XLIX.—*Experiments on the Synthesis of the Terpenes.*
Part X. Synthesis of Carvestrene and its Derivatives.

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AMONG the many remarkable molecular changes which have so frequently been met with in the camphor and terpene group, few are more interesting and instructive than the series of decompositions which Baeyer investigated during the course of his classical researches on carvone and which, besides other important results, ultimately led to the discovery of carvestrene.

When carvone, $C_{10}H_{14}O$, a substance which occurs in oil of carraway, is reduced by sodium and alcohol, it is converted into *dihydrocarveol*, and this, on oxidation with chromic acid, yields *dihydrocarvone*,

Leuckart (*Ber.*, 1887, 20, 114), Wallach (*Annalen*, 1893, 275, 110), Baeyer (*Ber.*, 1893, 26, 823).

Hydrobromic acid converts dihydrocarvone into a hydrobromide, $C_{10}H_{17}OBr$, which, when treated with alcoholic potash at 0° , readily loses hydrogen bromide. Instead, however, of the unsaturated substance, dihydrocarvone, being regenerated as the result of this decomposition, a remarkable formation of a trimethylene ring takes place and *carone* is produced.

In order to demonstrate the presence of the dimethyltrimethylene ring in carone, Baeyer and Ipatieff (*Ber.*, 1896, 29, 2796) studied the behaviour of this ketone on oxidation with permanganate and succeeded in isolating the *cis*- and *trans*-caronic acids,

The subsequent synthesis of these acids by Perkin and Thorpe (*Trans.*, 1899, 75, 48), by a method which left no doubt as to their constitutions, afforded additional evidence of the presence of the dimethyltrimethylene ring in carone.

When caroneoxime is reduced by sodium and alcohol it yields *carylamine*, $\text{C}_{10}\text{H}_{17}\text{NH}_2$, and since this base is stable to permanganate, Baeyer (*Ber.*, 1894, 27, 3486) concluded that it could not be unsaturated and must, therefore, still contain the dimethyltrimethylene ring. The constitution of *carylamine* is for this reason derived from that of caroneoxime in a simple manner without molecular change and is represented by the formula :

The most characteristic property of *carylamine* is the decomposition which it undergoes when its solution in dilute acids is evaporated, during which process the dimethyltrimethylene ring suffers disruption and the unsaturated isomeric base, *vestrylamine*,

is formed. Lastly, the hydrochloride of *vestrylamine* is readily decomposed on distillation, with elimination of ammonium chloride and formation of *carvestrene*, an inactive terpene to which Baeyer (*loc. cit.*, 3485) assigned the constitution :

This formula represents *carvestrene* as a derivative of *m*-cymene, and direct evidence in favour of this view was subsequently obtained by Baeyer (*Ber.*, 1898, 31, 1402), who showed that, when *carvestrene* dihydrobromide is treated with excess of bromine and the product reduced by zinc dust and alcoholic hydrochloric acid, it actually yields *m*-cymene. The position of the double linking in the above formula for *carvestrene* is rendered probable by the fact that it is formed from *vestrylamine* by the simple elimination of ammonia, but this decomposition might equally well lead to the expression :

The properties of carvestrene which are of special importance in connexion with the present investigation are these: It distils at 178°, yields a *dihydrochloride*, $C_{10}H_{16} \cdot 2HCl$, which melts at 52.5°, and a *dihydrobromide*, $C_{10}H_{16} \cdot 2HBr$,* of melting point 48–50°, and gives a deep blue coloration when a drop of sulphuric acid is added to its solution in acetic anhydride.

Carvestrene occupies the same position in the *m*-cymene group of terpenes as dipentene does in the *p*-cymene series and, for this reason, it is to be considered as one of the most important of the terpenes. It therefore seemed interesting to institute a series of experiments with the object of preparing it synthetically by some process which would leave no doubt as to the constitution of the terpene, and in this we were ultimately successful.

The starting point in this synthesis was *m*-hydroxybenzoic acid, which is reduced by sodium and alcohol to *cyclohexanol-3-carboxylic acid*:

In the first place we carefully investigated this interesting acid and found that it exists in well-defined *cis*- and *trans*-modifications, of which the former (m. p. 132°) had already been obtained by Einhorn (*Annalen*, 1896, 291, 298). The *trans*-acid melts at 120°, or considerably lower than the *cis*-modification.

The *cis*-acid yields a crystalline lactone which reacts readily with hydrobromic acid with formation of the *cis*-modification (m. p. 63°) of *3-bromocyclohexanecarboxylic acid*,

whereas the *trans*-hydroxy-acid is converted, by treatment with hydrobromic acid, into the corresponding *trans*-bromo-acid of melting point 167°. When the latter is digested with diethylaniline, it is decomposed apparently quantitatively, with elimination of hydrogen bromide and formation of Δ^3 -*cyclohexenecarboxylic acid* (Δ^3 -tetrahydrobenzoic acid):

The second step in the synthesis of carvestrene was the conversion of *cyclohexanol-3-carboxylic acid* into *cyclohexanone-3-carboxylic acid*,

by oxidation with chromic acid mixture, and in this way we have prepared large quantities of this important acid in a crystalline condition

* The product of the action of hydrobromic acid on carvestrene consists of this solid dihydrobromide and a liquid isomeride, and these, doubtless, represent *cis*- and *trans*-modifications.

(m. p. 76°), whereas it had previously only been obtained as a syrup. *Ethyl cyclohexanone-3-carboxylate* (b. p. 138° under 18 mm.) reacts readily with magnesium methyl iodide, and the product yields, on hydrolysis, *methylcyclohexanol-3-carboxylic acid* and a considerable quantity of an interesting neutral oil (B) the composition of which is discussed later (p. 485). The hydroxy-acid is decomposed by distillation under reduced pressure with elimination of water and formation of the lactone of *cis-1-methyl-1-cyclohexanol-3-carboxylic acid* (b. p. 145° under 20 mm.):

Hydrobromic acid converts this lactone into *cis-1-bromo-1-methylcyclohexane-3-carboxylic acid*,

a thick syrup which, when digested with pyridine, is decomposed with elimination of hydrogen bromide and formation of *1-methyl- Δ^1 -cyclohexene-3-carboxylic acid* (b. p. 142° under 20 mm.),

The constitution of this acid was controlled by oxidation first with permanganate and then with chromic acid, when it yielded adipic acid and a syrupy ketonic acid which was probably ω -acetylvaleric acid, since, when treated with sodium hypobromite, it yielded bromoform and adipic acid. The formation of these oxidation products leaves no doubt that the unsaturated acid is *1-methyl- Δ^1 -cyclohexene-3-carboxylic acid*, since the only other unsaturated acid which could result from the elimination of hydrogen bromide from *1-bromo-1-methylcyclohexane-3-carboxylic acid* is *1-methyl- Δ^6 -cyclohexene-3-carboxylic acid*,

and an acid of this constitution could not yield adipic acid on oxidation. The *1-methyl- Δ^1 -cyclohexene-3-carboxylic acid* was next converted into its ethyl ester (b. p. 128° under 60 mm.) and this was treated with an ethereal solution of magnesium methyl iodide, a decomposition which resulted in the synthesis of *dihydrocarvestrenol* or *Δ^1 -m-menthenol* (8),

a substance which had not previously been obtained.

