Allylic acetate 40. To a cooled (-20°C) solution of thiazole **28** (241 mg, 0.5 mmol) in 7 mL of THF was added 0.7 mL of buffered TBAF solution (1.0 M in THF with 20 mol % acetic acid added). After 1.5 h, the reaction was quenched with 3 mL of pH 7 buffer, diluted with 10 mL CH_2Cl_2 and warmed to 25°C. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography to give 156 mg (98%) of the alcohol as a yellow oil: R_f = 0.16 (1:1-EtOAc:hexanes); IR (thin film) 3706-3047, 2977, 2955, 1725, 1225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 5.97 (dq, *J* = 1.2, 8.7 Hz, 1H), 4.79 (dt, *J* = 5.7, 8.7 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.26 (d, *J* = 5.7 Hz, 2H), 2.90-3.20 (br s, 1H), 2.28 (d, *J* = 1.2 Hz, 3H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 161.2, 146.7, 132.8, 127.6, 124.6, 68.0, 61.5, 40.1, 24.0, 14.3; HRMS (FAB) Calcd for $C_{11}H_{14}{}^{81}BrNO_3S$[M+H]: 321.9935. Found: 321.9926. To a solution of the alcohol (156 mg, 0.5 mmol) in 5 mL of CH_2Cl_2 was added acetic anhydride (0.070 mL, 0.74 mmol), pyridine (0.060 mL, 0.74 mmol) and DMAP (6 mg, 0.05 mmol) sequentially. After 2.5 h, the reaction was quenched with 1 mL pH 7 buffer and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography on SiO_2 eluting with hexanes:EtOAc (4:1 → 1:1) gave 149.8 mg (83%) of acetate **40** as a clear colorless oil: R_f = 0.67 (1:1-EtOAc:hexanes); IR (thin film) 2986, 1739, 1229, 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 5.85 (dq, *J* = 1.2, 9.6 Hz, 1H), 5.70 (ddd, *J* = 5.7, 7.2, 9.6 Hz, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.42 (dd, *J* = 7.2, 14.9 Hz, 1H), 3.35 (dd, *J* = 5.7, 14.9 Hz, 1H), 2.33 (d, *J* = 1.2 Hz, 3H), 2.06 (s, 3H), 1.41 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 165.4, 161.2, 147.0, 128.6, 128.0, 127.8, 69.6, 61.5, 38.0, 24.4, 21.0, 14.4; HRMS (FAB) Calcd for $C_{13}H_{16}{}^{79}BrNO_4S$[M+H]: 362.0061. Found: 362.0063.

Triene 41. A solution of bromide **28** (9.8 mg, 0.02 mmol) in 0.1 mL of N-methyl pyrrolidinone (NMP) was degassed by several freeze/thaw cycles. Trifurylphosphine (0.6 mg, 0.002 mmol) and Pd_2dba_3 (0.9 mg, 0.0009 mmol) were added as solids resulting in a yellow homogenous solution. To this was added a solution of stannane **4** in 0.3 mL of NMP. After 18 h, the reaction was partitioned betweeen Et_2O and 10% aqueous NH_4OH. The aqueous layer was extracted with Et_2O and the combined organic layers were dried over Na_2SO_4. Concentration *in vacuo* and purification of the residue by flash chromatography on SiO_2 eluting with hexanes:EtOAc:Et_3N (89:10:1 → 79:20:1) to hexanes:acetone:Et_3N (79:20:1 → 77:20:3) gave 46 mg (46%) of triene **41** as a clear colorless oil: IR (thin film) 2943, 2863, 1719, 1066 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 6.24 (d, J = 15.9, 1H), 6.13 (d, J = 15.9 Hz, 1H), 5.60 (t, J = 6.9 Hz, 1H), 5.49 (d, J = 8.7 Hz, 1H), 5.02 (dt, J = 5.7, 8.4 Hz, 1H), 4.42 (q, J = 6.9 Hz, 2H), 3.35 (dd, J = 6.3, 14.4 Hz, 1H), 3.25 (dd, J = 5.4, 14.4 Hz, 1H), 3.06 (d, J = 6.6 Hz, 2H), 2.23 (s, 6H), 1.79 (s, 3H), 1.70 (s, 3H), 1.39 (t, J = 6.9 Hz, 3H), 1.01 (s, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 161.8, 146.5, 134.4, 134.0, 133.0, 131.6, 128.3, 69.0, 61.5, 57.3, 45.4, 42.7, 18.2, 18.1, 14.6, 13.4, 13.0, 12.6.

Triene 42. A stirred solution of bromide **40** (21 mg, 0.057 mmol) in 0.3 mL of THF was degassed by several freeze/thaw cycles. Trifurylphosphine (3.3 mg, 0.014 mmol) and Pd_2dba_3 (2.7 mg, 0.003 mmol) were added as solids resulting in a yellow-green colored homogenous solution after 15 min. A solution of stannane **4** in 0.3 mL of THF was then added via cannula. After 46 h, the reaction was diluted with EtOAc, filtered through Celite and concentrated *in vacuo*. Purification of the residue by flash chromatography on SiO_2 eluting with hexanes:EtOAc (4:1 → 0:1) to hexanes:acetone:Et_3N (35:6:1 → 24:25:1) gave 12.3 mg (53%) of triene **42** as an orange-yellow oil: IR ($CHCl_3$) 3017, 2971, 2926, 1797, 1715, 1214 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.34 (d, J = 15.9 Hz, 1H), 6.17 (d, J = 15.9 Hz, 1H), 5.93 (ddd, J = 5.9, 7.4, 9.3 Hz, 1H), 5.63 (t, J = 6.6 Hz, 1H), 5.44 (d, J = 9.3 Hz, 1H), 4.43

(q, J = 7.2 Hz, 2H), 3.45 (dd, J = 7.4, 14.9 Hz, 1H), 3.38 (dd, J = 5.9, 14.9 Hz, 1H), 3.05 (d, J = 6.9 Hz, 2H), 2.34 (s, 6H), 2.05 (s, 3H), 1.87 (d, J = 1.2 Hz, 3H), 1.79 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 166.2, 161.3, 146.8, 139.2, 135.8, 134.4, 130.7, 130.4, 127.9, 127.0, 69.9, 61.4, 57.2, 45.3, 38.7, 21.1, 14.4, 13.2, 12.6; HRMS (FAB) Calcd for $C_{21}H_{30}{}^{79}BrN_2O_4S$[M+Na]: 429.1836. Found:429.1824.

β-Hydroxyester 44. To a cooled (0°C) solution of diisopropylamine (6.82 mL, 52 mmol) in 200 mL of THF was added 21.0 mL of an *n*-butyllithium solution (48 mmol, 2.3 M in hexanes). After 30 min, the solution was cooled to -78°C and methyl acetate (3.82 mL, 48 mmol) was added. Hydrocinnamaldehyde (5.27 mL, 40 mmol) was added to the flask after an additional 30 min. The reaction was partitioned between pH 7 buffer and EtOAc after 7 h and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with NH_4Cl, H_2O, then brine, and dried over Na_2SO_4. Purification by flash chromatography on SiO_2 eluting with hexanes:EtOAc (7:3) gave 6.66 g (80%) of ester **44** as a clear colorless oil which correlated with data previously reported for this compound[41]: R_f = 0.40 (3:7-EtOAc:hexanes); IR (thin film) 3453, 3026, 2950, 2860, 1719, 1602, 1495 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.15-7.25 (m, 5H), 4.06 (m, 1H), 3.73 (s, 3H), 2.66-2.92 (m, 2H), 2.44-2.60 (m, 2H), 1.72-1.94 (m, 2H); ^{13}C NMR (300 MHz) δ 173.5, 141.9, 128.6, 128.6, 126.1, 67.4, 51.9, 41.3, 38.3, 31.9; HRMS (FAB) Calcd for $C_{12}H_{17}O_3$[M+H]: 209.1178. Found: 209.1184.

β-Hydroxyamide 45. To a cooled (0°C) suspension of *O*-benzylhydroxylamine hydrochloride (2.71 g, 17 mmol) in 20 mL of CH_2Cl_2 was added 8.5 mL of trimethylaluminum (17 mmol, 2.0 M in hexanes) and the solution was warmed to 25°C. After 1 h, the solution was recooled to 0°C and a solution of β-hydroxyester **44** (1.99 g, 9.6 mmol) in 10 mL of CH_2Cl_2 solution was added dropwise. After stirring for 12 h at 25°C, the reaction was cooled to 0°C and quenched with 50 mL of 10% aqueous citric acid. After 1 h, the layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with 10%

aqueous citric acid, saturated $NaHCO_3$ and brine then dried over Na_2SO_4. Concentration *in vacuo* gave white crystals that were washed with Et_2O to yield 1.79 g (63%) of amide **45** which was of sufficient purity to be used in the next step without further purification: R_f = 0.41 (1:1-EtOAc:hexanes); ^{1}H NMR (300 MHz, d_6-DMSO) δ 7.15-7.45 (m, 10H), 4.81 (s, 2H), 3.80-3.95 (m, 1H), 2.66-2.80 (m, 1H), 2.50-2.66 (m, 1H), 2.13 (d, *J* = 6.6 Hz, 2H), 1.52-1.76 (m, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) δ 167.7, 142.2, 136.1, 128.7, 128.3, 128.24, 128.18, 125.6, 76.8, 66.4, 40.9, 40.3, 38.8; HRMS (FAB) Calcd for $C_{18}H_{22}NO_3$[M+H]: 300.1600. Found: 300.1612.

β-Lactam 46a. To a solution of β-hydroxyamide **45** (1.6 g, 5.4 mmol) in 37 mL of acetonitrile was added 1.35 mL of carbon tetrachloride (14.0 mmol), 0.82 mL of Et_3N (5.9 mmol), and triphenylphosphine (1.55 g, 5.9 mmol). After stirring 12 h, the solvent was removed *in vacuo*. The residue was recrystallized from EtOAc/hexanes to give a white crystalline solid that was discarded (Ph_3P=O). The mother liquor was purified by flash chromatography on SiO_2 eluting with hexanes:EtOAc (7:3) to give 1.03 g (68%) of lactam **46a** as a white crystalline solid: IR (thin film) 3231, 3063, 3027, 2951, 2851, 1773, 1495, 1453 cm^1; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00-7.60 (m, 5H), 4.95 (s, 2H), 3.43-3.57 (m, 1H), 2.67 (dd, *J* = 5.1, 13.5 Hz, 1 H), 2.50-2.64 (m, 2H), 2.24 (dd, *J* = 2.7, 13.5 Hz, 1H), 1.90-2.06 (m, 1H), 1.60-1.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 140.8, 135.5, 129.4, 129.1, 128.8, 128.7, 128.5, 128.4, 126.4, 78.4, 57.7, 38.0, 34.2, 32.0; HRMS (FAB) Calcd for $C_{18}H_{20}NO_2$[M+H]: 282.1494. Found: 282.1506.

β-Lactam 46b. A solution of β-lactam (1.18 g, 4.2 mmol) in 2.4 mL of THF and 1.5 mL of water (83 mmol) was deoxygenated by several freeze/thaw cycles. To this solution was added 42 mL of SmI_2 solution (12.6 mmol, 0.3 M in Et_2O). After stirring for 10 h, the reaction was partitioned between EtOAc and saturated $NaHCO_3$ and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with $Na_2S_2O_3$, water, and brine and then dried

over Na_2SO_4. Concentration *in vacuo* followed by purification by flash chromatography eluting with hexanes:EtOAc (2:3) gave 652 mg (88%) of a white amorphous solid: R_f = 0.50 (1:1-EtOAc:hexanes) IR (thin film) 3252, 3026, 2938, 1735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.16-7.36 (m, 5H), 5.90-6.15 (br s, 1H), 3.53-3.69 (m, 1H), 3.03 (ddd, *J* = 1.8, 5.1, 14.9 Hz, 1H), 2.67 (td, *J* = 1.8, 7.5 Hz, 2H), 2.55 (dd, *J* = 1.8, 14.9 Hz, 1H), 1.95 (dd, *J* = 7.8, 14.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 168.2, 140.6, 129.1, 128.4, 128.4, 128.3, 128.2, 126.8, 126.1, 60.3, 47.6, 43.3, 36.8, 32.6, 20.9, 14.1; HRMS (FAB) Calcd for $C_{11}H_{14}NO$[M+H]: 176.1075. Found: 176.1073.

