Electronic Supplementary Material (ESI) for ChemComm.
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ESI for:

The Synthesis and Structure of Chiral Enamine *N*-Oxides

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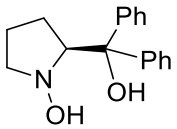
1. Experimental:

1.1. General

All reagents were purchased from commercial sources and used as received unless otherwise stated. ^{1}H- and ^{13}C- NMR spectra were recorded at 400.13 and 100.61 MHz, respectively, and chemical shift values (δ) reported with reference to the residual $CHCl_3$ signal at 7.28 ppm. IR spectra were recorded on an ATR-FTIR spectrometer with neat samples. Mass spectra were recorded on a TRIO-1000 and Micromass LCT mass spectrometers using either chemical ionisation (CI) in ammonia or electrospray ionisation (EI) in MeOH.

1.2 **Characterisation and spectral data:**

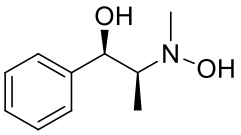
(S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (4):



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 - 7.72 (m, 2 H), 7.50 - 7.59 (m, 2 H), 7.28 - 7.44 (m, 5 H), 7.18 - 7.27 (m, 2 H), 4.21 (dd, J=9.2, 7.2 Hz, 1 H), 3.82 - 4.74 (bs, 2 H), 3.18 - 3.29 (m, 1 H), 2.98 (td, J=10.0, 7.2 Hz, 1 H), 1.58 - 2.03 ppm (m, 4 H)

^{13}C NMR (100 MHz $CDCl_3$): δ = 147.2, 145.4, 128.1, 126.6(2), 126.5(6), 126.1, 125.6, 78.0, 74.0, 59.1, 21.5

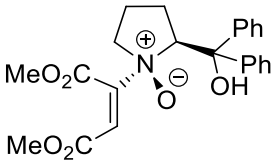
(1R,2S)-2-(hydroxy(methyl)amino)-1-phenylpropan-1-ol (13):



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 - 7.44 (m, 4 H), 7.25 - 7.32 (m, 1 H), 5.41 (s, 1 H), 2.89 (qd, J=6.7, 2.1 Hz, 1 H), 2.80 (s, 3 H), 0.97 ppm (d, J=6.8 Hz, 3 H)

^{13}C NMR (100 MHz $CDCl_3$): δ = 141.7, 128.5, 128.2, 127.0, 125.9, 69.1, 45.9, 11.9

(1S,2S)-1-((E)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide (7):



Dimethyl acetylendicarboxylate (10.6 mg, 0.074 mmol) was dissolved in 0.6 mL $CDCl_3$ and (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (20.2 mg, 0.074 mmol) was added as a solid. The mixture was shaken and the reaction was followed by ^{1}H-NMR spectroscopy. After 0.25 h the reaction was complete and the enamine *N*-Oxide was observed as the major product (>95 %) as essentially a single diastereoisomer.

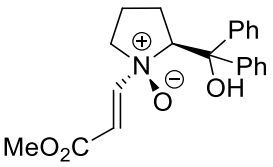
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, J=7.4 Hz, 2 H), 7.54 (dd, J=8.4, 1.0 Hz, 2 H), 7.24 - 7.41 (m, 3 H), 7.13 - 7.21 (m, 4 H), 6.96 - 7.06 (m, 1 H), 5.60 - 5.65 (m, 1 H), 3.70 - 3.95 (m, 2 H), 3.61 (s, 3 H), 3.19 - 3.25 (m, 1 H), 2.50 - 2.66 (m, 2 H), 2.21-1.93 (m, 2 H).

^{13}C NMR (100 MHz $CDCl_3$): δ = 164.9, 163.2, 148.7, 147.3, 145.6, 128.7, 128.5, 128.2, 128.1, 127.4, 127.1, 126.8, 126.7, 125.1, 78.3, 78.1, 73.5, 53.7, 52.6, 25.9, 22.3.

IR (neat)/cm^{-1}: 1726, 1666, 1264

HRMS (ES +) Calc. $C_{23}H_{25}NO_6Na$ 434.1580; Found. 434.1577

(1R,2S)-2-(hydroxydiphenylmethyl)-1-((E)-3-methoxy-3-oxoprop-1-en-1-yl)pyrrolidine 1-oxide (5)



Methyl propiolate (6.4 mg, 0.074 mmol) was dissolved in 0.6 mL $CDCl_3$ and (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (19.9 mg, 0.074 mmol) was added as a solid. The mixture was shaken and the reaction was followed by ^{1}H-NMR spectroscopy. After 0.25 h the reaction was complete and the enamine *N*-Oxide was observed as the major product (>95 %) as essentially a single diastereoisomer. The solvent was removed *in vacuo* and the yellow solid recrystallized by diffusion of pentane into a DCM solution of the crude product to obtain colourless needles of X-Ray quality (22 mg, 85 %).

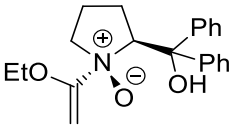
^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.52 (br. s., 1 H), 7.62 (d, J=7.6 Hz, 2 H), 7.49 - 7.59 (m, 2 H), 7.09 - 7.40 (m, 6 H), 6.97 - 7.08 (m, 1 H), 6.64 (d, J=12.7 Hz, 1 H), 6.28 (d, J=12.7 Hz, 1 H), 4.54 (t, J=9.1 Hz, 1 H), 3.60 (s, 3 H), 3.49 (td, J=11.1, 7.7 Hz, 1 H), 3.20 (dd, J=10.4, 8.0 Hz, 1 H), 2.65 - 2.79 (m, 1 H), 2.46 - 2.65 (m, 1 H), 1.96 - 2.20 ppm (m, 2 H)

^{13}C NMR (100 MHz $CDCl_3$): δ = 165.4, 152.3, 146.5, 146.1, 128.8, 128.5(1), 128.4(9), 128.1, 128.0, 127.3, 127.1, 126.8, 125.1, 117.8, 80.8, 77.6, 73.5, 52.1, 25.1, 24.8, 21.7.

IR ($CHCl_3$)/cm^{-1}:3435, 1668, 1601, 1447

HRMS (ES +) Calc. $C_{21}H_{23}NO_4Na$ 376.1525; Found. 376.1526

(1S,2S)-1-(1-ethoxyvinyl)-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide (10):



(1S,2S)-1-(1-ethoxyvinyl)-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide: (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (20.0 mg, 0.074 mmol) was dissolved in 0.6 mL $CHCl_3$. Ethoxy acetylene (26.1 mg, 0.15 mmol, 40 % solution in Hexanes) was added. The reaction was monitored by TLC and after 18 h the solvents were removed in vacuo. The crude solid was washed with cold hexane and dried in vacuo to yield the desired enamine *N*-Oxide as an off-white solid (23 mg, 91 %)

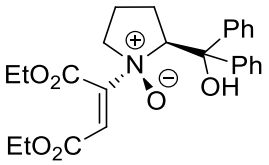
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 - 7.70 (m, 2 H), 7.55 - 7.61 (m, 2 H), 7.25 - 7.36 (m, 3 H), 7.09 - 7.21 (m, 3 H), 5.00 - 5.08 (m, 2 H), 3.98 (td, J=10.9, 8.2 Hz, 1 H), 3.50 - 3.59 (m, 1 H), 3.47 (d, J=3.3 Hz, 1 H), 3.23 (dd, J=9.2, 7.2 Hz, 1 H), 3.10 - 3.18 (m, 1 H), 2.41 - 2.71 (m, 2 H), 1.90 - 2.16 (m, 2 H), 1.39 (t, J=6.9 Hz, 3 H), 1.10 - 1.36 ppm (m, 2 H)

^{13}C NMR (100 MHz $CDCl_3$): δ = 159.4, 147.6, 146.2, 128.1, 127.0, 126.5, 126.4 126.2, 124.8, 80.0, 73.5, 71.7, 65.3, 24.7, 20.5, 14.3

IR (neat)/cm^{-1}: 1681, 1447

HRMS (ES +) Calc. $C_{21}H_{26}NO_3$ 340.1912; Found. 340.1913

(1S,2S)-1-((E)-1,4-diethoxy-1,4-dioxobut-2-en-2-yl)-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide (7):



Diethyl acetylendicarboxylate (12.6 mg, 0.074 mmol) was dissolved in 0.6 mL $CDCl_3$ and (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (20.0 mg, 0.074 mmol) was added as a solid. The mixture was left at room temperature and the reaction was followed by ^{1}H-NMR spectroscopy. After 0.25 h the reaction was complete and the enamine *N*-Oxide was observed as the major product (>95 %) as essentially a single diastereoisomer. The solvent was removed *in vacuo* and the yellow solid recrystallized by diffusion of pentane into a DCM solution of the crude product to obtain colourless prisms of suitable quality for X-ray analysis (27 mg, 83 %).

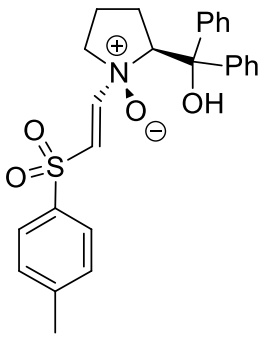
^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.24 (br. s., 1 H), 7.55 (d, *J*=7.4 Hz, 2 H), 7.46 (dd, *J*=8.3, 1.0 Hz, 2 H), 7.16 - 7.23 (m, 1 H), 7.05 - 7.13 (m, 1 H), 7.03 - 7.30 (m, 7 H), 6.88 - 6.99 (m, 1 H), 5.54 - 5.59 (m, 1 H), 4.07 - 4.27 (m, 2 H), 3.99 (qd, *J*=7.1, 1.9 Hz, 2 H), 3.89 (td, *J*=10.6, 7.5 Hz, 1 H), 3.12 (dd, *J*=8.9, 7.6 Hz, 1 H), 2.41 - 2.60 (m, 2 H), 1.85 - 2.10 (m, 2 H), 1.20 (t, *J*=7.2 Hz, 3 H), 1.18 (t, *J*=7.1 Hz, 3 H), 1.10 - 1.32 (m, 1 H)

^{13}C NMR (400 MHz, $CDCl_3$): δ 164.6, 16.5, 147.7, 145.7, 128.7, 128.5, 128.2, 127.1, 127.0, 126.7, 125.1, 78.3, 73.7, 63.2, 61.6, 26.0

IR (neat)/cm^{-1}:1731, 1719, 1666, 1251

HRMS (ES +) 440.2078, $C_{25}H_{30}NO_6$ requires 440.2068.

(1S,2S)-2-(hydroxydiphenylmethyl)-1-((E)-2-tosylvinyl)pyrrolidine 1-oxide (8):



Ethynyl *p*-tolyl sulphone (13.6 mg, 0.074 mmol) was dissolved in 0.6 mL CDCl3 and (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (20.2 mg, 0.074 mmol) was added as a solid. The mixture was left at room temperature and the reaction was followed by ^1H-NMR spectroscopy. After 4 h the reaction was complete and the enamine *N*-Oxide was observed as the major product (>95 %) as essentially a single diastereoisomer.

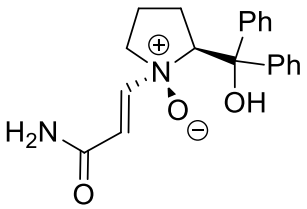
^1H NMR (400 MHz, $CDCl_3$): δ = 7.59 - 7.64 (m, 2 H), 7.44 - 7.50 (m, 3 H), 7.32 - 7.39 (m, 3 H), 7.25 - 7.32 (m, 2 H), 7.16 - 7.21 (m, J= 1 H), 7.06 - 7.12 (m, 2 H), 6.96 - 7.02 (m, 1 H), 5.64 (d, J=12.0 Hz, 1 H), 4.53 - 4.60 (m, J=9.0 Hz, 1 H), 3.25 - 3.48 (m, 1 H), 3.07 - 3.25 (m, J=11.2, 6.4 Hz, 1 H), 2.38 - 2.65 (m, 1 H), 2.49 (s, 3 H), 1.82 - 2.08 (m, 2 H), 1.69 - 1.81 ppm (m, 1 H)

^{13}C NMR (400 MHz, $CDCl_3$): δ = 159.9, 145.8, 144.7, 143.7, 143.5, 139.6, 129.6, 128.3, 128.1, 127.9, 127.8, 127.6, 127.1, 126.8(0), 126.7(6), 125.7, 125.3, 106.2, 74.0, 59.7, 56.2, 25.9, 22.5, 21.6

IR ($CHCl_3$)/cm^{-1}:1617, 1302

HRMS (ES +) Calc. $C_{26}H_{27}NO_4NaS$ 472.1559; Found. 472.1569

Synthesis of (*S*)-2-(hydroxydiphenylmethyl)pyrrolidin-1-acrylamide-*N*-oxide (9):



Propiolamide (5.2 mg, 0.074 mmol) was dissolved in 0.6 mL $CDCl_3$ and (S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-ol (20.0 mg, 0.074 mmol) was added as a solid. After stirring

for 18 h a white precipitate had formed. The mixture was filtered off and the resulting white solid dried *in vacuo* to yield the desired product (21 mg, 84 %).

