Supporting Information

Liquid-phase Split-type-combinatorial Synthesis of Tripeptide Derivatives
Encoded by Fluorous Fmoc Reagents

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**General Experimental Methods.**

Except as otherwise indicated, all reactions were carried out under a positive pressure of nitrogen. All the laboratory chemicals were purchased and used without purification. Solvents were removed at a heating bath temperature of 40 °C and reduced pressure by rotary evaporation. Non-volatile compounds were dried *in vacuo* at 0.01 mbar. All reactions were magnetically stirred and monitored by thin layer chromatography (TLC) using silica gel plates. Purification by chromatography was performed on silica gel (65-210 Å). NMR-spectra were recorded at 270 MHz (¹H) and 67.8 MHz (¹³C) and 466 MHz (¹⁹F) respectively. Chemical shifts δ are referred in terms of ppm and *J-coupling* constants are given in Hz. Abbreviations for multiplicity are as follows: *s* (singlet), *d* (doublet), *t* (triplet), *m* (multiplet), *br* (broad signal). HPLC analyses and separations were performed on a SHIMADZU system with a SHIMADZU LC-6AD, CBM-20A, FRC-10A, SPC-20A, DGU-20A λ₃. High resolution FAB mass spectra was calibrated with Ultramark 1621® prior to data acquisition.
**Premix**

**Preparation of f\textsubscript{14}-Fmoc-Ala-OH**

A solution of f\textsubscript{14}-Fmoc-OSu (5.50 g, 7.54 mmol) in MeCN (60 mL) was added to a solution of L-alanine (1.1 g, 12.3 mmol) in 10% aq. Na\textsubscript{2}CO\textsubscript{3} (20 mL) slowly at room temperature. The reaction mixture was stirred for 2 h. The reaction acidified with 1.0 M HCl aq. to pH 2.0. The organic layer was extracted with diethyl ether, dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated. The residue was purified by silica gel chromatography (CHCl\textsubscript{3}/MeOH = 5:1) to give f\textsubscript{14}-Fmoc-Ala-OH (5.3 g, 98%).

Pale yellow solid; mp 95.7-96.5 °C, \textsuperscript{1}H NMR (270 MHz, CDCl\textsubscript{3}) δ 1.49 (d, J = 7.0 Hz, 3H) 2.31-2.51 (m, 4H), 2.96-3.02 (m, 4H), 4.16-4.21 (m, 1H), 4.39-4.48 (m, 3H), 5.28 (d, J = 7.0 Hz, 1H), 7.25 (d, J = 7.3 Hz, 2H), 7.42 (s, 2H), 7.68 (d, J = 8.1 Hz, 2H); \textsuperscript{19}F NMR (466 MHz, CDCl\textsubscript{3}) δ -80.4 (6F), -115.4 (4F), -127.6 (4F); HRMS [FAB+] m/z calcd for C\textsubscript{28}H\textsubscript{23}NO\textsubscript{4}F\textsubscript{14} 704.1482, found: 704.1456.

**Preparation of f\textsubscript{18}-Fmoc-Phe-OH**

A solution of f\textsubscript{18}-Fmoc-OSu (5.50 g, 6.01 mmol) in 1,4-dioxane (40 mL) was added to a solution of L-phenylalanine (1.5 g, 9.02 mmol) in 10% aq. Na\textsubscript{2}CO\textsubscript{3} (40 mL) slowly at 0 °C. The reaction mixture was warmed to room temperature and was stirred for 2 h. The reaction acidified with 1.0 M HCl aq. to pH 2.0. The organic layer was extracted with diethyl ether, dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated. The residue was purified by silica gel chromatography (CHCl\textsubscript{3}/MeOH = 5:1) to give f\textsubscript{18}-Fmoc-Phe-OH (5.12 g, 95%).

White solid; mp 122.2-123.1 °C; \textsuperscript{1}H NMR (270 MHz, CDCl\textsubscript{3}) δ 2.33-2.50 (m, 4H), 2.94-3.00 (m, 4H), 3.09-3.25 (m, 2H), 4.13-4.17 (m, 1H), 4.33-4.47 (m, 2H), 4.66-4.73 (m, 1H), 5.21 (d, J= 7.8 Hz, 1H), 7.12 (d, J= 6.5 Hz, 2H), 7.23-7.26 (m, 5H), 7.39 (d, J= 3.8 Hz, 2H), 7.67 (d, J= 8.6 Hz, 2H); \textsuperscript{19}F NMR (466 MHz, CDCl\textsubscript{3}) δ -80.8 (6F), -114.7 (4F), -124.2 (4F), -125.9 (4F); HRMS [FAB+] m/z calcd for C\textsubscript{36}H\textsubscript{27}NO\textsubscript{4}F\textsubscript{18} 880.1731, found: 880.1685.

**f\textsubscript{26}-Fmoc-Leu-OH**

The same procedure employed above for compound f\textsubscript{18}-Fmoc-Phe-OH was repeated using a solution of f\textsubscript{26}-Fmoc-OSu (861.0 mg, 6.56 mmol) in 1,4-dioxane (30 mL) and a solution of
L-leucine (4.5 g, 4.37 mmol) in 10% aq. Na₂CO₃ (30 mL). The residue was purified by silica gel chromatography (CHCl₃/MeOH = 5:1) to give f₂₆-Fmoc-Leu-OH (4.13 g, 89%).

White solid; mp 134.5-135.4 °C; ¹H NMR (270 MHz, CDCl₃) δ 0.97 (d, J= 5.4 Hz, 6H), 1.59-1.76 (m, 3H), 2.32-2.45 (m, 4H), 2.96-3.02 (m, 4H), 4.17-4.22 (m, 1H), 4.39-4.44 (m, 3H), 5.11 (d, J= 8.3 Hz, 1H), 7.24 (d, J= 7.3 Hz, 2H), 7.43 (s, 2H), 7.67 (d, J= 8.1 Hz, 2H); ¹⁹F NMR (466 MHz, CDCl₃) δ -80.6 (6F), -114.4 (4F), -121.7 (4F), -122.7 (4F), -123.3 (4F), -125.9 (4F); HRMS [FAB+] m/z calcd for C₃₇H₂₉NO₄F₂₆ 1046.1760, found: 1046.1747.

Mixture Synthesis

Three-component mixture of f₁₄-Fmoc-Ala-Ala-benzyl ester, f₁₈-Fmoc-Phe-Ala-benzyl ester, and f₂₆-Fmoc-Leu-Ala-benzyl ester

f₁₄-Fmoc-Ala-OH (560.0 mg, 0.79 mmol), f₁₈-Fmoc-Phe-OH (714.4 mg, 0.79 mmol), f₂₆-Fmoc-Leu-OH (832.0 mg, 0.79 mmol) were mixed and dissolved in DMF (20 mL). The solution was HOBt•H₂O (438.8 mg, 2.86 mmol) and HBTU (1086 mg, 2.86 mmol) were added separately. After stirring for 5 min, the reaction mixture was added to Ala-OBn (1.01 g, 2.86 mmol), DIEA (974 µl, 5.72 mmol) were added separately. The reaction mixture was stirred for 24 h at room temperature. After the addition of 1.0 M HCl aq. and then diluted with ethyl acetate. The organic layer was washed with H₂O, saturated aq. NaHCO₃ and brine, dried over Na₂SO₄ and concentrated. The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 20:1) to give the title compound (2.4 g, 95% based on the average molecular weight of the mixture).

