A Novel Decarboxylation of an α-Keto-ester: Methyl Phenylpyruvate

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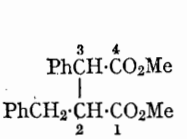
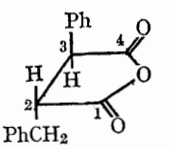
THE major neutral products of the sodium methoxide catalysed condensation of methyl phenylpyruvate in anhydrous dioxan have been shown to be the two diastereoisomers of dimethyl 2-benzylsuccinate (I), isomer A† (m.p. 86—88°, yield 49%) and isomer B (m.p. 121—123°, yield 41%). These compounds show virtually identical i.r., u.v., and mass spectral properties and the $CH_2{\cdot}CH{\cdot}CH{\cdot}$ groups form second-order ABCD systems which give rise to a complex series of signals between τ 5·9 and 7·5 in the n.m.r. spectrum of each isomer. However, differences occur in the n.m.r. signals associated with the aromatic and *O*-methyl protons. The aromatic region in the spectrum of isomer A shows one singlet (τ 2·66, 5H) and one complex band (centred at τ 2·80, 5H) whereas the spectrum of isomer B shows two singlets of equal intensity (τ 2·75, and 2·82) in this region. The two *O*-methyl signals from isomer A have normal chemical shifts (τ 6·38 and 6·42), but in the spectrum of isomer B the corresponding signals are at τ 6·36 and 6·85, showing that one *O*-methyl group is strongly shielded.

A mixture of two diastereoisomeric dicarboxylic acids, corresponding to the diesters A and B, was formed when either isomer A or B was hydrolysed with alkali. Presumably partial inversion at C(3) accompanied the hydrolysis in each case. The diacids were related to their corresponding esters by re-esterification with diazomethane. Under mild conditions (Ac_2O, room temp.) both diacids yielded the same anhydride, $C_{17}H_{14}O_3$ [m.p. 53—55, ν_{max} (CCl_4) 1785 and 1865 cm.$^{-1}$], which regenerated only the acid from isomer A on mild hydrolysis. We regard this anhydride as the more stable *trans*-anhydride (II), formed in the case of the diacid from isomer B by inversion of the highly hindered *cis*-anhydride at C(3), and on this basis formulate isomer A as the *threo*-diester

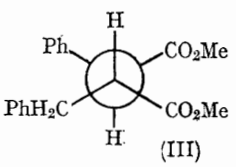


(I)

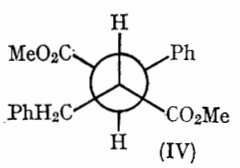


(II)

(III) and isomer B as the *erythro*-diester (IV). A similar conclusion is reached if it is assumed that the most stable conformation of each diester is a staggered conformation in which the four bulky substituents are arranged in two *trans*-diaxial pairs, as shown in (III) and (IV). Models indicate that the strong shielding of a methoxy-group, observed in isomer B, will occur only when the phenyl ring of the benzyl group and the C(4) ester group are juxtaposed as in (IV). Both diesters have been synthesised by a structurally unambiguous route.



(III)

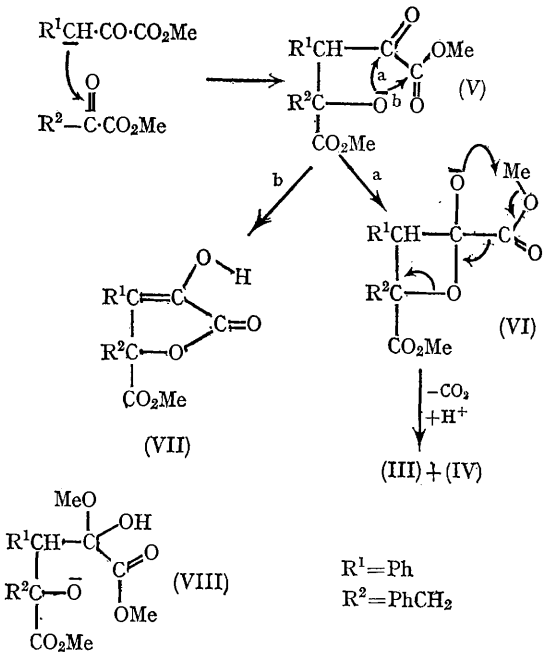


(IV)

The dimerisation and remarkable decarboxylation which lead to the formation of these products from the phenylpyruvate ester can be rationalised

† Satisfactory elemental analyses have been obtained for all new compounds reported.

in terms of the mechanism outlined in the scheme below.



An aldol condensation is followed by an intramolecular nucleophilic attack (a) on the highly electrophilic carbon of the carbonyl group. The anion formed (VI) displaces the carboxy-function from the methyl ester and the reaction to this stage can be regarded as an example of neighbouring group participation in an ester hydrolysis by alkyl oxygen fission. If this fission is part of a concerted process which also involves the loss of the carbon dioxide molecule and the opening of the four-membered ring, as indicated, it is probable that the relief of the strain in the ring facilitates the reaction.

No products associated with the intramolecular attack (b) on the ester carbonyl could be detected when dioxan was used as a solvent. However, when the reaction was carried out in anhydrous methanol the $\alpha\beta$-unsaturated γ-lactone (VII),[1] m.p. 156—158°, ν_{max} ($CHCl_3$) 1765 (C=O lactone str.) and 1745 cm.$^{-1}$ (C=O ester str.); λ_{max} (MeOH) 290 nm., log ϵ 3·26; λ_{max} (MeOH–NaOH) 330 nm., log ϵ 3·23, accounted for 30% of the neutral products (isomer A 41%, isomer B 28%). In methanol, the nucleophilicity of the anionic species would be considerably reduced by solvation but it seems unlikely that this would cause a marked change in the product ratio. The hydroxylic solvent may play a catalytic role in the rate-determining step of the lactonisation but we think that the principal cause of the change is solvation of the keto-group in (V) competing with the attack (a). In addition to reducing the rate of formation of (VI), the hemiacetal formed (VIII) could facilitate the lactonisation by the electrophilic participation of its hydroxy-group.[2]

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[1] *Cf.* I. H. Gault and R. Weick, *Compt. rend.*, 1920, **170**, 1392; **171**, 395.
[2] B. Capon, *Quart. Rev.*, 1964, **18**, 58.