

CCCLXXI.—*Piperitone. Part XI. Syntheses of Optically Inactive and Active Piperitylamines, Piperitols, and α -Phellandrenes.*

By JOHN READ and RALPH ALEXANDER STOREY.

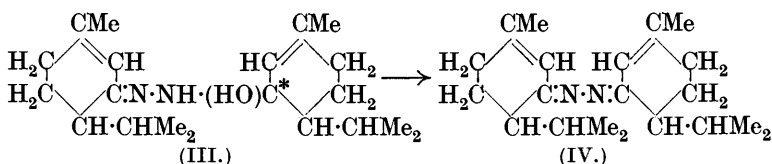
PIPERITOL, or Δ^1 -menthen-3-ol (I), the $\alpha\beta$ -unsaturated secondary alcohol corresponding to piperitone, was originally discovered by H. G. Smith in the essential oils of several members of the so-called "peppermint" group of eucalypts; it occurs in these oils in a lævorotatory form, together with *l*-piperitone and *l*- α -phellandrene (Baker and Smith, "A Research on the Eucalypts," 2nd edn, Sydney, 1920, p. 373). More recently, a dextrorotatory form of the same alcohol has been found by Simonsen (*Indian Forest Records*, 1924, **10**, part viii) in the essential oil of a new species of *Andropogon* growing in the United Provinces; in this instance the oil contained *d*- Δ^4 -carene and certain other constituents, but piperitone was absent.

Following unsuccessful attempts to reduce piperitone directly to piperitol (compare Gibson and Simonsen, *Chemistry and Industry*, 1930, **49**, 540), repeated endeavours have been made to attain the same end through the corresponding primary amine, piperitylamine (II):



Hitherto, however, such methods as the reduction of piperitone-oxime (Read, Cook, and Shannon, *J.*, 1926, 2226) and the treatment of piperitone with ammonium formate have not proved suitable for the preparation of this base, owing to the simultaneous production of menthylamines.

We now show that the viscid oil obtained by the interaction, under proper conditions, of *l*-piperitone and hydrazine may be readily reduced to optically inactive piperitylamine, which therefore becomes available in quantity. The constitution of the viscid oil remains in doubt. The analysis corresponds to a hydrated azine (III), and this structure affords an explanation of the curious fact that when heated to 95° under diminished pressure the substance loses water and undergoes a striking diminution in optical rotation, *e.g.*, from $[\alpha]_D + 201.1^\circ$ to $+ 48.3^\circ$. This change would be conditioned by the loss of asymmetry of the carbon atom marked with an asterisk:



The specimens of piperitylamine obtained by reducing the above viscous product with zinc and glacial acetic acid displayed only a feeble optical activity, and readily furnished characteristic, optically inactive *acetyl*, *benzoyl*, and *anisoyl* derivatives, in addition to a well-defined hydrochloride. The structure of the base (II) follows from its conversion into piperitol and piperitone.

When fractionally crystallised with a molecular proportion of *d*-tartaric acid, this base yielded a highly distinctive hydrogen tartrate of the form *dAlB*. The physical constants of the corresponding *l*-piperitylamine are compared below with those of the optically inactive base and of *l*-menthylamine (this vol., p. 2764) :

Piperitylamines and l-Menthylamine.

	B. p.	d_4^{25} (vac.).	n_D^{25} .	$[R_L]_D$.	$[\alpha]_D^{25}$.
<i>dl</i> -Piperitylamine	97.5—98.5°/16 mm.	0.8801	1.4769	49.20	—
<i>l</i> -Piperitylamine	98.2°/16 mm.	0.8789	1.4770	49.27	—80.35°
<i>l</i> -Menthylamine	81—82°/12 mm.	0.8525	1.4600	49.86	—44.53

The calculated values of $[R_L]_D$ for piperitylamine and menthylamine are 49.14 and 49.53, respectively.

The constants are thus markedly higher for the piperitylamines than for the menthylamines.

A detailed study, now in hand, of the optical resolution of inactive piperitylamine indicates that this base may possibly consist of a mixture of *dl*-piperitylamine and *dl*-*neopiperitylamine*. There is at present no evidence to indicate whether the above levorotatory piperitylamine corresponds configurationally to *d*-piperitol or to *d*-*neopiperitol* (*vide infra*), that is, whether it possesses the *cis*- or the *trans*-configuration. For the time being, it is called *l*-piperitylamine.

When treated with nitrous acid, these bases yield piperitols; in practice, however, the most satisfactory results have been attained by steam-distilling mixtures of the piperityltrimethylammonium iodides (VII) and silver oxide. In this way, both the *dl*- and the *l*-compound yield a mixture of two stereoisomeric piperitols, the physical constants of which are summarised below, together with the corresponding values recorded by Smith and by Simonsen (*loc. cit.*) for naturally occurring *l*- and *d*-piperitol, respectively :

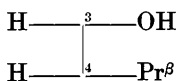
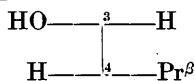
Piperitols.

