

**Preparation of oxime ether ( $\text{HO}_2\text{CC=NOBn}$ ).**

To a solution of glyoxylic acid monohydrate (5.0 g, 54 mmol) in MeOH (250 mL) were added *O*-benzyloxymine hydrochloride (13.0 g, 82 mmol) and AcONa (8.9 g, 109 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 12 h, the solvent was evaporated at reduced pressure, and the resulting residue was added to water and  $\text{CH}_2\text{Cl}_2$ . The layers were separated, and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic phase was dried over  $\text{MgSO}_4$  and concentrated at reduced pressure. Purification of the residue by recrystallization (AcOEt/hexane) afforded oxime ether (6.88 g, 71%) as a 2:1 mixture of *E/Z*-oxime.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.50 (2/3H, s), 7.29 (5H, s), 7.27 (1/3H, s), 5.18 (4/3, s), 4.89 (2/3, s)  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  165.6, 142.5, 136.0, 135.5, 128.6, 128.43, 128.41, 128.29, 128.25, 77.6, 77.5. HRMS: Calcd for  $\text{C}_9\text{H}_9\text{NO}_3$  ( $\text{M}^+$ ) : 179.0582, Found : 179.0569.

**Preparation of oxime ether (1).**

To a suspension of Wang resin (0.83 mmol/g, 25 g) in  $\text{CH}_2\text{Cl}_2$  (200 mL) were added oxime ether ( $\text{HO}_2\text{CC=NOBn}$ ) (14.9 g, 83 mmol), DCC (21.4 g, 104 mmol) and DMAP (1.27 g, 10 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h and then staid for 11 h, the resin was filtered, washed well with  $\text{CH}_2\text{Cl}_2$ , AcOEt followed by MeOH and then dried in vacuo.

**Preparation of oxime ether (2).**

To a suspension of TentaGel OH resin (0.26 mmol/g, 0.50 g) in DMF (2.5 mL) were added oxime ether ( $\text{HO}_2\text{CC=NOBn}$ ) (107 mg, 0.60 mmol), 2,6-dichlorobenzoyl chloride (0.086 mL, 0.60 mmol) and pyridine (0.08 mL, 0.99 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature

for 1 h and then staid for 11 h, the resin was filtered, washed well with CH<sub>2</sub>Cl<sub>2</sub>, AcOEt followed by MeOH and then dried in vacuo.

**Ethyl radical addition to oxime ether 1.**

To a suspension of oxime ether **1** (0.83 mmol/g, 274 mg, 0.28 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3.0 mL) was added Et<sub>3</sub>B (1.0 M in hexane, 1.0 mL, 1.0 mmol) under a nitrogen atmosphere at 20 or -78 °C. After the reaction mixture was stirred at the same temperature for 1 h, the resin was filtered, washed well with CH<sub>2</sub>Cl<sub>2</sub>, AcOEt followed by MeOH and then dried in vacuo. To a flask with the resulting resin **3a** was added TFA/CHCl<sub>3</sub> (1:3, v/v, 4.0 mL) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 30 min, the reaction mixture was filtered and washed with MeOH/CHCl<sub>3</sub> (1:11, v/v, 60 mL), and the filtrate was concentrated at reduced pressure. Purification of the residue by Amberlite IR-120B (eluting with MeOH) followed by preparative TLC (MeOH/CHCl<sub>3</sub> 1:10, v/v) afforded the α-amino acid derivative **4a**.

<sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.34-7.26 (5H, m), 4.68 (2H, s), 3.50 (1H, br t, *J*=10.2 Hz), 1.58 (2H, m), 0.95 (3H, t, *J*=11.1 Hz). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.2, 138.9, 129.4, 129.1, 128.7, 76.9, 66.1, 23.6, 10.7. HRMS: Calcd for C<sub>11</sub>H<sub>15</sub>NO<sub>3</sub> (M<sup>+</sup>) : 209.1051, Found : 209.1064.

