Reactions of Carbonyl Compounds in Basic Solutions. Part 18.[1] The Mechanisms of the Alkaline Hydrolysis of Methyl Benzil-2-carboxylates and 2-Phenylacetylbenzoates

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Rate coefficients have been measured for the alkaline hydrolysis of methyl 3′- and 4′-substituted benzil-2-carboxylates at 21.0 °C and methyl 2-(3- and 4-substituted phenylacetyl)benzoates at 24.0 °C in 70% (v/v) dioxane–water. Those for the two parent esters were also measured at several temperatures and the enthalpies and entropies of activation have been evaluated. The relative rates of hydrolysis, activation parameters and substituent effects have been used to demonstrate neighbouring group participation by keto-carbonyl groups in the alkaline hydrolysis of the esters under study. For the methyl benzil-2-carboxylates, the α-carbonyl group appears to participate by means of an intermediate having a five-membered ring.

A large number of studies[2] of neighbouring group participation by suitably situated carbonyl groups in the alkaline hydrolysis of esters have been made. The criteria used to detect such intramolecular catalysis have been varied and include significant rate enhancements,[3,4] distinctive activation parameters,[4,5] leaving group effects,[6,7] Hammett reaction constants[4,8] and ^{18}O labelling studies.[6,9,10] The carbonyl groups involved include formyl and varied keto substituents with exocyclic or endocyclic reactions involved. The rate determining step can be either the formation of the initial adduct at the carbonyl group or the intramolecular nucleophilic attack of the latter adduct on the ester group.

We describe here the alkaline hydrolysis of a series of methyl 3′- or 4′-substituted benzil-2-carboxylates and 2-(3- or 4-substituted phenyl) acetylbenzoates in aqueous dioxane.[11] The effects of substitution, relative rates and activation parameters are discussed in terms of a detailed mechanism.

Experimental

Materials.—The preparation of the normal methyl 2-(3- and 4-substituted phenyl)acetylbenzoates has been described previously.[12] The methyl 3′- or 4′-substituted benzil-2-carboxylates were prepared by esterification of the corresponding acids with diazomethane in ether and these normal esters are reported in a related study.[13]

The solvents for the kinetic studies were prepared as previously described.[6]

Measurements.—Rate coefficients for the alkaline hydrolysis of the esters were determined spectrophotometrically by use of a Perkin-Elmer lambda 5 UV–VIS spectrometer. The reactions were followed at 339–357 nm (2-phenylacetylbenzoate esters) and at 280–295 nm (benzil-2-carboxylate esters). The procedure used was that described previously.[7] The products of the reactions were found to be the anions of the corresponding acids in quantitative yield in all cases and were further confirmed spectrophotometrically by comparison of the spectrum of the acid in base with that of the reaction product.

Results

The alkaline hydrolysis of the methyl esters is of first-order both in ester and in hydroxide anion. Rate coefficients for alkaline hydrolysis of methyl 2-(substituted phenylacetyl)-benzoates at 24.0 °C and substituted benzil-2-carboxylates at 21.0 °C in 70% (v/v) dioxane–water are shown in Table 1 and, for the parent esters, at several temperatures in Table 2. The activation parameters for the parent esters are shown in Table 3. Previous measurements[4] for methyl 2-phenylacetylbenzoate had been made by a conductivity method between 1 °C and 20 °C at much higher concentrations of substrate and base (0.01

Table 1 Rate coefficients (k_2) for the alkaline hydrolysis of methyl 2-(substituted phenylacetyl)benzoates and substituted benzil-2-carboxylates in 70% (v/v) dioxane–water[a]

	k_2/dm^3 mol^{-1} s^{-1}	
Substituent	Benzil-2-carboxylates at 21.0 °C	2-Phenylacetylbenzoates at 24.0 °C
H	1110	14.0_5
4-CH_3	485	8.20_5
3-CH_3	520	9.38
4-OCH_3	250	7.67
3-OCH_3	1380	15.7
4-Cl	1590	35.8_5
3-Cl	2840	49.9
4-Br	1460	39.9_5

[a] Rate coefficients were reproducible to within ±3%.

Table 2 Rate coefficients (k_2) for the alkaline hydrolysis of methyl 2-phenylacetylbenzoate and benzil-2-carboxylate in 70% (v/v) dioxane–water[a]

	k_2/dm^3 mol^{-1} s^{-1}	
T/°C	2-Phenylacetylbenzoate	Benzil-2-carboxylate
21.0		1110
24.0	14.0_5	
30.0	19.5	
31.0		1390
40.0	36.1	
42.5		1650
50.0	60.0	
60.0	105	

[a] See Table 1.

