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Return of the lysergamides. Part II: Analytical and behavioural characterization of N6-allyl-6-norlysergic acid diethylamide (AL-LAD) and (2'S,4'S)-lysergic acid 2,4-dimethylazetidide (LSZ)

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Return of the lysergamides. Part II: Analytical and behavioural characterization of *N*^{6}-allyl-6-norlysergic acid diethylamide (AL-LAD) and (2'*S*,4'*S*)-lysergic acid 2,4-dimethylazetidide (LSZ)

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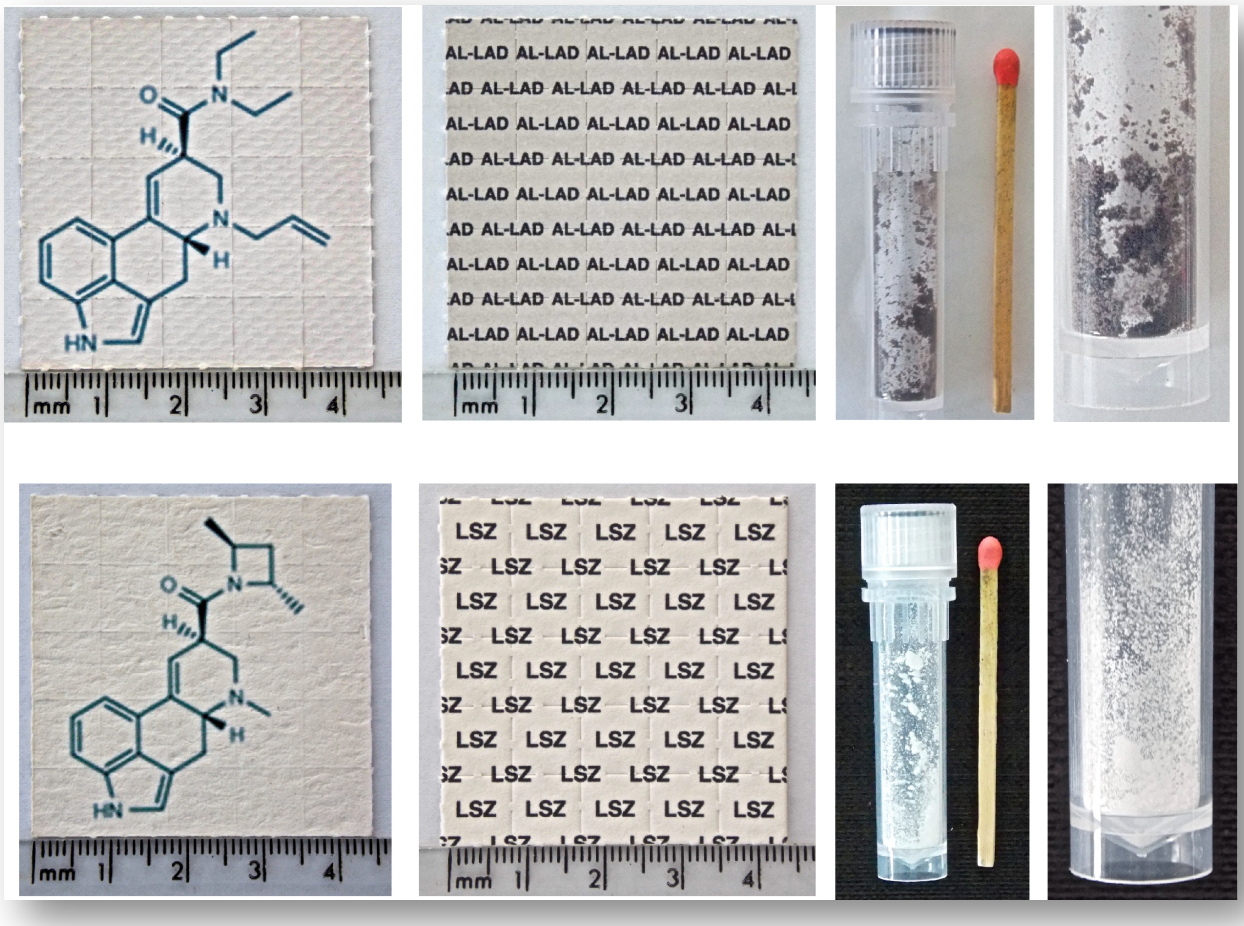
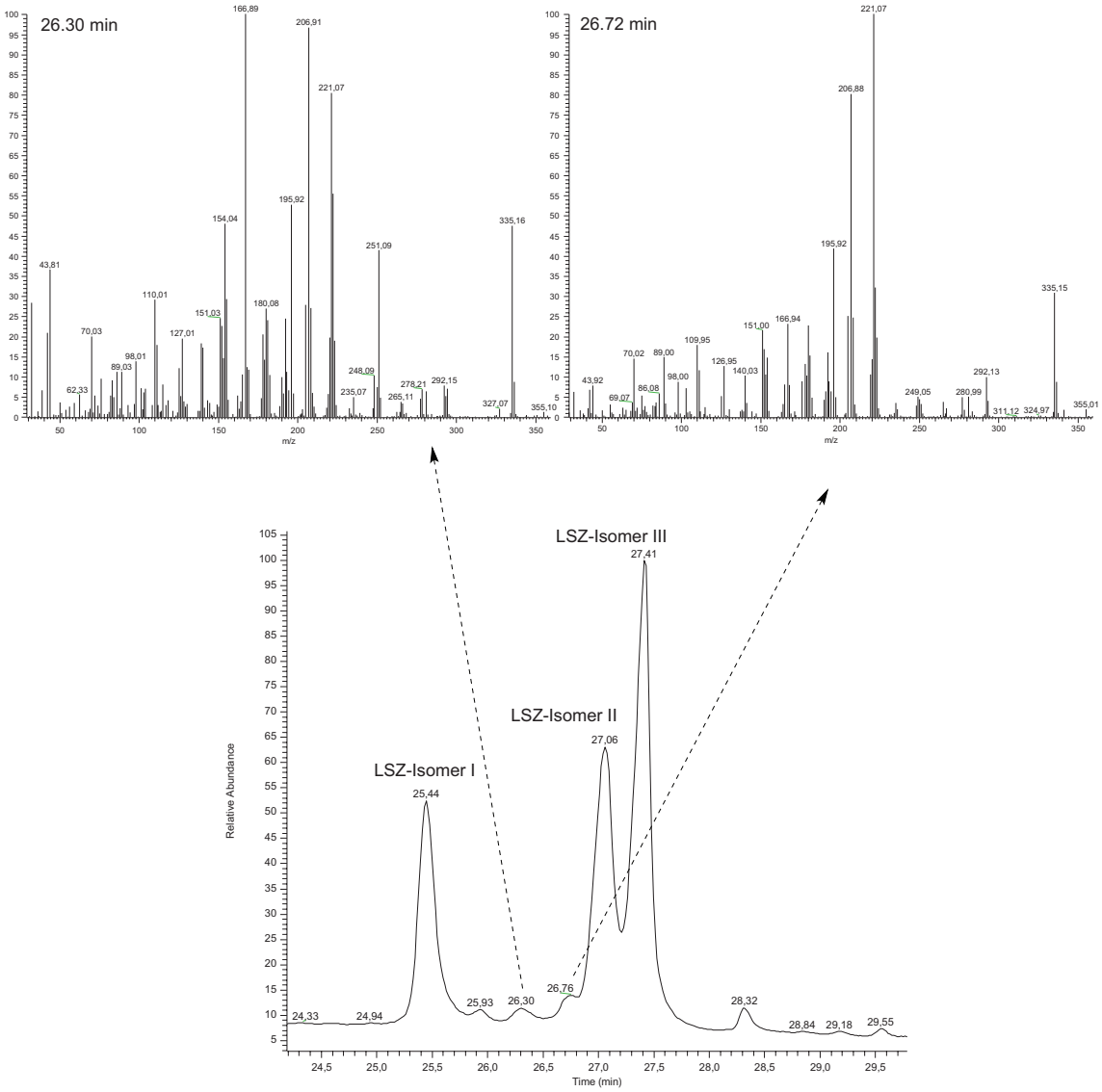
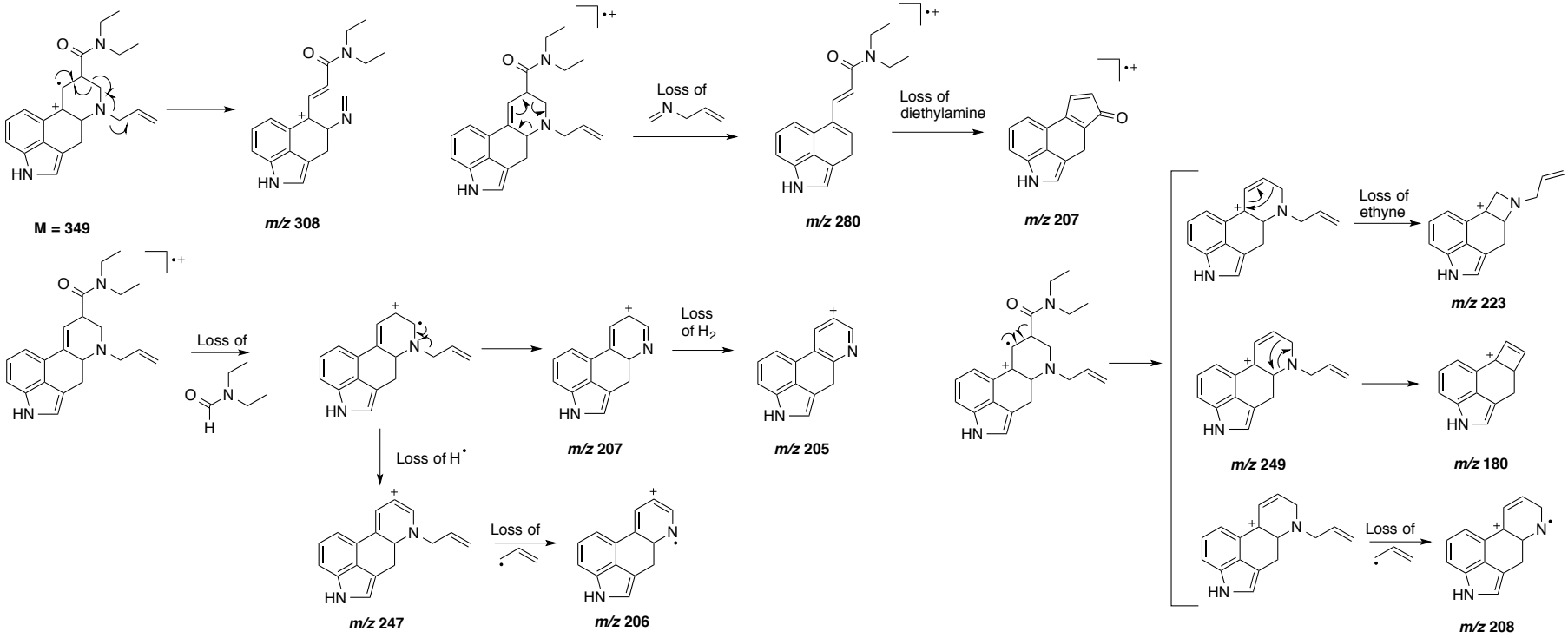
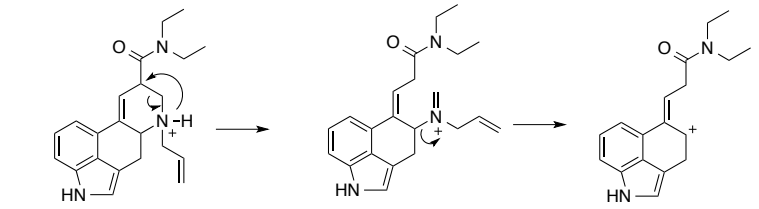


LSZ Isomers (minor)
(spectra background subtracted)

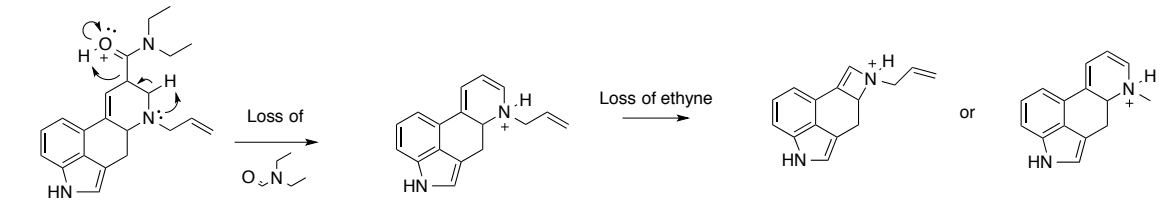



M = 349
m/z 308
m/z 280
Loss of
Loss of diethylamine
m/z 207
Loss of
Loss of H2
m/z 205
Loss of H•
m/z 247
Loss of
m/z 206
Loss of ethyne
m/z 223
m/z 249
m/z 180
Loss of
m/z 208
Loss of
Loss of ethyne
m/z 128
m/z 181
m/z 154
Loss of CO
m/z 100
and/or
α-1,2-H
m/z 72



Chemical Formula: $C_{22}H_{28}N_3O^+$
Exact Mass: 350.22269

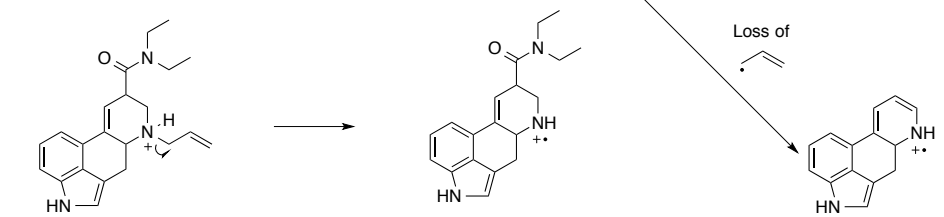
Chemical Formula: $C_{18}H_{21}N_2O^+$
Exact Mass: 281.16484



