One-pot synthesis of benzo[*f*]quinolin-3-ones and benzo[*a*]phenanthridein-5-ones by the photoanuulation of 6-chloropyridin-2-ones and 3-chloroisoquinolin-1-ones to phenylacetylene

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Supporting Information

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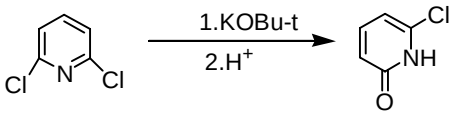
General remark:

All reagents were purchased from commercial suppliers and used without further purification. All solvents were dried and redistilled before use. Flash chromatography was carried out with silica gel (200-300 mesh). Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. Melting points were determined on a Yanagimoto melting point apparatus and uncorrected. Elementary analyses were carried out on a PERKIN-ELMER 2400 II analyzer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 NMR or a Bruker DRX-300 NMR spectrometers in $CDCl_3$ with TMS as an internal standard. EI-MS spectra were measured on an HP 5988A spectrometer by direct inlet at 70 eV. The HMRS spectra were measured on a Burker Dattonics APEX Ⅱ 47e sepectrometer by ESI.

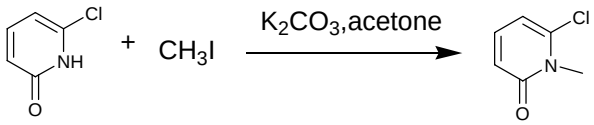
Experimental procedures:

The Preparation of 6-chloropyridin-2(1 H)-one.[1]



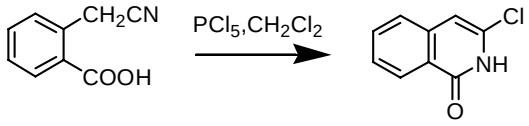
A mixture of 2,6-dichloropyridine (1.48g, 10 mmol),potassium t-butoxide (10g), and redistilled t-butyl alcohol (75 mL) was refluxed for 24 hrs. After cooling, the solvent was removed in vacuum, ice/water was carefully added, and the aqueous layer was extracted with chloroform to remove the unreacted starting material. The aqueous solution was acidified with 3 *N* hydrochloric acid and extracted with chloroform. The chloroform was washed with water, dried over anhydrous magnesium sulfate, and concentrated to afford pure 6-chloropyridin-2(1 H)-one (840 mg, yield 66%).

The preparation of 6-chloro-1-methylpyridin-2-one.[2]



A mixture of 6-chloropyridin-2-one (0.02 mol), potassium carbonate (0.07 mol) and methyl iodide (0.7 mol) were refluxed in acetone (100 mL) in a seal tube for 4 hrs. The reaction mixture was cooled, and potassium iodide was filtered off. The acetone was evaporated off and a small amount of water was added to the residue. This solution was extracted with chloroform. The mixture was concentrated and the residue was purified by chromatography on a silica gel column to yield 6-chloro-1-methylpyridin-2-one 2g (70%)

The Preparation of 3-chloroisoquinolin-1(2 H)-one.[3]



A mixture of PCl_5 (6.8 g, 0.033 mol) was added to o-cyanomethylbenzoic acid in 25 ml of dichloromethane under stirring at 0℃. The mixture was stirred for 3 hrs first at 0℃ and then at room temperature, then kept overnight. The dichloromethane was distilled off and the residue recrystallized from water to yield the product 5.0 g (94%).

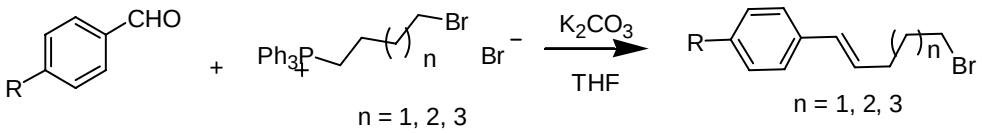
The Preparation of ω-Bromoalkanylphosphonium bromide.

4-Bromobutylphosphonium bromide is prepared by heating triphenylphosphine (10.49 g, 40 mmol) and 1,4-dibromobutane (8.64 g, 40 mmol) in dry xylene for 12 hrs at reflux. The crude material (95% yield) is washed with ether and dried at 100 ℃/8 torr prior to use.

The Preparation of 4-hydroxyalkanylphosphonium bromide.

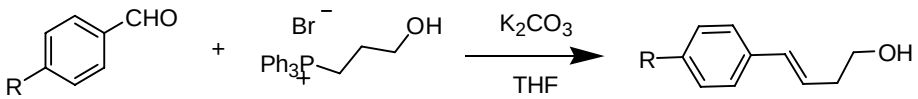
4-hydroxyalkanylphosphonium bromide is prepared by heating triphenylphosphine (10.49 g, 40 mmol) and 3-bromopropan-1-ol (5.52 g, 40 mmol) in dry xylene for 12 hrs at reflux. The crude material (93% yield) is washed with ether and dried at 100 ℃/8 torr prior to use.

The Preparation of ω-bromoalkanylstyrene by witting reaction. [4]



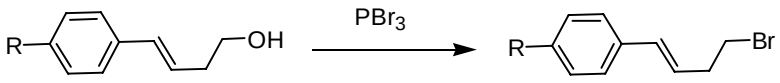
A mixture of phosphonium salt (44 mmol), aldehyde (40 mmol), potassium carbonate (80 mmol) and 40 mL THF was refluxed for 12 hrs, then filtered and separated by a short column chromatography on silica gel.

The Preparation of 4-phenylbut-3-en-1-ol by witting reaction.[5]



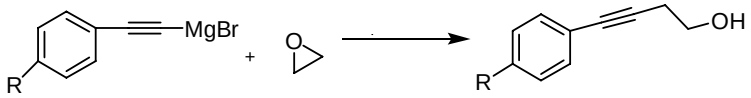
A mixture of 4-hydroxyalkanylphosphonium bromide (44 mmol), aldehyde (40 mmol), potassium carbonate (80 mmol) and 40 mL THF was refluxed for 12 hrs, filtered and separated by a short column chromatography on silica gel.

The preparation of 4-bromo-1-phenyl-1-butene.[6]



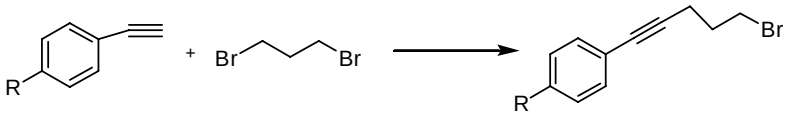
A solution of PBr_3 (2.71 g, 10 mmol) in benzene (20 mL) was added dropwise over a 10-min period to a stirred, ice-cooled solution of 4-phenylbut-3-en-1-ol (3.0 g, 20 mmol) in benzene (20 mL). The stirred solution was refluxed for 3 hrs and then cooled to 0 ℃, and ice (5.0 g) was added to the reaction mixture. The aqueous layer was separated and extracted twice with benzene (20 mL). The organic layers were combined and dried (Na_2SO_4/$MgSO_4$), and the solvent was evaporated under reduced pressure to give a cloudy, colorless oil. Distillation yielded 2.35 g (55%) of 4-bromo-1-phenyl-1-butene as a clear, colorless liquid,

The preparation of 4-phenylbut-3-yn-1-ol.[6]



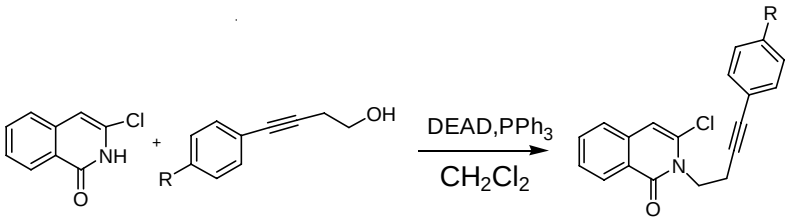
A solution of ethyl bromide (5.54 g, 50 mmol) in anhydrous ether (20 mL) was added dropwise to a stirred mixture of Mg turnings (1.32g, 55 mmol) and a catalytic mount of iodine in anhydrous ether (100mL). After the mixture stirred for 30 min, a solution of phenylacetylene (5.1 g. 50 mmol) in anhydrous ether (50 mL) was added in a dropwise manner, and the mixture was refluxed for 1 hr. The stirred mixture was cooled to 0℃, and a solution of ethylene oxide (15 g, 340 mmol) in anhydrous ether (25 mL) was added over a 5 min period . After the mixture was stirred at 0℃ for 1 hr and at room temperature for 30 min, a saturated solution of NH_4Cl was added until precipitation of magnesium salt was complete. The mixture was filtered, and the filtrate was dried over $NaSO_4$ and evaporated under reduced pressure. Distillation gave 2.96 g (41%) 4-phenylbut-3-yn-1-ol as a colorless liquid.

The preparation of 1-(5-bromopent-1-ynyl)benzene.[7]



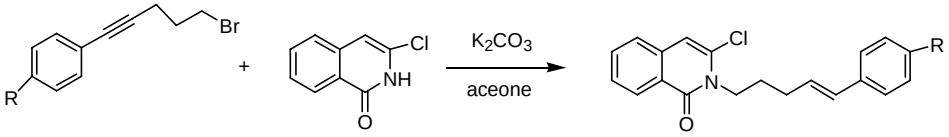
To a solution of phenylacetylene (6.51 g, 63.7 mmol) in THF (25 mL) was added dropwise nBuLi (39.8 mL, 63.7 mmol, 1.6 M in hexane) at 0℃. After addition the reaction mixture was allowed to warm up to 25 ℃ and stirring was continued for 1 hr. Afterwards, 1,3-dibromopropane (7.3 mL, 70 mmol) was added in one portion at -78℃. After 2 hr at this temperature the reaction mixture was stirred for another 12 hrs under reflux. The reaction was quenched by adding small pieces of ice at 0℃, H_2O (200 mL) was added and the mixture was extracted with Et_2O (3×200 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was subjected to silica gel flash chromatography (hexane) and concentration of the appropriate fractions in vacuum afforded the 1-(5-bromopent-1-ynyl)benzene (8.50 g, 60% yield) as colorless liquid.

The preparation of 3-chloro-2-(4-phenylbut-3-ynyl)isoquinolin-1(2 H)-one.[8]



To a mixture of 3-chloroisoquinolin-1(2 H)-one (90 mg, 0.5 mmol), the 4-phenylbut-3-yn-1-ol (88mg, 0.6 mmol), and PPh_3 (196 mg, 0.75 mmol) in CH_2Cl_2 (8mL), was added diethyl zaodicarboxylate (130 mg, 0.75mmol) at 0 ℃. The resulting mixture was flushed with Ar and stirred at room temperature for 24 hrs. The mixture was concentrated and the residue was purified by chromatography on a silica gel column to yield product 70mg (45%). Compounds **7a**, **7b** were prepared in the same manner.

The preparation of 3-chloro-2-(5-phenylpent-4-enyl)isoquinolin-1(2 H)-one.[9]



Potassium carbonate (414 mg, 3mmol) was added a solution of 3-chloro-1-isoquinolinol (179.5 mg, 1 mmol) and 5-bromo-1-phenylpentene (250 mg, 2 mmol) in acetone (18 mL). The mixture was heated to reflux for 10 hrs. When the starting materials were consumed completely monitored by TLC, the reaction was concentrated under vacuum and then the product was isolated by silica gel colum chromatography to give a clear liquid 130 mg (40%). Compounds **5a**, **5b**, **7c**, **7d**, **9a**, **9b**, **9c**, **11a**, **11b**, **11c**, **11d**, **11e**, **11f**, **11g**, **11 H**, **11i**, **11j**, **131**, **15a**, **15b** were prepared in the same manner.

General procedure for the photochemical reactions of 1a and 5a-b and 9a-c

6-chloro-1-methylpyridin-2-one (**1a**) (72 mg, 0.5 mmol) was dissolved in 40 mL dry dichloromethane. The solution was distributed into two quartz tubes and the two tubes were irradiated with a medium-pressure mercury lamp (500W) at ambient temperature for 36 hrs. The progress of the reaction was monitor by TLC at regular intervals. After allmost all substrte **1a** had been consumed the solvent was removed under reduced pressure and the residue was separated by colum chromatography on silica gel eluted by hexane-acetone 10:1(v/v) to afford photoreaction product **2a**.

General procedure for the photochemical reactions of 3a-c, 7a-d and 11a-j

6-chloro-1-(5-phenylpent-4-enyl)pyridin-2-one (**3a**) (90 mg, 0.5 mmol) was dissolved in 40 mL dry methylene dichloride and dry pyridine (160 mg) was added. The solution was distributed into two Pyrex tubes and the two tubes were irradiated with a medium-pressure mercury lamp (500W)

at ambient temperature for 40 hrs. The progress of the reaction was monitor by TLC at regular intervals. After almost all substrate **3a** had been consumed the solvent was removed under reduced pressure and the residue was separated by colum chromatography on silica gel eluted by hexane-acetone 10:1(v/v) to afford photoreaction product **4a**.

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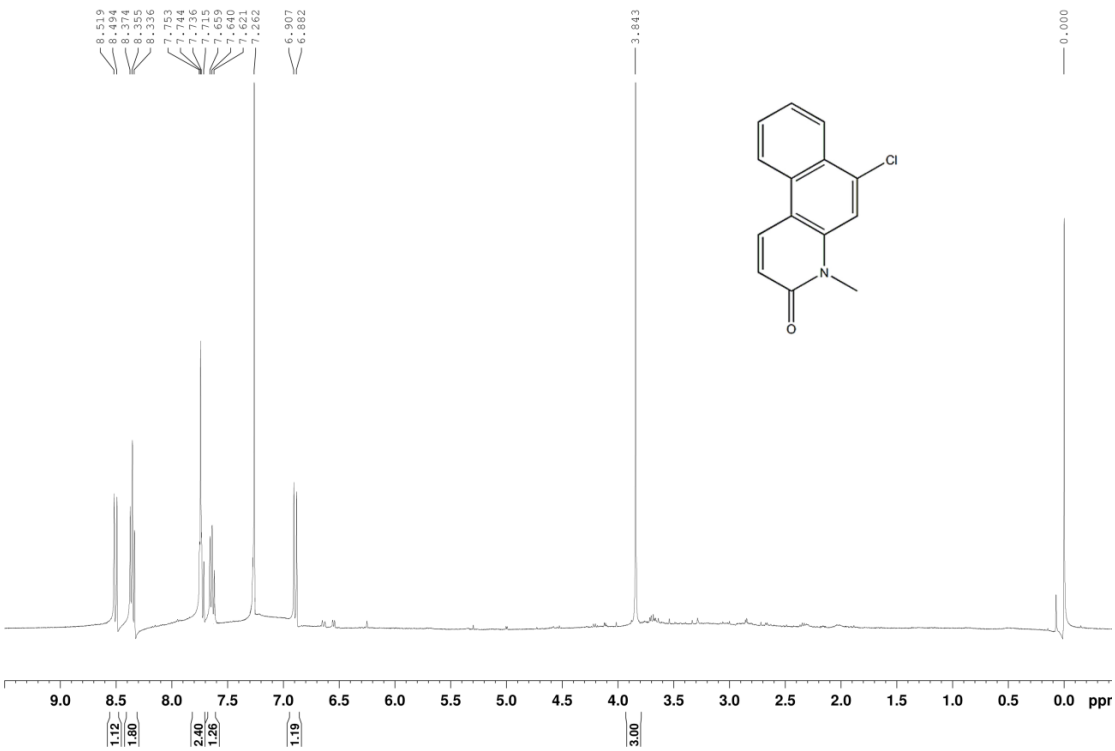
2a ^{1}H NMR



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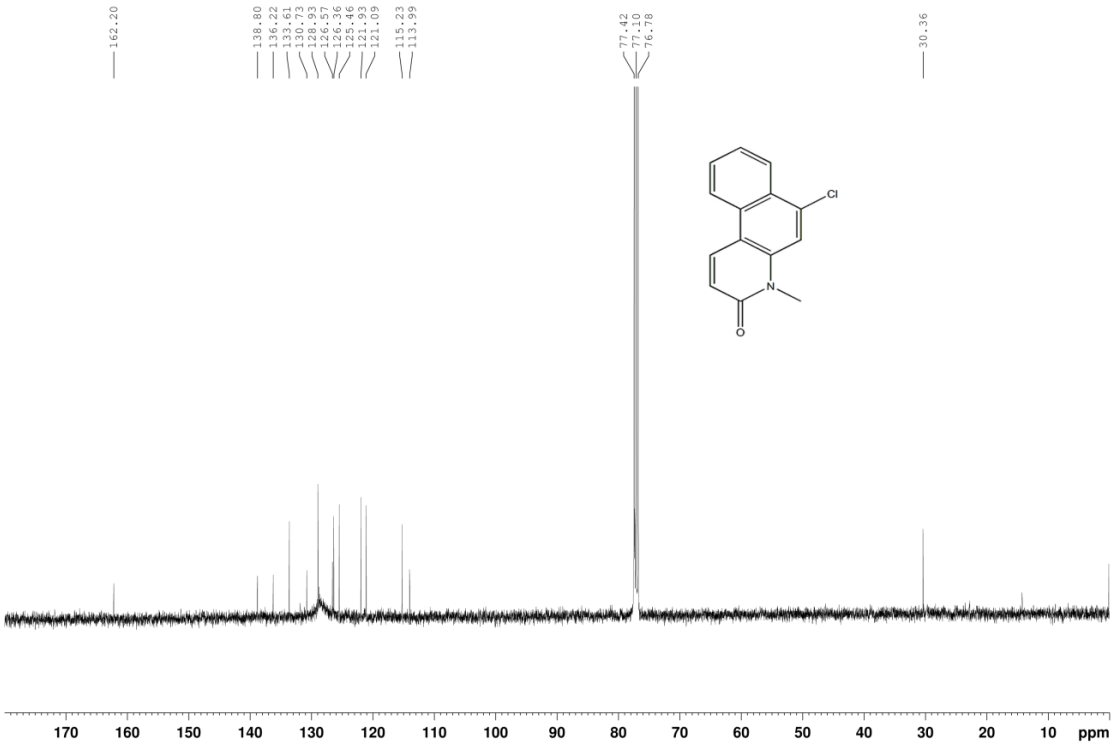

