

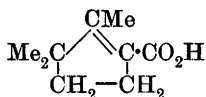
CXLV.—*The Action of Aluminium Chloride on
Camphoric Anhydride. Part II.*

By W. H. PERKIN, jun., and J. YATES.

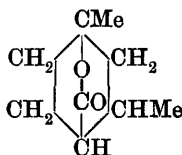
IN the first part of this paper, published a short time ago (Lees and Perkin, this vol., 332), it was shown that when camphoric anhydride, dissolved in chloroform, is treated in the cold with aluminium chloride, the camphor molecule undergoes a series of remarkable molecular changes.

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The substances formed during this decomposition and described in the first paper were solauronic acid,

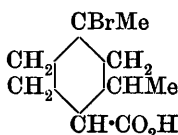


and a mixture of isomeric lactones, which, since they are readily converted into xylic acid on oxidation with sulphuric acid, were recognised as stereoisomeric modifications of the lactone of hydroxyhexahydro-xylic acid,



By hydrolysing the mixed lactones we succeeded, in a way described in detail in that paper, in isolating two well characterised stable hydroxyhexahydro-xylic acids melting at 160° and 113° respectively, which we called simply A and B, since we had no means of determining their configurations. When distilled, these acids were converted into the corresponding lactones with elimination of water, the lactone of the A-acid melted at 55° ,* and that of the B-acid at 44° .

We have since further examined these two hydroxy-acids and their lactones and find that the A-acid or its lactone, when treated with fuming hydrobromic acid, is converted into *A-bromohexahydro-xylic acid*,



which melts at 133° , whereas the B-hydroxy-acid and its lactone, under similar conditions, yield *B-bromohexahydro-xylic acid* melting at 126° .

In our earlier experiments, several results were obtained which seemed to indicate that the lactone mixture obtained by the action of aluminium chloride on camphoric anhydride did not consist entirely of the two lactones of A- and B-hydroxyhexahydro-xylic acid, but contained other isomeric lactones, which we were at that time unable to isolate. Since then, by experimenting with large quantities of material, this

* This lactone was described as an oil, but it subsequently solidified,

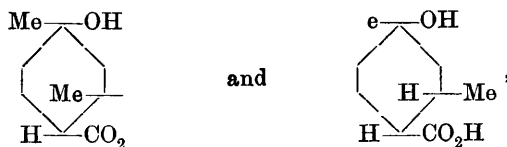
suspicion has been confirmed and we have now been able to identify all the constituents of the mixture.

The two hydroxy-acids, A and B, are characterised by remarkable stability, since, although they contain the hydroxyl and carboxyl groups in the δ -position, they are not converted into their lactones even by prolonged boiling with water, and it was found necessary, in order to prepare these lactones, to submit the acids to dry distillation.*

In order to explain this remarkable stability, we suggested in the earlier paper that the two hydroxy-acids, A and B, were probably the *trans*-modifications,

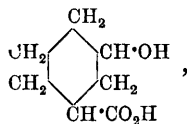


The corresponding *cis*-modifications,

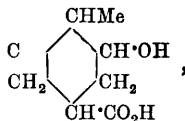


might be expected to exhibit much less stability, and be converted into their lactones when their salts are acidified, as is the case with the δ -hydroxy-acids in the fatty series.

* Somewhat similar cases of stable ring hydroxy-acids have already been observed. Thus, the hydroxycyclohexanecarboxylic acid of the formula



which Einhorn (*Annalen*, 1896, **291**, 298) prepared by reducing *m*-hydroxybenzoic acid, is quite stable although it is a γ -hydroxy-acid. Again, Tiemann and Semmler (*Ber.*, 1895, **28**, 2143) describe as stable the γ -hydroxyhexahydro-*p*-toluic acid of the formula :



Both these acids are probably *trans*-modifications.

The existence of *cis*- and *trans*-isomerism in the case of ring-acids containing the

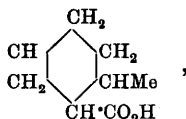
By making use of these differences in stability we have now succeeded in showing that the mixed lactones obtained by the action of aluminium chloride on camphoric anhydride contain, not only the lactones of the *trans*-A- and B-hydroxyhexahydro-xylic acids, but also the corresponding *cis*-lactones. The process employed in separating the latter is briefly as follows :

The mixed lactones are first converted into the hydroxy-acids by hydrolysis and these then submitted to distillation in steam ; in this way, the *cis*-hydroxy-acids are converted into lactones which pass over with the steam, whereas the *trans*-acids remain for the most part unchanged in the distilling flask, so that by repeating this process an almost complete separation is possible. The last traces of *trans*-acids are removed by hydrolysing the lactones and allowing the hydroxy-acids to stand for a few days, when the *cis*-modifications are spontaneously converted into lactones, which are separated from any traces of *trans*-hydroxy-acids by treatment with sodium carbonate. In this way, more than 100 grams of oil were obtained, which distilled constantly at 145° under 25 mm. pressure, and, like the *trans*-lactones, yielded xylic acid when treated with sulphuric acid ; there can therefore be no doubt that it consisted of the *cis*-lactones of hydroxyhexahydro-xylic acid.

Further examination showed that this oil contains two lactones (one, however, only in extremely small quantity), since when treated with fuming hydrobromic acid the oil yields a solid product which, when crystallised from light petroleum, may be separated into a small quantity of a very sparingly soluble C-bromohexahydro-xylic acid melting at 137° and a large quantity of the more soluble D-bromohexahydro-xylic acid, which melts at 130°. At first it was thought that the two bromo-acids, A and C, melting at 133° and 137°, and the two B, and D, melting at 128° and 130° were identical, but investigation showed that this is not the case.

If, for example, the first two are intimately mixed, the mixture melts at about 100° and a mixture of the two latter was found to melt at about 105°, and again, the four bromo-acids differ in their behaviour with sodium carbonate : a point which will be discussed at a later stage.

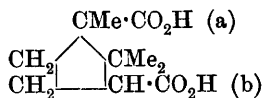
groups CHMe and CH·CO₂H has already been observed. Thus, hexahydro-*o*-toluic acid,



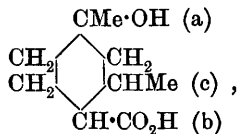
exists in well-defined *cis*- and *trans*-modifications (Goodwin and Perkin, *Trans.*, 1895, 67, 121).

It is therefore evident that there are four distinct bromo-acids, $C_9H_{15}O_2Br$, two *cis* and two *trans*, and this agrees with the assumption that the hydroxy-acids, $C_9H_{15}O_2\cdot OH$, from which they are derived, are stereoisomeric modifications of hydroxyhexahydro-xylic acid, and that the bromo-acids are therefore stereoisomeric bromohexahydro-xylic acids: this will be evident from the following considerations.

