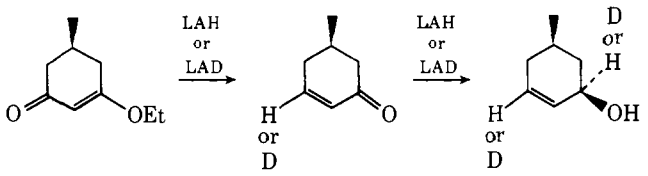
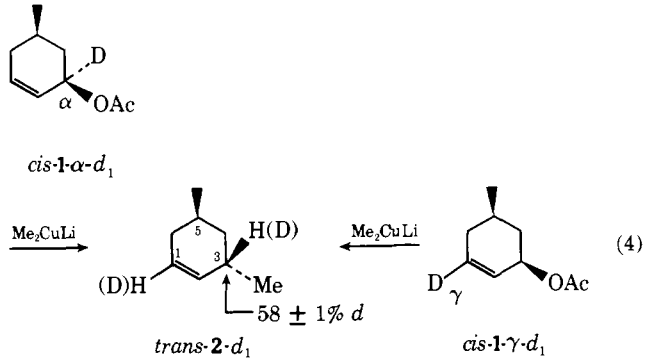
biased system. Synthesis of the 5-methyl-2-cyclohexenyl system involves two lithium aluminum hydride reductions.[5b] The final reduction gives 95% cis alcohol (**5**) from which pure *cis*-**5** can be obtained. This mixture can also be converted to *trans*-**5**.[5b,c] As illustrated, use of lithium aluminum deuteride in the appropriate step leads to either α- or γ-deutero-*cis*-**5**.



cis-**5**

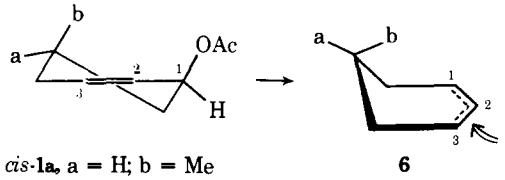
As shown by eq 4, *cis*-**1**-α-d_1 (96.7 ± 1.6% *d*) and *cis*-**1**-γ-d_1 (98.4 ± 1.4% *d*) gave *trans*-**2**-d_1 with the same fraction of total deuterium at C_3. Total deuterium contents were determined from mass spectra.[8] Expanded Eu(fod)$_3$-shifted 100-MHz NMR spectra of the deuterated acetates **1**-d_1 showed they were discretely labeled as indicated. Unreacted *cis*-**1**-α-d_1 was isolated and found to be unchanged which shows that scrambling does not occur prior to reaction. The deuterium distribution in *trans*-**2**-d_1 was determined from the total deuterium (same as for *cis*-**1**-d_1) and relative peak areas (planimeter) for the C_3 and C_5 proton signals in expanded 270-MHz NMR spectra which gave baseline separation of both signals. The data indicate that **2**-d_1 derived from either α- or γ-deuterio-**1** has somewhat more than half of the label at C_3. This probably results from a systematic error in determining the deuterium distribution. In any case it appears that the reaction involves a symmetrical intermediate (allyl radical or π-allyl complex) in which the two allylic positions are equivalent.



cis-**1**-α-d_1

trans-**2**-d_1 *cis*-**1**-γ-d_1 (4)

The data under eq 3 show that the 1 → 2 transformation is highly stereoselective. This system is unbiased with regard to substitution with and without allylic rearrangement. However, there may be an inconspicuous steric bias, unique to the cyclohexenyl system, that favors inversion of configuration. For reasons given earlier in another connection,[9] the quasi-axial conformation (**1a**) may be related to the best transition state for cleavage of the allylic bond. This leads to an allylic intermediate (**6**) with the out of plane C_5 carbon on the side from which the acetate group has departed. Clearly the oppposite side (**6**, arrow) is less hindered for capture to form product or an intermediate π-allyl complex.



cis-**1a**, a = H; b = Me
trans-**1a**, a = Me; b = H

6

Acknowledgment. We thank Professor C. P. Casey for helpful suggestions. This work was supported by the Research Committee of the Graduate School of the University of Wisconsin and by the National Science Foundation (MPS76-15879).