Chemical Formula: $C_{22}H_{28}N_3O^+$
Exact Mass: 350.22269

Chemical Formula: $C_{17}H_{17}N_2^+$
Exact Mass: 249.13862

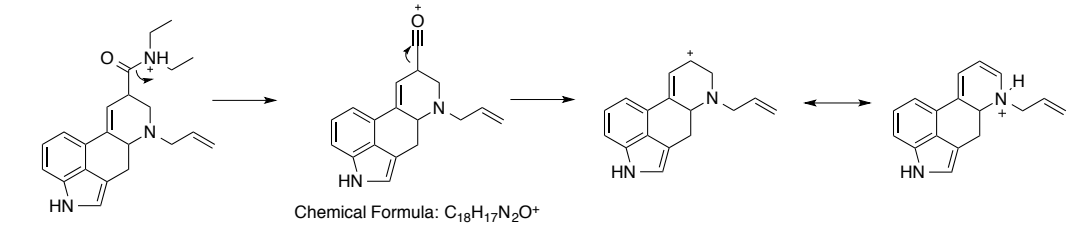
Chemical Formula: $C_{15}H_{15}N_2^+$
Exact Mass: 223.12297



Chemical Formula: $C_{22}H_{28}N_3O^+$
Exact Mass: 350.22269

Chemical Formula: $C_{19}H_{23}N_3O^{\cdot+}$
Exact Mass: 309.18356

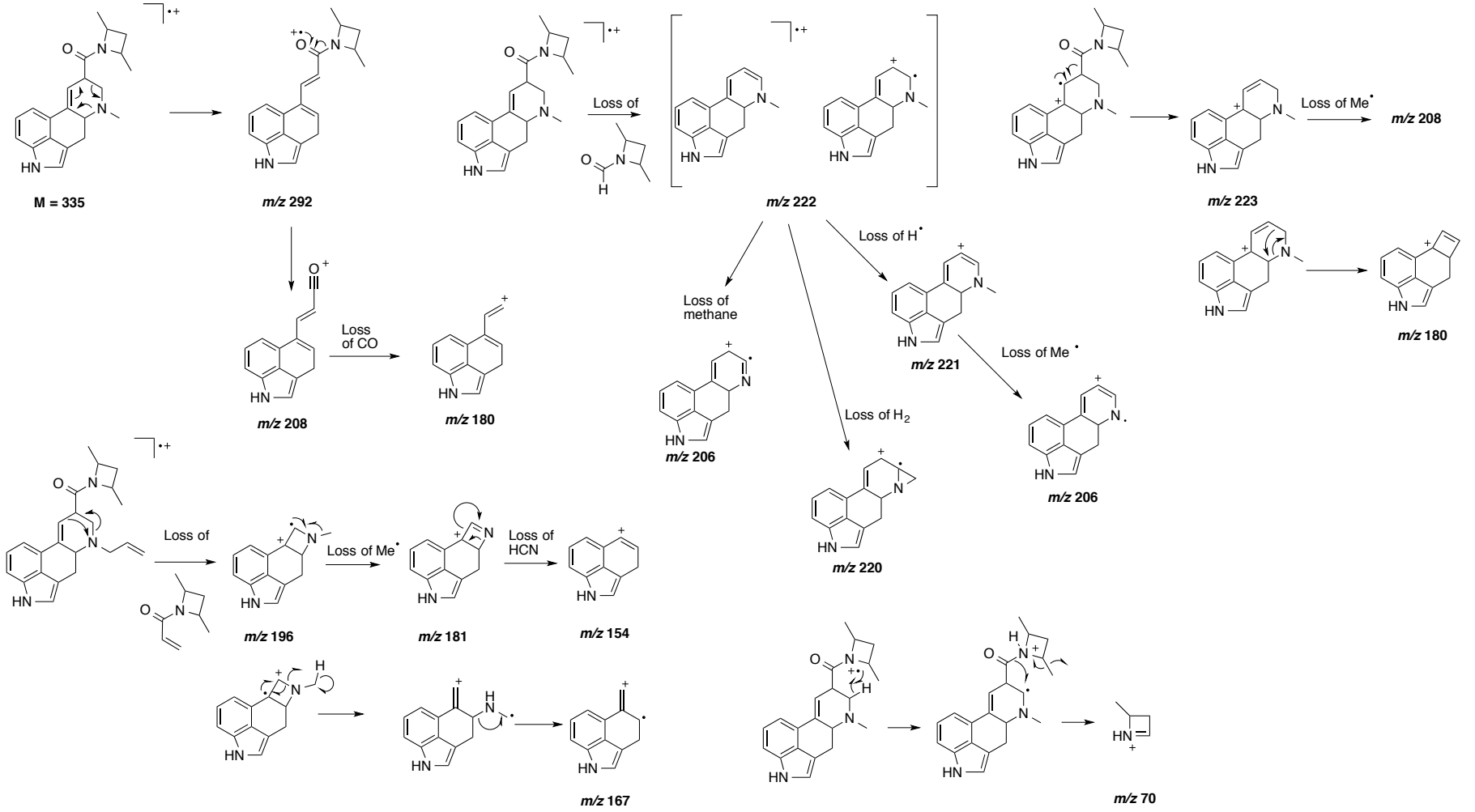
Chemical Formula: $C_{14}H_{12}N_2^{\cdot+}$
Exact Mass: 208.09950

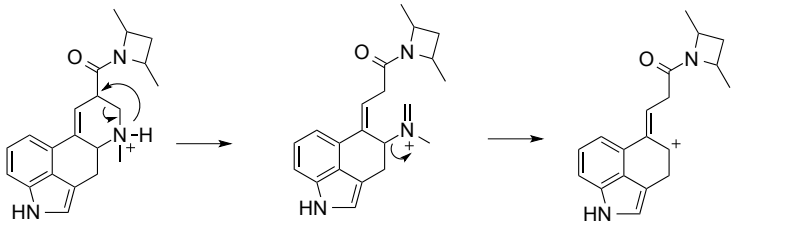


Chemical Formula: $C_{22}H_{28}N_3O^+$
Exact Mass: 350.22269

Chemical Formula: $C_{18}H_{17}N_2O^+$
Exact Mass: 277.13354

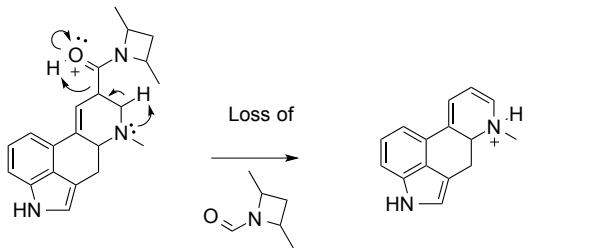
Chemical Formula: $C_{17}H_{17}N_2^+$
Exact Mass: 249.13862


M = 335
m/z 292
Loss of
m/z 222
Loss of Me•
m/z 223
m/z 208
Loss of CO
m/z 208
m/z 180
Loss of methane
m/z 206
Loss of H•
m/z 221
Loss of Me•
m/z 206
m/z 180
Loss of H2
m/z 220
Loss of
m/z 196
Loss of Me•
m/z 181
Loss of HCN
m/z 154
m/z 167
m/z 70



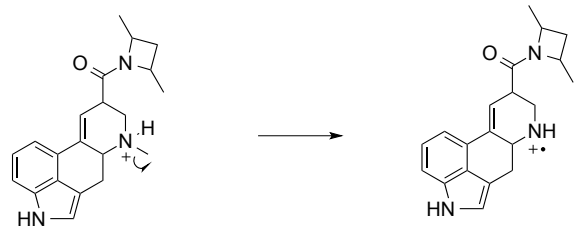
Chemical Formula: $C_{21}H_{26}N_3O^+$
Exact Mass: 336.20704

Chemical Formula: $C_{19}H_{21}N_2O^+$
Exact Mass: 293.16484



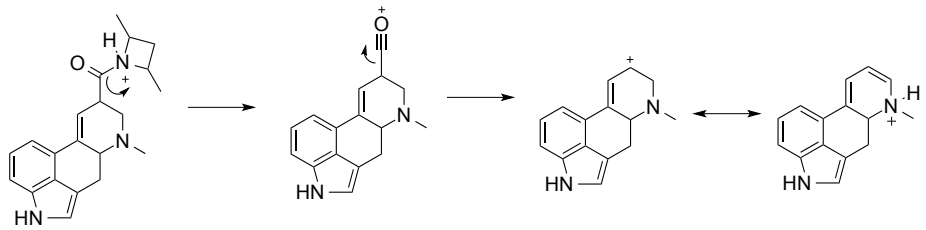
Chemical Formula: $C_{21}H_{26}N_3O^+$
Exact Mass: 336.20704

Chemical Formula: $C_{15}H_{15}N_2^+$
Exact Mass: 223.12297



Chemical Formula: $C_{21}H_{26}N_3O^+$
Exact Mass: 336.20704

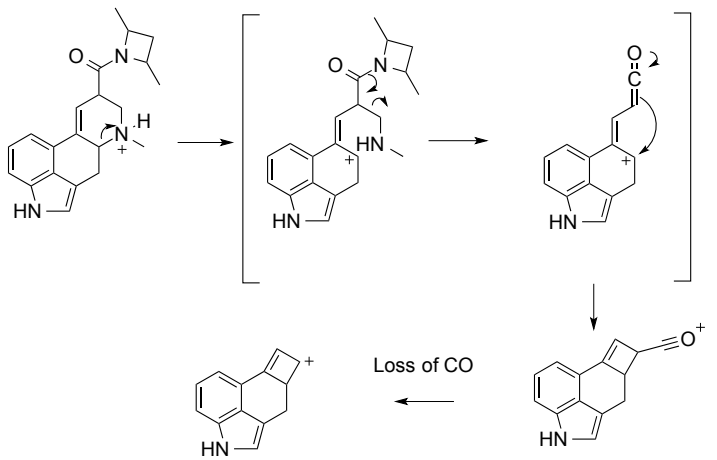
Chemical Formula: $C_{20}H_{23}N_3O^{\bullet+}$
Exact Mass: 321.18356



Chemical Formula: $C_{21}H_{26}N_3O^+$
Exact Mass: 336.20704

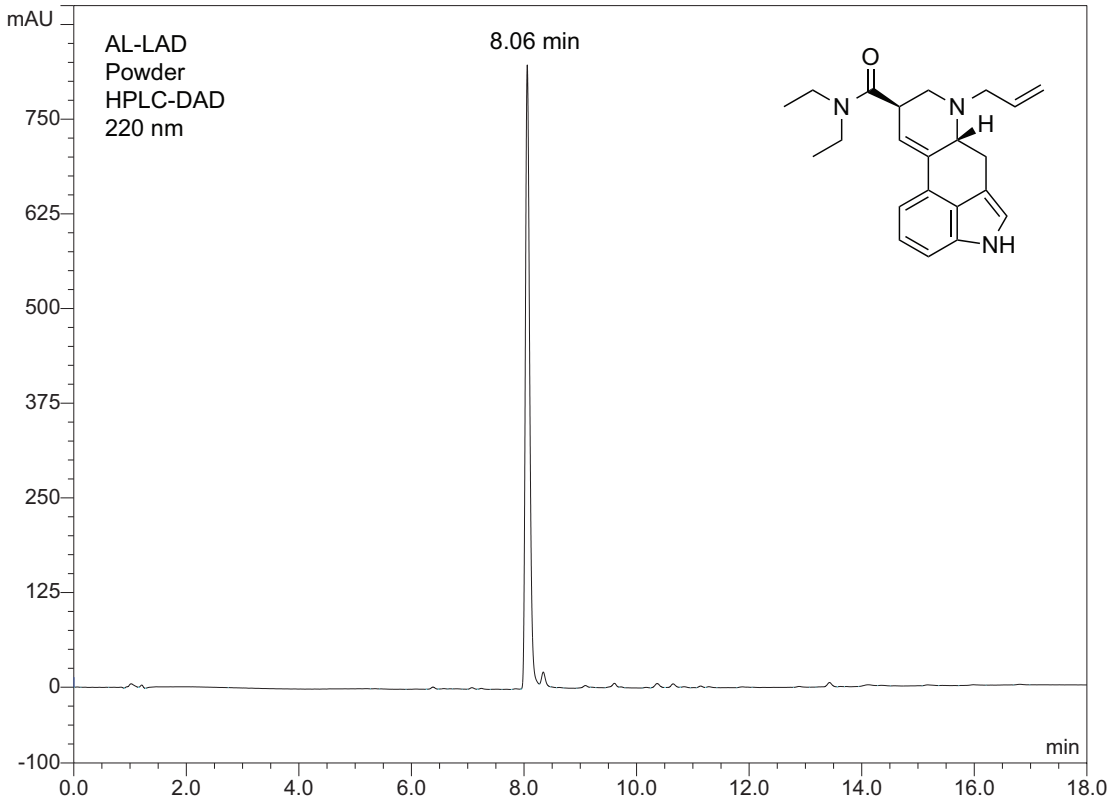
Chemical Formula: $C_{16}H_{15}N_2O^+$
Exact Mass: 251.11789

