Supporting Information

Catalytic Asymmetric Synthesis of Diketopiperazines by Intramolecular Tsuji-Trost Allylation

Matteo Faltracco[†], Silvia Cotogno[†], Christophe M. L. Vande Velde[‡] and Eelco Ruijter[*,†]

[†] Department of Chemistry & Pharmaceutical Sciences, Amsterdam Institute for Molecules, Medicines & Systems (AIMMS) Vrije Universiteit Amsterdam, De Boelelaan 1108, 1081 HZ Amsterdam, The Netherlands

[‡] Advanced Reactor Technology, Faculty of Applied Engineering, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerpen, Belgium

Email: e.ruijter@vu.nl

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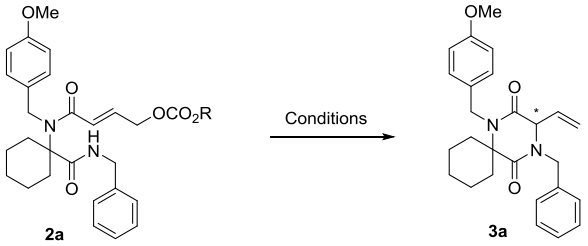
Optimization of reaction conditions

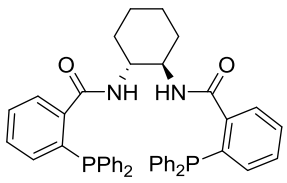
Table S1. Optimization study



Entry[a]	R	Catalyst	Ligand	Conc. (M)	Solvent	T°(C)	Yield (%)[b]	ee (%)[c]
1	Et	$Pd(PPh_3)_4$	-	0.025	MeCN	60	-	-
2	Et	$Pd(OAc)_2$	-	0.025	MeCN	60	-	-
3	Et	$PdCl_2$	-	0.025	MeCN	60	-	-
4	Et	Pd_2dba_3	-	0.025	MeCN	60	4%	-
5	Et	$[PdClAllyl]_2$	-	0.025	MeCN	60	-	-
6	Et	$Pd(PPh_3)_4$	dppe	0.025	MeCN	60	-	-
7	Et	$Pd(OAc)_2$	dppe	0.025	MeCN	60	-	-
8	Et	$PdCl_2$	dppe	0.025	MeCN	60	-	-
9	Et	Pd_2dba_3	dppe	0.025	MeCN	60	11%	-
10	Et	$[PdClAllyl]_2$	dppe	0.025	MeCN	60	traces	-
11	Et	$Pd(PPh_3)_4$	-	0.2	THF	50	28%	-
12	Et	$Pd(OAc)_2$	-	0.2	THF	50	-	-
13	Et	$PdCl_2$	-	0.2	THF	50	-	-
14	Et	Pd_2dba_3	-	0.2	THF	50	-	-
15	Et	$[PdClAllyl]_2$	-	0.2	THF	50	-	-
16	Et	$Pd(PPh_3)_4$	dppe	0.2	THF	50	56%	-
17	Et	$Pd(OAc)_2$	dppe	0.2	THF	50	33%	-
18	Et	$PdCl_2$	dppe	0.2	THF	50	-	-
19	Et	Pd_2dba_3	dppe	0.2	THF	50	86%	-
20	Et	$[PdClAllyl]_2$	dppe	0.2	THF	50	67%	-
21[d]	Et	Pd_2dba_3	**L1**	0.2	THF	50	-	-
22[d]	Et	Pd_2dba_3	**L2**	0.2	THF	50	41%	14%
23[d]	Et	Pd_2dba_3	**L3**	0.2	THF	50	22%	57%
24	Et	Pd_2dba_3	**L1**	0.2	THF	50	-	-
25	Et	Pd_2dba_3	**L2**	0.2	THF	50	35%	16%
26	Et	Pd_2dba_3	**L3**	0.2	THF	50	12%	60%
27[e]	Et	Pd_2dba_3	**L4**	0.2	THF	50	43%	76%
28	Et	Pd_2dba_3	**L4**	0.2	THF	50	46%	76%
29[f]	Et	Pd_2dba_3	**L4**	0.2	THF	50	56%	68%
30	Et	Pd_2dba_3	**L5**	0.2	THF	50	62%	16%
31	Et	Pd_2dba_3	**L6**	0.2	THF	50	17%	63%
32	Et	Pd_2dba_3	**L7**	0.2	THF	50	75%	26%
33	Et	Pd_2dba_3	**L8**	0.2	THF	50	72%	20%
34	Et	Pd_2dba_3	**L9**	0.2	THF	50	74%	2%
35[g]	Et	Pd_2dba_3	**L4**	0.2	THF	r.t.	31%	86%
36[h]	Et	Pd_2dba_3	**L4**	0.2	THF	r.t.	29%	89%
37	Et	Pd_2dba_3	**L4**	0.2	THF	r.t.	27%	91%
38[i]	Et	Pd_2dba_3	**L4**	0.2	THF	r.t.	22%	91%
39[j]	Et	Pd_2dba_3	**L4**	0.2	THF	r.t.	27%	88%
40	Et	Pd_2dba_3	**L4**	0.2	DCM	r.t.	75%	78%
41	Et	Pd_2dba_3	**L4**	0.2	Tol	r.t.	12%	78%

42	Et	Pd_2dba_3	**L4**	0.2	DMF	r.t.	-	-
43	Et	Pd_2dba_3	**L4**	0.2	Diox	r.t.	41%	88%
44	Et	Pd_2dba_3	**L4**	0.2	MeCN	r.t.	traces	n.d.
45	Et	Pd_2dba_3	**L4**	0.2	Et_2O	r.t.	17%	84%
46	Et	Pd_2dba_3	**L4**	0.2	MeO*t*Bu	r.t.	13%	81%
47	Et	Pd_2dba_3	**L4**	0.2	2-MeTHF	r.t.	40%	86%
48	Et	Pd_2dba_3	**L4**	0.2	Anisole	r.t.	36%	84%
49	Et	Pd_2dba_3	**L4**	0.2	DCM/Diox 1:1	r.t.	41%	87%
50	Et	Pd_2dba_3	**L4**	0.2	DCM/Diox 2:1	r.t.	48%	86%
51	Et	Pd_2dba_3	**L4**	0.2	DCM/Diox 4:1	r.t.	55%	86%
52	Et	Pd_2dba_3	**L4**	0.2	DCM/Diox 8:1	r.t.	40%	85%
53[k]	Et	Pd_2dba_3	**L4**	0.2	Diox	r.t.	31%	92%
54[l]	Et	Pd_2dba_3	**L4**	0.2	Diox	r.t.	11%	n.d.
55	Et	Pd_2dba_3	**L4**	0.2	DCM	0°C	22%	60%
56	Et	Pd_2dba_3	**L4**	0.5	Diox	r.t.	21%	86%
57	Et	Pd_2dba_3	**L4**	0.1	Diox	r.t.	54%	89%
58	Et	Pd_2dba_3	**L4**	0.05	Diox	r.t.	53%	90%
59	Et	Pd_2dba_3	**L4**	0.025	Diox	r.t.	86%	94%
60	Et	Pd_2dba_3	**L4**	0.01	Diox	r.t.	56%	94%
61	Et	Pd_2dba_3	**L10**	0.025	Diox	r.t.	-	-
62	Et	Pd_2dba_3	**L11**	0.025	Diox	r.t.	-	-
63	Et	Pd_2dba_3	**L12**	0.025	Diox	r.t.	46%	91%
64	Et	Pd_2dba_3	**L13**	0.025	Diox	r.t.	49%	42%
65	Et	Pd_2dba_3	**L14**	0.025	Diox	r.t.	81%	41%
66	Et	Pd_2dba_3	**L15**	0.025	Diox	r.t.	88%	90%
67	Me	Pd_2dba_3	**L4**	0.025	Diox	r.t.	80%	88%
68	*t*Bu	Pd_2dba_3	**L4**	0.025	Diox	r.t.	38%	78%
69[m]	Et	Pd_2dba_3	**L4**	0.025	Diox	r.t.	-	-
70[n]	Et	Pd_2dba_3	**L4**	0.025	Diox	r.t.	-	-
71[o]	Et	Pd_2dba_3	**L4**	0.025	Diox	r.t.	-	-

[a]Reactions were performed using **2a** (0.20 mmol), Pd source (10 mol%), ligand (20 mol% for monodentate ligands and 10% for bidentate ligands) for 24h, unless stated otherwise. [b] Isolated yield. [c] Determined by chiral SFC. [d] Reaction performed using 20 mol % of **L1**, **L2** and **L3**. [e] Reaction performed using 40 mol % of **L4**. [f] Reaction performed using 10 mol % of **L4**. [g] Reaction performed using 10 mol% of **L4**. [h] Reaction performed using 15 mol % of L4. [l] Reaction performed using 40 mol% of **L4**. [j] Reaction time 120 h. [k] Reaction performed using 20 mol % catalyst loading and 40 mol% of **L4**. [l] Addition of catalyst/ligand complex over 24h. [m] Reaction performed using 1 eq. of nBu$_4$NCl. [n] Reaction performed using 1 eq. of nBu$_4$NF. [o] Reaction performed using 1 eq. of LiCl.



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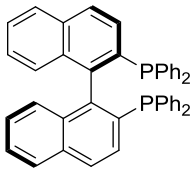

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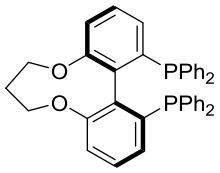

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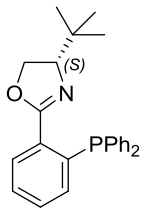

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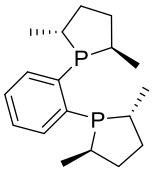

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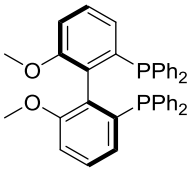

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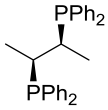

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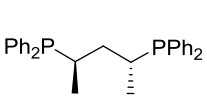

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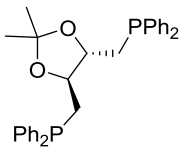

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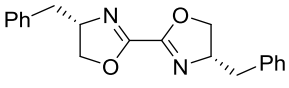

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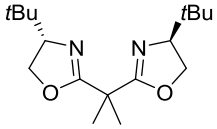

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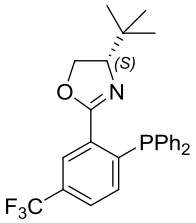

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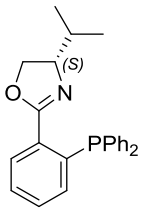

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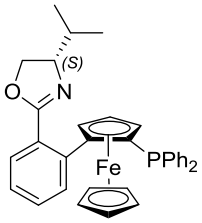

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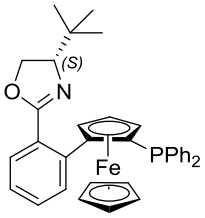
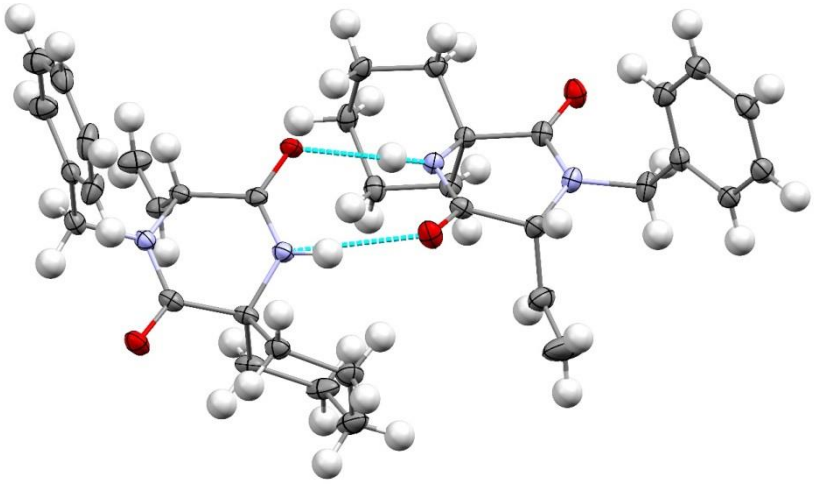


L15

X-Ray crystallography

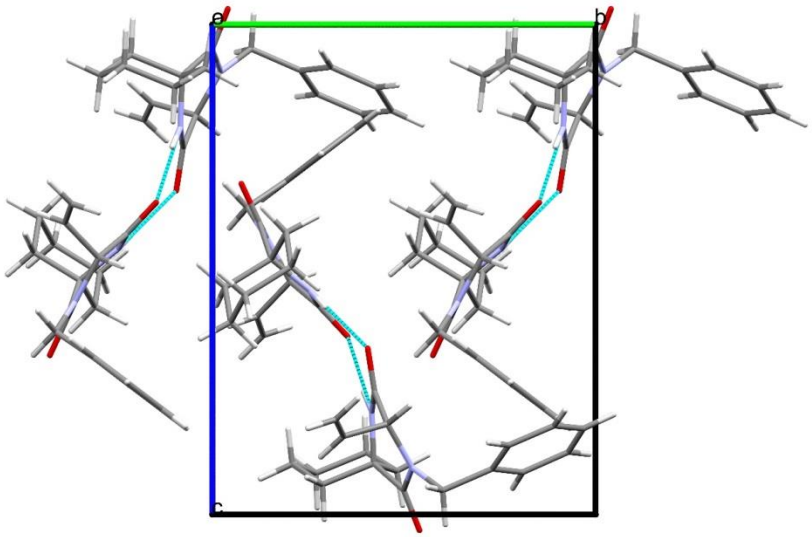
Crystals of **7** suitable for single crystal X-ray diffraction were obtained from recrystallization by slow solvent evaporation from cyclohexane. Crystals were mounted on a borate glass capillary on an Agilent Supernova Kappa diffractometer with Cu microsource, and cooled to 100.0(1)K for intensity measurement by 0.5° omega scans. Intensity data were scaled and corrected for absorption by CrysalisPro 1.171.39.45i.

The structure was solved with SHELXT (Sheldrick, 2015a) and refined with SHELXL 2016/4 (Sheldrick, 2015b). The space group was found to be $P2_1$, and the Flack parameter refined to -0.02(17) for absolute configuration R, with a Friedel pair coverage of 82%. (Figure 1)



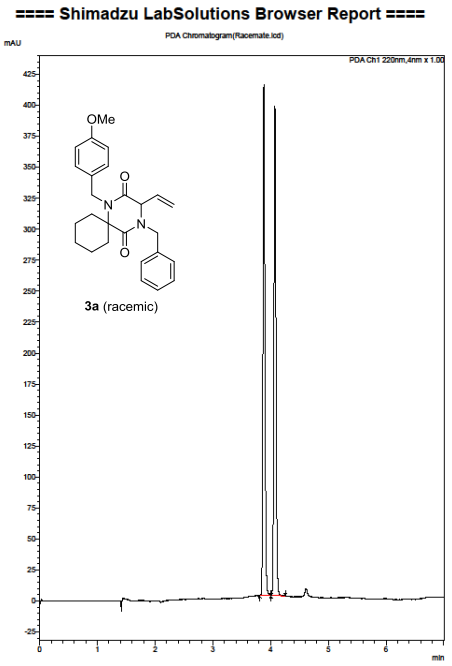
ORTEP plot of **7** with displacement ellipsoids at the 30% level and H atoms represented as spheres of arbitrary radius.

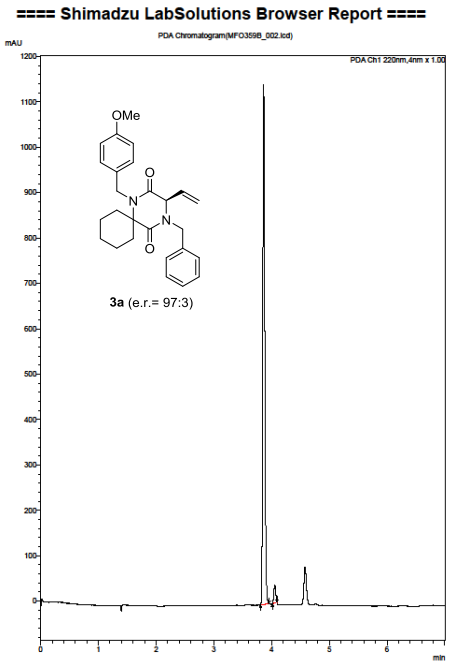
The structure forms N-H …O hydrogen bonded pairs between the 2,5-pyrazinediones of the two non-symmetry equivalent molecules. The structure can thus be described as two sets of U-shaped channels consisting of dimers running along the a axis, in which both non-symmetry equivalent molecules have the *R*-configuration.



View of the structure along the *a* direction. Hydrogen bonds between the non-symmetry equivalent molecules are indicated by cyan dotted lines.

Determination of enantiomeric ratio by SFC





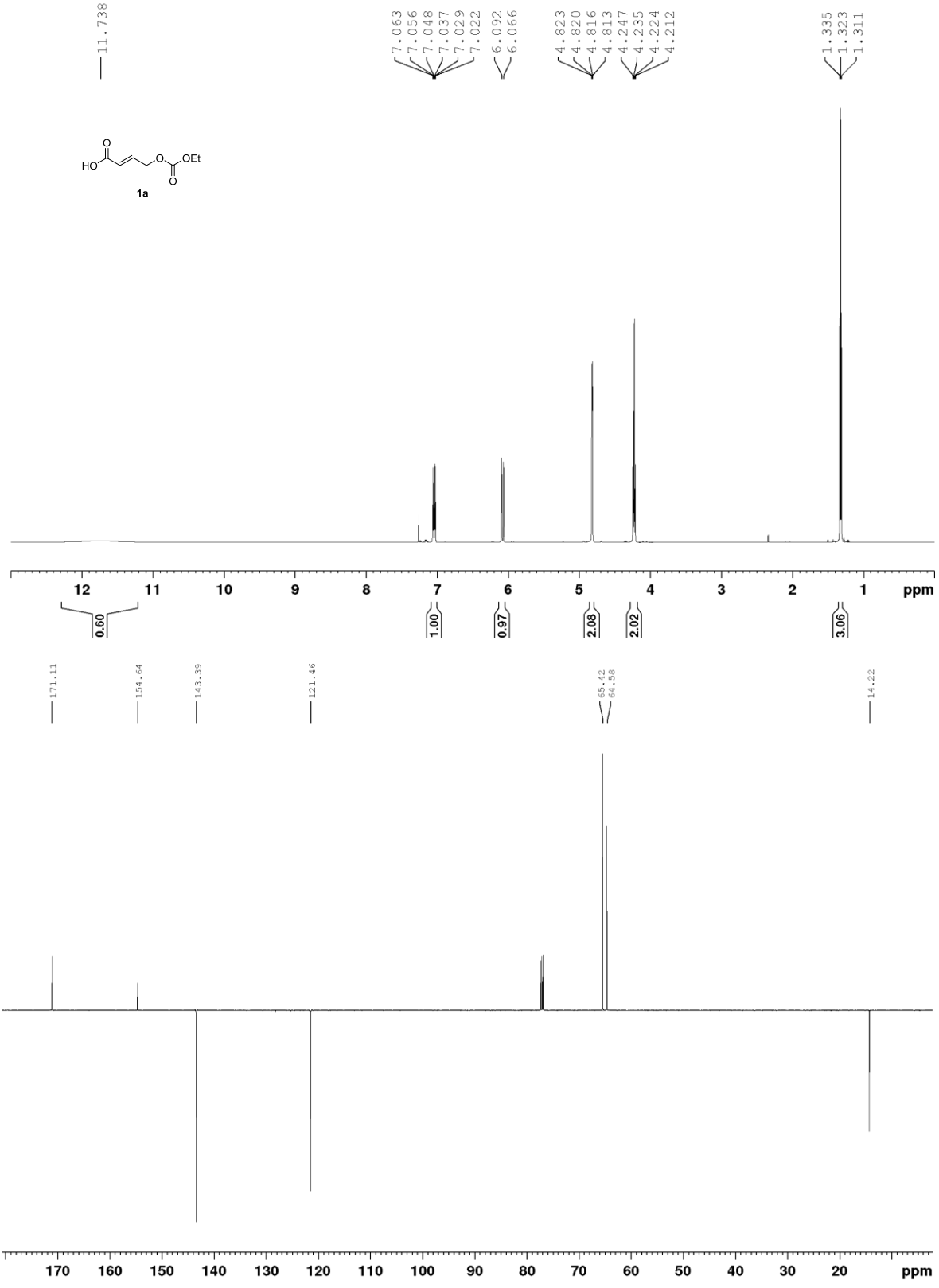
PDA Ch1 220nm

Peak#	Ret. Time	Area	Area%
1	3.884	981263	49.889
2	4.075	985629	50.111
Total		1966892	100.000

PDA Ch1 272nm

Peak#	Ret. Time	Area	Area%
1	3.863	256464	96.916
2	4.055	8160	3.084
Total		264624	100.000

