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.