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# Trisoxazoline/Cu(II)-promoted Kinugasa Reaction. Enantioselective Synthesis of $\beta$ -Lactams

Meng-Chun Ye, Jian Zhou and Yong Tang\*

*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, 354*

*Fenglin Road, Shanghai 200032, China.*

tangy@mail.sioc.ac.cn

## *Supporting Information*

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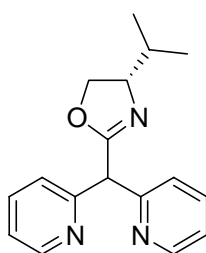
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**General Methods.** Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, alkynes and acetonitrile were used as received. Various alkyl amines were purchased from commercial suppliers and were distilled over potassium hydroxide pellets under air atmosphere. Nitrones were prepared according to literature procedures.<sup>1,2</sup> The synthesis of ligands **2a-2d**, **2e-2l**, **2m**, and **2n-2o** have been reported.<sup>3</sup>

### The Synthesis of Chiral Ligand **2p**.

#### (S)-2-(dipyridin-2-ylmethyl)-4-isopropyl-4,5-dihydrooxazole **2p**



To a solution of dipyridin-2-ylmethane (272 mg, 1.6 mmol) in dried THF (30 mL) was added dropwise *t*-BuLi (0.95 mL, 1.7 M in hexanes, 1.6 mmol) within 15-20 minutes at -78 °C under N<sub>2</sub>. The resulting yellow solution was stirred for an additional hour at this temperature. Then a solution of (4S)-2-bromo-4-isopropyl-4,5-dihydro-oxazole (357 mg, 1.9 mmol) in THF (10 mL) was added dropwise at -78 °C over 10 minutes. The solution was slowly warmed to room temperature and was stirred for an hour, then refluxed for six hours. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (30 mL) and was washed with H<sub>2</sub>O (5 mL). The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was purified by flash chromatography (EtOAc/Et<sub>3</sub>N = 200/1) to give the desired product (syrup): 257 mg (57%). [α]<sub>D</sub><sup>20</sup> -37.0 (c 0.75, CHCl<sub>3</sub>); IR (neat) 2961, 2891, 1671, 1586, 1567, 1467, 1432, 1356, 997, 989 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.57-8.54 (m, 2H), 7.64-7.60 (m, 2H), 7.48-7.42 (m, 2H), 7.18-7.15 (m, 2H), 5.46 (s, 1H), 4.30-4.22 (m, 1H), 4.05-3.97 (m, 2H), 1.84-1.76 (m, 1H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 65.4, 158.1, 158.0, 149.4, 149.4, 136.6, 123.7, 123.6, 122.2, 122.2, 72.0, 70.0, 56.2, 32.4, 18.9, 17.7; LRMS-EI(*m/z*): 281 (M<sup>+</sup>), 169 (100); HRMS-ESI (*m/z*): [M+H]<sup>+</sup>

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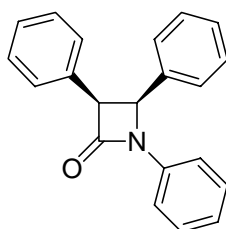
calcd for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O, 282.1601; found, 282.1617.

**General Procedures for Catalytic Asymmetric Synthesis of  $\beta$ -Lactams.**

**Procedure A:** A mixture of Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (9.3 mg, 0.025 mmol) and (S)-isopropyl-trisoxazoline **2a** (11.3 mg, 0.03 mmol) in CH<sub>3</sub>CN (4 mL) was stirred under air atmosphere at 15 °C for two hours. The solution was cooled to 0 °C and then Cy<sub>2</sub>NH (50  $\mu$ L, 0.25 mmol) was added. After ten minutes, alkyne (0.375 mmol) was added. When the color of the resulting mixture turned into light yellow, to this solution was added nitron (0.25 mmol). After the reaction was complete (monitored by TLC), the mixture was passed through a short silica gel column (neat CH<sub>2</sub>Cl<sub>2</sub> as the eluent). The filtrate was concentrated and the residue was purified by flash chromatography (PE/CH<sub>2</sub>Cl<sub>2</sub>) to afford the product. The diastereoselectivity was determined by <sup>1</sup>H NMR spectroscopic analysis of crude product. The determination of enantiomeric excess of *cis* isomer was performed by chiral HPLC with a Daicel Chiralcel OD-H column (eluent: Hexane/<sup>i</sup>PrOH (80/20), flow rate: 0.7 mL/min).

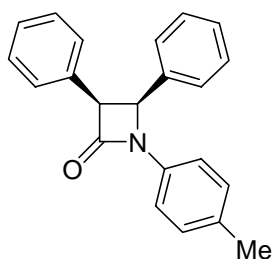
**Procedure B:** A mixture of Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (4.6 mg, 0.0125 mmol) and (S)-<sup>t</sup>Bu-BOX **1b** (4.5 mg, 0.015 mmol) in CH<sub>3</sub>CN (2 mL) was stirred under air atmosphere at 15 °C for two hours. The solution was cooled to 0 °C and then <sup>t</sup>Pr<sub>2</sub>NEt (9  $\mu$ L, 0.05 mmol) and nitron (0.25 mmol) was added. After ten minutes, ethyl propiolate (50.6  $\mu$ L, 0.5 mmol) was added. After the reaction was complete (monitored by TLC), the mixture was passed through a short silica gel column (neat CH<sub>2</sub>Cl<sub>2</sub> as the eluent). The filtrate was concentrated and the residue was purified by flash chromatography (PE/CH<sub>2</sub>Cl<sub>2</sub>) to afford the product. The diastereoselectivity was determined by <sup>1</sup>H NMR spectroscopic analysis of crude product. The determination of enantiomeric excess of *trans* isomer was performed by chiral HPLC with a Daicel Chiralcel OD-H column (eluent: Hexane/<sup>i</sup>PrOH (85/15), flow rate: 0.9 mL/min).

**(3S,4S)-1,3,4-triphenyl-2-azetidinone 6a<sup>5</sup>**



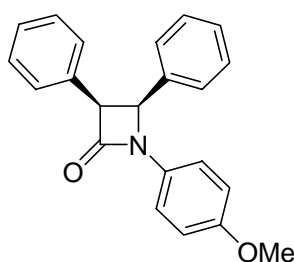
**Procedure A:** 56% yield (solid, 35 h);  $[\alpha]_{\text{D}}^{20}$  -8.0 (c 1.62,  $\text{CHCl}_3$ ; 82% ee);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.43-7.40 (m, 2H), 7.29-7.24 (m, 2H), 7.09-7.03 (m, 11H), 5.45 (d,  $J = 6.3$  Hz, 1H), 5.00 (d,  $J = 6.6$  Hz, 1H).

**(3S,4S)-1-(4-Methylphenyl)-3,4-diphenyl-2-azetidinone 6b<sup>6</sup>**



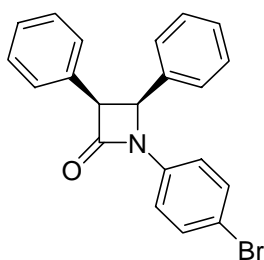
**Procedure A:** 36% yield (solid, 56 h);  $[\alpha]_{\text{D}}^{20}$  -10.5 (c 0.68,  $\text{CHCl}_3$ ; 82% ee);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.32-7.26 (m, 2H), 7.11-7.03 (m, 12H), 5.44 (d,  $J = 6.0$  Hz, 1H), 5.00 (d,  $J = 5.7$  Hz, 1H), 2.29 (s, 3H).

**(3S,4S)-1-(4-Methoxyphenyl)-3,4-diphenyl-2-azetidinone 6c<sup>7</sup>**



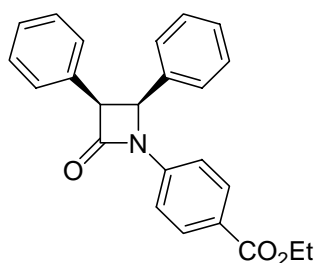
**Procedure A:** 36% yield (solid, 7 days);  $[\alpha]_{\text{D}}^{20}$  -4.8 (c 0.63,  $\text{CHCl}_3$ ; 84% ee);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36 (dd,  $J = 2.1, 6.9$  Hz, 2H), 7.11-7.03 (m, 10H), 6.82 (dd,  $J = 2.1, 6.6$  Hz, 2H), 5.42 (d,  $J = 6.0$  Hz, 1H), 5.00 (d,  $J = 6.3$  Hz, 1H), 3.76 (s, 3H).

**(3S,4S)-1-(4-Bromophenyl)-3,4-diphenyl-2-azetidinone 6d<sup>1</sup>**



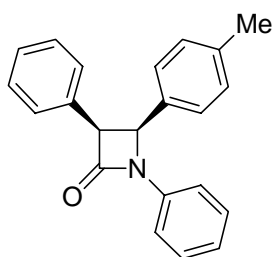
**Procedure A:** 70% yield (solid, 33 h);  $[\alpha]_D^{20}$  -16 (c 0.29,  $\text{CHCl}_3$ ; 75% ee);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39 (d,  $J = 8.7$  Hz, 2H), 7.30 (d,  $J = 9.0$  Hz, 2H), 7.12-7.02 (m, 10H), 5.45 (d,  $J = 6.3$  Hz, 1H), 5.03 (d,  $J = 6.6$  Hz, 1H).

**(3S,4S)-1-(4-Carboethoxyphenyl)-3,4-diphenyl-2-azetidinone 6e<sup>1</sup>**



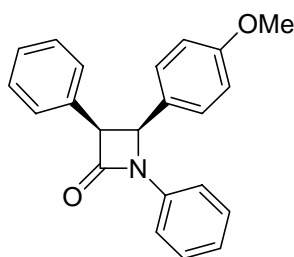
**Procedure A:** 98% yield (syrup, 9 h);  $[\alpha]_D^{20}$  -11.4 (c 1.43,  $\text{CHCl}_3$ ; 70% ee);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.98 (d,  $J = 8.7$  Hz, 2H), 7.44 (d,  $J = 9.0$  Hz, 2H), 7.12-7.03 (m, 10H), 5.51 (d,  $J = 6.6$  Hz, 1H), 5.06 (d,  $J = 6.3$  Hz, 1H), 4.34 (q,  $J = 6.9$  Hz, 2H), 1.36 (t,  $J = 6.9$  Hz, 3H).

**(3S,4S)-4-(4-Methylphenyl)-1,3-diphenyl-2-azetidinone 6f<sup>6</sup>**



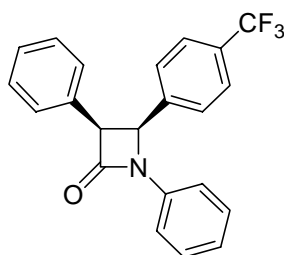
**Procedure A:** 50% yield (solid, 56 h);  $[\alpha]_D^{20}$  -14.2 (c 0.95,  $\text{CHCl}_3$ ; 82% ee);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43-7.39 (m, 2H), 7.30-7.25 (m, 2H), 7.10-7.05 (m, 6H), 6.97-6.90 (m, 4H), 5.44 (d,  $J = 6.0$  Hz, 1H), 4.98 (d,  $J = 6.0$  Hz, 1H), 2.18 (s, 3H).

**(3S,4S)-4-(4-Methoxyphenyl)-1,3-diphenyl-2-azetidinone 6g<sup>8</sup>**



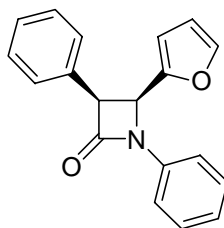
**Procedure A:** 58% yield (solid, 8 days);  $[\alpha]_D^{20}$  -11.6 (c 0.98,  $\text{CHCl}_3$ ; 83% ee);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43-7.40 (m, 2H), 7.31-7.25 (m, 2H), 7.12-7.07 (m, 6H), 7.00 (dd,  $J = 2.4, 6.9$  Hz, 2H), 6.65 (dd,  $J = 2.1, 6.6$  Hz, 2H), 5.43 (d,  $J = 6.0$  Hz, 1H), 4.99 (d,  $J = 6.3$  Hz, 1H), 3.67 (s, 3H).

**(3S,4S)-4-(4-Trifluoromethylphenyl)-1,3-diphenyl-2-azetidinone 6h**



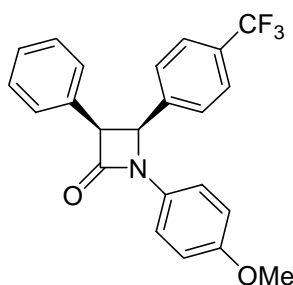
**Procedure A:** 75% yield (solid, 22 hours);  $[\alpha]_D^{20}$  -6.6 (c 0.89,  $\text{CHCl}_3$ ; 82% ee);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.40-7.26 (m, 6H), 7.18 (d,  $J = 8.4$  Hz, 2H), 7.13-7.01 (m, 6H), 5.51 (d,  $J = 6.0$  Hz, 1H), 5.06 (d,  $J = 6.0$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  165.2, 142.3, 138.7, 137.3, 131.4, 130.0 (q,  $^2J_{\text{C-F}} = 40$ ), 129.2, 128.7, 128.3, 127.6, 127.4, 125.2 (q,  $^3J_{\text{C-F}} = 3.8$ ), 124.4, 123.7 (q,  $^1J_{\text{C-F}} = 256$ ), 117.1, 60.4, 59.7; IR (KBr): 3033, 2925, 1755, 1621, 1599, 1498, 1454, 1422, 1379, 1326, 1168, 1125, 1069, 1018, 885, 837, 754, 698  $\text{cm}^{-1}$ ; EI (m/z): 367 ( $\text{M}^+$ ) (10), 248 (100); Anal. Calcd. For  $\text{C}_{22}\text{H}_{16}\text{F}_3\text{NO}$ : C, 71.93; H, 4.39; N, 3.81. Found: C, 71.71; H, 4.44; N, 3.65.

**(3S,4S)-4-(2-furyl)-1,3-diphenyl-2-azetidinone 6i<sup>9</sup>**



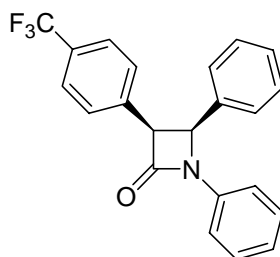
**Procedure A:** 56% yield (solid, 7 days);  $[\alpha]_D^{20}$  -37.4 (c 0.66, CHCl<sub>3</sub>; 85% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.45-7.41 (m, 2H), 7.33-7.26 (m, 2H), 7.22-7.19 (m, 5H), 7.13-7.09 (m, 2H), 6.12-6.11 (m, 2H), 5.47 (d, *J* = 5.7 Hz, 1H), 4.97 (d, *J* = 6.0 Hz, 1H).

**(3S,4S)-1-(4-Methoxyphenyl)-4-(4-trifluoromethylphenyl)-3-phenyl-2-azetidinoe 6j<sup>1</sup>**



**Procedure A:** 35% yield (solid, 7 days);  $[\alpha]_D^{20}$  -4.0 (c 0.80, CHCl<sub>3</sub>; 84% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 9.0 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.09-7.03 (m, 5H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.47 d, *J* = 5.7 Hz, 1H), 5.04 (d, *J* = 6.0 Hz, 1H), 3.76 (s, 3H).

**(3S,4S)-3-(4-Trifluoromethylphenyl)-1,4-diphenyl-2-azetidinone 6k**

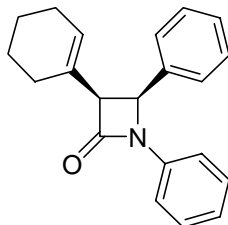


**Procedure A:** 65% yield (solid, 40 h);  $[\alpha]_D^{20}$  -6.5 (c 0.63, CHCl<sub>3</sub>; 73% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.42-7.30 (m, 6H), 7.20-7.05 (m, 8H), 5.51 (d, *J* = 6.0 Hz, 1H), 5.04 (d, *J* = 6.0 Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 164.6, 137.4, 136.2, 133.8, 129.9 (q, <sup>2</sup>*J*<sub>C-F</sub> = 40), 129.1, 128.5, 128.3, 126.9, 125.0 (q, <sup>3</sup>*J*<sub>C-F</sub> = 3.6), 124.3, 123.9 (q, <sup>1</sup>*J*<sub>C-F</sub> = 256), 117.2, 60.0, 59.6; IR (KBr): 3038, 2924, 1749, 1736, 1599, 1500, 1382, 1322, 1167, 1125, 1069, 885, 819, 763, 702 cm<sup>-1</sup>; EI (m/z): 367 (M<sup>+</sup>) (8), 181 (100); Anal. Calcd. For C<sub>22</sub>H<sub>16</sub>F<sub>3</sub>NO: C, 71.93; H, 4.39; N, 3.81. Found: C, 71.71; H, 4.13;

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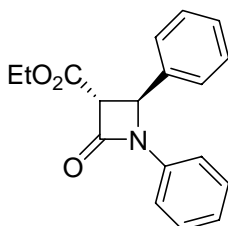
N, 3.52.

**(3S,4S)-3-(Cyclohex-1-enyl)-1,4-diphenyl-2-azetidinone 6l<sup>8</sup>**



**Procedure A:** 33% yield (solid, 5 days);  $[\alpha]_D^{20}$  -10.8 (c 0.72, CHCl<sub>3</sub>; 72% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.36-7.21 (m, 9H), 7.06-7.01 (m, 1H), 5.86-5.85 (m, 1H), 5.22 (d, *J* = 5.7 Hz, 1H), 4.18 (d, *J* = 6.0 Hz, 1H), 2.12-0.85(m, 8H).

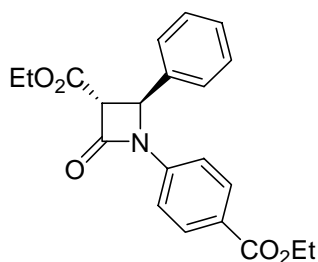
**(3R,4S)-ethyl 2-oxo-1,4-diphenylazetidine-3-carboxylate 6m<sup>10</sup>**



**Procedure B:** 67% yield (syrup, 1 h);  $[\alpha]_D^{20}$  34.9 (c 0.84, CHCl<sub>3</sub>; 50% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.41-7.23 (m, 9H), 7.09-7.07 (m, 1H), 5.35 (d, *J* = 3.0 Hz, 1H), 4.30 (q, *J* = 6.9 Hz, 2H), 3.99 (d, *J* = 2.7 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 166.1, 159.1, 137.0, 136.2, 129.2, 129.0, 128.9, 126.0, 124.3, 117.0, 63.4, 62.0, 57.4, 14.1.

