LXVII.—*Stereoisomeric Osazones.* Part I.

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ACCORDING to the theory of nitrogen isomerism proposed by Hantzsch and Werner, just as the 1 : 2-dioximes exist in several modifications, so also should the 1 : 2-dihydrazones or osazones show a similar isomerism. Anschütz and Pauly (*Ber.*, 1895, **28**, 64) have, in fact, quite recently succeeded in preparing the three theoretically possible forms of the osazone of dihydroxytartaric acid. With this exception, however, all attempts to obtain the various modifications of these substances have proved futile, the methods invariably leading to one and the same dihydrazone.

The osazone of benzile, being one of the easiest to prepare, has been the object of attack by several chemists. Anwers and his scholars (*Ber.*, **26**, 788; **27**, 1133), especially, have tried to obtain such stereoisomerides by the use of substituted hydrazines, and Smith and Ransom (*Amer. Chem. J.*, 1894, **16**, 115) have heated the stereoisomeric hydrazones of benzoin with phenylhydrazine in acetic acid solution. In all cases, however, only one modification could be isolated.

In continuation of an investigation on the derivatives of tetrazole, we had occasion to study the action of iodine on a mixture of sodium ethoxide and benzalphenylhydrazone. The fact that alkyllogens enter into reaction with the sodium derivative of this last-named compound was first noticed by B. Philips (*Ber.*, 1887, **20**, 2485), but the substitution of sodium alcoholates for sodium in similar reactions was first made by Landsberg (*vide* Japp and Klingemann, *Trans.*, 1888, **53**, 519). The application of Landsberg's modification of Philip's method to benzalphenylhydrazone does not appear to have been studied.

By the interaction of an ethereal solution of iodine with a mixture of sodium ethoxide and benzalphenylhydrazone, also dissolved in ether, and all in molecular proportion, the formation of a compound, $\text{C}_6\text{H}_5\cdot\text{N}:\text{N}:\text{CH}\cdot\text{C}_6\text{H}_5$, was to be expected. On carrying out the experiment we found that two well-defined crystalline substances were formed, melting at 208° and 186° respectively, the former in much the larger quantity. On analysis it was found that both had the formula $(\text{C}_{13}\text{H}_{11}\text{N}_2)_x$.

At this point it came to our knowledge that v. Pechmann (*Ber.*, 1893, **26**, 1045) had obtained a compound of the same composition by direct oxidation of benzalphenylhydrazone with amylic nitrite. The same substance had previously been obtained by Minunni (*Gazzetta*,

1892, **22**, ii, 217), using mercuric oxide as the oxidising agent.* v. Pechmann assigned the constitutional formula above suggested to this compound, and named it dibenzaldiphenylhydrotetrazone (*Ber.*, 1894, **27**, 2920). On repeating the experiments of these two chemists, we found that in both cases the same substance was formed, and that it was identical with the compound melting at 186°, previously obtained by the action of iodine on sodium benzalphenylhydrazone.

Thinking that the other substance, melting at 208°, might be obtained by the action of alkali on the hydrotetrazone first produced, we heated the latter, dissolved in benzene, with alcoholic potash, and found, to our surprise, that the compound produced was not the one melting at 208°, but that it melted at 225°, and was in every respect identical with benzileosazone. An intramolecular change has then occurred,

similar to that which takes place when hydrazobenzene is treated with acids,

nitrogen linkage giving place to that of carbon.

Just as the rearrangement in the latter case may be viewed as being occasioned by the acid inducing the formation of basic molecules, so in the present instance the presence of alkali determines the formation of acidic imido-groups.

v. Pechmann found that on heating the hydrotetrazone with phenylhydrazine, it suffered reduction to the original benzalphenylhydrazone (*loc. cit.*); we repeated his experiment with the same result, and it appeared of interest to examine the behaviour towards this reagent of the isomeric substance melting at 208°; it was found that partial decomposition took place, and benzileosazone, melting at 225° was formed. According to v. Pechmann, osotetrazones when heated with phenylhydrazine are reduced to the corresponding osazones:

The substance under consideration showed, however, none of the reactions of osotetrazones, and the fact that it is very readily oxidised indicates the presence of oxidisable hydrogen.

* v. Pechmann gives 190° as the melting point of this substance; Minunni 180°. The former also repeated Minunni's experiments, and corrects the melting point given by him. We, however, have not found a higher value than 186° for the substance prepared by any of the three methods.

