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ELIMINATION REACTIONS. SUBSTITUENT EFFECTS ON POSITIONS IN THE E2H-E2C SPECTRUM OF TRANSITION STATES

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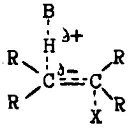
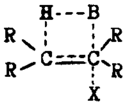
We are investigating the possibility that an E2H-E2C spectrum of transition state structures, II, which lie between the extreme structures I and III, can help to explain all existing observations on bimolecular elimination (E2) reactions (1-4).

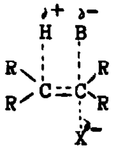


I

E2H



II



III

E2C

It seems likely that an E2 reaction of a particular substrate with RO$^-$, e.g. acetate, p-nitrophenoxide (OAr$^-$) or ethoxide, will always be *more* E2H-like than the corresponding E2 reaction with halide or mercaptide ions (RS$^-$), under the same conditions. The RO$^-$ species are very much *more* basic towards *hydrogen* than are Hal$^-$ or RS$^-$, (Table 2 and reference 5), whereas RO$^-$ species are only *slightly* more nucleophilic towards *carbon* than are halide ions and are often *less* C- nucleophilic than RS$^-$ (cf. Table 2). Reactions of different substrates with a particular base are expected to become more E2H-like as the acidity at β-hydrogen increases.

Rates of E2H reactions should obey the Brönsted relationship and correlate with H-basicity, whereas rates of E2C reactions should correlate with C- nucleophilicity (1). Most E2 reactions exhibit behaviour between these extremes. Structure I has the partial double bond less developed than in the E2C transition state, III, and rates of E2H reactions will depend on the acidity of the substrate at the β-hydrogen, i.e. on the electronic effect of substituents at Cβ. On the other hand, there is very little negative charge at Cβ in the E2C transition state, III, so that rates of E2C reactions do not respond to changes in acidity at β-hydrogen. Thus the free energy of the E2C transition state is not necessarily lowered by electron-withdrawing substituents, although, because of interactions with the well-developed double bond in the transition state, $\Delta G^{\ddagger}$ is decreased by groups like methyl, phenyl and CO_2Me (6). A steric factor should also be considered when evaluating substituent effects at Cβ in an E2C reaction. Non-bonding interactions between bulky groups at Cβ decrease as hybridisation at Cβ changes from Sp^3 in reactant to well advanced Sp^2 in the transition state, so that replacement of hydrogen by any other substituent should exert an accelerating effect on the E2C reaction.

Rate constants (k^E M^{-1} sec^{-1}) for formation of the Saytzeff olefin by an E2 <u>trans</u> elimination are in Tables 1 and 2. Analysis by vpc showed that this was >95% of the initial elimination product and that competition by Hofmann elimination and by <u>cis</u>-elimination, as well as elimination from substitution products, accounts for less than 5% of the olefins. These interesting minor reactions (6) will not be discussed here. The solvolysis in acetone containing excess 2,6-lutidine (1) was always < 1% of the slowest E2 reaction.

Values of k^E, for reactions of a series of substrates of increasing acidity, increase much more when the base is acetate rather than chloride ion in acetone (Table 1). The rate difference log $k^E(OAc)/k^E(Cl)$ is very much greater for elimination from <u>erythro</u>-methyl-2,3-dibromobutanoate, which has electron-withdrawing Br and CO_2Me β-substituents, than for elimination from 2-bromo-3-methylbutane, which has two electron-donating methyl substituents at Cβ. As expected, the difference is due to a strong increase in the rate of the acetate (more E2H-like) reaction rather than to any substantial change in the rate of the chloride reaction.

The reactions of 2-bromo-3-methylbutane (Table 1) are more E2C-like than those of the more acidic <u>dl</u>-2,3-dibromobutane, as shown by the closer correspondence between Δlog k^E with the former substrate and Δlog k^S for related S_N2 reactions (1).

There is a substantial increase in the rate of the E2C-like reaction of chloride ion in acetone when the β-substituents are changed from two hydrogens in 2-bromopropane to either two electron-donating methyl groups in 2-bromo-3-methylbutane or to the electron-withdrawing bromine and CO_2Me groups in <u>erythro</u>-methyl-2,3-dibromobutanoate. This "Saytzeff" substituent effect (6) is clearly not related to the acidity of the substrate, but may be an example of steric acceleration and or stabilization of the developing double bond, as anticipated above.

The rate data in Table 2 for reactions of cyclohexyl bromide and <u>cis</u>-1,2-dibromocyclohexane show much the same trends. An acidifying bromine substituent, which is <u>cis</u> and β- to the leaving group, has a much greater effect on the rate of the more E2H-like reactions of OEt$^-$ in ethanol and of OAc$^-$ and OAr$^-$ in acetone than it has on the rates of the more E2C-like reactions of Cl$^-$ and p-nitrothiophenoxide (SAr$^-$) in acetone. Azide ion shows intermediate behaviour. A rough Bronsted correlation between log k^E and pK_a emerges for E2 reactions of cis-1,2-dibromocyclohexane, if a Brönsted coefficient of ca. 0.3 can be accepted, but the more E2C-like reactions of cyclohexyl bromide give no indication of a Brönsted correlation, nor is there a satisfactory correlation between log k^E and log k^S (1). The E2 reactions of cyclohexyl bromide are less E2C-like than those of cyclohexyl tosylate (1).

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TABLE 1

Rates (log k)^a of S_N2 and E2 Reactions of RR'CH-CH(Br)$\cdot$CH$_3$ with B$^-$ to give RR'CH$\cdot$CH(B)$\cdot$CH$_3$ and RR'C=CH$\cdot$CH$_3$ in Acetone^b at 50°C.

R	R'	NBu$_4$Cl^b	NBu$_4$OAc^b	log k(OAc)/k(Cl)	Reaction
H	H	-2.7^c	-1.7^c	+1.0	S_N2
CH$_3$	CH$_3$	-3.32	-2.89	+0.43	S_N2
H	H	$<-4.7^c$	$<-3.7^c$	-	E2
CH$_3$	CH$_3$	-3.31	-1.97	+1.34	E2
CH$_3$	Br^d	-3.8^d	$-0.8^{d,f}$	+3.0	E2
CO$_2$Me	Br^e	-2.60^e	$+3.88^{e,f}$	+6.48	E2

(a) k in M^{-1} sec.$^{-1}$ (b) Acetone containing 0.05M 2,6-lutidine, NBu$_4$Cl at 0.035M, NBu$_4$OAc at 0.050M. (c) No propene (detection limit <1%) was detected by v.p.c. in the products of these S_N2 reactions. (d) d,l-2,3-dibromobutane gave >95% 2-bromo-trans-2-butene as the elimination product. There has been no statistical correction of log k for the two equivalent bromines. (e) erythro-methyl-2,3-dibromobutanoate (crotonate) gave >98% methyl-2-bromo-cis-but-2-enoate. (f) Rate constants extrapolated from measurements at lower temperatures.

TABLE 2

Rates of S_N2 (k^S M^{-1} sec^{-1}) and E2[a] Reactions of cis-2-R-bromocyclohexane in Acetone[b] at 76.4°C

R		NBu_4Cl	NBu_4SAr[c]	NBu_4N_3	NBu_4OAr[c]	NBu_4OAc	NaOEt[d]
H	log k^S	-3.50	-3.03	-2.21	-3.93	-2.88	-5.14
	Δ log k^S	0.00	+0.47	+1.29	-0.43	+0.62	-1.64
H	log k^E	-3.27	-3.34	-2.84	-3.14	-2.01	-2.98
	Δ log k^E	0.00	-0.07	+0.43	+0.13	+1.26	+0.29
Br	log k^E	-2.84	-2.23	-1.50	-1.04	+0.14	-0.70
	Δ log k^E	0.00	+0.61	+1.34	+1.80	+2.98	+2.14
Δ pK_a (HB-HCl)[e]		0.0	1.9	5.1	8	9	-

(a) The E2 product is >99% 1-R-cyclohexene by v.p.c. (b) Acetone contained 0.06M 2,6 lutidine, electrolytes were at 0.05 ± 0.004M. (c) Ar is 4-nitrophenyl. (d) In ethanol, unpublished work by D. Lloyd. (e) Reference 5.

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