XVI.—*Derivatives of Camphoric Acid. Part III.*

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THE first of these papers on derivatives of camphoric acid (Trans., 1896, 69, 913) contained an account of a number of optically active acids and other compounds which had been obtained from π -bromocamphoric acid, in the course of attempts to open the closed chain contained in this simple substitution product of camphoric acid at a different point from that at which it is broken in the oxidation of camphoric acid, the parent substance, to camphoronic acid.

The principal acids, which have already been described, were obtained in the following manner. π -Bromocamphoric acid was treated with an alkali and thus converted into (a) *trans*- π -camphanic acid,

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$C_{10}H_{14}O_4$, a monocarboxylic acid containing a lactone ring, and (b) π -hydroxycamphoric acid, $C_{10}H_{16}O_5$; these two compounds were oxidised by nitric acid to one and the same *trans*- π -camphotricarboxylic acid, from which the *cis*-isomeride was also obtained.

The further oxidation of *trans*- π -camphotricarboxylic acid being attended with considerable difficulty, owing to the great stability of the compound, it was converted into its monobromo-substitution product and the latter was then decomposed with water; in this way, two isomeric lactones of the composition $C_{10}H_{12}O_6$, derived from a hydroxycamphotricarboxylic acid, $C_{10}H_{14}O_7$, were obtained, but these derivatives, like the parent substance, were found to be very stable, and could not be made to yield satisfactory oxidation products.

Having failed to obtain any easily oxidisable derivative of camphoric acid by these means, attempts were next made to oxidise *cis*- π -camphanic acid, $C_{10}H_{14}O_4$, an interesting compound obtained by the distillation of its isomeride *trans*- π -camphanic acid; these experiments were successful in a measure, inasmuch as a crystalline hydroxy-*cis*- π -camphanic acid was thus obtained, but this compound, like the others just mentioned, effectually resisted further oxidation.

It will be seen from this brief statement that the main object of this investigation had been defeated by the stability of these different substitution products of camphoric acid, all of which still contained the closed chain of the parent substance; moreover, the difficulty of obtaining material sufficient for oxidation experiments on the large scale rendered it almost impossible to proceed further on these lines. It was necessary, therefore, to try and attack the π -bromocamphoric acid in a somewhat different manner, namely, to convert it, if possible, into a dibromo-compound, and then to substitute hydroxyl for one, or both, of the bromine atoms, and thus obtain in a more direct manner a substitution product which might be oxidisable.

The results of these experiments are described in this paper.

When π -bromocamphoric acid is brominated, it is converted, in almost theoretical quantities, into a substance of the composition $C_{10}H_{12}Br_2O_3$, which, for reasons given later, is named πw^* -dibromocamphoric anhydride; this substance crystallises in magnificent rhombic plates, and on hydrolysis with concentrated nitric acid it is transformed into πw -dibromocamphoric acid, $C_{10}H_{14}Br_2O_4$, a substance which in many respects is very similar to π -bromocamphoric acid and other halogen derivatives of this compound which have been described (compare Lapworth and Kipping, *Trans.*, 1897, 71, 15).

πw -Dibromocamphoric acid is decomposed when it is heated alone or with water, yielding hydrogen bromide and an acid of the composition

* The letter *w* has been previously used to denote a certain position in the molecule of camphoric acid (compare *Trans.*, 1896, 69, 61, and 916).

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$C_{10}H_{13}BrO_4$, which, from its method of formation, must be regarded as a lactonic monocarboxylic acid; for this and other reasons, this compound is named π -bromo-*w*-camphanic acid. It crystallises in orthorhombic prisms, and both its *amide*, $C_9H_{12}BrO_2 \cdot CO \cdot NH_2$, and *methylic salt*, $C_9H_{12}BrO_2 \cdot COOMe$, are well-defined compounds.

When π -bromo-*w*-camphanic acid is treated with alkalis, it yields a crystalline product which is identical with hydroxy-*cis*- π -camphanic acid, the oxidation product of *cis*- π -camphanic acid; this hydroxy-acid is also formed by the action of excess of alkali on *pw*-dibromocamphoric anhydride. When, on the other hand, π -bromo-*w*-camphanic acid is boiled with nitric acid and silver nitrate, it is converted into a compound of the composition $C_{10}H_{12}O_6$, which is identical with one of the isomeric lactones of hydroxycamphotricarboxylic acid.

These transformations, the chemical properties of the various compounds, and the relations existing between these and other substitution products of camphoric acid, can only be elucidated by making use of some structural formula for camphoric acid, and in previous papers Brecht's formula was employed because it accounted for all the facts under discussion in a satisfactory manner, and at the same time seemed to have more evidence in its favour than any other of the many formulæ which had then been suggested. The recent publication of an important paper by W. H. Perkin, junr. (Trans., 1898, 73, 796), in which a new formula for camphoric acid is propounded, has certainly necessitated a modification of this last statement; nevertheless, the difference between Brecht's and Perkin's formulæ is of such a kind as to require little, if any, alteration in the views which have been advanced in explaining the relationship of these π -derivatives.

On inspection, it will be seen that these two formulæ, which are given below, differ merely in this, namely, that one of the $>CH_2$ groups in Brecht's is transferred, in Perkin's formula, to a position between the $>CMe_2$ and $>CH \cdot COOH$ groups.

This change does not effect any of the author's previous arguments, which were mainly based on stereochemical considerations, and, in fact, only makes this difference, that the π -camphanic acids, according to Perkin's formula, may, but do not necessarily, contain a δ - instead of a γ -lactone ring.