**General procedure for the alkyl radical addition to oxime ether 1.**

To a suspension of oxime ether **1** (0.83 mmol/g, 274 mg, 0.28 mmol) in CH<sub>2</sub>Cl<sub>2</sub> or toluene (3.0 mL) were added RI (2.0 mmol), Bu<sub>3</sub>SnH (0.16 mL, 0.6 mmol) and Et<sub>3</sub>B (1.0 M in hexane, 0.30 mL, 0.30 mmol) under a nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h, the resin was filtered, washed well with CH<sub>2</sub>Cl<sub>2</sub>, AcOEt followed by MeOH and then dried in vacuo. To a flask with the resulting resin **3** was added TFA/CHCl<sub>3</sub> (1:3, v/v, 4.0 mL) under a

nitrogen atmosphere at 20 °C. After the reaction mixture was stirred at the same temperature for 30 min, the reaction mixture was filtered and washed with MeOH/CHCl<sub>3</sub> (1:11, v/v, 60 mL), and the filtrate was concentrated at reduced pressure. Purification of the residue by Amberlite IR-120B (eluting with MeOH) afforded the alkylated α-amino acids. Ethylated α-amino acid derivative **4a** was removed by preparative TLC (MeOH/CHCl<sub>3</sub>, 1:10, v/v) to afford the desired α-amino acid derivative **4b-g**.

**4b** : <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.38-7.26 (5H, m), 4.67 (2H, s), 3.30 (1H, br m), 1.90-1.70 (1H, m), 0.94 (6H, d, *J*=10.1 Hz). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.2, 139.0, 129.5, 129.1, 128.6, 76.7, 70.6, 29.9, 19.7. HRMS: Calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>3</sub> (M<sup>+</sup>) : 223.1207, Found : 223.1221.

**4c** : <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.34-7.26 (5H, m), 4.65 (2H, s), 3.31 (1H, m), 1.35-0.78 (11H, m). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.2, 139.0, 129.5, 129.1, 128.6, 76.7, 70.1, 39.5, 30.72, 30.66, 27.1, 27.0. HRMS: Calcd for C<sub>15</sub>H<sub>21</sub>NO<sub>3</sub> (M<sup>+</sup>) : 263.1520, Found : 263.1505.

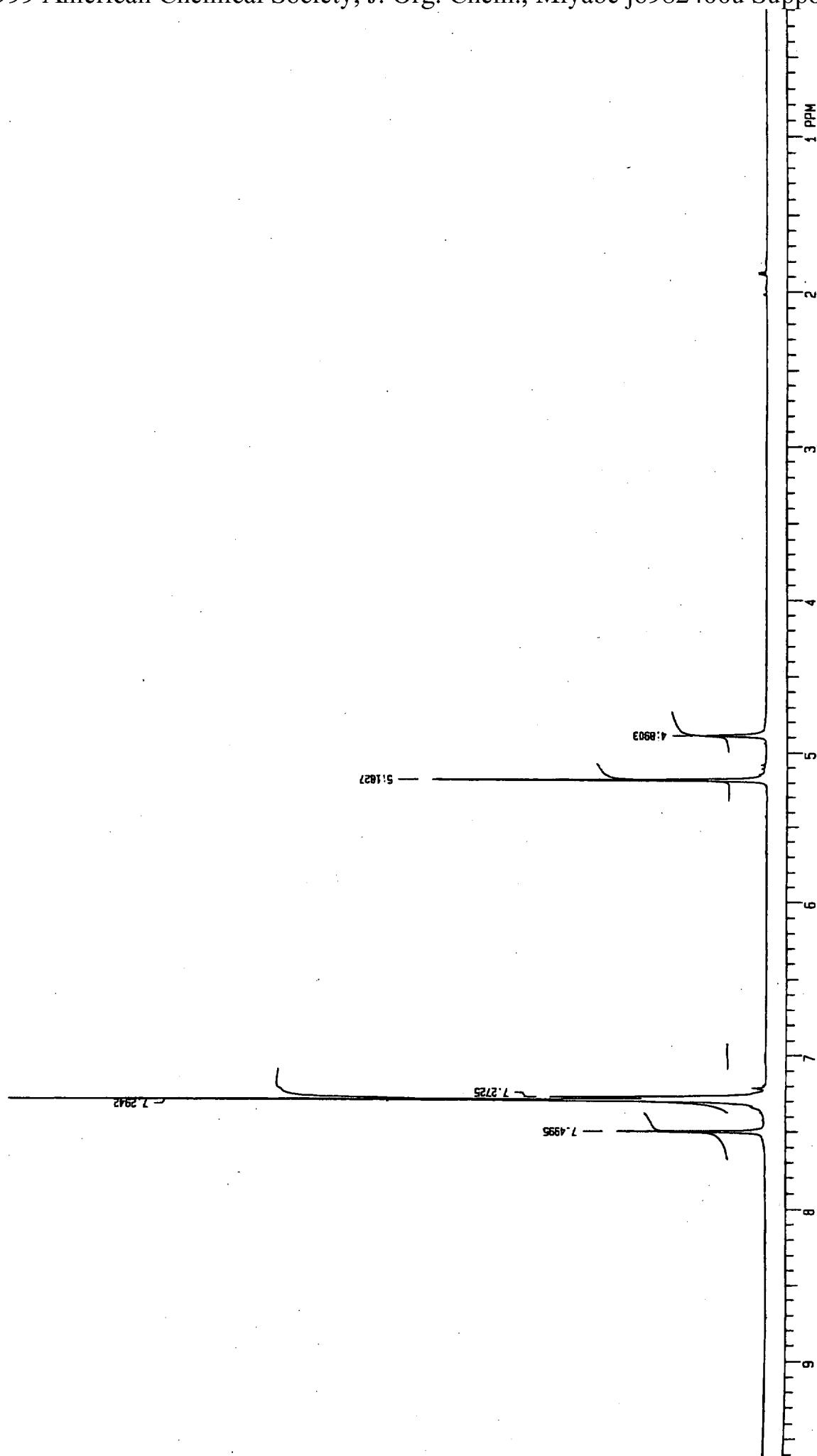
**4d** : <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.36-7.28 (5H, m), 4.65 (2H, s), 3.31 (1H, br m), 0.94 (9H, s). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.2, 139.1, 129.7, 129.1, 128.6, 76.5, 73.2, 33.3, 27.5. HRMS: Calcd for C<sub>13</sub>H<sub>19</sub>NO<sub>3</sub> (M<sup>+</sup>) : 237.1364, Found : 237.1344.

