Urea Hemispherand Complexation and Decomplexation Rates with t-Butylammonium Picrate Salts

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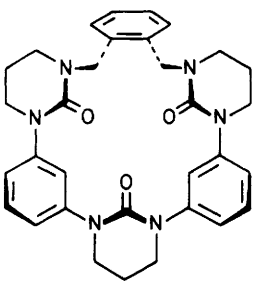
The complexation and decomplexation rate constants have been examined for t-butylammonium picrate as guest binding to seven hosts whose principal binding sites are cyclic urea units incorporated in macrorings.

Hemispherands (**1**)—(**7**) form one-to-one complexes with t-butylammonium picrate in which the cyclic urea units act as the main hydrogen bond accepting sites. This applies both to the structure in the crystal[1,2] and in solution. The latter is evident from the shifts induced in the ^{1}H n.m.r. spectra of the hosts by the gradual addition of t-butylammonium picrate. The shift curves for all of the hosts have a sharp knee at a molar ratio of 1:1. In contrast, with metal ions as guests, the complexation usually involves a 2:1 host-to-guest ratio. Compound (**6**) is the strongest known complexer of $Bu^tNH_3^+$,[1] with a binding free energy of $-\Delta G^\circ = 13.2$ kcal mol^{-1}† at 25 °C in $CDCl_3$ saturated with D_2O. Furthermore, (**8**), by collecting and orienting L-alanyl *p*-nitrophenyl ester perchlorate in $CDCl_3$, was acylated *ca.* 10^{11} faster than the non-complexing model compound, 3-phenylbenzyl alcohol under the same conditions.[3] The enormous rate enhancement for transacylation in this enzyme model makes it important to know the complexation and decomplexation rate constants for this type of host. This paper reports the results of kinetics studies of the decomplexation rates of the $Bu^tNH_3^+$ complexes of (**1**)—(**7**) determined through use of the differences between the ^{1}H n.m.r. chemical shifts of the CH_3 protons in complexed and uncomplexed guest.

The ^{1}H n.m.r. spectra of hosts (**4**)—(**7**) mixed with 2 mol of guest at a concentration of about 0.05 M in either $(CD_3)_2CO$ or $CDCl_3$ saturated with D_2O gave two signals with equal intensities for the CH_3 protons of the guest, one complexed and one noncomplexed, at accessible temperatures. As the temperature was raised, the two signals coalesced due to exchange between uncomplexed and complexed guest. From the differences in chemical shifts of the two signals ($\Delta\nu$) in the slow exchange limit, the rate constants for decomplexation at a series of temperatures, including that at the coalescence temperature (k_c), were calculated by line shape analysis. These values in turn provided the activation free energies at 298 K and at the

† 1 kcal = 4.18 kJ.



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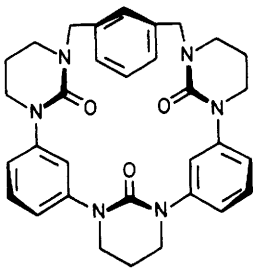

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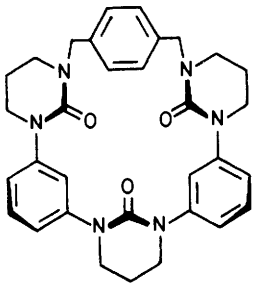

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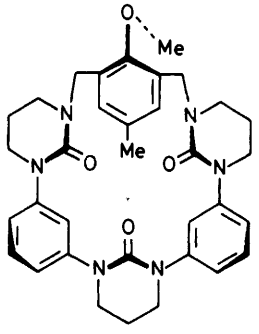

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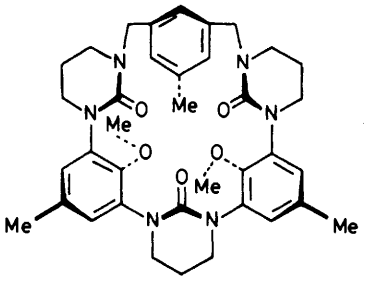

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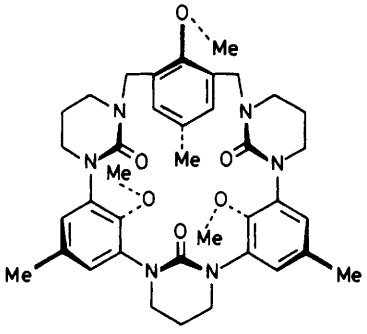

