

CCXXV.—*Studies in the Camphane Series. Part XXVIII. Stereoisomeric Hydrazones and Semicarbazones of Camphorquinone.*

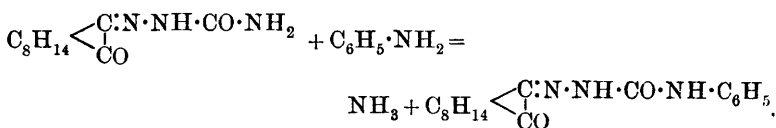
By MARTIN ONSLOW FORSTER and ADOLF ZIMMERLI.

THE expectation of stereoisomerism among semicarbazones is a natural corollary of the Hantzsch-Werner hypothesis. Up to the present time, however, it does not appear that any systematic attempt has been made to place the question of semicarbazone-isomerism on the basis occupied by that of the oximes. Apart from the distrust with which the hypothesis in question is still viewed in some quarters, the principal reason for this omission to bring the semicarbazones into line with oximes is the scattered and ill-defined nature of the evidence relating to the occurrence of isomerism in the former class. The cases of *isothujone*, *carvenone*, and *tetrahydrocarvone* appear to have been established by Wallach (*Ber.*, 1895, **28**, 1955), but the isomeric semicarbazones of *citral* and of *ionone* owe their formation to the existence of each ketone in two isomeric forms. Wallach has also shown that *synthetical pulegone*, obtained by condensation of *methylhexanone* with *acetone*, yields two semicarbazones (*Ber.*, 1896, **29**, 2955; also *Annalen*, 1898, **300**, 269), from both of which the ketone is regenerated by acid, but a claim for the production of isomerides from *phenyl-1-methyl- Δ^6 -cyclohexen-5-one* (Knoevenagel and Gold-

smith, *Ber.*, 1898, **31**, 2465) is not based on strong evidence. Benzoylmethylthiodiazole, on the other hand, gives rise to two derivatives (Wolff, *Annalen*, 1902, **325**, 173), but the supposed existence of two benzilmonosemicarbazones (Posner, *Ber.*, 1901, **34**, 3979) was shown to be fallacious by Biltz and Arnd (*Ber.*, 1902, **35**, 344; compare also Biltz, *Annalen*, 1905, **339**, 243), the second substance being 5:6-diphenyl-3-oxy-1:2:4-triazine, prepared by Thiele and Stange (*Annalen*, 1894, **283**, 27). Nef has recorded the production of two semicarbazones from propaldehyde (*Annalen*, 1904, **335**, 202), whilst Knoevenagel and Samel (*Ber.*, 1906, **39**, 681), and later Rupe and Dorschky (*Ber.*, 1906, **39**, 2112), found that when semicarbazide acts on carvone in the cold, the product is distinct from that described by von Baeyer, into which, however, it is convertible at raised temperatures.

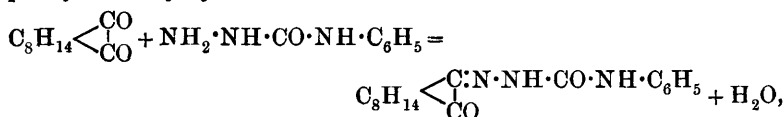
In reviewing the foregoing evidence relating to the existence of isomeric semicarbazones, we have not encountered any systematic attempt to explain the phenomenon, but the experiments described in this paper lead us to express the opinion that stereoisomerism of the type displayed by oximes must now be regarded as existing in this class also.

Our attention was drawn to the subject by an observation made in connexion with camphorquinonesemicarbazone (Lapworth and Chapman, *Trans.*, 1901, **79**, 381), and our thanks are due to Dr. Lapworth for his consent to our using this material. In preparing it by the slightly modified process of Diels and vom Dorp (*Ber.*, 1903, **36**, 3190), we noticed that the mother liquor contained a more soluble isomeride melting at a lower temperature than the modification already described, and calling the latter the α -derivative, we refer to the new compound as the β -semicarbazone. When this is heated above its melting point, it is converted into the α -semicarbazone, and the latter, under the influence of hot aniline, undergoes the change described by Borsche (*Ber.*, 1901, **34**, 4297; 1904, **37**, 3177), giving rise to camphorquinonephenylcarbamylhydrazones, with liberation of ammonia:



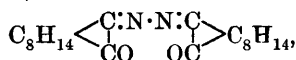
The product, however, is an equilibrium mixture of two isomerides, related to one another in a manner similar to the connexion between the semicarbazones. Both camphorquinonephenylcarbamylhydrazones are produced, also, when the β -semicarbazone is heated

with aniline, and by the condensation of camphorquinone with phenylcarbamyldiazide:

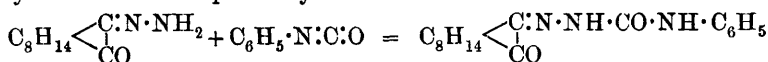


and they may be obtained separately by the action of phenylcarbimide on two new hydrazones of camphorquinone.

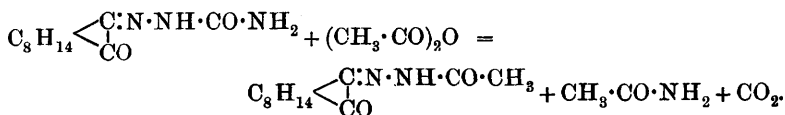
The action of hydrazine on camphorquinone is stated by Oddo (*Gazzetta*, 1897, **27**, ii, 117) to yield "biscamphanonazine," identical with Angeli's azocamphanone (*Gazzetta*, 1894, **24**, ii, 44), produced in association with camphenone by heating diazocamphor. As represented by Angeli, the formation of azocamphanone:



obviously depends on the condensation of hydrazine with two molecules of the diketone, but we find that if the substances interact in molecular proportion, two new derivatives of camphorquinone are produced; these, being isomeric, are referred to as the α - and β -hydrazones, and it is by the action of phenylcarbimide on these two substances that the above-mentioned α - and β -phenylcarbamyldhydrazones are respectively obtainable:

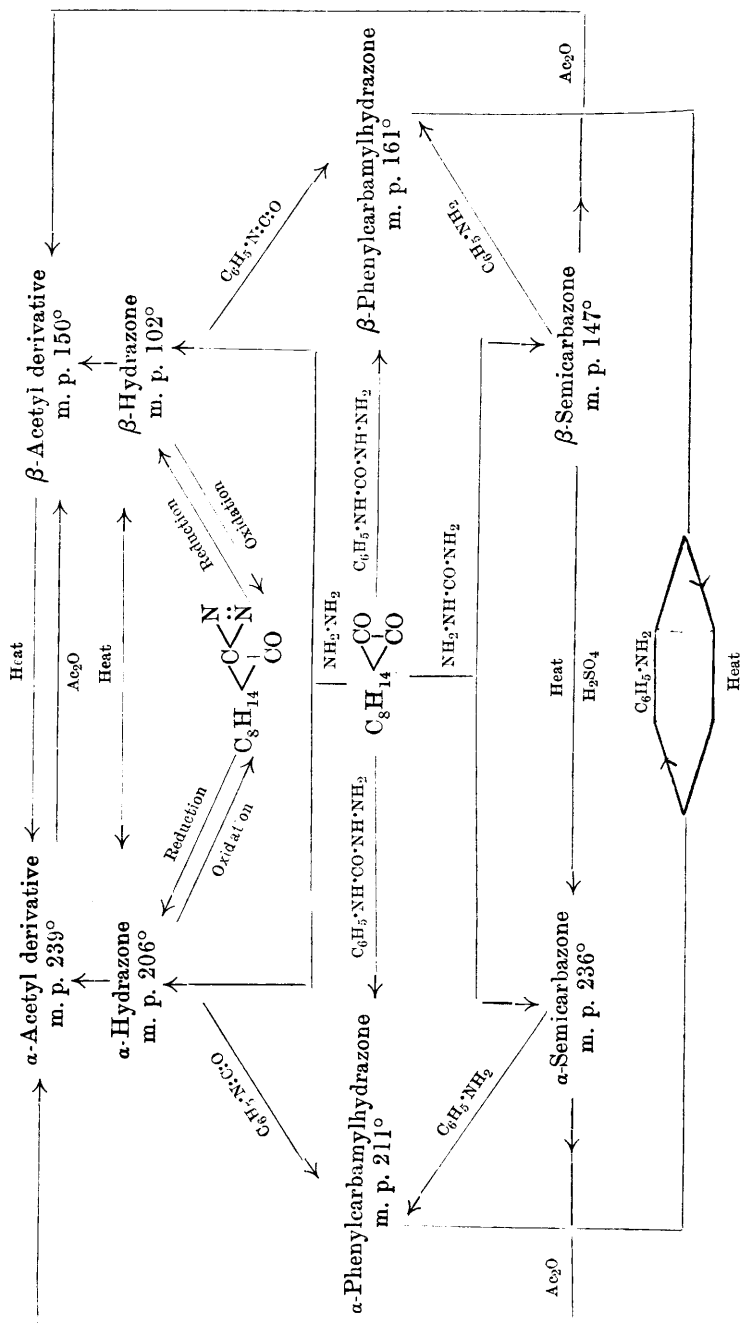


Thus, the isomeric hydrazones (m. p. 206° and 102°) are connected through the isomeric phenylcarbamyldhydrazones (m. p. 211° and 161°) with the isomeric semicarbazones (m. p. 236° and 147°) respectively, and the members of each pair bear to one another the same relation in respect of solubility, fusibility, and interconvertibility by heat. A further connexion between the hydrazones and semicarbazones is established by the fact that whilst acetic anhydride converts the hydrazones into acetyl derivatives (m. p. 239° and 150°), of which the β -compound is transformed into the α -modification by heat, an equilibrium mixture of these isomeric acetyl derivatives follows the action of hot acetic anhydride on the isomeric semicarbazones:



These reactions are summarised in the diagram on p. 2159.

It now becomes necessary to explain our grounds for ascribing the present case of isomerism to stereochemical rather than struc-

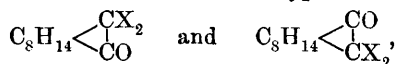


tural considerations, and since the only justification for a stereochemical explanation is the exclusion of structural differences, we proceed to deal with the possible causes of the foregoing relationships. These are:

1. Dimorphism, condemned by the distinct differences in optical activity which solutions of the respective pairs display under comparable conditions.

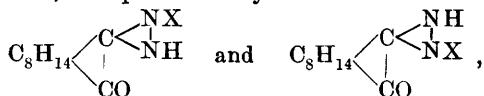
2. Polymerism, which might be suspected from the higher melting point and sparing solubility of the α -compounds. The latter property has precluded application of the freezing-point method of molecular-weight determination except in the case of the α -phenylcarbamylhydrazone; this is normal, and so is the α -semicarbazone in boiling chloroform, whilst for other reasons which become apparent later in this paper it is difficult to believe that the less fusible member of each pair is merely a polymericide of the corresponding β -modification.

3. The structural difference which, depending on the asymmetry of the camphane molecule, renders the types,

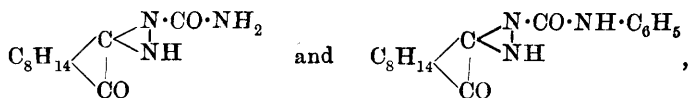


distinct from one another. The principal objection to this explanation is one which is familiar to all workers with camphor derivatives, namely, the immensely superior reactivity of the α -position. But it is excluded also by the formation of the hydrazones on reducing diazocamphor, supported by the improbability of the above types undergoing interconversion by merely heating the substances at 100–200°.

4. *cis-trans*-Isomerism, also depending on the asymmetry of the camphane nucleus, as represented by the formulæ:

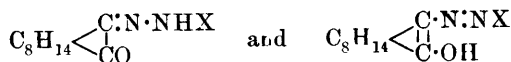


the possibility of which has been indicated by Armstrong and Robertson (*Trans.*, 1905, **87**, 1278). This point would be difficult to argue in the case of the semicarbazones and phenylcarbamylhydrazones if these had the constitution:

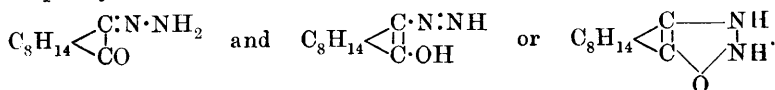


respectively, but is simplified by their experimental relation to the hydrazones, because it is obvious that *cis-trans*-isomerism of the order shown above could not occur in the case of the latter substances.

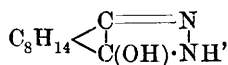
5. The structural difference arising from enolisation, namely:



as suggested by Betti in connexion with the phenylhydrazones (*Ber.*, 1899, **32**, 1995). Here again the test is furnished by the simple hydrazones, which would be represented as:

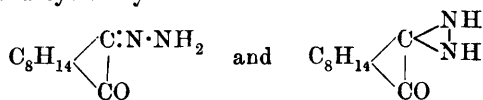


But this enolic formula represents the nitrogen in a condition hopelessly unprotected and quite incompatible with stability, whilst the alternative cycloid could not reasonably be expected to display chemical behaviour practically identical with the azethenoid compound represented by the first of the above expressions. The latter remark applies also to the formula:

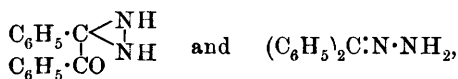


suggested by analogy to Hantzsch's representation of the alkali derivatives from oximinoketones. Thus the keystone of the discussion is the constitution of the simple hydrazones.

