LXVI.—*Experiments on the Synthesis of the Terpenes.*
Part I. Synthesis of Terpin, Inactive Terpeneol,
and Dipentene.

By WILLIAM HENRY PERKIN, jun.

IN that remarkable section of chemistry which deals with the terpenes and their derivatives, there are probably few substances of greater importance than the closely related group, terpin, terpeneol, and dipentene, and this is due, not only to the great interest attached to the substances themselves, but also to their intimate connection with pinene and many other members of the same section. Terpin, as is well known, combines very readily with water to form the highly characteristic compound, terpin hydrate, $C_{10}H_{18}(OH)_2 \cdot H_2O$, and from the first this hydrate has been specially selected by chemists for investigation, partly because of its extraordinary facility for crystallising and the consequent ease with which it is obtained pure from oil of turpentine, and partly because there was reason to suppose that the determination of its constitution would afford a valuable clue to the nature of the terpene group as a whole. The fact that the constitution of terpin and its derivatives is now fairly well understood is due principally to the laborious researches of Baeyer, Tilden, Tiemann and Schmidt, and Wallach, and to the brilliant theoretical deductions of Wagner, and to such of this work as has a direct bearing on the present investigation some mention is made below.

It must, however, be remembered that it is impossible, within the limits of a paper of this kind, to enter into anything like a complete historical discussion of the gradual progress of the development of the formulæ of terpin, terpeneol, and dipentene, and for this reason many valuable contributions to our knowledge of the subject must unavoidably remain unnoticed.

The difficulties which early investigators of terpin and its derivatives had to encounter were of a quite unusual kind, not only owing to the fact

that the chemical behaviour of the many partially unsaturated closed chain compounds belonging to this class was, at that time, not at all understood, but also because of the unexpected fundamental intramolecular changes which were frequently met with, and which gave rise to false deductions and the suggestion of many formulæ now known to be incorrect.

That a close relationship exists between terpin, terpineol, and dipentene was long ago evident from the work of Tilden (*Ber.*, 1879, 12, 848) and of Wallach (*Annalen*, 1885, 230, 258), who showed that when terpin is digested with dilute acids, it yields terpineol, and that the latter is converted by potassium hydrogen sulphate at 200° into dipentene, these changes being simply due to the successive elimination of water :

The first to represent terpineol as a derivative of cymene appears to have been Kanonnikoff (*J. Russ. Phys. Chem. Soc.*, 1883, 15, 472), who, mainly from physical considerations, proposed the formula

for this substance. In a remarkable paper (*Annalen*, 1893, 277, 105), which contains a careful investigation of terpineol, Wallach suggested the following modification of this formula,

and, shortly afterwards, Baeyer (*Ber.*, 1893, 26, 2558) published a research on the same subject, in which he expresses his agreement with Wallach's view of the constitution of terpineol, and at the same time suggests the formula

for terpin.

The strongest argument against the acceptance of these views was the fact that, in whichever way water is eliminated from Wallach's terpineol formula, a constitution for dipentene is arrived at which does not contain an asymmetric carbon atom, whereas it is well known that dipentene is an externally compensated mixture of the two active *d*- and *l*-limonenes. In order to get over this difficulty, Baeyer (*Ber.*, 1894, 27, 454) suggested the possibility that the activity of the limonenes was due to the asymmetry of the whole molecule, and not to the presence of an asymmetric carbon atom.

In 1894, Wagner published his classical paper "On the oxidation of

cyclic compounds" (*Ber.*, 27, 1636), in which he discusses the constitutions of some of the more important members of the terpene group. From a careful consideration of the relationship of terpineol to pinene, pinol, and sobrerol, he deduces the expression,

as best representing terpineol, and points out that, if this formula is adopted, the difficulty with regard to the activity of the limonenes disappears, since the constitution of limonene (dipentene) would then be represented thus :

that is to say, by a formula which contains an asymmetric carbon atom. The constitution of terpin itself, deduced from the above formula for terpineol, would then be

That the formula suggested by Wagner for terpineol is correct was rendered probable by the subsequent work of Wallach (*Ber.*, 1895, 28, 1776), who showed that this substance, on oxidation, is converted first into trihydroxyhexahydrocymene, which then breaks up further into a ketolactone, called methoethylheptanonolid, and then into acetic and terpenylic acids. With the aid of Wagner's formula, these changes may be expressed in the following simple manner :

but Wallach is careful to remark that the formation of these oxidation products cannot be accepted as a definite proof that the constitution of terpineol is that suggested by Wagner.

The present investigation was undertaken with the object of synthesising terpin, terpineol, and dipentene, not only on account of the interest which always attaches to syntheses of this kind, but also in the hope that a method of synthesis might be devised of such a

simple kind that there would no longer be room for doubt as to the constitution of these important substances.

