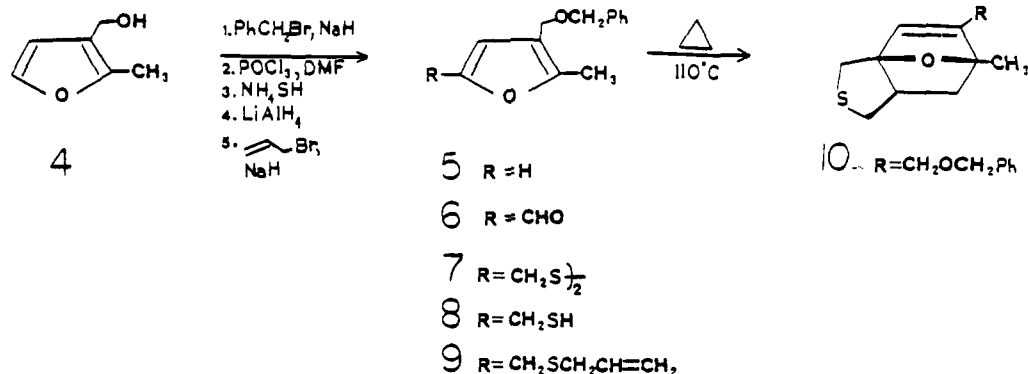
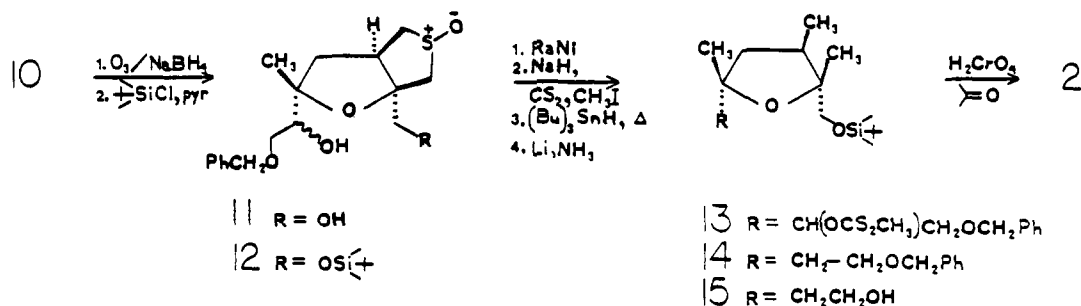


Scheme III

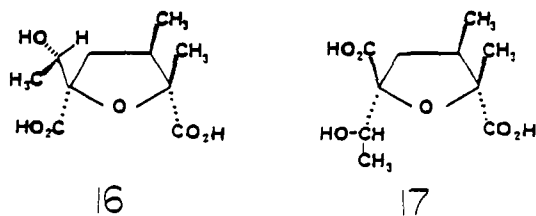


Scheme IV



11 was produced as a mixture of diastereomers, which were used in subsequent reactions without separation. Direct silylation of **11** with *t*-BuMe₂SiCl was performed (pyridine, 70 °C, 2 h) and treatment of **12** with Raney nickel¹³ in refluxing ethanol served to reduce the sulfoxide and desulfurize the resultant sulfide (in 68% from **10**). Deoxygenation of the epimeric hydroxy group proceeded cleanly using Barton's two-step method¹⁴ (i.e., xanthate formation followed by reduction of the crude xanthates **13** with (*n*-Bu)₃SnH in refluxing toluene) to give diprotected **14** in 80% yield. The benzyl group in **14** could be removed by reaction with lithium in ammonia (3:2, NH₃/THF) to yield silyl alcohol **15**. Finally, treatment of **15** with Jones' reagent at room temperature directly afforded in 60% yield a diacid that was identical with natural nemorensic acid in terms of its ¹³C and ¹H NMR spectra and its mass spectrum. Since compound **14** has the two pendant chains differentiated, through the use of deprotection and selective-oxidation strategies, one could have access to either monoacid.

