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Reactions of carbonyl compounds in basic solutions. Part 36:[†] The base-catalysed reactions of 1,2-dicarbonyl compounds[‡]

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ABSTRACT: 1,2-Dicarbonyl compounds can undergo base-catalysed reactions in three ways: rearrangement of the benzil–benzilic acid type, fission of the carbon–carbonyl carbon bond and fission of the carbonyl carbon–carbonyl carbon bond. The requirements for the observation of the variant reaction types are discussed *both* for open-chain *and* for ring systems in terms of electronic and stereochemical factors. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: 1,2-dicarbonyl compounds; base-catalysed rearrangement

The present communication is an attempt to review and interpret the base-catalysed reactions of 1,2-dicarbonyl compounds, particularly with regard to the effects of substituents and ring formation on the course of the reactions. The reactivity of 1,2-dicarbonyl compounds **1** with base can be related, in the first instance, to the powerful activation of *one* electron-withdrawing carbonyl group on the other towards nucleophiles. The first reaction is to form a relatively stable adduct of the 1,2-dicarbonyl compound with the base **2**. Further reaction can occur in three ways (Fig. 1):

(i) rearrangement of the benzil–benzilic acid type, with migration of R in **2** to form **3**;
(ii) fission of the R carbon–carbonyl carbon bond to form **5** and **6**; and
(iii) fission of the carbonyl carbon–carbonyl carbon bond to form **7** and **8**.

Benzils react in all three ways with base.[1] The benzil–benzilic acid rearrangement (case (i)) has been examined using an extensive range of physical organic techniques.[2–4] This occurs for benzils with ring substituents that are 'moderately' either electron-withdrawing or electron-releasing. We have attempted separation of the effects of *meta-* and *para*-substituents in both phenyl rings into the Hammett reaction constant: for overall migration $\rho_b \approx 3.8$; for non-migration $\rho_a \approx 1.8$.[1] However, others have criticized our assumption of additivity of ρ values on the basis of a theoretical treatment.[5] The latter study is unadorned by any experimental evidence. Furthermore, it refers to a cross-interaction term ρ_{ab}, whereas, in a previous review, Lee[6] indicates such a term is equal to zero for the only reaction reviewed analogous to the base-catalysed benzil–benzilic acid rearrangement, *i.e.* the alkaline hydrolysis of *meta/para*-substituted phenyl *meta/para*-substituted benzoates in which additivity was observed.[7] Approximate additivity in Hammett-type correlations has been observed for other analogous reactions by Exner.[8] In a reactivity–selectivity analysis by Johnson,[9] additivity of reaction constants in several analogous reactions has been demonstrated. However, our study[1] demonstrates unequivocally the overriding importance of 'moderately' electron-with-

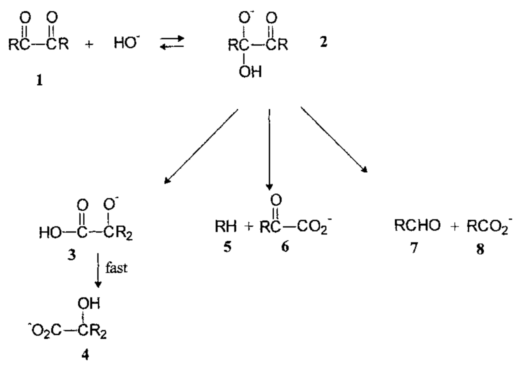

Figure 1. Reaction of 1,2-dicarbonyl compounds with base

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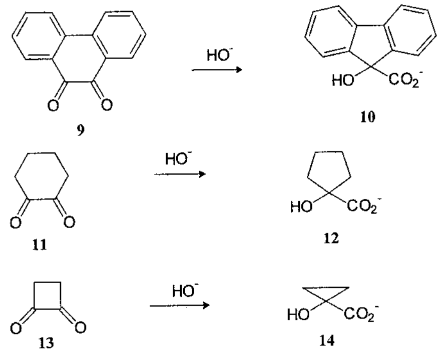
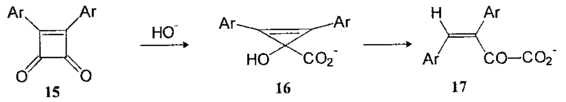
drawing substituents in facilitating the benzil–benzilic acid rearrangement.

