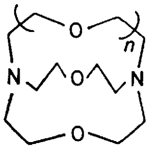
Kinetics and Mechanisms of Formation of the Di-*endo* Protonated Cryptand (2,1,1)H_2^{2+} including Trapping and *X*-Ray Structure Determination as its Diperchlorate Salt

Brian G. Cox,[a] **Judith Murray-Rust,**[a] **Peter Murray-Rust,**[a] **Nguyen van Truong,**[a] **and Hermann Schneider**[b]

[a] *Chemistry Department, University of Stirling, Stirling FK9 4LA, U.K.*
[b] *Max-Planck-Institut für biophys. Chemie, D-3400, Göttingen, West Germany*

The di-*endo*-protonated cryptand (2,1,1)H_2^{2+} is formed by slow direct proton transfer from acids HA to (2,1,1)H^+; the crystal structure of (2,1,1)H_2^{2+} as its diperchlorate salt is reported.

Proton transfer reactions of cryptands have been investigated kinetically[1–5] and shown to occur in two distinct steps, corresponding to formation of mono- and di-protonated species. The rates for the (1,1,1) cryptand (**1**) are extremely slow and several different species have been observed by n.m.r. spectroscopy, interconverting over periods of hours.[5] It was suggested that the mono- and di-protonated species can exist in various conformers differing in whether the nitrogens are *endo* or *exo*.



(**1**) $n = 1$

(**2**) $n = 2$

We have investigated proton transfer with the (2,1,1) cryptand (**2**). In acid solution the monoprotonation of (**2**) is fast, but the second protonation is sufficiently slow to be studied conveniently by stopped-flow methods in a number of solvents. Results obtained in methanol (Figure 1) show that

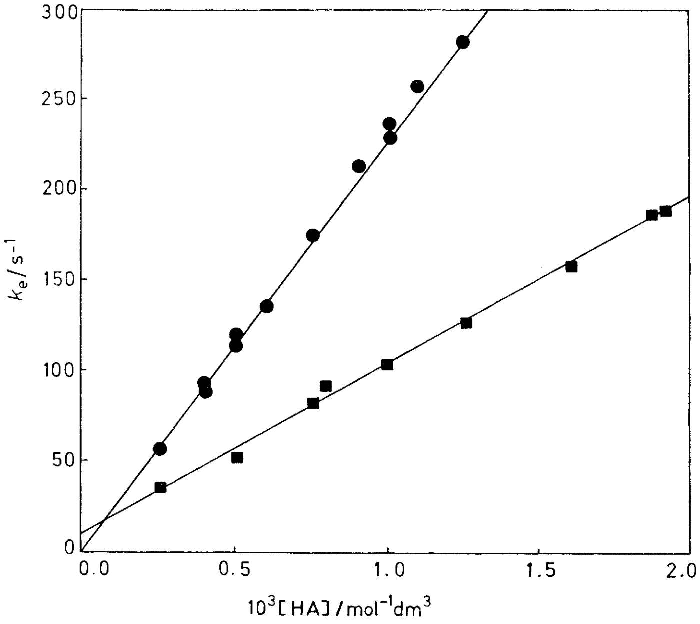
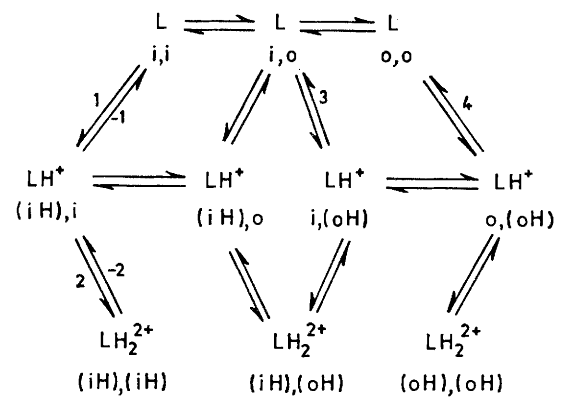


Figure 1. Rates of protonation of (2,1,1)H^+ in methanol at 25 °C. (●) Dichloroacetic acid; (■) chloroacetic acid.



Scheme 1. Possible interconversion pathways for (2,1,1) species. Only the 3 *endo*, *endo*-species and pathways 1 and 2 seem to be involved. i = *endo* N, iH = *endo* NH^+, o = *exo* N, oH = *exo* NH^+.

Table 1. Rates of protonation of (2,1,1)H^+ in methanol at 25 °C.