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Making use, then, of Perkin's formula, and representing π -bromocamphoric acid by I (below), the substitution of bromine for hydrogen would afford a dibromocamphoric acid which must be represented by formula II, because in the formation of this substance the bromine doubtless displaces the same tertiary hydrogen atom as that which is expelled in the formation of *w*-bromocamphoric anhydride from ordinary camphoric acid.

I. π -Bromocamphoric acid. II. πw -Dibromocamphoric acid.

π -Bromo-*w*-camphanic acid, which is formed from the dibromo-acid with the greatest readiness, just as *w*-camphanic acid is very easily produced from *w*-bromocamphoric acid, might be represented by one of several isomeric formulæ, of which, however, it is unnecessary to give examples, as it is possible to select the most probable one from a consideration of the following facts and arguments. In the first place, there are strong grounds for supposing that the π -bromine atom, namely, that which is a constituent of the $-\text{CH}_2\text{Br}$ group, is still present in this bromocamphanic acid, because it is known that the *w*-bromine atom in *w*-bromocamphoric acid is very easily eliminated as hydrogen bromide by the action of boiling water, whereas π -bromocamphoric acid is comparatively stable under these conditions; in the second place, the bromocamphanic acid in question offers considerable resistance to the attack of oxidising agents, whereas had it been formed by the elimination of the π -bromine atom, it should resemble *trans*- π -camphanic acid in behaviour and be easily oxidisable to a bromo-tricarboxylic acid.

A comparatively simple way of settling this question as to which of the two halogen atoms is eliminated from the dibromo-acid offered itself, namely, to prepare a π -bromo-*w*-chlorocamphoric anhydride by chlorinating the π -bromo-acid, and then to convert this substance into the substituted camphanic acid by treatment with boiling water. On making these experiments, it was found that the π -bromo-*w*-chlorocamphoric anhydride, $\text{C}_{10}\text{H}_{12}\text{BrClO}_3$ was readily acted on by boiling water with formation of hydrogen chloride and a bromocamphanic acid identical with that obtained from the dibromo-anhydride. It follows, therefore, that the bromo-acid in question is a π -bromo-*w*-camphanic acid, and its constitution may be expressed by one of the following stereoisomeric formulæ.

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III. π -Bromo-*cis*-*w*-camphanic acid. IV. π -Bromo-*trans*-*w*-camphanic acid.

Now it seems probable that the first of these two formulæ represents the configuration of the acid better than does the second, in spite of the fact that this view necessitates the assumption that intramolecular change occurs in the formation of the acid from πw -dibromocamphoric anhydride; when the properties of ordinary *w*-camphanic acid are considered, it must be admitted that this compound is probably a *cis*-lactonic acid, because the hydroxy-acid, of which it forms salts on treatment with alkalis, is not known in the free state, but immediately passes into its lactone; *w*-camphanic acid, therefore, is doubtless stereochemically analogous to *cis*- π -camphanic acid, whereas the *trans*-*w*-camphanic acid, corresponding with the unstable *trans*- π -camphanic acid, has not yet been prepared.

It is probable, then, that when *w*-bromocamphoric anhydride is converted into *w*-camphanic acid, the carboxyl group changes its position stereochemically, just as it is known to do to a considerable extent in the reduction of *w*-bromocamphoric anhydride, a reaction which affords a mixture of *cis*- and *trans*-, or *d*- and *d*-iso-camphoric acids (Aschan, *Acta Soc. Scient. fenn.*, 21, [v], p. 195).

The conclusion thus arrived at, namely, that π -bromocamphanic acid has the configuration represented by formula III, is in accordance with the behaviour of this substance, and also accounts for its conversion into hydroxy-*cis*- π -camphanic acid; when treated with potash, it may be supposed that it first gives a salt of *w*-hydroxy- π -bromocamphoric acid, the *w*-lactone ring undergoing hydrolysis, and that then potassium bromide is eliminated with formation of a different lactone ring, namely, that which is contained in *cis*- π -camphanic acid.

V. π -Bromo-*cis*-*w*-camphanic acid. VI. *w*-Hydroxy-*cis*- π -camphanic acid.

The last formula (VI) indicates the possible existence of a *dilactone*, which would be derived from hydroxy-*cis*- π -camphanic acid by the elimination of one molecule of water from the remaining -OH and

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—COOH groups; although the isolation of such a substance has not yet been accomplished, indications of its formation have been observed, and the neutral crystalline compound obtained by brominating *trans*- π -camphanic acid (Trans, 1896, 69, 934), or the neutral oily product formed in the decomposition of πw -dibromocamphoric anhydride (see later), may possibly be a compound of this kind; it is by no means improbable, however, that the existence of one lactone ring may, owing to stereochemical causes, hinder the formation of a second one, and thus render it difficult to obtain such a dilactone by ordinary methods.

The further oxidation of the compounds obtained from dibromocamphoric anhydride has not yet been accomplished with satisfactory results in a single case; to give an instance of the difficulty of oxidising some of these products, it may be mentioned that a small quantity of the lactone of *w*-hydroxycamphotricarboxylic acid may be heated at 100° with a mixture of concentrated nitric and hydrochloric acids, or with a mixture of concentrated nitric and sulphuric acids, and after several hours treatment, the lactone is deposited unchanged on keeping the solution at ordinary temperatures.

Most of the compounds described in this paper are readily obtainable in well-defined crystals, and the author has again to express his thanks to Mr. W. J. Pope for a number of interesting reports on the crystallographic characters of the various substances which have been submitted to him for examination.

Part of the cost of this, and of all the other investigations on camphor derivatives, which have been published by the author, alone and in conjunction with Mr. W. J. Pope and Dr. A. Lapworth, has been defrayed by grants from the Royal Society, for which the author desires to express his thanks to the Government Grant Committee.

EXPERIMENTAL.