Three-component mixture of f₁₄-Fmoc-Ala-Val-benzyl ester, f₁₈-Fmoc-Phe-Val-benzyl ester, and f₂₆-Fmoc-Leu-Val-benzyl ester

The same procedure employed above for compound three-component mixture of f₁₄-Fmoc-Ala-Ala-benzyl ester, f₁₈-Fmoc-Phe-Ala-benzyl ester, and f₂₆-Fmoc-Leu-Ala-benzyl ester was repeated using f₁₄-Fmoc-Ala-OH (420.0 mg, 0.60 mmol), f₁₈-Fmoc-Phe-OH (536.0 mg, 0.60 mmol), f₂₆-Fmoc-Leu-OH (624.0 mg, 0.60 mmol), HOBt•H₂O (329.1 mg, 2.15 mmol), HBTU (815.2 mg, 2.15 mmol), Val-OBn (523.9 mg, 2.15 mmol), and DIEA (730 µl, 4.30 mmol) in DMF (20 mL). The crude residue was
purified by silica gel chromatography (CHCl₃/MeOH = 20:1) to give the title compound (1.9 g, 98% based on the average molecular weight of the mixture).

Three-component mixture of f₁₄-Fmoc-Ala-Ala-OH, f₁₈-Fmoc-Phe-Ala-OH, and f₂₆-Fmoc-Leu-Ala-OH
The mixture of f₁₄-Fmoc-Ala-Ala-benzyl ester, f₁₈-Fmoc-Phe-Ala-benzyl ester, and f₂₆-Fmoc-Leu-Ala-benzyl ester (300 mg, 0.10 mmol based on molecular weight of the mixture) and Pd/C (2.20 mg, 0.02 mmol) in THF/MeOH (8 mL, 1/1 v/v) was stirred at room temperature for 3 h under H₂ balloon. The catalyst was removed by filtration through a pad of Celite® and washed with ethyl acetate. The filtrate was concentrated. The residue was purified by silica gel chromatography (CHCl₃/MeOH = 5:1) to give the title compound (291.0 mg, quantitative yield based on molecular weight of the mixture).

Three-component mixture of f₁₄-Fmoc-Ala-Val-OH, f₁₈-Fmoc-Phe-Val-OH, and f₂₆-Fmoc-Leu-Val-OH
The same procedure employed above for compound three-component mixture of f₁₄-Fmoc-Ala-Ala-OH, f₁₈-Fmoc-Phe-Ala-OH, and f₂₆-Fmoc-Leu-Ala-OH was repeated using three-component mixture of f₁₄-Fmoc-Ala-Val-benzyl ester, f₁₈-Fmoc-Phe-Val-benzyl ester, and f₂₆-Fmoc-Leu-Val-benzyl ester (300 mg, 0.09 mmol based on molecular weight of the mixture) and Pd/C (2.2 mg, 0.02 mmol) in THF/MeOH (8 mL, 1/1 v/v). The residue was purified by silica gel chromatography (CHCl₃/MeOH = 5:1) to give the title compound (290 mg, quantitative yield based on molecular weight of the mixture).

Three-component mixture of f₁₄-Fmoc-Ala-Ala-Ala benzyl ester, f₁₈-Fmoc-Phe-Ala-Ala benzyl ester, and f₂₆-Fmoc-Leu-Ala-Ala benzyl ester (Group A)
A solution of the mixture of f₁₄-Fmoc-Ala-Ala-OH, f₁₈-Fmoc-Phe-Ala-OH, and f₂₆-Fmoc-Leu-Ala-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture) in DMF (10 mL) was treated with HOBT·H₂O (95.4 mg, 0.62 mmol) and HBTU (236.2 mg, 0.62 mmol) at room temperature. After 5 min, Ala-OBn (218.0 mg, 0.62 mmol) and DIEA (210 μL,
1.24 mmol) were sequentially added to the above solution. The reaction mixture was stirred at room temperature for 24 h. After the addition of 1.0 M HCl aq. and then diluted with ethyl acetate, the organic layer was washed with H₂O, saturated aq. NaHCO₃ and brine, dried over Na₂SO₄ and concentrated. The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 20:1) to give the title compound (568.8 mg, 97% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate; 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): \( t_R = 2.7 \) min (f₁₄-Fmoc-Ala-Ala-Ala benzyl ester), 3.4 min (f₁₈-Fmoc-Phe-Ala-Ala benzyl ester), 12.5 min (f₂₆-Fmoc-Leu-Ala-Ala benzyl ester).

Three-component mixture of f₁₄-Fmoc-Ala-Ala-Val benzyl ester, f₁₈-Fmoc-Phe-Ala-Val benzyl ester, and f₂₆-Fmoc-Leu-Ala-Val benzyl ester (Group B)
The same procedure employed above for compound Group A was repeated using three-component mixture of f₁₄-Fmoc-Ala-Ala-OH, f₁₈-Fmoc-Phe-Ala-OH, and f₂₆-Fmoc-Leu-Ala-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture), HOBtH₂O (95.4 mg, 0.62 mmol), HBTU (236.2 mg, 0.62 mmol), Val-OBn (218.0 mg, 0.62 mmol), and DIEA (210 μL, 1.24 mmol) in DMF (10 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 20:1) to give the title compound (552.6 mg, 92% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate; 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): \( t_R = 3.1 \) min (f₁₄-Fmoc-Ala-Ala-Val benzyl ester), 4.3 min (f₁₈-Fmoc-Phe-Ala-Val benzyl ester), 11.3 min (f₂₆-Fmoc-Leu-Ala-Val benzyl ester).

Three-component mixture of f₁₄-Fmoc-Ala-Ala-Leu benzyl ester, f₁₈-Fmoc-Phe-Ala-Leu benzyl ester, and f₂₆-Fmoc-Leu-Ala-Leu benzyl ester (Group C)
The same procedure employed above for compound Group A was repeated using three-component mixture of f₁₄-Fmoc-Ala-Ala-OH, f₁₈-Fmoc-Phe-Ala-OH, and f₂₆-Fmoc-Leu-Ala-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture), HOBtH₂O (95.4 mg, 0.62 mmol), HBTU (236.2 mg, 0.62 mmol), Leu-OBn (218.0 mg, 0.62 mmol), and DIEA (210 μL, 1.24 mmol) in DMF (10 mL). The crude residue was purified by
silica gel chromatography (CHCl3/MeOH = 20:1) to give the title compound (594.5 mg, 98% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate; 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): $t_R = 2.7$ min ($f_{14}$-Fmoc-Ala-Ala-Leu benzyl ester), 3.3 min ($f_{18}$-Fmoc-Phe-Ala-Leu benzyl ester), 9.7 min ($f_{26}$-Fmoc-Leu-Ala-Leu benzyl ester).

