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A NOVEL SOLVENT DEPENDENCY OF ANCHIMERIC ASSISTANCE IN ESTER HYDROLYSIS - ALKALINE HYDROLYSIS OF GLYCOL MONOBENZOATES IN AQUEOUS DMSO, AQUEOUS ETHANOL AND AQUEOUS ACETONE

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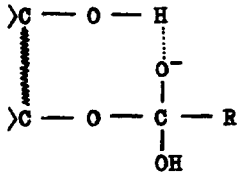
Anchimeric assistance in ester hydrolysis is well characterised[1,2]. An aliphatic hydroxyl group located in close proximity to an ester bond is known to facilitate alkaline hydrolysis. In regard to the mechanism of the above facilitation, Henbest and Lovell[3] favoured a hydrogen bonded structure involving the ether oxygen as important in the hydrolysis of cyclohexane-1,3-diol monoacetates. This problem was further investigated by Bruice and Pife[4] who examined the)C=O and -OH group IR absorptions as well as the rates of alkaline hydrolysis of a number of cyclopentane and norbornane acetates and diol monoacetates. The increased rates of hydrolysis of cyclopentyl or exo-2-norbornyl acetates on the substitution of a hydroxyl group in the α- or β-position was greater than could be explained on the basis of an inductive effect. The results of infrared studies demonstrated that the extent of facilitation of hydrolysis by a vicinal hydroxyl group is not greatly dependent on the type of possible internal hydrogen bonding in the ground state. These authors therefore postulated an intramolecular hydrogen bond stabilisation of the transition state.



(I)

Bruice and Benkovic[2] labelled this as a microscopic solvent change effect. Very little work is on record on the solvent dependency of such reactions involving anchimeric assistance[5].

We have investigated for the first time, the differential effects of solvents on ester hydrolysis proceeding with a participation by a neighbouring group. We report in this communication, the results obtained on the saponification of glycol monobenzoates, in which a similar intramolecular stabilisation of the transition state by the neighbouring hydroxyl group is possible. The rate coefficients for the two steps of the alkaline hydrolysis of glycol dibenzoates were determined using the approach of Frost and Schwemer[6] and the rate constants for the second step of hydrolysis viz., the hydrolysis of monobenzoates are presented in the table below.

TABLE

Rate coefficients for the alkaline hydrolysis of glycol monobenzoates at 30°C

Compound	10^3k litre mole^{-1} sec^{-1}			k_s	k_r
	80%EtOH	80%DMSO	80%Acetone		
Ethyl benzoate	1.47	173	5.95	118	4
Ethyleneglycol monobenzoate	0.625	626	39.1	1000	62
Neopentylglycol monobenzoate	0.986	219	8.81	220	9
Butan 1:4 diol monobenzoate	1.12	124	5.59	112	5

$k_s = k_{DMSO}/k_{EtOH}$ $k_r = k_{acetone}/k_{EtOH}$

We notice here that the reactivity pattern itself changes on changing the solvent. This novel finding can be rationalised in terms of the solvation of the transition state by the three solvents.

It is now well established that the transition state for the basic hydrolysis of esters has a negative charge localised on the carbonyl oxygen atom making this a good hydrogen bond acceptor[7] and hence solvated by protic solvents which are good hydrogen bond donors. In the case of ethyleneglycol monobenzoate, the negative charge on the carbonyl oxygen atom in the transition state is decreased by diffusion through intramolecular hydrogen bond formation as in (I) and consequently the transition state is considerably less solvated

by ethanol whereas there is a greater localisation of the negative charge on the carbonyl oxygen in the transition state for ethyl benzoate hydrolysis. This explanation is further justified by our finding that ethyleneglycol monoacetate is hydrolysed faster than ethyl acetate in water, but slower in aqueous ethanol. Typically at 25°C the rate constants for the hydrolysis of ethyleneglycol monoacetate and ethyl acetate in water are 0.227 and 0.111[8] and in 60% aqueous ethanol at 30°C are 0.018 and 0.027 litre $mole^{-1}$ sec^{-1} respectively.

The increased reactivity of neopentylglycol monobenzoate compared to ethyleneglycol monobenzoate in aqueous ethanol is due to the cumulative effect of two factors 1) the intramolecular hydrogen bonding in the transition state decreases because of the greater separation of reacting groups, thus making the transition state a better hydrogen bond acceptor to the solvent and 2) the increasing steric effects with the introduction of two methyl groups resulting in the "loosening up" of the transition state[9] and thus increasing its solvation by a protic solvent.

The near reactivity of butan 1:4 diol monobenzoate to ethyl benzoate is not surprising as there will be absolutely no <u>internal</u> hydrogen bonding stabilisation of the transition state. Consequently in aqueous DMSO also the same pattern of reactivity is observed with the ratios k_{DMSO}/k_{EtOH} being nearly the same.

However, in aqueous DMSO, we notice that ethyleneglycol monobenzoate and neopentylglycol monobenzoate are hydrolysed <u>faster</u> than ethyl benzoate. This behaviour is to be traced to the stabilisation of the transition state by the dipolar aprotic solvent DMSO. As stated earlier in the discussion, the negative charge on the carbonyl oxygen in the transition state is decreased by intramolecular hydrogen bonding and consequently this transition state has a charge distribution similar to that of a S_N2 one, unlike in the case of hydrolysis of normal esters, in which there is a localisation of a negative charge on the oxygen atom. It is well documented that bimolecular reactions, involving anions, passing through such transition states are considerably accelerated by a change from protic to dipolar aprotic solvent. This hypothesis is confirmed by

the high k_s value (1000) we have observed for the saponification of ethyleneglycol monobenzoate. To our knowledge this is the first instance where a slight change in the structure of the reactant alters solvent effects in a dramatic manner. In the hydrolysis of neopentylglycol monobenzoate, as stated earlier, the hydrogen bonding interaction between the hydroxyl group and the oxygen atom in the transition state decreases, thereby reducing the stabilisation of the transition state by DMSO and as a result the reactivity as well as the k_s value drops considerably. In the case of butan 1:4 diol monobenzoate there is no internal hydrogen bonding facilitation of the transition state and the k_s value is nearly the same as that for ethyl benzoate.

In acetone, another dipolar aprotic solvent, the same type of reactivity as in DMSO is observed. Of course the transition state stabilisation in acetone will be lower than with DMSO and hence the $k_{acetone}/k_{EtOH}$ values are lower than k_{DMSO}/k_{EtOH} values.

The present investigations therefore clearly indicate that the transition state solvation has an important part to play and this novel solvent dependency of reactivity pattern can be rationalised only in terms of transition state solvation.

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