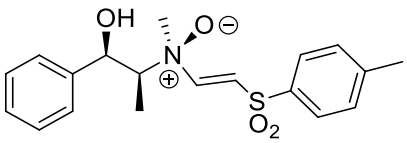
^{1}H NMR (400 MHz, CD_3OD): δ = 7.51 - 7.63 (m, 4 H), 7.25 - 7.37 (m, 3 H), 7.14 - 7.25 (m, 3 H), 7.03 (s, 1 H), 6.77 (d, J=12.5 Hz, 1 H), 6.21 (d, J=12.5 Hz, 1 H), 5.14 (s, 1 H), 3.68 - 3.81 (m, 1 H), 3.10 (dd, J=7.5, 6.8 Hz, 1 H), 2.28 - 2.58 (m, 2 H), 2.02 - 2.23 (m, 2 H), 1.11 - 1.42 (m, 1 H), 0.87 ppm (s, 1 H).

^{13}C NMR (100MHz, CD_3OD): δ = 166.3, 149.7, 146.1, 145.3, 127.9, 127.7, 127.0, 126.5, 125.9, 124.4, 118.9, 79.2, 77.6, 74.7, 72.4, 24.3, 20.5.

IR (neat)/cm^{-1}: 3312, 3170, 2943, 1689, 1515, 1392.

HRMS (ES +) 339.1706 $[M+H]^+$, $C_{20}H_{23}N_2O_3$ requires 339.1709.

(S,1R,2S)-1-hydroxy-N-methyl-1-phenyl-N-((E)-2-tosylvinyl)propan-2-amine oxide (16):



Ephedrine hydroxylamine (15.1 mg, 0.082 mmol) was added to a solution of ethynyl *p*-tolyl sulfone (15.0 mg mg, 0.082 mmol) in 0.6 mL $CDCl_3$. The mixture was reacted for 18 h at which point ^{1}H-NMR spectroscopy showed that conversion to the desired enamine *N*-oxide was complete and essentially quantitative. Evaporation of the solvent allowed IR and HRMS analysis.

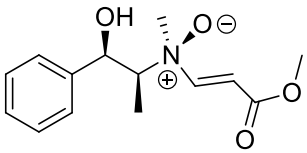
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 - 7.85 (m, 2 H), 7.63 (d, *J*=11.4 Hz, 1 H), 7.16 - 7.46 (m, 9 H), 6.02 (d, *J*=11.4 Hz, 1 H), 4.90 (br. s., 1 H), 3.09 (qd, *J*=6.7, 3.7 Hz, 1 H), 2.77 (s, 3 H), 2.39 - 2.57 (m, 4 H), 2.15 (br. s., 1 H), 1.01 ppm (br. s., 3 H)

^{13}C NMR (100MHz, $CDCl_3$) δ = 159.7, 143.7, 139.6, 129.8, 128.3, 127.5, 127.0, 126.0, 107.5, 68.8, 42.8, 21.6

IR (neat)/cm^{-1}: 3428, 1561, 1293, 1047

HRMS (ES +) Calc. $C_{19}H_{23}NO_4Na$ 384.1236; Found. 384.1245

(R,E)-N-((1R,2S)-1-hydroxy-1-phenylpropan-2-yl)-3-methoxy-N-methyl-3-oxoprop-1-en-1-amine oxide (14):



Ephedrine hydroxylamine (15.3 mg, 0.084 mmol) was added to a solution of methyl propiolate (6.9 mg mg, 0.082 mmol) in 0.6 mL $CDCl_3$. The mixture was reacted for 18 h at which point ^{1}H-NMR spectroscopy showed that conversion to the desired enamine N-oxide was complete and essentially quantitative. Evaporation of the solvent allowed IR and HRMS analysis.

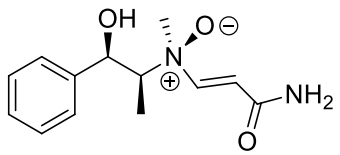
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J*=12.3 Hz, 2 H), 7.32 - 7.38 (m, 4 H), 7.28 (s, 1 H), 5.56 (d, *J*=12.3 Hz, 2 H), 5.03 (d, *J*=2.2 Hz, 1 H), 3.71 (s, 3 H), 3.06(qd, *J*=6.7,2.7, 1 H), 2.92 (s, 3 H), 2.79 (s, 3 H), 2.39 (bs, 1H) 0.94 ppm (d, *J*=6.3 Hz, 3 H)

^{13}C NMR (100MHz, $CDCl_3$): δ = 168.6, 162.9, 153.5, 128.6, 127.6, 126.3, 96.6, 75.3, 74.8, 69.3, 60.8, 53.3, 51.6, 43.5, 14.6

IR (neat)/cm^{-1}: 3464, 1708, 1626, 1109

HRMS (ES +) Calc. $C_{14}H_{19}NO_4Na$ 288.1206; Found. 288.1186

(R,S)-3-amino-N-((1R,2S)-1-hydroxy-1-phenylpropan-2-yl)-N-methyl-3-oxoprop-1-en-1-amine oxide (15):



Ephedrine hydroxylamine (14.9 mg, 0.082 mmol) was added to a solution of propiolamide (5.8 mg, 0.082 mmol) in 0.6 mL $CDCl_3$. The mixture was reacted for 18 h at which point ^{1}H-NMR spectroscopy showed that conversion to the desired enamine N-oxide was complete. Evaporation of the solvent allowed IR and HRMS analysis.

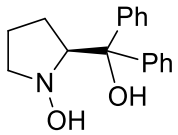
^{1}H NMR (400 MHz, $CDCl_3$): Shift = 7.65 (d, J=12.0 Hz, 1 H), 7.30 - 7.41 (m, 5 H), 7.23 - 7.29 (m, 2 H), 5.54 (d, J=12.0 Hz, 1 H), 5.47 (br. s., 2 H), 5.01 (d, J=2.8 Hz, 1 H), 3.04 (qd, J=6.7, 3.1 Hz, 1 H), 2.77 (s, 3 H), 0.95 ppm (d, J=6.5 Hz, 3 H)

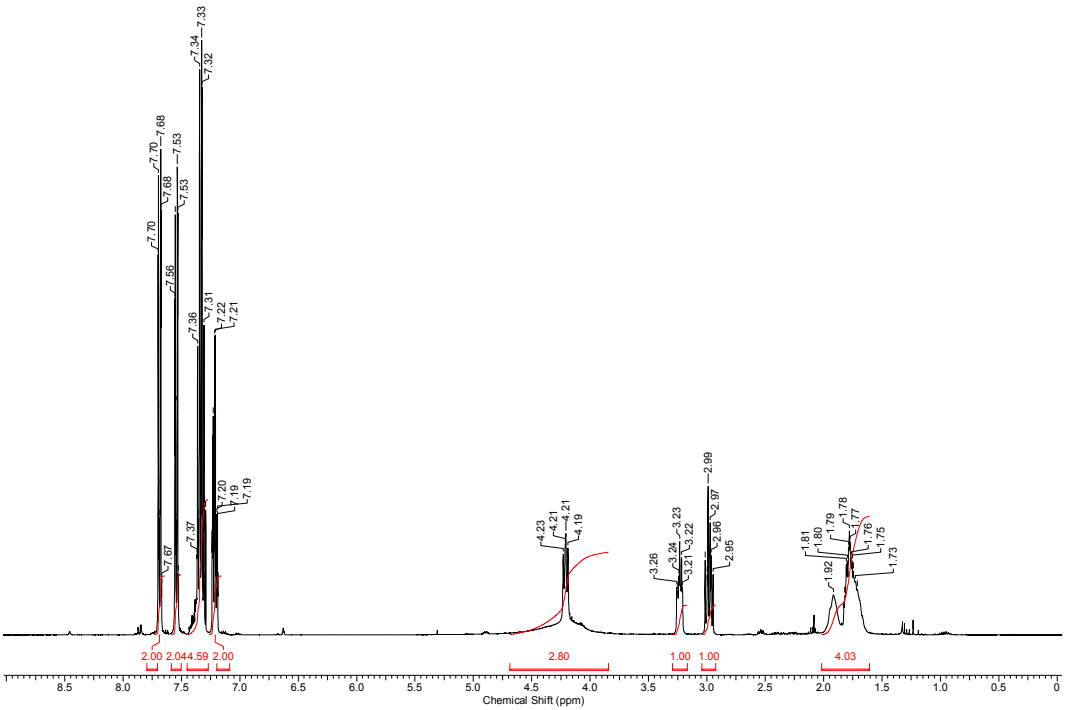
^{13}C NMR (100MHz, $CDCl_3$) δ = 167.1, 161.0, 141.4, 128.2, 127.2, 126.0, 97.5, 68.9, 43.0, 9.1

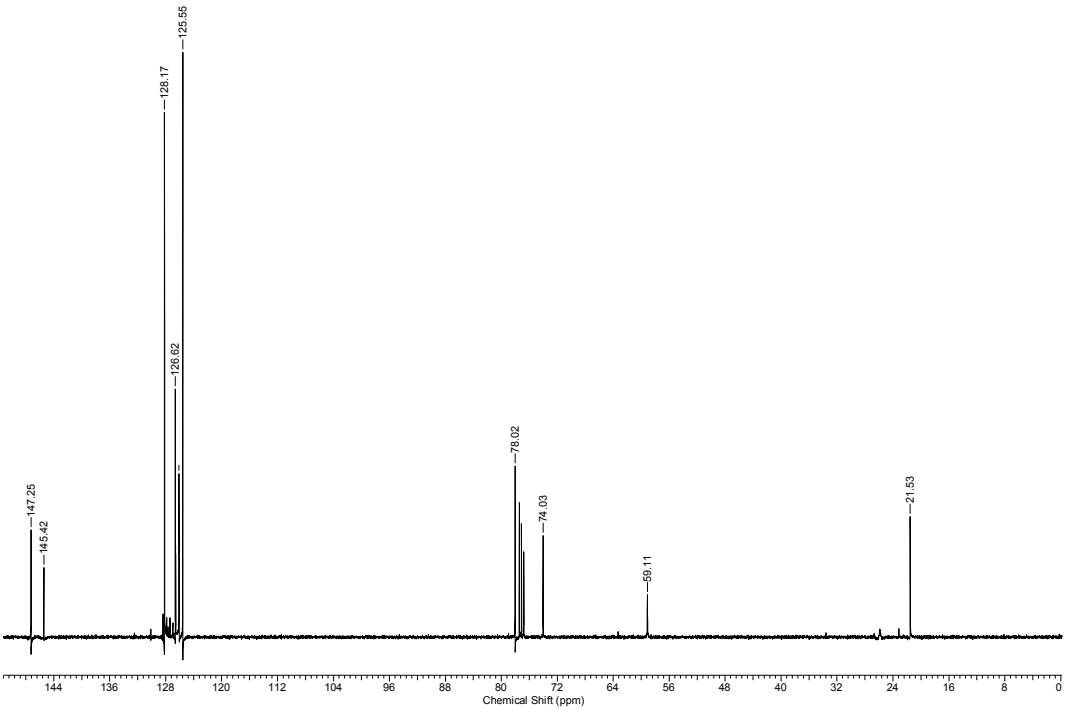
IR (neat)/cm^{-1}: 3332, 3191, 1658, 1583, 1382, 1178

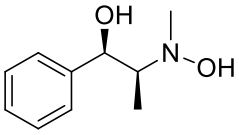
HRMS (ES +) Calc. $C_{13}H_{18}N_2O_3Na$ 273.1215; Found. 273.1209