	B. p.	d^* .	n_D^* .	$[R_L]_D$.	$\alpha_D^{25}(1\text{-dec.})$.
Smith, <i>l</i> -	95—96°/ 10 mm.	0.9230 ^{22°}	1.4760 ^{22°}	47.04	-34.1°
Simonsen, <i>d</i> -	165—170°/ 200 mm.	0.911 ^{30°}	1.474 ^{30°}	47.5	+41.9 ^{30°}
Read and Storey, <i>dl</i> - <i>neo</i> -	94—96°/ 15.5 mm.	—	1.4740 ^{19.5°}	—	—
Read and Storey, <i>dl</i> -	100—106°/ 19.5 mm.	—	1.4769 ^{18°}	—	—
Read and Storey, <i>d</i> - <i>neo</i>	96.5—98.5°/ 15.5 mm.	0.9119 ^{25°}	1.4729 ^{25°}	47.40	+21.22 ^{16°}
Read and Storey, <i>d</i> -	101—104°/ 16 mm.	0.9200 ^{25°}	1.4770 ^{18°}	—	+40.22 ^{16°}

The calculated value of $[R_L]_D$, irrespective of exaltation, is 47.16.

A complete separation of the two stereoisomeric *dl*- or *d*-piperitols is not claimed at this stage of the investigation, but from an examination of the foregoing data it is evident that the natural alcohols isolated by Smith and Simonsen correspond to the higher- rather than to the lower-boiling synthetic substances. That the two dextrorotatory piperitols derived from *l*-piperitylamine differ only in the asymmetry of carbon atom (3) is shown by the fact that upon oxidation with chromic acid they both furnish practically pure *d*-piperitone. Thus, the reversal of asymmetric carbon atom (3) in the piperitols does not affect the sign of the optical rotation of the molecule.

Since the higher-boiling substances possess also the higher density and refractive index, these stereoisomerides may provisionally be assigned the *cis*-configuration (V), in accordance with the Auwers-Skita rule (compare *Chemical Reviews*, 1930, 7, 4); further, in order to conform to the nomenclature adopted for the menthols and menthylamines (*loc. cit.*, p. 37), the *trans*-isomerides should be distinguished by the prefix *neo*-. The following relative molecular configurations are thus reached for the piperitols:

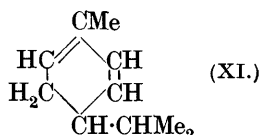
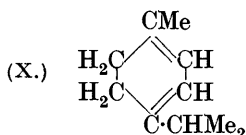
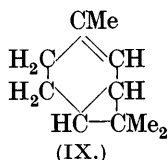
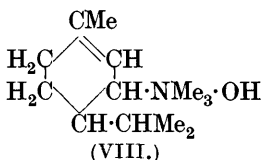
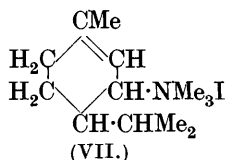
(V.) *d*(or *l*)-Piperitol.(VI.) *d*(or *l*)-*neo*Piperitol.

According to this representation it is interesting that the *cis*-isomeride displays the higher optical rotation, as with the menthones.

The piperitols may be hydrogenated catalytically to menthols, and this process is being studied in detail, particularly as it may furnish, *inter alia*, the hitherto unknown *neoisomenthols* (compare *Trans. Faraday Soc.*, 1930, 26, 450). As $\alpha\beta$ -unsaturated secondary alcohols, the piperitols undergo dehydration so readily (compare Simonsen, *loc. cit.*) that attempts to prepare crystalline esters, etc., have not yet

been successful. It will be of interest to ascertain whether one of the stereoisomerides can be dehydrated with greater ease than the other. It is suggestive that, according to the observations now recorded, natural piperitol appears to consist of the *cis*-form (V), which presumably should be less amenable to dehydration than the *trans*-form (VI). Moreover, as Simonsen (*loc. cit.*) has pointed out, *cis*-piperitol bears a close configurational relationship to Δ^4 -carene (IX), which accompanies *d*-piperitol and *d*-piperitone in *Andropogon* oils.

In treating *dl*- and *l*-piperityltrimethylammonium iodide with silver oxide and water, the possible formation of Δ^4 -carene (IX) or α -terpinene (X) was anticipated, either immediately from the quaternary hydroxide (VIII) or through the derived piperitol (I) :



Very remarkably, however, the terpene which is formed with the piperitols in this reaction appears to consist wholly of α -phellandrene (XI). When *l*-piperityltrimethylammonium iodide was used, the resulting terpene had $\alpha_D^{16} + 86.4^\circ$, and a comparison of its physical constants with those of *d*- α -phellandrene, α -terpinene, and *d*- Δ^4 -carene indicates that little, if any, of the last two substances could have been formed (compare J., 1923, **123**, 1660; 1922, **121**, 2295). Besides affording a direct passage from a Δ^1 - to a $\Delta^{2:6}$ -derivative, this reaction is important as establishing a chemical and stereochemical connexion between *d*-piperitol, *d*-piperitone, and *d*- α -phellandrene. New light is thus thrown upon the association of *l*- α -phellandrene with *l*-piperitone in eucalyptus oils (compare Read and Smith, J., 1921, **119**, 781).

