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Supplementary Information

Ligand Synthesis. Lysine monohydrochloride, di-*t*-butyl-dicarbonate and benzyl alcohol were purchased from Aldrich; D-alanine was purchased from Sigma; lithium D-lactate, *N,N*-dicyclohexylcarbodiimide (DCC) and 4-dimethylamino-pyridine (DMAP) were purchased from Fluka; 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and *N*-α-*t*-Boc-*N*-ε-acetyl-lysine were purchased from Novabiochem.

Reactions were monitored by t.l.c (type 60 F_{254}, 0.25 mm thickness) in a solvent system of methanol/chloroform (1:4, v/v) and examined under UV light (wavelength) and developed with either ninhydrin (0.2 g/100 ml ethanol) or Ce/Mo (prepared from $Ce(SO_4)_2$ (3 g), phosphomolybdic acid (7.5 g), water (150 ml) and sulfuric acid (18 M, 30 ml). Solvents were purified according to standard procedures.

Spectra were recorded at 300 K unless otherwise stated and referenced to residual protio solvent peaks. In those cases where unambiguous assignment of peaks was not obvious from examination of the one dimensional spectra, COSY spectra where used.

Electrospray mass spectra were recorded on a VG Bio-Q machine using a source temperature of 70 °C, a capillary potential of 4 kV and a cone voltage of 40 V. The eluent was a 1:1 mixture of water and acetonitrile at a flow rate of 4 $\mu l min^{-1}$.

Preparation of *t*-Boc-D-alanine. D-Alanine (10 g, 111 mmol) and di-*tert*-butyldicarbonate (27 g, 120 mmol) were dissolved in a mixture of acetonitrile (50 ml) and sodium hydroxide (3 M, 85 ml). The solution was stirred for 3 h, after which time further sodium hydroxide (3 M, 30 ml) was added so as to maintain the pH above 9.5. Stirring was continued overnight and the reaction mixture was then washed with ether (2 x 50 ml). The aqueous layer was then acidified to pH 1

with hydrochloric acid (3 M) and extracted into ethyl acetate (3 x 60 ml). The combined ethyl acetate extracts were washed with brine (80 ml), dried over anhydrous sodium sulfate and evaporated to dryness to afford a pale yellow oil. This was placed under vacuum to yield *t*-Boc-D-alanine (17 g, 82%) as an off-white waxy solid. ^{1}H NMR (500 MHz; $CDCl_3$, 310 K) δ 1.40 - 1.44 (12 H, m, Boc CH_3 and Ala CH_3), 4.21 - 4.29 (1 H, bs, Ala α), 4.90 - 5.10 (1 H, bs, NH).

Preparation of di-*t*-Boc-lysine. L-Lysine monohydrochloride (3.0 g, 16.4 mmol) and di-*tert*-butyldicarbonate (8.2 g, 37.6 mmol) were dissolved in a mixture of acetonitrile (18 ml) and sodium hydroxide (3 M, 24 ml) and the pH of the solution was adjusted to greater than 9 by the addition of further sodium hydroxide solution (3 M, 55 ml). The mixture was stirred overnight and then washed with ether (2 x 75 ml) and the aqueous layer acidified to pH 1 by the addition of hydrochloric acid (3 M, 40 ml), which resulted in a milky solution. The acidified aqueous layer was then extracted with ethyl acetate (3 x 75 ml) and the combined extracts were dried over anhydrous sodium sulfate, filtered and evaporated to dryness to afford crude di-*t*-Boc-L-lysine (4.7 g, 82%) as a pale brown glassy solid. ^{1}H NMR (500 MHz; $CDCl_3$; 283 K) δ 1.35 - 1.51 (22 H, m, Boc CH_3, Lys γ and Lys δ), 1.64 - 1.75 (1 H, m, Lys β), 1.77 - 1.88 (1 H, m, Lys β), 3.05 - 3.16 (2 H, m, Lys ε), 4.24 - 4.34 (1 H, m, Lys α), 4.72 - 4.80 (1 H, m, Boc NH), 5.33 - 5.41 (1 H, m, Boc NH), 9.50 - 10.25 (1 H, m, CO_2H).

