Synthesis of (+)-Hexacyclinol

Significance: (+)-Hexacyclinol is a metabolite isolated from *Panus rudis* strain HKI 0254 in 2002. The structure of this natural product has been the cause of recent controversy [*Chem. Eng. News* **2006**, 84(31), 11]. A synthesis of the proposed structure (J. La Clair *Angew. Chem. Int. Ed.* **2006**, 45, 2769-2773) has recently been revised on the basis of calculated ¹³C NMR shifts (S. D. Rychnovsky *Org. Lett.* **2006**, 8, 2895-2898). This work substantiates the revised structure and relates to a recent biomimetic synthesis of (+)-panepophenanthrin by Porco and co-workers (*Angew. Chem. Int. Ed.* **2003**, 42, 3913-3917) that amply displays the virtues of biomimetic strategy in natural product synthesis.

Comment: Stille coupling of bromide **B** and vinyl stannane **C** gave **D** that, upon silyl cleavage, underwent Diels-Alder dimerization via *exo* transition state **E** to afford **F**. Subsequent treatment with K10 clay induced S_N2' substitution of the allyl-methoxy group by the proximal *Re* face hydroxyl group giving the target.

Reviews: *The Stille Reaction*, V. Farina, V. Krishnamurthy, W. J. Scott *Org. React (N.Y.)* **1997**, 50, 1-652. *Clay and Clay-Supported Reagents in Organic Synthesis*, R. S. Varma *Tetrahedron* **2002**, 58, 1235-1255.

Category

Synthesis of Natural Products and Potential Drugs

Key words

Stille reaction

Diels-Alder reaction

acid-catalyzed rearrangement

SYNFACT
of the month