Dry π -bromocamphoric acid (Trans., 1896, 69, 924), which has been freed from α -nitro- $\alpha\pi$ -dibromocamphor by washing with chloroform, is ground up with about one-tenth of its weight of amorphous phosphorus, and gradually treated with bromine in a Würtz flask; when the first vigorous action has subsided, the flask is heated on a water-bath and the addition of bromine continued very slowly, so that the quantity added in the course of about 3 hours is approximately twice the weight of the acid taken. During this operation, the evolution of hydrogen bromide gradually slackens, but without ceasing entirely, and bromine also escapes in small quantities, so that the end of the

normal reaction is difficult to recognise. The excess of bromine having been expelled, the product, which consists of a red, crystalline mass, saturated with a red oil, is well agitated with successive small quantities of cold water, and then with a little cold dilute alcohol; these liquids remove most of the oily impurity, leaving a pale reddish or greenish crystalline product, the weight of which is rather greater than that of the original acid, the average yield amounting to about 90 per cent. of the theoretical. A small quantity of a crystalline by-product is obtained from the alcoholic washings, but the examination of this substance is not completed.

The crude anhydride is very easily purified, without appreciable loss, by dissolving it in boiling chloroform, and precipitating the filtered solution with ether, repeating these operations if necessary; a sample thus purified and dried over sulphuric acid was analysed.

0.1779 gave 0.2307 CO₂ and 0.0643 H₂O. C = 35.36; H = 4.01.

0.1248 „ 0.1426 AgBr. Br = 47.8.

C₁₀H₁₂Br₂O₃ requires C = 35.29; H = 3.52; Br = 47.06 per cent.

Dibromocamphoric anhydride is readily soluble in boiling chloroform, from which it crystallises in large, transparent plates (see below) melting at 209—210°*; it is also readily soluble in boiling ethylic acetate, acetic acid, and cold acetone, moderately in cold benzene, and sparingly in cold ether and alcohol. It sublimes readily when heated in a test-tube, giving a solid sublimate of lustrous prisms. It seems not to be acted on by boiling quinoline, from which it separates again on cooling, but when heated with aniline it is vigorously attacked; it dissolves in warm, concentrated, sulphuric acid with evolution of hydrogen bromide, and on heating more strongly the solution darkens in colour considerably.

Boiling water slowly converts the anhydride into bromocamphanic acid and hydrogen bromide, and a boiling solution of half a molecular proportion of sodium carbonate in dilute alcohol brings about a similar change; boiling alcoholic or aqueous potash in excess causes the elimination of both the bromine atoms with formation of the potassium salt of hydroxy-*cis*- π -camphanic acid or dihydroxycamphoric acid. Fusion with potash at a moderately low temperature also results in the formation of a salt, from which *w*-hydroxy-*cis*- π -camphanic acid is liberated on the addition of a mineral acid, but other products appear to be formed in small quantities. When silver nitrate is added to a solution of the dibromo-anhydride in acetic acid, the separation of silver bromide soon commences, and after prolonged boiling *w*-hydroxy-*cis*- π -camphanic acid can be isolated from the solution; the γ -lactone of hydroxycamphotricarboxylic acid (Trans., 1896,

* For corrections to be applied to these melting points, see Trans., 1897, **71**, 963.

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69, 961) also seems to be produced under these conditions by the oxidation of the dihydroxycamphoric acid, which is probably formed as an intermediate product, but the isolation of the lactone is not very easy.

Dibromocamphoric anhydride is lævorotatory. For the determination of its specific rotation, a solution in chloroform of 1.158 grams was diluted to 25 c.c., and examined at 14° in a 200 mm. tube; the mean of 7 observations gave $\alpha = -2.9^{\circ}$, from which $[\alpha]_D = -31.2^{\circ}$.*

The following is Mr. W. J. Pope's account of the crystals of the dibromo-anhydride, which were obtained by spontaneous evaporation of its solution in chloroform.

"*πw*-Dibromocamphoric anhydride crystallises in transparent, rhomboidal-shaped, orthorhombic plates (Fig. 1) possessing a calcite-like lustre. The dominant form is always the pinacoid $a\{100\}$, and the form $q\{011\}$ is usually the next largest; these two forms give fairly good reflections. The prism $p\{110\}$ is, as a rule, much smaller than $q\{011\}$, and the pinacoid $b\{010\}$ is generally very small; the form $r\{101\}$ is always small but bright, and is frequently absent.

FIG. 1.

"Crystalline system.—Orthorhombic.

$$a : b : c = 1.4844 : 1 : 0.7083.$$

"Forms observed.— $a\{100\}$, $b\{010\}$, $p\{110\}$, $q\{011\}$, $r\{101\}$.

"The following measurements were obtained.

Angle.	Number of observations.	Limits.	Mean.	Calculated.
$ap = 100 : 110$	34	$55^{\circ}44' - 56^{\circ}17'$	$56^{\circ} 2'$	—
$pp = 110 : \bar{1}10$	18	$67 31 - 68 12$	$67 54$	$67^{\circ}56'$
$bp = 010 : 110$	29	$33 30 - 34 24$	$33 59$	$33 58$
$qq = 011 : 0\bar{1}\bar{1}$	24	$109 1 - 109 40$	$109 24$	$109 23$
$bq = 010 : 011$	29	$54 23 - 54 59$	$54 41$	$54 41 30''$
$qq = 011 : 0\bar{1}\bar{1}$	37	$70 14 - 70 54$	$70 37$	—
$ar = 100 : 101$	18	$64 3 - 64 51$	$64 27$	$64 29 30$
$rr = 101 : \bar{1}01$	26	$50 47 - 51 35$	$51 2$	$51 1$

* The polarimeter used in these determinations could only be read to $6'$, and so the results may not be very accurate.

