General procedure

(R)-(+)-3-(2-Nitropropane-2-yl) cyclohexanone. A mixture of 2-cyclohexen-1-one (50 μL, 0.52 mmol), 2-nitropropane (100 μL, 1.1 mmol), 2,5-dimethylpiperazine (60 mg, 0.53 mmol) and a catalytic amount of L-Proline (0.2.2 mg, 0.02 mmol) were stirred in reagent grade chloroform previously passed through a bed of Brockmann 1 grade basic alumina.[17] (4 mL) for 62 h at rt. The reaction mixture was diluted with CH_2Cl_2 and washed with aqueous HCl (3%). The organic phase was dried ($MgSO_4$), filtered, concentrated and chromatographed on a silica gel column to obtain a colorless solid (84 mg, 88%). $[\alpha]_D$ +23.3 (c 1.0, $CHCl_3$, 93% *ee*). Lit.[9] $[\alpha]_D$ +15.0 (c 1.0, $CHCl_3$, 59% *ee*); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.45-2.30 (m, 3H), 2.28-2.17 (m, 1H), 2.17-2.05 (m, 2H), 1.83-1.74 (m, 1H), 1.74-1.48 (m, 1H), 1.55 (s, 3H), 1.54 (s, 3H), 1.48-1.33 (m, 1H),; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 208.9, 90.6, 46.5, 42.6, 40.7, 25.9, 24.3, 23.5, 22.4; IR (CH_2Cl_2) 1715.5, 1540.4, 1457.8, 1400.9, 1376.0, 1348.3 and 1267.0 cm^{-1} ; HRMS (FAB) calcd. for $C_9H_{16}NO_3^+$ ($(M+1)^+$) 186.1130, found 186.1138. Under argon atmosphere, a mixture of 3-(2-Nitropropane-2-yl) cyclohexanone (42.5 mg, 0.23 mmol), (2*R*,3*R*)-2,3-butane diol (40 μL, 0.44 mmol) and a catalytic amount of *p*-toluensulfonic acid in dry benzene (5 mL) were heated at reflux for 1 h. The reaction was cooled to rt, added ethyl acetate (20 mL) and washed with saturated $NaHCO_3$ (3 X 5 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated to obtain the corresponding ketal as a colorless oil (55 mg, 93%). (The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal, observing at δ 44.7/44.2, 38.8/37.7 and 37.2/36.1.

(+)-3-Nitromethyl cyclohexanone. $[\alpha]_D$ +8.1 (c 1.8, $CHCl_3$, 71% *ee*). Lit.[9] $[\alpha]_D$ +9.4 (c 1.0, $CHCl_3$, 45% *ee*). Lit. [10] $[\alpha]_D$ -0.67 (c 2.37, $CHCl_3$, 6% *ee*); HRMS (FAB) calcd. for $C_7H_{12}NO_3^+$ ($(M+1)^+$) 158.0817, found 158.0811; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 40.1/39.3, 36.4/35.5, 34.7/34.4 and 22.0/21.6.

(+)-3-(1-Nitrocyclopentyl) cyclohexanone. $[\alpha]_D$ -8.2 (c 1.3, $CHCl_3$, 93% *ee*); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.75-2.59 (m, 2H), 2.51-2.34 (m, 2H), 2.60-2.32 (m, 4H), 1.98-1.88 (m, 1H), 1.86-1.50 (m, 7H), 1.47-1.32 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 209.2, 103.3, 46.0, 43.6, 40.8, 35.0, 34.3, 26.9, 24.5, 23.6, 23.5; IR (neat) 1715.3, 1530.6, 1450.1, 1434.4, 1352.1 and 1320.7 cm^{-1}; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 43.2/42.8, 39.2/38.1 and 36.5/35.5.

(+)-3-(1-Nitrocyclohexyl) cyclohexanone. $[\alpha]_D$ +2.2 (c 1.4, $CHCl_3$, 93% *ee*); HRMS (FAB) calcd. for $C_{12}H_{20}NO_3^+$ ($(M+1)^+$) 226.1443, found 226.1437; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 44.6/44.0, 38.0/36.9 and 36.6/35.5.

(+)-3-(2-Nitroethyl) cyclohexanone. (Less polar). $[\alpha]_D$ +7.8 (c 0.4, $CHCl_3$, 51% *ee*); HRMS (FAB) calcd. for $C_8H_{14}NO_3^+$ ($(M+1)^+$) 172.0974, found 172.0979; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 22.1/21.7.

(+)-3-(2-Nitroethyl) cyclohexanone. (More polar). $[\alpha]_D$ +5.2 (c 0.4, $CHCl_3$, 49% *ee*); HRMS (FAB) calcd. for $C_8H_{14}NO_3^+$ ($(M+1)^+$) 172.0974, found 172.0979; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 22.3/22.0.

(+)-3-(5-Nitropentene) cyclohexanone. (Less polar). $[\alpha]_D$ +18.7 (c 0.4, $CHCl_3$, 81% *ee*); HRMS (FAB) calcd. for $C_{11}H_{18}NO_3^+$ ($(M+1)^+$) 212.1286, found 212.1294; The enantiomeric excess was determined by ^{13}C-NMR of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at (75 MHz, $CDCl_3$)δ 36.5/35.5 and 22.1/21.7 and (100 MHz, C_6D_6) at δ 23.0/22.5.

(-)-3-(5-Nitropentene) cyclohexanone. (More polar). $[\alpha]_D$ -6.6 (c 0.3, $CHCl_3$, 53% *ee*); HRMS (FAB) calcd. for $C_{11}H_{18}NO_3^+$ ($(M+1)^+$) 212.1286, found 212.1291; The enantiomeric excess was determined by ^{13}C-NMR of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at (75 MHz, $CDCl_3$)δ 36.5/35.5 and 22.4/22.1 and (100 MHz, C_6D_6) at δ 23.3/22.9(6).

(+)-3-Nitromethyl cycloheptanone. $[\alpha]_D$ +45.4 (c 1.6, $CHCl_3$, 72% *ee*). Lit.[9] $[\alpha]_D$ +25.1 (c 1.0, $CHCl_3$, 41% *ee*); HRMS (FAB) calcd. for $C_8H_{14}NO_3^+$ ($(M+1)^+$) 172.0974, found 172.0977; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 110.0/109.5, 42.6/42.0 and 27.5/25.8.

(+)-3-(2-Nitropropane-2-yl) cycloheptanone. $[\alpha]_D$ +67.7 (c 2.1, $CHCl_3$, 86% *ee*). Lit.[9] $[\alpha]_D$ +51.8 (c 1.0, $CHCl_3$, 73% *ee*); HRMS (FAB) calcd. for $C_{10}H_{18}NO_3^+$ $((M+1)^+)$ 200.1287, found 200.1278; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 110.2/109.5 and 28.9/28.5.

(+)-3-(1-Nitrocyclopentyl) cycloheptanone. $[\alpha]_D$ +44.0 (c 1.4, $CHCl_3$, 87% *ee*). Lit.[9] $[\alpha]_D$ +34.4 (c 1.0, $CHCl_3$, 67% *ee*); HRMS (FAB) calcd. for $C_{12}H_{20}NO_3^+$ $((M+1)^+)$ 226.1443, found 226.1448; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 110.4/109.6, 35.7/35.1 and 22.1/21.5.

(+)-3-(1-Nitrocyclohexyl) cycloheptanone. $[\alpha]_D$ +46.6 (c 2.2, $CHCl_3$, 89% *ee*). Lit.[9] $[\alpha]_D$ +41.7 (c 1.0, $CHCl_3$, 84% *ee*); HRMS (FAB) calcd. for $C_{13}H_{22}NO_3^+$ $((M+1)^+)$ 240.1599, found 240.1595; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 110.3/109.4, 28.5/27.9 and 26.3/24.7.

(+)-3-(Nitromethane) cyclopentanone. $[\alpha]_D$ +66.9 (c 0.6, $CHCl_3$, 62% *ee*); HRMS (FAB) calcd. for $C_6H_{10}NO_3^+$ $((M+1)^+)$ 144.0656, found 144.0661; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 41.5/41.1, 36.8/36.5, 35.5/35.1 and 27.2/26.8.

(+)-3-(2-Nitropropyl) cyclopentanone. $[\alpha]_D$ +84.2 (c 0.9, $CHCl_3$, 75% *ee*); HRMS (FAB) calcd. for $C_8H_{14}NO_3^+$ ($(M+1)^+$) 172.0974, found 172.0973; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 46.0/45.6, 39.4/39.2, 37.3/37.0 and 24.9/24.6.

(+)-3-(1-Nitrocyclopentyl) cyclopentanone. $[\alpha]_D$ +73.5 (c 1.3, $CHCl_3$, 76% *ee*); HRMS (FAB) calcd. for $C_{10}H_{16}NO_3^+$ ($(M+1)^+$) 198.1130, found 198.1127; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butandiol, observing at δ 44.4/43.9, 40.0/39.8 and 37.1/36.9.

(+)-3-(1-Nitrocyclohexyl) cyclopentanone. $[\alpha]_D$ +236.4 (c 0.2, $CHCl_3$, 76% *ee*); HRMS (EI) calcd. for $C_{11}H_{18}NO_3^+$ (M+) 211.1208, found 211.1203; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 47.2/47.6, 39.0/38.7, and 37.2/36.9.

(+)-3-(Nitroethyl) cyclopentanone. (Less polar). $[\alpha]_D$ +75.1 (c 0.7, $CHCl_3$, 65% *ee*); HRMS (EI) calcd. for $C_7H_{11}NO_3^+$ (M+) 157.0739, found 157.0738; HRMS (FAB) calcd. for $C_7H_{12}NO_3^+$ ($(M+1)^+$) 158.0817, found 158.0824; The enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 37.0/36.7 and 27.2/26.8.

(+)-3-(Nitroethyl) cyclopentanone. (More polar). $[\alpha]_D$ +83.8 (c 0.5, $CHCl_3$, 64% *ee*); HRMS (FAB) calcd. for $C_7H_{12}NO_3^+$ ($(M+1)^+$) 158.0817, found 158.0824; The

enantiomeric excess was determined by ^{13}C-NMR (100 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 37.2/36.9 and 26.2/25.9.

(+)-3-(5-Nitropentene) cyclopentanone. (Less polar). $[\alpha]_D$ +79.5 (c 0.7, $CHCl_3$, 72% *ee*); HRMS (FAB) calcd. for $C_{10}H_{16}NO_3^+$ ($(M+1)^+$) 198.1130, found 198.1124; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 36.9/36.6 and 27.1/26.7.

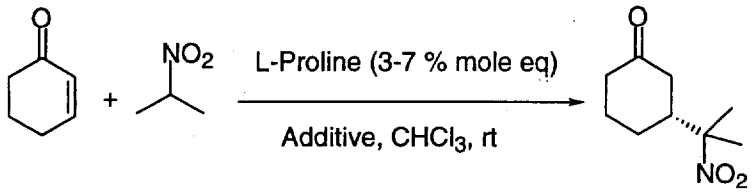
(+)-3-(5-Nitropentene) cyclopentanone. (More polar). $[\alpha]_D$ +41.8 (c 0.5, $CHCl_3$, 43% *ee*); HRMS (FAB) calcd. for $C_{10}H_{16}NO_3^+$ ($(M+1)^+$) 198.1130, found 198.1127; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 37.2/36.9 and 26.6/26.2.

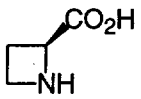
(+)-4-Phenyl-5-methyl-5-nitro-2-hexanone. $[\alpha]_D$ +29.4 (c 1.7, $CHCl_3$, 61 % *ee*) HRMS (FAB) calcd for $C_{13}H_{18}NO_3^+$ ($(M+1)^+$) 236.1287, found 236.1280; The enantiomeric excess was determined by ^{13}C-NMR (75 MHz, $CDCl_3$) of the ketal with (2*R*, 3*R*)-2,3-butane diol, observing at δ 49.7/49.4, 21.9/21.7 and 16.2/15.8.

(+)-5-Methyl-5-nitro-4-pentyl-2-hexanone. $[\alpha]_D$ +15.1 (c 1.0, $CHCl_3$, 68 % *ee*). Lit.[9] $[\alpha]_D$ +13.2 (c 1.0, $CHCl_3$, 60% *ee*)

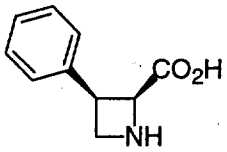
Comparison of highest *ee* values with different amino acids

Chart 1.[a]

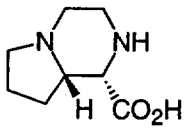




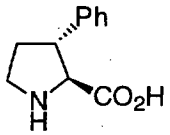
RbOH 59%
Quinine 56%



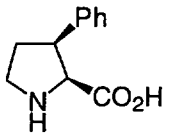
RbOH 74%
Quinine 17%
Ephedrine 40%
DMpiperazine 38%



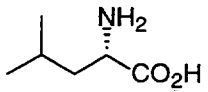
RbOH 7%
Quinine 17%



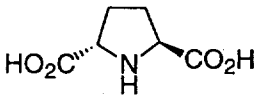
RbOH 59%
Quinine 72%
Ephedrine 43%
DMpiperazine 90%