NMR Spectra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4.235
4.224
4.212
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1.323
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O
OEt
O
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2.02
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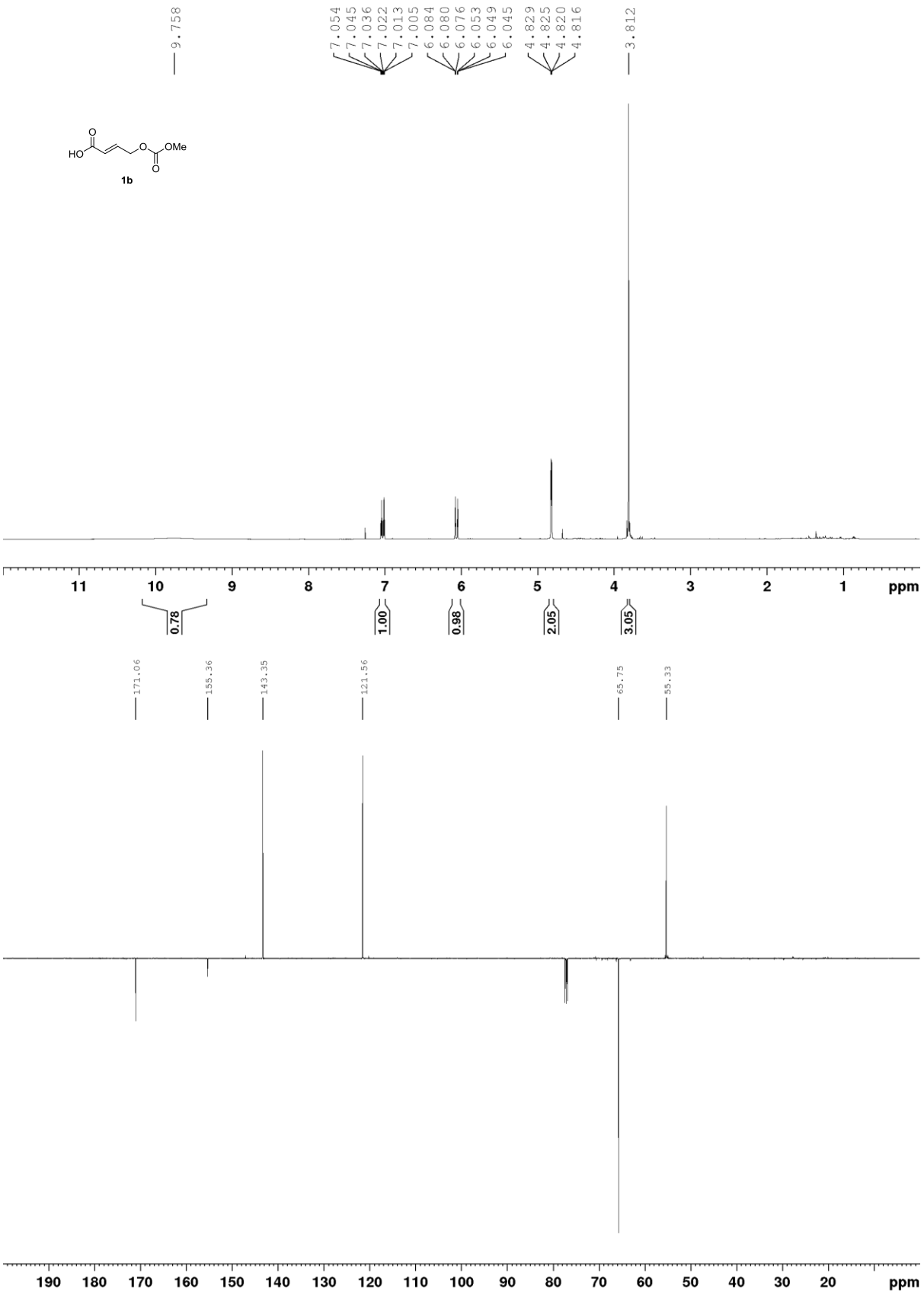
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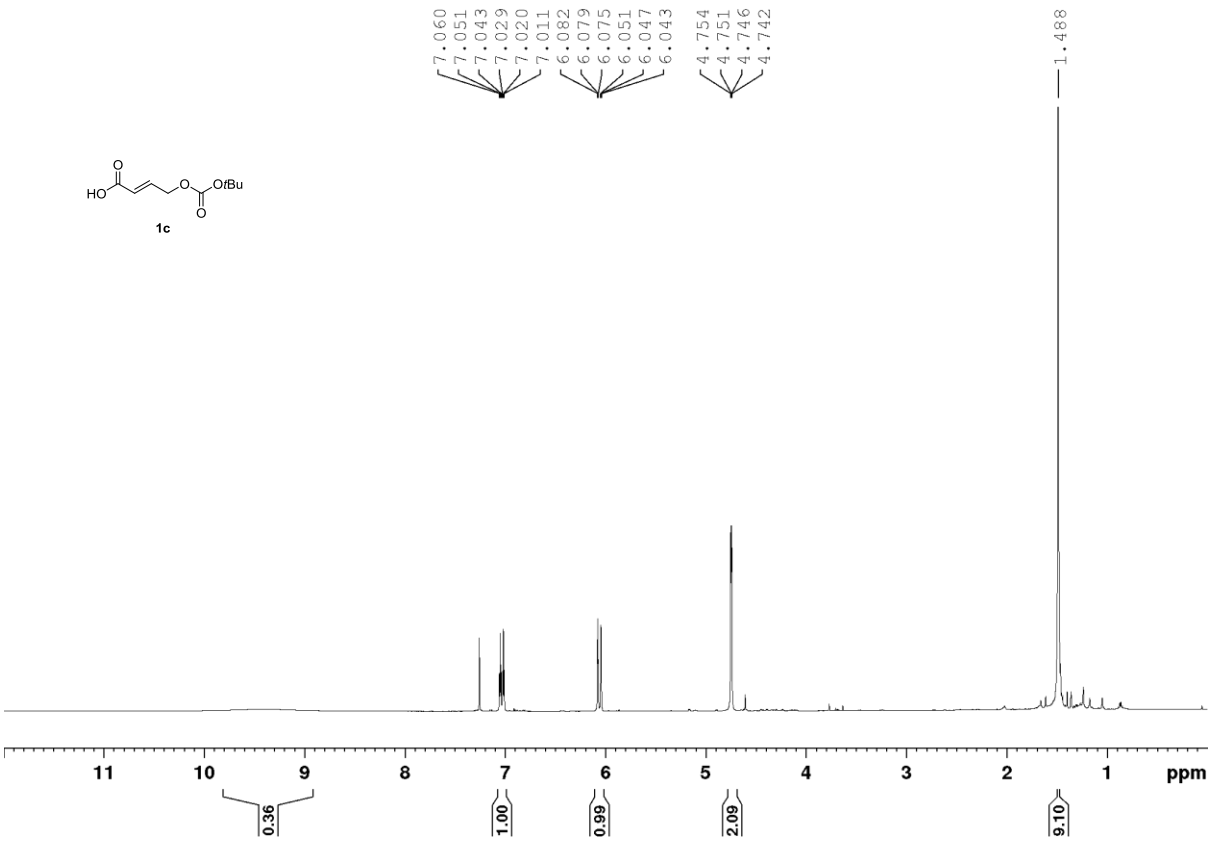
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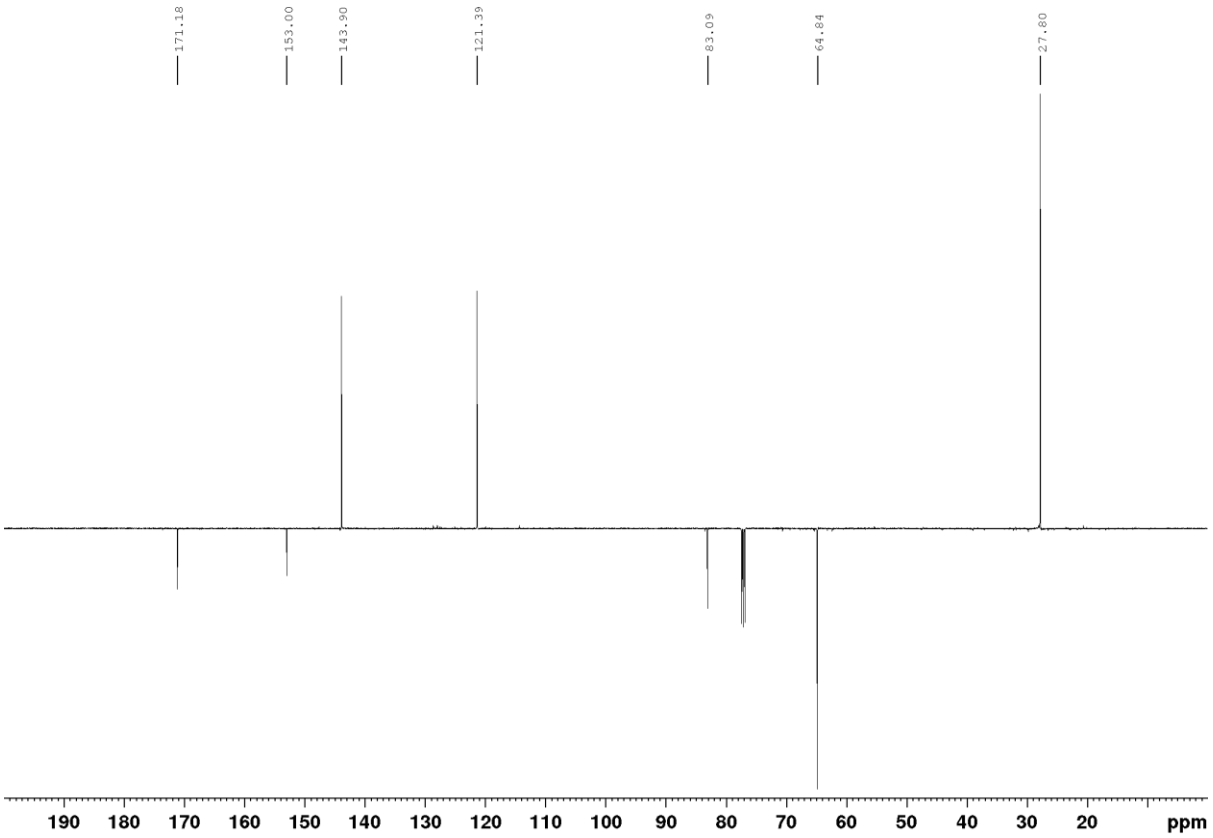
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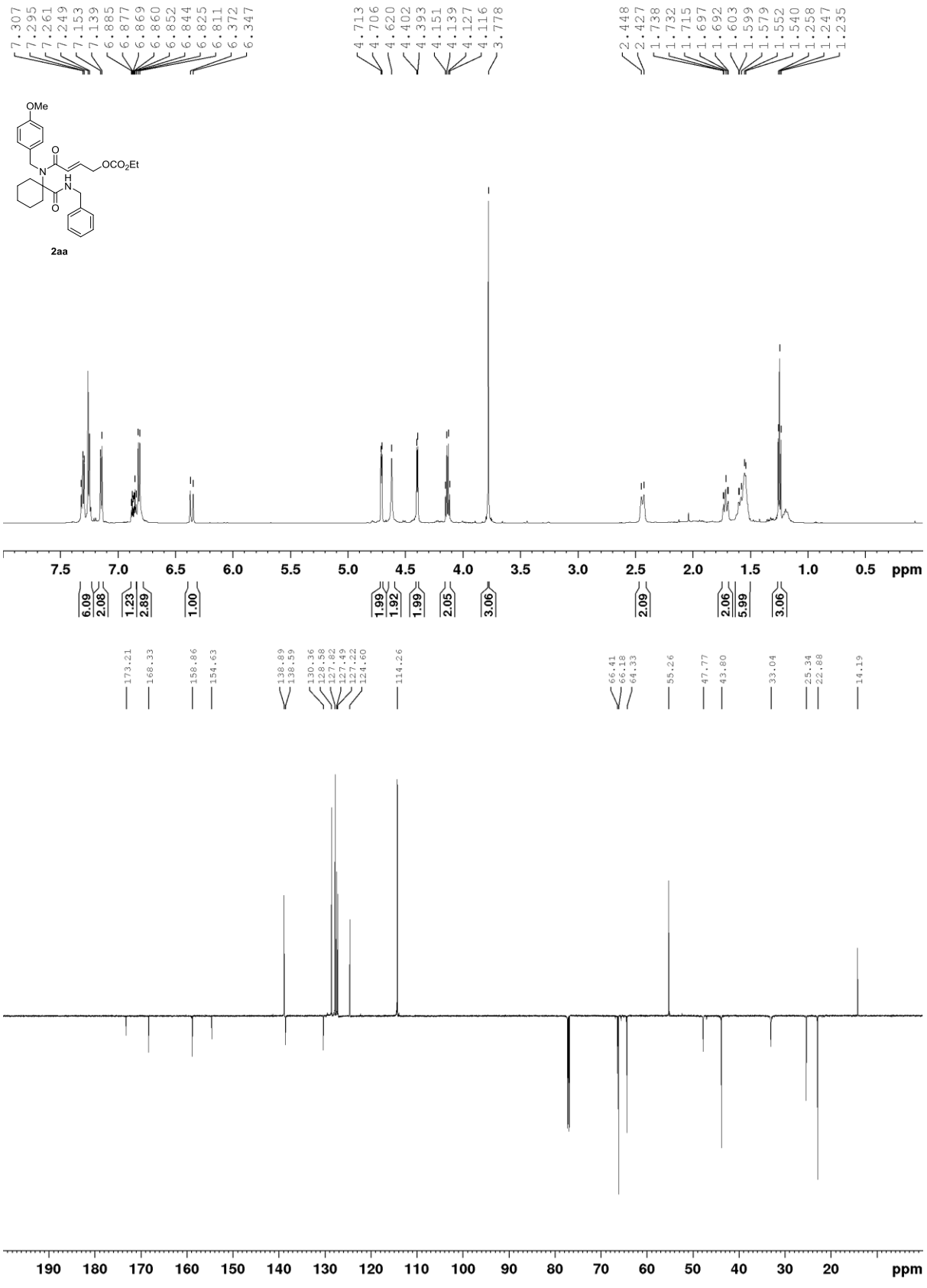
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OMe
OCO2Et
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2.05
3.06
2.09
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138.89
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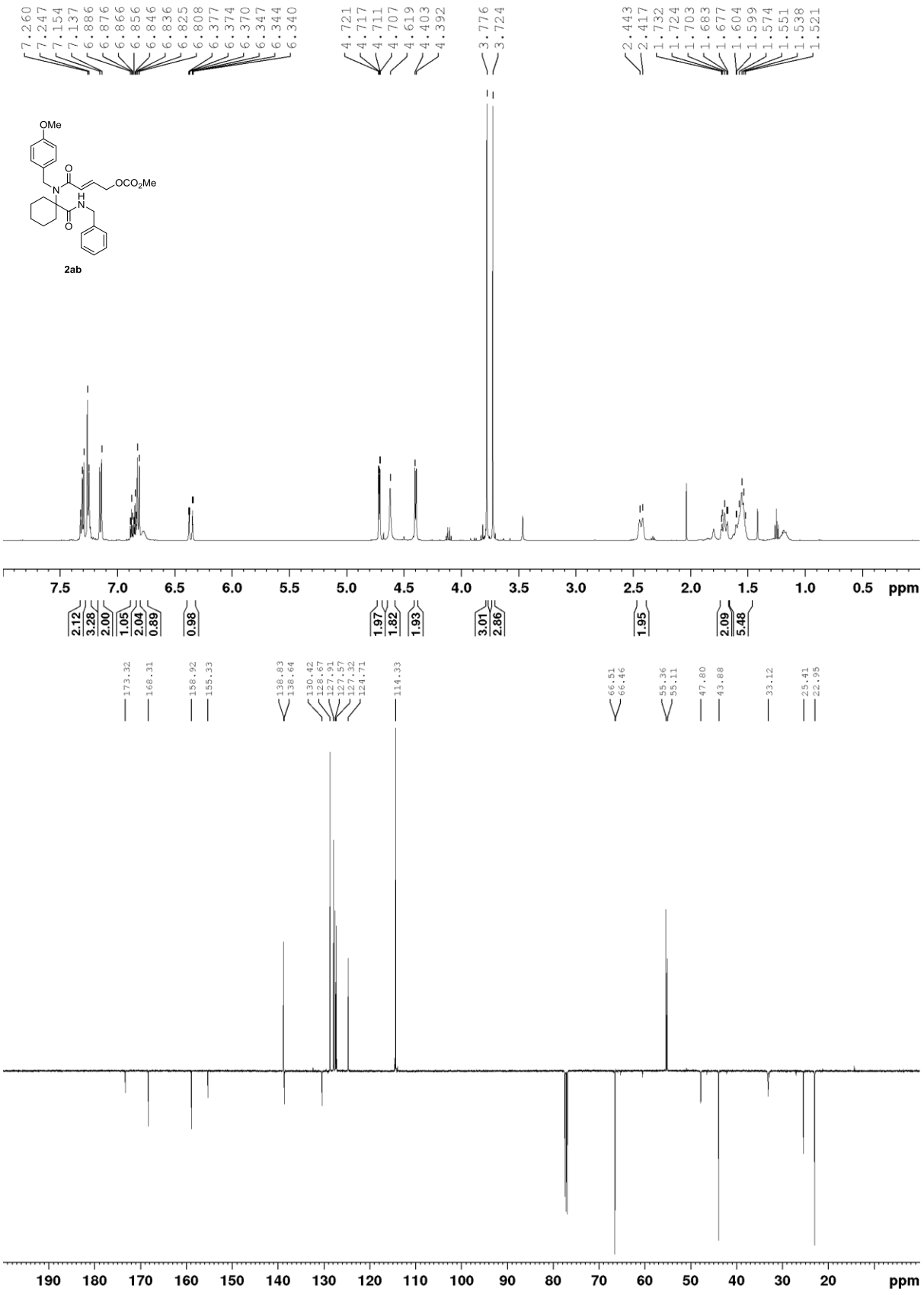
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6.377
6.374
6.370
6.347
6.344
6.340
4.721
4.717
4.711
4.707
4.619
4.403
4.392
3.776
3.724
2.443
2.417
1.732
1.724
1.703
1.683
1.677
1.604
1.599
1.574
1.551
1.538
1.521
OMe
O
N
OCO2Me
H
N
O
2ab
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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3.28
2.00
1.05
2.04
0.89
0.98
1.97
1.82
1.93
3.01
2.86
1.95
2.09
5.48
173.32
168.31
158.92
155.33
138.83
138.64
130.42
128.67
127.91
127.57
127.32
124.71
114.33
66.51
66.46
55.36
55.11
47.80
43.88
33.12
25.41
22.95
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80
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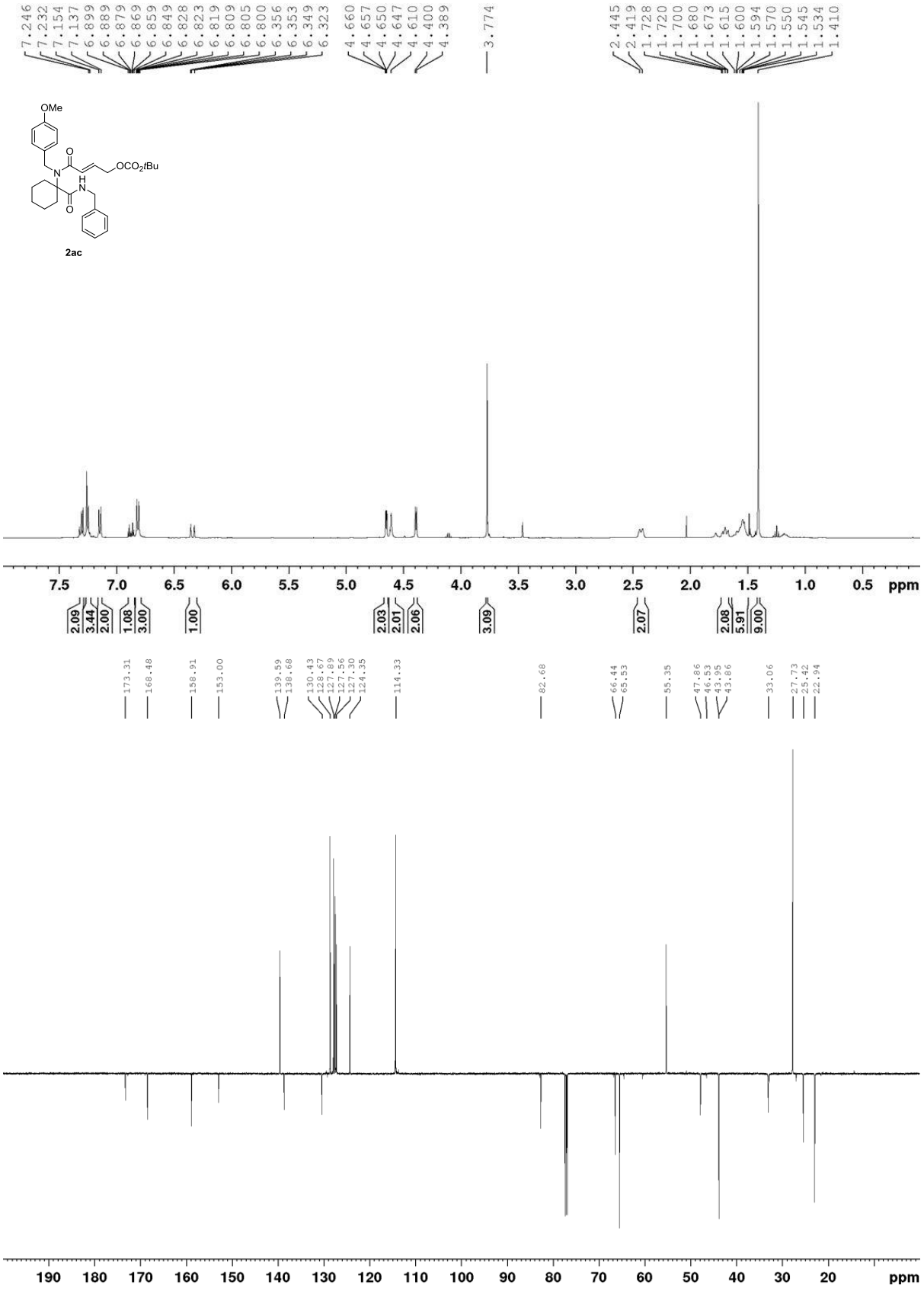
20
ppm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6.823
6.819
6.809
6.805
6.800
6.356
6.353
6.349
6.323
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4.657
4.650
4.647
4.610
4.400
4.389
3.774
2.445
2.419
1.728
1.720
1.700
1.680
1.673
1.615
1.600
1.594
1.570
1.550
1.545
1.534
1.410
OMe
OCO2tBu
2ac
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
ppm
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2.00
1.08
3.00
1.00
2.03
2.01
2.06
3.09
2.07
2.08
5.91
9.00
173.31
168.48
158.91
153.00
139.59
138.68
130.43
128.67
127.89
127.56
127.30
124.35
114.33
82.68
66.44
65.53
55.35
47.86
46.53
43.95
43.86
33.06
27.73
25.42
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160
150
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100
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80
70
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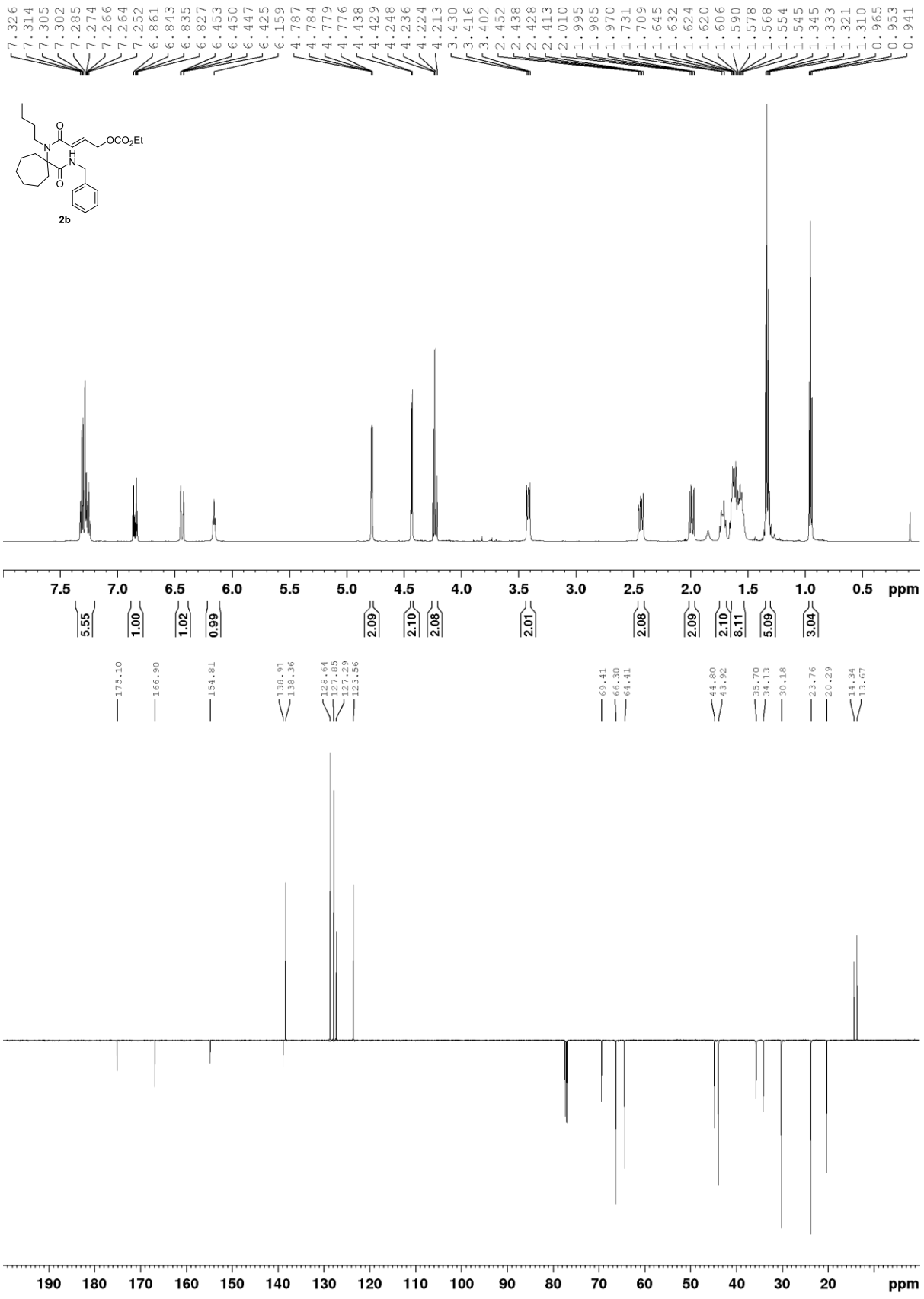
50
40
30
20
ppm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6.827
6.453
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6.447
6.425
6.159
4.787
4.784
4.779
4.776
4.438
4.429
4.248
4.236
4.224
4.213
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3.416
3.402
2.452
2.438
2.428
2.413
2.010
1.995
1.985
1.970
1.731
1.709
1.645
1.632
1.624
1.620
1.606
1.590
1.578
1.568
1.554
1.545
1.345
1.333
1.321
1.310
0.965
0.953
0.941
OCO2Et
2b
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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
ppm
5.55
1.00
1.02
0.99
2.09
2.10
2.08
2.01
2.08
2.09
2.10
8.11
5.09
3.04
175.10
166.90
154.81
138.91
138.36
128.64
127.85
127.29
123.56
69.41
66.30
64.41
44.80
43.92
35.70
34.13
30.18
23.76
20.29
14.34
13.67
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180
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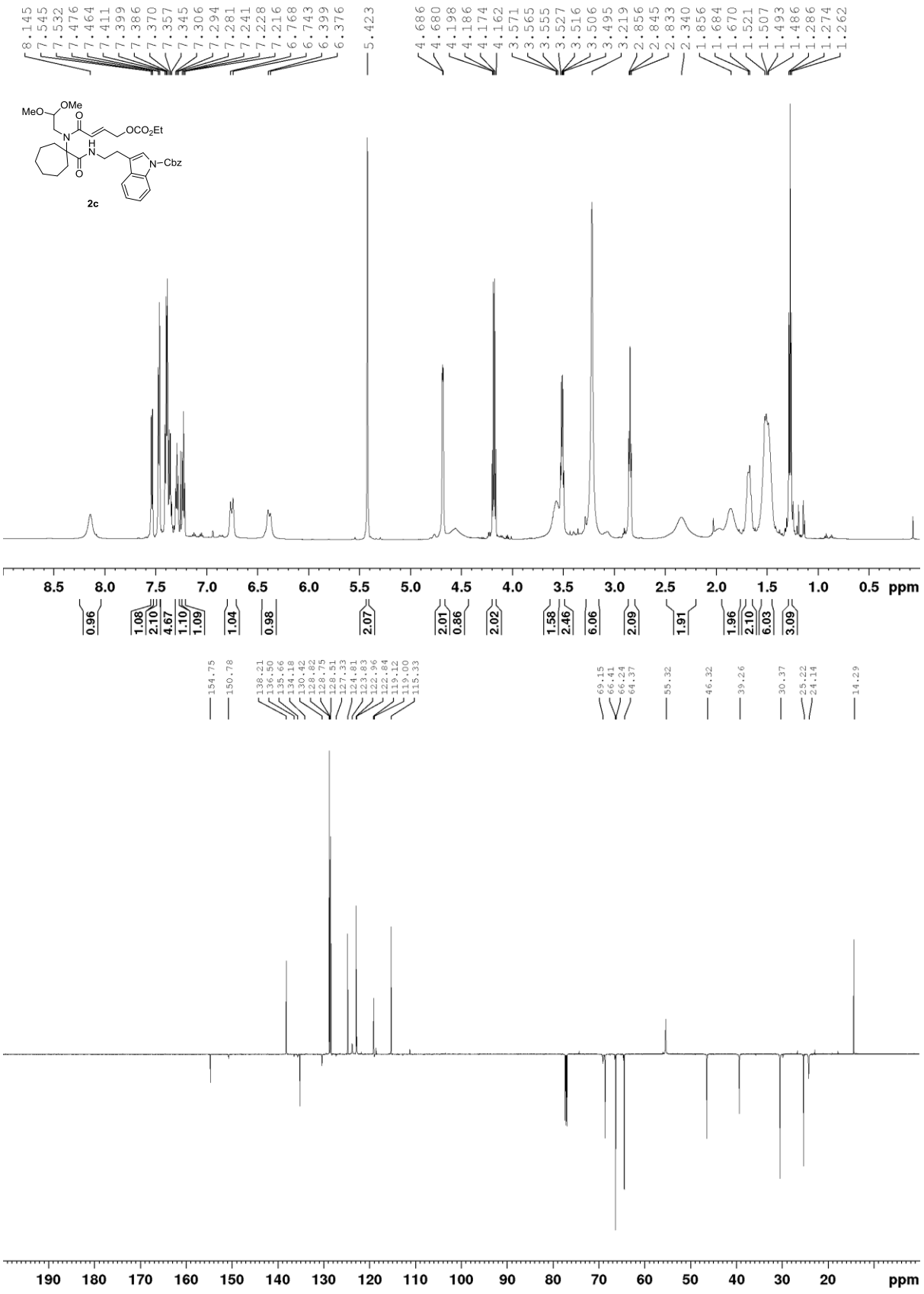
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.281
7.241
7.228
7.216
6.768
6.743
6.399
6.376
5.423
4.686
4.680
4.198
4.186
4.174
4.162
3.571
3.565
3.555
3.527
3.516
3.506
3.495
3.219
2.856
2.845
2.833
2.340
1.856
1.684
1.670
1.521
1.507
1.493
1.486
1.286
1.274
1.262
MeO
OMe
O
N
OCO2Et
H
N
O
N–Cbz
2c
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 ppm
0.96 1.08 2.10 4.67 1.10 1.09 1.04 0.98 2.07 2.01 0.86 2.02 1.58 2.46 6.06 2.09 1.91 1.96 2.10 6.03 3.09
154.75
150.78
138.21
136.50
135.66
134.18
130.42
128.82
128.75
128.51
127.33
124.81
123.83
122.96
122.84
119.12
119.00
115.33
69.15
66.41
66.24
64.37
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39.26
30.37
25.22
24.14
14.29
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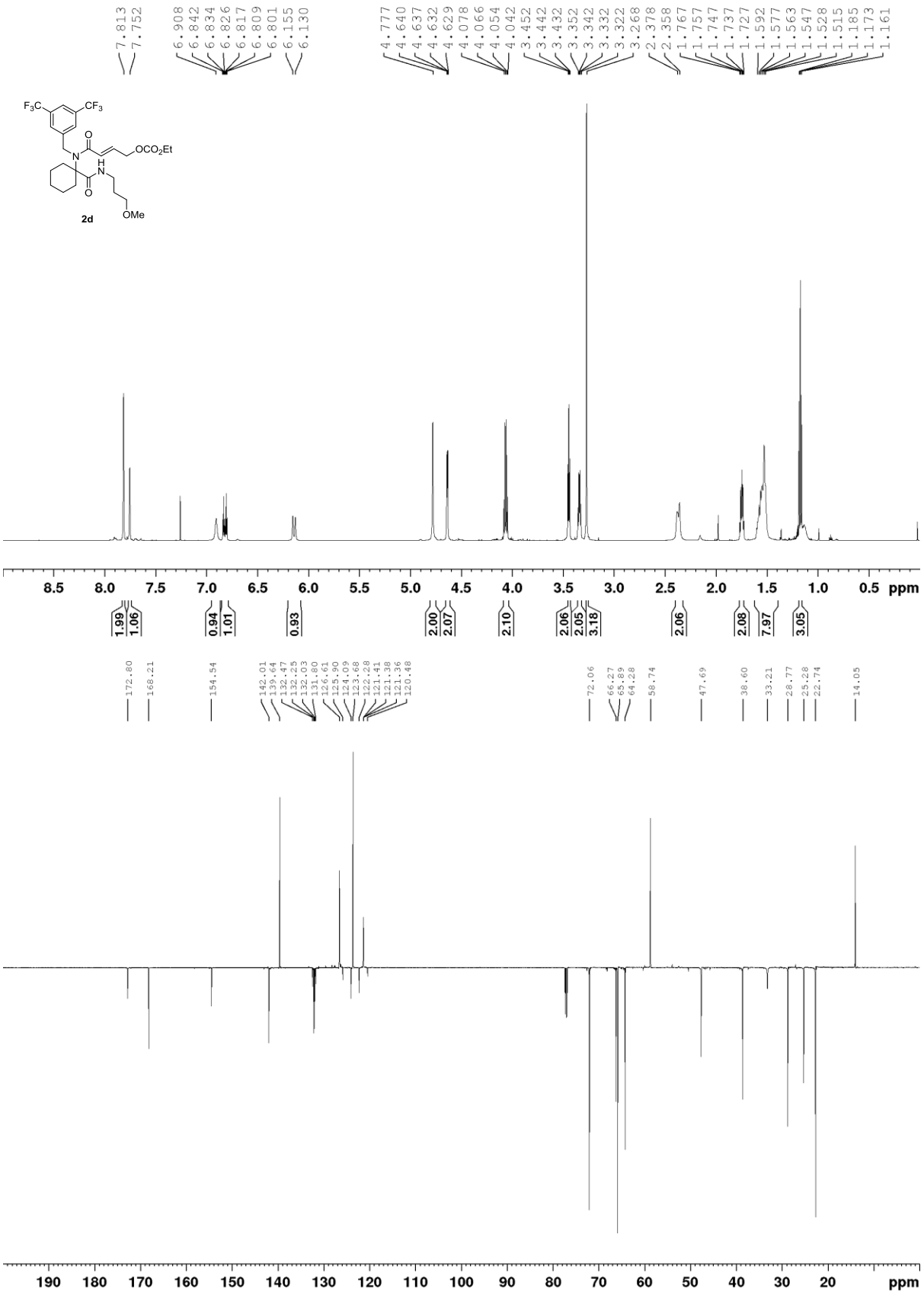
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6.826
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6.809
6.801
6.155
6.130
4.777
4.640
4.637
4.632
4.629
4.078
4.066
4.054
4.042
3.452
3.442
3.432
3.352
3.342
3.332
3.322
3.268
2.378
2.358
1.767
1.757
1.747
1.737
1.727
1.592
1.577
1.563
1.547
1.528
1.515
1.185
1.173
1.161
F3C
CF3
OCO2Et
OMe
2d
ppm
1.99
1.06
0.94
1.01
0.93
2.00
2.07
2.10
2.06
2.05
3.18
2.06
2.08
7.97
3.05
172.80
168.21
154.54
142.01
139.64
132.47
132.25
132.03
131.80
126.61
125.90
124.09
123.68
122.28
121.41
121.38
121.36
120.48
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28.77
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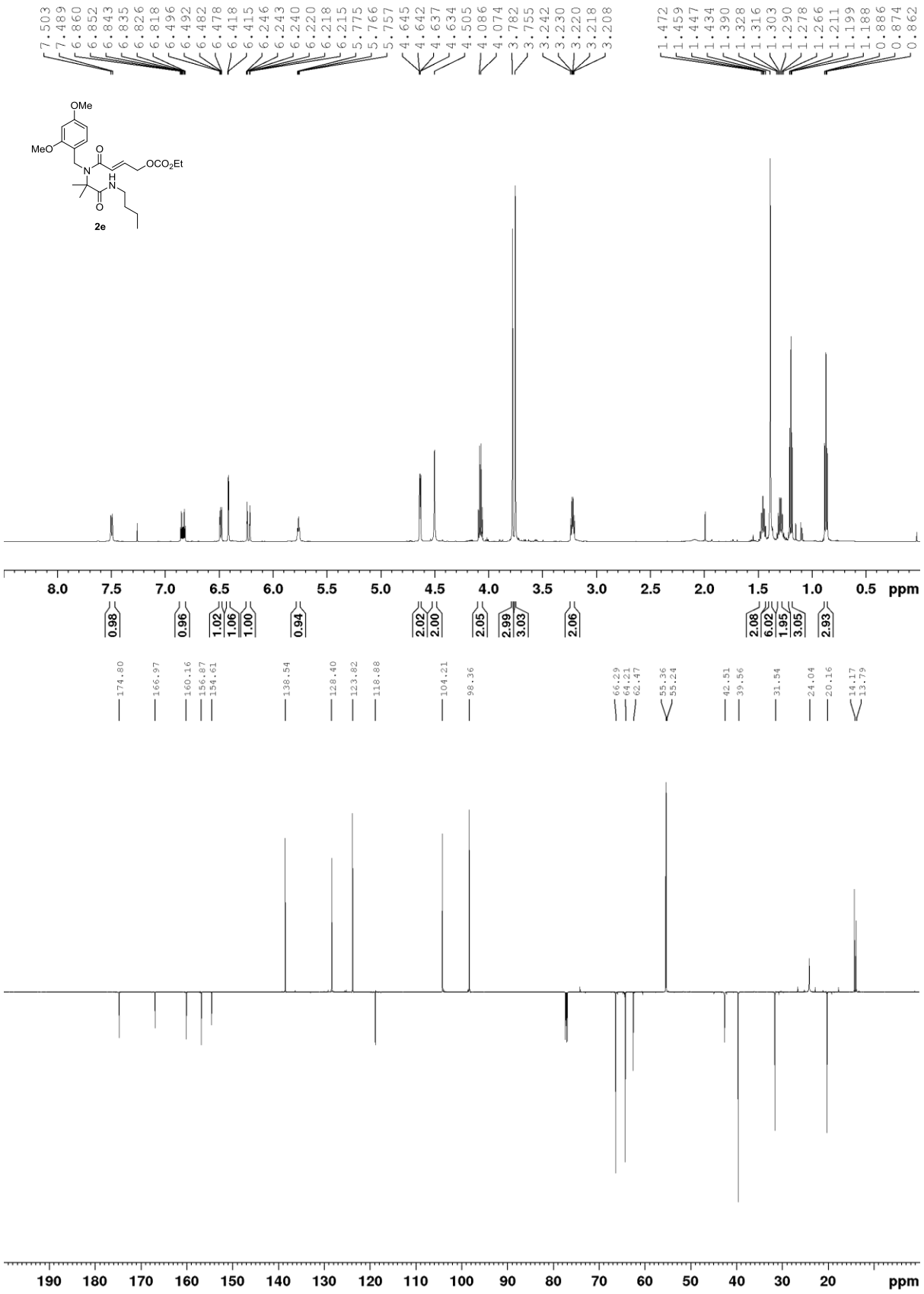
14.05
ppm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6.826
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6.492
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6.478
6.418
6.415
6.246
6.243
6.240
6.220
6.218
6.215
5.775
5.766
5.757
4.645
4.642
4.637
4.634
4.505
4.086
4.074
3.782
3.755
3.242
3.230
3.220
3.218
3.208
1.472
1.459
1.447
1.434
1.390
1.328
1.316
1.303
1.290
1.278
1.266
1.211
1.199
1.188
0.886
0.874
0.862
OMe
MeO
OCO2Et
2e
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 ppm