In attempting to dehydrate *d*-piperitol from *Andropogon* oil with magnesium methyl iodide, Simonsen (*loc. cit.*) obtained a hydrocarbon which yielded an oxidation product characteristic of α -terpinene; as, however, the hydrocarbon had $[\alpha]_D^{30} + 20.2^\circ$, while α -terpinene is optically inactive, it now appears possible that *d*- α -phellandrene was also present in this hydrocarbon. A mixture of α -terpinene and *d*- α -phellandrene is indeed formed upon heating

l-piperityltrimethylammonium iodide to about 88°; it then breaks down quantitatively in the following way: $C_{10}H_{17}NMe_3I \longrightarrow C_{10}H_{16} + NMe_3.HI$.

Since α -phellandrene is formed by heating the above quaternary iodide (VII) in the absence of water, the important possibility is here indicated of a direct passage from an ethylenic system to a conjugated system, a result which appears to be conditioned by the doubly-exerted activating effect (at positions 3 and 6) of the double bond. Reactions of this type may conceivably play an important part in biochemical processes: as a simple example, it now becomes unnecessary to postulate an intermediate hydration in the supposed natural formation of α -phellandrene from piperitol (Read, *Chemical Reviews*, 1930, 7, 44). It may also be recalled that *dl*- α -phellandrene is produced to some extent in the reduction of *dl*-piperitone with sodium and alcohol (Read and Cook, J., 1925, 127, 2784): it is now seen that piperitol is probably an intermediate substance in this process.

It appears that the new synthesis of *dl*- and *d*- α -phellandrene from piperityltrimethylammonium hydroxide furnishes the purest specimens of these substances which have yet been prepared by artificial means. *d*- α -Phellandrene obtained by treating *d*- Δ^2 -isopropylhexenone with magnesium methyl iodide (Wallach, *Annalen*, 1908, 359, 283) had $\alpha_D + 4^\circ 7'$ (1-dcm.); while the specimen resulting from the reduction of monochlorophellandrene from *d*- Δ^6 -menthen-2-one (Harries and Johnson, *Ber.*, 1905, 38, 1832) had $\alpha_D^{20} + 45^\circ$ (1-dcm.): neither of these synthetic products was chemically homogeneous (Gildemeister and Hoffmann, "Die Aetherischen Oele," 3rd edn, 1928, I, 338). *d*- α -Phellandrene from *l*-piperityltrimethylammonium hydroxide had $[R_L]_D$ 45.46, $\alpha_D^{16} + 86.4^\circ$, as compared with $[R_L]_D$ 45.51, $\alpha_D^{20} - 95.00^\circ$ (1-dcm.) for the purest specimen of *l*- α -phellandrene isolated by Smith, Hurst, and Read from the essential oil of *Eucalyptus dives* (J., 1923, 123, 1660). The identity of the substance was established by tracing the characteristic mutarotation, in chloroform solution, of its highly levorotatory α -nitrosite (Smith, Hurst, and Read, *loc. cit.*, p. 1665). The presence of α -terpinene in the α -phellandrene derived by heating the quaternary ammonium iodide was readily determined by utilising the solubility of α -terpinene nitrosite in cold ether.

As a further consequence of this work, it has become possible to proceed from *l*-piperitone of *Eucalyptus* oils to *d*-piperitol and *d*-piperitone of *Andropogon* species (compare Simonsen, *loc. cit.*; also J., 1921, 119, 1644): *l*-piperitone \longrightarrow *dl*-piperitylamine \longrightarrow *l*-piperitylamine \longrightarrow *d*- α -phellandrene + *d*-piperitols \longrightarrow *d*-piperitone. Syntheses of the antimeric substances are in progress.

EXPERIMENTAL.

Piperitylamines.

Conversion of Piperitone into Piperitylamines.—Powdered hydrazine sulphate (162 g.; 1.25 mols.) was gradually stirred into a cold solution of sodium hydroxide (100 g.; 2.5 mols.) in water (100 c.c.), with constant cooling and shaking. Methylated spirit (400 c.c.) was added, and the liquid heated on a briskly boiling water-bath for 10 minutes. Piperitone (152 g.; 1 mol.; $[\alpha]_D^{25} - 50.0^\circ$) was then introduced gradually, and the heating continued for 6—8 hours under reflux. After being kept over-night, the liquid was filtered, and the solid deposit of sodium sulphate washed with methylated spirit. When the filtrate was steam-distilled, the alcohol fraction was followed by a small quantity of oil consisting mainly of the unchanged ketone. The residual yellow mobile syrup (140 g.), when recovered from an ethereal solution which had been dried over sodium sulphate, had $\alpha_D + 9.42^\circ$, $[\alpha]_D + 161.6^\circ$ (*c* 2.9145, alcohol).* This material, heated to about 95° under diminished pressure, lost water and became darker, and 2 days' further drying in ethereal solution over calcium chloride furnished a dark red, viscid liquid, with $\alpha_D + 1.81^\circ$, $[\alpha]_D + 35.9^\circ$ (*c* 2.5240, alcohol) [Found: C, 74.6; H, 10.7; N, 10.5; O (diff.), 4.2. Calc. for $C_{20}H_{34}ON_2$: C, 75.4; H, 10.7; N, 8.8; O, 5.0%. Calc. for $C_{20}H_{32}N_2$: C, 80.0; H, 10.8; N, 9.3%]. Another preparation had $[\alpha]_D + 201.1^\circ$ and $+ 48.3^\circ$ before and after drying, respectively. Upon reducing the quantity of hydrazine to one molecular proportion, much of the piperitone was recovered unchanged, even after the mixture had been heated for 6 hours at 120° in a sealed tube.