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"The faces of the zone [001] are striated with lines parallel to the *c*-axis; these lines are sufficiently well developed as frequently to disturb the measurements in that zone. The optic axial plane is *c*(001), and the axis-*b* is a bisectrix of negative double refraction; the optic axial angle is very large, but the *b*-axis is probably the acute bisectrix. There is a fairly good cleavage on $a\{100\}$, and the cleavage faces are usually marked by the striations noted above; it is noteworthy that the crystals are always tabular on $a\{100\}$.

"After melting on a microscope slide under a cover slip in the usual way, the substance solidifies readily to a cubic modification; when the plate cools to about 60°, this changes to a doubly refracting biaxial modification made up of large individual fragments which, as cooling continues, crack across perpendicularly to their long directions. The pieces are frequently perpendicular to an optic axis, and are marked by interlaced straight striations. The double refraction seems to be of negative sign, and the modification is in all probability with the crystals measured above."

πw-Dibromocamphoric Acid, $C_8H_{12}Br_2(COOH)_2$.

It has been shown in previous papers that when an anhydride cannot be converted into the corresponding acid by treatment with alkalis or with boiling water, owing to elimination of the elements of a halogen acid, as, for example, in the case of the anhydrides of *w*-bromocamphoric acid (Trans., 1896, 69, 1), *π*-bromocamphoric acid (Trans., 1896, 69, 927), and *π*-chlorocamphoric acid (Lapworth and Kipping, Trans., 1897, 71, 1), this conversion is easily accomplished by using concentrated nitric acid as the hydrolysing agent. This method can be applied with very satisfactory results for the preparation of dibromocamphoric acid from its anhydride.

Dibromocamphoric anhydride dissolves readily in hot, concentrated nitric acid (sp. gr. 1.4), and if the solution be cooled after heating during a few minutes only, most of the anhydride is deposited unchanged; if, however, the nitric acid solution be heated on a water-bath in an evaporating dish, crystals of the dibromo-acid begin to separate after a short time, neither nitrous fumes nor bromine being evolved in any appreciable quantity. When most of the nitric acid has evaporated, a little water is added to precipitate the rest of the dibromo-acid, and the colourless crystals are then separated and dried in the air. This product is generally free from anhydride, but should the latter be present, it is easily removed by washing the crystals with a little cold chloroform, in which the acid is insoluble, or nearly so.

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For analysis, a sample was treated in this way, and then recrystallised from ether and dried at 100° until constant in weight.

0.1682 gave 0.2076 CO_2 and 0.0624 H_2O . $\text{C} = 33.66$; $\text{H} = 4.12$.

$\text{C}_{10}\text{H}_{14}\text{Br}_2\text{O}_4$ requires $\text{C} = 33.52$; $\text{H} = 3.91$ per cent.

πw -Dibromocamphoric acid crystallises from ether, in which it is very readily soluble, in microscopic, four-sided plates; it dissolves freely in cold acetone, ethylic acetate, and methylic alcohol, but is almost insoluble in benzene as well as in chloroform. It melts at about 210° , effervescing, owing to the escape of water vapour and hydrogen bromide, and becoming slightly brown, but like w -bromocamphoric acid and all the π -halogen derivatives of camphoric acid, it is stable at 100° , and does not lose in weight even after having been heated during several hours. It is practically insoluble in boiling water, although just sufficiently soluble to impart to the water an acid reaction after heating for a few minutes; it is probable, however, that the dibromo-acid does not dissolve unchanged, and that the acidity of the solution is due to hydrobromic and π -bromocamphanic acids, since these two compounds are rapidly produced when a solution of the dibromo-acid in dilute methylic alcohol is boiled.

Hot concentrated nitric acid dissolves dibromocamphoric acid freely, and on cooling beautiful, transparent, flat, four-sided crystals are deposited, but they are not large enough to be suitable for goniometric examination. The acid dissolves in dilute sodium carbonate, forming apparently the corresponding sodium salt, as on acidifying a freshly prepared solution with a mineral acid, dibromocamphoric acid is reprecipitated; when, however, such a solution of the acid is boiled for a few minutes and then acidified, crystals of π -bromocamphanic acid are deposited, hydrogen bromide having been eliminated.

When dibromocamphoric acid is heated in a test-tube over a small flame, it first melts with effervescence and then distils, charring very slightly but evolving hydrogen bromide, and apparently traces of carbonic anhydride; the crystalline distillate consists of a mixture of πw -dibromocamphoric anhydride and an acid melting at 176° , which is doubtless π -bromocamphanic acid.

No attempts were made to prepare salts of the dibromo-acid, on account of the readiness with which it is decomposed by water, alkali carbonates, and alkalis. It is interesting to note the relative stability of hot solutions of the acid in concentrated nitric acid and in water respectively; whereas the former may be heated during several hours without suffering any appreciable change, elimination of hydrogen bromide takes place rapidly in the aqueous solutions; this behaviour is similar to that of π -bromocamphoric acid.

π -Bromo- w -chlorocamphoric Anhydride, $C_8H_{12}BrCl\begin{smallmatrix} \diagup CO \\ \diagdown CO \end{smallmatrix}O$.

The object of preparing this compound has already been stated; the method was the following. Dry powdered π -bromocamphoric acid was treated with a slight excess of the theoretical quantity of phosphorus pentachloride, the colourless liquid product heated on a water-bath, and dry chlorine slowly bubbled into it for about 4 hours, or until the evolution of hydrogen chloride almost ceased. The pale yellow oil thus obtained was gradually treated with ice cold water, whereon it quickly solidified, and was then purified by washing with water and dilute alcohol successively; for analysis, a sample was recrystallised twice from chloroform and then dried over sulphuric acid.

