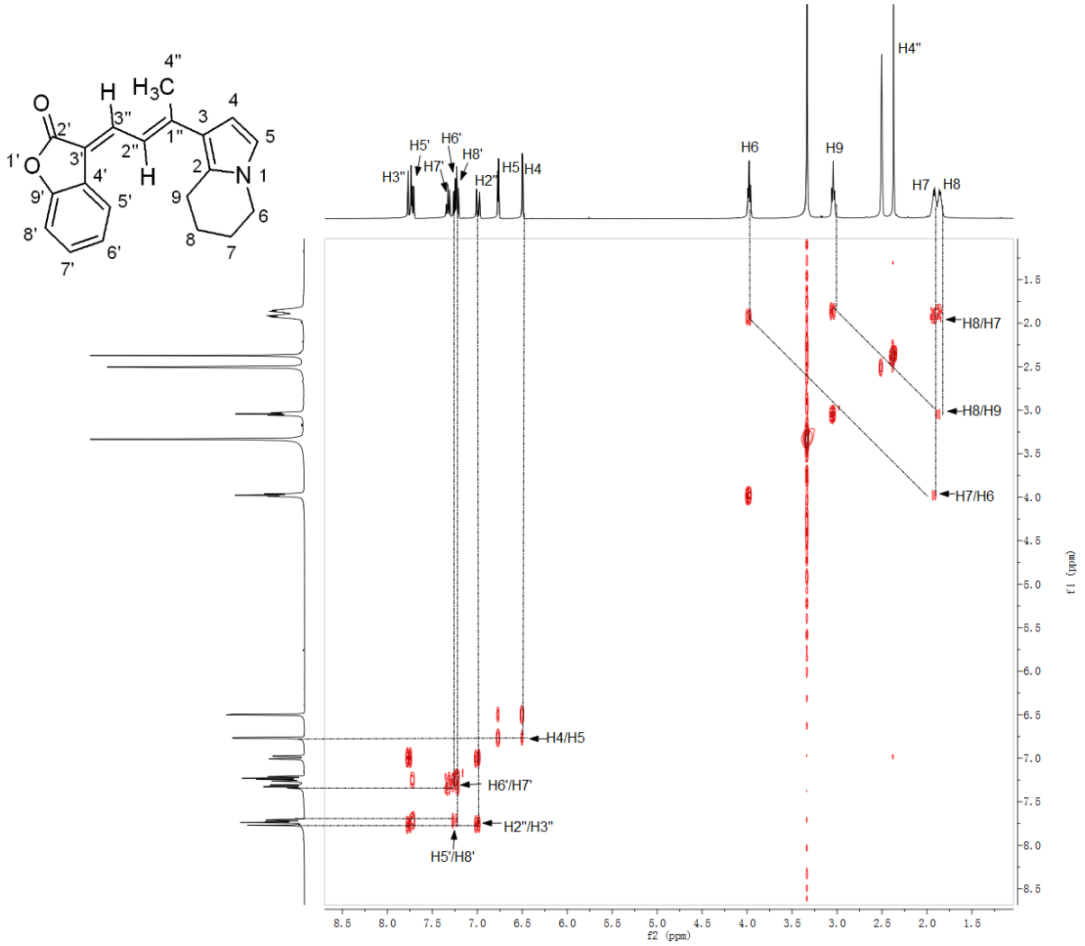
^{13}C NMR spectrum of **1a** in DMSO-d_6



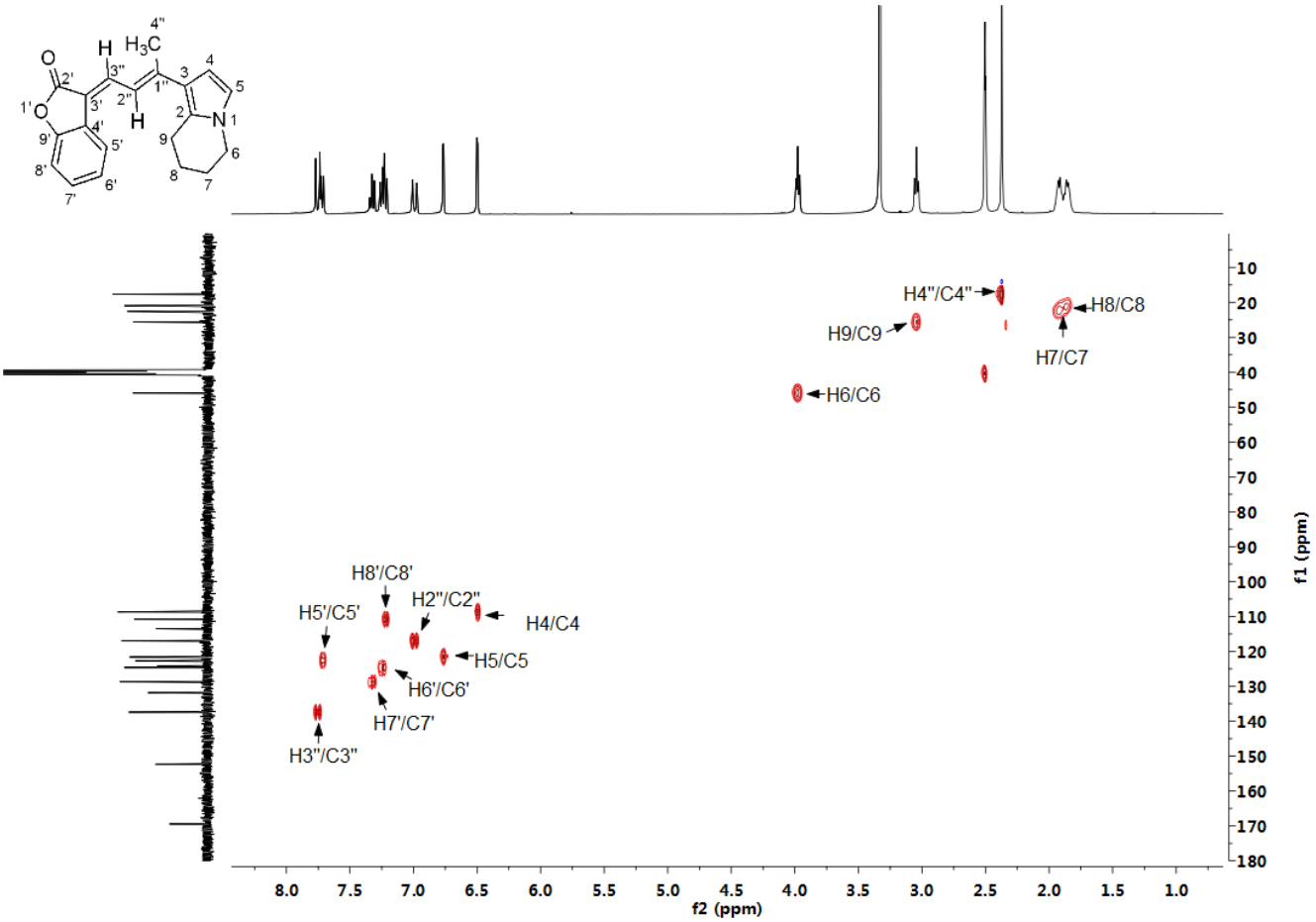
DEPT-135 spectrum of **1a** in DMSO-d_6



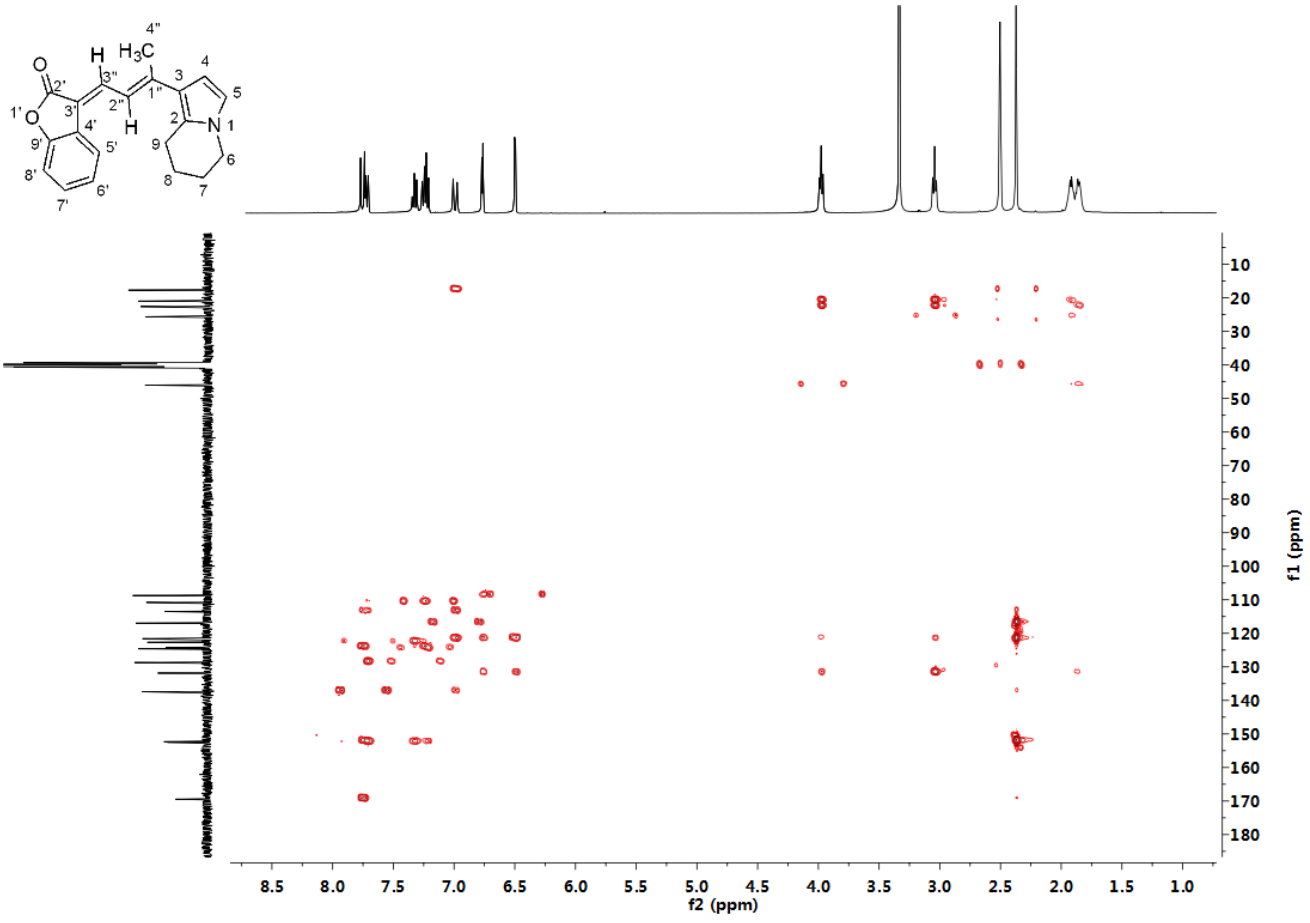
^{1}H-^{1}H COSY spectrum of **1a** in DMSO-d_6



