

General procedure

(R)-(+)-3-(2-Nitropropane-2-yl) cyclohexanone. A mixture of 2-cyclohexen-1-one (50 μ L, 0.52 mmol), 2-nitropropane (100 μ L, 1.1 mmol), 2,5-dimethylpiperazine (60 mg, 0.53 mmol) and a catalytic amount of L-Proline (0.22 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%). $[\alpha]_{\text{D}} +23.3$ (c 1.0, CHCl_3 , 93% *ee*). Lit.⁹ $[\alpha]_{\text{D}} +15.0$ (c 1.0, CHCl_3 , 59% *ee*); $^1\text{H-NMR}$ (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),; $^{13}\text{C-NMR}$ (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 $\text{C}_9\text{H}_{16}\text{NO}_3^+$ ((*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 μ L, 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 $^{13}\text{C-NMR}$ (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 $\text{C}_7\text{H}_{12}\text{NO}_3^+$ ((*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*); ^1H -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 $\text{C}_{12}\text{H}_{20}\text{NO}_3^+$ ((*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 $\text{C}_8\text{H}_{14}\text{NO}_3^+$ ((*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 $\text{C}_8\text{H}_{14}\text{NO}_3^+$ ((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 $\text{C}_{11}\text{H}_{18}\text{NO}_3^+$ ((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 $\text{C}_{11}\text{H}_{18}\text{NO}_3^+$ ((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 $\text{C}_8\text{H}_{14}\text{NO}_3^+$ ((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 $\text{C}_{10}\text{H}_{18}\text{NO}_3^+$ ((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 $\text{C}_{12}\text{H}_{20}\text{NO}_3^+$ ((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 $\text{C}_{13}\text{H}_{22}\text{NO}_3^+$ ((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 $\text{C}_6\text{H}_{10}\text{NO}_3^+$ ((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 $\text{C}_8\text{H}_{14}\text{NO}_3^+$ ((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 $\text{C}_{10}\text{H}_{16}\text{NO}_3^+$ ((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 $\text{C}_{11}\text{H}_{18}\text{NO}_3^+$ (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 $\text{C}_7\text{H}_{11}\text{NO}_3^+$ (M⁺) 157.0739, found 157.0738; HRMS (FAB) calcd. for $\text{C}_7\text{H}_{12}\text{NO}_3^+$ ((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 $\text{C}_7\text{H}_{12}\text{NO}_3^+$ ((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). $[\alpha]_{\text{D}} +79.5$ (c 0.7, CHCl_3 , 72% *ee*); HRMS (FAB) calcd. for $\text{C}_{10}\text{H}_{16}\text{NO}_3^+$ ((*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.

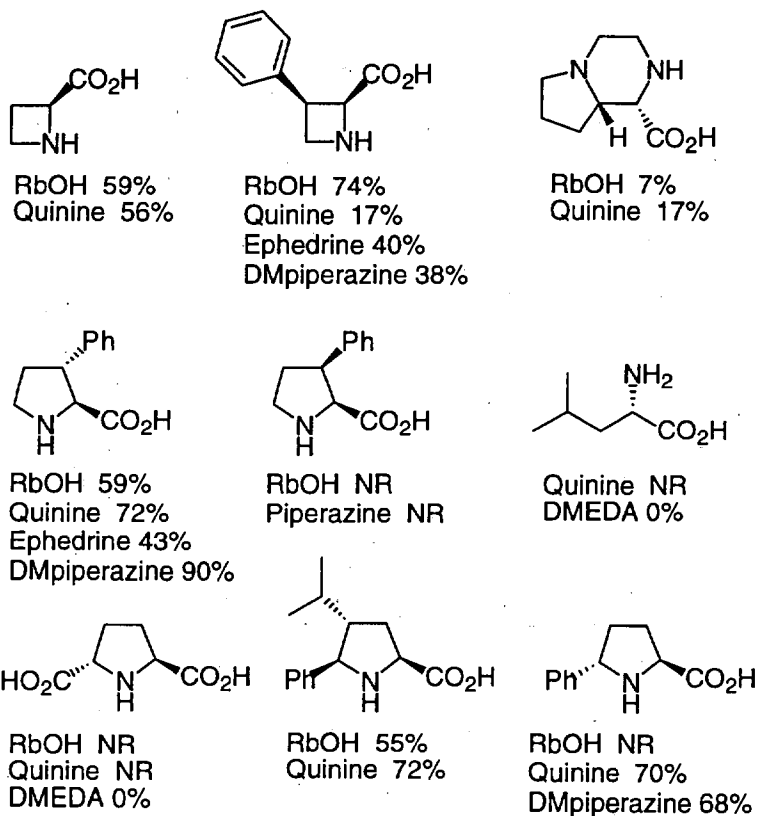
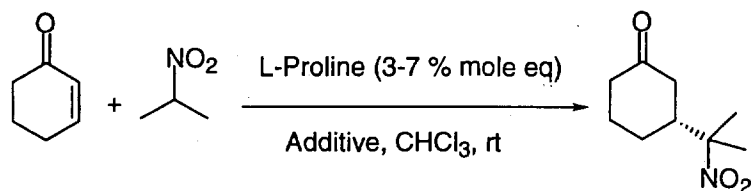
(+)-3-(5-Nitropentene) cyclopentanone. (More polar). $[\alpha]_{\text{D}} +41.8$ (c 0.5, CHCl_3 , 43% *ee*); HRMS (FAB) calcd. for $\text{C}_{10}\text{H}_{16}\text{NO}_3^+$ ((*M*+1) $^+$) 198.1130, found 198.1127; The enantiomeric excess was determined by ^{13}C -NMR (75 MHz, CDCl_3) of the ketal with (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. $[\alpha]_{\text{D}} +29.4$ (c 1.7, CHCl_3 , 61 % *ee*)
HRMS (FAB) calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_3^+$ ((*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.

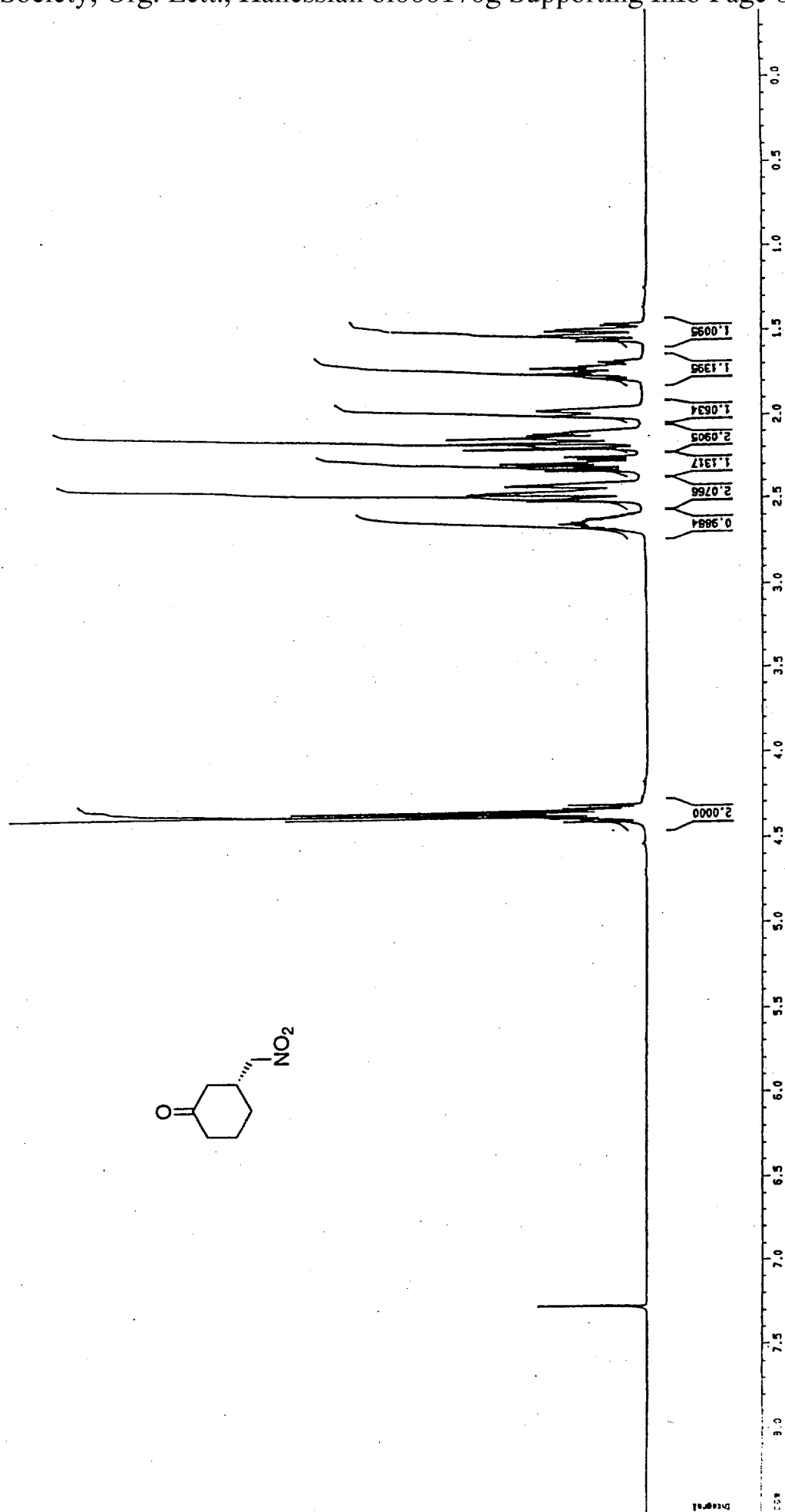
(+)-5-Methyl-5-nitro-4-pentyl-2-hexanone. $[\alpha]_{\text{D}} +15.1$ (c 1.0, CHCl_3 , 68 % *ee*). Lit.⁹
 $[\alpha]_{\text{D}} +13.2$ (c 1.0, CHCl_3 , 60% *ee*)

Comparison of highest *ee* values with different amino acids

Chart 1.^a



a. Bases: RbOH (as proline salt); Quinine; d-Ephedrine; DMEDA (N,N'-dimethylethylene diamine); piperazine; DMpiperazine (*trans*-2,5-dimethylpiperazine);

