LXXV.—*The Structure of the Glutaconic Acids and Esters. Part I. Cyanoglutaconic Esters.*

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In the recent general investigation of three-carbon tautomerism, which has been shown to occur in a variety of unsaturated compounds with an activating group at one end of the chain, no attempt was made to deal with the notoriously difficult problem presented by the glutaconic acids and their esters. The generalisations arising out of the study of three-carbon tautomerism are, however, necessarily incomplete if they do not account for the many peculiarities of the chemistry of glutaconic acid derivatives. It is proposed, therefore, to attempt, in the present series of papers, a general revision of our knowledge of these compounds in the light of the facts ascertained in the study of the simpler cases.

The cyanoglutaconic esters constitute, in virtue of their markedly unsymmetrical structure, a link between the two types.

The parent substance of the series, ethyl α-cyanoglutaconate (I), has been repeatedly obtained (Guthzeit and Eyssen, *J. pr. Chem.*, 1908, **80**, 41; Verkade, *Proc. K. Akad. Wetensch. Amsterdam*, 1919, **27**, 1132; Ingold and Perren, J., 1921, **119**, 1582), but its unstable character makes it unsuitable for investigation, although some additional observations have now been made (p. 565). Its β-methyl derivative, however, is stable and readily obtained. Rogerson and Thorpe (J., 1905, **87**, 1669) gave it the formula (II) and showed that it could be readily alkylated through its crystalline potassio-derivative, to which the formula (III) *

$$CO_2Et\cdot CH(CN)\cdot CH{:}CH\cdot CO_2Et \quad \text{(I.)}$$

$$CO_2Et\cdot CH(CN)\cdot CMe{:}CH\cdot CO_2Et \quad \text{(II.)}$$

$$CO_2Et\cdot C(CN){:}CMe\cdot CHK\cdot CO_2Et \quad \text{(III.)}$$

$$CO_2Et\cdot C(CN){:}CMe\cdot CHMe\cdot CO_2Et \quad \text{(IV.)}$$

$$CO_2Et\cdot CH(CN)\cdot CMe{:}CMe\cdot CO_2Et \quad \text{(V.)}$$

$$CO_2Et\cdot \underset{\cdot}{C}(CN)\cdot CMe[H]\cdot \underset{\cdot}{C}Me\cdot CO_2Et \quad \text{(VI.)}$$

was subsequently assigned by Thorpe (P., 1912, **28**, 51). The methylation product was formulated as (IV), and the isomeric ester obtained from ethyl cyanoacetate and ethyl methylacetoacetate had the structure (V). Bland and Thorpe (J., 1912, **101**, 871) assigned to the ester (IV) the " normal " structure (VI). On treatment of the " normal " ester with sodium ethoxide a sodio-derivative is formed, from which water liberates a part of the ester, and this was stated to be the unchanged " normal " ester, whereas the ester still remaining in solution, which can be recovered by saturating the solution with carbon dioxide, was termed the " labile " ester (V). This is in part contrary to the observation of Hope (J., 1922, **121**, 2216), who found that the ester IV (or VI) was converted into the ester (V) on treatment with ammonia or sodium ethoxide.

Of the related esters with a γ- but not a β-substituent, little was known except that the methyl, ethyl, and phenyl compounds had been prepared by Ingold, Perren, and Thorpe (J., 1922, **121**, 1765) and formulated as $CO_2Et\cdot CH(CN)\cdot CH{:}CR\cdot CO_2Et$, although no strict proof of their structure was given.

Consideration of the formula of the cyanoglutaconic esters suggests that these substances should exhibit tautomerism similar to that studied in cyanomonocarboxylic esters (Birch, Kon, and Norris, J., 1923, **123**, 1361; Hugh and Kon, J., 1930, 775), and react in the forms $CO_2Et\cdot C(CN){:}CR\cdot CHR'\cdot CO_2Et$ (αβ) and $CO_2Et\cdot CH(CN)\cdot CR{:}CR'\cdot CO_2Et$(βγ), although the point of equilibrium is somewhat difficult to predict.

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* The formulation representing the metal as attached to carbon has been used throughout the paper for the sake of simplicity.

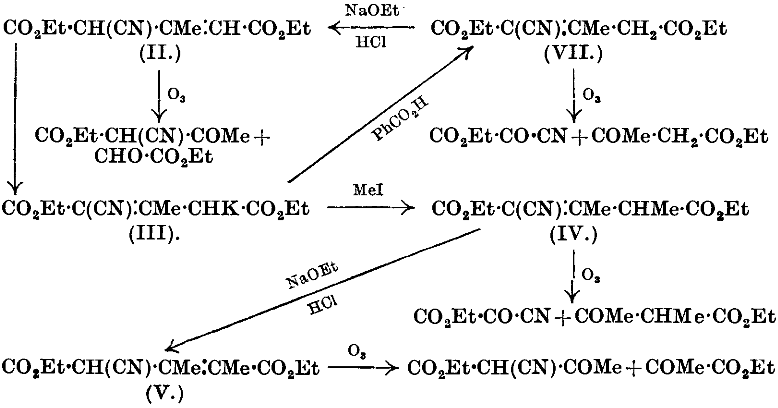
The presence of another activating group provides a second path for enolisation, and two modes of alkylation will therefore be possible: this is actually found in practice, although the rules governing the process are less simple than hitherto believed.

