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Syntheses, analytical and pharmacological characterizations of the "legal high" 4-[1-(3-methoxyphenyl)cyclohexyl]morpholine (3-MeO-PCMo) and analogues

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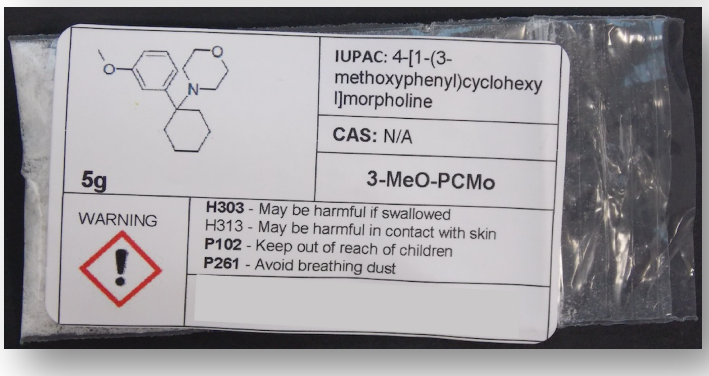

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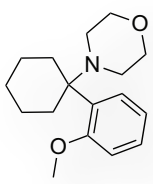

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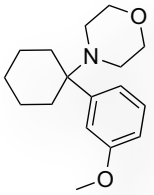

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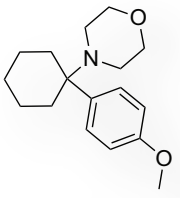

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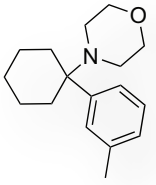
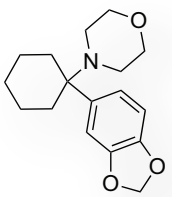
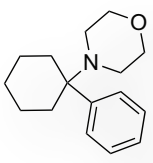


3-Me-PCMo



3,4-MD-PCMo



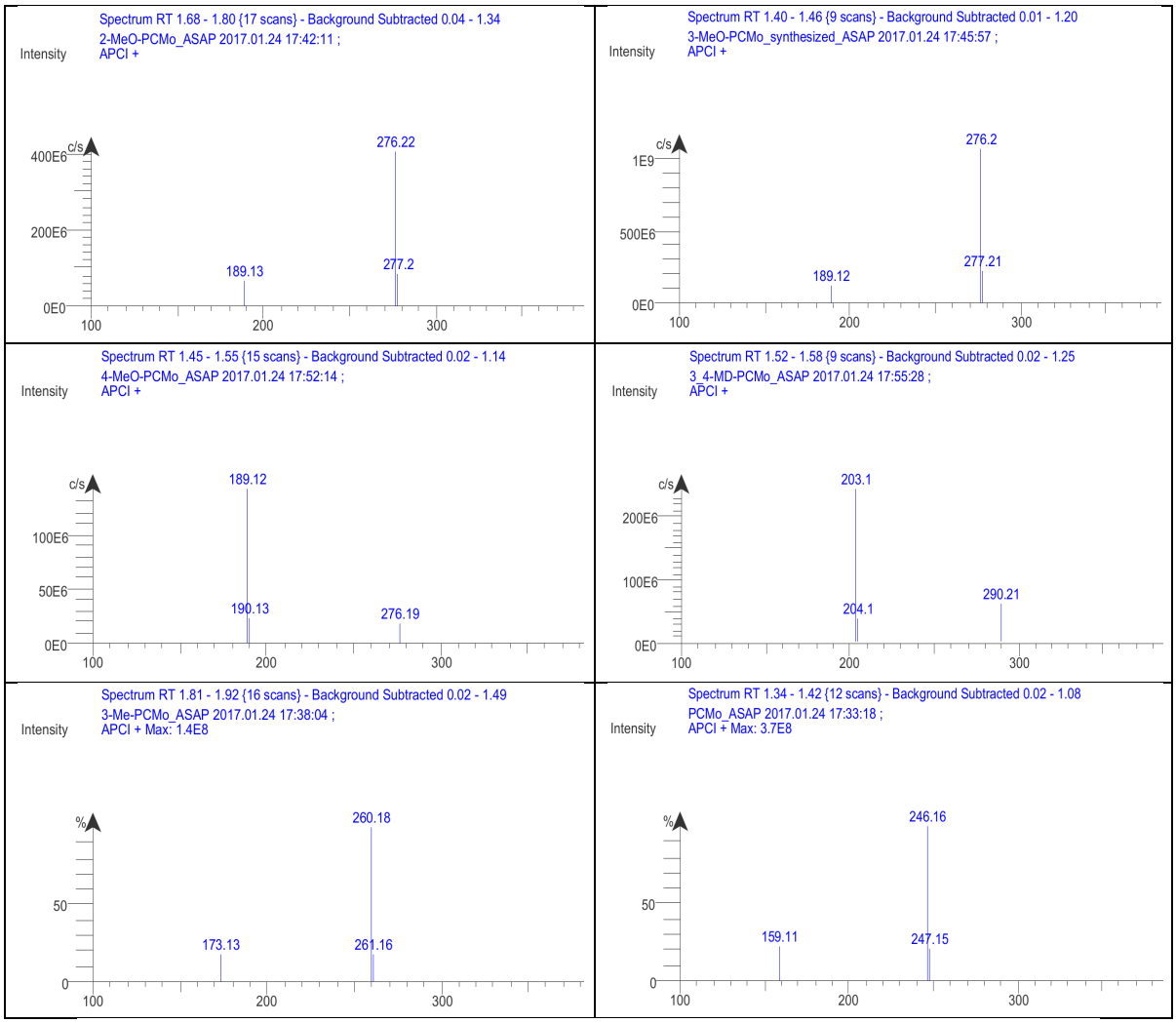
PCMo

Alternative PCMo PCC synthesis route description

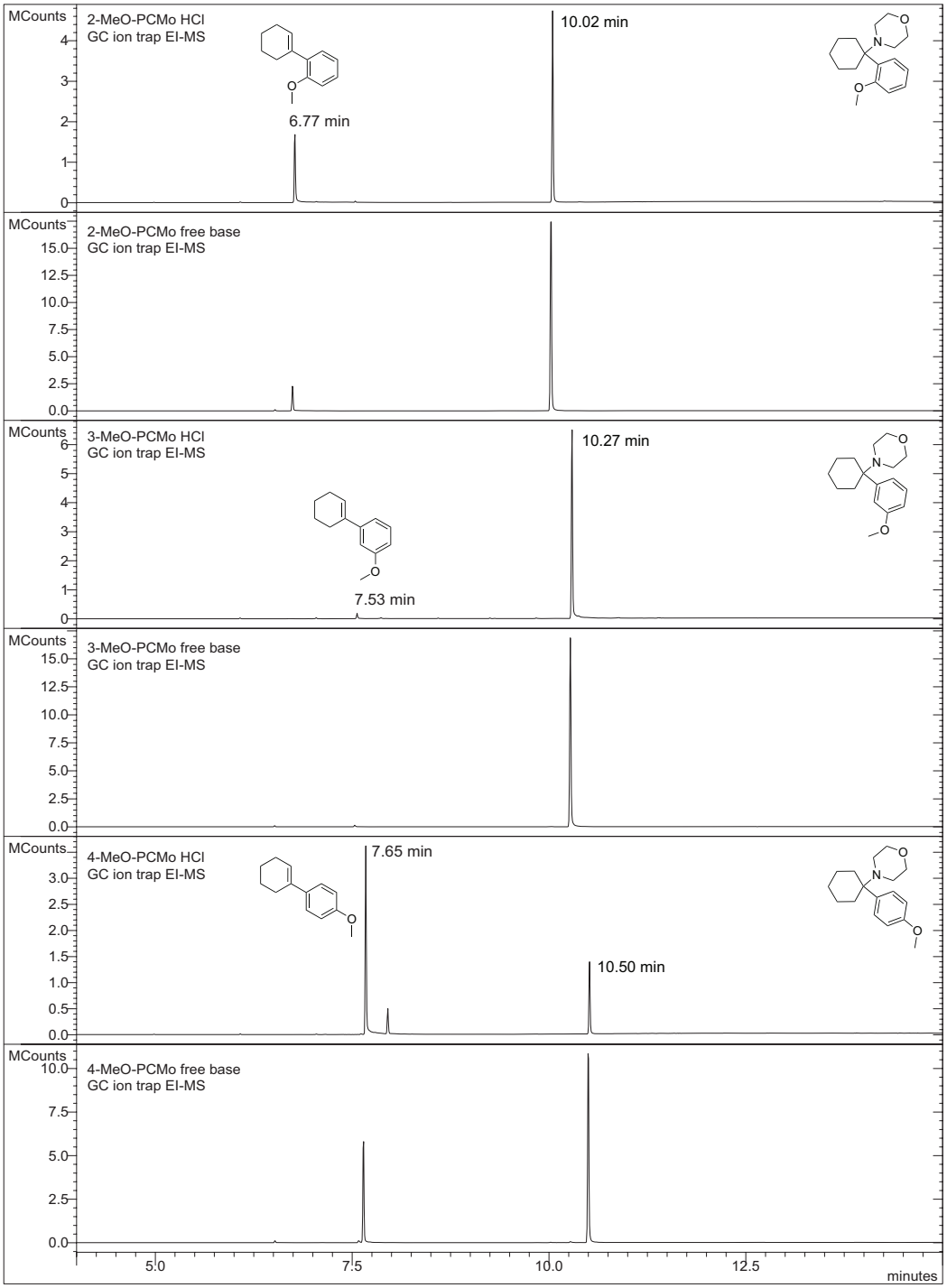
Cyclohexanone (0.0504 mol, 5.3 g) was added to a solution consisting of $NaHSO_3$ (6.3 g) in 100 mL distilled water (dH_2O) resulting in an amber solution. With vigorous stirring there was simultaneously added NaCN (0.0605 mol, 2.95 g) dissolved in 20 mL dH_2O and morpholine (0.0555 mol, 4.83 mL). The solution became very cloudy and was allowed to stir overnight at ambient temperature. The reaction was then removed from stir plate and allowed to sit which resulted in the formation of two separate layers. The top oil layer was obtained by extracting with ethyl acetate (2 x 60 mL). The organic extractions were pooled, washed with dH_2O (100 mL), saline (2 x 10 mL), dried with anhydrous Na_2SO_4 and the solvents evaporated under vacuum to provide 7.0 g (71.5% yield) of 1-(morpholin-4-yl)cyclohexane-1-carbonitrile as an amber oil which solidified on storage in the freezer (but melted at ambient temperature). Bromobenzene (0.0756 mol, 7.91 mL) was added to a stirred suspension of crushed magnesium (0.227 mol, 1.8 g) in Et_2O (20 mL) under argon. A small crystal of iodine was added to initiate reaction. The exothermic reaction was cooled on ice as needed and allowed to sit for approximately 20 minutes at which point the nitrile (0.036 mol, 7.0 g) dissolved in 10 mL of dry THF was slowly added with vigorous stirring under argon. This led to a violent exothermic reaction and the precipitate of white solids. The solution was allowed to sit overnight at which point the reaction appeared complete (MS and TLC). To work-up the reaction, Et_2O (100 mL) was added and the suspension extracted with 0.5 N aqueous HCl solution (2 x 150 mL). The pooled aqueous phase was washed with ethyl acetate (2 x 50 mL), made basic with KOH pellets and extracted with ethyl acetate (3 x 60 mL). The organic extractions were pooled, washed with saline (10 mL) dried with Mg_2SO_4, filtered and solvents evaporated under vacuum to give crude PCMo as a yellow oil. The material was purified using flash column chromatography as described previously and the desired fractions (TLC and MS) pooled and evaporated to give (1.5 g) PCMo, a colorless oil in 17% yield. The true yield was higher as a large number of fractions also contained product contaminated with unreacted nitrile a common issue encountered with this route. An attempt at short-path vacuum distillation was only partially successful so the material was thus discarded. The purified freebase was converted to the HCl salt as described previously.

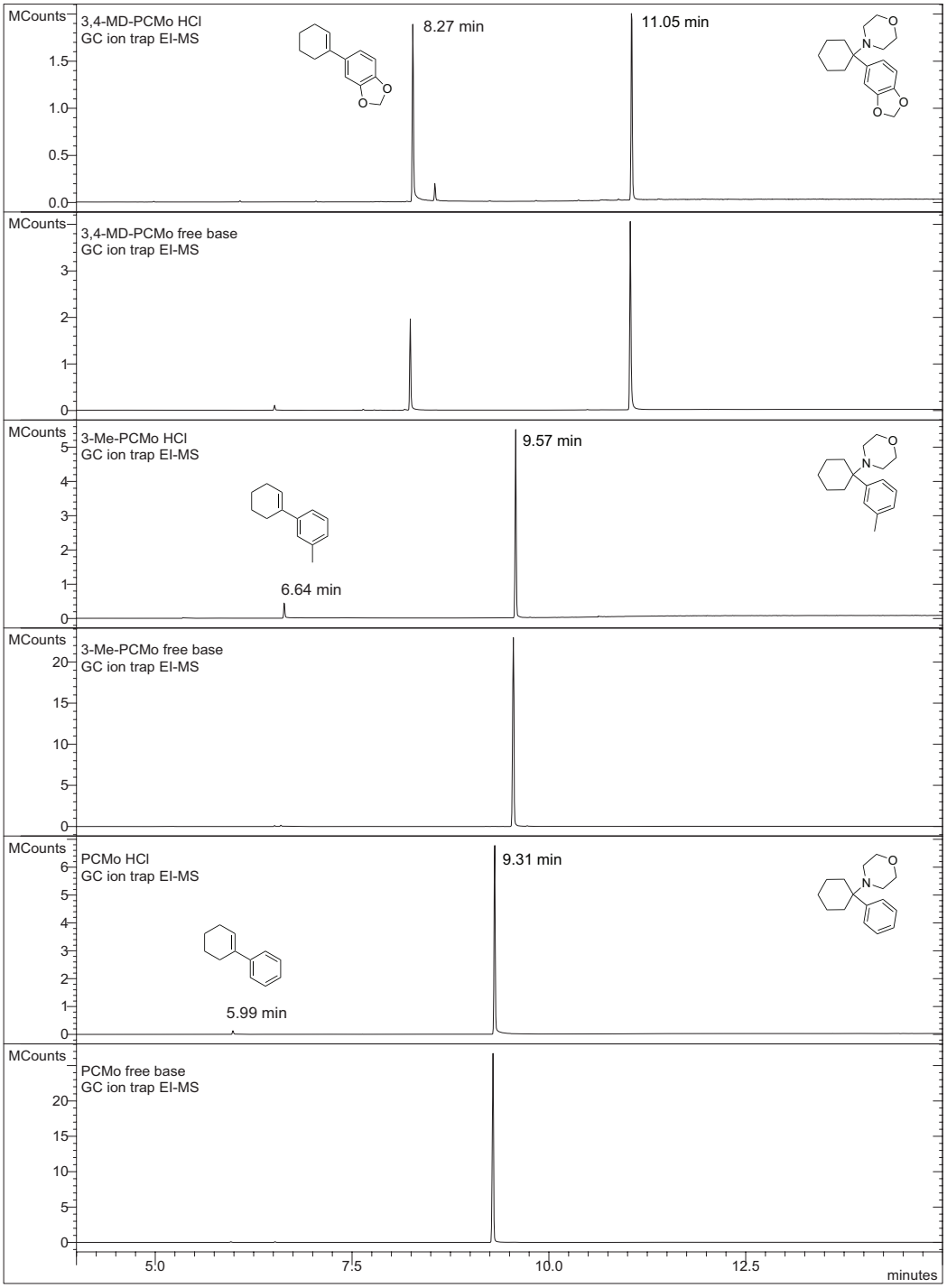
Atmospheric solids analysis probe mass spectrometry

Flash chromatography fractions of PCMo products were recorded on an Advion expression^{S} CMS system (New York, USA) using an atmospheric solids analysis probe (ASAP) source from Advion. Nitrogen was used as the source gas. Capillary temperature was set at 150ºC, with the capillary voltage of 120 V, source voltage offset was set to 20 and source voltage span to 0. Source gas temperature was 200ºC and APCI corona discharge set to 5 mA. Spectra were analyzed using Advion Data Express software, version 2.2.29.2. This method of analysis particularly helpful for the analysis of fractions obtained from flash column chromatography.

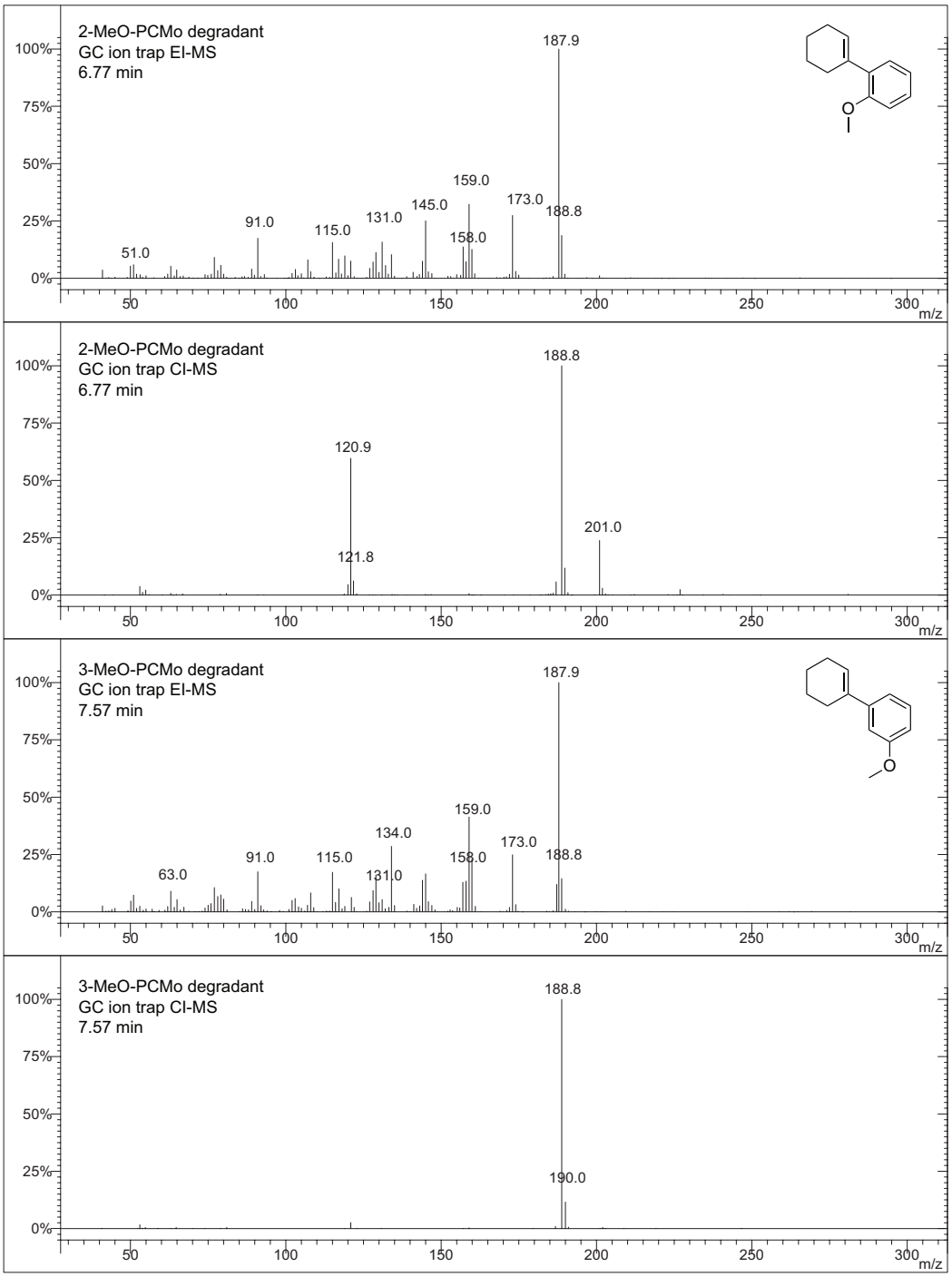


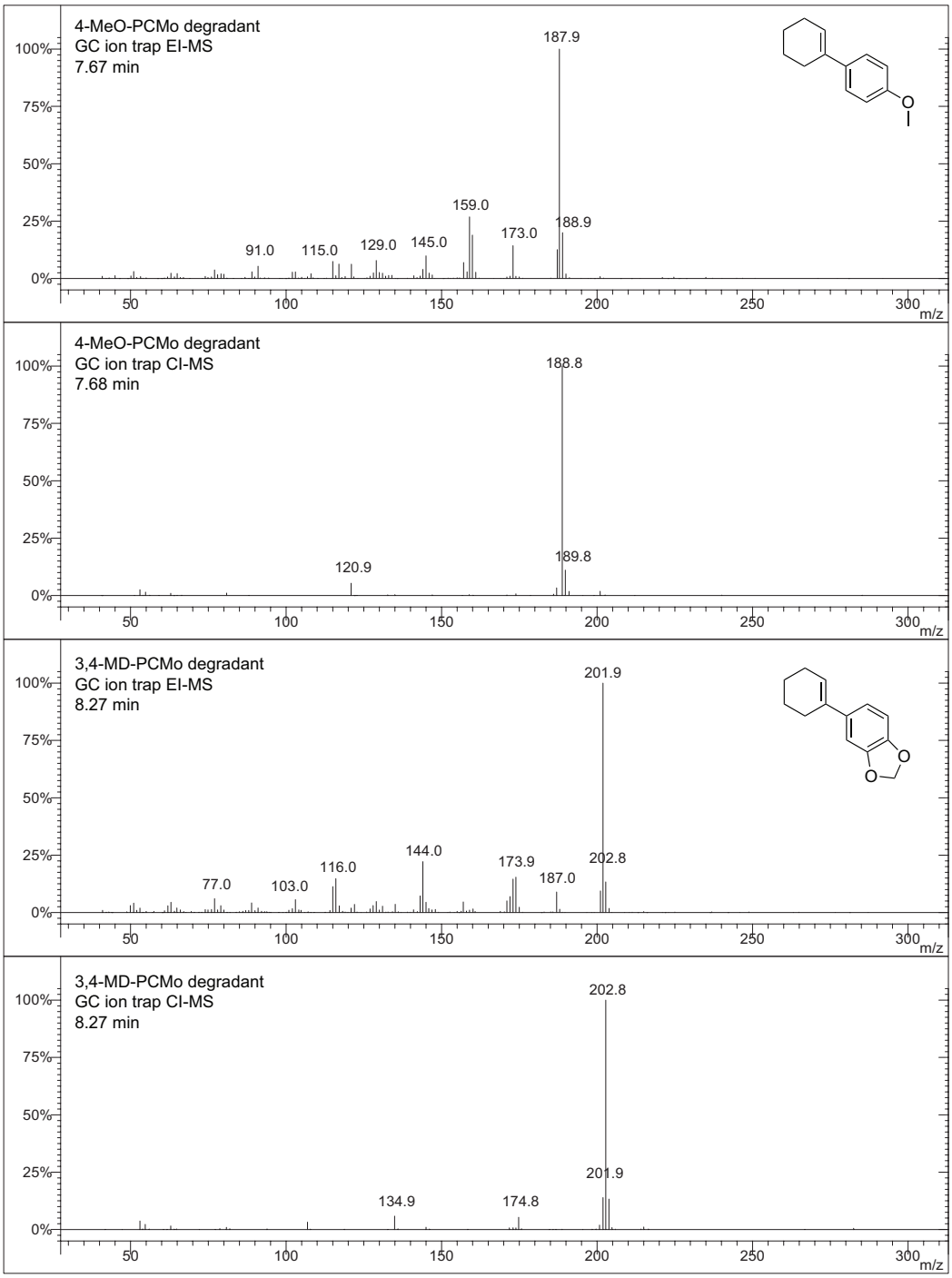
GC ion trap MS full scan traces HCl vs. freebase to compare GC-induced degradation

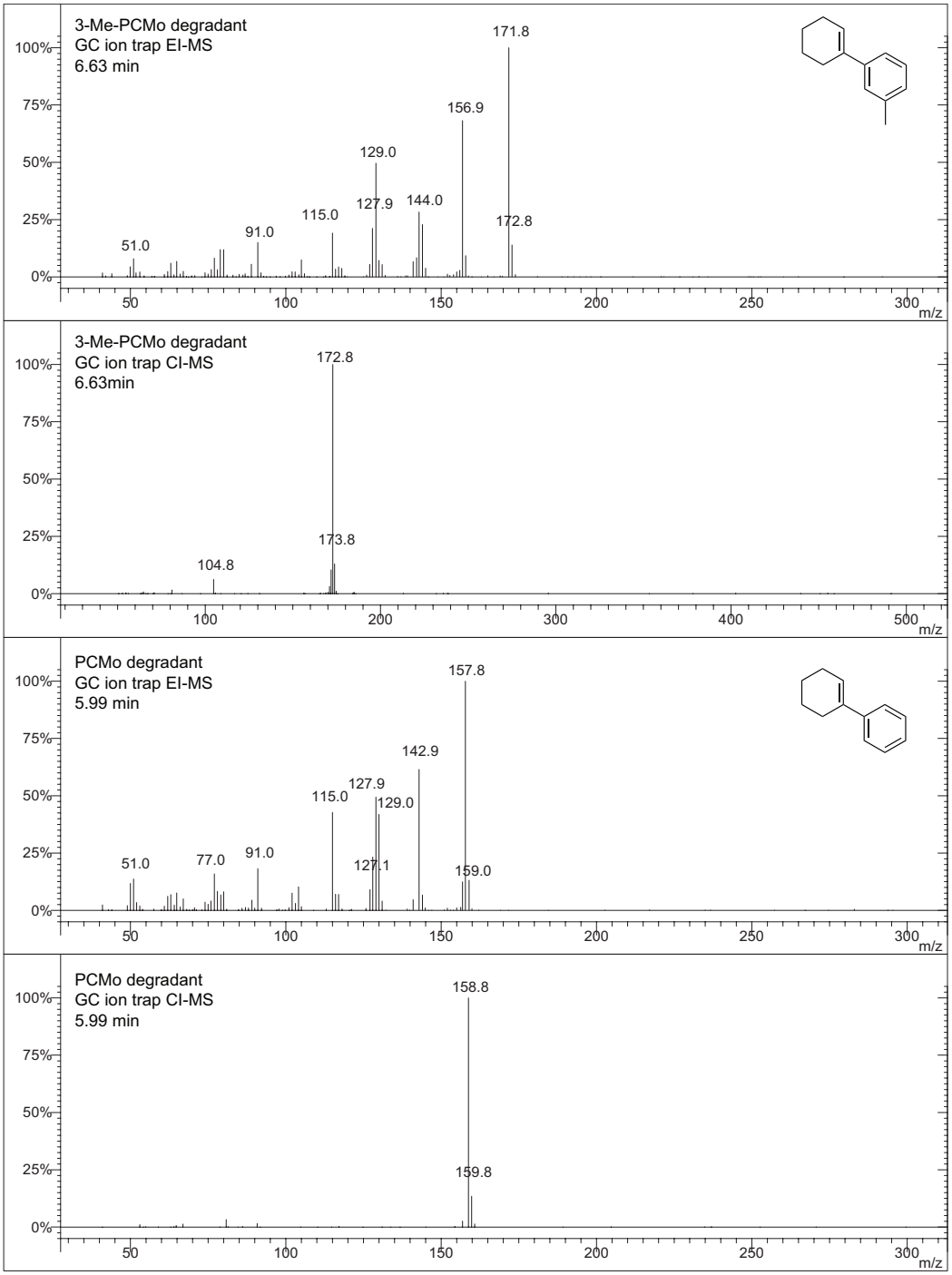



MCounts
3,4-MD-PCMo HCl
GC ion trap EI-MS
8.27 min
11.05 min
3,4-MD-PCMo free base
GC ion trap EI-MS
3-Me-PCMo HCl
GC ion trap EI-MS
9.57 min
6.64 min
3-Me-PCMo free base
GC ion trap EI-MS
PCMo HCl
GC ion trap EI-MS
9.31 min
5.99 min
PCMo free base
GC ion trap EI-MS
5.0
7.5
10.0
12.5
minutes

