

## Experimental Section

**Z-Ala-Oxime Resin (2a).**<sup>1</sup> A mixture of oxime resin (5.26 g, 0.76 mmol/g, 4.0 mmol), Z-Ala-OH (1.79 g, 8.0 mmol) and HBTU (3.03 g, 8.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (60 mL) was placed in a peptide synthesis apparatus. DIPEA (2.07 g, 16.0 mmol) was added to the mixture, which was then bubbled with N<sub>2</sub> at room temperature for 16 h. The solution was drained and the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3 and dried in vacuo. The unreacted oxime groups were capped by reaction with pivaloyl chloride (2.41 g, 20 mmol) and DIPEA (2.59 g, 20 mmol) in DMF (60 mL) at room temperature for 2 h. The solution was drained and the resin was washed with DMF x 4, MeOH x 4, CH<sub>2</sub>Cl<sub>2</sub> x 3 and dried in vacuo to obtain **2a** (6.04 g, 0.66 mmol/g).

**Boc-Leu-Ala-Oxime Resin (2b).**<sup>1</sup> A mixture of oxime resin (5.26 g, 0.76 mmol/g, 4.0 mmol), Boc-Ala-OH (1.51 g, 8.0 mmol), DMAP (0.98 g, 8.0 mmol) and DIC (1.25 mL, 8.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (80 mL) was placed in a peptide synthesis apparatus and was bubbled with N<sub>2</sub> at room temperature for 11 h. After the solution was drained, the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3, DMF x 3. The unreacted oxime groups were capped by reaction with pivaloyl chloride (2.46 mL, 20 mmol) and DIPEA (3.48 mL, 20 mmol) in DMF (30 mL) at room temperature for 2 h. After the solution was drained, the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3. The Boc-Ala-Oxime resin was then deprotected with 25% TFA in CH<sub>2</sub>Cl<sub>2</sub> (60 mL) for 40 min. After the solution was drained, the resin was washed with CH<sub>2</sub>Cl<sub>2</sub> x 3, MeOH x 3, DMF x 3. The resin was coupled to Z-Leu-OH•H<sub>2</sub>O (1.99 g, 8.0 mmol) with HBTU (3.03 g, 8.0 mmol), HOBut•H<sub>2</sub>O (1.22 g, 8.0 mmol) and DIPEA (4.18 mL, 24.0 mmol) in DMF (30 mL) for 2 h. After the solution was drained, the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3 and then dried in vacuo (6.46 g of **2b**, 0.62 mmol/g).

**Z-Leu-Ala-Oxime Resin (2c).**<sup>1</sup> A similar manner as **2b** was used from oxime resin (5.26 g, 0.76 mmol/g, 4.0 mmol) to prepare **2c** (6.46 g of the titled resin, 0.62 mmol/g).

**Boc-Tyr(OBu<sup>t</sup>)-Gly-Gly-Phe-Oxime Resin (2d).**<sup>1</sup> This resin was prepared in a similar manner as **2b** using Boc-Phe-OH, Boc-Gly-Gly-OH and Boc-Tyr(Bu<sup>t</sup>)-OH in order to avoid diketopiperazine formation at the dipeptide stage. A mixture of oxime resin (2.63 g, 0.76 mmol/g, 2.0 mmol), Boc-Phe-OH (2.12 g, 8.0 mmol), DMAP (25 mg, 0.20 mmol) and DIC (1.25 mL, 8.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (30 mL) was placed in a peptide synthesis apparatus and was bubbled with N<sub>2</sub> at room temperature for 62 h. After the solution was drained, the resin was washed with CH<sub>2</sub>Cl<sub>2</sub> x 4, DMF x 4. The unreacted oxime groups were capped by reaction with acetic anhydride (1.89 mL, 20 mmol) and DIPEA (3.48 mL, 20 mmol) in DMF (30 mL) at room temperature for 2 h. After the solution was drained,

the resin was washed with DMF x 4, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3. The Boc group was then deprotected with 50% TFA in CH<sub>2</sub>Cl<sub>2</sub> (30 mL) for 1 h. After the solution was drained, the resin was washed with CH<sub>2</sub>Cl<sub>2</sub> x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3. The resin was added a solution of Boc-Gly-Gly-OH (928 mg, 4.0 mmol), HBTU (1.52 g, 4.0 mmol), HOBr•H<sub>2</sub>O (612 mg, 4.0 mmol) and DIPEA (2.09 mL, 12 mmol) in DMF (30 mL) for 19 h. After the solution was drained, the resin was washed with DMF x 4, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3. The Boc group was then deprotected with 50% TFA in CH<sub>2</sub>Cl<sub>2</sub> (30 mL) for 1 h. After the solution was drained, the resin was washed with CH<sub>2</sub>Cl<sub>2</sub> x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3. The resin was added a solution of Boc-Tyr(OBu<sup>t</sup>)-OH (1.35 g, 4.0 mmol), HBTU (1.52 g, 4.0 mmol), HOBr•H<sub>2</sub>O (612 mg, 4.0 mmol) and DIPEA (2.09 mL, 12 mmol) in DMF (30 mL) for 20 h. After the solution was drained, the resin was washed with DMF x 4, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3 and then dried in vacuo (3.69 g, 0.54 mmol/g).

**Boc-Tyr(OBu<sup>t</sup>)-Gly-Gly-D-Phe-Oxime Resin (D-2d).**<sup>1</sup> The titled resin was prepared in a similar manner as the L-Phe isomer (3.68 g, 0.54 mmol/g).

**H-Phe-Wang Resin (5a).**<sup>2</sup> Fmoc-Phe-Wang resin (4.97 g, 0.51 mmol/g, 2.53 mmol) was placed in a peptide synthesis apparatus. To the resin was added 20% piperidine in DMF (50 mL) and N<sub>2</sub> was bubbled for 45 min. After the solution was drained, the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3 and dried in vacuo to obtain **5a** (4.35 g, 0.58 mmol/g).

**H-Ala-Phe-Wang Resin (5b).**<sup>2</sup> **5b** was prepared as described for the synthesis of L-**7ba** below.

**H-Val-Phe-Wang Resin (5c).**<sup>2</sup> **5c** was prepared in a similar manner as **5b**.

**H-Leu-Wang Resin (5d).**<sup>2</sup> Fmoc-Leu-Wang resin (2.50 g, 0.40 mmol/g, 1.0 mmol) was placed in a peptide synthesis apparatus. To the resin was added 20% piperidine in DMF (30 mL) and N<sub>2</sub> was bubbled for 15 min. After the solution was drained, the resin was washed with DMF x 3, MeOH x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3 and dried in vacuo (2.26 g, 0.44 mmol/g).

**H-Met-Wang Resin (5e).**<sup>2</sup> The titled resin was prepared in a similar manner as H-Leu-Wang resin (1.14 g, 0.88 mmol/g).

**H-Leu-Ala-Phe-OH (L-7ba).**<sup>2</sup> Fmoc-Phe-Wang resin (2.45 g, 0.51 mmol/g, 1.25 mmol) and 20% piperidine in DMF (20 mL) were placed in a bench-top peptide synthesis apparatus and N<sub>2</sub> was bubbled at room temperature for 20 min. The solution was drained and the resin was washed with DMF x 3, i-PrOH x 3, DMF x 3. A solution of Fmoc-Ala-OH (778 mg, 2.5 mmol, 2.0 eq.), HBTU (948 mg, 2.5 mmol, 2.0 eq.), HOBr•H<sub>2</sub>O (383 mg, 2.5 mmol, 2.0 eq.) in DMF (10 mL) was added to the resin. DIPEA (0.87 mL, 5.0 mmol, 4.0 eq.) was added to the mixture, which was then bubbled with N<sub>2</sub> at room