References and Notes

(1) R. Rona, L. Tökes, J. Tremble, and P. Crabbé, *Chem. Commun.*, 43 (1969).
(2) (a) R. J. Anderson, C. A. Henrick, J. B. Siddall, and R. Zurfluh, *J. Am. Chem. Soc.*, **94**, 5379 (1972); (b) R. J. Anderson, C. A. Henrick, and J. B. Siddall, *ibid.*, **92**, 735 (1970).
(3) E. J. Corey and J. Mann, *J. Am. Chem. Soc.*, **95**, 6832 (1973).
(4) G. E. Gream and C. F. Pincombe, *Aust. J. Chem.*, **27**, 543 (1974).
(5) (a) H. G. Goering, T. D. Nevit, and E. F. Silversmith, *J. Am. Chem. Soc.*, 77, 4042 (1955); (b) H. L. Goering and J. P. Blanchard, *ibid.*, **76**, 5405 (1954); (c) H. L. Goering and J. T. Doi, *ibid.*, **82**, 5850 (1960).
(6) H. O. House and W. F. Fischer, Jr.; *J. Org. Chem.*, **33**, 949 (1968).
(7) N. Muller and W. C. Tosche, *J. Chem. Phys.*, **37**, 1167 (1962); M. E. Peterkin, *Appl. Spectrosc.*, **28**, 41 (1974); see also M. Mousseron, *Bull. Soc. Chim. Fr.*, 218 (1946).
(8) K. Biemann, "Mass Spectra-Organic Chemistry Applications", McGraw-Hill, New York, N.Y., 1962, p 223.
(9) H. L. Goering and R. R. Josephson, *J. Am. Chem. Soc.*, **84**, 2779 (1962).

Harlan L. Goering,* Victor D. Singleton, Jr.
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706
Received August 26, 1976

Capped Cyclodextrin

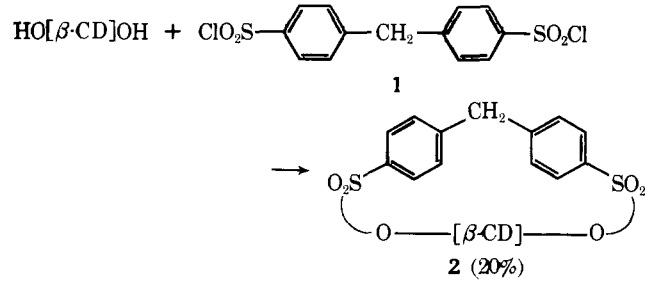
Sir:

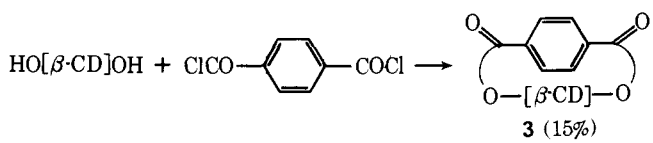
Inclusion recognition or host-guest recognition has attracted the rapidly increasing interest of chemists since the first structural recognition of benzene derivatives by cyclodextrins in ester hydrolyses,[1] the remarkable regio recognition of anisole by cyclodextrin in chlorination,[2] or the beautiful chiral recognition of α-amino acids by certain crown ethers[3] has been reported.

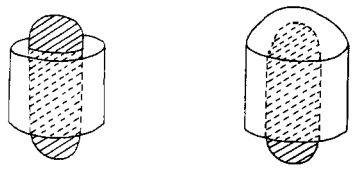
However, only a few host molecules are known to recognize a guest molecule mostly via *hydrophobic interaction.* For development and understanding of the concept of host-guest recognition, new families of hydrophobic binding hosts must be added into the list of known hosts.

According to Nèmethy-Sheraga theory,[4] hydrophobic destabilization originates mostly in the entropically unfavorable orientation of water molecules on the surface of the hydrophobic guest (and/or host) dissolved in water. From this standpoint, the driving force of hydrophobic host-guest binding, or *hydrophobic interaction,* should be closely correlated with a decrease of the hydrophobic surface exposed in water. Thus, it may be reasonably expected that the capping of well-known cylindrical hosts should cause a remarkable strengthening of hydrophobic binding[5] as is schematically exemplified by Figure 1.