***N*-Boc-β-lactam 46c.** To a solution of β-lactam **46b** (105 mg, 0.6 mmol) in 3.0 mL of CH_2Cl_2 was added a solution of di-*tert*-butyl dicarbonate (605 mg, 2.8 mmol) and dimethylaminopyridine (10 mg, 0.08 mmol) in 1 mL of CH_2Cl_2 at 25°C followed by 0.4 mL of Et_3N (2.73 mmol). After 2 h, the reaction was quenched with 1 mL pH 7 buffer and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 eluting with hexanes:EtOAc (1:4) to give 124 mg (75%) of lactam **46c** as a clear colorless oil: R_f = 0.50 (3:7-EtOAc:hexanes); IR (thin film) 3409, 3112, 2975, 2949, 2932, 2869, 1813, 1715 cm^{-1}; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.16-7.34 (m, 5H), 3.92 (qt, *J* = 3.3, 6.0 Hz, 1H), 3.01 (dd, *J* = 6.0, 16.1 Hz, 1H), 2.67 (t, *J* = 8.0 Hz, 2H), 2.56 (dd, *J* = 3.3, 16.1 Hz, 1H), 2.39-2.50 (m, 1H), 1.77-1.90 (m, 1H), 1.49 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 160.5, 148.0, 140.6, 128.7, 128.3, 126.3, 83.2, 51.2, 42.1, 34.4, 31.6, 28.1; HRMS (FAB) Calcd for $C_{16}H_{22}NO_3$[M+H]: 276.1600. Found: 276.1608.

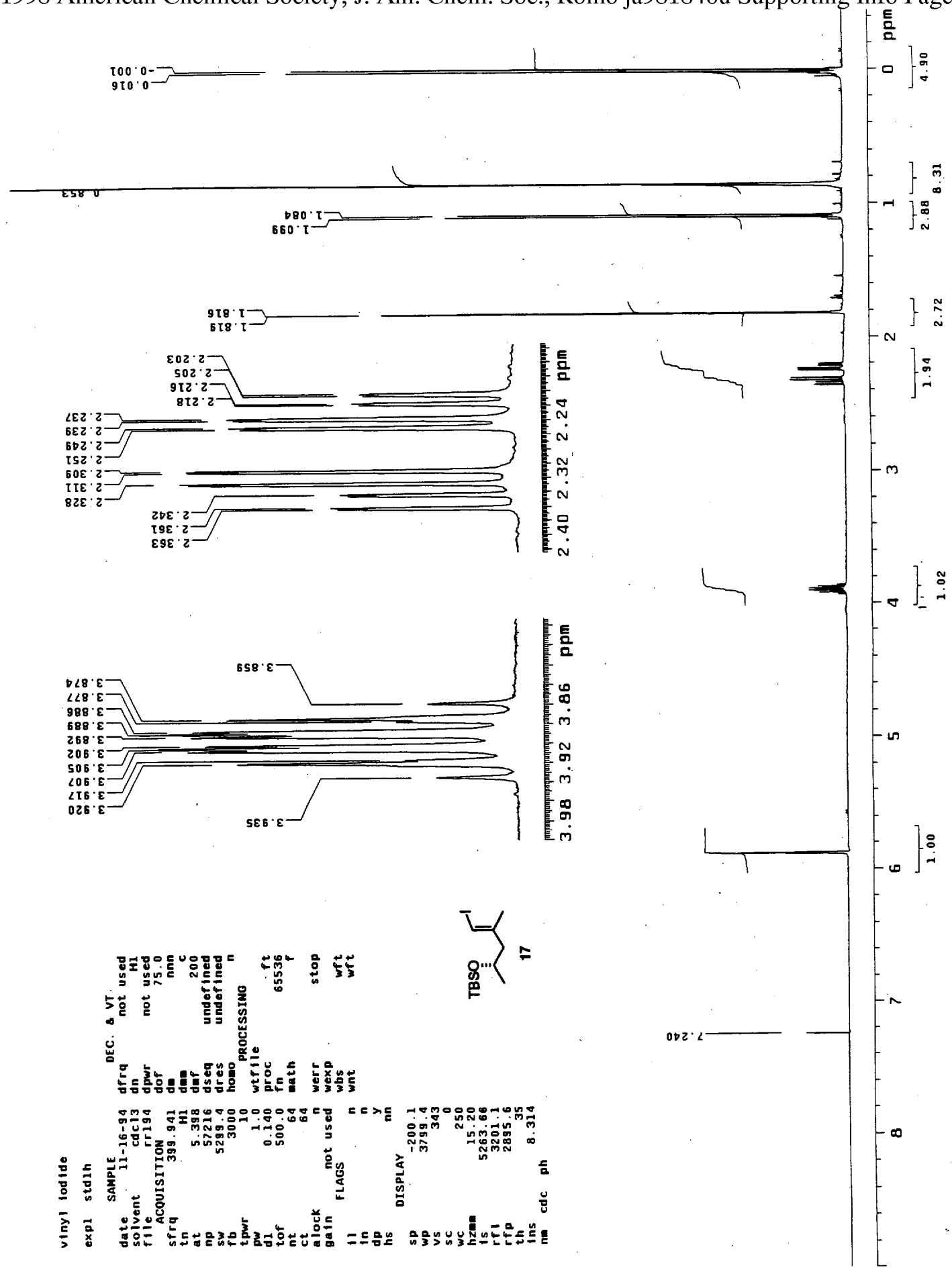
N-Trifluoroacetyl-β-lactam 46d. This compound was prepared using a similar procedure as for β-lactam **46c** using lactam **46b** (76 mg, 0.4 mmol), trifluoracetic anhydride (0.094 mL, 0.7 mmol) and pyridine (0.057 mL, 0.7 mmol) in 4.5 mL of CH_2Cl_2 to give 55 mg

(46%) of lactam **46d**: R_f = 0.48 (3:7-EtOAc:hexanes); IR (thin film) 3424, 3084, 3064, 3026, 2952, 2652, 2860, 1818, 1724 cm^{-1}; ^1H NMR (200 Mhz, $CDCl_3$) δ 7.2-7.5 (m, 5H), 4.15 (m, 1H), 3.23 (dd, *J* = 6.6, 16.9, 1H), 2.75 (dd, J = 4.0, 16.9, 1H), 2.5-2.8 (m, 2H), 1.8-2.0 (m, 2H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 161.4, 140.0, 129.0, 128.5, 126.8, 51.4, 43.0, 33.7, 31.6.

β-Aminoester 47a. Performed as described below for β-aminoester **47c** using 48 mg (0.2 mmol) of β-lactam **46a**, 0.094 mL of sodium bis(trimethylsilyl)amide (0.19 mmol, 2.0 M in THF), and 0.013 mL of isopropyl alcohol (0.2 mmol) in 1 mL of THF. Purification by flash chromatography on SiO_2 eluting with hexanes/EtOAc (17:3) gave 39 mg (67%) of β-lactam **47a**. IR (thin film) 3027, 2979, 2932, 1719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15-7.35 (m, 10H), 5.00 (m, 1H), 4.71 (s, 2H), 3.35 (m, 2H), 2.45 (m, 1H), 2.45-2.47 (m, 2H), 1.60-2.00 (m, 2H), 1.20-1.22 (m, 6H); ^{13}C (75 MHz, $CDCl_3$) δ 171.8, 141.8, 137.9, 128.4, 128.3, 128.3, 127.8, 125.8, 76.4, 67.7, 57.1, 37.2, 33.6, 32.3, 21.8; HRMS (FAB) Calcd for $C_{21}H_{27}NO_3$[M+H]: 342.2069. Found 342.2086.

β-Aminoester 47c. To a cooled (-42°C) solution of 0.010 mL of isopropyl alcohol (0.15 mmol) in 0.5 mL of THF was added 0.080 mL of sodium bis(trimethylsilyl)amide (0.16 mmol, 2.0 M in THF). After 30 minutes, a solution of β-lactam **46c** (39 mg, 0.15 mmol) in 1 mL of THF was transferred via cannula. After 1.5 hours, the reaction was quenched with pH 7 buffer, warmed to 25°C and extracted with EtOAc. The combined organic layers were washed with water and brine, then dried over Na_2SO_4. Purification by flash chromatography on SiO_2 eluting with hexanes:EtOAc (17:3) gave 39 mg (80%) of ester **47c** as solid: R_f = 0.61 (3:7-EtOAc:hexanes); IR (thin film) 3303, 2975, 1736, 1678, 1536 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.12-7.35 (m, 5H), 5.01 (app quin, *J* = 6.0 Hz, 1H), 3.90-4.10 (m, 1H), 2.60-2.77 (m, 2H), 2.42-2.58 (m, 2H), 1.70-1.90 (m, 2H), 1.55-1.70 (br s, 1H), 1.45 (s, 9H), 1.23 (d, *J* = 6.0 Hz,

6H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 171.1, 155.3, 141.5, 128.4, 128.3, 125.9, 79.2, 68.0, 47.5, 39.6, 36.5, 32.5, 28.3, 21.8, 21.7, 16.1; HRMS (FAB) Calcd for $C_{19}H_{30}NO_4$[M+H]: 336.2135. Found: 336.2181.



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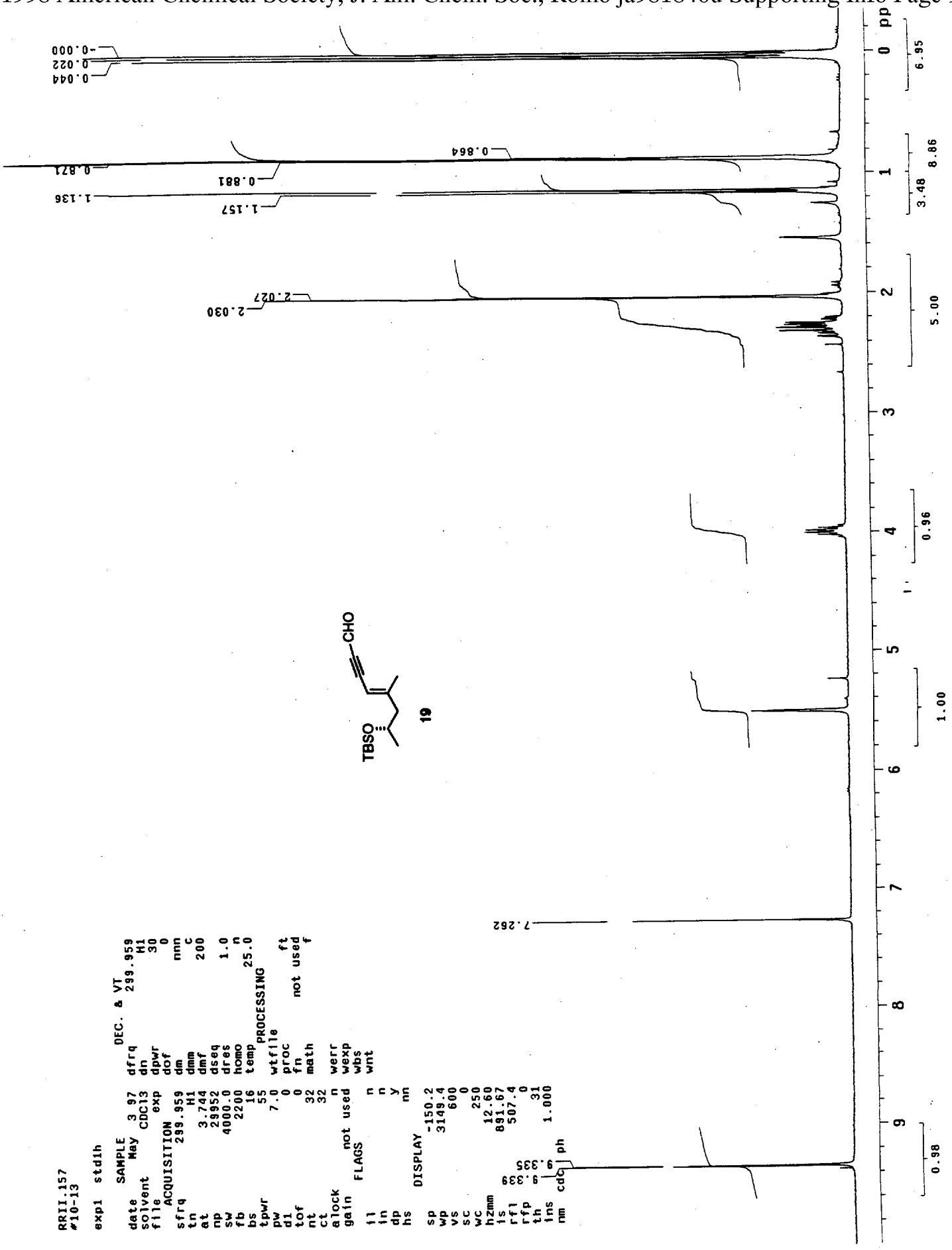