0.98 0.96 1.02 1.06 1.00 0.94 2.02 2.00 2.05 2.99 3.03 2.06 2.08 6.02 1.95 3.05 2.93
174.80
166.97
160.16
156.87
154.61
138.54
128.40
123.82
118.88
104.21
98.36
66.29
64.21
62.47
55.36
55.24
42.51
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31.54
24.04
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14.17
13.79
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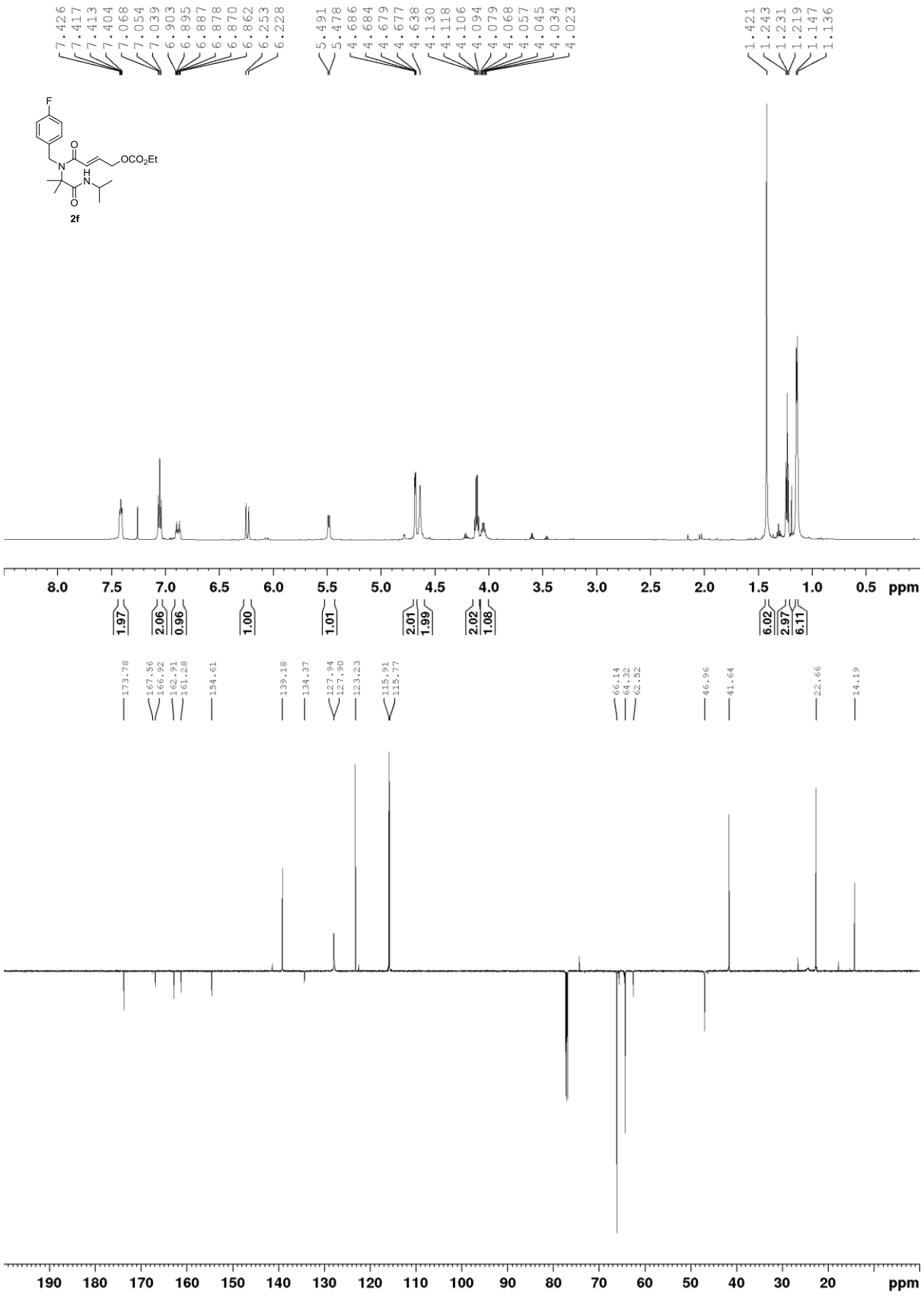
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7.404
7.068
7.054
7.039
6.903
6.895
6.887
6.878
6.870
6.862
6.253
6.228
5.491
5.478
4.686
4.684
4.679
4.677
4.638
4.130
4.118
4.106
4.094
4.079
4.068
4.057
4.045
4.034
4.023
1.421
1.243
1.231
1.219
1.147
1.136
F
O
N
OCO2Et
H
N
O
2f
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.97
2.06
0.96
1.00
1.01
2.01
1.99
2.02
1.08
6.02
2.97
6.11
173.78
167.56
166.92
162.91
161.28
154.61
139.18
134.37
127.94
127.90
123.23
115.91
115.77
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62.52
46.96
41.64
22.66
14.19
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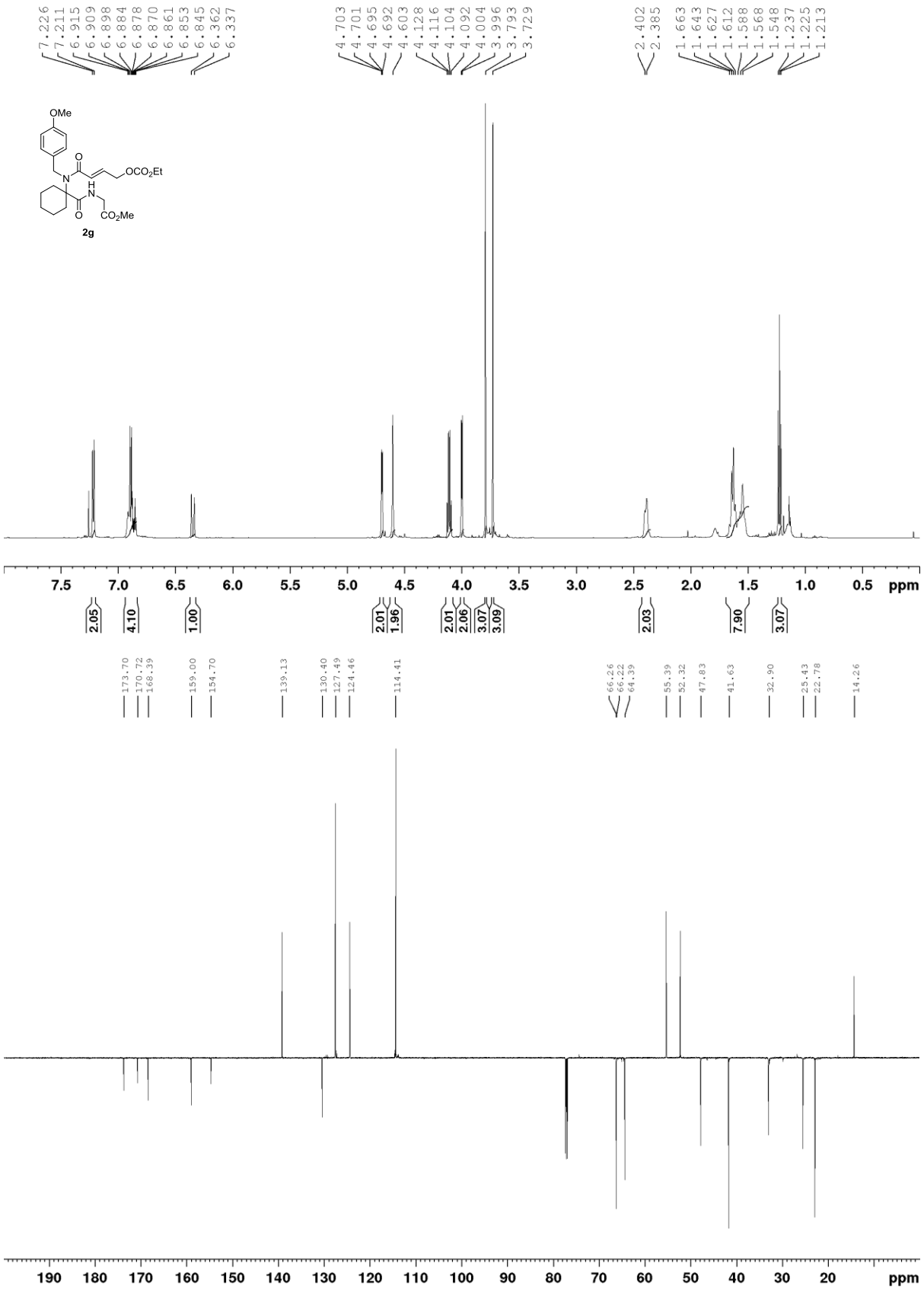
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6.870
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6.853
6.845
6.362
6.337
4.703
4.701
4.695
4.692
4.603
4.128
4.116
4.104
4.092
4.004
3.996
3.793
3.729
2.402
2.385
1.663
1.643
1.627
1.612
1.588
1.568
1.548
1.237
1.225
1.213
OMe
OCO2Et
CO2Me
2g
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 ppm
2.05 4.10 1.00 2.01 1.96 2.01 2.06 3.07 3.09 2.03 7.90 3.07
173.70
170.72
168.39
159.00
154.70
139.13
130.40
127.49
124.46
114.41
66.26
66.22
64.39
55.39
52.32
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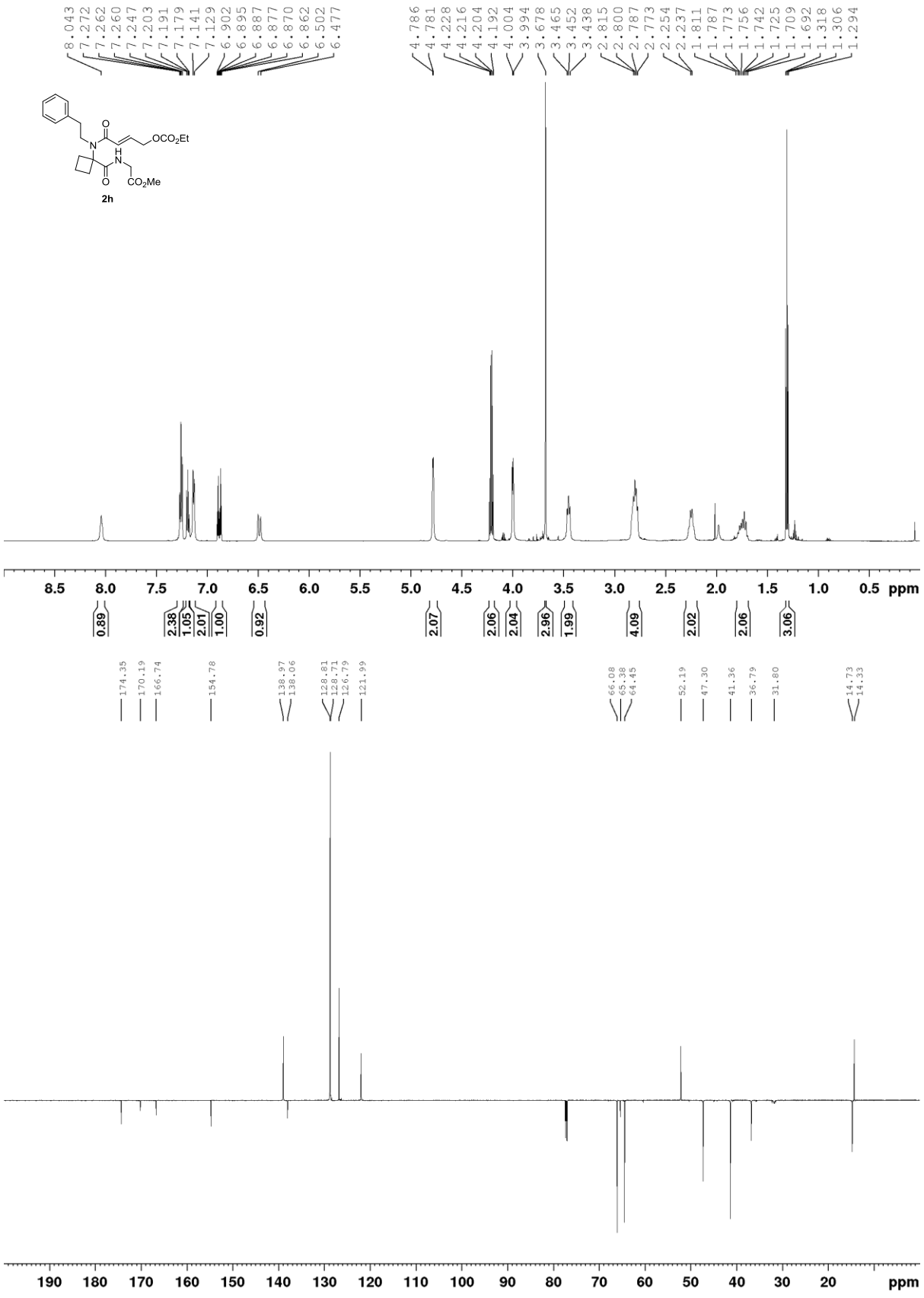
41.63
32.90
25.43
22.78
14.26
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.129
6.902
6.895
6.887
6.877
6.870
6.862
6.502
6.477
4.786
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4.216
4.204
4.192
4.004
3.994
3.678
3.465
3.452
3.438
2.815
2.800
2.787
2.773
2.254
2.237
1.811
1.787
1.773
1.756
1.742
1.725
1.709
1.692
1.318
1.306
1.294
OCO2Et
CO2Me
2h
ppm
0.89
2.38
1.05
2.01
1.00
0.92
2.07
2.06
2.04
2.96
1.99
4.09
2.02
2.06
3.06
174.35
170.19
166.74
154.78
138.97
138.06
128.81
128.71
126.79
121.99
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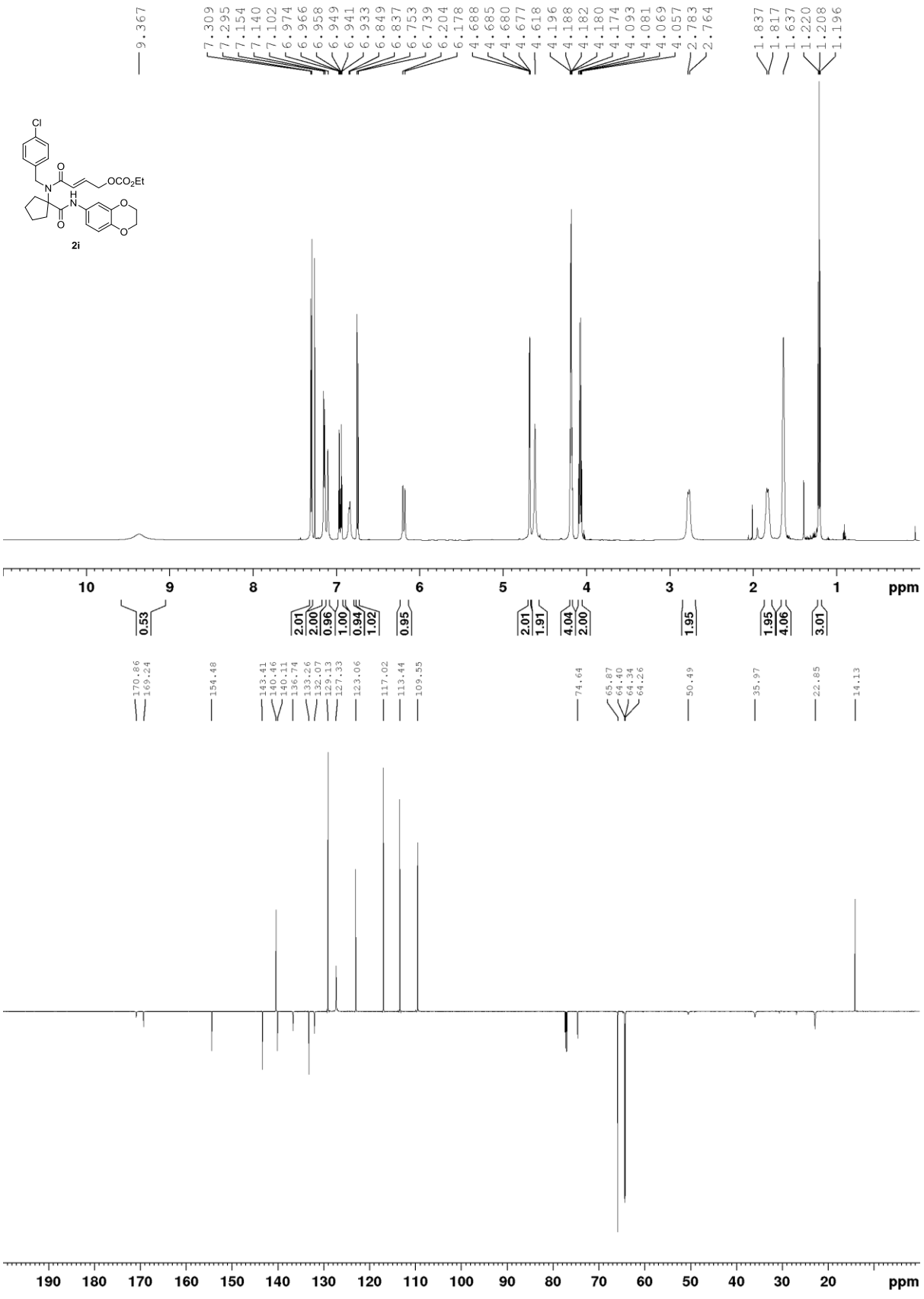
65.38
64.45
52.19
47.30
41.36
36.79
31.80
14.73
14.33
ppm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6.941
6.933
6.849
6.837
6.753
6.739
6.204
6.178
4.688
4.685
4.680
4.677
4.618
4.196
4.188
4.182
4.180
4.174
4.093
4.081
4.069
4.057
2.783
2.764
1.837
1.817
1.637
1.220
1.208
1.196
Cl
OCO2Et
2i
10 9 8 7 6 5 4 3 2 1 ppm
0.53
2.01
2.00
0.96
1.00
0.94
1.02
0.95
2.01
1.91
4.04
2.00
1.95
1.95
4.06
3.01
170.86
169.24
154.48
143.41
140.46
140.11
136.74
133.26
132.07
129.13
127.33
123.06
117.02
113.44
109.55
74.64
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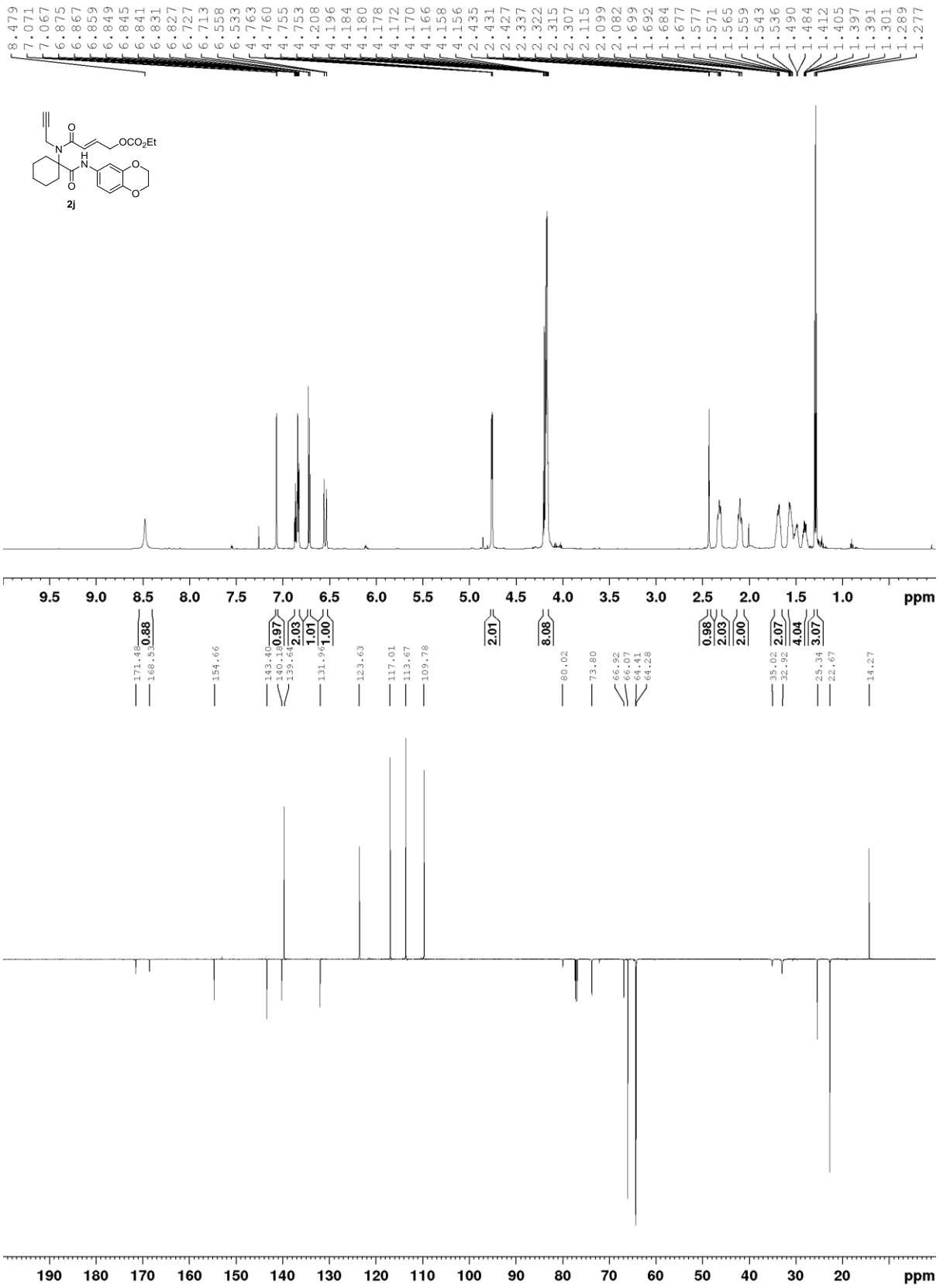
64.26
50.49
35.97
22.85
14.13
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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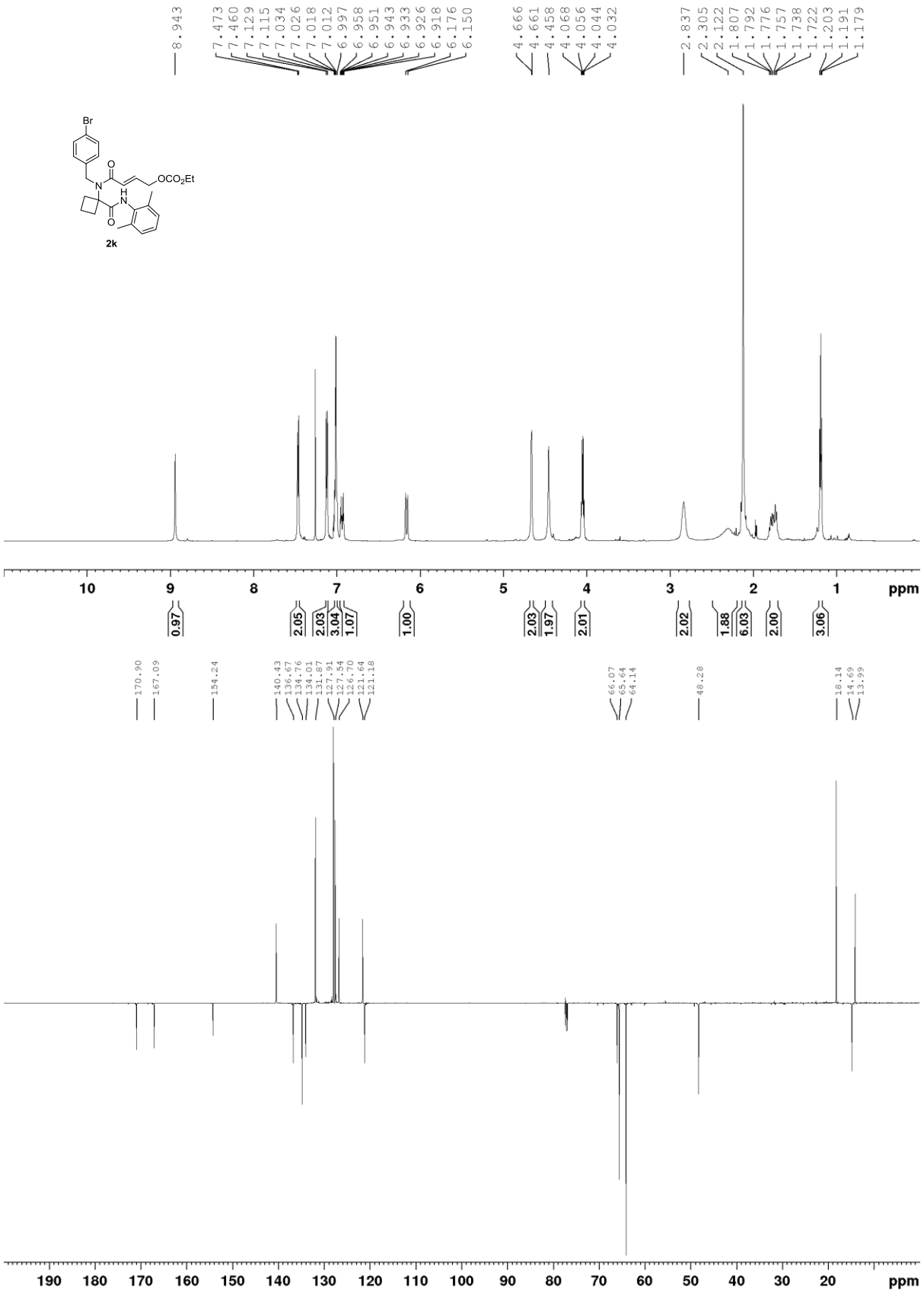
6.727
6.713
6.558
6.533
4.763
4.760
4.755
4.753
4.208
4.196
4.184
4.180
4.178
4.172
4.170
4.166
4.158
4.156
2.435
2.431
2.427
2.337
2.322
2.315
2.307
2.115
2.099
2.082
1.699
1.692
1.684
1.677
1.577
1.571
1.565
1.559
1.543
1.536
1.490
1.484
1.412
1.405
1.397
1.391
1.301
1.289
1.277
OCO2Et
2j
9.5 9.0 8.5 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 ppm
0.88
0.97
2.03
1.01
1.00
2.01
8.08
0.98
2.03
2.00
2.07
4.04
3.07
171.46
168.53
154.66
143.40
140.16
139.64
131.96
123.63
117.01
113.67
109.78
80.02
73.80
66.92
66.07
64.41
64.28
35.02
32.92
25.34
22.67
14.27
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.018
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6.943
6.933
6.926
6.918
6.176
6.150
4.666
4.661
4.458
4.068
4.056
4.044
4.032
2.837
2.305
2.122
1.807
1.792
1.776
1.757
1.738
1.722
1.203
1.191
1.179
Br
O
N
OCO2Et
H
N
O
2k
10
9
8
7
6
5
4
3
2
1
ppm
0.97
2.05
2.03
3.04
1.07
1.00
2.03
1.97
2.01
2.02
1.88
6.03
2.00
3.06
170.90
167.09
154.24
140.43
136.67
134.76
134.01
131.87
127.91
127.54
126.70
121.64
121.18
66.07
65.64
64.14
48.28
18.14
14.69
13.99
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180
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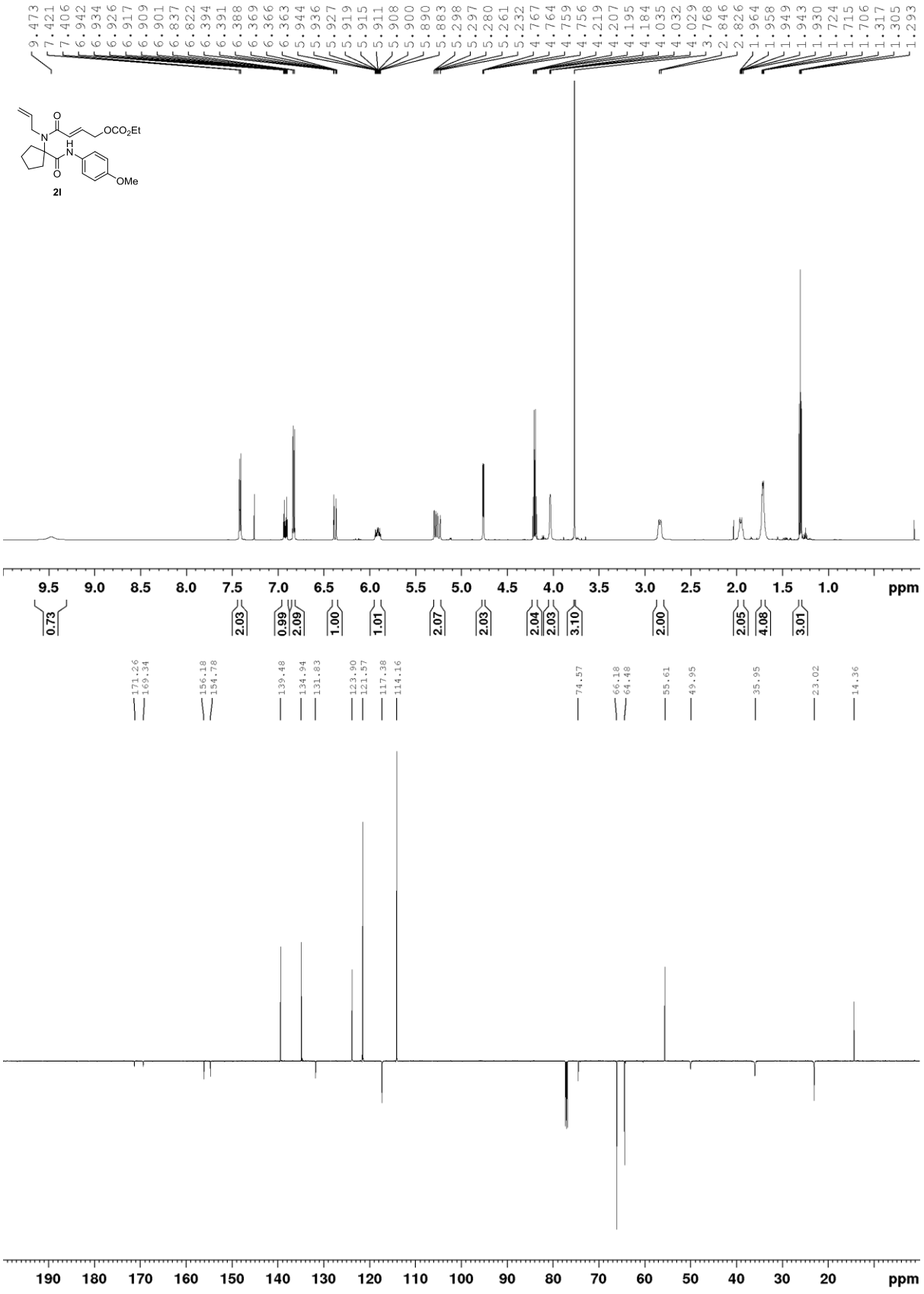
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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6.901
6.837
6.822
6.394
6.391
6.388
6.369
6.366
6.363
5.944
5.936
5.927
5.919
5.915
5.911
5.908
5.900
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5.232
4.767
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4.756
4.219
4.207
4.195
4.184
4.035
4.032
4.029
3.768
2.846
2.826
1.964
1.958
1.949
1.943
1.930
1.724
1.715
1.706
1.317
1.305
1.293
OCO2Et
N
H
O
OMe
2l
ppm
0.73
2.03
0.99
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1.01
2.07
2.03
2.04
2.03
3.10
2.00
2.05
4.08
3.01
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156.18
154.78
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131.83
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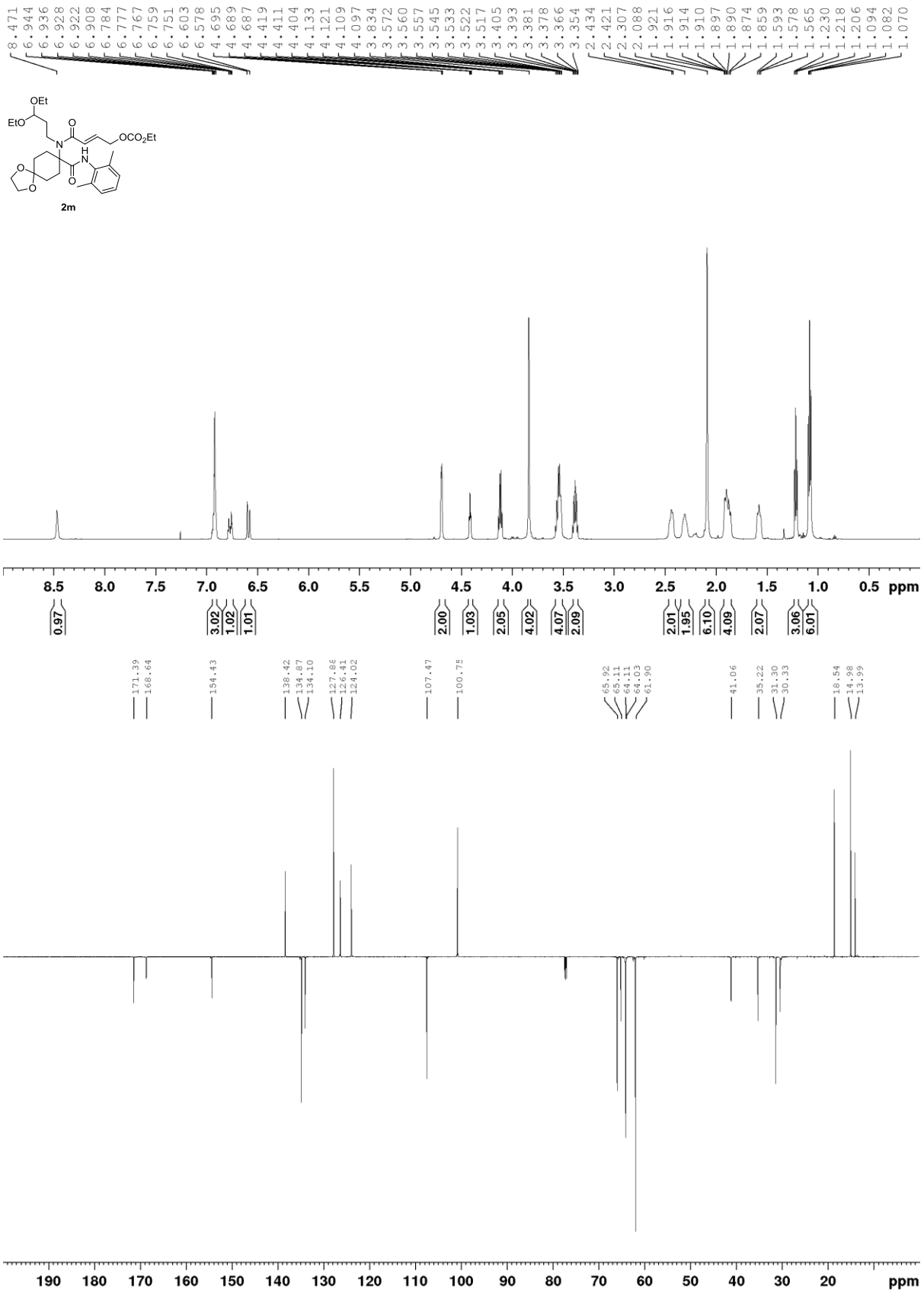
ppm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1.578
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OEt
EtO
OCO2Et
2m
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0.97
3.02
1.02
1.01
2.00
1.03
2.05
4.02
4.07
2.09
2.01
1.95
6.10
4.09
2.07
3.06
6.01
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154.43
138.42
134.87
134.10
127.86
126.41
124.02
107.47
100.75
65.92
65.11
