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1. *The Structure of Glutaconic Acids and Esters. Part II. α-Substituted Derivatives of β-Methylglutaconic Acid.*

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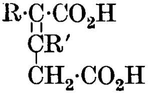
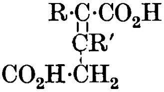
ANY unsymmetrically substituted glutaconic acid such as the α-methyl compound can theoretically exist in two isomeric forms differing in the position of the double bond; in addition, each of these should give rise to two stereoisomeric forms, thus:



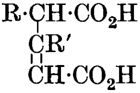
$$\begin{array}{l} R\cdot C\cdot CO_2H \\ \quad\| \\ \;\, CR' \\ \quad| \\ \;\, CH_2\cdot CO_2H \end{array}$$

(I) *cis-αβ.*



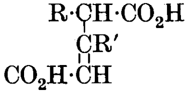
$$\begin{array}{r} R\cdot C\cdot CO_2H \\ \| \quad\quad \\ CR' \quad \\ | \quad\quad \\ CO_2H\cdot CH_2 \quad \end{array}$$

(II) *trans-αβ.*



$$\begin{array}{l} R\cdot CH\cdot CO_2H \\ \quad| \\ \;\, CR' \\ \quad\| \\ \;\, CH\cdot CO_2H \end{array}$$

(III) *cis-βγ.*



$$\begin{array}{r} R\cdot CH\cdot CO_2H \\ | \quad\quad\quad \\ CR' \quad\quad \\ \| \quad\quad\quad \\ CO_2H\cdot CH \quad\quad \end{array}$$

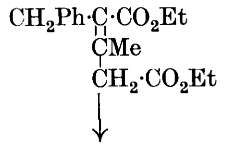
(IV) *trans-βγ.*

As the great majority of glutaconic acids exist in two forms, it had generally been assumed that these are stereoisomeric (Feist), although the position of the double bond was uncertain. The alternative view, representing the two forms as "normal" and "labile," the latter alone being capable of stereoisomerism, has recently been abandoned (compare McCombs, Packer, and Thorpe, J., 1931, 547; Packer and Thorpe, J., 1926, 1199), but it is clear that Feist's stereochemical explanation is not sufficient to account for the chemistry of the glutaconic acids. Thus, Feist's experiments on the αβ-dimethylglutaconic esters led him to the conclusion that these esters were mixtures of αβ- and βγ-isomerides (*Annalen*, 1922, **428**, 68), since oxidation products of both forms were isolated, although the αβ predominated; he merely concluded from this that there was no *chemical* difference between the two acids ("ein Unterschied mehr gradueller, als prinzipieller Natur"; *loc. cit.*, p. 75) and that they were therefore stereoisomerides. Such a conclusion is clearly unsatisfactory: a pure solid acid must, apart from its configuration, have either the αβ- or the βγ-unsaturated structure, and, even if one form be represented by such a formula as the "normal," the second form must have *one* of the unsaturated structures.

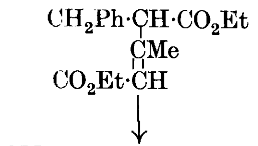
A repetition of Feist's work on the ozonisation of dimethylglutaconic esters led to similar results, but it soon became apparent that esters of different origin contained varying proportions of the two isomerides; the ester prepared from the pure high-melting form through the silver salt was practically homogeneous and had the αβ-structure, giving ethyl pyruvate and ethyl acetoacetate on ozonolysis, whilst the ester obtained by the methylation of ethyl *iso*dehydracetate, although a mixture, contained mostly the βγ-isomeride. A mixture containing even more of the βγ-form was obtained by methylating ethyl β-methylglutaconate through its potassium derivative. It is now clear that the method of esterification used by Feist (heating with sulphuric acid and alcohol) caused extensive isomerisation and accounts for his results; unfortunately, we were unable to obtain sufficient quantities of the lower-melting form of dimethylglutaconic acid in a state of purity to examine its ester and were therefore obliged to turn to the corresponding α-benzyl acids, both forms of which can be readily isolated.

