Supplementary Information

Virtually Epimerization-Free Synthesis of Peptide-alpha-Thioesters

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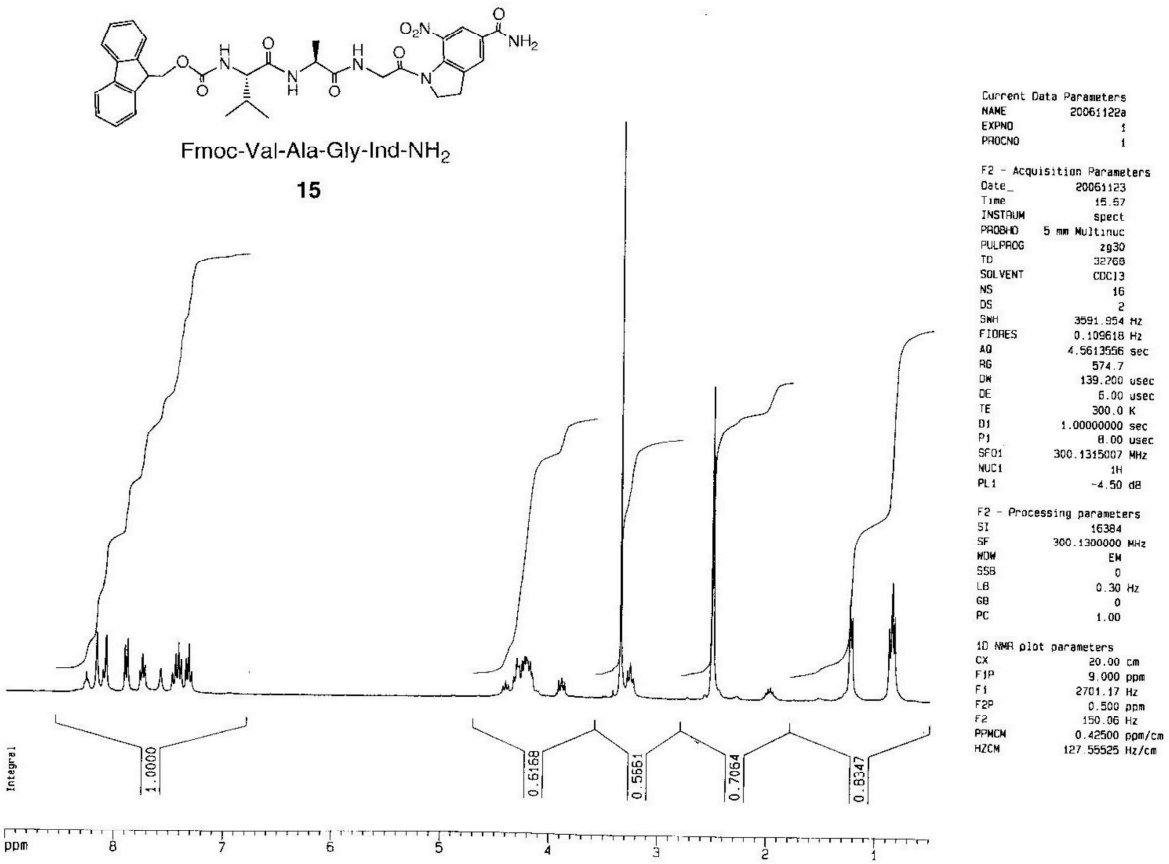
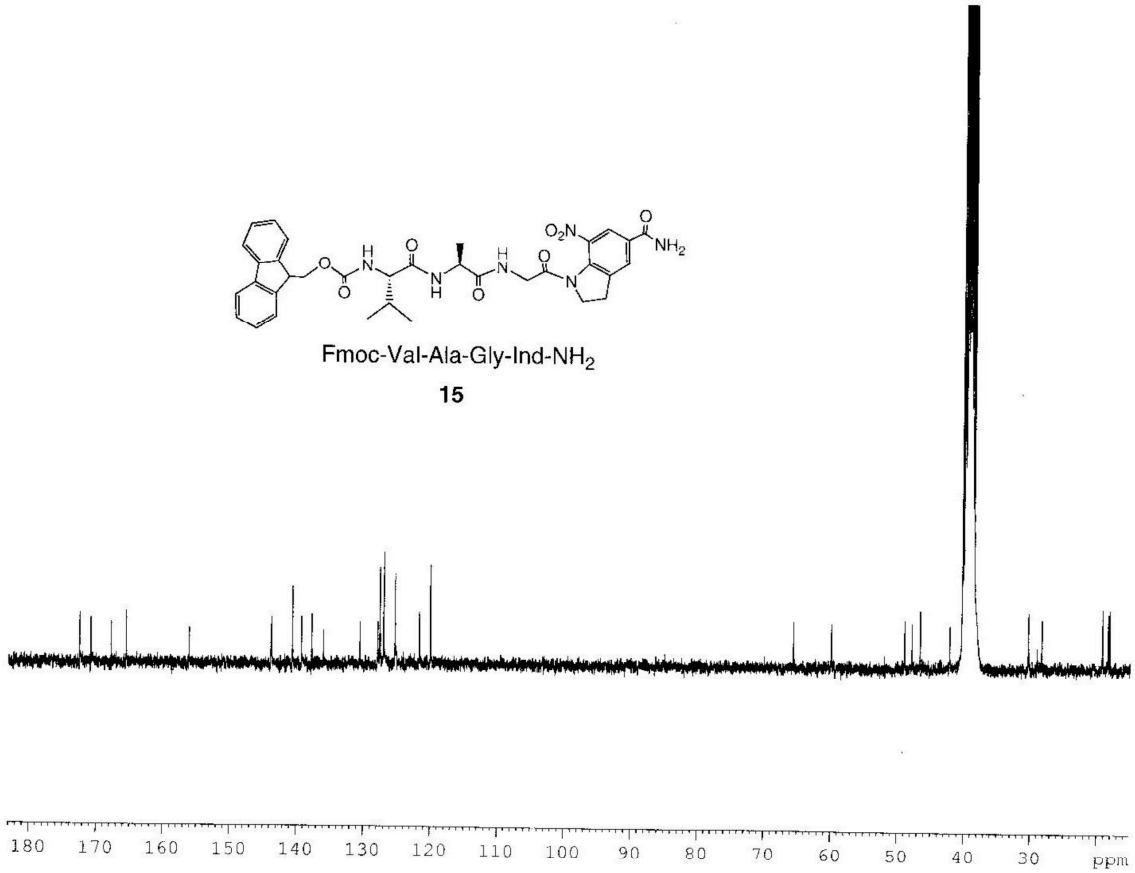
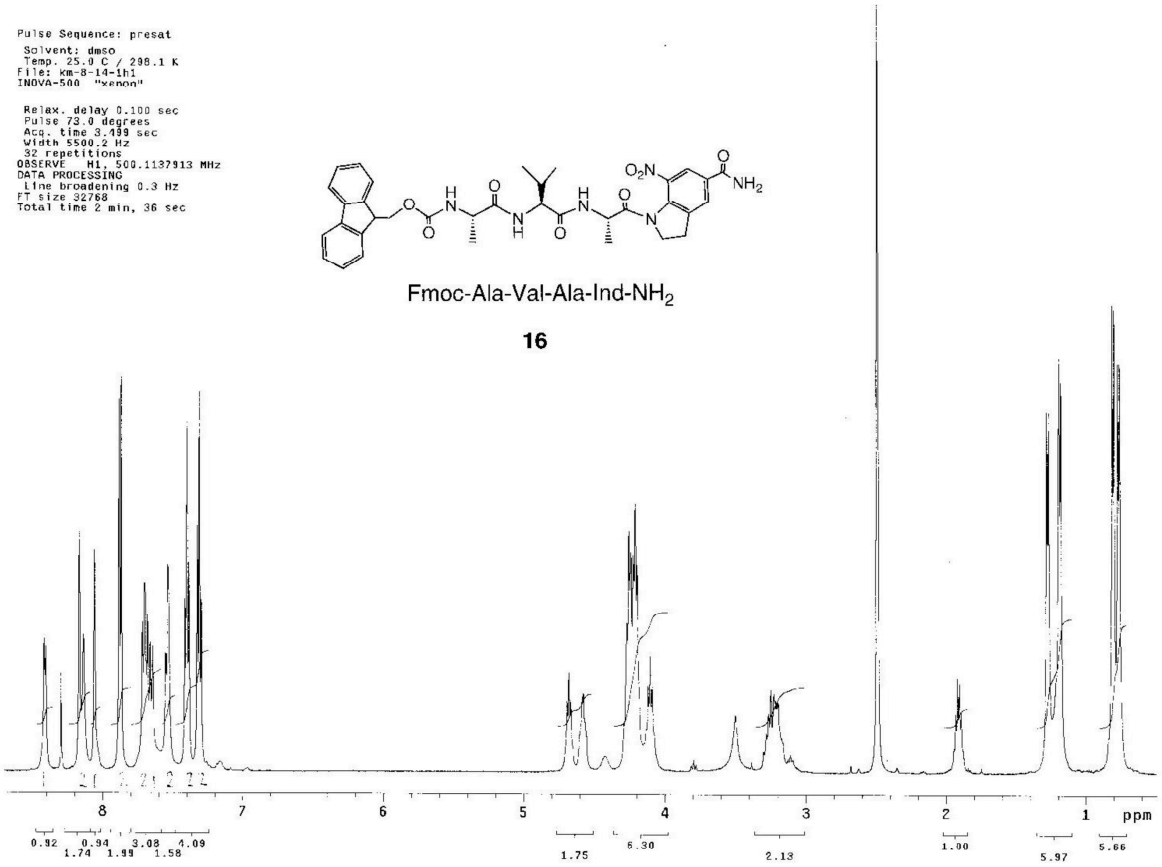


