CXXXII.—*Cyclic Di- and Tri-ketones.*

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THE close resemblance between isatin and the diketopyrrolines, which has been pointed out previously (Trans., 1909, **95**, 984, 1603; 1910, **97**, 462), exists also in the behaviour of these substances towards *o*-phenylenediamine. In the same way as this diamine condenses with isatin to indophenazine,

it yields similar compounds with the diketopyrrolines. I have prepared, thus, *diphenylpyrrolinophenazine*,

and *phenyl-p-tolylpyrrolinophenazine*,

which substances, like indophenazine, are yellow.

The red diketocyclopentene derivative, $\text{C}_{14}\text{H}_{12}\text{O}_3$, which is formed from the product of the action of sodioacetylacetone on phenyl-

propiolyl chloride (Ruhemann and Merriman, *Trans.*, 1905, **87**, 1383) also condenses with the diamine thus:

but the compound which is produced differs in colour from the phenazines, since it is purple. This fact leads to the conclusion that it has not the constitution:

and that its formation is preceded by the change of diketoacetylphenylmethylcyclopentene into its tautomeric form:

This view as to the formula of the purple condensation product, which is indicated by the similarity of its colour with that of the salts of the diketocyclopentene derivative, $\text{C}_{14}\text{H}_{12}\text{O}_3$, is supported by the following considerations. The hydrogen, marked by an

¹ An error occurs in my paper, "Condensation of Amides with Esters of Acetylenic Acids" (*Trans.*, 1909, **95**, 984), which requires correction. Whereas the tautomeric form of the cyclopentene derivative, $\text{C}_{14}\text{H}_{12}\text{O}_3$, is correctly represented thus:

the formula of the compound with the diketonic grouping (p. 986) is erroneously given as:

After having established the nature of the tautomeric change of this substance by a comparison of its properties with isatin and the diketopyrrolines (*loc. cit.*), another correction becomes imperative. This concerns the formulæ of some of the derivatives of the diketone, $\text{C}_{14}\text{H}_{12}\text{O}_3$, which were described previously (*Trans.*, 1906, **89**, 682). The formulæ given there must be changed to:

asterisk, has a greater mobility than the iminic hydrogen of isatin or the diketopyrrolines. Whereas the latter substances, with alkalis only, yield blue solutions which quickly change to yellow, the diketocyclopentene derivative, $C_{14}H_{12}O_3$, dissolves not only in alkalis, but also in alkali carbonates or acetates, to form blue salts, and these are considerably more stable than the salts of the former diketone. Again, the diketopyrrolines do not give blue solutions on the addition of piperidine, but form with it colourless additive products (this vol., p. 465); the diketocyclopentene derivative, $C_{14}H_{12}O_3$, on the other hand, dissolves in piperidine, as it does in alkalis or alkali carbonates, to yield a blue solution. It follows therefore that this diketone readily undergoes a transformation into its tautomeric form, which occurs, also, in its condensation with *o*-phenylenediamine. Reagents, like phenylhydrazine or hydroxylamine, do not effect this change, but form with the diketone a phenylhydrazone or an oxime (Ruhemann, Trans., 1906, **89**, 682). Nor does such a transformation occur in the reaction of phenylmercaptan with the diketone, which yields an additive product; this, in every respect, resembles the one which is formed by the union of the mercaptan with diketodiphenylpyrroline (*loc. cit.*).