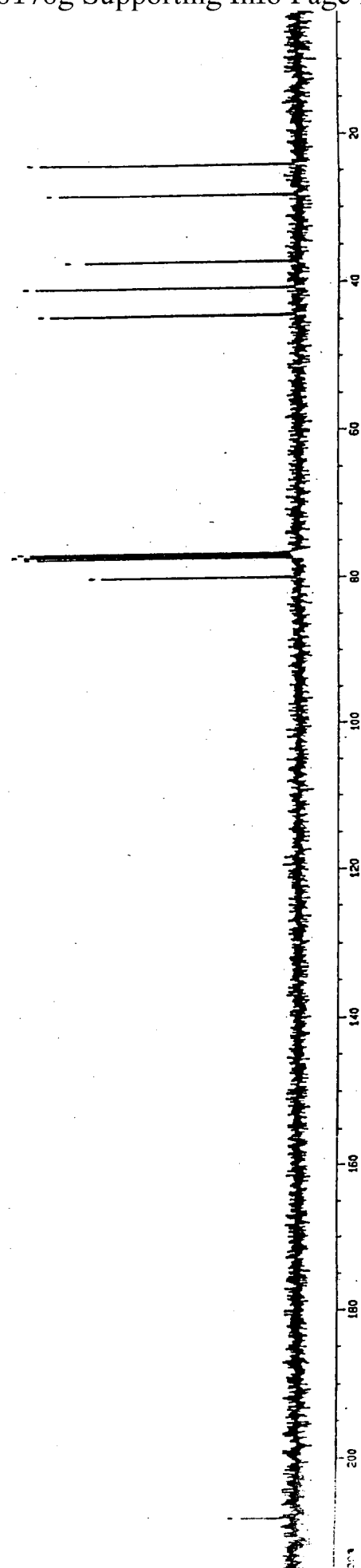
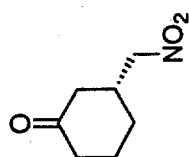


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— 28.095
— 37.061
— 40.717
— 44.317

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76.930
77.248
79.914

— 208.047

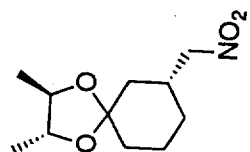
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16.778
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80.821

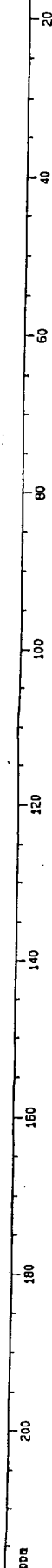
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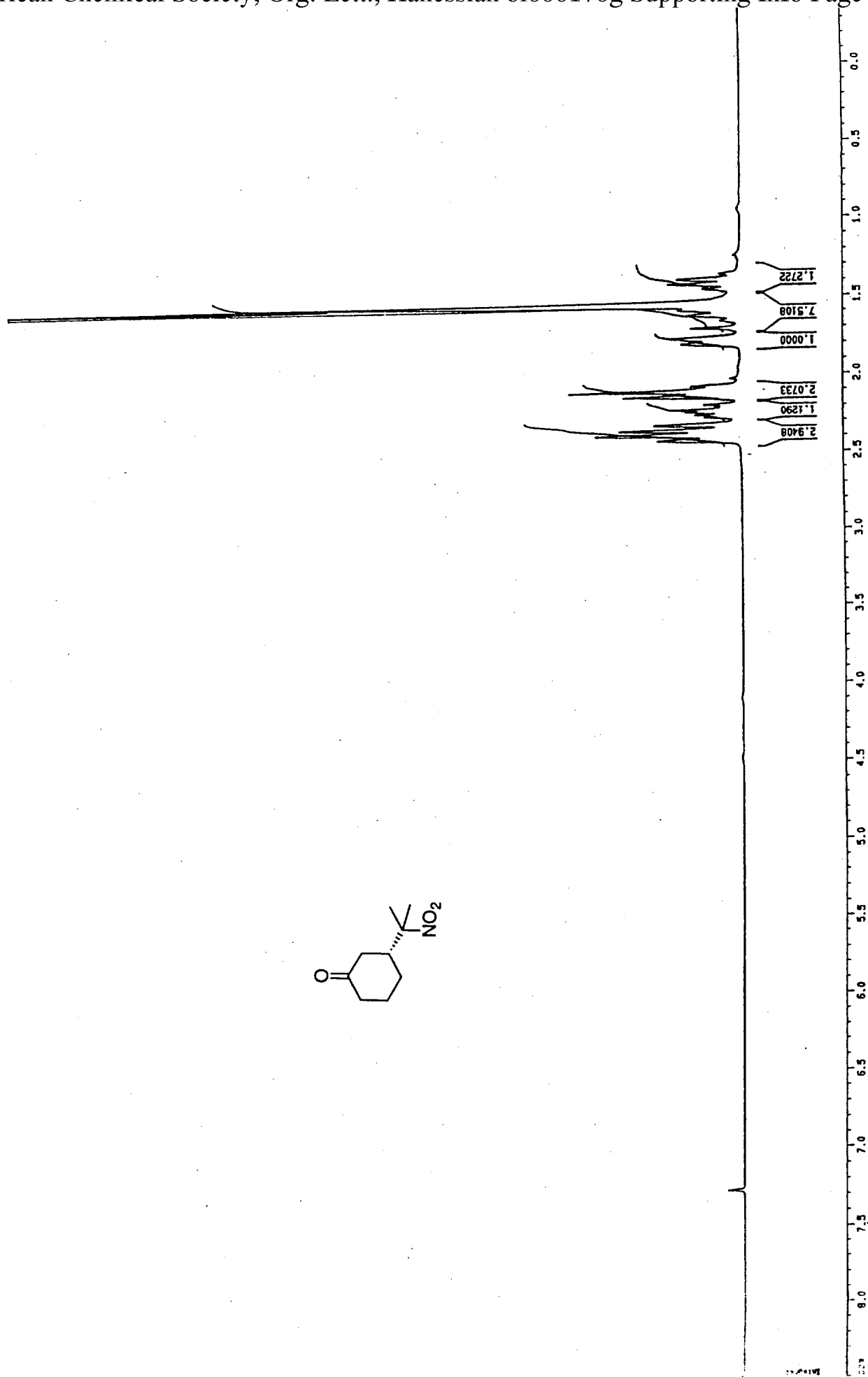


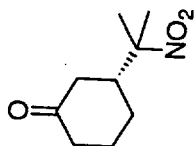
¹³C-NMR, 75 MHz

CDCl₃

71% ee

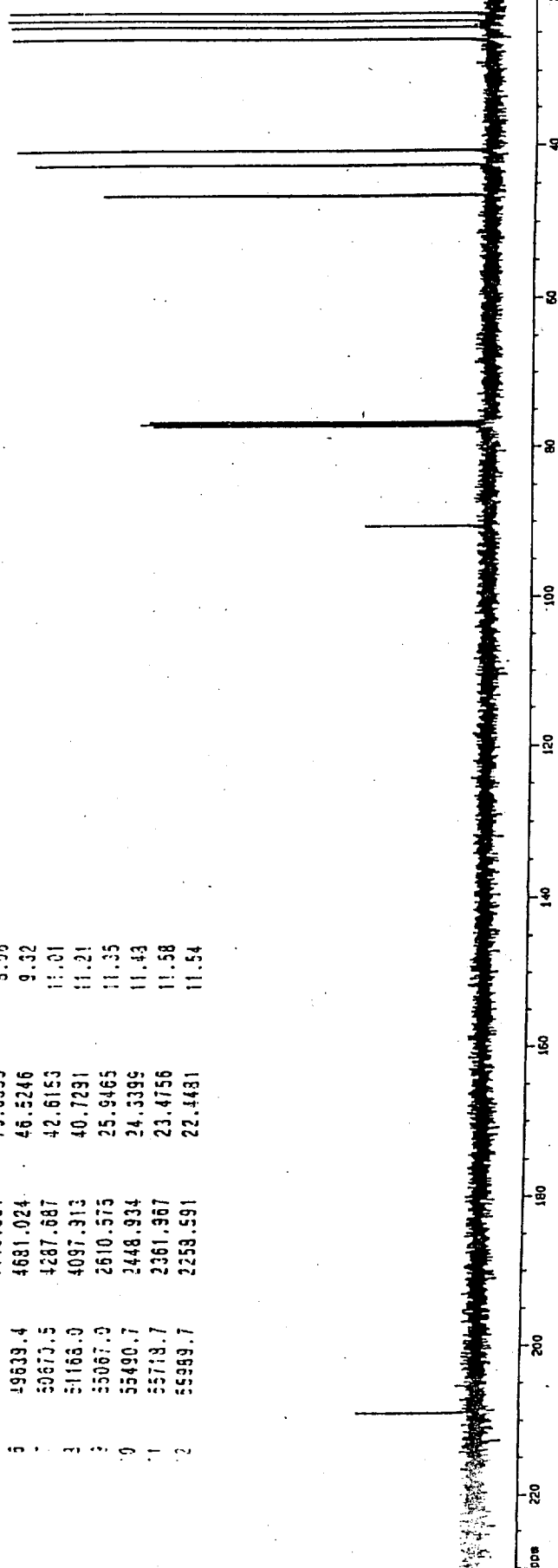


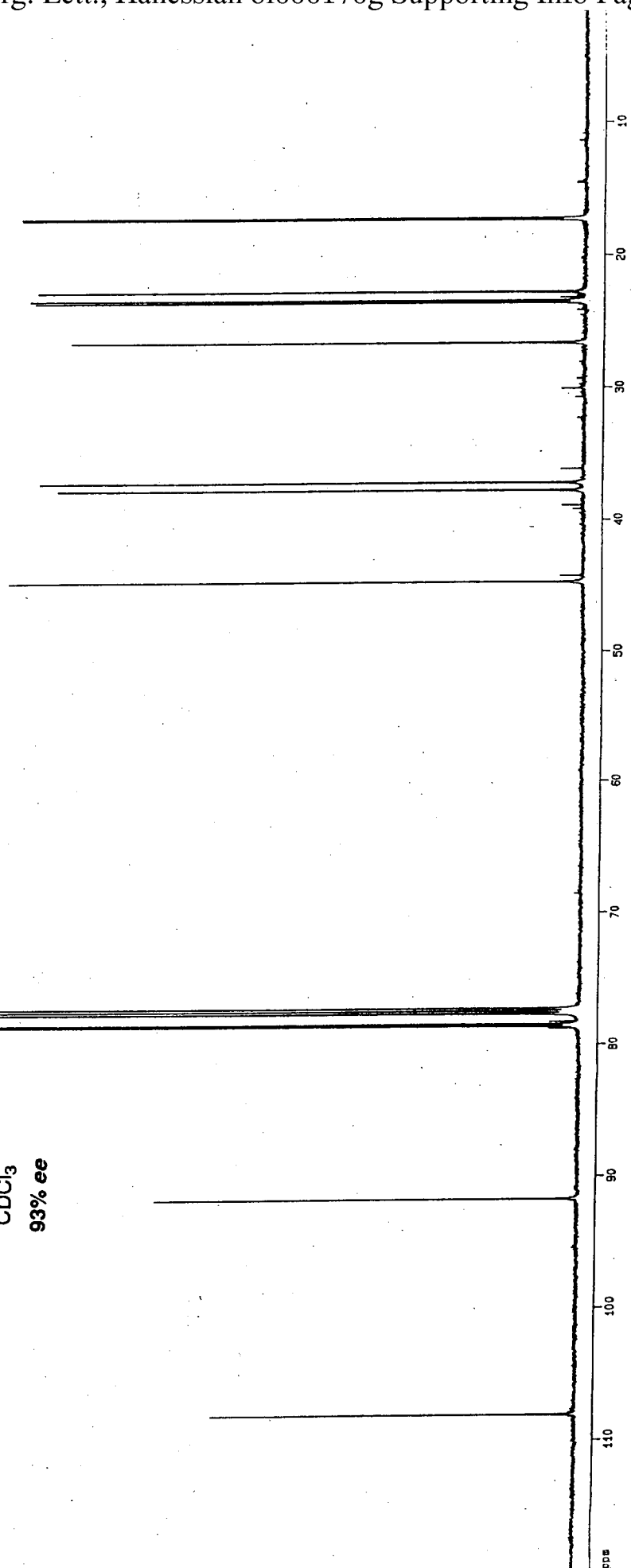
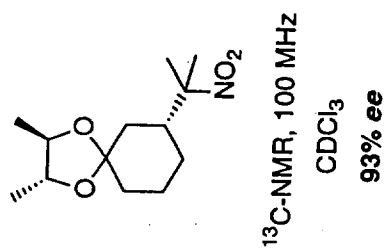


