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# ELIMINATION REACTIONS. THE E2C MECHANISM[1]

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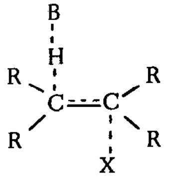
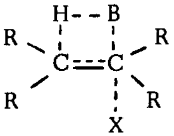
This Communication deals with an aspect of the question, do bimolecular elimination reactions proceed through transition states like I, like III, or through a spectrum of transition states, II, which can be E2H-like or E2C-like in different circumstances? The terms, E2H and E2C, signify attack at $\beta$-hydrogen and $\alpha$-carbon, respectively, in E2 reactions. An extreme form of E2C mechanism, involving an intermediate common to $S_N2$ substitution and E2 elimination, was suggested some time ago for certain elimination reactions.[2a, b] However, this extreme mechanism was disproved in certain test cases, elimination and substitution being shown to be independent processes.[2c]



I

E2H



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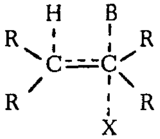


III

E2C

In considering criteria for the nature of E2 transition states, one would suppose that rate constants, $k^E$, for elimination via E2H transition states should show at least some correlation with the H-nucleophilicity of B.[3] In general, H-nucleophilicity, a kinetic property, is related to H-basicity, a thermodynamic property, through the Brönsted equation.[4] Therefore, one expects that $k^E$ for reaction of a variety of bases with any one substrate will fit the Brönsted relationship (1)[5] if such eliminations proceed through an E2H transition state. Some deviations from this equation[4a] would be expected, but the general trend should be clear.

$$\log k^E = \beta pK_a + \text{constant} \qquad (1)$$

If the E2 transition state has a partial bond between B and the $\alpha$-carbon atom of the substrate as in III, then we would expect $k^E$ to depend on the C-nucleophilicity[7] of B. Following Swain and Scott[4b, 8] we would anticipate for a variety of bases in the same solvent, that there would be a linear free energy relationship (2) between $k^E$ for eliminations proceeding through III and the rates, $k^S$, of $S_N2$ reactions with a model compound. Ideally, the substrates for the $E_2$ and $S_N2$ reactions should be as similar as possible.

$$\log k^E = S \log k^S + \text{constant} \qquad (2)$$

The bimolecular reactions of cyclohexyl tosylate with bases are admirably suited to test equations (1) and (2). Both E2 and $S_N2$ reactions are observed and each process usually accounts for 20-80% of the total reaction. Elimination and substitution take place, of course, from the same ground state free energy level, so that for reaction with any one base, the ratio of cyclohexene to substitution product reflects only the difference in free energy of the $S_N2$ and E2 transition states. Clearly the $S_N2$ reactions of cyclohexyl tosylate are the best model reactions for testing equation (2), as it applies to E2 reactions of cyclohexyl tosylate.

Elimination rates were determined from the rate of acid production and substitution rates were measured by the loss of base. Yields of cyclohexene, by v.p.c. analysis, agreed with the proportion of elimination, estimated from acid formation, for reaction of $Bu_4NCl$, $Bu_4NN_3$ and $Bu_4NSC_6H_4NO_2$-p with cyclohexyl tosylate in acetone containing an excess of 2,6-lutidine at 75°. Blank v.p.c. measurements showed that, over five half lives of elimination, hydrazoic, hydrochloric and acetic acid and 4-nitrothiophenol do not add to cyclohexene in acetone containing $Bu_4NOTs$ and 2,6-lutidine at 75°. The rate data are summarized in Table I.

A Brönsted plot of rates of elimination from cyclohexyl tosylate in acetone at 75° versus $pK_a$ of the appropriate acid in DMF[6] at 25° is shown in Figure 1. We do not have values for the $pK_a$ of acids in acetone, but there is an excellent linear correlation (3) of $pK_a$ in DMF with $pK_a$ in other dipolar aprotic solvents such as DMSO and acetonitrile.[6, 9] Since acetone is also a dipolar aprotic solvent,[10] one can be confident that (4) is valid. It follows that equation (5) provides an accurate assessment of the linearity of equation (1) for E2 reactions in acetone.

$$pK_a\ (\text{DMF}) = pK_a\ (\text{dipolar aprotic}) + \text{constant} \qquad (3)$$

$$pK_a\ (\text{DMF}) = pK_a\ (\text{acetone}) + \text{constant} \qquad (4)$$

$$\log K^E\ (\text{acetone}) = \beta pK_a\ (\text{DMF}) + \text{constant} \qquad (5)$$

It is clear from Figure 1 that there is absolutely no correlation between rates of E2 reactions of cyclohexyl tosylate and the H-basicity of the base. While it seems conceivable that

