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Total Synthesis of (–)-4-Hydroxyzinowol
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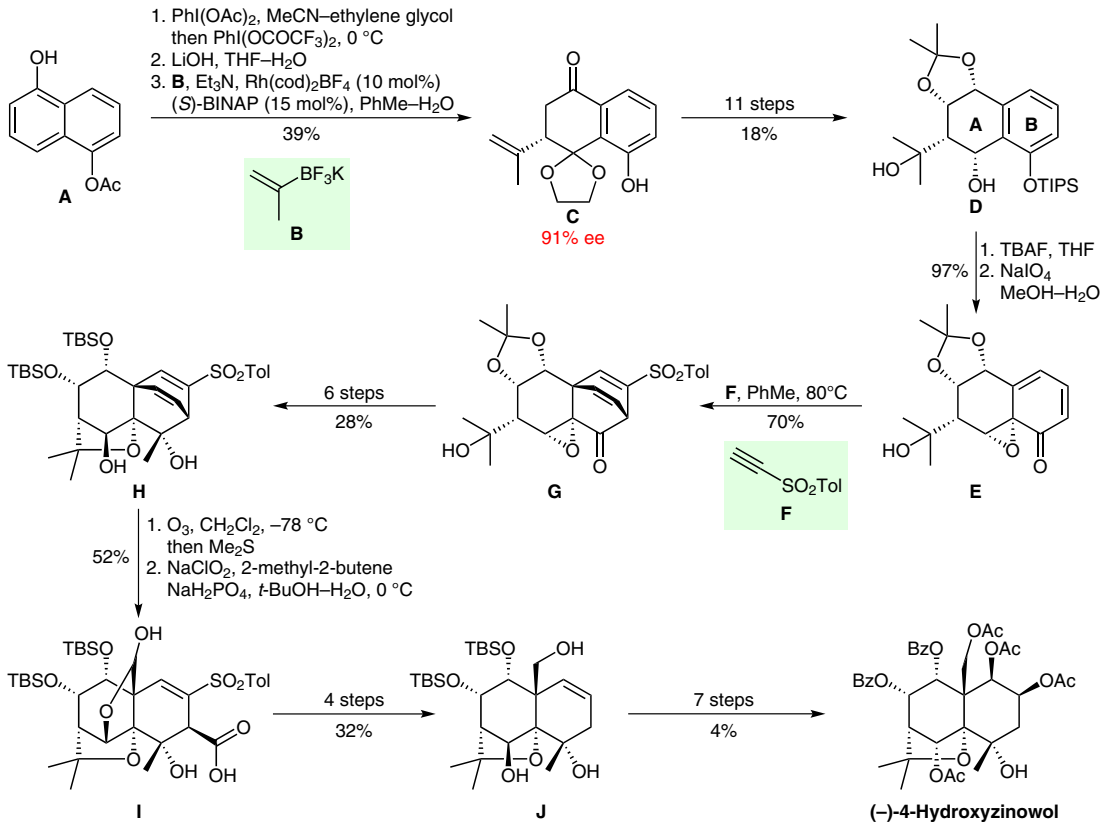
Synthesis of (–)-4-Hydroxyzinowol



Significance: 4-Hydroxyzinowol is a highly oxidized sesquiterpenoid of the dihydro-β-agarfuran family. Following its isolation from the plant *zinowiewia Costaricensis*, it was found to be a potent inhibitor of a daunorubicin related MDR transporter. Thus, 4-hydroxyzinowol is considered to be a potential lead structure for the treatment of cancers with acquired multi-drug resistance. In this work, the authors disclose the first total synthesis of this promising natural product.

Comment: Starting from naphthol **A**, oxidative dearomatization and asymmetric 1,4-addition of tetrafluoroborate **B** gave phenol **C** with good enantioselectivity. Further steps completed the oxidation state adjustment of the A-ring in **D** to set the stage for another oxidative dearomatization to yield epoxide **E**. Finally, Diels–Alder reaction followed by ozonolysis of the more electron-rich double bond in diene **H** gave **I**, which was transformed into 4-hydroxyzinowol in eleven additional steps.

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Synthesis of Natural Products and Potential Drugs

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Diels–Alder reaction