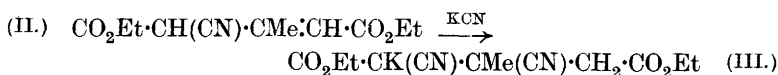


CCLXVI.—*The Addition of Hydrogen Cyanide to Derivatives of Glutaconic Acid. Part I. The Addition of Hydrogen Cyanide to Ethyl  $\alpha$ -Cyano- $\beta$ -methylglutaconate and its Homologues.*

By EDWARD HOPE and WILFRID SHELDON.

IN the course of an investigation carried out by one of us some years ago on the reaction occurring between ethyl citraconate and ethyl sodiomalonate (T., 1912, **101**, 892), it was found necessary to devise a means for the synthesis of  $\beta$ -methyltricarballic acid,  $\text{CO}_2\text{H}\cdot\text{CH}_2\cdot\text{CMe}(\text{CO}_2\text{H})\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$  (I). The method then adopted depended on the interaction of potassium cyanide with ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate in alcoholic solution according to the scheme :



Ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate, derived from the potassium compound (III), yielded  $\beta$ -methyltricarballic acid on hydrolysis. This method sufficed at the time, but it has been since found that

the addition of hydrogen cyanide occurs almost quantitatively and with remarkable ease when the conditions first described by Lapworth (T., 1903, **83**, 995) are employed, that is, when the unsaturated ester, dissolved in alcohol or aqueous alcohol, is treated with hydrogen cyanide in the presence of potassium cyanide (the latter ensuring the presence of the essential agent, cyanide ions).

It is noteworthy that addition of hydrogen cyanide takes place also when the unsaturated ester is shaken with an aqueous solution of potassium cyanide in the entire absence of alcohol. When ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate is treated with a strong aqueous solution of potassium cyanide, it first dissolves, but the homogeneous solution soon separates into two layers, the lower one of which consists of a solution of the potassium derivative of the additive product (III). The possibility of using purely aqueous solutions was important in investigating whether an ester without replaceable hydrogen, for example, ethyl  $\alpha$ -cyano- $\alpha\beta\gamma$ -trimethylglutaconate,

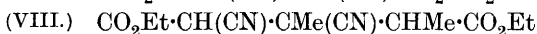
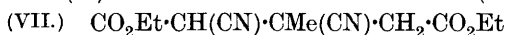
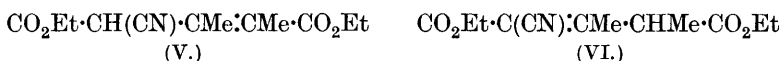


was capable of reacting with hydrogen cyanide or not.

The use of an aqueous alcoholic solution in a case like this results in the elimination of ethyl carbonate and the formation of ethyl  $\gamma$ -cyano- $\alpha\beta\gamma$ -trimethylcrotonate (compare Rogerson and Thorpe, T., 1905, **87**, 1669).

The present communication contains an account of the chemistry of the products of interaction of hydrogen cyanide and ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate (II), ethyl  $\alpha$ -cyano- $\beta$ -methyl- $\Delta^{\beta}$ -butene- $\alpha\gamma$ -dicarboxylate (V), and ethyl  $\alpha$ -cyano- $\beta$ -methyl- $\Delta^{\alpha}$ -butene- $\alpha\gamma$ -dicarboxylate (VI). The reactions in the latter two cases are almost certainly identical since, under the conditions of the experiment, the cyano-ester (VI) passes over into (V). In any case, the products of reaction with hydrogen cyanide are identical.

In these reactions, the products are, respectively, from (II), ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate (VII), and from (V) and (VI) ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII).

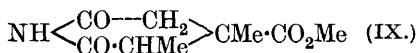


It is of interest to note that no addition of hydrogen cyanide could be detected in the case of ethyl  $\alpha$ -cyano- $\alpha\beta\gamma$ -trimethylglutaconate, which contains no hydrogen replaceable by metals. The general behaviour of the products VII and VIII is in accordance with the constitution given. For example, VII is hydrolysed by means of

concentrated hydrochloric acid or by 40 per cent. sulphuric acid to  $\beta$ -methyltricarballic acid, whilst VIII is hydrolysed by similar treatment to  $\alpha\beta$ -dimethyltricarballic acid\* (m. p. 165—167°).

