133. *The Structure of the Glutaconic Acids and Esters. Part III. α-Carbethoxyglutaconic Esters.*

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IN Part I (Kon and Nanji, J., 1931, 560) it was shown that α-cyanoglutaconic esters can exist in αβ- and βγ-unsaturated varieties, usually in the form of equilibrium mixtures in which the βγ-compound predominates.

The corresponding carbethoxyglutaconic esters should by analogy exist in two forms (I) (αβ) and (II) (βγ), and their general behaviour

$(CO_2Et)_2C{:}CR{\cdot}CHR'{\cdot}CO_2Et$ (I.) $\qquad$ $(CO_2Et)_2CH{\cdot}CR{:}CR'{\cdot}CO_2Et$ (II.)

has now been shown to be similar to that of the cyano-esters, although no counterpart is found to the abnormal mode of alkylation of some of the latter.

Carbethoxyglutaconic esters are usually obtained in the form of equilibrium mixtures; these contain only a small amount of the αβ-form, as shown by the results of ozonisation: there is no quantitative method available for the estimation of the isomerides present, Linstead and May's iodometric method (J., 1927, 2565) being inapplicable to these substances. The proportion of the αβ-form, however, appears in all cases to be less than in the corresponding cyanoglutaconic esters—a not unexpected result in view of the great tendency of the α-cyano-group to form the conjugated or αβ-compound (compare Kandiah and Linstead, J., 1929, 2139; Linstead, *ibid.*, p. 2498).

Carbethoxyglutaconic esters react with sodium ethoxide, forming sodio-derivatives $(CO_2Et)_2CNa{\cdot}CR{:}CR'{\cdot}CO_2Et$ (the metal is represented as attached to carbon for the sake of simplicity); these in presence of water are dissociated, regenerating the ester, the extent of dissociation depending on the dilution and the acidity of the particular ester employed. A further, generally small, amount of ester can be obtained by saturating the alkaline solution, remaining after the removal of the first portion of ester, with carbon dioxide. The esters successively obtained in this way have been distinguished as "normal" and "labile" respectively (Bland and Thorpe, J., 1912, **101**, 871), although it has since been shown that the "normal" and the "labile" forms of the cyano-glutaconic esters are identical and represent equilibrium mixtures (Kon and Nanji, *loc. cit.*). In the instances now studied, only the "normal" ester is a true equilibrium mixture; the "labile" ester consists almost entirely

of the βγ-ester. If the ester is liberated from the sodio (or potassio)-derivative by means of a weak organic acid in a neutral solvent, the pure βγ-ester is obtained, showing that under these conditions only the keto-enol change proceeds to completion whilst the change involving the three-carbon system is arrested and a true equilibrium is not established (compare Hugh and Kon, J., 1930, 775; Kon and Nanji, *loc. cit.*). From the comparative ease with which this false equilibrium can be attained it can be concluded that the mobility of the carbethoxyglutaconic esters is not of a high order.

All the esters now studied alkylate on the α-carbon atom in agreement with the formulation of the sodio-derivatives given above. The parent member of the series, ethyl carbethoxyglutaconate (I; R = R′ = H), has been stated to alkylate in the γ-position (Thorpe, J., 1911, **101**, 249), but we were unable to investigate this reaction because we could not prepare the ester either by Thorpe's method or by that of Easterfield and Silberrad (J., 1904, **85**, 864). The crude ester obtained by the former method appeared to contain some of the glutaconic ester, as shown by the results of ozonisation; but the separation of the ester from the accompanying *cyclo*propane derivative was impracticable. The process of extraction with alkali recommended for the separation of the glutaconic ester must lead to its conversion (through the sodium derivative) into the equilibrium mixture, and this can be more readily obtained from the βγ-isomeride, ethyl *iso*aconitate (II; R = R′ = H). The latter ester decomposes on distillation and cannot be purified, but its oxidation products show that it is correctly represented by the βγ-formula; indeed, we were unable to identify any oxidation products derived from the αβ-form, probably because the ethyl mesoxalate, which should have been isolated, may have undergone further oxidation.

Ethyl *iso*aconitate readily forms an alkyl derivative, but alkylation takes place in the α-, not the γ-position: the structure of the product was confirmed by oxidation and by its behaviour with sodium ethoxide, a carbethoxyl group being eliminated with the production of ethyl α-methylglutaconate.

Of the β-substituted esters studied, ethyl α-carbethoxy-β-methylglutaconate (I and II; R = Me, R′ = H) presents several features of interest. It was originally prepared by Fichter and Schwab (*Annalen*, 1906, **348**, 251), who hoped to obtain two stereoisomeric forms of it by condensing ethyl sodiomalonate with ethyl β-chlorocrotonate and ethyl β-chloro*iso*crotonate respectively; on hydrolysis (with hot baryta) *both* preparations gave a mixture of the two β-methylglutaconic acids and therefore gave no clue to their configuration.