64.11
64.03
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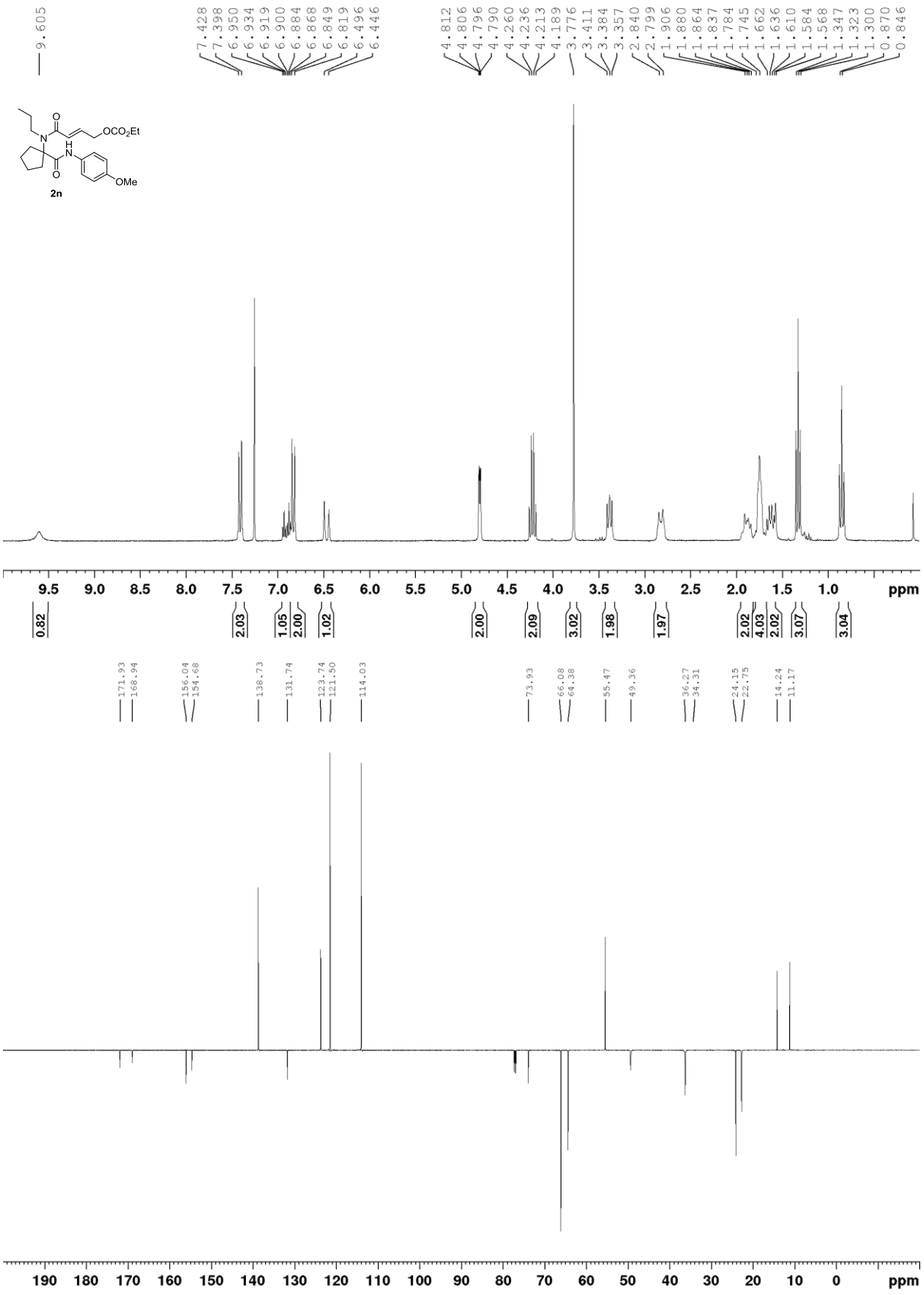
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1.662
1.636
1.610
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0.846
OCO2Et
N
H
N
O
O
OMe
2n
ppm
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1.05
2.00
1.02
2.00
2.09
3.02
1.98
1.97
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4.03
2.02
3.07
3.04
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123.74
121.50
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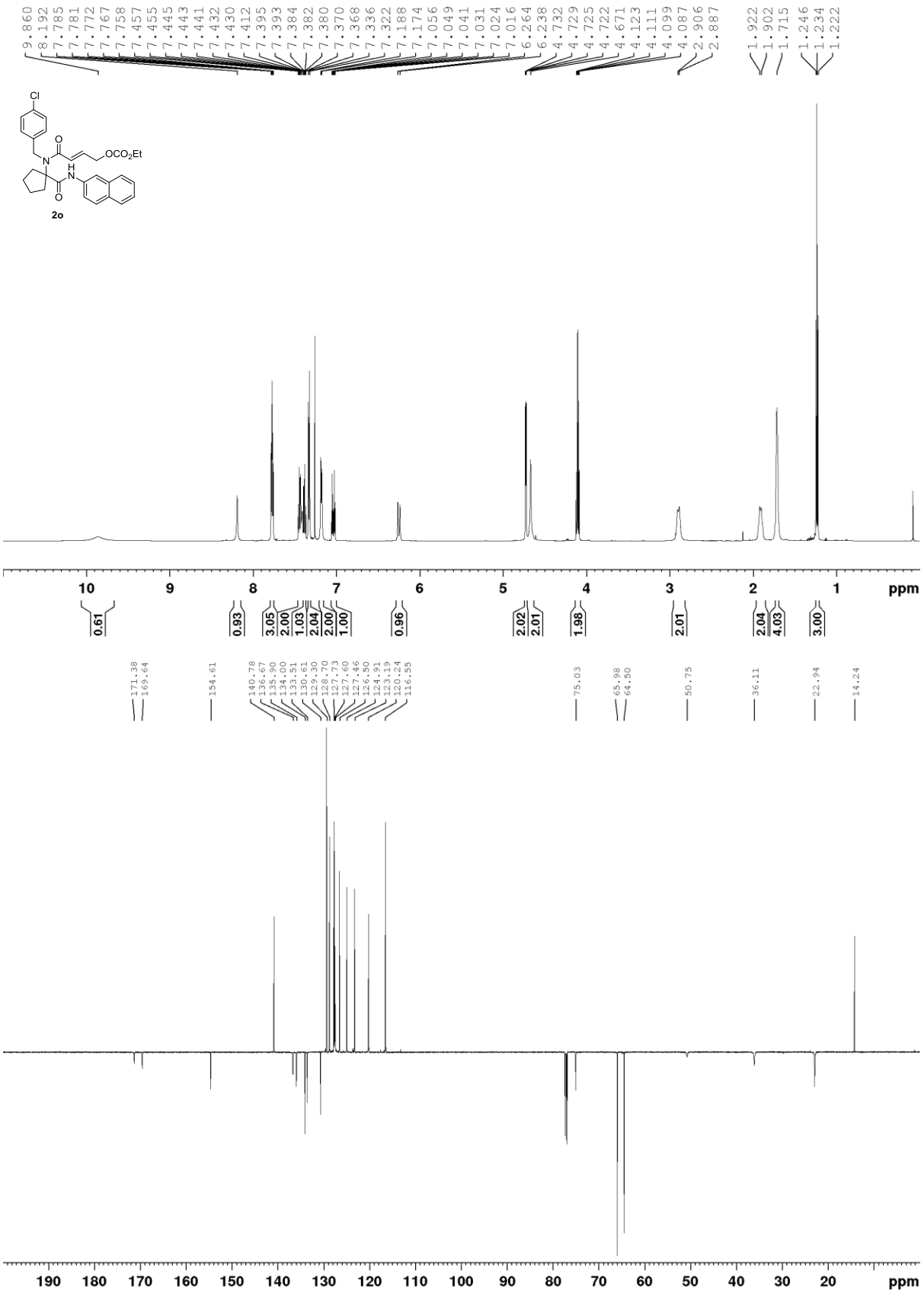
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7.430
7.412
7.395
7.393
7.384
7.382
7.380
7.370
7.368
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7.322
7.188
7.174
7.056
7.049
7.041
7.031
7.024
7.016
6.264
6.238
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4.729
4.725
4.722
4.671
4.123
4.111
4.099
4.087
2.906
2.887
1.922
1.902
1.715
1.246
1.234
1.222
Cl
OCO2Et
2o
10
9
8
7
6
5
4
3
2
1
ppm
0.61
0.93
3.05
2.00
1.03
2.04
2.00
1.00
0.96
2.02
2.01
1.98
2.01
2.04
4.03
3.00
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169.64
154.61
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136.67
134.00
133.51
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129.30
128.70
127.73
127.60
127.46
126.50
124.91
123.19
120.24
116.55
75.03
65.98
64.50
50.75
36.11
22.94
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140
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90
80
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50
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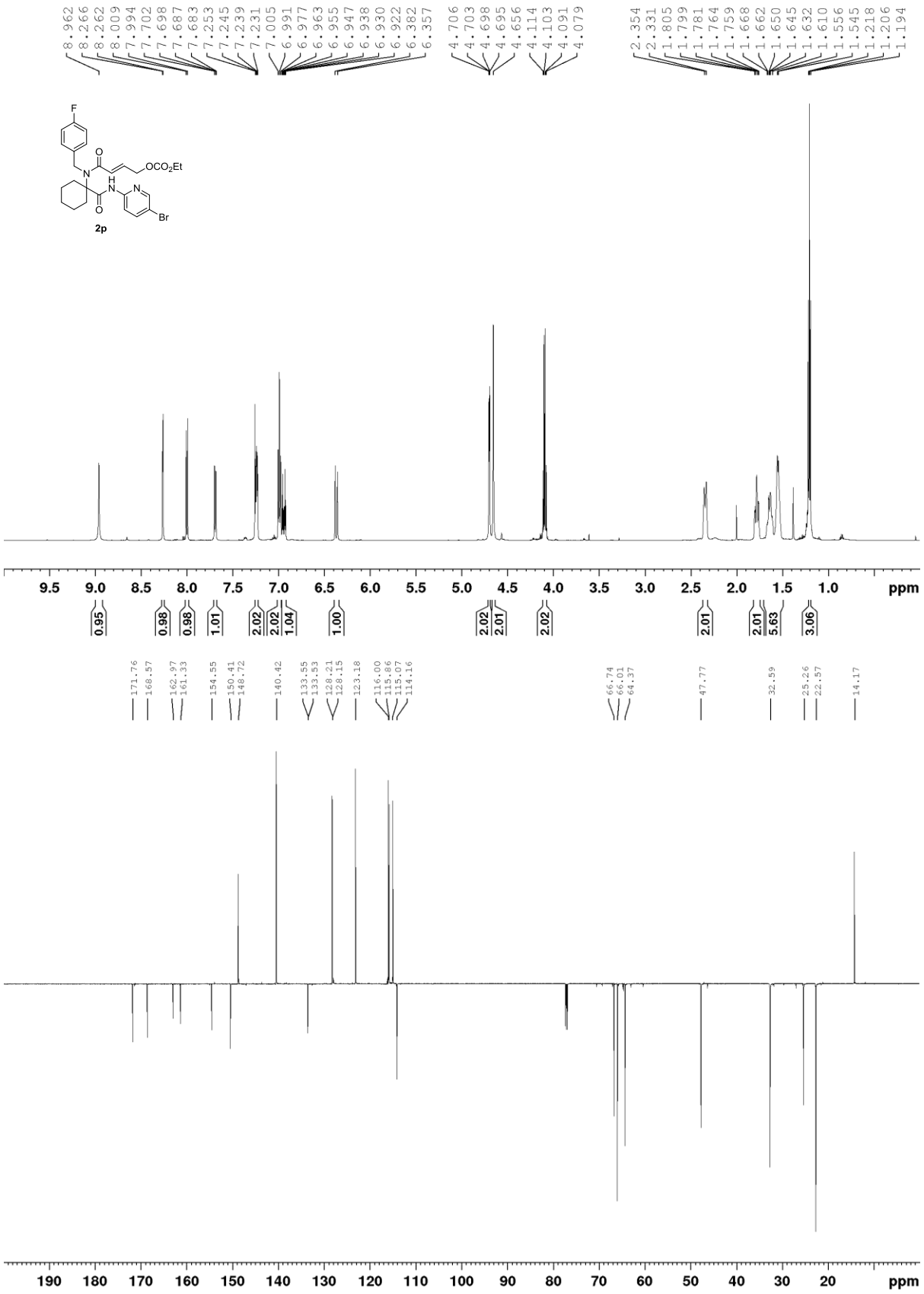
30
20
ppm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7.231
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6.977
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6.955
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6.930
6.922
6.382
6.357
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4.703
4.698
4.695
4.656
4.114
4.103
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4.079
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1.781
1.764
1.759
1.668
1.662
1.650
1.645
1.632
1.610
1.556
1.545
1.218
1.206
1.194
F
O
N
OCO2Et
H
N
N
O
Br
2p
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 ppm
0.95
0.98
0.98
1.01
2.02
2.02
1.04
1.00
2.02
2.01
2.02
2.01
2.01
5.63
3.06
171.76
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162.97
161.33
154.55
150.41
148.72
140.42
133.55
133.53
128.21
128.15
123.18
116.00
115.86
115.07
114.16
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47.77
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22.57
14.17
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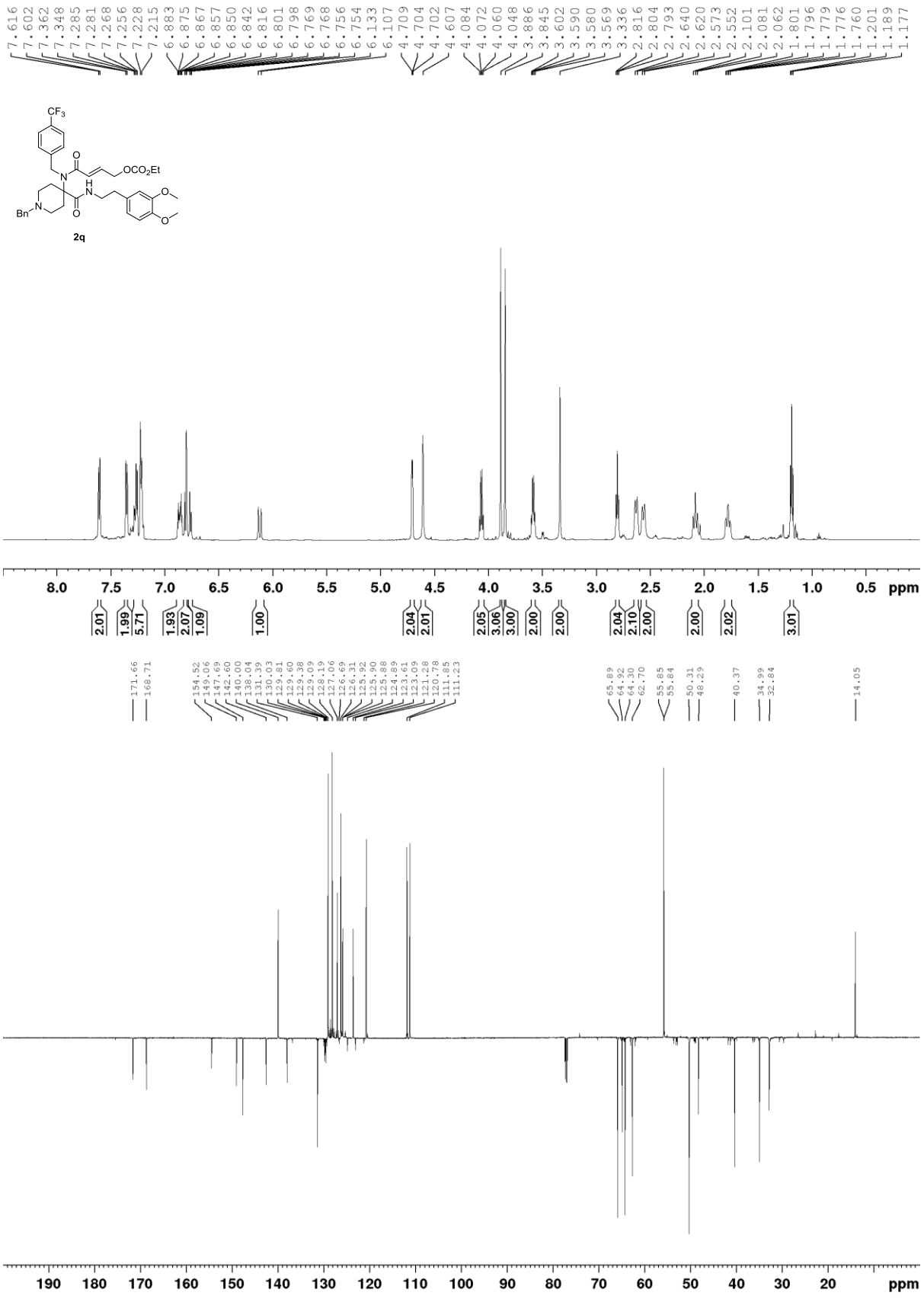
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6.857
6.850
6.842
6.816
6.801
6.798
6.769
6.768
6.756
6.754
6.133
6.107
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4.704
4.702
4.607
4.084
4.072
4.060
4.048
3.886
3.845
3.602
3.590
3.580
3.569
3.336
2.816
2.804
2.793
2.640
2.620
2.573
2.552
2.101
2.081
2.062
1.801
1.796
1.779
1.776
1.760
1.201
1.189
1.177
CF3
OCO2Et
Bn
2q
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2.01 1.99 5.71 1.93 2.07 1.09 1.00 2.04 2.01 2.05 3.06 3.00 2.00 2.00 2.04 2.10 2.00 2.00 2.02 3.01
171.66
168.71
154.52
149.06
147.69
142.60
140.00
138.04
131.39
130.03
129.81
129.60
129.38
129.09
128.19
127.06
126.69
126.31
125.92
125.90
125.88
124.89
123.61
123.09
121.28
120.78
111.85
111.23
65.89
64.92
64.30
62.70
55.85
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48.29
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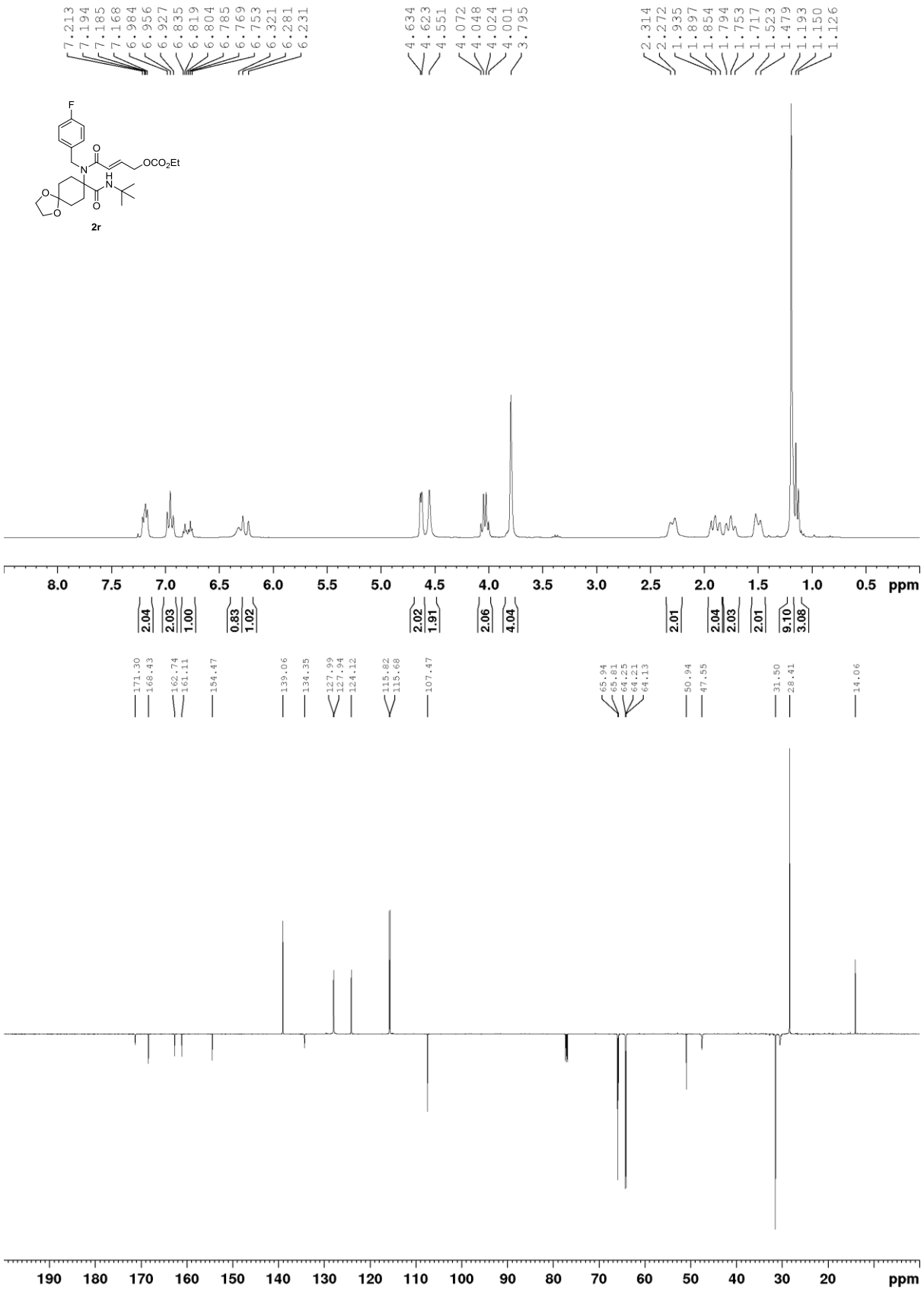
34.99
32.84
14.05
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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6.281
6.231
4.634
4.623
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4.072
4.048
4.024
4.001
3.795
2.314
2.272
1.935
1.897
1.854
1.794
1.753
1.717
1.523
1.479
1.193
1.150
1.126
F
O
N
OCO2Et
H
N
O
O
O
2r
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2.04 2.03 1.00 0.83 1.02 2.02 1.91 2.06 4.04 2.01 2.04 2.03 2.01 9.10 3.08
171.30
168.43
162.74
161.11
154.47
139.06
134.35
127.99
127.94
124.12
115.82
115.68
107.47
65.94
65.81
64.25
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50.94
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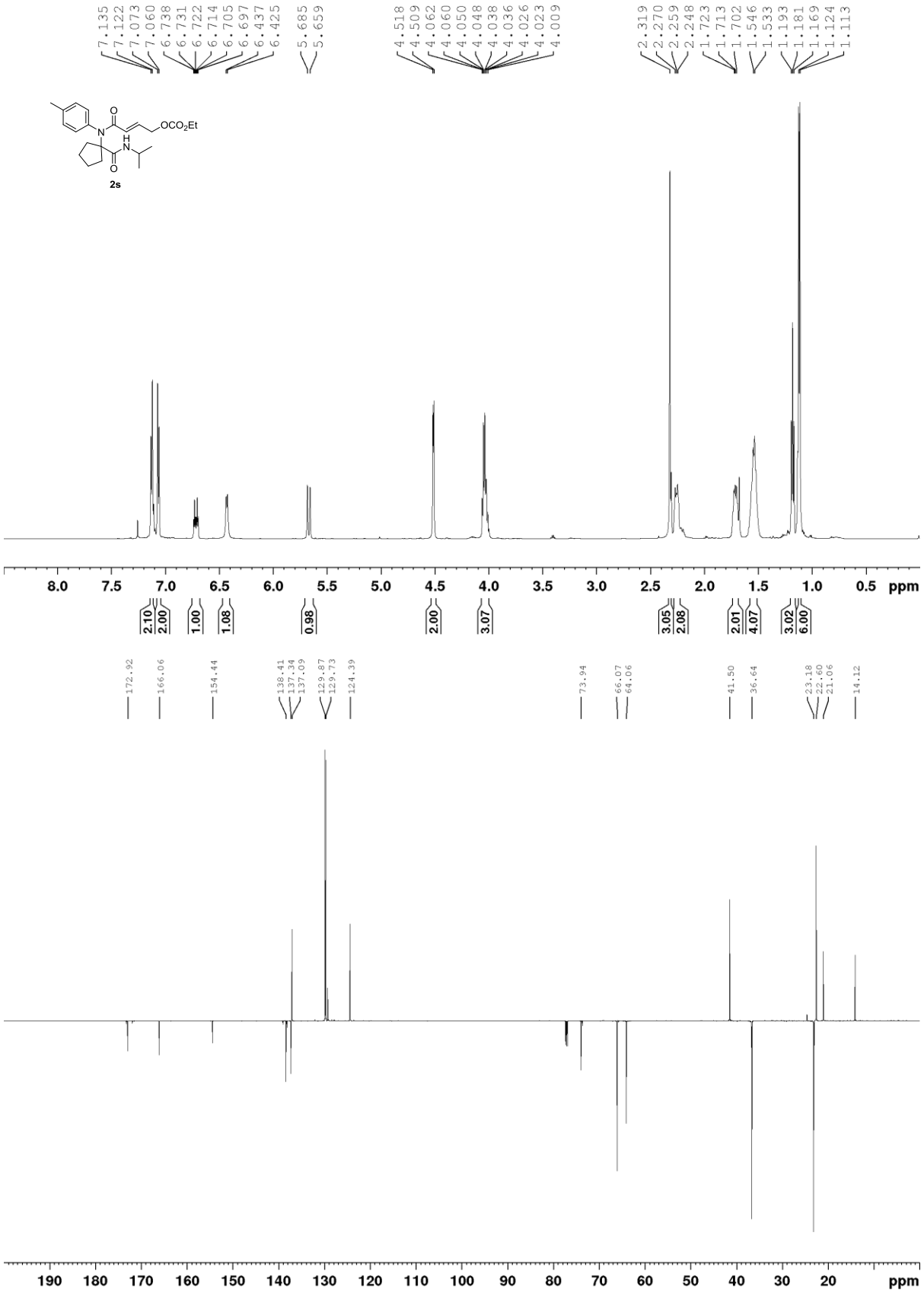
31.50
28.41
14.06
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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5.685
5.659
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4.509
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4.060
4.050
4.048
4.038
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4.023
4.009
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2.270
2.259
2.248
1.723
1.713
1.702
1.546
1.533
1.193
1.181
1.169
1.124
1.113
OCO2Et
2s
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172.92
166.06
154.44
138.41
137.34
137.09
129.87
129.73
124.39
73.94
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22.60
21.06
14.12
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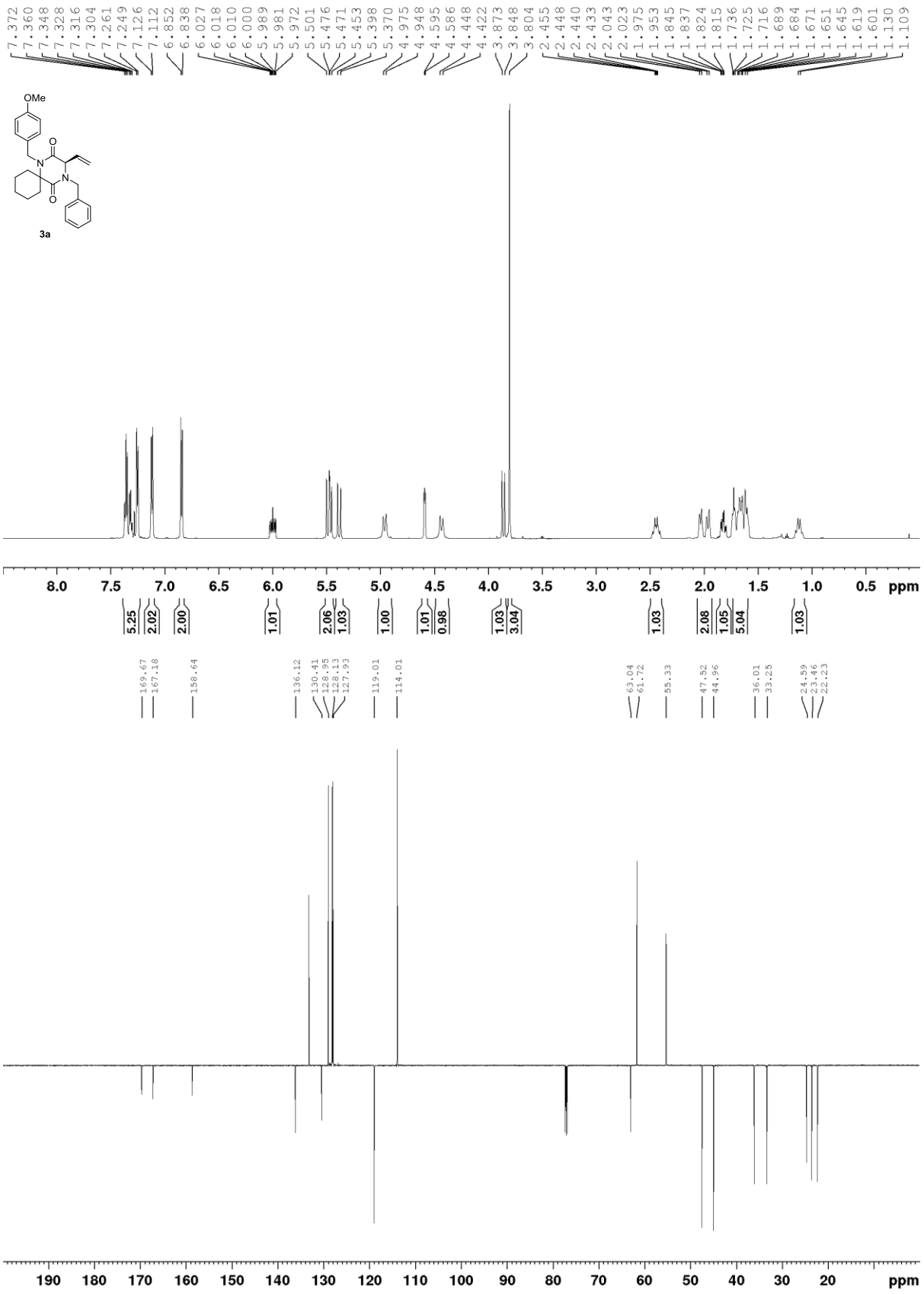
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5.972
5.501
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5.471
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4.586
4.448
4.422
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3.804
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2.448
2.440
2.433
2.043
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1.837