In the synthesis described in this paper, the first step was the preparation of ethyl γ -cyanopentane- $\alpha\gamma$ -tricarboxylate,

by the interaction of ethyl β -iodopropionate and ethyl sodiocyanoacetate. On hydrolysis with hydrochloric acid, this ester yields pentane- $\alpha\gamma$ -tricarboxylic acid, and on digesting with acetic anhydride and distilling, this acid is decomposed, with elimination of water and carbon dioxide and formation of δ -ketohexahydrobenzoic acid,

(compare Trans., 1904, 85, 418).

The ester of this acid reacts readily with magnesium methyl iodide in ethereal solution, and the product, on hydrolysis, yields δ -hydroxy-hexahydro-*p*-toluic acid, $\text{MeC}(\text{OH})\langle\begin{smallmatrix}\text{CH}_2\cdot\text{CH}_2 \\ \text{CH}_2\cdot\text{CH}_2\end{smallmatrix}\rangle\text{CH}\cdot\text{CO}_2\text{H}$, which melts at 153° and has already been prepared by Stephan and Helle (*Ber.*, 1902, 35, 2156) by the oxidation of $\Delta^{8(9)}$ -menthenol (I) (see p. 659). This hydroxy-acid dissolves readily in fuming hydrobromic acid, and the solution soon deposits crystals of δ -bromohexahydro-*p*-toluic acid (m. p. 126°), from which, by treatment with weak alkalis or pyridine, Δ^3 -tetrahydro-*p*-toluic acid (m. p. 99°) is obtained,

The last step was to convert the unsaturated acid into its ester and to act on this with an ethereal solution of magnesium methyl iodide, when an almost quantitative yield of an oil was obtained which, on examination, proved to be *terpineol*. This synthesis is readily understood with the aid of the formulæ,

the change being simply the conversion of the $-\text{CO}_2\text{Et}$ group into the group $-\text{CMe}_2\cdot\text{OH}$.

The *terpineol* thus synthesised had the pronounced odour of lilac which is so characteristic of this substance, and distilled constantly at 135° under 60 mm. pressure, and this was found to be exactly the temperature at which a sample of pure *terpineol*, from Schimmel & Co., distilled in the same apparatus and under the same conditions.

In order that there might be no room for doubt as to the identity of the synthetical product, it was converted into the *nitrosochloride*,

$C_{10}H_{18}O, NOCl$ (m. p. 122°), and *phenylurethane*, $C_{10}H_{17}O \cdot CO \cdot NH \cdot C_6H_5$ (m. p. 113°), and these were compared with specimens prepared from ordinary terpineol, with the result that the preparations obtained from both sources were found to be absolutely identical.

The next step was to convert the synthetical terpineol into dipentene, which was readily accomplished by heating with potassium hydrogen sulphate, when water was eliminated according to the scheme,

The *dipentene* produced in this way was converted into the *tetra-bromide*, $C_{10}H_{16}Br_4$ (m. p. 125°), the *dihydrochloride*, $C_{10}H_{16}, 2HCl$ (m. p. $48-50^\circ$), and the *nitrosochloride*, $C_{10}H_{16}, NOCl$ (m. p. 106°), and these derivatives were compared with the corresponding specimens obtained from ordinary dipentene, with which they were found to be identical in all respects.

Lastly, the synthetical terpineol was agitated with dilute sulphuric acid until the oil had become converted into a mass of crystals; these, on examination, were found to consist of pure terpin hydrate,

and thus the synthesis of the three substances, terpin, terpineol, and dipentene, which have played so prominent a part in the history of the terpene group, was accomplished, and in a way which can leave no further doubt as to their constitutions.

Recently, Stephan and Helle (*Ber.*, 1902, 35, 2147) have shown that one of the products of the dehydration of terpin is that isomeric modification of terpineol,

for which the name $\Delta^{8(9)}$ -menthenol (1) has been suggested (Meyer and Jacobson, *Lehrbuch*, II, 933). When this interesting substance is oxidised, it yields the following products

and the last of these is identical with the acid which is one of the steps in the foregoing synthesis of terpineol. For the purpose of this synthesis, this acid was prepared from ethyl *δ*-ketohexahydrobenzoate by the action of magnesium methyl iodide, the change being simply due to the conversion of the ketonic group into the group $\text{MeC(OH)}<$. The reaction does not, however, proceed entirely in this direction, for there is always produced, although in very small quantity, a neutral oil, the formation of which is due to the conversion of the $-\text{CO}_2\text{Et}$ group into the group $-\text{CMe}_2\cdot\text{OH}$:*

The hydroxyisopropyl-*p*-ketohexamethylene obtained in this way could only be somewhat imperfectly investigated, owing to the small amount of available material. It distils at 177—180° under 100 mm. pressure, and when treated with hydrobromic acid and then with alcoholic potash, is converted into isopropenyl-*p*-ketohexamethylene (b. p. 186°):

When this ketone is left in contact with magnesium methyl iodide, a substance, $\text{C}_{10}\text{H}_{18}\text{O}$, is produced, which distils at 127° (60 mm.) and crystallises on cooling. Assuming that, during this process, the ketonic group is converted in the usual way into the group $\text{MeC(OH)}<$, the substance, $\text{C}_{10}\text{H}_{18}\text{O}$, should be identical with the menthenol,

of Stephan and Helle. The most characteristic derivative of this menthenol appears to be the phenylurethane which melts at 85°, and, on preparing this derivative from the above synthetical substance, crystals were obtained which melted at 83—85°, so that there is little room for doubt that the synthetical substance is identical with the above $\Delta^{8(9)}$ -menthenol (1).

