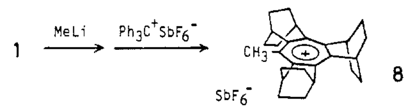
V/s) as compared with **7** (−0.765 V) or the unsubstituted tropylium ion (−0.510 V).

In pursuit of further possible stabilization, **1** was converted to the fully substituted cation **8**.[8] However, **8** was found to be somewhat less stable than **1** as is shown by its pK_{R^+} (12.4) and reduction potential (−1.094 V). This is ascribed to the decreased planarity of the seven-membered ring due to the steric repulsion between overcrowding substituents.[11]



A single straight line (slope 0.870, correlation coefficient 0.9988) is obtained when pK_{R^+} is plotted against E_{pc} for **1**, **7**, **8**, and a series of cyclopropyltropylium ions (c-$Pr_nC_7H_{7-n}{}^+$, $n = 0$–3). From this plot, stabilization by annelation with one bicyclo[2.2.2]octene unit is shown to be almost twice as effective as that by substitution with one cyclopropyl group. Thus, the cyclic 6π/7C system in **1** is strongly stabilized by the inductive effect plus σ–π conjugation of the tropylium 2p orbitals with the σ-bonds, which are rigidly fixed in the position nearly parallel to the vacant 2p orbitals.[12]

Acknowledgment. We thank the Ministry of Education, Science and Culture for a Grant-in-Aid for Scientific Research (no. 61134038).

Supplementary Material Available: Spectral and analytical data, UV spectra of **1** at different pH's, a plot of pK_{R^+} against E_{pc}, and results of INDO MO calculations (5 pages). Ordering information is given on any current masthead page.

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(11) For example, see: Takeuchi, K.; Kurosaki, T.; Yokomichi, Y.; Kimura, Y.; Kubota, Y.; Fujimoto, H.; Okamoto, K. *J. Chem. Soc., Perkin Trans. 2* **1981**, 670.

(12) This is supported by the results of INDO MO calculations on the cation **7** as a model, in comparison with the tropylium ions annelated with bicyclo[2.1.1]hexene and with cyclopentene. The results show that **7** has the lowest charge density on the cationic ring and the highest π-bond order between the tropylium ring and the σ-framework: see Supplementary Material.

Polar Host–Guest Interaction. Binding of Nonionic Polar Compounds with a Resorcinol–Aldehyde Cyclooligomer as a Lipophilic Polar Host[†][1]

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Received October 5, 1987

Recognition of nonionic polar moieties through the hydrogen-bonding interaction constitutes an important challenge in molecular recognition but still remains largely unexplored.[2,3] Especially important are the hydroxyl and amide groups and nitrogen heterocycles since they are constituents of such important biomolecules as sugars, peptides, nucleosides and nucleotides, vitamins, and coenzymes. We wish to report here that a lipophilic resorcinol–aldehyde cyclooligomer provides effective binding sites in apolar media for a variety of polar compounds of biological origin.

The acid-catalyzed reaction of resorcinol with dodecanal in ethanol under conditions similar to those for the reaction with CH_3CHO or C_6H_5CHO to give **1b**[4] or **1c**[5] afforded the cyclooligomer **1a** as a monohydrate having good solubilities in apolar solvents.[6] Acetylation of **1a** gave octaacetate **2a**.[6] The ^{1}H NMR spectra of **1a** and **2a**[6] in light of structures[4,5,7] of octaacyl derivatives **2b** and **2c** suggested that **1a** has a crown[5] or bowl-shaped[3a,3b,8] conformation with alkyl chains in an all-axial and all-cis configuration and OH groups which are hydrogen-bonded. Vapor pressure osmometry (VPO) indicated that **1a** is aggregated in $CHCl_3$ or C_6H_6, whereas **2a** is monomeric.[6] The polar substrates investigated are glycerol (**3**), D-glucose (**4**), D-ribose (**5**), riboflavin (vitamin B_2, **6a**), vitamin B_{12} (cyanocobalamin, **7a**), and hemin (**8**). They are all insoluble in CCl_4 and C_6H_6.