On the one hand, the similarity, on the other the difference, which exists between the diketocyclopentene derivative, $C_{14}H_{12}O_3$, and isatin, or the diketopyrrolines, induced me to attempt the preparation of diketopentenes with the grouping $\begin{array}{c} \cdot C - CO \\ | \quad \cdot \\ C \cdot CH_2 \cdot CO \end{array}$, in which the methylene radicle is intact. With this object in view, as well as for the purpose of arriving at a compound which in constitution closely resembles isatin, I chose α -hydrindone as starting point. I expected that this substance, by means of Sachs and Barschall's method of changing methylene groups into ketonic groups (*Ber.*, 1901, **34**, 3047), would be transformed into 1:2-diketohydrindene,

the isomeride of the known 1:3-diketohydrindene. The experiment, however, led to the remarkable result that, in the presence of potassium hydroxide or sodium carbonate, *p*-nitrosodimethylaniline mainly attacks both methylene groups of α -hydrindone. Analysis of the substance which is formed points to the formula $C_{25}H_{24}ON_4 \cdot H_2O$; accordingly, it is to be represented thus:

That, indeed, nitrosodimethylaniline has entered into both methylene groups of the hydrindone follows from the behaviour of

mineral acids towards the condensation product; thus, it is readily decomposed, and yields the *hydrate* of *triketohydrindene*.

Some years ago Kaufmann (*Ber.*, 1897, **30**, 387) stated that he obtained triketohydrindene, along with diphtalylethylene (indenigo),

on oxidation of 1:3-diketohydrindene by means of hydrogen peroxide, but that the amount which was formed did not suffice for analysis. He described his compound as crystallising from glacial acetic acid in yellowish-brown plates, which were insoluble in alkalis, and decomposed at 190—206°. The substance which is produced from α -hydrindone has quite different properties, and these fully characterise it as triketohydrindene. It crystallises from water or alcohol in the form of its colourless hydrate, which, on heating, first loses water and turns red, then melts, and decomposes at 239—240°. The triketone readily reduces Fehling's solution and ammoniacal silver solutions. This fact is undoubtedly due to the opening up of the five-carbon ring and the formation of the semialdehyde of phthalonic acid, namely, phenylglyoxal-*o*-carboxylic acid, thus:

which is finally oxidised to phthalonic acid. Of especial interest is the action of ammonia on the triketone. If the aqueous solution of the mixture of both substances is kept for a short time, it turns a deep reddish-violet, and no longer reduces silver nitrate. On the addition of dilute hydrochloric acid, a red solid is precipitated, which has the empirical formula $\text{C}_9\text{H}_5\text{O}_2\text{N}$. This formula, undoubtedly, should be doubled. The constitution of the substance may be deduced from a consideration of the action of ammonia on phenylglyoxal, $\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{COH}$. Müller and v. Pechmann (*Ber.*, 1889, **22**, 2557), who studied this reaction, did not arrive at the correct empirical formula of the compound which is formed. This was established by Pinner (*Ber.*, 1902, **35**, 4134), who showed, also, that the substance was identical with the one which Engler and Hassenkamp (*Ber.*, 1885, **18**, 2241) obtained on treatment of dibromoacetophenone with ammonia. Pinner, further, considered that it is to be represented thus:

and accordingly to be regarded as 2-benzoyl-5-phenylglyoxaline. Since the reducing action of triketohydrindene can only be explained by the opening up of the five-carbon ring and the formation of phenylglyoxal-*o*-carboxylic acid, the action of ammonia may be explained, as in the case of phenylglyoxal, by the assumption that the aldehydo-acid, first, condenses to the dicarboxylic acid,

which subsequently loses water and yields:

The product thus appears both to contain the indone ring and to be a derivative of glyoxaline. It may therefore be called 2-*o*-carboxybenzoylindonoglyoxaline. Experiments to prove the correctness of this view are in progress.

