Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Complexation of methylammonium salts and sugar-related alcohols with resorcinol cyclic tetramer in water: An implication of the CH-π interaction on polar guest binding

Kenji Kobayashi[a]; Yuji Asakawa[a]; Yasuhiro Aoyama[a]
[a] Department of Chemistry, Nagaoka University of Technology, Nagaoka, Niigata, Japan

To cite this Article Kobayashi, Kenji , Asakawa, Yuji and Aoyama, Yasuhiro(1993) 'Complexation of methylammonium salts and sugar-related alcohols with resorcinol cyclic tetramer in water: An implication of the CH-π interaction on polar guest binding', Supramolecular Chemistry, 2: 2, 133 — 135
To link to this Article: DOI: 10.1080/10610279308038307
URL: http://dx.doi.org/10.1080/10610279308038307

SUPRAMOLECULAR CHEMISTRY, Vol. 2, pp. 133–135
Reprints available directly from the publisher
Photocopying permitted by license only

Complexation of methylammonium salts and sugar-related alcohols with resorcinol cyclic tetramer in water: An implication of the CH-π interaction on polar guest binding

KENJI KOBAYASHI, YUJI ASAKAWA and YASUHIRO AOYAMA*

Department of Chemistry, Nagaoka University of Technology, Kamitomioka, Nagaoka, Niigata 940-21, Japan

(Received August 20, 1992)

Methylammonium cations and sugar-related alcohols are bound to the tetrasulphonate derivatives 1a–1c of the resorcinol cyclic tetramer in water. With respect to the change in substituent X on C-2 of the benzene rings of the host, both 1b (X = CH_3, highly hydrophobic and moderately electron-donating) and 1c (X = OH, highly hydrophilic and highly electron-donating) exhibit higher binding abilities than the parent host 1a (X = H). These results suggest that the CH-π interaction, involving polarized C–H bonds of the guest and electron-rich benzene rings of the host, makes a substantial contribution to the guest-binding process. Host 1c even binds more hydrophilic dioxygen-functionalized sugar models (*cis*-1,2-cyclohexanediol, 2-oxacyclohexyl-1-carbinol and 2-oxacyclopentyl-1-carbinol) more strongly than the corresponding more hydrophobic mono-ols (cyclohexanol, cyclohexylcarbinol and cyclopentylcarbinol).

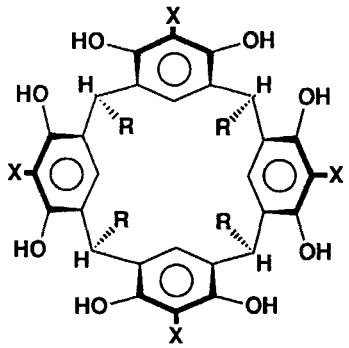
INTRODUCTION

Better understanding of intermolecular forces is a central theme of molecular recognition.[1] Dougherty and coworkers[2] have reported on the complexation of a new type of aromatic host and methylammonium guests in water. Systematic variation in guest structures led them to conclude that the primary binding force is a cation-π interaction between highly polarized CH_3–N^+ moieties of the guest and electron-rich aromatic rings of the host. On the other hand, we have recently found that the water-soluble resorcinol cyclic tetramer **1** binds relatively hydrophobic sugar derivatives in water.[3] We were able to change the substituents on the host benzene rings (**1a**, **1b** and **1c**)[4] and thereby showed that guest–host CH-π interaction is at least partially responsible for the present sugar-cyclophane complexation. In the present work, we have investigated the complexation of methylammonium salts and cyclic alcohols as simplified models of sugars. We report here that the CH-π interaction indeed plays an essential role in the binding of polar guests.

The interaction of tetrasulphonate host **1**[3] (Chart 1) and various guests in unbuffered D_2O was investigated by ^{1}H-NMR spectroscopy at 25°C. The host has substituents H (**1a**), CH_3 (**1b**), or OH (**1c**) on the 2-positions of the benzene rings. The intention of these modifications is to change the hydrophobicity of the guest-binding aromatic cavity as well as changing the electron density of the benzene rings. The guests studied are tetramethyl- (**2**), trimethyl- (**3**), dimethyl- (**4**), and methylammonium chloride (**5**), ammonium chloride (**6**), choline chloride (**7**), acetylcholine chloride (**8**), *tert*-butanol (**9**), cyclohexanol (**10**), *cis*-1,2-cyclohexanediol (**11**), cyclohexylcarbinol (**12**), 2-oxacyclohexyl-1-carbinol (**13**), cyclopentylcarbinol (**14**), and 2-oxacyclopentyl-1-carbinol (**15**) (Chart 1).