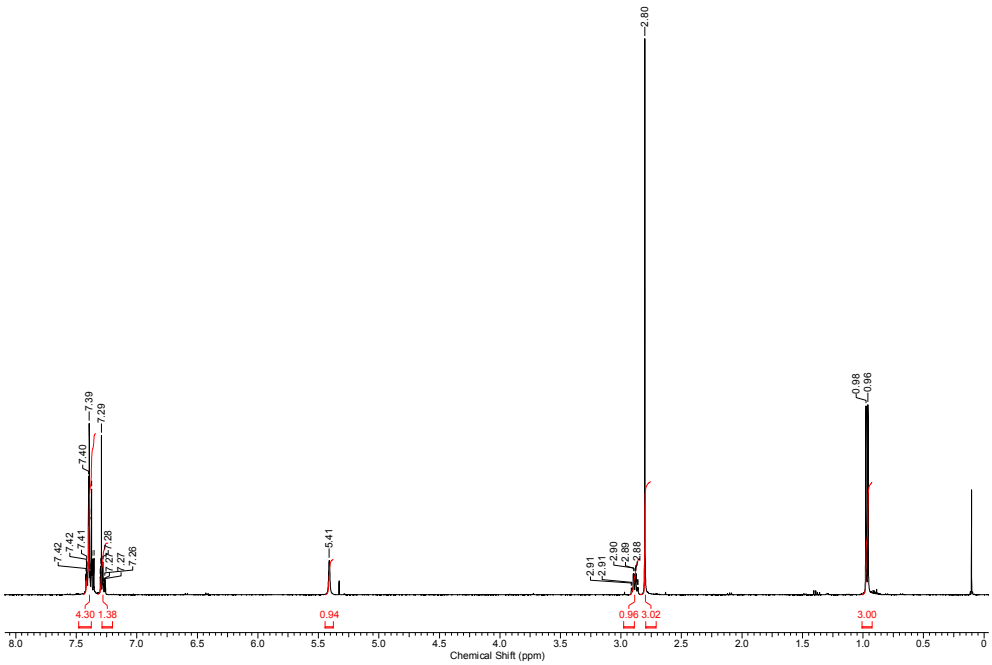
1.3 ^{1}H and ^{13}C spectra

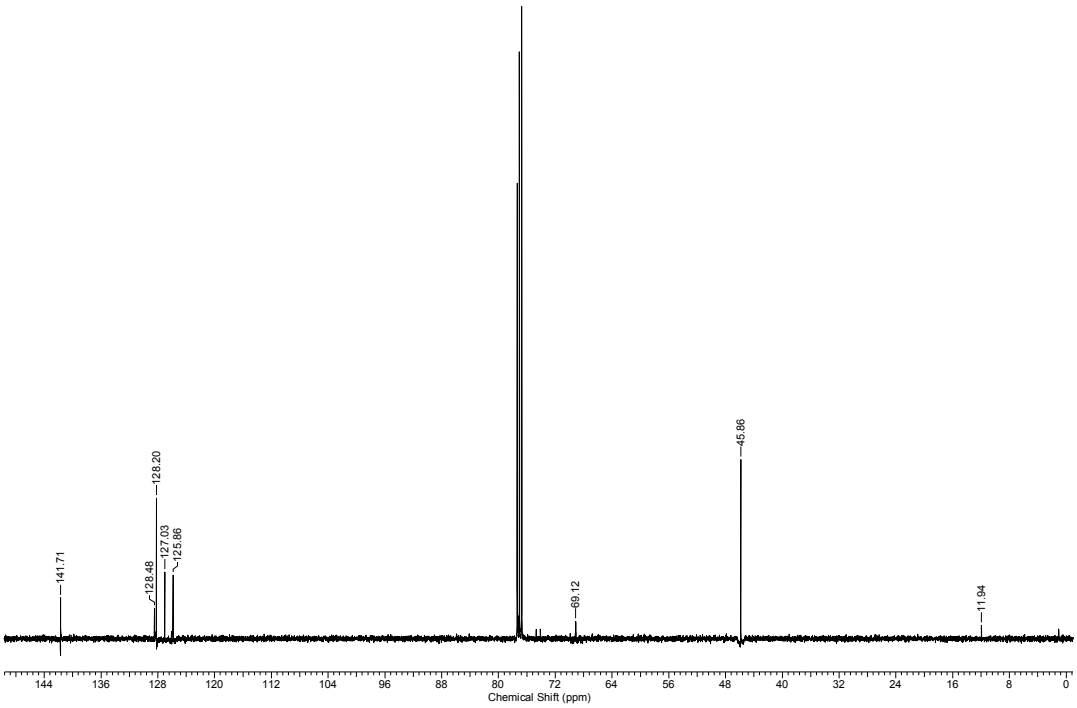


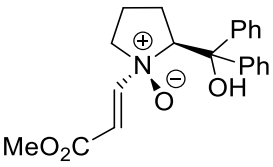


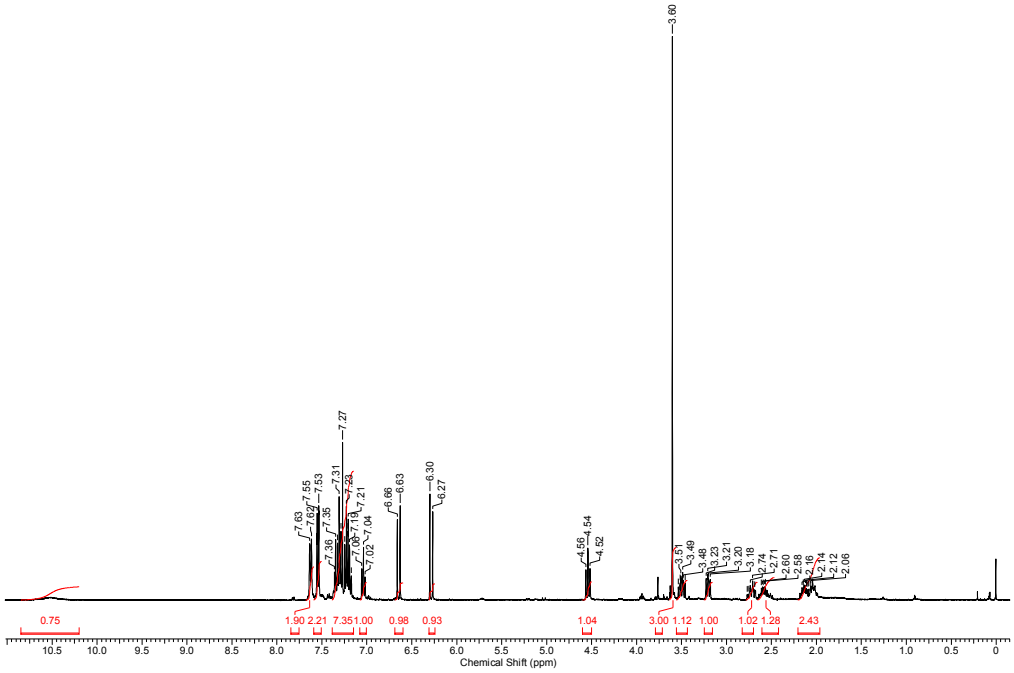


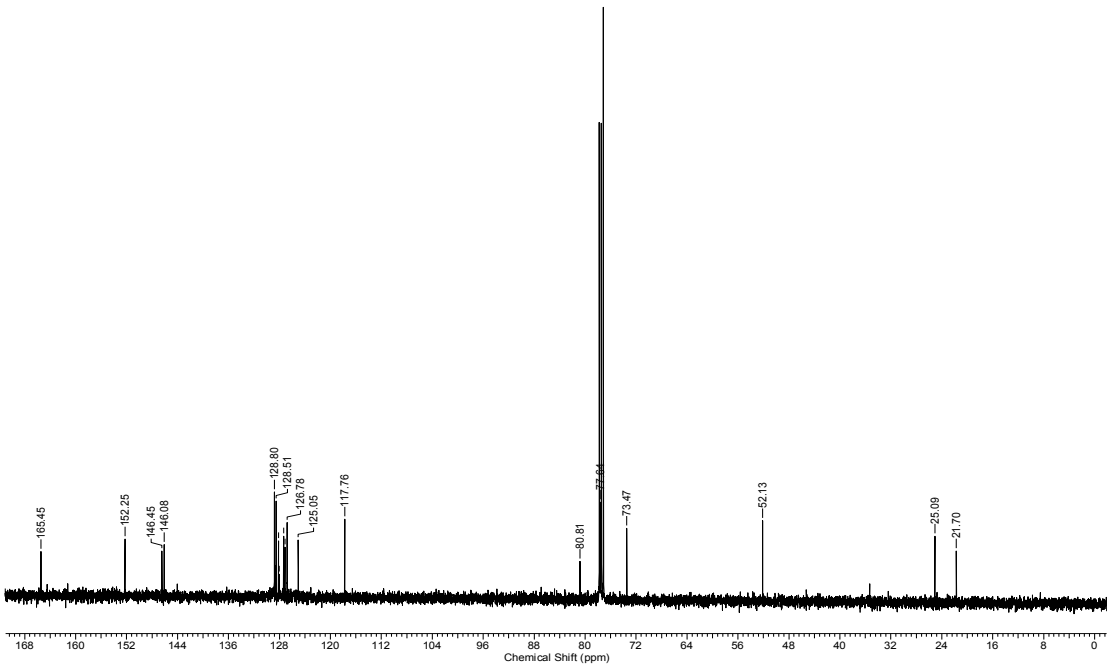

OH
N
OH

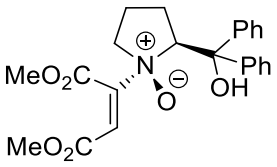

2.80
0.98
0.96
7.39
7.29
7.40
7.42
7.42
7.41
7.28
7.27
7.27
7.26
5.41
2.91
2.91
2.90
2.89
2.88
4.30
1.38
0.94
0.96
3.02
3.00
Chemical Shift (ppm)

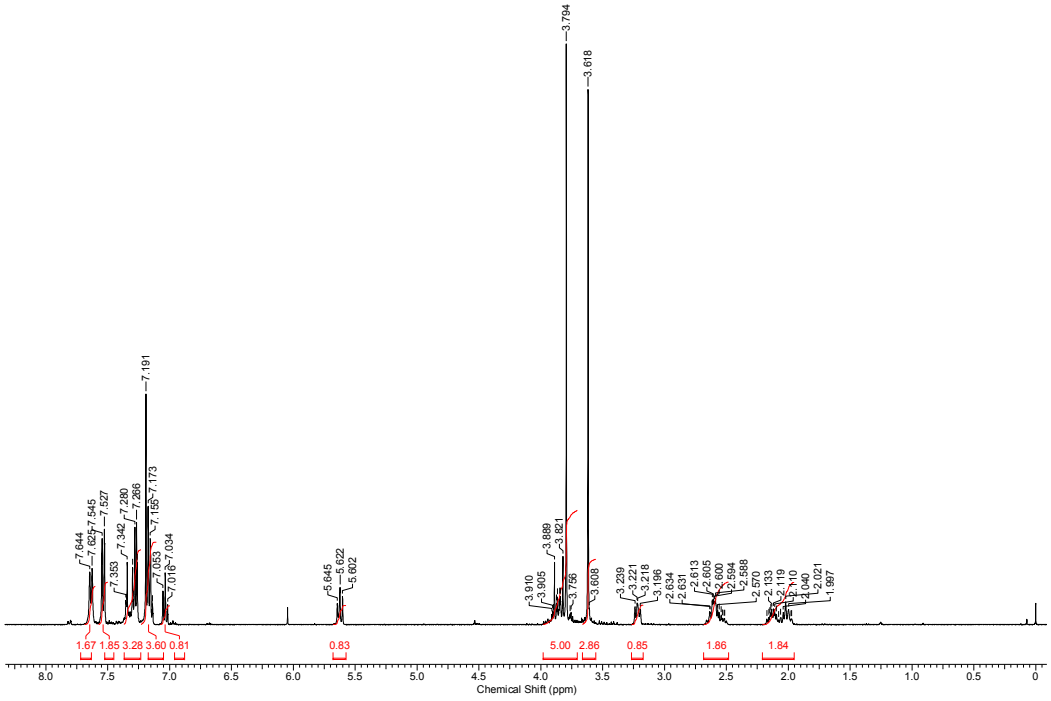

45.86
128.20
127.03
125.86
141.71
128.48
69.12
11.94
Chemical Shift (ppm)

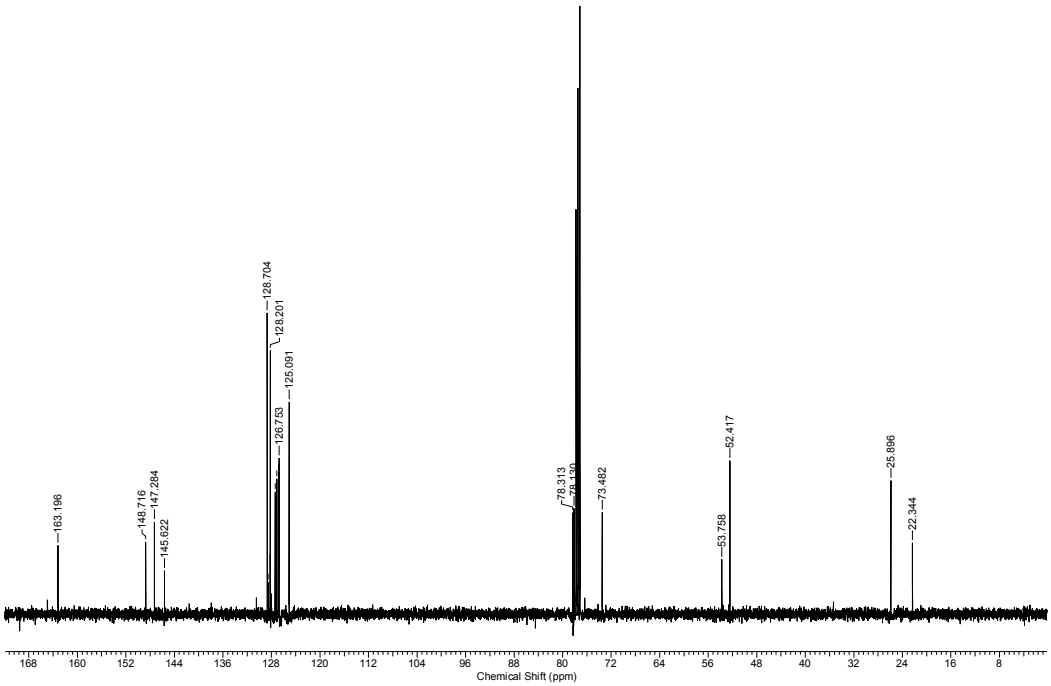

Ph
Ph
OH
N
O
MeO2C

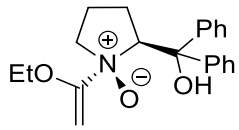

3.60
7.27
7.63
7.69
7.55
7.53
7.31
7.38
7.35
7.23
7.21
7.19
7.09
7.04
7.02
6.66
6.63
6.30
6.27
4.56
4.54
4.52
3.51
3.49
3.48
3.23
3.21
3.20
3.18
3.14
2.71
2.60
2.58
2.16
2.14
2.12
2.06
0.75
1.90 2.21 7.35 1.00
0.98
0.93
1.04
3.00 1.12
1.00
1.02 1.28
2.43
Chemical Shift (ppm)