**(3R,4S)-ethyl**

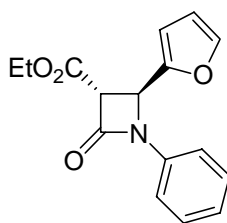
**1-(4-(ethoxycarbonyl)phenyl)-2-oxo-4-phenylazetidine-3-carboxylate 6n**



**Procedure B:** 80% yield (syrup, 1 h);  $[\alpha]_D^{20}$  17.4 (c 0.88, CHCl<sub>3</sub>; 49% ee); <sup>1</sup>H NMR

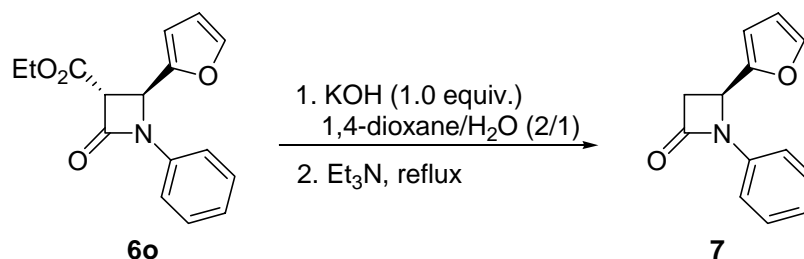
(300 MHz, CDCl<sub>3</sub>):  $\delta$  7.96-7.93 (m, 2H), 7.40-7.27 (m, 7H), 5.38 (d,  $J = 2.4$  Hz, 1H), 4.33 (q,  $J = 7.2$  Hz, 2H), 4.30 (q,  $J = 7.2$  Hz, 2H), 4.03 (d,  $J = 2.7$  Hz, 1H), 1.35 (t,  $J = 7.2$  Hz, 3H), 1.34 (t,  $J = 7.2$  Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  165.9, 165.8, 159.5, 140.5, 135.7, 130.8, 129.4, 129.2, 126.1, 126.0, 116.6, 36.7, 62.2, 60.9, 57.7, 14.2, 14.1; IR (KBr): 2982, 2938, 1768, 1723, 1606, 1514, 1456, 1365, 1173, 1114, 1013, 854, 769 cm<sup>-1</sup>; EI ( $m/z$ ): 367 (M<sup>+</sup>), 131 (100); Anal. Calcd. For C<sub>22</sub>H<sub>16</sub>F<sub>3</sub>NO: C, 68.31; H, 5.76; N, 3.81. Found: C, 68.31; H, 5.85; N, 3.46.

**(3R,4S)-ethyl 1-phenyl-2-oxo-4-(2-furyl)azetidine-3-carboxylate 6o**



**Procedure B:** 78% yield (syrup, 2 h); [ $\alpha$ ]<sub>D</sub><sup>20</sup> 13.9 (c 1.92, CHCl<sub>3</sub>; 45% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.42-7.25 (m, 5H), 7.11-7.06 (m, 1H), 6.54 (d,  $J = 3.6$  Hz, 1H), 6.38 (dd,  $J = 2.1, 3.3$  Hz, 1H), 5.38 (d,  $J = 2.4$  Hz, 1H), 4.33 (d,  $J = 2.7$  Hz, 1H), 4.28 (q,  $J = 7.2$  Hz, 2H), 1.33 (t,  $J = 7.5$  Hz, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  166.0, 158.9, 148.4, 143.6, 137.2, 129.0, 124.5, 116.8, 110.7, 110.6, 62.2, 60.2, 50.7, 14.1; IR (KBr): 2985, 2356, 1769, 1727, 1590, 1545, 1497, 1369, 1294, 1154, 1010, 752 cm<sup>-1</sup>; EI ( $m/z$ ): 285 (M<sup>+</sup>), 166 (100); HRMS-ESI ( $m/z$ ): [M+Na]<sup>+</sup> calcd for C<sub>16</sub>H<sub>15</sub>NO<sub>4</sub>, 308.0899; found, 308.0891.

Absolute configurations of  $\beta$ -lactams **6a-6l** were determined by comparison of their optical rotations with those of the known compounds. For  $\beta$ -Lactam **6o**, its configuration was determined by chemical transformation into a known compound **7**.<sup>4</sup> **(S)-4-(furan-2-yl)-1-phenyl-2-azetidinone 7**<sup>4</sup>



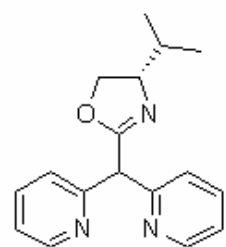
To a solution of compound **6o** (45% ee, 143 mg, 0.5 mmol) in 1,4-dioxane (4 mL) and H<sub>2</sub>O (2 mL) was added KOH (56 mg, 1.0 mmol) at room temperature. The resulting mixture was stirred overnight. Then the mixture was washed with CH<sub>2</sub>Cl<sub>2</sub> (3×6 mL). The aqueous layer was acidified with HCl (1 N, 2 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×10 mL), and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated to give the crude hydrolysate. Triethylamine (10 mL) was added and the mixture was refluxed for 10 hours. Cooled to rt, the mixture was concentrated in vacuo, washed with KOH (1 N, 2 mL), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×10 mL). The combined organic phases were concentrated and the residue was purified by flash chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give the desired product **7** (solid, 20% yield).  $[\alpha]_D^{20}$  -82.0 (c 0.42, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.40-7.35 (m, 3H), 7.27-7.24 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 2.7 Hz, 1H), 6.37-6.35 (m, 1H), 5.06 (dd, *J* = 2.7, 5.4 Hz, 1H), 3.47 (dd, *J* = 6.0, 15.6 Hz, 1H), 3.27 (dd, *J* = 2.4, 15.0 Hz, 1H).

Reference:

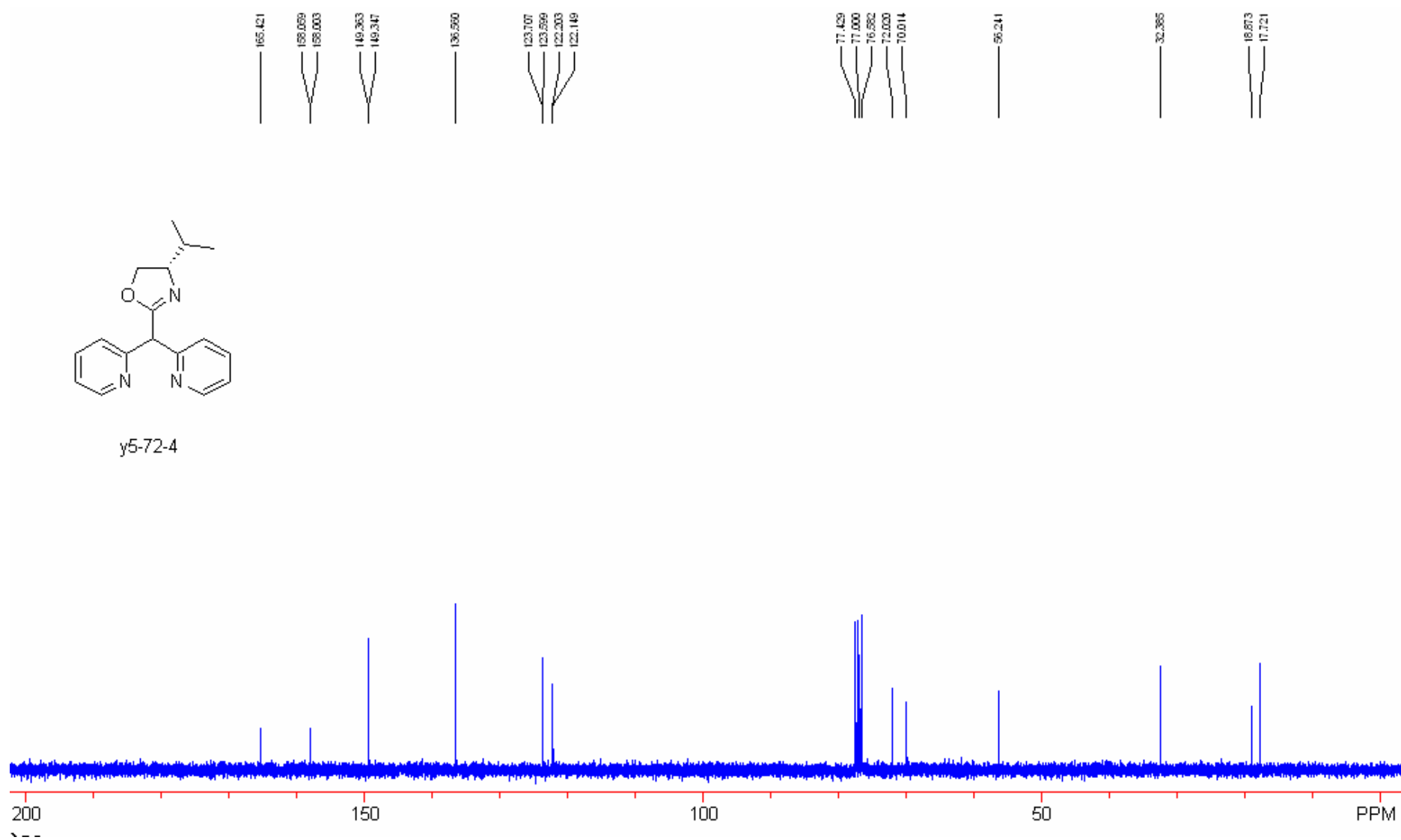
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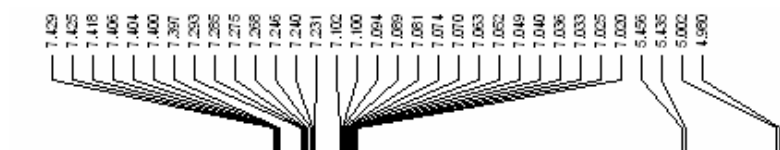
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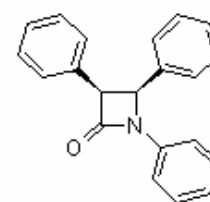


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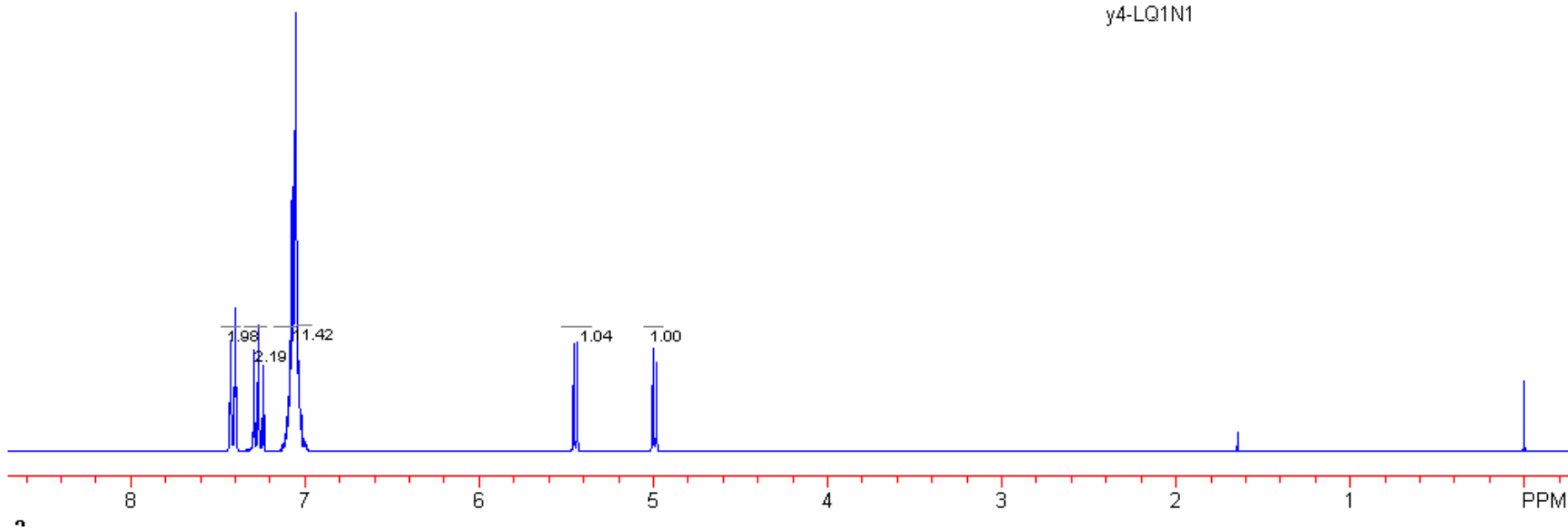




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y4-LQ1N1



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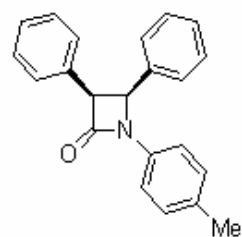
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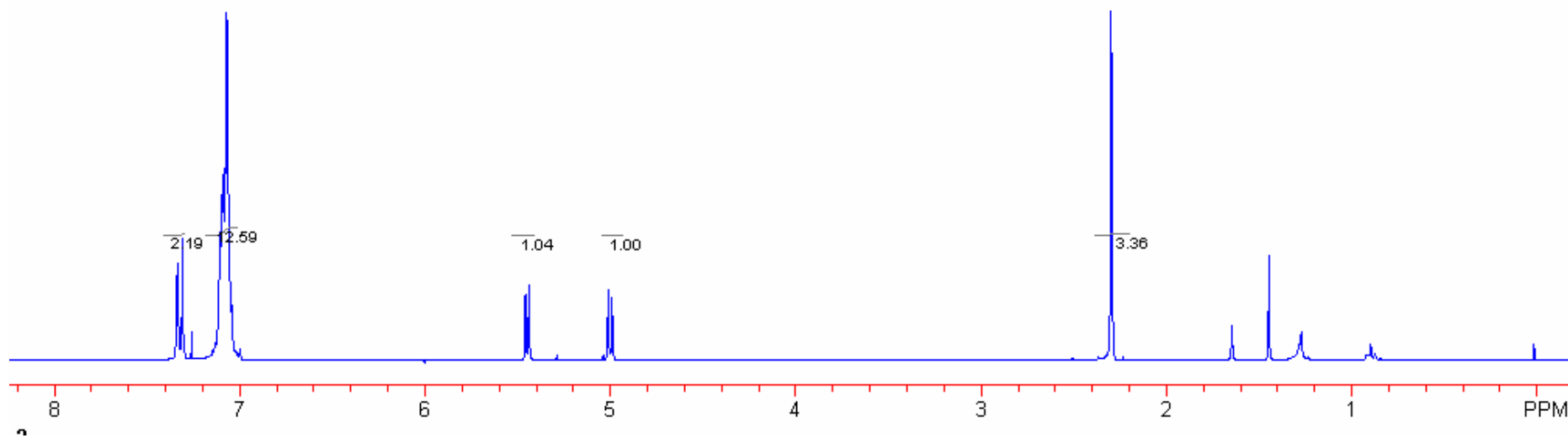
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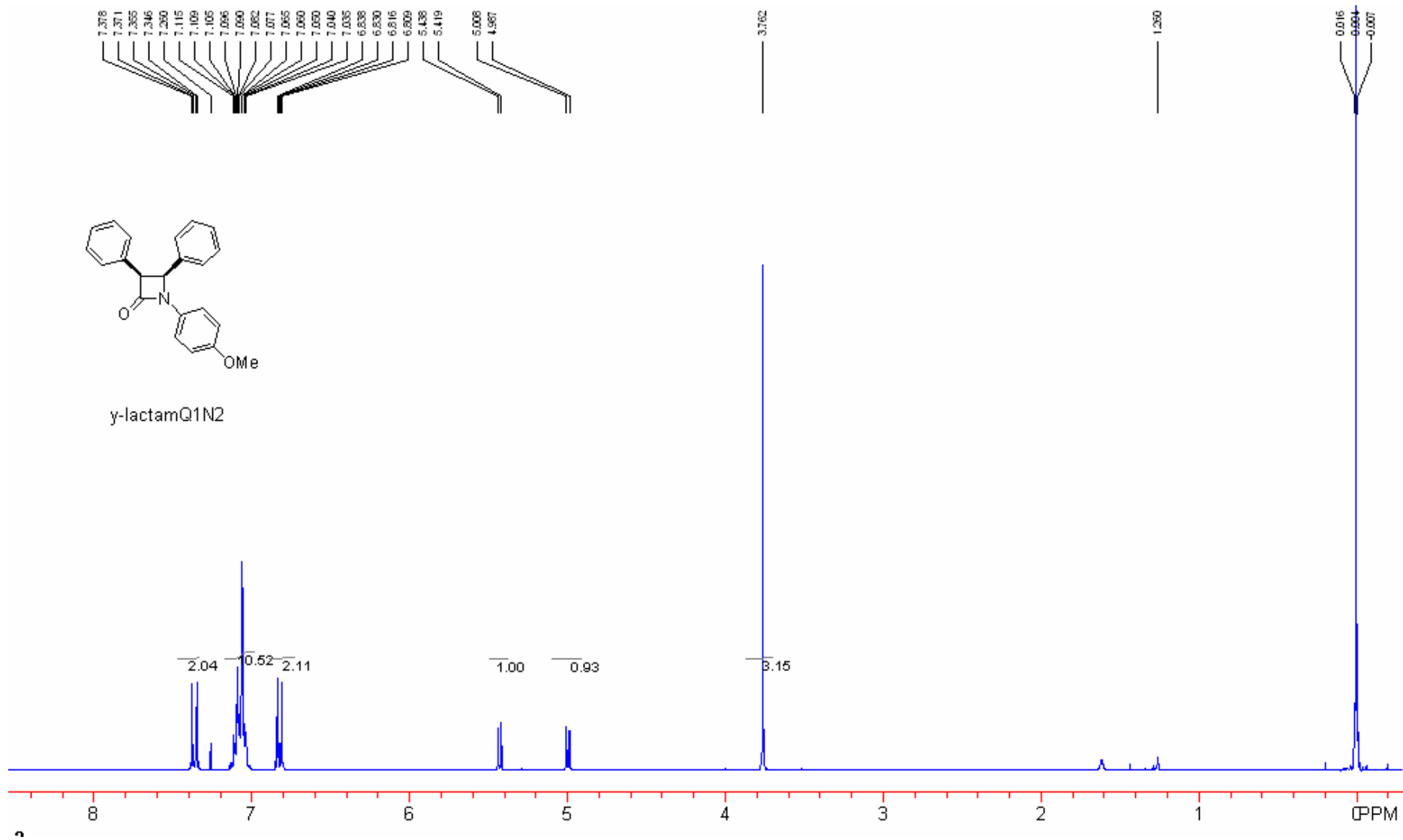
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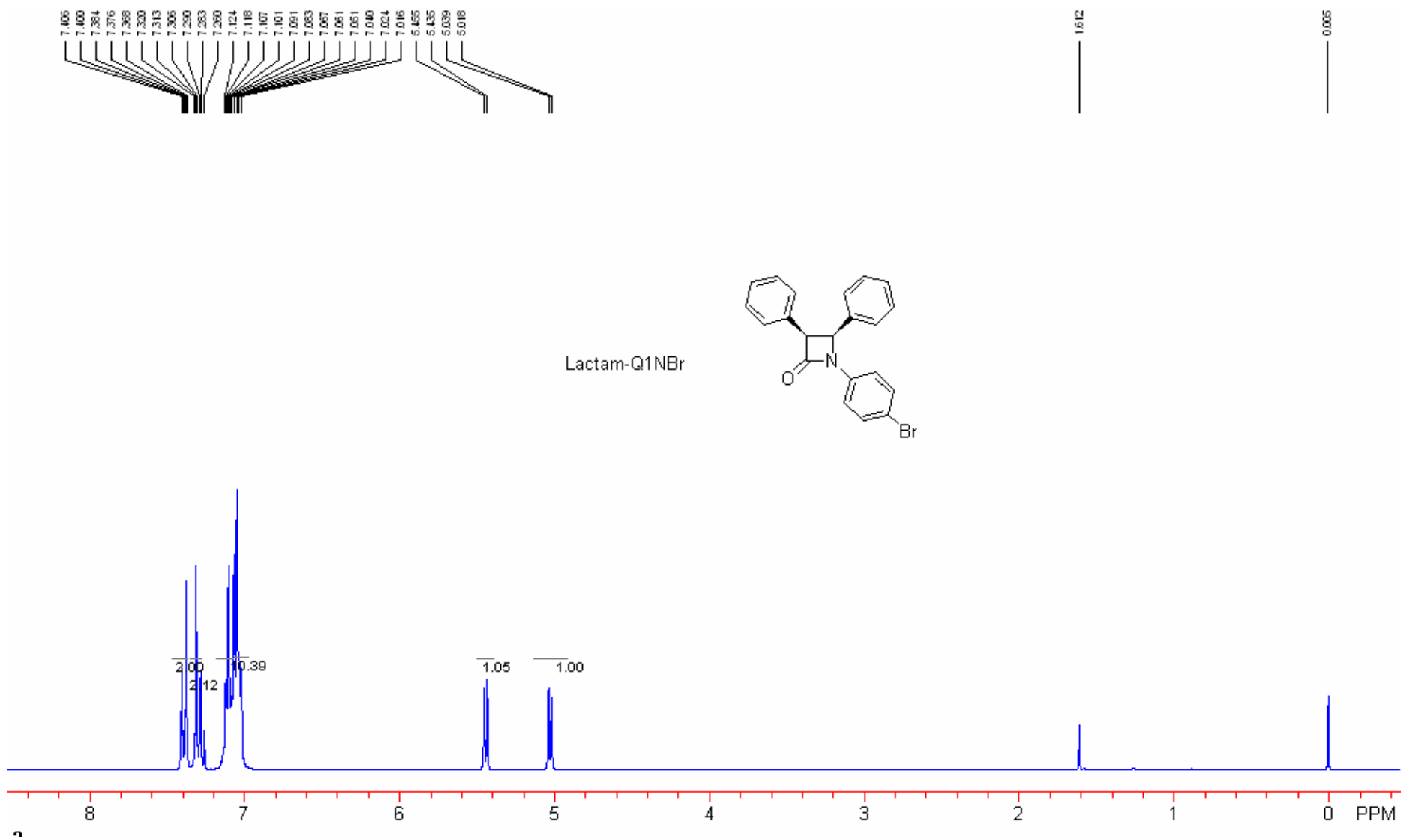
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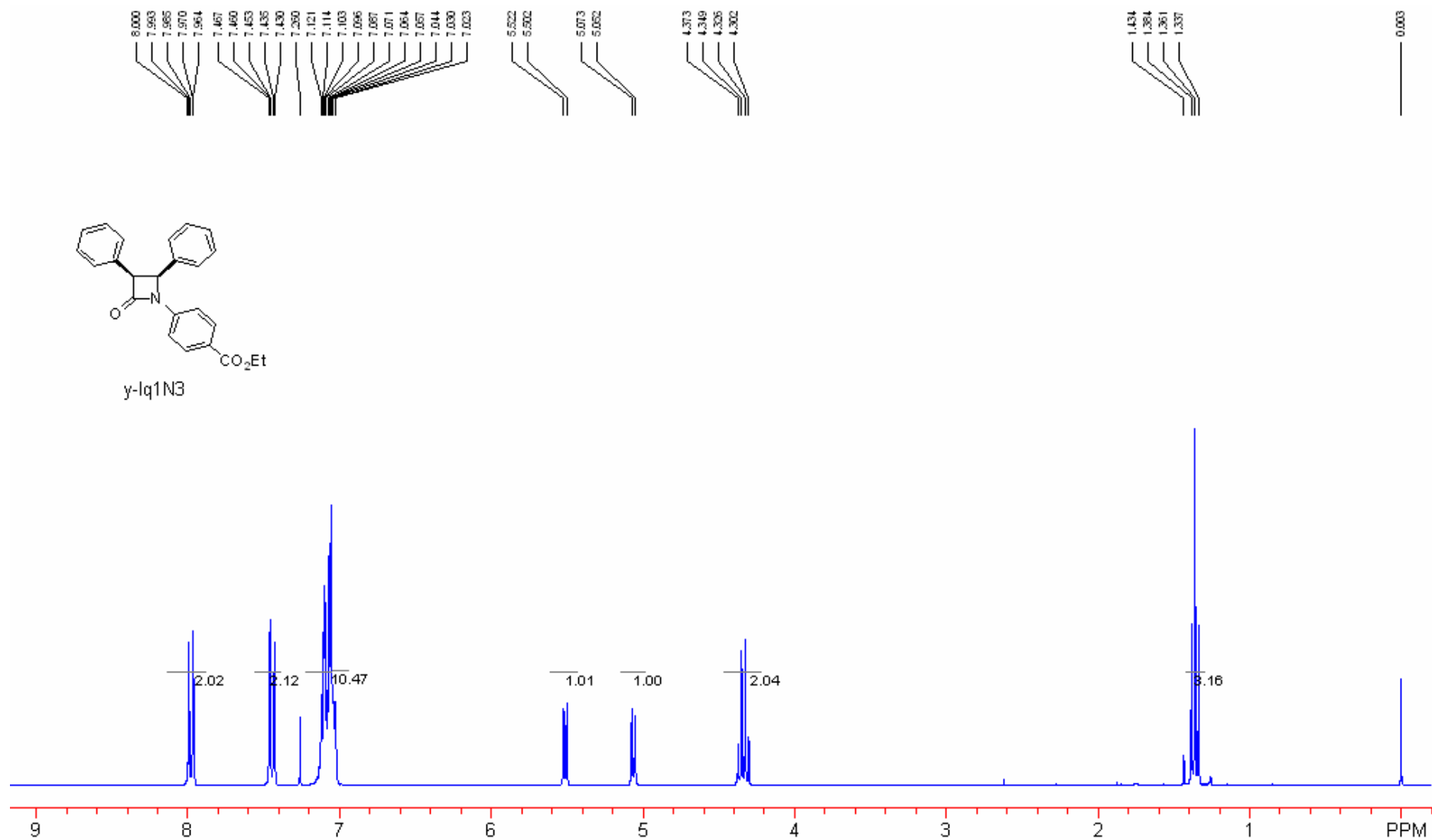
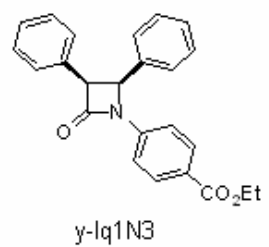