In summary, this efficient and stereoselective approach to the highly substituted cyclic necic acids will allow selective preparation of monoester and dilactone natural products and their analogues. Application of these methods toward structures such as jaconecic acid (**16**)^{15a} and petasitenecic acid (**17**),^{15b} which would not require



the deoxygenation steps, would be straightforward and is currently under way.

(13) Analogous to W-2, 50% slurry in H₂O, pH 10; Sigma Chemical Co., St. Louis, MO.

(14) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1*, 1975, 1574.

(15) (a) Masamune, S. *J. Am. Chem. Soc.* 1960, 82, 5253. (b) Yamada, K.; Tatamatsu, H.; Suzuki, M.; Hirata, Y.; Haga, M.; Hirono, I. *Chem. Lett.* 1976, 461.

Supplementary Material Available: ¹H NMR and HRMS data for compounds **5**–**10** and **15**, ¹³C NMR data for **5**–**10**, and ¹H NMR, ¹³C NMR, and MS (70 eV) data for **2** (2 pages). Ordering information is given on any current masthead page.

Complementary Solutes Enter Nonpolar Preorganized Cavities in Lipophilic Noncomplementary Media¹

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Ordinarily, when host and guest complex, each must desolvate. Most hosts containing enforced cavities of molecular dimensions (cavitands)² contain holes large enough to admit solvent.³ Only the anisyl-based spherands⁴ and the cyclotrimeratrylene-based cavitands⁵ contain unsolvated interior surfaces. We report here complexation studies in CDCl₃ and C₆D₆ between nonpolar partners containing complementary surfaces. New cavitands **1**–**3** contain cylindrical wells of varying depths whose limited diameters

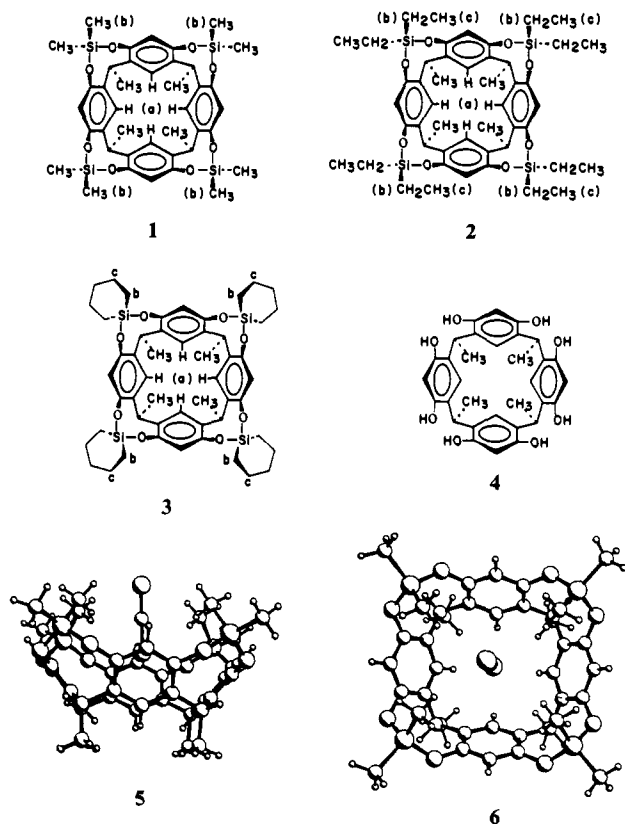
(1) We warmly thank the National Science Foundation for NSF Grant CHE 81-09532, which supported all of the work except the crystal structure determination, which was supported on NSF Grant CHE 82-05803.

(2) (a) Cram, D. J. *Science (Washington, D.C.)* 1983, 219, 1177–1183. (b) Moran, J. R.; Karbach, S.; Cram, D. J. *J. Am. Chem. Soc.* 1982, 104, 5826–5828.

(3) (a) Gutsche, C. D.; Levine, J. A. *J. Am. Chem. Soc.* 1982, 104, 2652–2653. (b) Miller, S. P.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* 1984, 106, 1492–1494. (c) Mock, W. L.; Shih, N. Y. *J. Org. Chem.* 1983, 48, 3618–3619. (d) Mock, W. L.; Irra, T. A.; Wepsiec, J. P.; Manimaran, T. L. *Ibid.* 1983, 48, 3619–3620.