In order, however, to eliminate the possibility of a mere reduction by the phenylhydrazine, the substance alone was dissolved in ethyl succinate (b. p. 217°), and heated to boiling; it was found that this treatment converted it into benzileosazone. It would appear, especially as the same result was afterwards obtained by heating with ethylic benzoate or malonate, and with alcohol at 200°, that the solvent did not exert any chemical action, but that we had here one of the much sought for stereoisomerides of benzileosazone, which we have named α -benzileosazone.

The preparation of osazones directly from aldehydrazones is not new. Japp and Klingemann (Trans., 1888, **53**, 519) have already prepared a number of them by the simple heating of these compounds. Under these conditions, the hydrazone loses hydrogen thus

and the dihydrazone of a 1 : 2-diketone is formed. The substances thus obtained do not appear to have differed from those formed by direct condensation of the ketone with hydrazine.

As a means of determining the configuration of the two osazones, we had recourse to the method employed by Hantzsch and Werner, and by Beckmann, in the case of the stereoisomeric oximes. The isomerides, when treated with such agents as sulphuric acid and phosphorus pentachloride, pentoxide, pentasulphide or oxychloride, gave different products, and from a study of these they were led to assign definite space configurations to them.

Of the three compounds derived from benzile, for example, the α and γ varieties gave substances whose formation could only be explained by the severance of the *ketonic carbon linking*, whilst in the case of the β -dioxime this linking remained intact in all the products. The γ -compound yielded benzoylphenylurea, and from experience with the monoximes, the *amphi*-configuration was assigned to this variety. The change was thus represented

dibenzénylazoxime (Gunther, *Annalen*, 1889, **252**, 44), and since it also readily yields an anhydride, the *syn*-configuration was assigned to it. The change would be represented as follows.

Thirdly, the β -modification gave oxanilide, and may therefore be considered to possess the *anti*-configuration. The reaction may be formulated thus

Seeing then that so much information is obtained by the use of these reagents with the dioximes, we determined to study the behaviour of the two benzileosazones towards concentrated sulphuric acid. Each of the osazones after treatment with the cold acid was mixed with water, and the product distilled with steam. Under these conditions the β -modification gave large quantities of benzile, and traces of a substance melting at 115° and crystallising in four-sided flat acute rhombic plates, the nature of which was not determined. The α -variety, on the other hand gave large quantities of benzaldehyde, benzile, and triphenylosotriazole (m. p. $120\text{--}121^\circ$)

On rendering the residue in the flask strongly alkaline with caustic potash and again distilling in steam, ammonia, aniline, and some phenylhydrazine were obtained from both modifications.

The production of benzaldehyde from the α -osazone can only be explained by severance of the ketonic carbon linking, and would therefore correspond to the behaviour of the *syn*- and *amphi*-dioximes already cited; the β -variety, yielding no benzaldehyde or allied compound, would be analogous to the *anti*-dioxime.

The formation of triphenylosotriazole corresponds exactly with that of an anhydride by the *syn*-dioxime, and it seems extremely probable that the anilido-groups are nearer in space in this case than in the β -compound.

Auwers and V. Meyer have prepared this osotriazole from ordinary or β -benzileosazone by dry distillation or by heating with alcohol at 210° . The stability of the molecule at the temperature necessary to bring about these reactions, is greatly decreased, and this change cannot therefore be used as an argument in favour of the *syn*-configuration of the ordinary osazone. The action of sulphuric acid is very different. Here the temperature at which the change takes place is one at which

both osazones are stable and under these conditions the normal or β -osazone, as already stated, does not yield this osotriazole whereas the α -osazone does.

Anschütz and Pauly (*loc. cit.*) as already mentioned, have recently prepared the stereoisomerides of dihydroxytartaric acid osazone, and on comparing the melting points of these with those of the two benzileosazones a remarkable agreement is noticed.

	Osazones of dihydroxytartaric acid.	Benzileosazones.
α -variety.....	120—121° C.	207—208° C.
β -variety (most stable)	136—137 „	225° C.
γ -variety.....	173—175 „	—

The difference between the melting points of the α and β varieties in the case of the osazones of dihydroxytartaric acid is 16°, and in that of the benzileosazones it is 17°. In each case, the form of the higher melting point is the most stable.

A similar agreement among the monhydrazones and oximes of lenzoïn has been noticed by Smith and Ransom (*loc. cit.*).

Of the three isomerides prepared by Anschütz and Pauly, the α -compound is attacked by oxidising agents with the formation of a dark violet osotetrazone, while the β - and γ -modifications are unaffected. Thus, since the α -compound most easily yields a ring, it is probably a *syn*-osazone. Of the stereoisomerides of benzileosazone, the α -modification is the more readily oxidisable, yielding, for example, a dark red coloration with potassium dichromate in acetic acid solution; the β -osazone does not yield this coloration. The oxidation products are still under examination.