It has already been suggested by Bland and Thorpe that the lower-melting form, m. p. 134°, has the *trans*-configuration (II) (J., 1912, **101**, 1740), whilst the isomeride, m. p. 148°, which readily passes into the anhydride, is a *cis*-form.

The ethyl esters have now been prepared from the pure acids through their silver salts under conditions precluding isomerisation (compare Hugh and Kon, J., 1930, 775), and their physical properties carefully examined. They showed distinct differences, that derived from the *cis*-acid having the higher density and lower molecular refraction in agreement with the observations of Auwers and Ottens (*Ber.*, 1924, **57**, 437) on the refractivities of *cis*-*trans*-isomerides. On ozonolysis, however, the two esters proved to be *structurally* different, for whilst the ester of the acid, m. p. 148°, gave ethyl phenylpyruvate and ethyl acetoacetate, that of the acid, m. p. 134°, gave ethyl glyoxylate (and oxalic acid) and ethyl benzylacetoacetate :



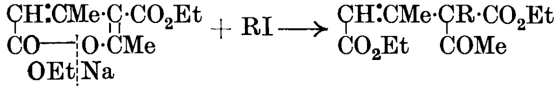
$$\begin{array}{c} \mathrm{CH_2Ph\cdot C\cdot CO_2Et} \\ \| \\ \mathrm{CMe} \\ | \\ \mathrm{CH_2\cdot CO_2Et} \\ \downarrow \\ \mathrm{CH_2Ph\cdot CO\cdot CO_2Et} + \\ \mathrm{COMe\cdot CH_2\cdot CO_2Et} \end{array}$$



$$\begin{array}{c} \mathrm{CH_2Ph\cdot CH\cdot CO_2Et} \\ | \\ \mathrm{CMe} \\ \| \\ \mathrm{CO_2Et\cdot CH} \\ \downarrow \\ \mathrm{COMe\cdot CH(CH_2Ph)\cdot CO_2Et} + \\ \mathrm{CHO\cdot CO_2Et} \end{array}$$

It must therefore be concluded that the acids represent structural as well as geometrical isomerides, the higher-melting form (Bland and Thorpe's " normal " acid) being the *cis*-αβ (I), the lower-melting isomeride being the *trans*-βγ (IV) and not the *trans*-αβ (II) as suggested by Bland and Thorpe (*loc. cit.*).

The crude ester from which these two acids are derived (by acid and alkaline hydrolysis respectively) is produced by benzylating the sodio-derivative formed from sodium ethoxide and ethyl *iso*dehydracetate and has properties closely resembling those of the *trans*-βγ-ester; oxidation shows that it consists largely of this ester, although the presence of some *cis*-αβ-ester is clearly proved. The *trans*-βγ-ester is evidently the primary product of the reaction and results from the opening of the pyrone ring of ethyl *iso*dehydracetate without change of configuration or wandering of the double bond, followed by alkylation, the acetyl ester then losing the acetyl group.



$$\begin{array}{l} \mathrm{CH{:}CMe{\cdot}C{\cdot}CO_2Et} \\ \mathrm{CO{-}{-}O{\cdot}CMe} \\ \mathrm{\ OEt|Na} \end{array} + \mathrm{RI} \longrightarrow \begin{array}{l} \mathrm{CH{:}CMe{\cdot}CR{\cdot}CO_2Et} \\ \mathrm{CO_2Et \quad COMe} \end{array}$$