Dihydrocarvestrenol is a colourless syrup which distils at $105\text{--}108^{\circ}$ (30 mm.), has a powerful odour of menthol and terpineol, and is a substance of much interest since it is the alcohol in the *m*-cymene

series which corresponds to terpineol, with which, indeed, it has many properties in common. It was prepared in considerable quantity in order that its physical properties might be investigated by Sir W. H. Perkin, and an account of these experiments is to be found on p. 499. The next step was to convert the dihydrocarvestrenol into the terpene, and this was readily accomplished, in the usual manner, by digesting with potassium hydrogen sulphate, and a careful examination of the hydrocarbon obtained proved conclusively that it was in all respects identical with the carvestrene of Baeyer.

This point was decided by a direct comparison which was rendered possible by the kindness of Prof. von Baeyer, who placed his specimen of carvestrene at our disposal for this purpose.

Both preparations gave exactly the same blue coloration when sulphuric acid was added to their solution in acetic anhydride.

Both yielded a *dihydrochloride* melting at 52.5° and a *dihydrobromide* melting at 48–50°; moreover, the mixture of the two specimens of the dihydrobromide melted sharply at 48–50°, proving conclusively that they were identical. This synthesis establishes the constitution of carvestrene and demonstrates that the double linking in the ring is in the position assigned to it by Baeyer when he adopted the formula

as representing the probable constitution of this terpene.

In possession of sufficient quantities of dihydrocarvestrenol and carvestrene, we instituted a series of experiments with the object of preparing the *cis*- and *trans*-modifications of *tetrahydrocarvestrenediol* (*m-menthane-1:8-diol*), $\text{C}_{10}\text{H}_{18}(\text{OH})_2$, which it was thought would be of special interest on account of their similarity in constitution and relationship to the *cis*- and *trans*-modifications of terpin. With this object in view, dihydrocarvestrenol was shaken for several days with 5 per cent. sulphuric acid, when it was converted, almost quantitatively, into a tetrahydrocarvestrenediol,

which melts at about 90°. This is the *cis*-modification and corresponds to *cis*-terpin, from which it, however, differs in being much more soluble in water and in not combining with water to form a hydrate.

In other respects the two substances have much in common. *cis*-Tetrahydrocarvestrenediol, for example, is converted by hydrobromic acid into a mixture of the *cis*- and *trans*-carvestrene dihydrobromides, the *trans*-modification largely predominating just as, in the

case of *cis*-terpin, the product of the action of hydrobromic acid in the cold consists principally of *trans*-dipentene dihydrobromide.

trans-Tetrahydrocarvestrenediol (m. p. 127°) was first prepared by Baeyer (*Ber.*, 1894, 27, 3490) from *trans*-carvestrene dihydrobromide (m. p. 48—50°) by treatment with silver acetate and subsequent hydrolysis of the diacetate produced, by alcoholic potash; a process exactly similar to the conversion of *trans*-dipentene dihydrobromide into *trans*-terpin. We have also prepared *trans*-tetrahydrocarvestrenediol and observed the same melting point, and the chief difference between *trans*-dihydrocarvestrenol and *trans*-terpin lies again in the fact that the former dissolves easily whereas the latter is sparingly soluble in water.

Direct Synthesis of Dihydrocarvestrenol [Δ^1 -*m*-menthenol(8)], *Tetrahydrocarvestrenediol* (*m*-menthane-1 : 8-diol) and its Anhydride (*m*-Cineol) from Ethyl cycloHexanone-3-carboxylate.

It has already been mentioned that a considerable quantity of a neutral oil (B) is formed when magnesium methyl iodide reacts with ethyl cyclohexanone-3-carboxylate, and examination has shown that this oil consists essentially of three substances.

I. A substance which distils at 177—178° and corresponds in the *m*-cymene series with *cineol* in the *p*-series, that is to say, it has the constitution

This interesting substance, which we have named *m-cineol*, is the anhydride of tetrahydrocarvestrenediol, and is probably formed by the dehydrating action of magnesium methyl iodide on *cis*-tetrahydrocarvestrenediol, which is doubtless one of the products of the action of this reagent on ethyl cyclohexanone-3-carboxylate (see below). It has a pungent odour of camphor and is very similar to cineol in its properties, thus when treated with hydrobromic acid it is converted into a mixture of the *cis*- and *trans*-modifications of carvestrene dihydrobromide in which the *cis*-modification greatly predominates, just as cineol under the same conditions yields principally *cis*-dipentene dihydrobromide.

II. A substance distilling constantly at 105—108° (30 mm.) and which amounted to nearly half of the neutral oil. This substance was found to be pure *dihydrocarvestrenol*.

III. A crystalline substance melting at 127°, which was found by direct comparison to be identical with the *trans*-tetrahydrocarvestrene-

diol obtained from *trans*-carvestrene dihydrobromide by the process just described.

It seems probable that one of the products of the action of magnesium methyl iodide on ethyl *cyclohexanone*-3-carboxylate is a mixture of the *cis*- and *trans*-modifications of tetrahydrocarvestrenediol, and that the *cis*-modification is then converted, by the further action of the reagent, into *m*-cineol, whereas the *trans*-modification remains unchanged.

In the communication preceding the present one, it was pointed out that *cis*-terpin is a direct product of the action of magnesium methyl iodide on ethyl *cyclohexanone*-4-carboxylate, and the fact that it was found possible to isolate *cis*-terpin in such considerable quantities from the product of the reaction seems to indicate that this substance is not so readily converted into its anhydride, cineol, as *cis*-tetrahydrocarvestrenediol into *m*-cineol.

The reduction of *m*-hydroxybenzoic acid to *cyclohexanol*-3-carboxylic acid by means of sodium and alcohol was first carried out by Einhorn (*Annalen*, 1896, 291, 298), but as the process which he describes is very laborious and we required large quantities of the hexahydro-acid, we instituted a number of comparative experiments which led us to adopt the following method for its preparation.

m-Hydroxybenzoic acid (40 grams) is dissolved in absolute alcohol (1 litre), the solution heated to boiling in a large flask connected with a long reflux condenser, and then sodium (150 grams) added as rapidly as possible. When the action slackens small quantities of alcohol are added from time to time, and the heating is continued until the sodium has completely dissolved. The product is mixed with water, nearly neutralised with hydrochloric acid and evaporated until all the alcohol has been removed and sodium chloride commences to separate. The mass is then mixed with excess of hydrochloric acid and extracted ten times with washed ether, and afterwards ten times on the shaking machine, and even then the whole of the hydroxy-acid will not have been extracted. The ethereal solution is dried over calcium chloride, and nearly all the ether removed by evaporation, when, after a few days, the syrupy residue will have become semi-solid. The crystals are collected, washed with ether and recrystallised from dry ether from which *cis*-*cyclohexanol*-3-carboxylic acid separates in hard crusts melting at 130—132°:

0.1241 gave 0.2648 CO_2 and 0.0936 H_2O . $\text{C}=58.2$; $\text{H}=8.4$.

$\text{C}_7\text{H}_{12}\text{O}_3$ requires $\text{C}=58.3$; $\text{H}=8.3$ per cent.

