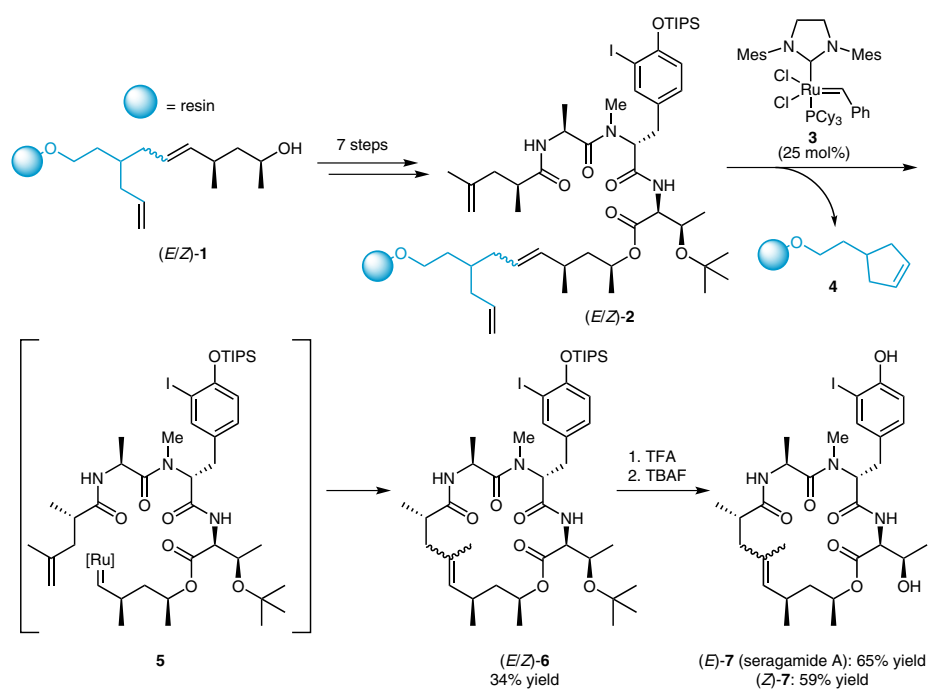


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Divergent Solid-Phase Synthesis of Natural Product-Inspired Bipartite Cyclodepsipeptides: Total Synthesis of Seragamide A

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SPS of Seragamide A via Relay-Ring-Closing Metathesis



Significance: The authors present the first total synthesis of seragamide A (isolated from the sponge *Suberites japonicus* Thiele in 2006) via a solid-phase synthesis–cyclorelease strategy utilizing relay-ring-closing metathesis. Starting from resin (E/Z)-1, the precursor (E/Z)-2 was prepared in seven steps. Relay-ring-closing metathesis of (E/Z)-2 proceeded in the presence of $\text{RuCl}_2(\text{SIMes})(\text{PCy}_3)(=\text{CHPh})$ (**3**) to give (E/Z)-6 in 34% yield based on (E/Z)-1 as a mixture of separable isomers. Treatment of (E)-6 with TFA followed by TBAF provided (E)-7 (seragamide A) in 65% yield (based on the crucial ring-closing step). Similarly, (Z)-6 was converted into (Z)-7 in 59% yield.

Comment: The present synthetic protocol was also applied to the preparation of a collection of structurally diverse cyclodepsipeptides using various peptides (9 examples) and ketide segments (4 examples).

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