Supporting Information for "Enforced Stacking in Crowded Arenes"

Mark L. Bushey, Austin Hwang, Peter W. Stephens, and Colin Nuckolls*
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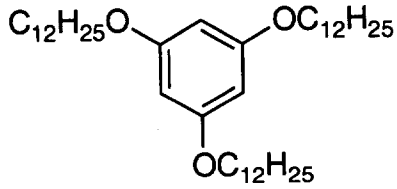
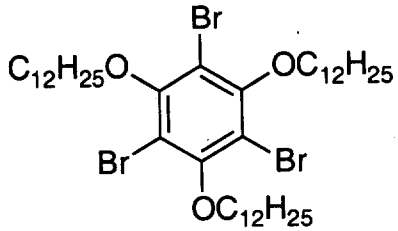
Synthesis of 1a-d.

General. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on a Bruker DRX 300 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Paragon 3000 FT-IR spectrometer. *t*-Butyllithium was purchased as a solution in hexane from Acros. THF (Aldrich), CH_2Cl_2 (Aldrich), Benzene (Aldrich) and DMF (Acros) were "anhydrous-grade" and used as received. All other reagents were purchased from Aldrich or Fluka. Unless otherwise noted, all reactions were run in oven-dried glassware under a nitrogen atmosphere. Flash chromatography was performed using 230-400 mesh silica gel.

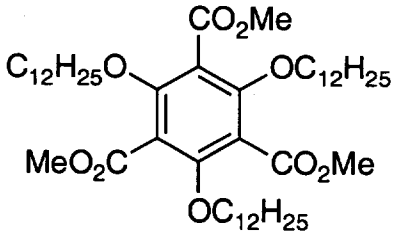


1,3,5-tridodecyloxybenzene. To phloroglucinol dihydrate (4.82 g, 29.7 mmol), potassium carbonate (24.64 g, 178.2 mmol), and 1-iodododecane (22 mL, 89.1 mmol) in a 250 mL round bottom flask with a magnetic stirring bar was added DMF (30 mL). The reaction mixture was heated under a nitrogen atmosphere for 12 hours at 60°C. After cooling to room temperature, H_2O (100 mL) was added. The solution was neutralized to pH ca. 7 with a concentrated HCl solution. The resulting slurry was extracted three times (100 mL each) with diethyl ether. The organic solutions were combined, dried over sodium sulfate, and concentrated under reduced pressure. Silica gel chromatography (0.5% diethyl ether in hexanes) yielded a viscous liquid that slowly solidified. (6.6 g, 10.5 mmol, 35%). R_f 0.3 (2% Et_2O/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.08 (s, 1H), 3.92 (t, J = 13.1 Hz, 2H), 1.78 (dt, J = 14.4, 14.5 Hz, 2H), 1.46 (m, 2H), 1.29 (m, 16H), 0.91 (t, J = 13.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 162.5, 95.2, 69.4, 33.5, 31.2, 30.9, 30.8, 27.6, 24.2, 15.6. IR (thin film) 2910, 2850, 1610, 1590, 1460 cm^{-1}; HRMS (FAB; M+H$^+$) calcd for $C_{42}H_{79}O_3$ 631.6029; found 631.6020.

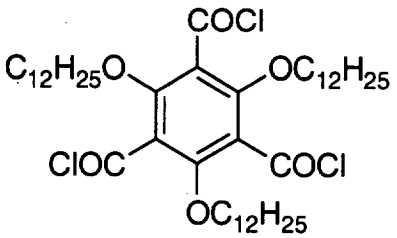


1,3,5-tribromo-2,4,6-tridodecyloxybenzene. To a 250 mL flask that had been outfitted with a magnetic stir bar was added 1,3,5-tridodecyloxybenzene (6.6 g, 10.5 mmol), $FeCl_3$ (0.17 g, 1.05 mmol), and chloroform (70 mL). Bromine (1.7 mL, 32.4 mmol) was added, and the mixture was heated under reflux for 3 hours and stirred an additional 12 hours at room temperature. 40 mL of a sodium thiosulfate solution (10% aqueous) was added vigorous stirring until the deep red colour had deminished (ca. 1h). The solution was diluted with H_2O (30 mL) and extracted three times with CH_2Cl_2 (50 mL each). The organic solutions were combined, dried over sodium

sulfate, then concentrated under reduced pressure. . Silica gel chromatography (0.5% diethyl ether/hexanes) yielded a white solid, (8.1 g, 9.3 mmol, 89%). R_f (2% Et_2O/hexanes) = 0.3; mp 42–45°C (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (t, J = 12.9 Hz, 2H), 1.89 (dt, J = 14.0, 14.3 Hz, 2H), 1.55 (m, 2H), 1.29 (m, 16H), 0.91 (t, J = 13.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 154.6, 110.7, 74.0, 32.4, 30.6, 30.4, 30.1, 29.9, 29.8, 26.3, 14.6. IR (thin film) 2970, 2850, 1540, 1470, 1410 cm^{-1}. HRMS (FAB, M^+) calcd for $C_{42}H_{75}Br_3O_3$ 864.3266; found 864.3247.



2,4,6-dodecyloxy-1,3,5-trimethyltricarboxylate. Into a dry 250 mL flask that was outfitted with a stir bar was added 1,3,5-tribromo-2,4,6-tridodecyloxybenzene (4.0g, 4.6 mmol), and THF (90 mL). The solution was evacuated and flushed with nitrogen several times and then cooled to –78 °C. With vigorous stirring, a *t*-butyllithium solution (25 mL, 1.5M solution in hexanes) was added dropwise. After the solution had stirred at –78 °C for 3hours it became intensely yellow. At –78 °C, the reaction was quenched by the addition of methyl chloroformate (3.6 mL, 46 mmol) at a medium pace. The mixture was warmed to room temperature and allowed to stir for ca. 12 h. H_2O (100 mL) was added to the solution and then extracted three times with diethyl ether (100 mL each). The organic phases were combined and dried over sodium sulfate followed by silica gel chromatography (2% Et_2O/hexanes) light-yellow liquid (1.1 g, 1.3 mmol, 29%). R_f (8 % Et_2O/hexanes) = 0.3. ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (t, J = 12.9 Hz, 2H), 3.89 (s, 3H), 1.66 (dt, J = 14.2, 14.3 Hz, 2H), 1.27 (s, 18H), 0.89 (t, J = 13.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 165.9, 156.8, 118.9, 76.7, 52.9, 32.3, 30.4, 30.0, 29.7, 26.2, 23.1, 14.5. IR (thin film) 2920, 2360, 2340, 1730, 1580, 1460, 1430 cm^{-1}; HRMS (FAB, M^+) calcd for $C_{48}H_{84}O_9Na$ 827.6013; found 827.6016.



2,4,6-tridodecyloxy-1,3,5-benzenetricarbonyl trichloride. In a 250ml flask outfitted with a reflux condenser and a magnetic stir bar was added 2,4,6-dodecyloxy-1,3,5-trimethyltricarboxylate (1.0 g, 1.2 mmol) and sodium hydroxide (4.97 g, 124.2 mmol) followed by isopropanol (38 mL) and then H_2O (19 mL). The mixture was heated under reflux (100 °C oil bath) for 12 hours, cooled to room temperature, and concentrated under reduced pressure. On ice, an HCl solution (1 N, 50 mL) was added to the gummy residue and made slightly acidic by addition of a concentrated HCl solution. After extracting this solution three times with Et_2O (50 mL each), the organic solutions were combined, washed with brine (100 mL), and dried over sodium sulfate. Concentration under reduced pressure yielded an off-white foam. To the flask containing the triacid was immediately added CH_2Cl_2 (40 mL) and 0.9 mL $SOCl_2$ (1.4 g, 11.8

mmol) under an inert atmosphere. The reaction mixture was heated at reflux for 2 h and the volatiles were removed by distillation under reduced pressure, yielding a viscous oil (0.94 g, 1.2 mmol, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (t, J = 13.0 Hz, 2H), 1.78 (dt, J = 14.4, 14.6 Hz, 2H), 1.29 (m, 18H), 0.90 (t, J = 13.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 165.9, 156.8, 123.8, 79.2, 33.5, 31.3, 31.2, 31.1, 31.0, 30.9, 30.7, 27.0, 24.2, 15.7. IR (thin film) 2920, 2850, 1780, 1570, 1470, 1430 cm^{-1}; Low resolution mass spec for $C_{45}H_{76}Cl_3O_6$ found (M^+) 817.5 and 781.5 ($M–Cl^+$).

General procedure for the synthesis of 1a–d. To a 5 mL flask with a magnetic stirbar under nitrogen was added sequentially 2,4,6-tridodecyloxy-1,3,5-benzenetricarbonyl trichloride (0.11g, 0.13 mmol), CH_2Cl_2 (1.5 mL), Et_3N [62 μL, 0.4 mmol (twice as much if the amine hydrochloride was used)], and the amine or amine hydrochloride (0.4 mmol). After stirring for 2 h, the mixture was diluted with CH_2Cl_2 (20 mL) and $NaHCO_3$ (20 mL, sat. aqueous). The phases were seperated and the aqueous one extracted twice with CH_2Cl_2 (20 mL each). The organic phases were combined, dried over sodium sulfate, concentrated under reduced pressure. For **1a-c** the solids were recrystallization from methanol afford white solids. **1d** was chromatographed on silica gel with a gradient elution (30% to 45% diethyl ether/hexanes).

(1a). (135 mg, 0.11 mmol, 81 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ δ 5.96 (br s, 1H), 3.98 (t, J = 12.6 Hz, 2H), 3.40 (dt, J = 6.0 Hz, 2H), 1.62 (m, 4H), 1.27 (s, 18H), 0.90 (t, J = 13.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 164.8, 156.0, 122.6, 40.6, 32.3, 30.6, 30.1, 29.8, 27.526.2, 23.1, 14.5. IR (thin film) 3280, 2950, 2920, 2850, 1730, 1650, 1580, 1540, 1470, 1440 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{81}H_{154}N_3O_6$ 1265.1838; found 1265.1840.

(1b). (100 mg, 0.1 mmol, 77 %). R_f (2% MeOH/CH_2Cl_2) = 0.3. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.22 (m, 5H), 5.90 (br s, 1H), 3.91 (t, J = 13.0 Hz, 2H), 3.68 (dt, J = 6.1, 6.1 Hz, 2H), 2.91 (t, J = 14.2 Hz, 2H), 1.64 (s, 4H), 1.25 (s, 16H), 0.89 (t, J = 13.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 164.9, 156.1, 139.0, 129.1, 129.0, 127.0, 122.5, 76.8, 41.6, 36.1, 32.3, 30.6, 30.1, 29.9, 29.8, 26.3, 23.1, 14.6. IR (thin film) 3300, 3030, 2920, 2850, 1640, 1580, 1540, 1490, 1450, 1430 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{69}H_{106}N_3O_6$ 1072.8082; found 1072.8055.