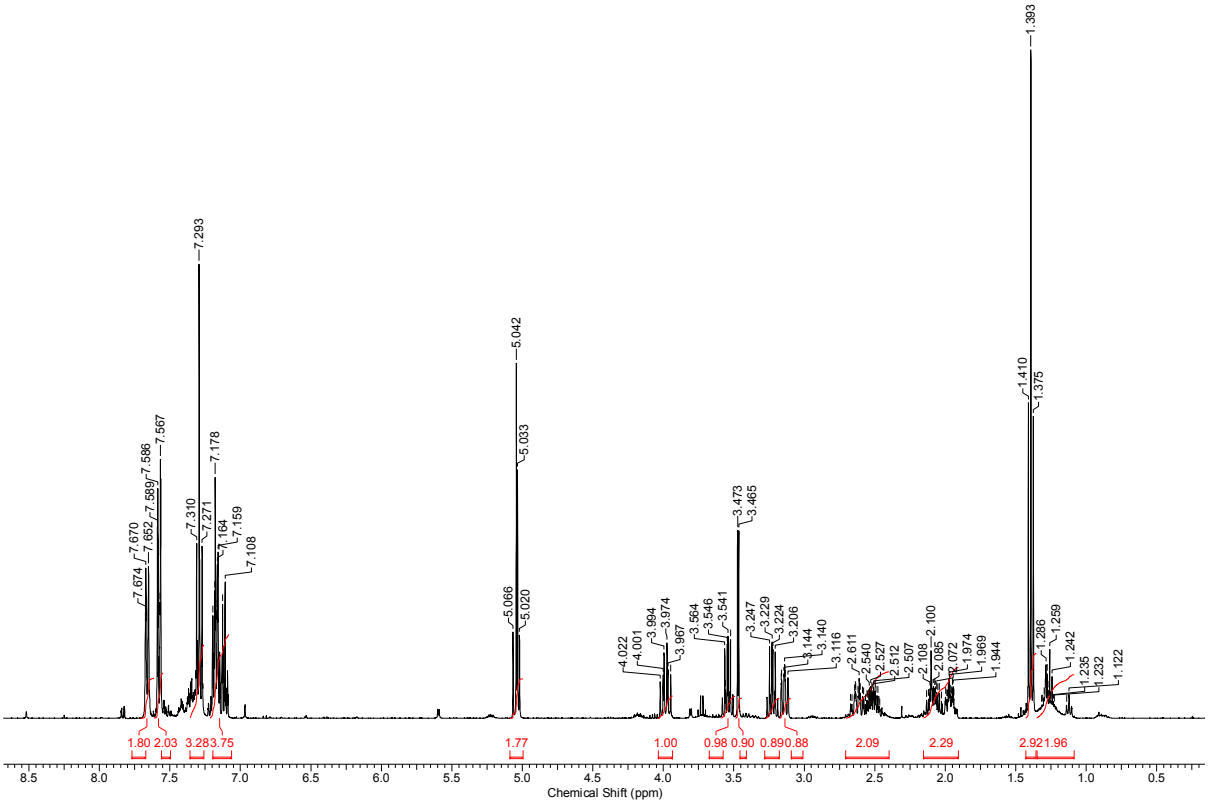

165.45
152.25
146.45
146.08
128.80
128.51
126.78
125.05
117.76
80.81
73.64
73.47
52.13
25.09
21.70
Chemical Shift (ppm)

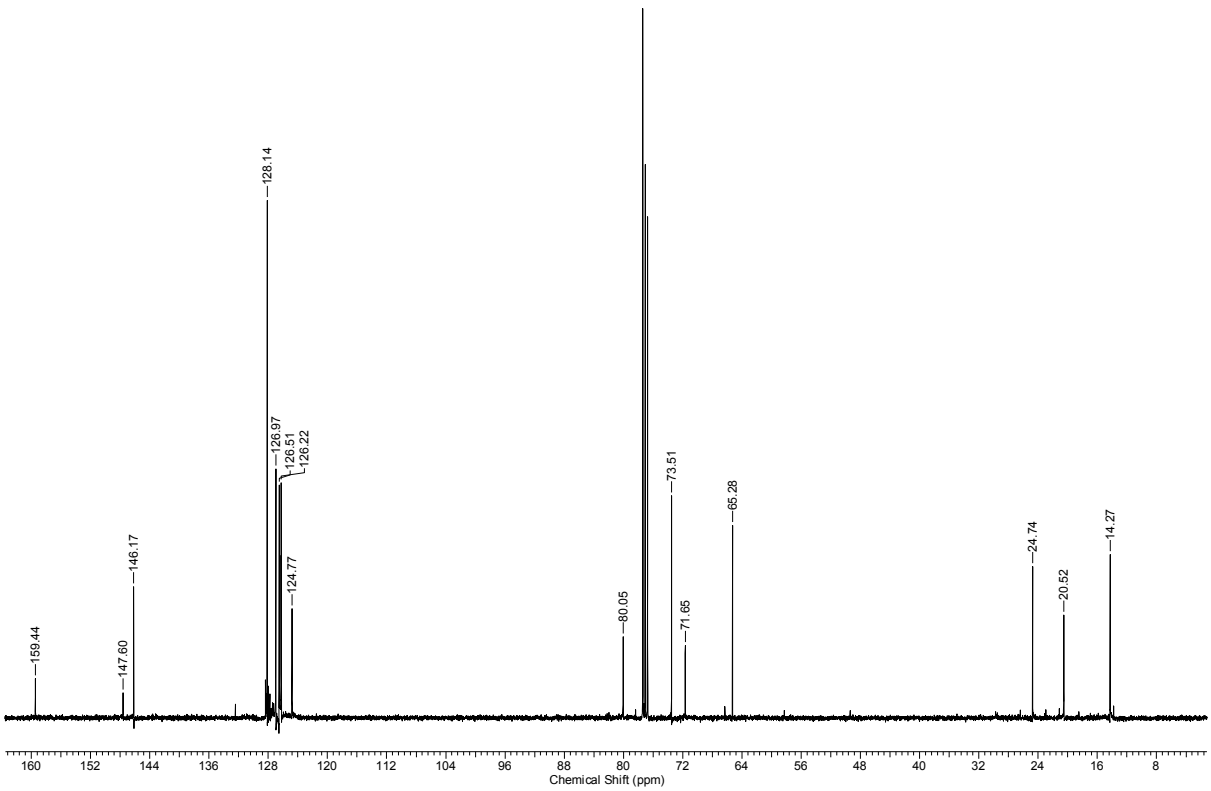

MeO2C
MeO2C
N
O
Ph
Ph
OH

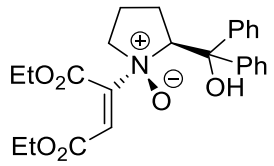

3.794
3.618
7.191
7.644
7.625
7.545
7.527
7.353
7.342
7.280
7.266
7.173
7.155
7.059
7.034
7.016
5.645
5.622
5.602
3.910
3.905
3.889
3.821
3.756
3.608
3.239
3.221
3.218
3.196
2.634
2.631
2.613
2.605
2.600
2.594
2.588
2.570
2.133
2.119
2.110
2.060
2.021
1.997
1.67 1.85 3.28 3.60 0.81
0.83
5.00 2.86
0.85
1.86
1.84
Chemical Shift (ppm)

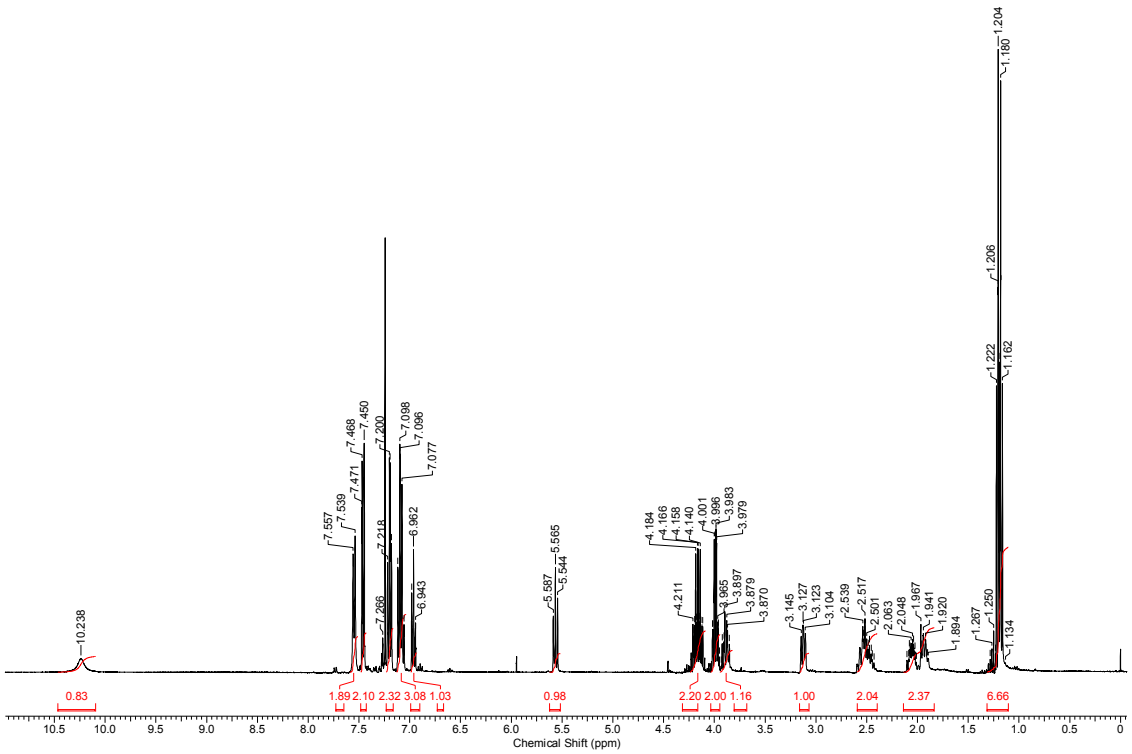

128.704
128.201
125.091
126.753
163.196
148.716
147.284
145.622
78.313
78.130
73.482
53.758
52.417
25.896
22.344
Chemical Shift (ppm)

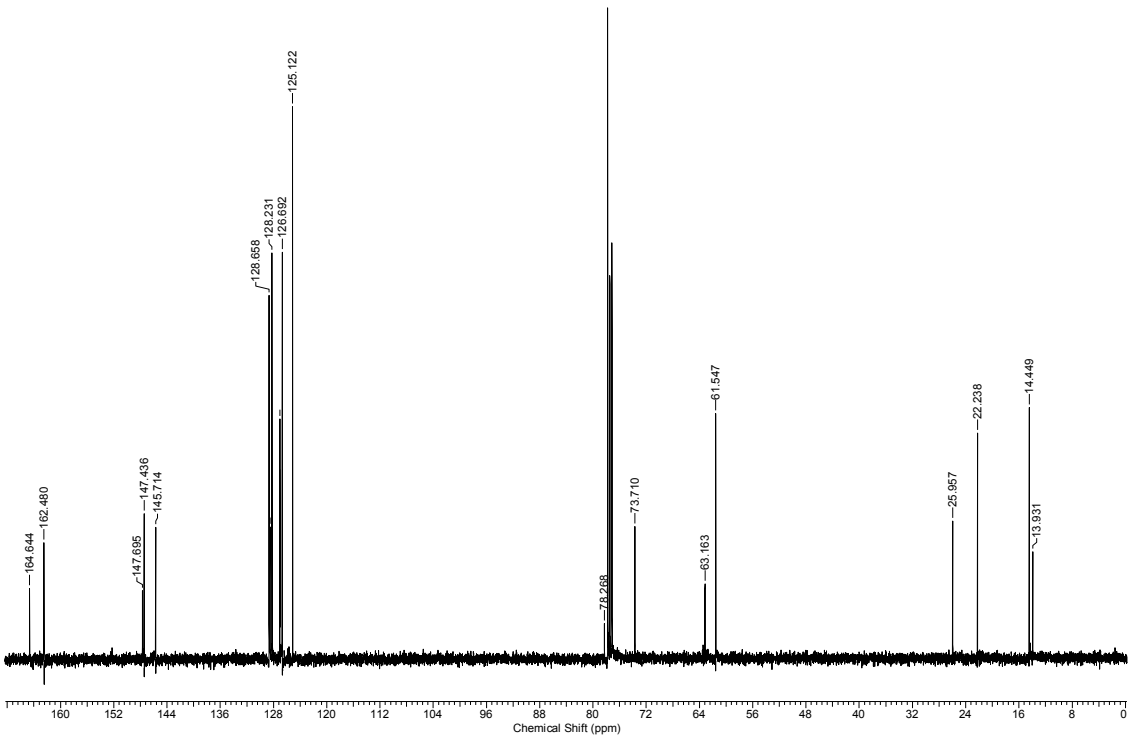

Ph
Ph
EtO
N
O
OH

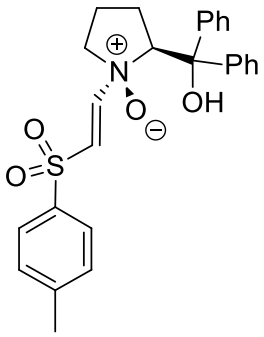

7.674
7.670
7.652
7.589
7.586
7.567
7.310
7.293
7.271
7.178
7.164
7.159
7.108
5.066
5.042
5.033
5.020
4.022
4.001
3.994
3.974
3.967
3.564
3.546
3.541
3.473
3.465
3.247
3.229
3.224
3.206
3.144
3.140
3.116
2.611
2.540
2.527
2.512
2.507
2.108
2.100
2.085
2.072
1.974
1.969
1.944
1.410
1.393
1.375
1.266
1.259
1.242
1.235
1.232
1.122
1.80 2.03 3.28 3.75
1.77
1.00
0.98 0.90 0.89 0.88
2.09
2.29
2.92 1.96
Chemical Shift (ppm)