When either of the pure esters is treated with potassium ethoxide a potassio-derivative is formed but does not separate from the solution; on careful neutralisation with benzoic acid (Hugh and Kon, *loc. cit.*) an ester is produced which differs somewhat in properties from the two parent esters and gives on ozonolysis an appreciable quantity of benzaldehyde in addition to products derived from the αβ-ester; oxidation products derived from the βγ-ester could not be identified with certainty, so this can only be present in small quantities. These results point to the presence of a new ester of the formula $\mathrm{CO_2Et{\cdot}C({:}CHPh){\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Et}$; and the corresponding *acid*, m. p. 173°, can be isolated by fractional crystallisation of the mixture obtained on cold alkaline hydrolysis of the ester. The latter is evidently produced from the potassio-αβ-ester by the further wandering of the double bond:

$$\begin{array}{l} \mathrm{CO_2Et{\cdot}CH(CH_2Ph){\cdot}CMe{:}CH{\cdot}CO_2Et} \longrightarrow \\ \qquad\qquad \mathrm{CO_2Et{\cdot}C(CH_2Ph){:}CMe{\cdot}CH{\cdot}CO_2Et\}K} \longrightarrow \\ \qquad \mathrm{CO_2Et{\cdot}C({:}CHPh){\cdot}CHMe{\cdot}CH_2{\cdot}CO_2Et.} \end{array}$$

This reaction supplies a remarkable example of the change of a true glutaconic system into one containing a phenyl*iso*crotonic skeleton and is, we believe, the first of its kind to be recorded. The change is doubtless connected with the great stability of systems in which a double bond is conjugated with the double bonds of a benzene ring (Linstead and Williams, J., 1926, 2735; compare Johnson and Kon, *ibid.*, p. 2748).

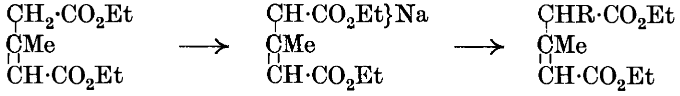
It is at present impossible to decide whether the intermediate potassium derivative is that shown above or is derived from the benzylidene ester; it is hoped that alkylation experiments may throw a light on this problem.

The new acid is remarkably stable to the action of alkalis and undergoes no change under conditions which cause interconversion of both the *cis*-αβ- and the *trans*-βγ-acid. Similarly, the acid of m. p. 173° must be fairly stable to the action of acids, because it was on one occasion isolated in small amount in the preparation of the *cis*-αβ-acid from the crude ester by hydrolysis with concentrated hydrochloric acid.

Similar experiments were also performed on the β-methyl-α-ethylglutaconic acids, m. p. 164° and 98° respectively (Bland and Thorpe, J., 1912, **101**, 1557). It was again possible to esterify them without isomerisation, and oxidation with ozone supplied conclusive proof that the higher-melting form is the αβ, the lower-melting the βγ. Here again, the αβ-form appears to have the *cis*-configuration, being readily converted into the anhydride, whilst the lower-melting form is only slowly attacked by acetyl chloride and is probably the *trans*-βγ-acid. (Although inability to form an anhydride can be taken to denote a *trans*-configuration, the converse is by no means necessarily true; anhydride formation may proceed as the result of *tautomeric* change leading to change of configuration : compare Packer and Thorpe, *loc. cit.*).

The ester obtained by the direct ethylation of ethyl *iso*dehydracetate consists almost entirely of the *trans*-βγ-ester. There is evidently less conversion into the αβ-isomeride than in the benzyl esters, because ethylation proceeds readily at low temperatures whereas benzylation requires heating.

Now it is evident that if it were possible to convert the two stereoisomeric forms of ethyl β-methylglutaconate into sodio- or potassio-derivatives without change of configuration and replace the metal by an alkyl group, two stereoisomeric forms of the *same* α-alkyl-β-methyl-βγ-unsaturated ester should result. Thus, the *cis*-



$$\begin{array}{l}CH_2\cdot CO_2Et\\ |\\ CMe\\ \|\\ CH\cdot CO_2Et\end{array} \longrightarrow \begin{array}{l}CH\cdot CO_2Et\}Na\\ |\\ CMe\\ \|\\ CH\cdot CO_2Et\end{array} \longrightarrow \begin{array}{l}CHR\cdot CO_2Et\\ |\\ CMe\\ \|\\ CH\cdot CO_2Et\end{array}$$

ester should yield the *cis*-βγ-ester, and the *trans*-compound should be similarly formed from ethyl *trans*-β-methylglutaconate.