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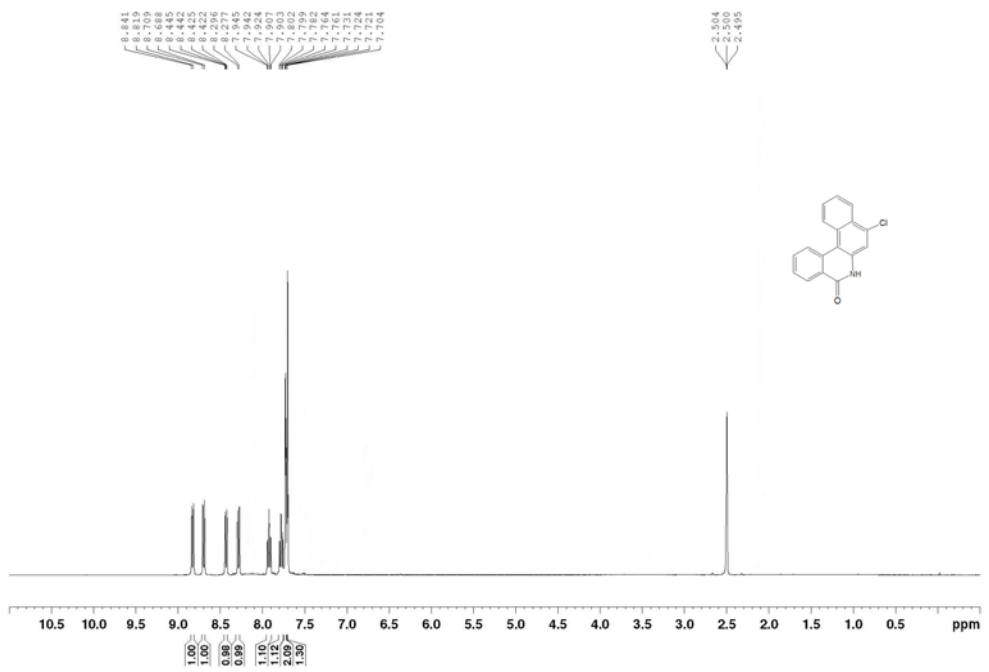

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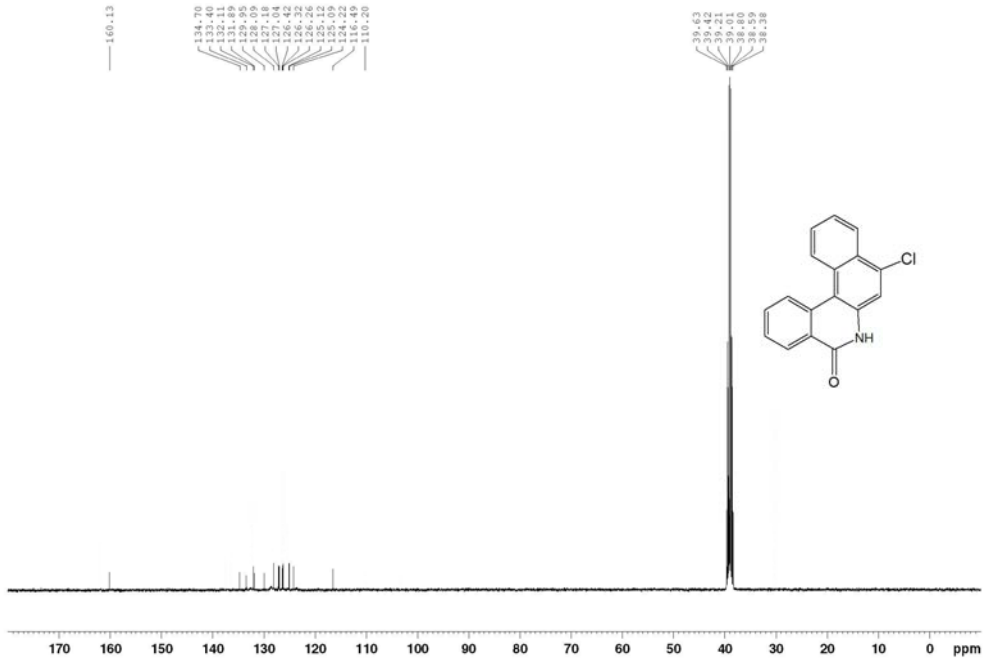

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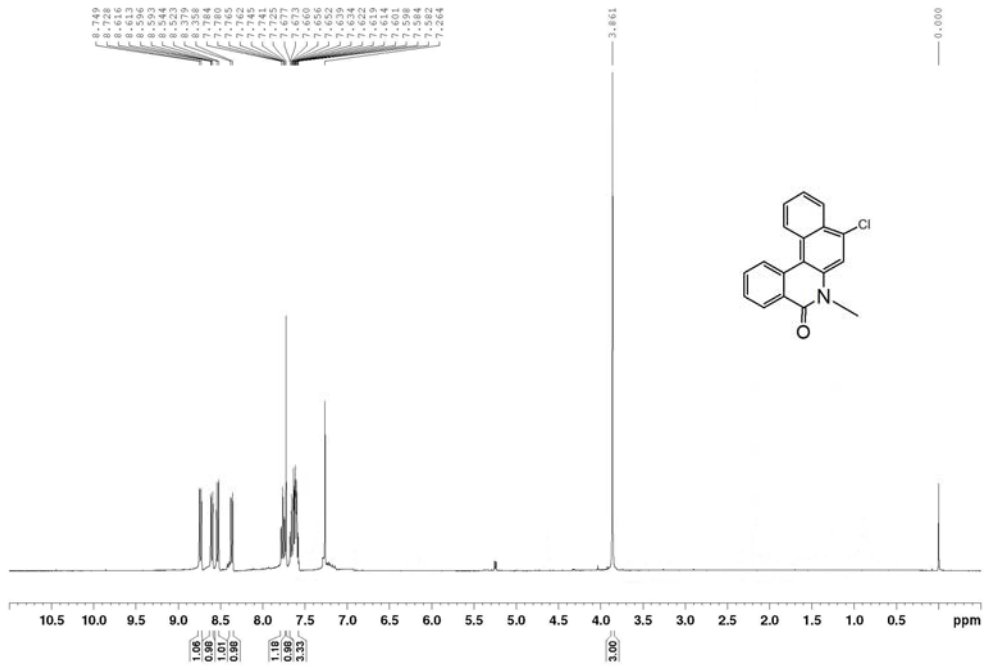

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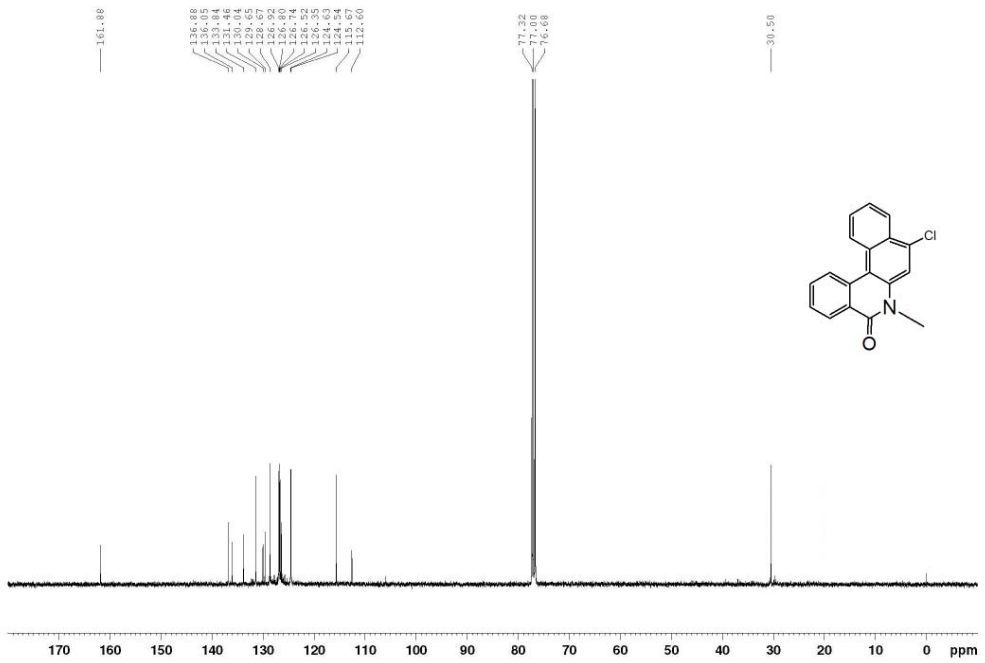

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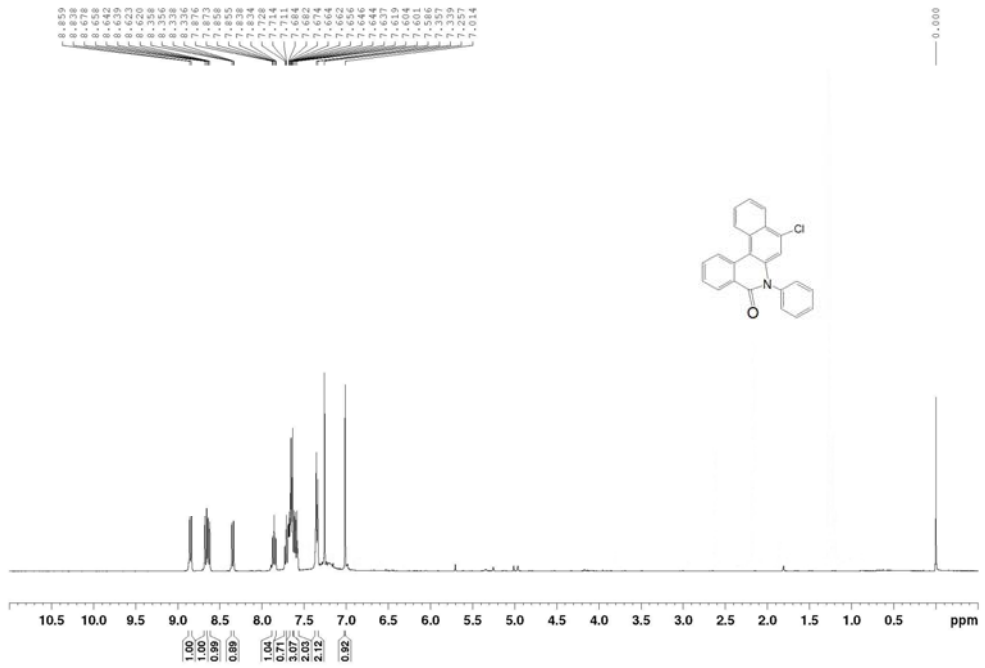

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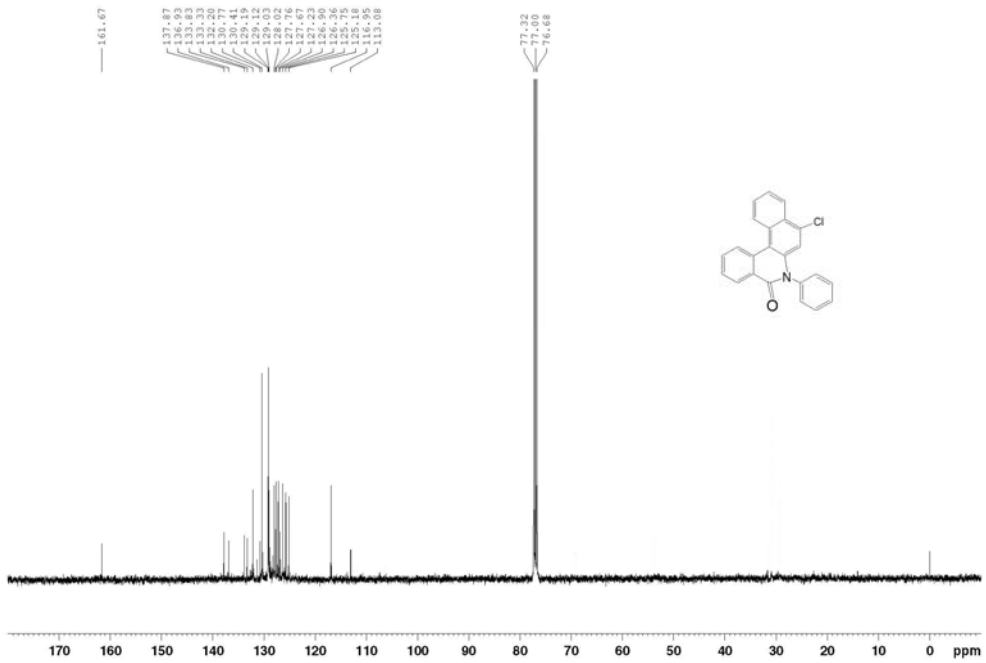

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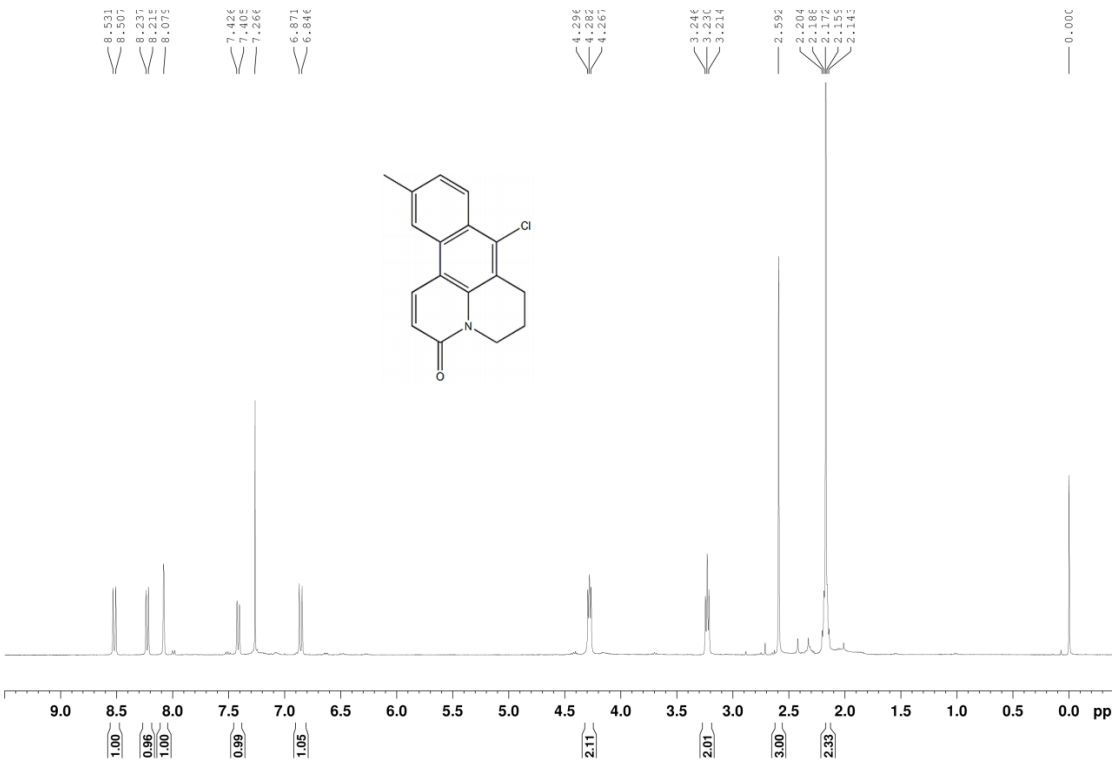

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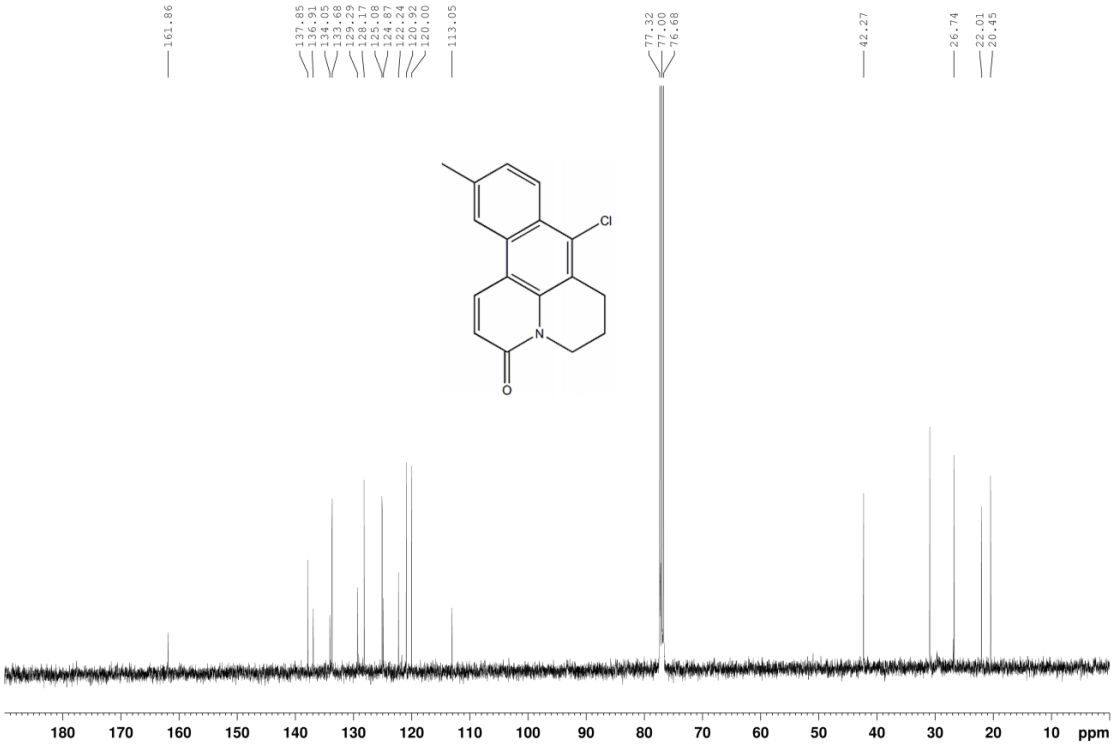