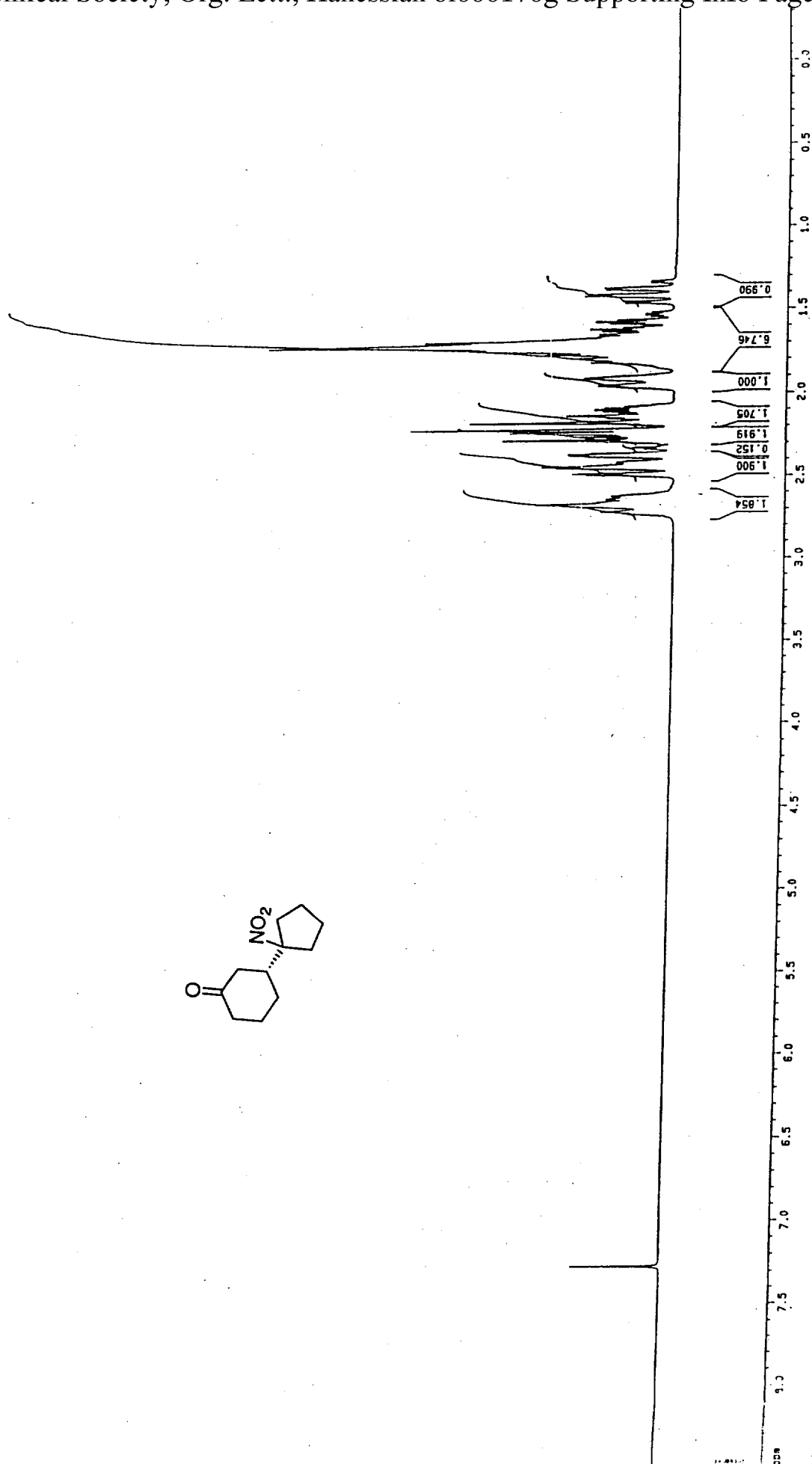


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3	41523.7	7775.033	77.2759	7.34
4	41612.5	7743.051	76.3581	8.30
5	41696.6	7710.394	75.6395	3.05
6	49639.4	4681.024	46.5246	9.32
7	50673.5	4287.687	42.6153	11.01
8	51166.0	4097.313	40.7291	11.21
9	55067.0	2610.575	25.9465	11.35
10	55490.7	2448.934	24.3395	11.43
11	55718.7	2361.967	23.4756	11.58
12	55989.7	2259.591	22.4481	11.54







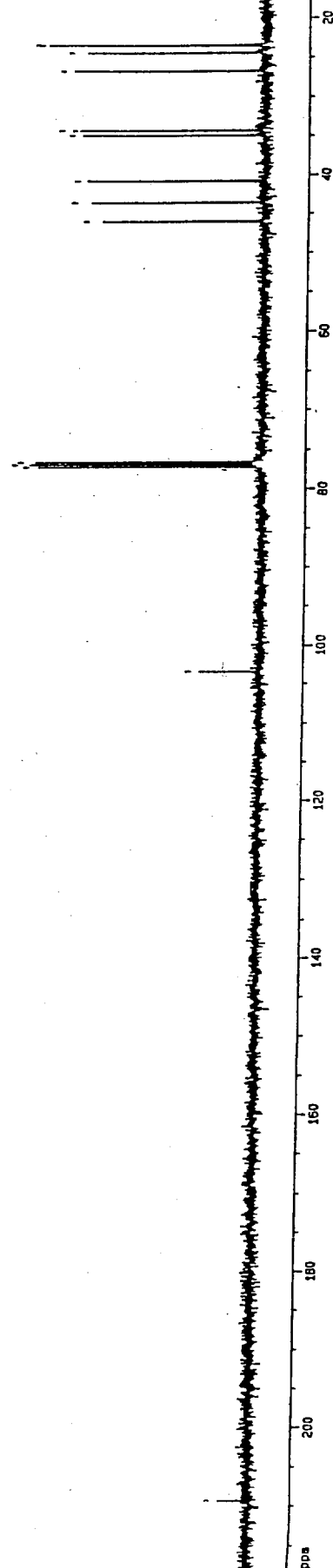
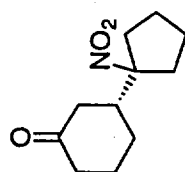
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77.231

103.340

209.212

ppm



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38.076

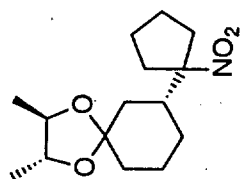
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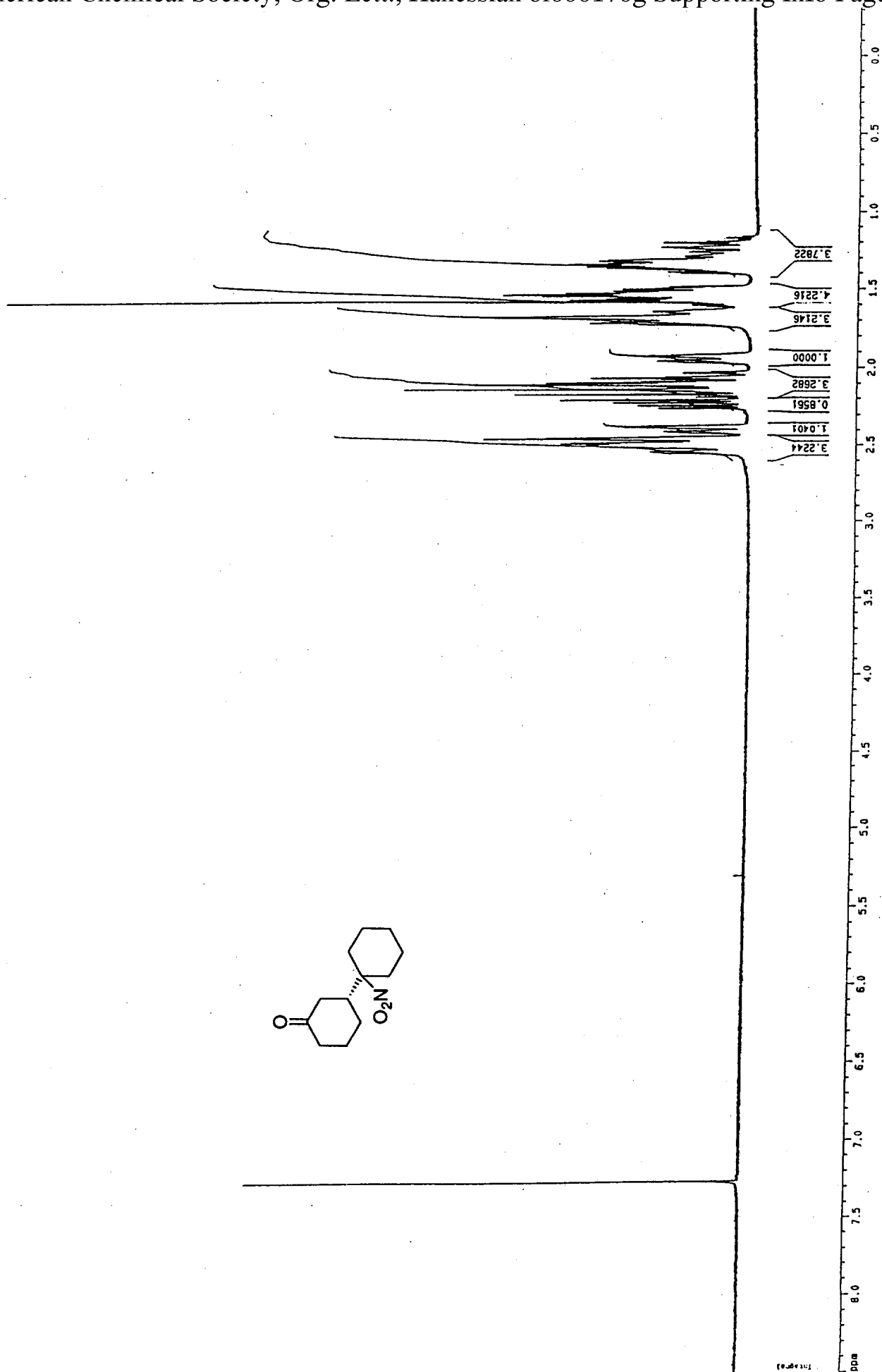
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¹³C-NMR, 100 MHz

