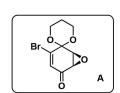
## Total Synthesis and Structure Assignment of (+)-Hexacyclinol

Porco, J.A., Jr.; Su, S.; Lei, X.; Bardhan, S.; Rychnovsky, S.D.

Angew. Chem. Int. Ed. 2006, 35, 5790 - 5792

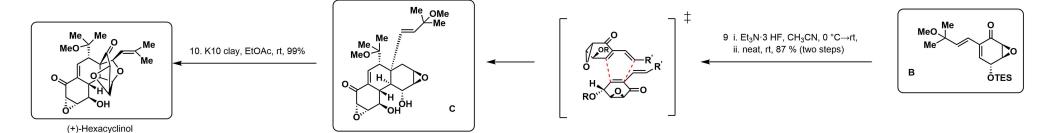
- OMe Br
- 1. PIDA, MeOH, RT 96%
- 2. 1,3-propanediol, BF<sub>3</sub>·Et<sub>2</sub>O, DME, rt, 75%
- 3. Ph<sub>3</sub>COOH, NaHMDS, (+)-DIPT,
- 4 Å mol sieves, PhMe, -55 °C, 80%

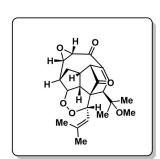


- 4. LiEt<sub>3</sub>BH, THF, -78°C, 98%
- 5 i. PPh<sub>3</sub>, DIAD, 4-nitrobenzoic acid, THF, -50 °C→rt ii. NaOMe 1 M, MeOH, rt, 80%
- 6. K10 clay (acidic silicate), CH2Cl2, 98%

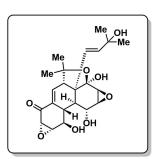


- 7. Et<sub>3</sub>SiCl, 2,6-lutidin, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, 83%
- 8. [Pd<sub>2</sub>(dba)<sub>3</sub>], AsPh<sub>3</sub>, PhMe, 110 °C, 96%





- Structure proposed by U. Gräfe (J. Antibiotics 2002 814) isolated from fungus panus rudis found in sibiria
- Allegedly first total synthesis by J.J. La Clair (34 Steps) (Angew. Chem. Int. Ed. 2006 2769-2773 Retracted 2012)
- NMR DFT prediction by S.D. Rychnovsky (Org. Lett. 2006 2895–2898) shows discrepancy between NMR spectra from naturally obtained hexacyclinol and Gräfes proposed structure
- S.D. Rychnovsky noted similarities of the spectral data to previously synthesized panepophenanthrin by J.A. Porco
- Rychnovsky also believed that hexacyclinol could be an isolation artefact deriving from panepophenanthrin (later refuted by J.A. Porco)



Panepophenanthrin

Proposed structure for Hexacyclinol by U. Gräfe

Bonus question: How could paneophenanthrin react to hexacyclinol during silica gel chromatography purification?