If the formula of camphoric acid is compared with that of hydroxyhexahydro-xylic acid,



Camphoric acid.



Hydroxyhexahydro-xylic acid.

it will be seen that not only are the two asymmetric carbon atoms in the camphoric acid (marked a, b) present in the hydroxyhexahydro-xylic acid, although in a somewhat altered form, but that in the formation of the latter acid from the former a new asymmetric carbon (marked c) has been created: in other words, hydroxyhexahydro-xylic acid contains *three* asymmetric carbon atoms. In order to discuss this point, we may conveniently select the four bromo-acids A, B, C, and D, and it may be stated at once that experiment has shown that these are all inactive and that, therefore, racemisation must have taken place in their formation from the strongly dextrorotatory camphoric anhydride. In the case of a substance containing three asymmetric carbon atoms, a, b, c, the possible combinations, using the signs + and - are:

+ a - a		+ a - a		+ a - a		- a + a
+ c - c		- c + c		- c + c		- c + c
+ b - b		+ b - b		- b + b		+ b - b
1 2		3 4		5 6		7 8

that is to say, there are four possible externally compensated combinations, 1:2, 3:4, 5:6, and 7:8, and it is highly probable that the four bromo-acids, A, B, C, and D, and their corresponding hydroxy-acids, are these combinations. Unfortunately, it is not possible at this stage to assign to *each* modification its particular configuration. We may, however, select the combination [+a-c-b, -a+c+b] for C, in which case D will be [-a-c+b, +a+c-b], and the acids A and B will be represented by [+a+c+b, -a-c-b] and [+a-c+b, -a+c-b], but which of these symbols belongs to A, and which to B, must be left an open question.

In connection with this question of the introduction of a new asymmetric carbon atom into a molecule containing already one or more u carbon atoms, we may perhaps be allowed to call attention

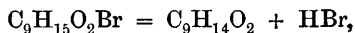
following very interesting aspect of the subject, since it arises directly from our experimental work.

It has already been stated that the results briefly described above leave little room for doubting that during the conversion of *d*-camphoric acid the change proceeds in such a way as to yield the four externally compensated hydroxyhexahydro-xylic acids, to which only the configurations given on page 1377 can be assigned. It thus follows that the camphor residue has, during the treatment with aluminium chloride, undergone racemisation in a manner similar to, although probably more complete than, that observed by Kipping and Pope (Trans., 1897, 71, 956) to occur on sulphonating camphor; and whilst in the latter case the complex $+a+b$ became converted into $-a-b$, in the case now described the other two complexes, $+a-b$ and $-a+b$, are also produced at some stage during the series of reactions. The formation of a third asymmetric carbon atom in addition to the two already present results in the ultimate production of all eight possible configurations of the substance containing three dissimilar asymmetric carbon atoms.

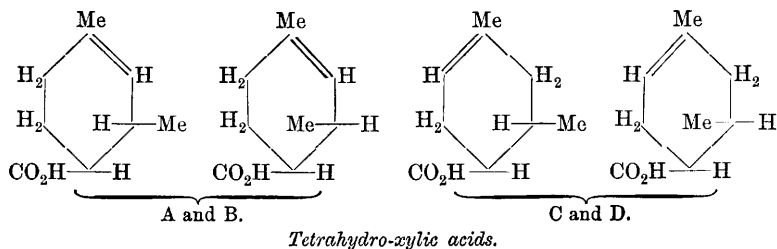
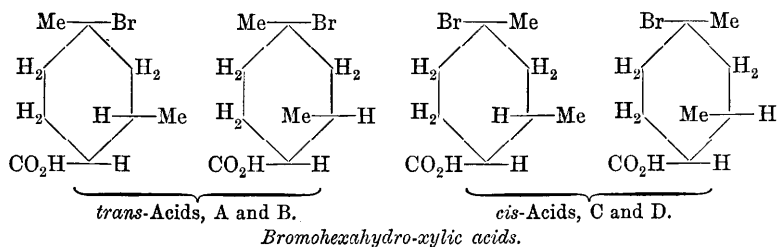
Quite recently (Cohen and Whiteley, Proc., 1900, 16, 212; Kipping, *ibid.*, 226), the question has again been opened as to whether in converting an optically active substance containing n -asymmetric carbon atoms into one containing $n+1$ such atoms, the configuration of the n -asymmetric carbon atoms originally present exercises a directive influence on the configuration of the new asymmetric carbon atom. This question seems to have been answered in the affirmative by Fischer's work, and more especially by his observation that *d*-mannose, which contains four asymmetric carbon atoms, gives an almost quantitative yield of *d*-mannoheptonic acid (*Ber.*, 1889, 22, 370), which contains five asymmetric carbon atoms in the molecule. A number of well-known facts leading to the same conclusion are available and the work now described also points in the same direction. Thus, it is well known that on brominating succinic acid two optically inactive dibromosuccinic acids are obtained in different quantities, the isomeride (*isodibromosuccinic acid*) produced in much the smaller amount having the configuration $[+a+a, -a-a]$, whilst ordinary dibromosuccinic acid is the internally compensated compound having the configuration $[+a-a]$. Since monobromosuccinic acid containing one asymmetric carbon atom is first produced and on further bromination yields more internally than externally compensated dibromosuccinic acid, it follows that the presence of one asymmetric carbon atom in this case causes the second to assume, by preference, the opposite configuration to the first. The literature concerning the tartaric acids reveals similarly convincing proofs of the same proposition. The possibility of drawing, from the behaviour of optically

inactive substances, sound conclusions as to the directive influence exerted by the configuration of asymmetric carbon atoms already existent in the substance upon that of others ultimately produced, seems hitherto to have been overlooked. In the formation of the hydroxyhexahydro-xylic acids with three asymmetric carbon atoms from camphoric acid containing only two, we show that the four externally compensated isomerides produced are formed in widely different proportions, which may be roughly stated to be as follows: A, 12 per cent.; B, 5 per cent.; C, 3 per cent.; D, 80 per cent. Although we are unable at present to definitely distribute the four pairs of possible configurations amongst these four acids, the fact that these acids are formed in different quantities is convincing proof that the configurations of the two original asymmetric carbon atoms have exercised a directive influence on the configuration of the carbon atom, which becomes asymmetric during the action of the aluminium chloride.

When the four bromo-acids, A, B, C, D, are boiled with sodium carbonate, they are all decomposed with elimination of hydrogen bromide and formation of tetrahydro-xylic acids,



and according to theory, four different externally compensated acids should be formed in this way, as will be seen at once if the bromo-acids are represented graphically and the corresponding tetrahydro-xylic acids written underneath.