(4) (a) Cram, D. J.; Kaneda, T.; Helgeson, R. C.; Lein, G. M. *J. Am. Chem. Soc.* 1979, 101, 6752–6754. (b) Cram, D. J.; Kaneda, T.; Helgeson, R. C.; Brown, S. B.; Knobler, C. B.; Maverick, E.; Trueblood, K. N. *Ibid.*, in press.

(5) (a) Canceill, J.; Lacombe, L.; Collet, A. *C. R. Acad. Sci., Ser. 2* 1984, 298, 39–42. (b) Canceill, J.; Collet, A.; Gabard, J.; Kotzyba-Hibert, F.; Lehn, J.-M. *Helv. Chim. Acta* 1982, 65, 1894–1897.



deny occupancy to all but slim linear guests.

Treatment of **4** (conformationally mobile)⁶ with appropriate dialkyldichlorosilanes in THF-Et₃N at high dilution closed four eight-membered rings to give **1**, **2**, and **3**⁷ in 37%, 9%, and 7% yields, respectively. Although melting at >320 °C, **1-3** were soluble in nonpolar solvents. Evaporation of **1** in CS₂ gave crystalline 1·2CS₂ of X-ray quality.

The Benesi-Hildebrand method⁸ for determining association constants (K_a) from ¹H NMR chemical shift changes⁹ was applied to **1** (0.001 M) complexing CS₂ (0.1-2 M) in CDCl₃ (five to ten points per run). Upon complexation, protons "a" lining the well bottom in **1** moved upfield from 7.35 maximally by 0.18 ppm. Protons "b" lining the upper sides in **1** moved downfield from -0.55 maximally by 0.40 ppm. The outward-facing protons remained unchanged (±0.04 ppm). Similar experiments produced similar changes for protons "a", "b", and "c" of **2** and **3**. At 250 K, K_a (M⁻¹) values were, **1**, 0.82, **2**, 8.1, and **3**, 13.2.¹⁰ From the differences in K_a values determined at 212, 250, 275, and 300 K for **1** binding CS₂, the following values were estimated (kcal mol⁻¹ at 212 K): ΔG , -0.4; ΔH , -3.5; $T\Delta S$, -3.1. Thus enthalpy favors and entropy disfavors complexation. At 300 K, **1** binds CS₂ in CDCl₃ with $\Delta G = +0.91$ and, in C₆D₆, with $\Delta G = +1.02$ kcal mol⁻¹.¹¹ Even at 212 K in CDCl₃, the signals for free **1** and 1-CS₂ merged. Thus ΔG^\ddagger for decomplexation is <10 kcal mol⁻¹. Similar experiments with **1** and CH₃C≡CH in CDCl₃ produced similar spectral shifts. However, mixing C₆H₆, I₂, CH₃I, K₃Fe(CN)₆, *t*-BuNH₃SCN, H₂O, CO₂, or CH₂Cl₂ with **1** in CDCl₃ produced none, nor did mixing of CHCl₃ with solutions of **1** in C₆D₆. The signals for only protons "a" and "b" of **1** were significantly broadened when **1** in CDCl₃ was saturated with O₂ at 250 K.

Displacement of O₂ with N₂ reproduced sharp peaks. Thus 1-3 complex linear molecules CS₂, CH₃C≡CH, and O₂ but not detectably noncomplementary guest candidates.

In drawings **5** and **6** of the crystal structure of 1·2CS₂^{12a}, the CS₂ molecule which lies between molecules of complex is omitted. The other CS₂ beautifully occupies the well of the host.^{12b} The magnitudes and directions of the ¹H NMR resonance shifts in the spectra of 1-CS₂, 2-CS₂, and 3-CS₂ are consistent with the solution structures of these complexes being similar to the crystal structure of 1-CS₂. Molecular model examination and the chemical shift patterns of the indicator protons at the bottom and top of the well in 1-HC≡CCH₃ require that the C≡CH end of CH₃C≡CH is inserted into the well. The existence of a totally organized organic complex for O₂ is unprecedented¹³ and is striking considering the importance of the storage and transport of O₂ in biological systems.