**4e** : <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.36-7.29 (5H, m), 4.68 (2H, s), 3.59 (1H, t, *J*=10.7 Hz), 1.69 (1H, m), 1.34 (2H, m), 0.90 (3H, d, *J*=11.0 Hz), 0.81 (3H, d, *J*=11.0 Hz). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.8, 138.9, 129.4, 129.1, 128.6, 76.8, 63.2, 39.5, 26.0, 23.0, 22.7. HRMS: Calcd for C<sub>13</sub>H<sub>19</sub>NO<sub>3</sub> (M<sup>+</sup>) : 237.1364, Found : 237.1348.

**4f** (diastereomeric mixture) : <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 7.38-7.26 (5H, m), 4.65 (2H, s), 3.42 (1H, br m), 1.68-1.38 (2H, m), 1.26-1.11 (1H, m), 0.87 (6H, m). <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 177.4, 177.1, 139.0, 129.5, 129.1, 128.6, 76.1, 69.1, 68.6, 36.8, 36.2,

27.3, 26.9, 16.0, 15.7, 11.8, 11.5. HRMS: Calcd for  $C_{13}H_{19}NO_3$  ( $M^+$ ) : 237.1364, Found : 237.1354.

**4g** :  $^1H$  NMR ( $CD_3OD$ )  $\delta$  7.38-7.24 (5H, m), 4.62 (2H, s), 3.13 (1H, br s), 2.00-1.26 (15H, m).  $^{13}C$  NMR ( $CD_3OD$ )  $\delta$  176.6, 139.1, 129.6, 129.1, 128.6, 76.5, 74.2, 40.3, 37.8, 35.6, 29.6. HRMS: Calcd for  $C_{19}H_{25}NO_3$  ( $M^+$ ) : 315.1833, Found : 315.1825.