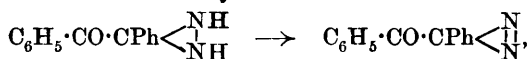
6. The structural difference of compounds derived from the azethenoid and cyclic hydrazones:



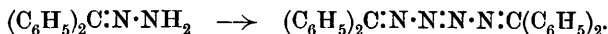
respectively. The discussion of this possibility involves a reference to the early work of Curtius on the interaction of hydrazine hydrate and ketonic substances. In dealing with the constitution of hydrazine derivatives from benzil and benzophenone, Curtius and Thun (*J. pr. Chem.*, 1891, [ii], **44**, 161) and, later, Curtius and Rauterberg (*loc. cit.*, p. 192) distinguish the products by the formulæ:



respectively. Their principal reasons for doing so were the superior reactivity of the benzophenone derivative towards benzaldehyde, although the benzilhydrazone also condenses with that substance, and the oxidation of the benzilhydrazone to the corresponding derivative of diazomethane by the action of mercuric oxide:

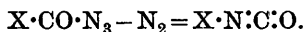
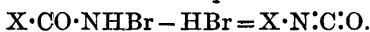


the benzophenonehydrazone being stated to yield a tetrazone by this treatment:

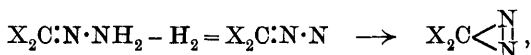


The evidence of tetrazone-formation will be found on examination, however, to be noticeably slender, and in the light of our own experiments we suggest that the "tetrazones" derived from benzophenonehydrazone (Curtius and Rauterberg, *loc. cit.*), benzyldenehydrazone (Curtius and Pflug, *loc. cit.*, p. 535), and acetophenonehydrazone (Curtius and Pflug, *loc. cit.*) are unstable derivatives of diazomethane, corresponding with that obtained from benzylhydrazone.

If this suggestion is justified it would, at first sight, appear to confirm the cyclic representation of the hydrazones. But it has been already pointed out that *cis-trans*-isomerism of an unsubstituted cyclic hydrazone does not seem possible, and the direct consequence of revealing isomerism in a simple hydrazone is therefore to discredit the cyclic structure for at least one member of the pair in favour of the azethenoid representation. How, then, is the formation of a diazomethane derivative from an azethenoid hydrazone to be explained? We suggest the following interpretation, first pointing out that it is probably the self-evidence of the conclusion that a hydrazone, convertible into a diazomethane derivative by mercuric oxide, must be derived from a cyclic type, which has obscured the possibility of an alternative explanation. It seems to us most likely that the cause of this change is to be found in the Hofmann-Curtius reaction, which, without quoting other examples (Trans., 1909, **95**, 433; Schroeter, *Ber.*, 1909, **42**, 2336) may be summarised in the equations:



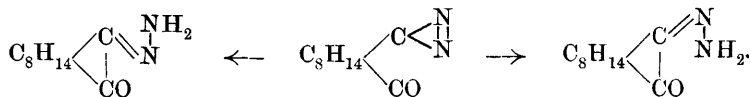
Applying this to the present question, we have to deal with a case of arrested transformation:



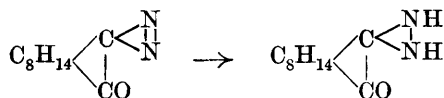
it being impracticable for the denuded atom of nitrogen to displace carbon from its position in the molecule, with the result that the azethenoid linking incurs a redistribution of valency.

Although a superficial criticism of this explanation might dismiss it as forced, and less probable than the one at present accepted, it is strongly supported by the following circumstances. As already pointed out, the isomeric camphorquinonehydrazones cannot both have the cyclic structure; if, on the other hand, one were cyclic and the other azethenoid, some difference in behaviour towards an oxidising agent should evince itself. But there is none. The

α - and β -hydrazones, dissolved in cold pyridine, have been oxidised with aqueous mercury acetamide to diazocamphor, and the precipitation of mercury takes place instantaneously in both cases. Moreover, by reducing diazocamphor in cold alcohol with ammonium sulphide, both hydrazones have been regenerated. It appears to us that these experiments point incontestably to stereoisomerism of the Hantzsch-Werner type. Theoretical considerations make it clear that at least one of the hydrazones must be azethenoid, and since oxidation of both leads to diazocamphor, the production of a diazomethane derivative from a hydrazone by this step cannot be accepted any longer as evidence of the cyclic structure. Furthermore, the fact that diazocamphor yields both hydrazones on reduction vitiates the conclusion that because diazomethane is cycloid, a hydrogenised diazocamphor must be a cyclic hydrazone. On the other hand, formation of both hydrazones on reducing diazocamphor gives colour to our hypothesis, because if it be admitted that ring-scission occurs on reduction, *anti*- and *syn*-modifications would be produced simultaneously:



Moreover, from relationships developed recently between structure and optical activity in the camphane series (Trans., 1909, **95**, 942), it is to be expected that a substance derived from diazocamphor in the manner indicated by the formulæ:

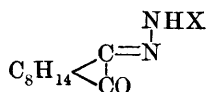


would display lower rotatory power than diazocamphor itself, whereas the α - and β -hydrazones of camphorquinone both have distinctly higher molecular rotation. Furthermore, they do not differ greatly from one another in respect of this property, although a considerable difference might be anticipated between an azethenoid and a cyclic hydrazone.

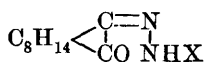
The second chemical distinction which has been mentioned as leading Curtius to differentiate between cyclic and azethenoid hydrazones, namely, condensation with benzaldehyde, corroborates the evidence from oxidation. When suspended in cold water and shaken with this agent, both hydrazones undergo immediate condensation, indicated by a change of colour, since the benzylidene derivative is deep yellow. The final product is the same whether the α - or the β -hydrazone is employed as starting-material, but the

deeper colour generated by the latter substance, and the delay in solidification shown by the product, suggest the preliminary formation of an unstable β -benzylidene compound.

Before concluding, we ought to mention that there is one distinction existing between the members of each pair which will doubtless be quoted as evidence in conflict with our explanation. It is a fact that whilst the α -hydrazone, α -semicarbazone, and α -phenylcarbamylhydrazone are colourless, the β -modifications are faintly yellow. It was by a distinction of this order that Armstrong and Robertson (*loc. cit.*) attempted to justify their representation of the phenylmethylhydrazone and phenylbenzylhydrazone of camphorquinone as "phanes," whilst retaining the azethenoid structure for the diphenylhydrazone, and if the same principle were applied to the substances described herein, the colourless α -hydrazone and its derivatives would be represented as cycloid, whilst the yellow β -compounds would be labelled azethenoid. In the foregoing remarks we have endeavoured to show that this cannot be accepted, but even if that evidence could be swept aside, we still hold that the conclusion from colour is in support of our hypothesis, which regards the α - and β -derivatives as *anti*- and *syn*-carbonylic respectively:

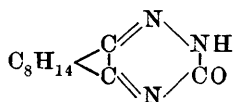


α -Hydrazone, α -semicarbazone,
and α -phenylcarbamylhydrazone.

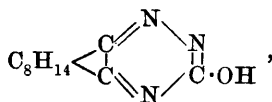


β -Hydrazone, β -semicarbazone,
and β -phenylcarbamylhydrazone.