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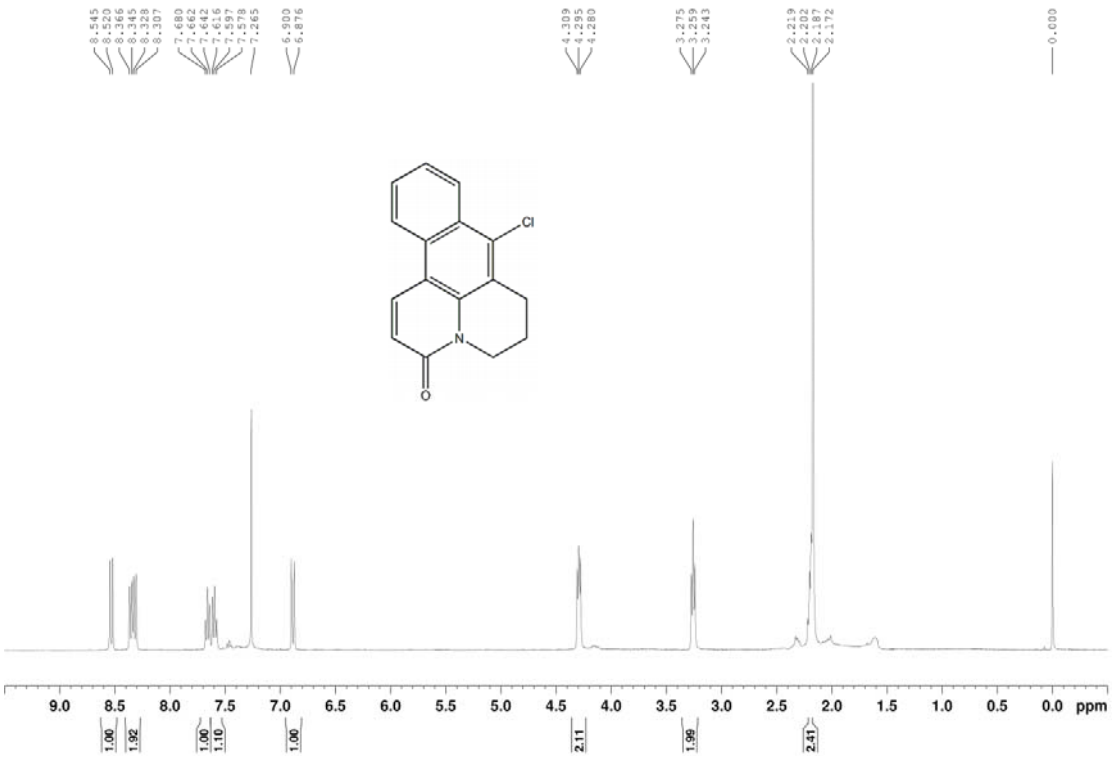

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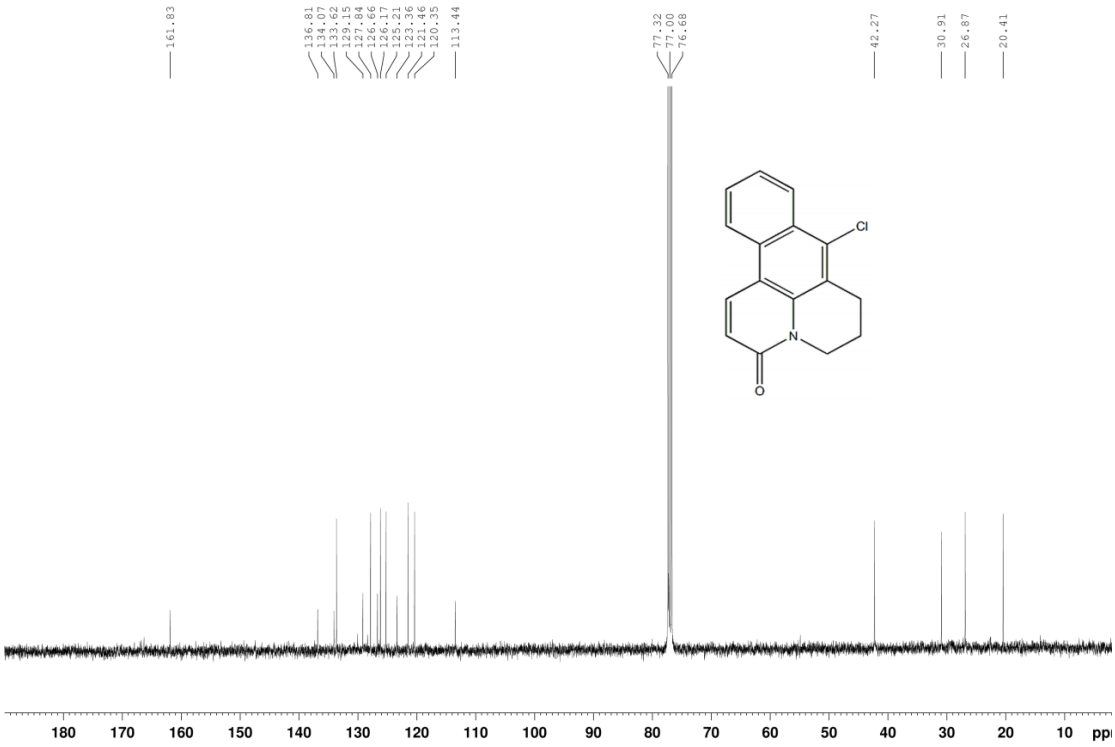

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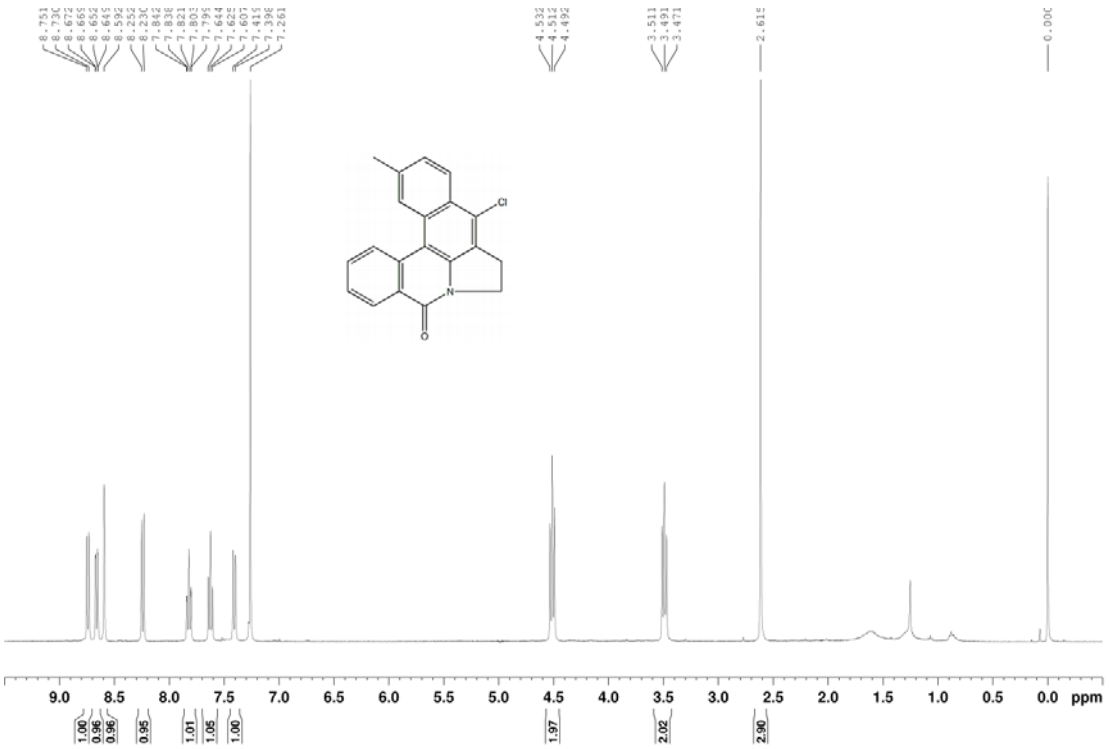

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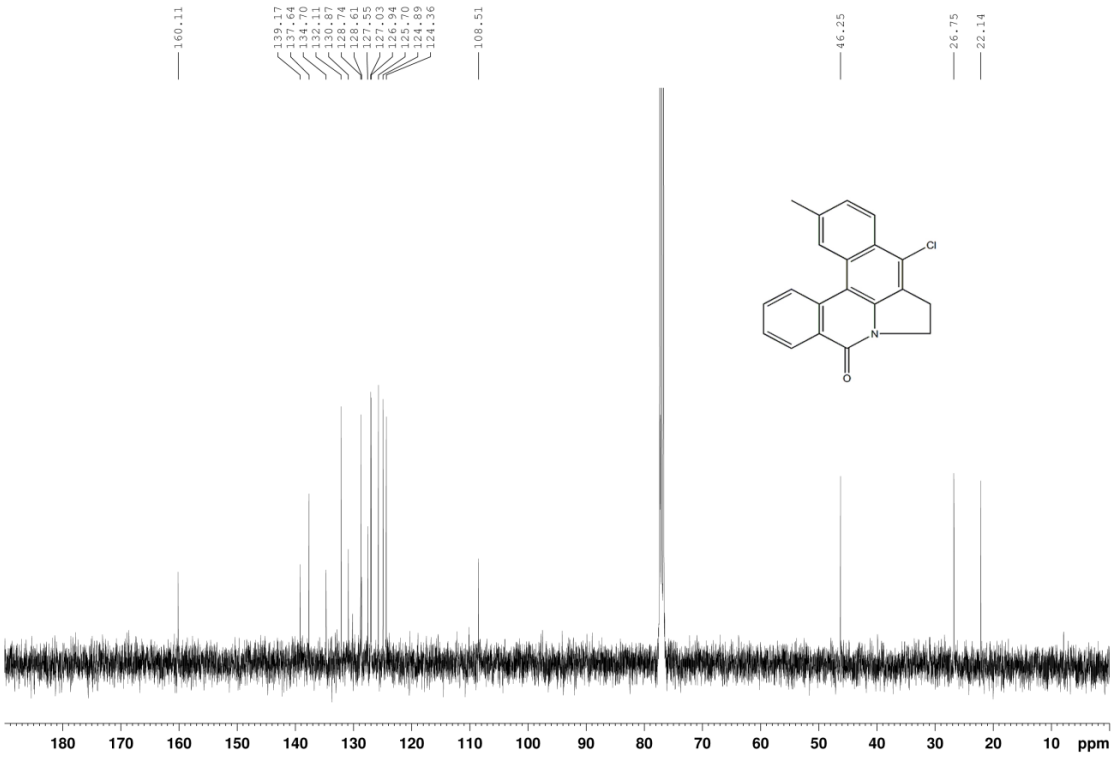

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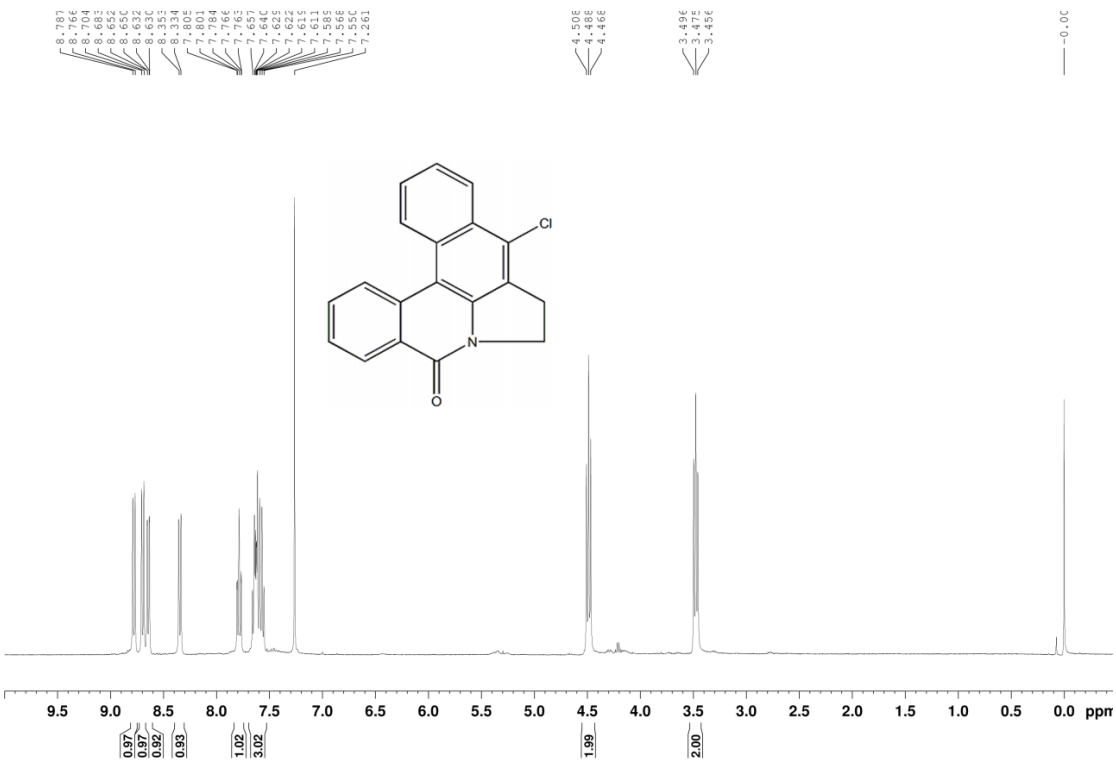

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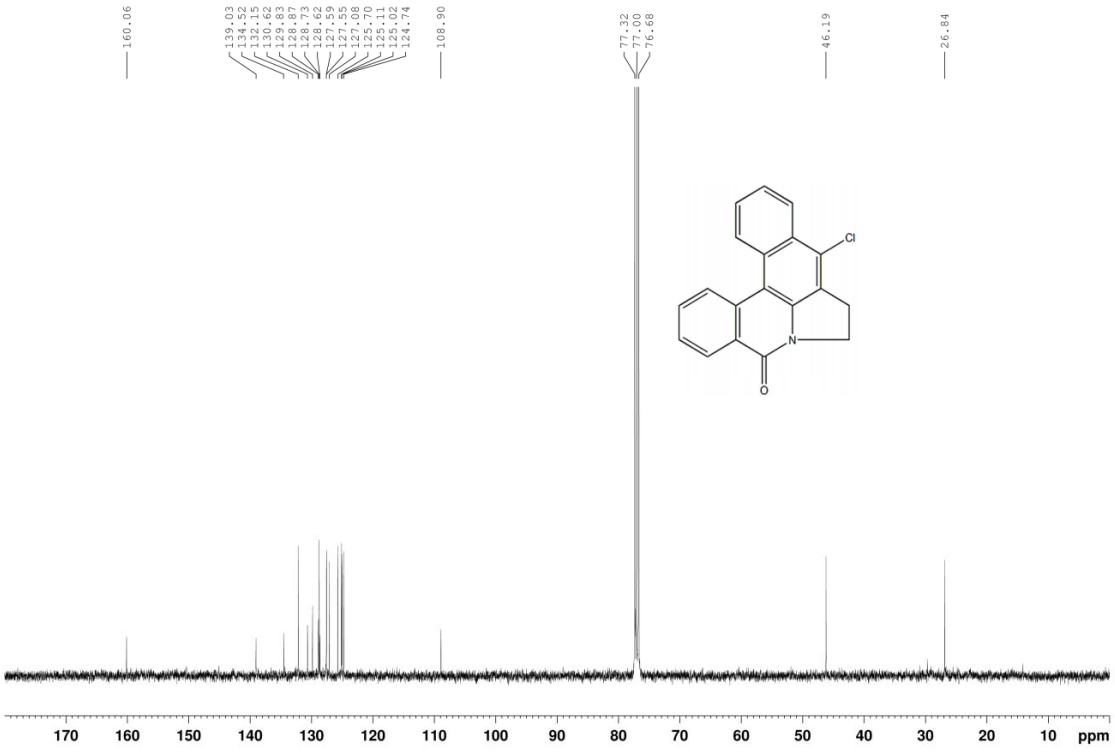

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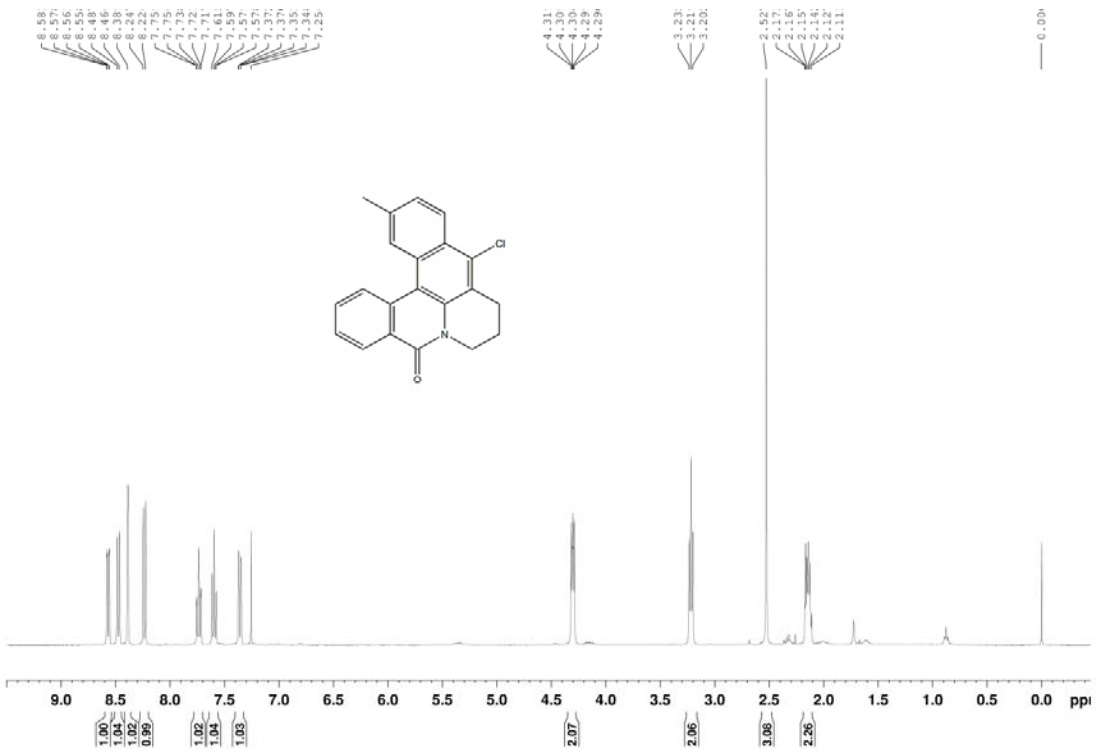

