XCI.—*Studies of the Terpenes and allied Compounds.*
Note on Ketopinic acid—a product of the Oxidation
of the solid Hydrichloride (Chlorocamphydrene)
prepared from Pinene.

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NOTWITHSTANDING the amount of attention lavished on the study of the terpenes and allied compounds, we are still unaware of the genetic connection subsisting among the greater number; in fact, it can scarcely be definitely asserted of any one of them that we know its constitution: the arguments made use of too often involve assumptions, the acceptance of which requires an excess of credulity not easily exercised.

The protean transformations to which they give rise are truly remarkable; in no other group is such extraordinary plasticity noticeable; but this fecundity is a source of perplexity, and, in a measure, the bane of progress, however gratifying to the vanity of the worker anxious to associate his name with the preparation of new compounds.

The group is apparently one altogether peculiar in type, and the difficulty of arriving at final decisions is greatly enhanced by the

fact that hitherto our studies have been entirely analytical; synthetic observations calculated to give fixity to our opinions are sorely needed. But in ultimately solving the problems which the terpenes and their congeners present, we shall undoubtedly enormously increase our knowledge of chemical processes, and more especially of a class of operations of great biological significance; hence the importance of not relaxing our efforts.

Among the many interesting educts to which terpenes give rise, perhaps the most striking of all is the solid hydrichloride obtained by the interaction of terebenthene or pinene and hydrogen chloride; its extreme stability especially is very remarkable when the readiness with which it is produced is taken into account. Although prepared directly from pinene, it is open to question whether it be an immediate derivative of that hydrocarbon; indeed, its properties are such as clearly to suggest that it is related more closely to camphene than to pinene. In any case, we are not at present justified in terming it pinene hydrochloride, and as it is obviously closely related to the saturated camphene-like hydrocarbon, $C_{10}H_{18}$, into which it is converted by the action of sodium, which may conveniently be termed camphydrene, I propose to speak of it provisionally as *chlorocamphydrene*.

It is very noteworthy, as I have pointed out in a recent note in the *Proceedings* (1896, 161, 44) on the relation of pinene to citrene, that whereas chlorocamphydrene is highly active, the dibromide and nitrosochloride prepared from pinene are both optically inactive. Such differences in optical characters are deserving of greater consideration than they have hitherto received if, as there is every reason to suppose is the case, inversion of optical activity can only be conditioned by the occurrence of change immediately within the sphere of activity of an asymmetric carbon atom. It is, in fact, probable for this reason that the dibromide and nitrosochloride are not mere products of the addition of Br_2 or $NOCl$ respectively to pinene, and that their formation involves a change in which the asymmetric carbon atom in pinene is involved.

To repeat what I said in the note in question—

“It is to be remembered that the carbon atoms which are connected by an ethenoid linkage in pinene cannot be the origin of its optical activity, and that, whatever it may be, its formula must be one containing at least one asymmetric carbon atom. But, this being the case, it is difficult to understand how the addition either of bromine or of nitrosyl chloride can give rise to optically inactive products capable of affording an inactive pinene; the occurrence of “racematisation” in such a case would seem to indicate that the region in which the asymmetric carbon is situated also becomes affected, although, apparently, but temporarily: *i.e.*, whatever be the change, it is subsequently reversed—even when pinene is converted into the nitrosochloride. If we cannot accept this conclusion, we must admit that

the formulæ hitherto attributed to pinene are all unsatisfactory expressions to a far greater extent than we have ever supposed. The difficulty, it may be added, is greater in the case of such a formula as Tiemann's—as this contains two asymmetric carbons—than in the case of those proposed by v. Baeyer, or by the writer.*

"A similar argument is applicable in the case of camphor. If the argument of the following note (reproduced below)† be admitted, the production of an inactive

* The possibility of pinene being a trimethylene derivative was considered in the note in question; the formula given by way of illustration—as the simplest expression of such a view—was the following.

† "The Conditions involved in the occurrence of Inversion in the case of Asymmetric Optically Active Compounds.—Having formed the opinion that the changes which attend the production of what are supposed to be pinene derivatives merit much closer attention, the writer has been led to carefully consider Walden's recent very remarkable observations on the formation from each of the two active malic acids by means of phosphorus pentachloride or bromide of an oppositely active chloro- or bromo-succinic acid, from each of which in turn a malic acid of its own order of activity may be obtained (*Ber.*, 1896, 133). It does not appear difficult to explain these results without any modification of our current theory, and attention is now called to considerations which, perhaps, may prove to be of importance in discussions of the behaviour, and of other questions relating to, asymmetric compounds.

"When optical inversion is effected by hydrolytic agents, in the case of either an aldose or a ketose or acid, it is probable that, in the first instance, the keto-group becomes hydrated, and that either an 'aldehydrol,' $\text{CH}(\text{OH})_2$, or a 'ketohydrol,' $\text{C}(\text{OH})_2$, or an 'acidhydrol,' $\text{C}(\text{OH})_3$, is produced. When water is withdrawn from such compounds, if the water be formed from an OH group of the hydrol complex and a hydrogen atom attached to the carbon contiguous to that of the hydrol complex, an ethenoid derivative will be formed, thus

"On hydration, according as hydration takes place at the one or the other junction of the ethenoid linkage, such a compound will afford one or the other of the two possible asymmetric forms; and if, as in the case of tartaric acid, the compound be symmetrical, it is to be expected that the two forms will be produced in equal proportions. But if an unsymmetrical compound be thus changed, such as a hexose or an acid like glucosonic acid, it is to be expected that the severance will take place to a greater extent at one of the two junctions, and in some cases, perhaps, only at one. The striking results recently obtained by Lobry de Bruyn, and all E. Fischer's observations, are in accordance with this view, which, in fact, is the generally accepted one.

