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Multicomponent Reaction for the Synthesis of Pyrido[1, 2-*b*] isoquinoline derivatives *via* [3+2] Cycloaddition Reaction between Alkynes and *in situ* Generated Isoquinolinium ylides

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Supporting Information

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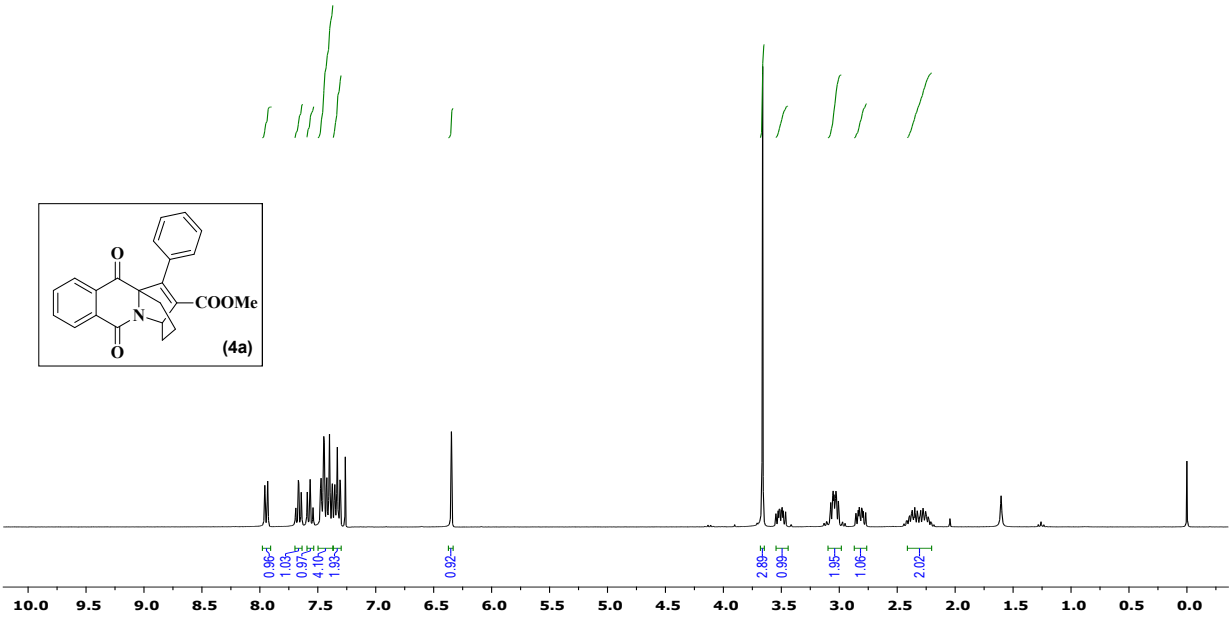
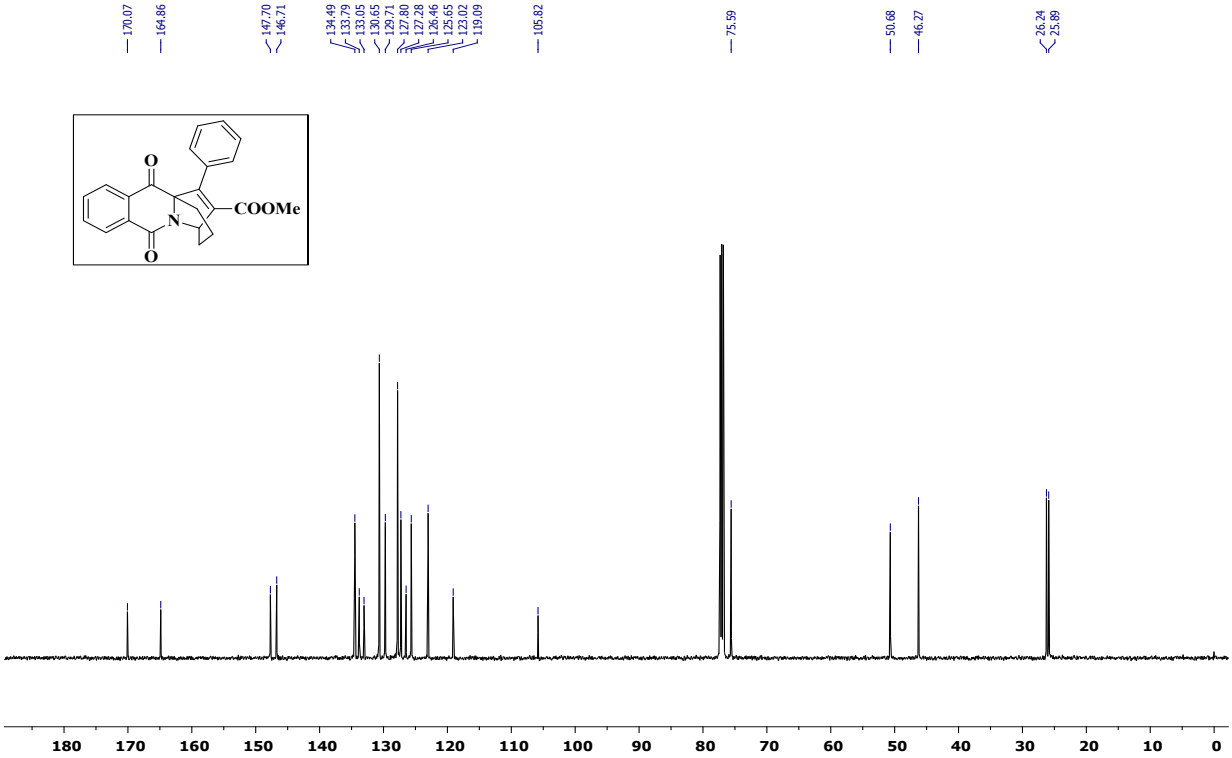
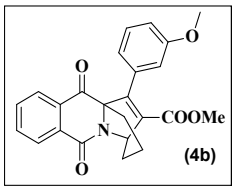
1. General Information:

All substrates and reagents were readily and commercially available.TLC analysis was performed using pre-coated glass plates. Column chromatography was conducted using silica gel (60-120 mesh). All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform ($CDCl_3$) on Avance 300 or 400 or Avance 500 spectrometers. Chemical shift (δ) are reported in parts per million (ppm) relative to residual $CHCl_3$ (^{1}H: δ 7.26 (ppm), ^{13}C: δ 77.00 (ppm) as an internal reference. Coupling constant (*j*) is reported in (Hz). Peak multiplicities are indicated as: s-singlet, t-triplet, q-quartet, m-multiplate and dd-doublet of doublet. Mass spectra were recorded by using 70 Ev spectrometer. High resolution mass spectrums (HRMS) were recorded using Applied Bio-sciences HRMS spectrometer at national center for mass spectroscopy.

