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A PERTURBATIONAL INTERPRETATION OF ENOLATE ALKYLATION: C/O SELECTIVITY AND ELECTROPHILE LEAVING GROUP EFFECT.≠

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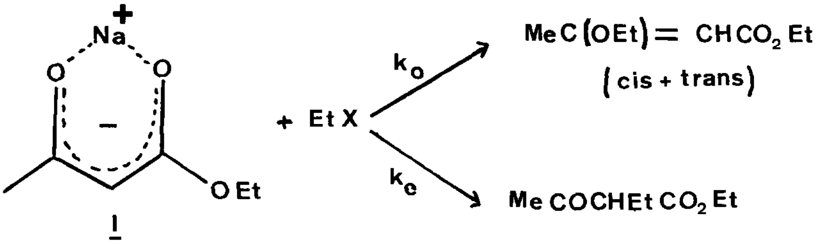
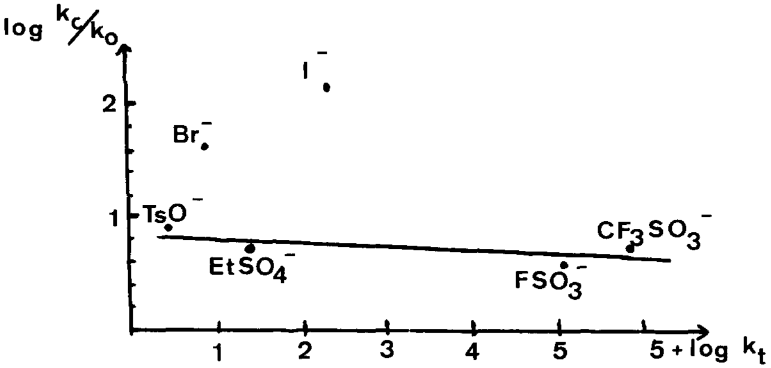
We have studied ambident anion <u>1</u> ethylation in DME at 0°C (1) and observed there is no simple relationship between reactivity (k_T) and selectivity ($[C]/[O] = k_C/k_O$) on changing the leaving group.



$$k_t = k_o + k_c \qquad [C]/[O] = k_c/k_o$$

When these results are plotted on a diagram of log (k_C/k_O) = f(log k_T) (figure 1) (reactivity-selectivity diagram) (2), the sulphonate points are found to lie along a line while the corresponding points for BrEt and IEt fall wide of the line.



The explanations usually proposed to rationalise leaving group effects involve either HSAB theory (3), reaction exothermicity (4), or alkylating agent electrophilicity (5). While the last two are totally inconsistent with our data, the first cannot rationalize all our results.

In this paper we discuss these results in terms of perturbation theory. Until now it was generally considered that for an enolate, O-alkylation is under charge control, while

≠ This work is part of the thèse d'Etat of P.Sarthou, Orsay, February 22, 1978.

C-alkylation is orbital controlled (6). Such an approach can be valid only when free anions or loose ion pairs are involved such as in HMPA (11). When the nucleophilic species are tight ion pairs or aggregates (as for 1 in DME), in our opinion, only orbital control is to be invoked, as the reagent as a whole is "neutral".

The interactions to be taken into account are those between the electrophile σ^*_{C-X} orbital and the two highest occupied molecular orbitals of the nucleophile:

- a π type orbital, with a large coefficient on carbon, which is responsible for C-alkylation (HOMO, frontier control)
- an n lone pair orbital, essentially located on oxygen (σ type) responsible for O-alkylation (subjacent MO, subjacent control).

Figure 2 shows the structure of acetaldehyde sodium enolate (7). Type 1 enolates have very closely related electronic structures (8,9).

