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NUCLEOPHILIC REACTIVITY AT UNSATURATED CENTERS

I. METHANOLYSIS OF SUBSTITUTED METHYL BENZOATES

by

Lee B. Jones and Thompson M. Sloane*
Department of Chemistry, University of Arizona, Tucson, Arizona

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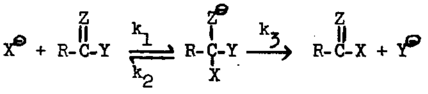
A detailed study of nucleophilic reactivity at centers of unsaturation is difficult because most reactions proceed by an addition-elimination mechanism.[1] The observed rate constant under normal conditions is thus dependent upon the addition step k_1, as well as the ratio of the rate constants for the two possible elimination steps (k_2/k_3).



$$X^{\ominus} + R\text{-}\overset{\overset{Z}{\|}}{C}\text{-}Y \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R\text{-}\underset{X}{\overset{Z^{\ominus}}{C}}\text{-}Y \xrightarrow{k_3} R\text{-}\overset{\overset{Z}{\|}}{C}\text{-}X + Y^{\ominus} \qquad (1)$$

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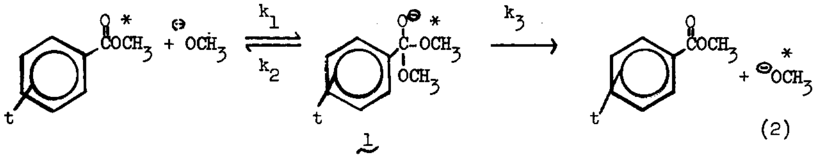
The observed rate constant for the majority of such reactions is $k_1/({}^{k_2}/k_3 + 1)$. In order to study factors affecting only k_1 (the nucleophilic addition step) we have studied as our first system for investigation the symmetrical reaction shown in equation 2. The substituted esters (labeled with tritium in the methyl groups) were prepared by the method of Melander.[14]



(2)

Since the intermediate (1) contains two equivalent leaving groups (one labeled with tritium and denoted by an asterisk), the partition of this intermediate between reactant and product must be statistical and hence $k_{obs.} = k_1/2$. Any isotope effect on k_2/k_3 will certainly be within the limits of experimental error for small enrichments of tritium in the methyl group. In this manner we were able to study by direct means the nature of the nucleophilic addition step. We now report the results of this initial study. The rate measurements were determined by following the loss of radioactivity from the starting ester.

A series of <u>para</u>-substituted methyl benzoates has been studied in pure methanol at a series of temperatures. The reactions were observed to be pseudo-first order since the base concentration (sodium methoxide) remains unchanged during the course of reaction. The second order rate constants for the addition step k_1 were obtained by dividing the observed first order constants by the concentration of added base. The results of these measurements are presented in Table 1.

Table 1

Kinetic Data for Base Catalyzed Methanolysis of Substituted Methyl Benzoates

	Rate Constants, k_1(M.$^{-1}$sec.$^{-1}$ x 10^2)			Activation Parameters (25°)	
$ArCO_2Me$	30.1°	41.0°	51.7°	$\Delta H^{\ddagger}\left(\frac{kcal.}{mole}\right)$	$\Delta S^{\ddagger}$(e.s.u.)
p-Methoxy	1.06	2.48	5.58	14.3	-20.3
p-Methyl	1.86	4.20	9.62	14.1	-20.1
p-Hydrogen	4.81	10.0	21.4	12.7	-22.8
p-Bromo	21.2	38.0	76.4	11.0	-25.4
p-Nitro	416	670	1098	8.1	-29.5

These data show good Hammett $\rho\sigma$ plots at each temperature. The observed ρ values are as follows: 2.41 (30.1°), 2.32 (41.0°) and 2.18 (51.7°). Correlation coefficients for the Hammett plots were all in the vicinity of 0.995.

The enthalpy-entropy values give a reasonable good iso-kinetic plot as defined by Leffler[2] (β = 660°K). The p-methyl compound deviates slightly. An analysis of these data in accordance with Petersen's[3] discussion shows no "iso-kinetic correlation."[a]

It is of interest to compare these results with previous studies of ester hydrolysis and methanolysis. In all previous studies,[4] as in this one, the enthalpy of activation shows a continuous decrease as electron withdrawing substituents are substituted for electron supplying groups. This is consistent with the fact that electron withdrawing groups are known to facilitate these