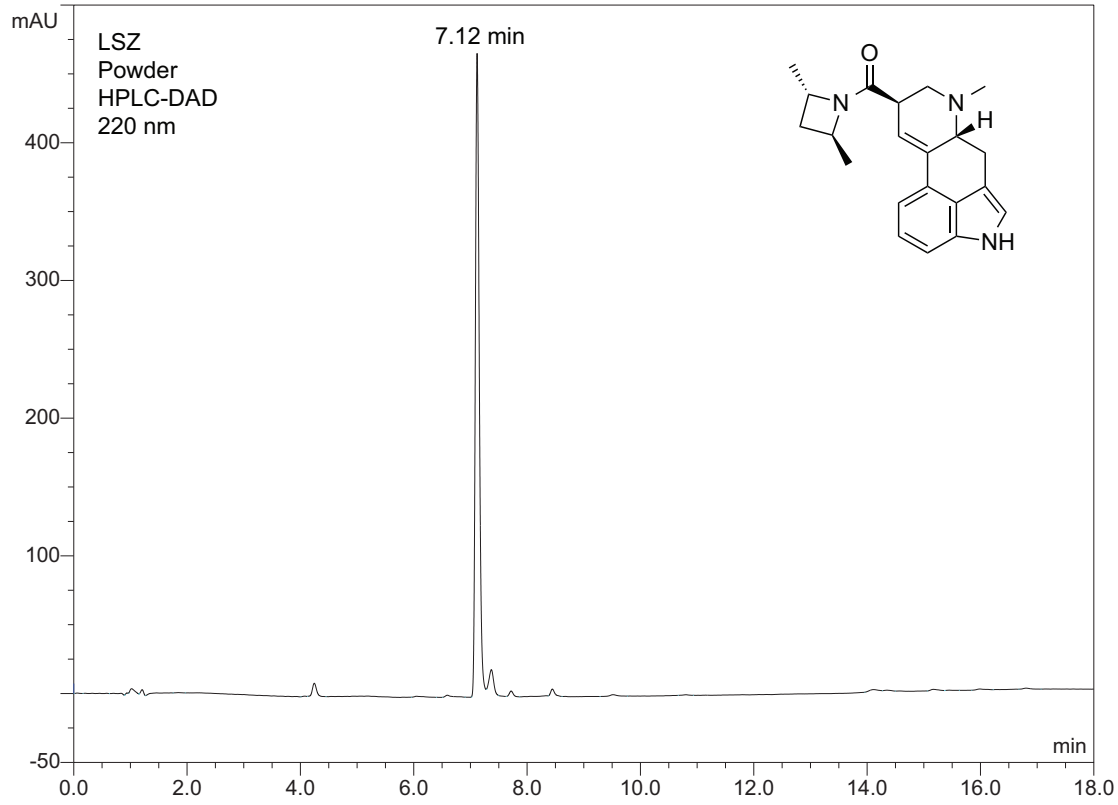
Chemical Formula: $C_{15}H_{15}N_2^+$
Exact Mass: 223.12297

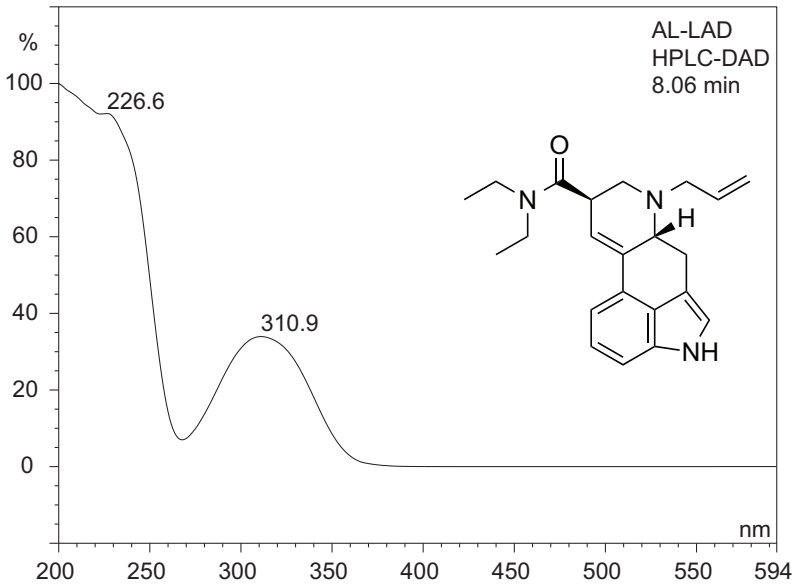


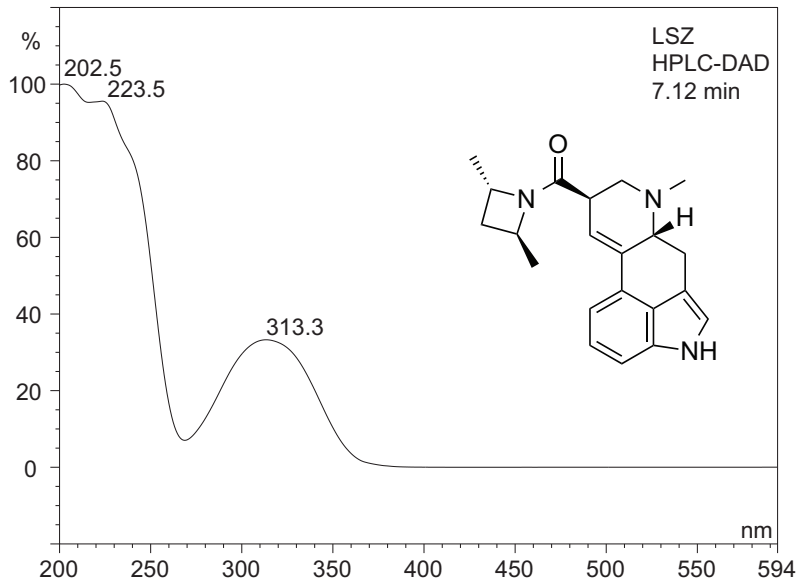
Chemical Formula: $C_{13}H_{10}N^+$
Exact Mass: 180.08078

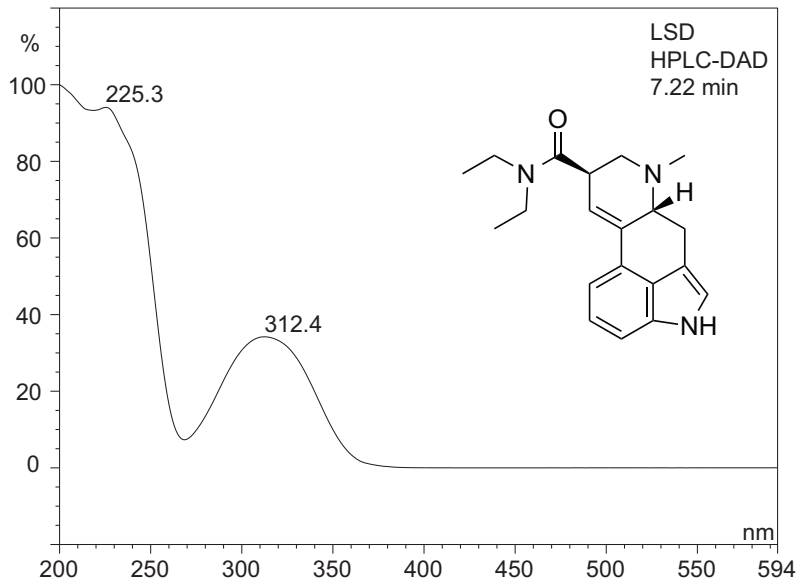
Chemical Formula: $C_{14}H_{10}NO^+$
Exact Mass: 208.07569

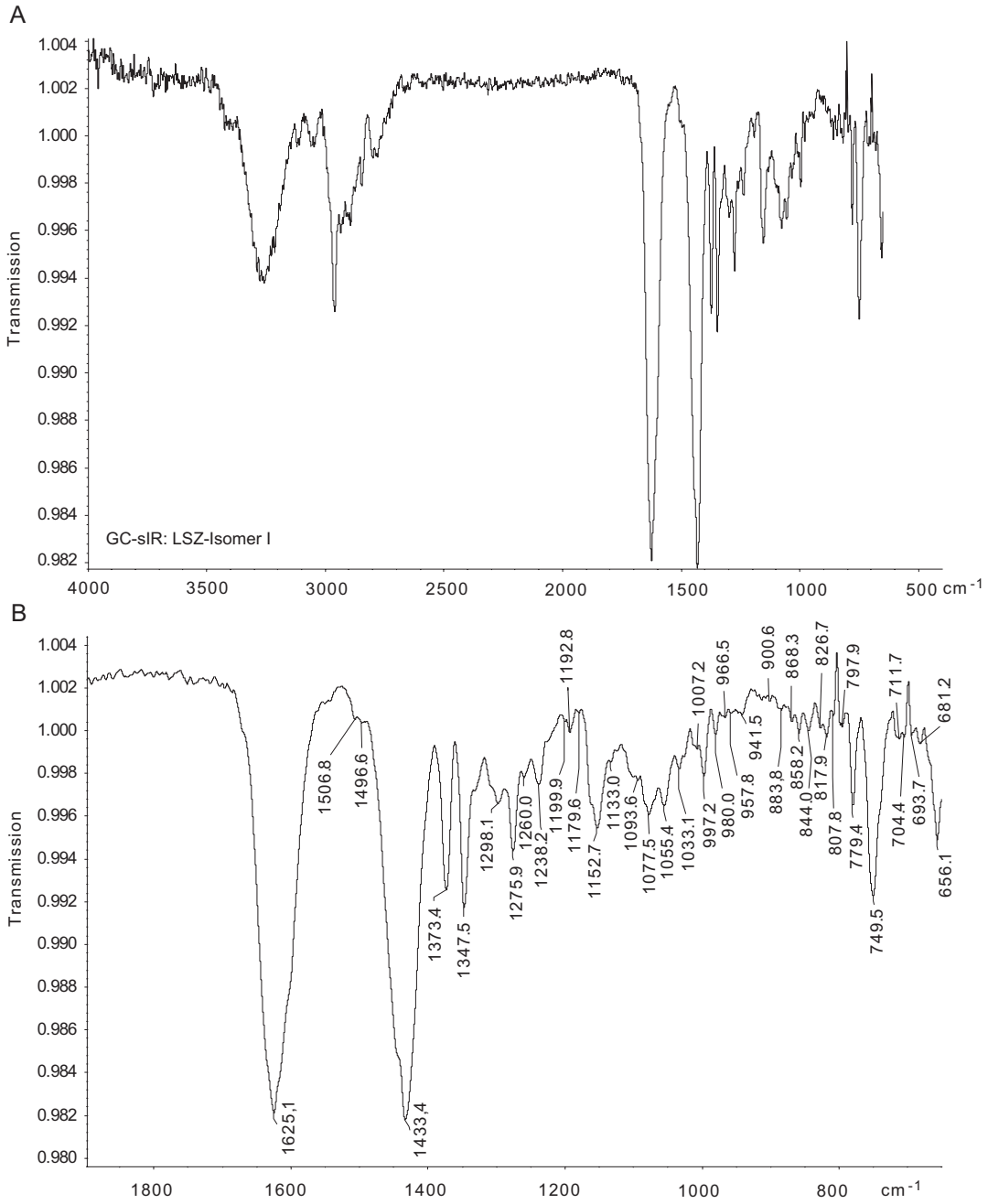

mAU
AL-LAD
Powder
HPLC-DAD
220 nm
8.06 min
O
N
N
H
NH
750
625
500
375
250
125
0
-100
min
0.0
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0

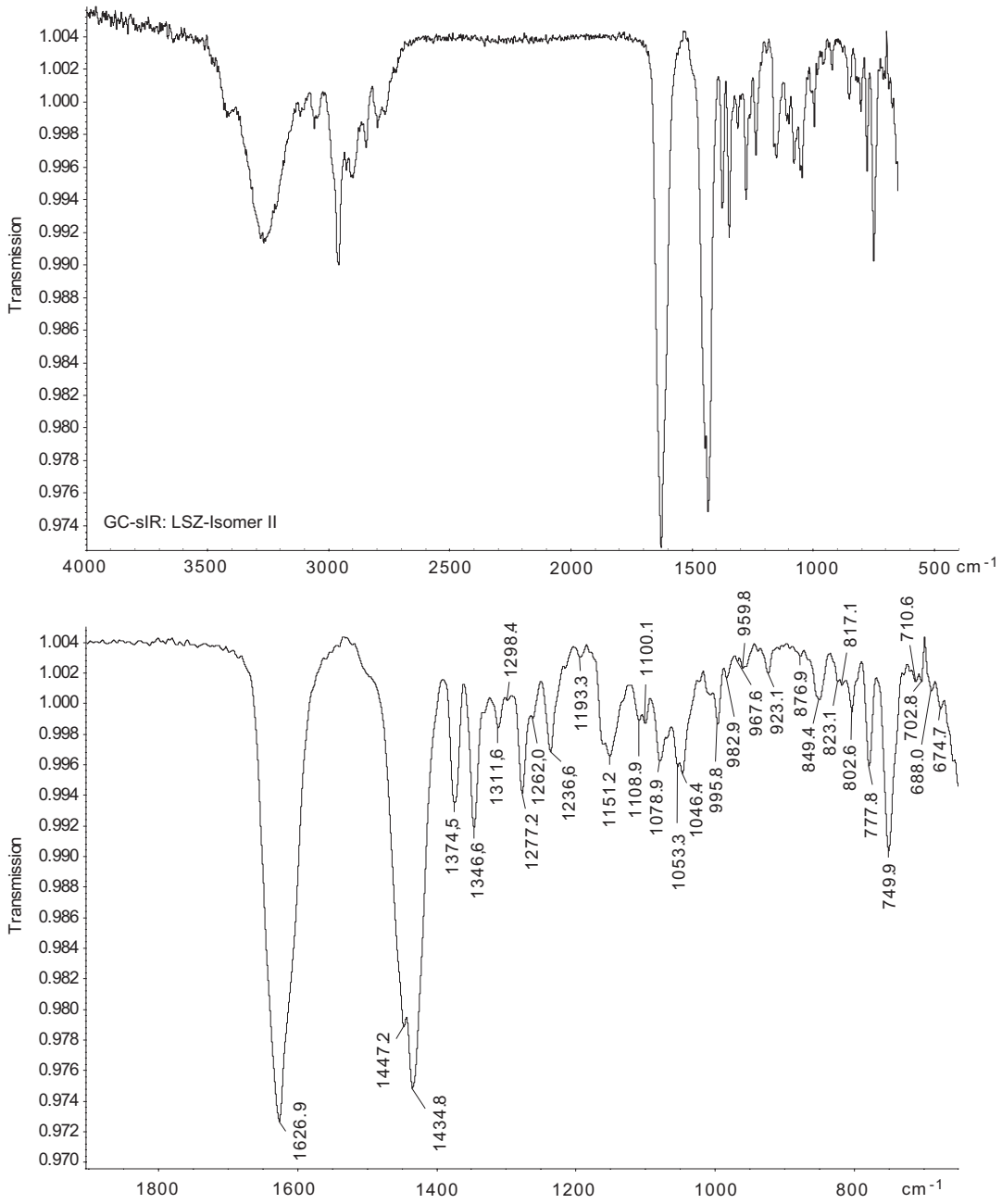

mAU
LSZ
Powder
HPLC-DAD
220 nm
7.12 min
O
N
N
H
NH
400
300
200
100
-50
min
0.0
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0