The dicyano-esters also are much more acid in character than the cyanoglutaconates from which they are derived. The esters VII and VIII, for example, dissolve to some extent in a 10 per cent. solution of sodium carbonate and readily in potassium carbonate of equivalent strength, in both cases giving yellow solutions. Both esters, too, are readily attacked by a concentrated aqueous solution of ammonia. The cyanoglutaconates from which these esters are derived are practically not affected by alkali carbonates. They are, however, attacked by concentrated ammonia. The behaviour of the above dicyano-esters with ammonia is most remarkable, for it consists in nothing less than the complete reversal of the whole synthetical process from ethyl cyanoacetate and ethyl acetoacetate or a derivative. The product of interaction with ammonia, of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate (VII), for example, gives exactly the same products as arise in the similar treatment of ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate, namely,  $\beta$ -aminocrotonic ester and the hydroxypyridine derivative described in the preceding paper (p. 2220). The same kind of reaction occurs with the dimethyl derivative (VIII),  $\beta$ -amino- $\alpha$ -methylcrotonic ester being produced along with the corresponding hydroxypyridine derivative.

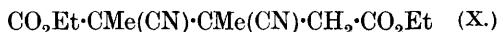
In view of the fact that ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate (VII) contains hydrogen replaceable by metals, a methyl homologue was prepared by the action of methyl iodide on the sodium derivative. A substance isomeric with the dimethyl derivative (VIII) was produced. The individuality of the new ester was established in several ways. When hydrolysed with 40 per cent. sulphuric acid, it yielded a substance which, on treatment with methyl-alcoholic hydrochloric acid, gave a new and highly crystalline solid containing nitrogen, which is probably an imide with the constitution (IX).



\* This is apparently the first preparation of this acid. The acid described by Michael (*Ber.*, 1900, **33**, 3757) as  $\beta$ -methylbutane- $\alpha\beta\gamma$ -tricarboxylic acid (that is,  $\alpha\beta$ -dimethyltricarballic acid), melting at 196—198°, was obtained by the hydrolysis of the methylation product of the substance which he formulated thus:  $(\text{CO}_2\text{Et})_2\text{CH} \cdot \text{CMe}(\text{CO}_2\text{Et}) \cdot \text{CH}_2 \cdot \text{CO}_2\text{Et}$ . The substance obtained by condensing ethyl citraconate with ethyl sodiomalonate is not, however, as Michael thought, ethyl  $\beta$ -methylpropane- $\alpha\beta\gamma\gamma$ -tetracarboxylate, but ethyl butane- $\alpha\alpha\beta\gamma$ -tetracarboxylate,  $(\text{CO}_2\text{Et})_2\text{CH} \cdot \text{CH}(\text{CO}_2\text{Et}) \cdot \text{CHMe} \cdot \text{CO}_2\text{Et}$  (Hope, T., 1912, **101**, 900), and Michael's acid is without doubt pentane- $\beta\gamma\delta$ -tricarboxylic acid,  $\text{CO}_2\text{H} \cdot \text{CHMe} \cdot \text{CH}(\text{CO}_2\text{H}) \cdot \text{CHMe} \cdot \text{CO}_2\text{H}$ , which does, in fact, melt at about 200°.

Under precisely the same conditions, ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII) yields the trimethyl ester of  $\alpha\beta$ -dimethyltricarballic acid.

The imido-ester is a white, crystalline solid melting at 135—136°. It dissolves in and can be titrated by *N*-potassium hydroxide solution. It suffers further hydrolysis when heated with concentrated hydrochloric acid in a sealed tube and gives  $\alpha\beta$ -dimethyltricarballic acid and ammonium chloride. The behaviour of the new ester (X) towards strong ammonia solution is also characteristic. It yields a sparingly soluble solid which gives no coloration with ferric chloride. This substance is probably an amide and not a pyridine derivative as in the other cases. The new dicyano-ester has without doubt the constitution



It would appear that in the case of these saturated substances, as in the case of the cyanoglutaconic esters, the hydrolytic action of ammonia depends on the presence of replaceable hydrogen in the cyanoacetic ester residue.

