Comparisons of Activation Energies for Dimethyl Sulfoxide Rotations in the Inner Phase of Seven Carcerands

Siavash K. Kurdistani, Timothy A. Robbins and Donald J. Cram*

Department of Chemistry and Biochemistry, University of California at Los Angeles, Los Angeles, CA 90095, USA

The syntheses and characterizations of nine new carceplexes are reported, the $\Delta G^{\ddagger}$ values for rotations of Me_2SO in the inner phases of seven of them are determined and found to be unaffected by changes in bulk solvent.

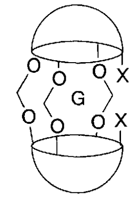
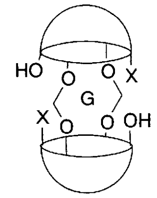
Prior papers reported the synthesis of three carceplexes **1**⊙G (G = Me_2SO, Me_2NCOMe or Me_2NCHO) by shell closures with $BrCH_2Cl$–Cs_2CO_3 or two molecules of tetrol **3** in G as solvent.[1] Similarly, two molecules of diol **4** were shell closed in the same three solvents to give three hemicarceplexes **2**⊙G (G = Me_2SO, Me_2NCOMe and Me_2NCHO).[2] However, when triol **5** was submitted to shell closure in Me_2SO, hemicarceplex **9**⊙Me_2SO and carceplex **14**⊙Me_2SO were obtained, corresponding to the two possible ways the rims of the triols can be attached to one another.[2] Furthermore, ^1H NMR spectra of the guest of **1**⊙Me_2SO demonstrated that, at temperatures below 0 °C, the guests' rotations relative to the host were slow on the spectral timescale.

The current study has three objectives. The first is to determine how solvent changes and rim-located substituents on the bowls affect the balance of products produced by the different ways rim-to-rim coupling can occur. The second is to use the activation free energies and coalescence temperatures for incarcerated guest rotations as a measure of the cavity size of the host. The third is to determine whether bulk solvent change alters the activation free energies for rotations.

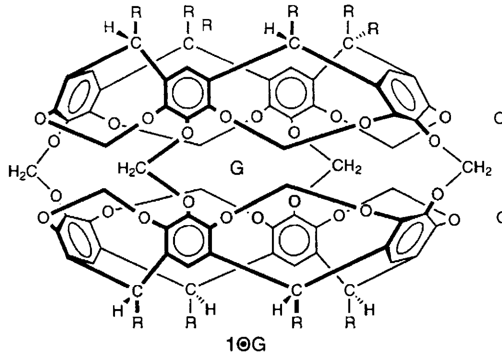
Tetrol **3**[1] when treated with excess MeI, EtI or $PhCH_2Br$ in Me_2NCHO containing 1.5 equiv. of CsF[3] at 40 °C, gave 20–25% yields of the respective easily-purified triols, **6**, **7** and **8**.[†] Shell closure of each triol was conducted in Me_2SO, Me_2NCOMe and Me_2NCHO ($BrCH_2Cl$–Cs_2CO_3, 65 to 100 °C, 3–5 d)[2] to give the product distributions shown in Table 1.

Sherman *et al.* have demonstrated that the yields of shell closed products of an analogue of tetrol **3** (R = Me rather than CH_2CH_2Ph) correlate with the stability of hydrogen bonded dimers as solvent (guest) is changed.[4] Such an effect would explain why tris-bridged products generally dominated over the bis-bridged products, three hydrogen bonds being more stabilizing than two. There is no correlation of shell-closure yields with

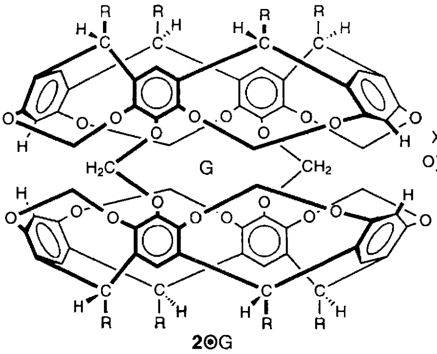
Table 1 Distribution of shell-closed products