Experiment shows that the two isomeric esters can be prepared in a state of purity by the silver salt method and are readily converted into potassio-derivatives. It was hoped to convert them by means of benzyl chloride into the two stereoisomeric forms of the α-benzyl compound (R = CH_2Ph), of which only the *trans*-form is known. The treatment necessary to produce the benzyl compound (high temperature) is, however, too drastic, and extensive isomerisation takes place leading to a mixture containing the two esters already discussed. Ethylation can, however, be carried out at a lower temperature and two esters are produced which appear to be the expected stereoisomeric forms of ethyl β-methyl-α-ethyl-Δ^{β}-propenedicarboxylate; of these the *trans*-compound is identical with that already described (IV), but the *cis* (III) is new; we have not yet succeeded in obtaining a solid acid from it, but the method appears to be promising and it is proposed to extend its application.

EXPERIMENTAL.

Ethyl αβ-*Dimethylglutaconate.*—This ester was prepared from ethyl *iso*dehydracetate by Feist's modification (*loc. cit.*) of Bland and Thorpe's method (J., 1912, **101**, 1567), consisting in using 2 mols. of sodium ethoxide. The yield of ester, b. p. 129—135°/15 mm., $d_{4°}^{20\cdot0°}$ 1·0217, $n_{\mathrm{D}}^{20\cdot0°}$ 1·4543, $[R_L]_{\mathrm{D}}$ 56·79, was 80%.

Ozonisation. 10 G. of redistilled ester (b. p. 130°/11 mm.), dissolved in 90 c.c. of pure ethyl acetate, were treated with ozonised oxygen at 0° until no more was absorbed. The solvent was removed in a vacuum at room temperature, and the ozonide decomposed by shaking over-night with 100 c.c. of water, the products being taken up in pure ether. The extract was shaken with aqueous sodium bicarbonate (which removed appreciable quantities of oxalic acid), dried, and evaporated, and the residue distilled under 18 mm., the following fractions being obtained: (i) below 60°, (ii) 60—80°, (iii) above 80°, very small, mainly 135—140°, consisting of unchanged ester. The first fraction slowly developed a red colour with ferric chloride and gave with phenylhydrazine acetate the phenylhydrazone of ethyl pyruvate, m. p. 119°, and a little 1-phenyl-3-methylpyrazolone derived from ethyl acetoacetate. The second fraction developed an immediate, intense purple-red colour with ferric chloride and gave both phenylmethylpyrazolone and the phenylhydrazone of ethyl methylacetoacetate, m. p. 152° (mixed m. p. 152—153°).

Ethyl αβ-*Dimethyl-*Δ^{α}*-propene-*αγ*-dicarboxylate.*—The pure high-melting form of dimethylglutaconic acid (I, R and R′ = Me) (Bland and Thorpe, *loc. cit.*) (11 g.) was covered with 300 c.c. of water, and the theoretical quantity of 2*N*-ammonia slowly added with shaking, any rise of temperature being prevented. The solution was further diluted with 200 c.c. of water, and a slight excess of silver nitrate solution added. The silver salt was collected, washed with alcohol and ether, and dried in a desiccator. It was then covered with dry ether and refluxed for 6 hours with an excess of ethyl iodide. The ester solution was washed with sodium sulphite solution, dried, and evaporated. The ester boiled at 141°/18 mm. and had $d_{4^\circ}^{20\cdot0^\circ}$ 1·0289, $n_{\rm D}^{20\cdot0^\circ}$ 1·4545, $[R_L]_{\rm D}$ 56·38.