Three-component mixture of $f_{14}$-Fmoc-Ala-Val-Ala benzyl ester, $f_{18}$-Fmoc-Phe-Val-Ala benzyl ester, and $f_{26}$-Fmoc-Leu-Val-Ala benzyl ester (Group D)
The same procedure employed above for compound Group A was repeated using three-component mixture of $f_{14}$-Fmoc-Ala-Val-OH, $f_{18}$-Fmoc-Phe-Val-OH, and $f_{26}$-Fmoc-Leu-Val-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture), HOBt$\cdot$H2O (92.7 mg, 0.61 mmol), HBTU (229.5 mg, 0.61 mmol), Ala-OBn (212.7 mg, 0.61 mmol), and DIEA (204 µL, 1.22 mmol) in DMF (10 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 20:1) to give the title compound (554.3 mg, 95% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate; 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): $t_R = 3.1$ min ($f_{14}$-Fmoc-Ala-Val-Ala benzyl ester), 4.3 min ($f_{18}$-Fmoc-Phe-Val-Ala benzyl ester), 11.3 min ($f_{26}$-Fmoc-Leu-Val-Ala benzyl ester).

Three-component mixture of $f_{14}$-Fmoc-Ala-Val-Leu benzyl ester, $f_{18}$-Fmoc-Phe-Val-Leu benzyl ester, and $f_{26}$-Fmoc-Leu-Val-Leu benzyl ester (Group E)
The same procedure employed above for compound Group A was repeated using three-component mixture of $f_{14}$-Fmoc-Ala-Val-OH, $f_{18}$-Fmoc-Phe-Val-OH, and $f_{26}$-Fmoc-Leu-Val-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture), HOBt$\cdot$H2O (92.7 mg, 0.61 mmol), HBTU (229.5 mg, 0.61 mmol), Leu-OBn (238.1 mg, 0.61 mmol), and DIEA (204 µL, 1.22 mmol). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 20:1) to give the title compound (571.1 mg, 94% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate; 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): $t_R = 2.8$ min ($f_{14}$-Fmoc-Ala-Val-Leu benzyl ester), 3.7 min ($f_{18}$-Fmoc-Phe-Val-Leu benzyl ester), 10.5
min (f_{26}-Fmoc-Leu-Val-Leu benzyl ester).

Three-component mixture of f_{14}-Fmoc-Ala-Val-Met methyl ester, f_{18}-Fmoc-Phe-Val-Met methyl ester, and f_{26}-Fmoc-Leu-Val-Val-Met methyl ester (Group F)

The same procedure employed above for compound Group A was repeated using three-component mixture of f_{14}-Fmoc-Ala-Val-OH, f_{18}-Fmoc-Phe-Val-OH, and f_{26}-Fmoc-Leu-Val-OH (500.0 mg, 0.17 mmol based on molecular weight of the mixture), HOBt\(\overline{H}_2O\) (92.7 mg, 0.61 mmol), HBTU (229.5 mg, 0.61 mmol), Met-OMe (238.1 mg, 0.61 mmol), and DIEA (204 \(\mu\)L, 1.22 mmol) in DMF (10 mL). The crude residue was purified by silica gel chromatography (CHCl\(_3\)/MeOH = 20:1) to give the title compound (494.4 mg, 86% based on molecular weight of the mixture). Fluorous analytical HPLC (flow rate: 1.0 ml/min; 0 to 30 min: 80% MeCN to 100% MeCN; 30 to 60 min: 100% MeCN): \(t_R = 2.7\) min (f_{14}-Fmoc-Ala-Val-Met methyl ester), 3.2 min (f_{18}-Fmoc-Phe-Val-Met methyl ester), 8.5 min (f_{26}-Fmoc-Leu-Val-Met methyl ester).

Demix

Group A

Preparative Separation of Group A. The preparative separation of Group A was carried out on a SHIMADZU HPLC system. Group A was dissolved in THF (2.0 mL) and filtered through a syringe filter (0.45 \(\mu\)m pore size) prior to injection. The separation was carried out on a FluoroFlash® HPLC Columns, 20 mm i.d., 250 mm length. The separation was achieved by gradient elution with 80 % MeCN/H\(_2\)O up to 100% MeCN in 30.0 minutes, followed by isocratic elution with 100% MeCN over 120 minutes with a constant flow rate of 4.0 mL/min. A UV detector (254 nm) was used to manually identify the peaks. Group A (100 mg/mL) was injected per chromatographic run. The yield of demixing over two injections was 96% and the following three compounds were isolated: f_{14}-Fmoc-Ala-Ala-Ala benzyl ester (43 mg), f_{18}-Fmoc-Phe-Ala-Ala benzyl ester (63 mg), f_{26}-Fmoc-Leu-Ala-Ala benzyl ester (86 mg).

f_{14}-Fmoc-Ala-Ala-Ala benzyl ester

White solid; mp 153.8-154.6 °C; \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 1.36-1.42 (m, 9H), 2.31-2.44
(m, 4H), 2.96-3.02 (m, 4H), 4.16-4.19 (m, 1H), 4.22-4.28 (m, 1H), 4.39-4.50 (m, 3H), 4.56-4.61 (m, 1H), 5.13 (d, J= 11.9 Hz, 1H), 5.19 (d, J= 12.7 Hz, 1H), 5.44 (d, J= 7.3 Hz, 1H), 6.55-6.62 (m, 2H), 7.24 (d, J= 9.9 Hz, 2H), 7.31-7.36 (m, 5H), 7.42 (s, 2H), 7.68 (d, J= 8.1 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) δ -80.3 (6F), -115.4 (4F), -127.6 (4F); HRMS [FAB+] m/z calcd for C$_{41}$H$_{40}$N$_3$O$_6$F$_{14}$ 936.2694, found: 936.2704.

f$_{18}$-Fmoc-Phe-Ala-Ala benzyl ester
White solid; mp 171.5-172.4 °C; $^1$H NMR (270 MHz, CDCl$_3$) δ 1.30 (d, J= 6.8 Hz, 3H), 1.40 (d, J= 7.3 Hz, 3H), 2.34-2.44 (m, 4H), 2.95-3.02 (m, 4H), 3.07-3.11 (m, 2H), 4.10-4.15 (m, 1H), 4.30-4.46 (m, 4H) 4.52-4.58 (m, 1H), 5.13 (d, J= 11.9 Hz, 1H), 5.19 (d, J= 12.7 Hz, 1H), 5.35 (d, J= 6.8 Hz, 1H), 6.38 (d, J= 5.9 Hz, 1H), 6.45 (d, J= 7.0 Hz, 1H), 7.13-7.16 (m, 2H), 7.23-7.40 (m, 12H), 7.68 (d, J= 7.8 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) δ -80.6 (6F), -114.5 (4F), -124.1 (4F), -125.8 (4F); HRMS [FAB+] m/z calcd for C$_{52}$H$_{45}$N$_3$O$_5$F$_{18}$ 1112.2943, found: 1112.2969.

f$_{26}$-Fmoc-Leu-Ala-Ala benzyl ester
White solid; mp 179.9-181.0 °C; $^1$H NMR (270 MHz, CDCl$_3$) δ 0.94 (d, J= 5.4 Hz, 6H), 1.36-1.42 (m, 6H), 1.50-1.70 (m, 3H), 2.35-2.48 (m, 4H), 2.96-3.02 (m, 4H), 4.15-4.20 (m, 2H), 4.36-4.59 (m, 3H), 4.45-4.59 (m, 1H), 5.16-5.22 (m, 3H), 6.48 (d, J= 6.5 Hz, 2H), 7.32-7.43 (m, 9H), 7.68 (d, J= 7.2 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) δ -80.6 (6F), -114.4 (4F), -121.6 (4F), -122.6 (4F), -123.2 (4F), -125.9 (4F); HRMS [FAB+] m/z calcd for C$_{52}$H$_{46}$N$_3$O$_6$F$_{26}$ 1278.2971, found: 1278.3009.

