Neighbouring Group Participation by a Carbonyl Group in the Hydrolysis of Methyl Benzil-2-carboxylates

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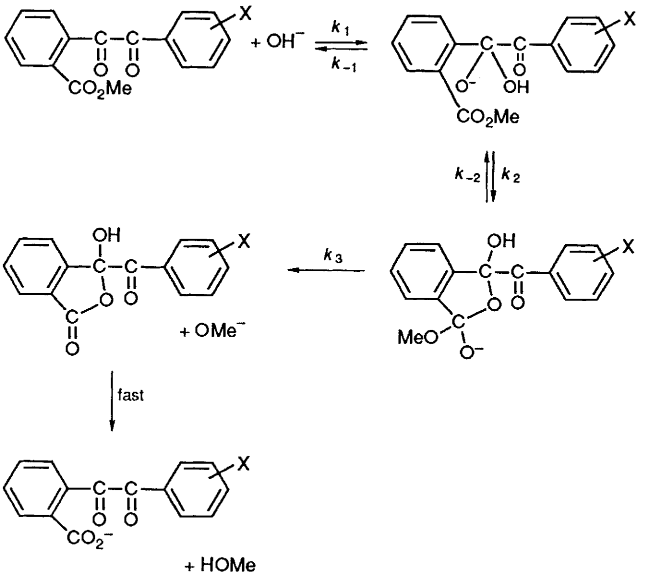
Intramolecular catalysis by the neighbouring carbonyl group occurs in the alkaline hydrolysis of methyl benzil-2-carboxylates. The α-carbonyl group participates by giving rise to an intermediate having a five-membered ring.

Neighbouring group participation by suitably oriented carbonyl groups in the alkaline hydrolysis of esters has been clearly established by various criteria.[1] These include significant rate enhancements,[2,3] distinctive activation parameters,[3,4] Hammett reaction constants,[5,6] leaving group effects [3,7] and ^{18}O labelling studies.[5,8,9] Such participation has been found in a wide variety of systems having keto or formyl substituents, in which initial attack of hydroxide anion occurs at the acyl carbonyl group.[1] The present investigation demonstrates for the first time such intramolecular catalysis in the alkaline hydrolysis of esters of benzil-2-carboxylic acid. The group participating is the 2-phenyloxoacetyl substituent. The addition of nucleophiles to benzil is known to be facile.[10] In this system the ring-size of the intermediate could be either five- or six-membered and the reaction is exocyclic.

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}. This represents a rate ratio for the hydrolysis of the latter ester, compared to methyl benzoate, of 1.3×10^5. However, for unassisted hydrolysis a rate ratio of *ca.* 15 might be expected on the basis of the known steric and polar effects of *ortho*-substituents on the alkaline hydrolysis of methyl benzoates.[11] Furthermore, the activation parameters, $\Delta H^\ddagger$ and $\Delta S^\ddagger$, for the hydrolysis of the benzil ester at 20 °C in 70% (v/v) dioxane–water are 2800 cal mol^{-1} and -35 cal mol^{-1} K^{-1}, respectively.† Such small enthalpies of activation and more negative entropies of activation appear to be characteristic for a class of esters undergoing intramolecular catalysis by carbonyl groups.[1,3,4] 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. The Hammett reaction constants, ρ, for the benzil and 2-phenylacetyl esters in 70% (v/v) dioxane–water are *ca.* 1.52 at 21 °C and 1.43 at 24 °C, respectively. The corresponding ρ values found for the hydrolysis of methyl benzoates and methyl 2-(3- and 4-substituted benzoyl)benzoates in the same medium at 30 °C are 2.20 and 2.07, respectively.[5] Both the 2-phenylacetyl and 2-benzoylbenzoate esters are hydrolysed with neighbouring group participation by the carbonyl group. However, in the former series, the effect of the substituted phenyl group is transmitted by a methylene link to the carbonyl group; whereas, in the latter series, the transmission to the carbonyl group is direct. A transmission factor of *ca.* 0.5 for methylene would be expected,[12] which is close to that observed. Thus, the result for the benzil ester is in accord with transmission of the substituent polar effect to the α-carbonyl group of the benzil-2-carboxylate.



Scheme 1

The reaction pathway, shown in Scheme 1, involves a five-membered intermediate. The rate determining step for these esters could be either the formation of the initial adduct, k_1, or the intramolecular nucleophilic attack, k_2. For very reactive 2-formyl and 2-acetyl systems,[1,7,9] the former would appear to be likely, whereas, for less reactive 2-benzoyl systems,[1,7] the latter appears to be the case. The reactivity and activation parameter evidence appears to indicate that the rate determining step for benzil esters is more likely to be k_1. A study[13] 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. A five-membered cyclic tautomer appears to occur in the ring–chain tautomerism of benzil-2-carboxylic acids.[14,15]

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† 1 cal = 4.184 J.

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