

144. *The Structure of the Glutaconic Acids and Esters. Part IX.*
 α -Methyl- and α -Ethyl-glutaconic Acids.

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It has been shown by Kon and Watson (J., 1932, 2434) that the well-known α -benzylglutaconic acid is the *trans*-form with the double bond in the $\beta\gamma$ -position (I, R = CH₂Ph), and a new isomeride, the *cis*- Δ^{α} -acid (II, R = CH₂Ph) was also described.



The corresponding α -methyl- and α -ethyl-acids have now been examined.

The stable forms of the acids have been prepared by a slight modification of the method of Thole and Thorpe (J., 1911, 99, 2208); the preparation of the ethyl acid was very tedious owing to the ready fission of the parent carboxyglutaconic ester with the production of butyric acid. Since Kon and Watson (*loc. cit.*) had found it impossible to esterify the α -benzyl acid without isomerisation, even by the silver salt method, an attempt was made to prepare the methyl esters of these acids with the aid of diazomethane in the cold. The ester of the α -methyl acid prepared in this way was homogeneous and the products obtained from it on ozonisation (oxalic acid, derived from the methyl glyoxylate first formed, and methyl α -formylpropionate) showed that the parent acid had the formula (I, R = Me). The ester of the α -ethyl acid was similar, although the neutral oxidation product could not be identified with certainty.

These stable acids are therefore the Δ^{β} -compounds of the structure (I), and doubtless have the *trans*-configuration, since they are not the primary products obtained by the hydration of the anhydrides formed from them.

The latter method is the only one available for the preparation of the *cis*-forms and presents considerable experimental difficulties. For instance, it is difficult to obtain the hydroxy-anhydride of the α -methyl acid free from the corresponding chloro-anhydride, the presence of which is prejudicial because it liberates hydrogen chloride on hydration; and we were unable to obtain the hydroxy-anhydride of the α -ethyl acid in a pure condition. Moreover, the conditions employed by Thole and Thorpe and also by Feist (*Annalen*, 1909, 370, 41) for the hydration of these anhydrides involve the use of alkali and are therefore unsuitable. For this reason we adopted the method of Malachowski (*Ber.*, 1929, 62, 1323), who used cold water. The hydrolysis under these conditions is slow and some hydroxy-anhydride remains unchanged at the end of two months, whilst the interconversion of the two forms of the acid under these conditions proceeds at a comparable rate, so that the *trans*-acid is isolated at the end of the experiment. However, if the acid formed is isolated at the end of a few hours, the *cis*-form is obtained and in this way the pure *cis*- α -methyl acid was prepared. It melts some 7° higher than the "labile" acid of Thole and Thorpe (= *cis*-acid of Feist); the latter acid is doubtless the eutectic of the two forms similar to that formed from the α -benzyl acids. The new acid has the Δ^{α} -structure (II, R = Me), as shown by the ozonisation of the ester prepared by means of diazomethane: no oxalic acid was produced, and methyl pyruvate was identified in the neutral portion of the products.

Owing to our failure to obtain the pure hydroxy-anhydride of the α -ethyl acid, the pure *cis*-form of this acid was not obtained; the acid of m. p. 108° (Thole and Thorpe, *loc. cit.*) was isolated, but ozonisation of the ester proved that it was not homogeneous, since oxalic acid was detected in the mixture of oxidation products.

EXPERIMENTAL.

trans- α -Methyl- Δ^{β} -propene- $\alpha\gamma$ -dicarboxylic Acid (I, R = Me).—The stable form of α -methylglutaconic acid was prepared by Linstead and Millidge's modification of Thole and Thorpe's method (J., 1936, 478), but it was found possible to hydrolyse ethyl α -methyl- $\alpha\gamma$ -dicarboxyglutaconate in one stage by keeping it for 10 days with an excess of 30% aqueous potassium hydroxide and enough alcohol to give a homogeneous solution. The yield of crude acid obtained was somewhat less than 50% and a 65% yield was obtained by hydrolysing ethyl α -methyl- γ -carboxyglutaconate under the same conditions. In either case the acid obtained was evidently contaminated with some acid ester, as the amount diminished considerably on recrystallisation; the pure acid melted at 145°. The methyl ester was prepared by adding the acid slowly to a freshly prepared solution of diazomethane in dry ether, the reagent being present in excess. After some hours the solution was evaporated, and the residue distilled; the ester had b. p. 92—93°/1.5 mm., $d_4^{20.5}$ 1.1055, $n_D^{20.5}$ 1.4578, $[R_L]_D$ 42.44.