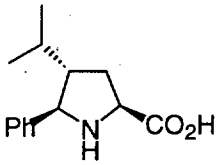
RbOH NR
Piperazine NR



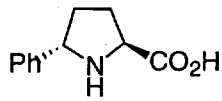
Quinine NR
DMEDA 0%



RbOH NR
Quinine NR
DMEDA 0%

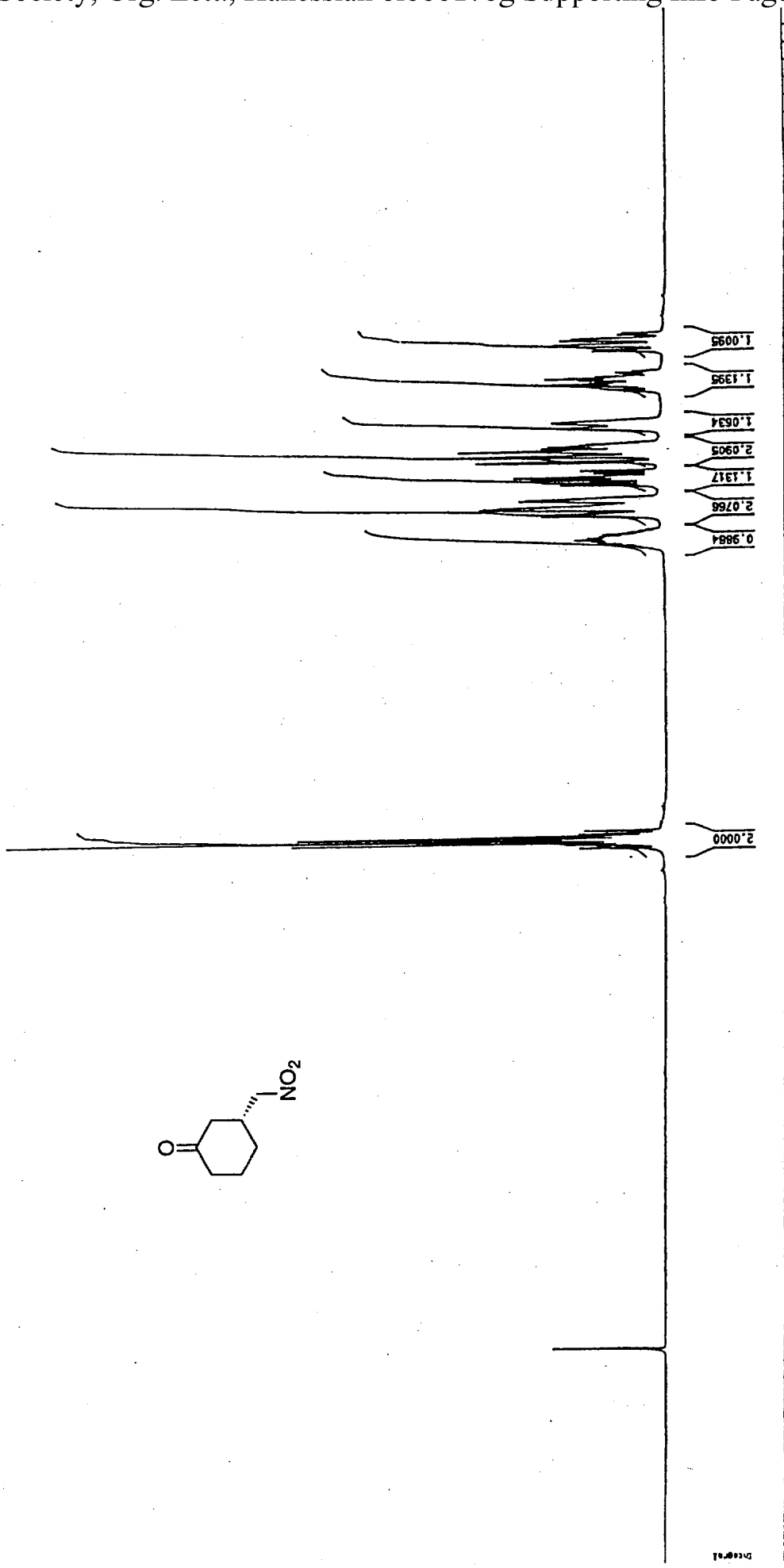


RbOH 55%
Quinine 72%



RbOH NR
Quinine 70%
DMpiperazine 68%

a. Bases: RbOH (as proline salt); Quinine; d-Ephedrine; DMEDA (N,N'-dimethylethylene diamine); piperazine; DMpiperazine (*trans*-2,5-dimethylpiperazine);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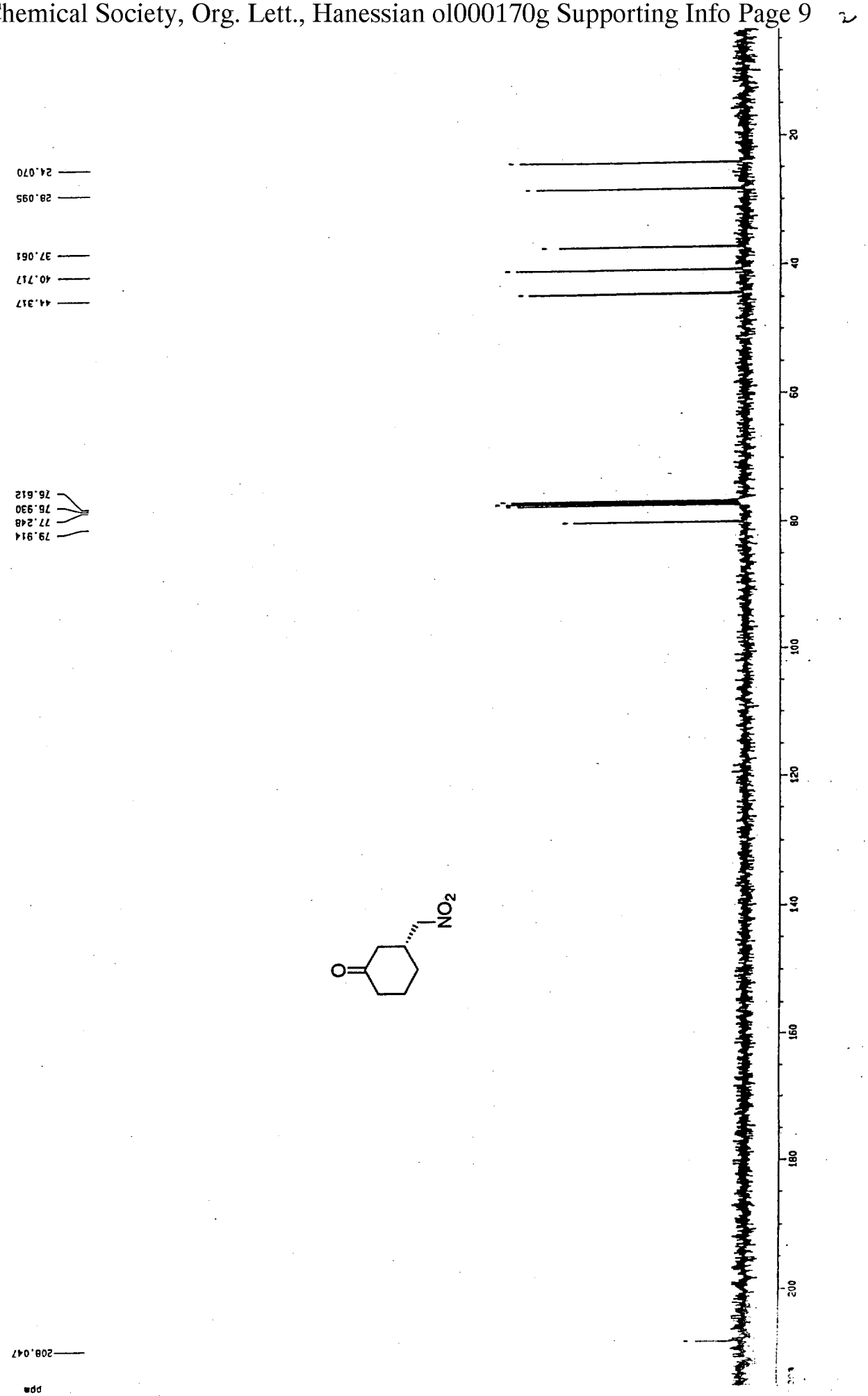
NO2
O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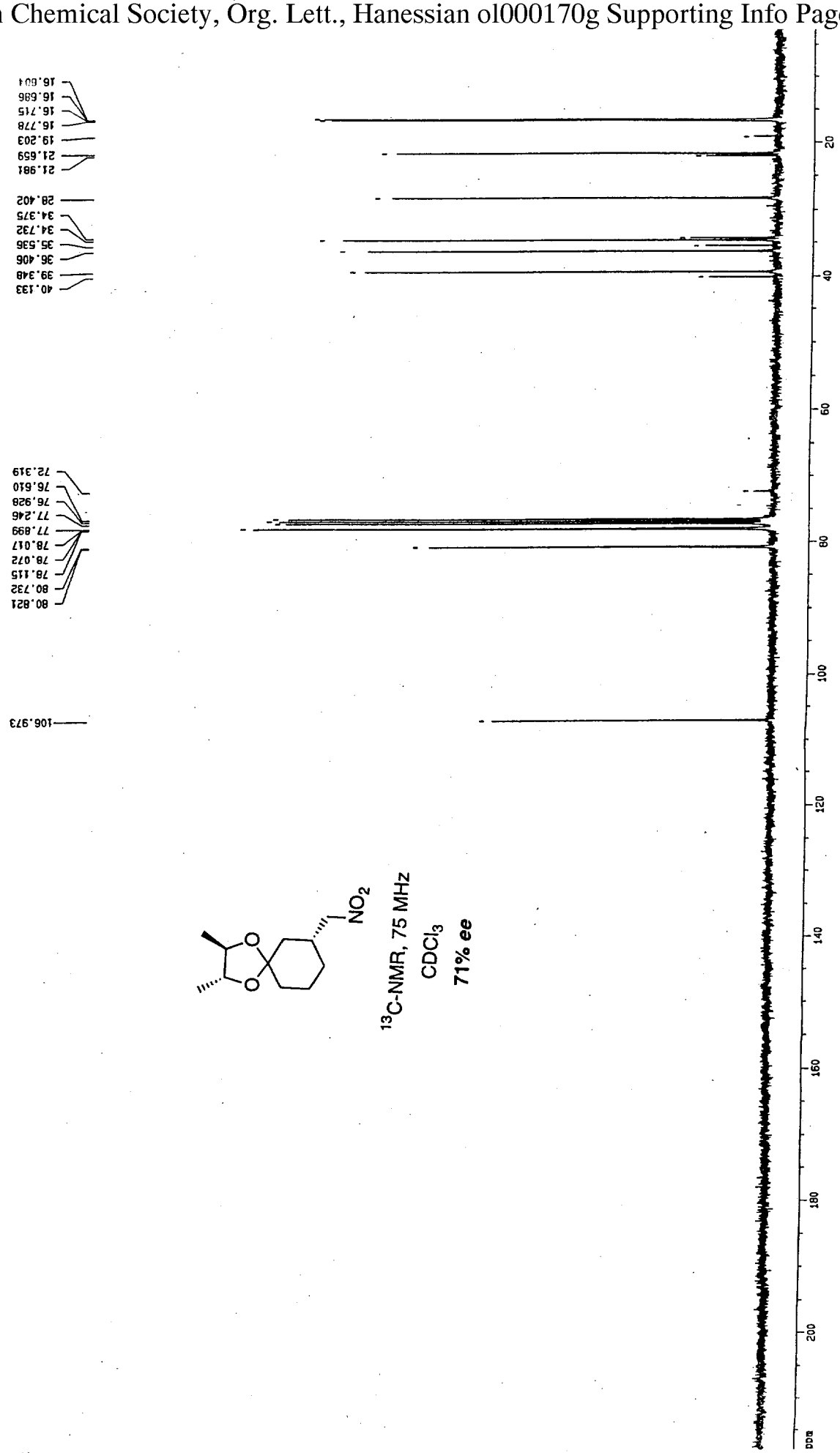
O
NO2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76.928
77.246
77.899
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80.732
80.821
106.973
20
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140
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180
200
ppm
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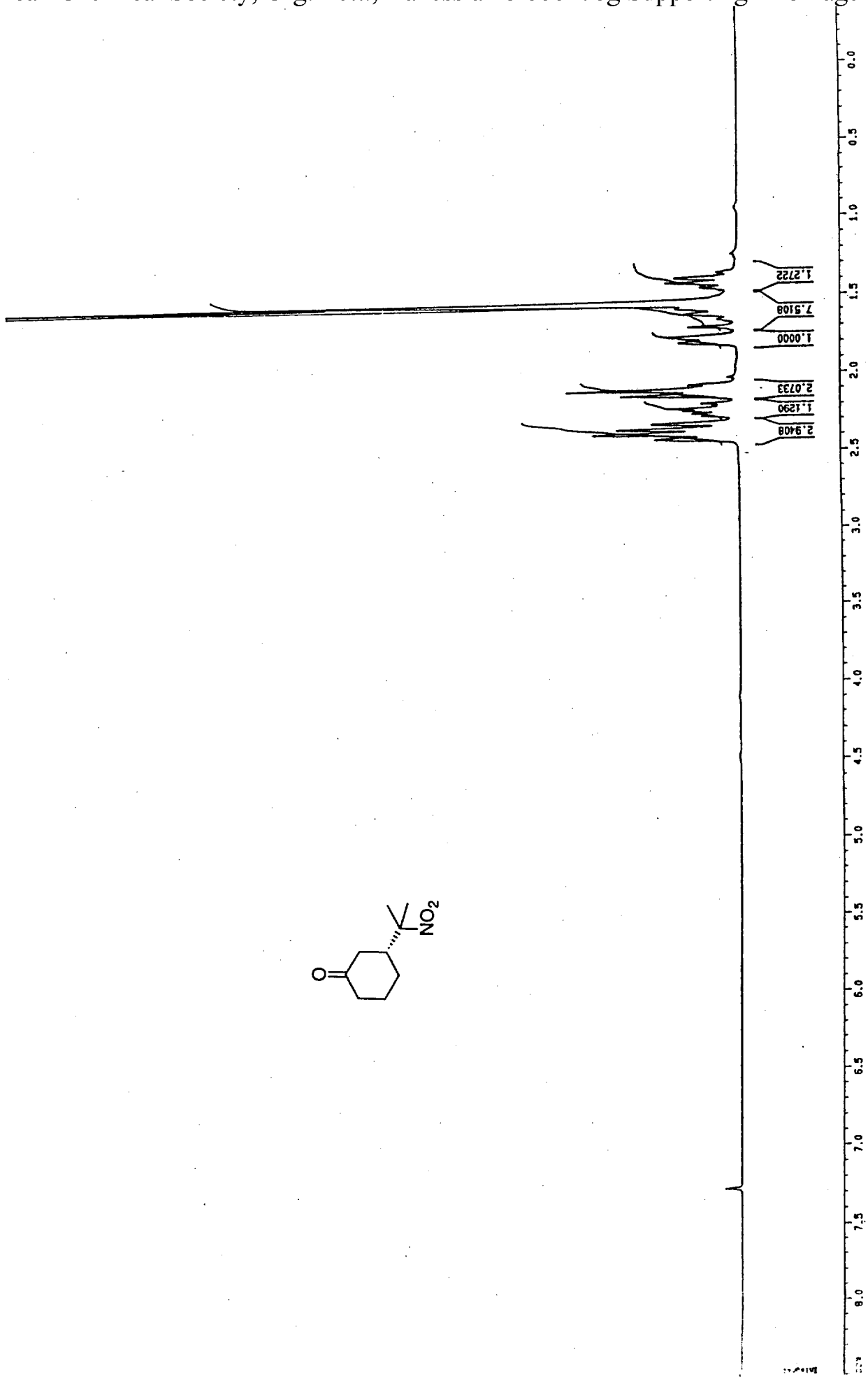
^{13}C-NMR, 75 MHz
$CDCl_3$
71% ee



