Decomplexation rate comparisons of hemicarceplexes whose single unique host bridge is changed in length and blocking power

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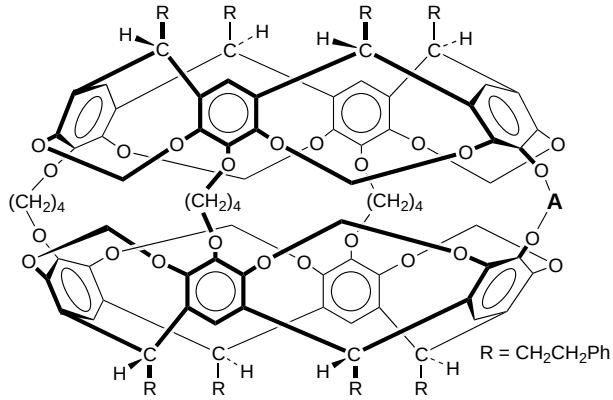
Decomplexation rates of hemicarceplexes can be manipulated by changes in solvent, guest, one of four host-bridge lengths and one of four host-bridge's blocking power.

Prior papers reported the syntheses and characterizations of hosts **1**–**6**, as well as crystal structures of **1**⊙4-MeC_6H_4OMe, **2**⊙$CHCl_3$, **4**⊙$PhNO_2$ and **6**⊙guests.[1–3] In five crystalline complexes of **6**, the host parts were essentially isostructural and changed only in minor ways when guests of generally similar size were involved (*e.g.* 1,4-$I_2C_6H_4$, 1,4-$Me_2C_6H_4$, $PhNO_2$, 2-BrC_6H_4OH and Me_2NCOMe). Decomplexation rates for **7**⊙guests were generally on the human time scale only at temperatures of 100–200 °C, indicating that considerable constrictive binding must be overcome during the decomplexation process.[4,5]



1, A = $(CH_2)_5$; **2**, A = 1,3-$(CH_2)_2C_6H_4$; **3**, A = $(CH_2)_6$; **4**, A = 1,4-$(CH_2)_2C_6H_4$; **5**, A = 9,10-$(CH_2)_2$anthracene; **6**, A = $(CH_2)_4$; **7**, all four bridging units are 1,2-$(CH_2)_2C_6H_4$

We report here the results of a survey of decomplexation rates as a function of host structure (**1**–**5**), guest structure (4-MeO-C_6H_4OMe, 3-$MeOC_6H_4OMe$, 4-$MeOC_6H_4Me$ and 4-MeC_6H_4Me), temperature (25–120 °C) and solvent ($CDCl_3$ and $CDCl_2CDCl_2$).† Hemicarceplex **2**⊙4-$MeOC_6H_4OMe$ was selected as a standard complex, whose first order rate constants were determined by following the appearance in their ^1H NMR spectra of methyl proton signals for free guest in $CDCl_3$ at four temperatures (25, 35, 45 and 55 °C) and in $CDCl_2CDCl_2$ at four temperatures (90, 100, 110, 120 °C). The decomplexations exhibited good first order behaviour over several half-lives. The technique and treatment of the data are described in a prior publication as applied to decomplexation kinetics of **7**⊙guests, in which empty host was demonstrated to be the initial product.[4]‡ Table 1 records the activation parameters ($\Delta H^‡$, $\Delta S^‡$ and $\Delta G^‡_{308}$) and $t_{1/2}$ values for decomplexations of **2**⊙4-$MeOC_6H_4OMe$ in the two solvents at 35 °C.§

First order rate constants were also determined for decomplexations involving hosts **1**–**4** and the four disubstituted benzene guests at 35 °C in $CDCl_3$. With use of eqn. 1, $k_{relative}$

$$k_{relative} = k_{H⊙G}/k_{\mathbf{2}⊙4\text{-}MeOC_6H_4OMe} \quad (1)$$

values were obtained, from which $\Delta G^‡$ values for nine complexes were calculated, and a lower limit of $\Delta G^‡$ for **5**⊙4-$MeOC_6H_4OMe$ was estimated. Table 2 provides the structures of the eleven complexes, the values of rate constants, and $\Delta G^‡_{308}$.