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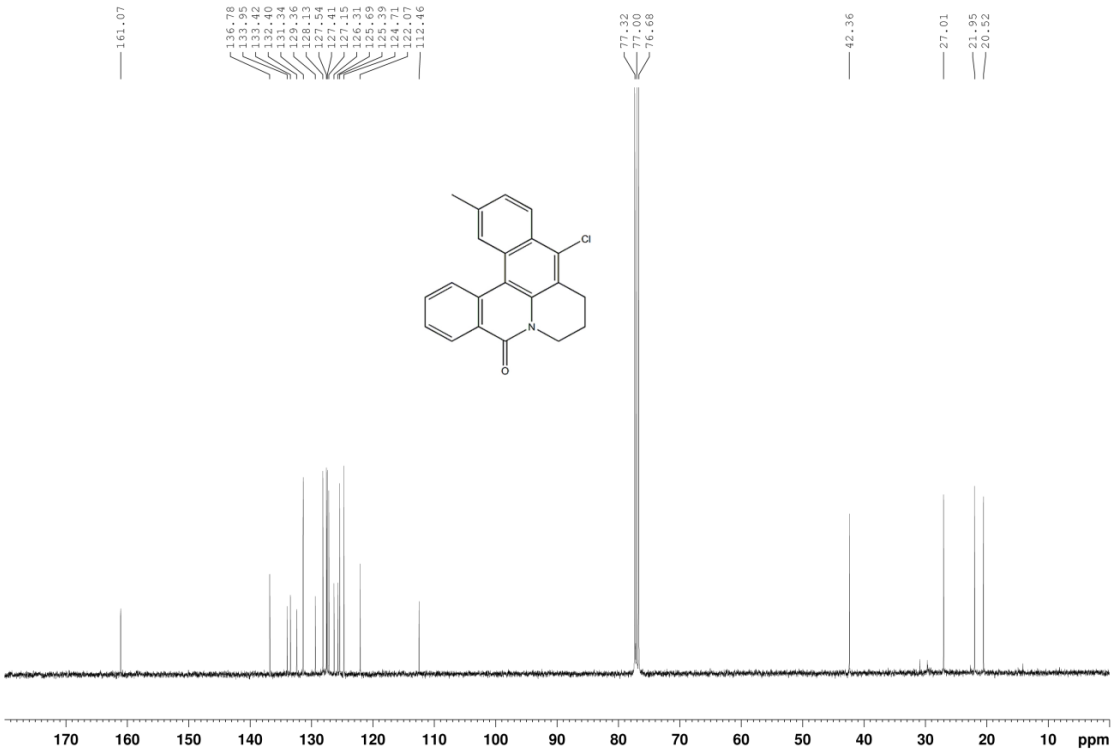

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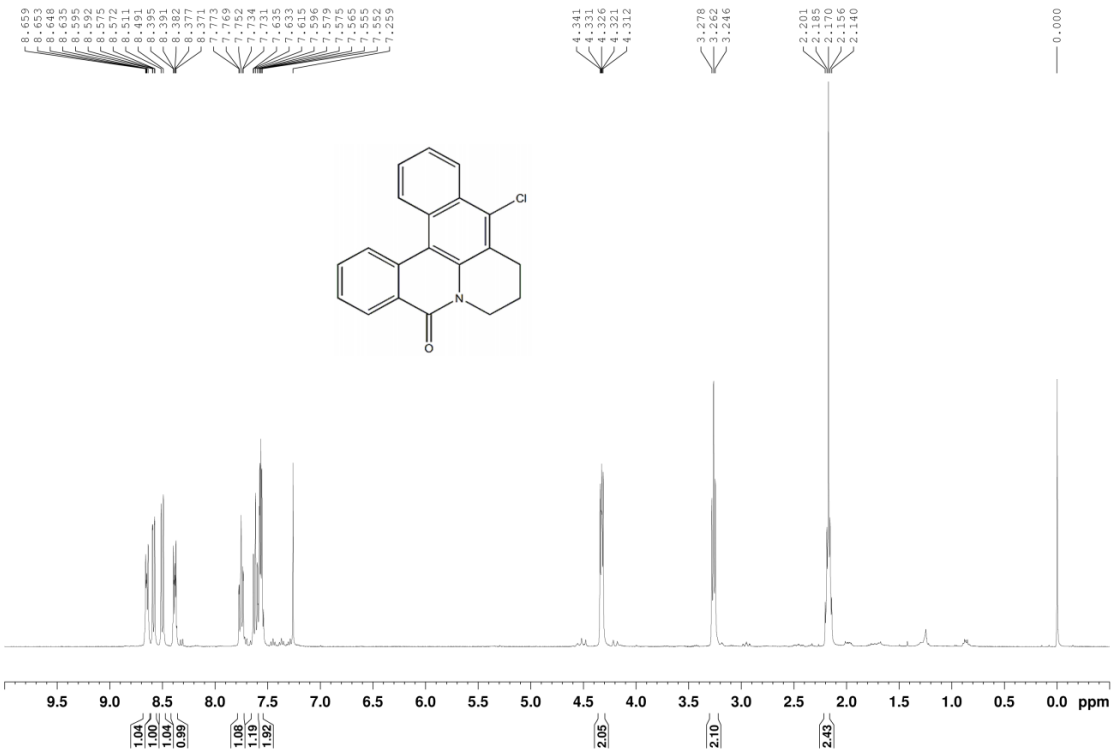

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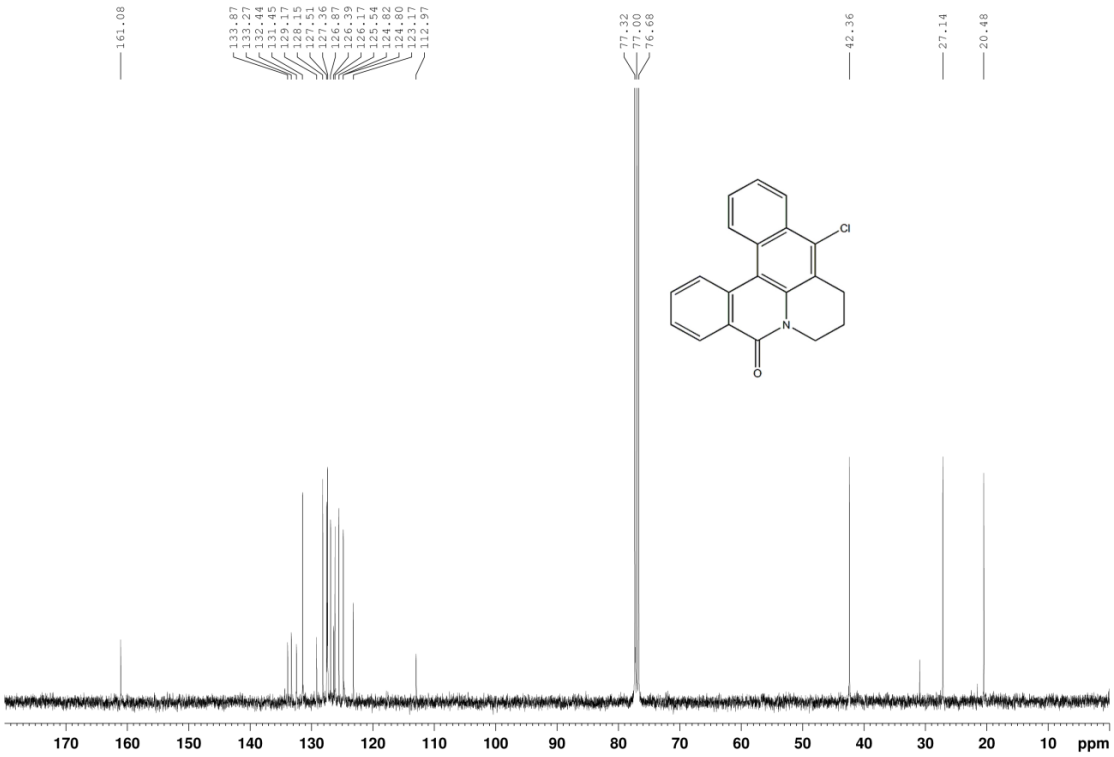

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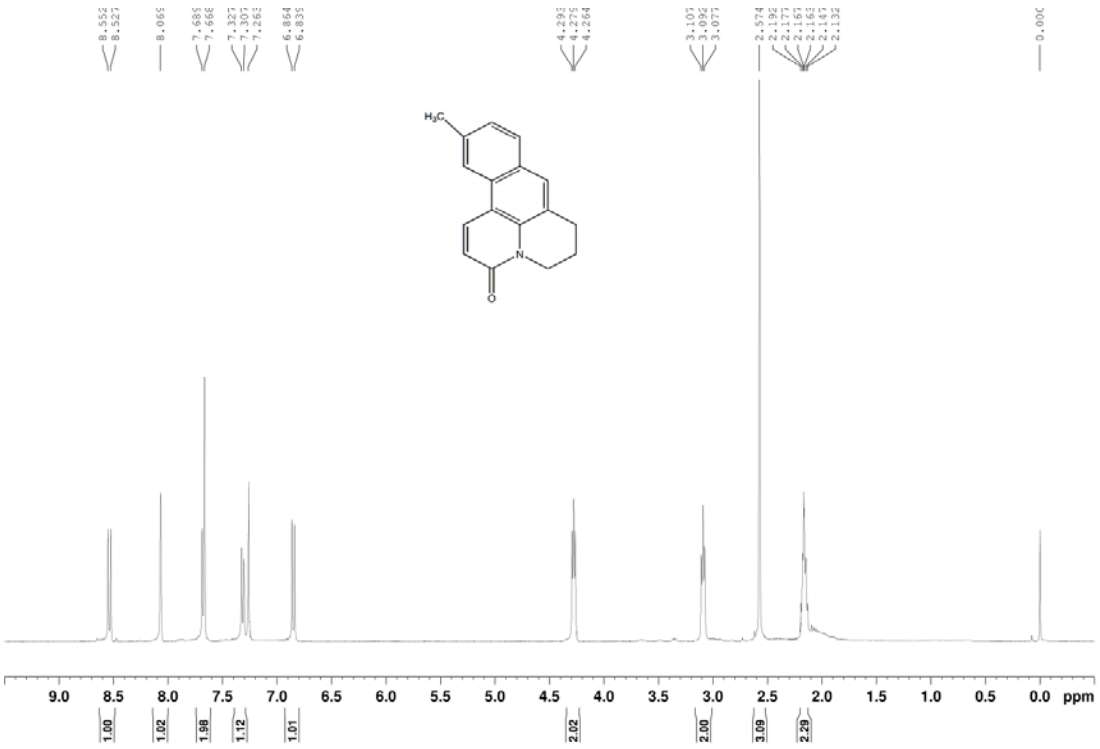

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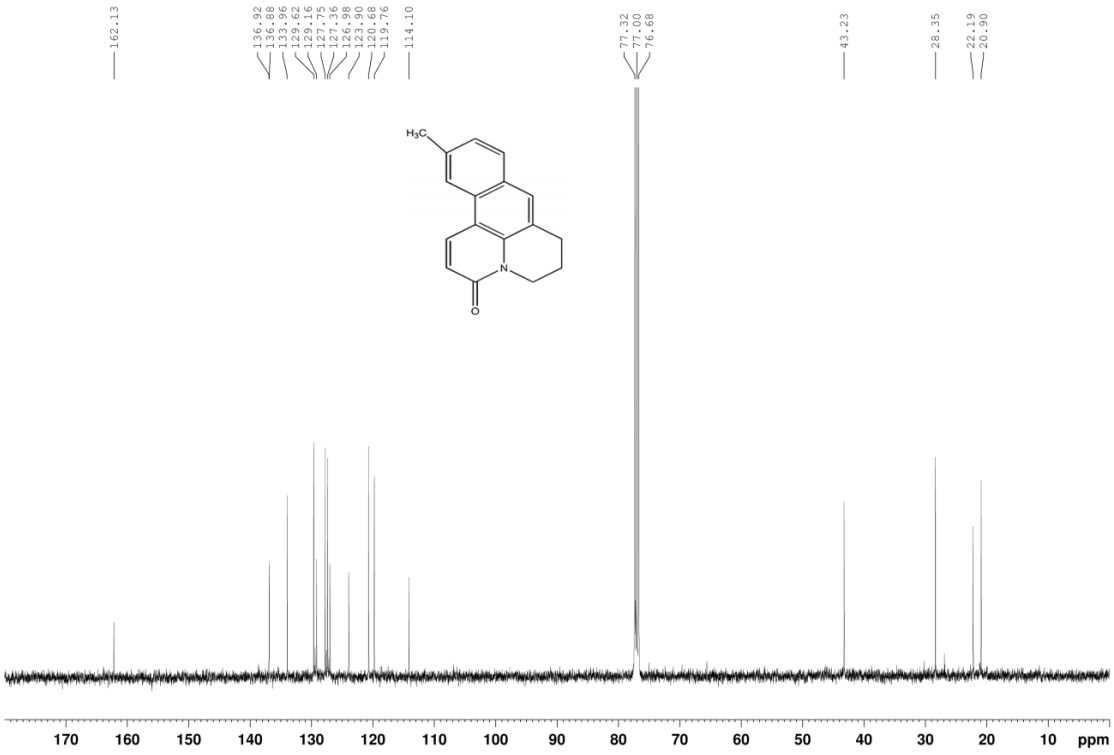

