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 $Total\ Synthesis\ of\ (\pm)-Lysergic\ Acid\ by\ an\ Intramolecular\ Imino-Diels-Alder\ Reaction$ Helv. Chim. Acta 1981, 64, 478-481, DOI: 10.1002/hlca.19810640212.

## Total Synthesis of (±)-Lysergic Acid

**Significance:** In 1981, Oppolzer and co-workers reported a concise synthesis of (±)-lysergic acid, a precursor for many ergoline alkaloids. Their synthesis improved upon earlier approaches in terms of efficiency and length by utilizing a Diels-Alder cycloaddition as the key step.

Comment: Intermediate F was accessed from 4hydroxymethyl-1-tosylindole (A) in four steps and was converted to I either directly by treatment with **G**, or more efficiently over two steps. Nef reaction gave rise to K, which underwent retro-Diels-Alder followed by Diels-Alder cycloaddition in one pot at 200 °C. Three more steps gave (±)-lysergic acid.

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Category

**Synthesis of Natural** Products and **Potential Drugs** 

## Key words

lysergic acid Diels-Alder reaction Appel reaction **Nef reaction** Wittig olefination Mannich reaction ergoline alkaloids



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