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THE EFFECT OF DMSO ON THE BASIC METHANOLYSIS OF BENZANILIDES

T.J. Broxton, L.W. Deady, and Y.T. Pang

Department of Organic Chemistry, La Trobe University,

Bundoora, Victoria 3083, Australia.

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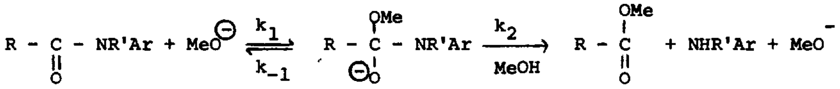
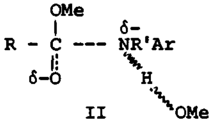
In the basic methanolysis of anilides, formation of I or its decomposition can be



$$R-\underset{\underset{O}{\|}}{C}-NR'Ar + MeO^{\ominus} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R-\underset{\underset{\ominus O}{|}}{\overset{\overset{OMe}{|}}{C}}-NR'Ar \xrightarrow[MeOH]{k_2} R-\underset{\underset{O}{\|}}{\overset{\overset{OMe}{|}}{C}} + NHR'Ar + MeO^-$$

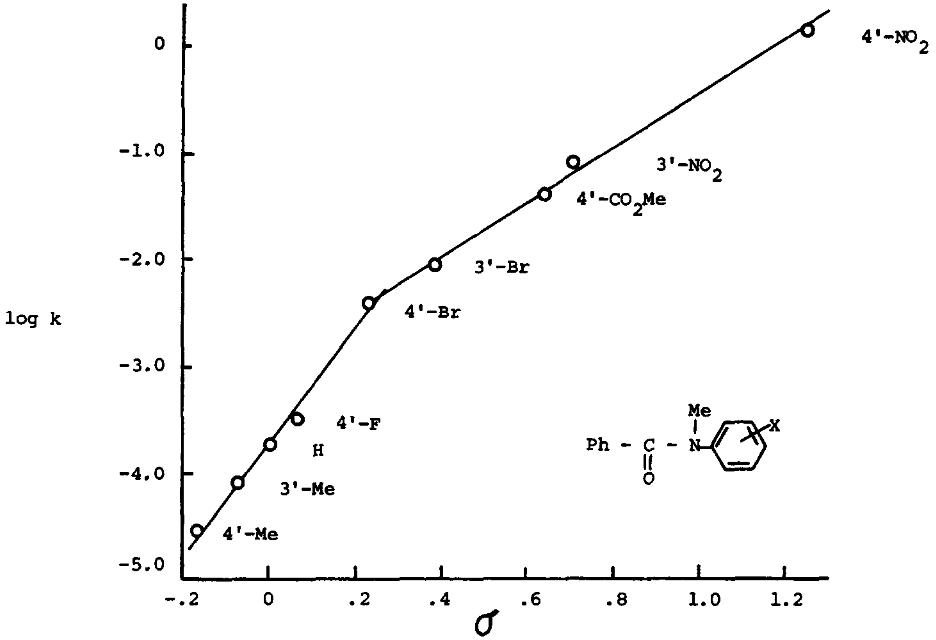
I

rate-determining. Within the latter category, a spectrum of transition states is possible[1] and transition state II has been suggested for good leaving groups (strong electron withdrawing aryl substituents). The addition of DMSO to the solvent markedly increases the rate of reaction of N-methylnitroacetanilides[2,3] but mechanistically this is equivocal since rate-determining formation of I (mechanism A[2]) or rate-determining breakdown of I via II (mechanism B[3]) would be similarly enhanced by this solvent change. However, mechanism A has a smaller ρ value than does B[4] and a change from B to A (for the best leaving groups) should thus produce a concave downward Hammett plot. Such behaviour has not been observed.



II

The results for the basic methanolysis of benzanilides (R = Ph) in methanol afford a linear Hammett plot,[4] best explained by invoking the operation of mechanism B throughout the series. We have now studied the effect of added DMSO on this reaction. The reactions were carried out in 80% (v/v) DMSO/MeOH by a standard method.[4,5] The results at 298K[6] are summarised in the figure (k is the observed second order rate constant). This represents the first example in this field of a downward break in the Hammett plot and is consistent with a change in rate-determining step from mechanism B (poor leaving groups) to A (for substituents with better withdrawing power than 4'-Br). The effect of DMSO is apparently to enhance the loss of amine from I relative to loss of methoxide. This is reasonable in a solvent system which is poor at solvating anions, as the localised charge on the methoxide would be more affected than the diffuse charge on the aromatic amine. Thus $^{k_2}/k_{-1} > 1$ for substituents with better withdrawing power than 4'-Br and here the k_1 step becomes rate-determining. Support for this interpretation comes from hydrolysis studies; Pollack[7] has shown that $^{k}2/k_{-1}$ (DMSO) > $^{k}2/k_{-1}$ (H_2O) for reaction of 4'-nitroacetanilide.



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5. We found for each compound that the k value was increased by about 10% by a doubling of the MeO^- concentration. Infinity spectra were stable and agreed with those of authentic product mixtures. The addition of $LiClO_4$ did not affect the rate. We have no explanation for this observed base dependence. The uncertainty in individual rate constants is not significant when the large range of values is considered and the result quoted for each compound was obtained at 0.054M MeO^- to minimise relative uncertainties.
6. The value for the 4'-CH_3 compound was obtained by extrapolation: $10^4k = 2.15$ (316K), 7.32 (327.5K), 20.9 (339.5K) $M^{-1}sec^{-1}$.
7. R.M. Pollack, J. Org. Chem., **39**, 2109 (1974).