775. *The Constitution of Two Piperitone Dimers.*

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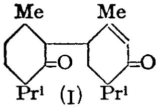
Evidence is adduced for the structure of two stereoisomeric dipiperitones formed through dimerisation of piperitone by the action of heat or alkali. Dimerisation probably occurs through primary Michael addition followed by aldolisation. The isomers are considered to be derivatives of *tricyclo*[7 : 3 : 1 : $0^{2:7}$]tridec-2(7)-ene, containing a tertiary hydroxyl group and one keto-group conjugated with a double bond (see VI). All these groups show marked inactivity due to steric hindrance.

TREIBS (*Ber.*, 1930, **63**, 2738) reported the formation of three dimers of piperitone by irradiation of its solution in glacial acetic acid or aqueous alcohol with a mercury-vapour lamp: (*a*) needles, m. p. 162°, which did not form a semicarbazone, (*b*) silky needles, m. p. 142—144° (semicarbazone, m. p. 228—235°), and (*c*) leaflets, m. p. 157—159°, which gave no semicarbazone. No structures were suggested for these compounds. Later (*J. pr. Chem.*, 1933, **138**, 299), he recorded the formation of a fourth dimer by the action of hot methyl-alcoholic potassium hydroxide on piperitone. It crystallised in plates and prisms, m. p. 105°, and slowly absorbed bromine in chloroform solution with the formation of hydrogen bromide. He suggested structure (I) for this dimer with no further evidence supporting it.



(I)

In the commercial production of piperitone through the bisulphite derivative the residue from the distillation often crystallises. During a series of experiments aimed at preparing a racemic product, piperitone was treated with a 2% alcoholic solution of sodium ethoxide at room temperature for ten days. On distillation, the residue (18%) crystallised to give the same product. A preliminary purification produced crystals, m. p. 107·5—108°, of empirical formula, $C_{10}H_{16}O$, possibly identical with the fourth dimer described by Treibs. A more complete investigation of this material has now been made.

First, fractional crystallisation, coupled with hand-sorting of the crystals, has afforded two isomeric products: (*a*) thin rectangular flat prisms, m. p. 110°, and (*b*) thick rectangular prisms, m. p. 94·5°, with the opposite angles more acute (almost twice as acute) and more obtuse than the respective angles of the (*a*) form. Both isomers are insoluble in water but soluble in all other common solvents, and separation by fractional crystallisation alone is very difficult. By analysis and determination of their molecular weight both have been shown to be dimers of piperitone with a molecular formula $C_{20}H_{32}O_2$. We suggest the names, α- and β-dipiperitone, respectively for these compounds, which exhibit similar and unusual properties.

FIG. 1.

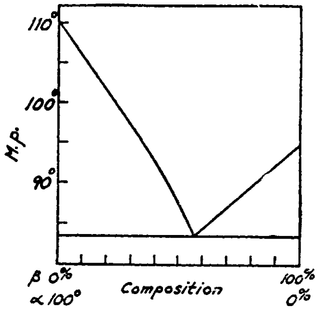
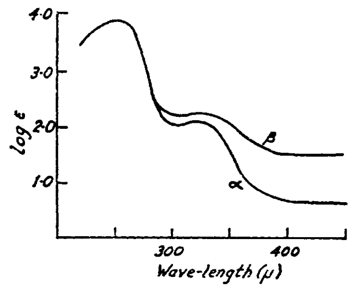


FIG. 2.



A thermal phase diagram (Fig. 1) illustrates the formation of a eutectic mixture, m. p. 83·5°, containing 43% of the α- and 57% of the β-isomer. This fact is important since in many reactions (see p. 3795) interconversion of the α- and the β-form occurred, as a result of which the eutectic crystallised out.

Each isomer when treated with hot glacial acetic acid or dilute alcoholic sodium hydroxide is converted into a mixture of the two.

Constitution of α-Diperitone.—α-Diperitone contains a hydroxyl group, a keto-group, and a double bond, all of which are unreactive owing to steric hindrance.