It is hoped that further experiments, which are in progress, will result in the synthesis of other important members of the terpene series.

* This behaviour has been also observed in the case of other keto-esters, and a description of the interesting substances obtained in this way is reserved for a future communication.

The preparation of these substances may be conveniently carried out in the following way.

In a large flask, connected with a reflux condenser, magnesium (12 grams) is covered with anhydrous ether* (300 c.c.), and then methyl iodide (100 grams) added in four portions, the vigorous reaction being kept under control by means of running water. As soon as all the magnesium has dissolved, the flask is well cooled, and ethyl δ -keto-hexahydrobenzoate† (50 grams) is then gradually run in. The decomposition is not energetic, the rise of temperature being comparatively small, and as this seemed to point to the reaction being a gradual one, the whole was always left for 24 hours.

Excess of dilute hydrochloric acid is then cautiously added in small quantities at a time, the flask being carefully cooled after each addition, the ethereal solution is separated, washed with a little water and evaporated, and the residual yellow oil mixed with a solution of caustic potash (50 grams) in methyl alcohol. After heating for a few minutes on the water-bath, water is added, and the small quantity of neutral oil (the examination of which is described on p. 670) extracted with ether.

The aqueous liquor is then evaporated until free from methyl alcohol, transferred to a flask, acidified with hydrochloric acid, and heated for half an hour on the water-bath, when the crude lactone of δ -hydroxyhexahydro-*p*-toluic acid separates as a brown oil which has a powerful odour of peppermint. In order to extract completely the whole of the products of the reaction, the aqueous liquors must be treated at least 20 times with ether in the ordinary way or 10 times on the shaking machine: the ethereal solution is then repeatedly extracted with sodium carbonate (A, see p. 661), dried over calcium chloride, and evaporated. The residual crude lactone distils for the most part at 140—150° under 45 mm. pressure and the distillate gradually becomes semi-solid. After cooling in ice and salt, the crystals are rapidly collected at the pump,‡ drained on porous porcelain, and purified by recrystallisation

* The ether used in these experiments was first dehydrated over sodium and then distilled over phosphoric oxide; the methyl iodide was also distilled over phosphoric oxide.

† For the preparation of this ester, see Trans., 1904, 85, 427.

‡ The oily filtrate from these crystals may be used, without further purification, in the preparation of δ -bromohexahydro-*p*-toluic acid (p. 663).

from light petroleum (b. p. 60—70°), from which the lactone separates in glistening leaflets.

0.1240 gave 0.3098 CO₂ and 0.0962 H₂O. C = 68.2; H = 8.6.

0.1363 „ 0.3421 CO₂ „ 0.1061 H₂O. C = 68.4; H = 8.7.

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

The lactone of *cis*- δ -hydroxyhexahydro-*p*-toluic acid has already been described by Stephan and Helle (*Ber.*, 1902, 35, 2154); it melts at 69—70°, and possesses a penetrating odour closely resembling that of thymol. When the lactone is warmed with barium hydroxide, it readily dissolves, and the solution, after acidifying, remains clear, but if boiled with excess of hydrochloric acid, oily drops of the lactone soon separate. In order to isolate the corresponding hydroxy-acid, a considerable quantity of the lactone was hydrolysed by boiling with excess of barium hydroxide, the acidified solution being then extracted 10 times with ether. After drying over calcium chloride and evaporating to a small bulk, the ethereal solution gradually deposited a crystalline crust, which was collected, washed with a little ether, and re-crystallised from the same solvent.

0.1395 gave 0.3099 CO₂ and 0.1143 H₂O. C = 60.5; H = 9.1.

C₈H₁₄O₃ requires C = 60.8; H = 8.8 per cent.

cis- δ -Hydroxyhexahydro-*p*-toluic acid melts at about 153°, and is readily soluble in hot water, from which it crystallises, on cooling, in colourless, glistening leaflets.

Examination of the Sodium Carbonate Extract A (see p. 660).

After the lactone of δ -hydroxyhexahydro-*p*-toluic acid had been separated as described above, the extract (A) was acidified, saturated with ammonium sulphate, and extracted 10 times with ether; the ethereal solution was dried over calcium chloride and evaporated, when a brown syrup was obtained, which, when left over sulphuric acid in a vacuum desiccator, became semi-solid. In contact with porous porcelain, the dark, oily impurity was soon absorbed, and the residual yellow, crystalline mass was readily purified by crystallisation from water with the aid of animal charcoal. The colourless, glistening crystals thus obtained melted at 153°, and consisted of pure δ -hydroxyhexahydro-*p*-toluic acid.