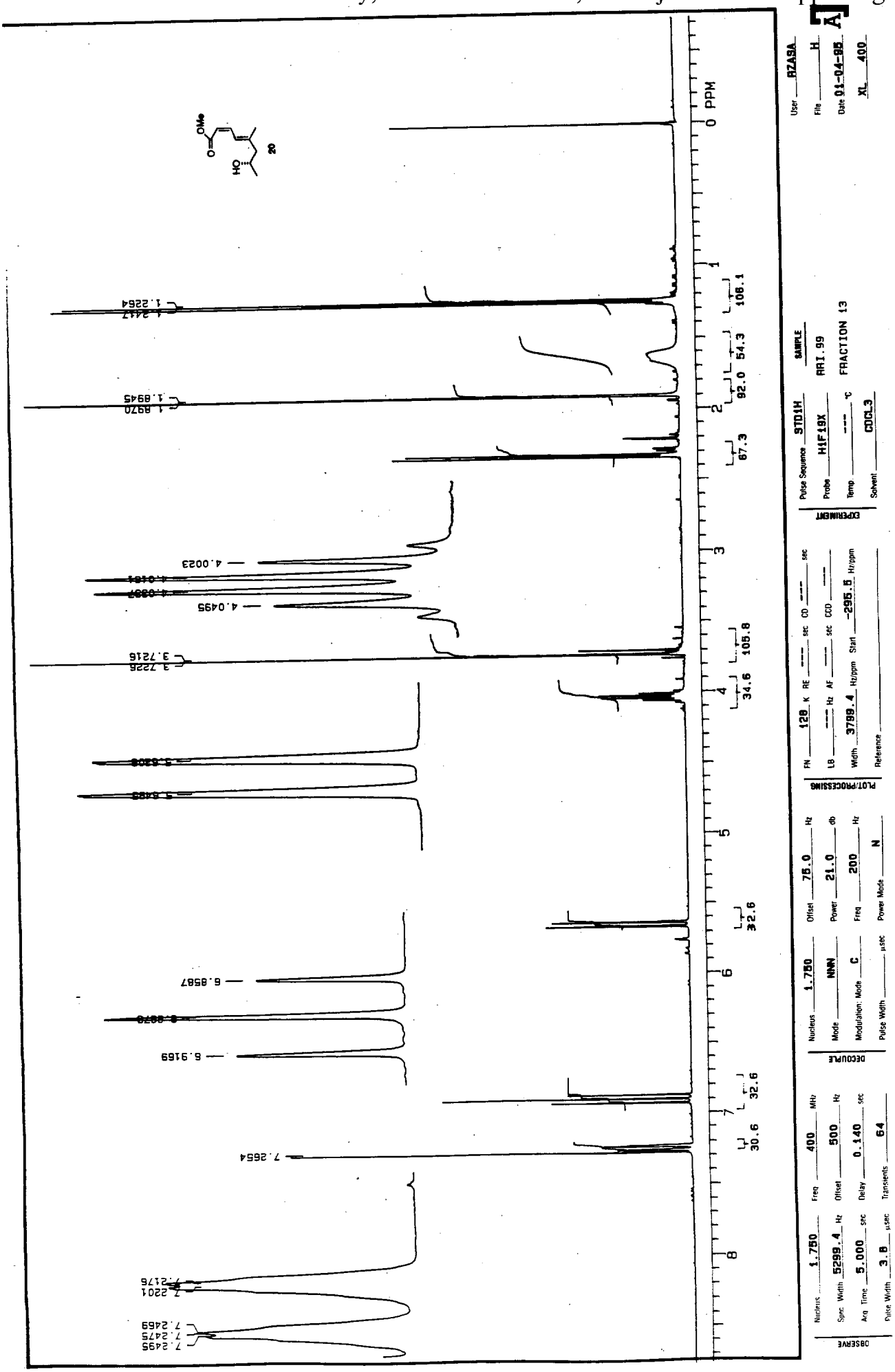

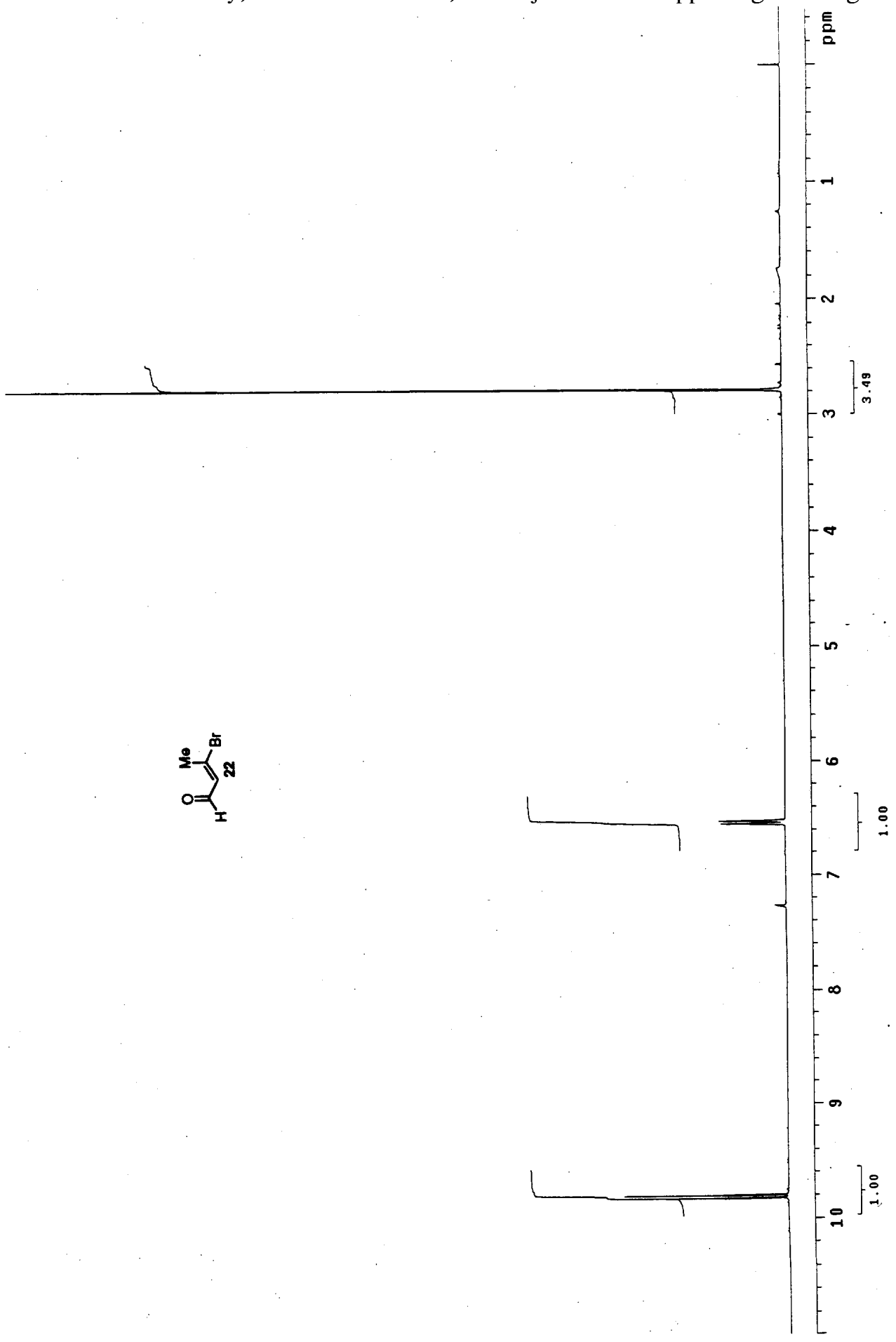

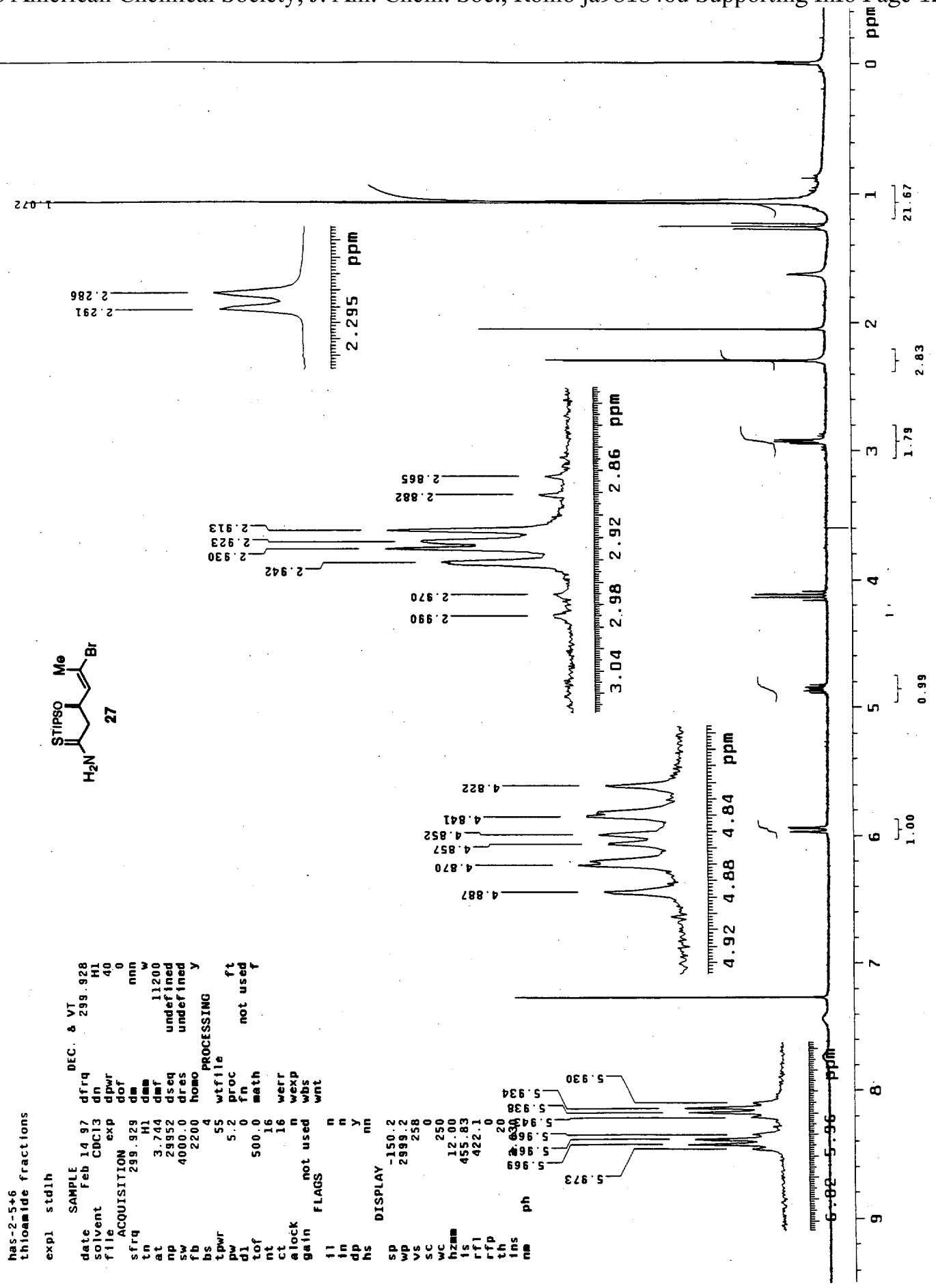

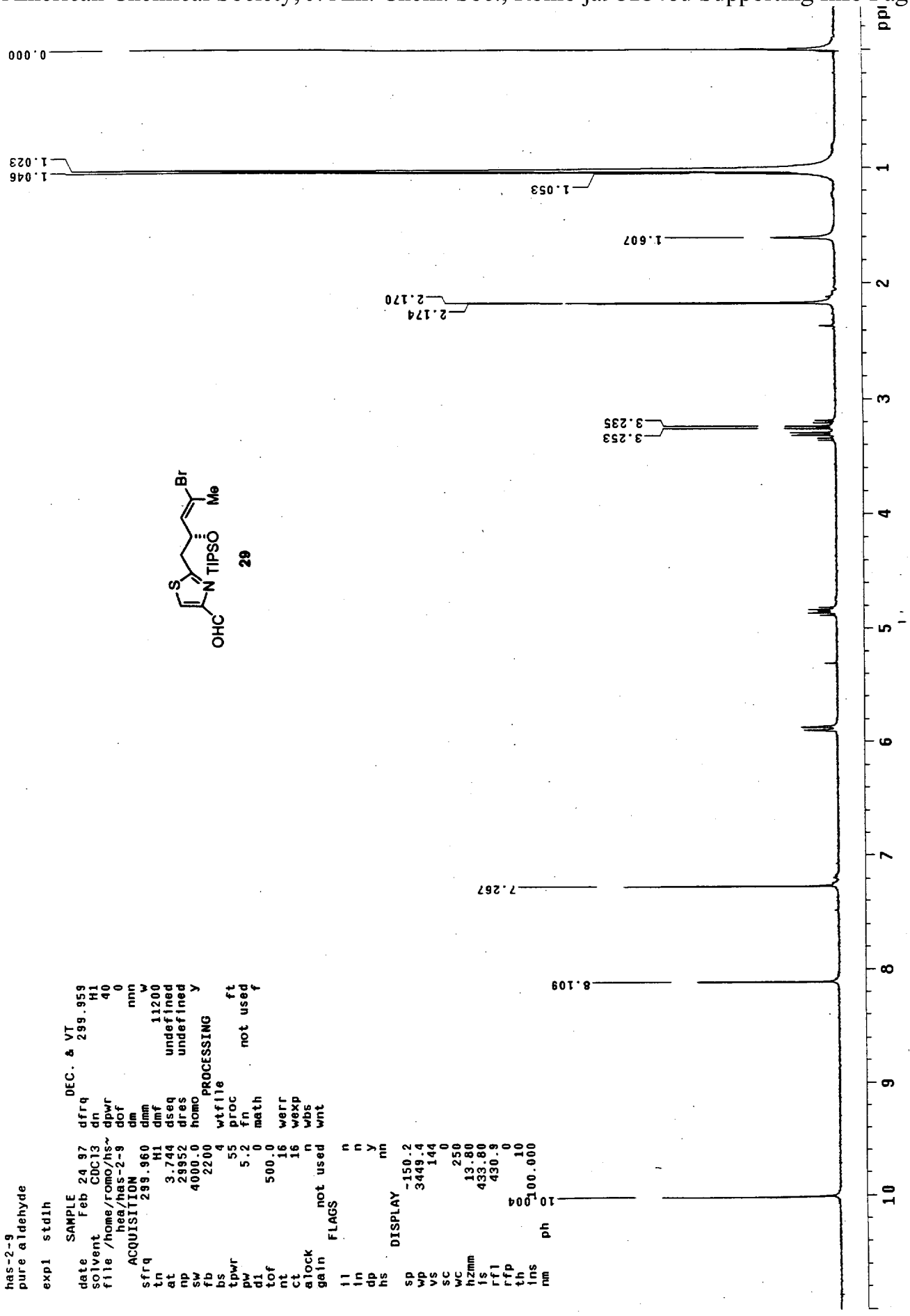