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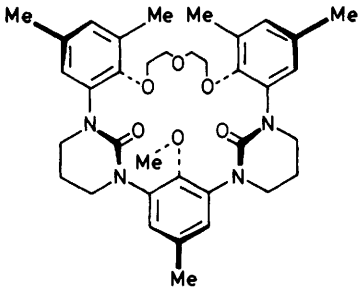

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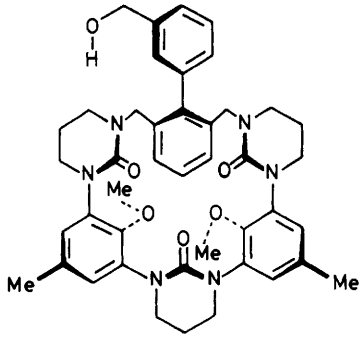

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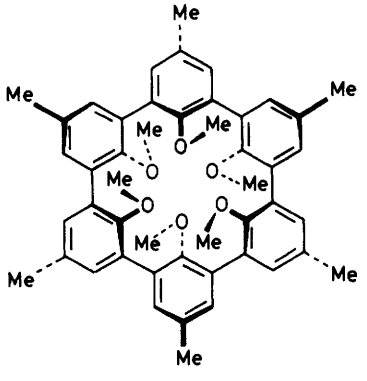

(9)

coalescence temperature ($\Delta G^{\ddagger}_{298}$ and $\Delta G^{\ddagger}_{c}$), from which were calculated the dissociation rate constants at 25 °C, k_{-1}. Moreover, the activation enthalpies ($\Delta H^{\ddagger}$) and entropies ($\Delta S^{\ddagger}$) were obtained. The coalescence temperatures for hosts (**1**)—(**3**) in $(CD_3)_2CO$ could not quite be reached, so only limits can be set on the values of t_c and $\Delta G^{\ddagger}_{c}$ for these compounds. The values of the association constants (K_a) for hosts and guests equilibrating with their complexes at 25 °C in $CDCl_3$ saturated with D_2O are available from other studies.‡[1,2] From values of k_{-1} and K_a, the association rate constants (k_1) were calculated for those runs made in $CDCl_3$ saturated with D_2O. Table 1 records the results.

The association constants (k_1 values) for (**4**)—(**7**) vary by two powers of ten, and are in the 10^{10}—10^{12} mol^{-1} s^{-1} range, which indicates the complexation rates are diffusion controlled. Spherand (**9**) complexing lithium or sodium picrate in the same medium ($CDCl_3$) gave values in the 10^4—10^5 mol^{-1} s^{-1} range.[4] The crystal structure of (**6**)·$Bu^tNH_3^+$ indicates the guest perches on the binding sites (the C=O groups) of the host,[1] whereas those of (**9**)·Na^+ and (**9**)·Li^+ indicate the guest is encapsulated.[5] Therefore, the difference is not surprising. Although not calculable, the k_1 values for (**1**)—(**3**) are probably in the 10^{11}—10^{12} mol^{-1} s^{-1} range as well, which places their k_{-1} values in the 10^5—10^6 s^{-1} range (off scale for direct measurement by these techniques). Thus the dissociation constants in $CDCl_3$ for (**1**)—(**7**) probably vary from *ca.* 10^3 to *ca.* 10^6. As has been observed earlier with other systems, the k_{-1} values roughly correlate inversely with the K_a values as structure is changed, whereas the k_1 values change much less.[4,6]

For hosts (**4**)—(**7**), change in solvent from $(CD_3)_2CO$ to $CDCl_3$ saturated with water changes the value of k_{-1} by one power of ten at the most. However in $(CD_3)_2CO$, $\Delta H^{\ddagger}$ values range from 4.9—5.6 kcal mol^{-1}, whereas in $CDCl_3$ saturated with D_2O, they range from 9.3—10.6 kcal mol^{-1}. The $-T\Delta S^{\ddagger}$ contribution to $\Delta G^{\ddagger}_{298}$ varies in the opposite direction to

‡ Compound (**5**) has been prepared by a method (ref. 1) very similar to that employed for (**6**) (D. J. Cram and M. Miesch), whereas (**7**) was prepared by conventional reactions (D. J. Cram and H. E. Katz). Both compounds were fully characterized, and their syntheses and binding properties will be reported in the near future.

Table 1. Complexation (k_1) and decomplexation (k_{-1}) rate constants, complexation equilibrium constants (K_a), and attendant thermodynamic parameters for cyclic urea hosts and t-butylammonium picrate guest.