h

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5	41696.6	7710.394	76.6395	3.06
6	49639.4	4681.024	46.5246	9.32
7	50670.5	4287.687	42.6153	11.01
8	51168.0	4097.313	40.7291	11.21
9	55067.0	2610.575	25.9465	11.35
10	55490.7	2448.934	24.3395	11.43
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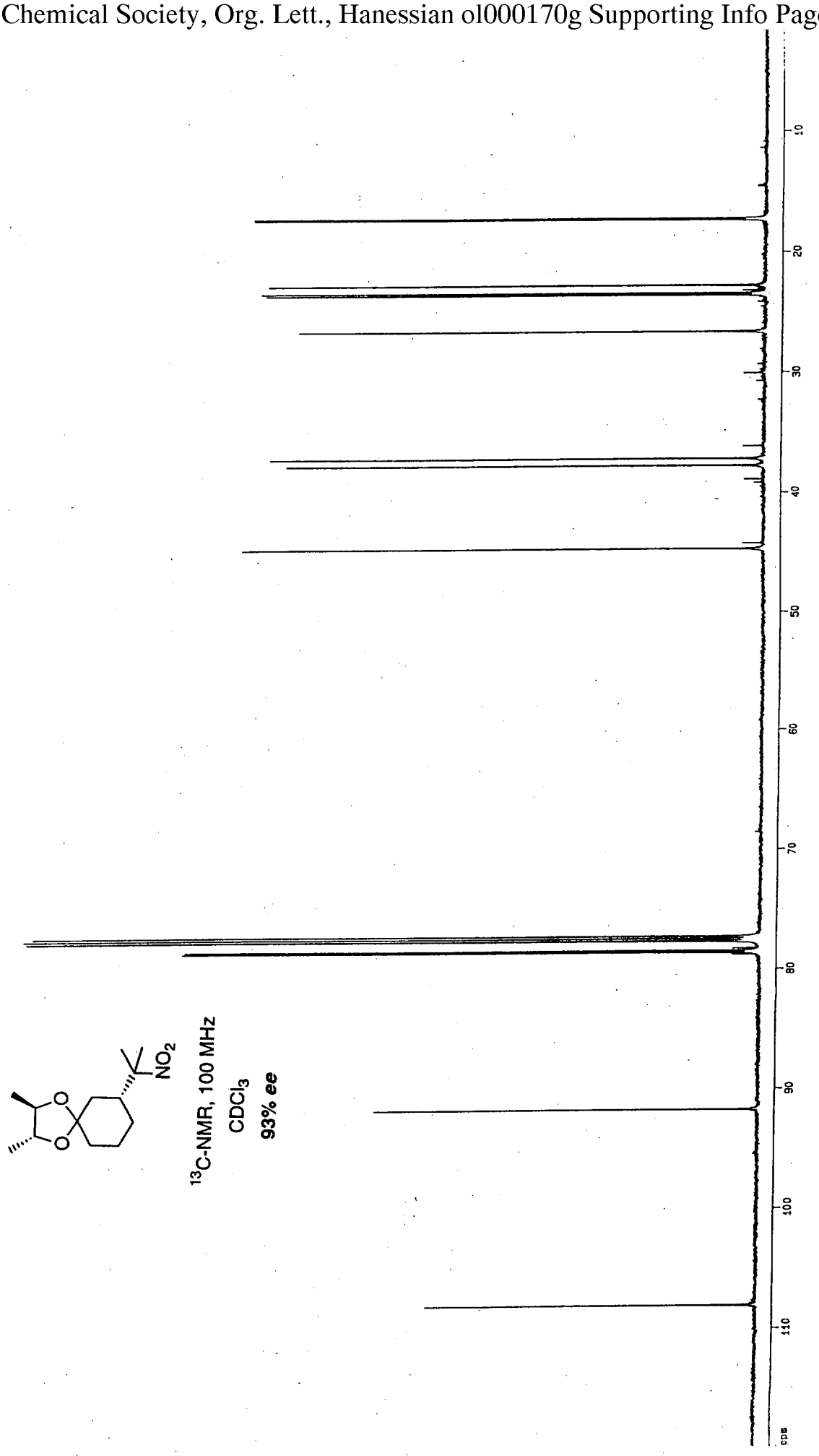
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80
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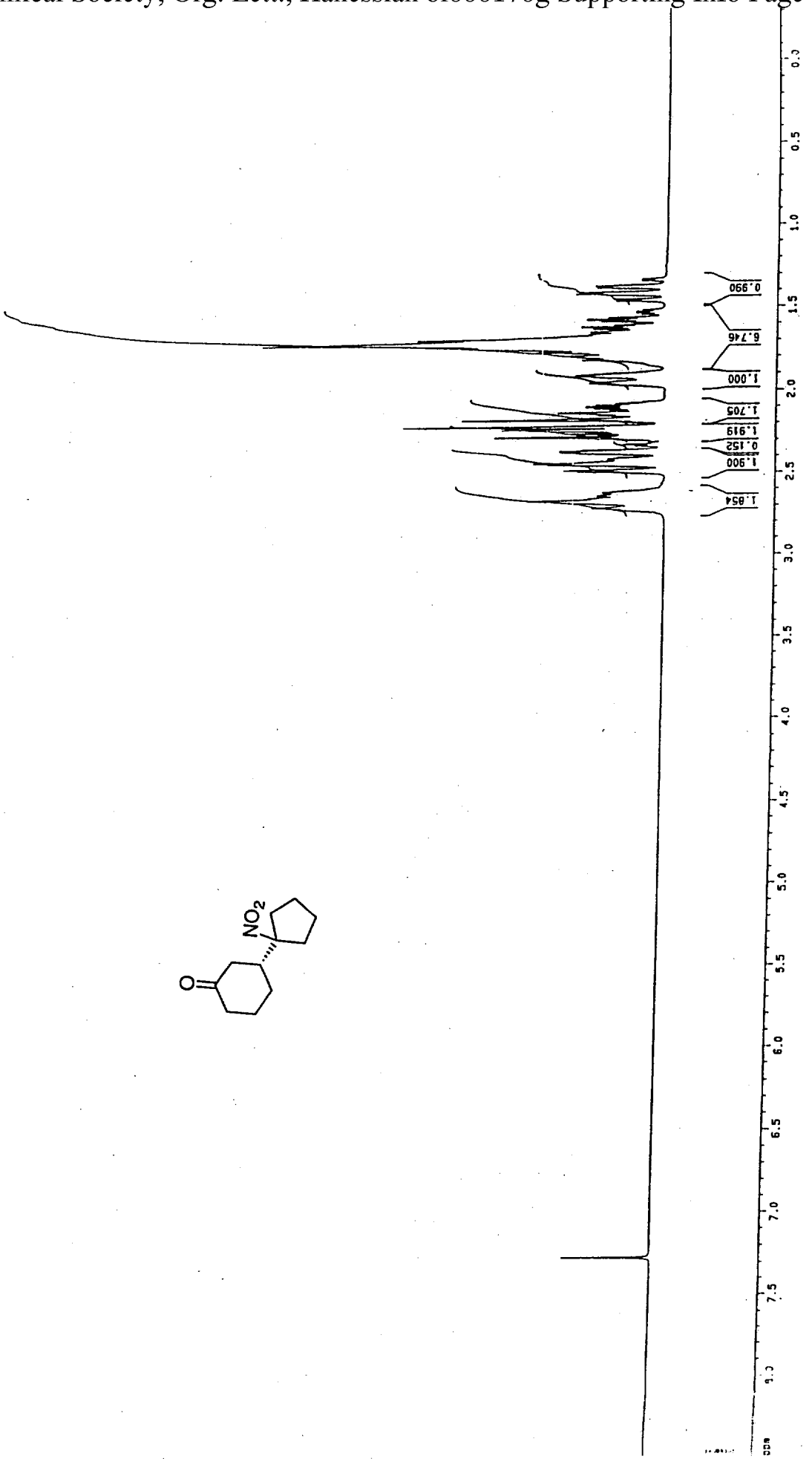
ppm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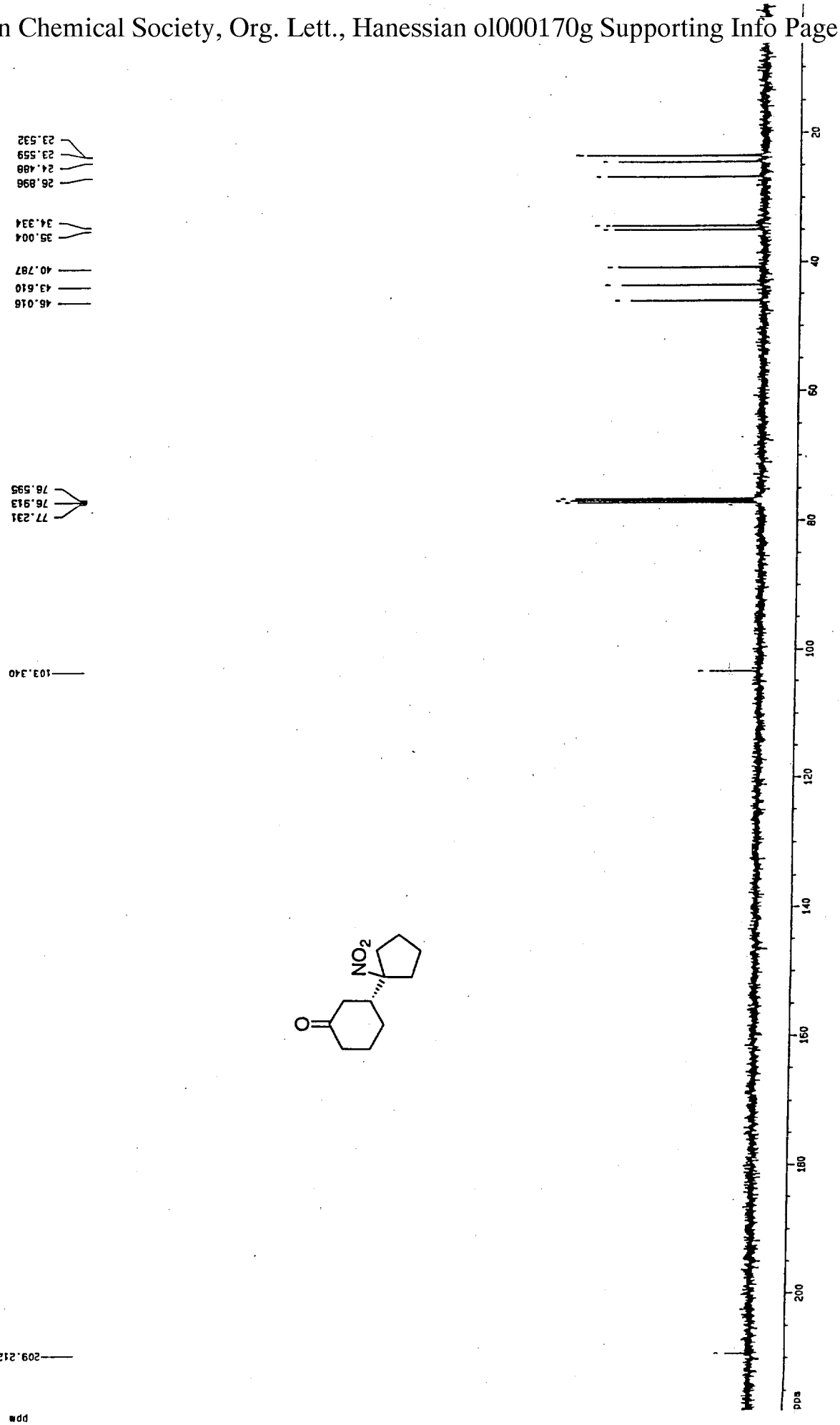
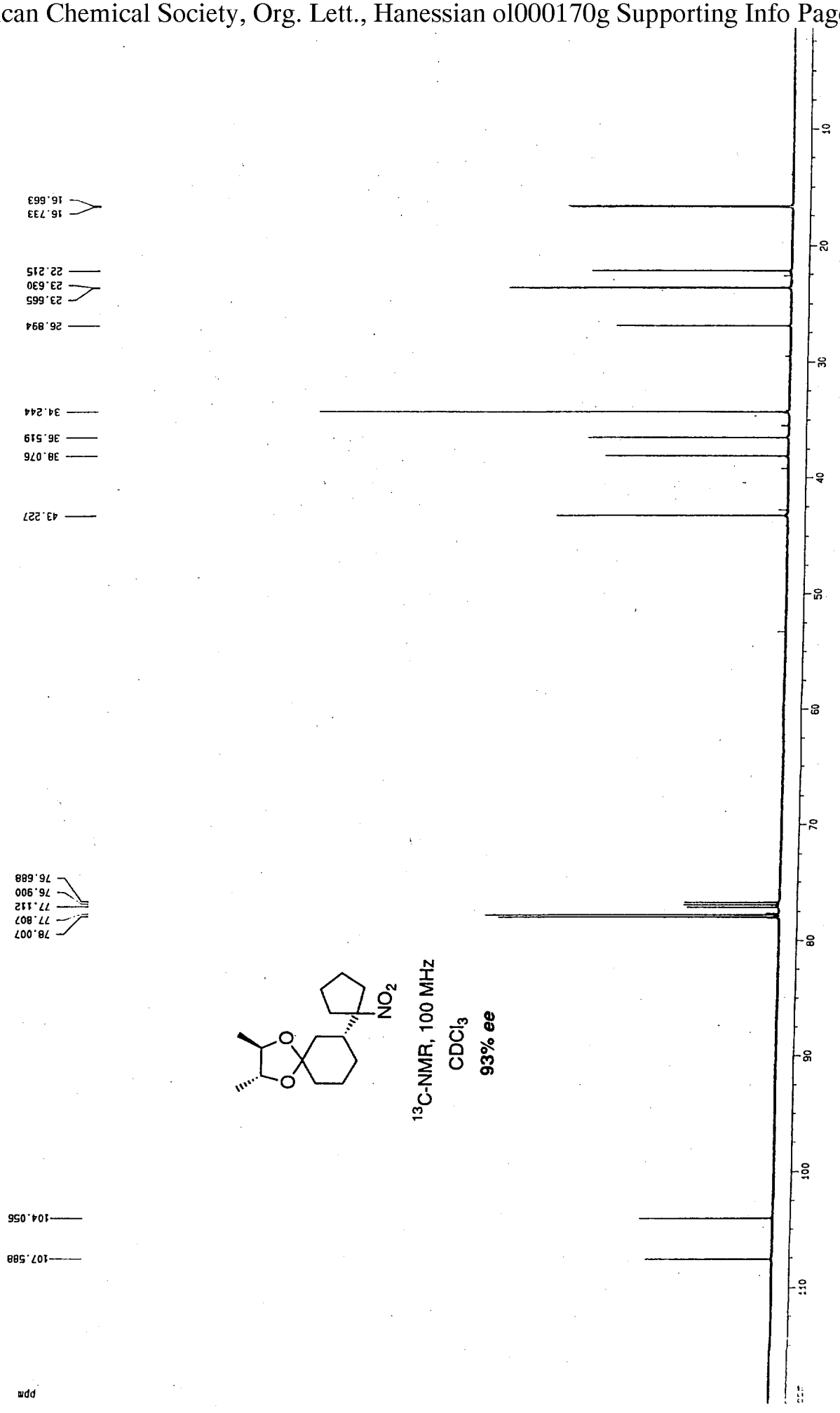
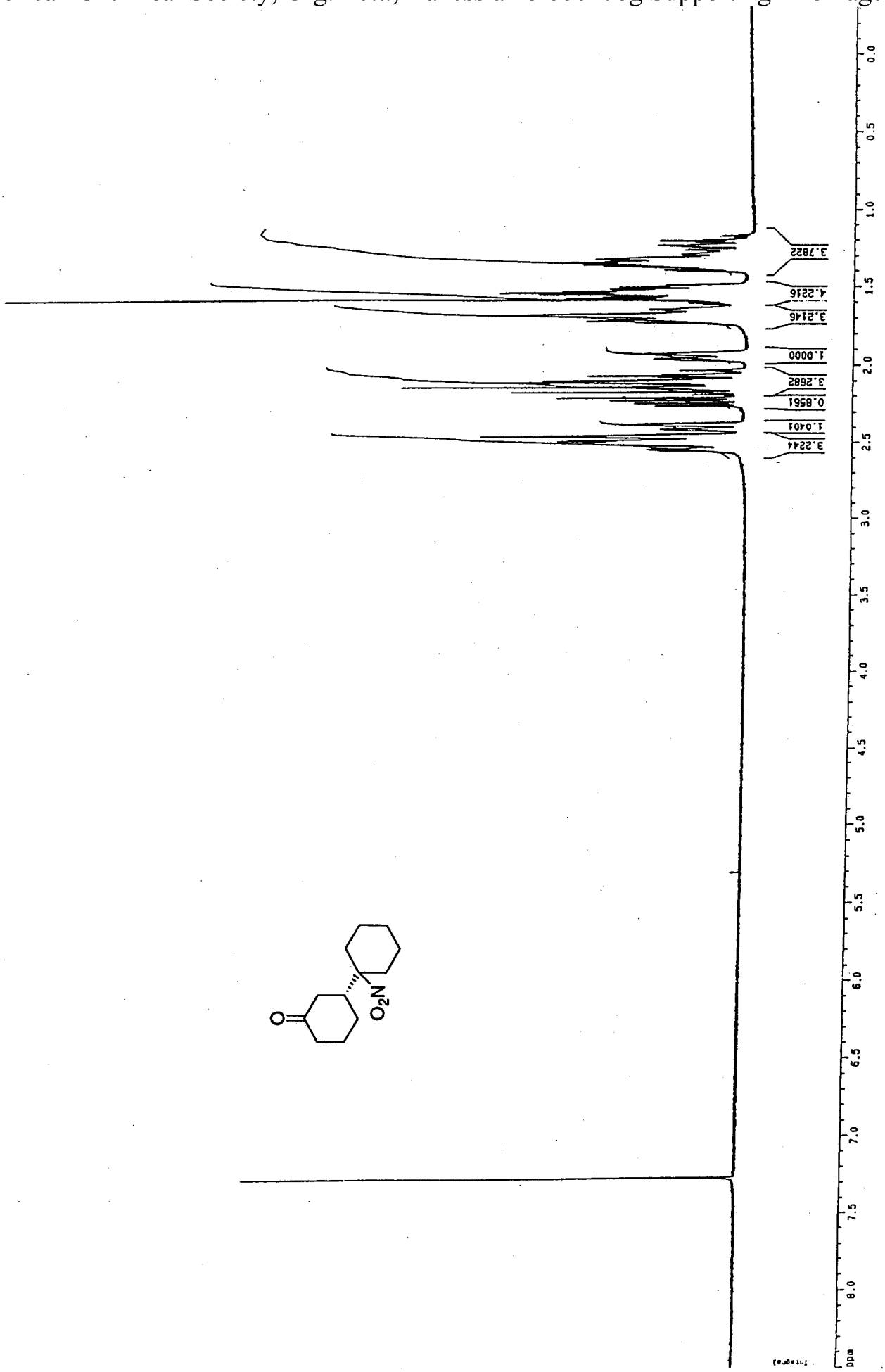
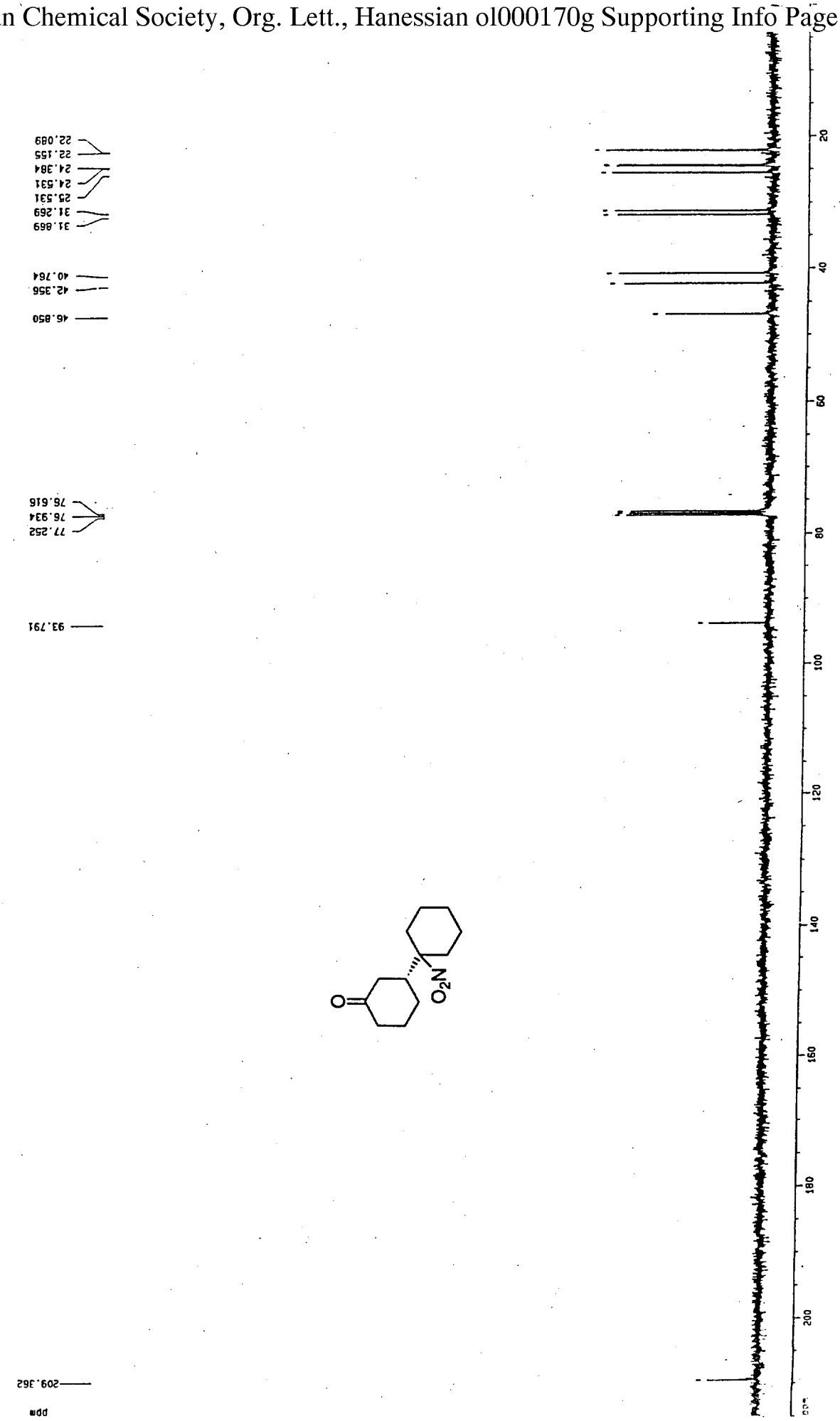
O