0.1576 gave 0.2349 CO_2 and 0.0602 H_2O . $C = 40.65$; $H = 4.24$.

$C_{10}H_{12}ClBrO_4$ requires $C = 40.62$; $H = 4.06$ per cent.

π -Bromo- w -chlorocamphoric anhydride, like the corresponding dibromo-compound, crystallises best from chloroform, from which it is deposited in lustrous prisms (see later) melting at $214-215^\circ$, or 5° higher than its analogue; a mixture of the dibromo- and chlorobromo-anhydrides shows no sign of melting until the temperature rises to $209-210^\circ$ —the melting point of the former—an indication of the isomorphism of the two compounds which was confirmed by the crystallographic examination made by Mr. W. J. Pope (see p. 136).

In most respects, the properties of π -bromo- w -chlorocamphoric anhydride are so similar to those of the corresponding dibromo-compound that further description is unnecessary, but one rather interesting difference in behaviour may perhaps be noted. When the chlorobromo-compound is crystallised from a mixture of chloroform and ether, it is sometimes deposited in long, slender prisms, or needles, as well as in the compact prisms already referred to; these two kinds of crystals differ, not only in appearance, but also in behaviour, as the former become opaque when kept over sulphuric acid or heated on a water-bath, whereas the latter remain transparent; both forms, however, melt at $214-215^\circ$.

Experiments showed that the needles are formed when the crystallisation of the ethereal chloroform solution takes place at low temperatures, as, for example, at -5° , whereas, when the solution is kept at about the ordinary atmospheric temperature, one or other, or both forms may be deposited; ethereal chloroform solutions of the dibromo-anhydride, crystallised at temperatures just below 0° , did not deposit anything but the rhombic prisms described above.

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This anhydride, like the corresponding dibromo-compound, is lævoptatory; a solution of 1.153 grams in chloroform diluted to 25 c.c., and examined at 14° in a 200 mm. tube, gave $\alpha = -2.4^{\circ}$ as the average of seven observations: hence $[\alpha]_D = -26.1^{\circ}$.*

"*πw*-Chlorobromocamphoric anhydride crystallises in large, transparent, orthorhombic prisms (Fig. 2), which appear rather more lustrous than the crystals of the corresponding dibromo-compound. The dominant form, as in the latter case, is usually the pinacoid $a\{100\}$, but the form $p\{100\}$ is sometimes the most developed; the pinacoid $b\{010\}$ is also usually well developed, and $q\{011\}$ is generally broader than in dibromocamphoric anhydride. The crystals of the latter give much better results on measurement than do those of the compound now described.

FIG. 2.

"Crystalline system.—Orthorhombic.

$$a : b : c = 1.4789 : 1 : 0.7107.$$

"Forms observed: $a\{100\}$, $b\{010\}$, $p\{110\}$, $q\{011\}$, $r\{101\}$.

"The following measurements were obtained.

Angle.	Number of observations.	Limits.	Mean.	Calculated.
$ap = 100 : 110$	47	$55^{\circ} 1' - 56^{\circ} 54'$	$55^{\circ} 56'$	—
$pp = 110 : \bar{1}10$	32	$67^{\circ} 49' - 69^{\circ} 2'$	$68^{\circ} 31'$	$68^{\circ} 8'$
$bp = 010 : 110$	21	$33^{\circ} 20' - 34^{\circ} 48'$	$34^{\circ} 7'$	$34^{\circ} 4'$
$qq = 011 : 0\bar{1}\bar{1}$	38	$108^{\circ} 42' - 109^{\circ} 57'$	$109^{\circ} 16'$	$109^{\circ} 12'$
$bq = 010 : 011$	43	$53^{\circ} 39' - 55^{\circ} 10'$	$54^{\circ} 38'$	$54^{\circ} 36'$
$qq = 011 : 0\bar{1}\bar{1}$	44	$69^{\circ} 57' - 71^{\circ} 28'$	$70^{\circ} 48'$	—
$ar = 100 : 101$	13	$63^{\circ} 19' - 65^{\circ} 6'$	$64^{\circ} 24'$	$64^{\circ} 20'$

"The forms in the zone $[001]$, and more especially the pinacoid $a\{100\}$, are marked with striations parallel to the c -axis. The optic axial plane is $c\{001\}$, and the axis b is the acute bisectrix; the double

* Compare footnote, p. 132.

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refraction is negative in sign, and the optic axial angle is large. There is a very poor conchoidal cleavage on $a\{100\}$.

"After melting on a microscope slide under a cover slip, the compound solidifies readily, yielding a singly-refracting cubic modification; this, before it cools to the atmospheric temperature, changes to a biaxial doubly-refracting modification, which is formed in large plates very similar to those constituting the film of the corresponding dibromo-derivative. These plates are marked with interlaced, straight striations, and are frequently perpendicular to an acute bisectrix of large axial angle and of negative double refraction.

"As would be expected from the chemical relationship between the two compounds, πw -dibromo- and πw -chlorobromo-camphoric anhydride are isomorphous; the axial ratios are of the same order and corresponding angles, as shown in the following table, do not differ greatly in the two cases.