Now we wish to report the preparation of β-cyclodextrins (β-CD), capped by hydrophobic moieties, **2**, and **3**, which bind







a. binding by a common cylindrical host

b. binding by a capped cylindrical host

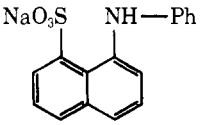
Figure 1. Schematic representation of hydrophobic binding. Obliquely lined areas are exposed in water, not contributing to binding. Obliquely dotted lined areas are contributing to binding.

sodium 1-anilino-8-naphthalenesulfonate 11-24 times stronger than the parent cyclodextrin.

Treatment of β-CD (0.010 mol) with diphenylmethane-*p,p'*-disulfonyl chloride (**1**) (0.012 mol) in pyridine gave crude **2** in ca. 70% yield based on TLC analysis. Careful workup (decantation, condensation, precipitation with $CHCl_3$, recrystallization from water) gave pure **2** in 20% yield. IR (KBr), 1595, 1495, 1360, 1180, and 880 cm^{-1}; UV (H_2O) 236 and 257 nm. NMR spectrum, multiplet centered at 7.69 (aromatic 8 H), multiplet centered at 4.87 (C_1H, 7 H), and multiplet centered at 3.50 (others, 42 H)

The reaction of β-CD (0.0020 mol) and terephthaloyl chloride (0.0026 mol) in pyridine afforded practically pure **3** in 15% yield after repeated recrystallizations from water. IR (KBr), 1710, 1280, and 730 cm^{-1}; UV (H_2O) 246 nm. NMR spectrum, multiplet centered at 7.97 (aromatic 4 H), multiplet centered at 4.80 (C_1H, 7 H), and multiplet centered at 3.50 (others, 42 H)

Binding of 1,8-ANS, **4**, by capped β-CD's was investigated by fluorescence measurements.[6] A strong increase in the fluorescence intensity was observed, and the Benesi-Hildebrand plot[7] gave a straight line in the concentration range of a capped β-CD from 4.2×10^{-5} to 2.5×10^{-4} M at a concentration of 5×10^{-6} M of **4**, which gave the binding constant for the complexation of **4** by **2** to be 1.3×10^3 M^{-1}. The constant for the binding of **4** by **3** was 6.4×10^2 M^{-1}, interestingly in a good accord with that by **2**. Thus, binding by a capped β-CD becomes 11-24 times stronger than that by the parent β-CD and is relatively insensitive to the capping groups.



4

A cyclodextrin with pendant hydrophobic substituents[5] was reported to bind aromatic guests more poorly ($K_{diss} = 2.6 \times 10^{-2}$ for *m*-nitrophenyl acetate) than the parent CD ($K_{diss} = 5.3 \times 10^{-3}$) does but it binds 1-adamantanecarboxylic acid more strongly ($K_{diss} = 6.7 \times 10^{-5}$) than the parent CD ($K_{diss} = 1.6 \times 10^{-3}$). The capped CD **2** in the present work also binds adamantanecarboxylic acid strongly ($K_{diss} = 2.0 \times 10^{-5}$ at pH 6.86).[8] That capped CD's in this present work bind even an aromatic **4** much more strongly than the parent CD is, therefore, very interesting, and is in good agreement with the Nèmethy-Sheraga's concept of the hydrophobic interaction.

Thus, we may safely say that one can design a structure of an appropriate hydrophobic host primarily based on this concept.

