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PITFALLS IN THE DETERMINATION OF THE α-EFFECT BY A TWO-POINT ANALYSIS. THE EFFECT OF SOLVENT ON THE α-EFFECT.

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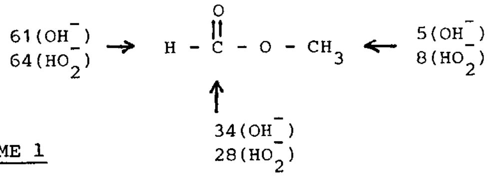
Summary The methodology for evaluation of the α-effect is examined and it is shown that the two-point analysis method is generally of limited value. This leads to a re-examination of the effect of solvent on the α-effect.

The α-effect, defined as the positive deviation of an α-nucleophile (e.g., HOO^-, NH_2-NH_2 etc.) from a Bronsted type (log k vs. pK_a) plot, remains one of the most intriguing problems in the field of nucleophilic reactions.[1-4] The procedure needed to produce sufficient data points for the construction of the Bronsted type plot as well as determination of the rate constant for the α-nucleophile is oftentimes quite laborious. A common shortcut is to replace this procedure by two rate constant determinations: one for the α-nucleophile (α-N) and the other for a "normal" nucleophile (N) used as a reference point. In this communication, the possible consequences of such a short cut will be analysed.

Since the ordinate of the Bronsted type plot is the basicity of the nucleophiles, three different situations can exist - a: $pK_a(\alpha\text{-N}) > pK_a(\text{N})$; b: $pK_a(\alpha\text{-N}) = pK_a(\text{N})$; and c: $pK_a(\alpha\text{-N}) < pK_a(\text{N})$. For obvious reasons, the first combination of α and "normal" nucleophile is not expected to be very informative and to the best of our knowledge such a combination has never been employed. A typical example of the second combination, where the two nucleophiles possess the same pK_a, is NH_2-NH_2 (α-N) and glycylglycine (N).[5] Probably the most commonly encountered combination is that of HOO^- and OH^- which fits into the third category.[6]

The two combinations b and c must be examined in light of the β_{nuc} value, namely, the slope of the Bronsted plot for a series of nucleophiles of which N is a member. The case where $\beta_{nuc} = 0$ (line I in Fig. 1) is in fact irrelevant to the α-effect since both experimental observation[7] as well as theoretical considerations[8,9] have shown that the α-effect can be exhibited only when the reactions are characterized by β_{nuc} values of an appreciable magnitude. The more pertinent case is when $\beta_{nuc} > 0$. In this event the most reliable information is achieved when the α-nucleophile and the "normal" one are of the same pK_a. Thus an observation of log k(α-N) > log k(N) clearly indicates the existence of an α-effect whereas identity of the rate constants points to its absence. However, when the pK_a of the α-nucleophile is smaller than that of the normal one (combination c), the analysis become somewhat more complex. As shown in the figure (line II), the α-nucleophile can display a reactivity which is larger (point 1), identical (point 2) and lower (points 3 and 4) than that of the reference nucleophile. Since, as was mentioned above, the α-effect is defined as a positive deviation from the Bronsted type plot, an α-effect can be observed even in cases where the two-point analysis results in log k(α-N) < log k(N) (point 3). Needless to say an α-effect is clearly evident in the cases where log k(α-N) $\geq$ log k(N) (points 2 and 1). It is only in one case (point 4) that the α-effect does not exist. However, in order to distinguish between the cases represented by points 2, 3 and 4, the β_{nuc} value must be known.

In order to demonstrate the importance of this analysis, we will employ as a "case study" a recently published report which utilized the two-point analysis method to investigate the α-effect in the gas phase. In this study,[10] the reactions of hydroxide and hydroperoxide anions with methyl formate were investigated by means of the flowing afterglow technique. These anions were found to react with the substrate in three competitive ways: proton abstraction, carbonyl addition and S_N2 displacement. Product distribution (values in percent are given in the following scheme) was taken as a criterion for the nucleophiles' affinities towards the various sites.[10b] The authors suggested that the fact



SCHEME 1

that HO_2^- exhibits an almost identical product distribution ratio to OH^- indicates the absence of the α-effect and points to a solvent effect as the most probable origin of this phenomenon. While this conclusion could in general be a valid one, in light of the previous analysis we would like to outline an alternative possible interpretation of the data.