The hydroxyl group. α-Dipiperitone fails to react with acetic anhydride and sodium acetate, phenyl *iso*cyanate, phenyl *iso*thiocyanate, 3 : 5-dinitrobenzoyl chloride, Denigès's reagent, or chromic acid in chloroform solution. The presence of a hydroxyl group, however, is inferred from one active hydrogen atom disclosed in Zerewitinoff estimation and the presence of an absorption band at 3413 cm.$^{-1}$ in the infra-red spectrum. Acetylation in the cold with acetic anhydride and a trace of perchloric acid, however, afforded a crystalline monoacetyl derivative, no longer exhibiting an absorption band at *ca.* 3413 cm.$^{-1}$. The difficulty of acetylation indicates the presence of a tertiary alcohol, coupled with some steric hindrance. Tertiary alcohols are usually readily dehydrated by mild reagents. The α-isomer, however, did not undergo dehydration with boiling 98% formic acid but was isomerised into a mixture of the α- and the β-form. This could be accounted for if the carbon atoms adjacent to the carbon atom carrying the hydroxyl group were both quaternary, which is most unlikely in the present case, or that the carbon atom carrying the hydroxyl group is at a bridgehead. It has been shown that in cases such as the latter (cf. Rabe, Ehrenstein, and Jahr, *Annalen*, 1908, **360**, 1465) dehydration does not occur, since the resultant olefin, if formed, would be under considerable strain. The formation of such an olefin would contravene Bredt's rule (for a discussion on which see Fawcett, *Chem. Reviews*, 1950, **47**, 219). In our proposed structure for both isomers (see p. 3792) the tertiary alcoholic group is indeed attached to a bridgehead carbon atom.

The carbonyl group. α-Dipiperitone fails to react with hydroxylamine, semicarbazide, 2 : 4-dinitrophenylhydrazine, or Girard's reagent-T, and does not give a colour reaction with *m*-dinitrobenzene and alcoholic potassium hydroxide. It is also recovered unchanged from the Zerewitinoff estimation. The presence of a carbonyl group, however, is indicated from both the ultra-violet and the infra-red spectrum. The former (Fig. 2) shows maxima at 253 (log ε 3·90) and 321 mμ (log ε 2·08), indicative of an αβ-unsaturated ketone. These values are different from those of piperitone itself which exhibits maxima at 235·5 (log ε 4·25) and 321 mμ (log ε 1·73) (Gillam, Lynas-Gray, Penfold, and Simonsen, *J.*, 1941, 60). Woodward (*J. Amer. Chem. Soc.*, 1941, **63**, 1123) has correlated the absorption bands of αβ-unsaturated ketones with structure, and the above maxima correspond with an αβ-unsaturated ketone fully substituted in the α- and the β-position (Woodward quotes a value of 254 ± 5 mμ). The presence of a carbonyl group is also shown by an absorption band in the infra-red spectrum at 1618 cm.$^{-1}$. This is considerably lower than that of a normal carbonyl band and even of an αβ-unsaturated ketone which causes a shift of *ca.* 40 cm.$^{-1}$ to lower frequencies (cf. Jones, Williams, Whalen, and Dobriner, *J. Amer. Chem. Soc.*, 1948, **70**, 2024). Piperitone itself exhibits a maximum at 1667 cm.$^{-1}$ at the lower limit of αβ-unsaturated ketones, while substitution at the α- and both β-positions of an αβ-unsaturated ketone, even where the double bond lies between two rings as in the proposed structure for the dimers (see p. 3792), has little effect on this value. Djerassi, Batres, Velasco, and Rosenkranz (*ibid.*, 1952, **74**, 1715), for example, record for 11α-hydroxy-$\Delta^{8(9)}$-22-*isoallo*spirostene-3 : 7-dione maxima in a Nujol mull at 1718 cm.$^{-1}$, assigned to the carbonyl group at $C_{(3)}$, and at 1660 cm.$^{-1}$, assigned to the trebly substituted αβ-unsaturated ketone, with the double bond between two rings. Hydrogen bonding with a carbonyl group causes a considerable shift to lower wave-numbers as in 1-hydroxyanthraquinone (Flett, *J.*, 1948, 1441) but, at the same time, the characteristic hydroxyl band disappears. This cannot be the explanation in the present case, since bands characteristic of both groups are present. Perhaps the very marked steric hindrance exhibited by the dimers is the reason for the low carbonyl value. Although the carbonyl group of α-dipiperitone does not react with methylmagnesium iodide in the Zerewitinoff estimation, yet it does react with lithium aluminium hydride to give a crystalline compound, $C_{20}H_{34}O_2$. Since carbonyl groups are reduced by this reagent to alcohols, and double bonds are not normally attacked, this compound is in all probability the corresponding dihydroxy-derivative, which failed, however, to give a crystalline acetyl derivative. The infra-red spectrum confirms this contention by the presence of an absorption maximum at 3521 cm.$^{-1}$, characteristic of the hydroxyl group, and the complete lack of absorption from 3521 to 1290 cm.$^{-1}$, which includes the region characteristic of carbonyl groups.