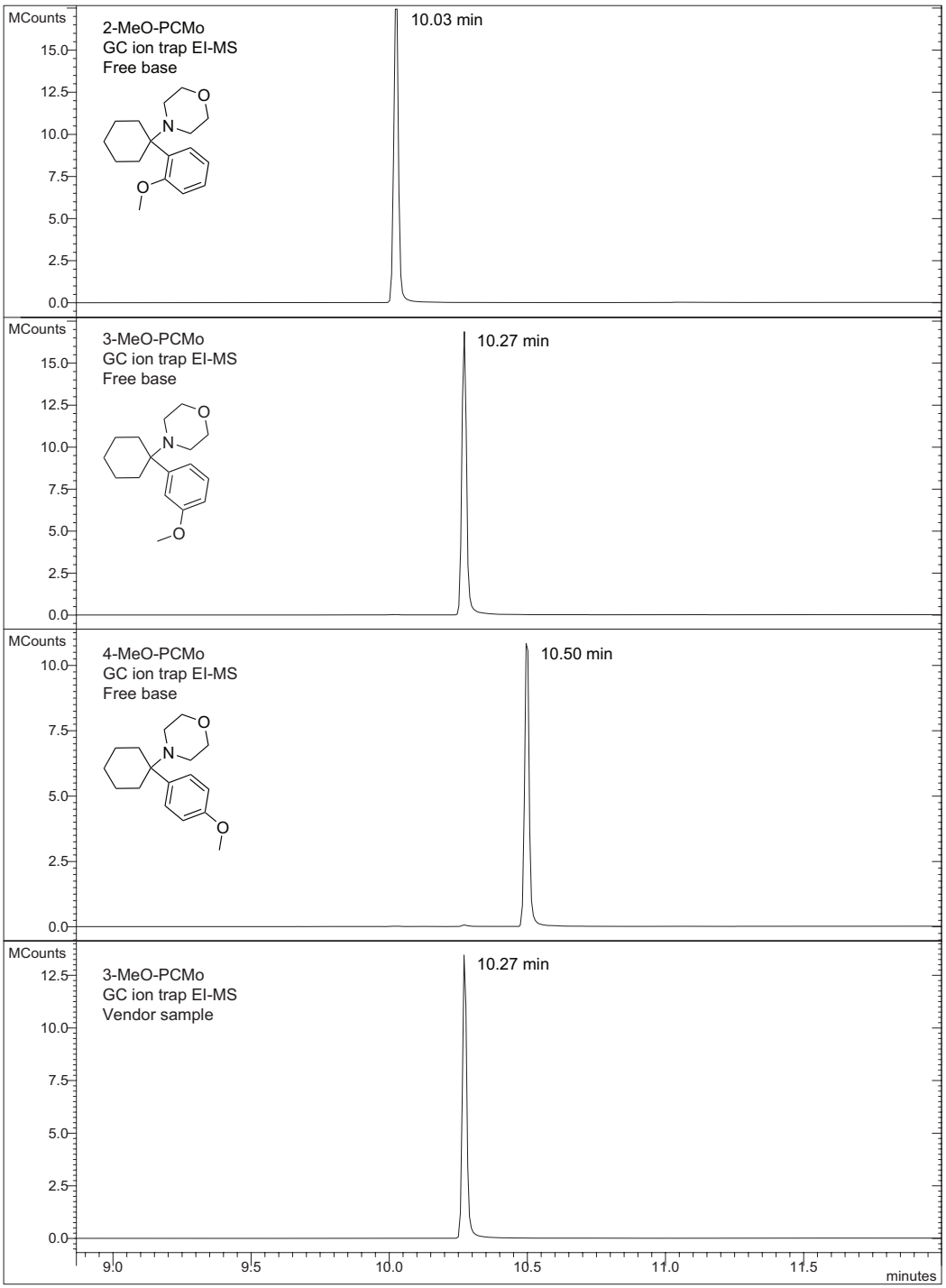
Ion trap EI/CI mass spectra of GC-induced PCMo degradation products



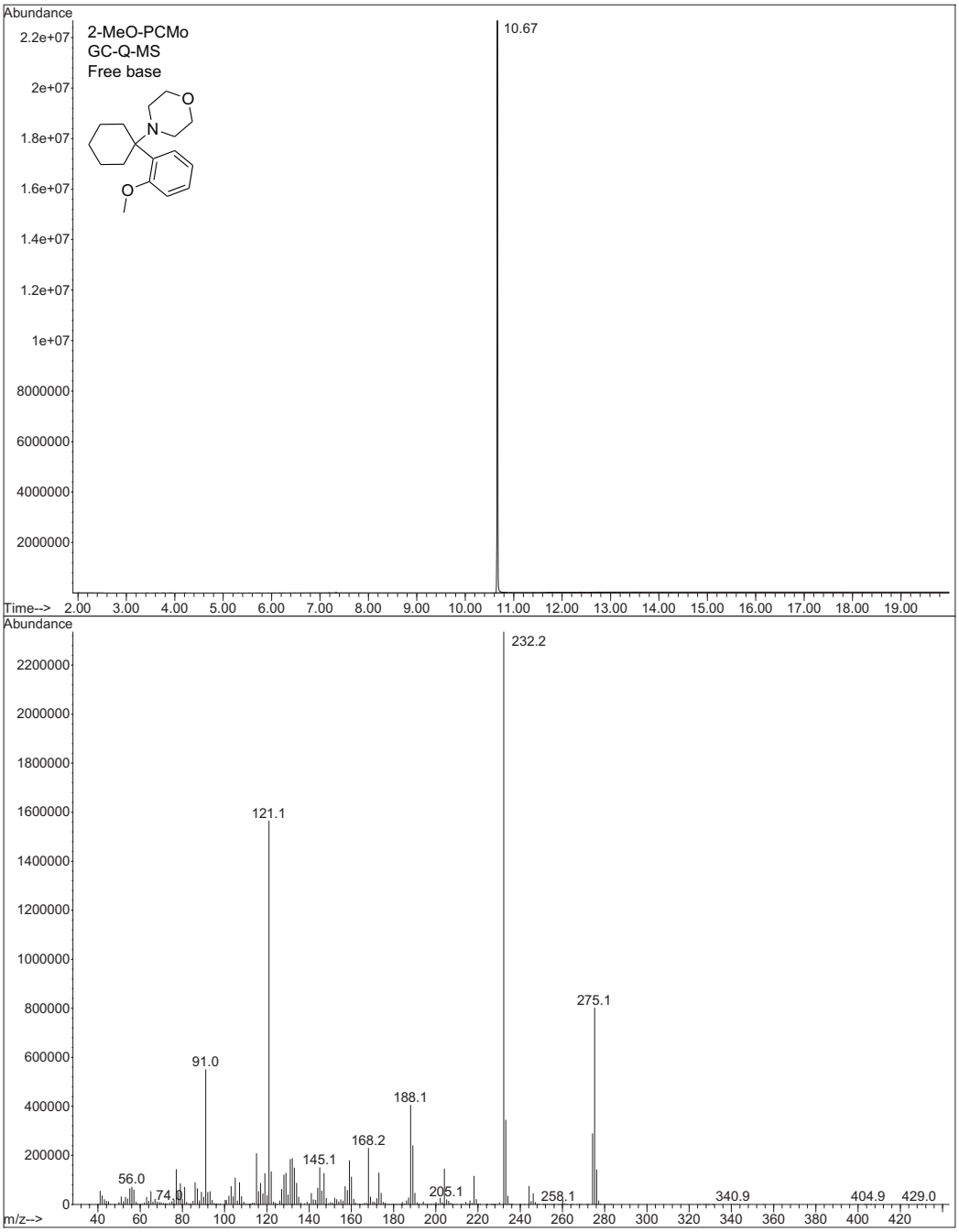

4-MeO-PCMo degradant
GC ion trap EI-MS
7.67 min
187.9
159.0
188.9
173.0
91.0
115.0
129.0
145.0
O
4-MeO-PCMo degradant
GC ion trap CI-MS
7.68 min
188.8
189.8
120.9
3,4-MD-PCMo degradant
GC ion trap EI-MS
8.27 min
201.9
144.0
173.9
202.8
116.0
187.0
77.0
103.0
O
O
3,4-MD-PCMo degradant
GC ion trap CI-MS
8.27 min
202.8
201.9
134.9
174.8
100%
75%
50%
25%
0%
50
100
150
200
250
300
m/z

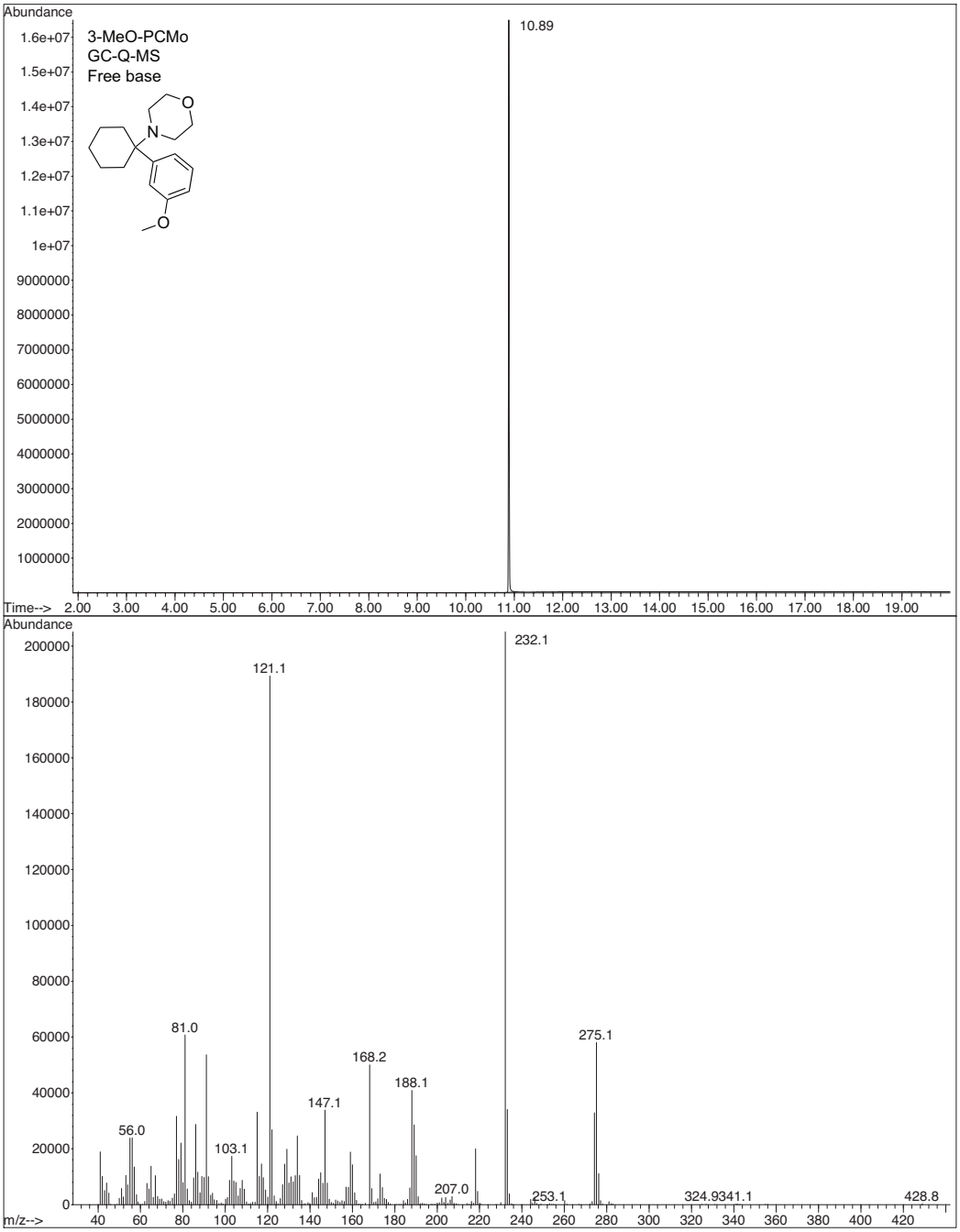

3-Me-PCMo degradant
GC ion trap EI-MS
6.63 min
171.8
156.9
129.0
127.9
144.0
115.0
172.8
91.0
51.0
3-Me-PCMo degradant
GC ion trap CI-MS
6.63min
172.8
173.8
104.8
PCMo degradant
GC ion trap EI-MS
5.99 min
157.8
142.9
127.9
115.0
129.0
51.0
77.0
91.0
127.1
159.0
PCMo degradant
GC ion trap CI-MS
5.99 min
158.8
159.8
100%
75%
50%
25%
0%
50
100
150
200
250
300
400
500
m/z

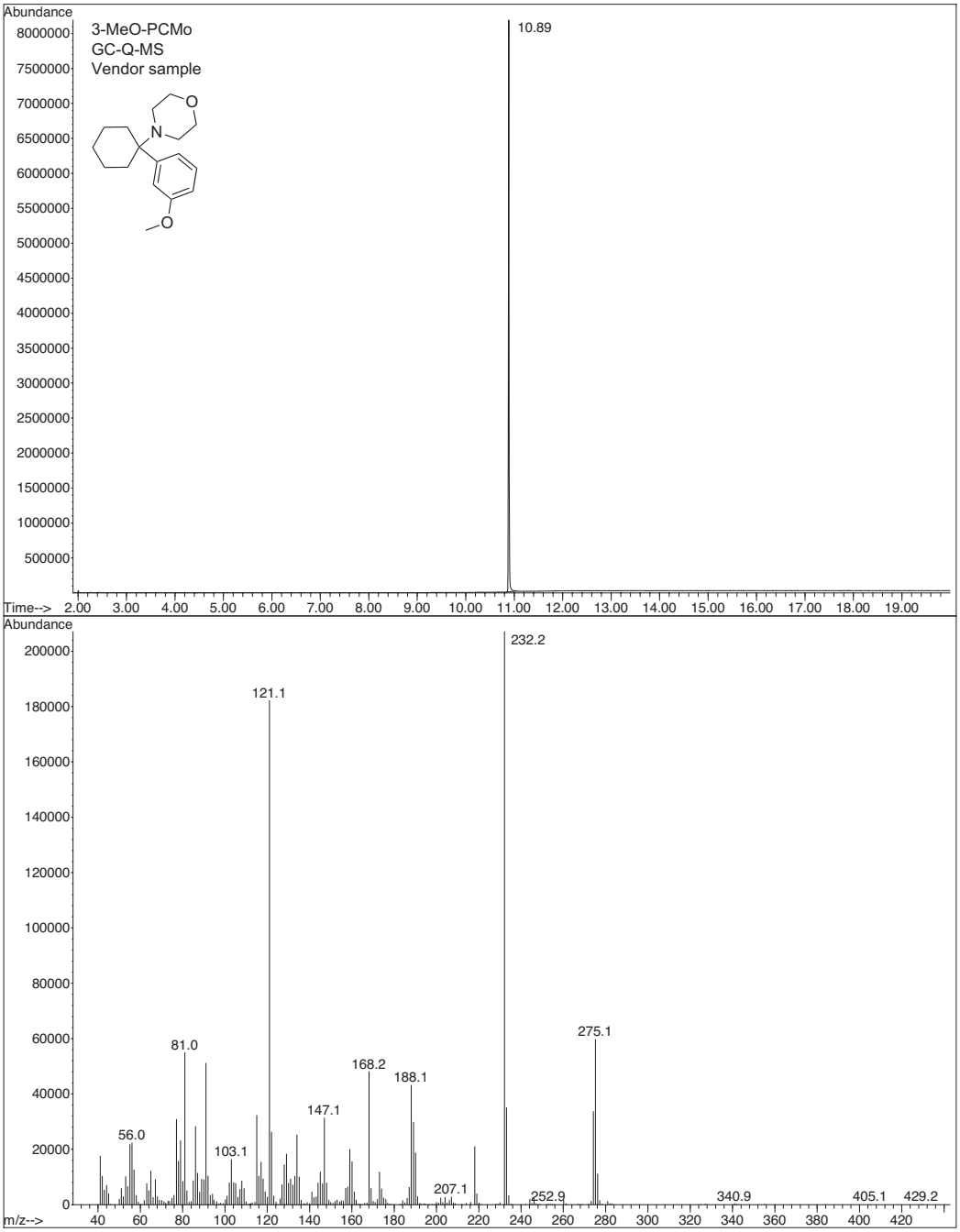
Partial GC ion trap MS full scan traces of MeO isomers vs. 3-MeO-PCMo vendor sample

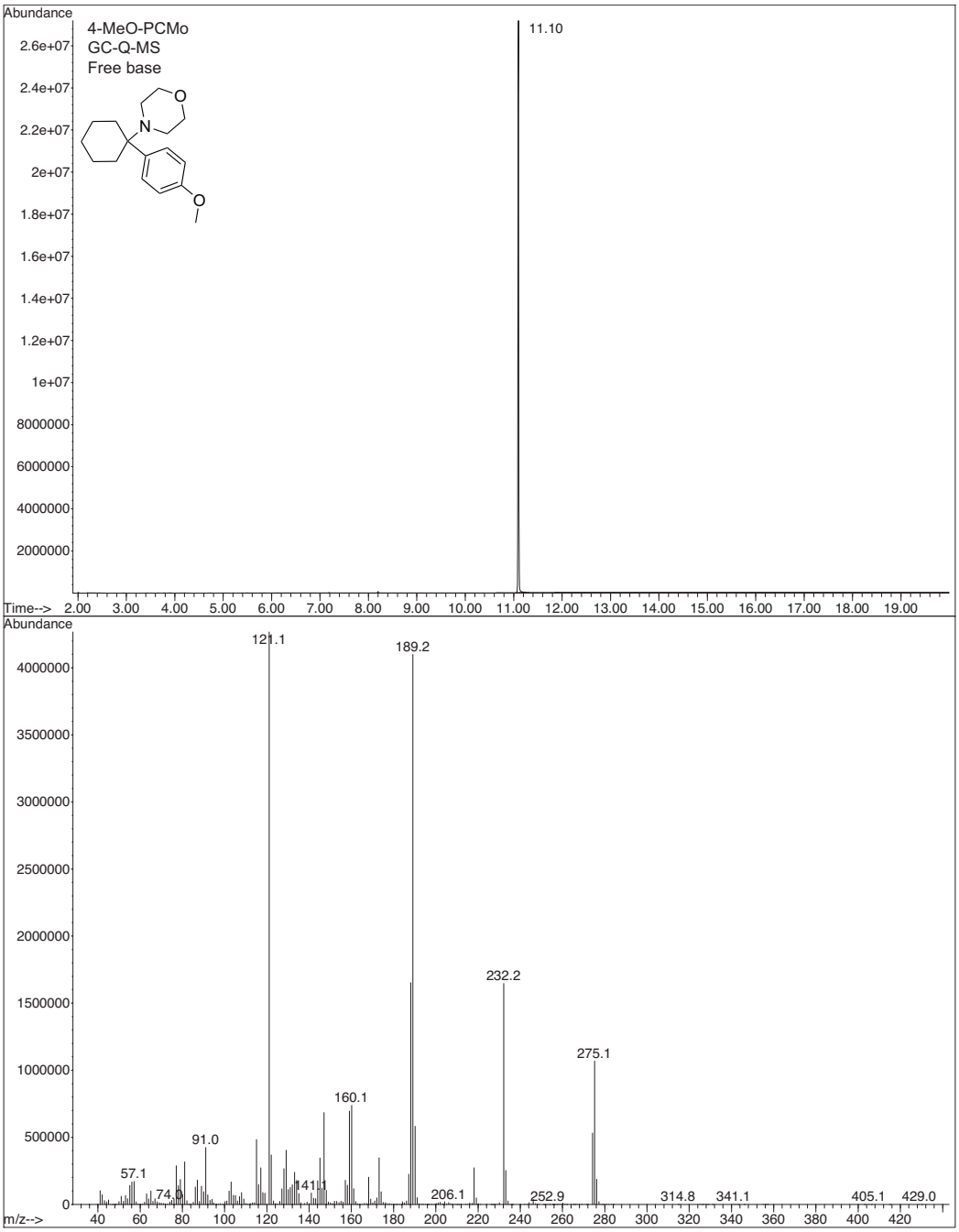


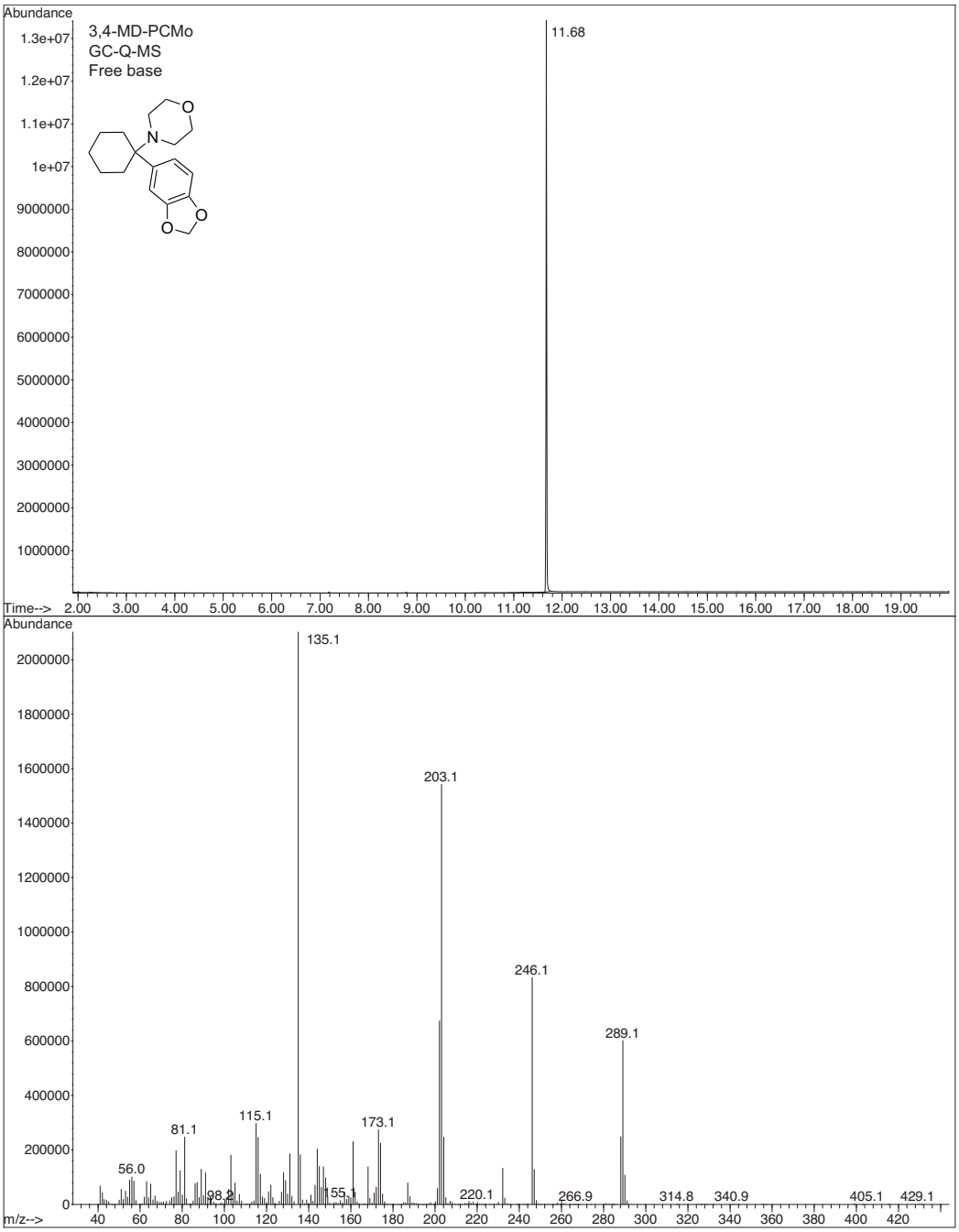
GC quadrupole EI-MS (GC-Q-MS) full scan traces of PCMo analogues

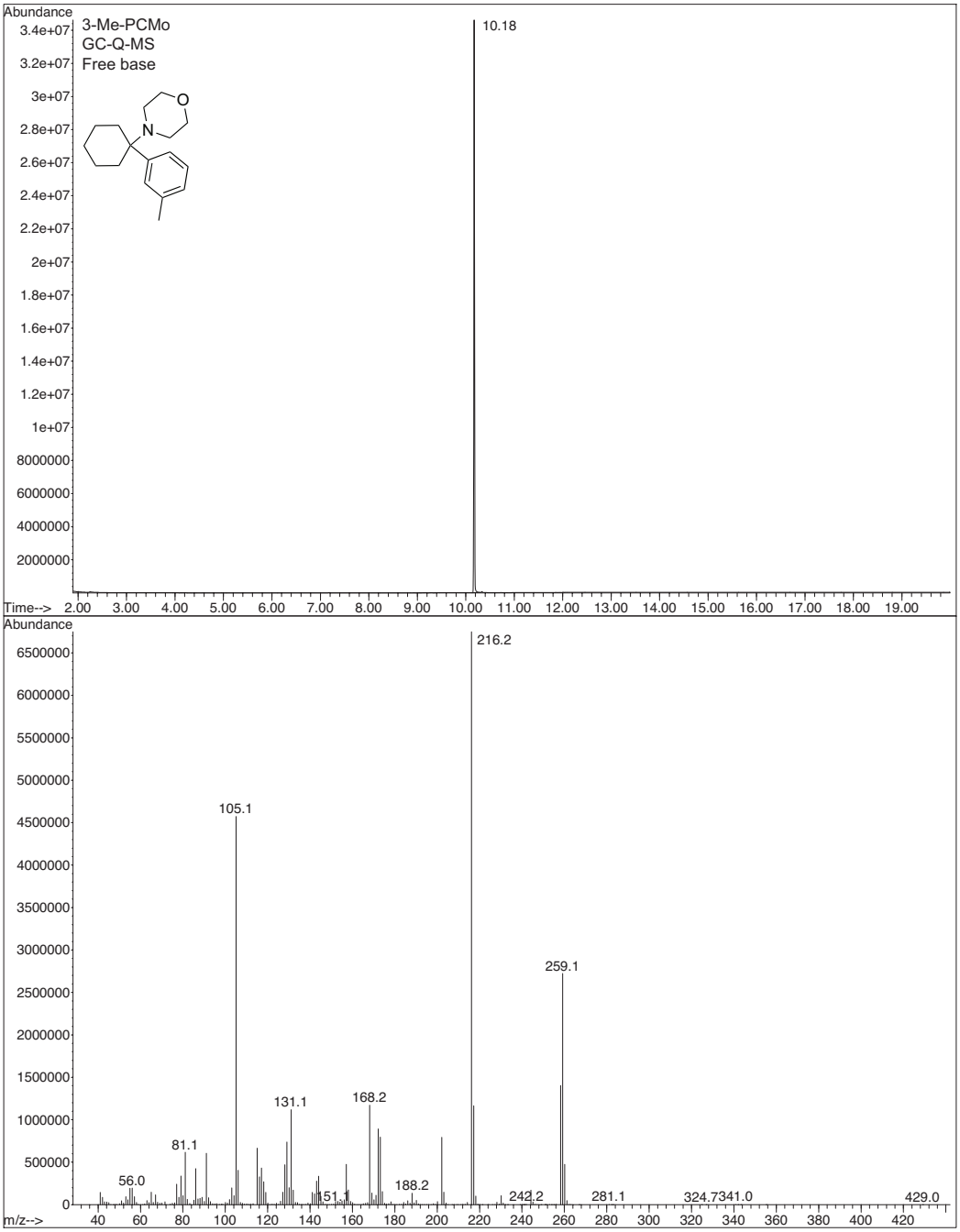


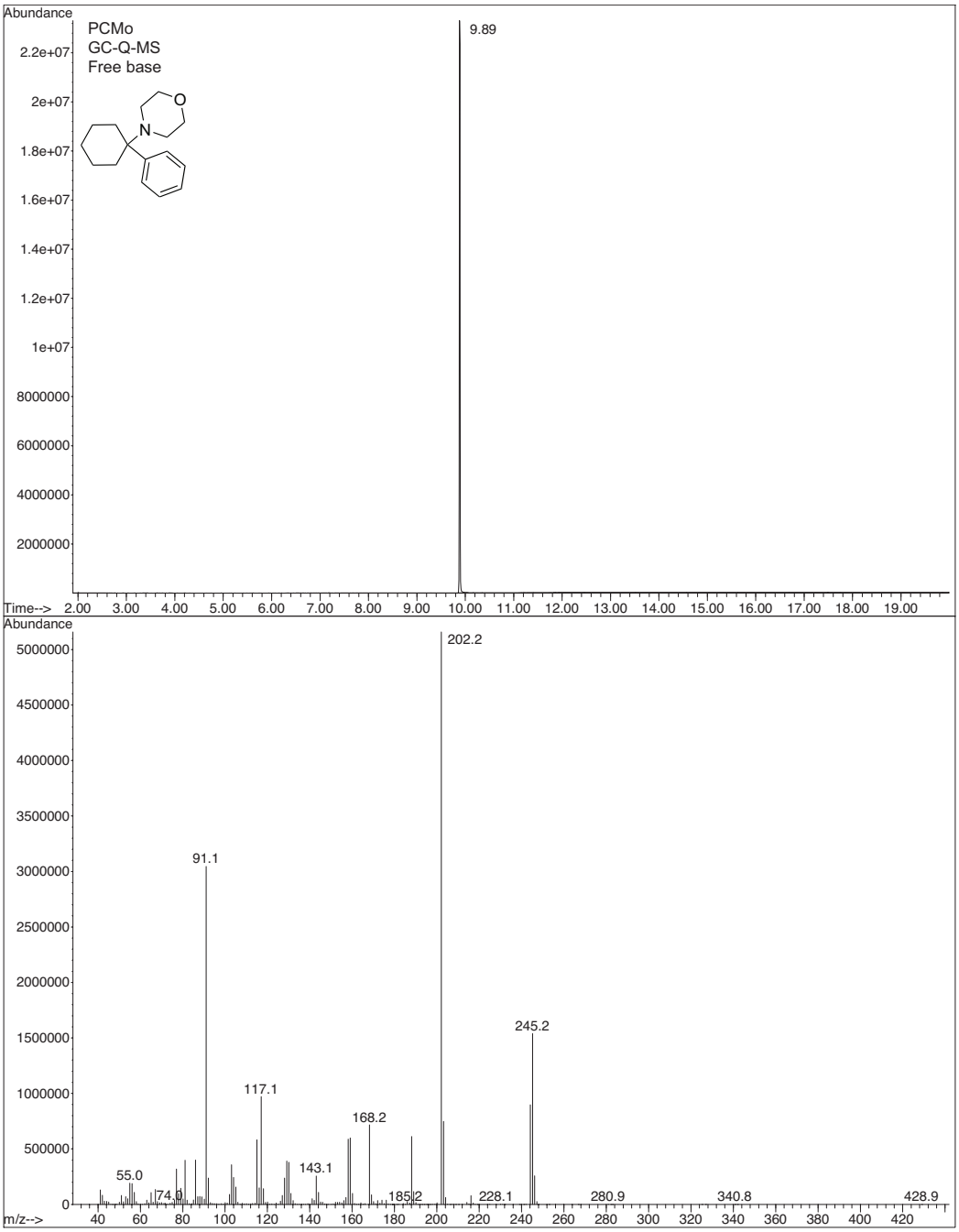

Abundance
3-MeO-PCMo
GC-Q-MS
Free base
10.89
Time-->
Abundance
232.1
121.1
81.0
275.1
168.2
188.1
147.1
56.0
103.1
207.0
253.1
324.9341.1
428.8
m/z-->


