

Kinetic Deuterium Isotope Effect in the Protonation of Cryptand [2,1,1], (1,10-Diaza-4,7,13,18-tetraoxabicyclo[8.5.5]eicosane) by Water

By ANNA M. KJÆR, POUL E. SØRENSEN, and JENS ULSTRUP*

(Chemistry Department A, Building 207, The Technical University of Denmark, 2800 Lyngby, Denmark)

Summary The protonation of cryptand [2,1,1] by water displays large kinetic deuterium effects suggesting that the process involves direct proton transfer through the cryptand molecular framework.

It is commonly found that proton transfer reactions involving nitrogen and oxygen donor and acceptor atoms are fast and display small kinetic deuterium isotope effects.^{1,2} Notable exceptions to this are the slow protonation and deprotonation reactions of small cryptands^{3,4} for which the molecular framework presumably prevents the

proton donor or acceptor from an energetically favourable approach to the cryptand reaction site. The proton transfer would then require either that a major structural reorganization of the cryptand molecule occurs, *e.g.* an *endo-exo* conversion,⁴ or that the proton transfer occurs by tunnelling.

In order to elucidate the prevalence of either of these two alternatives we have measured the rate of protonation of the dibasic form of cryptand [2,1,1] by L₂O (L = H or D) in aqueous and 99.8% D₂O solutions. Equimolar solutions of the cryptand (Kryptofix, Merck) and *m*-nitrophenol

(recrystallized several times from 5×10^{-3} mol dm $^{-3}$ HCl) in H $_2$ O or D $_2$ O, 10^{-2} mol dm $^{-3}$ with respect to caesium chloride, were mixed in a Durrum-Gibson stopped-flow apparatus, and the rate of formation of the phenolate anion was followed spectrophotometrically at 440 nm to an equilibrium corresponding to about 10% of unchanged components. The phenol is thus a scavenger for the liberated hydroxide ions, and the equimolarity ensures that diprotonation of the cryptand is avoided.⁵ Moreover, the liberation of phenolate is initially dominated by direct proton transfer from phenol to cryptand (details of which will be reported later) but otherwise exhibited first-order behaviour over several half-lives.

The following rate constants, k_L (25 °C; in s $^{-1}$), and activation parameters were found: $k_H = 2.2$, $k_D = 0.57$; $k_H/k_D = 3.9$; $E_A^H = 48.8 \pm 0.6$ kJ mol $^{-1}$; $E_A^D = 52.7 \pm 1$ kJ mol $^{-1}$; $A_H = 7.5 \times 10^8$; $A_D = 9.4 \times 10^8$, and $A_H/A_D = 0.80$, where E_A^L and A_L are the appropriate activation energies and Arrhenius pre-exponential factors, respectively. These substantial isotope effects strongly suggest

that the proton is transferred directly from water to the cryptand and are hard to reconcile with a slow conformational change followed by a rapid proton transfer to the exposed nitrogen atom. Analysis of the data in terms of the quantum mechanical formulation of the kinetic isotope effect of proton transfer reactions^{6,7} shows that the proton is most likely transferred along an O-H bending mode (of frequency *ca.* 1600 cm $^{-1}$) to a cryptand N-H bending mode, and that the proton transfer distance would then be 0.5–0.6 Å.

We notice finally that the protonation of a series of mono- and di-basic cryptands by ethyl nitroacetate displays somewhat larger kinetic isotope effects ($k_H/k_D = 7.2$ – 8.5). This reaction is, however, less suitable for elucidation of the influence of the cryptand molecule dynamics on the proton transfer path, since the deprotonation of ethyl nitroacetate by more 'conventional' oxygen and nitrogen acceptors also displays large kinetic isotope effects.¹

(Received 2nd August 1979; Com. 842.)

¹ R. P. Bell, 'The Proton in Chemistry,' 2nd edn., Chapman and Hall, London, 1973.

² A. J. Kresge, *Accounts Chem. Res.*, 1975, **8**, 354.

³ J. Cheney and J. M. Lehn, *J.C.S. Chem. Comm.*, 1972, 487.

⁴ B. G. Cox, D. Knop, and H. Schneider, *J. Amer. Chem. Soc.*, 1978, **100**, 6002.

⁵ J. M. Lehn and J. P. Sauvage, *J. Amer. Chem. Soc.*, 1975, **97**, 6700.

⁶ E. D. German and Yu. I. Kharkats, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1972, **5**, 1031; E. D. German, *ibid.*, 1977, **10**, 2802; 1978, **11**, 959.

⁷ N. Brüniche-Olsen and J. Ulstrup, *J.C.S. Faraday I*, 1979, **75**, 205.

⁸ B. G. Cox and H. Schneider, *J.C.S. Perkin II*, in the press.