The ultra-violet absorption spectrum indicates substitution in the α-position of the conjugated double bond, and in conformity α-dipiperitone fails to condense with benzaldehyde. Substitution at both α-carbon atoms and the suppression of carbonyl activity due to the presence of the αβ-double bond thus account for the inability of α-dipiperitone to react with carbonyl reagents. Newman and Mosby (*J. Amer. Chem. Soc.*, 1951, **73**, 3738) record another ketone, unreactive through steric hindrance, which fails to react with Grignard reagents but may be reduced with lithium aluminium hydride (cf. also May and Mosettig, *ibid.*, p. 1301).

The double bond. α-Dipiperitone did not give any chemical tests for unsaturation. It gave no colour with tetranitromethane or antimony trichloride. It reacted only very slowly with bromine in glacial acetic acid but the product did not contain bromine (see p. 3794). It was recovered unchanged after attempts to hydrogenate it with palladium–charcoal or with platinum oxide catalysts of proved activity at room temperature and 3 atm., and even with two Raney nickel catalysts of proved activity at 100°/125 atm. It was unchanged by neutral permanganate solution. The presence of a double bond, however, conjugated with the carbonyl group, is indicated by the ultra-violet spectrum discussed above. Both the chemical and the physical evidence point to the presence of a tetrasubstituted double bond. Final chemical proof of the presence of a double bond was afforded by reduction with Raney nickel catalyst at 250°/170 atm. to a liquid hydrocarbon, $C_{20}H_{36}$. This corresponds with reduction of the hydroxyl and the carbonyl group and one double bond.

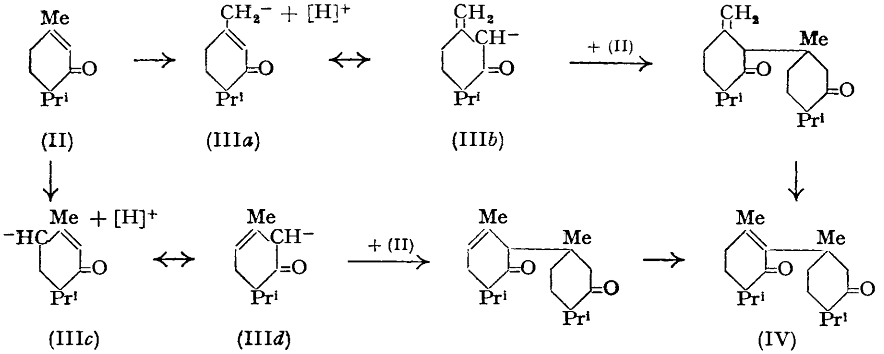
A solution of α-dipiperitone in glacial acetic acid only slowly decolorised bromine in the same solvent. Two atoms were decolorised in 24 hours, the mixture then fuming in moist air [compare the action of bromine on Treibs's dimer (*loc. cit.*)]. The crystalline product, however, did not contain bromine and the molecular formula, $C_{20}H_{30}O_2$, showed that dehydrogenation had taken place. It gave a test for unsaturation with tetranitromethane but none with antimony trichloride, and it failed to undergo reduction with a palladium–charcoal catalyst in low-pressure hydrogenation. The ultra-violet absorption spectrum no longer exhibits the characteristics of an αβ-unsaturated carbonyl group, and the infra-red absorption spectrum shows two strong bands at 3289 and 3185 $cm.^{-1}$, characteristic of an alcoholic and a phenolic group, respectively. The dehydrogenated product does not dissolve in sodium hydroxide solution nor does it give a ferric chloride colour. The insolubility in alkali, however, is again due to steric hindrance, since the compound exhibits phenolic properties in other ways. It dissolves in Claisen's cryptophenol reagent (*Annalen*, 1919, **418**, 96), couples with diazotised *p*-nitroaniline, and as a phenol in the Molisch test for carbohydrates it gives a positive colour. The phenol has a free *para*-position since it gives a positive test with 2 : 6-dibromoquinone chloroimide (Gibbs, *J. Biol. Chem.*, 1927, **72**, 649).