	$C_{10}H_{12}Br_2O_3$.	$C_{10}H_{12}ClBrO_3$.	Differences.
a/b	1.4844	1.4789	+ 0.0055
c/b	0.7083	0.7107	- 0.0024
a/c	2.0958	2.0809	+ 0.0149
$ap=100:110$	$56^\circ 2'$	$55^\circ 56'$	+ 0.6'
$bp=010:110$	$33^\circ 58'$	$34^\circ 4'$	- 0.6'
$cq=001:011$	$35^\circ 18' 30''$	$35^\circ 24'$	- 0.530"
$bq=010:011$	$54^\circ 41' 30''$	$54^\circ 36'$	+ 0.530"
$ar=100:101$	$64^\circ 29' 30''$	$64^\circ 20'$	+ 0.930"
$cr=001:101$	$25^\circ 30' 30''$	$25^\circ 40'$	- 0.930"

"It will be seen that the dimensions measured in the zone $[001]$ differ least in the two cases, whilst those in the parametral zone $[010]$ exhibit the greatest differences. The same forms are present on crystals of both anhydrides and striations parallel to the zone axis observed in the zone $[001]$ are also observed in both cases.

"Amongst the differences may be noted that the crystals of the dibromo-compound show a much better cleavage parallel to $\{100\}$ than do those of the chlorobromo-derivative; again, the crystals of the former are really much better developed and give more trustworthy measurements than those of the latter substance. Further, there is a well-marked difference in habit. Crystals of the dibromo-anhydride are always tabular, whilst those of the chlorobromo-derivative are much more prismatic in habit; this is mainly due to a large development of the forms $p\{110\}$ and $b\{010\}$ on the latter crystals.

"The behaviour of the two substances after melting and solidification is, in accordance with the isomorphism, extremely similar."

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 π -Bromo- ω -chlorocamphoric Acid, $C_8H_{12}BrCl(COOH)_2$.

This acid can be prepared from its anhydride by the same method as that employed in the case of the dibromo-anhydride, namely, by dissolving the anhydride in concentrated nitric acid (sp. gr. 1.4), and then evaporating the solution on the water-bath. The colourless crystals of the acid are dried on porous earthenware, washed with a little chloroform to remove traces of unchanged anhydride which may be present, and then dried at 100° ; for the analysis, a sample was re-crystallised from ether, as the crystals retain small quantities of occluded nitric acid, which is not easily expelled even at 100° .

0.1689 gave 0.2395 CO_2 and 0.0693 H_2O . $C = 38.67$; $H = 4.56$.

$C_{10}H_{14}BrClO_4$ requires $C = 38.29$; $H = 4.46$ per cent.

π -Bromo- ω -chlorocamphoric acid is a microcrystalline, colourless powder, as prepared in the above manner; it melts at about 197° when heated fairly slowly from about 80° , effervescing vigorously, but as this temperature is a decomposition rather than a melting point, it varies a little with the rapidity of heating. There is, however, a much larger difference between the melting points of the bromochloro- and dibromo-acids, than between those of the corresponding anhydrides. In all ordinary properties, the bromochloro-acid resembles the dibromo-compound; it is, however, rather more soluble in boiling water, from which it separates in long, transparent prisms, which seem to contain water of crystallisation, as they become opaque when heated and melt at about 197° . It separates from cold concentrated nitric acid in nodular, opaque masses, and from ethereal chloroform in colourless, transparent, well-defined microscopic prisms; its behaviour towards boiling water is referred to later.

 π -Bromocamphanic Acid, $COOH \cdot C_8H_{12}Br \begin{smallmatrix} \diagup CO \\ \diagdown \end{smallmatrix}$.

Various methods can be adopted for preparing this compound from dibromocamphoric anhydride, or from the corresponding acid, some of which have already been mentioned. It may be obtained in large quantities by boiling the finely divided anhydride with a large volume of water, but as this process occupies a long time, owing to the slight solubility of the anhydride, the following method is more convenient.

The anhydride is dissolved in a small quantity of boiling acetic acid, and after adding a little water until a turbidity is just produced in the hot solution, the latter is heated on a sand-bath, more water

being added from time to time as the anhydride decomposes; during this process, the solution almost invariably acquires a distinct bright pink colour, which slowly changes to brown, the liquid then depositing traces of some tarry matter, doubtless due to impurity in the (crude) anhydride used. The hot solution is finally filtered, and on cooling the π -bromocamphanic acid is deposited in almost colourless needles; further quantities are obtained on evaporating the mother liquors, the yield being practically theoretical.

For analysis, a sample was purified by recrystallisation from a mixture of ethylic acetate and chloroform and dried at 100°.

0.1576 gave 0.2518 CO₂ and 0.0697 H₂O. C = 43.57; H = 4.91.

C₁₀H₁₃BrO₄ requires C = 43.32; H = 4.69 per cent.

π -Bromocamphanic acid usually separates from hot water, in which it is only moderately easily soluble, in small, well-defined, lustrous prisms, which do not lose in weight at 100°. It is comparatively sparingly soluble in boiling benzene, and only moderately so in boiling chloroform, but it dissolves readily in acetic acid, alcohol, and ethylic acetate; it crystallises best from cold, dilute acetic acid, from which it is deposited in transparent prisms described later. It melts at 176–177° without decomposing, but when heated at its boiling point it darkens considerably and seems to give off a little hydrogen bromide; the distillate soon crystallises on cooling, and consists of slightly impure bromocamphanic acid.

π -Bromocamphanic acid is a very stable substance in many respects, and boiling nitric acid, dilute or concentrated, does not oxidise any appreciable quantity of it in the course of a few hours. Prolonged boiling with a solution of chromic anhydride and dilute sulphuric acid seems to result simply in the elimination of hydrogen bromide, the bromocamphanic acid being converted into hydroxy-*cis*- π -camphanic acid; the last-named compound is also formed when the bromo-acid is boiled with an aqueous solution of silver nitrate, but other substances are also produced. When the acid is treated with ammonia under suitable conditions, a product is obtained which is almost insoluble in water, but which has not yet been analysed or examined.