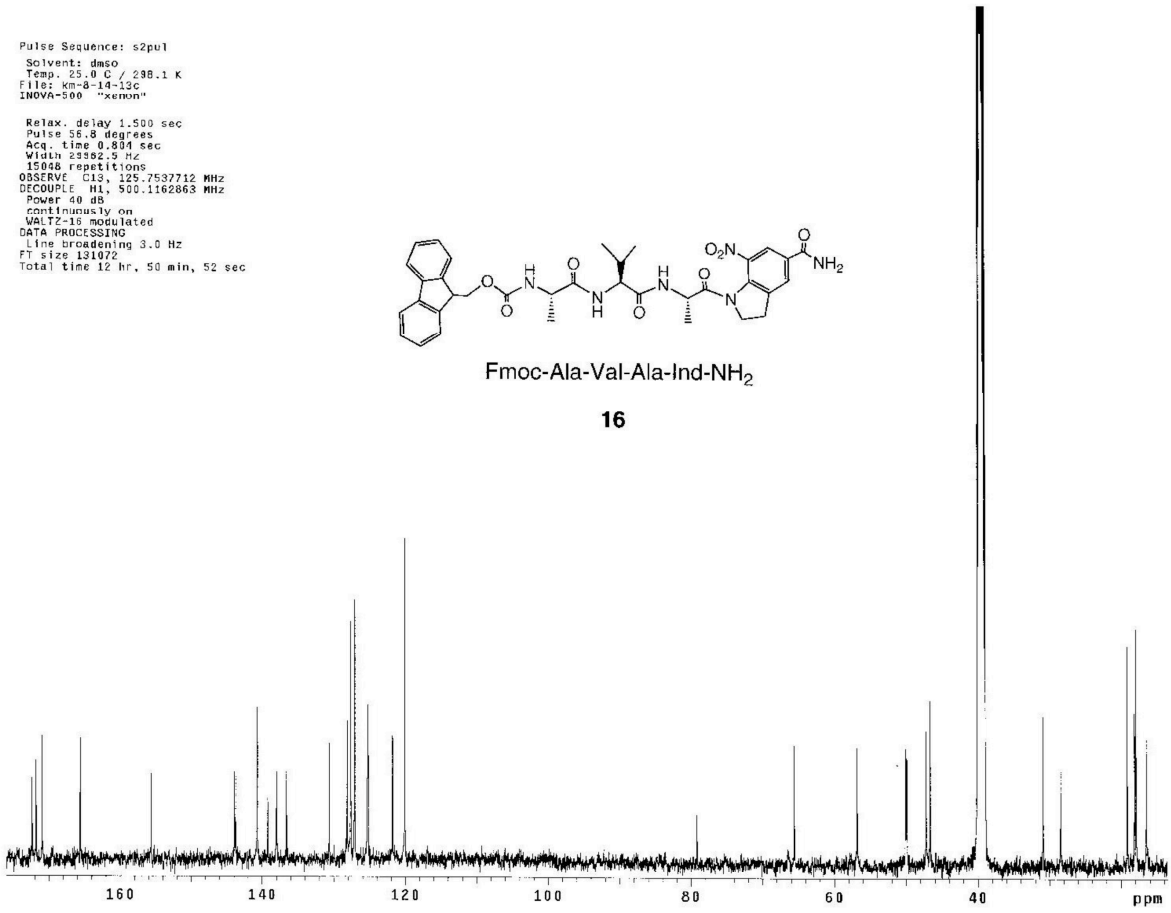
^{1}H NMR (dmso-d_6, 298K, 300 MHz) δ 8.26 (m, 1H, NH-Gly); 8.16 (s, 2H, H-4, H-6); 8.10 (d, 1H NH-Ala, $^{3}J_{NH,\alpha}$ 8.3 Hz); 8.08 (s, 1H, C-terminal NH); 7.89 (d, 2H, Fmoc, ^{3}J 7.4 Hz); 7.70 (m, 2H, Fmoc); 7.74 (t, 2H, Fmoc, ^{3}J 6.7 Hz); 7.58 (s, 