Our attention was principally devoted to the study of ethyl α-cyano-β-methylglutaconate and its methyl derivatives. The compounds were carefully purified, their physical properties examined, and their structures determined by ozonolysis. A partly successful attempt was also made to apply Linstead and May's iodometric method (J., 1927, 2565) to these compounds.

Ethyl α-cyano-β-methylglutaconate, the preparation of which has been considerably improved, appeared at first to have the βγ-structure (II); the molecular refraction has only a moderate exaltation and the compound has a considerable affinity for iodine chloride, especially under the modified conditions employed in the present work (up to 72% addition). Ozonolysis proved, however, that although the βγ-form preponderates, an appreciable amount of the isomeric αβ-form is also present (see Table I).

Such a result is quite understandable, because the ester (II) is obtained by the acidification of its sodio- or potassio-derivative under conditions which lead to equilibrium mixtures (Hugh and Kon, *loc. cit.*). Now it has been shown by Hugh and Kon (*loc. cit.*) that when the liberation of an ester from its sodio-derivative is carried out in the absence of water and polar catalysts, it is sometimes possible to arrest the production of an equilibrium mixture. The enolic form of the βγ-ester, which is first produced, passes into its own keto-form, without conversion into the keto-form of the αβ-ester, and in this manner the βγ-isomeride of ethyl *cyclo*pentylidenemalonate was isolated.

TABLE I.



moreover, again consisted of the equilibrium mixture. As the reaction was carried out in the absence of alcohol, it may be that the production of the equilibrium mixture is not due to the equilibration of the ester formed but to a different mode of reaction, for it is possible for the two components to undergo a Michael reaction with the subsequent elimination of hydrogen chloride, which can proceed in two directions :

$$\mathrm{CO_2Et{\cdot}CHNa{\cdot}CN + CMeCl{:}CH{\cdot}CO_2Et \longrightarrow}$$
$$\mathrm{CO_2Et{\cdot}CNa(CN){\cdot}CMeCl{\cdot}CH_2{\cdot}CO_2Et - \rightarrow (II)\ and\ (VII).}$$

The examination of the $\beta\gamma$-dimethyl esters (IV) and (V) showed that they were related in the same way as the lower homologues just described. The molecular refraction of the methylation product of the potassium compound (III) has a considerable exaltation over those of the parent compound (II) and the isomeric ester (V), suggesting a difference of structure. An endeavour was made to compare their additive power towards iodine chloride, but under the conditions successfully used for the parent ester both methyl compounds were practically inert and could not be distinguished.

By oxidation with ozone, however, it was found that the ester (IV) was the pure $\alpha\beta$-compound, giving ethyl cyanoglyoxylate, $\mathrm{CN{\cdot}CO{\cdot}CO_2Et}$, and ethyl methylacetoacetate as sole products. The isomeric ester, on the other hand, proved to be *mainly* the $\beta\gamma$-ester (V) but contained small amounts of the $\alpha\beta$-form (IV). Such a result is quite understandable, for, whereas the ester (IV) is prepared from the pure solid potassium compound (III) in the absence of equilibrating reagents, the ester (V) (like the parent ester II) is liberated from solutions of its sodio-derivative by means of hydrochloric acid and is therefore an equilibrium mixture (compare Hugh and Kon, *loc. cit.*). This view was confirmed by treating the ester (IV) with sodium ethoxide; the ester liberated from the solution by addition of water and hydrochloric acid had the lower molecular refraction and all the other properties of the ester (V) (compare Hope, *loc. cit.*). Similarly, Bland and Thorpe's " normal " and " labile " esters proved to be the *same* equilibrium mixture, consisting mainly of the ester (IV) and *not* identical with the ester from which they were derived; this was proved by ozonolysis of the two esters and it is plain that the amount of " normal " ester precipitated on addition of water to the alcoholic solution of the sodio-derivative is entirely dependent on the degree of dissociation of the latter in water. Thus, the amount of " normal " ester obtained from the more acid or enolisable γ-benzyl ester is less, and the amount of the " labile " ester liberated by carbon dioxide greater than in the preceding case, but these two esters again appear to be identical.

The sodio-derivative of the ester (V) has the structure

$CO_2Et{\cdot}CNa(CN){\cdot}CMe{:}CMe{\cdot}CO_2Et$,

as it yields ethyl α-cyano-αβγ-trimethylglutaconate on treatment with methyl iodide (Rogerson and Thorpe, *loc. cit.*); it should therefore be possible to obtain the pure βγ-ester from it by treatment with benzoic acid. The ester so obtained proved to be similar to the equilibrium mixture in properties except for a somewhat lower molecular refraction, but the products obtained on oxidation with ozone indicated that it consisted of the pure βγ-ester (V), as no trace of the easily recognisable ethyl methylacetoacetate was found in addition to the expected products, ethyl pyruvate and ethyl α-cyanoacetoacetate.

