

## Marked small molecule libraries: A truncated approach to molecular probe design

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### Supporting Information

#### Synthesis of 2b

##### Methyl (2*R*)-2-amino-3-(4'-hydroxyphenyl)-propionate hydrochloride salt

To a stirred solution of methanol (200 ml) at 0 °C, was added the acetyl chloride (11.8 ml, 165 mmol). The solution was stirred for 15 min at 0 °C, and then *D*-tyrosine **3** (10.0 g, 55.2 mmol) was added portionwise to the solution. The resulting solution was heated at reflux for 3 h, before concentration *in vacuo* to give the hydrochloride salt. The salt was recrystallised using methanol to give as a colorless solid (12.8 g, 55.2 mmol, 100%); **mp** 192-193 °C;  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 4256, 3338, 1744, 1613, 1592, 1515; <sup>1</sup>H NMR  $\delta$  (200 MHz, CD<sub>3</sub>OD) 7.07 (2H, d, *J* 8.5, *ArH*), 6.78 (2H, d, *J* 8.5, *ArH*), 4.88 (2H, br s, *NH*<sub>2</sub>), 4.24 (1H, t, *J* 6.6, *C*<sub>2</sub>*H*), 3.80 (3H, s, *OMe*), 3.20-3.06 (2H, m, *C*<sub>3</sub>*H*<sub>2</sub>); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CD<sub>3</sub>OD) 168.6 (1C, Q), 156.4 (1C, Q), 129.6 (2C, CH), 123.7 (1C, Q), 115.0 (2C, CH), 51.6 (1C, CH<sub>3</sub>), 53.5 (1C, CH), 34.7 (1C, CH<sub>2</sub>); *m/z* (ESI+) 196 ([M+H]<sup>+</sup>, 100%).

##### Methyl (2*R*)-2-dibenzylamino-3-(4'-hydroxyphenyl)-propionate

To a solution of the hydrochloride salt (12.8 g, 55.2 mmol) in acetonitrile (400 ml) was added potassium carbonate (22.9 g, 166 mmol) followed by benzyl bromide (15.1 ml, 127 mmol), and the solution stirred for 48 h. The reaction was quenched by addition of water (100 ml). The organics were separated and the aqueous extracted with ethyl acetate (3 x 100 ml). The combined organics were washed with brine (100 ml), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo* to give a yellow oil. The oil was chromatographed on silica gel [10% EtOAc/hexane] to give the product as a clear oil (16.1 g, 42.3 mmol, 76 %); **R<sub>f</sub>** [30% EtOAc/hexane] = 0.50; [ $\alpha$ ]<sub>D</sub> +75.2 (*c* 1.25, CHCl<sub>3</sub>);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3411, 1708, 1614, 1514; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.17-7.08 (10H, m, *ArH*), 6.75 (2H, d, *J* 8.5, *ArH*), 6.61 (2H, d, *J* 8.5, *ArH*), 5.95 (1H, br s, *OH*), 3.84 (2H, d, *J* 14.0, *NCH<sub>x</sub>H<sub>y</sub>Ph* x 2), 3.60 (3H, s, *OMe*), 3.53 (1H, t, *J* 7.8, *C*<sub>2</sub>*H*), 3.43 (2H, d, *J* 14.0, *NCH<sub>x</sub>H<sub>y</sub>Ph* x 2), 2.95 (1H, dd, *J* 14.0, 7.8, *C*<sub>3</sub>*H<sub>A</sub>H<sub>B</sub>*), 2.81 (1H, dd, *J* 14.0, 7.8, *C*<sub>3</sub>*H<sub>A</sub>H<sub>B</sub>*); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 173.2 (1C, Q), 154.1 (1C, Q), 139.0 (2C, Q), 130.3 (2C, CH), 129.7 (1C, Q), 128.5 (4C, CH), 128.0 (4C, CH), 126.8 (2C, CH), 114.9 (2C, CH), 62.5 (1C, CH), 54.3 (2C, CH<sub>2</sub>), 51.1 (1C, CH<sub>3</sub>), 34.7 (1C, CH<sub>2</sub>); *m/z* (FAB, NOBA) 398 ([M+Na]<sup>+</sup>, 25%), 376 ([M+H]<sup>+</sup>, 85%), 316 (73), 268 (98), 91 (100); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 376.1912. C<sub>24</sub>H<sub>26</sub>NO<sub>3</sub> requires *m/z*, 376.1913).

##### (2*R*)-2-Dibenzylamino-3-(4'-hydroxyphenyl)-propanoic acid

To a solution of ester (16.1 g, 42.3 mmol) in THF:H<sub>2</sub>O (200 ml, 4:1) was added lithium hydroxide (9.03 g, 215 mmol) and the solution heated at 82 °C for 48 h. The reaction was quenched by addition of 1N HCl until the solution was judged to be pH 2 by litmus paper. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 100 ml). The combined organics were washed with water (100 ml), brine (100 ml), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo* to give a yellow foam (14.9 g, 41.4 mmol, 96%); **R<sub>f</sub>** [30% EtOAc/hexane] = 0.13; [ $\alpha$ ]<sub>D</sub> +52.1 (*c* 3.55, EtOH);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3407, 1731, 1614, 1515; <sup>1</sup>H NMR  $\delta$  (250 MHz, CD<sub>3</sub>OD) 7.56-7.44 (10H, m, *ArH*), 7.13 (2H, d, *J* 8.5, *ArH*), 6.95 (2H, d, *J* 8.5, *ArH*), 4.16 (2H, d, *J* 13.8, *NCH<sub>x</sub>H<sub>y</sub>Ph* x 2), 3.94 (2H, d, *J* 13.8, *NCH<sub>x</sub>H<sub>y</sub>Ph* x 2), 3.86 (1H, dd, *J* 8.4, 6.8, *C*<sub>2</sub>*H*), 3.33 (1H, dd, *J* 14.2, 6.8, *C*<sub>3</sub>*H<sub>A</sub>H<sub>B</sub>*), 3.17 (1H, dd, *J* 14.2, 8.4, *C*<sub>3</sub>*H<sub>A</sub>H<sub>B</sub>*); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 173.2 (1C, Q), 155.0 (1C, Q), 137.7 (2C, Q), 129.5 (2C, CH), 128.4 (1C, Q), 128.1 (4C, CH), 127.4 (4C, CH), 126.4 (2C, CH), 114.1 (2C, CH), 62.5

(1C, CH), 53.6 (2C, CH<sub>2</sub>), 33.4 (1C, CH<sub>2</sub>); *m/z* (FAB, NOBA) 384 ([M+Na]<sup>+</sup>, 63%), 362 ([M+H]<sup>+</sup>, 100%), 316 (49), 254 (73), 91 (72); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 362.1756. C<sub>23</sub>H<sub>24</sub>NO<sub>3</sub> requires *m/z*, 362.1756).

#### **(2R)-3-(4'-tert-Butyldimethylsilyloxyphenyl)-2-dibenzylamino-propanoic acid 4**

To a solution of phenol (14.9 g, 41.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (200 ml) at 0 °C was added 2,6-lutidine (19.6 ml, 168 mmol) and the solution stirred for 30 min. TBSOTf (19.8 ml, 86.3 mmol) was added to the solution and stirred for a further 3.5 h. The reaction was poured onto iced 1M phosphoric acid (50 ml) and the aqueous extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 100 ml). The combined organics were washed with water (100 ml), brine (100 ml), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo* to give the di-TBS protected compound.

The crude material was dissolved in acetic acid:THF:H<sub>2</sub>O (200 ml, 3:1:1) and stirred for 6 h. The reaction was quenched by addition of sodium hydrogen carbonate (~35 g), diluted with water (200 ml) and extracted with EtOAc (5 x 100 ml). The combined organics were washed with brine (100 ml), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo* to give a foam (15.2 g, 32.1 mmol, 78%); **R<sub>f</sub>** [30% EtOAc/hexane] = 0.28; **[α]<sub>D</sub>** +23.4 (*c* 3.40, CHCl<sub>3</sub>); **ν<sub>max</sub>** (neat)/cm<sup>-1</sup> 3407, 1731, 1614, 1514; **<sup>1</sup>H NMR** δ (250 MHz, CDCl<sub>3</sub>) 9.50 (1H, br s, CO<sub>2</sub>H), 7.22-7.07 (10H, m, ArH), 6.88 (2H, d, *J* 8.5, ArH), 6.67 (2H, d, *J* 8.5, ArH), 3.70 (2H, d, *J* 13.6, NCH<sub>X</sub>H<sub>Y</sub>Ph x 2), 3.68 (2H, d, *J* 13.6, NCH<sub>X</sub>H<sub>Y</sub>Ph x 2), 3.61 (1H, dd, *J* 9.1, 5.8, C<sub>2</sub>H), 3.15 (1H, dd, *J* 14.4, 5.8, C<sub>3</sub>H<sub>A</sub>H<sub>B</sub>), 2.90 (1H, dd, *J* 14.4, 9.1, C<sub>3</sub>H<sub>A</sub>H<sub>B</sub>), 0.89 (9H, s, *t*-Bu), 0.12 (6H, s, Me<sub>2</sub>Si); **<sup>13</sup>C NMR** δ (62.9 MHz, CDCl<sub>3</sub>) 175.7 (1C, Q), 154.2 (1C, Q), 137.7 (2C, Q), 130.6 (1C, Q), 130.2 (2C, CH), 128.8 (4C, CH), 128.3 (4C, Q), 127.4 (2C, CH), 119.9 (2C, CH), 62.5 (1C, CH), 54.2 (2C, CH<sub>2</sub>), 33.2 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 18.1 (1C, Q), -4.5 (2C, CH<sub>3</sub>); *m/z* (FAB, NOBA) 498 ([M+Na]<sup>+</sup>, 85%), 476 ([M+H]<sup>+</sup>, 89%), 430 (84), 91 (100); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 476.2618. C<sub>29</sub>H<sub>38</sub>NO<sub>3</sub>Si requires *m/z*, 476.2621).

#### **Ethyl (4R)-5-(4'-tert-butyldimethylsilyloxyphenyl)-4-dibenzylamino-3-oxo-pentanoate**

To a solution of acid (7.27 g, 15.3 mmol) in THF (50 ml) was added carbonyl diimidazole (7.44 g, 45.9 mmol) and the solution stirred for 2 h, before cooling to -78 °C. Meanwhile, a stirred solution of ethyl acetate (5.21 ml, 53.6 mmol) was cooled to -78 °C, LiHMDS (54.0 ml, 1.0 M in THF) was added and the solution stirred for 20 min. The enolate was then transferred *via* cannula to the imidazole and the solution stirred at -78 °C for 40 min. The reaction was warmed to 0 °C over 30 min, and stirred for a further 1 h at 0 °C. The reaction was quenched by addition of 1% HCl (15 ml) and diluted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml). The organic layer was separated and the aqueous phase extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 50 ml). The combined organics were combined and washed sequentially with water (50 ml) and brine (50 ml), then dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo*. The residue was chromatographed on silica gel [8% EtOAc/hexane] to give a clear oil (6.66 g, 12.2 mmol, 79 %); **R<sub>f</sub>** [30% EtOAc/hexane] = 0.83; **[α]<sub>D</sub>** +12.7 (*c* 1.10, CHCl<sub>3</sub>); **ν<sub>max</sub>** (neat)/cm<sup>-1</sup>, 1745, 1717 1608, 1509; **<sup>1</sup>H NMR** δ (250 MHz, CDCl<sub>3</sub>) 7.34-7.03 (10H, m, ArH), 7.01 (2H, d, *J* 8.6, ArH), 6.74 (2H, d, *J* 8.6, ArH), 4.03 (2H, q, *J* 7.1, OCH<sub>2</sub>CH<sub>3</sub>), 3.85 (2H, d, *J* 14.0, NCH<sub>X</sub>H<sub>Y</sub>Ph x 2), 3.68 (1H, d, *J* 15.6, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 3.60 (1H, dd, *J* 9.1, 3.9, C<sub>4</sub>H), 3.56 (2H, d, *J* 14.0, NCH<sub>X</sub>H<sub>Y</sub>Ph x 2), 3.37 (1H, d, *J* 15.6, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 3.14 (1H, dd, *J* 14.0, 9.1, C<sub>5</sub>H<sub>5</sub>H<sub>T</sub>), 2.81 (1H, dd, *J* 14.0, 3.9, C<sub>5</sub>H<sub>5</sub>H<sub>T</sub>), 1.12 (3H, t, *J* 7.1, OCH<sub>2</sub>CH<sub>3</sub>), 1.01 (9H, s, *t*-Bu), 0.20 (6H, s, Me<sub>2</sub>Si); **<sup>13</sup>C NMR** δ (62.9 MHz, CDCl<sub>3</sub>) 202.5 (1C, Q), 167.1 (1C, Q), 153.8 (1C, Q), 138.7 (2C, Q), 131.5 (1C, Q), 131.0 (2C, CH), 128.9 (4C, CH), 128.5 (4C, CH), 127.2 (2C, CH), 119.8 (2C, CH), 68.2 (1C, CH), 60.9 (1C, CH<sub>2</sub>), 54.4 (2C, CH<sub>2</sub>), 46.7 (1C, CH<sub>2</sub>), 27.7 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 18.0 (1C, Q), 14.0 (1C, CH<sub>3</sub>), -4.6 (2C, CH<sub>3</sub>); *m/z* (FAB, THIOG) 546 ([M+H]<sup>+</sup>, 37%), 430 (85), 221 (71), 91 (100); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 546.3042. C<sub>33</sub>H<sub>44</sub>NO<sub>4</sub>Si requires *m/z*, 546.3038).

### Ethyl (3*R*,4*R*)-5-(4'-*tert*-butyldimethylsilyloxyphenyl)-4-dibenzylamino-3-hydroxy-pentanoate 5

To a solution of  $\beta$ -keto ester (6.66 g, 12.2 mmol), in ether (100 ml), was added methanol (20.0 ml) and the solution adjusted to pH 4 by addition of a few drops of acetic acid. Sodium cyanoborohydride (11.5 g, 183 mmol) was added to the solution at 0 °C, the solution was allowed to warm to room temperature and stirred for 19 h. The solution was quenched by addition of saturated ammonium chloride (40 ml). The organic phase was separated and the aqueous extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 ml). The combined organics were washed with brine (40 ml), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [8% EtOAc/hexane] to give a clear oil (5.77 g, 10.5 mmol, 86%);  $R_f$  [10% EtOAc/hexane] = 0.28;  $[\alpha]_D$  -30.2 (*c* 3.05, CHCl<sub>3</sub>);  $\nu_{max}$  (neat)/cm<sup>-1</sup> 3453, 1732, 1607, 1509; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.41-7.30 (10H, m, ArH), 7.11 (2H, d, *J* 8.5, ArH), 6.85 (2H, d, *J* 8.5, ArH), 4.25 (1H, br s, OH), 4.18 (2H, d, *J* 13.7, NCH<sub>x</sub>H<sub>y</sub>Ph x 2), 4.09 (2H, q, *J* 7.2, OCH<sub>2</sub>CH<sub>3</sub>), 4.05-4.02 (1H, m, C<sub>3</sub>H), 3.48 (2H, d, *J* 13.7, NCH<sub>x</sub>H<sub>y</sub>Ph x 2), 3.14 (1H, m, C<sub>4</sub>H), 2.85-2.75 (2H, m, C<sub>5</sub>H<sub>2</sub>), 2.40 (1H, dd, *J* 15.7, 9.3, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 2.18 (1H, dd, *J* 15.7, 2.7, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 1.26 (3H, t, *J* 7.2, OCH<sub>2</sub>CH<sub>3</sub>), 1.06 (9H, s, <sup>*t*</sup>Bu), 0.28 (6H, s, Me<sub>2</sub>Si); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 172.5 (1C, Q), 153.9 (1C, Q), 139.0 (2C, Q), 132.4 (1C, Q), 129.9 (2C, CH), 128.9 (4C, CH), 128.3 (4C, CH), 127.1 (2C, CH), 120.1 (2C, CH), 67.8 (1C, CH), 63.0 (1C, CH), 60.4 (1C, CH<sub>2</sub>), 54.2 (2C, CH<sub>2</sub>), 39.7 (1C, CH<sub>2</sub>), 30.1 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 18.1 (1C, Q), 14.0 (1C, CH<sub>3</sub>), -4.6 (2C, CH<sub>3</sub>); *m/z* (FAB, NOBA) 570 ([M+Na]<sup>+</sup>, 82%), 548 ([M+H]<sup>+</sup>, 98%), 430 (100), 91 (96); HRMS (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 548.3191. C<sub>33</sub>H<sub>46</sub>NO<sub>4</sub>Si requires *m/z*, 548.3196); Chiral HPLC (*R* enantiomer) *R*<sub>f</sub> = 5.30 min, (*S* enantiomer) *R*<sub>f</sub> = 6.26 min [2% ethanol/hexane], 97% ee.