(1c). (80 mg, 0.10 mmol, 75 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (br s, 1H), 3.99 (t, J = 12.9 Hz, 2H), 2.95 (d, J = 4.7 Hz, 3H), 1.65 (m, 2H), 1.27 (s, 18H), 0.90 (t, J = 12.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 164.8, 155.4, 123.7, 32.3, 30.6, 30.1, 29.9, 29.8, 27.0, 26.2, 23.1, 20.0, 14.5. IR (thin film) 3283, 2920, 2850, 1640, 1580, 1560, 1540, 1470, 1460, 1400 cm^{-1}; HRMS (FAB M+H)$^+$ calcd for $C_{48}H_{88}N_3O_6$ 802.6673; found 802.6697

(1d). (115 mg, 0.1046 mmol, 80%). R_f (50% Et_2O/hexanes) = 0.3. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (br t, J = 9.5 Hz, 1H), 4.08 (d, J = 4.9 Hz, 2H), 4.01 (t, J = 13.1 Hz, 2H), 1.63 (m, 2H), 1.50 (s, 9H), 1.26 (s, 18H), 0.89 (t, J = 13.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 168.6, 164.6, 156.8, 121.9, 82.7, 77.0, 42.8, 32.3, 30.4, 30.0, 29.8, 28.4, 26.1, 23.1, 14.5. IR (thin film) 3280, 3070, 2920, 2850, 1760, 1650, 1580, 1540, 1470, 1440 cm^{-1}; HRMS (FAB M+H$^+$) calcd for $C_{63}H_{112}N_3O_{12}$ 1101.8246; found 1102.8199.

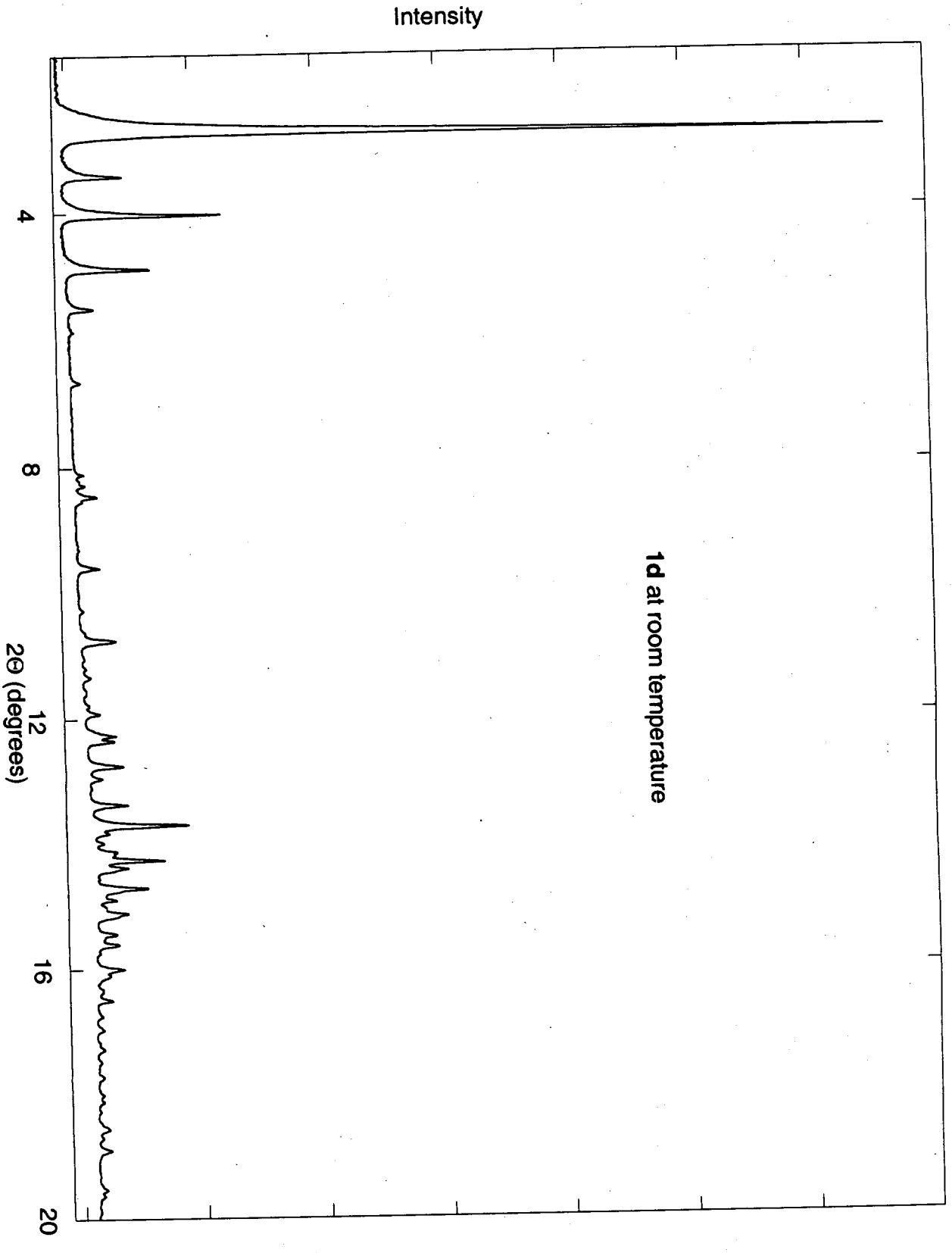
Molecular modeling. Modeling was performed on a VA Linux 420 work-station (733 Mhz Intel Pentium III processor) outfitted with the Maestro Interface (Schrodinger Inc., MacroModel v. 7.0, Linux version). All models were minimized using the Amber* molecular force-field.

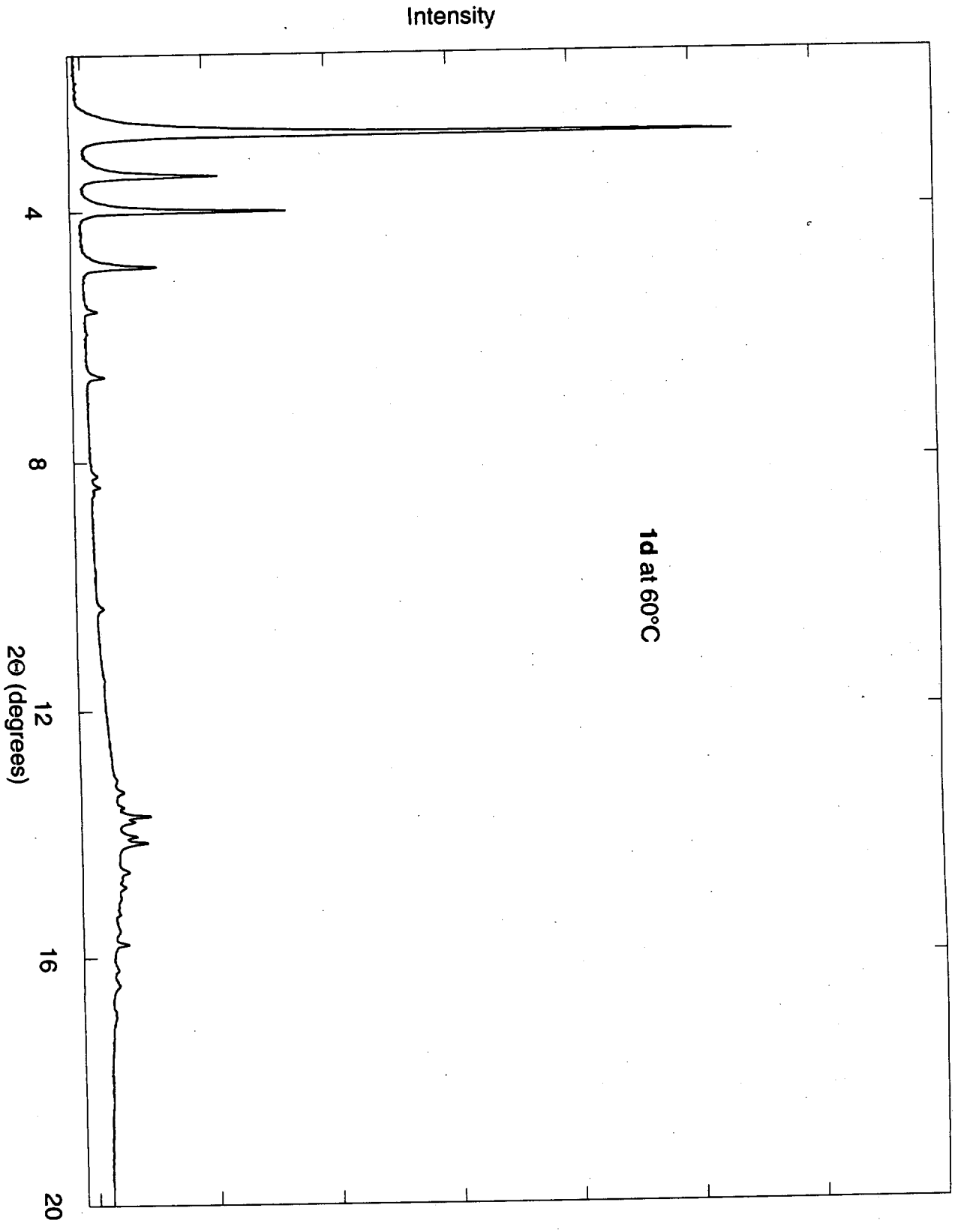
Microscopy. Polarized light microscopy was performed on a Leica DMLP polarized light microscope with a 20X objective and a DMLD camera system with spot-metering. Samples were placed between a coverslip and glass slide. Photographic images were captured as the samples were cooled (1°C/min) from their clearing temperature. The temperature was varied with a Linkam TMS 350E heating and cooling stage.