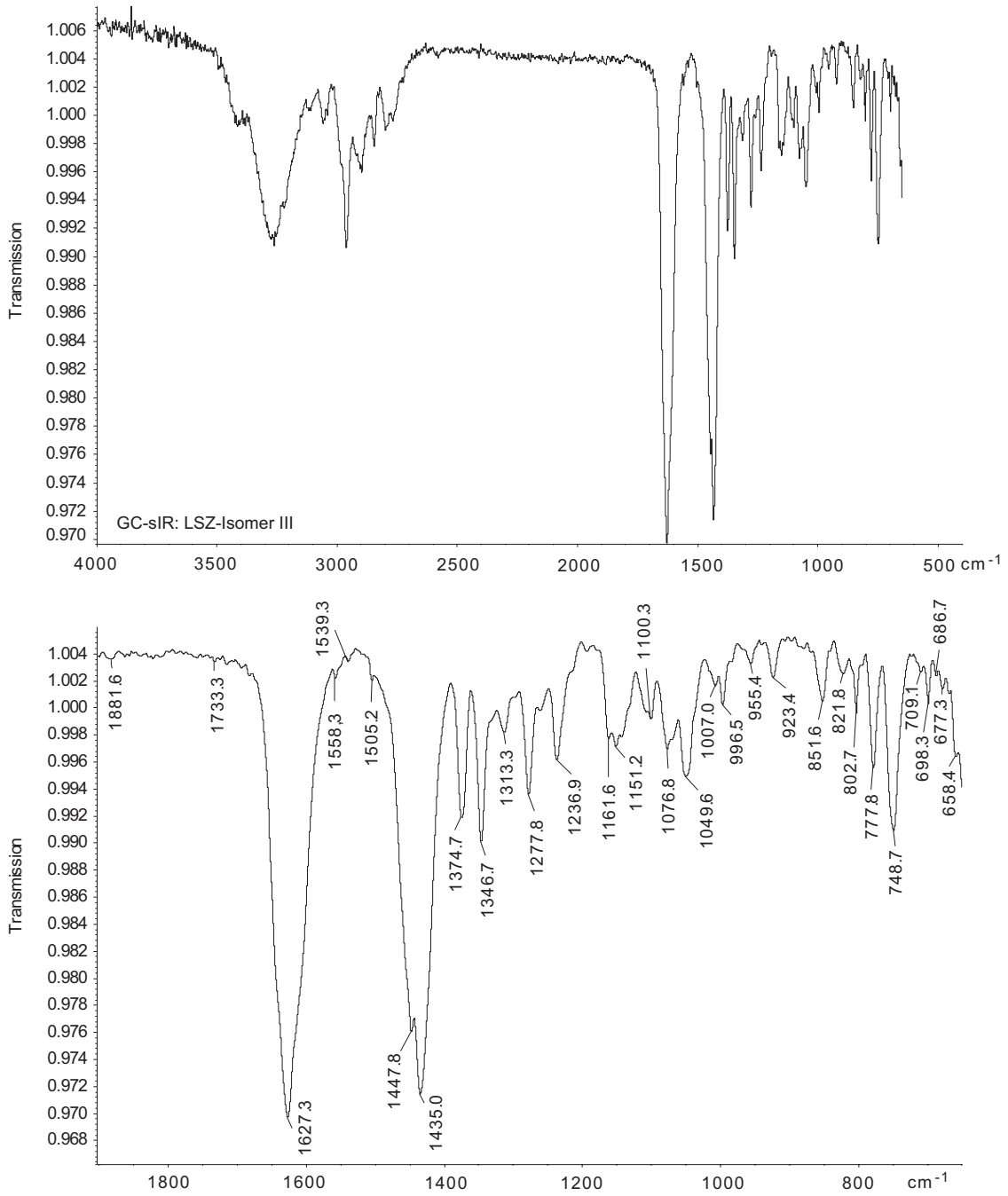

AL-LAD
HPLC-DAD
8.06 min
%
100
80
60
40
20
0
226.6
310.9
nm
200
250
300
350
400
450
500
550
594
O
N
N
H
NH

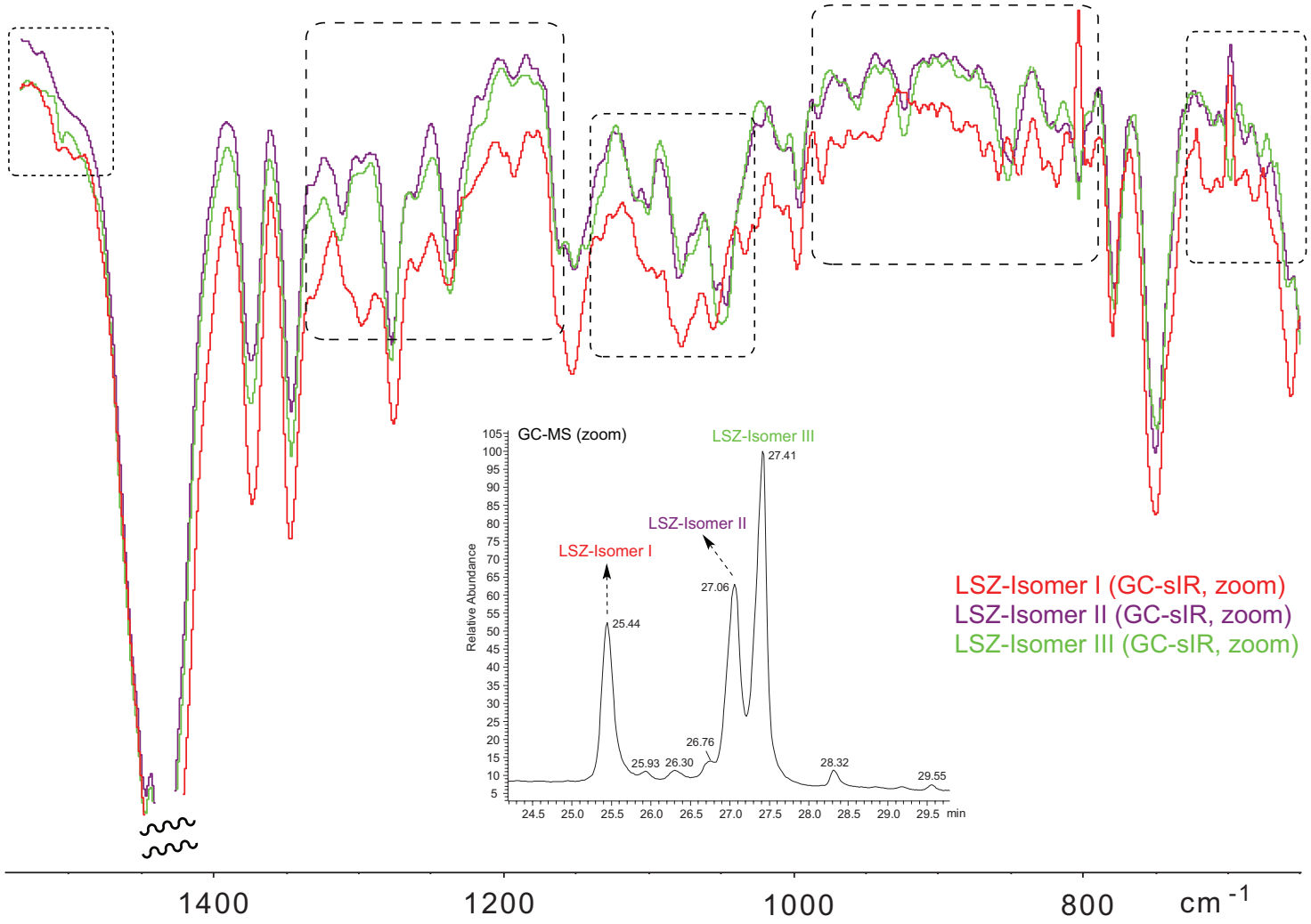

LSZ
HPLC-DAD
7.12 min
%
100
80
60
40
20
0
202.5
223.5
313.3
nm
200
250
300
350
400
450
500
550
594
O
N
N
H
NH

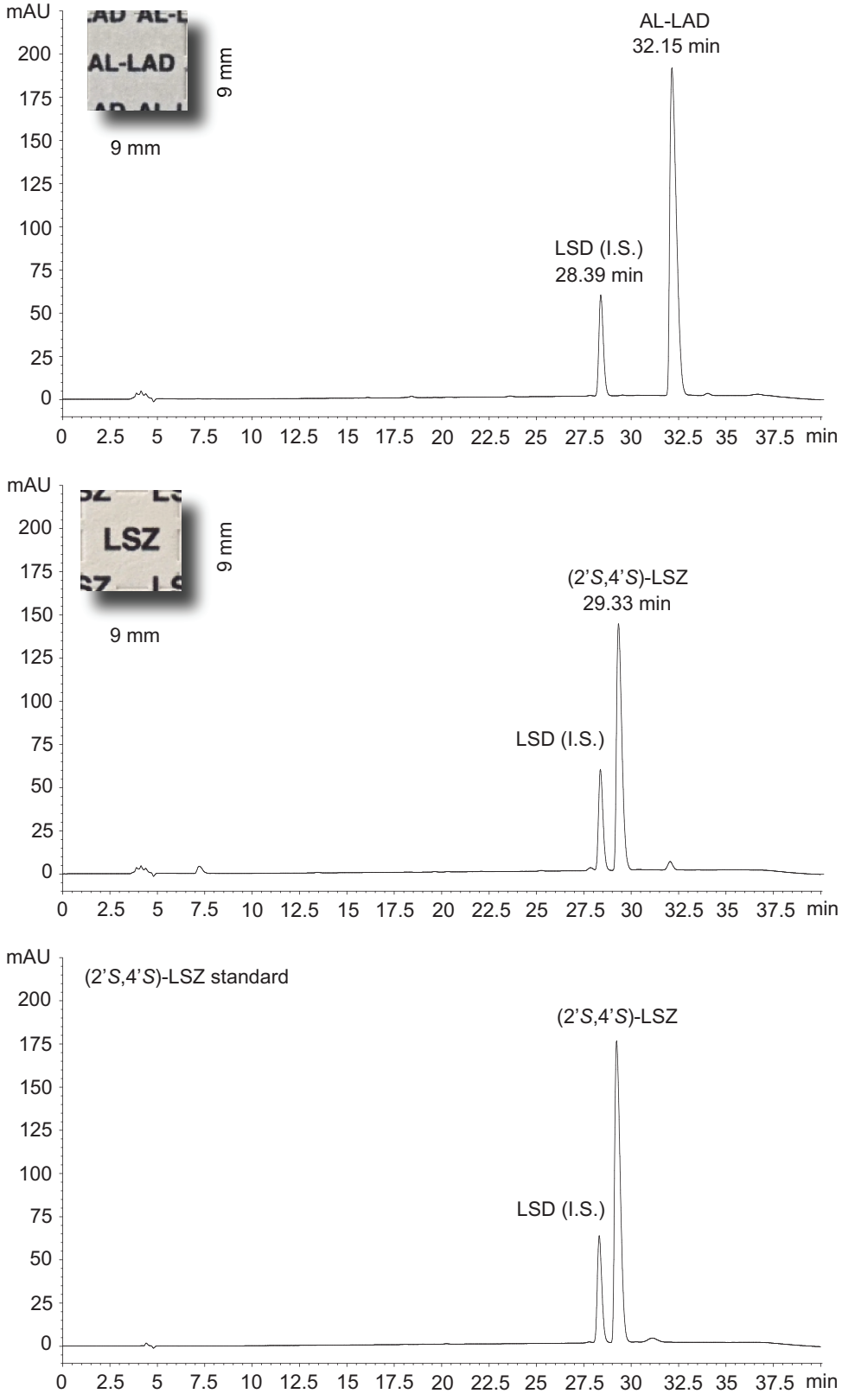

LSD
HPLC-DAD
7.22 min
%
100
80
60
40
20
0
225.3
312.4
nm
200
250
300
350
400
450
500
550
594
O
N
N
H
NH