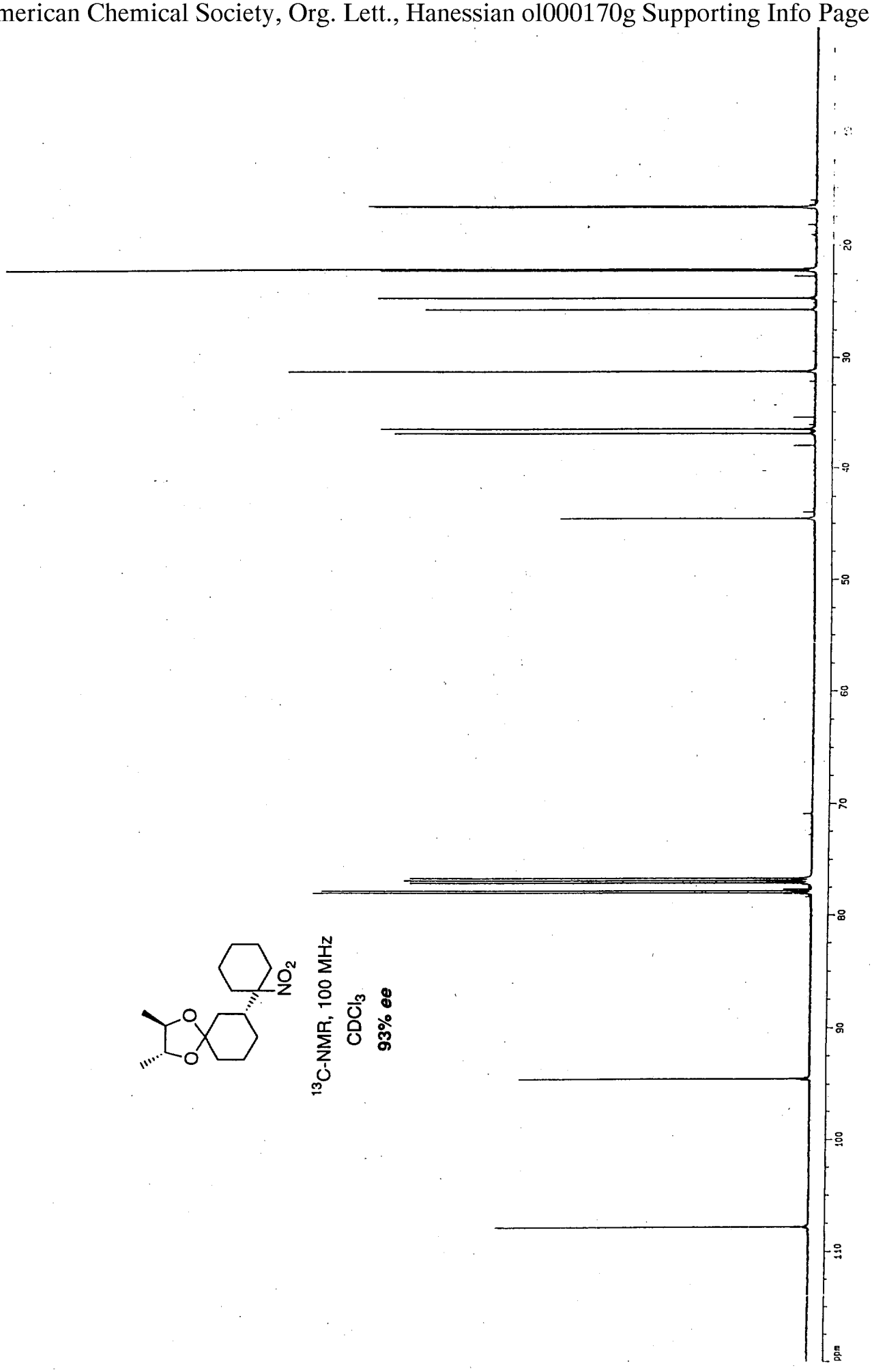


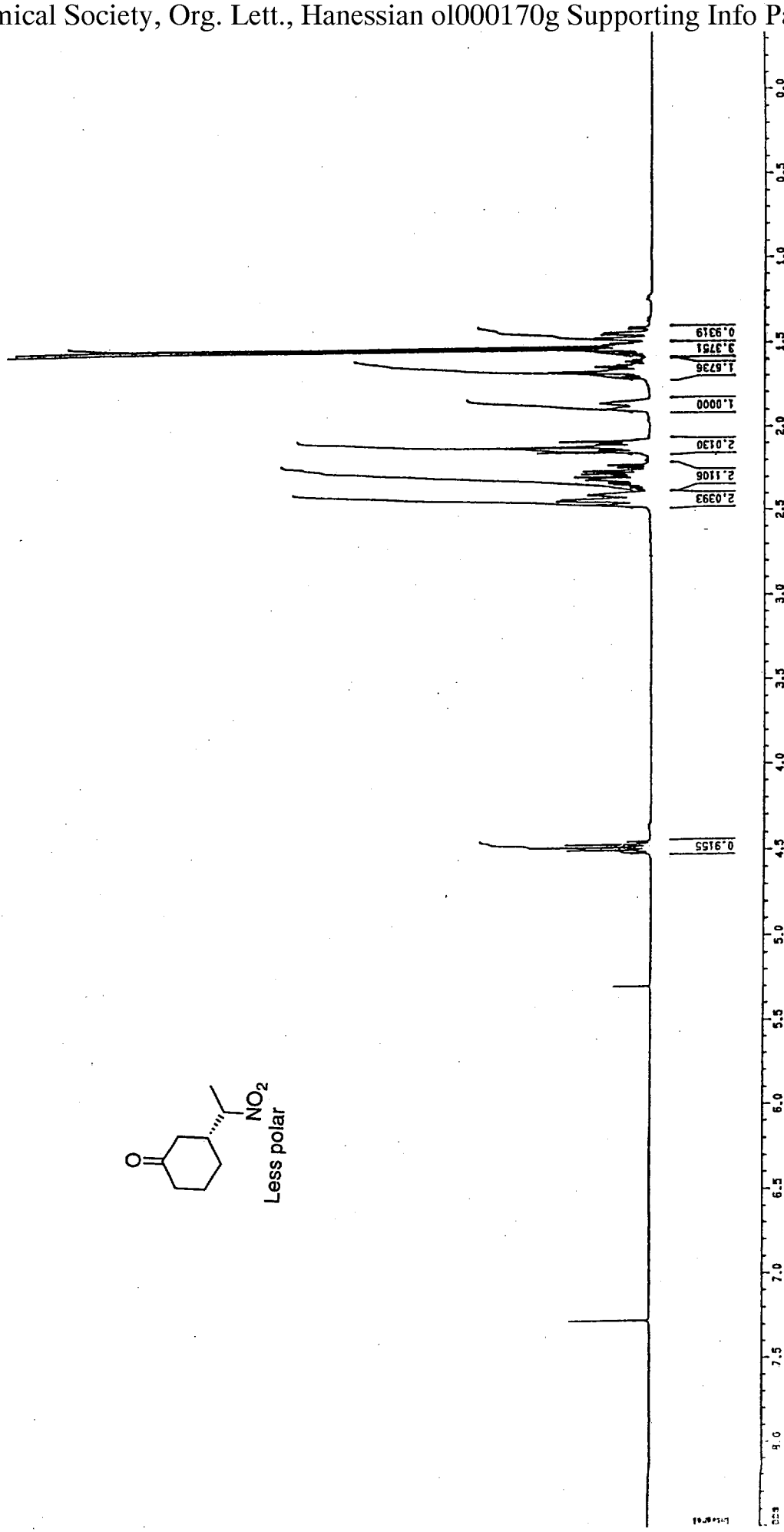


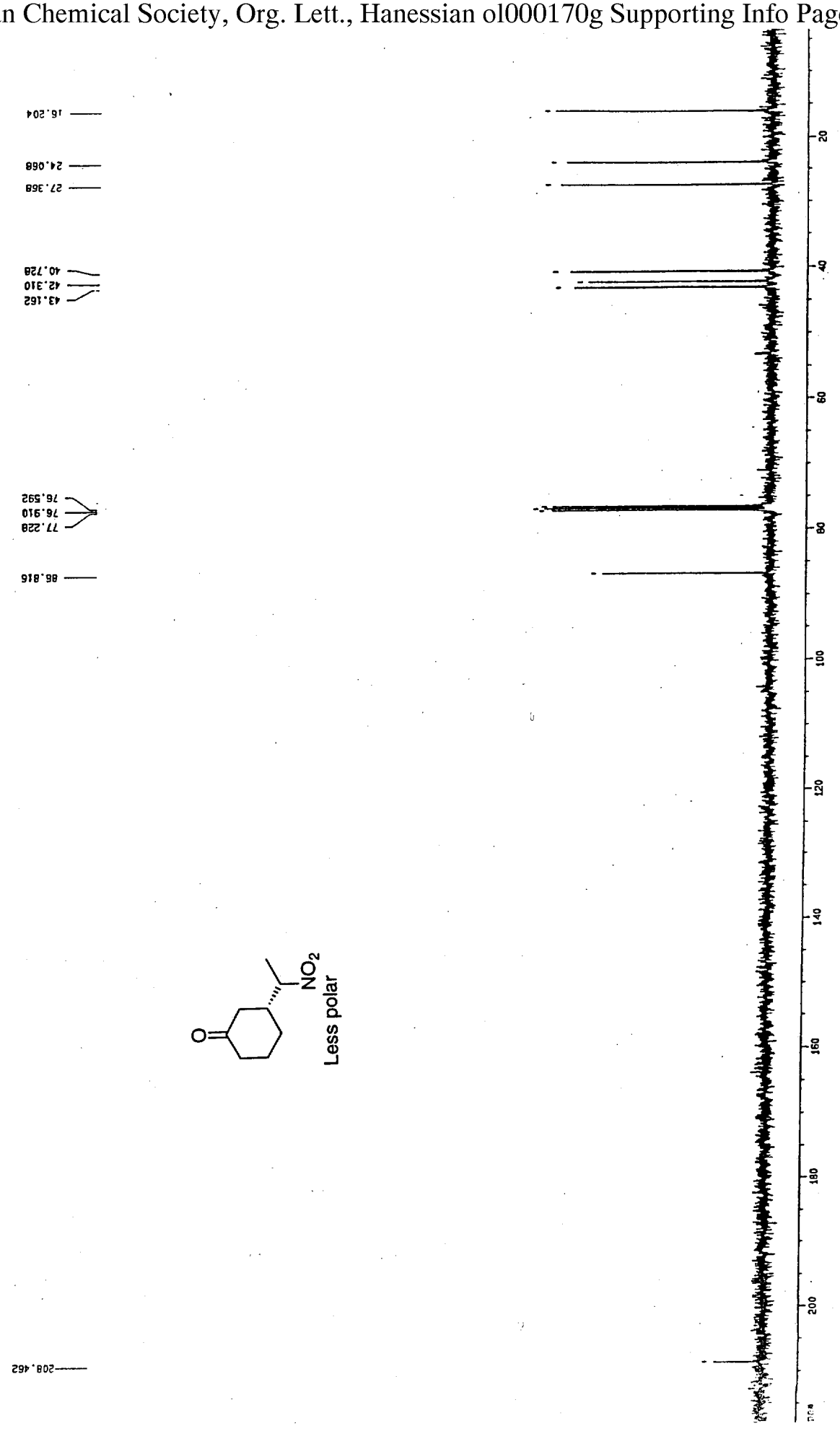
b

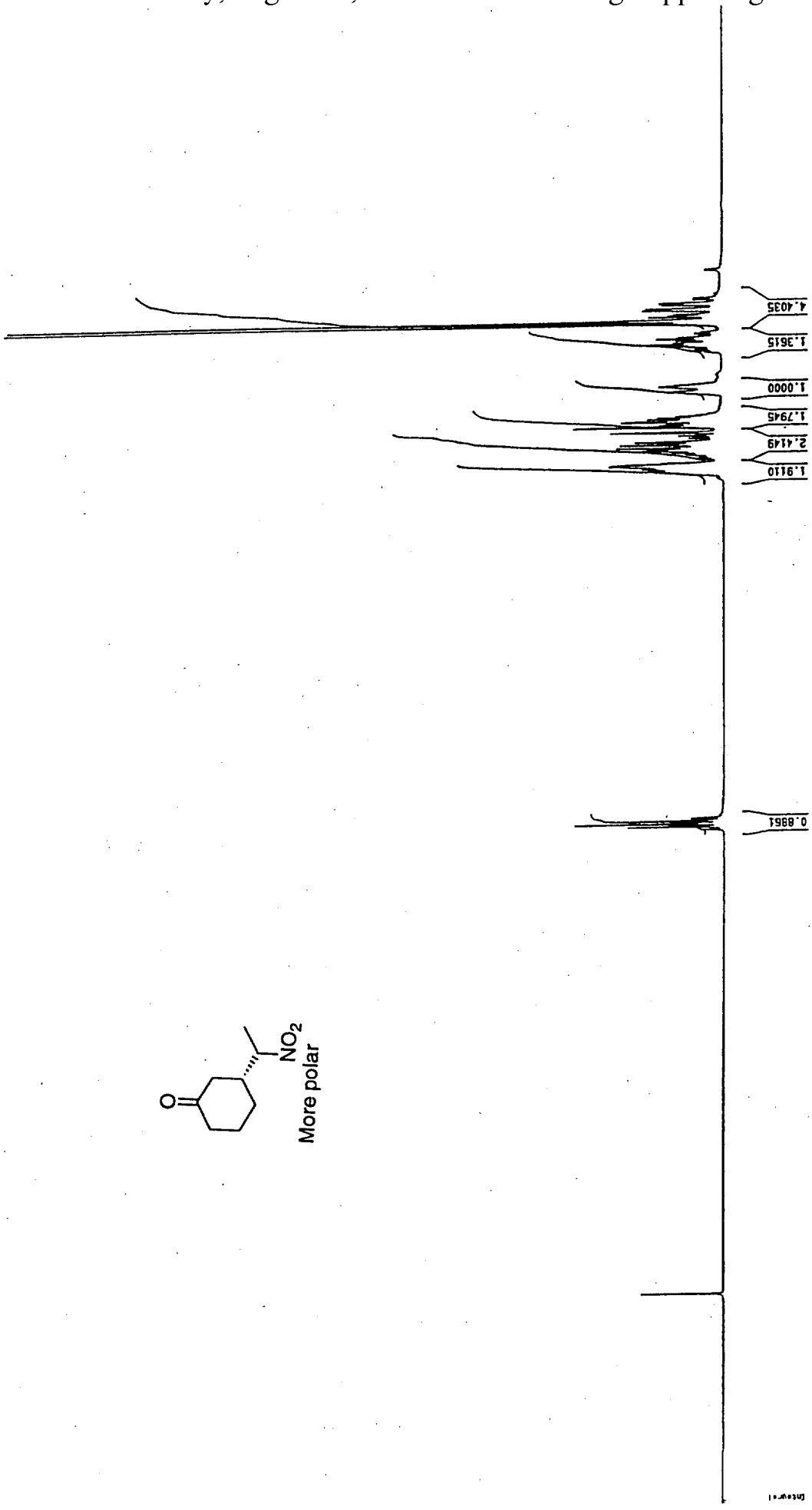





NO2
O
O
13C-NMR, 100 MHz
CDCl3
93% ee
20
30
40
50
60
70
80
90
100
110
ppm

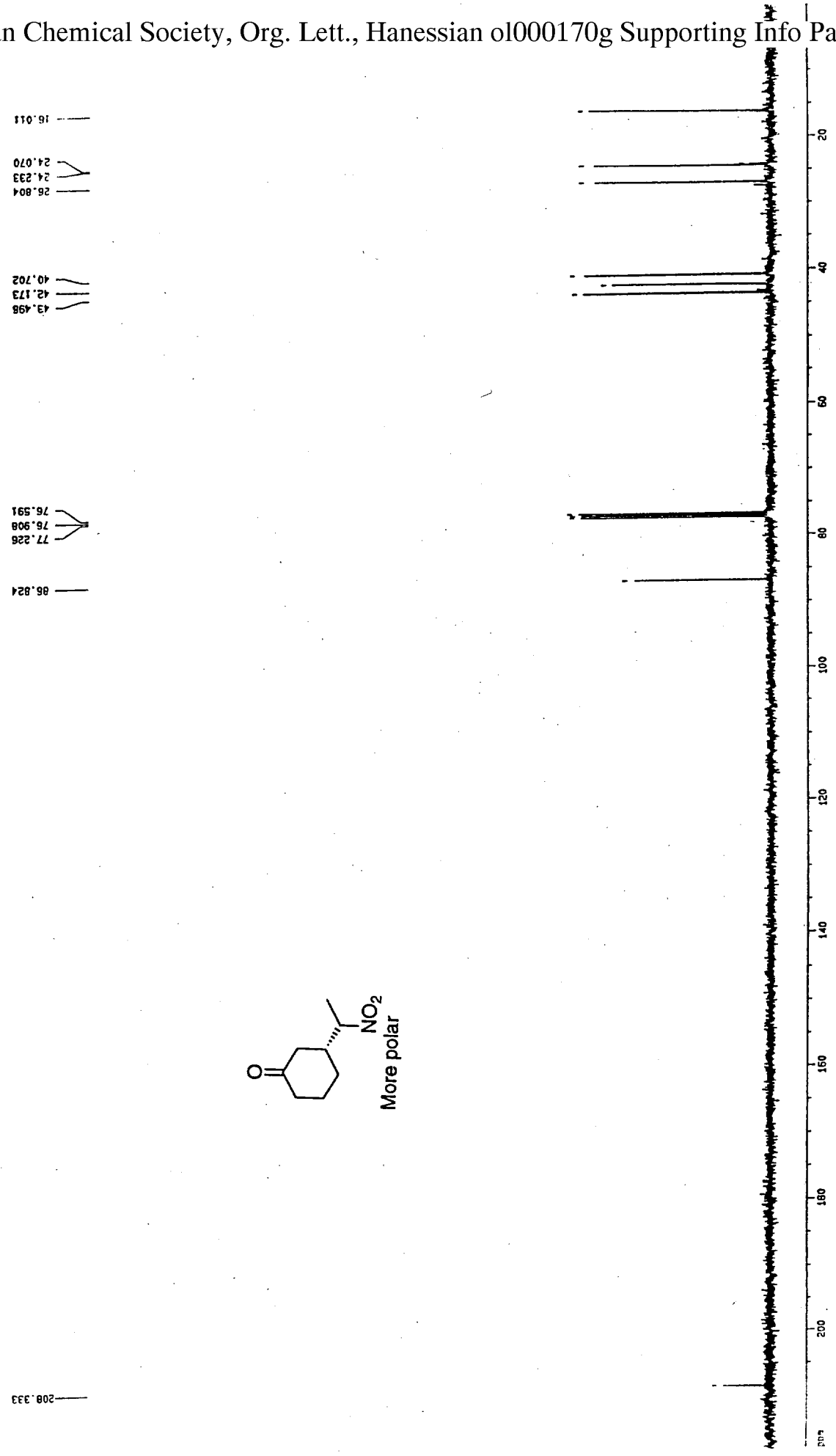

0.9319
9.3751
1.6736
1.0000
2.0130
2.1106
2.0393
0.9155
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
O
NO2
Less polar