Finally, therefore, the constitution of the two osazones, as based on the arguments we have adduced would be represented by the following formulæ.

EXPERIMENTAL.

Action of Iodine and Sodium Ethoxide on Benzalphenylhydrazone.

Ten grams of benzalphenylhydrazone were dissolved in ether, to this a solution of 1.4 grams of sodium in 20 c.c. of alcohol was added, and an ethereal solution of 6.5 grams of iodine gradually run in, the mixture being shaken from time to time; sodium iodide at once separated, and the liquid became intensely red. On adding water,

the sodium iodide dissolved, and the last traces of iodine were removed by shaking with sodium sulphite solution. On evaporating the ether, a brownish-red, somewhat resinous residue remained, which left a bright yellow crystalline substance on treatment with alcohol; this, after purification by washing with hot alcohol, weighed 1.6 grams. The crystalline substance on boiling with ethylic acetate was separated into two portions, one soluble, α -benzileosazone, the other a canary-yellow insoluble powder identical with v. Pechmann's dibenzaldiphenylhydrotetrazone (*loc. cit.*); on recrystallisation from benzene, the latter formed silky needles melting at 186° . The air-dried substance was analysed.

0.2115 gave 27.4 c.c. moist nitrogen at 15° and 732 mm. $N = 14.8$.

Calculated for $C_{26}H_{22}N_4$. $N = 14.36$ per cent.

It is very insoluble in almost all solvents, and dissolves but sparingly in hot benzene and chloroform. With sulphuric acid, it gives a characteristic blue coloration, and on heating with phenylhydrazine it is reduced to the original benzalphenylhydrazone.

Action of Alcoholic Potash on Dibenzaldiphenylhydrotetrazone.

The hydrotetrazone (0.5 gram) was dissolved in benzene, and caustic potash (1.5 grams) in alcoholic solution added; a precipitate formed at first, but on heating it dissolved and a dark brown liquid was obtained. After boiling for half-an-hour, using a reflux condenser, alcohol was added and the crystals which separated were collected and recrystallised from a mixture of benzene and alcohol. They melted at 224 — 225° and showed all the properties of β -benzileosazone. On analysis, they gave the following numbers.

0.156 gave 0.4560 CO_2 and 0.0805 H_2O . $C = 79.72$; $H = 5.73$.

Calculated for $C_{26}H_{22}N_4$. $C = 80.00$; $H = 5.64$ per cent.

α -Benzileosazone. That portion of the substance obtained by the action of sodium ethoxide and iodine on benzalphenylhydrazone, which is soluble in ethylic acetate, and which forms the bulk of the product, separates from the concentrated solution in small prismatic yellow crystals melting at 206° . When purified by recrystallisation from a mixture of benzene and alcohol, it forms yellow prismatic needles, melting and decomposing at 208° . On analysis, it gave numbers agreeing with those required for benzileosazone. The substance was dried in a vacuum.

0.1196 gave 15.5 c.c. moist nitrogen at 15.5° and 731 mm. $N = 14.56$

0.1330 gave 0.3915 CO_2 and 0.0660 H_2O . $C = 80.25$; $H = 5.51$.

Calculated for $C_{26}H_{22}N_4$. $C = 80.00$; $H = 5.64$; $N = 14.36$ per cent.

It is practically insoluble in alcohol, but dissolves slightly in ether

and more easily in acetone, ethylic acetate, chloroform and benzene. A determination of the molecular weight was made in benzene solution by Raoult's method, and gave the following numbers.

Weight of substance taken. . . .	= 0.2425 gram.
Weight of benzene taken	= 13.6595 grams.
Depression of freezing point ..	= 0.21°.

	Calculated for $C_{26}H_{22}N_4$.	Found.
Molecular weight.	390	414

It undergoes no change when heated with dilute acids, the residue melting as before at 208°, but with concentrated sulphuric acid a wine red coloration is produced identical in shade with that produced from β -benzileosazone; this changes to green on adding a drop of ferric chloride, or potassium dichromate solution. If water be added to the sulphuric acid solution, a strong smell of benzaldehyde is produced, and the colour changes to yellowish-brown.

Transformation of α -Benzileosazone into the β -modification.