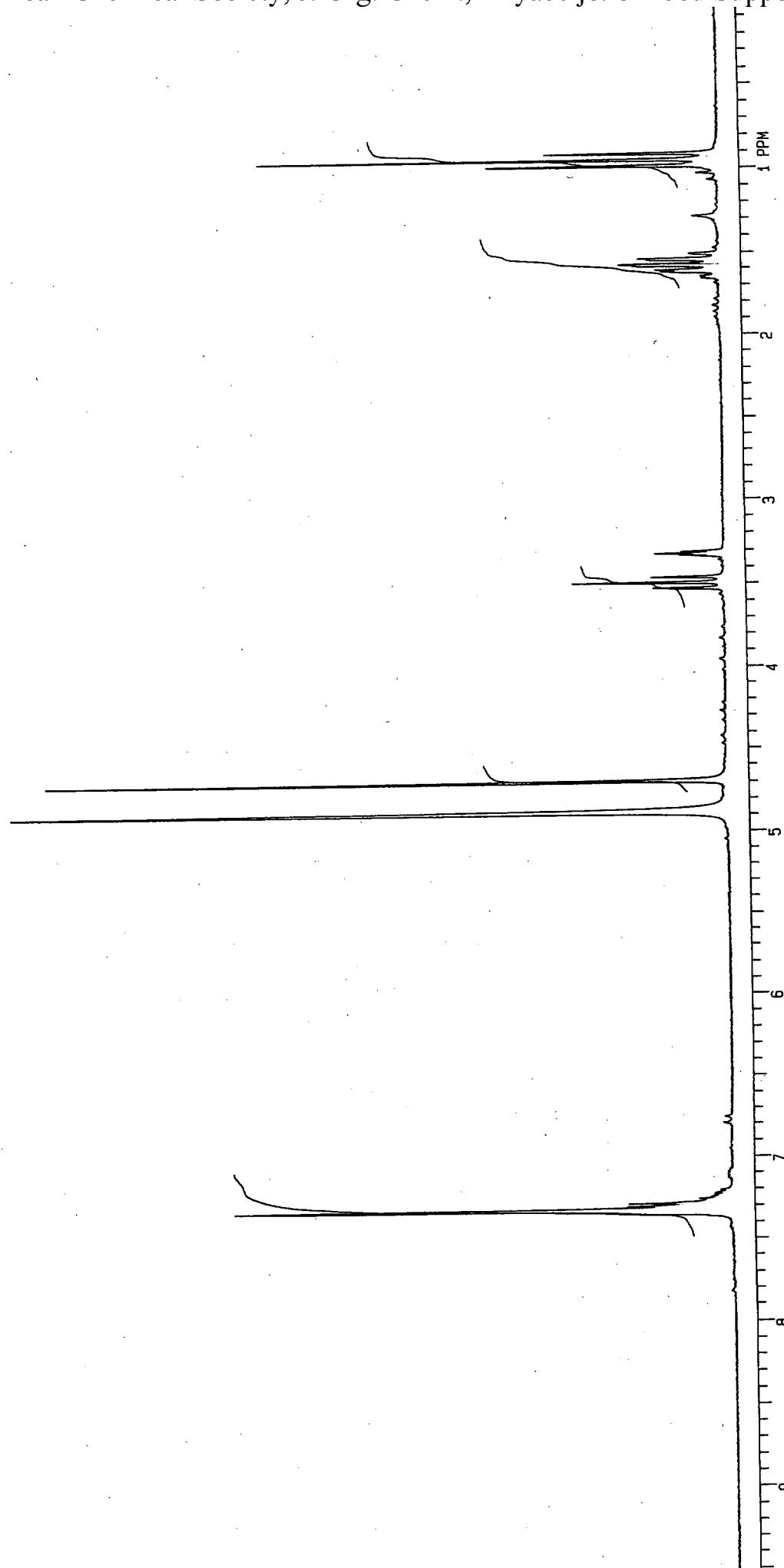


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Transients	15	Modulation	Mode C	Freq.	200
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Width, 9.4	usec	Power Mode	A/B/C	Hz/ppm	Hz/ppm
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				Ticks	mm
				Time QD	sec