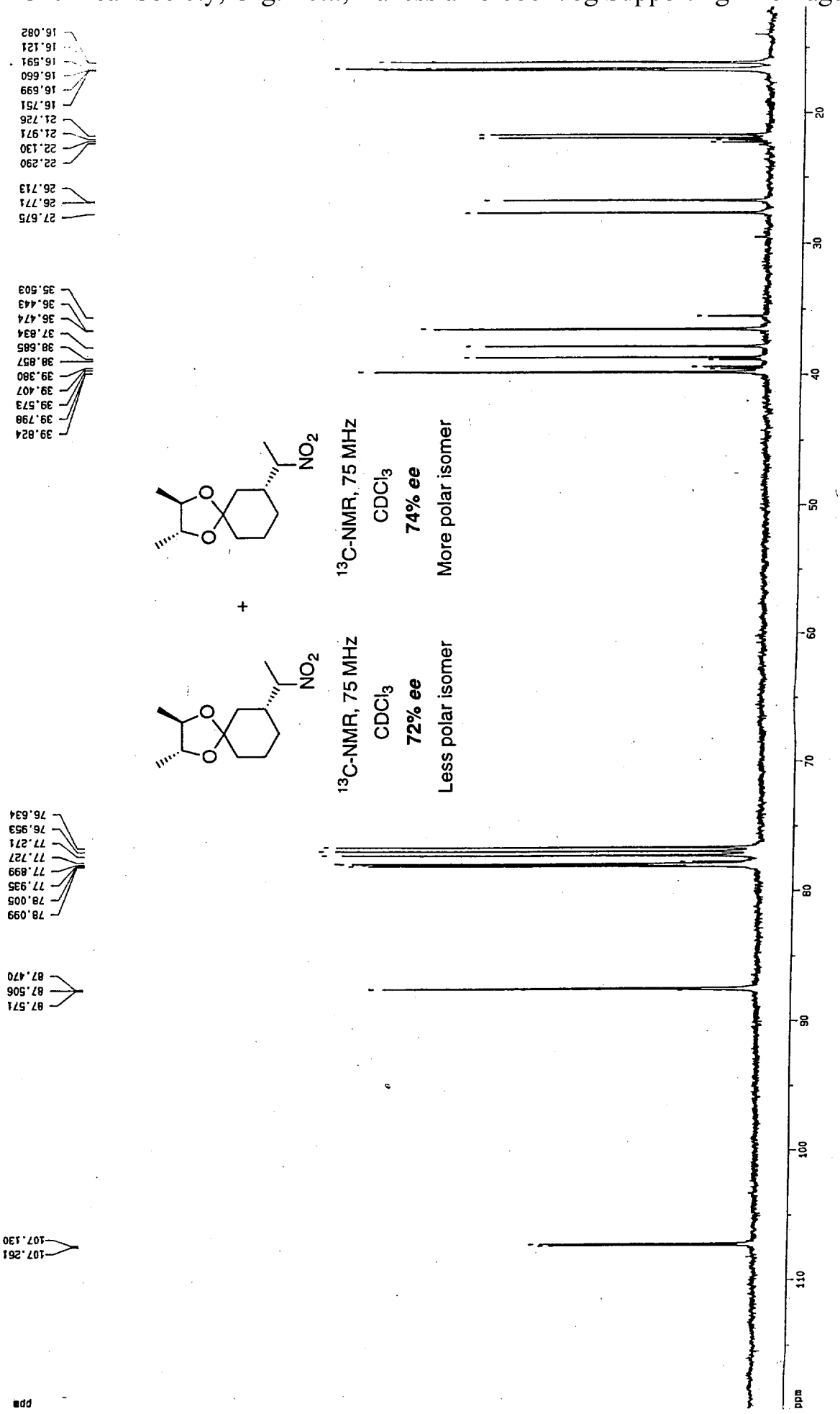

16.204
24.068
27.368
40.728
42.310
43.162
76.592
76.910
77.228
86.816
208.462
ppm
20
40
60
80
100
120
140
160
180
200
NO2
O
Less polar

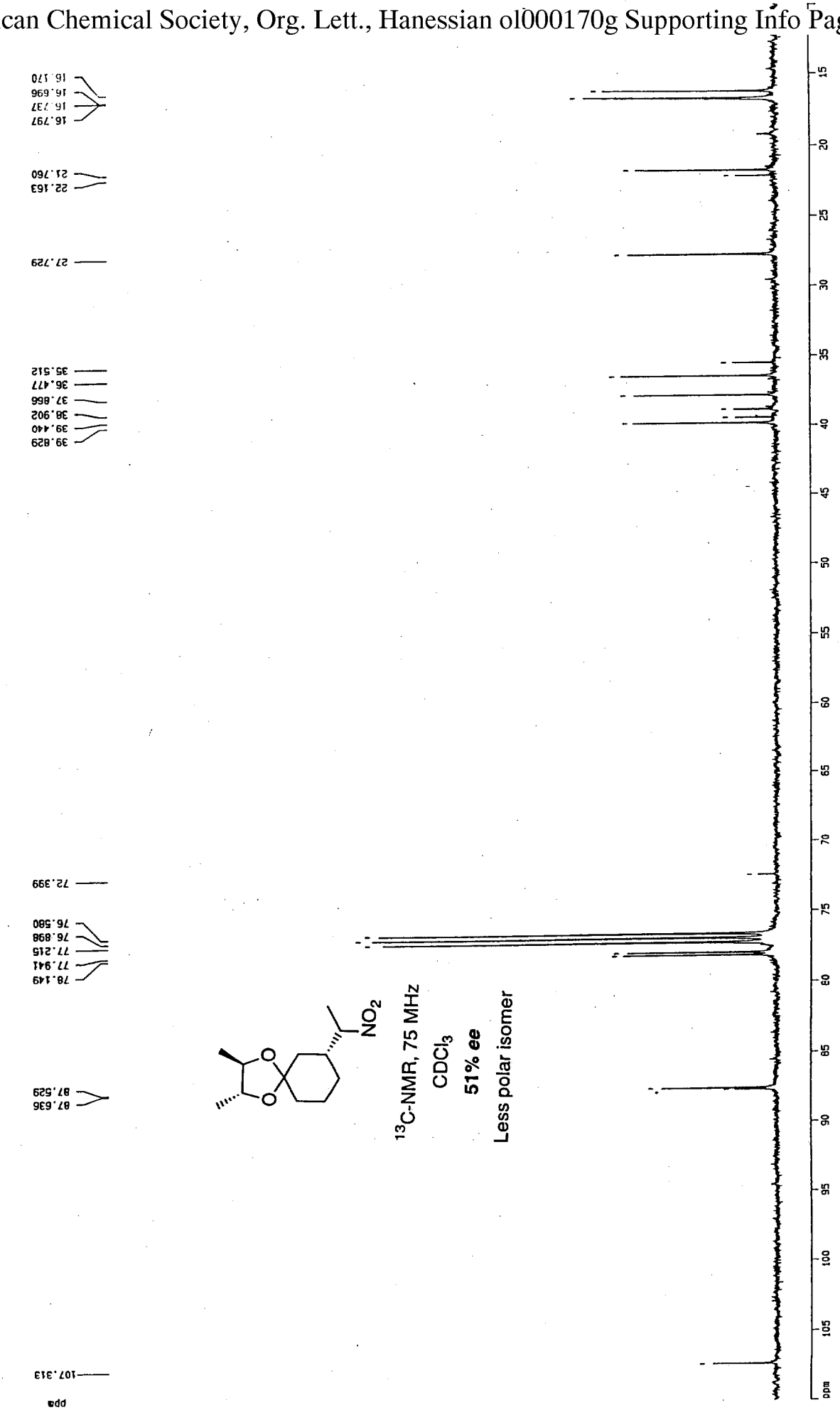

4.4035
1.3615
1.0000
1.7945
2.4149
1.9110
0.8861
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
ppm

