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An Eight-Step Synthesis of Epicolactone Reveals its Biosynthetic Origin

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## **Total Synthesis of Epicolactone**

Significance: Trauner and co-workers report the total synthesis of epicolactone, isolated from fungi living on sugar and cocoa trees belonging to the *Epicoccum* species. Besides the intriguing complexity of the carbon skeleton, this metabolite shows promising antimicrobial and antifungal biological activity. Based on structural similarities with purpurogallin, known to be formed by oxidative dimerization of pyrogallol, they propose the biosynthesis of epicolactone involving an oxidative dimerization of epicoccine and epicoccone B, both metabolites of the *Epicoccum* species, and support it by means of a highly efficient synthesis.

**Comment:** The sequence commences with the synthesis of **A**, prepared from vanillyl alcohol in six steps (12% overall yield), and epicoccine, prepared from eudesmic acid in five steps (43% overall yield). The exposure of **A** and epicoccine to  $K_3[Fe(CN)_6]$  generates the respective quinones, which undergo the following reaction cascade: (5+2) cycloaddition gives intermediate **C**, which undergoes retro-Claisen condensation forming intermediate **D**, followed by vinylogous aldol reaction affording **E** in 42% yield. Epicolactone was obtained by demethylation of **E**.

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**Key words** 

(5+2) cycloaddition

retro-Claisen condensation

vinylogous aldol reaction

cascade reaction

biomimetic synthesis