When four atoms of bromine are used in the above bromination, a *para*-substituted bromo-derivative of the above phenol is obtained, $C_{20}H_{29}O_2Br$. This likewise fails to dissolve in sodium hydroxide solution but readily dissolves in a solution containing a little alcohol. A colour is no longer given by Gibbs's reagent.

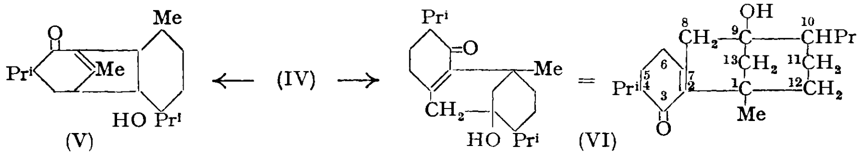
When heated with solid sodium hydroxide, α-dipiperitone decomposes with the formation of (±)-*iso*menthone in <50% yield.

α-Dipiperitone is not appreciably affected by selenium at 290°, almost all being recovered as the eutectic mixture of α- and β-forms. It does undergo dehydrogenation, however, at 320°, yielding a liquid product with a possible molecular formula, $C_{16}H_{24}O_2$, which fails to yield a crystalline derivative with picric acid or trinitrobenzene, indicating that complete aromatisation has not occurred.

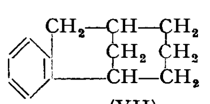
If we assume that α-dipiperitone is identical with the dimer obtained by Treibs (*loc. cit.*) by the action of methyl-alcoholic potassium hydroxide on piperitone, it is obvious that his proposed constitution as a diketone does not fit the above facts. We suggest that the

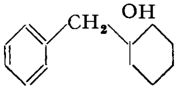


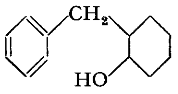
dimer is formed in two stages, by a Michael condensation followed by aldolisation. Only reaction in this order can give rise to products with the requisite properties. The influence of the carbonyl group of piperitone (II) may be transferred by electromeric change to the methyl group on $C_{(1)}$ or to the methylene group at $C_{(6)}$, leading, in the ultimate case, particularly in the presence of alkali, to the ions (III*a*) and (III*c*). These in turn can resonate with the canonical forms (III*b*) and (III*d*) respectively. We suggest that Michael addition then occurs between the second of these forms and another molecule of piperitone [cf. the Michael addition of an αβ-unsaturated ketone to acrylonitrile in Woodward's synthesis of a steroid (Woodward *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 2404; 1952, **74**, 4223)], followed by rearrangement of the double bond to a position conjugated with the carbonyl group. Either form finally leads to the same intermediate product (IV). Only by condensation in this way can an αβ-unsaturated ketone arise substituted in the α- and both β-positions to agree with the ultra-violet spectrum. The intermediate compound (IV), we suggest, then undergoes aldolisation, which could theoretically lead to two isomeric compounds (V) and (VI). The constitution (V) is most unlikely as it contains a bridgehead double bond and, therefore, contravenes Bredt's rule. For a discussion on analogous compounds containing nitrogen atoms in the rings, see Fawcett (*loc. cit.*, p. 265).

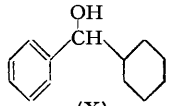

(V) (VI)

The structure (VI), however, is similar to the tricyclic compound (VII) obtained by Cook and Hewett (*J.*, 1936, 62). They have shown that this compound has considerable stability similar to that of the parent hydrocarbon *bicyclo*[3 : 3 : 1]nonane, itself (Meerwein, *Annalen*, 1913, **398**, 196; *J. pr. Chem.*, 1922, **104**, 161). It is formed by dehydration of any of the three compounds (VIII), (IX), or (X), and does not undergo dehydration with selenium or platinum catalysts. Nitrogen analogues of this system also

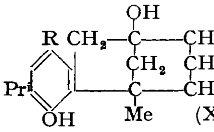

(VII)

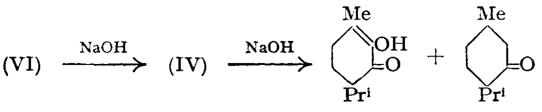

(VII)


(IX)