temperature for 1 h. The solution was drained and washed with DMF x 3. 20% piperidine in DMF (20 mL) was added to the resin and N<sub>2</sub> was bubbled at room temperature for 10 min. The solution was drained and the resin was washed with DMF x 3, i-PrOH x 3, DMF x 3. A solution of Boc-Leu-OH (578 mg, 2.5 mmol, 2.0 eq.), HBTU (948 mg, 2.5 mmol, 2.0 eq.), HOBr•H<sub>2</sub>O (383 mg, 2.5 mmol, 2.0 eq.) in DMF (8 mL) was added to the resin. DIPEA (0.87 mL, 5.0 mmol, 4.0 eq.) was added to the mixture, which was then bubbled with N<sub>2</sub> at room temperature for 2 h. The solution was drained and washed with DMF x 3, CH<sub>2</sub>Cl<sub>2</sub> x 3, MeOH x 3. The resulting resin was treated with 50% TFA in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) at room temperature for 1 h. The solution was collected and the resin was washed with CH<sub>2</sub>Cl<sub>2</sub> x 3. All filtrates were combined and evaporated to give the crude product as a yellow syrup. The crude product was triturated from Et<sub>2</sub>O and an ivory gel appeared. The gel was collected on a Buchner funnel and dried in vacuo to obtain the tripeptide as an ivory powder (393 mg, 90%): HPLC retention time (0% B → 40% B in 30 min), 19.0 min; mp 185 - 187 °C; <sup>1</sup>H NMR (250 MHz, DMSO-d<sub>6</sub>) δ 8.64 (d, J = 7.7 Hz, 1H, NH), 8.39 (d, J = 7.8 Hz, 1H, NH), 8.12 (br, 2H, NH<sub>2</sub>), 7.24 (m, 5H, Ph), 4.40 (m, 2H, 2 x NHCH), 3.77 (m, 1H, NH<sub>2</sub>CH), 3.07 (dd, J = 13.8, 4.9 Hz, 1H, CHCHHPh), 2.99 (dd, J = 13.8, 9.0 Hz, 1H, CHCHHPh), 1.62 (m, 1H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.48 (m, 2H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.22 (d, J = 7.0 Hz, 3H, Ala-CH<sub>3</sub>), 0.86 (t, J = 5.8 Hz, 6H, Leu-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, DMSO-d<sub>6</sub>) δ 172.6, 171.5, 168.3, 158.1, 157.9, 137.4, 129.0, 128.1, 126.3, 53.3, 50.6, 48.0, 36.5, 23.3, 22.6, 21.8, 18.3; HRMS m/e calcd for C<sub>18</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub> (M + H<sup>+</sup>) 350.2080, found 350.2061.

**H-Leu-D-Ala-Phe-OH (D-7ba).**<sup>2</sup> The titled tripeptide was synthesized in 96% yield by standard Fmoc peptide chemistry starting from commercially available Fmoc-Phe-Wang resin in a similar manner as L-7ab: HPLC retention time (0% B → 40% B in 30 min), 21.8 min; mp 70 - 73 °C; <sup>1</sup>H NMR (250 MHz, DMSO-d<sub>6</sub>) δ 8.72 (d, J = 7.8 Hz, 1H, NH), 8.50 (d, J = 8.5 Hz, 1H, NH), 8.13 (br, 2H, NH<sub>2</sub>), 7.25 (m, 5H, Ph), 4.46 (m, 2H, 2 x NHCH), 3.81 (br, 1H, NH<sub>2</sub>CH), 3.11 (dd, J = 13.8, 4.9 Hz, 1H, CHCHHPh), 2.85 (dd, J = 13.8, 3.3 Hz, 1H, CHCHHPh), 1.57 (m, 3H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 0.96 (d, J = 7.0 Hz, 3H, Ala-CH<sub>3</sub>), 0.86 (m, , 6H, Leu-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, DMSO-d<sub>6</sub>) δ 127.8, 171.3, 168.3, 137.4, 129.1, 128.0, 126.3, 53.1, 50.6, 47.9, 37.0, 23.5, 22.5, 22.1, 18.8; HRMS m/e calcd for C<sub>18</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub> (M + H<sup>+</sup>) 350.2080, found 350.2076.

**Z-Ala-Ala-Phe-OH (7ab).** A pale yellow powder (90%): HPLC retention time (0% B → 100% B in 60 min), 27.9 min; mp 159 - 162 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 8.02 (d, J = 7.8 Hz, 1H, NH), 7.87 (d, J = 7.6 Hz, 1H, NH), 7.4 - 7.1 (m, 11H, 2 x Ph, OCONH), 5.01 (s, 2H, OCH<sub>2</sub>Ph), 4.41 (m, 1H, NHCH), 4.28 (quintet, J = 7.2 Hz, 1H, Ala-Ala-NHCH), 4.04 (quintet, J = 7.2 Hz, 1H, Z-Ala-NHCH), 3.05 (dd, J = 14.0, 4.0

Hz, 1H, CHCHHPh), 2.90 (dd,  $J = 13.9, 8.5$  Hz, 1H, CHCHHPh), 1.17 (m, 6H, 2 x Ala- $CH_3$ );  $^{13}C$  NMR (125 MHz, DMSO-d<sub>6</sub>)  $\delta$  172.6, 172.0, 171.9, 155.6, 137.3, 137.0, 129.1, 128.3, 128.1, 127.7, 127.6, 126.3, 65.3, 53.4, 49.8, 47.8, 36.6, 25.2, 18.2, 18.0; HRMS m/e calcd for C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>6</sub>Na (M + Na<sup>+</sup>) 464.1798, found 464.1781.

**Z-Ala-Val-Phe-OH (7ac).** A pale yellow powder (75%): HPLC retention time (0% B ---> 100% B in 60 min), 30.7 min; mp 199 - 200 °C;  $^1H$  NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  12.56 (br, 1H, COOH), 8.20 (d,  $J = 7.7$  Hz, 1H, NH), 7.57 (d,  $J = 9.0$  Hz, 1H, NH), 7.46 (d,  $J = 7.7$  Hz, 1H, OCONH), 7.4 - 7.1 (m, 10H, 2 x Ph), 5.01 (s, 2H, OCH<sub>2</sub>Ph), 4.44 (m, 1H, Phe-NHCH), 4.19 (m, 1H, Ala-NHCH), 4.09 (t,  $J = 7.3$  Hz, 1H, Val-NHCH), 3.05 (dd,  $J = 14.0, 5.3$  Hz, 1H, CHCHHPh), 2.89 (dd,  $J = 14.0, 9.0$  Hz, 1H, CHCHHPh), 1.92 (m, 1H, Val-CH(CH<sub>3</sub>)<sub>2</sub>), 1.15 (d,  $J = 7.1$  Hz, 3H, Ala-CH<sub>3</sub>), 0.79 (m, 6H, Val-CH<sub>3</sub>);  $^{13}C$  NMR (125 MHz, DMSO-d<sub>6</sub>)  $\delta$  172.7, 172.1, 170.7, 137.4, 137.0, 129.0, 128.3, 128.1, 127.7, 127.6, 126.3, 65.3, 57.0, 53.2, 50.0, 36.6, 30.9, 19.0, 17.8; HRMS m/e calcd for C<sub>25</sub>H<sub>32</sub>N<sub>3</sub>O<sub>6</sub> (M + H<sup>+</sup>) 470.2291, found 4670.2310.

**H-Leu-Ala-Ala-Phe-OH (7bb).** A pale brown powder (70%): HPLC retention time (0% B ---> 100% B in 60 min), 18.6 min; mp 190 - 193 °C;  $^1H$  NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.59 (d,  $J = 7.5$  Hz, 1H, NH), 8.05 (d,  $J = 7.8$  Hz, 1H, NH), 7.99 (d,  $J = 7.5$  Hz, 1H, NH), 7.23 (m, 5H, Ph), 4.39 (m, 2H, 2 x NHCH), 4.28 (quintet,  $J = 7.2$  Hz, 1H, Ala-NHCH), 3.76 (t,  $J = 7.0$  Hz, 1H, Leu-NHCH), 3.05 (dd,  $J = 13.9, 5.2$  Hz, 1H, CHCHHPh), 2.90 (dd,  $J = 13.8, 8.5$  Hz, 1H, CHCHHPh), 1.64 (m, 1H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.52 (m, 2H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.20 (d,  $J = 7.1$  Hz, Ala-CH<sub>3</sub>), 1.17 (d,  $J = 7.1$  Hz, Ala-CH<sub>3</sub>), 0.89 (m, 6H, Leu-CH<sub>3</sub>);  $^{13}C$  NMR (125 MHz, DMSO-d<sub>6</sub>)  $\delta$  173.0, 172.3, 171.4, 168.8, 137.7, 129.5, 128.5, 126.8, 53.7, 51.0, 48.4, 48.3, 37.0, 23.8, 23.0, 22.3, 18.6, 18.5; HRMS m/e calcd for C<sub>21</sub>H<sub>33</sub>N<sub>4</sub>O<sub>5</sub> (M + H<sup>+</sup>) 421.2451, found 421.2452.