The syrupy product was not sensibly affected when treated with zinc powder in presence of hot alcoholic potassium hydroxide (compare Meyer and Jacobson, "Lehrbuch der organischen Chemie," 1907, I, i, 763), but it was readily reduced when treated in the following manner. A solution of the syrupy material (70 g.) in glacial acetic acid (300 c.c.) was placed in a flask (2 litre), the vessel being immersed in cold water and provided with a mechanical stirring apparatus (mercury seal) and reflux condenser. Zinc powder (75 g.) was added, and the mixture vigorously stirred, a further charge of zinc powder (25 g.) and glacial acetic acid (50 c.c.) being introduced at the end of $\frac{1}{2}$ hour. After $2\frac{1}{2}$ hours the water-bath was heated very gradually to boiling, at which point it was kept for about an hour. Hot water (500 c.c.) was then added, and the reaction mixture was rapidly filtered, any residual zinc being washed with a

* Unless otherwise stated, all the determinations of optical rotatory power recorded in this paper were observed in a 2-dcm. tube at about 16° .

little hot water. The filtrate, when basified with a concentrated solution of sodium hydroxide and steam-distilled, yielded an oily layer, together with an aqueous liquid containing ammonia. The distillate was acidified and extracted with light petroleum to remove the neutral oil, which contained piperitone and menthones. The base was recovered from the acid solution in the usual way, the ethereal extract being washed with water and dried over solid potassium hydroxide. When distilled in a dry atmosphere free from carbon dioxide, about 90% of the crude base passed over at 97.5—98.5°/16 mm.; 100 g. of the original syrup furnished about 72 g. of base.

Specimens of piperitylamine thus prepared showed values of α_D ranging from +0.5° to +3.7° ($l = 1$). The product was a clear colourless liquid, resembling the menthylamines closely in its physical properties and odour. It absorbed carbon dioxide avidly from the air, forming a highly crystalline deposit. The following additional physical constants were observed: n_D^{15} 1.4802, n_D^{20} 1.4769; d_4^{25} (vac.) 0.8801; $[R_L]_D$ 49.20 (calc. for $C_{10}H_{17}NH_2$ $[\bar{=}$, 49.14).

Acetyl-dl-piperitylamine separated from light petroleum in colourless needles, m. p. 108° (Found: C, 73.6; H, 10.6. $C_{12}H_{21}ON$ requires C, 73.8; H, 10.8%). *Benzoyl-dl-piperitylamine* crystallised from aqueous alcohol in small colourless needles, m. p. 130°; a mixture of this substance with benzoyl-*d-isomenthylamine* (m. p. 128°) melted at about 102° (Found: C, 79.3; H, 8.8; N, 5.7. $C_{17}H_{23}ON$ requires C, 79.3; H, 9.0; N, 5.5%). *Anisoyl-dl-piperitylamine* was deposited from aqueous alcohol in small needles, m. p. 161° (Found: C, 74.8; H, 8.8. $C_{18}H_{25}O_2N$ requires C, 75.2; H, 8.8%). The melting points of these derivatives remained unaltered after recrystallisation. None of the substances showed any appreciable optical rotation when dissolved in chloroform (c 1.7, l 2). The base gave rise to a hydrochloride which formed fine colourless needles, m. p. 191°.

Preparation of l-Piperitylamine.—The crystalline residue obtained when an alcoholic solution of equimolecular amounts of *dl*-piperitylamine and *d*-tartaric acid was evaporated to dryness had $[\alpha]_D + 12.6^\circ$, $[M]_D + 39.4^\circ$ (c 1.5, water). After two recrystallisations from hot methylated spirit, the salt gave the constant value $[\alpha]_D - 43.0^\circ$. Larger quantities of the base were resolved as follows.

Powdered *d*-tartaric acid (150 g.; 1 mol.) was dissolved in a hot mixture of methylated spirit (1000 c.c.) and water (500 c.c.). To this solution was added a hot solution of *dl*-piperitylamine (153 g.; 1 mol.) in methylated spirit (300 c.c.), the vessel containing the basic solution being then washed out with warm spirit (200 c.c.), which was

added to the main solution. When allowed to cool over-night, the solution deposited a mass of colourless prisms. Two recrystallisations from boiling water furnished pure *l*-piperitylamine hydrogen *d*-tartrate in stout prisms, attaining several centimetres in length, m. p. 217° , $\alpha_D - 0.93^{\circ}$, $[\alpha]_D - 43.0^{\circ}$, $[M]_D - 130^{\circ}$ (*c* 1.0800, water) (Found: C, 55.5; H, 8.3. $C_{14}H_{25}O_6N$ requires C, 55.4; H, 8.3%).

