

## Origin of the So-called $\alpha$ -Effect

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The  $\alpha$ -effect is attributed primarily to the relative affinity of the  $\alpha$ -nucleophile for the electrophilic centre under consideration compared to the proton affinity, as indicated by thermochemical data, and by calculations of HOMO's and charge distribution at the 4-31G and 6-311G\* levels.

Many explanations have been given<sup>1</sup> of the abnormally high reactivity of certain nucleophiles (the so-called  $\alpha$ -effect)<sup>2</sup> but the subject remains a matter of controversy.

We suggest here that the effect is thermodynamic in origin and is due to the differences in the affinities of nucleophiles for a particular electrophile relative to the proton. It was noted<sup>4</sup> some years ago that the magnitude of the  $\alpha$ -effect increases with the extent of bond formation in the transition state (as given by the Brønsted  $\beta$ ). A simple extrapolation shows that the effect should be a maximum for complete bond formation.

Abnormally high affinities of HO<sub>2</sub><sup>-</sup> and *N*-substituted hydroxamic acids towards carbon have been reported,<sup>5</sup> and in the preceding communication we report that aromatic oximes, but not phenols of comparable p*K*<sub>a</sub> form adducts with acyl isothiocyanates.

Equilibria can be treated by a classical thermodynamic argument<sup>6</sup> as follows. Consider the equilibria (1)–(4), where N<sub>1</sub><sup>-</sup> represents a 'normal' nucleophile, N<sub>2</sub><sup>-</sup> an  $\alpha$ -nucleophile,

and E = an electrophile. Each process is imagined to involve (i) desolvation, (ii) electron transfer, (iii) bond formation. Thus equation (5) is obtained, where  $\Delta H_N^S$  is the solvation enthalpy of N<sup>-</sup>,  $E_N$  the electron affinity of N, and  $D_{N-E}$  the dissociation energy of the N–E bond.  $\Sigma E^+$  represents energy terms for E which are constant when two nucleophiles are compared, and  $\Sigma \Delta S$  is the net entropy change in the reaction, which can be neglected in the following treatment.

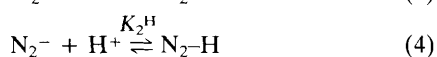
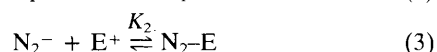
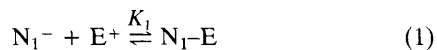
Applying equation (5) to equilibria (1)–(4) we have expression (6).

Thus an  $\alpha$ -effect will be observed *in an equilibrium* when the relative proton affinity  $\Delta D_{H-N}$  is greater than the relative affinity towards the electrophile  $\Delta D_{E-N}$ . This is supported by the thermochemical calculations and *ab initio* calculations at the 4-31G level (see Table 1). From the estimated values of the affinities towards carbon and hydrogen from thermochemical data, we find that  $\Delta D_{H-N}$  = approx.  $\Delta D_{C-N}$  for CH<sub>3</sub>O<sup>-</sup> and HCO<sub>2</sub><sup>-</sup>, two 'normal' nucleophiles of very different basicity.

**Table 1.** HOMO Energies,<sup>a</sup> Mulliken charges  $q_o$ ,<sup>b</sup> and calculated<sup>c</sup> and experimental<sup>d</sup> proton and methyl cation affinities (kcal mol<sup>-1</sup>; 1 cal = 4.184 J) of some oxyanions.

	$\epsilon_{\text{HOMO}}$		Proton affinity		Methyl cation affinity		Electronic charge on oxygen ( $q_o$ )	
	4-31G	6-311G*	4-31G	Exptl.	4-31G	Exptl.	4-31G	6-311G*
HO <sup>-</sup>	-0.0340	-0.0483	426.0	390.8	292.8	276.3	-1.144	-1.193
CH <sub>3</sub> O <sup>-</sup>	-0.0635	-0.0773	409.8	379.2	279.1	267.6	-0.949	-0.859
HO <sub>2</sub> <sup>-</sup>	-0.0868	-0.0942	387.4	379.4	259.6	272.6	-0.607	-0.614
FO <sup>-</sup>	-0.1371	-0.1514	360.5		235.4		-0.471	-0.457
HCO <sub>2</sub> <sup>-</sup>	-0.1510		360.0	345.2	229.8	233.1	-0.788	

<sup>a</sup> In Hartrees. <sup>b</sup> Units of electrons on the nucleophilic atom. <sup>c</sup> At 0 K, uncorrected for zero-point vibration. <sup>d</sup>  $-\Delta H_{298}$  for the process N<sup>-</sup> + A<sup>+</sup> → NA (A = H, C).



$$\Delta G^\circ = -RT \ln K = \Delta H_N^\ddagger + E_N - D_{N-E} + \Sigma E^+ + T \Sigma \Delta S \quad (5)$$

$$\begin{aligned} RT \ln \frac{K_2}{K_1} - RT \ln \frac{K_2^H}{K_1^H} &= (D_{H-N_1} - D_{H-N_2}) - (D_{E-N_1} - D_{E-N_2}) \\ &= \Delta D_{H-N} - \Delta D_{E-N} \end{aligned} \quad (6)$$

However,  $\Delta D_{H-N} - \Delta D_{C-N} = 4.8 \text{ kcal mol}^{-1}$  when  $\text{CH}_3\text{O}^-$  and  $\text{HO}_2^-$  are compared, corresponding to an  $\alpha$ -effect of  $10^{3.5}$  at 298 K. This may be compared with the experimental value<sup>7</sup> of  $10^{2.4}$  for the  $\alpha$ -effect in the reaction of *p*-nitrophenyl acetate with  $\text{HO}_2^-$ , where the value of  $\beta$  is found to be 0.65. Thus for complete bond formation, a value of  $10^{3.6}$  would be found for the  $\alpha$ -effect, if this is assumed to be proportional to  $\beta$ .

Examination of the MO data in Table 1 shows that a decrease in  $\epsilon_{\text{HOMO}}$  (*i.e.* an increase in ionisation potential) of a 'normal' nucleophile is accompanied by a decrease in  $q_o$ , the charge on the nucleophilic atom. However, substitution at the nucleophilic atom to form an  $\alpha$ -nucleophile, *e.g.*  $\text{HO}_2^-$ ,

produces a large decrease in  $q_o$  for a smaller decrease in  $\epsilon_{\text{HOMO}}$ . For example,  $\epsilon_{\text{HOMO}}$  for  $\text{HCO}_2^-$  is considerably *less* than  $\epsilon_{\text{HOMO}}$  for  $\text{HO}_2^-$  but the negative charge,  $q_o$  is *greater* for the  $\text{HCO}_2^-$  ion.

These calculations suggest that the increased value of  $\Delta D_{H-N}$  relative to  $\Delta D_{C-N}$  may be explained in terms of bond polarities. The abnormally large decrease in negative charge  $q_o$  (for  $\text{HO}_2^-$ ) reduces the Coulombic contributions to the H-O and C-O bonds.<sup>3</sup> This reduction is greater for the short, highly polar O-H bond than for the C-O bond, *i.e.*  $\Delta D_{H-N} > \Delta D_{C-N}$ . It follows therefore that  $\text{HO}_2^-$  (and other  $\alpha$ -nucleophiles) has a greater relative affinity than  $\text{HO}^-$  (or  $\text{CH}_3\text{O}^-$ ) for carbon. This is equivalent to saying that  $\text{HO}^-$  (or  $\text{CH}_3\text{O}^-$ ) has an abnormally high affinity for the proton.

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