(X)

occur in certain alkaloids of the lupinane group such as cytisine (Henry, " The Plant Alkaloids," Churchill, London, 4th Edn., pp. 116—151). The structure (VI), 9-hydroxy-1-methyl-4 : 10-di*iso*propyl*tricyclo*[7 : 3 : 1 : $0^{2:7}$]tridec-2(7)-en-3-one, is in harmony with nearly all the properties of α-dipiperitone so far described. It contains a sterically hindered tertiary alcoholic group at a bridgehead. The αβ-unsaturated carbonyl group is substituted as required. The double bond is tetrasubstituted and lies between two rings, a position well known for its inactivity [cf. lanosterol (Barton, Fawcett, and Thomas, *J.*, 1951, 3147) and 1 : 2 : 3 : 4 : 4*b* : 5 : 6 : 7 : 8 : 8*a* : 9 : 10-dodecahydrophenanthrene (Durland and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 1501)]. Bromination of α-dipiperitone probably occurs initially at $C_{(4)}$, and subsequent loss of hydrogen bromide and aromatisation gives the phenol (XI; R = H). Further bromination leads to the *para*-substituted bromophenol (XI; R = Br).


(XI)


(XIII) (XII)

In the action of solid sodium hydroxide on α-dipiperitone we suggest that dealdolisation first occurs followed by hydrolysis leading to *iso*menthone (XII) (isolated) and diosphenol (XIII), which, however, we were unable to isolate.

The Constitution of β-*Dipiperitone*.—Although a complete examination of this dimer has not been made, there is sufficient evidence to show that it differs from α-dipiperitone only by epimerisation at $C_{(4)}$. The hydroxyl group does not react with the normal reagents, but a monoacetate, isomeric with the α-isomer derivative, is formed by the action of acetic anhydride and perchloric acid. It produces one molecule of methane in the Zerewitinoff estimation. The infra-red absorption spectrum is very similar to that of the α-isomer and includes a band at 3436 cm.$^{-1}$ characteristic of hydroxyl groups.

An αβ-unsaturated carbonyl group is indicated by the ultra-violet absorption spectrum (Fig. 2) where maxima appear at 253 (log ε 3·90), and 327 mμ (log ε 2·24). These are in similar positions to those of the α-isomer and indicate an αβ-unsaturated ketone substituted in the α- and both β-positions. Like the α-isomer, also, it fails to condense with benzaldehyde, showing that the other group adjacent to the carbonyl group is substituted.

The β-isomer failed to give the normal tests for unsaturation and failed to undergo reduction with a palladium–charcoal or a platinum oxide catalyst and hydrogen at 3 atm. The presence of a double bond, however, conjugated with the carbonyl group, is evident from the ultra-violet absorption spectrum mentioned above.

When distilled with solid sodium hydroxide, the β-isomer afforded *iso*menthone similarly to the α-isomer. When treated with two atoms of bromine in acetic acid it undergoes dehydrogenation and aromatisation and affords the same phenol as that obtained by the action of bromine on the α-isomer. Further bromination likewise yields the same bromophenol as that produced from the α-isomer. Since the isomerism between the two isomers disappears in the reaction, they can differ only by the different steric arrangement of the *iso*propyl group at $C_{(4)}$.

EXPERIMENTAL

The microanalyses are by Dr. T. S. Ma and Dr. A. D. Campbell, University of Otago, Dunedin.

Isolation and Separation of α- and β-Dipiperitone.—The crude material remaining from the commercial distillation of piperitone was a dark brown mass of large crystals. A preliminary purification from colouring matter and insoluble material was effected by crystallisation from alcohol or acetone. The partially purified material was then allowed to crystallise slowly from an acetone solution at room temperature. The large crystals so formed were hand-sorted, where possible, into two fractions, obviously different in crystalline shape. Material which could not be sorted was recrystallised, and the process repeated. The separate fractions thus obtained were again crystallised from acetone and hand-sorted, and the process repeated four times. The thin, rectangular, flat prisms of the first fraction, *α-dipiperitone,* were finally crystallised repeatedly from alcohol and then had m. p. 110°, unaltered by change of solvent [Found : C, 78·6, 78·6; H, 10·4, 10·5%; *M* (Rast), 309, 313; *M* (cryoscopic in benzene), 279, 298. $C_{20}H_{32}O_2$ requires C, 79·0; H, 10·5%; *M*, 304. Anomalous results (618, 568, 569) were obtained for the molecular weight determined ebullioscopically in benzene].