1.824
1.815
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1.689
1.684
1.671
1.651
1.645
1.619
1.601
1.130
1.109
OMe
3a
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169.67
167.18
158.64
136.12
130.41
128.95
128.13
127.93
119.01
114.01
63.04
61.72
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24.59
23.46
22.23
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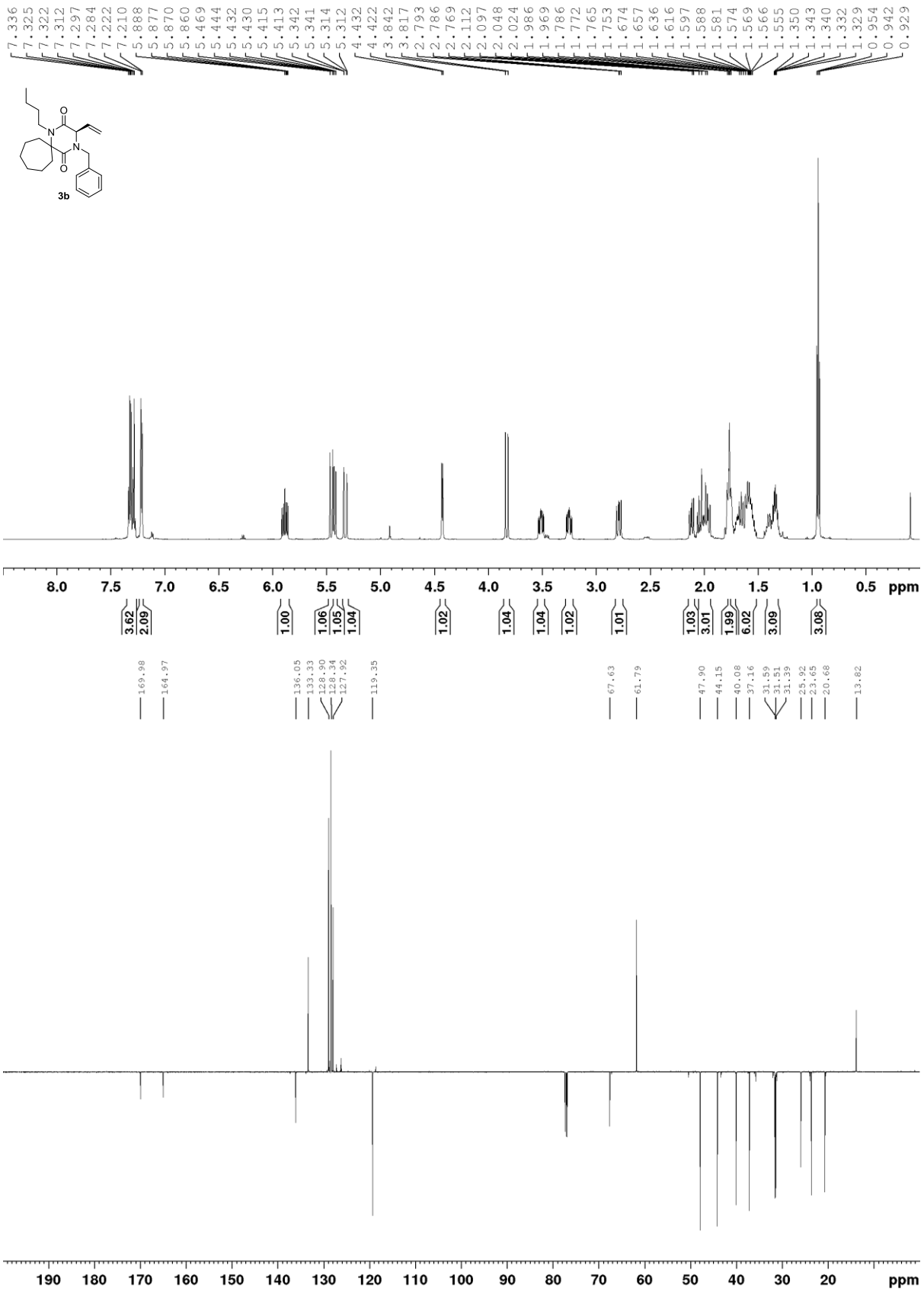
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1.569
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1.329
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0.929
3b
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3.62 2.09 1.00 1.06 1.05 1.04 1.02 1.04 1.04 1.02 1.01 1.03 3.01 1.99 6.02 3.09 3.08
169.98
164.97
136.05
133.33
128.90
128.34
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67.63
61.79
47.90
44.15
40.08
37.16
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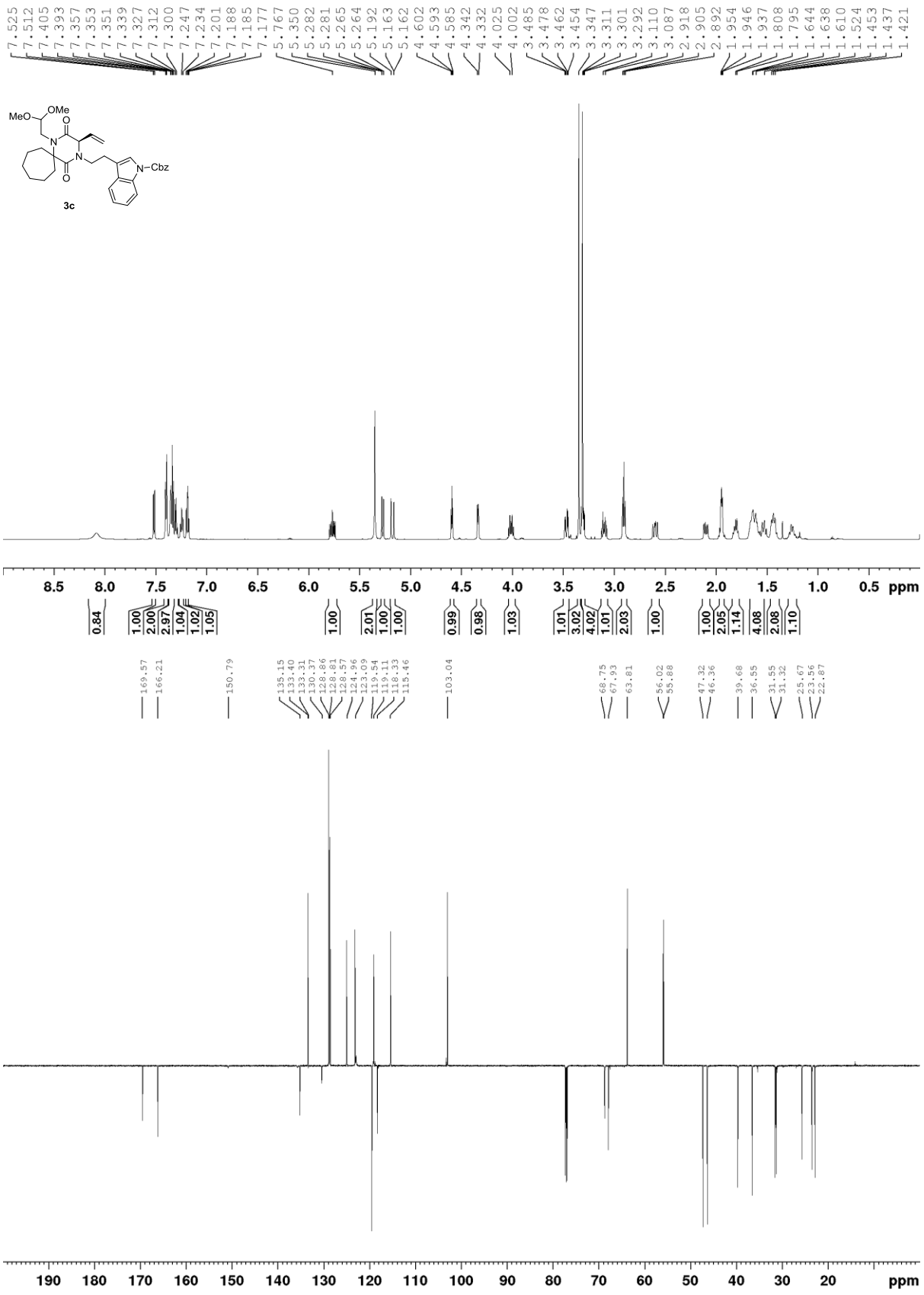
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.188
7.185
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1.610
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1.453
1.437
1.421
MeO
OMe
N
O
N
O
N–Cbz
3c
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150.79
135.15
133.40
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130.37
128.86
128.81
128.57
124.96
123.09
119.54
119.11
118.33
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103.04
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56.02
55.88
47.32
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31.55
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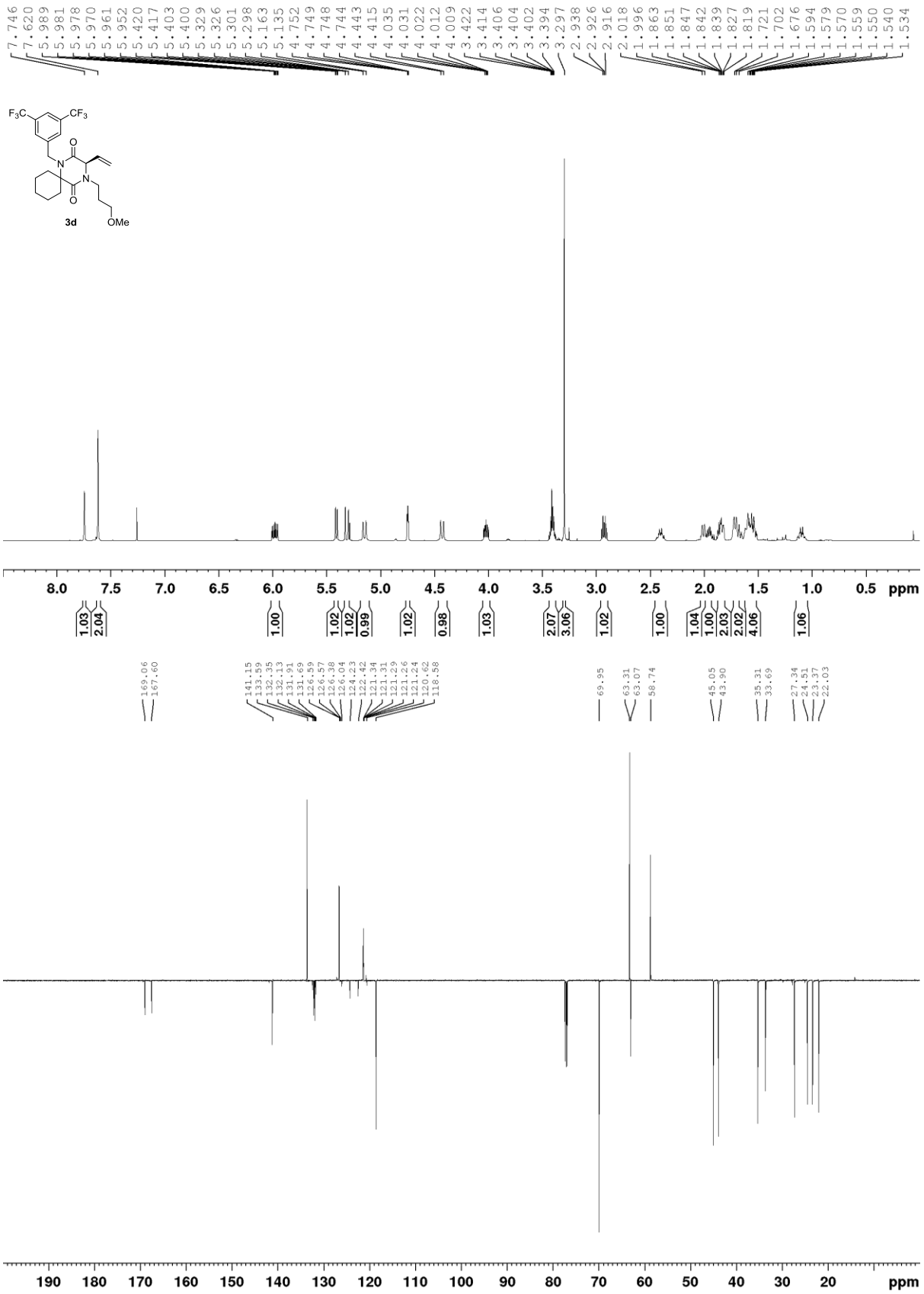
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CF3
O
N
N
O
3d
OMe
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5.0
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3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.04
1.00
1.02
1.02
0.99
1.02
0.98
1.03
2.07
3.06
1.02
1.00
1.04
1.00
2.03
2.02
4.06
1.06
169.06
167.60
141.15
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132.35
132.13
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126.59
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122.42
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121.29
121.26
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69.95
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27.34
24.51
23.37
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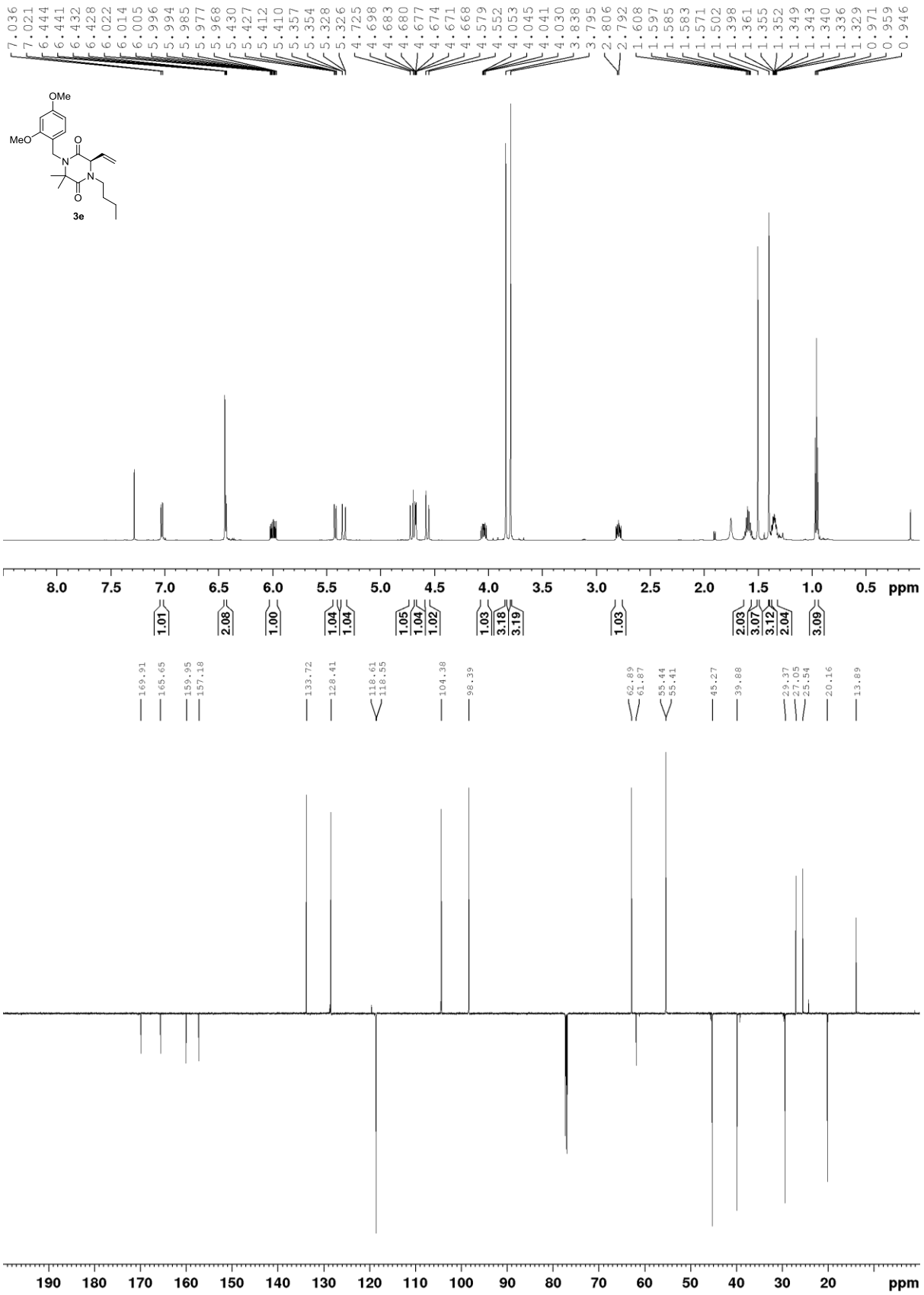
ppm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4.680
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4.668
4.579
4.552
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4.030
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1.597
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0.946
OMe
MeO
O
N
N
O
3e
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3.5
3.0
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1.0
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ppm
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1.04
1.04
1.05
1.04
1.02
1.03
3.18
3.19
1.03
2.03
3.07
3.12
2.04
3.09
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159.95
157.18
133.72
128.41
118.61
118.55
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98.39
62.89
61.87
55.44
55.41
45.27
39.88
29.37
27.05
25.54
20.16
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120
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80
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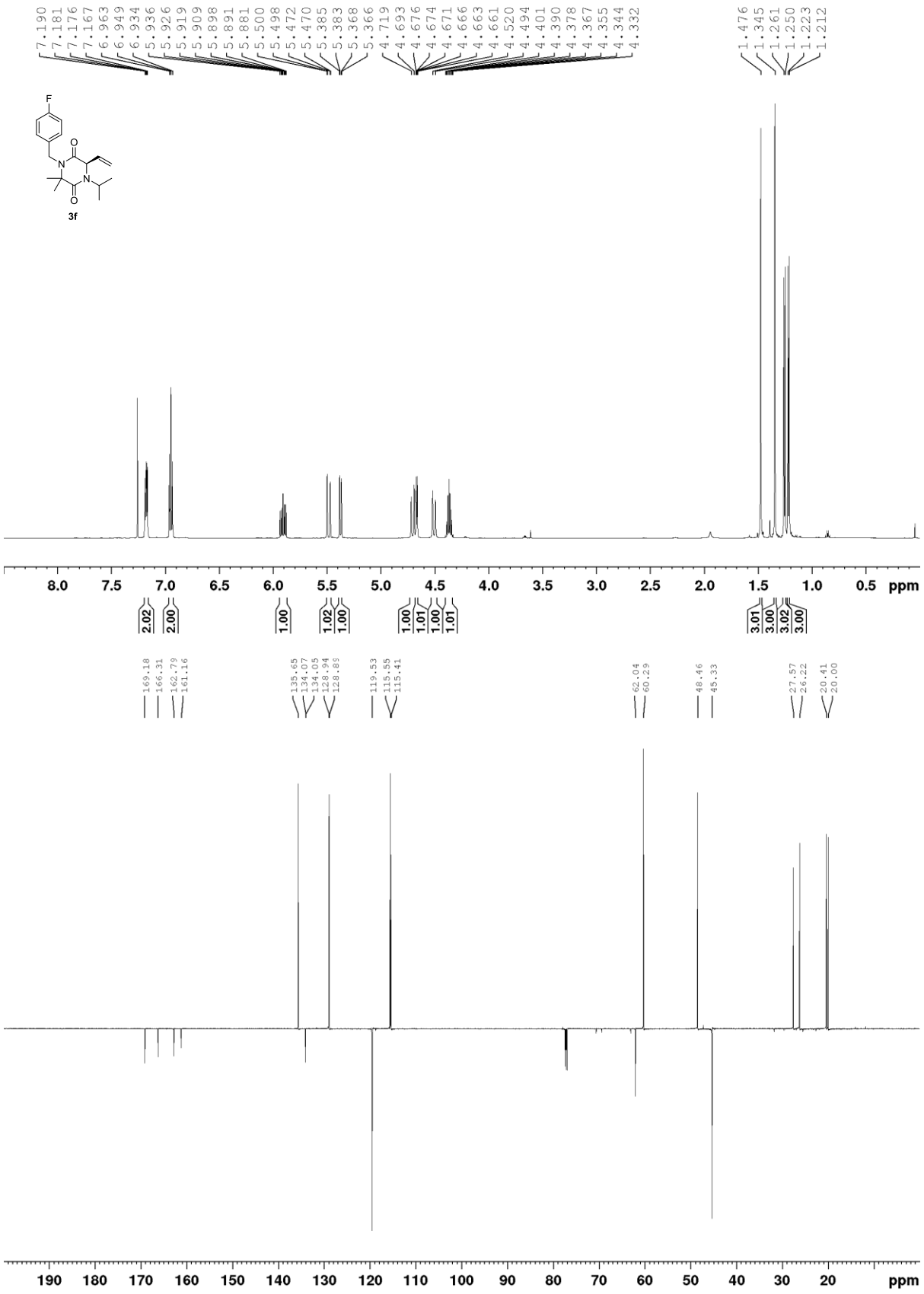
20
ppm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5.366
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4.693
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4.674
4.671
4.666
4.663
4.661
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4.367
4.355
4.344
4.332
1.476
1.345
1.261
1.250
1.223
1.212
F
O
N
N
O
3f
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169.18
166.31
162.79
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134.05
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128.88
119.53
115.55
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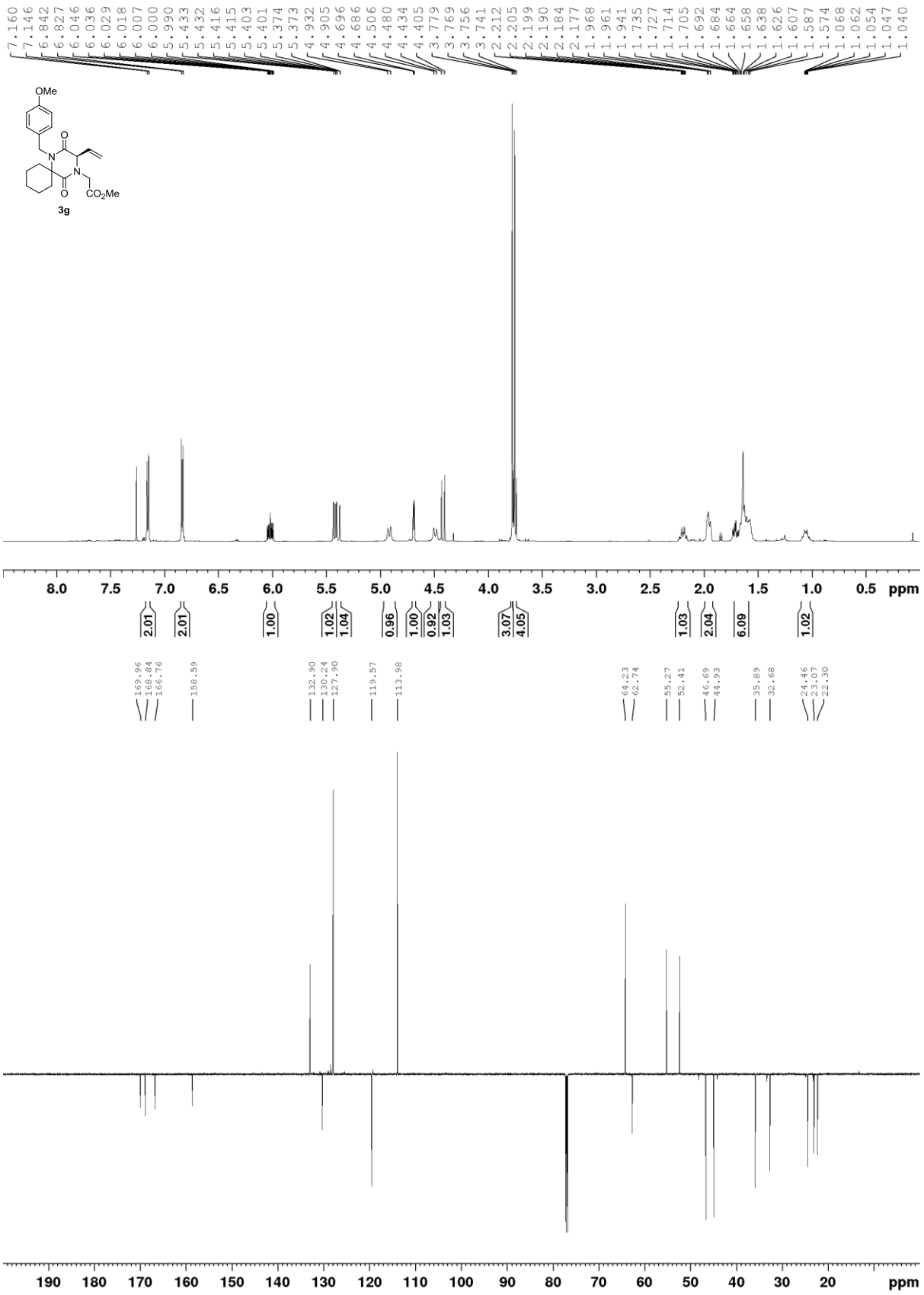
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5.401
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5.373
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4.480
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4.405
3.779
3.769
3.756
3.741
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2.205
2.199
2.190
2.184
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1.727
1.714
1.705
1.692
1.684
1.664
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1.638
1.626
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1.587
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1.040
OMe
O
N
O
N
CO2Me
3g
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166.76
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127.90
119.57
113.98
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55.27
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24.46
23.07
22.30
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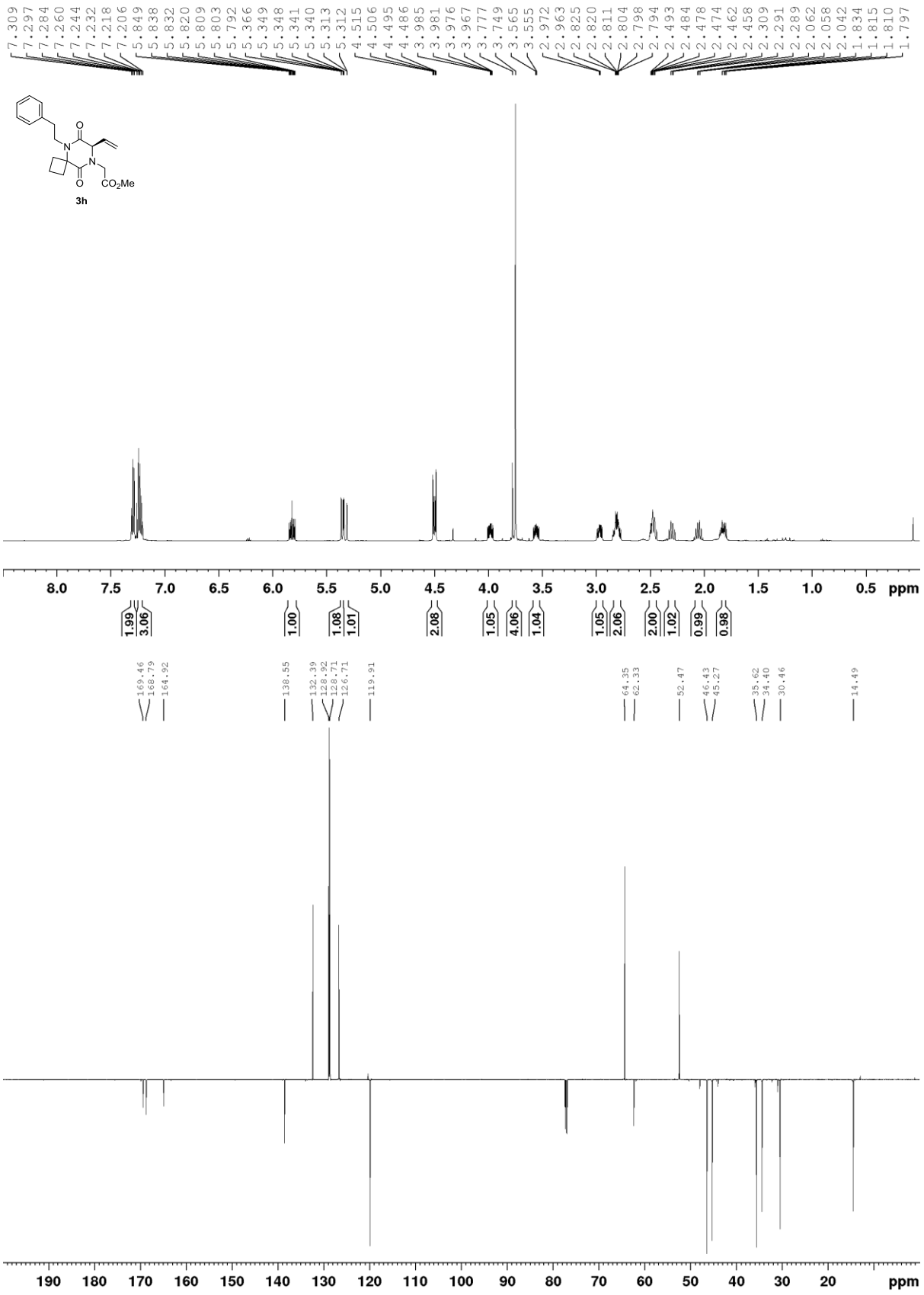
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5.341
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5.312
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4.495
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3.565
3.555
2.972
2.963
2.825
2.820
2.811
2.804
2.798
2.794
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2.478