Mr. Pope's description of this substance is as follows. "The crystals of bromocamphanic acid are very beautiful, transparent, orthorhombic prisms (Fig. 3), which have a very brilliant, glassy lustre. The prism $p\{110\}$ is always dominant, but gives poor results on measurement owing to the presence of vicinal faces and of striations parallel to the *c*-axis; the forms $q\{011\}$ and $r\{101\}$ are next in size, $r\{101\}$ being usually rather the larger, and give very brilliant reflections, so that the measurements obtained from them may be relied upon. The pinacoid $c\{001\}$ is very small and frequently absent.

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FIG. 3.

"Crystalline System.—Orthorhombic.

$$a : b : c = 1.4654 : 1 : 0.9501.$$

"Forms observed.— $c\{001\}$, $p\{110\}$, $q\{011\}$, $r\{101\}$.

"The following angular measurements were obtained.

Angle.	Number of measurements.	Limits.	Mean.	Calculated.
$cr = 001 : 101$	9	$35^{\circ}17' - 35^{\circ}59'$	$35^{\circ}41'$	$35^{\circ}39'30''$
$rr = 101 : \bar{1}01$	29	$71\ 12 - 71\ 26$	$71\ 19$	—
$rr = 101 : 10\bar{1}$	25	$108\ 34 - 108\ 48$	$108\ 40$	$108\ 41\ 8$
$pq = 110 : 011$	34	$70\ 41 - 70\ 56$	$70\ 49$	—
$qr = 011 : 101$	29	$55\ 49 - 56\ 15$	$56\ 59$	$56\ 57$
$rp = 101 : 110$	31	$53\ 5 - 53\ 24$	$53\ 15$	$53\ 14$
$qq = 011 : 01\bar{1}$	16	$86\ 52 - 87\ 20$	$87\ 4$	$87\ 8$
$qq = 011 : 0\bar{1}1$	14	$92\ 37 - 93\ 11$	$92\ 55$	$92\ 52$
$cq = 001 : 011$	15	$46\ 1 - 46\ 54$	$46\ 21$	$46\ 26$
$pp = 110 : 1\bar{1}0$	37	$110\ 47 - 111\ 58$	$111\ 26$	$111\ 23$
$pp = 110 : \bar{1}10$	24	$68\ 20 - 69\ 13$	$68\ 47$	$68\ 37$

"The plane $c(001)$ is the optic axial plane, and an optic axis emerges obliquely through each face of the form $p\{110\}$; the double refraction is strong and the optic axial dispersion slight. After melting, the substance solidifies readily, and is thus obtained in large individual flakes, which are often marked by striæ crossing each other at about 60° , and cracked across their longest dimension on cooling; the flakes are frequently perpendicular to an optically negative bisectrix of a large axial angle."

This ethereal salt is conveniently prepared by passing hydrogen chloride into a solution of the acid in methylic alcohol and then

evaporating at the ordinary temperature; the product, which is slowly deposited in felted needles, can be purified by recrystallisation from a mixture of ether and chloroform.

0.1662 gave 0.2777 CO_2 and 0.0832 H_2O . $\text{C} = 45.57$; $\text{H} = 5.56$.

$\text{C}_{11}\text{H}_{15}\text{BrO}_4$ requires $\text{C} = 45.36$; $\text{H} = 5.15$ per cent.

Methylic π -bromocamphanate crystallises from ether and from most other solvents in long, transparent needles melting at $87-88^\circ$; it is very readily soluble in cold chloroform, methylic alcohol, and boiling ether, but comparatively sparingly soluble in light petroleum. Massive crystals are easily obtained from a solution in a mixture of ether and chloroform, and a specimen of the compound thus obtained was examined by Mr. W. J. Pope, whose report is now given.

"The crystals of methylic bromocamphanate are transparent orthorhombic plates or prisms, possessing a high lustre (Fig. 4); the habit of the crystals varies considerably, those of prismatic habit are lengthened in the direction of the axis- a , and somewhat flattened in that of the b -axis, the dominant forms being $a\{100\}$ and $r\{101\}$; the tabular crystals are flattened on two parallel faces of the form $r\{101\}$. Very good results are obtained on measuring the crystals.

FIG. 4.

"Crystalline System.—Orthorhombic.

$$a:b:c = 1.0977 : 1 : 0.6561.$$

"Forms observed.— $a\{100\}$, $b\{010\}$, $p\{110\}$, $r\{101\}$.

"The following angular measurements were obtained.

Angle.	Number of measurements.	Limits.	Mean.	Calculated.
$ap = 100 : 110$	18	$47^\circ 34' - 47^\circ 47'$	$47^\circ 40'$	—
$pb = 110 : 010$	12	$42^\circ 12' - 42^\circ 27'$	$42^\circ 18'$	$42^\circ 20'$
$ar = 100 : 101$	24	$59^\circ 0' - 59^\circ 23'$	$59^\circ 8'$	—
$rr = 101 : \bar{1}01$	16	$61^\circ 31' - 61^\circ 50'$	$61^\circ 42'$	$61^\circ 44'$
$pr = 110 : 101$	7	$69^\circ 39' - 69^\circ 52'$	$69^\circ 45'$	$69^\circ 47'$

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"There is a poor conchoidal cleavage parallel to $b\{010\}$, and the axis- b is the acute bisectrix; the optic axial plane is $c(001)$, and the double refraction is positive in sign, and strong. The optic axial angle is fairly large and the optic axial dispersion is slight.

"The substance solidifies readily after melting on a microscope slide under a cover slip, giving large, individual flakes; most of these are nearly perpendicular to an optically negative bisectrix of a very large optic axial angle, and these are full of symmetrically arranged egg-shaped bubbles and of intersecting striations. A few fragments are usually to be observed which show no bubbles or striæ; these are nearly perpendicular to the optically positive bisectrix of a fairly large optic axial angle. This modification is doubtless identical with the crystals measured above."