The salt obtained by evaporating the mother-liquors from this optical resolution was very readily soluble in most of the usual solvents. The yield of pure *l*-piperitylamine hydrogen *d*-tartrate was about 22% of the total weight of salt prepared.

l-Piperitylamine was isolated from the hydrogen *d*-tartrate in the usual way. It resembled the above *dl*-base in its ordinary properties, and had b. p. $101-102^{\circ}/19$ mm., $98.2^{\circ}/16$ mm.; d_4^{25} (vac.) 0.8789; n_D^{16} 1.4800, n_D^{25} 1.4770; $[R_L]_D$ 49.27 (calc., 49.14).

The rotatory power of the homogeneous base was observed ($l = 1$): $\alpha_D^{16} - 71.31^{\circ}$; $\alpha_{5461}^{15} - 84.37^{\circ}$; $\alpha_D^{25} - 70.62^{\circ}$, $[\alpha]_D^{25} - 80.35^{\circ}$; $\alpha_{5461}^{25} - 83.61^{\circ}$, $[\alpha]_{5461}^{25} - 95.15^{\circ}$. In chloroform solution ($l = 2$): $\alpha_D^{25} - 5.38^{\circ}$, $[\alpha]_D^{25} - 70.0^{\circ}$; $\alpha_{5461}^{25} - 6.37^{\circ}$, $[\alpha]_{5461}^{25} - 82.8^{\circ}$ (*c* 3.8455).

l-Piperitylamine hydrochloride separated from water, ethyl acetate, or absolute alcohol—light petroleum in small transparent needles, m. p. 213° (decomp.), $\alpha_D^{16} - 1.98^{\circ}$, $[\alpha]_D^{16} - 83.5^{\circ}$, $[M]_D^{16} - 158^{\circ}$ (*c* 1.1855, water) (Found: C, 63.0; H, 10.7. $C_{10}H_{19}N, HCl$ requires C, 63.3; H, 10.6%).

Acetyl-l-piperitylamine crystallised from aqueous alcohol in large flat prisms, m. p. $102-103^{\circ}$, $\alpha_D^{25} - 3.74^{\circ}$, $[\alpha]_D^{25} - 153^{\circ}$; $\alpha_{5461}^{25} - 4.48^{\circ}$, $[\alpha]_{5461}^{25} - 183^{\circ}$ (*c* 1.2225, chloroform) (Found: C, 73.4; H, 11.1. $C_{12}H_{21}ON$ requires C, 73.8; H, 10.8%).

Benzoyl-l-piperitylamine separated from aqueous alcohol in long colourless needles, m. p. $102-103^{\circ}$, $\alpha_D^{25} - 4.13^{\circ}$, $[\alpha]_D^{25} - 173^{\circ}$; $\alpha_{5461}^{25} - 4.99^{\circ}$, $[\alpha]_{5461}^{25} - 208^{\circ}$ (*c* 1.1975, chloroform) (Found: C, 79.1; H, 8.9. $C_{17}H_{23}ON$ requires C, 79.3; H, 9.0%).

Anisoyl-l-piperitylamine, was deposited from aqueous alcohol in clusters of fine needles, m. p. $142-143^{\circ}$, $\alpha_D^{25} - 3.75^{\circ}$, $[\alpha]_D^{25} - 175^{\circ}$; $\alpha_{5461}^{25} - 4.55^{\circ}$, $[\alpha]_{5461}^{25} - 212^{\circ}$ (*c* 1.0725, chloroform) (Found: C, 74.9; H, 8.7. $C_{18}H_{25}O_2N$ requires C, 75.2; H, 8.8%).

Phenylacetyl-l-piperitylamine separated from aqueous alcohol in magnificent prisms, showing an unusually perfect development, m. p. $89-90^{\circ}$, $\alpha_D^{20} - 3.13^{\circ}$, $[\alpha]_D^{20} - 130.5^{\circ}$ (*c* 1.1990, chloroform) (Found: C, 79.4; H, 9.3. $C_{18}H_{25}ON$ requires C, 79.7; H, 9.3%).

Methylation of Piperitylamine.—(1) In a preliminary experiment, a solution of *dl*-piperitylamine (25 g.; 1 mol.) and methyl iodide (46.5 g.; 2 mols.) in dry methyl alcohol (100 c.c.) was boiled under reflux for an hour. Sodium (3.75 g.; 1 at.), dissolved in dry methyl alcohol, was added and the heating was continued for 10 minutes.

The whole treatment with methyl iodide and sodium was then repeated. Finally, a third addition of methyl iodide (46.5 g.) was made and the mixture was boiled for an hour.

After removal of some of the solvent by distillation, the crystalline separation (38 g.) was collected and fractionally crystallised from hot methyl alcohol containing a little water : the solution deposited successive fractions consisting essentially of tetramethylammonium iodide (4.5 g.), trimethylamine hydriodide (2 g.), and sodium iodide (30 g.), respectively.

The filtrate containing the residual portion of the original reaction product was concentrated under diminished pressure and then taken to dryness on the water-bath. The resulting hard brown mass, when fractionally crystallised from methyl alcohol, and eventually from chloroform, was shown to consist of a mixture of trimethylamine hydriodide and sodium iodide. The final chloroform washings yielded only a trace of a mobile brown oil, with a terpene-like odour. Hence the quaternary iodide had decomposed, and the resulting terpené had been lost during the distillation and evaporation of the different solutions.