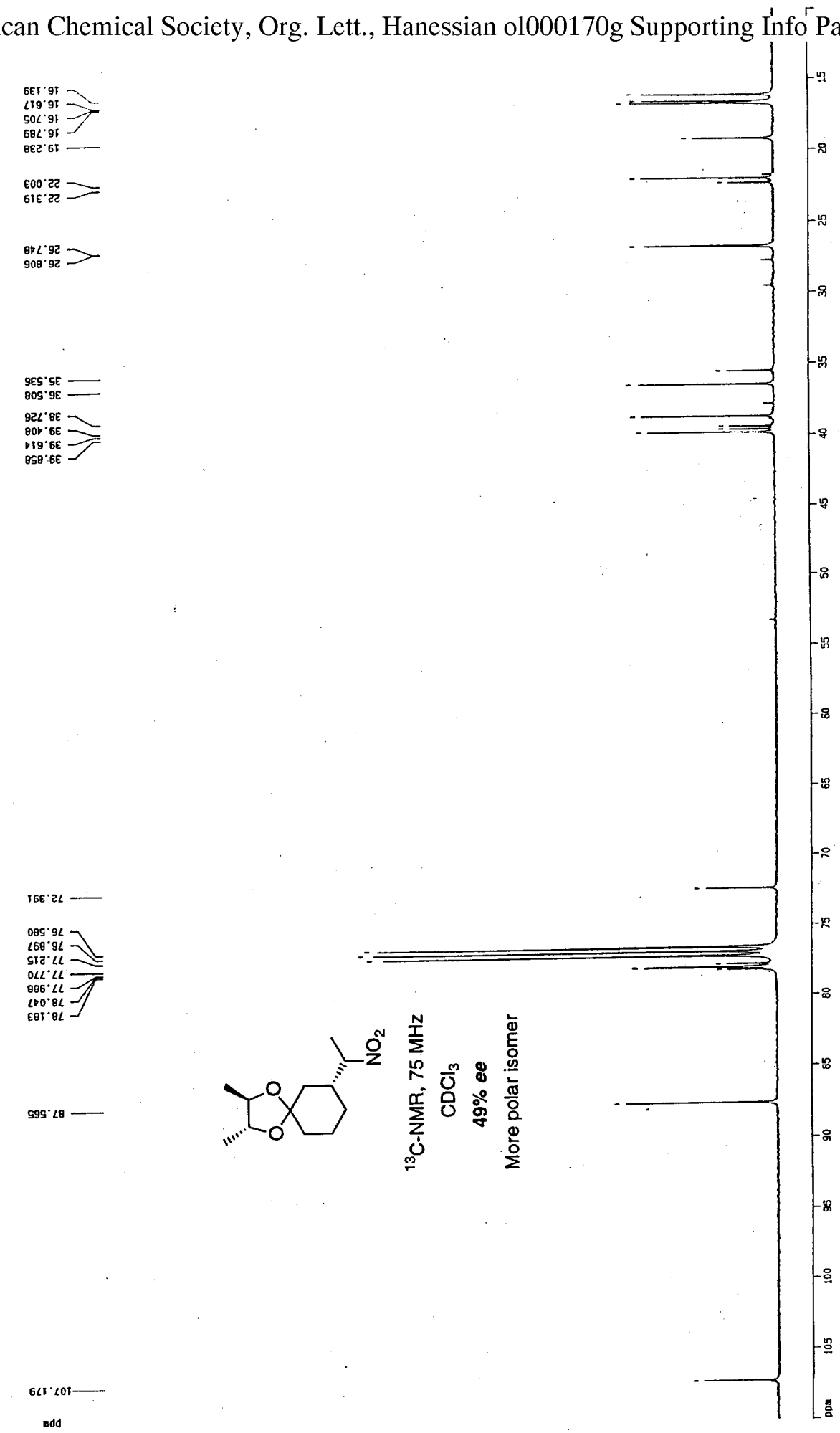
O
NO2

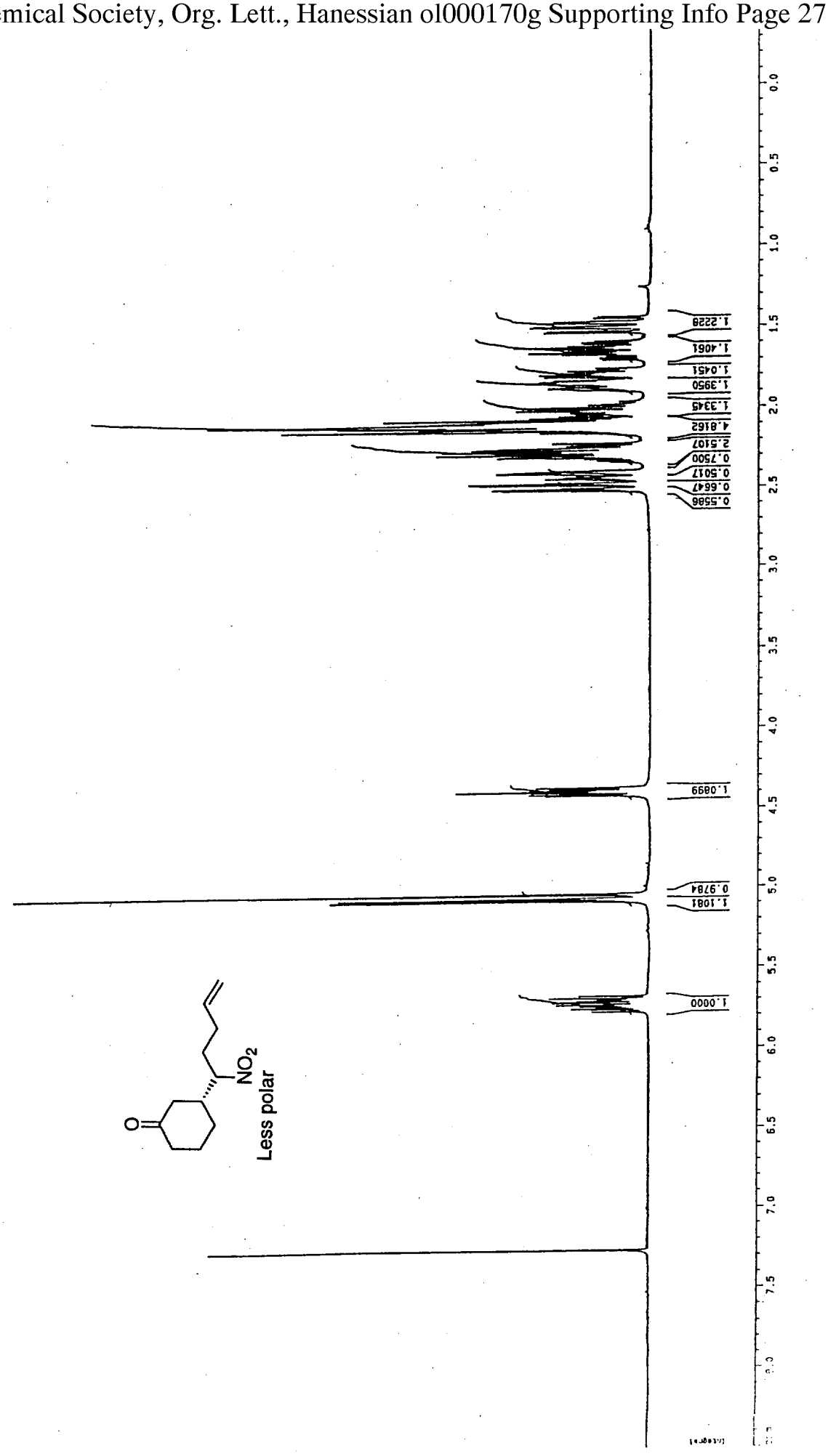
More polar

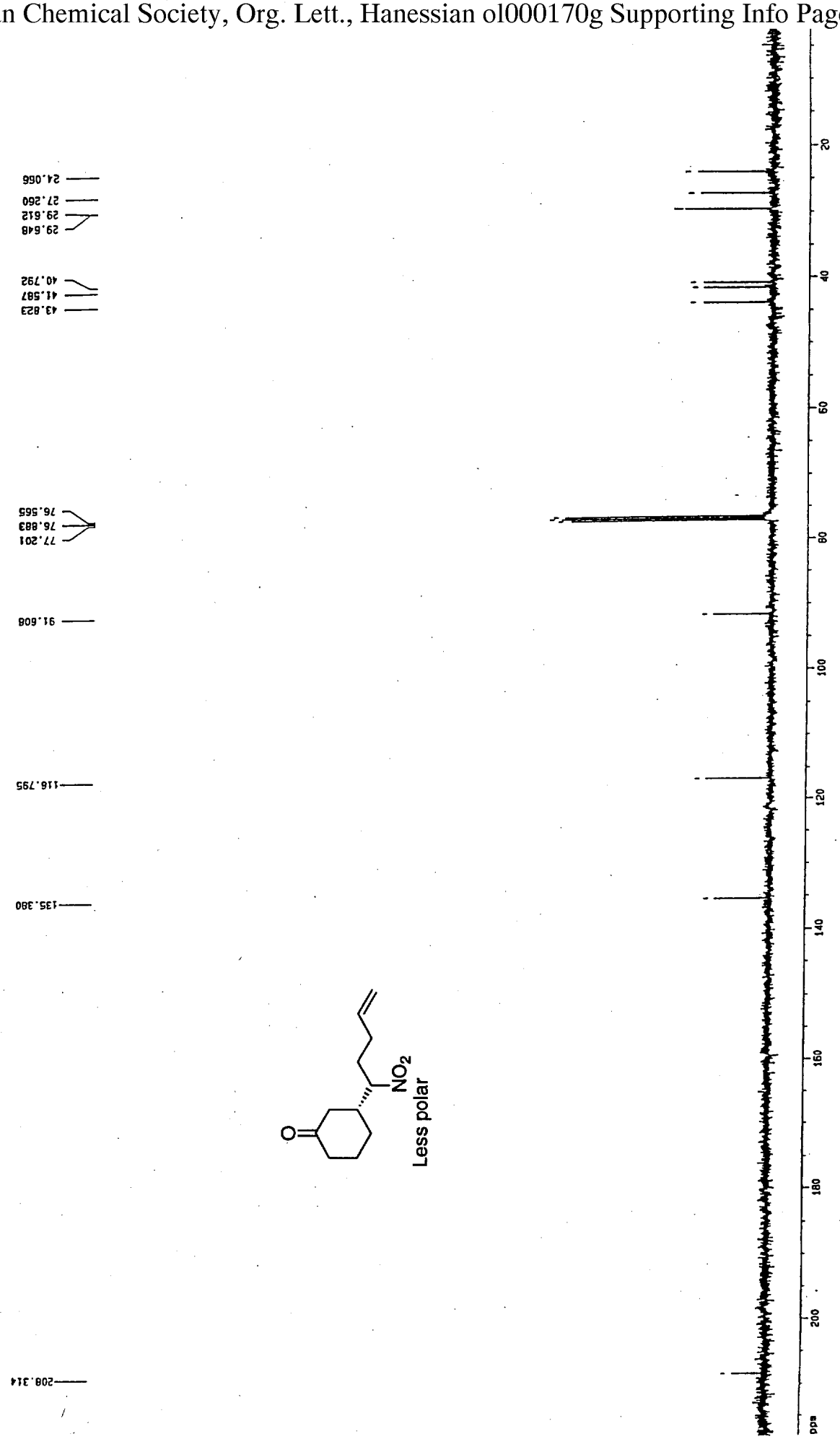


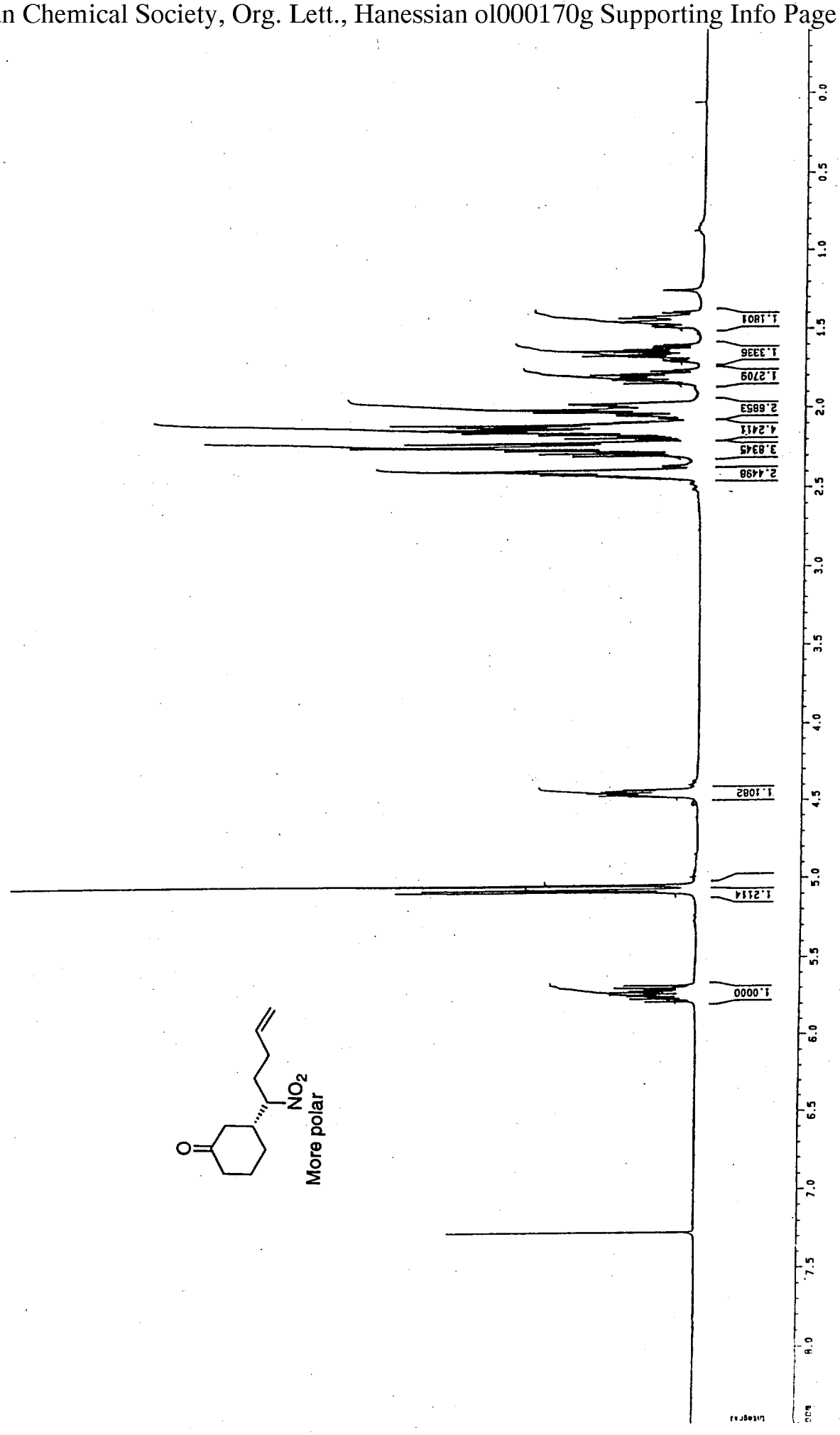


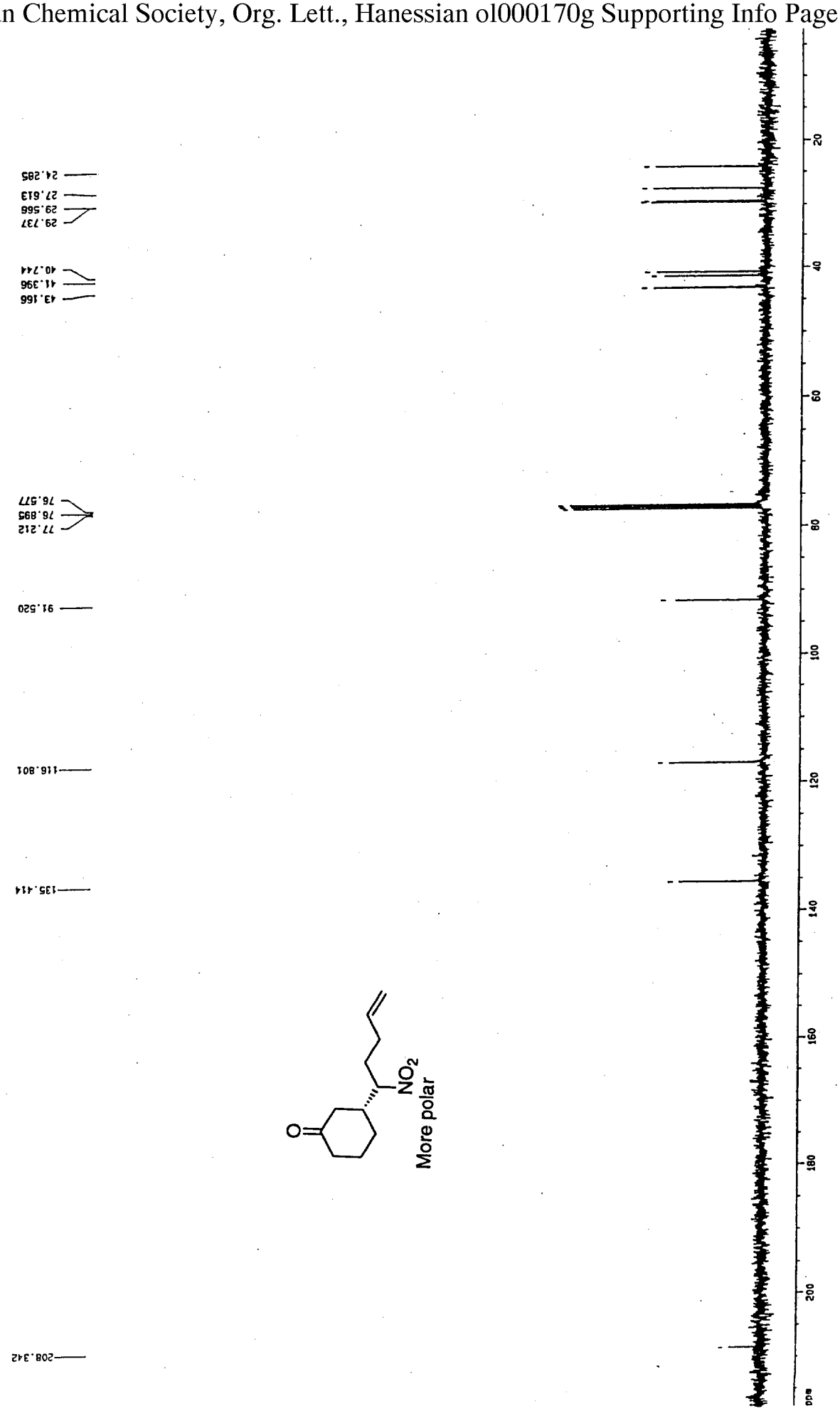


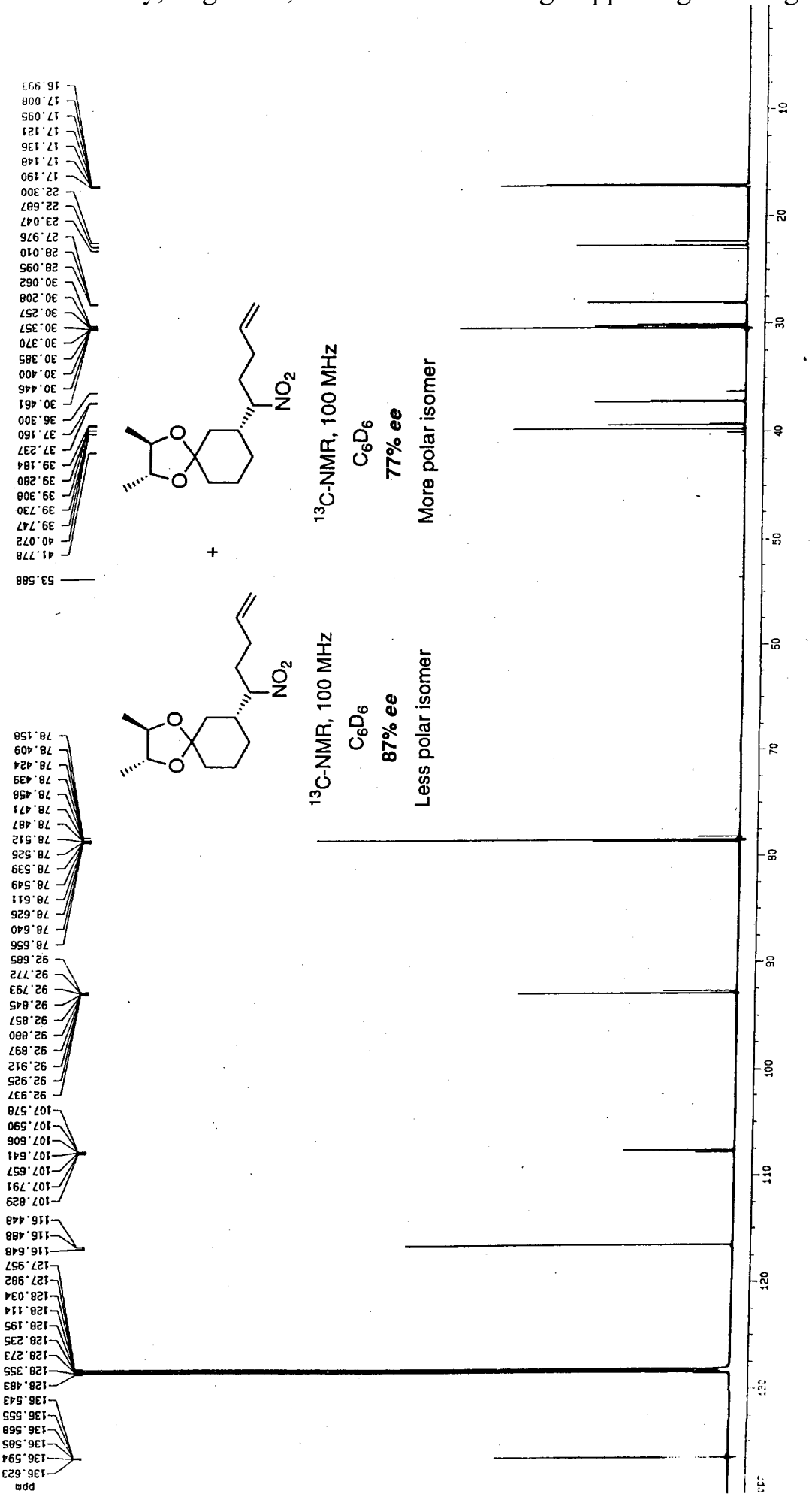


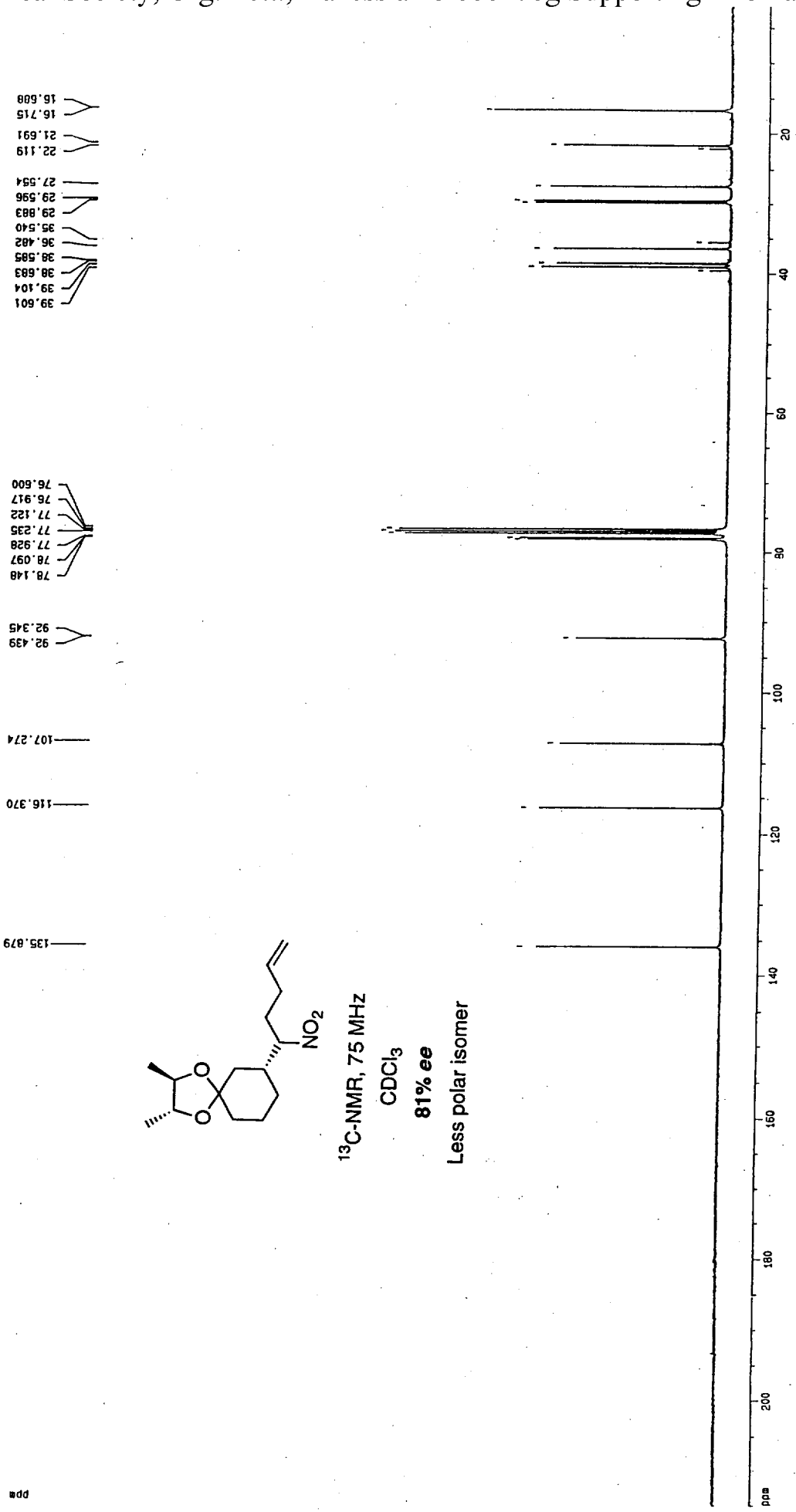

1.2228
1.4061
1.0451
1.3950
1.3345
4.8162
2.5107
0.7500
0.5017
0.6647
0.5586
1.0899
0.9784
1.1081
1.0000
O
NO2
Less polar