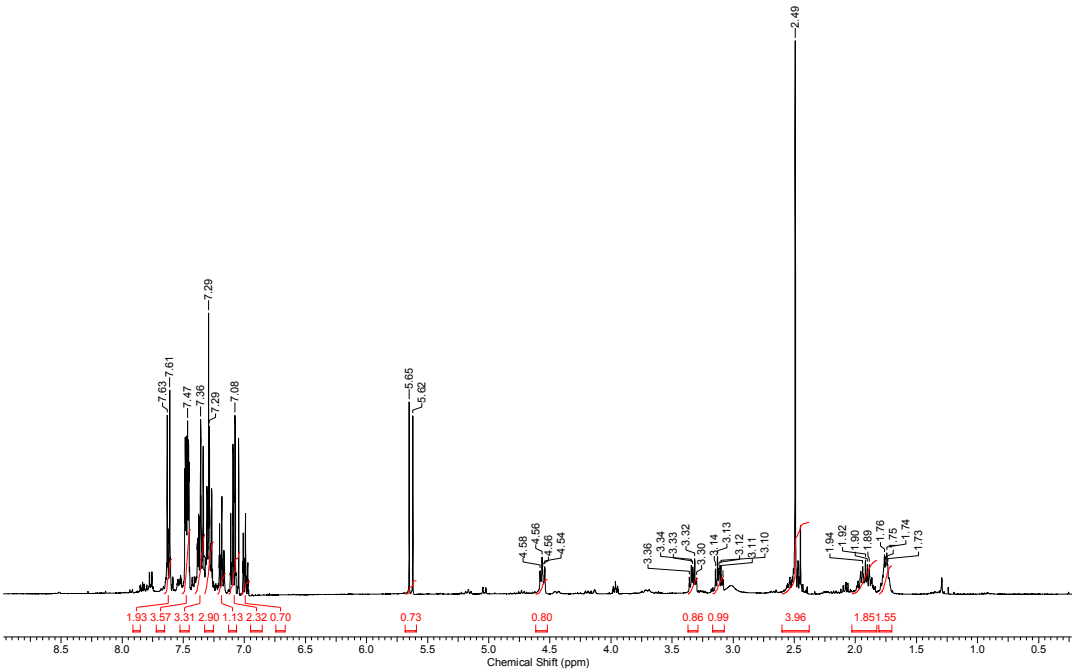

159.44
147.60
146.17
128.14
126.97
126.51
126.22
124.77
80.05
73.51
71.65
65.28
24.74
20.52
14.27
Chemical Shift (ppm)

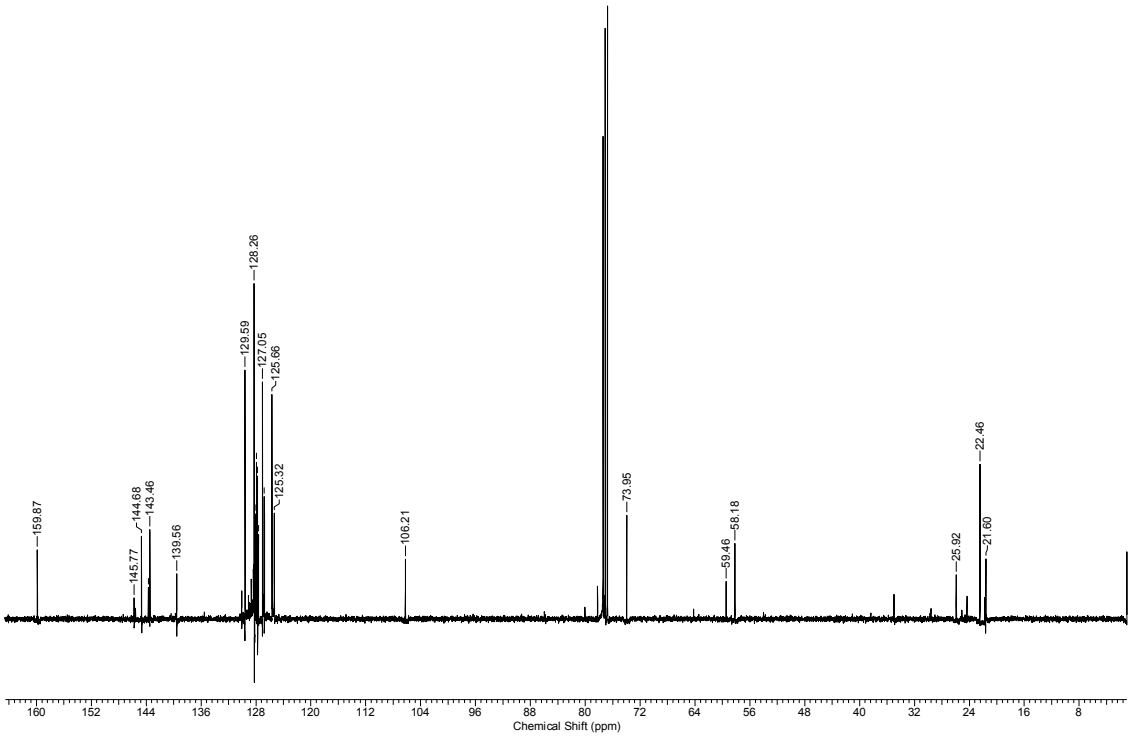

Ph
Ph
OH
EtO2C
EtO2C
N
O

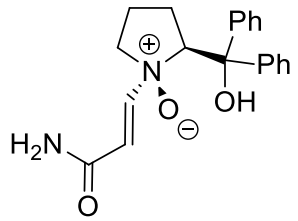

10.238
7.557
7.539
7.471
7.468
7.450
7.218
7.200
7.266
7.098
7.096
7.077
6.962
6.943
5.587
5.565
5.544
4.211
4.184
4.166
4.158
4.140
4.001
3.996
3.983
3.979
3.965
3.897
3.879
3.870
3.145
3.127
3.123
3.104
2.539
2.517
2.501
2.063
2.048
1.967
1.941
1.920
1.894
1.267
1.250
1.222
1.204
1.180
1.162
1.134
0.83
1.89
2.10
2.32
3.08
1.03
0.98
2.20
2.00
1.16
1.00
2.04
2.37
6.66
Chemical Shift (ppm)

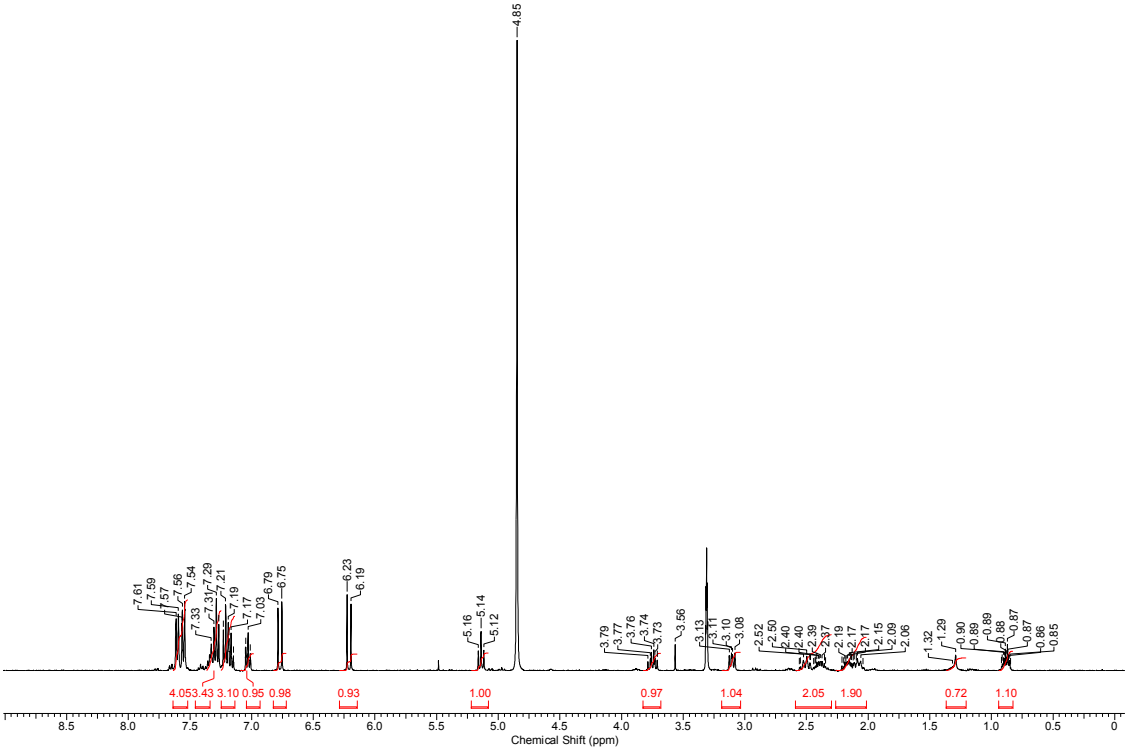

164.644
162.480
147.695
147.436
145.714
128.658
128.231
126.692
125.122
78.268
73.710
63.163
61.547
25.957
22.238
14.449
13.931
Chemical Shift (ppm)

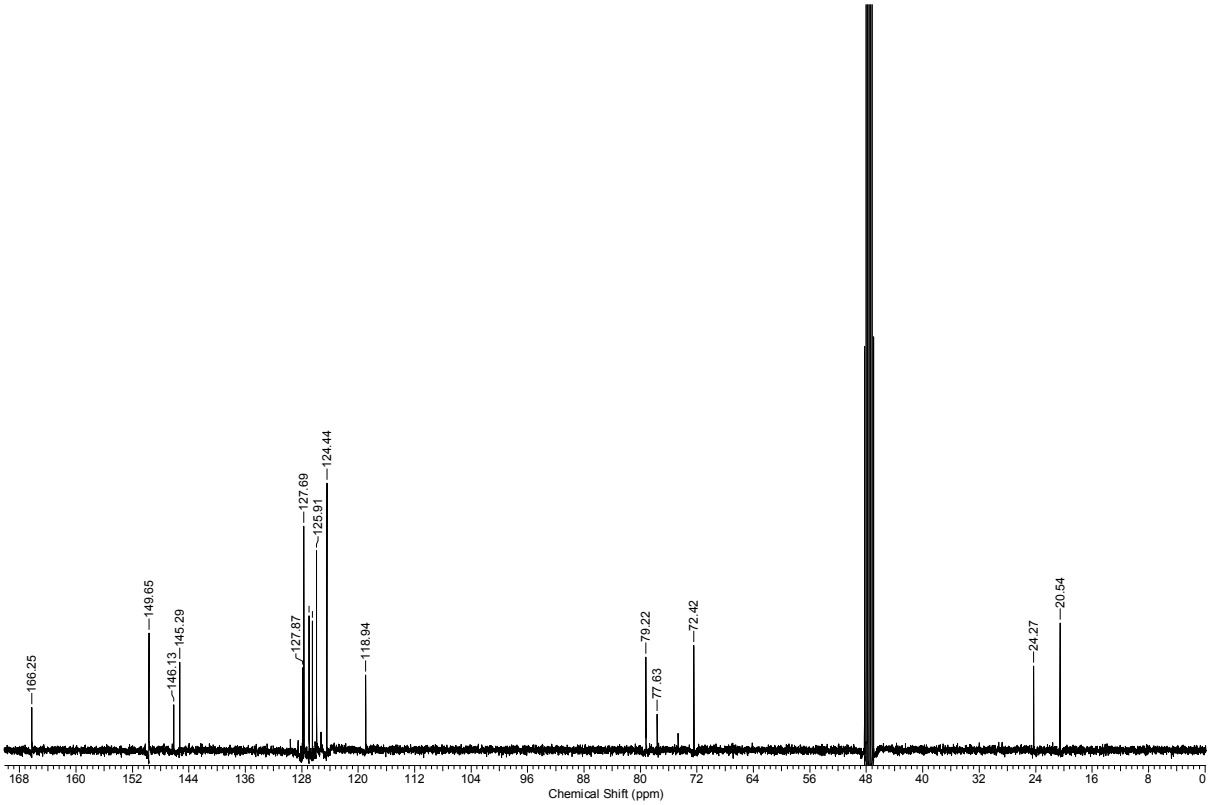

Ph
Ph
OH
N
O
O
O
S

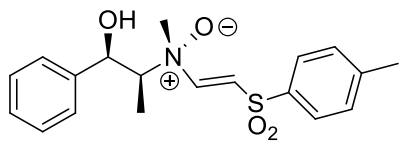

2.49
7.29
7.63
7.61
7.47
7.36
7.29
7.08
5.65
5.62
4.58
4.56
4.56
4.54
3.36
3.34
3.33
3.32
3.30
3.14
3.13
3.12
3.11
3.10
1.94
1.92
1.90
1.89
1.76
1.75
1.74
1.73
1.93 3.57 3.31 2.90 1.13 2.32 0.70
0.73
0.80
0.86 0.99
3.96
1.85 1.55
Chemical Shift (ppm)