For it cannot be denied that from the conflict of views as to the relation between colour and constitution there does emerge this principle, that colour appears to be associated with a concentration of unsaturated atoms. Clearly there is a more intimate massing of such atoms in the β -compounds as represented above than in their isomerides, and it is fair to claim this point as favouring the stereochemical hypothesis. In further support of the latter, it may be stated that the only chemical distinction between the members of each pair which has yet come to light is to be found in the behaviour of the semicarbazones towards aqueous alkali. Whilst the α -semicarbazone forms a yellow solution which does not undergo spontaneous alteration, the dissolved β -semicarbazone quickly loses its colour, and on acidifying the liquid there is liberated the oxytriazine:



or



production of which is obviously more favoured by the *syn*-carbonylic configuration than by the alternative one.

These, then, are our principal reasons for inclining to the stereochemical representation of the camphorquinonehydrazones and their derivatives described in this paper. If this interpretation finds acceptance, it carries with it fresh evidence in support of the Hantzsch-Werner hypothesis.

EXPERIMENTAL.

Action of Hydrazine Hydrate on Camphorquinone.

Azocamphanone.—Twelve grams of hydrazine hydrochloride, dissolved in 100 c.c. of water, were treated with 12 grams of potassium hydroxide, and, when cold, mixed with 33 grams of camphorquinone in 100 c.c. of hot alcohol. During one hour at 40° the appearance of the liquid had completely changed, owing to the separation of a bulky, pale yellow precipitate; this was collected, washed with 50 per cent. alcohol, and found to weigh 29 grams. The product was dissolved in 400 c.c. of boiling alcohol, which deposited lustrous, six-sided, transparent plates, almost rhombohedral in form; becoming deep yellow at 195°, it melted and decomposed at 218°. (Found, N=8.75; $C_{20}H_{28}O_2N_2$ requires N=8.53 per cent.) This compound is the "azocamphanone" of Angeli (*loc. cit.*), who records 222° as the melting point, whilst Oddo gives 217–218°. It does not reduce hot Fehling's solution, and is not hydrolysed by a hot 20 per cent. solution of alcoholic potassium hydroxide; concentrated hydrochloric acid, however, when mixed with an alcoholic solution and boiled, eliminates hydrazine, but cold concentrated sulphuric acid, although forming a deep yellow solution, does not resolve azocamphanone into hydrazine and camphorquinone. An alcoholic solution does not change when heated with an aqueous solution of mercury acetamide.

When powdered or in separate crystals, azocamphanone appears colourless, but when viewed in bulk it has a yellow tinge, and solutions are deep yellow; 0.3104 gram, dissolved in chloroform and made up to 25 c.c., gave α_D 4°20' in a 2-dcm. tube, whence $[\alpha]_D$ 174.5° and $[M]_D$ 571°, not 790°, as previously stated in error (Trans., 1909, 95, 948).

The Isomeric Camphorquinonehydrazones, $C_8H_{14} \begin{smallmatrix} < \\ C:N \cdot NH_2 \\ CO \end{smallmatrix}$.—An

aqueous solution of hydrazine hydrate prepared from 30 grams of hydrazine sulphate and 24 grams of potassium hydroxide in 150 c.c. of water was mixed with 33 grams of camphorquinone, dissolved in 150 c.c. of hot alcohol. After three hours at 40°,

23 grams of pale brown crystals had separated, quite distinct in appearance from the bulky precipitate of azocamphanone, and a current of steam having been passed through the filtrate until all volatile matter was removed, a further 2 grams crystallised from the hot liquid, so that under these conditions the yield of α -hydrazone amounted to 75 per cent. There was not any azocamphanone or camphorquinone, and after recrystallisation from about 400 c.c. of boiling alcohol, the α -hydrazone separated in long, lustrous, transparent prisms, melting and evolving gas at 206° :

0.2538 gave 0.6189 CO_2 and 0.2037 H_2O . $\text{C}=66.51$; $\text{H}=8.98$.

0.1418 „ 18.9 c.c. N_2 at 15° and 751.5 mm. $\text{N}=15.43$.

$\text{C}_{10}\text{H}_{16}\text{ON}_2$ requires $\text{C}=66.66$; $\text{H}=8.88$; $\text{N}=15.55$ per cent.

The α -hydrazone and its solutions are colourless, but large crystals frequently have a brown tinge; 0.3110 gram, dissolved in chloroform and made up to 25 c.c., gave α_D $7^{\circ}9'$ in a 2-dcm. tube, whence $[\alpha]_D$ 287.4° . The compound is insoluble in petroleum, and is not readily soluble in other media even when these are boiled; acetone or benzene is a convenient solvent from which to obtain it in colourless crystals, but upwards of 100 c.c. of the latter solvent at the boiling point are required to dissolve 1 gram of the substance. It is readily soluble, however, in warm phenol, and sparingly so in cold pyridine.

A solution in chloroform decolorises bromine immediately, and ammoniacal silver oxide is reduced when warmed with the alcoholic solution. On adding solid sodium nitrite to a cold suspension of the α -hydrazone in glacial acetic acid, the salt assumed a transient purple tint, whilst the liquid became yellow and evolved gas; on diluting the acetic acid with water, azocamphanone was precipitated.

On passing a current of steam through the filtrate from the α -hydrazone as prepared under the foregoing conditions, 3 grams of a straw-yellow, crystalline material were carried over. The yield of this compound, however, was trebled by adding 40 grams of hydrazine hydrate to 50 grams of camphorquinone dissolved in 75 c.c. of alcohol, when the deep yellow colour changed immediately to pale brown; copious precipitation of the α -hydrazone took place after a very short interval, and at the end of half an hour the liquid was filtered and subjected to a current of steam. The solid distillate, consisting of β -hydrazone, weighed 12.5 grams, whilst 2 grams more were obtained by extracting the distilled water (1200 c.c.) with ether; the yield of accompanying α -hydrazone was 66.6 per cent., and if both compounds are required, the above conditions of procedure are the most economical. The β -hydrazone was recrystallised twice from boiling petroleum (b. p. 60 – 80°), 12 grams requiring 120 c.c. of the solvent, which deposited long,

lustrous, straw-yellow needles or transparent prisms, melting at 102°:

0.2038 gave 0.4975 CO₂ and 0.1632 H₂O. C=66.59; H=8.96.

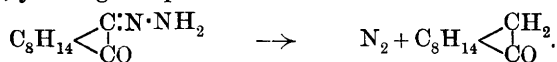
0.1864 „, 26.6 c.c. N₂ at 25° and 754 mm. N=15.79.

C₁₀H₁₆ON₂ requires C=66.66; H=8.88; N=15.55 per cent.

The substance has a faint odour suggesting that of bornylamine; it is readily soluble in organic media, excepting petroleum. A solution containing 0.3134 gram, made up to 25 c.c. with chloroform, gave α_D 5°48' in a 2-dcm. tube, whence $[\alpha]_D$ 231.3°. An alcoholic solution reduces cold ammoniacal silver oxide, and a solution in chloroform decolorises bromine immediately.