By the action of sodium and methyl iodide, it was found possible to prepare the next homologue of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate, namely, the ester



which gives rise to  $\alpha\beta\gamma$ -trimethyltricarballic acid on hydrolysis.

Trimethyltricarballic acid appears to be incapable of separate existence, but its anhydride (m. p. 188—190°) and its trimethyl ester (b. p. 166—172°/26 mm.) were prepared.

## EXPERIMENTAL.

### *Addition of Hydrogen Cyanide to Ethyl $\alpha$ -Cyano- $\beta$ -methylglutaconate.*

#### *Formation of Ethyl $\alpha\beta$ -Dicyano- $\beta$ -methylglutarate (VII).*

This substance has been described in a previous communication (Hope, T., 1912, **101**, 911), but the method of preparation there employed gave neither a good yield nor a pure product. The following method gives excellent results. Ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate (22.5 grams; 1 mol.), dissolved in alcohol (95 per cent.) (120 c.c.), is treated with a solution of potassium cyanide (13 grams; 2 mols.) in water (70 c.c.). The homogeneous solution is cooled in ice-water and further treated with a quantity of approximately 20 per cent. aqueous hydrochloric acid containing 5.4 grams (1.5 mols.) of the acid. The reaction mixture, after standing at the ordinary temperature for fifteen minutes, is poured into about 500 c.c. of dilute hydrochloric acid, the precipitated oil extracted

with ether, the ethereal solution washed with water several times and dried with calcium chloride. After evaporation of the ether, the residual oil is distilled under reduced pressure. In such an experiment, 21 grams of the pure product were obtained, boiling at 200—205°/20 mm. (yield 83 per cent. of the theoretical) (Found: C = 57.1; H = 6.7. Calc., C = 57.2; H = 6.3 per cent.).

Ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate is a colourless or slightly yellow, rather viscid oil not appreciably soluble in water. It dissolves readily in a 10 per cent. aqueous solution of potassium or sodium hydroxide, being apparently hydrolysed, since it is not reprecipitated on acidification of the solution. It is somewhat soluble in a 10 per cent. solution of sodium carbonate, forming a faintly yellow solution, but it is quite readily soluble in a potassium carbonate solution of equivalent strength. The ester is reprecipitated from these solutions in alkali carbonates on acidification. In its easy solubility in solutions of sodium and potassium carbonates the behaviour of this ester is in marked contrast to that of ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate, which is unchanged by these reagents—and indicates considerably greater acidity of one of the hydrogen atoms.

*Action of Ammonia.*—The ester is readily soluble in concentrated ammonia, giving at once a slightly opalescent solution. After keeping for twenty-four hours at the ordinary temperature, the solution was subjected to reduced pressure, and the cooling effect caused the crystallisation of a low-melting solid which proved to be  $\beta$ -aminocrotonic ester. The ester was purified and recognised as described under the account of the action of ammonia on ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate (this vol., p. 2219). There remained in the aqueous mother-liquors a high-melting solid which, exactly as did the corresponding glutaconate, gave, on boiling with alkali, a substance melting at 316—318°, which is identical with that obtained from the cyanoglutaconate and is evidently 6-hydroxy-2-keto-4-methyl-2 : 3-dihydropyridine-3-carboxylonitrile (Guareschi, *Mem. Accad. Sci. Torino*, 1896, 46, 1).

*Hydrolysis of Ethyl  $\alpha\beta$ -Dicyano- $\beta$ -methylglutarate by Mineral Acids.*  
*Formation of  $\beta$ -Methyltricarballic Acid.*—The best agent for effecting this hydrolysis was found to be concentrated hydrochloric acid (sulphuric acid was used in the earlier experiments, but the ultimate isolation of the acid is somewhat troublesome in this method). Usually 12 grams of the dicyano-ester were boiled with 100 c.c. of concentrated hydrochloric acid until all the oil had passed into solution, five to six hours being the time generally required. The clear liquid was then evaporated to dryness and the solid mass thus obtained, extracted for a long period with ether. On evapor-

ation of the latter, 6 grams of the acid remained and readily solidified. On recrystallisation from formic or hydrochloric acid, the product melted at  $164^{\circ}$ , and the melting point was unchanged by further crystallisation. The acid was, of course, identical with the  $\beta$ -methyltricarballic acid previously prepared by one of us (T., 1912, **101**, 909), using more or less the same method.