Spectral copies of ^{1}H NMR and ^{13}C NMR



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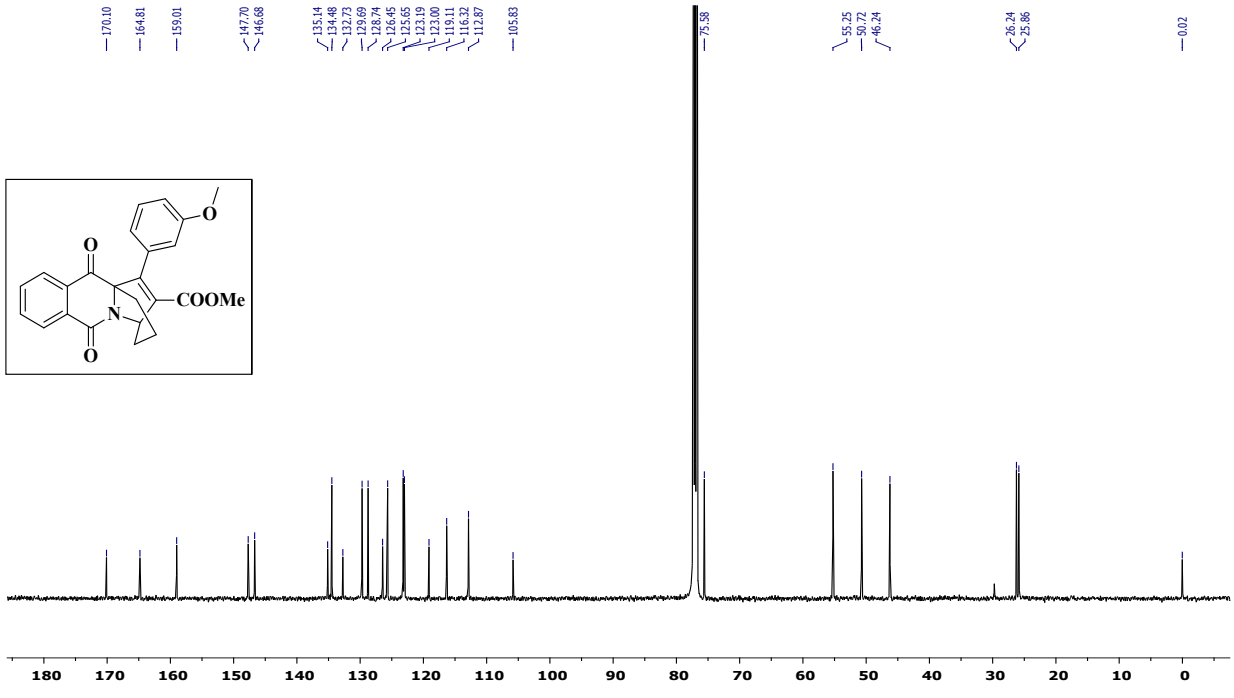
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170
160
150
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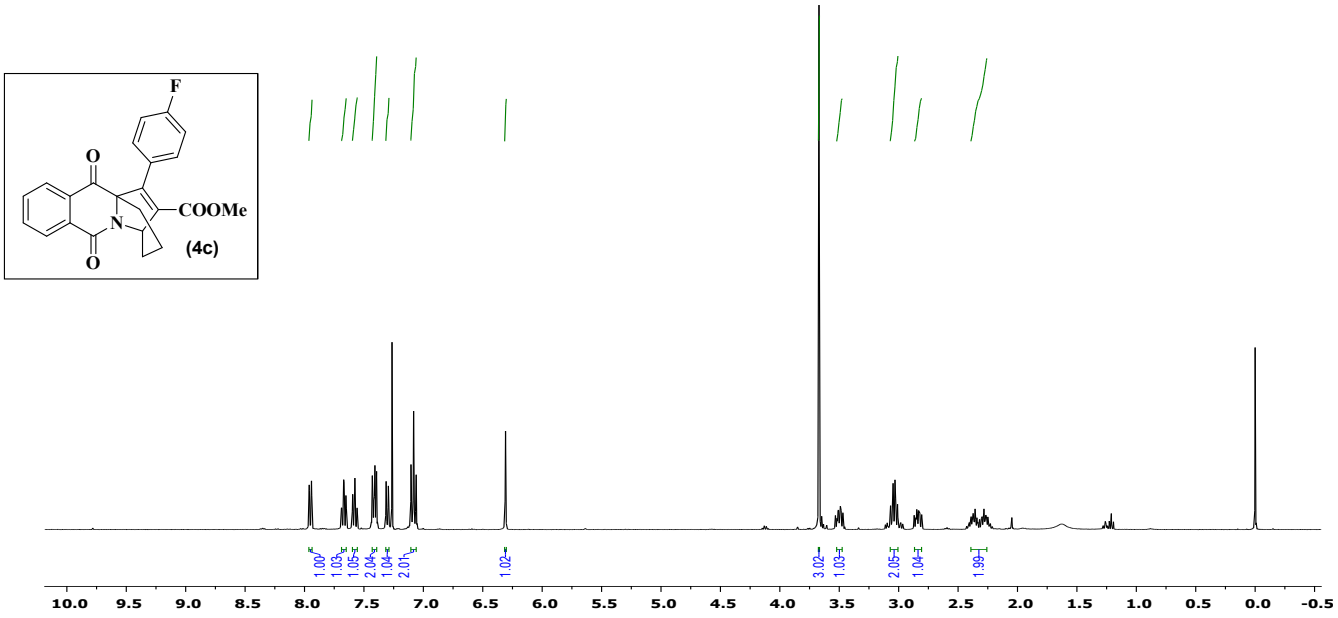
COOMe
N
O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1.03
2.05
1.04
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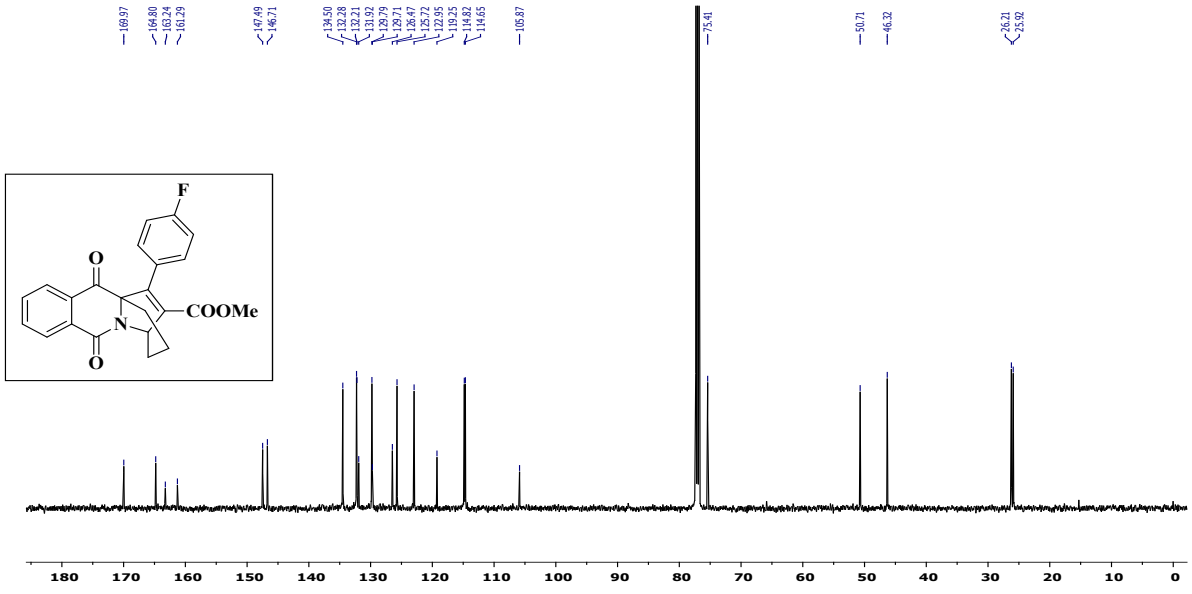
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114.82
114.65
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75.41
50.71
46.32
26.21
25.92
F
O
COOMe
N
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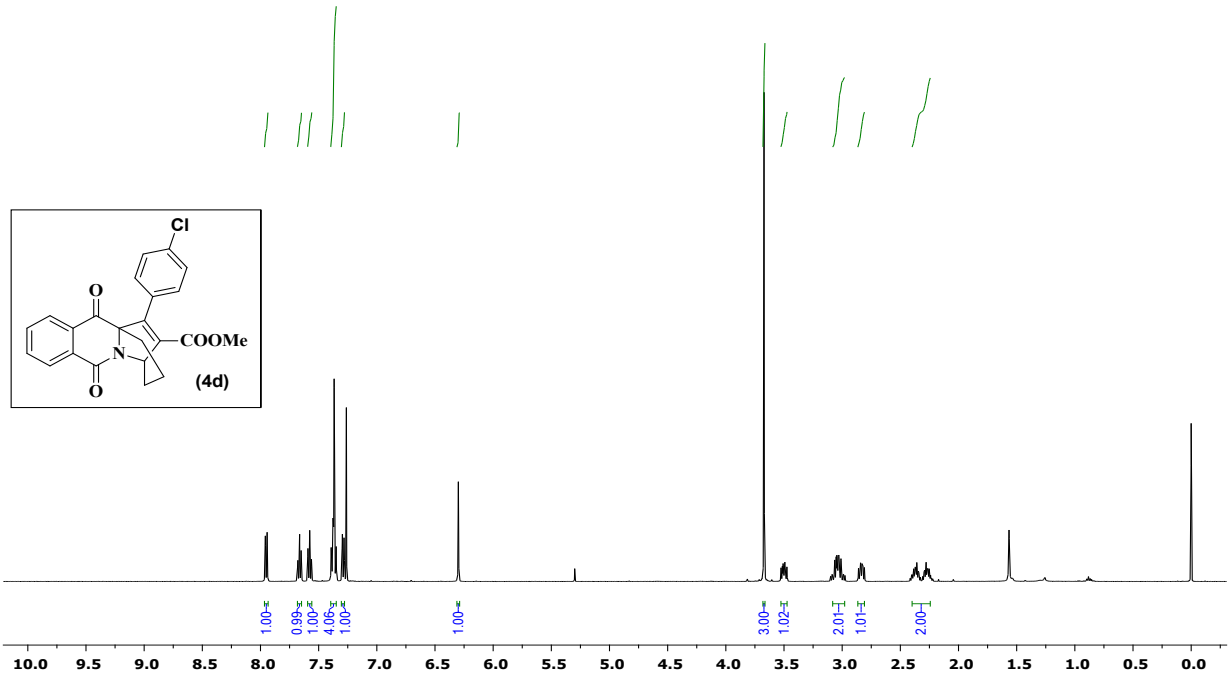
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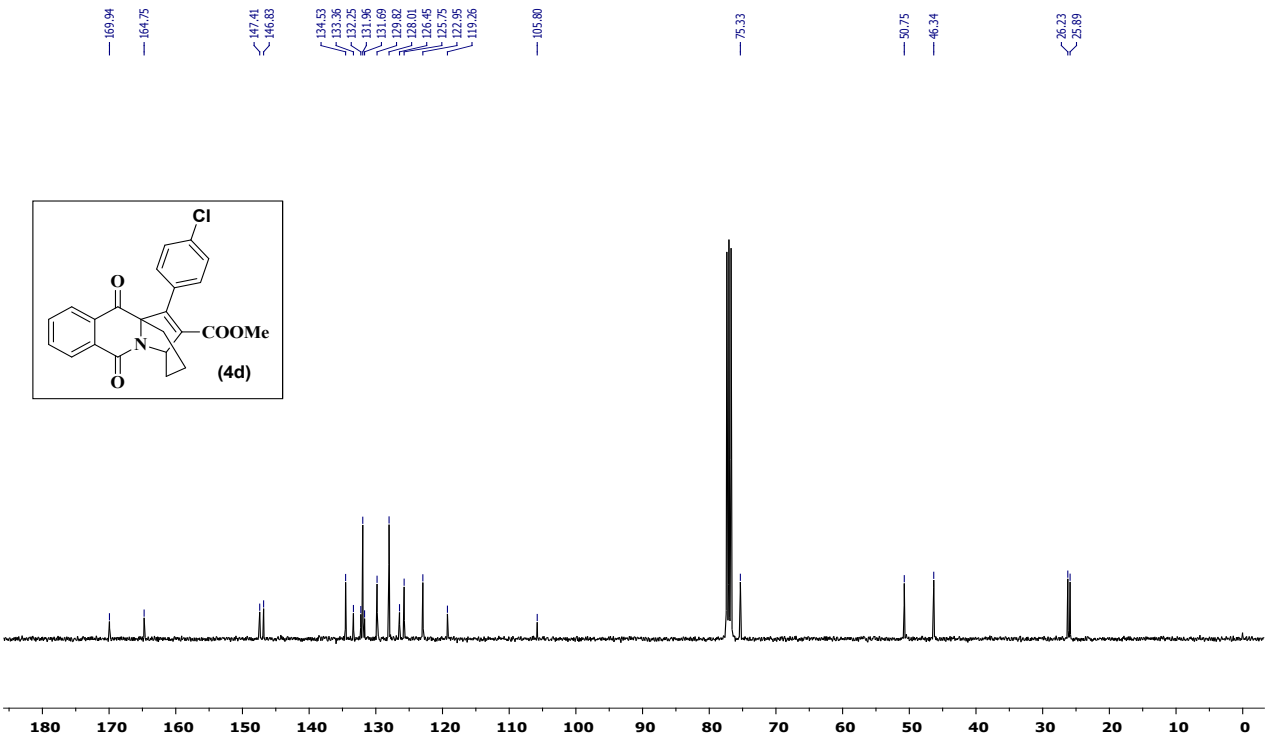
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46.34
26.23
25.89
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O
O
N
COOMe
(4d)
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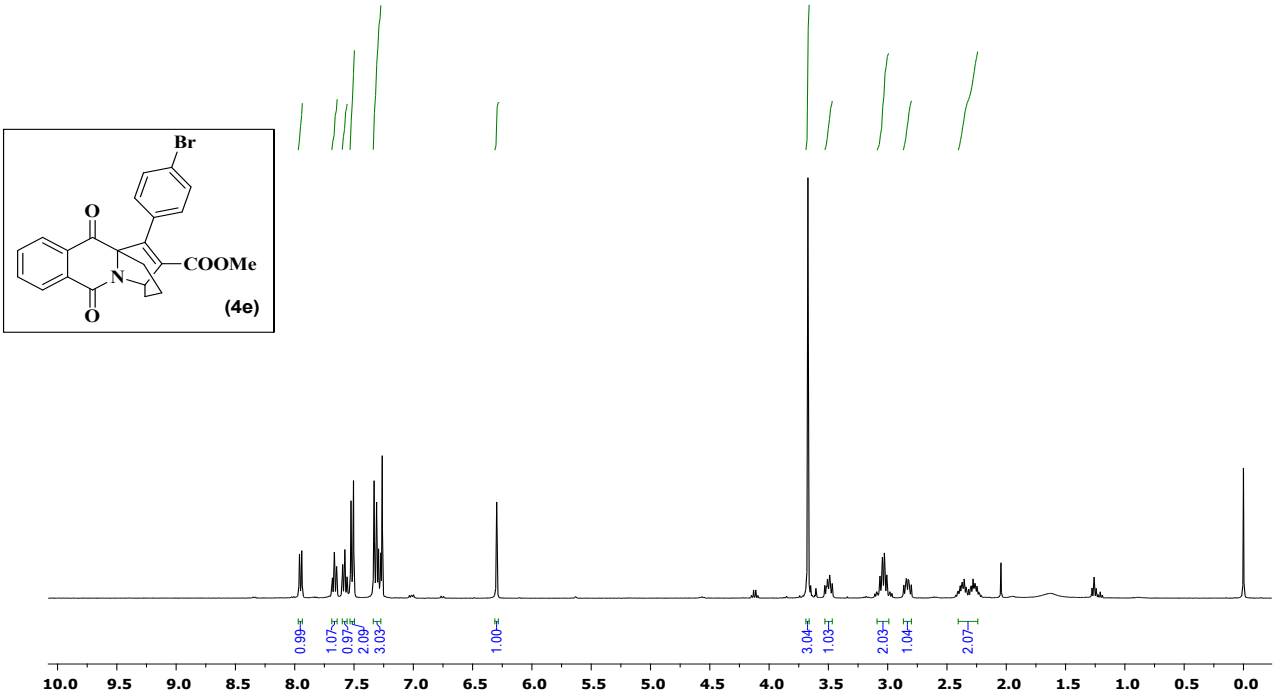
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2.07
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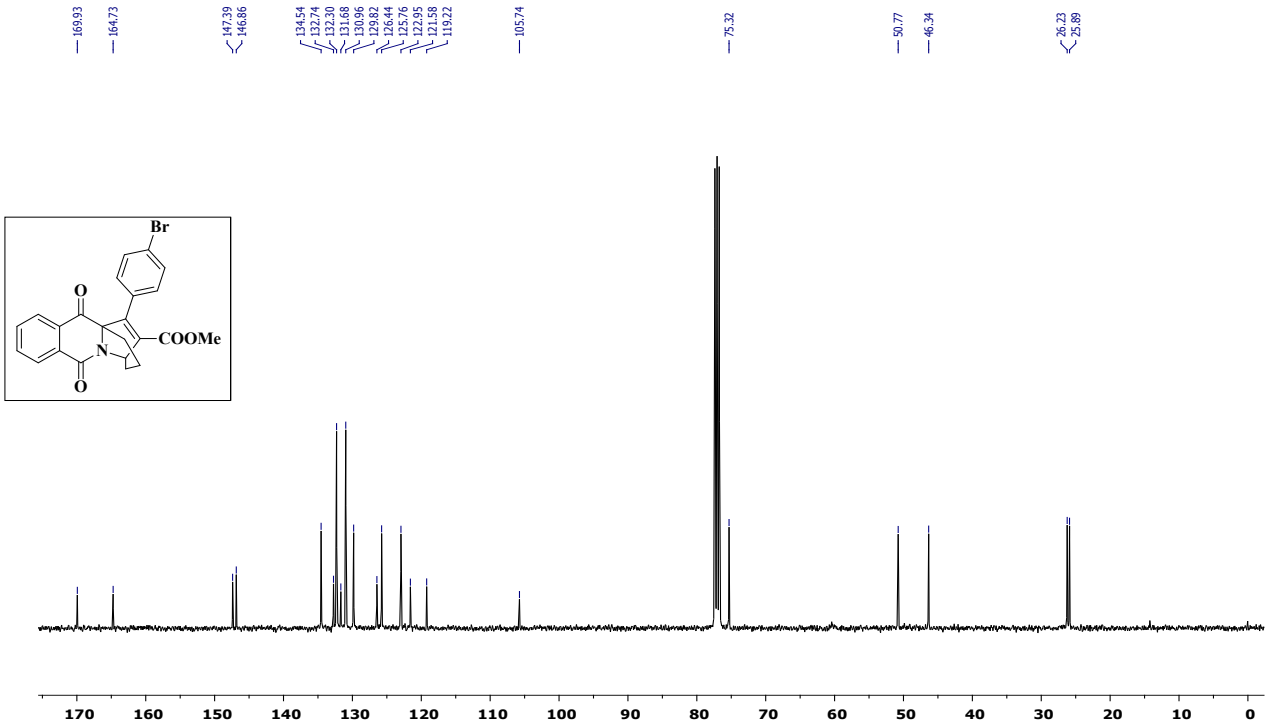
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COOMe
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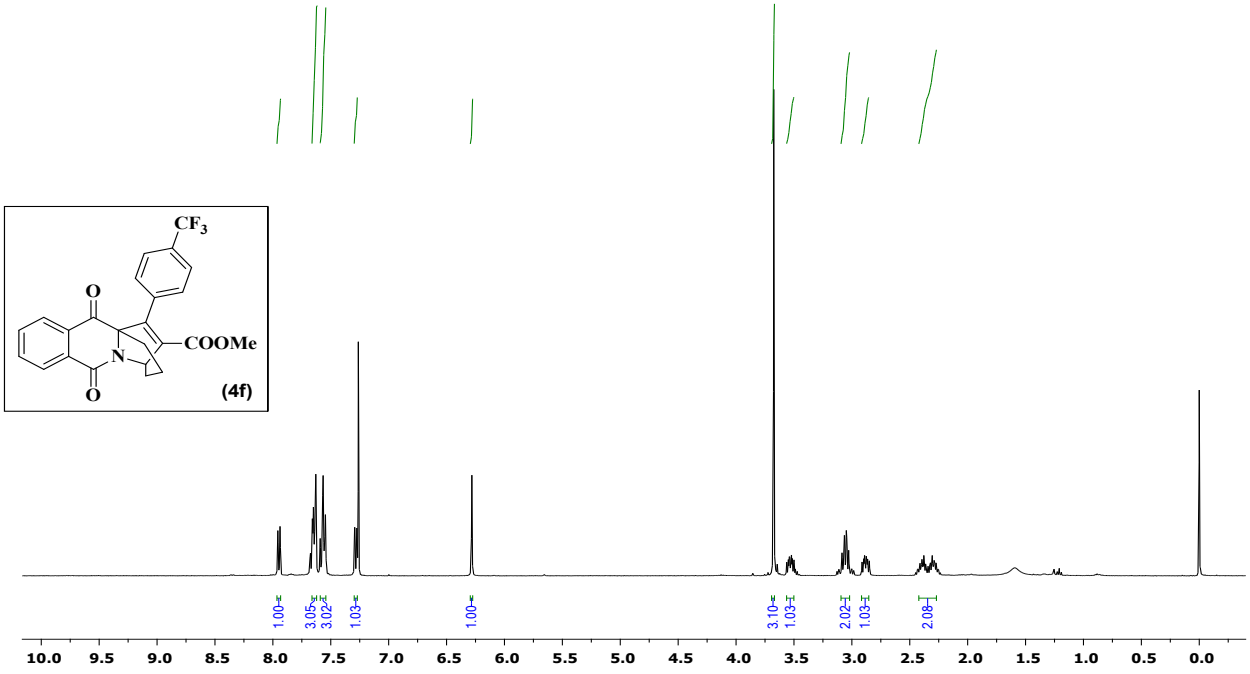
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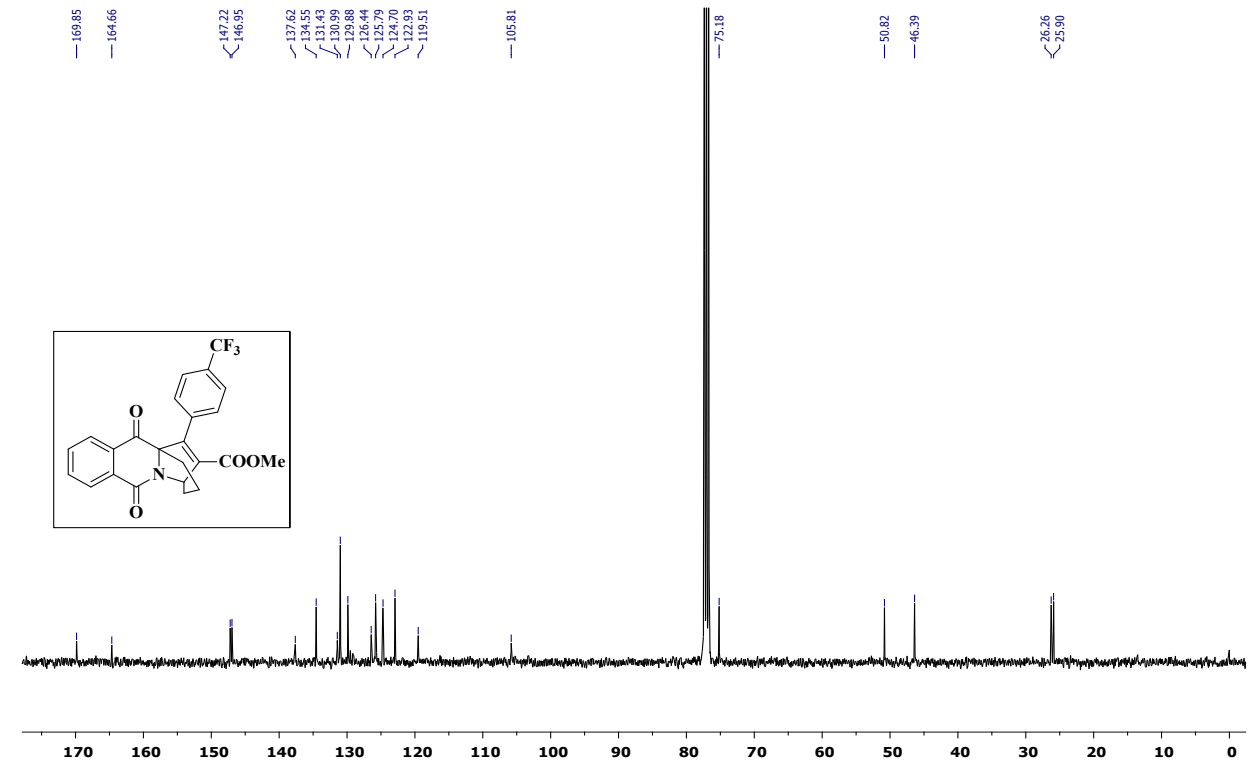
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25.90
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COOMe
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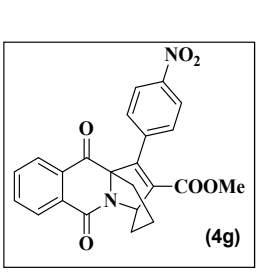
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N
O
(4g)

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2.11
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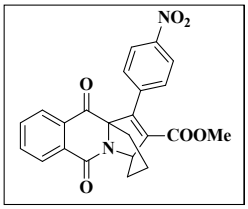
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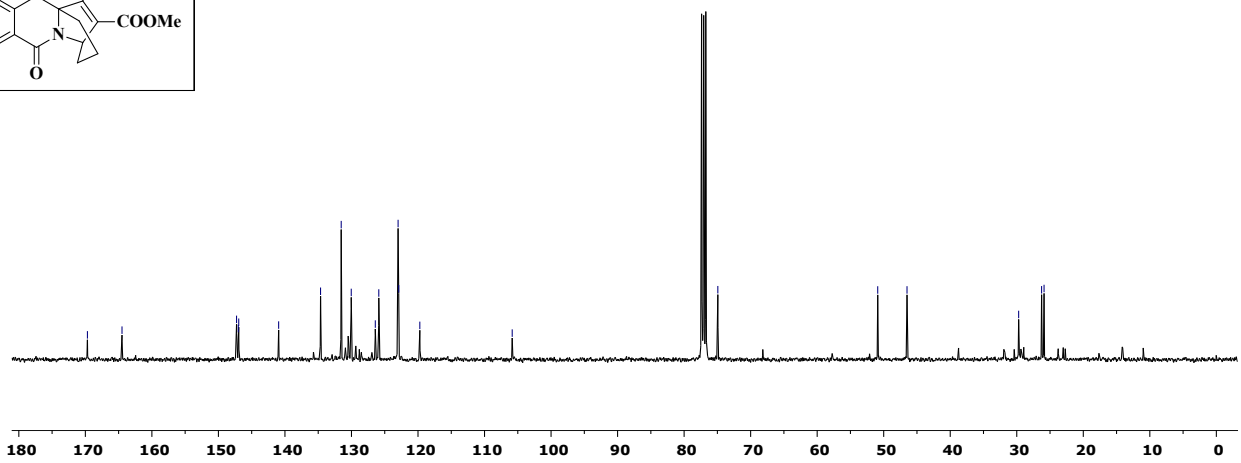
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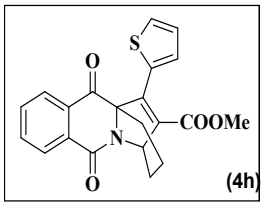
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COOMe
N
O
(4h)

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0.96
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1.00
1.00
1.05
1.03
2.01
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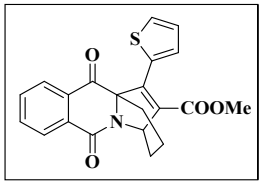
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N
O