As in the previous case of sugar binding,[3] the complexation was conveniently followed by monitoring either guest-induced downfield shifts of aromatic H-5 of host **1** or host-induced upfield shifts of the guest-proton responances as a result of the ring-current effect of the benzene rings of the host. Both of these exhibited saturation with increasing guest or host concentrations. The saturation shift for the methyl protons of guest **2**, for example, was found to be as large as 3.6 ppm. This result, coupled with the binding selectivity presented below, indicates that the methyl groups of **2** are incorporated in the polyhydroxy aromatic cavity of host **1a**,[5] and direct ammonium sulphate guest-host electrostatic interaction, if any, plays only a minor role. This binding geometry is also

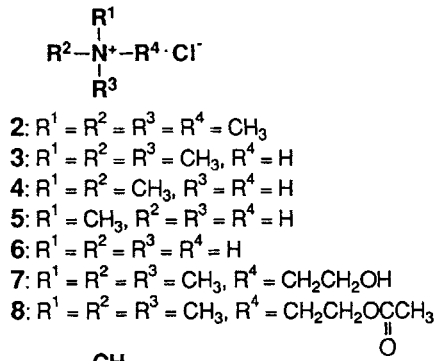
* To whom correspondence should be addressed.



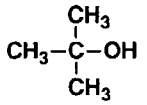
1a: R = $(CH_2)_2SO_3Na$; X = H

1b: R = $(CH_2)_2SO_3Na$; X = CH_3

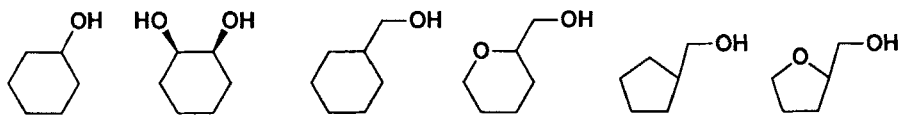
1c: R = $(CH_2)_2SO_3Na$; X = OH



2: $R^1 = R^2 = R^3 = R^4 = CH_3$
3: $R^1 = R^2 = R^3 = CH_3$, $R^4 = H$
4: $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$
5: $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$
6: $R^1 = R^2 = R^3 = R^4 = H$
7: $R^1 = R^2 = R^3 = CH_3$, $R^4 = CH_2CH_2OH$
8: $R^1 = R^2 = R^3 = CH_3$, $R^4 = CH_2CH_2OCCH_3$ (O)



9



10 **11** **12** **13** **14** **15**

Chart 1

Table 1 Binding constants (K) for the complexation of hosts **1a**, **1b** and **1c** with various guests in D_2O at 25°C

	$K\ (M^{-1})$													
Guest	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Host														
1a	160	30	3	<1	<1	240	360	4	16	14	30	29	19	18
1b	1500					1700	2000	19	130	80	200	180	100	90
1c	1800					2100	1800	24	64	80	92	160	60	80

supported by NOE measurements.* The binding constants (K) were evaluated, as summarized in Table 1, by the Benesi-Hildebrand analysis ($r > 0.99$ in every case) of the titration data for the aromatic H-5 resonances of the host (0.5 ~ 2 mM) in the presence of varying amounts of the guest.

Trimethylammonium salt **3** shows a greater binding ability than its neutral counterpart **9**, exemplifying a sort of charge effect, as has already been noted by Dougherty *et al.*[2] This is, however, not a simple charge effect. In fact, there is a remarkable span in the K values of host **1a** for a series of ammonium salts, decreasing in the order **2** > **3** > **4** > **5** and **6**. Some kind of apolar interaction involving the methyl groups polarized by a nitrogen positive charge must come into play. Examination of the effects of substituents in the host reveals some essential aspects of this interaction. For every guest, both hosts **1b** (X = CH_3, highly hydrophobic and moderately electron-donating) and **1c** (X = OH, highly hydrophilic and highly electron-donating) show significantly larger binding constants than the parent host **1a** (X = H). Thus, the electron density or the π-basicity of the benzene rings of the host is an important factor. This is taken as evidence that, in collaboration with the hydrophobic effect, the CH-π interaction[2f,3,6] involving polarized C–H bonds of the guest and electron-rich benzene rings of the host makes a substantial contribution to the present guest-binding process.