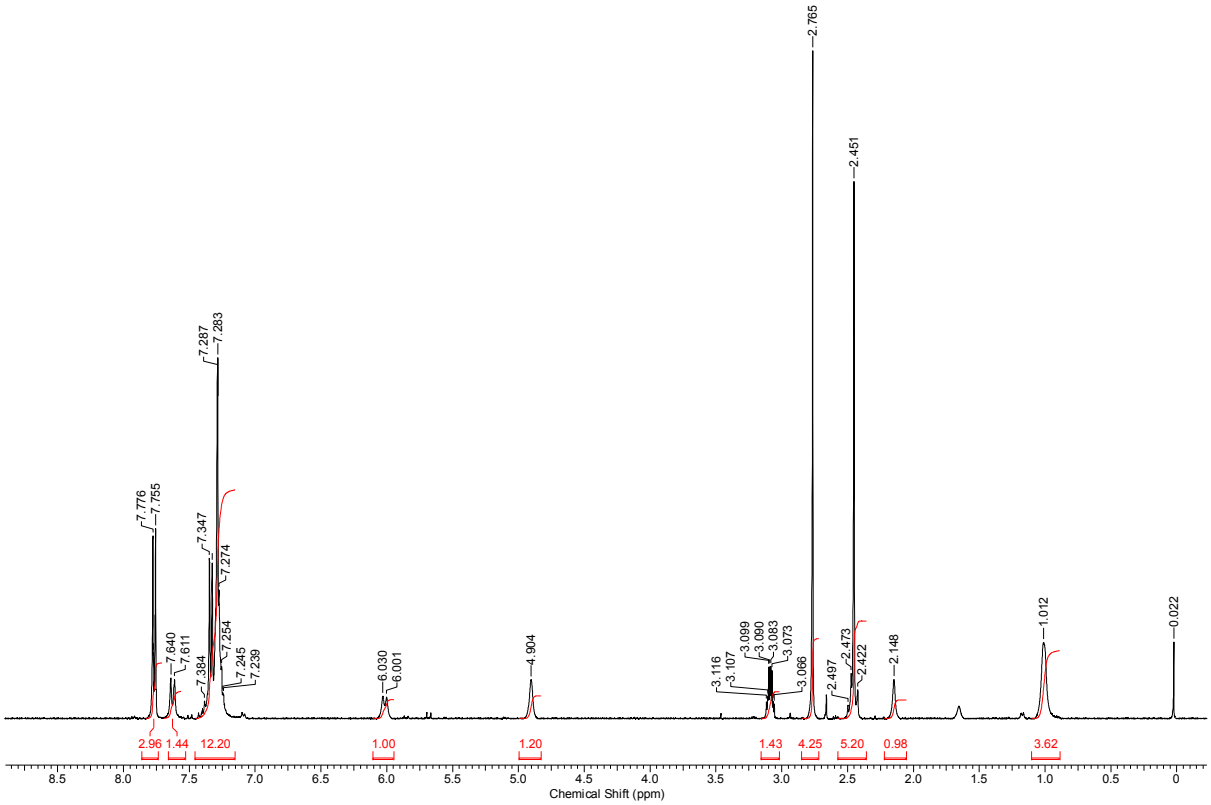

159.87
145.77
144.68
143.46
139.56
129.59
128.26
127.05
125.66
125.32
106.21
73.95
59.46
58.18
25.92
22.46
21.60
Chemical Shift (ppm)

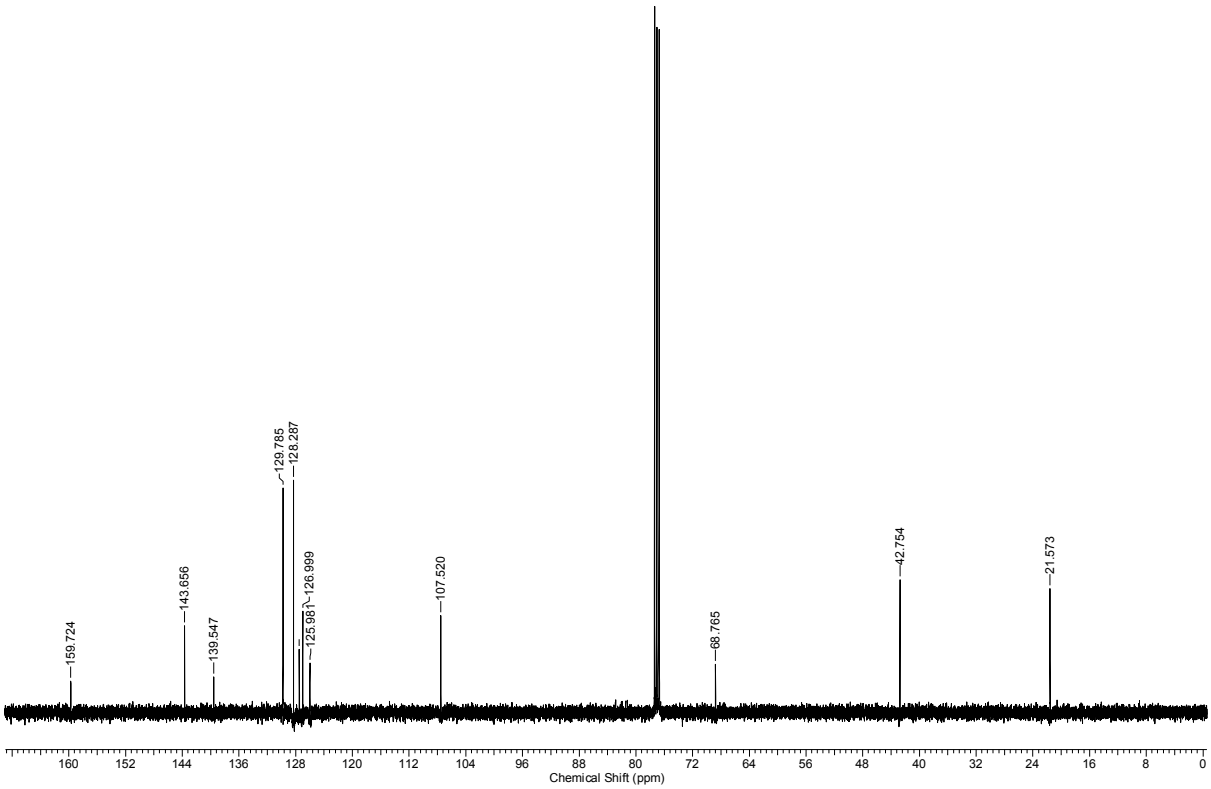

Ph
Ph
OH
N
O
H2N
O

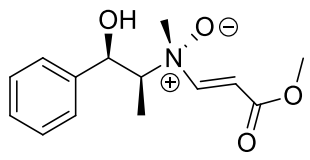

4.85
7.61
7.59
7.57
7.56
7.54
7.33
7.31
7.29
7.21
7.19
7.17
7.03
6.79
6.75
6.23
6.19
5.16
5.14
5.12
3.79
3.77
3.76
3.74
3.73
3.56
3.13
3.11
3.10
3.08
2.52
2.50
2.40
2.39
2.19
2.17
2.15
2.09
2.06
1.32
1.29
0.90
0.89
0.88
0.87
0.86
0.85
4.05 3.43 3.10 0.95 0.98
0.93
1.00
0.97
1.04
2.05 1.90
0.72
1.10
Chemical Shift (ppm)

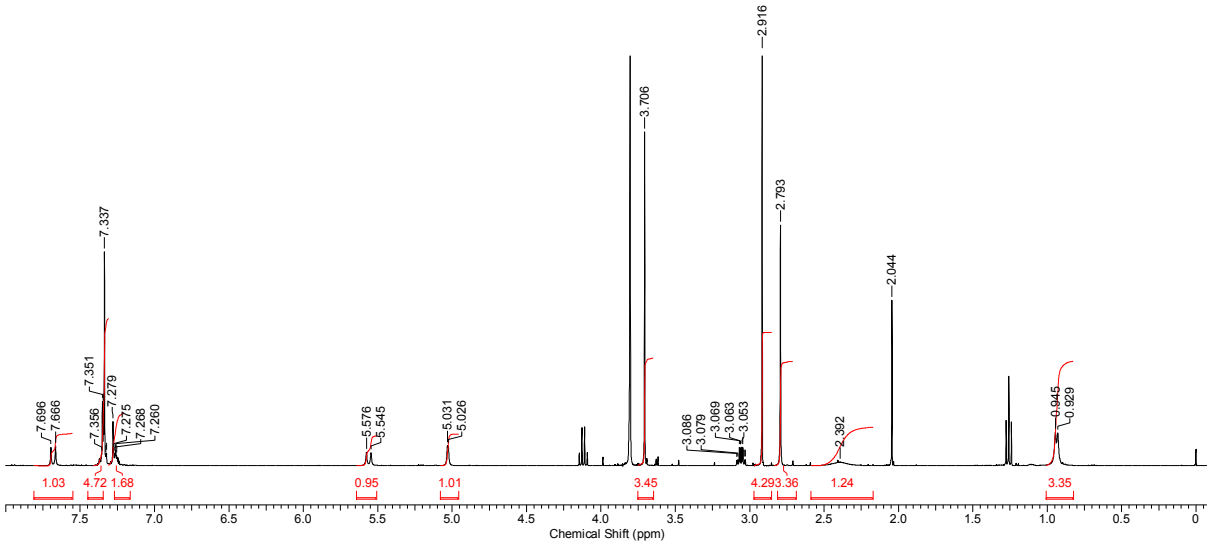

166.25
149.65
146.13
145.29
127.87
127.69
125.91
124.44
118.94
79.22
77.63
72.42
24.27
20.54
Chemical Shift (ppm)

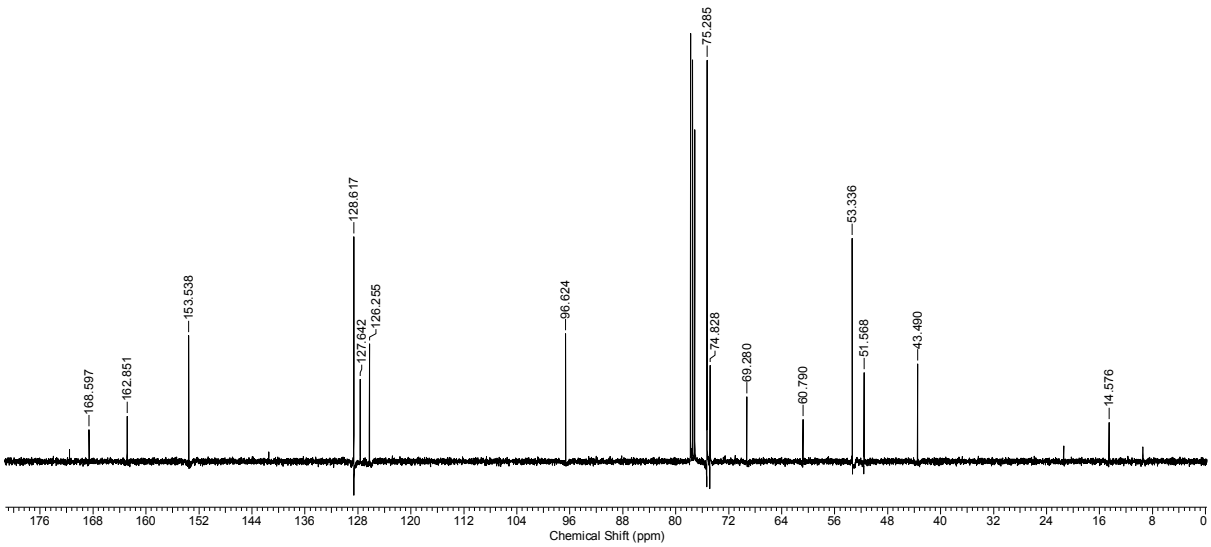

OH
N
O
S
O2

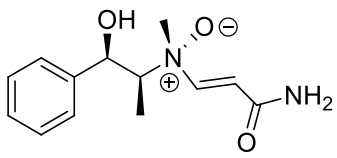

2.765
2.451
7.287
7.283
7.776
7.755
7.347
7.274
7.640
7.611
7.384
7.254
7.245
7.239
6.030
6.001
4.904
3.116
3.107
3.099
3.090
3.083
3.073
3.066
2.497
2.473
2.422
2.148
1.012
0.022
2.96
1.44
12.20
1.00
1.20
1.43
4.25
5.20
0.98
3.62
Chemical Shift (ppm)