Ozonisation. The ester, dissolved in 5 vols. of ethyl acetate, was cooled in ice and treated with ozonised oxygen until no more was absorbed. The solvent was removed under reduced pressure below 40°, and the residue decomposed by shaking with cold water for some hours and finally warmed with water under reflux for 15 minutes. The products were taken up in ether, and the extract shaken with aqueous sodium bicarbonate, which removed oxalic acid; this was identified in the usual way. The ethereal extract was dried and evaporated and was shown to contain methyl α -formylpropionate by preparing 1-phenyl-4-methylpyrazolone, m. p. and mixed m. p. 148—149°, from it with phenylhydrazine.

cis- α -Methyl- Δ^{α} -propene- $\alpha\gamma$ -dicarboxylic Acid (II, R = Me).—The *trans*-acid was heated with acetyl chloride (2 mols.) in a sealed tube for 5—6 hours at 110°: in some experiments a crystalline solid, m. p. 70—76°, separated in small amount. The liquid was evaporated to dryness, the residue taken up in ether, and the solution extracted with aqueous sodium bicarbonate until the latter remained alkaline; the dark red extract was acidified with dilute hydrochloric acid and extracted with ether. The extract was still highly coloured, but a colourless preparation was obtained by distilling the hydroxy-anhydride under reduced pressure in a sabre flask; the yield did not exceed 40%. Hydration under Thole and Thorpe's conditions gave an acid, m. p. 110—118°, consisting mainly of the *cis*-acid. To prepare the pure acid, the hydroxy-anhydride was finely powdered and left covered with water for several hours; the water was

then evaporated without heating in a vacuum desiccator at 2 mm.; a solid was then obtained, m. p. 123—125°, which was crystallised from chloroform. The m. p., now 125—126°, was depressed by the *trans*-acid (Found: C, 49.7; H, 5.7. $C_6H_8O_4$ requires C, 50.0; H, 5.6%). The methyl ester was prepared with diazomethane and had b. p. 82—85°/2 mm., $d_4^{18.5^\circ}$ 1.1041, $n_D^{18.5^\circ}$ 1.4546, $[R_L]_D$ 42.24.

Ozonisation. This was carried out as described on p. 726. No oxalic acid was obtained; the neutral portion gave the usual colour reactions of pyruvates and methyl pyruvate was identified as the 2:4-dinitrophenylhydrazone, m. p. 180°; it also gave a violet colour with ferric chloride.

trans- α -Ethyl- Δ^{β} -propene- α -dicarboxylic Acid (I, R = Et).—Both the tricarboxylic and the tetracarboxylic ester in this case gave an acid contaminated with various amounts of butyric acid, although both acid and alkaline hydrolytic agents were tried; the method described on p. 726 was on the whole the best. The acid after several crystallisations had m. p. 131—132° (Thole and Thorpe give m. p. 133—134°). The methyl ester was prepared with diazomethane and had b. p. 95—98°/5 mm., $d_4^{19.0^\circ}$ 1.0762, $n_D^{19.0^\circ}$ 1.4574, $[R_L]_D$ 47.10.

Ozonisation. This was carried out as before; oxalic acid was isolated in large quantity and identified. The neutral product reacted with phenylhydrazine, but the resulting pyrazolone would not crystallise (1-phenyl-4-ethylpyrazolone is described as melting at 78°).

cis- α -Ethylglutaconic Acid.—All attempts to obtain a pure hydroxy-anhydride from the *trans*-acid were unsuccessful; the material prepared as described on p. 726 was semi-solid and crude *cis*-acid could be prepared from it by rubbing with benzene; after recrystallisation from chloroform this melted at 108—109°. The methyl ester prepared from it had b. p. 90—96°/5 mm., $d_4^{19.0^\circ}$ 1.0728, $n_D^{19.0^\circ}$ 1.4558, $[R_L]_D$ 47.12. The products obtained on ozonisation are referred to on p. 726.

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