XXIV.—*The Condensation Products of Triacetic Lactone with Acetoacetic Ester and β -Aminocrotonic Ester.*

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ALTHOUGH many members of the γ -pyrone series have long been known, no substance has hitherto been obtained containing two adjacent γ -pyrone rings. The possibility of such a substance being produced by the condensation of triacetic lactone with suitable reagents and the hope that its properties would throw some light on the constitution of the γ -pyrone nucleus led to this research.

With this object in view the reactions of triacetic lactone with ethyl acetoacetate and with β -aminocrotonic ester in presence of condensing agents were investigated.

The reaction between ethyl acetoacetate and triacetic lactone was examined first. Theoretically two different compounds might be formed by the complete condensation of the substances with the elimination of water and alcohol, (1) a $\gamma\gamma$ -dipyrone, (2) a γ -pyrone-lactone.

One compound, however, only was formed which from the reactions of one of its derivatives was proved to be the pyrone lactone and not the dipyrone.

A completely analogous reaction takes place between triacetic lactone and ethyl β -aminocrotonate. In this case, if the condensation is complete, the production of a $\gamma\gamma$ -dipyrone or of a pyrone lactone with the elimination of ammonia and alcohol is possible, as is also the formation of a substance containing nitrogen in the second ring, with the elimination of water and alcohol.

On investigating the condensation, two substances were isolated, namely, the same substance as was formed when triacetic lactone and ethyl acetoacetate interact, and a substance containing nitrogen which, from its reactions, was shown to be a condensation product of two molecules of β -aminocrotonic ester with one of the lactone.

EXPERIMENTAL.

Condensation of Triacetic Lactone and Acetoacetic Ester.

The best condensing agent was found to be hydrogen chloride, the yield being nearly twice as much as when concentrated sulphuric acid was used, and several times greater than in the cases of acetic anhydride and piperidine.

Thirty grams of triacetic lactone and 60 grams of ethyl acetoacetate (theory 30·9) were dissolved in 300 c.c. of dry absolute alcohol, and the solution slowly saturated in the cold with dry hydrogen chloride. After standing for twenty-four hours the flask was filled with a fine mass of feathery crystals, which after being separated, washed with a little alcohol, and dried in a vacuum, weighed 10·6 grams. A further quantity was deposited by the filtrate on standing, the total yield after the solution had stood for fourteen days being 20·8 grams, or 44·3 per cent. of the theoretical quantity. The product was colourless and almost pure.

For analysis the substance was twice recrystallised from benzene ; it then melted at 213—214° with decomposition.

0·1941 gave 0·4431 CO₂ and 0·0754 H₂O. C = 62·24 ; H = 4·31.

C₁₀H₈O₄ requires C = 62·50 ; H = 4·16 per cent.

The substance is readily soluble in chloroform or hot glacial acetic acid, moderately so in hot benzene or ethyl acetate, sparingly so in hot alcohol or ether, and insoluble in water or light petroleum.

Reactions of the Substance C₁₀H₈O₄.

The condensation product obtained in this way is extremely stable towards acids, with which, unlike dimethylpyrone, it forms no salts. It can be heated to a high temperature with strong sulphuric acid, forming a markedly blue fluorescent solution,* from which it can be recovered unchanged. In glacial phosphoric acid the fluorescence is but slight. The substance is not altered when boiled with a mixture of phosphorus tri- and penta-chlorides, and does not form an oxime or a hydrazone. On the other hand, it yields crystalline nitro- and monobromo-derivatives.

When heated with phosphorus and hydriodic acid in a sealed tube it

* This fluorescence is similar to that given by umbelliferone, $\text{HO}\cdot\text{C}_6\text{H}_3\begin{matrix} \diagup \text{O}-\text{CO} \\ \diagdown \text{CH}:\text{CH} \end{matrix}$, in strong sulphuric acid. The substance was subsequently proved to be of a similar type to that compound.

is entirely destroyed. With ferric chloride in alcoholic solution it gives a deep brown colour.

Reactions with Alkalis.—The behaviour of the substance towards alkalis is remarkable; definite salts, however, could not in all cases be prepared.

The substance dissolves in dilute sodium hydroxide forming a deep yellow solution; if the excess of alkali is considerable and the solution is boiled for a few minutes, it assumes a pale straw colour, and at the same time much decomposition takes place. Both solutions, however, yield the original substance on acidification.

With ammonia a deep yellow solution is likewise formed; if, however, the solution is evaporated on the water-bath the original substance begins to separate as soon as the excess of ammonia is removed.