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2.462
2.458
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2.291
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N
O
N
O
CO2Me
3h
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6.0
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4.0
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ppm
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1.00
1.08
1.01
2.08
1.05
4.06
1.04
1.05
2.06
2.00
1.02
0.99
0.98
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128.92
128.71
126.71
119.91
64.35
62.33
52.47
46.43
45.27
35.62
34.40
30.46
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160
150
140
130
120
110
100
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80
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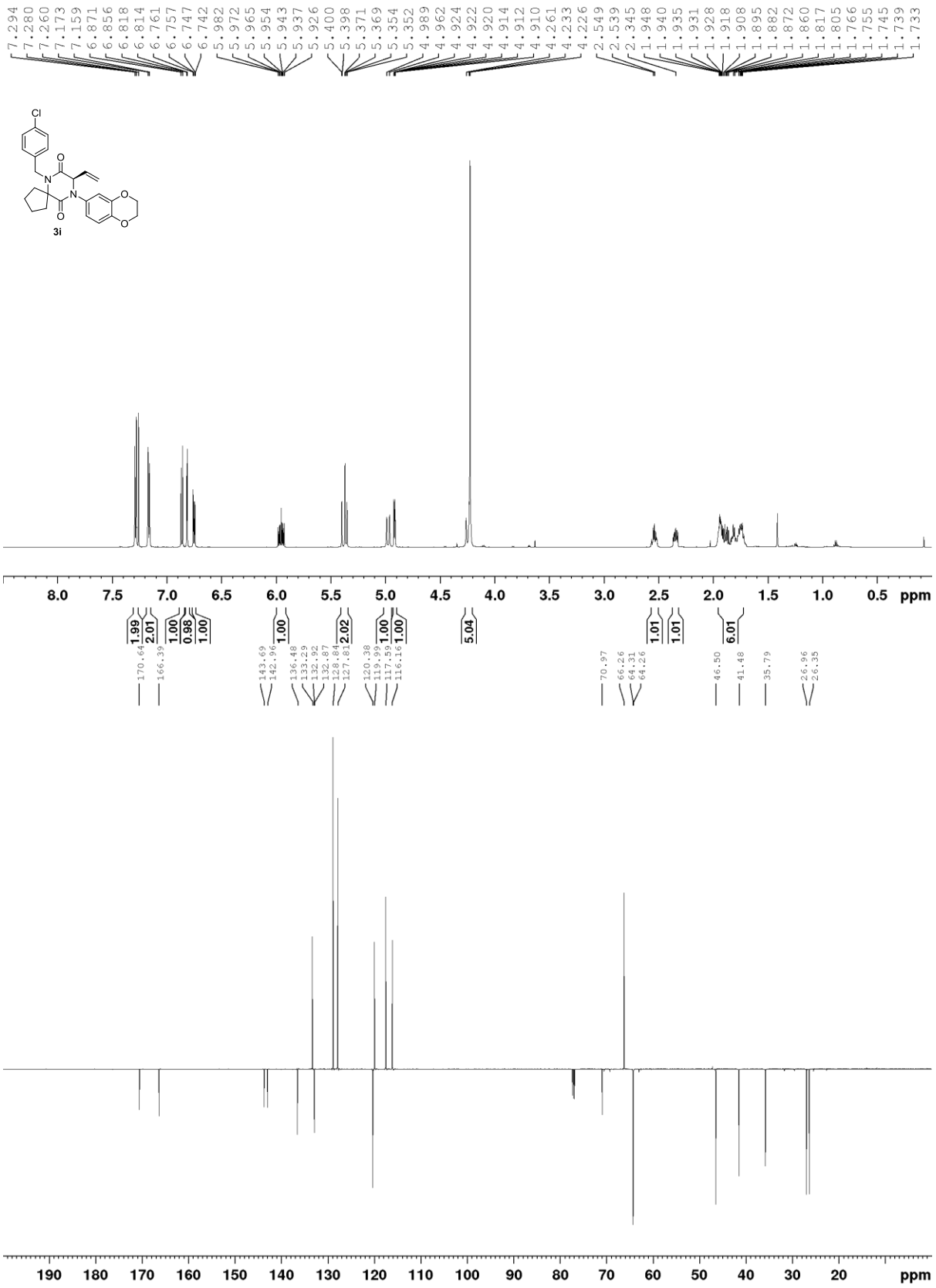
50
40
30
20
ppm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6.742
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5.972
5.965
5.954
5.943
5.937
5.926
5.400
5.398
5.371
5.369
5.354
5.352
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4.962
4.924
4.922
4.920
4.914
4.912
4.910
4.261
4.233
4.226
2.549
2.539
2.345
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1.940
1.935
1.931
1.928
1.918
1.908
1.895
1.882
1.872
1.860
1.817
1.805
1.766
1.755
1.745
1.739
1.733
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N
N
O
O
O
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6.0
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4.0
3.5
3.0
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0.5
ppm
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1.00
0.98
1.00
1.00
2.02
1.00
1.00
5.04
1.01
1.01
6.01
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166.39
143.69
142.96
136.48
133.29
132.92
132.87
128.84
127.81
120.38
119.99
117.59
116.16
70.97
66.26
64.31
64.26
46.50
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26.96
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150
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120
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80
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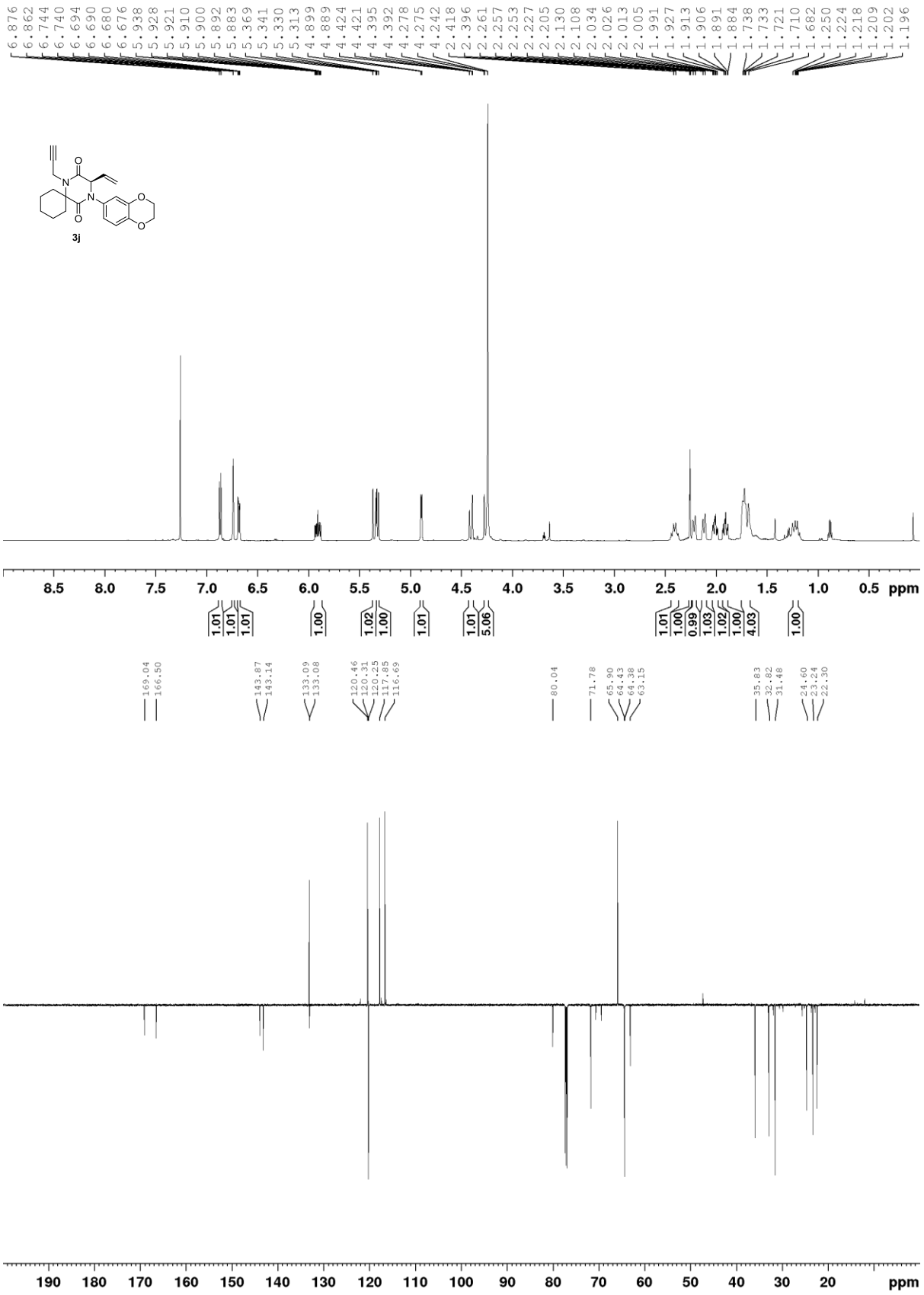
40
30
20
ppm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5.900
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5.883
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5.341
5.330
5.313
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4.889
4.424
4.421
4.395
4.392
4.278
4.275
4.242
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2.396
2.261
2.257
2.253
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2.205
2.130
2.108
2.034
2.026
2.013
2.005
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1.927
1.913
1.906
1.891
1.884
1.738
1.733
1.721
1.710
1.682
1.250
1.224
1.218
1.209
1.202
1.196
3j
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169.04
166.50
143.87
143.14
133.09
133.08
120.46
120.31
120.25
117.85
116.69
80.04
71.78
65.90
64.43
64.38
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32.82
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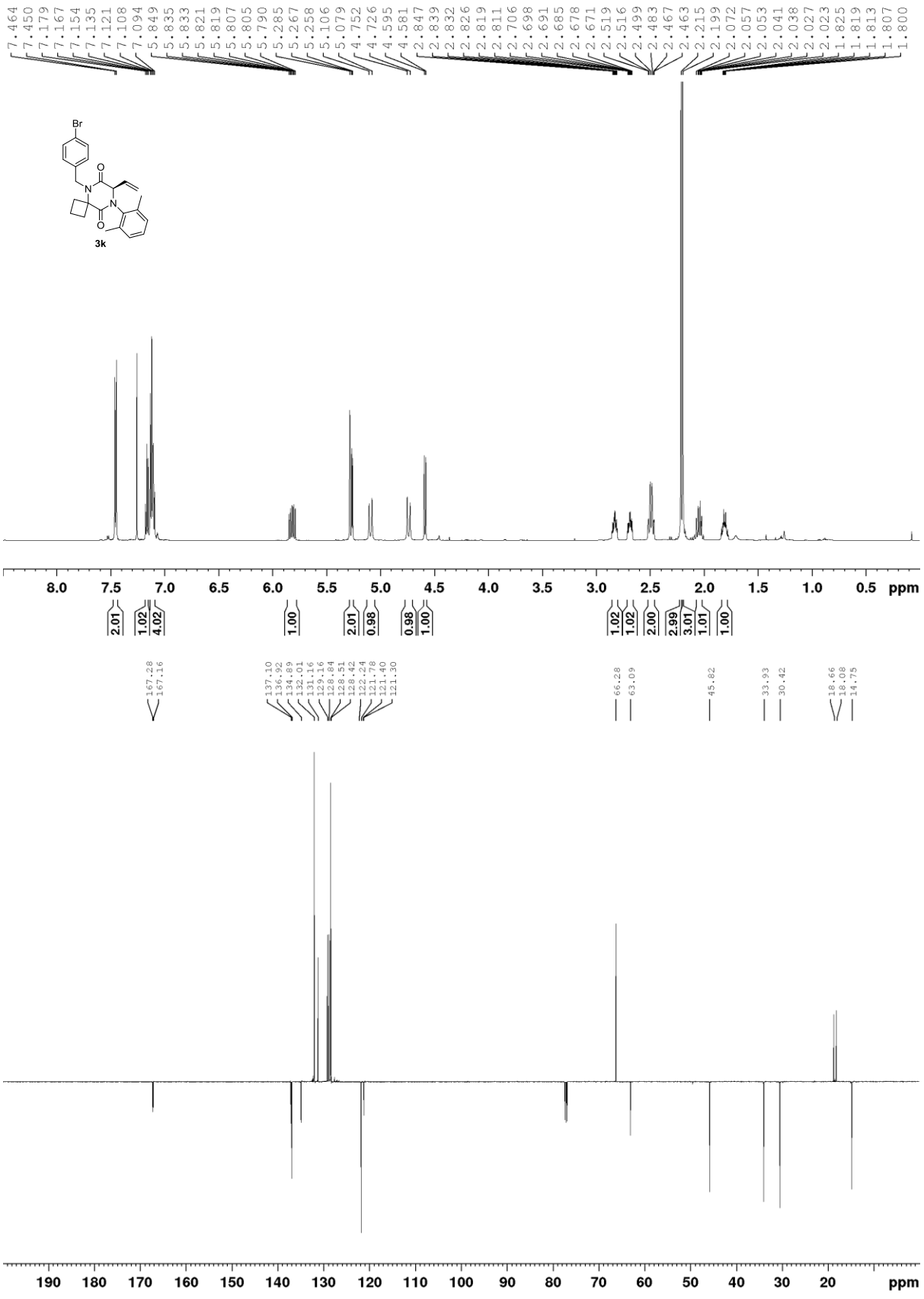
24.60
23.24
22.30
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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5.821
5.819
5.807
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5.267
5.258
5.106
5.079
4.752
4.726
4.595
4.581
2.847
2.839
2.832
2.826
2.819
2.811
2.706
2.698
2.691
2.685
2.678
2.671
2.519
2.516
2.499
2.483
2.467
2.463
2.215
2.199
2.072
2.057
2.053
2.041
2.038
2.027
2.023
1.825
1.819
1.813
1.807
1.800
Br
O
N
N
O
3k
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2.01 1.02 4.02 1.00 2.01 0.98 0.98 1.00 1.02 1.02 2.00 2.99 3.01 1.01 1.00
167.28
167.16
137.10
136.92
134.89
132.01
131.16
129.16
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128.51
128.42
122.24
121.78
121.40
121.30
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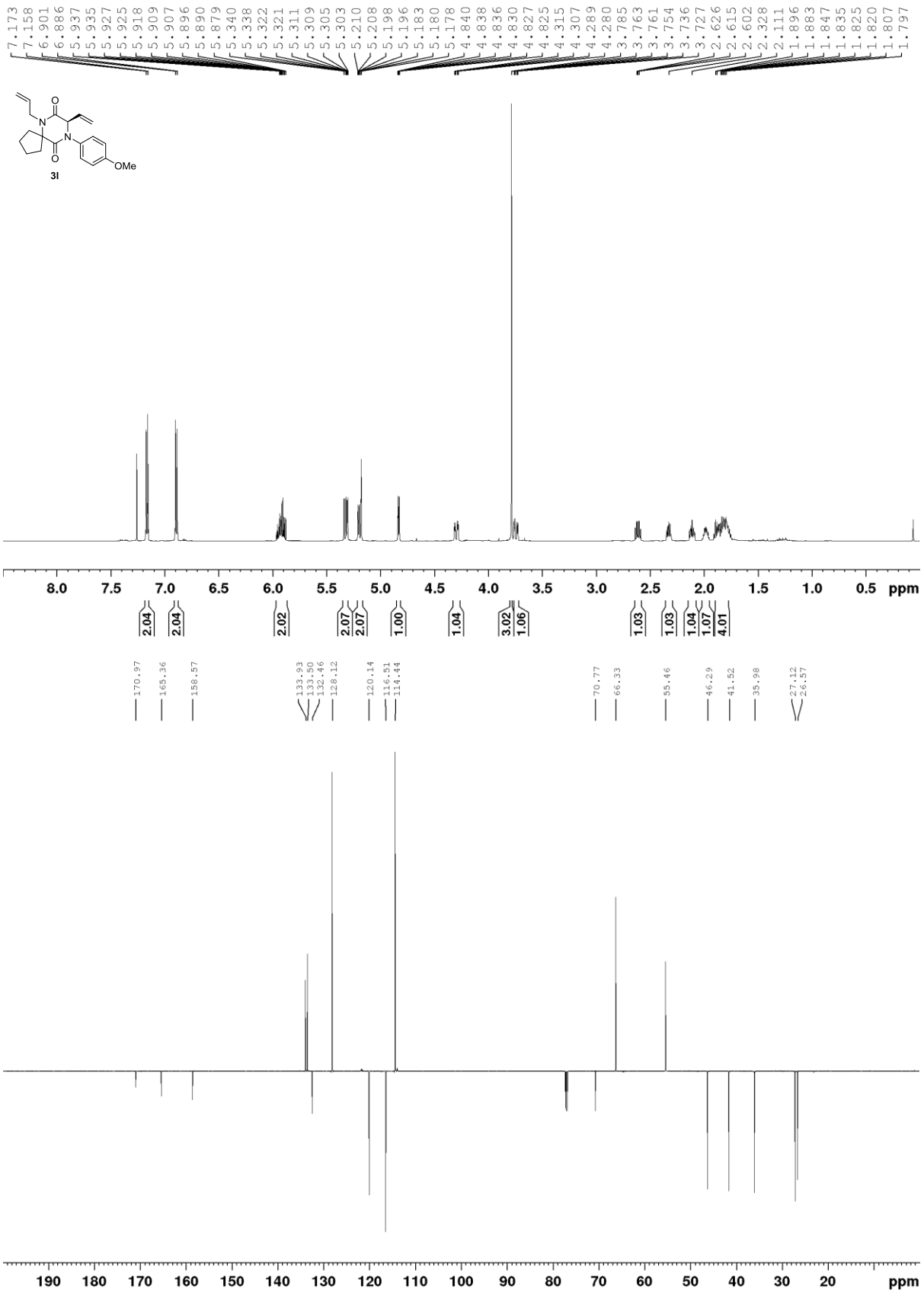
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5.322
5.321
5.311
5.309
5.305
5.303
5.210
5.208
5.198
5.196
5.183
5.180
5.178
4.840
4.838
4.836
4.830
4.827
4.825
4.315
4.307
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3.754
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2.626
2.615
2.602
2.328
2.111
1.896
1.883
1.847
1.835
1.825
1.820
1.807
1.797
O
N
O
N
OMe
3l
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2.04
2.04
2.02
2.07
2.07
1.00
1.04
3.02
1.06
1.03
1.03
1.04
1.07
4.01
170.97
165.36
158.57
133.93
133.50
132.46
128.12
120.14
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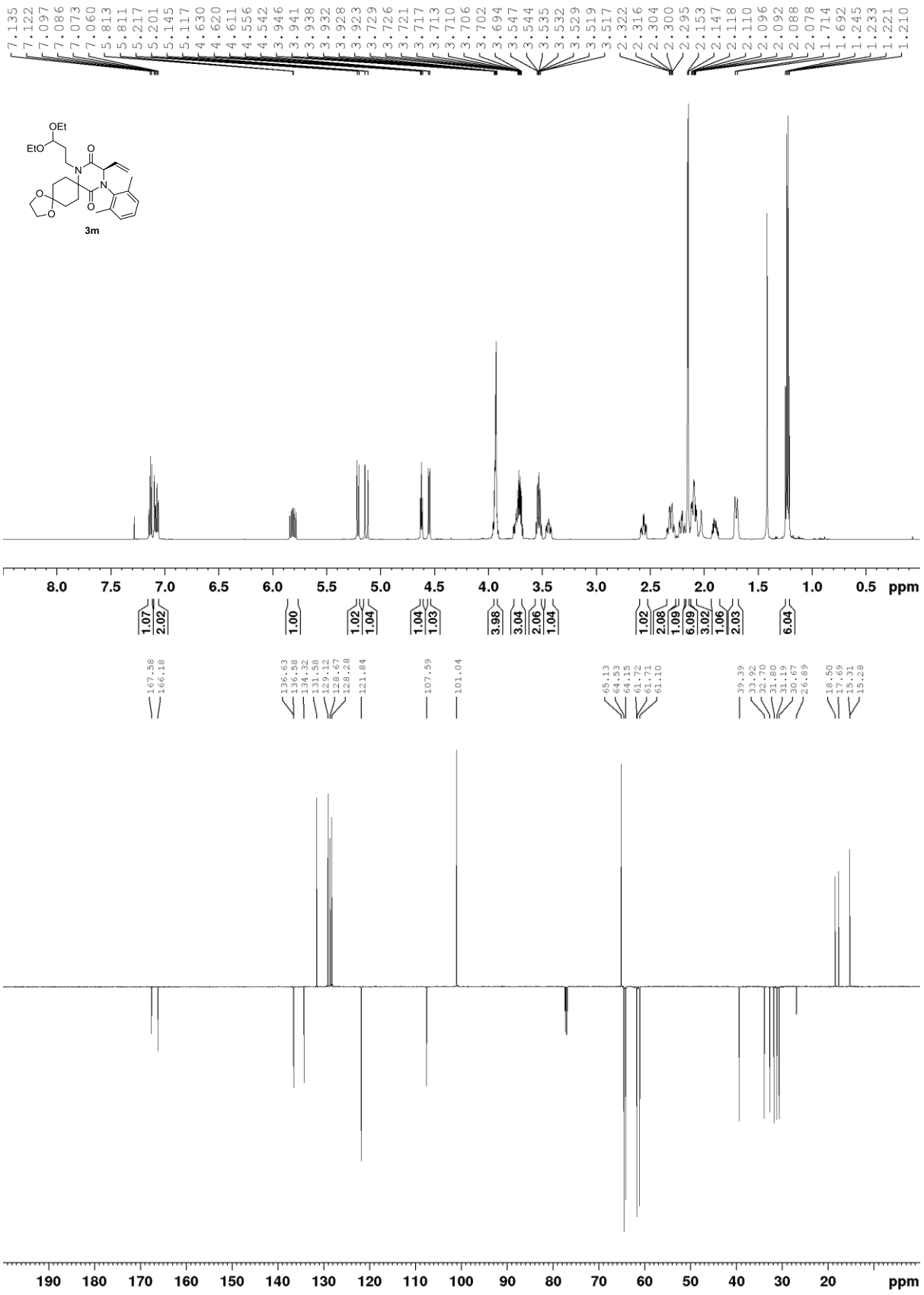
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4.542
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3.941
3.938
3.932
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3.729
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3.702
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2.110
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2.092
2.088
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1.714
1.692
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1.233
1.221
1.210
OEt
EtO
O
N
O
N
O
O
O
3m
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166.18
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131.58
129.42
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128.28
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101.04
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61.71
61.10
39.39
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32.70
31.80