Group B
The preparative separation of Group B was carried out in the same manner as Group A. Group B (150 mg/mL) was injected per chromatographic run. The yield of the demixing over two injections was 96% yield and the following three compounds were isolated: f$_{14}$-Fmoc-Ala-Ala-Val benzyl ester (82 mg), f$_{18}$-Fmoc-Phe-Ala-Val benzyl ester (100 mg), f$_{26}$-Fmoc-Leu-Ala-Val benzyl ester (106 mg).
White solid; mp 156.2-157.1 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.84-0.90 (m, 6H), 1.38 (d, $J$= 6.5 Hz, 6H), 2.1-2.21 (m, 1H), 2.34-2.47 (m, 4H), 2.96-3.02 (m, 4H), 4.11-4.27 (m, 2H), 4.39-4.56 (m, 4H), 5.13 (d, $J$= 11.9 Hz, 1H), 5.21 (d, $J$= 12.7 Hz, 1H), 5.38 (d, $J$= 6.5 Hz, 1H), 6.47 (d, $J$= 7.8 Hz, 2H), 7.23-7.26 (m, 2H), 7.35 (s, 5H), 7.42 (s, 2H), 7.68 (d, $J$= 8.1 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB+] m/z calcd for C$_{43}$H$_{44}$N$_3$O$_6$F$_{14}$ 964.3007, found: 964.3029.

f$_{18}$-Fmoc-Phe-Ala-Val benzyl ester
White solid; mp 145.0-145.8 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.84-0.91 (m, 6H), 1.31 (d, $J$= 6.8 Hz, 3H), 2.12-2.22 (m, 1H), 2.34-2.47 (m, 4H), 2.95-3.09 (m, 6H), 4.09-4.14 (m, 1H), 4.27-4.33 (m, 1H), 4.40-4.56 (m, 4H), 5.10 (d, $J$= 12.4 Hz, 1H), 5.20 (d, $J$= 11.8 Hz, 1H), 5.41 (d, $J$= 7.3 Hz, 1H), 6.55 (d, $J$= 7.3 Hz, 2H), 7.14-7.16 (s, 2H), 7.20-7.40 (m, 12H), 7.67 (d, $J$= 8.1 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.6 (6F), -114.5 (4F), -124.1 (4F), -125.8 (4F); HRMS [FAB+] m/z calcd for C$_{51}$H$_{48}$N$_3$O$_6$F$_{18}$ 1140.3256, found: 1140.3217.

f$_{26}$-Fmoc-Leu-Ala-Val benzyl ester
White solid; mp 175.0-176.0 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.83-0.94 (m, 12H), 1.37 (d, $J$= 7.3 Hz, 3H), 1.53-1.67 (m, 3H), 2.14-2.22 (m, 1H), 2.32-2.52 (m, 4H), 2.96-3.02 (m, 4H), 4.17-4.19 (m, 2H), 4.43-4.55 (m, 4H), 5.09-5.25 (m, 3H), 6.53 (d, $J$= 7.3 Hz, 2H), 7.23-7.26 (m, 2H), 7.34 (s, 5H), 7.42 (d, $J$= 5.9 Hz, 2H), 7.68 (d, $J$= 7.3 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.6 (6F), -114.3 (4F), -121.6 (4F), -122.6 (4F), -123.2 (4F), -126.0 (4F); HRMS [FAB+] m/z calcd for C$_{51}$H$_{50}$N$_3$O$_6$F$_{26}$ 1306.3284, found: 1306.3319.

**Group C**
The preparative separation of Group C was carried out in the same manner as Group A. Group C (150 mg/mL) was injected per chromatographic run. The yield of demixing over two injections was 99% yield and the following three compounds were isolated: f$_{14}$-Fmoc-Ala-Ala-Leu benzyl ester (84.3 mg), f$_{18}$-Fmoc-Phe-Ala-Leu benzyl ester (99.2 mg), f$_{26}$-Fmoc-Leu-Ala-Leu benzyl ester (113.5 mg).
White solid; mp 170.1-170.9 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.89 (d, $J$= 4.6 Hz, 6H), 1.36-1.38 (m, 6H), 1.54-1.65 (m, 3H), 2.38-2.47 (m, 4H), 2.96-3.10 (m, 4H), 4.16-4.30 (m, 2H), 4.38-4.54 (m, 3H), 4.59-4.65 (m, 1H), 5.11 (d, $J$= 12.7 Hz, 1H), 5.18 (d, $J$= 12.4 Hz, 1H), 5.43 (d, $J$= 7.3 Hz, 1H), 6.44 (d, $J$= 8.6 Hz, 1H), 6.60 (d, $J$= 7.0 Hz, 1H), 7.23-7.26 (m, 2H), 7.34 (s, 5H), 7.42 (s, 2H), 7.67 (d, $J$= 8.1 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB+] $m/z$ calcd for C$_{44}$H$_{46}$N$_3$O$_6$F$_{14}$ 978.3163, found: 978.3136.

f$_{18}$-Fmoc-Phe-Ala-Leu benzyl ester

White solid; mp 141.5-142.4 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.90-0.91 (m, 6H), 1.30 (d, $J$= 6.8 Hz, 3H), 1.53-1.68 (m, 3H), 2.31-2.51 (m, 4H), 2.95-3.10 (m, 6H), 4.10-4.14 (m, 1H), 4.31-4.44 (m, 4H), 4.57-4.60 (m, 1H), 5.11 (d, $J$= 12.4 Hz, 1H), 5.18 (d, $J$= 11.8 Hz, 1H), 5.33 (d, $J$= 8.1 Hz, 1H), 6.31 (d, $J$= 7.8 Hz, 1H), 6.43 (d, $J$= 7.3 Hz, 1H), 7.13-7.16 (m, 2H), 7.23-7.40 (m, 12H), 7.68 (d, $J$= 7.8 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.8 (6F), -114.5 (4F), -124.1 (4F), -125.8 (4F); HRMS [FAB+] $m/z$ calcd for C$_{52}$H$_{50}$N$_3$O$_6$F$_{18}$ 1154.3412, found: 1154.3413.