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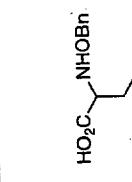
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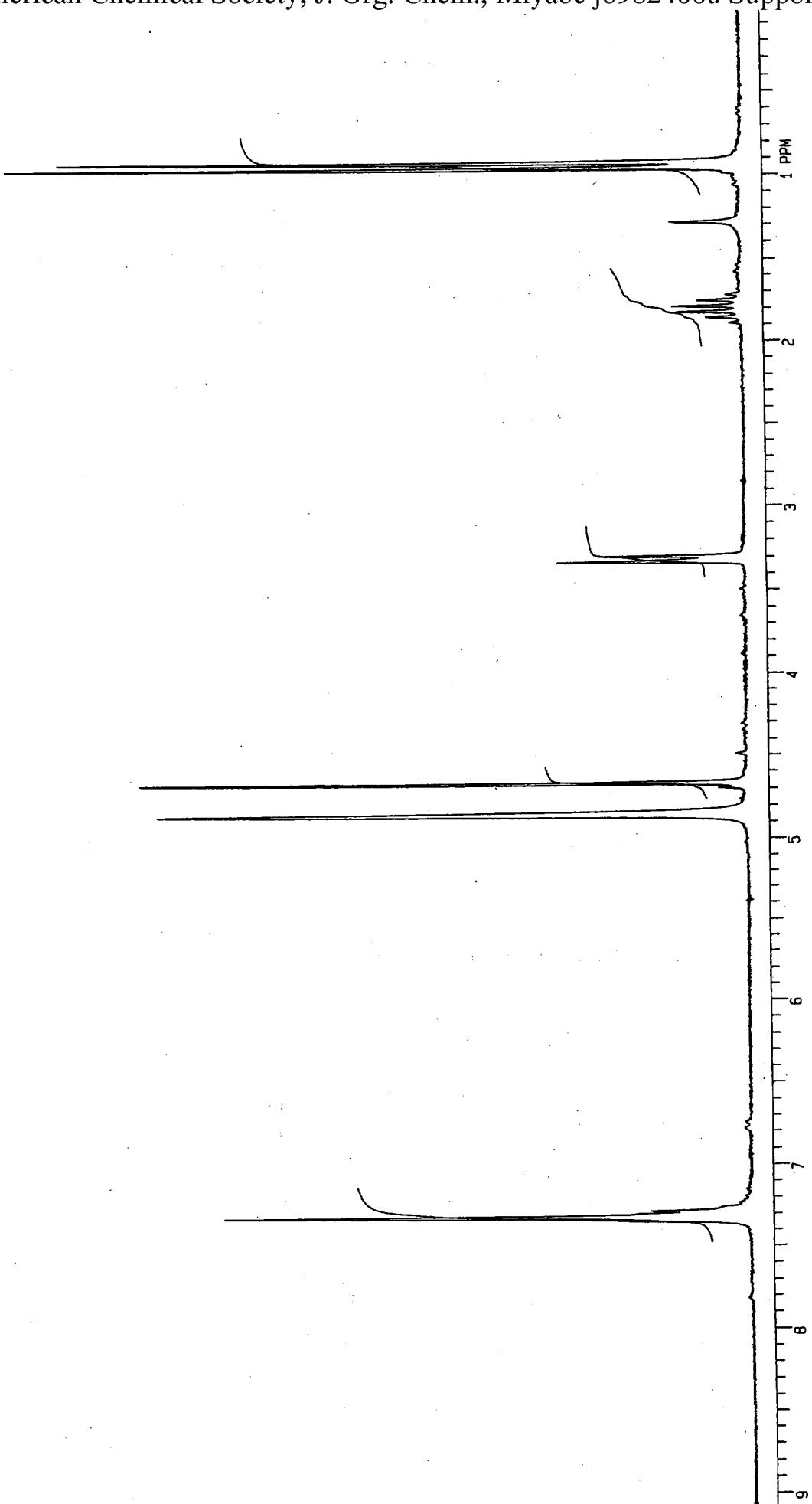
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Mode	NNN	Temp	°C
Modulation	MSBC	Solvent	CDCl <sub>3</sub>
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Notch	11.5 μsec		



