cis,cis,cis,cis-1,2,3,4,5-Pentakis(hydroxymethyl)cyclopentane[1]

Summary: The synthesis of *cis,cis,cis,cis*-1,2,3,4,5-pentakis(hydroxymethyl)cyclopentane is described.

Sir: Molecules with chemically distinct surfaces play an increasingly important role in complexation chemistry (e.g., crown ethers), in synthetic enzymology, in ion-transport phenomena, and in surfactant chemistry. We are particularly interested in systems for which the polar substituents, e.g., hydroxymethyl groups, are maintained cis to each other on a carbocyclic backbone. We now report the synthesis of the first member of this series—*cis,cis,cis,cis*-1,2,3,4,5-pentakis(hydroxymethyl)cyclopentane (**1**).

Formation of an all-cis pentasubstituted pentacycle in which the stereochemical integrity is not maintained by additional rings presented a synthetic challenge with few precedents. The all-cis cyclitol 1,2,3,4,5-cyclopentanepentol has been synthesized, although in a mixture of geometric isomers.[2] Our approach used the sine qua non of stereospecific reactions, the Diels-Alder cycloaddition (see Figure 1). Addition of a chilled ethereal solution of maleic anhydride to a <10 °C solution of 5-[(benzyloxy)methyl]cyclopentadiene[3] (**2**) yielded the bicyclo[2.2.1] derivative **3** in an average 60% yield as a colorless crystalline solid, mp 104–105 °C.[4] In bicycloheptene **3**, the double bond masked two of the cis substituents while the endo approach of the dienophile to the least hindered diene face provided the requisite endo, anti disposition of the remaining substituents. Single-crystal X-ray diffractometry provided unambiguous confirmation of the stereochemistry of **3** (see Figure 2).[5]

Since direct ozonation/reduction of the bicycloheptene **3** produced poor yields, methanol/HCl esterification to dimethyl ester **4** (92% yield) preceded ozonation. Moreover, to avoid the possibility of epimerization of the polycarbonyl derivative during workup, the ozonide was subjected to *direct* reduction with $LiAlH_4$. The resulting tetraol **4** was finally debenzylated with Na/NH_3 (l) and the pentaol **1** extracted from the inorganic residue with *tert*-butyl alcohol. Solvent removal yielded pure *cis,cis,cis,cis*-1,2,3,4,5-pentakis(hydroxymethyl)cyclopentane (**1**) in 45% yield from **4** as a colorless viscous oil having an NMR spectrum consistent with a C_5 symmetric molecule.[6]

Pentamethanol **1** is water miscible and soluble in Me_2SO but insoluble in most organic solvents. We are currently studying the surfactant behavior of **1**. Our ultimate goal is the dehydrative dimerization of **1** into dodecahedrane[7] (**5**) through a novel, high-symmetry approach.

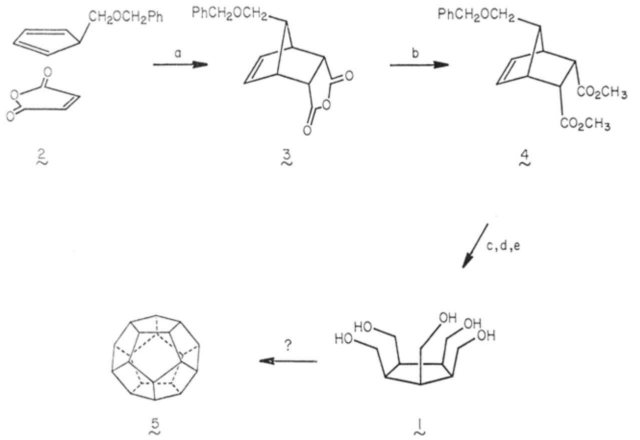

Figure 1. Synthesis of cyclopentanepentamethanol (**1**): (a) 10 °C, THF; (b) CH_3OH/HCl; (c) O_3; (d) $LiAlH_4$; (e) Na/NH_3 (l).

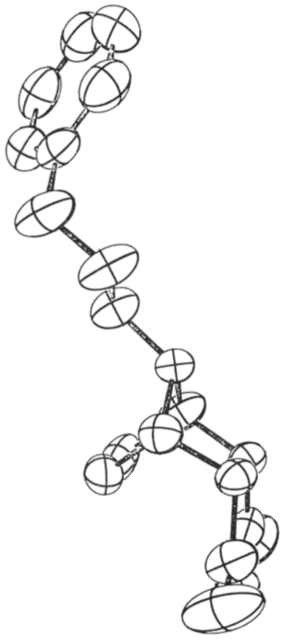

Figure 2. Crystal structure of adduct **3**.

Acknowledgment. Support of this research by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

Supplementary Material Available: Positional and thermal parameters refined for the non-hydrogen atoms and hydrogen atom parameters (3 pages). Ordering information is given on any current masthead page.

Laren M. Tolbert,*[†] J. Carlin Gregory
Carolyn P. Brock

Department of Chemistry
University of Kentucky
Lexington, Kentucky 40506-0055

Received October 30, 1984

---

(1) Taken from the M.S. thesis of J. Carlin Gregory, University of Kentucky, 1983.

(2) Cocu, F. G.; Posternak, T. *Helv. Chim. Acta* **1971**, *54*, 1676.

(3) Corey, E. J.; Koelliker, U.; Neuffer, J. *J. Am. Chem. Soc.* **1971**, *93*, 1489.

(4) ^1H NMR (90 MHz, Me_2CO-d_6) δ 2.46 (1 H, br t, $J = 8$), 3.37 (3 H, d, $J = 7$), 3.81 (2 H, d of d), 4.43 (2 H, s), 6.16 (2 H, m), 7.27 (5 H, s); MS, *m/e* 284, 91 (100%); IR (KBr) 1880, 1790 cm^{-1}. Anal. Calcd for $C_{17}H_5O_4$: C, 71.82; H, 5.67. Found: C, 71.62; H, 6.83.

(5) Compound **3** crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 6.2161$ (8) Å, $b = 9.0987$ (10) Å, $c = 26.0744$ (18) Å, and $Z = 4$ at 295 K. The structure was refined (full-matrix least-squares) to agreement factors R and R_w on F_o of 0.043 and 0.046 with 190 variables and the 1013 observations having $F_o^2 \geq 3\sigma(F_o^2)$ out of the 2480 unique data measured with an Enraf-Nonius CAD4/F diffractometer using Mo K_α radiation ($2\lambda_{max} = 60°$). There was no important decomposition, absorption, or extinction. The features of the final difference map have heights of ±0.17 e Å^{-3}.

(6) ^1H NMR (D_2O, 200 MHz) δ 2.45 (5 H, br m), 3.65 (10 H, br m); ^{13}C NMR (D_2O, 200 MHz) 57.46, 42.38. Anal. Calcd for $C_{10}H_{20}O_5$: 220.131. Found: 220.130.

(7) Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4503.

[†] Fellow of the Alfred P. Sloan Foundation, 1983–85.