The mother liquors of the crystalline hydroxy-acid are best purified by conversion into the ester, the syrup (60 grams) being dissolved in a 4 per cent. solution of hydrogen chloride in alcohol (200 c.c.) and allowed to remain for twenty-four hours. After boiling for four hours, water is added, the crude ester extracted with ether, the ethereal solution washed with water and dilute sodium carbonate,* evaporated, and the oil fractionated under 35 mm. pressure. It began to boil at 120° , and a large fraction was obtained between this and 140° ,† then the ester of the hydroxy-acid distilled between 148 — 155° leaving a considerable quantity of a viscid residue in the flask. When the latter fraction was redistilled almost the whole quantity passed over at 147° (20 mm.) and consisted of pure *ethyl cyclohexanol-3-carboxylate* :

0.1698 gave 0.3930 CO_2 and 0.1405 H_2O . $\text{C}=63.1$; $\text{H}=9.2$.

$\text{C}_9\text{H}_{16}\text{O}_3$ requires $\text{C}=62.8$; $\text{H}=9.3$ per cent.

Einhorn (*Annalen*, 1896, 291, 301), who first prepared this substance, states that it boils at about 148 — 158° under 20 mm. pressure.

The results of hydrolysis indicate that this ester is a mixture of the *cis*- and *trans*-modifications, the former largely predominating.

The ester (200 grams) was mixed with a warm solution of potash (100 grams) in methyl alcohol when the temperature rose to the boiling point, and, after remaining for two hours, water was added, the solution evaporated until free from methyl alcohol, acidified, saturated with ammonium sulphate, and repeatedly extracted with washed ether. The ethereal extract, after drying over calcium chloride and evaporating, deposited a syrup which soon became semi-solid, and, after remaining for several days, the mass was filtered and washed several times with pure ether, when a colourless crystalline acid was obtained which melted at 128 — 130° and consisted of nearly pure *cis*-cyclohexanol-3-carboxylic acid.

The mother liquor was evaporated and the residue allowed to crystallise, and this operation repeated until the syrupy acid either did not crystallise at all or only after very long standing; it was then treated as explained in the next section.

* When evaporated and heated with alcoholic hydrogen chloride, this sodium carbonate extract yields a further quantity of hydroxy-ester.

† When this fraction was twice distilled under the ordinary pressure, almost the whole quantity came over at 200 — 202° and gave, on analysis :

0.1711 gave 0.4377 CO_2 and 0.1447 H_2O $\text{C}=69.8$; $\text{H}=9.5$.

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

It is evident that this substance is the ester of one of the tetrahydrobenzoic acids, and, as a large quantity has accumulated, it will be further investigated.

The Lactone of cis-cycloHexanol-3-carboxylic Acid and its Conversion into cis-3-Bromocyclohexanecarboxylic Acid.

When the uncrystallisable hydroxy-acid, obtained as explained in the last section, is slowly distilled under a pressure of 30 mm., water is eliminated, and an oil passes over at 125—140° which becomes semi-solid on cooling. The thermometer then rises rapidly to 180°, between which temperature and 195° a large amount of a colourless oil (A) distils and also solidifies on cooling. The lower fraction was redistilled, when a considerable quantity passed over at 125—130° (20 mm.) and crystallised in the condenser to a camphor-like mass. This substance, which was found to be the lactone of the *cis*-hydroxy-acid, was left in contact with porous porcelain until quite free from oil, and then crystallised from light petroleum.

0.1067 gave 0.2600 CO₂ and 0.0756 H₂O. C = 66.5; H = 7.9.

C₇H₁₀O₂ requires C = 66.7; H = 7.9 per cent.

The lactone of *cis*-cyclohexanol-3-carboxylic acid separates from light petroleum in groups of small needles, but, even when freshly crystallised, it is of such a curious sticky nature that it was found impossible to introduce it into a capillary tube, and the quantity was too small to allow of its melting point being determined by any other process. It is insoluble in sodium carbonate in the cold, but is readily hydrolysed by methyl-alcoholic potash, and if the solution is evaporated until free from alcohol, acidified, and repeatedly extracted with ether, the ethereal solution, after drying over calcium chloride and evaporating to a small bulk, deposits colourless crusts which melt at 132°, and consist of the pure *cis*-hydroxy-acid:

0.1535 gave 0.3269 CO₂ and 0.1181 H₂O. C = 58.1; H = 8.5.

C₇H₁₂O₃ requires C = 58.3; H = 8.4 per cent.

The lactone dissolves in aqueous hydrobromic acid (saturated at 0°) and, on standing, crystalline crusts gradually separate. These were collected, drained on porous porcelain, rapidly washed on porous porcelain with formic acid (sp. gr. 1.22), and dried over sulphuric acid under reduced pressure:

0.2347 gave 0.2185 AgBr. Br = 38.1.

C₇H₁₁O₂Br requires Br = 38.6 per cent.

Purified in this way, *cis*-3-bromocyclohexanecarboxylic acid melts at about 62—63°, and differs from the corresponding *trans*-isomeride (m. p. 167°, see p. 489) by its much lower melting point and by the fact that it is much more soluble in formic acid and other solvents.

trans-cycloHexanol-3-carboxylic Acid and its Conversion into trans-3-Bromocyclohexanecarboxylic Acid and into Δ^3 -cyclo-Hexenecarboxylic Acid.

In the last section mention is made of an oil (A) which distilled at about 195° (30 mm.) and solidified on cooling, and investigation has shown that this consists of *trans-cyclohexanol-3-carboxylic acid*. The crystalline mass was left in contact with porous porcelain until free from oil, and several times crystallised from ether, from which the new acid separated in colourless crusts :

0.1686 gave 0.3598 CO_2 and 0.1289 H_2O . $\text{C} = 58.2$; $\text{H} = 8.5$.

$\text{C}_7\text{H}_{12}\text{O}_3$ requires $\text{C} = 58.3$; $\text{H} = 8.4$ per cent.

trans-cyclo-Hexanol-3-carboxylic acid melts at $119\text{--}120^\circ$, and is readily soluble in water or alcohol, but very sparingly so in dry ether. In its other properties it shows great similarity to the corresponding *cis*-acid, but when it is intimately mixed with an equal quantity of the *cis*-acid (m. p. 132°) the mixture shrinks at 90° and is almost completely melted at 100° , a behaviour which clearly proves that the acids are distinct. The *trans*-acid dissolves readily in aqueous hydrobromic acid (saturated at 0°) and no separation takes place even after twenty-four hours, but when heated at 100° for a few minutes the solution separates into two layers, of which the upper is the bromo-acid. This was isolated by diluting with water and extracting with ether, and, after the ethereal solution had been well washed with water, dried over calcium chloride, and evaporated, a viscid syrup remained which soon commenced to crystallise. The crystalline mass was drained on porous porcelain and twice recrystallised from light petroleum, when crystalline crusts were obtained which gave the following results on analysis :

0.3476 gave 0.3112 AgBr. $\text{Br} = 38.2$.

$\text{C}_7\text{H}_{11}\text{O}_2\text{Br}$ requires $\text{Br} = 38.6$ per cent.

trans-3-Bromocyclohexanecarboxylic acid melts at 167° , and is characterised by the facility with which it crystallises from organic solvents. It dissolves readily in boiling benzene, and separates on cooling in four-sided plates with bevelled edges. It is also readily soluble in methyl alcohol, chloroform, or ethyl acetate, from all of which it crystallises beautifully.