(2) A solution of *dl*-piperitylamine (30.6 g.; 1 mol.) and methyl iodide (42.6 g.; 1.5 mols.) in dry methyl alcohol (90 c.c.) was boiled gently under reflux for $\frac{1}{2}$ hour. A solution of sodium (4.6 g.; 1 at.) in dry methyl alcohol was added, and the boiling renewed for 10 minutes. Further quantities of methyl iodide (42.6 g.), sodium (4.6 g.) dissolved in methyl alcohol, and methyl iodide (28.4 g.) were introduced separately, the mixture being boiled for 10 minutes after each of the first two of these additions and finally for an hour. The liquid was then removed by distillation under diminished pressure below 75°. The crystalline residue was extracted for a few minutes with boiling chloroform (150 c.c.). The mixture was then cooled, and the undissolved solid, consisting of sodium iodide, was filtered off and washed with a little chloroform. The chloroform was removed by distillation under the conditions noted above, leaving a yield (65 g.) of crude *dl*-piperityltrimethylammonium iodide equal to the calculated amount. Some of the product was washed with ether and dissolved in cold acetone, a small quantity of insoluble material (trimethylamine hydriodide) being removed by filtration. When the solvent was allowed to evaporate at the ordinary temperature, the pure quaternary iodide separated in pale yellow prisms (Found : I, 39.5. $C_{13}H_{26}NI$ requires I, 39.3%). The substance is very soluble in acetone, alcohol, or water, readily soluble in warm chloroform, slightly soluble in ethyl acetate, and practically insoluble in ether. It melts and decomposes at 88°, forming trimethylamine hydriodide and a mixture of *dl*- α -phellandrene and α -terpinene (*vide infra*); it

breaks down in a similar way when submitted to continued treatment with hot solvents.

Piperitols.

Optically Inactive Piperitols.—(1) Well-washed silver oxide, freshly prepared by treating silver nitrate (100 g.; 1.5 mols.) with barium hydroxide, was covered with water; a solution of *dl*-piperityltrimethylammonium iodide (126 g.; 1 mol.) in cold water (700 c.c.) was added and the mixture was thoroughly shaken and heated on the water-bath under reflux for 2 hours, trimethylamine being evolved. An ethereal extract of the cooled product yielded an oil (22.5 g.). The extracted aqueous liquid, when steam-distilled for 2 hours in contact with the silver oxide and silver iodide, gave more oil (11.5 g.); and the filtered liquid yielded a third oily fraction (8 g.) when distilled. The washed and dried oil (42 g.), when fractionally distilled twice under diminished pressure, yielded the following main fractions: (I) b. p. 63—65°/15.5 mm., $n_D^{19.5}$ 1.4772 (7.2 g.); (II) b. p. 94—96°/15.5 mm., $n_D^{19.5}$ 1.4740 (9.7 g.); (III) b. p. 100—106°/19.5 mm., $n_D^{19.5}$ 1.4769 (4.8 g.).

Fraction (II) appeared to consist of *dl*-neopiperitol (Found: C, 78.1; H, 11.5. $C_{10}H_{18}O$ requires C, 77.9; H, 11.8%). It was a colourless, somewhat viscid liquid with an agreeable and characteristic odour; immiscible with water, but readily soluble in organic solvents. When oxidised with Beckmann's reagent, it yielded an oil having the characteristic odour of piperitone. Fraction (III) was regarded (*vide supra*) as *dl*-piperitol; it was rather more viscid than Fraction (II), which it resembled closely (Found: C, 77.4; H, 11.6%). Treatment of these fractions with various reagents gave results similar to those obtained with the corresponding dextro-rotatory preparations.

(2) A solution of *dl*-piperitylamine (20 g.) in dilute hydrochloric acid (3 mols.; 500 c.c.) was titrated in the cold with an aqueous solution of sodium nitrite (1 mol.). After remaining in the freezing mixture for 15 minutes, the turbid solution was warmed on the water-bath until effervescence had ceased. The resulting reddish oil, when purified by steam distillation, followed by distillation under diminished pressure, passed over almost completely at 103—105°/15 mm., and had $n_D^{19.5}$ 1.4779 (3 g.). This product appeared to consist largely of piperitol (Found: C, 73.5; H, 10.6%). When it was oxidised with Beckmann's reagent the mixture developed heat, and the resulting oil had the characteristic odour of piperitone. Further, when condensed with anisaldehyde (J., 1926, 2073) it yielded pale yellow prisms, which melted, alone or mixed with anisylidene-*dl*-piperitone, at 98°.

No appreciable terpene fraction was obtained in several experi-

ments of this kind. Tarry matter was formed, and a good deal of the base was recovered unchanged by basifying and steam-distilling the residual aqueous liquid.