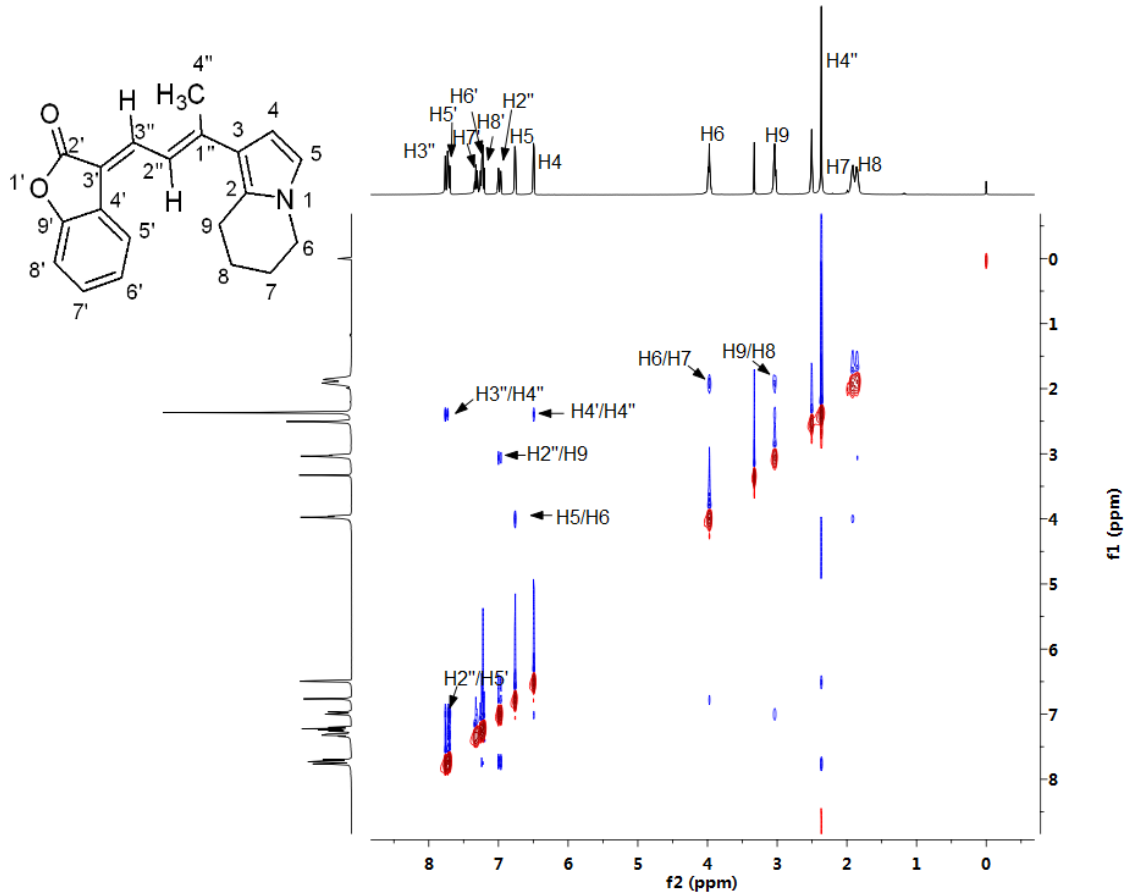
HSQC spectrum of **1a** in DMSO-d_6



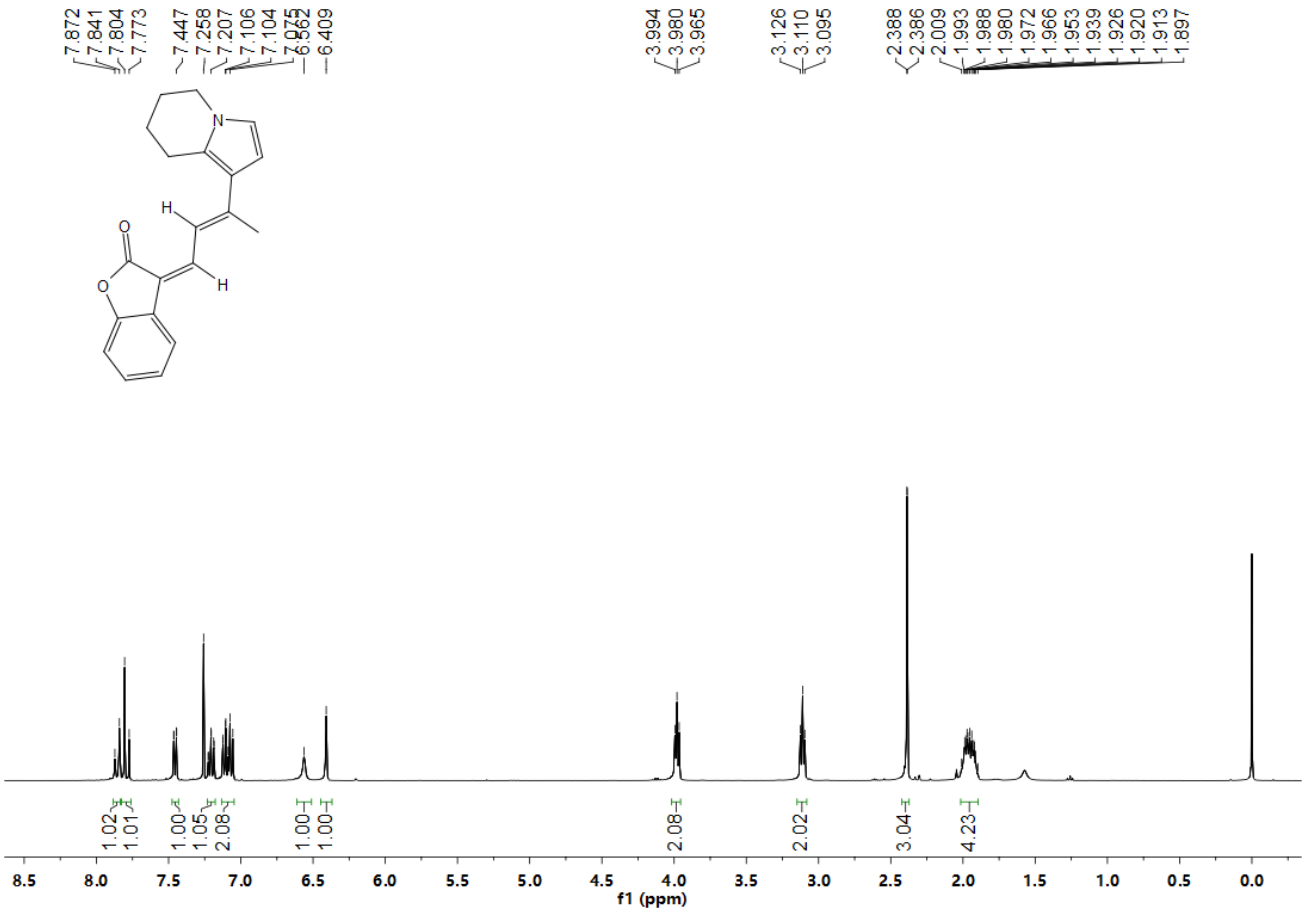
HMBC spectrum of **1a** in DMSO-d_6



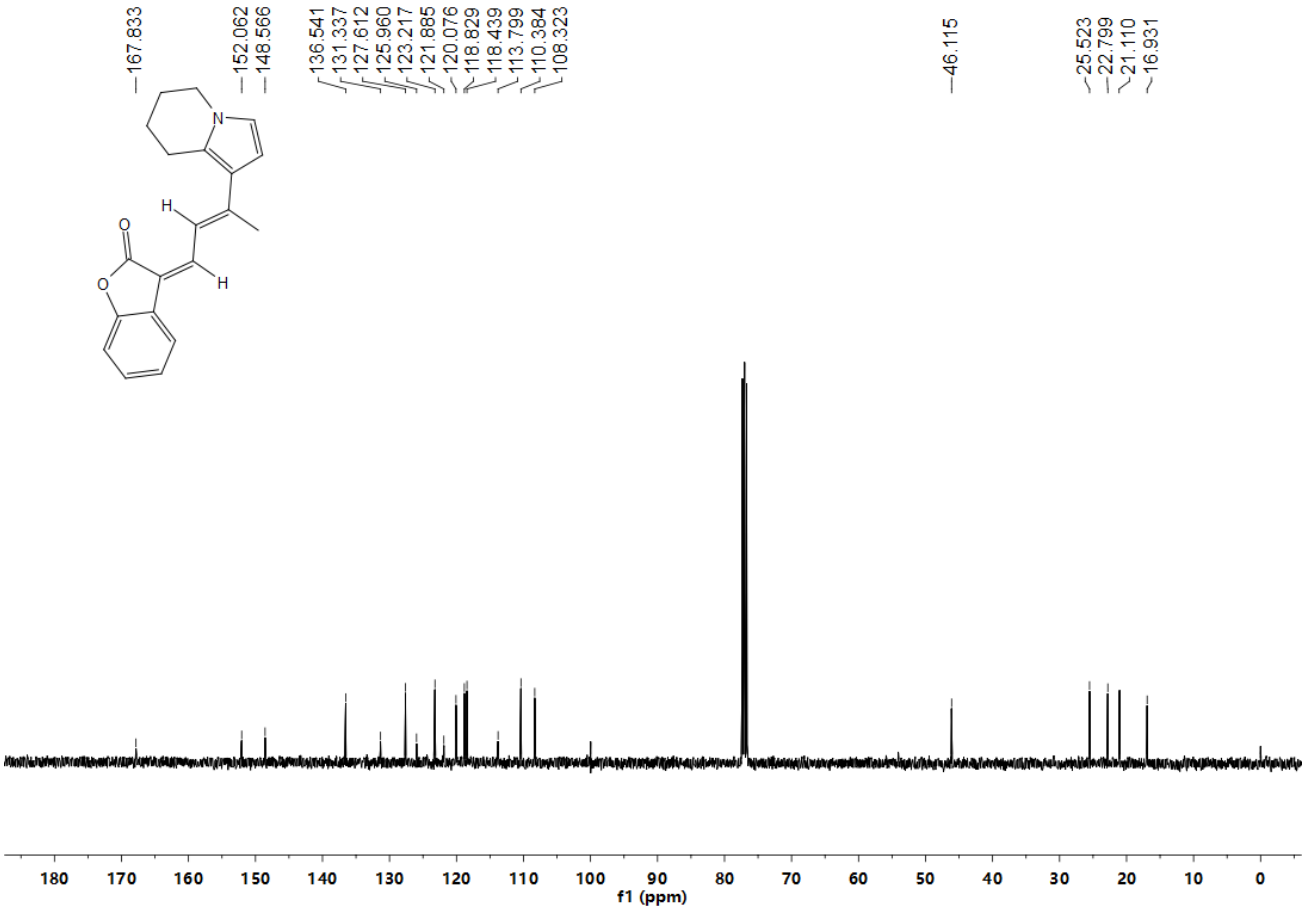
NOESY spectrum of **1a** in DMSO-d_6



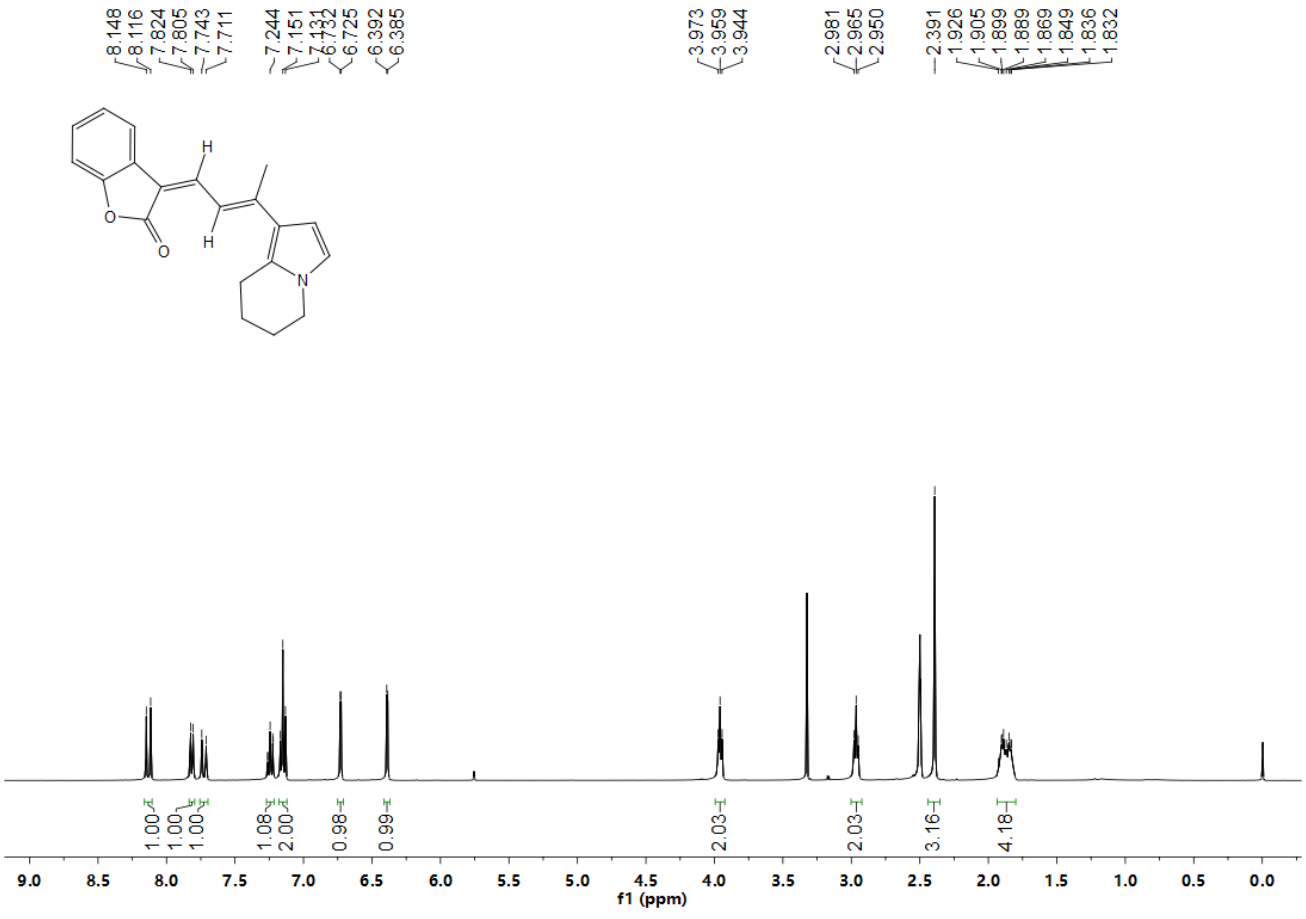
^{1}H NMR spectrum of **1b** in $CDCl_3$



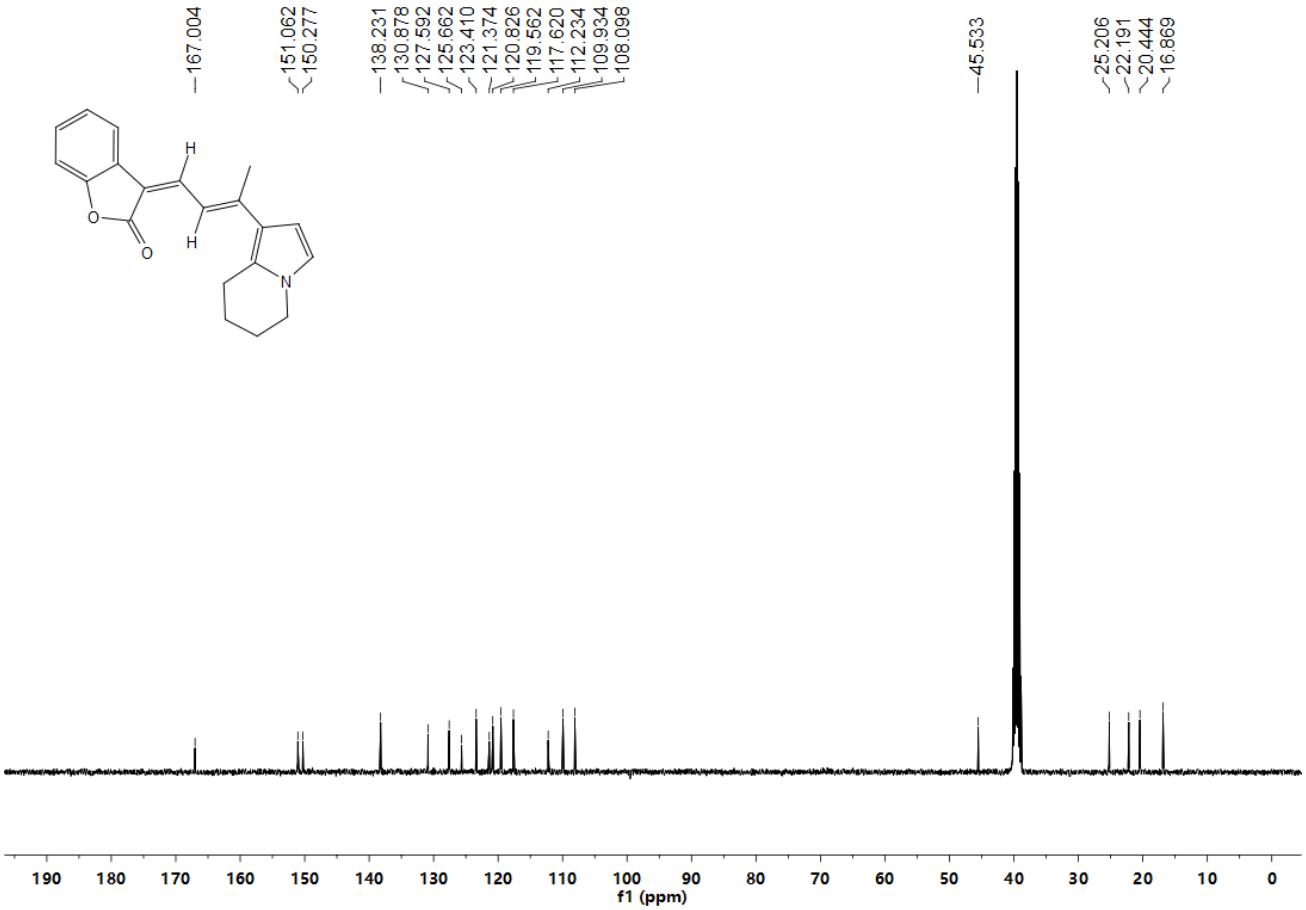
^{13}C NMR spectrum of **1b** in $CDCl_3$



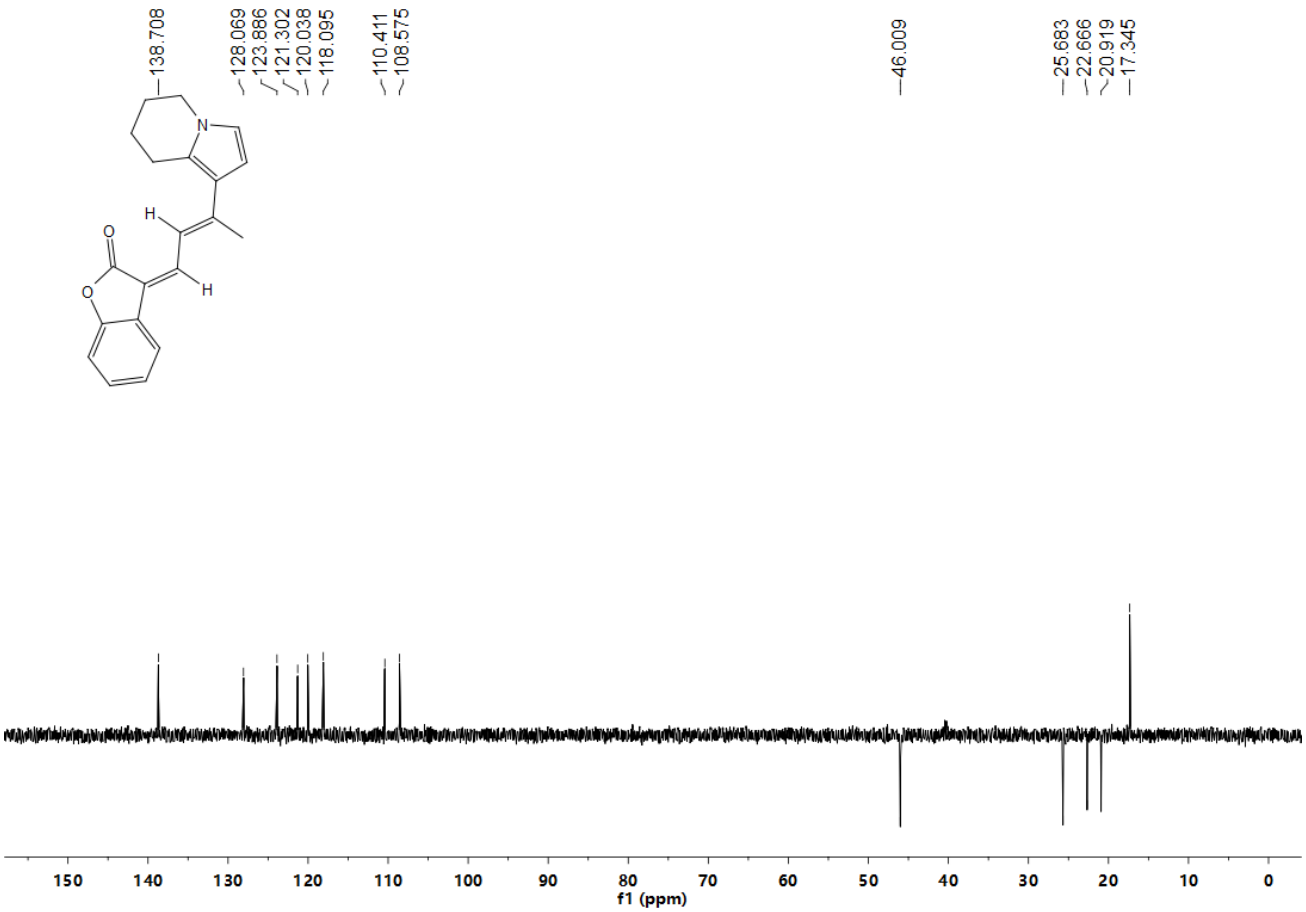
^{1}H NMR spectrum of **1b** in DMSO-d_6