Ethyl α-cyano-γ-methylglutaconate was found to have physical properties similar to those of its β-methyl isomeride (the slightly lower molecular refraction is due to "crossed" conjugation) and a fairly high iodine addition, in agreement with the βγ structure.

$CO_2Et{\cdot}CH(CN){\cdot}CH{:}CMe{\cdot}CO_2Et$ (VIII.)

On oxidation with ozone, however, it gave products indicating the presence of the αβ-form as well, so it also is an equilibrium mixture, as would be expected from the method used in its preparation.

The ester readily forms a solid potassium derivative like the ester (II) but having the potassium attached to the cyanoacetic residue. This is proved by the ready formation of a methylation product consisting of *ethyl α-cyano-αγ-dimethylglutaconate*,

$CO_2Et{\cdot}CMe(CN){\cdot}CH{:}CMe{\cdot}CO_2Et$,

and not the γγ-compound $CO_2Et{\cdot}C(CN){:}CH{\cdot}CMe_2{\cdot}CO_2Et$; its structure was proved by ozonolysis and by the characteristic reaction with sodium ethoxide, which leads to the rapid elimination of a carbethoxyl group. It was clearly impossible to prepare the αβ-isomeride of the ester (VIII) by the method successfully employed with the β-methyl esters; actually the potassium compound gives on treatment with benzoic acid in dry ether an ester which has an even higher affinity for iodine chloride than the original ester. The point of equilibrium is approximately the same as in the isomeric β-methyl esters.

Finally, the alkylation of ethyl α-cyanoglutaconate was investigated. As neither the α- nor the γ-position in this ester is substituted, it can be alkylated in two ways; should the methyl group enter the γ-position, as in the ester (II), Ingold, Perren, and Thorpe's γ-methyl ester should result. The ester obtained is, however, an isomeric compound, the methyl group entering the α-position as shown by ozonolysis; a similarly constituted ethyl compound,

$CO_2Et{\cdot}CEt(CN){\cdot}CH{:}CH{\cdot}CO_2Et$,

is also readily produced.

It is certainly remarkable that ethyl α-cyanoglutaconate is alkylated in the α-position, whereas esters with a positive substituent in the β-position, such as the β-methyl compound discussed above and the β-amino-ester investigated by Baron, Remfry, and Thorpe (J., 1904, **85**, 1737; compare J., 1910, **97**, 1299), give γ-alkyl derivatives (the α-alkylation of the γ-methyl ester is to be expected). It is clear that alkylation follows the entrance of the alkali metal into the molecule, forming an enolate, and that the positive β-substituent in some way favours the enolisation of the γ- rather than the α-carbethoxyl group, although the reason for this is not apparent. Further experiments are being undertaken with the object of shedding light on this problem.

A survey of the above facts leads to several important conclusions.

The cyanoglutaconic esters display tautomerism of the same type as that of many other unsaturated cyano-esters. They can in some cases be isolated in two distinct forms; the reactions of these isomerides are fully accounted for by the αβ- and βγ-unsaturated formulæ, and the "normal" formulation suggested for some of them is no longer necessary. These isomerides are interconvertible in the presence of suitable catalysts, forming equilibrium mixtures, notably when they are liberated from their sodio-derivatives, and for this reason the method of distinguishing between "normal" and "labile" isomerides used by Thorpe and Bland (*loc. cit.*) is not effective. This statement applies only to α-cyano- and α-carbethoxyglutaconic esters (an account of the latter will shortly be published), because the terms "normal" and "labile" have also been used to denote the esters of the glutaconic acids themselves. These are no doubt distinct and their isomerism presents a separate problem in which stereoisomerism unquestionably plays an important part.

Finally, it is shown that in the equilibrium mixtures the βγ-ester predominates.

EXPERIMENTAL.

Ethyl α-Cyano-β-methylglutaconate (equilibrium ester, II and VII).—Several modifications, enumerated below, of Rogerson and Thorpe's method (*loc. cit.*) were tried for the preparation of this ester: following Hope's suggestion (*loc. cit.*), the alcohol used was carefully dehydrated with calcium before use.

1. Rogerson and Thorpe's method. Yield, 33%.
2. Excess of alcohol removed in a vacuum at 60°. Yield, 35%.
3. Sodium ethoxide prepared from "molecular" sodium suspended in dry ether with the theoretical quantity of alcohol. Mixture kept cold for 2 days. Yield, 35%.
4. As (3) but potassium used in place of sodium. Yield, 56%.
5. A solution of potassium (20 g.) in alcohol (150 c.c.) was cooled,

ethyl cyanoacetate (56 g.) added with shaking, then ethyl acetoacetate (65 g.), and the flask kept in a freezing mixture for some hours and at room temperature for 2 days. There was very little darkening under these conditions. Yield, 80%.