### (3*R*,4*R*)-5-(4'-*tert*-Butyldimethylsilyloxyphenyl)-4-dibenzylamino-3-hydroxy-pentan-1-ol

A solution of ester (5.77 g, 10.5 mmol) in THF (100 ml) was cooled to -78 °C and lithium aluminium hydride (53.0 ml, 52.5 mmol, 1.0 M in THF) added. The solution was stirred at -78 °C for 6 h, then allowed to warm to RT over 1 h. The reaction was quenched by addition of 1 M sodium hydroxide (30 ml), diluted with CH<sub>2</sub>Cl<sub>2</sub> (30 ml) and saturated sodium potassium tartrate (30 ml) and stirred for 16 h. The organic phase was separated and the aqueous phase extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 80 ml). The combined organics were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [30% EtOAc/hexane] to give a clear oil (5.17 g, 10.2 mmol, 97%);  $R_f$  [30% EtOAc/hexane] = 0.39;  $[\alpha]_D$  -28.3 (*c* 2.40, CHCl<sub>3</sub>);  $\nu_{max}$  (neat)/cm<sup>-1</sup> 3376, 1607, 1509; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.41-7.24 (10H, m, ArH), 7.12 (2H, d, *J* 8.4, ArH), 6.88 (2H, d, *J* 8.4, ArH), 4.88 (1H, brs, OH), 3.95 (2H, d, *J* 13.2, NCH<sub>x</sub>H<sub>y</sub>Ph x 2), 3.84 (1H, td, *J* 2.7, 9.0, C<sub>3</sub>H), 3.73-3.69 (2H, m, C<sub>1</sub>H<sub>2</sub>OH), 3.45 (2H, d, *J* 13.2, NCH<sub>x</sub>H<sub>y</sub>Ph x 2), 3.10 (1H, dd, *J* 14.2, 6.5, C<sub>5</sub>H<sub>S</sub>H<sub>T</sub>), 2.99-2.94 (2H, m, C<sub>4</sub>H, OH), 2.65 (1H, dd, *J* 14.2, 6.5, C<sub>5</sub>H<sub>S</sub>H<sub>T</sub>), 1.66-1.64 (1H, m, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 1.36-1.31 (1H, m, C<sub>2</sub>H<sub>A</sub>H<sub>B</sub>), 1.06 (9H, s, <sup>*t*</sup>Bu), 0.27 (6H, s, Me<sub>2</sub>Si); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 154.0 (1C, Q), 138.5 (2C, Q), 132.5 (1C, Q), 129.9 (2C, CH), 128.9 (4C, CH), 128.4 (4C, CH), 127.2 (2C, CH), 120.2 (2C, CH), 70.4 (1C, CH), 63.8 (1C, CH), 61.1 (1C, CH<sub>2</sub>), 53.6 (2C, CH<sub>2</sub>), 35.6 (1C, CH<sub>2</sub>), 31.3 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 18.1 (1C, Q), -4.6 (2C, CH<sub>3</sub>); *m/z* (FAB, THIOG) 506 ([M+H]<sup>+</sup>, 9%), 430 (12), 284 (35), 221 (55), 91 (100); HRMS (FAB, THIOG) (Found: [M+H]<sup>+</sup>, 506.3091. C<sub>31</sub>H<sub>44</sub>NO<sub>3</sub>Si requires *m/z*, 506.3091).

### (2*R*,3*R*)-2-(4'-*tert*-Butyldimethylsilyloxybenzyl)-1,1-dibenzyl-3-hydroxy-pyrrolidinium chloride 6

To a solution of alcohol (5.17 g, 10.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 ml) at 0 °C was added DMAP (2.05 g, 16.8 mmol) and trisopropylbenzene sulfonyl chloride (3.40 g, 11.2 mmol). The solution was stirred for 19 h before being diluted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml) and water (50 ml). The organic phase was separated and washed with 1% HCl (2 x 20 ml) then dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] to give a colourless foam. The salt was subjected to ion exchange chromatography [Dowex Cl<sup>-</sup>]; prepared by treating Dowex resin with methanol, then 1% HCl, followed by flushing with methanol until the eluent returned to pH 7] eluting with methanol to give the chloride salt (5.14 g, 9.82 mmol, 96%) as an amorphous solid;  $R_f$  [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] = 0.12;  $[\alpha]_D$

-42.1 (c 1.50, CHCl<sub>3</sub>);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3397, 1607, 1508; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.78-7.29 (10H, m, ArH), 7.26 (2H, d, *J* 8.5, ArH), 6.65 (2H, d, *J* 8.5, ArH), 6.56 (1H, br s, OH), 5.73 (1H, d, *J* 13.4, NCH<sub>X</sub>H<sub>Y</sub>Ph), 5.08 (2H, m, NCH<sub>X</sub>H<sub>Y</sub>Ph x 2), 4.32 (1H, br s, C<sub>3</sub>H), 4.23 (1H, d, *J* 13.4, NCH<sub>X</sub>H<sub>Y</sub>Ph), 3.91 (1H, br d, *J* 11.1, CH<sub>5</sub>H<sub>T</sub>Ar), 3.84-3.81 (1H, m, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 3.53 (1H, br d, *J* 11.1, CH<sub>5</sub>H<sub>T</sub>Ar), 3.33 (1H, br t, *J* 11.1, C<sub>2</sub>H), 3.04 (1H, td, 11.1, 8.7, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.58 (1H, td, *J* 14.1, 7.9, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 1.94-1.87 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 0.98 (9H, s, <sup>t</sup>Bu), 0.17 (6H, s, Me<sub>2</sub>Si); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 154.4 (1C, Q), 133.4 (2C, CH), 133.0 (2C, CH), 130.5 (3C, CH), 130.2 (1C, CH), 129.2 (2C, CH), 129.0 (2C, CH), 128.3 (1C, Q), 127.9 (1C, Q), 127.3 (1C, Q), 120.1 (2C, CH), 76.1 (1C, CH), 67.6 (1C, CH), 62.2 (1C, CH<sub>2</sub>), 61.6 (1C, CH<sub>2</sub>), 55.6 (1C, CH<sub>2</sub>), 31.2 (1C, CH<sub>2</sub>), 27.4 (1C, CH<sub>2</sub>), 25.5 (3C, CH<sub>3</sub>), 17.9 (1C, Q), -4.6 (2C, Q); *m/z* (FAB, NOBA) 488 ([M]<sup>+</sup>, 100%), 396 (21), 307 (14), 91 (75); HRMS (FAB, NOBA) (Found: [M]<sup>+</sup>, 488.2978. C<sub>31</sub>H<sub>42</sub>NO<sub>2</sub>Si requires *m/z*, 488.2985).

### **(2R,3R)-1-Benzyl-2-(4'-tert-butyltrimethylsilyloxybenzyl)-3-hydroxy-pyrrolidine**

To a solution of the chloride salt (4.32 g, 8.25 mmol) in methanol (40 ml) was added 5% Pd/C (300 mg) and potassium carbonate (3.42 g, 24.8 mmol). The mixture was exposed to a hydrogen atmosphere and stirred vigorously for 20 min. The suspension was filtered through a pad of celite and concentrated under reduced pressure. The residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 ml) and washed with water (15 ml). The organic phase was separated and the aqueous phase extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 15 ml). The combined organic phases were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo* to give an oil (2.90 g, 7.30 mmol, 89%); *R<sub>f</sub>* [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] = 0.12; [ $\alpha$ ]<sub>D</sub> -64.3 (c 2.10, CHCl<sub>3</sub>);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3397, 1607, 1508; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.35-7.26 (5H, m, ArH), 7.19 (2H, d, *J* 8.5, ArH), 6.78 (2H, d, *J* 8.5, ArH), 4.17 (1H, d, *J* 13.0, NCH<sub>X</sub>H<sub>Y</sub>Ph), 3.96-3.92 (1H, m, C<sub>3</sub>H), 3.26 (1H, d, *J* 13.0, NCH<sub>X</sub>H<sub>Y</sub>Ph), 3.05 (1H, td, *J* 9.2, 3.9, C<sub>2</sub>H), 2.90-2.93 (2H, m, CH<sub>5</sub>H<sub>T</sub>Ar), 2.50 (1H, td, *J* 7.1, 3.9, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.15 (1H, td, *J* 9.6, 7.1, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.01-1.97 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 1.71-1.68 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 0.98 (9H, s, <sup>t</sup>Bu), 0.19 (6H, s, Me<sub>2</sub>Si); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 153.8 (1C, Q), 138.3 (1C, Q), 131.8 (1C, Q), 130.1 (2C, CH), 128.8 (2C, CH), 128.2 (2C, CH), 127.0 (1C, CH), 119.9 (2C, CH), 71.9 (1C, CH), 70.8 (1C, CH), 57.6 (1C, CH<sub>2</sub>), 51.4 (1C, CH<sub>2</sub>), 32.8 (1C, CH<sub>2</sub>), 32.1 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 18.1 (1C, Q), -4.5 (2C, CH<sub>3</sub>); *m/z* (FAB, NOBA) 398 [M+H]<sup>+</sup>, (100%), 221 (61), 176 (90), 91 (99); HRMS (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 398.2511. C<sub>24</sub>H<sub>36</sub>NO<sub>2</sub>Si requires *m/z*, 398.2515).

### **(2R,3R)-3-Acetoxy-1-benzyl-2-(4'-tert-butyltrimethylsilyloxybenzyl)-pyrrolidine**

To a solution of the alcohol (2.90 g, 7.30 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 ml) was added a catalytic amount of DMAP, freshly distilled acetic anhydride (1.38 ml, 14.6 mmol) and triethylamine (2.02 ml, 14.6 mmol). The solution was stirred for 18 h and then quenched by addition of saturated aq. sodium bicarbonate solution (40 ml). The organic phase was separated and the aqueous phase extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 ml). The combined organics were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [30% EtOAc/hexane] to give an oil (3.11 g, 7.08 mmol, 96%); *R<sub>f</sub>* [30% EtOAc/hexane] = 0.62; [ $\alpha$ ]<sub>D</sub> -93.1 (c 2.90, CHCl<sub>3</sub>);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 1738, 1608, 1509; <sup>1</sup>H NMR  $\delta$  (250 MHz, CDCl<sub>3</sub>) 7.35-7.18 (5H, m, ArH), 7.04 (2H, d, *J* 8.4, ArH), 6.75 (2H, d, *J* 8.4, ArH), 5.02-4.98 (1H, m, C<sub>3</sub>H), 4.05 (1H, d, *J* 13.1, NCH<sub>X</sub>H<sub>Y</sub>Ph), 3.33 (1H, d, *J* 13.1, NCH<sub>X</sub>H<sub>Y</sub>Ph), 3.00-2.75 (4H, m, CH<sub>2</sub>Ar, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>, C<sub>2</sub>H), 2.23-2.13 (2H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub> + C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.07 (3H, s, OAc), 1.72-1.70 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 0.97 (9H, s, <sup>t</sup>Bu), 0.18 (6H, s, Me<sub>2</sub>Si); <sup>13</sup>C NMR  $\delta$  (62.9 MHz, CDCl<sub>3</sub>) 170.4 (1C, Q), 153.8 (1C, Q), 138.1 (1C, Q), 131.6 (1C, Q), 129.6 (2C, CH), 129.0 (2C, CH), 128.1 (2C, CH), 126.9 (1C, CH), 119.9 (2C, CH), 74.6 (1C, CH), 68.0 (1C, CH), 58.2 (1C, CH<sub>2</sub>), 51.5 (1C, CH<sub>2</sub>), 33.4 (1C, CH<sub>2</sub>), 30.5 (1C, CH<sub>2</sub>), 25.6 (3C, CH<sub>3</sub>), 21.1 (1C, CH<sub>3</sub>), 18.1 (1C, Q), -4.6 (2C, CH<sub>3</sub>); *m/z* (FAB, NOBA) 540 ([M+H]<sup>+</sup>, 100%), 380 (51), 218 (96), 91 (90); HRMS (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 440.2630. C<sub>26</sub>H<sub>38</sub>NO<sub>3</sub>Si requires *m/z*, 440.2621).

### **(2R,3R)-3-Acetoxy-2-(4'-tert-butyldimethylsilyloxybenzyl)-pyrrolidine**

A solution of monobenzylamine (1.01 g, 2.29 mmol) and Pearlman's catalyst (20% Pd(OH)<sub>2</sub>/C; 300 mg) in EtOH (15 ml) was exposed to a hydrogen atmosphere (1 atm) and stirred vigorously for 2.5 h. The solution was filtered through a pad of Celite (prewashed with EtOH, CH<sub>2</sub>Cl<sub>2</sub>) and concentrated *in vacuo* to give an oil (785 mg, 2.25 mmol, 98%); **R<sub>f</sub>** [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] = 0.16; [**α**]<sub>D</sub> -42.3 (c 1.30, CHCl<sub>3</sub>); **v**<sub>max</sub> (neat)/cm<sup>-1</sup> 2930, 1742, 1608, 1510; **<sup>1</sup>H NMR** δ (250 MHz, CDCl<sub>3</sub>) 7.05 (2H, d, *J* 8.4, ArH), 6.75 (2H, d, *J* 8.4, ArH), 5.12 (1H, br s, C<sub>3</sub>H), 3.86 (1H, br s, C<sub>2</sub>H), 3.33-3.23 (2H, m, C<sub>5</sub>H<sub>2</sub>), 3.07-2.89 (2H, m, CH<sub>2</sub>Ar), 2.23-2.17 (H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 2.17 (3H, s, OAc), 2.13-1.92 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 0.93 (9H, s, <sup>*t*</sup>Bu), 0.17 (6H, s, Me<sub>2</sub>Si); **<sup>13</sup>C NMR** δ (62.9 MHz, CDCl<sub>3</sub>) 170.5 (1C, Q), 154.4 (1C, Q), 130.8 (1C, Q), 129.8 (2C, CH), 120.3 (2C, CH), 74.4 (1C, CH), 64.4 (1C, CH), 43.8 (1C, CH<sub>2</sub>), 33.9 (1C, CH<sub>2</sub>), 32.6 (1C, CH<sub>2</sub>), 25.8 (3C, CH<sub>3</sub>), 21.3 (1C, CH<sub>3</sub>), 18.3 (1C, Q), -4.3 (2C, CH<sub>3</sub>); **m/z** (FAB, NOBA) 350 ([M+H]<sup>+</sup>, 100%), 290 (34), 221 (60); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 350.2154. C<sub>19</sub>H<sub>32</sub>NO<sub>3</sub>Si requires *m/z*, 350.2152).