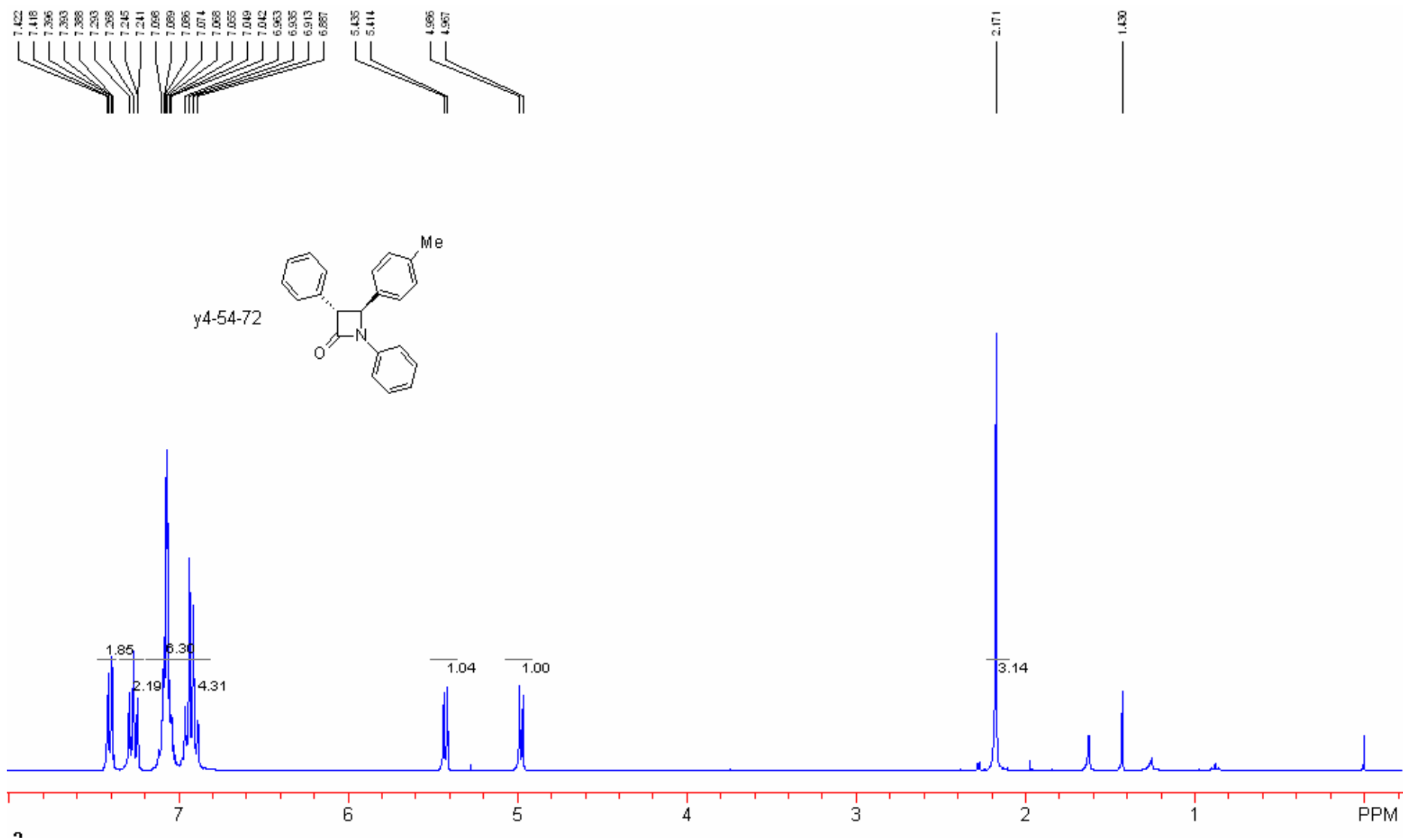
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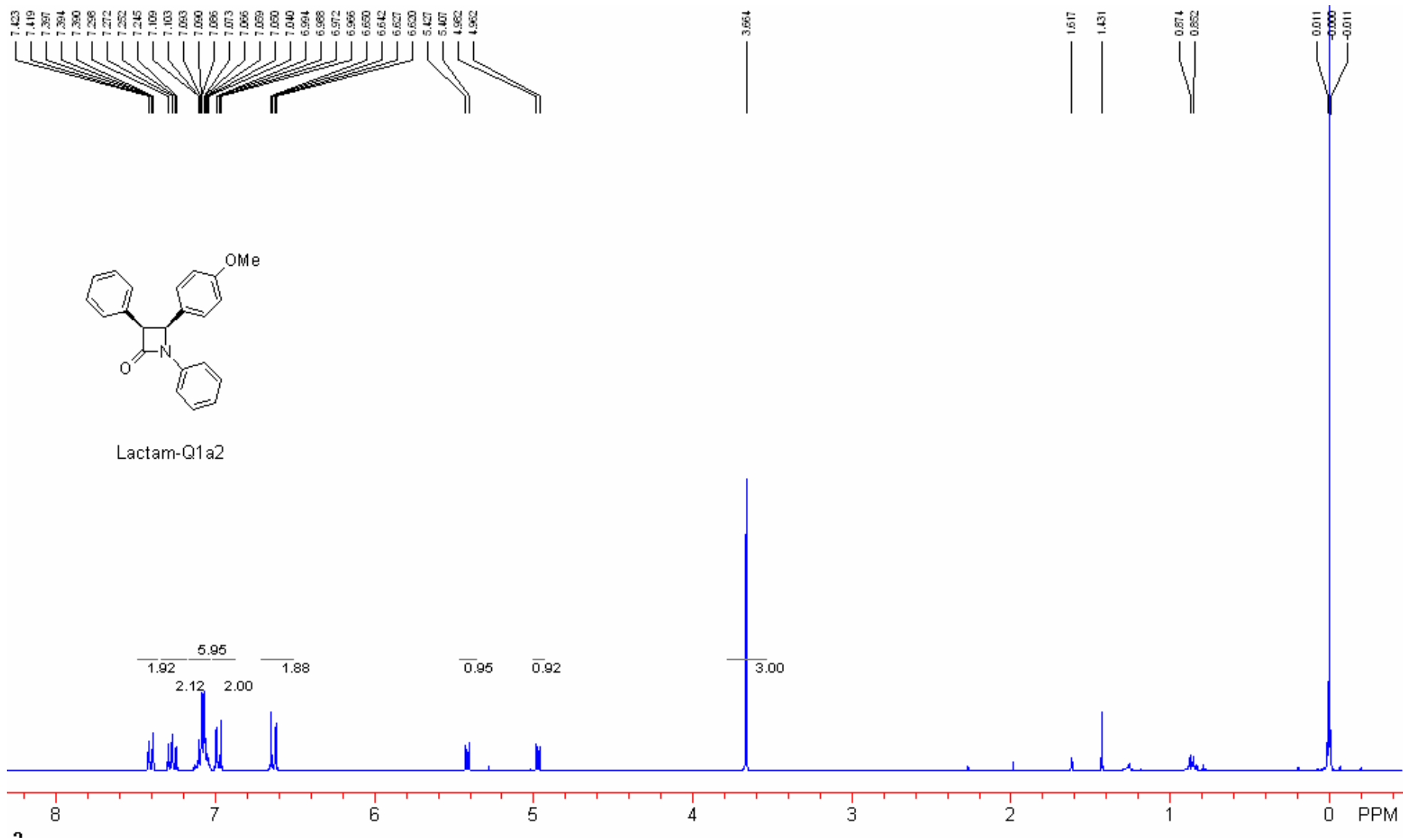


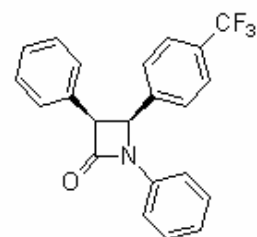
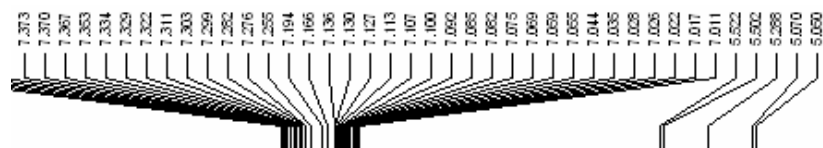




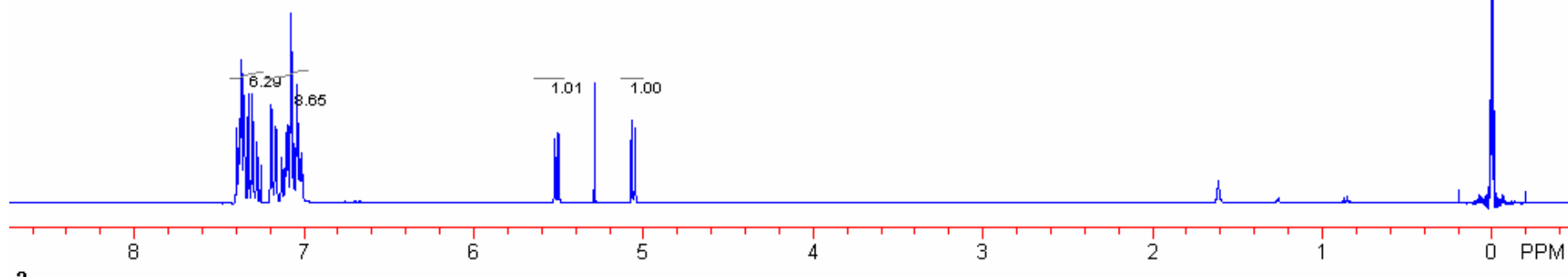
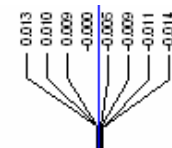