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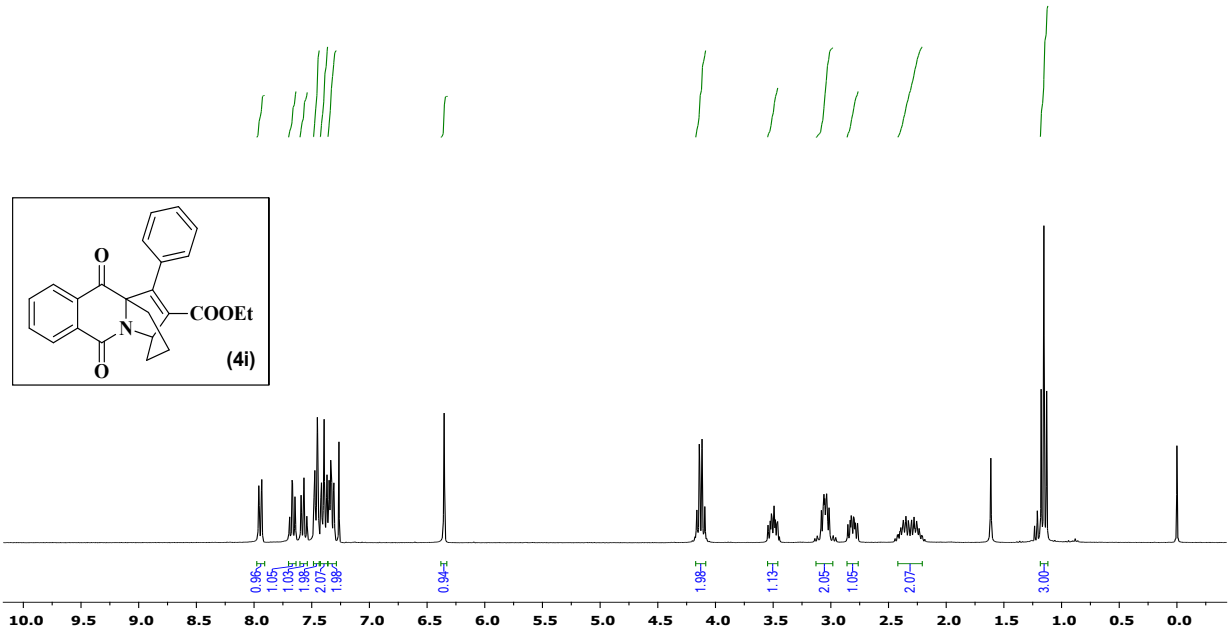
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O
(4i)
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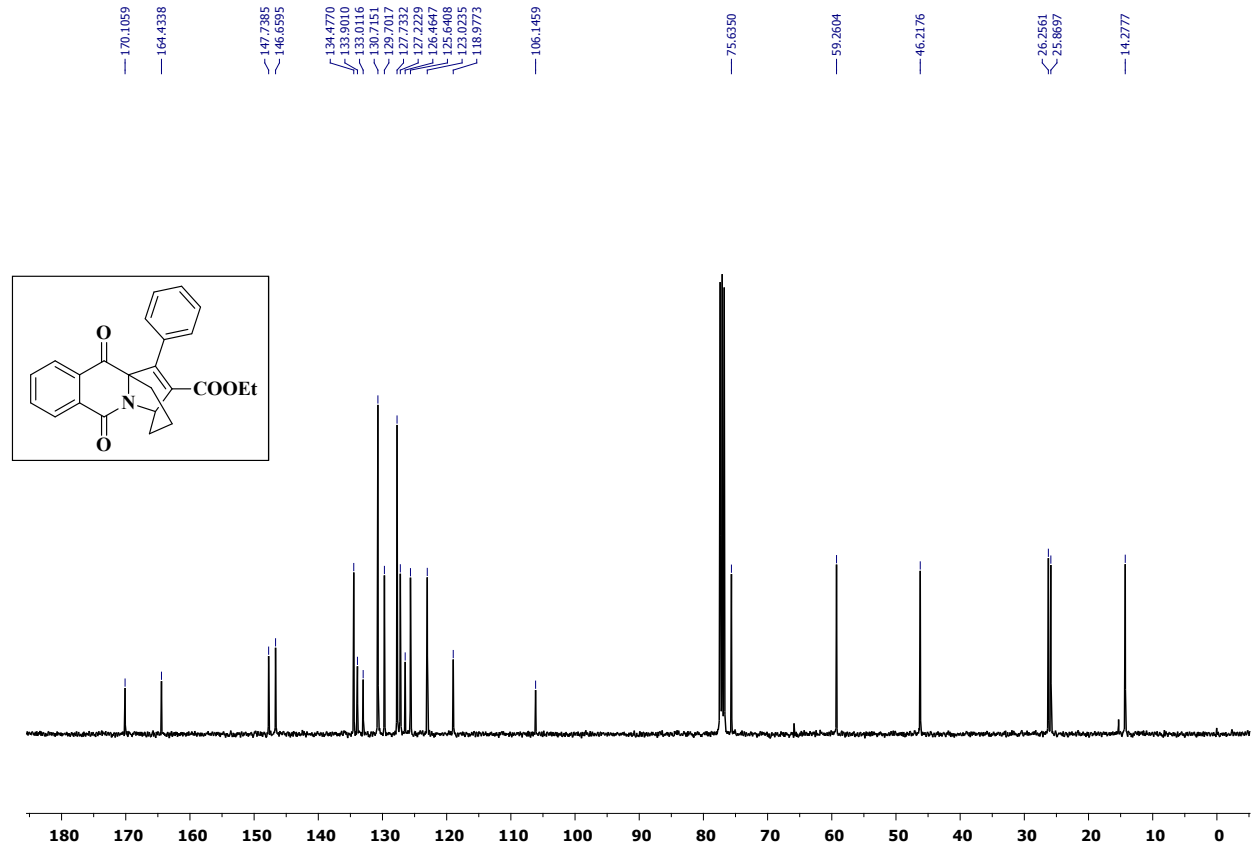
1.13
2.05
1.05
2.07
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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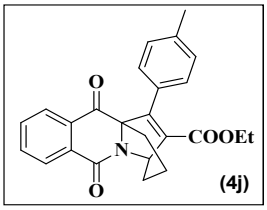
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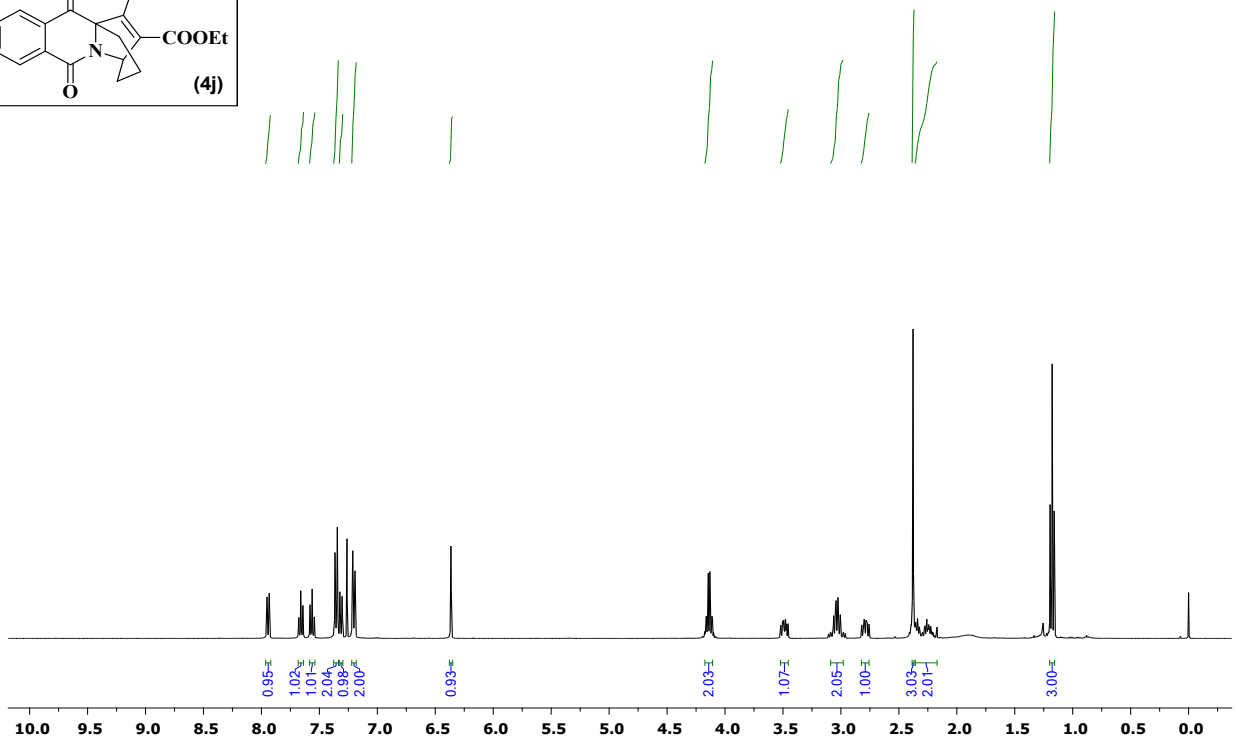
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3.00
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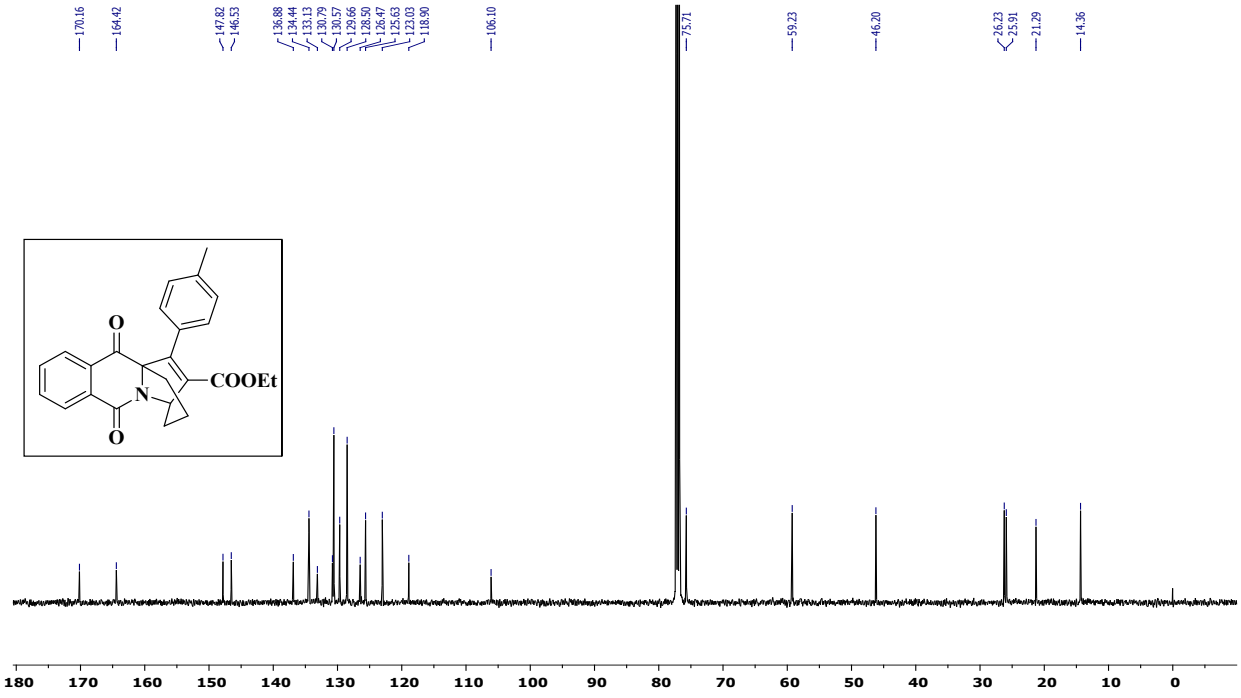
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N
COOEt
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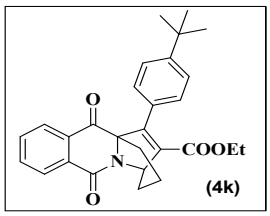
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(4k)