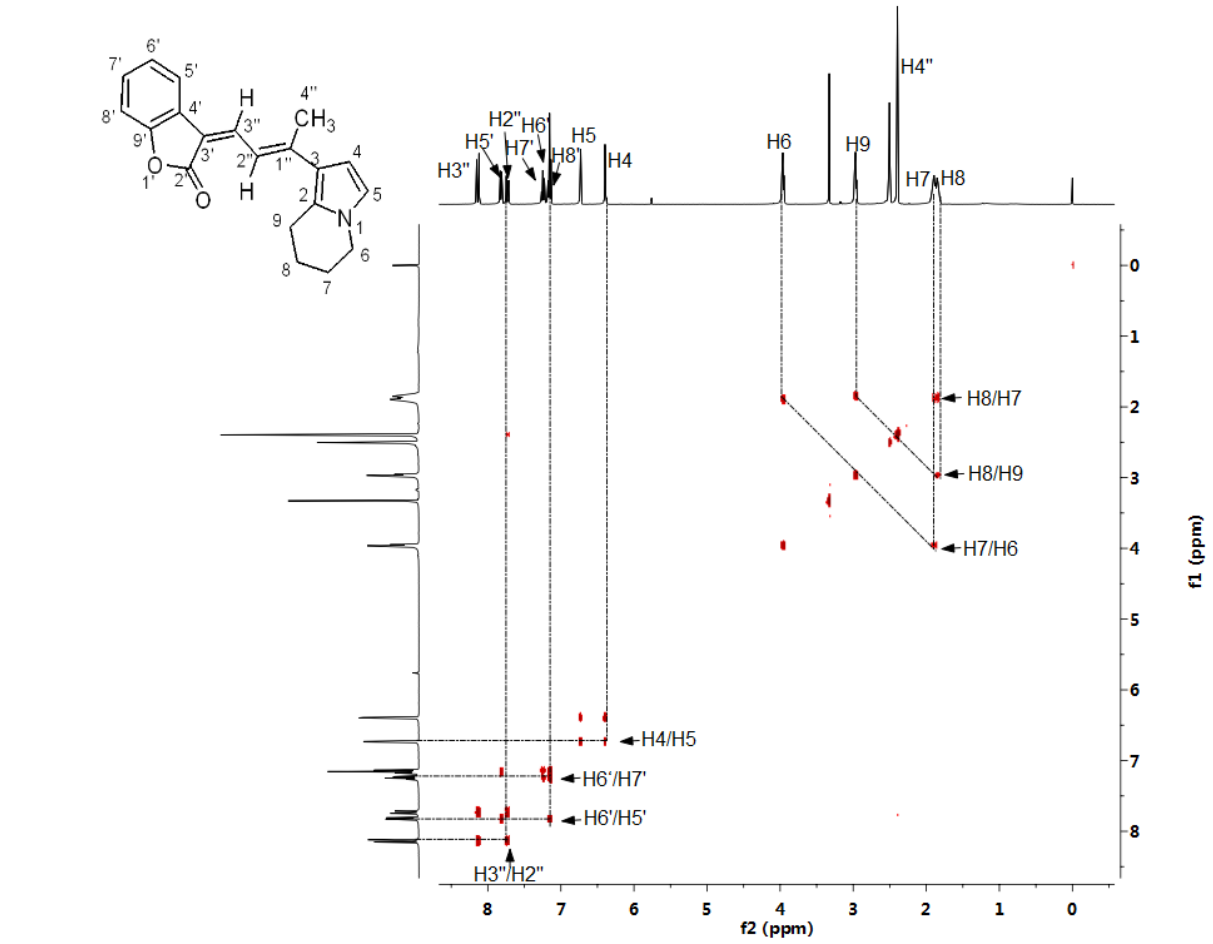
^{13}C NMR spectrum of **1b** in DMSO-d_6



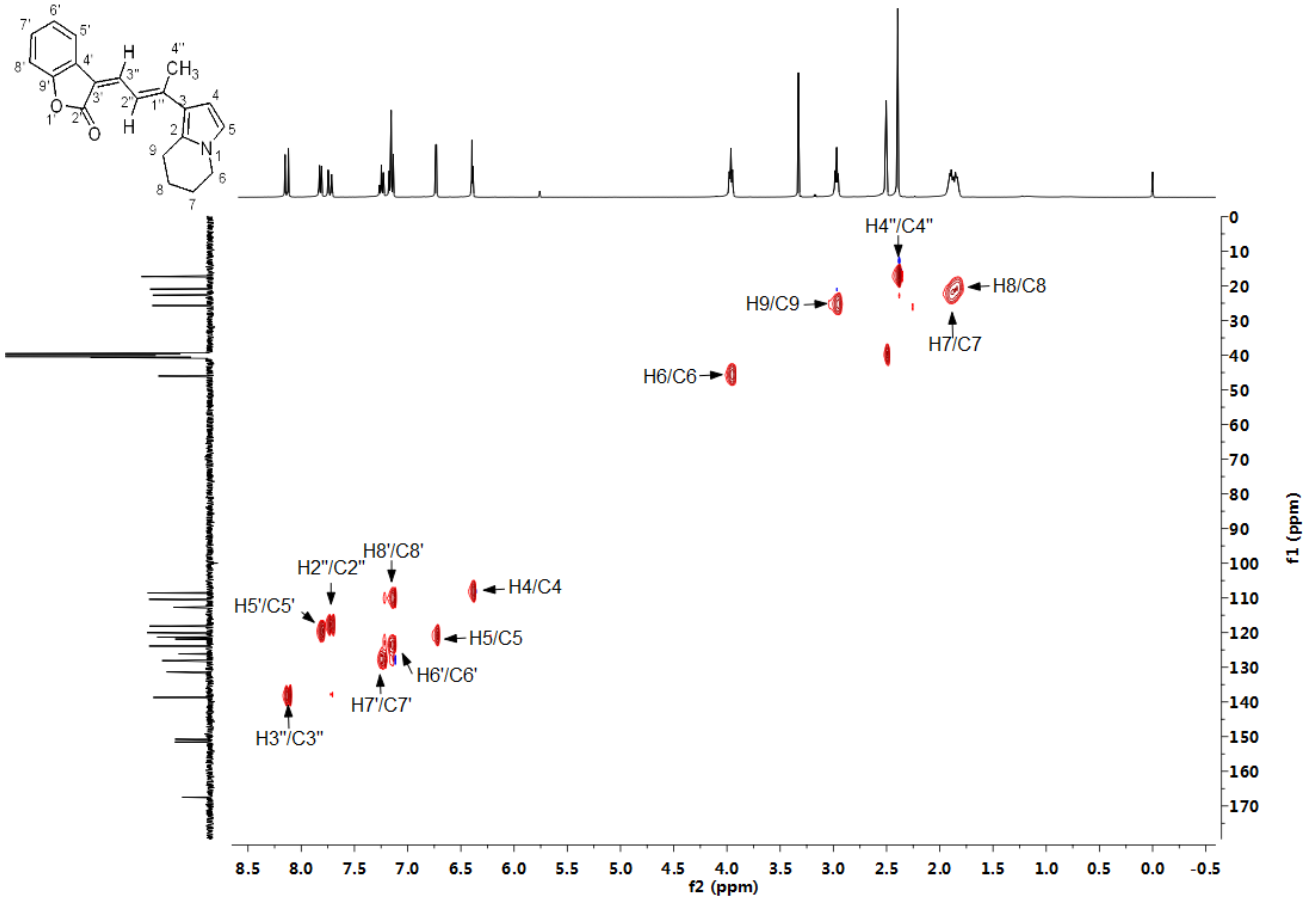
DEPT-135 spectrum of **1b** in DMSO-d_6



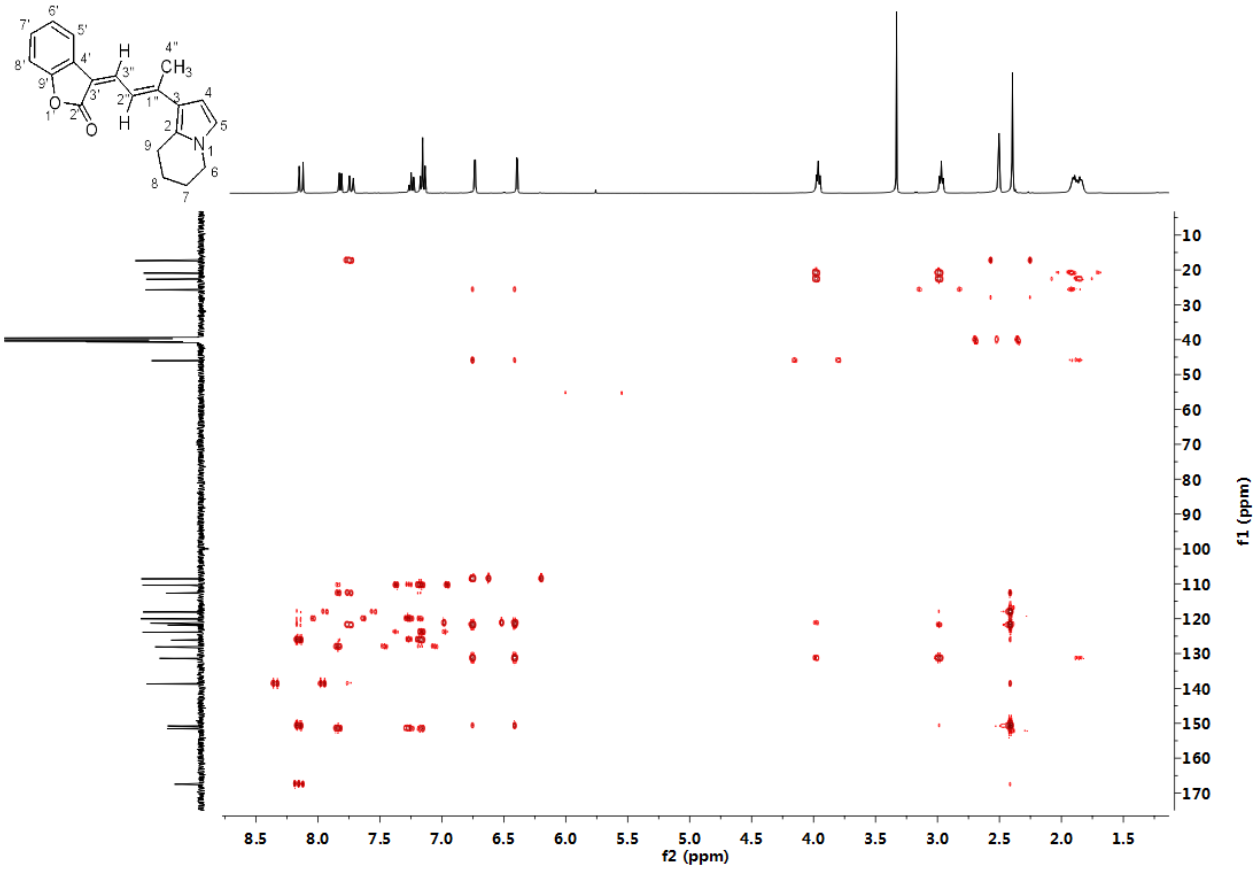
^{1}H-^{1}H COSY spectrum of **1b** in DMSO-*d*$_6$