0.1401 gave 0.3112 CO₂ and 0.1140 H₂O. C = 60.6; H = 9.0.

C₈H₁₄O₃ requires C = 60.8; H = 8.8 per cent.

The amount of hydroxy-acid obtained in this way was considerable (p. 662), and it is therefore evident that only a portion of this acid is

converted into its lactone when it is digested with dilute hydrochloric acid under the conditions described on p. 660.

The porous porcelain, which had been used to absorb the dark, oily mother liquors of the hydroxy-acid (see above), was broken up and extracted with ether in a Soxhlet apparatus, and the extract dried over calcium chloride and evaporated. On distilling the residue under 15 mm. pressure, water was eliminated, and, with the exception of a small quantity of a dark brown, resinous substance, the whole passed over below 210° , and most of it distilled at 140 — 150° . The distillate was dissolved in ether, the ethereal solution extracted with sodium carbonate, dried over calcium chloride, and evaporated, and the residue fractionated under 100 mm. pressure, when the whole passed over at 175 — 185° as a colourless oil, which gradually became semi-solid, and on examination was found to consist of the lactone of δ -hydroxyhexahydro-*p*-toluic acid.*

The sodium carbonate extract was acidified and extracted, when, after drying and evaporating to a small bulk, small hexagonal plates were deposited which melted at 65 — 67° , and consisted of δ -keto-hexahydrobenzoic acid, which had escaped the action of the magnesium methyl iodide, and in some experiments a good deal of this valuable acid was recovered in this way. In order to obtain an approximate estimate of the yields obtained in the above preparation of δ -hydroxyhexahydro-*p*-toluic acid and its lactone, two special experiments were made, and the average of these gave the following results. After treatment with magnesium methyl iodide, 100 grams of ethyl keto-hexahydrobenzoate were found to yield 21 grams of lactone (obtained direct), and, from the sodium carbonate-extract (A), 12 grams of the same lactone, 10 grams of the hydroxy-acid, and 8 grams of unchanged keto-hexahydrobenzoic acid. No doubt the considerable loss shown by these numbers is partly accounted for by the formation of resinous substances which remain in the distilling flasks, but it is also due largely to the great difficulty experienced throughout this research in extracting completely the products of the reactions, even when the solutions were treated on the shaking machine with large quantities of ether.

The δ -hydroxyhexahydro-*p*-toluic acid described in this section is evidently the *cis*-modification, since it readily yields a lactone, and, in spite of very careful search, no trace of the corresponding *trans*-acid, which it was thought should also have been present, could be detected.

* Stephan and Helle (*loc. cit.*, p. 2153) state that pure δ -hydroxyhexahydro-*p*-toluic acid distils unchanged under 10—15 mm. pressure, but yields the lactone when distilled under the ordinary pressure.

The above experiment shows that the crude acid is completely converted into its lactone on distillation under 15 mm. pressure.

Attention has already been directed (Trans., 1904, 85, 421) to the fact that in many cases where stereoisomeric modifications should be capable of existence it sometimes happens either that, as in the above case, only one of the modifications is actually obtained, or more frequently that the one is found to be present in very much larger quantities than the other.

δ-Bromohexahydro-p-toluic Acid, $\text{MeCBr} \begin{smallmatrix} \text{CH}_2 \cdot \text{CH}_2 \\ \text{CH}_2 \cdot \text{CH}_2 \end{smallmatrix} \text{CH} \cdot \text{CO}_2\text{H}$, and
 Δ^3 -*Tetrahydro-p-toluic Acid*, $\text{MeC} \begin{smallmatrix} \text{CH} - \text{CH}_2 \\ \text{CH}_2 \cdot \text{CH}_2 \end{smallmatrix} \text{CH} \cdot \text{CO}_2\text{H}$, and its
Derivatives.

When the finely powdered lactone of *δ*-hydroxyhexahydro-*p*-toluic acid (p. 661) was mixed with aqueous hydrobromic acid (saturated at 0°) it dissolved, and almost immediately the liquid became clouded and an oil separated which rapidly solidified. After two hours, water was added, the crystalline precipitate of the bromo-acid collected, and left in contact with porous porcelain until quite dry; it was then dissolved in boiling light petroleum (b. p. 70–80°), from which it separated in groups of glistening needles. The dry substance has a satiny lustre, and closely resembles benzoic acid in appearance.

0.1368 gave 0.1156 AgBr. Br = 36.0.

$\text{C}_8\text{H}_{13}\text{O}_2\text{Br}$ requires Br = 36.2 per cent.

δ-Bromohexahydro-p-toluic acid softens at 122° and melts at about 126°; it is readily soluble in alcohol, but almost insoluble in water; it dissolves readily in boiling light petroleum, but sparingly in the cold. Much of the bromo-acid which was required for this research was prepared direct from *δ*-hydroxyhexahydro-*p*-toluic acid itself. This acid dissolves in concentrated hydrobromic acid, but the solution soon begins to deposit crystals, and, after two hours, water is added and the bromo-acid purified as described above. Again, in preparing the bromo-acid from the lactone, it should be mentioned that it is not at all necessary to use the recrystallised lactone; the semi-solid fraction boiling at 140–150° (45 mm.) was always employed with excellent results (compare p. 660 and footnote).