As in this change (elimination of hydrogen bromide), only one of

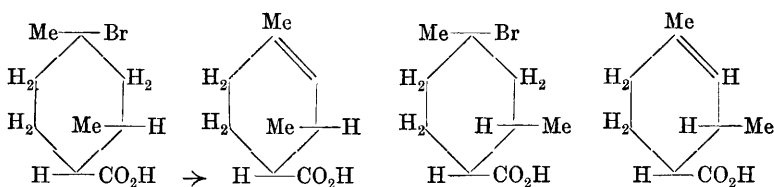
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the three asymmetric carbon atoms in the bromohexahydro-xylic acids disappears, each of [the unsaturated acids formulated above still contains two asymmetric carbon atoms and is an externally compensated compound; the optical relationship of these four racemic compounds may therefore be expressed by the same signs as before, omitting that given to the $>\text{CMeBr}$ -group. The tetrahydro-xylic acid, C, will therefore be $[-c-b, +c+b]$, D will be $[-c+b, +c-b]$, and A and B will be either $[+c+b, -c-b]$ or $[-c+b, +c-b]$.

The actual results of the experiments on the behaviour of the four bromo-acids with sodium carbonate show that the three bromo-acids, A, B, and D, give three distinct tetrahydro-xylic acids, A, B, and D, which melt at 80° , 68° , and 87° respectively, but in the case of the bromo-acid, C, the material at our disposal was so small that we were unable to purify the acid formed sufficiently to determine its melting point accurately; most probably it is the fourth isomeride indicated by theory.

There is, however, at present no proof of the actual position of the double linkings in the tetrahydro-xylic acids, and the formulæ given above are only intended as examples of the direction in which elimination of hydrogen bromide may possibly take place.

It is clear that the relationship, for example, between the *cis*-bromo-acids, C and D, and their corresponding tetrahydro-xylic acids might equally well be written thus :

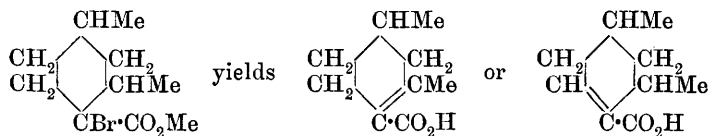


In order, if possible, to obtain some clue as to the constitution of these unsaturated acids, experiments (see pp. 1388, 1393) were instituted on the oxidation of the tetrahydro-xylic acids, A and D, but the results obtained with the small quantities of these acids available were not sufficient to throw much light on this point.

When treated with fuming hydrobromic acid, the three tetrahydro-xylic acids A, B, and D are quantitatively reconverted into the bromo-acids from which they were derived by elimination of hydrogen bromide, the bromine atom becoming attached in each case, therefore, to the tertiary carbon atom carrying the methyl group.

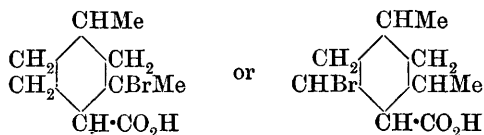
Another characteristic of these acids is that when warmed with sulphuric acid at 80° they are rapidly oxidised to xylic acid and, indeed, this change takes place at the ordinary temperature if the solution in sulphuric acid is allowed to stand for some days.

During the course of a series of experiments on the reduction of xylic acid by means of sodium and *iso*amyl alcohol, Bentley and Perkin (Trans., 1897, 71, 173) obtained a tetrahydro-xylic acid which melts at 107° and is isomeric with the tetrahydro-xylic acids, A, B, and D, described in the present paper. That this acid is either Δ^1 - or Δ^6 -tetrahydro-xylic acid is conclusively proved by the fact that it is formed from methyl α -bromohexahydro-xylate by hydrolysis and elimination of hydrogen bromide.



In order to obtain further evidence in support of the assumption that the acids A, B, and D are tetrahydro-xylic acids, we decided to further examine this acid of melting point 106°, and as the result of our experiments we find in properties and behaviour with reagents it shows a quite striking similarity to the acids A, B, and D.

Thus, for example, when heated with sulphuric acid, it is readily oxidised to xylic acid, and it combines readily with hydrogen bromide, yielding a new bromohexahydro-xylic acid which melts at 127° and the constitution of which is doubtless represented by one of the formulæ,



It is remarkable that the five bromohexahydro-xylic acids described in this paper should all melt between 127° and 137°, and that the three tetrahydro-xylic acids, A, B, and D, should all melt close together and be so very similar in properties. The impossibility of readily distinguishing between these different isomeric modifications has very greatly added to the difficulties of this research.

EXPERIMENTAL.

Separation of the Lactones produced by the action of Aluminium Chloride on Camphoric Anhydride.

In the introduction, it was stated that a new method for separating these lactones had been worked out, which gives much more satisfactory results than that described in the previous paper and is especially convenient for the rapid isolation of the *cis*-lactones. This method is as follows:

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The solution of the camphoric anhydride in chloroform is first treated with aluminium chloride exactly as described in the previous paper, and after separating the *isolauronic* acid by means of potash, the chloroform solution of the lactones is distilled from the water-bath until as much chloroform as possible has been removed. The dark-brown residue, which often still contains 50 per cent. of its weight of chloroform, is fractionated twice under reduced pressure, when the whole passes over at $170-180^{\circ}$ (80 mm.) as a colourless oil, the weight of which from 1 kilo. of camphoric anhydride is usually about 130 grams. The mixed lactones from 2 kilos. of camphoric anhydride were now treated on the water-bath with sufficient moderately concentrated barium hydroxide to just dissolve them, the solution filtered from a small quantity of a dark-coloured impurity, the filtrate acidified, saturated with calcium chloride, and extracted at least 20 times with pure ether. The ethereal solution was then evaporated and the residual thick oil submitted to distillation in a rapid current of steam (*a*). When oil ceased to come over with the condensed water, the distillate was saturated with ammonium sulphate, repeatedly extracted with ether, and after evaporating off the ether, the oily lactone mixture was again boiled with barium hydroxide until dissolved; the solution was then cooled to 60° , acidified with excess of hydrochloric acid, and kept at 60° for 5 minutes.

After saturating with calcium chloride, the whole was extracted twenty times with ether; the ethereal solution was then well washed with strong sodium carbonate (*b*), dried over calcium chloride, evaporated, and the residual colourless oil distilled under reduced pressure.

During the first distillation, the whole quantity passed over at $174-177^{\circ}$ (80 mm.) and weighed 120 grams; on distilling again, more than 100 grams passed over between 175° and 176° under the same pressure. On analysis:

0.1176 gave 0.3017 CO_2 and 0.099 H_2O . $\text{C} = 70.0$; $\text{H} = 9.3$.