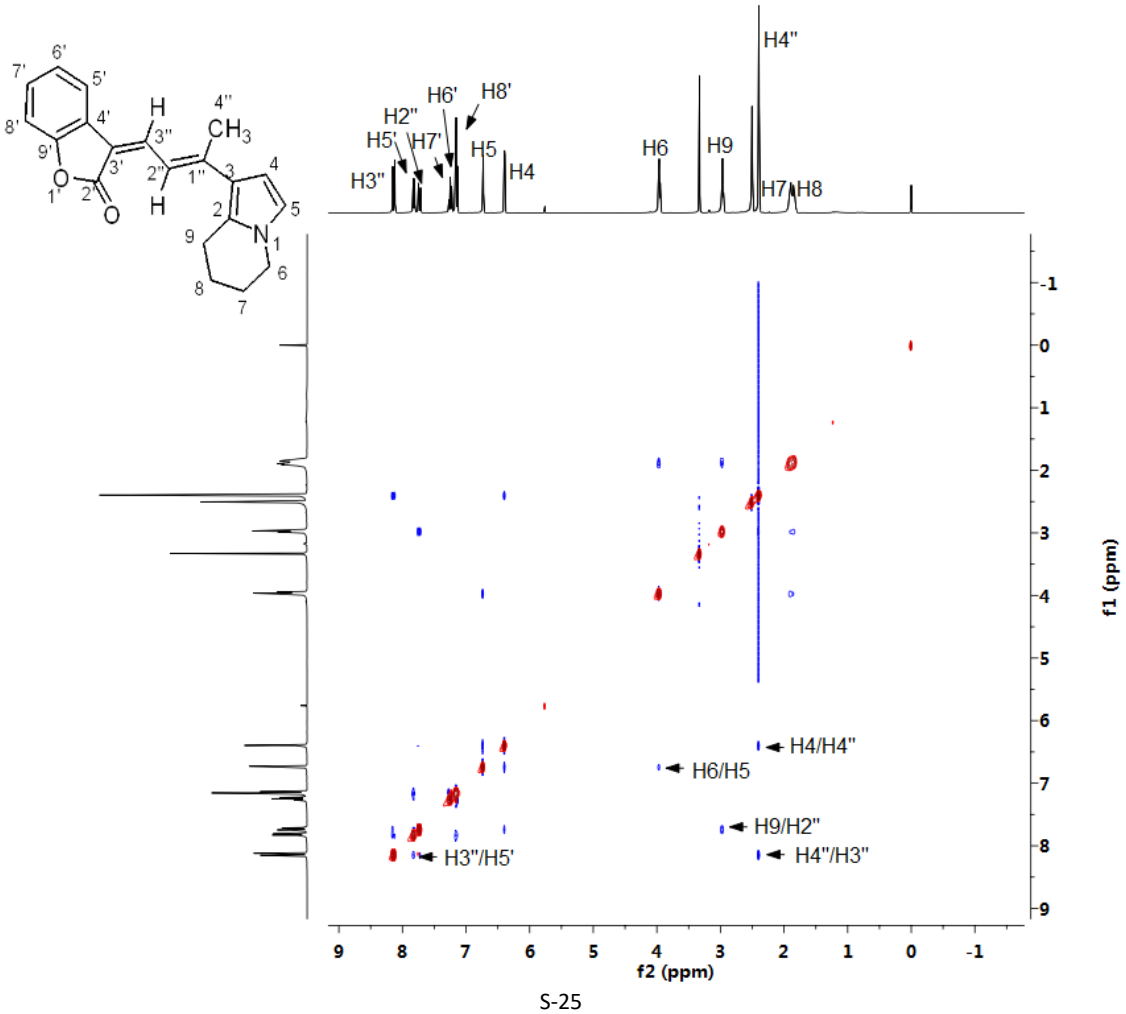
HSQC spectrum of **1b** in DMSO-*d*$_6$



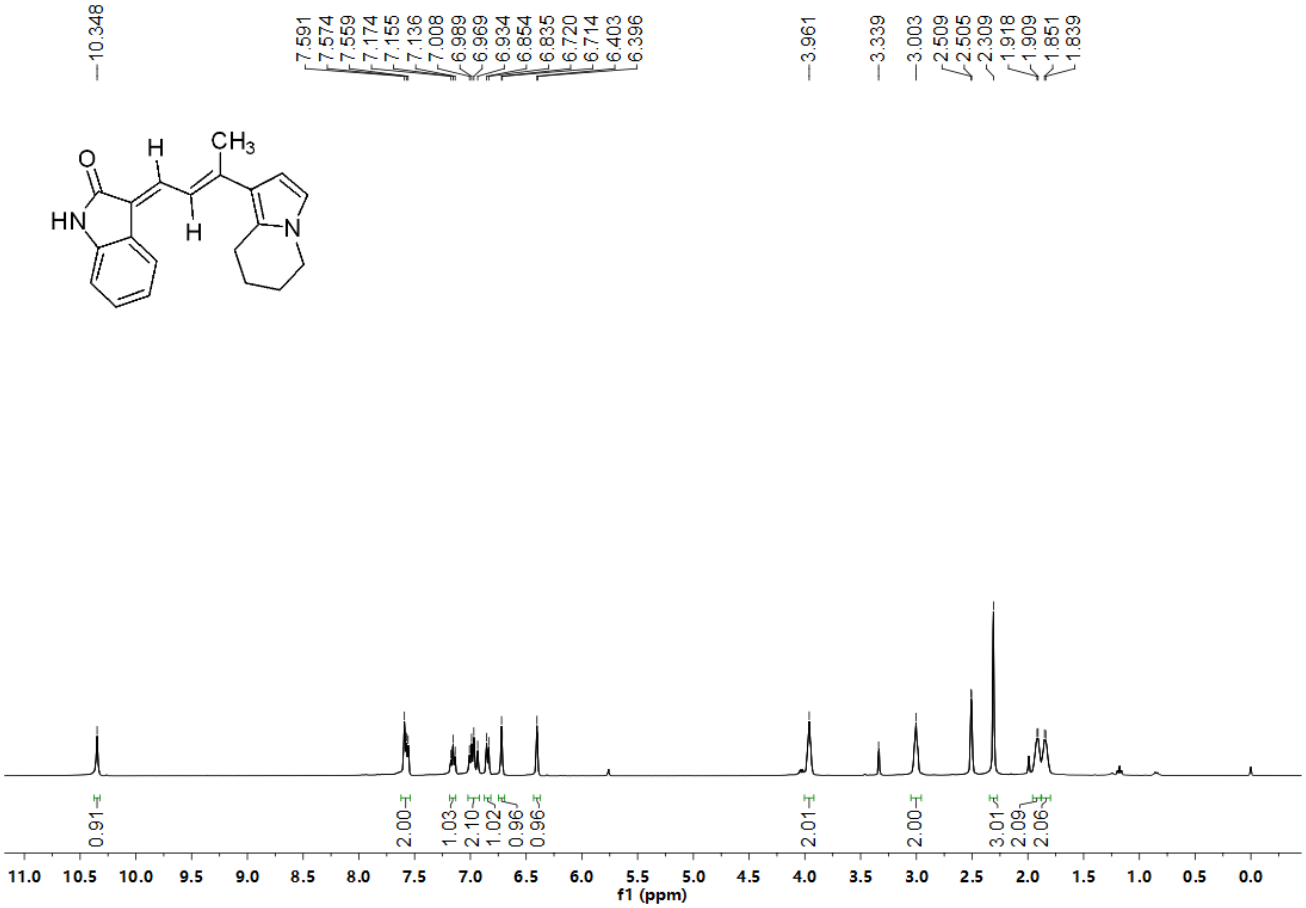
HMBC spectrum of **1b** in DMSO-d_6



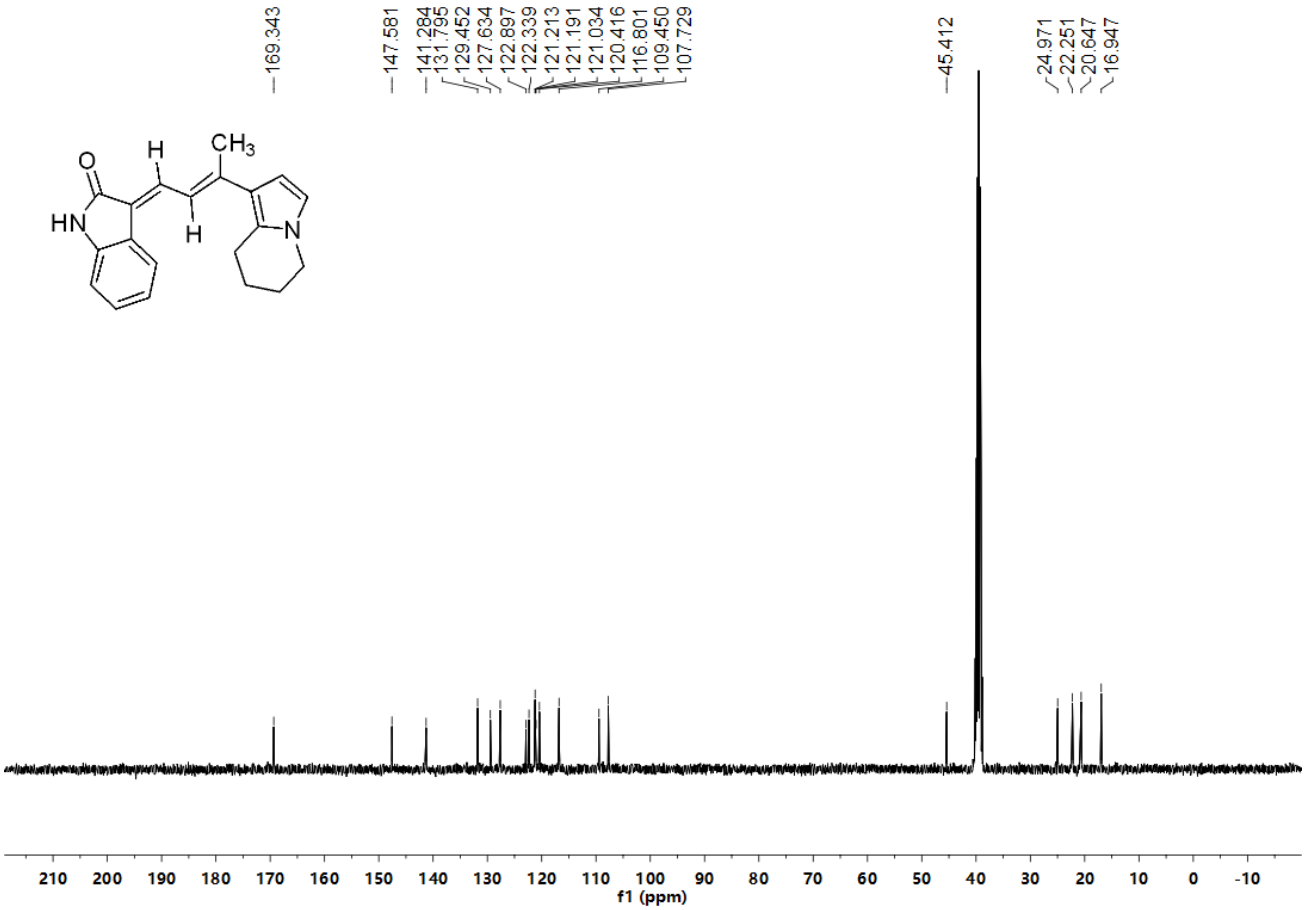
NOESY spectrum of **1b** in DMSO-d_6



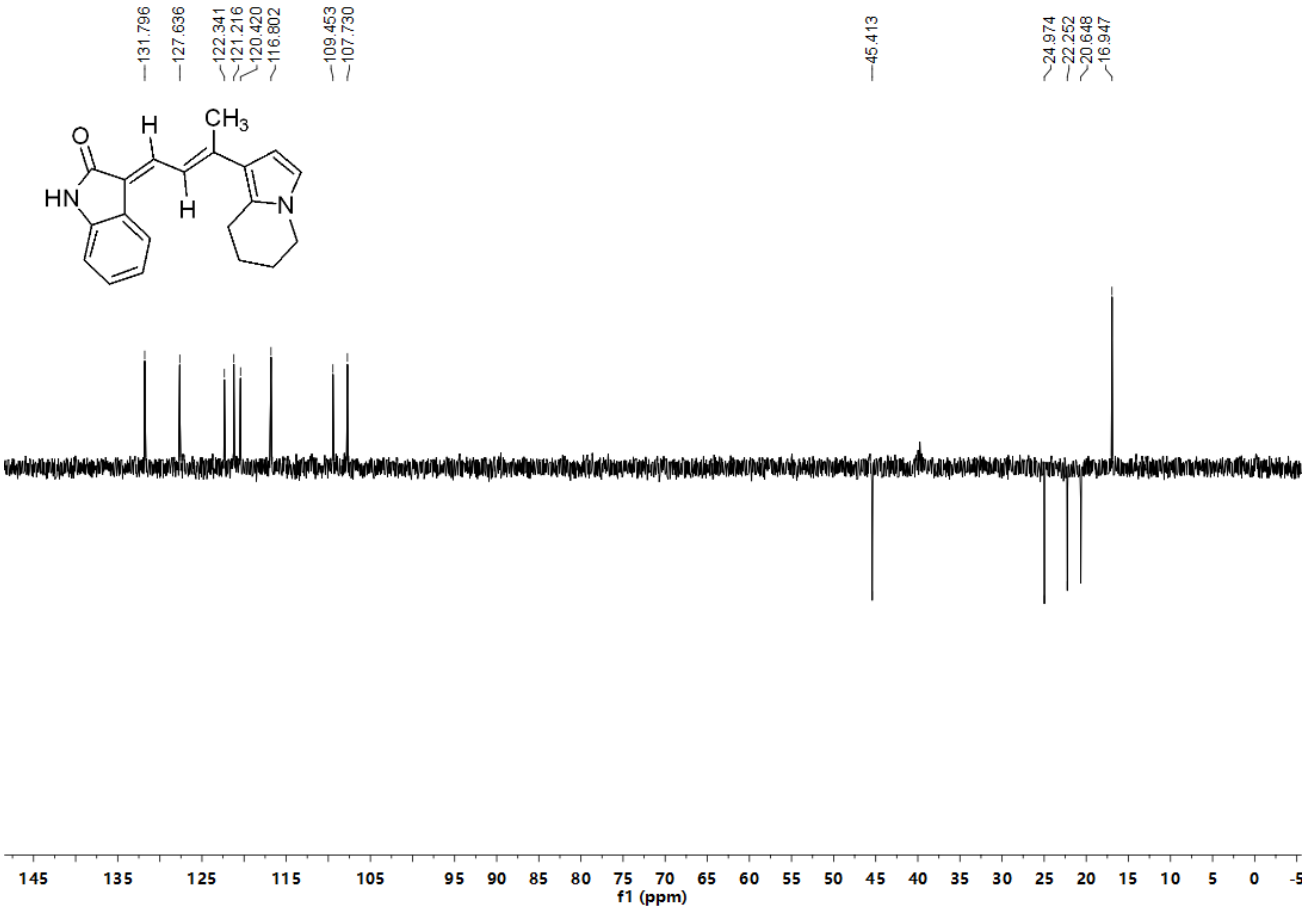
^{1}H NMR spectrum of **2a** in DMSO-d_6



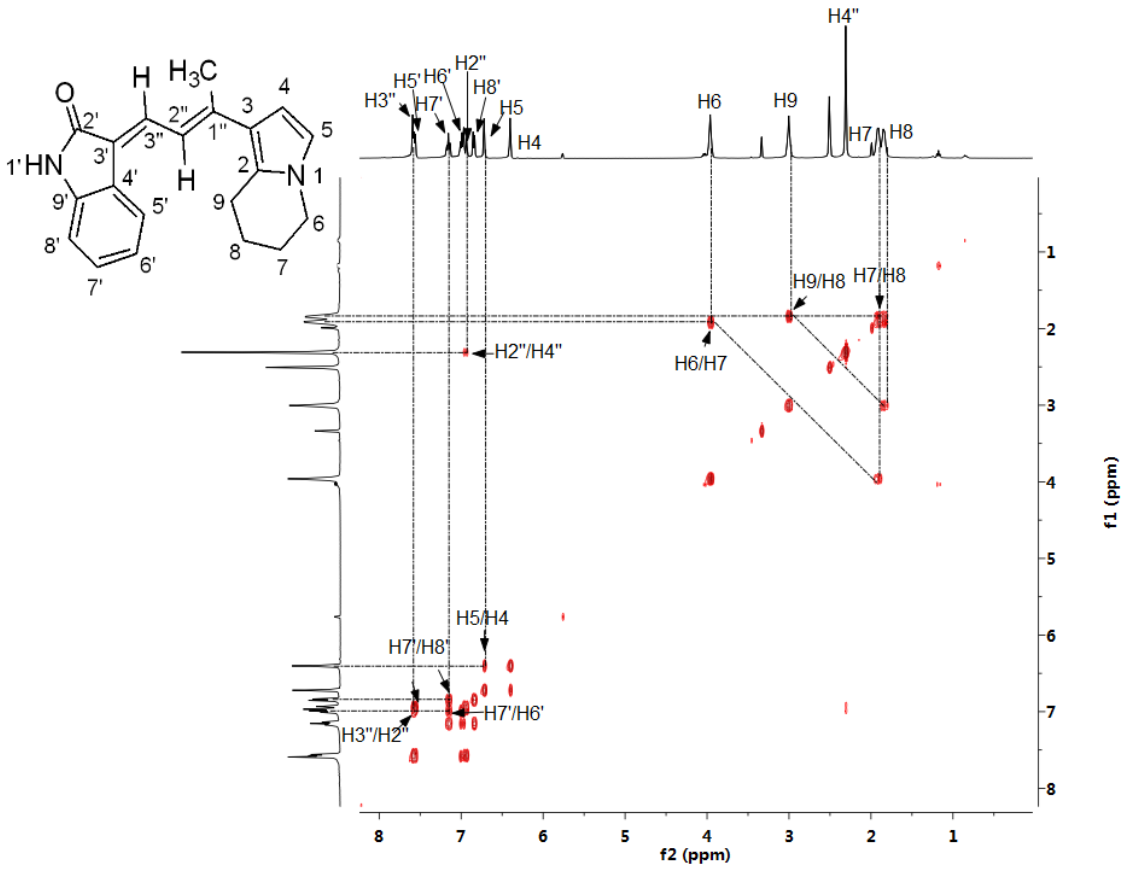
^{13}C NMR spectrum of **2a** in DMSO-d_6