It is now found that the tricarboxylic esters so obtained show

small but distinct differences in physical properties; and hydrolysis under carefully regulated conditions leads to *different* acids. The acid, m. p. 149°, is the sole product derived from the *trans*-ester (from ethyl chlorocrotonate), whilst its isomeride, m. p. 115—116°, is produced from the *cis*-ester (from ethyl chloro*iso*crotonate); the latter is probably also identical with the condensation product of ethyl tetrolate with ethyl sodiomalonate. The density of the *trans*-ester is distinctly higher than that of the *cis*, which is contrary to the general rule, but perhaps too great an importance should not be attached to this observation in view of the complicated structure of the compound; and it must be remembered that a carboxyl group is lost in the course of the hydrolysis and this may well be the factor determining the configuration of the acid obtained. It is clear that Fichter and Schwab's failure to obtain the two stereoisomeric acids was due to the drastic method of hydrolysis adopted.

For ordinary purposes the ester is prepared from the mixture of *cis*- and *trans*-chlorocrotonic esters consisting mostly of the *cis*-ester; the condensation product closely resembles the ester obtained from pure ethyl chloro*iso*crotonate.

Ozonisation shows that this ester contains a small amount of the αβ-isomeride (II); the latter cannot exist in *cis*- and *trans*-forms and it is difficult to say which acid it should give on hydrolysis; but the amount present is small in any case.

The reaction of the ester with sodium ethoxide is of special interest in view of the abnormal behaviour encountered in the closely related α-cyano-β-methylglutaconic ester, which forms a γ-sodio-derivative and alkylates on the γ-carbon atom. No such abnormal features are encountered in the present instance, except that a small portion of the ester, presumably the αβ-ester contained in it, reacts with the loss of a carbethoxyl group (as ethyl carbonate), a behaviour which recalls that of ethyl α-cyano-βγ-dimethyl-Δ^{α}-propenedicarboxylate (Hope, J., 1922, **121**, 2216; Kon and Nanji, *loc. cit.*). The sodio-derivative formed from the remainder of the ester has the ordinary structure, gives an α-methyl derivative with methyl iodide, and when treated with benzoic acid regenerates the pure βγ-ester; the latter is quite free from the αβ-isomeride, because no trace of the easily detected ethyl acetoacetate is formed from it on oxidation with ozone.

The closely related β-phenylcarbethoxyglutaconic esters (I and II; R = Ph, R′ = H) are similar in their general behaviour. A remarkable feature of their chemistry is that the yellow crystalline sodio-derivative from which these esters are derived, and which is formed in the condensation of ethyl phenylpropiolate with ethyl sodio-

malonate in benzene (Michael, *J. pr. Chem.*, 1894, **49**, 20), appears to differ in constitution from those usually obtained. For instance, the ester is only slowly liberated from it by treatment with benzoic acid in dry ether and it cannot be methylated in a neutral solvent; methylation does, however, take place in boiling alcoholic solution (Thorpe and Wood, J., 1913, **103**, 1569). The ester liberated from it by means of mineral acids is a liquid, although it generally deposits a quantity of the solid ester, m. p. 38°, on keeping. Oxidation with ozone shows that, whilst the solid is the pure $\beta\gamma$-ester (II), the liquid contains some of the $\alpha\beta$-isomeride (I). The free ester forms a sodio-derivative which is practically colourless and from which the solid ester can be liberated with the aid of benzoic acid in a few minutes; it can, in addition, be readily methylated in a neutral solvent. The methylation product is in every case the compound obtained by Thorpe and Wood; and it has already been shown by Feist (*Annalen*, 1922, **428**, 25) that the alkyl group enters the α-position. This fact, together with the formation of the $\beta\gamma$-ester with benzoic acid, proves that the colourless sodio-derivative has the usual structure with the metal attached to the malonic residue (III). On the other hand, it seems probable that the yellow sodium compound first formed from ethyl sodiomalonate and ethyl phenylpropiolate has the metal attached to the other end of the chain (IV).

$(CO_2Et)_2CNa{\cdot}CPh{:}CH{\cdot}CO_2Et$ (III.) $\qquad$ $(CO_2Et)_2CH{\cdot}CPh{:}CNa{\cdot}CO_2Et$ (IV.)

The formula is similar to that originally proposed by Bland and Thorpe (J., 1912, **101**, 868) except for the position of the double bond, which these authors assume to be in the $\alpha\beta$-position. The reason for the formulation now suggested is that a similar condensation product can be prepared, although in poor yield, from ethyl phenylpropiolate and ethyl sodiomethylmalonate. This could give rise to either of the two sodio-derivatives (V) and (VI) according to whether the sodium or the methyl group of the addendum separated from the malonic residue:

$(CO_2Et)_2CMe{\cdot}CPh{:}CNa{\cdot}CO_2Et$ (V.) $\qquad$ $(CO_2Et)_2CNa{\cdot}CPh{:}CMe{\cdot}CO_2Et$ (VI.)