Why do 1-3 complex slim linear molecules? In the cavitation model for dissolution, the free energy for cavity formation in the solvent (ΔG_c) is of opposite sign and similar magnitude to the free energy for solvent-solute interactions (ΔG_i).¹⁴ Compounds 1-3 are the equivalent of benzene-alkane solvent molecules organized to form a cavity whose ΔG_c is supplied during synthesis, leaving ΔG_i unopposed.¹⁵ Solvophobic driving forces¹⁶ for expelling CS₂ from CDCl₃ are likely negligible, as are host-guest charge-transfer attractions between like species.¹⁷ Thus ΔG_i appears composed of overall attractive dipole-dipole interactions. The fact that K_a^2 and $K_a^3 > K_a^1$ supports this conclusion, since host-guest interactions should increase with increasing areas of contact. Thus the principles of preorganization and complementarity¹⁸ are applicable to designing complexes between lipophilic entities.

(12) (a) At 115 K, $a = 11.233$ Å, $b = 20.018$ Å, $c = 10.069$ Å, $\beta = 90.84^\circ$, space group $P2_1/m$, $Z = 2$, $R = 0.040$. (b) The depth of the guest penetration into the well of the host is measured by these distances: the CS₂ carbon is located 0.47 Å below the plane defined by the C atoms of the four axial CH₃'s which form the upper rim of the cavity; the inserted sulfur lies 2.02 Å below this plane and 0.68 Å below the plane defined by the four Si atoms. The good steric fit between the complexing partners is reflected in the amplitudes of atomic thermal vibrations exhibited by the linear guest. They are relatively low and comparable to those of the rigid host. Details will be published elsewhere.

(13) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev.* **1984**, *84*, 137-203.

(14) (a) Eyring, H.; Jhon, M. S. "Significant Liquid Structure"; Wiley: New York, 1969; Chapter 3. (b) Pierotti, R. A. *J. Phys. Chem.* **1965**, *69*, 281-288. (c) Sinanoglu, O. "Molecular Associations in Biology"; Pullman, E., Ed.; Academic Press: New York, 1968; pp 427-445.

(15) We warmly thank Professor J. Reisse, Universite Libre de Bruxelles, and Professor H. Reiss, University of California, Los Angeles, for helpful discussions of these ideas.

(16) Ben-Naim, A. *Biopolymers* **1975**, *14*, 1337-1355.

(17) Person et al. (Person, W. B.; Humphrey, R. E.; Deskin, W. E.; Popov, A. I. *J. Am. Chem. Soc.* **1958**, *80*, 2049-2053) report a charge-transfer complex between CS₂ as donor and I-Cl as acceptor.

(18) Cram, D. J.; Cram, J. M. "Selectivity, A Goal for Synthetic Efficiency"; Bartman, W., Trost, B. M., Eds.; Verlag Chemie: Weinheim, Germany, **1983**; pp 42-64.

Shell Closure of Two Cavitands Forms Carcerand Complexes with Components of the Medium as Permanent Guests¹

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Absent among the over six million organic compounds reported are closed surface hosts with enforced interiors, large enough to imprison behind covalent bars guests (G) the size of ordinary solvents. We report here the shell closure of two hemispherical cavitands to form carcerand **1**, in whose interior are trapped

(6) Högberg, A. G. S. *J. Org. Chem.* **1980**, *45*, 4498-4500.

(7) All new compounds gave C, H, and Si analyses within 0.20% of theory, MS molecular ions, and expected ¹H NMR spectra.

(8) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703-2707.

(9) Foster, R.; Fyfe, C. A. *Prog. Nucl. Magn. Reson. Spectrosc.* **1969**, *4*, 1-89.

(10) Spectra were taken on a 200-MHz instrument. The R values of least-square plots were 0.98 or higher and the limit of error (twice the standard deviation) ranged from 2% to 7%.

(11) ±20%.