Interconversion of the Hydrazones.

On melting the β -hydrazone, it was noticed that if the temperature of the bath is raised to 150—160° the liquid solidifies, and this change was found to be due to conversion into the isomeride, which is readily isolated by recrystallisation from hot alcohol. The converse transformation cannot be brought about by merely melting the α -hydrazone, because this modification slowly loses nitrogen at 205—210°, yielding camphor:



If, however, the α -hydrazone is dissolved in molten paraffin wax, and maintained at 180° during a few minutes, it is a simple matter to demonstrate the formation of the β -hydrazone by suspending the product in hot water, and passing a current of steam through the liquid, when the volatile modification is carried into the condenser.

Action of Sulphuric Acid on the Hydrazones.

The hydrazones behave exactly alike towards sulphuric acid. When covered with the warm agent of 30 per cent. strength, a clear solution is formed almost immediately, and this at once becomes turbid, setting to a paste of azocamphanone in the course of a few minutes; on extracting the filtered product with boiling alcohol, crystals of hydrazine sulphate remain undissolved. With 10 per cent. acid, a clear solution is not produced, because the dissolution of the hydrazone is overtaken by the separation of azocamphanone.

Acyl Derivatives of the Hydrazones

The α -Formyl Derivative, $\text{C}_8\text{H}_{14} \begin{smallmatrix} \text{C:N}\cdot\text{NH}\cdot\text{CHO} \\ \diagup \text{CO} \end{smallmatrix}$.—On dissolving

1 gram of the α -hydrazone in 10 grams of formic acid (D 1.2), the pale yellow solution remained clear during a few seconds, when a shower of crystals separated; the derivative was recrystallised from boiling alcohol, of which about 70 c.c. were required by 1 gram, and was deposited in colourless, lustrous, six-sided plates, which displayed frequent twinning. It melts at 234° :

0.1240 gave 14.6 c.c. N_2 at 18° and 757 mm. $\text{N}=13.54$.

$\text{C}_{11}\text{H}_{16}\text{O}_2\text{N}_2$ requires $\text{N}=13.45$ per cent.

The formyl derivative is insoluble in boiling petroleum, and dissolves sparingly in methyl alcohol, benzene, acetone, and chloroform unless these solvents are heated, 15 c.c. of the last-named, for example, dissolving about one decigram until warmed; it is more readily soluble in pyridine and glacial acetic acid. A solution containing 0.1720 gram, made up to 25 c.c. with chloroform, gave $\alpha_D 3^\circ 33'$ in a 2-dcm. tube, whence $[\alpha]_D 258.0^\circ$. On adding ferric chloride to an alcoholic solution, a pale brown coloration is developed, whilst that with copper acetate is grass-green. Aqueous alkalis dissolve the substance readily, producing a bright yellow solution, and on adding ferrous sulphate to the diluted liquid a dark bluish-green precipitate is formed; when the alkaline solution is left at the laboratory temperature, the colour quickly fades, and the α -hydrazone separates.

The same formyl derivative was also produced by the action of the acid on the β -hydrazone. An attempt to prepare a benzoyl derivative by the action of benzoyl chloride on the formyl compound dissolved in pyridine was not successful.

The α -Acetyl Derivative, $\text{C}_8\text{H}_{14} \begin{smallmatrix} \text{C:N}\cdot\text{NH}\cdot\text{CO}\cdot\text{CH}_3 \\ \diagup \text{CO} \end{smallmatrix}$.—Although

dissolving readily in cold formic acid, the α -hydrazone is only moderately soluble in cold glacial acetic acid; it dissolves on warming the liquid, but does not crystallise readily even on dilution, owing to partial acetylation. The substance was therefore warmed with five parts of acetic anhydride, when the acetyl derivative separated as a paste of crystals at the moment of complete dissolution in the hot liquid; recrystallisation from a considerable proportion of boiling alcohol gave long, lustrous, snow-white needles, melting and decomposing at 239° :

0.1047 gave 11.8 c.c. N_2 at 17° and 760 mm. $\text{N}=13.07$.

$\text{C}_{12}\text{H}_{18}\text{O}_2\text{N}_2$ requires $\text{N}=12.61$ per cent.

A solution containing 0.2226 gram, made up to 20 c.c. with chloroform, gave α_D $5^{\circ}54'$ in a 2-dcm. tube, whence $[\alpha]_D$ 265.5° . The compound dissolves freely in dilute aqueous alkali, developing a bright yellow coloration, and the solution yields an intense bluish-green precipitate with ferrous sulphate; 0.2083 gram, dissolved in 5 c.c. of 10 per cent. sodium hydroxide and diluted to 25 c.c. with water, gave α_D $4^{\circ}12'$ in a 2-dcm. tube, whence $[\alpha]_D$ 252.0° . In process of time, the colour of the alkaline solution fades, and the α -hydrazone separates from the liquid.

The β -Acetyl Derivative.—On dissolving the β -hydrazone in five parts of cold acetic anhydride, the temperature rose slightly, and long, flat, transparent prisms began to separate in the course of a few minutes; after recrystallisation from boiling petroleum, the substance was found to be pale yellow, and melted at 150° :

0.1297 gave 14.5 c.c. N_2 at 18° and 760 mm. $N=12.91$.

$C_{12}H_{18}O_2N_2$ requires $N=12.61$ per cent.

A solution containing 0.3890 gram, made up to 25 c.c. with chloroform, gave α_D $6^{\circ}58'$ in a 2-dcm. tube, whence $[\alpha]_D$ 223.8° . The solution in aqueous alkali has the same appearance as that of the α -acetyl derivative, developing a similar precipitate with ferrous sulphate; in the course of some hours, the yellow colour fades, and the liquid deposits crystals of the α -hydrazone.

When the β -acetyl derivative is heated at temperatures above its melting point, varying proportions of the α -acetyl compound are produced, but the conversion is not complete; moreover, on heating the α -acetylhydrazone in acetic anhydride, a certain amount of the β -isomeride may be isolated from the product.

The α -Benzoyl Derivative, $C_8H_{14} \begin{smallmatrix} \text{C:N} \cdot \text{NH} \cdot \text{CO} \cdot \text{C}_6\text{H}_5 \\ \text{CO} \end{smallmatrix}$.—The

α -hydrazone requires about 25 parts of pyridine to maintain a clear solution at zero, and on adding the calculated amount of benzoyl chloride, also dissolved in ice-cold pyridine, the hydrochloride of the base separated, the benzoyl derivative being precipitated on dilution with water; recrystallisation from boiling alcohol, in which it is sparingly soluble, gave tough, lustrous, snow-white needles, becoming yellow above 200° , and melting at 219 – 222° , according to the rate at which the temperature is raised:

0.1322 gave 11.4 c.c. N_2 at 16° and 757 mm. $N=10.01$.

