Isothiourea-Mediated Asymmetric Functionalization of 3-Alkenoic Acids

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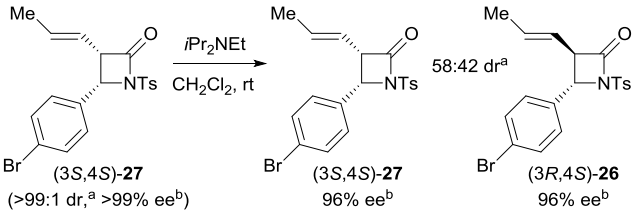
SUPPORTING INFORMATION

Contents

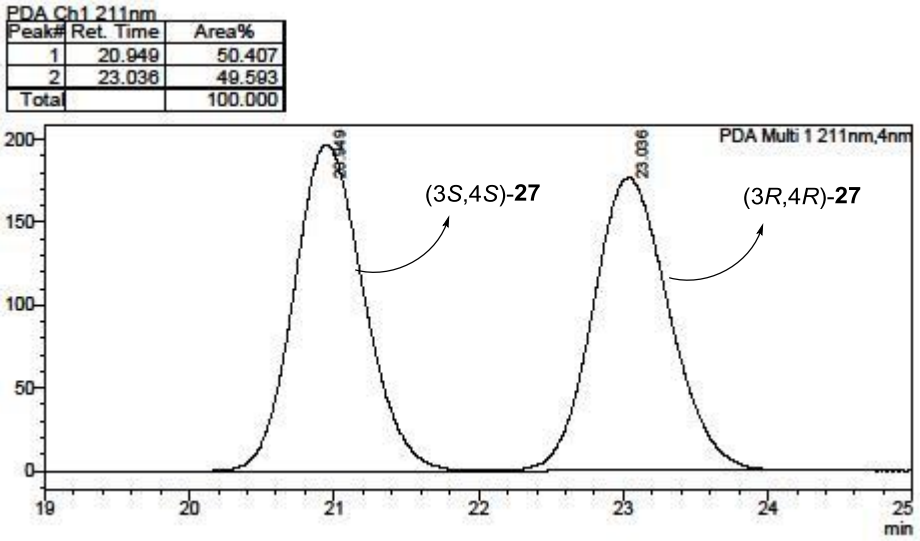
1.1 β-Lactone Epimerisation Experiment



[a] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture; [b] Determined by HPLC analysis.

A solution of lactone (3*S*,4*S*)-**27** (8.4 mg, 0.02 mmol) (>99:1 dr >99% ee) in CH_2Cl_2 (1 mL) was added *i*-Pr_2NEt (8.65 μL, 0.05 mmol) and the reaction mixture was stirred at rt for 16 h. The reaction mixture was quenched with HCl (1M in H_2O) and poured into H_2O. The reaction mixture was extracted with CH_2Cl_2 (x 3) and the combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude reaction mixture (58:42 dr *syn*:*anti*). Chiral HPLC analysis of the crude reaction mixture showed the following composition: *syn*-β-lactam (3*S*,4*S*)-**27** (96% ee) and *anti*-β-lactam (3*R*,4*S*)-**26** (96% ee). The configuration of the *anti*-β-lactam is opposite to that observed experimentally. Assuming epimerisation occurs *via* C(3), this allows the absolute configuration of the *anti*-β-lactam formed in Table 2 to be assigned (3*S*,4*R*). Refer to the traces below.

Racemic sample of *syn* diastereoisomer:

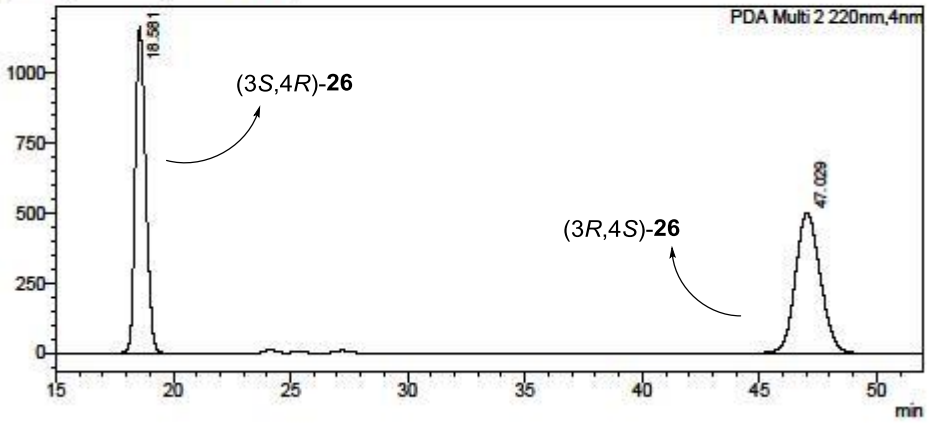


Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 20.9 min, t_R(3*R*,4*R*): 23.0 min.

Racemic sample of *anti* diastereoisomer:

PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	18.581	49.441
2	47.029	50.559
Total		100.000

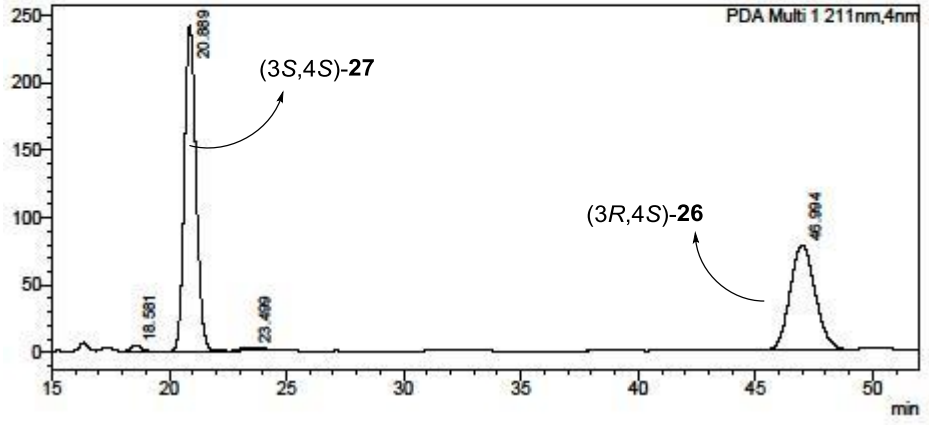


Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 18.6 min, t_R(3*R*,4*S*): 47.0 min.

Epimerisation experiment:

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	18.581	0.800
2	20.889	57.453
3	23.499	1.275
4	46.994	40.471
Total		100.000

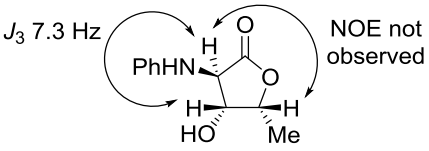


Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 18.6 min, t_R(3*S*,4*S*): 20.9 min, t_R(3*R*,4*R*): 23.5 min, t_R(3*R*,4*S*): 47.0 min.

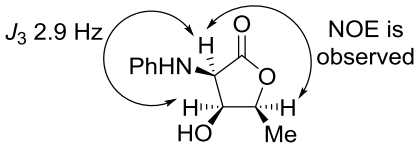
1.2 Assignment of Diastereoisomers 49 and 50

The relative configurations of lactones **49** and **50** were assigned after derivatization towards lactones **79** and **80**. Diastereoisomers (3*R*,4*R*,5*R*)-**79** and (3*R*,4*S*,5*S*)-**80** were assigned based upon the J_3 coupling constant at between C(3)*H* and C(4)*H* which is 7.3 Hz for (3*R*,4*R*,5*R*)-**79** due to the *anti* relationship and 2.9 Hz for (3*R*,4*S*,5*S*)-**80** due to the *syn* relationship. Additional evidence was found using NOE

experiments. Upon irradiation of C(5)*H* in (3*R*,4*R*,5*R*)-**79** there is a NOE with both C(4)*H* and CH_3. However, irradiation of C(5)*H* in (3*R*,4*S*,5*S*)-**80** gives NOE with C(4)*H*, CH_3 and importantly C(3)*H*, indicating that C(3)*H*, C(4)*H* and C(5)*H* are all on the same face of the 5-membered lactone as shown below:

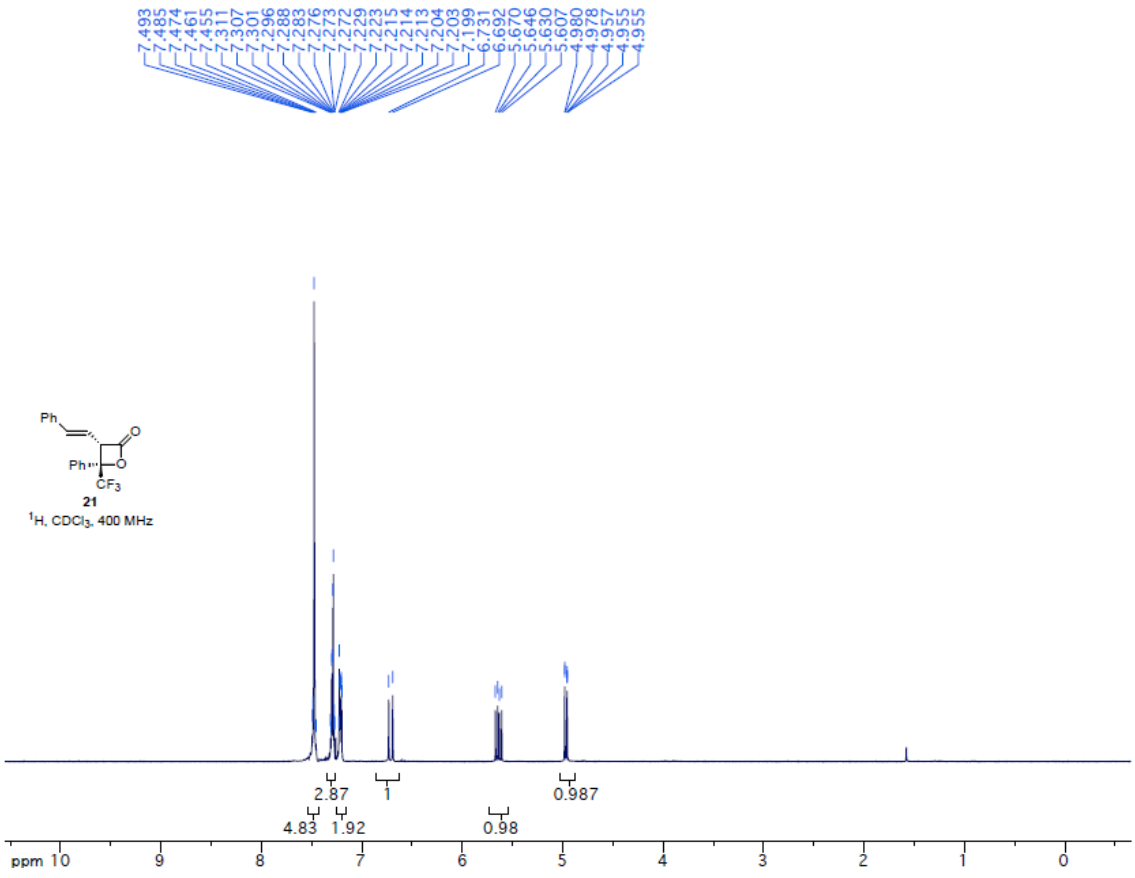


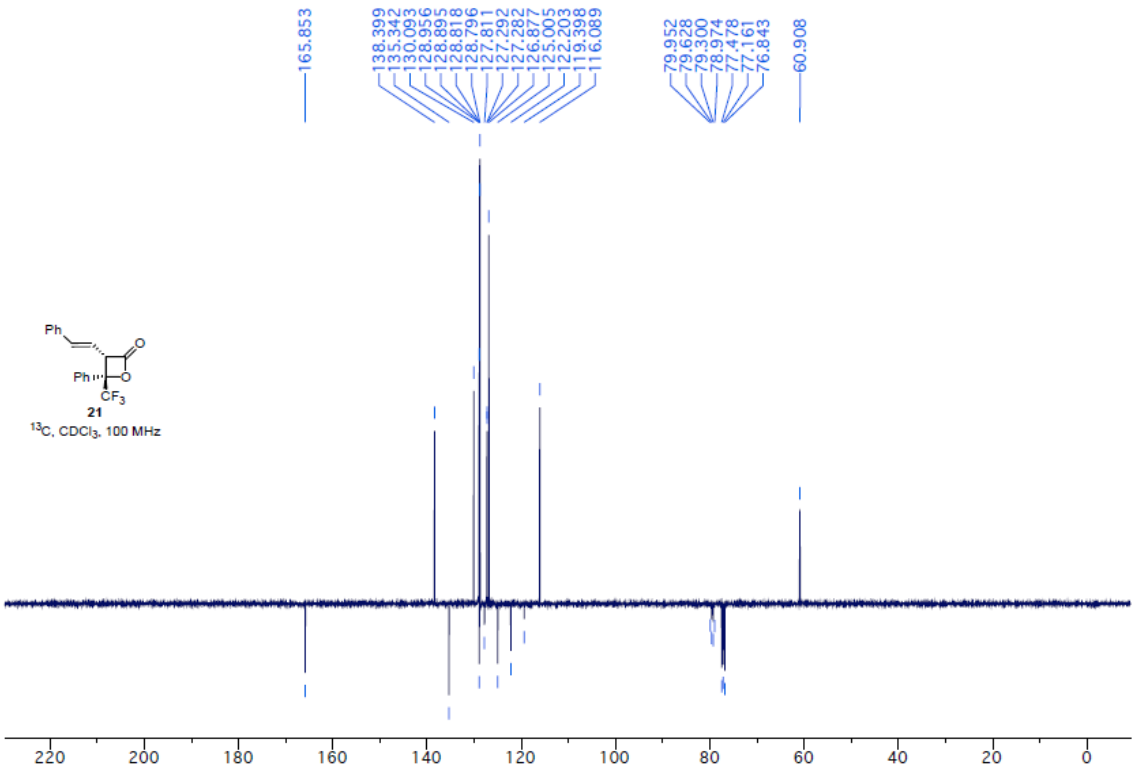
(3*R*,4*R*,5*R*)-**79**

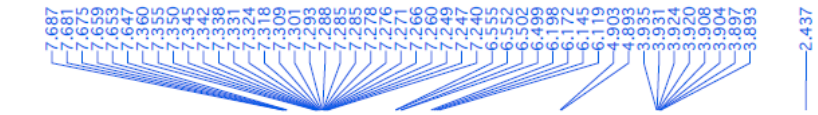


(3*R*,4*S*,5*S*)-**80**

1.3 NMR Spectra of novel compounds



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7.647
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7.345
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7.331
7.324
7.318
7.309
7.301
7.293
7.288
7.285
7.278
7.276
7.271
7.266
7.260
7.249
7.247
7.240
6.555
6.552
6.502
6.499
6.198
6.172
6.145
6.119
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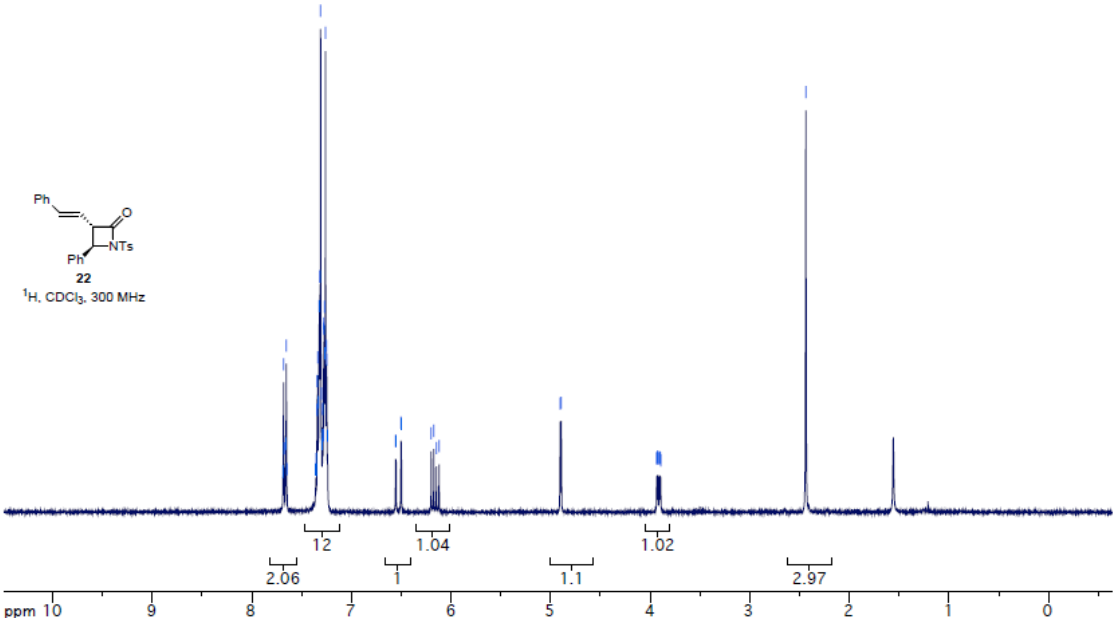
3.935
3.931
3.924
3.920
3.908
3.904
3.897
3.893
2.437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NTs
Ph
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1H, CDCl3, 300 MHz
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1.02
2.06
1
1.1
2.97
ppm 10
9
8
7
6
5
4
3
2
1
0


165.172
145.400
135.825
135.805
135.752
129.965
129.211
129.055
128.806
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126.757
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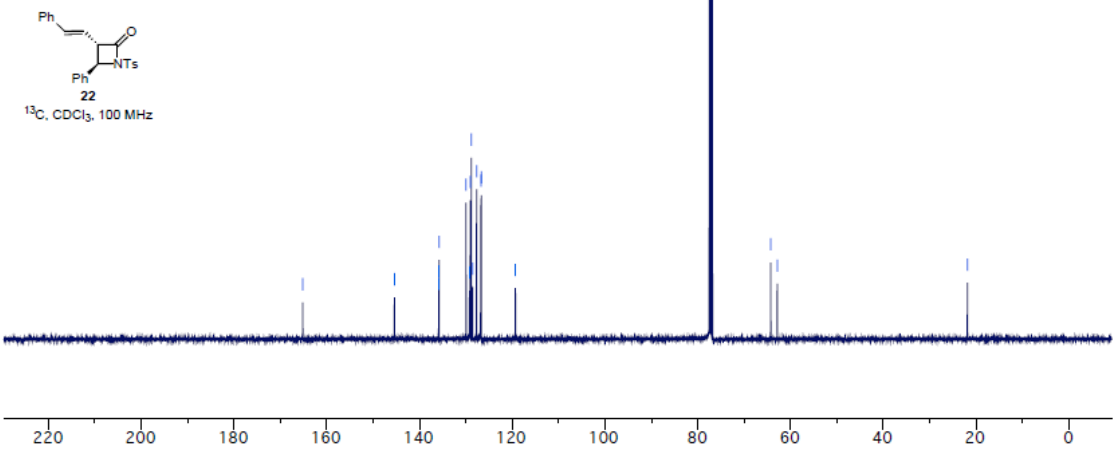
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NTs
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100
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60
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20
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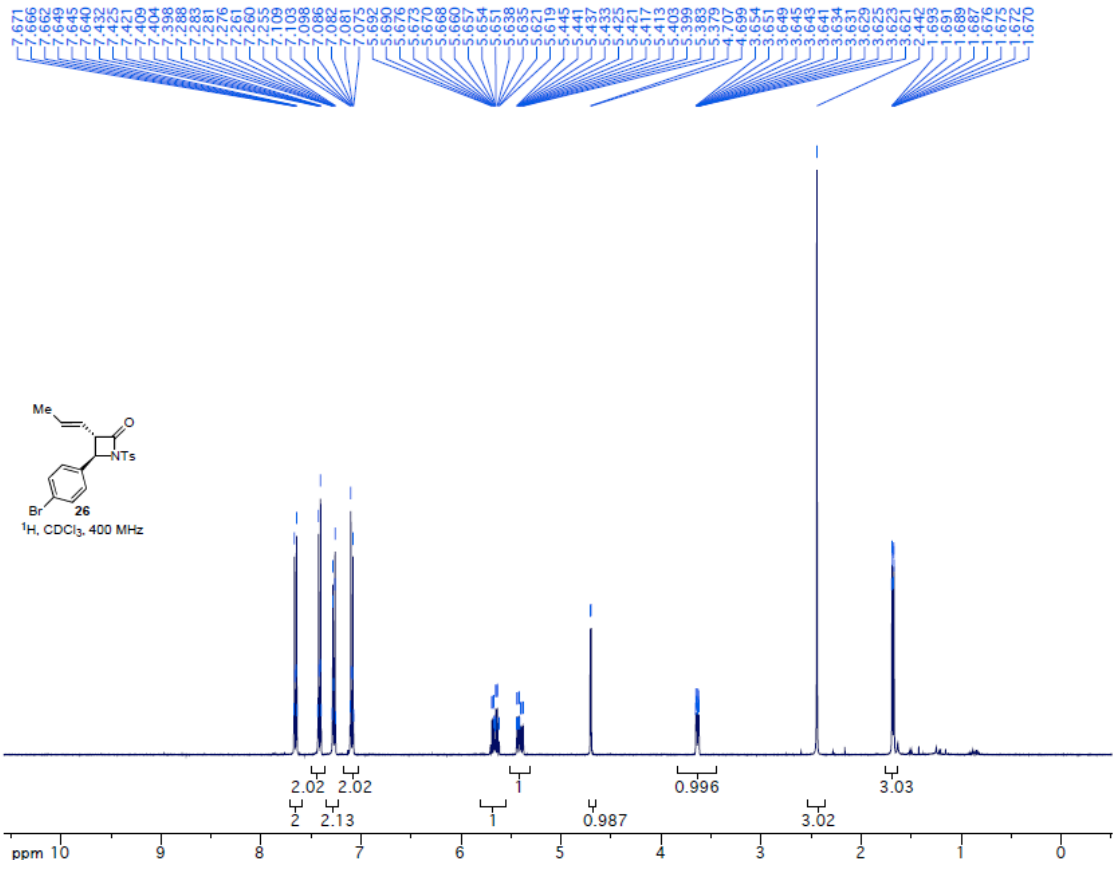
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NTs
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2
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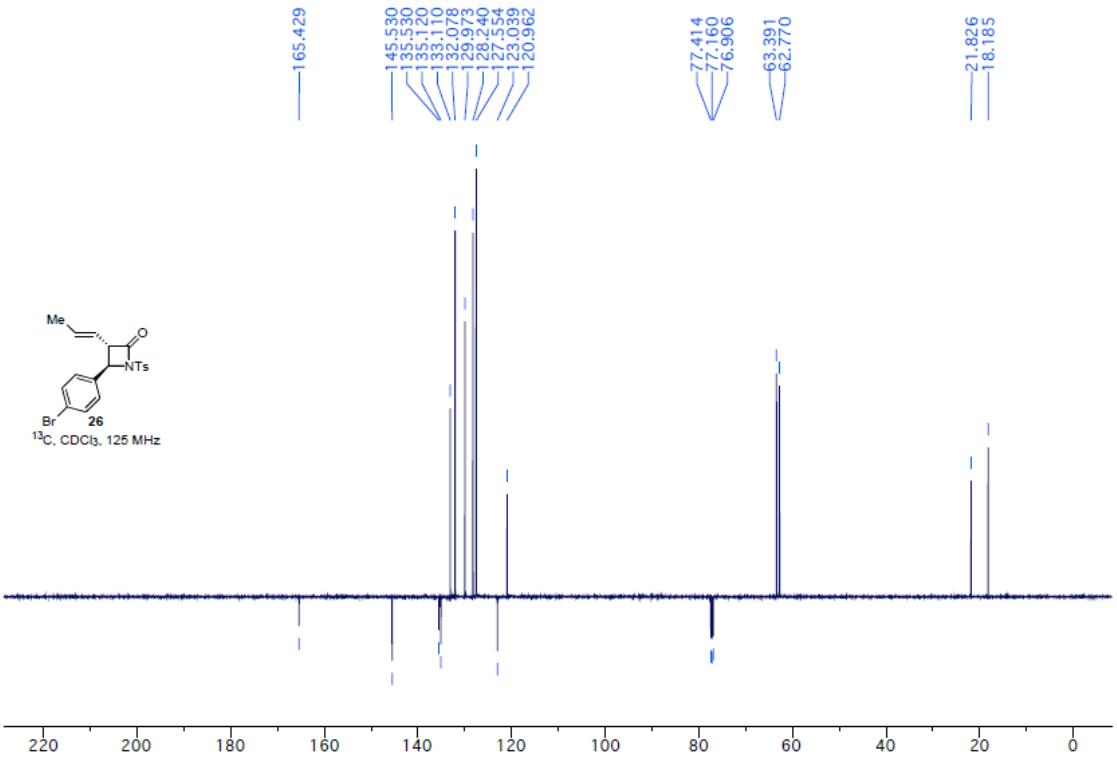
1
0.987
3.02
ppm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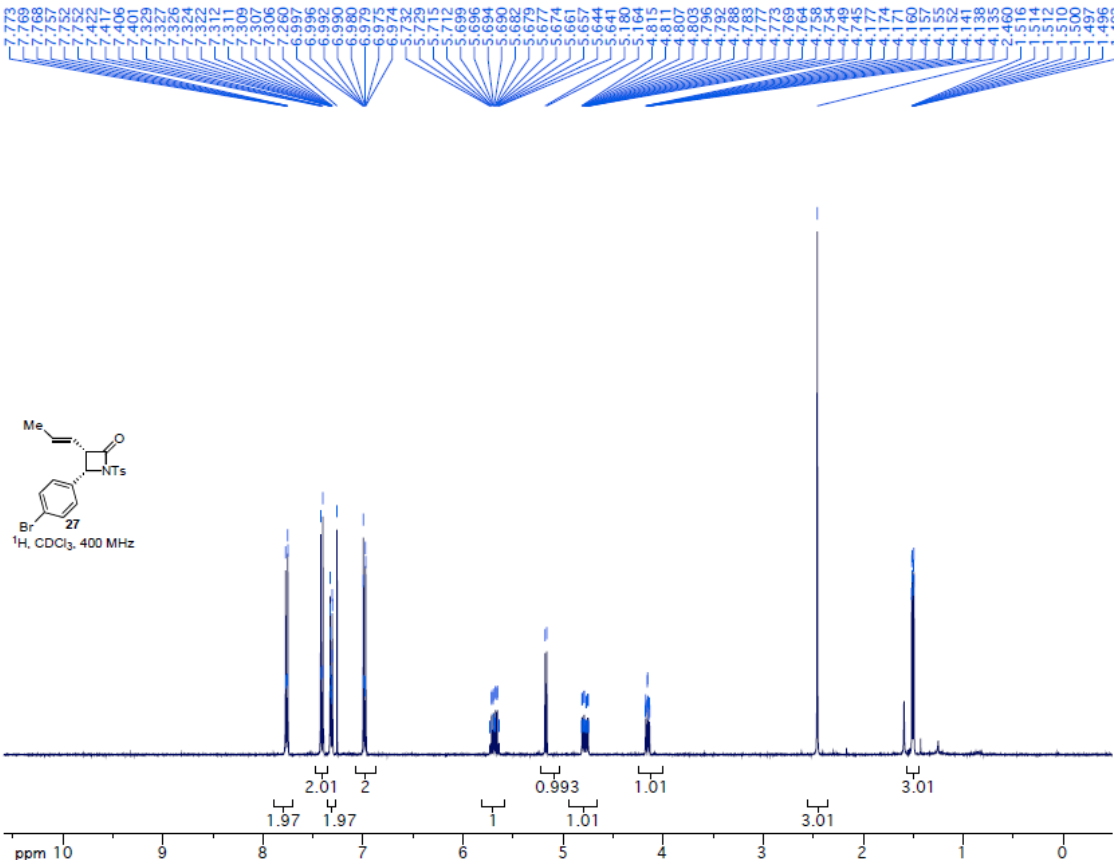
O
NTs
Br
26
13C, CDCl3, 125 MHz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O
NTs
Br
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1H, CDCl3, 400 MHz
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0.993
1.01
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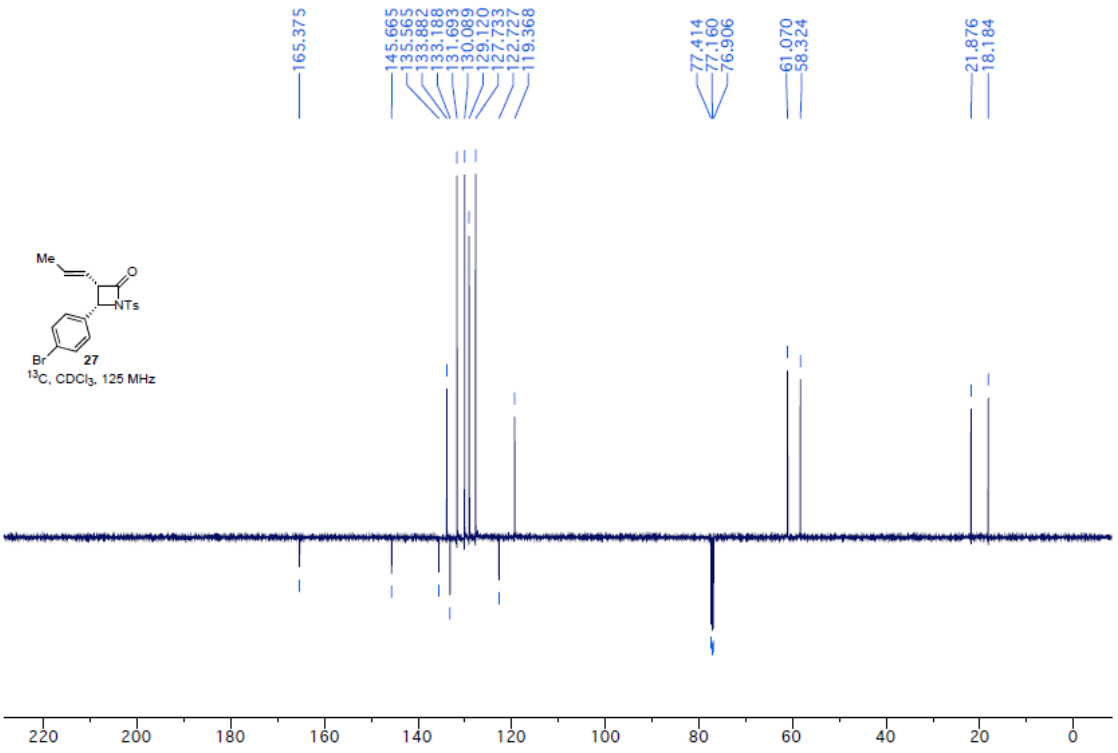
1
1.01
3.01
ppm 10
9
8
7
6
5
4
3
2
1
0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Br
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200
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160
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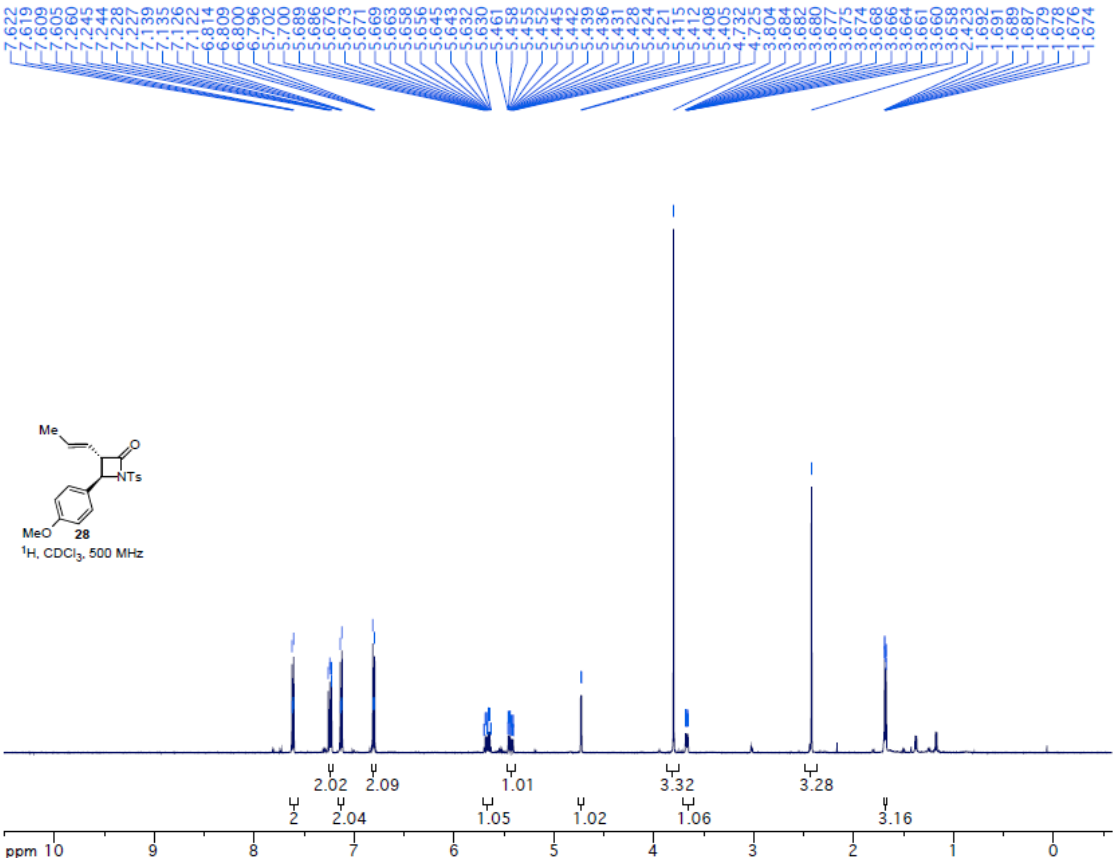
120
100
80
60
40
20
0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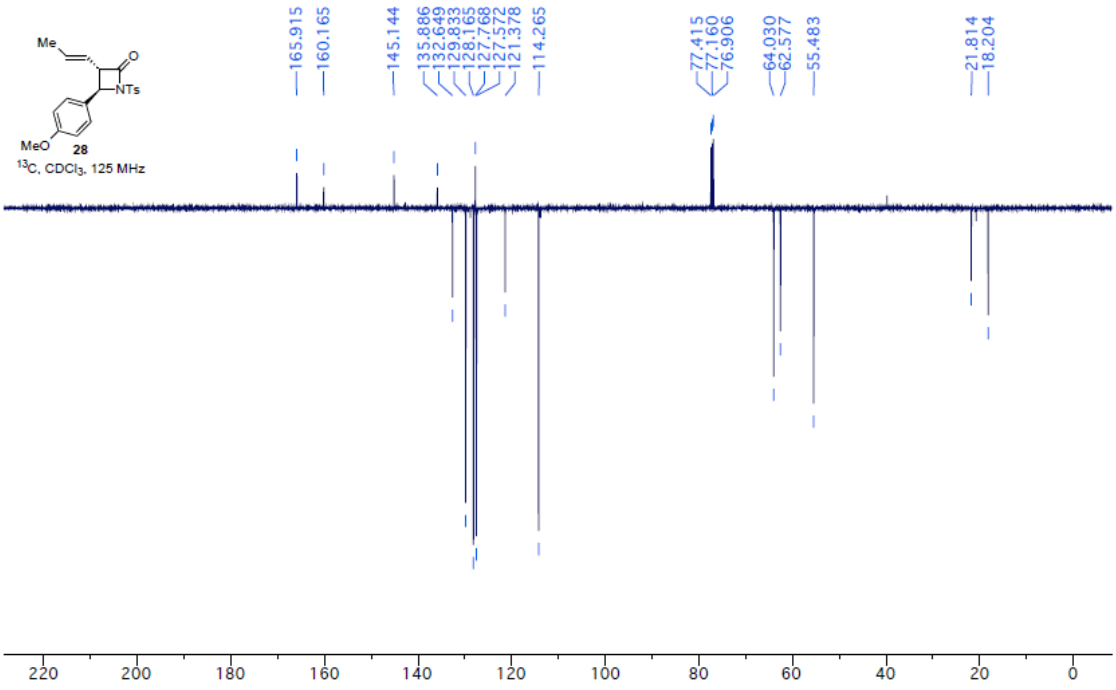
7.227
7.139
7.135
7.126
7.122
6.814
6.809
6.800
6.796
5.702
5.700
5.689
5.686
5.676
5.673
5.671
5.669
5.663
5.658
5.656
5.645
5.643
5.632
5.630
5.461
5.458
5.455
5.452
5.445
5.442
5.439
5.436
5.431
5.428
5.424
5.421
5.415
5.412
5.408
5.405
4.732
4.725
3.804
3.684
3.682
3.680
3.677
3.675
3.674
3.668
3.666
3.664
3.661
3.660
3.658
2.423
1.692
1.691
1.689
1.687
1.679
1.678
1.676
1.674
Me
O
NTs
MeO
28
1H, CDCl3, 500 MHz
2.02
2.09
1.01
3.32
3.28
2
2.04
1.05
1.02
1.06
3.16
ppm 10
9
8
7
6
5
4
3
2
1
0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135.886
132.649
129.833
128.165
127.768
127.572
121.378
114.265
77.415
77.160
76.906
64.039
62.577
55.483
21.814
18.204
Me
O
NTs
MeO
28
13C, CDCl3, 125 MHz
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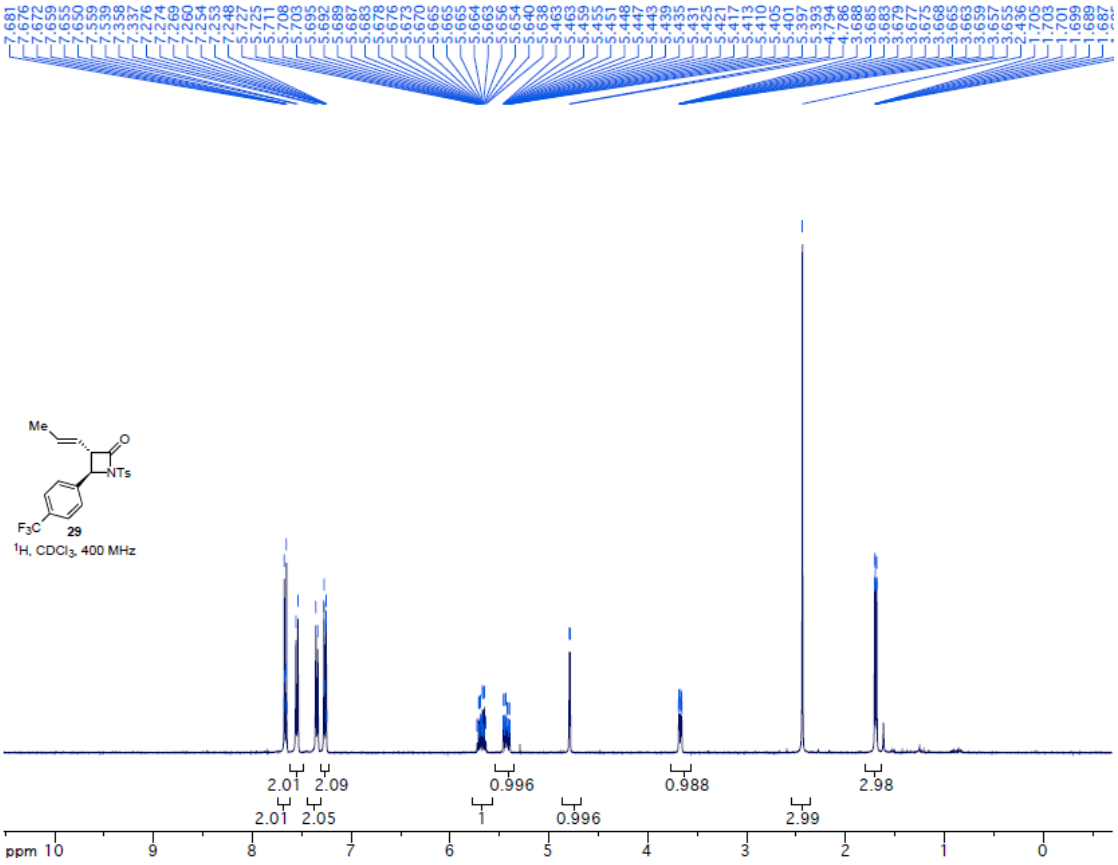
200
180
160
140
120
100
80
60
40
20
0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O
NTs
F3C
29
1H, CDCl3, 400 MHz
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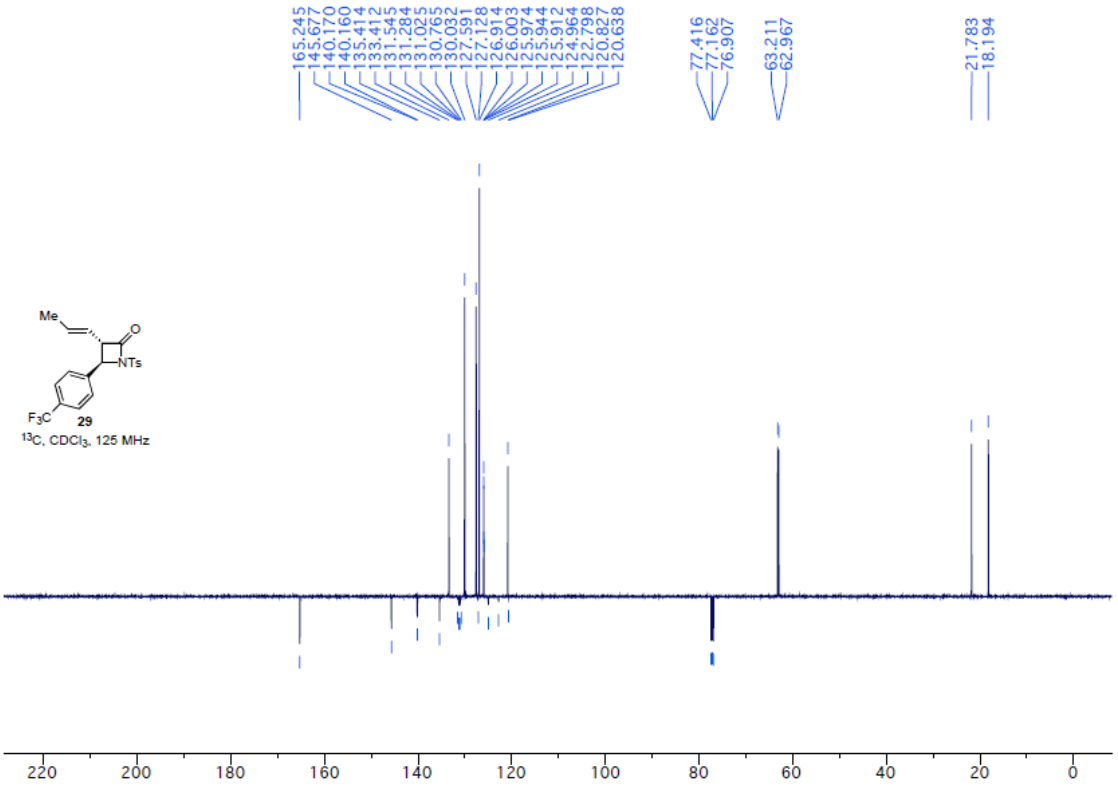
2.09
0.996
0.988
2.98
2.01
2.05
1
0.996
2.99
ppm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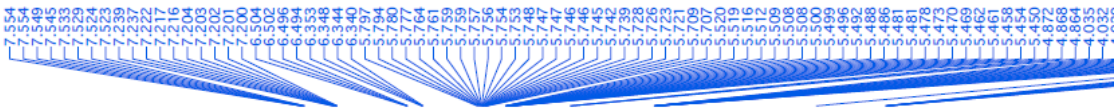
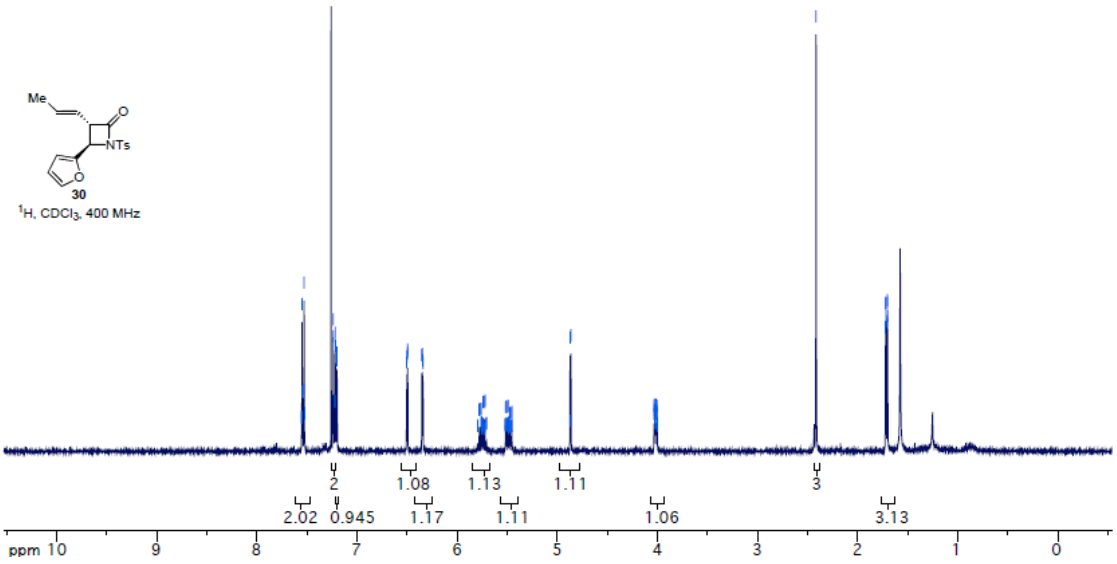
NTs
F3C
29
13C, CDCl3, 125 MHz