Although certain gas phase reactions exhibit some selectivity,[11] the practically identical product distribution observed in the reactions of HOO^- and OH^- with methyl formate strongly indicates that these reactions are remarkable in their unusually low selectivity with respect to the nucleophiles.[12] This low selectivity becomes even more striking in light of the ca. 20 kcal/mol difference in the proton affinities of the two nucleophiles.[13] In terms of the Bronsted type relationship used to define the α-effect, such a low selectivity will be expressed as β_{nuc} values approaching zero. Since, as stated earlier, $\beta_{nuc} > 0$ is an essential condition for the manifestation of the α-effect and since this gas phase reaction[10] fails to meet this demand, it follows that a priori no α-effect is expected to be observed in this case. Therefore, this study can not invalidate any of the previously suggested explanations concerning the origin of the α-effect which had not utilized the solvent effect argument.

It follows also that if, however, one were led to believe that the reactions of OH^- and HOO^- with methyl formate in the gas phase are characterized by a non-zero β_{nuc} value[14] and that $k_{OH^-} \approx k_{HOO^-}$ (rate constants refer in this case to the crossing of the barier at the bottom of the ion-dipole potential well), then the results of this study[10] would actually constitute direct evidence for the existence of the α-effect in the gas phase (see point 2 in Fig. 1).

We may conclude therefore that a two point analysis of the α-effect can in certain cases be misleading. In these cases a direct and unambiguous determination of β_{nuc} is essential in order to obtain a meaningful conclusion. Such studies will be necessary in order to determine whether the origin of the α-effect is primarily a solvent effect, or whether initial state and transition state (and/or other) effects are also important.[15-17]

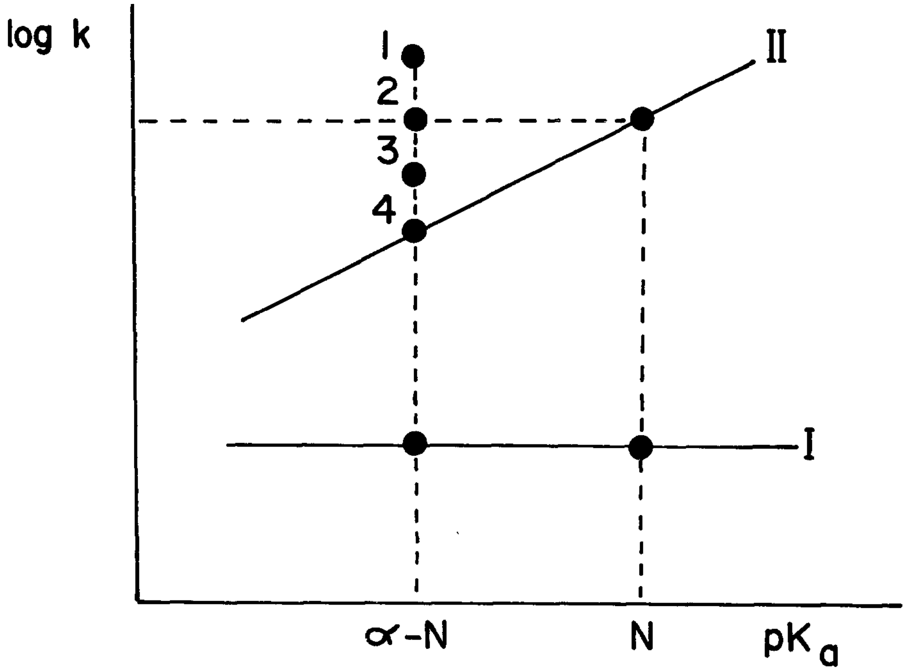


Figure 1. Bronsted type plot showing rate constants (log k) for an α-nucleophile (α-N) and a normal nucleophile (N) as a function of pK_a, for pK_a (α-N) < pK_a (N). Line I corresponds to $\beta_{nuc} = 0$ and line II to $\beta_{nuc} > 0$; see text for discussion of points marked 1, 2, 3 and 4.