Preparation of D-lactate benzyl ester. A solution of lithium D-lactate (1 g, 10.4 mmol) was stirred in benzyl alcohol (9 ml) containing hydrochloric acid (1 g) for 48 h. Ethyl acetate (20 ml) was added to the reaction mixture which was then washed with water (20 ml), sodium hydrogen carbonate solution (10%, 20 ml) and brine (20 ml). The organic layer was the dried over anhydrous sodium sulfate, filtered and the solvent removed under vacuum. Purification of the residue by Krugelrohr distillation (210 °C, 21 mbar) afforded D-lactate benzyl ester (0.94 g, 52%) as a clear colorless oil. ^{1}H NMR (500 MHz; $CDCl_3$) δ 1.44 (3 H, d, *J* 6.9 Hz, Lac

CH_3), 2.78 (1 H, d, *J* 5.4 Hz, OH), 4.30 - 4.35 (1 H, m, Lac α), 5.21 and 5.23 (2 H, ABq, J_{AB} 12.6 Hz, benzylic CH_2), 7.35 - 7.40 (5 H, m, aryl H).

Preparation of *t*-Boc-D-alanyl-D-lactate benzyl ester. *t*-Boc-D-alanine (560 mg, 2.96 mmol), D-lactate benzyl ester (800 mg, 4.44 mmol) were dissolved in dichloromethane (20 ml). To this was added a solution of DCC (610 mg, 2.96 mmol) and DMAP (18 mg, 0.15 mmol) in dichloromethane (5 ml) in 5 portions over a 40 min period and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was then filtered and the solvent removed under vacuum. The residue was chromatographed over silica (chloroform) to afford *t*-Boc-D-alanyl-D-lactate benzyl ester (820 mg, 79%) as a white crystalline solid. ^1H NMR (500 MHz; $CDCl_3$) δ 1.38 (3 H, d, *J* 7.2 Hz, Ala CH_3), 1.44 (9 H, s, Boc CH_3), 1.52 (3 H, d, *J* 7.2 Hz, Lac CH_3), 4.30 - 4.38 (1 H, m, Ala α), 4.92 - 5.01 (1 H, m, Boc NH), 5.12 - 5.22 (3 H, m, benzylic CH_2 and Lac α), 7.31 - 7.39 (5 H, m, aryl H).

Preparation of di-*t*-Boc-lysyl-D-alanyl-D-lactate benzyl ester. *t*-Boc-D-alanyl-D-lactate benzyl ester (420 mg, 1.20 mmol) was dissolved in dichloromethane (4 ml) and a solution of hydrochloric acid in dioxane (4 M, 4 ml) and the resulting solution was allowed to stir at room temperature for 1 h. The solvent was then removed and the last traces of hydrogen chloride were removed by the successive addition and evaporation of dichloromethane (3 x 10 ml). A solution of di-*t*-Boc-lysine (460 mg, 1.30 mmol), *N*,*N*-diisopropylethylamine (170 mg, 1.30 mmol) and HBTU (490 mg, 1.30 mmol) in dichloromethane (5 ml) was stirred for 10 min and to this was added the crude D-alanyl-D-lactate benzyl ester hydrochloride and *N*,*N*-diisopropylethylamine (550 mg, 4.25 mmol) in dichloromethane (10 ml). The resulting mixture was stirred at room temperature for 2 h and then washed with hydrochloric acid (3 M, 2 x 30 ml), sodium hydrogen carbonate solution (10%, 2 x 30 ml), brine (50 ml), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue obtained was then chromatographed over silica (chloroform, initially, then chloroform/methanol, 95:5) to afford di-*t*-Boc-

lysyl-D-alanyl-D-lactate benzyl ester (621 mg, 89%) as a white crystalline solid. ^{1}H NMR (500 MHz; $CDCl_3$) δ 1.35 - 1.40 (2 H, m, Lys γ), 1.41 (3 H, d, *J* 7.2 Hz, Ala CH_3), 1.43 - 1.46 (18 H, m, Boc CH_3), 1.47 - 1.50 (2 H, m, Lys δ), 1.53 (3 H, d, *J* 7.1 Hz, Lac CH_3), 1.60 - 1.66 (1 H, m, Lys β), 1.80 - 1.88 (1 H, m, Lys β), 3.07 - 3.15 (2 H, m, Lys ε), 4.05 - 4.11 (1 H, m, Lys α), 4.55 - 4.61 (2 H, m, Ala α and side chain Boc NH), 5.04 - 5.11 (1 H, m, Boc NH), 5.12 - 5.21 (3 H, m, Lac α and benzylic CH_2), 5.97 - 6.62 (1 H, m, Ala NH), 7.28 - 7.39 (5 H, m, aryl H).

