Comment on the Transition-state Structure for Menschutkin Reactions

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Summary Based on the influence of substitution at the α-carbon atom, solvent effects, and substitution within the attacking anion for an onium salt decomposition, it is proposed that Menschutkin reactions are best considered as proceeding through normal S_N2 transition states rather than the transition state with extensive bond breaking and little bond making recently proposed by Arnett and Reich.

IN a recent publication, Arnett and Reich[1] have suggested that Menschutkin reactions (1) in the absence of severe

$$R^1R^2R^3N + R^4X \rightleftharpoons R^1R^2R^3R^4N^+X^- \qquad (1)$$

steric hindrance or stongly hydrogen bonding solvents can be accommodated by a transition-state structure with about one-third positive charge development on the nitrogen (based upon free-energy changes accompanying variation within the nucleophile) and approaching complete negative charge development at and solvent reorganization around the leaving group (based upon comparison of entropies of activation with entropies of reaction). The incorporation of extensive bond breaking within the transition state leads to a picture which differs substantially from the essentially 'classical' S_N2 scheme advocated by Abraham.[2–5]

The Arnett and Reich[1] model for the transition state requires considerable positive charge (approaching two-thirds) to have developed on the α-carbon atom and it is extremely similar to what would be expected for the transition state of the rate-determining step for an S_N2C^+ reaction[6] of an ion-pair, expecially if residual bonding between the α-carbon atom and the leaving group is incorporated.[7,8] Several criteria which we have used [9–11] to test proposed S_N2C^+ reactions of methyl derivatives can also be applied to this one-step process.

One criterion of mechanism which is usually found to be highly reliable is the concept that a charged structure will be stabilized by dispersal of charge and *vice versa*. Solvation is one mechanism by which this can be achieved[1] but another powerful mechanism is through substitution at the reaction centre.[12–15] Schleyer has estimated that the rate of formation of the incipient carbenium ion in a limiting S_N1 reaction is increased by a factor of 10^8 on replacement of a α-hydrogen atom by a methyl group.[13]

Second-order rate coefficients for the reaction with pyridine in 2-nitropropane at 25 °C give MeX/EtX ratios of 28 for the fluorosulphonates and 20 for the iodides,[1] indicating that steric factors outweigh polar factors. The Arnett and Reich model would necessarily incorporate an appreciable facilitating polar effect upon α-methyl substitution and would require an unreasonably[16] large counterbalancing steric factor. Indeed, the observed ratios are of the magnitude to be expected on the basis of negligible charge development on the α-carbon atom within the transition state.[16]

A major difference between t-butyl halide solvolysis and Menschutkin reactions is that the former are accelerated (by as much as 10^5 fold[17]) and the latter decelerated on transfer from aprotic to hydroxylic solvents.[3] The model proposed by Arnett and Reich was restricted to non-hydrogen-bonding solvents[1] but it does suggest that transfer from acetonitrile to the almost isodielectric[18] methanol should facilitate reaction through a considerable strengthening of the solvation of the highly developed anionic leaving group. For reaction of methyl iodide with *NN*-dimethylanilines a modest retardation is actually observed.[19] If the model were to be accurate, this would require that desolvation of the only weakly bonded amine should be a more important rate-determining factor than the solvation of the highly developed iodide ion. Breaking of the hydrogen bonding to the amine nitrogen would be favoured by electron-withdrawing substituents and would be expected to contribute a positive component to the overall Hammett ρ value. Calculations from the available data[19] give ρ values in methanol and acetonitrile of $-2{\cdot}44$ and $-2{\cdot}53$ at 40 °C and $-2{\cdot}40$ and $-2{\cdot}44$ at 50 °C, arguing against any appreciable increased contribution from the desolvation of the amine in methanol relative to acetonitrile. Indeed, Abraham[2,5] has presented evidence that the transfer to a hydroxylic solvent increases the free energy of the transition state rather than lowering the initial-state free energy; this was a major consideration in his proposal that the transition state is more like a polarisable non-electrolyte (with about two-fifths charge separation) than an ion-pair.

The principle of microscopic reversibility requires the transition state for the reverse reaction (1) to have appreciable breaking of the bond to the departing amine and little bonding or desolvation of the attacking anion, if the model of Arnett and Reich is applied. Such a reaction would be expected to be extremely insensitive to the nature of substitution within the attacking anion. Rate data are available[20] for a related 'onium ion decomposition (2) in acetonitrile and, for a series of *meta*- and *para*-substitutents within

$$\mathrm{ArSO_3^-} + \mathrm{Me{-}O^+(Me)_2} \xrightarrow[-23{\cdot}4\ ^\circ\mathrm{C}]{\mathrm{MeCN}} \mathrm{MeOSO_2Ar} + \mathrm{Me_2O} \qquad (2)$$

the arenesulphonate (0·04 M), a ρ value of $-1{\cdot}18 \pm 0{\cdot}04$ was obtained. This appreciable value is identical to that obtained for attack on methyl trifluoromethanesulphonate,[11] a neutral methylating agent of very similar reactivity,[21] indicating essentially identical bonding to the attacking anion both in a reaction of the same type as the reverse Menschutkin reaction and in a reaction involving attack on a neutral substrate. Further, the ρ value can be compared with that for the methanolyses (3) of methyl arenesulphonates.[22] The ρ value of $+1{\cdot}25 \pm 0{\cdot}04$ is virtually identical in absolute magnitude to that for reaction (2).

$$\mathrm{MeOH} + \mathrm{MeOSO_2Ar} \xrightarrow[50\ ^\circ\mathrm{C}]{\mathrm{MeOH}} \mathrm{Me_2\overset{+}{O}H} + \mathrm{ArSO_3^-} \qquad (3)$$

The above considerations point to a classical S_N2 transition state with approximately synchronous bond making and bond breaking, so as to produce little charge on the α-carbon atom. The actual charge separation would be expected to vary with the reactants and the solvent but would be expected to be in the neighbourhood of one-half. It is not obvious why the entropies of activation for reactions of pyridines with methyl iodide in acetonitrile constitute 72—80% of the entropies of reaction for the unsubstituted and 3- and 4-substituted pyridines, and as much as 93% for the one 2-substituted pyridine studied.[1] These observations appear to imply that solvent reorganization is more advanced at the transition state than charge development.

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