Action of Sodium Carbonate on δ-Bromohexahydro-p-toluic Acid.—In studying this decomposition, the pure bromo-acid was ground with water to a fine paste, excess of a warm saturated solution of sodium carbonate was then added, and, after the acid had dissolved, the whole was heated to boiling for a few minutes. On acidifying the cold liquid, a crystalline precipitate separated at once and was collected, washed well, and purified by recrystallisation from much water, from which the substance separated in needles resembling benzoic acid.

0.1258 gave 0.3162 CO₂ and 0.0980 H₂O. C = 68.5; H = 8.6.

0.1513 „ 0.3795 CO₂ „ 0.1179 H₂O. C = 68.4; H = 8.7.

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

This Δ³-tetrahydro-*p*-toluic acid has already been obtained by Stephan and Helle (*Ber.*, 1902, 35, 2154) from Δ⁸⁽⁹⁾-menthenol (1) by the action of oxidising agents. It softens at 95° and melts at 99–100°; it is almost insoluble in cold water, and very sparingly so even on boiling; it dissolves readily in acetic acid, and dilute acetic acid appears to be the most convenient solvent from which to crystallise it.

The aqueous mother liquors from which this acid had separated on acidifying were extracted repeatedly with ether, the ethereal solution dried over calcium chloride and evaporated, when a considerable quantity of a solid acid was obtained which crystallised from water in glistening needles and melted at 153°. This substance on analysis proved to be δ-hydroxyhexahydro-*p*-toluic acid, which had evidently been produced from the bromo-acid by simple hydrolysis.

Action of Pyridine on δ-Bromohexahydro-p-toluic Acid.—As the yield of the tetrahydro-acid produced in the above experiment was only about 60 per cent. of the theoretical (nearly 40 per cent. being converted into the hydroxy-acid), the action of pyridine as an agent for eliminating hydrogen bromide was investigated, and excellent results were obtained. The bromo-acid dissolves readily in pyridine, and if, after boiling for 5 minutes, the excess of pyridine is removed by evaporation and the residue decomposed by dilute sulphuric acid, a white, crystalline deposit of nearly pure tetrahydro-acid is obtained at once, the yield being almost quantitative. After recrystallising from dilute acetic acid, a sample of the acid prepared in this way was analysed with the following result:

0.1390 gave 0.3489 CO₂ and 0.1082 H₂O. C = 68.5; H = 8.7.

C₈H₁₄O₂ requires C = 68.6; H = 8.6 per cent.

Ethyl Δ³-Tetrahydro-p-toluate.—This ester could not be prepared from the acid by treatment with alcohol and hydrogen chloride in the ordinary way, owing to the great ease with which it unites with hydrogen chloride; it was, however, obtained pure in the following manner. The pure acid (25 grams) was digested for three hours on the water-bath with 100 c.c. of a mixture of 1 volume of sulphuric acid and 10 volumes of alcohol, and, after remaining overnight, water was added and the oily ester extracted with ether. The ethereal solution was washed well with water and dilute sodium carbonate, dried over calcium chloride, and evaporated, the residual oil being fractionated under 100 mm. pressure.

Almost the whole distilled at 155—157° as a colourless oil having a pungent and unpleasant odour.

0.1109 gave 0.2893 CO₂ and 0.0949 H₂O. C = 71.0; H = 9.5.

C₁₀H₁₆O₂ requires C = 71.4; H = 9.5 per cent.

γδ-Dibromohexahydro-p-toluic Acid.—Tetrahydro-*p*-toluic acid shows all the properties of an unsaturated acid, since its solution in sodium carbonate rapidly decolorises permanganate, and the powdered acid is at once attacked by bromine with considerable development of heat and evolution of some hydrogen bromide. In order to prepare the dibromo-additive product, the acid was dissolved in dry chloroform, the solution cooled to -10°, and bromine added drop by drop until the colour just remained permanent. The solution was then exposed in a shallow basin and, when the chloroform had evaporated, a solid residue was obtained which crystallised from formic acid (sp. gr. 1.22) in satiny plates.

0.1396 gave 0.1754 AgBr. Br = 53.4.

C₈H₁₂O₂Br₂ requires Br = 53.3 per cent.

γδ-Dibromohexahydro-p-toluic acid melts at about 104°, but it softens a few degrees below this temperature. It dissolves readily in sodium carbonate, and the solution is stable to permanganate in the cold and, even on warming, reduction takes place only gradually.

Conversion of Δ³-Tetrahydro-p-toluic Acid into p-Toluic Acid by Oxidation with Sulphuric Acid.—In carrying out this oxidation, the tetrahydro-acid (1 gram) dissolved in concentrated sulphuric acid (10 grams) was heated on the water-bath until the evolution of sulphur dioxide was complete, which was the case after about 10 minutes. The dark brown liquid was diluted with water, the solid mass which separated was collected, washed with water, dried on porous porcelain, and distilled. The distillate was then recrystallised from dilute acetic acid, and the colourless mass of crystals dried at 100°.