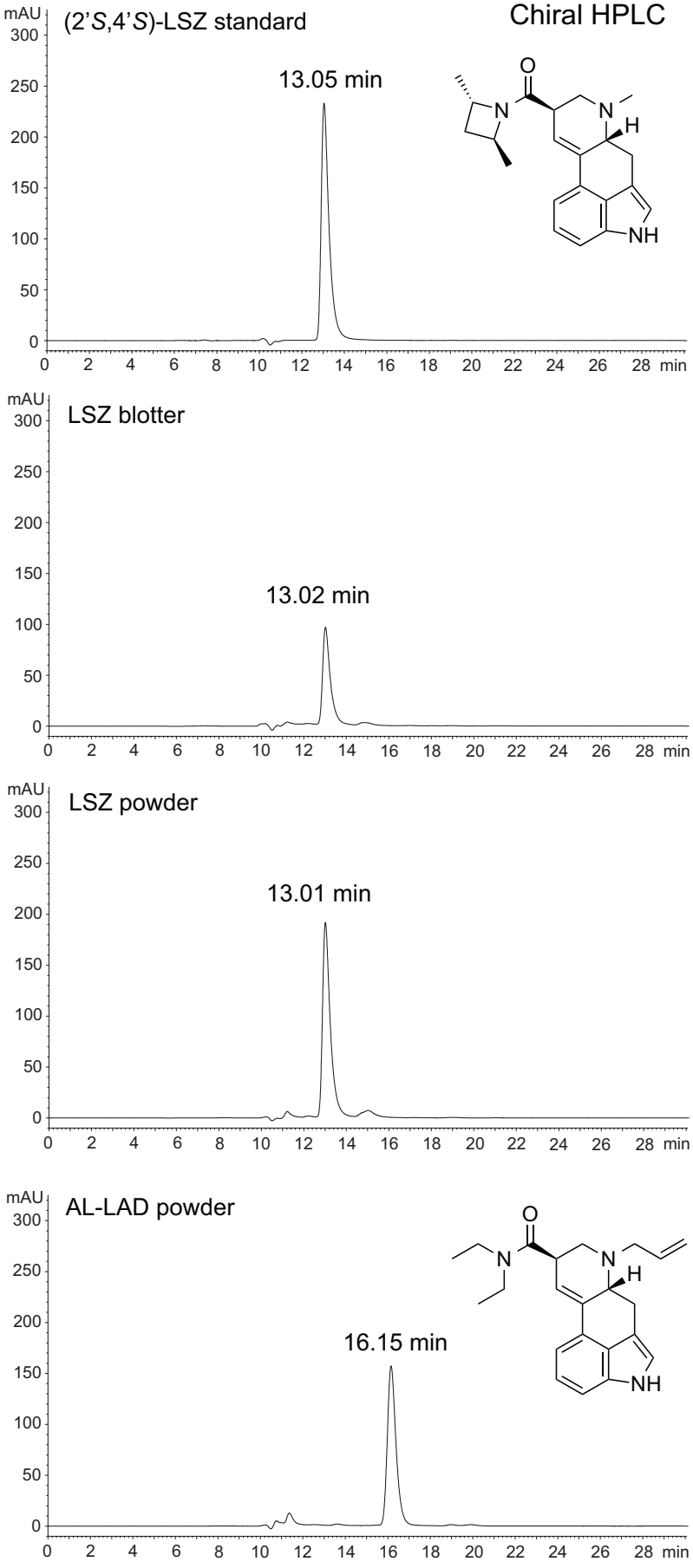

A
Transmission
GC-sIR: LSZ-Isomer I
cm-1
B
Transmission
1625,1
1506.8
1496.6
1433,4
1373.4
1347.5
1298.1
1275.9
1260.0
1238.2
1199.9
1192.8
1179.6
1152.7
1133.0
1093.6
1077.5
1055.4
1033.1
1007.2
997.2
980.0
966.5
957.8
941.5
900.6
883.8
868.3
858.2
844.0
826.7
817.9
807.8
797.9
779.4
749.5
711.7
704.4
693.7
681.2
656.1
cm-1


Transmission
GC-sIR: LSZ-Isomer II
cm-1
1626.9
1447.2
1434.8
1374.5
1346.6
1311.6
1298.4
1277.2
1262.0
1236.6
1193.3
1151.2
1108.9
1100.1
1078.9
1053.3
1046.4
995.8
982.9
967.6
959.8
923.1
876.9
849.4
823.1
817.1
802.6
777.8
749.9
710.6
702.8
688.0
674.7


Transmission
GC-sIR: LSZ-Isomer III
cm-1
1881.6
1733.3
1627.3
1539.3
1558.3
1505.2
1447.8
1435.0
1374.7
1346.7
1313.3
1277.8
1236.9
1161.6
1151.2
1100.3
1076.8
1049.6
1007.0
996.5
955.4
923.4
851.6
821.8
802.7
777.8
748.7
709.1
698.3
677.3
658.4
686.7


GC-MS (zoom)
LSZ-Isomer III
27.41
LSZ-Isomer II
27.06
LSZ-Isomer I
25.44
26.76
25.93
26.30
28.32
29.55
Relative Abundance
min
LSZ-Isomer I (GC-sIR, zoom)
LSZ-Isomer II (GC-sIR, zoom)
LSZ-Isomer III (GC-sIR, zoom)
1400
1200
1000
800
cm -1

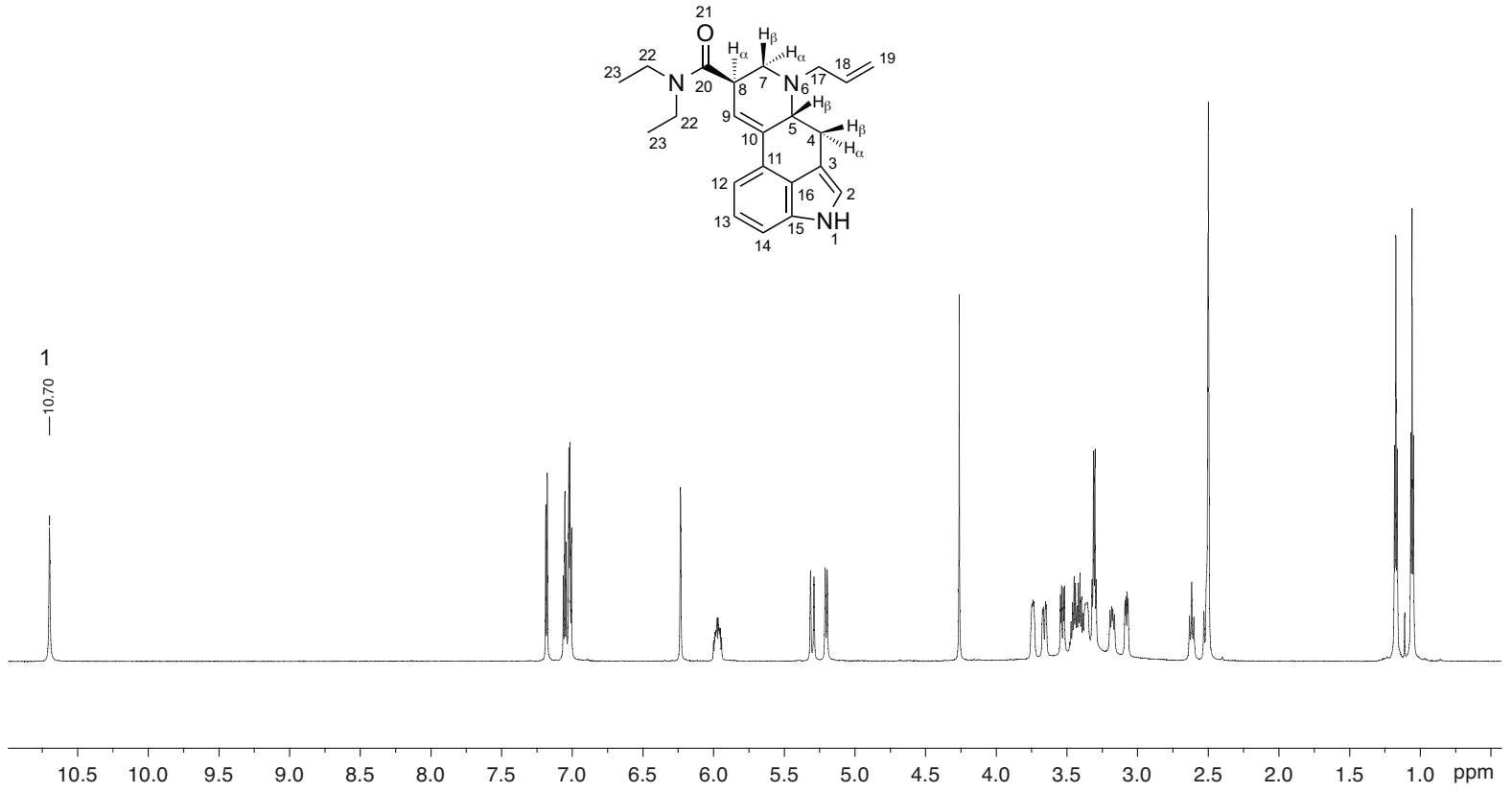

mAU
AL-LAD
9 mm
9 mm
AL-LAD
32.15 min
LSD (I.S.)
28.39 min
min
LSZ
9 mm
9 mm
(2'S,4'S)-LSZ
29.33 min
LSD (I.S.)
min
(2'S,4'S)-LSZ standard
(2'S,4'S)-LSZ
LSD (I.S.)
min


Chiral HPLC
(2'*S*,4'*S*)-LSZ standard
13.05 min
LSZ blotter
13.02 min
LSZ powder
13.01 min
AL-LAD powder
16.15 min
mAU
min
O
N
H
NH

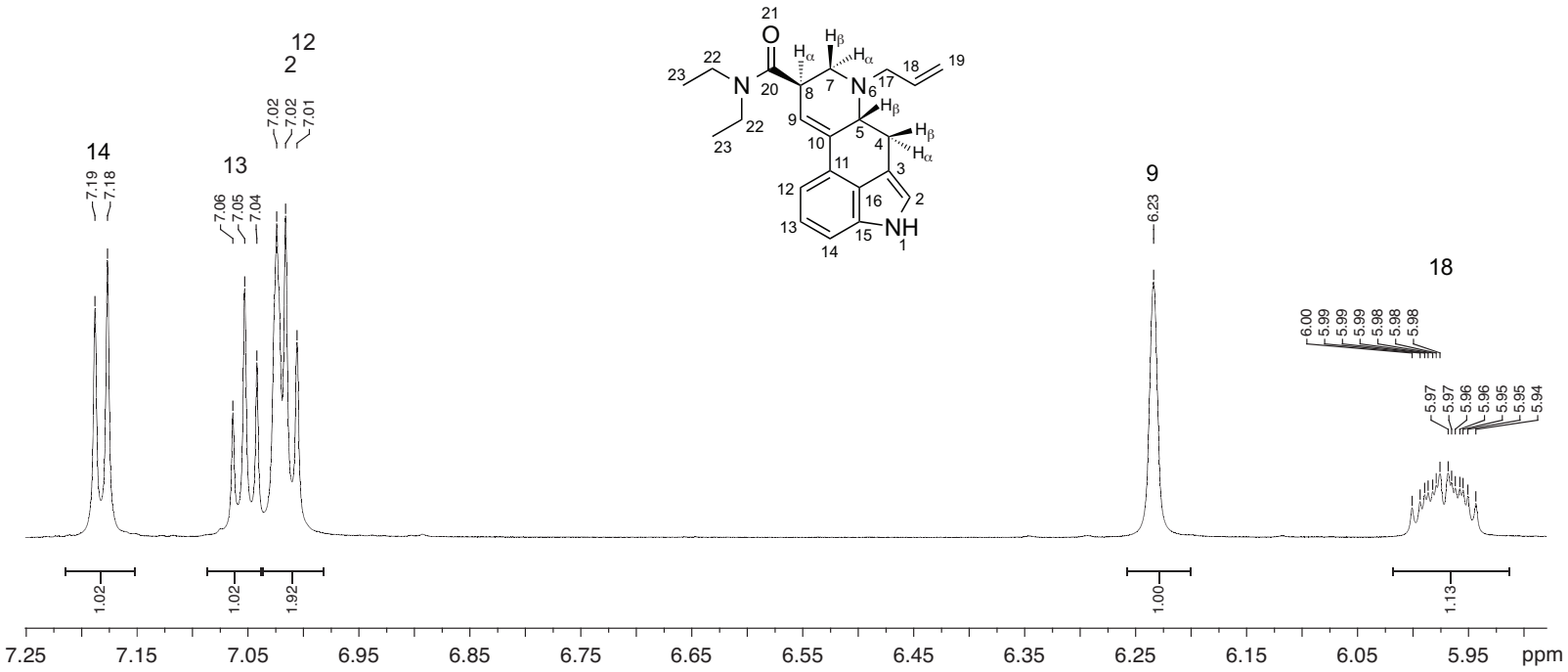
Chiral HPLC analysis

Chiral HPLC analyses were performed used the equipment described in the manuscript. Separation was obtained on a CHIRALPAK® AD-H column (250 × 4.6 mm, 5 µm) from Daicel Chemical Industries, Ltd. (Cedex, France). An isocratic mobile phase consisting of 9:1, 2-propanol: *n*-hexane was used. Powdered AL-LAD and LSZ, and LSZ reference material was dissolved individually in the isocratic mobile phase and diluted to a final concentration of 0.1 mg/mL. LSZ blotter was dissolved and extracted into the isocratic mobile phase following the procedure described in the manuscript. Injection volume was 10 µL, flow rate was 0.3 mL/min, and the column temperature was set at 25 °C. The total run time was 30 minutes.