$\text{C}_9\text{H}_{14}\text{O}_2$ requires $\text{C} = 70.1$; $\text{H} = 9.1$ per cent.

This lactone was slightly *laevorotatory*, the observed rotation in a 100 mm. tube being only -4.24° .

In order to make quite sure that this oil was quite free from even traces of the lactones of the *trans*-acids A and B, it was again dissolved in baryta water, and the solution, after standing until quite cold, acidified with excess of hydrochloric acid, care being taken that the temperature did not rise above 15° . The whole was then allowed to stand for 24 hours, when it was noticed that the oily layer, which at first was quite thick, had become much more mobile. After extracting as usual with ether, the ethereal solution was washed repeatedly with

sodium carbonate (*c*), dried over calcium chloride, and evaporated, when 90 grams of a lactone were obtained which distilled constantly at 145° under 25 mm., and at 255° under 760 mm. pressure, and had a rotation in a 100 mm. tube of -5.3° . Experiment showed that further treatment with baryta, exactly as just described, did not alter this rotation or the other physical constants of the oil. It was therefore clear that it was now quite free from the lactones of the *trans*-A- and B-acids, and consisted of the lactones of the *cis*-acids only. In this condition, it was employed in the experiments described in this paper. On analysis, the following numbers were obtained :

0.1646 gave 0.4237 CO_2 and 0.1376 H_2O . $\text{C} = 70.2$; $\text{H} = 9.3$.

$\text{C}_9\text{H}_{14}\text{O}_2$ requires $\text{C} = 70.1$; $\text{H} = 9.1$ per cent.

The density and magnetic rotation of this oil were determined by W. H. Perkin, sen., with the following results :

Density determinations : $d\ 10^{\circ}/10^{\circ} = 1.0503$; $d\ 15^{\circ}/15^{\circ} = 1.0471$; $d\ 20^{\circ}/20^{\circ} = 1.0441$.

Magnetic rotation.

<i>t.</i>	Sp. rotation.	Mol. rotation.
15°	1.0562	8.632

These numbers differ considerably from the previous determinations made with the mixture of *cis*- and *trans*-lactones, the density was then at $10^{\circ}/10^{\circ} = 1.0606$ and the magnetic rotation 8.200 , and they naturally differ still more for the values found for the lactone of the *trans*-acid A (see p. 1390), which are as follows : Density, $d\ 10^{\circ}/10^{\circ} = 1.0640$; magnetic rotation, 8.174 .

Action of Sulphuric Acid on the cis-Lactones. Formation of Xylic Acid.—The oily lactone just described dissolves in concentrated sulphuric acid with development of a good deal of heat, and if the solution is heated at 80° it rapidly darkens and much sulphur dioxide is evolved. After heating for 15 minutes, the product was poured into water and allowed to stand overnight ; the dark precipitate was then collected, dissolved in sodium carbonate, and boiled with purified animal charcoal. On acidifying, a rather dark coloured crystalline mass separated, and this, after drying, was distilled and the distillate crystallised from dilute acetic acid, when almost colourless crystals separated which melted at 124 — 125° and consisted of *xylic acid*, $\text{C}_6\text{H}_8(\text{CH}_3)_2 \cdot \text{CO}_2\text{H}$. On analysis :

0.1298 gave 0.3422 CO_2 and 0.0794 H_2O . $\text{C} = 71.9$; $\text{H} = 6.8$.

$\text{C}_9\text{H}_{10}\text{O}_2$ requires $\text{C} = 72.0$; $\text{H} = 6.7$ per cent.

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Separation of the Substances Removed during the Purification of the cis-Lactones.

During the purification of the *cis*-lactones, as described in the previous section, more than half of the original mixture of *cis*- and *trans*-lactones was removed during the steam distillation and afterwards by the repeated extractions with sodium carbonate. The investigation of this material was carried out briefly as follows. The sodium carbonate extract *b* (p. 1382) was acidified, saturated with calcium chloride, and repeatedly extracted with ether; the ethereal solution, after carefully drying over calcium chloride and evaporating to a small bulk, yielded, on standing, 17 grams of colourless crystals, which, after recrystallisation from ether, melted at 158—160° and consisted of pure A-hydroxyhexahydro-xylic acid (this vol., p. 345).

The ethereal mother liquors of these crystals deposited, on spontaneous evaporation, several crops of crystals which, when left in contact with porous porcelain to remove oily impurity, became hard and colourless, and on subsequently recrystallising from ether, yielded further quantities of the A-acid.

The total amount of pure A-acid obtained from this sodium carbonate extract was 27 grams.

It is rather remarkable that such considerable quantities of the A-acid should be found at this place, since its presence here shows that it must have been carried over during the steam distillation, yet in the previous paper (p. 345) it was shown that the pure A-acid is not volatile as such with steam, nor is it converted into its volatile lactone under these conditions. It therefore follows that in the present case its volatility must be due to the presence of the lactones of the *cis*-acids, which carry it over during the steam distillation.

The sodium carbonate extract *c* (p. 1383) was acidified with excess of hydrochloric acid, when a thick, heavy oil separated, which on standing at the ordinary temperature for 3 weeks became much less dense and more mobile. The whole was then saturated with calcium chloride, repeatedly extracted with ether, the ethereal solution washed well with strong sodium carbonate (*d*), dried over calcium chloride, and evaporated. In this way, about 80 grams of an oil were obtained which distilled constantly at 163° (40 mm.), and had a rotation of -4.4° in a 100 mm. tube. This was further purified by solution in baryta water and treatment with hydrochloric acid at the ordinary temperature, as previously described in purifying the main bulk of the *cis*-lactones (p. 1382); it then yielded more than 70 grams of pure *cis*-lactones. Thus, without allowing for considerable loss during purification, the total yield of the *cis*-lactones from 250 grams of the mixed lactones

is at least 170 grams. The sodium carbonate extract *d* was treated in exactly the same way as *c*, and yielded small quantities of the *cis*-lactones and about 0.5 gram of pure crystalline A-acid.

The steam distillation flask, *a*, contained a considerable quantity of a thick oil; this was repeatedly extracted with ether and after drying the ethereal solution and evaporating, the residual oil was several times carefully distilled. During the first distillation, much water was given off and a colourless oil was collected at 160–170° under 35 mm. pressure, leaving in the flask a slight crystalline residue of camphoric anhydride which had escaped the action of the aluminium chloride. In order to remove this as far as possible, the oil was carefully dried and several times slowly fractionated under 35 mm. pressure, when almost the whole passed over at 155–160°.