Ozonisation. This was carried out exactly as described above and with similar results except that only a minute amount of oxalate was present in the bicarbonate washings and a very small amount of the phenylhydrazone of ethyl methylacetoacetate, m. p. 152°, was isolated, the product being almost entirely ethyl pyruvate and ethyl acetoacetate. It is clear, however, that a small amount of conversion had taken place in the process of esterification.

Methylation of Ethyl β*-Methylglutaconate.*—Thorpe and Wood's method (J., 1913, **103**, 1758) was modified as follows : 3·15 g. of potassium were dissolved in 25 c.c. of alcohol dried over calcium, and the excess of alcohol removed in a vacuum. Dry ether was then added, and the evacuation repeated 3 times; the potassium ethoxide was covered with ether and 17·5 g. of the ester in 50 c.c. of ether were added, followed by an equal volume of dry petroleum (b. p. 60—80°). The potassium derivative, which formed very rapidly, was filtered off and well washed with petroleum, care being taken to keep it covered with petroleum; it was then rapidly transferred to a flask, covered with ether, and refluxed with an excess of methyl iodide. The ester finally obtained had b. p. 131°/15 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0179, $n_{\rm D}^{20\cdot0^\circ}$ 1·4525, $[R_L]_{\rm D}$ 56·81.

Ozonisation. The same fractions were obtained as before. The first fraction gave a reddish colour with ferric chloride and a small amount of phenylmethylpyrazolone was obtained from it, together with the phenylhydrazone of ethyl glyoxylate, m. p. and mixed m. p. 157° (compare Kon and Nanji, J., 1931, 560). The second fraction, which constituted nearly the whole of the distillate, gave a reddish-purple colour with ferric chloride and contained mainly ethyl methylacetoacetate, although a little ethyl acetoacetate was isolated in the form of phenylmethylpyrazolone. The ester thus consists very largely of the βγ-form.

"*Labile*" αβ*-Dimethylglutaconic Acid* (? IV, R and R′ = Me).—This acid was repeatedly prepared by the alkaline hydrolysis of the ester, but was generally liquid and sufficient quantities of the solid, m. p. 103°, have not yet been obtained for investigation. By analogy it can be assumed that this acid is the *trans*-Δ^{β}-form.

Ethyl α*-Benzyl-*β*-methylglutaconate.*—This ester was prepared as described by Bland and Thorpe (*loc. cit.*) except that 2 mols. of sodium ethoxide were employed. The ester had b. p. 195—205°/16 mm. (mainly 199°), $d_{4^\circ}^{20\cdot0^\circ}$ 1·0645, $n_{\rm D}^{20\cdot0^\circ}$ 1·5084, $[R_L]_{\rm D}$ 81·31. A very similar product was obtained in an alternative preparation in which the benzylation and extraction of the ester were carried out in the cold (48 hours).

Ozonisation. This was carried out exactly as described on p. 5. Fractions were obtained from 10 g. of ester at 18 mm.: (i) below 90°, 2·05 g.; (ii) 90—140°, 2·4 g.; (iii) 140—155°, 2·8 g.; (iv) 155—165°, 1·0 g.; (v) above 165°, a few drops of the original ester.

Fraction (i) gave a red colour with ferric chloride, and with phenylhydrazine the soluble phenylhydrazone of ethyl glyoxylate, m. p. 157°, and phenylmethylpyrazolone.

Fractions (ii) and (iii) both gave a greenish-purple colour with ferric chloride and were evidently mixtures of ethyl phenylpyruvate, which gives a green colour, and ethyl benzylacetoacetate, which gives a purple; the former gave the *semicarbazone*, plates, m. p. 159—160°, from dilute alcohol (Found: C, 58·1; H, 5·8. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·0%); whilst the latter ester gave the known semicarbazone, m. p. and mixed m. p. 169°, and with phenylhydrazine the pyrazolone, m. p. and mixed m. p. 138°.