Vigorous stirring of a two-phase mixture of a solution of **1a** in CCl_4 or C_6D_6 (1–2 × 10^{-2} M, 4 vols) and **3** (neat) or H_2O (1 vol) at 20 °C for 24 h resulted in transfer of the latter into the former solution, the stoichiometries **3**:**1a** = H_2O:**1a** = 4:1 being established by ^{1}H NMR integration.[9] When a 50% (mol/mol) aqueous solution of **3** ([**3**] = [H_2O] = 11 M) was used, only ca. 4 mol of H_2O was incorporated with little extraction of **3**. Similar extraction studies using saturated or very concentrated aqueous solutions of **4** (3.1 M) and **5** (5.5 M) showed a striking difference in their affinities to **1a** in CCl_4; little extraction of **4**, while ready extraction of **5** (ca. 1 mol per mol of **1a**).[9] The selectivity may be explained in terms of directions of OH groups.[10] The formation of a stable complex between **1a** (3.6 × 10^{-4} M) and **6a** or **7a** in C_6H_6 was suggested by the extraction of **6a** or **7a** from a very dilute solution in water or even in 1 N aqueous HCl in which **6a** was protonated.[11] The distributions of **6a** or **7a** (G) between

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[†] This paper is dedicated to the late Professor Iwao Tabushi.

(1) Molecular Recognition. 1. Presented at the 12th International Symposium on Macrocyclic Chemistry, Hiroshima, Japan, 1987; Abstracts, p 89.

(2) For recent studies on the polar organic-substrate binding in apolar media, see: (a) Rebek, J., Jr.; Askew, B.; Killoran, M.; Nemeth, D.; Lin, F.-T. *J. Am. Chem. Soc.* **1987**, *109*, 2426 and references therein. (b) Rebek, J., Jr.; Askew, B.; Nemeth, D.; Parris, K. *Ibid.* **1987**, *109*, 2432. (c) Rebek, J., Jr.; Nemeth, D.; Ballester, P.; Lin, F.-T. *Ibid.* **1987**, *109*, 3474. (d) Rebek, J., Jr.; Askew, B.; Ballester, P.; Buhr, C.; Jones, S.; Nemeth, D.; Williams, K. *Ibid.* **1987**, *109*, 5033. (e) Hamilton, A. D.; Van Engen, D. *Ibid.* **1987**, *109*, 5035. (f) Gutsche, C. D.; Iqbal, M.; Alam, I. *Ibid.* **1987**, *109*, 4314. (g) Sheridan, R. E.; Whitlock, H. W. *Ibid.* **1986**, *108*, 7120. (h) van Staveren, C. J.; Fenton, D. E.; Reinhoudt, D. N.; van Eerden, J.; Harkema, S. *Ibid.* **1987**, *109*, 3456 and references therein. (i) Menger, F. M.; Dulany, M. A. *Tetrahedron Lett.* **1985**, *26*, 267. (j) Kobiro, K.; Takahashi, M.; Nishikawa, N.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Ibid.* **1987**, *28*, 3825. (k) Komiyama, M.; Yamamoto, H.; Hirai, H. *Chem. Lett.* **1984**, 1081. (l) Toda, F.; Kai, A.; Tagami, Y. *Ibid.* **1987**, 1393 and references therein.

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(6) **1a**: yield 70% after thorough washing with water followed by recrystallization from methanol or ethanol: mp 270–271 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.20 and 6.10 (each s, each 4 H, Ar-H), 4.28 (t, 4 H, Ar-CRH-Ar), 2.21 and 1.29 (CH_2, 80 H), 0.90 (t, 12 H, CH_3), 9.60 and 9.28 (each s, each 4 H, Ar-OH), 4.95 (br s, 2 H, H_2O). Anal. ($C_{72}H_{112}O_8{\cdot}H_2O$) C, H. **2a**: yield 72% after recrystallization from petroleum ether; mp 132–132.5 °C; ^{1}H NMR ($CDCl_3$) 6.89 (s, 4 H, Ar-H), ca. 6 (very br, 4 H, Ar-H), 4.14 (t, 4 H, Ar-CRH-Ar), 2.16 (br s, 24 H, CH_3CO), 1.84 and 1.26 (80 H, CH_2), 0.88 (t, 12 H, CH_3). Anal. ($C_{88}H_{128}O_{16}$) C, H. Molecular weights by VPO for C_6H_6 or $CHCl_3$ solutions are as follows: **1a**, 7066 (C_6H_6) or ca. 5000 ($CHCl_3$) (calcd 1124); **2a**, 1445 (C_6H_6) or 1447 ($CHCl_3$) (calcd 1442).