1H, C-terminal NH'); 7.48-7.38 (m, 3H, NH-Val, Fmoc); 7.32 (t, 2H, Fmoc); 4.41 (t, 1H, Hα-Ala); 4.35-4.14 [m, 7H, Hα-Gly, Hα'-Gly, CH, CH_2 (Fmoc), H-2, H-2']; 3.89 (dd, 1H, Hα-Val), 3.26 (t, 2H, H-2, H-2'), 1.98 (m, 1H, H-β-Val); 1.23 (d, 3H, 3×Hβ-Ala); 0.65 (t, 6H, 3×Hγ-Val, 3×H-γ'-Val) ppm.



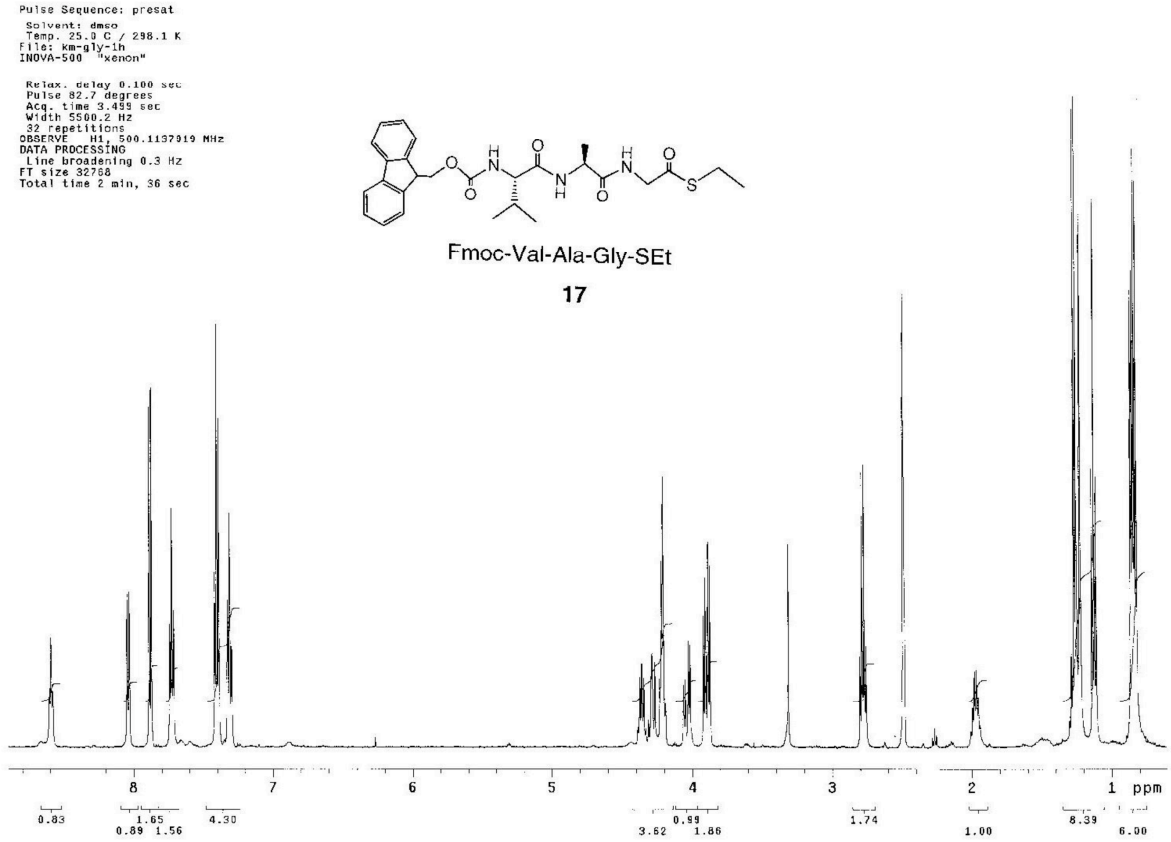
^{13}C NMR (dmso-d_6, 298K, 75 MHz) δ 172.5; 170.9; 167.8; 165.6; 156.1; 143.9; 143.8; 140.7; 139.4; 137.8; 136.1; 130.6; 128.0; 127.7; 127.1; 125.4; 121.8; 120.1; 65.7; 60.0; 49.0; 47.9; 46.7; 42.2; 30.4; 28.4; 19.3; 18.4; 18.2 ppm.