Acid (HA)	k_{HA}/mol^{-1} dm^3 s^{-1}	k_A[a]/mol^{-1} dm^3 s^{-1}
H^+	4 (±1.5) × 10^5 [b]	5 × 10^{-3} (s^{-1})[b,c]
$CHCl_2CO_2H$	2.3 × 10^5	7.8 × 10^3 [c]
CH_2ClCO_2H	8.0 × 10^4	7.0 × 10^4 [c]
CH_3CO_2H	4.8 × 10^3	2.8 × 10^5 [d]

[a] Deprotonation of (2,1,1)H_2^{2+} by A^-. [b] Approximate value obtained by extrapolation from lower temperatures. [c] Obtained by combining k_{HA} with the equilibrium constants for proton transfer between HA and (2,1,1)H^+ $\{K_{HA}/K[(2,1,1)H_2^{2+}]\}$. K_{HA} values from B. W. Clare, D. Cook, E. T. C. Ko, Y. C. Mac, and A. J. Parker, *J. Am. Chem. Soc.*, 1966, **88**, 1911. $K[(2,1,1)H_2^{2+}]$ from B. Speiss, F. Arnaud-Neu, and M.-J. Schwing-Weill, *Helv. Chim. Acta*, 1979, **62**, 1531 corrected to zero ionic strength. [d] Measured directly by mixing an excess of NEt_4OAc with (2,1,1)H_2^{2+}, ionic strength ⩽10^{-3} M.

the reaction involves a rate-determining proton transfer from acid HA to (2,1,1)H^+, as in equations (1) and (2). Table 1 lists

$$LH^+ + HA \underset{k_A}{\overset{k_{HA}}{\rightleftharpoons}} LH_2^{2+} + A^- \qquad (1)$$

$$-d[LH^+]/dt = k_{HA}\,[LH^+][HA] \text{ (in an excess of HA)} \qquad (2)$$

values of k_{HA} and k_A. The (2,1,1) system reacts much faster than the (1,1,1) system,[5] but k_{HA} values are still several orders of magnitude lower than those expected for a diffusion-controlled reaction in the thermodynamically favoured direction.[6]

Possible interconversions (Scheme 1) are suggested on the assumption that proton transfer and conformational change are independent, and that inversion can occur only at unprotonated nitrogen. The conformation of the free ligand (a liquid) has not been determined but, by analogy with (2,2,2) in the solid state,[7] is expected to be *endo*, *endo* ($L_{1,1}$). The slow rates of protolysis of (2,1,1) under conditions where only the monoprotonated species is formed (both in water and methanol)[1,4,8] are inconsistent with simple *exo*-protonation in LH^+ (steps 3 and 4) and, we believe, by analogy with the LiI complex,[9] that LH^+ is in the *endo*, *endo*-conformation, though not necessarily involving an internal N–H . . . N bond. The second protonation step presumably involves *endo*-protonation, evidence being provided by the slow rate and the involvement of HA in the transition state.

The very slow rate of deprotonation of LH_2^{2+} in strong acid suggests the possibility of trapping it in the solid state. When 1M $HClO_4$ is added to L/LH^+ in water, crystals of $LH_2(ClO_4)_2$ precipitate instantaneously (*i.e.* their rate of production depends on mixing time). This is much faster than the H_2O-catalysed deprotonation of LH_2^{2+},† so that the diperchlorate is likely to have trapped kinetically the thermodynamically most stable cation in solution.‡ We now report the *X*-ray structure of this salt.

Crystal data for (2)·2$HClO_4$: $C_{14}H_{30}N_2O_{12}Cl_2$, M_r = 488.9, monoclinic, space group $P2_1/c$, Z = 4, a = 8.56(1), b =

---

† We estimate $t_{\frac{1}{2}}$ ($LH_2^{2+} \rightarrow LH^+$) as several minutes, based on data in Table 1 and relative rates of deprotonation/protonation steps in the (2,1,1) systems in water and methanol (ref. 8).

‡ Since the diperchlorate can be recrystallised unchanged from water it is also the most stable cation in the solid state.

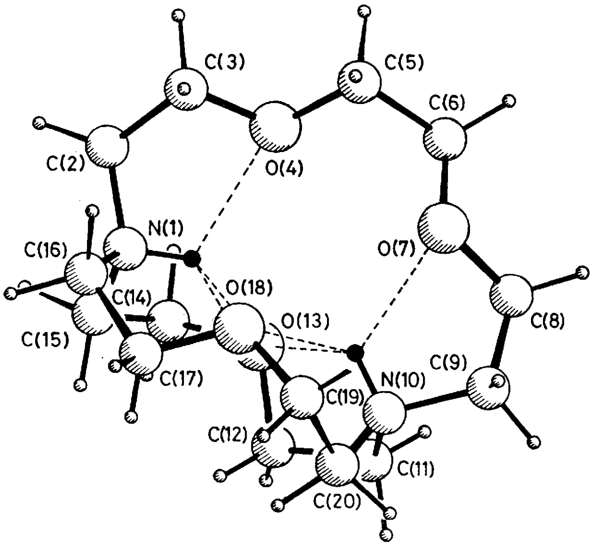
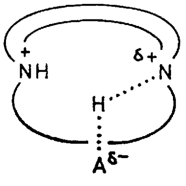


Figure 2. The deprotonated (2,1,1) ligand (approximate C_2 symmetry) in its perchlorate salt. The (disordered) perchlorates are omitted; so are some of the H atoms for clarity. The two protons on the N atoms (black) each make contacts with 3 O atoms. The N . . . O distances are in the range 2.72—2.82Å and the H . . . H distance is 2.64 Å.

19.43(2), $c = 13.17(2)$ Å, $\beta = 91.85(2)°$; $\mu(\text{Mo-}K_\alpha) = 3.05 \text{ cm}^{-1}$, crystal size *ca.* 0.5 × 0.3 × 0.3 mm^3. 3405 reflexions with $I > 3\sigma(I)$ were collected on a Stoe 2-circle diffractometer and the structure was solved by direct methods (SHELX-76).[10] Hydrogen atoms on both nitrogens were located by difference synthesis and refined isotropically; hydrogen atoms on C were placed in calculated positions. Both perchlorate ions are disordered. Full matrix refinement with anisotropic heavy atoms converged at $R = 0.068$.§

The cation (Figure 2) has an approximate C_2 axis and the ligand geometry is extremely similar to that in LiL^+I^-,[9] differences in torsion angles being usually 3° or less. Clearly the presence of two formal charges in the cavity, which might be thought to show severe electrostatic repulsion, has little effect on the geometry. This may, in part, be due to the lone pairs on the O atoms, and 3 formal NH . . .O bonds can be drawn for each N. It is probable also that the ligand is rather rigid because the 12-membered ring [containing O(13), O(18)] has the same conformation as free cyclododecane. Unlike the (2,2,2) and larger systems therefore, we feel that the (2,1,1) cryptand is rather rigid and has a high preference for the *endo*, *endo*-state whether or not the nitrogens are co-ordinated.



(3)

This rigidity can explain the abnormally slow rates of proton transfer. *exo*-Attack is not favoured and step 1 seems to involve direct entry of the proton into the cavity.[3,4] Step 2 is linked to the acid strength of the proton donor HA, acting as a general acid, so that the transition state might be (**3**). This is clearly a much slower process than simple proton attack because of steric hindrance and the non-linear geometry. It is even more pronounced in the (1,1,1) system but, without structural data, we are less able to speculate on the detailed geometries of LH^+ and LH_2^{2+} in this case.

Received, 21st December 1981; Com. 1443

References

1 B. G. Cox, D. Knop, and H. Schneider, *J. Am. Chem. Soc.*, 1978, **100**, 6002.
2 R. Pizer, *J. Am. Chem. Soc.*, 1978, **100**, 4239.
3 B. G. Cox and H. Schneider, *J. Chem. Soc., Perkin Trans.* 2, 1979, 1293.
4 A. M. Kjaer, P. E. Sørensen, and J. Ulstrup, *J. Chem. Soc., Chem. Commun.*, 1979, 965.
5 P. B. Smith, J. L. Dye, J. Cheney, and J.-M. Lehn, *J. Am. Chem. Soc.*, 1981, **103**, 6044.
6 A. J. Kresge, *Pure Appl. Chem.*, 1981, **53**, 189.
7 B. Metz, D. Moras, and R. Weiss, *J. Chem. Soc., Perkin Trans.* 2, 1976, 423.
8 N. van Truong, unpublished results.
9 D. Moras and R. Weiss, *Acta Crystallogr., Sect. B*, 1973, **29**, 400.
10 G. M. Sheldrick, 'SHELX-76' University of Cambridge, 1976.

---

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.