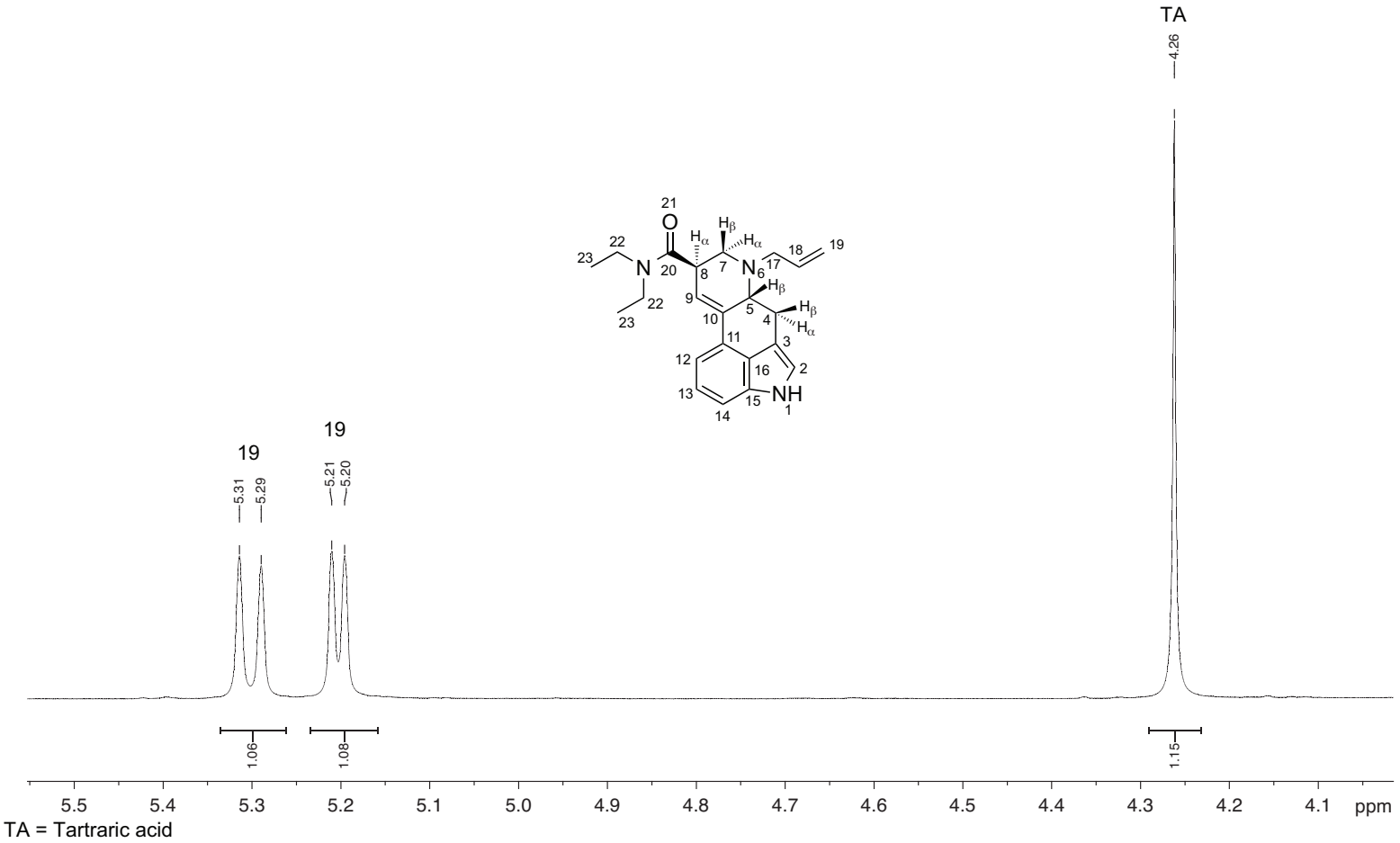
AL-LAD hemitartrate
^{1}H-NMR (700 MHz)
d_6-DMSO



AL-LAD hemitartrate
^{1}H-NMR (700 MHz)
d_6-DMSO

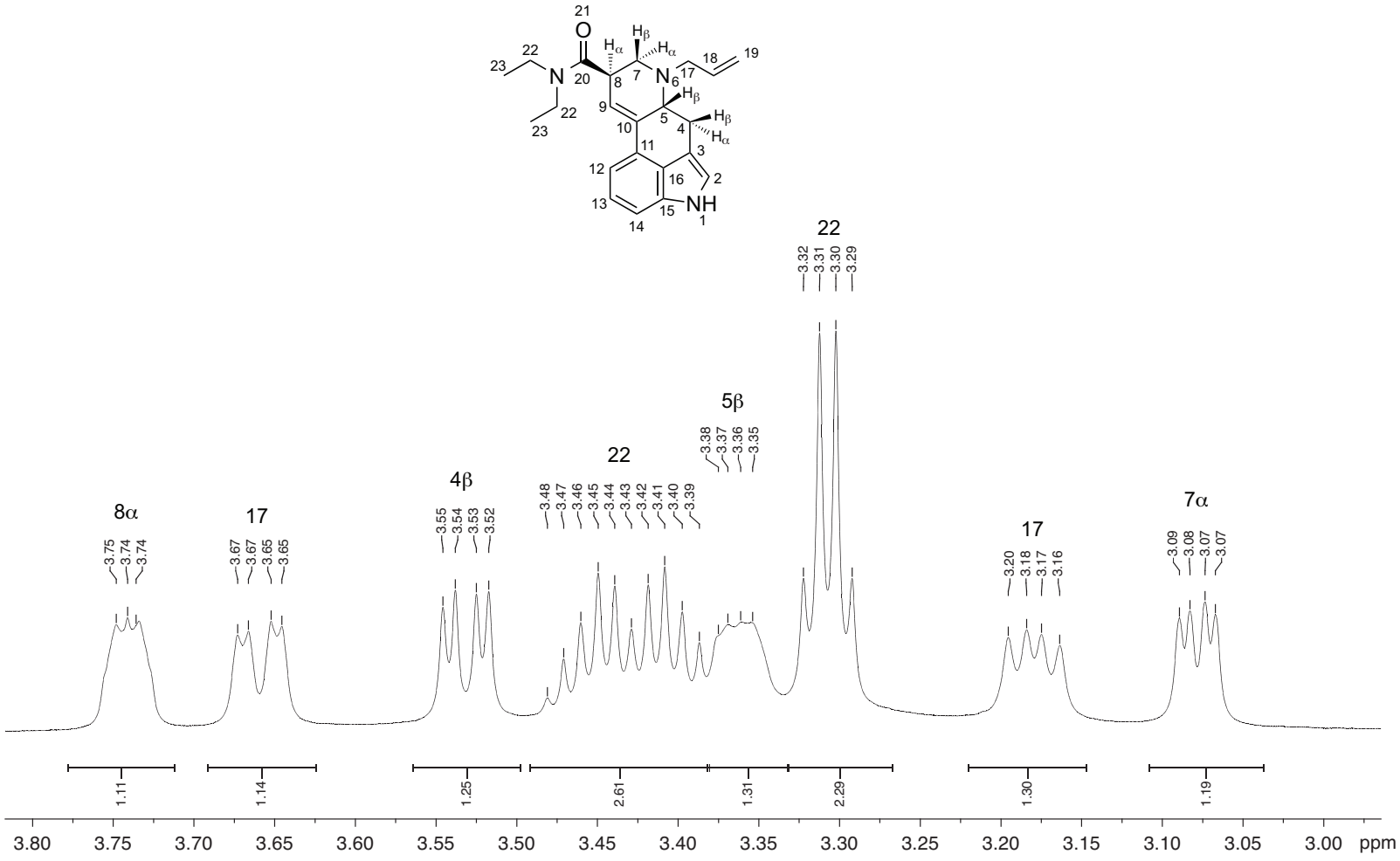


AL-LAD hemitartrate
^{1}H-NMR (700 MHz)
d_6-DMSO

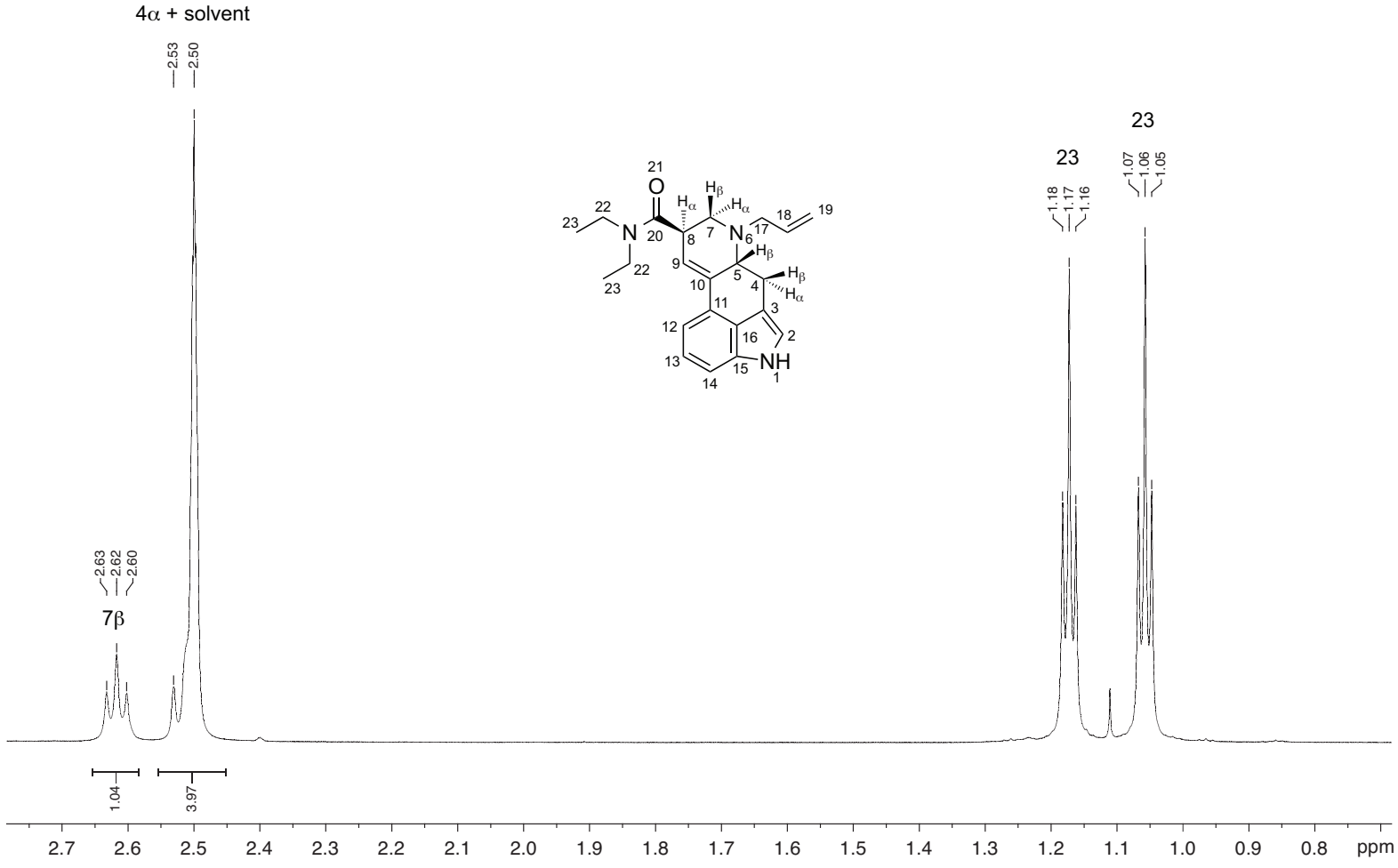


TA = Tartraric acid

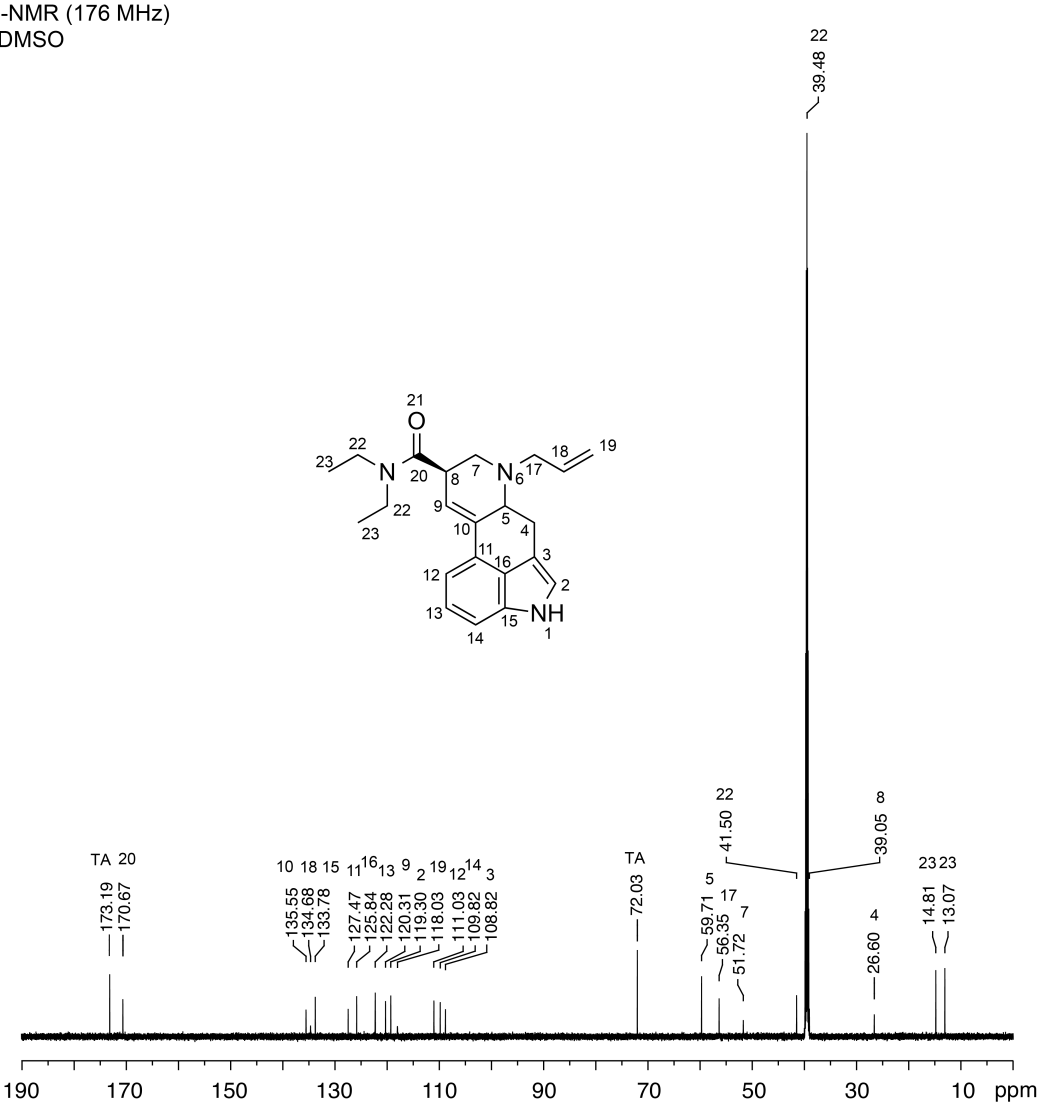
AL-LAD hemitartrate
^{1}H-NMR (700 MHz)
d_6-DMSO