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(9) Clear solutions containing **1a** were separated by centrifugation and filtration. The ^{1}H NMR spectra showed a broad singlet at δ 9.6–9.7 for OH protons (8 H) of **1a** and signals due to substrates, e.g., at δ 3.34 (CH, 20 H) and 4.98 (OH, 12 H) for **3** and 2.93 (8 H) for H_2O. The assignments were confirmed by use of the substrates deuteriated at OH groups, i.e., **3**-d_3, **5**-d_4, and D_2O. The substrates solubilized (**3** and **5**) could also be reextracted with D_2O and identified further by means of ^{1}H NMR spectroscopy.

(10) Three cis secondary and one primary OH groups in **5** can interact simultaneously with OH groups of **1a** (CPK model). This is, however, not the case for **4** which has OH groups in various directions. The observation of some highly shielded C–H proton resonances at 0.2 ppm for bound **5** may be consistent with multipoint **5**–**1a** interaction which places some C–H protons of **5** in the vicinity of benzene rings of **1a**.

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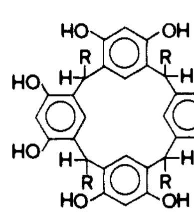
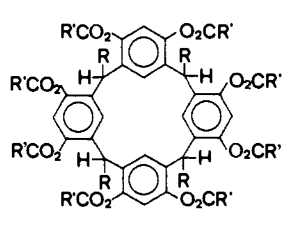
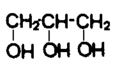


1a ; R = (CH$_2$)$_{10}$CH$_3$
1b ; R = CH$_3$
1c ; R = C$_6$H$_5$

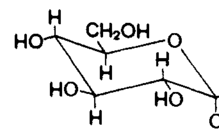


2a ; R = (CH$_2$)$_{10}$CH$_3$, R' = CH$_3$
2b ; R = CH$_3$, R' = CH$_3$, C$_2$H$_5$
2c ; R = C$_6$H$_5$, R' = C$_3$H$_7$

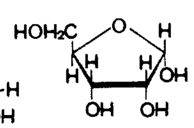


$CH_2CH\text{-}CH_2$ (OH OH OH)

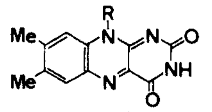
3



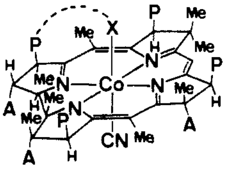
4 (α form)



5 (α form)

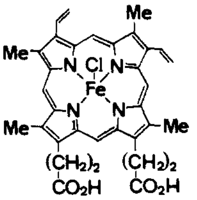


6a; R = CH$_2$(CH)$_3$CH$_2$ (OH OH)
6b; R = CH$_2$(CH)$_3$CH$_2$ (OAc OAc)
6c ; R = (CH$_2$)$_4$CH$_3$



A = CH$_2$CONH$_2$
P = (CH$_2$)$_2$CONH$_2$

7a ; X = dimethylbenzimidazole ribonucleotide linked to P
7b ; X = CN



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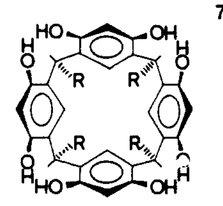

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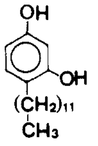

10

aqueous (a) and organic (o) phases were such that could be correlated with the equation, G$_a$ + **1a**$_o$ ⇌ (G-**1a**)$_o$; K = [(G-**1a**)]$_o$/[G]$_a$[**1a**]$_o$ = 2.1 × 10^2 and 2.3 × 10^2 M^{-1} for **6a** (aqueous phase, 1 N HCl) and **7a**, respectively.[11] The maximal guest/host ratios of **6a**:**1a** ≅ 1:5 and **7a**:**1a** ≅ 1:2 were obtained by using aqueous solutions saturated with **6a** (in the order of 10^{-4} M) and **7a** (~1 × 10^{-2} M), respectively.[12] Hemin (**8**) as a solid could be solubilized slowly in benzene containing **1a**.