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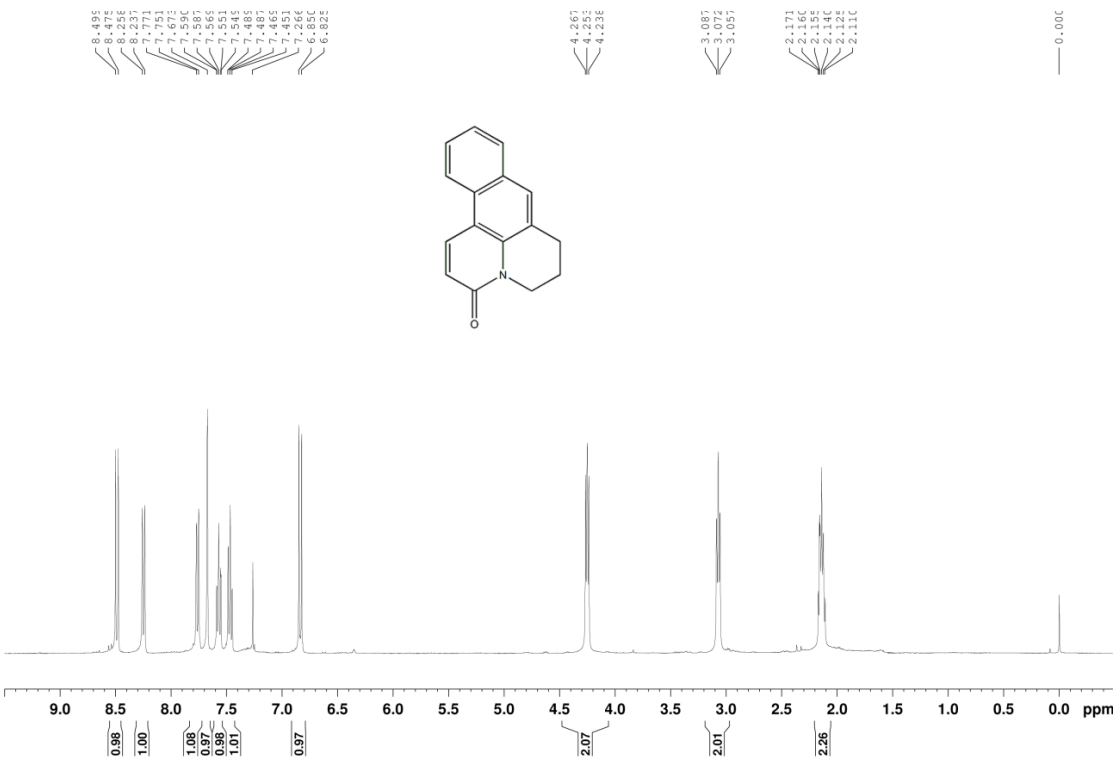
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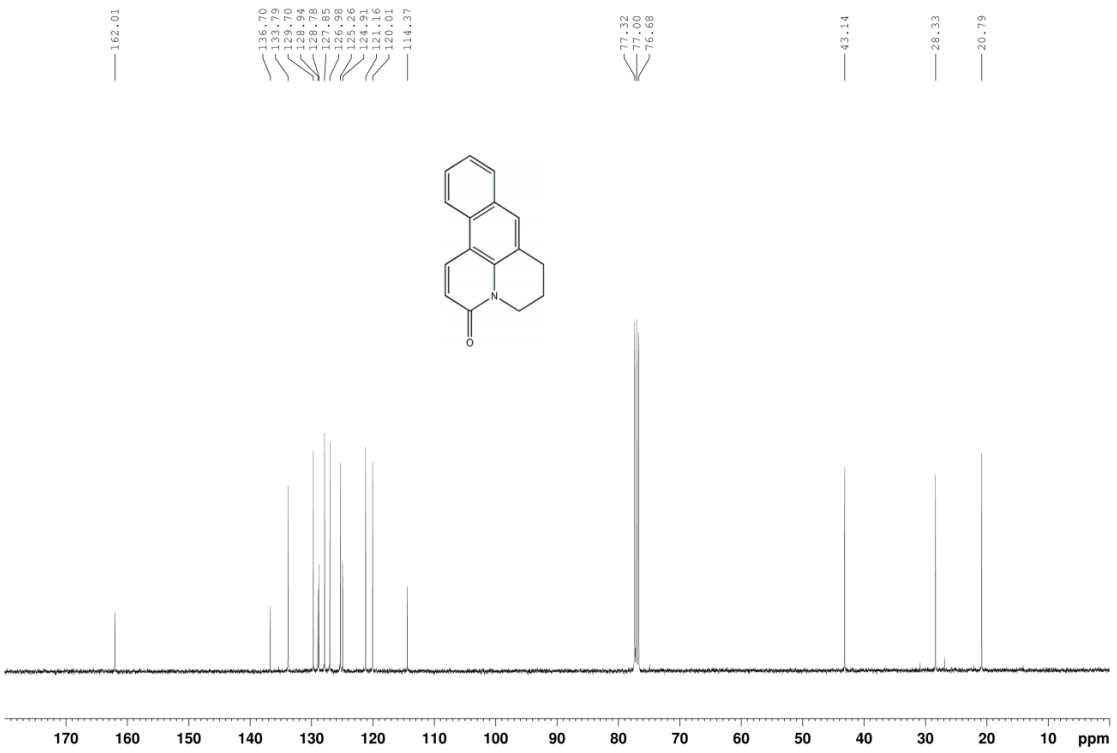
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N
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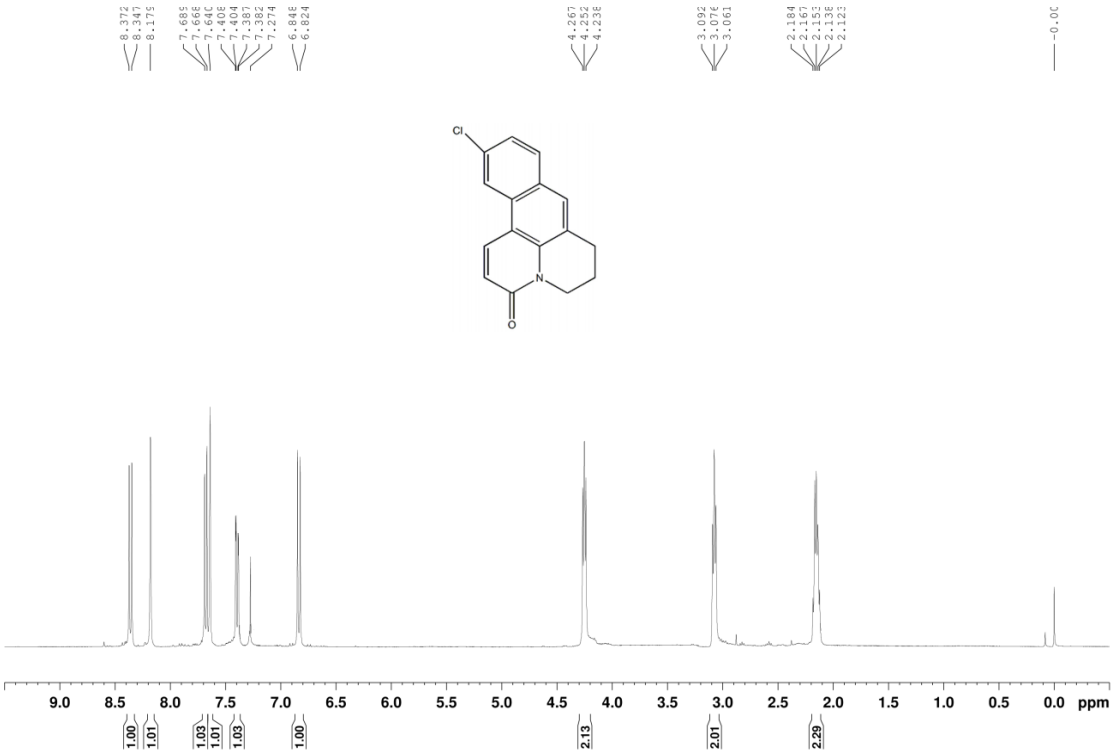
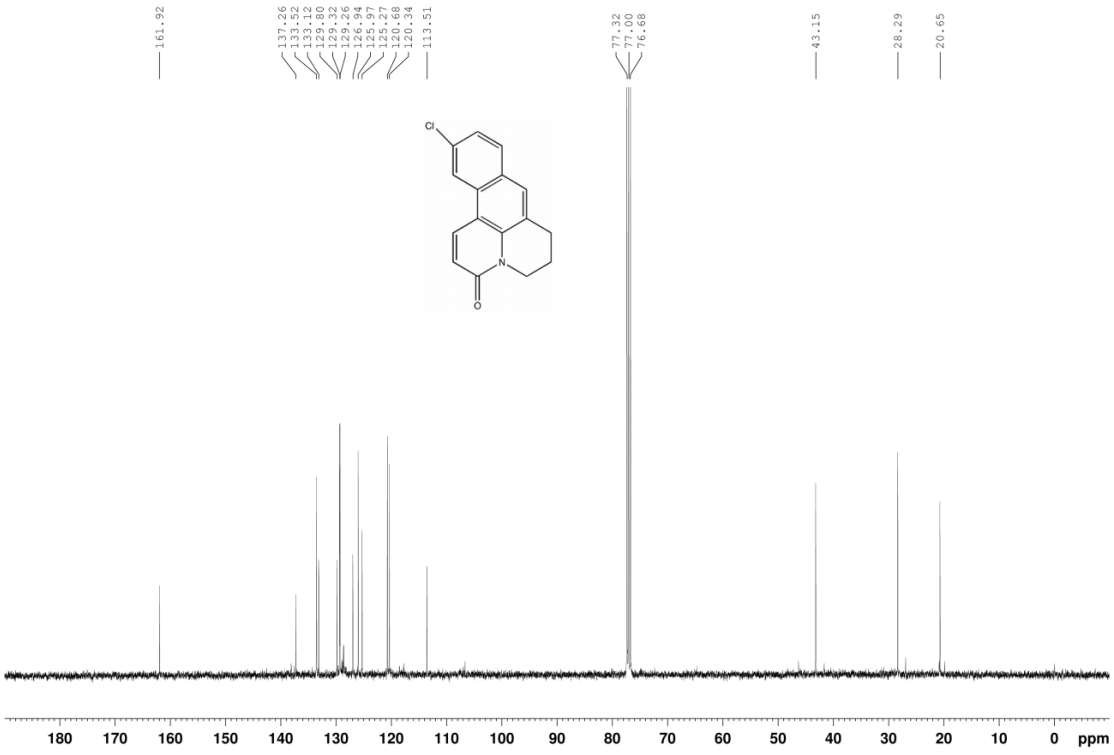
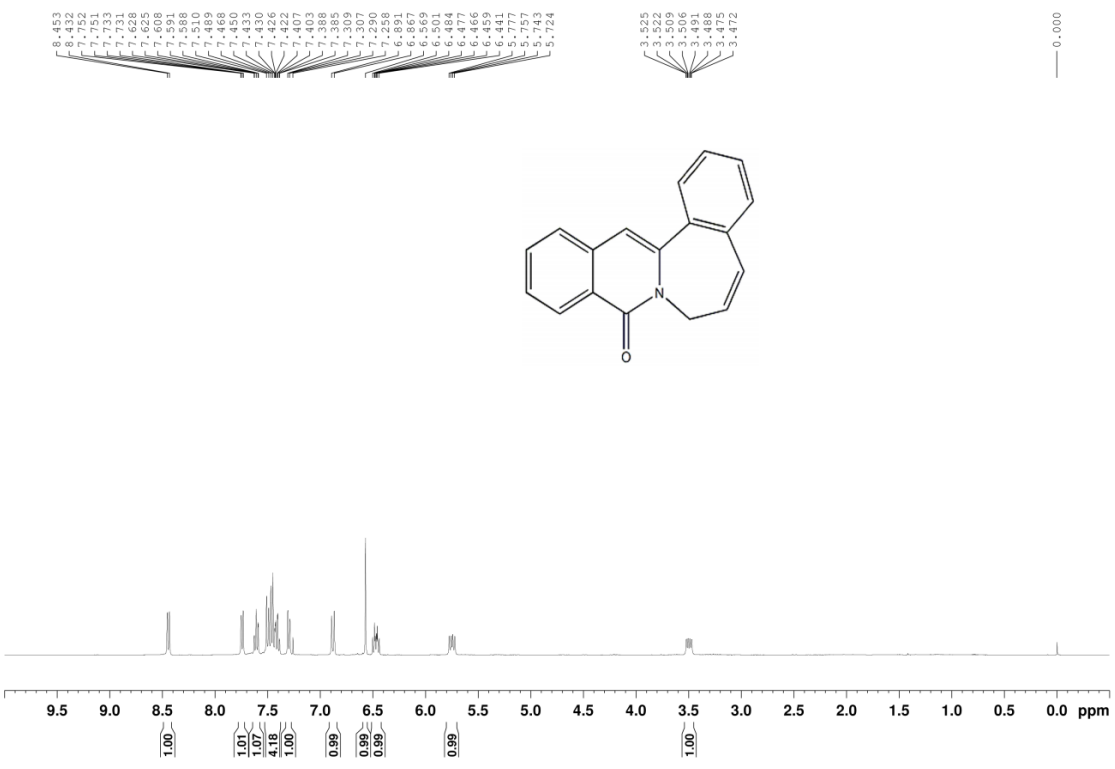
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

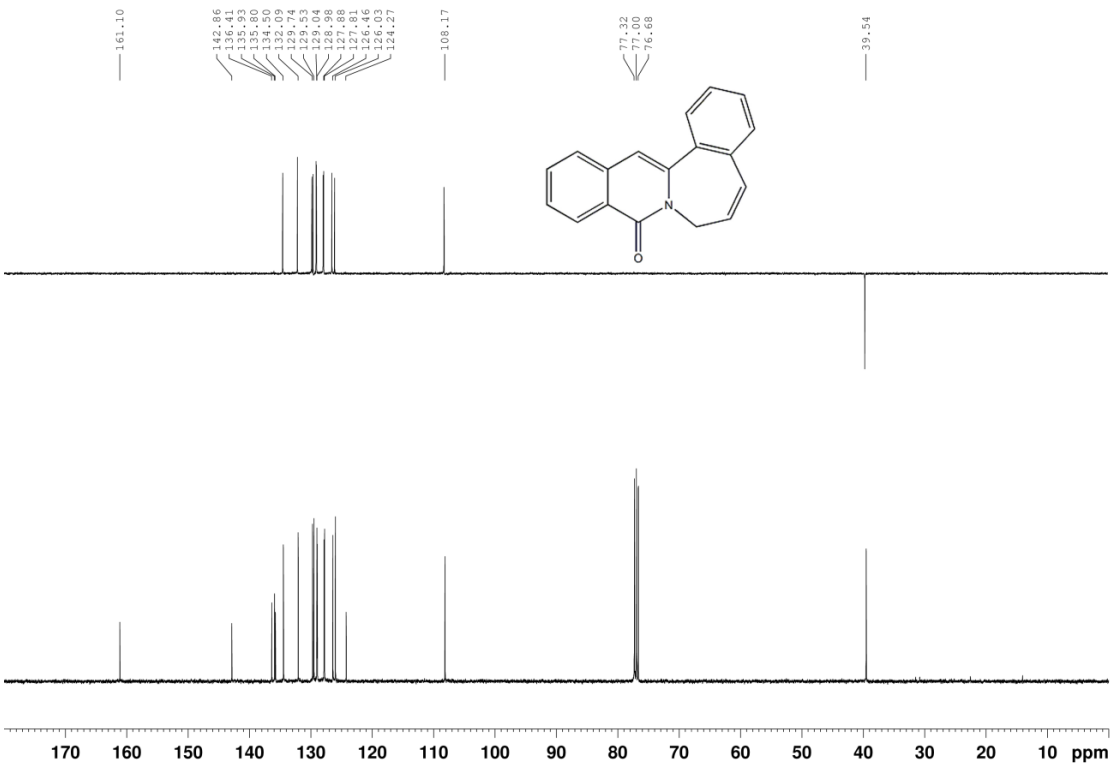
10c ^{1}H NMR



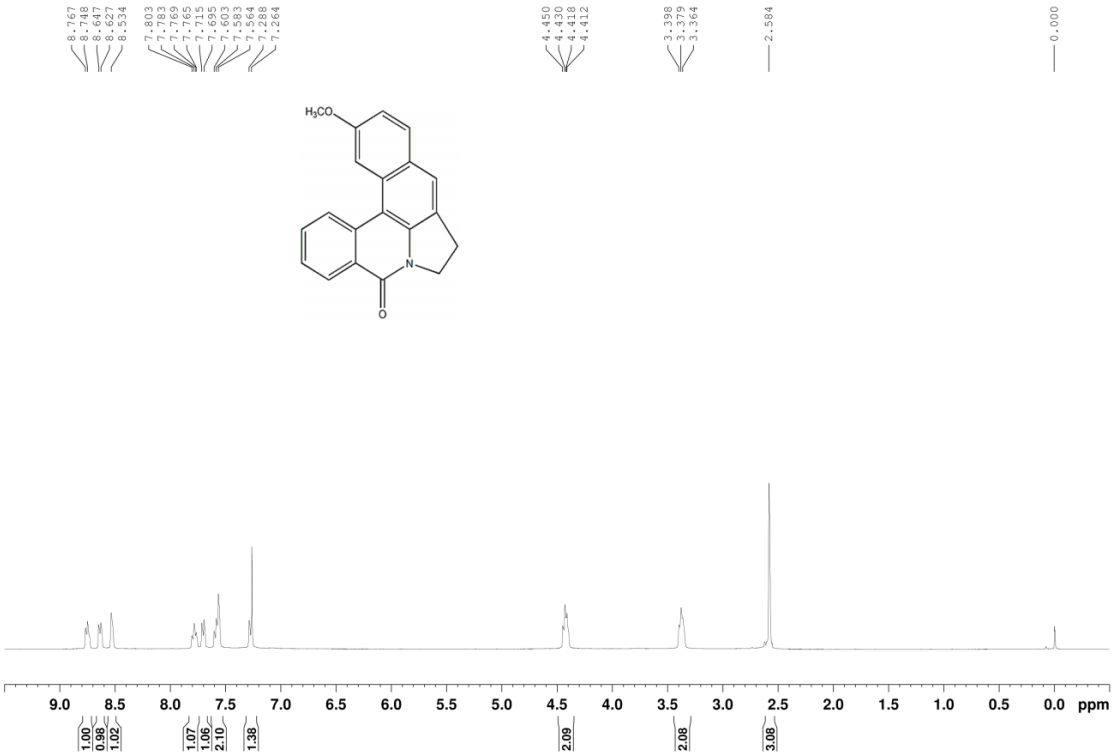
10c ^{13}C NMR



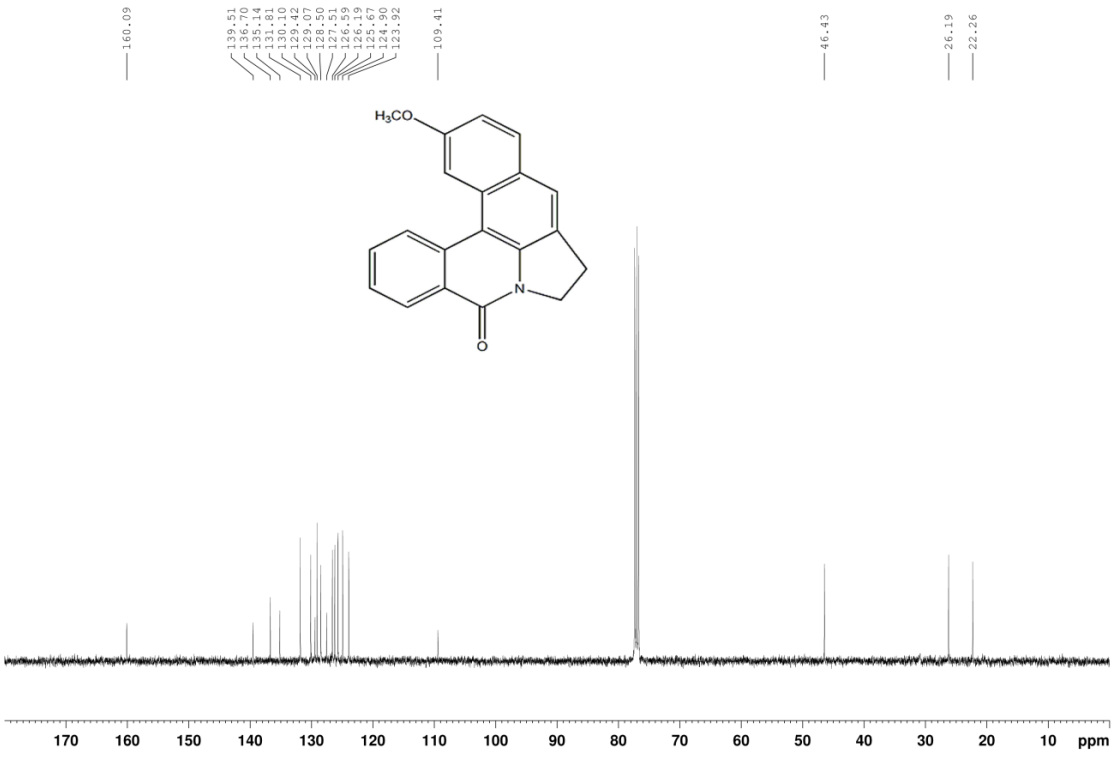

8.453
8.432
7.752
7.751
7.733
7.731
7.628
7.625
7.608
7.591
7.588
7.510
7.489
7.468
7.450
7.433
7.430
7.426
7.422
7.407
7.403
7.388
7.385
7.309
7.307
7.290
7.258
6.891
6.867
6.569
6.561
6.484
6.477
6.466
6.459
6.441
5.777
5.757
5.743
5.724
3.525
3.522
3.509
3.506
3.491
3.488
3.475
3.472
0.000
N
O
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.01
1.07
4.18
1.00
0.99
0.99
0.99
0.99
1.00


161.10
142.86
136.41
135.93
135.80
134.50
132.09
129.74
129.53
129.04
128.98
127.88
127.81
126.46
126.03
124.27
108.17
77.32
77.00
76.68
39.54
N
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