The most striking feature of the results is that the simple change of solvent from $CDCl_3$ to $CDCl_2CDCl_2$ resulted in an increase of activation free energy for decomplexation of **2**⊙4-$MeOC_6H_4OMe$ of $\Delta(\Delta G^‡_{308})$ = 4.1 kcal mol^{-1}. The enthalpy, $\Delta(\Delta H^‡)$ = 6.2, and entropy changes, $\Delta(T\Delta S^‡)_{308}$ = 2.1, both contribute to the change in free energy, but the enthalpy change is the larger contributor by 4.1 kcal mol^{-1}. The decomplexation half-life for **2**⊙4-$MeOC_6H_4OMe$ is 800 times *longer* in $CDCl_2CDCl_2$ than in $CDCl_3$. The fact that solvation plays such a large role in the transition state for decomplexation suggests that it resembles in structure the dissociated rather than the starting state of the complex. Models (Corey–Pauling–Koltun or CPK) of possible transition states show that to be significantly solvated, the guest must protrude substantially from the portal for multiple guest–solvent contacts to be made. The fact that $CDCl_2CDCl_2$ is much larger than $CDCl_3$ suggests that steric inhibition of solvation of the transition state for decomplexation is responsible for this very large effect of solvent on rate. The only other study of the effects of solvent on rates of decomplexation of hemicarceplexes involved **7**⊙Me_2NCOMe (100 °C).[4] The rate constants decreased by an overall factor of about 45, and in the following order as solvent was changed: C_6D_5Br > C_6D_5Cl > 1,2-$(CD_3)_2C_6D_4$ > 1,4-$(CD_3)_2C_6D_4$ > $CDCl_2CDCl_2$ > $C_6D_5CD_3$. The six solvents vary considerably in their polarity and polarizability, but little in their overall size, compared to $CDCl_3$ *vs.* $CDCl_2CDCl_2$.

An examination of a CPK model of host **6** which contains four $O(CH_2)_4O$ bridges indicates that although the four portals are 26-membered rings, there is little chance of the substituted benzenes of this study entering or departing the inner phase of this hemicarcerand except at very high temperatures. Experimentally, **6**⊙4-MeC_6H_4OMe was formed only when **6** was heated in molten guest at 170 °C for 3.5 days.[3] Decomplexation of **6**⊙Me_2NCOMe required heating a solution of the complex in Ph_2O at 195 °C for 5 days. We conclude that the complexations and decomplexations of **1**–**5** occur through the two 27- or 28-membered ring portals partially defined by the unique bridge.

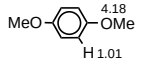
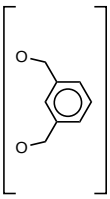
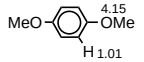
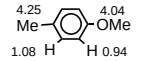
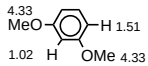
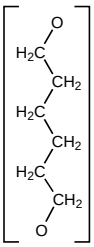
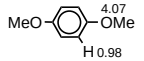
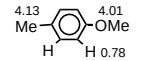
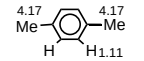
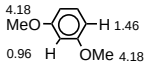
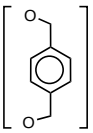
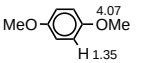
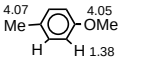
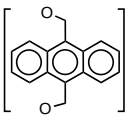
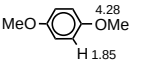
Comparisons of the activation free energies (Table 2) for decomplexations in $CDCl_3$ at 35 °C of various complexes of 4-$MeOC_6H_4OMe$ as a common guest show the effects of portal

Table 1 Activation parameters and half-lives for decomplexation of **2**⊙4-$MeOC_6H_4OMe$ in $CDCl_3$ and $CDCl_2CDCl_2$

Solvent	$t_{1/2}$/min[a]	$\Delta H^‡$/ kcal mol^{-1}	$\Delta S^‡$/cal mol^{-1} K^{-1}	$\Delta G^‡_{308}$/ kcal mol^{-1}
$CDCl_3$	182	19.0	−15.3	23.7
$CDCl_2CDCl_2$	147 000	25.2	−8.4	27.8

[a] At 35 °C.

Table 2 Decomplexation rate constants and activation free energies for host⊙guest at 35 °C in $CDCl_3$, and ^1H NMR spectral $\Delta\delta$ values ($\delta_{free\ guest} - \delta_{complexed}$, ppm)[a]

Host No.	Bridge O–A–O	Guest	k/ 10^{-3} min^{-1}	$\Delta G^{\ddagger b}$/ kcal mol^{-1}
1	[O(CH$_2$)$_5$O]		0.324	25.2
2			3.81	23.7
2			1.12	24.5
2			0.257	25.4
3			57.2	22.0
3			48.0	22.2
3			22.4	22.6
3			16.9	22.8
4			6.00	23.4
4			5.35	23.5
5			≪0.1	> 27

[a] 400 MHz in $CDCl_3$ at 25 °C. [b] $\Delta G^{\ddagger}_{308} = 23.7 - RT\ln k_{relative}$.