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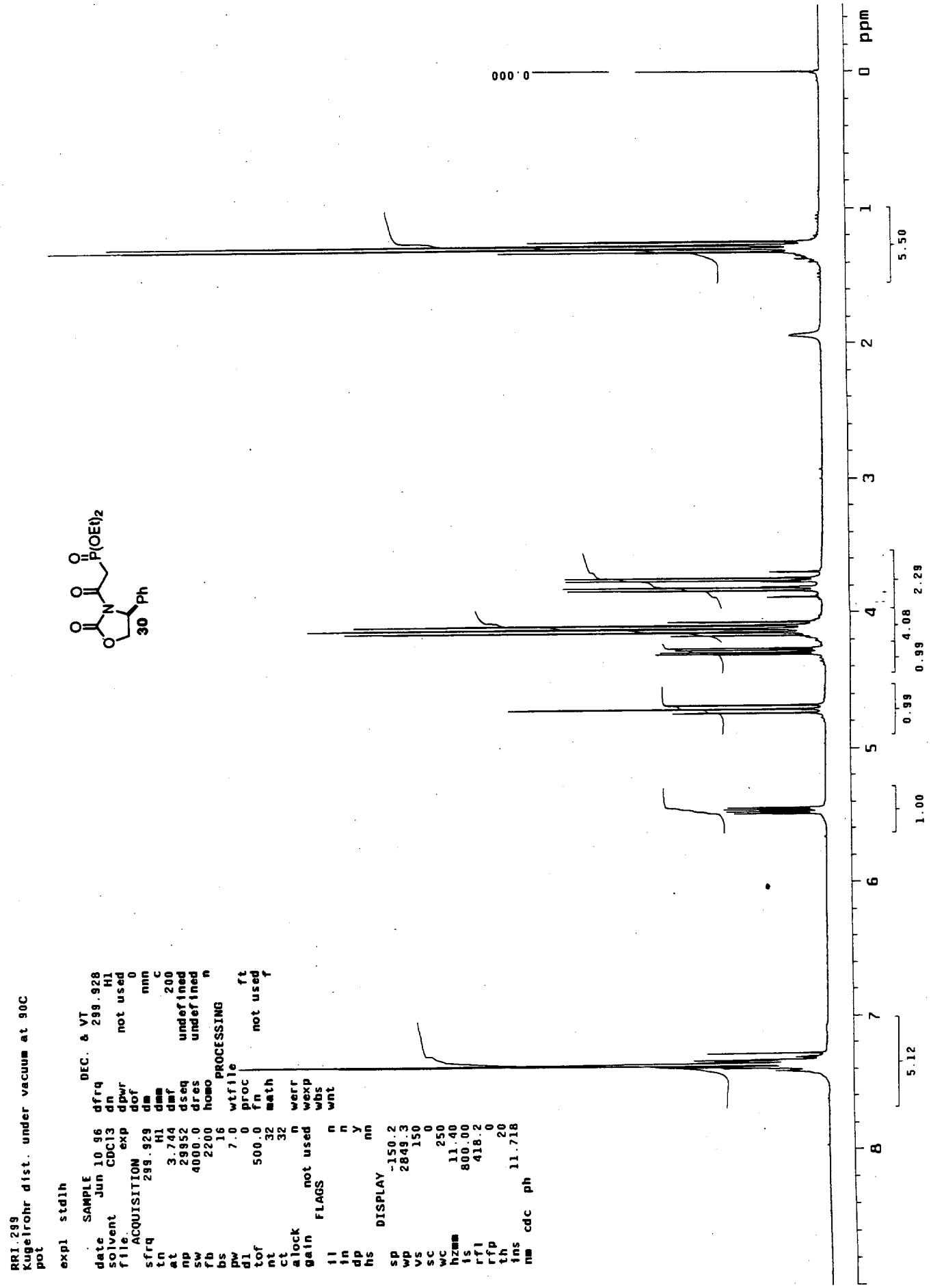

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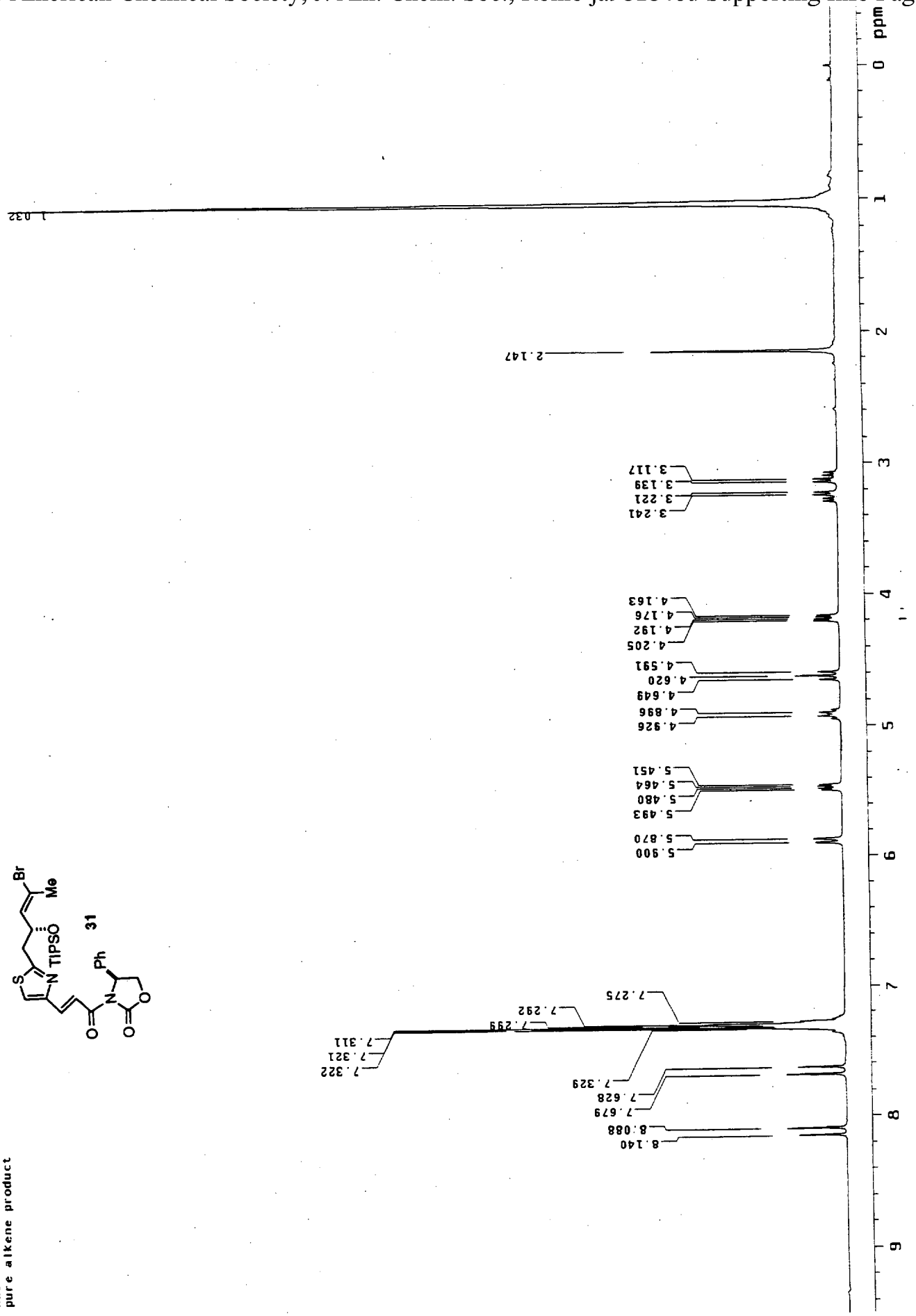