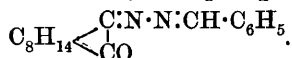
$C_{17}H_{20}O_2N_2$ requires $N=9.86$ per cent.

The substance is not readily soluble in chloroform, and a solution containing 0.2135 gram, made up to 50 c.c. with this solvent, gave α_D $1^{\circ}45'$ in a 2-dcm. tube, whence $[\alpha]_D$ 204.9° . Although in part dissolved by 2 per cent. aqueous sodium hydroxide, the benzoyl derivative did not form a clear solution; 0.1904 gram, suspended

in about 20 c.c. of the agent, was made up to 50 c.c. with absolute alcohol, the clear, deep yellow liquid giving α_D $1^\circ 50'$ in a 2-dcm. tube, whence $[\alpha]_D$ 240.7° .

On attempting to prepare a benzoyl derivative of the β -hydrazone, the principal product was found to consist of the substance just described, but the residue from the mother liquor remained oily during many months, suggesting that both isomerides are formed. The α -benzoyl derivative was obtained also by mixing equal quantities of camphorquinone and benzoylhydrazine in dilute alcohol, crystals separating after two hours at 40° ; in this case, also, the filtrate deposited an oil, indicating the presence of a mixture.

Benzylidene Derivative of Camphorquinonehydrazone,



The α -hydrazone was finely powdered, mixed with the calculated amount of benzaldehyde, and heated with a few c.c. of alcohol during two or three minutes; crystals did not separate on cooling, but water precipitated a yellow oil, which quickly became solid, and was recrystallised from boiling petroleum (b. p. $60-80^\circ$). The massive, yellow crystals melted at 109.5° :

0.1253 gave 12.0 c.c. N_2 at 20.5° and 758 mm. $\text{N}=10.90$.

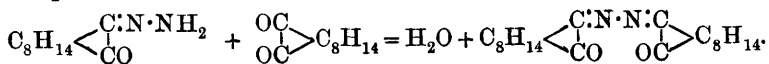
$\text{C}_{17}\text{H}_{20}\text{ON}_2$ requires $\text{N}=10.44$ per cent.

The substance is freely soluble in chloroform, benzene, acetone, alcohol, and ethyl acetate, but only moderately so in warm petroleum; a solution containing 0.3035 gram, made up to 20 c.c. with chloroform, gave α_D $4^\circ 50'$ in a 2-dcm. tube, whence $[\alpha]_D$ 159.2° . It is also produced immediately on shaking the finely powdered hydrazone with water and benzaldehyde, but the method is not convenient, as a portion of the hydrazone remains mechanically protected.

The same benzylidene derivative is produced on agitating the β -hydrazone suspended in water with the aldehyde, the deep yellow colour of the condensation product becoming noticeable immediately. Owing to the solubility of the β -hydrazone in water, none escapes combination, but the product remains liquid during many days, although rapidly becoming solid when heated to 100° and scratched.

Another example of the capacity of the hydrazones for taking part in condensation changes was given by heating an alcoholic solution of the α -hydrazone and camphorquinone in molecular pro-

portion during twelve hours under reflux, when azocamphanone was produced:



Oxidation of the Hydrazones to Diazocamphor.

Since it was desirable to study the oxidation of the hydrazones under conditions precluding the likelihood of preliminary inter-conversion, it occurred to us that mercury acetamide, owing to its solubility in cold water, might be a more suitable agent than mercuric oxide, a study of the acetamide compound having shown that it acts rapidly on primary hydrazines with precipitation of mercury (Trans., 1898, **73**, 783). Experiment showed that the behaviour of the isomeric hydrazones of camphorquinone towards this agent distinguishes itself sharply from the indifference of azocamphanone. It having been first ascertained that the β -hydrazone is not transformed into the isomeride by dissolution in pyridine, 1 gram dissolved in 3 c.c. of the cold solvent was treated with 2 grams of mercury acetamide in 3 c.c. of cold water, the metal being precipitated immediately. The production of the diazo-compound was indicated on extracting with ether, which became deep yellow, and, after evaporation, the pyridine residue yielded 0.8 gram of diazocamphor on dilution with water; recrystallisation from petroleum (b. p. 40°) gave long, striated, yellow prisms, melting at $73\text{--}74^\circ$.

Procedure in the case of the α -hydrazone was modified by the sparing solubility of the substance, 5 grams of which were dissolved in 80 c.c. of hot pyridine, cooled to $50\text{--}60^\circ$, and treated with 10 grams of mercury acetamide in 30 c.c. of warm water; mercury was precipitated immediately, and 4 grams of diazocamphor obtained. A solution containing 0.4605 gram of the diazo-compound, made up to 25 c.c. with chloroform, gave α_D $4.58'$ in a 2-dcm. tube, whence $[\alpha]_D$ 134.8° .

Reduction of Diazocamphor to the Hydrazones.

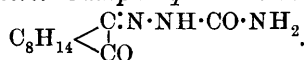
A 20 per cent. solution of diazocamphor in absolute alcohol was saturated with hydrogen sulphide without undergoing any change in appearance, but on adding a few drops of dilute ammonia and again passing the gas, the liquid became pale brown, and gradual separation of the α -hydrazone took place; on subjecting the filtrate to steam distillation, a small proportion of the β -hydrazone was carried over. As it is a matter of importance to establish the production of both compounds without question, the experiment

was repeated at zero, when it was found that the precipitation of the α -hydrazone was diminished, and the yield of β -hydrazone was proportionately increased.

Reduction of the α -Hydrazone to α -Aminocamphor.

Owing to the readiness with which the hydrazones undergo acetylation, a certain amount of the α -acetyl derivative is formed on attempting to reduce the α -hydrazone with zinc dust and acetic acid; it is precipitated, however, when the acid is neutralised. On adding a further quantity of alkali to the filtrate, ammonia is set free, and ether extracts aminocamphor, which may be identified by conversion into the oxime; a specimen of aminocamphoroxime obtained in this way melted at 144—145°.

The Isomeric Camphorquinonesemicarbazones,



The discovery of a second camphorquinonesemicarbazone arose from the observation that on evaporating the filtrate from the substance described by Lapworth and Chapman, there is deposited an oil which, by treatment with very dilute aqueous alkali, is divisible into two solids; one passes into solution, and consists of the derivative already known, whilst the new semicarbazone remains suspended.

