

Supplemental material:

Toward The Synthesis of Artificial Proteins: The Discovery of an Amphiphilic Helical Peptoid Assembly

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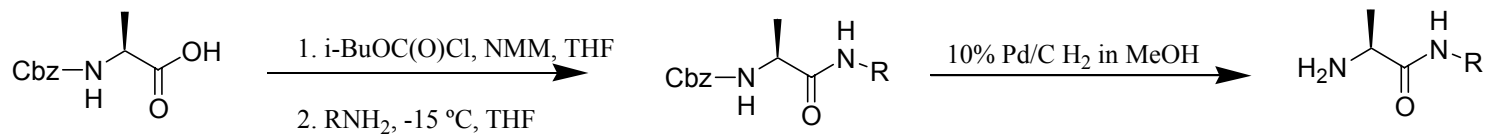
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Monomer Synthesis:

We found that the chiral *N'*-substituted propanamide side chain motif allowed for the synthesis of water soluble folded peptoid sequences with a variety of different side chain functionality. A general and efficient synthesis procedure which retains chirality was developed (Scheme 1) and applied to a variety of different amines. The alanine *N'*-substituted amide submonomers were prepared in high yield in two steps from Cbz-protected L-alanine. Upon completion of the procedure, no further purification was needed for incorporation of these submonomers into peptoid synthesis. Anhydrous solvents and reagents were obtained from commercial sources and used without further purification. A representative synthesis is presented below.

Scheme 1



R- (sidechain amine)	Coupling step yield	Deprotection step yield
<chem>H2N-CH2-CH2-O-TIPS</chem>	92%	>98%
<chem>H2N-CH2-CH2-O-CH3</chem>	65%	>98%
<chem>H2N-CH2-CH2-NH-Boc</chem>	81%	>98%
<chem>H2N-CH2-CH2-C(=O)OC(C)(C)C</chem>	93%	90%
<chem>H2N-CH2-CH2-CH3</chem>	84%	>98%
<chem>H2N-CH(CH3)2</chem>	66%	93%
<chem>H2N-CH2-CH(CH3)2</chem>	87%	>98%
<chem>H2N-CH2-C1=CC=CC=C1</chem>	91%	>98%
<chem>H2N-CH2-C1CCCCC1</chem>	88%	>98%

Cbz-L-alanine *N'*-2-[(triisopropylsilyl)oxy]ethylamide

To Cbz protected L-Alanine (55mmol) in 80mL anhydrous THF in flame dried glassware under inert atmosphere at room temperature, *N*-methyilmorpholine (1eq.) was added dropwise via syringe over 10 minutes. The reaction vessel was then cooled to -15°C using an ice/acetone/dry ice bath (55/40/5 by volume). To the cooled, vigorously stirring solution, isobutyl chloroformate (1eq) was added dropwise via syringe over 20 minutes and then allowed to stir for another 15 minutes. The desired amine, in this case [(triisopropylsilyl)oxy]ethylamine, (1eq.) in THF (2M) was added dropwise via syringe over 15 minutes. Upon completion of the procedure, the reaction was allowed to equilibrate to room temperature and stirred for 15 hours. The solvent was then removed *in vacuo* and then taken up in 200mL ethylacetate and 200mL water. The organic layer was washed with 10% sodium bicarbonate (3 x 150mL), 10% citric acid (3 x 150mL), and 10% sodium bicarbonate (3 x 150mL). The organic layer was dried (Na_2SO_4) and the solvent was removed *in vacuo* to yield 21.4 g (92%) of a yellowish oil: ^1H NMR (300MHz, CDCl_3) δ 7.34 (s, 5H, arom H), 6.36 (br s, 1H, NH), 5.34 (br s, 1H, NH), 5.12 (s, 2H, arom $-\text{CH}_2$), 4.25 (m, 1H, CH), 3.76 (t, $J = 7$ Hz, 2H, CH_2), 3.41 (t, $J = 7$ Hz, 2H, CH_2), 1.39 (d, 3H, CH_3), 1.08 (m, 21 H, CH_3 and isopropyl)

L-alanine *N'*-2-[(triisopropylsilyl)oxy]ethylamide

To Cbz-L-alanine *N'*-2-[(triisopropylsilyl)oxy]ethylamide (50.6 mmol) in 300 mL anhydrous methanol under an inert atmosphere, was added 0.5g of 10%

palladium/carbon. The reaction vessel was flushed with hydrogen gas and then sealed under hydrogen for 12 hours. The solution was filtered through celite and the solvent was removed *in vacuo* to yield 14.3 g (98%) of a yellowish oil: ^1H NMR (300MHz, CDCl_3) δ 7.62 (br s, 1H, NH), 3.77 (t, $J = 7$ Hz, 2H, CH_2), 3.48 (m, 1H, CH), 3.38 (t, $J = 7$ Hz, 2H, CH_2), 1.33 (d, 3H, CH_3), 1.08 (m, 21 H, CH_3 and isopropyl).