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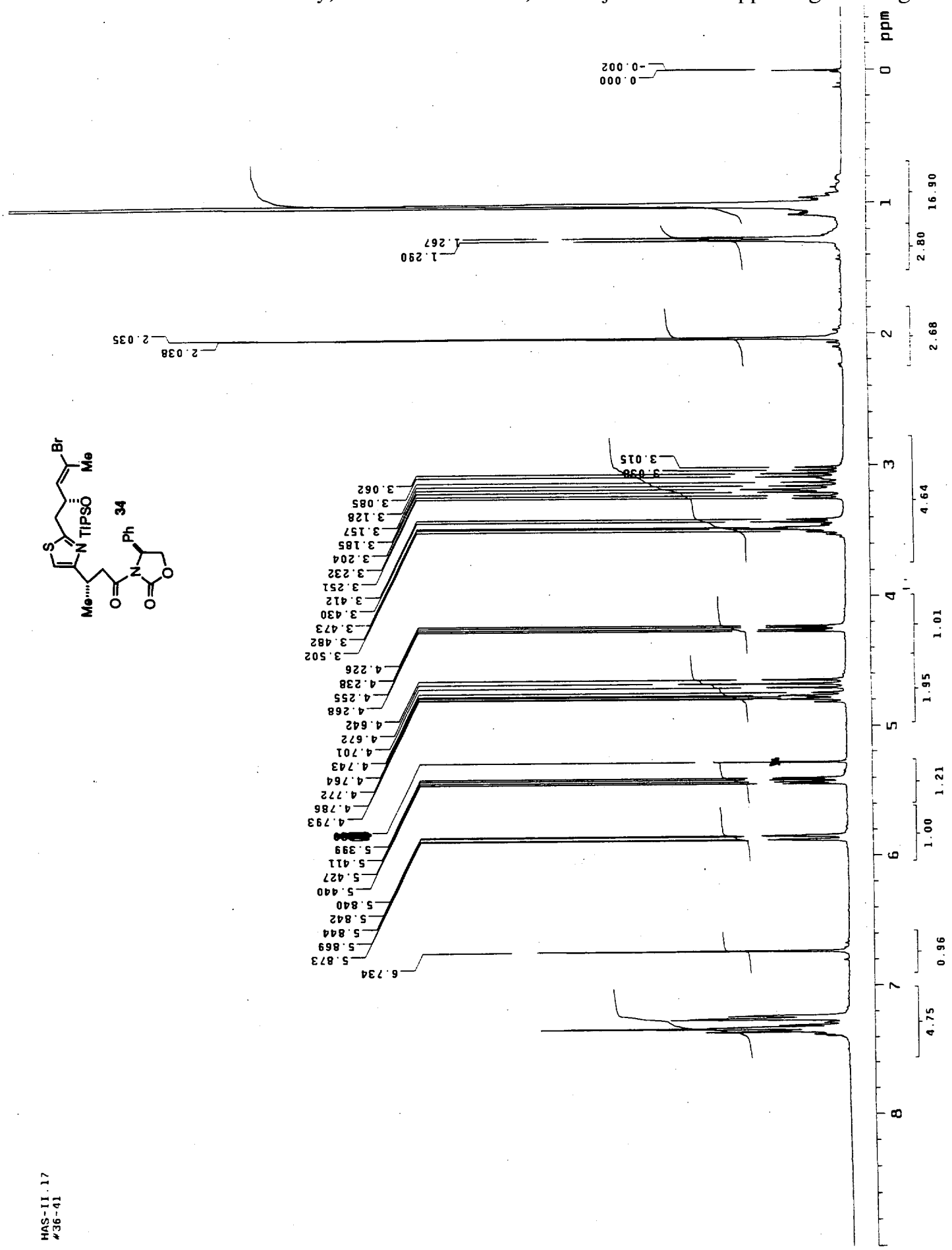

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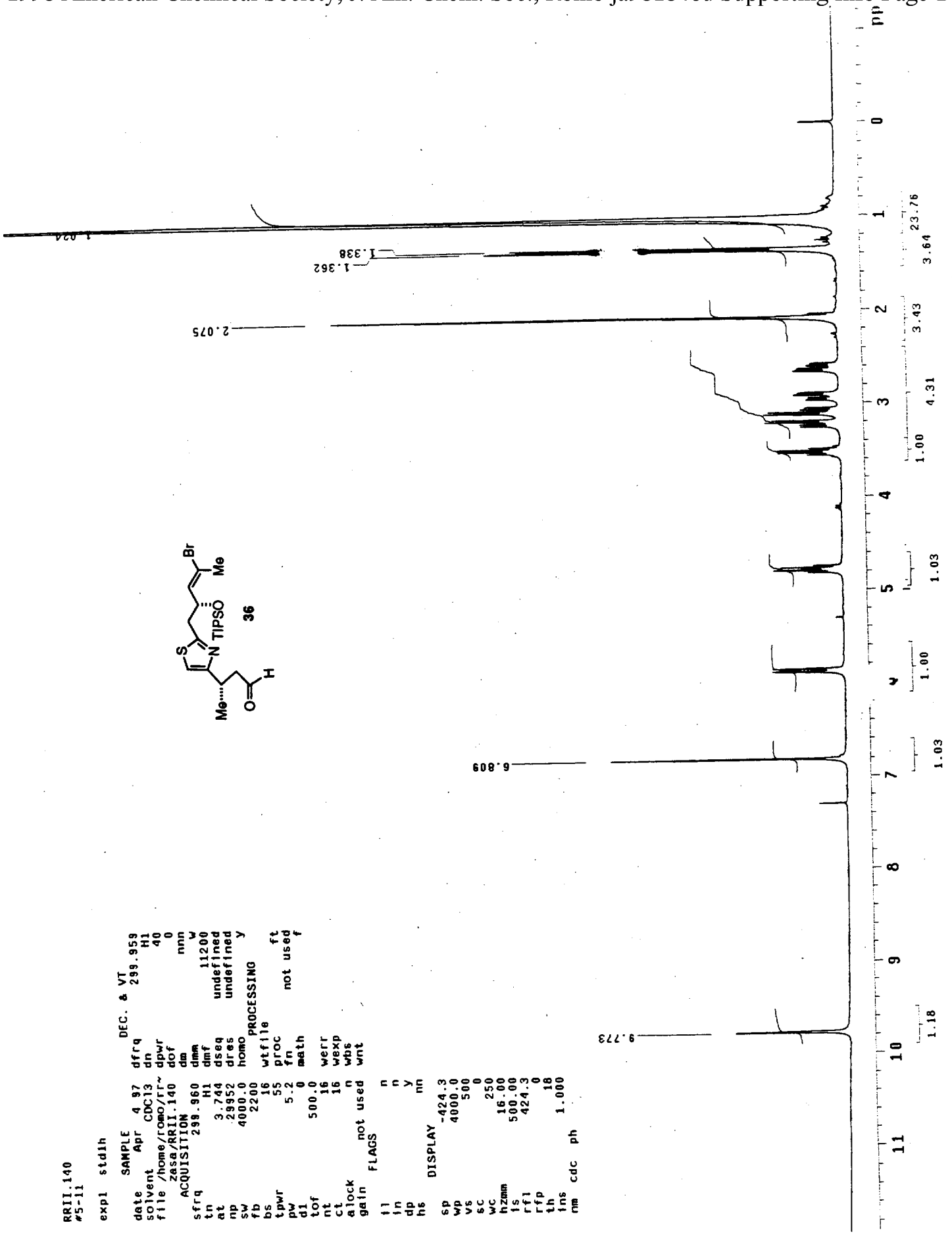

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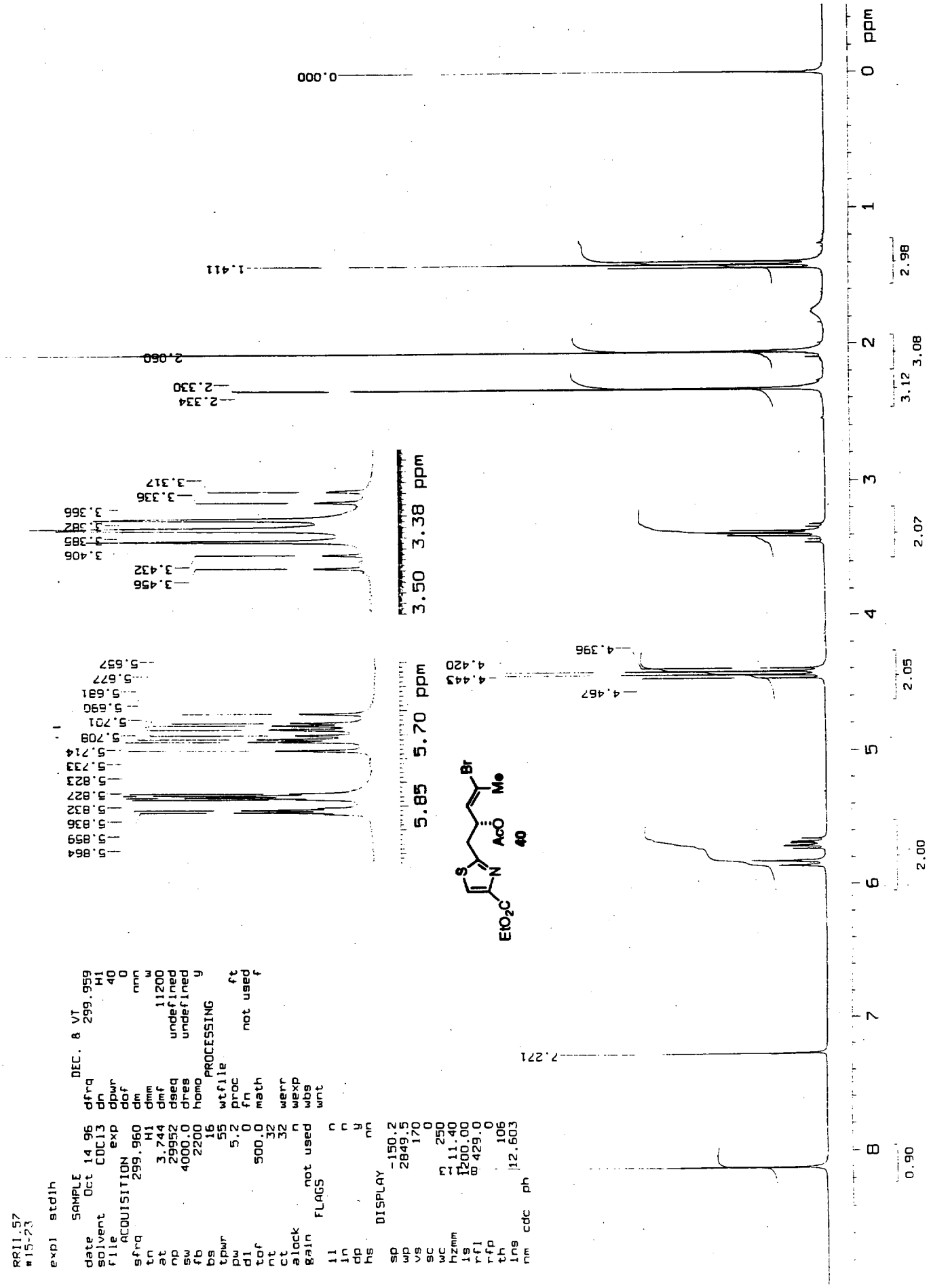
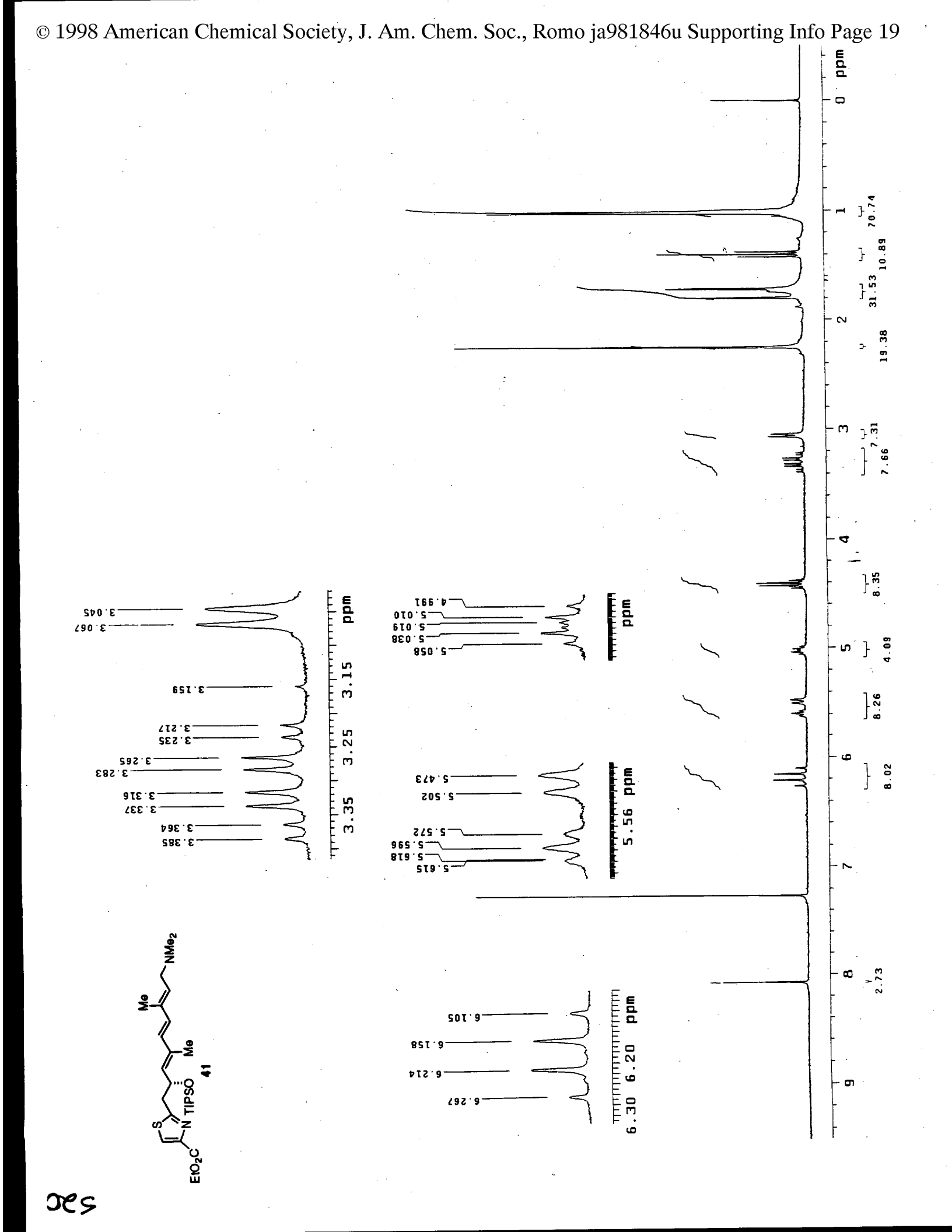