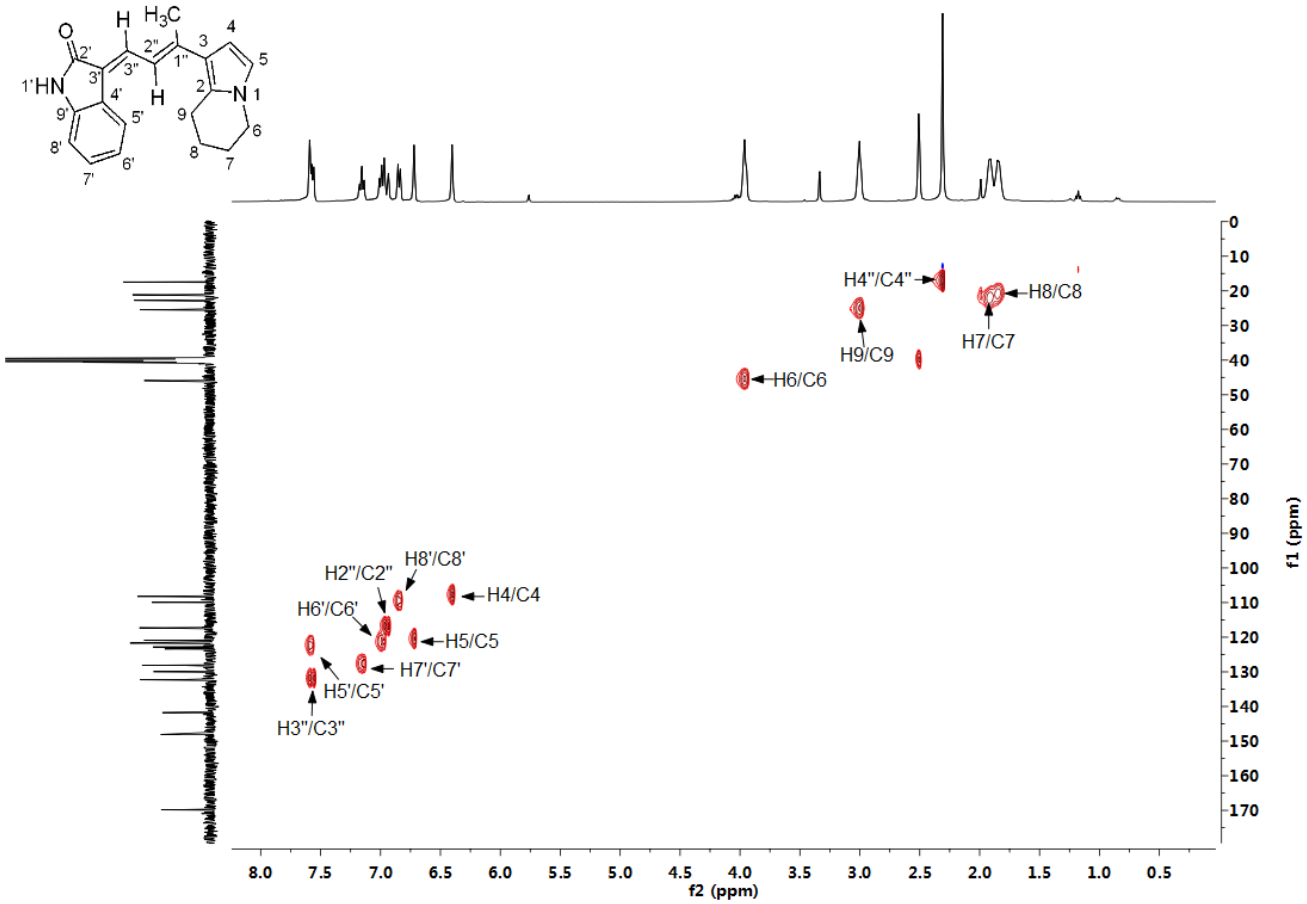
DEPT-135 spectrum of **2a** in DMSO-d_6



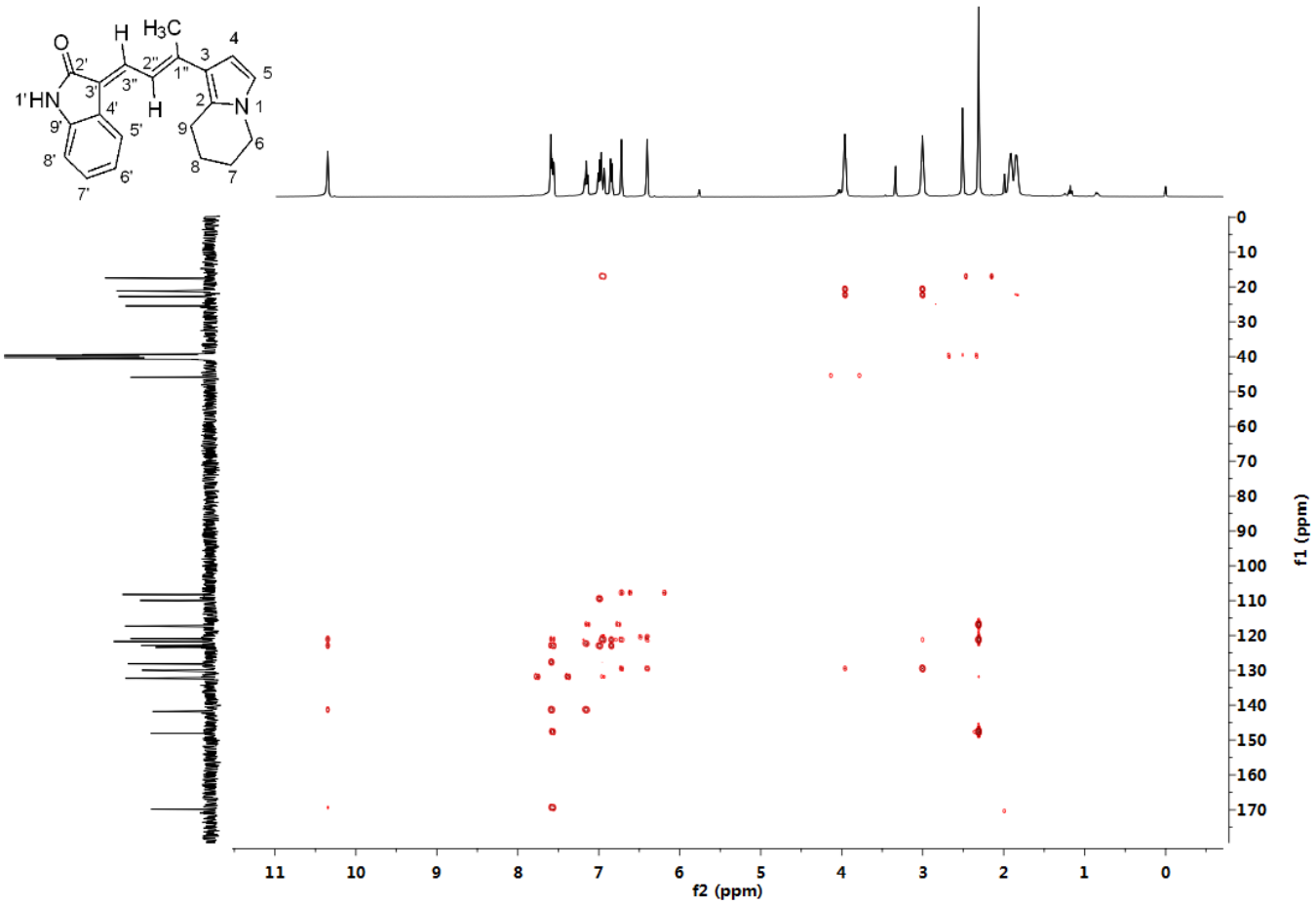
^{1}H-^{1}H COSY spectrum of **2a** in DMSO-d_6



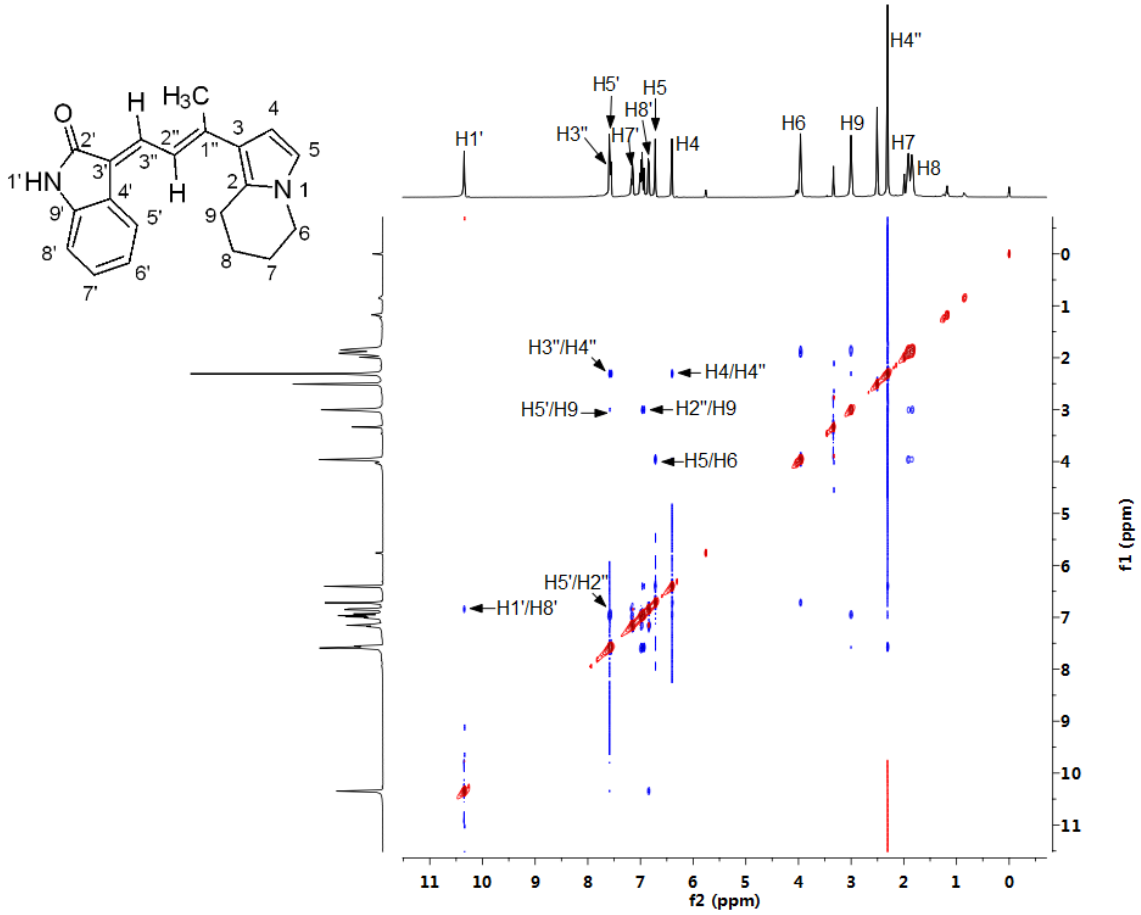
HSQC spectrum of **2a** in DMSO-d_6



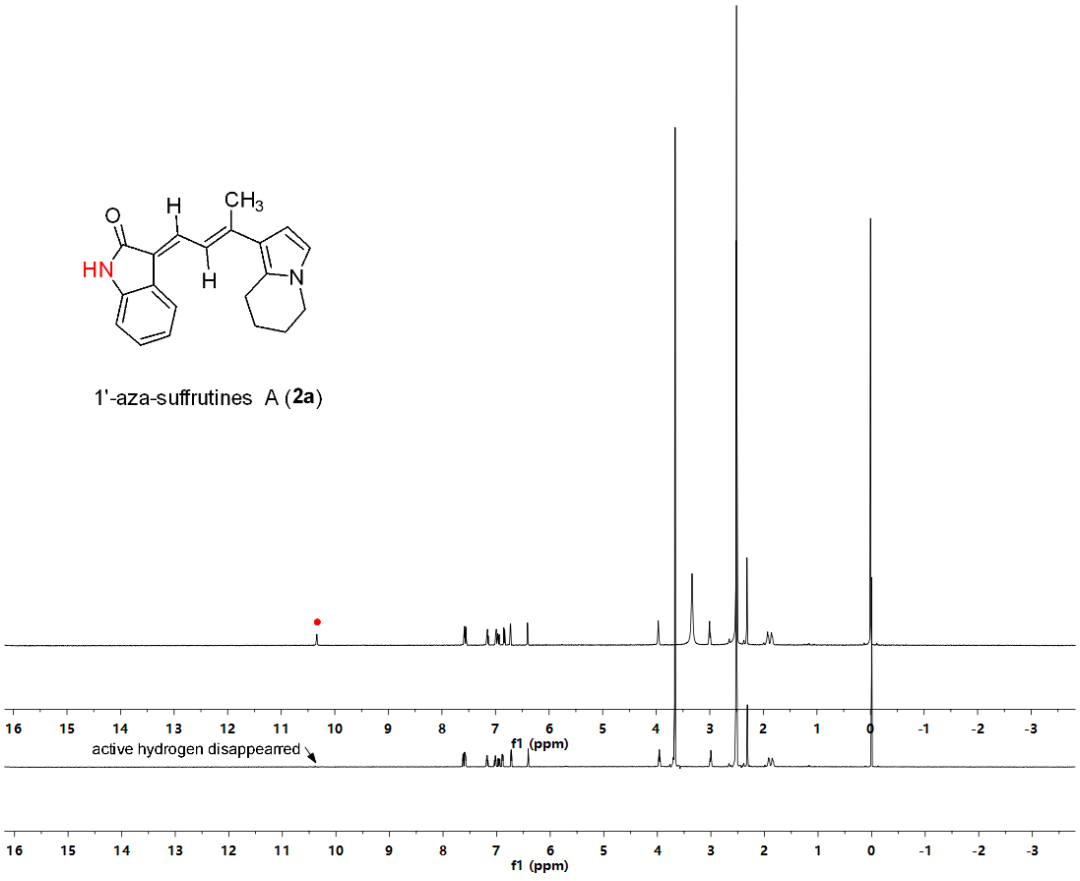
HMBC spectrum of **2a** in DMSO-d_6



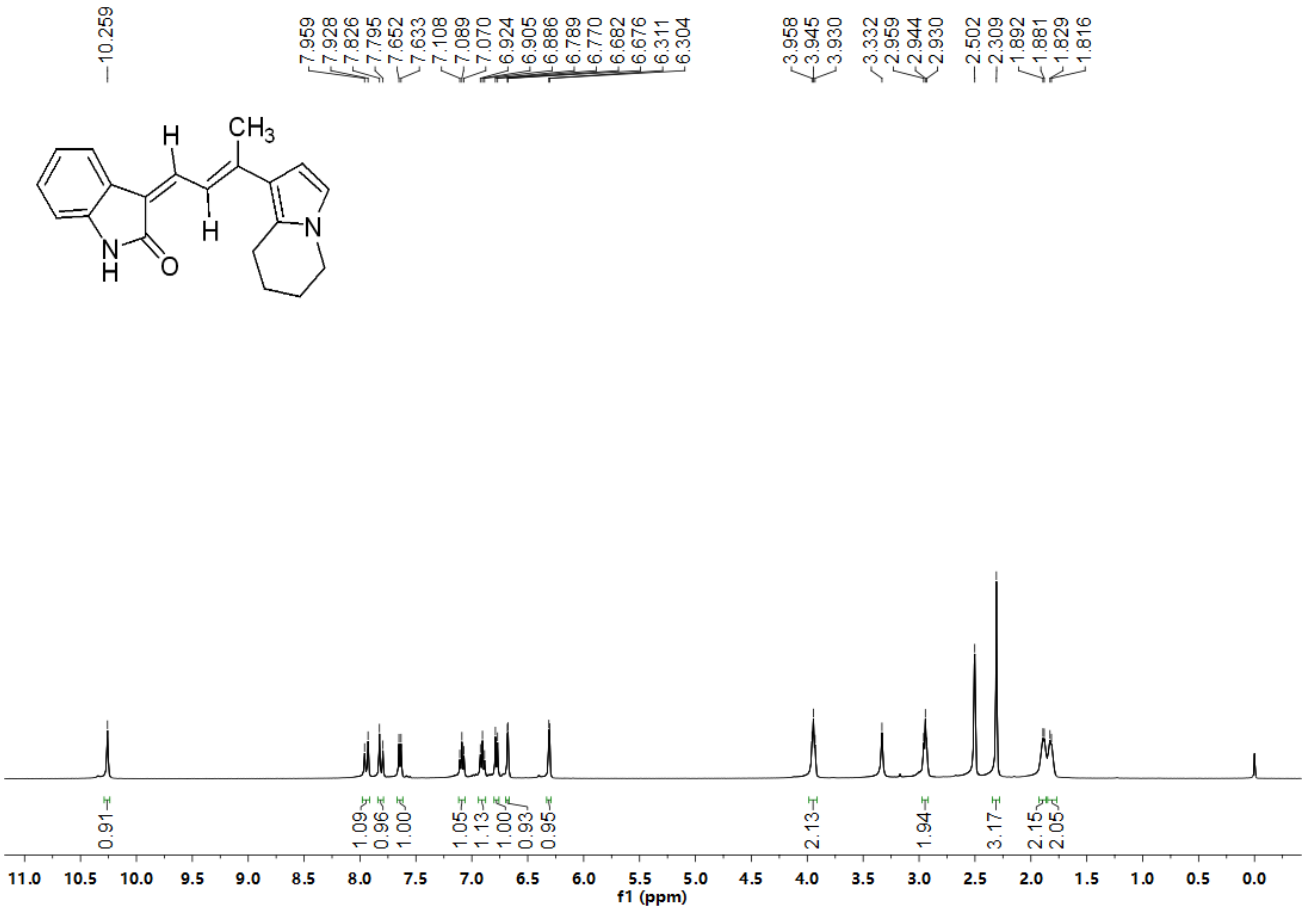
NOESY spectrum of **2a** in DMSO-d_6



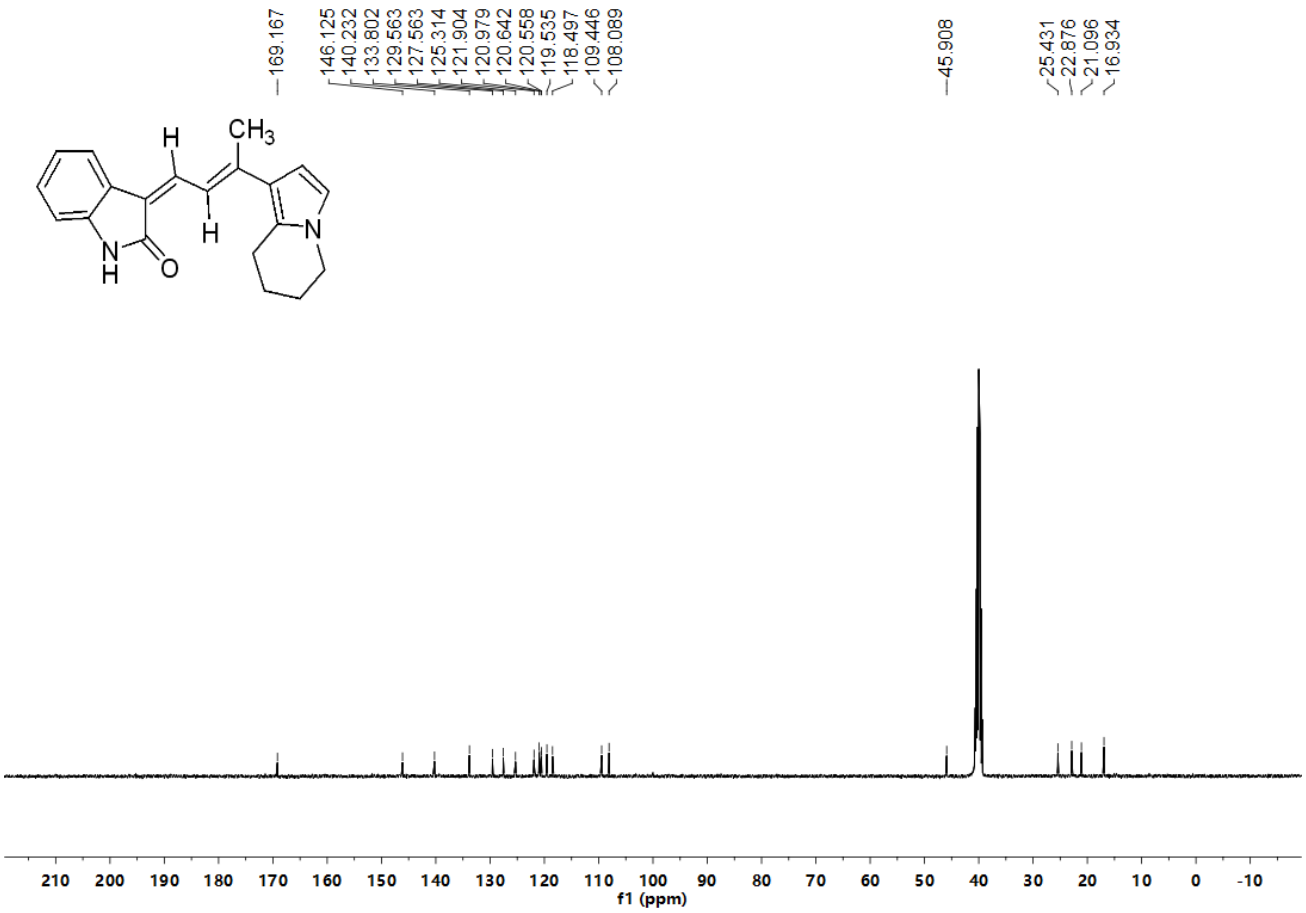
^{1}H NMR D_2O exchange experiment of **2a** in DMSO-d_6