Fraction (iv) gave a purple colour with ferric chloride and contained ethyl benzylacetoacetate, which gave the semicarbazone, m. p. 169°, and the pyrazolone, m. p. 138°.

The aqueous and bicarbonate washings gave a positive test for oxalate.

The ester thus contained both the αβ- and the βγ-isomeride, roughly in equal amounts.

Ethyl trans-*α-Benzyl-β-methyl-*Δ^{β}*-propene-αγ-dicarboxylate.*—The *trans*-βγ-acid (IV; $R = CH_2Ph$, $R' = Me$) (Bland and Thorpe's "labile" acid) prepared as described by these authors was esterified by the method given on p. 5. The ester had b. p. 195°/13 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0643, $n_D^{20\cdot0^\circ}$ 1·5085, $[R_L]_D$ 81·34. The ester can be hydrolysed to the pure *trans*-βγ-acid by cold dilute alkali.

Ozonisation. This gave the same results as the mixed ester, but fraction (i) weighed only 0·1 g. and contained a minute amount of ethyl acetoacetate, identified as phenylmethylpyrazolone. The second fraction was also insignificant and gave a greenish-purple colour with ferric chloride, and therefore contained a small quantity of ethyl phenylpyruvate; no pure derivatives could be obtained from it. The third fraction, b. p. 145—170°/18 mm., made up nearly the whole distillate, the major portion boiling at 157°/18 mm. and consisting of ethyl benzylacetoacetate, which was identified as before.

Quantities of oxalic acid were present in the aqueous and bicarbonate extracts.

The ester was therefore the βγ-form, but contained a very small amount of the αβ-isomeride.

Ethyl cis-*α-Benzyl-β-methyl-*Δ^{α}*-propene-αγ-dicarboxylate.*—The *cis-*

αβ-acid (I; R = CH_2Ph, R′ = Me) (Bland and Thorpe's "normal" acid), prepared as described by these authors, was esterified by the method given on p. 5. The ester had b. p. 191°/10 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0702, $n_D^{20\cdot0^\circ}$ 1·5090, $[R_L]_D$ 80·95.

Ozonisation. From 10 g. of ester the following fractions were obtained at 13 mm.: (i) below 70°, 3·4 g.; (ii) 70—120°, 0·6 g.; (iii) 120—160°, 5·0 g.; (iv) above 160°, a few drops.

Fraction (i) gave a red colour with ferric chloride and consisted entirely of ethyl acetoacetate, identified as phenylmethylpyrazolone; no ethyl glyoxylate was detected and no oxalic acid was present in the aqueous or alkaline washings. Fraction (ii) gave a dirty greenish colour with ferric chloride and contained both ethyl acetoacetate and ethyl phenylpyruvate. The latter constituted the whole of fraction (iii) and was identified as before; no trace of ethyl benzylacetoacetate could be detected. The highest fraction also gave a green colour with ferric chloride, but consisted mainly of the original ester.

The ester is thus the pure αβ-compound.

Action of Potassium Ethoxide on the Benzylmethylglutaconic Esters.—The pure *trans*-βγ-ester (28 g.) was treated with potassium ethoxide in ether exactly as described on p. 6; no solid potassium derivative separated even on addition of a large volume of petroleum. When the mixture was treated with a slight deficiency (10·3 g.) of dry benzoic acid, the dark red colour rapidly faded; after being mechanically shaken over-night, and filtered from potassium benzoate, the solution was evaporated and the residual ester distilled: b. p. 200—201°/18 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0630, $n_D^{20\cdot0^\circ}$ 1·5085, $[R_L]_D$ 81·44.