S19



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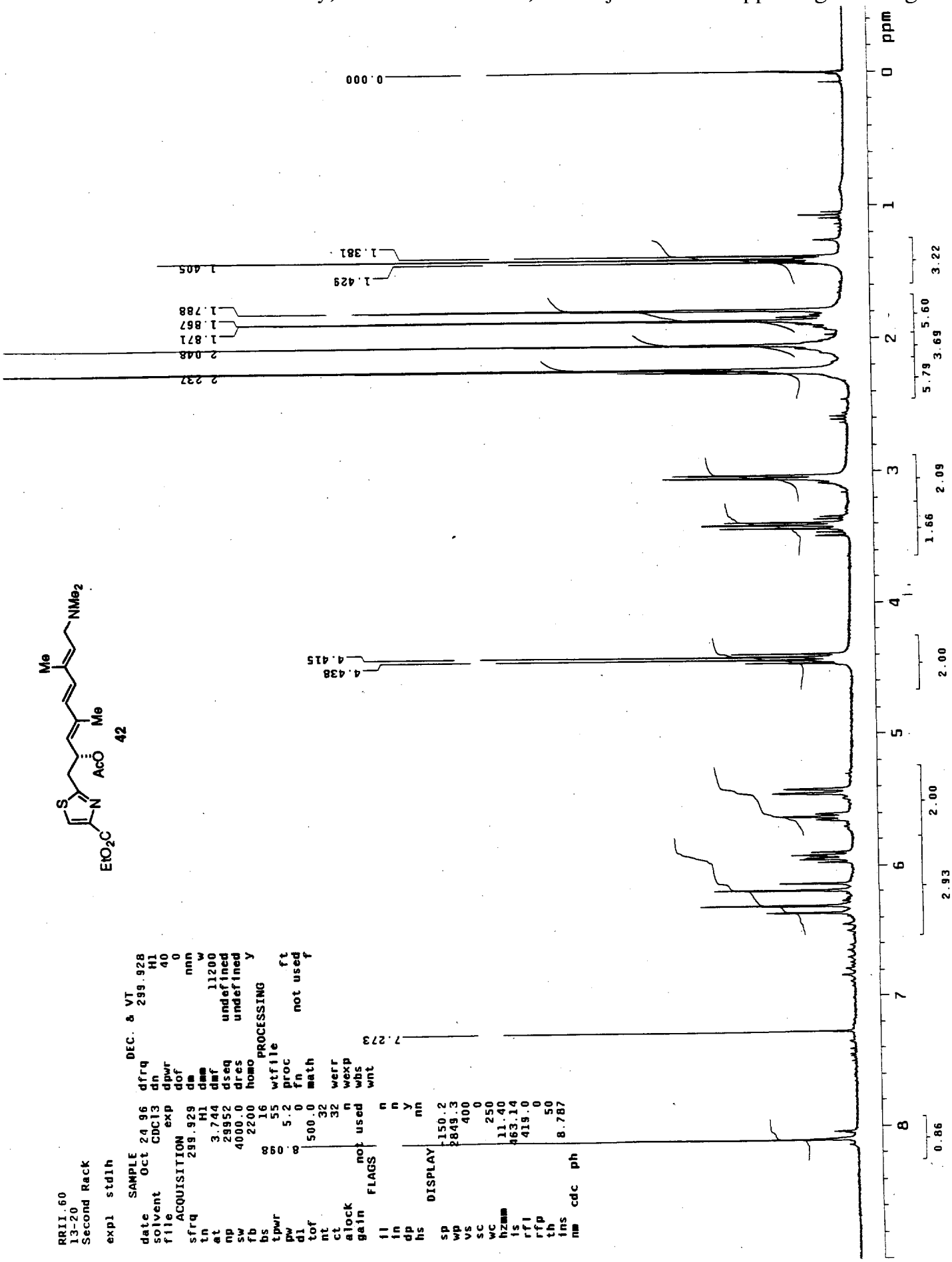

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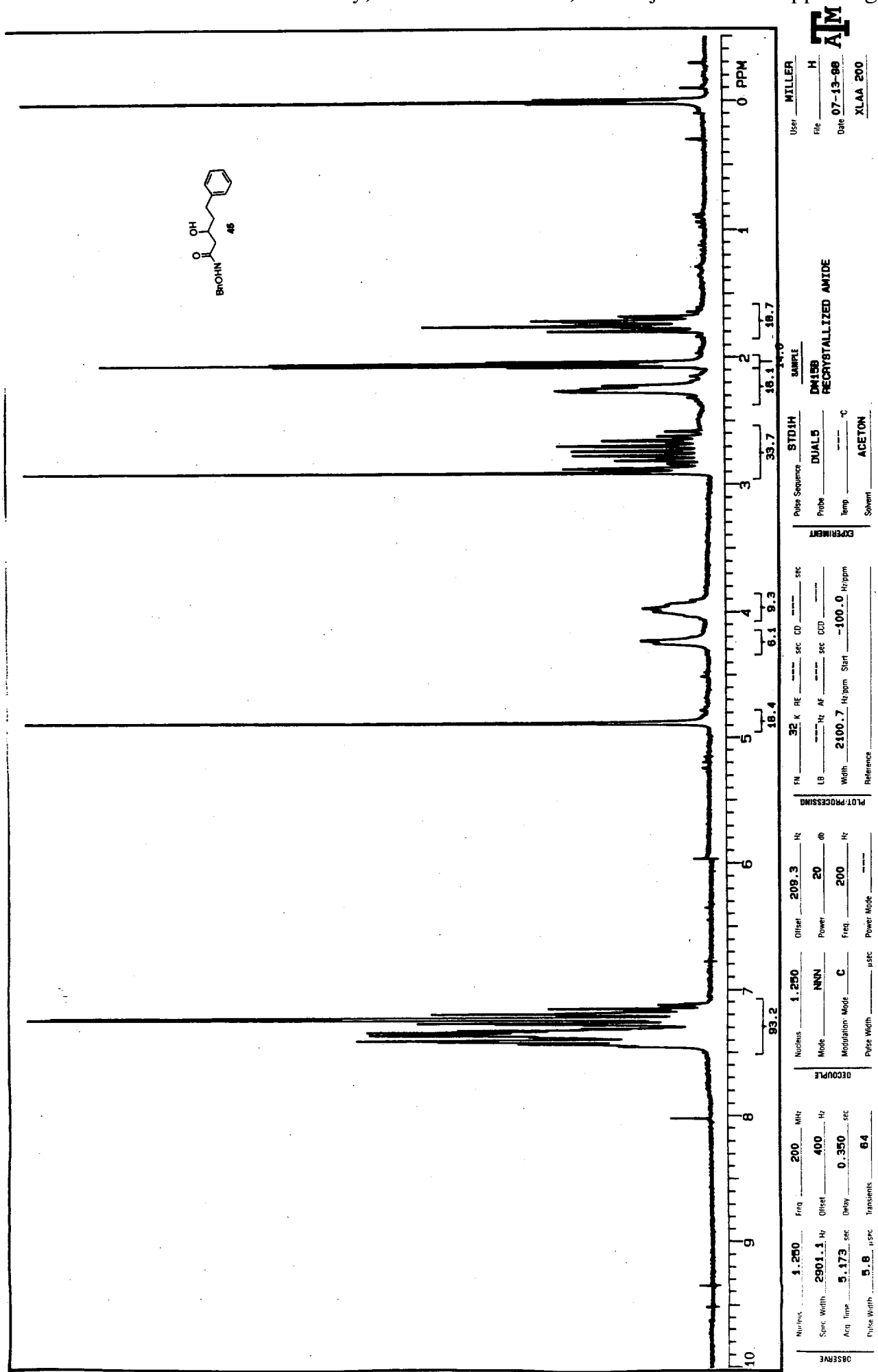