An attempt to prepare a barium salt yielded rather better results, although owing to the instability of the salt a pure substance was not obtained. About 5 grams of the substance were boiled with a large excess of barium hydroxide until the deep yellow solution first formed had assumed a pale straw colour. In the process a considerable quantity of carbonate was produced owing to decomposition. The excess of barium was removed by means of a stream of carbon dioxide and the solution filtered. The mother liquor was then evaporated to a syrup under reduced pressure and the syrup quickly filtered (to remove carbonate formed during the distillation) into a large volume of alcohol. An extremely hygroscopic white precipitate was obtained which was purified by solution in the smallest quantity of water possible and reprecipitation with alcohol. This was repeated several times, and the substance was finally dried in a vacuum.

Found (mean of two analyses) Ba = 37.1.

$C_{10}H_8O_4Ba(OH)_2$ requires Ba = 37.7 per cent.

The *barium* salt decomposed on heating and on keeping. On acidification it yielded the original substance. A solution gave, on addition of a mercuric salt, an insoluble yellow *mercuric* salt; on addition of a mercurous salt the latter was reduced. With silver nitrate a colourless insoluble salt was formed, which, however, was at once reduced on heating, giving a remarkably good silver mirror.

In these reactions it is clear that two types of salts are formed, namely, those giving the deep yellow solution and those produced from the latter by boiling. That neither of these two are normal salts of the free acid corresponding to the pyrone lactone (the original substance was subsequently proved to have that constitution) is shown in the first case by the yellow colour of their solutions and in the second from the analysis of the barium salt, for the normal salt would require only

24·8 per cent. of barium. Neither do they correspond to a type of salt represented by the constitution

which requires 39·7 per cent. of barium and would be colourless.

Bromination of the Substance C₁₀H₈O₄.

Five grams of the substance were dissolved in hot glacial acetic acid, and to the solution 4·5 grams of bromine dissolved in glacial acetic acid were slowly added. The colour of the solution did not change on standing. On pouring into water, a white, voluminous precipitate was formed. This was crystallised from boiling alcohol and obtained in fine needles, which, on standing, changed completely to a mass of granular crystals. After drying in a vacuum, these melted at 191° with slight decomposition.

The yield was 5·2 grams, or 73·5 per cent. of the theoretical.

No dibromo-derivative was produced by using a larger quantity of bromine, but only a diminished yield of the monobromo-derivative was obtained.

For analysis the substance was recrystallised from benzene, from which it separated in brilliant needles containing benzene of crystallisation. This compound readily loses its benzene on heating or standing in the air.

1·4077 lost 0·1830. C₆H₆ = 13·0.

(C₁₀H₇O₄Br)₂, C₆H₆ requires C₆H₆ = 12·6 per cent.

The residue melted at 191°, and on analysis :

0·2056 gave 0·3317 CO₂ and 0·0489 H₂O. C = 44·40 ; H = 2·63.

0·2308 „ 0·3714 CO₂ „ 0·0573 H₂O. C = 43·89 ; H = 2·75.

0·2233 „ 0·1565 AgBr. Br = 29·76.

C₁₀H₇O₄Br requires C = 44·28 ; H = 2·58 ; Br = 29·52 per cent.

The substance, besides being readily soluble in hot benzene, is very soluble in chloroform or hot glacial acetic acid, moderately so in hot acetone, ethyl acetate, or alcohol, slightly so in light petroleum, and insoluble in water.

From glacial acetic acid, acetone, or alcohol, the fine needles first formed on crystallisation change to the granular condition on standing. The substance is also readily soluble in hot toluene, giving a compound similar to that obtained with benzene ; on analysis :

1·5188 lost 0·2158. C₇H₈ = 14·2.

(C₁₀H₇O₄Br)₂, C₇H₈ requires C₇H₈ = 14·5 per cent.

When the bromo-derivative is boiled with zinc dust and acetic acid, it is converted into the substance C₁₀H₈O₄ (m. p. 213—214°) from which it was produced.

Nitration of the Substance $C_{10}H_8O_4$.

Three grams of the substance $C_{10}H_8O_4$ were dissolved in 10 c.c. of strong sulphuric acid and the solution cooled to 0° . To this solution a cold mixture of 2 c.c. of nitric acid, sp. gr. 1.2 (the theoretical amount for a dinitro-derivative), and 8 c.c. of strong sulphuric acid were slowly added. The temperature during the process was not allowed to rise above 4° . The mixture, which had become deep yellow and began to evolve gases, was then poured into 100 grams of a mixture of ice and water.