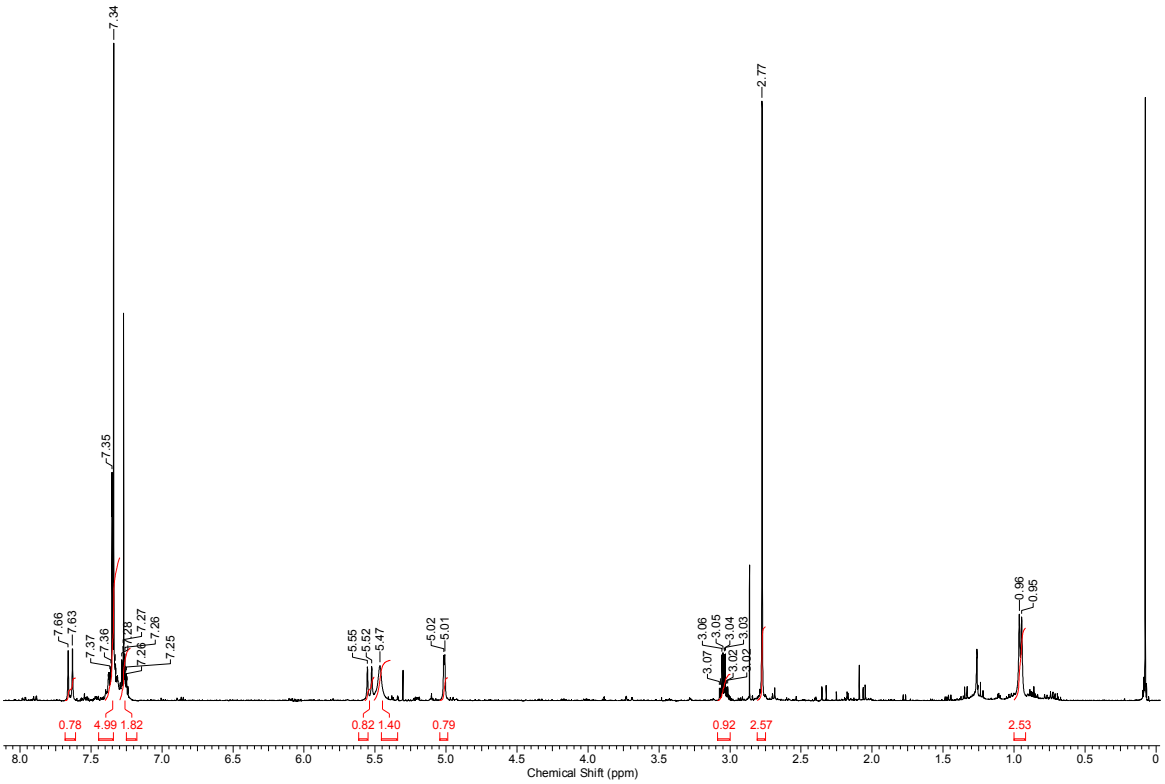

129.785
128.287
126.999
125.981
143.656
139.547
159.724
107.520
68.765
42.754
21.573
Chemical Shift (ppm)

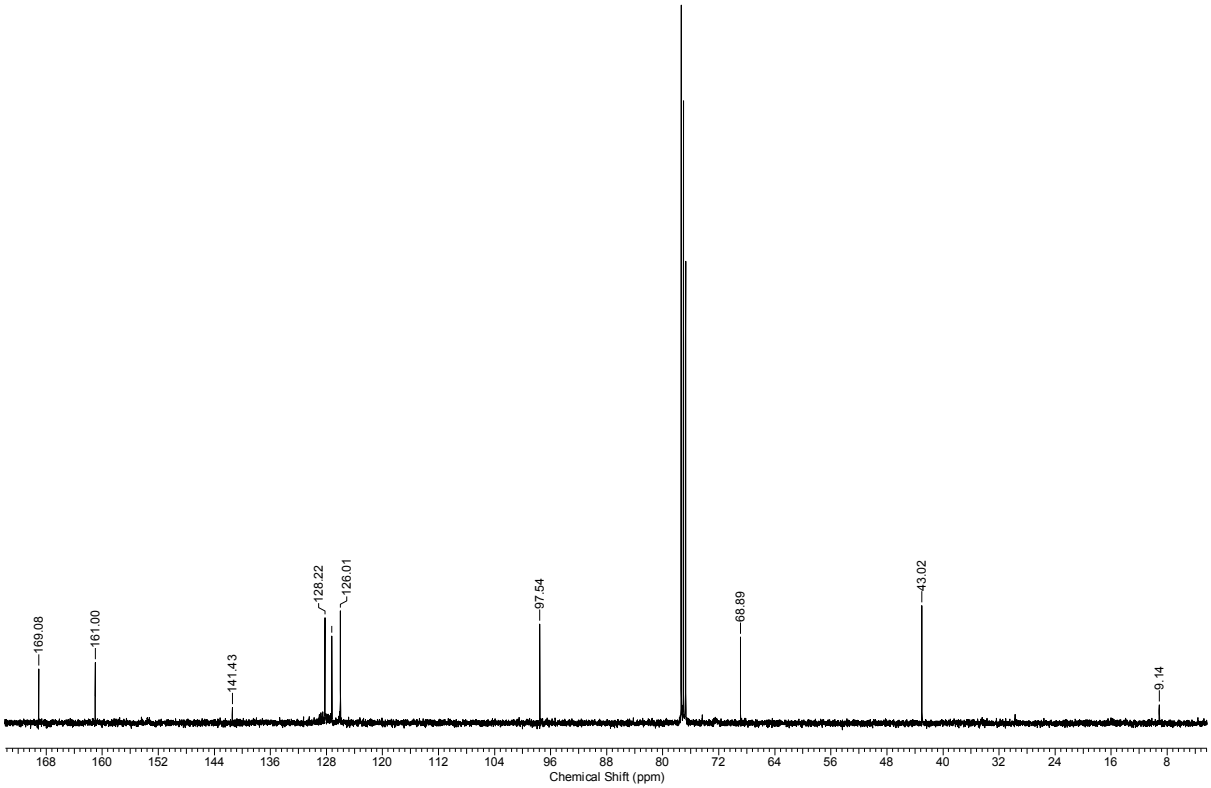



7.696
7.666
7.356
7.351
7.337
7.279
7.275
7.268
7.260
5.576
5.545
5.031
5.026
3.706
3.086
3.079
3.069
3.063
3.053
2.916
2.793
2.392
2.044
0.945
0.929
1.03
4.72
1.68
0.95
1.01
3.45
4.29
3.36
1.24
3.35
Chemical Shift (ppm)


168.597
162.851
153.538
128.617
127.642
126.255
96.624
75.285
74.828
69.280
60.790
53.336
51.568
43.490
14.576
Chemical Shift (ppm)


OH
N
O
NH2
O

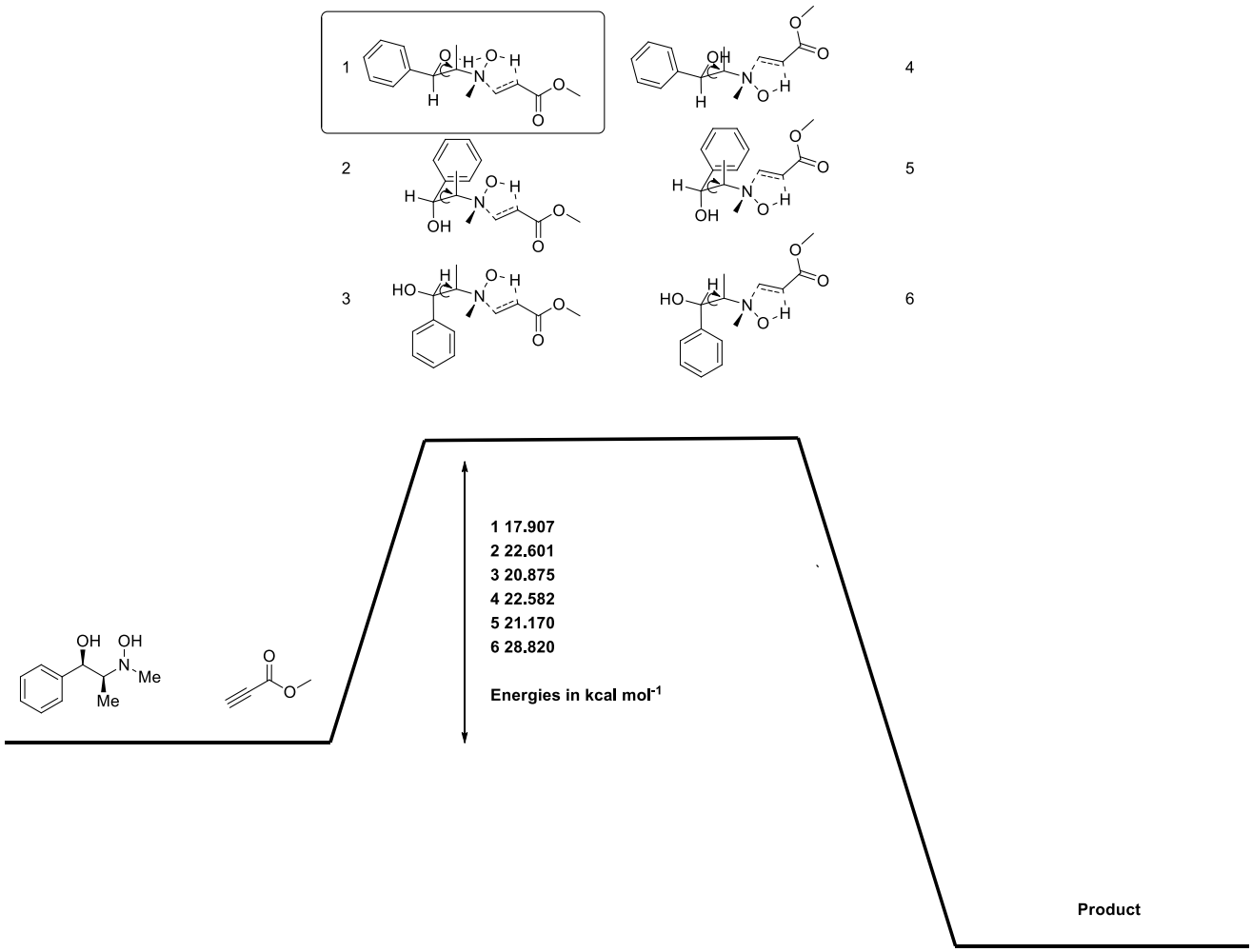

7.34
7.35
2.77
7.66
7.63
7.37
7.36
7.28
7.27
7.26
7.25
7.24
5.55
5.52
5.47
5.02
5.01
3.06
3.05
3.04
3.03
3.07
3.02
3.02
0.96
0.95
0.78
4.99
1.82
0.82
1.40
0.79
0.92
2.57
2.53
Chemical Shift (ppm)


169.08
161.00
141.43
128.22
126.01
97.54
68.89
43.02
9.14
Chemical Shift (ppm)

2. Computational methods

All stationary points were fully optimized with Gaussian 09 (Frisch, M. J.; et al. Gaussian 09, revision A.02; Gaussian, Inc.: Wallingford, CT, 2009) using M06-2X/6-311++(d.p) (Zhao, Y.; Truhlar, D. G. Theor. Chem. Acc. 2008, 120, 215– 241). An ultrafine grid density was used for numerical integration in all DFT calculations. Harmonic vibrational frequencies were computed for all optimized structures to verify that they were either minima or transition states, possessing zero imaginary frequencies and one imaginary frequency, respectively. Calculations were performed with M06-2X functional, which is constructed to include nonlocal effects of electronic dispersion and is found to give good estimates for reaction enthalpies in bond-forming reactions.