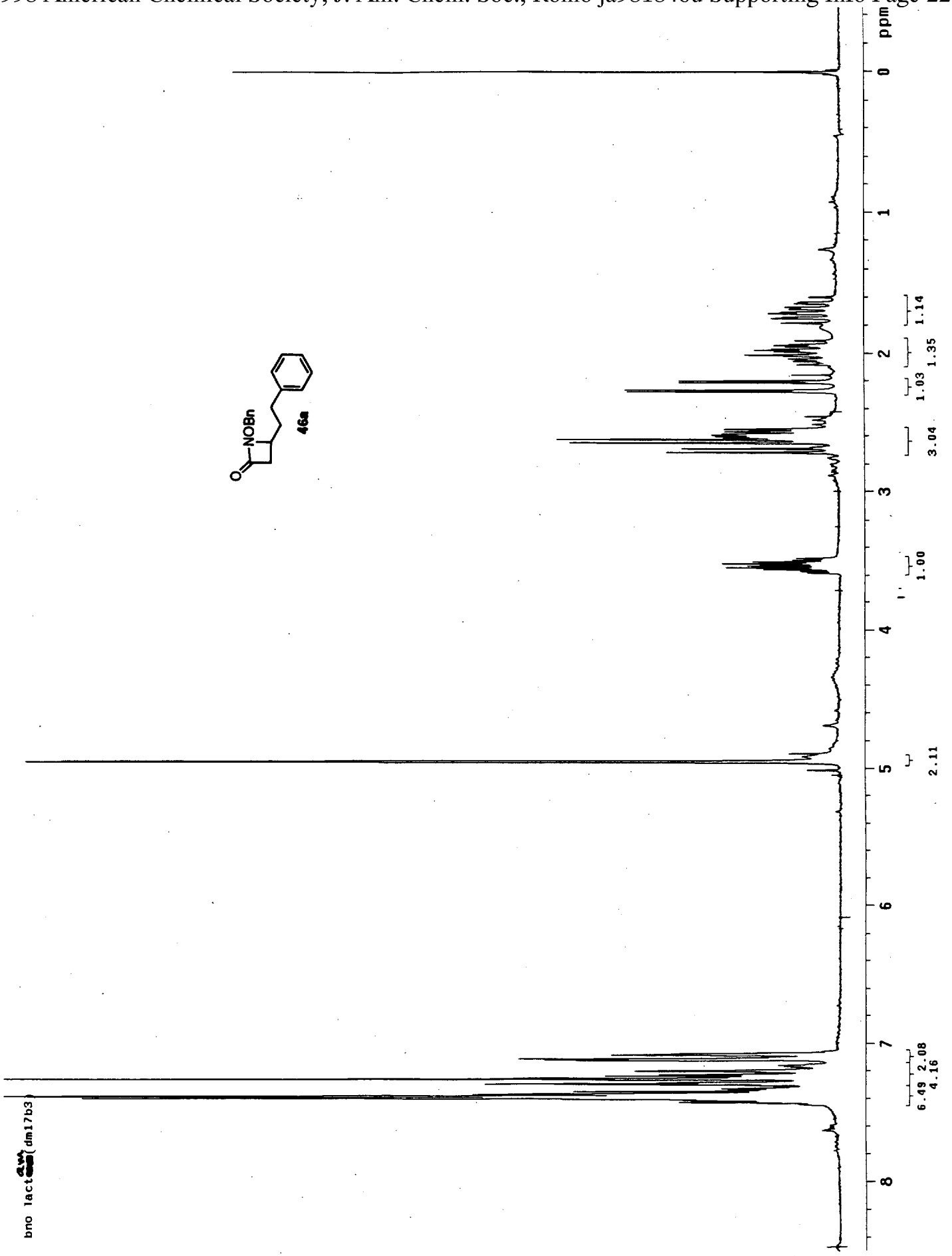

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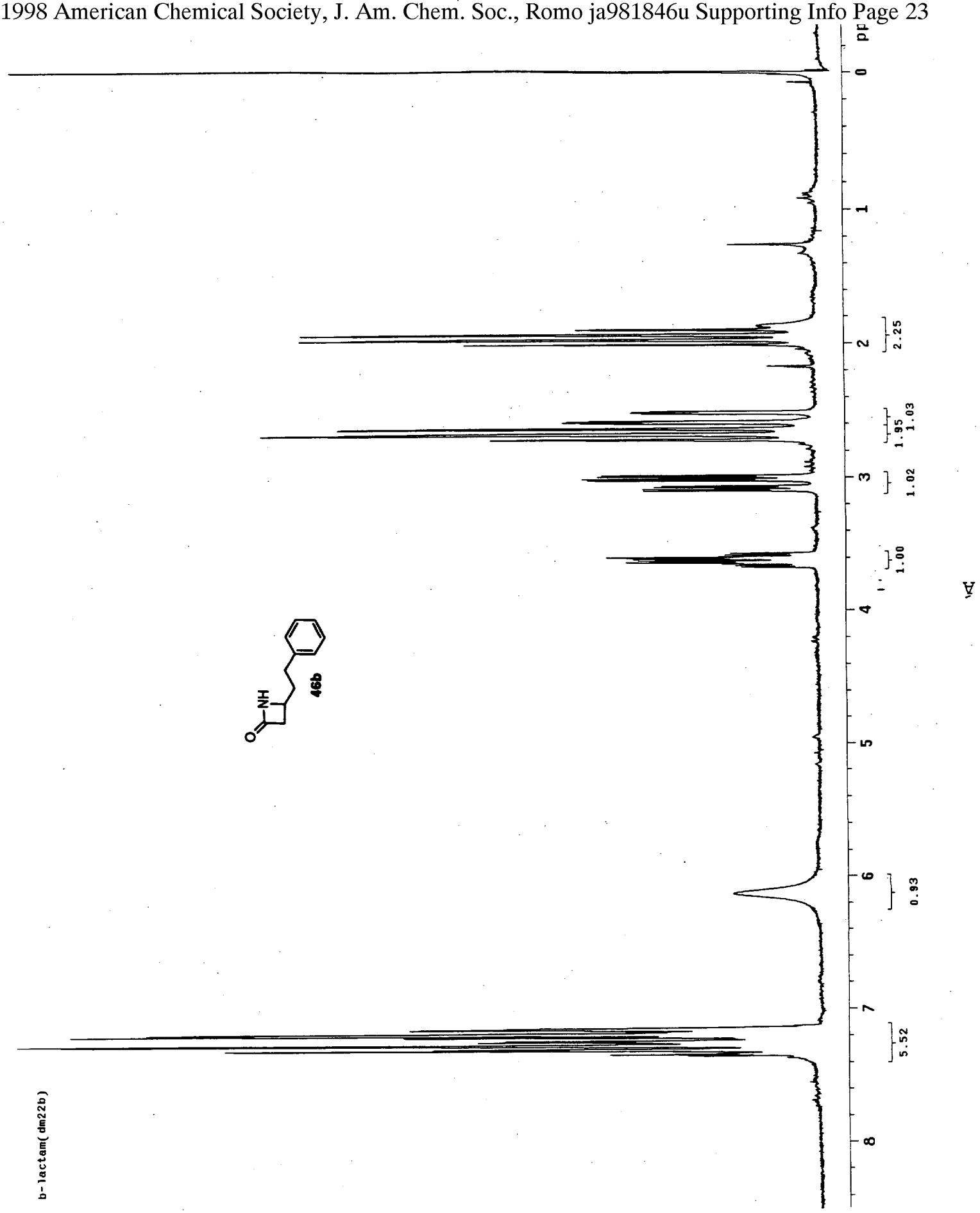

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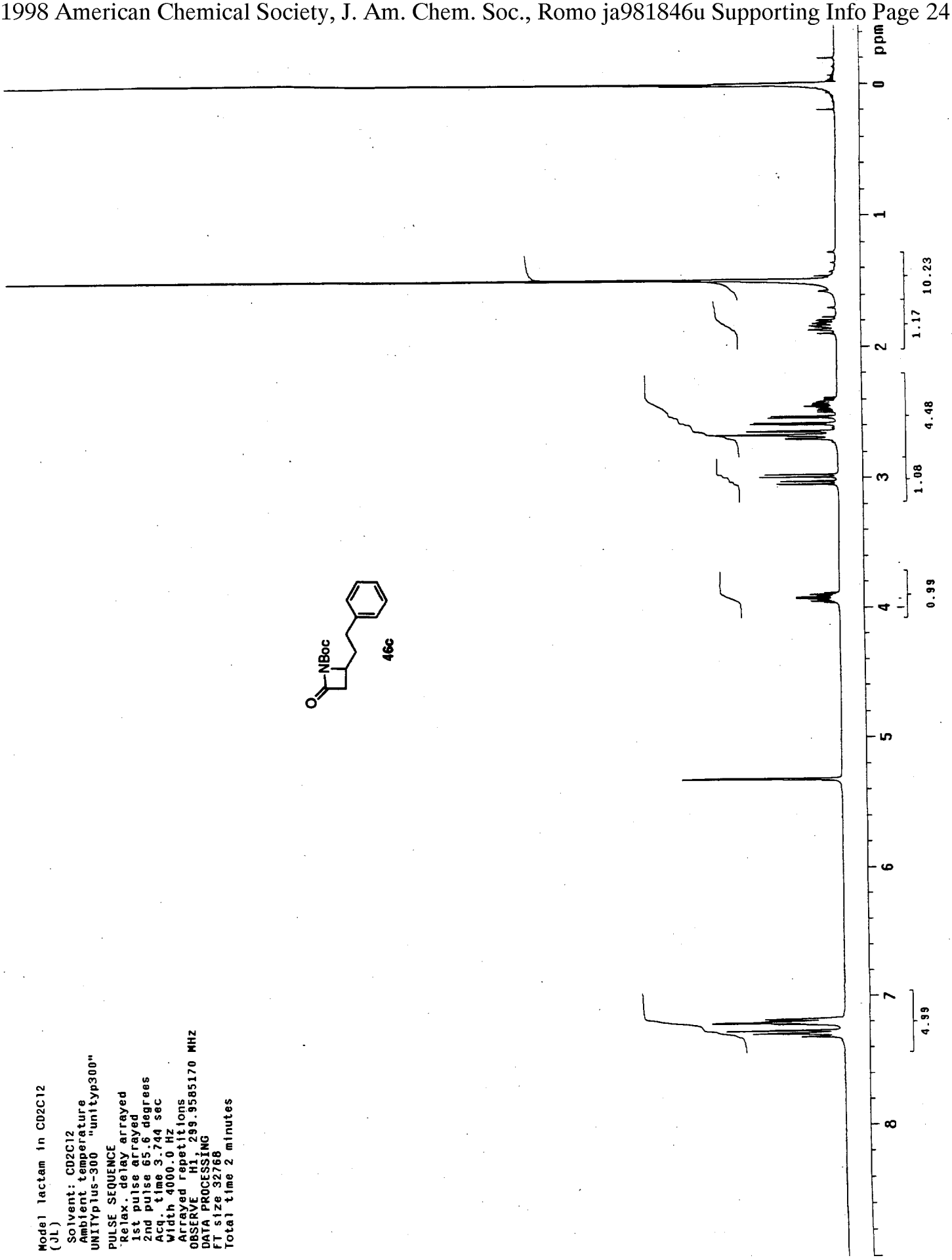

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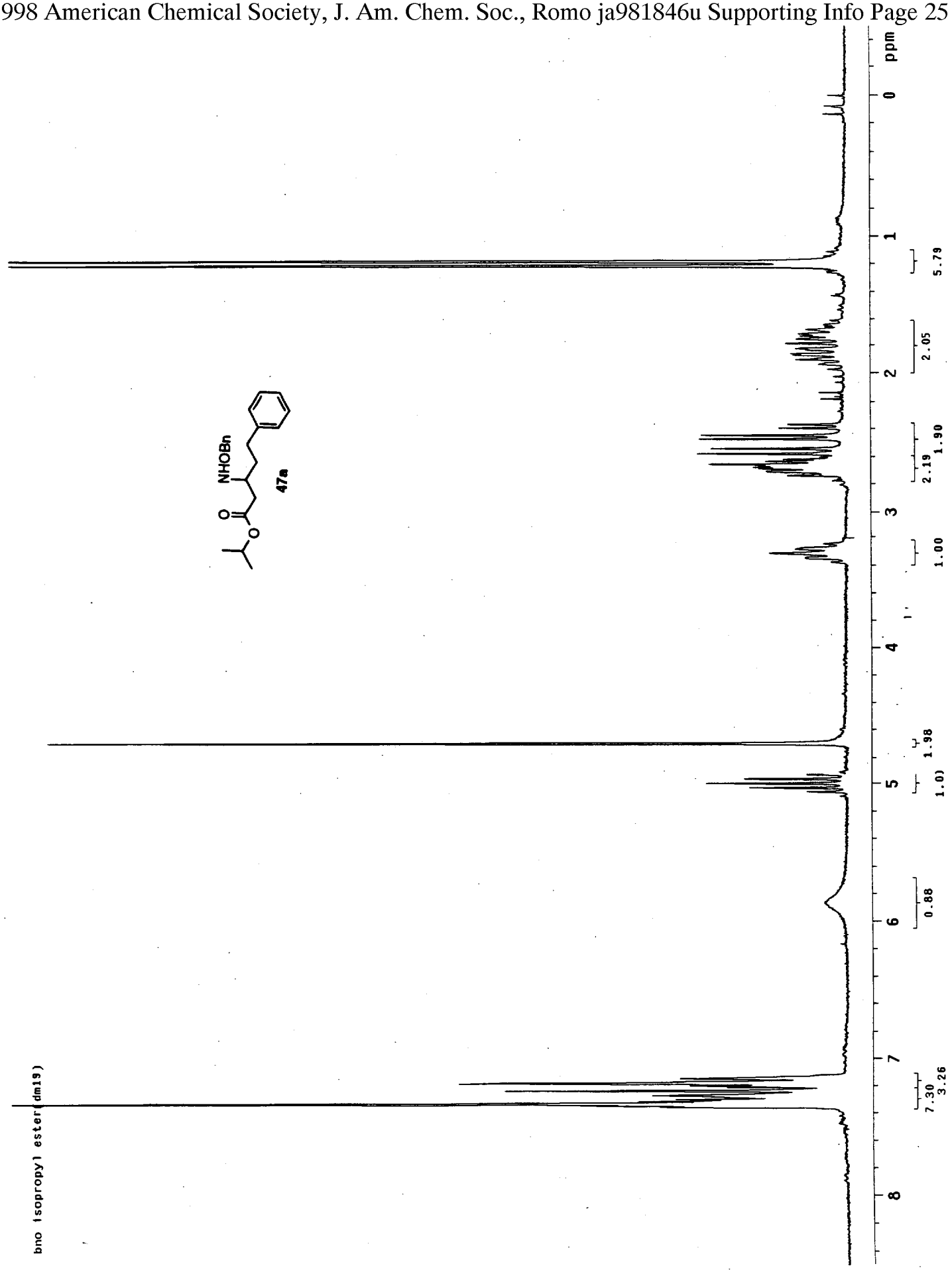

