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CAN GROUND-STATE DESTABILIZATION OF AN α-NUCLEOPHILE INDUCE AN α-EFFECT?

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Summary The possible importance of ground-state destabilization as the origin of the enhanced reactivity of α-nucleophiles is critically examined and it is concluded that, in general, this factor will contribute only slightly, if at all, to the manifestation of α-effects.

The α-effect has attracted wide attention during the past two decades.[1-4] No doubt a major source of this attraction has been the multitude of theories invoked in order to explain this phenomenon.[5-13] In this paper we would like to analyze critically one of these, namely ground state destabilization of the α-nucleophile.

It is clear that ground state destabilization resulting either directly from lone pair-lone pair interactions or indirectly via other phenomena such as solvation will increase the reactivity of the nucleophile. However, this will simultaneously increase its basicity as well. Since in general for structurally related series of reactions nucleophilicity is expected to increase linearly with basicity, and since the α-effect is defined[3] as a positive deviation from such a linear correlation, it follows that the α-effect will be manifested only in cases where the increased nucleophilic reactivity due to ground state destabilization will exceed that of a "normal" nucleophile possessing a correspondingly increased basicity.

In order to analyze the effect quantitatively, let us examine a "normal" nucleophile A_o[14] which is a member of a series of nucleophiles for which a β_{nuc} ($\Delta \log k/\Delta\ pK_a$) value is defined. Using the thermodynamic and extrathermodynamic quantities $\Delta G°$ and $-\Delta G^{\ddagger}$ directly instead of the related parameters log k and pK_a,[15] the nucleophile will be defined by the aforementioned coordinates, basicity, $\Delta G°(A_o)$, and nucleophilicity, $-\Delta G^{\ddagger}(A_o)$, Fig. 1. Destabilization of the ground state by the amount δ to generate the α-nucleophile A' will affect simultaneously the nucleophilicity and basicity by the quantity δ, assuming that the transition state is unaffected and that the free energies of the two conjugate acids A_oH and A'H are also identical. This perturbation will shift the position of the nucleophile to the new location for which the coordinates will be $\Delta G°(A')$ and $-\Delta G^{\ddagger}(A')$ as shown in Figure 1. The