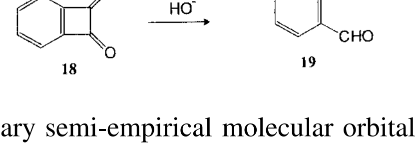
More recently the effects of the 1,2-dicarbonyl groups being part of ring have been systematically examined.[10–12] Early studies[2,3] demonstrated the benzil–benzilic acid type rearrangement (case (i)) of, among others, 9,10-phenanthraquinone (**9**) to 9-hydroxyfluorene-9-carboxylic acid (**10**) (six- to five-membered ring contraction) and cyclohexane-1,2-dione (**11**) to 1-hydroxycyclopentane-1-carboxylic acid (**12**) (six- to five-membered ring contraction). The base-catalysed reaction of cyclobutane-1,2-diones (**13**) has been demonstrated to produce 1-hydroxycyclopropane-1-carboxylic acids (**14**) (case (i)) (four- to three-membered ring contraction).[13]



Nevertheless, the reaction of 3,4-diphenyl-cyclobut-3-ene-1,2-diones (**15**) gives (*Z*)-2-oxo-3,4-diphenylbut-3-enoic acids (**17**) (four-membered ring to open chain) (*apparently* case (ii)). However, the mechanistic pathway proposed[12] involves the formation of 1-hydroxy-2,3-diphenylcycloprop-2-ene-1-carboxylic acids (**16**) (*actually* case (i)), *prior* to ring fission.

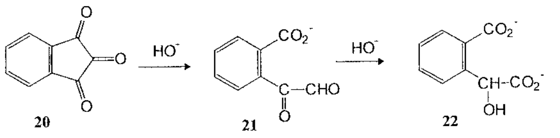


The base-catalysed ring fission of related 2,3-diphenylcyclopropen-1-ones has been shown to be a comparatively facile process.[14] In contrast, benzocyclobutene-1,2-diones (**18**) suffer base-catalysed ring fission to form 2-formylbenzoic acids (**19**) (case (iii)). There is *no* evidence for an intermediate involving ring contraction in this reaction.

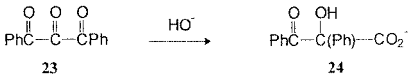


Preliminary semi-empirical molecular orbital calculations[15] using the AM1 Hamiltonian[16,17] on the mechanism of ring fission of **18** clearly indicate that breaking of the carbonyl carbon–carbonyl carbon bond has a significantly lower barrier ($\sim$ 4 kcal mol^{-1}) than breaking of the aryl carbon–carbonyl carbon bond. Thus, according to these calculations, case (iii)-type ring fission should be greatly favoured over case (i)-or case (ii)-type reactions. The situation appears to be more complex for 3,4-diaryl-cyclobut-3-ene-1,2-diones (**17**). According to the calculations, ring opening of the proposed 1-hydroxycycloprop-2-ene-1-carboxylic acid intermediate **16** indeed appears to be quite facile. However, until now, localization of the transition state for formation of this compound has been elusive. *Ab initio*,[18] or, more precisely, hybrid density functional theory/HF calculations using Becke's three-parameter density functional[19] with the Lee–Yang–Parr correlation functional (B3LYP/6-311 ++ G**)[20] on a simplified model system (cyclobut-3-ene-1,2-dione) led to similar results.[21]

Indane-1,2,3-trione (**20**), as the hydrate (ninhydrin), rearranges in base to give *ortho*-carboxymandelic acid (**22**) as the *final* product; but the intermediate product has been shown to be *ortho*-carboxyphenylglyoxal (**21**) (five-membered ring to open chain).[10]



Thus, in this pathway, the first step is the fission of carbonyl carbon–carbonyl carbon (case (iii)), which is followed by an intramolecular Cannizzaro reaction. There is *no* evidence for an intermediate formed by a benzil–benzilic acid type rearrangement involving a ring contraction. This is in contrast to the rearrangement of the related open-chain compound, 1,3-diphenylpropane-1,2,3-trione (**23**), to give 2-benzoylmandelic and **24** (case (i)) by a benzil–benzilic acid type rearrangement, before reacting further.[2]



$$\overset{O}{\overset{\|}{\mathrm{PhC}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{Ph} \xrightarrow{HO^-} \overset{O}{\overset{\|}{\mathrm{PhC}}}-\overset{OH}{\overset{|}{\mathrm{C}}}(\mathrm{Ph})-CO_2^-$$