A solution containing 33.2 grams of camphorquinone in 150 c.c. of alcohol was mixed with semicarbazide acetate prepared from 22.2 grams of the hydrochloride and 27 grams of crystallised sodium acetate in 100 c.c. of water; the liquid, from which crystals of the α -semicarbazone quickly separated, was transferred to a stoppered filtering flask connected with a water-pump, the alcohol being evaporated at the laboratory temperature during six to eight hours, when drops of oil became noticeable among the crystals. From the resulting sludge about 16 grams of the less soluble α -semicarbazone were filtered, the mother liquor being poured into water and treated with alkali hydroxide until a faint yellow colour persisted; the suspended oil became solid when stirred, and consisted of the more soluble β -semicarbazone mixed with a small proportion of the isomeride. In order to remove the latter, the filtered product was ground three or four times with 10 c.c. of 2 per cent. aqueous sodium hydroxide, the filtration necessary after each extraction being carried out as quickly as possible, because although the α -semicarbazone dissolves in weak alkali without delay, the β -modification is also soluble, but very slowly. The pale yellow powder was then extracted twice with 300 c.c. of boiling water, the

crystalline deposit (6 grams) from this being recrystallised from 25 c.c. of warm benzene, to which the same volume of petroleum was added. At this stage the purification was complicated by the fact that following closely on the slender, yellow crystals of the β -semicarbazone there appeared opaque nodules containing the isomeride.

Camphorquinone- α -semicarbazone is the substance described by Lapworth and Chapman (*loc. cit.*). It crystallises from alcohol in lustrous, colourless prisms, melting and evolving gas at 236° , after sintering and becoming yellow at about 230° ; it is much less readily soluble in organic media than the isomeride, and is insoluble in petroleum. A solution containing 0.3152 gram, made up to 20 c.c. with methyl alcohol, gave α_D $8^\circ 45'$ in a 2-dcm. tube, whence $[\alpha]_D$ 277.6° . As distinguished from the β -compound, it dissolves immediately in dilute alkali, and 0.3344 gram in sufficient potassium hydroxide, made up to 25 c.c. with water, gave α_D $8^\circ 55'$ in a 2-dcm. tube, whence $[\alpha]_D$ 333.3° ; this remained constant during six days, and the semicarbazone precipitated from the solution by acetic acid was unchanged material. Nevertheless, on heating with 10 per cent. potassium hydroxide during three to four days, camphor was gradually produced. Cold concentrated sulphuric acid dissolves the α -semicarbazone, and gradually changes it to azocamphanone, which is precipitated on pouring the liquid into water; if, however, the hot acid is used, a certain amount of camphorquinone is produced. An estimation of the molecular weight in boiling chloroform gave 236 instead of 223.

Camphorquinone- β -semicarbazone crystallises in pale yellow prisms, melts at 147° , and is readily soluble in alcohol, acetone, ethyl acetate, chloroform, ether, or benzene, but dissolves only sparingly in hot water or boiling petroleum:

0.2328 gave 0.5037 CO_2 and 0.1539 H_2O . $\text{C}=59.03$; $\text{H}=7.66$.

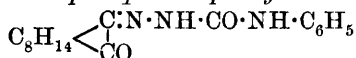
0.3225 „ 54.8 c.c. N_2 at 25° and 754 mm. $\text{N}=18.79$.

$\text{C}_{11}\text{H}_{17}\text{O}_2\text{N}_3$ requires $\text{C}=59.19$; $\text{H}=7.62$; $\text{N}=18.83$ per cent.

A solution containing 0.3152 gram, made up to 20 c.c. with methyl alcohol, gave α_D $6^\circ 20'$ in a 2-dcm. tube, whence $[\alpha]_D$ 200.9° . When covered with aqueous alkali hydroxide, the β -semicarbazone does not appear to dissolve; if, however, the solid substance is thrown into hot 10 per cent. sodium hydroxide, there is produced immediately a deep yellow solution, the colour of which gradually fades, owing to the formation of the oxytriazine (see below). On raising the temperature of the fused β -semicarbazone to about 190° , the substance became solid, and the α -semicarbazone was found to have been produced.

Conversion of the Semicarbazones into the Acetylhydrazones.

The semicarbazones were separately heated with boiling acetic anhydride during one hour, the solid product obtained in each case, on pouring the liquid into water, being found to consist of a mixture of the α - and β -acetyl derivatives of the hydrazones. The transformation was not easy to establish experimentally, because the relative solubility of the acetyl derivatives in alkali exactly resembles that of the semicarbazones themselves, and as the melting points of the latter differ from those of the respective acetyl hydrazones by 3° only in each case, the preliminary experiments led to the supposition that the semicarbazones are directly interconvertible by the action of the agent in question.

The Isomeric Camphorquinonephenylcarbamyldhydrazones,

These derivatives were prepared by three different methods.

(1) Action of hot aniline on the α - and β -semicarbazones, each of which gave both phenylcarbamyldhydrazones.

(2) Condensation of camphorquinone with phenylcarbamyldhydrazide, also yielding a mixture.

(3) Interaction of phenylcarbimide and the α - and β -hydrazones, which led to the individual phenylcarbamyldhydrazones, respectively.

Camphorquinone- α -phenylcarbamyldhydrazone.—Four grams of the α -semicarbazone were dissolved in 20 c.c. of aniline, and heated ten minutes at the boiling point of the solvent, ammonia being liberated freely before this temperature was reached; the cooled liquid was diluted with its volume of alcohol, and poured into 200 c.c. of 10 per cent. acetic acid at zero. The precipitated oil quickly hardened when scratched, and on dissolving the product in 80 c.c. of hot methyl alcohol, the α -phenylcarbamyldhydrazone crystallised in thick, colourless plates, melting at 211° , whilst the isomeride remained dissolved:

0.2494 gave 0.6096 CO_2 and 0.1656 H_2O . $\text{C}=66.67$; $\text{H}=7.43$.

0.1660 „ 20.3 c.c. N_2 at 24° and 761.5 mm. $\text{N}=13.75$.

$\text{C}_{17}\text{H}_{21}\text{O}_2\text{N}_3, \frac{1}{2}\text{CH}_4\text{O}$ requires $\text{C}=66.64$; $\text{H}=7.30$; $\text{N}=13.33$ per cent.

The transparent crystals became opaque in the steam-oven, owing to loss of crystal-alcohol:

0.2462 gave 0.6158 CO_2 and 0.1546 H_2O . $\text{C}=68.23$; $\text{H}=7.03$.

$\text{C}_{17}\text{H}_{21}\text{O}_2\text{N}_3$ requires $\text{C}=68.23$; $\text{H}=7.03$ per cent.

Ordinary solvents, excepting petroleum, dissolve the substance readily, but, unlike the α -semicarbazone, it is insoluble in cold

aqueous alkali hydroxide, although dissolving when heated, with development of a yellow coloration. A solution containing 0.2207 gram, made up to 25 c.c. with chloroform, gave α_D $4.03'$ in a 2-dcm. tube, whence $[\alpha]_D$ 229.3° . An estimation of the molecular weight by depression of the melting point of benzene gave 327 instead of 299.

Camphorquinone- β -phenylcarbamyldrazone.—From the mother liquor of the foregoing substance there gradually separated long, slender, silky needles, in which a few small crystals of the α -compound were embedded, and as the latter remained undissolved on rapidly warming the liquid, it was possible to isolate the β -modification without much difficulty, the final recrystallisation being effected by adding petroleum to a solution of the needles in benzene. The substance is very pale yellow, and melts at 161° :

0.2142 gave 0.5346 CO_2 and 0.1372 H_2O . $\text{C}=68.10$; $\text{H}=7.17$.