6. Equimolecular quantities of the two esters were kept at room temperature with a few drops of triethanolamine or piperidine. The yield in both cases was very poor (10% and 3% respectively); the product was in every way identical with that obtained with potassium ethoxide (Found for a specimen prepared with triethanolamine: C, 58·4; H, 6·7. Calc.: C, 58·6; H, 6·6%) in physical properties and iodine addition (see below).

The ester, purified by redistillation, boiled at 170°/25 mm. and had $d_{4°}^{18·0°}$ 1·0897, $n_{D}^{18·0°}$ 1·46917, $[R_L]_D$ 57·55.

Oxidation. 10 G. of the ester, dissolved in 100 c.c. of pure ethyl acetate, were treated with a rapid stream of ozonised oxygen until no more absorption took place (48 hours). The solvent was removed in a vacuum at room temperature, and the ozonide decomposed by shaking with water for several hours. The products were taken up in ether, the extract shaken with sodium carbonate, dried, and evaporated, and the residue distilled under 14 mm. pressure. Fractions were obtained: (1) up to 70°, (2) 70—90°, (3) 90—120°, (4) 120—150°, (5) a small amount above 150° consisting of unchanged ester.

Fraction (1) gave a red colour with ferric chloride and yielded with phenylhydrazine acetate a mixture of two compounds which were separated by extraction with methyl alcohol. The soluble component was the phenylhydrazone of glyoxylic ester, m. p. 157° * (Found: C, 62·6; H, 6·2. Calc.: C, 62·5; H, 6·3%), and the sparingly soluble compound was 1-phenyl-3-methylpyrazolone; both were identified by comparison with genuine specimens.

Fraction (2) developed a deep red colour with ferric chloride and readily gave phenylmethylpyrazolone unaccompanied by any other compound.

Fraction (3) gave a faint colour with ferric chloride, yielded a trace of phenylmethylpyrazolone, and gave with semicarbazide the semicarbazone of ethyl α-cyanoacetoacetate (m. p. 189°; mixed m. p. 189—190°) (Michael, *Ber.*, 1905, **38**, 51).

Fraction (4) gave no colour with ferric chloride and yielded the *phenylhydrazone* of *ethyl cyanoglyoxylate*, which crystallised from alcohol in yellow plates, m. p. 127° (Found: C, 60·8; H, 5·1. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·1%); it also gave the characteristic reduction of ammoniacal silver nitrate observed by Scheiber

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* This phenylhydrazone has been repeatedly obtained in these laboratories in the course of ozonisations and found to have the above melting point.

and Meisel (*Ber.*, 1915, **48**, 255), who were the first to obtain the ester but did not characterise it. The ester was repeatedly obtained by us in the course of ozonisation experiments, although invariably in small quantities; it appears to boil at 130—135°/15 mm.

The oxidation products are therefore ethyl glyoxylate, ethyl acetoacetate, ethyl α-cyanoacetoacetate, and ethyl cyanoglyoxylate.

Iodine Additions.—Preliminary experiments were made with ethyl α-cyano-β-methylglutaconate and its two methyl derivatives (IV) and (V). Under Linstead and May's standard conditions (*loc. cit.*) an $M/300$-chloroform solution of the parent ester had some 30% addition in 1 hour, the ester (IV) had no addition, and the ester (V) one of 5·7%; the last was due to the presence in (V) of some of the parent ester, as it had been prepared from a specimen of ethyl methylacetoacetate which had not been specially purified. The pure βγ-ester has no measurable addition. In carbon tetrachloride solution, the addition of the parent ester was somewhat higher (29% in 30 minutes, 42% in 1 hour). The strength of the ester solution was then trebled, and that of the iodine chloride doubled (5·1 g. of mercuric chloride and 3·38 g. of iodine per 100 c.c.). The addition observed with the parent ester in chloroform was 57·5% in 1 hour, and these conditions were adopted as standard throughout this investigation. In carbon tetrachloride, somewhat higher additions (40%, 59%, and 72% in ½, 1, and 1½ hours) were observed. Bromine in chloroform ($N/10$) gave only 8% addition in 1 hour, and iodine chloride in acetic acid about 4%. The dimethyl esters showed no addition under any of the conditions tried.

Attempts to prepare the Pure βγ-Ester.—(1) Ethyl cyanoacetate (56 g.) was added to "molecular" sodium (11·5 g.) in benzene (300 c.c.), and the sodio-derivative boiled under reflux with ethyl β-chlorocrotonate (80 g.) (prepared by the method of Mamert, *Bull. Soc. chim.*, 1895, **13**, 71) for 6 hours. Water was then added and the benzene layer was separated, washed, dried, and distilled under reduced pressure. Yield of fraction b. p. 160—162°/18 mm., 4 g.