It was found that the above hydrolysis could be very rapidly effected (in about an hour) by heating at about  $140^{\circ}$  with sulphuric acid of 70 per cent. strength.

In the preparation of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate from ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate, a number of alterations in the method of adding the hydrogen cyanide were tried—more particularly because it was necessary in some later experiments to avoid the presence of alcohol in performing this reaction.

It was found, in the first place, that no alcohol is really necessary, although it is convenient, provided that the cyanoglutaconate is sufficiently violently agitated with the hydrogen cyanide solution. A larger excess of potassium cyanide, 3, 4, and 5 molecular proportions to 1.5 of hydrochloric acid, did not alter the yield of the product in any way.

In the case of ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate, vigorous agitation with a concentrated solution of potassium cyanide leads to the same result. In this experiment, vigorous shaking from time to time during ten minutes results in the formation of a deep yellow emulsion, from which nothing can be extracted by means of ether. After allowing the emulsion to settle, it is found that a layer of potassium cyanide solution forms the upper portion, the yellowish-brown lower layer being apparently an aqueous solution of the potassium derivative of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate. The free ester is obtained by acidifying and extracting with ether. From an experiment like this, 9 grams of ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate yielded 8 grams of the pure dicyano-ester of b. p.  $197\text{--}200^{\circ}/19$  mm.

*Condensation of the Cyanohydrin of Ethyl Acetoacetate with Ethyl Sodiocynoacetate. Formation of Ethyl  $\alpha\beta$ -Dicyano- $\beta$ -methylglutarate (VII).*

On account of the difficulty of obtaining ethyl  $\alpha$ -cyano- $\beta$ -methylglutaconate in good yield, it was decided to try the preparation of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate by the direct condensation of the cyanohydrin of ethyl acetoacetate with ethyl sodiocynoacetate—a method suggested by the interesting experiments of Thorpe and Higson (T., 1906, **89**, 1455) on the synthesis of substituted succinic acids by the condensation, for example, of acetone cyano-

hydrin with ethyl sodiocyanoacetate. The condensation was carried out as follows. To a solution of sodium ethoxide (4.4 grams of sodium in 70 c.c. of absolute alcohol) 22.6 grams of ethyl cyanoacetate were added, and the solution was cooled and added, in small quantities at a time, with continual shaking, to a solution of 31.4 grams of the cyanohydrin of ethyl acetoacetate in 30 c.c. of absolute alcohol. The reaction took place without appreciable rise of temperature, and the slightly yellow solution was found on the next day to have set to a solid yellow mass, the solid being essentially the sodium derivative of ethyl dicyano- $\beta$ -methylglutarate. The mass was stirred with dilute hydrochloric acid, the precipitated oil extracted with ether, and the extract distilled under reduced pressure, when 20 grams of the expected condensation product were obtained, b. p. 197—202°/18 mm. The fact that the yield (40 per cent.) is the same as that obtained in proceeding through the stage of the cyanoglutaconate suggests that the mechanism of the formation of the dicyano-ester is essentially the same as that in the previously described experiments.

That the dicyano-ester prepared by this method is identical with that prepared by other methods was amply proved by a number of reactions. It gave  $\beta$ -methyltricarballic acid on hydrolysis. It was easily soluble in alkali hydroxides and in 10 per cent. potassium carbonate solution. When treated with ammonia, it gave the same results as other specimens.

*Addition of Hydrogen Cyanide to Ethyl  $\alpha$ -Cyano- $\beta$ - $\gamma$ -dimethylglutaconate (V). Formation of Ethyl  $\alpha\beta$ -Dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII).*

The cyanodimethylglutaconic ester necessary for these experiments was prepared by Rogerson and Thorpe's method (*loc. cit.*) with the difference that potassium was substituted for the sodium used by them (this vol., p. 2219).