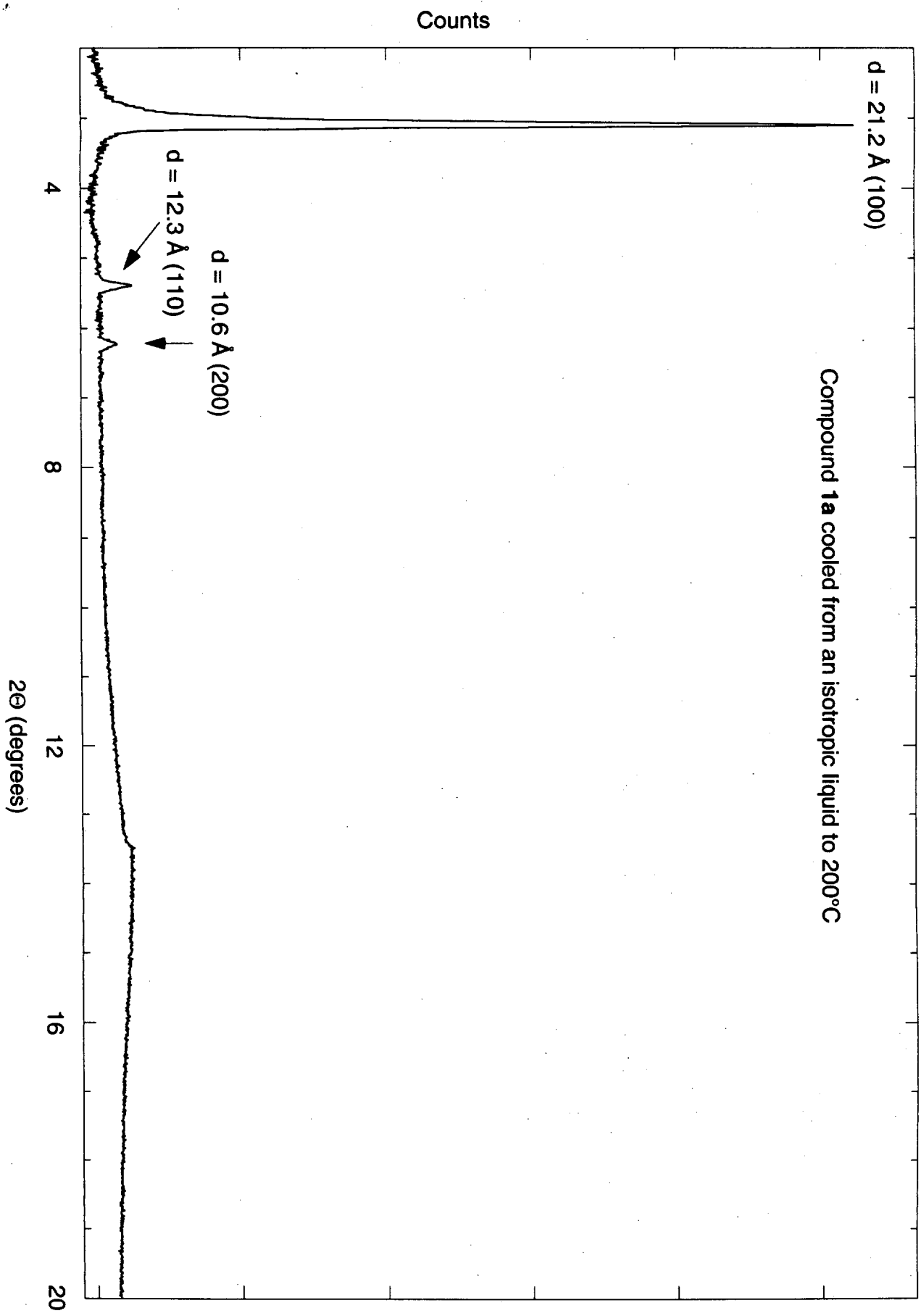
X-ray Diffraction. Lindemann capillary tubes (1 mm) were filled with the samples. They were heated in a thermostatically controlled furnace with Kapton windows. The sample was rotated around the long axis of the capillary to average out any effects of preferential orientation. The x-ray diffraction measurements were performed at beamline X3B1 of the National Synchrotron Light Source. X-rays of wavelength 1.151 Å, selected by a double crystal Si(111) monochromator, were incident on the sample. X-rays diffracted in the vertical plane passed through a Söller collimator of 0.03 degrees FWHM and were detected by a conventional NaI scintillation counter. Counts were normalized to the incident flux via an ionization chamber in the incident beam.

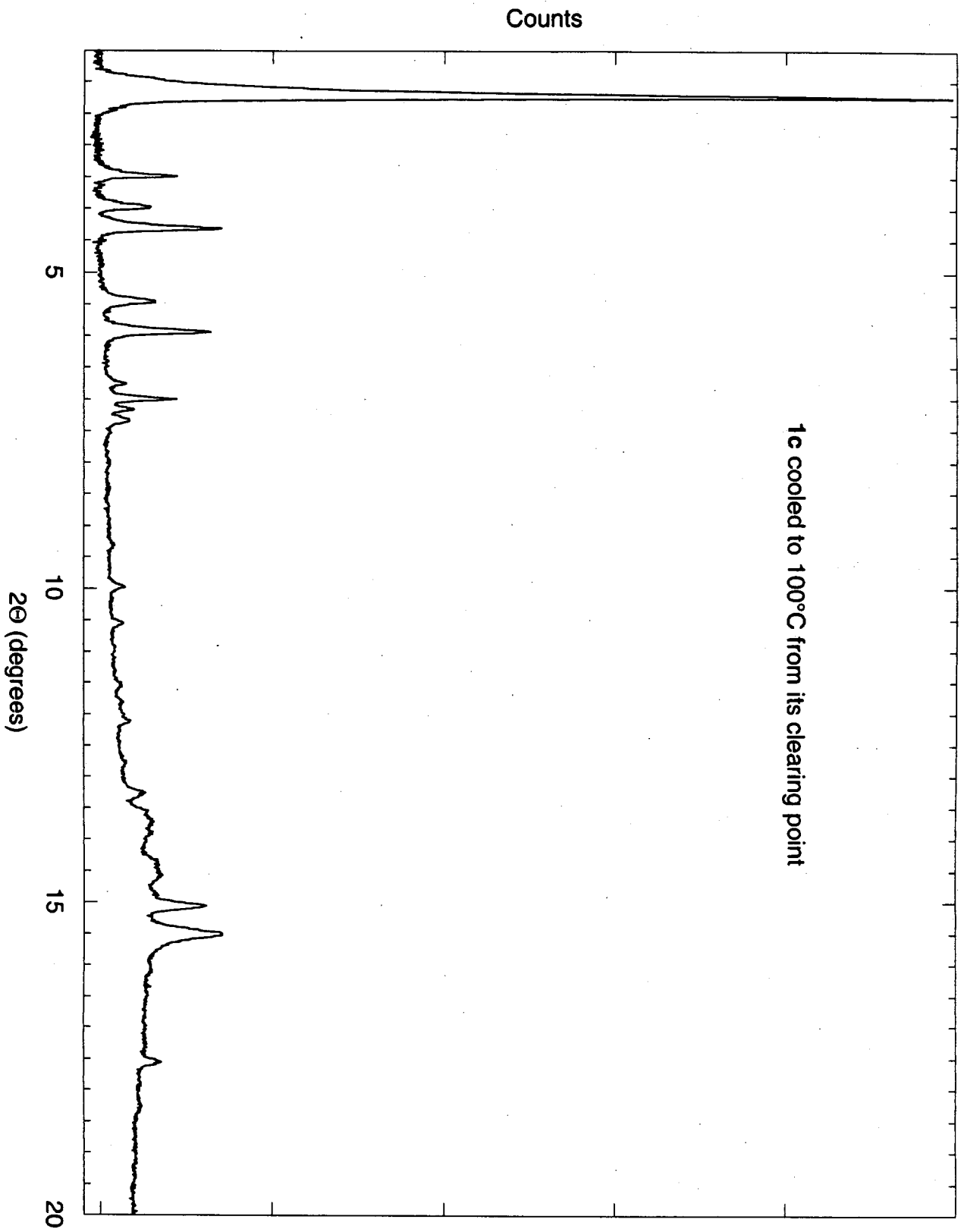
Differential Scanning Calorimetry. DSC was performed on a Perkin-Elmer Pyris 1. Between 1 and 3 mgs for of each of the sample was weighed into aluminum calorimetry pans. The pans were sealed and analyzed. The scan rate was 20°C/min.

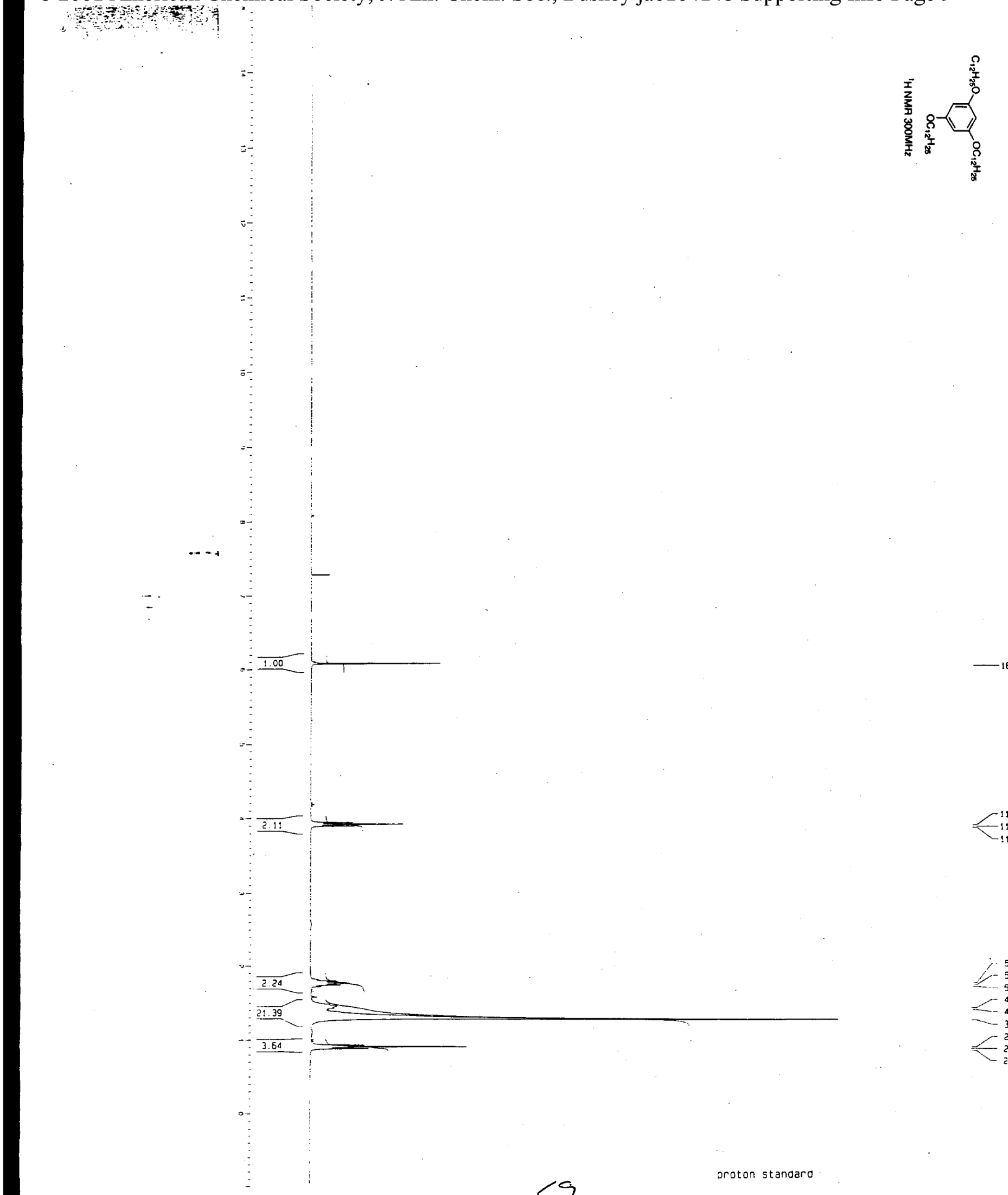
Variable temperature IR. The glass windows were removed from the Linkam TMS 350E heating and cooling stage, and it was mounted in a Perkin-Elmer Paragon 3000 FT-IR spectrometer. Samples were heated on KBr plates and their IR spectra recorded.