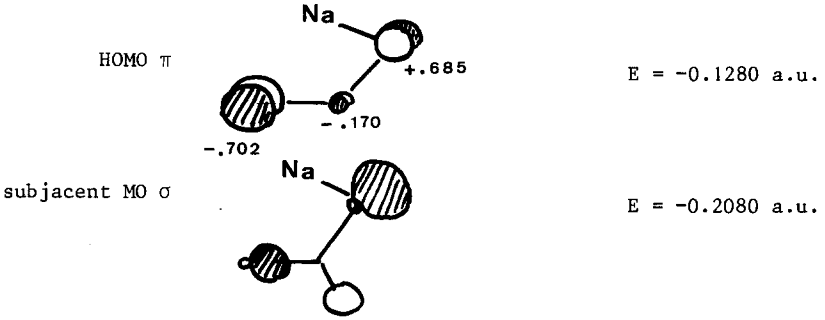
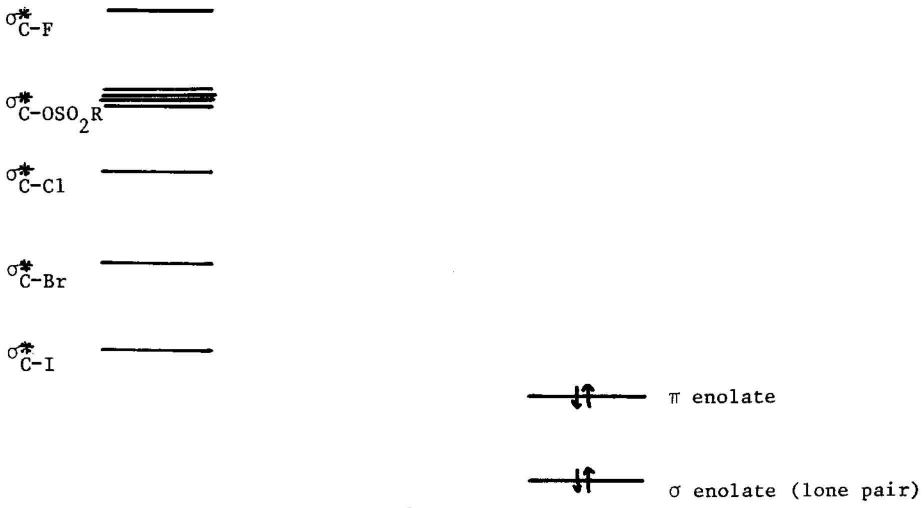


Figure 2

The perturbational scheme is thus, the following one (10):



$$C/O = \Delta\Delta E_p = \frac{(\beta_\pi, \sigma^*_{C-X})^2}{(\beta_\sigma, \sigma^*_{C-X})^2} \cdot \frac{E_\sigma - E_{\sigma^*_{C-X}}}{E_\pi - E_{\sigma^*_{C-X}}}$$

From this scheme, and assuming that changes in β^2 are negligible, it appears that the lower the σ^*_{C-X} MO level, the higher the differenciation between the two occupied MO's. Thus one would expect a C/O ratio which decreases in the order I>Br>OSO_2R and very similar selectivity for the different sulphonates.

KARTON and PROSS (12) have proposed a similar interpretation for the relative selectivities of m-chloroaniline and ethanol toward 1-octyl halides and sulphonates as a function of the leaving group.

However one would expect that when the levels of σ^*_{C-X} and of the nucleophile occupied MO are closer in energy, the reaction rate should increase (2b): this is the case when one compares the reactions of 1 with EtBr and EtI. However, one could expect very close rates for the reactions of different sulphonates: our results show the opposite. Furthermore, some sulphonates are even more reactive than EtBr and EtI while the opposite would be expected (fig.1)

Therefore, if perturbational treatment can, in this case, justify the selectivity dependence upon the leaving group nature, it does not account for the relative reactivities: factors such as geometries of transition states (degree of bond making and bond breaking), leaving group electronic reorganization and entropy factors should be of importance in some cases. We note that recently GIESE (13) interpreted the failure of reactivity-selectivity relationships by invoking differences in transition state geometries.

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