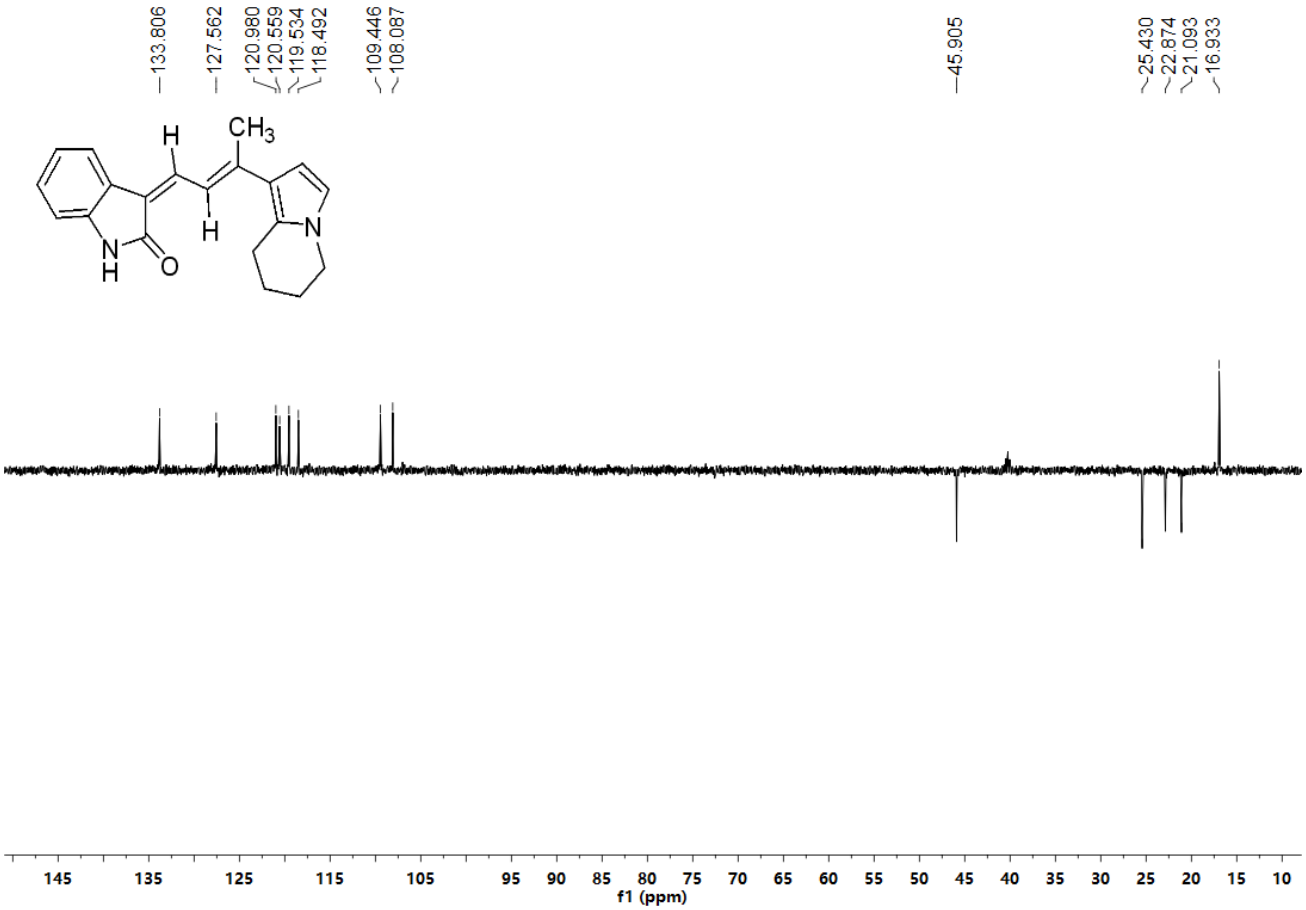
^{1}H NMR spectrum of **2b** in DMSO-d_6



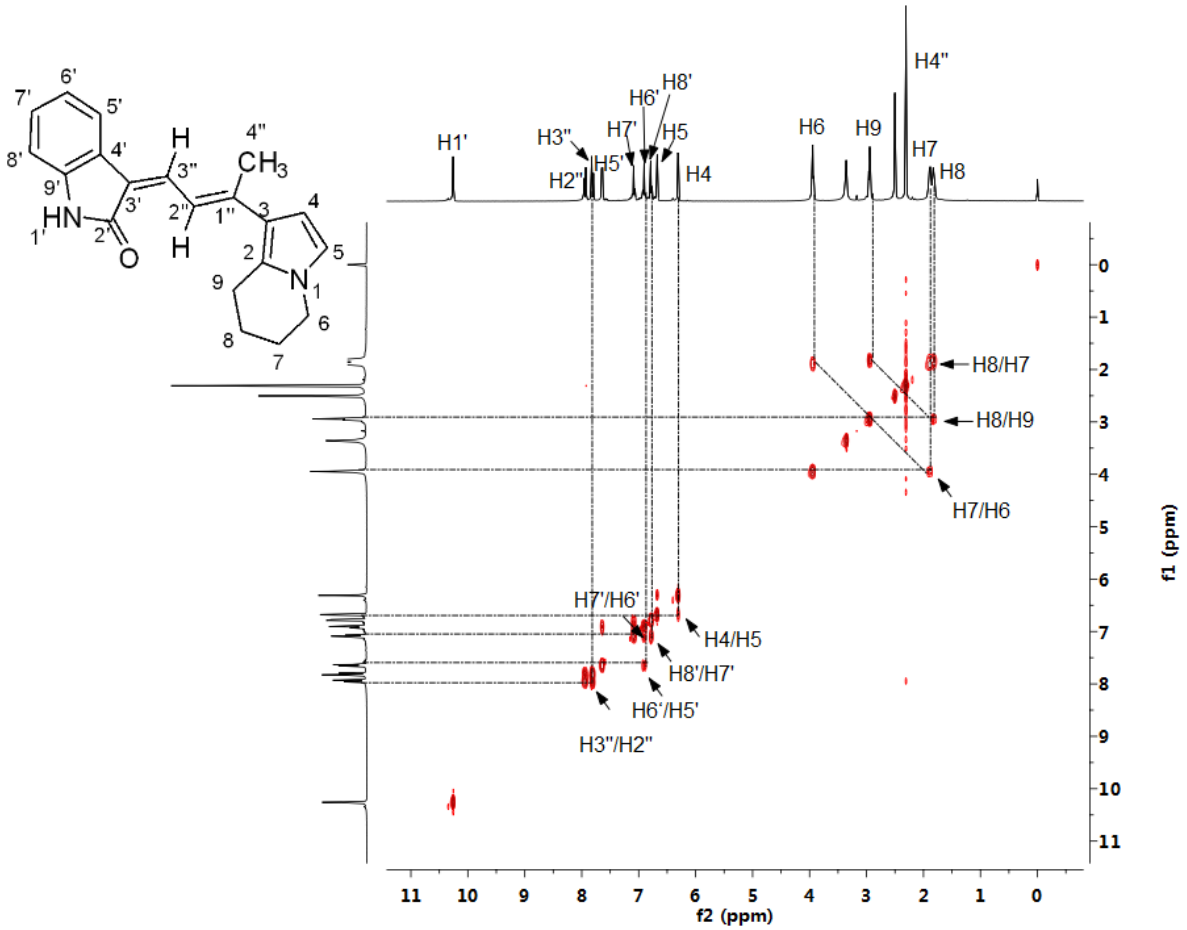
^{13}CNMR spectrum of **2b** in DMSO-d_6



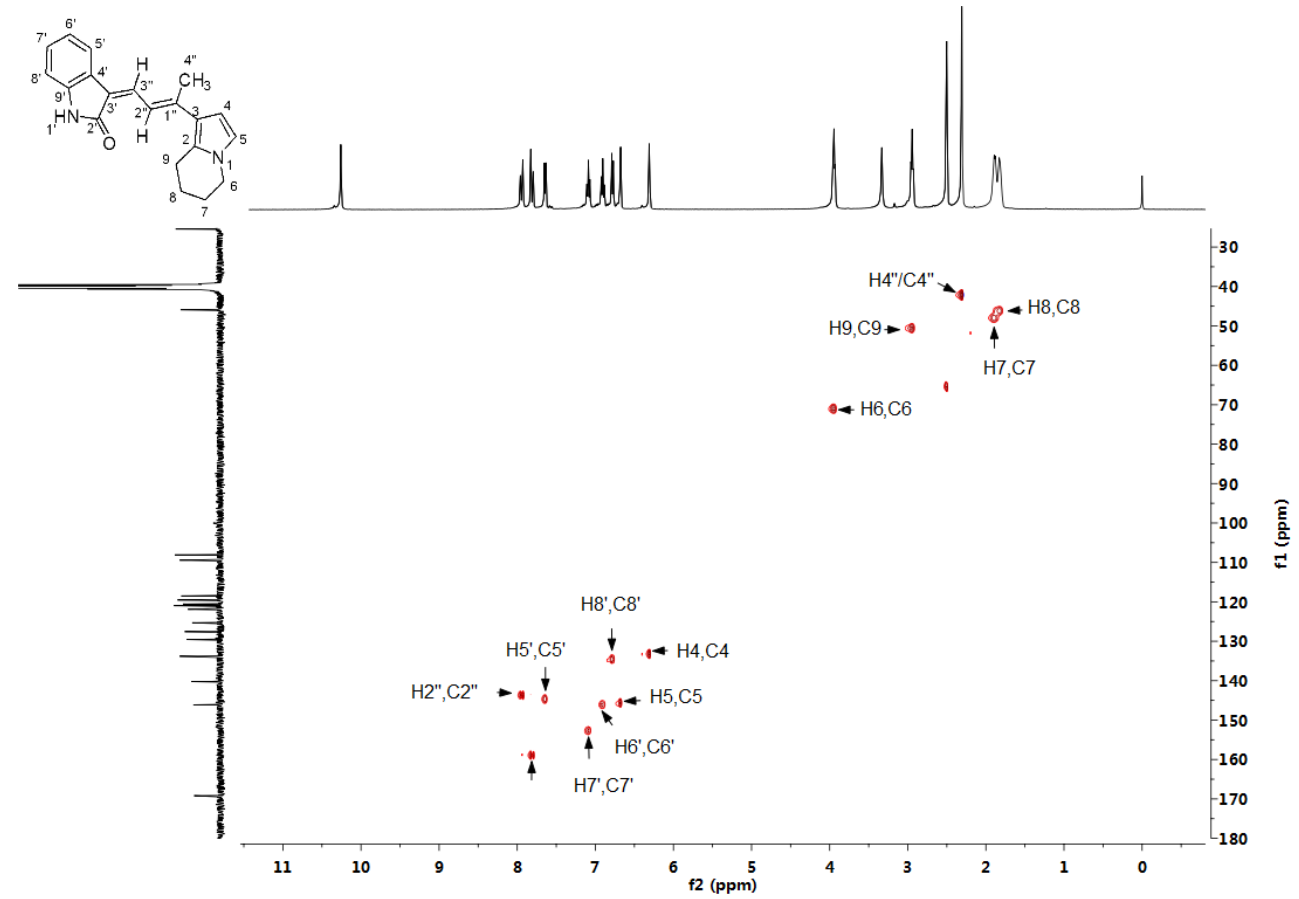
DEPT-135 spectrum of **2b** in DMSO-d_6



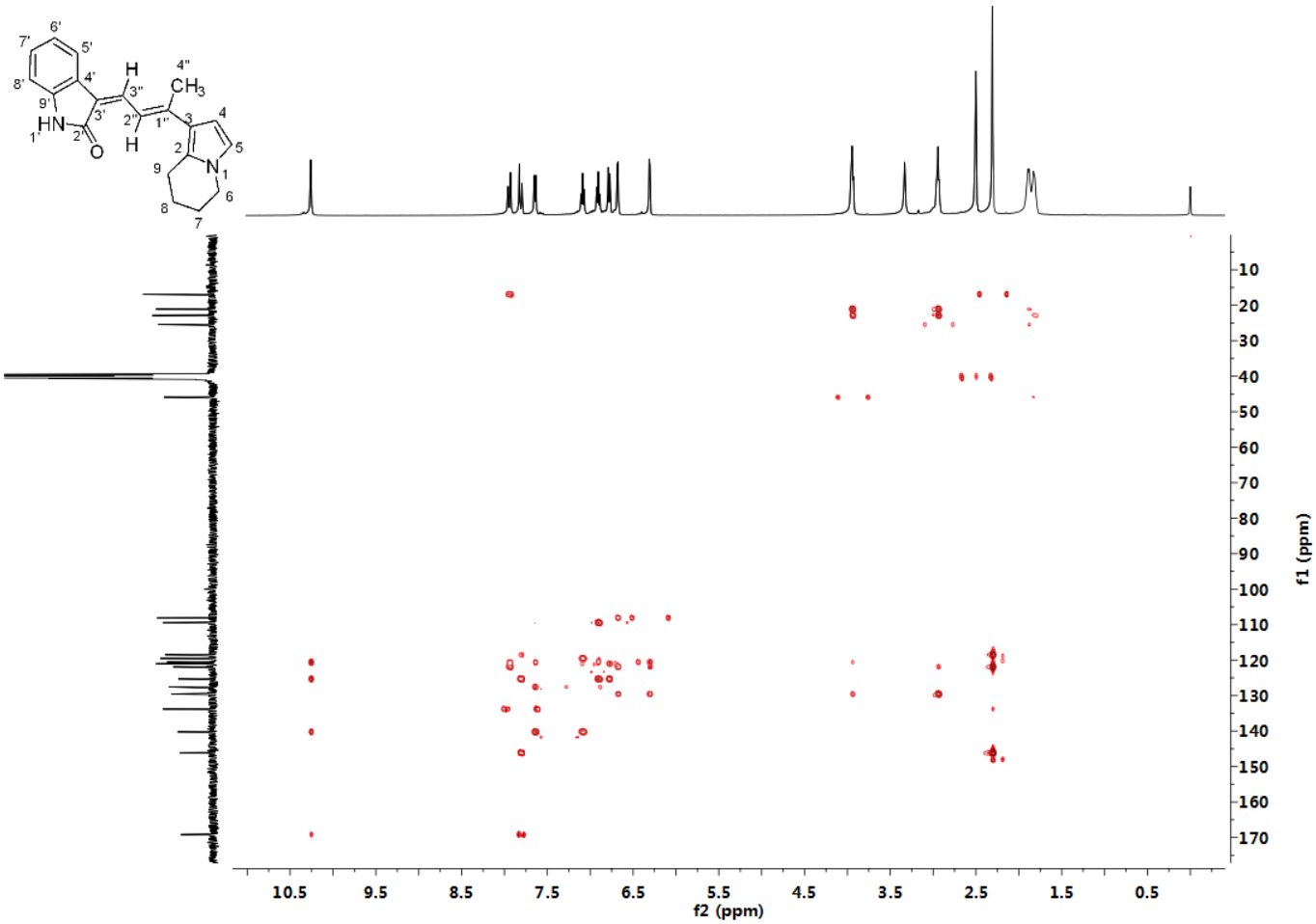
^{1}H-^{1}H COSY spectrum of **2b** in DMSO-d_6