Me
O
NTs
O
30
^{1}H, $CDCl_3$, 400 MHz
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1.08
1.13
1.11
3
2.02
0.945
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1.11
1.06
3.13
ppm 10
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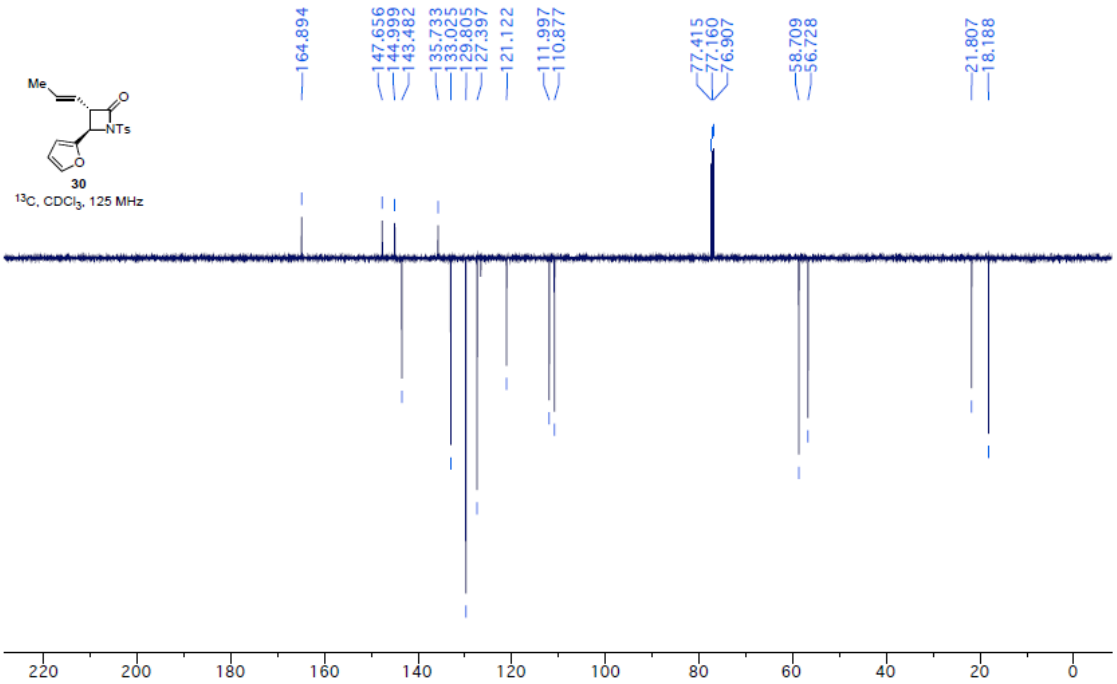
8
7
6
5
4
3
2
1
0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135.733
133.025
129.805
127.397
121.122
111.997
110.877
77.415
77.160
76.907
58.709
56.728
21.807
18.188
Me
O
NTs
O
30
^{13}C, $CDCl_3$, 125 MHz
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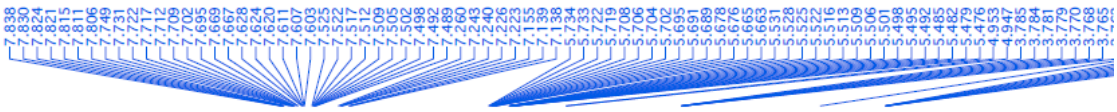
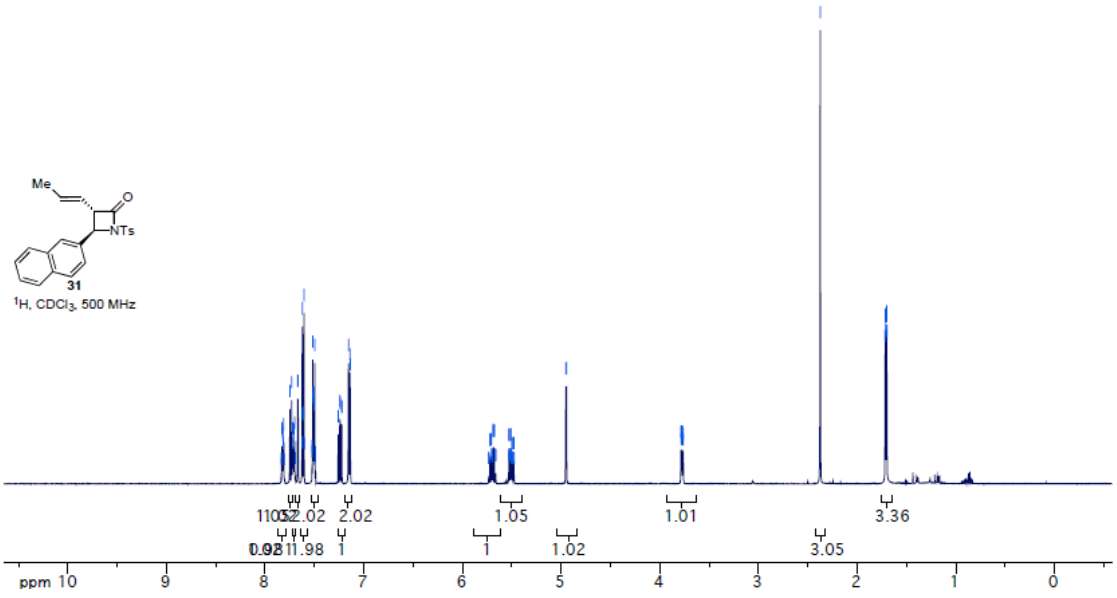
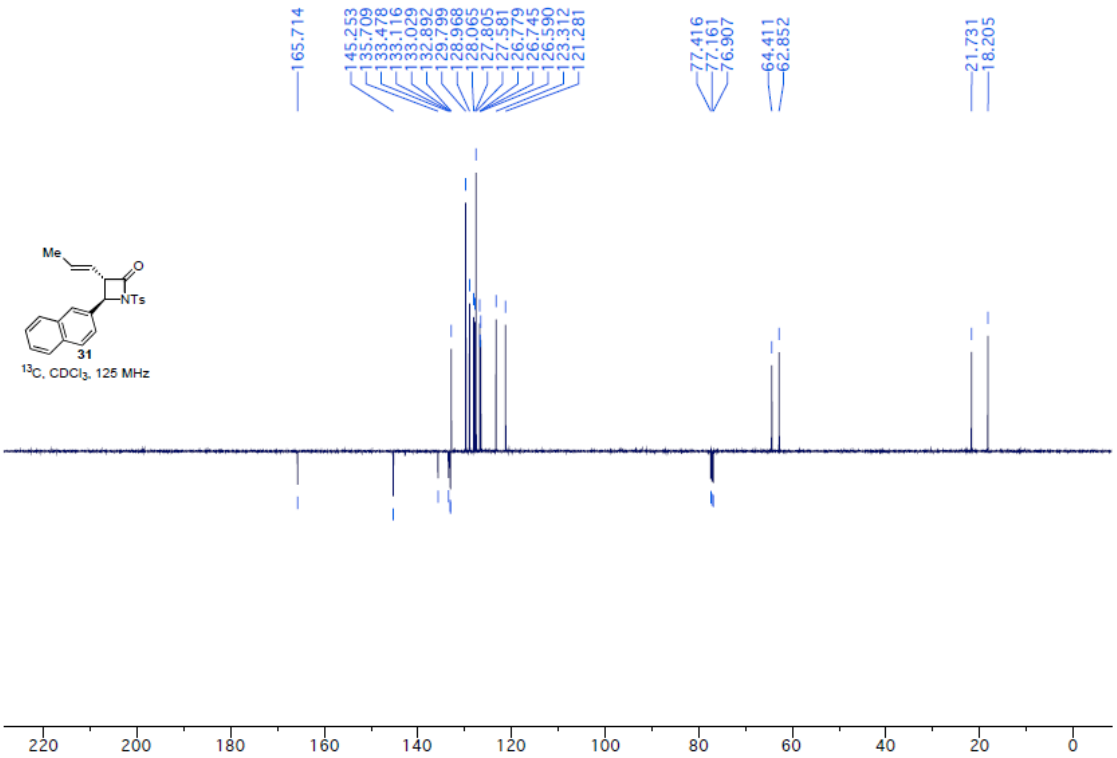
200
180
160
140
120
100
80
60
40
20
0




Me
O
NTs
31
1H, CDCl3, 500 MHz
2.02
2.02
1.05
1.01
3.36
11.98
1
1
1.02
3.05
ppm 10
9
8
7
6
5
4
3
2
1
0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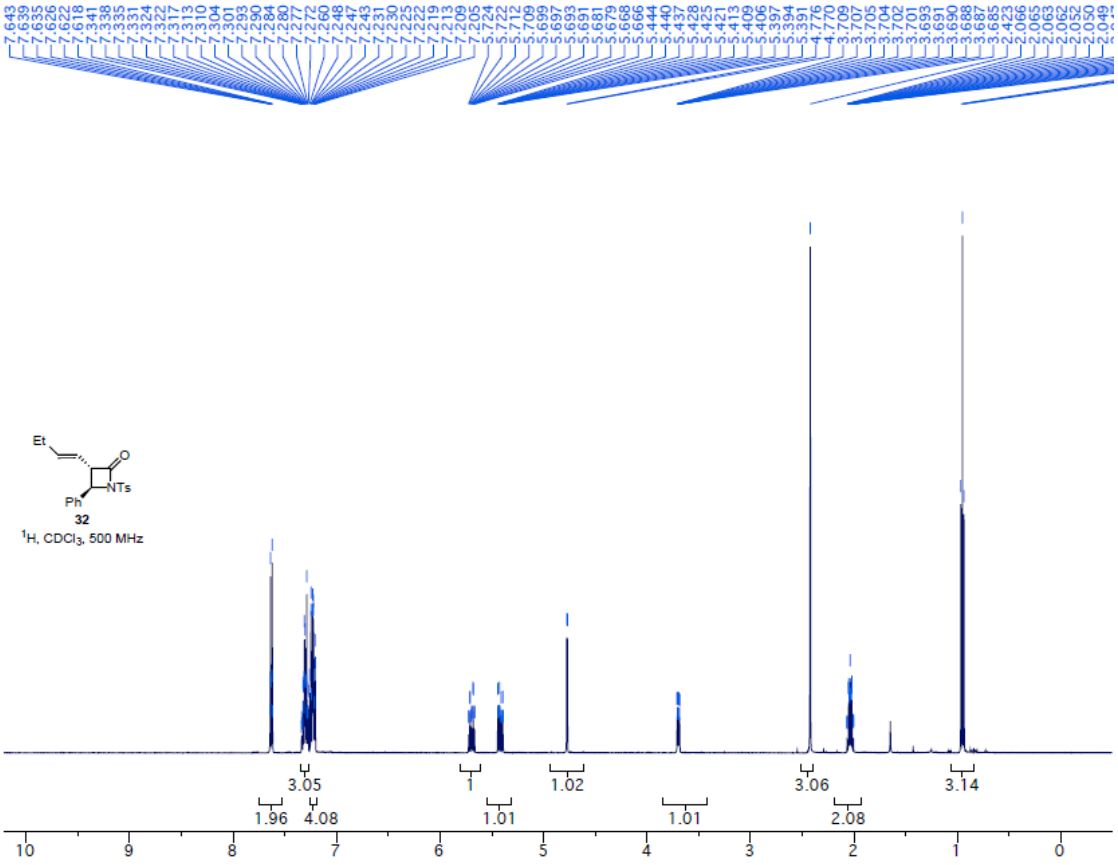
135.709
133.478
133.116
133.029
132.892
129.799
128.968
128.065
127.805
127.581
126.779
126.745
126.590
123.312
121.281
77.416
77.161
76.907
64.411
62.852
21.731
18.205
Me
O
NTs
31
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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7.635
7.626
7.622
7.618
7.341
7.338
7.335
7.331
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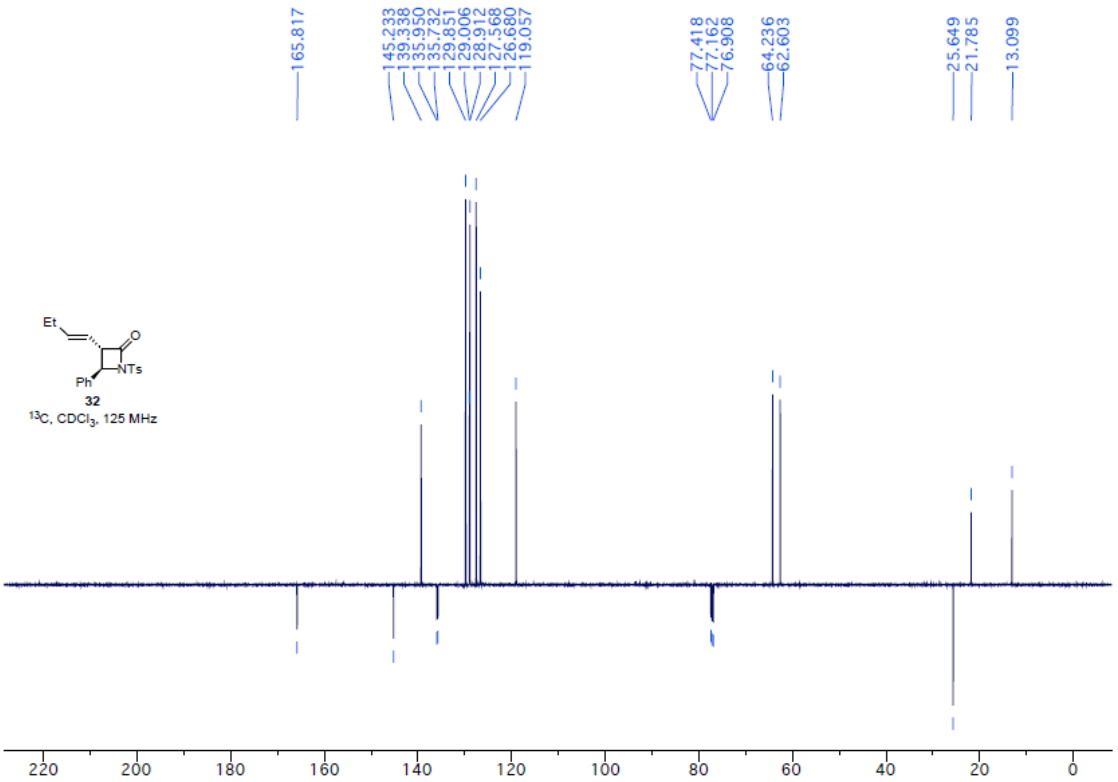
7.322
7.317
7.313
7.310
7.304
7.301
7.293
7.290
7.284
7.280
7.277
7.272
7.260
7.248
7.247
7.243
7.231
7.230
7.225
7.222
7.219
7.213
7.209
7.205
5.724
5.712
5.709
5.699
5.697
5.693
5.691
5.681
5.679
5.668
5.666
5.444
5.440
5.437
5.428
5.425
5.421
5.413
5.409
5.406
5.397
5.394
5.391
4.776
4.770
3.709
3.707
3.705
3.704
3.702
3.701
3.693
3.691
3.690
3.688
3.687
3.685
3.423
2.066
2.063
2.062
2.052
2.050
2.049
Et
O
NTs
Ph
32
1H, CDCl3, 500 MHz
3.05
1
1.02
3.06
3.14
1.96
4.08
1.01
1.01
2.08
10
9
8
7
6
5
4
3
2
1
0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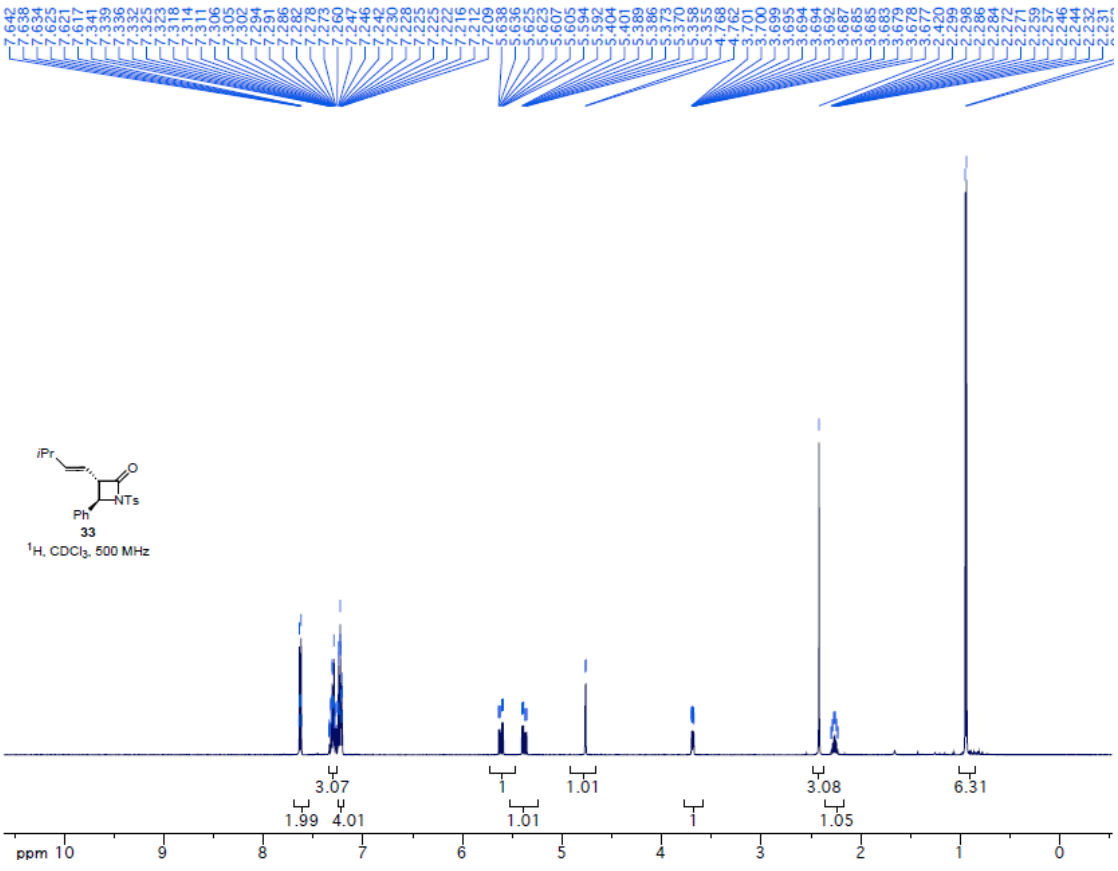
145.233
139.338
135.950
135.732
129.851
129.006
128.912
127.568
126.680
119.057
77.418
77.162
76.908
64.236
62.603
25.649
21.785
13.099
Et
O
NTs
Ph
32
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


iPr
O
NTs
Ph
33
1H, CDCl3, 500 MHz
3.07
1
1.01
3.08
6.31
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1.01
1
1.05
ppm 10
9
8
7
6
5
4
3
2
1
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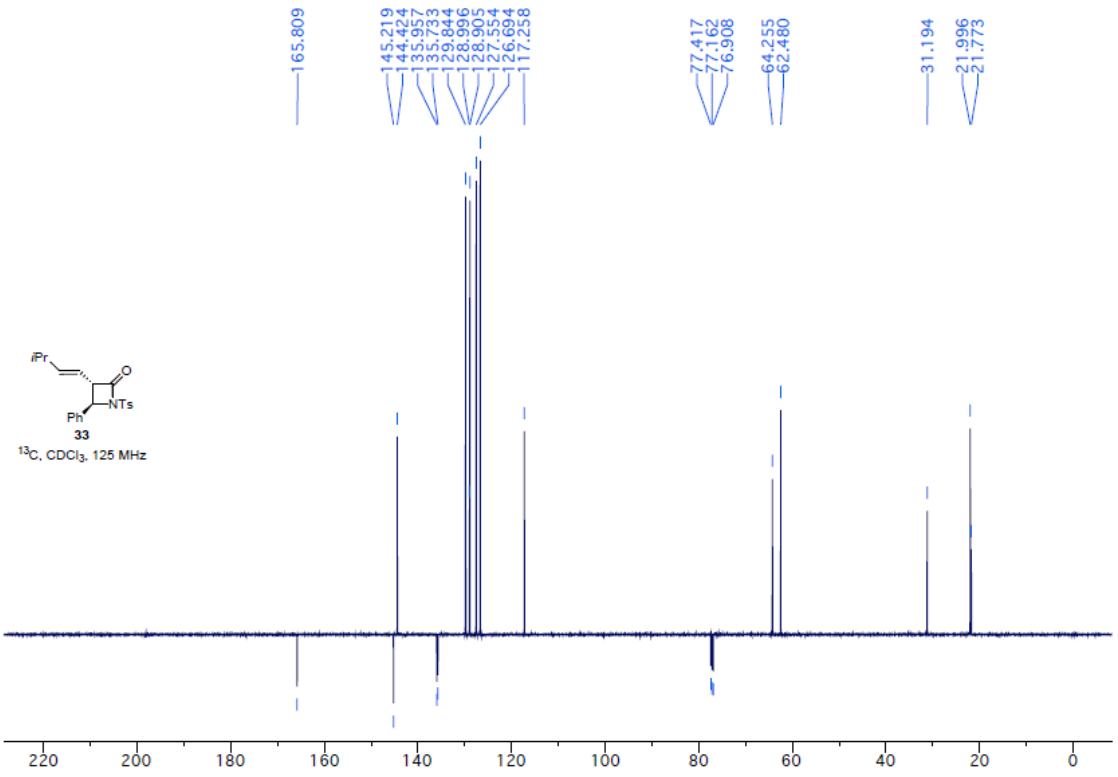
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144.424
135.957
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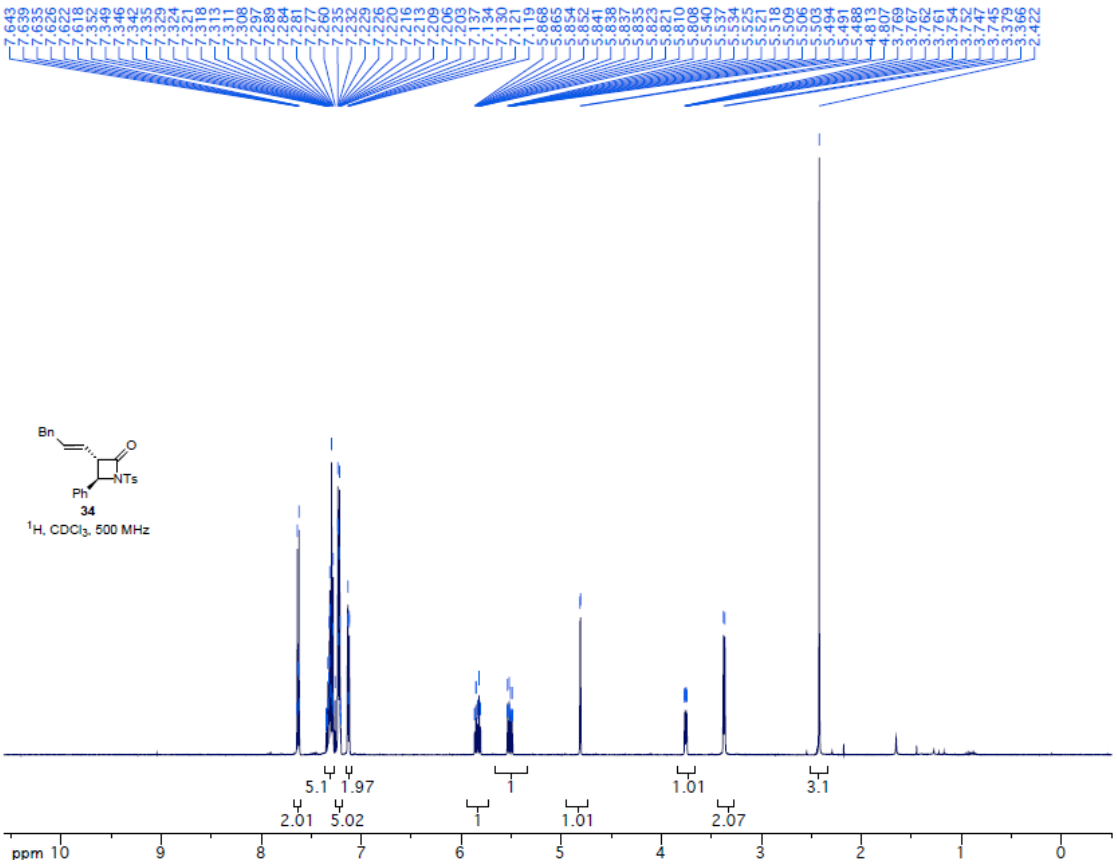
128.996
128.905
127.554
126.694
117.258
77.417
77.162
76.908
64.255
62.480
31.194
21.996
21.773
iPr
O
NTs
Ph
33
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


7.643
7.639
7.635
7.626
7.622
7.618
7.352
7.349
7.346
7.342
7.335
7.329
7.324
7.321
7.318
7.313
7.311
7.308
7.297
7.289
7.284
7.281
7.277
7.260
7.235
7.232
7.229
7.226
7.220
7.216
7.213
7.209
7.206
7.203
7.137
7.134
7.130
7.121
7.119
5.868
5.865
5.854
5.852
5.841
5.838
5.837
5.835
5.823
5.821
5.810
5.808
5.540
5.537
5.534
5.525
5.521
5.518
5.509
5.506
5.503
5.494
5.491
5.488
4.813
4.807
3.769
3.767
3.762
3.761
3.754
3.752
3.747
3.745
3.379
3.366
2.422
Bn
O
NTs
Ph
34
1H, CDCl3, 500 MHz
5.1
1.97
1
1.01
3.1
2.01
5.02
1
1.01
2.07
ppm 10
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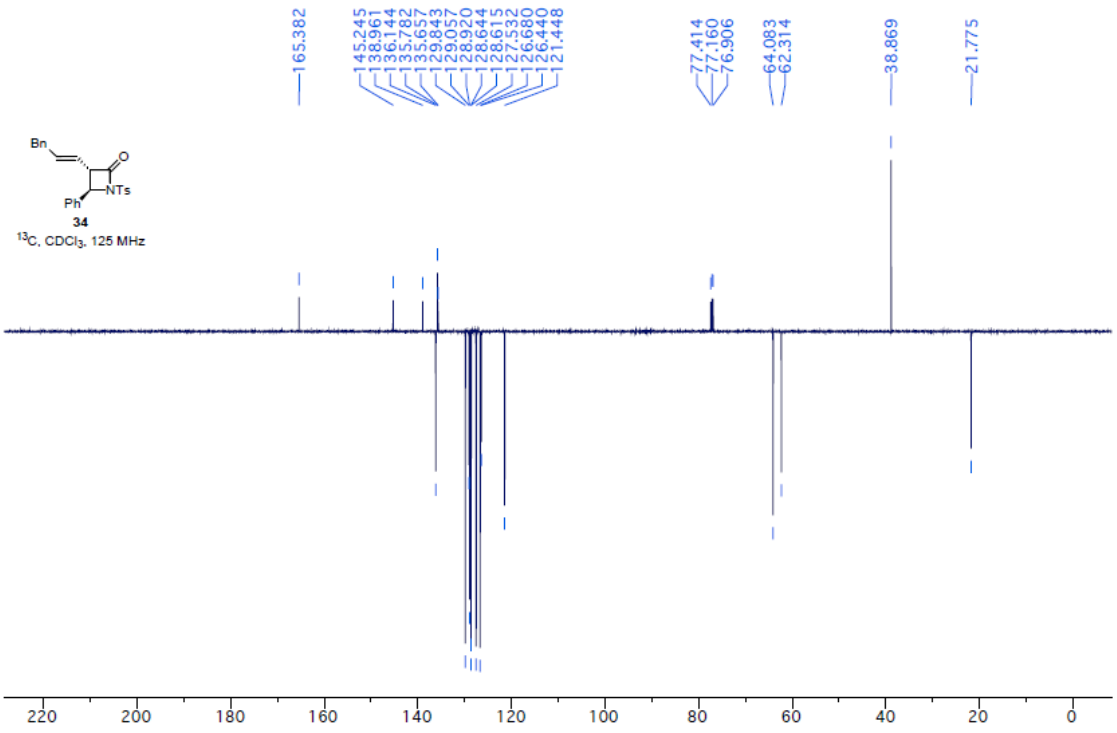
8
7
6
5
4
3
2
1
0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138.961
136.144
135.782
135.657
129.843
129.057
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128.615
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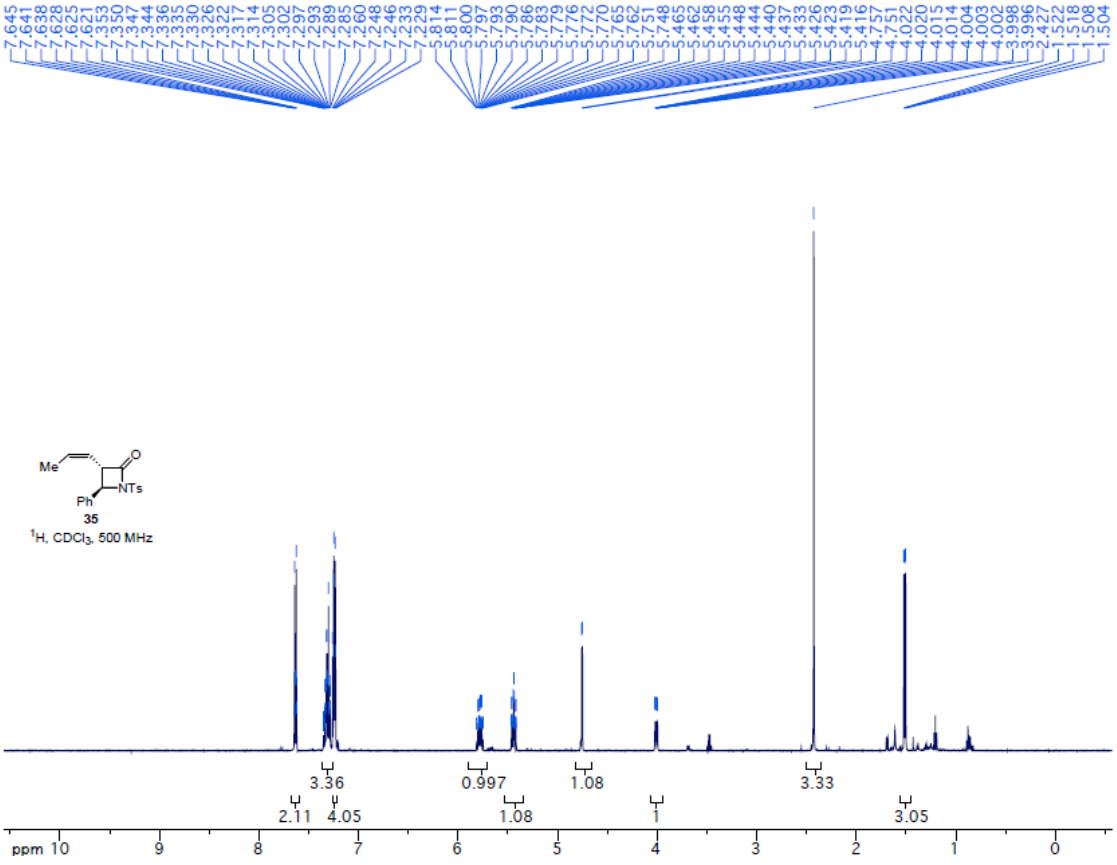
126.680
126.440
121.448
77.414
77.160
76.906
64.083
62.314
38.869
21.775
Bn
O
NTs
Ph
34
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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7.641
7.638
7.628
7.625
7.621
7.353
7.350
7.347
7.344
7.336
7.335
7.330
7.326
7.322
7.317
7.314
7.305
7.302
7.297
7.293
7.289
7.285
7.260
7.248
7.246
7.233
7.229
5.814
5.811
5.800
5.797
5.793
5.790
5.786
5.783
5.779
5.776
5.772
5.770
5.765
5.762
5.751
5.748
5.465
5.462
5.458
5.455
5.448
5.444
5.440
5.437
5.433
5.426
5.423
5.419
5.416
4.757
4.751
4.022
4.020
4.015
4.014
4.004
4.003
4.002
3.998
3.996
2.427
1.522
1.518
1.508
1.504
Me
Ph
NTs
O
35
1H, CDCl3, 500 MHz
3.36
0.997
1.08
3.33
2.11
4.05
1.08
1
3.05
ppm 10
9
8
7
6
5
4
3
2
1
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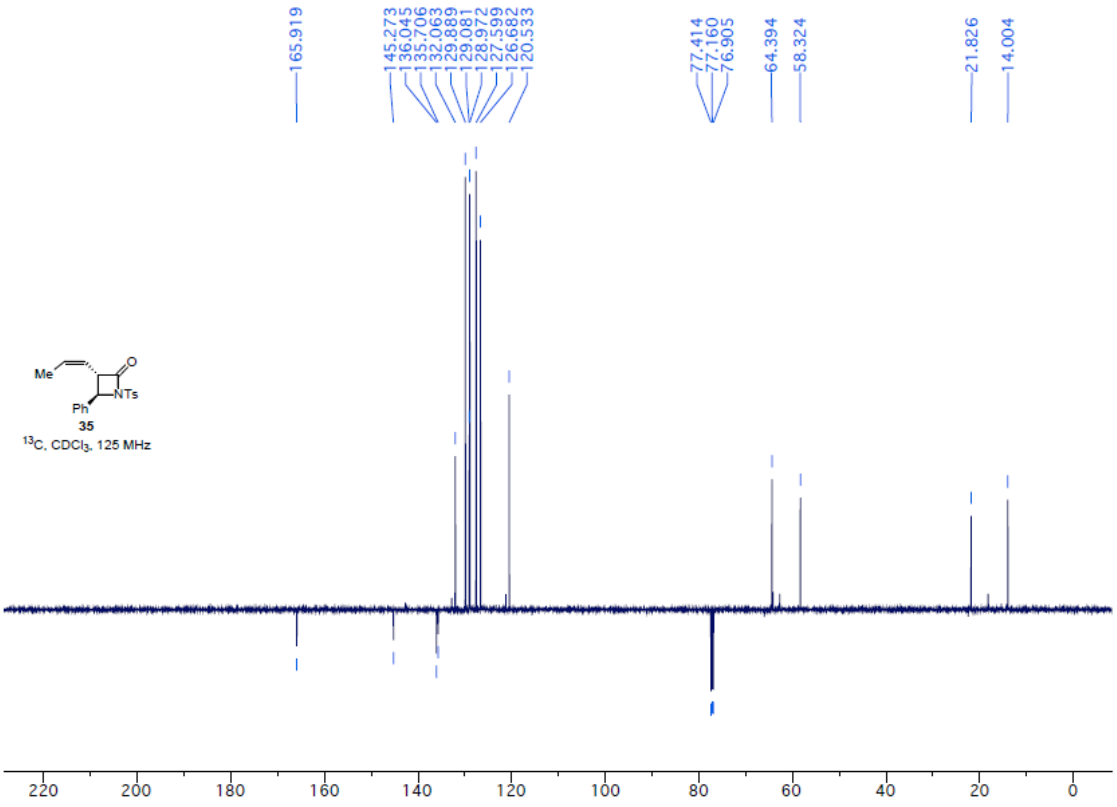
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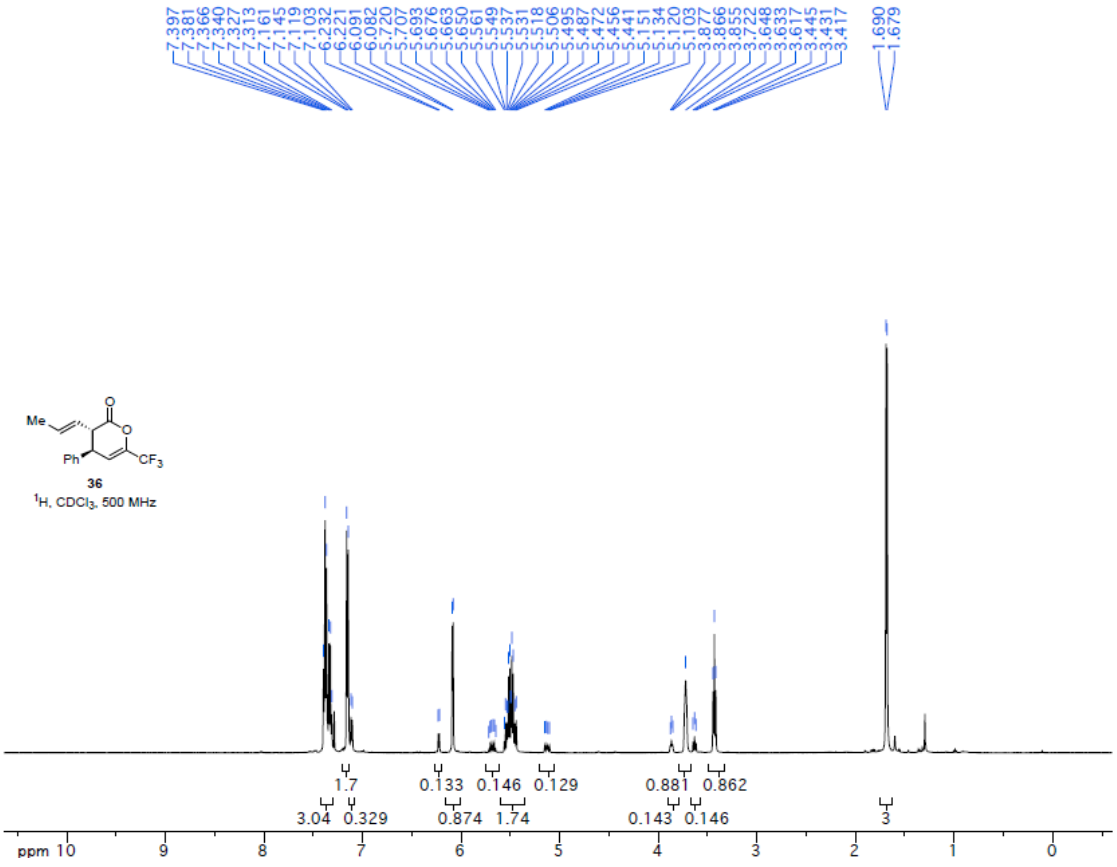
145.273
136.045
135.706
132.063
129.889
129.081
128.972
127.599
126.682
120.533
77.414
77.160
76.905
64.394
58.324
21.826
14.004
Me
Ph
NTs
O
35
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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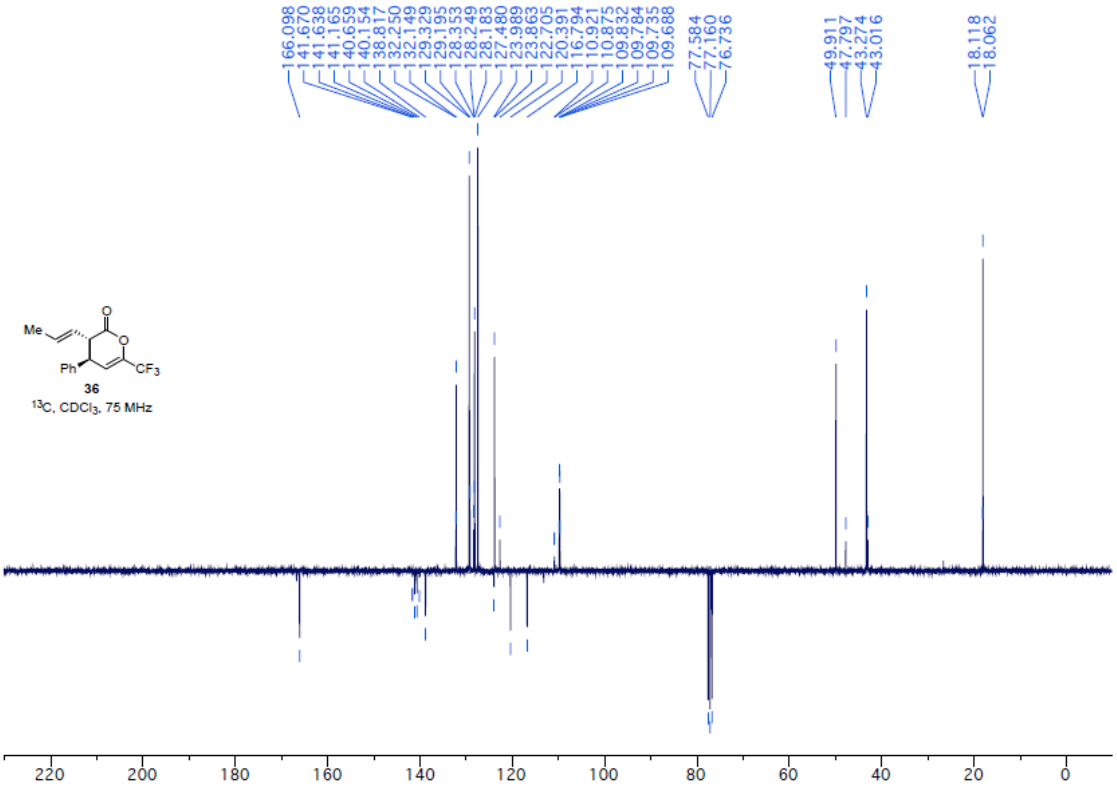
7.381
7.366
7.340
7.327
7.313
7.161
7.145
7.119
7.103
6.232
6.221
6.091
6.082
5.720
5.707
5.693
5.676
5.663
5.650
5.561
5.549
5.537
5.531
5.518
5.506
5.495
5.487
5.472
5.456
5.441
5.151
5.134
5.120
5.103
3.877
3.866
3.855
3.722
3.648
3.633
3.617
3.445
3.431
3.417
1.690
1.679
Me
Ph
O
O
CF3
36
1H, CDCl3, 500 MHz
1.7
0.133
0.146
0.129
0.881
0.862
3.04
0.329
0.874
1.74
0.143
0.146
3
ppm 10
9
8
7
6
5
4
3
2
1
0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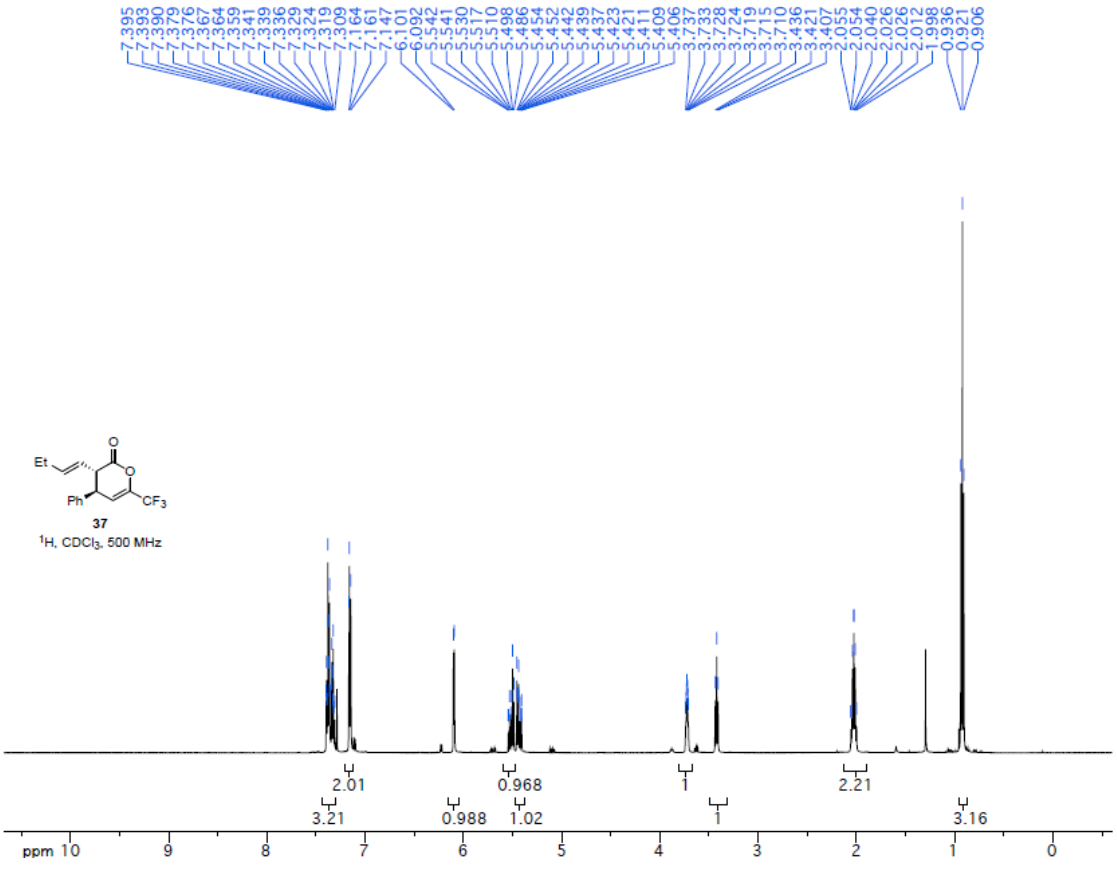
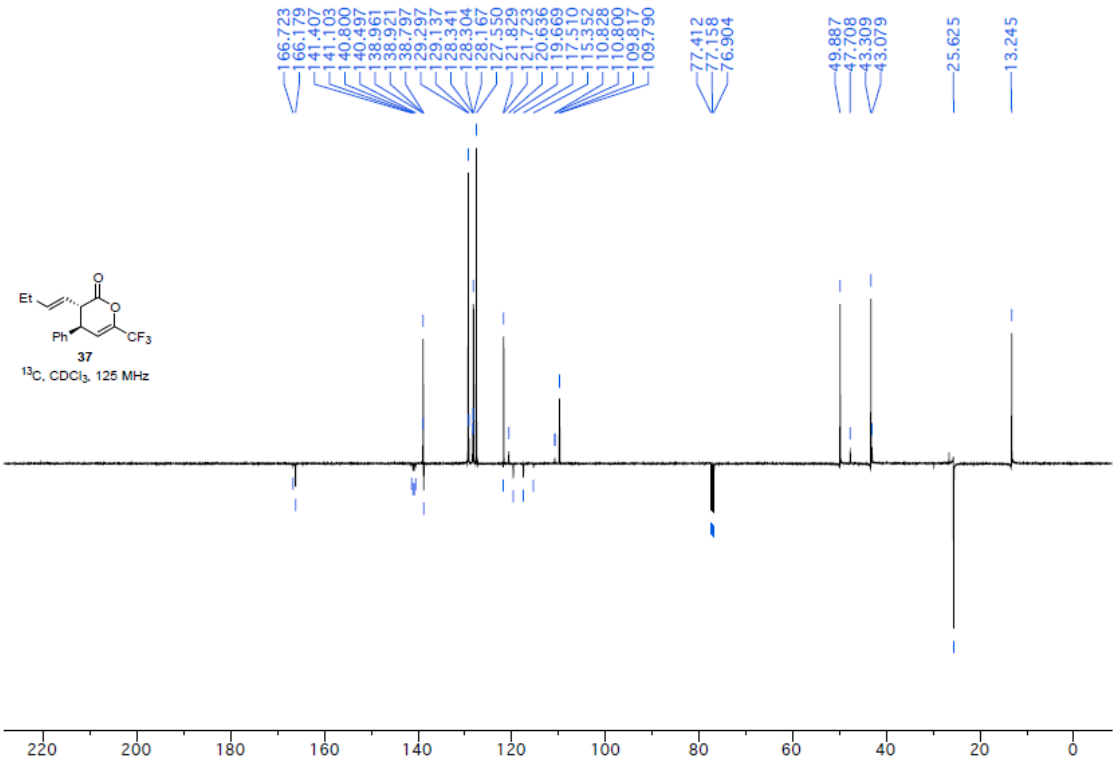
141.670
141.638
141.165
140.659
140.154
138.817
132.250
132.149
129.329
129.195
128.353
128.249
128.183
127.480
123.989
123.863
122.705
120.391
116.794
110.921
110.875
109.832
109.784
109.735
109.688
77.584
77.160
76.736
49.911
47.797
43.274
43.016
18.118
18.062
Me
Ph
O
O
CF3
36
13C, CDCl3, 75 MHz
220
200
180
160
140
120
100
80
60
40
20
0