Towards hydrobromic acid the *cis*- and *trans*-modifications of *cyclohexanol-3-carboxylic acid* show apparently an exactly similar behaviour. The acids dissolve readily in the hydrobromic acid and no change takes place at the ordinary temperature. When the solution is heated at 100° , a thick syrup separates which consists of the *trans*-bromo-acid of melt-

ing point 167° , together with a more soluble bromo-acid of much lower melting point which is doubtless the *cis*-modification. Apparently hydrobromic acid at 100° yields, in each case, an equilibrium mixture of the two modifications of the bromo-acid.

Δ^3 -cycloHexenecarboxylic Acid (Δ^3 -tetrahydrobenzoic acid).—*trans*-3-Bromocyclohexanecarboxylic acid is a very stable substance, since it is only very slowly decomposed by boiling pyridine; when, however, it is digested with diethylaniline for one hour, complete decomposition takes place with elimination of hydrogen bromide and formation of Δ^3 -cyclohexenecarboxylic acid. The product was treated with excess of dilute hydrochloric acid, extracted with ether, the ethereal solution well washed, dried over calcium chloride, evaporated, and the residue distilled under reduced pressure, when almost the whole quantity passed over at 133° (20 mm.) and solidified readily in a freezing mixture:

0.1635 gave 0.3981 CO_2 and 0.1175 H_2O . C = 66.4; H = 8.0.

$\text{C}_7\text{H}_{10}\text{O}_2$ requires C = 66.6; H = 7.9 per cent.

In order to prove that this substance was Δ^3 -cyclohexenecarboxylic acid, its behaviour towards bromine was investigated, when it was found that 4.26 grams, dissolved in chloroform and cooled to -10° , absorbed about 5.5 grams of bromine without evolution of hydrogen bromide, but the end point was not quite sharp. The quantity of bromine which should, theoretically, have been absorbed in converting the above amount of an unsaturated acid, $\text{C}_7\text{H}_{10}\text{O}_2$, into the dibromo-addition product, $\text{C}_7\text{H}_{10}\text{O}_2\text{Br}_2$, is 5.41 grams. The product was allowed to remain on a clock glass exposed to air until almost the whole of the chloroform had evaporated, the syrupy residue was then left over sulphuric acid in contact with a crystal of 3:4-dibromocyclohexanecarboxylic acid, when crystallisation soon commenced. After traces of oily impurity had been removed by contact with porous porcelain, the residue was washed on porous porcelain with formic acid and recrystallised from this solvent, when colourless plates separated which melted at 86° :

0.1585 gave 0.2072 AgBr. Br = 55.6.

$\text{C}_7\text{H}_{10}\text{O}_2\text{Br}_2$ requires Br = 55.9 per cent.

That this substance was 3:4-dibromocyclohexanecarboxylic acid ($\gamma\delta$ -dibromohexahydrobenzoic acid) was shown by mixing it with a specimen of this acid which had previously been prepared (Trans., 1904, 85, 433) from cyclohexanol-4-carboxylic acid, when no alteration in melting point could be observed.

cycloHexanone-3-carboxylic Acid (γ -keto-hexahydrobenzoic acid),

This acid is produced by the oxidation of *cis*-cyclohexanol-3-carboxylic acid, and after many comparative experiments we finally adopted the following process for the preparation of the large quantities of the acid and its ester which were required for this research. The *cis*-acid* (50 grams) is dissolved in water (200 c.c.) warmed to 45°, and then a solution of potassium dichromate (70 grams) and sulphuric acid (50 c.c.) in water (300 c.c.) is added in small quantities at a time, a fresh quantity only being added after the previous one had been completely reduced. The product is cooled, saturated with ammonium sulphate and extracted at least ten times on the shaking machine; the extract is dried over calcium chloride, evaporated, and the crude acid converted at once into its ester. In doing this care must always be taken to use only weak alcoholic solutions of hydrochloric or sulphuric acids, otherwise condensation takes place with formation of oils of very high boiling point. The crude acid (20 grams) is left in contact with a 2.5 per cent. solution of alcoholic hydrogen chloride (75 c.c.) for three days and then heated to boiling for one hour. After diluting with water and extracting with ether, the ethereal solution is washed with water and dilute sodium carbonate, evaporated, and the residue fractionated several times under reduced pressure from a distilling flask with a long neck in order that the separation of the keto-ester from any unchanged hydroxy-ester may be as complete as possible:

0.2891 gave 0.6711 CO₂ and 0.2236 H₂O. C = 63.3; H = 8.6.

0.1777 „ 0.4161 CO₂ „ 0.1380 H₂O. C = 63.3; H = 8.7.

C₉H₁₄O₃ requires C = 63.5; H = 8.3 per cent.

Ethyl cyclohexanone-3-carboxylate distils at 138° under 18 mm. pressure, and not at 170—180° (16 mm.) as stated by Einhorn (*Annalen*, 1896, 291, 303).

In order to prepare the keto-acid, the pure ester was digested with dilute hydrochloric acid until solution was complete, the product was then evaporated on the water-bath until free from alcohol, saturated with ammonium sulphate, and repeatedly extracted with ether.

The ethereal solution was dried over calcium chloride, evaporated, and the residue distilled under reduced pressure (30 mm.), when almost the whole quantity passed over at 205° as a viscid, colourless oil, which

* In some of our experiments we oxidised the crude mixture of *cis*- and *trans*-isomerides (p. 487), but the yield of keto-acid always seemed to be much more satisfactory when the pure *cis*-acid was employed,

gradually and almost completely crystallised. After remaining in contact with porous porcelain for some days, the acid was crystallised from benzene, from which it separates in hard crusts, or if the cold saturated solution is allowed to evaporate slowly the acid is obtained in the form of small glistening prisms :

0.1835 gave 0.3981 CO_2 and 0.1179 H_2O . $\text{C} = 59.1$; $\text{H} = 7.1$.

0.1464 „ 0.3174 CO_2 „ 0.0936 H_2O . $\text{C} = 59.2$; $\text{H} = 7.1$.

$\text{C}_7\text{H}_{10}\text{O}_3$ requires $\text{C} = 59.1$; $\text{H} = 7.0$ per cent.

cycloHexanone-3-carboxylic acid melts at $75-76^\circ$ and is very soluble in water, alcohol, or benzene, but sparingly so in light petroleum.

The *silver* salt, $\text{C}_7\text{H}_9\text{O}_3\text{Ag}$, was prepared by adding silver nitrate to a hot slightly alkaline solution of the ammonium salt when the filtered liquid, on slowly cooling, deposited the silver salt as a voluminous felted mass of minute needles :

0.3011 gave 0.1309 Ag. $\text{Ag} = 43.4$.

$\text{C}_7\text{H}_9\text{O}_3$ Ag requires $\text{Ag} = 43.3$ per cent.

This silver salt is somewhat readily soluble even in cold water. The neutral solution of the ammonium salt of the keto-acid gives no precipitate with barium or calcium chlorides, or with lead acetate or copper sulphate.

The oxime.—In order to prepare this derivative, *cyclohexanone-3-carboxylic acid* (2 grams) was dissolved in water and mixed with a solution of hydroxylamine hydrochloride (2 grams) and caustic potash (4 grams). After twenty-four hours a slight excess of hydrochloric acid was added, the clear solution extracted ten times with ether, and the ethereal solution dried over calcium chloride and evaporated. The syrupy residue gradually crystallised, and, after draining on porous porcelain, the oxime was purified by crystallisation from ether.