f$_{26}$-Fmoc-Leu-Ala-Leu benzyl ester

White solid; mp 171.9-172.8 °C; $^1$H NMR (270 MHz, CDCl$_3$) $\delta$ 0.88-0.94 (m, 12H), 1.36 (d, $J$= 7.3 Hz, 3H), 1.54-1.65 (m, 6H), 2.39-2.48 (m, 4H), 2.95-3.01 (m, 4H), 4.16-4.20 (m, 2H), 4.31-4.52 (m, 3H), 4.59-4.65 (m, 1H), 5.11 (d, $J$= 12.7 Hz, 1H), 5.18 (d, $J$= 12.4 Hz, 1H), 5.27 (d, $J$= 8.6 Hz, 1H), 6.45 (d, $J$= 7.3 Hz, 1H), 6.55 (d, $J$= 7.3 Hz, 1H), 7.23-7.26 (m, 2H), 7.34 (s, 5H), 7.42 (d, $J$= 5.7 Hz, 2H), 7.67 (d, $J$= 8.1 Hz, 2H); $^{19}$F NMR (466 MHz, CDCl$_3$) $\delta$ -80.6 (6F), -114.3 (4F), -121.7 (4F), -122.6 (4F), -123.2 (4F), -125.9 (4F); HRMS [FAB+] $m/z$ calcd for C$_{53}$H$_{52}$N$_3$O$_6$F$_{26}$ 1320.3441, found: 1320.3402.

**Group D**

The preparative separation of Group D was carried out in the same manner as Group A. Group D (150 mg/mL) was injected per chromatographic run. The yield of demixing over two injections was 97% and the following three compounds were isolated:
**f_{14}-Fmoc-Ala-Val-Ala benzyl ester** (82.2 mg), **f_{18}-Fmoc-Phe-Val-Ala benzyl ester** (97.3 mg), **f_{26}-Fmoc-Leu-Val-Ala benzyl ester** (111.4 mg).

**f_{14}-Fmoc-Ala-Val-Ala benzyl ester**
White solid; mp 171.2-172.3 °C; \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 0.90-0.94 (m, 6H), 1.40-1.42 (m, 6H), 2.04-2.19 (m, 1H), 2.37-2.51 (m, 4H), 2.95-3.02 (m, 4H), 4.16-4.26 (m, 3H), 4.39 (d, \(J=6.8\) Hz, 2H), 4.56-4.66 (m, 1H), 5.12 (d, \(J=10.0\) Hz, 1H), 5.19 (d, \(J=11.8\) Hz, 1H), 5.41 (d, \(J=6.5\) Hz, 1H), 6.35 (d, \(J=7.3\) Hz, 1H), 6.57 (d, \(J=8.6\) Hz, 1H), 7.23-7.26 (m, 2H), 7.33-7.35 (m, 5H), 7.42 (s, 2H), 7.67 (d, \(J=8.1\) Hz, 2H); \(^{19}\)F NMR (466 MHz, CDCl\(_3\)) \(\delta\) -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB+] \(m/z\) calcld for C\(_{43}\)H\(_{44}\)N\(_3\)O\(_6\)F\(_{14}\) 964.3007, found: 964.2957.

**f_{18}-Fmoc-Phe-Val-Ala benzyl ester**
White solid; mp 174.2-175.2 °C; \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 0.82-0.88 (m, 6H), 1.40 (d, \(J=6.5\) Hz, 3H), 2.03-2.09 (m, 1H), 2.38-2.51 (m, 4H), 2.95-3.09 (m, 6H), 4.13-4.21 (m, 2H), 4.30-4.42 (m, 3H), 4.53-4.58 (m, 1H), 5.12 (d, \(J=11.8\) Hz, 1H), 5.19 (d, \(J=11.8\) Hz, 1H), 5.42 (d, \(J=7.8\) Hz, 1H), 6.34 (d, \(J=7.3\) Hz, 1H), 6.46 (d, \(J=6.8\) Hz, 1H), 7.17-7.40 (m, 14H), 7.67 (d, \(J=8.1\) Hz, 2H); \(^{19}\)F NMR (466 MHz, CDCl\(_3\)) \(\delta\) -80.8 (6F), -114.5 (4F), -124.1 (4F), -125.8 (4F); HRMS [FAB+] \(m/z\) calcld for C\(_{51}\)H\(_{48}\)N\(_3\)O\(_6\)F\(_{18}\) 1140.3256, found: 1140.3287.

**f_{26}-Fmoc-Leu-Val-Ala benzyl ester**
White solid; mp 177.2-178.1 °C; \(^1\)H NMR (270 MHz, CDCl\(_3\)) \(\delta\) 0.90-0.94 (m, 12H), 1.40 (d, \(J=6.5\) Hz, 3H), 1.54-1.71 (m, 3H), 2.04-2.09 (m, 1H), 2.38-2.45 (m, 4H), 2.95-3.01 (m, 4H), 4.14-4.27 (m, 3H), 4.36-4.41 (m, 2H), 4.58-4.64 (m, 1H), 5.12 (d, \(J=11.8\) Hz, 1H), 5.19 (d, \(J=12.4\) Hz, 1H), 5.28 (d, \(J=8.6\) Hz, 1H), 6.38 (d, \(J=7.3\) Hz, 1H), 6.59 (d, \(J=7.8\) Hz, 1H), 7.22-7.26 (m, 2H), 7.34 (s, 5H), 7.41 (d, \(J=4.6\) Hz, 2H), 7.67 (d, \(J=8.1\) Hz, 2H); \(^{19}\)F NMR (466 MHz, CDCl\(_3\)) \(\delta\) -80.6 (6F), -114.4 (4F), -121.7 (4F), -122.7 (4F), -123.2 (4F), -126.0 (4F); HRMS [FAB+] \(m/z\) calcld for C\(_{52}\)H\(_{50}\)N\(_3\)O\(_6\)F\(_{26}\) 1306.3284, found: 1306.3307.

**Group E**
The preparative separation of Group E was carried out in the same manner as Group A. Group E (150 mg/mL) was injected per chromatographic run. The yield of demixing over two injections was 90% and the following three compounds were isolated: 

**f₄-Fmoc-Ala-Val-Leu benzyl ester** (76.8 mg), **f₁₈-Fmoc-Phe-Val-Leu benzyl ester** (90.2 mg), **f₂₆-Fmoc-Leu-Val-Leu benzyl ester** (102.9 mg).

**f₁₄-Fmoc-Ala-Val-Leu benzyl ester**

White solid; mp 165.7-166.8 °C; ¹H NMR (270 MHz, CDCl₃) δ 0.89-0.93 (m, 12H), 1.38 (d, J = 6.5 Hz, 3H), 1.54-1.68 (m, 3H), 2.04-2.14 (m, 1H), 2.34-2.51 (m, 4H), 2.96-3.02 (m, 4H), 4.13-4.26 (m, 3H), 4.39 (d, J = 6.8 Hz, 2H), 4.62-4.65 (m, 1H), 5.12 (d, J = 11.8 Hz, 1H), 5.19 (d, J = 12.7 Hz, 1H), 5.42 (d, J = 6.8 Hz, 1H), 6.20 (d, J = 7.8 Hz, 1H), 6.55 (d, J = 8.6 Hz, 1H), 7.23-7.26 (m, 2H), 7.33 (s, 5H), 7.42 (s, 2H), 7.67 (d, J = 7.8 Hz, 2H); ¹⁹F NMR (466 MHz, CDCl₃) δ -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB+] m/z calcd for C₄₆H₅₀N₃O₆F₁₄ 1006.3476, found: 1006.3470.