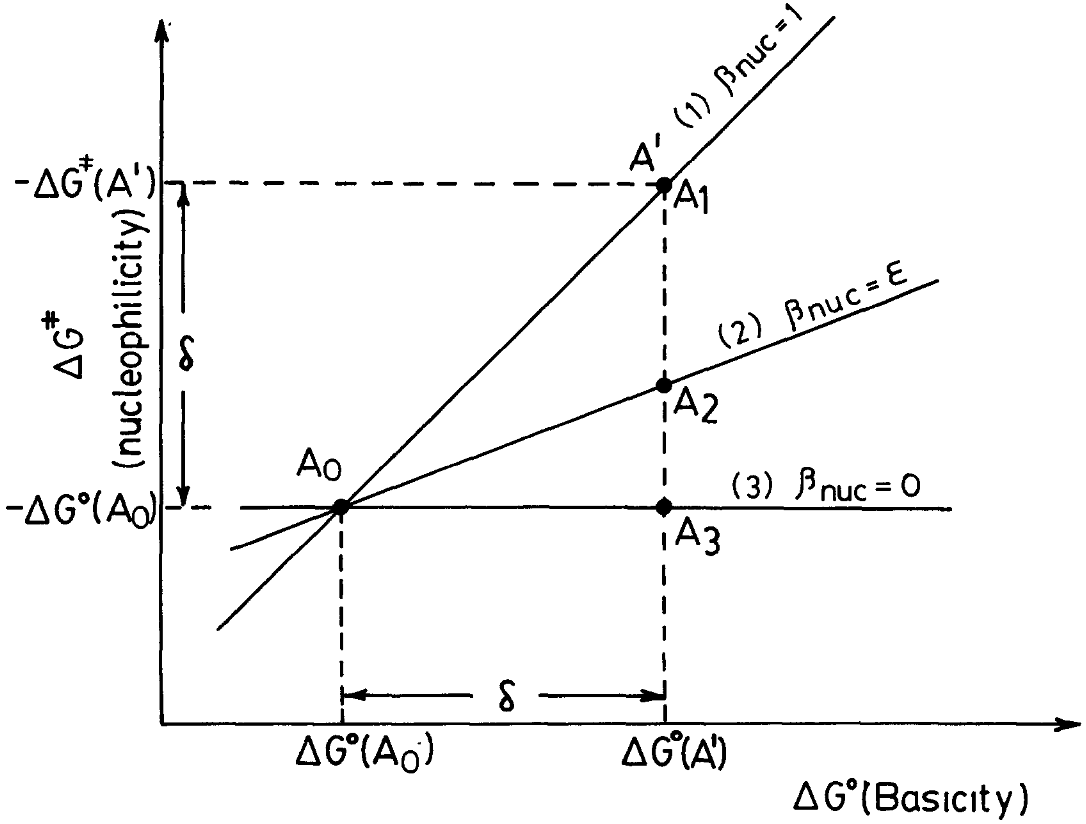

Figure 1. Bronsted type plots for nucleophilic reactions and ground state destabilization effects on basicity and nucleophilicity.

slope of the line connecting A_o and A' will be given by the expression[16]

$$\frac{-\Delta G^{\ddagger}(A') - (-\Delta G^{\ddagger}(A_o))}{\Delta G^{\circ}(A') - \Delta G^{\circ}(A_o)} = \frac{\Delta\Delta G^{\ddagger}}{\Delta\Delta G^{\circ}} = \frac{\delta}{\delta} = 1$$

Let us now consider three different cases of "normal" nucleophiles A_1, A_2, A_3 corresponding to (1) $\beta_{nuc} = 1$, (2) $\beta_{nuc} = \varepsilon$ where $0 < \varepsilon < 1$, and (3) $\beta_{nuc} = 0$, such that A_1, A_2, A_3 have the same basicity as A'.[17] In the first case, it will be seen (Fig. 1) that A' and A_1 are coincident on the Bronsted type plot of unit slope passing through A_o. Since the α-effect is defined as the positive deviation of A' from the Bronsted type plot, there will be no α-effect manifested in this case $(-\Delta G^{\ddagger}(A') - (-\Delta G^{\ddagger}(A_1) = 0)$. For case (2) it can easily be shown that the nucleophilicity of A_2 will exceed that of A_o by $\delta\varepsilon$ and therefore the α-effect will be given by $-\Delta G^{\ddagger}(A') - (-\Delta G^{\ddagger}(A_2)) = \delta(1-\varepsilon)$. Finally in case (3), where the increase in basicity of A_3 does not cause any increase in its nucleophilicity, the ground state destabilization will be manifested to its full size $(-\Delta G^{\ddagger}(A') - (-\Delta G^{\ddagger}(A_3)) = \delta)$ as an α-effect.

One can thus conclude that introduction of a pair of electrons at a position α to the nucleophilic center which destabilizes only the ground state of the nucleophile (either directly or indirectly as above) will cause an α-effect whose magnitude is expected to increase as β_{nuc} values decrease, being zero for $\beta_{nuc} = 1$ and reaching the maximum value for $\beta_{nuc} = 0$.[18]

In the previous discussion we have not considered any reflection of the ground state destabilization on the transition state. However, using the traditional interpretation of β_{nuc} as a measure of the bond order between the nucleophile and the electrophile at the transition state and assuming for simplicity a direct proportionality in the ground state and transition state effects, it follows that at the transition state the nucleophile will be destabilized by the fraction $(1-\beta_{nuc})$ of its original ground state destabilization. Thus for a ground state destabilization of δ and $\beta_{nuc} = \varepsilon$, the nucleophilicity enhancement for the α-nucleophile in thermodynamic units will be $\delta - \delta(1-\varepsilon) = \delta\varepsilon$ (see Fig. 2). However this is in fact merely the increase in nucleophilicity for a normal nucleophile whose basicity has been increased from $\Delta G°(A_o)$ by the amount δ (Fig. 1, A_2), i.e. no α-effect is manifested.