					At 25 °C				In kcal mol^{-1}				
Host	^{1}H N.m.r. solvent[a]	t_c/°C	$\Delta\nu$[b](Hz)	k_c(s^{-1})[c]	k_1 (mol^{-1} s^{-1})[d]	k_{-1}(s^{-1})[c]	K_a (l mol^{-1})[d]	$\Delta S^{\ddagger}$ cal K^{-1} mol^{-1}	$-\Delta G^{\circ}$[e]	$\Delta G^{\ddagger}_{298}$[c]	$\Delta G^{\ddagger}_c$[c]	$\Delta H^{\ddagger}$[c]	$-T\Delta S^{\ddagger}$[e]
(1)	$(CD_3)_2CO$	$\leqslant -93$	—	—	—		2.3×10^5	—	7.3	—	$\leqslant 8.9$	—	—
(2)	$(CD_3)_2CO$	$\leqslant -91$	—	—	—		2.0×10^6	—	8.6	—	$\leqslant 9.0$	—	—
(3)	$(CD_3)_2CO$	$\leqslant -99$	—	—	—		4.7×10^6	—	9.1	—	$\leqslant 8.6$	—	—
(4)	$(CD_3)_2CO$	−70.5	45.9	102	—	6.7×10^4	—	−24.5	—	12.2	9.8	4.9	7.3
(4)	$CDCl_3$	−49	53.0	118	3.9×10^{11}	4.2×10^4	9.3×10^6	−3.1	9.5	11.1	10.9	10.2	0.9
(5)	$(CD_3)_2CO$	+27	53.2	118	—	1.1×10^2	—	−31.4	—	14.6	14.7	5.3	9.3
(5)	$CDCl_3$	−5	49.8	111	1.4×10^{12}	6.1×10^2	2.2×10^9	−17.2	12.7	13.6	13.1	8.5	5.1
(6)	$(CD_3)_2CO$	+63[f]	63.0	140	—	4.2×10	—	−32.1	—	15.2	16.4	5.6	9.6
(6)	$CDCl_3$	−1	60.5	134	3.1×10^{12}	6.9×10^2	4.5×10^9	−14.3	13.2	13.6	13.2	9.3	4.3
(7)	$(CD_3)_2CO$	−53.5	51.3	114	—	2.9×10^3	—	−26.0	—	12.7	10.5	5.0	7.7
(7)	$CDCl_3$	−25.5	51.8	115	3.3×10^{10}	2.2×10^3	1.5×10^7	−5.7	9.8	12.3	12.0	10.6	1.7

[a] $(CD_3)_2CO$ was dry and $CDCl_3$ was saturated with D_2O at 25 °C. [b] $\Delta\nu = \nu_G - \nu_{H\cdot G}$, where G is $Bu^tNH_3^+$ picrate, H·G, the complex, and ν is the chemical shift of guest protons at 90 MHz at the slow exchange limits; the molar ratio of guest to host is 2:1, and the guest concentration is *ca.* 5×10^{-2} M. [c] $k_c = (\pi\Delta\nu)/2^{1/2}$, where k_c is the first order rate constant for decomplexation at the coalescence temperature. Line shape analysis provided the rate constants at other temperatures (6—9 points), to provide Eyring plots from which were calculated k_{-1} at 25 °C, $\Delta G^{\ddagger}_{298}$, $\Delta G^{\ddagger}_c$ (activation free energy at the coalescence temperature), $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$. These values always apply to $CDCl_3$ saturated with water as the medium. [d] Calculated with $k_1 = K_a k_{-1}$ at 25 °C; k_{-1} is the first order rate constant for decomplexation (see footnote c), k_1 is the second order rate constant for complexation, and K_a is the equilibrium constant measured at 25 °C for host in $CDCl_3$ extracting guest picrate salt from D_2O (ref. 2). [e] At $T = 298$ K. [f] Obtained by extrapolation.

compensate, so the $\Delta G^{\ddagger}_{298}$ values in the two solvents are almost within a kcal of one another. This effect probably reflects the presence of the small amount of water in the $CDCl_3$ [absent in the $(CD_3)_2CO$], which presumably takes the place of the t-butylammonium ion in the host upon complex dissociation. Thus the molecularity of the decomplexation changes when the solvent is changed.

We warmly thank the National Science Foundation, the U.S. Public Health Service, and the Norges Teknisk-Naturvitenskapelige Forskningaråd for support of this research. We are also grateful to Professor F. A. L. Anet for the use of computer and program for line shape analysis.

Received, 12th August 1983; Com. 1104

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