A slightly coloured precipitate was obtained which after filtration was crystallised from glacial acetic acid, when it separated in shining, yellow needles. The yield was 2 grams, corresponding to 55.7 per cent. of the theoretical.

The yield was not improved by using either more or less nitric acid. In an experiment in which the theoretical quantity was used the reaction was incomplete, whilst when a greater excess was employed or the temperature allowed to rise, decomposition ensued accompanied with a copious evolution of gases and a much diminished yield.

For analysis, the substance was recrystallised from ethyl acetate, from which it separated in pale yellow needles which began to darken at about 180° and melted with violent decomposition at about 200° .

0.3127 gave 16.7 c.c. moist nitrogen at 16° and 759.5 mm. $N = 6.2$.

$C_{10}H_7O_6N$ requires $N = 5.9$ per cent.

The substance is readily soluble in cold acetone, hot glacial acetic acid, ethyl acetate, benzene, or chloroform, slightly so in hot alcohol, and almost insoluble in ether, light petroleum, or water. With ferric chloride in alcoholic solution, a deep yellow colour is produced. With alkalis, it forms deep yellow to red solutions, and in the case of ammonia a further reaction takes place.

It is not attacked by hydrogen sulphide in boiling alcoholic solution, but is reduced, with elimination of the nitro-group, to the original substance, $C_{10}H_8O_4$, when boiled with zinc dust and acetic acid.

Reaction between Ammonia and the Substance $C_{10}H_7O_4NO_2$.—The nitro-derivative dissolves slowly in cold concentrated aqueous ammonia, giving a deep red solution which at once begins to deposit a colourless solid, the solution at the same time becoming pale yellow.

Five grams of the nitro-derivative were continuously shaken with 30 c.c. of aqueous ammonia (sp. gr. 0.88) until the original solid was entirely dissolved and the colour of the solution had changed to pale yellow. The colourless precipitate which had subsequently formed was filtered, washed with a little water, and dried in a vacuum: yield 2.5 grams.

The substance dissolved readily in hot water and the solution, when cooled slowly, set to a jelly, which on standing furnished a mass of fine crystals. For analysis, it was recrystallised from hot water and dried in a vacuum :

0.1947 gave 14.7 c.c. moist nitrogen at 18.5° and 755 mm. N = 8.65.

0.1977 „ 14.8 c.c. „ „ „ 18° „ 757 mm. N = 8.62.

C₈H₉O₃N requires N = 8.38 per cent.

An examination of the properties of this substance and a comparison with those of aminodehydracetic acid prepared by the action of strong aqueous ammonia on dehydracetic acid (Oppenheim and Precht, *Ber.*, 1876, 9, 1100 ; Collie and Myers, *Trans.*, 1893, 63, 128) proved the identity of the two substances. The substance here described melted at 208° (uncorr.) whilst aminodehydracetic acid melts at 208.5° (corr.) (O. and P.).

The mother liquor from the preparation of this substance gave on acidification the reaction for nitrous acid with potassium iodide and starch. This reaction therefore affords a proof of the constitution of the series of substances in question, and fixes the position of the nitro-group in the nitro-derivatives, for, of the two possible types of condensation products, that containing the lactone ring is the only one which could yield aminodehydracetic acid :

Reaction between Triacetic Lactone and Ethyl-β-aminocrotonate.

Triacetic lactone reacts with ethyl β-aminocrotonate in presence of sulphuric acid, alcoholic hydrochloric acid, or glacial acetic acid to give in each case the pyrone lactone already described, and, in the latter case, a second substance containing nitrogen. The effect of all three reagents was examined. When hydrochloric acid was used under similar conditions to those of the previous experiment a very small yield was always obtained, with sulphuric acid the yield was much increased, but the best results were given by the use of glacial acetic acid as follows :

6.2 grams of triacetic lactone, 7.5 grams of ethyl β-aminocrotonate, and 25 c.c. of glacial acetic acid were heated almost to boiling and left to cool. A mass of fine needles separated which were found to consist of nearly pure pyrone lactone. 3.1 grams were obtained, corresponding to a yield of 32.5 per cent.

The mother liquor was poured into 70 c.c. of water, quickly filtered from a small quantity of impure pyrone lactone which separated, diluted with 100 c.c. of water, and left to stand. A granular crystalline precipitate slowly formed, which after twenty-four hours' standing was collected, washed with a little water, and dried in a vacuum. 2.5 grams were obtained.

The substance was recrystallised from a mixture of methyl alcohol and water (1:4), from which it separated in colourless granular crystals melting indefinitely, from about 180° to about 200°.

