XXVII.—*Studies in the Camphane Series. Part VII.*
.Conversion of Hydroxycamphene into β -Halogen
Derivatives of Camphor.

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IN a recent communication (Trans., 1901, 79, 644) I described, under the name hydroxycamphene, an isomeride of camphor which exhibited some remarkable properties. The method by which it was obtained from camphor, although circuitous, leads by steps, apparently straightforward, through camphoroxime, bromonitrocamphane, nitrocamphene, and aminocamphene. The substance itself behaves like an unsaturated compound towards bromine and potassium permanganate, and is readily converted into camphor by the agency of dilute mineral acids; it also contains the hydroxyl group. On the strength of these facts, it was regarded as the tautomeric modification of camphor:

It was necessary to admit, however, that in some respects the behaviour of hydroxycamphene was dissimilar from that which is usually associated with compounds of this type. Its unsaturated character, and its ready conversion into the ketonic isomeride were certainly in accordance with this view of its constitution, but its insolubility in alkalis, the indifference of an alcoholic solution towards ferric chloride, and the extraordinary stability of the substance on distillation, were

points which demanded an explanation more complete than that which was put forward at the time. It was suggested, namely, that the abnormal behaviour of hydroxycamphene might be due to the fact that, unlike the enolic modifications of the ketonic esters which have received so much attention during recent years, it contains no acyl substituent attached to the β -carbon atom. This view received some support from the observation (Trans., 1901, 79, 987) that α -benzoylcamphor, in which the acyl radicle occupies a β -position relative to the ketonic oxygen, is readily converted into an enolic modification which has all the general properties of compounds belonging to this class. On the other hand, it must be borne in mind that the constitution of enolic α -benzoylcamphor is by no means assured, because although, at present, the evidence is in favour of representing it as 1-hydroxy-2-benzoylcamphene, the matter is still under investigation, which may produce facts in support of the alternative structure, namely, that of phenylhydroxymethylenecamphor:

1-Hydroxy-2-benzoylcamphene.

Phenylhydroxymethylenecamphor.

With the object of gaining further evidence relating to the constitution of hydroxycamphene, the action of bromine on this compound has been studied. It was anticipated that if the structure of hydroxycamphene is that which has been assigned to it, addition of bromine, followed by elimination of hydrogen bromide, would yield α -bromocamphor, either alone, or mixed with the unknown α' -bromocamphor:

The product actually obtained by the action of bromine on hydroxycamphene dissolved in glacial acetic acid containing sodium acetate is a new bromocamphor, which melts at 78° , and when dissolved in alcohol has $[\alpha]_D +19^\circ$; α -bromocamphor melts at 76° and has $[\alpha]_D +135^\circ$. No addition to the list of mono-halogen derivatives of camphor has been made since Kipping and Pope described π -chlorocamphor and π -bromocamphor (Trans., 1895, 67, 371), prepared by eliminating sulphur dioxide from camphorsulphonic chloride and bromide respectively. Since the new bromocamphor does not agree in properties with those attributed to any of the isomerides previously

described, it seemed probable at first that it was α' -bromocamphor, the unknown stereoisomeride of ordinary α -bromocamphor. Such a substance, however, would be expected to yield α -bromocamphor on treatment with the usual transforming agents, but the new derivative resists the action of fuming hydrogen bromide and concentrated sulphuric acid. Moreover, alcoholic potash should convert it into camphor, and although zinc and acetic acid reduce it to that substance, showing it to be a true camphor derivative, alcoholic potash acts as a hydrolytic agent, giving rise to α -campholenic acid:

Finally, bromine, which would yield α -dibromocamphor in the case of α' -bromocamphor, converts the new substance into β -dibromocamphor.

These facts have only one explanation. The substance obtained by the action of bromine on hydroxycamphene must be the unknown β -bromocamphor, bearing the relation to β -dibromocamphor that α -bromocamphor has to α -dibromocamphor. In the last-named substance both bromine atoms occupy the α -position, whilst in β -dibromocamphor, which is more suitably named $\alpha\beta$ -dibromocamphor, one bromine atom is attached to the α -carbon atom, the other occupying the β -position, of which the exact situation is unknown.

A bromo-derivative of camphor has been described by Marsh, who refers to the substance as " β -bromocamphor." Without disparaging the claims of this compound to be regarded as an individual substance, it may be questioned whether the bromine atom occupies the β -position in the sense just indicated, it being nowhere stated that bromine converts it into $\alpha\beta$ -dibromocamphor, or that alcoholic potash resolves it into α -campholenic acid.