1.—*By means of phenylhydrazine.*—0.5 gram of the α -osazone was heated for an hour with excess of phenylhydrazine in a tube provided with a reflux condenser. On cooling the orange-red liquid, and adding acetic acid and water, a substance separated which was practically insoluble in alcohol; it was purified by repeated washing on the filter with this liquid, and by twice recrystallising from a mixture of chloroform and alcohol. It then melted at 224° and showed all the properties of the β -osazone.

2.—*By ethylic succinate.*—1 gram of α -benzileosazone was heated with 4 grams of ethylic succinate (b. p. 217°) to the boiling point of the mixture. The osazone dissolved, and the liquid darkened in colour until it became a deep brown. After five minutes, the action was complete; the flame was then removed, alcohol added, and the precipitate recrystallised from benzene and alcohol. A substance melting at 224–225° was thus obtained, the yield being 50 per cent. on the α -osazone used. On analysis the product gave the following numbers:

0.1550 gave 0.4545 CO_2 and 0.084 H_2O . C = 79.98; H = 6.02.

0.1350 gave 0.3970 CO_2 and 0.0745 H_2O . C = 80.20; H = 6.13

Calculated for $C_{26}H_{22}N_4$. C = 80.00; H = 5.64.

It has, in addition, all the properties of β -benzileosazone.

3.— β -benzileosazone is similarly produced on heating the α -compound dissolved in ethylic benzoate (b. p. = 211°) or ethylic malonate (b. p. = 195°). Since it is obtained in the latter case, it would

appear that the change may be brought about at a temperature below but near to the melting point of the α -osazone.

4.—*By heating with alcohol at 200°.* 1 gram of the α -osazone was heated in a sealed tube with 20 c.c. of absolute alcohol at a temperature from 180° to 205° for two to three hours. The clear orange-coloured liquid contained long needles of the β -osazone and on opening the tube a smell of benzaldehyde was noticed, as well as the presence of alkaline vapour. A partial decomposition of the osazone has, therefore, taken place. The crystals proved to be the β -osazone melting at 225°.

Relative Properties of the two Osazones.

1.—*Solubilities.*—Since there is a very great difference in the solubilities of the stereoisomeric osazones described by Anschütz and Pauly (*loc. cit.*) it was of interest to examine the two osazones with respect to this property. For this purpose, acetone was chosen as the solvent, and the two isomerides were found to give small though definite differences in their solubility in this liquid.

α -Benzileosazone.—1.699 grams of the acetone solution at 18–19° left on evaporation 0.0275 gram of the osazone; hence 100 parts of acetone dissolve 1.65 parts of the α -compound.

β -Benzileosazone.—2.4165 grams of the acetone solution at 18–19° left on evaporation 0.0565 gram of the solid; hence 100 parts of acetone dissolve 2.4 parts of the β -compound.

The solubility of the two substances in ether was likewise shown to differ to a small extent.

2.—*Behaviour towards Oxidising Agents.*—When dissolved in acetic acid and treated with potassium dichromate solution, the α -osazone instantaneously gives a dark red coloration; this quickly disappears, and on the addition of more dichromate the liquid assumes an orange-red colour. The β -osazone does not yield the initial red colour when treated in this way but, after standing, acquires a similar orange-red tint. On carrying out the oxidation in ethereal solution with potassium permanganate and hydrochloric acid (*see* Anschütz and Pauly, *loc. cit.*), a dark red solid was obtained from the α osazone, but it could not be crystallised.

v. Pechmann has proposed amylic nitrate as an oxidising agent for imido-hydrogen groups, and it was hoped by this means to obtain an osotetrazone from the α -osazone. For this purpose, the α -osazone was dissolved in benzene, and treated with excess of this oxidising agent. As each drop of the nitrite touched the liquid, a bright red coloration was produced which immediately disappeared, but on boiling the mixture, the colour returned. After heating for half an hour, a precipitate had formed in the liquid, and this was removed

by filtration and crystallised from alcohol. It did not melt below 250° , but since it gave Liebermann's reaction with phenol and sulphuric acid it is probably a nitrosamine; the quantity obtained was too small to admit of further examination. The resinous residue left on evaporating the filtrate was extracted with light petroleum, and this, on evaporation, yielded a dark red resin, which, although it was not obtained in a crystalline form, gave β -benzileosazone on heating with excess of phenylhydrazine, so that it is probably an osotetrazone.

When β -benzileosazone is subjected to similar treatment with amyl nitrite, it does not yield a dark red, but rather an orange-yellow solution, and appears to suffer decomposition. We were unable to obtain either the nitrosamine, or a resin similar to that above-mentioned.

