
Literature Report

Synthetic Route Development for the Laboratory Preparation of Eupalinilide E

Reporter: Chang-Bin Yu

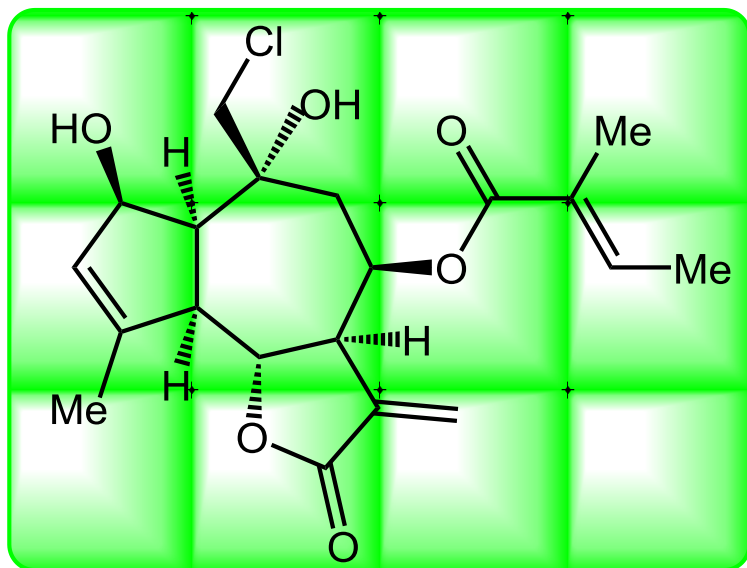
Checker: Hong-Qiang Shen

2017-05-15



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Eupalinilide E

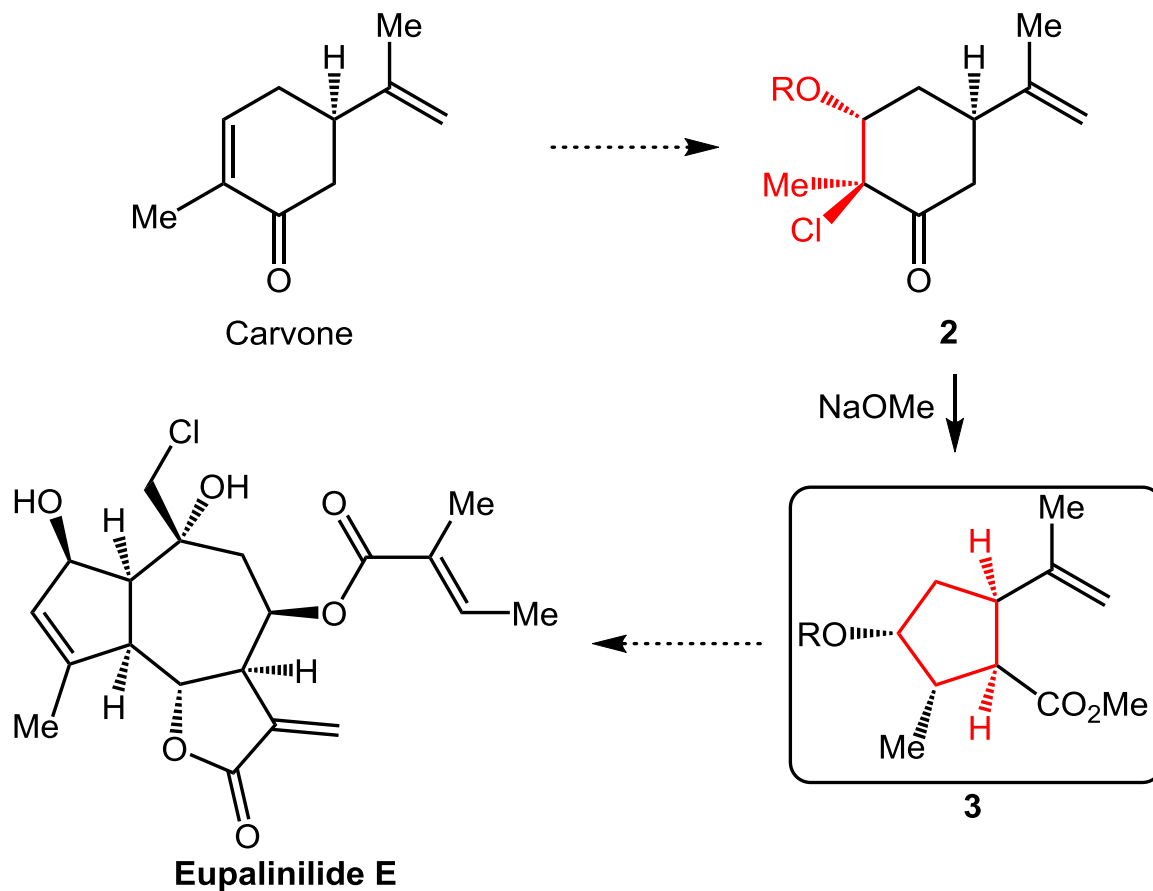


Eupatorium lindleyanum (林泽兰)

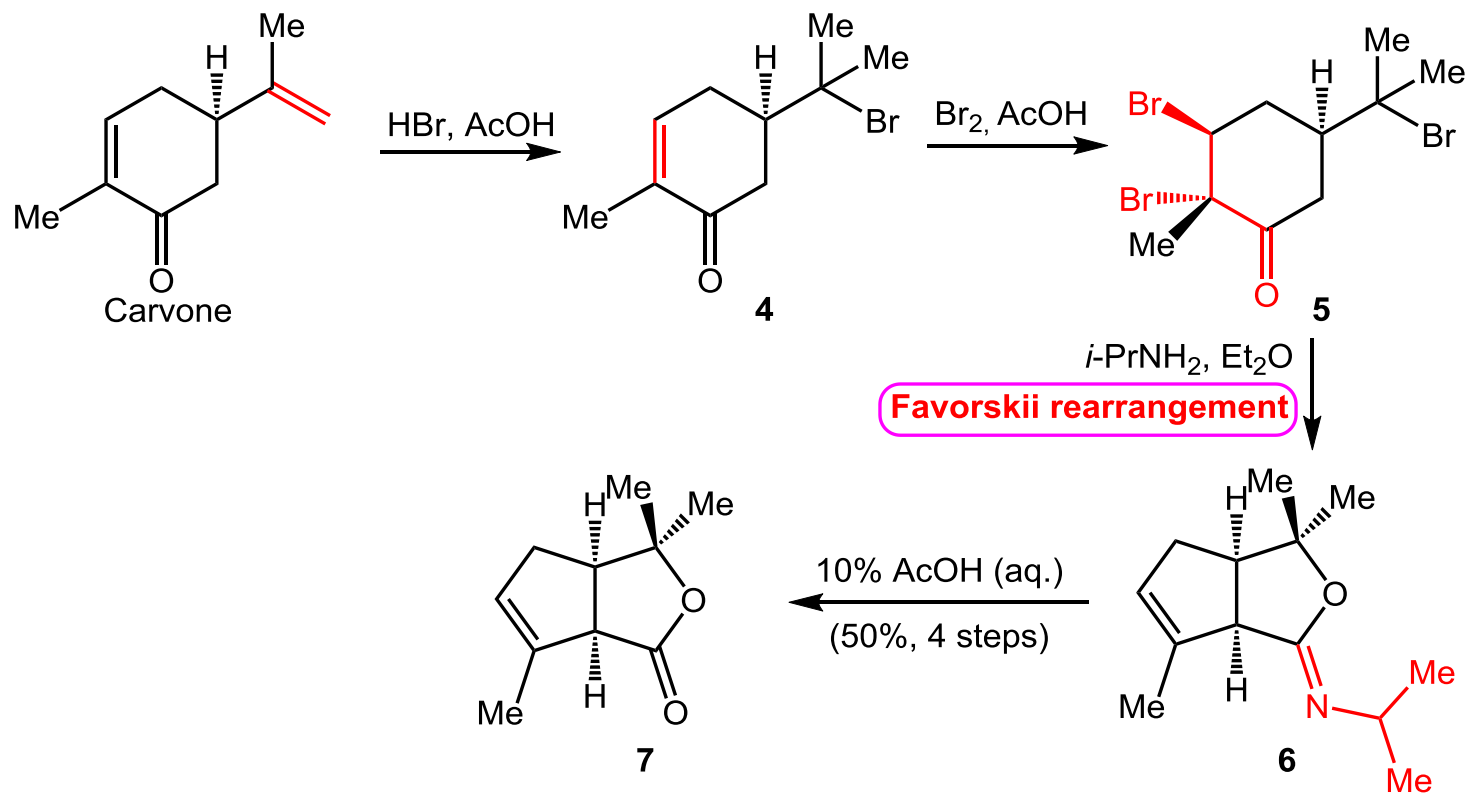
Eupalinilide E was isolated in 2004 from Eupatorium lindleyanum.