### **(2R,3R)-3-Acetoxy-1-tert-butoxycarbonylamino-2-(4'-tert-butyldimethylsilyloxybenzyl)-pyrrolidine 7**

To a solution of the amine (726 mg, 2.08 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (15 ml) was added triethylamine (456 μl, 3.27 mmol) and the solution cooled to 0 °C. Di-*tert*-butoxy carbamate (713 mg, 3.27 mmol) was added and the solution stirred for 5 min, before warming to RT and stirring for 15 h. The reaction was quenched with saturated sodium bicarbonate (30 ml) and diluted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml). The organic phase was separated and washed with 1% HCl (20 ml) then dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [2% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] to give an oil (903 mg, 2.01 mmol, 97%); **R<sub>f</sub>** [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] = 0.68; [**α**]<sub>D</sub> +3.50 (c 2.00, CHCl<sub>3</sub>); **v**<sub>max</sub> (neat)/cm<sup>-1</sup> 1743, 1697, 1608, 1509; **<sup>1</sup>H NMR** δ (360 MHz, CDCl<sub>3</sub>, 323 K) 7.06 (2H, d, *J* 8.4, ArH), 6.73 (2H, d, *J* 8.4, ArH), 5.13 (1H, br q, *J* 6.7 C<sub>3</sub>H), 4.29-4.24 (1H, m, C<sub>2</sub>H), 3.45-3.40 (1H, m, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 3.34-3.27 (1H, m, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.94 (1H, br d, CH<sub>5</sub>H<sub>T</sub>Ar), 2.86-2.80 (1H, dd, *J* 13.8, 8.3, CH<sub>5</sub>H<sub>T</sub>Ar) 2.08-2.04 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 2.01 (3H, s, OAc), 1.83-1.76 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 1.47 (9H, s, <sup>*t*</sup>BuO), 0.99 (9H, s, <sup>*t*</sup>BuSi), 0.19 (6H, s, Me<sub>2</sub>Si); **<sup>13</sup>C NMR** δ (90.7 MHz, CDCl<sub>3</sub>, 323 K) 170.8 (1C, Q), 155.1 (1C, Q), 154.6 (1C, Q), 131.8 (1C, Q), 130.9 (2C, CH), 120.5 (2C, CH), 80.4 (1C, Q), 73.9 (1C, CH), 59.6 (1C, CH), 42.0 (1C, CH<sub>2</sub>), 34.1 (1C, CH<sub>2</sub>), 33.1 (1C, CH<sub>2</sub>), 29.1 (3C, CH<sub>3</sub>), 26.3 (3C, CH<sub>3</sub>), 21.6 (1C, CH<sub>3</sub>), 18.9 (1C, Q), -4.4 (2C, CH<sub>3</sub>); **m/z** (FAB, NOBA) 450 ([M+H]<sup>+</sup>, 9%), 221 (83), 91 (22); **HRMS** (FAB, NOBA) (Found: [M+H]<sup>+</sup>, 450.2671. C<sub>24</sub>H<sub>40</sub>NO<sub>5</sub>Si requires *m/z*, 450.2676).

### **(2R,3R)-3-Acetoxy-1-tert-butoxycarbonylamino-2-(4'-hydroxy-benzyl)-pyrrolidine**

To a solution of the silyl ether (572 mg, 1.27 mmol) in THF (15 ml) at 0 °C was added triethylamine trihydrofluoride (1.02 ml, 6.35 mmol), the solution was stirred for 5 min at 0 °C, before warming to RT and stirring for 2 h. The reaction was quenched with saturated sodium bicarbonate (30 ml) and diluted with EtOAc (50 ml). The organic phase was separated and washed with saturated brine (20 ml) then dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated *in vacuo*. The residue was chromatographed on silica gel [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] to give an oil (415 mg, 1.23 mmol, 96%); **R<sub>f</sub>** [5% MeOH/CH<sub>2</sub>Cl<sub>2</sub>] = 0.25; [**α**]<sub>D</sub> +9.30 (c 0.80, CHCl<sub>3</sub>); **v**<sub>max</sub> (neat)/cm<sup>-1</sup> 3350, 1741, 1666, 1615, 1515; **<sup>1</sup>H NMR** δ (360 MHz, CDCl<sub>3</sub>, 323 K) 7.02 (2H, d, *J* 8.2, ArH), 6.73 (2H, d, *J* 8.2, ArH), 5.13 (1H, br q, *J* 6.8, C<sub>3</sub>H), 4.26 (1H, br q, *J* 6.8, C<sub>2</sub>H), 3.48-3.41 (1H, m, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 3.36-3.29 (1H, m, C<sub>5</sub>H<sub>M</sub>H<sub>N</sub>), 2.91 (1H, br s, CH<sub>5</sub>H<sub>T</sub>Ar), 2.80 (1H, dd, *J* 13.7, 8.1, CH<sub>5</sub>H<sub>T</sub>Ar), 2.09-2.04 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 2.02 (3H, s, OAc), 1.85-1.62 (1H, m, C<sub>4</sub>H<sub>E</sub>H<sub>F</sub>), 1.45 (9H, s, <sup>*t*</sup>BuO); **<sup>13</sup>C NMR** δ (90.7 MHz, CDCl<sub>3</sub>, 323 K) 170.8 (1C, Q), 155.4 (1C, Q), 155.3 (1C, Q), 130.9 (2C, CH), 130.4 (1C, Q), 115.8 (2C, CH), 80.6 (1C, Q), 73.9 (1C, CH), 59.8 (1C, CH), 43.6 (1C, CH<sub>2</sub>), 34.6 (1C, CH<sub>2</sub>), 29.4 (1C, CH<sub>2</sub>), 29.0 (3C, CH<sub>3</sub>), 21.2 (1C, CH<sub>3</sub>); **m/z** (FAB, THIOG) 336 ([M+H]<sup>+</sup>, 50%), 176 (70); **HRMS** (FAB, THIOG) (Found: [M+H]<sup>+</sup>, 336.1810. C<sub>18</sub>H<sub>26</sub>NO<sub>5</sub> requires *m/z*, 336.1811).

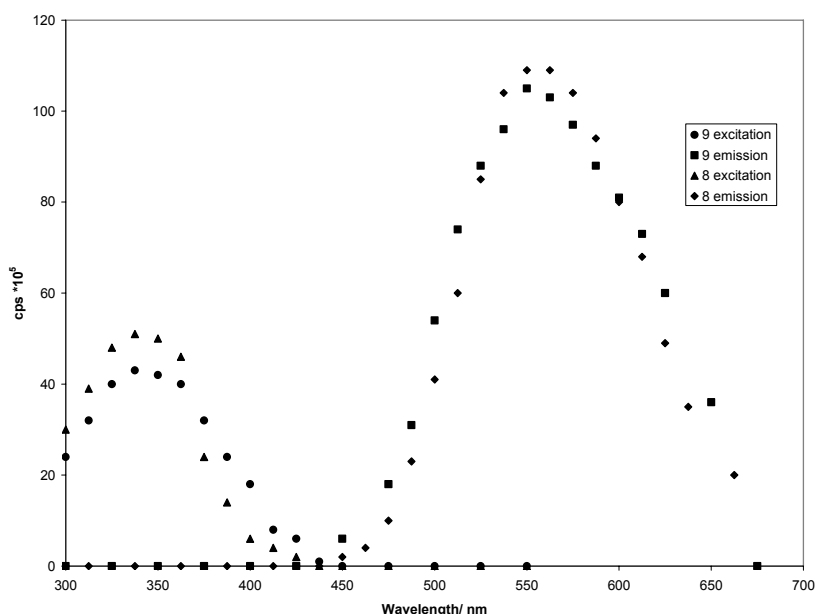
### (2R,3R)-3-Acetoxy-1-tert-butoxycarbonylamino-2-(4'-propargyloxybenzyl) pyrrolidine

To a solution of the phenol (27.0 mg, 80.0  $\mu\text{mol}$ ) in DMF (2 ml) was added potassium carbonate (17 mg, 120  $\mu\text{mol}$ ) and propargyl bromide (15.0  $\mu\text{l}$ , 120  $\mu\text{mol}$ ), the solution was stirred at RT for 12 h, before quenching with water (5 ml) and diluting with ether (10 ml). The organic phase was separated and washed with saturated brine (10 ml) then dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was chromatographed on silica gel [2% MeOH/ $\text{CH}_2\text{Cl}_2$ ] to give an oil (30.0 mg, 80.0  $\mu\text{mol}$ , 100%);  $R_f$  [5% MeOH/ $\text{CH}_2\text{Cl}_2$ ] = 0.70;  $[\alpha]_D^{+9.00}$  (*c* 1.50,  $\text{CHCl}_3$ );  $\nu_{\text{max}}$  (neat)/ $\text{cm}^{-1}$  3286, 1739, 1692, 1610, 1510;  $^1\text{H NMR}$   $\delta$  (360 MHz,  $\text{CDCl}_3$ , 318 K) 7.20 (2H, d, *J* 8.6, ArH), 6.89 (2H, d, *J* 8.6, ArH), 5.13 (1H, br q, *J* 6.5,  $\text{C}_3\text{H}$ ), 4.66 (1H, d, *J* 2.4,  $\text{HC}\equiv\text{CCH}_2$ ) 4.3 (1H, ddd, *J* 8.2, 6.5, 4.7,  $\text{C}_2\text{H}$ ), 3.48-3.41 (1H, m,  $\text{C}_5\text{H}_\text{M}\text{H}_\text{N}$ ), 3.36-3.31 (1H, m,  $\text{C}_5\text{H}_\text{M}\text{H}_\text{N}$ ), 2.96 (1H, br s,  $\text{CH}_3\text{H}_\text{T}\text{Ar}$ ), 2.86-2.80 (1H, dd, *J* 13.8, 8.2,  $\text{CH}_3\text{H}_\text{T}\text{Ar}$ ), 2.49 (1H, t, *J* 2.4,  $\text{HC}\equiv\text{CCH}_2$ ), 2.08-2.04 (1H, m,  $\text{C}_4\text{H}_\text{E}\text{H}_\text{F}$ ), 1.99 (3H, s, OAc), 1.84-1.78 (1H, m,  $\text{C}_4\text{H}_\text{E}\text{H}_\text{F}$ ), 1.45 (9H, s, *t*-BuO);  $^{13}\text{C NMR}$   $\delta$  (90.7 MHz,  $\text{CDCl}_3$ , 318 K) 170.2 (1C, Q), 156.4 (1C, Q), 154.6 (1C, Q), 131.9 (1C, Q), 130.6 (2C, CH), 115.1 (2C, CH), 79.9 (1C, Q), 79.0 (1C, CH), 75.4 (1C, Q), 73.4 (1C, CH), 59.4 (1C, CH), 56.2 (1C,  $\text{CH}_2$ ), 42.0 (1C,  $\text{CH}_2$ ), 34.4 (1C,  $\text{CH}_2$ ), 33.1 (1C,  $\text{CH}_2$ ), 28.6 (3C,  $\text{CH}_3$ ), 21.0 (1C,  $\text{CH}_3$ ); *m/z* (FAB, THIOG) 374 ( $[\text{M}+\text{H}]^+$ , 8%), 318 (100), 274 (39), 214 (61), 91 (93); HRMS (FAB, THIOG) (Found:  $[\text{M}+\text{H}]^+$ , 374.1966.  $\text{C}_{21}\text{H}_{28}\text{NO}_5$  requires *m/z*, 374.1968).

### (2R,3R)- 3-Acetoxy-2-(4'-propargyloxybenzyl)-pyrrolidine 2b

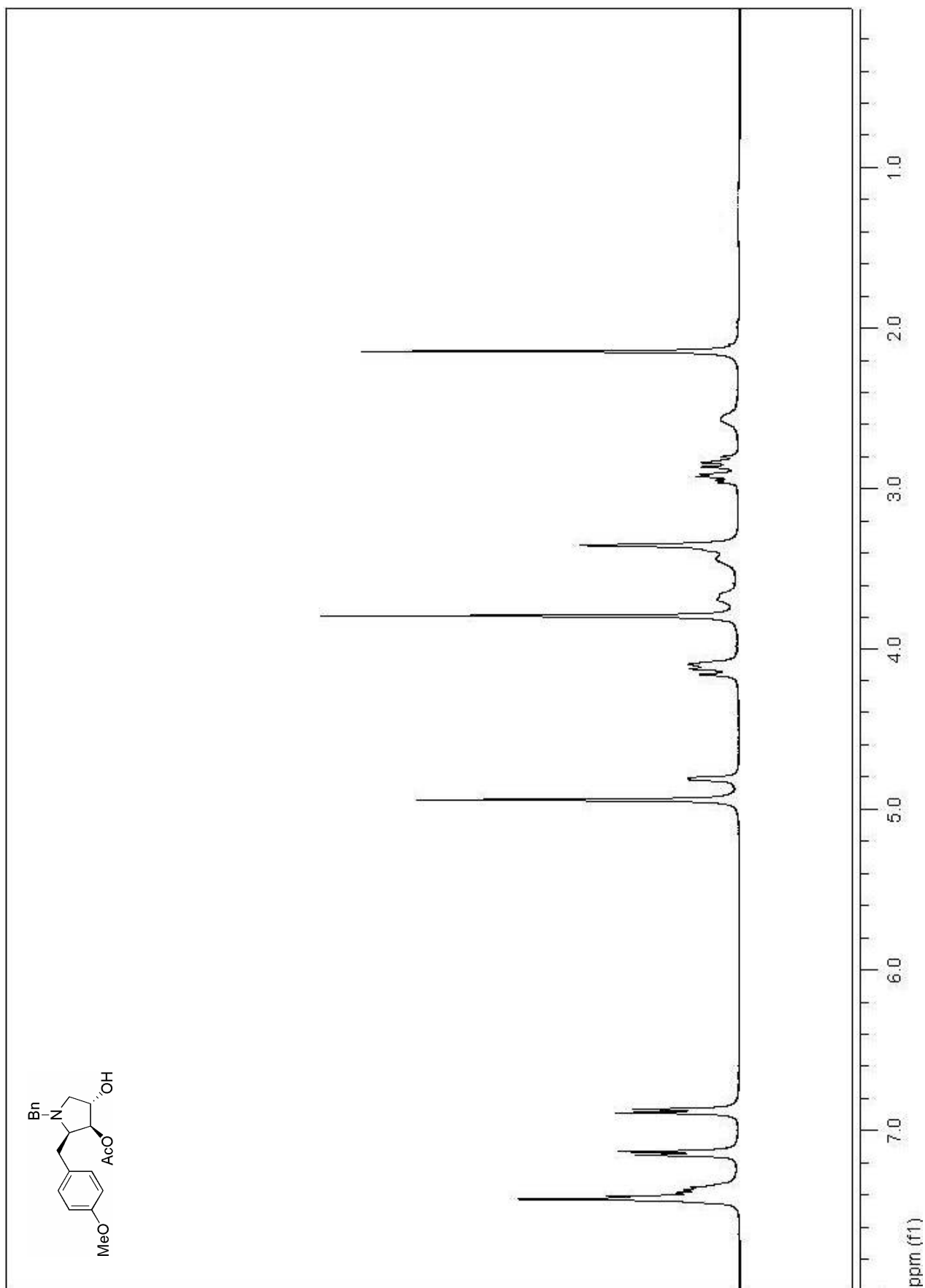
To a solution of carbamate (30.0 mg, 80.0  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (2 ml) was added TFA (0.20 ml, 0.80 mmol) and the solution stirred for 15 h. The solution was quenched with saturated aq. sodium bicarbonate (5 ml). The organic phase was separated and the aqueous phase extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 ml). The combined organic phases were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo* to give an oil (18.0 mg, 70.0  $\mu\text{mol}$ , 87%);  $R_f$  [5% MeOH/ $\text{CH}_2\text{Cl}_2$ ] = 0.11;  $[\alpha]_D^{-24.2}$  (*c* 0.95,  $\text{CHCl}_3$ );  $\nu_{\text{max}}$  (neat)/ $\text{cm}^{-1}$  3282, 2925, 1730, 1610, 1510;  $^1\text{H NMR}$   $\delta$  (360 MHz,  $\text{CDCl}_3$ , 323 K) 7.09 (2H, d, *J* 8.7, ArH), 6.90 (2H, d, *J* 8.7, ArH), 5.29-5.27 (1H, m,  $\text{C}_3\text{H}$ ), 4.63 (2H, d, *J* 2.4,  $\text{HC}\equiv\text{CCH}_2$ ), 3.85-3.80 (1H, m,  $\text{C}_2\text{H}$ ), 3.45-3.32 (2H, m,  $\text{C}_5\text{H}_2$ ), 3.05-2.99 (2H, m,  $\text{CH}_2\text{Ar}$ ), 2.50 (1H, t, *J* 2.4,  $\text{HC}\equiv\text{CCH}_2$ ), 2.29-2.17 (2H, m,  $\text{C}_4\text{H}_2$ ), 2.18 (3H, s, OAc);  $^{13}\text{C NMR}$   $\delta$  (90.7 MHz,  $\text{CDCl}_3$ , 323 K) 169.9 (1C, Q), 157.3 (1C, Q), 130.0 (2C, CH), 128.2 (1C, Q), 115.9 (2C, CH), 78.7 (1C, Q), 75.8 (1C, CH), 72.6 (1C, CH), 64.5 (1C, CH), 56.2 (1C,  $\text{CH}_2$ ), 43.2 (1C,  $\text{CH}_2$ ), 31.8 (1C,  $\text{CH}_2$ ), 33.3 (1C,  $\text{CH}_2$ ), 20.7 (1C,  $\text{CH}_3$ ); *m/z* (FAB, THIOG) 274 ( $[\text{M}+\text{H}]^+$ , (87%)), 214 (57); HRMS (FAB, THIOG) (Found:  $[\text{M}+\text{H}]^+$ , 274.1441.  $\text{C}_{16}\text{H}_{19}\text{NO}_3$  requires *m/z*, 274.1443).