(2) Ethyl cyanoacetate (56 g.) was added to sodium (11·5 g.) dissolved in absolute alcohol (150 c.c.) and the mixture was kept at 0° while ethyl β-chlorocrotonate (80 g.) was gradually added with shaking. After 2 days, the product was worked up as before and gave the same yield of condensation product, b. p. 166°/13 mm., with an iodine addition of 57% in 1 hour (Found: C, 58·3; H, 6·4. Calc.: C, 58·6; H, 6·6%).

Finally an attempt was made to see whether the αβ-ester present in the equilibrium ester could be eliminated in the form of a bimolecular reduction product by treatment with aluminium amalgam in ether (Harries and Eschenbach, *Ber.*, 1896, **29**, 389). The whole of the product, however, boiled at 175°/14 mm., and was fully saturated, consisting of ethyl α-cyano-β-methylglutarate (Darbishire and Thorpe, J., 1905, **87**, 1716) (Found: C, 58·2; H, 7·5. Calc.: C, 58·1; H, 7·5%), as it gave β-methylglutaric acid, m. p. and mixed m. p. 87°, on hydrolysis with sulphuric acid.

Ethyl α-Cyano-β-methyl-Δ^α^-propene-αγ-dicarboxylate (VII).—(1) Ethyl α-cyano-β-methylglutaconate was converted into the potassium compound (III) as described by Rogerson and Thorpe (*loc. cit.*) and the salt was washed with alcohol and ether and dried in a desiccator. 100 G. of the salt were suspended in dry ether, a little less than the theoretical quantity of benzoic acid (48 g.), dissolved in dry ether, was added, and the mixture mechanically shaken for 2 days. The potassium benzoate was filtered off and washed with ether, the ethereal solution, which gave a distinct colour with ferric chloride, was evaporated, and the residue distilled under reduced pressure. About 50 g. of the new αβ-*ester*, b. p. 178—180°/22 mm., were collected; it had $d_{4^\circ}^{19\cdot5^\circ}$ 1·0918, $n_D^{19\cdot5^\circ}$ 1·47409, $[R_L]_D$ 57·89, and an iodine addition of 3% in one hour (Found: C, 58·7; H, 6·5. $C_{11}H_{15}O_4N$ requires C, 58·6; H, 6·6%). The distilled ester no longer gave a colour with ferric chloride.

(2) The pure dry potassium salt was suspended in dry petroleum (b. p. 40—60°), cooled in a freezing mixture, and dry hydrogen chloride bubbled in, the process being interrupted when rather less than the theoretical amount of acid had been introduced; the ester formed was isolated as before and had b. p. 174°/20 mm., $d_{4^\circ}^{23^\circ}$ 1·0920, $n_D^{23^\circ}$ 1·47429, $[R_L]_D$ 57·88, and an iodine addition of 2% in one hour (Found: C, 58·3; H, 6·6%).

It was subsequently found that the best method of preparing the potassium compound (III) is by the action of alcoholic potassium ethoxide on the equilibrium ester (II), the ester being taken in slight excess. The precipitation of the potassium compound is completed by adding dry ether; the precipitate is filtered off, washed with dry ether, and is then ready for use, and the process of drying the solid is unnecessary. The above method was used in all the regenerations of esters described below. The use of potassium in place of the sodium originally employed by Hugh and Kon (*loc. cit.*) is advantageous because potassium benzoate is much more easily filtered off than the gelatinous sodium salt.

The proportion of αβ-ester obtained by the above methods varies within wide limits owing to causes which are still under investigation. The experiments described above gave the best yield.

Oxidation. The αβ-ester was ozonised, and the product worked up exactly as described on p. 567. The fractions obtained at 15 mm. were: (1) 70—90°, (2) 90—130°, (3) 130—150°, (4) above 150°, unchanged ester. Fractions (1) and (2) gave an intense red colour with ferric chloride and contained ethyl acetoacetate, identified in the form of phenylmethylpyrazolone; no ethyl glyoxylate could be found. Fraction (3) did not give a colour with ferric chloride and consisted of ethyl cyanoglyoxylate, which was identified by means of the phenylhydrazone, m. p. 127°. The oxidation products are therefore those which would be expected from the pure ester (VII).

Action of sodium ethoxide on the $\alpha\beta$*-ester.* The $\alpha\beta$-ester was added to a cold solution of sodium in absolute alcohol in slight excess. After a few minutes, water and dilute hydrochloric acid were added, the ester was taken up in ether, and the extract washed with sodium carbonate solution and with water, dried, and evaporated. The equilibrium ester boiled at 163°/19 mm. and had $d_{4^\circ}^{20^\circ}$ 1·0894, $n_{\mathrm{D}}^{20 \cdot 0^\circ}$ 1·46917, $[R_L]_{\mathrm{D}}$ 57·56, iodine addition 56·4% in 1 hour (Found: C, 58·6; H, 6·5. Calc.: C, 58·6; H, 6·6%).