References and Notes

(1) (a) N. Hennrich and F. Cramer, *J. Am. Chem. Soc.*, **87**, 1121 (1965); (b) R. L. VanEtten, J. F. Sebastian, G. A. Clowes, and M. L. Bender, *ibid.*, **89**, 3242, 3253 (1967).
(2) R. Breslow and P. Campbell, *J. Am. Chem. Soc.*, **91**, 3085 (1969).
(3) E. B. Kyba, K. Koga, L. R. Sousa, M. G. Siegel, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 2692 (1973).
(4) G. Nèmethy and H. A. Sheraga, *J. Phys. Chem.*, **66**, 1773 (1962).
(5) This idea is first suggested by Breslow in his noncapped (or "flexibly" capped) cyclodextrin. J. Emert and R. Breslow, *J. Am. Chem. Soc.*, **97**, 670 (1975).
(6) D. C. Turner and L. Brand, *Biochemistry*, **7**, 3381 (1968).
(7) (a) H. A. Benesi and H. Hildebrand, *J. Am. Chem. Soc.*, **71**, 2703 (1949); (b) T. Kinoshita, F. Inuma, and A. Tsuji, *Chem. Pharm. Bull.*, **22**, 2413 (1974).
(8) Although pH for the present measurement and the Emert-Breslow measurement were different, being 6.86 and 9.00, respectively, the K_{diss} for the binding of 1-adamantanecarboxylic acid was only slightly dependent on pH of this region, since its pK_a is ca. 5.
(9) The binding of *m*-nitrophenyl acetate, a Emert-Breslow substrate, by the capped cyclodextrin **2** has not been examined and, therefore, a direct comparison of **2** with the Emert-Breslow's cyclodextrin is not possible. One of the referees pointed out the reasonable possibility that the polar nitro group may destabilize the inclusion complex to show large K_{diss} value. However, the solubility of ANS, the present guest, in water (more than 2.2 M) is considerably higher than that of *m*-nitrophenyl acetate (ca. 0.1 M), suggesting that polar destabilization is not the sole determining factor.

Iwao Tabushi,* Kazuhiro Shimokawa, Nobuaki Shimizu Hiroko Shirakata, Kahee Fujita

Department of Pharmaceutical Sciences, Kyushu University Maidashi, Fukuoka, 812 Japan

Received July 6, 1976

Stereoselective Formation of Diepoxides by an Enzyme System of *Pseudomonas oleovorans*

Sir:

In previous work, we have established that an enzyme system from *Pseudomonas oleovorans* catalyzes the conversion of terminal olefins to the corresponding 1,2-oxides.[1-12] Among the highly unusual characteristics of this enzymatic epoxidation reaction are a specificity far different from that observed in peracid epoxidations, a lack of retention of the original olefinic geometry during the course of the reaction, and the fact that the conversion of 1,7-octadiene to 7,8-epoxy-1-octene proceeds with a high degree of stereoselectivity with more than 90% of the product being the *R*(+) isomer. Although each of these characteristics imparts potential synthetic utility to this enzymatic system, the latter is of particular interest since optically active epoxides with a high degree of optical purity cannot be produced from simple olefins via any known chemical epoxidizing agent.[13] We now wish to report that highly stereoselective syntheses of diepoxides from simple diolefins can also be achieved using this enzymatic system. Furthermore, we have found that the configuration of a preformed asymmetric center at one end of a substrate profoundly affects the stereochemical consequences of enzymatic oxygen insertion into a double bond at the other end of the molecule. These findings not only establish the unique suitability of this system for the facile production of both mono and diepoxides of high optical purity, but also provide information about the mode of substrate binding at the active site.

Enzymatic epoxidation of 1,7-octadiene to produce 7,8-epoxy-1-octene or 1,2;7,8-diepoxyoctane on a preparative scale was accomplished using growing cells of *P. oleovorans* in the presence of octane according to the procedures that we have previously described.[5,7] Enzymatic epoxidation of racemic 7,8-epoxy-1-octene was accomplished as follows. Shake flasks (100 300-ml) each containing 100 ml of P_1 minimal salts medium,[5] 1 ml of octane, 100 μl (87 mg) racemic 7,8-epoxy-1-octene and a 10-ml inoculum of a resting cell suspension of *P. oleovorans* (~10^9 cells/ml) were incubated for 20 h at 30 °C on a gyrotory shaker. The broths were then extracted with toluene and concentrated, and both the diepoxide product and unreacted 7,8-epoxy-1-octene isolated by vacuum distillation. Typical recoveries (before distillation) from a single shake flask