No solubilization of the guests (**3**–**8**) was observed when **2a** instead of **1a** was used as the host, indicating that the hydrogen bonding of the OH groups of **1a** with the polar groups of the guests, the OH groups in cases of **3**, **5**, and H$_2$O, is responsible for the present host–guest association. On the other hand, the imide moiety (CO–NH–CO) seems to be primarily responsible for the binding of **6a**, since **6a** is rendered nonfluorescent[13] upon complex formation with **1a** and the benzene-soluble tetraacetate (**6b**)[13] and pentyl (**6c**)[14] derivatives also form stable complexes with **1a** in C$_6$H$_6$, as shown by fluorescence quenching. For **7a** the seven amide groups can be the sites of binding, since dicyanocobinamide (**7b**) is also bound with **1a**. The 4:1 stoichiometry for the complexes **3**–**1a** and H$_2$O–**1a** strongly suggests that a pair of hydrogen-bonded OH groups on adjacent benzene rings in **1a** provide the essential binding site; four such sites (refer to **9**) may independently interact with four molecules of small polar guests such as **3** and H$_2$O or may undergo multisite interaction with **5** and also with the four upward and three downward amide side chains of **7a** in a sandwich form as the 1:2 stoichiometry for **7a**–**1a** suggests. In fact, 4-dodecylresorcinol (**10**) (1.4 × 10^{-3} M in C$_6$H$_6$) which is unable to form such an OH pair fails to solubilize **3**–**8** to any detectable extent. It is also interesting to note that the complexes **3**–**1a** (4:1) and **7a**–**1a** (1:2) are monomeric as such in CHCl$_3$ as demonstrated by VPO.[15]

This study presents a novel example of polar substrate binding with macrocyclic polar hosts rendered soluble in apolar media. It is significant that the present polar host–guest interaction can compete favorably with the host–host, host–H$_2$O, and guest–H$_2$O interactions. These findings provide a basis for the elaborate molecular recognition of biological polar compounds and may also open a new synthetic chemistry thereof in apolar organic solvents.

Acknowledgment. This work was supported by a Grant-in-Aid for Special Projects from the Ministry of Education, Science, and Culture of Japan.

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(11) Monitored by electronic spectroscopy until equilibria were attained. Electronic spectra for species solubilized with **1a** in C$_6$H$_6$: **6a**, λ_{max} (ϵ) 382 (8.5 × 10^3), 452 (10.3 × 10^3), 477 nm (8.7 × 10^3); **7a**, 363 (28.1 × 10^3), 552 nm (8.4 × 10^3).

(12) In case of **6a** which has a very low solubility in water, the apparent ratio **6a**:**1a** may not necessarily be the stoichiometry.

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(15) Molecular weights are as follows: **3**–**1a**, 1497 (calcd for 4(**3**)·**1a**, 1474); **7a**–**1a**, 3678 (calcd for **7a**·2(**1a**), 3567).

The Distance Dependence of Intramolecular Electron-Transfer Rates: Importance of the Nuclear Factor

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Received August 31, 1987

The factors determining the distance dependence of intramolecular electron-transfer rates in small molecule systems[1-6] and metalloproteins[7-10] are of considerable current interest. In the semiclassical formalism[1,11] the rate constant k for intramolecular electron transfer is given by eq 1 where κ_{el} is the electronic

$$k = \kappa_{el}\nu_n\kappa_n \tag{1a}$$

$$\kappa_n = \exp\left[-\frac{(\lambda + \Delta G^\circ)^2}{4\lambda RT}\right] \tag{1b}$$

$$\lambda = \lambda_{out} + \lambda_{in} \tag{1c}$$

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