7.395
7.393
7.390
7.379
7.376
7.367
7.364
7.359
7.341
7.339
7.336
7.329
7.324
7.319
7.309
7.164
7.161
7.147
6.101
6.092
5.542
5.541
5.530
5.517
5.510
5.498
5.486
5.454
5.452
5.442
5.439
5.437
5.423
5.421
5.411
5.409
5.406
3.737
3.733
3.728
3.724
3.719
3.715
3.710
3.436
3.421
3.407
2.055
2.054
2.040
2.026
2.026
2.012
1.998
0.936
0.921
0.906
Et
Ph
CF3
37
1H, CDCl3, 500 MHz
2.01
0.968
1
2.21
3.21
0.988
1.02
1
3.16
ppm 10
9
8
7
6
5
4
3
2
1
0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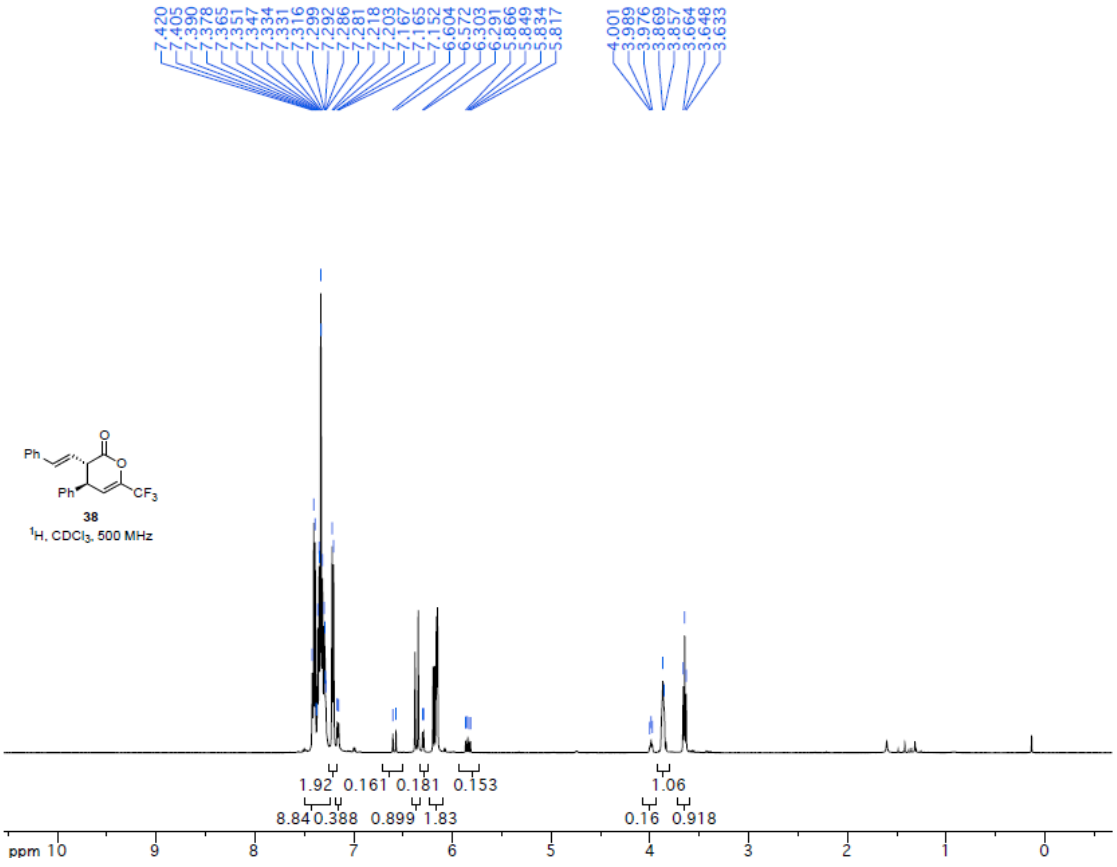
166.179
141.407
141.103
140.800
140.497
138.961
138.921
138.797
138.797
129.297
129.137
128.341
128.304
128.167
127.550
121.829
121.723
120.636
119.669
117.510
115.352
110.828
110.800
109.817
109.790
77.412
77.158
76.904
49.887
47.708
43.309
43.079
25.625
13.245
Et
Ph
CF3
37
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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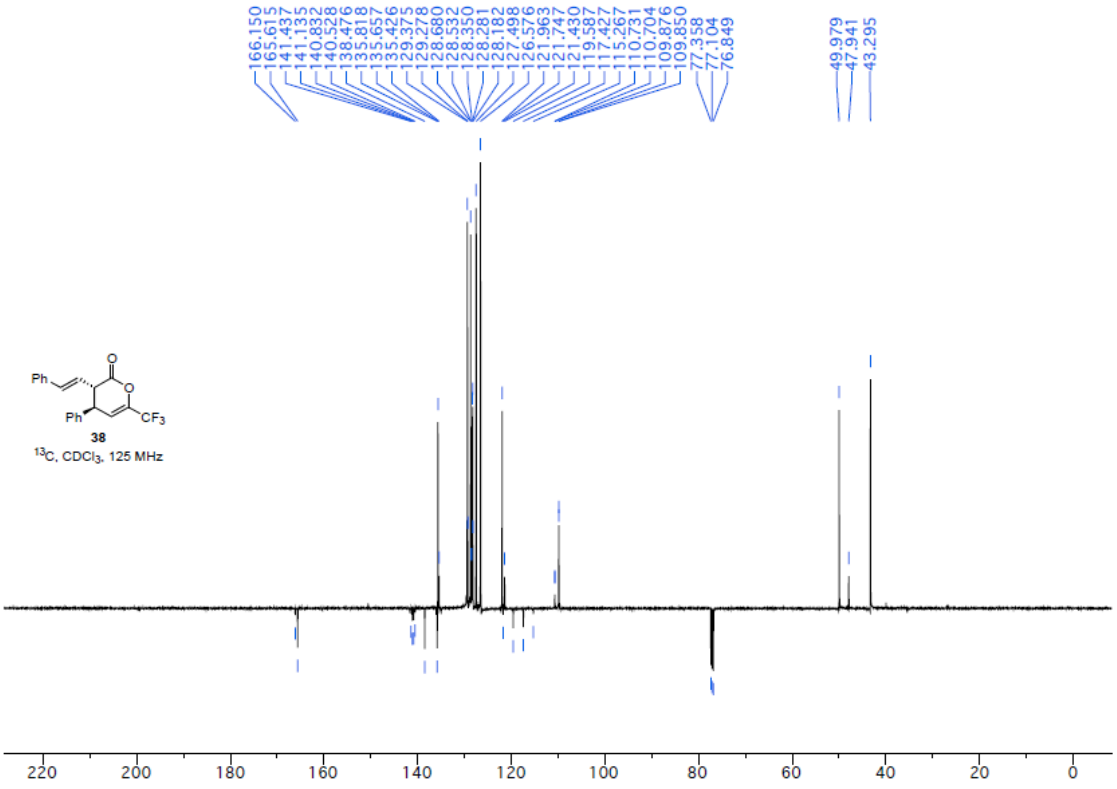
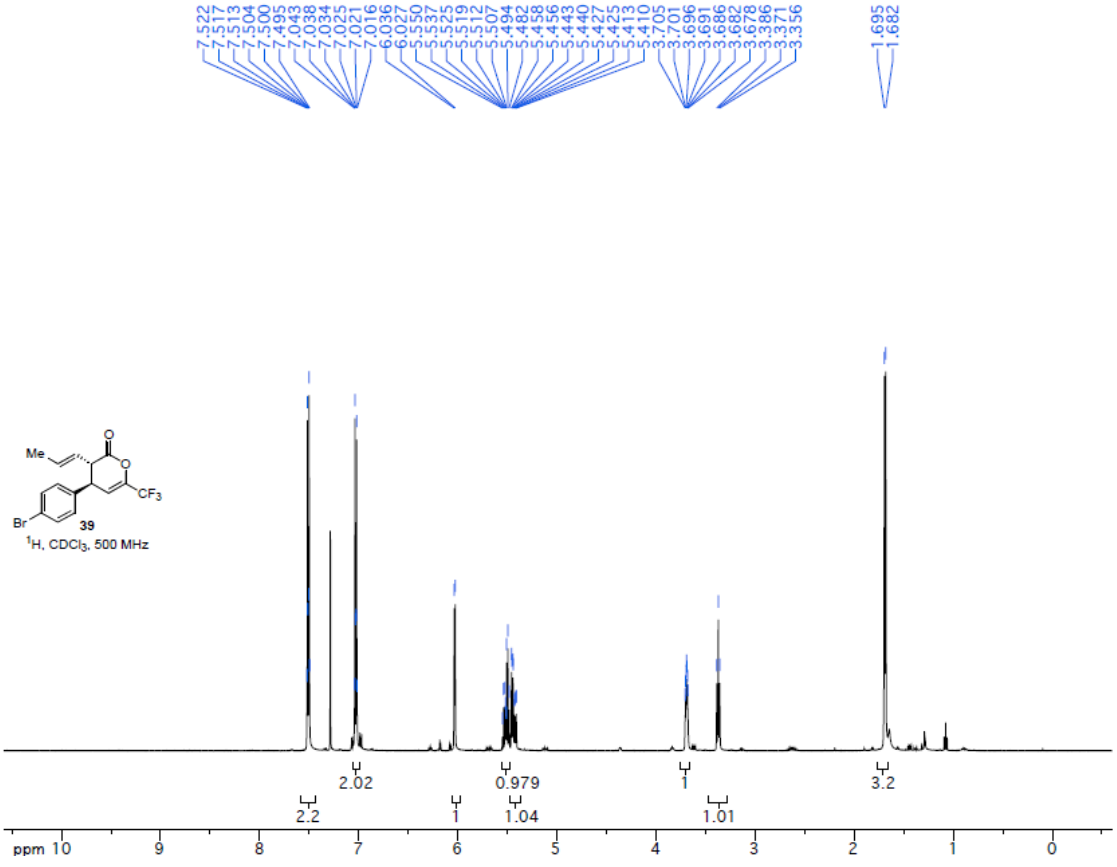
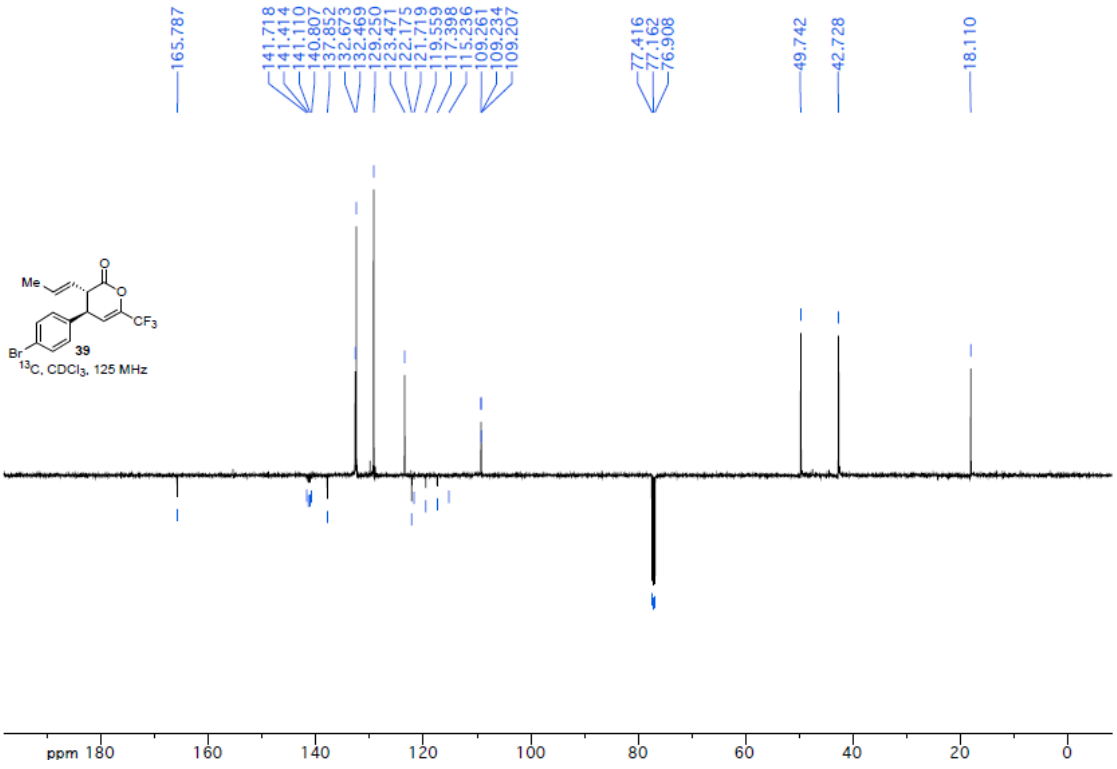
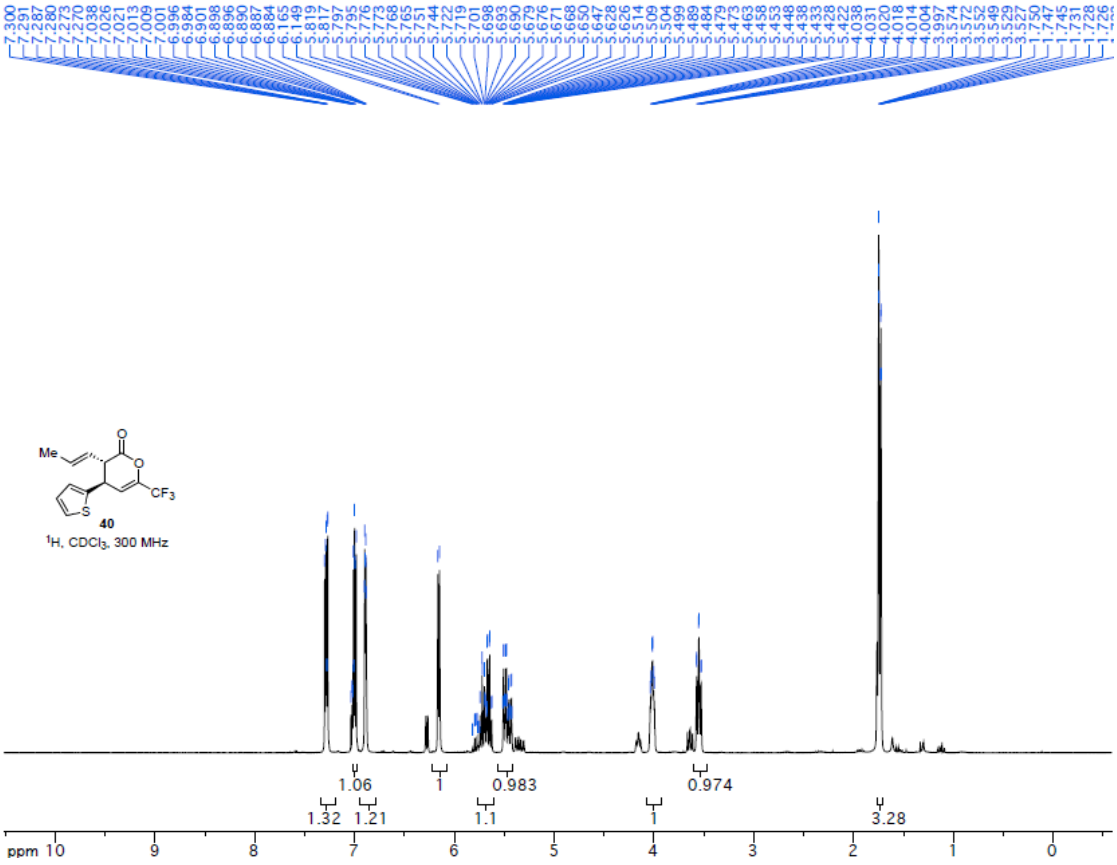
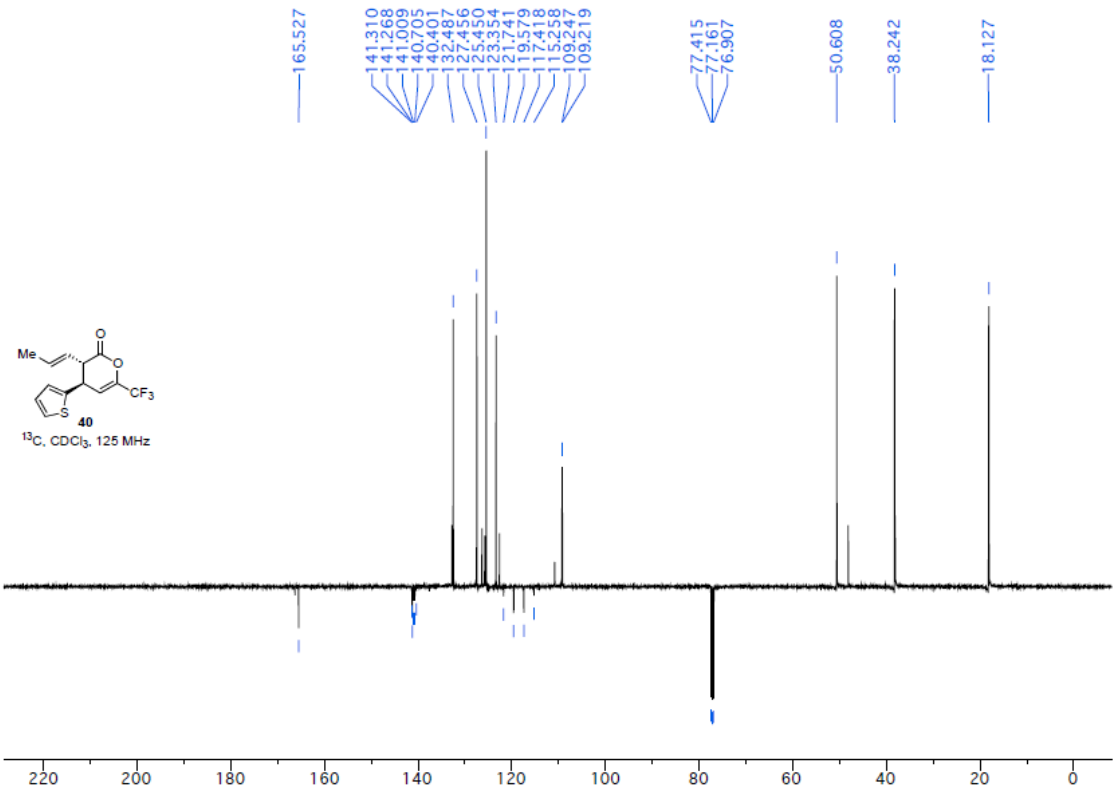
7.405
7.390
7.378
7.365
7.351
7.347
7.334
7.331
7.316
7.299
7.292
7.286
7.281
7.218
7.203
7.167
7.165
7.152
6.604
6.572
6.303
6.291
5.866
5.849
5.834
5.817
4.001
3.989
3.976
3.869
3.857
3.664
3.648
3.633
Ph
Ph
CF3
38
1H, CDCl3, 500 MHz
1.92
0.161
0.181
0.153
1.06
8.84
0.388
0.899
1.83
0.16
0.918
ppm 10
9
8
7
6
5
4
3
2
1
0


166.150
165.615
141.437
141.135
140.832
140.528
138.476
135.818
135.657
135.426
129.375
129.278
128.680
128.532
128.350
128.281
128.182
127.498
126.576
121.963
121.747
121.430
119.587
117.427
115.267
110.731
110.704
109.876
109.850
77.358
77.104
76.849
49.979
47.941
43.295
Ph
Ph
CF3
38
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


7.522
7.517
7.513
7.504
7.500
7.495
7.043
7.038
7.034
7.025
7.021
7.016
6.036
6.027
5.550
5.537
5.525
5.519
5.512
5.507
5.494
5.482
5.458
5.456
5.443
5.440
5.427
5.425
5.413
5.410
3.705
3.701
3.696
3.691
3.686
3.682
3.678
3.386
3.371
3.356
1.695
1.682
Me
O
O
CF3
Br
39
1H, CDCl3, 500 MHz
2.02
0.979
1
3.2
2.2
1
1.04
1.01
ppm 10
9
8
7
6
5
4
3
2
1
0


165.787
141.718
141.414
141.110
140.807
137.852
132.673
132.469
129.250
123.471
122.175
121.719
119.559
117.398
115.236
109.261
109.234
109.207
77.416
77.162
76.908
49.742
42.728
18.110
Me
O
O
CF3
Br
39
13C, CDCl3, 125 MHz
ppm 180
160
140
120
100
80
60
40
20
0


Me
O
O
CF3
S
40
1H, CDCl3, 300 MHz
1.06
1
0.983
0.974
1.32
1.21
1.1
1
3.28
ppm 10
9
8
7
6
5
4
3
2
1
0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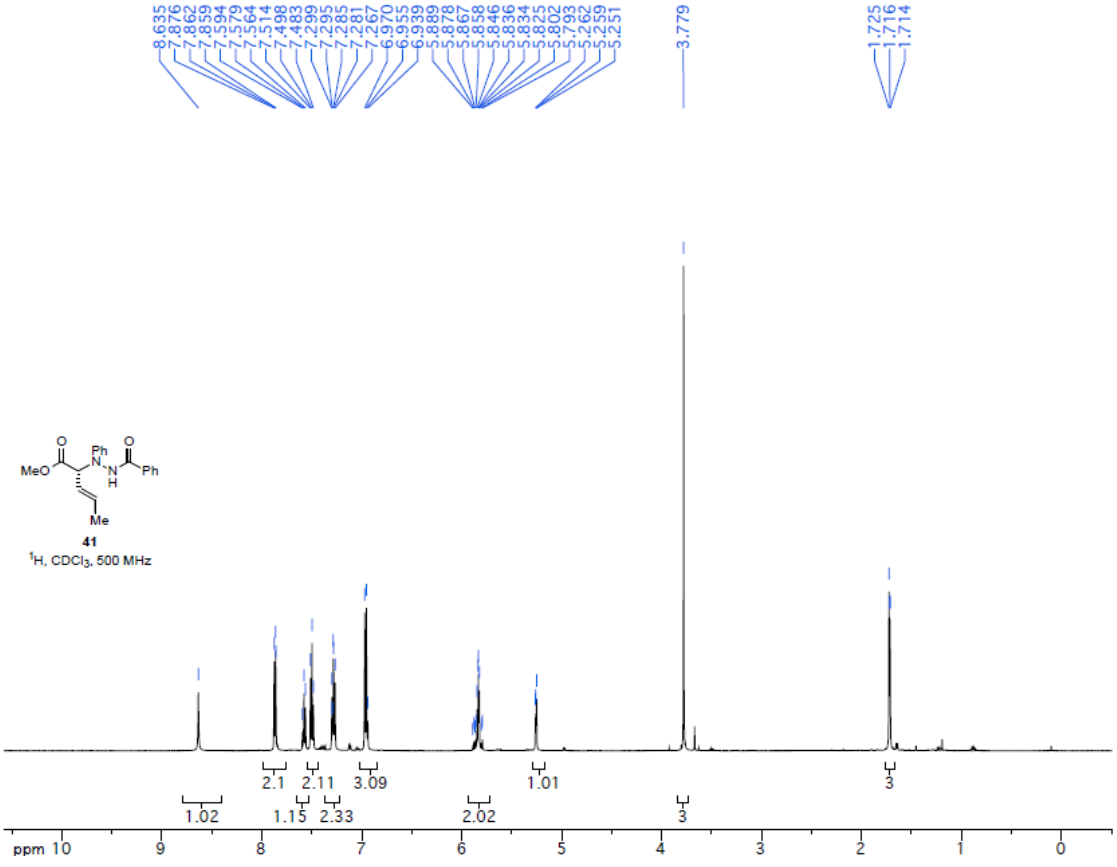
141.268
141.009
140.705
140.401
132.487
127.456
125.450
123.354
121.741
119.579
117.418
115.258
109.247
109.219
77.415
77.161
76.907
50.608
38.242
18.127
Me
O
O
CF3
S
40
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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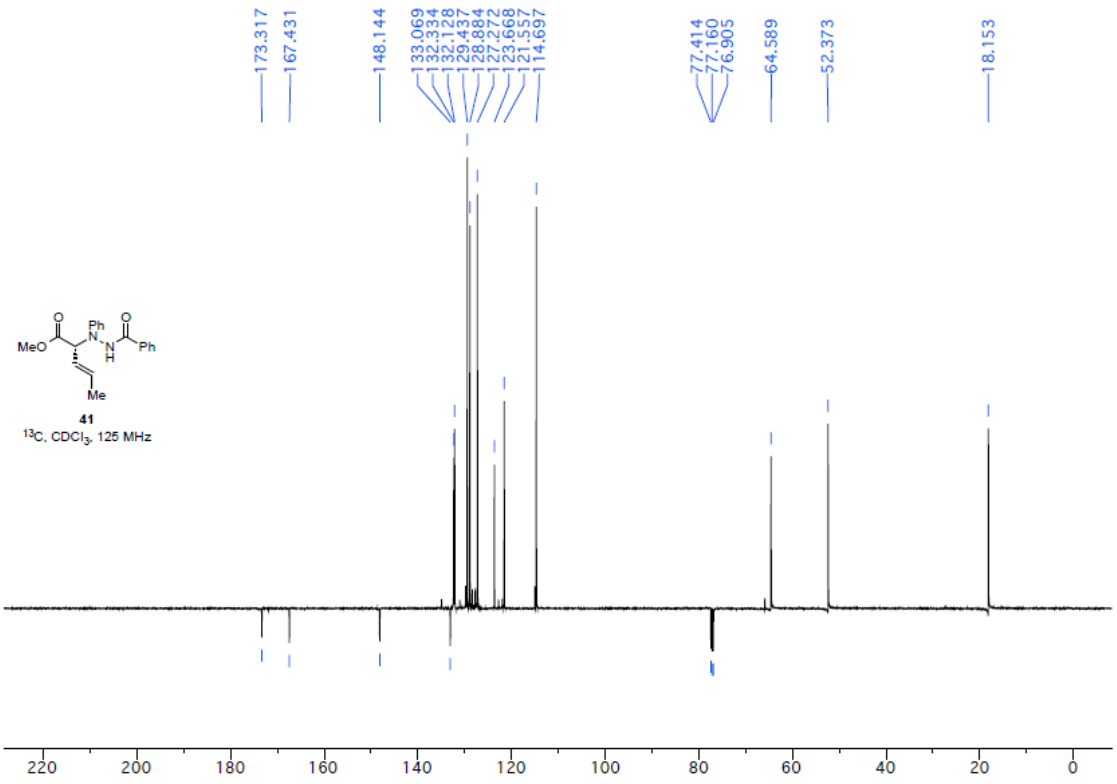
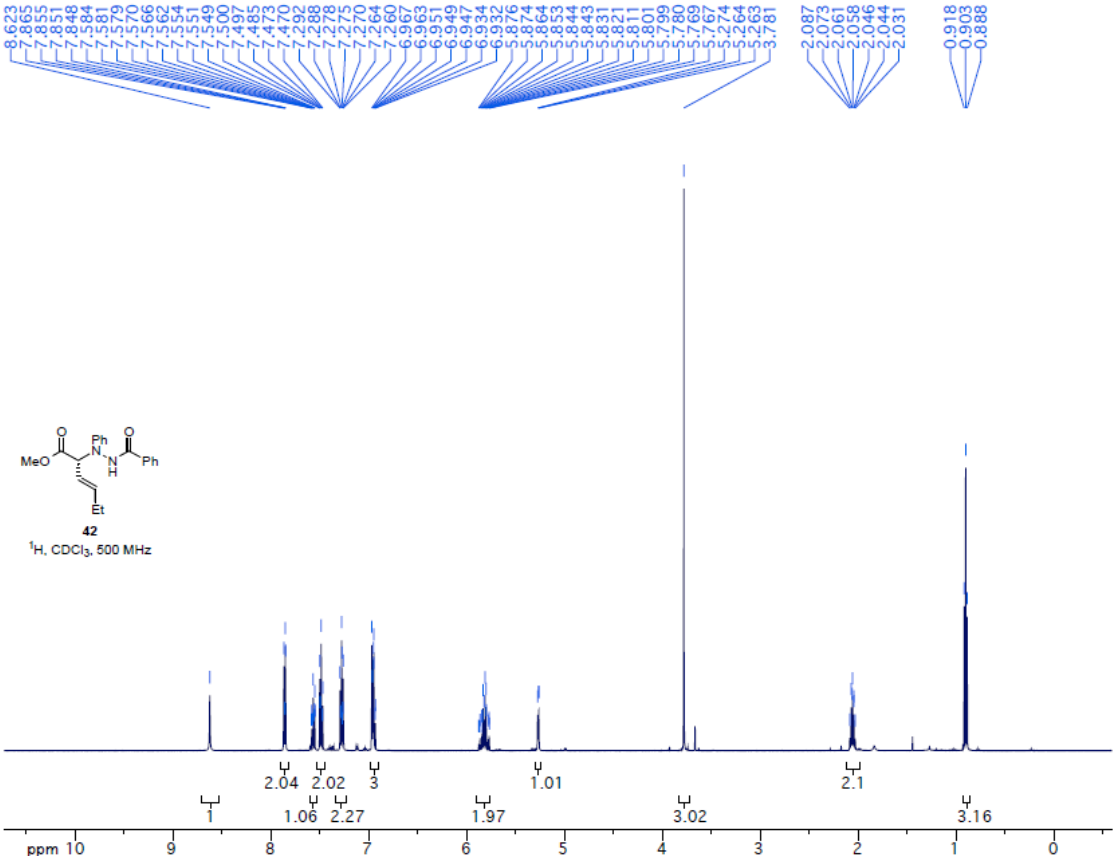
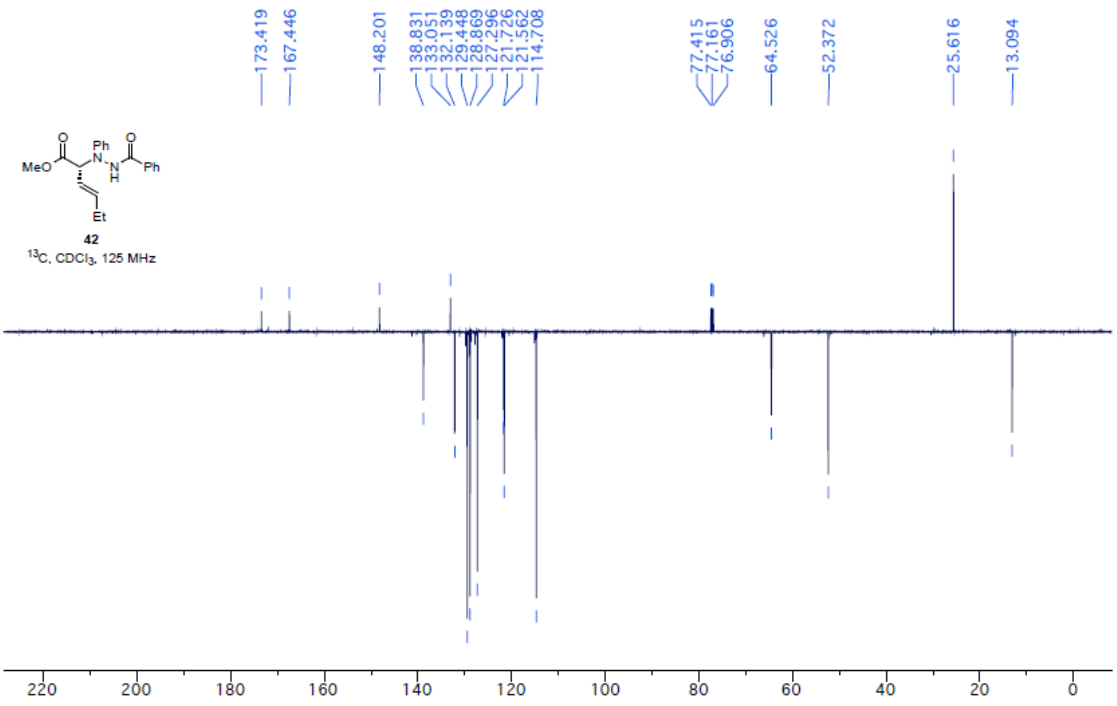
7.876
7.862
7.859
7.594
7.579
7.564
7.514
7.498
7.483
7.299
7.295
7.285
7.281
7.267
6.970
6.955
6.939
5.889
5.878
5.867
5.858
5.846
5.836
5.834
5.825
5.802
5.793
5.262
5.259
5.251
3.779
1.725
1.716
1.714
MeO
Ph
N
N
H
O
Ph
Me
41
1H, CDCl3, 500 MHz
2.1
2.11
3.09
1.01
3
1.02
1.15
2.33
2.02
3
ppm 10
9
8
7
6
5
4
3
2
1
0


173.317
167.431
148.144
133.069
132.334
132.128
129.437
128.884
127.272
123.668
121.557
114.697
77.414
77.160
76.905
64.589
52.373
18.153
MeO
Ph
N
N
H
O
Ph
Me
41
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