Abundance
3-MeO-PCMo
GC-Q-MS
Vendor sample
10.89
Time-->
Abundance
232.2
121.1
275.1
81.0
168.2
188.1
147.1
56.0
103.1
207.1
252.9
340.9
405.1
429.2
m/z-->

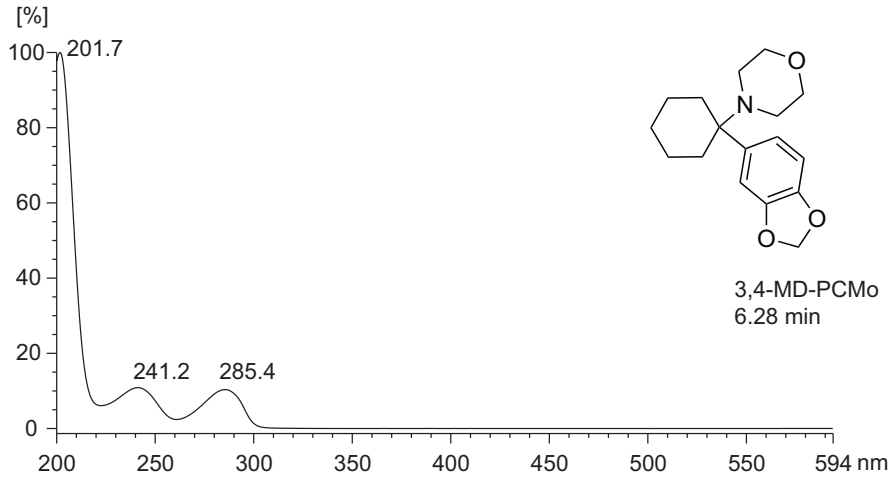

Abundance
4-MeO-PCMo
GC-Q-MS
Free base
11.10
Time-->
Abundance
121.1
189.2
232.2
275.1
160.1
91.0
57.1
74.0
141.1
206.1
252.9
314.8
341.1
405.1
429.0
m/z-->

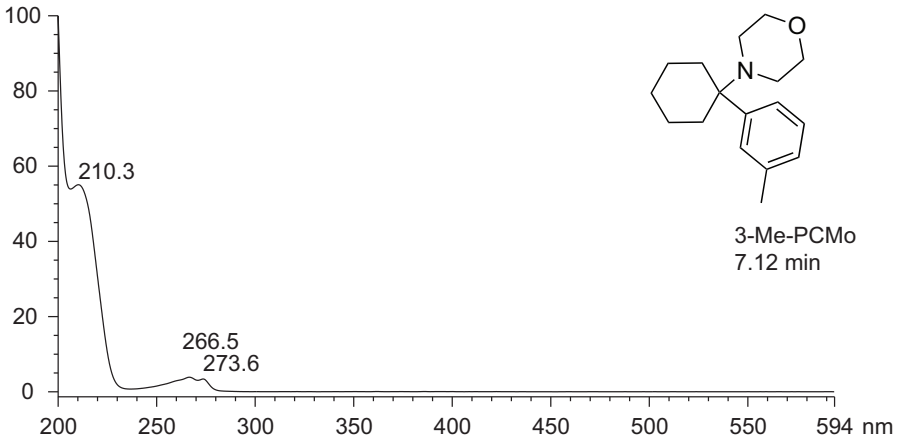

Abundance
3,4-MD-PCMo
GC-Q-MS
Free base
11.68
Time-->
Abundance
135.1
203.1
246.1
289.1
115.1
81.1
173.1
56.0
98.2
155.1
220.1
266.9
314.8
340.9
405.1
429.1
m/z-->

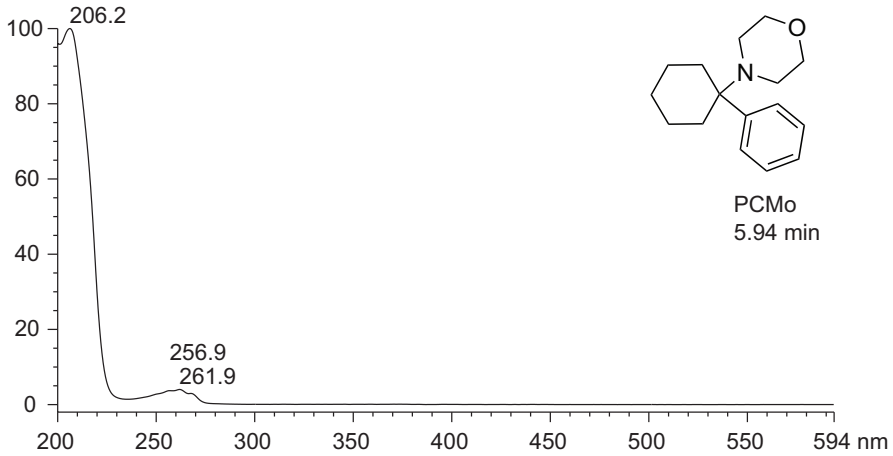

Abundance
3-Me-PCMo
GC-Q-MS
Free base
10.18
Time-->
Abundance
216.2
105.1
259.1
131.1
168.2
81.1
56.0
188.2
242.2
281.1
324.7341.0
429.0
m/z-->


Abundance
PCMo
GC-Q-MS
Free base
9.89
Time-->
Abundance
202.2
91.1
245.2
117.1
168.2
143.1
55.0
74.0
185.2
228.1
280.9
340.8
428.9
m/z-->

UV full scan spectra via HPLC-DAD of 3,4-MD-PCMo, 3-Me-PCMo and PCMo

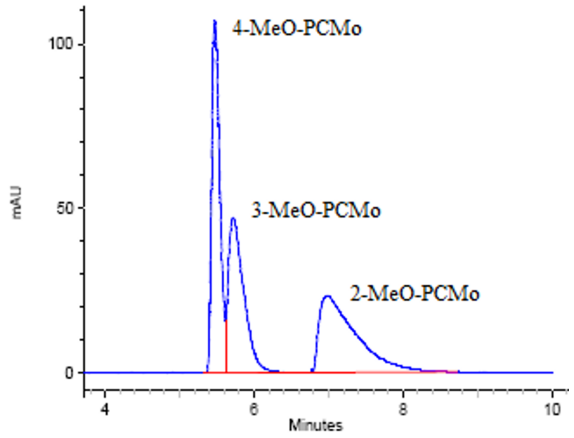






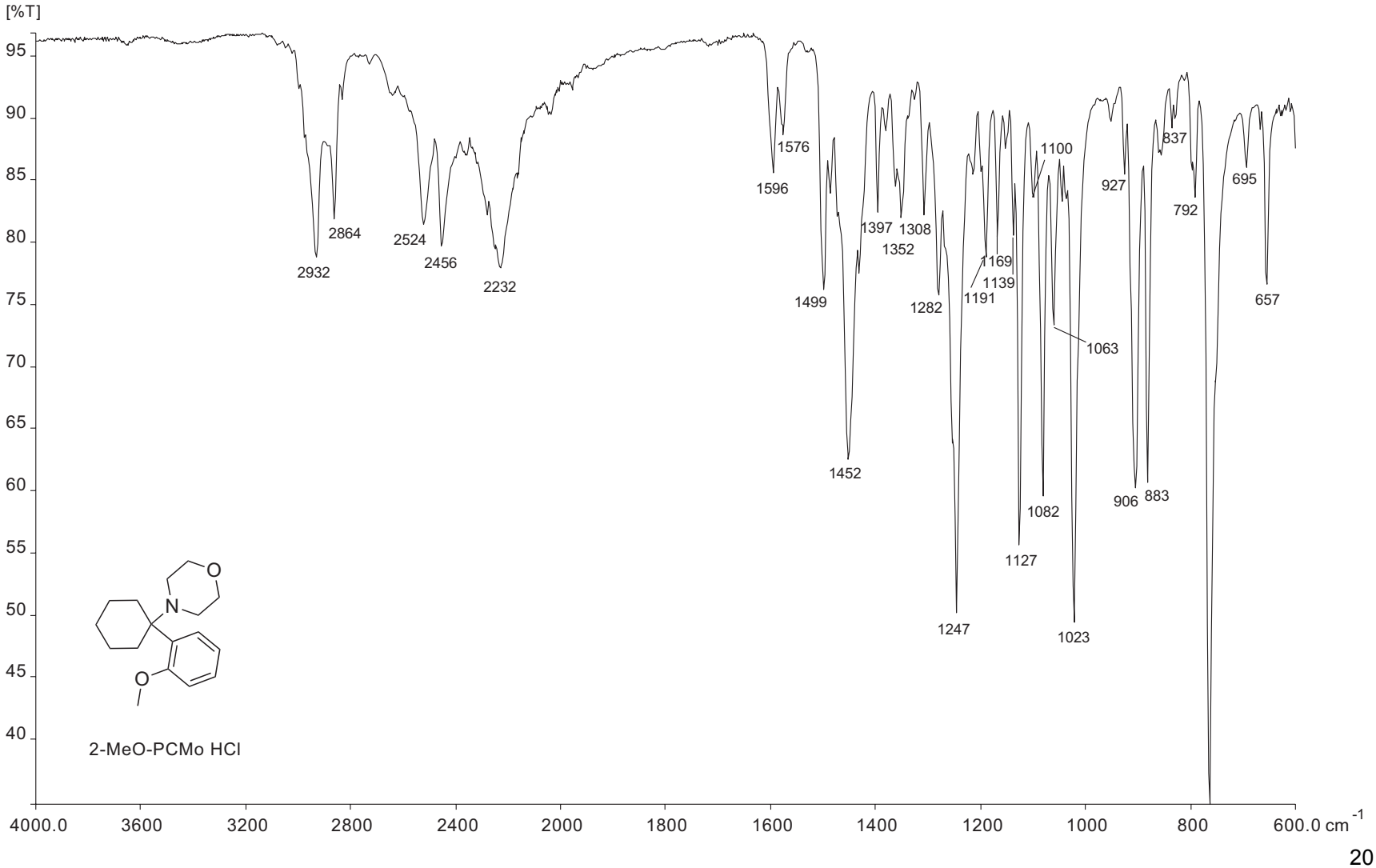
Alternative HPLC method to attempt separation between 2-, 3-, and 4-MeO-PCMo

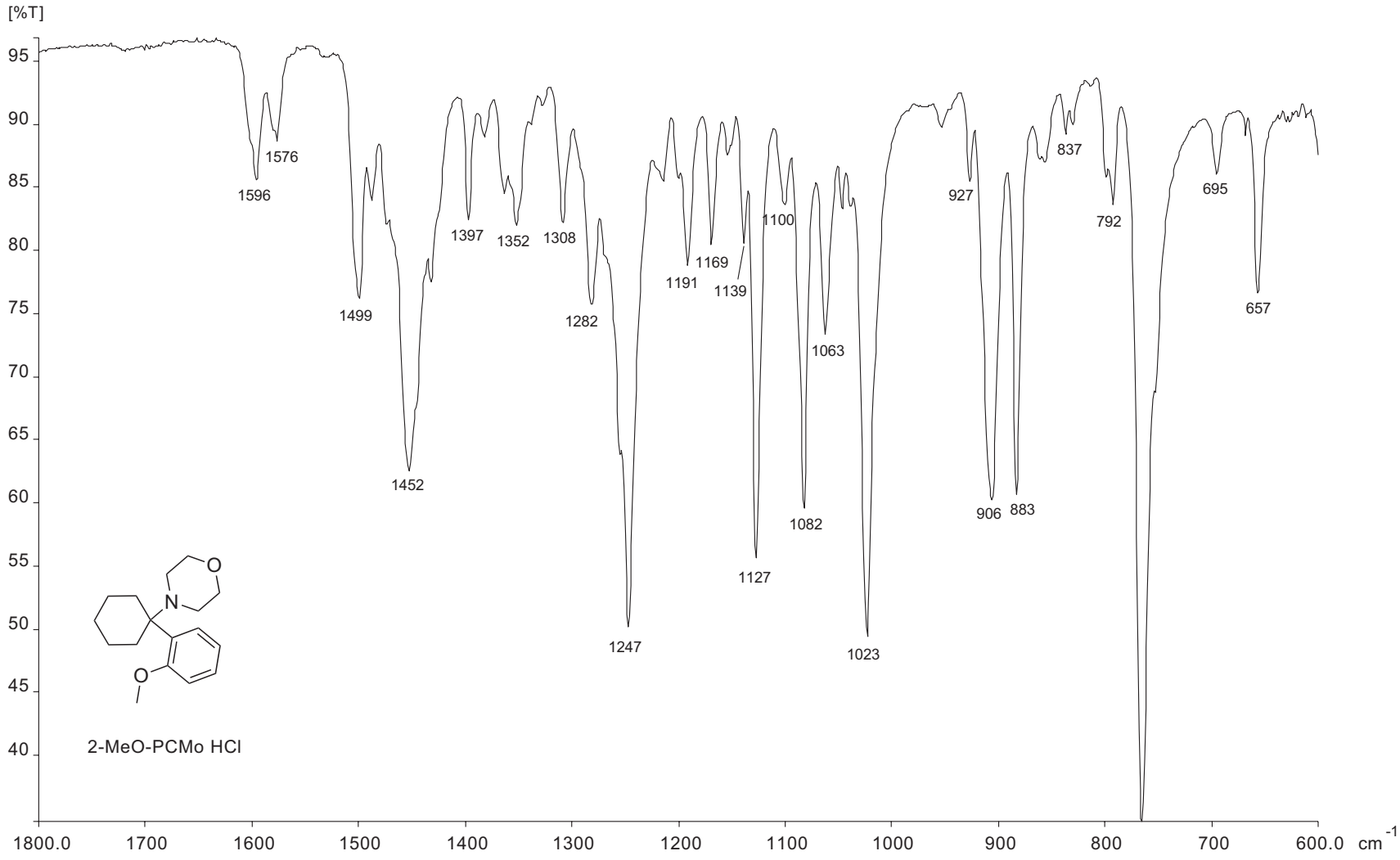
RP-HPLC analyses were performed on a Hitachi LaChrom Elite system with L-2130 pump, L-2200 autosampler, L-2300 column oven, and L-2400 UV detector, respectively (Hitachi High Technologies America, Inc., San José, CA, USA). The detection wavelength was set at 250 nm. Individual samples were prepared in acetonitrile at a concentration of 1 mg/mL, and then combined into a mixture of three equal parts with 1% 2-propanol (v/v). Separation was obtained using a Zorbax Eclipse Plus C18 column (5 µm, 250 mm × 4.6mm) from Agilent Technologies (Santa Clara, CA, USA). Mobile phase A consisted of water with 10 mM formate; mobile phase B was acetonitrile with 1% 2-propanol (v/v). The following gradient was used for elution: 0–4.5 min 93% B, followed by an increase to 100% within 0.5 min and held for 2min. This was followed by a decrease to 93% B within 1 min and held for 2 min to give a total run time of 10 min. Injection volume was 10 mL, flow rate was 1 mL/min, and column temperature was maintained at 35°C using an external column oven from Cole-Palmer (Cole-Palmer, Indiana, USA) due to the long column length. Chromatograms were analyzed using Agilent OpenLAB CDS EZChrom Edition (Agilent Technologies, Santa Clara, CA, USA).



Using the method described, and despite various modifications of the mobile phase compositions, complete separation between the 3- and 4-MeO isomers were not achieved. 4-MeO-PCMo eluted at 5.473 minutes, 3-MeO-PCMo at 5.717 minutes, and 2-MeO-PCMo at 6.980 minutes, respectively. An improvement of tailing observed with 2-MeO-PCMo was not achieved under the conditions used without compromising separation.

ATR-IR spectra of PCMo analogues (HCl salts)

