5.37 Introduction to Organic Synthesis Laboratory
Spring 2009

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Lecture 1
Introduction to Organic Synthesis
The Diels–Alder Reaction

Our results will play a role not only in the discussion of theoretically interesting questions . . . . but probably also will yield greater significance in a practical sense. Thus it appears to us that the possibility of synthesis of complex compounds related to or identical with natural products such as terpenes, sesquiterpenes, perhaps also alkaloids, has been moved to the near prospect. . . . . We explicitly reserve for ourselves the application of the reaction discovered by us to the solution of such problems.

Otto Diels and Kurt Alder  Justus Liebigs Annalen der Chemie 460, 98 (1928)

For Additional Reading . . . .


General Principles of Retrosynthetic Analysis

Strategy

- overall plan to achieve the ultimate synthetic target
- intellectual retrosynthetic planning

Tactics

- means by which plan is implemented
- experimental synthetic execution

TRANSFORMS

REACTIONS

Target  ➔  Precursor  ➔  Target

Strategies for the Assembly of Cyclic Compounds

Cyclization

Annulation

Concerted Cycloadditions
Non-Concerted "Single-Operation" Annulations
Multistep Annulation Strategies
**General Principles of Retrosynthetic Analysis**

The first principle of retrosynthetic planning: **convergent strategies** are the most efficient strategies for the assembly of complex molecules.

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**The Power of Convergent Synthesis**

<table>
<thead>
<tr>
<th>Molecular Complexity (Mwt)</th>
<th># Steps</th>
<th>Starting Materials</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9</td>
<td>62.1 g</td>
<td>3278 mL</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>20.8 g</td>
<td>714 mL</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>20.4 g</td>
<td>346 mL</td>
</tr>
</tbody>
</table>

*Calculations based on 70% yield per step*
"Tragt man in eine Suspension von 1 Mol. Maleinsäure-anhydrid in der 5 fachen Menge von reinem Benzol unter Kuhlung allmählich 1 Mol. Cyclopentadien ein, so reagieren die Komponenten augenblicklich unter starker Warmentwicklung. Das Maleinsäure-anhydrid geht in Lösung, und schon während des Prozesses scheidet sich das Anhydrid der neuen Säure in schneeweissen, glanzenden Kristallen ab. Die Ausbeute ist nahezu quantitativ."

Otto Diels and Kurt Alder Justus Liebigs Annalen der Chemie 460, 98 (1928)