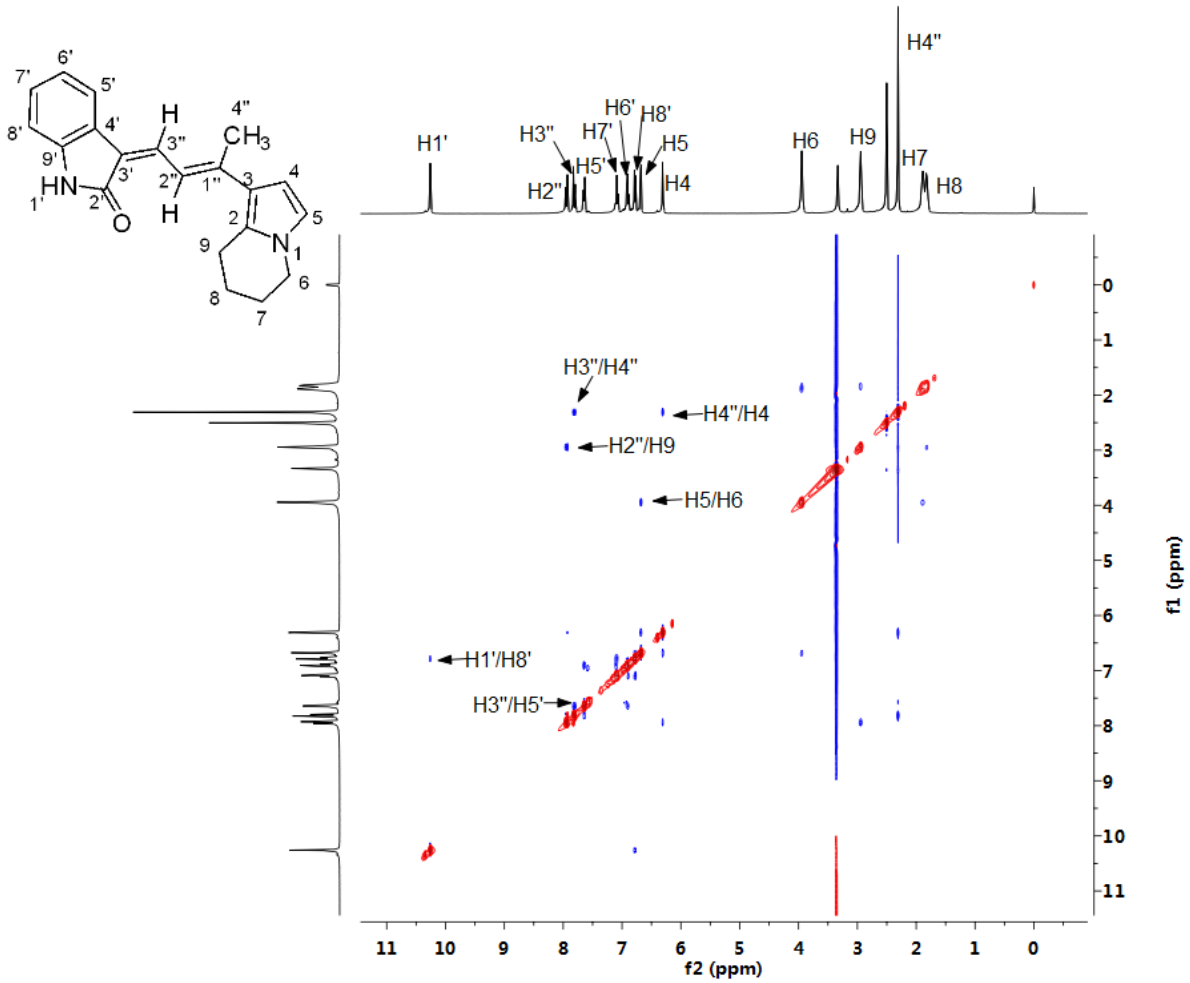
HSQC spectrum of **2b** in DMSO-d_6



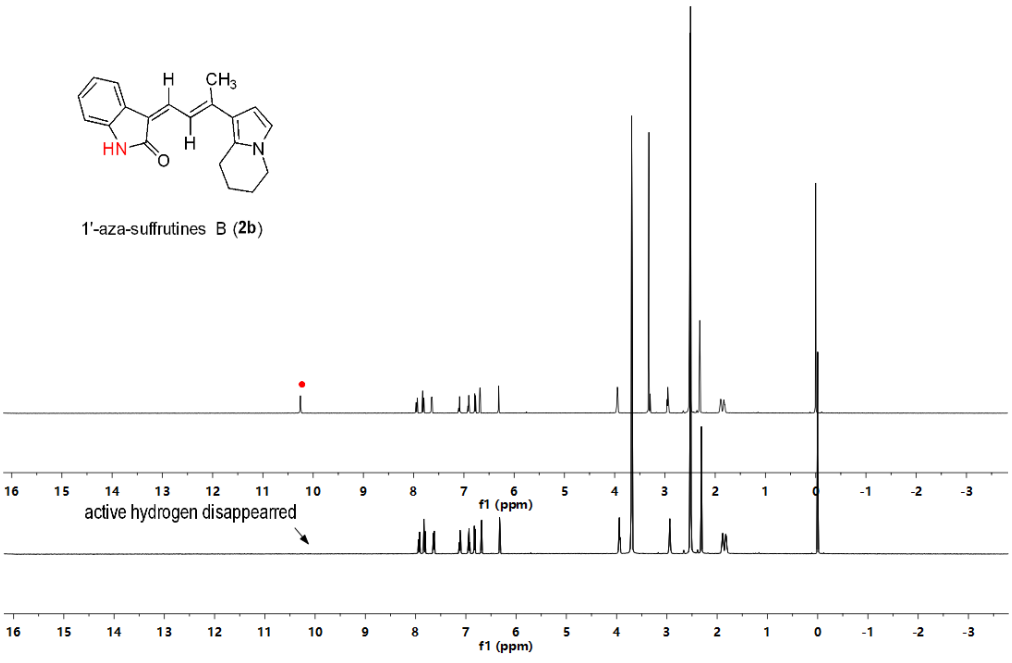
HMBC spectrum of **2b** in DMSO-d_6



NOESY spectrum of **2b** in DMSO-d_6



^{1}H NMR D_2O exchange experiment of **2b** in DMSO-d_6



5. HRMS spectra for 1a, 1b and 2a, 2b

Formula Predictor Report - suffru-1a.lcd

Data File: \\Deep-20160624ld\data1\邹永\ZZF\suffru-1a.lcd

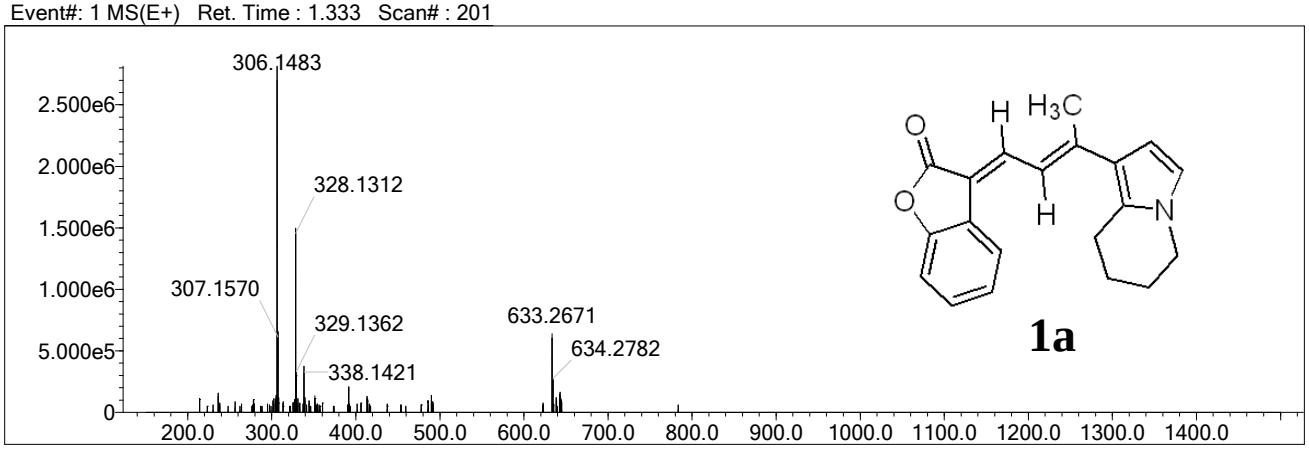
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	19	F	1	0	0	Se	2	0	0	H
2H	1	0	0	Si	4	0	0	Br	1	0	0	Na
B	3	0	0	P	3	0	0	Pd	2	0	0	NH4
C	4	0	20	S	2	0	0	I	3	0	0	K
N	3	0	1	Cl	1	0	0	Pt	2	0	0	
O	2	0	2	K	1	0	0					

Error Margin (ppm): 100
HC Ratio: unlimited
Max Isotopes: all
MSn Iso RI (%): 75.00

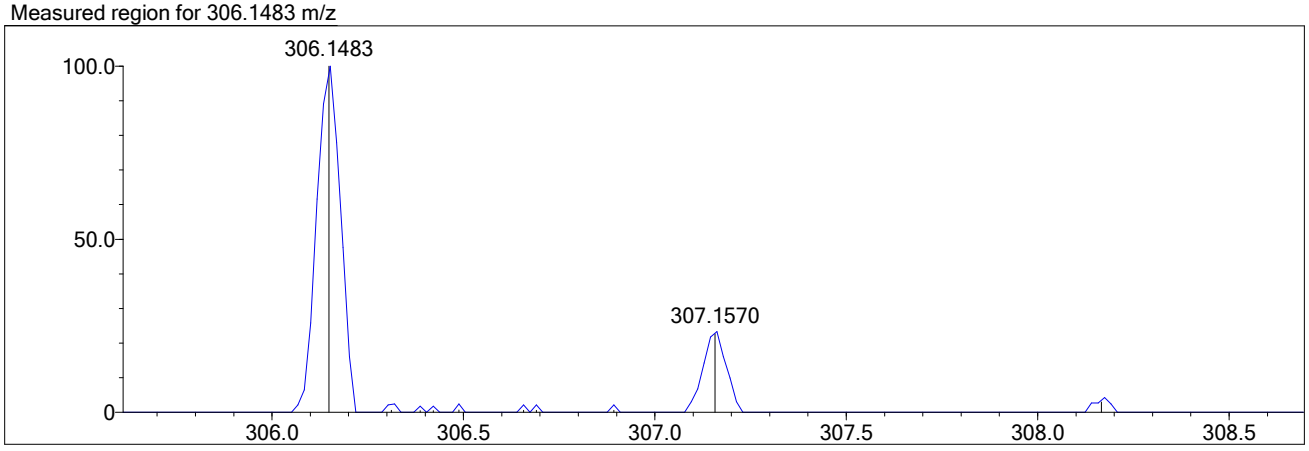
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 50

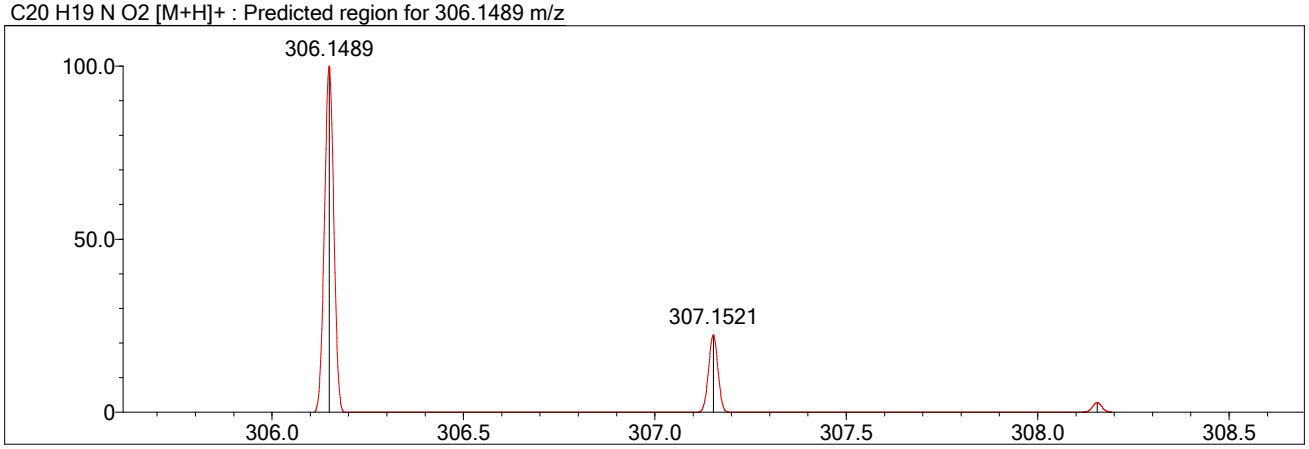
Event#: 1 MS(E+) Ret. Time : 1.333 Scan# : 201



Measured region for 306.1483 m/z



C20 H19 N O2 [M+H]+ : Predicted region for 306.1489 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	86.12	C20 H19 N O2	[M+H]+	306.1483	306.1489	-0.6	-1.96	88.24	12.0

Data File: \\Deep-20160624ld\data1\邹永\ZZF\suffru-1b.lcd

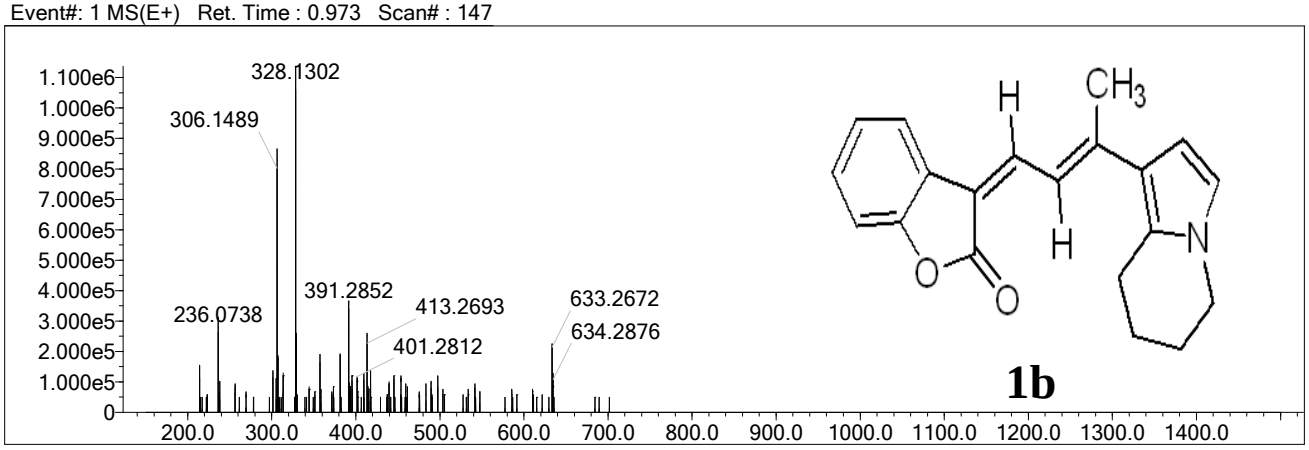
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	19	F	1	0	0	Se	2	0	0	H
2H	1	0	0	Si	4	0	0	Br	1	0	0	Na
B	3	0	0	P	3	0	0	Pd	2	0	0	NH4
C	4	0	20	S	2	0	0	I	3	0	0	K
N	3	0	1	Cl	1	0	0	Pt	2	0	0	
O	2	0	2	K	1	0	0					

Error Margin (ppm): 100
HC Ratio: unlimited
Max Isotopes: all
MSn Iso RI (%): 75.00

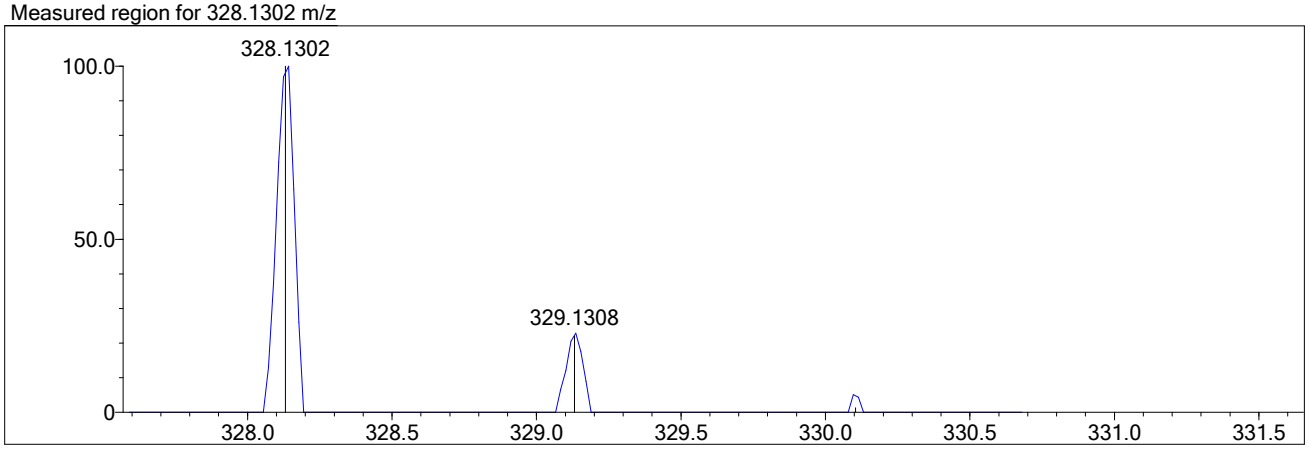
DBE Range: not fixed
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 50