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1247
1191
1169
1139
1127
1100
1082
1063
1023
927
906
883
837
792
695
657
2-MeO-PCMo HCl
1800.0
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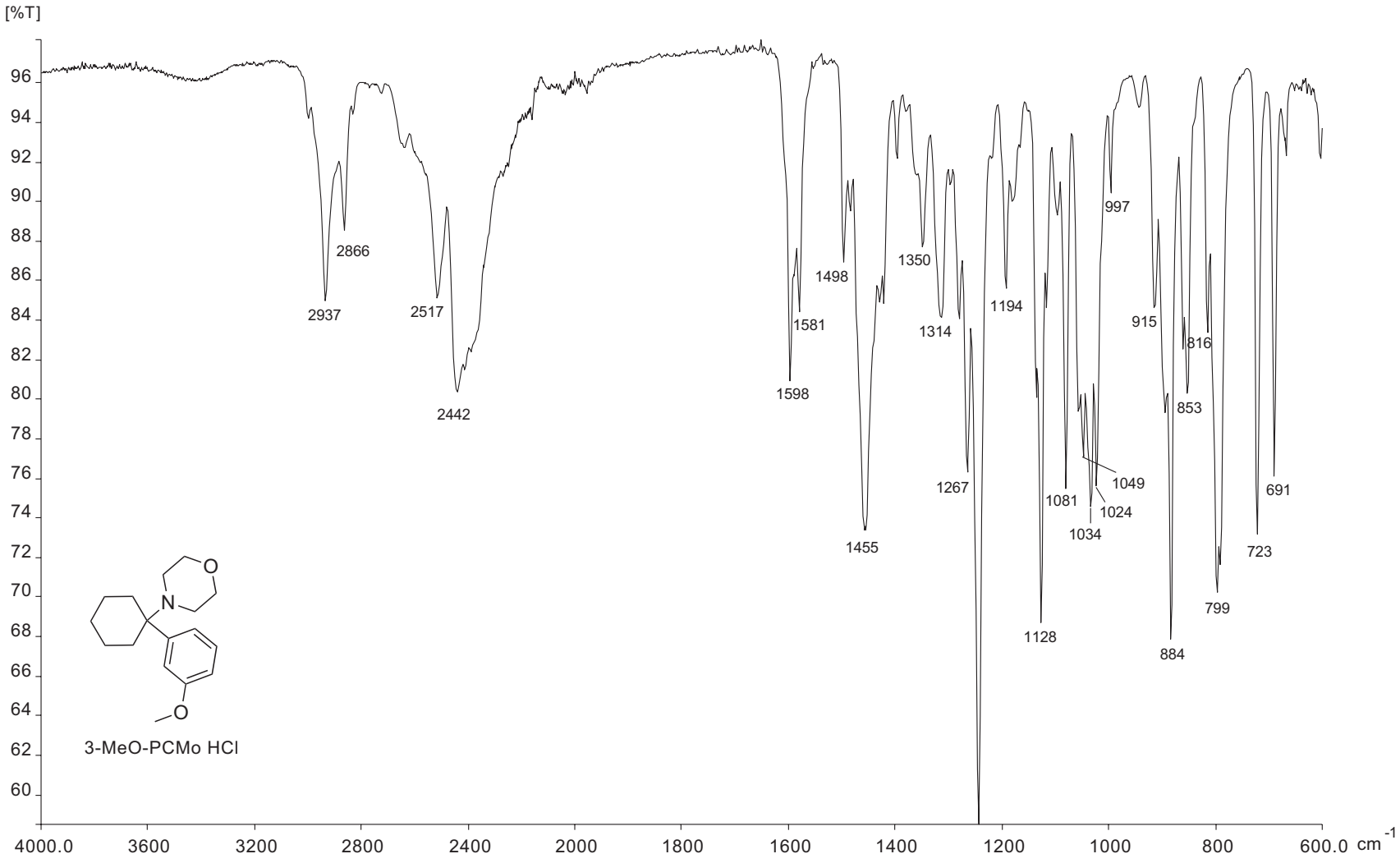
1500
1400
1300
1200
1100
1000
900
800
700
600.0
cm-1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1581
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1128
1081
1049
1034
1024
997
915
884
853
816
799
723
691
4000.0
3600
3200
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1800
1600
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1200
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800
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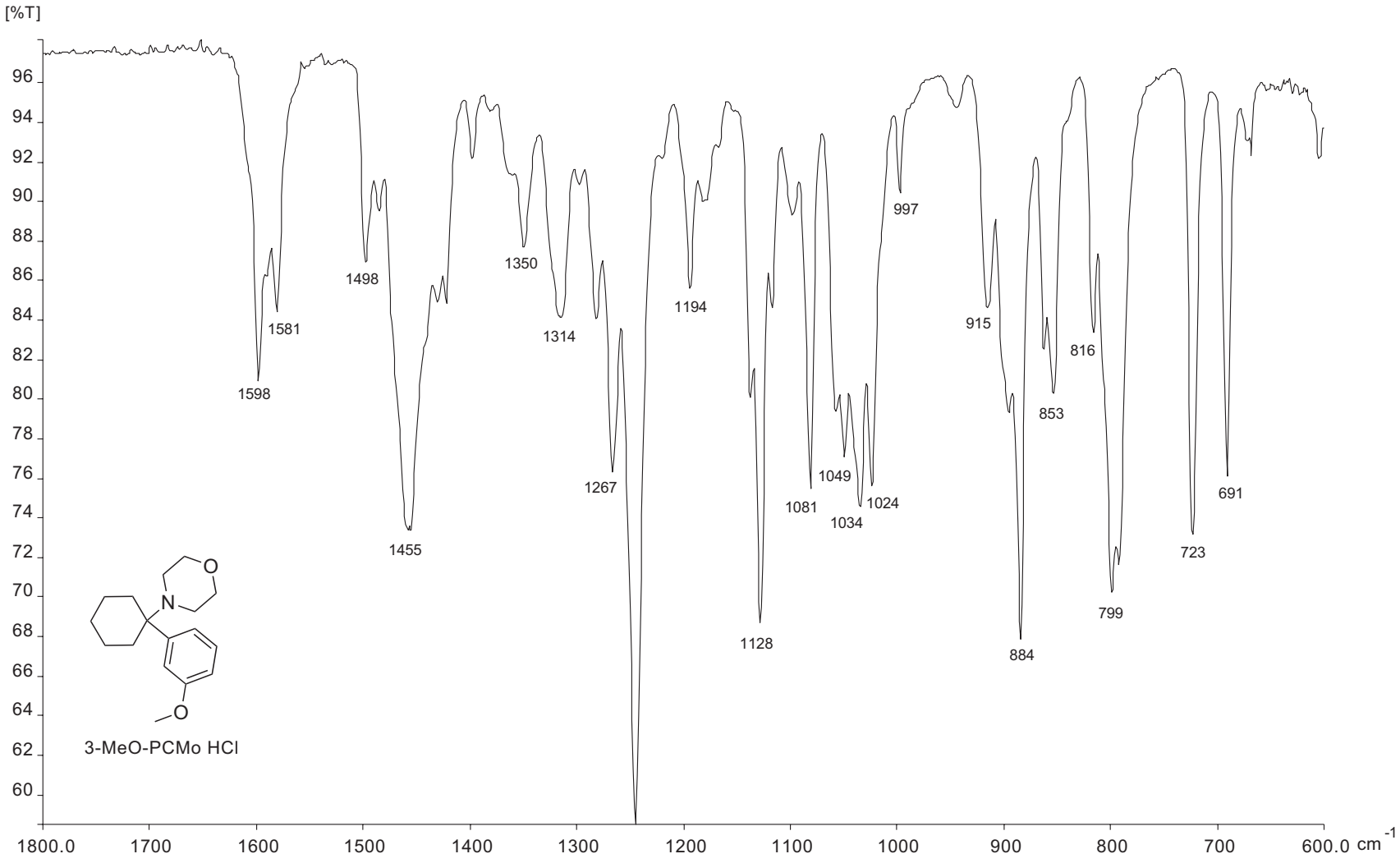
N
O
3-MeO-PCMo HCl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1455
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1314
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1128
1081
1049
1034
1024
997
915
884
853
816
799
723
691
1800.0
1700
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800
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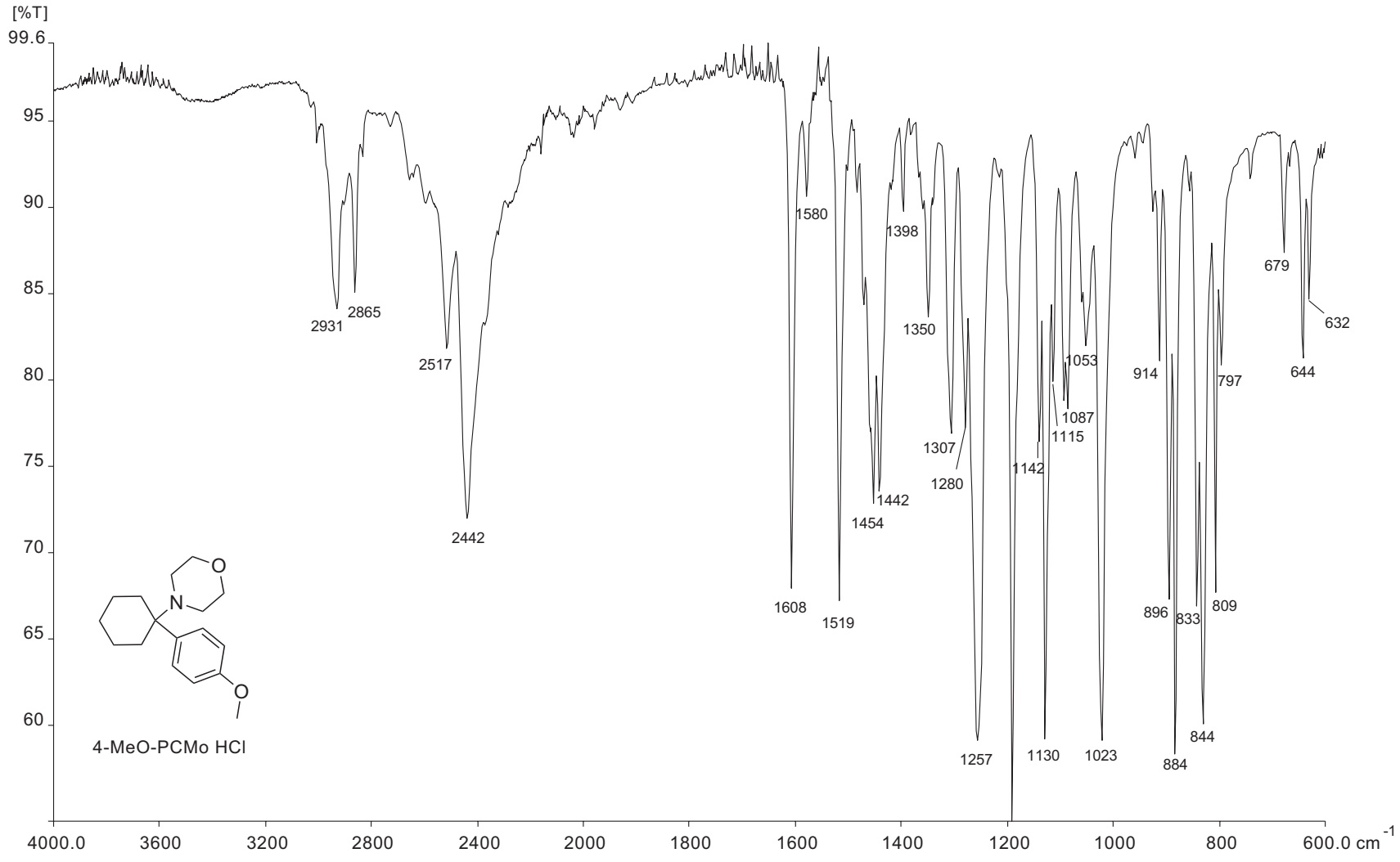
O
3-MeO-PCMo HCl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1257
1142
1130
1115
1087
1053
1023
914
896
884
844
833
809
797
679
644
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4-MeO-PCMo HCl
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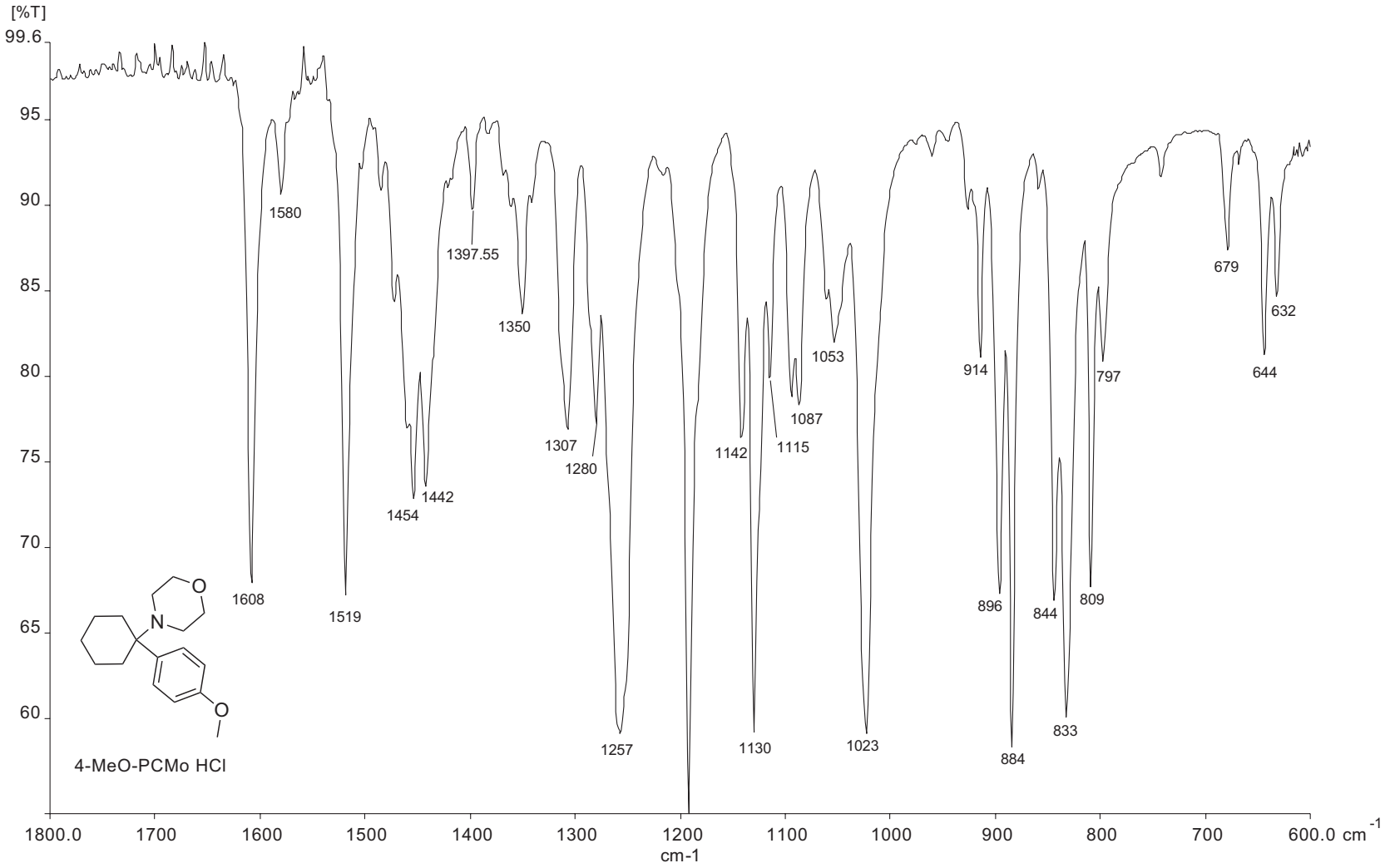
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4-MeO-PCMo HCl
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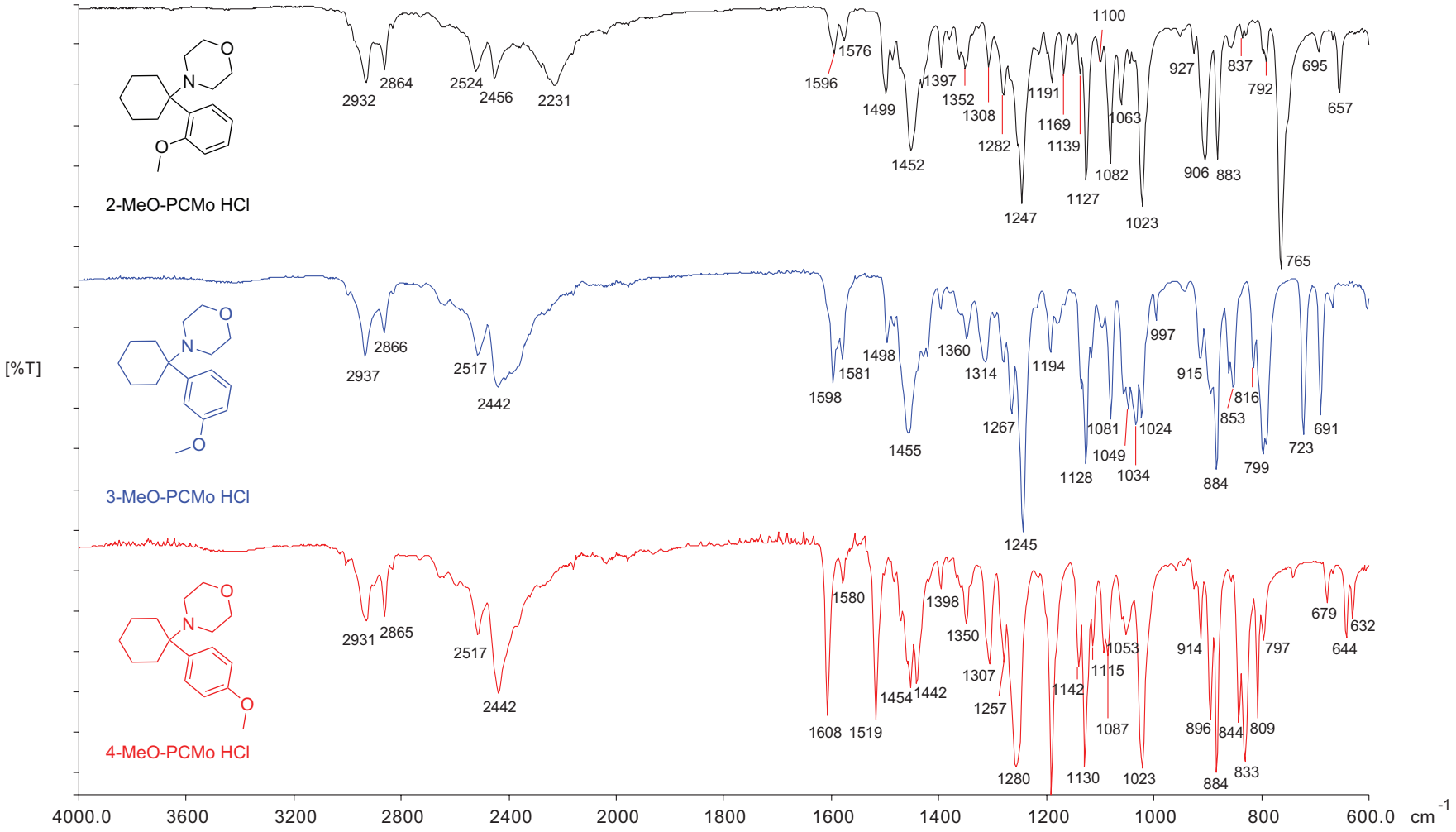
cm-1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1191
1169
1139
1127
1100
1082
1063
1023
927
906
883
837
792
765
695
657
3-MeO-PCMo HCl
2937
2866
2517
2442
1598
1581
1498
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1360
1314
1267
1245
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1128
1081
1049
1034
1024
997
915
884
853
816
799
723
691
4-MeO-PCMo HCl
2931
2865
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1608
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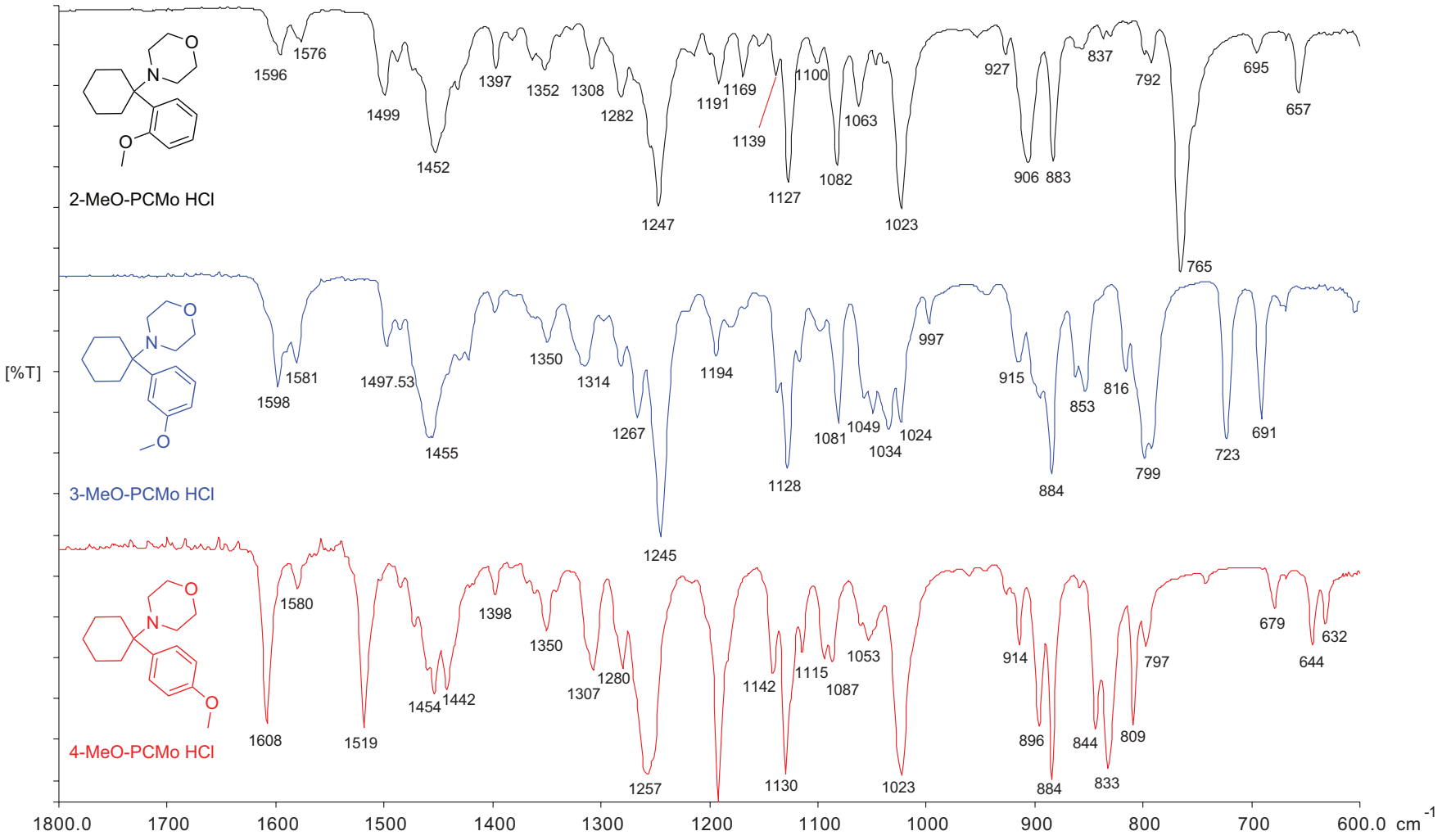
cm -1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1082
1063
1023
927
906
883
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792
765
695
657
3-MeO-PCMo HCl
1598
1581
1497.53
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1267
1245
1194
1128
1081
1049
1034
1024
997
915
884
853
816
799
723
691
4-MeO-PCMo HCl
1608
1580
1519
1454
1442
1398
1350
1307
1280
1257
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679
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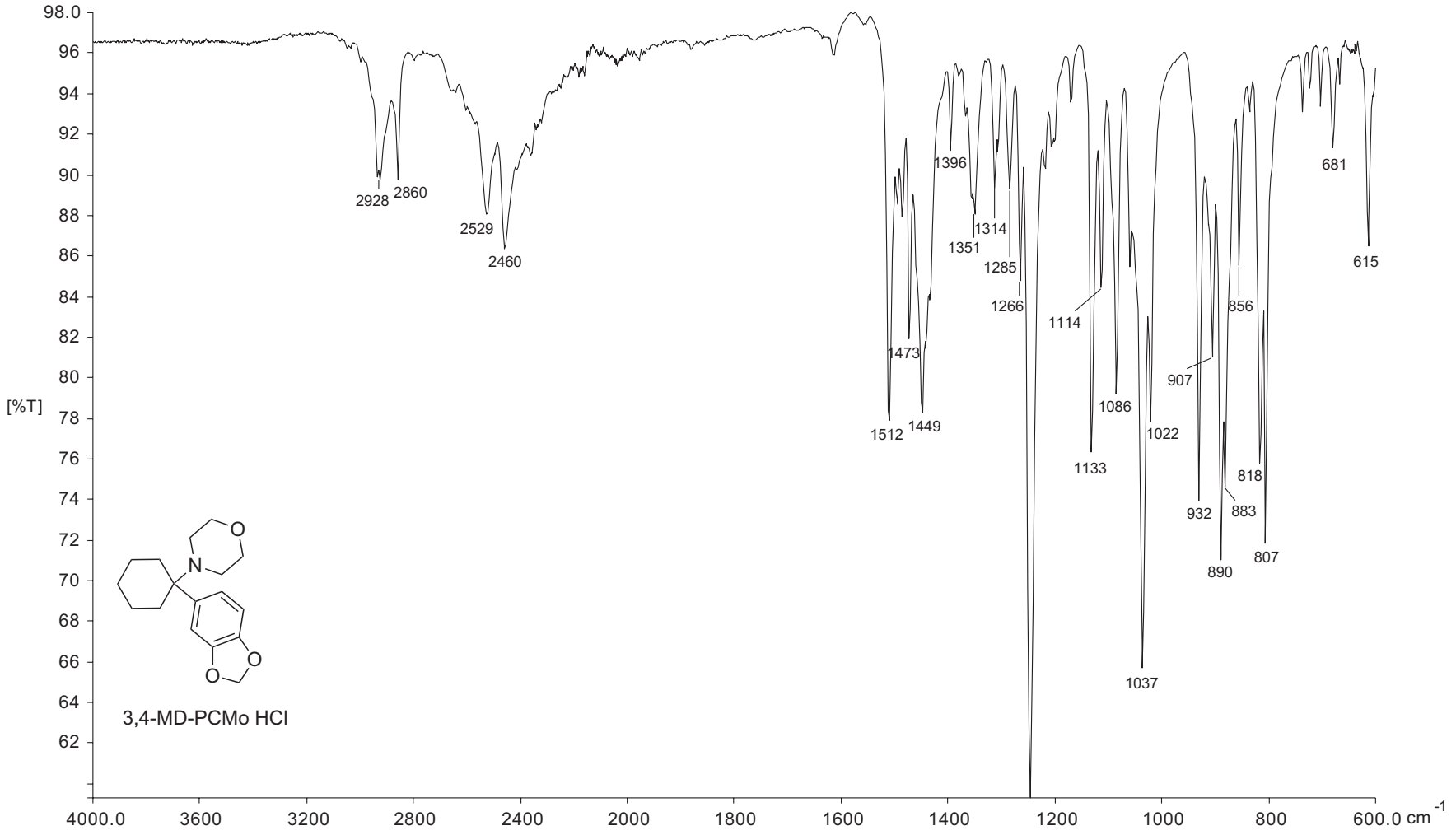
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2860
2529
2460
1512
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1351
1314
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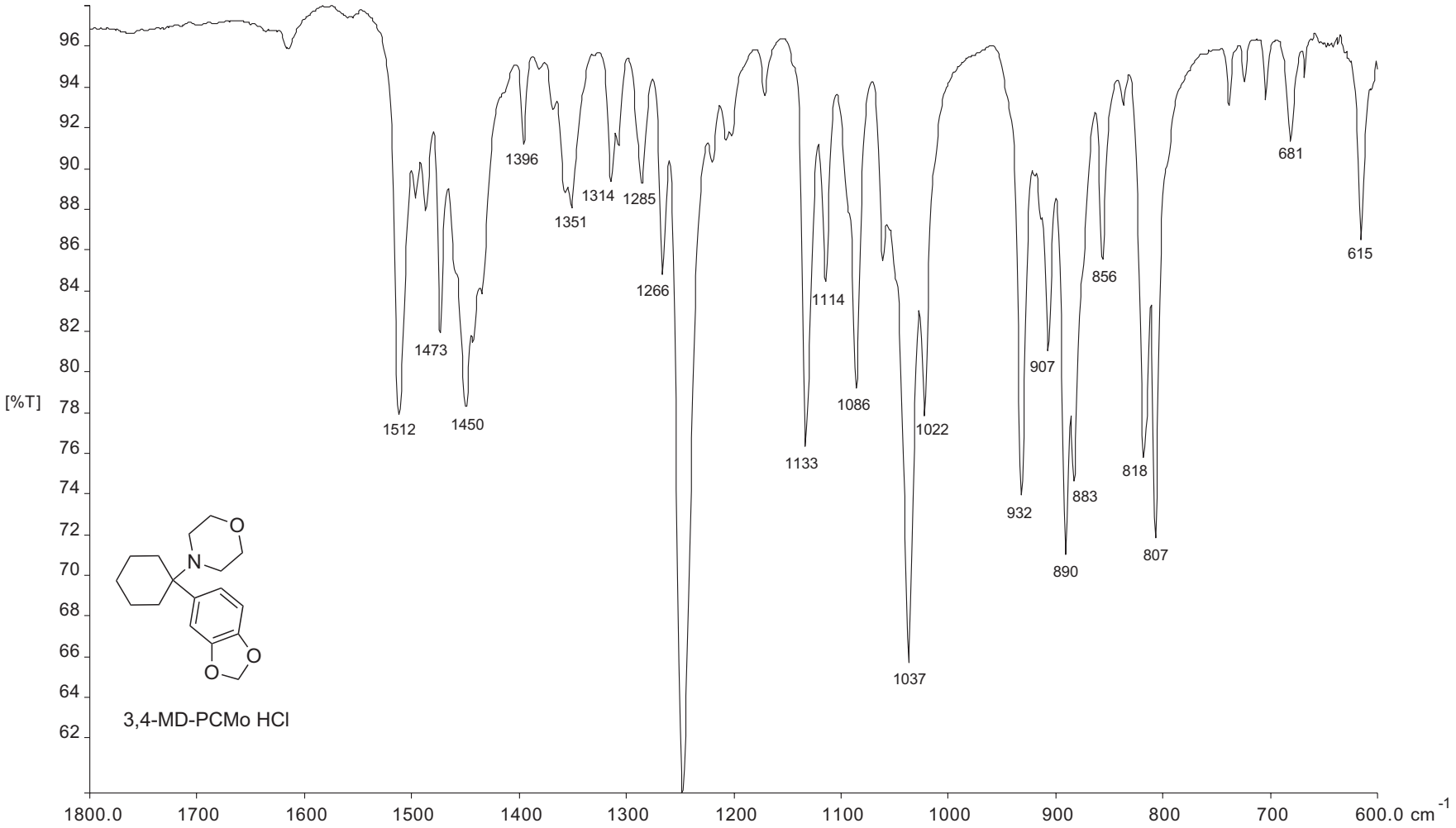
1266
1114
1133
1086
1037
1022
907
932
890
883
856
818
807
681
615
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0 cm -1
O
N
O
O
3,4-MD-PCMo HCl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72
70
68
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64
62
1800.0
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600.0 cm-1
1512
1473
1450
1396
1351
1314
1285
1266
1133
1114
1086
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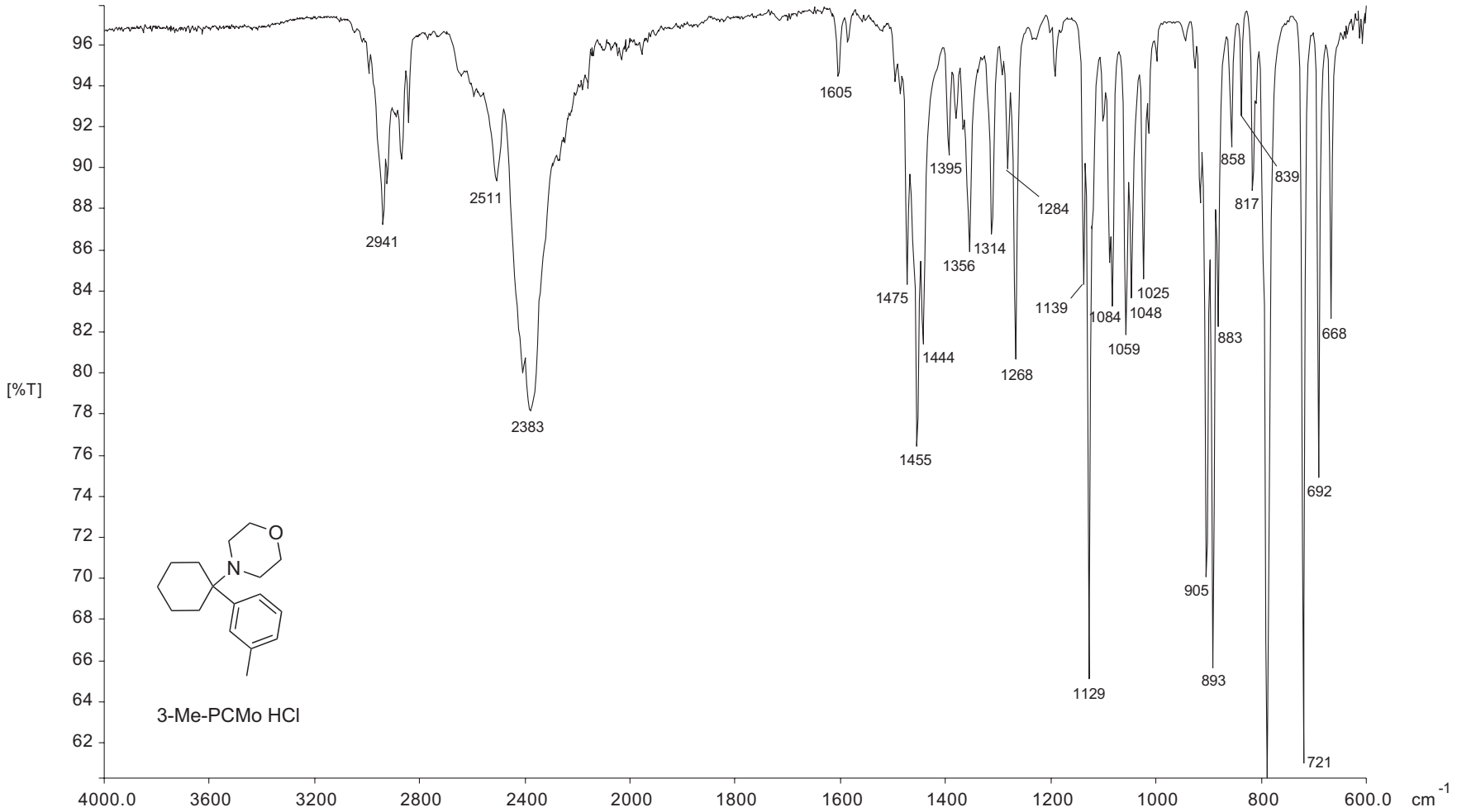
856
818
807
681
615
O
N
O
O
3,4-MD-PCMo HCl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94
92
90
88
86
84
82
80
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76
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72
70
68
66
64
62
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm -1
2941
2511
2383
1605
1475
1455
1444
1395
1356
1314
1284
1268
1139
1129
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905
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883
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839
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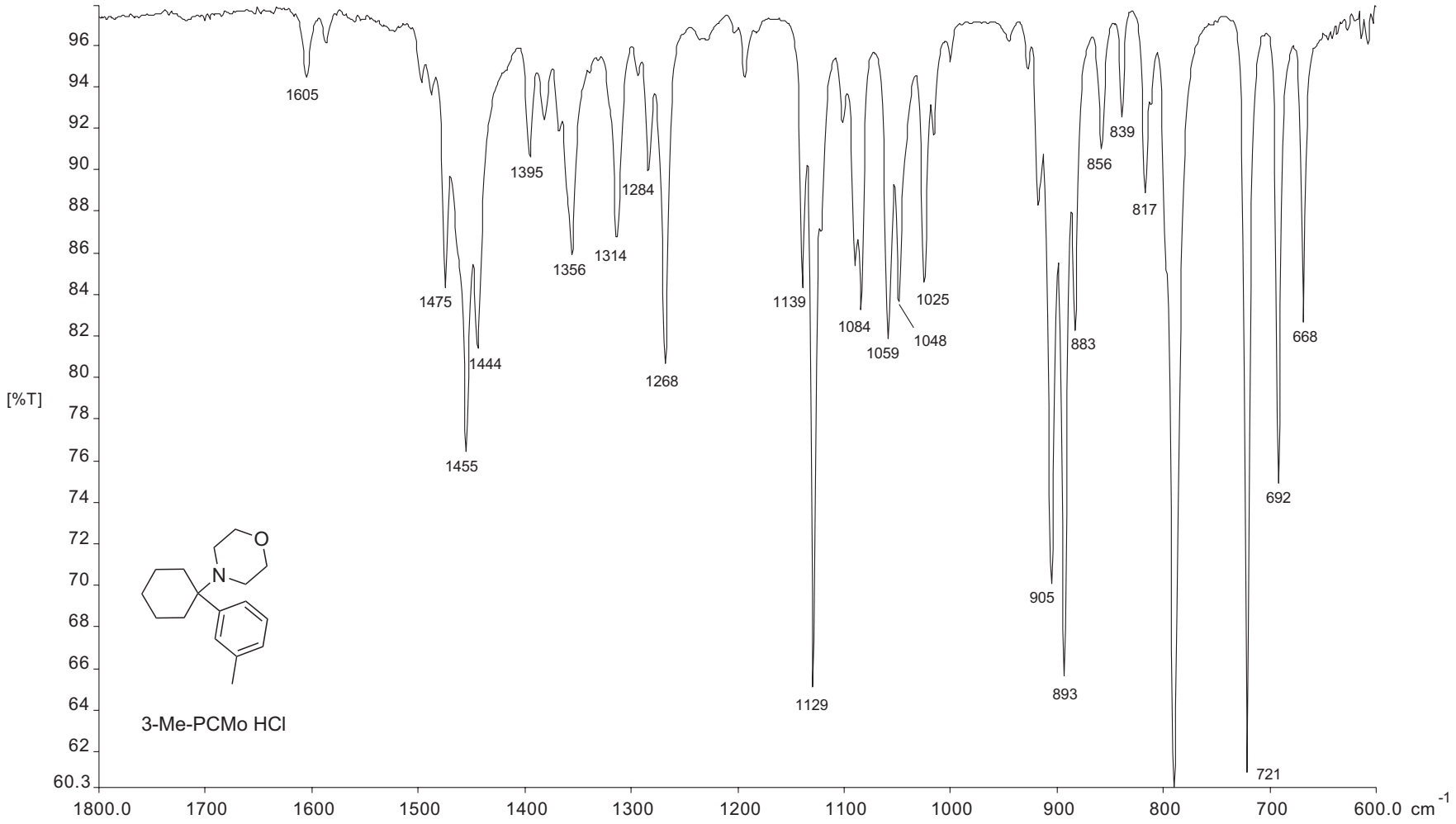
721
692
668
O
N
3-Me-PCMo HCl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64
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60.3
1800.0
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600.0 cm-1
1605
1475
1444
1455
1395
1356
1314
1284
1268
1139
1129
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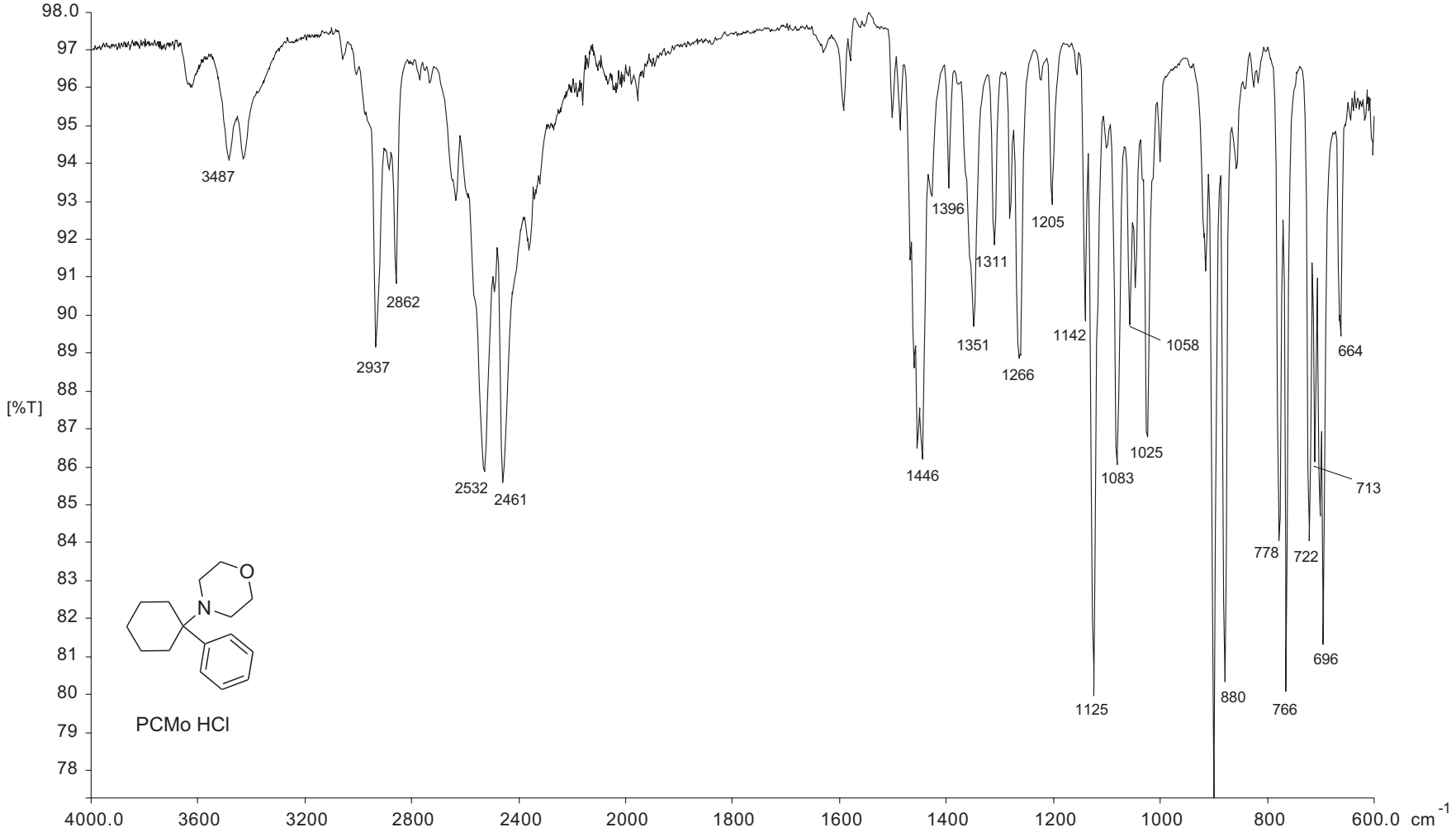
721
692
668
O
N
3-Me-PCMo HCl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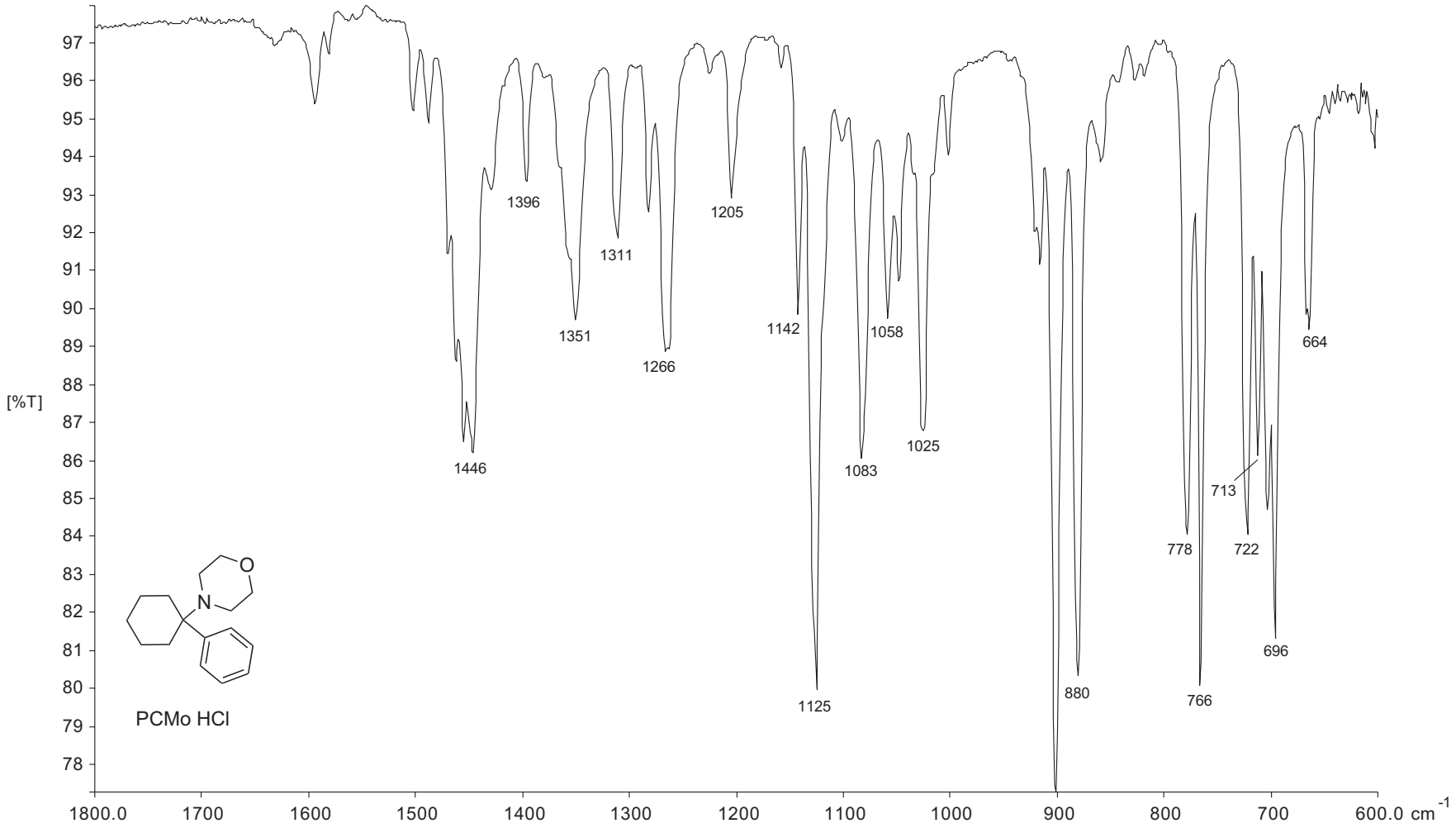
78
[%T]
3487
2937
2862
2532
2461
1446
1396
1351
1311
1266
1205
1142
1125
1083
1058
1025
880
778
766
722
713
696
664
O
N
PCMo HCl
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1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81
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79
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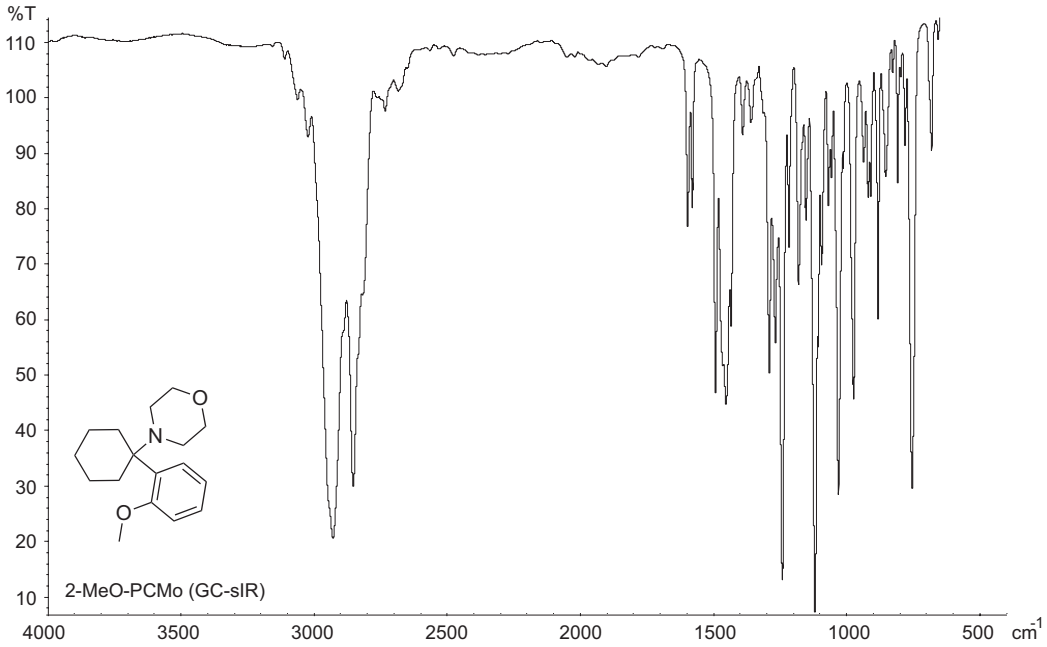
1800.0
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600.0 cm-1
1446
1396
1351
1311
1266
1205
1142
1125
1083
1058
1025
880
778
766
722
713
696
664
O
N
PCMo HCl