Oxidation of the resulting ester shows that the former assumption is correct; the sodio-derivative (V) cannot, of course, have the double bond in the $\alpha\beta$-position, and it is reasonable to suppose that the sodio-ester (IV) is produced in an analogous manner and has a similar structure.

If the above explanation be accepted, the behaviour of the yellow sodium compound (IV) becomes clear; the compound is not unlike

the well-known ethyl sodiodicarbethoxyglutaconate. The sodium is very strongly held and owing to the sparing solubility of the compound in neutral solvents it is not alkylated and is only slowly attacked by benzoic acid. In alcoholic solution it is evidently dissociated to some extent; the ester liberated can then react with sodium ethoxide to form the ordinary sodio-derivative (III), which is readily alkylated if a suitable reagent is present. The alkyl group accordingly enters the α-position even though the sodium was originally at the opposite end of the chain. The facts summarised above are in good agreement with Lapworth and Holden's explanation of the mechanism of some seemingly abnormal cases of the Michael reaction (J., 1931, 2368) and would appear to provide further experimental support for their views.

The formation of the sodio-derivative (IV) and of the corresponding compound from ethyl sodiomethylmalonate and ethyl phenylpropiolate is of great interest, especially in view of the more recent work on the mechanism of the Michael reaction (compare Holden and Lapworth, *loc. cit.*); it is hoped to subject them to further study.

Little need be said about the γ-alkylcarbethoxyglutaconic esters (I and II; R = H, R′ = Me, Et or CH_2Ph) except that they conform to the general description already given. Oxidation of the γ-benzyl esters shows, however, that the ordinary equilibrium ester contains, in addition to the isomerides (I and II; R′ = CH_2Ph), a third substance to which the formula

$$(CO_2Et)_2CH\cdot CH_2\cdot C(:CHPh)\cdot CO_2Et$$

must be assigned; it is recognised by the formation of benzaldehyde on oxidation with ozone. When the equilibrium ester is converted into the potassio-derivative and this is acidified with benzoic acid in a neutral solvent, the ester produced no longer contains the αβ-form (I) originally present, but some of the benzylidene ester is again formed. The formation of this compound is in every way analogous to that of the ester $CO_2Et\cdot CH_2\cdot CHMe\cdot C(:CHPh)\cdot CO_2Et$ observed by Kon and Watson (this vol., p. 1) and constitutes another example of the conversion of a true glutaconic system into a phenyl*iso*crotonic system.

In connexion with the present work we were asked by Prof. J. F. Thorpe, F.R.S., to repeat the work originally carried out by Thole and Thorpe (J., 1911, **99**, 2187) with the object of proving the identity of the α- and γ-positions of glutaconic acid. These authors found that if ethyl dicarbethoxyglutaconate is methylated in the α-position, the product treated with sodium ethoxide to remove the γ-carbethoxyl group, and the tribasic ester ethylated in the γ-position, the ester on hydrolysis gives the same α-methyl-γ-ethylglutaconic acid as the ester obtained by reversing this sequence

of operations, *i.e.*, that α-methyl-γ-ethyl- and α-ethyl-γ-methyl-glutaconic acid are the same substance, although it is clear that the tricarboxylic esters from which they are derived are different, being respectively

$CO_2Et{\cdot}CMe{:}CH{\cdot}CEt(CO_2Et)_2$ and $CO_2Et{\cdot}CEt{:}CH{\cdot}CMe(CO_2Et)_2$.

These two esters were prepared and treated with sodium ethoxide to obtain the dibasic esters. The two specimens had practically identical physical properties and proved, on oxidation with ozone, to consist of an equilibrium mixture of the two isomerides

$CO_2Et{\cdot}CMe{:}CH{\cdot}CHEt{\cdot}CO_2Et$ and $CO_2Et{\cdot}CEt{:}CH{\cdot}CHMe{\cdot}CO_2Et$.

It is clear that interconversion of the dibasic esters occurs as soon as they are liberated from the sodio-derivatives formed on elimination of the carbethoxyl group; and a similar interconversion occurs on hydrolysis of the isomeric tricarboxylic esters to the dibasic acids. Their formation cannot, therefore, be used to prove or disprove the identity of the α- and γ-positions in glutaconic acid. We have made numerous attempts to convert the pure α-methyl-γ-ethylglutaconic acid into an individual ester with the view of ascertaining the position of the double bond by oxidation with ozone; in spite of all precautions the ester obtained was in every case a mixture of two forms.

EXPERIMENTAL.