A considerable quantity of the substance was prepared by this method.

Attempts to purify it by recrystallisation and fractionation failed, no substance of definite melting point being obtained, whilst at the same time each sample was proved to contain a small amount of the pyrone lactone, since it gave the same blue fluorescence when dissolved in strong sulphuric acid. The substance was therefore treated with a small quantity of alcoholic potash.

Two grams of the substance dissolved in a little alcohol were heated on the water-bath for fifteen minutes with 10 c.c. of a 10 per cent. solution of alcoholic potash. The solution was then poured into 100 c.c. of water acidified with hydrochloric acid and left to stand overnight. A white, crystalline solid separated which, after being dried in a vacuum, amounted to 1.1 grams. On recrystallisation from methyl alcohol the substance separated in flat plates melting at 193°, and which no longer showed fluorescence when dissolved in strong sulphuric acid. The pyrone lactone originally present had therefore been destroyed.

After a second recrystallisation :

0.2391 gave 0.5210 CO₂ and 0.1319 H₂O. C = 59.42 ; H = 6.13.

0.2684 „ 10.3 c.c. moist nitrogen at 11.0° and 759 mm. N = 4.57.

C₁₆H₁₂O₆N requires C = 59.81. H = 5.91 ; N = 4.36 per cent.

The substance is insoluble in water, light petroleum, or ether readily soluble in hot alcohol, methyl alcohol, or chloroform, and slightly so in ethyl acetate or benzene. It dissolves in dilute aqueous sodium hydroxide without giving a coloured solution, and if boiled for some time with very concentrated alkali, ammonia is evolved.

With ferric chloride in alcoholic solution no coloration is produced. The mother liquor from the preparation of this substance was rendered faintly acid and evaporated to a very small bulk, when an oily substance separated which quickly solidified on cooling. On addition of hydrochloric acid the greater part dissolved, leaving a very small quantity of a brown residue, which was filtered off and the solution made nearly neutral. On standing for some time a white,

feathery solid separated which was collected, washed with a little water and dried in a vacuum. This substance, which contained nitrogen, melted at 138° ; yield 0.2 gram.

In order to ascertain whether it was present in the original impure substance, a series of experiments were made in which the quantity of alcoholic potash and time of boiling were increased. In each case a greater quantity of the substance was formed, thus showing that it was a decomposition product.

Reaction between Alcoholic Potash and the Substance $C_{16}H_{19}O_6N$.—Two grams of the compound $C_{16}H_{19}O_6N$ were boiled for one hour with 30 c.c. of alcoholic potash of the same strength as before, poured into 150 c.c. of water, acidified and left to stand when 0.6 gram of the original substance $C_{16}H_{19}O_6N$ separated, and, after evaporation as before, 0.83 gram of the second substance was obtained. This was mixed with the former preparations and the whole crystallised from hot water, being obtained in fine needles, which slowly changed to granular crystals on standing.

The substance melted at 138° and proved to be identical with the ethyl ester of ψ -lutidostyrylcarboxylic acid, corresponding to the formula

previously obtained by the action of pure, dry hydrogen chloride on β -aminocrotonic ester at 120° (Collie, Trans., 1897, 71, 303), and by the action of ammonia on the ethyl ester of isodehydracetic acid at 150 – 160° (Anschütz, Bendix, and Kerp, *Annalen*, 1890, 259, 173), for on treatment with strong aqueous alkali for some time, it yielded the corresponding acid melting at 295° (given as 304° approx. in the literature).

The production of this ester makes it evident that in the formation of the substance $C_{16}H_{19}O_6N$ two molecules of ethyl β -aminocrotonate had taken part, thus:

or

giving a compound of the type

or of the type

of which the latter is the more probable, since the lactone is produced at the same time.

The lactone ring is then separated under the influence of alcoholic potash and a free acid is obtained which at once yields the lutidone ester with loss of water :

The last reaction is practically quantitative. In the above experiment, out of 2 grams of the original substance $\text{C}_{16}\text{H}_{19}\text{O}_6\text{N}$, 0.6 gram was recovered unchanged, and the remaining 1.4 grams gave 0.83 gram of the lutidone ester, corresponding to a yield of 97 per cent.

That the substance $\text{C}_{16}\text{H}_{19}\text{O}_6\text{N}$ is not merely a molecular compound of triacetic lactone and the lutidone ester is proved by the fact that, if a solution of the two is evaporated to dryness and the product very carefully fused, the lutidone remains unchanged, whilst the lactone is partly decomposed.

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