Gas chromatography solid-state infrared analysis (GC-sIR)

Samples were analyzed using a GC-solid phase-IR-system that consisted of an Agilent GC 7890B (Waldbronn, Germany) with probe sampler Agilent G4567A and a DiscovIR-GC™ (Spectra Analysis, Marlborough, MA, USA). The column eluent was cryogenically accumulated on a spirally rotating ZnSe disk cooled by liquid nitrogen. IR spectra were recorded through the IR-transparent ZnSe disk using a nitrogen-cooled MCT detector. GC parameters: injection in splitless mode with an injection port temperature set at 240°C and a DB-1 fused silica capillary column (30 m × 0.32 mm i.d., 0.25 µm film thickness). The carrier gas was helium with a flow rate of 2.5 mL/min and the oven temperature program was as follows: 80°C for 2 min, ramped to 290°C at 20°C/min, and held at for 20 min. The transfer line was heated at 280°C. Infrared conditions: oven temperature, restrictor temperature, disc temperature, and Dewar cap temperatures were 280°C, 280°C, −40°C, and 35°C, respectively. The vacuum was 0.2 mTorr, disc speed 3 mm/s, spiral separation was 1 mm, wavelength resolution 4 cm^{-1} and IR range 650–4000 cm^{-1}. Acquisition time was 0.6 s/file with 64 scans/spectrum. Data were processed using GRAMS/AI Ver. 9.1 (Grams Spectroscopy Software Suite, Thermo Fischer Scientific, Dreieich, Germany) followed by implementation of the OMNIC Software, Ver. 7.4.127 (Thermo Electron Corporation, Dreieich, Germany).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110
100
90
80
70
60
50
40
30
20
10
4000
3500
3000
2500
2000
1500
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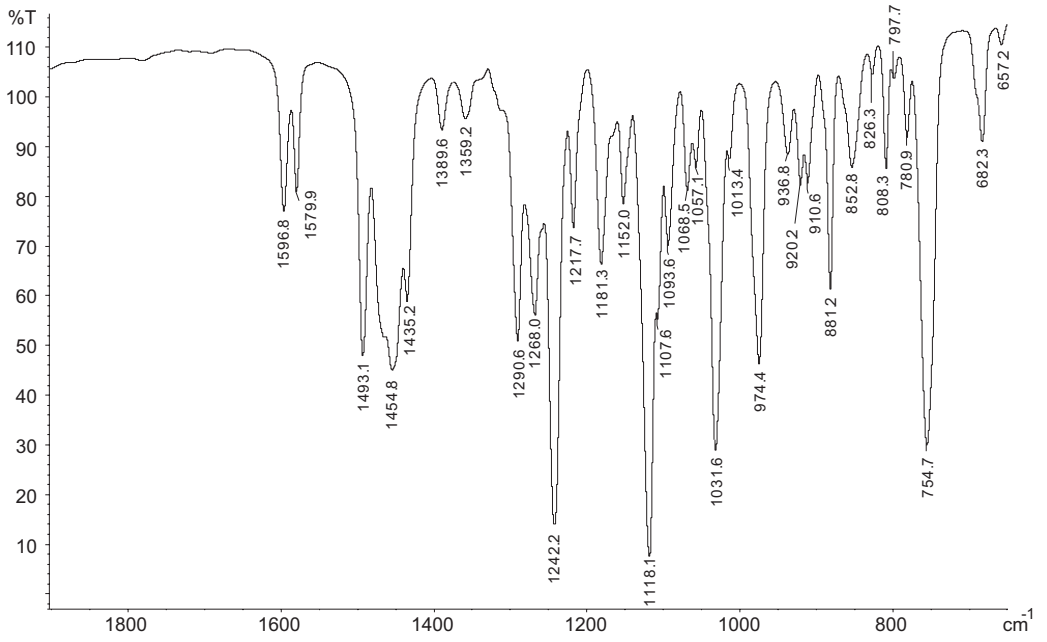
500
cm-1
O
N
O
2-MeO-PCMo (GC-sIR)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80
70
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30
20
10
1800
1600
1400
1200
1000
800
cm-1
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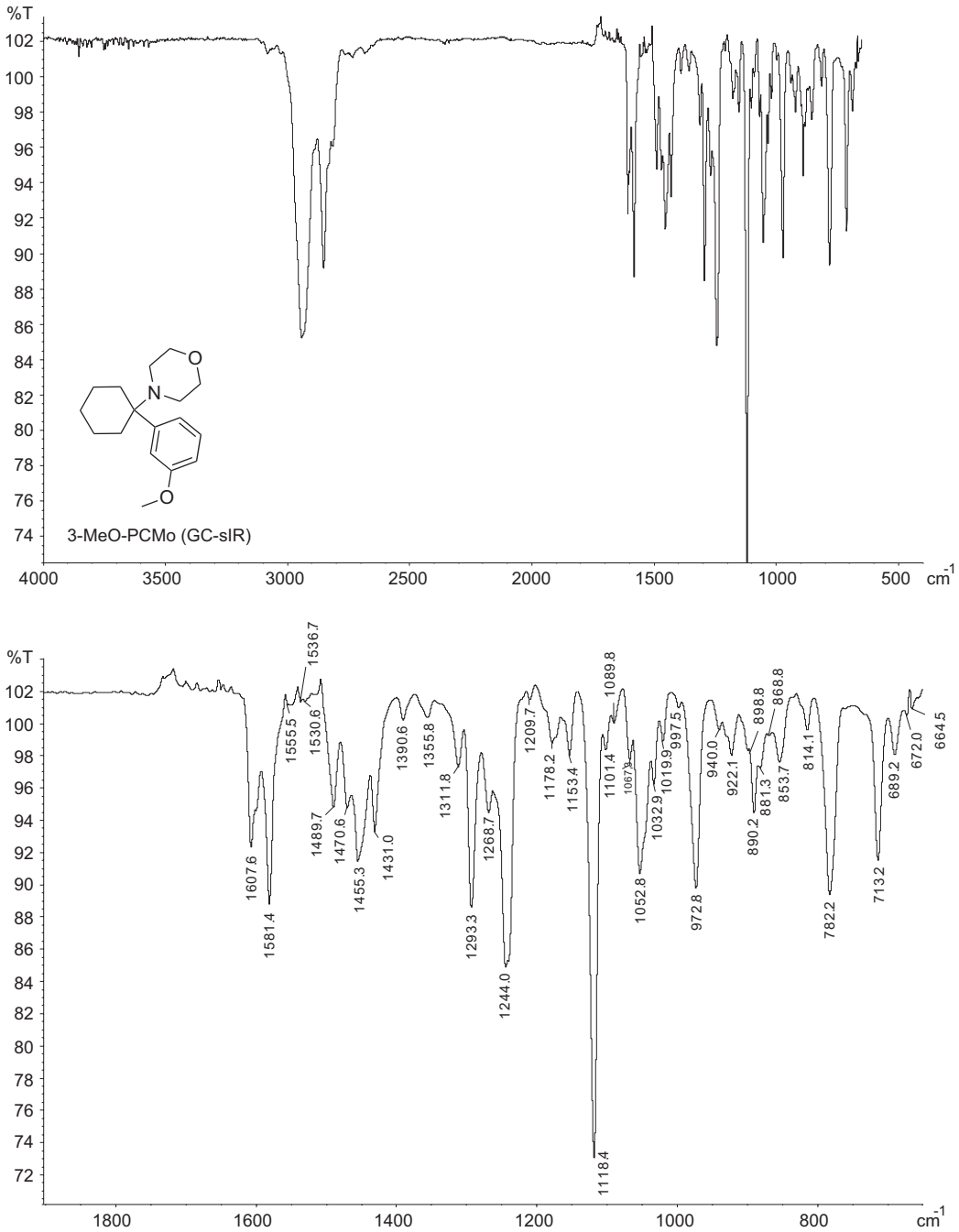
1579.9
1493.1
1454.8
1435.2
1389.6
1359.2
1290.6
1268.0
1242.2
1217.7
1181.3
1152.0
1118.1
1107.6
1093.6
1068.5
1057.1
1031.6
1013.4
974.4
936.8
920.2
910.6
881.2
852.8
826.3
808.3
797.7
780.9
754.7
682.3
657.2


%T
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100
98
96
94
92
90
88
86
84
82
80
78
76
74
4000
3500
3000
2500
2000
1500
1000
500
cm-1
O
N
O
3-MeO-PCMo (GC-sIR)
%T
102
100
98
96
94
92
90
88
86
84
82
80
78
76
74
72
1800
1600
1400
1200
1000
800
cm-1
1607.6
1581.4
1555.5
1536.7
1530.6
1489.7
1470.6
1455.3
1431.0
1390.6
1355.8
1311.8
1293.3
1268.7
1244.0
1209.7
1178.2
1153.4
1118.4
1101.4
1089.8
1067.3
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1019.9
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972.8
940.0
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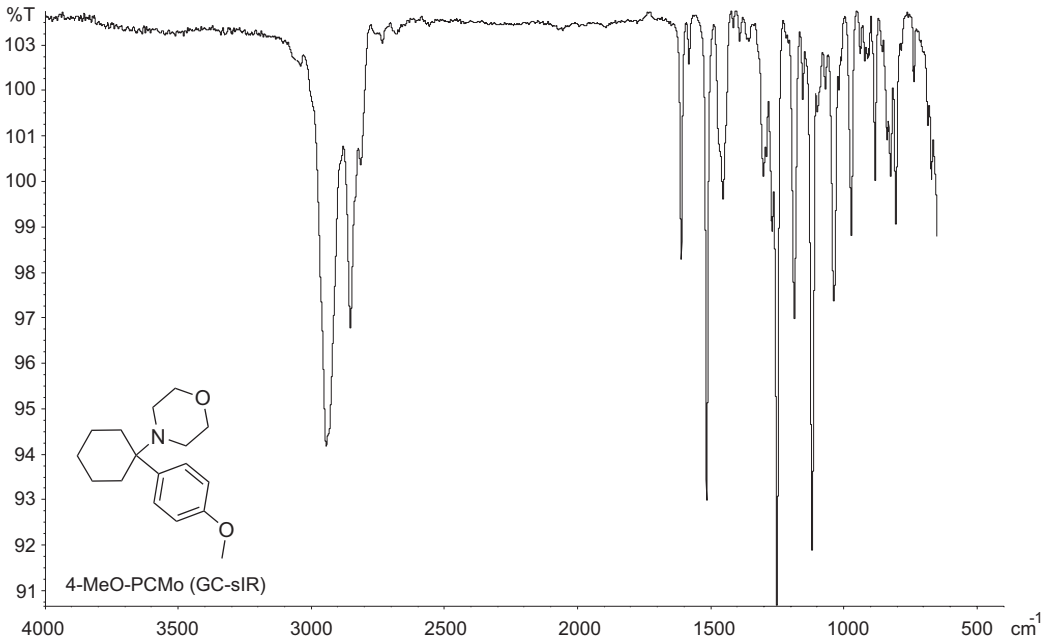
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103
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100
99
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96
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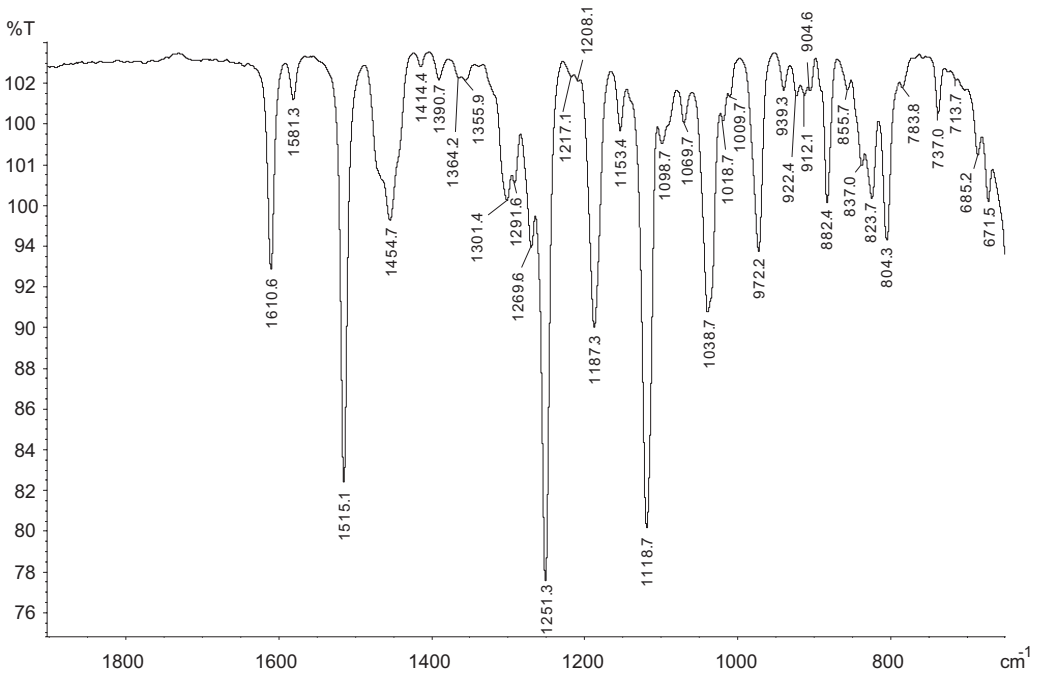
94
93
92
91
O
N
O
4-MeO-PCMo (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1