Ethyl Δ^{β}*-Propene-*αα*γ-tricarboxylate* (*Ethyl* iso*Aconitate*) (II; R = R′ = H).—This ester was prepared by the method of Guthzeit and Dressel (*Ber.*, 1889, **22**, 1413); we were unable to purify it by distillation, as it decomposed even under 2 mm. pressure.

Ozonisation. A solution of the ester (10 g.) in 30 c.c. of ethyl acetate was treated at 0° with ozonised oxygen until no more was absorbed, the ozonide freed from solvent under reduced pressure and decomposed by shaking with cold water over-night, and the products dissolved in ether. The extract was shaken with dilute sodium bicarbonate solution, dried, and evaporated, and the residue distilled, the following fractions being obtained at 16 mm.: (1) below 40°, (2) 50—65°, (3) 65—90°. The lowest fraction (a few drops) gave no colour with ferric chloride, and with phenylhydrazine yielded the orange phenylhydrazone of ethyl glyoxylate, m. p. and mixed m. p. 157° (Found: N, 14·4. Calc.: N, 14·6%). Fraction (3) gave a deep red colour with ferric chloride and a phenylhydrazone, m. p. 129°, which was identified as that of ethyl formylmalonate. The intermediate fraction was a mixture from which both the above phenylhydrazones were isolated. The aqueous and the bicarbonate washings contained oxalic acid. The products were thus derived from the βγ-form of the ester.

Methylation. Ethyl *iso*aconitate (39 g.) in alcohol (35 c.c.) was added to a solution of 3·5 g. of sodium in 45 c.c. of alcohol, the solution assuming a deep orange colour; 23 g. of methyl iodide were then added and the mixture was refluxed for 12 hours. Water was added and the oil was taken up in either, washed alternately with sodium hydroxide solution and water until the alkali was no longer coloured, and then dried, and evaporated. The residue of ethyl α-methyl-Δ^{β}-propene-ααγ-tricarboxylate, b. p. 168—169°/9 mm., had $d_4^{20\cdot0°}$ 1·0778, $n_D^{20\cdot0°}$ 1·4520, and $[R_L]_D$ 68·12.

Ozonisation. The methylated ester, ozonised exactly as described on p. 1032, gave two main fractions: (1) 40—60°/35 mm., (2) 60—80°/20 mm., neither of which gave a colour with ferric chloride. The low fraction contained ethyl glyoxylate (phenylhydrazone, m. p. 157°) and the second was evidently ethyl α-formylmethylmalonate. It was characterised by its *phenylhydrazone*, m. p. 128° (Found: C, 62·0; H, 6·9. $C_{15}H_{20}O_4N_2$ requires C, 61·6; H, 6·9%).

Action of sodium ethoxide. The methylated ester (27 g.) in 30 c.c. of alcohol was added to 2·3 g. of sodium dissolved in 25 c.c. of alcohol. The solution, which developed an odour of ethyl carbonate and became deep orange, was poured into dilute hydrochloric acid after an hour, and the ester isolated by means of ether. On distillation, some ethyl carbonate was first collected, then a fraction, b. p. 130°/15 mm., $d_4^{20\cdot0°}$ 1·0336, $n_D^{20\cdot0°}$ 1·4482, $[R_L]_D$ 65·29, consisting of ethyl α-methylglutaconate (Found: C, 59·8; H, 8·0. Calc.: C, 60·0; H, 8·0%); on hydrolysis with hydrochloric acid this gave α-methylglutaconic acid, m. p. and mixed m. p. 145—146°

Ethyl Δ^{α}-*Propene-ααγ-tricarboxylate* (I; R = R′ = H).—Easterfield and Silberrad's preparation (*loc. cit.*) was repeated several times without success, all the fractions obtained on distillation consisting either of ethyl propane-ααγ-tricarboxylate or of mixtures of this with esters containing bromine. Attempts to substitute ethyl sodiomalonate for the sodio-derivative of the tricarboxylic ester were also unsuccessful, ethyl ethanetetracarboxylate being one of the products isolated.

Thorpe's method (*loc. cit.*) gave variable results; in a large number of experiments the *cyclo*propane derivative was the sole product obtained and a satisfactory separation of the glutaconic derivative was impossible. The fraction, b. p. 183°/15 mm. (slight decomp.), appeared to contain some of the desired ester, as it gave, on ozonisation, in addition to a small indefinite fraction, b. p. 80—100°/20 mm., a greenish-yellow oil, b. p.. 100—111°/20 mm., which developed no colour with ferric chloride and was converted, on shaking with water and evaporation of the aqueous solution,

into crystals of ethyl mesoxalate hydrate, m. p. 59° (Found: C, 43·9; H, 6·2. Calc.: C, 43·7; H, 6·2%).