### Absorption and Emission Spectra of 8 and 9

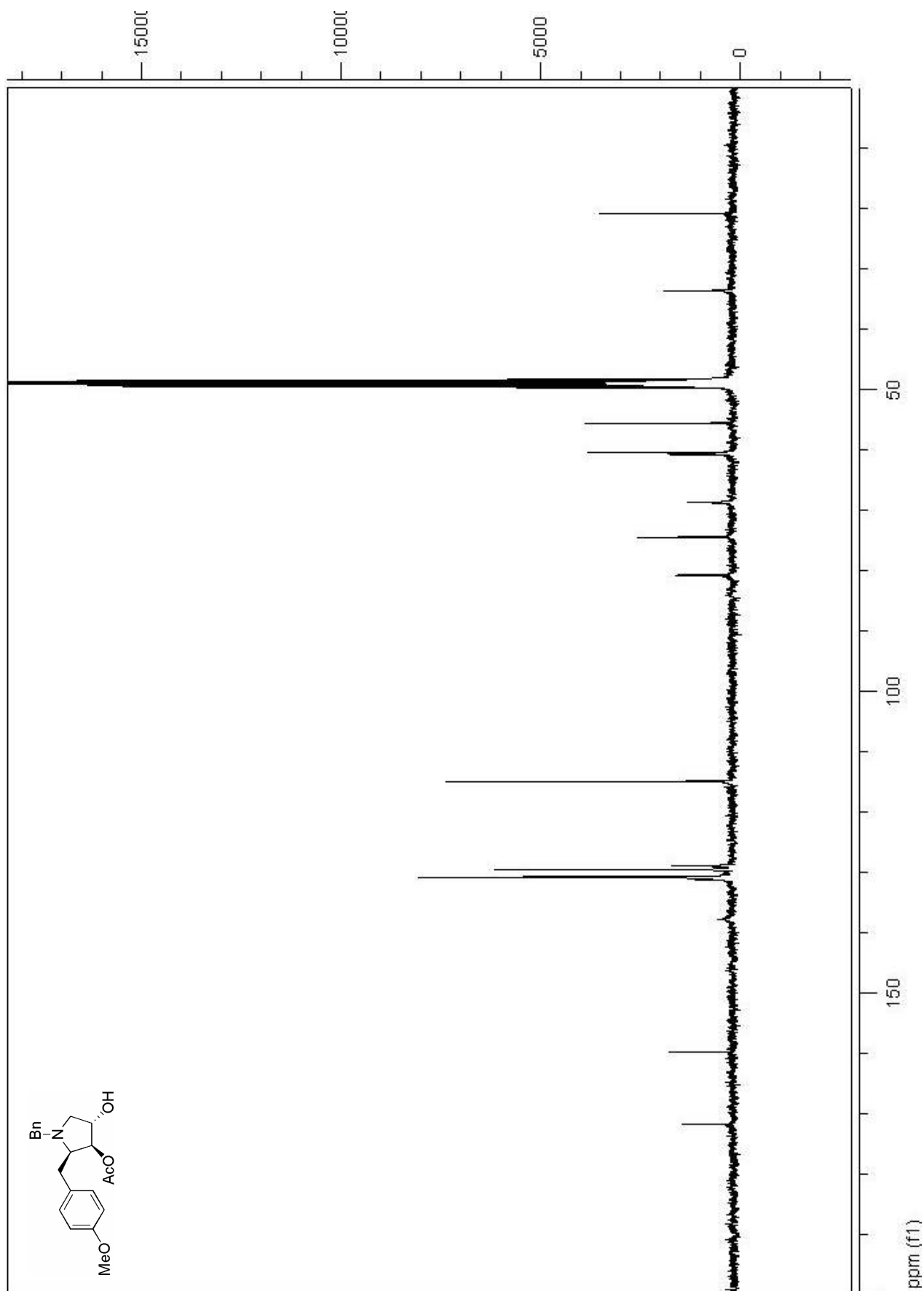


Emission spectra of 8 and 9 were recorded with excitation at 350 nm.

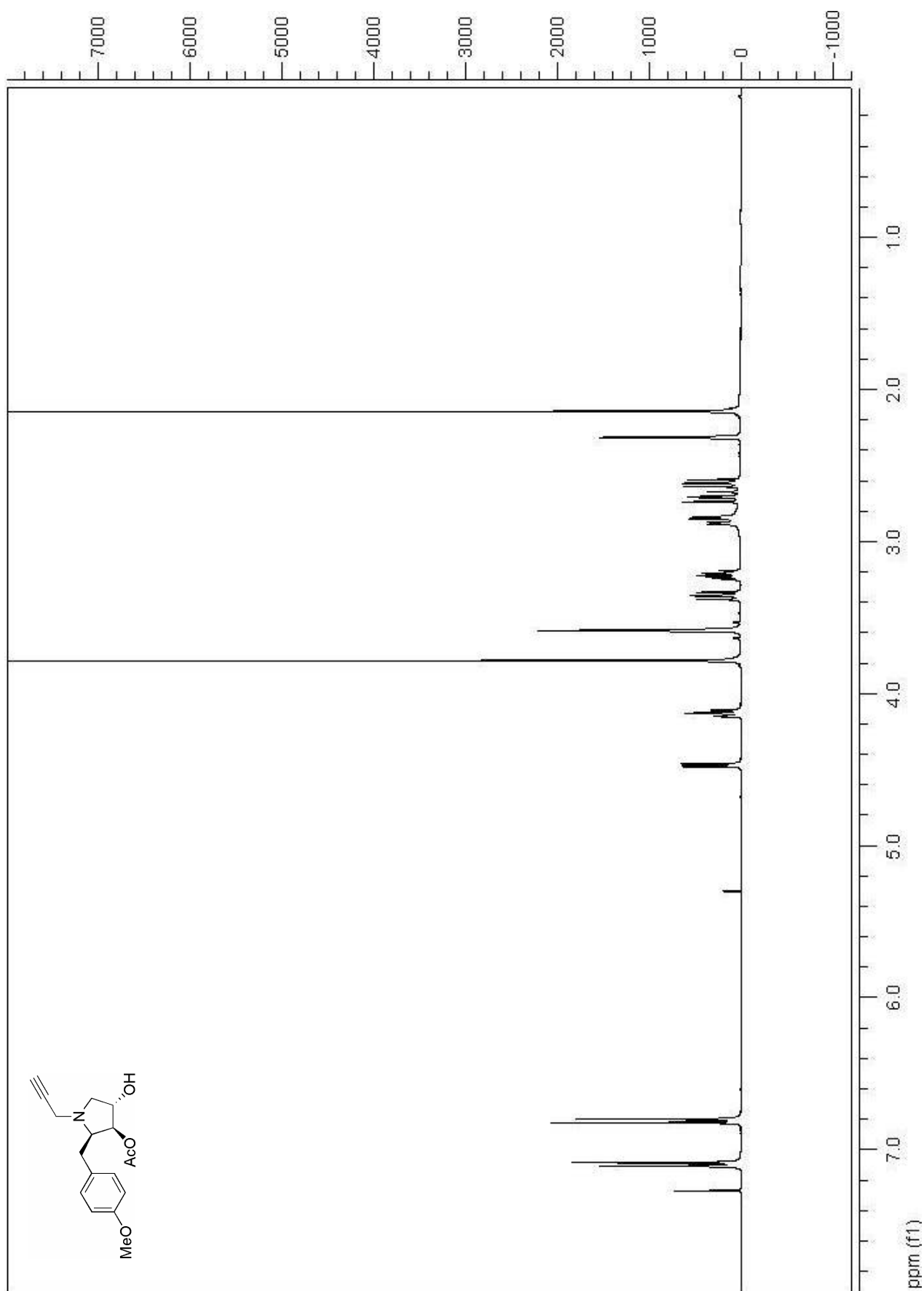
(2*R*,3*S*,4*S*)-3-Acetoxy-1-benzyl-4-hydroxy-2-(4'-methoxybenzyl)-pyrrolidine 1c



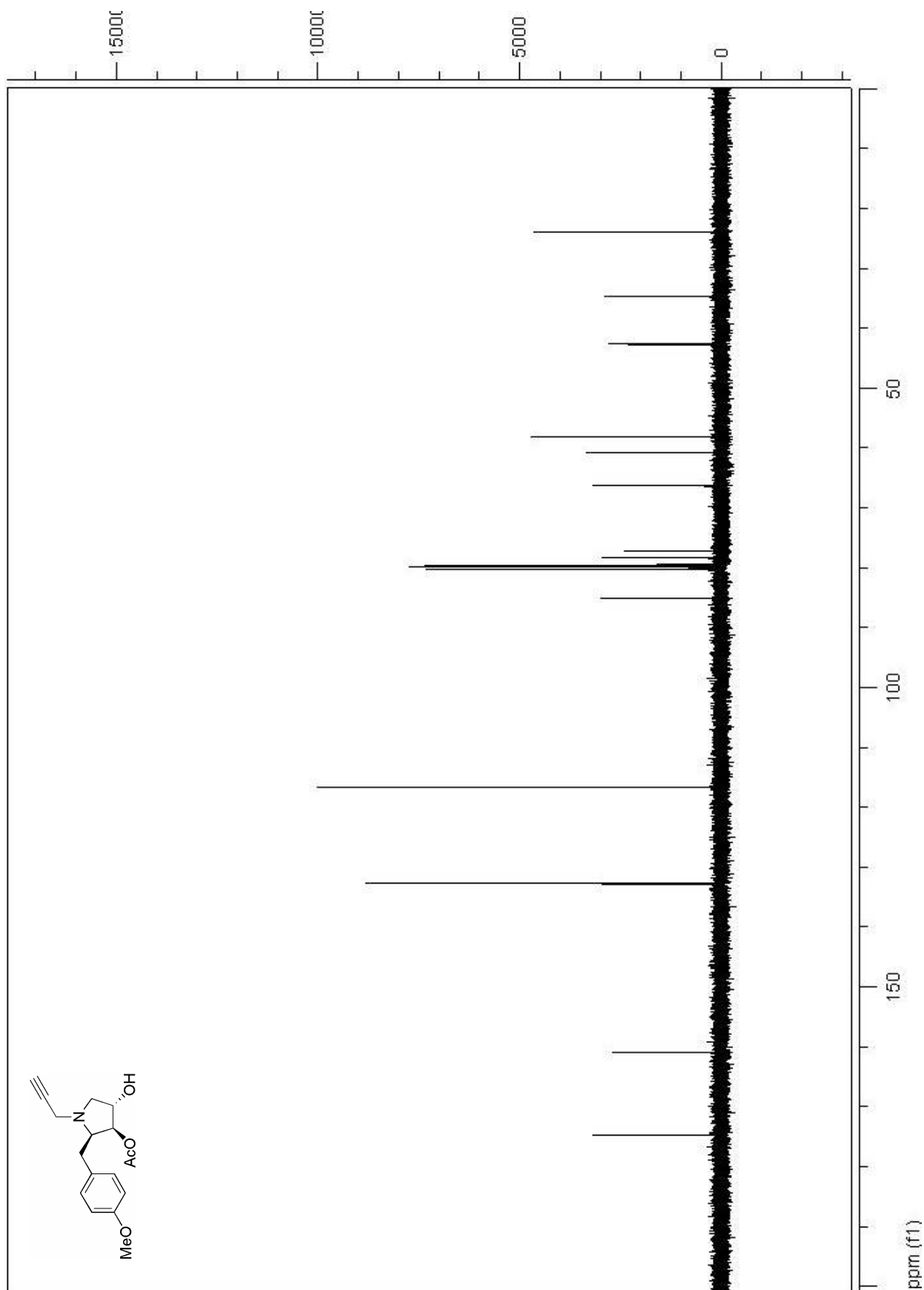
(2*R*,3*S*,4*S*)-3-Acetoxy-1-benzyl-4-hydroxy-2-(4'-methoxybenzyl)-pyrrolidine 1c