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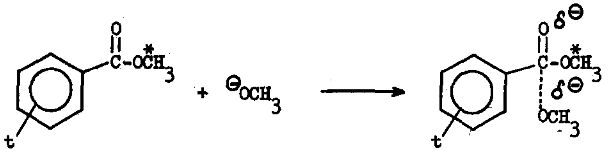
[a] However, it has been pointed out by a referee that Petersen's[3] views seem somewhat tenuous when two extreme cases are considered. If $\beta = \infty$ for a two point "iso-kinetic relationship" and $\delta\Delta H^{\ddagger}$ is small the rates of each compound will be essentially the same at all temperatures. However, when β = 0° and $\delta\Delta S^{\ddagger}$ is small the rates will again be approximately the same at all temperatures. Thus, an apparent inconsistency exists in Petersen's treatment.

reactions. However, in most previous studies the entropy of activation was found to be essentially invariant with substituent change. The major difference between this study and those reported previously is that we are looking only at the addition step k_1, whereas earlier studies of ester hydrolysis or alcoholysis have been dependent upon the overall reaction rate involving k_1, k_2 and k_3. Newman[5] did observe a small variation in $\Delta S^{\ddagger}$ when he studied the base catalyzed methanolysis of meta-alkyl l-menthyl benzoates. Such a variation was not noted for the para-alkyl compounds. The variations in $\Delta S^{\ddagger}$ for the meta isomers were attributed to steric effects. When the same reaction was studied with substituents of widely varying Hammett σ values (p-NO_2 to p-OCH_3), the entropy of activation was found to be constant.[4b]

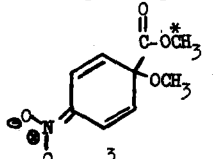
It is interesting to speculate as to the significance of such a systematic entropy variation. The rate determining transition state formation may be formulated as shown in equation 3.



2 (3)

This transformation involves the conversion of one oxygen anion into another. Since the transition state must be well along toward the "tetrahedral intermediate"[1,6] there is only a relatively small amount of charge dispersion and hence solvation interactions are probably not the dominant feature of the observed entropy variations. Further, one observes that the standard entropies (ΔS°) for ionization of the corresponding para-substituted benzoic acids[7] show small variations but in the opposite direction to those observed here. That is, the standard entropy of ionization for the para-nitro acid is less negative than that for the para-toluic acid. Solvation effects due to hydration of the proton are the same in ease case and therefore do not have any effect on the difference, $\Delta\Delta S^o$, for any two substituents. Hence, our observed entropy effects are probably not due to differential solvation of the substituents.

Valence bond structures such as 3 and 4 cannot be considered important contributors to the resonance hybrid of the transition state because such "neighboring orbital participation" is considered unimportant for first row elements.[8]



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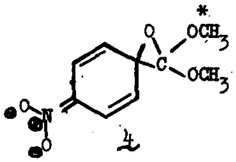

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It appears that one very reasonable interpretation of the entropy data can be based on translational entropy considerations. When two species come together a certain amount of translational freedom (entropy) must necessarily be lost. In this study, we are considering a symmetrical reaction with relatively little alteration of charge in going from reactant to transition state. Since solvation forces are of minor importance the results suggest that somewhat more translational entropy is lost when methoxide ion reacts with methyl p-nitrobenzoate than with the p-methyl compound. This implies that as the substituents are varied from electron supplying to electron withdrawing groups, bonding in the transition state becomes more nearly complete (equation 3). Conclusions about the extent of bonding from entropy measurements have been drawn previously.[9]

This conclusion is opposite to what one might have anticipated from a consideration of an extension of the Hammond postulate,[10] but appears to conform to the "reacting-bond rule" recently proposed by Swain.[11] This conclusion is further strengthened by preliminary results of our study of solvent effects on this symmetrical reaction. When this reaction is carried out in mixtures of dioxane-methanol only small solvent effects are noted. Hinshelwood[12] and Tommila[13] have similarly observed small solvent effects on the hydrolysis rates of ethyl benzoate in mixed solvents. The important observation, however, is that even though the results are small an electron withdrawing substituent renders the ester methanolysis rate less sensitive to a change in solvent than does an electron supplying group. This implies that when such an electron withdrawing substituent is present there is a smaller amount of charge dispersion in the transition state (2). Since the transition state occurs well along the reaction coordinate[1] one concludes that bond formation must be more complete when electron withdrawing substituents are present. A detailed investigation of solvent effects on this symmetrical reaction is continuing.

Thus, it seems apparent that the correlation of transition state structure with substituent change in carbonyl addition reactions is better described by the "reacting-bond rule" than by the Hammond postulate. This is not surprising in view of the fact that Hammond probably did not intend that his postulate be applied to fine details of reactions such as substituent changes.

We are continuing our work on this and similar symmetrical substitution reactions at unsaturated centers and will report on these results in the future.

Acknowledgement

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