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# TRANSITION STATES OF SOME ACYL TRANSFER REACTIONS IN ACETONITRILE[1]

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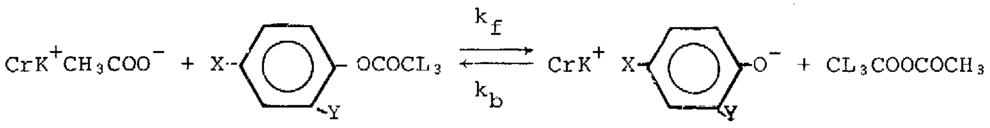
SUMMARY: β-Deuterium isotope effect (β-DIE) studies of acyl transfer from aryl acetates to acetate ion in acetonitrile indicate the degree of tetrahedral character at the transition state (TS) to be small, and the same as in protic solvents.

Velocities of reactions of acetate ion, solubilized as its potassium salt by 18-crown-6 in dry acetonitrile, with *p*-nitrophenyl acetate (PNPA) and 2,4-dinitrophenyl acetate (DNPA) are increased by trideuteration in the acyl group of the esters. These β-DIEs are temperature independent within experimental error with values of 0.958±0.007, 5-45°C for PNPA and 0.964±0.011, 5-20°C for DNPA. The degree of tetrahedral character at the TS is calculated to be 0.32 and 0.28, respectively, taking 0.87 from the equilibrium β-DIE[2,3,4] of ketone hydration for the limiting fully $sp^3$ TS when three deuteriums are involved. The transition state for these reactions therefore, occurs at a point where the tetrahedral character, as measured by the βDIE, is less than half. Activation parameters for the two reactions, especially the positive values of $\Delta S^{\ddagger}$(+5-9 e.u.) are also consistent with the proposition of TSs not resembling the tightly bound intermediate. This finding is in strong agreement with data from studies of α-[5,6] and β-DIEs[2,3] and of Brønsted correlations[7,8,9] of acyl transfer reactions to oxyanions in protic solvents, and indicates that this quite drastic alteration in environmental conditions has had little or no influence on the structure of the TS within this group of acyl transfer reactions.

Studies of ionic reactions in aprotic solvents have become possible recently with the advent of macrocyclic polyethers[10,11] for solubilization of alkali salts. In this study, the acetate reagent was prepared in 1.5 - $4\times10^{-3}$ M concentration in a solution of 2 fold excess of 18-crown-6[12] in acetonitrile[13]. Rates were followed spectrophotometrically. The rate law for reversible formation of acetic anhydride:



could be simplified to follow first order kinetics for DNPA even when the nucleophile was in 50-100 fold excess. Preliminary measurements of the reaction rate between acetic anhydride and *p*-nitrophenoxide allowed an estimate of $k_b \sim 150k_f$ for PNPA. Indeed, negative deviations from first order kinetics were perceptible even when the nucleophile was in $10^3$ excess, thus initial rate measurements to 1-2% completion were used. There was no detectable reaction when X=Y=H, due to the predominance of the back reaction with the strong nucleophile, phenoxide. This behavior is predicted by structure reactivity correlations of ester formation in water[14] ($\rho$=-1.40), allowing calculation of relative values of the equilibrium constant ($K_X/K_H$) of 1:60:6000 for (X=Y=H):(X=$NO_2$, Y=H):(X=Y-$NO_2$). The observations in acetonitrile suggest no change in the order or approximate magnitude of the substituent effect.

Second order rate constants and β-DIEs are tabulated in Table I as a function of temperature and activation parameters are in Table II. Addition of water in 1-10 fold excess of KOAc retarded the rates as shown in Table III.

Despite the substantial rate acceleration, $2.7 \times 10^4$ for PNPA[7] and $2.7 \times 10^5$ for DNPA at 25°C relative to the corresponding reactions in water, the β-DIEs are not different within experimental error from the 0.950±0.009 value observed for DNPA in water, 25°C[3]. All β-DIEs measured in protic solvents for nucleophilic reactions of oxy-anions, such as hydroxide[3], methoxide[2], phenoxide[3], and acetate[3] ions with the aryl acetates studied are less inverse than anticipated for TSs that resemble the tetrahedral intermediate. Instead, the reactions appear to have progressed only by fractions of 0.15-0.2, ∿0.2, 0.2-0.4, and 0.37, respectively, as estimated from β-DIEs, and from αDIEs for reactions of the same nucleophiles with aryl formates[5]. Another indicator of reaction progress, $\beta_{nuc}$ from a Brønsted correlation[7,8], yielded similar result (0.2) for strong bases (pK>12) and a larger value (0.7) for weak bases (pK 8-11) reacting as nucleophiles. It has been suggested that the value of 0.2 is too small because of ground-state solvation effects and that 0.7 is too large because of losses of resonance energy in the TS[3].