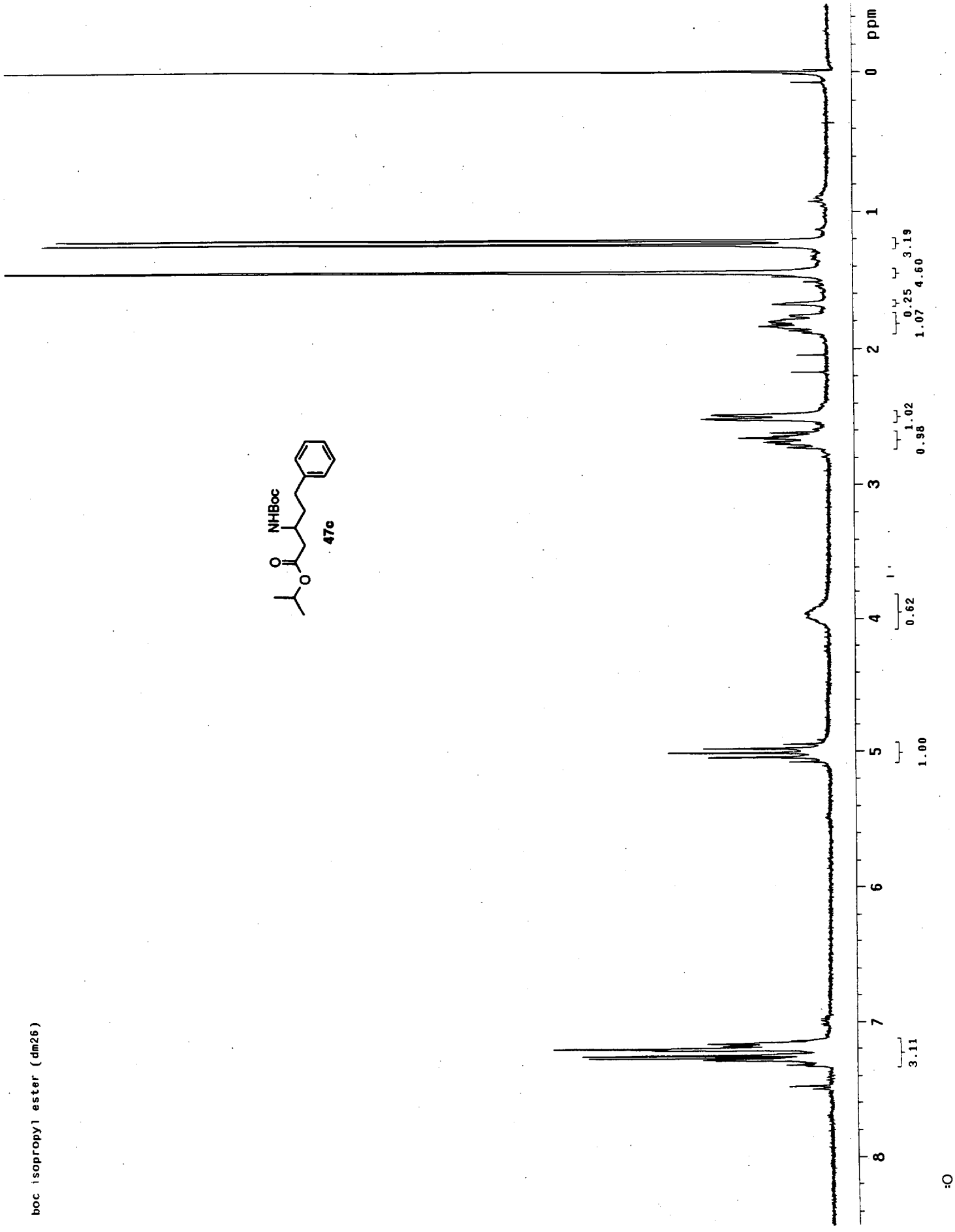

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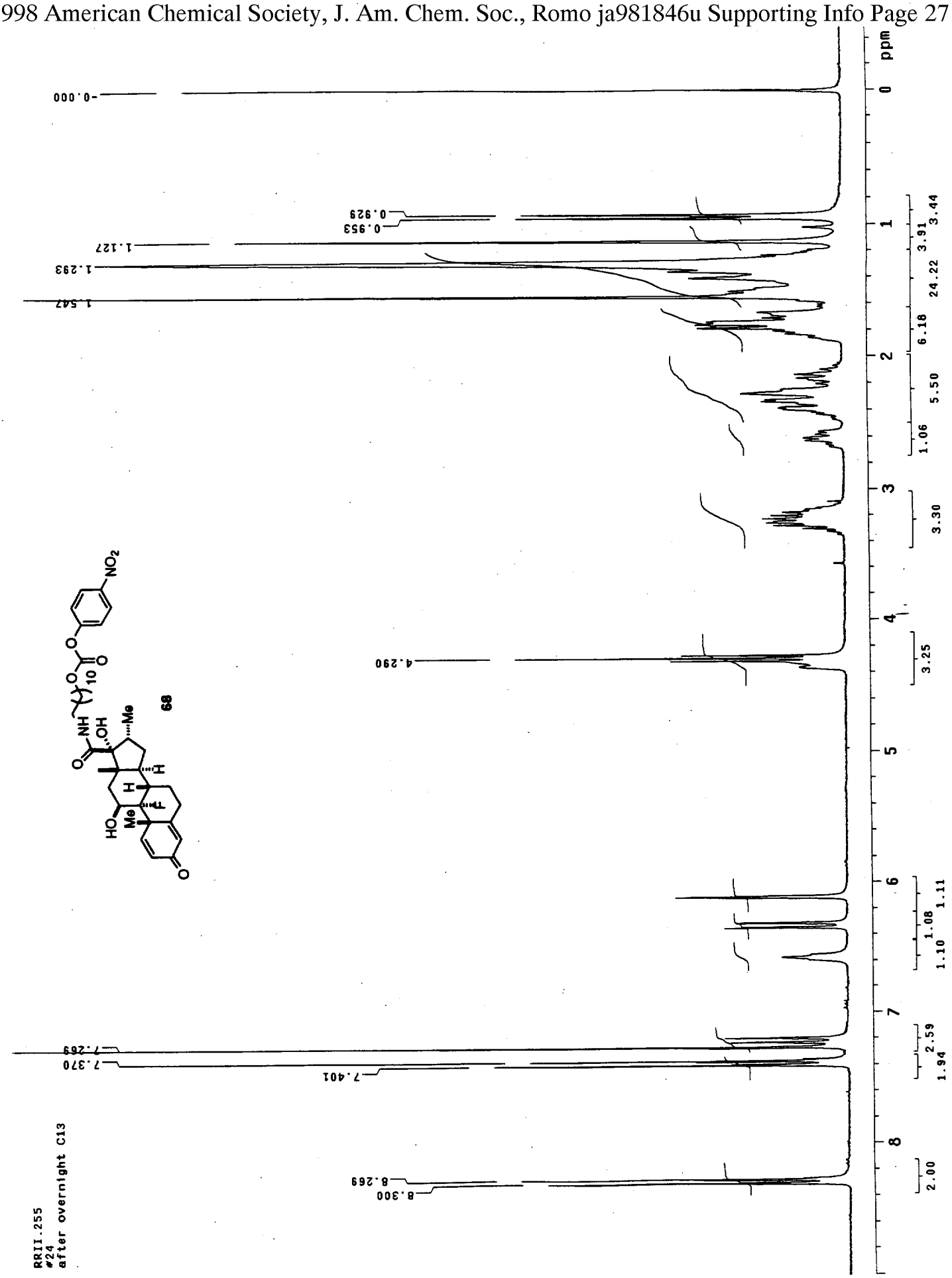

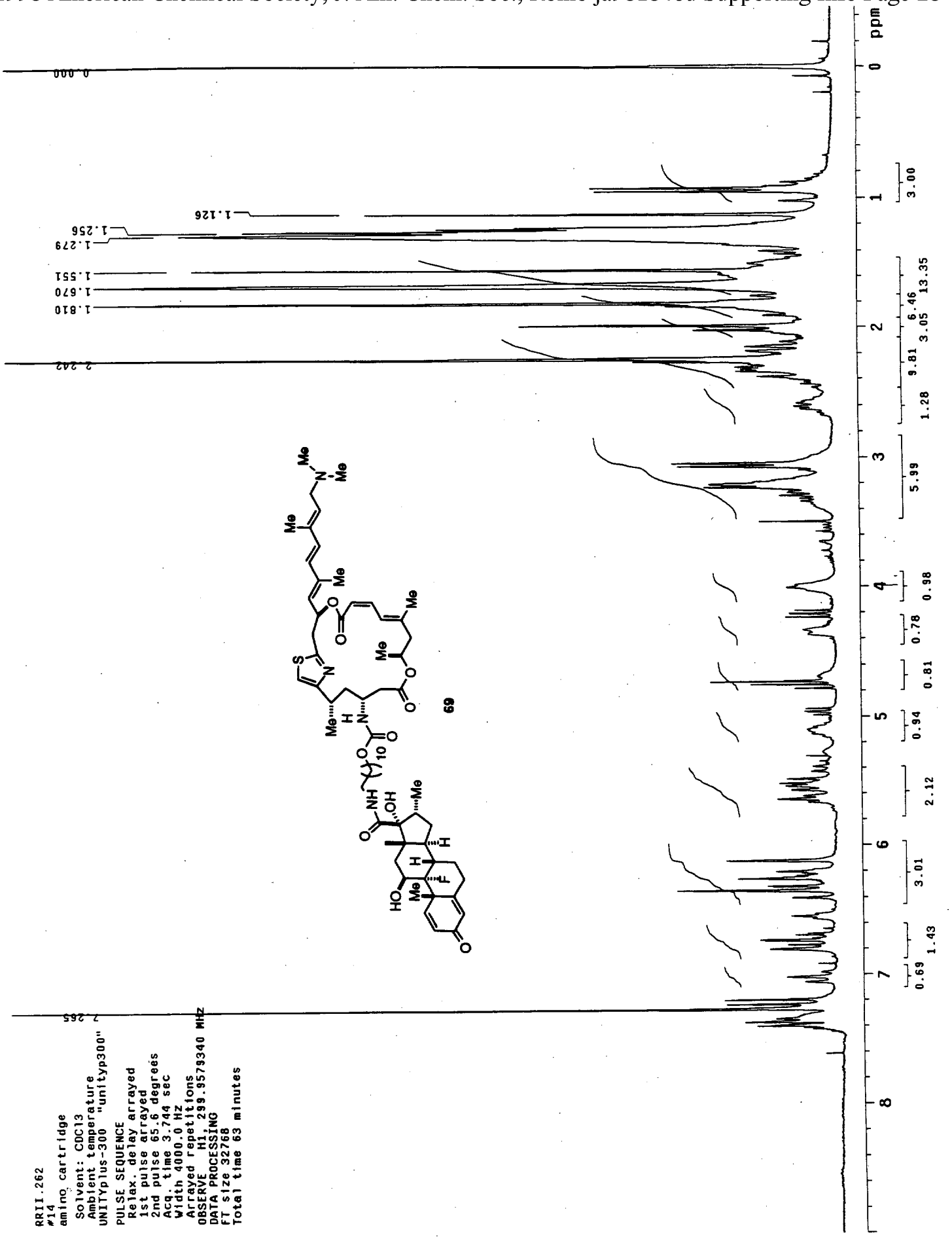

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