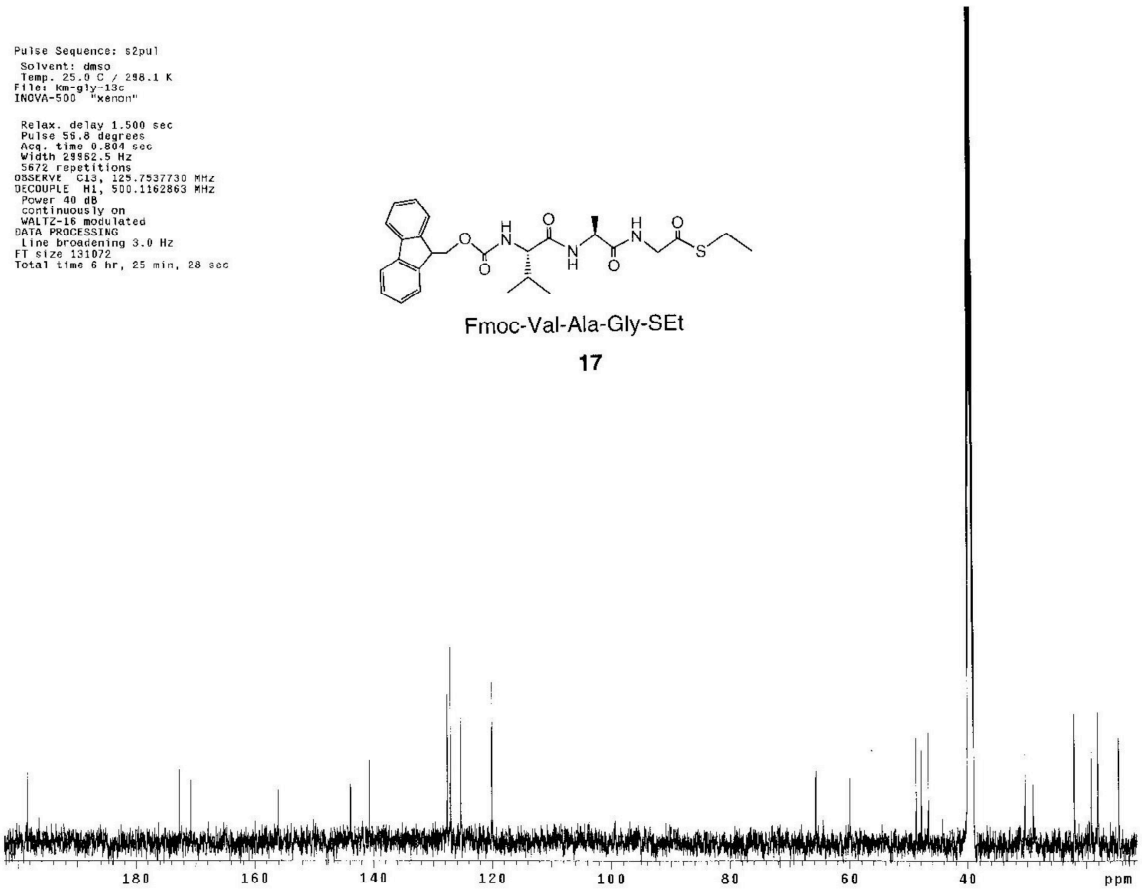
^{1}H NMR (dmso-d_6, 298K, 500 MHz) δ 8.41 (d, 1H, NH-Ala-2, $^{3}J_{NH,\alpha}$ 6.1 Hz); 8.17, 8.14, 8.06 (3s, 3H, H-4, H-6, C-terminal NH); 7.87 (d, 2H, Fmoc, ^{3}J 7.4 Hz); 7.70 (m, 2H, Fmoc); 7.65 (d, 1H, NH-Val, $^{3}J_{NH,\alpha}$ 9.0 Hz); 7.54 (m, 2H, NH-Ala-1, C-terminal NH'); 7.40 (t, 2H, Fmoc, ^{3}J 7.3 Hz); 7.31 (t, 2H, Fmoc); 4.68 (m, 1H, H-α-Ala-2); 4.58 (m, 1H, H-2); 4.29-4.17 (m, 5H, H-α-Val, CH-Fmoc, CH_2-Fmoc, H-2'); 4.10 (m, 1H, H-α-Ala-1); 3.29-3.15 (m, 2H, H-3, H-3'); 1.91 (m, 1H, H-β-Val); 1.28, d, 3H, 3×H-β-Ala-2, $^{3}J_{\alpha,\beta}$ 6.7 Hz); 1.18 (d, 3H, 3×H-β-Ala-1, $^{3}J_{\alpha,\beta}$ 7.0 Hz); 0.81 (d, 3H, 3 × H-γ-Val, $^{3}J_{\alpha,\beta}$ 6.7 Hz); 0.77 (d, 3H, 3 × H-γ'-Val, $^{3}J_{\alpha,\beta}$ 6.4 Hz) ppm.