When this oil was dissolved in baryta water and, after acidifying, the acids extracted with ether, an oil was obtained which, even after standing for months, deposited only a very few crystals; it was therefore distilled under the ordinary pressure, when almost the whole quantity came over at 252–255° (750 mm.) The distillate was dissolved in ether and repeatedly extracted with dilute potash, and the alkaline solution, after freeing from ether, was acidified, when a considerable quantity of an oil was precipitated which, on standing, became semi-solid.

In contact with a porous plate, the oily impurity was soon absorbed and a crystalline mass resulted, which after crystallising from dilute acetic acid melted at 78–80° and consisted of A-tetrahydro-xylic acid (p. 1392).

0.1481 gave 0.3802 CO₂ and 0.1224 H₂O. C = 70.0; H = 9.2.

C₉H₁₄O₂ requires C = 70.1; H = 9.1 per cent.

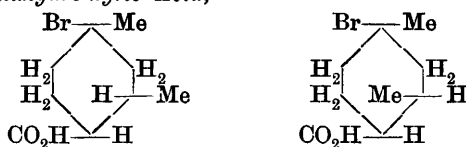
This acid, which weighed about 3 grams, is undoubtedly formed by the elimination of water from A-hydroxyhexahydro-xylic acid, during the frequent distillations, since it is elsewhere proved (p. 1391) that small quantities of A-tetrahydro-xylic acid are always produced when the A-hydroxy-acid is distilled. The ethereal solution which had been separated from the alkaline extract, gave, on evaporation, a colourless oil, and this was converted into the hydroxy-acid by treatment with baryta in the usual way.

On long standing, the thick, oily acid partially crystallised and when spread on a porous plate a colourless mass of crystals was obtained, which, after recrystallisation from ether, melted at 158–160° and consisted of A-hydroxyhexahydro-xylic acid. The porous plate was broken up and extracted in a Soxhlet apparatus with ether, and the ethereal extract, after a long series of fractional crystallisations, yielded about 2 grams of A-hydroxy-acid and 5 grams of pure B-hydroxy-

hexahydro-xylic acid, which melted at 113° and on distillation was decomposed with elimination of water and formation of the pure B-lactone melting at 44° .

It is remarkable that so little of the B-acid should have been obtained on this occasion, because in the previous experiments (*loc. cit.*, p. 346), a relatively large quantity of it could always be isolated with comparative ease. This great difference in yield proves that the relative quantity of the lactones formed by the action of aluminium chloride on camphoric anhydride varies with unavoidable slight alterations in the conditions of the experiment.

Action of Hydrobromic Acid on the cis-Lactones of Hydroxyhexahydro-xylic Acid. Formation of the cis-Modifications (C and D) of Bromohexahydro-xylic Acid,



When the mixed *cis*-lactones, in quantities of not more than 5 grams are rapidly mixed with four times the volume of fuming hydrobromic acid (saturated at 0°), they rapidly and completely dissolve, but in a few seconds the solution becomes opaque owing to the separation of oil. The oil collects as a clear layer on the surface of the acid and after standing for 24 hours solidifies to a colourless, crystalline mass. This is powdered, washed with water on the pump, and left in contact with porous porcelain until quite dry; it is then ground up with light petroleum (b. p. $35-40^{\circ}$), in which it is very sparingly soluble, and washed with this solvent on the pump. The latter operation not only removes traces of coloured impurity but dissolves a small quantity of unchanged lactone, which always appears to be present, even when a large excess of hydrobromic acid is used. The colourless residue is *rapidly** dissolved in boiling light petroleum (b. p. $80-90^{\circ}$), a pinch of purified animal charcoal added, the liquid filtered, and carefully watched as it crystallises. A small crop of prismatic crystals of the C-bromo-acid quickly forms, then there is a pause in the crystallisation, and if the liquid is quickly poured off and well stirred, a mass of needles of the D-bromo-acid rapidly separates. By repeating this operation, it is quite easy to completely separate these two acids.

C-Bromohexahydro-xylic Acid crystallises in glistening, prismatic needles and melts at about $137-138^{\circ}$ if the determination is rapidly

* Unless this operation is very rapidly performed, the bromo-acids decompose with evolution of quantities of hydrogen bromide.

carried out, but as it decomposes on heating with evolution of hydrogen bromide, a considerably lower melting point will be observed if the operation is conducted slowly. On analysis:

0.2108 gave 0.1697 AgBr. Br = 34.2

$C_9H_{15}O_2Br$ requires Br = 34.0 per cent.

This C-bromo-acid is very sparingly soluble in light petroleum and so similar in its other properties to A-bromohexahydro-xylic acid (m. p. 133°, p. 1391) that it was at first thought that the two were identical. Carefully purified specimens of each of these two acids were therefore intimately mixed, and it was then found that the melting point of the mixture was about 100–105°, a conclusive proof that the two bromo-acids C and A are not identical.

So far as could be seen with the small quantity of material at our disposal (2 grams dissolved in 100 c.c. of pure ether), C-bromohexahydro-xylic acid is inactive; it dissolves readily in sodium carbonate, and on acidifying the solution and heating to boiling, some of the tetrahydro-xylic acid formed appears to be converted into the C-lactone; if this is removed by making alkaline with sodium carbonate and extracting with ether and the alkaline solution acidified, an oil separates which solidifies on standing and probably consists of C-tetrahydro-xylic acid. From this small experiment, the C-bromo-acid appears to behave somewhat differently from the A-, B-, and D-bromo-acids, which do not yield lactones when treated in this way. This difference, however, requires confirmation before it can be definitely accepted.

The *D-bromohexahydro-xylic acid*, after complete separation from the C-acid by repeated recrystallisation from light petroleum, melts at about 128–130° and separates from light petroleum, in which it is sparingly soluble in the cold, as a voluminous mass of needles, which completely fill the liquid. It is readily soluble in ether and a solution in this solvent containing 5 grams in 100 c.c. was found, on examination, to be quite inactive.

It dissolves readily in dilute sodium carbonate, and on boiling the solution elimination of hydrogen bromide takes place with formation of *D-tetrahydro-xylic acid* (see next section). An analysis of D-bromohexahydro-xylic acid yielded the following results:

0.1896 gave 0.1514 AgBr. Br = 34.1.

$C_9H_{15}O_2Br$ requires Br = 34.0 per cent.

It may, at first sight, seem remarkable that the bromo-acids C and D should show no signs of activity, although the *cis*-lactones from which they were prepared had a rotation of -5.3° in a 100 mm. tube. It has, however, already been pointed out that, in the formation of these lactones from camphoric anhydride, racemisation must have taken

place, and the fact that the *cis*-lactones always have a small rotation simply shows that it has not been quite complete.

