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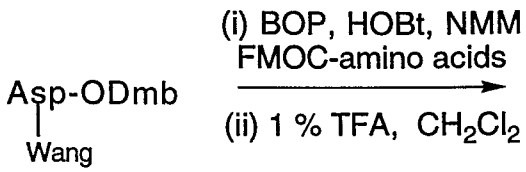
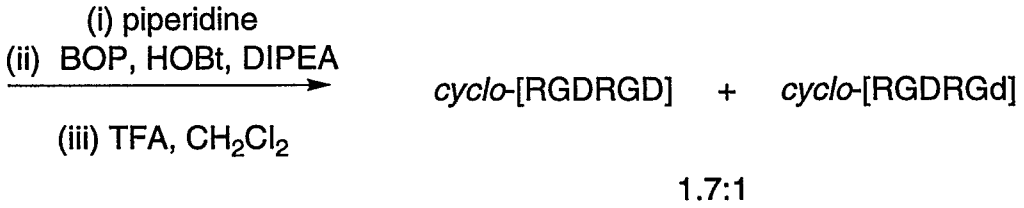
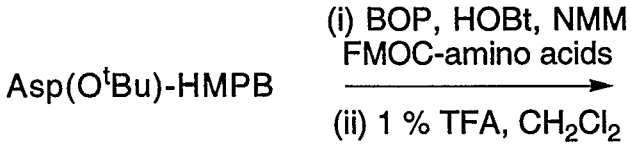
first method



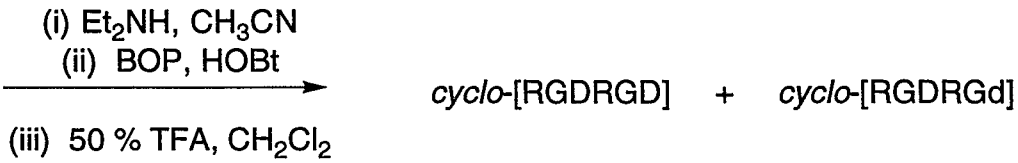
FMOC-Arg(Mtr)-Gly-Asp(^{t}Bu)-Arg(Mtr)-Gly-Asp-OH
Wang



second method



FMOC-Arg(Mtr)-Gly-Asp(^{t}Bu)-Arg(Mtr)-Gly-Asp(O^{t}Bu)-OH



Scheme S1. Syntheses of *cyclo*-[RGDRGD] and *cyclo*-[RGDRGd]. Abbreviations: Dmb, 2,4-dimethoxybenzyl; HMPB, 4-hydroxymethyl-3-methoxyphenoxybutyrate; MBHA, 4-methylbenzhydrylamine; Wang, 4-benzyloxybenzylalcohol.

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Table S1. Chemical shifts, coupling constants and temperature coefficients of various protons in *cyclo*-RGDRGD and *cyclo*-RGDRGd (ref. Arg-δ; 3.10 ppm)

amino acid proton		δ (ppm) {important coupling (Hz)} [temperature coefficient (ppb K^{-1})][c]	
		***cyclo*-RGDRGD**	***cyclo*-RGDRGd**[a]
Arg	NH	8.08 {d, 8.0} [-5.8]	8.31 {d, 8.5} [-7.6]
	α	4.32	4.40
	β	1.83	1.72
	β	1.69	1.72
	γ	1.50	1.54 {m}
	δ	3.10	3.10
	NHε	7.10 [-2.6]	7.10 [-3.0]
Gly	NH	8.25 {5.5} [-6.3]	7.48 {dd, 7.5, 4.0} [-0.6]
	pro-*R*-α[b]	3.95 {16.0}	4.16 {dd, 17.5, 7.5}
	pro-*S*-α[b]	3.72 {16.0}	3.58 {dd, 17.5, 4}
Asp	NH	8.38 {d, 7.0} [-3.6]	8.50 {d, 5.5} [-7.6])
	α	4.41	4.54
	β	2.61	2.70
	β'	2.61	2.70
Arg	NH		8.59 {d, 8.5} [-10.6]
	α		~4.33
	β		1.68
	β		1.68
	γ		1.54 {m}
	δ		3.10
	NHε		7.10 [-3.0]
Gly	NH		8.03 {dd, 7.5, 3.5} [-2.3]
	pro-*R*-α		4.28 {dd, 17.0, 7.5}
	pro-*S*-α		3.89 {dd, 17.0, 3.5}
Asp	NH		8.49 {d, 5} [-6.8]
	α		4.39
	β		2.78
	β'		2.78

[a] Asp^1 and Asp^4 were indistinguishable, *ie* Asp^1 can be either L- or D- form. [b] Prochirality of two α protons. [c] In general, temperature dependence of amide NH protons *in aqueous environments* do not correlate well with intramolecular hydrogen bonding. Consequently, this data is not contradictory to the H/D exchange results given in the main text; it is just uninformative.

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Figure S1. ϕ, ψ Scatter plots for the R, G, and D residues in the 30 lowest energy conformers from the QMD simulation of *cyclo*-[RGDRGD].