Asymmetric Total Synthesis of Arcutinidine, Arcutinine, and Arcutine

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1: the originally described structure of arcutine; R = (R)-s-BuCO
2: arcutinine; R = i-PrCO
3: arcutinidine; R = H
1: the originally described structure of arcutine; $R = (R)-s$-BuCO
2: arcutinine; $R = i$-PrCO
3: arcutinidine; $R = H$

4: atropurpuran
5: tongolinine

the hetidine skeleton

1,2-alkyl shift

the arcutine skeleton
3. arcutininidine

dehyde reductive amination

Prins/Wagner-Meerwein

anionic Diels-Alder

Diels-Alder
<table>
<thead>
<tr>
<th>entry</th>
<th>conditions(^a)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TFA, 0 °C, 24 h</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>TESOTf, 0 °C, 1 h</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>BF(_3)·OEt(_2), −15 °C, 6 h</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>TiCl(_4), −15 °C, 1 h</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>SnCl(_4), −15 °C, 1 h</td>
<td>63</td>
</tr>
<tr>
<td>6</td>
<td>SnCl(_4), TMSOAc, −15 °C, 1 h</td>
<td>55</td>
</tr>
</tbody>
</table>

\(^a\) 1.0 equiv. acid. Reactions performed in CH\(_2\)Cl\(_2\).
Mechanism of the Mukaiyama Hydration
a) NH₂OH•HCl, NaOAc; NaBH₄ → 65% →

b) TiCl₃, NaBH₃CN → 71% →

3: arcutinidine; R = H
2: arcutinine; R = i-PrCO

c) i-PrCO₂H, DCC, DMAP, 77% →
3: arcuminidine

1: the originally described structure of arcutine

25: arcutine

a) (R)-s-BuCO₂H, DCC, 4-DMAP

b) (S)-s-BuCO₂H, DCC, DMAP

74%