Triketohydrindene condenses with phenylhydrazine to an orange-coloured diphenylhydrazone, the constitution of which is either

I am inclined to regard the first formula as correct; a similar formula would represent the yellow disemicarbazone, $C_9H_4O(:N \cdot NH \cdot CO \cdot NH_2)_2$, which triketohydrindene forms with semicarbazide. The formation of a trihydrazone or trisemicarbazone does not take place; hydroxylamine, however, is capable of producing a trioxime. Oximes of triketohydrindene are already known, namely, 2-oximino-1:3-diketohydrindene,

(Wislicenus, *Annalen*, 1888, **246**, 347); further, 1:3-dioximino-2-hydrindone,

(Heusler and Schieffer, *Ber.*, 1899, **32**, 32), and finally trioximino-hydrindene, $C_9H_4(:NOH)_3$, which Wislicenus and Koetzle (*Annalen*, 1889, **252**, 74) prepared by treating 2-oximino-1:3-diketohydrindene with hydroxylamine. The latter substance is the chief product contained in the mixture of oximes which is formed by the action of hydroxylamine on triketohydrindene. Although I have been unable to isolate the trioxime in the pure state, its formation is sufficiently established by the analytical result of the

mixture. Triketohydrindene condenses with *o*-phenylenediamine to ketohydrindenophenazine,

which is yellow.

The behaviour of *p*-nitrosodimethylaniline towards α -hydrindone induced me to ascertain whether, besides the compound $C_{25}H_{26}O_2N_4$, the dimethylaminoanil,

is formed in the reaction. On examining the mother liquor from the black solid, $C_{25}H_{26}O_2N_4$, which separates if the alcoholic solution of the mixture of *p*-nitrosodimethylaniline and α -hydrindone is treated with potassium hydroxide, I found that, in the course of a few days, it deposited a red solid, which separated from alcohol in beautiful red crystals, but the yield was so small that it sufficed only for an analysis. Although the analytical data are not in full agreement with the theory, they indicate that the substance is indeed the dimethylaminoanil of α -hydrindone.

EXPERIMENTAL.

Diphenylpyrrolinophenazine,

This compound separates as a yellow solid when the mixture of diketodiphenylpyrroline and *o*-phenylenediamine, dissolved in dilute acetic acid, is digested on the water-bath. It is sparingly soluble in cold, moderately so in boiling, alcohol, and crystallises in yellow needles, which melt at 240—241°:

0.1750 gave 0.5272 CO_2 and 0.0765 H_2O . $C=82.16$; $H=4.86$.

0.1855 „ 20.8 c.c. N_2 at 15° and 759 mm. $N=13.11$.

$C_{22}H_{15}N_3$ requires $C=82.24$; $H=4.67$; $N=13.08$ per cent.

The substance dissolves in cold concentrated sulphuric acid, yielding a solution which is purple in transmitted, green in reflected, light; the solution in hydrochloric acid is red.

Phenyl-p-tolylpyrrolinophenazine,

This is prepared from diketophenyl-*p*-tolylpyrroline and *o*-phenylenediamine in the same way as the former substance, with the only exception that a more concentrated solution of acetic acid must be used on account of the fact that this diketone is less soluble than diketodiphenylpyrroline. The phenazine is moderately soluble in boiling alcohol, and, on cooling the solution, slowly separates in yellow needles, which melt at 258°:

0.1833 gave 0.5532 CO₂ and 0.0865 H₂O. C=82.30; H=5.24.

0.1788 „, 19.4 c.c. N₂ at 17° and 762 mm. N=12.62.

C₂₃H₁₇N₃ requires C=82.38; H=5.07; N=12.54 per cent.

Action of o-Phenylenediamine on 2:3-Diketo-1-acetyl-4-phenyl-5-methylcyclopentene.

On adding to the red diketocyclopentene derivative, C₁₄H₁₂O₃ (1 gram), dissolved in hot alcohol or acetic acid, *o*-phenylenediamine (0.5 gram), the whole sets to a mass of dark-coloured crystals. The product of the reaction is almost insoluble in alcohol, but dissolves in boiling glacial acetic acid, from which it crystallises in bunches of purple needles, softening at 245° and melting at 250°:

0.1782 gave 0.5225 CO₂ and 0.0855 H₂O. C=79.97; H=5.33.

0.1720 „, 14.2 c.c. N₂ at 21° and 747 mm. N=9.23.