Activation Energies for the Six Verified TS



Coordinates of Reactants and Transition States

Methyl propiolate

6	3.683894000	-1.283334000	0.979796000
6	2.797307000	-0.788020000	1.615073000

1	2.008691000	-0.348308000	2.179492000
6	4.799334000	-1.848735000	0.234846000
8	5.935926000	-1.484109000	0.347179000
8	4.389408000	-2.819113000	-0.583649000
6	5.424672000	-3.433350000	-1.358432000
1	6.167079000	-3.886209000	-0.701396000
1	5.910129000	-2.691251000	-1.992129000
1	4.927659000	-4.189272000	-1.959287000

Ephedrine hydroxylamine

6	-0.382604000	1.270207000	0.312093000
1	-0.695652000	1.082319000	1.343582000
7	1.086383000	1.361038000	0.400310000
6	1.542389000	2.518287000	1.160022000
1	1.289169000	3.466262000	0.673551000
1	2.624701000	2.458209000	1.277285000
1	1.081428000	2.477657000	2.148781000
8	1.589849000	1.527065000	-0.936250000
1	2.304000000	0.884270000	-0.985861000
6	-1.076095000	2.528214000	-0.213895000
1	-1.011176000	3.347006000	0.503709000
1	-2.132020000	2.317987000	-0.392895000
1	-0.632225000	2.853796000	-1.155984000
6	-0.767434000	0.019335000	-0.508402000
1	-0.056598000	-0.771186000	-0.230392000
6	-2.163215000	-0.447913000	-0.154927000
6	-4.735792000	-1.272220000	0.569074000
6	-2.392127000	-1.055927000	1.080355000
6	-3.231264000	-0.265610000	-1.029301000
6	-4.511968000	-0.675453000	-0.666127000
6	-3.669189000	-1.464768000	1.443466000
1	-1.560028000	-1.219100000	1.759446000
1	-3.045781000	0.188604000	-1.994368000
1	-5.336611000	-0.529969000	-1.354303000
1	-3.832027000	-1.939345000	2.404064000
1	-5.732618000	-1.592419000	0.848186000
8	-0.712234000	0.259448000	-1.899517000
1	0.109137000	0.734604000	-2.067002000

TS 1

6	-0.336365000	1.295042000	0.267608000
1	-0.591190000	1.014744000	1.296631000
7	1.133229000	1.483958000	0.294068000
6	1.596303000	2.673506000	1.002936000
1	1.310877000	3.585988000	0.475843000
1	2.681709000	2.615708000	1.078632000
1	1.159157000	2.670464000	2.004016000
8	1.674585000	1.464273000	-0.974514000
1	2.344111000	0.720044000	-0.890731000
6	2.897433000	-0.547893000	0.368187000
6	2.063426000	-0.084045000	1.149988000

1	1.526958000	-0.015730000	2.077408000
6	3.977949000	-1.400425000	-0.055914000
8	5.148725000	-1.165722000	0.098910000
8	3.513940000	-2.497660000	-0.682024000
6	-1.101537000	2.555984000	-0.124391000
1	-1.018800000	3.329075000	0.640255000
1	-2.157760000	2.310741000	-0.246986000
1	-0.734508000	2.950299000	-1.072992000
6	-0.693122000	0.099957000	-0.648275000
1	0.063376000	-0.678961000	-0.493485000
6	-2.042662000	-0.463291000	-0.259195000
6	-4.523827000	-1.474534000	0.534522000
6	-2.161618000	-1.205458000	0.916493000
6	-3.172423000	-0.241455000	-1.041676000
6	-4.408280000	-0.745038000	-0.643067000
6	-3.394040000	-1.707934000	1.314410000
1	-1.277784000	-1.404440000	1.516702000
1	-3.070410000	0.314331000	-1.965310000
1	-5.282505000	-0.569493000	-1.259096000
1	-3.472569000	-2.288366000	2.226095000
1	-5.486041000	-1.867521000	0.840518000
8	-0.733592000	0.480643000	-2.005259000
1	0.133662000	0.842928000	-2.217547000
6	4.522918000	-3.392672000	-1.152539000
1	3.988384000	-4.209332000	-1.630257000
1	5.123663000	-3.760796000	-0.320562000
1	5.175166000	-2.889361000	-1.866680000

TS 2

6	-2.326362000	0.443084000	-0.353921000
1	-2.855997000	0.019528000	-1.213730000
7	-1.842973000	-0.743489000	0.405352000
6	-2.905423000	-1.690807000	0.756277000
1	-3.608626000	-1.248477000	1.462931000
1	-2.433345000	-2.560012000	1.212074000
1	-3.425642000	-1.989551000	-0.155818000
8	-1.201025000	-0.356255000	1.557912000
1	-0.277975000	-0.706877000	1.414260000
6	0.558614000	-1.837410000	0.124232000
6	-0.508215000	-1.836950000	-0.506616000
1	-1.129750000	-2.150473000	-1.326046000
6	1.948261000	-2.094040000	0.353107000
8	2.849576000	-1.413286000	-0.079715000
6	-3.291607000	1.274099000	0.490842000
1	-4.205149000	0.721167000	0.710980000
1	-3.580756000	2.175133000	-0.053105000
1	-2.820205000	1.564713000	1.430211000
6	-1.198963000	1.301868000	-0.988830000
1	-1.741837000	2.128429000	-1.458032000
8	-0.596317000	0.622442000	-2.066550000
1	0.048439000	-0.006336000	-1.727315000

6	-0.201511000	1.922421000	-0.020333000
6	1.572715000	3.085901000	1.813788000
6	-0.582258000	3.030717000	0.738120000
6	1.097355000	1.435828000	0.117727000
6	1.974425000	2.007192000	1.034342000
6	0.292055000	3.604651000	1.653641000
1	-1.568921000	3.461228000	0.605183000
1	1.465466000	0.609092000	-0.477751000
1	2.975581000	1.602328000	1.125259000
1	-0.024139000	4.464088000	2.233169000
1	2.257056000	3.531642000	2.525813000
8	2.143740000	-3.164983000	1.142556000
6	3.511105000	-3.453334000	1.437113000
1	4.064200000	-3.658215000	0.520282000
1	3.492196000	-4.331336000	2.077310000
1	3.975432000	-2.612054000	1.952326000

TS 3

6	-0.916221000	1.937586000	0.181765000
1	-1.427914000	1.870412000	1.150207000
7	0.463027000	1.442772000	0.434377000
6	1.301039000	2.398683000	1.168477000
1	1.504720000	3.281621000	0.562634000
1	2.234171000	1.893854000	1.412238000
1	0.784734000	2.681610000	2.088567000
8	1.095266000	1.109633000	-0.743023000
1	1.454154000	0.196716000	-0.511088000
6	1.452396000	-0.943704000	0.954449000
6	0.644256000	-0.174857000	1.499617000
1	-0.030803000	0.100956000	2.289231000
6	2.221667000	-2.156330000	0.942257000
8	1.893057000	-3.207955000	0.448386000
8	3.423266000	-1.972863000	1.533875000
6	-0.934589000	3.380761000	-0.322569000
1	-0.602810000	4.086759000	0.438723000
1	-1.953048000	3.640092000	-0.606398000
1	-0.289431000	3.475856000	-1.199826000
6	-1.682856000	1.035921000	-0.804203000
1	-1.225407000	1.149740000	-1.792843000
8	-3.003051000	1.574762000	-0.807073000
1	-3.571031000	0.955166000	-1.273137000
6	-1.691465000	-0.423659000	-0.424104000
6	-1.576400000	-3.088290000	0.384199000
6	-0.978901000	-1.354290000	-1.174365000
6	-2.386706000	-0.842994000	0.710178000
6	-2.328848000	-2.172320000	1.113255000
6	-0.910598000	-2.681147000	-0.766971000
1	-0.439076000	-1.026209000	-2.056848000
1	-2.966207000	-0.122057000	1.278740000
1	-2.860875000	-2.491655000	2.002018000
1	-0.312360000	-3.390608000	-1.323691000

1	-1.502524000	-4.117651000	0.713350000
6	4.273419000	-3.117867000	1.531792000
1	5.187912000	-2.804323000	2.029095000
1	4.483024000	-3.437771000	0.510465000
1	3.807857000	-3.942888000	2.071875000

TS 4

6	-2.489398000	-0.200635000	0.266552000
1	-3.384194000	-0.408708000	-0.335171000
7	-1.512025000	-1.284547000	-0.044566000
6	-2.103325000	-2.624979000	0.068717000
1	-1.369665000	-3.335759000	-0.305522000
1	-3.021818000	-2.685785000	-0.521176000
1	-2.309257000	-2.843463000	1.116162000
8	-1.035178000	-1.132050000	-1.329418000
1	-0.031988000	-1.230111000	-1.165602000
6	1.091454000	-1.516582000	0.167093000
6	0.145616000	-1.424978000	0.969949000
1	-0.264369000	-1.418866000	1.960899000
6	2.502908000	-1.719436000	-0.040824000
8	3.343364000	-0.859526000	-0.127349000
6	-2.870574000	-0.252105000	1.744020000
1	-3.396399000	-1.173933000	1.993584000
1	-3.547208000	0.574973000	1.964882000
1	-2.001129000	-0.155643000	2.393768000
6	-2.022216000	1.201486000	-0.203312000
1	-2.727414000	1.901145000	0.255953000
6	-0.624485000	1.570519000	0.261123000
6	1.970124000	2.049101000	1.190068000
6	0.452434000	1.575536000	-0.621429000
6	-0.396713000	1.878569000	1.602434000
6	0.894439000	2.107676000	2.068196000
6	1.742453000	1.804166000	-0.159844000
1	0.286116000	1.384267000	-1.674575000
1	-1.232668000	1.953989000	2.290358000
1	1.057174000	2.336486000	3.115168000
1	2.577441000	1.760651000	-0.847255000
1	2.980341000	2.200839000	1.549928000
8	-2.213560000	1.346464000	-1.590703000
1	-1.763885000	0.607022000	-2.015777000
8	2.783158000	-3.033902000	-0.174745000
6	4.156333000	-3.331317000	-0.424079000
1	4.489593000	-2.854038000	-1.346189000
1	4.209883000	-4.413425000	-0.512624000
1	4.779649000	-2.982995000	0.399973000

TS 5

6	-0.961716000	1.841183000	0.098842000
1	-1.761493000	1.945549000	0.842784000
7	0.274833000	1.481972000	0.844168000
6	0.865405000	2.583130000	1.609517000

1	1.655905000	2.153165000	2.220805000
1	0.115652000	3.056436000	2.250510000
1	1.293070000	3.317843000	0.927834000
8	0.001611000	0.457386000	1.721048000
1	0.588624000	-0.275263000	1.380268000
6	1.945433000	-0.428068000	0.056222000
6	1.709730000	0.745581000	-0.262579000
1	1.906208000	1.628788000	-0.841228000
6	2.556648000	-1.717312000	-0.059188000
8	2.187468000	-2.597537000	-0.801948000
8	3.589163000	-1.860389000	0.794518000
6	-0.774257000	3.157418000	-0.652025000
1	-0.650888000	4.001529000	0.025716000
1	-1.657176000	3.335686000	-1.261997000
1	0.091995000	3.109168000	-1.318146000
6	-1.380819000	0.736085000	-0.895209000
1	-0.587595000	0.634598000	-1.646465000
8	-2.561161000	1.253331000	-1.508556000
1	-3.016232000	0.519705000	-1.931144000
6	-1.658389000	-0.626625000	-0.299483000
6	-2.185575000	-3.145588000	0.779536000
6	-0.892879000	-1.726273000	-0.675743000
6	-2.711923000	-0.799791000	0.600719000
6	-2.974638000	-2.052861000	1.136850000
6	-1.146432000	-2.981635000	-0.128502000
1	-0.073900000	-1.610116000	-1.376584000
1	-3.320280000	0.052528000	0.884925000
1	-3.789681000	-2.179264000	1.839832000
1	-0.522195000	-3.819073000	-0.416428000
1	-2.386491000	-4.121133000	1.206743000
6	4.229430000	-3.135239000	0.754781000
1	3.521896000	-3.925891000	1.006343000
1	5.025339000	-3.085020000	1.493301000
1	4.638482000	-3.327455000	-0.237481000

TS 6

6	-0.479387000	1.135687000	-0.034378000
1	-1.109622000	1.696331000	0.664405000
7	0.908315000	1.646355000	0.213217000
6	1.060087000	3.078124000	-0.061864000
1	2.041602000	3.377215000	0.299971000
1	0.280761000	3.646628000	0.450578000
1	0.998546000	3.242385000	-1.137045000
8	1.194739000	1.448059000	1.562789000
1	1.952699000	0.832320000	1.543016000
6	2.727946000	-0.246748000	-0.176261000
6	2.203781000	0.753237000	-0.715448000
1	2.241231000	1.349186000	-1.612885000
6	2.721158000	-1.321160000	0.735794000
8	1.959327000	-2.276450000	0.661298000
8	3.641370000	-1.216118000	1.717665000

6	-0.914741000	1.396430000	-1.468477000
1	-1.016872000	2.459378000	-1.687080000
1	-1.889844000	0.928989000	-1.616113000
1	-0.220677000	0.928301000	-2.166735000
6	-0.604532000	-0.369743000	0.309818000
1	0.012591000	-0.577617000	1.188110000
8	-0.195156000	-1.157289000	-0.776526000
1	0.531330000	-1.724243000	-0.470744000
6	-2.050862000	-0.658513000	0.684934000
6	-4.710726000	-1.149672000	1.383585000
6	-2.864299000	-1.421142000	-0.146718000
6	-2.575359000	-0.151135000	1.874608000
6	-3.896888000	-0.395177000	2.224443000
6	-4.190850000	-1.662014000	0.201329000
1	-2.439013000	-1.830858000	-1.054137000
1	-1.936626000	0.427108000	2.536818000
1	-4.291033000	-0.003551000	3.154778000
1	-4.817526000	-2.257519000	-0.452241000
1	-5.741891000	-1.342324000	1.654522000
6	3.688194000	-2.323635000	2.618282000
1	4.475272000	-2.086808000	3.329190000
1	3.920926000	-3.242556000	2.080132000
1	2.732786000	-2.446715000	3.129240000

3. X-ray crystallographic data: All crystallographic data has been deposited in the Cambridge Crystallographic Data Centre and can be found online.

CCDC numbers:

(1R,2S)-2-(hydroxydiphenylmethyl)-1-((E)-3-methoxy-3-oxoprop-1-en-1-yl)pyrrolidine 1-oxide = **CCDC 963296**

(1S,2S)-1-((E)-1,4-diethoxy-1,4-dioxobut-2-en-2-yl)-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide = **CCDC 963298**