Ozonisation. The following fractions were obtained from 10 g. of the ester at 20 mm.: (i) below 70°, (ii) 70—100°, (iii) 100—160°, (iv) above 160°, a small amount of unchanged ester. Fraction (i) had a strong smell of benzaldehyde, which could be isolated in quantity as the semicarbazone, m. p. and mixed m. p. 220°. It also gave a red colour with ferric chloride, and phenylmethylpyrazolone with phenylhydrazine, confirming the presence of ethyl acetoacetate. Fraction (ii) was insignificant in amount and consisted entirely of ethyl acetoacetate. The third fraction made up the bulk of the distillate and gave with ferric chloride a green colour tinged with purple, suggesting the presence of ethyl benzylacetoacetate; this could not, however, be identified with certainty, the only compound isolated being the semicarbazone of ethyl phenylpyruvate. No ethyl glyoxylate or oxalic acid appeared to be formed, so the ester consisted entirely of the *cis*-αβ- and the benzylidene esters. Another specimen similarly prepared from the pure *cis*-αβ-ester had the same properties and gave the same results on ozonisation. We have so far been unable to isolate the second oxidation product, presumably ethyl α-keto-β-methylglutarate, which should be formed from the benzylidene ester.

α-Phenyl-γ-methyl-Δ^{a}-butene-βδ-dicarboxylic Acid.—The mixture of esters described above was kept at room temperature for 4 days with 1·5 times the calculated volume of 10% aqueous potassium hydroxide and enough alcohol to give a homogeneous solution. The alcohol was removed under reduced pressure and the acids were liberated by careful acidification with 3*N*-hydrochloric acid in presence of a large volume of ether. The mixture of acids obtained on evaporation of the ethereal solution readily solidified; it was extracted with successive small quantities of hot benzene, which removed the *trans*-βγ-acid; the residue was recrystallised from water and formed small iridescent plates, m. p. 173°, sparingly soluble even in hot water, consisting of *α-phenyl-γ-methyl-Δ^{a}-butene-βδ-dicarboxylic acid* (*α-benzylidene-β-methylglutaric acid*) [Found : C, 66·3; H, 5·9; *M* (dibasic), 233·6. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%; *M*, 234·0]. The barium salt, like that of the *trans*-βγ-acid, is soluble in water.

Oxidation. A solution of the acid in dilute aqueous sodium carbonate was covered with ether, and cold 3% potassium permanganate solution added with vigorous shaking until the pink colour persisted. The ethereal layer on evaporation gave a good yield of benzaldehyde, which was identified as its semicarbazone, m. p. 220°.

Action of alkali. 0·7 G. of the new acid, dissolved in 25 c.c. of 20% potassium hydroxide solution, was heated in a closed tube for 90 minutes in boiling water; the solution was then cooled, diluted, covered with ether, and cautiously acidified; the recovered acid solidified at once, and gave the characteristic plates, m. p. 173°, on recrystallisation from water, and its barium salt was soluble, thus showing the absence of the *cis*-αβ-acid. Specimens of the *cis*-αβ- and *trans*-βγ-acids were similarly treated; the product in each case contained both acids, which were separated by means of their barium salts.

Ethyl β-Methyl-α-ethylglutaconate.—This ester, prepared from ethyl *iso*dehydracetate in the same way as the lower homologue, had b. p. 136—138°/15 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0057, $n_{D}^{20\cdot0^\circ}$ 1·4545, $[R_L]_D$ 61·44.

Ozonisation. The following fractions were obtained at 15 mm. from 10 g. of ester : (i) 65—80°, 2·4 g.; (ii) 80—100°, 5·2 g.; (iii) above 100°, a small amount of unchanged ester. There was no distillate below 65°, indicating the absence of ethyl glyoxylate, but a quantity of oxalic acid was found in the aqueous and alkaline washings. Fraction (i) gave an intense red colour with ferric chloride, and with sodium nitroprusside a deep violet colour, changing to red with potassium hydroxide and blue with acetic acid; these colour reactions point to the presence of ethyl α-ketobutyrate, but all attempts to isolate it in the form of phenylhydrazone were unsuccessful; ethyl acetoacetate was readily identified in the form of phenylmethylpyrazolone. Fraction (ii) gave a purple colour with ferric chloride and contained ethyl ethylacetoacetate, which was identified as its semicarbazone, m. p. and mixed m. p. 154°. The ester ozonised thus consisted of a mixture of αβ- and βγ-esters, the latter predominating.

