

A Bicyclic Analog of the Linear Peptide Arodyn Is a Potent and Selective Kappa Opioid Receptor Antagonist

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Table S1. Yield of intermediate **6** following RCM with HG II under various microwave heating conditions.^{a,b}

Entry	Temp (°C)	Time	RCM Pdt yield (%)
1	75	2 h	- ^c
2	100	2 h	46
3	150	5 min	63
4	150	15 min	73
5	150	30 min	73
6	175	15 min	67
^a 15 mol% HG II, 0.3 mM, in DCE; ^b product yield was determined by analytical HPLC (5-50% aqueous MeCN containing 0.1% TFA over 45 min; see Table S2 for retention times of products); ^c <10%			

Table S2. Analytical data for peptides **5-9**.

Compound	HPLC t_R (min) ^a	ESI-MS	
		Calcd.	Obsvd.
5	25.3	[M+3H] ³⁺ 428.6	[M+3H] ³⁺ 428.7
6	23.3	[M+3H] ³⁺ 419.2	[M+3H] ³⁺ 419.5
7	30.8	[M+3H] ³⁺ 544.0	[M+3H] ³⁺ 543.9
		[M+4H] ⁴⁺ 408.2	[M+4H] ⁴⁺ 408.2
8	32.9	[M+3H] ³⁺ 553.3	[M+3H] ³⁺ 553.2
		[M+4H] ⁴⁺ 415.3	[M+4H] ⁴⁺ 415.2
9	28.7	[M+2H] ²⁺ 815.5	[M+2H] ²⁺ 815.4
		[M+3H] ³⁺ 544.0	[M+3H] ³⁺ 543.9

^a5-50% aqueous MeCN (0.1% TFA) over 45 min

Figure S1. HPLC chromatograms of pure bicyclic peptide 4.

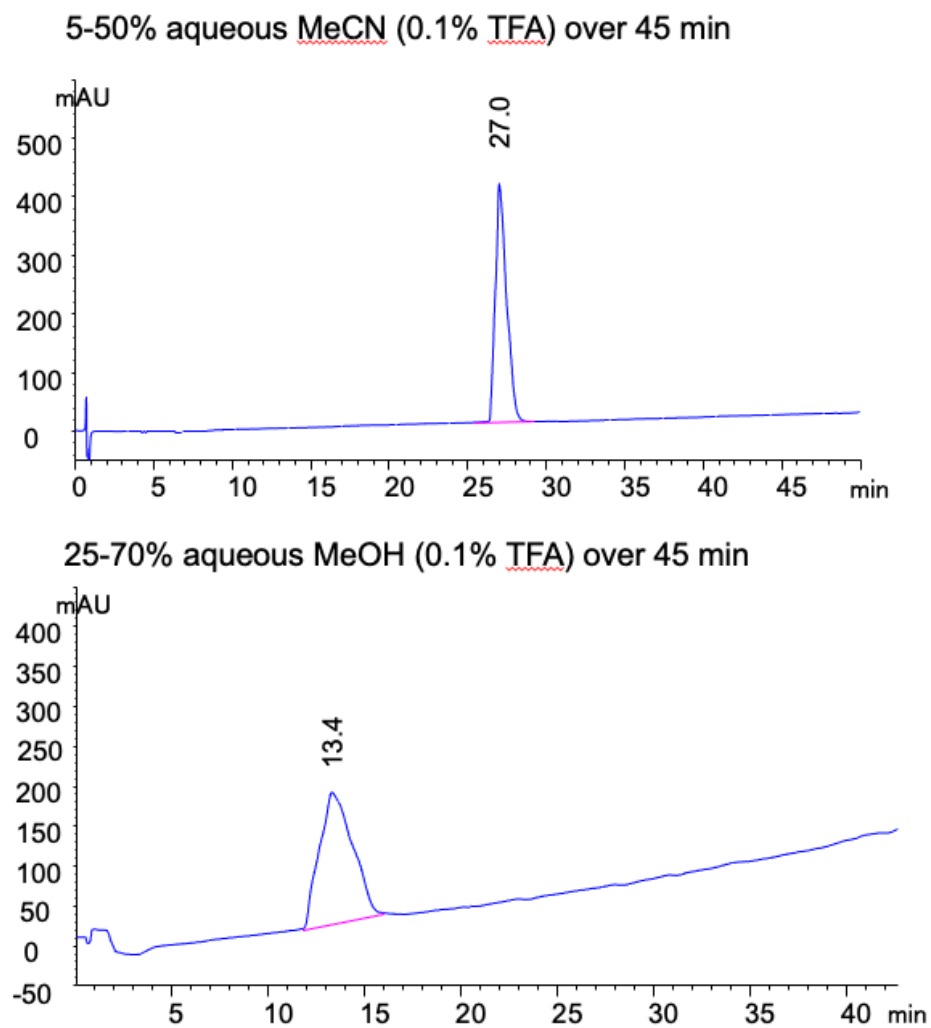


Figure S2. Electrospray ionization mass spectrum of pure bicyclic peptide 4.