C₂₀H₁₆ON₂ requires C=80.00; H=5.33; N=9.33 per cent.

The substance dissolves in cold concentrated sulphuric or hydrochloric acids to yield purple solutions. It has been pointed out before (p. 1439) that this compound must be represented thus:

it may be called *isophenylmethylacetylcyclopentenephenazine*.

With phenylmercaptan, the diketocyclopentene derivative, C₁₄H₁₂O₃, unites to yield the additive compound, C₁₄H₁₂O₃·C₆H₅S. This is formed when the diketone (0.5 gram), dissolved in hot alcohol, is mixed with phenylmercaptan (0.3 gram). The red colour of the solution changes to yellow, and, on adding water until turbidity is produced, yellow prisms separate, which soften at 125° and melt at 130° to a red liquid:

0.2344 (dried in a vacuum) gave 0.1650 BaSO₄. S=9.67.

C₂₀H₁₈O₃S requires S=9.47 per cent.

This compound, like the product of the union of diketodiphenylpyrroline with phenylmercaptan, readily decomposes into its constituents, the diketone and the mercaptan.

Action of p-Nitrosodimethylaniline on α-Hydrindone.

α-Hydrindone was prepared by the action of aluminium chloride on phenylpropionyl chloride, according to the method elaborated by Kipping (Trans., 1894, **65**, 484), and the yield was found to be the same as stated by this author, if his directions are closely followed. The action of nitrosodimethylaniline on the hydrindone takes place under the influence of alcoholic potassium hydroxide, and is accompanied by development of heat. After several experiments, the following mode of procedure was adopted as giving the best results. The hydrindone (6 grams) and nitrosodimethylaniline (24 grams), dissolved in equal volumes of alcohol (about 50 c.c.), are mixed, the solution is cooled by ice, and gradually treated with a small quantity of alcoholic potassium hydroxide. The mixture soon turns deep brown and deposits a black solid; after being kept for a day at the ordinary temperature, the reaction is complete. The solid is collected, washed with cold alcohol, and dissolved in boiling methylated spirit (about 2·5 litres are required); on cooling, beautiful green prisms (9 to 9·5 grams) separate from the bluish-black solution, which, after a second crystallisation from the same solvent, melt and decompose at 174°:

0·1862 gave 0·4960 CO₂ and 0·1020 H₂O. C=72·65; H=6·08.

0·1948 „ 0·5194 CO₂ „ 0·1045 H₂O. C=72·73; H=5·96.

0·1890 „ 21·8 c.c. N₂ at 18° and 761 mm. N=13·33.

0·1895 „ 22·2 c.c. N₂ „ 21° „ 765 mm. N=13·41.

C₂₅H₂₆O₂N₄ requires C=72·46; H=6·28; N=13·56 per cent.

It will be noticed that the agreement between the analytical and theoretical numbers is not so close as might be desired, and that, especially, the percentage of hydrogen was found lower than required for the formula. On account of this discrepancy, I have frequently analysed this compound after repeated crystallisations, but without arriving at results which differ appreciably from those stated above.

The substance C₂₅H₂₆O₂N₄ may be regarded as the *hydrate* of 2:3-bis(p-dimethylaminoanilo)-α-hydrindone,

It is only sparingly soluble in alcohol, moderately so in hot benzene, but does not readily crystallise from this solution without the addition of alcohol; it dissolves with great ease in glacial acetic acid to yield an indigo-blue solution, which, in a short time, changes

to yellow, and finally, if warmed, becomes reddish-violet. The dark brown filtrate from the compound $C_{25}H_{26}O_2N_4$, when kept for a few days, deposits a very small quantity of a yellowish-red solid. This is moderately soluble in boiling alcohol to form a red solution, from which, on cooling, dark red crystals separate. These have a bluish-green, metallic lustre, and melt at 238° . As mentioned before, the substance is most probably the *p*-dimethylaminoanil of α -hydrindone,

The following analysis indicates that it is not quite pure:

0.1910 gave 0.5348 CO_2 and 0.1100 H_2O . $C = 76.36$; $H = 6.39$.