8.623
7.865
7.855
7.851
7.848
7.584
7.581
7.579
7.570
7.566
7.562
7.554
7.551
7.549
7.500
7.497
7.485
7.473
7.470
7.292
7.288
7.278
7.275
7.270
7.264
7.260
6.967
6.963
6.951
6.949
6.947
6.934
6.932
5.876
5.874
5.864
5.853
5.844
5.843
5.831
5.821
5.811
5.801
5.799
5.780
5.769
5.767
5.274
5.264
5.263
3.781
2.087
2.073
2.061
2.058
2.046
2.044
2.031
0.918
0.903
0.888
MeO
Ph
N
H
Ph
Et
42
1H, CDCl3, 500 MHz
2.04
2.02
3
1.01
2.1
1
1.06
2.27
1.97
3.02
3.16
ppm 10
9
8
7
6
5
4
3
2
1
0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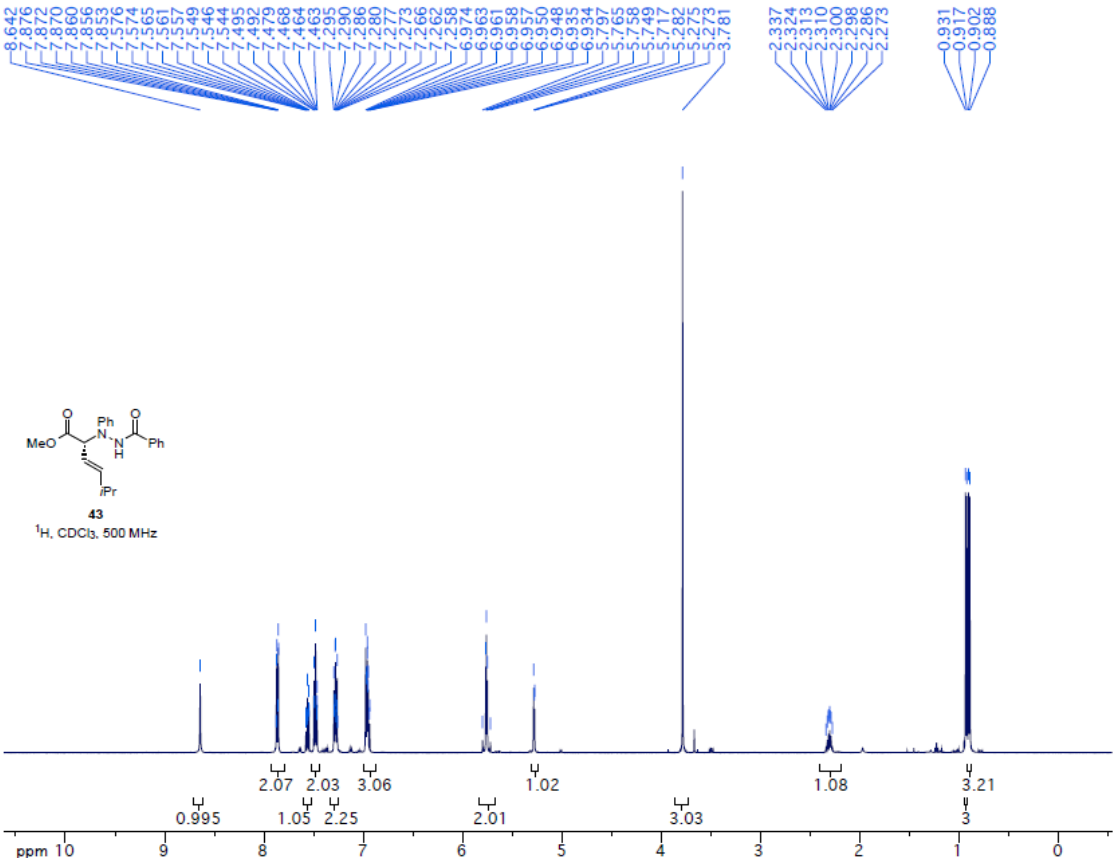
167.446
148.201
138.831
133.051
132.139
129.448
128.869
127.296
121.726
121.562
114.708
77.415
77.161
76.906
64.526
52.372
25.616
13.094
MeO
Ph
N
H
Ph
Et
42
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0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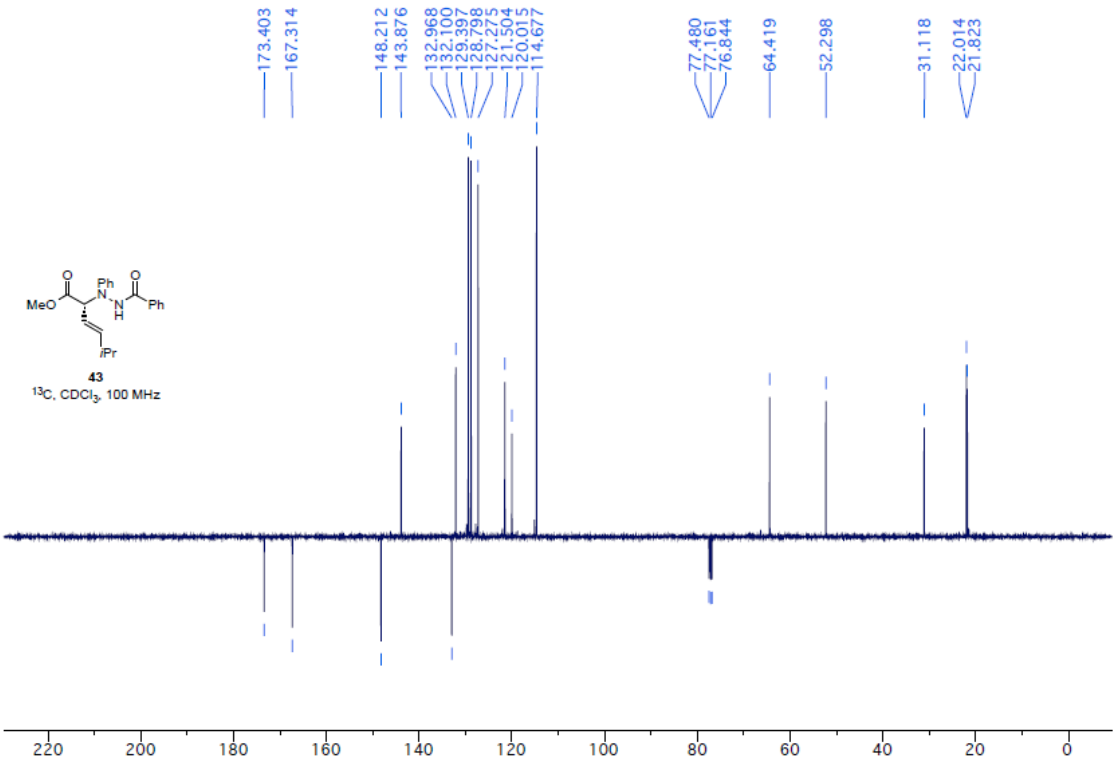
7.876
7.872
7.870
7.860
7.856
7.853
7.576
7.574
7.565
7.561
7.557
7.549
7.546
7.544
7.495
7.492
7.479
7.468
7.464
7.463
7.295
7.290
7.286
7.280
7.277
7.273
7.266
7.262
7.258
6.974
6.963
6.961
6.958
6.957
6.950
6.948
6.933
6.934
5.797
5.765
5.758
5.749
5.717
5.282
5.275
5.273
3.781
2.337
2.324
2.313
2.310
2.300
2.298
2.286
2.273
0.931
0.917
0.902
0.888
MeO
Ph
N
N
H
O
O
Ph
iPr
43
1H, CDCl3, 500 MHz
2.07
2.03
3.06
1.02
1.08
3.21
0.995
1.05
2.25
2.01
3.03
3
ppm 10
9
8
7
6
5
4
3
2
1
0


173.403
167.314
148.212
143.876
132.968
132.100
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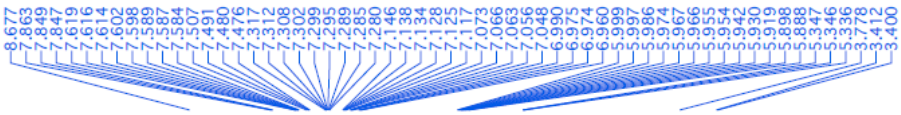
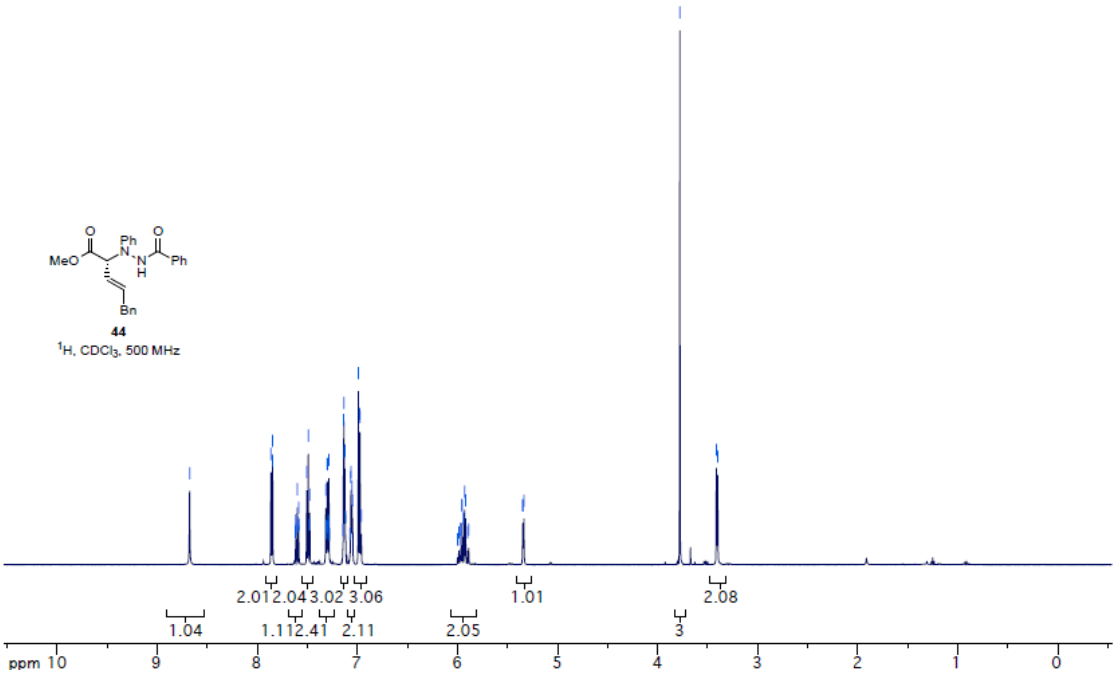
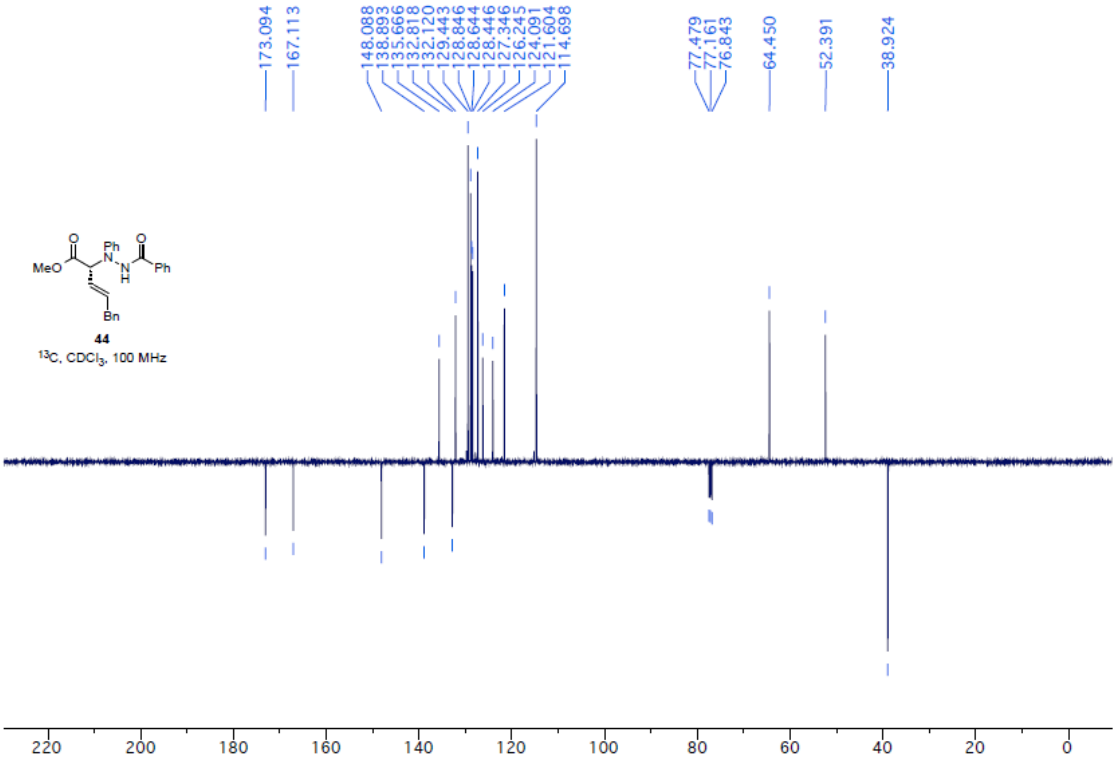
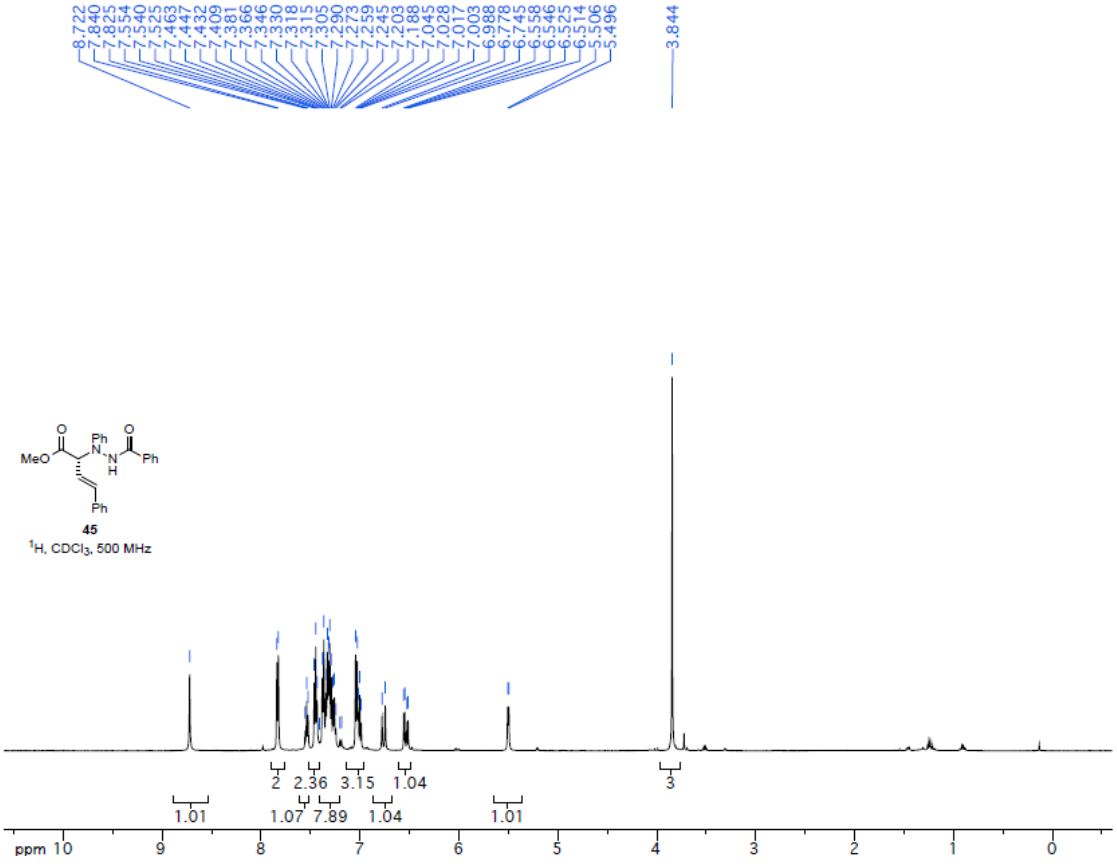
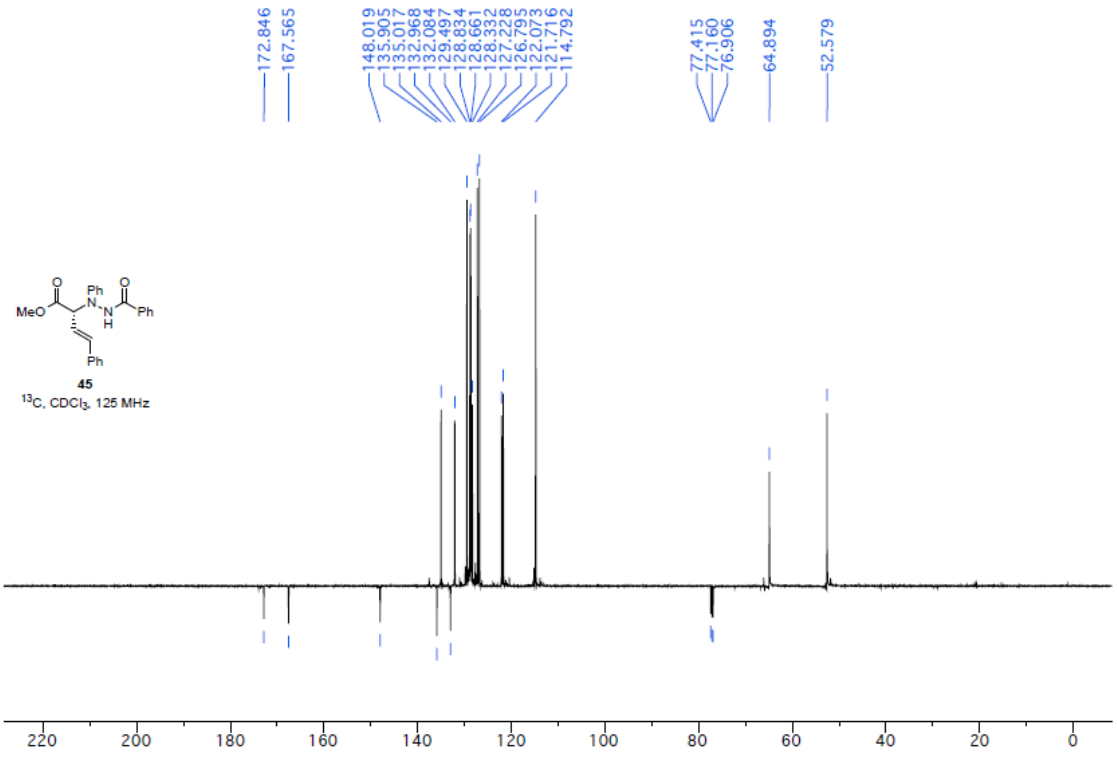
128.798
127.275
121.504
120.015
114.677
77.480
77.161
76.844
64.419
52.298
31.118
22.014
21.823
MeO
Ph
N
N
H
O
O
Ph
iPr
43
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

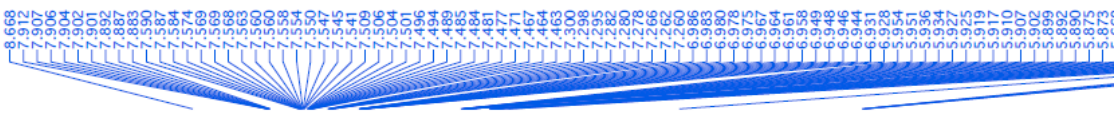

8.677
7.863
7.849
7.847
7.619
7.616
7.614
7.602
7.598
7.589
7.587
7.584
7.507
7.491
7.480
7.476
7.317
7.312
7.308
7.302
7.299
7.295
7.289
7.285
7.280
7.146
7.138
7.134
7.128
7.125
7.117
7.073
7.066
7.063
7.056
7.048
6.990
6.975
6.974
6.960
5.999
5.997
5.986
5.974
5.967
5.966
5.955
5.954
5.942
5.930
5.919
5.898
5.888
5.347
5.346
5.336
3.778
3.412
3.400

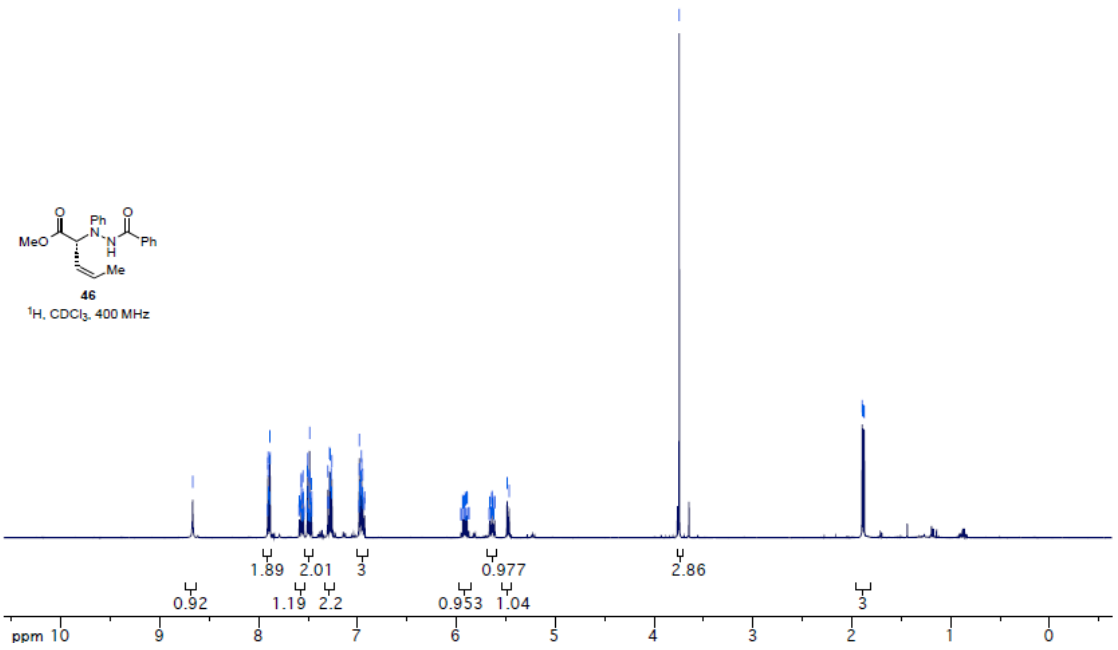

MeO
Ph
N
N
H
O
Ph
Bn
44
1H, CDCl3, 500 MHz
2.01
2.04
3.02
3.06
1.01
2.08
1.04
1.11
2.41
2.11
2.05
3
ppm 10
9
8
7
6
5
4
3
2
1
0

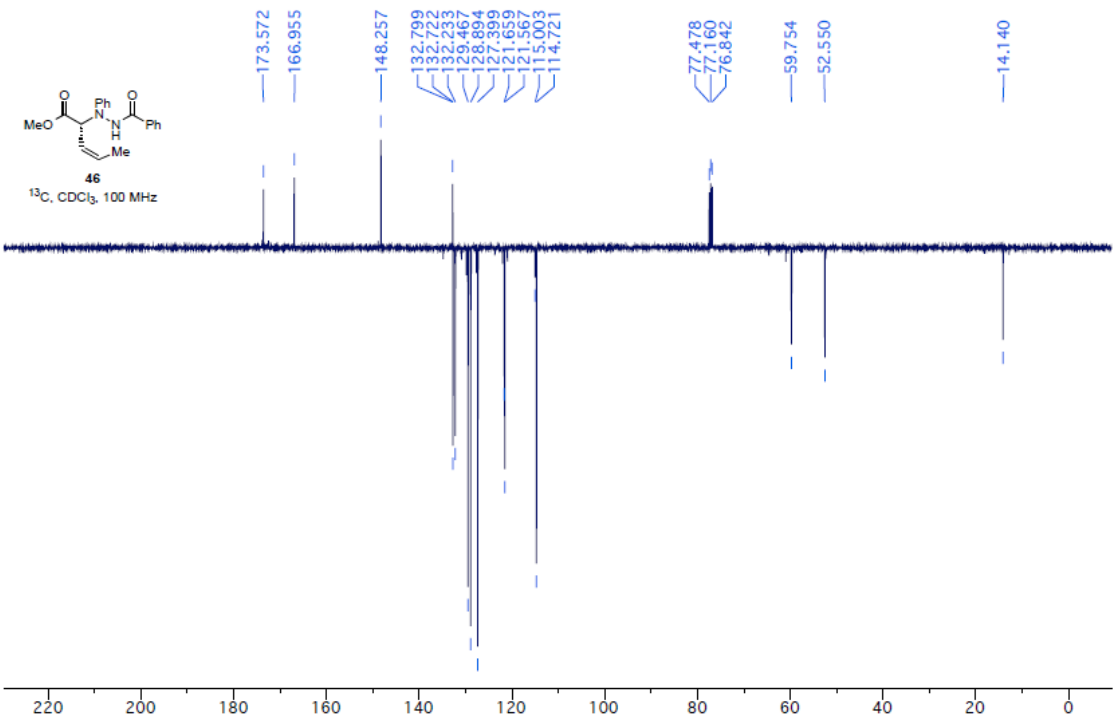

173.094
167.113
148.088
138.893
135.666
132.818
132.120
129.443
128.846
128.644
128.446
127.346
126.245
124.091
121.604
114.698
77.479
77.161
76.843
64.450
52.391
38.924
MeO
Ph
N
N
H
O
Ph
Bn
44
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

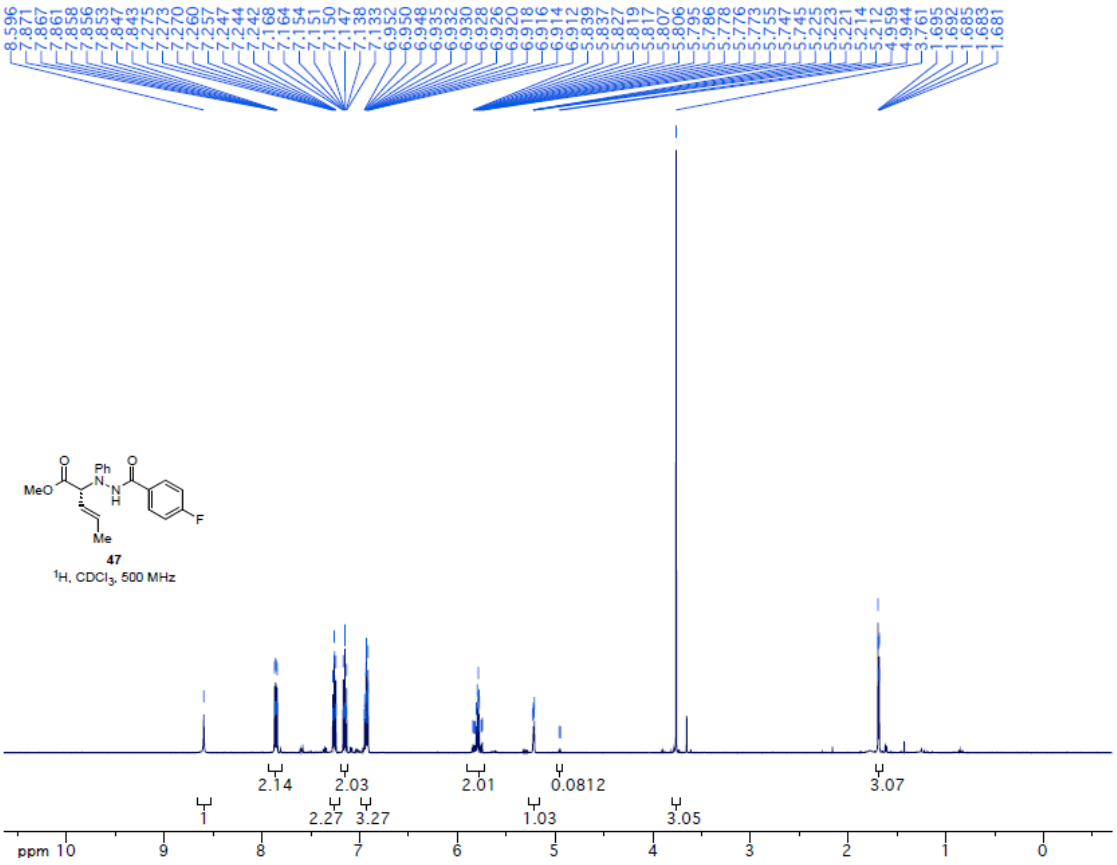

8.722
7.840
7.825
7.554
7.540
7.525
7.463
7.447
7.432
7.409
7.381
7.366
7.346
7.330
7.318
7.315
7.305
7.290
7.273
7.259
7.245
7.203
7.188
7.045
7.028
7.017
7.003
6.988
6.978
6.745
6.558
6.546
6.525
6.514
5.506
5.496
3.844
MeO
Ph
N
N
H
O
O
Ph
Ph
45
1H, CDCl3, 500 MHz
2
2.36
3.15
1.04
3
1.01
1.07
7.89
1.04
1.01
ppm 10
9
8
7
6
5
4
3
2
1
0

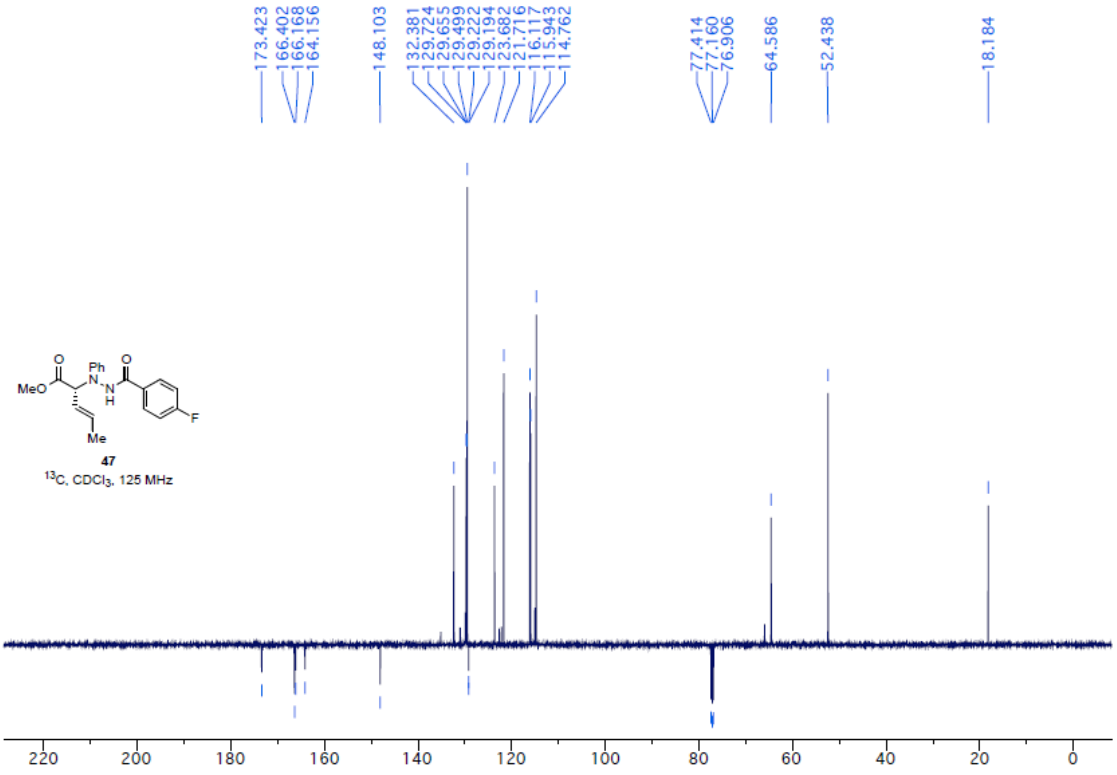

172.846
167.565
148.019
135.905
135.017
132.968
132.084
129.497
128.834
128.661
128.332
127.228
126.795
122.073
121.716
114.792
77.415
77.160
76.906
64.894
52.579
MeO
Ph
N
N
H
O
O
Ph
Ph
45
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0

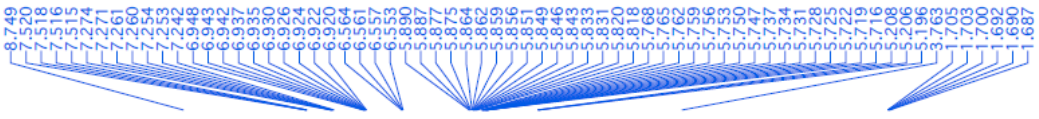


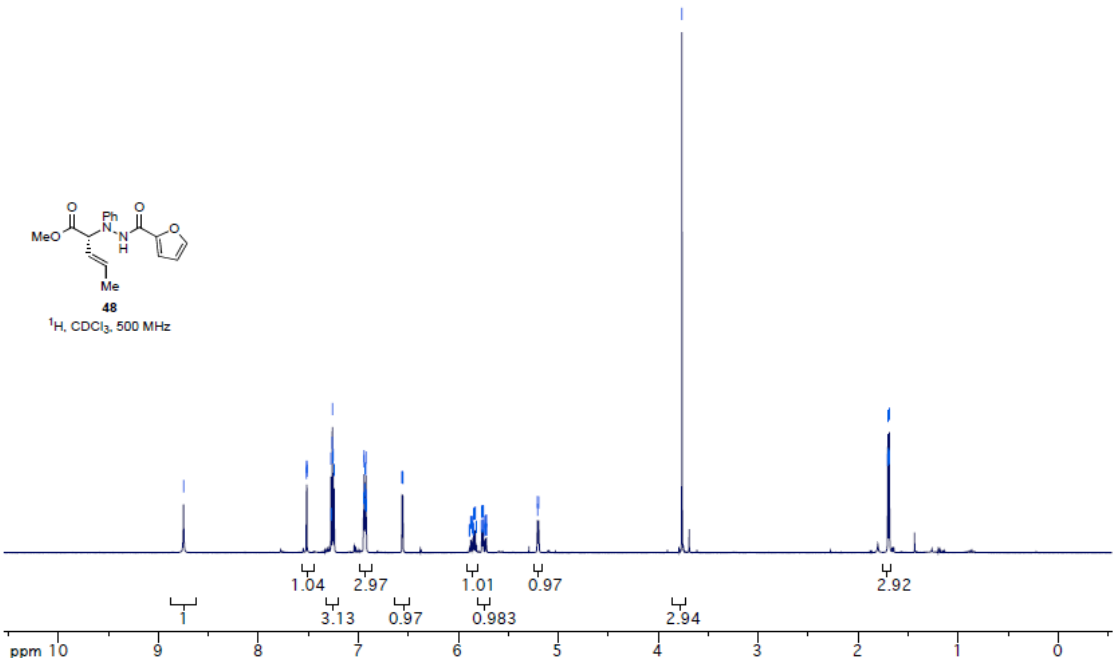

46
1H, CDCl3, 400 MHz
1.89
2.01
3
0.977
2.86
0.92
1.19
2.2
0.953
1.04
3
ppm

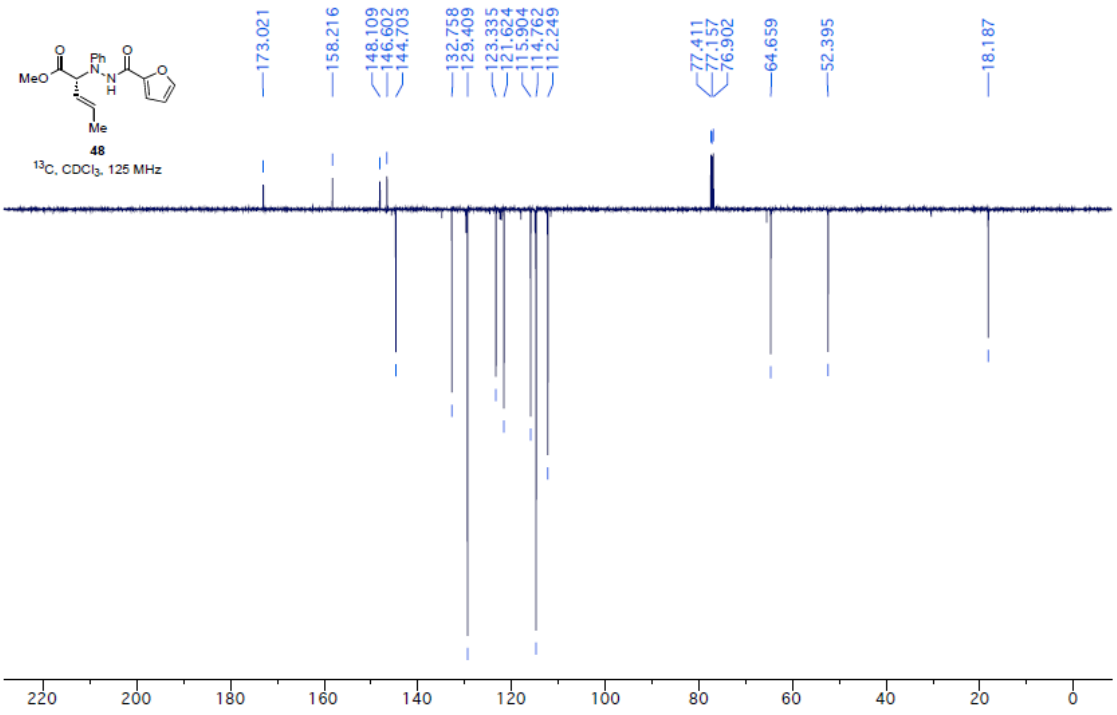

173.572
166.955
148.257
132.799
132.722
132.233
129.467
128.894
127.399
121.659
121.567
115.003
114.721
77.478
77.160
76.842
59.754
52.550
14.140
46
13C, CDCl3, 100 MHz

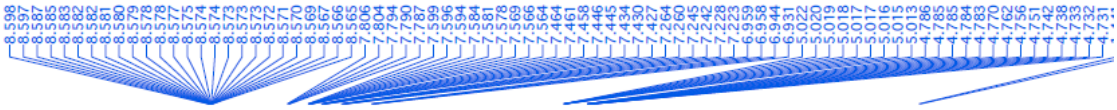

8.596
7.871
7.867
7.861
7.858
7.856
7.853
7.847
7.843
7.275
7.273
7.270
7.260
7.257
7.247
7.244
7.242
7.168
7.164
7.154
7.151
7.150
7.147
7.138
7.133
6.952
6.950
6.948
6.935
6.932
6.930
6.928
6.926
6.920
6.918
6.916
6.914
6.912
5.839
5.837
5.827
5.819
5.817
5.807
5.806
5.795
5.786
5.778
5.776
5.773
5.755
5.747
5.745
5.225
5.223
5.221
5.214
5.212
4.959
4.944
3.761
1.695
1.692
1.685
1.683
1.681
MeO
Ph
N
N
H
O
O
F
Me
47
1H, CDCl3, 500 MHz
2.14
2.03
2.01
0.0812
3.07
1
2.27
3.27
1.03
3.05
ppm 10
9
8
7
6
5
4
3
2
1
0

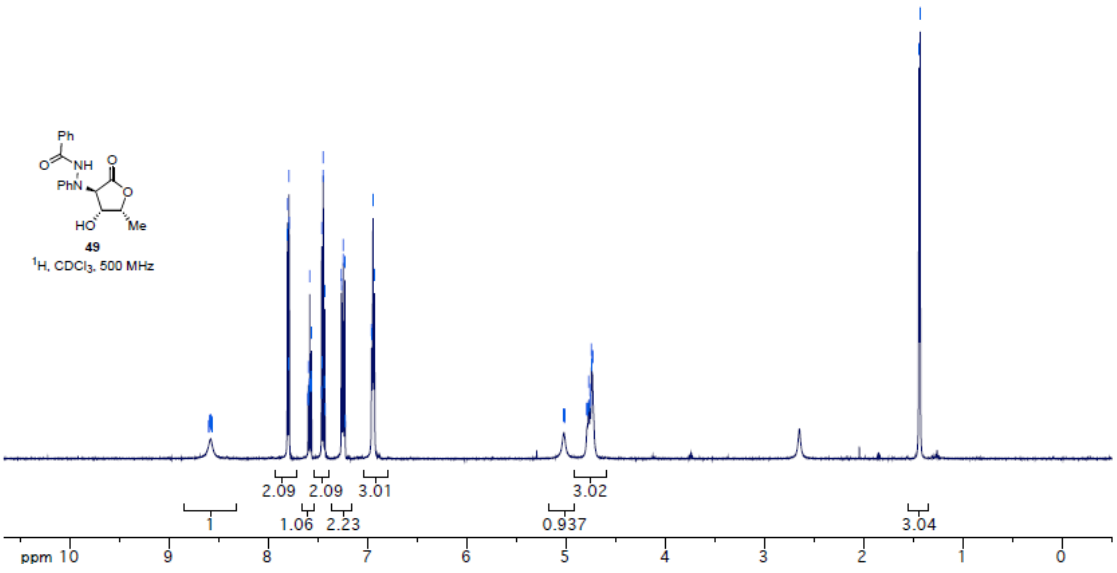

173.423
166.402
166.168
164.156
148.103
132.381
129.724
129.655
129.499
129.222
129.194
123.682
121.716
116.117
115.943
114.762
77.414
77.160
76.906
64.586
52.438
18.184
MeO
Ph
N
N
H
O
O
F
Me
47
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0

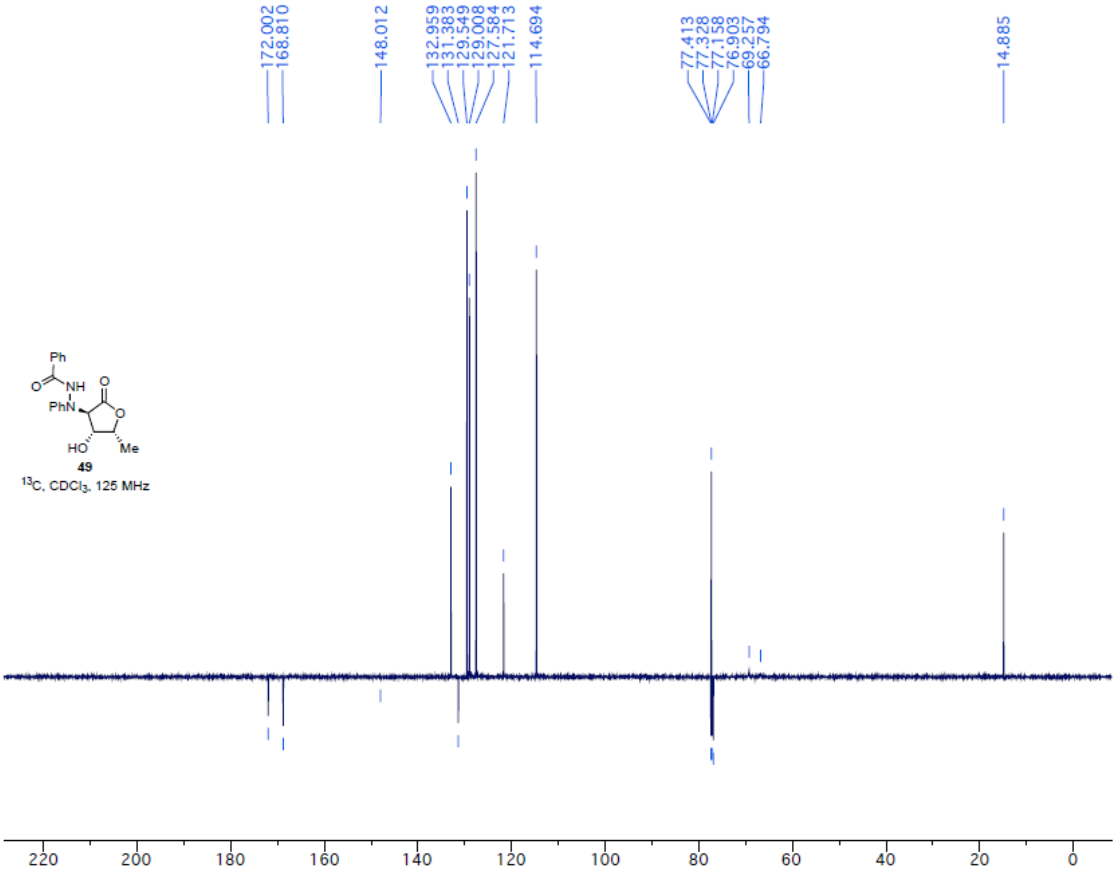

8.749
7.520
7.518
7.516
7.515
7.274
7.271
7.261
7.260
7.254
7.253
7.242
6.948
6.943
6.942
6.937
6.935
6.930
6.926
6.924
6.922
6.920
6.564
6.561
6.557
6.553
5.890
5.887
5.877
5.875
5.864
5.862
5.859
5.856
5.851
5.849
5.846
5.843
5.833
5.831
5.820
5.818
5.768
5.765
5.762
5.759
5.756
5.753
5.750
5.747
5.737
5.734
5.731
5.728
5.725
5.722
5.719
5.716
5.208
5.206
5.196
3.763
1.705
1.703
1.700
1.692
1.690
1.687