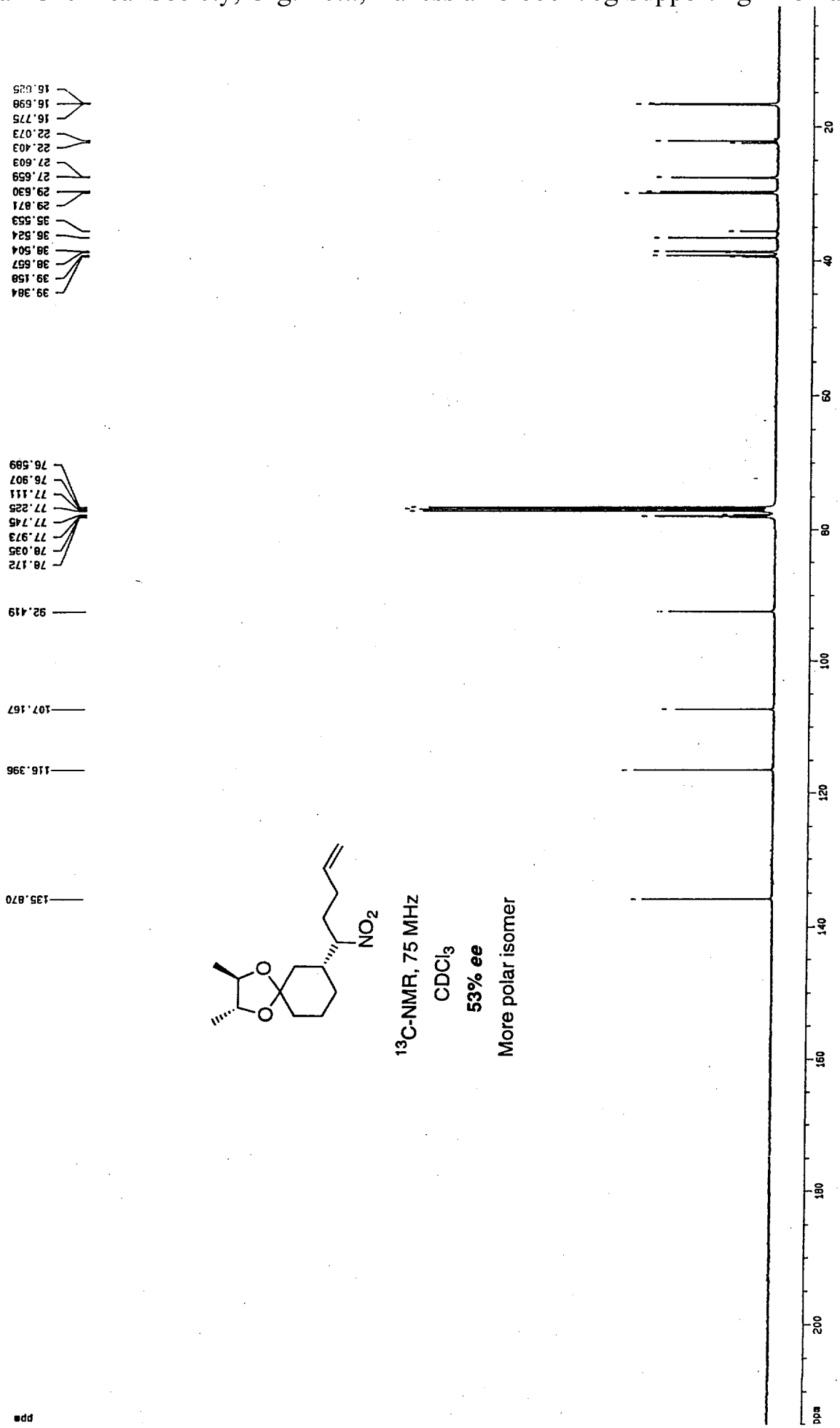

24.056
27.260
29.612
29.648
40.792
41.587
43.823
76.565
76.883
77.201
91.608
116.795
135.390
208.314
ppm
20
40
60
80
100
120
140
160
180
200
ppm
O
NO2
Less polar

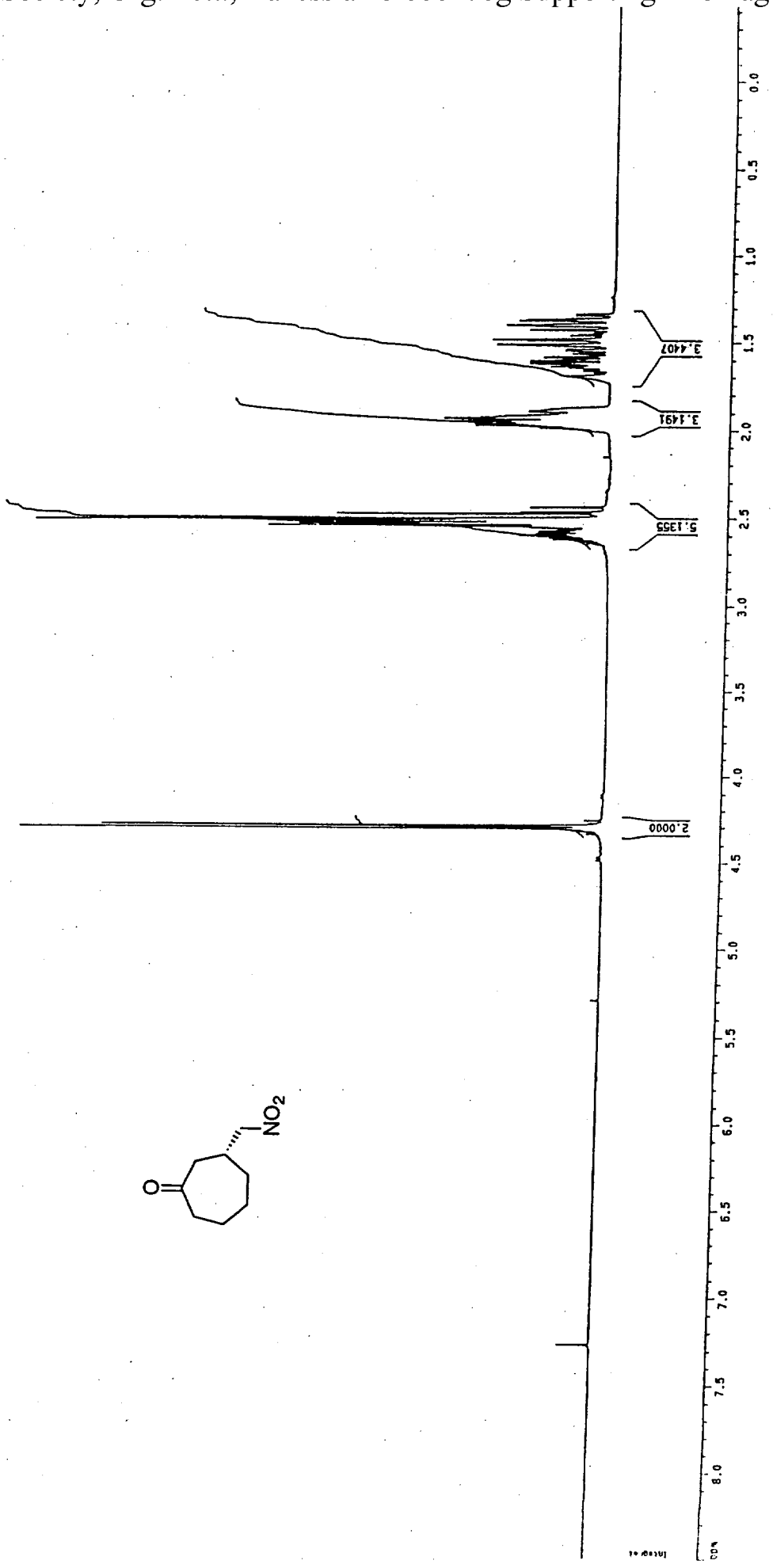

1.1808
1.3338
1.2709
2.6853
4.2411
3.8345
2.4498
1.1082
1.2114
1.0000
NO2
More polar

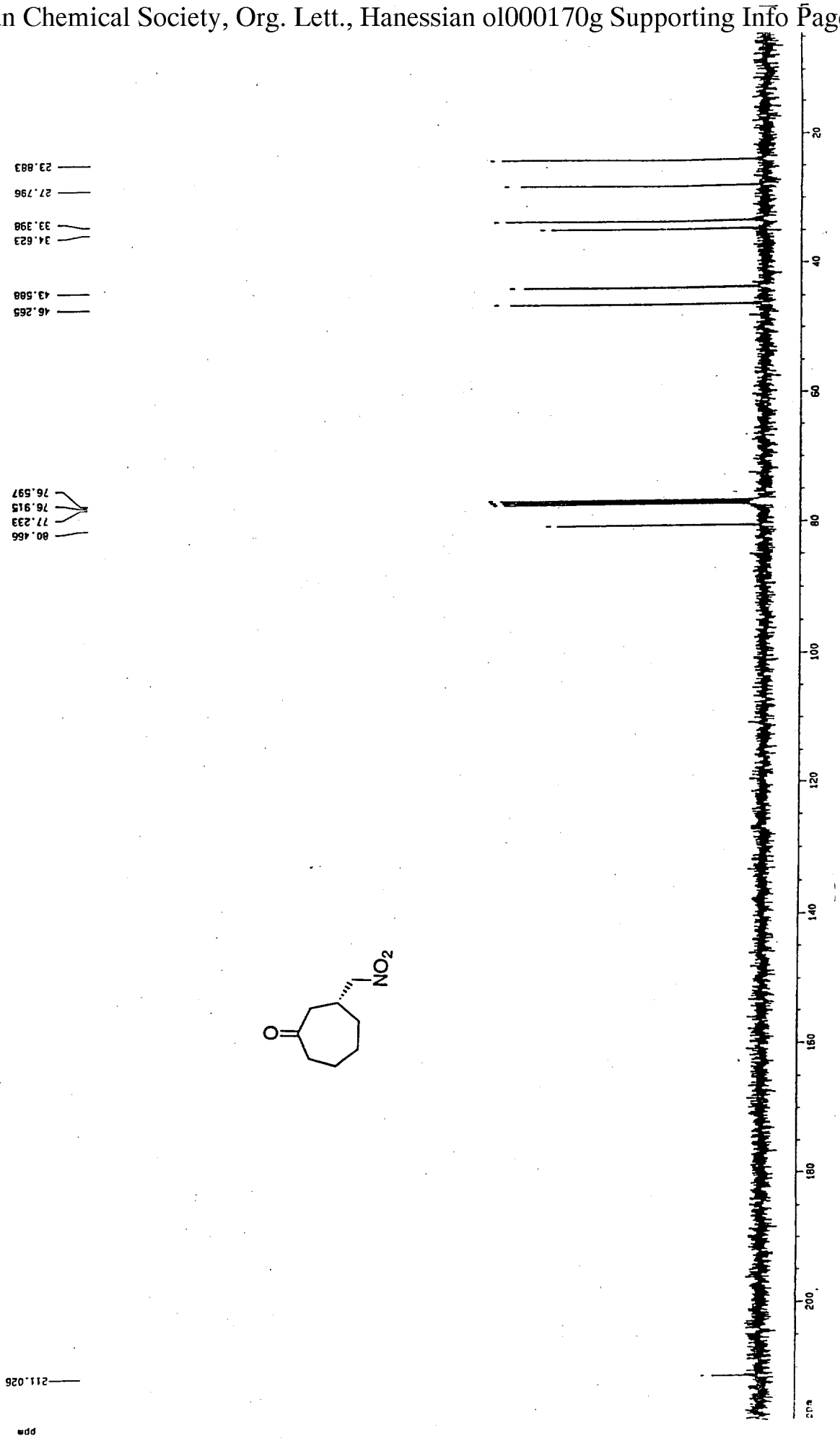

24.285
27.613
29.566
29.737
40.744
41.396
43.166
76.577
76.895
77.212
91.520
116.801
135.414
208.342
ppm
20
40
60
80
100
120
140
160
180
200
ppm
NO_2
O
More polar

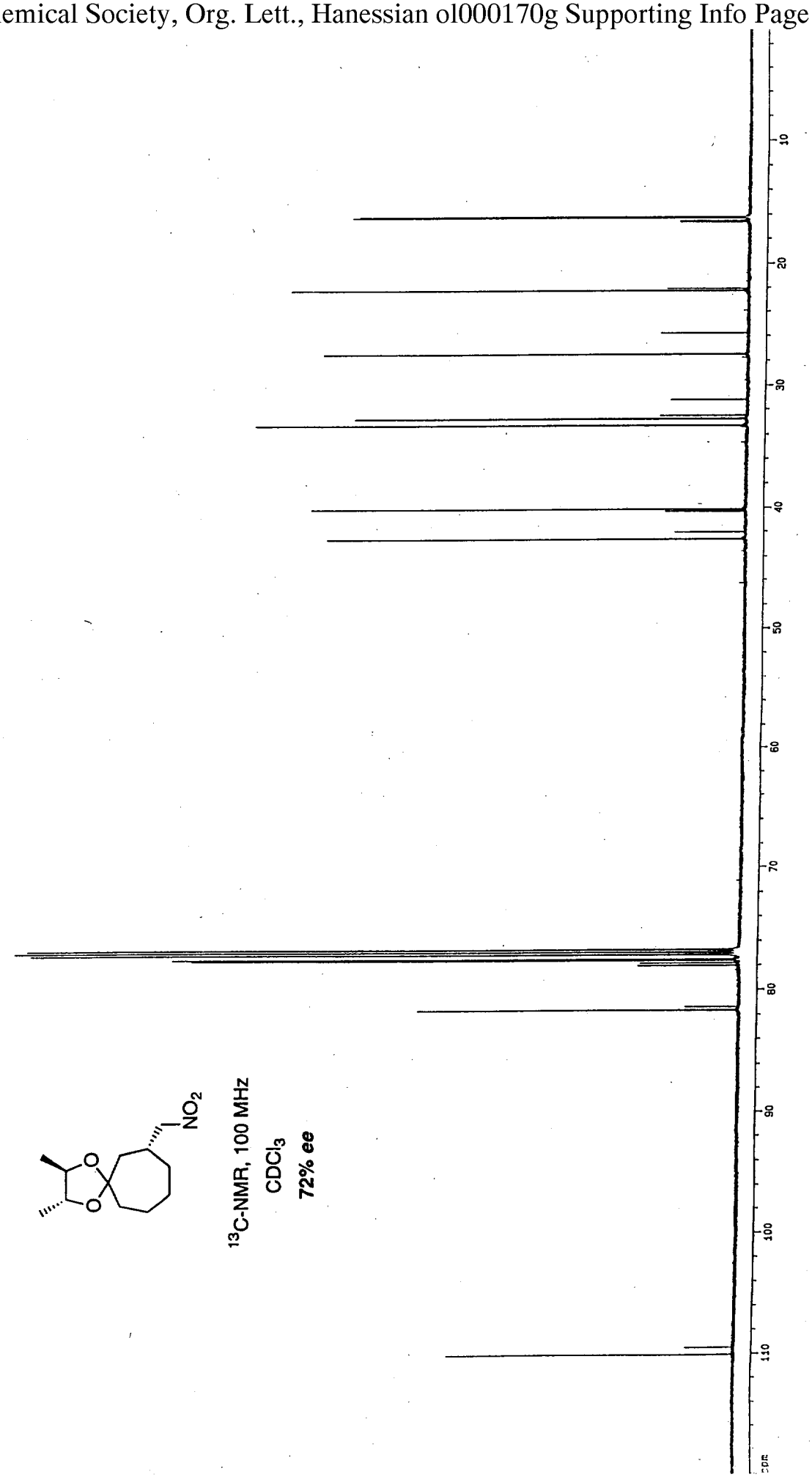

^{13}C-NMR, 100 MHz
C_6D_6
77% ee
More polar isomer
NO_2
+
^{13}C-NMR, 100 MHz
C_6D_6
87% ee
Less polar isomer
NO_2
ppm