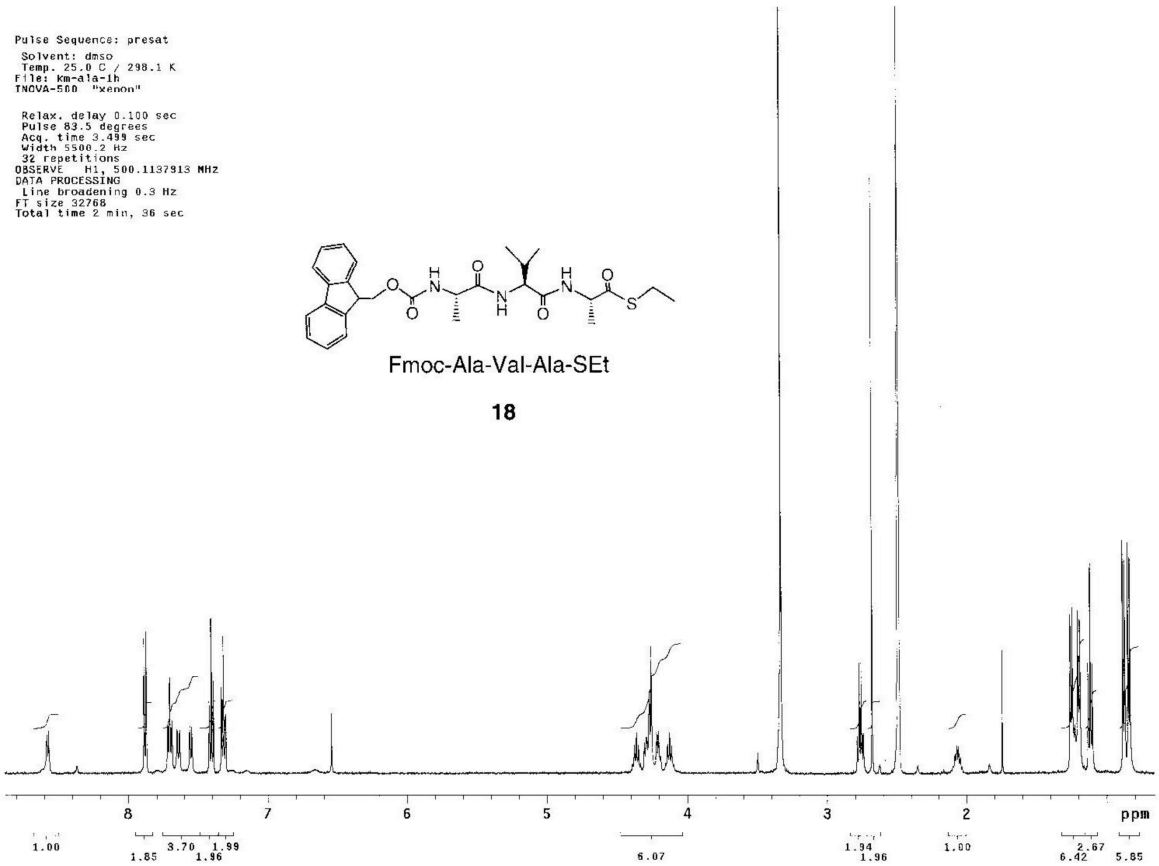
^{13}C NMR (dmso-d_6, 298K, 126 MHz) δ 172.3; 171.8; 170.9; 165.6; 155.6; 143.9; 143.7; 140.7; 139.2; 138.0; 136.6; 130.6; 128.1; 127.6; 127.1; 125.3; 125.2; 121.8; 120.1; 79.2; 65.6; 56.9; 50.1; 49.9; 47.2; 46.6; 30.9; 28.4; 19.1; 18.1; 17.9; 16.5 ppm.



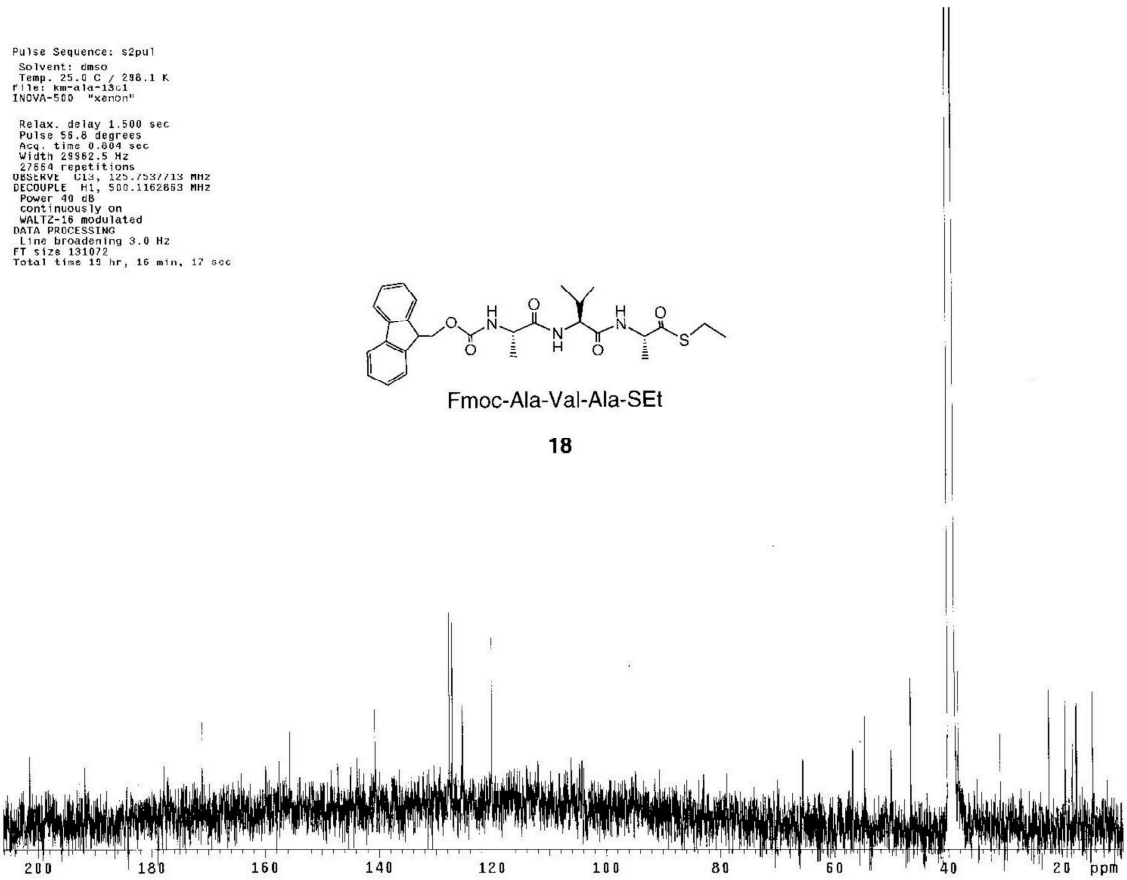
^{1}H NMR (dmso-d_6, 298K, 500 MHz) δ 8.53 (m, 1H, NH-Gly); 8.04 (d, 2H, NH-Ala, $^{3}J_{NH,\alpha}$ 7.4); 8.10 (d, 1H NH-Ala, $^{3}J_{NH,\alpha}$ 8.3 Hz); 7.88 (d, 2H, Fmoc, ^{3}J 7.7 Hz); 7.23 (t, 2H, Fmoc); 7.43-7.38 (m, 3H, NH-Val, Fmoc); 7.31 (t, 2H, Fmoc); 4.36 (m, 1H, Hα-Ala); 4.32-4.18 [m, 3H, CH, CH_2 (Fmoc)]; 4.04 (dd, 