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17.69
15.31
15.28
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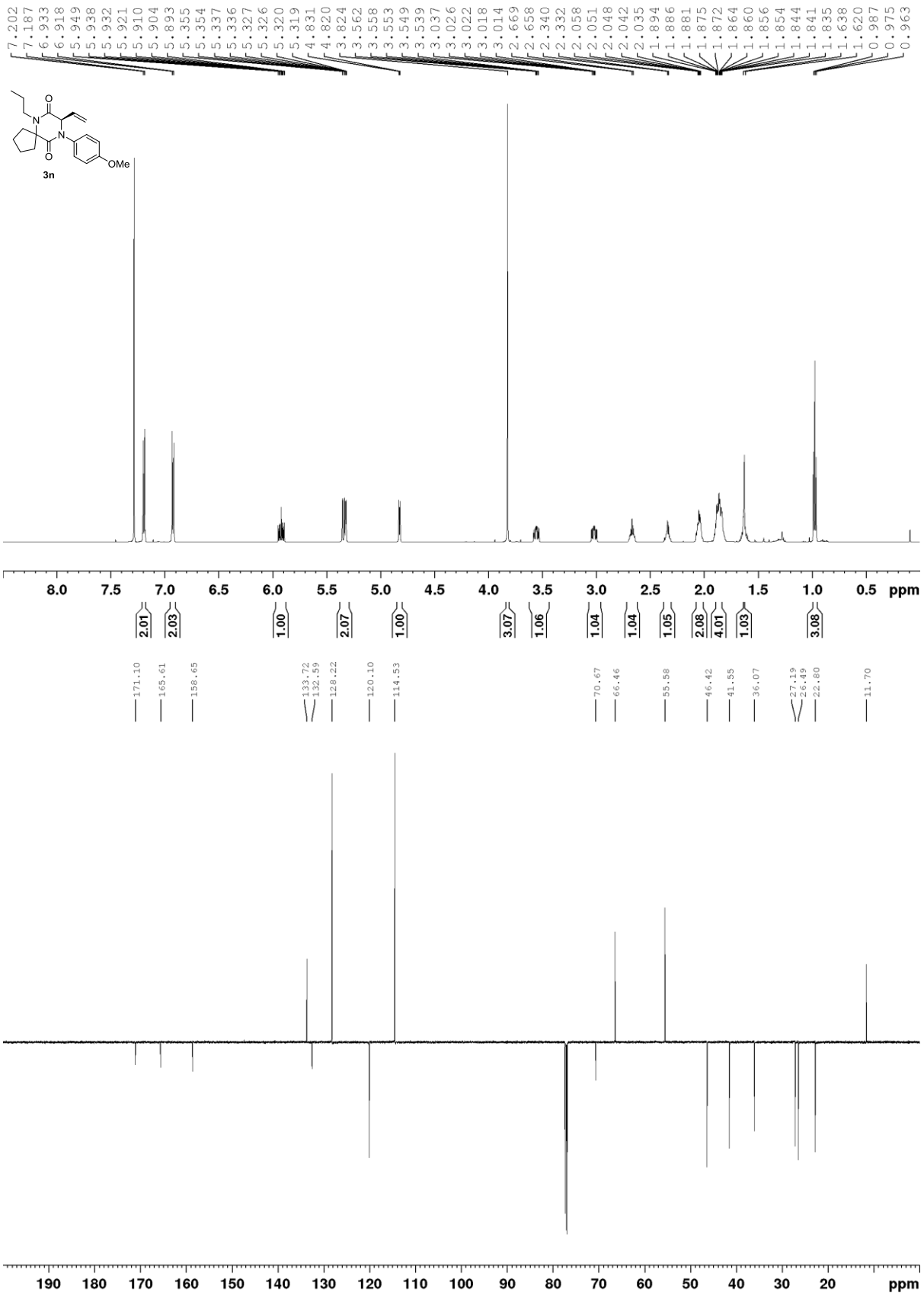
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5.319
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4.820
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1.844
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1.835
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0.975
0.963
OMe
3n
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.03
1.00
2.07
1.00
3.07
1.06
1.04
1.04
1.05
2.08
4.01
1.03
3.08
171.10
165.61
158.65
133.72
132.59
128.22
120.10
114.53
70.67
66.46
55.58
46.42
41.55
36.07
27.19
26.49
22.80
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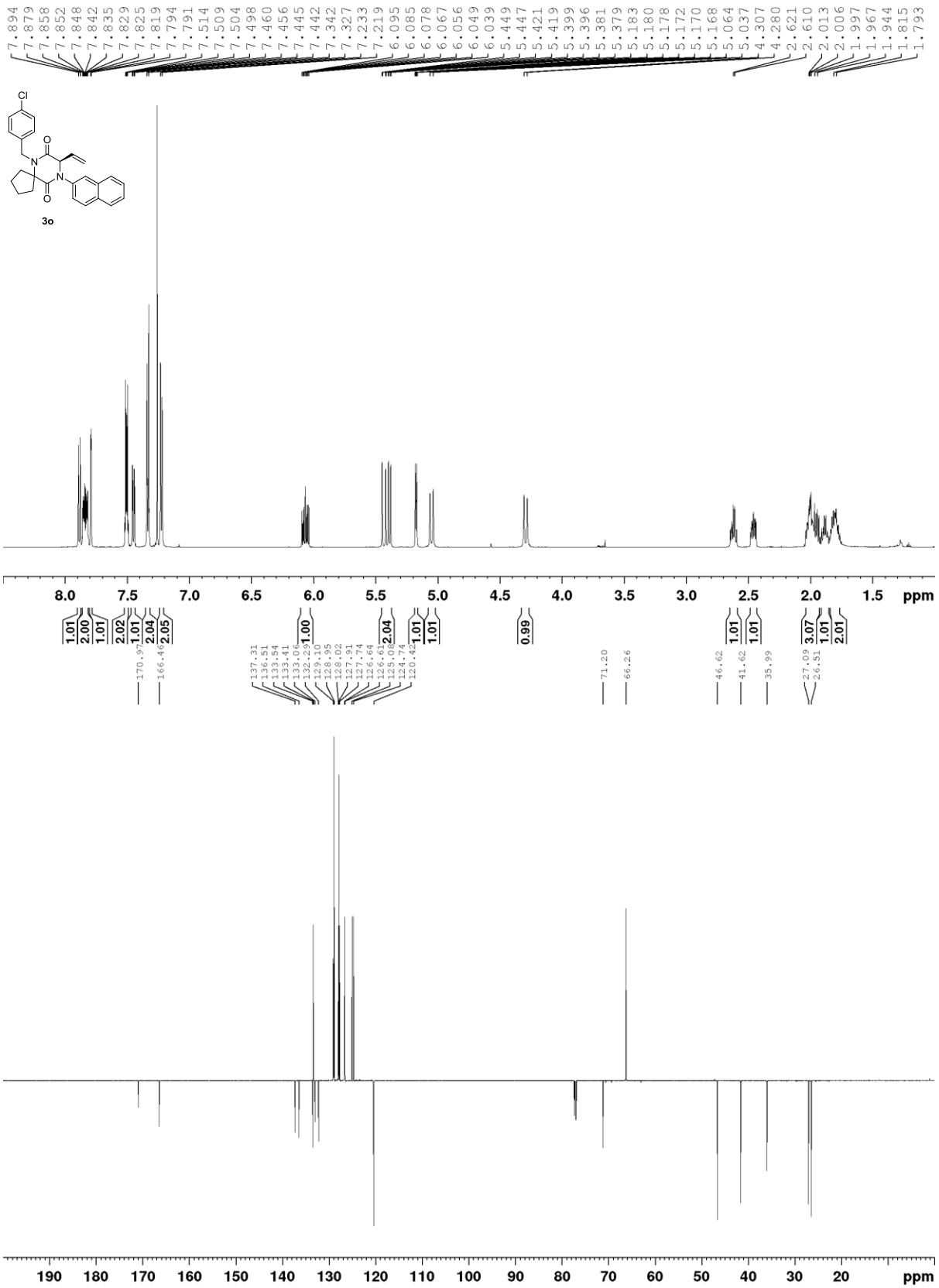
20
ppm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6.085
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O
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ppm
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2.00
1.01
2.02
1.01
2.04
2.05
1.00
2.04
1.01
1.01
0.99
1.01
1.01
3.07
1.01
2.01
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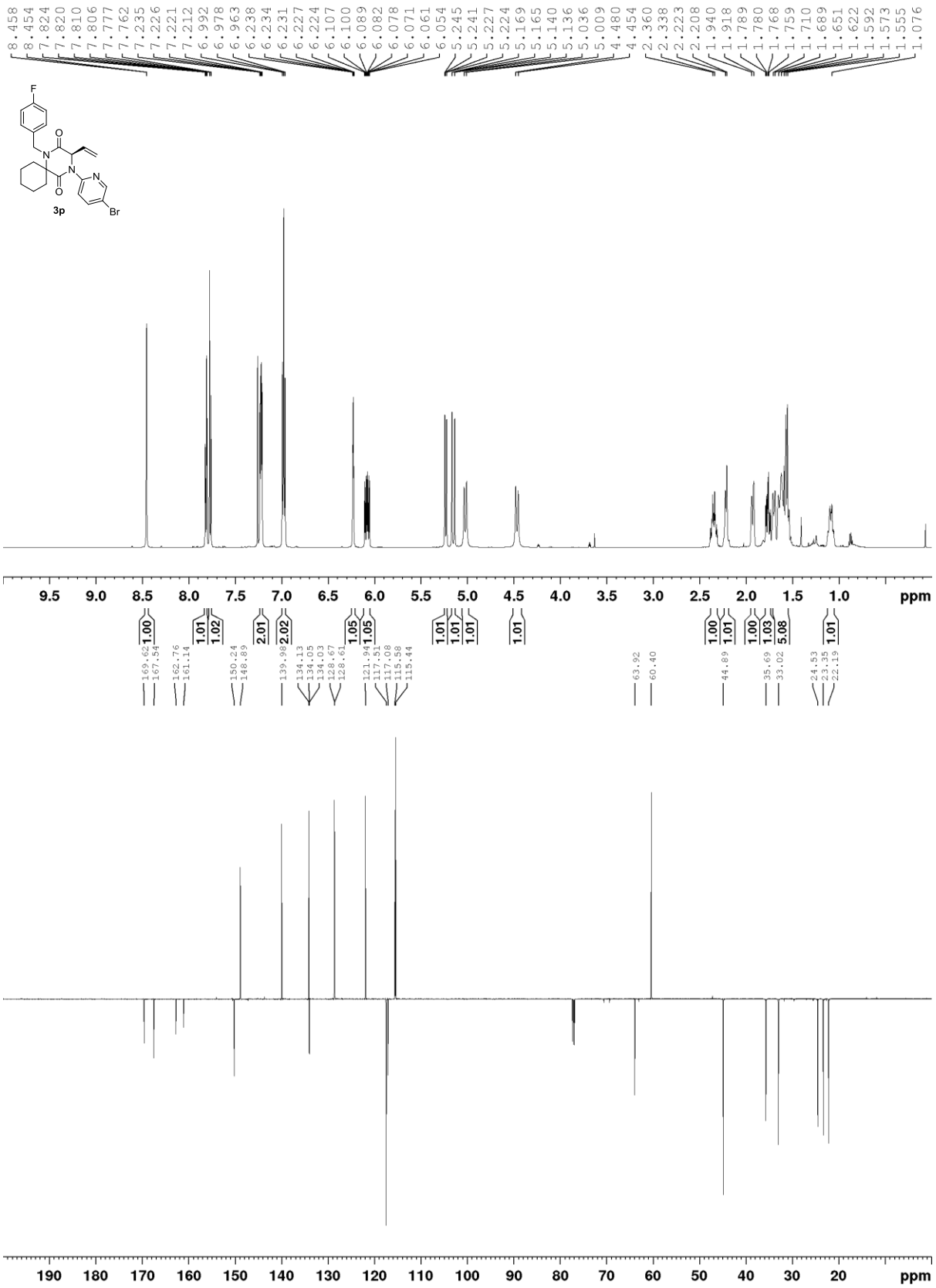
ppm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F
O
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O
N
3p
Br
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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167.54
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161.14
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134.13
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128.61
121.94
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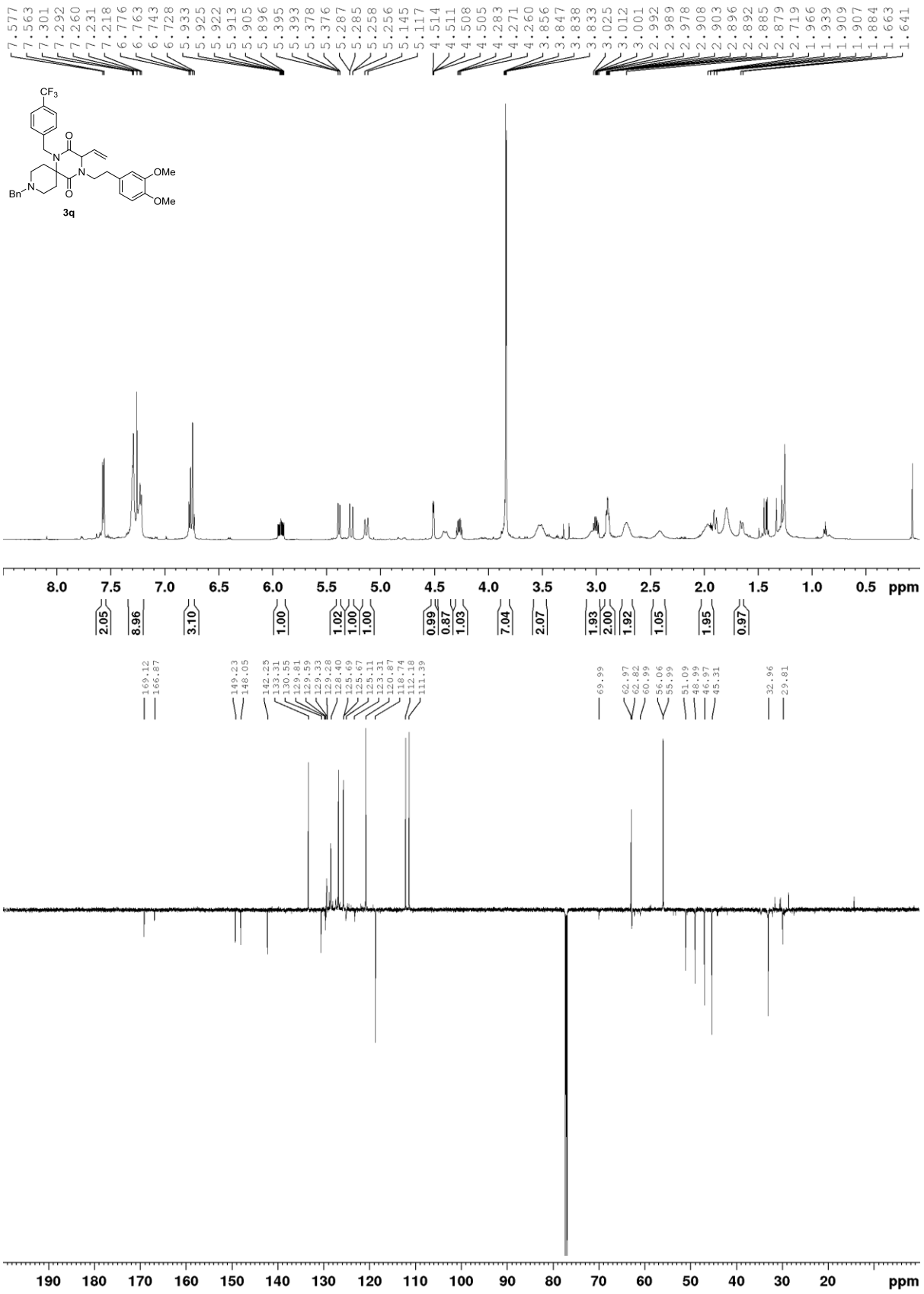
117.08
115.58
115.44
63.92
60.40
44.89
35.69
33.02
24.53
23.35
22.19
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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7.563
7.301
7.292
7.260
7.231
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6.776
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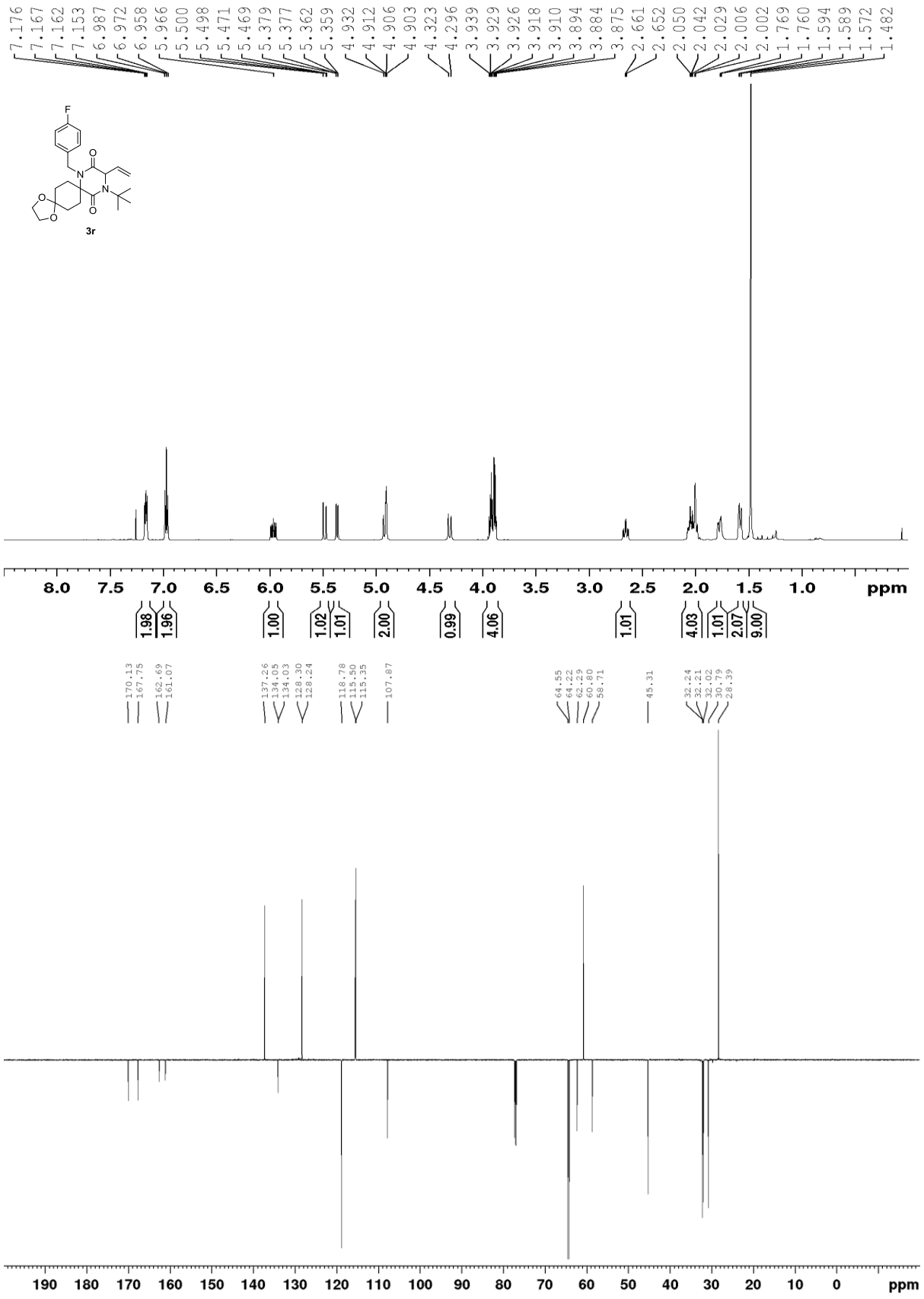
6.743
6.728
5.933
5.925
5.922
5.913
5.905
5.896
5.395
5.393
5.378
5.376
5.287
5.285
5.258
5.256
5.145
5.117
4.514
4.511
4.508
4.505
4.283
4.271
4.260
3.856
3.847
3.838
3.833
3.025
3.012
3.001
2.992
2.989
2.978
2.908
2.903
2.896
2.892
2.885
2.879
2.719
1.966
1.939
1.909
1.907
1.884
1.663
1.641
CF3
OMe
OMe
Bn
3q
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 ppm
2.05 8.96 3.10 1.00 1.02 1.00 1.00 0.99 0.87 1.03 7.04 2.07 1.93 2.00 1.92 1.05 1.95 0.97
169.12
166.87
149.23
148.05
142.25
133.31
130.55
129.81
129.59
129.33
129.28
128.40
125.69
125.67
125.11
123.31
120.87
118.74
112.18
111.39
69.99
62.97
62.82
60.99
56.06
55.99
51.09
48.99
46.97
45.31
32.96
29.81
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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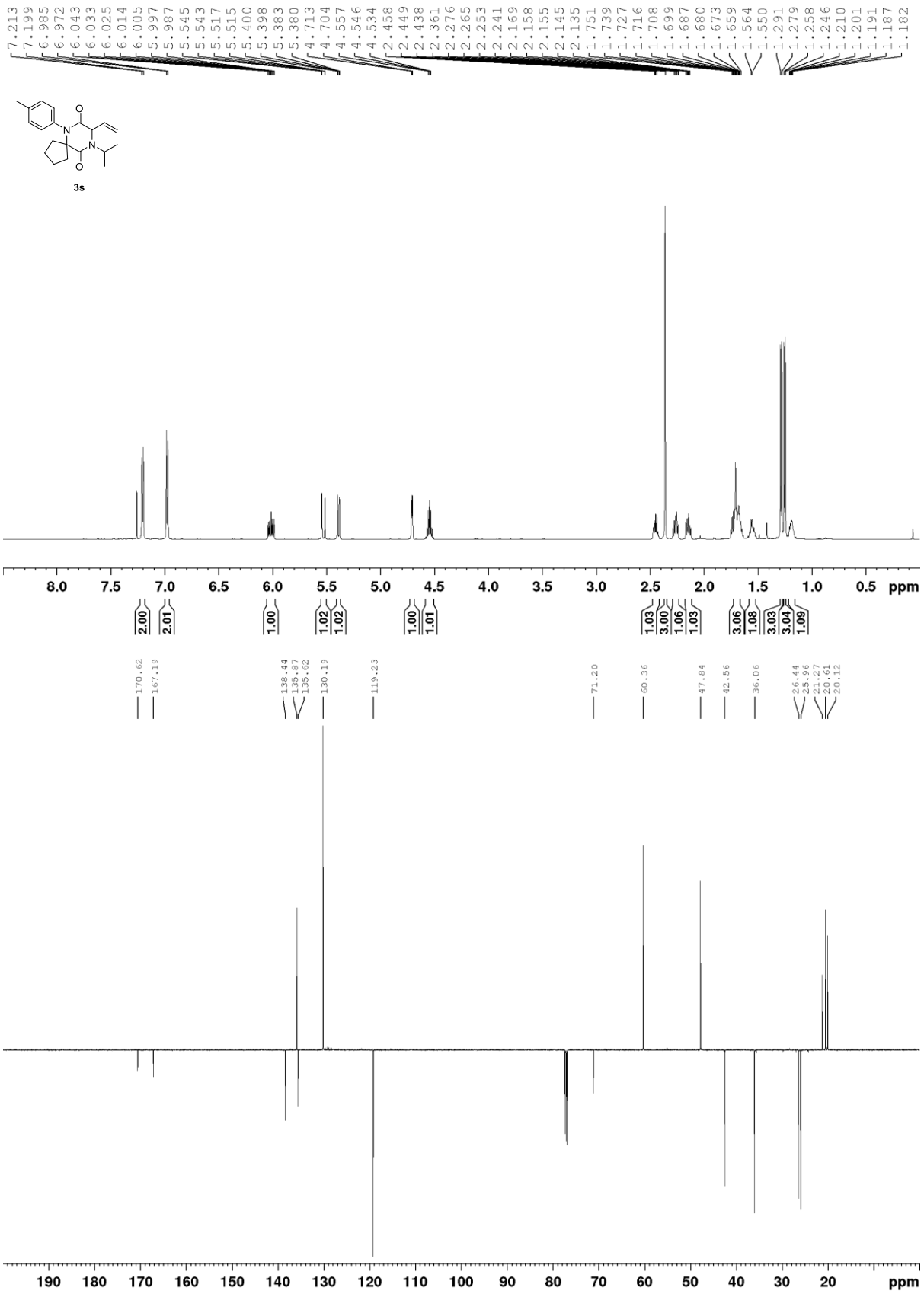
7.162
7.153
6.987
6.972
6.958
5.966
5.500
5.498
5.471
5.469
5.379
5.377
5.362
5.359
4.932
4.912
4.906
4.903
4.323
4.296
3.939
3.929
3.926
3.918
3.910
3.894
3.884
3.875
2.661
2.652
2.050
2.042
2.029
2.006
2.002
1.769
1.760
1.594
1.589
1.572
1.482
F
O
N
O
N
O
O
O
3r
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.98
1.96
1.00
1.02
1.01
2.00
0.99
4.06
1.01
4.03
1.01
2.07
9.00
170.13
167.75
162.69
161.07
137.26
134.05
134.03
128.30
128.24
118.78
115.50
115.35
107.87
64.55
64.22
62.29
60.80
58.71
45.31
32.24
32.21
32.02
30.79
28.39
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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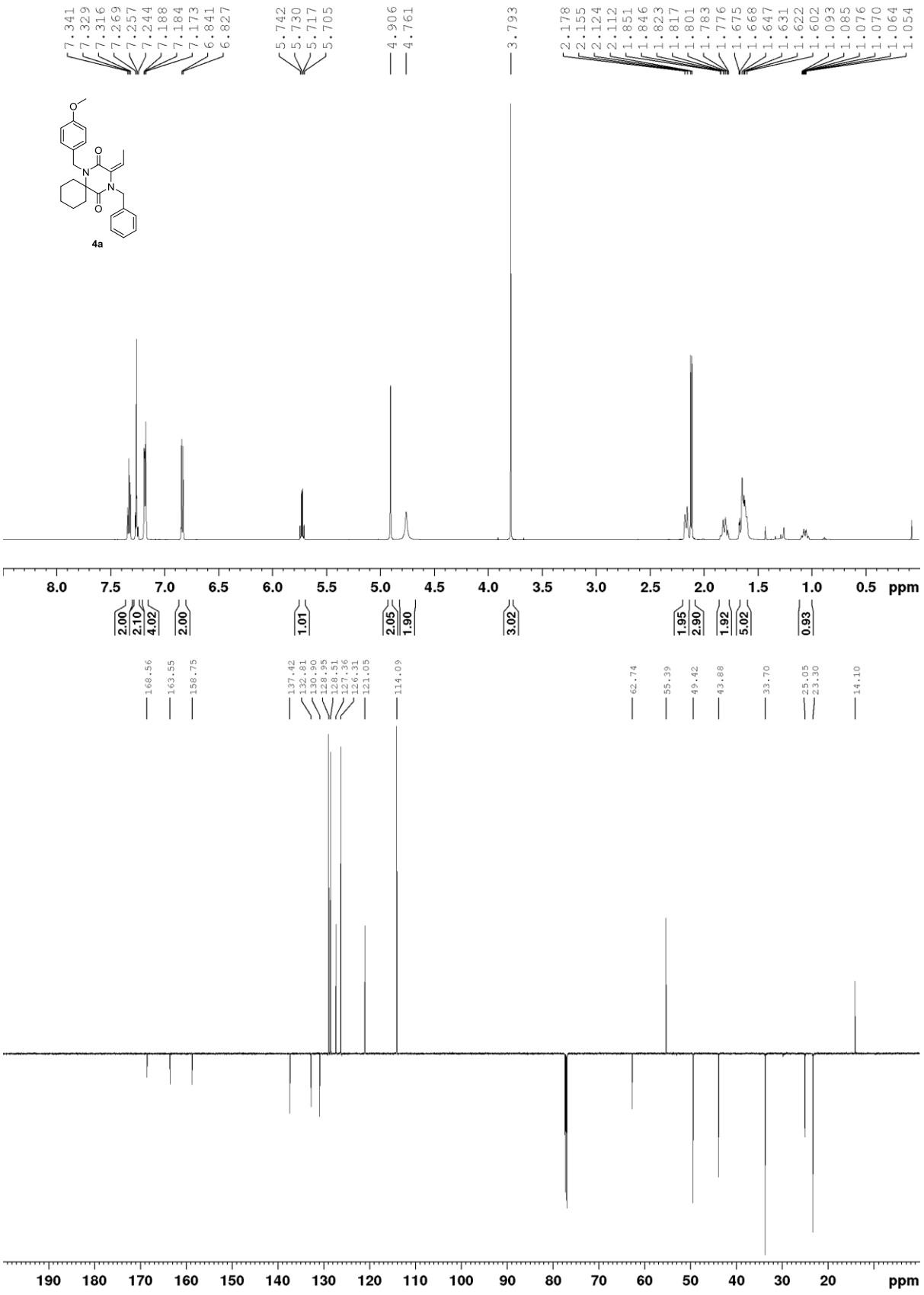
6.985
6.972
6.043
6.033
6.025
6.014
6.005
5.997
5.987
5.545
5.543
5.517
5.515
5.400
5.398
5.383
5.380
4.713
4.704
4.557
4.546
4.534
2.458
2.449
2.438
2.361
2.276
2.265
2.253
2.241
2.169
2.158
2.155
2.145
2.135
1.751
1.739
1.727
1.716
1.708
1.699
1.687
1.680
1.673
1.659
1.564
1.550
1.291
1.279
1.258
1.246
1.210
1.201
1.191
1.187
1.182
3s
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 ppm
2.00 2.01 1.00 1.02 1.02 1.00 1.01 1.03 3.00 1.06 1.03 3.06 1.08 3.03 3.04 1.09
170.62
167.19
138.44
135.87
135.62
130.19
119.23
71.20
60.36
47.84
42.56
36.06
26.44
25.96
21.27
20.61
20.12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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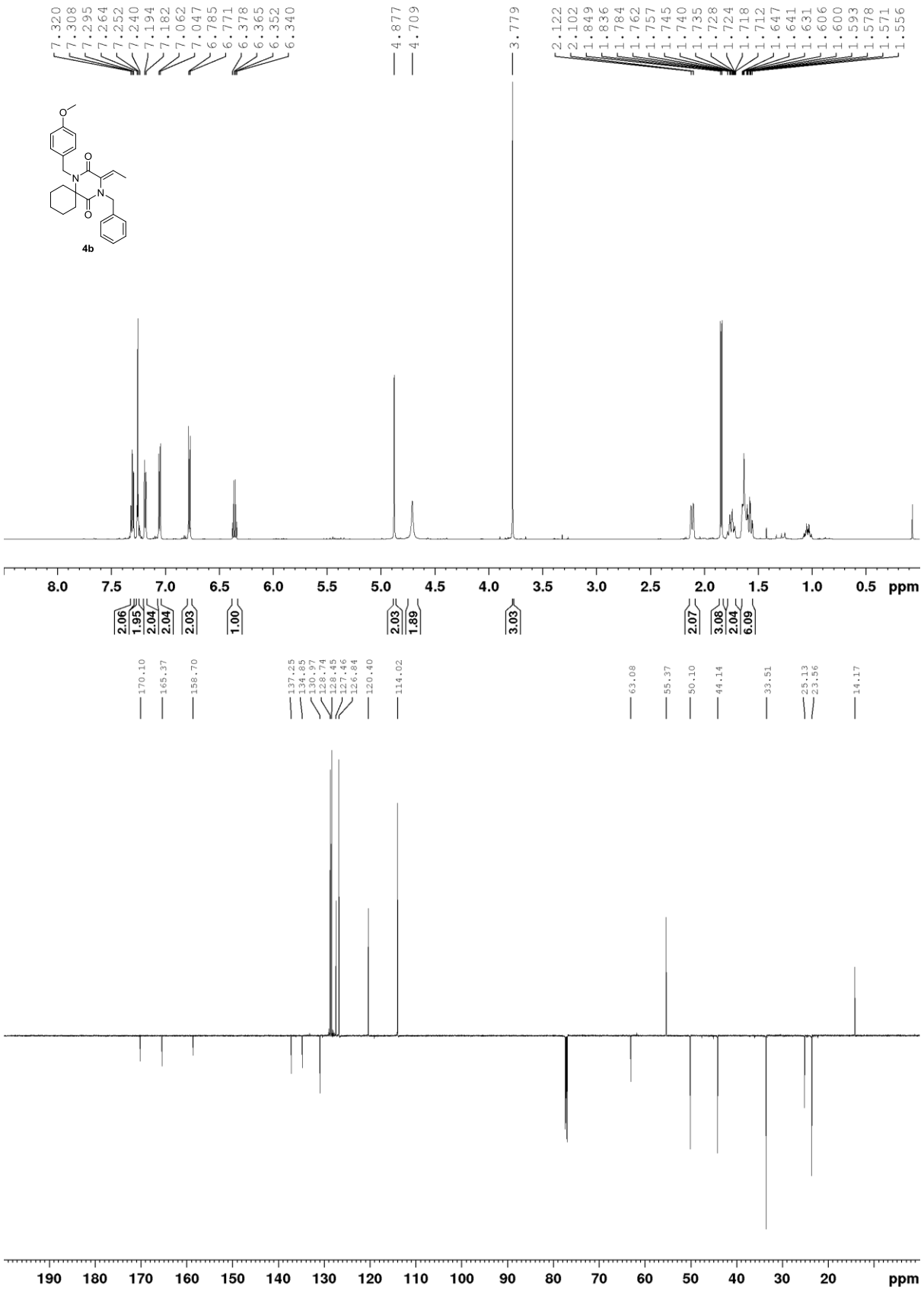
7.329
7.316
7.269
7.257
7.244
7.188
7.184
7.173
6.841
6.827
5.742
5.730
5.717
5.705
4.906
4.761
3.793
2.178
2.155
2.124
2.112
1.851
1.846
1.823
1.817
1.801
1.783
1.776
1.675
1.668
1.647
1.631
1.622
1.602
1.093
1.085
1.076
1.070
1.064
1.054
4a
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00 2.10 4.02 2.00 1.01 2.05 1.90 3.02 1.95 2.90 1.92 5.02 0.93
168.56
163.55
158.75
137.42
132.81
130.90
128.95
128.51
127.36
126.31
121.05
114.09
62.74
55.39
49.42
43.88
33.70
25.05
23.30
14.10
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.320
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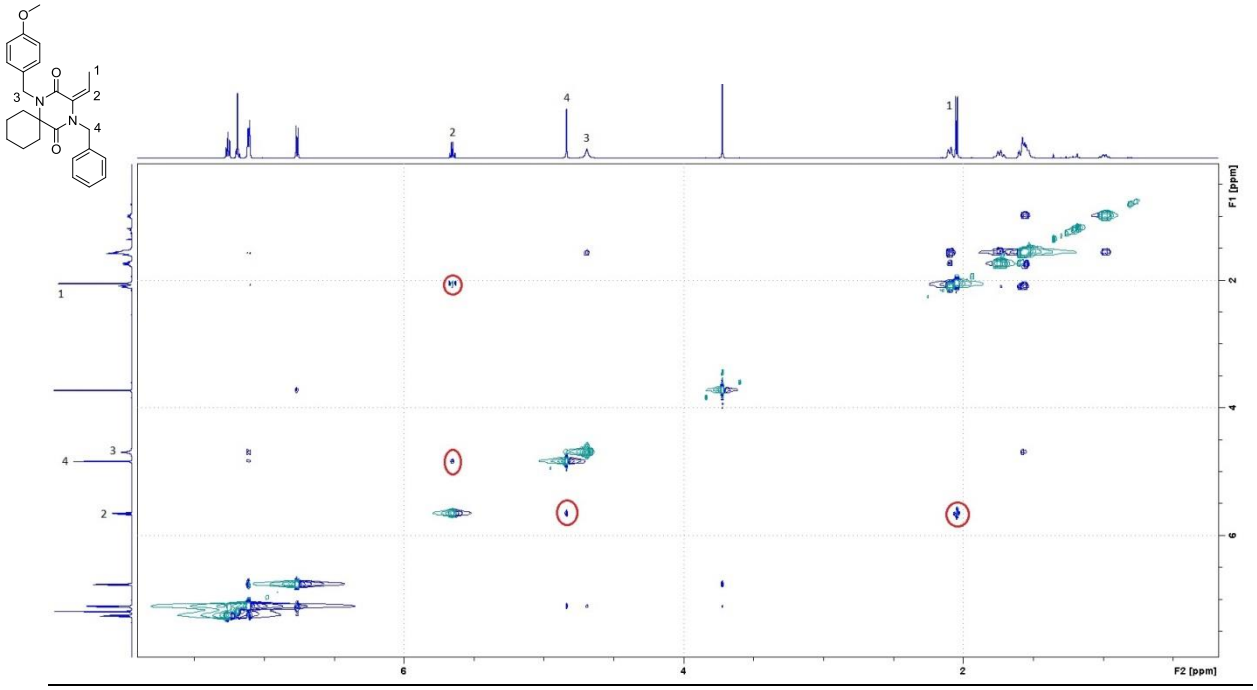
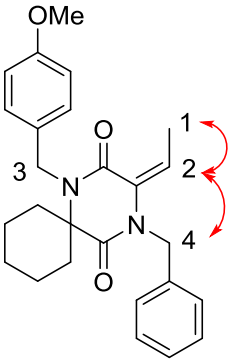
7.295
7.264
7.252
7.240
7.194
7.182
7.062
7.047
6.785
6.771
6.378
6.365
6.352
6.340
4.877
4.709
3.779
2.122
2.102
1.849
1.836
1.784
1.762
1.757
1.745
1.740
1.735
1.728
1.724
1.718
1.712
1.647
1.641
1.631
1.606
1.600
1.593
1.578
1.571
1.556
4b
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.06 1.95 2.04 2.04 2.03 1.00 2.03 1.89 3.03 2.07 3.08 2.04 6.09
170.10
165.37
158.70
137.25
134.85
130.97
128.74
128.45
127.46
126.84
120.40
114.02
63.08
55.37
50.10
44.14
33.51
25.13
23.56
14.17
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