Determination of the point of equilibrium. 10·0 G. of the equilibrium ester were ozonised in ethyl acetate and the ozonide was worked up as described above, but the products were not distilled after removal of the ether. The residue (8 g.) was treated with an equal volume of phenylhydrazine, a few c.c. of water were added and enough acetic acid to give a clear solution, which was then kept at 100° for 3 hours and at room temperature for 2 days. The solid was collected (2·87 g. after drying) and extracted with methyl alcohol, and the insoluble residue of phenylmethylpyrazolone dried (0·468 g.). The experiment was repeated to ensure that the result was not accidental and an ozonisation of the pure $\alpha\beta$-ester was carried out at the same time; 3·1 g. of "total phenylhydrazones" and 2·0135 g. of pyrazolone were obtained. From the amount of pyrazolone recovered, the minimum % of $\alpha\beta$-form present in the equilibrium ester would be 7·6 and in the $\alpha\beta$-ester 32·8, or, in other words, about 1/3 of the total $\alpha\beta$-ester is recovered in the form of pyrazolone; allowing for this, the $\alpha\beta$-content of the equilibrium ester becomes about 23%, whereas the maximum deduced from the iodine addition in $1\frac{1}{2}$ hours is 28%.

Ethyl α*-Cyano-*$\beta\gamma$*-dimethyl-*Δ^{α}*-propene-*$\alpha\gamma$*-dicarboxylate* (IV).—This ester was prepared by treating the potassium compound (III) with methyl iodide as described by Rogerson and Thorpe (*loc. cit.*); a better yield is, however, obtained if alcoholic potassium ethoxide is used in the preparation of the potassium compound. The ester has b. p. 162°/14 mm., $d_{4^\circ}^{18 \cdot 0^\circ}$ 1·0456, $n_{\mathrm{D}}^{18 \cdot 0^\circ}$ 1·46619, $[R_L]_{\mathrm{D}}$ 63·37; iodine addition nil.

Oxidation. The ester was ozonised and the product worked up exactly as described on p. 567, and the following fractions were obtained at 10 mm.: (1) 70—80°, (2) 80—130°, (3) 130—150°,

(4) above 150°, unchanged ester. Fraction (1) gave a fine violet colour with ferric chloride, and yielded the phenylhydrazone of ethyl methylacetoacetate, orange needles, m. p. 153°, identified by direct comparison with a genuine specimen. Fraction (2) gave a faint colour with ferric chloride and a little of the same phenylhydrazone was isolated from it. Fraction (3) did not give a colour with ferric chloride and yielded the phenylhydrazone of ethyl cyanoglyoxylate, m. p. 127°; the ester was also recognised by the reducing action on ammoniacal silver nitrate. No trace of ethyl pyruvate or ethyl α-cyanoacetoacetate could be detected and the ester was thus the pure αβ-form (IV).

Ethyl α-Cyano-βγ-dimethylglutaconate (equilibrium ester IV and V).—This ester was prepared in 25% yield by the modification of Rogerson and Thorpe's method described on p. 567. It is essential to purify the ethyl methylacetoacetate by repeated shaking with dilute aqueous ammonia (Michael, *Ber.*, 1905, **38**, 2091), otherwise the product is liable to contain some of the parent ester (II); this can be detected by the fact that the ester then has an appreciable affinity for iodine chloride (6—8% addition in 1 hour). The pure equilibrium ester boils at 160°/13 mm. and has $d_{4^\circ}^{18\cdot0^\circ}$ 1·0708, $n_{\mathrm{D}}^{18\cdot0^\circ}$ 1·46996, $[R_L]_{\mathrm{D}}$ 62·26, iodine addition 1% in 1 hour.

Oxidation. The ester was ozonised and the product worked up exactly as described on p. 567, the following fractions being obtained at 15 mm.: (1) up to 70°, (2) 70—110°. Fraction (1) gave a deep violet colour with ferric chloride and a reddish-violet with sodium nitroprusside, changing to deep violet with ammonia, red with potassium hydroxide and blue with acetic acid (test for ethyl pyruvate). It gave the phenylhydrazone of ethyl methylacetoacetate, m. p. 153°, and that of ethyl pyruvate, m. p. 119° (Found: C, 63·6; H, 6·8. Calc.: C, 64·1; H, 6·8%), which were separated by fractional crystallisation from alcohol. Fraction (2) gave a faint reddish-violet colour with ferric chloride, and a phenylhydrazone could not be obtained from it, but the semicarbazone of ethyl α-cyanoacetoacetate, m. p. 189°, was isolated. No high fraction, corresponding to ethyl cyanoglyoxylate, was found in this experiment, but the isolation of ethyl methylacetoacetate proves the presence of the ester (IV) beyond all doubt.

Ethyl α-Cyano-βγ-dimethyl-Δ^{β}-propene-αγ-dicarboxylate (V).—This ester was prepared by treating the equilibrium ester with potassium ethoxide and shaking the potassium derivative with benzoic acid exactly as described on p. 569. The ester obtained boiled at 154°/9 mm. and had $d_{4^\circ}^{20\cdot0^\circ}$ 1·0729, $n_{\mathrm{D}}^{20\cdot0^\circ}$ 1·46916, $[R_L]_{\mathrm{D}}$ 62·05.