In adding hydrogen cyanide to ethyl  $\alpha$ -cyano- $\beta$ - $\gamma$ -dimethylglutaconate, 24 grams of the latter were dissolved in 150 c.c. of alcohol and the solution was cooled in ice. A concentrated solution of potassium cyanide (13 grams) was added and subsequently a quantity of a 20 per cent. solution of hydrochloric acid equivalent to 5.4 grams of the anhydrous acid. After standing for fifteen minutes, the product was isolated by pouring into water and extracting with ether, 20 grams of pure ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII), b. p. 200—206°/20 mm., being obtained. This is 75 per cent. of the theoretical (Found: C = 58.5; H = 7.2; N = 10.3.  $C_{13}H_{18}O_4N_2$  requires C = 58.6; H = 6.8; N = 10.5 per cent.).



*Ethyl*  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate resembles ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate very closely in its general properties. It is a colourless oil insoluble in 10 per cent. sodium carbonate solution, slightly soluble in 10 per cent. potassium carbonate solution and in 10 per cent. potassium or sodium hydroxide.

*Action of Ammonia.*—When ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (5 grams) was vigorously shaken with concentrated ammonia (60 c.c.), it gradually dissolved, solution being complete in about ten to fifteen minutes, the liquid taking on a yellow colour. After twenty-four hours, crystals had separated. A part of these proved to be soluble in ether and were identified as ethyl  $\beta$ -amino- $\alpha$ -methylcrotonate (this vol., p. 2221), whilst the other portion was soluble in hot water, from which it crystallised on cooling. This substance blackened considerably above  $300^\circ$  and melted at about  $320^\circ$ . By decomposing this compound with boiling caustic alkali, a substance, m. p.  $276^\circ$ , was produced and this showed itself in every way identical with the substance obtained by the action of ammonia on  $\alpha$ -cyano- $\beta\gamma$ -dimethylglutaconic ester (this vol., p. 2221). It is clearly the substance first described by Guareschi (*loc. cit.*) and stated by him to be 6-hydroxy-2-keto-4 : 5-dimethyl-2 : 3-dihydropyridine-3-carboxylonitrile.

*Hydrolysis of Ethyl*  $\alpha\beta$ -Dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII). *Formation of*  $\alpha\beta$ -Dimethyltricarballic Acid,  
 $\text{HO}_2\text{C}\cdot\text{CHMe}\cdot\text{CMe}(\text{CO}_2\text{H})\cdot\text{CH}_2\cdot\text{CO}_2\text{H}.$

—The cyano-ester was hydrolysed by boiling with concentrated hydrochloric acid for about twelve hours, the resulting solution being evaporated to dryness and the residual solid extracted several times with ether. After the evaporation of the ethereal solution, the gummy residue of acid was dissolved in methyl alcohol, saturated with dry hydrogen chloride, kept over-night, and treated again in the same way after evaporating off at reduced pressure water and excess of alcohol. The acid was thus almost quantitatively converted into the trimethyl ester. The ester was extracted in the usual way and was obtained as a colourless liquid, b. p.  $162^\circ/22$  mm. (Found : C = 53.3 ; H = 7.3.  $\text{C}_{11}\text{H}_{18}\text{O}_6$  requires C = 53.7 ; H = 7.3 per cent.).

The trimethyl ester was hydrolysed in the ordinary way with alcoholic potassium hydroxide solution, and the resulting acid extracted with several lots of ether. After evaporation of the ether, an acid remained which showed no signs of crystallisation. Even after repeated evaporation of an aqueous solution and ultimately leaving for many weeks not only in a vacuum over sulphuric acid, but also for a period exposed to the air, it still remained a