The thick rectangular prisms of the second fraction, *β-dipiperitone,* were also finally repeatedly crystallised from alcohol and then had m. p. 94·5°, unaltered by change of solvent [Found : C, 78·7, 79·0, 79·0; H, 10·4, 10·65, 10·5%; *M* (Rast), 295]. Consistently low carbon values were obtained when large crystals were used owing to the retention of water, and the correct result could only be obtained on the powdered material.

Very approximately, equal amounts of the two dimers were obtained by the above process.

α-Dipiperitone.—This isomer decomposes when heated to its b. p. at atmospheric pressure but sublimes unchanged at 101—104°/0·1 mm. In a Zerewitinoff determination in anisole, it showed 0·98 active H; pure α-dipiperitone was recovered from the reaction mixture.

The molecular refractivity was obtained from data derived from solutions of the α-isomer in acetophenone. The acetophenone used had n_D^{25} 1·5310, d_4^{25} 1·023. The constants of three separate solutions of 0·2513, 0·7007, and 0·2001 g. in 5 c.c. of acetophenone were n_D^{25} 1·5296, 1·5282, 1·5298, and d_4^{25} 1·0319, 1·0330, 1·0250, respectively, whence the molecular refractivity can be calculated to be 86·94, 87·43, 86·70. These observed results, however, are not in agreement with the result calculated on assuming the presence of a double bond and an alcoholic and a ketonic group, as outlined on p. 3789. Increments known to occur when the double bond is in the αβ-position to the carbonyl group do not explain these anomalous results.

O-*Acetyl-α-dipiperitone.* A solution of α-dipiperitone (640 mg.) in acetic anhydride (3 c.c.) and concentrated perchloric acid (2 drops) was kept for 2 days. The large square plates of *acetyl* derivative that formed (up to 5 mm. in size), after repeated crystallisation from alcohol, had m. p. 113°, depressed to 86—96° on admixture with the starting material (Found : C, 75·7, 75·9, 76·0; H, 9·5, 9·7, 9·5; Ac, 8·6. $C_{22}H_{34}O_3$ requires C, 76·4; H, 9·8; 1Ac, 12·1%).

Reduction with lithium aluminium hydride. α-Dipiperitone (5 g.) was added in small portions to a solution of lithium aluminium hydride (1·22 g.) in dry ether (100 c.c.), a vigorous evolution of gas taking place at each addition. After the last addition the mixture was refluxed for 24 hr., and the excess of hydride destroyed by addition of ether saturated with water. The metals were dissolved in 10% sulphuric acid (40 c.c.), and the ethereal layer was separated, washed with alkali and water, and dried. Crystals were formed when the ether was allowed to evaporate at room temperature. The crude product (4·81 g.) could only be crystallised with difficulty from acetone or light petroleum (b. p. 40—60°) with great loss of material and, after repeated crystallisation from acetone, formed needles and rhombs, m. p. 87° (Found : C, 78·1 ; H, 10·8. $C_{20}H_{34}O_2$ requires C, 78·5; H, 11·1%). The resulting *diol* is insoluble in water but very soluble in organic solvents. It decomposed on attempted acetylation with acetic anhydride and perchloric acid, and when acetylated with acetic anhydride and pyridine at the b. p. it formed a viscous oil which could not be crystallised.

Hydrogenation of α-Dipiperitone.—α-Dipiperitone (2 g.) in *cyclo*hexane (40 c.c.) was hydrogenated with a Raney nickel catalyst (0·5 g.; Homer and Pavlic, *J. Amer. Chem. Soc.*, 1946, **68**, 1471) at 2660 lb./sq. in. at 250° for 3 hr. The colourless, somewhat viscous liquid, obtained after removal of the catalyst and the solvent, was distilled in a micro-column. The four fractions collected had approximately the same refractive index, n_D^{20} 1·4918, and were homogeneous (Found : C, 86·8; H, 13·1. $C_{20}H_{36}$ requires C, 87·0; H, 13·0%).