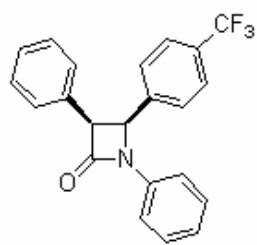




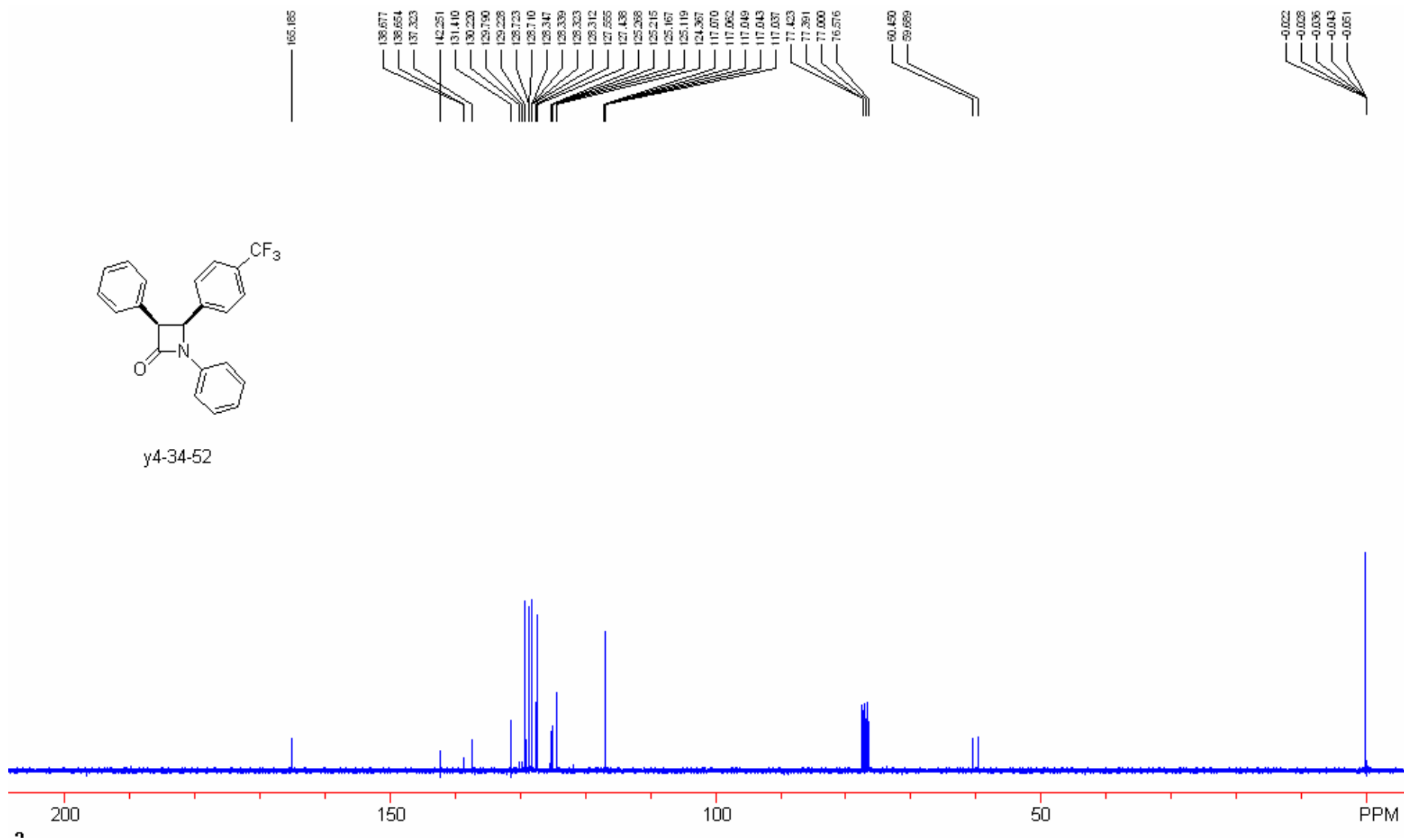


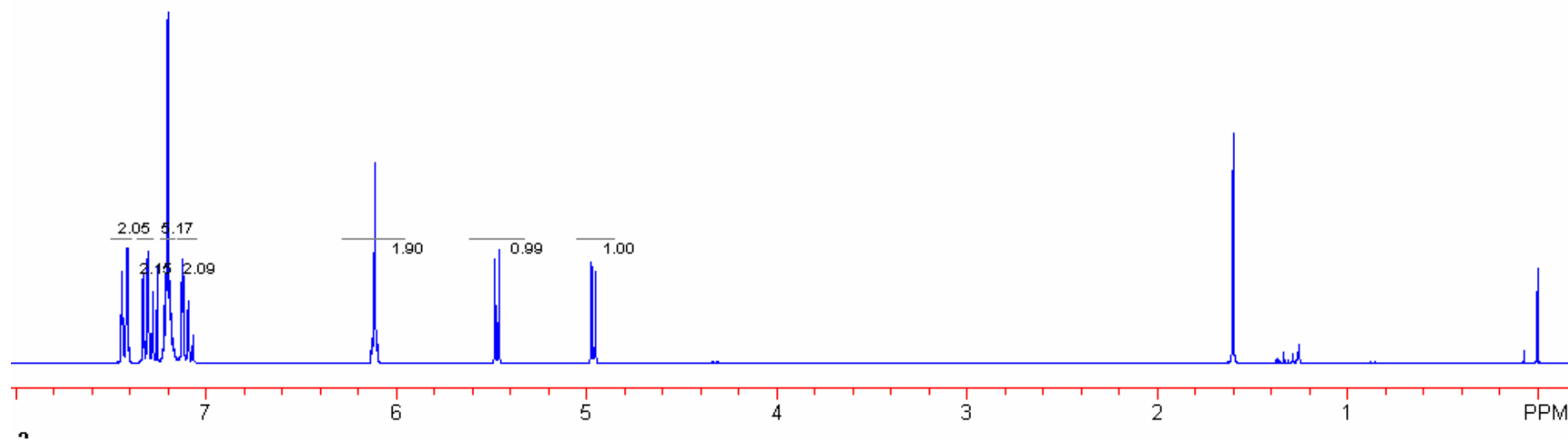
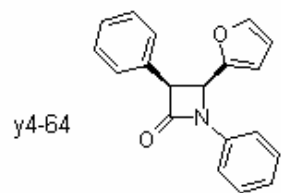
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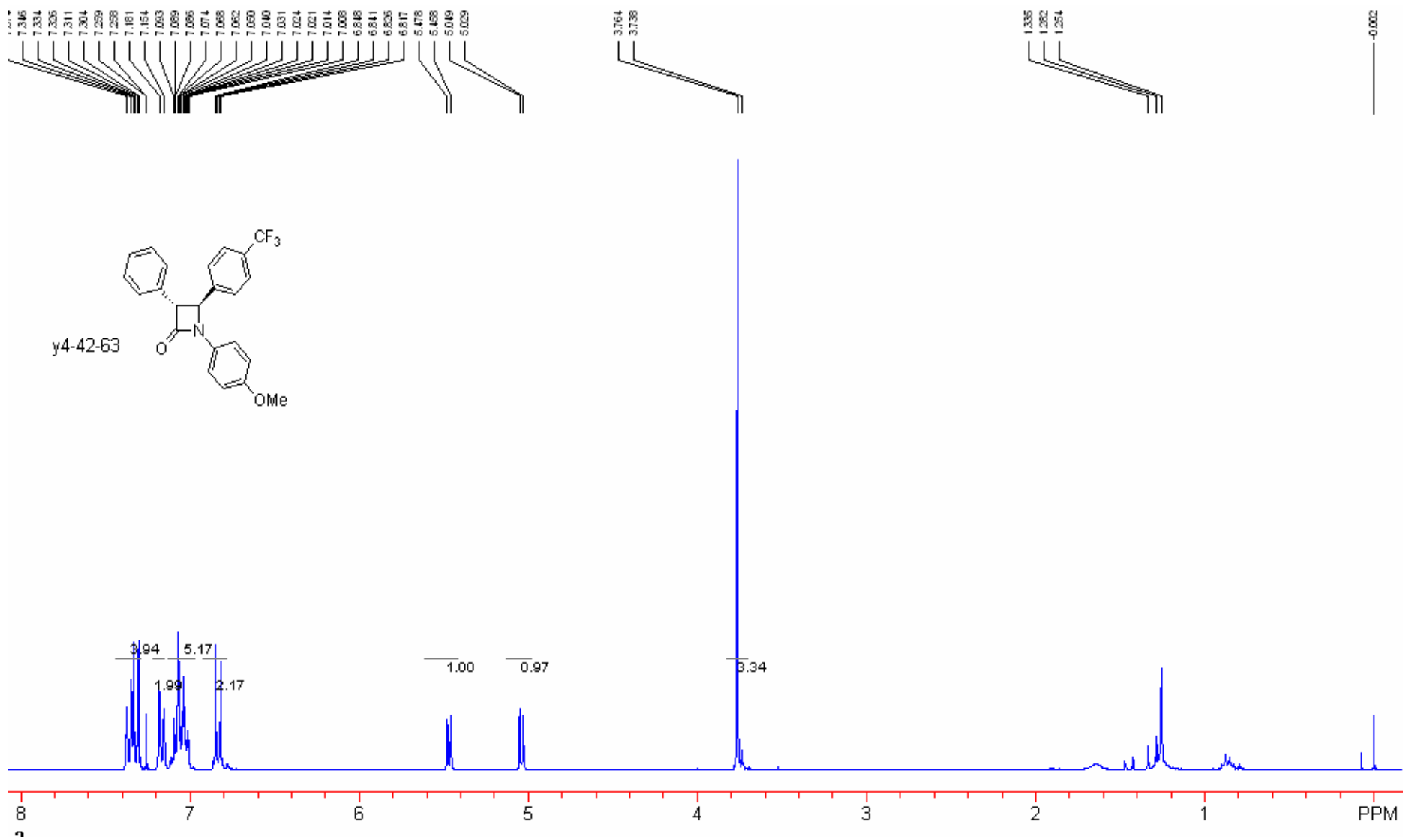


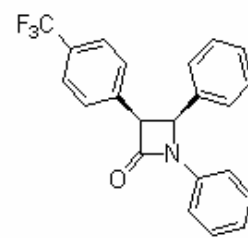
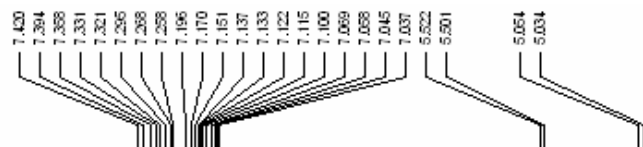


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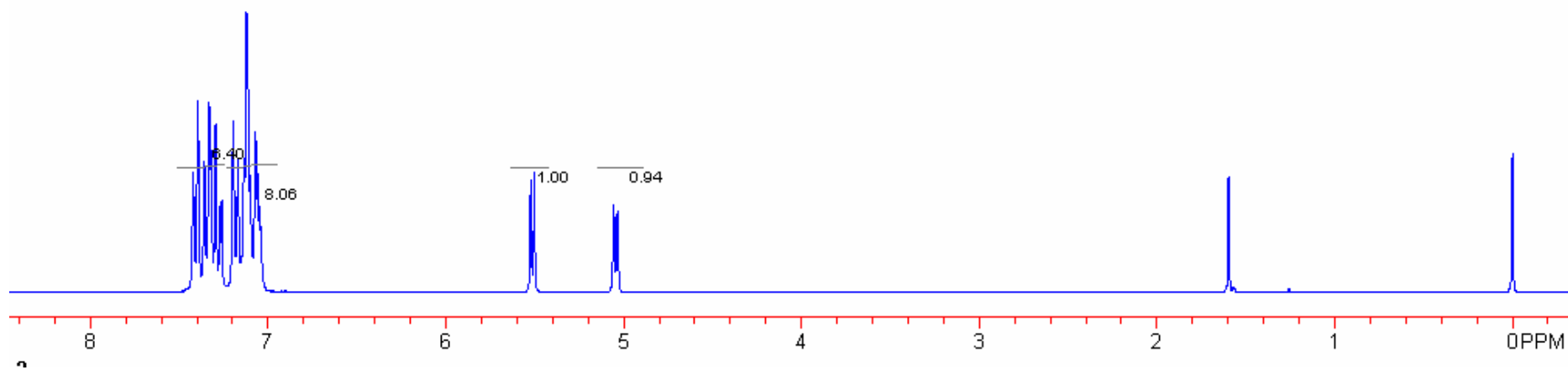


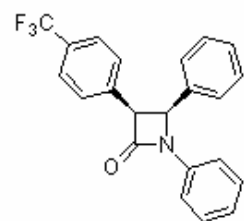




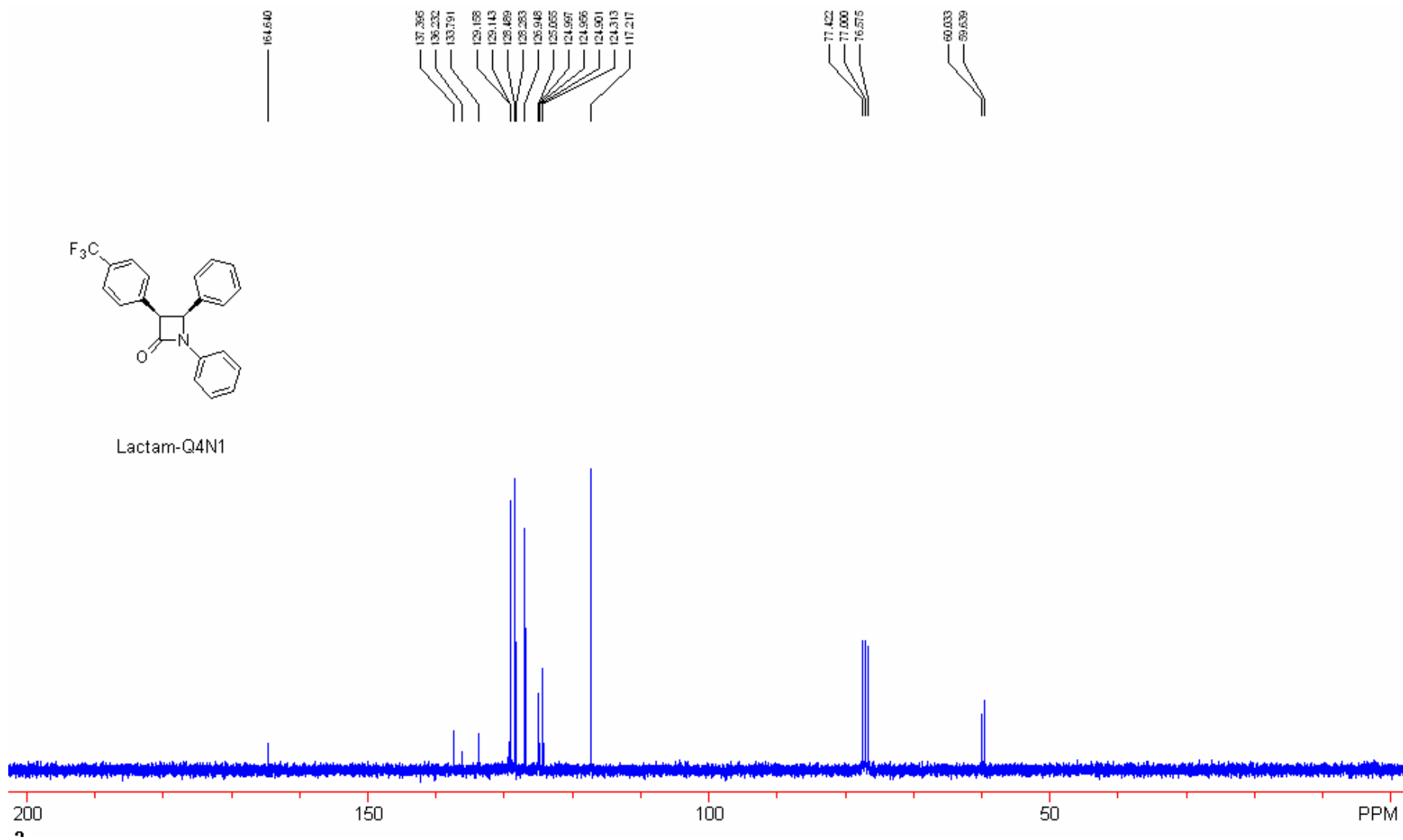


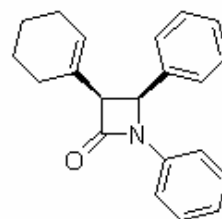
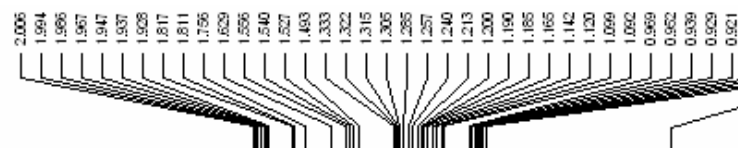
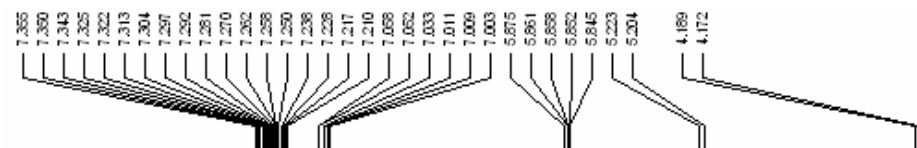
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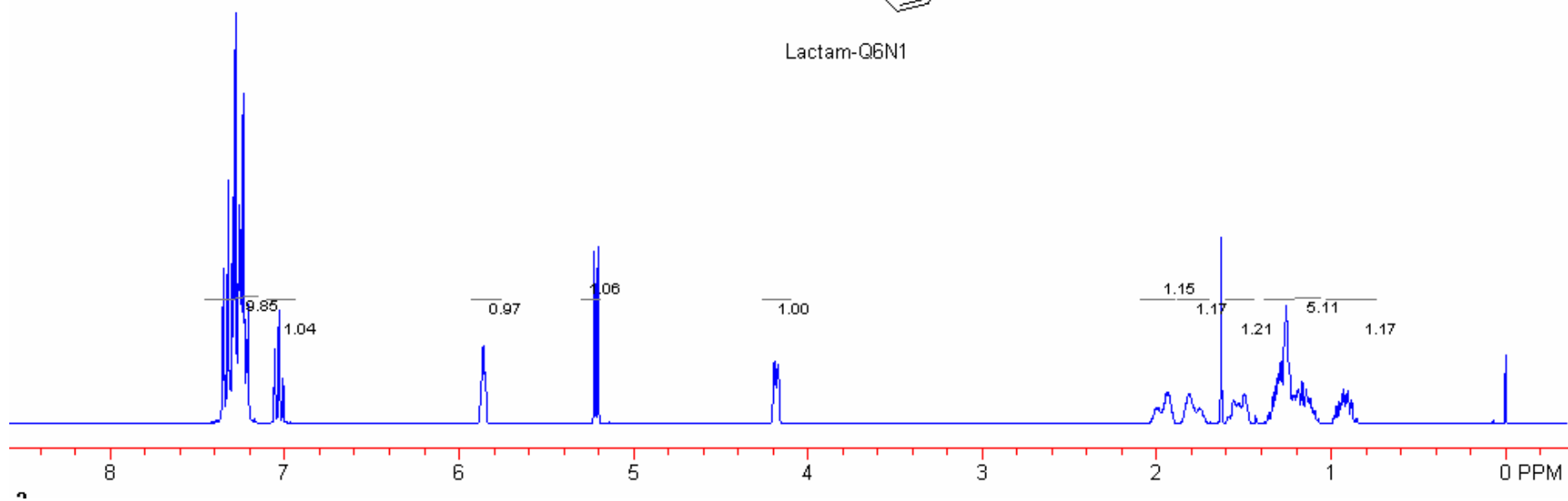


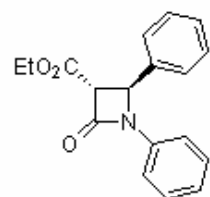
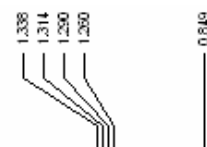
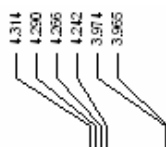
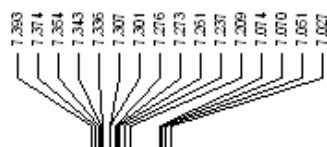
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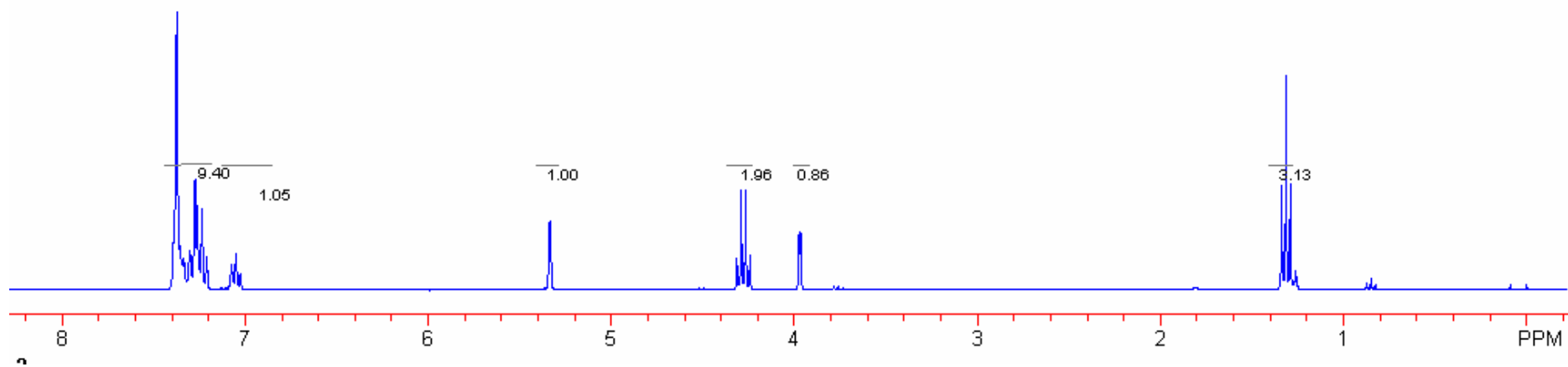