Ethyl cis-β-*Methyl-α-ethyl-Δ^{α}-propene-αγ-dicarboxylate.*—The pure *cis*-αβ-acid, m. p. 164° (I; R = Et, R′ = Me) (Thorpe and Bland's "normal" acid), obtained by the acid hydrolysis of the above mixed ester, was converted into the ester as described on p. 5; this had b. p. 126°/10 mm., $d_{4°}^{20\cdot0°}$ 1·0076, $n_{D}^{20\cdot0°}$ 1·4528, $[R_L]_D$ 61·18.

Ozonisation. The results were similar to those described above, but only traces of oxalic acid were formed and ethyl glyoxylate was absent; ethyl acetoacetate was present in quantity and a small amount of ethyl ethylacetoacetate was also identified. The ester thus consisted of the αβ-form, but contained a small amount of the isomeric form.

Ethyl trans-β-*Methyl-α-ethyl-Δ^{β}-propene-αγ-dicarboxylate.*—The acid, m. p. 98° (IV; R = Et, R′ = Me) (Bland and Thorpe's "labile" acid), obtained by the alkaline hydrolysis of the mixed ester (Bland and Thorpe, *loc. cit.*), contains the *cis*-αβ-acid as impurity; the latter can be removed in the form of the insoluble barium salt or by taking advantage of its sparing solubility in ether. There is an appreciable difference in the rates at which the two acids react with acetyl chloride in the cold, the higher-melting form being the more reactive, in accordance with the configurations assigned to them. The ester, prepared through the silver salt, had b. p. 136°/12 mm., $d_{4°}^{20\cdot0°}$ 1·0055, $n_{D}^{20\cdot0°}$ 1·4540, $[R_L]_D$ 61·45.

Ozonisation. Only one drop of distillate was obtained below 80°/13 mm. from 10 g. of the ester; this gave a reddish-purple colour with ferric chloride. The remainder, except for a small amount of unchanged initial material, boiled at 80—100° and gave a violet colour with ferric chloride; the semicarbazone of ethyl ethylacetoacetate, m. p. and mixed m. p. 154°, was isolated in quantity, and much oxalic acid was identified in the washings. The ester thus appears to be the pure βγ-compound.

Ethylation of Ethyl cis- *and* trans-β-*Methylglutaconates.*—The two forms of β-methylglutaconic acid were esterified through their silver salts, the ester from the acid of m. p. 149° having b. p. 130°/18 mm.,

$d_{4^\circ}^{20\cdot0^\circ}$ 1·0296, $n_D^{20\cdot0^\circ}$ 1·4505, $[R_L]_D$ 52·29, and that from the acid of m. p. 115—116° having b. p. 136°/23 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0329, $n_D^{20\cdot0^\circ}$ 1·4505, $[R_L]_D$ 52·12. The ester of the lower-melting acid is thus appreciably denser than its isomeride, in agreement with the *cis*-configuration assigned to it.

The two esters were ethylated exactly as described on p. 6. The *trans*-ester gave a product identical in properties with the *trans*-βγ-ester (p. 10), b. p. 136°/13 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0054, $n_D^{20\cdot0^\circ}$ 1·4541, $[R_L]_D$ 61·46, and gave similar results on ozonisation, although it was found to contain a small amount of the isomeric αβ-ester. The ester derived from the *cis*-ester was appreciably different, b. p. 146°/22 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0028, $n_D^{20\cdot0^\circ}$ 1·4537, $[R_L]_D$ 61·58; it is characterised by its lower density and refractive index and higher molecular refraction.

The results of ozonisation were similar to the above, although a good deal of unchanged initial material was recovered. A solid acid has not yet been obtained on hydrolysis.

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