4a

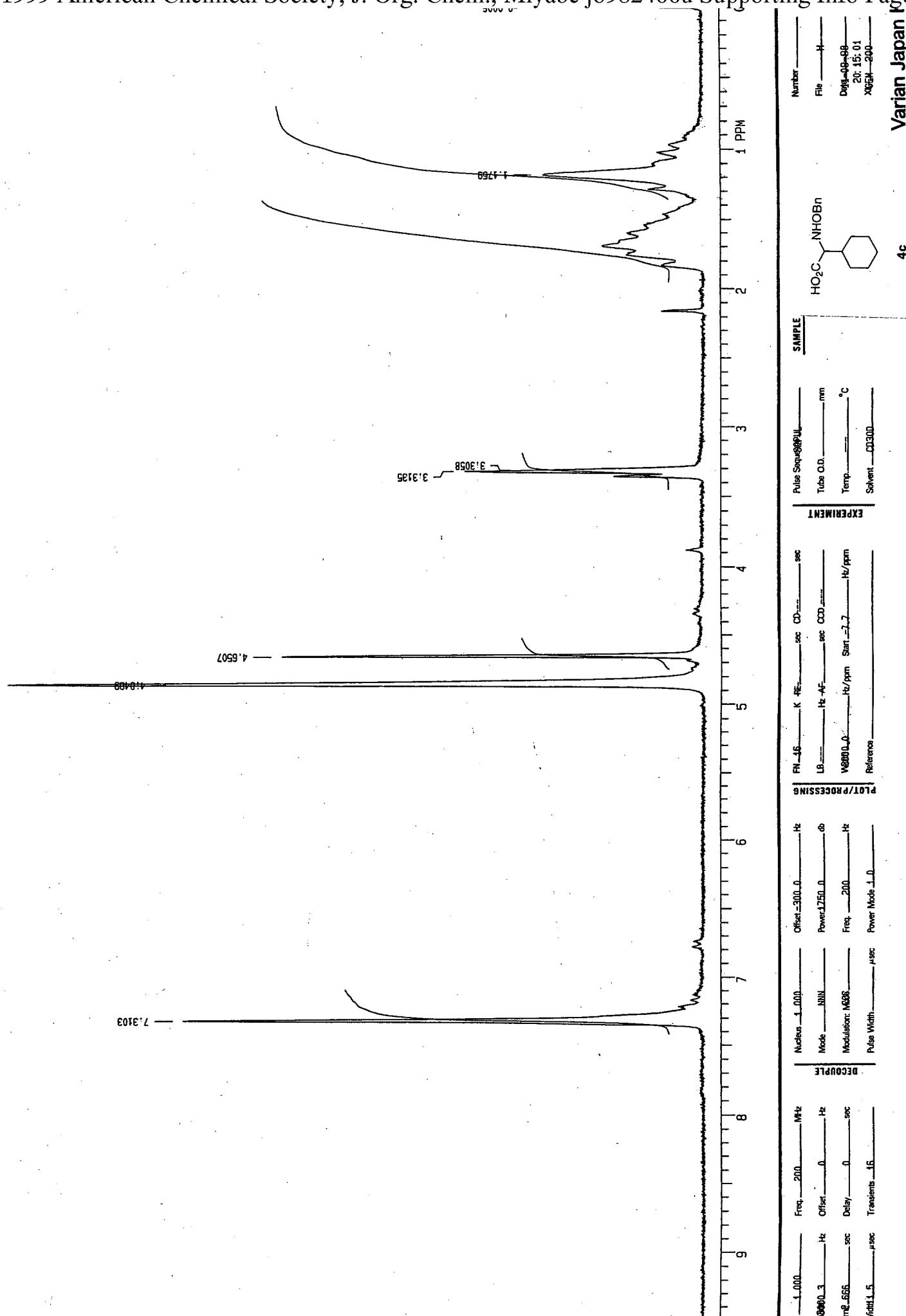
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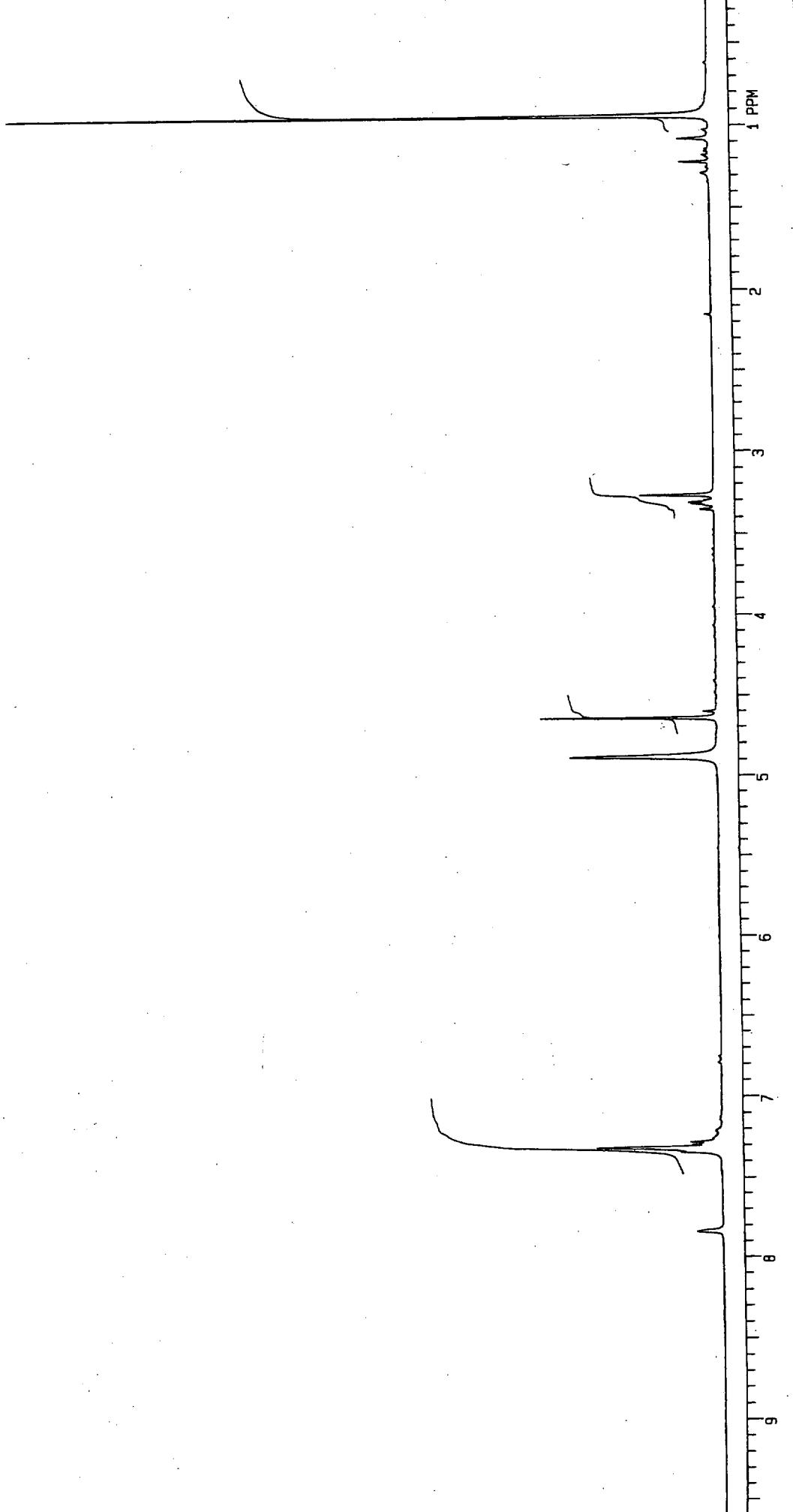
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4b