Oxidation. The ester was ozonised and the product worked up exactly as described before. The same fractions were obtained as in the preceding case, but fraction (1) did not give the characteristic violet colour with ferric chloride, due to ethyl methylacetoacetate, nor could its phenylhydrazone be isolated, although ethyl pyruvate was readily identified. Similarly, no trace of ethyl cyanoglyoxylate could be found; the ester thus appeared to be the pure βγ-compound (V).

Action of Sodium Ethoxide on the Ester (IV).—The pure αβ-ester was treated with sodium ethoxide and separated into the "normal" and the "labile" ester exactly as described by Thorpe and Bland (*loc. cit.*). The "normal" ester had $d_{4°}^{17·0°}$ 1·0731, $n_D^{17·0°}$ 1·46818, $[R_L]_D$ 62·17. It was ozonised, giving the same products as the equilibrium ester (see above) except that ethyl cyanoglyoxylate was also identified by means of its phenylhydrazone, m. p. 127°. The "labile" ester had $d_{4°}^{17·0°}$ 1·0733, $n_D^{17·0°}$ 1·46996, $[R_L]_D$ 62·09, and gave precisely the same result on oxidation with ozone, all four oxidation products being isolated. Both the "normal" and the "labile" ester thus consist of the equilibrium ester (compare Hope, *loc. cit.*). Neither "normal" nor "labile" ester gave a colour with ferric chloride.

The formation of small quantities of ethyl carbonate and ethyl γ-cyano-βγ-dimethylcrotonate in the action of sodium ethoxide on the ester (IV) was also observed.

Ethyl α-Cyano-γ-benzyl-β-methyl-Δ^α-propene-αγ-dicarboxylate.—This ester was prepared as described by Rogerson and Thorpe by the benzylation of the potassium compound (III). It boiled at 213°/15 mm. and had $d_{4°}^{19·2°}$ 1·0997, $n_D^{19·2°}$ 1·51800, $[R_L]_D$ 87·29, iodine addition nil.

Ethyl α-Cyano-γ-benzyl-β-methylglutaconate (equilibrium ester).—This was prepared in 33% yield from ethyl cyanoacetate and ethyl benzylacetoacetate in the presence of potassium ethoxide in exactly the same way as the βγ-dimethyl ester. The *ester* boiled at 216°/14 mm. and had $d_{4°}^{19·3°}$ 1·1082, $n_D^{19·3°}$ 1·52005, $[R_L]_D$ 86·46, iodine addition nil (Found: C, 68·4; H, 6·5. $C_{18}H_{21}O_4N$ requires C, 68·7; H, 6·6%).

Action of sodium ethoxide on the γ-benzyl ester. The ester was treated with one equivalent of sodium ethoxide and separated into "normal" and "labile" portions as described by Thorpe and Bland (*loc. cit.*). The esters isolated had the following properties: "normal," b. p. 215°/11 mm., $d_{4°}^{19·0°}$ 1·1043, $n_D^{19·0°}$ 1·51989, $[R_L]_D$ 86·42; "labile," b. p. 214°/11 mm., $d_{4°}^{18·9°}$ 1·1042, $n_D^{18·9°}$ 1·51999, $[R_L]_D$ 86·47; they were thus identical with the equilibrium ester described above, the latter being characterised by a somewhat higher density and refractive index than the pure αβ-ester. Neither the "labile" nor the "normal" ester gave a colour with ferric chloride.

Ethyl α-cyanoglutaconate was prepared by the method of Verkade (*loc. cit.*) and purified as far as possible as recommended by Ingold and Perren (*loc. cit.*).

Ethyl α-Cyano-α-methyl-Δ^{β}-propene-αγ-dicarboxylate.—Ethyl α-cyanoglutaconate was converted into the sodio-derivative by means of sodium ethoxide and treated with an excess of methyl iodide, the reaction being completed by warming. The methylated *ester* was obtained in 30% yield as a colourless oil, b. p. 160—161°/16 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0662, $n_{D}^{20\cdot0^\circ}$ 1·45543, $[R_L]_D$ 57·31 (Found: C, 58·9; H, 6·8. $C_{11}H_{15}O_4N$ requires C, 58·6; H, 6·6%); it did not react with iodine chloride.

Oxidation. The ester was ozonised and the product worked up as described on p. 567. The following fractions were obtained at 16 mm.: (1) up to 75°, (2) 75—120°, (3) 120—150°. Fraction (1) gave no colour with ferric chloride, and the phenylhydrazone of ethyl glyoxylate, m. p. 157°, was prepared from it and identified. Neither of the other fractions gave a colour with ferric chloride, showing the absence of ethyl formylpropionate. Fraction (2) gave a phenylhydrazone, melting indefinitely above 200°, which has not yet been identified. The isolation of ethyl glyoxylate definitely establishes the βγ-position of the double bond.

Action of sodium ethoxide. A small amount of the methylated ester was treated with an equivalent quantity of sodium ethoxide. The mixture soon developed the characteristic odour of ethyl carbonate, indicating that a carbethoxyl group had been eliminated.