When the *cis*-lactones are converted into the bromo-acids and then purified by recrystallisation from light petroleum, the externally compensated modifications being less soluble (as is frequently the case) are easily obtained in a pure state, and the traces of the active modifications remain in the mother liquor.

That the light petroleum mother liquor of these inactive bromo-acids contains active substances was proved by direct experiment, but the solutions were unfortunately too highly coloured to allow of exact measurements being made.

D-Tetrahydro-xylic Acid, $C_8H_{15} \cdot CO_2H$.

D-Bromohexahydro-xylic acid dissolves readily in sodium carbonate solution, and if the solution is heated to boiling for a few seconds and then cooled and acidified, an acid separates either at once in the crystalline form, or else as an oil which rapidly solidifies. The solid mass, after drying on a porous plate, melts at about 80° , and is so soluble in organic solvents that it is difficult to purify it by recrystallisation.

It crystallises, however, in the form of pearly plates from dilute methyl alcohol, but the operation is rather troublesome, since, unless exactly the right conditions of concentration and temperature have been found, the acid always separates as an oil.

D-Tetrahydro-xylic acid melts at 87° , and distils without decomposition; it is almost insoluble in water, but readily volatile in a current of steam. On analysis :

0.1571 gave 0.4020 CO_2 and 0.1298 H_2O . $C = 69.8$; $H = 9.2$.

$C_8H_{14}O_2$ requires $C = 70.1$; $H = 9.1$ per cent.

When left in contact with fuming hydrobromic acid, this acid is rapidly converted into the D-bromohexahydro-xylic acid from which it had been prepared.

Oxidation of D-Tetrahydro-xylic Acid.—When this unsaturated acid is dissolved in dilute sodium carbonate and mixed with potassium permanganate, the latter is instantaneously reduced, and as it seemed probable that results throwing light on the position of the double linking in this acid (p. 1380) might be obtained by studying this oxidation, the following experiment was carried out.

The pure acid (5 grams) was dissolved in dilute sodium carbonate mixed with a quantity of powdered ice and oxidised, in a porcelain dish fitted with a turbine, with small quantities of permanganate until the colour remained permanent for 3 minutes. Sodium sulphite was then added to destroy the excess of permanganate, the

liquid heated to boiling, and the filtrate and washings of the manganese precipitate evaporated to a small bulk. The concentrated solution, after acidifying with acetic acid, gave no precipitate with calcium sulphate, showing that no oxalic acid had been formed. The whole was then acidified with hydrochloric acid and distilled in steam to remove a very small quantity of a volatile substance which appeared to be present. The residue in the steam distillation flask was saturated with ammonium sulphate, and repeatedly extracted with ether, the ethereal solution was dried over calcium chloride and evaporated, when a pale yellow oil was obtained which, after standing over sulphuric acid in a vacuum desiccator for some days, showed no signs of crystallising. It was analysed with the following result :

0.1571 gave 0.3290 CO_2 and 0.1105 H_2O . $\text{C} = 57.1$; $\text{H} = 7.8$.

$\text{C}_9\text{H}_{14}\text{O}_4$ requires $\text{C} = 58.0$; $\text{H} = 7.5$ per cent.

This acid is very readily soluble in water and is monobasic, since 0.207 gram was found, on titration with decinormal caustic soda, to neutralise 0.045 NaOH , whereas this amount of a monobasic acid, $\text{C}_9\text{H}_{14}\text{O}_4$, should have neutralised 0.044 NaOH .

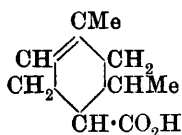
The remainder of the acid was dissolved in water and oxidised with a slight excess of potassium dichromate and dilute sulphuric acid on the water-bath, the product was then saturated with ammonium sulphate and extracted 20 times with ether. After drying over calcium chloride and evaporating, an oil was obtained which on standing over sulphuric acid became semi-solid ; when this was spread on a porous plate, the oily impurity was soon completely absorbed, leaving a hard, crystalline mass which melted roughly at 140° .

This crude acid is very soluble in water, but a concentrated solution on standing deposits colourless plates like sugar crystals which, after recrystallisation, melt at 167° with slight previous softening. On analysis :

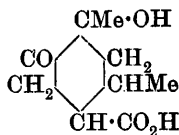
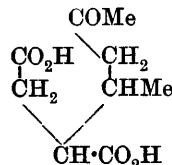
0.1121 gave 0.2206 CO_2 and 0.0704 H_2O . $\text{C} = 53.6$; $\text{H} = 7.0$.

$\text{C}_9\text{H}_{14}\text{O}_5$ requires $\text{C} = 53.5$; $\text{H} = 6.9$ per cent.

The new acid is dibasic, since 0.1076 gram required for neutralisation 0.0420 NaOH , whereas this quantity of a dibasic acid, $\text{C}_9\text{H}_{14}\text{O}_5$, should neutralise 0.0426 NaOH . It shows all the reactions of a ketonic acid, and when treated with potassium hydroxide and bromine it yields bromoform ; it therefore probably contains the group $\text{Me}\cdot\text{CO}$; unfortunately, the amount of material at our disposal was too small to allow of the isolation and identification of the acid which is formed during this oxidation. These results seem, nevertheless, to indicate the probability of the oxidation of D-tetrahydro-xylic acid proceeding somewhat in the following way



D-Tetrahydro-xylic acid.

Acid, $C_9H_{14}O_4$.Acid, $C_9H_{14}O_5$
(m. p. 167°).

The position of the double-bond in D-tetrahydro-xylic acid has, of course, not been definitely ascertained, and the formula given here has simply been selected to serve as an illustration of the possible mechanism of the oxidation.

The Lactone of A-Hydroxyhexahydro-xylic Acid and its Conversion into A-Bromohexahydro-xylic Acid and into A-Tetrahydro-xylic Acid.

Twenty grams of pure A-hydroxyhexahydro-xylic acid (m. p. 160°) were distilled and the distillate dissolved in ether and extracted three times with carbonate of soda to remove traces of an acid which was present (see below). The ethereal solution was then dried over calcium chloride, evaporated and the residual lactone twice fractionated, when practically the whole quantity distilled at $263\text{--}265^\circ$ under 748 mm. pressure the fraction boiling constantly at 264° being collected separately and forwarded to W. H. Perkin, sen., in order that its specific gravity and magnetic rotation might be determined. This specimen had a permanent rotation of $+1.96^\circ$ in a 100 mm. tube. The density and magnetic rotation determinations gave the following results :

Density. $d\ 10^\circ/10^\circ = 1.0640$; $d\ 15^\circ/15^\circ = 1.0606$; $d\ 20^\circ/20^\circ = 1.0575$.

Magnetic rotation.

<i>t.</i>	Sp. rotation.	Mol. rotation.
15.4°	1.0131	8.174.