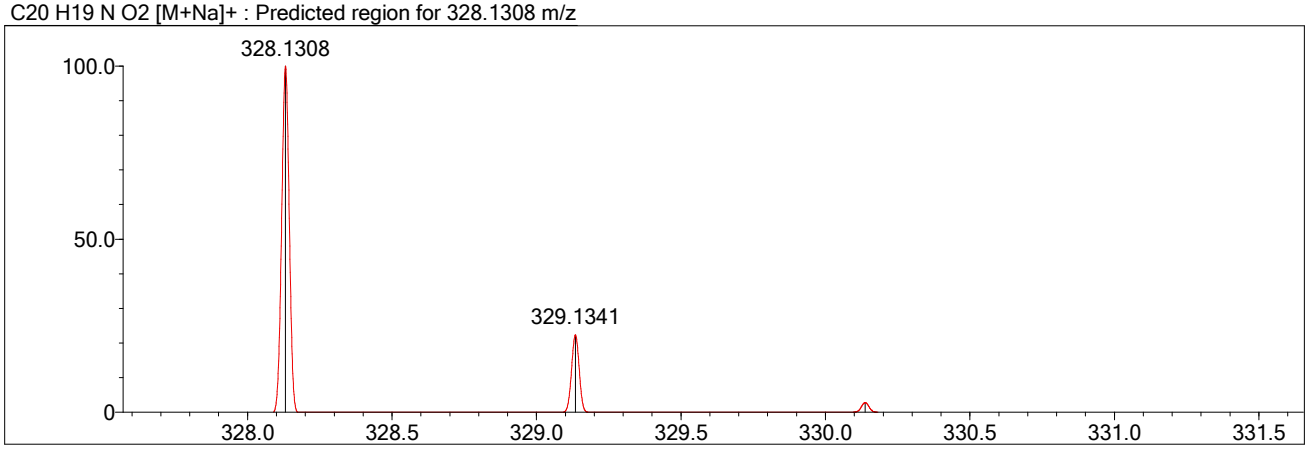
Event#: 1 MS(E+) Ret. Time : 0.973 Scan# : 147



Measured region for 328.1302 m/z



C20 H19 N O2 [M+Na]+ : Predicted region for 328.1308 m/z



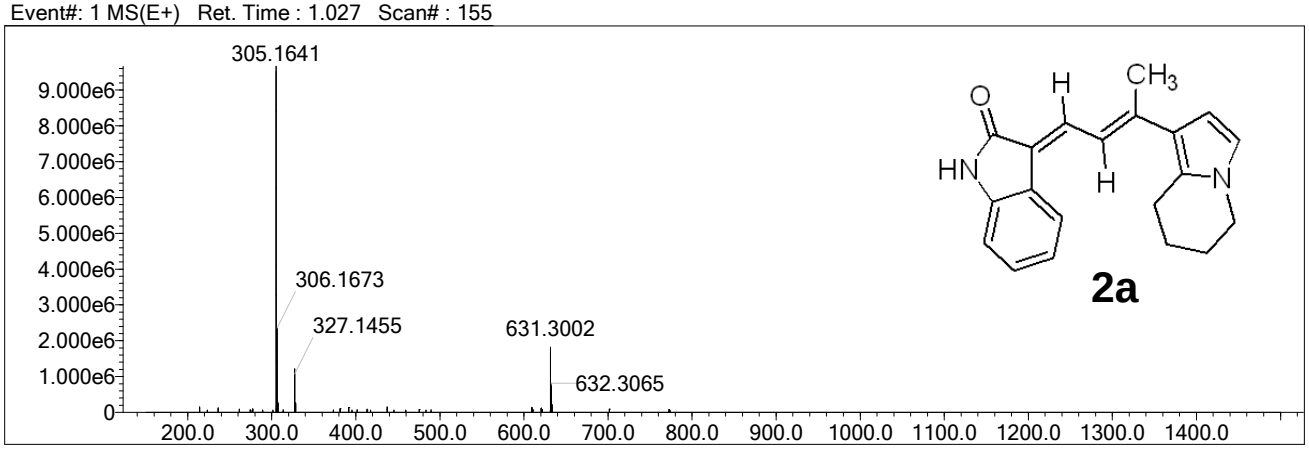
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	87.74	C20 H19 N O2	[M+Na]+	328.1302	328.1308	-0.6	-1.83	89.59	12.0

Data File: \\Deep-20160624ld\data1\邹永\ZZF\N-A-2a.lcd

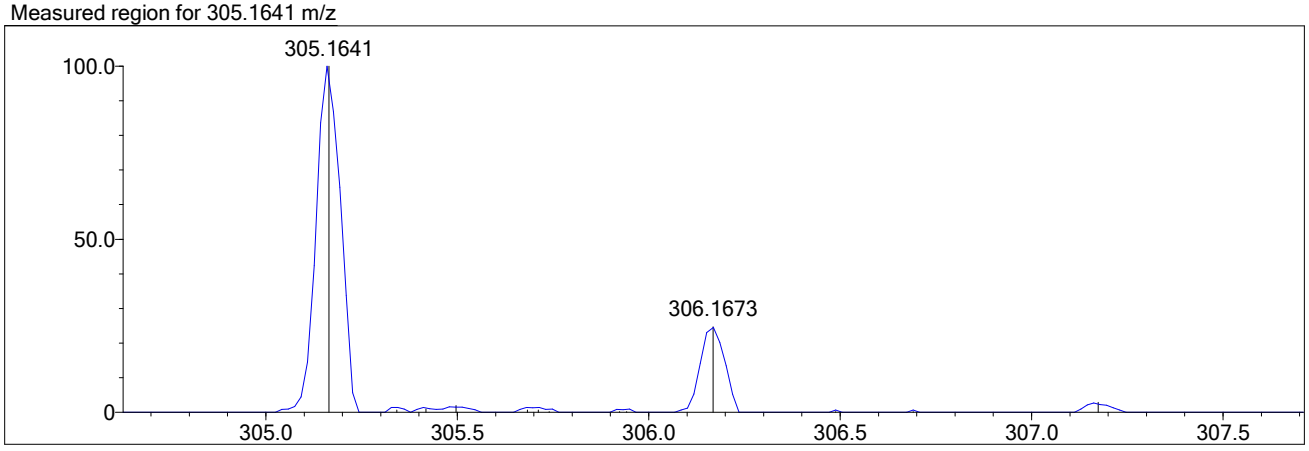
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	20	F	1	0	0	Se	2	0	0	H
2H	1	0	0	Si	4	0	0	Br	1	0	0	Na
B	3	0	0	P	3	0	0	Pd	2	0	0	NH4
C	4	0	20	S	2	0	0	I	3	0	0	
N	3	0	2	Cl	1	0	0	Pt	2	0	0	
O	2	0	1	K	1	0	0					

Error Margin (ppm):	100	DBE Range:	not fixed	Electron Ions:	both
HC Ratio:	unlimited	Apply N Rule:	yes	Use MSn Info:	no
Max Isotopes:	all	Isotope RI (%):	1.00	Isotope Res:	10000
MSn Iso RI (%):	75.00	MSn Logic Mode:	AND	Max Results:	50

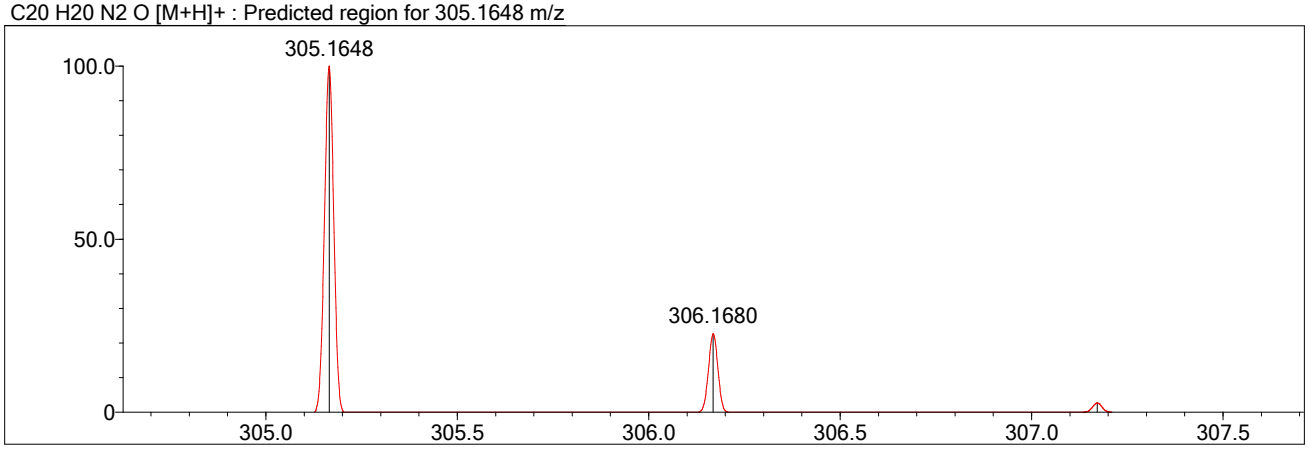
Event#: 1 MS(E+) Ret. Time : 1.027 Scan# : 155



Measured region for 305.1641 m/z



C20 H20 N2 O [M+H]+ : Predicted region for 305.1648 m/z



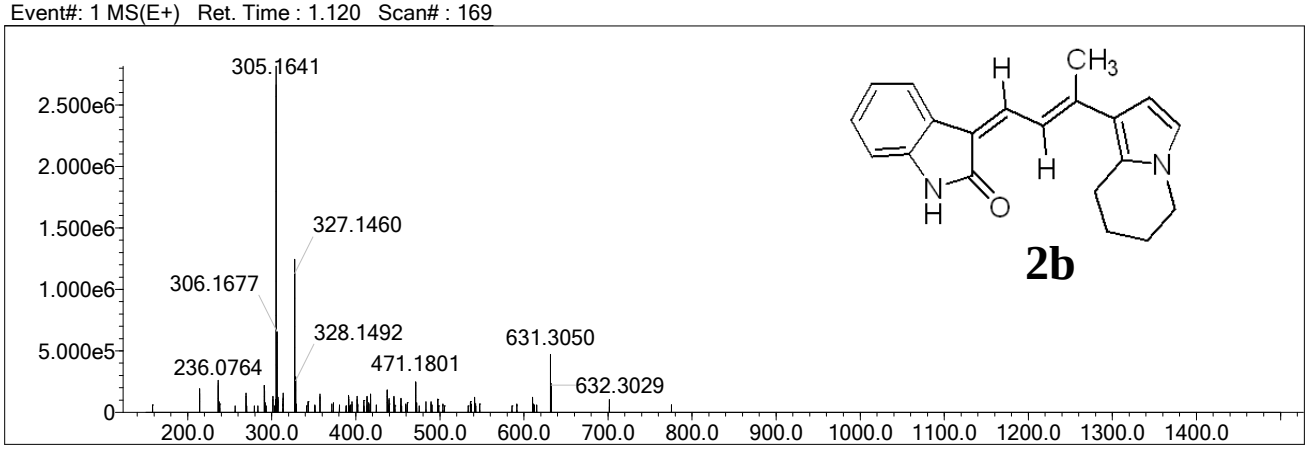
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	67.30	C20 H20 N2 O	[M+H]+	305.1641	305.1648	-0.7	-2.29	69.55	12.0

Data File: \\Deep-20160624ld\data1\邹永\ZZF\N-B-2b.lcd

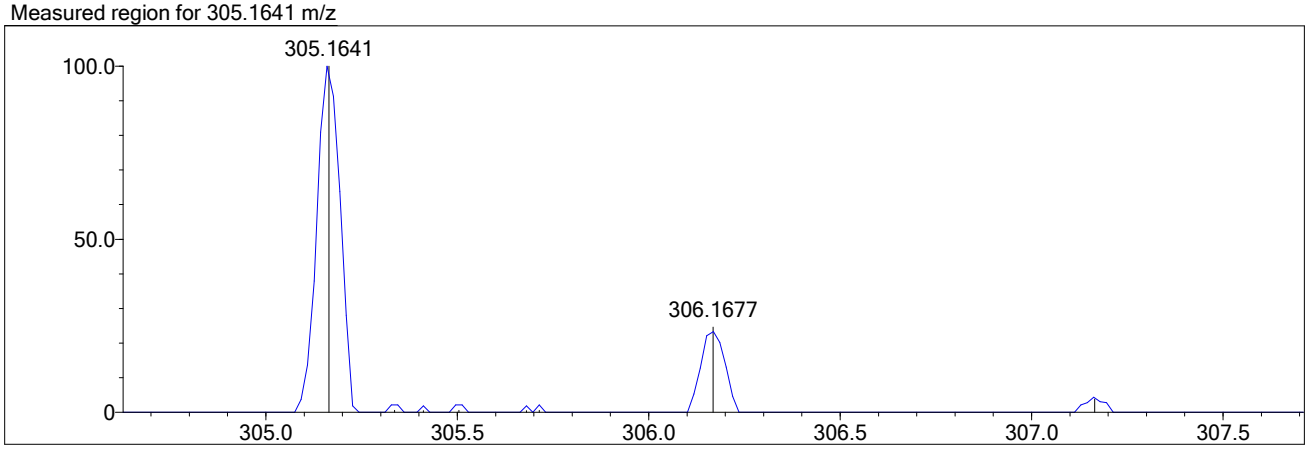
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	0	20	F	1	0	0	Se	2	0	0	H
2H	1	0	0	Si	4	0	0	Br	1	0	0	Na
B	3	0	0	P	3	0	0	Pd	2	0	0	NH4
C	4	0	20	S	2	0	0	I	3	0	0	
N	3	0	2	Cl	1	0	0	Pt	2	0	0	
O	2	0	1	K	1	0	0					

Error Margin (ppm):	100	DBE Range:	not fixed	Electron Ions:	both
HC Ratio:	unlimited	Apply N Rule:	yes	Use MSn Info:	no
Max Isotopes:	all	Isotope RI (%):	1.00	Isotope Res:	10000
MSn Iso RI (%):	75.00	MSn Logic Mode:	AND	Max Results:	50

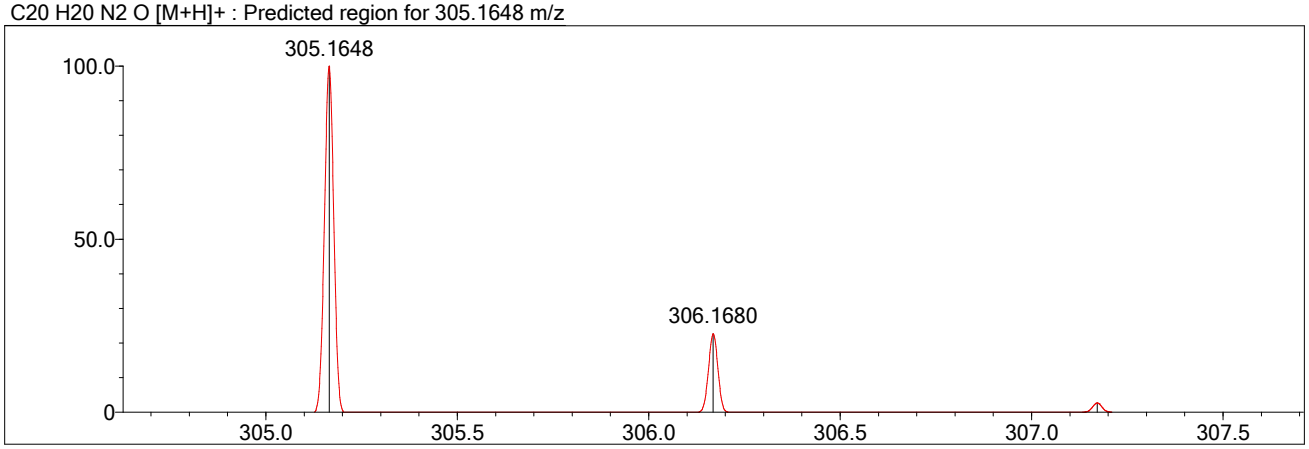
Event#: 1 MS(E+) Ret. Time : 1.120 Scan# : 169



Measured region for 305.1641 m/z



C20 H20 N2 O [M+H]+ : Predicted region for 305.1648 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	70.94	C20 H20 N2 O	[M+H]+	305.1641	305.1648	-0.7	-2.29	73.31	12.0