Ethyl α-Carbethoxy-β-methylglutaconate (I and II; R = Me, R′ = H).—This ester was prepared, as described by Fichter and Schwab (*loc. cit.*), from the mixture of ethyl β-chlorocrotonate and ethyl β-chloro*iso*crotonate obtained from phosphorus pentachloride and ethyl acetoacetate (Thomas-Mamert, *Bull. Soc. chim.*, 1895, **13**, 70), the yield being 50%; this could be raised to 65% by employing two molecules of ethyl malonate. The ester had b. p. 170°/14 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0912, $n_D^{20\cdot0^\circ}$ 1·4581, and $[R_L]_D$ 68·07.

Ozonisation. The ester was ozonised as described on p. 1032 and gave, in addition to oxalic acid, the following fractions at 12 mm.: (1) below 40°, (2) 74—100°, (3) 100—120°, (4) 120—150°. Fraction (1) contained ethyl glyoxylate (phenylhydrazone, m. p. 157°). Fraction (2) gave a deep red colour with ferric chloride and consisted mainly of ethyl acetoacetate, identified in the form of phenylmethylpyrazolone. Fraction (3) was deep yellow, gave no colour with ferric chloride, and consisted of ethyl mesoxalate, from which the solid hydrate was readily obtained. The last fraction gave with ferric chloride a deep red colour due to ethyl acetylmalonate (semicarbazone, m. p. and mixed m. p. 106—107°; β-acetphenylhydrazide, m. p. 128·5°).

Ethyl β-Methyl-Δ$^\beta$-propene-ααγ-tricarboxylate (II; R = Me, R′ = H).—The above equilibrium ester was converted into the potassio-derivative, and this treated with benzoic acid as described by Kon and Nanji (*loc. cit.*, p. 569), except that petroleum (b. p. 40—60°) was used to precipitate the potassio-derivative; the ester had b. p. 139°/2 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0892, $n_D^{20\cdot0^\circ}$ 1·4566, and $[R_L]_D$ 68·01. When the equilibrium ester is converted into the sodio- or potassio-derivative, especially in alcoholic solution, a small amount of ethyl carbonate is usually formed, together with the corresponding dibasic ester. When the solution is poured into water the equilibrium ester is recovered unchanged ($d_{4^\circ}^{20\cdot0^\circ}$ 1·0853, $n_D^{20\cdot0^\circ}$ 1·4555) without much loss.

Ozonisation. In addition to oxalic acid, only ethyl glyoxylate and ethyl acetylmalonate were produced, so the compound was evidently the pure βγ-form.

Methylation. The equilibrium ester was methylated in alcoholic solution as described on p. 1033; the reaction appeared to be complete in about an hour. The product, ethyl αβ-dimethyl-Δ$^\beta$-propene-ααγ-tricarboxylate, had b. p. 132—133°/2 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0786, $n_D^{20\cdot0^\circ}$ 1·4575, and $[R_L]_D$ 72·33. The same product was obtained by boiling the pure potassio-derivative of the βγ-ester with methyl iodide in benzene solution for some hours ($d_{4^\circ}^{20\cdot0^\circ}$ 1·0807, $n_D^{20\cdot0^\circ}$ 1·4579).

Ozonisation. The methylated ester was ozonised as described on p. 1032. In addition to oxalic acid the following fractions were obtained at 20 mm.: (1) below 55°, (2) 60—125°, (3) 125—132°. The lowest fraction gave a faint, rapidly fading, colour with ferric chloride and formed with phenylhydrazine the phenylhydrazone of glyoxylic ester, m. p. and mixed m. p. 157°. The third fraction gave no colour with ferric chloride; with phenylhydrazine acetate it formed β-acetphenylhydrazide, m. p. 128·5°, but with the base in ethereal solution a colourless *pyrazolone*, m. p. 176°, was produced (Found: C, 64·5; H, 6·0. $C_{14}H_{16}O_3N_2$ requires C, 64·6; H, 6·1%), proving the presence of ethyl acetylmethylmalonate. Fraction (2) was a mixture of (1) and (3).

Action of sodium ethoxide on the methylated ester. This was carried out as described on p. 1033, but the mixture was allowed to stand over-night; a good yield of ethyl αβ-dimethylglutaconate was obtained, b. p. 136—138°/18 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0213, $n_D^{20\cdot0^\circ}$ 1·4525, and $[R_L]_D$ 56·62 (Found: C, 61·6; H, 8·2. Calc.: C, 61·7; H, 8·4%); it was further characterised by hydrolysis with hydrochloric acid to the *cis*-αβ-acid, m. p. and mixed m. p. 148°.