$C_{17}H_{16}ON_2$ requires $C = 77.27$; $H = 6.06$ per cent.

Triketohydrindene Hydrate,

Dilute sulphuric acid attacks the compound $C_{25}H_{26}O_2N_4$ even at the ordinary temperature, but more readily on slightly warming on the water-bath; the green crystals disappear, and a dark solution is produced which contains the hydrate of triketohydrindene. Owing to the fact that it is moderately soluble in cold, readily so in boiling, water, but sparingly so in ether, its isolation is rather troublesome. It was found necessary to shake the deep brown liquor which is formed by the action of the acid on the condensation product (10 grams) twenty times with fresh quantities of ether to extract the triketone hydrate (3.2 grams) which was formed. The red, ethereal extracts are decolorised with animal charcoal and evaporated on the water-bath, when a yellow oil is left which solidifies on stirring with a glass rod. The solid readily dissolves in hot water, and, on cooling the concentrated solution, crystallises in colourless prisms, which turn red at 125° , froth at 139° , and melt and decompose at 239 — 240° . The compound, after drying in a vacuum desiccator over sulphuric acid, gave the following results:

0.2083 gave 0.4637 CO_2 and 0.0640 H_2O . $C = 60.71$; $H = 3.41$.

$C_9H_6O_4$ requires $C = 60.67$; $H = 3.37$ per cent.

The aqueous solution of this substance colours the skin purple; this is similar to the behaviour of alloxan, which, in constitution, shows a certain resemblance to triketohydrindene. This substance reduces Fehling's solution as well as ammoniacal silver solutions.

Action of Ammonia on Triketohydrindene.

If the solution of triketohydrindene in dilute ammonia is kept for a short time, it becomes reddish-violet, and no longer reduces silver nitrate. On the addition of dilute hydrochloric acid to the ammoniacal solution, a red, gelatinous precipitate is formed.

This is insoluble in water, sparingly soluble in ether, readily so in hot glacial acetic acid, moderately so in boiling alcohol, and, on cooling the alcoholic solution, crystallises in scarlet prisms. On heating, their colour changes to yellow at about 245°, and above 330° they melt to a dark liquid:

0.1910 gave 0.4760 CO₂ and 0.0540 H₂O. C=67.96; H=3.14.

0.2013 „ 15.6 c.c. N₂ at 20° and 758 mm. N=8.83.

C₁₈H₁₀O₄N₂ requires C=67.92; H=3.14; N=8.80 per cent.

As mentioned above (p. 1442), the compound is most probably to be represented thus:

It dissolves in ammonia, potassium hydroxide, or sodium carbonate to yield reddish-violet solutions, which do not reduce silver nitrate or alkaline copper oxide solutions. The deep violet *silver* compound which it forms on the addition of silver nitrate to its solution in ammonia (containing only a slight excess of the base) is characteristic. If the solution is hot, a curdy, violet precipitate is produced, which is insoluble in water, and can be dried in the water-bath without undergoing any change:

0.2168 gave 0.0880 Ag. Ag=40.59.

C₁₈H₈O₄N₂Ag₂ requires Ag=40.60 per cent.

In the light of the view expressed above concerning the constitution of the condensation product of the triketone with ammonia, the formula of the silver salt is to be expressed thus:

Action of Aniline on Triketohydrindene.

Aniline reacts with the triketone as readily as does ammonia, and yields a yellow compound which separates in needles on bringing the aqueous solution of the triketone into contact with the base. This substance, however, is very unstable, it darkens at 78°, melts indefinitely at 97°, and, on heating with alcohol, suffers a change which is indicated by a deep violet coloration of the solution. I have not yet further examined this reaction.

Action of Potassium Hydroxide on Triketohydrindene.

