Abstract
Olfaction is a dominate sense in the activities of many insects, yet the chemical cues used to mediate their activities are often unknown. Here, we describe our effort to synthesize natural products that mediate the interactions of parasitoid wasps of the genus Leptopolina. These minute insects naturally produce insufficient quantities of olefactory cues, such as sex pheromones and defensive secretions, to fully characterize them spectroscopically and biologically. We have undertaken the synthesis of these natural products to corroborate their identities and, through a collaboration with chemical ecologist Dr. Joachim Ruther, establish their biological activities. We devised a novel synthesis of five natural products with similar iridoid substructures, and have succeeded in preparing three:

- Iridomyrmecin
- Isoiridomyrmecin
- Dolicholactone

and isoiridomyrmecin were both prepared in six steps, with an overall yield of 19%. Prepared teucriumlactone in seven steps with a 3% overall yield. Iridomyrmecin was hindered by low yields. In the optimization of this step, we determined that the ionic hydrogenation of nepetalactol to form a common intermediate (6) to all five natural products. Using this strategy, we prepared teucriumlactone in seven steps with a 3% overall yield. Iridomyrmecin and isoiridomyrmecin were both prepared in six steps, with an overall yield of 19%.

Background
Iridomyrmecin (1) is naturally produced by the parasitoid wasp of the genus Leptopolina, in which it acts as a sex pheromone. Although this specific ecological role spurred our synthesis, iridomyrmecin (1), isoiridomyrmecin (2), teucriumlactone (3), dolichodial (4), and dolicholactone (5) can be isolated from many other plants and animals.

Target Iridoid | Natural Source
---|---
Iridomyrmecin (1) | *Linhepitha humile* (Argentine worker ants)\(^2\)
Isoiridomyrmecin (2) | *Nepeta erecta* Benth.\(^3\)
Teucriumlactone (3) | *Antismorpha buprestoides* (the walkingstick insect)\(^4\)
Dolichodial (4) | *Teucrium muranum* (the mint plant)\(^5\)
Dolicholactone (5) | *Teucrium marum* (the mint plant)\(^6\)

Retrosynthetic Analysis of Natural Products

[Diagram showing retrosynthetic analysis]

Ionic Hydrogenation of 9

**Optimization:**

The ionic hydrogenation of nepetalactol (9) forms the common intermediate to all five natural products. Therefore, success of this one reaction governs the yield of all the targets. However, the synthesis of the enol ether (6) was hindered by low yields. In the optimization of this step, we determined that the ionic hydrogenation of (9) is highly sensitive to temperature and both the concentration and the rate of addition of the Lewis acid, boron trifluoride etherate.

Relative Product Proportions:

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Equivalence of BF(_3)OEt(_2)</th>
<th>Rate of Addition of BF(_3)OEt(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30°C</td>
<td>3, 2, 8</td>
<td>(i) 5, 25</td>
</tr>
<tr>
<td>35°C</td>
<td>3, 5, 6</td>
<td>(ii) 6, 1</td>
</tr>
<tr>
<td>40°C</td>
<td>2, 1, 5</td>
<td>(iii) 3, 5</td>
</tr>
</tbody>
</table>

Acknowledgements

I would like to thank Kenyon College for the funding and opportunity to perform this research. I would also like to thank Dr. Hofferberth for his guidance throughout the course of the synthesis, and both he and Snow Adler for their work on the collaborative aspects of this research.

References