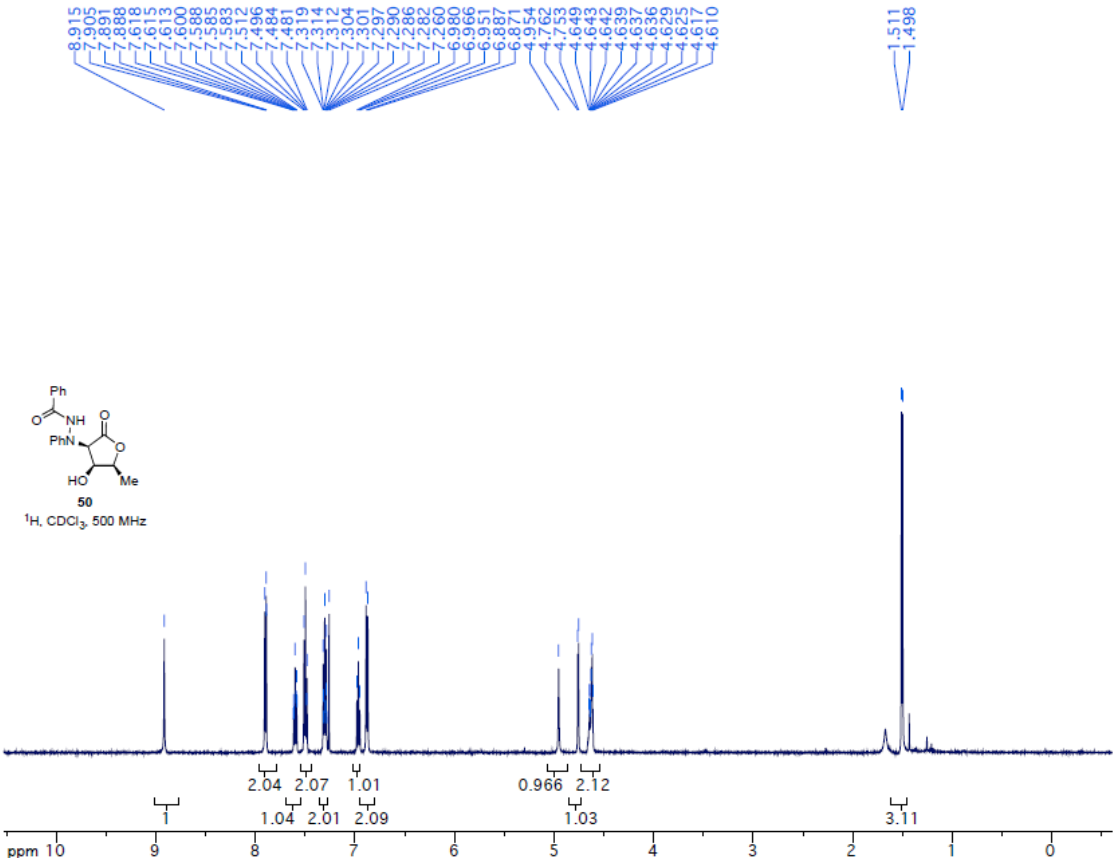

MeO
Ph
N
N
H
O
O
Me
48
^{1}H, $CDCl_3$, 500 MHz
1.04
2.97
1.01
0.97
2.92
1
3.13
0.97
0.983
2.94
ppm 10
9
8
7
6
5
4
3
2
1
0

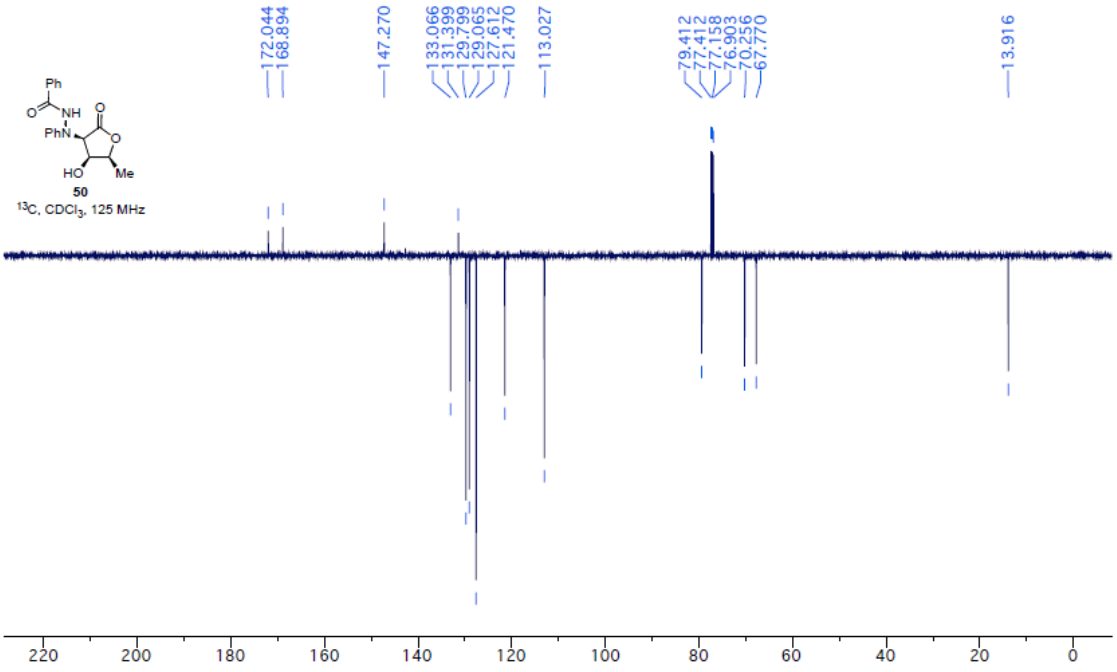

MeO
Ph
N
N
H
O
O
Me
48
^{13}C, $CDCl_3$, 125 MHz
173.021
158.216
148.109
146.602
144.703
132.758
129.409
123.335
121.624
115.904
114.762
112.249
77.411
77.157
76.902
64.659
52.395
18.187
220
200
180
160
140
120
100
80
60
40
20
0

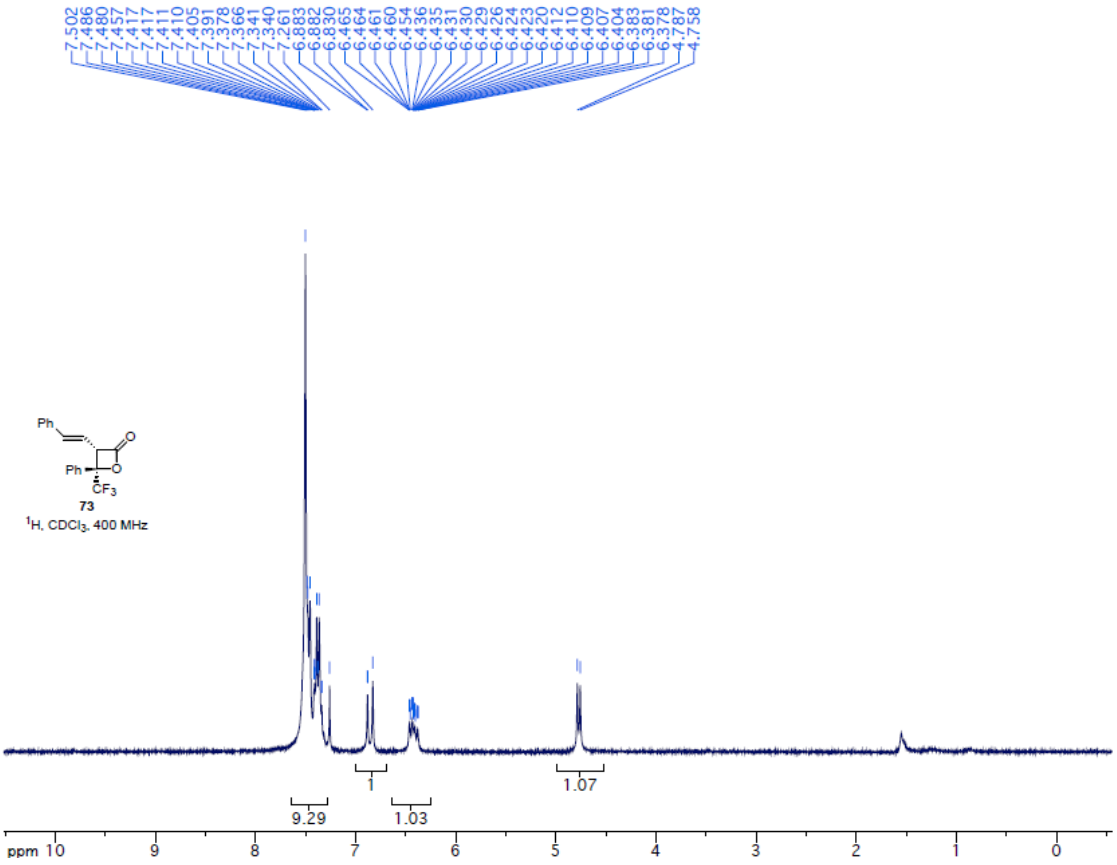


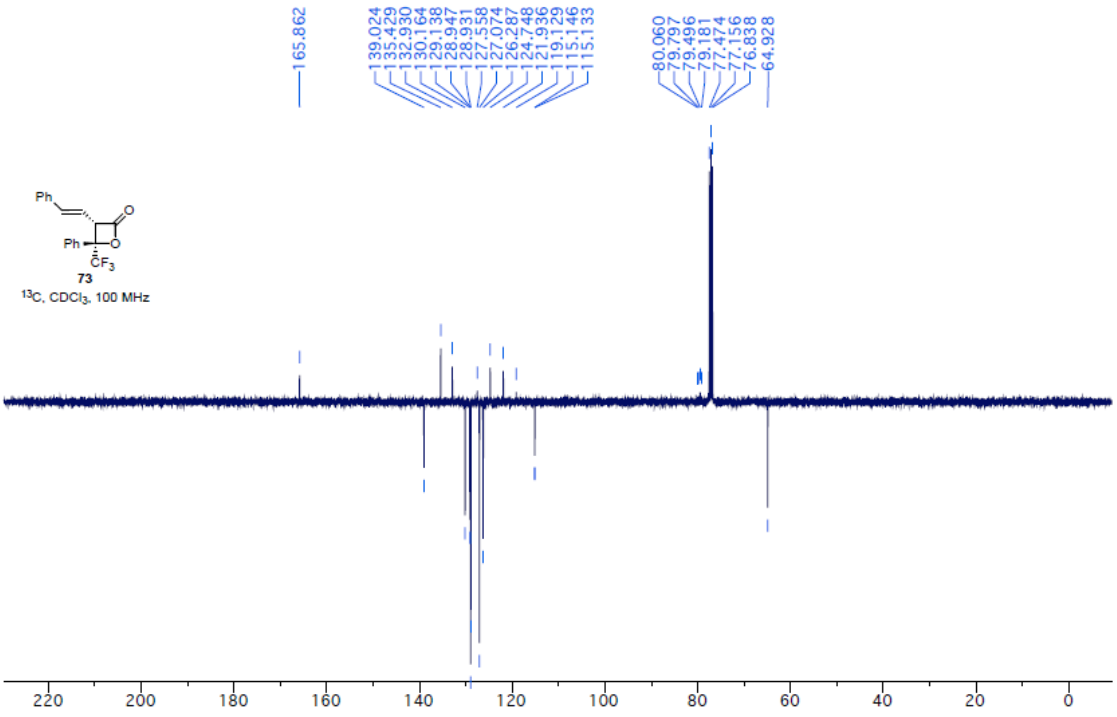

Ph
NH
PhN
O
O
HO
Me
49
1H, CDCl3, 500 MHz
2.09
2.09
3.01
3.02
1
1.06
2.23
0.937
3.04
ppm 10
9
8
7
6
5
4
3
2
1
0

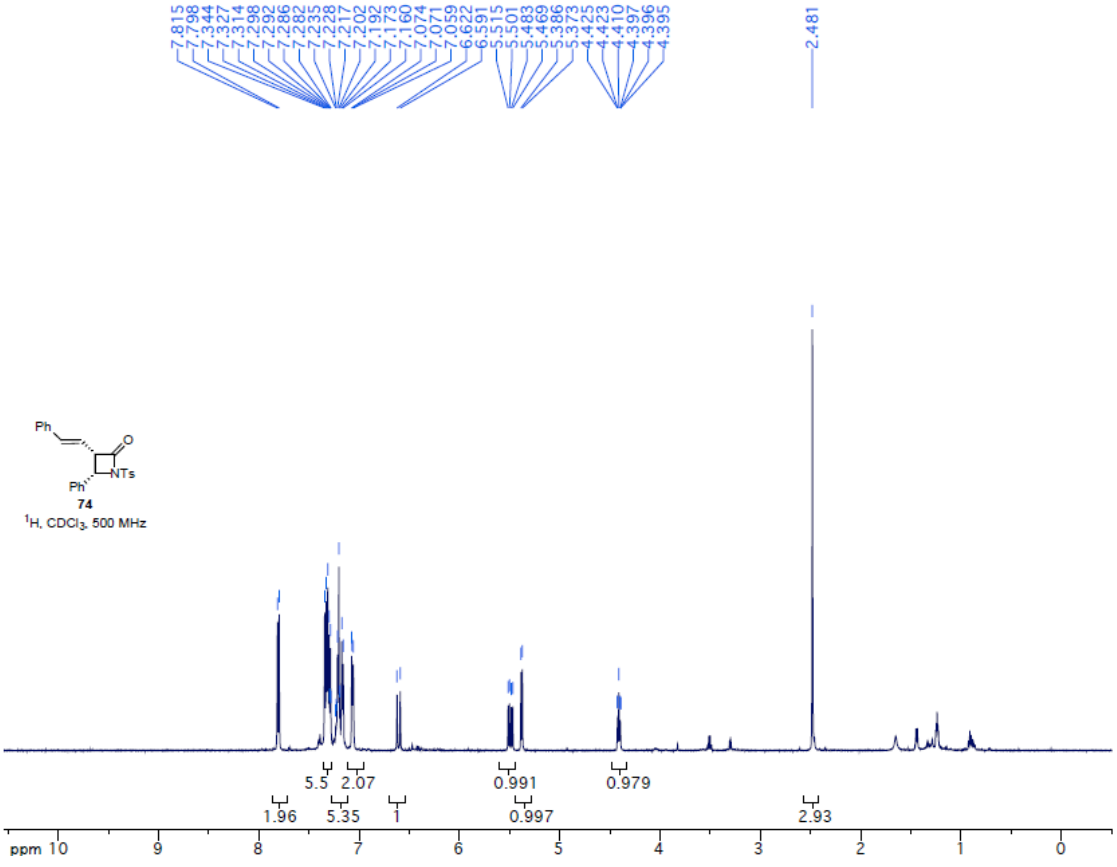

172.002
168.810
148.012
132.959
131.383
129.549
129.008
127.584
121.713
114.694
77.413
77.328
77.158
76.903
69.257
66.794
14.885
Ph
NH
PhN
O
O
HO
Me
49
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0

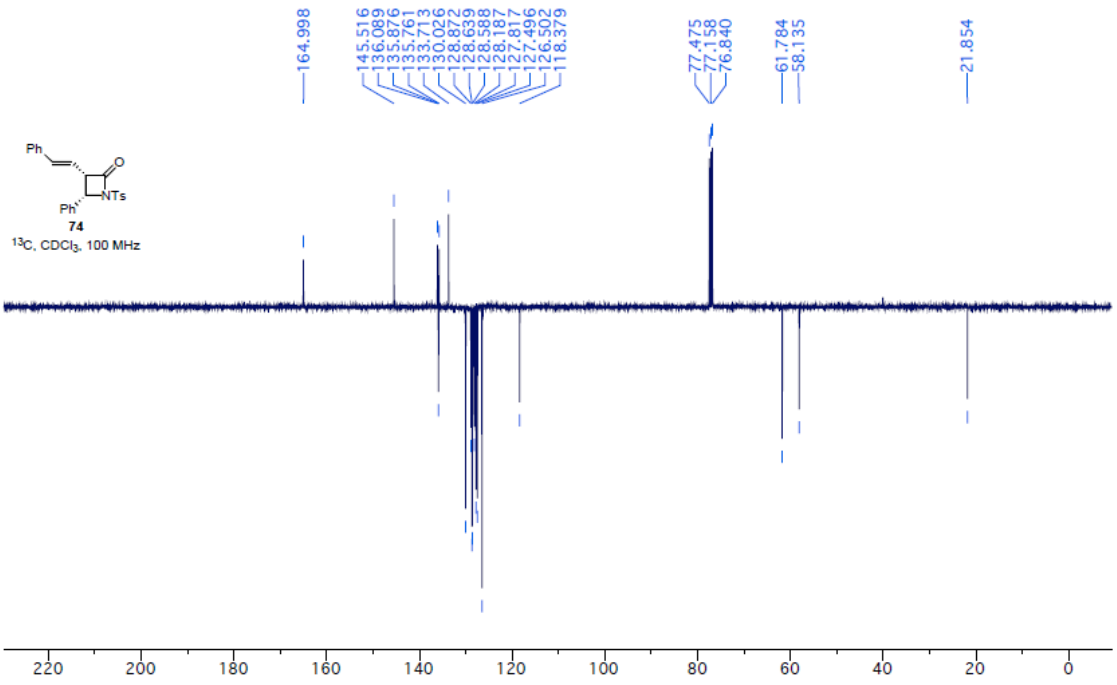

8.915
7.905
7.891
7.888
7.618
7.615
7.613
7.600
7.588
7.585
7.583
7.512
7.496
7.484
7.481
7.319
7.314
7.312
7.304
7.301
7.297
7.290
7.286
7.282
7.260
6.980
6.966
6.951
6.887
6.871
4.954
4.762
4.753
4.649
4.643
4.642
4.639
4.637
4.636
4.629
4.625
4.617
4.610
1.511
1.498
Ph
NH
PhN
O
HO
Me
50
1H, CDCl3, 500 MHz
2.04
2.07
1.01
0.966
2.12
1
1.04
2.01
2.09
1.03
3.11
ppm 10
9
8
7
6
5
4
3
2
1
0

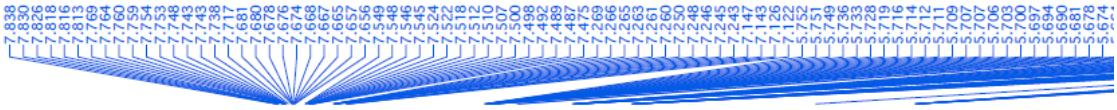

172.044
168.894
147.270
133.066
131.399
129.799
129.065
127.612
121.470
113.027
79.412
77.412
77.158
76.903
70.256
67.770
13.916
Ph
NH
PhN
O
HO
Me
50
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0

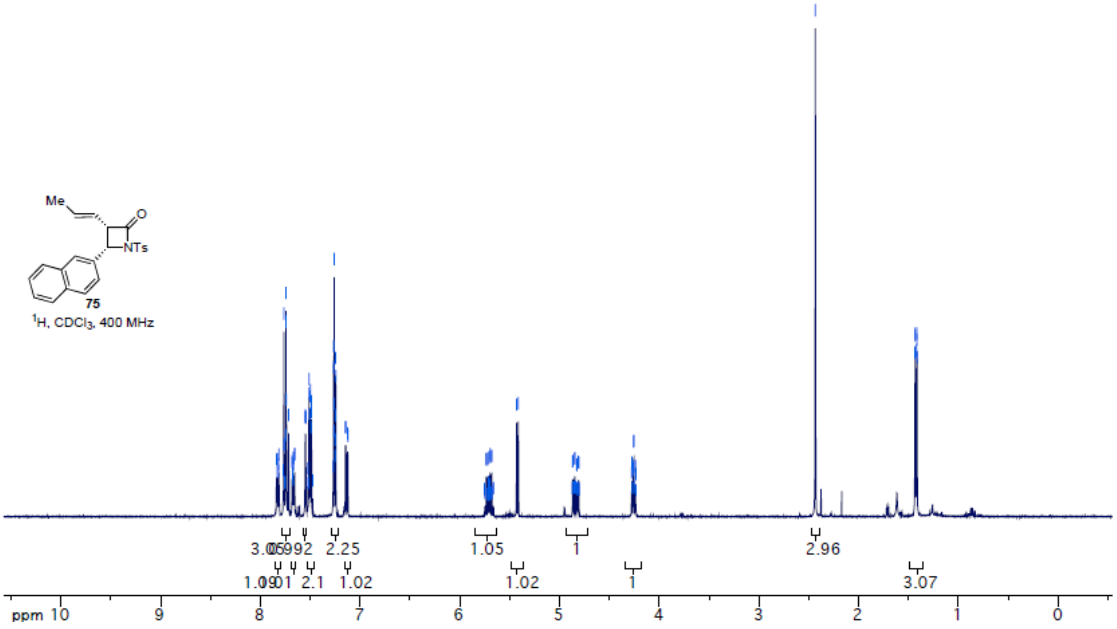

7.502
7.486
7.480
7.457
7.417
7.417
7.411
7.410
7.405
7.391
7.378
7.366
7.341
7.340
7.261
6.883
6.882
6.830
6.465
6.464
6.461
6.460
6.454
6.436
6.435
6.431
6.430
6.429
6.426
6.424
6.423
6.420
6.412
6.410
6.409
6.407
6.404
6.383
6.381
6.378
4.787
4.758
Ph
Ph
O
O
CF3
73
1H, CDCl3, 400 MHz
9.29
1
1.03
1.07
ppm 10
9
8
7
6
5
4
3
2
1
0

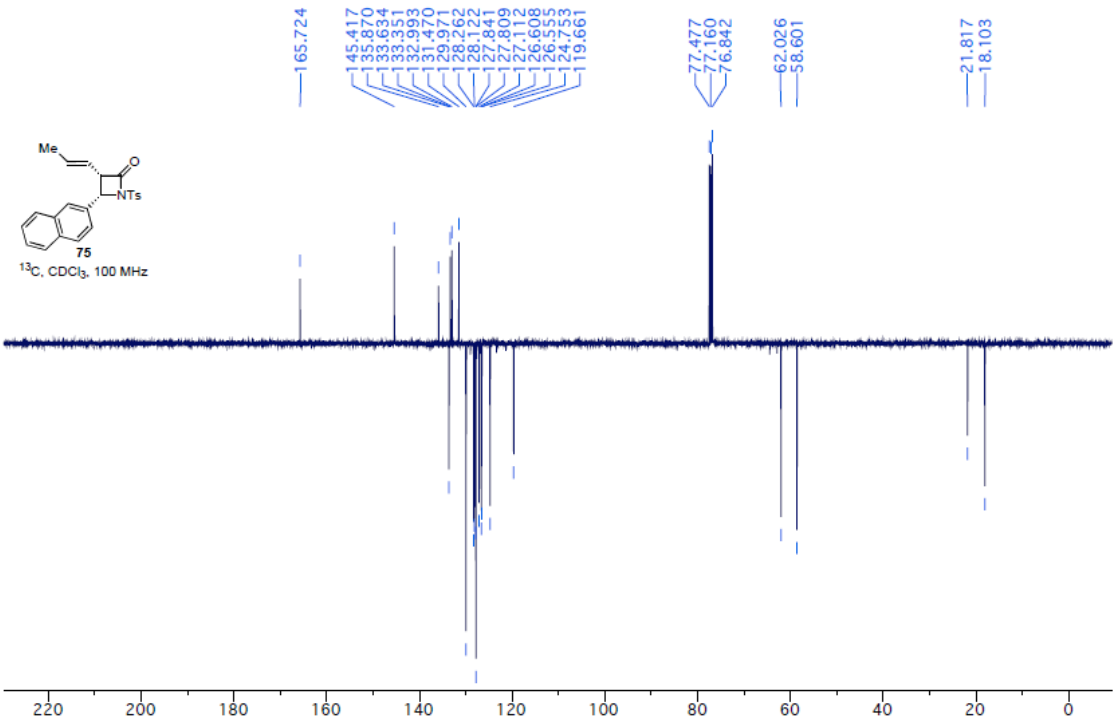

165.862
139.024
135.429
132.930
130.164
129.138
128.947
128.931
127.558
127.074
126.287
124.748
121.936
119.129
115.146
115.133
80.060
79.797
79.496
79.181
77.474
77.156
76.838
64.928
Ph
Ph
O
O
CF3
73
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

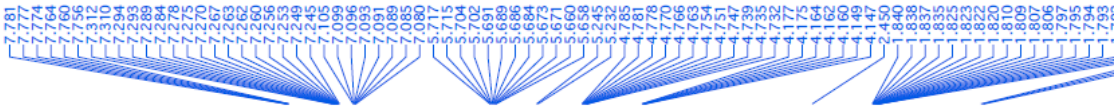

7.815
7.798
7.344
7.327
7.314
7.298
7.292
7.286
7.282
7.235
7.228
7.217
7.202
7.192
7.173
7.160
7.074
7.071
7.059
6.622
6.591
5.515
5.501
5.483
5.469
5.386
5.373
4.425
4.423
4.410
4.397
4.396
4.395
2.481
Ph
O
NTs
Ph
74
1H, CDCl3, 500 MHz
5.5
2.07
0.991
0.979
1.96
5.35
1
0.997
2.93
ppm 10
9
8
7
6
5
4
3
2
1
0

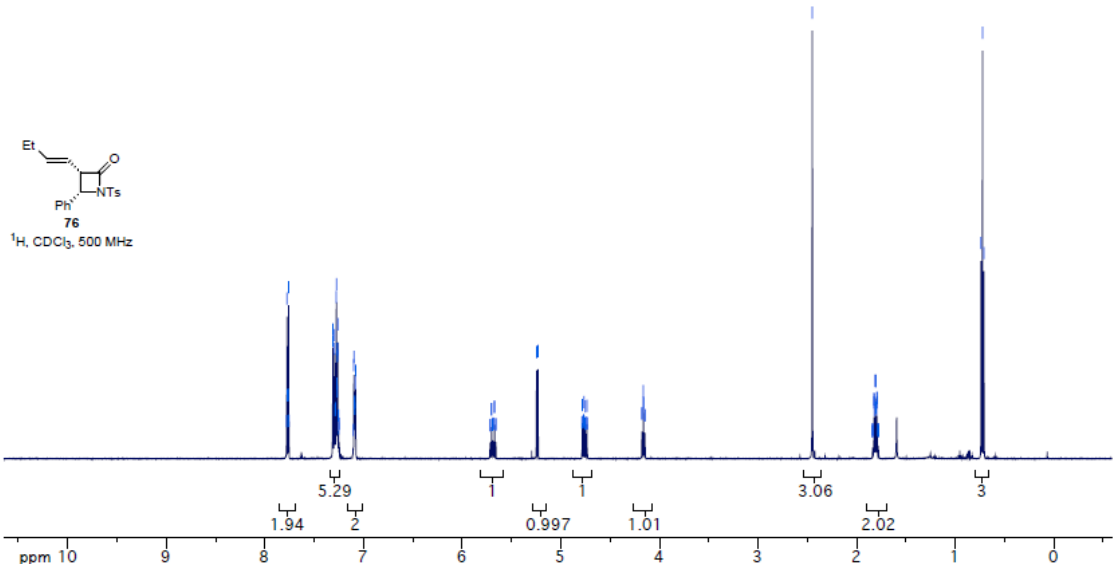

164.998
145.516
136.089
135.876
135.761
133.713
130.026
128.872
128.639
128.588
128.187
127.817
127.496
126.502
118.379
77.475
77.158
76.840
61.784
58.135
21.854
Ph
O
NTs
Ph
74
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

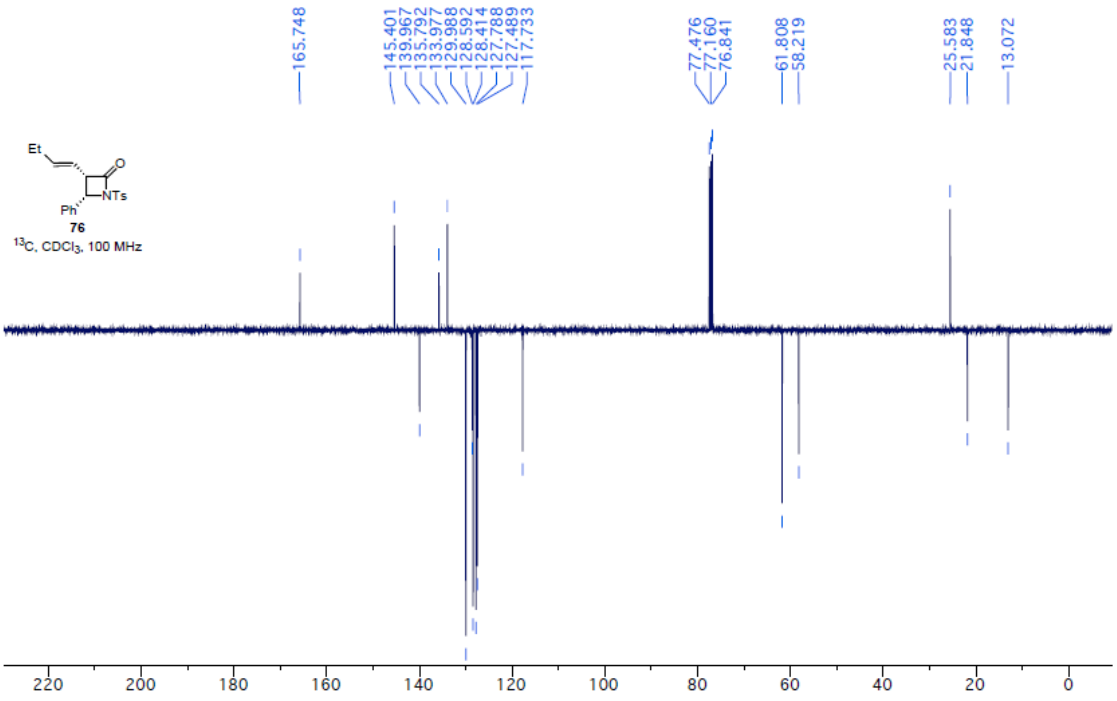


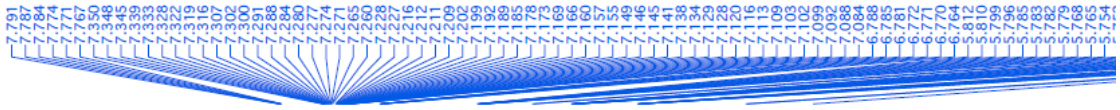

Me
O
NTs
75
1H, CDCl3, 400 MHz
3.06
1.09
1.01
2.1
2.25
1.02
1.05
1.02
1
1
2.96
3.07
ppm 10
9
8
7
6
5
4
3
2
1
0

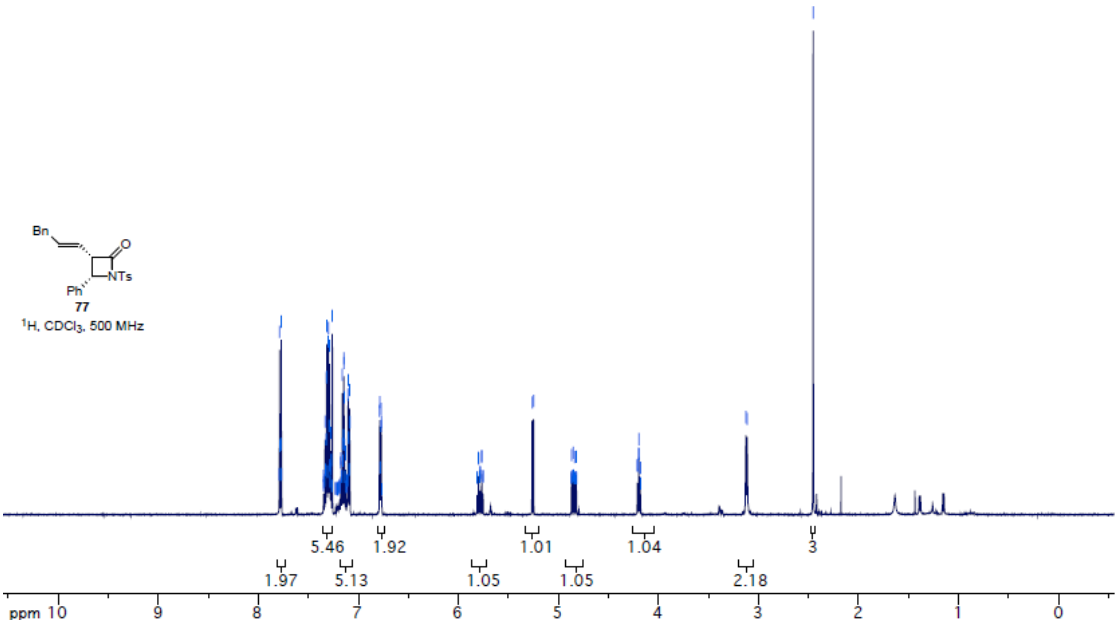

165.724
145.417
135.870
133.634
133.351
132.993
131.470
129.971
128.262
128.122
127.841
127.809
127.112
126.608
126.555
124.753
119.661
77.477
77.160
76.842
62.026
58.601
21.817
18.103
Me
O
NTs
75
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

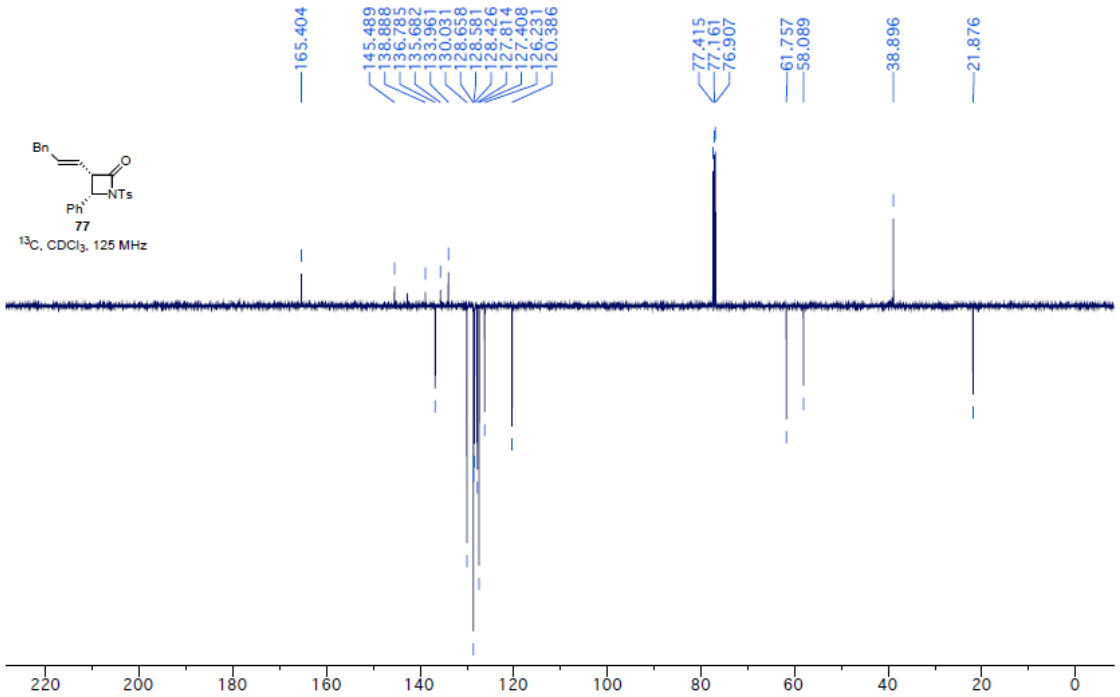

7.781
7.777
7.774
7.764
7.760
7.756
7.312
7.310
7.294
7.293
7.289
7.284
7.278
7.275
7.270
7.267
7.263
7.262
7.260
7.256
7.253
7.249
7.245
7.105
7.099
7.096
7.093
7.091
7.089
7.085
7.080
5.717
5.715
5.704
5.702
5.691
5.689
5.686
5.684
5.673
5.671
5.660
5.658
5.245
5.232
4.785
4.781
4.778
4.770
4.766
4.763
4.754
4.751
4.747
4.739
4.735
4.732
4.177
4.175
4.164
4.162
4.160
4.149
4.147
2.450
1.840
1.838
1.837
1.835
1.825
1.823
1.822
1.820
1.810
1.809
1.807
1.806
1.797
1.795
1.794
1.793

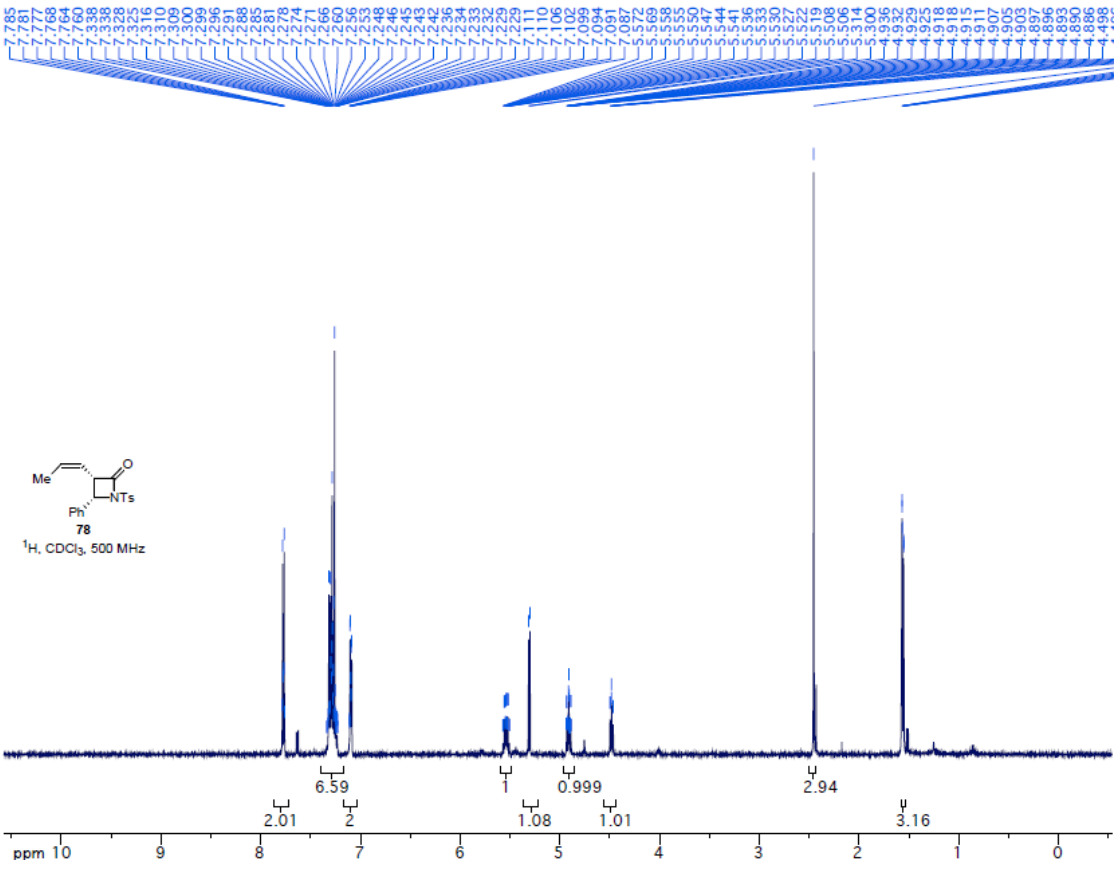

Et
O
NTs
Ph
76
1H, CDCl3, 500 MHz
5.29
1
1
3.06
3
1.94
2
0.997
1.01
2.02
ppm 10
9
8
7
6
5
4
3
2
1
0

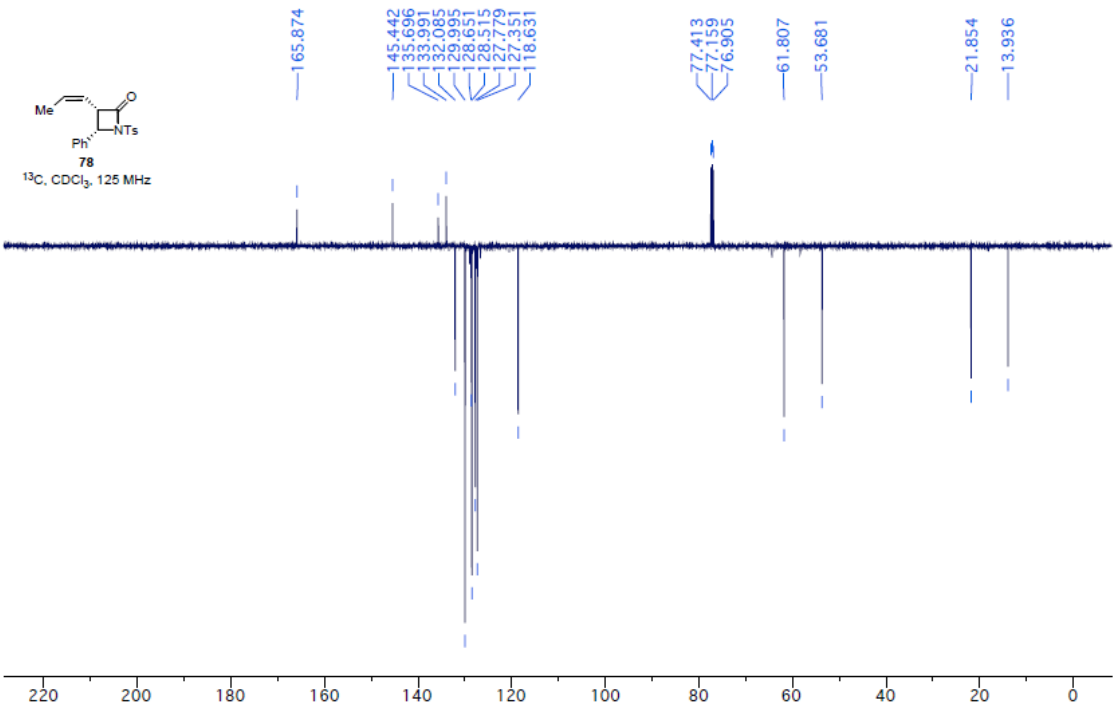

165.748
145.401
139.967
135.792
133.977
129.988
128.592
128.414
127.788
127.489
117.733
77.476
77.160
76.841
61.808
58.219
25.583
21.848
13.072
Et
O
NTs
Ph
76
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