0.1385 gave 0.3575 CO₂ and 0.0748 H₂O. C = 70.4; H = 6.0.

C₈H₈O₂ requires C = 70.6; H = 5.9 per cent.

This acid melted sharply at 179°, and consisted of pure *p*-toluic acid.

Action of Magnesium Methyl Iodide on Ethyl Δ³-Tetrahydro-p-toluate.
Synthesis of Inactive Terpeneol.

In carrying out this synthesis, magnesium (21 grams) was covered with pure dry ether (500 c.c.) and then gradually treated with an

excess of methyl iodide (120 grams),* the vigorous reaction being kept under control by cooling in running water. As soon as the magnesium had dissolved, ethyl tetrahydro-*p*-toluate (30 grams) was added in one portion, since the reaction takes place apparently only gradually, and with evolution of very little heat. After 24 hours, the product was cautiously decomposed by adding water and dilute hydrochloric acid, the ethereal solution was separated, washed with dilute hydrochloric acid, and evaporated. In order to remove any unchanged ester which might have escaped the action of the magnesium methyl iodide, the yellow, oily residue was mixed with a solution of caustic potash (10 grams) in methyl alcohol and heated on the water-bath for 15 minutes; water was then added and the oil again extracted with ether.

The ethereal solution was carefully freed from methyl alcohol by washing with water, dried over anhydrous sodium sulphate, and the residue, after evaporation, distilled under 60 mm. pressure.

With the exception of a small quantity of a more volatile fraction which had the odour of dipentene, almost the whole quantity distilled at 134–135° as a viscid, colourless oil† which proved to be *inactive terpineol*. After a second fractionation, the following analytical results were obtained:

0.1592 gave 0.4536 CO₂ and 0.1670 H₂O. C=77.7; H=11.7.

0.1431 „ 0.4086 CO₂ „ 0.1529 H₂O. C=77.8; H=11.9.

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

That the boiling point given above is that of terpineol was proved by distilling a specimen of pure terpineol in the same apparatus and under the same conditions, when a boiling point identical with that given above was observed. Furthermore, the synthetical substance possessed in a marked degree the odour of lilac, which is so characteristic of terpineol. In order, however, that there should be no doubt as to the identity of the synthetical substance, it was converted into the crystalline nitrosochloride and phenylurethane, which were then compared, and found to be identical with specimens prepared from ordinary terpineol.

Terpineolnitrosochloride, C₁₀H₁₈O.NOCl.

This derivative was obtained by mixing synthetical terpineol (1.5 grams) with glacial acetic acid (1.5 c.c.) and *isoamyl* nitrite (1.5 c.c.);

* See footnote, p. 660.

† When this oil was cooled in a freezing mixture, it became very viscid, but did not crystallise even on rubbing with a glass rod, and the same behaviour was noticed in the case of a carefully fractionated sample of liquid terpineol. Subsequently, a specimen of solid terpineol was obtained from Schimmel & Co., and, on adding a minute crystal of this to the synthetical terpineol and cooling in ice, the whole became quite solid.

hydrochloric acid (0.7 c.c.) was then added drop by drop, the whole being carefully cooled in ice and salt during the operation. After 2 hours, the pale green liquid was poured on to powdered ice, when an oil separated which gradually solidified.

In contact with porous porcelain, traces of oily mother liquor were rapidly absorbed, and the residue, after recrystallisation from ethyl acetate, melted at about 119—122°, whereas a specimen of the nitrosochloride, prepared from crystallised terpineol in the same way, melted at 121—123°. The identity was further proved by the fact that the mixture of the two specimens melted at 120—122°.

The specimen from synthetical terpineol was analysed with the following result:

0.1129 gave 0.0724 AgCl. Cl = 15.9.

$C_{10}H_{18}O_2NCl$ requires Cl = 16.1 per cent.

Terpineolphenylurethane, $C_{10}H_{17}O \cdot CO \cdot NH \cdot C_6H_5$.

In preparing this substance, synthetical terpineol (1.5 grams) was mixed with phenylcarbimide (1.2 grams), and the whole heated at 60° for one hour and then at 90° for half an hour. On pouring the product on to a watch glass, it soon solidified completely, and was easily purified by recrystallisation from dilute methyl alcohol, from which it separated in colourless needles melting at 113° (compare Wallach, *Annalen*, 1893, 275, 104).

0.1406 gave 6.2 c.c. of nitrogen at 16° and 760 mm. N = 5.2.

$C_{17}H_{23}O_2N$ requires N = 5.1 per cent.

A quantity of the phenylurethane was prepared from crystallised terpineol, and found to melt at the same temperature; moreover, on mixing this with the specimen obtained from synthetical terpineol, no alteration in the melting point could be observed.

Conversion of Synthetical Terpineol into Terpin Hydrate.