**H-Leu-Ala-Val-Phe-OH (7bc).** A pale brown powder (80%): HPLC retention time (0% B ---> 100% B in 60 min), 28.2 min; mp 287 - 290 °C;  $^1H$  NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  12.66 (br, 1H, COOH), 8.60 (d,  $J = 7.5$  Hz, 1H, NH), 8.19 (d,  $J = 7.8$  Hz, 1H, NH), 8.08 (br, 2H, NH<sub>2</sub>), 7.78 (d,  $J = 9.0$  Hz, 1H, NH), 7.3 - 7.1 (m, 5H, Ph), 4.45 (m, 2H, 2 x NHCH), 4.18 (dd,  $J = 8.9, 6.8$  Hz, 1H, Val-NHCH), 3.77 (t,  $J = 6.9$  Hz, 1H, Leu-NHCH), 3.06 (dd,  $J = 14.0, 5.2$  Hz, 1H, CHCHHPh), 2.89 (dd,  $J = 14.0, 9.1$  Hz, 1H, CHCHHPh), 1.93 (m, 1H, Val-CH(CH<sub>3</sub>)<sub>2</sub>), 1.63 (m, 1H, Leu-CH(CH<sub>3</sub>)<sub>2</sub>), 1.51 (m, 2H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.18 (d,  $J = 7.0$  Hz, 3H, Ala-CH<sub>3</sub>), 0.9 - 0.7 (m, 12H, Leu- and Val-CH<sub>3</sub>);  $^{13}C$  NMR (125 MHz, DMSO-d<sub>6</sub>)  $\delta$  172.7, 171.2, 170.6, 168.4, 137.4, 129.0, 128.0, 126.3, 64.8, 57.2, 53.2, 50.7, 48.1, 36.6, 30.8, 23.4, 22.5, 22.0, 19.0, 17.8; HRMS m/e calcd for C<sub>23</sub>H<sub>37</sub>N<sub>4</sub>O<sub>5</sub> (M + H<sup>+</sup>) 449.2764, found 449.2771.

**Z-Leu-Ala-Phe-OH (7ca).** A pale brown powder (83%): HPLC retention time (0% B ---> 100% B in 60 min), 33.7 min; mp 179 - 180 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 7.92 (m, 2H, 2 x NH), 7.4 - 7.1 (m, 11H, 2 x Ph, OCONH), 5.02 (s, 2H, OCH<sub>2</sub>Ph), 4.36 (m, 1H, NHCH), 4.27 (quintet, J = 7.2 Hz, 1H, Ala-NHCH), 4.03 (m, 1H, NHCH), 3.05 (dd, J = 13.8, 5.2 Hz, 1H, CHCHHPh), 2.90 (dd, J = 13.8, 8.0 Hz, 1H, CHCHHPh), 1.60 (m, 3H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.41 (m, 3H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.18 (d, J = 7.0 Hz, 3H, Ala-CH<sub>3</sub>), 0.84 (m, , 6H, Leu-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, DMSO-d<sub>6</sub>) δ 172.7, 171.8 (2C), 155.9, 137.5, 137.0, 129.1, 129.2, 128.0, 127.7, 127.5, 126.2, 65.3, 53.6, 52.9, 47.9, 36.7, 24.1, 23.0, 21.3, 18.2; HRMS m/e calcd for C<sub>26</sub>H<sub>33</sub>N<sub>3</sub>O<sub>6</sub>Na (M + Na<sup>+</sup>) 506.2267, found 506.2284.

**Z-Leu-Ala-Ala-Phe-OH (7cb).** A pale brown powder (67%): HPLC retention time (0% B ---> 100% B in 60 min), 33.2 min; mp 162 - 164 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 12.69 (s, 1H, COOH), 8.02 (d, J = 7.8 Hz, 1H, NH), 7.94 (d, J = 7.4 Hz, 1H, NH), 7.84 (d, J = 7.5 Hz, 1H, NH), 7.4 - 7.1 (m, 11H, 2 x Ph, OCONH), 5.02 (s, 2H, OCH<sub>2</sub>Ph), 4.41 (m, 1H, NHCH), 4.26 (m, 2H, 2 x NHCH), 4.03 (m, 1H, NHCH), 3.05 (dd, J = 13.9, 5.3 Hz, 1H, CHCHHPh), 2.90 (dd, J = 13.9, 8.5 Hz, 1H, CHCHHPh), 1.62 (m, 1H, CH(CH<sub>3</sub>)<sub>2</sub>), 1.42 (m, 2H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.16 (d, J = 7.0 Hz, 6H, 2 x Ala-CH<sub>3</sub>), 0.85 (m, 6H, Leu-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, DMSO-d<sub>6</sub>) δ 172.6, 171.9, 171.8, 171.5, 155.9, 137.3, 137.0, 129.1, 128.3, 128.1, 127.7, 127.5, 126.4, 65.3, 53.3 (2C), 53.0, 47.8, 36.6, 24.1, 23.0, 21.3, 18.2, 18.0; HRMS m/e calcd for C<sub>29</sub>H<sub>38</sub>N<sub>4</sub>O<sub>7</sub>Na (M + Na<sup>+</sup>) 577.2638, found 577.2643.

**Z-Leu-Ala-Val-Phe-OH (7cc).** A pale brown powder (68%): HPLC retention time (0% B ---> 100% B in 60 min), 35.2 min; mp 216 - 218 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 12.53 (br, 1H, COOH), 8.16 (d, J = 7.8 Hz, 1H, NH), 8.00 (d, J = 7.4 Hz, 1H, NH), 7.55 (d, J = 9.1 Hz, 1H, NH), 7.5 - 7.1 (m, 11H, 2 x Ph, OCONH), 5.02 (s, 2H, OCH<sub>2</sub>Ph), 4.44 (m, 1H, NHCH), 4.31 (quintet, J = 7.2 Hz, 1H, Ala-NHCH), 4.16 (dd, J = 8.9, 6.5 Hz, 1H, Val-NHCH), 3.05 (dd, J = 14.0, 5.3 Hz, 1H, CHCHHPh), 2.89 (dd, J = 14.0, 9.0 Hz, 1H, CHCHHPh), 1.92 (m, 1H, Val-CH(CH<sub>3</sub>)<sub>2</sub>), 1.62 (m, 1H, Leu-CH(CH<sub>3</sub>)<sub>2</sub>), 1.42 (m, 2H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.15 (d, J = 6.9 Hz, 3H, Ala-CH<sub>3</sub>), 0.9 - 0.7 (m, 12H, Leu- and Val-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, DMSO-d<sub>6</sub>) δ 172.7, 172.0, 171.7, 170.6, 155.9, 137.4, 137.0, 128.9, 128.3, 128.1, 127.7, 127.5, 126.3, 65.3, 57.1, 53.2, 52.9, 47.9, 36.6, 30.8, 24.1, 23.0, 21.3, 19.0, 17.7; HRMS m/e calcd for C<sub>31</sub>H<sub>43</sub>N<sub>4</sub>O<sub>7</sub> (M + H<sup>+</sup>) 583.3132, found 583.3148.

**Leu-Enkephalin (H-Tyr-Gly-Gly-Phe-Leu-OH, 7dd).** A pale brown powder (87%): HPLC retention time (0% B ---> 100% B in 60 min), 21.2 min (the same retention

time as the authentic sample from Sigma); LRMS m/e calcd for  $C_{28}H_{37}N_5O_7$  ( $M + H^+$ ) 556.3, found 556.4.