0.1813 gave 13.7 c.c. nitrogen at 10° and 752 mm. $\text{N} = 8.8$.

$\text{C}_7\text{H}_{11}\text{O}_3\text{N}$ requires $\text{N} = 8.9$ per cent.

cycloHexanoneoxime-3-carboxylic acid separates from ether in hard, crystalline crusts and melts at 170° as stated by Baeyer.

It dissolves very readily in warm water and crystallises from a saturated solution, on long standing, in warty masses.

The semicarbazone.—When an aqueous solution of the keto-acid is mixed with semicarbazide hydrochloride and sodium acetate and allowed to stand, the semicarbazone gradually separates as a hard, crystalline crust. It is very sparingly soluble in alcohol or water, but may be crystallised from either solvent, and is thus obtained as a sandy, crystalline precipitate which melts at $182-183^\circ$ with decomposition :

0.1601 gave 28.5 c.c. nitrogen at 16° and 758 mm. $\text{N} = 20.9$.

$\text{C}_8\text{H}_{13}\text{O}_3\text{N}_3$ requires $\text{N} = 21.2$ per cent.

*Formation of cycloHexanone-3-carboxylic Acid from
Terephthalic Acid.*

During his investigation of the reduction products of terephthalic acid, Baeyer (*Ber.*, 1889, **22**, 2178) showed that this acid may be converted into *cyclohexanone-3-carboxylic acid* by the following interesting series of reactions.

Terephthalic acid is nitrated and the nitro-acid reduced to aminoterephthalic acid, which, when treated with sodium nitrite, yields *hydroxyterephthalic acid*,

This hydroxy-acid is readily reduced by sodium amalgam with the formation of *cyclohexanone-3:6-dicarboxylic acid*, the constitution of which is probably represented by the formula

When this acid is warmed with water it is decomposed with evolution of carbon dioxide and formation of *cyclohexanone-3-carboxylic acid*,

which was obtained as a syrup, but was characterised by conversion into the oxime, which melted at 170° (compare p. 492).

When we commenced the present research, this series of decompositions, discovered by Baeyer, was very carefully investigated, because it seemed possible that this process might prove to be the simplest method for the preparation of the large quantities of *cyclohexanone-3-carboxylic acid* which we required for our synthetical experiments. We therefore prepared a large amount of *hydroxyterephthalic acid*, and carefully purified it by converting it into its methyl ester, which, after crystallisation from methyl alcohol, melted at 96°:

0.1956 gave 0.4093 CO₂ and 0.0829 H₂O. C = 57.0; H = 4.7.

C₁₀H₁₀O₅ requires C = 57.1; H = 4.8 per cent.

This ester was hydrolysed, reduced by sodium amalgam, and the *cyclohexanone-3:6-dicarboxylic acid*, isolated in the manner recommended by Baeyer, was obtained in the form of pale yellow crusts which gave correct numbers on analysis:

0.1505 gave 0.2848 CO₂ and 0.0781 H₂O. C = 51.7; H = 5.7.

C₈H₁₀O₅ requires C = 51.6; H = 5.4 per cent.

When this acid was boiled with water, carbon dioxide was slowly eliminated, and the solution, on standing, deposited a considerable quantity of a very sparingly soluble acid. This was collected and

purified by recrystallisation from glacial acetic acid, from which it separated as a pale ochre, granular, crystalline mass.

Two different specimens gave the following results on analysis :

0.1577 gave 0.3286 CO₂ and 0.0645 H₂O. C = 56.8 ; H = 4.6.

0.1735 „ 0.3624 CO₂ „ 0.0736 H₂O. C = 56.9 ; H = 4.7.

C₈H₈O₄ requires C = 57.1 ; H = 4.8 per cent.

The investigation of this acid has proved conclusively that it is Δ^{1:4}-cyclohexadiene-1:4-dicarboxylic acid (Δ^{1:4}-dihydroterephthalic acid),

and had evidently been formed by the elimination of water from *cyclohexanone-3:6-dicarboxylic acid* during the boiling with water.

This acid was obtained by Baeyer (*Annalen*, 1888, **245**, 145 ; 1889, **251**, 272), by the direct reduction of terephthalic acid with sodium amalgam. It gives a dimethyl ester of melting point 130°, which is characterised by yielding an intense yellow colour when its alcoholic solution is warmed with alcoholic potash, and these properties were also exhibited by the acid obtained by us.

The aqueous solution, from which the *cyclohexadiene-1:4-dicarboxylic acid* had been separated, was saturated with ammonium sulphate and extracted twenty times with ether, when the ethereal solution, after drying over calcium chloride and evaporating, deposited, as Baeyer describes, a syrupy acid which yielded an oxime of melting point 170°, and obviously consisted of impure *cyclohexanone-3-carboxylic acid*.

This crude acid distilled with considerable decomposition even under low pressures ; it was therefore converted into its ester (compare p. 491), and this, on distillation under 18 mm. pressure, yielded a quantity of oil boiling at 135—145°, but there was a considerable amount of an oil of higher boiling point left in the flask.

When this oil was hydrolysed, a syrupy acid was obtained which distilled at about 205° (30 mm.) and gradually solidified ; after crystallisation from benzene, the hard crusts melted at 76° and were found, by direct comparison, to be identical with *cyclohexanone-3-carboxylic acid* (p. 492).

0.1317 gave 0.2854 CO₂ and 0.0845 H₂O. C = 59.1 ; H = 7.2.

C₇H₁₀O₃ requires C = 59.1 ; H = 7.0 per cent.

These experiments clearly indicated that the above process was not suitable for preparing *cyclohexanone-3-carboxylic acid* in quantity, and it was therefore abandoned in favour of the method of preparation described on p. 491.

The Lactone of cis-1-Methylcyclohexanol-3-carboxylic Acid (cis- γ -Hydroxyhexahydro-m-toluic Acid) and its Conversion into cis-1-Bromo-1-methylcyclohexane-3-carboxylic Acid.

When ethyl cyclohexanone-3-carboxylate (50 grams) is gradually added to an ethereal solution of magnesium methyl iodide (containing 15 grams of magnesium) a vigorous action takes place which must be moderated by cooling in ice water, and a thick, oily layer separates which gradually crystallises. After remaining overnight, the product is decomposed with dilute hydrochloric acid in the usual manner, extracted at least twenty times with ether on the shaking machine, the ethereal solution evaporated, and the residue (45 grams) digested for one hour with potash (50 grams) dissolved in methyl alcohol. Water is then added, the neutral oil (B, 10 grams, see p. 502) extracted several times with ether, the alkaline solution neutralised, evaporated until free from alcohol, acidified, and extracted many times with ether. The ethereal solution is dried over calcium chloride and evaporated, and the thick, syrupy methylhydroxy-acid converted into the lactone by distillation under reduced pressure (20 mm.).

At first much water is given off, and then about two-thirds distils at 130—150°, but a considerable fraction, 180—200°, is also obtained, which probably contains the *trans*-methylhydroxy-acid, and a thick residue remains in the flask. The distillate is dissolved in ether dried over calcium chloride and again several times fractionated, when the lactone (15—20 grams) is readily obtained pure :

0.1933 gave 0.4844 CO₂ and 0.1504 H₂O. C = 68.3 ; H = 8.6.