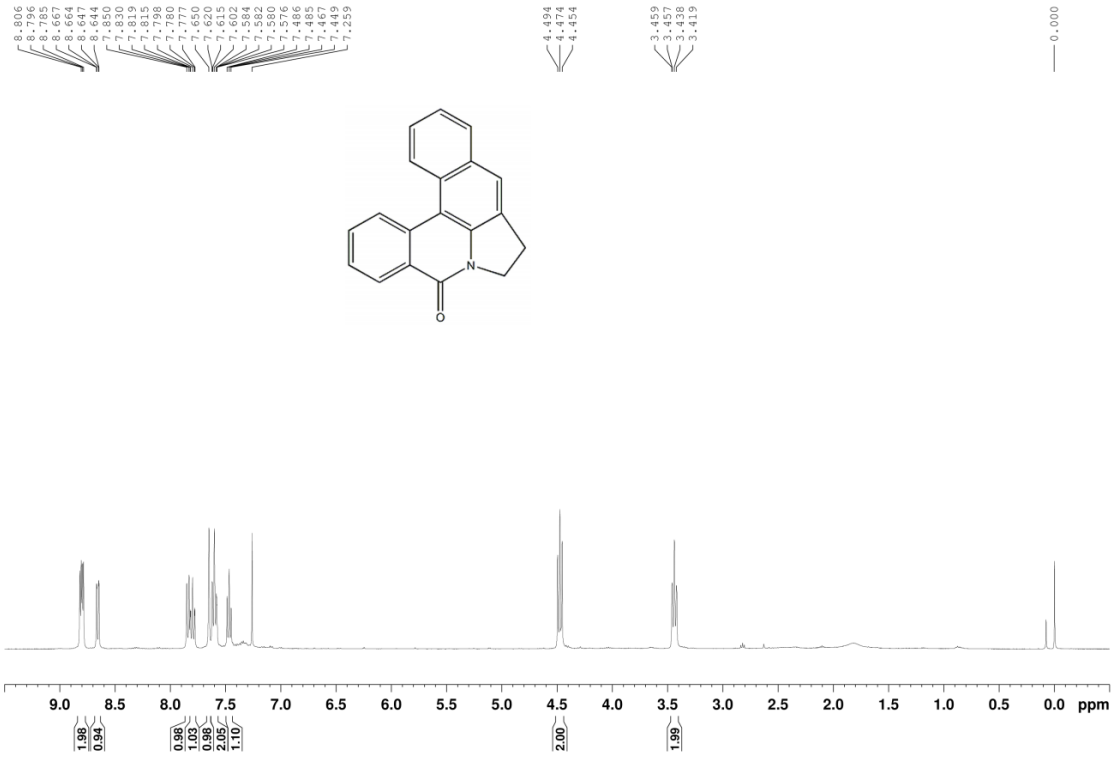
12a ^{1}H NMR



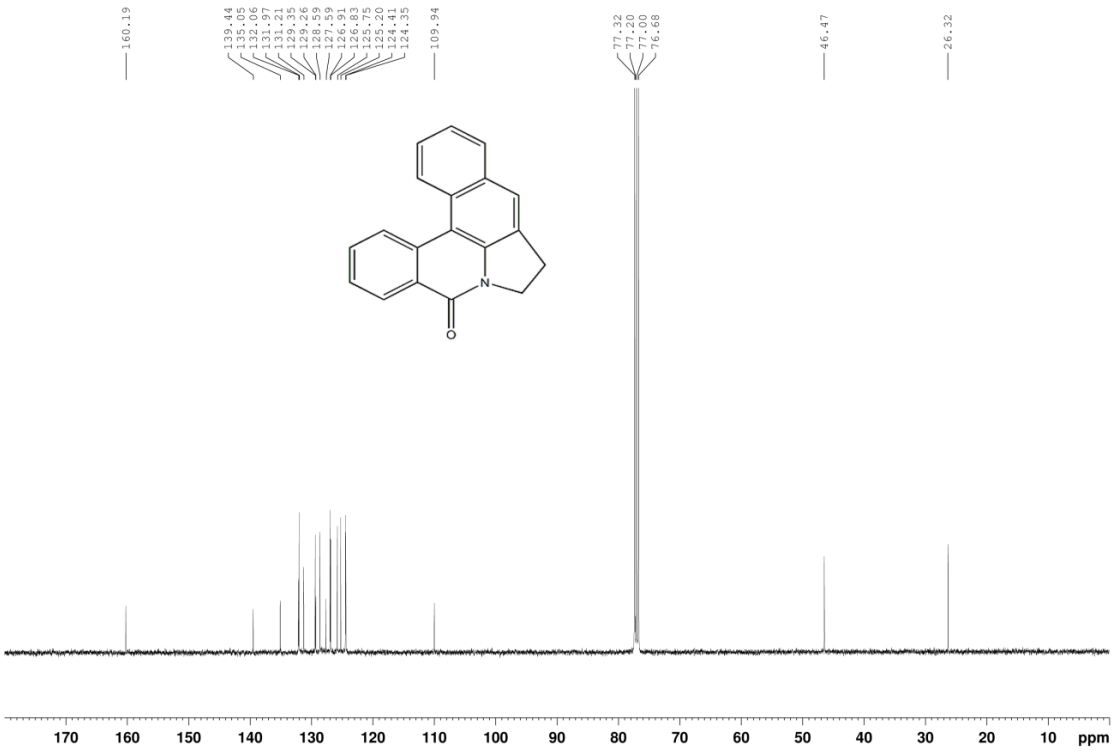
12a ^{13}C NMR



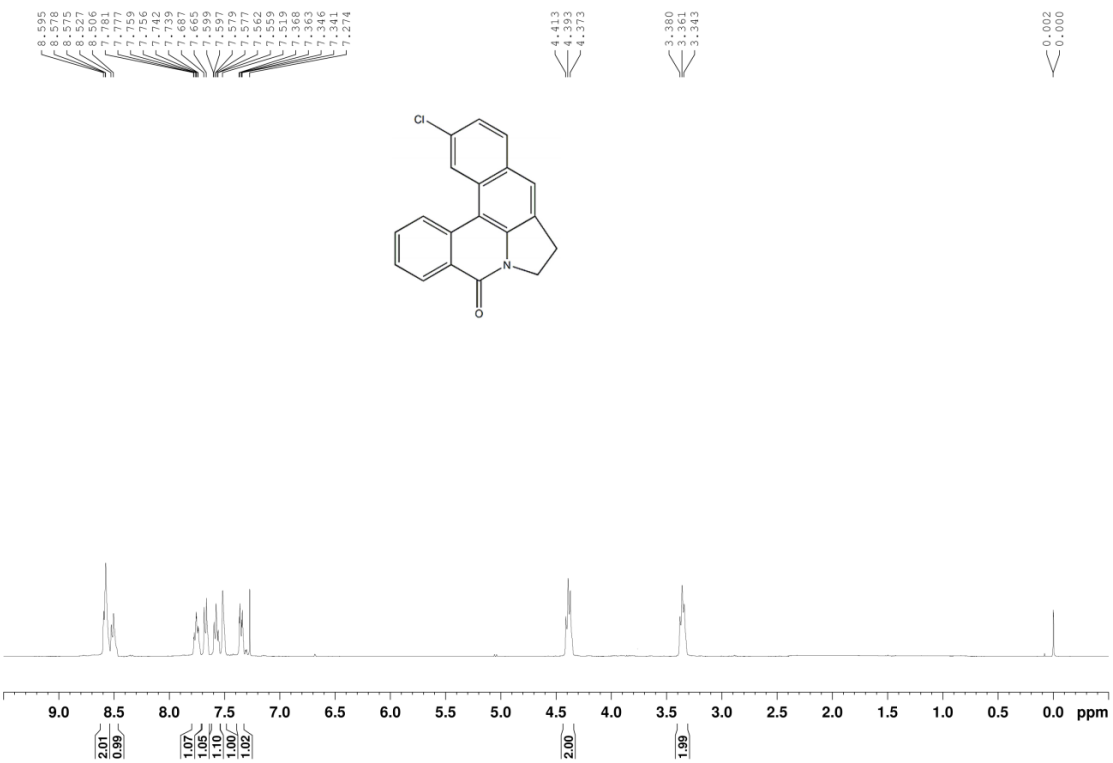
12b ^{1}H NMR



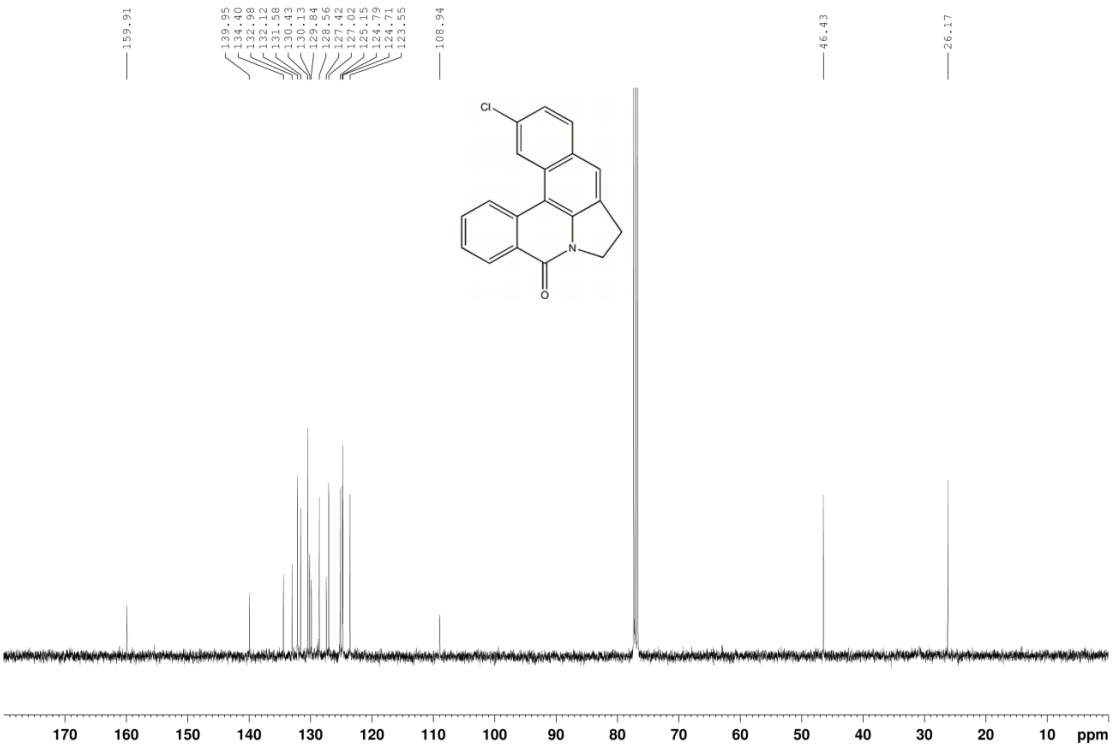
12b ^{13}C NMR



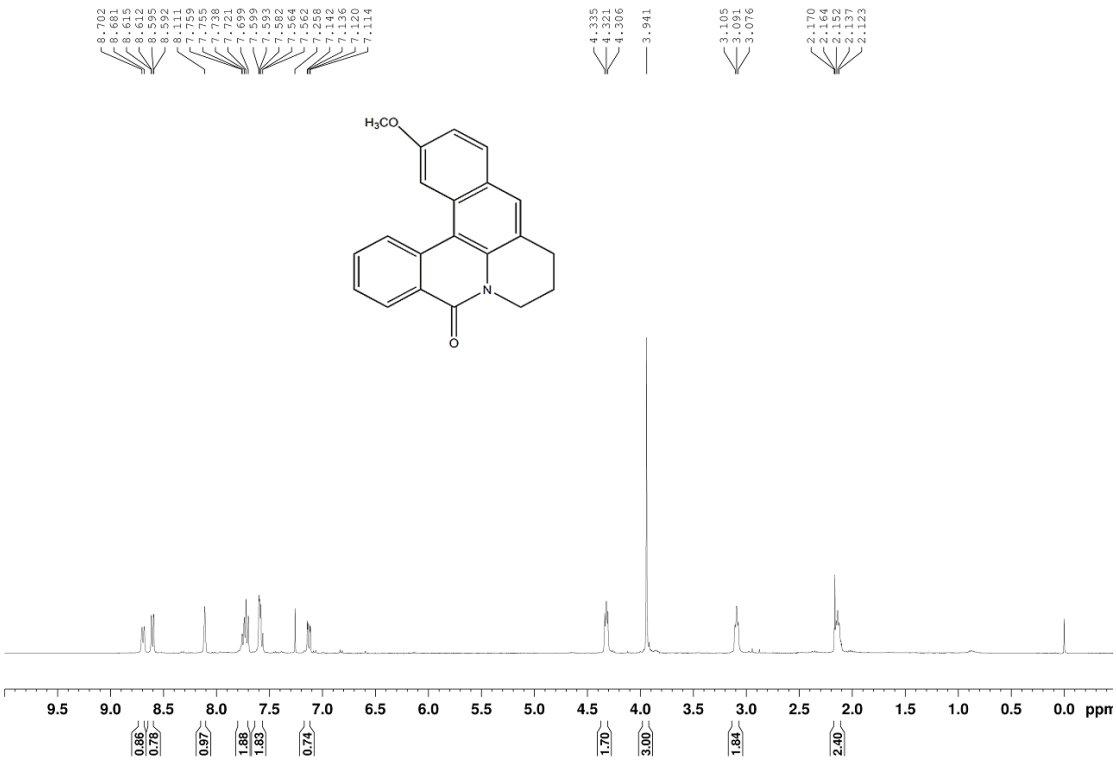
12c ^{1}H NMR



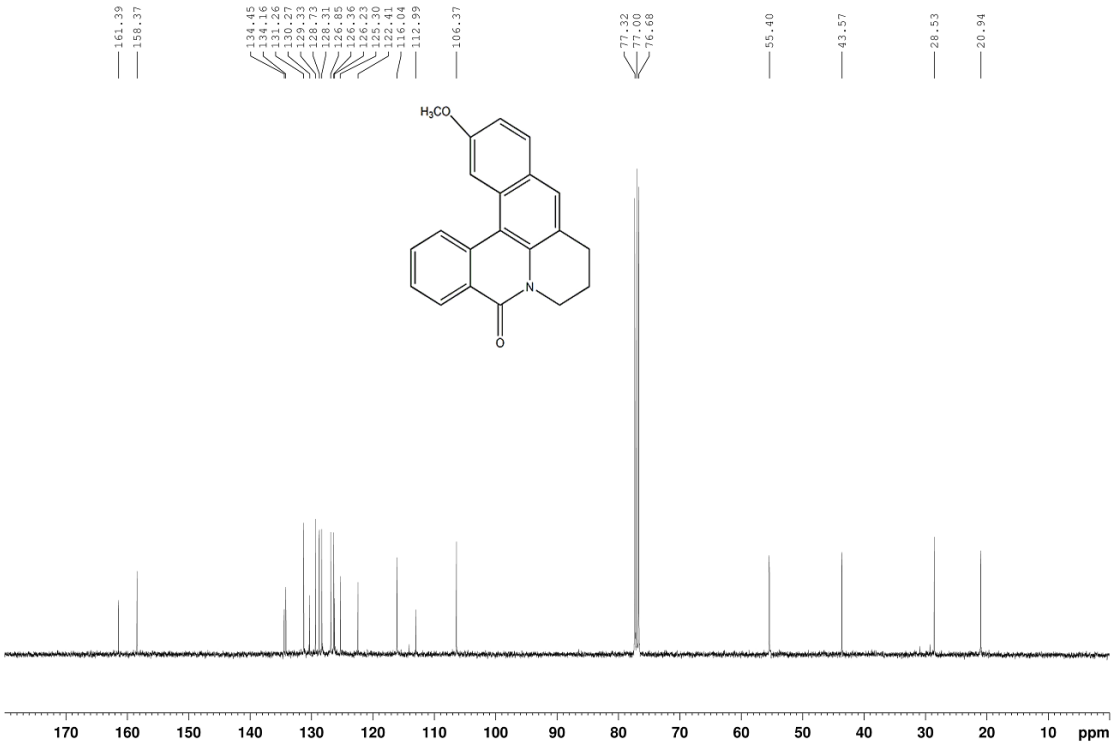
12b ^{13}C NMR



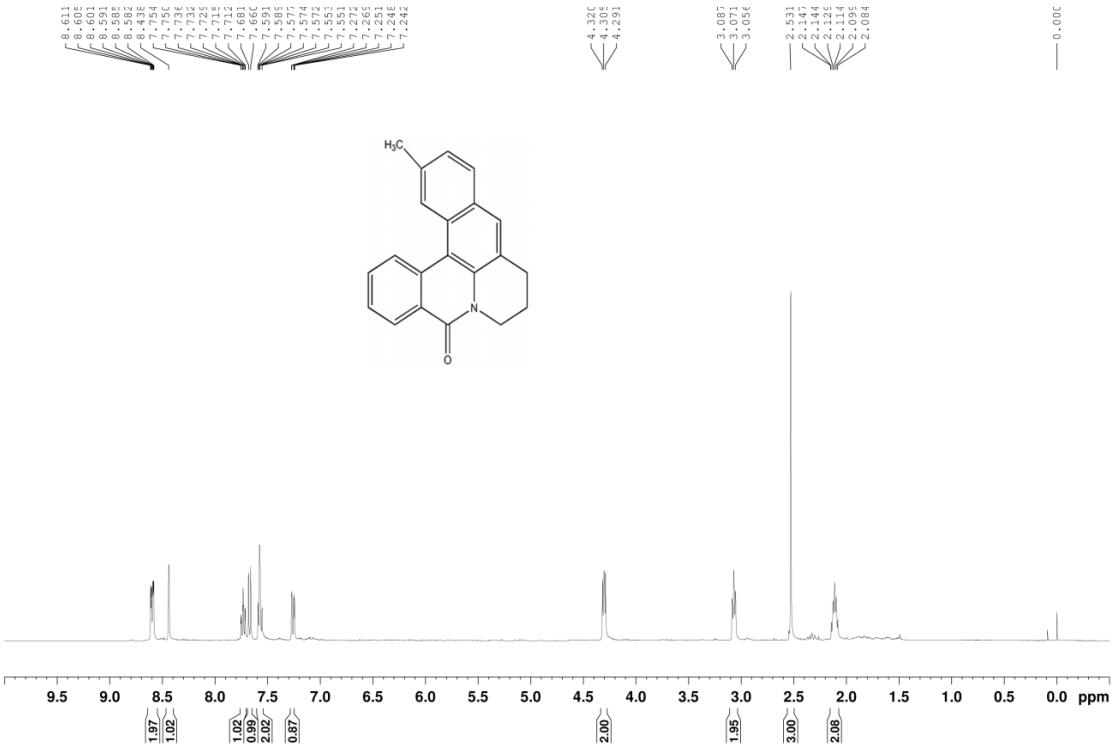
12c ^{1}H NMR



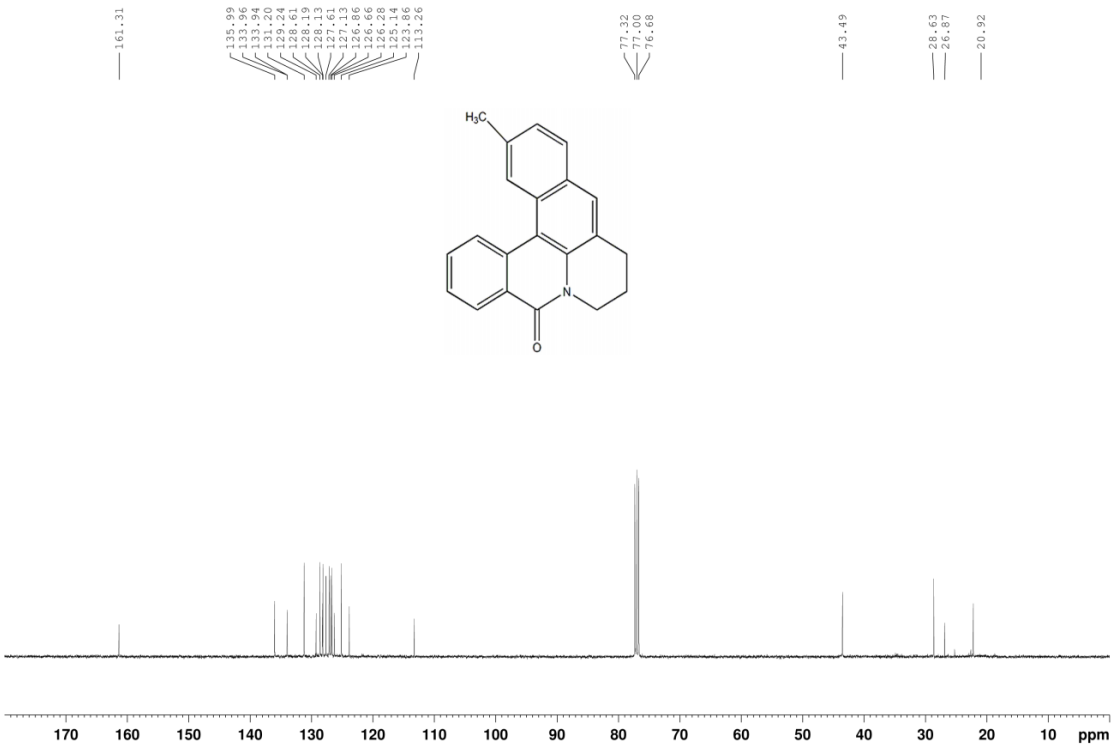
12c ^{13}C NMR



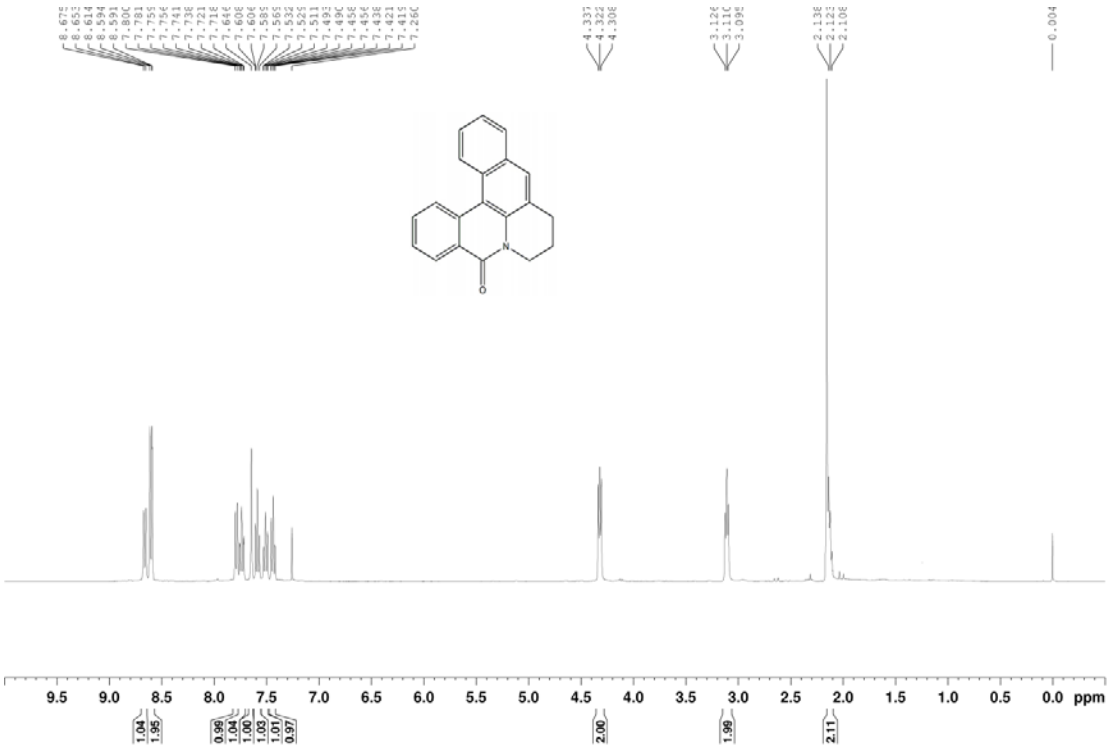
12d ^{1}H NMR


8.611
8.603
8.601
8.591
8.588
8.582
8.438
7.754
7.750
7.738
7.734
7.725
7.715
7.712
7.681
7.661
7.591
7.585
7.577
7.574
7.572
7.553
7.551
7.272
7.265
7.251
7.248
7.242
4.320
4.305
4.291
3.087
3.071
3.054
2.531
2.147
2.144
2.125
2.114
2.095
2.084
0.000
H3C
N
O
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.97
1.02
1.02
0.99
2.02
0.87
2.00
1.95
3.00
2.08

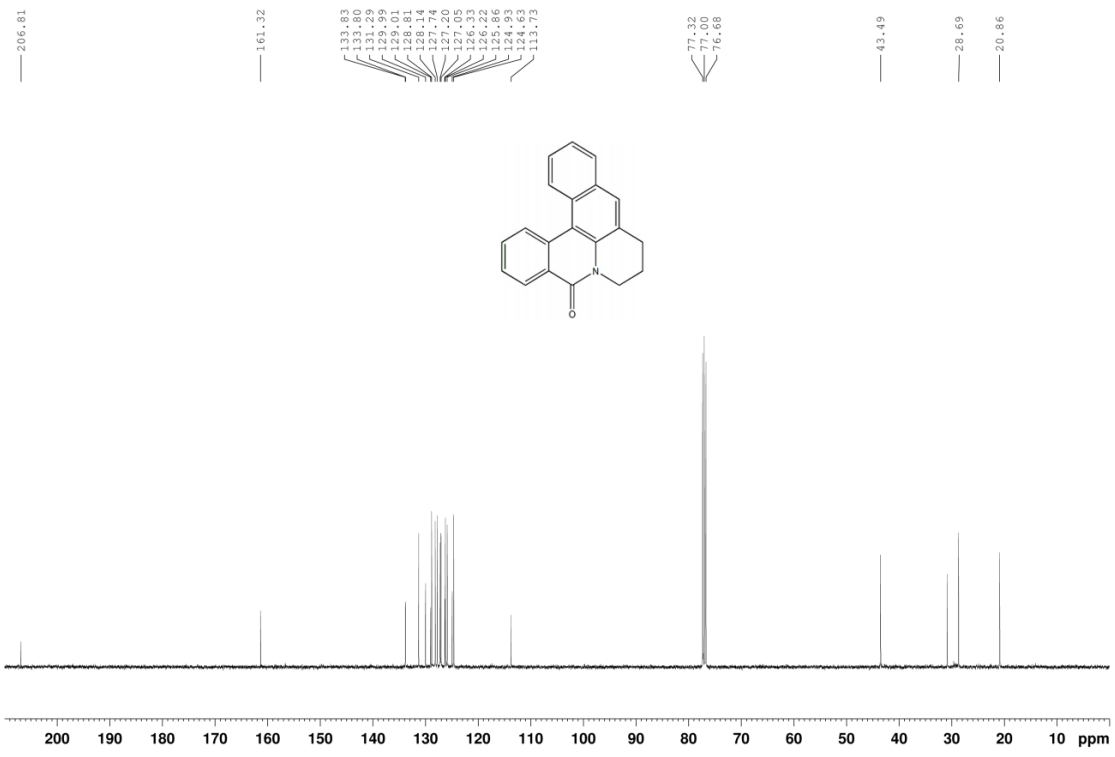
12d ^{13}C NMR


161.31
135.99
133.96
133.94
131.20
131.04
128.61
128.19
128.13
127.61
127.13
126.86
126.66
126.28
125.14
123.86
113.26
77.32
77.00
76.68
43.49
28.63
26.87
20.92
H3C
N
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