TABLE I

Rates of Substitution ($k^S$) and Elimination ($k^E$) in Reactions of Cyclohexyl Tosylate in Acetone at 75.0°

| $10^2$M [ROTs] | Salt | $10^2$M [Salt] | $10^2$M [Lut]$^a$ | $10^2F_E{}^b$ | $10^3k_2{}^c$ $M^{-1}$ sec$^{-1}$ | $10^3k^S$ $M^{-1}$sec$^{-1}$ | $10^3k^E$ $M^{-1}$sec$^{-1}$ |
|---|---|---|---|---|---|---|---|
| 1.99 | | - | 3.396 | - | $5.6 \times 10^{-3d}$ | - | - |
| 1.99 | $LiClO_4$ | 3.264 | 3.378 | - | $1.8 \times 10^{-2d}$ | - | - |
| 1.99 | $Bu_4NCl$ | 3.701 | 3.410 | 72.3 | 7.40 | 2.05 | 5.35 |
| 1.99 | $Bu_4NBr$ | 4.133 | 3.469 | 61.6 | 1.76 | 0.68 | 1.08 |
| 4.03 | $Bu_4NN_3$ | 2.42 | - | 9.6 | 22.1 | 20.0 | 2.1 |
| 2.15 | $Bu_4NN_3$ | 4.61 | 4.20 | 9.6 | 22.1 | 20.0 | 2.1 |
| 6.30 | $Bu_4NOC_6H_4NO_2$-p | 4.11 | - | 50.0 | 0.86 | 0.43 | 0.43 |
| 6.38 | $Bu_4NSC_6H_4NO_2$-p | 2.90 | - | - | 2.54 | - | - |
| 1.64 | $Bu_4NSC_6H_4NO_2$-p | 5.75 | - | $56^e$ | 2.23 | 0.98 | 1.25 |
| 3.17 | $Bu_4NOAc$ | 5.65 | - | 66 | 21.0 | 7.1 | 13.9 |
| 2.33 | $Bu_4NOAc$ | 4.42 | 4.04 | - | - | - | $12.7^f$ |
| 1.89 | $Bu_4NI$ | 3.98 | 3.71 | $-^g$ | $6.8 \times 10^{-2}$ | $<0.068$ | $<0.068$ |
| 2.01 | $KOBu^{t\ h}$ | 3.75 | 3.00 | $>99$ | $0.60^h$ | $<0.006$ | $0.60^h$ |
| 2.09 | $Bu_4NSC_6H_4NO_2$-$p^i$ | 4.46 | - | $60^i$ | $4.82^i$ | $1.93^i$ | $2.89^i$ |

(a) 2,6-lutidine, added to prevent addition of HB to cyclohexene, does not influence the rate of reaction. Ref. 16. (b) $F_E$ = fraction of total $S_N2$ and E2 reaction which gives acid. (c) $k_2 = k^S + k^E$. (d) Initial rate of acid production by solvolysis, expressed as a second order rate "constant" for attack by a hypothetical 0.03M reagent. This allows ready comparison of solvolysis, E2 and $S_N2$ rates. (e) $F_E$ determined in presence of 0.10 M lutidine. (f) Rate of acid production calculated on 66% of theoretical infinity. (g) The substitution product, cyclohexyl iodide, is solvolyzed more rapidly than cyclohexyl tosylate, so that the $S_N2$ reaction cannot be measured. (h) Solvent t-butanol. Rate constant is for loss of base but reaction gives >99% cyclohexene by v.p.c. (i) Solvent methanol.