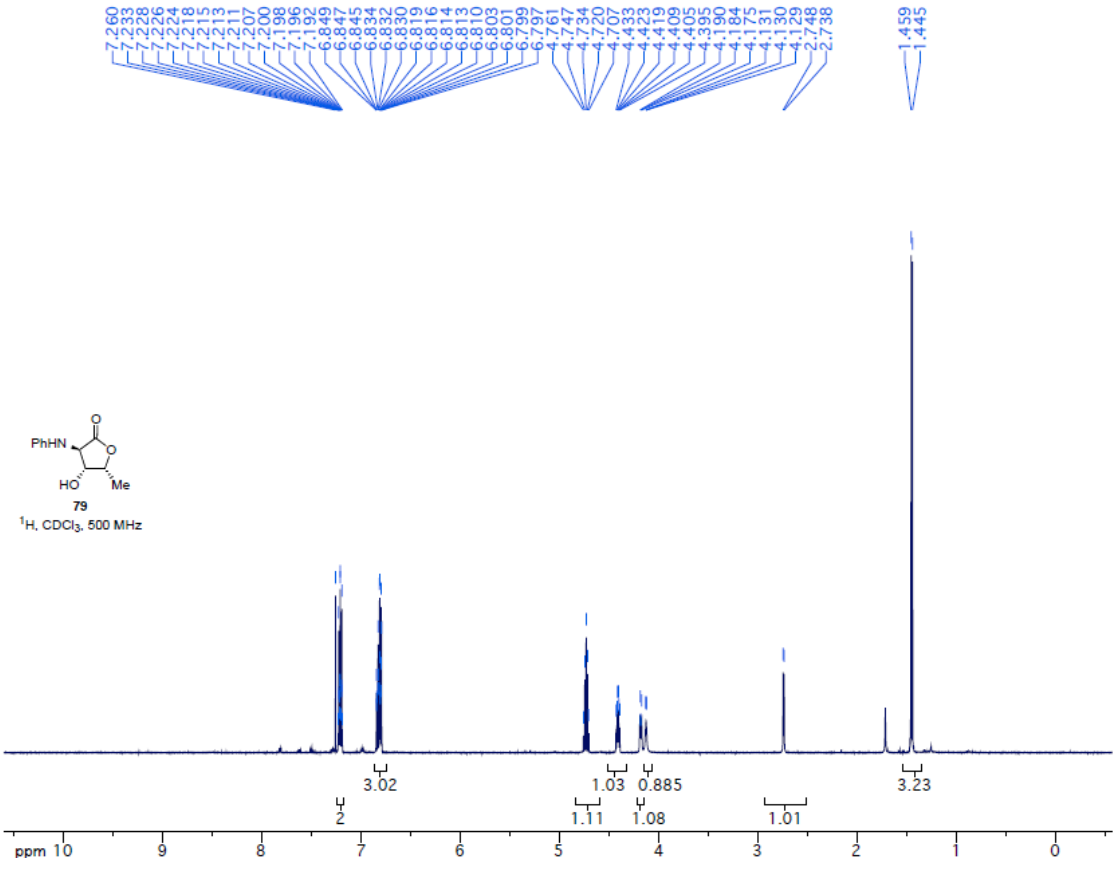


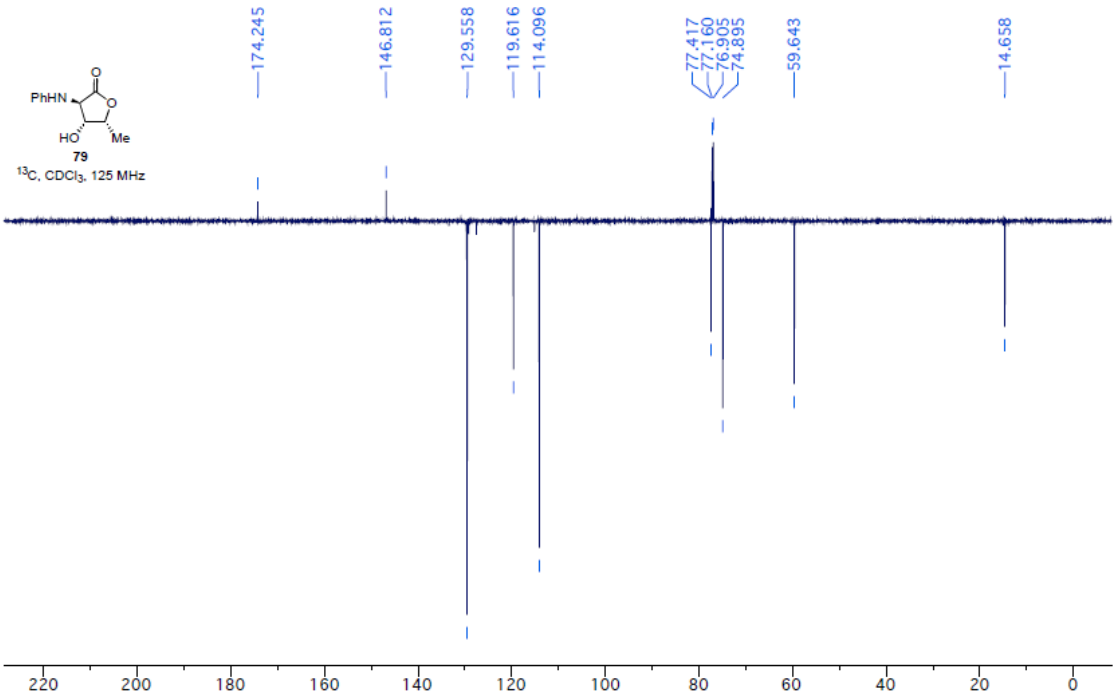

Bn
O
NTs
Ph
77
^{1}H, CDCl$_3$, 500 MHz
5.46
1.92
1.01
1.04
3
1.97
5.13
1.05
1.05
2.18
ppm 10
9
8
7
6
5
4
3
2
1
0

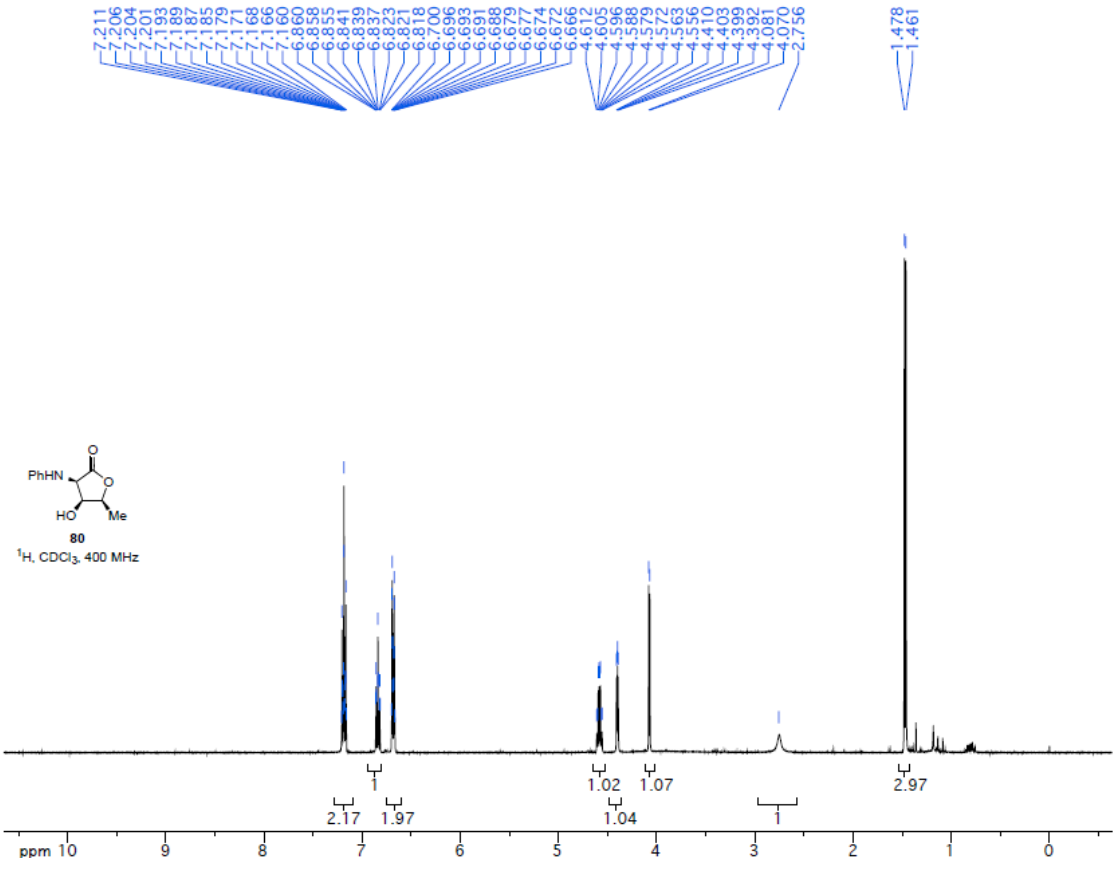

165.404
145.489
138.888
136.785
135.682
133.961
130.031
128.658
128.581
128.426
127.814
127.408
126.231
120.386
77.415
77.161
76.907
61.757
58.089
38.896
21.876
Bn
O
NTs
Ph
77
^{13}C, CDCl$_3$, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0

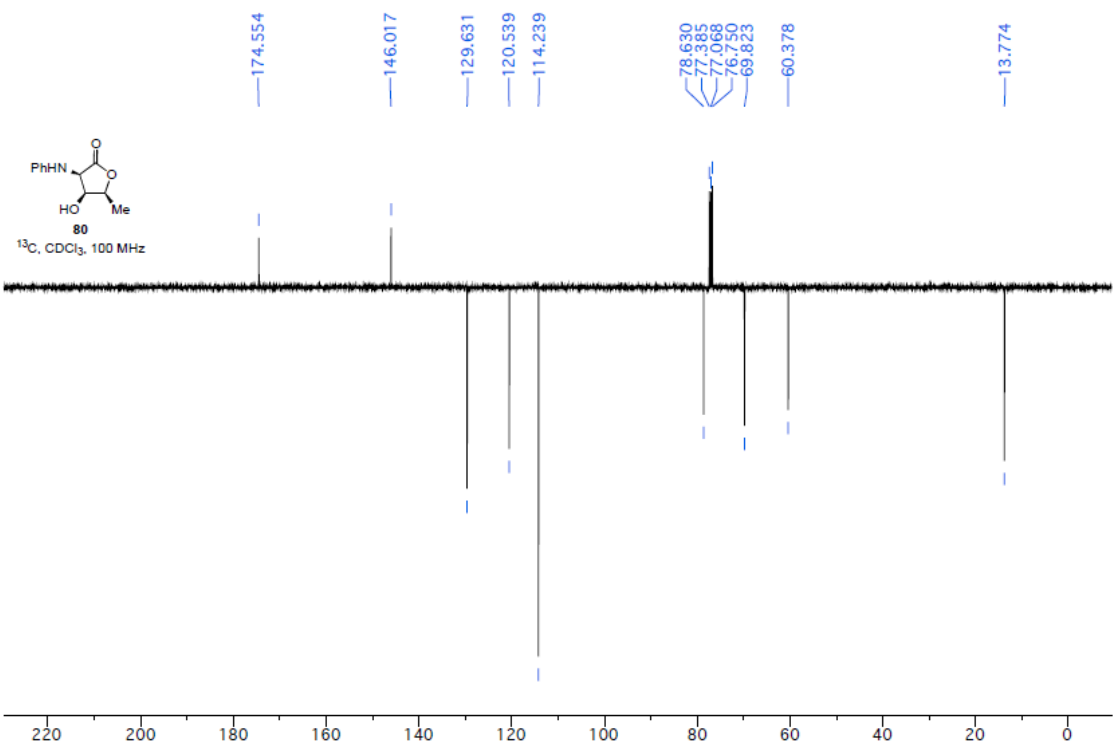

7.785
7.781
7.777
7.768
7.764
7.760
7.338
7.328
7.325
7.316
7.310
7.309
7.300
7.299
7.296
7.291
7.288
7.285
7.281
7.278
7.274
7.271
7.266
7.260
7.256
7.253
7.248
7.246
7.245
7.243
7.242
7.236
7.234
7.233
7.232
7.229
7.229
7.111
7.110
7.106
7.102
7.099
7.094
7.091
7.087
5.572
5.569
5.558
5.555
5.550
5.547
5.544
5.541
5.536
5.533
5.530
5.527
5.522
5.519
5.508
5.506
5.314
5.300
4.936
4.932
4.929
4.925
4.918
4.915
4.911
4.907
4.905
4.903
4.897
4.896
4.893
4.890
4.886
4.498
Me
O
NTs
Ph
78
1H, CDCl3, 500 MHz
6.59
1
0.999
2.94
2.01
2
1.08
1.01
3.16
ppm 10
9
8
7
6
5
4
3
2
1
0


165.874
145.442
135.696
133.991
132.085
129.995
128.651
128.515
127.779
127.351
118.631
77.413
77.159
76.905
61.807
53.681
21.854
13.936
Me
O
NTs
Ph
78
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


7.260
7.233
7.228
7.226
7.224
7.218
7.215
7.213
7.211
7.207
7.200
7.198
7.196
7.192
6.849
6.847
6.845
6.834
6.832
6.830
6.819
6.816
6.814
6.813
6.810
6.803
6.801
6.799
6.797
4.761
4.747
4.734
4.720
4.707
4.433
4.423
4.419
4.409
4.405
4.395
4.190
4.184
4.175
4.131
4.130
4.129
2.748
2.738
1.459
1.445
PhHN
O
O
HO
Me
79
1H, CDCl3, 500 MHz
3.02
1.03
0.885
3.23
2
1.11
1.08
1.01
ppm 10
9
8
7
6
5
4
3
2
1
0

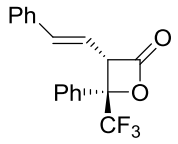

174.245
146.812
129.558
119.616
114.096
77.417
77.160
76.905
74.895
59.643
14.658
PhHN
O
O
HO
Me
79
13C, CDCl3, 125 MHz
220
200
180
160
140
120
100
80
60
40
20
0


7.211
7.206
7.204
7.201
7.193
7.189
7.187
7.185
7.179
7.171
7.168
7.166
7.160
6.860
6.858
6.855
6.841
6.839
6.837
6.823
6.821
6.818
6.700
6.696
6.693
6.691
6.688
6.679
6.677
6.674
6.672
6.666
4.612
4.605
4.596
4.588
4.579
4.572
4.563
4.556
4.410
4.403
4.399
4.392
4.081
4.070
2.756
1.478
1.461
PhHN
O
O
HO
Me
80
1H, CDCl3, 400 MHz
1
2.17
1.97
1.02
1.04
1.07
1
2.97
ppm 10
9
8
7
6
5
4
3
2
1
0


174.554
146.017
129.631
120.539
114.239
78.630
77.385
77.068
76.750
69.823
60.378
13.774
PhHN
O
O
HO
Me
80
13C, CDCl3, 100 MHz
220
200
180
160
140
120
100
80
60
40
20
0

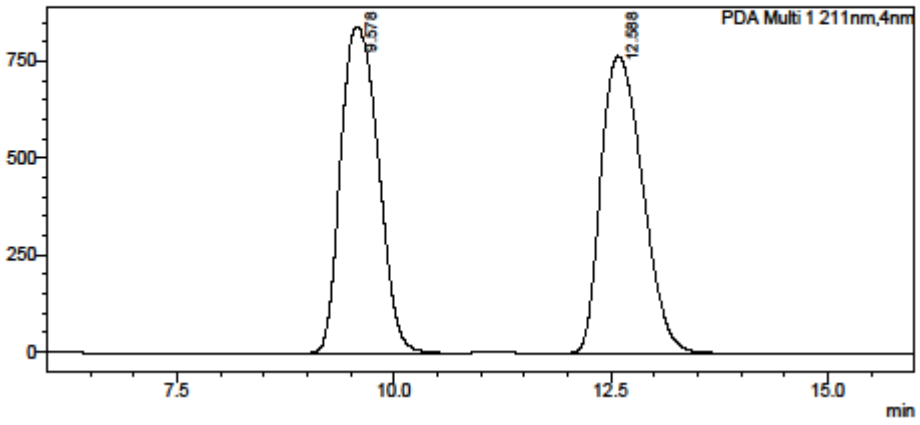
1.4 HPLC Traces

HPLC data compound **21**: Chiral HPLC Chiralcel OD-H (0.5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*R*,4*R*): 9.6 min, t_R(3*S*,4*S*): 12.6 min, 79% *ee* at rt.



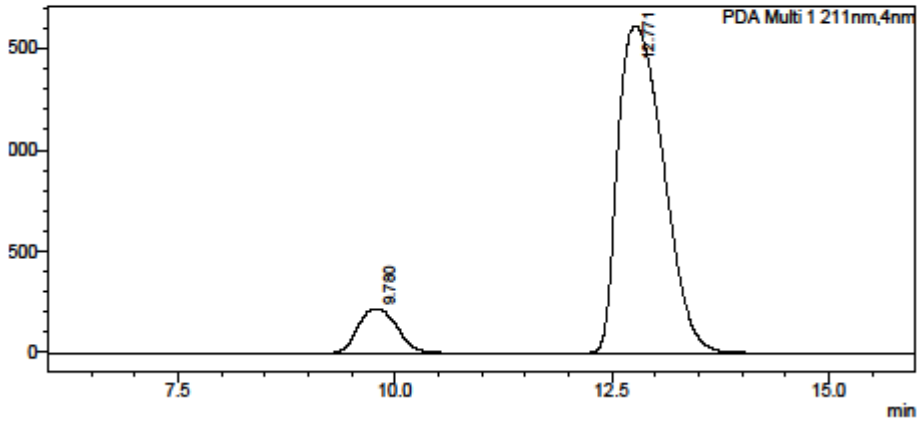
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.578	49.832
2	12.588	50.168
Total		100.000

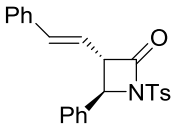


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.780	10.430
2	12.771	89.570
Total		100.000

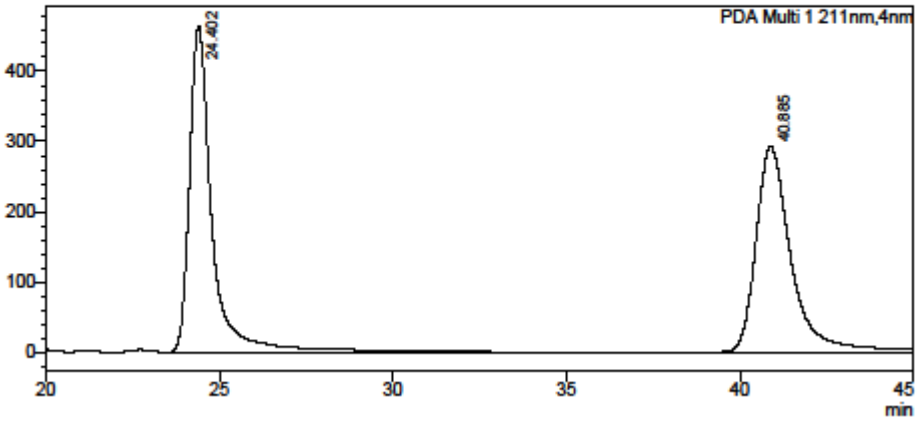


HPLC data compound **22**: HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 24.4 min, t_R(3*R*,4*S*): 40.9 min, 72% *ee* at rt.



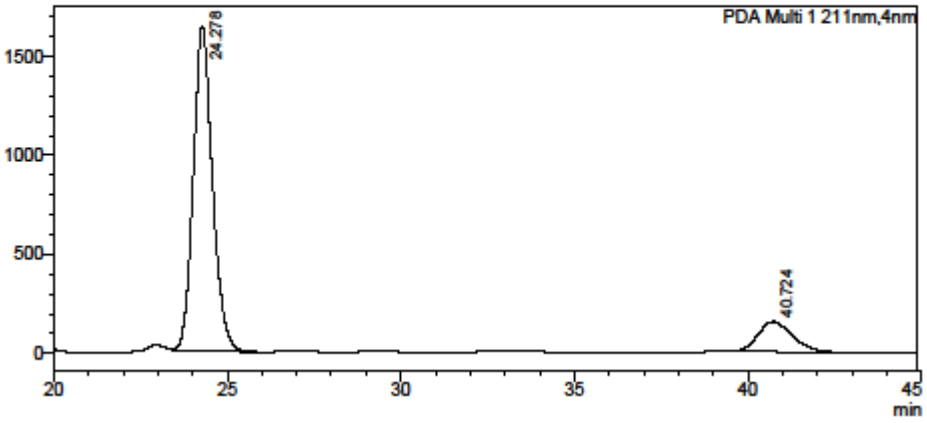
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	24.402	50.320
2	40.885	49.680
Total		100.000

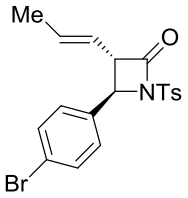


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	24.278	85.803
2	40.724	14.197
Total		100.000

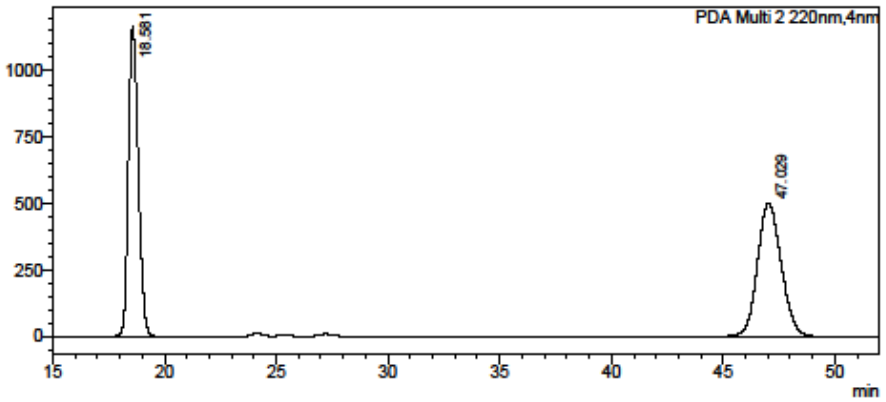


HPLC data compound **26**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(3*S*,4*R*): 18.6 min, t_R(3*R*,4*S*): 47.0 min, 79% *ee* at rt and 97% *ee* at -78 °C.



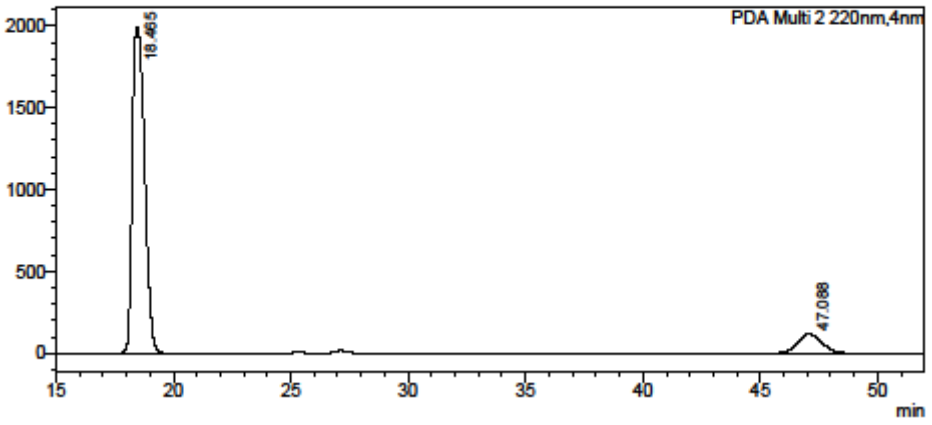
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	18.581	49.441
2	47.029	50.559
Total		100.000



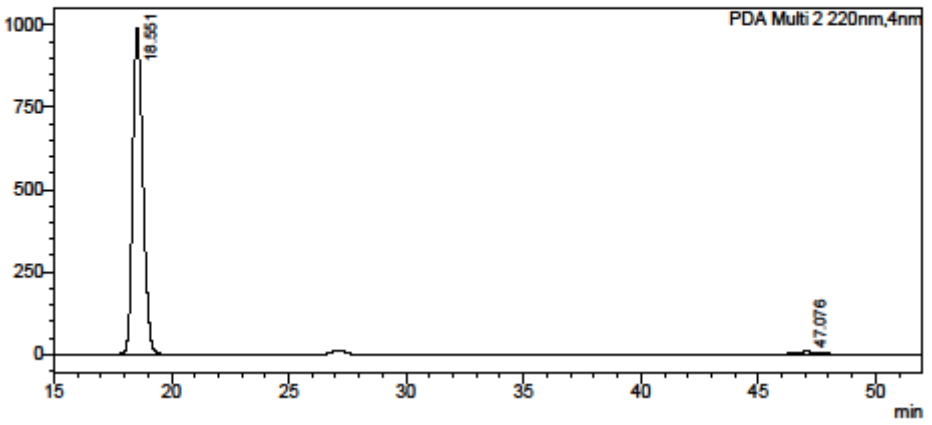
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	18.465	89.549
2	47.088	10.451
Total		100.000

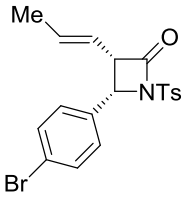


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	18.551	98.275
2	47.076	1.725
Total		100.000

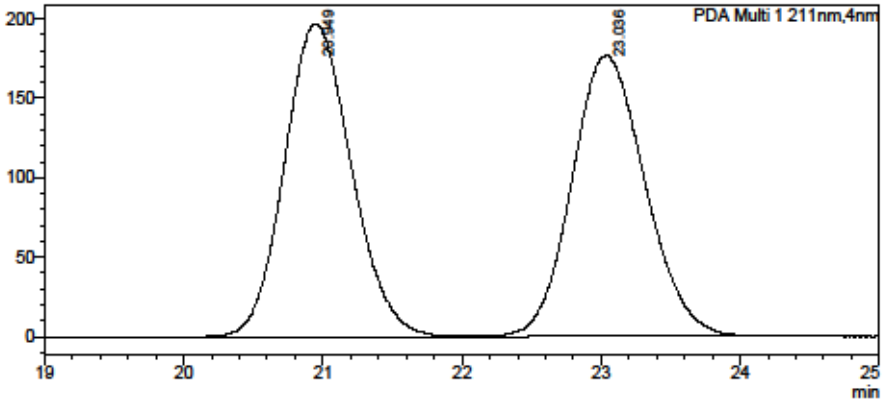


HPLC data compound **27**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 20.9 min, t_R(3*R*,4*R*): 23.0 min, 72% *ee* at rt and >99% *ee* at -78 °C



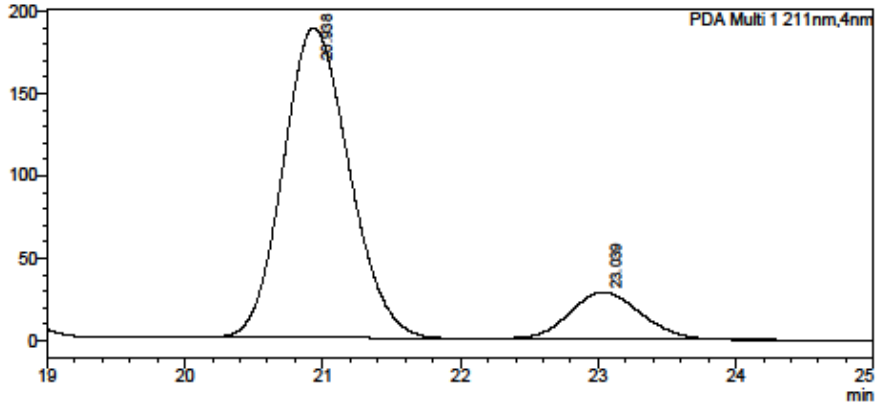
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.949	50.407
2	23.036	49.593
Total		100.000



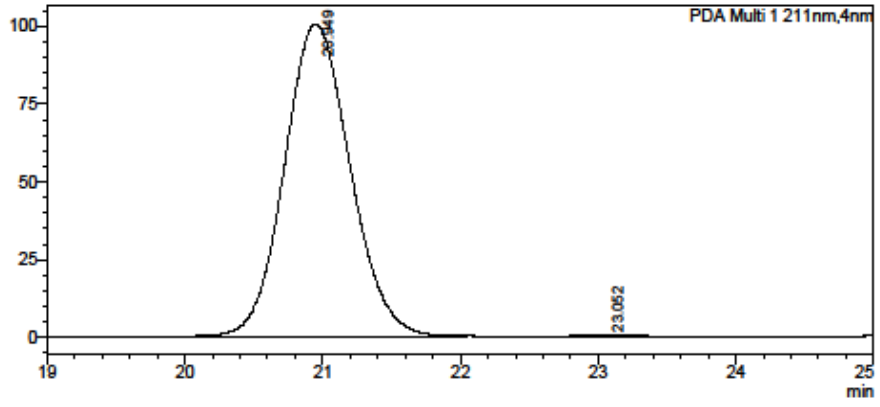
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.938	86.152
2	23.039	13.848
Total		100.000

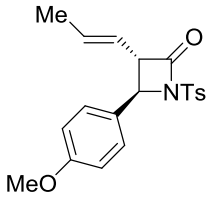


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.949	99.837
2	23.052	0.163
Total		100.000

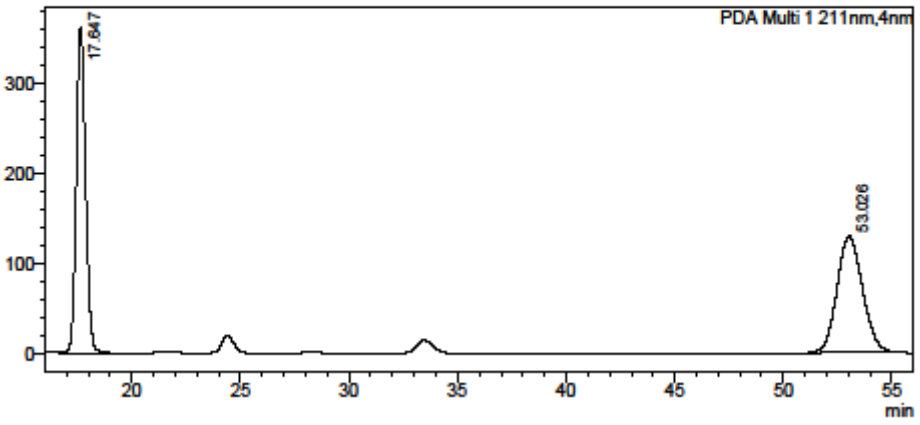


HPLC data compound **28**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 17.6 min, t_R(3*R*,4*S*): 53.0 min, 86% *ee*.



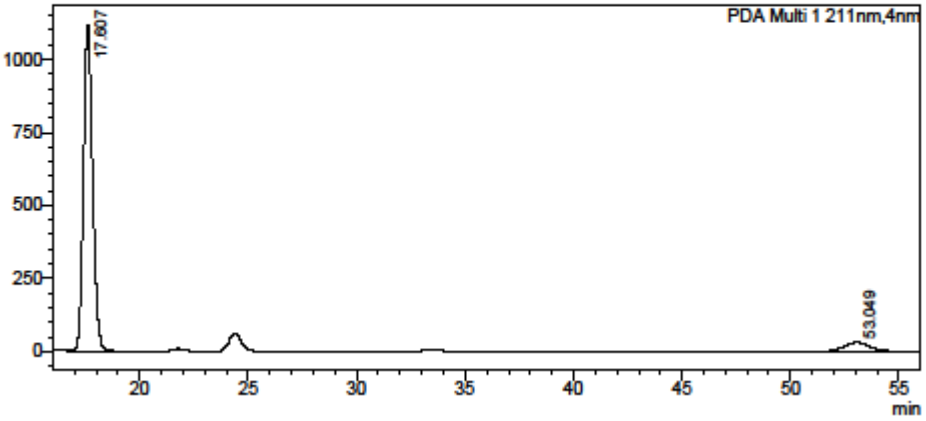
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.647	50.222
2	53.026	49.778
Total		100.000

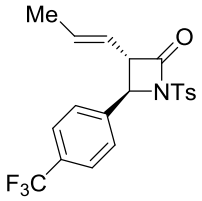


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.607	93.101
2	53.049	6.899
Total		100.000

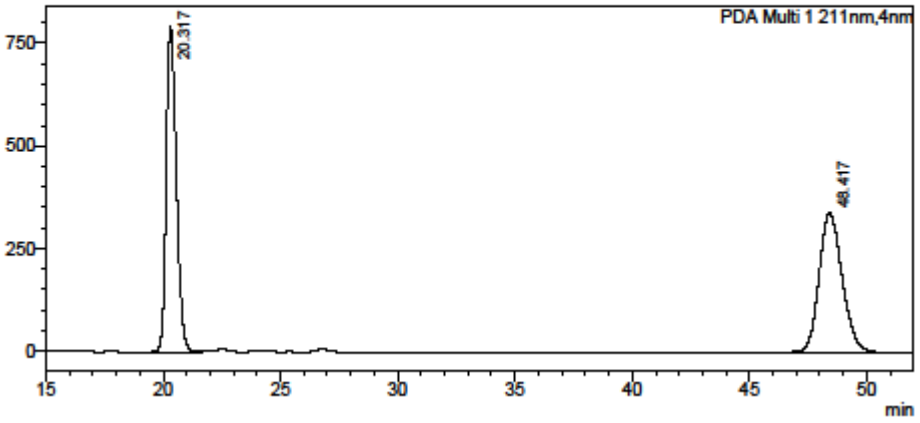


HPLC data compound **29**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 20.3 min, t_R(3*R*,4*S*): 48.4 min, 44% *ee* at rt.



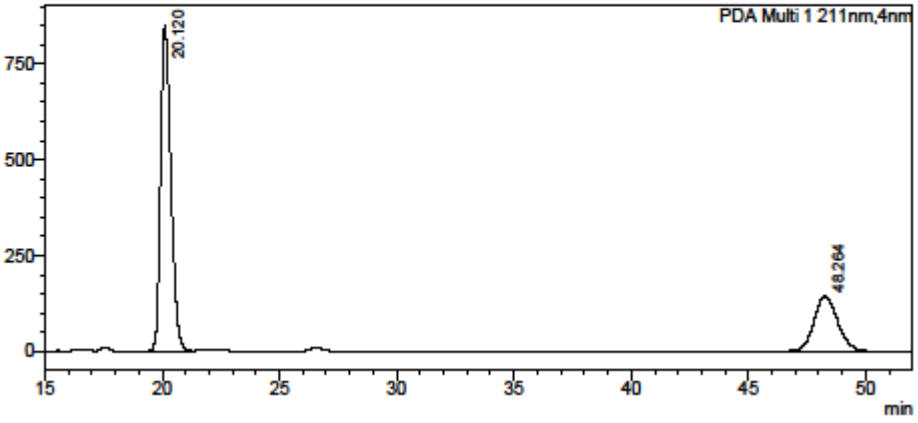
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.317	50.624
2	48.417	49.376
Total		100.000

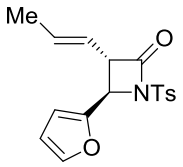


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	20.120	72.129
2	48.264	27.871
Total		100.000

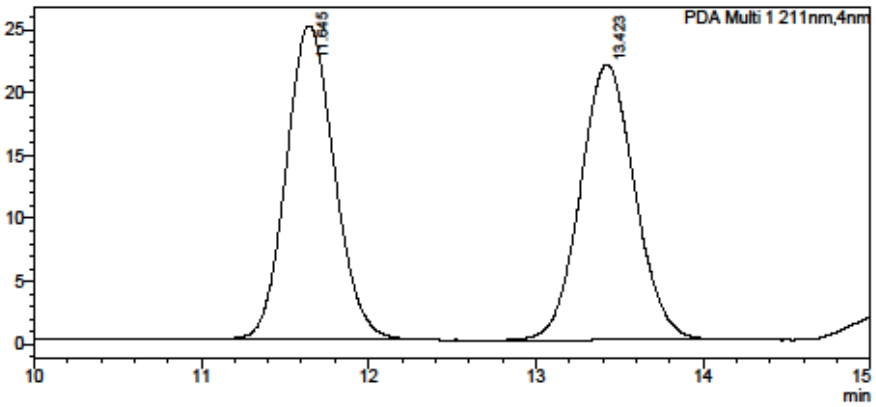


HPLC data compound **30**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 11.6 min, t_R(3*R*,4*S*): 13.4 min, 45% *ee* at rt and 95% *ee* at -78 °C



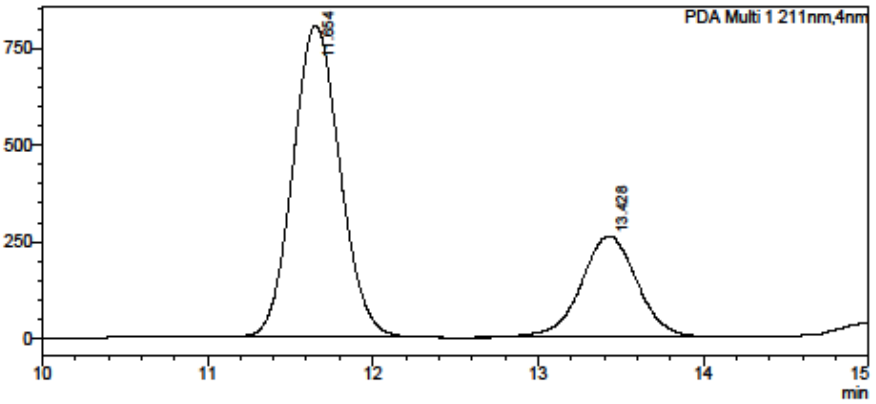
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.645	50.044
2	13.423	49.956
Total		100.000



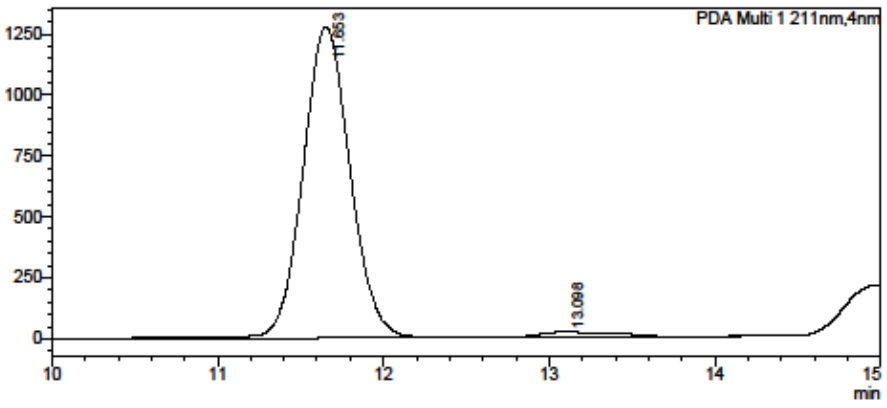
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.654	72.372
2	13.428	27.628
Total		100.000

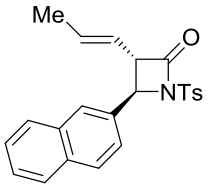


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.653	97.712
2	13.098	2.288
Total		100.000

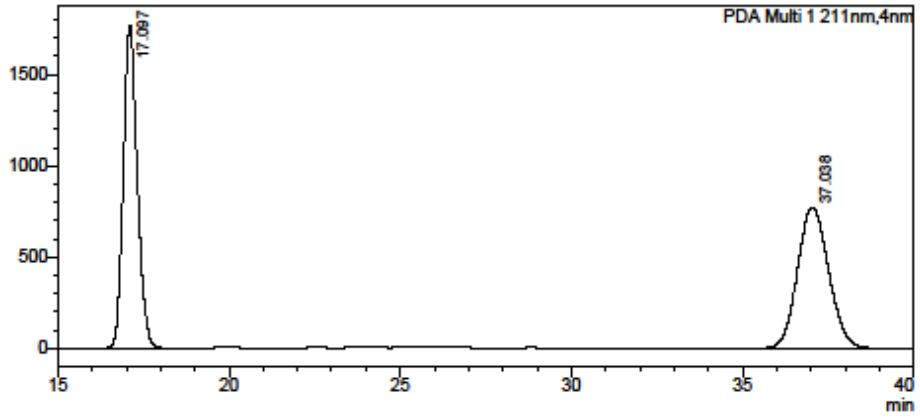


HPLC data compound **31**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 17.1 min, t_R(3*R*,4*S*): 37.0 min, 81% *ee* at rt and 97% *ee* at -78 °C



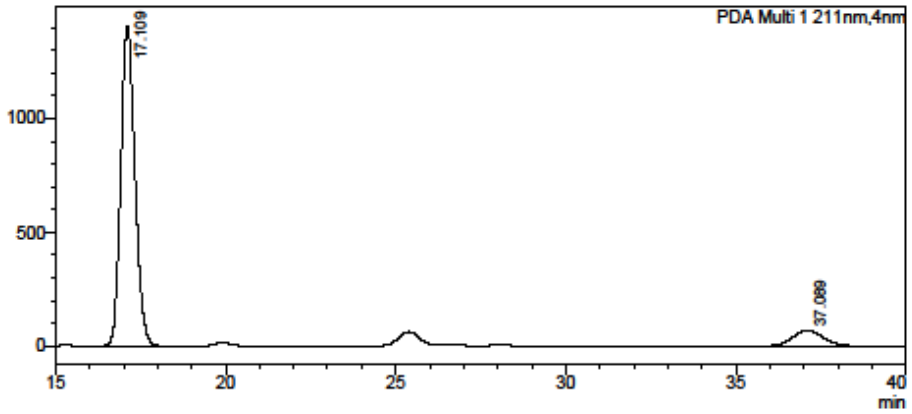
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.097	50.738
2	37.038	49.262
Total		100.000



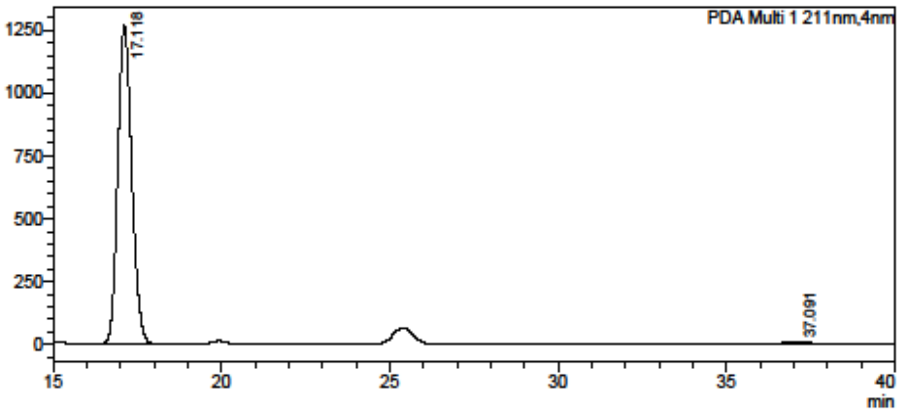
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.109	90.415
2	37.089	9.585
Total		100.000

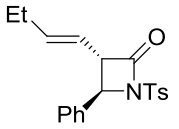


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.118	98.276
2	37.091	1.724
Total		100.000

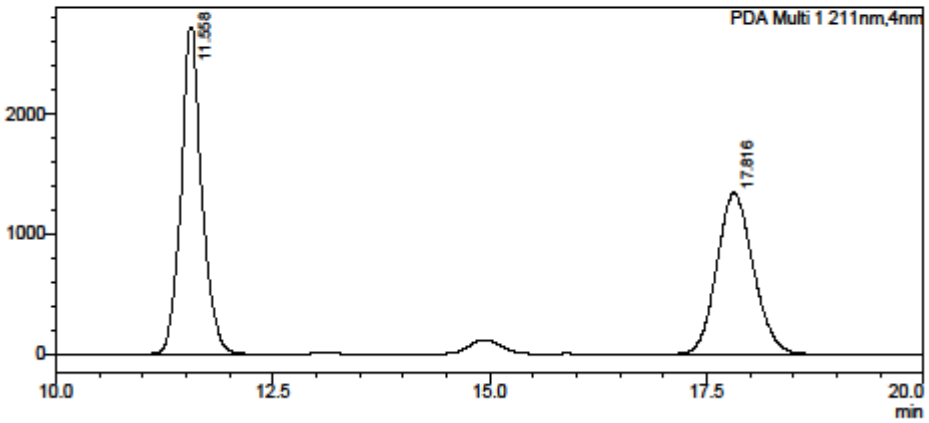


HPLC data compound **32**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 11.5 min, t_R(3*R*,4*S*): 17.8 min, 81% *ee* at rt and 98% *ee* at -78 °C.