**[D-Phe<sup>4</sup>]-Leu-Enkephalin (H-Tyr-Gly-Gly-D-Phe-Leu-OH, D-7dd).** A pale brown powder (61%): HPLC retention time (0% B --> 100% B in 60 min), 24.2 min; LRMS m/e calcd for  $C_{28}H_{37}N_5O_7$  ( $M + H^+$ ) 556.3, found 556.4.

**Met-Enkephalin (H-Tyr-Gly-Gly-Phe-Met-OH, 7de).** A pale brown powder (87%): HPLC retention time (0% B --> 100% B in 60 min), 24.0 min (the same retention time as the authentic sample from Sigma); LRMS m/e calcd for  $C_{27}H_{35}N_5O_7S$  ( $M + H^+$ ) 573.3, found 573.4.

**[D-Phe<sup>4</sup>]-Met-Enkephalin (H-Tyr-Gly-Gly-D-Phe-Met-OH, D-7de).** A pale brown powder (61%): HPLC retention time (0% B --> 100% B in 60 min), 19.1 min; LRMS m/e calcd for  $C_{27}H_{35}N_5O_7S$  ( $M + H^+$ ) 573.3, found 573.4.

## References

- (1) Jackson, S.; DeGrado, W.; Dwivedi, A.; Parthasarathy, A.; Higley, A.; Krywko, J.; Rockwell, A.; Markwalder, J.; Wells, G.; Wexler, R.; Mousa, S.; Harlow, R. *J. Am. Chem. Soc.* **1994**, *116*, 3220-3230.
- (2) For a manual peptide synthesis on Wang resin, see *Novabiochem Catalog & Peptide Synthesis Handbook*; 1997, pp S58-S59.

*Result Table*

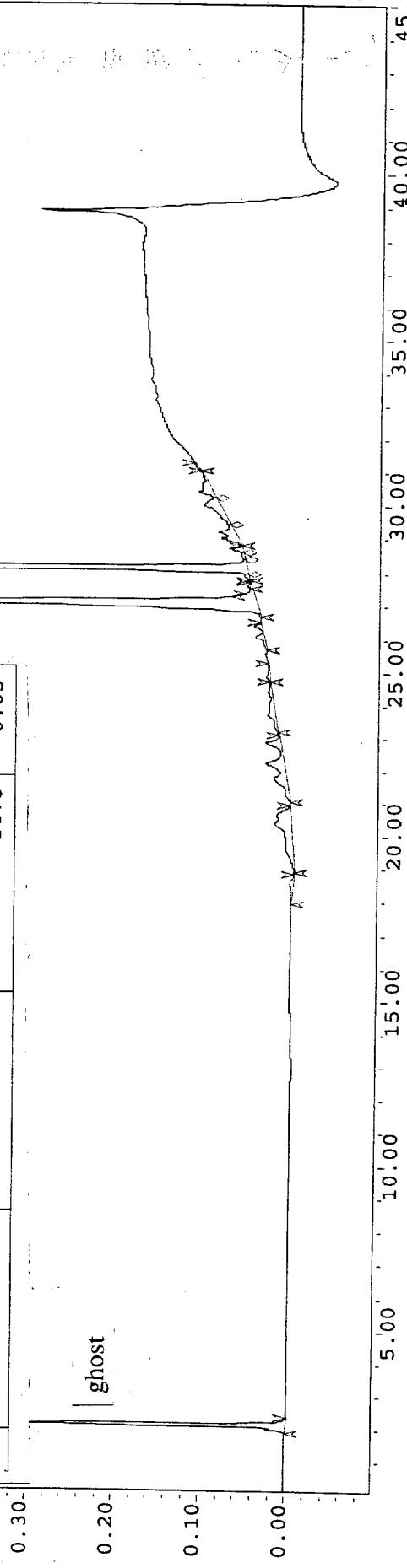
**7aa**

#	Retention Time (min)	Area (uV*sec)	Height (uV)	% Area
1	2.137	1871968	347037	9.86
2	18.603	89688	4048	0.47
3	20.403	916319	18450	4.83
4	22.270	861222	19897	4.54
5	23.720	308058	8311	1.62
6	24.853	38923	3337	0.21
7	26.087	156090	9707	0.82
8	27.070	7235123	640389	38.11
9	27.353	8093	2564	0.04
10	27.620	18643	3658	0.10
11	27.887	25073	3770	0.13
12	28.153	6439189	984641	33.92
13	28.520	16613	2398	0.09
14	28.703	70012	11627	0.37
15	29.053	311672	17320	1.64
16	30.037	379699	17324	2.00
17	30.437	230867	15317	1.22
18	31.187	8639	1478	0.05

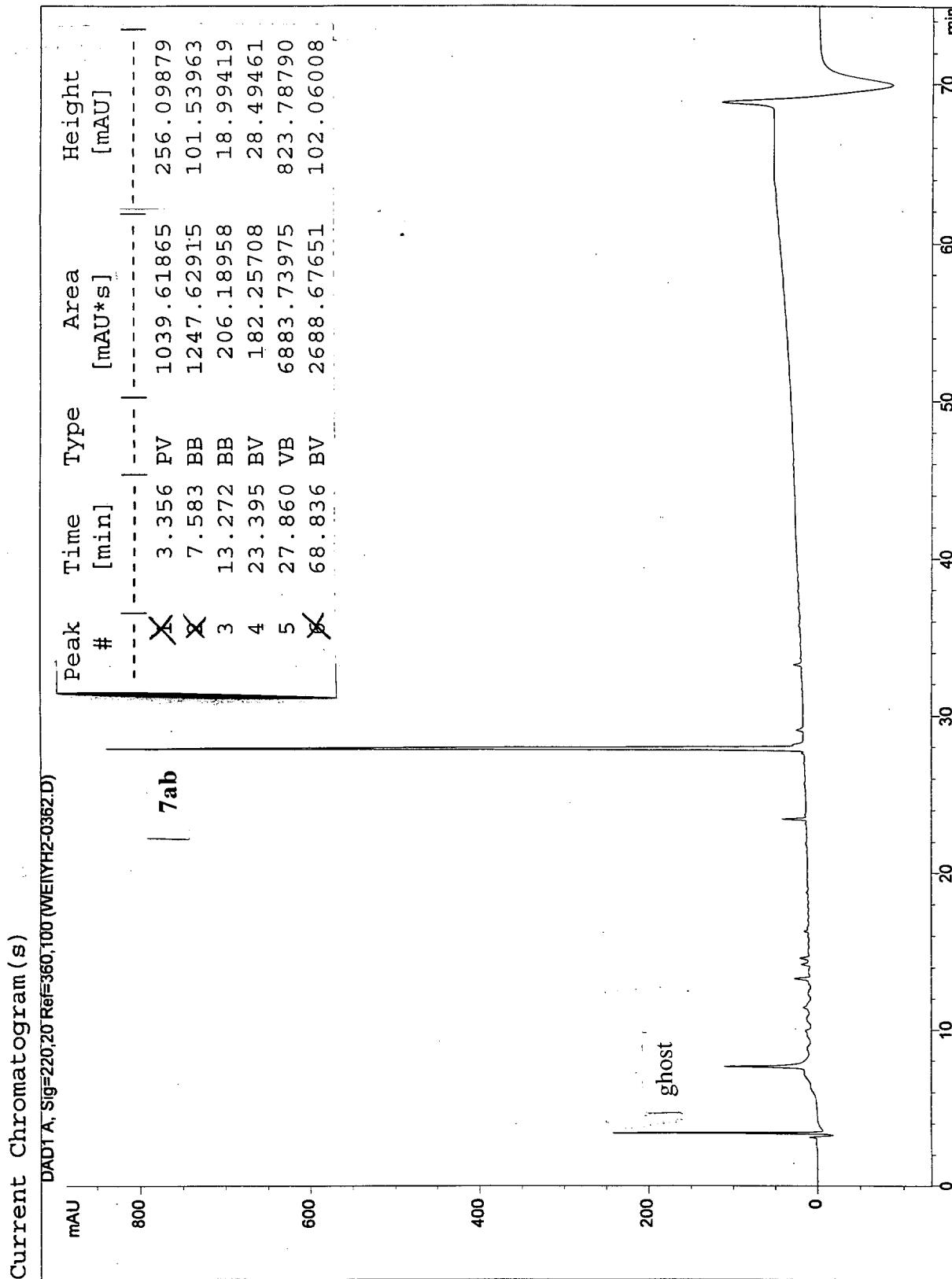
DA

Internal Standard  
(PhNO<sub>2</sub>)