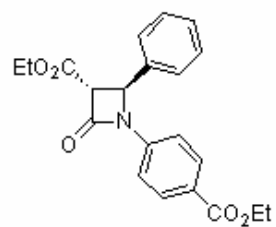
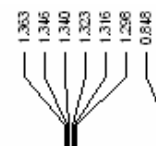
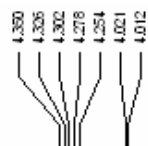
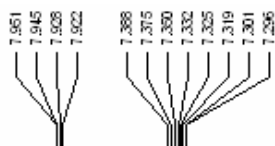
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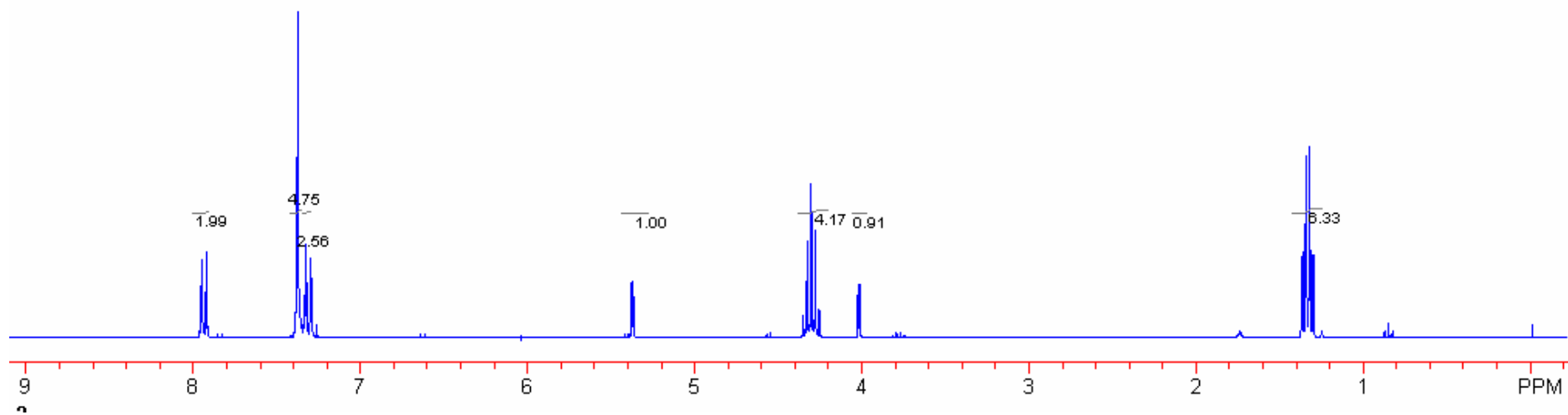


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Lactam-11-85-17



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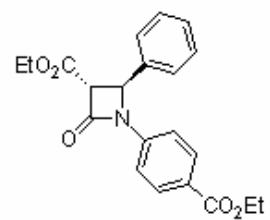
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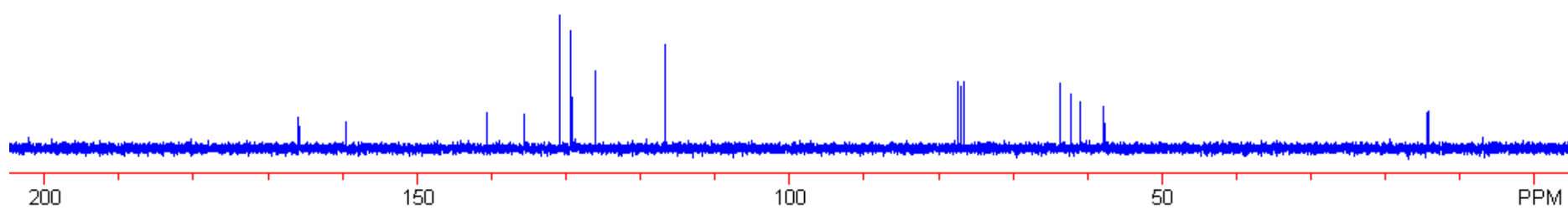
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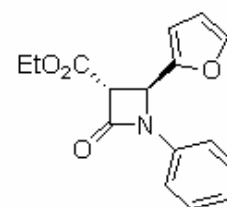
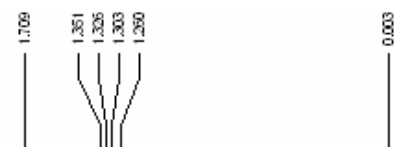
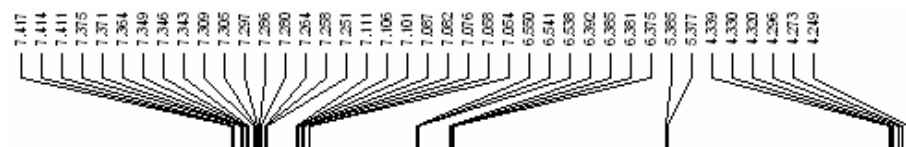
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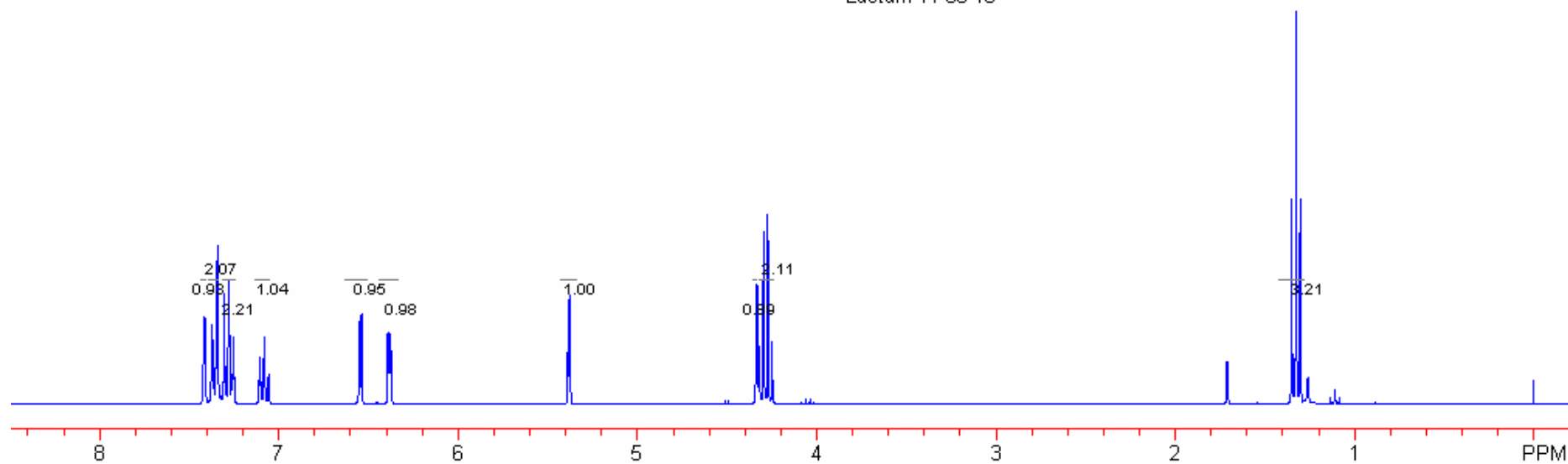


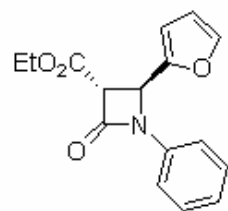
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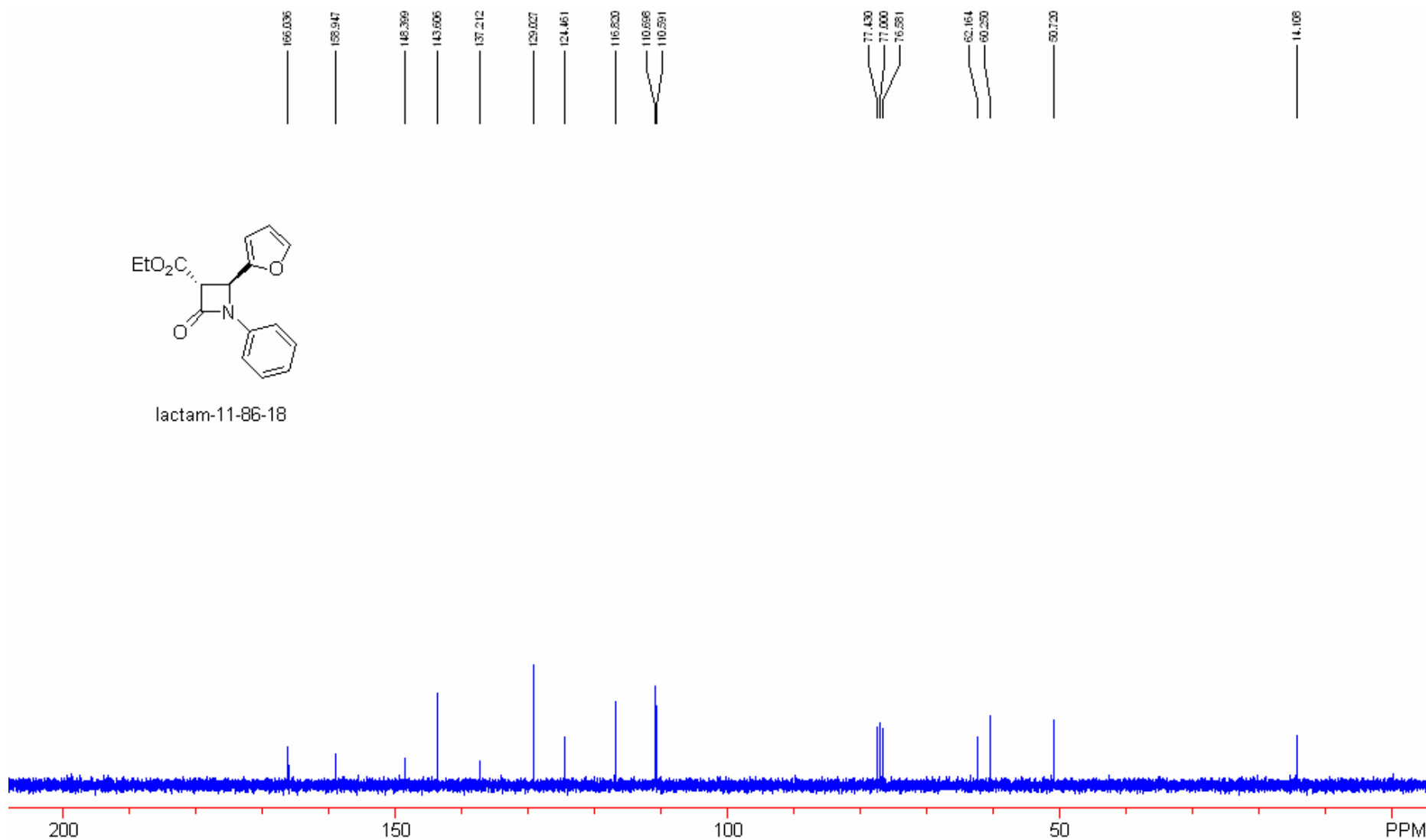


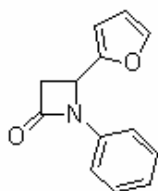
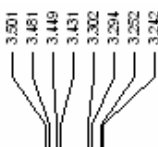
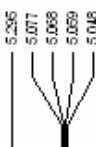
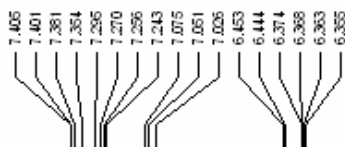
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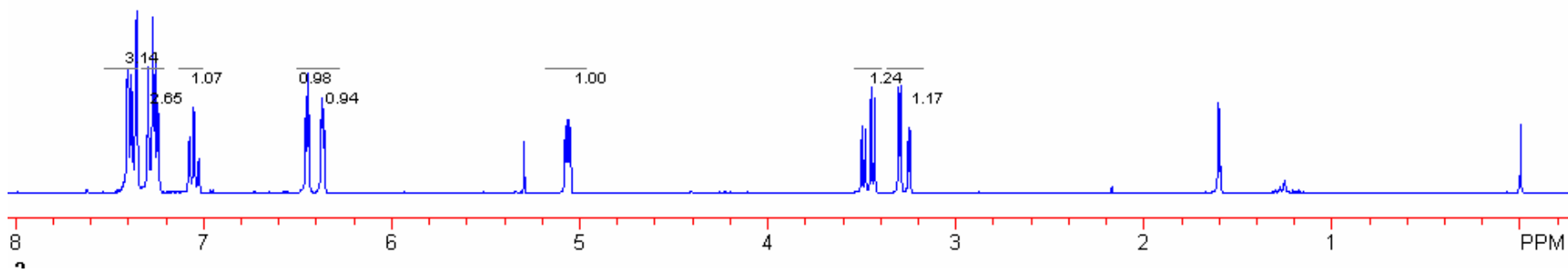


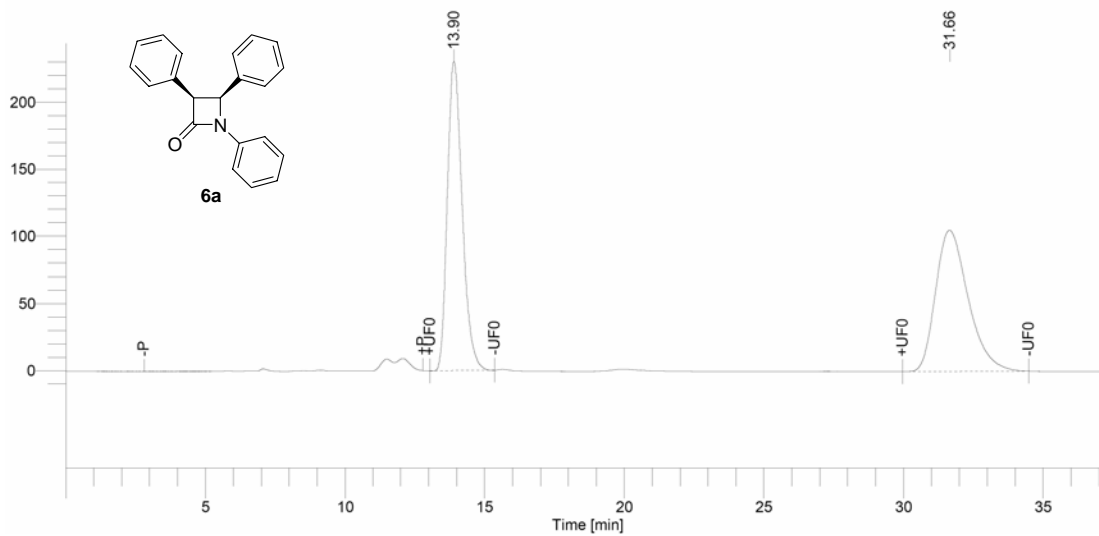
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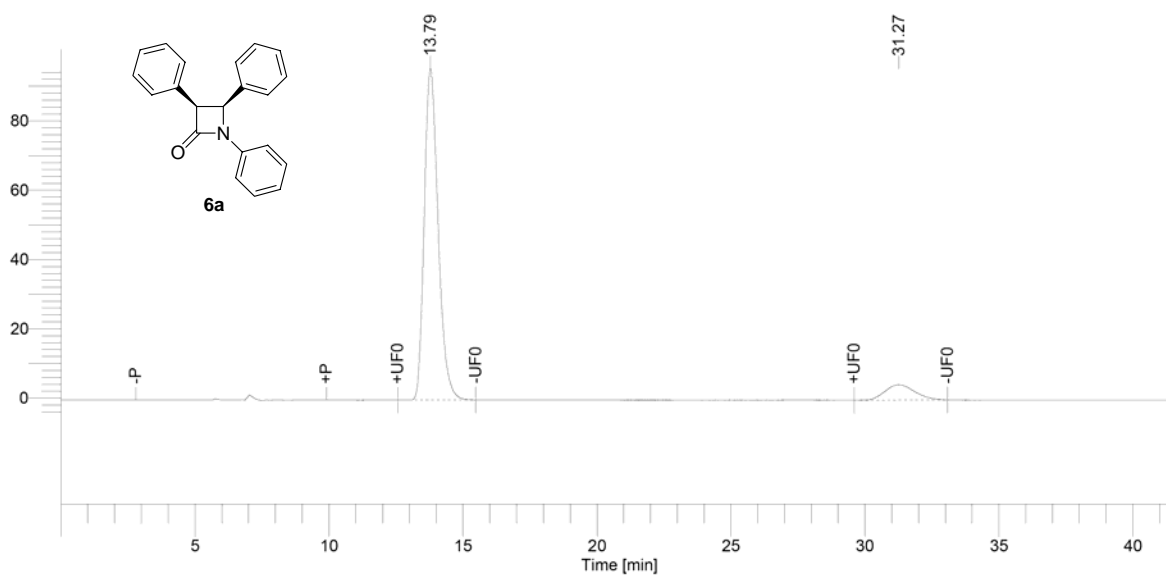


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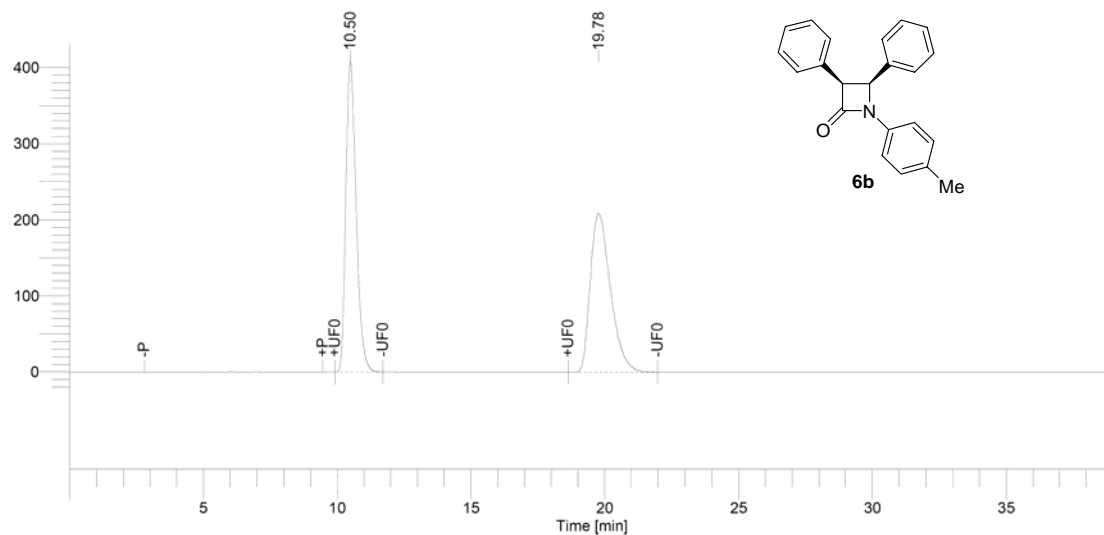