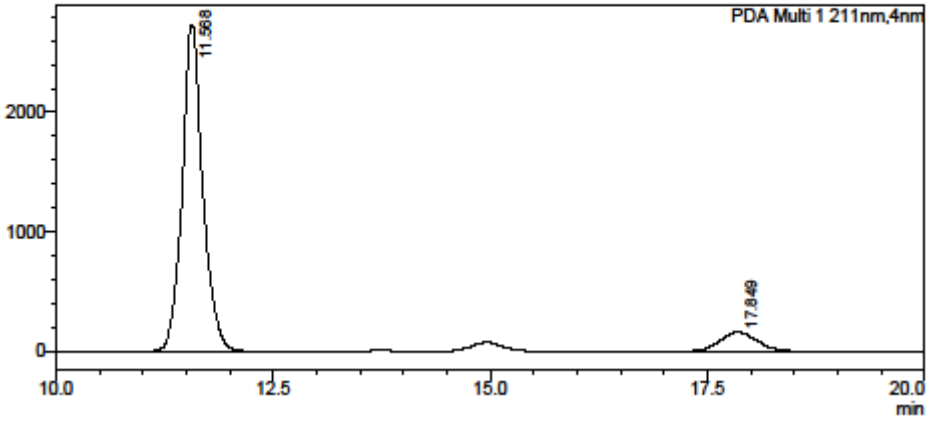
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.558	53.814
2	17.816	46.186
Total		100.000



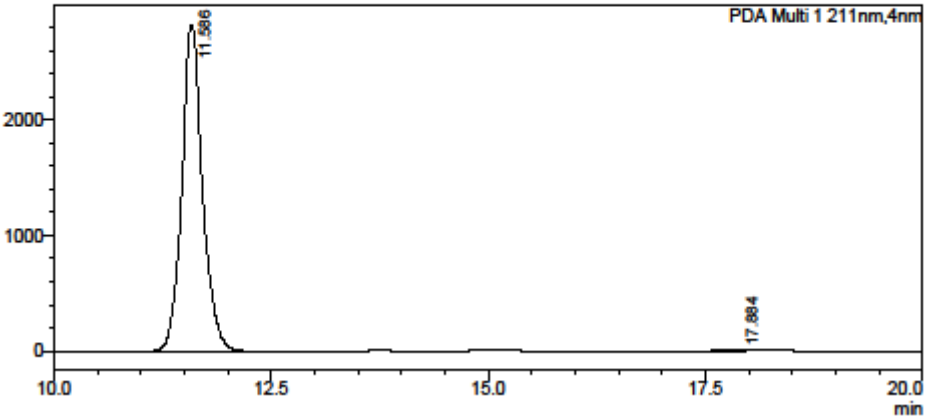
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.568	90.618
2	17.849	9.382
Total		100.000

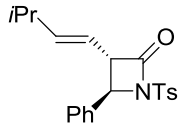


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.586	99.133
2	17.884	0.867
Total		100.000

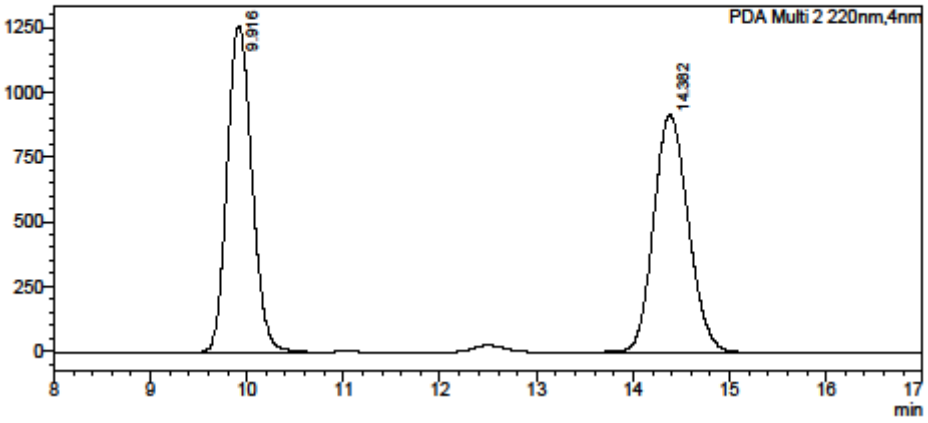


HPLC data compound **33**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(3*S*,4*R*): 9.9 min, t_R(3*R*,4*S*): 14.4 min, 82% *ee* at rt and 97% *ee* and -78 °C



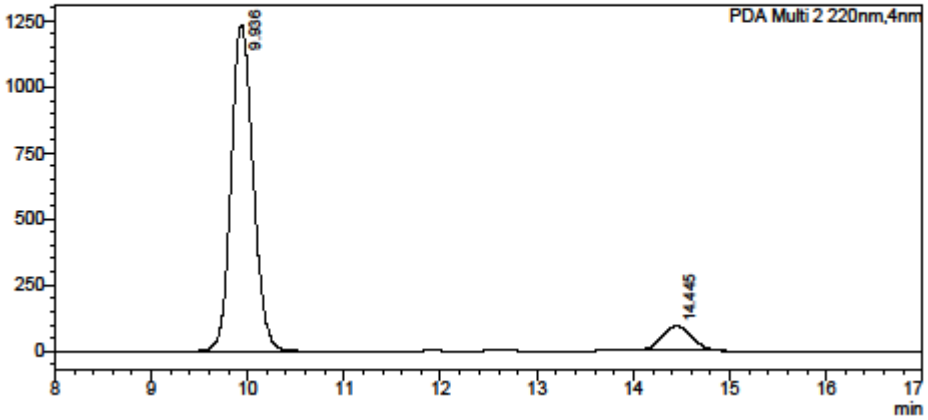
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	9.916	49.662
2	14.382	50.338
Total		100.000



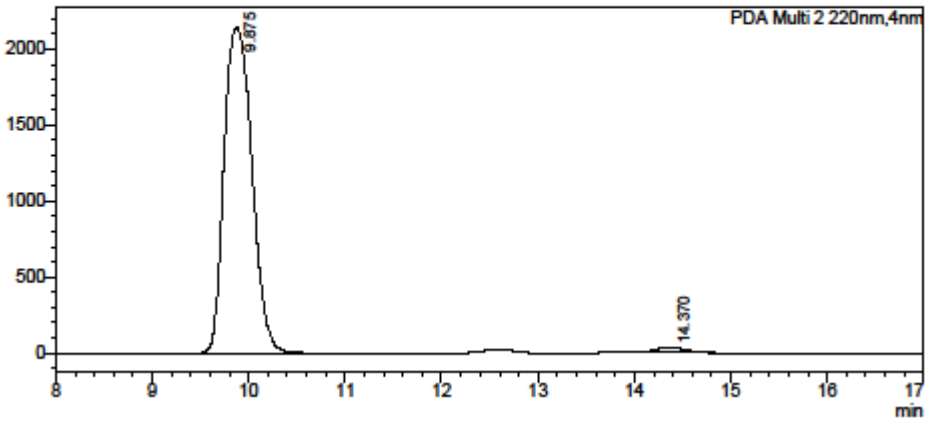
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	9.936	91.140
2	14.445	8.860
Total		100.000

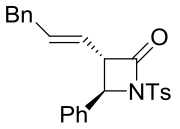


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	9.875	98.506
2	14.370	1.494
Total		100.000

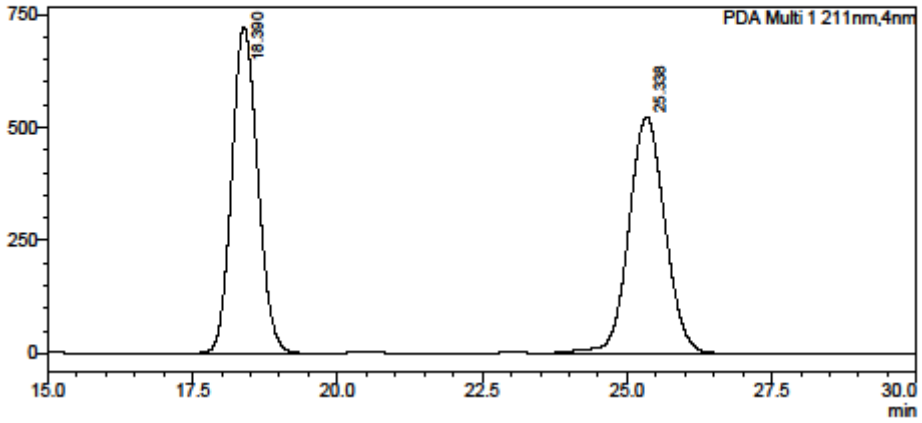


HPLC data compound **34**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*): 18.4 min, t_R(3*R*,4*S*): 25.3 min, 62% *ee* at rt and 95% *ee* at -78 °C



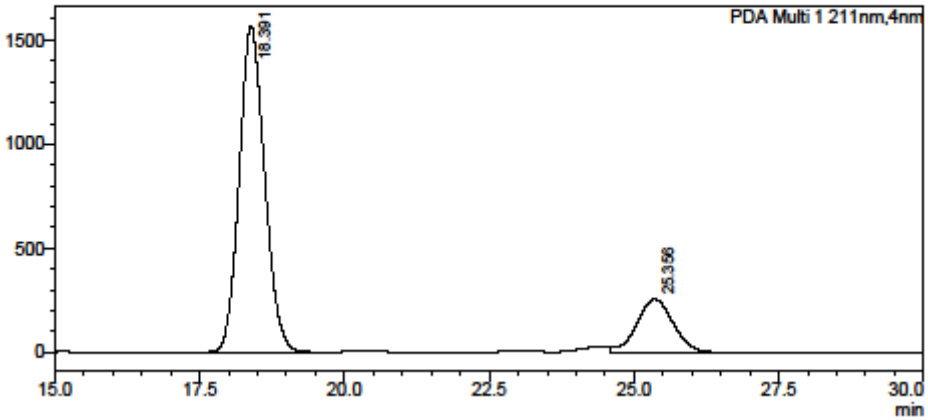
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	18.390	49.852
2	25.338	50.148
Total		100.000



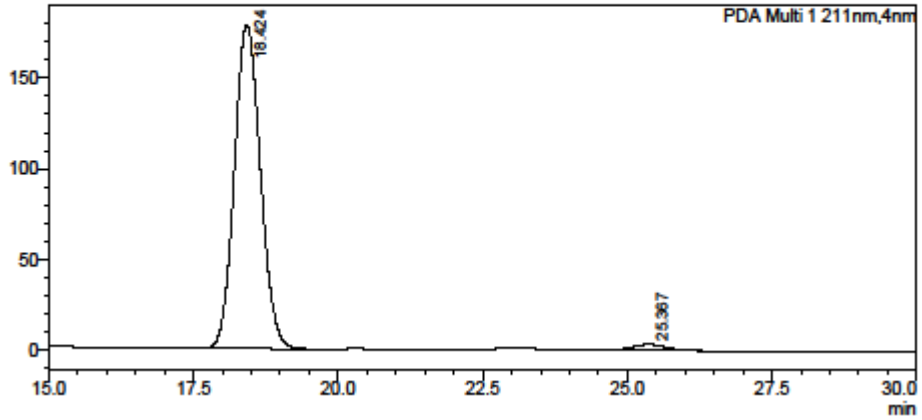
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	18.391	81.200
2	25.356	18.800
Total		100.000

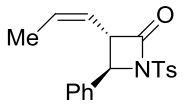


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	18.424	97.745
2	25.367	2.255
Total		100.000

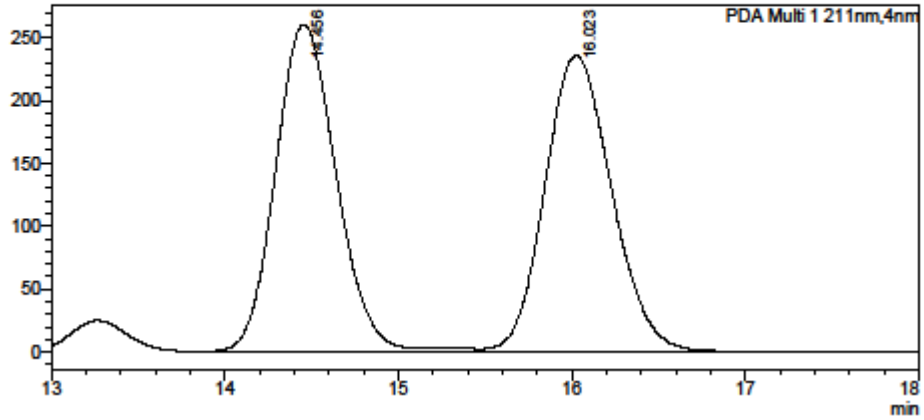


HPLC data compound **35**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*R*,4*S*): 14.5 min, t_R(3*S*,4*R*): 16.0 min, 92% *ee* at rt and 99% *ee* at -78 °C.



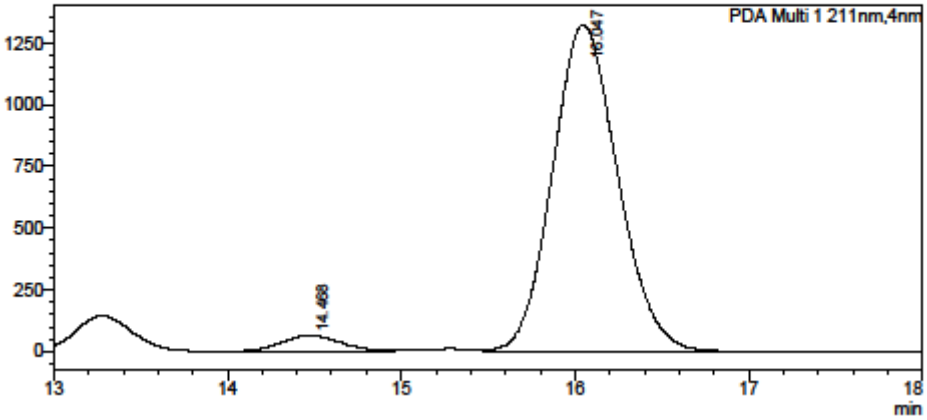
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.456	50.198
2	16.023	49.802
Total		100.000



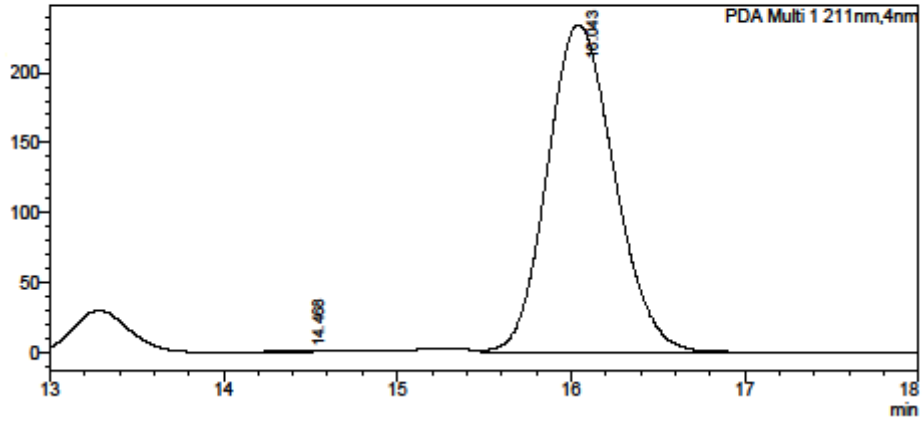
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.468	4.210
2	16.047	95.790
Total		100.000

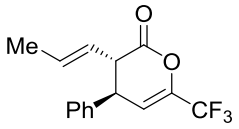


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.468	0.265
2	16.043	99.735
Total		100.000

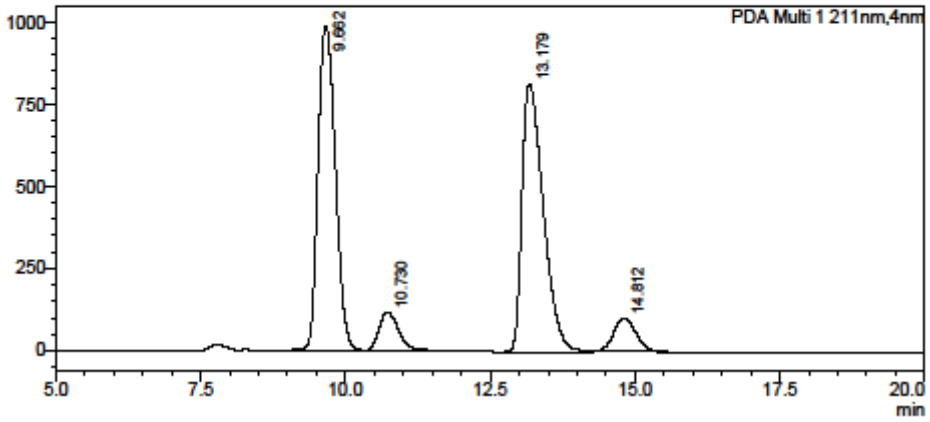


HPLC data compound **36**: Chiral HPLC Chiralpak Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer: t_R(3*S*,4*R*): 9.7 min, t_R(3*R*,4*S*): 13.2 min, 96% *ee*; minor diastereoisomer t_R: 10.7 min, t_R: 14.8 min, 15% *ee*.



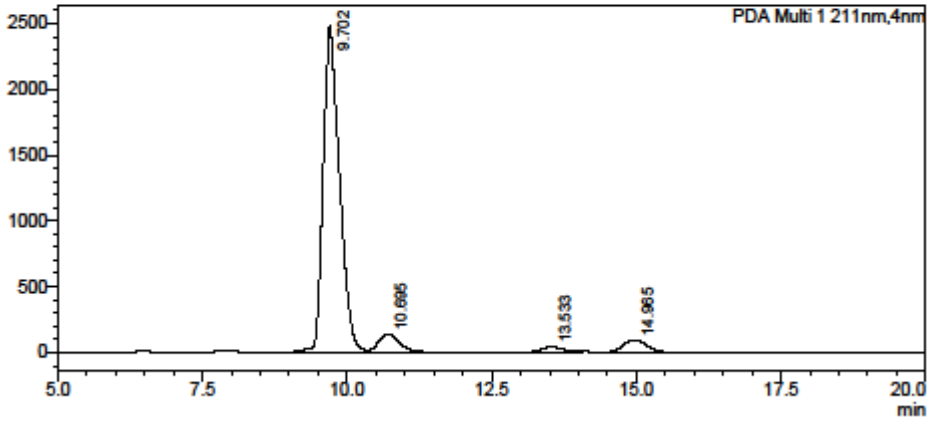
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.662	44.001
2	10.730	6.342
3	13.179	43.818
4	14.812	5.839
Total		100.000

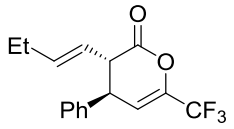


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.702	87.707
2	10.695	6.042
3	13.533	1.744
4	14.965	4.506
Total		100.000

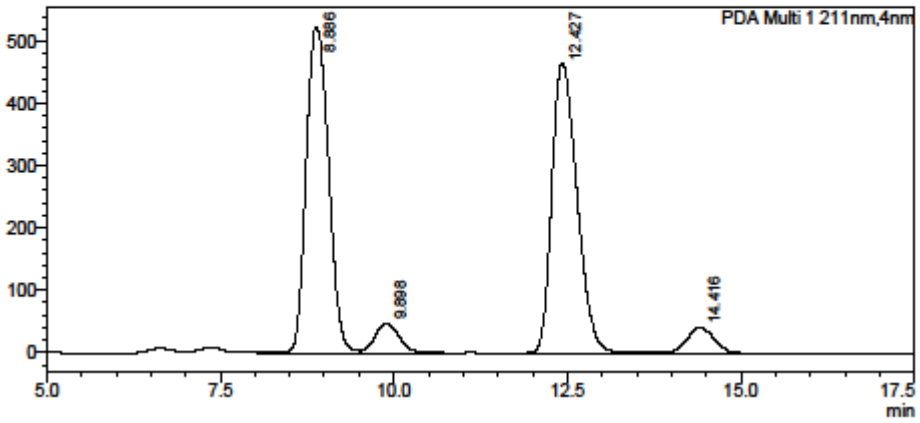


HPLC data compound **37**: Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer: t_R(3*S*,4*R*): 8.9 min, t_R(3*R*,4*S*): 12.4 min, 96% *ee*; minor diastereoisomer t_R: 9.9 min, t_R: 14.4 min, 12% *ee*.



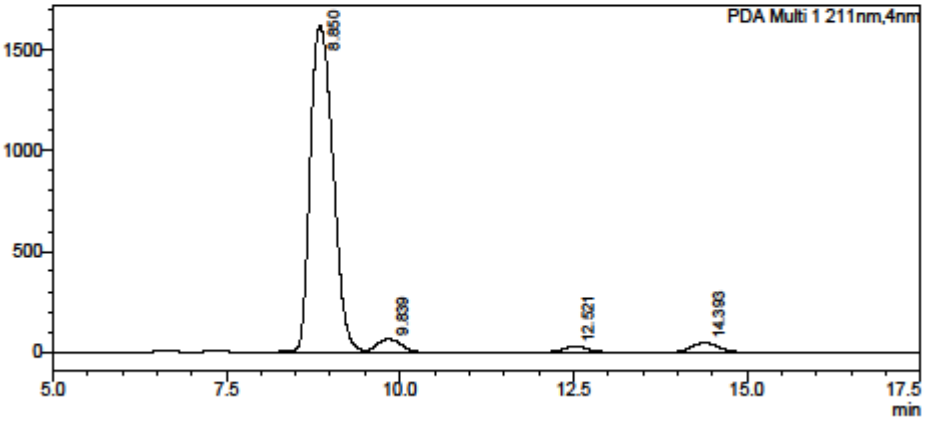
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	8.886	45.755
2	9.898	4.506
3	12.427	45.475
4	14.416	4.264
Total		100.000

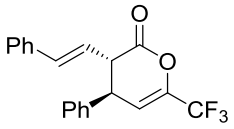


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	8.850	91.430
2	9.839	3.878
3	12.521	1.669
4	14.393	3.023
Total		100.000

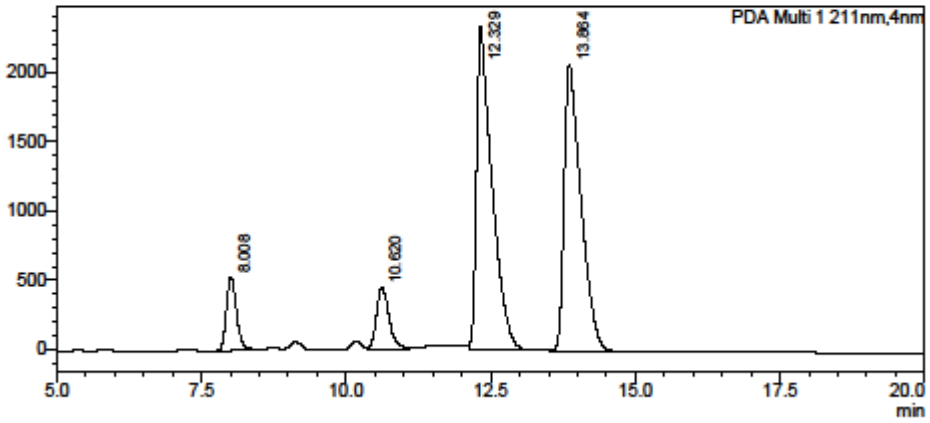


HPLC data compound **38**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer: t_R(3*R*,4*S*): 12.3 min, t_R(3*S*,4*R*): 13.9 min, 60% *ee*; minor diastereoisomer t_R: 8.00 min, t_R: 10.6 min, 52% *ee*.



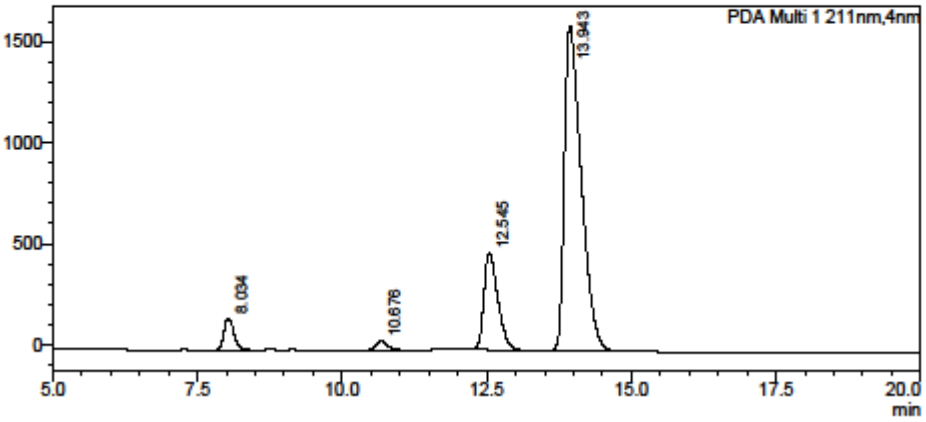
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	8.008	6.682
2	10.620	6.711
3	12.329	43.710
4	13.864	42.897
Total		100.000

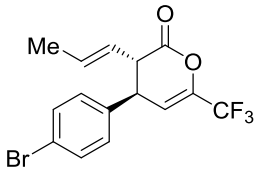


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	8.034	4.742
2	10.676	1.513
3	12.545	18.662
4	13.943	75.083
Total		100.000

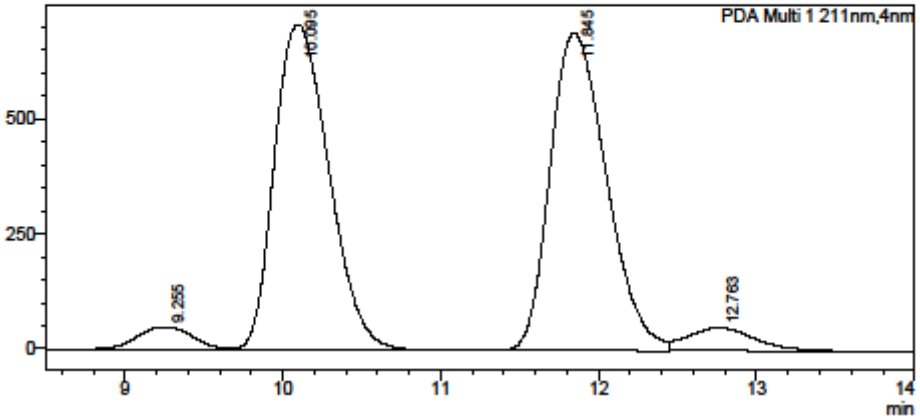


HPLC data compound **39**: Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer: t_R(3*R*,4*S*): 10.1 min, t_R(3*S*,4*R*): 11.8 min, 92% *ee*; minor diastereoisomer t_R: 9.3 min, t_R: 12.8 min, 90% *ee*.



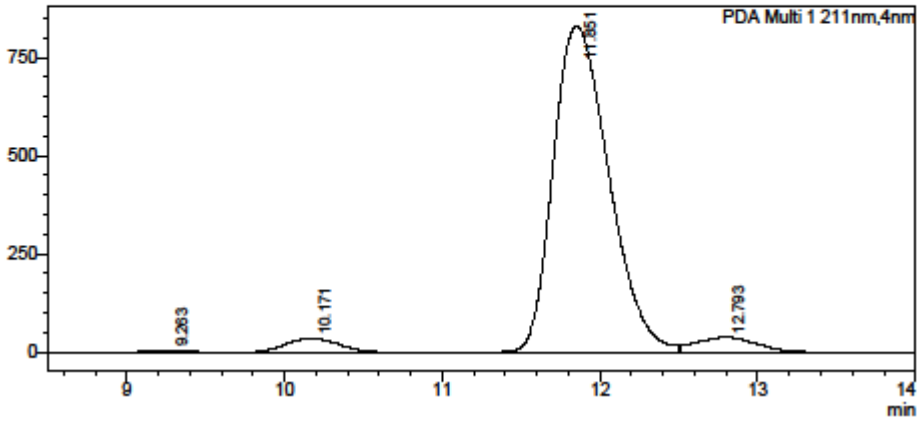
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.255	3.371
2	10.095	46.198
3	11.845	46.487
4	12.763	3.944
Total		100.000

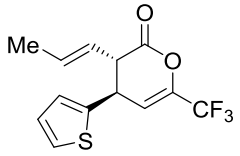


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.263	0.246
2	10.171	3.679
3	11.851	91.581
4	12.793	4.494
Total		100.000

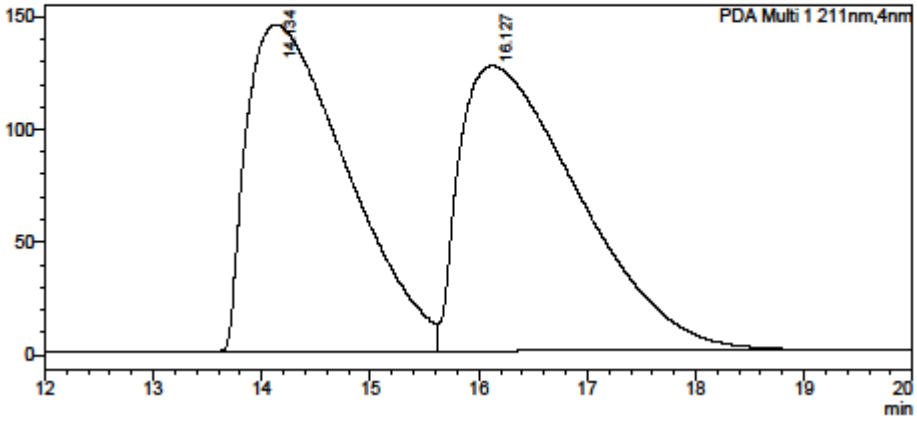


HPLC data compound **40**: Chiral HPLC Chiralpak AS-H (0.5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer: t_R(3*S*,4*R*): 14.1 min, t_R(3*R*,4*S*): 16.1 min, 93% *ee*.



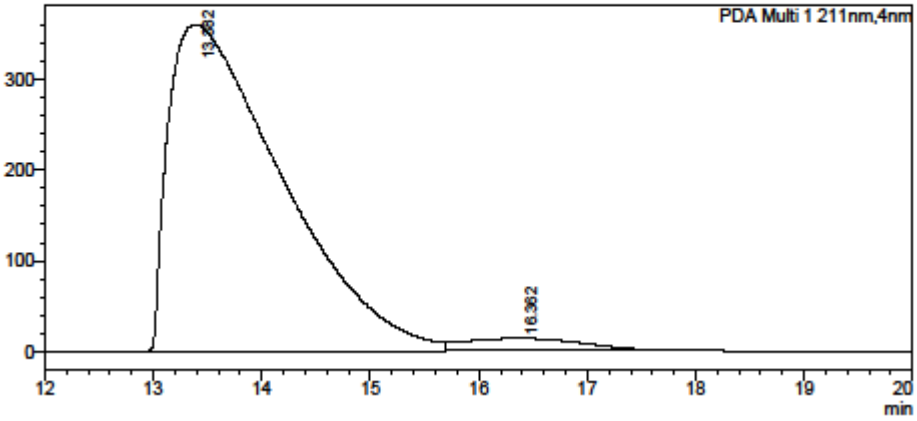
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.134	48.839
2	16.127	51.161
Total		100.000

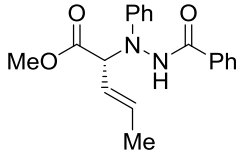


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.382	96.258
2	16.362	3.742
Total		100.000

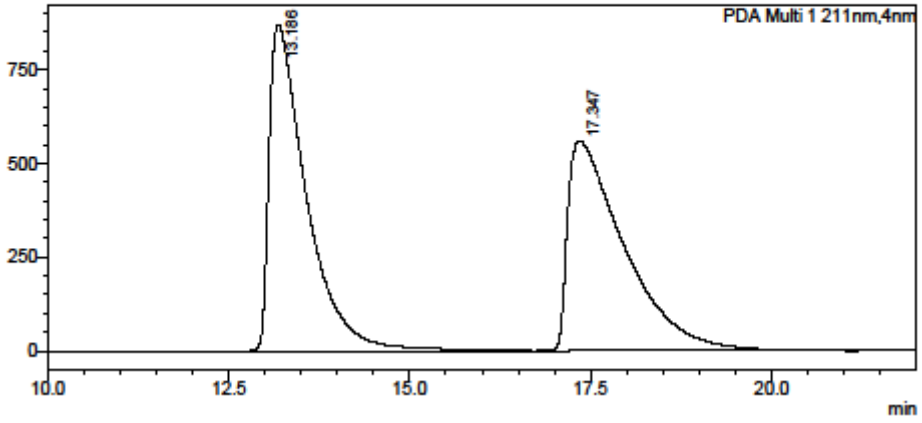


HPLC data compound **41**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 13.2 min, t_R(2*R*): 17.3 min, 96% *ee*.



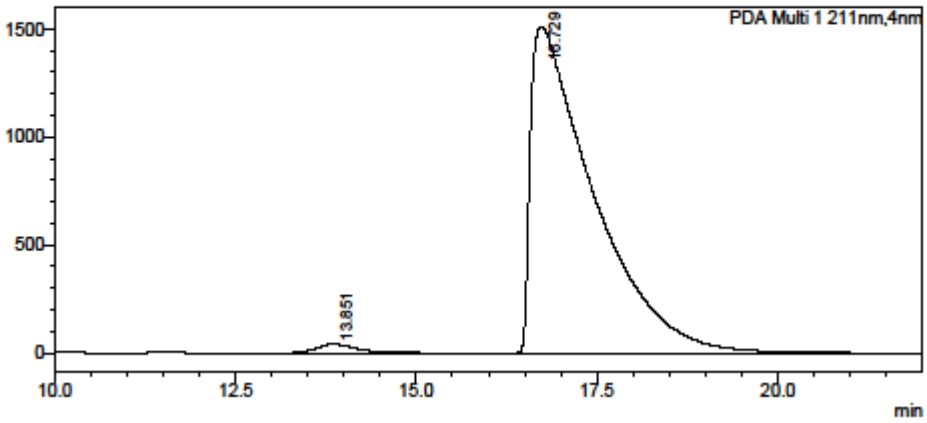
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.186	50.693
2	17.347	49.307
Total		100.000

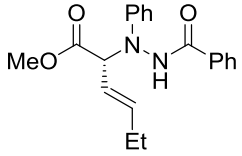


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.851	1.913
2	16.729	98.087
Total		100.000

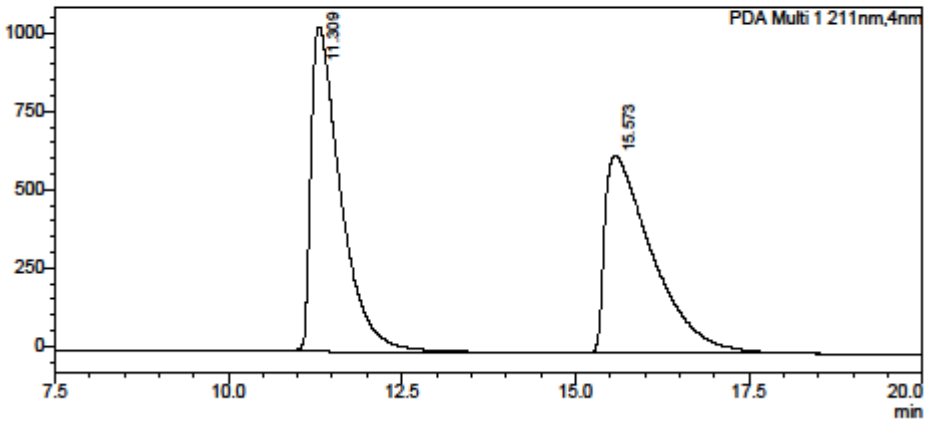


HPLC data compound **42**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 11.3 min, t_R(2*R*): 15.6 min, 99% *ee*.



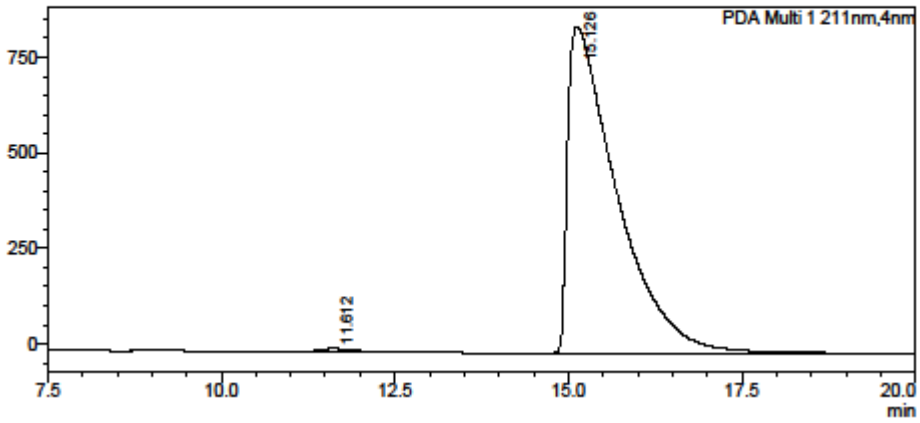
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.309	50.637
2	15.573	49.363
Total		100.000

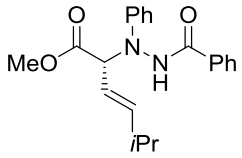


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.612	0.522
2	15.126	99.478
Total		100.000

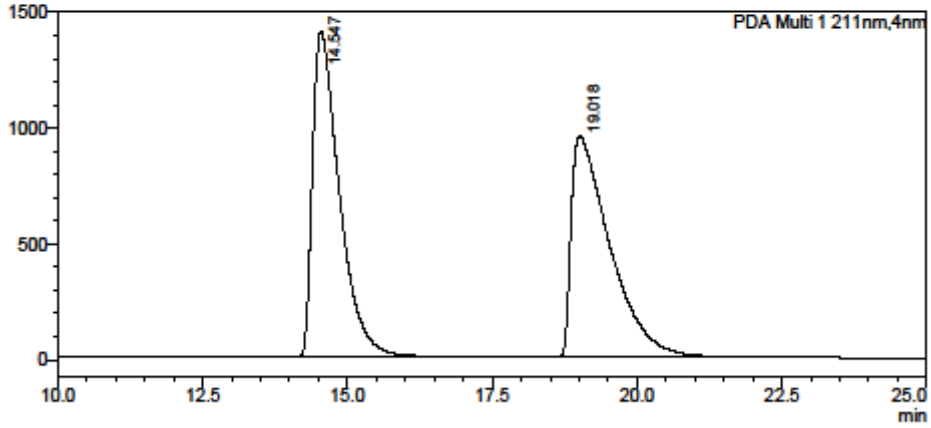


HPLC data compound **43**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 14.5 min, t_R(2*R*): 19.0 min, 99% *ee*.