comparatively mobile liquid. This was doubtless a mixture of the two possible isomeric forms of inactive  $\alpha\beta$ -dimethyltricarballic acid. A crystalline acid was ultimately obtained by heating the syrupy acid at  $180^\circ$  for six hours in a sealed tube with 30 c.c. of hydrochloric acid (22 c.c. of the concentrated acid and 10 c.c. of water). On extracting the product with pure ether, an acid was obtained which solidified readily and melted (after remaining in contact with porous porcelain) at  $147\text{--}151^\circ$ . Afterwards it was found that an acid of this melting point could readily be obtained by hydrolysing the trimethyl ester with concentrated hydrochloric acid and evaporating to dryness. The further purification of the acid proved to be a tedious piece of work, for apparently traces of an isomeric acid of lower melting point accompany it. It was crystallised five times from hydrochloric acid before a constant melting point was obtained. Ultimately the acid melted at  $165\text{--}167^\circ$  (effervescing violently at this temperature, doubtless forming an anhydride). A mixture of this acid with  $\beta$ -methyltricarballic acid (m. p.  $164\text{--}165^\circ$ ) melted at about  $152\text{--}155^\circ$  (Found: C = 46.7; H = 6.1.  $\text{C}_8\text{H}_{12}\text{O}_6$  requires C = 47.0; H = 6.0 per cent.). Attempts were made to isolate the isomeric acid the presence of which was suspected, but it must have been present in small quantity, for from the mother-liquors of the above crystallisation nothing could be isolated except what was obviously principally the acid of melting point  $165\text{--}167^\circ$ .

$\alpha\beta$ -Dimethyltricarballic acid shows in neutral solution precisely the same uncharacteristic behaviour towards various metallic salts as  $\beta$ -methyltricarballic acid (compare T., 1912, **101**, 910). It is insoluble in light petroleum, chloroform, or benzene, but readily soluble in water or acetic acid. It crystallises well from formic acid and from hydrochloric acid. On being heated above its melting point, it loses water easily, apparently forming an anhydride. This remained gummy and no solvent was found from which it could be crystallised. The acid was regenerated on crystallising the gum from hydrochloric acid.

*The Addition of Hydrogen Cyanide to Ethyl  $\alpha$ -Cyano- $\beta$ -methyl- $\Delta^{\alpha}$ -butene- $\alpha\gamma$ -dicarboxylate (VI).*

In the preceding paper (p. 2222), it is shown that the above ester is converted by the action of sodium ethoxide in cold alcoholic solution into the isomeric ester, ethyl  $\alpha$ -cyano- $\beta\gamma$ -dimethylglutaconate. In the circumstances in which hydrogen cyanide is added on, that is, in the presence of potassium cyanide and the free alkali formed from it by hydrolysis, it is almost certain that isomeric change precedes the additive process. If such change did not

occur, it is clear that the same product is to be expected. In fact, the dicyano-ester obtained showed itself in its behaviour on hydrolysis, in its behaviour with ammonia, and in its behaviour on treatment with sodium and methyl iodide, to be identical with that derived from ethyl  $\alpha$ -cyano- $\beta$ - $\gamma$ -dimethylglutaconate.

*Methylation of Ethyl  $\alpha\beta$ -Dicyano- $\beta$ -methylglutarate. Formation of  $\beta\gamma$ -Dicyano- $\gamma$ -methylbutane- $\beta\delta$ -dicarboxylate (X).*

In the preparation of this substance, ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylglutarate (25 grams) was added to a solution of sodium (2.3 grams) in alcohol (50 c.c.), and the mixture, after the addition of methyl iodide (25 grams), heated on a boiling water-bath for two and a half hours. The product, which was isolated in the usual way, boiled at  $196\text{--}197^\circ/17\text{mm.}$  and was a colourless, viscous oil (Found : C = 58.9; H = 7.3.  $\text{C}_{13}\text{H}_{18}\text{O}_4\text{N}_2$  requires C = 58.6; H = 6.8 per cent.).

When the ester was boiled with sulphuric acid of about 60 per cent. strength for three and a half hours and the liquor saturated with ammonium sulphate, an oil separated which showed no signs of solidification. It was extracted with ether, the ethereal solution dried, and the residue after the distillation of the ether treated with methyl alcohol and dry hydrogen chloride. After standing over-night, the methyl alcohol and hydrochloric acid were evaporated in a partial vacuum, the flask being immersed in boiling water, and the residue again treated with methyl-alcoholic hydrogen chloride. This second treatment resulted in the separation of a white, crystalline solid. Water was added and the mixture extracted with ether. The ethereal solution was washed with dilute sodium carbonate solution, dried with calcium chloride, and the solvent distilled. The residue solidified readily and completely. On distillation at reduced pressure, it boiled without decomposition at  $219\text{--}224^\circ/19\text{ mm.}$  From 10 grams of the original ester a total of 4.5 grams of the new substance\* was obtained. The distillate crystallised to a hard solid, which was recrystallised from water. Two recrystallisations raised its melting point to  $136\text{--}137^\circ$  and this was unaltered by further crystallisation. The substance dissolved in dilute alkali hydroxides and also in concentrated sodium carbonate solution, being reprecipitated on the addition of acids. It contains nitrogen and is in all probability an imide—the imido-group explaining the solubility in alkalis. Formula (IX) explains the behaviour of the substance so far as it has been examined