An interesting aspect shown in Table 1 is the relative binding abilities of hosts **1b** and **1c** toward three pairs of sugar-related neutral alcohols, i.e. mono-ol **10** and diol **11**, six-membered carbinol **12** and pyranose model **13**, and five-membered carbinol **14** and furanose model **15**. Host **1b** (X = CH_3) of an enhanced hydrophobicity binds, as expected, the more hydrophobic counterparts more strongly than the less hydrophobic ones, i.e. **10** > **11**, **12** > **13**, and **14** > **15**. In marked contrast,

* Irradiation of the methyl protons of guest **2** bound to host **1b** resulted in an NOE at the aromatic 2-CH_3 groups of the host, but not at its sulphonated side chains.

the opposite is true for the more electron-rich and less hydrophobic host **1c** (X = OH). This might be because an additional oxygen functionality in guests **11**, **13**, and **15** polarizes the adjacent C–H bonds more effectively so as to allow a better CH-π interaction with the highly electron-rich dialkyltrihydroxybenzene rings of host **1c**. This interpretation provides an insight into the significance of the structure of sugars. They have many such oxygen-activated C–H bonds. X-ray crystallography for sugar–protein complexes in fact indicates that the sugar C–H bonds are stacked or even sandwiched with the aromatic amino acid side chains of the protein.[7]

ACKNOWLEDGMENT

A part of this work was presented at the 7th International Symposium on Molecular Recognition and Inclusion (Kyoto, 1992). Y.A. is grateful to the Organizing Committee, especially Professor H. Ogoshi (Kyoto University).

REFERENCES AND NOTES

1 (a) Rebek, J. Jr.; *Angew. Chem. Intl. Edn. Engl.* **1990**, *29*, 245. (b) Schneider, H.J.; *Angew. Chem. Intl. Edn. Engl.* **1991**, *30*, 1417.
2 (a) Shepodd, T.J.; Petti, M.A.; Dougherty, D.A.; *J. Am. Chem. Soc.* **1986**, *108*, 6085. (b) Shepodd, T.J.; Petti, M.A.; Dougherty, D.A.; *J. Am. Chem. Soc.* **1988**, *110*, 1983. (c) Petti, M.A.; Stepodd, T.J.; Barrans, R.E., Jr.; Dougherty, D.A.; *J. Am. Chem. Soc.* **1988**, *110*, 6825. (d) Stauffer, D.A.; Dougherty, D.A.; *Tetrahedron Lett.* **1988**, *29*, 6039. (e) Stauffer, D.A.; Barrans, R.E. Jr.; Dougherty, D.A.; *Angew. Chem. Intl. Edn. Engl.* **1990**, *29*, 915. (f) Dougherty, D.A.; Stauffer, D.A.; *Science* **1990**, *250*, 1558.
3 Kobayashi, K.; Asakawa, Y.; Aoyama, Y.; *J. Am. Chem. Soc.* **1992**, *114*, 10307.
4 For the binding abilities of free and deprotonated derivatives of a water-soluble calix[4]arene see: Shinkai, S.; Araki, K.; Matsuda, T.; Nishiyama, N.; Ikeda, H.; Takasu, I.; Iwamoto, M.; *J. Am. Chem. Soc.* **1990**, *112*, 9053.
5 Very strong binding of ammonium salts to a tetradeprotonated derivative of host **1** (R = CH_3 and X = H) due to electrostatic interaction was originally reported by Schneider, *et al*: (a) Schneider, H.-J.; Güttes, D.; Schneider, U.; *Angew. Chem. Intl. Edn. Engl.* **1986**, *25*, 647. (b) Schneider, H.-J.; Karmer, R.; Simova, S.; Schneider, U.; *J. Am. Chem. Soc.* **1988**, *110*, 6442. (c) Schneider, H.-J.; Güttes, D.; Schneider, U.; *J. Am. Chem. Soc.* **1988**, *110*, 6449. Host **1a** has a $pK_a \approx 10$ for the dissociation of the OH groups.[3] They are therefore not deprotonated under the present conditions.
6 Nishio, M.; Hirota, M.; *Tetrahedron Lett.* **1989**, *35*, 7201.
7 (a) Quiocho, F.A.; Vyas, N.K.; *Nature* **1984**, *310*, 381. (b) Quiocho, F.A.; Wilson, D.K.; Vyas, N.K.; *Nature* **1989**, *340*, 404.