CDCl₃

93% ee



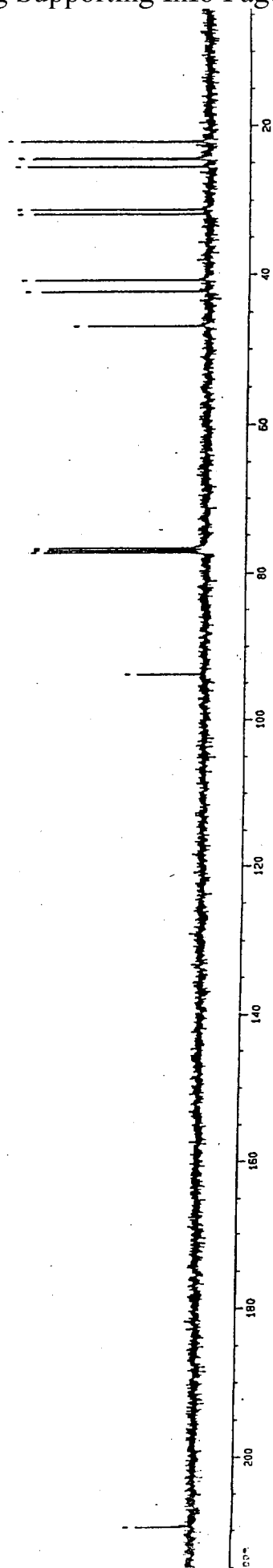
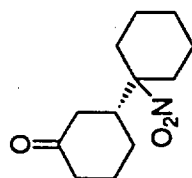
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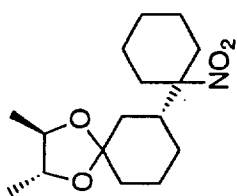
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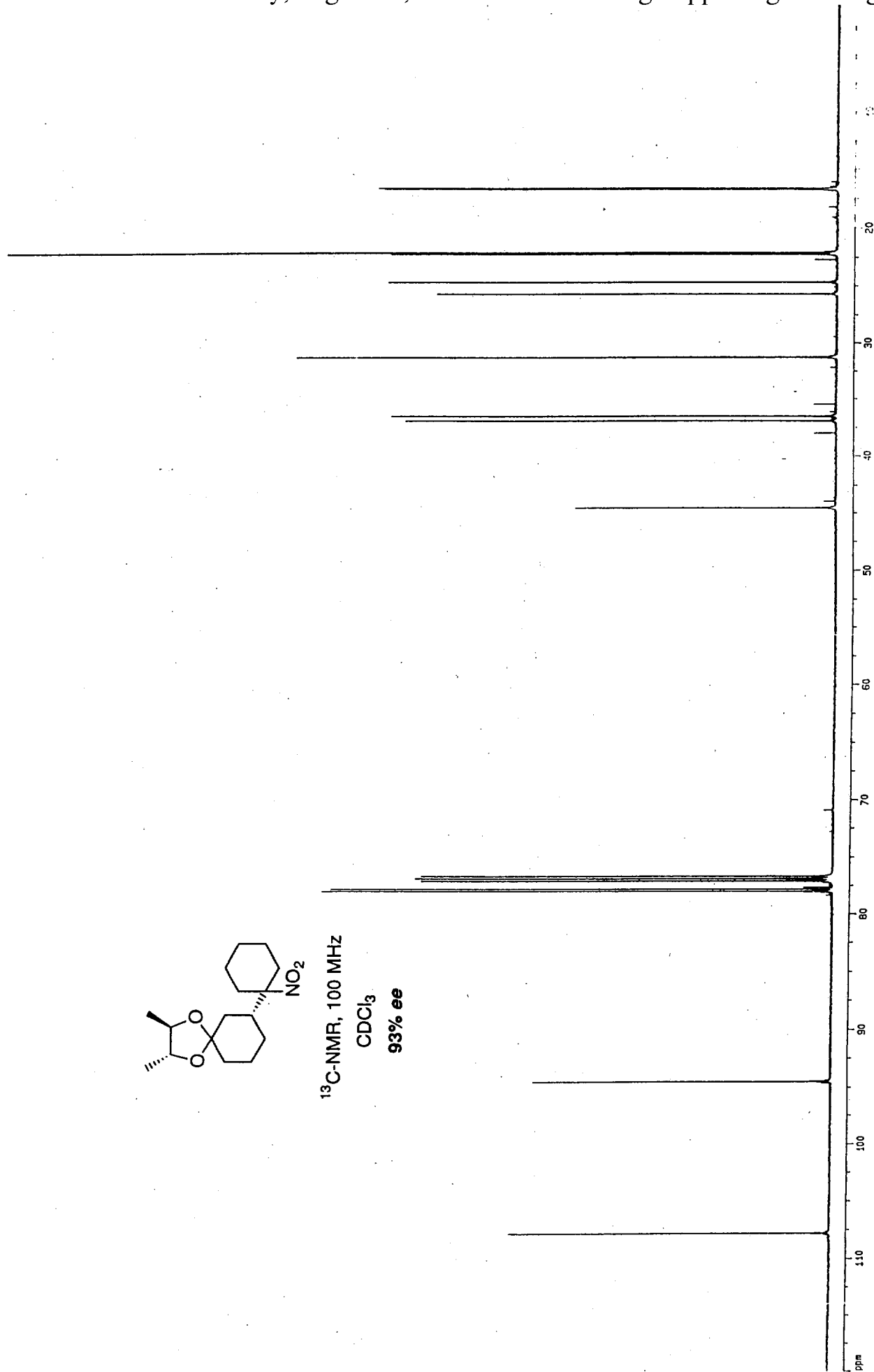


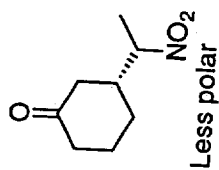
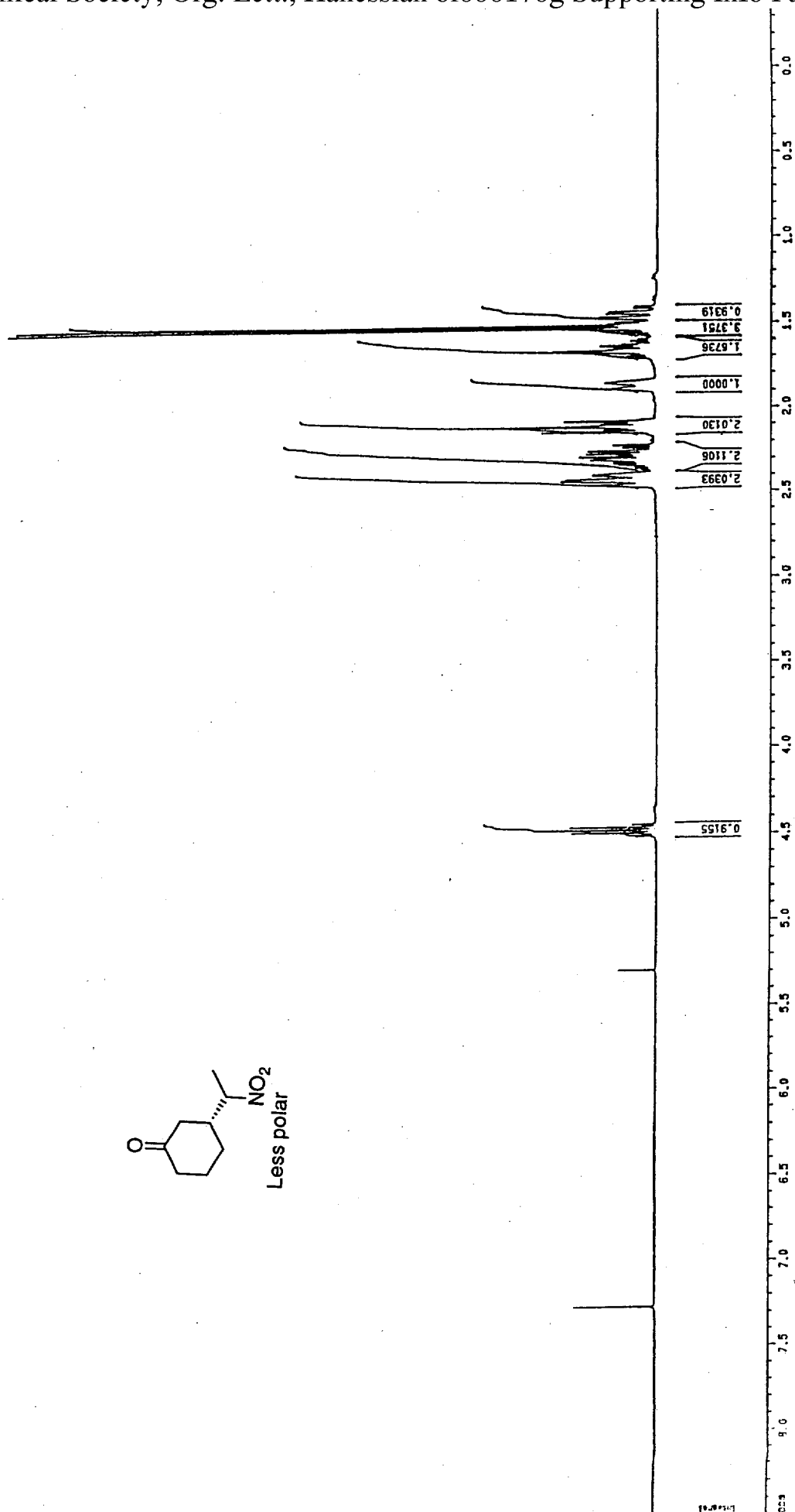