ghost

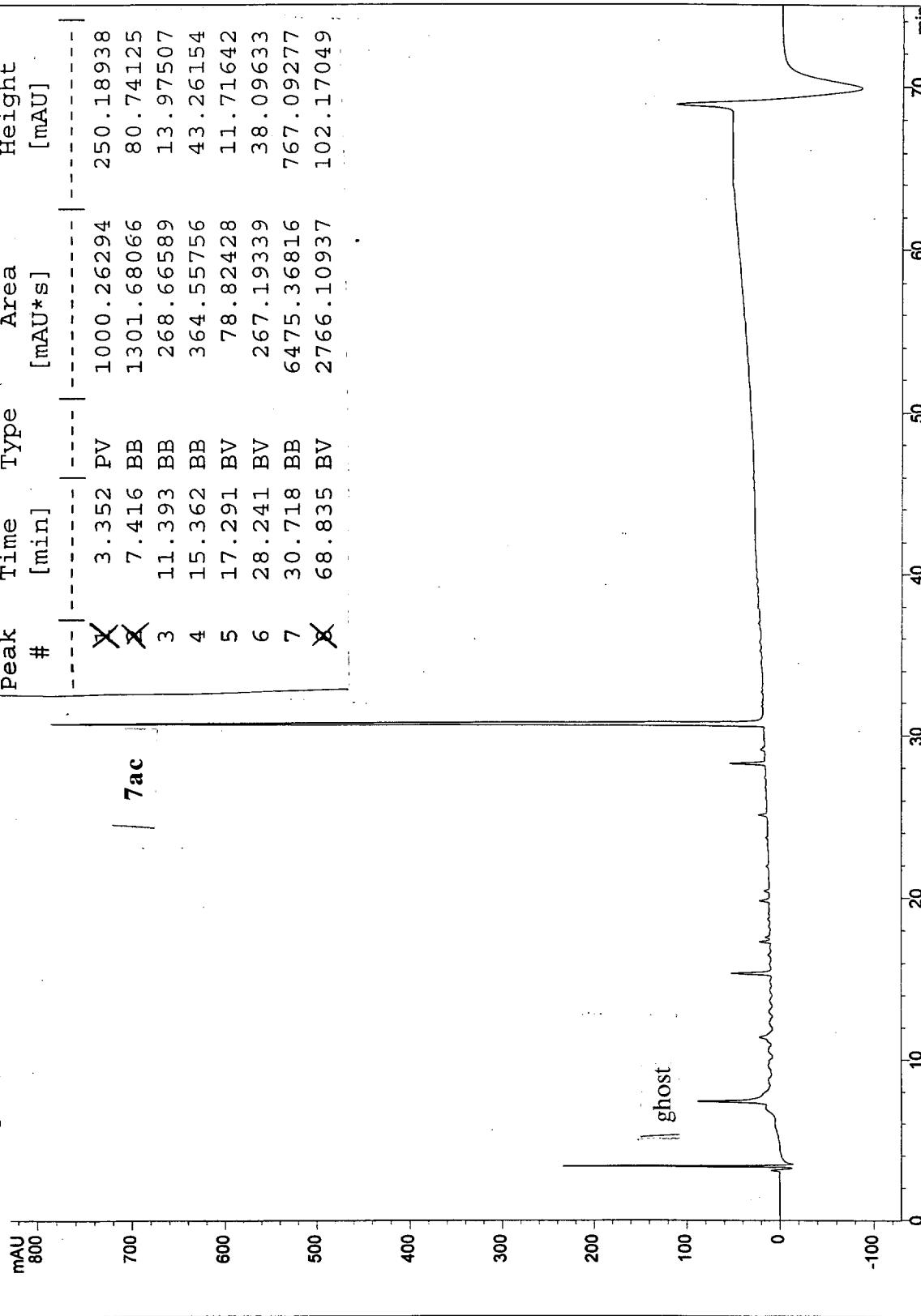


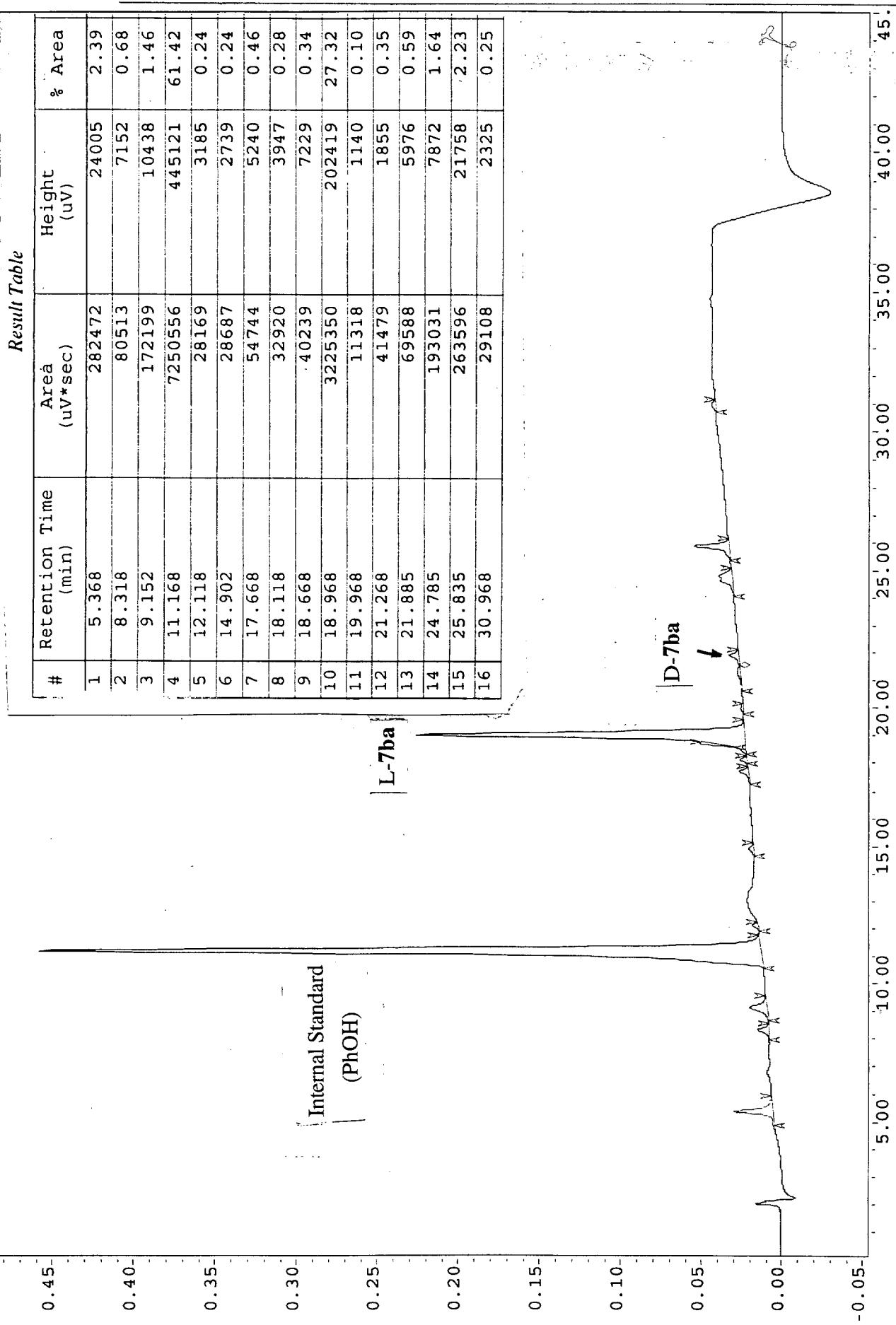
Minutes



## Print of Window 38: Current Chromatogram(s)

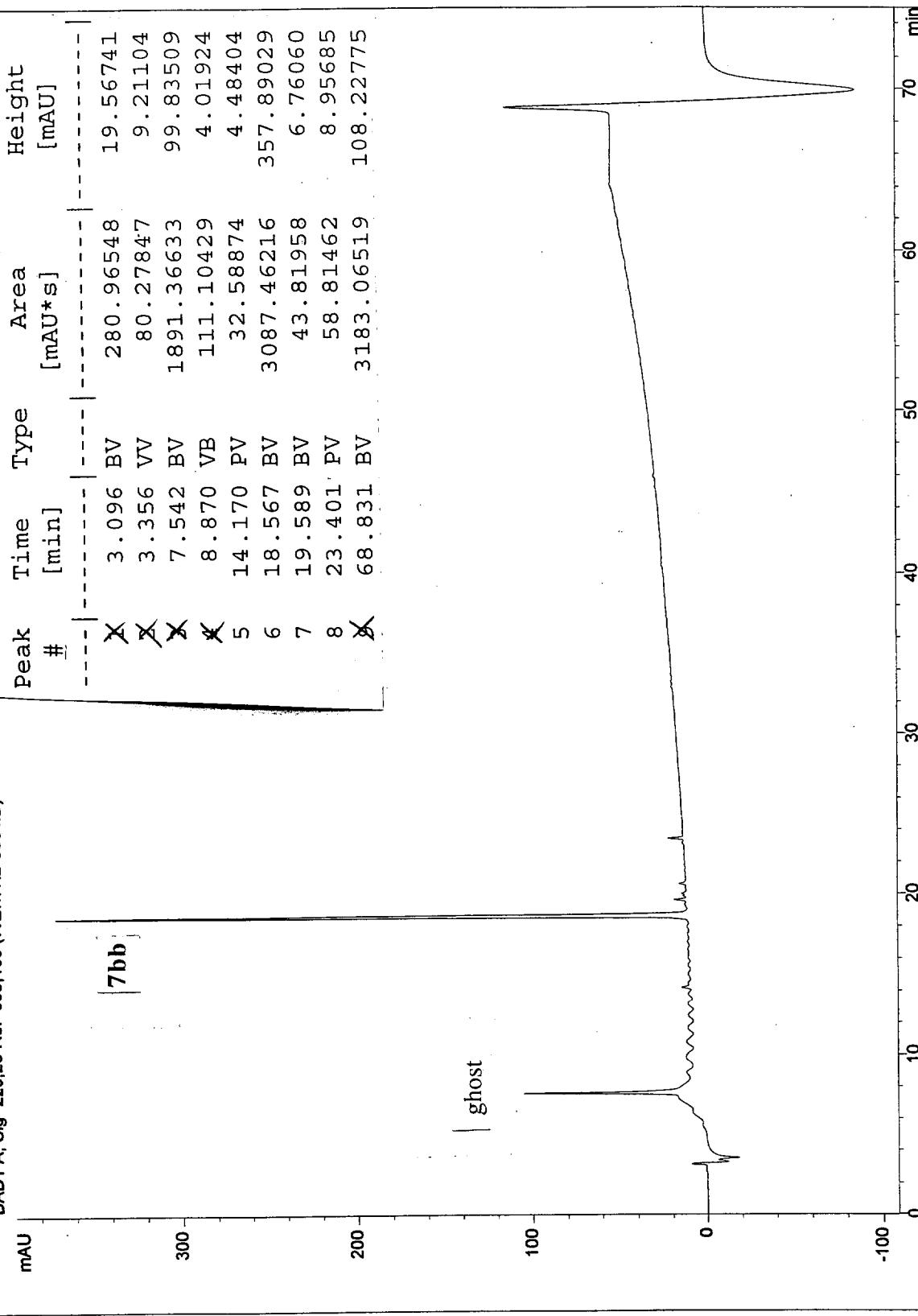
DAD1 A, Sig=220.20 Ref=350.100 (WE1VH2-0366.D)