Antibacterial and antihistamine(抗菌和抗组胺).

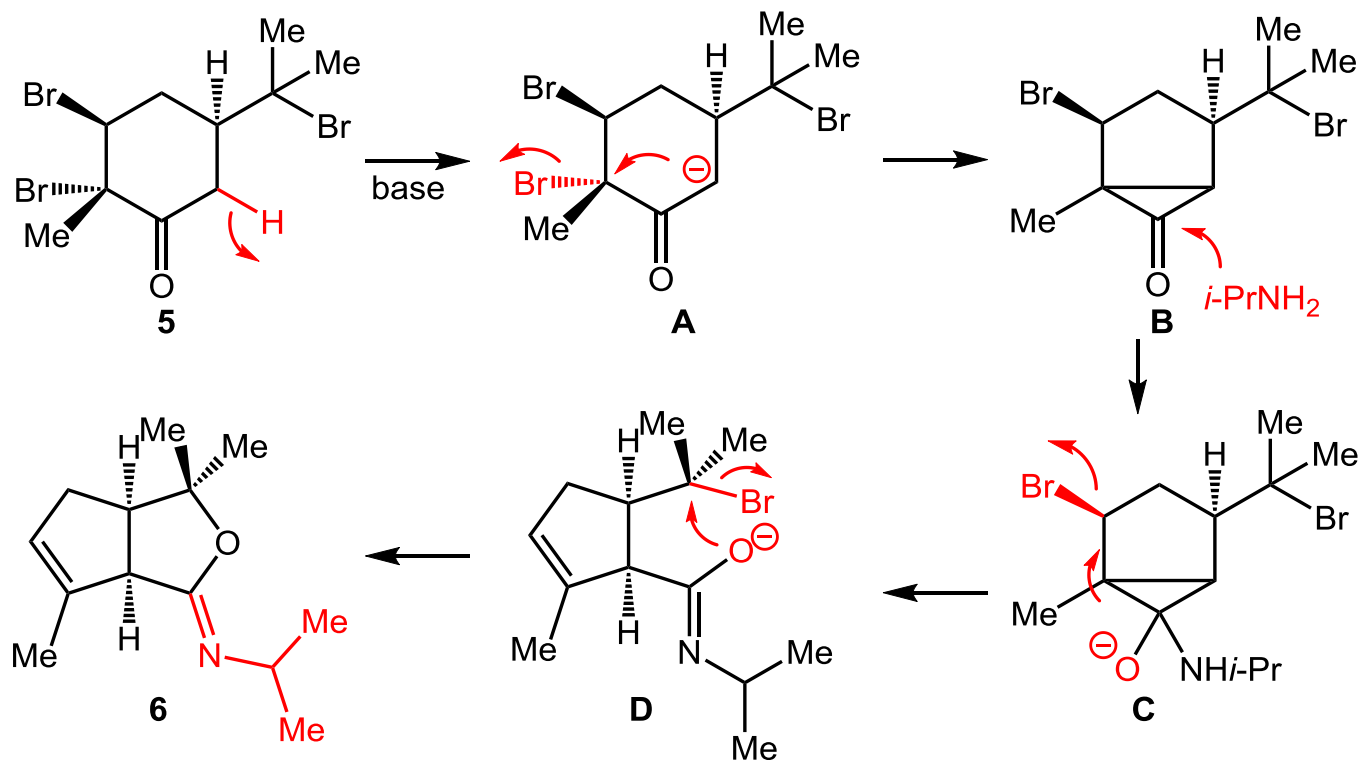
Proposed Retrosynthesis:



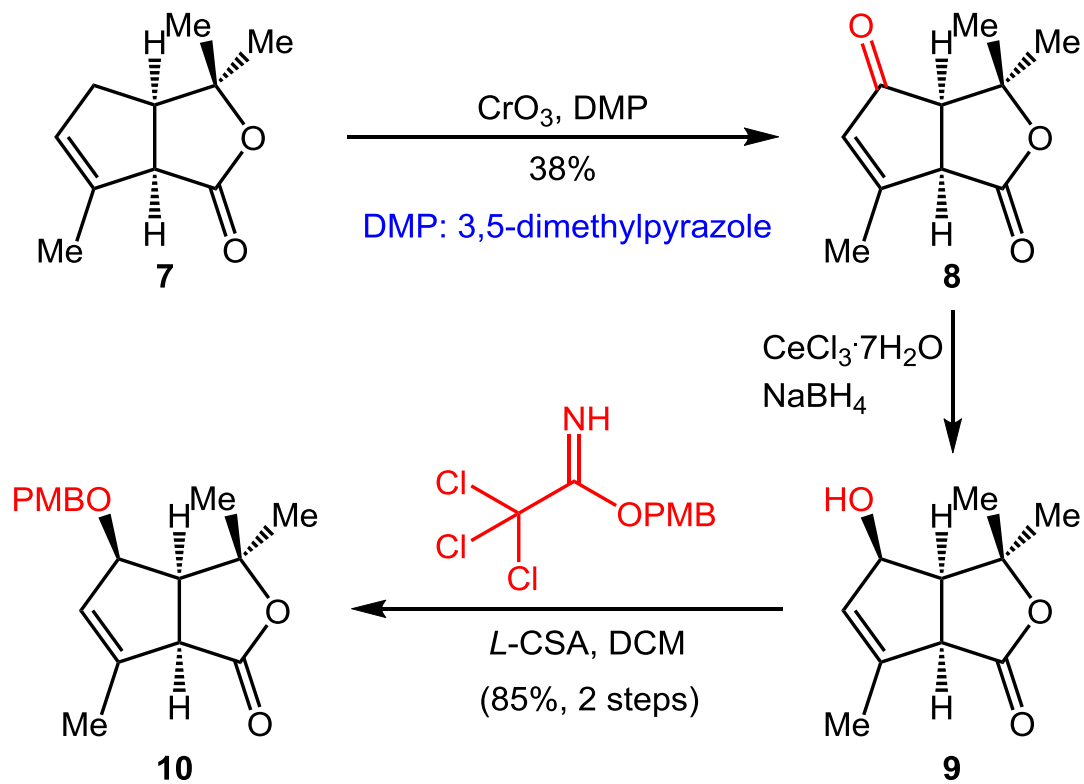
Synthesis of Lactone 7:



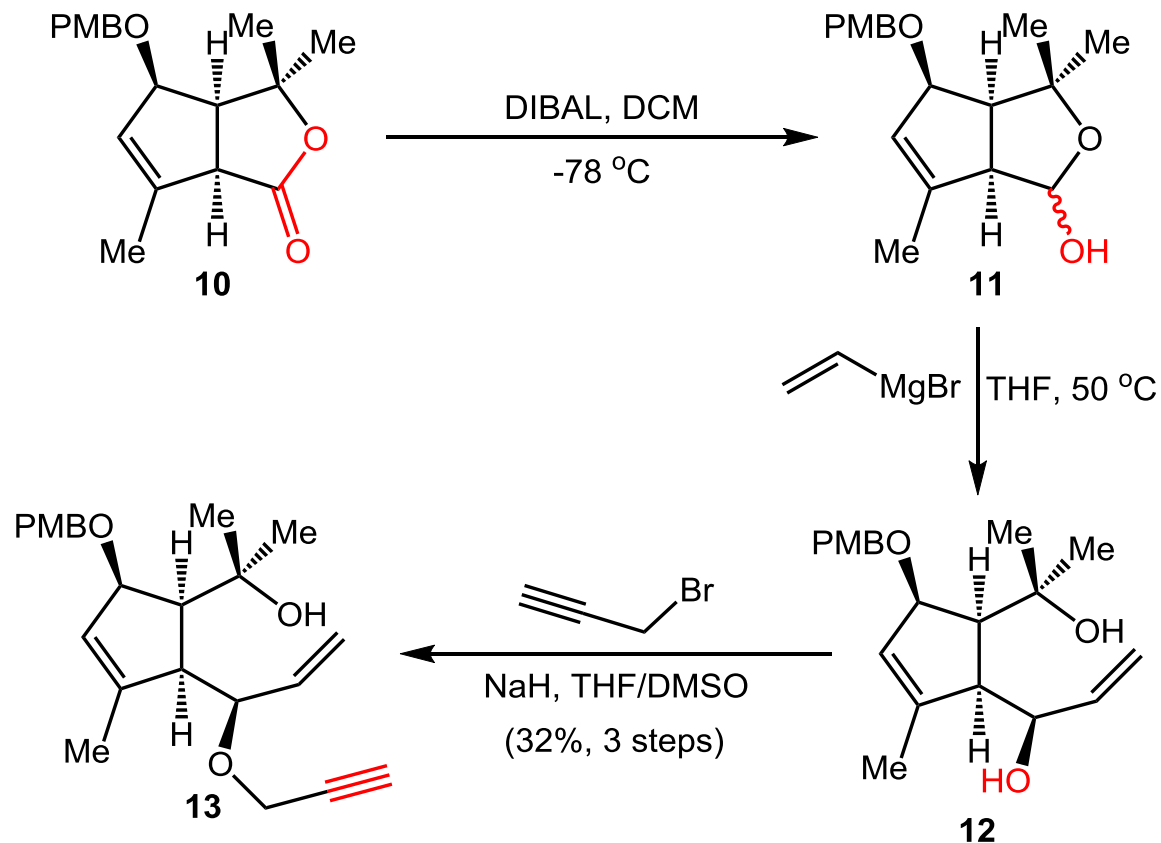
Favorskii Rearrangement :



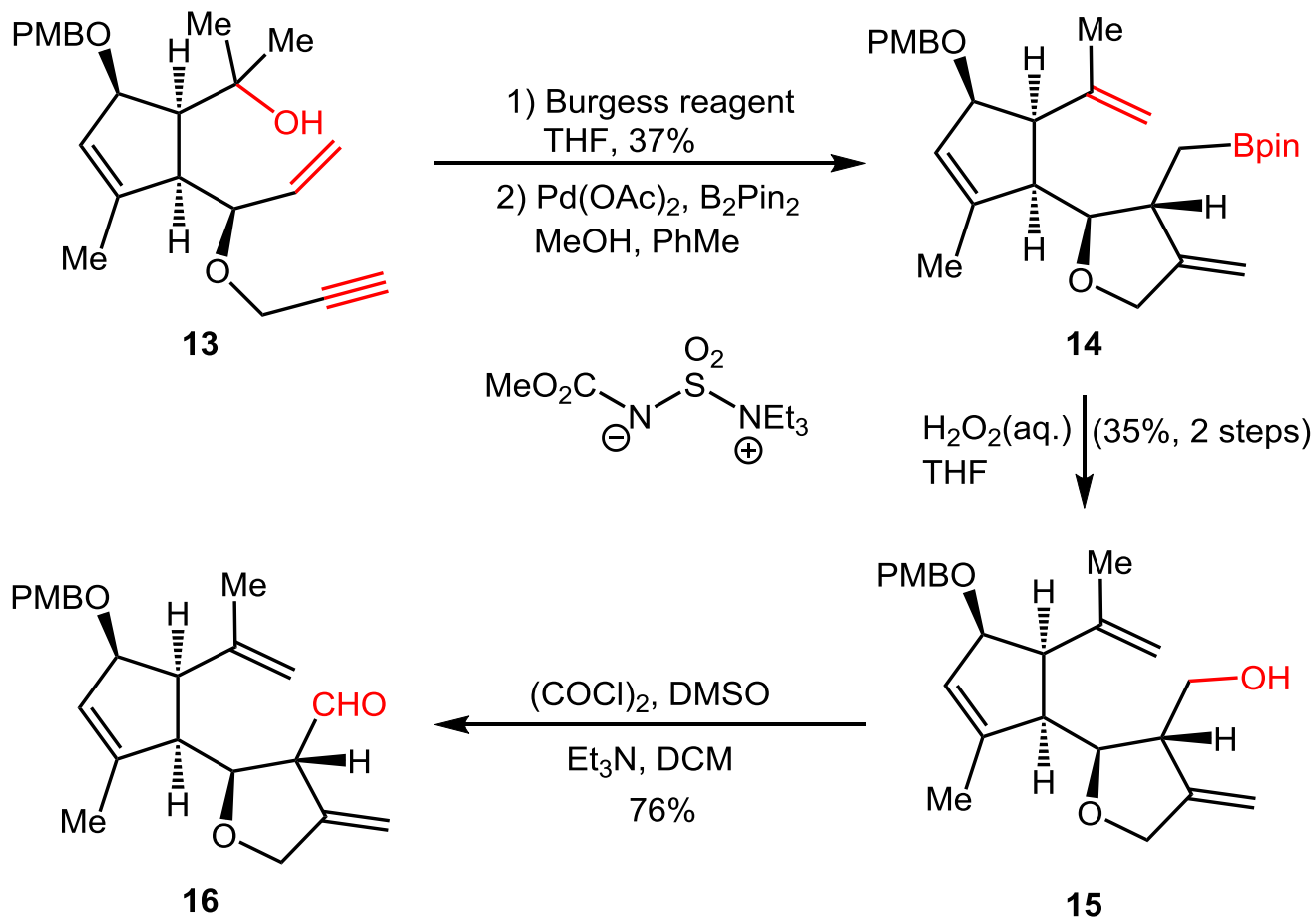
Synthesis of Intermediate 10:



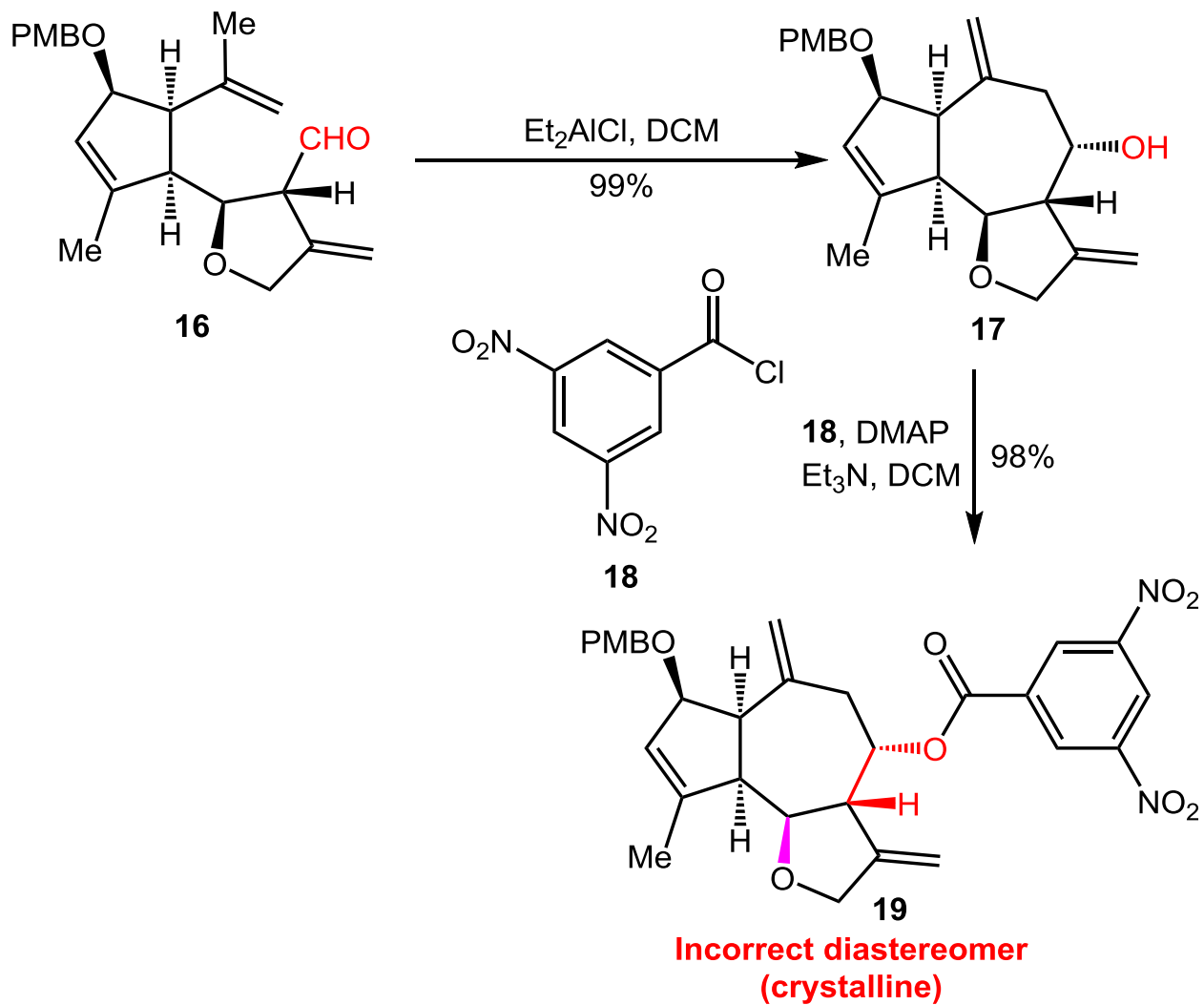
Synthesis of Intermediate 13:



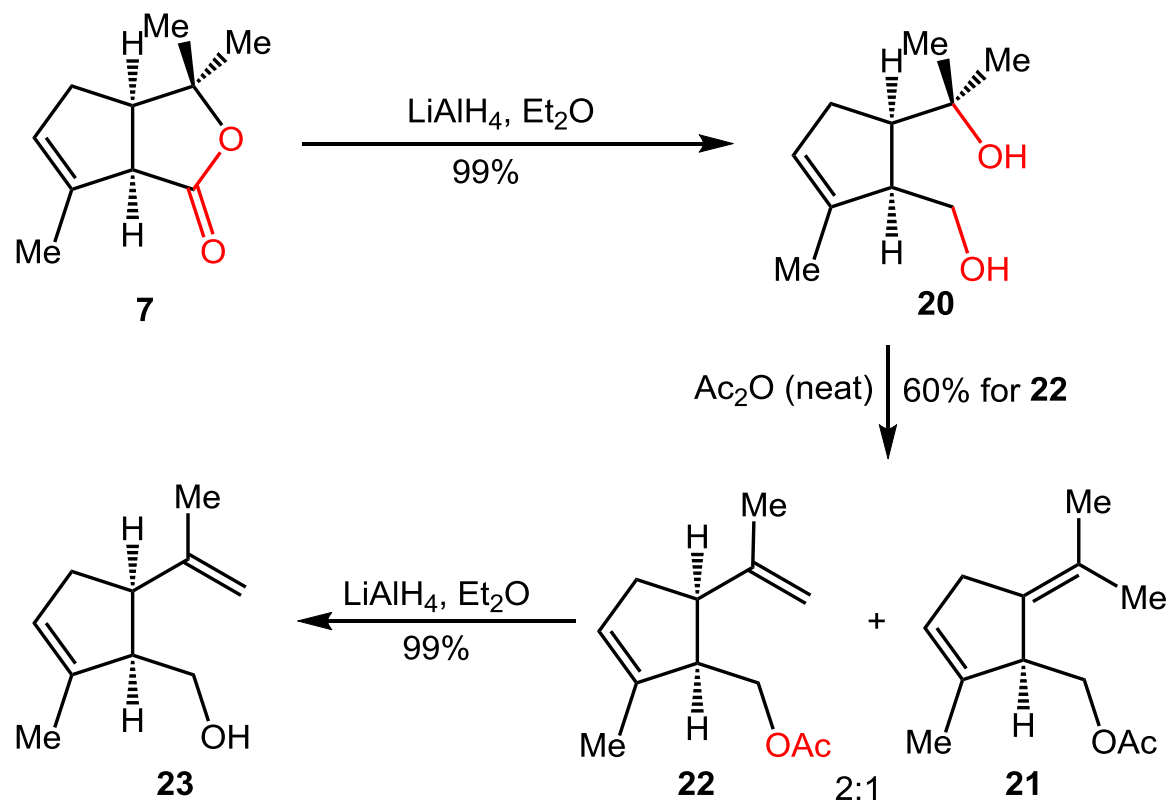
Synthesis of Intermediate 16:



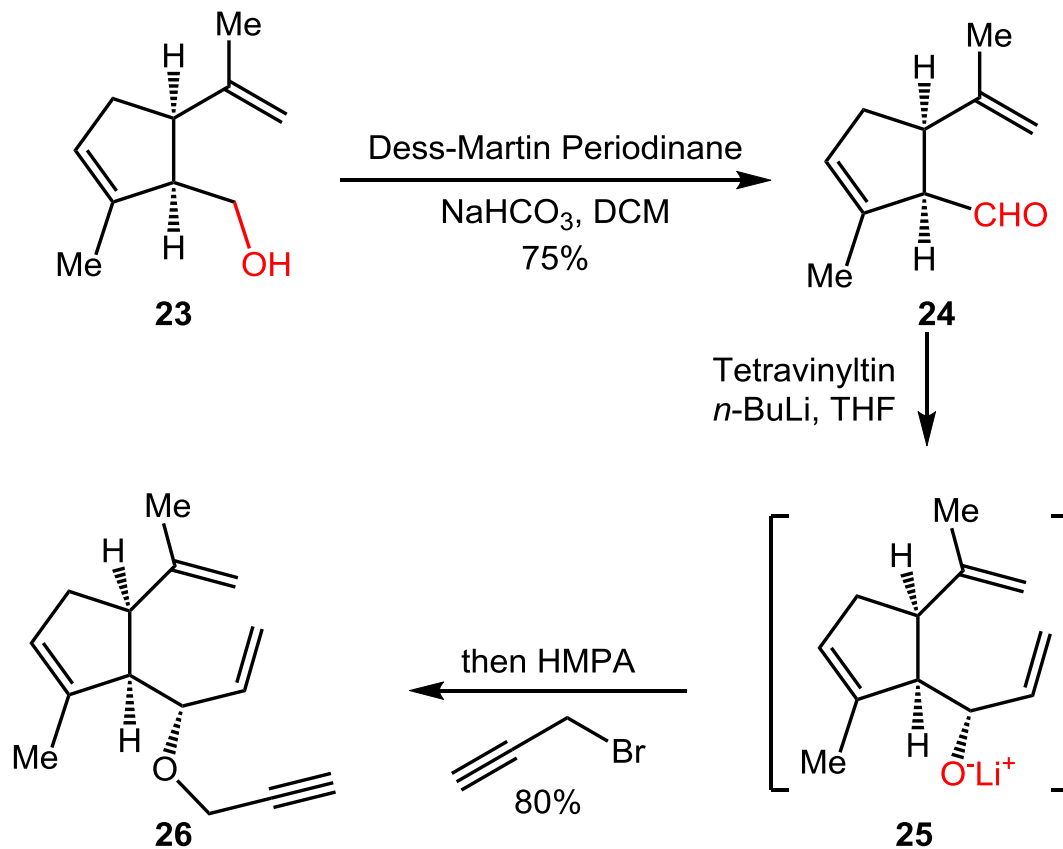
Synthesis of Intermediate 19:



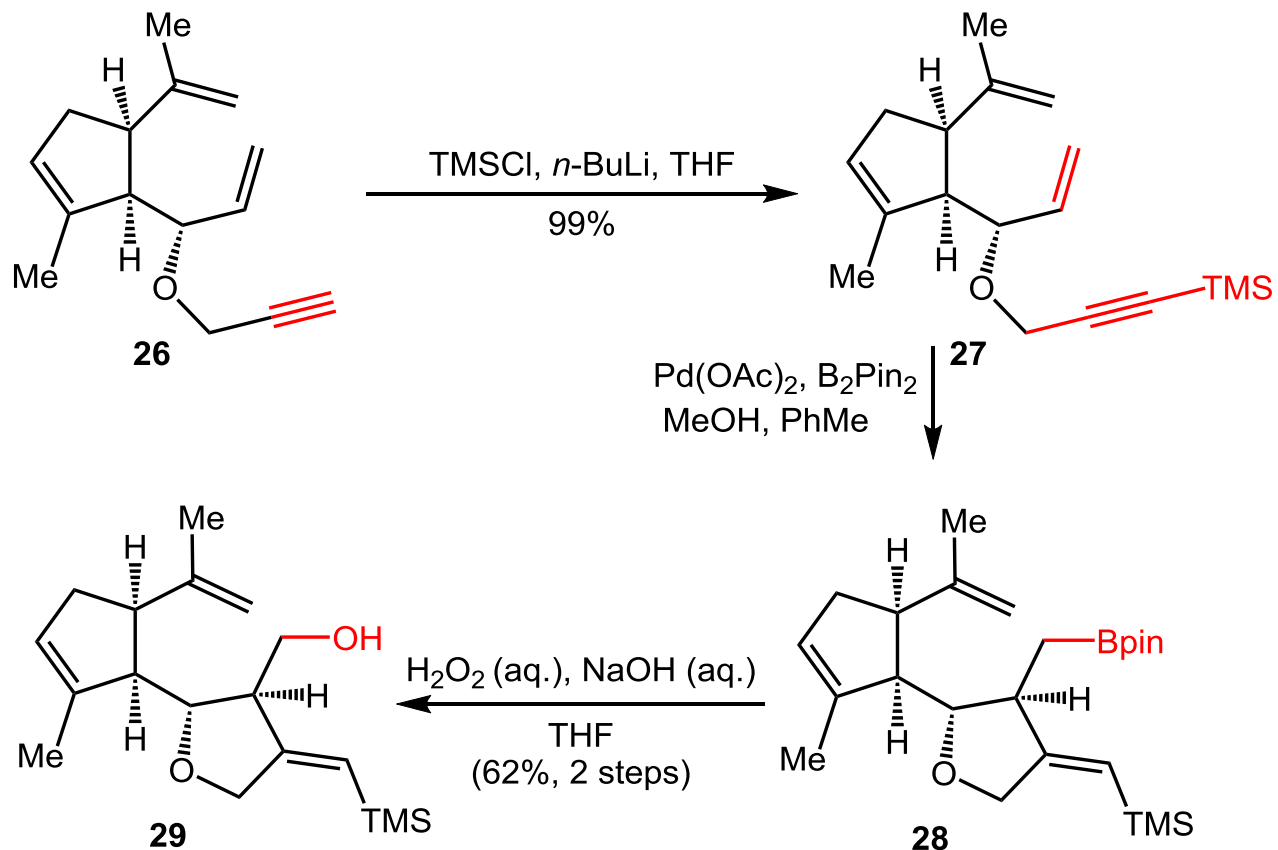
Synthesis of Intermediate 23:



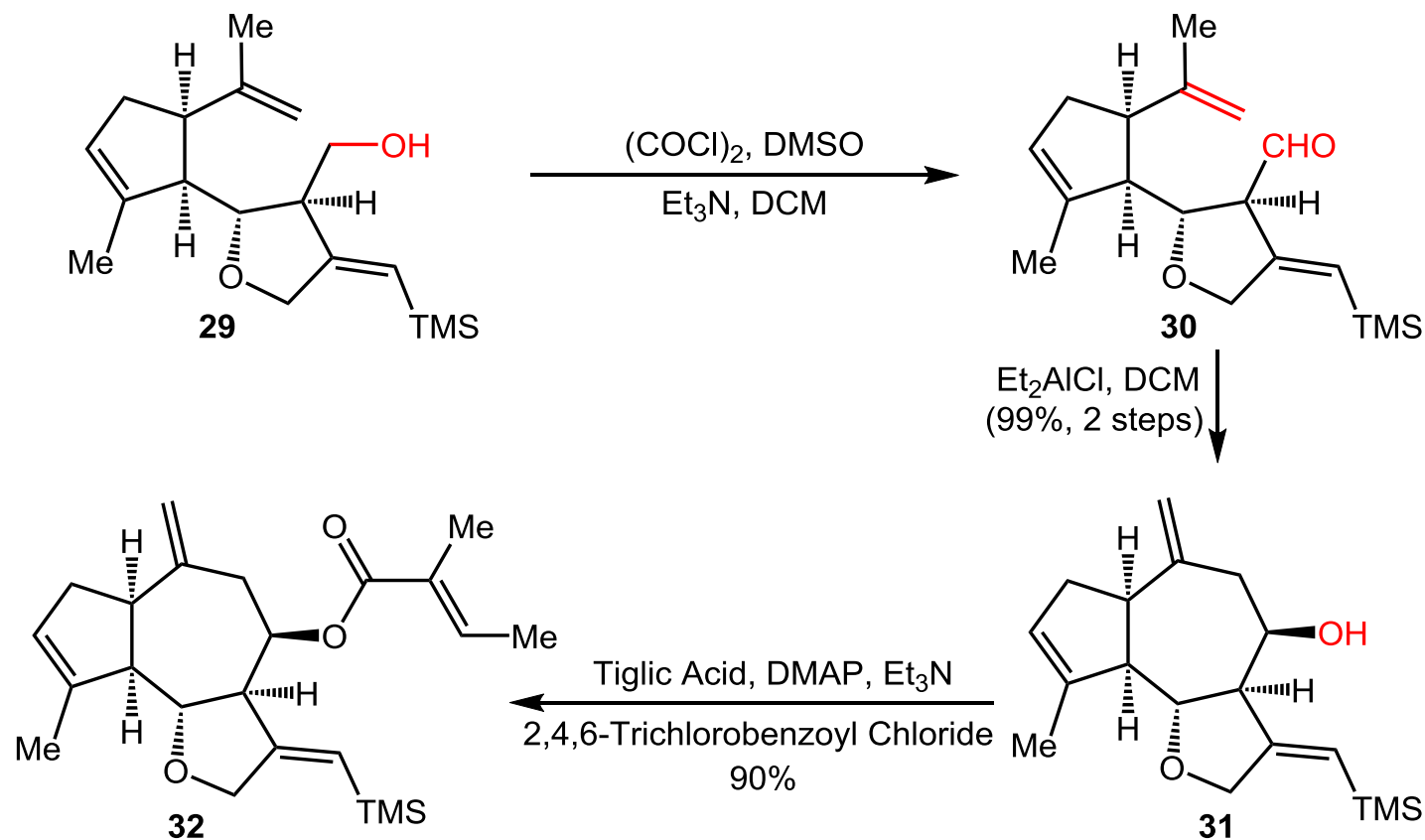
Synthesis of Intermediate 26:



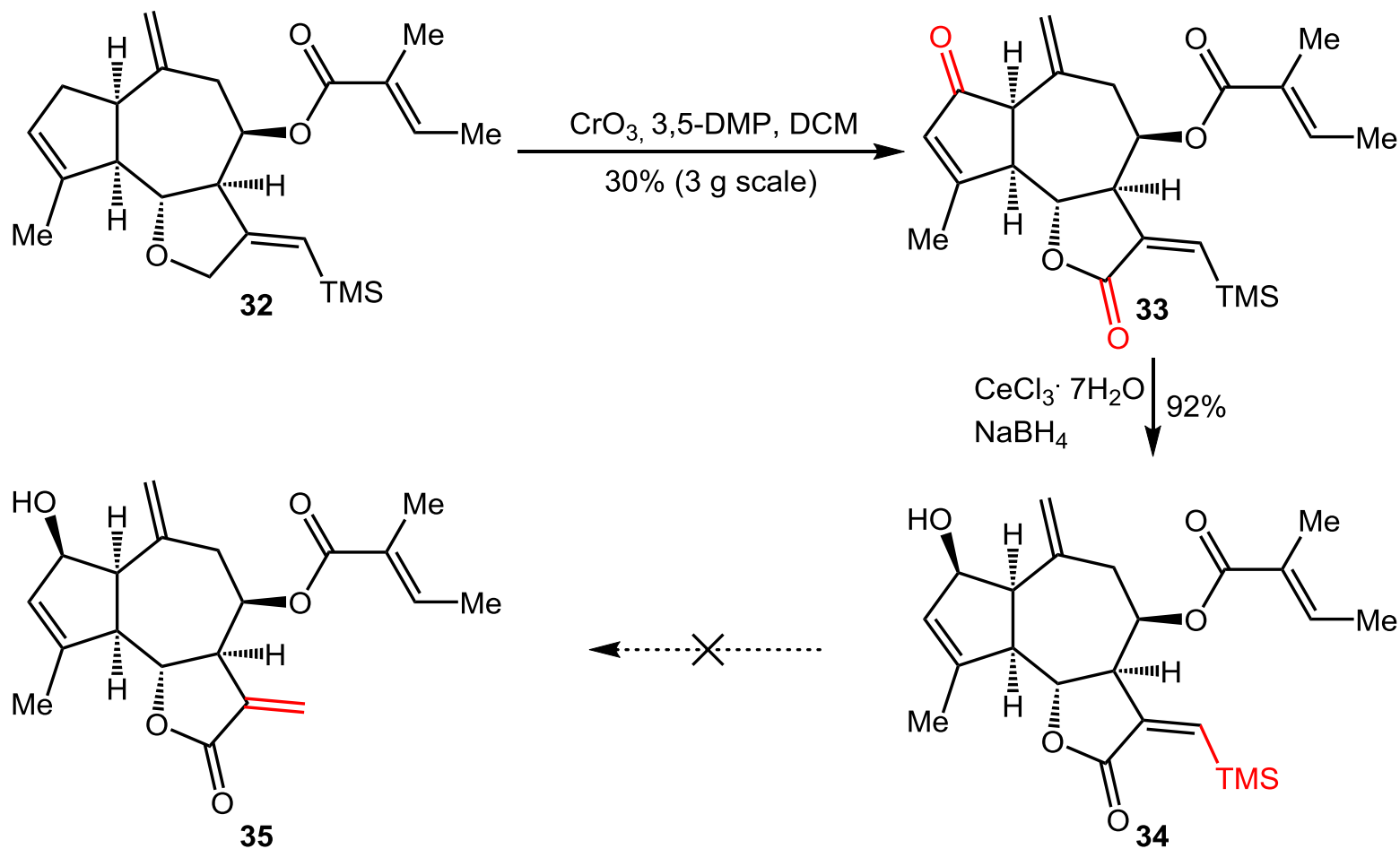
Synthesis of Intermediate 29:



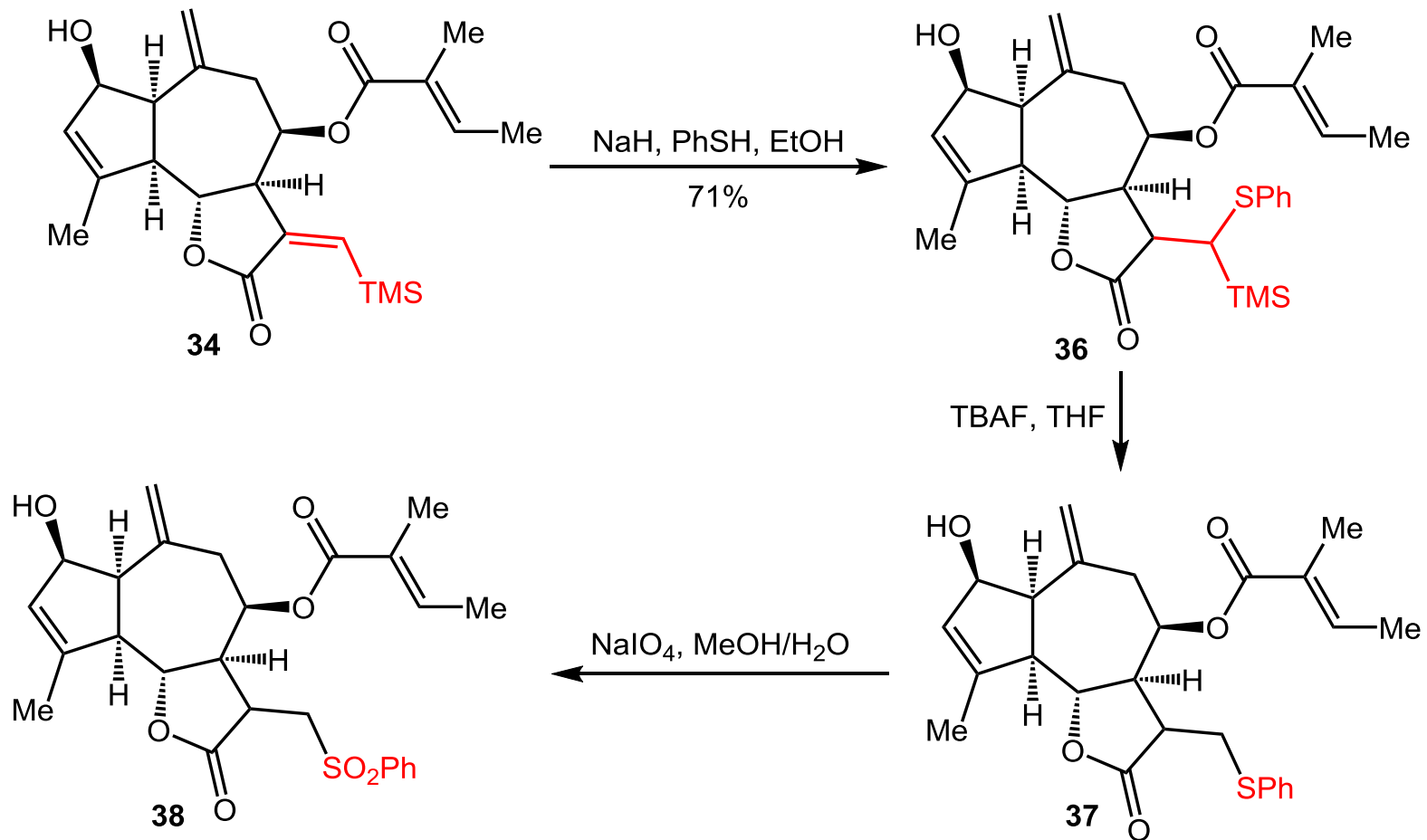
Synthesis of Intermediate 32:



Synthesis of Intermediate 35:



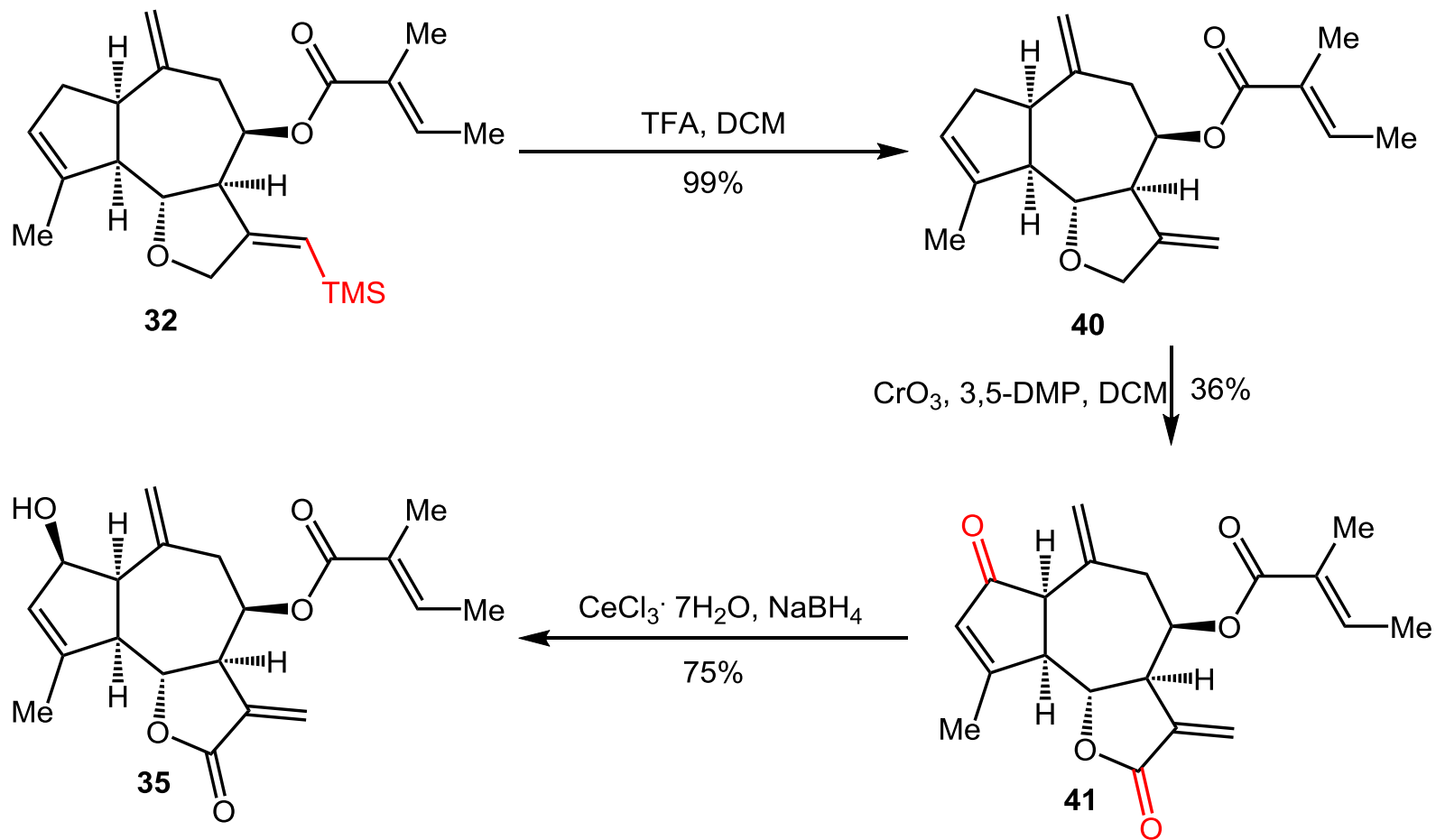
Synthesis of Intermediate 35:



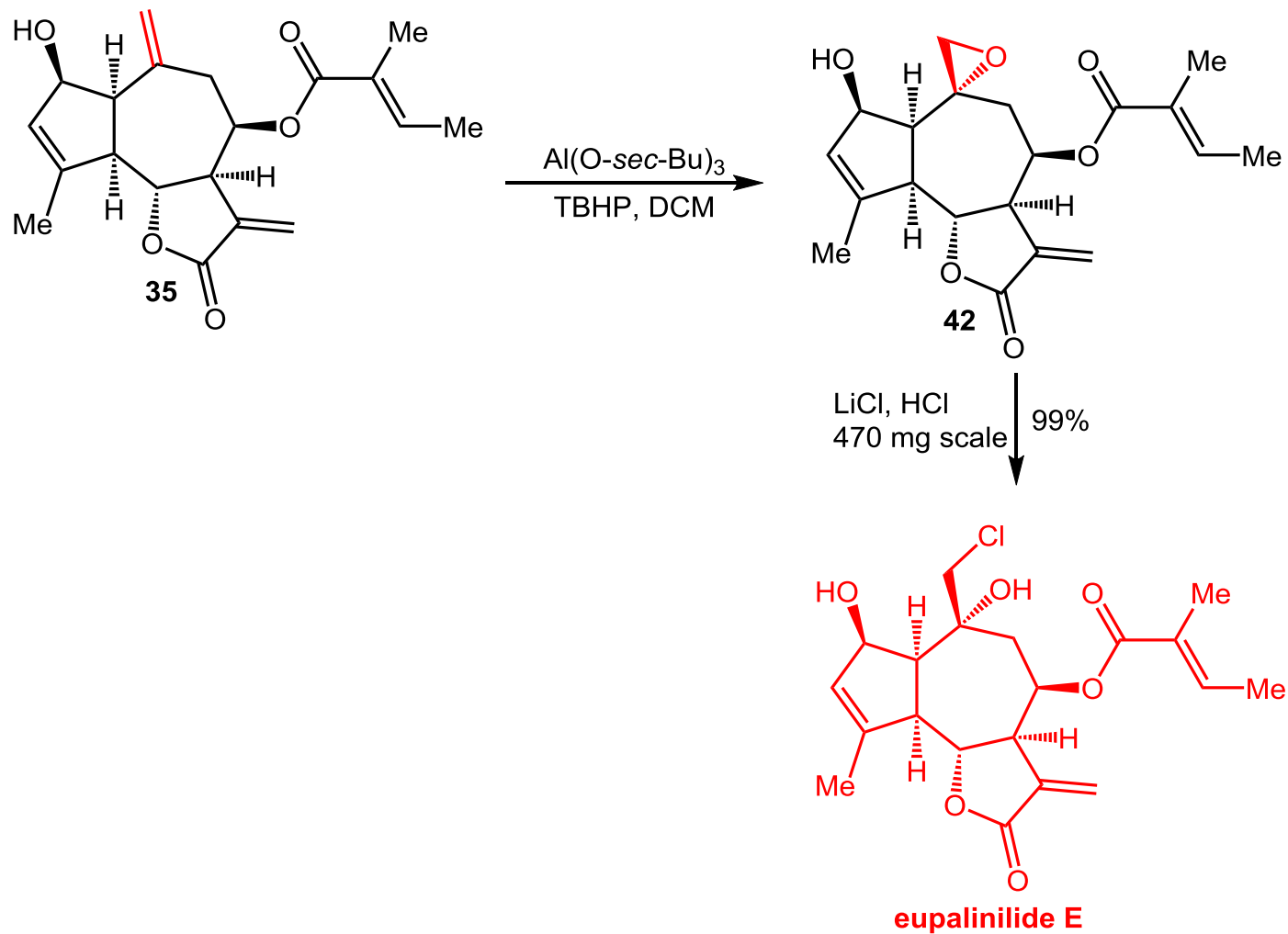
Synthesis of Intermediate 35:



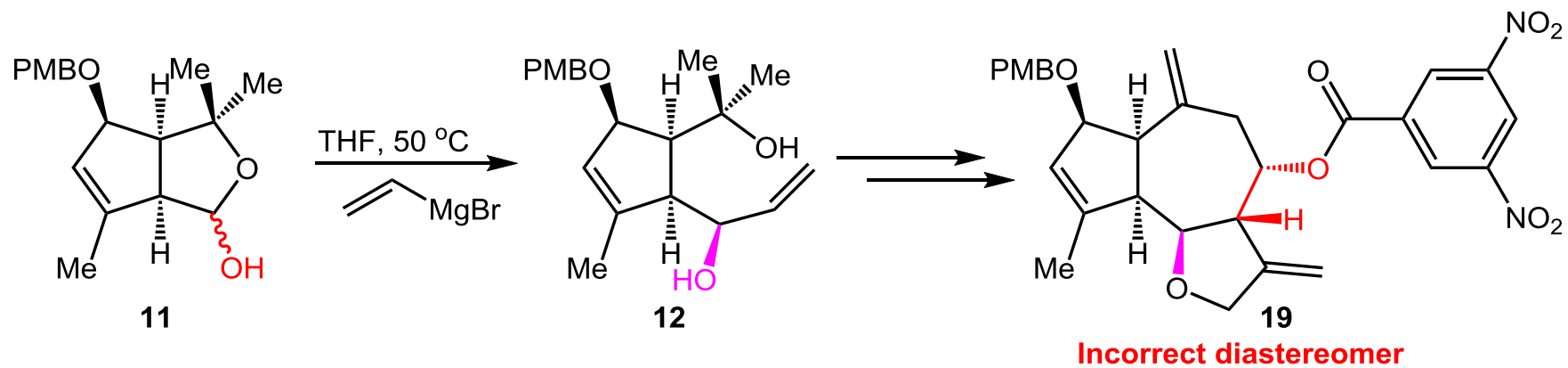
Synthesis of Intermediate 35:



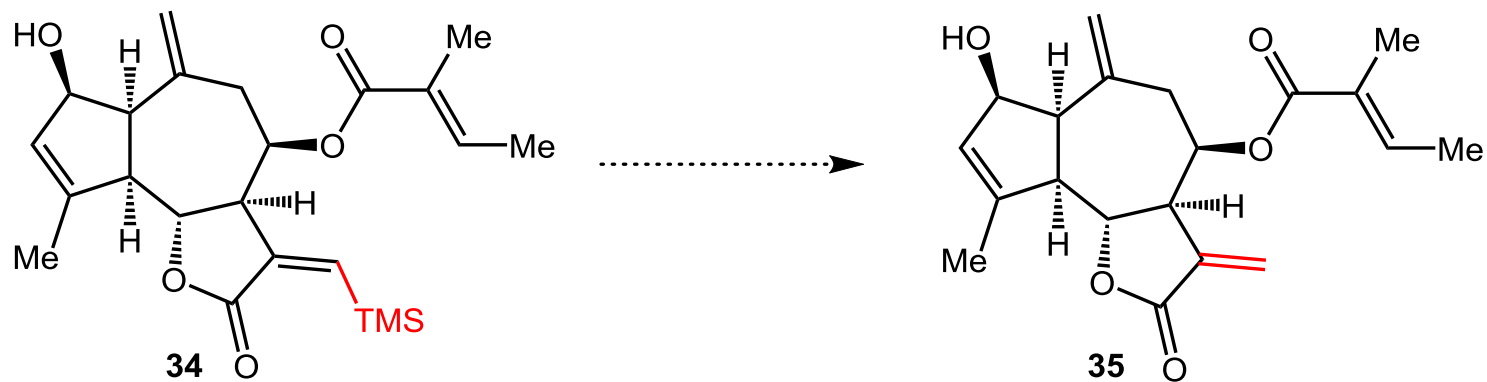
Synthesis of Intermediate 35:



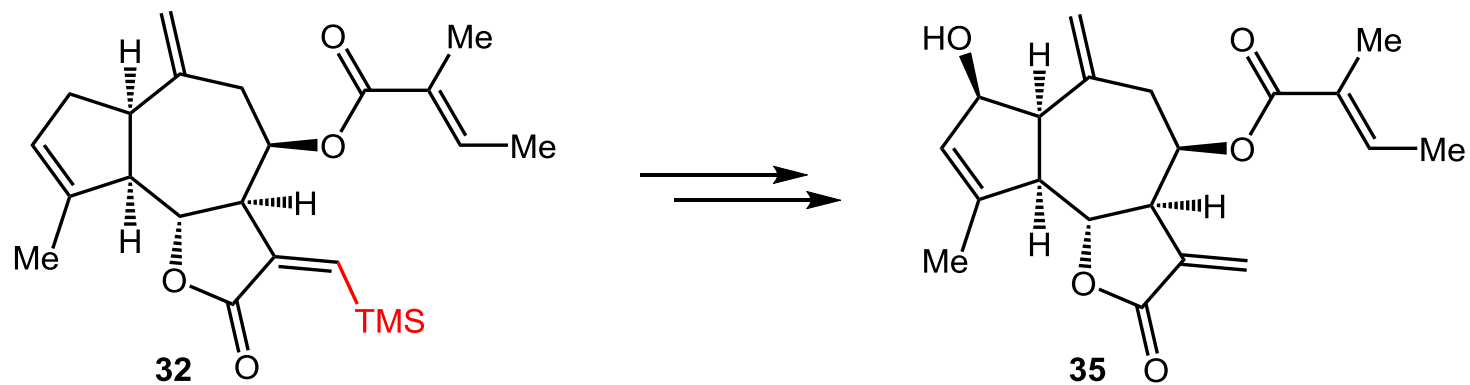
Summary:



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The First paragraph:

A series of sesquiterpene lactones, including eupalinilide E, were isolated in 2004 from *Eupatorium lindleyanum*, a plant which has ethnopharmacological uses as an antibacterial and antihistamine. Eupalinilide E was unique among coisolated compounds, as it possessed selective antiproliferative activity against A549. As a consequence of this resistance, there is an urgent need to develop drugs for this form of nonsmall cell lung cancer.

The First paragraph:

Patients with cancers possessing KRAS mutations have reduced benefit from adjuvant chemotherapy, are resistant to EGFR inhibitors, and experience less clinical success from medication in comparison to other forms of cancer, all of which significantly contribute to a low expectancy of survival for the patient. While it had been shown to possess selective cytotoxicity against a difficult cancer cell line, further evaluation of eupalinilide E did not occur beyond the initial isolation until the discovery of its ability to control stem cell fate.

The Last paragraph:

The chemistry and biology of eupalinilide E inspired the development of the first laboratory route to the natural product. With the evolution of multiple synthetic approaches a final strategy was developed that yielded eupalinilide E (>400 mg in a single batch), generating ample material for testing and probe development. Preliminary route failure could be retrospectively traced to premature introduction of oxygen into synthetic intermediates. As a consequence, the successful strategy introduced oxygen at a late stage through oxidation of activated methylene groups, providing carbonyls. This approach maximized substrate compatibility with different reagents up to the late-stage oxidation.
