Rates and Kinetic Hydrogen Isotope Effects for the Ionization of Phenylnitromethane

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Summary The general-base catalyzed ionization of phenylnitromethane is subject to large primary kinetic hydrogen isotope effects; these effects, their activation parameters, and the Brønsted catalysis coefficient for the reaction are used to discuss possible transition-state structures.

DURING recent years there have been a number of studies attempting to test and evaluate Westheimer's prediction[1] that the magnitude of the primary kinetic hydrogen isotope effect should be at a maximum for a reaction proceeding through a transition state in which the isotopic hydrogen is partially bound with equal strengths to the two groups between which it is being transferred. A way of varying experimentally the relative values of the two pertinent force constants is necessary for such tests. For proton transfer reactions a suggestion of Bell and Goodall[2] has been used—that the transition state should be approximately symmetrical, according to the equal force constant criterion, when the pK values of AH and HB [equation (1)] are

$$\text{A–H} + :\text{B} \rightleftharpoons \text{A}: + \text{H–B} \qquad (1)$$

approximately equal, *i.e.*, when $\mathrm{p}K_{\mathrm{AH}} - \mathrm{p}K_{\mathrm{BH}} = \Delta\mathrm{p}K_{\mathrm{a}} \approx 0$. Similarly, it has been supposed that for hydrogen atom transfer reactions, a symmetrical transition state will occur when the homolytic bond strengths of A–H and H–B are equal.[3,4] Although the methods mentioned above for varying transition state symmetry have not been proved,

TABLE 1. Kinetic parameters for the reaction $\text{Ph–CL}_2\text{–NO}_2 + :\text{B} \rightarrow \text{LB} + \text{Ph–CL} = \text{NO}_2^-$ (L = hydrogen or deuterium)

$$\Delta\mathrm{p}K_{\mathrm{a}}' = (\mathrm{p}K_{\mathrm{PNM}} - \mathrm{p}K_{\mathrm{BH}}) + \log\,(q_{\mathrm{H}}/q_{\mathrm{BH}})$$

Reaction	Base	$\mathrm{p}K_{\mathrm{HB}}^{\mathrm{a}}$ (25°)	k_{H} (25 °C) /l mol^{-1} s^{-1}	$\Delta\mathrm{p}K_{\mathrm{a}}'$	$k_{\mathrm{H}}/k_{\mathrm{D}}$ (25°C)
(1)	Hydroxide	15·74	151 ± 3	−8·94	7·4 ± 0·2
(2)	Piperidine	11·12	19·8 ± 0·3	−4·32	8·5 ± 0·1
(3)	Ethylamine	10·81	3·00 ± 0·04	−4·01	10·5 ± 0·3
(4)	Carbonate	9·80	0·515 ± 0·007	−2·52	9·4 ± 0·2
(5)	Morpholine	8·33	1·13 ± 0·01	−1·53	9·3 ± 0·2
(6)	Tris[b]	8·15	0·101 ± 0·002	−1·35	10·6 ± 0·3
(7)	Imidazole	6·95	3·51 ± 0·04 × 10^{-2}	−0·45	11·5 ± 0·2
(8)	Monohydrogen phosphate	6·50	2·75 ± 0·05 × 10^{-2}	+0·45	9·3 ± 0·5
(9)	Acetate	4·75	1·40 ± 0·02 × 10^{-3}	+2·35	8·3 ± 0·2
(10)	Formate	3·75	3·39 ± 0·05 × 10^{-4}	+3·35	7·3 ± 0·2
(11)	Chloroacetate	2·85	1·07 ± 0·01 × 10^{-4}	+4·25	7·4 ± 0·1
(12)	Water	−1·74	5·2 × 10^{-8}[c]	+8·54	5·5 ± 0·2[d]
(13)	Guanidine	13·6	—	−6·8	6·7 ± 0·3[e]
(14)	Fluoride	3·18	10^{-4}[f]	+3·62	4·8 ± 0·1
(15)	2,6-Lutidine .. .. (+4-nitroPNM)	6·7	0·556 ± 0·008	−0·9	12·3 ± 0·3