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mm	
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Temp.	— °C
Solvent	CDCl <sub>3</sub>

**EXPERIMENT**

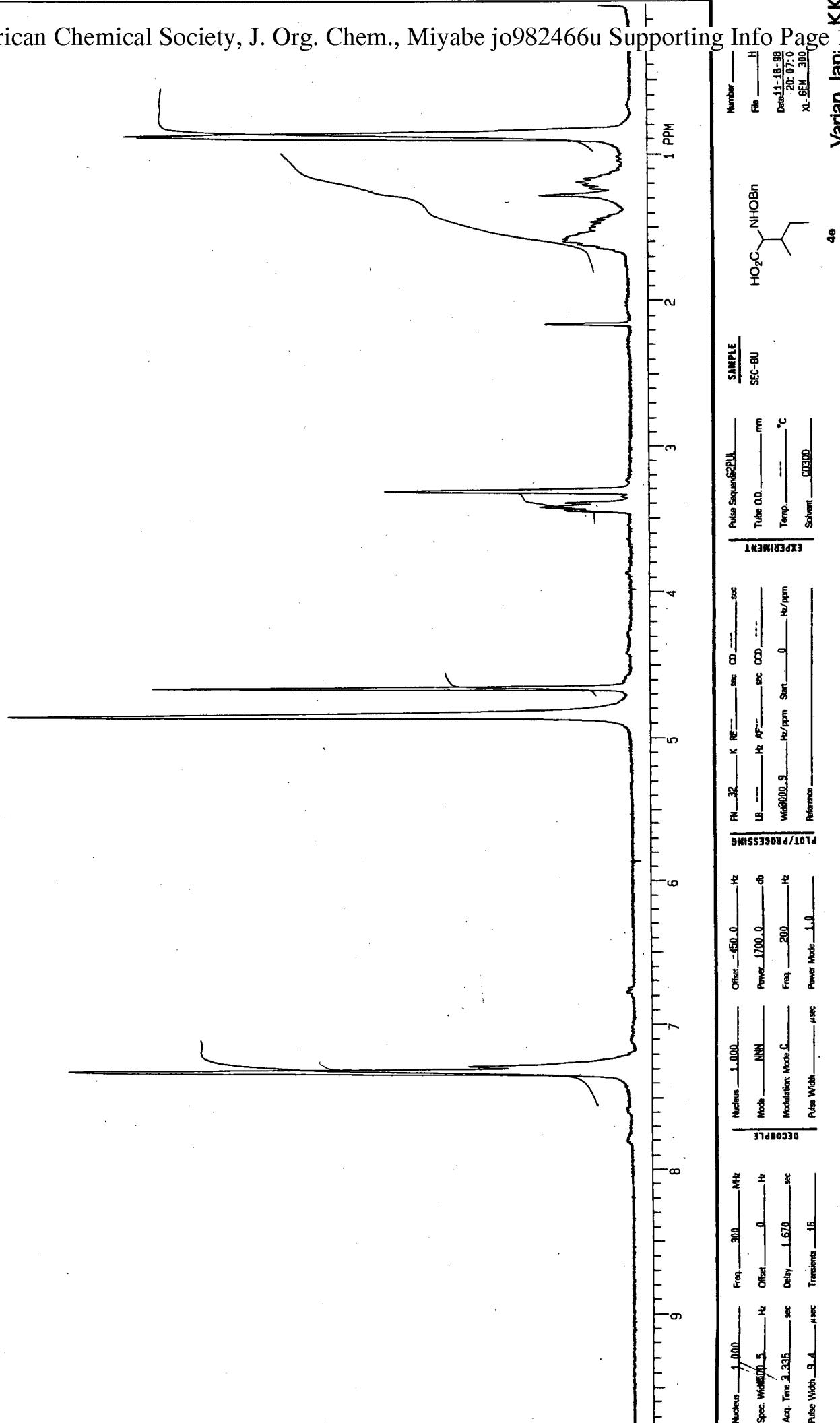
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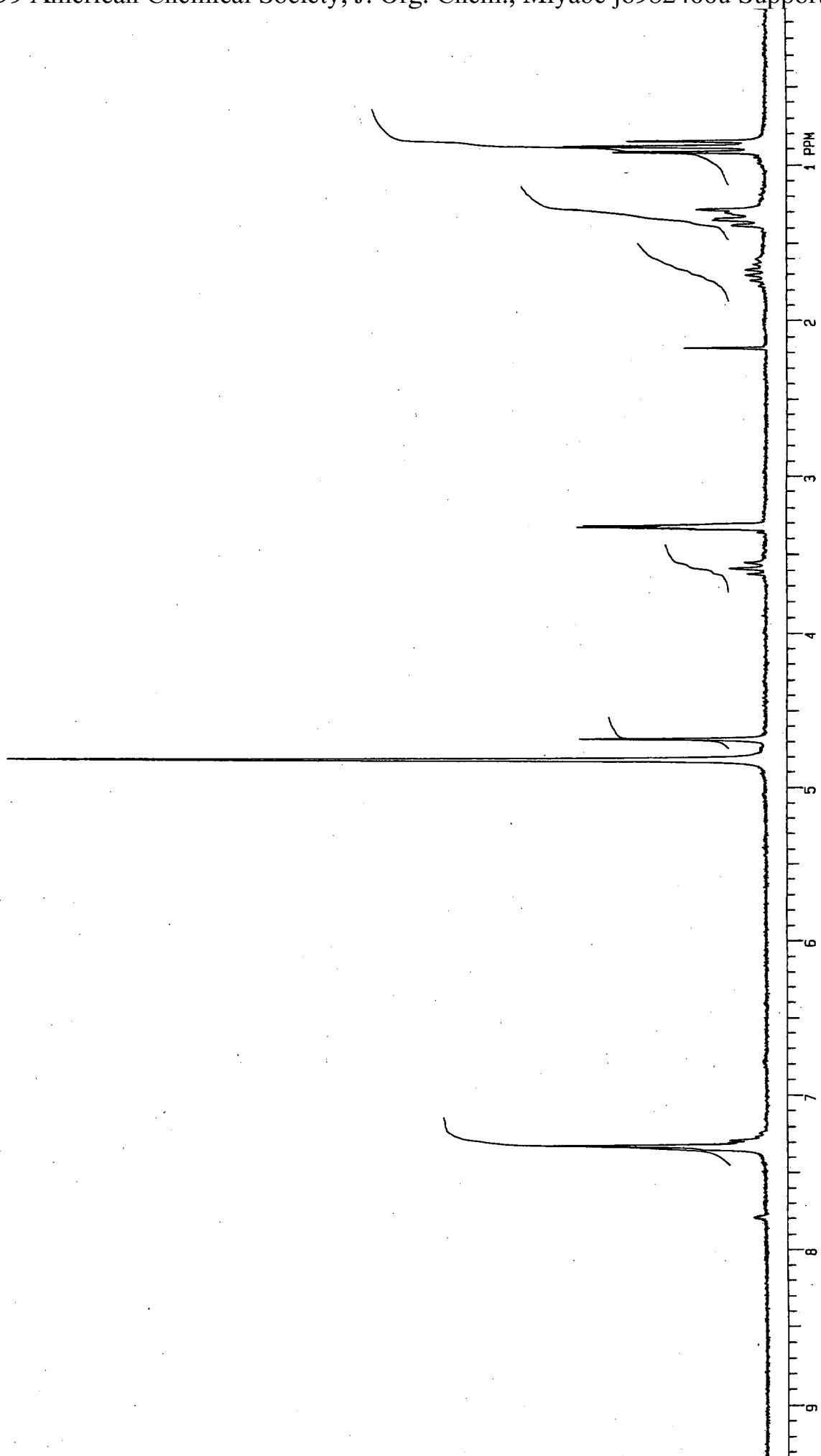
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**DECOUPLE**

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MHz	
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Hz	
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dB	
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sec	
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Date 4-18-98  
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