**f₁₈-Fmoc-Phe-Val-Leu benzyl ester**

White solid; mp 163.0-164.1 °C; ¹H NMR (270 MHz, CDCl₃) δ 0.82-0.90 (m, 12H), 1.54-1.67 (m, 3H), 2.04-2.06 (m, 1H), 2.31-2.51 (m, 4H), 2.95-3.08 (m, 4H), 3.06-3.08 (m, 2H), 4.10-4.15 (m, 1H), 4.21-4.24 (m, 1H), 4.28-4.34 (m, 1H), 4.40-4.46 (m, 2H), 4.59-4.63 (m, 1H), 5.12 (d, J = 11.8 Hz, 1H), 5.17 (d, J = 11.8 Hz, 1H), 5.38 (d, J = 7.8 Hz, 1H), 6.15 (d, J = 7.8 Hz, 2H); ¹⁹F NMR (466 MHz, CDCl₃) δ -80.8 (6F), -114.6 (4F), -124.2 (4F), -125.9 (4F); HRMS [FAB+] m/z calcd for C₅₄H₅₄N₃O₆F₁₈ 1182.7725, found: 1182.7756.

**f₂₆-Fmoc-Leu-Val-Leu benzyl ester**

White solid; mp 171.1-171.9 °C; ¹H NMR (270 MHz, CDCl₃) δ 0.88-0.92 (s, 18H), 1.47-1.72 (m, 6H), 2.04-2.10 (m, 1H), 2.31-2.52 (m, 4H), 2.95-3.01 (m, 4H), 4.14-4.24 (m, 3H), 4.36-4.41 (m, 2H), 4.60-4.68 (m, 1H), 5.12 (d, J = 12.4 Hz, 1H), 5.17 (d, J = 12.7 Hz, 1H), 5.27 (d, J = 7.3 Hz, 1H), 6.19 (d, J = 7.8 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 7.23-7.26 (m, 2H), 7.33 (s, 5H), 7.40-7.42 (m, 2H), 7.67 (d, J = 7.8 Hz, 2H); ¹⁹F NMR (466 MHz, CDCl₃) δ -80.6
(6F), -114.4 (4F), -121.7 (4F), -122.7 (4F), -123.2 (4F), -126.0 (4F); HRMS [FAB] m/z calcd for C_{54}H_{56}N_{3}O_{6}F_{26} 1348.3754, found: 1348.3715.

**Group F**

The preparative separation of Group F was carried out in the same manner as Group A. Group F (150 mg/mL) was injected per chromatographic run. The yield of demixing over two injections was 96% and the following three compounds were isolated: 

*f_{14}*-Fmoc-Ala-Val-Met methyl ester (81.2 mg), *f_{18}*-Fmoc-Phe-Val-Met methyl ester (96.2 mg), *f_{26}*-Fmoc-Leu-Val-Met methyl ester (110.5 mg).

**f_{14}*-Fmoc-Ala-Val-Met methyl ester**

White solid; mp 182.1-183.1 °C; ^1H NMR (270 MHz, CDCl\textsubscript{3}) δ 0.93-0.97 (m, 6H), 1.37-1.45 (d, J = 6.5 Hz, 3H), 1.98-2.17 (m, 6H), 2.31-2.50 (m, 6H), 2.96-3.02 (m, 4H), 3.76 (s, 3H), 4.14-4.19 (m, 1H), 4.24-4.29 (m, 2H), 4.40 (d, J = 6.5 Hz, 2H), 4.66-4.70 (m, 1H), 5.38 (d, J = 7.3 Hz, 1H), 6.54-6.60 (m, 2H), 7.23-7.26 (m, 2H), 7.42 (s, 2H), 7.68 (d, J = 7.3 Hz, 2H); ^19F NMR (466 MHz, CDCl\textsubscript{3}) δ -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB] m/z calcd for C_{39}H_{44}N_{3}O_{6}F_{14}S 948.2727, found: 948.2736.

**f_{18}*-Fmoc-Phe-Val-Met methyl ester**

White solid; mp 161.9-162.8 °C; ^1H NMR (270 MHz, CDCl\textsubscript{3}) δ 0.85-0.92 (m, 6H), 2.04-2.25 (m, 3H), 2.31-2.61 (m, 9H), 2.95-3.10 (m, 4H), 3.11-3.13 (m, 2H), 3.75 (s, 3H), 4.10-4.15 (m, 1H), 4.22-4.45 (m, 4H), 4.59-4.68 (m, 1H), 5.36 (d, J = 6.8 Hz, 1H), 6.43-6.60 (m, 2H), 7.12-7.40 (m, 9H) 7.68 (d, J = 7.3Hz, 2H); ^19F NMR (466 MHz, CDCl\textsubscript{3}) δ -80.8 (6F), -114.6 (4F), -124.1 (4F), -125.8 (4F); HRMS [FAB+] m/z calcd for C_{47}H_{48}N_{3}O_{6}F_{18}S 1124.2976, found: 1124.3014.

**f_{26}*-Fmoc-Leu-Val-Met methyl ester**

White solid; mp 187.6-188.5 °C; ^1H NMR (270 MHz, CDCl\textsubscript{3}) δ 0.93-0.96 (m, 12H), 1.54-1.68 (m, 3H), 2.03-2.17 (m, 6H), 2.47-2.52 (m, 6H), 2.95-3.01 (m, 4H), 3.75 (s, 3H), 4.14-4.16 (m, 1H), 4.24-4.30 (m, 1H), 4.36-4.42 (m, 2H), 4.66-4.74 (m, 1H), 5.33 (d, J = 7.8 Hz, 1H), -80.3 (6F), -115.3 (4F), -127.5 (4F); HRMS [FAB] m/z calcd for C_{54}H_{56}N_{3}O_{6}F_{26} 1348.3754, found: 1348.3715.
Hz, 1H), 6.61-6.68 (m, 3H), 7.25 (d, J= 7.0 Hz, 2H), 7.42 (d, J= 4.6 Hz, 2H), 7.67 (d, J= 7.3 Hz, 2H); 19F NMR (466 MHz, CDCl3) δ -80.6 (6F), -114.3 (4F), -121.6 (4F), -122.7 (4F), -123.2 (4F), -125.9 (4F); HRMS [FAB+] m/z calcd for C_{48}H_{50}N_{3}O_{6}F_{26}S 1290.3005, found: 1290.3042.

**Detag**

**Ala-Ala-Ala benzyl ester**

Diethylamine (DEA) (1 mL) was added to a solution of f14-Fmoc-Ala-Ala-Ala benzyl ester (70.0 mg, 0.075 mmol) in MeCN (2 mL), and the reaction mixture was stirred at room temperature for 30 min. After concentration in vacuo, the reaction mixture was azeotroped to dryness with MeCN (3 x 3 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (22.8 mg, 95%).