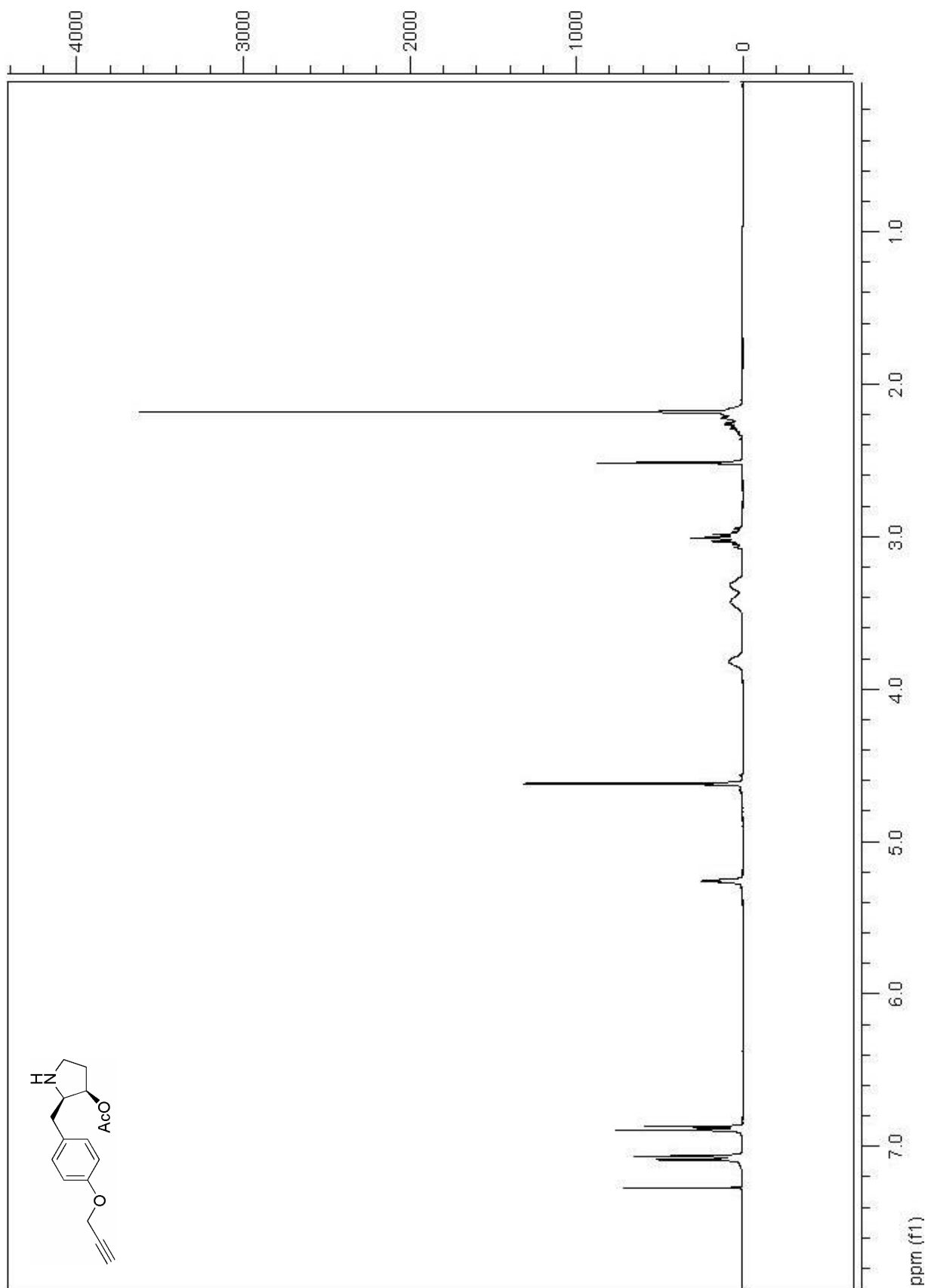
(2*R*,3*S*,4*S*)-3-Acetoxy-4-hydroxy-2-(4'-methoxybenzyl)-1-propargylpyrrolidine 1d



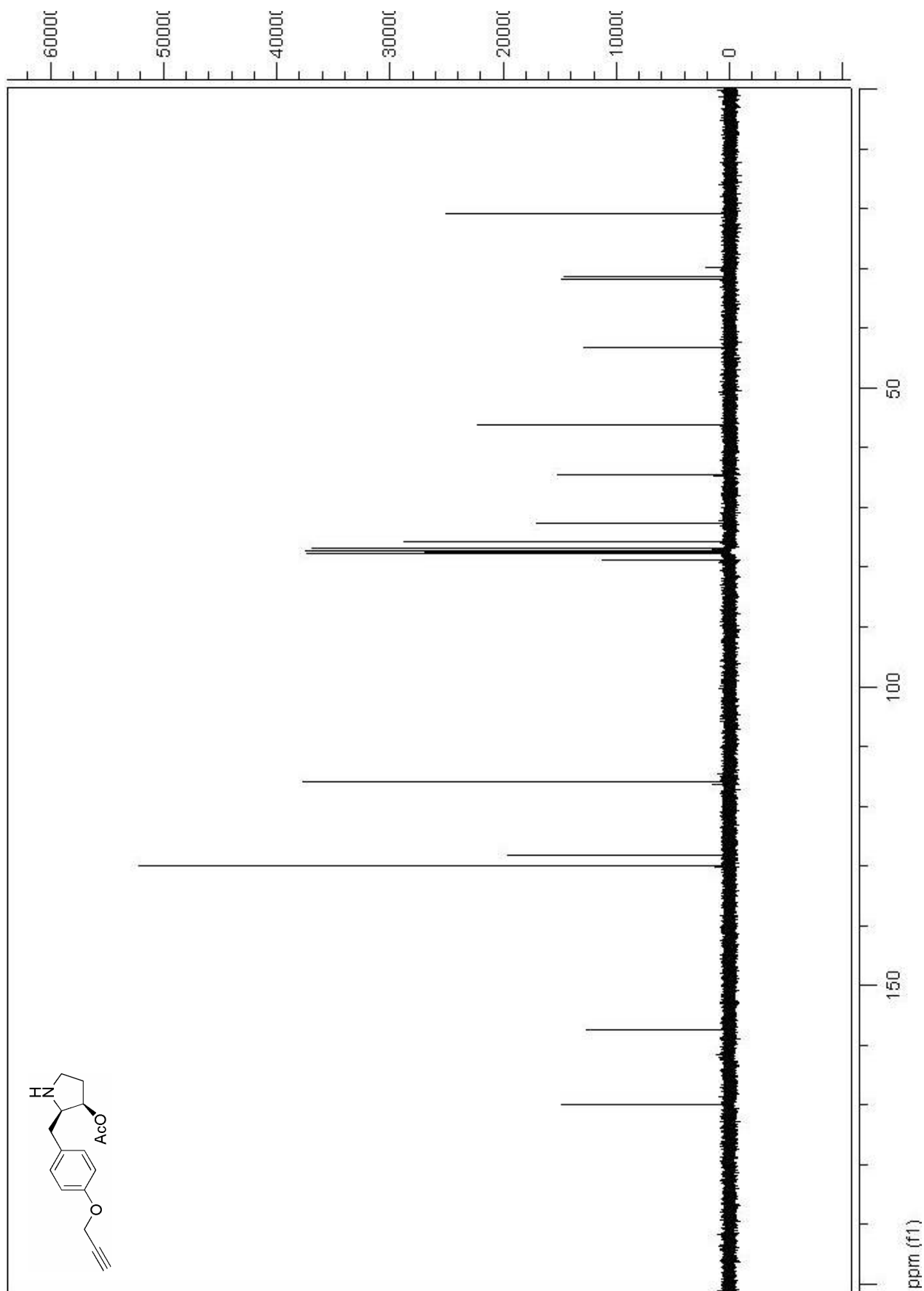
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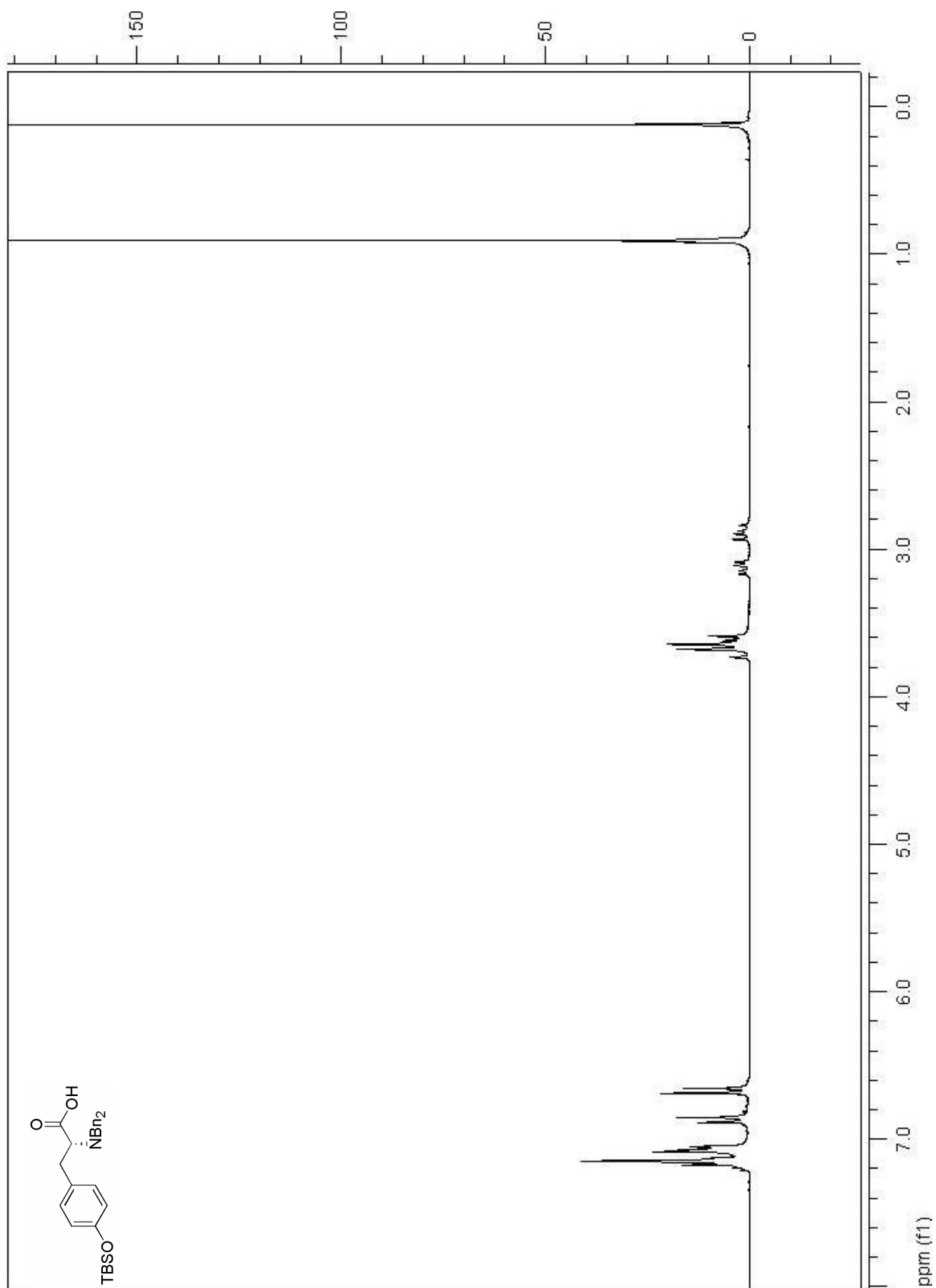
**(2*R*,3*R*)- 3-Acetoxy-2-(4'-propargyloxybenzyl)-pyrrolidine 2b**



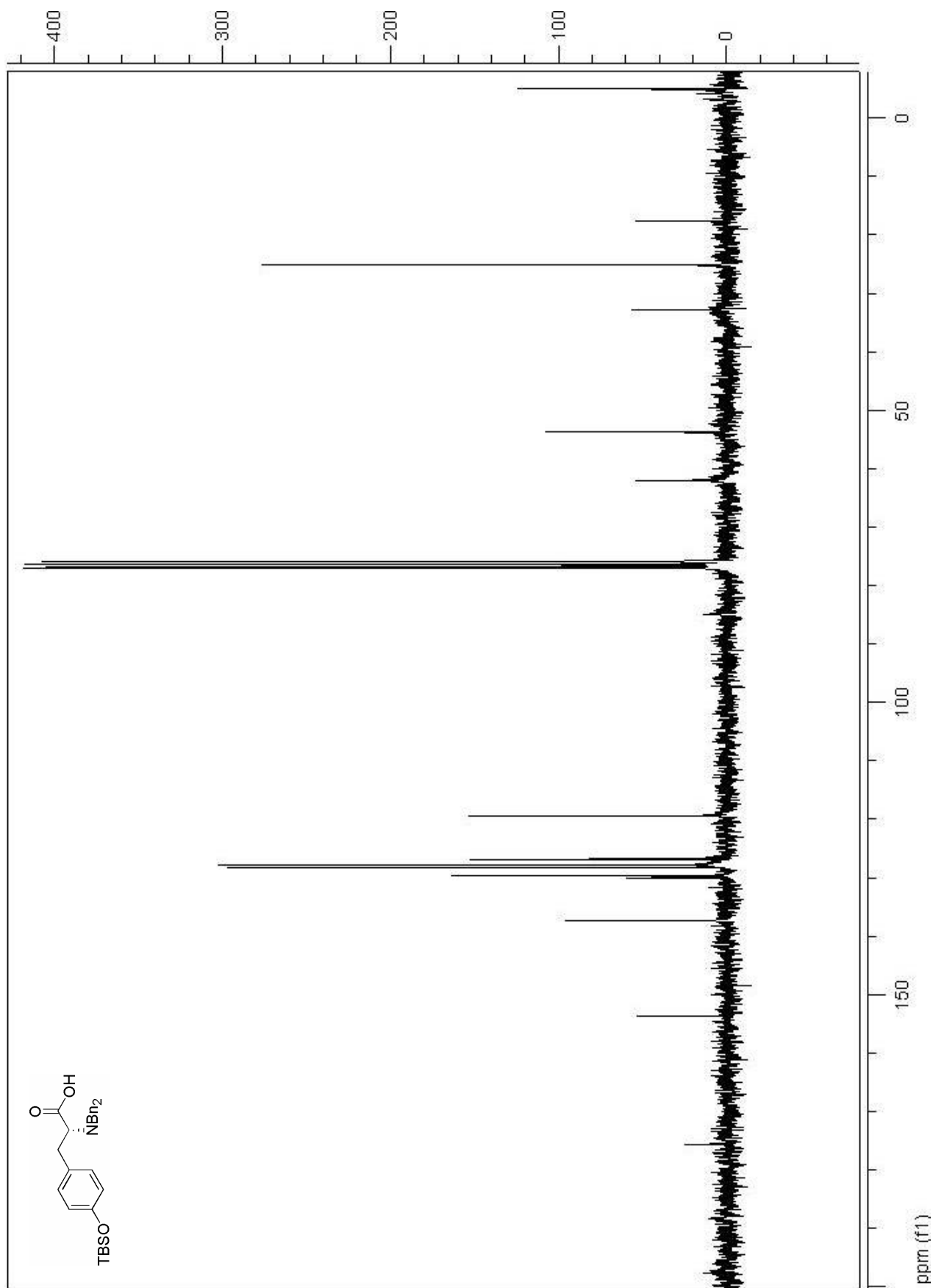
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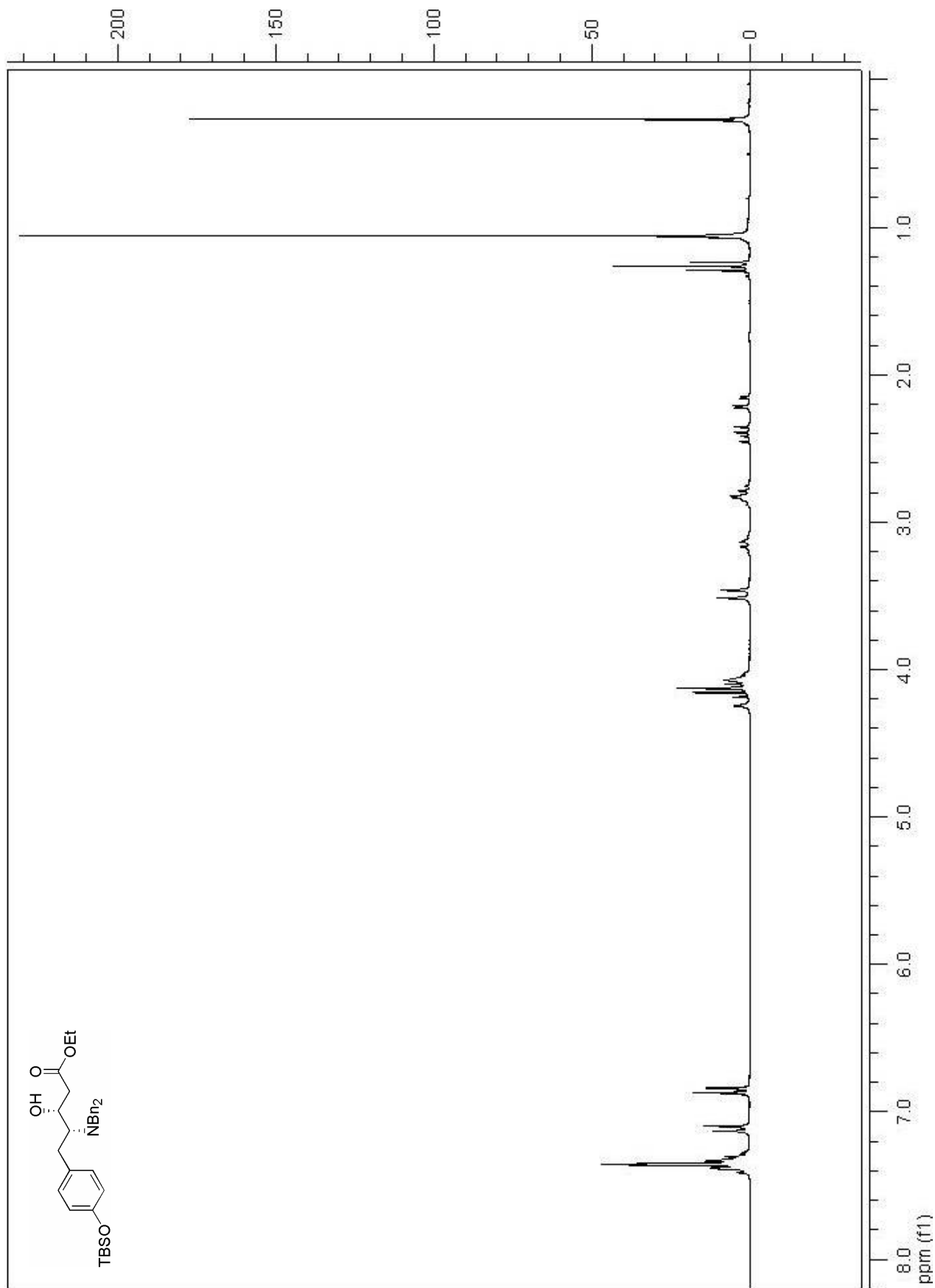