%T
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101
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82
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78
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1414.4
1390.7
1364.2
1355.9
1301.4
1291.6
1269.6
1251.3
1217.1
1208.1
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1153.4
1118.7
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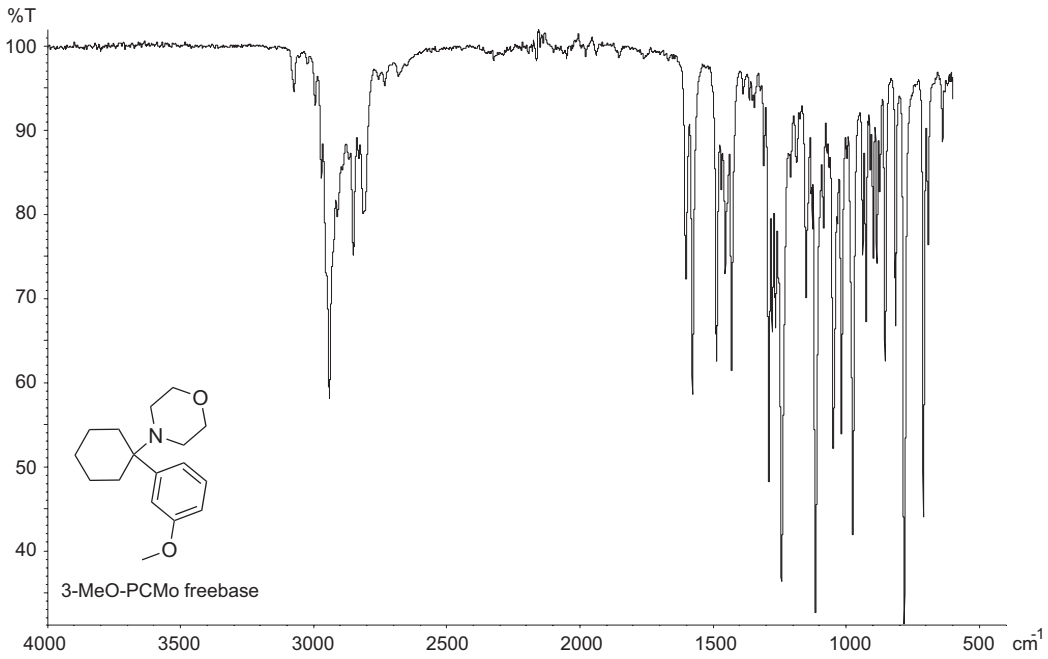
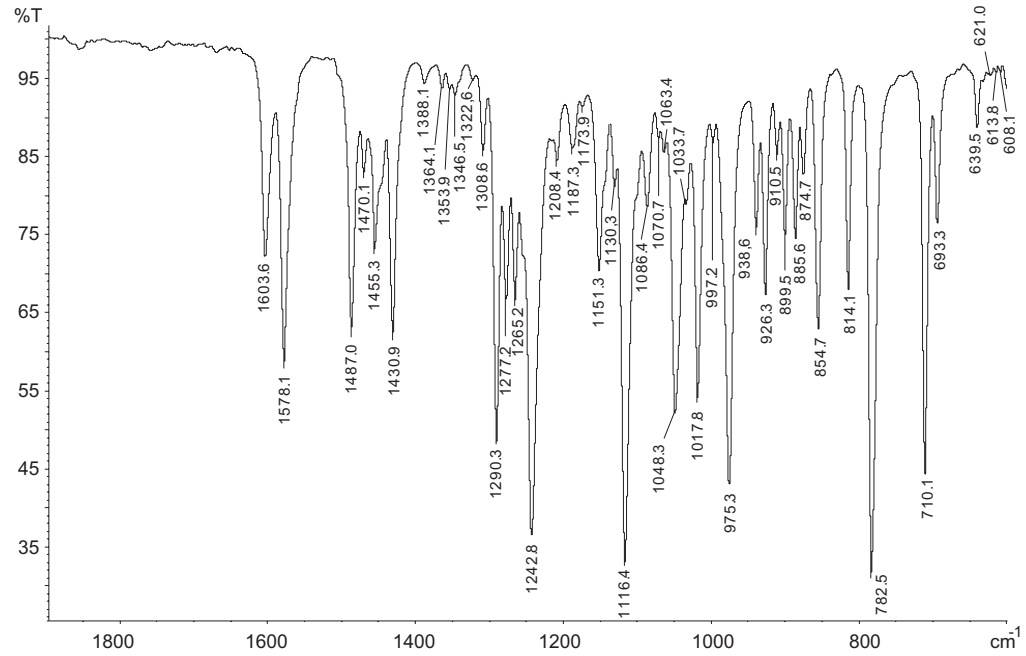
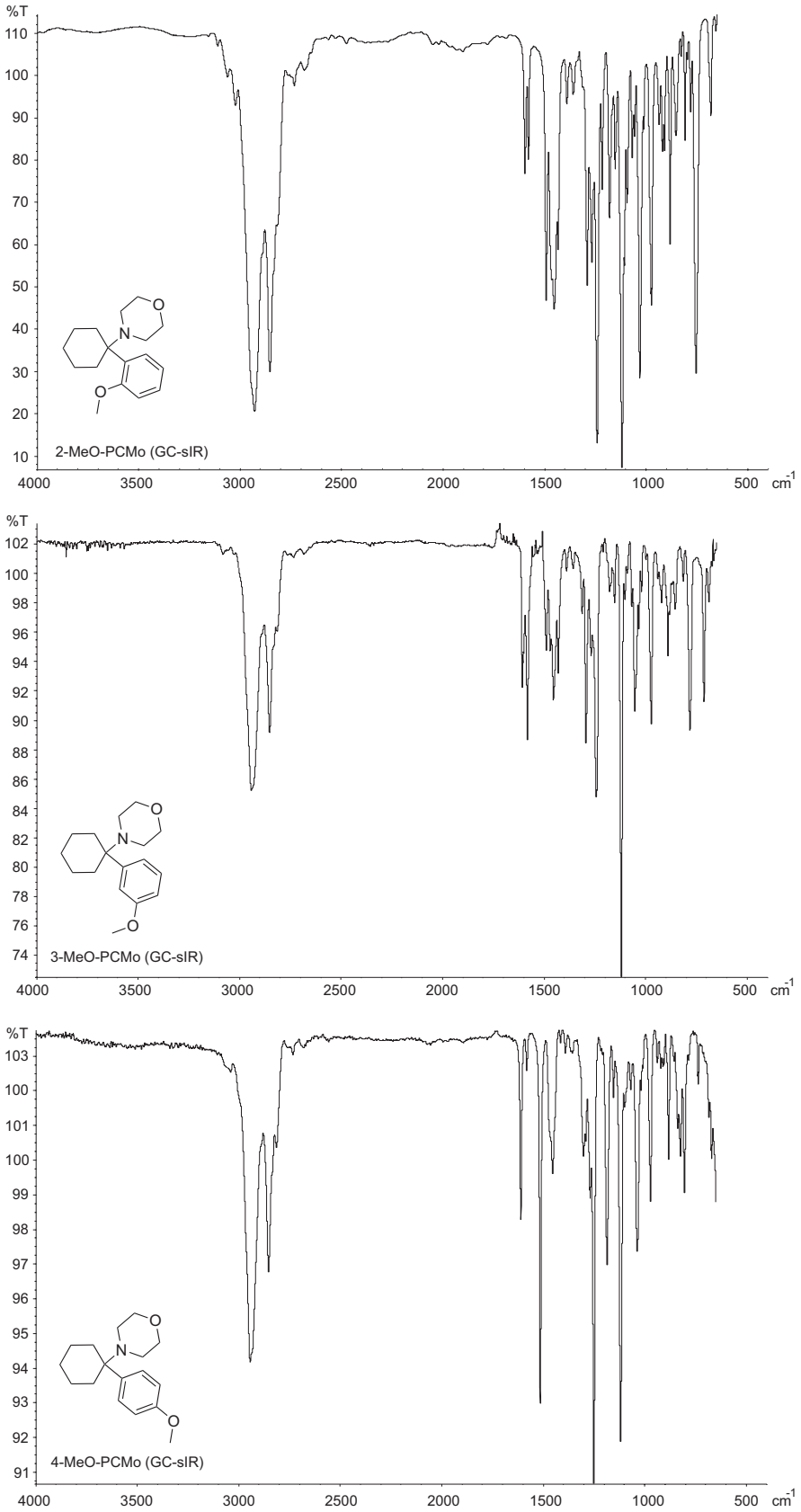
1069.7
1038.7
1018.7
1009.7
972.2
939.3
922.4
912.1
904.6
882.4
855.7
837.0
823.7
804.3
783.8
737.0
713.7
685.2
671.5
1800
1600
1400
1200
1000
800
cm-1

ATR-IR spectrum of 3-MeO-PCMo freebase

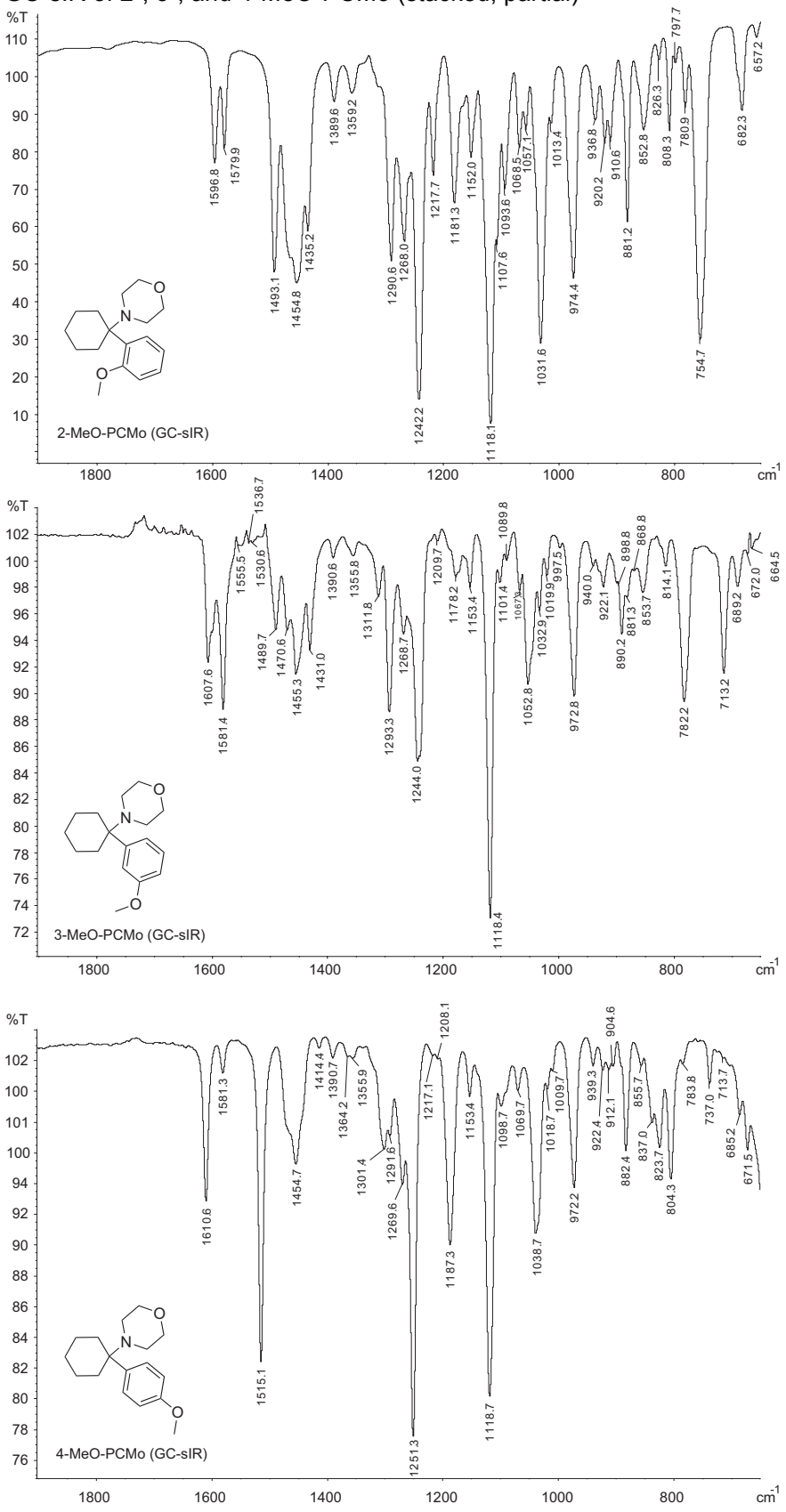




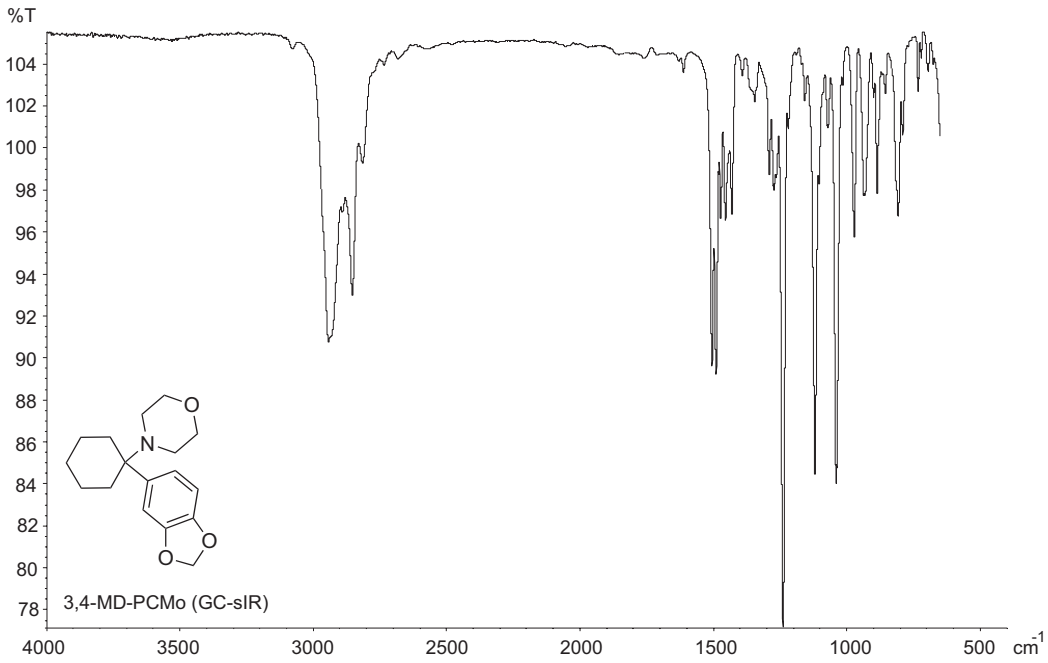
GC-sIR of 2-, 3-, and 4-MeO-PCMo (stacked)

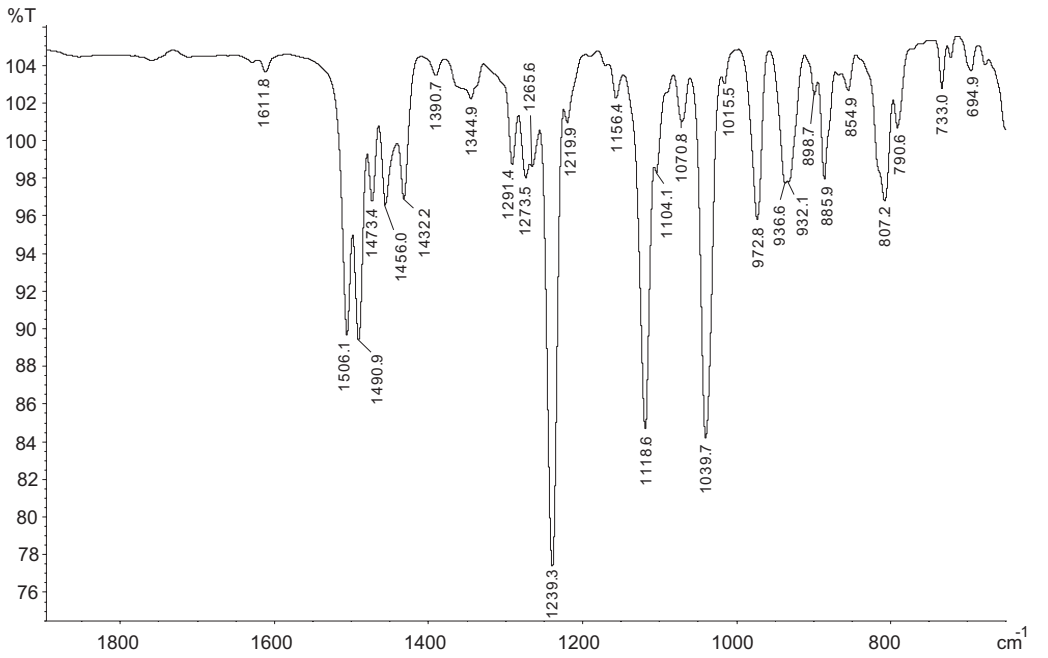


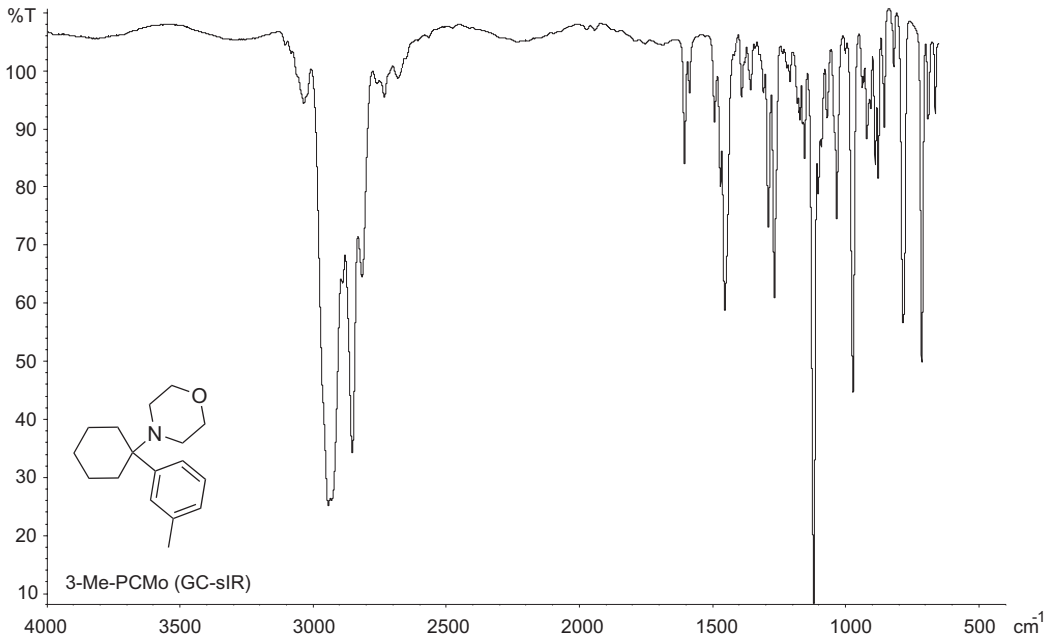
GC-sIR of 2-, 3-, and 4-MeO-PCMo (stacked, partial)



GC-sIR of 3,4-MD-PCMo, 3-Me-PCMo and PCMo






%T
100
90
80
70
60
50
40
30
20
10
O
N
3-Me-PCMo (GC-sIR)
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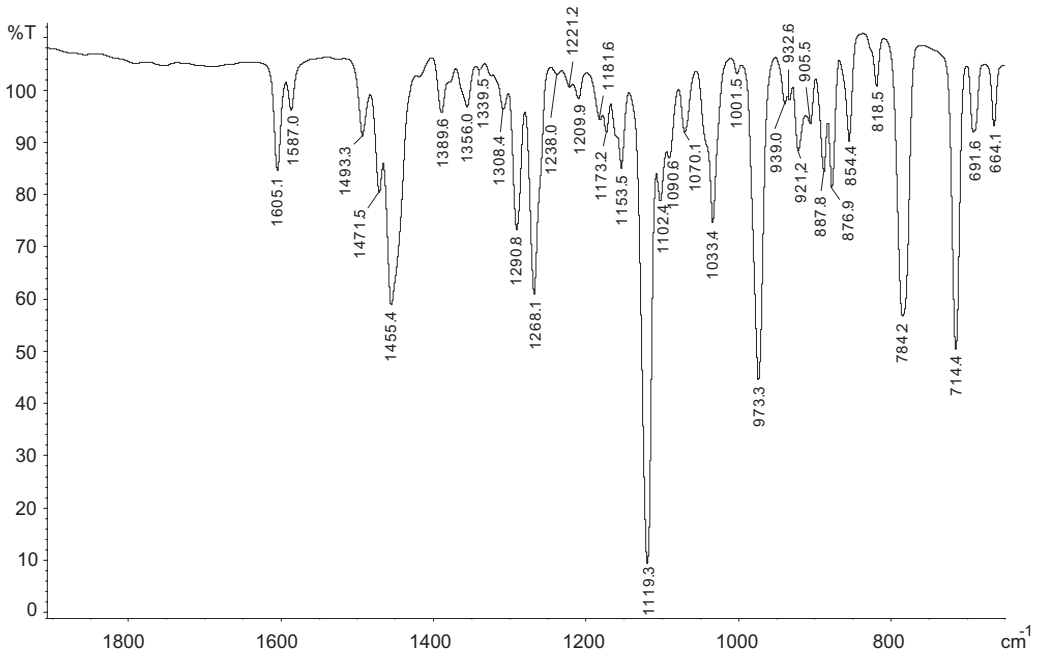
3500
3000
2500
2000
1500
1000
500
cm-1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70
60
50
40
30
20
10
0
1605.1
1587.0
1493.3
1471.5
1455.4
1389.6
1356.0
1339.5
1308.4
1290.8
1268.1
1238.0
1221.2
1209.9
1181.6
1173.2
1153.5
1119.3
1102.4
1090.6
1070.1
1033.4
1001.5
973.3
939.0
932.6
921.2
905.5
887.8
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854.4
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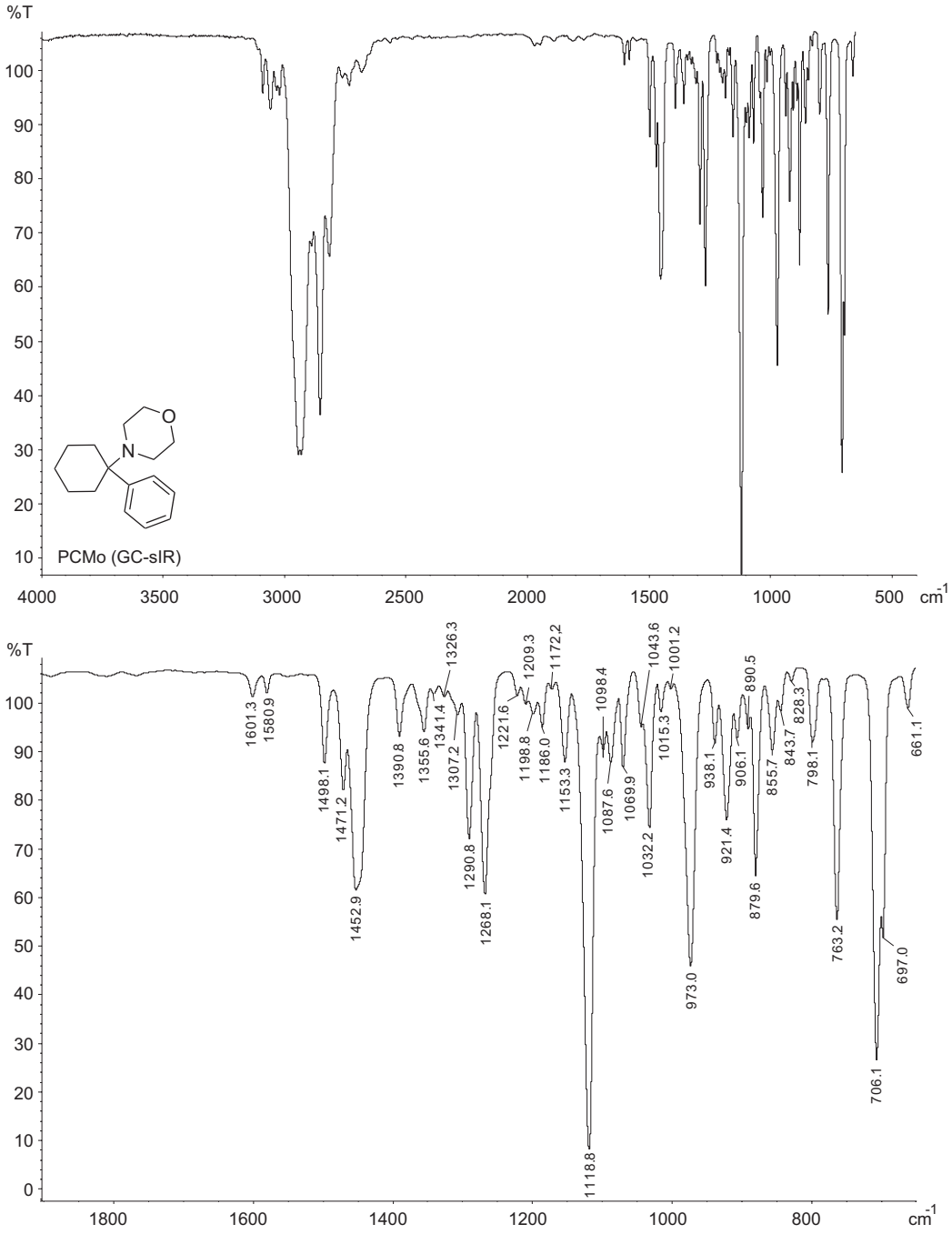
784.2
714.4
691.6
664.1
1800
1600
1400
1200
1000
800
cm-1


%T
100
90
80
70
60
50
40
30
20
10
O
N
PCMo (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1
%T
100
90
80
70
60
50
40
30
20
10
0
1601.3
1580.9
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1471.2
1452.9
1390.8
1355.6
1341.4
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1153.3
1118.8
1098.4
1087.6
1069.9
1043.6
1032.2
1015.3
1001.2
973.0
938.1
921.4
906.1
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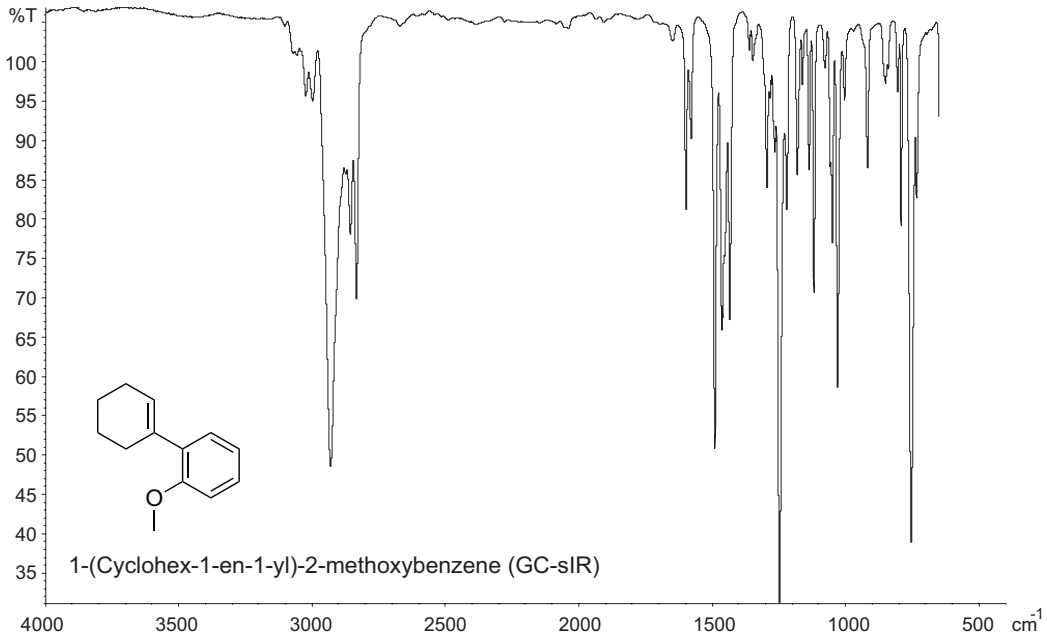
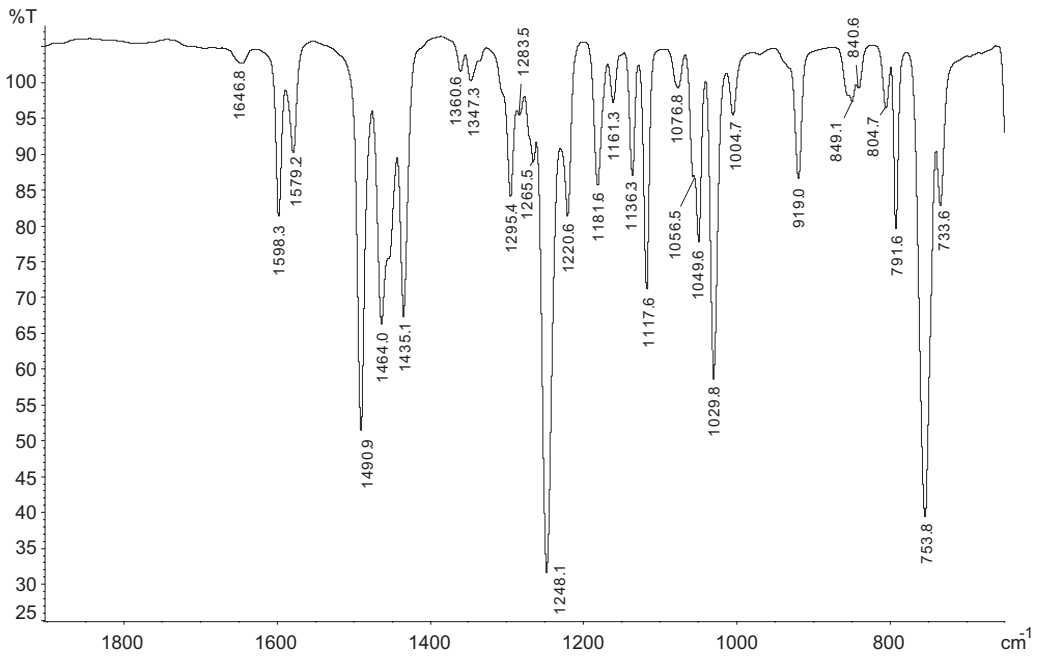
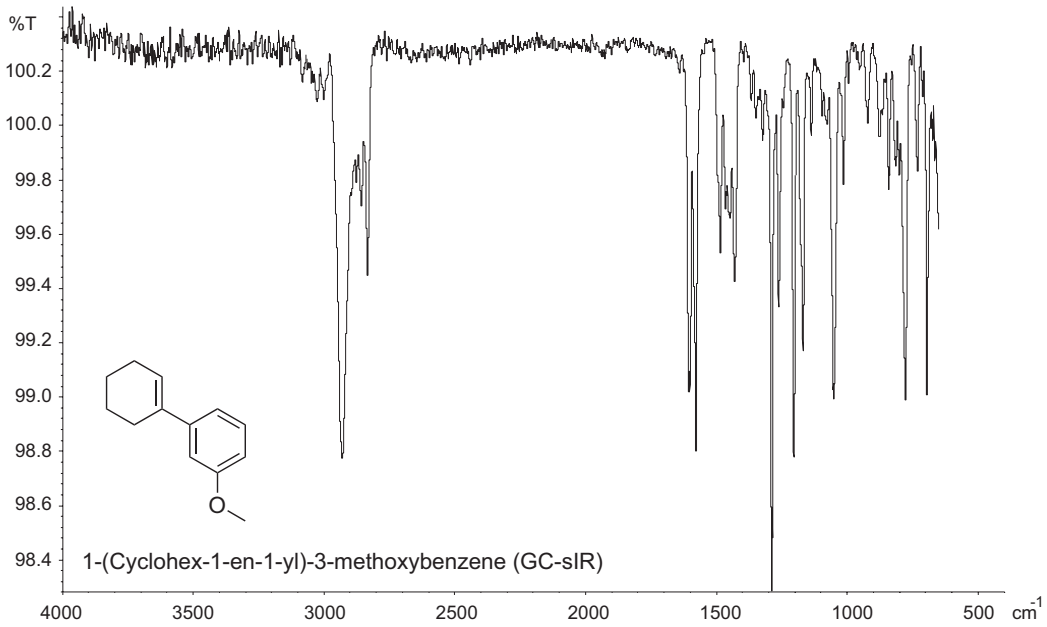
879.6
855.7
843.7
828.3
798.1
763.2
706.1
697.0
661.1
1800
1600
1400
1200
1000
800
cm-1