[a] These values were taken mainly from standard sources, *e.g.* 'The Handbook of Chemistry and Physics,' The Chemical Rubber Co., Cleveland, 1967. All kinetics were done at an ionic strength of 0·400(KCl) with the exception of reactions (8) (I = 0·300*M*) and (13) (I = 5·00*M*). The $\mathrm{p}K_{\mathrm{BH}}$ values quoted are for infinite dilution except those for carbonate and monohydrogen phosphate which are rather sensitive to ionic strength and which were estimated from data in L. G. Sillen and A. E. Martell, Eds., 'Stability Constants of Metal-Ion Complexes,' Special Publ. No. 17, The Chemical Society, London, 1964, pp. 133—135 (carbonate), and Supplement No. 1, Special Publ. No. 25, 1971, p. 107 (monohydrogen phosphate). [b] Tris(hydroxymethyl)aminomethane. [c] V. M. Belikov *et al.*, *Bull. Acad. Sci., U.S.S.R., Div. Chem. Soc.*, 1969, 1284. [d] Ratio determined using 40% (w/w) aq. acetic acid as solvent. [e] Upper limit. [f] Fluoride concentration not accurately determined.

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a number of groups have shown that the kinetic isotope effect does go through a maximum for a reaction having ΔpK_a (or ΔE° as appropriate) nearly zero.[2,5]

It has also been pointed out,[6] in discussions of work of this kind, that proton tunnelling will probably increase the isotope effect and that this influence too will be maximized when (for a proton transfer reaction) $\Delta pK_a = \Delta G^\circ =$ zero. Recently, Bell, Sachs, and Tranter[7] have shown that at least one transition state model (a "charge cloud" model) can be used to calculate isotope effect bows, of magnitudes comparable to experiment, entirely on the basis of tunnelling; *i.e.* as their "reaction series" was varied between $\Delta pK_a = +22$ and -22, the variation in the isotope effect was produced without significant alterations in partial bond force constants in the transition state. The question is thus raised: what aspect of transition-state structure is manifested by the isotope effect?

TABLE 2. Entropy and enthalpy changes for reactions (1), (2), (5), (7), and (8). (See Table 1).

Reaction	Base	$\Delta H^\ddagger_H$ /kcal mol^{-1}	$\Delta S^\ddagger_H$ /cal K^{-1} mol^{-1}	$\Delta H^\ddagger_D - \Delta H^\ddagger_H$ /kcal mol^{-1}	log (A_H/A_D)
(1)	Hydroxide	$11\cdot6 \pm 0\cdot1$	$-9\cdot4 \pm 0\cdot3$	$1\cdot70 \pm 0\cdot10$	$-0\cdot38 \pm 0\cdot08$
(2)	Piperidine	$12\cdot2 \pm 0\cdot3$	$-11\cdot5 \pm 1\cdot0$	$0\cdot46 \pm 0\cdot37$	$+0\cdot57 \pm 0\cdot26$
(5)	Morpholine	$13\cdot3 \pm 0\cdot2$	$-13\cdot8 \pm 0\cdot6$	$2\cdot60 \pm 0\cdot22$	$-0\cdot98 \pm 0\cdot15$
(7)	Imidazole	$13\cdot8 \pm 0\cdot2$	$-19\cdot2 \pm 0\cdot6$	$1\cdot80 \pm 0\cdot31$	$-0\cdot33 \pm 0\cdot22$
(8)	Monohydrogen phosphate ..	$16\cdot6_5 \pm 0\cdot2$	$-9\cdot8 \pm 0\cdot5$	$2\cdot30 + 0\cdot40$	$-0\cdot72 \pm 0\cdot29$

Bell has proposed that tunnelling can be detected by determining the Arrhenius pre-exponential ratio, log (A_H/A_D), for the isotope effect.[8] Values of the quantity more negative than $-0\cdot30$ are taken to indicate tunnelling. The "exact" calculations of Schneider and Stern[9] seem to confirm this proposal. To test it experimentally, activation parameters must be determined. In this communication we report a study of the rates, the isotope effects (k_H/k_D), and the temperature dependence of the isotope effect for the reaction of phenylnitromethane (PNM) with a number of bases in water.