This *trans*-lactone has therefore a higher sp. gr. and lower magnetic rotation than the *cis*-lactones (p. 1383). During its journey by train, it solidified to a hard mass of crystals which although very soluble in light petroleum (b. p. $30\text{--}35^\circ$), crystallised from this solvent in colourless needles melting at about 55° . On analysis :

0.1963 gave 0.5034 CO_2 and 0.1641 H_2O . C = 69.9 ; H = 9.2.

$C_9H_{14}O_2$ requires C = 70.1 ; H = 9.1 per cent.

In order to prove that this solid lactone was really the *lactone* of A-hydroxyhydro-xylic acid, it was warmed with a little baryta water,

in which it very readily dissolved with formation of the barium salt of the hydroxy-acid. The solution was acidified, extracted repeatedly with ether, and the ethereal solution, after drying over calcium chloride, evaporated to a small bulk, when crystalline crusts were deposited which melted at 160° and consisted of pure A-hydroxyhexahydro-xylic acid. The lactone of this acid was previously described (this vol., 345) as an oil boiling at $261\text{--}264^{\circ}$ under 748 mm. pressure, and this specimen showed no signs of crystallising either after standing for 6 months or on cooling in a mixture of ice and salt; when, however, a crystal of the lactone melting at 55° was put into the liquid, crystallisation started at once and the whole soon solidified to a hard mass of crystals.

The sodium carbonate solution which had been employed in purifying the lactone (see above) gave, on acidifying, no precipitate, but it was noticed that after standing for some days a small quantity of needle-shaped crystals had separated. These were collected and dried on a porous plate at the ordinary temperature; they then melted at 80° , and were found to consist of pure A-tetrahydro-xylic acid (see below). It is therefore evident that A-hydroxyhexahydro-xylic acid on distillation is almost quantitatively converted into its lactone, but that a very small amount of the acid is decomposed in another direction with elimination of water and formation of A-tetrahydro-xylic acid.

A-Bromohexahydro-xylic Acid.—The lactone of A-hydroxyhexahydro-xylic acid dissolves rapidly and completely in fuming hydrobromic acid (saturated at 0°), but the solution soon becomes cloudy and an oily layer separates which becomes crystalline in a few minutes. After standing for about an hour, the hard, crystalline mass was ground up with water, washed well on the pump, dried on a porous plate at the ordinary temperature, and then rapidly recrystallised from boiling light petroleum (b. p. $60\text{--}70^{\circ}$). The minute, glistening prisms which rapidly separated were analysed, with the following results:

0.1511 gave 0.1121 AgBr. Br = 33.9.

$\text{C}_9\text{H}_{15}\text{O}_2\text{Br}$ requires Br = 34.0 per cent.

A-Bromohexahydro-xylic Acid melts at about 133° almost without decomposition; it is readily soluble in most organic solvents, but only very sparingly so in cold light petroleum; its solution in ether is inactive. In appearance and melting point it is so similar to C-bromohexahydro-xylic acid that we were at first inclined to believe in the identity of the two. We therefore mixed equal quantities of the pure substances, and found that the melting point of the mixture was about $100\text{--}105^{\circ}$; it is therefore clear that the acids are not identical.

Considerable quantities of A-bromohexahydro-xylic acid were also prepared by grinding up A-hydroxyhexahydro-xylic acid with fuming

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hydrobromic acid. The crystals of the acid become converted into a gummy mass, but this soon solidifies, and after washing well on the pump and drying on a plate, a mass of colourless crystals is obtained which consists of the almost pure A-bromo-acid.

A-Chlorohexahydro-xylic Acid.—When A-hydroxyhexahydro-xylic acid is boiled for a few seconds with concentrated hydrochloric acid, it does not yield the corresponding lactone, but is converted into an oil which, on cooling, solidifies. This was collected, washed well with water, and, after drying over sulphuric acid, rubbed on a porous plate with light petroleum (b. p. 35–40°) until free from traces of oil. The colourless, crystalline residue, which was not sufficient for recrystallisation, melted at about 92°, and, on analysis, gave numbers which showed that it evidently consisted of A-chlorohexahydro-xylic acid :

0·1547 gave 0·1146 AgCl. Cl = 18·3.

$C_9H_{15}O_2Cl$ requires Cl = 18·5 per cent.

A-Tetrahydro-xylic Acid.—This acid is readily obtained by dissolving A-bromohexahydro-xylic acid in excess of sodium carbonate and boiling the solution for a few minutes ; it separates on acidifying in an almost pure condition as a colourless, crystalline precipitate. For analysis, it was recrystallised from dilute acetic acid, and thus obtained in the form of colourless groups of needles, which melt at 80° :

0·1587 gave 0·4066 CO_2 and 0·1321 H_2O . C = 69·9 ; H = 9·2.

$C_9H_{14}O_2$ requires C = 70·1 ; H = 9·1 per cent.

The acid is almost insoluble in cold water ; if, however, it is boiled with water, a small quantity dissolves, and on cooling separates in four-sided plates which melt at 80° ; it is readily volatile in steam. Most organic solvents dissolve it freely, but it is comparatively sparingly soluble in cold light petroleum (b. p. 35–40°). The acid seems to have no tendency to yield a lactone on boiling with dilute acids ; it separates, for example, unchanged from 20 per cent. sulphuric acid, even after boiling for 5 minutes. When mixed with fuming hydrobromic acid, it becomes soft, but does not dissolve, and from the mixture, after standing for 3 hours, water precipitates a mass of colourless crystals which, after washing with water, drying on a porous plate, and recrystallising from light petroleum, melts at 133°, and consists of pure A-bromohexahydro-xylic acid.

Oxidation of A-Tetrahydro-xylic Acid.—This acid, when dissolved in sodium carbonate, instantly decolorises permanganate, even at temperatures considerably below 0°, and it therefore seemed possible that, by studying this oxidation, results might be obtained which would throw some light on the position of the double bond in the molecule (see p. 1380).

Six grams of the pure acid were therefore dissolved in dilute sodium carbonate, mixed with powdered ice, and treated with a 3 per cent. solution of permanganate until the pink colour remained permanent for at least 2 minutes.

The slight excess was then removed with sodium sulphite, the whole heated to boiling, filtered, and the filtrate and washings of the manganese precipitate evaporated to a small bulk and tested for oxalic acid, but no trace of this acid could be detected. After acidifying and extracting repeatedly with pure ether, the ethereal solution was dried over calcium chloride and evaporated, when a thick, brownish, oily acid was obtained, which was left over sulphuric acid in a vacuum desiccator for 4 days and then analysed, with the following result :

0.1254 gave 0.2622 CO_2 and 0.0887 H_2O . $\text{C}=57.0$; $\text{H}=7.9$.