GC-sIR data of GC-induced degradation products



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99.6
99.4
99.2
99.0
98.8
98.6
98.4
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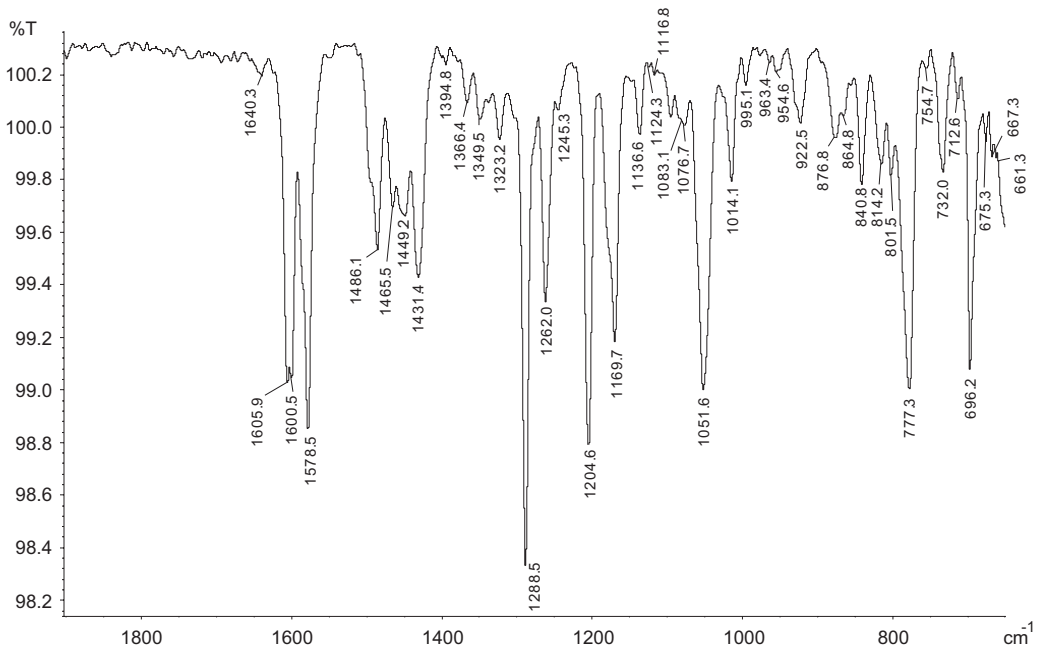
4000
3500
3000
2500
2000
1500
1000
500
cm-1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1431.4
1394.8
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1349.5
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1204.6
1169.7
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1116.8
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1076.7
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995.1
963.4
954.6
922.5
876.8
864.8
840.8
814.2
801.5
777.3
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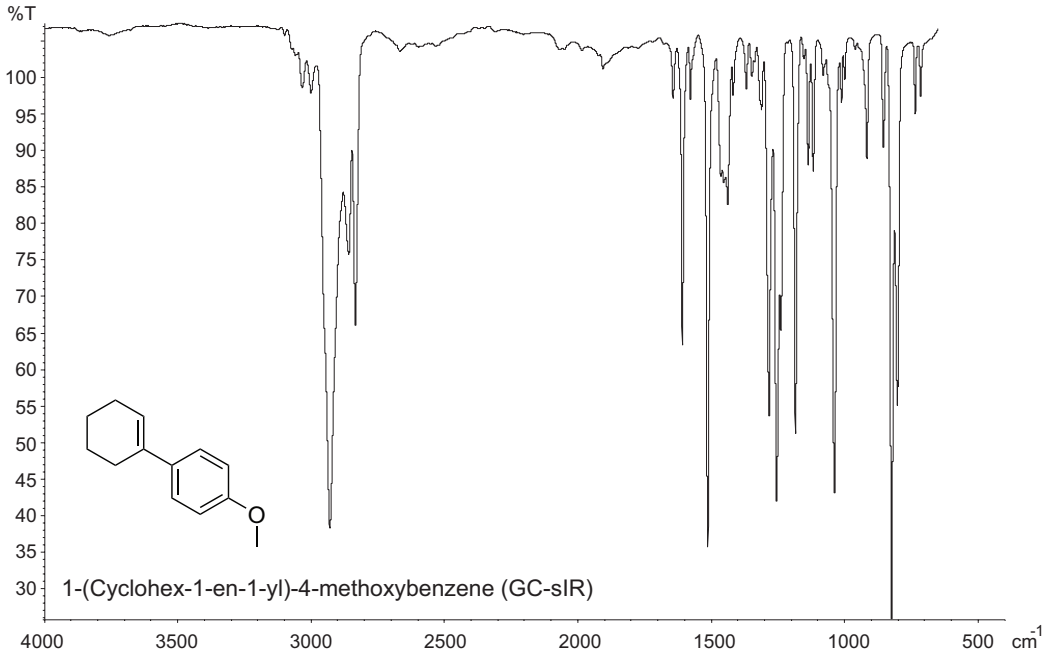
1000
800
cm-1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30
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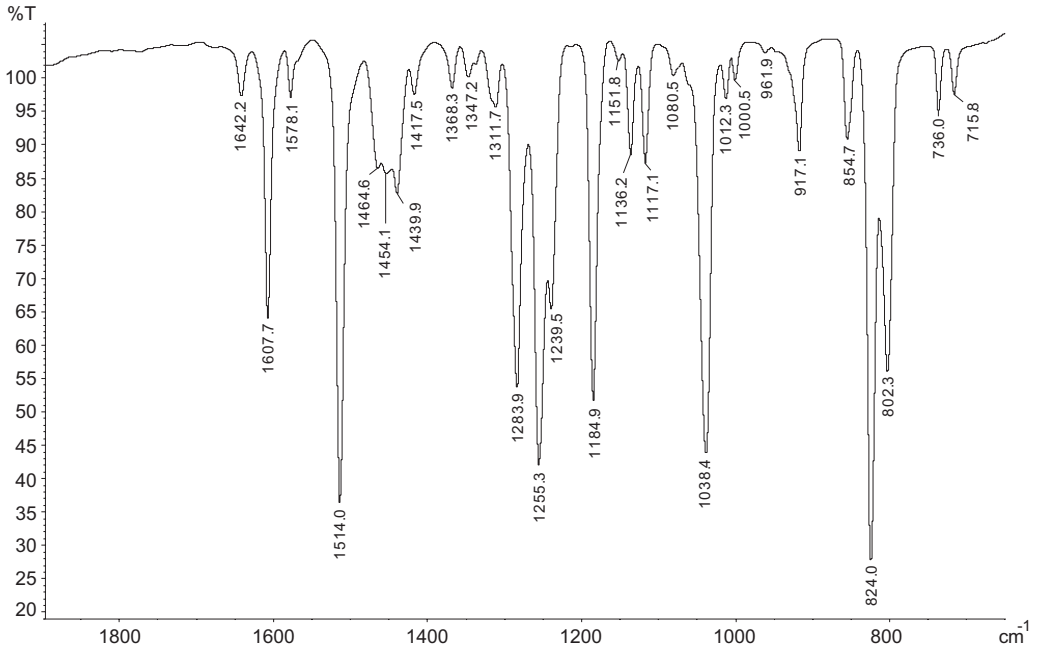
4000
3500
3000
2500
2000
1500
1000
500
cm-1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20
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1607.7
1514.0
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1454.1
1439.9
1417.5
1368.3
1347.2
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1283.9
1255.3
1239.5
1184.9
1151.8
1136.2
1117.1
1080.5
1038.4
1012.3
1000.5
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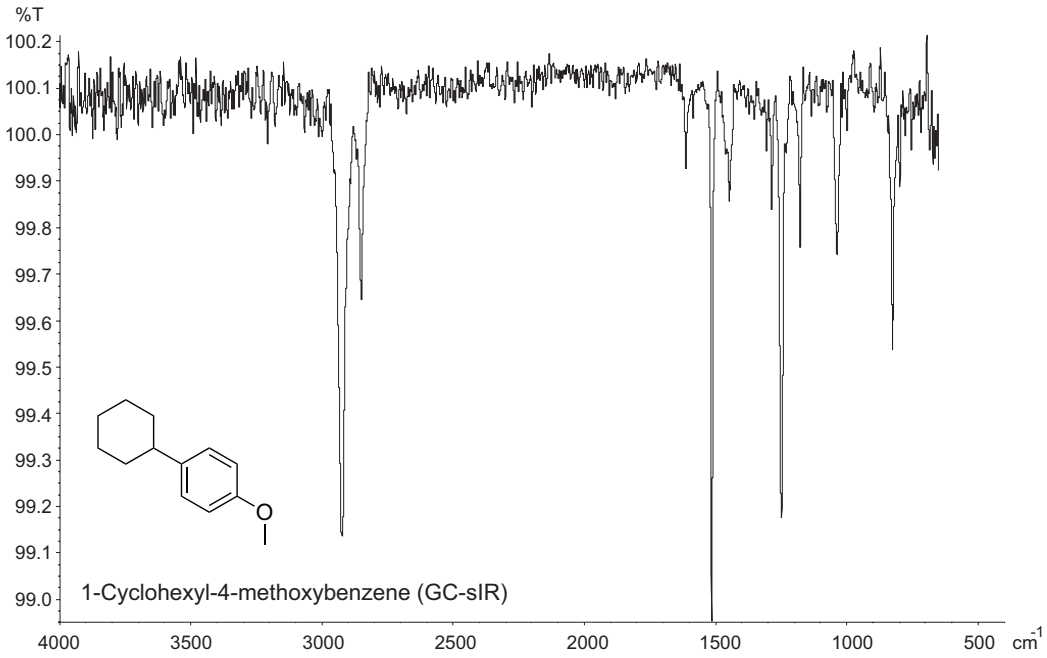
1800
1600
1400
1200
1000
800
cm-1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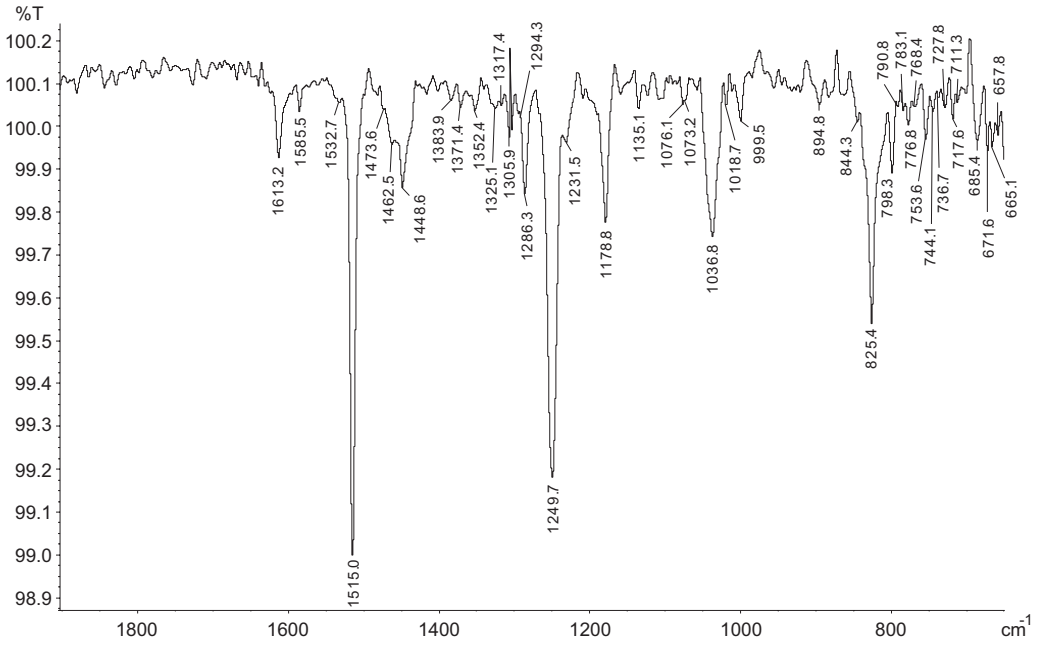
99.7
99.6
99.5
99.4
99.3
99.2
99.1
99.0
O
1-Cyclohexyl-4-methoxybenzene (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1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1305.9
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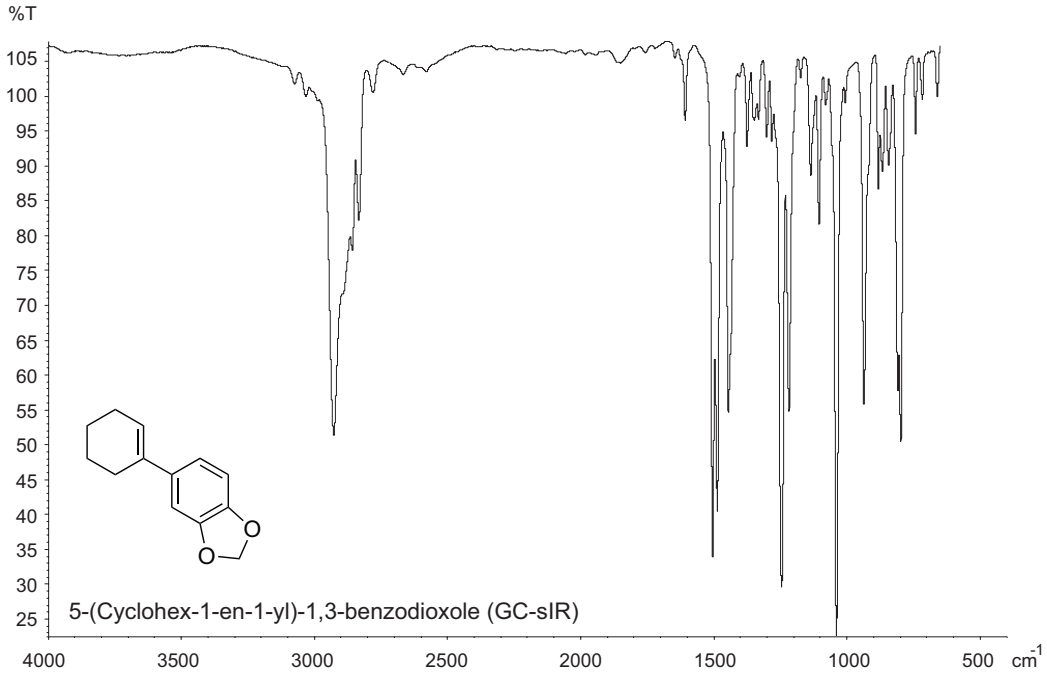
1249.7
1231.5
1178.8
1135.1
1076.1
1073.2
1036.8
1018.7
999.5
894.8
844.3
825.4
798.3
790.8
783.1
776.8
768.4
753.6
744.1
736.7
727.8
717.6
711.3
685.4
671.6
657.8
665.1
1800
1600
1400
1200
1000
800
cm-1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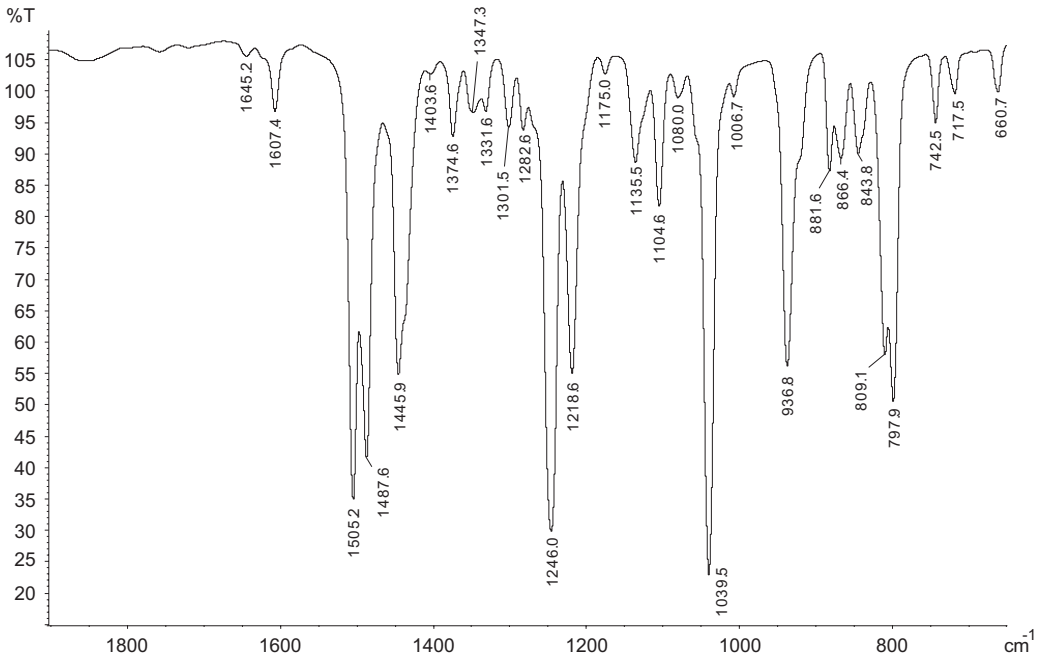
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
O
O
5-(Cyclohex-1-en-1-yl)-1,3-benzodioxole (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1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30
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20
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1607.4
1505.2
1487.6
1445.9
1403.6
1374.6
1347.3
1331.6
1301.5
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1218.6
1175.0
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1104.6
1080.0
1039.5
1006.7
936.8
881.6
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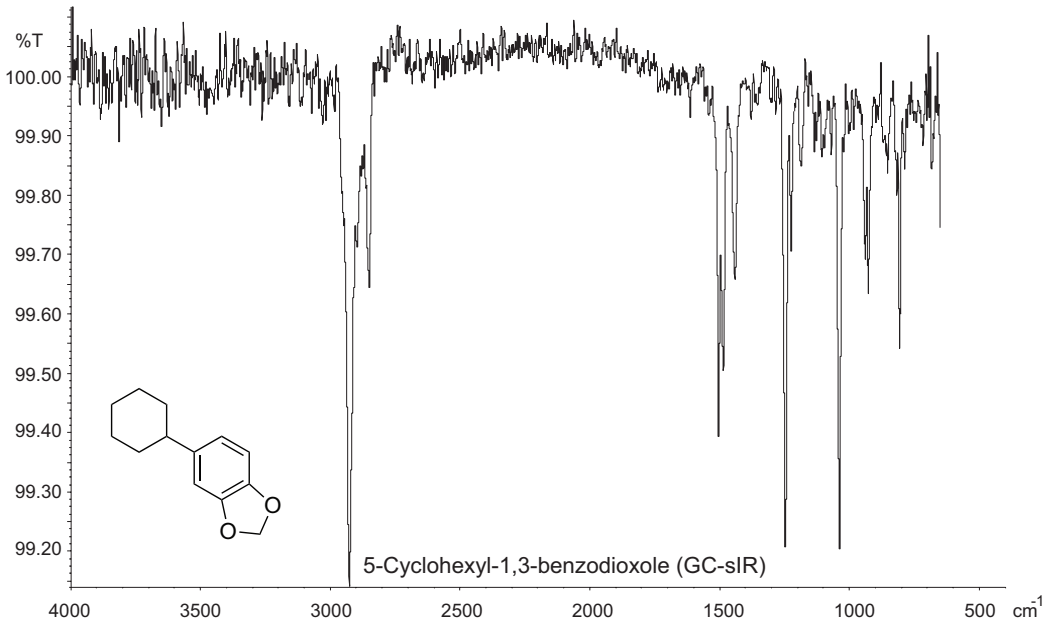
843.8
809.1
797.9
742.5
717.5
660.7
1800
1600
1400
1200
1000
800
cm-1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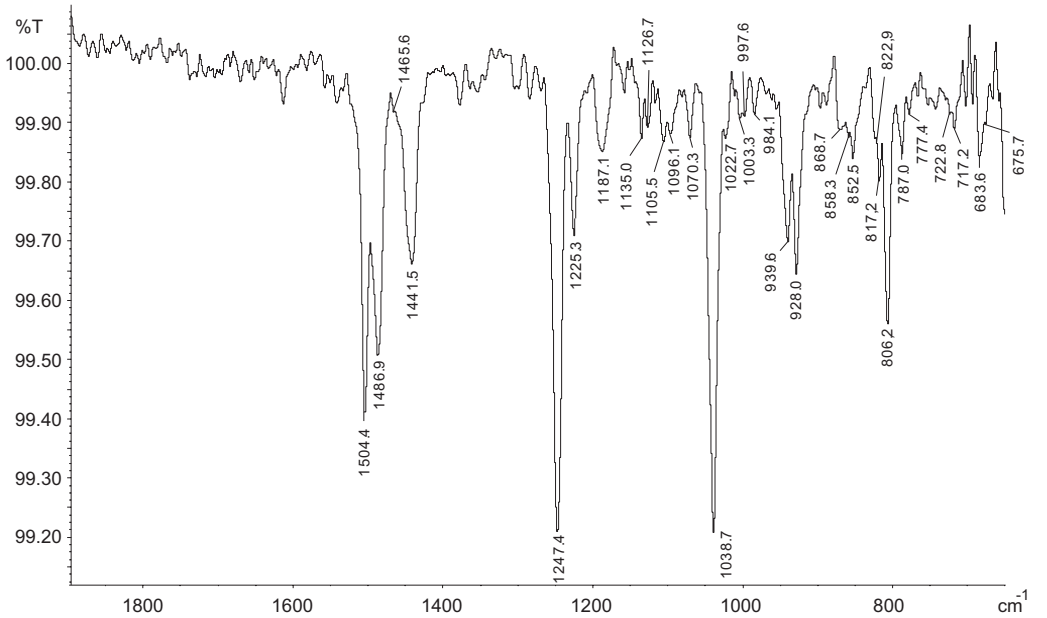
99.60
99.50
99.40
99.30
99.20
O
O
5-Cyclohexyl-1,3-benzodioxole (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1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99.50
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1247.4
1225.3
1187.1
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1126.7
1105.5
1096.1
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1038.7
1022.7
1003.3
997.6
984.1
939.6
928.0
868.7
858.3
852.5
822.9
817.2
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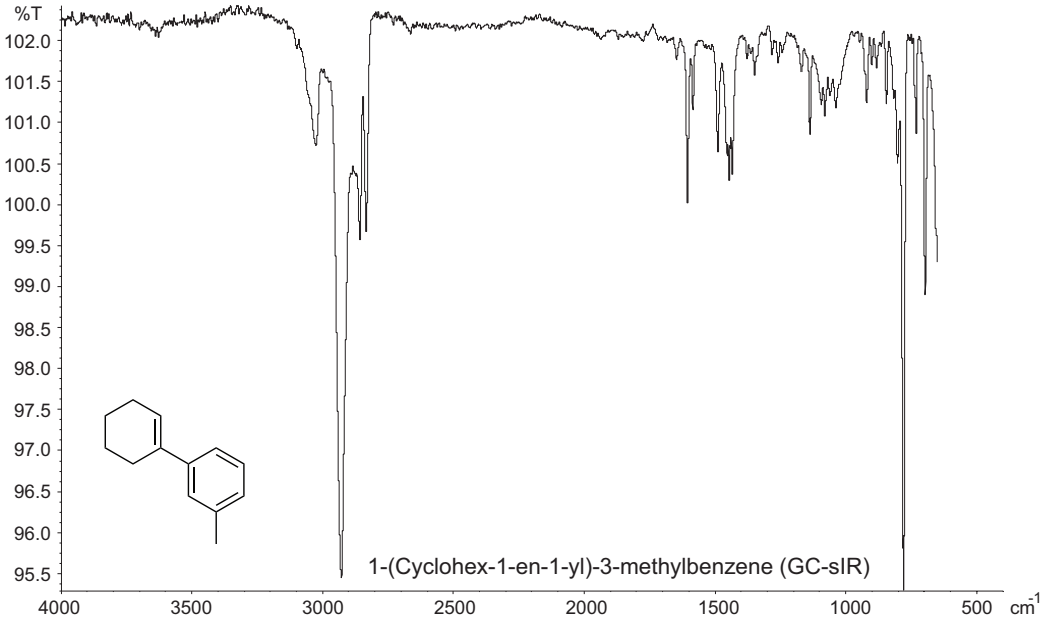
777.4
722.8
717.2
683.6
675.7
1800
1600
1400
1200
1000
800
cm-1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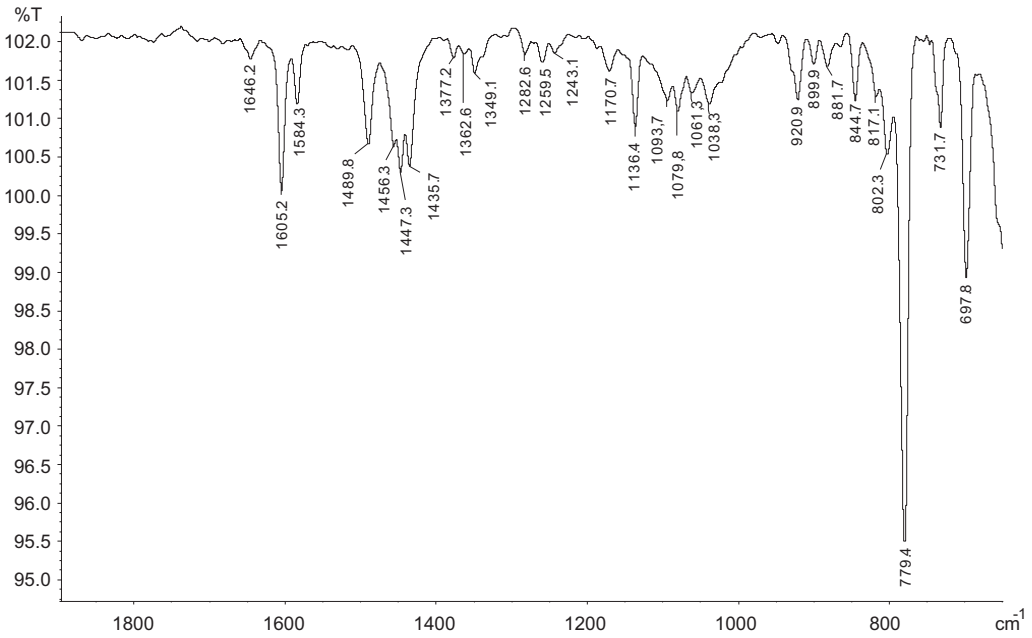
97.5
97.0
96.5
96.0
95.5
1-(Cyclohex-1-en-1-yl)-3-methylbenzene (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1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1038.3
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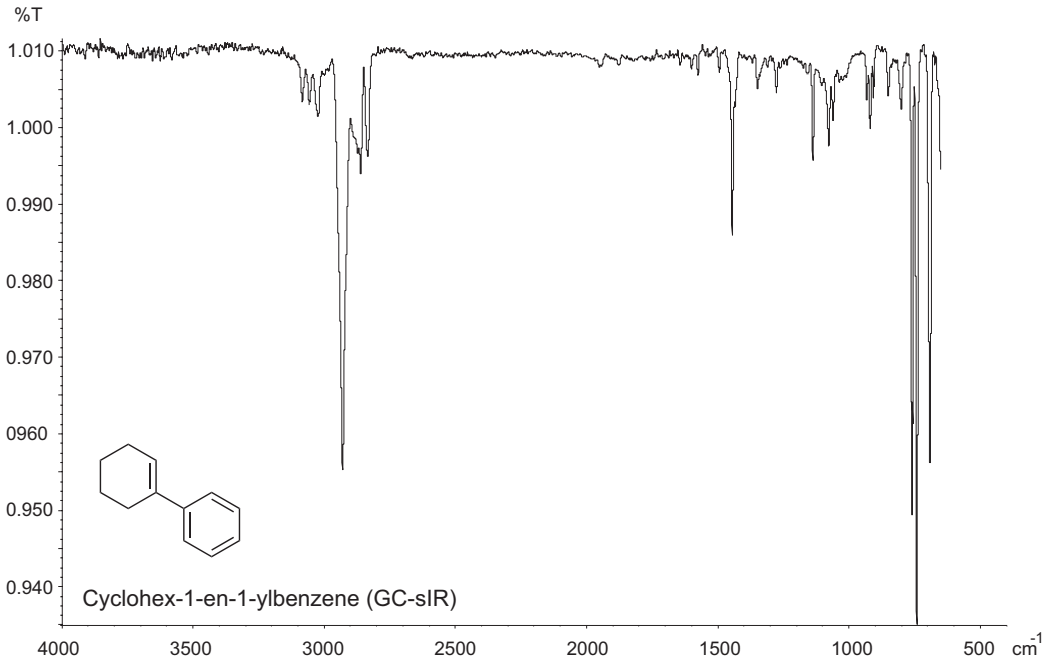
1800
1600
1400
1200
1000
800
cm-1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1.000
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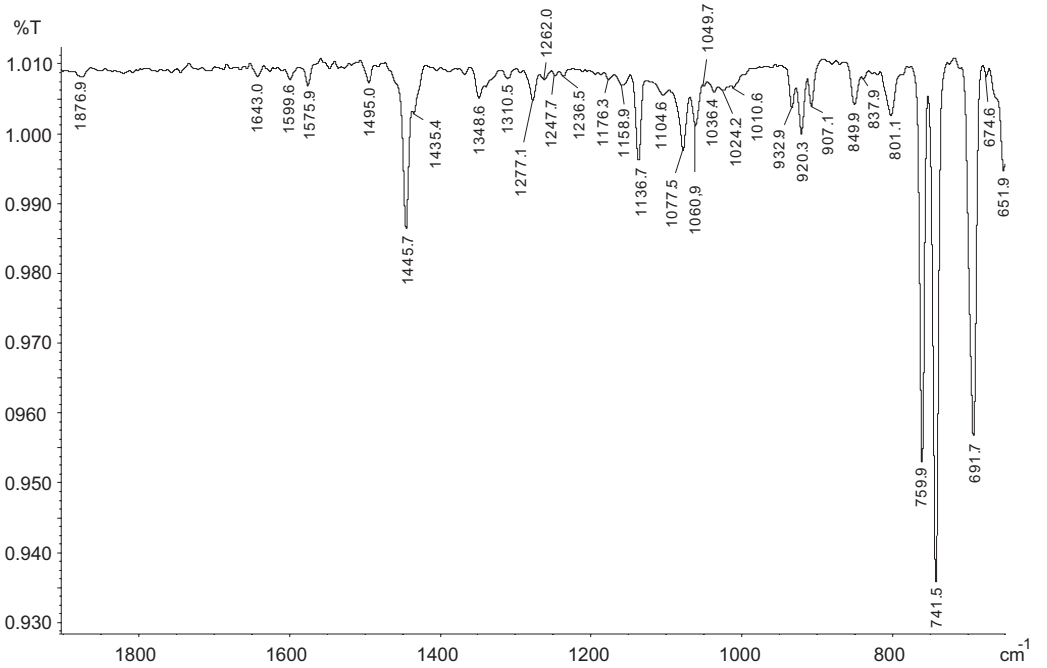
0.980
0.970
0960
0.950
0.940
Cyclohex-1-en-1-ylbenzene (GC-sIR)
4000
3500
3000
2500
2000
1500
1000
500
cm-1