		Yields (%)	
X	Solvent (G)		
OMe	Me_2SO	11	11
OMe	Me_2NCHO	24	0
OMe	Me_2NCOMe	0	0
OEt	Me_2SO	22	11
OEt	Me_2NCHO	20	0
OEt	Me_2NCOMe	0	0
OCH_2Ph	Me_2SO	15	0
OCH_2Ph	Me_2NCHO	40	0
OCH_2Ph	Me_2NCOMe	12	0
H[a]	Me_2SO	51	5
H[a]	Me_2NCHO	20	0
H[a]	Me_2NCOMe	42	0

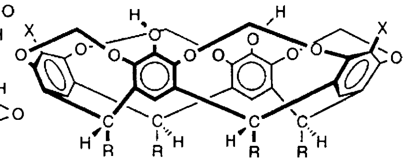
[a] Taken from ref. 1.



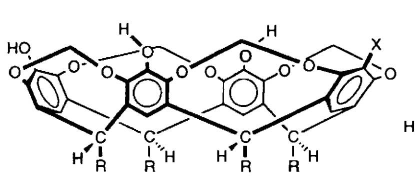
1⊙G



2⊙G

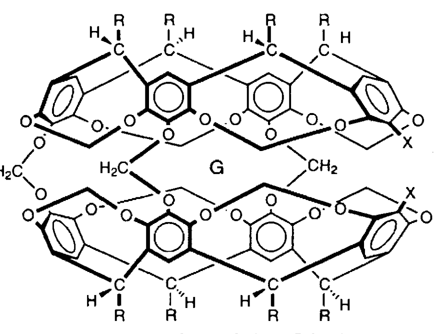


3 X = OH, **4** X = H

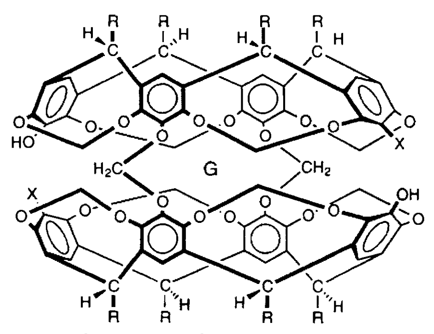


5 X = H, **6** X = OMe, **7** X = OEt, **8** X = OCH_2Ph

1–**17** R = CH_2CH_2Ph



9⊙G X = H, **10**⊙G X = OH, **11**⊙G, X = OMe, **12**⊙G X = OEt, **13**⊙G X = OCH_2Ph



14⊙G X = H, **15**⊙G X = OMe, **16**⊙G, X = OEt, **17**⊙G X = OCH_2Ph

the size of the rim substituents running from X = H to X = OCH_2Ph. This fact strongly suggests that in the ground and transition states for shell closures, the Me, Et and CH_2Ph groups are oriented away from the bowl cavities in a conformation which minimizes the O–C dipole–dipole repulsions in the attached 1,2,3-trisoxygen-substituted benzenes in the study.

Table 2 shows the coalescence temperatures (T_c) and activation free energies ($\Delta G^\ddagger$) for rotations of Me_2SO relative to the hosts for seven carceplexes, determined using a Bruker MA-360 MHz ^1H NMR spectrometer. The method employed was modelled after that previously reported for **1**⊙G, in which the signals for the guest's methyl proton singlets change upon cooling.[‡] Their occurrence at δ values below 0 ($SiMe_4$ standard) simplified their observation. Unfortunately, **2**⊙Me_2SO and **10**⊙Me_2SO were too insoluble at low temperatures to be included in the study.