^{13}C -NMR, 100 MHz

CDCl_3

93% ee





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27.366

40.726

42.310

43.162

76.592

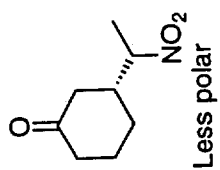
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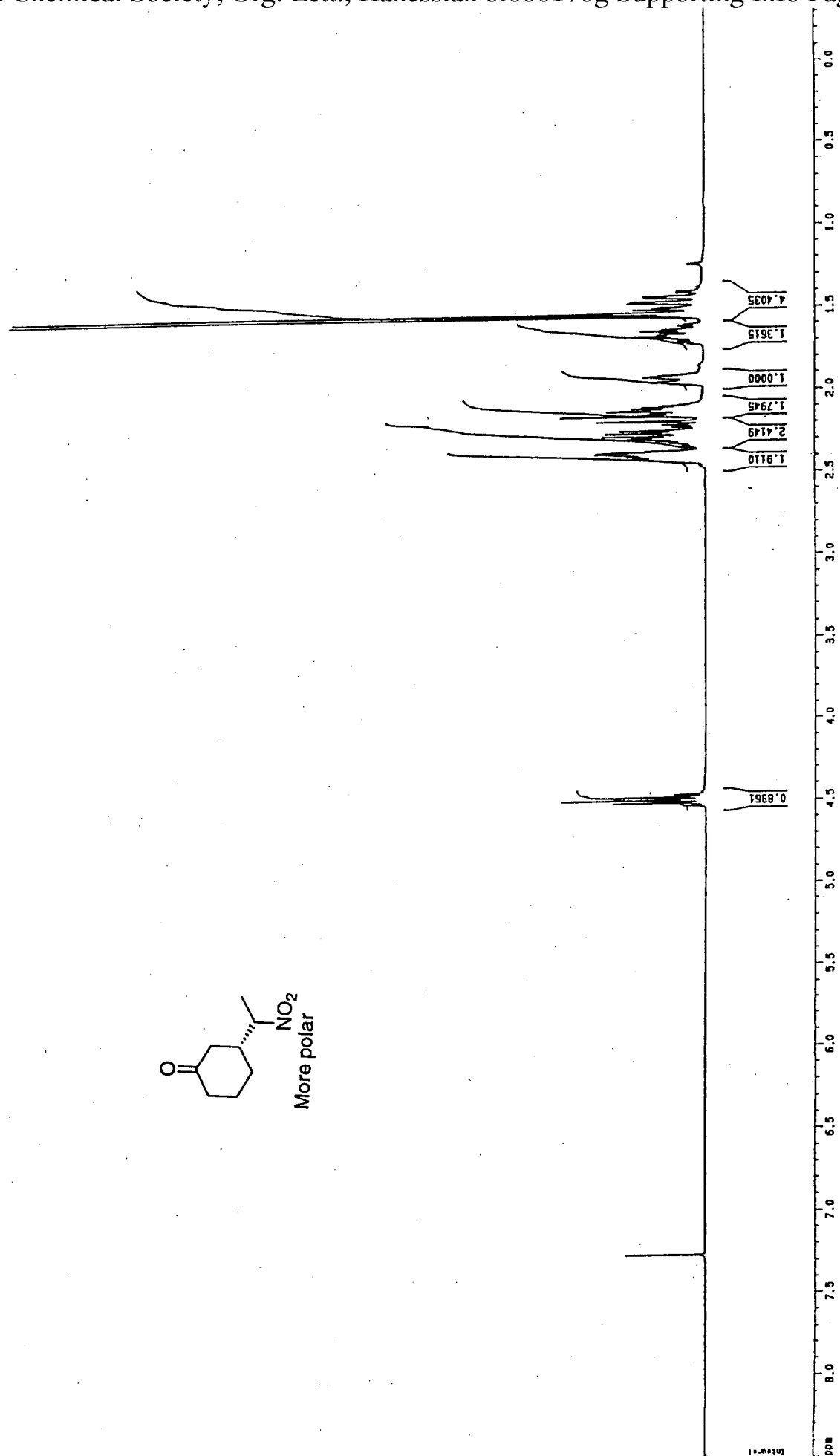
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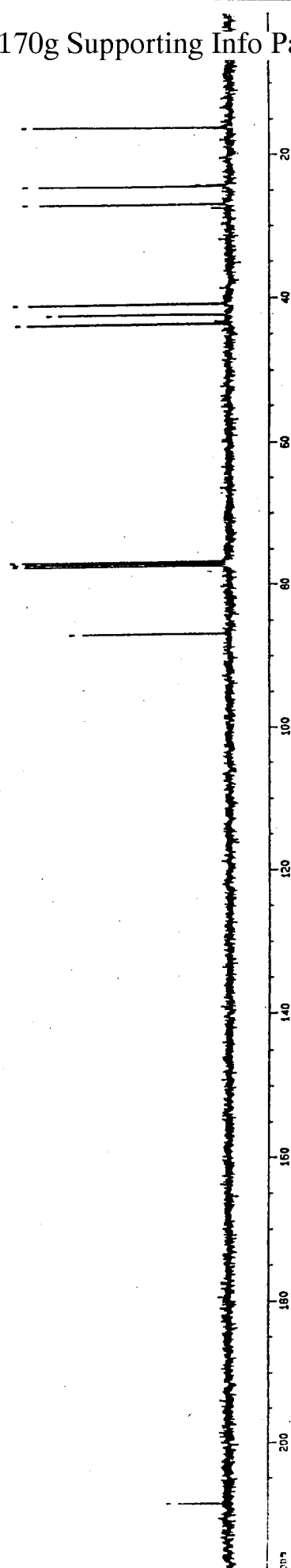
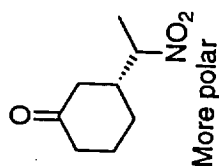
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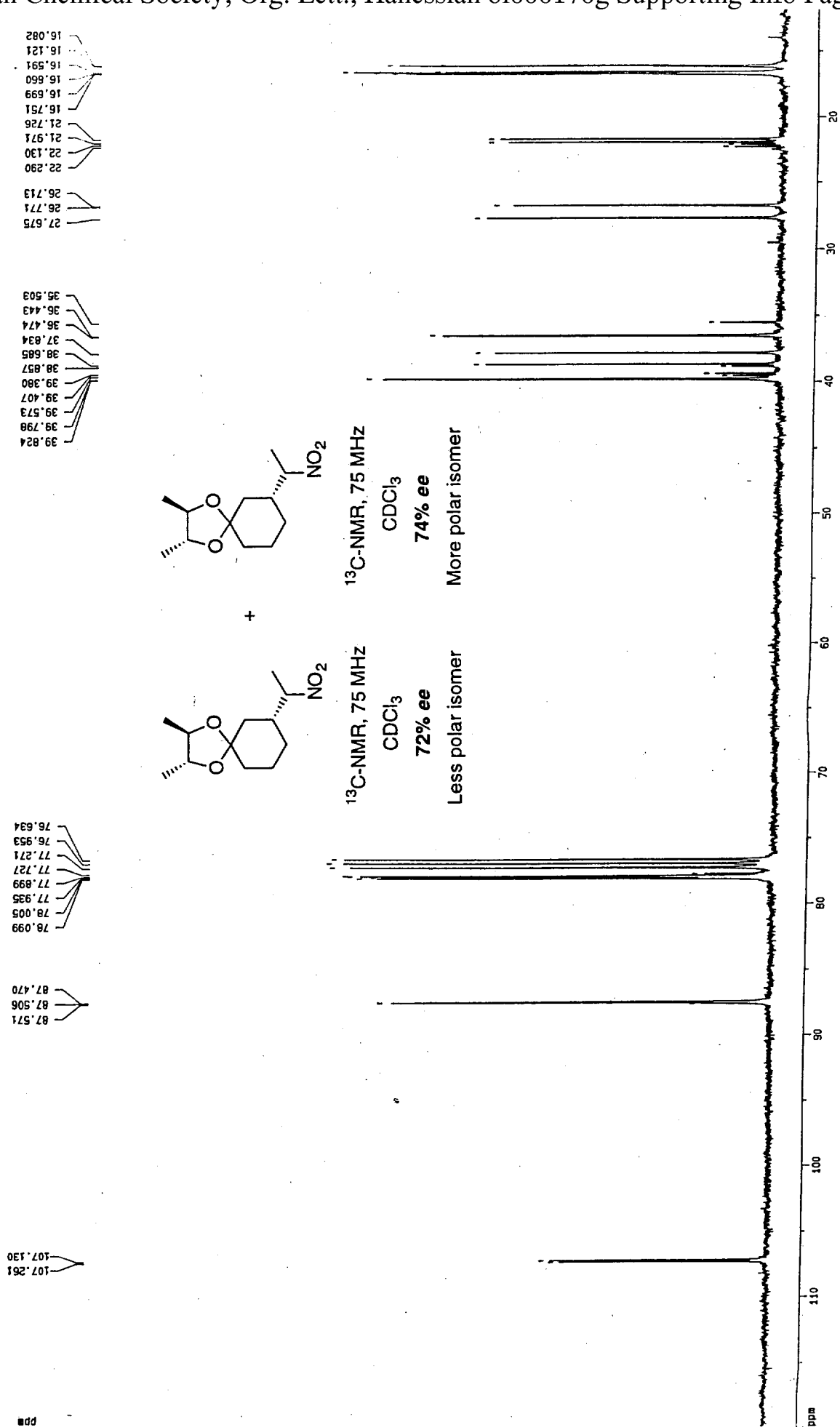
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86.824

208.333

ppm





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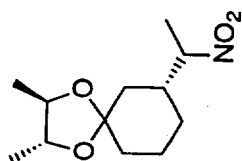
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76.149
77.941
77.215
76.898
76.580

87.636
87.529

107.313

ppm

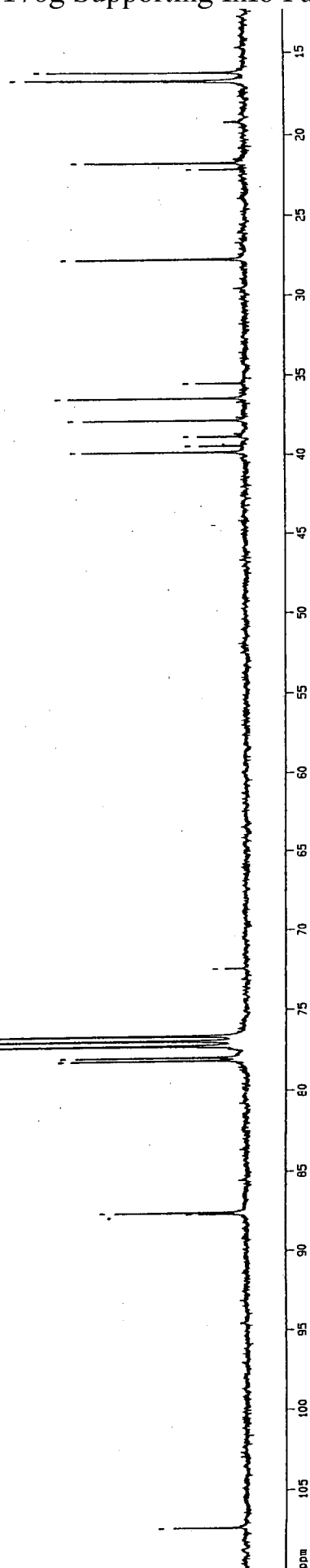


¹³C-NMR, 75 MHz

CDCl₃

51% ee

Less polar isomer



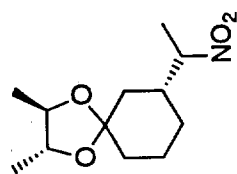
16.139
16.617
16.705
16.789
19.238
22.003
22.319
26.748
26.806