We hope to be able to repeat these oxidation experiments with larger quantities of the substances.

3.—*Behaviour towards Sulphuric Acid*.—(a.) α -osazone, *m. p.* 208° .—1 gram of the finely powdered substance, placed in a small round-bottomed flask, was well shaken with 10 c.c. of concentrated sulphuric acid; after half an hour, 100 c.c. of water was run in, when the original wine red colour immediately changed to a dull brick red. The contents of the flask were now distilled in a brisk current of steam, the concentration of the liquid being kept approximately constant; the distillation was continued for five hours and large amounts of benzile (*m. p.* $93-94^{\circ}$) passed over together with benzaldehyde. On making the contents of the flask alkaline, and again distilling in steam, ammonia, aniline, traces of phenylhydrazine and of an isonitrile were detected.

The experiment was repeated with 2 grams of the α -osazone, but this time the flask was allowed to stand only 10 minutes before the addition of the water, and further, towards the end of the experiment, the concentration was allowed to increase. Under these conditions white shining hexagonal plates were deposited in the condenser; they crystallised from alcohol in nacreous laminæ, melting at $120-121^{\circ}$, and showing all the properties of triphenylosotriazole (Auwers and V. Meyer, *loc. cit.*); the other products before-mentioned were likewise formed.

(b.) β -osazone, *m. p.* 225° .—One gram of the finely powdered substance was treated exactly as the first portion in (a). In this case, the distillate contained no trace of benzaldehyde, but benzile was formed in large quantity. On rendering alkaline and again distilling in steam, ammonia, aniline, and traces of phenylhydrazine were found in the distillate.

If the experiment be varied by allowing the substance to stand

only 10 minutes with the concentrated acid, and also gradually concentrating the liquid during the distillation, another product was formed in addition to the above. Towards the end of the operation, a white crystalline substance was deposited in very small quantity in the condenser; this crystallised from alcohol in flat rhombic plates, and melted at 115° . It was soluble in ether, but insoluble in alkalis, acids, and water, and differs both in melting point, crystalline form, and solubility from the triphenylosotriazole obtained with the isomeric substance. The quantity, however, was too small for further examination.

These experiments with the two osazones were several times repeated, and under the above conditions the same characteristic substances were always formed.

Oxidation of Benzalphenylhydrazone by Amylic Nitrite.—As mentioned in the introduction, v. Pechmann obtained dibenzaldiphenylhydrotetrazone by oxidising benzalphenylhydrazone with amylic nitrite in ethereal or light petroleum solution. On repeating his experiments, we obtained somewhat different results and an account of them will perhaps be of interest. Five grams of benzalphenylhydrazone was dissolved in ether, and about 5 grams of amylic nitrite added to the solution; the mixture, heated on the water bath, gave an orange-yellow solution at first, but on further heating this darkened and deposited yellow crystals. After six hours, these were collected and washed with ether and alcohol; the yield of dibenzaldiphenylhydrotetrazone (m. p. 185° – 186°) thus obtained was about 0.8 gram.

The filtrate from the crystals was concentrated by evaporation, treated with alcohol and filtered. On the filter there remained about 0.8 gram of a yellow crystalline substance which, after recrystallisation from a mixture of alcohol and benzene, melted at 202° . An analysis gave the following results.

0.154 gave 0.4505 CO_2 and 0.076 H_2O . $\text{C} = 79.79$; $\text{H} = 5.49$.

It is more soluble in alcohol than the α -osazone, and gives benzaldehyde on boiling with dilute acids, and a blue-green coloration on treatment with concentrated sulphuric acid. It does not appear to be changed by heating with alcoholic potash or with ethylic succinate, but phenylhydrazine, on boiling, reduces it to benzalphenylhydrazone. On treatment in acetic acid solution with potassium dichromate, a claret colour which rapidly darkens is produced. This would seem to indicate the presence of oxidisable hydrogen.

The constitution of this substance is not yet absolutely determined, but from this summary of its properties it appears not to be identical either with the α -osazone, or with dibenzaldiphenylhydro-

tetrazone. Its behaviour corresponds more nearly with the constitution represented by the formula

$$\begin{array}{c} \text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{N}:\text{C}\cdot\text{C}_6\text{H}_5 \\ | \\ \text{C}_6\text{H}_5\cdot\text{CH}\cdot\text{N}\cdot\text{N}\cdot\text{C}_6\text{H}_5 \end{array}$$

We are at present engaged in a further study of the whole subject, and hope to be able to extend the reactions described in this paper to other aldehydrazones.

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