Dextrorotatory Piperitols.—The quaternary iodide (186 g.) obtained by methylating *l*-piperitylamine with methyl iodide and sodium methoxide, according to method (2) described above for the *dl*-base, was a crystalline solid resembling the optically inactive quaternary iodide in its general properties. It was treated with silver oxide and water in the manner noted under (1) above, except that the mixture was steam-distilled without any preliminary heating under reflux. Trimethylamine was evolved, and the colourless oil (58 g.) collecting in the receiver was washed and dried. When submitted to two successive fractional distillations under diminished pressure, the oil yielded the following main fractions: (I) b. p. 66—68°/16 mm., $n_D^{16^\circ}$ 1.4827, $n_D^{25^\circ}$ 1.4777, $d_4^{25^\circ}$ (vac.) 0.8463, $\alpha_D^{16^\circ} + 86.4^\circ$ in a 1-dm. tube (8.5 g.); (II) b. p. 96.5—98.5°/15.5 mm., $n_D^{17^\circ}$ 1.4769, $n_D^{25^\circ}$ 1.4729, $d_4^{25^\circ}$ (vac.) 0.9119, $\alpha_D^{16^\circ} + 21.22^\circ$ (13.2 g.); (III) b. p. 101—104°/16 mm., $n_D^{16^\circ}$ 1.4770, $d_4^{25^\circ}$ (vac.) 0.9200, $\alpha_D^{16^\circ} + 40.22^\circ$ (3.0 g.).

Fraction (II) appeared to consist of *d*-neopiperitol (Found: C, 77.6; H, 11.7. $C_{10}H_{18}O$ requires C, 77.9; H, 11.8%); in odour and appearance it resembled closely the corresponding fraction furnished by the optically inactive quaternary iodide. The observed value of $[R_L]_D$ at 25° was 47.40 (calc. for $C_{10}H_{17}OH$ 47.16). When a portion of this fraction (2.3 g.) was oxidised with Beckmann's chromic acid mixture (20 c.c.) the temperature rose to 65° and a dark oil was formed; this was extracted with ether and washed successively with water, very dilute sodium hydroxide solution, and again with water. The oil (1.7 g.) recovered from the dried ethereal solution had $\alpha_D^{16^\circ} + 2.75^\circ$, $[\alpha]_D^{16^\circ} + 61.5^\circ$ (*c* 2.2345, benzene), and possessed the characteristics of piperitone; from the rotatory power it appeared to consist of the optically pure dextrorotatory ketone (compare J., 1923, 123, 2269).

Fraction (III) was closely similar in appearance to Fraction (II), except that possibly it possessed a slightly higher viscosity. As indicated above, it appeared to consist of *d*-piperitol (Found: C, 77.4; H, 11.6%); upon oxidation with Beckmann's reagent it yielded *d*-piperitone having $\alpha_D^{16^\circ} + 2.96^\circ$, $[\alpha]_D^{16^\circ} + 53.3^\circ$ (*c* 1.6665, benzene).

It was not found possible to isolate any crystalline derivative of piperitol by treatment with phenylcarbimide under various conditions. When a mixture of the two substances was slowly heated, reaction occurred suddenly with liberation of carbon dioxide and formation of carbanilide and a terpene-like oil. Apparently the piperitol underwent dehydration in this reaction, as also when

warmed in anhydrous pyridine solution with *p*-nitrobenzoyl chloride or 3 : 5-dinitrobenzoyl chloride; in these last instances there was no evidence of reaction at the ordinary temperature. Most of these experiments were carried out with the first piperitol fraction; a detailed physical and chemical examination of each fraction will be undertaken when larger quantities become available.

α-Phellandrenes and α-Terpinene.

(1) *dl-α-Phellandrene*.—When heated with silver oxide and water, *dl*-piperityltrimethylammonium iodide yielded a mixture of *dl*-piperitols, together with a fraction of a colourless mobile oil distilling at 63—65°/15.5 mm. and having n_D^{20} 1.4772 (*vide supra*) (Found : C, 85.9; H, 11.5. $C_{10}H_{16}$ requires C, 88.2; H, 11.8%). Part of this fraction, which possessed the characteristic odour of phellandrene, was dissolved in light petroleum and treated with nitrous acid in the manner adopted by Smith, Hurst, and Read (J., 1923, **123**, 1663). The petroleum layer soon became filled with a copious crystalline deposit, which was collected after $\frac{1}{2}$ hour. The filtrate deposited only a small quantity of oily material when kept for several hours longer in the freezing mixture. The somewhat sticky solid was washed successively with water, light petroleum, and ether. The residual hard white solid was allowed to dry in the air; its solution in a little warm chloroform was filtered, concentrated in a current of cold air, and diluted, after warming, with an equal bulk of methyl alcohol. Clusters of fine colourless needles, m. p. 113°, separated rapidly as the liquid cooled (Found : C, 56.5; H, 7.5. Calc. for $C_{10}H_{16}, N_2O_3$: C, 56.6; H, 7.6%). The filtrate yielded a further quantity of similar crystals, m. p. 109°. The crystals resembled those of *dl-α*-phellandrene α -nitrosite prepared by Carter (*Diss.*, St. Andrews, 1926), who has shown that the α - and the β -nitrosite of *dl-α*-phellandrene have melting points almost identical with those of the respective nitrosites derived from the optically active forms of α -phellandrene. It thus appears that the above crystalline substance was *dl-α*-phellandrene α -nitrosite (compare J., 1923, **123**, 1664).