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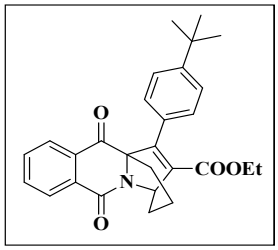
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COOEt
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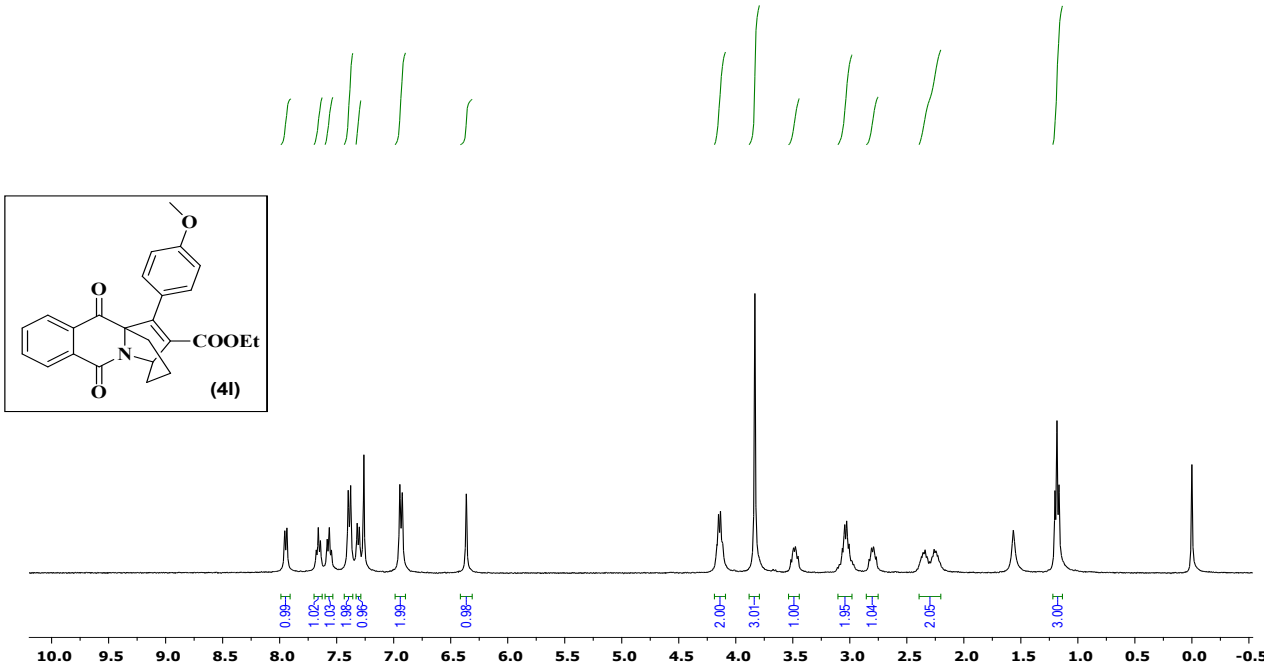
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1.00
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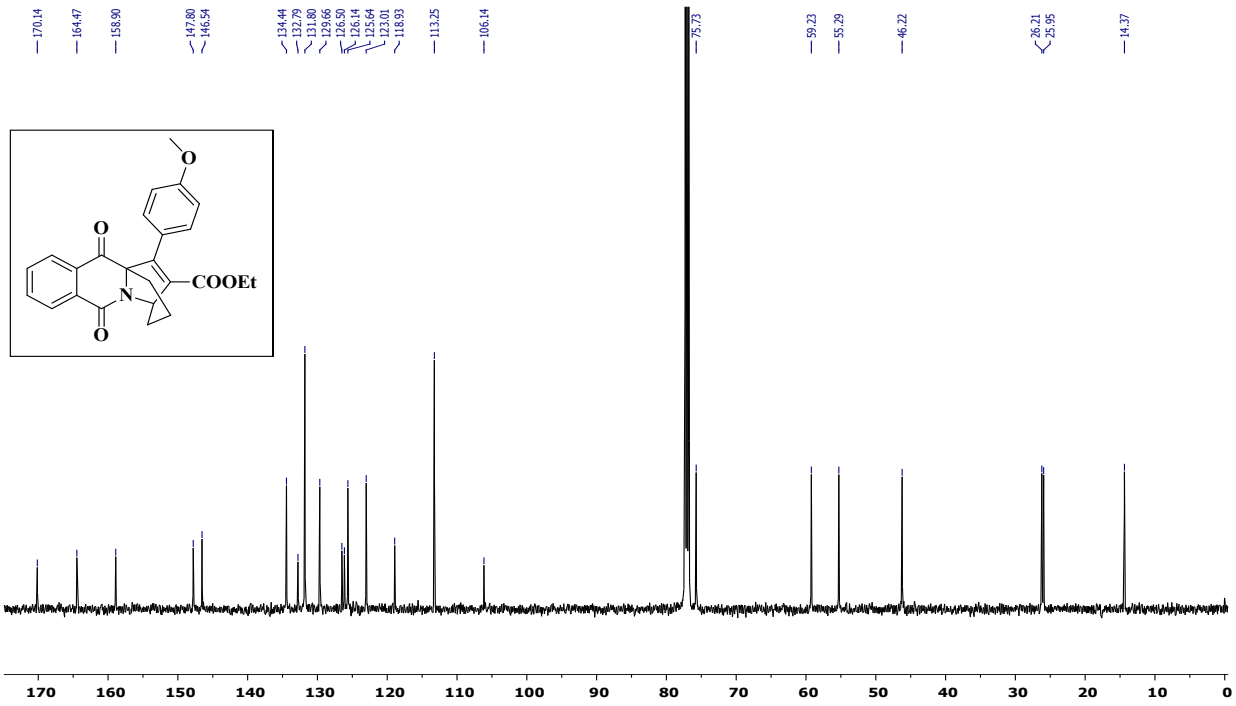
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123.01
118.93
113.25
106.14
75.73
59.23
55.29
46.22
26.21
25.95
14.37
O
O
COOEt
N
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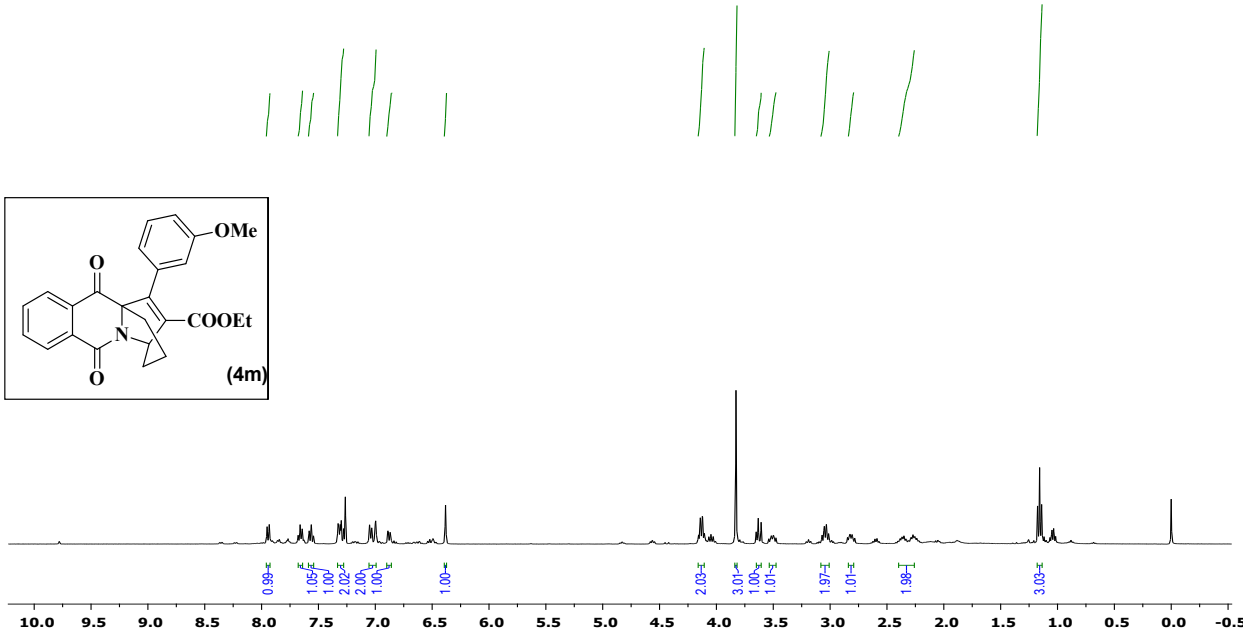
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O
(4m)
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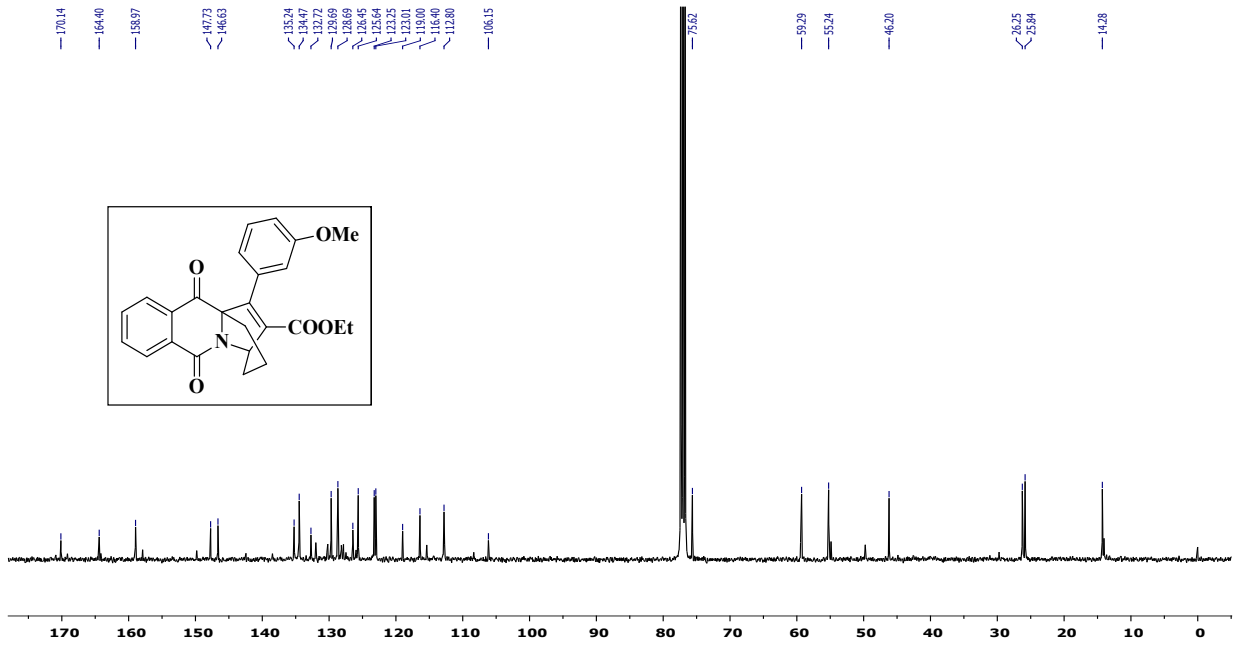
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158.97
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132.72
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128.69
126.45
125.64
123.25
123.01
119.00
116.40
112.80
106.15
75.62
59.29
55.24
46.20
26.25
25.84
14.28
OMe
O
COOEt
N
O
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150
140
130
120
110
100
90
80
70
60
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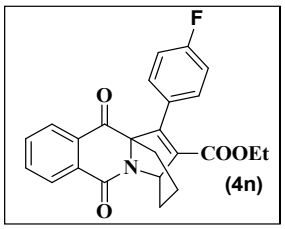
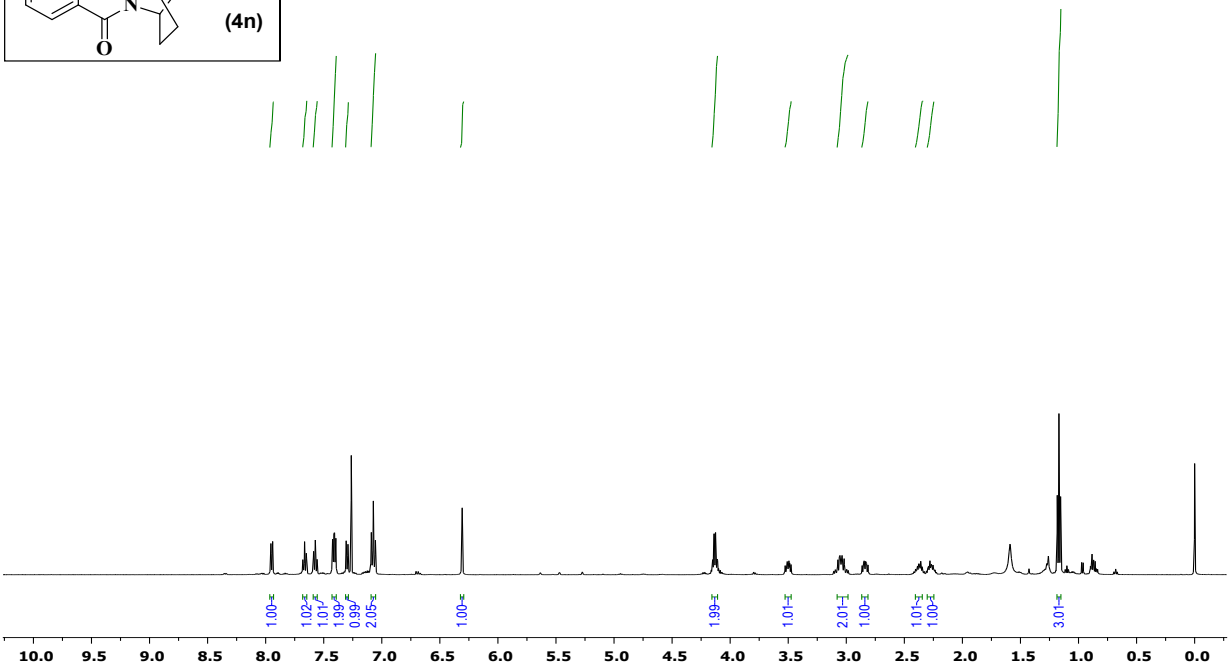
40
30
20
10
0


F
O
N
COOEt
O
(4n)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1.01
1.99
0.99
2.05
1.00
1.99
1.01
2.01
1.00
1.01
1.00
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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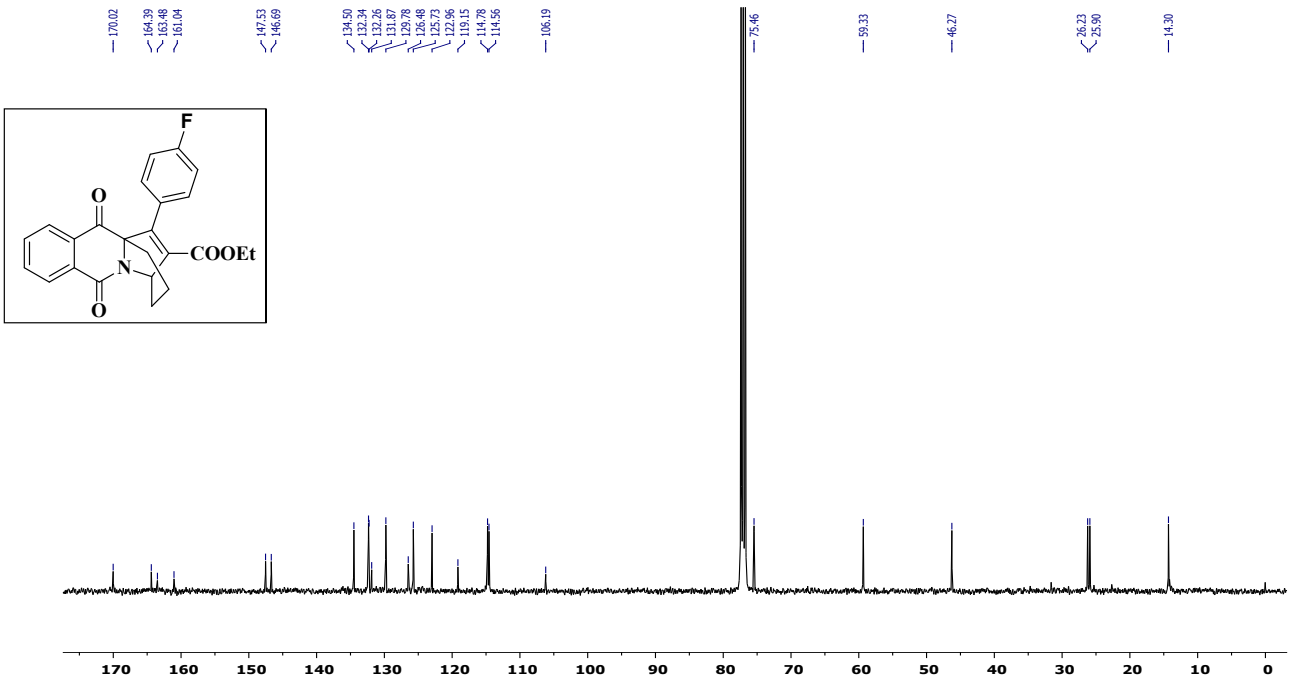
0.0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164.39
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134.50
132.34
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126.48
125.73
122.96
119.15
114.78
114.56
106.19
75.46
59.33
46.27
26.23
25.90
14.30
F
O
N
COOEt
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110
100
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70
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50
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30
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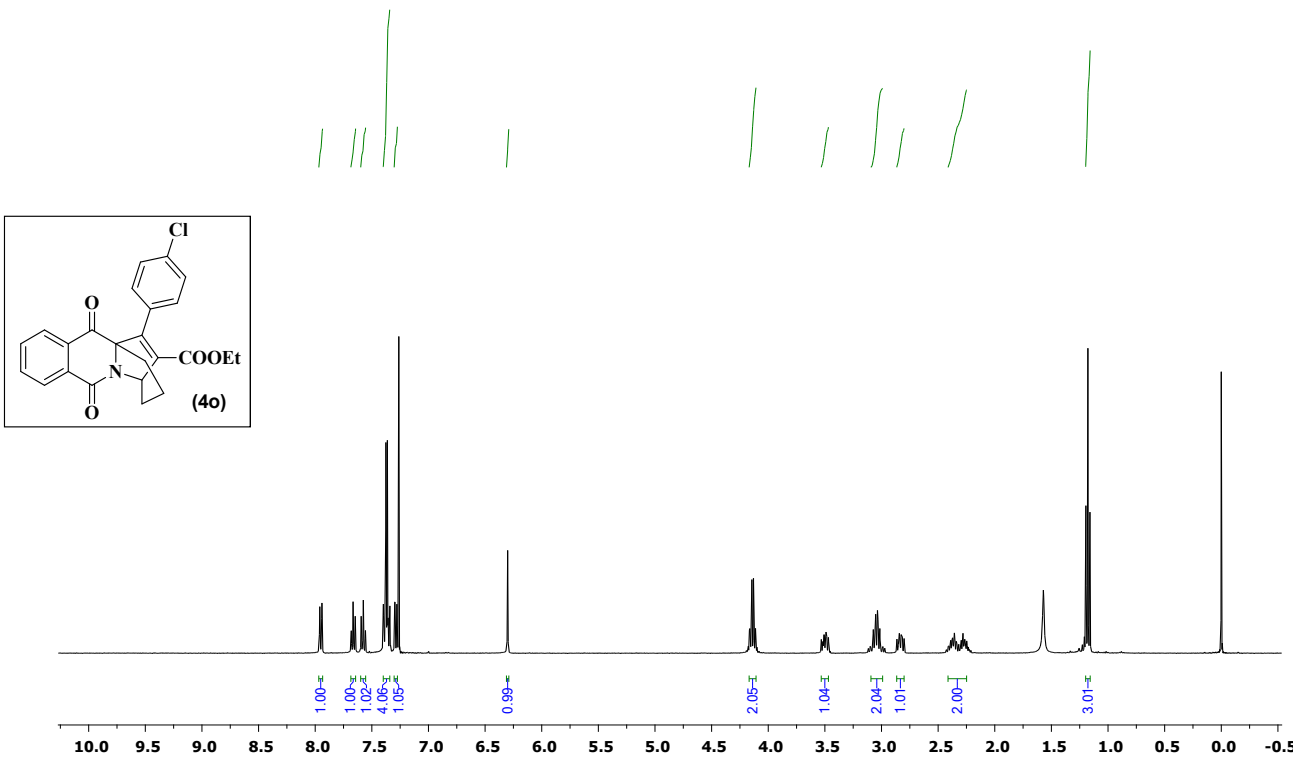
Cl
O
O
N
COOEt
O
(4o)
1.00
1.00
1.02
4.06
1.05
0.99
2.05
1.04
2.04
1.01
2.00
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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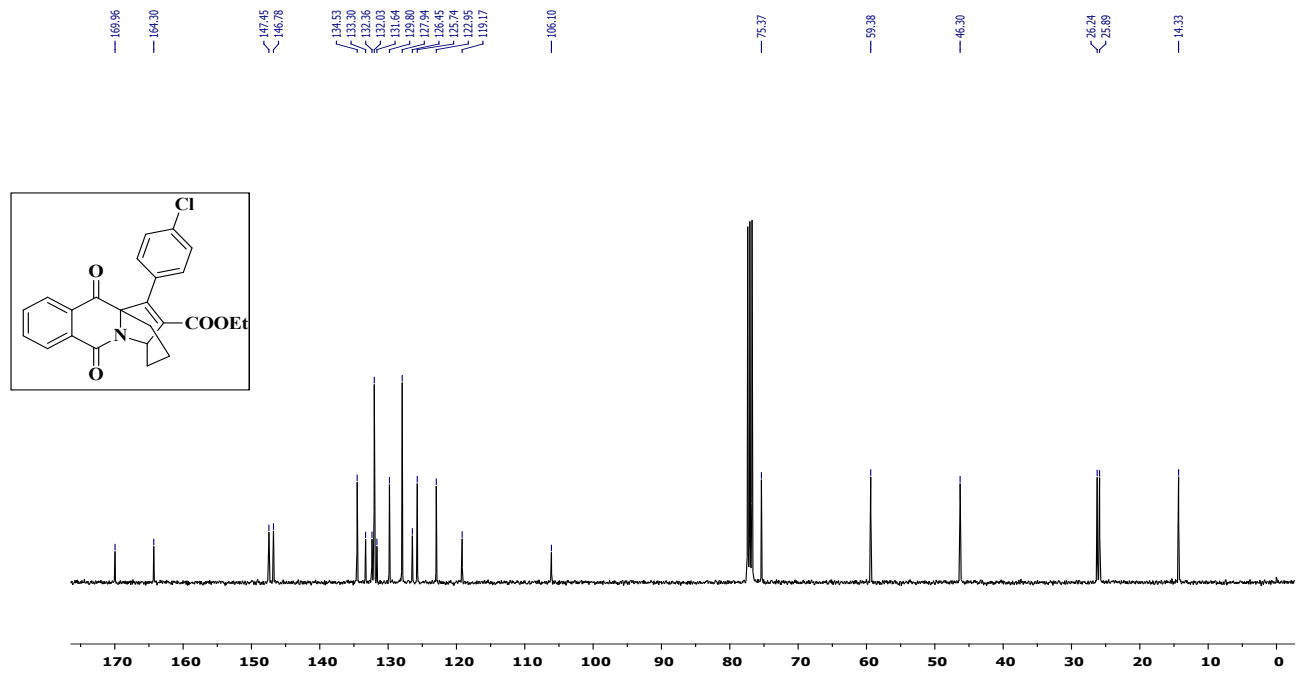
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5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132.36
132.03
131.64
129.80
127.94
126.45
125.74
122.95
119.17
106.10
75.37
59.38
46.30
26.24
25.89
14.33
Cl
O
O
N
COOEt
O
170
160
150
140
130
120
110
100
90
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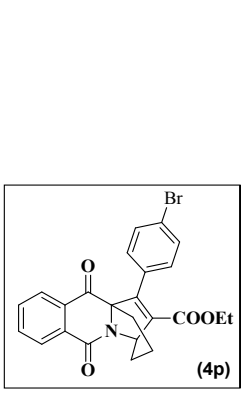
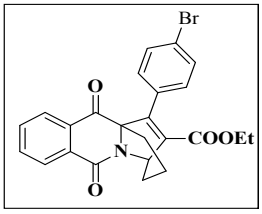
70
60
50
40
30
20
10
0