Table 3 Activation parameters for the alkaline hydrolysis of methyl 2-phenylacetylbenzoate and benzil-2-carboxylate in 70% (v/v) dioxane–water at 20.0 °C[a]

Ester	$\Delta H^{\ddagger}$/kcal mol^{-1} [c]	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1} [c]
2-Phenylacetylbenzoate	10.4 (13.3)[b]	−18 (−15)[b]
Benzil-2-carboxylate	2.80	−35

[a] Value of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are considered accurate to ±400 cal mol^{-1} and ±1 cal mol^{-1} K^{-1}, respectively. [b] Lit.[4] values (see text). [c] 1 cal = 4.184 J.

Table 4 Hammett reaction constants (ρ) for the alkaline hydrolysis of the methyl esters in 70% (v/v) dioxane–water[a]

System	ρ	$\log k_o$	*r*	*s*	*n*
3′- or 4′-substituted benzil-2-carboxylates at 21.0 °C	1.50	2.89	0.967	0.16	8
2-(3- or 4-substituted phenylacetyl)benzoates at 24.0 °C	1.43	1.17	0.963	0.16	8

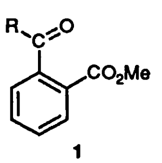
[a] *r* is the correlation coefficient, *s* the standard deviation and *n* the number of substituents used.

mol dm^{-3}). The agreement between the activation parameters shown in Tables 2 and 3 is not very good; but as would be expected in the particular circumstances.

Discussion

Reactivity and Structure of Benzil.—Benzil itself has a structure[14] that has been of interest for some while. The carbonyl groups in benzil are rotated about 110° from one another, with the phenyl rings nearby coplanar with the carbonyl groups. The carbonyl groups in benzil are highly reactive and benzil exchanges its oxygen in alkaline ^{18}O-enriched water very rapidly.[15] The latter reaction is very much faster than the benzilic rearrangement which occurs under much more vigorous conditions.[16,17] In effect, the reactivity of a carbonyl group of benzil is that of the benzoyl carbonyl group strongly activated by a powerfully electron-withdrawing benzoyl group. However, benzil is not significantly hydrated in aqueous solution,[18] but a compound of stoichiometry PhCOCOPh : KOH has been isolated.[19]

Alkaline Hydrolyis of Methyl Esters.—The rate of alkaline hydrolysis of methyl benzil-2-carboxylate is very rapid, *i.e.* k_2 at 20 °C in 70% (v/v) dioxane–water is 1.10×10^3 dm^3 mol^{-1} s^{-1}. A rate ratio for the hydrolysis of the latter ester to that of methyl benzoate[2,4] can be calculated as 1.3×10^5. For unassisted hydrolysis a rate ratio of *ca.* 15 might be expected on the basis of the known steric and polar effect of *ortho*-substituents on the alkaline hydrolysis of methyl benzoates.[20] Thus the enhanced ratio, r_e, of the benzil ester is 7.3×10^4 and can be compared to those derived from the effects of the *o*-formyl, -acetyl and -benzoyl groups on the hydrolysis of methyl benzoate, which are equal to 6.4×10^3, 760 and 5.6, respectively, under the same conditions.[2] The remarkable reactivity of the *o*-phenyloxoacetyl group must arise from the powerful electron-withdrawing effect of the benzoyl substituent on the neighbouring carbonyl group. It is now possible to extend the correlation[4] of the rates of alkaline hydrolysis of the system **1** using σ* and E_s for R, as shown in eqn. (1). The



1

$$\log(k/k_o) = 1.30(\pm 0.15)\,\sigma^* + 1.08(\pm 0.16)\,E_s + 2.00 \qquad (1)$$

$$n = 7, s = 0.32, r = 0.986$$

expected dependence on steric effects previously found is now complemented by a dependence on polar effects of the expected sign and a reasonable magnitude.[21] A closely related relation exists for the correlation of the equilibria hydration of carbonyl compounds which was reported by Bell[22] and is shown in eqn. (2) below. Both relations clearly demonstrate the inhibition of

$$\log K_H = 2.6\,\sigma^* + 1.3\,E_s - 2.70 \qquad (2)$$

formation of the tetrahedral state by steric crowding and enhancement of formation by electron-withdrawing substituents. The latter relations are also closely analogous to the defining reaction for both σ* and E_s, *i.e.* the alkaline hydrolysis of esters.[21]

The activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, for the hydrolysis of the benzil ester are shown in Table 3. The very small enthalpy of activation and more negative entropy of activation observed here appear to be characteristic for a class of esters undergoing intramolecular catalysis by carbonyl groups in which the rate determining step has been considered to be the addition of hydroxide anion to the acyl carbonyl group (*i.e.* k'_1 in Scheme 1). This is probably simplistic, but the evidence from leaving group studies of the alkaline hydrolysis of 3-substituted phenyl 2-acetylbenzoates,[8] in comparison to the corresponding 2-benzoylbenzoates, indicates that the negative charge is being developed on the keto-carbonyl group as the hydroxide develops its bond to the carbonyl carbon for the 2-acetyl system. The 2-acetyl system displays the pattern of enthalpy and entropy observed also for the 2-phenyloxoacetyl substituent.

Hammett Reaction Constants.—The effects of substitution on the alkaline hydrolysis of both methyl 3′- or 4′-substituted benzil-2-carboxylates and 2-(3- or 4-substituted phenylacetyl)-benzoates have been investigated and have been correlated successfully by the Hammett equation, but use of the substituent constants σ.[23] The correlations are shown in Table 4 and the ρ values for the benzil and 2-phenylacetyl esters in 70% (v/v) dioxane–water are 1.52 at 21 °C and 1.43 at 24 °C, respectively. The corresponding ρ values found for the alkaline hydrolysis of methyl benzoates and 2-(3- and 4-substituted benzoyl)-benzoates in the same medium at 30 °C are 2.20 and 2.07, respectively.[6] Attack by hydroxide at the keto carbonyl group for the 2-phenylacetyl system would be predicted to give a ρ of *ca.* 1.1 and at the α-carbonyl group of the benzil-2-carboxylates a ρ of *ca.* 1.5, using the transmission factors previously found for the C_{sp^3} and C_{sp^2} links,[24] respectively. The latter results appear to be in agreement with the pathway shown in Scheme 1 involving a five-membered intermediate.† A five-membered cyclic tautomer appears to occur in the ring-chain tautomerism of benzil-2-carboxylic acids.[13,25] Furthermore, intramolecular nucleophilic participation in base-catalysed reactions of 2,2′-di(bromomethyl)benzil involves the formation of five-membered rings.[26] A study[27] of the alkaline hydrolysis of methyl 3-benzoylpropionates, 4-benzoylbutyrates and 5-benzoylvalerates indicated that significant neighbouring group participation occurs only in the former system, which involves a five-membered ring intermediate.

Mechanistic pathway.—The reaction pathway is shown in Scheme 1 and involves a five-membered ring intermediate. The

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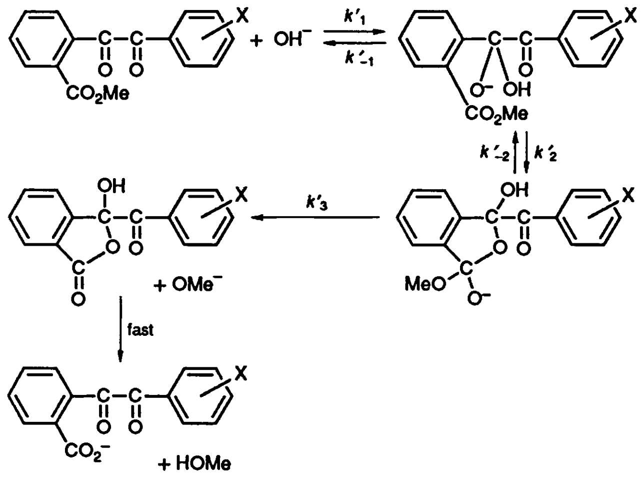
† However, the range of substituents studied is limited and, if more powerfully electron-withdrawing substituents were included, the result might differ.



Scheme 1

rate determining step for these esters could be either the formation of the initial adduct, k_1', or the intramolecular nucleophilic attack, k_2'. Thus, for the very reactive 2-formyl and 2-acetyl systems,[2,8,10] the former appears to be the case; whereas, for the less reactive 2-benzoyl system,[2,8] the latter appears to occur. The high reactivity of the benzil esters, as well as the pattern of activation parameters found, indicates that the rate determining step is likely to be k_1'.

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Paper 2/05039K
Received 21*st September* 1992
Accepted 14*th October* 1992