Colorless oil; 1H NMR (270 MHz, CDCl3) δ 1.32-1.43 (m, 9H), 1.59 (s, 2H) 3.45-3.53 (m, 1H), 4.42-4.63 (m, 2H), 5.14 (d, J= 12.4 Hz, 1H), 5.20 (d, J= 11.8 Hz, 1H), 6.81 (d, J= 6.8 Hz, 1H), 7.36 (s, 5H), 7.71 (d, J= 6.5 Hz, 1H).

**Phe-Ala-Ala benzyl ester**

The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f18-Phe-Ala-Ala benzyl ester (100.0 mg, 0.075 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (39.1 mg, quant).

Colorless oil; 1H NMR (270 MHz, CDCl3) δ 1.35 (d, J= 7.3 Hz, 3H), 1.42 (d, J= 7.3 Hz, 3H), 1.62 (bs, 2H), 2.67-2.79 (m, 1H), 3.20-3.27 (m, 1H), 3.60-3.65 (m, 1H), 4.45-4.64 (m, 2H), 5.13 (d, J= 12.4 Hz, 1H), 5.20 (d, J= 10.5 Hz, 1H), 6.96 (d, J= 6.8 Hz, 1H), 7.19-7.34 (m, 10H), 7.79 (d, J= 8.4 Hz, 1H); HRMS [FAB+] m/z calcd for C_{22}H_{28}N_{3}O_{4} 398.2082, found: 398.2083.

**Leu-Ala-Ala benzyl ester**

The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f26-Leu-Ala-Ala benzyl ester (80.0 mg, 0.063 mmol) and DEA (1 mL) in
MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (30.1 mg, quant).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.91-0.97 (m, 6H), 1.33-1.42 (m, 8H) 1.63-1.70 (m, 1H), 1.89 (bs, 2H), 3.39-3.43 (m, 1H), 4.44-4.62 (m, 2H), 5.17 (d, J= 11.9 Hz, 1H), 5.20 (d, J= 12.4 Hz, 1H), 6.98 (d, J= 7.3 Hz, 1H), 7.35 (s, 5H), 7.80 (d, J= 7.8 Hz, 1H); HRMS [FAB+] m/z calcd for C₁⁹H₃₀N₃O₄ 364.2238, found: 364.2265.

Ala-Ala-Val benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f₁₄-Ala-Ala-Val benzyl ester (90.0 mg, 0.093 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (31.1 mg, 95%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.84-0.90 (m, 6H), 1.34-1.39 (m, 6H), 2.00 (bs, 2H), 2.16-2.20 (m, 1H), 3.52-3.59 (m, 1H), 4.42-4.56 (m, 2H), 5.15 (d, J= 12.7 Hz, 1H), 5.20 (d, J= 11.8 Hz, 1H), 6.78 (d, J= 8.3 Hz, 1H), 7.35 (s, 5H), 7.71 (d, J= 7.3 Hz, 1H); HRMS [FAB+] m/z calcd for C₁₈H₂₈N₃O₄ 350.2082, found: 350.2078.

Phe-Ala-Val benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f₁₈-Phe-Ala-Val benzyl ester (70.0 mg, 0.061 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (24.1 mg, 92%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.86-0.95 (m, 6H), 1.35 (d, J= 7.3 Hz, 3H), 1.64 (bs, 2H), 2.17-2.24 (m, 1H), 2.68-2.77 (m, 1H), 3.22-3.29 (m, 1H), 3.61-3.66 (m, 1H), 4.44-4.57 (m, 2H), 5.13 (d, J= 12.7 Hz, 1H), 5.21 (d, J= 12.7 Hz, 1H), 6.75 (d, J= 8.4 Hz, 1H), 7.19-7.37 (m, 10H), 7.76 (d, J= 8.1 Hz, 1H); HRMS [FAB+] m/z calcd for C₂₄H₃₂N₃O₄ 426.2395, found: 426.2441.

Leu-Ala-Val benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f_{26}-Leu-Ala-Val benzyl ester (100.0 mg, 0.077 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (32.2 mg, quant).

Colorless oil; $^1$H NMR (270 MHz, CDCl$_3$) δ 0.87-0.94 (m, 12H), 1.36 (d, $J = 6.5$ Hz, 3H), 1.64-1.74 (m, 3H), 1.92 (bs, 1H), 2.16-2.20 (m, 1H), 3.36-3.40 (m, 1H), 4.51-4.63 (m, 2H), 5.11 (d, $J = 11.9$ Hz, 1H), 5.21 (d, $J = 12.7$ Hz, 1H), 7.09 (d, $J = 8.6$ Hz, 1H), 7.35 (m, 5H), 7.80 (d, $J = 7.3$ Hz, 1H); HRMS [FAB+] m/z calcd for C$_{21}$H$_{34}$N$_3$O$_4$ 392.2551, found: 392.2564.

Ala-Ala-Leu benzyl ester

The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f$_{14}$-Ala-Ala-Leu benzyl ester (90.0 mg, 0.081 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (28.5 mg, 96%).

Colorless oil; $^1$H NMR (270 MHz, CDCl$_3$) δ 0.87-0.91 (m, 6H), 1.36 (t, $J = 4.7$ Hz, 6H), 1.53-1.68 (m, 3H), 2.06 (bs, 2H), 3.51 (q, $J = 5.3$ Hz, 1H), 4.45-4.63 (m, 2H), 5.12 (d, $J = 11.9$ Hz, 1H), 5.15 (d, $J = 12.4$ Hz, 1H), 6.76 (d, $J = 7.8$ Hz, 1H), 7.34 (s, 5H), 7.70 (d, $J = 7.3$ Hz, 1H).

Phe-Ala-Leu benzyl ester

The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f$_{18}$-Phe-Ala-Leu benzyl ester (80.0 mg, 0.069 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (29.0 mg, 95%).

Colorless oil; $^1$H NMR (270 MHz, CDCl$_3$) δ 0.89-0.92 (m, 6H), 1.34 (d, $J = 7.3$ Hz, 3H), 1.57-1.70 (m, 3H), 1.76 (bs, 2H), 2.68-2.77 (m, 1H), 3.21-3.27 (m, 1H), 3.61-3.63 (m, 1H), 4.47-4.61 (m, 2H), 5.13 (d, $J = 12.4$ Hz, 1H), 5.18 (d, $J = 12.6$ Hz, 1H), 6.73 (d, $J = 8.1$ Hz, 1H), 7.22-7.36 (m, 10H), 7.78 (d, $J = 7.3$ Hz, 1H).

Leu-Ala-Leu benzyl ester

Leu-Ala-Leu benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f26-Leu-Ala-Leu benzyl ester (90.0 mg, 0.068 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (27.8 mg, 95%).

Ala-Val-Ala benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f14-Ala-Val-Ala benzyl ester (80.0 mg, 0.083 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (26.0 mg, 90%).

Phe-Val-Ala benzyl ester
The same method employed in the preparation of Ala-Ala-Ala benzyl ester above was followed using f18-Phe-Val-Ala benzyl ester (90.0 mg, 0.078 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl3/MeOH = 10:1) to give the title compound (29.2 mg, 87%).