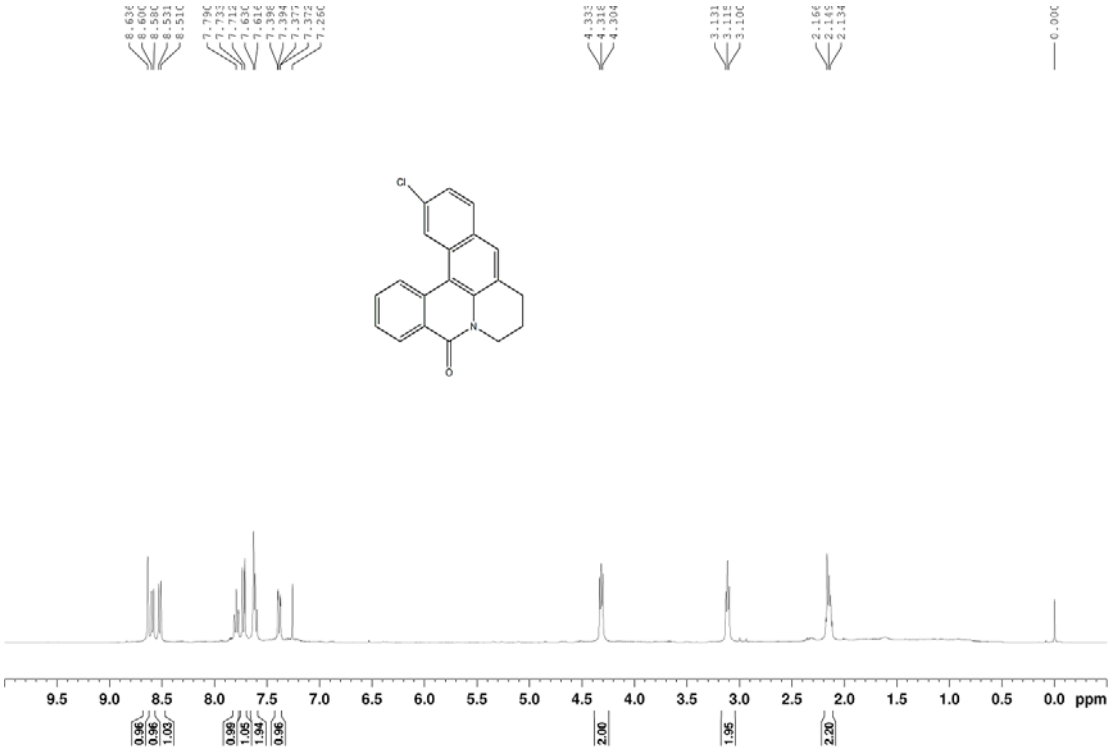
12e ^{1}H NMR



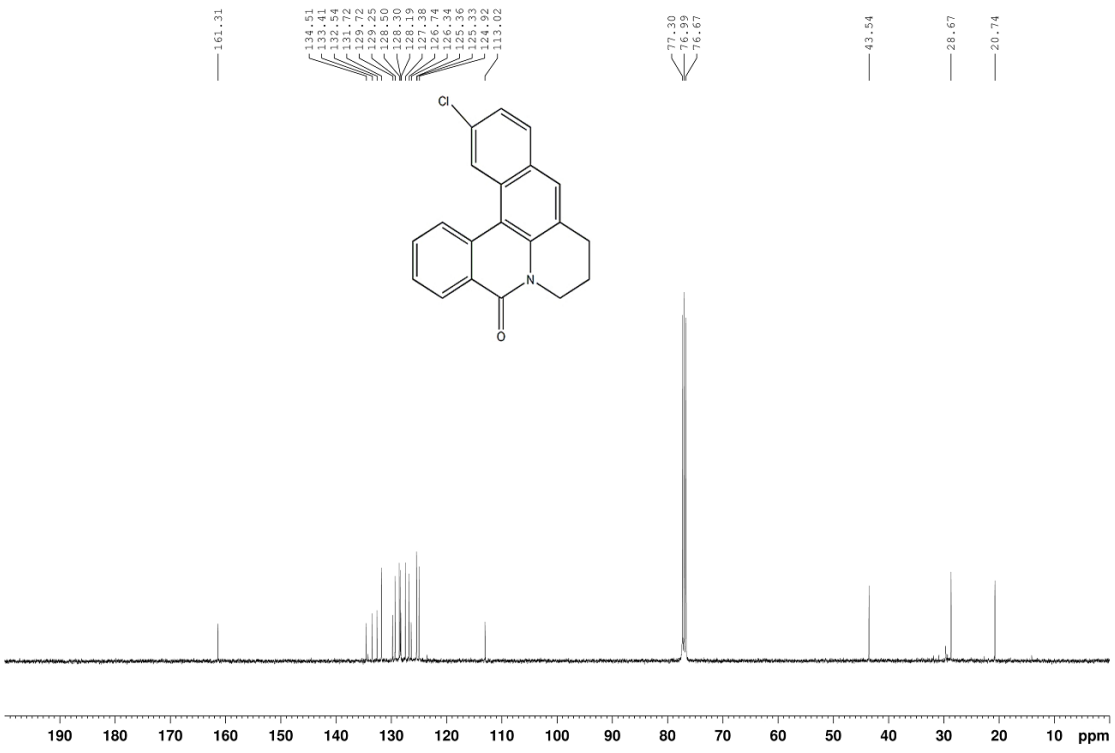
12e ^{13}C NMR



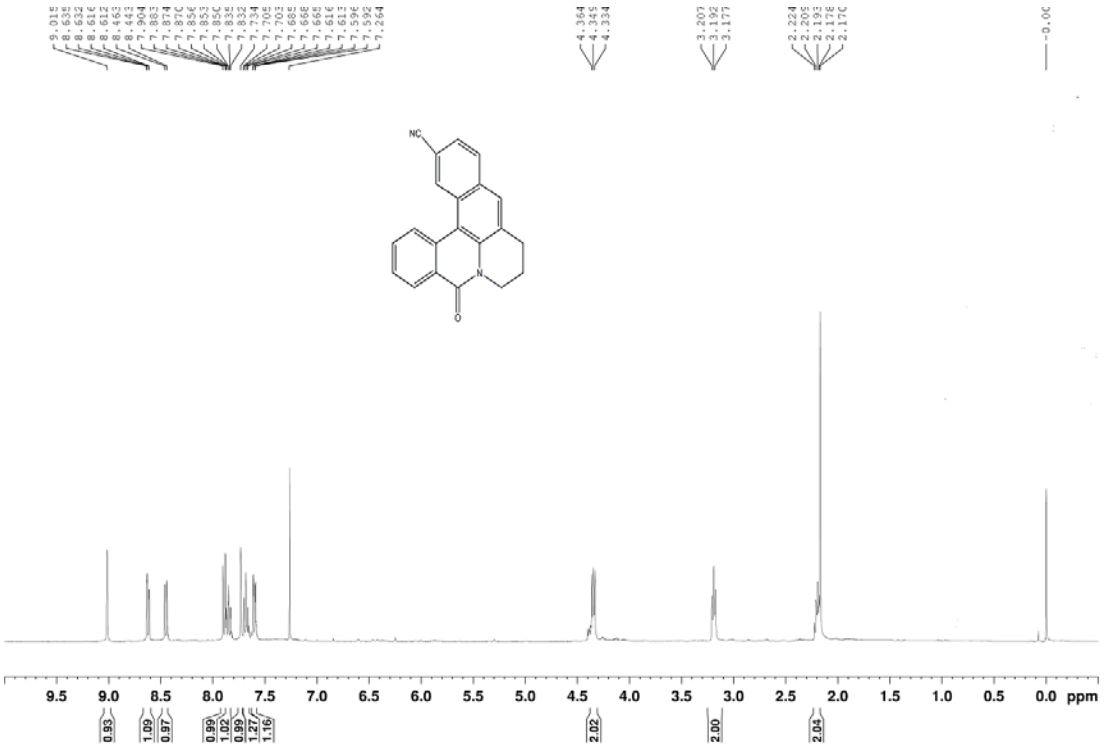
12f ^{1}H NMR



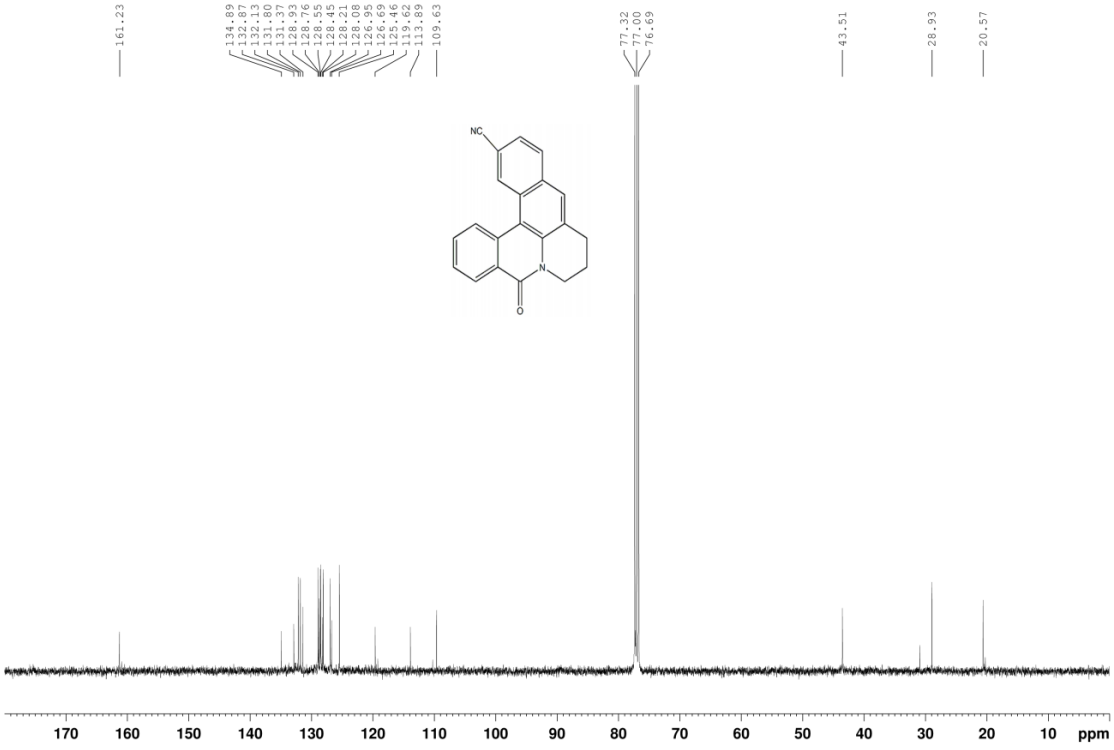
12f ^{13}C NMR



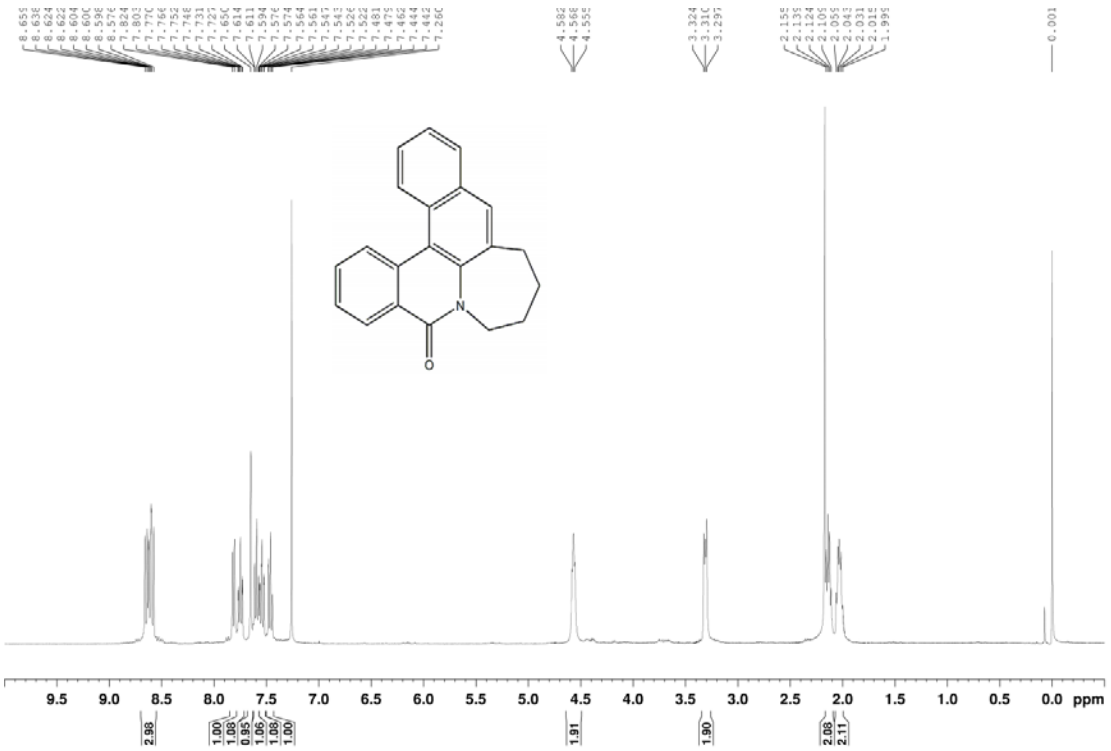
12g ^{1}H NMR



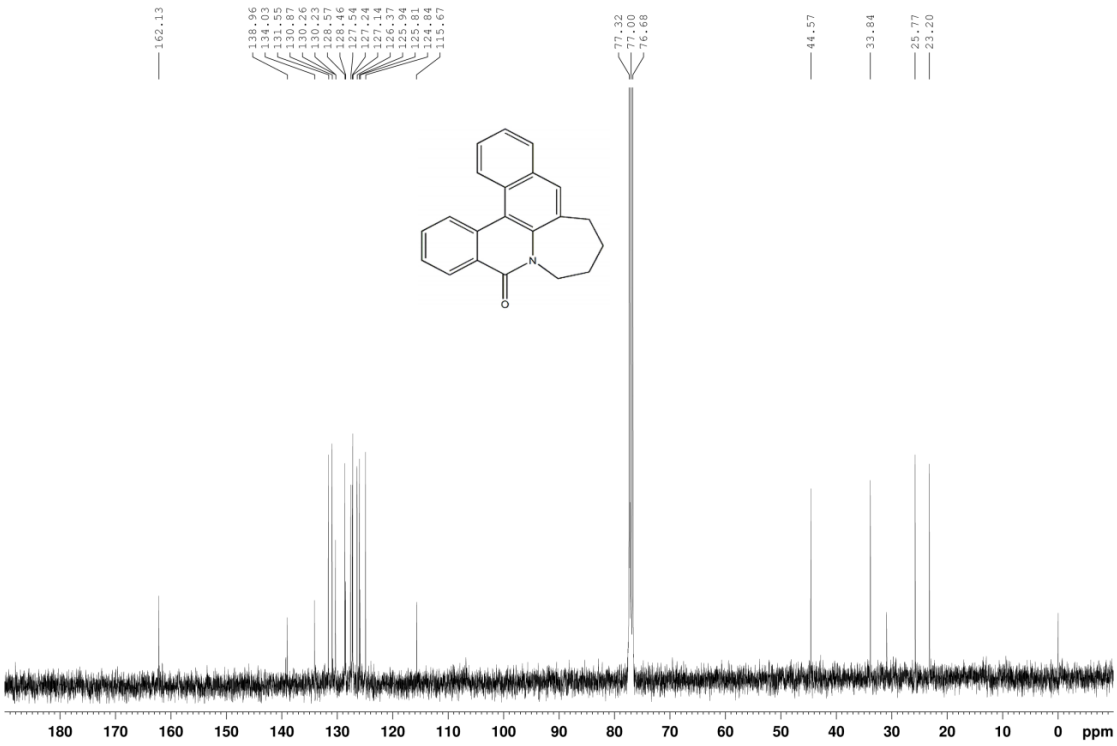
12g ^{13}C NMR



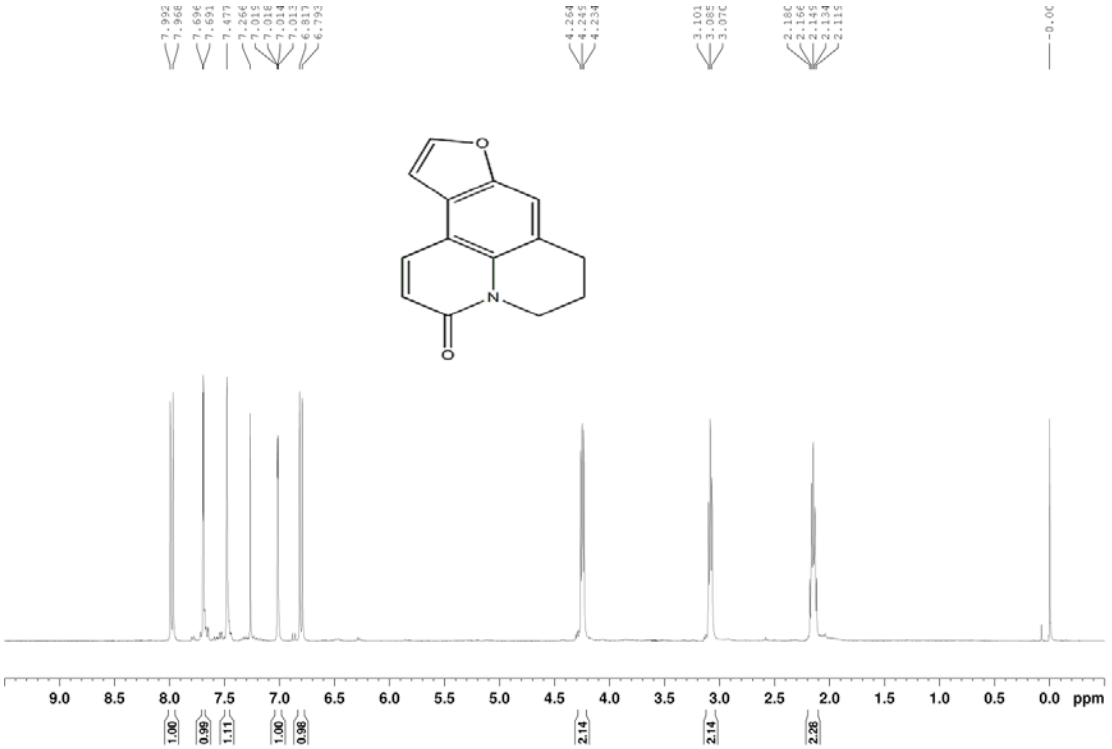
12h ^{1}H NMR


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.98
1.00
1.08
0.95
1.06
1.08
1.00
1.91
1.90