If potassium hydroxide (containing about 15 per cent. KOH) is added to the triketone, the crystals turn yellow, and then dissolve to yield a solution which, at first, is yellow, but, on keeping for a short time at the ordinary temperature, becomes colourless. The result is, however, different if one does not wait until the last change occurs, but warms at once after the addition of the alkali to the triketone; under these conditions, a deep blue solution is formed, which retains its colour even on boiling, but becomes colourless on dilution with water, and then does no longer reduce alkaline copper oxide. The interpretation of this remarkable phenomenon I hope to be able to give in my next paper on triketohydrindene.

Diphenylhydrazone of Triketohydrindene, $C_9H_4O(:N \cdot NH \cdot C_6H_5)_2$.

This compound is formed on adding phenylhydrazine to the solution of the triketone in acetic acid; after a short time, a red, crystalline solid separates, which dissolves in a large quantity of boiling alcohol, and, on cooling, crystallises in orange needles, melting at 207—208°:

0.1737 gave 0.4717 CO_2 and 0.0735 H_2O . $C = 74.06$; $H = 4.70$.

0.1738 „, 25.2 c.c. N_2 at 19° and 755 mm. $N = 16.56$.

$C_{21}H_{16}ON_4$ requires $C = 74.12$; $H = 4.70$; $N = 16.47$ per cent.

The dihydrazone dissolves in cold concentrated sulphuric acid to yield a deep brown solution, which turns indigo-blue on the addition of a trace of potassium dichromate.

Disemicarbazone of Triketohydrindene, $C_9H_4O(:N \cdot NH \cdot CO \cdot NH_2)_2$.

On mixing aqueous solutions of the triketone (1 gram) and semicarbazide hydrochloride (2 grams), an orange coloration is produced, and a yellow solid soon begins to separate. The reaction is complete after keeping the mixture at the ordinary temperature for a day. The substance is sparingly soluble in water or alcohol, and crystallises from these solutions in microscopic, yellow needles, which darken at 175° and melt at 208° with evolution of gas:

0.1620 gave 43.4 c.c. N_2 at 20° and 758 mm. $N = 30.55$.

$C_{11}H_{10}O_3N_6$ requires $N = 30.66$ per cent.

Action of Hydroxylamine on Triketohydrindene.

This reaction takes place if the aqueous solution of the mixture of triketohydrindene hydrate (1 gram) and hydroxylamine hydro-

chloride (2 grams) is kept at the ordinary temperature; a white solid is gradually formed, and after three days the separation is complete. The solid is sparingly soluble in water or alcohol, but separates very slowly from these solutions in the form of an amorphous powder, which dissolves in potassium hydroxide to yield a red solution, and melts at 174° with rapid evolution of gas. This product is a mixture of oximino-derivatives of triketohydrindene; its chief constituent is the trioxime, $C_9H_4(:NOH)_3$; this is indicated by the following analysis:

0.1875 gave 30.8 c.c. N_2 at 20° and 755 mm. $N=18.66$.

$C_9H_7O_3N_3$ requires $N=20.49$ per cent.

Ketohydrindenophenazine,

On mixing equal weights of triketohydrindene hydrate and *o*-phenylenediamine, dissolved in hot dilute acetic acid, a yellow solid is precipitated. This is sparingly soluble in cold, moderately so in boiling, alcohol, and, on cooling, crystallises in yellow prisms, which melt at $218-219^{\circ}$. The yield is almost theoretical:

0.1950 gave 0.5550 CO_2 and 0.0635 H_2O . $C=77.62$; $H=3.62$.

0.1755 „, 18.8 c.c. N_2 at 24° and 767 mm. $N=12.13$.

$C_{15}H_8ON_2$ requires $C=77.59$; $H=3.45$; $N=12.07$ per cent.

In conclusion, I may state that I am continuing the research on triketohydrindene as well as the study of the cyclic diketonic compounds which stand in a close relation to isatin.

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