Fig 1 - Bronsted Plot of Elimination Rates for Cyclohexyl Tosylate

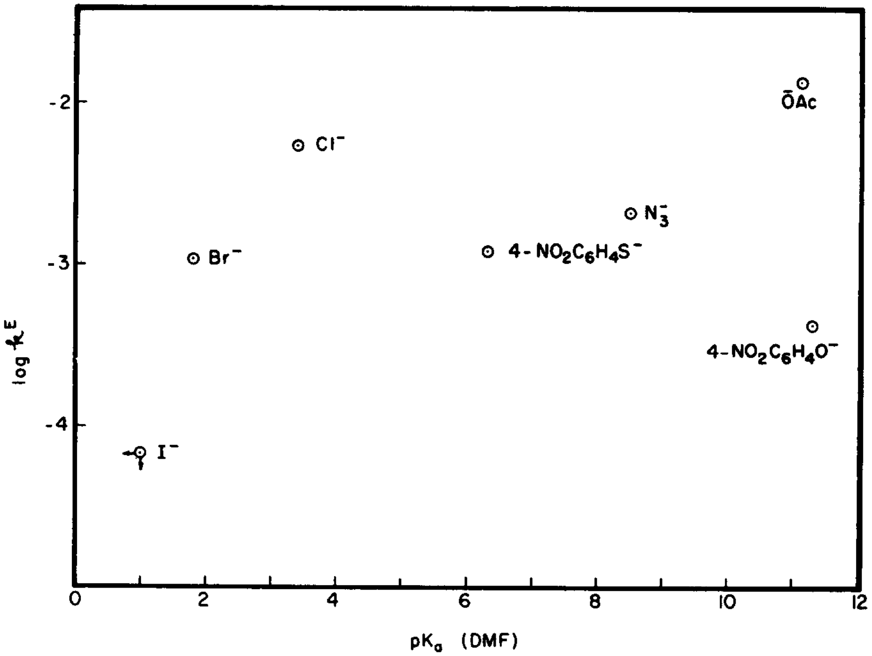
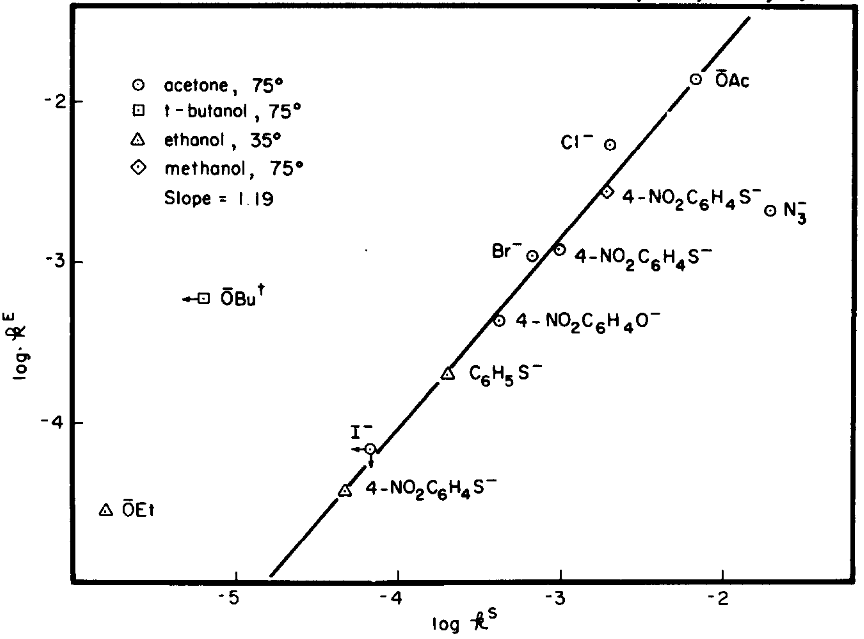


Fig 2 - Plot of Elimination vs. Substitution Rates for Cyclohexyl Tosylate



the correlation of H-nucleophilicity with H-basicity could turn out to be this poor, it seems more likely that $k^E$ for the E2 reactions in acetone does not depend mainly on the H-nucleophilicity of the base; also, that these E2 reactions do not proceed through a transition state like I, involving attack only at β-hydrogen.

A plot of rates of elimination from cyclohexyl tosylate versus rates of $S_N2$ substitution in cyclohexyl tosylate at 75° in acetone and in methanol is in Figure 2. Rate data for reactions of bases in ethanol with cyclohexyl tosylate at 35° are included.[11] Equation (2) is followed and the slope is close to unity, suggesting that the E2 transition state is responding to C-nucleophilicity in a very similar fashion to the $S_N2$ transition state.

Serious deviations from equation (2) occur for reactions of NaOEt in ethanol at 35°, of $KOBu^t$ in t-butanol at 75° and of $Bu_4NN_3$ in acetone at 75°. The alkoxides are very strong H-nucleophiles, but relatively weak C-nucleophiles.[4b] They cause elimination much more rapidly than expected from their rates in $S_N2$ reactions. Presumably they can utilize an E2H transition state, I, or an E2H-like transition state, II. Azide ion is considerably less effective at promoting elimination than is expected from its C-nucleophilicity. The linear azide ion is small and exhibits greatly enhanced nucleophilicity relative to halide ions when attacking carbon carrying some positive charge and/or sterically hindered carbon as in $S_NAr$ reactions and $S_N2$ reactions of neopentyl halides.[12, 13] The $S_N2$ transition state for reactions of cyclohexyl tosylate is thought to have a better developed $C_\alpha$-B bond with more positive charge on $C_\alpha$ than in the E2C transition state,[14] so that the special advantages of azide ion relative to other nucleophiles are utilized in the $S_N2$ transition state, but not in the E2C transition state.

The fact that many of the base systems promote E2 reactions at a rate which depends quantitatively on their C-nucleophilicity (Fig. 2) and also qualitatively on their ability to accept hydrogen bonds,[10, 15] but at a rate which has no correlation with H-basicity (Fig. 1), suggests that such E2 reactions proceed through a transition state II, which is much like III. We would describe this transition state as being E2C-like. The position of any one E2 transition state in the spectrum between I and III will depend on the structure of the substrate, the nature of the base and the nature of the leaving group.[14] An E2C-like transition state, II, also explains the marked preference for Saytzeff trans-elimination shown by E2 reactions of halide ions in acetone.[2c, 16]

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