35.536
36.508
38.726
39.408
39.614
39.858

72.391
76.580
76.897
77.215
77.770
77.988
78.047
78.183

87.565

107.179
ppm

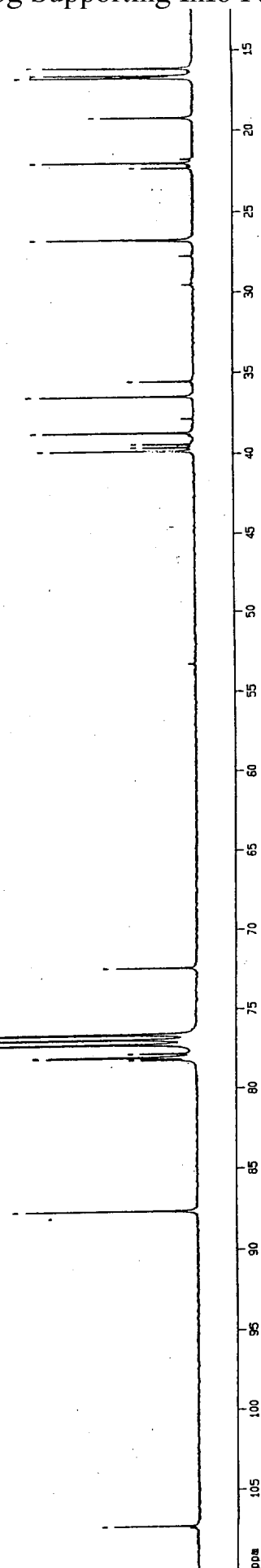


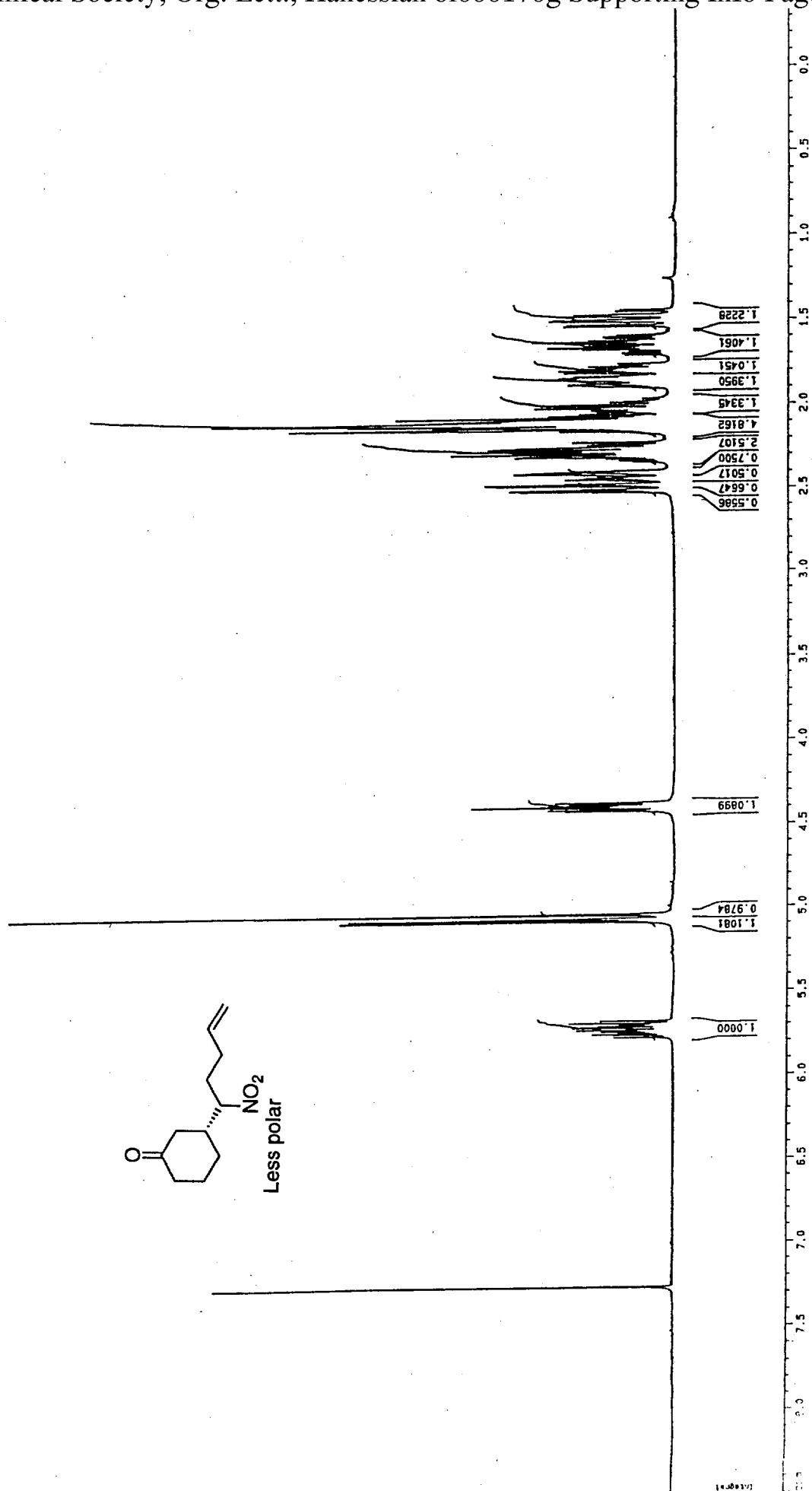
¹³C-NMR, 75 MHz

CDCl₃

49% ee

More polar isomer





24.056
27.260
29.512
29.548

40.792
41.587
43.823

76.565
76.883
77.201

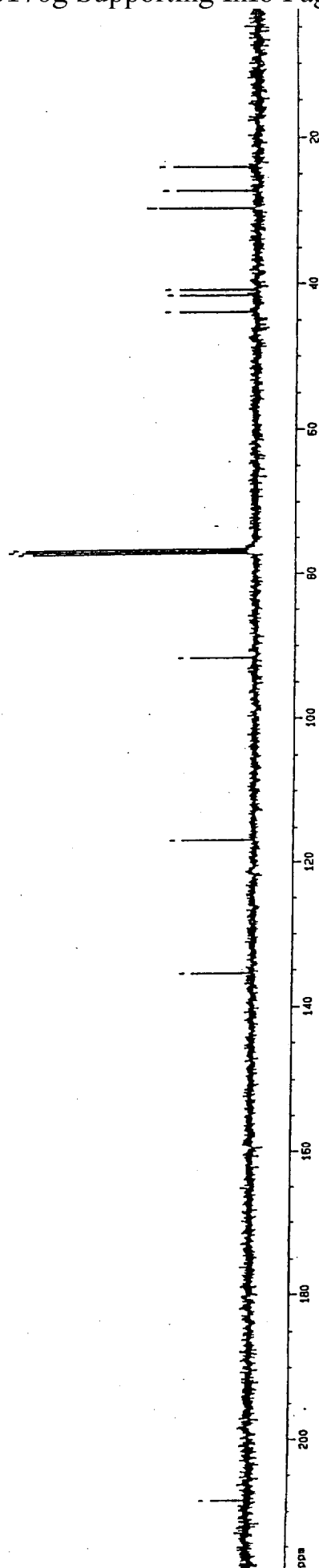
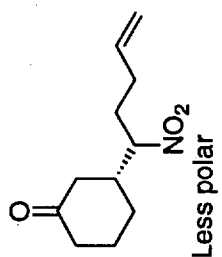
91.608