Br
O
COOEt
N
O
(4p)

0.98
1.04
1.06
1.99
3.00
0.98
2.01
1.02
2.02
1.00
2.00
3.00
10.0
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


169.94
164.28
147.43
146.79
134.53
132.84
132.36
131.63
130.89
129.80
126.45
125.74
122.95
121.51
119.13
106.06
75.36
59.38
46.30
26.24
25.89
14.33


Br
O
COOEt
N
O

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150
140
130
120
110
100
90
80
70
60
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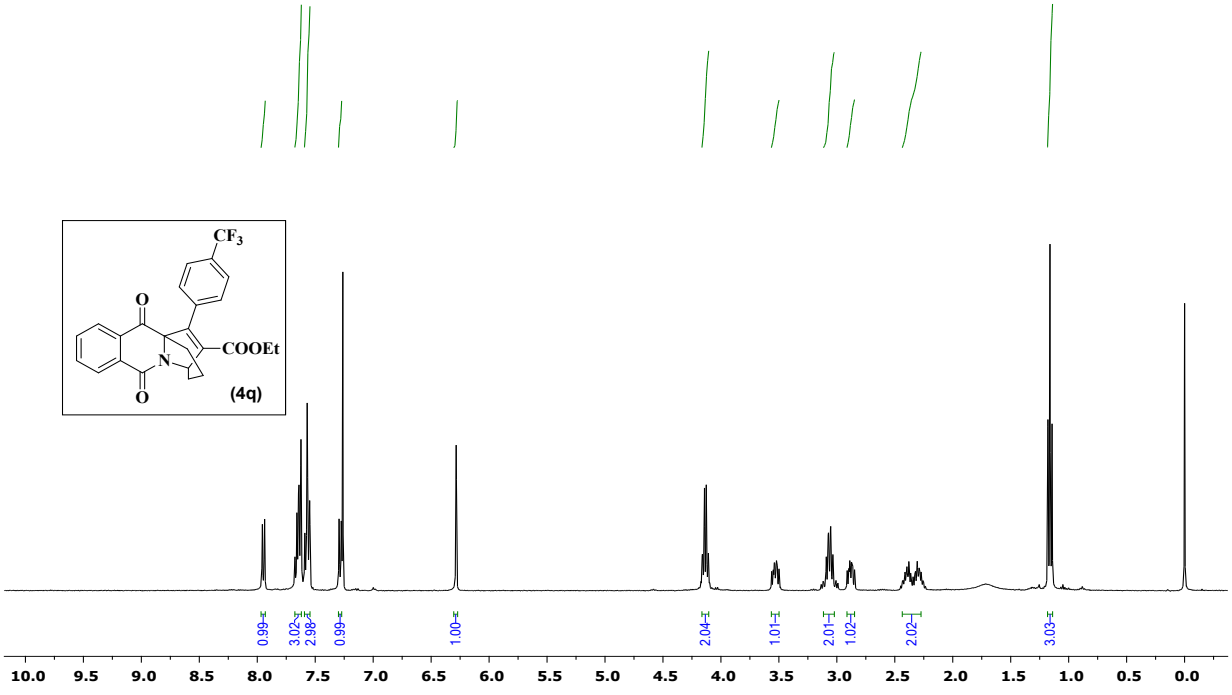
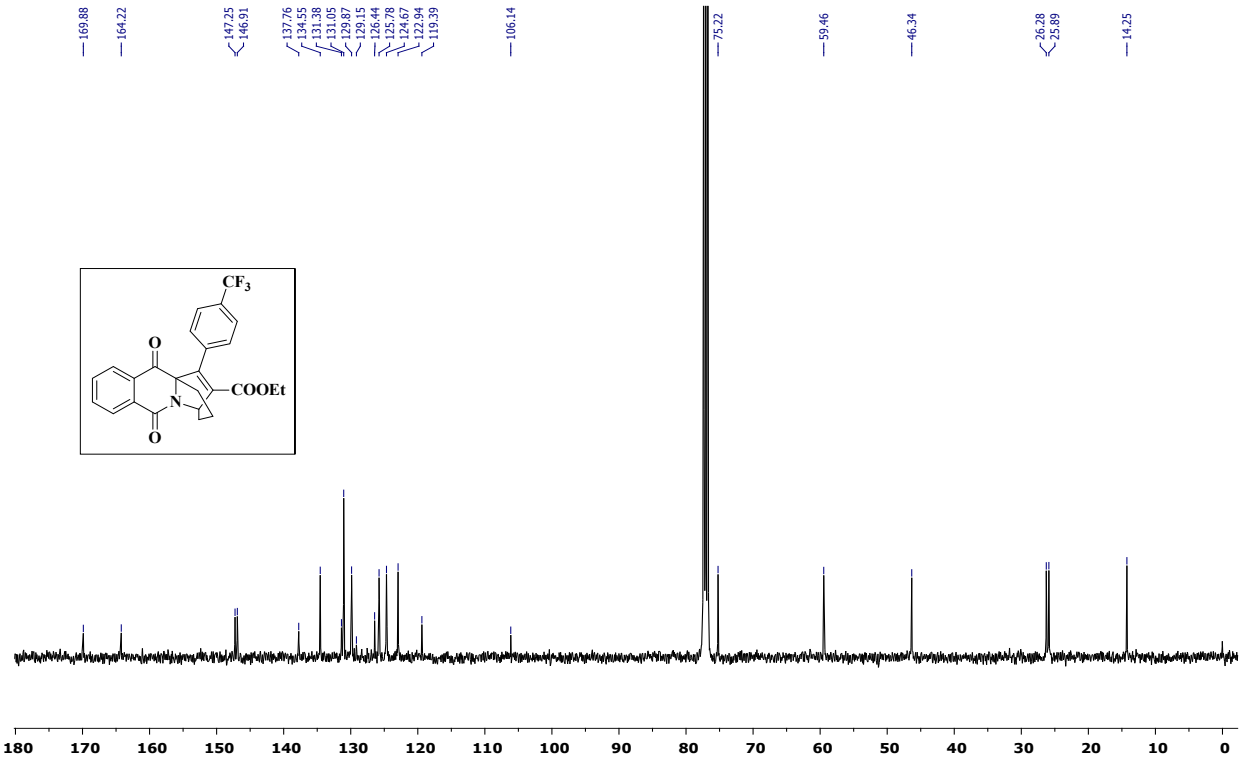
30
20
10
0


CF3
O
O
N
COOEt
O
(4q)
0.99
3.02
2.98
0.99
1.00
2.04
1.01
2.01
1.02
2.02
3.09
10.0 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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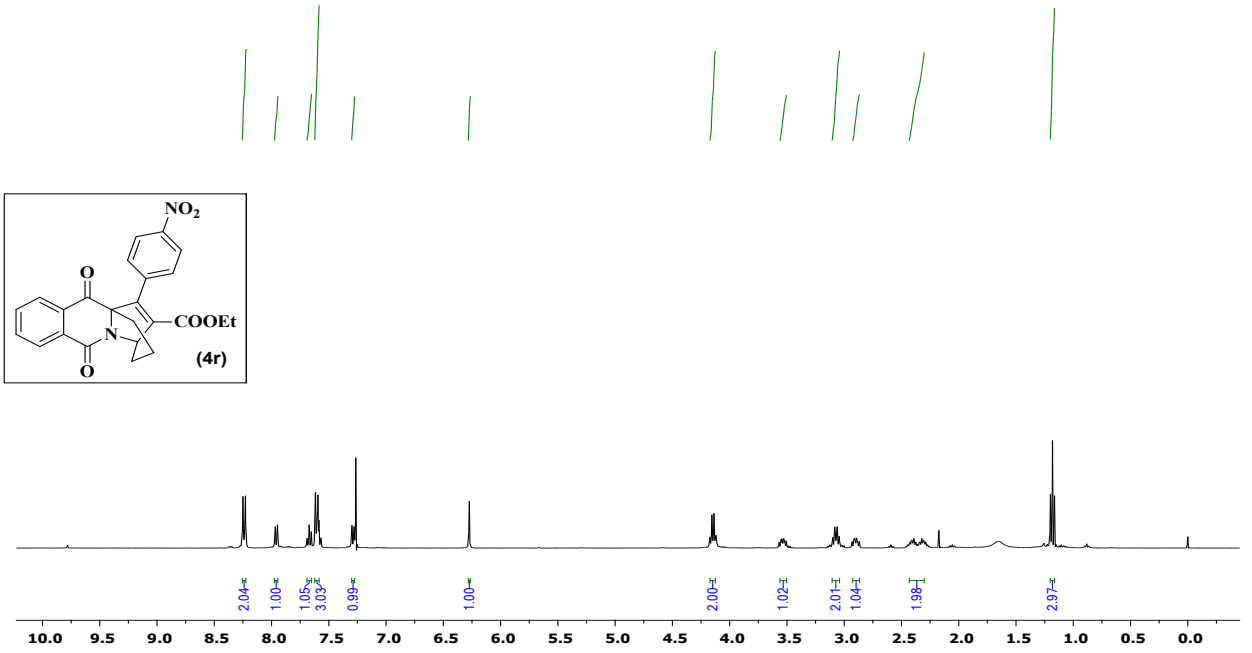
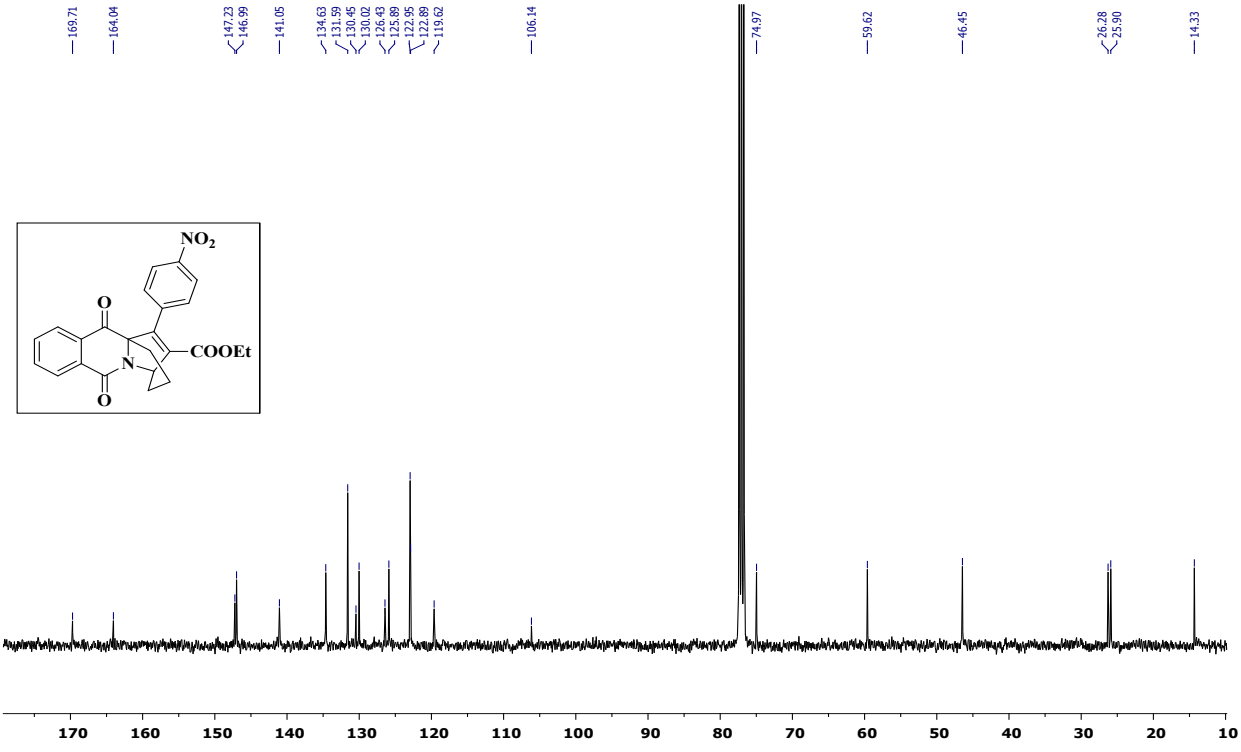
134.55
131.38
131.05
129.87
129.15
126.44
125.78
124.67
122.94
119.39
106.14
75.22
59.46
46.34
26.28
25.89
14.25
CF3
O
O
N
COOEt
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


NO2
O
COOEt
N
O
(4r)
2.04
1.00
1.05
3.03
0.99
1.00
2.00
1.02
2.01
1.04
1.98
2.97
10.0
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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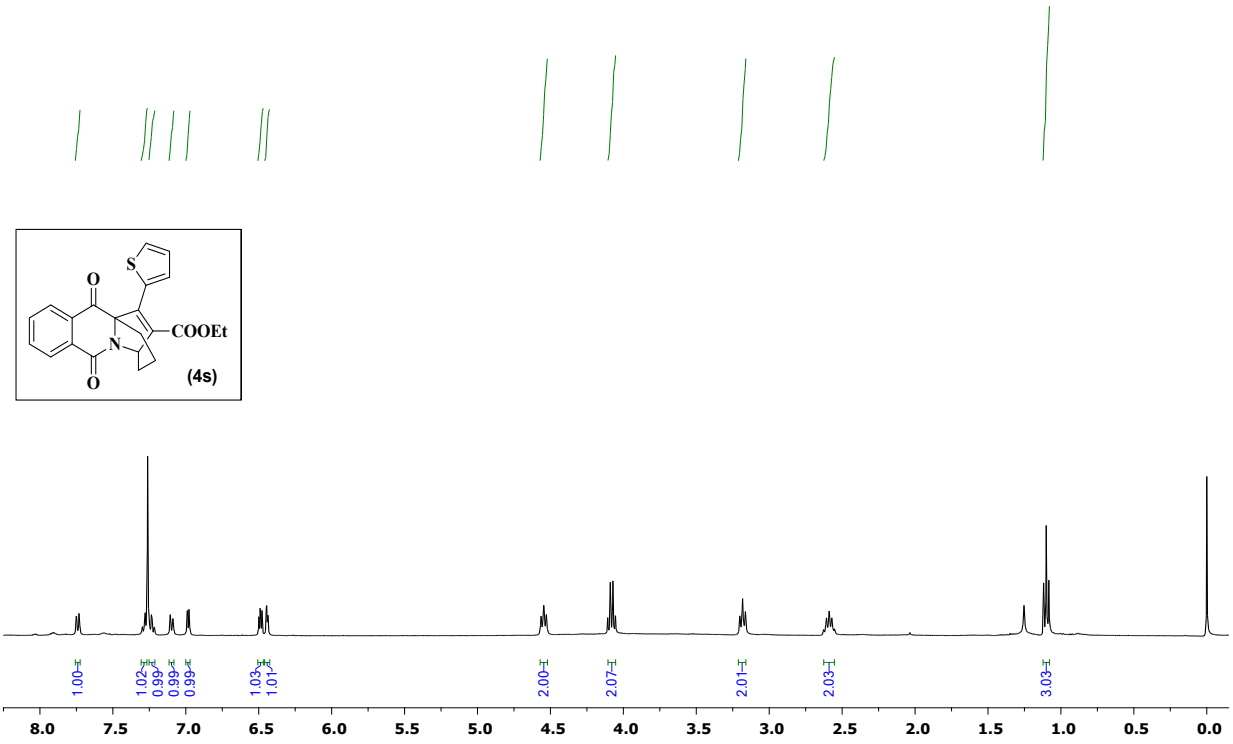
131.59
130.45
130.02
126.43
125.89
122.95
122.89
119.62
106.14
74.97
59.62
46.45
26.28
25.90
14.33
NO2
O
COOEt
N
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