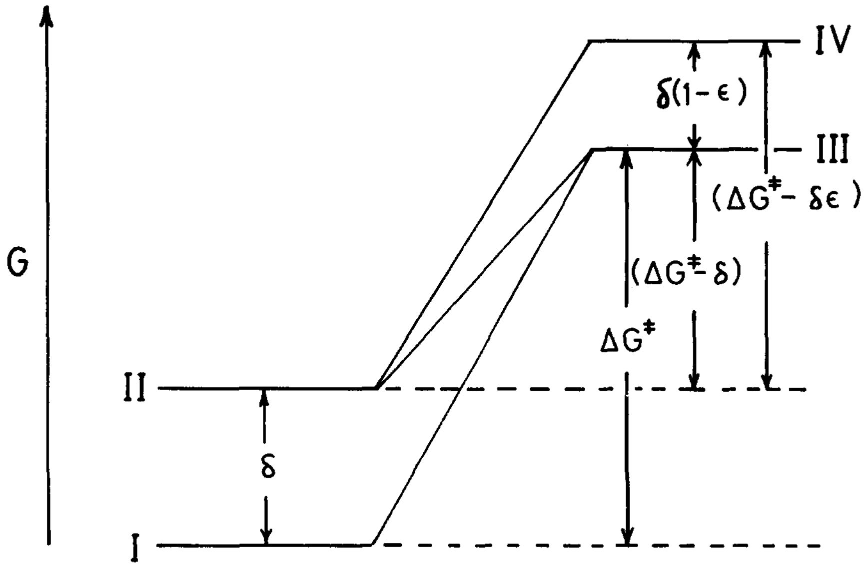

Figure 2. Ground and transition state destabilization effects on the barrier heights for nucleophilic reactions. I, ground state; II, destabilized ground state; III, transition state; IV, partly destabilized transition state.

It is thus concluded that, in general, ground-state destabilization of an α-nucleophile does not induce a rate enhancement and that the answer to the question posed in the title will be in the negative. However in the probably unique or rare cases where it is entirely or principally the ground state of the nucleophile which is destabilized by an alpha lone pair, a decrease in β_{nuc} will be accompanied by an increase in the α-effect. The fact that α-effects of appreciable magnitude are observed almost exclusively with certain classes of substrates but not with others[3,4,19] lends much support to the argument that the origin of the α-effect is not embodied in destabilization of the α-nucleophile itself but rather in the unique way by which it interacts with the substrate in the course of reaction.[11,12] The finding by Bruice[20] that the α-effect increases in magnitude as β_{nuc} increases is also in accord with this conclusion as β reflects the degree of bond formation in the transition state. We therefore believe that there is now strong evidence that the α-effect is a phenomenon associated largely with transition state stabilization rather than ground state destabilization.

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14. The symbols A_o, A_1, A_2,A_3 and A' are used to designate the nucleophiles as well as their location on Figure 1.
15. Since log k is proportional to $-\Delta G^{\ddagger}$, the ordinate in this figure has been labelled $-\Delta G^{\ddagger}$. The upward direction corresponds to an algebraic increase in the quantity $-\Delta G^{\ddagger}$. Thus the graph is similar to the conventional plot of log k vs. pK_a.
16. Note that slopes derived in this way are identical with β_{nuc} obtained from the expression Δ log k/Δ log pK_a.
17. The discussion is limited to cases where $0 < \beta_{nuc} < 1$.
18. Note that the experimentally observed relationship[20] between the α-effect and β_{nuc} is in fact the inverse of the one deduced hereby.
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