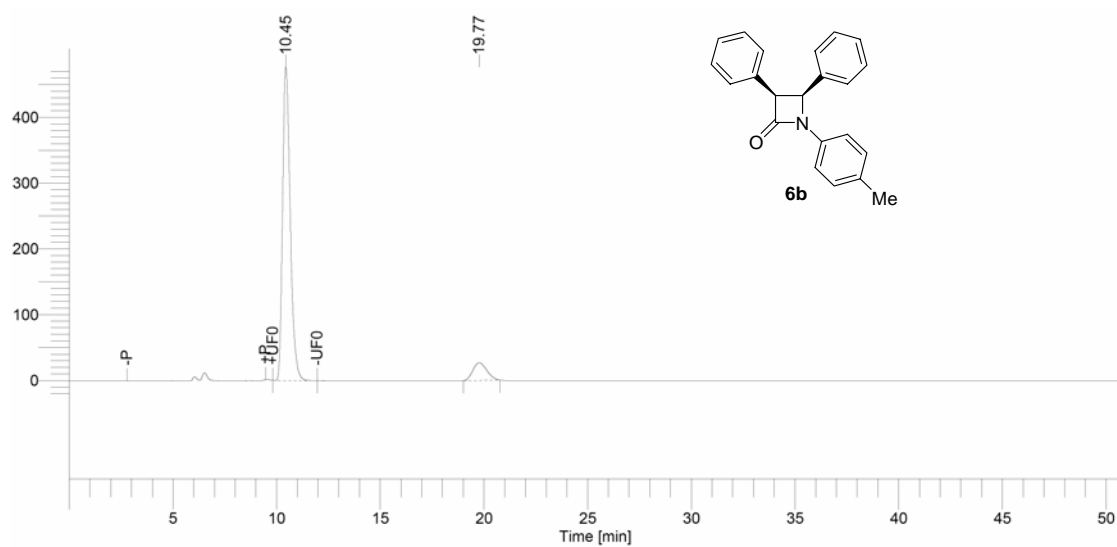
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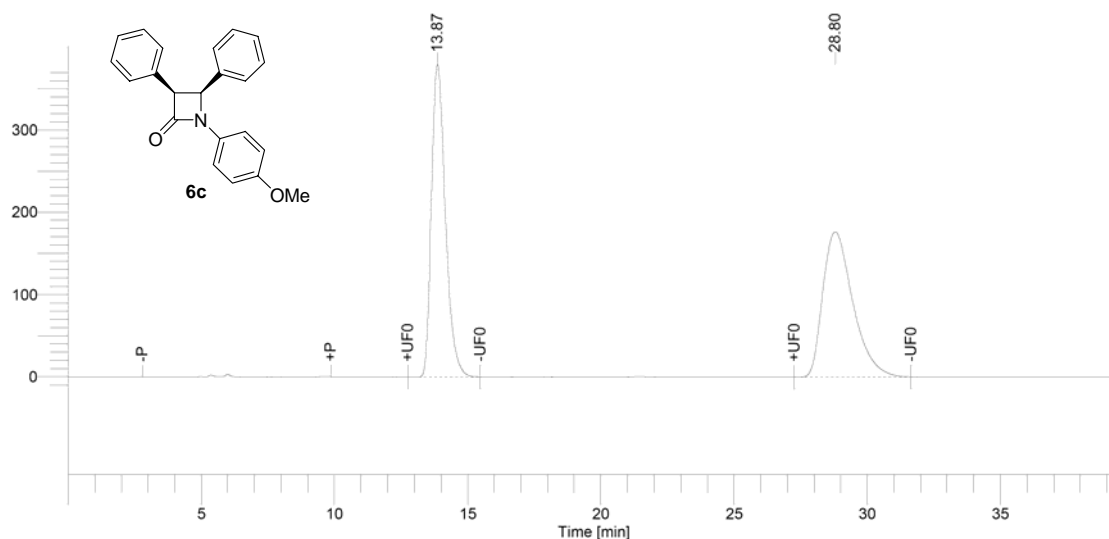
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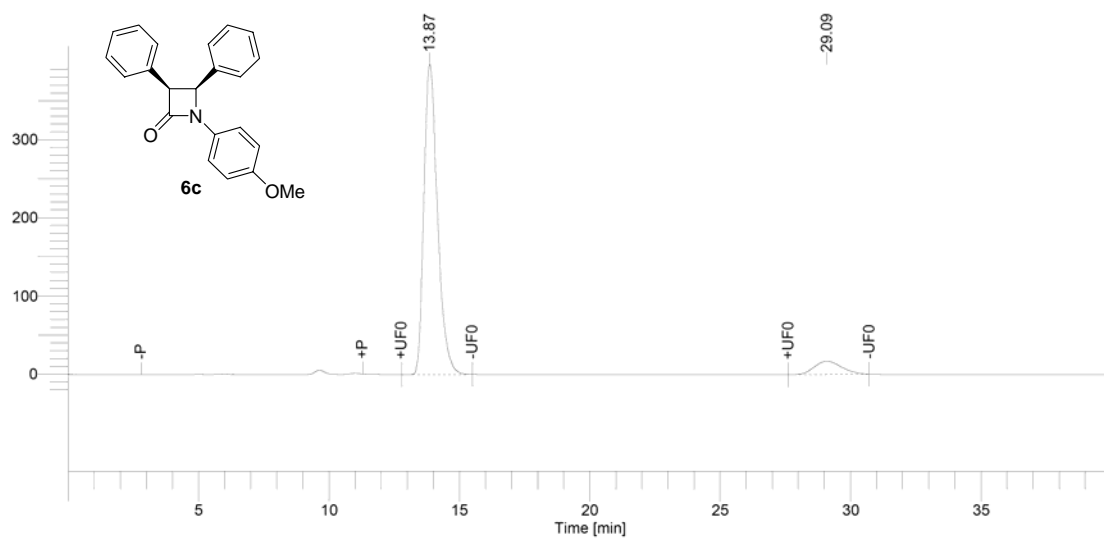
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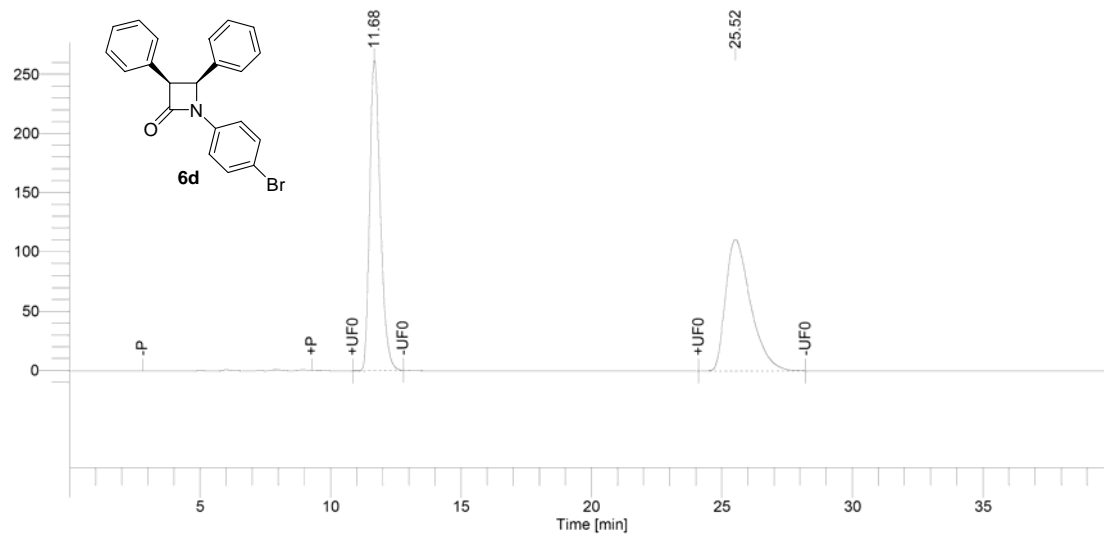
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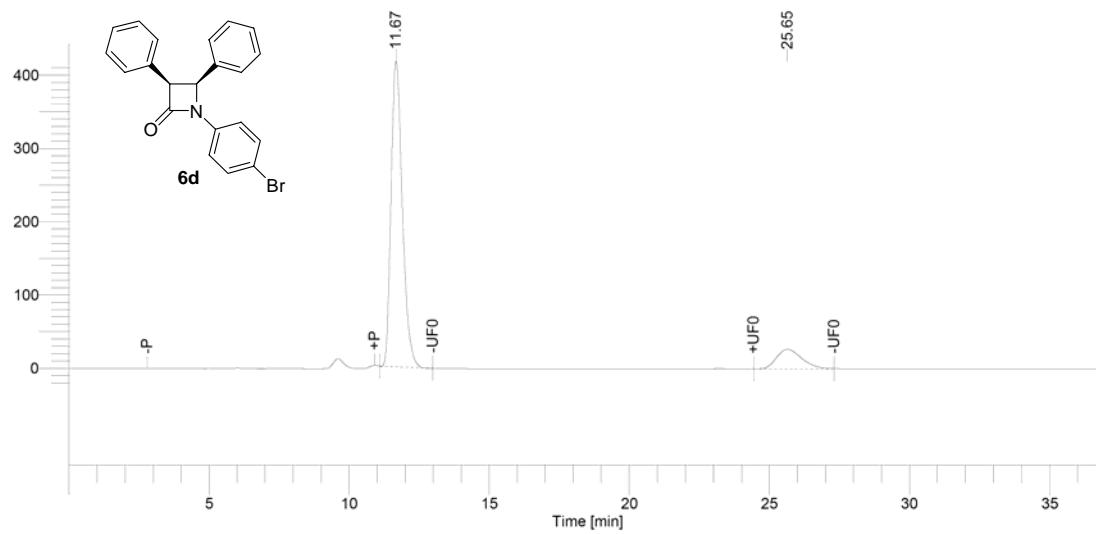
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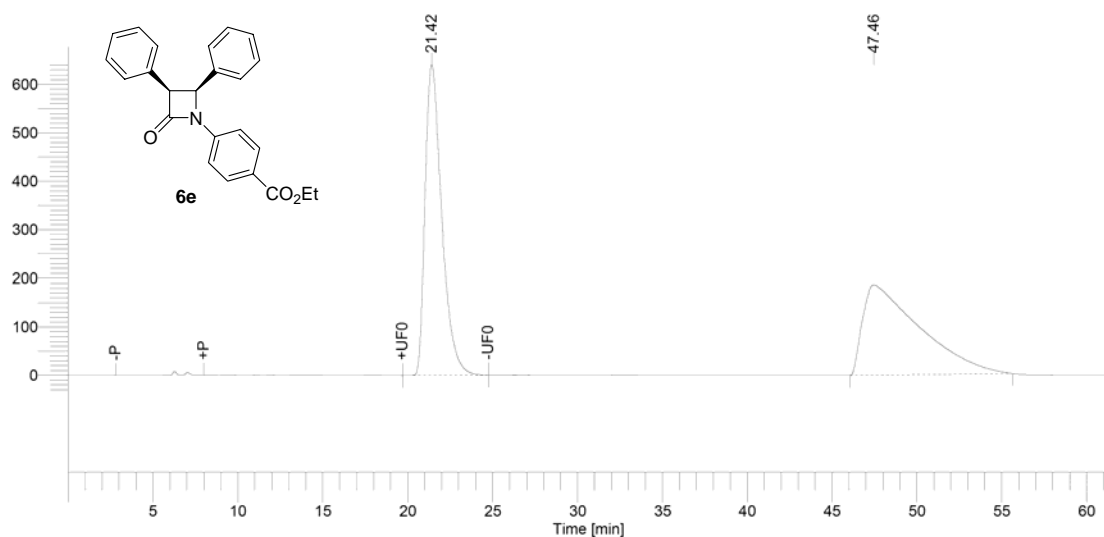
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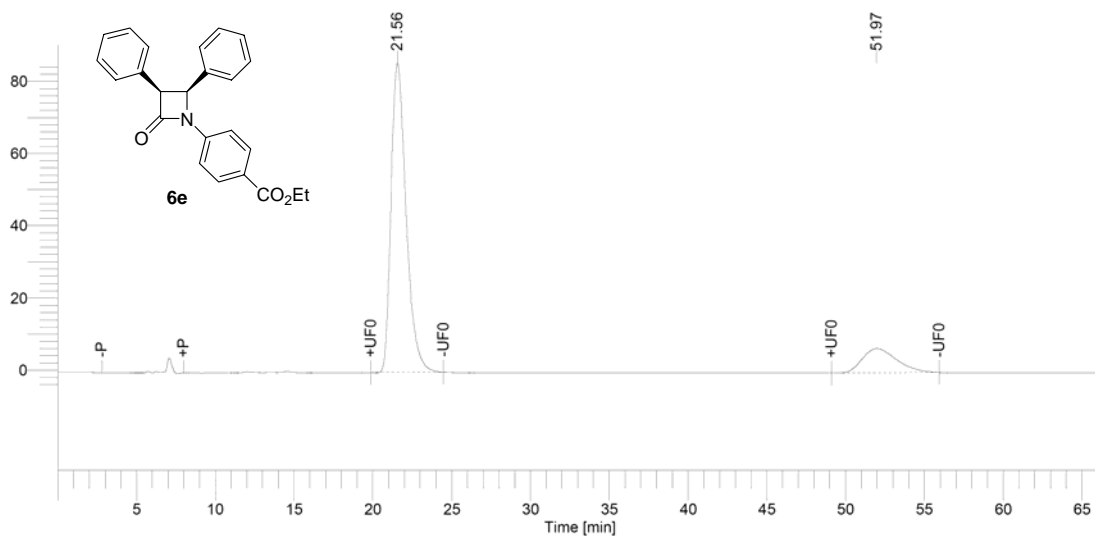
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25.517	14392759.27	215631.62	49.80	49.80	MM	14.3928
	28898323.32	724728.10	100.00	100.00		28.8983



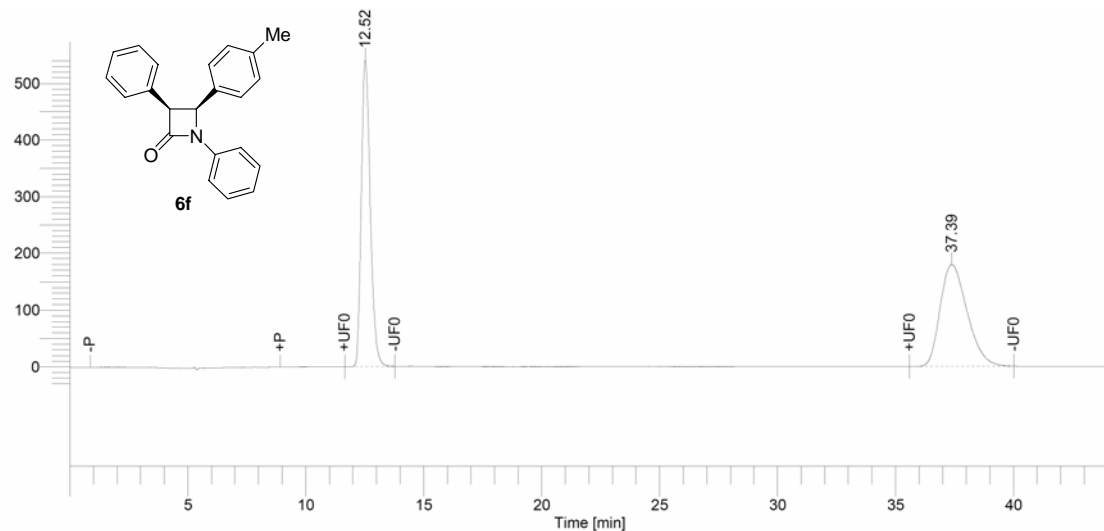
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25.645	3232797.20	51480.25	12.46	12.46	MM	3.2328
	25935206.74	861927.83	100.00	100.00		25.9352



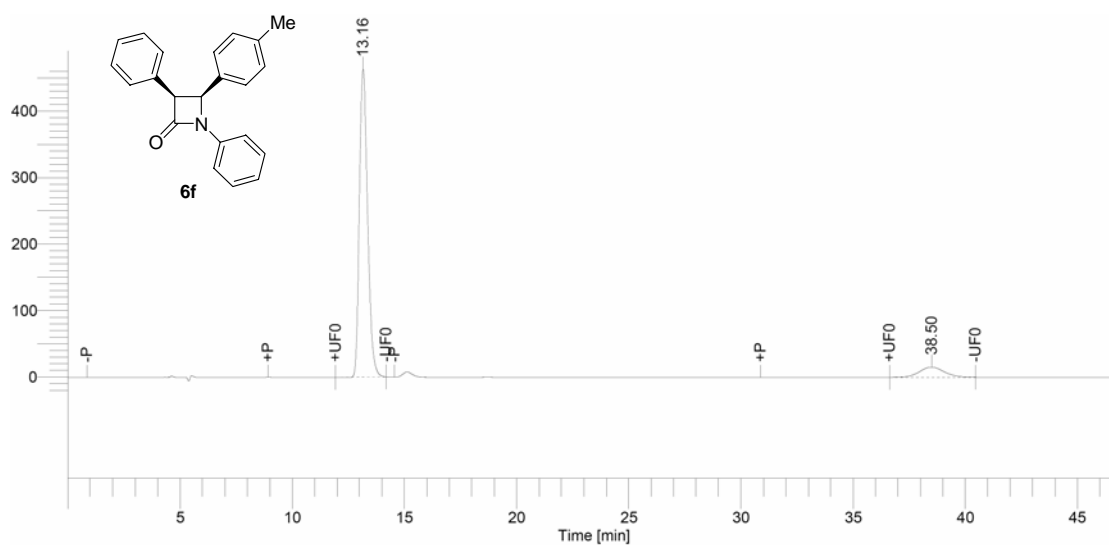
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
21.417	85164003.94	1.25e+06	50.11	50.11	MM	85.1640
47.461	84803075.02	362622.56	49.89	49.89	BB	84.8031
	1.70e+08	1.61e+06	100.00	100.00		169.9671



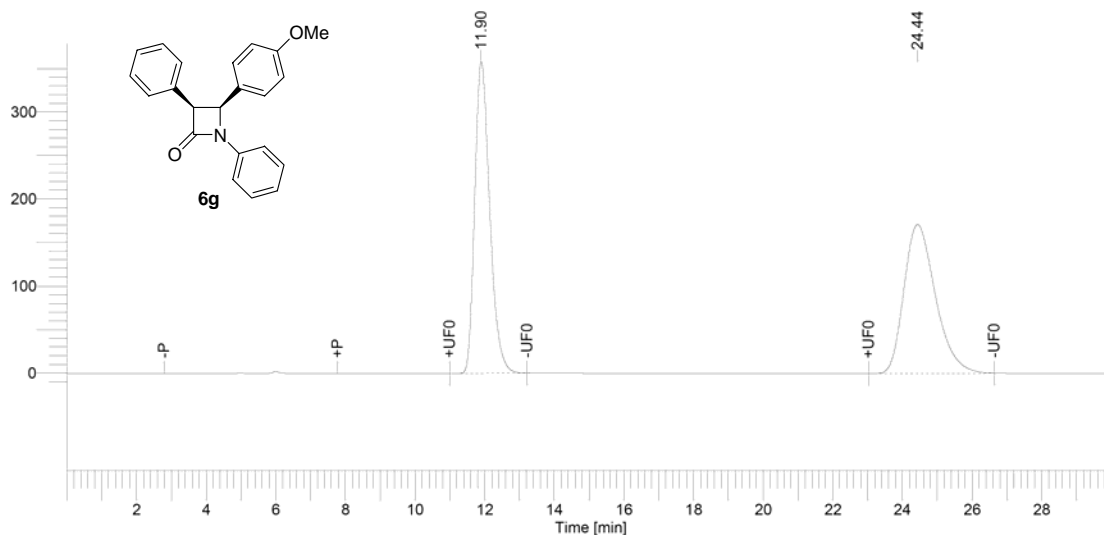
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
21.558	11040415.73	166749.33	84.77	84.77	MM	11.0404
51.970	1983520.21	13092.47	15.23	15.23	MM	1.9835
	13023935.94	179841.80	100.00	100.00		13.0239