Tiemann and Schmidt have made the interesting observation (*Ber.*, 1895, 28, 1781) that when terpineol is shaken with dilute sulphuric acid it is slowly converted into terpin hydrate, and as this change is highly characteristic, it was thought important to endeavour to bring it about in the case of the synthetical substance.

Synthetical terpineol (10 grams) was therefore mixed with benzene (5 grams) and shaken in a stoppered bottle, partly by hand and partly on the machine, with 1500 c.c. of 5 per cent. sulphuric acid.

After three days, crystals began to appear on the sides of the bottle, and when the formation of these seemed to be complete (in about 10 days), the whole was filtered and the pasty mass left in contact with porous porcelain until quite dry. The residue, together with a further crop of crystals which were obtained from the sulphuric acid mother liquors by saturating with ammonium sulphate, was then slowly recrystallised from water, and in this way magnificent crystals of *terpin hydrate* were obtained, which, after remaining exposed to the air for 2 days, were analysed.

0.1545 gave 0.3578 CO_2 and 0.1607 H_2O . $\text{C} = 63.1$; $\text{H} = 11.6$.

$\text{C}_{10}\text{H}_{22}\text{O}_3$ requires $\text{C} = 63.2$; $\text{H} = 11.6$ per cent.

When rapidly heated, this substance melted at 120° with vigorous decomposition,* due to evolution of steam, and, when kept in a water oven at 90° , the glistening crystals gradually became opaque and partially sublimed, and the *anhydrous terpin* thus obtained melted at 105° , which is the melting point of ordinary terpin (Wallach, *Annalen*, 1885, 230, 248). Furthermore, an intimate mixture of synthetical and ordinary terpin hydrate melted at exactly the same point as the components, so that there can be no doubt that the synthetical substance is identical in all respects with ordinary terpin hydrate.

Conversion of Synthetical Terpeneol into Dipentene,

It is well known that when ordinary terpeneol is heated with potassium hydrogen sulphate it is readily converted, with loss of water, into dipentene, and in order to accomplish this important transformation in the case of synthetical terpeneol, the following experiment was carried out. Synthetical terpeneol (21 grams) was mixed with powdered potassium hydrogen sulphate (30 grams) and heated to boiling for 1 hour in a reflux apparatus, during which it was noticed that much water was produced. After distilling in steam, the oil was extracted with ether, dried over calcium chloride, and roughly fractionated, and the portion boiling above 185° , which contained unchanged terpeneol, again heated with potassium hydrogen sulphate. The dipentene obtained from both experiments was carefully fractionated, and 15 grams were obtained, which distilled at $180-183^\circ$, and possessed in a marked degree the characteristic odour of lemons; but this did not

* This decomposition point is usually given as $116-117^\circ$, but if capillary tubes containing terpin hydrate are plunged into sulphuric acid heated in different experiments at temperatures between 116° and 122° , it will be seen that the correct point of decomposition is about $120-121^\circ$.

give satisfactory results on analysis. Experiments with ordinary dipentene clearly showed that it is a matter of considerable difficulty to prepare a specimen of dipentene in so pure a condition that it will give good results on analysis, and this is partly due to the rapidity with which this terpene absorbs oxygen from the air. The desired result was, however, ultimately accomplished in the case of the synthetical product by repeated distillation over sodium in a current of dry carbon dioxide, and the sample analysed distilled constantly at 180—181°.

0·1351 gave 0·3365 CO₂ and 0·1451 H₂O. C=88·1; H=11·9.

C₁₀H₁₆ requires C=88·2; H=11·8 per cent.

In order to demonstrate clearly the identity of this synthetical hydrocarbon with ordinary dipentene, the following derivatives were prepared from it, and directly compared with specimens made under exactly the same conditions from pure dipentene.

Dipentene Dihydrochloride, C₁₀H₁₆, 2HCl.—Synthetical dipentene (2 grams) was mixed with glacial acetic acid (1 gram) in a beaker, and gaseous hydrogen chloride led over the surface for about an hour. On mixing the solution with ice and water, an oil separated which readily solidified, and after remaining in contact with porous porcelain until quite dry, the substance was further purified by dissolving in alcohol and precipitating with water as recommended by Wallach (*Annalen*, 1887, 239, 12).

0·1282 gave 0·1767 AgCl. Cl=34·1.

C₁₀H₁₈Cl₂ requires Cl=34·0 per cent.

This dihydrochloride melted at 48—50°, and was identical in all respects with a specimen prepared from ordinary dipentene.

Dipentenetetra bromide, C₁₀H₁₆Br₄.—This substance was readily obtained by dissolving synthetical dipentene in twice its volume of pure, dry chloroform, cooling to -10°, and adding bromine drop by drop until the yellow colour persisted for 5 minutes.

The solution was freed from chloroform by aspirating a rapid current of dry air over it, and the crystalline residue was dried on porous porcelain and recrystallised from ethyl acetate, when it separated in colourless, glistening needles.

0·1344 gave 0·2213 AgBr. Br=70·1.