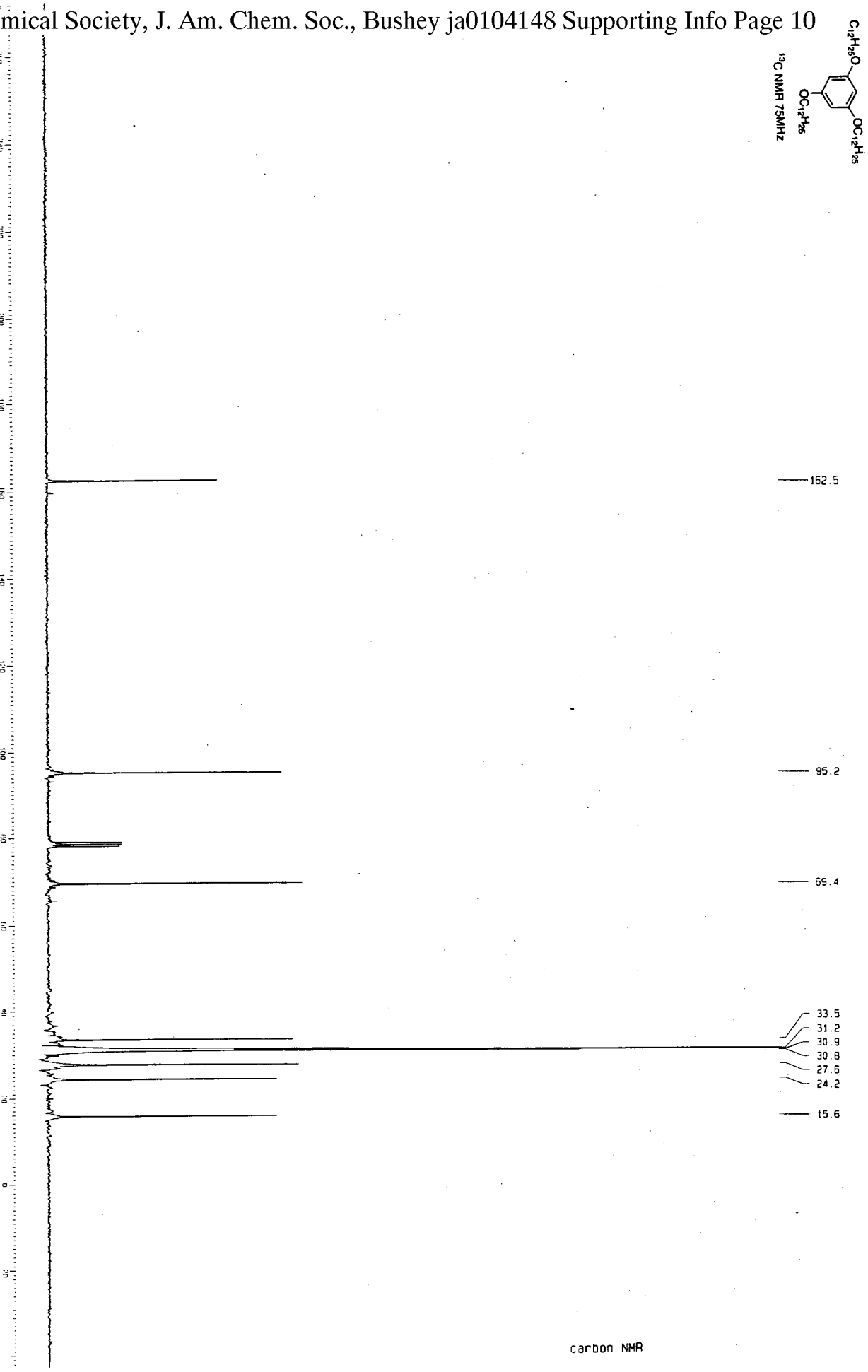

Intensity
4
8
12
16
20
2Θ (degrees)
1d at room temperature

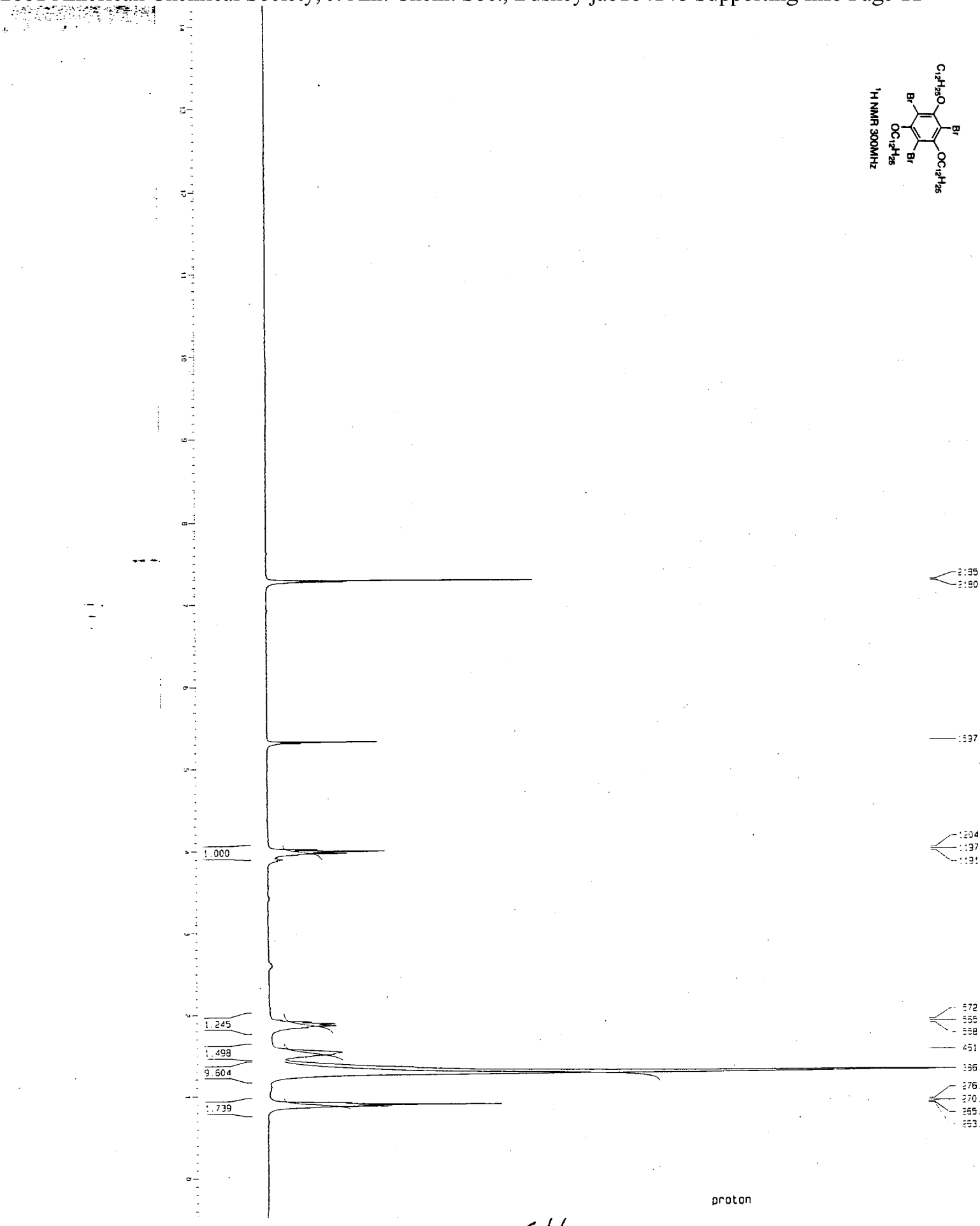

Intensity
4
8
12
16
20
2Θ (degrees)
1d at 60°C

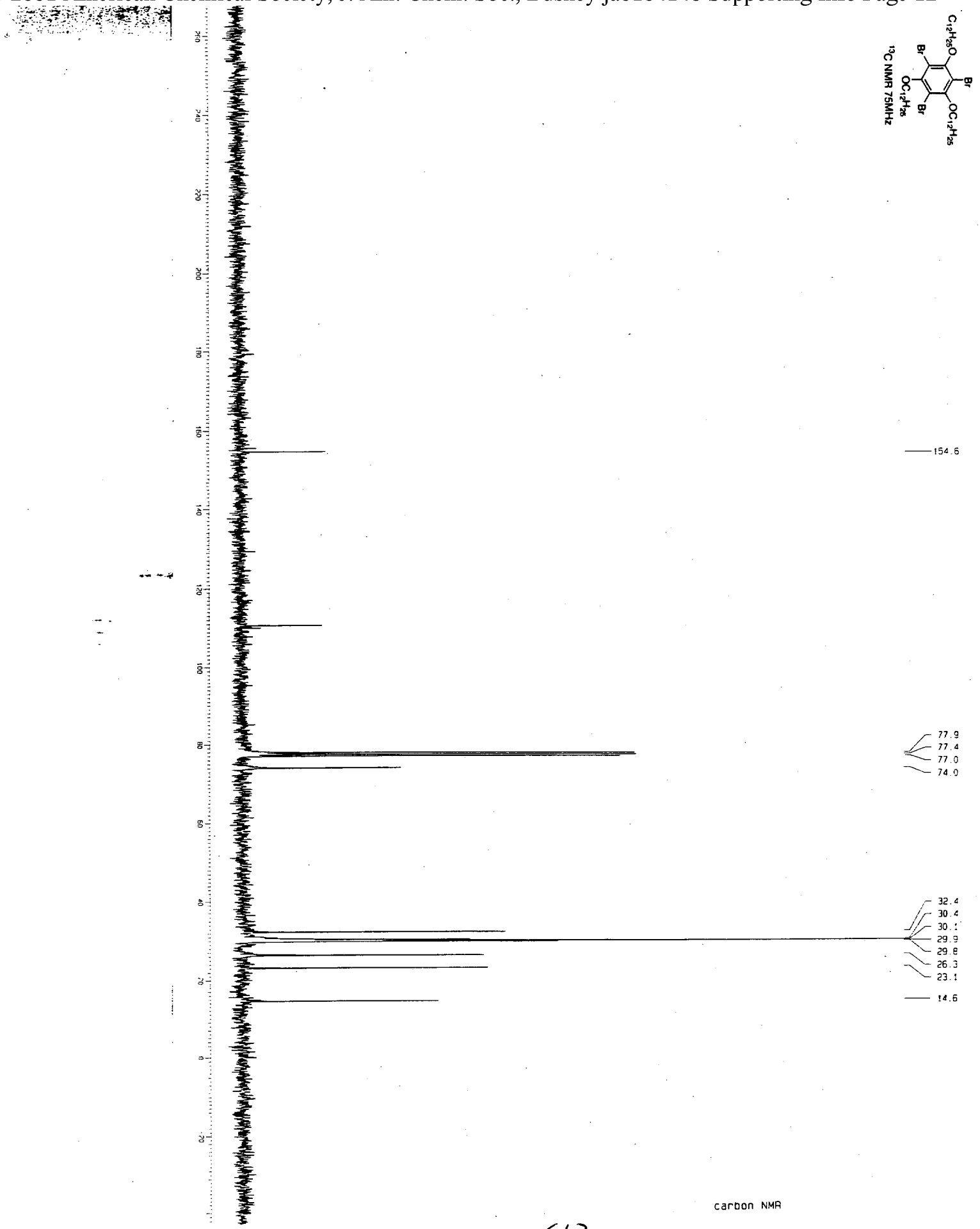



Counts
