Origin of the So-called α-Effect

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The α-effect is attributed primarily to the relative affinity of the α-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[1] of the abnormally high reactivity of certain nucleophiles (the so-called α-effect)[2] 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[4] some years ago that the magnitude of the α-effect increases with the extent of bond formation in the transition state (as given by the Brönsted β). A simple extrapolation shows that the effect should be a maximum for complete bond formation.

Abnormally high affinities of HO_2^- and *N*-substituted hydroxamic acids towards carbon have been reported,[5] and in the preceding communication we report that aromatic oximes, but not phenols of comparable pK_a form adducts with acyl isothiocyanates.

Equilibria can be treated by a classical thermodynamic argument[6] as follows. Consider the equilibria (1)—(4), where N_1^- represents a 'normal' nucleophile, N_2^- an α-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 ΔH_N^S is the solvation enthalpy of N^-, E_N the electron affinity of N, and D_{N-E} the dissociation energy of the N–E bond. ΣE^+ 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 α-effect will be observed *in an equilibrium* when the relative proton affinity ΔD_{H-N} is greater than the relative affinity towards the electrophile ΔD_{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 ΔD_{H-N} = approx. ΔD_{C-N} for CH_3O^- and HCO_2^-, two 'normal' nucleophiles of very different basicity.

Table 1. HOMO Energies,[a] Mulliken charges q_o,[b] and calculated[c] and experimental[d] proton and methyl cation affinities (kcal mol^{-1}; 1 cal = 4.184 J) of some oxyanions.

	ε_{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^-	−0.0340	−0.0483	426.0	390.8	292.8	276.3	−1.144	−1.193
CH_3O^-	−0.0635	−0.0773	409.8	379.2	279.1	267.6	−0.949	−0.859
HO_2^-	−0.0868	−0.0942	387.4	379.4	259.6	272.6	−0.607	−0.614
FO^-	−0.1371	−0.1514	360.5		235.4		−0.471	−0.457
HCO_2^-	−0.1510		360.0	345.2	229.8	233.1	−0.788	

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

$$N_1^- + E^+ \overset{K_1}{\rightleftharpoons} N_1\text{–}E \qquad (1)$$

$$N_1^- + H^+ \overset{K_1^H}{\rightleftharpoons} N_1\text{–}H \qquad (2)$$

$$N_2^- + E^+ \overset{K_2}{\rightleftharpoons} N_2\text{–}E \qquad (3)$$

$$N_2^- + H^+ \overset{K_2^H}{\rightleftharpoons} N_2\text{–}H \qquad (4)$$

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

$$RT\ln\frac{K_2}{K_1} - RT\ln\frac{K_2^H}{K_1^H} = (D_{H\text{-}N_1} - D_{H\text{-}N_2}) - (D_{E\text{-}N_1} - D_{E\text{-}N_2})$$

$$= \Delta D_{H\text{-}N} - \Delta D_{E\text{-}N} \qquad (6)$$

However, $\Delta D_{H\text{-}N} - \Delta D_{C\text{-}N} = 4.8$ kcal mol^{-1} when CH_3O^- and HO_2^- are compared, corresponding to an α-effect of $10^{3.5}$ at 298 K. This may be compared with the experimental value[7] of $10^{2.4}$ for the α-effect in the reaction of *p*-nitrophenyl acetate with HO_2^-, where the value of β is found to be 0.65. Thus for complete bond formation, a value of $10^{3.6}$ would be found for the α-effect, if this is assumed to be proportional to β.

Examination of the MO data in Table 1 shows that a decrease in ε_{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 α-nucleophile, *e.g.* HO_2^-, produces a large decrease in q_o for a smaller decrease in ε_{HOMO}. For example, ε_{HOMO} for HCO_2^- is considerably *less* than ε_{HOMO} for HO_2^- but the negative charge, q_o is *greater* for the HCO_2^- ion.

These calculations suggest that the increased value of $\Delta D_{H\text{-}N}$ relative to $\Delta D_{C\text{-}N}$ may be explained in terms of bond polarities. The abnormally large decrease in negative charge q_o (for HO_2^-) reduces the Coulombic contributions to the H–O and C–O bonds.[3] This reduction is greater for the short, highly polar O–H bond than for the C–O bond, *i.e.* $\Delta D_{H\text{-}N} > \Delta D_{C\text{-}N}$. It follows therefore that HO_2^- (and other α-nucleophiles) has a greater relative affinity than HO^- (or CH_3O^-) for carbon. This is equivalent to saying that HO^- (or CH_3O^-) has an abnormally high affinity for the proton.

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