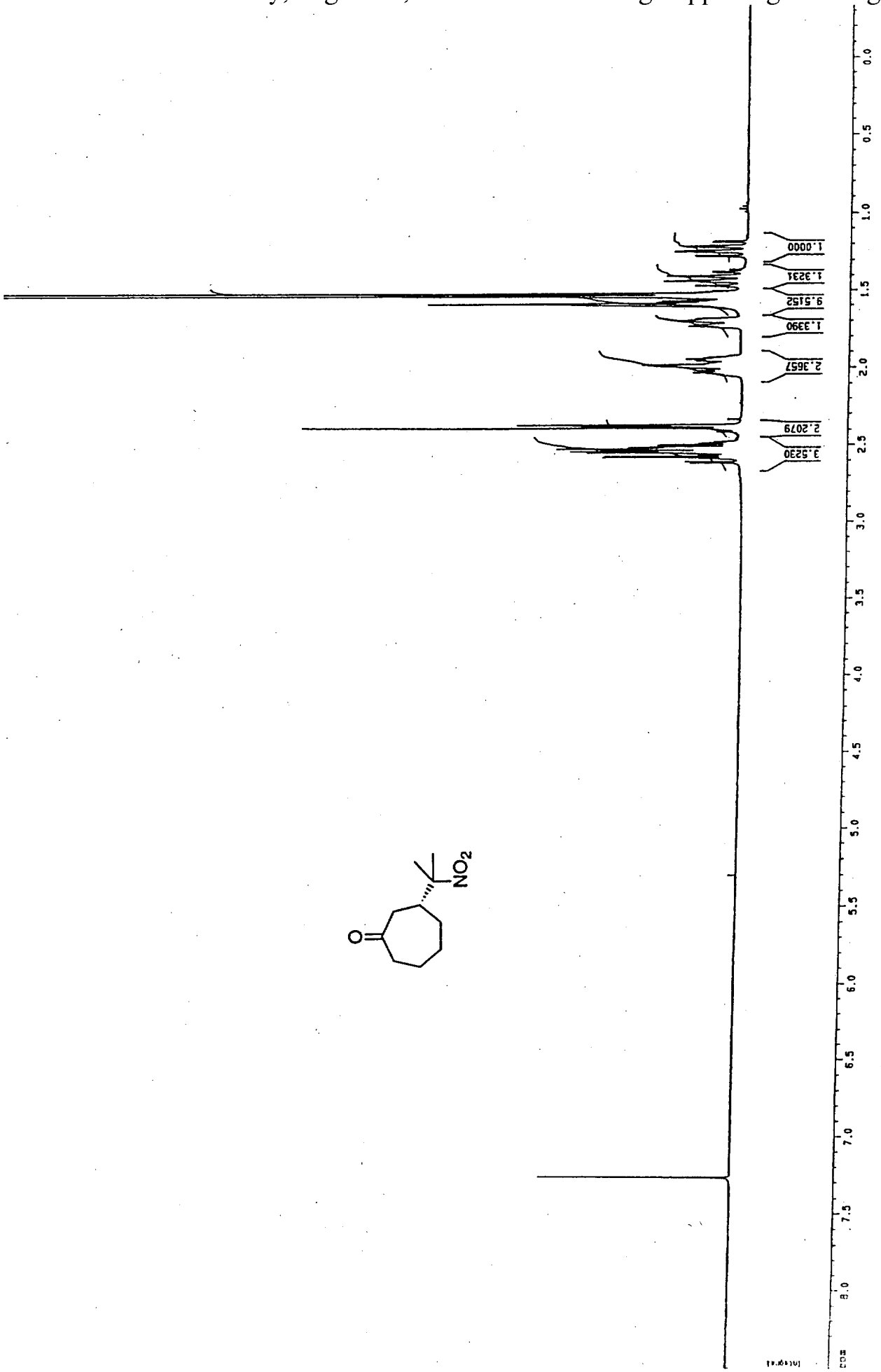

16.608
16.715
21.691
22.119
27.554
29.596
29.883
35.540
36.482
38.585
38.683
39.104
39.601
76.600
76.917
77.122
77.235
77.928
78.097
78.148
92.345
92.439
107.274
116.370
135.879
NO2
13C-NMR, 75 MHz
CDCl3
81% ee
Less polar isomer
ppm

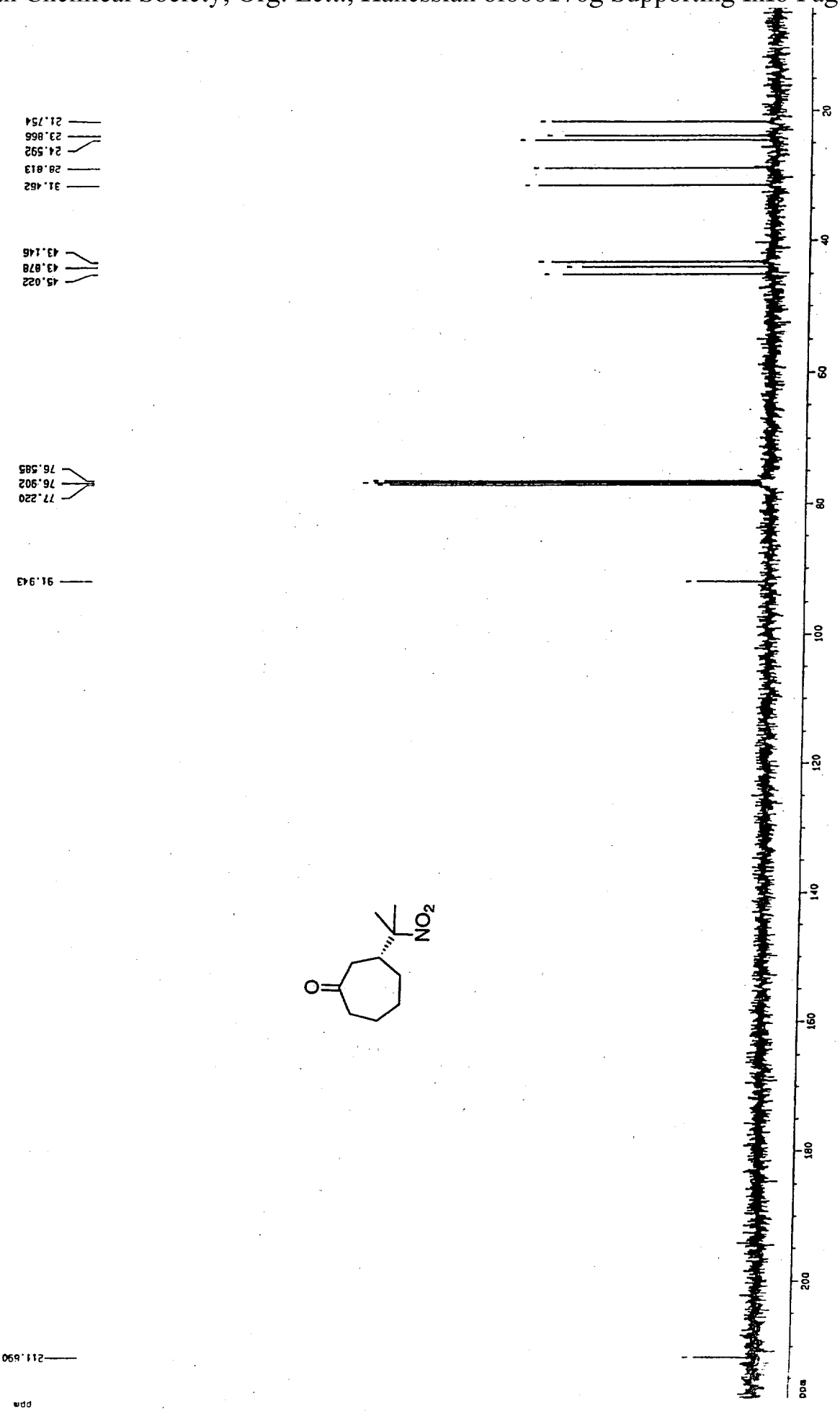


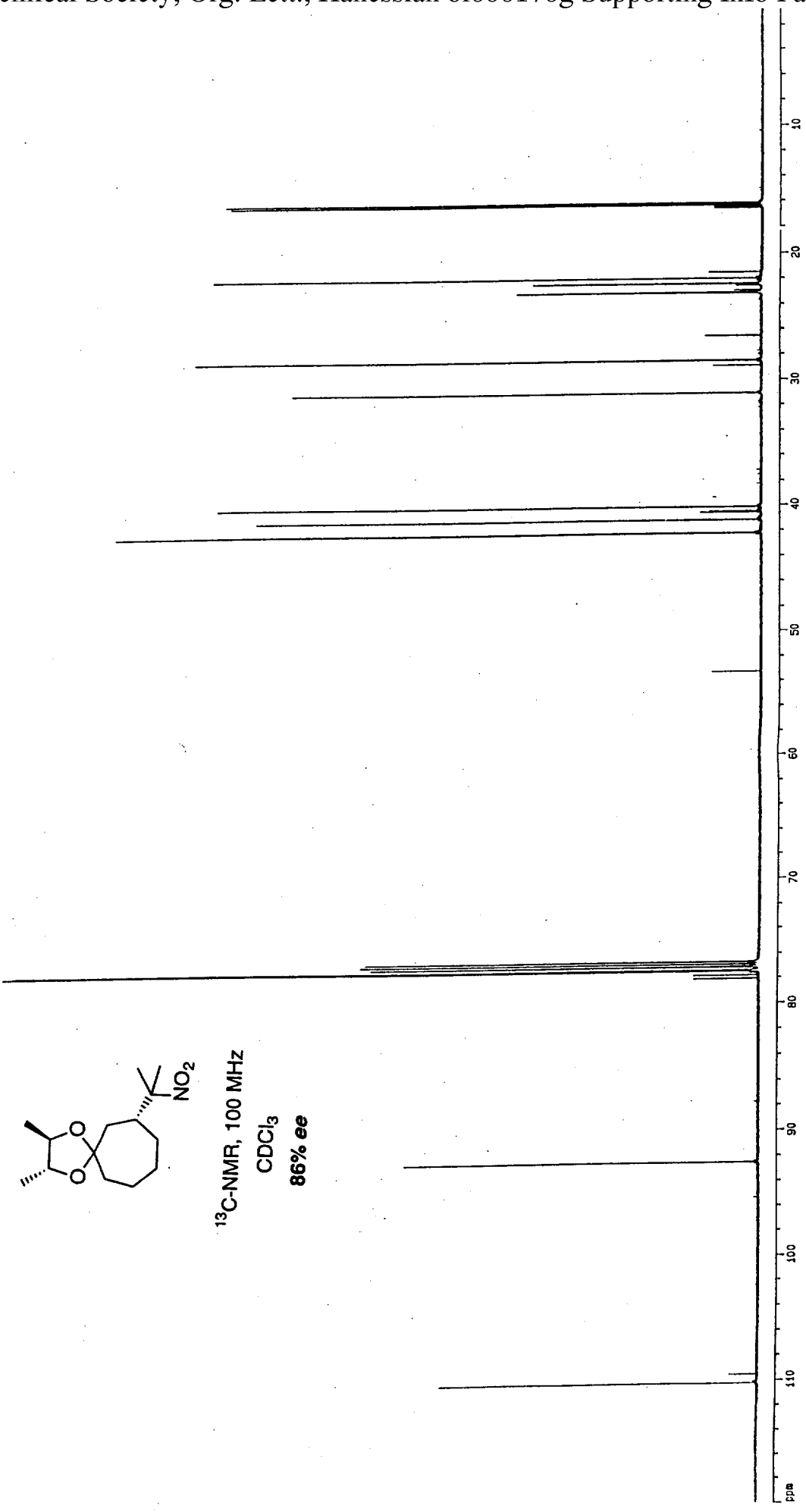

3.4407
3.1491
5.1353
2.0000
NO2
O

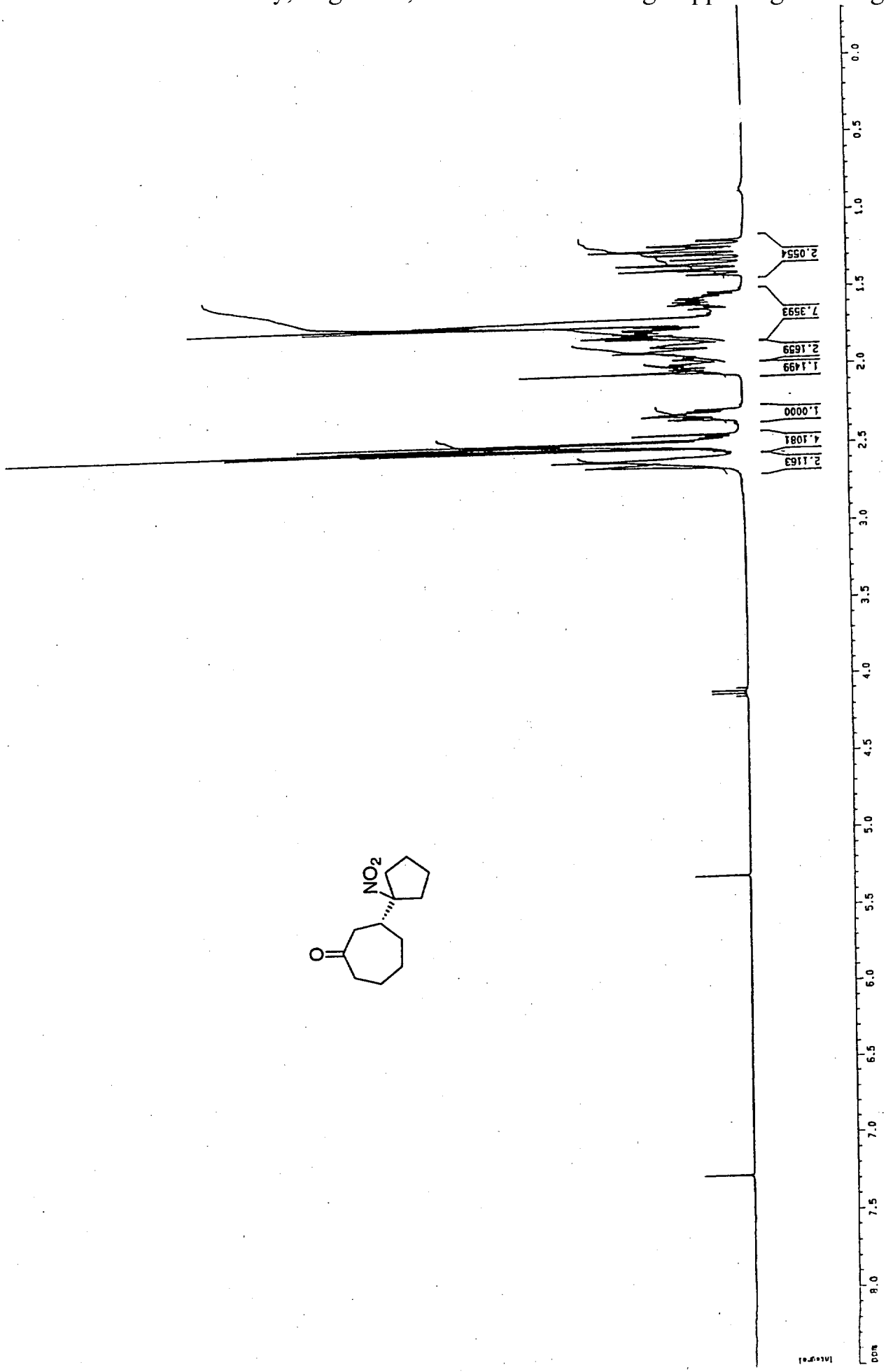





1.0000
1.3231
9.5152
1.3390
2.3657
2.2079
3.5230
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
O
NO2




NO2
13C-NMR, 100 MHz
CDCl3
86% ee
10
20
30
40
50
60
70
80
90
100
110
ppm


2.0554
7.3593
2.1639
1.1499
1.0000
4.1081
2.1163
NO2
O
PPM