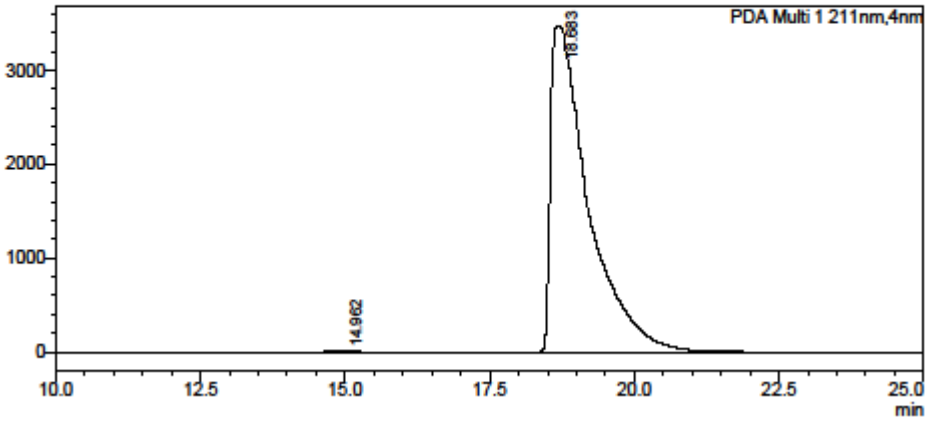
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.547	50.400
2	19.018	49.600
Total		100.000

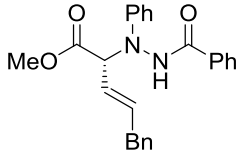


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.962	0.348
2	18.683	99.652
Total		100.000

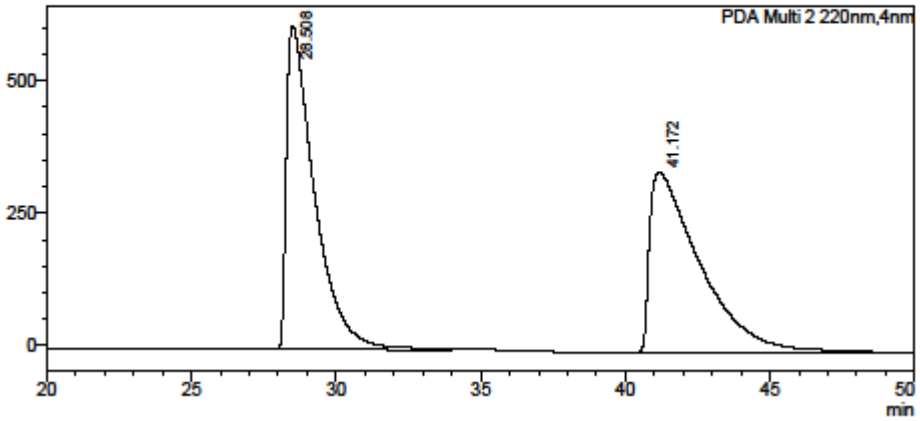


HPLC data compound **44**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*S*): 28.5 min, t_R(2*R*): 41.2 min, 99% *ee*.



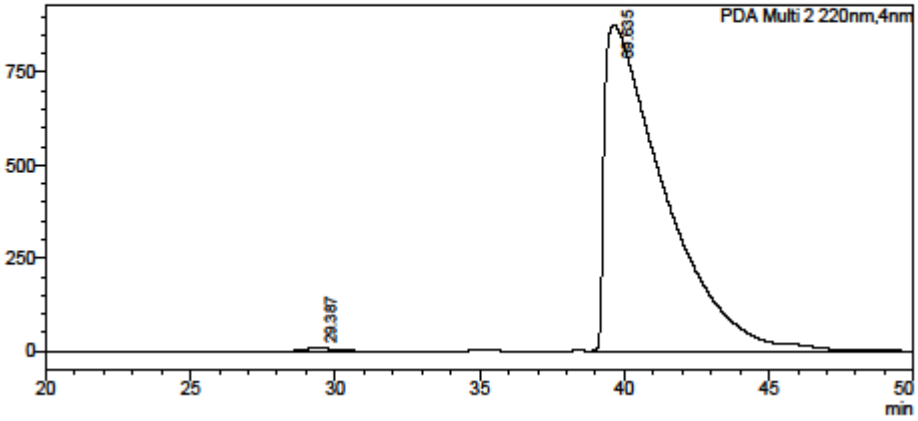
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	28.508	50.366
2	41.172	49.634
Total		100.000

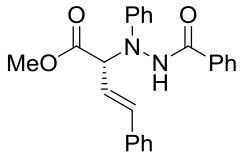


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	29.387	0.566
2	39.635	99.434
Total		100.000

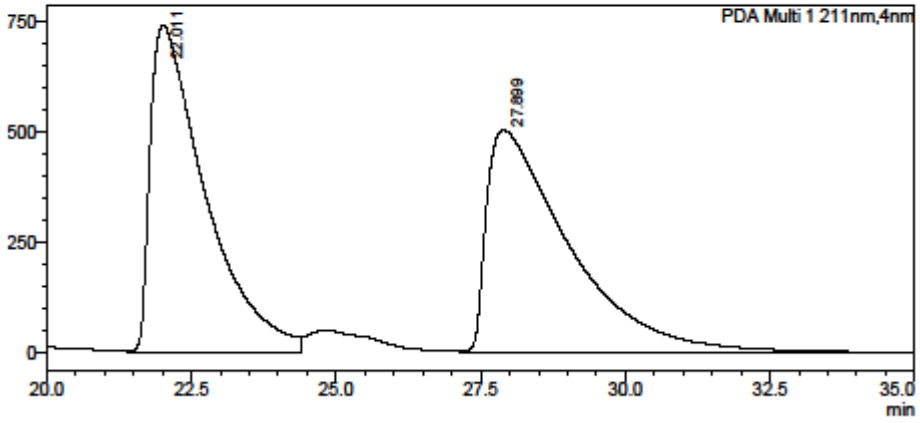


HPLC data compound **45**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 22.0 min, t_R(2*R*): 27.9 min, 91% *ee*.



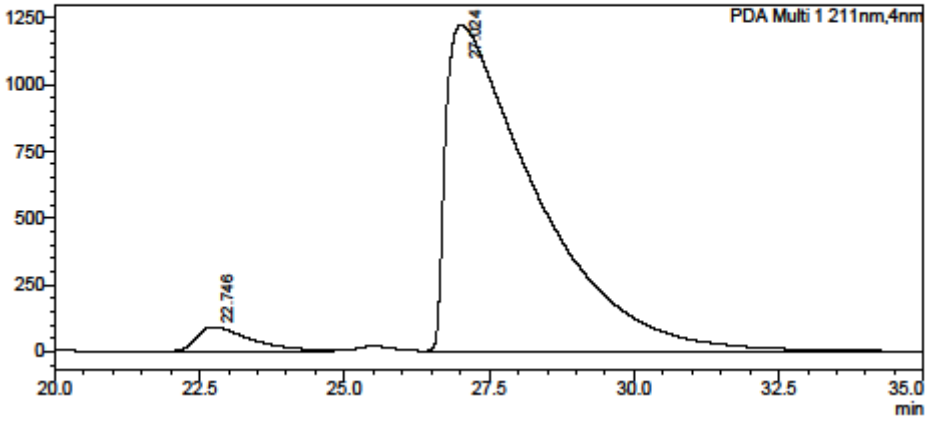
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	22.011	49.772
2	27.899	50.228
Total		100.000

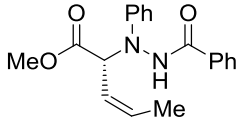


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	22.746	4.321
2	27.024	95.679
Total		100.000

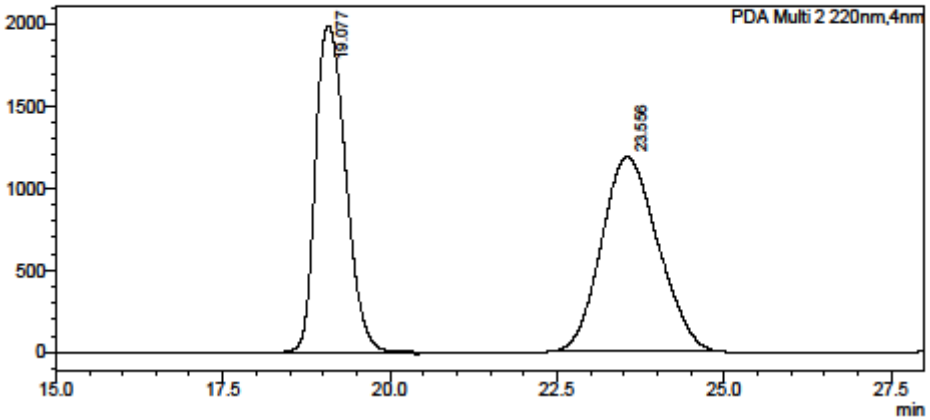


HPLC data compound **46**: Chiral HPLC Chiralpak AD-H (20% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*S*): 19.1 min, t_R(2*R*): 23.6 min, 99% *ee*.



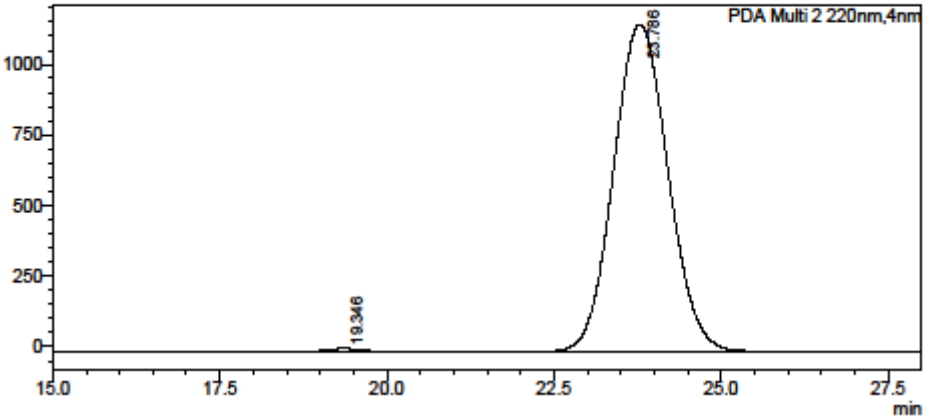
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	19.077	48.159
2	23.556	51.841
Total		100.000

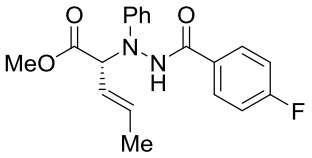


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	19.346	0.470
2	23.786	99.530
Total		100.000

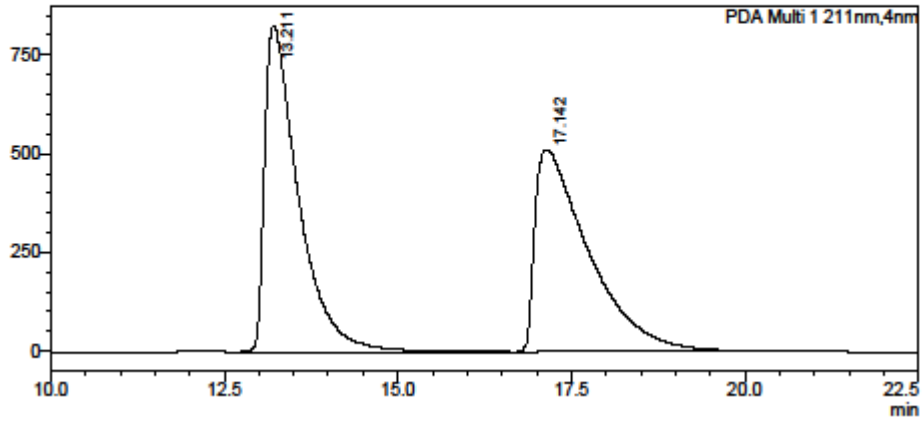


HPLC data compound **47**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 13.2 min, t_R(2*R*): 17.1 min, 99% *ee*.



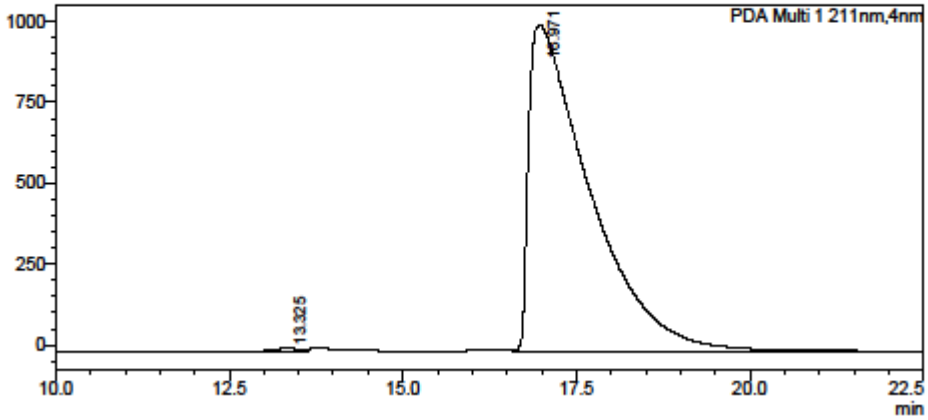
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.211	50.398
2	17.142	49.602
Total		100.000

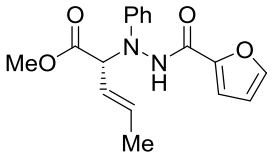


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.325	0.380
2	16.971	99.620
Total		100.000

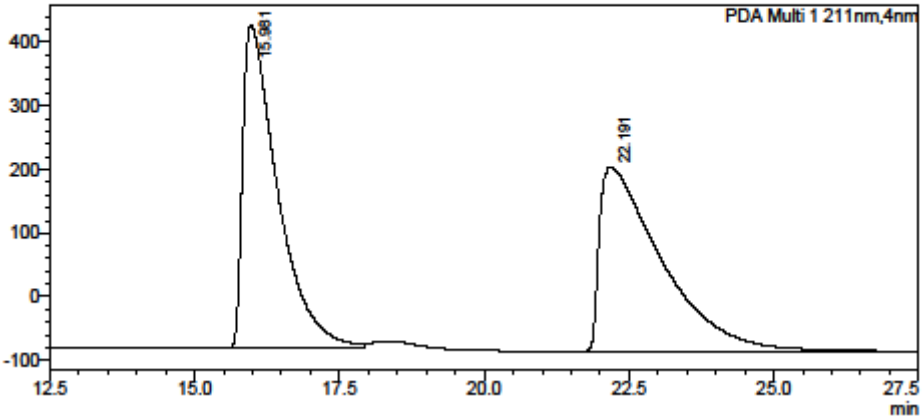


HPLC data compound **48**: Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 16.0 min, t_R(2*R*): 22.2 min, 99% *ee*.



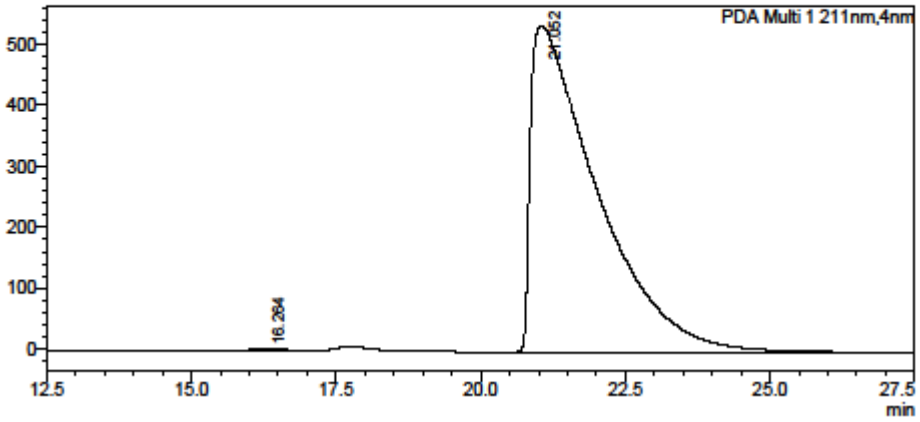
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	15.981	49.707
2	22.191	50.293
Total		100.000

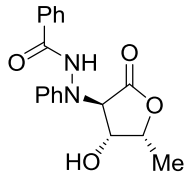


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	16.264	0.329
2	21.052	99.671
Total		100.000

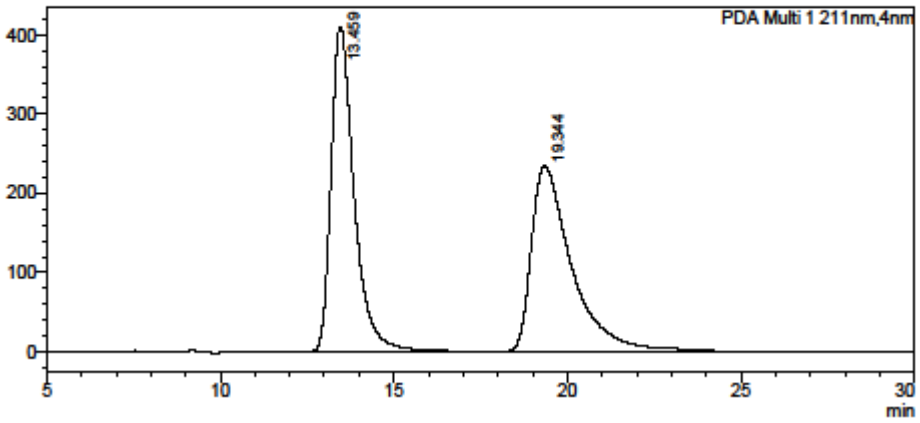


HPLC data compound **49**: Chiral HPLC Chiralcel OJ-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*,5*S*): 13.5 min, t_R(3*R*,4*R*,5*R*): 19.3 min, 99% *ee*.



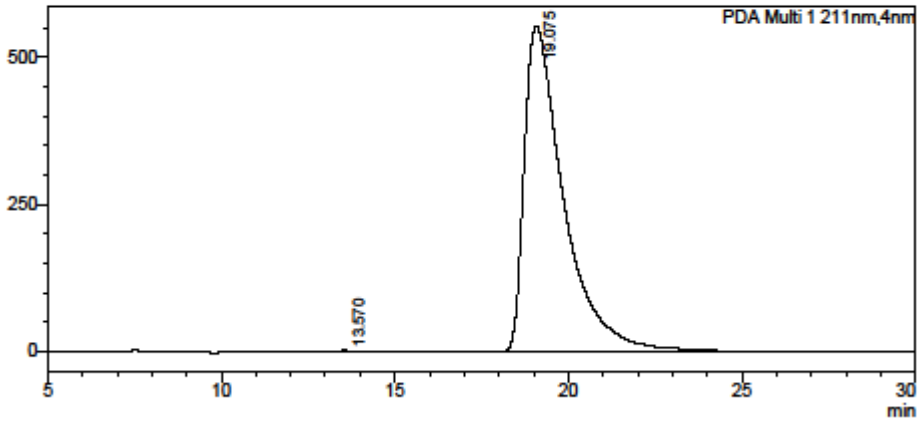
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.459	50.070
2	19.344	49.930
Total		100.000

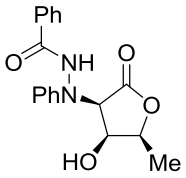


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.570	0.305
2	19.075	99.695
Total		100.000

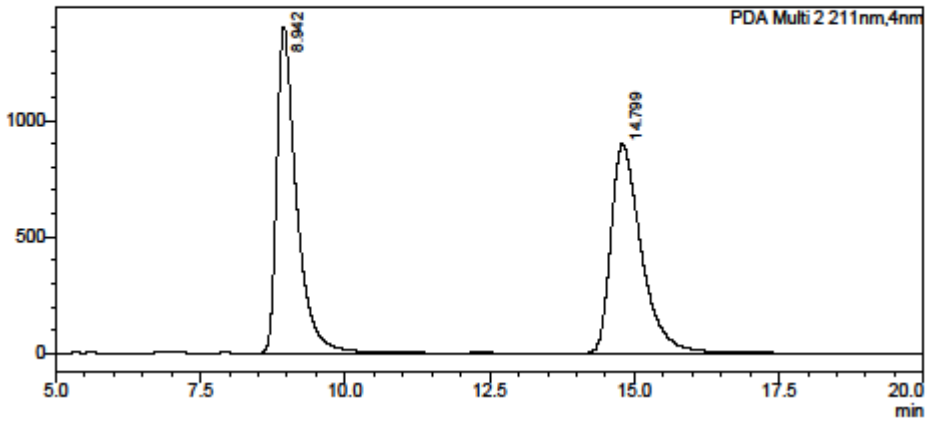


HPLC data compound **50**: Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*,5*R*): 8.9 min, t_R(3*R*,4*S*,5*S*): 14.8 min, 99% *ee*.



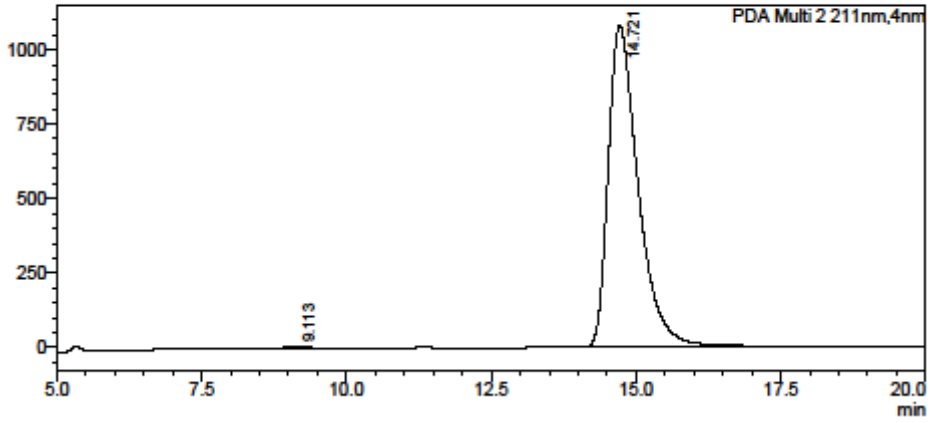
PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	8.942	50.833
2	14.799	49.167
Total		100.000

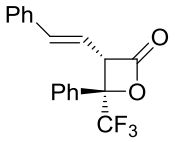


PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	9.113	0.281
2	14.721	99.719
Total		100.000

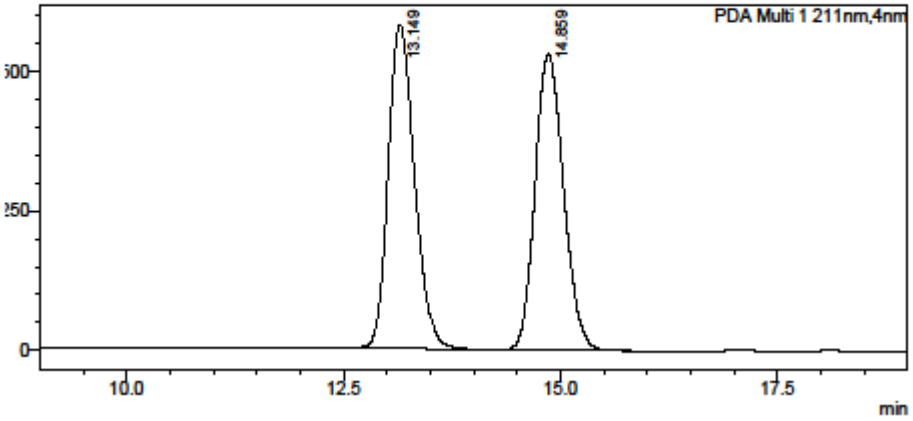


HPLC data compound **73**: Chiral HPLC Chiralcel OD-H (2% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 13.1 min, t_R(3*R*,4*R*): 14.9 min, 77% *ee* at rt.



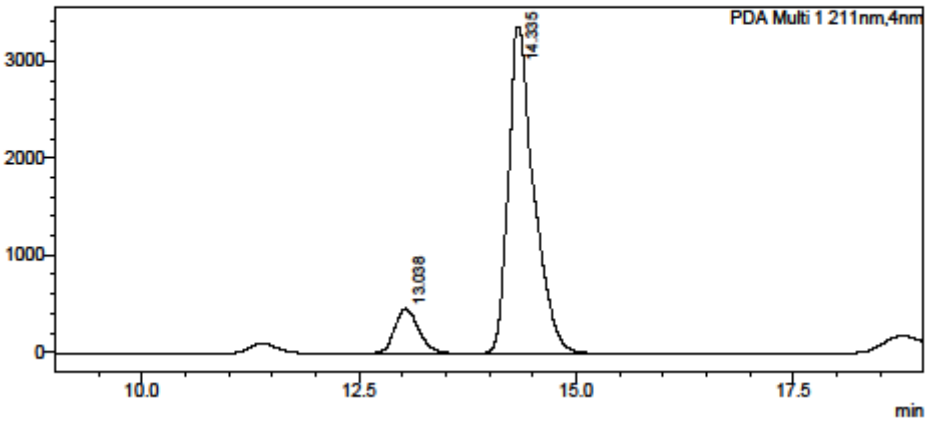
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.149	50.102
2	14.859	49.898
Total		100.000

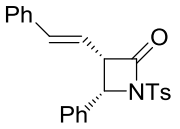


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.038	11.384
2	14.335	88.616
Total		100.000

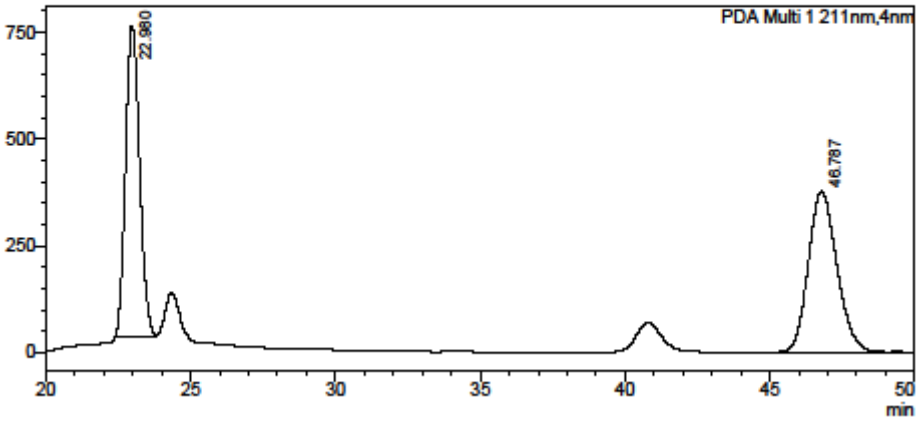


HPLC data compound **74**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 23.0 min, t_R(3*R*,4*R*): 46.8 min, 16% *ee* at -78 °C.



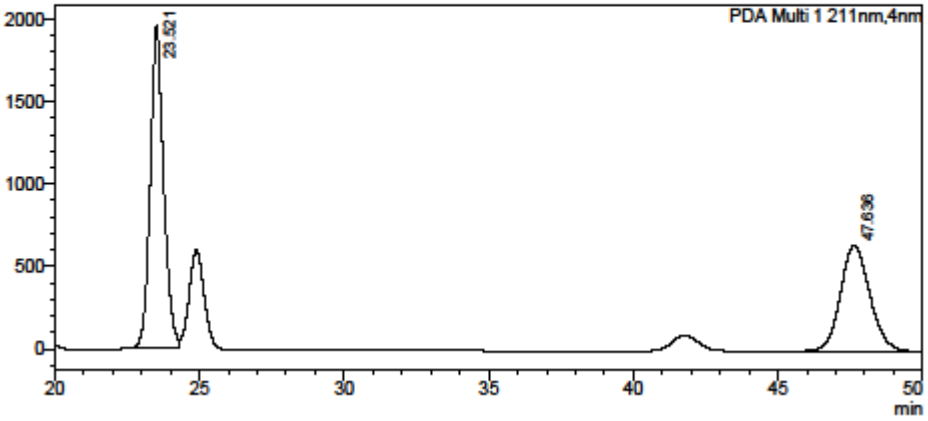
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	22.980	48.640
2	46.787	51.360
Total		100.000

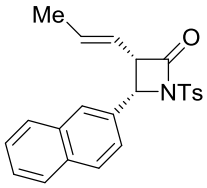


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	23.521	58.065
2	47.636	41.935
Total		100.000

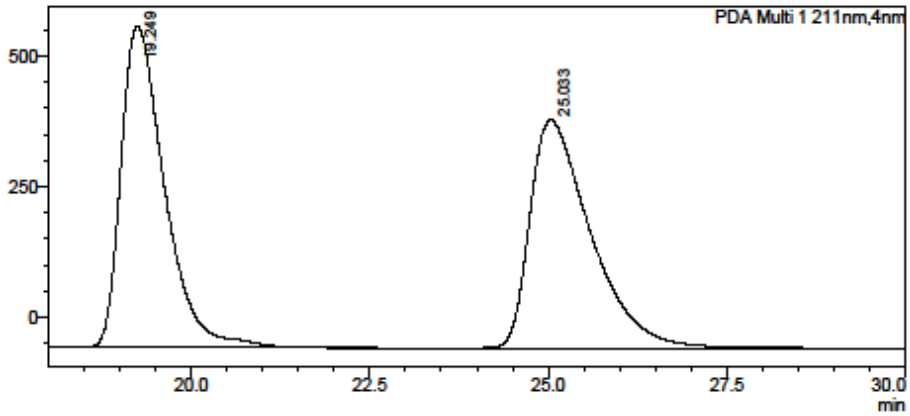


HPLC data compound **75**: Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 19.2 min, t_R(3*R*,4*R*): 25.0 min, 81% *ee* at rt and 99% *ee* at -78 °C



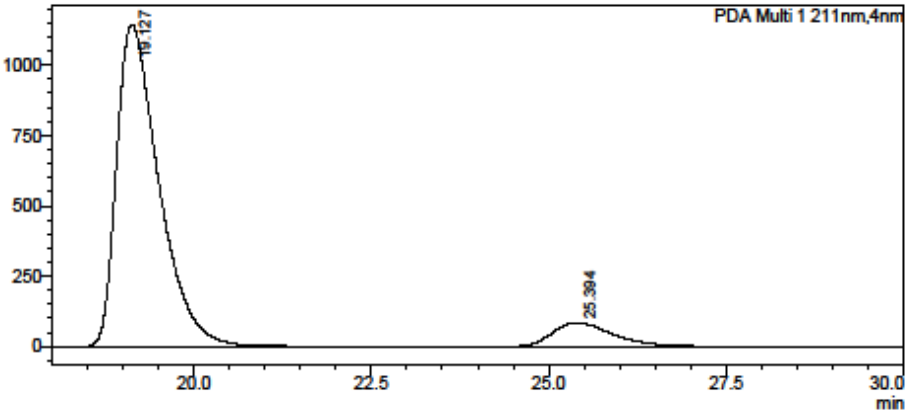
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	19.249	50.154
2	25.033	49.846
Total		100.000



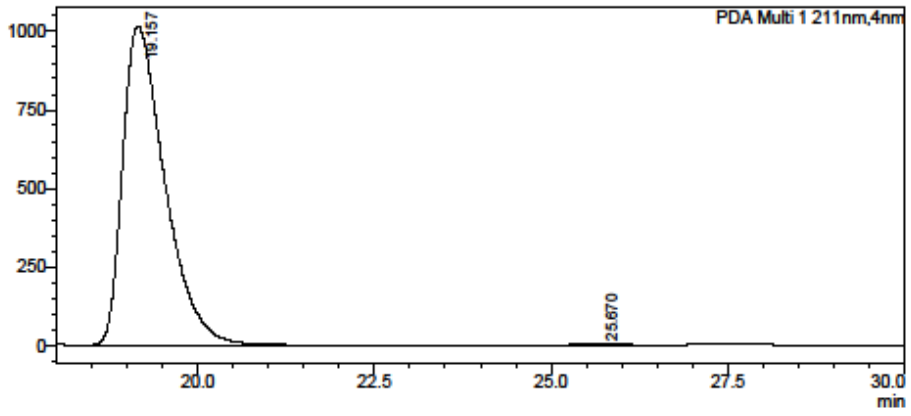
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	19.127	90.423
2	25.394	9.577
Total		100.000

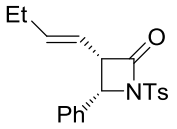


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	19.157	99.694
2	25.670	0.306
Total		100.000

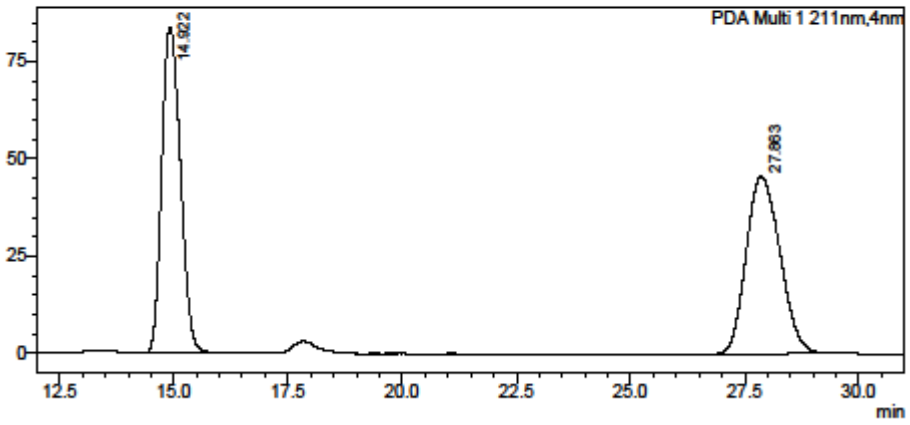


HPLC data compound **76**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 14.9 min, t_R(3*R*,4*R*): 27.9 min, 74% *ee* at rt and >99% *ee* at -78 °C.



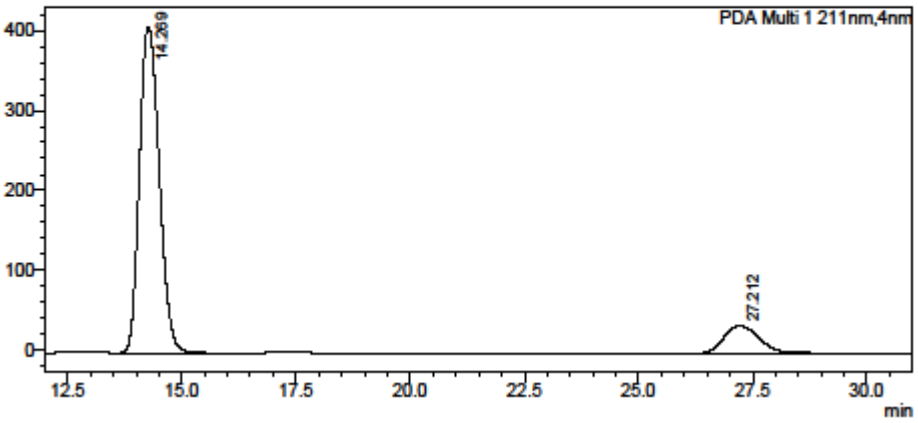
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.922	50.131
2	27.863	49.869
Total		100.000



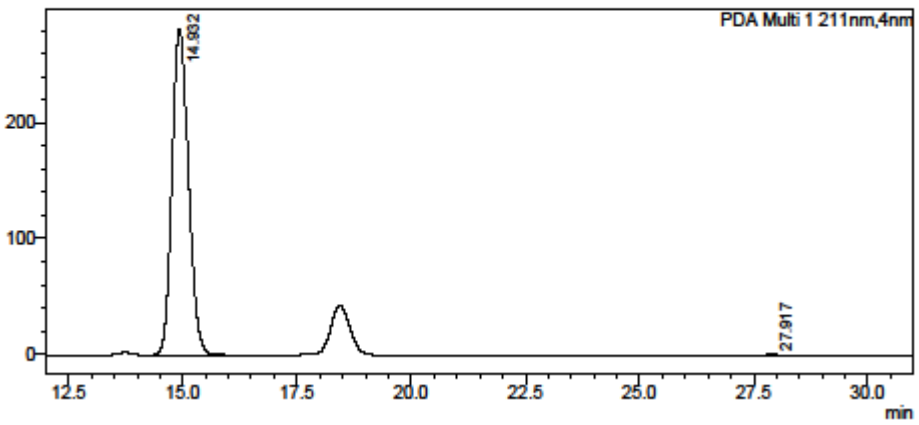
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.269	86.976
2	27.212	13.024
Total		100.000

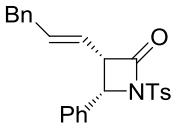


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.932	99.758
2	27.917	0.242
Total		100.000

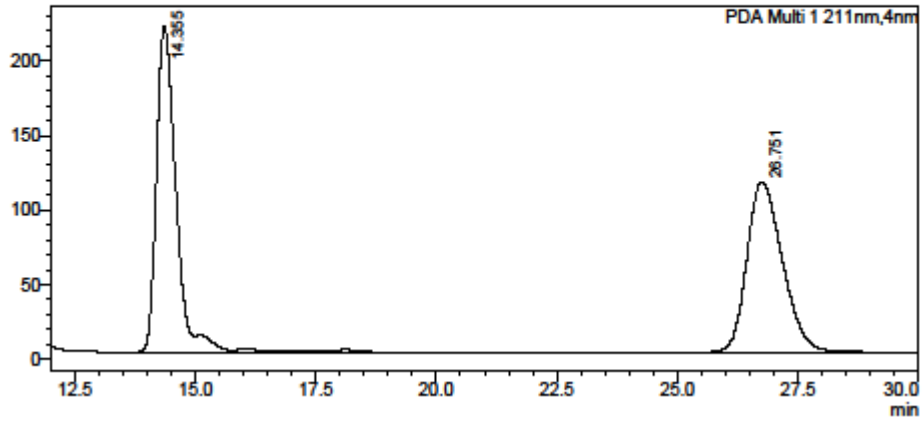


HPLC data compound **77**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 14.4 min, t_R(3*R*,4*R*): 26.7 min, 39% *ee* at rt and 97% *ee* at -78 °C.



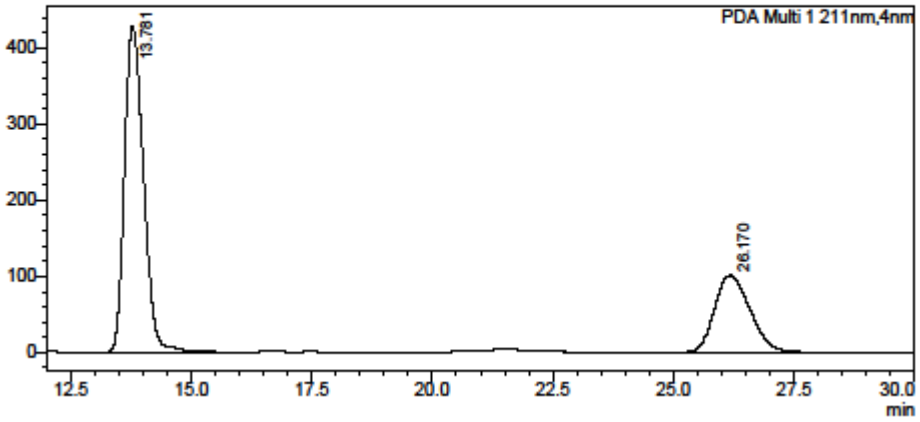
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	14.355	51.242
2	26.751	48.758
Total		100.000



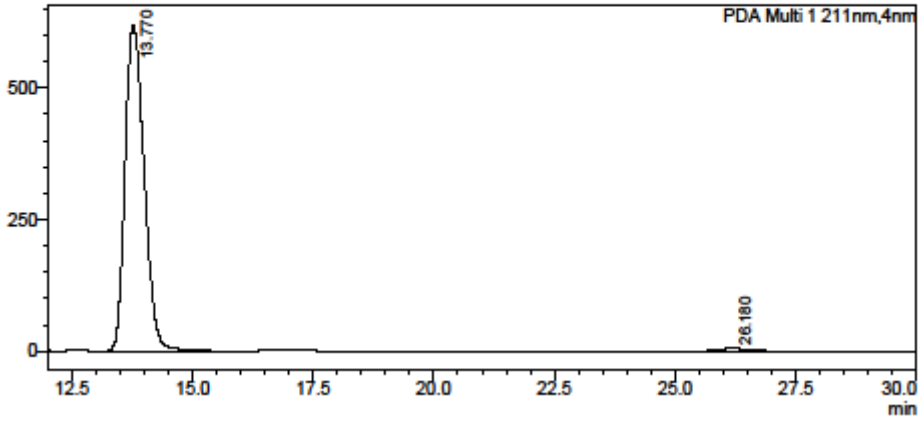
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.781	69.624
2	26.170	30.376
Total		100.000

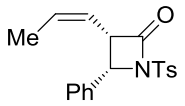


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.770	98.518
2	26.180	1.482
Total		100.000

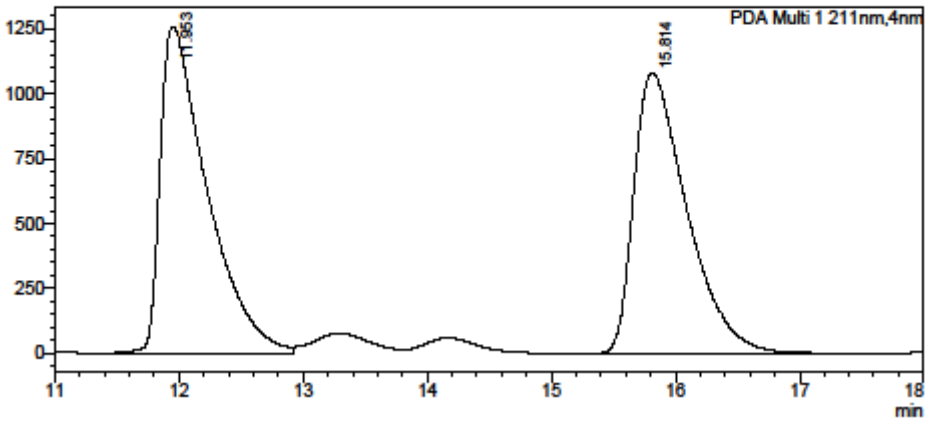


HPLC data compound **78**: Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*): 12.0 min, t_R(3*R*,4*R*): 15.8 min, 98% *ee* at rt and 99% *ee* at -78 °C



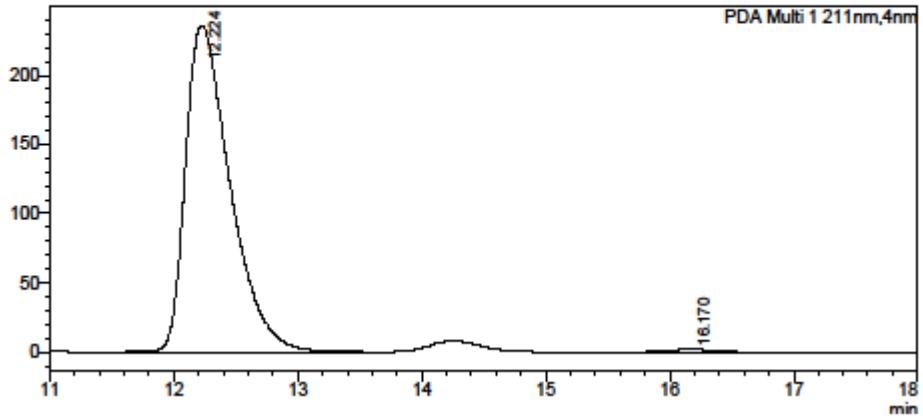
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.953	50.723
2	15.814	49.277
Total		100.000



PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	12.224	99.076
2	16.170	0.924
Total		100.000



PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	12.056	99.683
2	16.161	0.317
Total		100.000