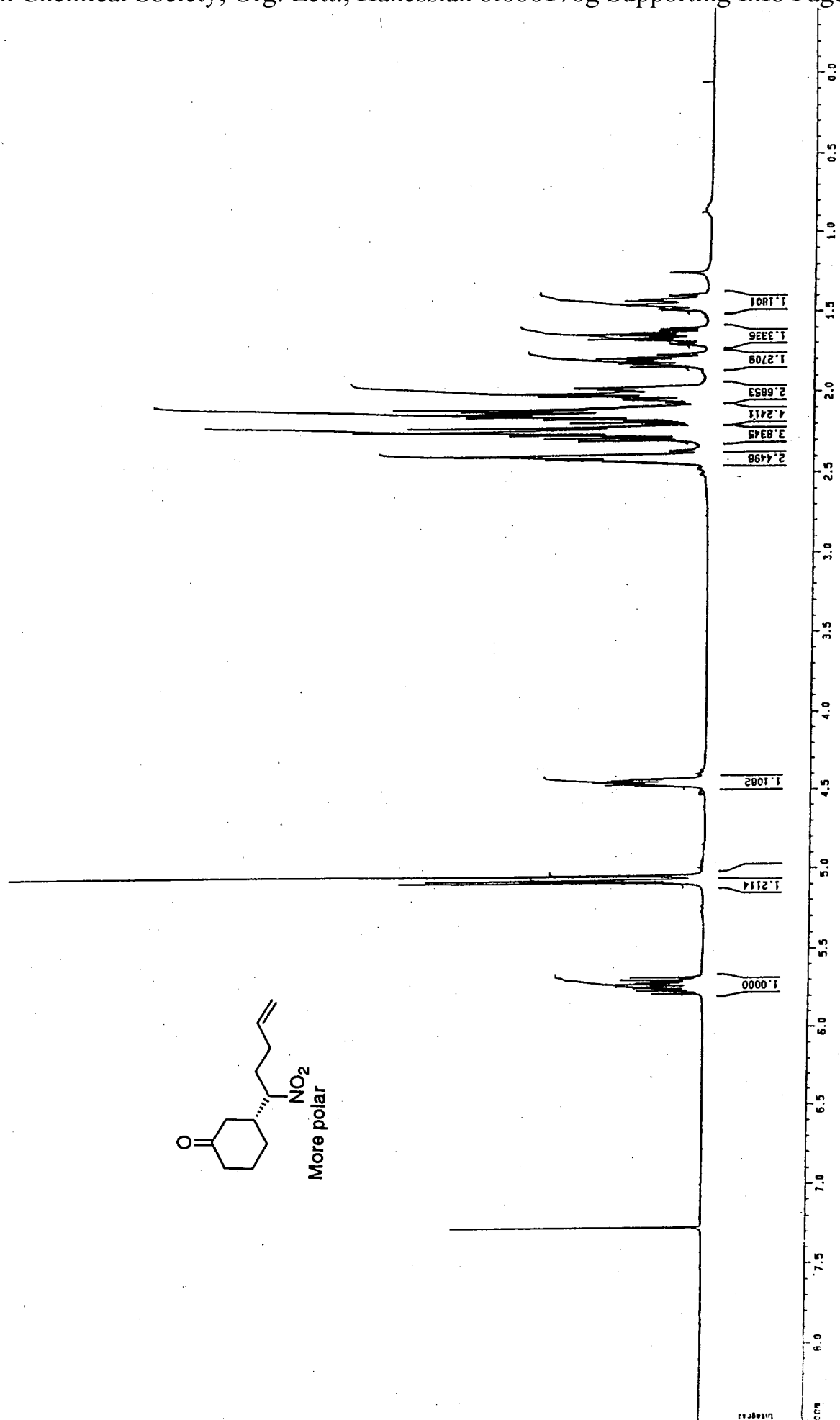
116.795

135.380

208.314

ppm





24.285
27.613
29.566
29.737
40.744
41.396
43.166

76.577
76.895
77.212

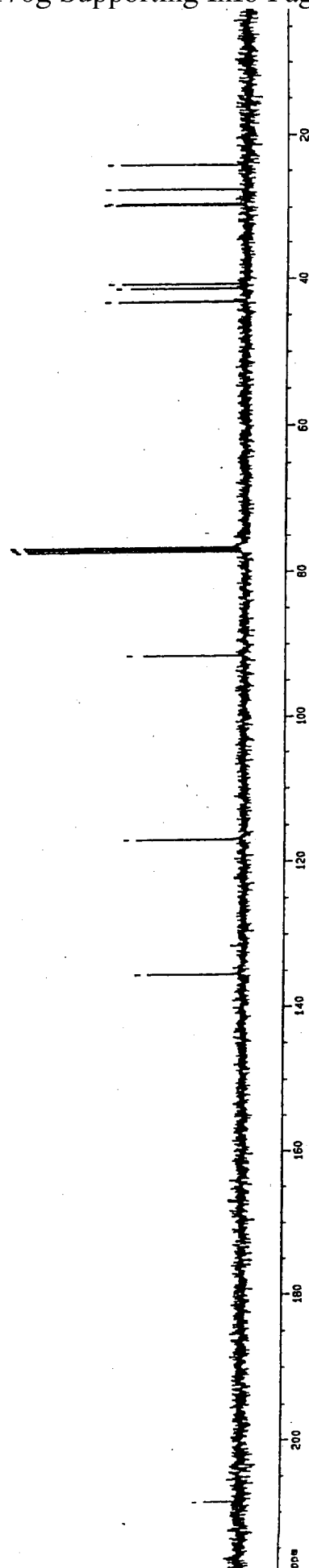
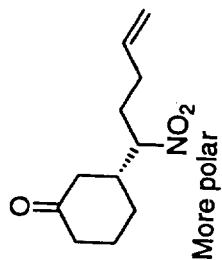
91.520

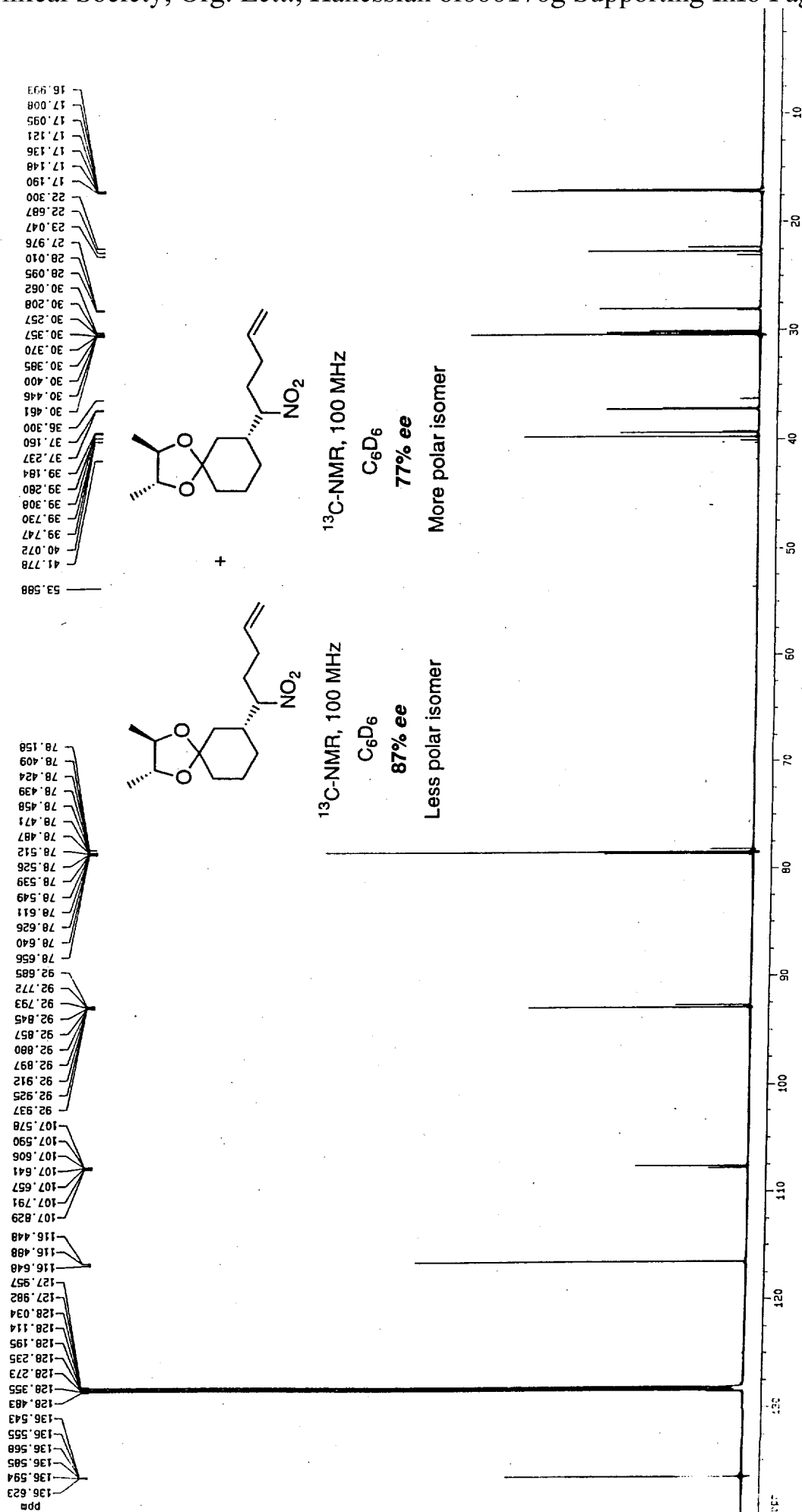
116.801

135.414

208.342

ppm





16.608
16.715
21.691
22.119
27.594
29.596
29.883
35.540
36.482
38.585
38.683
39.104
39.601

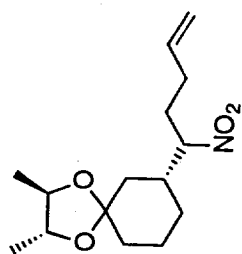
76.600
76.917
77.122
77.235
77.928
78.097
78.148

92.439
92.345

107.274

116.370

135.879



¹³C-NMR, 75 MHz

CDCl₃

81% ee

Less polar isomer

ppm

ppm

16.025
16.698
16.775
22.073
22.403
27.603
27.659
29.630
29.871
35.553
36.524
38.504
38.657
39.158
39.384

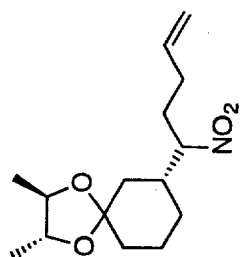
76.589
76.907
77.111
77.225
77.745
77.973
78.035
78.172

