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

Chem. Eur. J. **2015**, *21*, 5311–5316.

Category

Polymer-Supported Synthesis

Key words

solid-phase synthesis

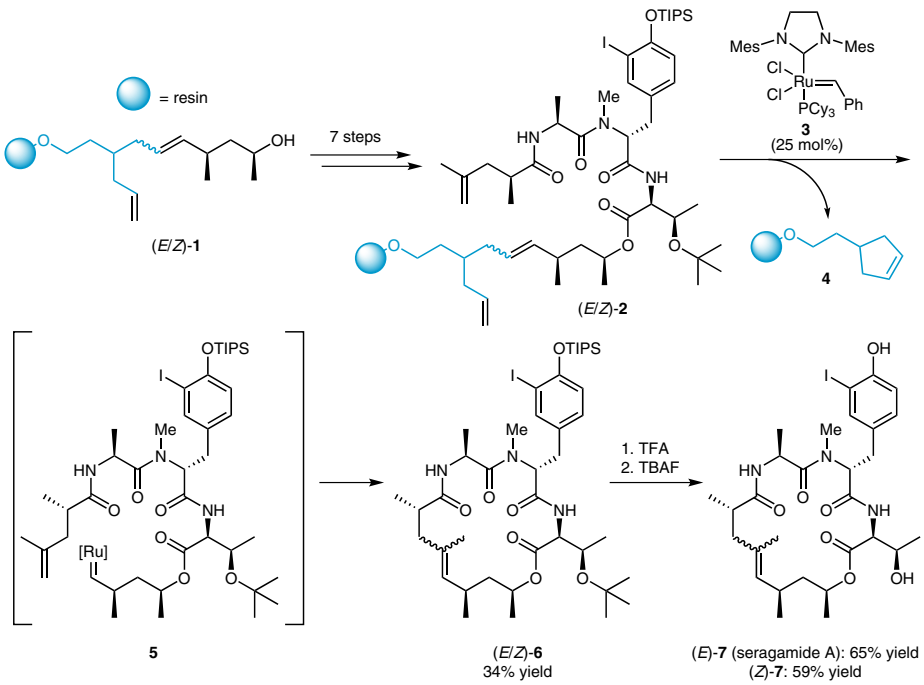
total synthesis

cyclodepsipeptides

relay-ring-closing metathesis

ruthenium

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 $RuCl_2(SIMes)(PCy_3)(=CHPh)$ (**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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Synfacts 2015, 11(6), 0665 Published online: 18.05.2015
DOI: 10.1055/s-0034-1380860; **Reg-No.:** Y05615SF