Leu-Val-Ala benzyl ester
The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f26-Leu-Val-Ala benzyl ester** (100.0 mg, 0.077 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (30.1 mg, quant).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.91-0.96 (m, 12H), 1.41 (d, J= 7.3 Hz, 3H), 1.68-1.72 (m, 3H), 2.10-2.19 (m, 1H), 2.51 (bs, 2H), 3.49-3.51 (m, 1H), 4.24-4.30 (m, 1H), 4.54-4.64 (m, 1H), 5.13 (d, J= 11.9 Hz, 1H), 5.20 (d, J= 12.7 Hz, 1H), 6.87 (d, J= 5.4 Hz, 1H), 7.34 (s, 5H), 7.91 (d, J= 8.6 Hz, 1H); HRMS [FAB+] m/z calcd for C₂₁H₃₄N₃O₄ 392.2551, found: 426.2516.

**Ala-Val-Leu benzyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f14-Ala-Val-Leu benzyl ester** (100.0 mg, 0.099 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (38.0 mg, 91%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.88-0.95 (m, 12H), 1.34 (d, J= 6.8 Hz, 3H), 1.56-1.69 (m, 3H), 1.92 (bs, 2H), 2.10-2.18 (m, 1H), 3.51-3.56 (m, 1H), 4.19-4.25 (m, 1H), 4.60-4.65 (m, 1H), 5.13 (d, J= 12.4 Hz, 1H), 5.18 (d, J= 12.7 Hz, 1H), 6.56 (d, J= 7.0 Hz, 1H), 7.36 (s, 5H), 7.81 (d, J= 9.2 Hz, 1H); HRMS [FAB+] m/z calcd for C₂₁H₃₄N₃O₄ 392.2551, found: 392.2511.

**Phe-Val-Leu benzyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f18-Phe-Val-Leu benzyl ester** (100.0 mg, 0.099 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (37.6 mg, 95%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.88-0.93 (m, 12H), 1.56-1.69 (m, 5H), 2.09-2.17 (m, 1H), 2.68-2.77 (m, 1H), 3.22-3.29 (m, 1H), 3.62-3.66 (m, 1H), 4.18-4.24 (m, 1H), 4.60-4.63 (m, 1H), 5.16 (d, J= 12.7 Hz, 1H), 5.18 (d, J= 12.7 Hz, 1H), 6.37 (d, J= 7.8 Hz, 1H), 7.25-7.38 (m, 10H), 7.87 (d, J= 9.1 Hz, 1H); HRMS [FAB+] m/z calcd for C₂₇H₃₈N₃O₄
468.2864, found: 468.2836.

**Leu-Val-Leu benzyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f26-Leu-Val-Leu benzyl ester** (90.0 mg, 0.066 mmol) and DEA (1 mL) in MeCN (4 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (23.6 mg, 82%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.88-0.96 (m, 18H), 1.60-1.71 (m, 6H), 2.05-2.09 (m, 3H), 3.43-3.47 (m, 1H), 4.33-4.39 (m, 1H), 4.59-4.65 (m, 1H), 5.11 (d, J = 12.4 Hz, 1H), 5.18 (d, J = 12.7 Hz, 1H), 7.10 (d, J = 7.8 Hz, 1H), 7.33 (s, 5H), 7.90 (d, J = 9.1 Hz, 1H); HRMS [FAB+] m/z calcd for C₂₄H₄₀N₃O₄ 434.3021, found: 434.2985.

**Ala-Val-Met methyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f14-Ala-Val-Met methyl ester** (70.0 mg, 0.074 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (22.2 mg, 90%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.95-0.99 (m, 6H), 1.36 (d, J = 7.3 Hz, 3H), 1.93-2.19 (m, 8H), 2.48-2.53 (m, 2H), 3.53-3.61 (m, 1H), 3.75 (s, 3H), 4.21-4.26 (m, 1H), 4.64-4.72 (m, 1H), 6.87 (d, J = 6.5 Hz, 1H), 7.86 (d, J = 9.5 Hz, 1H); HRMS [FAB+] m/z calcd for C₁₄H₂₈N₃O₄S 334.1802, found: 334.1814.

**Phe-Val-Met methyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f18-Ala-Val-Met methyl ester** (90.0 mg, 0.080 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (27.6 mg, 84%).

Colorless oil; ¹H NMR (270 MHz, CDCl₃) δ 0.91-0.97 (m, 6H), 1.81 (bs, 2H), 1.99-2.20 (m, 6H), 2.49-2.54 (m, 2H), 2.70-2.79 (m, 1H), 3.23-3.29 (m, 1H), 3.65-3.69 (m, 1H), 3.75 (s, 3H), 4.23-4.26 (m, 1H), 4.64-4.72 (m, 1H), 6.90 (d, J = 7.8 Hz, 1H), 7.22-7.35 (m, 5H), 7.91
(d, J= 9.1 Hz, 1H); HRMS [FAB+] m/z calcd for C_{20}H_{32}N_{3}O_{4}S 410.2115, found: 410.2102.

**Leu-Val-Met methyl ester**

The same method employed in the preparation of **Ala-Ala-Ala benzyl ester** above was followed using **f_{26}-Leu-Val-Met methyl ester** (100.0 mg, 0.078 mmol) and DEA (1 mL) in MeCN (2 mL). The crude residue was purified by silica gel chromatography (CHCl₃/MeOH = 10:1) to give the title compound (29.3 mg, quant).

Colorless oil; ^1^H NMR (270 MHz, CDCl₃) δ 0.94-0.99 (m, 12H), 1.96-2.23 (m, 6H), 2.48-2.53 (m, 3H), 2.61 (bs, 2H), 3.47-3.51 (m, 1H), 3.75 (s, 3H), 4.23-4.28 (m, 1H), 4.65-4.70 (m, 1H), 6.89 (d, J= 7.3 Hz, 1H), 7.90 (d, J= 9.5 Hz, 1H); HRMS [FAB+] m/z calcd for C_{17}H_{34}N_{3}O_{4}S 376.2272, found: 376.2280.

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**References**


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**Copies of NMR Spectra**
$f_{14}$-Fmoc-Ala-Val-OBn
$f_{18}$-Fmoc-Phe-Val-OBn
$f_{26}$-Fmoc-Leu-Val-OBn

(a mixture of 3 compounds)
\( f_{14} \)-Fmoc-Ala-Val-OH
\( f_{18} \)-Fmoc-Phe-Val-OH
\( f_{26} \)-Fmoc-Leu-Val-OH

(a mixture of 3 compounds)
(a mixture of 3 compounds)
(a mixture of 3 compounds)
$f_{18}$-Fmoc-Phe-Ala-Ala-OBn
$f_{14}$-Fmoc-Ala-Val-Ala-OBn
f_{26}-Fmoc-Leu-Val-Ala-OBn
$f_{14}$-Fmoc-Ala-Val-Leu-OBn
$f_{26}$-Fmoc-Leu-Val-Met-OMe
Ala-Ala-Ala-OBn

H₂N-\text{Ala}-\text{Ala}-\text{Ala}-\text{OBn}
Phe-Val-Ala-OBn
Ala-Val-Leu-OBn