cis- *and* trans-*Forms of Ethyl* α-*Carbethoxy*-β-*methylglutaconate.*—The preparation of the ester was repeated, pure ethyl β-chlorocrotonate, b. p. 76—77°/14 mm., and pure ethyl β-chloro*iso*crotonate, b. p. 56—57°/13 mm., respectively, being used; the former gave the *trans*-ester, b. p. 169—170°/13 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0937, $n_D^{20\cdot0^\circ}$ 1·4595, $[R_L]_D$ 68·09; the latter the *cis*-ester, b. p. 164—165°/12 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0884, $n_D^{20\cdot0^\circ}$ 1·4579, and $[R_L]_D$ 68·21. The ester prepared from ethyl tetrolate by Feist's method (*Annalen*, 1906, **345**, 104) was evidently similar to the *cis*-ester, b. p. 172°/18 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0898, $n_D^{20\cdot0^\circ}$ 1·4578 (the somewhat higher b. p. is probably due to superheating). The two stereoisomeric esters were hydrolysed by keeping for 3 days with cold 5% aqueous potassium hydroxide, enough alcohol being added (with care to avoid all rise of temperature) to give a homogeneous solution. The alcohol was evaporated off in a vacuum at room temperature and the acids were liberated in presence of ether by means of dilute hydrochloric acid. The *trans*-ester gave *trans*-β-methylglutaconic acid, m. p. 149° after one crystallisation, and the *cis*-ester gave the isomeride, m. p. 115—116°, also in the pure state.

Ethyl α-*Carbethoxy*-β-*phenylglutaconate* (I and II; R = Ph, R′ = H).—The yellow sodium compound of this ester was prepared as described by Bland and Thorpe (*loc. cit.*). The ester liberated from it with mineral acid was a yellow oil which could not be distilled without decomposition.

Ozonisation. The crude ester was treated as described on p. 1032 and gave, in addition to oxalic and benzoic acids, the following

fractions at 20 mm.: (1) below 40°, 2 drops; (2) 80—120°, (3) 120—165°; above 165° there was a good deal of decomposition with the formation of benzoic acid. The first fraction consisted of ethyl glyoxylate; the second was yellow, did not give a colour with ferric chloride, and formed the hydrate of ethyl mesoxalate, m. p. 59°, on treatment with water. The third fraction gave a red colour with ferric chloride and evidently contained ethyl benzoylacetate, as it gave 1 : 3-diphenylpyrazolone, m. p. and mixed m. p. 136°, with phenylhydrazine. The benzoic acid was principally derived from the decomposition of the ethyl benzoylmalonate, which was not isolated as such in this experiment.

Ethyl β-Phenyl-Δ^{β}-propene-ααγ-tricarboxylate (II; R = Ph, R′ = H).—The solid ester, m. p. 38° (Bland and Thorpe, *loc. cit.*), was the sole product when the yellow sodium compound mentioned above was treated with benzoic acid; the mixture had to be mechanically shaken for 3—4 days. The same ester was also obtained by the action of benzoic acid on the colourless potassio-derivative obtained from ethyl α-carbethoxy-β-phenylglutaconate as described on p. 1034, the reaction being complete in an hour.

Ozonisation. The solid ester, treated as described on p. 1032, gave a quantity of oxalic acid, and some benzoic acid in addition to a yellow oil giving an intense red colour with ferric chloride. This on distillation gave a few drops of low fraction containing ethyl glyoxylate (in another experiment this fraction was not obtained), the next fraction coming over as a yellow oil at 180—200°/18 mm.; there was, however, much decomposition and solid benzoic acid collected in the receiver. The yellow oil contained ethyl benzoylmalonate, giving a red colour with ferric chloride and characterised by the formation of the diphenylhydrazide of malonic acid, m. p. and mixed m. p. 191° (Found: C, 63·3; H, 5·9; N, 19·7. Calc.: C, 63·4; H, 5·7; N, 19·7%), and of β-benzoylphenylhydrazide, m. p. and mixed m. p. 168° (Fischer, *Annalen*, 1878, **190**, 125) (Found: C, 73·7; H, 5·7; N, 13·2. Calc.: C, 73·6; H, 5·7; N, 13·2%). Both these compounds were also obtained from a specimen of ethyl benzoylmalonate prepared for comparison.

Methylation. All attempts to methylate the original yellow sodium compound of ethyl phenylcarbethoxyglutaconate in a neutral solvent were unsuccessful, the salt being recovered unchanged.

The free ester (15 g.) was added to molecular sodium (1 g.) suspended in benzene; when the reaction was complete an excess of methyl iodide was added and the mixture warmed over-night; a good yield of the methylated ester (Thorpe and Wood, *loc. cit.*) was obtained. In another experiment, the potassio-derivative,

prepared as described above, was filtered off and carefully washed with ether until free from alcohol; it was then suspended in benzene and boiled with methyl iodide for 4½ hours, the same result being obtained. The methylated ester prepared in this way solidified completely after distillation (m. p. and mixed m. p. 50°).

Condensation of Ethyl Phenylpropiolate with Ethyl Sodiomethylmalonate.—Ethyl methylmalonate (17·4 g.) was added to molecular sodium (2·3 g.) suspended in benzene; when the formation of the sodio-derivative was complete (8 hours), ethyl phenylpropiolate (17·4 g.) was added and the mixture refluxed for 8 hours; the benzene was then removed under reduced pressure and petroleum added to assist in precipitation of the sodio-derivative; the latter was collected after 24 hours.