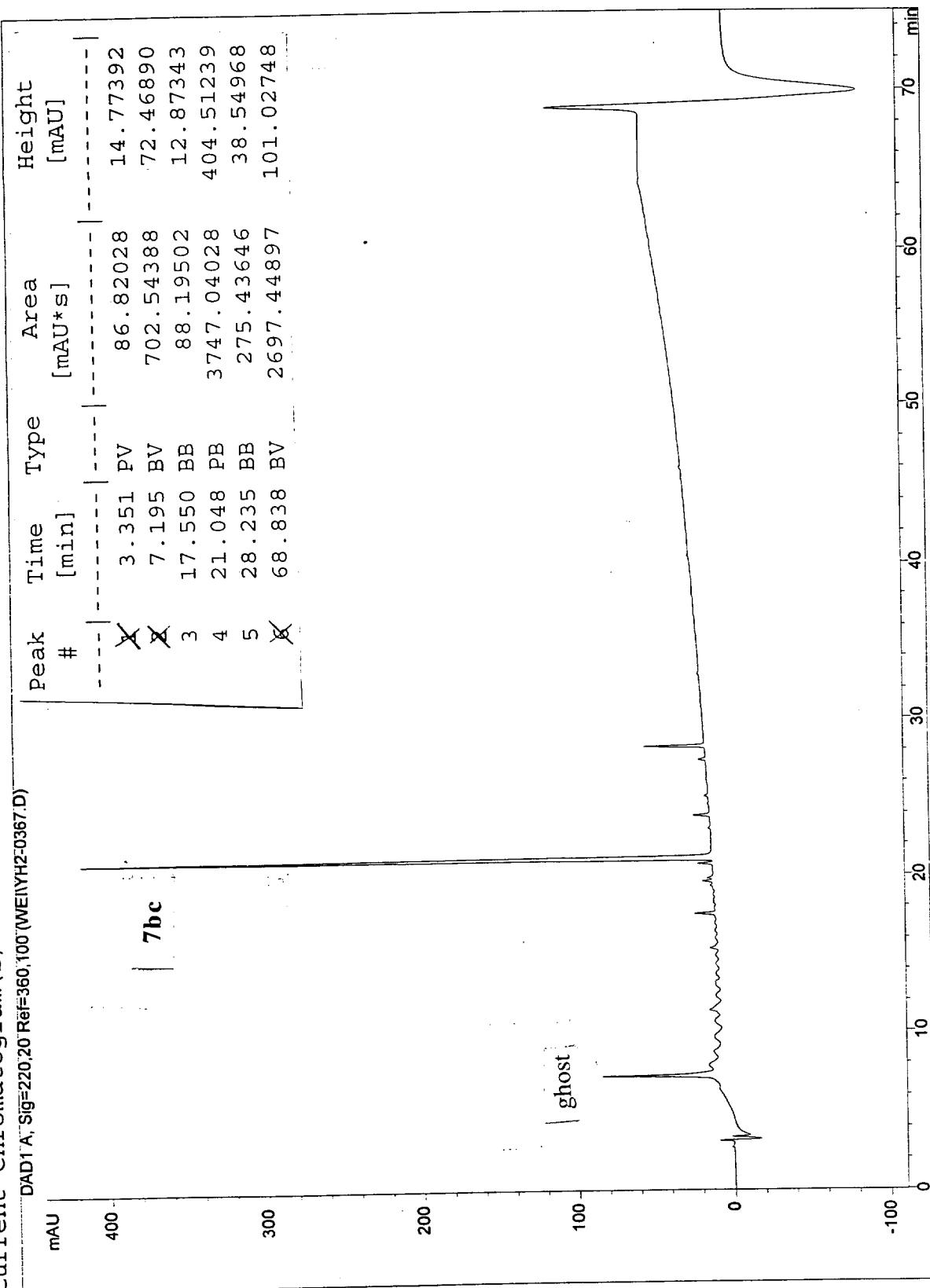




## Current Chromatogram (s)

DADTA, Sig=220.20 Ref=360.100 (WEIYH2-0364.D)



Current Chromatogram (s)  
DAD1A, Sig=220,20 Ref=360,100 (WEIVYH2-0367.D)