23 24

Thus, all three ways of reaction, cases (i), (ii) and (iii), can be *apparently* observed in systems in which the 1,2-dicarbonyl groups are part of a ring; but only cases (i) and (iii) are *actually* observed in the mechanistic sense. The observation of a rearrangement of the benzil–benzilic acid type appears to be the norm for such ring systems. However, when *very* excessive ring angle strain in a fused bicyclo system, such as **18**,[11] would occur in a rearrangement of the type of case (i), the system responds by effecting fission of the carbonyl carbon–carbonyl carbon link (case (iii)). When *both* the potential migrating *and* receiving groups are carbonyl groups held in a rigid ring and they are *cisoid* to each other, as in **20**, reaction does *not* proceed *either* by addition of the nucleophile to the 2-carbonyl group of the 1,2,3-tricarbonyl compound, followed by migration of the 1-

carbonyl group causing ring contraction, *or* by addition of the nucleophile at the 1-carbonyl group followed by migration of the aryl group causing ring contraction,[10] *both* giving rise to fused ring systems. In contrast, the former reaction path *does* occur for the open-chain analogue **22**.[1] Thus compound **20** responds to base-catalysed reaction by diverting to give carbonyl carbon–carbonyl carbon fission (case (iii)). The cause of this appears to lie in the stereochemical demands for a migration in **20**, which can involve both angular and ring strain.

Substituent effects on the base-catalysed reactions of **15**, **18** and **20** have been studied.[10–12] Separation of the effects into migration and non-migration contributions is neither possible nor meaningful. However, the Hammett reaction constant $\rho \approx 1.3$ for *para*-substitution in the 3- or 4-phenyl groups, as well as their equality, in **15** for the rates of reaction indicates the importance of electron-withdrawing substituents in facilitating the reaction and that the transition state structure is close to **16** in structure.[12] Study[11] of the effects of 4-substituents on the rates of reaction of **18** gave a Hammett reaction constant of *ca* 3.8, again clearly showing the powerful facilitation of the reaction by electron-withdrawing substituents comparable to that for overall migration in the reaction of benzil.[1] The effect of 5-substituents on the rates of the base-catalysed fission of **20** gave a Hammett reaction constant $\rho \approx 0.9$ to 1.4, showing yet again the facilitation of the reaction by electron-withdrawing substituents.[10]

Benzil has a structure in which the carbonyl groups are rotated about 110° from each other, with the phenyl rings nearly coplanar with the carbonyl groups.[22] Deslongchamps[23] has explicitly described the benzil–benzilic acid rearrangement as occurring with stereoelectronic control, with the most favourable path being that with the nucleophilic migrating phenyl group approaching the carbonyl group perpendicularly or close to that. Rotation about the carbonyl carbon–carbonyl carbon bond in the adduct **3** can facilitate this. However, in the systems in which the 1,2-dicarbonyl groups are part of a ring, their dicarbonyl structure will be *cisoid*, or close to that, having an unfavourable carbonyl dipole–dipole interaction, which has been significantly reduced in benzil by rotation. Some flexibility in the ring structures of the adducts of type **3** can assist in moving towards the most favourable path for stereoelectronic control in rearrangement, but such pathways cannot be ideal from the point of view of the latter control. Nevertheless, the systems **9**, **11**, **13**, and **15** suffer reasonably facile rearrangement of this type. Only systems **18** and **20** suffer ring fission rather than rearrangement. In both cases, the main factor giving rise to this is excessive fused ring strain.

Our conclusions are that both the course of and the facilitation of reactions in *both* open-chain and ring 1,2-dicarbonyl compounds by electron-withdrawing substituents arises from the stabilization of the adduct **3**, formed by the addition of the base, and of negative charge transferring in the transition state for rearrangement or fission. Furthermore, control of the course of reaction in compounds in which the 1,2-carbonyl groups are part of a ring depends, mainly, on the occurrence, or not, of excessive ring strain.

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