Shaking the sodio-derivative with benzoic acid for a week failed to liberate the ester; it was therefore treated with cold dilute hydrochloric acid, and the ester taken up in ether. It could not be purified by distillation, as it decomposed even under a pressure of 3 mm.

Ozonisation. The crude ester was treated as described on p. 1032. The alkaline and the aqueous washings contained benzoic and methylmalonic acids and much oxalic acid. The neutral products gave the following fractions, none giving a colour with ferric chloride: (1) 58—70°/25 mm., (2) 70—170°/18 mm., (3) 170—210°/18 mm.; there was much decomposition above 210°. The lowest fraction gave, with phenylhydrazine acetate, a small amount of oxaldiphenylhydrazide, m. p. 262—264°, suggesting the presence of ethyl α-benzoylpropionate (compare Feist, *loc. cit.*, p. 46); none of the other fractions gave characteristic derivatives, but as no ethyl pyruvate or benzoylmalonate could be present and oxalic acid was isolated in quantity, the ester must have the βγ-structure (V).

Ethyl α-Carbethoxy-γ-methylglutaconate (I and II; R = H, R′ = Me).—This ester was prepared as described by Thole and Thorpe (*loc. cit.*) and had b. p. 166—167°/15 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0880, $n_{D}^{20\cdot0^\circ}$ 1·4547, and $[R_L]_D$ 67·84.

Ozonisation. The ester was ozonised exactly as described on p. 1032 and gave the following fractions at 20 mm.: (1) below 60°, (2) 60—90°, (3) 90—110°. Fraction (1) gave a faint purple colour with ferric chloride (probably due to the presence of ethyl α-formylpropionate), a violet colour with sodium nitroprusside, and the phenylhydrazone of ethyl pyruvate, m. p. and mixed m. p. 119°, with phenylhydrazine. Fraction (2) gave a fine orange colour with ferric chloride, was soluble in 10% sodium hydroxide solution with the formation of malonic acid, and formed the phenylhydrazone of

ethyl formylmalonate, m. p. and mixed m. p. 129°, with phenylhydrazine. Fraction (3) consisted of a few drops of a greenish-yellow oil containing ethyl mesoxalate, which was identified by means of the hydrate, m. p. 59°.

"Normal" and "Labile" Forms of Ethyl α-Carbethoxy-γ-methylglutaconate.—The ester was separated into "normal" and "labile" fractions exactly as described by Bland and Thorpe (*loc. cit.*). The "normal" ester had b. p. 170°/16 mm., $d_4^{20\cdot0°}$ 1·0873, $n_D^{20\cdot0°}$ 1·4564; the "labile," b. p. 168—169°/16 mm., $d_4^{20\cdot0°}$ 1·0875, $n_D^{20\cdot0°}$ 1·4556. The latter may sometimes contain a small amount of the enol form, which gives rise to the pyrone, m. p. 92—93°, on distillation (compare Ingold and Perren, J., 1921, **119**, 1601).

Ozonisation. The "normal" ester gave exactly the same products as the original equilibrium ester; the "labile" ester gave only qualitative traces of the products derived from the αβ-form (oxalic acid and ethyl formylpropionate, recognised by the ferric chloride test but not isolated), whilst ethyl pyruvate and ethyl formylmalonate were isolated and identified as before.

Ethyl γ-Methyl-Δ^{β}-propene-ααγ-tricarboxylate (II; R = H, R′ = Me).—The equilibrium ester was converted into the potassio-derivative, and the pure βγ-ester liberated from it exactly as described on p. 1034; the ester, isolated in good yield, had b. p. 166°/12 mm., $d_4^{20\cdot0°}$ 1·0771, $n_D^{20\cdot0°}$ 1·4574.

Ozonisation. The results were similar to those of the "labile" ester given above, but no traces of ethyl mesoxalate or ethyl formylpropionate were isolated, the sole products being ethyl pyruvate and ethyl formylmalonate.

Attempt to prepare the αβ-ester (I; R = H, R′ = Me). The equilibrium ester was treated with aluminium amalgam in ether (Harries and Eschenbach, *Ber.*, 1896, **29**, 389), giving a good yield of *ethyl α-carbethoxy-γ-methylglutarate*, b. p. 159—161°/14 mm. (Found: C, 56·7; H, 8·1. $C_{13}H_{22}O_6$ requires C, 56·9; H, 8·1%). This ester was then brominated, and the bromo-ester treated with diethylaniline exactly as described by Thorpe (*loc. cit.*). The product boiled for the most part at 164°/18 mm., and was fully saturated; it was not further investigated.