REFERENCES AND NOTES

1. J.O. Edwards and R.G. Pearson, J. Am. Chem. Soc., 84, 16 (1962).
2. J.F. Bunnett, Ann. Rev. Phys. Chem., 14, 271 (1963).
3. N.J. Fina and J.O. Edwards, Int. J. Chem. Kinet., 5, 1 (1973).
4. W.P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw Hill, New York, 1969, p.107.
5. J.E. Dixon and T.C. Bruice, J. Am. Chem. Soc., 93, 3248 (1971).
6. J.L. Kice and A.R. Puls, J. Am. Chem. Soc., 99, 3455 (1977).
7. J.E. Dixon and T.C. Bruice, J. Am. Chem. Soc., 94, 2052 (1972).
8. E. Buncel, C. Chuaqui, and H. Wilson, J. Org. Chem., 45, 3621 (1980); E. Buncel, H. Wilson, and C. Chuaqui, J. Am. Chem. Soc., 104, 4896 (1982).
9. S. Hoz, J. Org. Chem., 47, 3545 (1982).
10. (a) C.H. DePuy, E.W. Della, J. Filley, J.J. Grabowski, and V.M. Bierbaum, J. Am. Chem. Soc., 105, 2481 (1983).
    (b) It has been pointed out by Dr. DePuy that the experimental data (footnote 14 in ref. 10 a) can be interpreted differently, leading to a product distribution somewhat different from the one given in Scheme 1. We are grateful to Prof. DePuy for this personal communication.
11. J.H.J. Dawson, Th. A.M. Kaandorp and N.M.M. Nibbering, Org. Mass Spectrom., 12, 330 (1977).
12. It is assumed throughout the discussion that product distribution indeed reflects activation barrier heights within the ion dipole potential well in the same sense as in solution chemistry. It should be noted however that in the gas phase reactions the rate determining step is in many cases a barrierless encounter of the reactants. Certain complications may arise also as a result of a possible equilibration of reactants and products at the potential well of the ion-dipole stabilized species (see for example the H/D exchange in the reaction of $PhCH_2^-$ with D_2O. J.H. Stewart, R.H. Shapiro, C.H. DePuy and V.M. Bierbaum, J. Am. Chem. Soc., 99, 7650 (1977)).
13. S.W. Benson and P.S. Nangia, J. Am. Chem. Soc., 102, 2843 (1980); V.M. Bierbaum, R.J. Schmitt and C.H. DePuy, J. Am. Chem. Soc., 103, 6262 (1981); D.J. Mitchell, Ph.D. Thesis, Queen's University, 1982.
14. When two nucleophiles, differing largely in their basicity, show the same selectivity in different reactions such as proton abstraction, carbonyl addition and nucleophilic displacement, the most reasonable conclusion would seem to be that these reactions are not sensitive to the pK_a of the nucleophile, i.e. $\beta = 0$. Alternatively, one could assume that the three reactions are equaly sensitive to the pK_a of the nucleophile i.e. $\beta_{\text{deprotonation}} = \beta_{C=O\ \text{addition}} = \beta_{SN2}$. This however would seem much less likely.
15. M. Laloi-Diard, J.F. Verchere, P. Gosslin and F. Terrier, Tetrahedron Lett., 25, 1267(1984).
16. E. Buncel and H. Wilson, Acc. Chem. Res., 12, 42 (1979).
17. E. Buncel and S. Hoz, Tetrahedron Lett., 24, 4777 (1983).

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