C₁₀H₁₆Br₄ requires Br=70·2 per cent.

Thus prepared, the tetrabromide melted at 125°, and when mixed with an equal quantity of ordinary dipentenetetra bromide, no alteration in the melting point could be detected.

Dipentenitrosochloride, C₁₀H₁₆, NOCl.—This substance was prepared from synthetical dipentene by the method recommended by

Wallach (*Annalen*, 1888, 245, 268); it melted at 106°, and was identical in all respects with ordinary dipentenitrosochloride.

Hydroxyisopropyl-p-ketohexamethylene, isoPropenyl-p-ketohexamethylene, and the Conversion of the latter into $\Delta^{8(9)}$ -Menthenol (1),

In describing the action of magnesium methyl iodide on ethyl δ -keto-hexahydrobenzoate (p. 660), it was mentioned that a neutral oil, unaffected by the treatment with methyl-alcoholic potash, and having an intense odour of peppermint, is always produced in small quantity.

During the course of this research, about 30 grams of this oil were gradually accumulated and then treated as follows.

It was first distilled in steam and then repeatedly fractionated under 100 mm. pressure, and thus separated into two portions boiling at 135—150° and 177—180°. The latter, which was about two-thirds of the whole, was analysed with the following result :

0.1113 gave 0.2799 CO₂ and 0.1048 H₂O. C = 68.6 ; H = 10.4.
CO(CH₂·CH₂)₂CH·CMe₂·OH or C₉H₁₆O₂ requires C = 69.2 ; H = 10.2 per cent.

As explained in the introduction (p. 659), this analysis and the method of formation of the substance leave scarcely any doubt that it is hydroxyisopropyl-*p*-ketohexamethylene. It is a viscid oil which is readily volatile in steam.

The lower fraction, boiling at 135—150° (100 mm.), was repeatedly distilled under the ordinary pressure, and about 10 grams were thus isolated, which boiled, not quite constantly, at 184—186°.

0.1507 gave 0.4286 CO₂ and 0.1369 H₂O. C = 77.3 ; H = 10.1.
CO(CH₂·CH₂)₂CH·CMe·CH₂ or C₉H₁₄O requires C = 78.2 ; H = 10.1 per cent.

This substance evidently has the composition C₉H₁₄O, and is derived from hydroxyisopropylketohexamethylene by the elimination of water, but as it could not be completely separated from this hydroxy-compound by fractionation, it was shaken with aqueous hydrobromic acid (saturated at 0°), and the heavy bromide thus produced digested with methyl-alcoholic potash. After extracting in the usual way, the resulting oil distilled at the same temperature as before, and gave on analysis numbers agreeing rather more closely with the formula C₉H₁₄O.

0·1211 gave 0·3449 CO₂ and 0·1110 H₂O. C = 77·6 ; H = 10·2.

C₉H₁₄O requires C = 78·2 ; H = 10·1 per cent.

This *isopropenyl-p-ketohexamethylene* is isomeric with phorone, acetophorone, camphorone, and many other similar ketones, and with these it shares the property of possessing a penetrating odour of peppermint. The conversion of this ketone into $\Delta^{8(9)}$ -menthenol (1), which is discussed in the introduction (p. 659), was carried out as follows. Magnesium (3 grams) was covered with dry ether (100 c.c.) and converted into magnesium methyl iodide by treatment with 25 grams of methyl iodide ; the ketone (6 grams), dissolved in ether (20 c.c.), was then added, and the whole left for 24 hours. The product was then decomposed by dilute hydrochloric acid, the ethereal solution separated, washed with water, evaporated, and the residual oil, after distilling in steam, fractionated under 60 mm. pressure. Almost the whole quantity distilled at 125–127°, or about 8° lower than terpineol, with which it is isomeric, and there can be no doubt that this synthetical substance is identical with the $\Delta^{8(9)}$ -menthenol (1) of Stephan and Helle (*Ber.*, 1902, 35, 2147), and which melts at 32°.

0·1506 gave 0·4298 CO₂ and 0·1625 H₂O. C = 77·9 ; H = 11·9.

C₁₀H₁₈O requires C = 77·9 ; H = 11·7 per cent.

The viscid oil thus obtained had a very pronounced odour of hyacinths, and when cooled in ice and well stirred, it crystallised ; but owing to the small amount of material available no attempt could be made to recrystallise it and determine its melting point.

On treatment with *isoamyl* nitrite and hydrochloric acid in acetic acid solution, it yielded a crystalline nitrosochloride, and phenylcarbimide converted it into a phenylurethane, which, after crystallisation from dilute methyl alcohol, melted at 85–87°, whereas Stephan and Helle give 85° as the melting point of the phenylurethane of $\Delta^{8(9)}$ -menthenol (1).

The author wishes to express his thanks to Mr. S. S. Pickles, B.Sc., for his valuable assistance in carrying out this difficult investigation, and to state that much of the expense incurred has been met by repeated grants from the Government Grant Fund of the Royal Society.

THE OWENS COLLEGE,
MANCHESTER.