Action of Sodium Hydroxide on α-Dipiperitone.—The α-isomer (5 g.) was gradually fused with sodium hydroxide (2 g.) and vacuum-distilled directly from the alkali. The main product (3·55 g.) had b. p. 138°/55 mm. and was identified as (±)-*iso*menthone by preparation of the 2 : 4-dinitrophenylhydrazone, m. p. 145°. The m. p. was sharply depressed by the corresponding menthone derivative of the same m. p. (Allen, *J. Amer. Chem. Soc.*, 1930, **52**, 2955) but undepressed by a sample of the 2 : 4-dinitrophenylhydrazone of (±)-*iso*menthone of the same m. p. The *iso*menthone used for this purpose was prepared according to Read and Cook (*J.*, 1925, **127**, 2782). From the yield of the 2 : 4-dinitrophenylhydrazone, 38% of *iso*menthone was produced in the above reaction. The residue from the distillation was steam-distilled and gave a little more *iso*menthone. It still contained unchanged dimer which was removed by ether. The aqueous layer was again steam-distilled after acidification with sulphuric acid but the odoriferous volatile product was too small for characterisation.

Action of Bromine on α-Dipiperitone.—(*a*) Two atoms per mole. Bromine (0·934 g., 1 mol.) in glacial acetic acid (10 c.c.) was added to α-dipiperitone (1·7784 g., 1 mol.) in the same solvent (25 c.c.). Even the first drop was decolorised slowly but the solution was completely colourless in 24 hr. and then fumed in moist air. The colourless *product* (1·68 g.) formed on pouring of the mixture into water (100 c.c.) was washed with sodium hydrogen carbonate solution and water and crystallised five times from alcohol. It then formed rectangular plates, m. p. 136°, which gave a deep orange colour with tetranitromethane [Found : C, 78·9; H, 9·9%; *M* (Rast), 302. $C_{20}H_{30}O_2$ requires C, 79·6; H, 9·9%; *M*, 302].

(*b*) Four atoms per mole. Bromine (1·24 g., 1 mol.) was added to a solution of α-dipiperitone (2·36 g., 1 mol.) in glacial acetic acid (30 c.c.). Decolorisation occurred after 2 hr.' stirring at room temperature. Further bromine (1·24 g., 1 mol.) in glacial acetic acid (20 c.c.) was then added, and the mixture stirred for ½ hr. and set aside for 24 hr., decolorisation then being complete. The *bromo-phenol* obtained when the mixture was poured into water (200 c.c.), after three crystallisations from alcohol, formed colourless needles, m. p. 154° (Found : C, 63·1; H, 8·5; Br, 20·9. $C_{20}H_{29}O_2Br$ requires C, 63·0; H, 7·8; Br, 21·0%).

Selenium Dehydrogenation of α-Dipiperitone.—α-Dipiperitone (10 g.) and selenium (30 g.) were intimately mixed and heated under a reflux condenser for 4 hr. at 320°. The black oil yielded to ether, after appropriate washing, a greenish-yellow viscous oil which was distilled in a micro-column (Craig, *Ind. Eng. Chem., Anal.*, 1936, **8**, 219). Three yellow, viscous, fractions were collected but they showed little difference in physical properties: (1) b. p. 312—318°, n_D^{25} 1·5330, $n_D^{16·5}$ 1·5361, $d_4^{16·5}$ 1·0175; (2) b. p. 314—320°, n_D^{25} 1·5330, $n_D^{17·5}$ 1·5359, $d_4^{17·5}$ 1·0156; (3) b. p. 328°, n_D^{25} 1·5339 [Found, in fraction (2): C, 77·4; H, 9·7. Calc. for $C_{16}H_{24}O_2$: C, 77·5; H, 9·7%].

Boiling with chloranil in xylene solution for 2 hr. caused dehydrogenation, as judged by the separation of the quinol, but the brownish-black, semi-solid product did not crystallise.

β-Dipiperitone.—This isomer is somewhat more soluble than the α-isomer in organic solvents. It can be sublimed unchanged under reduced pressure. It gives no reaction with *m*-dinitrobenzene and potassium hydroxide, antimony trichloride, or tetranitromethane. Zerewitinoff determinations in anisole showed 1·3, 1·11, and 0·97 active H.

O-*Acetyl-β-dipiperitone.*—A solution of the β-dimer (1 g.) in acetic anhydride (3 c.c.) and concentrated perchloric acid (2 drops) was kept for 24 hr. Water was added to promote crystallisation, and after recrystallisation from alcohol the *acetyl* derivative separated in needles, m. p. 99° (Found : C, 76·4; H, 9·4; Ac, 10·1. $C_{22}H_{34}O_3$ requires C, 76·3; H, 9·8; 1Ac, 12·4%).