0.1543 „ 0.3881 CO₂ „ 0.1201 H₂O. C = 68.6 ; H = 8.6.

C₈H₁₂O₂ requires C = 68.6 ; H = 8.6 per cent.

The lactone of *cis*-1-methylcyclohexanol-3-carboxylic acid is a colourless oil which distils at 145° (20 mm.) and at 170—171° (100 mm.).

In order to prepare *cis*-1-bromo-1-methylcyclohexane-3-carboxylic acid, the lactone (10 grams) is dissolved in aqueous hydrobromic acid (saturated at 0°, 20 c.c.), when an oil soon separates, and, after remaining for twenty-four hours, water is added, the heavy oily layer extracted with ether, dried over calcium chloride, and evaporated. The residual, almost colourless syrup did not crystallise, but after remaining for twelve hours in an evacuated desiccator, it yielded analytical results which agree approximately with those required for the bromo-acid :

0.1715 gave 0.1421 AgBr. Br = 35.3.

C₈H₁₃O₂Br requires Br = 36.2 per cent.

1-Methyl- Δ^1 -cyclohexene-3-carboxylic Acid, $\text{CH}_2 \left\langle \begin{smallmatrix} \text{CMe} \cdot \text{CH} \\ \text{CH}_2 \cdot \text{CH}_2 \end{smallmatrix} \right\rangle \text{CH} \cdot \text{CO}_2\text{H}$.

In the preparation of this acid, 1-bromo-1-methylcyclohexane-3-carboxylic acid was dissolved in anhydrous pyridine (3 vols.) and heated on the water-bath for two hours, when crystals of pyridine hydrobromide separated in quantity. After heating to boiling for ten minutes, the mass was mixed with water and distilled in steam, the distillate was acidified with hydrochloric acid, extracted with ether, and the ethereal solution dried over calcium chloride and evaporated. The residue distilled almost constantly at $140\text{--}142^\circ$ (20 mm.), but the unsaturated acid was nevertheless not quite pure, since it dissolved in sodium carbonate, yielding an opalescent solution, a behaviour probably due to the presence of traces of lactone, and it also contained traces of bromine:

0.2055 gave 0.5113 CO_2 and 0.1588 H_2O . C = 67.7; H = 8.6.

0.1438 „ 0.3588 CO_2 „ 0.1137 H_2O . C = 68.0; H = 8.6.

$\text{C}_8\text{H}_{12}\text{O}_2$ requires C = 68.6; H = 8.6 per cent.

1-Methyl- Δ^1 -cyclohexene-3-carboxylic acid is a colourless oil which does not crystallise when cooled to -10° ; it shows the behaviour of an unsaturated acid, since it decolorises bromine, and its solution in sodium carbonate instantly reduces permanganate.

In order to determine whether this acid was a single substance or a mixture, a considerable quantity was converted into the calcium salt by boiling with water and an excess of freshly precipitated calcium carbonate. The solution was concentrated and five crops of calcium salt were collected, but no difference in the appearance of the crops could be detected. They were all analysed and found to contain the same percentage of water of crystallisation and of calcium, and it will be only necessary to give details of the analyses of Crops I and V in illustration of this point:

Crop I.—0.4201, heated at 100° , lost 0.0879 H_2O and yielded 0.1369 CaSO_4 . $\text{H}_2\text{O} = 20.9$; Ca = 9.6.

Crop V.—0.4532, heated at 100° , lost 0.0948 H_2O and yielded 0.1514 CaSO_4 . $\text{H}_2\text{O} = 20.8$; Ca = 9.7.

$\text{C}_{16}\text{H}_{22}\text{O}_4\text{Ca}, 5\text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 22.0$; Ca = 9.8 per cent.

These results indicate that the unsaturated acid, prepared as explained above, is a single substance. In order to determine the position of the double linking in this acid, its behaviour on oxidation was next investigated.

In carrying out this experiment, the acid (15 grams) was dissolved in dilute sodium carbonate, and, after mixing with powdered ice, a 1 per cent. solution of potassium permanganate was slowly run in until

the colour remained, carbon dioxide being passed through and the liquid well stirred with a turbine during the operation. The excess of permanganate was destroyed by the addition of sodium sulphite, the product heated on the water-bath, filtered, and the filtrate and washings of the manganese precipitate evaporated to a small bulk. After acidifying with hydrochloric acid, saturating with ammonium sulphate, and extracting twenty times * with ether on the shaking machine, a viscoid oil (12 grams) was obtained which had a strong odour of acetic acid and did not crystallise. This was dissolved in water, warmed to 60°, and a dilute solution of sodium dichromate and sulphuric acid gradually added until the oxidation was complete. After saturating with ammonium sulphate and extracting twenty times with ether, a brown oil was obtained which was converted into the ester by treating with alcohol and sulphuric acid in the usual manner. When this ester was fractionated under 20 mm. pressure, about one-third distilled at 130–140° and almost the whole of the remainder at 175–185°. The lower fraction contained ethyl adipate, since, on hydrolysis, it yielded an acid which, after crystallising from water, melted at 148° and proved to be adipic acid, because, when mixed with a specimen of pure adipic acid, no alteration in the melting point could be observed. The fraction 175–185° (20 mm.) probably contains ethyl ω -acetylvalerate, $\text{COMe}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}_2\text{Et}$, since, on analysis, it gave numbers agreeing approximately with this formula and showed the following behaviour. Hydrolysis with methyl-alcoholic potash yielded a syrupy acid which did not crystallise (ω -acetylvaleric acid, when quite pure, crystallises and melts at 40–42°), but which gave an immediate precipitate with *p*-bromophenylhydrazine acetate and yielded bromoform and adipic acid when it was treated with bromine and caustic potash.

Ethyl 1-Methyl- Δ^1 -cyclohexene-3-carboxylate.—In preparing this ester, the acid (25 grams) was mixed with alcohol (250 c.c.) and sulphuric acid (20 c.c.), and, after remaining for 12 hours, heated on the water-bath for half an hour. Water was then added and the ester extracted with ether, the ethereal solution washed with dilute sodium carbonate, dried over calcium chloride, and fractionated under reduced pressure:

0.1365 gave 0.3552 CO_2 and 0.1153 H_2O . $\text{C} = 70.9$; $\text{H} = 9.4$.

$\text{C}_{10}\text{H}_{12}\text{O}_2$ requires $\text{C} = 71.4$; $\text{H} = 9.5$ per cent.

* When the fifteenth to twentieth extractions were evaporated to a small bulk, a very small quantity of a crystalline acid separated which melted at 193° and, on analysis, gave numbers agreeing with $\text{C}_8\text{H}_{16}\text{O}_4$ and also approximately with $\text{C}_8\text{H}_{14}\text{O}_4$. This acid is readily soluble in warm water, but almost insoluble in cold ether, and when heated in a test-tube, part decomposes and part sublimes unchanged and the distillate gives an immediate precipitate with *p*-bromophenylhydrazine.

Possibly this acid is one of the modifications of 1-methylcyclohexane-1:2-diol-3-carboxylic acid, but the amount available was too small for further investigation.

Ethyl 1-methyl- Δ^1 -cyclohexene-3-carboxylate distils at 128° (60 mm.) and has a very penetrating, sickly odour.