5
10
15
20
2Θ (degrees)
1c cooled to 100°C from its clearing point

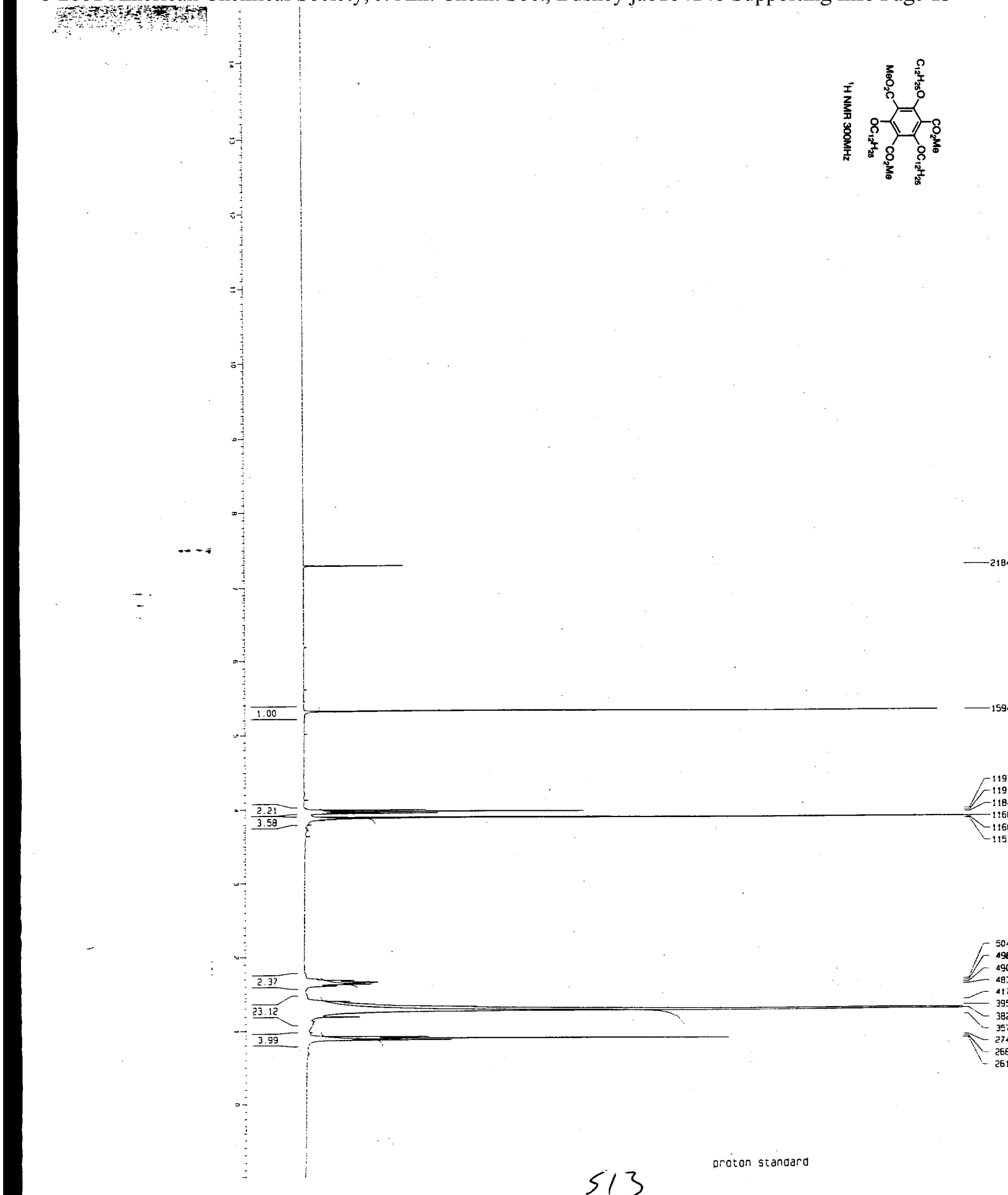



^{13}C NMR 75MHz
$C_{12}H_{25}O$
$OC_{12}H_{25}$
$OC_{12}H_{25}$
162.5
95.2
69.4
33.5
31.2
30.9
30.8
27.6
24.2
15.6
carbon NMR