The crystal structures of **1**⊙Me_2NCOMe[1] and **9**⊙Me_2NCHO[2] demonstrated that the unshared electron pairs of the interhemispheric OCH_2O bridges orient inward toward the cavity and the hydrogens outward away from the cavity. Corey–Pauling–Koltun molecular models of the carceplexes of Table 2 indicate that such a conformation is mandatory for the OMe, OEt and OCH_2Ph groups found in **11–13**, **15** and **16**. The $\Delta G^\ddagger$ values for rotation of the Me_2SO guest about the short axes of the host for **11–13** are all within experimental error of one another at 12.3 ± 0.3 kcal mol^{-1} (1 cal = 4.184 J), indicating the three cavities have about the same size and shape in concert with expectations based on model examination. The $\Delta G^\ddagger$ and T_c values for **13** in $(CD_2)_4O$, $CDCl_3$, CD_2Cl_2 and $CDCl_2CDCl_2$ are identical as expected, since the shell insulates the Me_2SO from varying solvent effects. When the OR groups are replaced with H as in **9**, the activation energy for rotation decreases to 9.8 kcal mol^{-1} since the cavity becomes somewhat wider in the equatorial region of the globe-shaped host. When the two OR groups are replaced by a fourth OCH_2O group as in **1**, the whole structure becomes more rigid (model examination), and the $\Delta G^\ddagger$ value increases to 13.6 kcal mol^{-1}.

Table 2 Free energies of activation for rotations of incarcerated Me_2SO[†]

Carceplex	Solvent	$\Delta G^\ddagger$/ kcal mol^{-1}	T_c/K
1⊙Me_2SO	$CDCl_3$	13.6	275
9⊙Me_2SO	$(CD_2)_4O$	9.8	193
11⊙Me_2SO	$(CD_2)_4O$	12.1	261
12⊙Me_2SO	$(CD_2)_4O$	12.6	272
13⊙Me_2SO	$(CD_2)_4O$	12.1	258
13⊙Me_2SO	$CDCl_3$	12.1	258
13⊙Me_2SO	CD_2Cl_2	12.1	258
13⊙Me_2SO	$CDCl_2CDCl_2$	12.1	258
15⊙Me_2SO	$(CD_2)_4O$	12.1	261
16⊙Me_2SO	$(CD_2)_4O$	13.0	283

In **15** and **16**, the two hemispheres are bridged by only two OCH_2O groups and the other two sets of positions each contain OH and OR groups. Model examination shows that the carcerands become more crowded and rigid as the R of the OR group increases in bulk, elongating the cavity along the long polar axis but shortening it along the shorter equatorial axes. Inhibition of Me_2SO rotation in models is more limited by the length of the equatorial axes. This effect appears to take hold in passing from **15**⊙Me_2SO to **16**⊙Me_2SO, in which X = OMe ($\Delta G^\ddagger$ = 12.1 kcal mol^{-1}) and X = OEt ($\Delta G^\ddagger$ = 13.0 kcal mol^{-1}), respectively. Compound **17**⊙Me_2SO failed to form, probably for steric reasons.

The authors warmly thank the US Public Health Service for supporting Grant GM-12640.

Received, 24th March 1995, Com. 5/01901J

Footnotes

[†] All new compounds gave C and H elementary analyses within 0.30% of theory, M^+ *m/z* signals of substantial intensity in their MS or FAB-MS, and ^1H NMR spectra consistent with their structures.

[‡] Values for $\Delta G^\ddagger$ of rotation were calculated using $\Delta G^\ddagger = 19.14\,T_c\,[9.97 + \log(T_c/\Delta v)]$ where T_c is the coalescence temperature and Δv is the difference in chemical shift of the Me_2SO guest proton signals.

References

1. J. C. Sherman and D. J. Cram, *J. Am. Chem. Soc.*, 1989, **111**, 4527; J. C. Sherman, C. B. Knobler and D. J. Cram, *J. Am. Chem. Soc.*, 1991, **113**, 2194.
2. M. E. Tanner, C. B. Knobler and D. J. Cram, *J. Am. Chem. Soc.*. 1990, **112**, 1659; D. J. Cram, M. E. Tanner and C. B. Knobler, *J. Am. Chem. Soc.*, 1991, **113**, 7717.
3. L. C. Groen, B. H. M. Ruël, A. Casnati, W. Verboom, A. Pochini, R. Ungaro and D. N. Reinhoudt, *Tetrahedron*, 1991, **47**, 8379.
4. R. G. Chapman, N. Chopra, E. D. Cochien and J. C. Sherman, *J. Am. Chem. Soc.*, 1994, **116**, 369; R. G. Chapman, J. Fraser, N. Chopra, E. D. Cochien and J. C. Sherman, *Symposium Honoring D. J. Cram*, UCLA, Los Angeles, CA, March 1994.