Preparation of di-*N*-acetyl-lysyl-D-alanyl-D-lactate benzyl ester. Di-*t*-Boc-lysyl-D-alanyl-D-lactate benzyl ester (300 mg, 0.52 mmol) was dissolved in dichloromethane (4 ml) and a solution of hydrochloric acid in dioxane (4 M, 4 ml) and the resulting mixture was allowed to stir for 2 h. The solvent was then removed and the last traces of hydrogen chloride were removed by the successive addition and evaporation of dichloromethane (3 x 5 ml). The crude lysyl-D-alanyl-D-lactate benzyl ester dihydrochloride was dissolved in a mixture of dichloromethane (20 ml), *N*,*N*-diisopropylethylamine (500 mg, 3.87 mmol) and acetic anhydride (800 mg, 7.85 mmol) and stirred for 3 h. The solvent was removed under vacuum and the residue chromatographed over silica (methanol:chloroform 1:4). The major band was collected and evaporated to dryness to afford di-*N*-acetyl-lysyl-D-alanyl-D-lactate benzyl ester (186 mg, 77%) as a glassy solid. ^{1}H NMR (500 MHz; DMSO-d_6) δ 1.14 - 1.28 (5 H, m, Lys γ and Ala CH_3), 1.30 - 1.37 (2 H, m, Lys δ), 1.41 (3 H, d, *J* 7.0 Hz, Lac CH_3), 1.42 - 1.49 (1 H, m, Lys β), 1.51 - 1.59 (1 H, m, Lys β), 1.75 (3 H, s, acetyl CH_3), 1.81 (3 H, s, acetyl CH_3), 2.95 (2 H, app q, Lys ε), 4.20 - 4.32 (2 H, m, Ala α and Lys α), 5.07 (1 H, q, *J* 7.0 Hz, Lac α), 5.14 (2 H, s, benzylic CH_2), 7.30 - 7.40 (5 H, m, aryl H), 7.71 - 7.77 (1 H, m, side-chain acetyl NH), 7.87 (1 H, d, *J* 8.4 Hz, NH), 8.34 (1 H, d, *J* 7.1 Hz, NH).

Preparation of di-*N*-acetyl-lysyl-D-alanyl-D-lactic acid. Di-*N*-acetyl-lysyl-D-alanyl-D-lactate benzyl ester (165 mg, 0.36 mmol) was dissolved in absolute ethanol (10 ml) and hydrogenated for 12 h at 1 atm over 5% palladium on charcoal (10 mg).

The reaction mixture was then evacuated, filtered through celite and evaporated to dryness to afford di-*N*-acetyl-lysyl-D-alanyl-D-lactic acid (120 mg, 90%) as a white solid. ^{1}H NMR (500 MHz; DMSO-d_6) δ 1.17 - 1.26 (2 H, m, Lys γ), 1.28 (3 H, d, *J* 7.2 Hz, Ala CH_3), 1.33 - 1.37 (2 H, m, Lys δ), 1.35 (3 H, d, *J* 7.1 Hz, Lac CH_3), 1.40 - 1.49 (1 H, m, Lys β), 1.52 - 1.60 (1 H, m, Lys β), 1.76 (3 H, s, acetyl CH_3), 1.82 (3 H, s, acetyl CH_3), 2.98 (2 H, app q, Lys ε), 4.22 - 4.30 (2 H, m, Lys α and Ala α), 4.85 (1 H, q, *J* 7.0 Hz, Lac α), 7.71 - 7.77 (1 H, m, side-chain acetyl NH), 7.89 (1 H, d, *J* 8.4 Hz, NH), 8.30 (1 H, d, *J* 7.2 Hz, NH). Electrospray MS m/z: 374.1 (MH^+)