Methylic π -bromocamphanate is slowly attacked by concentrated aqueous ammonia at ordinary temperatures, and is thereby converted into a crystalline substance, which, judging by its melting point and other ordinary properties, is identical with the π -bromocamphanamide produced by the action of aqueous ammonia on πw -dibromocamphoric anhydride. This compound may now be described.

When finely divided πw -dibromocamphoric anhydride is left in contact with concentrated aqueous ammonia at ordinary temperatures, it slowly changes into a rather more bulky mass of small prisms, but without passing into solution to any noticeable extent; after keeping the mixture for about two days, the product is separated by filtration from the ammoniacal solution, which contains a small quantity of a readily soluble, crystalline, ammonium salt, washed with cold water, and recrystallised from dilute methylic alcohol. The substance obtained in this way is the amide of π -bromo- w -camphanic acid, and an analysis of it gave the following result.

0.1678 gave 0.2671 CO_2 and 0.0796 H_2O . $\text{C} = 43.41$; $\text{H} = 5.27$.

$\text{C}_{10}\text{H}_{14}\text{O}_3\text{BrN}$ requires $\text{C} = 43.47$; $\text{H} = 5.07$ per cent.

The nature of this compound is further established by the fact already mentioned, namely, that it is formed on treating methylic π -bromocamphanate with aqueous ammonia, and also by its behaviour on hydrolysis; when boiled for a short time with concentrated hydrochloric acid, it is converted into a crystalline acid, which melts at $176\text{--}177^\circ$, and has all the properties of π -bromocamphanic acid.

π -Bromo- w -camphanamide crystallises from most solvents in lustrous, transparent needles or prisms melting at $161\text{--}162^\circ$; it is very readily

soluble in cold chloroform, acetone, ethylic acetate, acetic acid, and most other solvents, and it also dissolves freely in boiling water, but it is insoluble, or nearly so, in a cold dilute solution of sodium carbonate. It seems to be dimorphous, as the transparent crystals deposited from dilute methylic alcohol become opaque at about 140° when slowly heated, and do so at even lower temperatures when the tube containing them is rubbed gently.

Formation of π -Bromocamphanic Acid from π -Bromo- ω -chlorocamphoric Anhydride.—It was stated in the introduction that π -bromo- ω -chlorocamphoric anhydride is decomposed by boiling water, giving hydrogen chloride, and an acid identical with the π -bromo- ω -camphanic acid, prepared in a similar manner from $\pi\omega$ -dibromocamphoric anhydride; this statement rests on the following experimental evidence.

When bromochlorocamphoric anhydride is boiled for some hours with diluted acetic acid, and the filtered solution then allowed to cool, a substance crystallising in colourless prisms is deposited; this compound, after having been purified, melted at 176 — 177° , and in appearance and other properties seemed to be identical with π -bromocamphanic acid. The great similarity between dibromo- and bromochloro-camphoric anhydrides, however, if repeated in the case of the bromo- and chloro-camphanic acids, might render the distinction between the two latter a matter of some difficulty; for this reason, it was necessary to make the following analysis, the results of which show that the decomposition product of the bromochloro-anhydride is really a π -bromocamphanic acid.

0.1572 gave 0.2521 CO_2 and 0.0679 H_2O . $\text{C} = 43.74$; $\text{H} = 4.80$.

$\text{C}_{10}\text{H}_{13}\text{BrO}_4$ requires $\text{C} = 43.32$; $\text{H} = 4.69$ per cent.

Hydroxy-cis- π -camphanic Acid.

It has been shown in earlier papers that *cis*- π -camphanic acid is slowly oxidised by potassium permanganate in alkaline solution, being converted into a hydroxy-*cis*- π -camphanic acid, which is the lactone of a dihydroxycamphoric acid; this hydroxy-acid can be obtained in various ways from dibromocamphoric anhydride and its derivatives.

When, for example, dibromocamphoric anhydride is boiled for some time with alcoholic potash, or fused with potash at a moderate temperature, both the bromine atoms are removed, and hydroxy-*cis*- π -camphanic acid can be isolated from the product by methods which it is unnecessary to describe. Again, when π -bromocamphanic acid is heated with silver nitrate in aqueous solution, silver bromide is rapidly deposited, and an acid having all the properties of hydroxy-*cis*- π -camphanic acid can be obtained from the solution.

A number of experiments were made in the hope of isolating a

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dihydroxycamphoric acid, or the corresponding dilactone; for this purpose, the dibromo-anhydride, dibromo-acid, and π -bromocamphanic acid, were separately treated with aqueous silver nitrate under various conditions; in nearly every case the product seemed to be a mixture of two or three organic compounds, and it was not easily separable into its components by fractional crystallisation or by other methods; hydroxy-*cis*- π -camphanic acid was isolated in almost every instance, and also a crystalline substance, which from its melting point and other properties was found to be identical with the γ -lactone of hydroxycamphotricarboxylic acid. Further, in several experiments, small quantities of an oily product were obtained; this substance, when purified, was only sparingly soluble in boiling water (the other two products are readily soluble), and apparently insoluble in cold dilute sodium carbonate; it was vigorously attacked by hot concentrated nitric acid, being converted into the γ -lactone of camphotricarboxylic acid. These observations seem to show the existence of a dilactone of dihydroxycamphoric acid amongst the products of the action of silver nitrate on the bromo- and dibromo-compounds in question.

Hydroxy-*cis*- π -camphanic acid is prepared far more easily by one of these methods than by the oxidation of *cis*- π -camphanic acid, and its investigation, as well as that of some of the other compounds related to it, is being continued; the crystals of this acid, obtained from an acetone solution, are of large size and suitable for goniometric examination.

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