The reaction is a clean general-base-catalyzed deprotonation. The rates are first-order in substrate and in base, and were determined by several spectrophotometric methods: the first-order appearance of phenylmethanenitronate anion; the zero-order (initial) appearance of the anion; and the zero-order disappearance of bromine. The rate constants were corrected, as necessary, for small (<5%) contributions from hydroxide catalysis and for incomplete deuteriation (assuming a 15% secondary isotope effect). The results are given in the Tables.

Several features are evident from the data. The isotope effect goes through a maximum near $\Delta pK_a = 0$, as expected. The curve is not smooth, however, perhaps because of the structural variety of the bases used. The isotope effects are all rather large, the only major exceptions being for the bases water and fluoride. A good Brønsted correlation is obtained, with $\beta = 0\cdot57$. The rate constants for water and hydroxide ion show negative deviations from the Brønsted plot (as is common); the only other notable exceptions are the cyclic secondary amines morpholine and piperidine for both of which the reaction is faster than predicted. No clear trend emerges from consideration of the activation parameters. It is not obvious that the observed difference in isotopic activition energy is systematically greater, nor the value of A_H/A_D systematically lower, for the reactions having the lowest values of ΔG°. The results for piperidine seem anomalous, and no explanation is offered. It is possible similar bases, *e.g.* primary amines, would reveal a trend not here seen. However, it is noteworthy that even for a reaction with ΔG° as negative as that of hydroxide with PNM, evidence of tunnelling persists. Since tunnelling is extremely sensitive to the effective mass along the reaction coordinate, it may be argued that, for the reactions reported here, the motion of the isotope in the transition state is unaccompanied, at least along the reaction co-ordinate, by the motions of other nuclei. This result provides experimental support for the view that the proton-transfer process may be approximated to the movement of the proton between two fixed centres.

The results of this study, along with results on the Brønsted coefficients[10] and isotope effects[2,5] for similar reactions, substituent effects on the rates and equilibria of arylnitromethane and ethane ionization reactions,[11] and other data assembled by Bordwell[11], lead most consistently to the conclusion that, in the transition states for nitroalkane ionization, the partial bonds to the transferred isotope are roughly equal in strength, even for reactions having ΔG° rather different from zero. Further, the extent of delocalisation of the developing negative charge is probably not great, although rehybridisation has certainly begun, as shown by the magnitude (*ca.* 10—15%) of the secondary α-deuterium isotope effect for the ionisation of nitroalkanes.

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[1] F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265.

[2] R. P. Bell and D. M. Goodall, *Proc. Roy. Soc. A*, 1966, **294**, 273.

[3] W. A. Pryor and K. G. Kneipp, *J. Amer. Chem. Soc.*, 1971, **93**, 5586.

[4] E. S. Lewis and M. M. Butler, *Chem. Comm.*, 1971, 941.

[5] (a) R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 1970, 194; D. J. Barnes and R. P. Bell, *Proc. Roy. Soc. A*, 1970, **318**, 421; (b) F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, 1971, **93**, 512.

[6] R. P. Bell, *Discuss Faraday Soc.*, 1965, **39**, 16.

[7] R. P. Bell, W. H. Sachs, and R. L. Tranter, *Trans. Faraday Soc.*, 1971, **67**, 1995.

[8] R. P. Bell, 'The Proton in Chemistry,' Methuen, London, 1959, p. 211.

[9] M. E. Schneider and M. J. Stern, *J. Amer. Chem. Soc.*, 1972, **94**, 1517.

[10] F. G. Bordwell and W. J. Boyle, Jr., *J. Amer. Chem. Soc.*, 1971, **93**, 511.

[11] F. G. Bordwell, W. J. Boyle, Jr., and K. C. Yee, *J. Amer. Chem. Soc.*, 1970, **92**, 5926.

[12] (a) Refs. 2, 5 (b); M. H. Davies, personal communication; (c) N. H. Muderloh, M.S. Thesis, California State University, San Francisco, 1973.