It will be recognised that the production of β -bromocamphor from hydroxycamphene by a process so simple as addition of bromine followed by elimination of hydrogen bromide, necessitates a reconsideration of the relationship between camphor and hydroxycamphene. The last-named substance is indifferent towards hydroxylamine and phenylhydrazine, but readily forms alkyl ethers; its hydroxylic character seems therefore assured, apart from the fact that it is produced by the action of nitrous acid on a primary amine. There is no reason to doubt that the nitro-group in 1:1-bromonitrocamphane, and consequently the nitro-group in nitrocamphene, and the amino-group in aminocamphene, are attached to the carbon atom which, in camphor, is ketonic, because bromonitrocamphane yields camphoroxime on reduction, and aminocamphene gives rise to camphor when heated with acetic anhydride; moreover, hydroxycamphene is converted so readily into camphor that the action of nitrous acid on aminocamphene can scarcely have been abnormal. The only uncertain step, therefore,

in the series connecting camphoroxime with hydroxycamphene, is the removal of hydrogen bromide from 1:1-bromonitrocamphane. The question arises, How does this change take place?

Adopting Bredt's formula for camphor as the basis of representation, the constitution of 1:1-bromonitrocamphane is expressed as follows :

The point to be decided, therefore, is the source of the hydrogen atom which is eliminated in association with bromine when bromonitrocamphane is converted into nitrocamphene. In view of the unsaturated character of the latter, and the fact that, of the two carbon atoms united with that to which the bromine is attached, only one is combined with hydrogen, it was natural to conclude that nitrocamphene is represented by the formula :

It is this expression which is now shown to be incorrect. It is, however, the sole possible formula for a compound which is not only produced by the removal of hydrogen bromide from 1:1-bromonitrocamphane, but also contains an ethylenic link. The obvious conclusion is that nitrocamphene, and consequently hydroxycamphene, are compounds which owe their unsaturated nature to a trimethylene or tetramethylene ring, which is resolved so easily into the original form as to simulate an ethylenic structure.

Although, theoretically, this change might occur in each of six ways, the production of α -campholenic acid by the action of alcoholic potash on β -bromocamphor renders all improbable excepting two; these would involve the representation of hydroxycamphene by one of the formulæ :

the structure of β -bromocamphor being then indicated by one of the expressions :

respectively.

So far as the evidence in this paper is concerned, it is scarcely possible to come to a definite conclusion, although the transformation of β -bromocamphor into α -campholenic acid is distinctly in favour of the former representation, according to which the change in question, although fundamental, would appear quite simple, as follows :

Moreover, although the plane formula I represents union to have occurred between two carbon atoms which appear to be at some distance from one another, it is possible that they are in reality comparatively close, in accordance with the tetrahedral conception of the combining power of carbon. This is illustrated by the following representation of bromonitrocamphane :

Simultaneously with the publication of a preliminary notice of β -bromocamphor (Proc., 1901, 243, 245), Armstrong and Lowry recorded the properties of the same substance obtained by the action of heat on the camphorsulphonic bromide belonging to the Reychler series. These authors have converted β -bromocamphor by direct oxidation into β -bromocamphoric acid, and the investigation of the latter should make it possible to determine which, if either, of the two formulæ suggested in this paper correctly represents the constitution of β -bromocamphor.

An examination of β -bromocamphoroxime has already produced two observations of some interest. In the first place, the oxime does not yield the nitrile of an unsaturated acid when treated with hot dilute sulphuric acid, thereby differing completely from camphoroxime, which is converted into α -campholenonitrile. This again may be construed in

favour of the expression for β -bromocamphor corresponding with formula I for hydroxycamphene, as it accords with the simplest possible explanation of the last-named reaction :

In the second place, although β -bromocamphor is hydrolysed to α -campholenic acid by alcoholic potash, this agent is without action on β -bromocamphoroxime, a result which seems to suggest that, in the change undergone so readily by β -bromocamphor, disruption of the ring precedes replacement of bromine by hydroxyl, and the subsequent elimination of water. Indirectly, this also favours the formula for β -bromocamphor in which the bromine is represented as replacing hydrogen in the ring, because if substitution had occurred in a methyl group, it would be reasonable to expect the halogen to be more easily removed.