## Current Chromatogram (s)

DAD1A, Sig=220.20 Ref=360.100 (WEINH2-0361.D)

MAU

1000

800

600

400

200

0

7ca

ghost

0 10 20 30 40 50 60 70 min

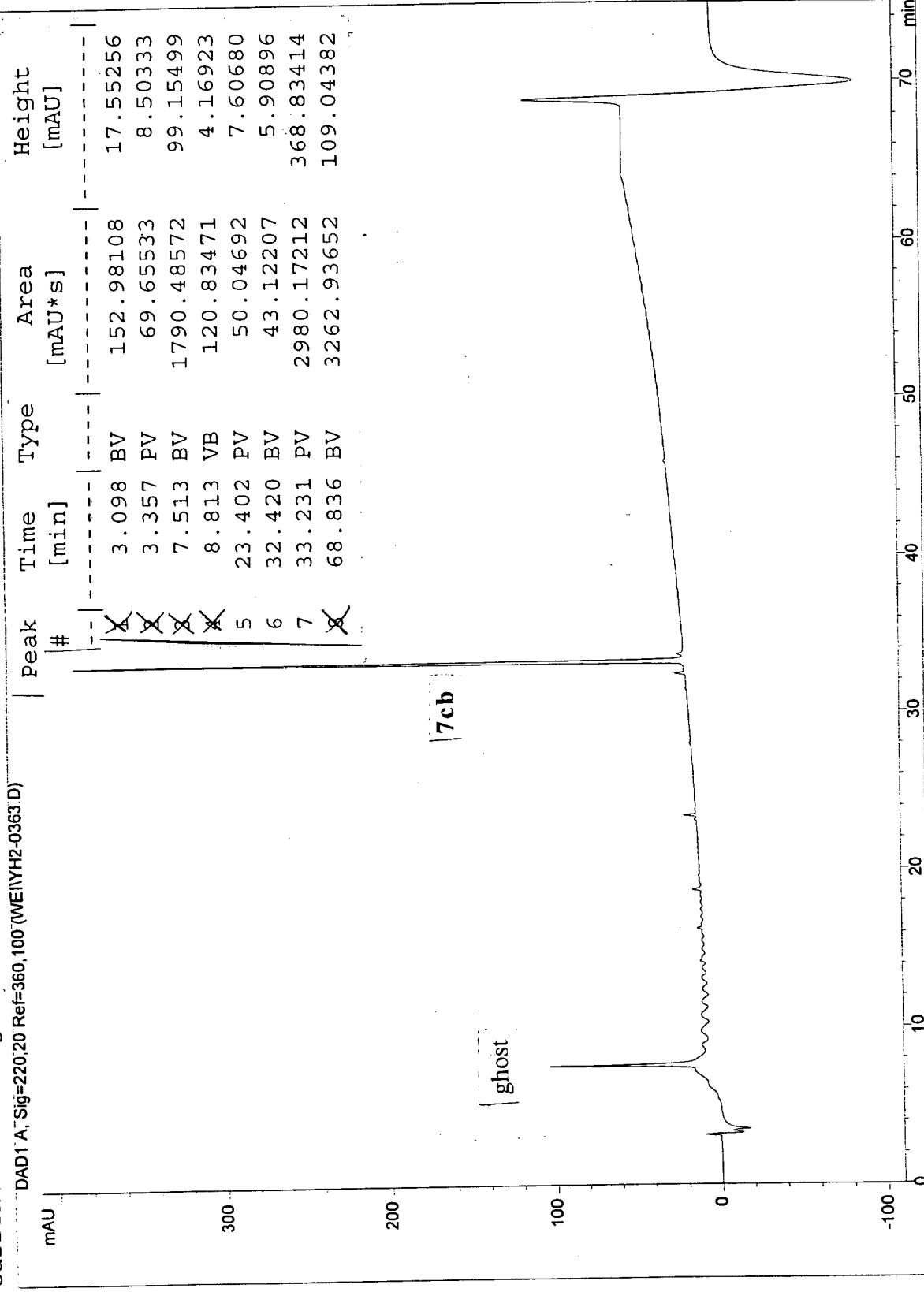
Peak #	Time [min]	Type	Area/ [mAU*s]	Height [mAU]
X	3.343	VV	109.91896	18.46451
X	7.522	BB	1225.63831	93.75051
3	19.592	BB	100.87581	15.56614
4	24.352	BB	127.36435	17.90916
5	25.308	BB	124.44821	18.26267
6	33.220	BV	348.40060	45.15500
7	33.669	PV	9667.33496	995.21417
X	68.834	BV	2713.37720	102.11051

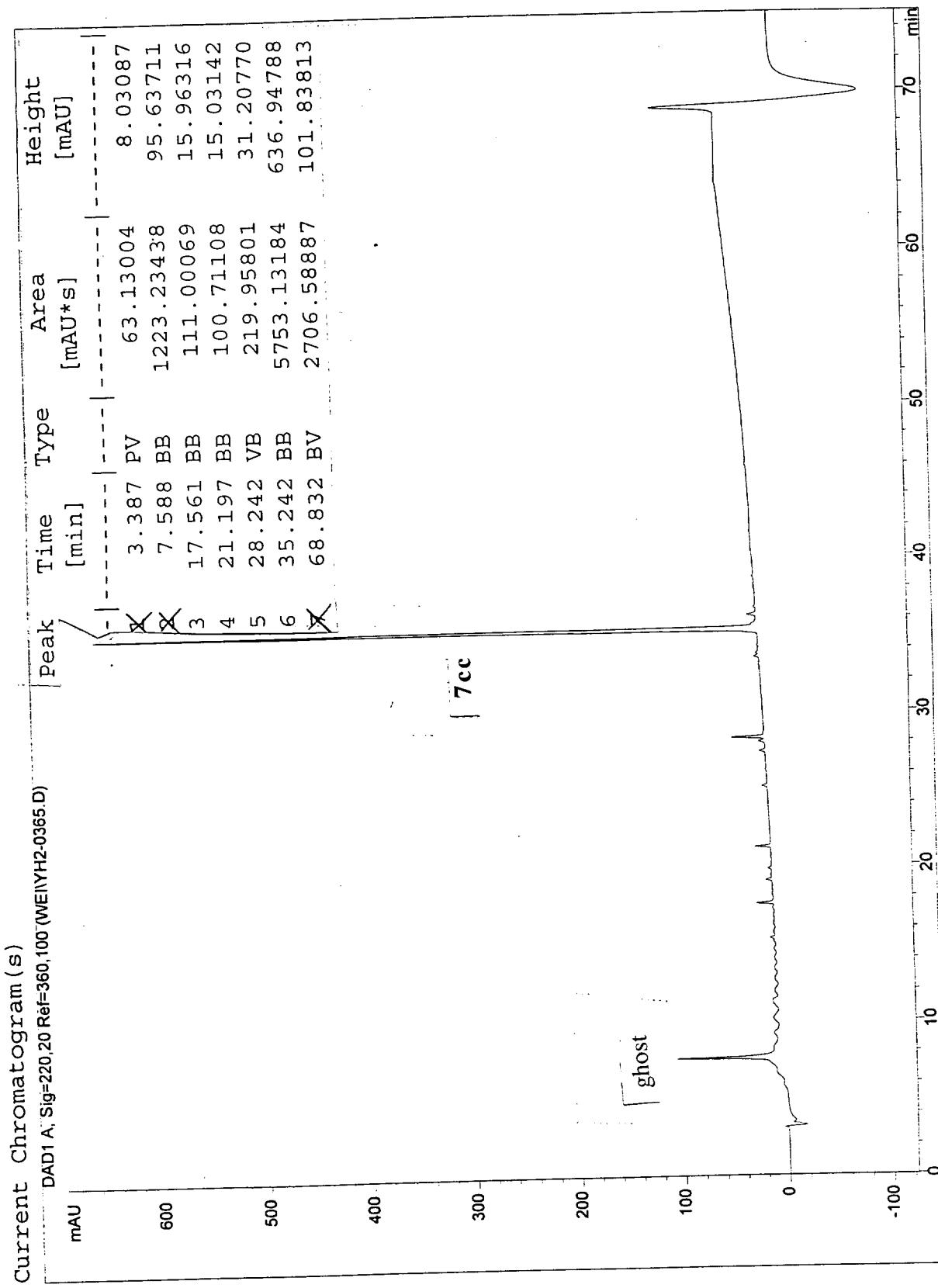
Printed on window 38: Current Chromatogram(s)