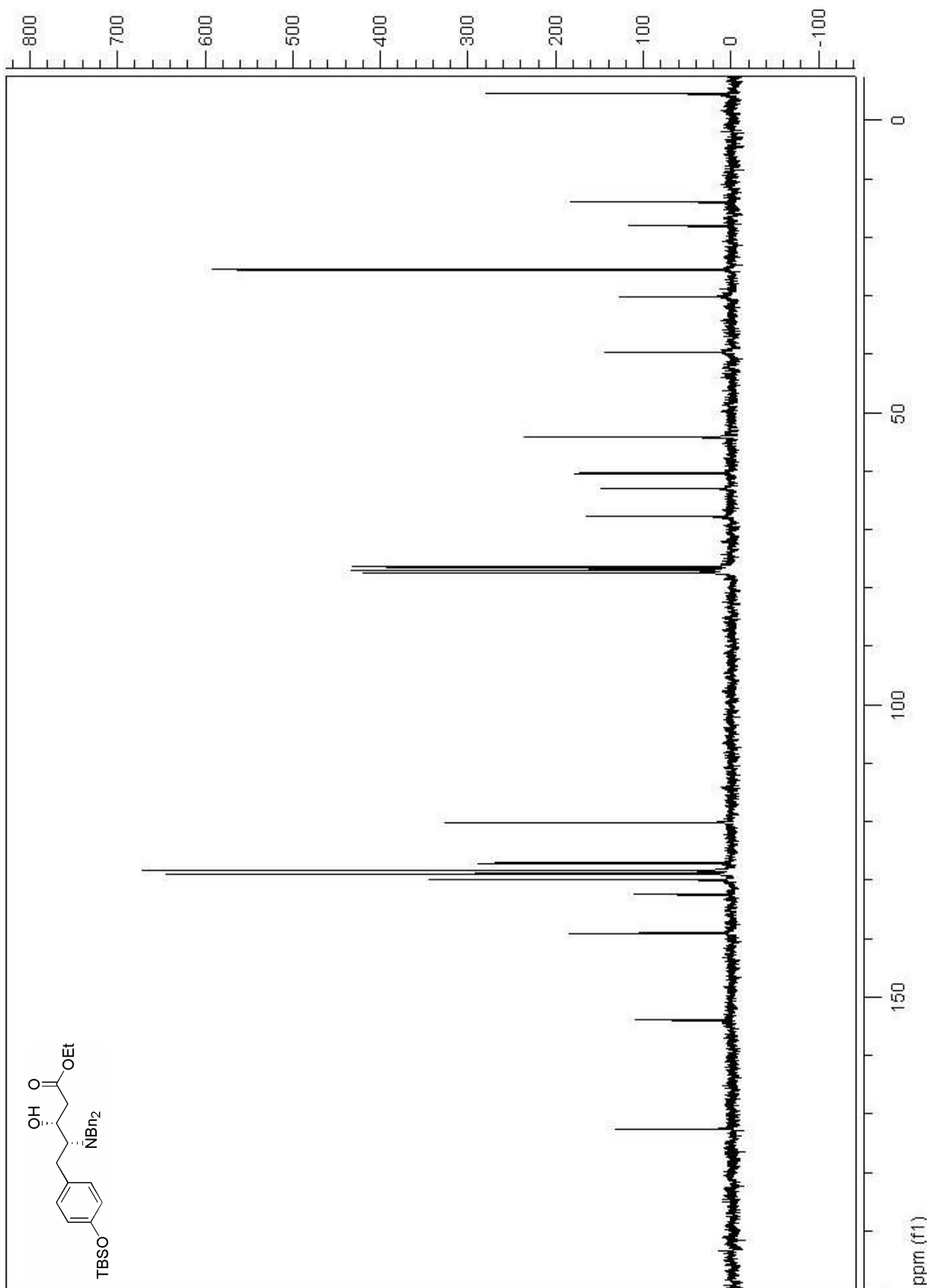
(2R)-3-(4'-*tert*-Butyldimethylsilyloxyphenyl)-2-dibenzylamino-propanoic acid 4

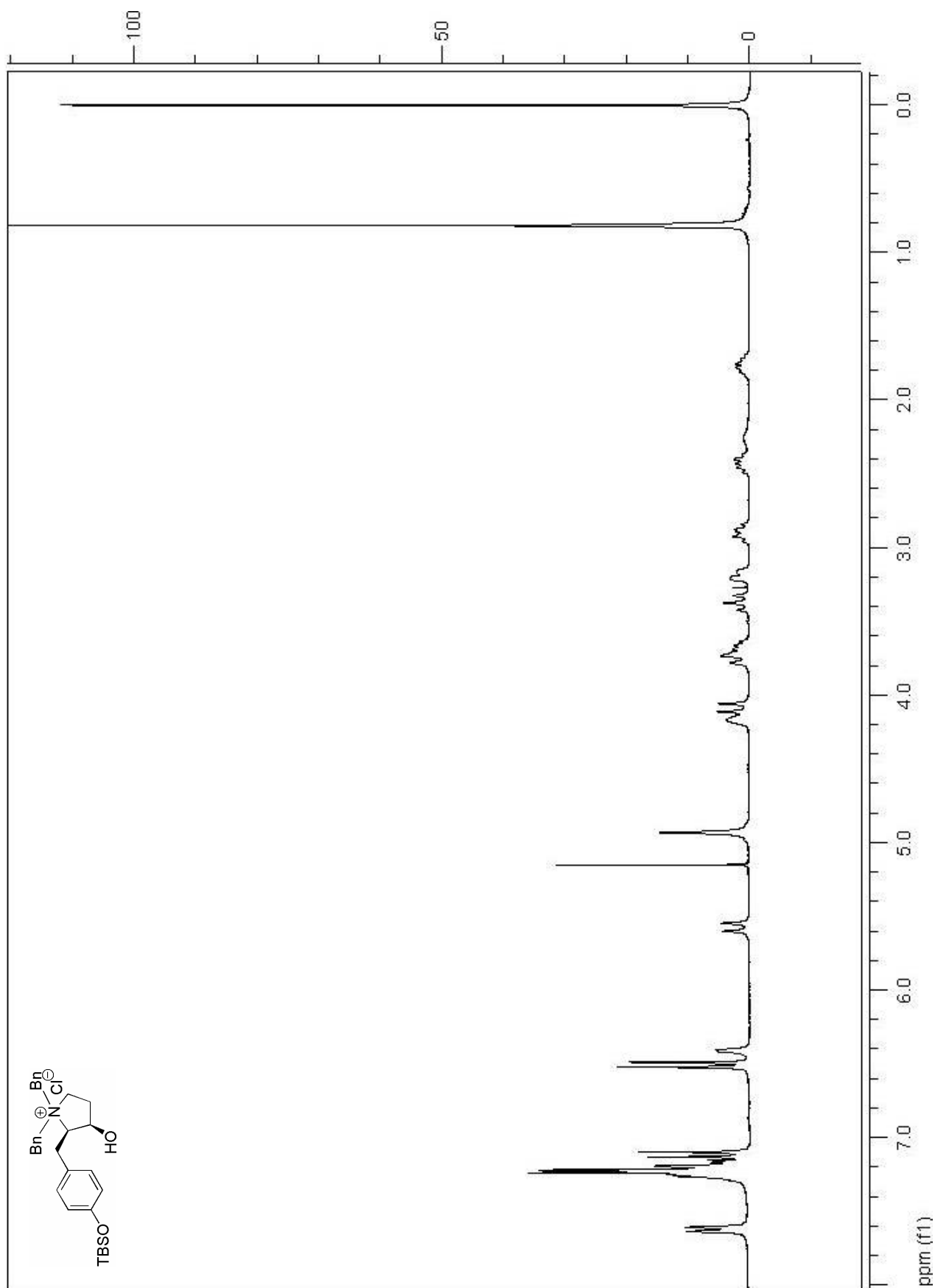


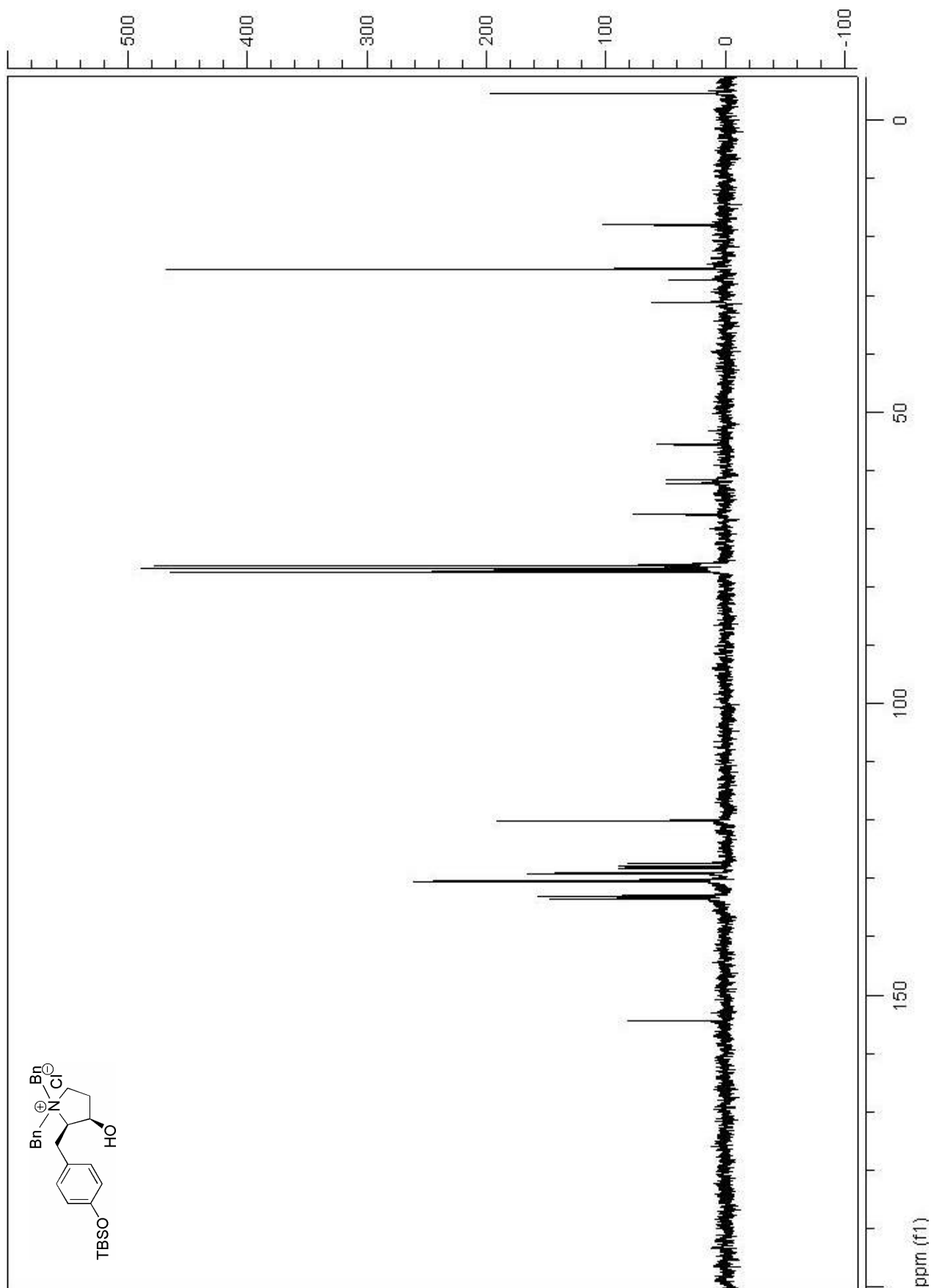
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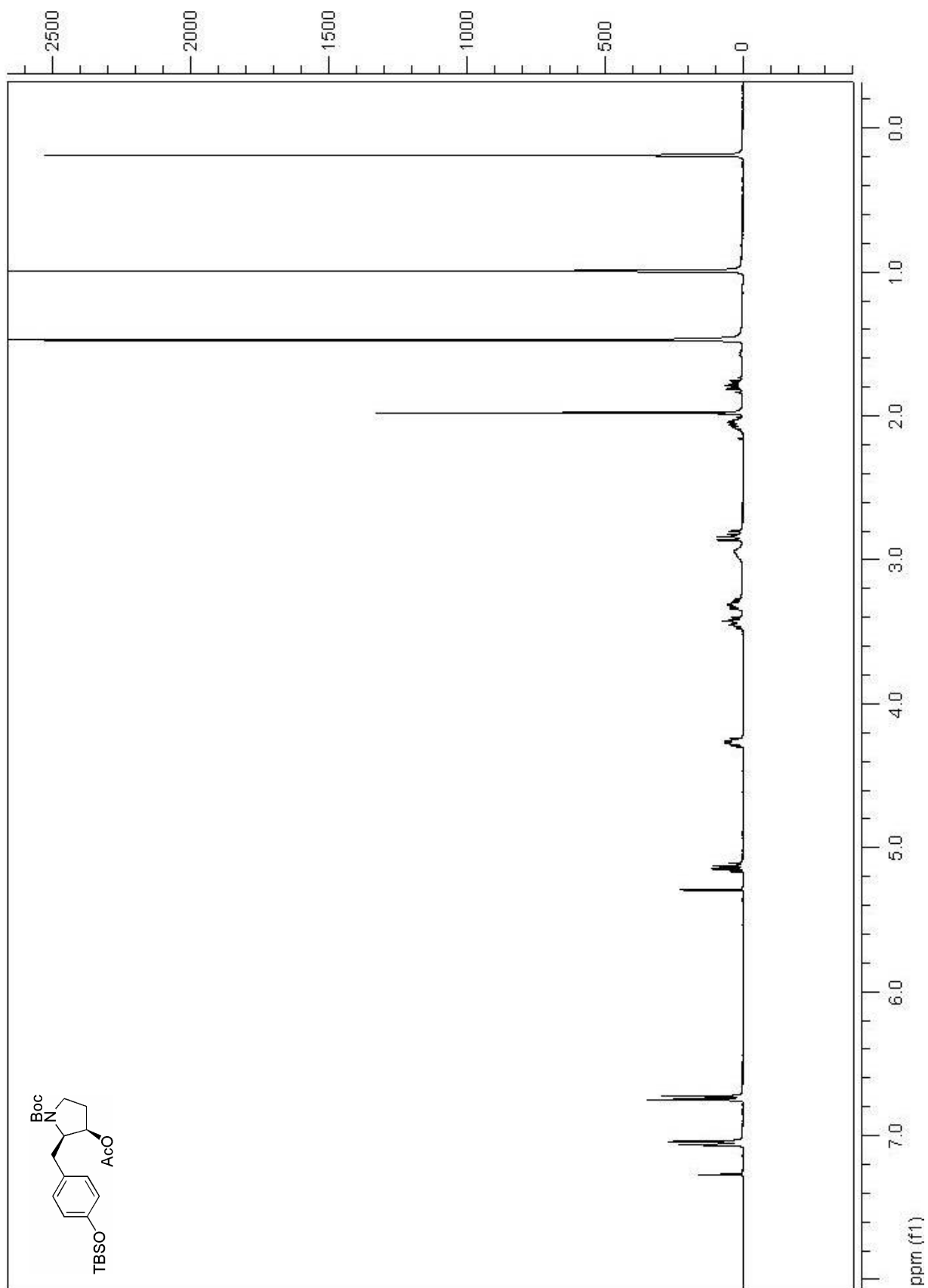