Synthesis of Dihydrocarvestrenol [Δ^1 -m-Menthenol (8)]

and Carvestrene [Δ^1 : $\text{S}^{(n)}$ -m-Menthadiene]

from *Ethyl 1-Methyl- Δ^1 -cyclohexene-3-carboxylate*.

The synthesis of dihydrocarvestrenol was carried out as follows. Ethyl 1-methyl- Δ^1 -cyclohexene-3-carboxylate (30 grams) was gradually added to an ethereal solution of magnesium methyl iodide (containing 12 grams of magnesium), when very little evolution of heat was noticed at the time of mixing, but, on standing, the temperature gradually rose to the boiling point of the ether so that the flask had to be cooled from time to time. After remaining for twenty-four hours, the product was decomposed by water and dilute hydrochloric acid, the ethereal solution evaporated, and the residue digested for a few minutes with methyl-alcoholic potash (containing 5 grams of KOH) in order to remove any unchanged ester which might be present. The product was diluted with water, extracted with ether, and the ethereal solution, after washing with water and drying over calcium chloride, evaporated, when an almost colourless oil remained which, after two fractionations, distilled constantly at 105 — 108° (30 mm.):

0.1650 gave 0.4711 CO_2 and 0.1751 H_2O . C = 77.8; H = 11.7.

0.1322 „ 0.3765 CO_2 „ 0.1411 H_2O . C = 77.6; H = 11.8.

$\text{C}_{10}\text{H}_{18}\text{O}$ requires C = 77.9; H = 11.7 per cent.

Dihydrocarvestrenol is a viscous, colourless oil which has a penetrating odour of menthol and terpineol and, so far, has not been obtained in a crystalline condition. Its solution in acetic anhydride gives, with a drop of sulphuric acid, at first a violet coloration, but this soon changes to an intense methylene-blue.

The determination of the physical properties of dihydrocarvestrenol was undertaken by Sir W. H. Perkin, with the following results:

$d\ 4^\circ/4^\circ = 0.9338$; $d\ 15^\circ/15^\circ = 0.9257$; $d\ 25^\circ/25^\circ = 0.9196$.

Magnetic rotation:

t .	Sp. rot.	Mol. rot.
14.45°	1.1945	11.035

Refractive power :

$$t = 15^{\circ}; d \ 15^{\circ}/4^{\circ} = 0.92299.$$

	$\mu.$	$\frac{\mu-1}{d}.$	$\frac{\mu-1}{d}p.$
α	1.47521	0.50934	78.438
β	1.48532	0.52018	80.107
γ	1.49144	0.52673	81.116

$$\text{Dispersion } \gamma - \alpha = 2.678.$$

In order to compare these numbers with the physical properties of terpineol, a very pure sample of the latter was prepared by fractionating crystalline terpineol from Schimmel. The examination of this specimen gave the following results :

Density (surfused) : $d \ 15^{\circ}/15^{\circ} = 0.9415$; $d \ 25^{\circ}/25^{\circ} = 0.9358$.

Magnetic rotation :

$t.$	Sp. rot.	Mol. rot.
17°	1.1951	10.876

Refractive power :

$$t = 14.8^{\circ}; d \ 14.8^{\circ}/4^{\circ} = 0.94080.$$

	$\mu.$	$\frac{\mu-1}{d}.$	$\frac{\mu-1}{d}p.$
α	1.48211	0.51244	78.916
β	1.49183	0.52278	80.508
γ	1.49763	0.52894	81.457

$$\text{Dispersion } \gamma - \alpha = 2.541.$$

It will be seen from these numbers that the similarity in physical properties between dihydrocarvestrenol and terpineol is very striking.

When dihydrocarvestrenol is mixed with an equal weight of powdered potassium hydrogen sulphate and heated to boiling in a reflux apparatus by means of an oil-bath, water is readily eliminated and *carvestrene* is formed. After boiling for half an hour, the product is treated with water to dissolve the salt, extracted with ether, the ethereal solution is washed with water, dried over calcium chloride and evaporated, and the oil distilled, when almost the whole quantity passes over at $175-185^{\circ}$, the conversion of the alcohol into the hydrocarbon taking place nearly quantitatively. After twice distilling over sodium, the hydrocarbon boiled constantly at $178-179^{\circ}$ (750 mm.) :

0.1449 gave 0.4658 CO_2 and 0.1568 H_2O . C=88.7; H=12.0.

0.1313 „ 0.4240 CO_2 „ 0.1401 H_2O . C=88.1; H=11.9.

$\text{C}_{10}\text{H}_{16}$ requires C=88.2; H=11.8 per cent.

Synthetical carvestrene has a pungent odour of lemons, and its solution in acetic anhydride is coloured a deep methylene-blue when a drop of sulphuric acid is added. It oxidises in the air, but not nearly so rapidly as dipentene does. The identity of synthetical carvestrene with the hydrocarbon prepared by Baeyer (*Ber.*, 1894, 27, 3485) from vestrylamine was proved by the preparation of the following derivatives.

Carvestrene Dihydrochloride, $C_{10}H_{16}, 2HCl$.—In order to prepare this characteristic derivative, synthetical carvestrene was dissolved in an equal volume of pure ether and slowly saturated with dry hydrogen chloride, the temperature being kept at -10° during the operation.

The solution gradually became dark brown, and, after remaining over night, it was poured on a clock glass and the ether allowed to evaporate, when an oil remained which soon crystallised. In contact with porous porcelain, the dark coloured impurities were quickly absorbed and the almost colourless residue separated from methyl alcohol in needles of melting point 52.5° :

0.1988 gave 0.2711 AgCl. $Cl = 33.7$.

$C_{10}H_{18}Cl_2$ requires $Cl = 33.9$ per cent.

Carvestrene Dihydrobromide, $C_{10}H_{16}, 2HBr$.—In preparing this derivative a saturated solution of hydrogen bromide in acetic acid (5 c.c.) was cooled to -10° and mixed with synthetical carvestrene (1 c.c.).

At first the hydrocarbon floated, but, after 24 hours, a heavy oil had separated below the acid, and shortly afterwards this began to crystallise. The crystals were left in contact with porous porcelain until quite free from oil (see below) and then crystallised from methyl alcohol:

0.2317 gave 0.2920 AgBr. $Br = 53.6$.

$C_{10}H_{18}Br_2$ requires $Br = 53.7$ per cent.

Carvestrene dihydrobromide separates from methyl alcohol in hard, prismatic needles and melts at $48-50^{\circ}$.

The dihydrochloride and dihydrobromide prepared from synthetical carvestrene have exactly the same melting points as the corresponding derivatives obtained by Baeyer (*Ber.*, 1894, 27, 3490) from carvestrene from vestrylamine. Baeyer was kind enough to send the authors a small quantity of his carvestrene, which was converted into the dihydrobromide of melting point $48-50^{\circ}$. When this was mixed with an equal quantity of the dihydrobromide from synthetical carvestrene, no alteration in melting point could be observed, and this fact clearly proves that the synthetical hydrocarbon is identical with carvestrene from vestrylamine.

When carvestrene is treated with hydrobromic acid under the con-

ditions mentioned above, only about half of the theoretical quantity of crystalline hydrobromide is obtained. If the porous porcelain, used in its purification, is extracted with ether and the ethereal solution evaporated, a heavy oil is obtained which contains about 50 per cent. of bromine and deposits only a few crystals on long standing. This behaviour seems to point, as Baeyer has suggested, to the formation of *cis*- and *trans*-modifications when carvestrene reacts with hydrobromic acid.