S
O
COOEt
N
O
(4s)
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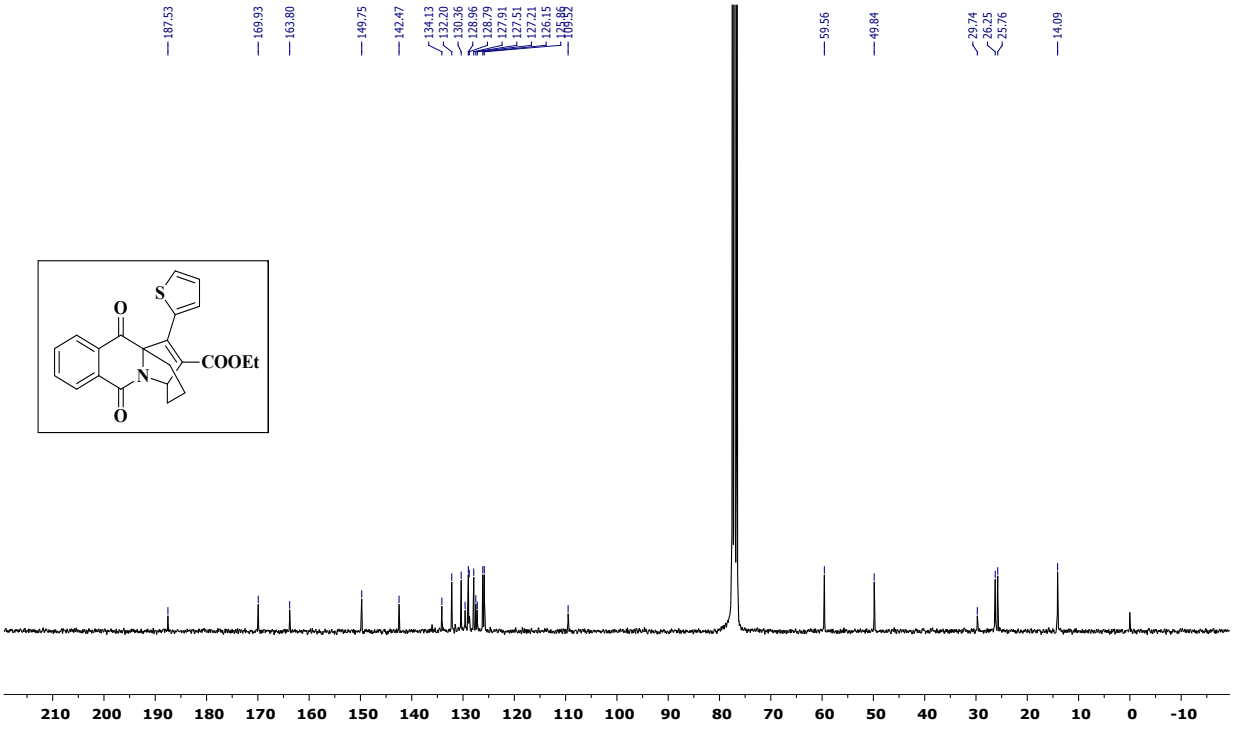
1.02
0.99
0.99
0.99
1.03
1.01
2.00
2.07
2.01
2.03
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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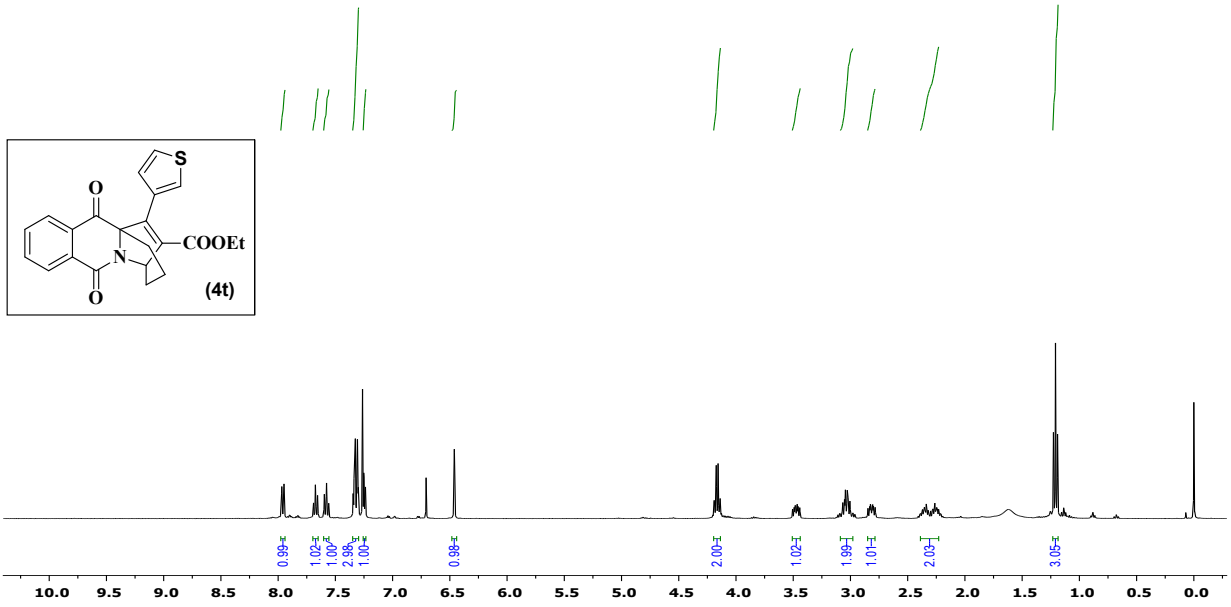
134.13
132.20
130.36
128.96
128.79
127.91
127.51
127.21
126.15
59.56
49.84
29.74
26.25
25.76
14.09
S
O
COOEt
N
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


S
O
O
N
COOEt
(4t)
0.99
1.02
1.00
2.98
1.00
0.98
2.00
1.02
1.99
1.01
2.03
3.05
10.0
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
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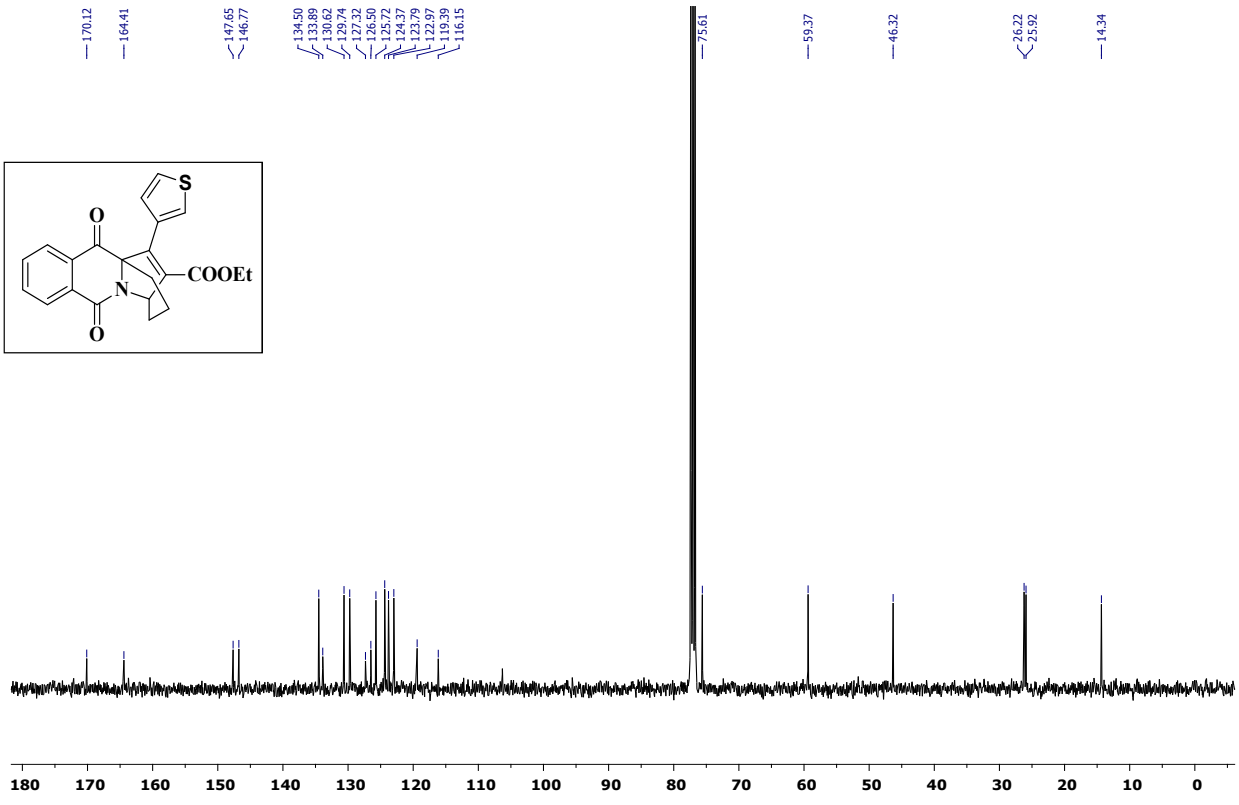
1.0
0.5
0.0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133.89
130.62
129.74
127.32
126.50
125.72
124.37
123.79
122.97
119.39
116.15
75.61
59.37
46.32
26.22
25.92
14.34
S
O
O
N
COOEt
180
170
160
150
140
130
120
110
100
90
80
70
60
50
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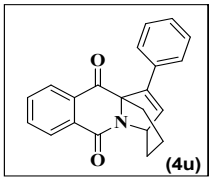
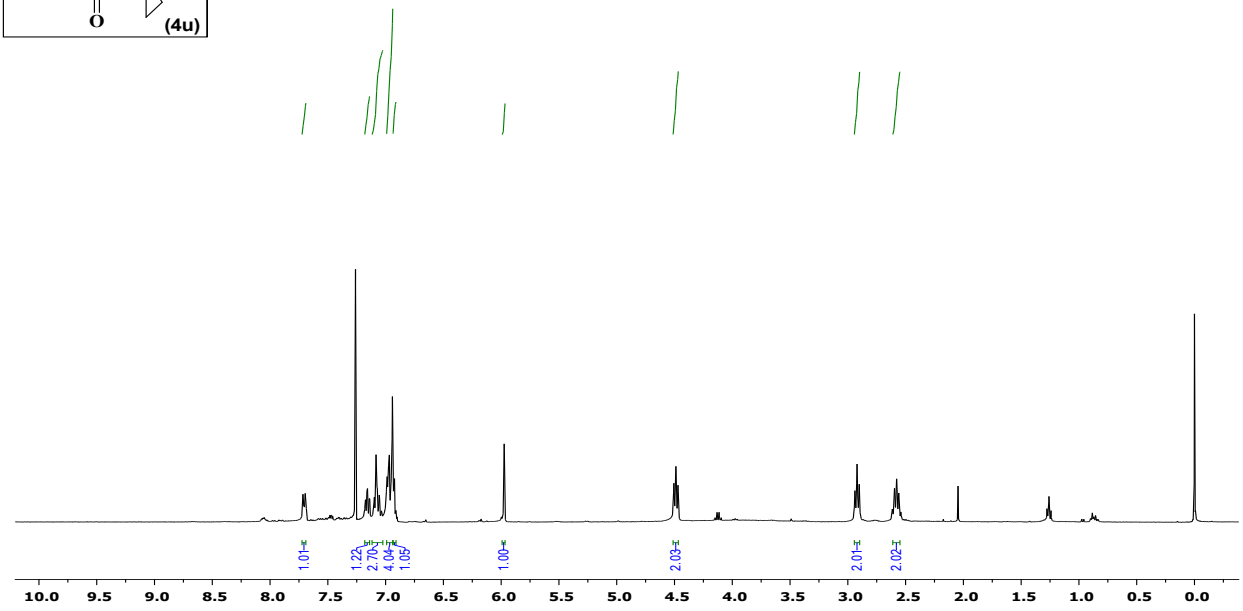
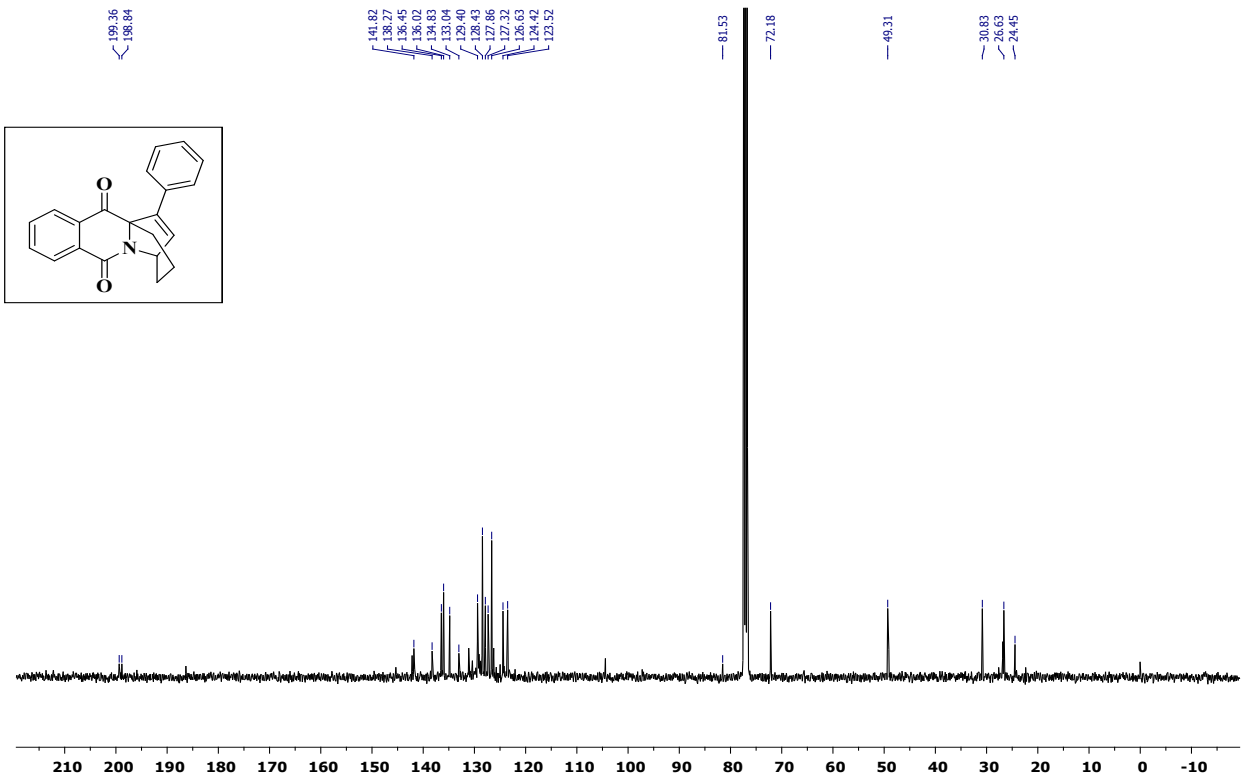
30
20
10
0


O
N
O
(4u)


1.01
1.22
2.70
4.04
1.05
1.00
2.03
2.01
2.02
10.0 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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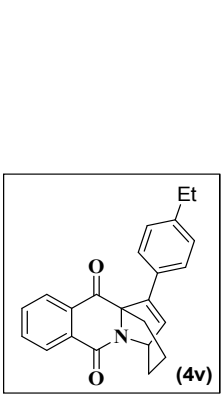
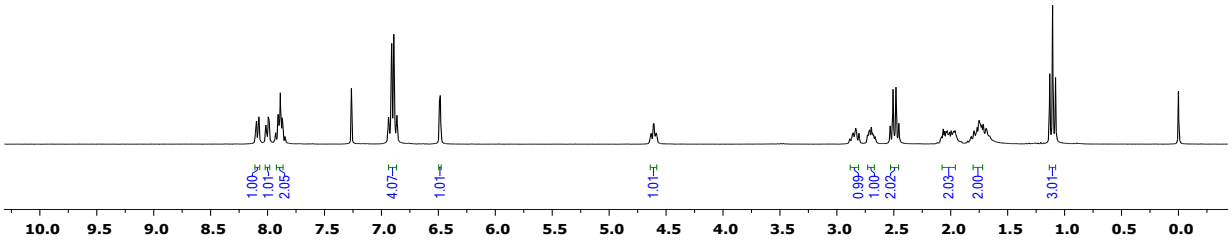
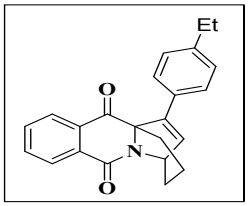
198.84
141.82
138.27
136.45
136.02
134.83
133.04
129.40
128.43
127.86
127.32
126.63
124.42
123.52
81.53
72.18
49.31
30.83
26.63
24.45
O
N
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Et
O
N
O
(4v)


1.00
1.01
2.05
4.07
1.01
1.01
0.99
1.00
2.02
2.03
2.00
3.01
10.0 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