AL-LAD hemitartrate
^{1}H-NMR (700 MHz)
d_6-DMSO

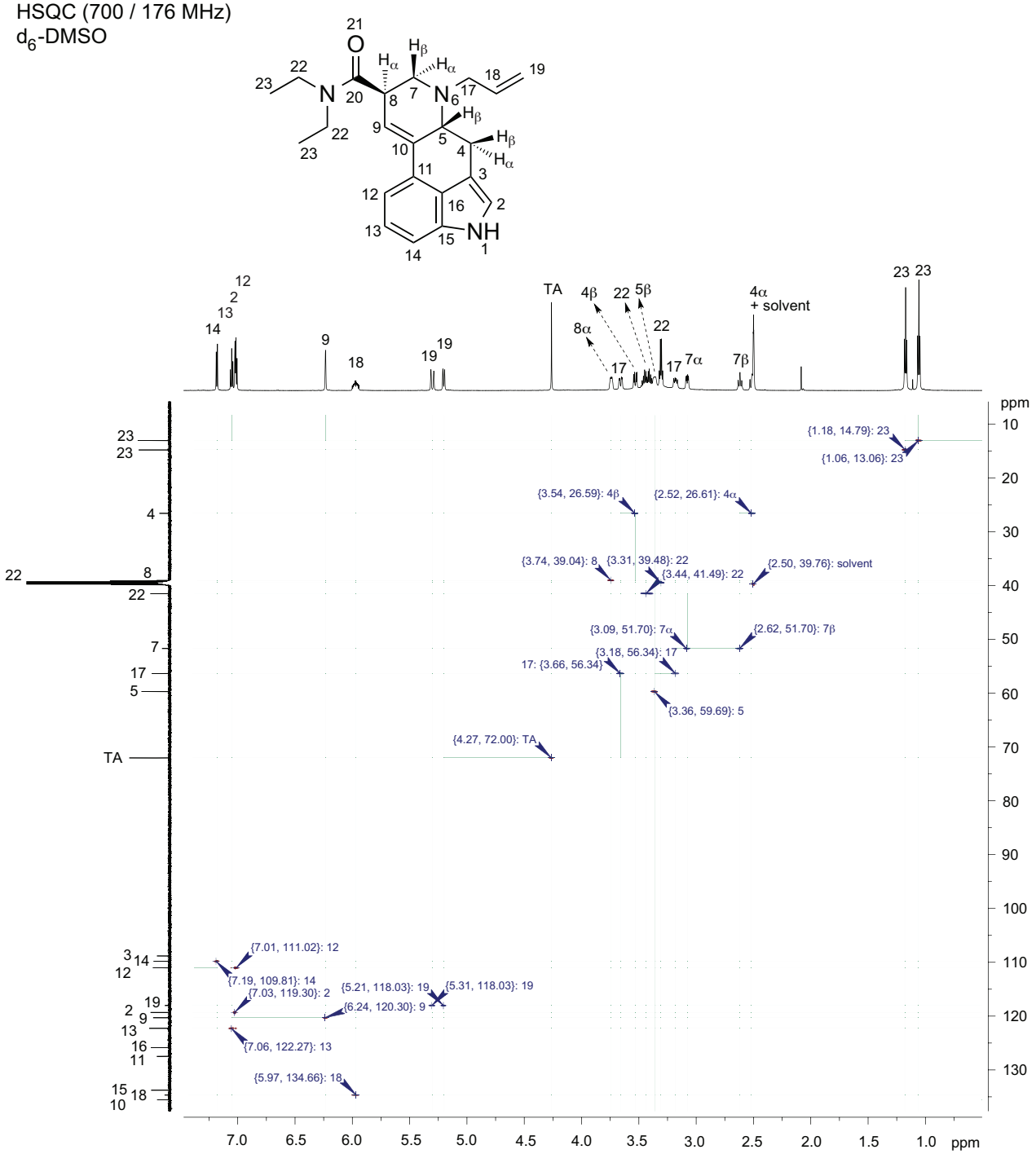


AL-LAD hemitartrate
^{13}C-NMR (176 MHz)
d_6-DMSO



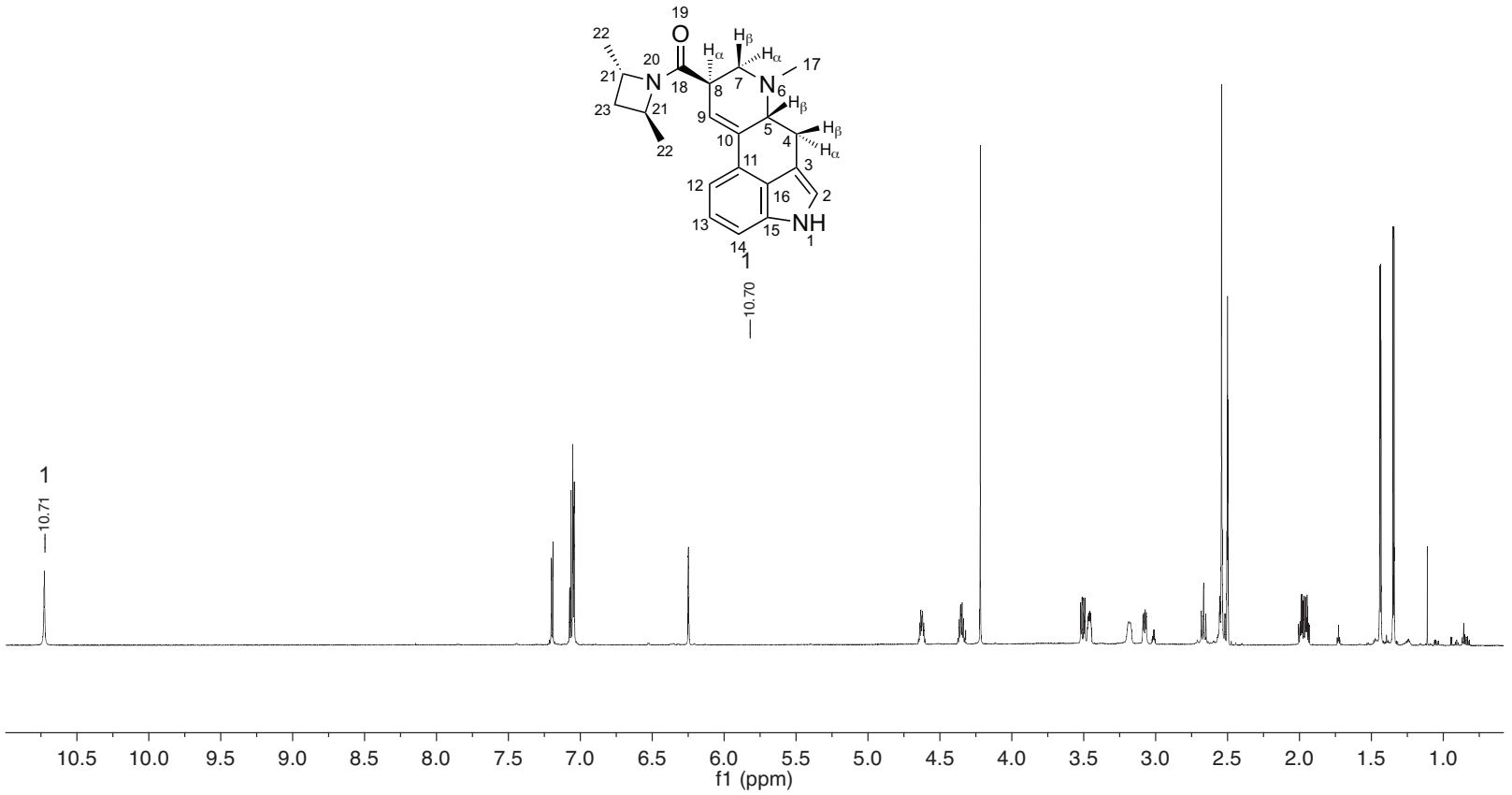
TA = Tartaric acid

AL-LAD hemitartrate
HSQC (700 / 176 MHz)
d_6-DMSO

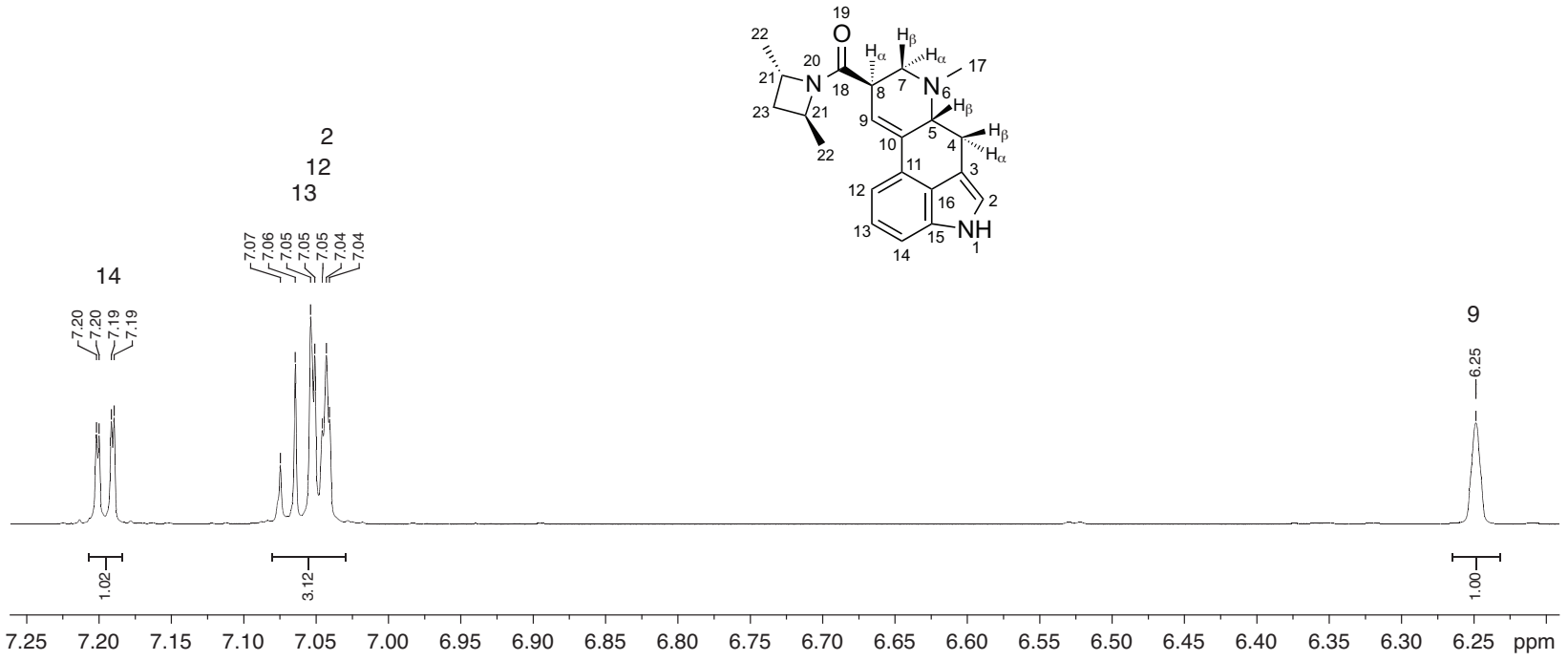


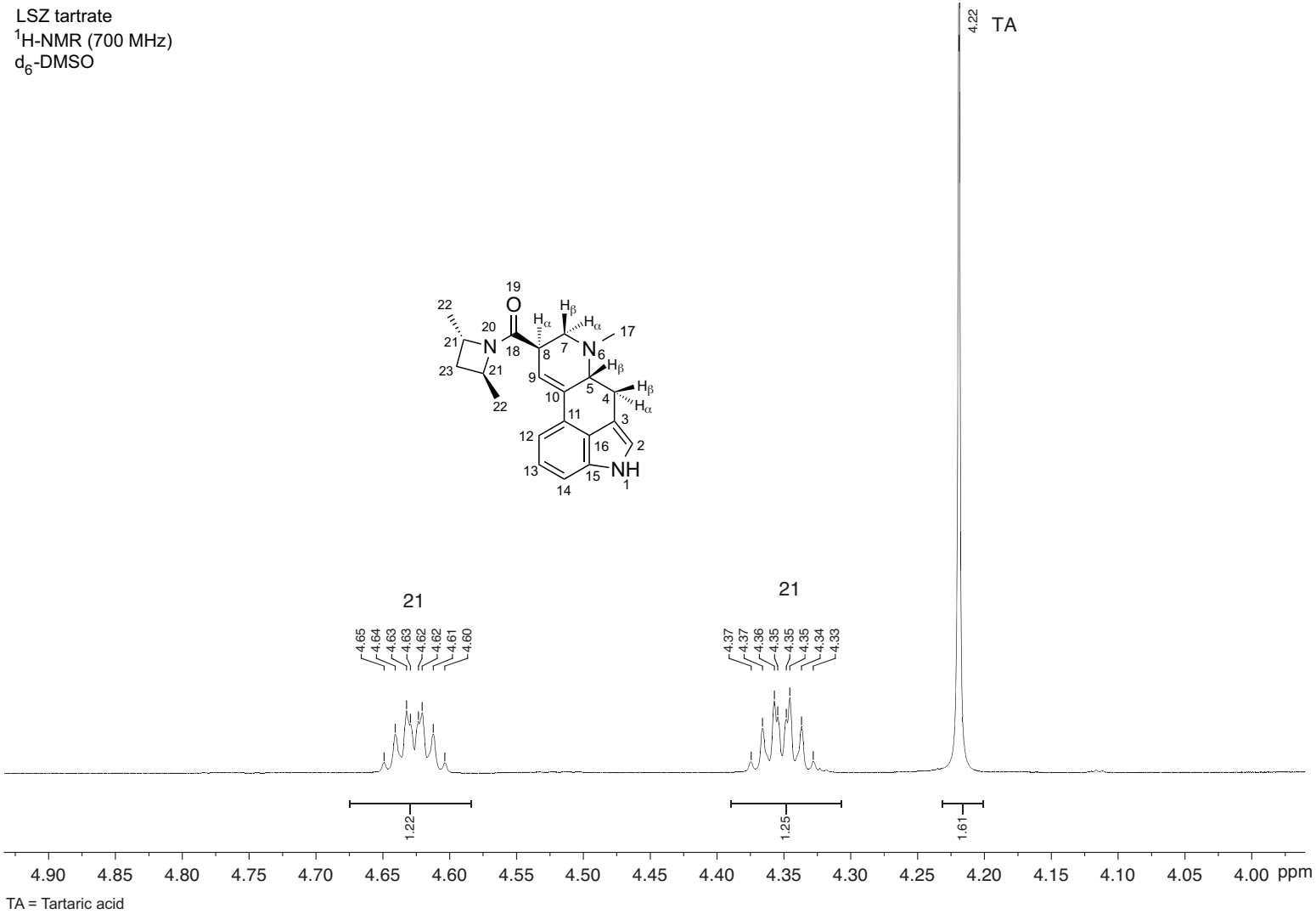
TA = Tartaric acid

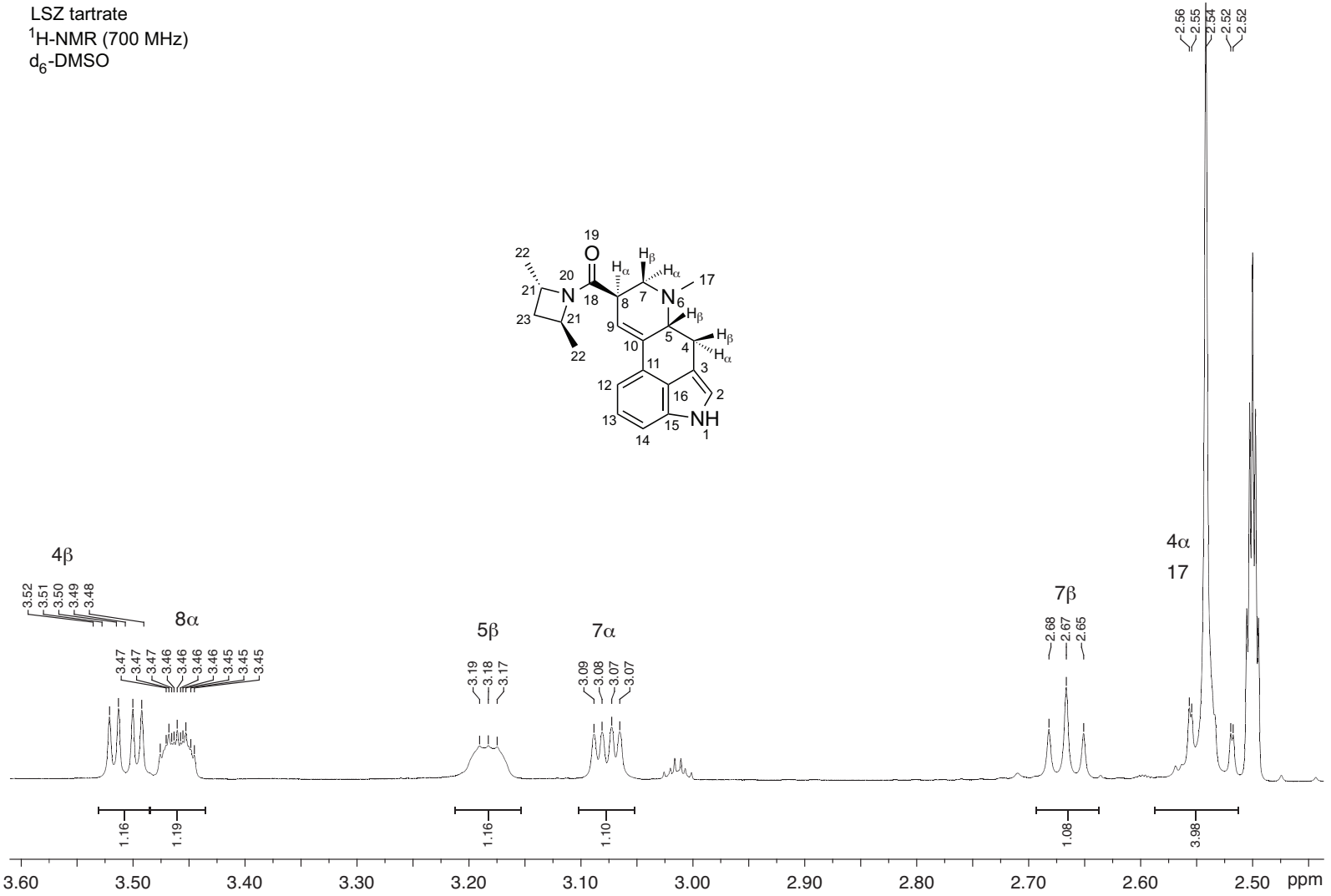
LSZ tartrate
^{1}H-NMR (700 MHz)
d_6-DMSO

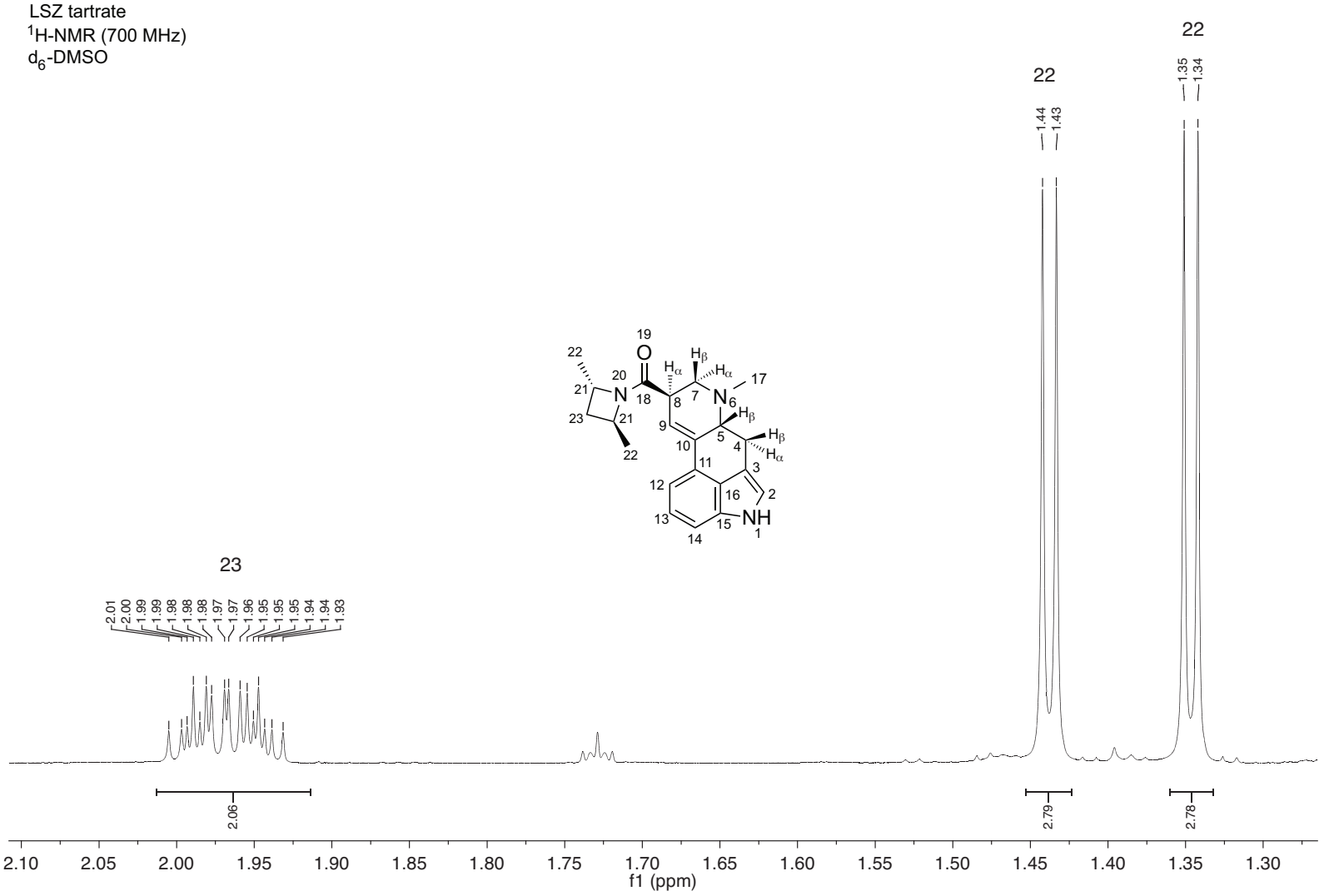


LSZ tartrate
^{1}H-NMR (700 MHz)
d_6-DMSO

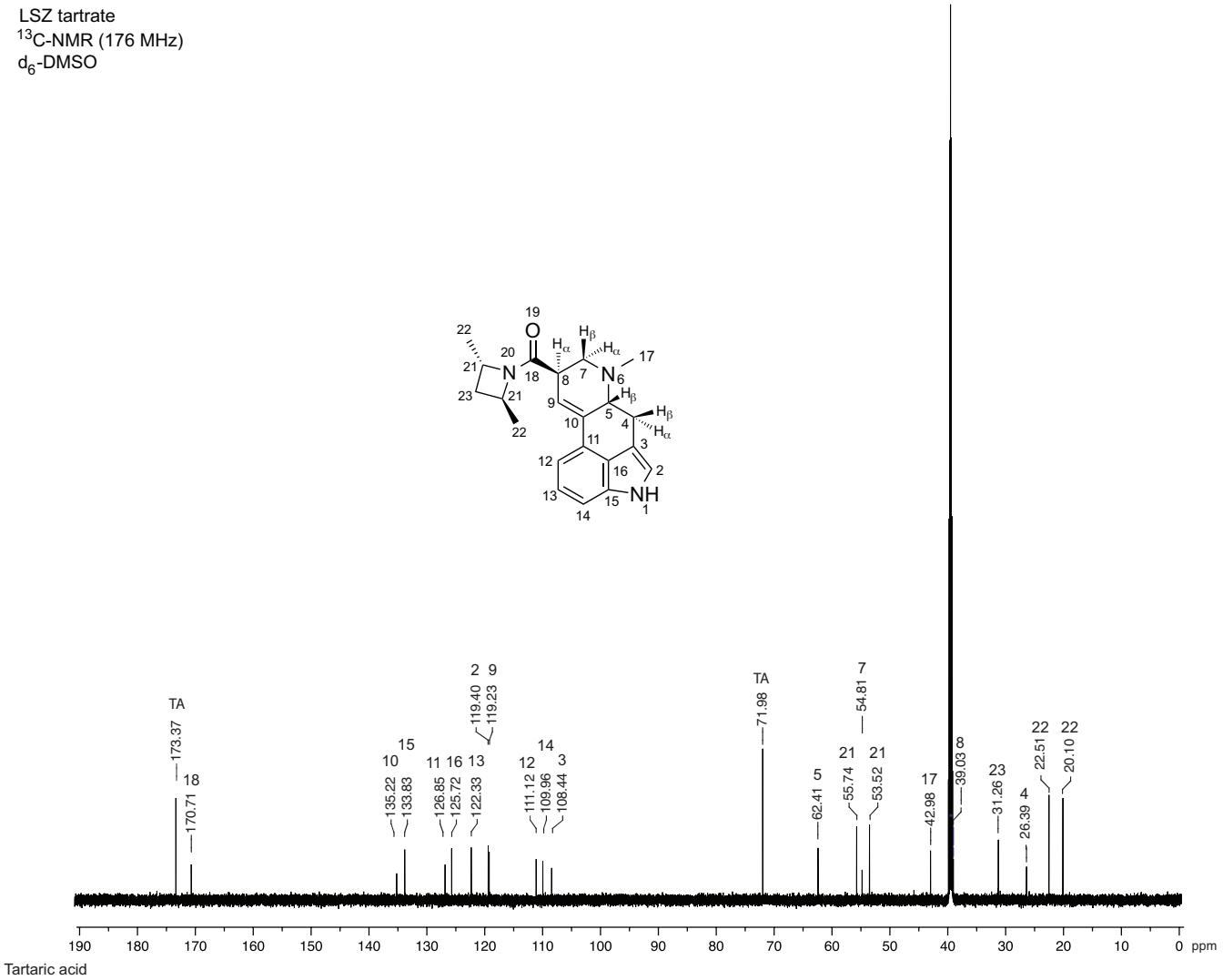



LSZ tartrate
1H-NMR (700 MHz)
d6-DMSO
TA
4.22
21
21
4.65
4.64
4.63
4.63
4.62
4.62
4.61
4.60
4.37
4.37
4.36
4.35
4.35
4.35
4.34
4.33
1.22
1.25
1.61