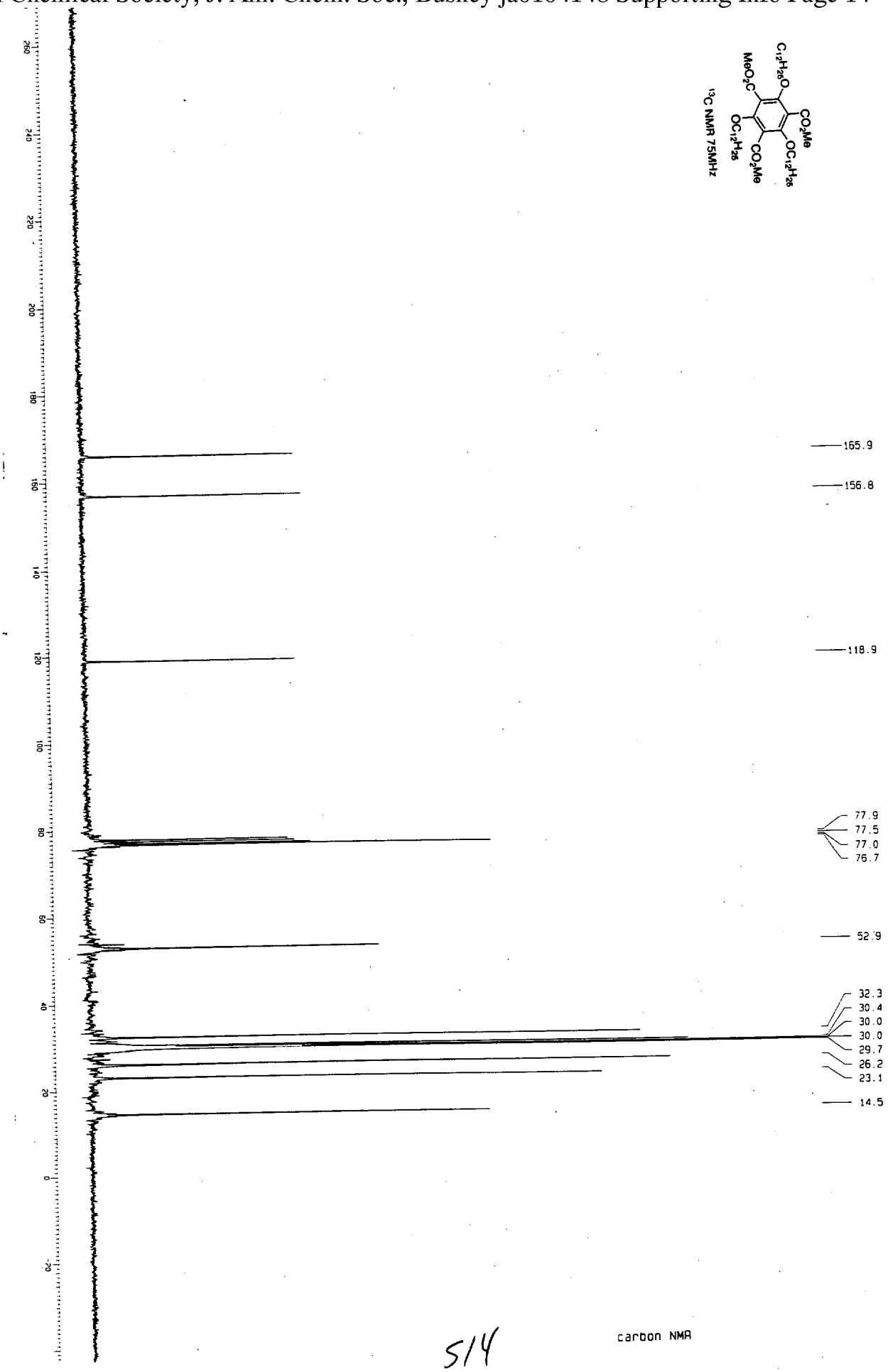




S12



513



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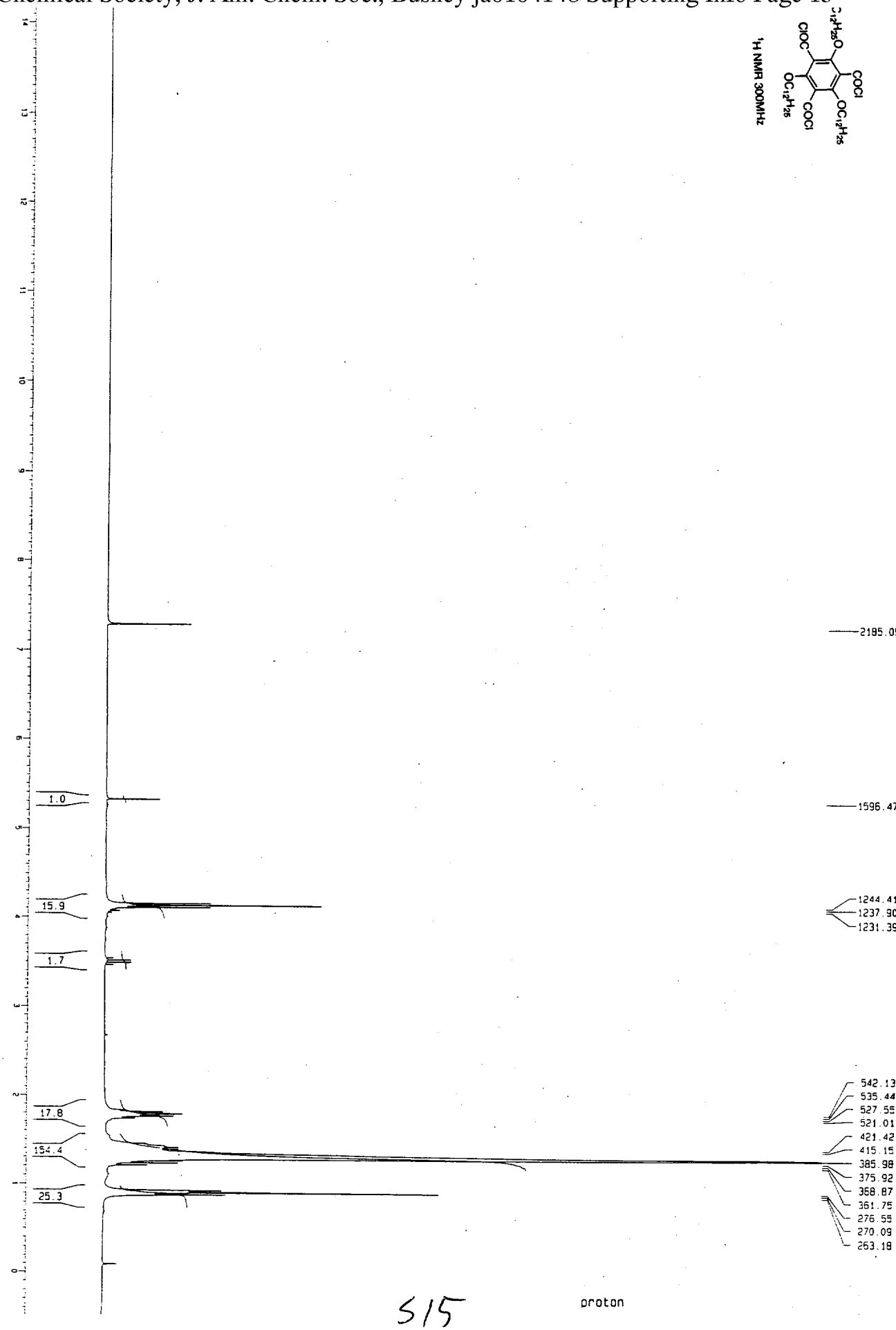
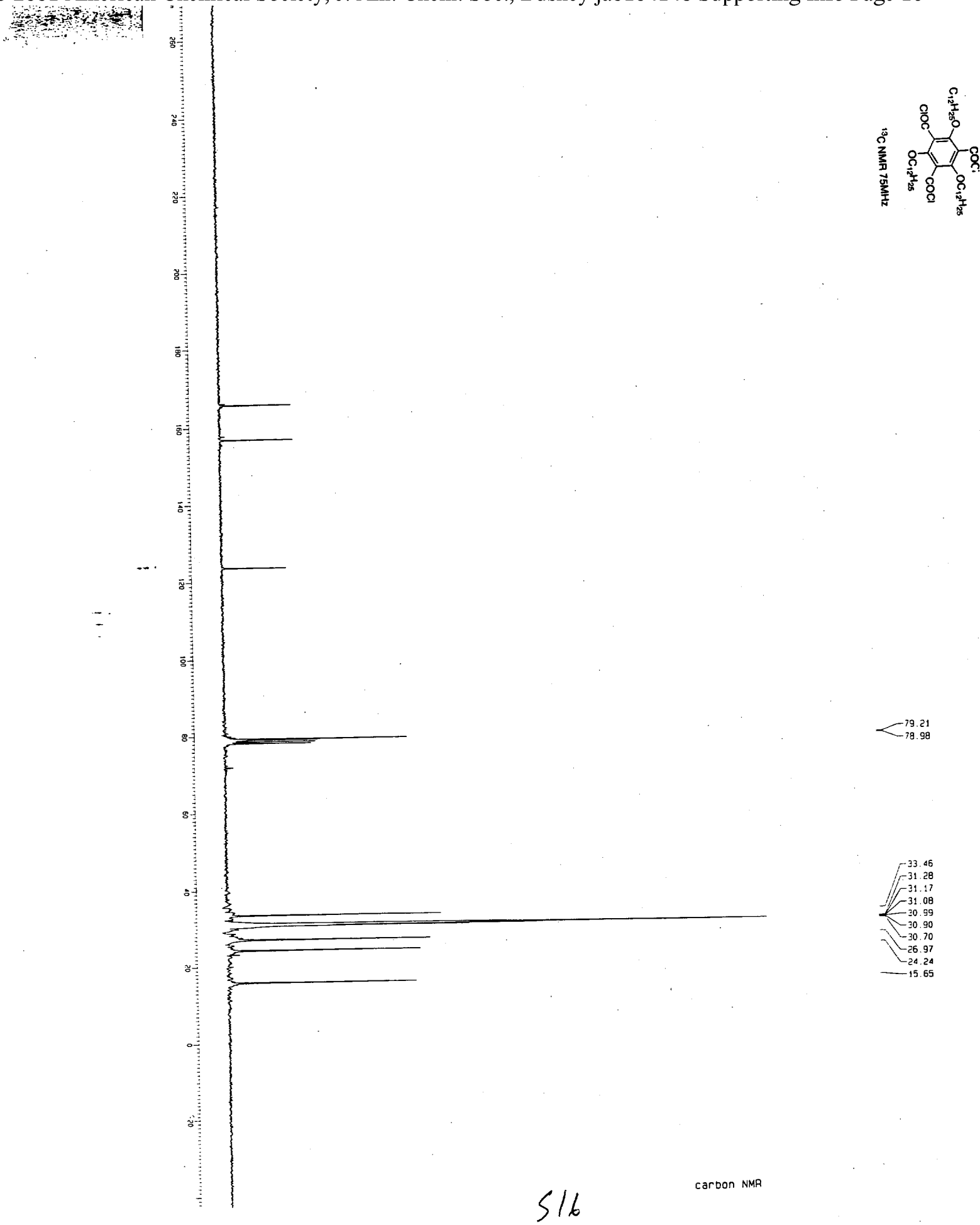
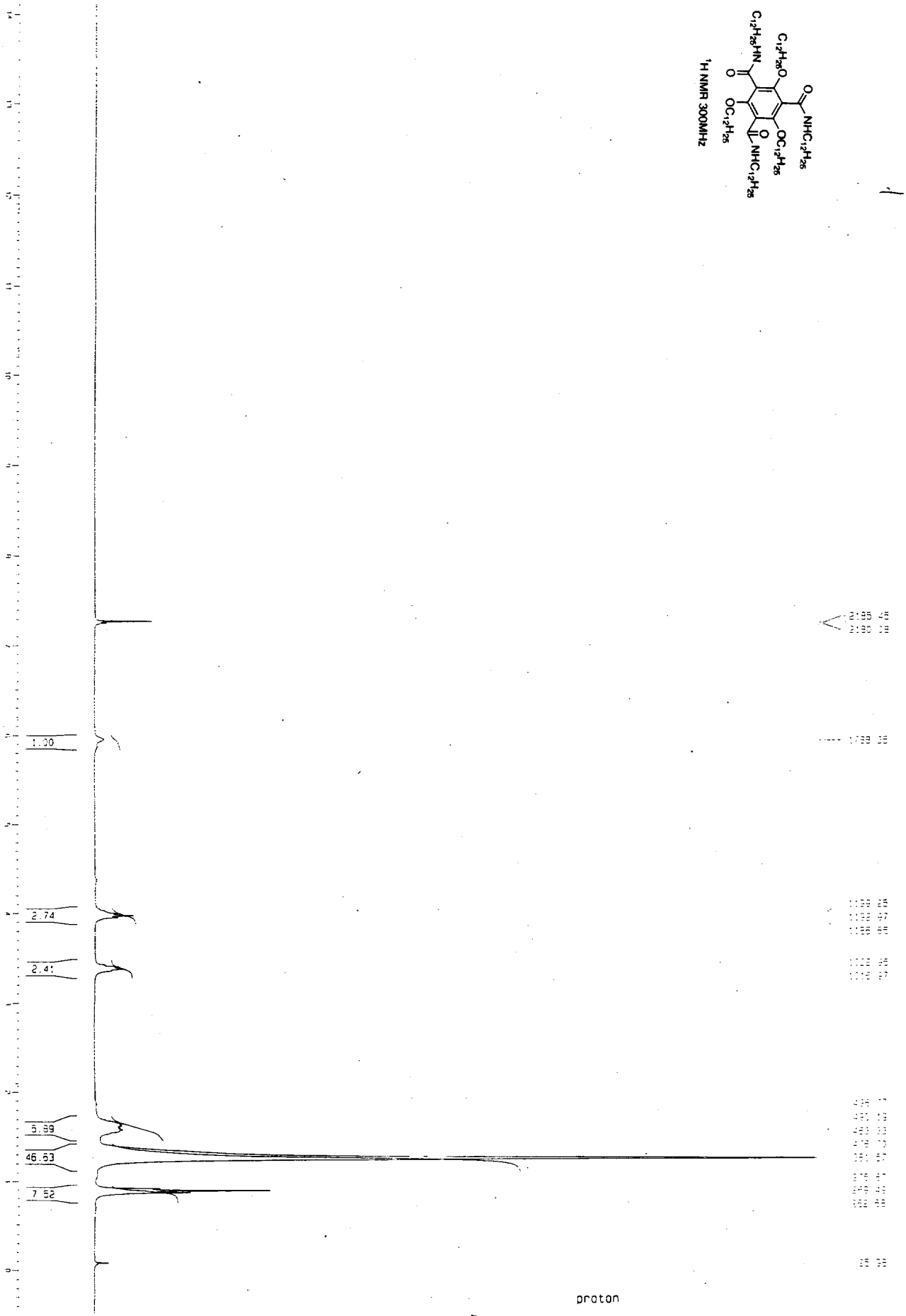