Et
O
N
O

199.25
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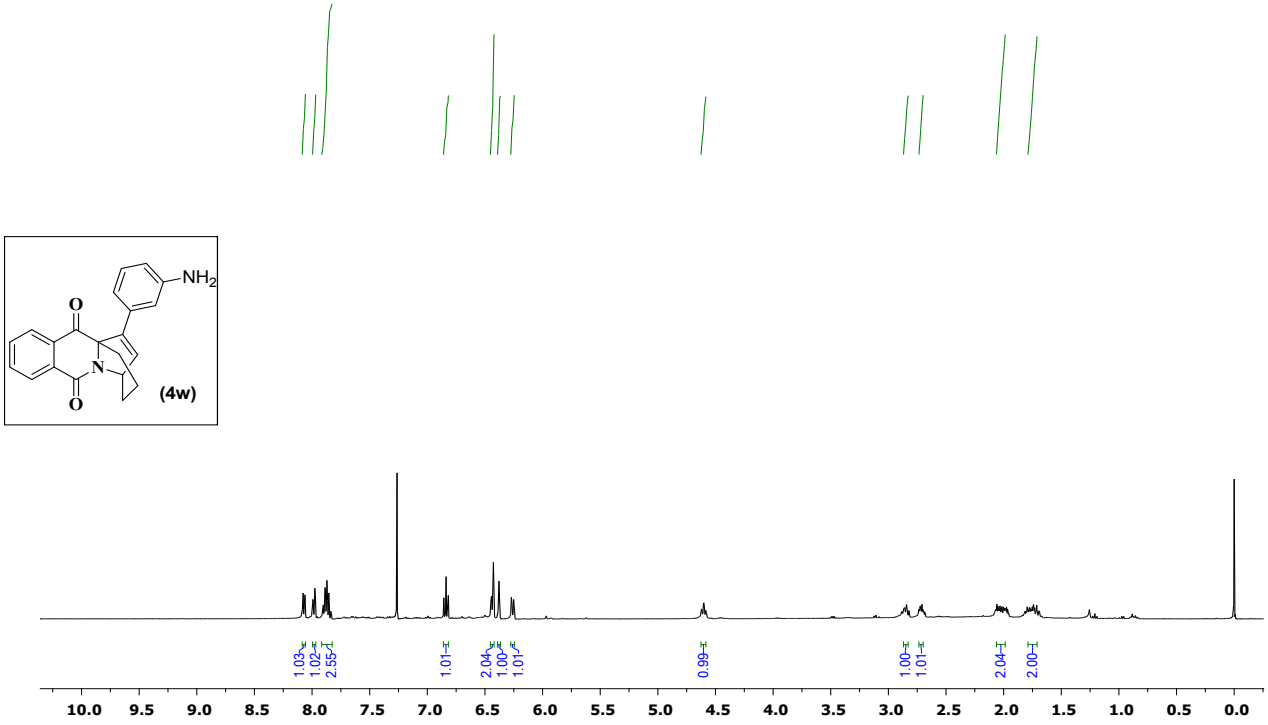
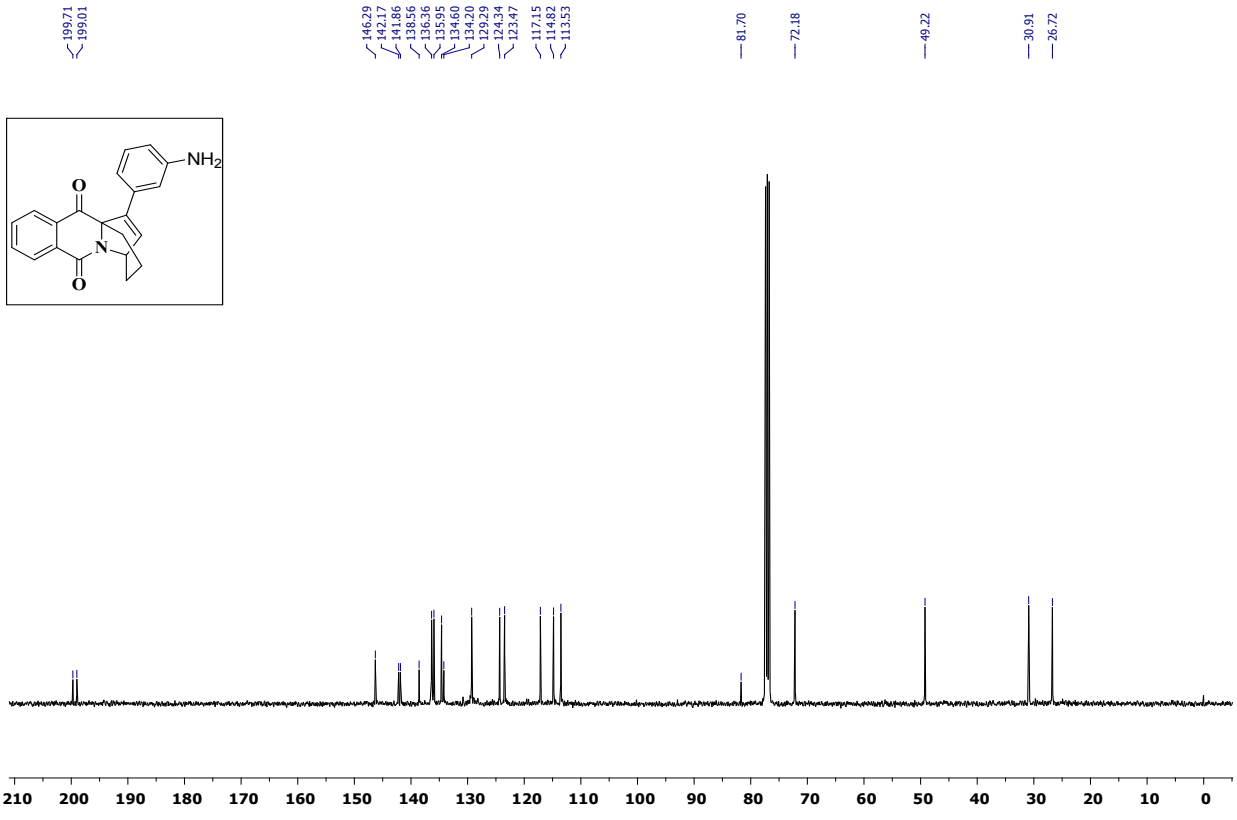
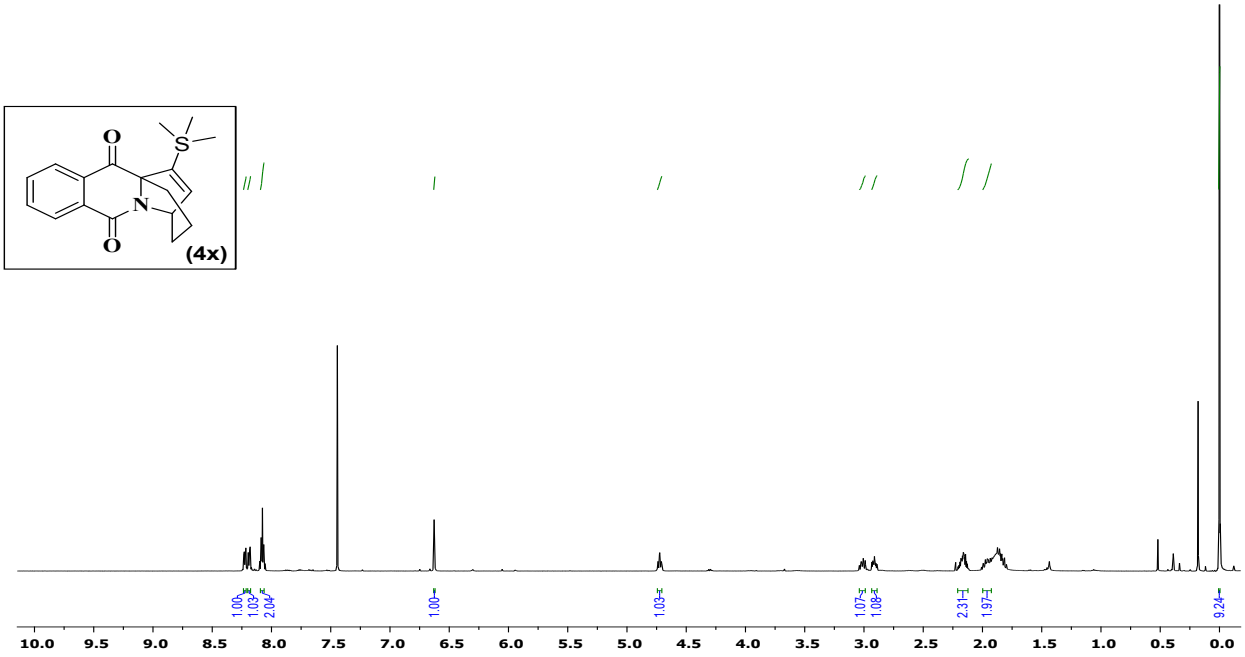
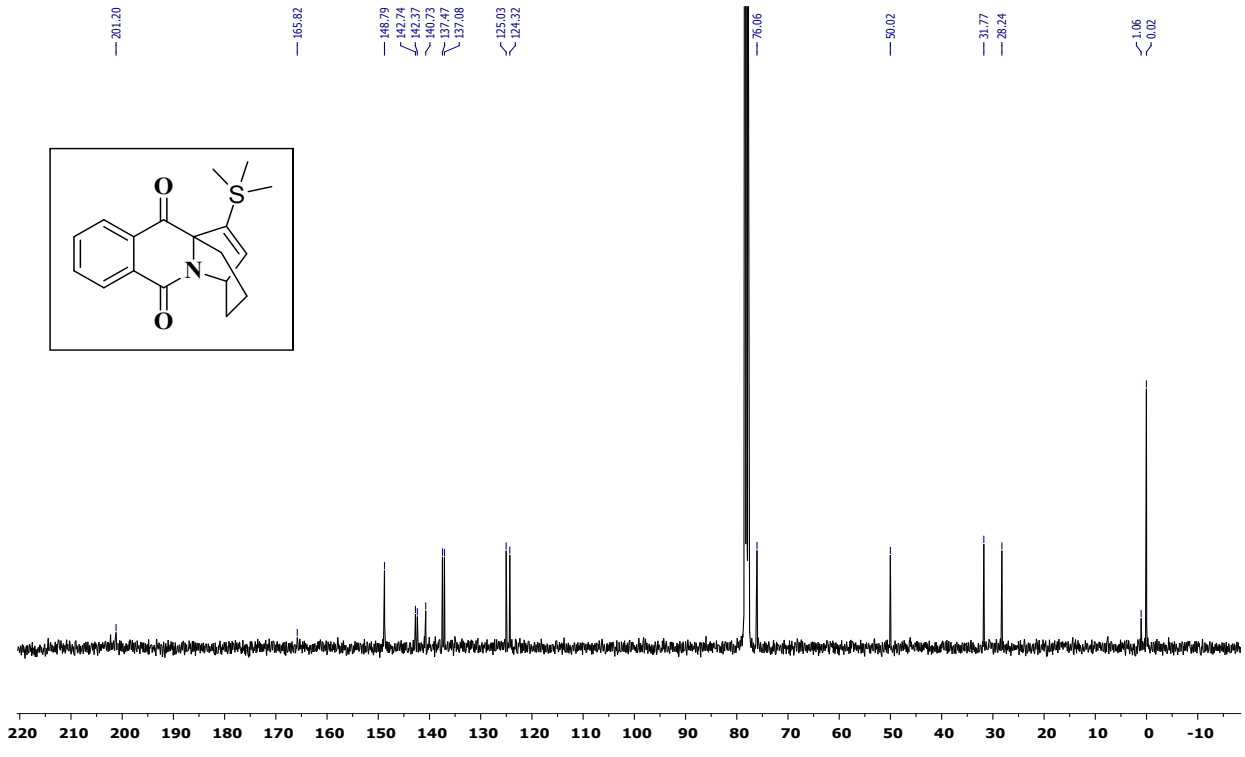
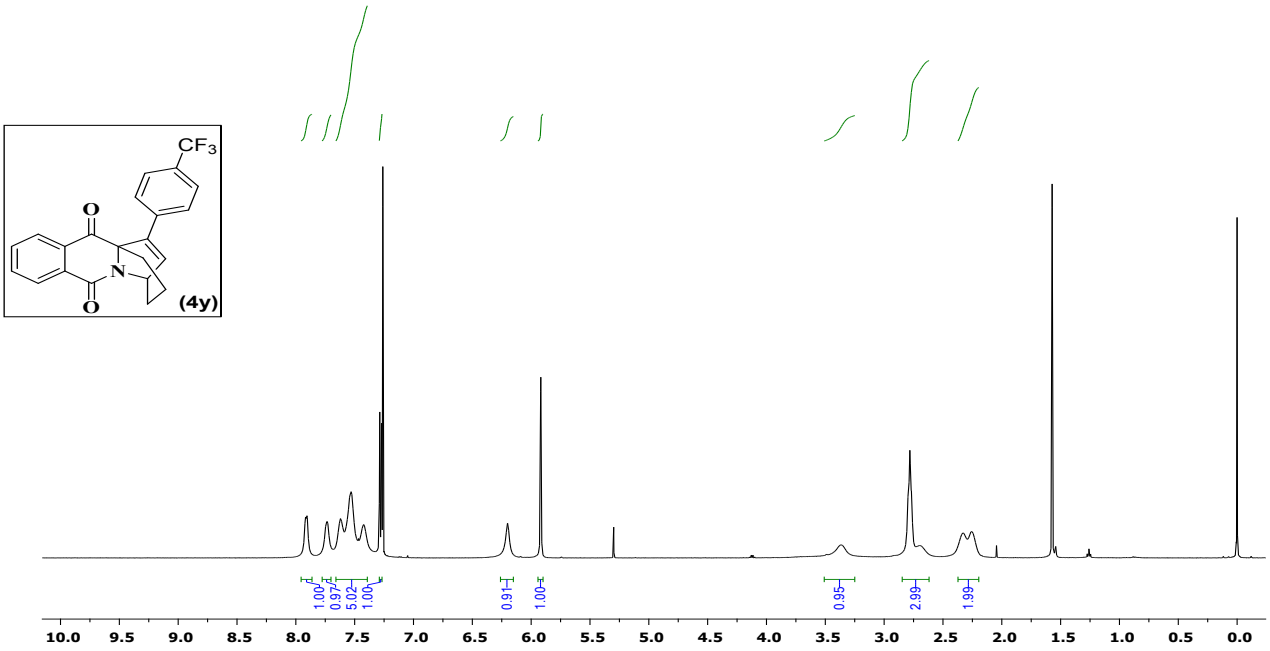
138.14
136.46
136.04
133.88
130.24
127.95
126.52
125.73
124.42
123.55
81.29
72.17
49.38
30.82
28.42
26.58
15.27
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

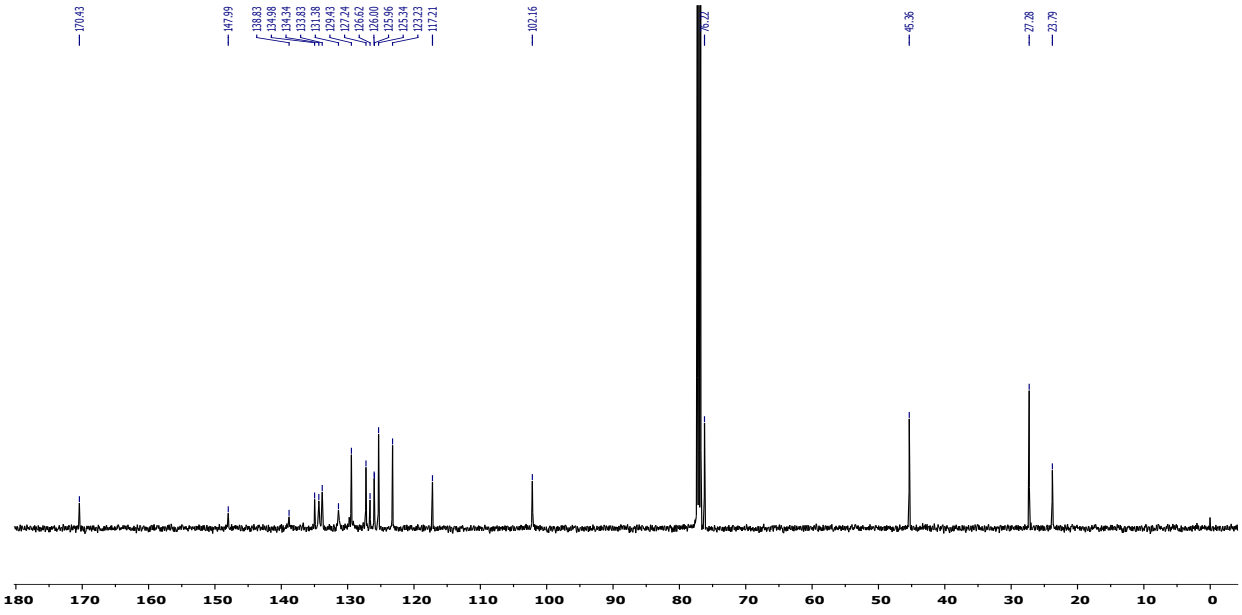

NH2
O
N
O
(4w)
1.03
1.02
2.55
1.01
2.04
1.00
1.01
0.99
1.00
1.01
2.04
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


199.71
199.01
146.29
142.17
141.86
138.56
136.36
135.95
134.60
134.20
129.29
124.34
123.47
117.15
114.82
113.53
81.70
72.18
49.22
30.91
26.72
NH2
O
N
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

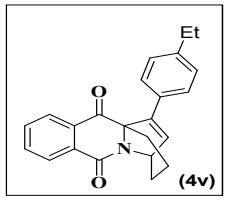

(4x)
1.00
1.03
2.04
1.00
1.03
1.07
1.08
2.31
1.97
9.24
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

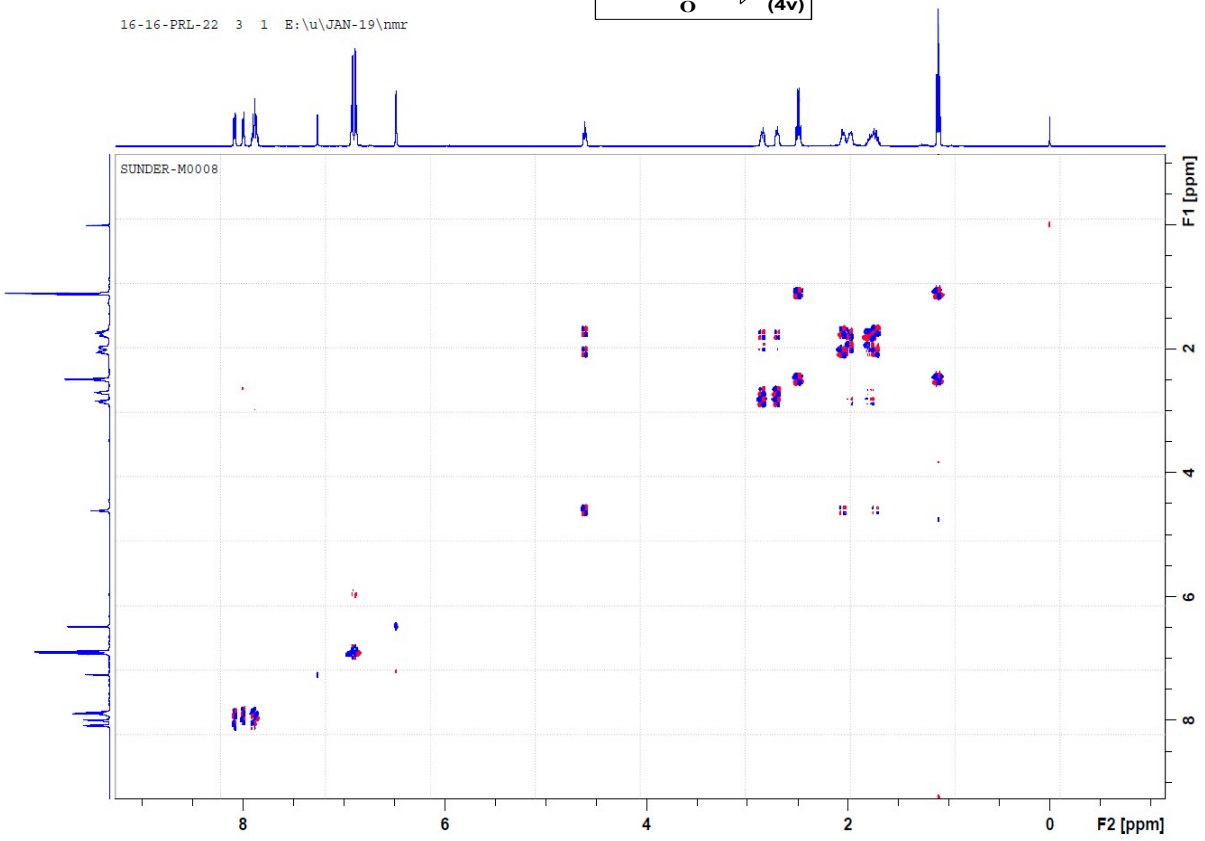

201.20
165.82
148.79
142.74
142.37
140.73
137.47
137.08
125.03
124.32
76.06
50.02
31.77
28.24
1.06
0.02
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

