Asymmetric Total Synthesis of Rumphellclovane E

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- isolated from the gorgonian coral *Rumphella antipathies*
- tricyclo[6.3.1.0]dodecane ring system
- 3 stereocenters
- 8 steps synthesis in B–AB–ABC construction sequence
- this synthesis serves as a general platform to concisely access the clovane-type sesquiterpenoids.

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Total Synthesis Presentation
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**Figure 1.** Representative examples of clovane-type sesquiterpenoids.
Scheme 1. Progress in Syntheses of Clovane-type Natural Products

(a) Becker et al (1965), A-AB-ABC strategy

(b) Schultz et al (1983), B-BC-ABC strategy

(c) Dreiding et al (1985), B-BC-ABC strategy

(d) Raphael et al (1965), C-BC-ABC strategy

(e) Funk et al (1988), C-BC-ABC strategy

(f) Kundu et al (1965), B-AB-ABC strategy

(g) Mukherjee et al (2003), B-BC-ABC strategy

(h) Yu et al (2017), AB-ABC strategy
Retrosynthetic analysis of Rumphellclovane E
(R)-carvone, 10 + EtOCONEt 2 → Rh₂(esp)₂ \[\text{PhMe, rt, 89\% (1:0.6 dr)}\] → inseparable diastereomers

From 10 to 11: Rh-catalyzed cyclopropanation

From 9 to 12: Intramolecular acylation

bis[rhodium(α,α,α’,α’'-tetramethyl-1,3-benzenedipropionic acid]
From 12 to 8: Michael addition

From 8 to 7a/7b: Metal-catalyzed reductive aldol reaction
From 7a/7b to 15a/15b: TBS protection of alcohol

From 15a/15b to 16: Hydrogenolysis under heterogeneous Catalysis

From 16 to 17: Hydrolysis and decarboxylation
From 17 to 18: Selective reduction of carbonyl

\[ \text{Edited text from 17 to 18: Selective reduction of carbonyl} \]

From 18 to 4: TBS deprotection

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 equiv of NaBH₄, MeOH, -78 °C</td>
<td>19, 73</td>
</tr>
<tr>
<td>2</td>
<td>1 equiv of LiAlH₄, THF, -78 °C</td>
<td>19, 69</td>
</tr>
<tr>
<td>3</td>
<td>1 equiv of (R)-CBS, 1.5 equiv of BH₃, THF, -78 °C</td>
<td>20, 65</td>
</tr>
<tr>
<td>4</td>
<td>1 equiv of (S)-CBS, 1.5 equiv of BH₃, THF, -78 °C</td>
<td>20, 51 (72% brsm)</td>
</tr>
<tr>
<td>5</td>
<td>0.1 mol/L of Sml₂, THF/H₂O (10:1 v/v), 0 °C</td>
<td>18, 76</td>
</tr>
<tr>
<td>6</td>
<td>0.1 mol/L of Sml₂, THF/MeOH (10:1 v/v), 0 °C</td>
<td>nr</td>
</tr>
</tbody>
</table>

(a) Rationale for achieving 19 & 20

(b) Rationale for achieving 18