Ethyl α-Methyl-γ-ethylglutaconate.—Ethyl α-methyldicarbethoxyglutaconate, prepared as described by Thole and Thorpe (*loc. cit.*), b. p. 208°/16 mm., $d_4^{19\cdot9°}$ 1·1095, $n_D^{19\cdot9°}$ 1·4530, $[R_L]_D$ 83·89, was converted into ethyl α-carbethoxy-γ-methyl-α-ethylglutaconate, b. p. 180—181°/20 mm., $d_4^{21\cdot0°}$ 1·0430, $n_D^{21\cdot0°}$ 1·4532, $[R_L]_D$ 77·80, and this on removal of the carbethoxyl group with sodium ethoxide gave the dicarboxylic ester, b. p. 160°/20 mm., $d_4^{20\cdot2°}$ 1·0087, $n_D^{20\cdot0°}$ 1·4495, $[R_L]_D$ 60·73. Similarly, ethyl α-ethyldicarbethoxyglutaconate,

b. p. 213°/20 mm., $d_4^{19\cdot5°}$ 1·0857, $n_D^{19\cdot5°}$ 1·4456, $[R_L]_D$ 87·98, gave ethyl α-carbethoxy-α-methyl-γ-ethylglutaconate, b. p. 180°/20 mm., $d_4^{19\cdot9°}$ 1·0596, $n_D^{19\cdot9°}$ 1·4505, $[R_L]_D$ 77·57, and finally the dicarboxylic ester, b. p. 161°/21 mm., $d_4^{17\cdot0°}$ 1·0091, $n_D^{17\cdot0°}$ 1·4495, $[R_L]_D$ 60·71.

Ozonisation. Both specimens of the dicarboxylic ester gave the same result. The fractions obtained at 23 mm. were: (1) 50—63°, (2) 63—66°, (3) 66—71°, (4) 71—92°. Fraction (1) gave a reddish-violet colour with ferric chloride, and a pyrazolone, m. p. 148°, identical with that prepared from ethyl α-formylpropionate. Fraction (3) also gave a colour with ferric chloride, but the phenylhydrazone of pyruvic ester, m. p. 119°, was the principal product isolated in the pure state and identified. Fraction (2) was evidently a mixture of (1) and (3), whilst the highest fraction gave a mixture of phenylhydrazones which could not be separated.

Ethyl α-methyl-γ-ethylglutaconate was also prepared by the esterification of the pure acid through the silver salt in the manner described by Kon and Watson (*loc. cit.*), but the ester was similar to those described above, b. p. 158°/18 mm., $d_4^{20\cdot0°}$ 1·0089, $n_D^{20\cdot0°}$ 1·4485, and gave similar results on ozonisation.

Ethyl α-Carbethoxy-γ-benzylglutaconate (I and II; R = H, R′ = CH_2Ph).—The ester was prepared as described by Thole and Thorpe (*loc. cit.*), but we were unable to distil it even at 2 mm. pressure.

Ozonisation. The crude ester was treated as described on p. 1032 and gave, in addition to a small amount of phenylacetic acid, isolated from the alkaline washings, the following fractions at 16 mm.: (1) up to 60°, (2) 60—85°, (3) 85—110°, (4) 110—150°, (5) 150—165°. Fraction (1) consisted of 3 drops with a strong odour of benzaldehyde and gave the characteristic semicarbazone of the latter. Fraction (2) gave a deep red colour with ferric chloride, and formed a mixture of phenylhydrazones from which those of ethyl formylmalonate (m. p. 129°) and of ethyl phenylpyruvate (m. p. 176°) could be isolated by fractional crystallisation. Fraction (3) was small, gave a faint colour with ferric chloride, and had a greenish-yellow colour which disappeared on shaking with water; ethyl mesoxalate hydrate was isolated from the aqueous solution. Fraction (4) gave a deep green colour with ferric chloride, due to ethyl phenylpyruvate, which was identified by means of its phenylhydrazone, m. p. 176°; another phenylhydrazone, m. p. 262° (decomp.), was also formed in very small amount but was not identified. The last fraction was very small, gave a purplish-green colour with ferric chloride, and the phenylhydrazone of ethyl formylphenylpropionate (m. p. and mixed m. p. 248°) was isolated from it in minute amount.

Similar results were obtained with Bland and Thorpe's " normal " and " labile " esters.

Attempts to prepare the pure $\beta\gamma$*-ester.* The equilibrium ester was converted into the potassium derivative and liberated from it as described on p. 1034, but the ester could not be distilled.

Ozonisation. The result was similar to that obtained with the equilibrium ester, but ethyl mesoxalate was not isolated, nor could ethyl formylphenylpropionate be identified, although some 2 drops of the relevant fraction, giving a purple colour with ferric chloride, were actually obtained; benzaldehyde, ethyl formylmalonate, and ethyl phenylpyruvate were again identified.

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