S15

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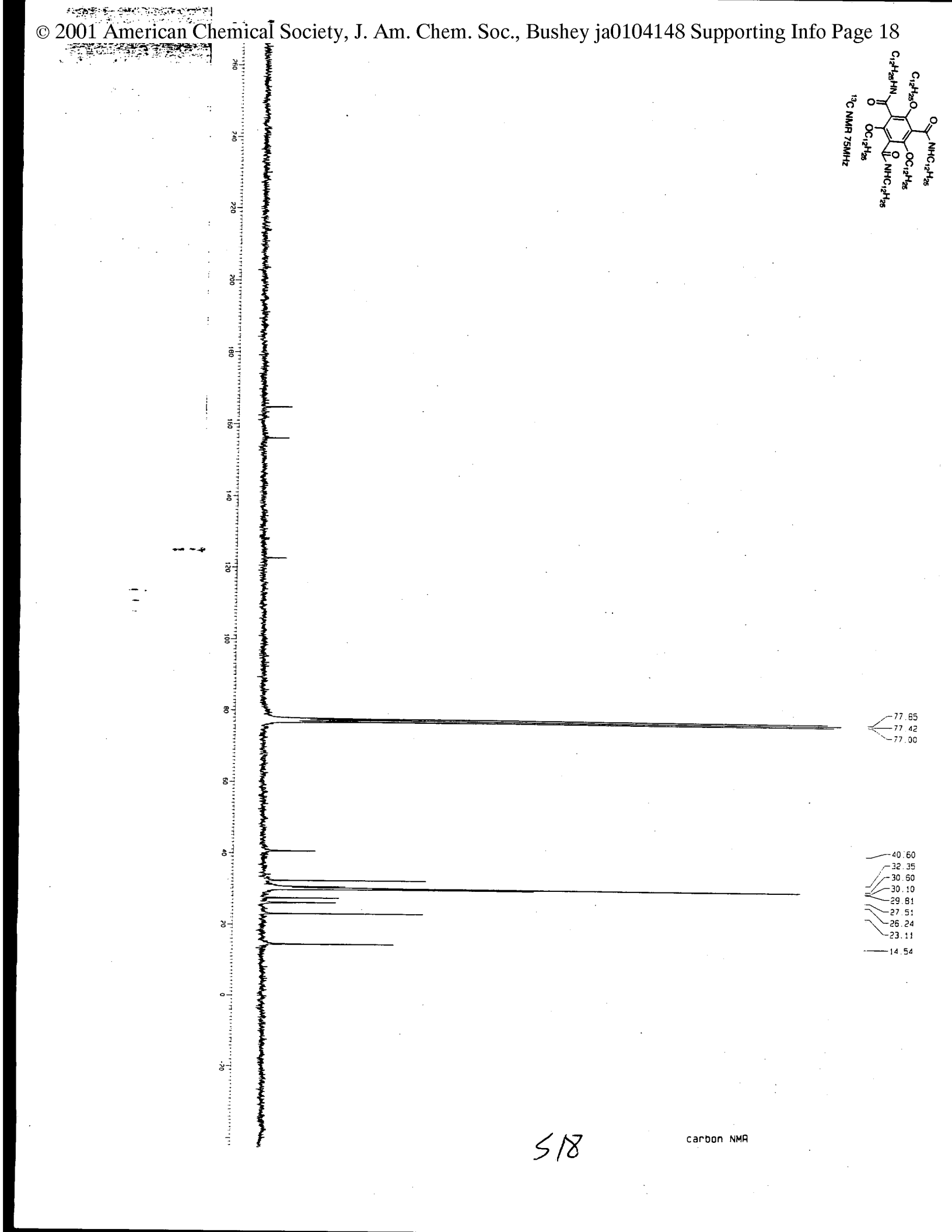
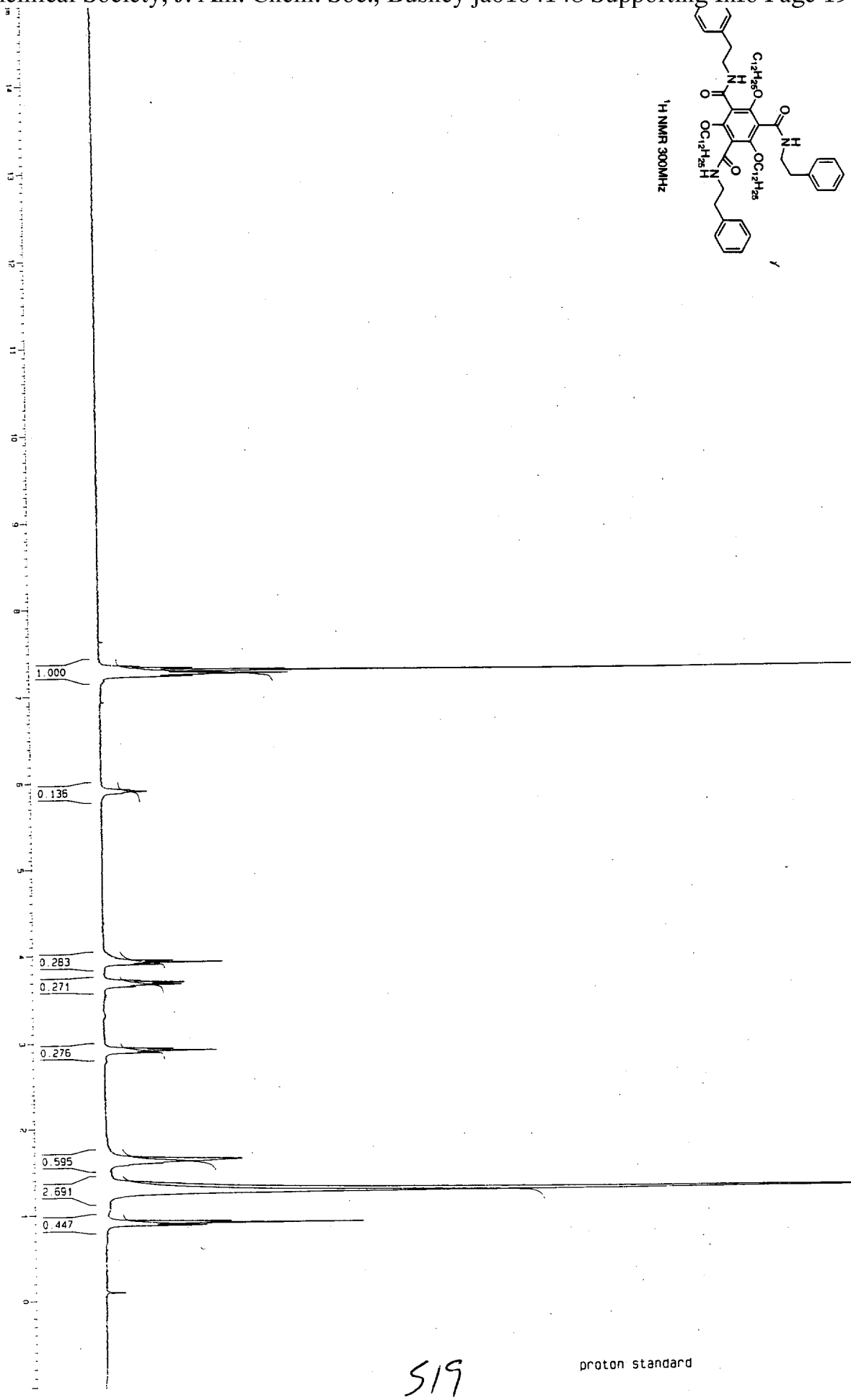
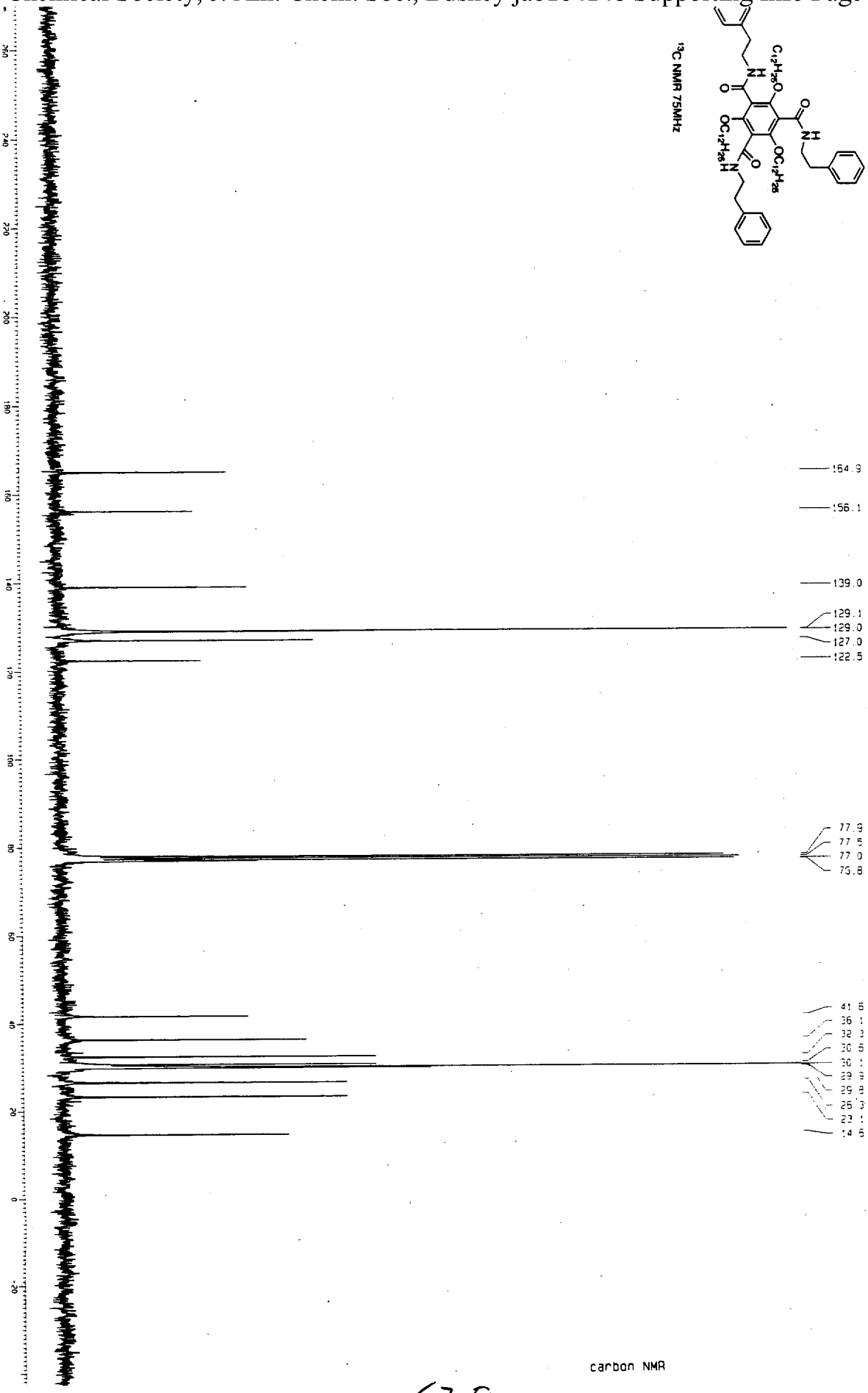
1.00
2.74
2.41
5.99
46.63
7.52
proton