Ethyl α-Cyano-α-ethyl-Δ^{β}-propene-αγ-dicarboxylate.—The ethylation of ethyl cyanoglutaconate was carried out in the same way as the methylation. The *ester* was obtained in 25% yield; b. p. 158—160°/11 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0503, $n_{D}^{20\cdot0^\circ}$ 1·5323, $[R_L]_D$ 61·54, iodine addition nil; it did not solidify in a freezing mixture (Found: C, 60·0; H, 7·3. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·1%).

A small amount of the ester was mixed with piperidine and kept at room temperature. Long needles began to form at the end of 2 hours and the separation was complete at the end of a day. The solid melted at 77—79° and evidently consisted of Guthzeit and Eyssen's ethylation product; the quantity obtained was insufficient for identification.

Ethyl α-Cyano-γ-methylglutaconate (VIII).—This ester was prepared by the method of Ingold and Perren (*loc. cit.*), but the yield was increased to 65% by the use of potassium ethoxide in the cold. The ester had b. p. 156°/13 mm., $d_{4^\circ}^{19\cdot5^\circ}$ 1·0743, $n_{D}^{19\cdot5^\circ}$ 1·45933, $[R_L]_D$ 57·28, iodine addition 59% in 1 hour. The end point in the titration was not very satisfactory, as the purple colour of the starch indicator reappeared after a short time; this was no doubt due to the splitting off of the halogen which had formed a substitution product with the unsaturated ester, a difficulty already met with in ketones, especially those which have a very high iodine addition.

The ester shows a characteristic behaviour when aqueous ferric chloride is added to its solution in alcohol. The colour of the reagent quickly fades and further quantities of it can be added, producing the same effect; the purple colour mentioned by Ingold and Perren (*loc. cit.*) was not observed. The fading of the ferric chloride is due to reduction of the reagent, because on addition of a drop of aqueous ammonia to the solution a green precipitate of ferrous hydroxide is produced.

Oxidation. The ester was ozonised and the product worked up as described on p. 567, the following fractions being obtained at 20 mm.: (1) up to 90°, (2) 90—125°, (3) 125—150°, (4) above 150°, consisting of unchanged ester. Fraction (1) gave a deep violet colour with ferric chloride and formed a mixture of derivatives, from which the phenylhydrazone of ethyl pyruvate, m. p. 119°, was isolated, together with long needles, m. p. 125°, consisting of 1-phenyl-2-methylpyrazolone (Michael, *Ber.*, 1905, **38**, 2108), identical with a specimen prepared from ethyl formylpropionate. Fraction (2) gave a slight colour with ferric chloride; no solid derivatives were isolated from it. Fraction (3) gave the phenylhydrazone of ethyl cyanoglyoxylate, m. p. 127°. The oxidation products thus point to the presence of both the αβ- and the βγ-ester.

Ethyl α-Cyano-αγ-dimethyl-Δ^{β}-propene-αγ-dicarboxylate.—Ethyl α-cyano-γ-methylglutaconate, alcoholic potassium ethoxide (1 equiv.), and an excess of methyl iodide were warmed together until the mixture was neutral in reaction. The methylated *ester* was obtained in 70% yield, b. p. 176—177°/22 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0729, $n_{\mathrm{D}}^{20\cdot0^\circ}$ 1·46818, $[R_L]_{\mathrm{D}}$ 61·89; it had no affinity for iodine chloride (Found: C, 60·2; H, 7·2. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·2%).

Oxidation. The ester was ozonised and the product worked up as described on p. 567, the following fractions being obtained at 16 mm.: (1) up to 70°, (2) 70—86°, mostly at 85—86°; no high fraction was formed. Fraction (1) gave no colour with ferric chloride, a positive test with sodium nitroprusside, and an abundant precipitate of ethyl pyruvate phenylhydrazone, m. p. 119°. Fraction (2) gave no colour with ferric chloride, and formed a *phenylhydrazone* crystallising in buff plates, m. p. 237—238°, doubtless derived from the ester $CHO{\cdot}CMe(CN){\cdot}CO_2Et$ (Found: C, 63·7; H, 5·8. $C_{13}H_{15}O_2N_3$ requires C, 63·7; H, 6·1%).

Action of sodium ethoxide. The methylated ester (16 g.), dissolved in 5 c.c. of alcohol, was mixed with a cold solution of 1·6 g. of sodium in 25 c.c. of alcohol. After an hour, the mixture was poured into water and extracted with ether, the extract repeatedly washed, dried, and evaporated, and the residue distilled, at atmospheric pressure until the temperature was 130°, then at 12 mm.; an oil distilled at 110—115°. The first fraction on redistillation boiled at 127° and consisted of ethyl carbonate; the second boiled at 103°/12 mm. and was evidently *ethyl α-cyano-αγ-dimethylcrotonate* (Found: C, 64·0; H, 7·9. $C_9H_{13}O_2N$ requires C, 64·1; H, 7·8%).

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