Deuterium Kinetic Isotope Effects in β-Elimination from Phenethyl Bromide promoted by *para*-Substituted Sodium Phenoxides in Dimethylformamide

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Deuterium kinetic isotope effects have been measured for elimination from phenethyl bromide promoted by *para*-substituted sodium phenoxides in dimethylformamide. Despite the large basicity range considered variations in the magnitude (in the range 7·6—9·0) of the isotope effects were practically within experimental error. Some evidence for proton tunnelling was obtained and this has made difficult a straightforward interpretation of the k_2^H/k_2^D values in terms of transition state geometry.

THE problem of the influence of the basicity of the nucleophile on the transition state structure of bimolecular β-eliminations is still a matter of controversy. When the three more important models, devised to rationalize the effects of structural changes in the transition state structure of *E*2 reactions, are examined, we find that each of these leads to a different prediction.

According to the theory of the variable transition state, as reviewed by Bunnett,[1] the bond which is more easily broken should exhibit the more extensive rupture in the transition state; thus, a stronger base is expected to favour a transition state of greater carbanionic character, as a consequence of a larger degree of C_β–H bond breaking. On the other hand, Thornton [2] has considered the effects exerted by structural changes along the reaction coordinate (parallel effects) or in a direction perpendicular to it (perpendicular effects). Parallel effects correspond closely to the predictions based on the Hammond postulate [3] while perpendicular effects are the opposite of these predictions. Thornton suggests that parallel effects are usually more important and, therefore, concludes that eliminations with a stronger base should be characterized by a more ' reactant-like ' transition state with less C_β–H bond rupture. Finally, More O'Ferrall [4] has discussed the effect of changes in the energy of reactants, products, and intermediates, that would be formed if the mechanism were not concerted, on the energy and structure of *E*2 transition state. The effects which increase the product stability are transmitted along the reaction coordinate, and operate by shifting the transition state structure towards that of the reactants; those increasing the stability of the intermediate, which are in contrast exerted in a direction perpendicular to the reaction coordinate, shift the transition state structure towards that of the intermediate itself.

Thus, a strong base, which stabilizes both the product and the carbanion, will have effects on the transition state structure which are complementary for C_α-leaving group bond breaking and opposite for C_β–H bond rupture. The resulting effect to be expected is a decrease in the extent of C_α–leaving group bond breaking whereas the degree of C_β–H bond rupture undergoes a small increase or decrease.

Unfortunately, despite the enormous amount of work on the mechanism of *E*2 elimination, no clear choice among the above theories has been possible so far. One reason is that in most of the studies the change in base has been accompanied by a change in solvent, thus making the results difficult to interpret.

Recently we investigated the kinetics of β-elimination from *p*-substituted phenethyl bromides induced by sodium phenoxide and *p*-nitrophenoxide in *NN*-dimethylformamide (DMF) [5] and observed that the ρ value for the reaction with sodium phenoxide (+2·64) is significantly larger than that (+1·84) for the reaction with sodium *p*-nitrophenoxide. Thus, it may be concluded that, at least in this system, the stronger base produces a transition state with greater carbanionic character.

However, in a reaction such as an *E*2 elimination, where two bonds are formed and two bonds are broken in concert, an increase in the carbanionic character of the transition state may occur in several ways; for example, it may be the consequence of an *increase* in the extent of the C_β–H bond breaking whereas the degree of formation or breaking of the other bonds remains practically un-

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[1] J. F. Bunnett, *Angew. Chem. Internat. Edn.*, 1962, **1**, 225; *Survey Progr. Chem.*, 1969, 5.

[2] E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 2915; L. J. Steffa and E. R. Thornton, *ibid.*, p. 6149.

[3] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[4] R. A. More O'Ferrall, *J. Chem. Soc.* (*B*), 1970, 224.

[5] S. Alunni and E. Baciocchi, *Tetrahedron Letters*, 1973, 4665.

changed; alternatively, it may be determined by a *decrease* in the extent of C_α–leaving group bond breaking and, consequently in C=C double bond formation, whereas negligible or less important variations take place in the degree of C_β–H bond breaking.

To acquire information on this problem we have determined the deuterium kinetic isotope effect for elimination from phenethyl bromide promoted by some *para*-substituted sodium phenoxides in DMF. Even if the interpretation of the deuterium kinetic isotope effect in terms of transition state geometry may sometimes be uncertain,[6-9] the results give, in several cases, important insight to the extent of C–H bond breaking in the transition state of reactions involving proton transfer, especially when, as in the present case, there is a continuous change in the nature of one of the reactants.

TABLE 1

Rate constants for the reaction of phenethyl bromide with sodium phenoxide in DMF

In the absence of $NaClO_4$ at 0° [a]			In the presence of 0·85M-$NaClO_4$ at 21° [b]		
t/s	Reaction (%)	k_2^E/l mol^{-1} s^{-1}	t/s	Reaction (%)	$10^2k_2^E$/l mol^{-1} s^{-1}
40	36·0	0·204	135	21·8	1·11
75	54·5	0·192	250	37·5	1·14
120	67·8	0·183	398	51·8	1·12
160	75·2	0·159	570	62·8	1·07
			875	78·6	1·08

[a] PhONa] 0·054M; [substrate] 0·0048M. [b] [PhONa] 0·15M; [substrate] 0·0139M.

TABLE 2

Rate constants and deuterium kinetic isotope effect for the elimination reaction of $PhCX_2CH_2Br$ induced by *para*-substituted phenoxides in DMF

Nucleophile	X	Temp. (°C)	$10^3k_2^E$/ l mol^{-1} s^{-1}	Olefin Yield (%)	k_2^H/k_2^D	A_H/A_D
Sodium phenoxide [a]	H	21	10·97	92·2	7·6 ± 0·7	
	D	21	1·44	52·8		
Sodium *p*-chlorophenoxide [b]	H	21	4·35	87·8	7·8 ± 0·4	
	D	21	0·56	51·4		
Sodium *p*-nitrophenoxide [c]	H	21	0·058	59·0	9·0 ± 0·6	
	D	21	0·00646	14·5		
	H	41	0·33	55·0	7·0 ± 0·5	0·17
	D	41	0·047	14·6		

[a] [PhONa] 0·15M; [$NaClO_4$] 0·85M. [b] [p-ClC_6H_4ONa] 0·17M; [$NaClO_4$] 0·8M. [c] [p-$NO_2C_6H_4ONa$] 0·45M.

RESULTS AND DISCUSSION

The kinetics of the reaction with sodium phenoxide and *p*-chlorophenoxide was complicated by the fact that these salts are not completely dissociated in DMF.[10] Accordingly, we found that the second-order rate constant k_2 decreases significantly with the progress of the reaction and increasing the initial concentration of the nucleophile. The phenomenon is due to ion association as is shown by the fact that in the presence of an excess of $NaClO_4$, which acts as a buffer on the concentration ratio dissociated ion : ion-pair, the kinetics followed a regular second-order pattern. Some representative results obtained with sodium phenoxide are reported in Table 1. As expected, a significant decrease in rate was also observed, since $NaClO_4$ should reduce the concentration of dissociated ions which are, probably, the only active nucleophiles in the reaction medium. This follows from observations by Brändström [11] on reactions of sodium phenoxide in alcohols and by the fact that the sensitivity of the reaction to substituent effects is practically the same as that measured in the absence of sodium perchlorate, when the temperature effect is allowed for,* and in the presence of crown ether.[5] Thus, rate constants for the reactions with sodium phenoxide and *p*-chlorophenoxide were determined in the presence of sodium perchlorate.

The effect of ion-pairing was less evident when sodium *p*-nitrophenoxide was the nucleophile. Accordingly, on using a large excess of nucleophile, first-order plots were obtained up to 70% reaction. However, some decrease in the second-order rate constant as the concentration of the nucleophile increases was observed. Buffering with $NaClO_4$ was, in this case, of less value owing to the high sodium *p*-nitrophenoxide concentrations used. In this case all the kinetics were carried out at the same sodium *p*-nitrophenoxide concentration (*ca.* 0·5M).

The rate constants for elimination from phenethyl and β-phenyl-β-dideuterioethyl bromide on treatment with sodium phenoxide, *p*-chlorophenoxide, and *p*-nitrophenoxide at 21° are reported in Table 2 together with the calculated values of the deuterium kinetic isotope effect k_2^H/k_2^D. In the case of the reaction with sodium *p*-nitrophenoxide k_2^H/k_2^D was also measured at 41°.

Though the three nucleophiles cover a basicity range of *ca.* 10^6,[12] we observe that the values of k_2^H/k_2^D are practically constant within experimental error. The

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* The reactivity ratio k_H/k_{OCH_3} is 4·2 at 0° in the absence of $NaClO_4$ and 3·4 at 21° in the presence of $NaClO_4$.

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[7] F. G. Bordwell and W. G. Boyle, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 562.

[8] L. F. Blackwell, P. D. Buckley, K. W. Jolley, and A. K. H. MacGibbon, *J.C.S. Perkin II*, 1973, 169.

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

[10] A. Berge and J. Ugelstad, *Acta Chem. Scand.*, 1965, **19**, 742.

[11] A. Brändström, *Arkiv. Kemi*, 1957, **11**, 567.

[12] C. D. Ritchie in ' Solute–Solvent Interaction,' eds. J. F. Coetzee and C. D. Ritchie, Dekker, New York and London, 1969, p. 224.

more obvious conclusion, therefore, is that in elimination from phenethyl bromide the extent of C_β–H bond breaking in the transition state is not dependent on the basicity of the nucleophile; as a consequence, the increase in ρ observed in passing from sodium *p*-nitrophenoxide to phenoxide should be mainly caused by a decrease in C_α–bromine bond breaking in the reaction with the stronger base. Interestingly, this conclusion is in agreement with the predictions of the More O'Ferrall model [4] for the transition state of *E*2 eliminations.

Unfortunately, the possible presence of a quantum mechanical tunnelling effect may require this conclusion to be modified. The values of k_2^H/k_2^D (Table 2) are larger than the theoretical estimates and this is some evidence of proton tunnelling. Moreover, we have determined the temperature dependence of the kinetic isotope effect for elimination promoted by sodium *p*-nitrophenoxide (which exhibits the largest effect) and found a value of A_H/A_D (0·17) which is significantly smaller than that expected in the absence of tunnelling.[13] Even though this value is subject to a large uncertainty, because k_2^H/k_2^D values are also influenced by errors in measuring the yield of olefin, this is an important indication of the presence of tunnelling in our system. Clearly, if tunnelling is present the interpretation of the values of the deuterium kinetic isotope effect becomes more difficult.

Saunders and Cockerill,[14] and More O'Ferrall [15] suggest that tunnelling should not necessarily preclude the interpretation of k_2^H/k_2^D values in terms of transition state geometry. The above conclusions could therefore still be valid, even if tunnelling is present. However, a different view is that of Wolfsberg and Willi [16] who predict that, in the presence of tunnelling, k_2^H/k_2^D will remain practically unchanged, at about the maximum value, for a wide range of proton transfer from substrate to base.

In this respect it is noteworthy that in the elimination from substituted phenethyl bromides k_2^H/k_2^D is virtually insensitive to changes in the nature of base, solvent, and substrate structure. Accordingly, k_2^H/k_2^D values very similar to those reported here were found in the elimination from substituted phenethyl bromides for a large variety of conditions (Bu^tOK–Bu^tOH,[17] EtONa–EtOH,[17] Bu^tOK–Bu^tOH–DMSO [18]) and no significant variation in k_2^H/k_2^D was observed upon the introduction of *para*-substituents in the phenyl ring.[8] Clearcut evidence for the presence of tunnelling was obtained for reactions in Bu^tOK–Bu^tOH.[8]

Undoubtedly, the constancy of k_2^H/k_2^D values in elimination from substituted phenethyl bromides could simply indicate that in this system (characterized by the presence of a good leaving group such as bromine) the degree of C_β–H bond breaking is not significantly influenced by structural changes, but could also be considered, following Wolfsberg and Willi, as the consequence of tunnelling contributions to the deuterium kinetic isotope effect.

Another point of interest is that elimination from phenethyl'onium salts [19-22] proceeds differently from elimination from substituted phenethyl bromides; thus, in the former reaction k_2^H/k_2^D is sensitive to substrate structure and reaction conditions. Moreover, in eliminations from phenethyl'onium salts a change to a stronger base produces a transition state with less C_β–H bond breaking.* These findings may be due to the fact that tunnelling is not present in elimination from phenethyl'onium salts; [21] however, they could also be related to the fact that charged groups are poorer leaving groups than bromine. As suggested recently,[22] the relative role of parallel and perpendicular effects (which oppose each other in determining transition state geometry) may depend upon the degree of the carbanionic character of the transition state and therefore upon the nature of the leaving group. When, as in the elimination from phenethyl'onium salts, the transition state has much carbanionic character, parallel effects prevail and a change to a stronger base may lead to a more ' reactant-like ' transition state with less C_β–H bond breaking. In contrast, when elimination occurs *via* a more ' central ' transition state, as should be the case for phenethyl bromide, perpendicular effects balance parallel effects and the extent of C_β–H bond breaking in the transition state may not be significantly influenced.

In conclusion, it appears that the k_2^H/k_2^D values obtained in the present study cannot be interpreted in a straightforward way and that, therefore, it is not possible to draw from these values, as hoped, definitive conclusions on the problem of the effect of nucleophile basicity on transition state structure in *E*2 reactions. Perhaps better information can be obtained by an investigation of leaving group kinetic isotope effects.

EXPERIMENTAL

Materials.—Phenethyl bromide was a redistilled commercial sample. Phen[2-$^2H_2$]ethyl bromide was prepared as described by Saunders and Edison.[17] The mass spectrum showed that the sample contained 1·92 atoms of deuterium per molecule. Sodium phenoxide and *p*-chlorophenoxide were prepared by treating phenol and *p*-chlorophenol, respectively, with equimolecular amounts of NaOH in water. Water was removed at reduced pressure and the residue recrystallized from dry acetone. Sodium *p*-nitrophenoxide was prepared from 4-nitrophenol and sodium methoxide in methanol using the same procedure.

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* It must be noted, however, that data in EtO^-–EtOH were compared with data in Bu^tO^-–Bu^tOH; thus, the change in base was also accompanied by a change in solvent.

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[22] P. J. Smith and A. N. Bourns, *Canad. J. Chem.*, 1974, **52**, 749.

Before use, phenoxides were kept at 100° and 1 mmHg for 90 min. DMF (Erba, R.P.) was stored over molecular sieves (B.D.H.; type 4M, 8—12 mesh beads), then distilled under nitrogen and at reduced pressure. Anhydrous sodium perchlorate was commercial (B.D.H.) and used without further purification.

Kinetics.—The formation of bromide ions was followed by potentiometric analysis with $AgNO_3$. The concentration of nucleophile was always *ca.* 10-fold larger than that of substrate.

Olefin Analysis.—The yield of styrene was determined by g.l.c. analysis (isopropylbenzene as internal standard) with an SE30 (2 m) column.

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