92.419

107.167

116.396

135.870

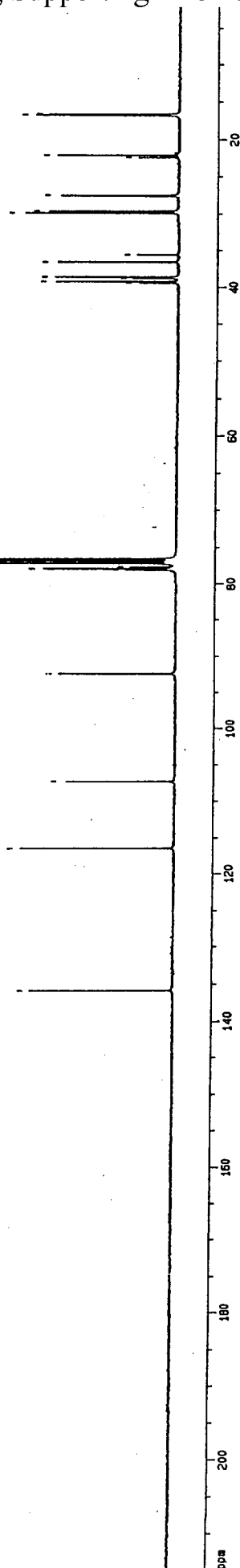


¹³C-NMR, 75 MHz

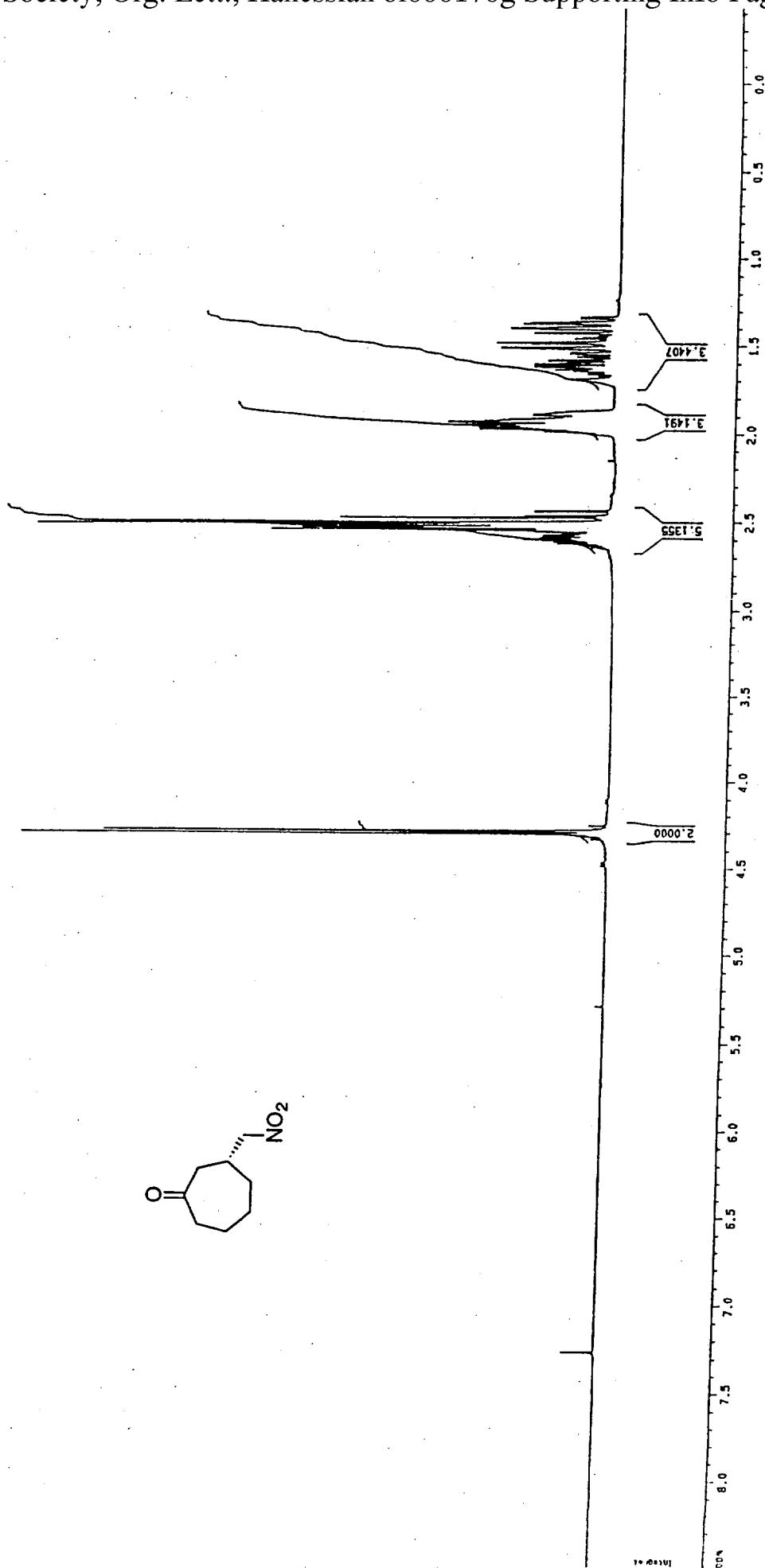
CDCl₃

53% ee

More polar isomer

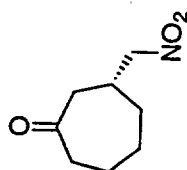


ppm



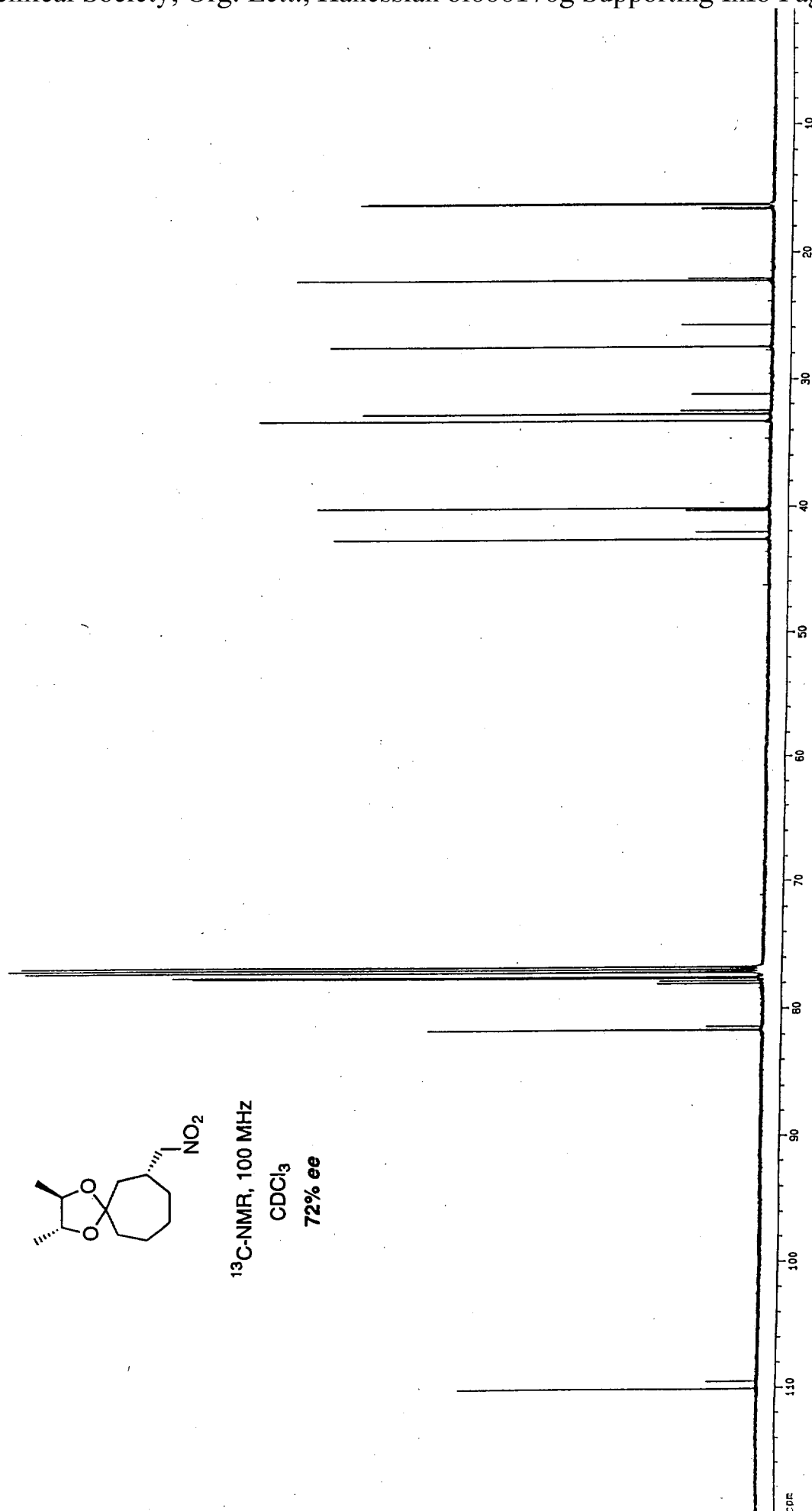
23.883
27.796
33.398
34.623
43.588
46.265

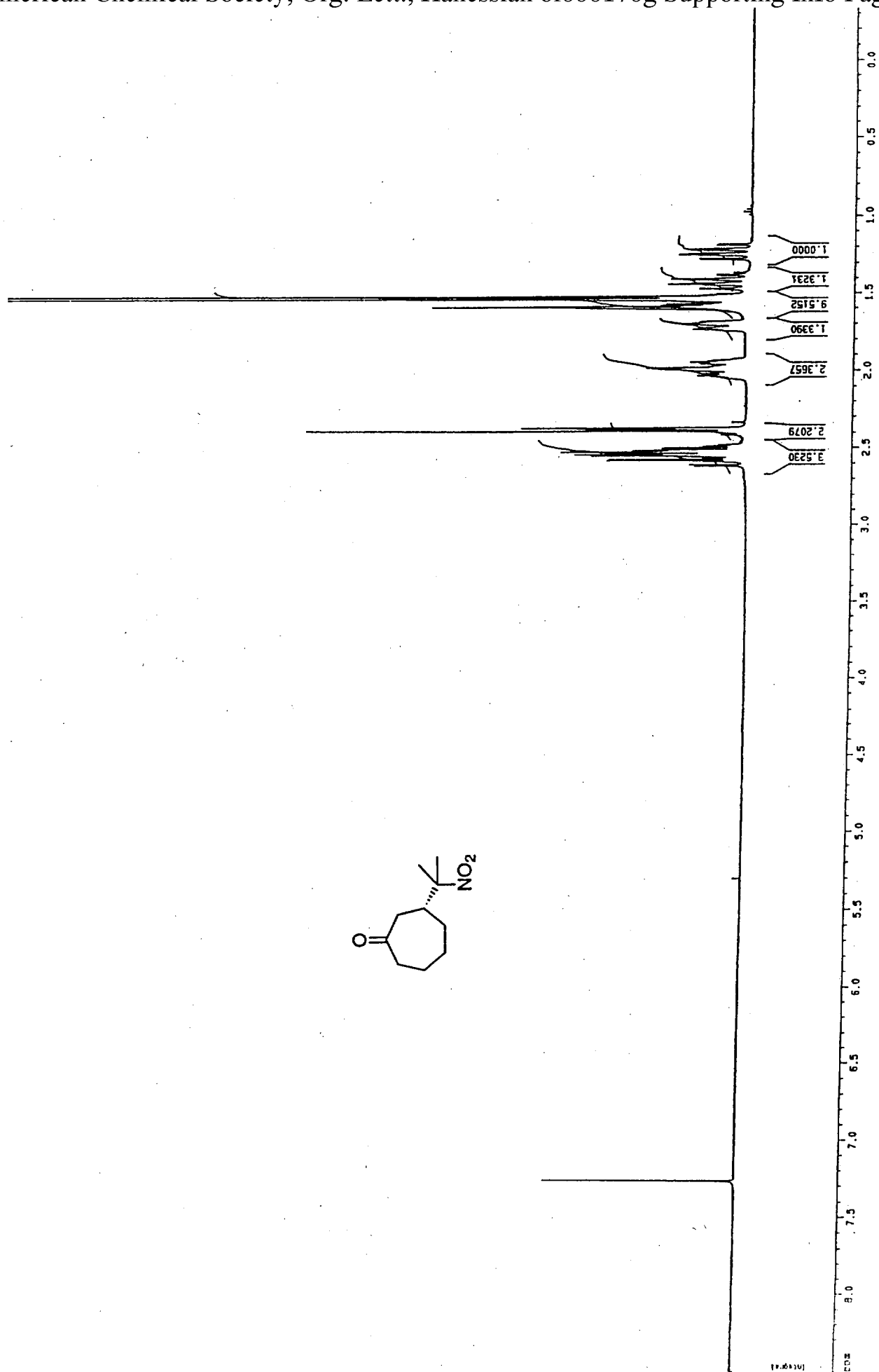
76.597
76.915
77.233
80.466



211.026

ppm



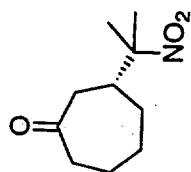


21.754
23.866
24.592
29.813
31.462

43.146
43.878
45.022

76.585
76.902
77.220

91.943



211.690

ppm