The cis- and trans-Modifications of Tetrahydrocarvestrenediol
(*m*-Menthane-1:8-diol).

When dihydrocarvestrenol (10 grams) was mechanically shaken with 5 per cent. sulphuric acid (350 c.c.) it gradually dissolved and, after remaining for ten days, the clear solution was saturated with ammonium sulphate and extracted twenty times with pure ether. The ethereal solution was dried over calcium chloride and evaporated, when a thick syrup resulted which soon began to crystallise and ultimately became almost solid. After remaining in contact with porous porcelain until quite free from oil, the residue was rapidly washed with a little ether and recrystallised from this solvent :

0·1408 gave 0·3600 CO₂ and 0·1458 H₂O. C = 69·7 ; H = 11·5.

C₁₀H₂₀O₂ requires C = 69·8 ; H = 11·6 per cent.

cis-Tetrahydrocarvestrenediol is readily soluble in dry ether and separates from the concentrated solution as a voluminous mass of slender needles ; it melts at about 90°, and is excessively soluble in water.

In order to determine whether this substance combined with water to form a hydrate, corresponding to *cis*-terpin hydrate, it was dissolved in a little water and the solution allowed to evaporate under ordinary conditions. The crystalline residue was left exposed to the air until dry and then analysed :

0·1126 gave 0·2871 CO₂ and 0·1169 H₂O. C = 69·5 ; H = 11·6.

C₁₀H₂₀O₂ requires C = 69·8 ; H = 11·6 per cent.

It is therefore obvious that *cis*-tetrahydrocarvestrenediol does not yield a hydrate under these conditions. *cis*-Tetrahydrocarvestrenediol dissolves in a solution of hydrogen bromide in acetic acid (saturated at 0°) and, on standing, crystals gradually separate. These were collected and recrystallised from methyl alcohol, when colourless needles were obtained which melted at 48—49° and consisted of *trans*-carvestrene dihydrobromide. The acetic acid mother liquor from

these crystals gave, on dilution with water, a quantity of an oily bromo-compound which was doubtless the crude *cis*-modification.

trans-Tetrahydrocarvestrenediol.—This interesting substance was first prepared, in small quantities, by Baeyer (*Ber.*, 1894, 27, 3490), and found to melt at 127°, but it was not analysed. We have repeated Baeyer's experiments, using material prepared from synthetical carvestrene, with the following results. *trans*-Carvestrene dihydrobromide (5 grams) was dissolved in glacial acetic acid (50 grams) in the cold, and silver acetate (10 grams) added in small quantities at a time, the whole being shaken after each addition and any rise of temperature avoided by cooling in ice-water. The decomposition took place at once with separation of silver bromide, and, after remaining overnight, the product was filtered and the silver bromide washed with a little acetic acid. The filtrate was then mixed with water, neutralised with potassium carbonate, and repeatedly extracted with ether. The ethereal solution, on evaporation, deposited an oily acetate which was digested with methyl-alcoholic potash (containing 5 grams of KOH) for a few minutes; water was then added and the *trans*-tetrahydrocarvestrenediol repeatedly extracted with ether. After washing with a little water, the ethereal solution was dried over calcium chloride and evaporated, when a crystalline mass remained which melted at 118—122°. This was dissolved in much light petroleum (b. p. 70—75°) and the solution rapidly concentrated, during which operation the pure substance separated in long, slender needles:

0.0854 gave 0.2165 CO₂ and 0.0913 H₂O. C = 69.2; H = 11.8.

C₁₀H₂₀O₂ requires C = 69.8; H = 11.6 per cent.

trans-Tetrahydrocarvestrenediol melts at 126—127°, and is very readily soluble in water, alcohol, or ether, but very sparingly so in cold light petroleum.

Direct Synthesis of Dihydrocarvestrenol [Δ^1 -*m*-*Menthenol* (8)], *Tetrahydrocarvestrenediol* (*m*-*Menthane*-1 : 8-*diol*), and its *Anhydride* (*m*-*Cineol*) from *Ethyl cycloHexanone-3-carboxylate*.

In describing the preparation of 1-methylcyclohexanol-3-carboxylic acid from ethyl cyclohexanone-3-carboxylate and magnesium methyl iodide, attention was called to the fact that a neutral oil (B, p. 495) with a strong odour of camphor is formed in considerable quantity during the reaction. This oil was collected from several experiments, and when 75 grams had accumulated it was fractionated under reduced pressure (20 mm.), when about 30 grams distilled at 85—95°, 25 grams at 95—120°, and most of the remainder (10 grams) at 130—150°.

The fraction 85—95° (20 mm.) was again distilled under the same pressure, when 23 grams passed over below 85°, and on fractionating this under ordinary pressures, and finally over sodium, an oil was obtained which distilled constantly at 177—178°, and consisted of the nearly pure *anhydride* of *cis-tetrahydrocarvestrenediol* (*m-cineol*):

0.1482 gave 0.4258 CO₂ and 0.1583 H₂O. C = 78.4; H = 11.9.

C₁₀H₁₈O requires C = 77.9; H = 11.7 per cent.

The oil was, however, unstable to permanganate, and evidently contained traces of some unsaturated substance, probably carvestrene; it was therefore shaken with ice and very dilute permanganate and again fractionated, when the analytical results were more satisfactory:

0.1186 gave 0.3388 CO₂ and 0.1268 H₂O. C = 78.1; H = 11.8.

m-Cineol is a colourless oil readily volatile in steam, which possesses a most pungent odour of camphor and distils at 177—178° (765 mm.).

It appears to form salts similar to those which are so characteristic of ordinary cineol, but the amount of material available was not sufficient to allow of these being investigated.

Unlike carvestrene, *m-cineol* dissolves at once in a saturated solution of hydrobromic acid in acetic acid with evolution of heat, and in a few minutes the solution clouds and an oil separates, but even after remaining for several days in a cool place this did not show any signs of crystallising. The product was diluted with water, extracted with ether, the ethereal solution washed with dilute sodium carbonate, dried over calcium chloride and evaporated, and the residue exposed over sulphuric acid in an evacuated desiccator.

A very small quantity of *trans*-carvestrene dihydrobromide (m. p. 48—49°) slowly separated, and the oil was found to contain 49.4 per cent. of bromine. There can therefore be little doubt that the main product of the fraction of hydrobromic acid at low temperatures on *m-cineol* is *cis*-carvestrene dihydrobromide.

The second fraction of the neutral oil boiling at 95—129° (20 mm.) was repeatedly fractionated, and yielded a large quantity of an oil which distilled constantly at 105—108° (30 mm.), and was found to be *dihydrocarvestrenol*:

0.1092 gave 0.3113 CO₂ and 0.1152 H₂O. C = 77.6; H = 11.7.

C₁₀H₁₈O requires C = 77.9; H = 11.7 per cent.

The highest fraction, 130—150° (20 mm.), gradually deposited crystals, and after some weeks the semi-solid mass was left in contact with porous porcelain until the oily impurity had been absorbed, and the colourless residue was then crystallised from light petroleum, from which long, slender needles separated. This substance melted at

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126—127°, and was found to be *trans-tetrahydrocarvestrenediol*, since, when mixed with the specimen of this substance obtained as explained on p. 502, no alteration in the melting point could be observed.

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