2.08
2.11

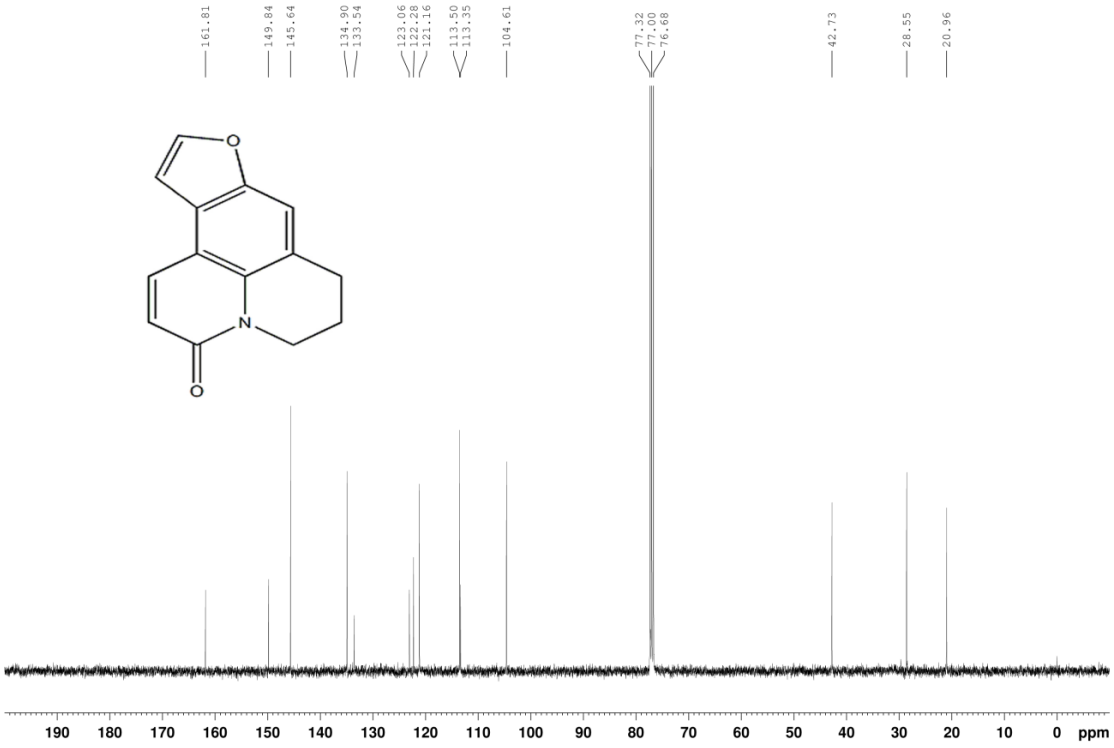
12h ^{13}C NMR


162.13
138.96
134.03
131.55
130.87
130.26
130.23
128.57
128.46
127.54
127.24
127.14
126.37
125.94
125.81
124.84
115.67
77.32
77.00
76.68
44.57
33.84
25.77
23.20
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

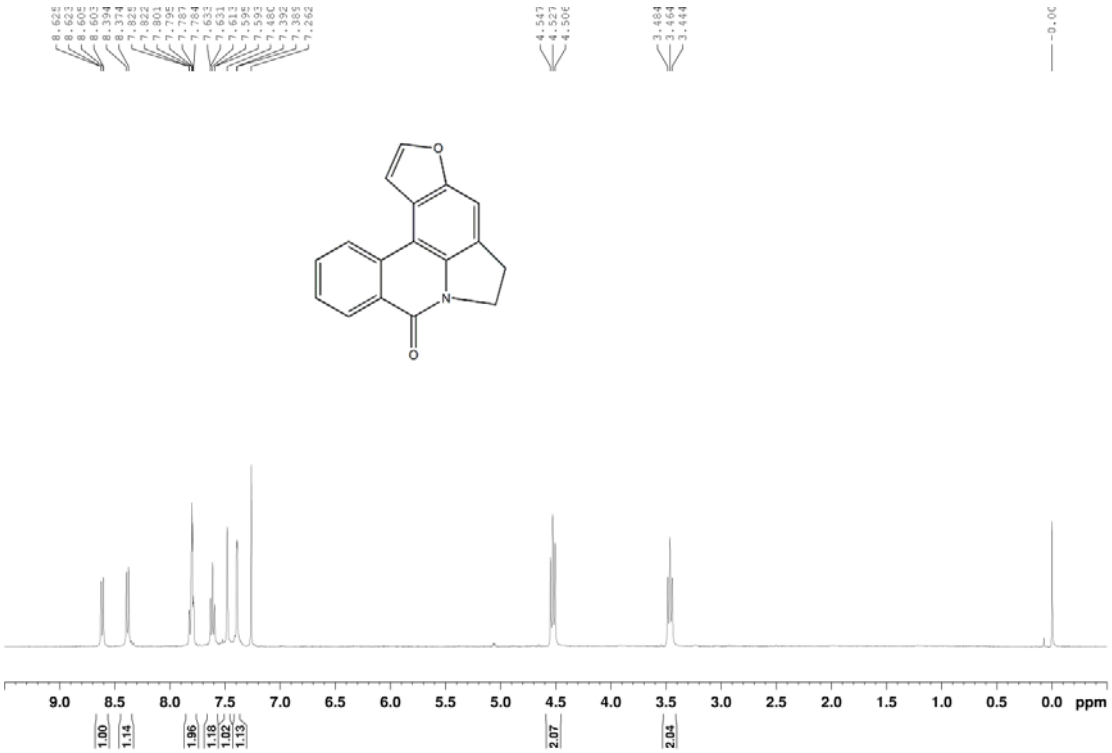
14a ^{1}H NMR



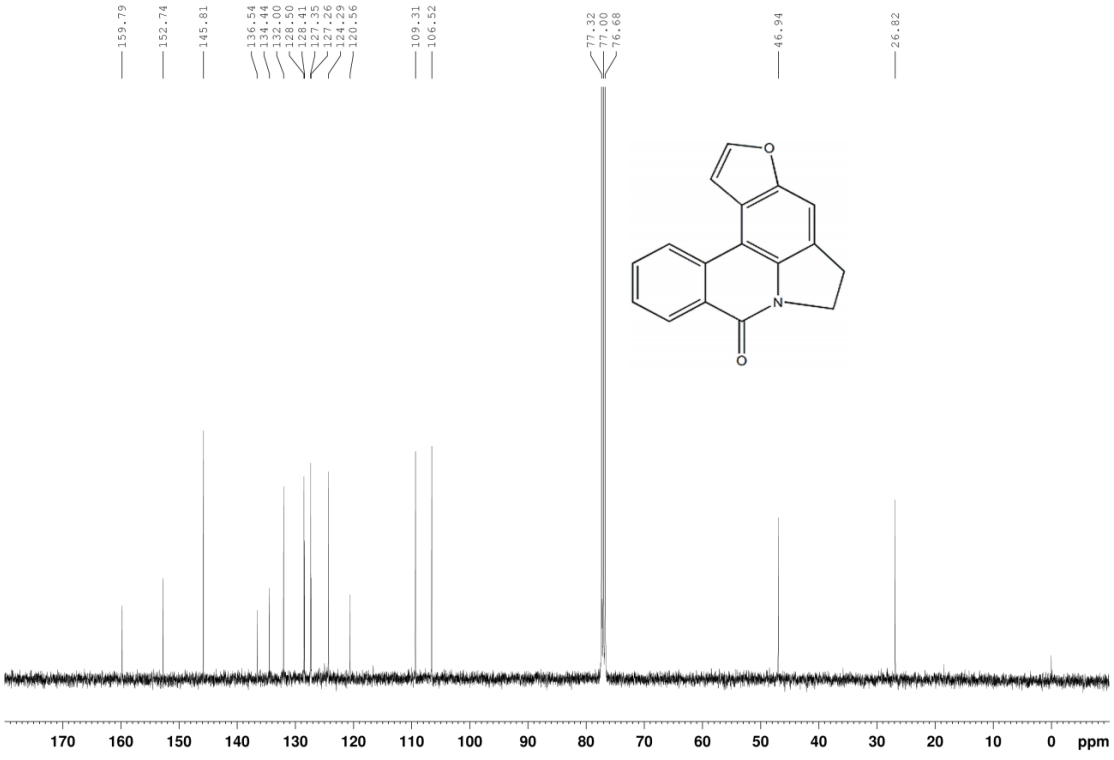
14a ^{13}C NMR



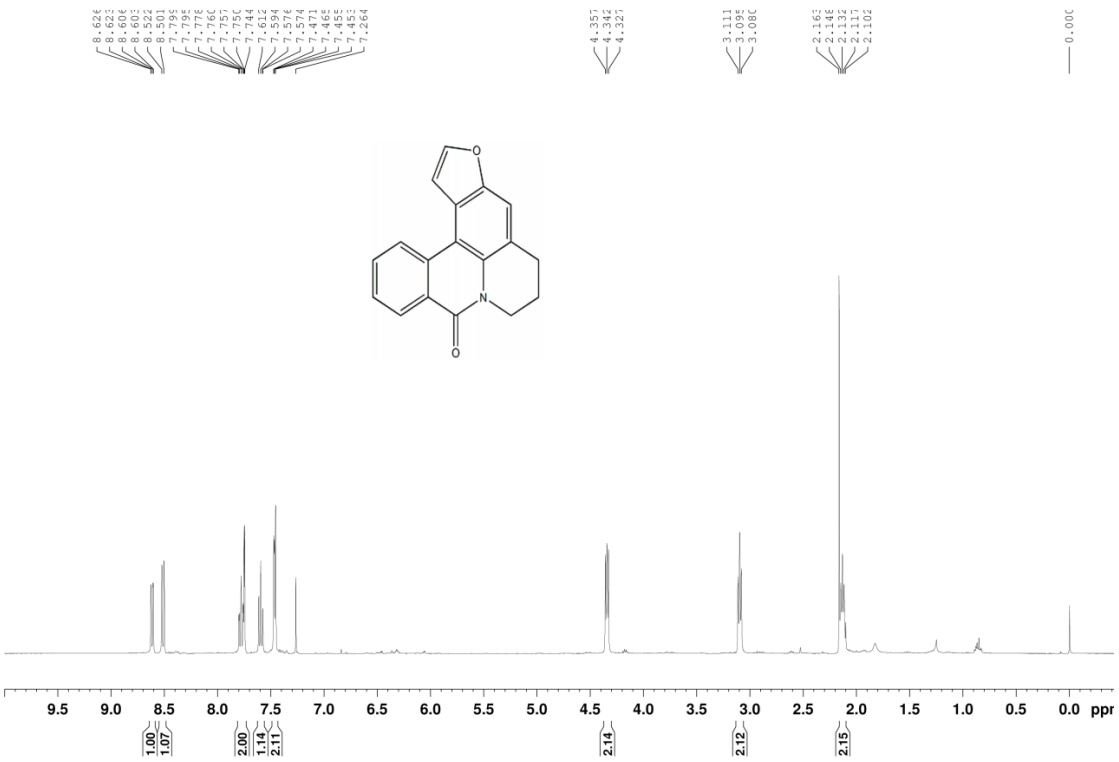
16a ^{1}H NMR



16a ^{13}C NMR



16b ^{1}H NMR



16b ^{13}C NMR