EXPERIMENTAL.

Twenty-five grams of 1-hydroxycamphene were dissolved in 400 c.c. of glacial acetic acid containing 25 grams of anhydrous sodium acetate. To the well cooled liquid were added in small quantities 26.5 grams of bromine dissolved in 100 c.c. of glacial acetic acid; the colour of the halogen was immediately destroyed, and heat being developed, the temperature of the liquid was allowed to return to about 20° before each addition of bromine. When the stated quantity had been added, the pale yellow liquid was poured into a large volume of cold water, which precipitated a colourless, crystalline substance. This was filtered, washed with water, and dried in the desiccator, when it weighed 38 grams.

β -Bromocamphor dissolves very readily in warm petroleum, and after being recrystallised twice from this solvent, melts at 78°, the second crystallisation producing no change in the specific rotatory power, and a very slight increase only in the fusion temperature. If the substance, purified in this way, is then recrystallised from absolute alcohol, the melting point is lowered about 1°.

0.2053 gave 0.1656 AgBr. Br = 34.32.

$\text{C}_{10}\text{H}_{15}\text{OBr}$ requires Br = 34.63 per cent.

The substance dissolves very readily in chloroform, benzene, or glacial acetic acid, also in warm petroleum or hot alcohol, crystallising from the last solvent named in long, striated prisms; when deposited slowly by petroleum, it crystallises in large, well formed, transparent prisms. It is readily volatile in steam, the vapour having a faint odour of camphor.

A solution containing 0.5014 gram in 25 c.c. of chloroform at 20°, gave α_D 39' in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D +16.2^\circ$; 0.5012 gram dissolved in 25 c.c. of absolute alcohol at 20°, gave α_D 46' in the same tube, corresponding with $[\alpha]_D +19.1^\circ$.

β -Bromocamphor may be dissolved in fuming hydrobromic acid (sp. gr. 1.83) or in concentrated sulphuric acid without undergoing any chemical change or alteration of rotatory power.

Conversion into Camphor.—Two grams of β -bromocamphor were dissolved in glacial acetic acid and treated with 5 grams of zinc dust. After remaining on the water-bath during 2 hours, the liquid was diluted with water, neutralised with sodium carbonate, and distilled in a current of steam. Camphor was deposited in the condenser, and was converted into the oxime by the usual process; the product was crystallised from petroleum, which deposited the characteristic crystals melting at 118°.

Conversion into $\alpha\beta$ -Dibromocamphor.—Five grams of the new bromocamphor were covered with one molecular proportion of bromine and heated on the water-bath, when evolution of hydrogen bromide soon occurred. When this gas was no longer liberated, the pale yellow liquid solidified almost immediately on being withdrawn from the water-bath. The product was washed with water, and recrystallised several times from alcohol, until the melting point was constant at 114°, when a mixture of the substance with $\alpha\beta$ -dibromocamphor melted at the same temperature; 1.0005 gram dissolved in 25 c.c. of chloroform at 21° gave α_D 8°4' in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D +100.8^\circ$.

Action of Alcoholic Potash on β -Bromocamphor.

Twenty grams of recrystallised β -bromocamphor were dissolved in 100 c.c. of alcohol which had been distilled from caustic soda; 15 grams of caustic potash, dissolved in the minimum quantity of water, were then added to the liquid, which was heated in a reflux apparatus during 8 hours. Alcohol was then removed by distillation, and a current of steam passed through the residual liquid, a preliminary experiment having shown that if an insufficient quantity of alkali has been employed any bromocamphor remaining unchanged can be removed conveniently at this stage. The contents of the distilling flask were

then cooled, just acidified with dilute sulphuric acid, and extracted with ether, the extract being washed several times with water, dried with calcium chloride, and evaporated on the water-bath. The residue was then distilled, passing over completely at 256—257° under 767 mm. pressure :

0.1570 gave 0.4087 CO₂ and 0.1330 H₂O. C = 71.00 ; H = 9.41.

C₁₀H₁₆O₂ requires C = 71.43 ; H = 9.52 per cent.

The substance is slowly volatile in steam, and has a very faint odour ; it dissolves in sodium carbonate, forming a solution which immediately decolourises potassium permanganate. It has a sp. gr. 0.9974 at 20°/20°, and gives α_D 16°40' in a 2-dcm. tube at 20°, whence the specific rotatory power $[\alpha]_D + 8.34^\circ$. The product was thus identified with α -campholenic acid.