4.90 4.85 4.80 4.75 4.70 4.65 4.60 4.55 4.50 4.45 4.40 4.35 4.30 4.25 4.20 4.15 4.10 4.05 4.00 ppm
TA = Tartaric acid


LSZ tartrate
1H-NMR (700 MHz)
d6-DMSO
4β
8α
5β
7α
7β
4α
17
3.52
3.51
3.50
3.49
3.48
3.47
3.47
3.47
3.46
3.46
3.46
3.46
3.45
3.45
3.45
3.19
3.18
3.17
3.09
3.08
3.07
3.07
2.68
2.67
2.65
2.56
2.55
2.54
2.52
2.52
1.16
1.19
1.16
1.10
1.08
3.98
3.60
3.50
3.40
3.30
3.20
3.10
3.00
2.90
2.80
2.70
2.60
2.50
ppm


LSZ tartrate
1H-NMR (700 MHz)
d6-DMSO
22
22
1.35
1.34
1.44
1.43
23
2.01
2.00
1.99
1.99
1.98
1.98
1.98
1.97
1.97
1.96
1.95
1.95
1.95
1.94
1.94
1.93
2.06
2.79
2.78
2.10
2.05
2.00
1.95
1.90
1.85
1.80
1.75
1.70
1.65
1.60
1.55
1.50
1.45
1.40
1.35
1.30
f1 (ppm)

LSZ tartrate
^{13}C-NMR (176 MHz)
d_6-DMSO



TA = Tartaric acid