684. *The Reactive Methyl Group of Ethyl β-Ethoxycrotonate.*

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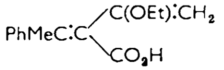
Base-catalysed condensation of ethyl β-ethoxycrotonate and acetophenone gives β-ethoxy-δ-phenylsorbic acid in two forms geometrically isomeric about the γδ-double bond.

The preparation of 1 : 3 : 5-triketones is of importance in connection with the acetate theory of biogenesis propounded by Birch *et al.*,[1] but cannot be achieved by Claisen condensations with ethyl acetoacetate because of inactivation of the ester and methyl groups in the enolate. Ethyl β-ethoxycrotonate is free from this drawback but has now been found to react at the active methyl group rather than at the ester group. Thus sodium hydride induced condensation of ethyl β-ethoxycrotonate with acetophenone, giving β-ethoxy-δ-phenylsorbic acid (I) in two isomers, A, m. p. 142°, $\lambda_{max.}$ (in EtOH) 231, 296 mμ (log ε 4·08, 4·20), and B, m. p. 108°, $\lambda_{max.}$ 230, 287 mμ (log ε 3·99, 4·20).

The absence of carbonyl groups was evident from the lack of reaction of either isomer with semicarbazide and similar carbonyl reagents, with sodium borohydride, and with ferric chloride. The carboxyl group was abnormal since it is vinylogous with carbonic acid but was clearly responsible for the very weak acidity (in 50% alcohol, isomer A had pK_a 6·85 and B had pK_a 6·98: benzoic acid has pK_a 5·55) and for the broad infrared absorption bands at 3 μ. The conjugated carboxyl group was also responsible for complex and intense absorption bands near 6·5 μ, and for the hypsochromic shift in the ultraviolet spectrum produced by alkaline alcohol in which compound A had $\lambda_{max.}$ 290 mμ (log ε 4·22) and B had $\lambda_{max.}$ 281 mμ (log ε 4·22).

$PhMeC\overset{a}{=}CH\cdot C(OEt)\overset{b}{=}CH\cdot CO_2H$

(I)



$PhMeC{:}C\begin{smallmatrix} \diagup C(OEt){:}CH_2 \\ \diagdown CO_2H \end{smallmatrix}$

(II)

$PhMeCH\cdot CH_2\cdot C(OEt){:}CH\cdot CO_2H$

(III)

The presence of a β-ethoxyacrylic acid system was disclosed by the stability of both isomers A and B to alkali, as opposed to their ready hydrolysis by cold dilute acids which gave oils initially giving a bluish-red ferric reaction but owing to decarboxylation affording the semicarbazone [2] of 4-phenylpent-3-en-2-one.

Care was taken to exclude structure (II) because this type of condensation product can be important and sometimes dominant.[3] Hydrogenation of isomers A and B gave the same dihydro-derivative (III), retaining a weakly acidic carboxyl group (pK_a in 50% alcohol, 7·02), having $\lambda_{max.}$ 238 mμ (log ε 4·11) similar to that of β-ethoxycrotonic acid [4] and yielding, by acid hydrolysis, 4-phenylpentan-2-one (carbonyl absorption at 1724 cm.$^{-1}$) characterised as the semicarbazone. Ozonolysis of this dihydro-derivative gave a neutral

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[1] Birch, Massey-Westropp, Rickards, and Smith, *J.*, 1958, 360.

[2] Ghate, Kaushal, and Deshapande, *J. Indian Chem. Soc.*, 1950, **27**, 633.

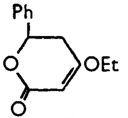
[3] Bohlmann, *Chem. Ber.*, 1957, **90**, 1519.

[4] Russoff, *J. Amer. Chem. Soc.*, 1945, **67**, 677.

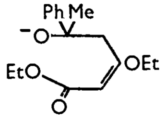
oil which on hydrolysis furnished β-phenylbutyric acid identified with authentic material [5] by means of the *S*-benzyl*iso*thiuronium salt, thus excluding structure (II) for either compound A or B.

Because the ultraviolet spectra precluded the existence of either isomer in the form of a lactone (IV), the isomerism must involve either or both the bonds (a) and (b); but it was difficult to define this further because both isomers gave the same dihydro-derivative (III) and 4-phenylpent-3-en-2-one. Since the inversions involved could have arisen either by 1 : 4-addition of hydrogen or by acid-catalysed rearrangement, configurations have been tentatively allocated by indirect means.

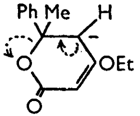
Reid and Ruby [6] obtained lactone (IV) from the Reformatsky reaction between benzaldehyde and ethyl γ-bromo-β-ethoxycrotonate and isomerised it with alkali to the corresponding acid [(I) H for Me]: these reactions are of course closely related to those now being discussed. Hydrolysis of β-alkoxyacrylates by the usual methods is difficult because of the reduced carbonyl character of the ester system, and under the conditions employed in this work ethyl β-ethoxycrotonate was hardly affected. Consequently the apparent hydrolysis of the ester group during the formation of acid (I) possibly results from the formation of ion (V) in which extrusion of ethoxide is aided by the stereochemical factor. The resulting lactone still possesses an active methylene group and with sodium hydride would yield the carbanion (VI) and thence the carboxylate without the intervention of hydrolysis.