The above ether washings, which should have contained any α -terpinene nitrosite present, were shaken with water, dried, and allowed to evaporate at the ordinary temperature. A small quantity of a yellowish oil remained, and this could not be induced to crystallise when treated with various solvents and seeded with crystalline α -terpinene nitrosite. In consideration of the ready detection of α -terpinene in this way (*vide infra*), its absence from the fraction of oil here concerned is thus indicated.

(2) *d-α-Phellandrene*.—The most readily volatile fraction of the oil formed in the treatment of *l*-piperityltrimethylammonium iodide

with silver oxide and hot water (*vide supra*) had b. p. 66—68°/16 mm., n_D^{16} 1.4827, n_D^{25} 1.4777, d_4^{25} (vac.) 0.8463, $[R_L]_D$ 45.46, α_D^{16} + 86.4° (1-dcm. tube). This fraction appeared to consist of almost pure *d*- α -phellandrene (Found: C, 87.8; H, 11.5%); it possessed the characteristic phellandrene odour and readily yielded a highly lævrotatory nitrosite, identical with the derivative described under (4) below. α -Terpinene was not detected in this fraction.

(3) *dl*- α -Phellandrene and α -Terpinene.—Crude *dl*-piperityltrimethylammonium iodide (30 g.) was dry-distilled, at a pressure of about 30 mm., from an oil-bath maintained at 150—200°. The oily distillate was washed in ethereal solution successively with water, dilute hydrochloric acid, and water. After being recovered from the dried ethereal solution, the oil (8.5 g.) distilled completely at 66.5—68.5°/19.5 mm. and had $n_D^{17.5}$ 1.4799. When part of the fraction was treated with nitrous acid, as described under (1) above, a crystalline deposit ensued. This was collected after an hour, and a further quantity of crystalline material was obtained from the filtrate overnight. Part of the crystalline product was insoluble in cold ether, and melted at 104°; when recrystallised from warm chloroform-methyl alcohol, it separated rapidly in fine needles, m. p. 112°, identical with *dl*- α -phellandrene α -nitrosite described under (1) above. When allowed to evaporate, the ethereal extract of the crude crystalline nitrosite yielded fine colourless needles, m. p. 147—150°; this material separated slowly from cold chloroform-methyl alcohol in long square-ended prisms, m. p. 155°, and a mixture of this product with authentic α -terpinene nitrosite (m. p. 155°) melted at the same temperature. The oil thus contained *dl*- α -phellandrene and α -terpinene.

The crystalline non-volatile product of the original dry distillation separated from hot methyl alcohol in lustrous plates, and gave reactions characteristic of trimethylamine hydriodide (Found: C, 19.5; H, 5.3; N, 7.7; I, 67.8. Calc.: C, 19.3; H, 5.4; N, 7.5; I, 67.9%).

(4) *d*- α -Phellandrene and α -Terpinene.—Crude *l*-piperityltrimethylammonium iodide (30 g.), when dry-distilled in the above manner, gave an oil (9.7 g.) distilling completely at 70—71°/19.5 mm. and having n_D^{20} 1.4798, n_D^{25} 1.4780, d_4^{25} (vac.) 0.8467, $[R_L]_D$ 45.47, α_D^{16} + 29.03° (1-dcm. tube) (Found: C, 87.6; H, 11.7%).

The oil was a mobile colourless liquid with the odour of phellandrene. The crystalline nitrosite, obtained as described under (3) above, was only partly soluble in cold ether. The insoluble portion melted at 105°, and upon recrystallisation from warm chloroform-methyl alcohol separated rapidly in fine needles, m. p. 110°; one further recrystallisation raised the melting point to 115°. A solution

of this substance in chloroform (c 0.2570) at 17.5° gave the following readings at the intervals stated ($l = 2$): 10 mins., $\alpha_D - 0.71^\circ$, $[\alpha]_D - 138.1^\circ$; 29 mins., $\alpha_D - 0.69^\circ$, $[\alpha]_D - 134.2^\circ$; 49 mins., $\alpha_D - 0.67^\circ$, $[\alpha]_D - 130.3^\circ$; 2 hours, $\alpha_D - 0.62^\circ$, $[\alpha]_D - 120.6^\circ$. The substance was therefore *d*- α -phellandrene α -nitrosite (Found: C, 56.4; H, 7.5. Calc.: C, 56.6; H, 7.6%) (compare J., 1923, **123**, 1664—5). The ethereal extract of the original crystalline nitrosite deposited long, lustrous, square-ended prisms when kept over-night; these melted at 155° , and showed no alteration of melting point when mixed with authentic α -terpinene nitrosite (m. p. 155°). A chloroform solution (c 0.5, $l = 2$) of this substance showed no appreciable optical activity in mercury-green light at 16° . The oil thus contained *d*- α -phellandrene and α -terpinene.

The crystalline residue obtained in the original dry distillation consisted of trimethylamine hydriodide.

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UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD,

UNIVERSITY OF ST. ANDREWS.

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