size and blocking power of the unique bridge. For example, $\Delta G^{\ddagger}$ is 25.2 kcal mol^{-1} with O(CH$_2$)$_5$O as the unique bridge, but decreases to 22.0 kcal mol^{-1} with O(CH$_2$)$_6$O as the unique bridge. This decrease of 3.2 kcal mol^{-1} reflects the increase of portal size by one CH_2 group added to the portal ring members (27 increased to 28), and corresponds to an increase in rate constant by a factor of 177. When the unique bridge is not increased in portal ring members but is decreased in blocking power by substitution of a 1,3-C$_6$H$_4$ for the internal (CH$_2$)$_3$ of the O(CH$_2$)$_5$O bridge, the $\Delta G^{\ddagger}$ value decreases by 1.5 kcal mol^{-1}, and the rate constant increases by a factor of 12. When the unique bridge is not changed from 28 portal ring members, but is increased in blocking power by substitution of a 1,4-C$_6$H$_4$ group for the central (CH$_2$)$_4$ moiety of O(CH$_2$)$_6$O, the $\Delta G^{\ddagger}$ value increases by 1.4 kcal mol^{-1}, and the rate constant decreases by a factor of 9.5. These trends correlate with the near-planarity of the 3-OCH$_2$C$_6$H$_4$CH$_2$O bridges in crystal structures of complexes containing these bridges,[6] and the near-perpendicularity of the aryl plane and the OCH$_2$··CH$_2$O plane in the crystal structure of **4**⊙C$_6$H$_5$NO$_2$.[2] When the 9,10-(OCH$_2$)$_2$-anthracenyl bridge is substituted for the O(CH$_2$)$_6$O bridge, the $\Delta G^{\ddagger}$ value increases by > 5 kcal mol^{-1}, and the rate constant decreases by a factor of at least 600. Model examination of **5** shows that the near perpendicularity of the two near planes of this bridge is enforced, and that the blocking ability of this bridge is greatly increased by the extension of its central ring by the two attached benzo groups. Model examination shows that in spite of this additional blocking effect, the 28-membered rings are still more available for use as portals than are the two 26-membered rings present in **5**.

Notice that independent of whether the host is **2**, **3** or **4** the increasing order of activation energy correlates with guest structural changes as follows: 4-MeOC$_6$H$_4$OMe < 4-MeC$_6$H$_4$OMe < 4-MeC$_6$H$_4$Me < 3-MeOC$_6$H$_4$OMe (see Table 2). For host **2** (27-membered ring portals), the $\Delta G^{\ddagger}$ values provide a spread of only 1.7 kcal mol^{-1}. For **3** (28-membered ring portals) an even lower spread of 0.8 kcal mol^{-1} is observed. The more confined entryway is the more selective, as expected.

We interpret the above correlations in terms of the relative contributions of *intrinsic* and *constrictive* binding that must be overcome for decomplexation to occur.[4] The five hosts have similarly shaped cavities generally complementary to the similarly shaped guests, suggesting that the intrinsic binding energies for the complexes are close to one another. In the transition states for decomplexation, the portals of each host must become slot-shaped and complementary to the slot-shaped cross section of the departing guest. Also, by guest rotation, the Me groups must pass from occupying the hosts' axial bowls to being aligned with the equatorially disposed portals. These shape and location adaptations in the transition state must overcome constrictive binding, which should be sensitive to portal-guest complementarity, and to exposure of protruding guest parts to bulk solution.

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Footnotes and References

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† All new complexes gave elemental analyses within 0.30% of theory, and expected ^1H NMR and FAB (*m/z*, M + H$^+$) mass spectra.

‡ The reaction G′ + H⊙G → H⊙G′ + G, where G′ is solvent, should give first order kinetics for appearance of G. Formally, a mechanism might apply in which G′ enters H in the same transition state that G departs. When H has multiple potential entryways whose equilibrium dimensions are comparable to cross sections of G′, activation energies for guest substitution are very low, and concerted mechanisms might apply. However, $\Delta G^{\ddagger}$ values for **2**⊙4-MeOC$_6$H$_4$OMe are rather high. Molecular model examinations show that for one portal to become large enough to accommodate guest departure, the other three must decrease their apertures through many small conformational adjustments, thus becoming unavailable for simultaneous solvent entry.

§ Decomplexation kinetics were conducted on 0.5 ml samples of 2 mM solutions of complexes in degassed $CDCl_3$ or $CDCl_2CDCl_2$ in sealed ^1H NMR tubes in the probe of a 400 MHz spectrometer adjusted to the desired temperature (±1 °C) after the probe temperature was calibrated with HOCH$_2$CH$_2$OH (ref. 7). The $CDCl_3$ or $CDCl_2CDCl_2$ had recently been passed through a plug of neutral activated alumina. About 20–25 spectra were recorded at appropriate time intervals. The first order rate constants were calculated from the strong signals of the guest methyl groups upon decomplexation. Tables 1 and 2 record the results.

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