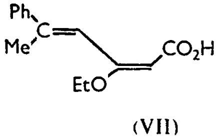
(IV)



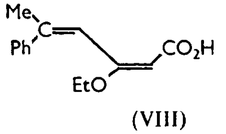
(V)



(VI)



(VII)



(VIII)

Because the electronic interaction of ethoxyl and carboxyl in the carboxylate is minimal, inversion at bond (b) would be most improbable, and therefore the above hypothesis requires both isomers to have ethoxyl *trans* to carboxyl. The isomerism is therefore confined to bond (a). Clearly, ring fission in the pyranone (VI) with phenyl in the quasi-equatorial position leads to an acid (I) in which phenyl is *cis* to hydrogen as in (VII), whereas with methyl in the quasiequatorial position ring fission leads to (VIII). The production of but one acid [6] from lactone (IV) is intelligible since in this lactone the form with a quasiequatorial phenyl group must predominate.

The solubilities, melting points, and ultraviolet spectra all indicate that isomer A should be allocated the more nearly "*trans*"-configuration and more highly conjugated structure. Therefore isomer A has structure (VII) and isomer B has structure (VIII).

EXPERIMENTAL

Isomers A and B of β-Ethoxy-δ-phenylsorbic Acid (I).—To sodium hydride (14·4 g.) in ether (1 l.) stirred under nitrogen were added ethyl β-ethoxycrotonate (32 g.) and acetophenone (24 g.) also in ether (200 ml.). After 9 hr. at the b. p. the orange mixture was freed from sodium hydride by water, and the ethereal layer was distilled, giving ethyl β-ethoxycrotonate, b. p. 99°/25 mm. (16 g.). When acidified at 10° by 2N-hydrochloric acid, the aqueous layer gave a solid (10·4 g.), separated by fractional crystallisation from light petroleum (b. p. 60—80°) into a less soluble component, *isomer A*, long needles, m. p. 142° (decomp.) (Found: C, 72·2; H, 7·2; OEt, 20·0. $C_{12}H_{11}O_2{\cdot}OEt$ requires C, 72·3; H, 6·9; OEt, 19·4%), and a more soluble component, *isomer B*, prisms, m. p. 108° (decomp.) (Found: C, 72·1; H, 7·1; OEt, 22·0%).

Hydrolysis of Isomers A and B.—When isomer A or B (1 g.) was shaken for 1 day with 2N-hydrochloric acid (80 ml.) it furnished an oil having a reddish-blue ferric reaction in alcohol and

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[5] Lipkin and Stewart, *J. Amer. Chem. Soc.*, 1939, **61**, 3295.

[6] Reid and Ruby, *ibid.*, 1951, **73**, 1054.

yielding the semicarbazone, m. p. 188° (Found: C, 66·2; H, 6·9; N, 19·1. Calc. for $C_{12}H_{15}ON_3$: C, 66·4; H, 7·0; N, 19·4%), of 4-phenylpent-3-en-2-one identical with an authentic specimen.[2]

3-*Ethoxy*-5-*phenylhex*-2-*enoic Acid* (III).—Isomer A or B (200 mg.) in ethyl acetate (50 ml.) containing palladium–barium sulphate (50 mg.) absorbed hydrogen (22 ml.) in 1½ hr., giving the *hexenoic acid,* which crystallised from light petroleum (b. p. 40—60°) and then aqueous alcohol in needles, m. p. 104—106° (Found: C, 72·0; H, 7·8; OEt, 19·6. $C_{12}H_{13}O_2{\cdot}OEt$ requires C, 71·8; H, 7·7; OEt, 19·2%).

Reactions of Acid (III).—(*a*) The acid (0·6 g.) was shaken with 2N-hydrochloric acid (100 ml.) for 1 day, giving an oil with a wine-red ferric reaction and furnishing the semicarbazone, m. p. 138° (Found: C, 65·2; H, 8·2; N, 19·8. Calc. for $C_{12}H_{17}ON_3$: C, 65·7; H, 7·8; N, 19·2%), of 4-phenylpentan-2-one.[7]

(*b*) The acid (0·3 g.) in ethyl acetate (40 ml.) at −10° was ozonised for 40 min. The residue after removal of the solvent was kept with warm water (25 ml.) and zinc dust. Next day the neutral fraction of the product was hydrolysed by 8% aqueous sodium hydroxide on the steam-bath for 4 hr., giving β-phenylbutyric acid as an oil which supplied the S-*benzyl*iso*thiuronium salt* in plates (from water), m. p. 148—149° (Found: C, 65·6; H, 6·3. $C_{18}H_{22}O_2N_2S$ requires C, 65·5; H, 6·7%), identified by the mixed m. p. and infrared methods with a sample prepared from authentic β-phenylbutyric acid.[5]

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[7] Chiang, *J. Chinese Chem. Soc.* (*Formosa*), 1951, **18**, 65.