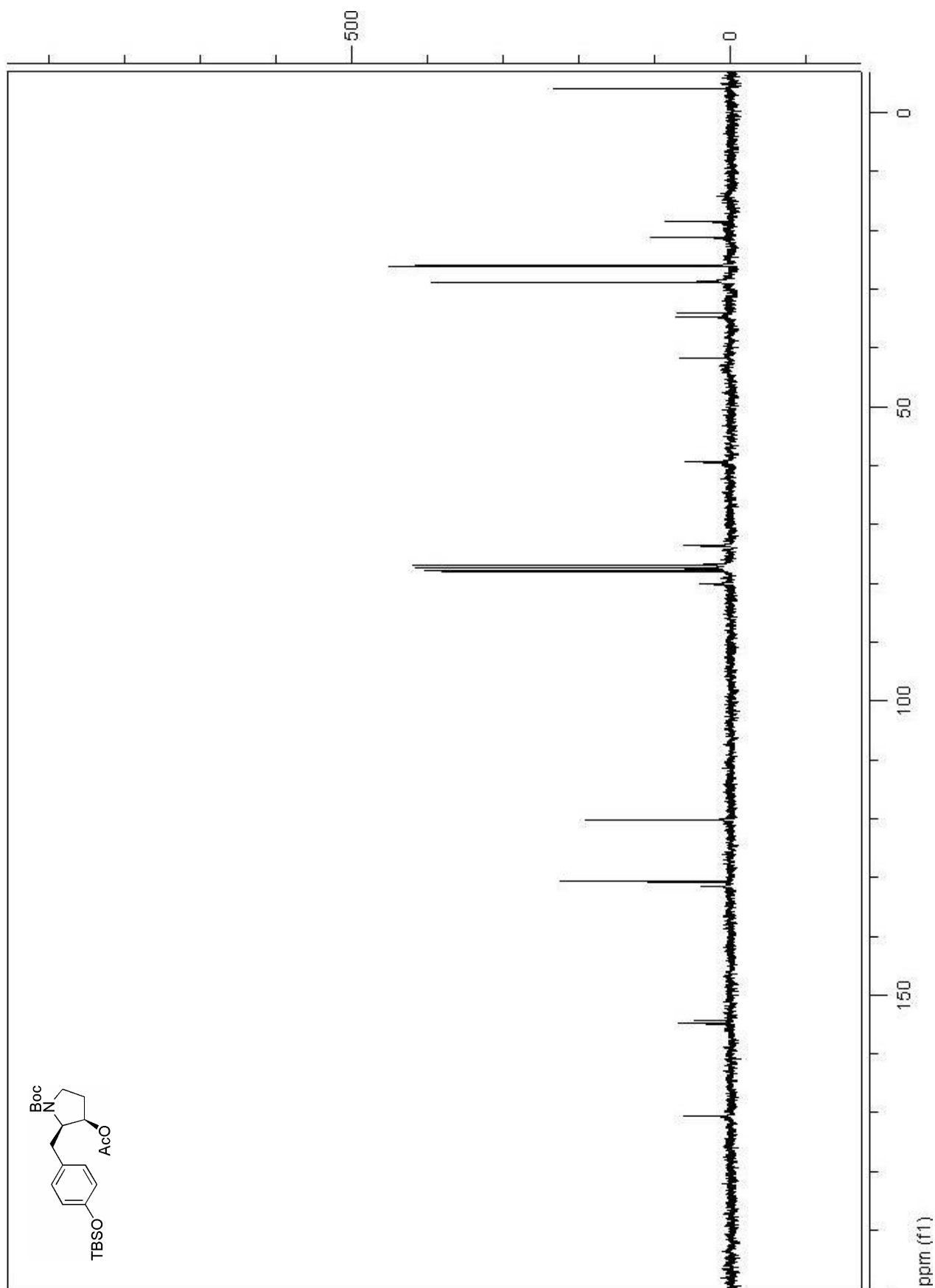




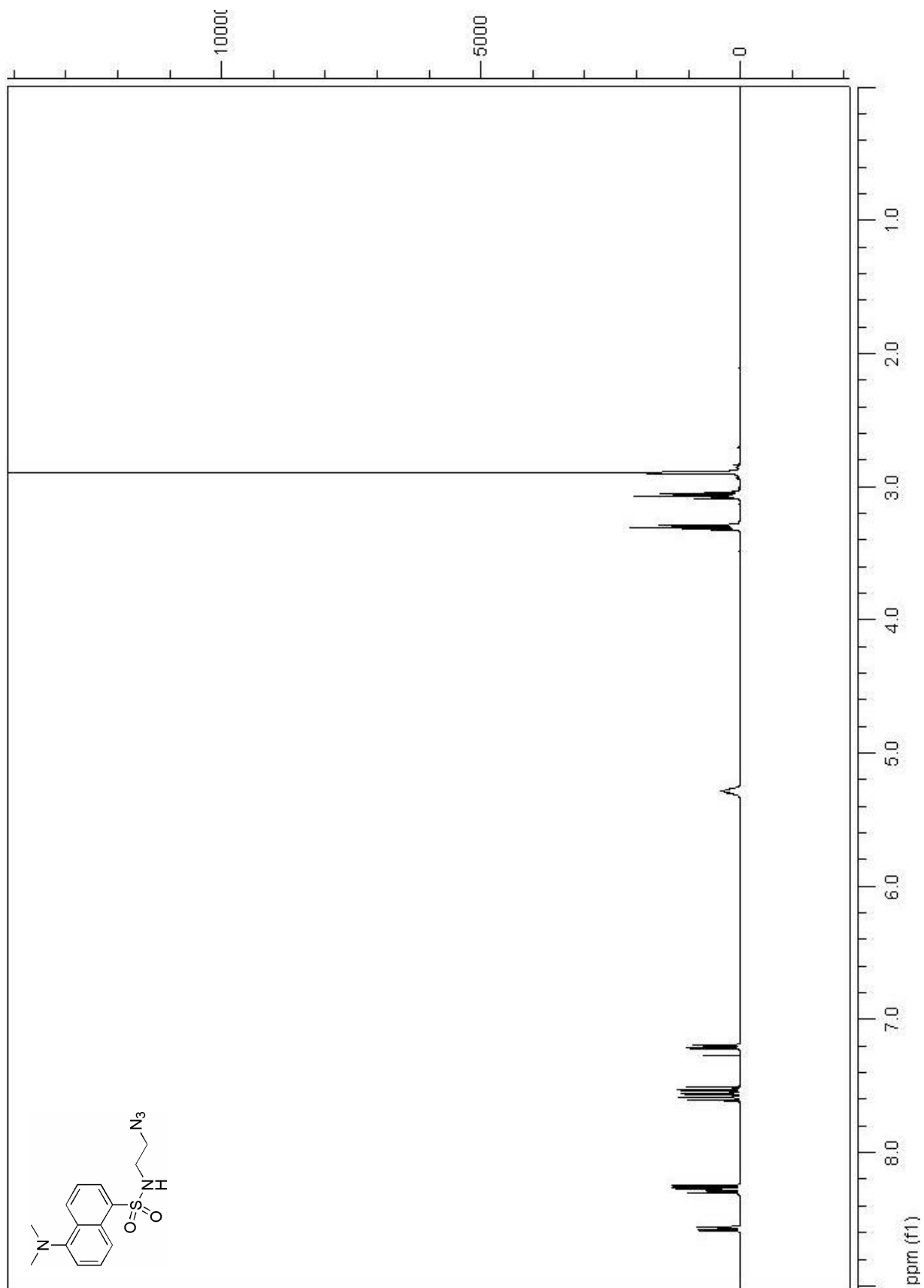
(2*R*,3*R*)-3-Acetoxy-1-*tert*-butoxycarbonylamino-2-(4'-*tert*-butyldimethylsilyloxybenzyl)-pyrrolidine 7



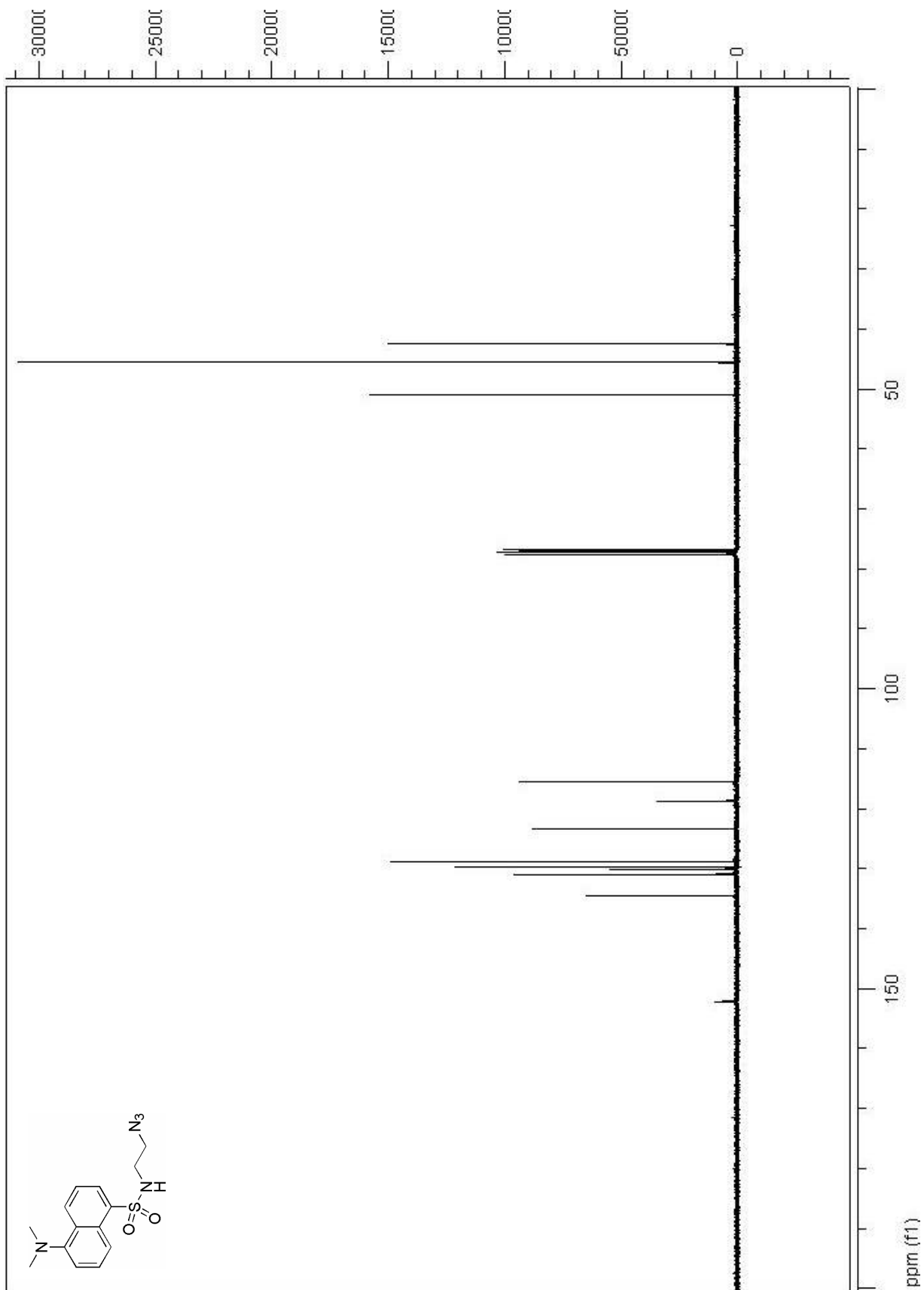
(2R,3R)-3-Acetoxy-1-tert-butoxycarbonylamino-2-(4'-tert-butyldimethylsilyloxybenzyl)-pyrrolidine 7