$\text{C}_9\text{H}_{14}\text{O}_4$ requires $\text{C}=58.0$; $\text{H}=7.5$ per cent.

This acid is readily soluble in water, and is evidently ketonic in character, since its aqueous solution gives at once a yellow, oily precipitate with phenylhydrazine acetate. That it is monobasic is shown by the results of the titration with decinormal sodium hydroxide, when 0.2366 gram required for neutralisation 0.0508 gram NaOH , whereas this quantity of a monobasic acid, $\text{C}_9\text{H}_{14}\text{O}_4$, should neutralise 0.0509 gram NaOH .

We next oxidised this acid with potassium dichromate and dilute sulphuric acid, exactly as described in the case of the isomeric acid from D-tetrahydro-xylic acid (p. 1389), and on extracting the product with ether, an oily acid was obtained which did not crystallise even after standing over sulphuric acid in a vacuum desiccator for some weeks. This oil gives an oily precipitate with phenylhydrazine acetate, and yields bromoform in considerable quantity when treated with bromine and potassium hydroxide ; it is, therefore, evidently a ketonic acid, but as it did not solidify it was not further investigated.

Formation of B-Bromohexahydro-xylic Acid and of B-Tetrahydro-xylic Acid from the Lactone of B-Hydroxyhexahydro-xylic Acid.

The lactone used in these experiments was prepared by distilling the pure B-hydroxy-acid as described in the previous communication, it boiled at $258-260^\circ$ under 745 mm. pressure and melted at 44° ; it was particularly noticed that even after repeated distillation there was no appreciable alteration in the melting point, clearly proving that even at the high temperature of the distillation, no change into a *cis*-modification takes place. When this lactone is melted and mixed with three times its volume of fuming hydrobromic acid (saturated at 0°), it dissolves, but the solution suddenly becomes opaque and an oil

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separates which begins to crystallise at once, the change from B-lactone to crystalline bromo-acid being apparently even more rapid than when the A-lactone is similarly treated (p. 1391). The product was mixed with water, the crystals collected, allowed to dry on a porous plate at the ordinary temperature, and then crystallised from light petroleum (b. p. 60—70°). On analysis :

0.1520 gave 0.1212 AgBr. Br = 33.8.

$C_9H_{15}O_2Br$ requires Br = 34.0 per cent.

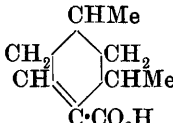
B-Bromohexahydro-xylic Acid melts at about 128° with decomposition, and is more readily soluble in light petroleum than the corresponding A-acid. It dissolves easily in sodium carbonate, and if the solution is boiled for a few minutes, then cooled and acidified, a crystalline precipitate separates which, after crystallising from dilute acetic acid, melts at about 68° and consists of B-tetrahydro-xylic acid.

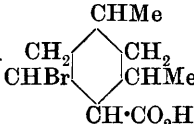
0.1592 gave 0.4078 CO_2 and 0.1303 H_2O . C = 69.9 ; H = 9.1.

$C_9H_{14}O_2$ requires C = 70.1 ; H = 9.1 per cent.

B-Tetrahydro-xylic Acid is very sparingly soluble in cold water, but it may be crystallised from large quantities of boiling water ; its solution in sodium carbonate instantly decolorises permanganate.

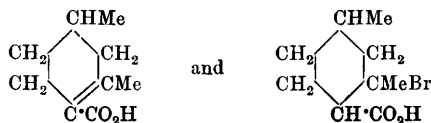
When left in contact with fuming hydrobromic acid, it becomes soft but does not dissolve, and if after 2 hours water is added, a white, crystalline precipitate separates which crystallises from light petroleum in woolly needles melting at 128° and consisting of pure B-bromohexahydro-xylic acid.

Δ^1 -Tetrahydro-xylic Acid, , and its conversion into

2-Bromohexahydro-xylic Acid,* , and into Xylic Acid.

Δ^1 -Tetrahydro-xylic acid is structurally isomeric with the tetrahydro-xylic acids, A, B, and D, and is the acid which is formed when

* The only other formulæ possible for these acids are :



xylic acid is reduced with sodium and *isoamyl* alcohol, and when methyl α -bromohexahydro-xylic acid is hydrolysed with alcoholic potash (Bentley and Perkin, *Trans.*, 1897, **71**, 173; Lees and Perkin, *this vol.*, 338), it melts at 107°. When it is mixed with fuming hydrobromic acid, it does not readily dissolve, but the crystals are seen to undergo gradually a change in appearance. In order to ensure the reaction being complete, the mixture was sealed up in a tube and shaken from time to time, and after two days water was added, the crystals collected on the pump, and allowed to dry on a porous plate in contact with air. The substance then melted at about 124–125°, but after crystallising from light petroleum (b. p. 50–60°), colourless, glistening prisms were obtained which melted at 127° without decomposition. On analysis :

0.152 gave 0.1208 AgBr. Br = 33.8.

$C_9H_{15}O_2Br$ requires Br = 34.0 per cent.

When treated with sodium carbonate, 2-bromohexahydro-xylic acid shows quite a different behaviour from that observed in the case of the A, B, and D-bromohexahydro-xylic acids (pp. 1388, 1392, 1394). It dissolves at first in the sodium carbonate, forming a clear solution which then rapidly becomes cloudy, and an oil separates which is very readily volatile in steam, smells like a hydrocarbon, and is evidently tetrahydro-*m*-xylene.



After boiling until the hydrocarbon was expelled, the clear solution gave on acidifying a colourless, crystalline precipitate which, when drained on a tile and dried at 90°, melted sharply at 107–108°, and evidently consisted of Δ^1 -tetrahydro-xylic acid.

Action of Sulphuric Acid on Δ^1 -Tetrahydro-xylic Acid.—This acid dissolves in concentrated sulphuric acid, and when the solution is heated at 100° for 10 minutes, sulphur dioxide is rapidly evolved and the dark coloured liquid, on dilution with water, deposits a yellow, crystalline precipitate. This was collected, distilled, and recrystallised from dilute acetic acid, when colourless crystals were obtained which melted at 124° and consisted of xylic acid. It is therefore evident that, in its behaviour with hydrobromic acid and with sulphuric acid Δ^1 -tetrahydro-xylic acid shows the greatest similarity to the A, B, and D tetrahydro-xylic acids described in this paper.

In conclusion we wish to express our thanks to Professors F. S. Kipping and W. J. Pope for many valuable suggestions that they were good enough to make during the course of this research.

We also wish to state that the cost of the large amount of material which was required in this research has been to a large extent defrayed by repeated grants from the Government Grant Fund of the Royal Society.

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