Synthesis and Stereochemical Assignment of Enteropeptin A

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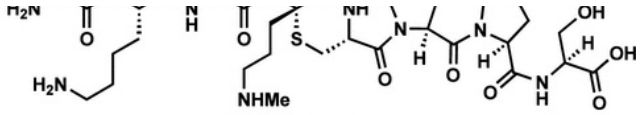


enteropeptin A
[14 steps]
[first total synthesis]
[structural elucidation]

the first total synthesis of a sactipeptide

MarKovnikov hyorothiolation

thioaminoketal group

thiomorpholine ring.

a general platform for the synthesis of stereochemically defined thiomorpholine-containing peptides,

cheme 1. Total Synthesis of Enteropeptin A (1) and Its Thioaminoketal Diastereomer (*epi*-1)[a]

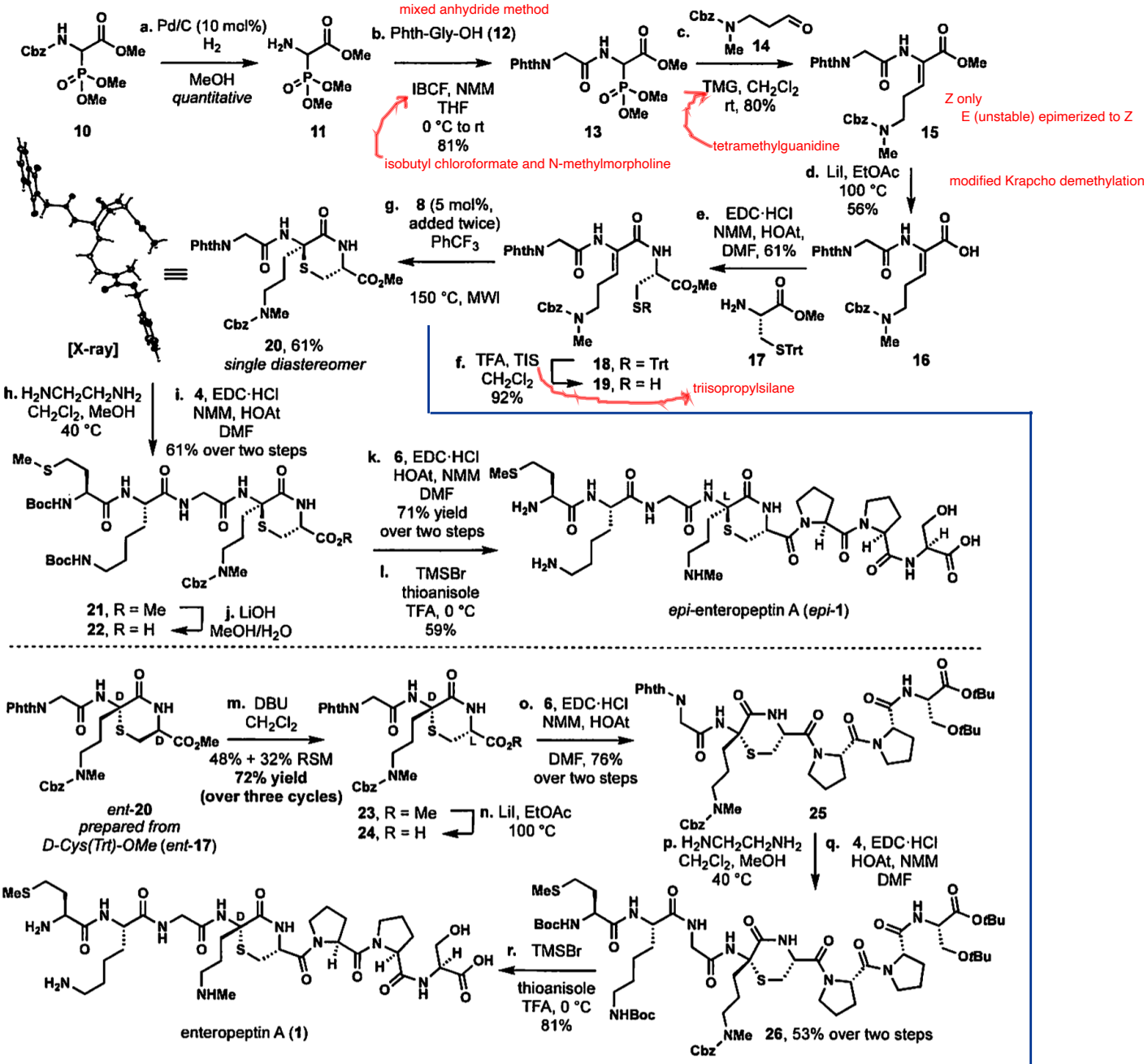
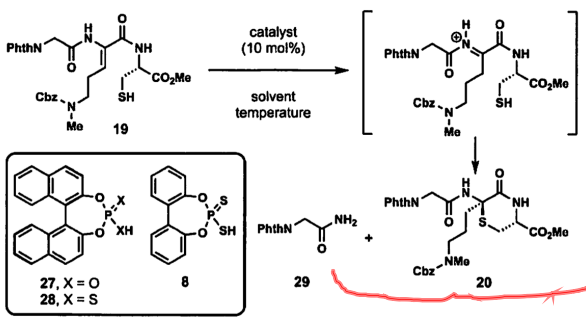


Table 1. Optimization of the Markovnikov Hydrothiolation[a]



catalyst	solvent, time	temp	yield of 20[b]	yield of 29[b]
MsOH	DCE, 12 h	rt	0	0
(R)-27	PhF, 12 h	rt	0	0
(R)-27	PhF, 12 h	90 °C	0	0
(R)-28	PhF, 12 h	rt	0	0
(R)-28	PhF, 12 h	90 °C	15	11
(R)-28'	PhF, 4 h	140 °C, MWI	46	6
8	PhF, 4 h	140 °C, MWI	50	4

formed by the fragmentation of the thioaminoketal in compound 20.

Preliminary attempts at transition metal catalyzed hydrothiolation using rhodium or hydrogen atom transfer conditions did not form the desired product 20.

SM recovered, no conjugate addition

no SM, the same diastereomer with (S)-28