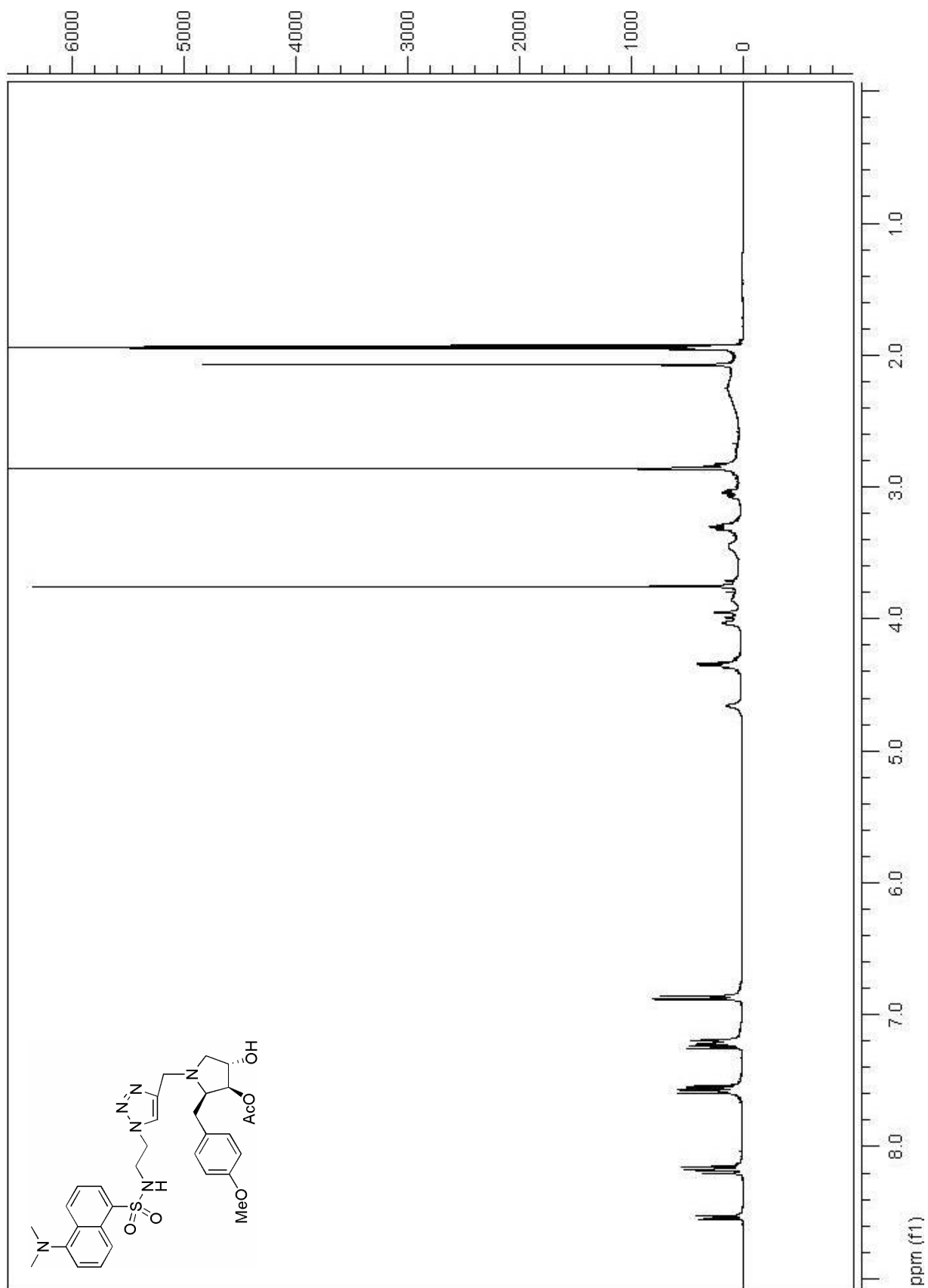
2-azido-1-*N*-dansylethylamine 8



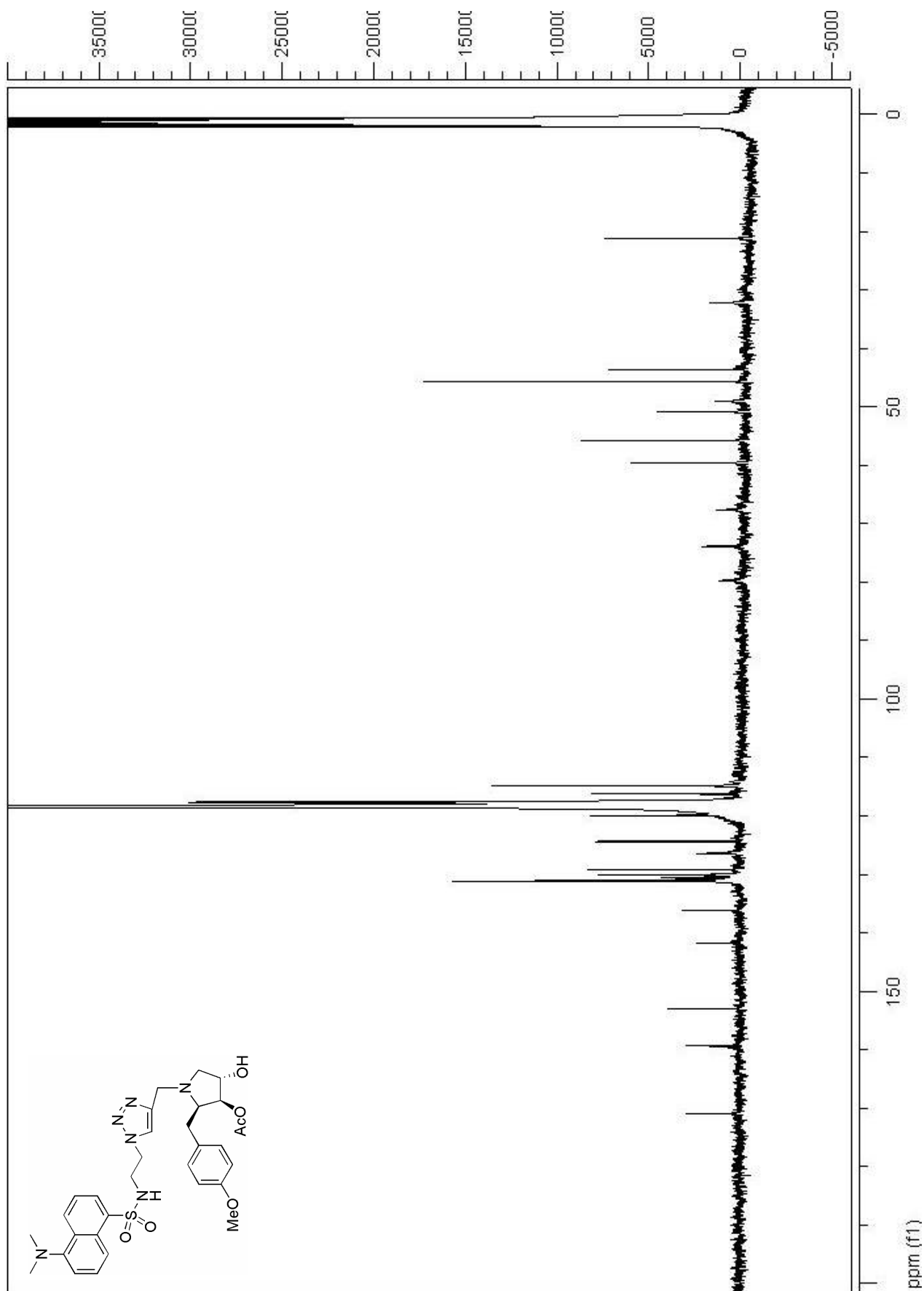
2-azido-1-N-dansylethylamine 8



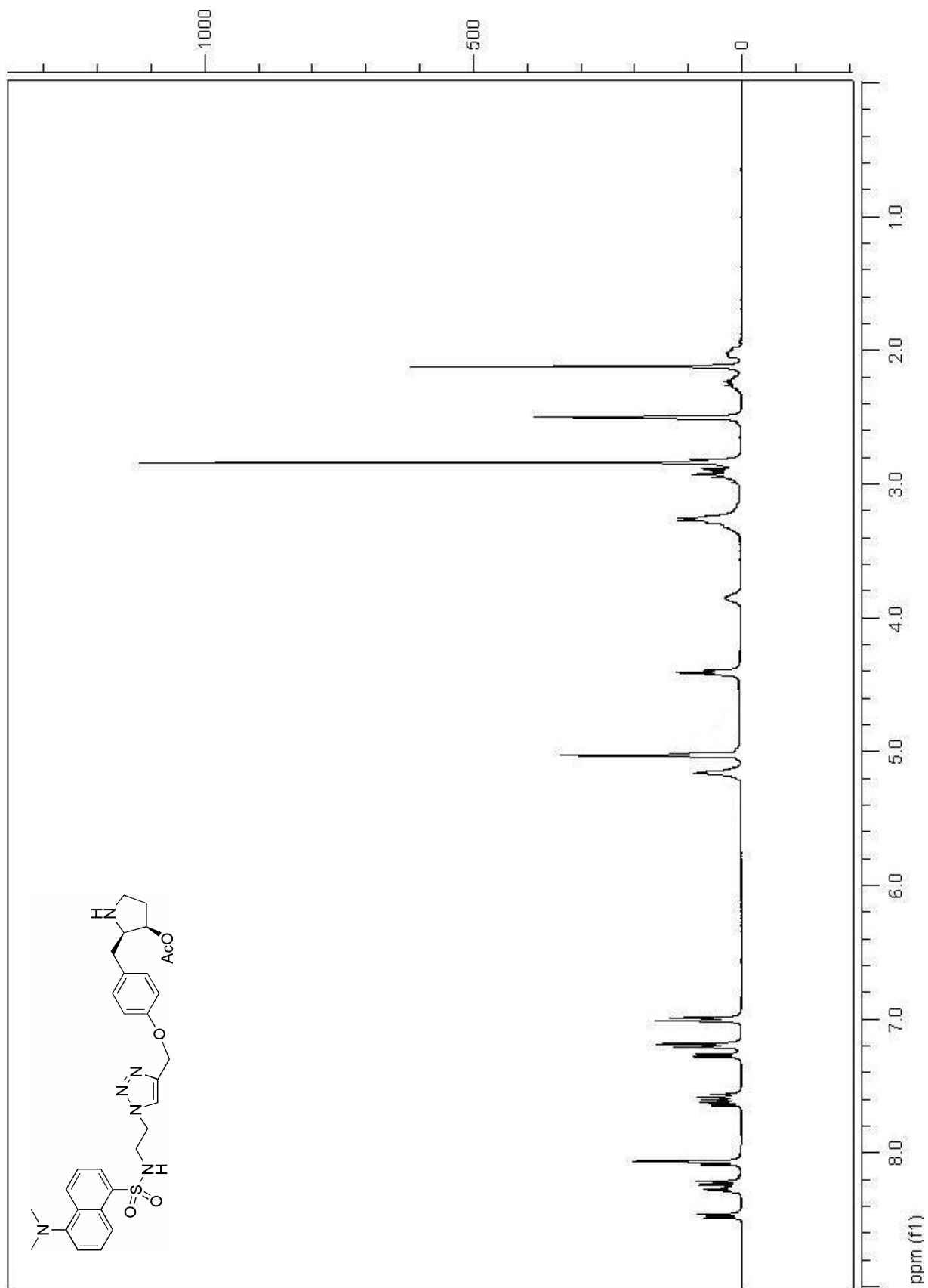
N-Linked dansyl molecular probe 9



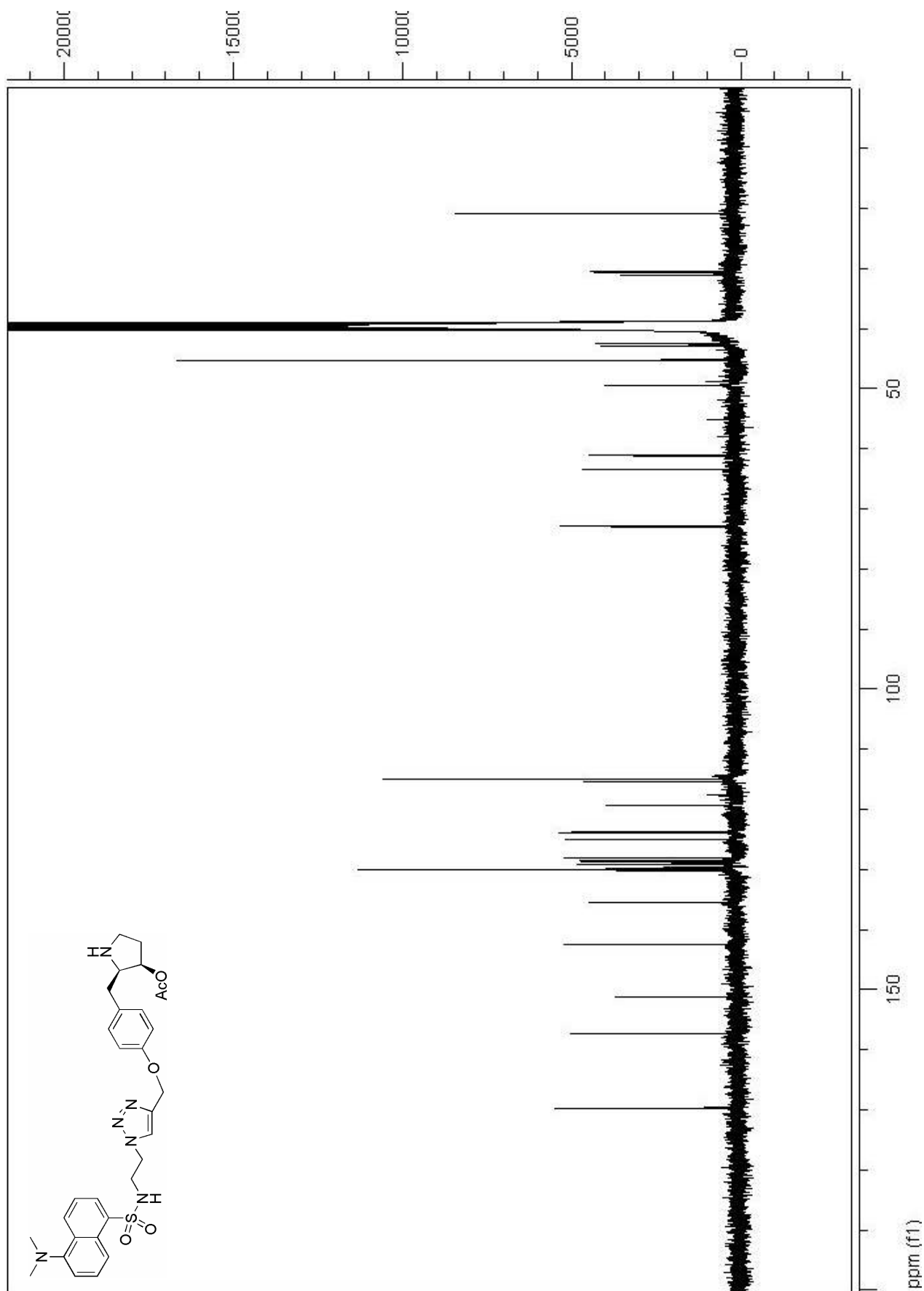
N-Linked dansyl molecular probe 9



O-Linked dansyl molecular probe 10



O-Linked dansyl molecular probe 10



O-Linked dansyl molecular probe 10