0.1062 „ 13.9 c.c. N_2 at 24° and 754 mm. $\text{N}=14.55$.

$\text{C}_{17}\text{H}_{21}\text{O}_2\text{N}_3$ requires $\text{C}=68.23$; $\text{H}=7.03$; $\text{N}=14.09$ per cent.

In all common media the solubility of the β -phenylcarbamyldrazone scarcely differs from that of the isomeride, but the tendency to form supersaturated solutions is much greater. A solution containing 0.2128 gram, made up to 25 c.c. with chloroform, gave α_D $3.016'$ in the 2-dcm. tube, whence $[\alpha]_D$ 191.9° .

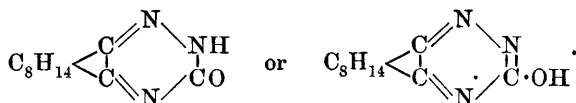
As in the case of the β -semicarbazone, transformation into the α -modification was readily accomplished by heating the β -phenylcarbamyldrazone above its melting point; the clear liquid which had been carried to 200° remained vitreous on cooling, but immediately became crystalline on being scratched in presence of a small quantity of methyl alcohol.

In preparing the phenylcarbamyldrazones by the foregoing method, it was noticed that the proportion of the two modifications depends on the duration of heating and on the temperature reached. This is explained by the fact that either is convertible into the other isomeride by the action of hot aniline, each individual yielding an equilibrium mixture when a solution in that base is heated until the solvent boils; roughly speaking, the relation between the constituents of this mixture is $\alpha : \beta = 2 : 1$.

The second process for obtaining the phenylcarbamyldrazones was practised by mixing solutions containing 5 grams of camphorquinone and 4.5 grams of phenylcarbamyldrazide, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}\cdot\text{NH}_2$, each in 15 c.c. of hot methyl alcohol, and heating the liquid on the water-bath during a few minutes; 2.8 grams of the α -phenylcarbamyldrazone separated on cooling, whilst the mother liquor deposited a mixture of this with the characteristic, silky needles of the β -modification,

The third method is the most convenient when the hydrazones are available, because it leads to the individuals, and thus obviates the necessity of a tedious separation. The finely powdered α -hydrazone (1.8 gram), suspended in 250 c.c. of boiling benzene, in which it was not completely soluble, was heated with 3 grams of phenylcarbimide on the water-bath during two hours, when the liquid did not deposit crystals on cooling. After distilling off the solvent until only 30 c.c. remained, twice this volume of petroleum was added, precipitating 2.7 grams of a crystalline powder, readily identified with the α -phenylcarbamyldhydrazone on recrystallisation. In preparing the β -modification by this process, 0.9 gram of the β -hydrazone, dissolved in 10 c.c. of benzene, was treated with 0.7 gram of phenylcarbimide, the mixture being left at the laboratory temperature, and after the lapse of twelve hours diluted with petroleum until pale yellow needles appeared; after recrystallisation it melted at 161° , and did not depress the melting point of the β -phenylcarbamyldhydrazone prepared by the other methods.

Camphane-oxytriazine,



Whilst the α -semicarbazone is dissolved immediately by aqueous alkali hydroxide, forming a permanent yellow solution, the β -modification is transformed into the anhydride represented above, the conversion taking place at rates depending on the temperature.

Camphorquinone- β -semicarbazone was covered with 10 parts of 10 per cent. aqueous sodium hydroxide, and shaken at intervals during five hours, when the solid substance, at first coloured yellow by the agent, had passed into a colourless solution. After extraction with ether, dilute sulphuric acid was added until the initial precipitate was redissolved, when the liquid was shaken eight times with ether; the solvent deposited 85 per cent. of viscous residue, which quickly solidified. Recrystallisation from warm benzene, to which petroleum was added, gave colourless, transparent pyramids, melting at 166 — 167° :

0.2183 gave 0.5137 CO_2 and 0.1406 H_2O . $\text{C} = 64.18$; $\text{H} = 7.21$.

0.1950 „ 35.6 c.c. N_2 at 21° and 759 mm. $\text{N} = 20.75$.

$\text{C}_{11}\text{H}_{15}\text{ON}_3$ requires $\text{C} = 64.39$; $\text{H} = 7.31$; $\text{N} = 20.49$ per cent.

The substance is somewhat readily soluble in warm water, and does not crystallise completely on cooling; alcohol, ether, chloroform and benzene dissolve it readily, but it is insoluble in petroleum. It

does not reduce Fehling's solution, and when heated with ammoniacal silver oxide yields a voluminous, white precipitate, freely soluble in ammonia. A solution in sodium carbonate is strongly alkaline, and gives a transient violet precipitate with ferrous sulphate, becoming bright green when excess is added; copper salts produce an apple-green precipitate, also formed by nickel sulphate, excess of which yields a clear solution. The optical activity of the oxytriazine and its derivatives is very much lower than that of the foregoing compounds of camphorquinone; a solution containing 0.2855 gram, made up to 25 c.c. with chloroform, gave α_D $0^{\circ}31'$ in a 2-dcm. tube, whence $[\alpha]_D$ 22.6° .

The *acetyl* derivative was readily formed on heating the oxytriazine with acetic anhydride; after recrystallisation from a mixture of benzene and petroleum, it melted at $168-169^{\circ}$:

0.1765 gave 0.4096 CO_2 and 0.1127 H_2O . $\text{C}=63.30$; $\text{H}=7.14$.

$\text{C}_{13}\text{H}_{17}\text{O}_2\text{N}_3$ requires $\text{C}=63.16$; $\text{H}=6.88$ per cent.

The substance dissolves freely in cold benzene, chloroform, acetone, or methyl alcohol, but is less readily soluble in ethyl alcohol or ethyl acetate, from which it crystallises in lustrous, colourless needles. A solution containing 0.2444 gram, made up to 20 c.c. with chloroform, gave α_D $1^{\circ}2'$ in a 2-dcm. tube, whence $[\alpha]_D$ 42.2° .

The *benzoyl* derivative, prepared by the action of benzoyl chloride in pyridine solution and purified by precipitation from acetic acid, followed by recrystallisation from a mixture of benzene and petroleum, melted at $193-194^{\circ}$:

0.2021 gave 0.5150 CO_2 and 0.1108 H_2O . $\text{C}=69.51$; $\text{H}=6.13$.

$\text{C}_{18}\text{H}_{19}\text{O}_2\text{N}_3$ requires $\text{C}=69.90$; $\text{H}=6.15$ per cent.

The compound is freely soluble in cold acetone or chloroform, but ethyl acetate, methyl alcohol, benzene, or ethyl alcohol dissolve it less readily, and it is very sparingly soluble in boiling petroleum. A solution containing 0.2808 gram, made up to 20 c.c. with chloroform, gave only α_D $0^{\circ}13'$ in a 2-dcm. tube, whence $[\alpha]_D$ 7.7° .

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