Ten grams of β -bromocamphor were dissolved in 50 c.c. of alcohol and heated with 5 grams of hydroxylamine hydrochloride and 5 grams of dry sodium acetate in a reflux apparatus during 2 hours ; 3 grams of the hydrochloride and the same quantity of sodium acetate were then added, and the heating continued during 3 hours, a preliminary experiment having shown that conversion into the oxime is incomplete unless a considerable excess of the hydrochloride is employed. On pouring the liquid into twice its own volume of cold water, a crystalline precipitate was obtained ; this was filtered, washed, and recrystallised twice from hot alcohol, which deposited lustrous, rhomboidal plates melting at 156° :

0.2566 gave 0.1944 AgBr. Br = 32.23.

C₁₀H₁₆ONBr requires Br = 32.52 per cent.

The oxime is readily soluble in chloroform, benzene, or ethyl acetate, but dissolves very sparingly in hot petroleum, which deposits it in aggregates of rhomboidal plates.

A solution containing 0.5017 gram in 25 c.c. of chloroform at 21° gave $\alpha_D - 2^\circ 57'$ in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D - 73.5^\circ$.

β -Bromocamphoroxime dissolves in caustic alkalis and in 50 per cent. sulphuric acid ; it may be warmed with concentrated sulphuric acid without undergoing conversion into a nitrile. It is also indifferent to alcoholic potash, with which a specimen has been heated in a reflux apparatus during 4 hours without becoming hydrolysed.

The *benzoyl* derivative is readily obtained by the Schotten-Baumann method. It is very readily soluble in hot alcohol, from which it

separates in tufts of white needles. Warm petroleum dissolves it less readily, and it is scarcely soluble in the cold solvent, which deposits it in long, snow-white, silky needles melting at 71—73°.

0.2695 gave 0.1437 AgBr. Br = 22.69.

$C_{17}H_{20}O_2NBr$ requires Br = 22.86 per cent.

The substance dissolves very readily in chloroform, ethyl acetate, or benzene. A solution containing 0.5040 gram in 25 c.c. of chloroform at 21° gave $\alpha_D - 1^\circ 35'$, whence the specific rotatory power $[\alpha]_D - 39.2^\circ$.

Twenty grams of hydroxycamphene were dissolved in 400 c.c. of glacial acetic acid containing 20 grams of anhydrous sodium acetate. The liquid was immersed in cold water and treated with a solution of chlorine in glacial acetic acid, which was added in small quantities at a time until, after an interval, the halogen was found to be in slight excess. As the precipitate obtained on pouring the liquid into a large volume of water weighed only 16 grams, the filtrate was neutralised with solid sodium carbonate, 6 grams more being obtained in this way; the product was then recrystallised three times from alcohol.

0.2064 gave 0.1565 AgCl. Cl = 18.76.

$C_{10}H_{15}OCl$ requires Cl = 19.03 per cent.

The new chlorocamphor is very similar to the bromo-derivative in appearance and properties; it melts, however, at 132.5°. It is readily soluble in chloroform, acetic acid, petroleum, benzene, or ethyl acetate, but dissolves less freely in alcohol, from which it crystallises in slender, striated prisms, sometimes exceeding an inch in length; it is readily volatile in steam, and the vapour has a faint odour of camphor.

A solution containing 0.5012 gram in 25 c.c. of chloroform at 21° gave $\alpha_D 1^\circ 35'$ in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D + 39.5^\circ$; 0.5019 gram dissolved in 25 c.c. of absolute alcohol at 19° gave $\alpha_D 1^\circ 38'$, corresponding to $[\alpha]_D + 40.7^\circ$.

The oxime of β -chlorocamphor was obtained by the same process as the bromo-derivative, which it closely resembles in appearance and properties. It separates from alcohol in colourless crystals isomorphous with those of β -bromocamphoroxime, and melts at 134°.

0.2412 gave 0.1662 AgCl. Cl = 17.05.

$C_{10}H_{16}ONCl$ requires Cl = 17.62 per cent.