%T
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1495.0
1445.7
1435.4
1348.6
1310.5
1277.1
1262.0
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1236.5
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1010.6
932.9
920.3
907.1
849.9
837.9
801.1
759.9
741.5
691.7
674.6
651.9
1800
1600
1400
1200
1000
800
cm-1

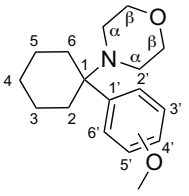
NMR data for PCMo analogues (HCl salts, $CDCl_3$, 400/100 MHz)

Carbon	2-MeO- PCMo	3-MeO- PCMo	4-MeO- PCMo	3,4-MD-PCMo	3-Me-PCMo	PCMo
C_1	73.01	71.33	71.42	71.54	71.42	71.42
$C_{2,6}$	31.74 32.59	30.29	30.34	30.61	30.26	30.19
$C_{3,5}$	22.82	22.60	22.54	22.56	22.59	22.53
C_4	24.70	24.51	24.63	24.52	24.57	24.58
$C_{1'}$	117.38	131.48	121.39	123.30	129.62	129.74
$C_{2'}$	160.28	116.83	130.86	109.37	129.82	129.46
$C_{3'}$	113.47	160.29	114.60	148.72	139.18	129.37
$C_{4'}$	131.81	113.68	160.44	148.89	126.57	129.91
$C_{5'}$	121.37	130.33	114.60	108.70	129.18	129.37
$C_{6'}$	132.76	121.46	130.86	123.73	130.62	129.46
C_α	45.39 46.99	45.63	45.35	45.46	45.49	45.53
C_β	63.89	63.61	65.59	63.60	63.32	63.59
C_c	55.54 (OCH_3)	55.51 (OCH_3)	55.38 (OCH_3)	101.88 (OCH_2O)	21.67 (CH_3)	-

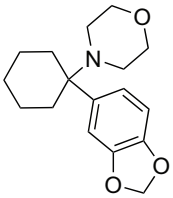
Proton	2-MeO- PCMo	3-MeO- PCMo	4-MeO- PCMo	3,4-MD-PCMo	3-Me-PCMo	PCMo
H_1	-	-	-	-	-	-
$H_{2,6}$	2.35 t (*J* = 12.3 Hz, 1H) 2.73–2.50 (1H) [a] 2.84 d (*J* = 12.1 Hz) 3.62 s (1H)	2.59 td (*J* = 13.0, 3.3 Hz, $2H_{ax}$)[c] 2.77 d (*J* = 12.4 Hz, $2H_{eq}$)	2.58–2.47 m ($2H_{ax}$)[e] 2.82–2.73 m ($2H_{eq}$)	2.65–2.49 m ($2H_{ax}$)[i] 2.70 d (*J* = 12.2 Hz, $2H_{eq}$)	2.56–2.41 m ($2H_{ax}$)[k] 2.73 d (*J* = 12.5 Hz, $2H_{eq}$)	2.59 td (*J* = 12.9, 3.3 Hz, $2H_{ax}$)[m] 2.88–2.78 m ($2H_{eq}$)
$H_{3,5}$	1.12–0.96 m (1H) 1.31–1.12 m (1H) 1.81 d (*J* = 13.1 Hz, 2H)	1.18 qt (*J* = 13.4, 3.6 Hz, $2H_{ax}$) 1.82 dm (*J* = 13.3 Hz, $2H_{eq}$)	1.17 qt (*J* = 13.4, 3.4 Hz, $2H_{ax}$) 1.83–1.76 m ($2H_{eq}$)	1.18 qt (*J* = 13.4, 3.4 Hz, $2H_{ax}$) 1.82 d (*J* = 13.1 Hz, $2H_{eq}$)	1.11 qt (13.4, 3.4 Hz, $2H_{ax}$) 1.75 d (*J* = 13.4 Hz, $2H_{eq}$)	1.16 qt (*J* = 13.5, 3.6 Hz, $2H_{ax}$) 1.84 dm (*J* = 13.1 Hz, $2H_{eq}$)
H_4	1.43 qt (*J* = 13.1, 4.2 Hz, $1H_{ax}$) 1.59–1.49 m ($1H_{eq}$)	1.43 qt (*J* = 13.1, 3.9 Hz, $1H_{ax}$) 1.48 dm (*J* = 13.1 Hz, H_{eq})	1.43 qt (*J* = 13.1, 4.1 Hz, $1H_{ax}$) 1.57 d (*J* = 13.2 Hz,1 H_{eq})	1.38 qt (*J* = 13.1, 4.0 Hz, $1H_{ax}$) 1.58 d (*J* = 13.1 Hz, $1H_{eq}$)	1.37 qt (*J* = 13.1, 4.2 Hz, $1H_{ax}$) 1.49 d (*J* = 13.0 Hz, $1H_{eq}$)	1.45 qt (*J* = 13.1, 4.1 Hz, $1H_{ax}$) 1.65–1.53 m ($1H_{eq}$)

$H_{1'}$	-	-	-	-	-	-
$H_{2'}$	-	7.01 dd (*J* = 8.1, 2.3 Hz, 1H)	7.42 dm (*J* = 8.94 Hz, 1H)	6.95 d (*J* = 1.9 Hz, 1H)	7.20 s (1H)	7.61–7.45 m (1H)
$H_{3'}$	7.06 dd (*J* = 8.4, 1.1 Hz, 1H)	-	7.02 dm (*J*= 8.95 Hz, 1H)	-	-	7.61–7.45 m (1H)
$H_{4'}$	7.47 ddd (*J* = 8.5, 7.2, 1.6 Hz, 1H)	7.01 dd (*J* = 8.1, 2.3 Hz, 1H)	-	-	7.34–7.19 m (1H)	7.61–7.45 m (1H)
$H_{5'}$	7.10 ddd (*J* = 8.1, 7.2, 1.2 Hz, 1H)	7.45 t (*J* = 8.0 Hz, 1H)	7.02 dm (*J* = 8.95 Hz, 1H)	6.93 d (*J* = 8.2 Hz, 1H)	7.34 t (*J* = 7.6 Hz, H)	7.61–7.45 m (1H)
$H_{6'}$	7.40 dd (*J* = 8.1, 1.7 Hz, 1H)	7.06 dd (*J* = 8.1, 1.7 Hz, 1H)	7.42 dm (*J* = 8.94 Hz, 1H)	6.98 dd (*J* = 8.2, 2.0 Hz, 1H)	7.34–7.19 m (1H)	7.61–7.45 m (1H)
Hα	2.73–2.45 m ($2H$)[b] 3.45 d (*J* = 12.1 Hz, 1H) 3.76 d (*J* = 12.2 Hz, 1H)	2.65–2.53 m ($2H_{ax}$)[d] 3.46 d (*J* = 12.1 Hz, $2H_{eq}$)	2.58–2.47 m ($2H_{ax}$)[f] 3.46 dm (*J* = 11.8 Hz, $2H_{eq}$)	2.65–2.49 m ($2H_{ax}$)[j] 3.45 d (*J* = 11.7 Hz, $2H_{eq}$)	2.56–2.41 m ($2H_{ax}$)[l] 3.41 d (*J* = 11.8 Hz, $2H_{eq}$)	2.88–2.78 m ($2H_{ax}$)[n] 3.50 d (*J* = 12.0 Hz, $2H_{eq}$)
Hβ	3.82 dd (*J* = 13.2, 3.3 Hz, $2H_{eq}$) 4.53 td (*J* = 12.5, 2.1 Hz, $2H_{ax}$)	3.87 dd (*J* -= 13.1, 3.4 Hz, $2H_{eq}$) 4.50 t (*J* = 12.5 Hz, $2H_{ax}$)	3.83 dd (*J* = 13.1, 3.4 Hz, $2H_{eq}$)[g] 4.49 td (*J* = 12.5, 2.1 Hz, $2H_{ax}$)	3.86 dd (*J* = 12.6, 3.5 Hz, $2H_{eq}$) 4.50 t (*J* = 12.4 Hz, $2H_{ax}$)	3.77 dd (*J* = 12.8, 3.6 Hz, $2H_{eq}$) 4.43 t (*J* = 12.0 Hz, $2H_{ax}$)	3.84 dd (*J* = 13.0, 3.6 Hz, $2H_{eq}$) 4.50 td (*J* = 12.5, 2.0 Hz, $2H_{ax}$)
Cc	3.87 s (OCH_3)	3.88 s (OCH_3)	3.87 s (OCH_3)[h]	6.07 s (OCH_2O)	2.37 s (CH_3)	-
NH^+	12.11 s (1H)	12.32 s (1H)	12.21 s (1H)	12.29 s (1H)	12.22 s (1H)	12.37 s (1H)

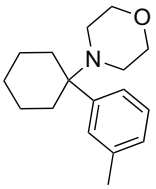
a. Overlap with Hα
b. Overlap with $H_{2,6}$
c. Overlap with $H\alpha_{ax}$
d. Overlap with $H_{2,6ax}$
e. Overlap with $H\alpha_{ax}$
f. Overlap with $H_{2,6ax}$
g. Overlap with Cc
h. Overlap with $H\beta_{eq}$
i. Overlap with $H\alpha_{ax}$
j. Overlap with $H_{2,6ax}$
k. Overlap with $H\alpha_{ax}$
l. Overlap with $H_{2,6ax}$
m. Overlap with $H\alpha_{ax}$
n. Overlap with $H_{2,6ax}$



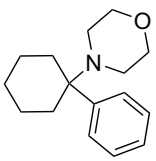
2-MeO-PCMo
3-MeO-PCMo
4-MeO-PCMo



3,4-MD-PCMo

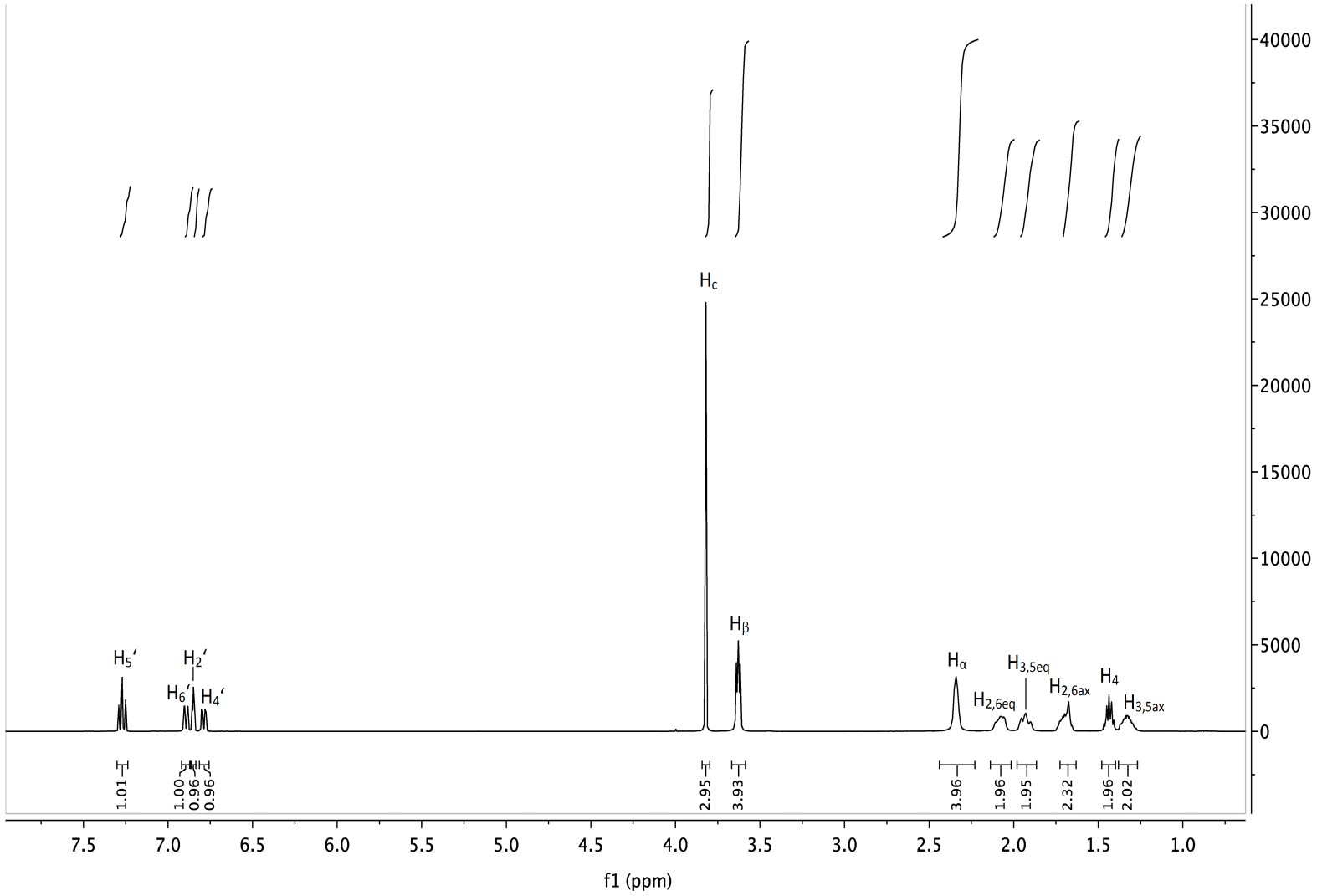


3-Me-PCMo

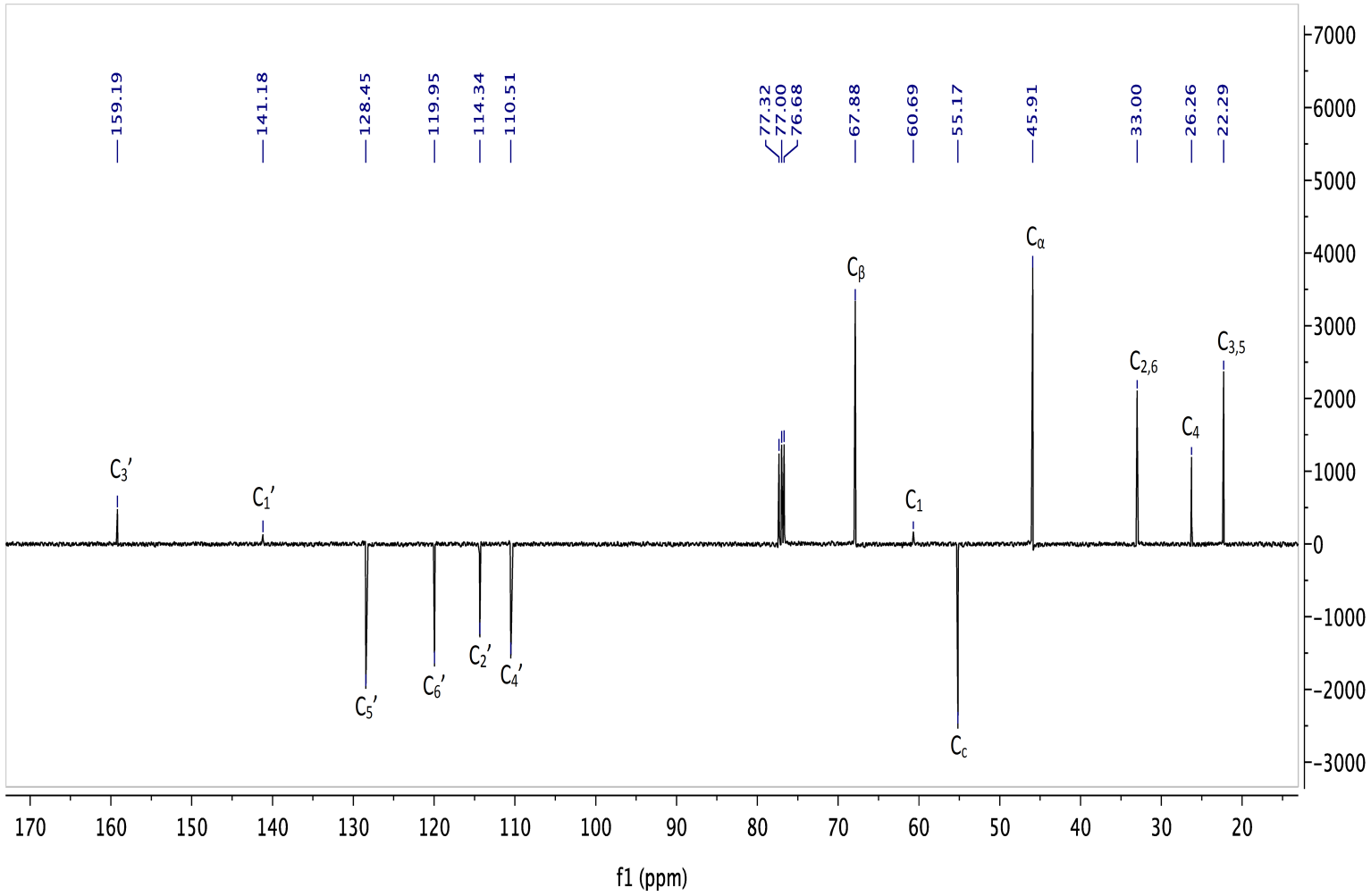


PCMo

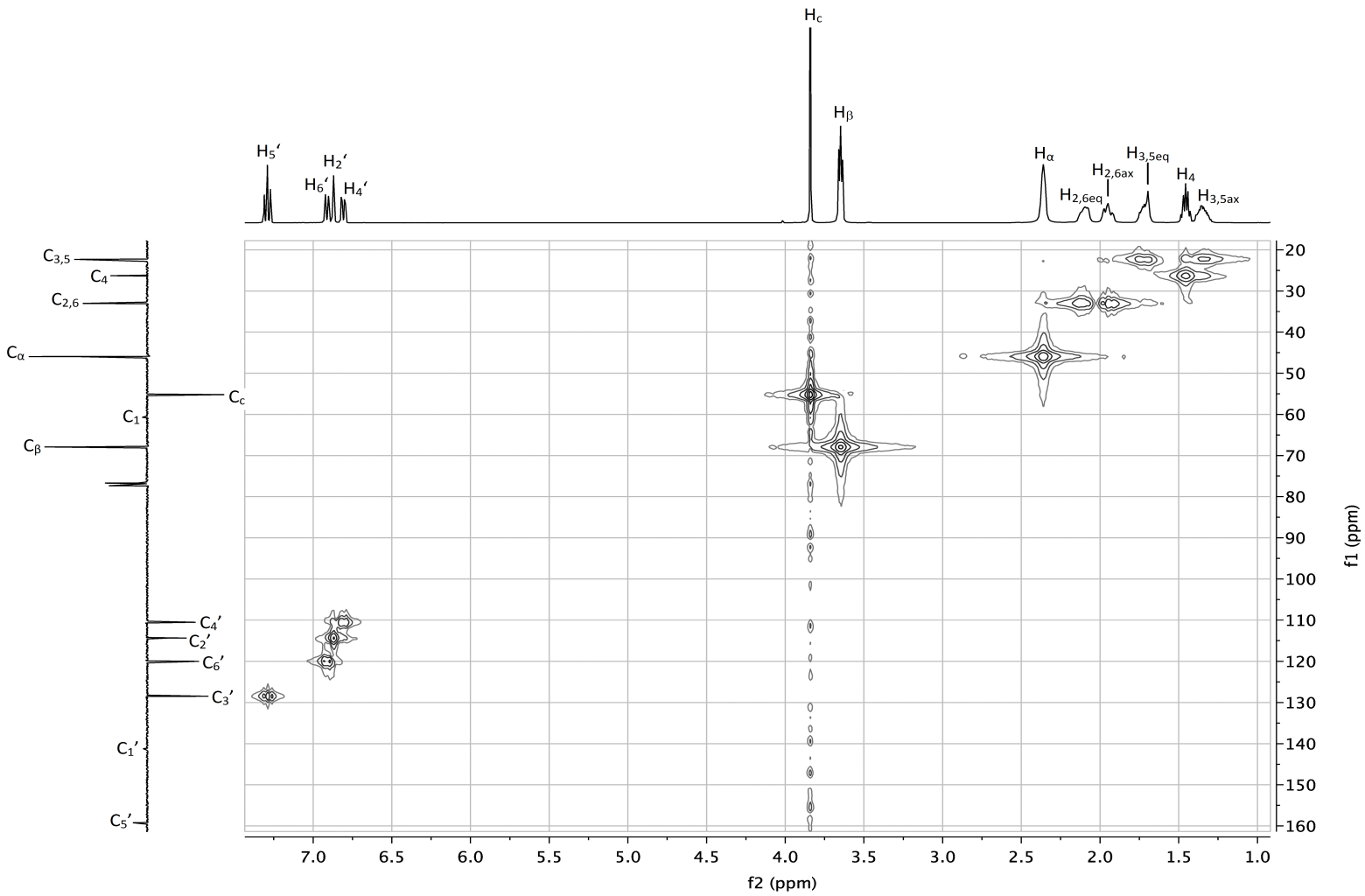
^{1}H NMR of 3-MeO-PCMo freebase (400 MHz, $CDCl_3$)



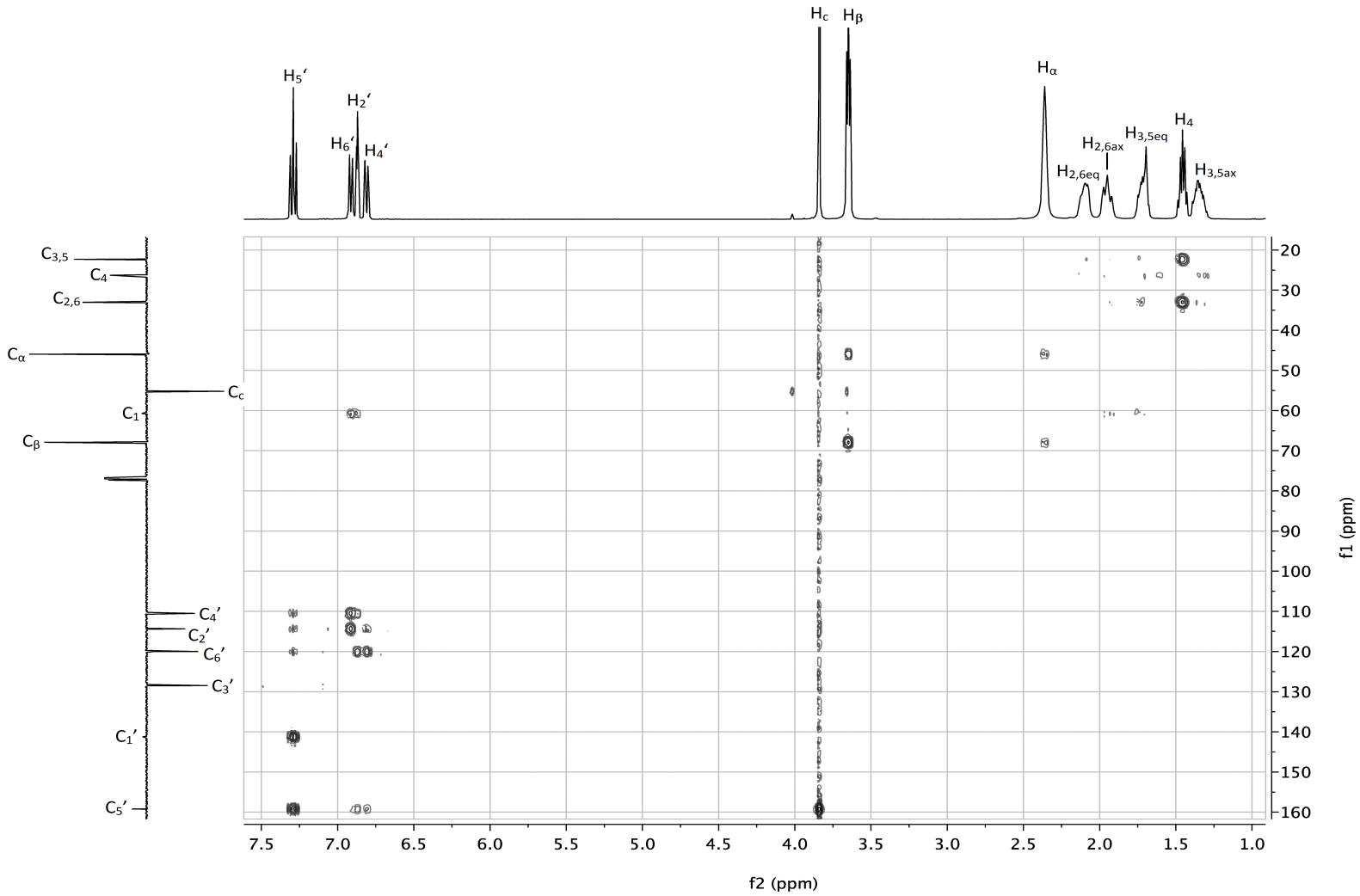
^{13}C PENDANT NMR of 3-MeO-PCMo freebase (100 MHz, $CDCl_3$)



HMQC 2-D NMR of 3-MeO-PCMo freebase ($CDCl_3$)



HMBC 2-D NMR of 3-MeO-PCMo freebase ($CDCl_3$)



COSY-45 2-D NMR of 3-MeO-PCMo freebase ($CDCl_3$)