\* A specimen of 10 grams of ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII), prepared from ethyl  $\alpha$ -cyano- $\beta\gamma$ -dimethylglutaconate and hydrogen cyanide, was subjected to *precisely* the same treatment as that described above. In this case exactly 4.5 grams of the trimethyl ester of  $\alpha\beta$ -dimethyltricarballic acid were obtained.

(Found : C = 53.7; H = 6.3; N = 7.3.  $C_9H_{13}O_4N$  requires C = 54.2; H = 6.5; N = 7.0 per cent.).

The imido-ester can be roughly titrated with aqueous alkali : 0.203 gram neutralised 0.03564 gram of sodium hydroxide, whereas 0.203 gram of a compound of the above formula, if it neutralised one gram-equivalent, would require 0.0408 gram.

Further evidence in favour of the view expressed above regarding the constitution, was obtained on hydrolysis with concentrated hydrochloric acid.

This operation required five hours, using a sealed tube, at a temperature of about  $175^\circ$ . The aqueous solution was evaporated to dryness on the steam-bath, and the solid residue extracted with pure ether. A residue of ammonium chloride was left and the substance which passed into solution was shown to be  $\alpha\beta$ -dimethyltricarballic acid, for after two crystallisations from hydrochloric acid it melted at  $162$ — $164^\circ$  (alone or mixed with an authentic specimen). (To obtain  $\alpha\beta$ -dimethyltricarballic acid of maximum melting point,  $165$ — $166^\circ$ , requires, as a rule, five or six crystallisations.)

On vigorously shaking the cyano-ester (X) with concentrated ammonia solution, it gradually passed into solution and after six or seven hours a sandy solid separated in small amount. This substance, which increased a little in quantity after the mixture had been kept for some days, was excessively sparingly soluble both in methyl alcohol and in water. It melted at about  $265^\circ$  and, unlike the substances obtained by the action of ammonia on the other cyano-esters, showed no colour reaction with ferric chloride. It is probably an amide, no hydrolysis of the carbon chain having occurred in this case.

#### *Hydrogen Cyanide and Ethyl $\alpha$ -Cyano- $\alpha\beta\gamma$ -trimethylglutaconate.*

Some of the trimethylglutaconate was made in the manner described by Rogerson and Thorpe (T., 1905, **87**, 1669) by the action of sodium ethoxide and methyl iodide on ethyl  $\alpha$ -cyano- $\alpha\gamma$ -dimethylglutaconate in alcoholic solution. Owing to the formation of considerable amounts of ethyl  $\gamma$ -cyano- $\alpha\beta\gamma$ -trimethylcrotonate by the action of traces of sodium ethoxide on the trimethylglutaconate, attempts were made to substitute metallic sodium and metallic potassium for the sodium ethoxide, alcohol being replaced by benzene.

Sodium was found scarcely to react, but with the aid of potassium, which formed an insoluble potassium derivative with the cyano-dimethylglutaconate, considerable quantities of the trimethylglutaconate, b. p.  $174$ — $178^\circ/28$  mm., were obtained. Unaltered

cyanodimethylglutaconate could be removed by the action of concentrated ammonia, the trimethyl derivative being unacted upon by this reagent.

In the investigation of the action of hydrogen cyanide on ethyl  $\alpha$ -cyano- $\alpha\beta\gamma$ -trimethylglutaconate, it was necessary to avoid the use of alcohol, since, owing to the presence of potassium cyanide, a certain amount of potassium ethoxide would have been formed, with the consequent elimination of ethyl carbonate and the formation of cyanotrimethylcrotonate. Agitation with an *aqueous* solution of potassium and hydrogen cyanides was the method adopted. The product in two separate experiments was identical with the starting material. It can therefore be safely concluded that ethyl  $\alpha$ -cyano- $\alpha\beta\gamma$ -trimethylglutaconate does not add on hydrogen cyanide.