1H, Hα-Gly, $^{2}J_{\alpha,\alpha'}$ 17.5Hz, $^{3}J_{\alpha,NH}$ 6.4Hz), 3.93-3.86 (m, 2H, Hα'-Gly, Hα-Val), 2.78 [q, 2H, CH_2 (Et), ^{3}J 7.4 Hz]; 1.98 (m, 1H, Hβ-Val); 1.26 (d, 3H, 3×HβAla); 1.12 [t, 3H, CH_3 (Et)]; 0.85 (d, 3H, 3×Hγ-Val, $^{3}J_{\beta,\gamma}$ 6.7Hz); 0.83 (d, 3H, 3×H-γ'-Val, $^{3}J_{\beta,\gamma'}$ 7.1Hz) ppm.



^{13}C NMR (dmso-d_6, 298K, 126 MHz) δ 198.4; 172.7; 170.8; 156.1; 143.9; 143.8; 140.7; 127.6; 127.0; 125.3; 120.1; 65.6; 59.9; 48.7; 47.9; 46.7; 30.3; 29.0; 22.1; 19.2; 18.1; 14.6 ppm.



^{1}H NMR (dmso-d_6, 298K, 500 MHz) δ 8.57 (d, 1H, NH-Ala-2, $^{3}J_{NH,\alpha}$ 7.1 Hz); 7.88 (d, 2H, Fmoc, ^{3}J 7.4 Hz); 7.70 (m, 2H, Fmoc); 7.64 (d, 1H, NH-Val, $^{3}J_{NH,\alpha}$ 9.4 Hz); 7.55 (d, 