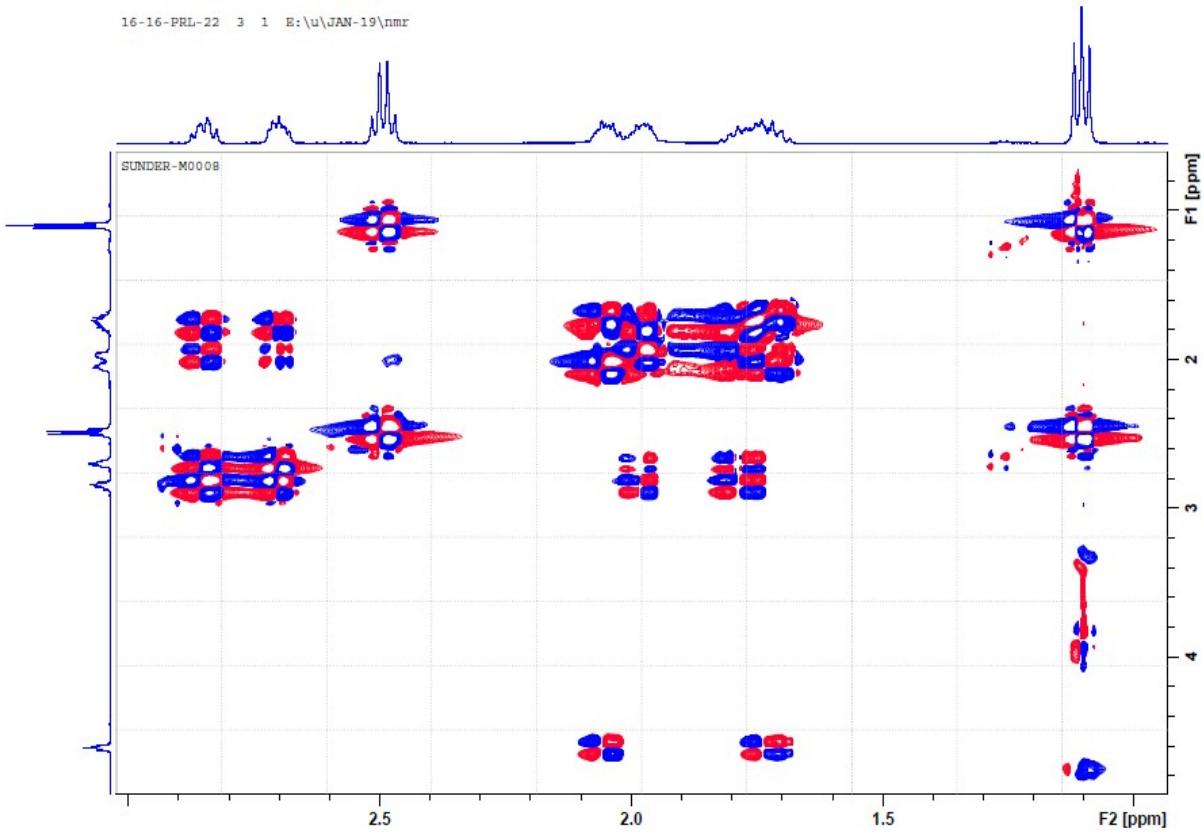

CF3
O
N
O
(4y)
1.00
0.97
5.02
1.00
0.91
1.00
0.95
2.99
1.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


170.43
147.99
138.83
134.98
134.34
133.83
131.38
129.43
127.24
126.62
126.00
125.96
125.34
123.23
117.21
102.16
76.72
65.36
27.28
23.79
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

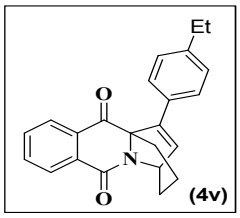
COSY for compound (4v):

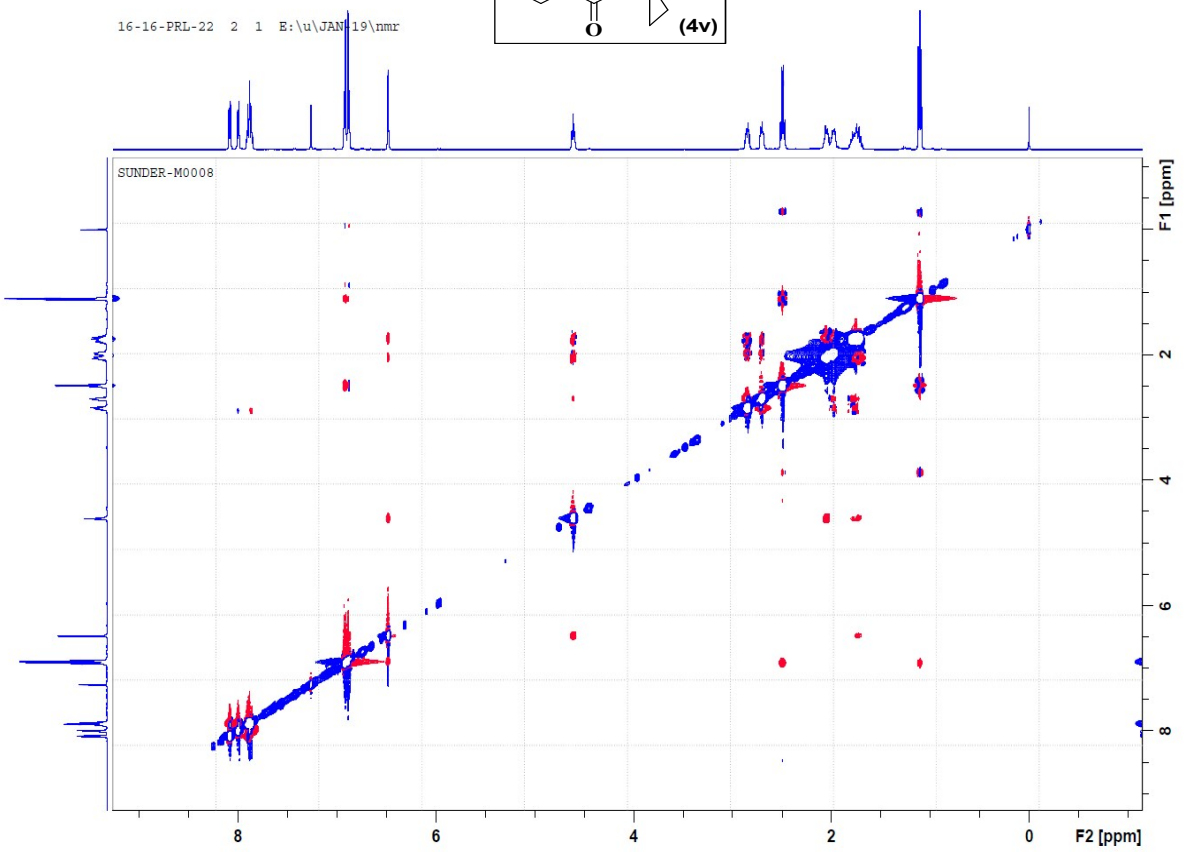


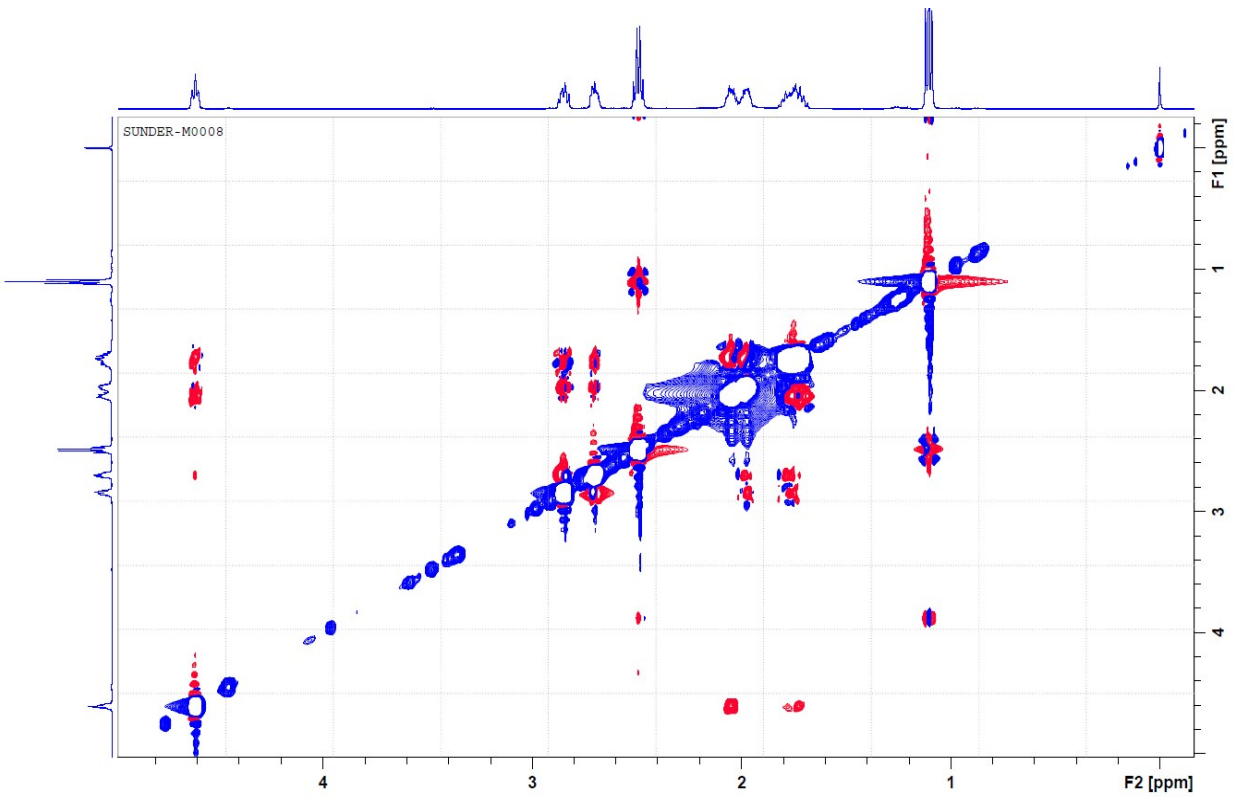




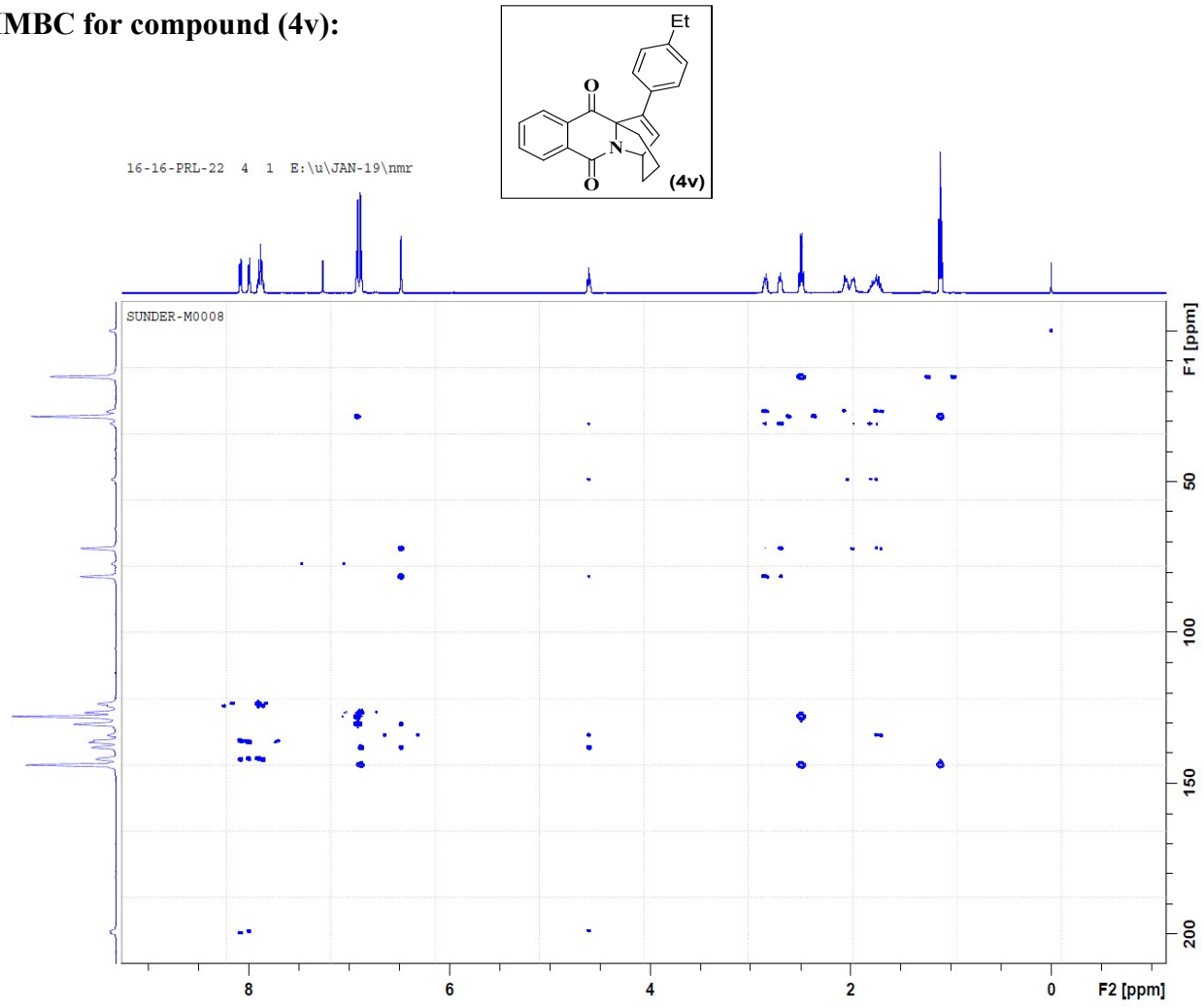
NOESY for compound (4v):



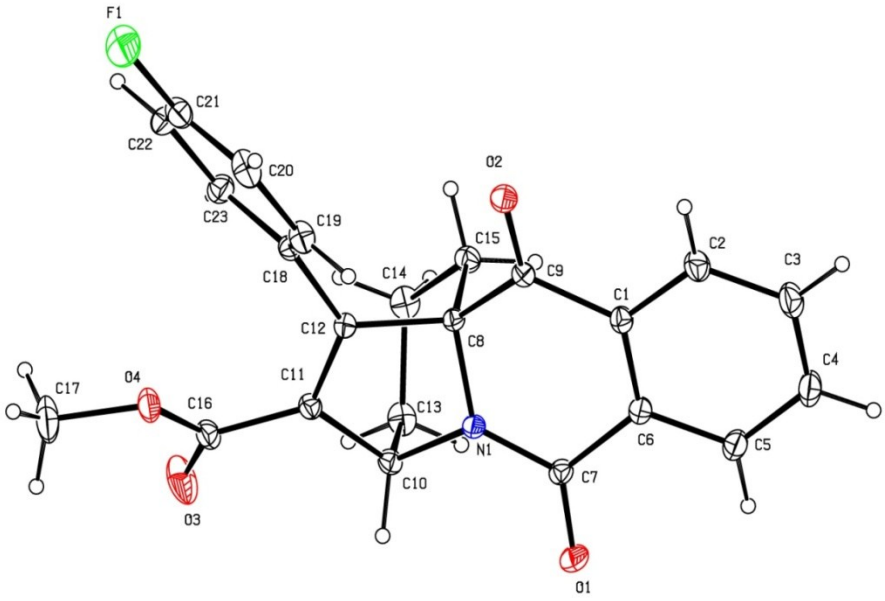




HMBC for compound (4v):



X-ray crystallography



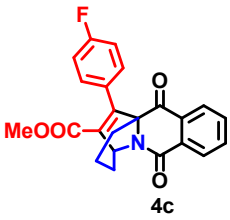


Figure caption: (4c) The molecular structure of KA181, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

X-ray crystallography study

X-ray data for the compound was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames of KA181 were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms of were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

Crystal Data for KA181: C23H18FNO4 (M =391.38 g/mol): triclinic, space group P-1 (no. 2), a = 8.66220(10) Å, b = 10.7712(2) Å, c = 11.1760(2) Å, α = 102.4181(5)°, β = 97.3598(5)°, γ = 113.4266(4)°, V = 907.47(3) Å3, Z = 2, T = 294.15 K, μ(MoKα) = 0.105 mm-1, Dcalc = 1.432 g/cm3, 31589 reflections measured (4.31° ≤ 2Θ ≤ 56.928°), 4553 unique (Rint = 0.0238, Rsigma = 0.0189) which were used in all calculations. The final R1 was 0.0457 (I > 2σ(I)) and wR2 was 0.1321 (all data). CCDC 1584703 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1.SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.

2.Sheldrick, G. M. (2015). Acta Cryst. C71, 3–8.

Figure caption: The molecular structure of KA181, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.