NOESY analysis of 4a

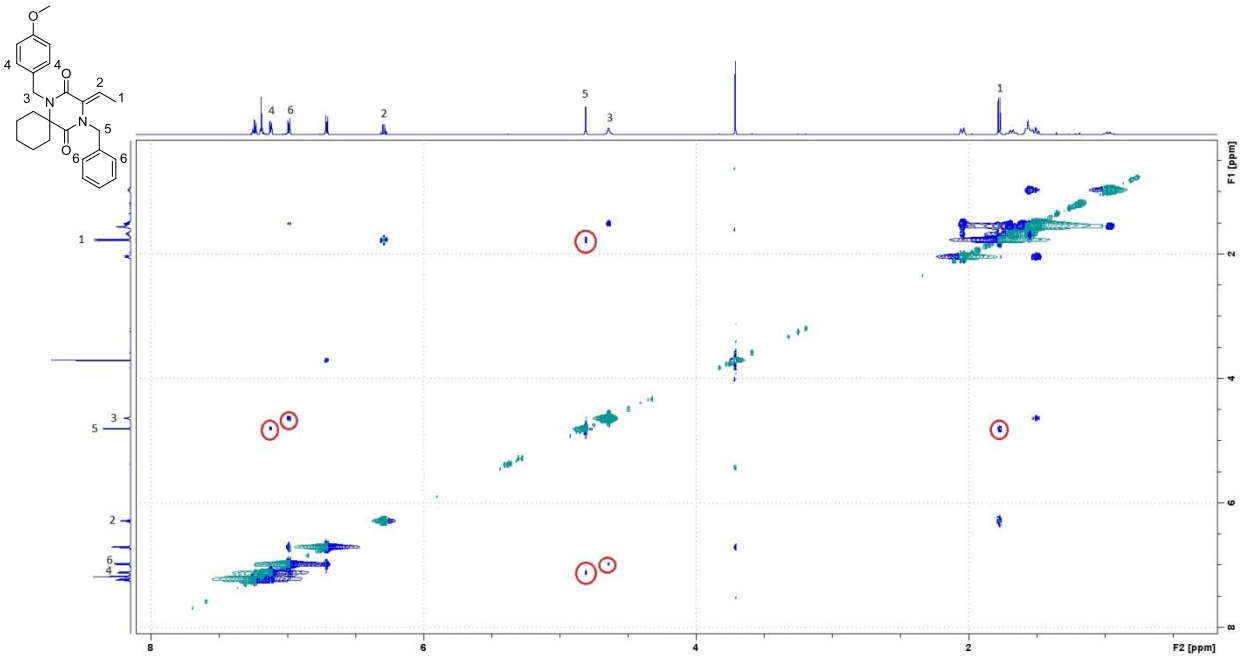
All relevant correlations are indicated by a red outline.

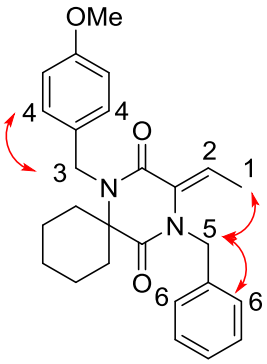


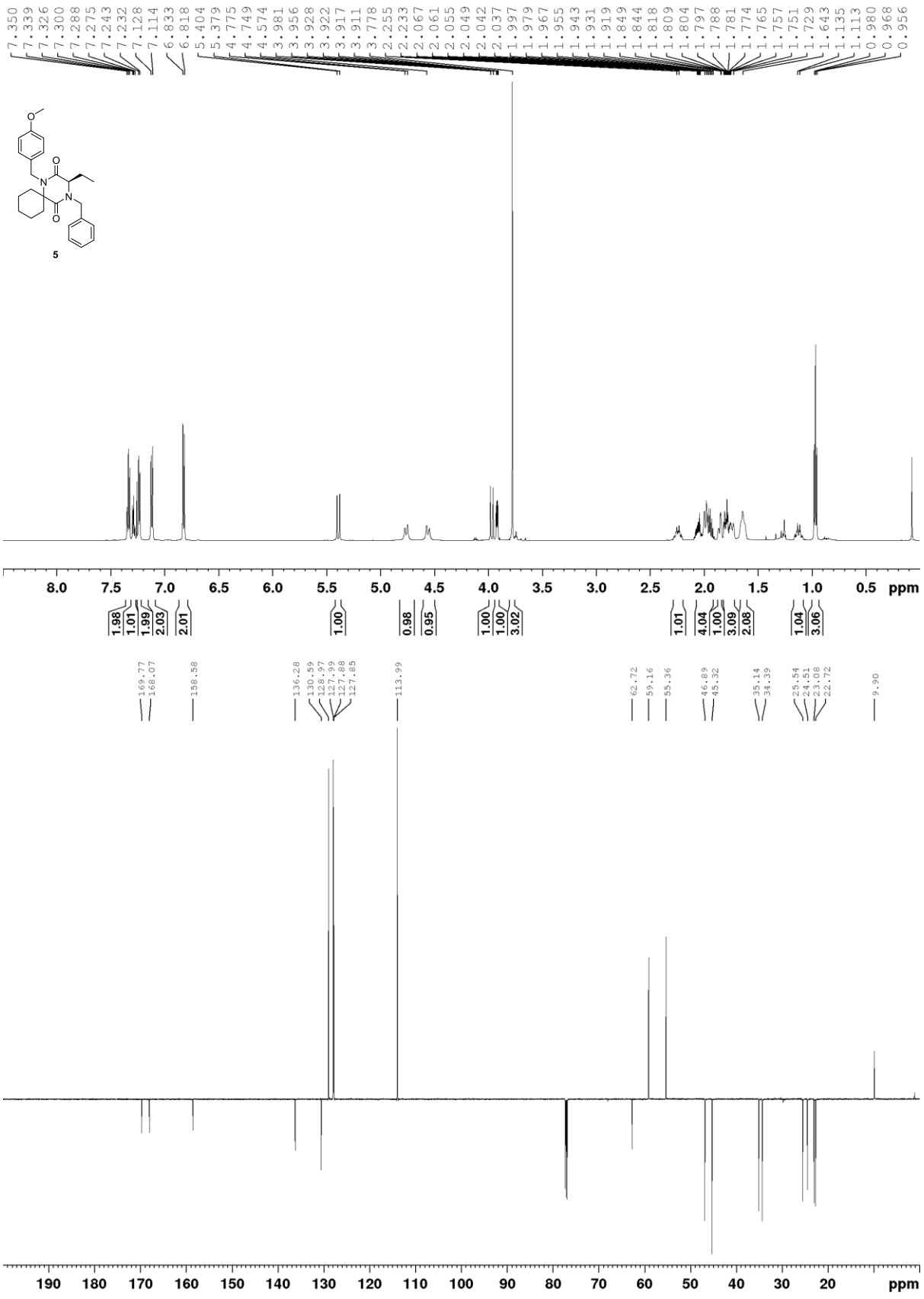


NOESY analysis of 4b

All relevant correlations are indicated by a red outline.



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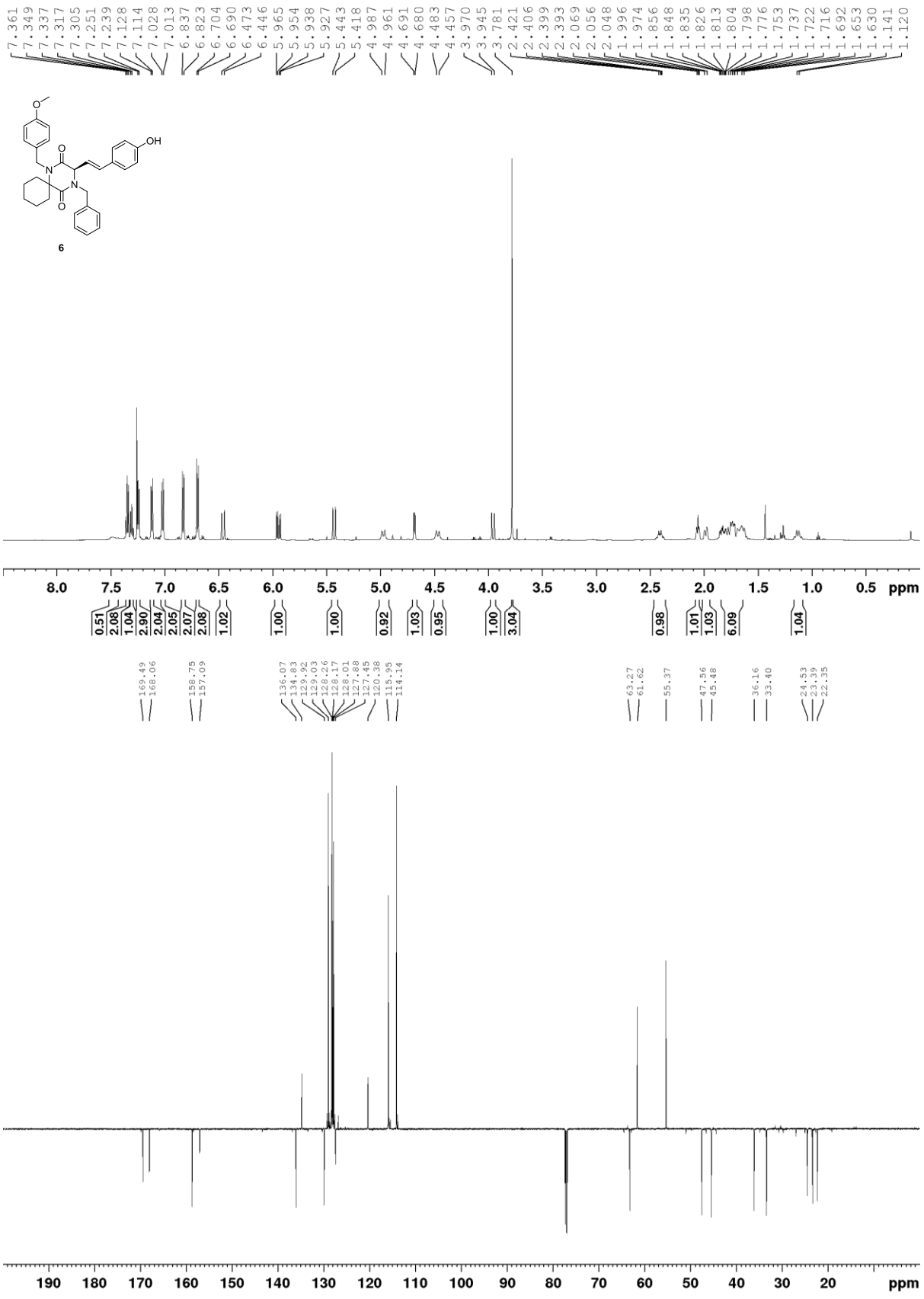
7.326
7.300
7.288
7.275
7.243
7.232
7.128
7.114
6.833
6.818
5.404
5.379
4.775
4.749
4.574
3.981
3.956
3.928
3.922
3.917
3.911
3.778
2.255
2.233
2.067
2.061
2.055
2.049
2.042
2.037
1.997
1.979
1.967
1.955
1.943
1.931
1.919
1.849
1.844
1.818
1.809
1.804
1.797
1.788
1.781
1.774
1.765
1.757
1.751
1.729
1.643
1.135
1.113
0.980
0.968
0.956
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 ppm
1.98 1.01 1.99 2.03 2.01 1.00 0.98 0.95 1.00 1.00 3.02 1.01 4.04 1.00 3.09 2.08 1.04 3.06
169.77
168.07
158.58
136.28
130.59
128.97
127.99
127.88
127.85
113.99
62.72
59.16
55.36
46.89
45.32
35.14
34.39
25.54
24.51
23.08
22.72
9.90
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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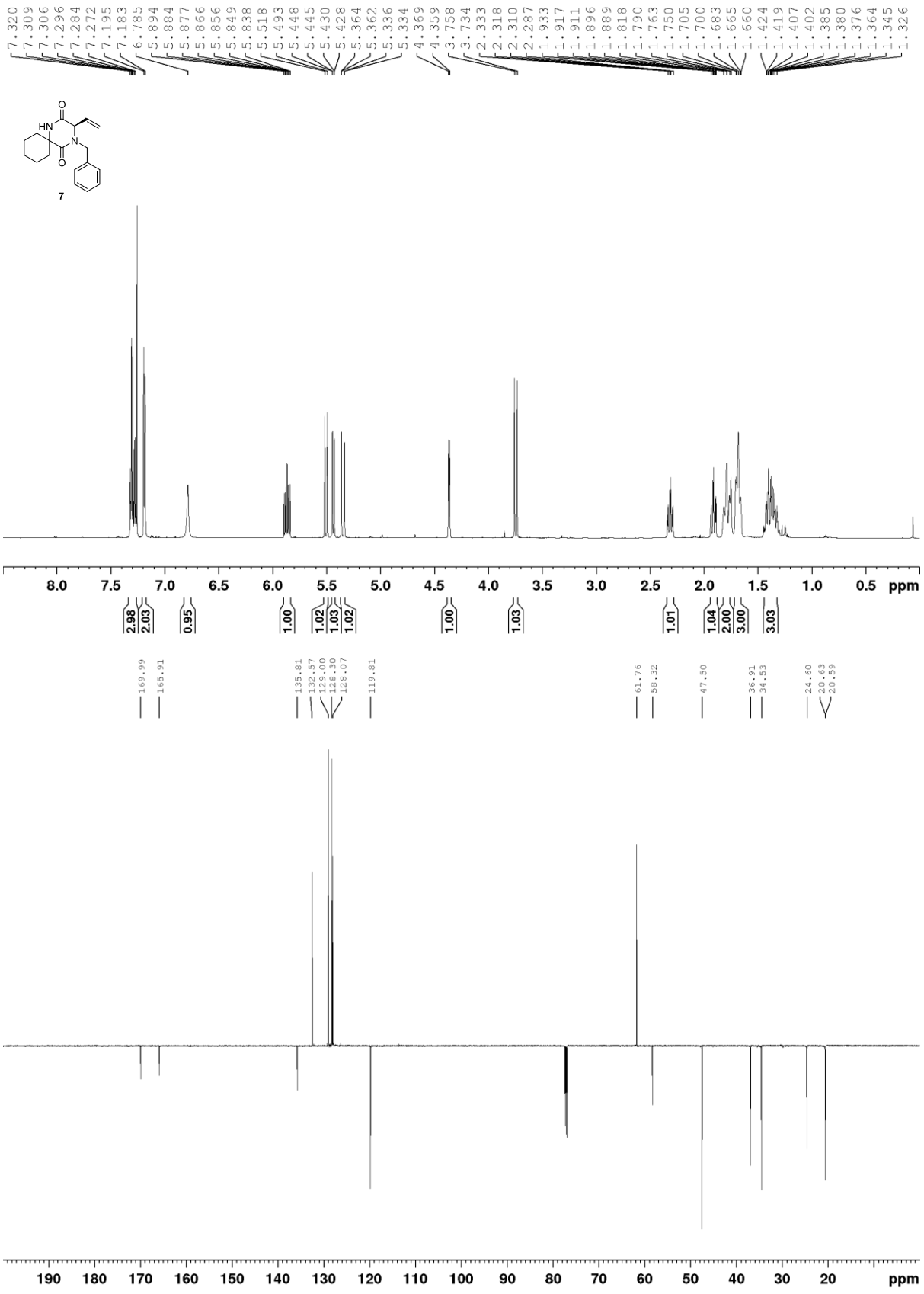
7.251
7.239
7.128
7.114
7.028
7.013
6.837
6.823
6.704
6.690
6.473
6.446
5.965
5.954
5.938
5.927
5.443
5.418
4.987
4.961
4.691
4.680
4.483
4.457
3.970
3.945
3.781
2.421
2.406
2.399
2.393
2.069
2.056
2.048
1.996
1.974
1.856
1.848
1.835
1.826
1.813
1.804
1.798
1.776
1.753
1.737
1.722
1.716
1.692
1.653
1.630
1.141
1.120
O
OH
N
N
O
O
6
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 ppm
0.51 2.08 1.04 2.90 2.04 2.05 2.07 2.08 1.02 1.00 1.00 0.92 1.03 0.95 1.00 3.04 0.98 1.01 1.03 6.09 1.04
169.49
168.06
158.75
157.09
136.07
134.83
134.82
129.03
128.26
128.17
128.01
127.88
127.45
120.38
115.95
114.14
63.27
61.62
55.37
47.56
45.48
36.16
33.40
24.53
23.39
22.35
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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5.894
5.884
5.877
5.866
5.856
5.849
5.838
5.518
5.493
5.448
5.445
5.430
5.428
5.364
5.362
5.336
5.334
4.369
4.359
3.758
3.734
2.333
2.318
2.310
2.287
1.933
1.917
1.911
1.896
1.889
1.818
1.790
1.763
1.750
1.705
1.700
1.683
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1.660
1.424
1.419
1.407
1.402
1.385
1.380
1.376
1.364
1.345
1.326
HN
O
O
N
7
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
ppm
2.98
2.03
0.95
1.00
1.02
1.03
1.02
1.00
1.03
1.01
1.04
2.00
3.00
3.03
169.99
165.91
135.81
132.57
129.00
128.30
128.07
119.81
61.76
58.32
47.50
36.91
34.53
24.60
20.63
20.59
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm