Tetrahedron Letters No.50, pp. 5183-5188, 1968. Pergamon Press. Printed in Great Britain.

ELIMINATION REACTIONS. LEAVING GROUP TENDENCIES IN E2C, E2H AND S_N2 REACTIONS

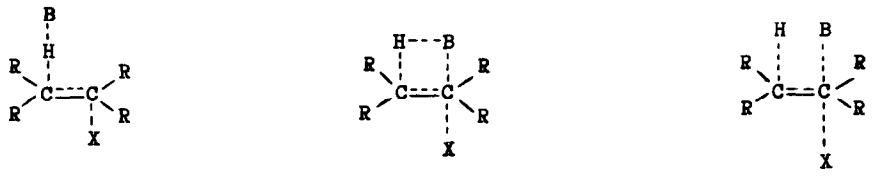
D.J. Lloyd and A.J. Parker

Department of Organic Chemistry, University of Western Australia,

Nedlands, Western Australia

(Received in UK 2 September 1968; accepted for publication 16 September 1968)

This communication deals with another aspect of the question, do bimolecular elimination reactions proceed through a spectrum of transition states II, which lie between the extreme structures I (for E2H reactions) and III (for E2C reactions) (1-4)?



I
E2H

II

III
E2C

Rates of the E2C-like reactions, but <u>not</u> rates of the E2H-like reactions of cyclohexyl-bromide and tosylate, respond in much the same way to solvent transfer as do the concurrent S_N2 reactions, which take place from the same reactant free energy level (2,3). Rates of the E2C-like reactions, but <u>not</u> rates of the E2H-like reactions of cyclohexyl tosylate, respond in much the same way to the carbon nucleophilicity of the base B, as do the concurrent S_N2 reactions (1) We now examine the effect of a further variable, the leaving group X, on the relative free energies of S_N2, E2C-like and E2H-like transition states.

We classify E2 reactions of chloride or mercaptide ions as E2C-like, because these are strong carbon but relatively weak hydrogen bases. Conversely, E2 reactions of alkoxides are classified as E2H-like, because these are strong hydrogen bases (1). There are often linear free energy relationships between leaving group tendencies, $\delta_X \log k^S$, in various S_N2 reactions at a saturated carbon atom (5) (e.g. Figure 1). The relationships are most satisfactory when

the transition states being compared are of much the same degree of tightness or looseness (2,3,6). For this condition to hold, then, among other things, the solvent should be of the same type, e.g. protic or dipolar aprotic and the reaction centre should have much the same pattern of substitution, e.g. primary carbon, secondary carbon, tertiary carbon, or benzylic carbon (2,3,6). In such situations, the behaviour shown in Figure 1 is not unusual although tosylate does not always correlate as well as shown there (6).

There is also an excellent linear correlation shown in Figure 2 between $\delta_X \log k^E$ for the E2C-like reactions and $\delta_X \log k^S$ for the concurrent S_N2 reactions of cyclohexyl derivatives with chloride ion in DMF. Thus the effect of the leaving group on rate, $\delta_X (\log k)_{S,B}$ can be included with the effect of solvent, (2), $\delta_S (\log k)_{B,X,}$ and the effect of base (1), $\delta_B (\log k)_{S,X,}$ as factors which support the concept of an E2C-like transition state, having much the same type of bonding and charge distribution between Y, C_α, and X, as is present in the concurrent S_N2 transition state.

There is <u>not</u> a linear relationship between $\delta_X \log k^E$ for E2H-like reactions and $\delta_X \log k$ for the concurrent S_N2 reactions of ethyl X derivatives with sodium ethoxide in ethanol, as seen in Figure 3. This suggests that there is a difference in the bonding between C_α and X in these E2H-like and S_N2 transition states. It follows that there is a difference in the bonding between C_α and X in the E2H-like and the E2C-like transition states.

We expect and do not attach a great deal of significance to linear relationships between leaving group tendencies within a series where the halogens are the only leaving groups. However Hoffman has shown (7-9) that the relative rates of displacement of tosylate and bromide, are a sensitive probe into the nature of bonding between C_α and X, in E2 and S_N2 transition states.

It seems that "loose" transition states often have high k^{OTS}/k^{Br} rate ratios, whereas "tight" transition states often have low k^{OTS}/k_{Br} rate ratios (6). A recent study of solvent effects on rate (2) has suggested that E2H-like transition states are tighter than E2C-like or S_N2 transition states, but that the latter two are of a similar degree of looseness for reactions of the same substrate. If this is so, we would expect to find similar values of $\log k^{OTS}/k^{Br}$, for S_N2 and their concurrent E2C-like reactions and these would be more positive than $\log k^{OTS}/k_{Br}$, for related E2H-like reactions. This expectation is confirmed by the data in Table 1.

TABLE 1

Leaving Group Tendencies of Tosylate and Bromide in S_N2, E2C and E2H Reactions

Reactants[a]	T°C	Solvent	log k (OTS) - log k (Br)[b] S_N2	E2C-like	Int.	E2H-like[d]	$\delta(S_N2 - E2)$[c]
Cyclohex X + SAr^-[e]	75°	Me_2CO	0.00	0.41	-	-	-0.41
Cyclohex X + Cl^-[f]	75°	Me_2CO	0.78	0.97	-	-	-0.19
Cyclohex X + PhS^-[g]	55°	EtOH	0.79	0.69	-	-	+0.10
Cyclohex X + SAr^-[g]	55°	EtOH	1.06	0.95	-	-	+0.11
Cyclohex X + N_3^-[h]	75°	Me_2CO	0.48	-	0.13	-	+0.35
Cyclohex X + OAc^-[e]	75°	Me_2CO	0.70	-	0.12	-	+0.58
Cyclohex X + OAr^-[e]	75°	Me_2CO	0.53	-	-0.26	-	+0.79
Cyclohex X + OEt^-[f]	75°	EtOH	1.28	-	-	0.00	+1.28
Cyclohex X + OBu^t-[f]	75°	t-BuOH	>1.6	-	-	0.38	>+1.2
$CH_3CH_2CH_2X + OEt^-$[i]	55°	EtOH	0.57	-	-	-1.10	+1.67
$CH_3CH_2CH_2X + OBu^t$-[i]	40°	t-BuOH	1.04	-	-	-0.80	+1.84
$(CH_3)_2CHX + OEt^-$[i]	55°	EtOH	1.08	-	-	-0.05	+1.13
$(CH_3)_2CH-\underset{X}{CH}-CH_3 + Cl^-$[j]	50°	Me_2CO	0.25	0.24	-	-	+0.01
$PhCH_2CH_2X + OEt^-$[i]	30°	EtOH	1.00	-	-	-1.00	+2.00

(a) Ar is 4-nitrophenyl. (b) i.e. log k for the reaction with X as tosylate minus log k for the same reaction with X as bromine. (c) i.e. log k (OTS) - log k (Br) for the S_N2 reaction minus log k (OTS) - log k (Br) for the E2 reaction. (d) Position in spectrum I - III move from like III to like I down the series of cyclohexyl X reactions. The classification is rough but is according to the principle outlined in the text. Reactions of azide, acetate and p-nitrophenoxide ion in acetone, with cyclohexyl bromide in particular, are more E2H-like than are reactions of chloride ion or p-nitrothiophenoxide in acetone, so are shown as having an intermediate mechanism, (Int.), but they are thought to be more E2C-like than E2H-like. (e) Data for cyclohexyl tosylate is from reference 1, that for cyclohexyl bromide is unpublished work by M. Ruane. (f) This work, rates were determined titrimetrically for acid and leaving group production or for entering group consumption. Product analysis by Vpc for elimination and substitution product. (g) D.J. McLennan, J. Chem. Soc. (B), 705 (1966). (h) Reference 1 and reference 3. (i) References 8 and 9. (j) G. Biale, A.J. Parker, I.D.R. Stevens, J. Takahashi and S. Winstein, Paper in preparation.

TABLE 2

S_N2 and E2C Reactions of Cyclohexyl X Compounds with NEt_4Cl in DMF at 75°C[a]

X	10^4k^{S+E} $M^{-1}sec^{-1}$	$100F_E$ Vpc[e]	H^+ [f]	10^4k^S $M^{-1}sec^{-1}$	10^4k^E $M^{-1}sec^{-1}$
Cl	-	50[i]	-	0.41[b,d]	0.42[b,c]
Br	13.70[g]	55	54	6.16	7.54
I	362 [g]	66	68	114	248
OTS	47.5[g]	70	70	14.3	33.2
SMe_2I	3.97[g,h]	69	-	1.24	2.73

(a) [cyclohexyl X] = 0.02M; [NEt_4Cl] = 0.04M. (b) At 100.0°C. (c) Rate of elimination from $\frac{dH^+}{dt}$. (d) Rate of substitution from rate of exchange, using Cl^{36}. (e) Products analysed by Vpc for cyclohexene and cyclohexyl chloride. (f) Fraction of elimination calculated from acid produced, which was estimated by titration. (g) Total rate estimated from production of halide ion, consumption of chloride in the substitution process and production of acid in the elimination process. The substitution reaction consumes chloride ion but the elimination reaction does not and this is allowed for in the calculation of the rate constant. (h) Only 1% of the reaction between dimethylcyclohexyl sulphonium cation and chloride ion is S_N2 and E2 in the cyclohexyl system. About 99% of the reaction is S_N2 at methyl, but the 1% at cyclohexyl is easily detected by Vpc analysis for cyclohexene and cyclohexyl chloride. (i) Mixture analysed for cyclohexene at various stages of the exchange reaction.

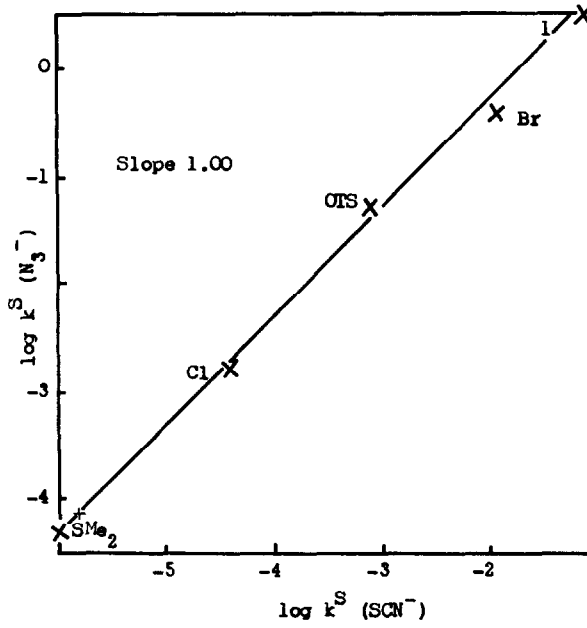


Fig. 1. Rates of S_N2 reactions of CH_3X compounds with azide ion versus rates with SCN^- in DMF at 25°. Data from Ref. 3.

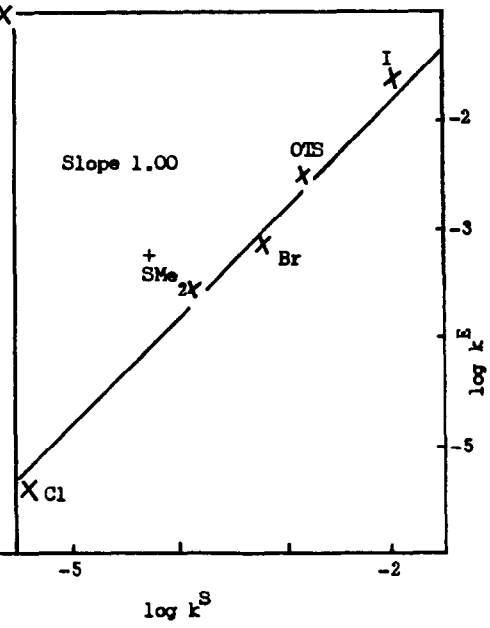


Fig. 2. Rates of E2C reactions versus rates of S_N2 reactions of cyclohexyl X compounds with chloride ion in DMF at 75°. This work. Cyclohexene and cyclohexyl chloride estimated by Vpc. The point for cyclohexyl chloride is extrapolated from measurements at 100° of the exchange rate and the rate of acid production. 99% of cyclohexyl $^+SMe_2$ reacts by S_N2 at methyl.

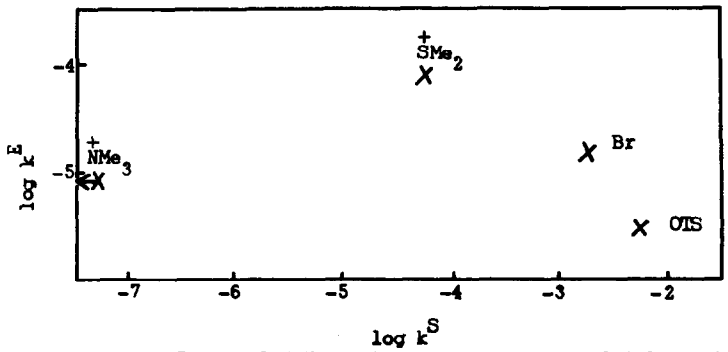


Fig. 3. Rates of E2H reactions versus rates of S_N2 reactions of ethyl X compounds with NaOEt at 55°C. Data from references 9 and 10. The point for $Et\overset{+}{N}Me_3$ is only approximate because log k^S is a maximum value, based on a negligible yield of EtOEt reported in reference 10. Data for this compound were extrapolated from measurements at 104.2°.

The behaviour towards cyclohexyl derivatives of the moderately strong hydrogen bases acetate and azide ion in acetone, is interesting. Reactions of these bases lead to values of $\log k^{OTS}/k_{Br}$ (S_N2) - $\log k^{OTS}/k_{Br}$ (E2) which are intermediate between the values for the strongly E2C-like bases, chloride and p-nitrothiophenoxide in acetone and those for the strongly E2H-like bases, ethoxide in ethanol and t-butoxide in t-butanol. The behaviour shown in Table 1 is consistent with a movement through the spectrum I to III from E2H-like to E2C-like in the order of bases, OBu^{t-}/t-BuOH; OEt^-/EtOH; $OC_6H_4NO_2^-/Me_2CO$; OAc^-/Me_2CO; N_3^-/Me_2CO; $C_6H_5S^-$/EtOH; Cl^-/Me_2CO; $4\text{-}NO_2C_6H_4S^-/Me_2CO$, in their reactions with cyclohexyl bromide and tosylate.

It cannot of course be claimed that the E2H-E2C spectrum is the only explanation for the results presented here, but as yet we have not made, nor have we heard of any observations on E2 reactions which cannot be explained in terms of this spectrum of transition states. Certainly E2 reactions promoted by strong carbon but weak hydrogen bases in dipolar aprotic solvents, have many features which distinguish them from the E2 reactions of the "classical" base systems, NaOEt in ethanol or $KOBu^t$ in t-butanol.

Acknowledgement: This research followed consideration of unpublished work by Professor S. Winstein and his co-workers. We thank him for helpful discussion and the opportunity to study that work.

REFERENCES

1. A.J. Parker, M. Ruane, G. Biale and S. Winstein, This Journal, 2113 (1968).
2. E.C.F. Ko and A.J. Parker, J. Am. Chem. Soc., 90, 000 (1968).
3. R. Alexander, E.C.F. Ko, A.J. Parker and T.J. Broxton, J. Am. Chem. Soc., 90, 000 (1968).
4. J. Csapilla, Chimia (Swiss), 18, 37 (1964); N.H. Cromwell, et al, J. Am. Chem. Soc., 79 230 (1957); 80, 901 (1958); 88, 4489 (1966); E.L. Eliel and R.S. Ro, Tetrahedron, 2, 353 (1958).
5. R.E. Davis, J. Am. Chem. Soc., 87, 3010 (1965).
6. A.J. Parker, Chem. Revs., 69, 000 (1969).
7. H.M.R. Hoffman, J. Chem. Soc., 6753, 6762 (1965).
8. G.M. Fraser and H.M.R. Hoffman, J. Chem. Soc. (B), 265 (1967).
9. G.M. Fraser and H.M.R. Hoffman, J. Chem. Soc. (B), 425 (1967).
10. D.V. Banthorpe, E.D. Hughes, and C.K. Ingold, J. Chem. Soc., 4054 (1960).