It dissolves very readily in chloroform, ethyl acetate, or benzene, but is sparingly soluble in boiling light petroleum, from which it crystallises on cooling. A solution containing 0.5015 gram dissolved in 25 c.c. chloroform at 21° gave $\alpha_D - 2^\circ 20'$ in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D - 58.1^\circ$. The *benzoyl* derivative was prepared by the Schotten-Baumann method; it dissolves very readily in alcohol and in warm petroleum, crystallising from the latter in lustrous, silky needles, which begin to shrink about 70°, and melt at 86°.

A solution containing 0.5012 gram dissolved in 25 c.c. of chloroform at 21° gave $\alpha_D - 1^\circ 9'$ in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D 28.7^\circ$.

Five grams of β -chlorocamphor were heated with 5 grams of bromine in an open flask on the water-bath, when, after a short interval, hydrogen bromide was evolved. Heating was continued until the gas was no longer liberated, the pale yellow liquid solidifying to a camphor-like mass on cooling; this was washed with water until free from acid, dried in the desiccator, and crystallised from a small quantity of boiling petroleum, in which it dissolves readily. After being recrystallised several times from this solvent, it was obtained in tabular aggregates of white prisms, melting at 101°.

0.1445 gave 0.1790 AgCl + AgBr. $Cl + Br = 43.15$.

$C_{10}H_{14}OClBr$ requires $Cl + Br = 43.50$ per cent.

The substance dissolves very readily in cold ethyl acetate, benzene, or chloroform; also in hot alcohol, from which it crystallises in well-formed, oblong prisms. A solution containing 0.5021 gram in 25 c.c. of chloroform at 20° gave $\alpha_D 5^\circ 5'$ in a 2-dcm. tube, whence the specific rotatory power $[\alpha]_D + 126.5^\circ$.

Ethers of 1-Hydroxycamphene.

Further evidence of the hydroxylic character of hydroxycamphene was obtained by converting it into ethers, the method which has been studied by Lander (Trans., 1900, 77, 729) having been found very suitable for this purpose.

The *methyl ether*, $C_{10}H_{15} \cdot OCH_3$, was prepared by treating 15 grams of hydroxycamphene, dissolved in 45 grams of methyl iodide, with 35 grams of dried silver oxide; no apparent action took place in the cold, and the mixture was therefore heated in a reflux apparatus on the

water-bath during 8 hours. The product was then filtered, and the residue washed several times with dry ether, which was afterwards removed by evaporation. The residual oil was heated with a further quantity of methyl iodide (30 grams) and silver oxide (24 grams) during a period of 8 hours, and subsequently, after removing excess of methyl iodide and the ether employed in washing the silver residue, distilled under the ordinary pressure.

The substance obtained in this manner is a colourless, limpid oil, readily volatile in steam, and having a pleasant odour. It boils at $193\text{--}194^\circ$ under 766 mm. pressure, has the sp. gr. 0.9314 at $20^\circ/20^\circ$, and gives $a_D - 50.53'$ in a 2-dcm. tube at 20° , whence the specific rotatory power $[\alpha]_D - 27.31^\circ$; a solution containing 0.5012 in 25 c.c. of benzene at 20° gave $a_D - 58'$ in the same tube, corresponding with $[\alpha]_D - 24.5^\circ$.

0.1621 gave 0.4743 CO_2 and 0.1531 H_2O . $\text{C} = 79.80$; $\text{H} = 10.50$.

$\text{C}_{11}\text{H}_{18}\text{O}$ requires $\text{C} = 79.52$; $\text{H} = 10.84$ per cent.

A solution of methoxycamphene in chloroform decolorises bromine immediately in the cold.

The *ethyl ether*, $\text{C}_{10}\text{H}_{15}\cdot\text{OC}_2\text{H}_5$, was obtained by the same process from hydroxycamphene and ethyl iodide; it boils at $203\text{--}204^\circ$ under a pressure of 760 mm.

An attempt to hydrolyse the substance with alcoholic potash was unsuccessful, a specimen which was heated with that agent during several hours in a reflux apparatus remaining unchanged.

Bromine converts ethoxycamphene into β -bromocamphor. Five grams were dissolved in glacial acetic acid containing sodium acetate and treated with bromine in the same solvent; on pouring the liquid into water, a crystalline precipitate was obtained, and this, when recrystallised from petroleum, melted at 78° .

An attempt to prepare the benzoyl derivative of hydroxycamphene by the action of benzoyl chloride (2 mols.) on the hydroxy-compound dissolved in pyridine (3 mols.) gave rise to a pale yellow, viscous oil, which did not crystallise.

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