Reactions that pass through an unstable intermediate (in this case the tetrahedral adduct referred to above) are commonly (correctly or incorrectly) expected to have TSs that resemble the intermediate, whether its formation or decomposition determines the rate. Whether formation or breakdown or some combination of the two is rate determining in these reactions, the conclusions remain the same; the TS(s) shows more trigonal character like the reactant and product than tetrahedral character like the adduct. Furthermore, the near trigonal character of the TS is independent of the protic/aprotic character of the solvent, and this conclusion is independent of whether the rate-determining step is the same in the two solvents. Requirements for desolvation of the nucleophile, specific to protic solvent, can therefore not be responsible for this structural feature of the TS.

The results reported here are thus most clearly in agreement with a hypothesis that a highly reactive, presumably desolvated nucleophile or leaving group, in a common solvent cage with the electrophile, precedes and succeeds the tetrahedral adduct. If these unstable species lie above the tetrahedral adduct in energy, then the TSs would be expected (as is observed) to resemble the trigonal form of the ester present in the high-

Table I. Temperature dependence of the second order rate constants and of the β-DIEs for reactions of KOAc in dry $CH_3CN$ and 18-crown-6:

A. PNPA and PNPA-$d_3$

| C° | $k^{CH_3}$, $M^{-1}s^{-1}$ | $k^{CD_3}$, $M^{-1}s^{-1}$ | $k^{CH_3}/k^{CD_3}$ |
|---|---|---|---|
| 5 | 0.02995 ± 0.00042 | 0.03121 ± 0.00089 | 0.960 ± 0.030 |
| 10 | 0.04847 ± 0.00089 | 0.05108 ± 0.00119 | 0.949 ± 0.028 |
| 15 | 0.07137 ± 0.00160 | 0.07505 ± 0.00162 | 0.951 ± 0.027 |
| 20 | 0.1137 ± 0.00062 | 0.1184 ± 0.0010 | 0.960 ± 0.010 |
| 25 | 0.1685 ± 0.0030 | 0.1753 ± 0.0039 | 0.957 ± 0.027 |
| 30 | 0.2567 ± 0.0039 | 0.2689 ± 0.0075 | 0.956 ± 0.030 |
| 35 | 0.3422 ± 0.0050 | 0.3585 ± 0.0086 | 0.955 ± 0.027 |
| 40 | 0.5339 ± 0.01581 | 0.5500 ± 0.0164 | 0.97 ± 0.04 |
| 45 | 0.6816 ± 0.0119 | 0.7070 ± 0.0143 | 0.964 ± 0.026 |

B. DNPA and DNPA-$d_3$

| C° | $k^{CH_3}$, $M^{-1}s^{-1}$ | $k^{CD_3}$, $M^{-1}s^{-1}$ | $k^{CH_3}/k^{CD_3}$ |
|---|---|---|---|
| 5 | 45.33 ± 0.131 | 47.61 ± 1.007 | 0.952 ± 0.020 |
| 10 | 60.96 ± 1.175 | 62.78 ± 1.764 | 0.971 ± 0.022 |
| 15 | 87.46 ± 1.353 | 91.11 ± 1.234 | 0.960 ± 0.020 |
| 20 | 124.21 ± 2.86 | 127.8 ± 2.56 | 0.972 ± 0.030 |

Table II. Activation parameters

| Compound | $\Delta H^{\ddagger}$, Kcal/mol | $\Delta S^{\ddagger}$e.u. |
|---|---|---|
| PNPA | 13.29 ± 0.18 | 5.35 ± 0.11 |
| PNPA-$d_3$ | 13.24 ± 0.18 | 5.28 ± 0.11 |
| DNPA | 10.38 ± 0.34 | 9.32 ± 0.33 |
| DNPA-$d_3$ | 10.22 ± 0.41 | 8.83 ± 0.38 |

Table III. The effect of added $H_2O$ to the reaction mixtures in $CH_3CN$

PNPA

| $H_2O$, $10^2$M | 0.0 | 0.456 | 0.912 | 1.368 | 2.280 | 4.560 |
|---|---|---|---|---|---|---|
| $\frac{v_0(CH_3CN + H_2O)}{v_0(CH_3CN)}$ | 1.0 | 0.794 | 0.712 | 0.685 | 0.594 | 0.508 |

DNPA

| $H_2O$, $10^2$M | 0.0 | 1.140 | 2.280 | 3.42 | 4.56 |
|---|---|---|---|---|---|
| $\frac{k_0(CH_3CN + H_2O)}{k_0(CH_3CN)}$ | 1.0 | 0.629 | 0.565 | 0.526 | 0.400 |

energy, desolvated complexes. Perhaps, the anionic species in acetonitrile, exist more or less close to this high energy state, which seems to be manifest in the much higher rate, but with a quite similar TS structure to the one in protic solvents.

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## References and Notes

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