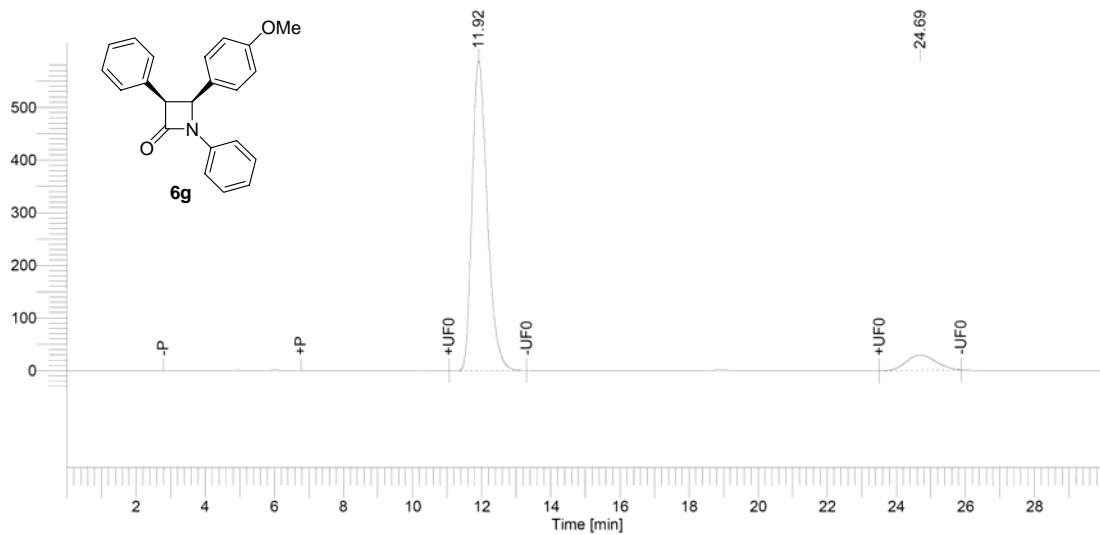
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
12.522	14290321.46	540667.90	49.98	49.98	MM	14.2903
37.388	14300670.99	179135.88	50.02	50.02	MM	14.3007
	28590992.45	719803.79	100.00	100.00		28.5910



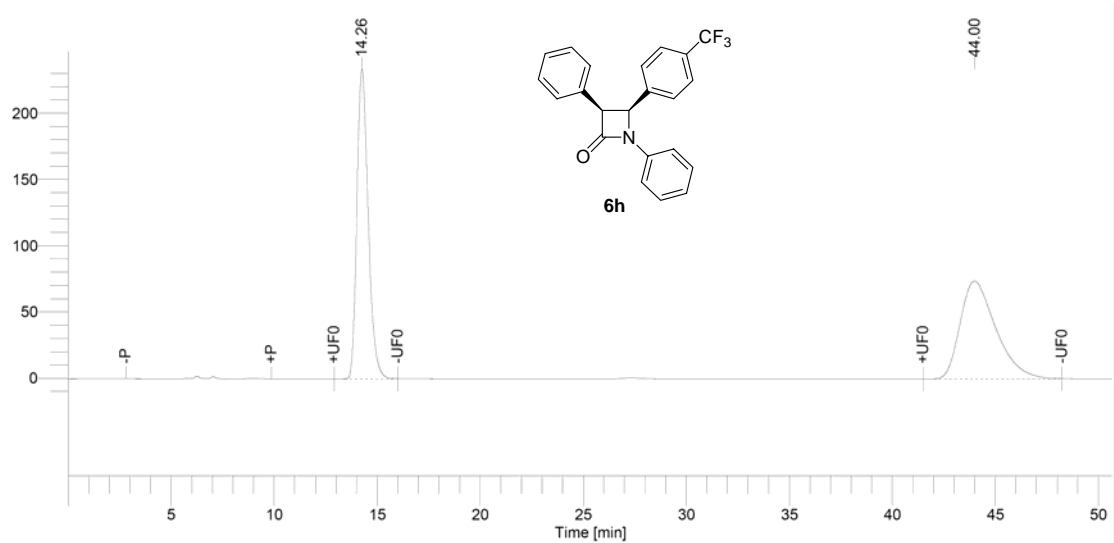
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
13.155	11810082.17	463081.03	91.00	91.00	MM	11.8101
38.500	1167581.82	15179.49	9.00	9.00	MM	1.1676
	12977663.99	478260.53	100.00	100.00		12.9777



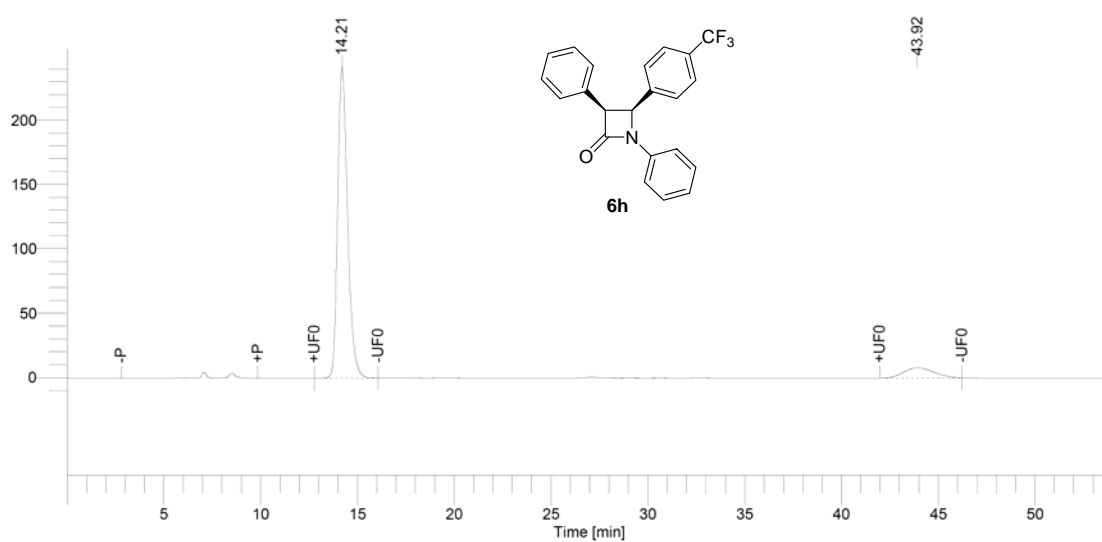
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
11.902	20896031.94	696644.54	49.99	49.99	MM	20.8960
24.435	20905555.52	332410.69	50.01	50.01	MM	20.9056
	41801587.46	1.03e+06	100.00	100.00		41.8016



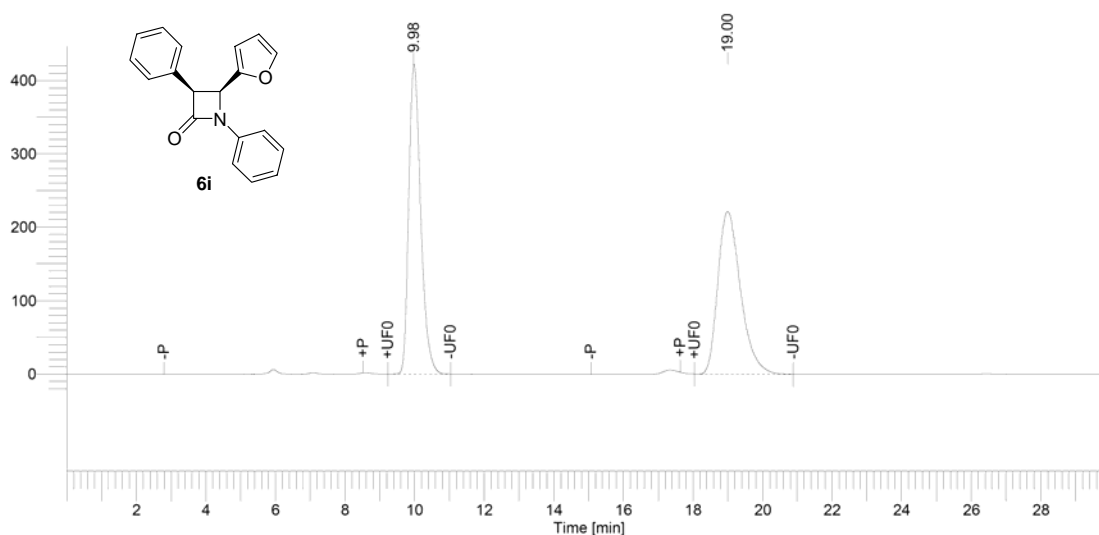
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
11.917	34985048.95	1.15e+06	91.26	91.26	MM	34.9850
24.692	3352523.32	56395.25	8.74	8.74	MM	3.3525
	38337572.26	1.20e+06	100.00	100.00		38.3376



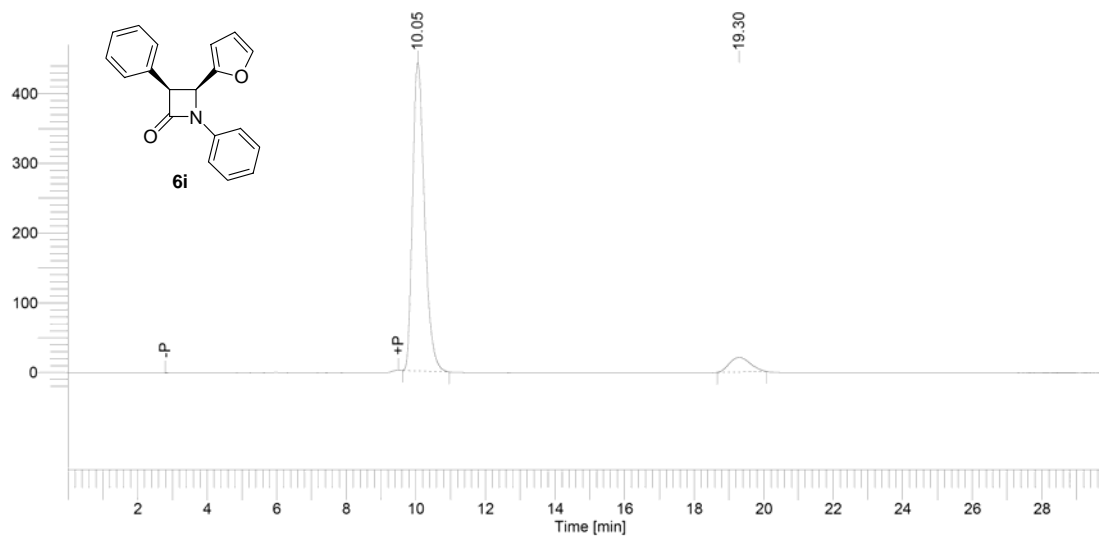
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
14.258	17318063.84	455082.79	50.09	50.09	MM	17.3181
43.997	17254070.93	143673.01	49.91	49.91	MM	17.2541
	34572134.77	598755.80	100.00	100.00		34.5721



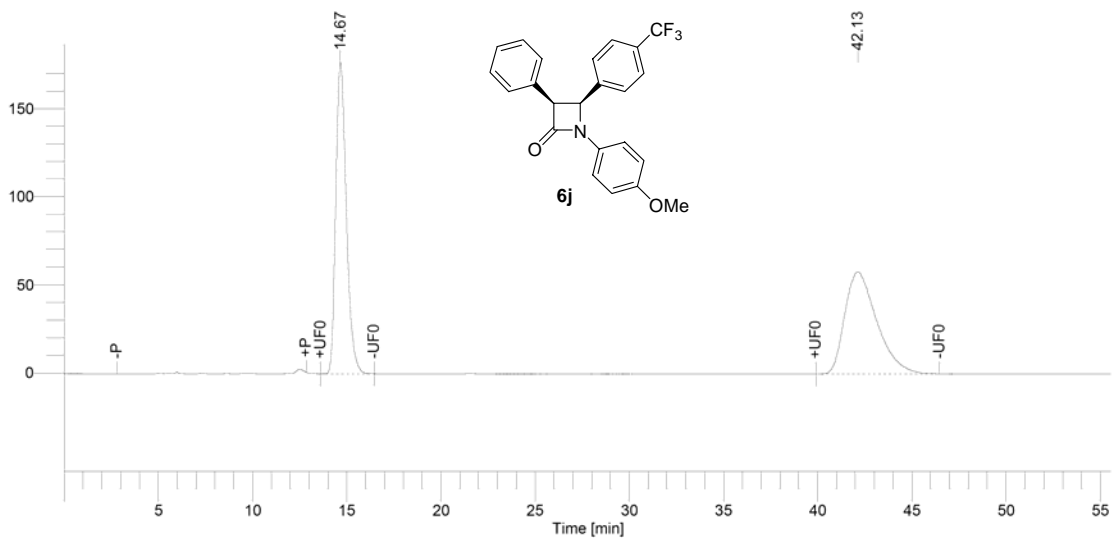
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
14.205	16834563.97	470227.25	90.86	90.86	MM	16.8346
43.920	1693434.03	15533.27	9.14	9.14	MM	1.6934
	18527998.00	485760.52	100.00	100.00		18.5280



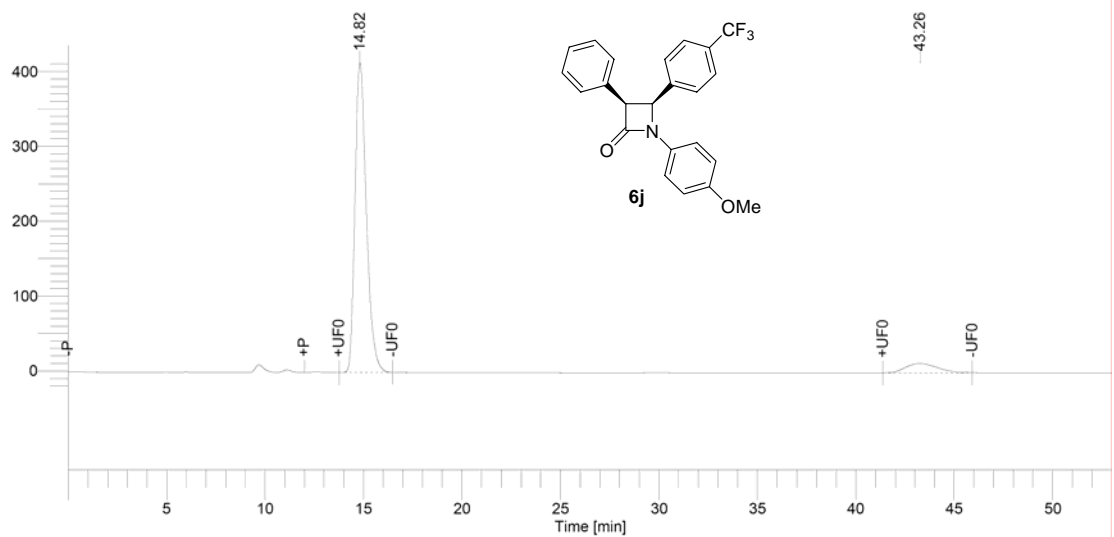
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
9.980	19651747.27	821624.39	50.05	50.05	MM	19.6517
18.995	19612682.41	430469.81	49.95	49.95	MM	19.6127
	39264429.67	1.25e+06	100.00	100.00		39.2644



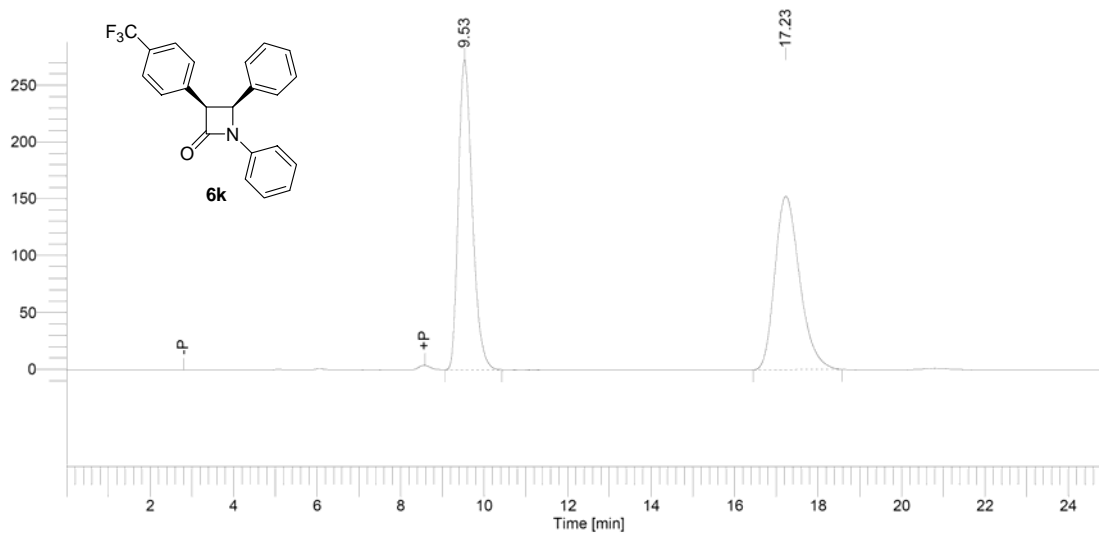
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
10.054	20510295.84	860574.40	92.35	92.35	BB	20.5103
19.295	1698225.38	41144.43	7.65	7.65	BB	1.6982
	22208521.23	901718.82	100.00	100.00		22.2085