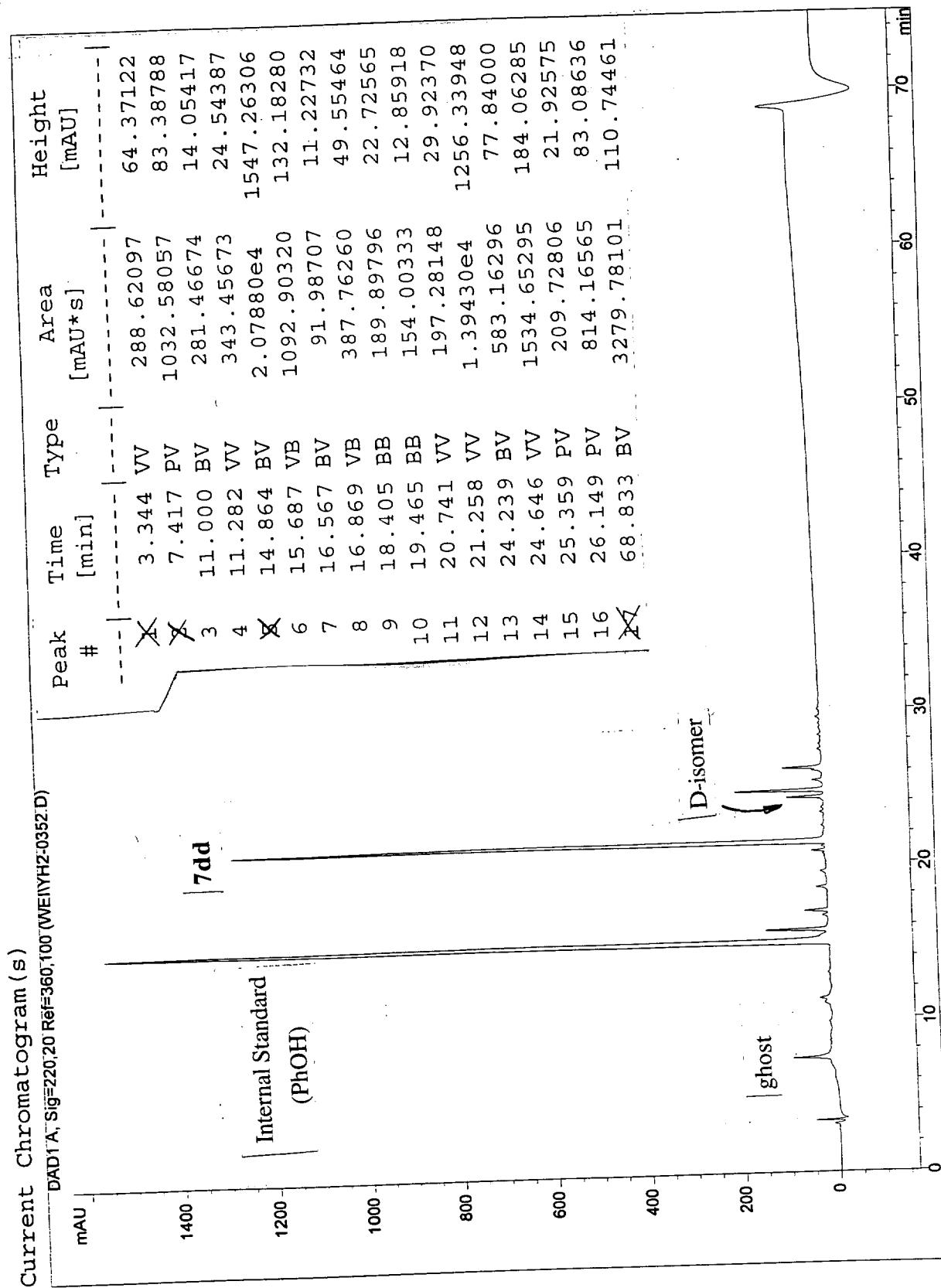
## Current Chromatogram(s)

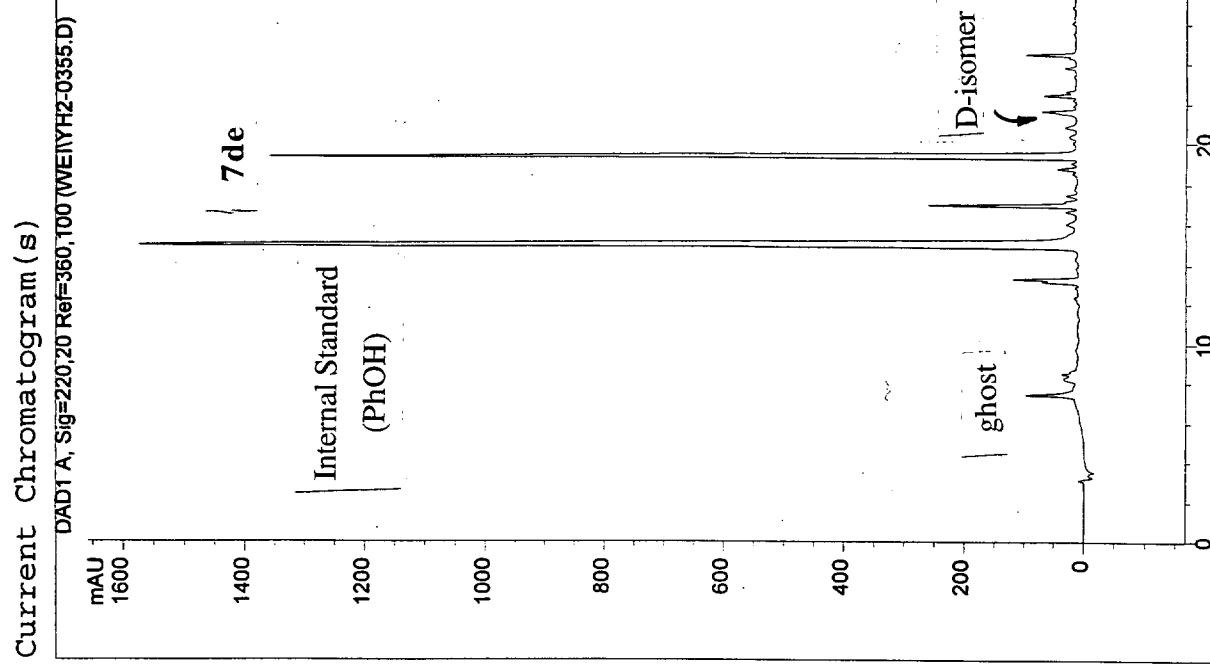
DAD1A, Sig=220,20 Ref=3660,100\WEN\YH2-0363.D

mAU









Peak #	Time [min]	Type	Area [mAU*s]	Height [mAU]
X	7.417	BV	1060.29700	86.74217
2	8.234	VV	358.26703	21.22660
3	8.478	VB	263.80530	24.99622
4	13.105	PV	393.12671	58.64240
5	13.242	VB	779.45868	109.72698
X	14.926	BV	2.32863e4	1561.98303
7	16.001	VB	210.68468	16.12795
8	16.601	BV	129.65639	17.23054
9	16.894	VV	1922.02258	247.29573
10	17.098	VV	118.05170	20.37566
11	17.407	PV	144.49854	17.27331
12	18.733	VV	213.71387	31.55186
13	19.259	VB	1.40394e4	1339.37341
14	20.793	BB	195.15762	17.89154
15	21.603	BV	568.97852	56.51904
16	22.389	VV	375.25092	53.40028
17	22.572	VV	106.87543	16.24875
18	23.765	BB	133.07782	18.66135
19	24.441	BB	679.06934	82.62572
X	68.838	BV	2934.46875	104.69134