"When malic acid is acted on by, say, phosphorus pentachloride, probably the campholide on reduction of camphoric anhydride (*Haller, C. R.*, 1896, 295) may,

in fact, be regarded not only as a proof that the CO group undergoing reduction is connected with a hydrogenised asymmetric carbon atom, but also as evidence of the presence of but a single asymmetric carbon in camphor.*

Taking the evidence afforded by optical characters into account, the argument here used would justify the conclusion that the hydri-chloride rather than either the dibromide or the nitrosochloride is an immediate derivative of pinene; and yet, apparently, the two last are alone reconvertible into pinene.

Attempts that I have made from time to time to obtain derivatives from chlorocamphydrene have always been failures. Many years ago I succeeded in oxidising it by prolonged digestion with dilute nitric acid, but the results were unsatisfactory both as regards quality and quantity of product; owing to the difficulty of securing contact between the acid and the chloride, the action took place with extreme slowness, and it was impossible to prevent further oxidation of the immediate product. It is noteworthy, however, that a minute quantity of camphoric acid was obtained in these experiments—a fact which was referred to under camphoric acid in the 1880 edition of the organic part of Miller's *Chemistry*, prepared by Mr. Groves and myself.*

first action to occur is one involving the formation of a chlorophosphonium compound, thus

"The next stage in the change may be assumed to be one involving 'internal condensation.'

"Supposing that this compound be then acted on by hydrogen chloride and resolved into chlorosuccinic acid and phosphorus oxychloride, if the attack became *directed* by the phosphorus, so that the chlorine took up the position of the phosphorus, complete inversion would be effected.†

"It will be obvious that such an explanation may be of general application, especially in connection with the exclusive production, under natural conditions, of a single asymmetric form."

* "Dextracamphene from the monohydrochloride from American turpentine yields a dextrorotatory camphoric acid having similar properties, which apparently is also produced on directly oxidising the monohydrochloride prepared from American turpentine with nitric acid (Armstrong)."

† The result would be the same if the oxygen exercised the orienting effect, as the hydrogen would thereby be brought into position *b*.

The discovery that the very strongest nitric acid could be used with advantage in oxidising dibromocamphor made in my laboratory by Dr. Forster, induced me again to attempt the oxidation of chlorocamphydrene, substituting such acid—in which it readily dissolves—for the diluted acid previously used. Experiments made at my suggestion by two of my students, Messrs. W. S. Gilles and F. F. Renwick, have been rewarded with success, and have led to the discovery of a remarkable acid, which apparently has not been previously obtained; as it exhibits ketonic functions, and is indirectly derived from pinene, it is proposed to term it *ketopinic* acid.

Messrs. Gilles and Renwick find that great care must be exercised in effecting the oxidation, as if the temperature be allowed to rise to 30° or 40°, only oxalic acid is produced, whilst if it fall to 17° or 18°, the action does not take place; the hydrichloride should be added (1 part) to the acid (5 parts) at such a rate that the acid is maintained at a temperature as near to 20° as possible. After 48 hours the acid solution is poured into several times its bulk of water, and the liquid is afterwards neutralised with chalk sludge.

The separation of the acid is facilitated by the fact that it forms a sparingly soluble calcium salt the solubility of which is not increased by heating; consequently, on evaporating the solution, the salt separates first along with some calcium nitrate, which is removed by digesting the crude salt with dehydrated spirit. The acid may be obtained by adding the calculated quantity of oxalic acid to a solution of the calcium salt, and subsequently concentrating the liquid; it separates as an oil, which solidifies on cooling. The amount obtained is equal in weight to about 10—15 per cent. of the hydrichloride used.

Ketopinic acid crystallises from water in colourless plates melting at 234° (uncorr.); but, in contact with water, it melts below 100°. Although sparingly soluble in water and light petroleum, it is very soluble in alcohol, benzene, chloroform, ether and ethylic acetate, and crystallises well from the last mentioned of these. It is optically inactive even when prepared from the most highly active hydrichloride.

The methylic salt is very soluble in all ordinary solvents except water; when purified by distillation, it forms a colourless mass melting at 28°.

The baric and calcic salts, which are sparingly soluble in water and insoluble in alcohol, separate in white needles on evaporating their aqueous solutions.

On digesting a solution of the acid in acetic acid with phenylhydrazine, a hydrazone was obtained, which, after recrystallisation

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from acetic acid, fused sharply at 146° ; it was soluble in a solution of sodic carbonate.

The corresponding hydroxime was obtained by warming a solution of the acid in a slight excess of caustic soda with hydroxylamine hydrochloride. This was almost insoluble in water and light petroleum, but readily soluble in alcohol, acetic acid, chloroform and ethylic acetate. It fused at 216° .

Bromine was without action on the acid.

The analyses which have been made of the acid and its educts justify the formula $C_{10}H_{14}O_3$, thus

		Found.	Calculated.
Acid.....	C	65.97, 65.96, 65.90, 65.70	65.93
	H	7.72, 7.48, 8.8, 8.13	7.69
Methylic salt ..	C	67.17, 67.06, 67.29	67.35
	H	8.41, 8.44, 8.20	8.16
Baric salt	Ba	27.4	27.4
Calcic salt	H ₂ O	3.6	1 mol. 4.3
	Ca	9.90	9.95
Hydrazone	N	10.40	10.30
Hydroxime....	N	7.66, 7.41	7.11

It is proposed to fully investigate ketopinic acid, and to apply the method used in its production to other derivatives of terpenes, &c., containing halogens; experiments made with pinene nitrosochloride have hitherto been unsuccessful.

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