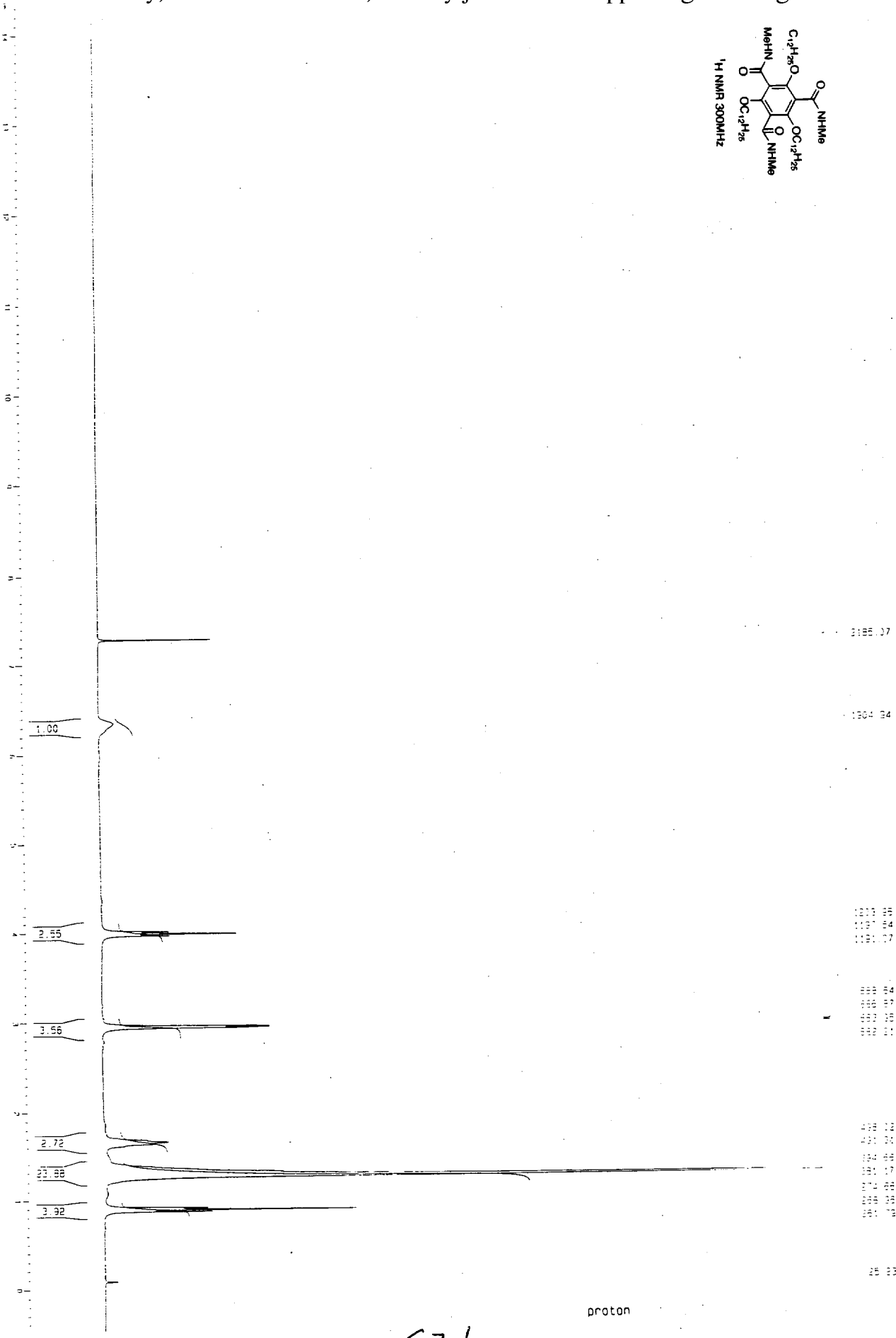



^{1}H NMR 300MHz
1.000
0.136
0.283
0.271
0.276
0.595
2.691
0.447
519
proton standard

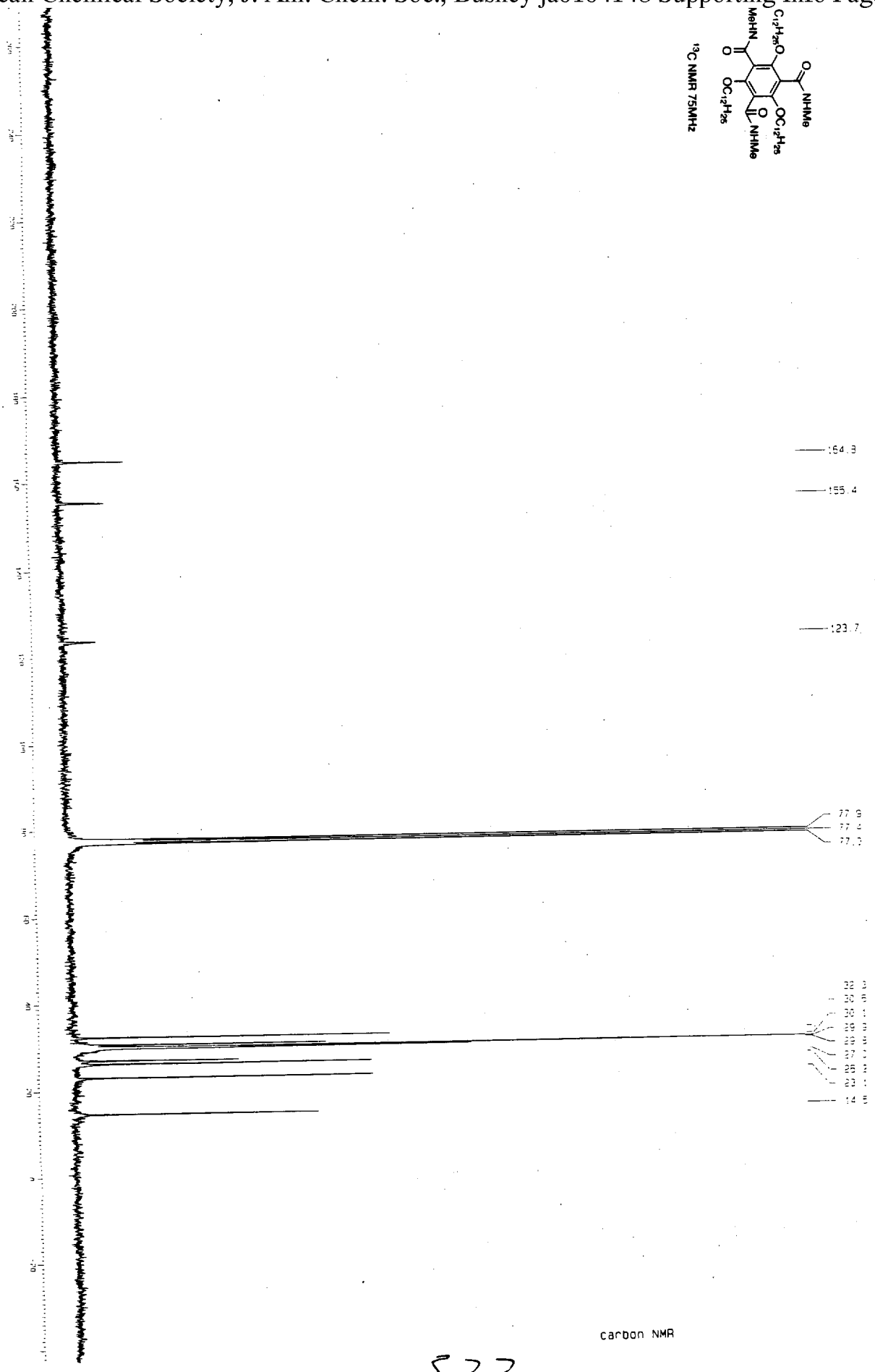


carbon NMR

520

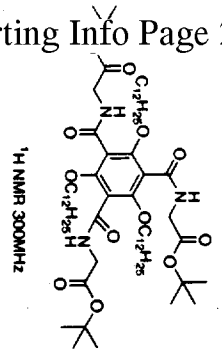

^{1}H NMR 300MHz
MeHN
$C_{12}H_{25}O$
NHMe
$OC_{12}H_{25}$
1.00
2.55
3.56
2.72
23.88
3.92
proton

S21



carbon NMR

522



523

proton standard