*Methylation of Ethyl  $\alpha\beta$ -Dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate (VIII).*

*Formation of Ethyl  $\beta\gamma$ -Dicyano- $\gamma$ -methylpentane- $\beta\delta$ -dicarboxylate (XI).*

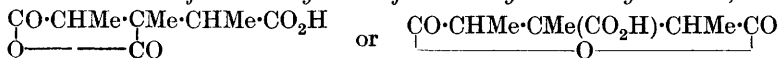
Since the above method for producing this substance failed, an attempt was next made to methylate ethyl  $\alpha\beta$ -dicyano- $\beta$ -methylbutane- $\alpha\gamma$ -dicarboxylate and was found to be successful.

In methylating this substance, 18.9 grams of it were treated with sodium ethoxide, prepared by dissolving sodium (1.61 grams) in absolute alcohol (40 c.c.). Subsequently methyl iodide (20 grams) was added. The addition of the sodium ethoxide resulted in a bright red colour, and there was no evolution of heat. The mixture became hot, however, on the addition of methyl iodide. The reaction was allowed to proceed by itself for about one hour and the mixture was then heated gently for a similar period on the steam-bath. On pouring into water and extracting with ether in the usual way, 16 grams of a new substance, b. p. 202—207°/23 mm., were isolated (Found : C = 59.6; H = 6.8.  $C_{14}H_{20}O_4N_2$  requires C = 60.0; H = 7.0 per cent.).

This new substance, which is a colourless oil, is quite insoluble in 10 per cent. aqueous potassium hydroxide, and is hence readily distinguishable from the original cyano-ester. It dissolves with great difficulty on prolonged standing with concentrated ammonia, but the product has not been examined.

*Hydrolysis of Ethyl  $\beta\gamma$ -Dicyano- $\gamma$ -methylpentane- $\beta\delta$ -dicarboxylate.*

*Formation of the Anhydride of Trimethyltricarballic Acid,*



When the cyano-ester is boiled with 40 per cent. sulphuric acid, it is slowly hydrolysed, the original oil being replaced by the

hydrolysis product, which is itself insoluble and floats on the sulphuric acid. Some of the product solidified without further treatment and was filtered off and crystallised from formic acid, when, after two crystallisations, it melted at 188—190°. The bulk of the product, however, required extraction with ether. The extract was treated with methyl alcohol and dry hydrogen chloride, and the ester thus formed isolated in the usual way. Practically the whole quantity boiled at 166—172°/26 mm. Redistillation gave a good specimen of boiling point 164—167°/24 mm. (Found : C = 54.9; H = 7.3.  $C_{12}H_{20}O_6$  requires C = 55.4; H = 7.7 per cent.). There can be no doubt that this is the trimethyl ester of trimethyltricarballic acid.

*Hydrolysis of Methyl Trimethyltricarballicate.*—By means of alcoholic potassium hydroxide solution an acid was obtained which remained gummy and crystallised only on boiling its solution in hydrochloric acid to almost complete dryness. By a somewhat wasteful crystallisation from hydrochloric acid a substance, m. p. 187—189°, was obtained, identical with the compound, m. p. 188—190°, already referred to. A specimen crystallised from hydrochloric acid and dried in an exhausted desiccator over sulphuric acid was analysed (Found : C = 53.8; H = 5.9.  $C_9H_{12}O_5$  requires C = 54.0; H = 6.0 per cent.).

The substance is evidently the anhydride of trimethyltricarballic acid, for the acid itself requires C = 49.5; H = 6.4 per cent. This is further borne out by the titration of the above compound : 0.1554 gram required 20 c.c. of *N*/10-NaOH, whereas 0.1554 of an anhydro-acid,  $C_9H_{12}O_5$ , should require 23.3 c.c. The end-point, using phenolphthalein, was very difficult to find, and a pink colour of reasonable permanence was obtained only after long standing.

It was at once noticeable that the substance of melting point 188—190° did not effervesce on melting (or on heating even at 240°), whilst the other methyltricarballic acids evolve water with violence at their melting points.

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