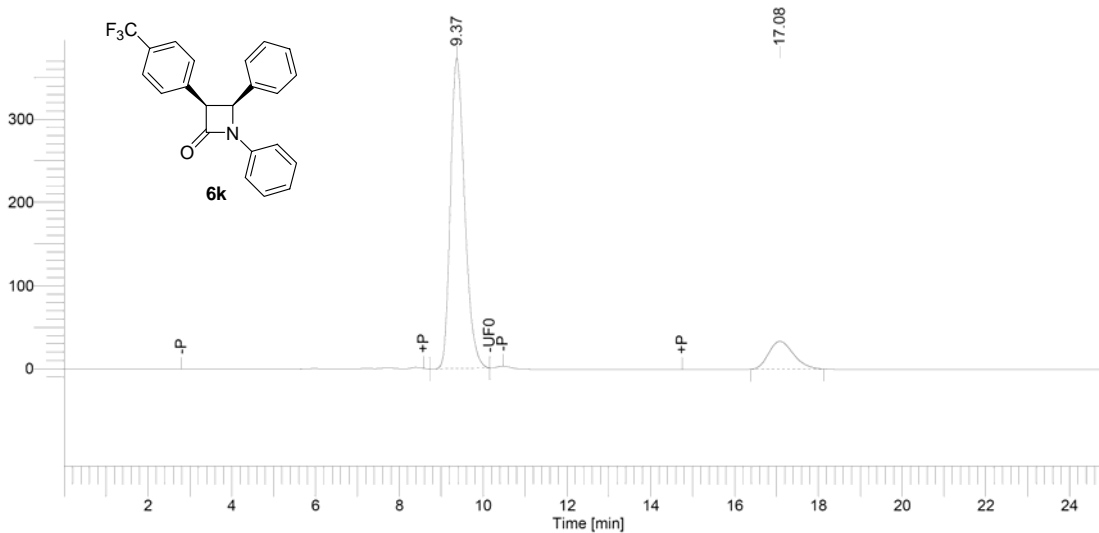
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
14.668	13390985.77	344165.44	50.02	50.02	MM	13.3910
42.132	13382093.05	112362.94	49.98	49.98	MM	13.3821
	26773078.82	456528.38	100.00	100.00		26.7731



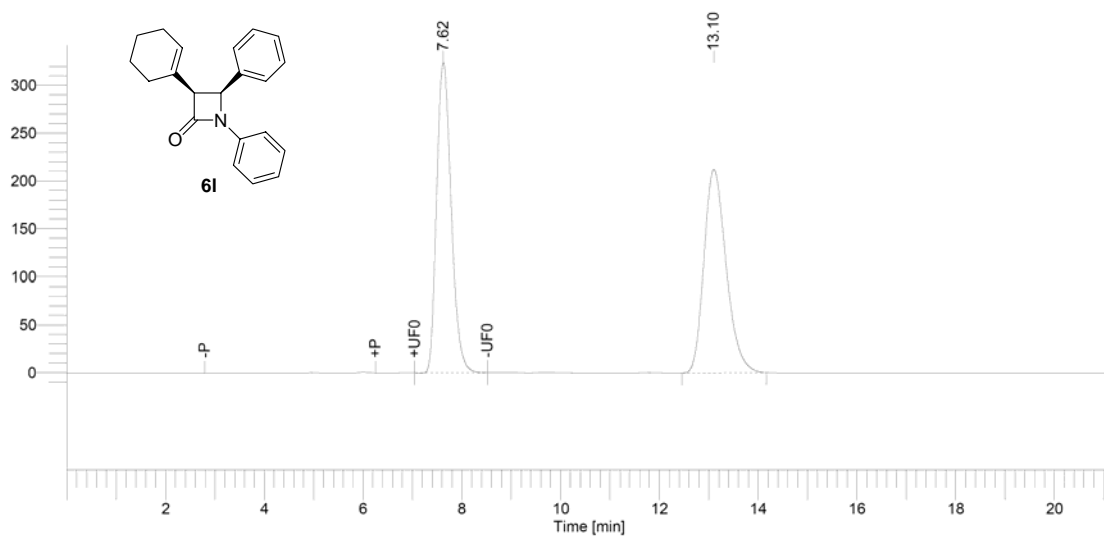
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
14.818	32326952.03	803594.37	92.11	92.11	MM	32.3270
43.260	2768211.34	24712.28	7.89	7.89	MM	2.7682
	35095163.37	828306.65	100.00	100.00		35.0952



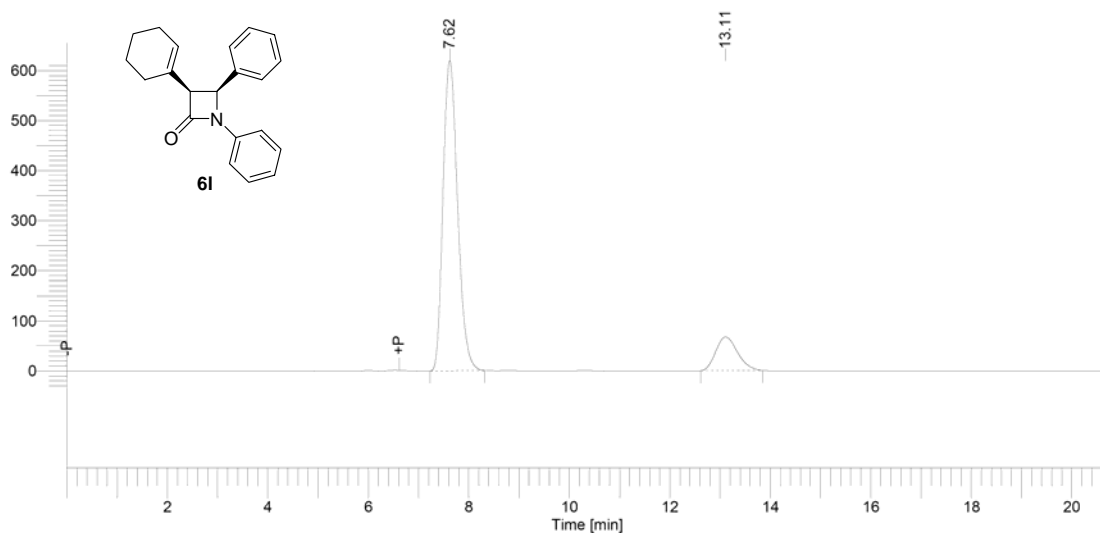
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
9.530	12309660.21	530408.59	50.04	50.04	BB	12.3097
17.229	12287981.39	296485.68	49.96	49.96	BB	12.2880
	24597641.60	826894.27	100.00	100.00		24.5976



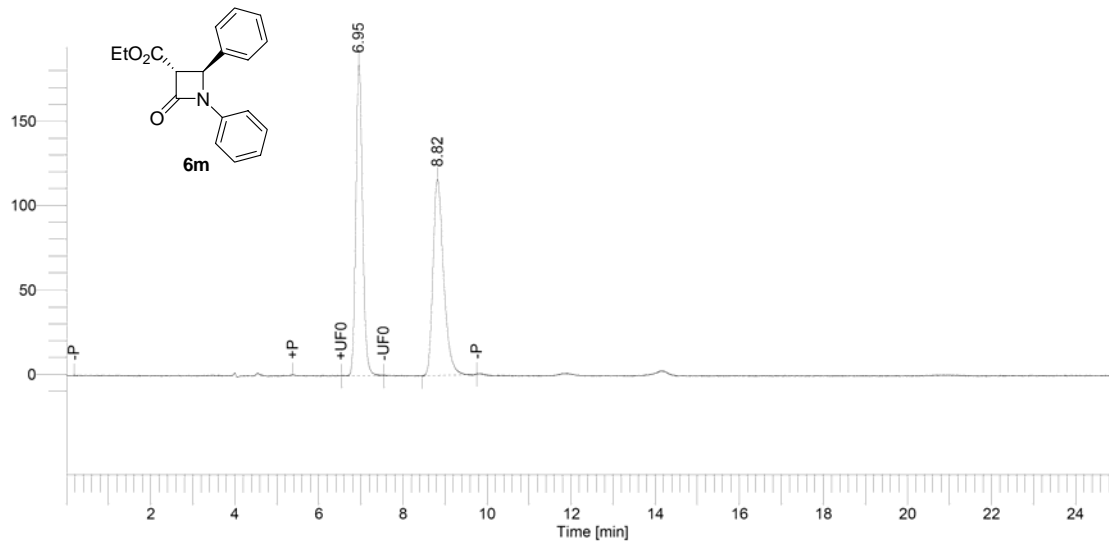
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
9.370	17148194.97	726107.26	86.39	86.39	MM	17.1482
17.082	2701824.45	65469.44	13.61	13.61	BB	2.7018
	19850019.42	791576.70	100.00	100.00		19.8500



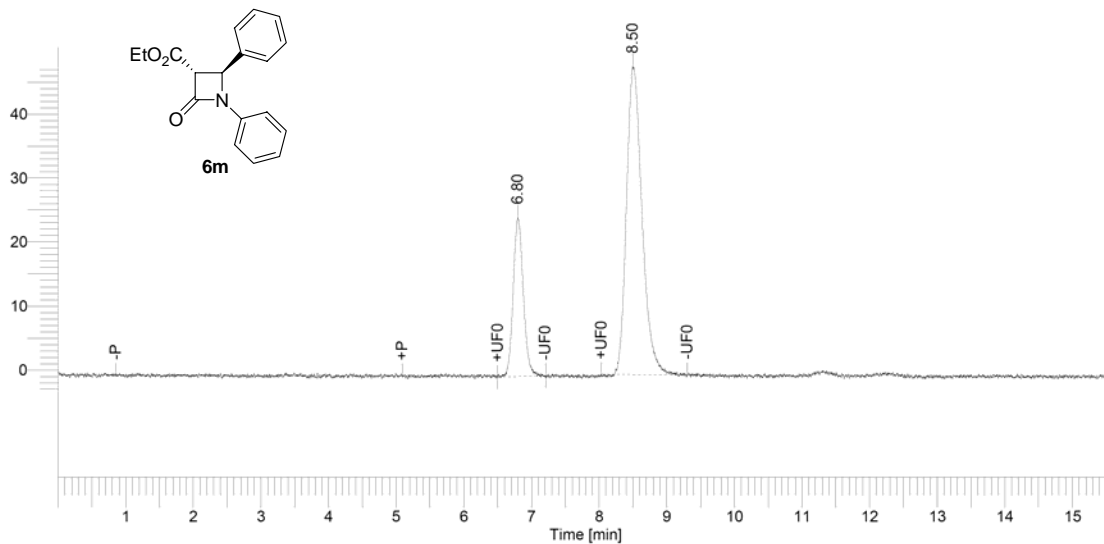
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
7.623	12922773.44	629766.48	49.99	49.99	MM	12.9228
13.102	12930138.73	413164.55	50.01	50.01	BB	12.9301
	25852912.17	1.04e+06	100.00	100.00		25.8529



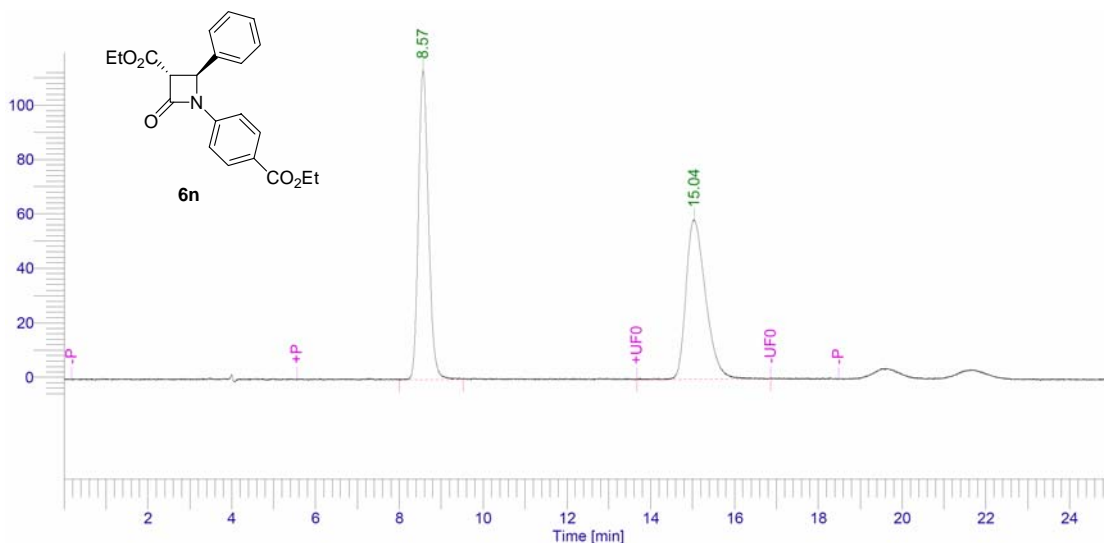
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
7.619	24242364.86	1.20e+06	85.91	85.91	BB	24.2424
13.109	3976118.74	131891.10	14.09	14.09	BB	3.9761
	28218483.60	1.34e+06	100.00	100.00		28.2185



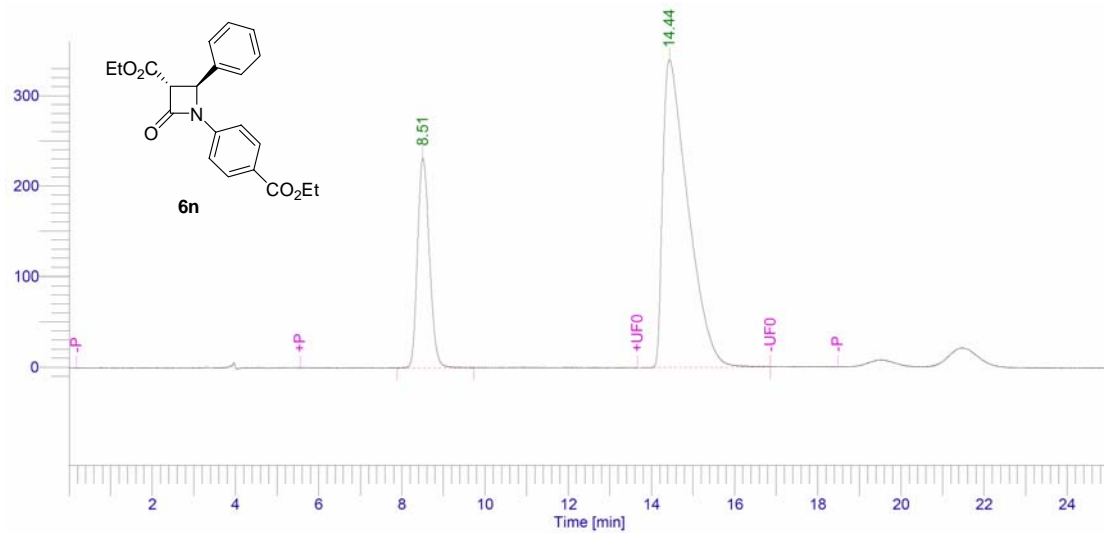
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
6.948	2068795.71	184132.30	50.29	50.29	MM	2.0688
8.822	2044704.27	116163.96	49.71	49.71	*BB	2.0447
	4113499.98	300296.25	100.00	100.00		4.1135



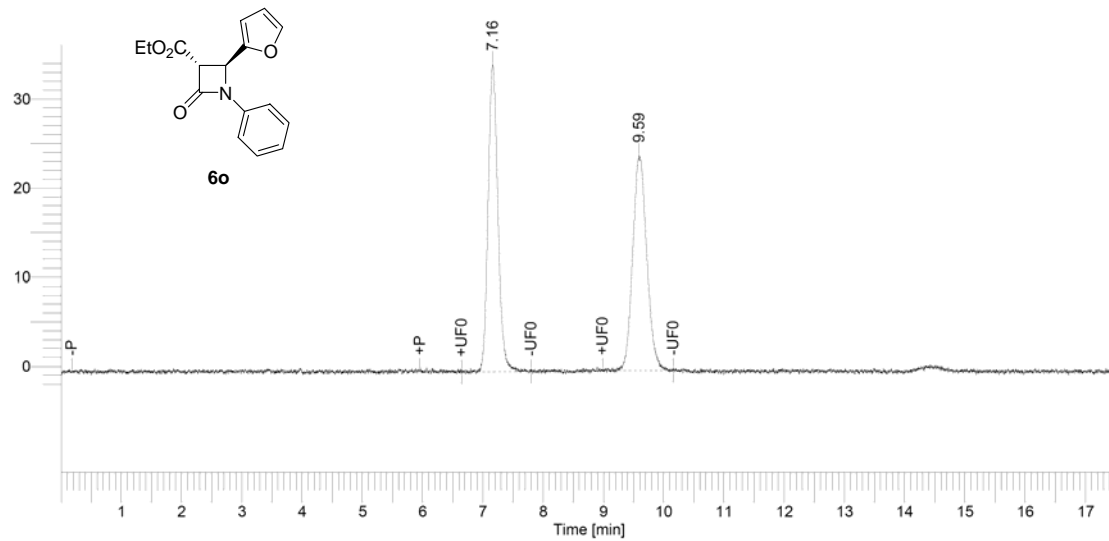
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
6.798	257886.37	24955.76	25.02	25.02	MM	0.2579
8.497	772845.46	48308.98	74.98	74.98	MM	0.7728
	1030731.83	73264.74	100.00	100.00		1.0307



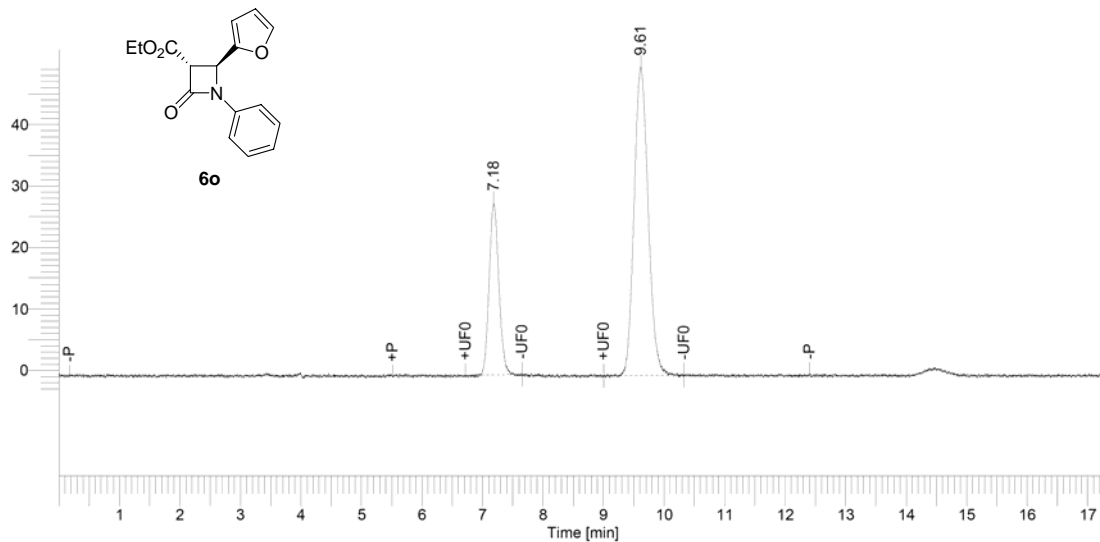
Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
8.566	1910751.98	113541.05	50.11	50.11	BB	1.9108
15.038	1902223.19	58470.15	49.89	49.89	MM	1.9022
	3812975.17	172011.20	100.00	100.00		3.8130



Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
8.505	4638793.75	231679.50	24.51	24.51	BB	4.6388
14.435	14287970.91	339889.30	75.49	75.49	MM	14.2880
	18926764.66	571568.80	100.00	100.00		18.9268



Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
7.162	390477.54	34638.93	49.93	49.93	MM	0.3905
9.593	391578.26	24138.59	50.07	50.07	MM	0.3916
	782055.79	58777.52	100.00	100.00		0.7821



Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	BL	Adjusted Amount
7.183	310570.34	27891.24	27.68	27.68	MM	0.3106
9.613	811567.62	50088.51	72.32	72.32	MM	0.8116
	1122137.96	77979.75	100.00	100.00		1.1221