1H, NH-Ala-1, $^{3}J_{NH,\alpha}$ 8.1 Hz); 7.41 (t, 2H, Fmoc, ^{3}J 7.4 Hz); 7.32 (t, 2H, Fmoc); 4.36 (m, H-α-Ala-2); 4.31-4.18 (m, 4H, H-α-Val, CH-Fmoc, CH_2-Fmoc); 4.13 (m, 1H, H-α-Ala-1); 2.76 (q, 2H, CH_2-SEt, ^{3}J 7.4 Hz); 2.06 (m, 1H, H-β-Val); 1.25 (d, 3H, 3×H-β-Ala-2, $^{3}J_{\alpha,\beta}$ 7.1 Hz); 1.20 (d, 3H, 3×H-β-Ala-1, $^{3}J_{\alpha,\beta}$ 7.1 Hz); 1.12 (t, 3H, CH_3-SEt); 0.87 (d, 3H, 3×H-γ-Val, $^{3}J_{\alpha,\beta}$ 6.7 Hz); 0.84 (d, 3H, 3 × H-γ'-Val, $^{3}J_{\alpha,\beta}$ 6.7 Hz) ppm.



^{13}C NMR (dmso-d_6, 298K, 126 MHz) δ 201.5; 191.8; 177.8; 171.0; 159.8; 155.6; 147.3; 144.9; 143.9; 140.7; 131.2; 127.6; 127.1; 125.2; 120.1; 65.6; 56.8; 54.7; 50.0; 46.6; 38.2; 30.8; 22.3; 19.4; 18.2; 17.5; 17.4; 14.6 ppm.