Action of Sodium Hydroxide on β-*Dipiperitone.*—By treating the β-dimer (2 g.) similarly to the α-dimer (see p. 3794), 1·30 g. of distilled liquid were obtained, identified as (±)-*iso*menthone by preparation of the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 145°.

Action of Bromine on β-*Dipiperitone.*—(*a*) Two atoms per mole. Bromine reacted with β-dipiperitone similarly to the α-isomer yielding the same product, m. p. and mixed m. p. with the phenol obtained from the α-isomer, 136°.

(*b*) Four atoms per mole. The same bromophenol, m. p. and mixed m. p. 154°, was obtained as from the α-isomer under similar conditions.

Isomerisation of α- *and* β-*Dipiperitone.*—(a) *With glacial acetic acid.* α-Dipiperitone (500 mg.) was heated in boiling glacial acetic acid (5 c.c.) for 10 hr., and the mixture poured into water (50 c.c.). The product on crystallisation from alcohol gave a first crop of unchanged α-dimer, but from the mother-liquor the two obviously different crystalline forms of α- and β-dipiperitone separated out and were hand-sorted. The thin, rectangular, flat prisms had m. p. 103° raised to 106° on admixture with α-dipiperitone. The thick rectangular prisms had m. p. 89°, raised to 92° on admixture with β-dipiperitone. Other experiments gave the eutectic, m. p. 84°.

In a similar experiment with anhydrous formic acid, designed to dehydrate α-dipiperitone, the α-isomer and the eutectic, m. p. 84°, undepressed by the product above, were recovered.

β-Dipiperitone, when treated similarly with boiling glacial acetic acid, gave mainly the β-isomer as the first crop on crystallisation from alcohol, but from the mother-liquors the two different crystalline forms of α- and β-dipiperitone separated and were hand-sorted; they had (α) m. p. 105° and mixed m. p. 109°, and (β) m. p. 88° and mixed m. p. 92°.

(b) *With 5% alcoholic sodium hydroxide.* α-Dipiperitone (500 mg.) was heated in alcoholic sodium hydroxide (500 mg. in 10 c.c.) for 1 hr. at 50°, and the solution poured into water (100 c.c.). The product, on crystallisation from alcohol, gave mainly the unchanged material in the first crop but from the mother-liquor the two obviously different crystalline forms of the α- and β-isomers separated, having m. p.s almost identical with those obtained from acid isomerisation, and raised in m. p. on admixture with the respective isomers.

In further experiments, fractional crystallisation of the product from aqueous alcohol (1 : 1) yielded the α-isomer, m. p. 110—112°, and the eutectic, m. p. 83—84°.

β-Dipiperitone, on similar treatment, also afforded a mixture of α- and β-dipiperitone, m. p.s 88° and 104° respectively, raised in m. p. on admixture with the respective isomers.

Thermal Phase Diagram for α- *and* β-*Dipiperitone.*—Mixtures of α- and β-dipiperitones with the following proportions of the β-isomer were finely ground in a mortar and heated in m. p. tubes, and the temperatures were recorded at which the last crystals disappeared on melting: 78%, m. p. 89°; 59%, m. p. 84°; 50%, m. p. 87·5°; 43%, m. p. 91°; 19%, m. p. 102°. From these results Fig. 1 was constructed.

Ultra-violet Spectra.—These spectra (see Fig. 2) were measured in a Beckman spectrophotometer, model DU, *ca.* 0·01% alcoholic solutions being used.

Infra-red Spectra.—We are indebted to Dr. B. Cleverley for the following spectra determined in a Beckman spectrophotometer, model IR2, with rock-salt optics (s = strong, m = medium, w = weak, vw = very weak, i = inflexion) :

α- *and* β-*Dipiperitone* (β in parentheses). Measurements were made on powdered form only : 3413 (3436) w, 2933 (2933) m, 2865 m (2874 w), 1618 s (1629 m), 1597 m (1587 w), 1447 (1443) m, 1401 (1404) w, 1359 (1351) m, 1332 (1328) vw, 1304 w (1300 m), 1248 s (1250 m), 1221 s (1217 m), 1178 (1172) w, 1148 (1145) w, 1117 (1116) w, 1075 (1083) w, 1054 (1048) m, 1040 w (1036 m), —— (1008 w), 983 (980) w, 962 (962) w, 942 (939) w, 902 (918) w, 887 (895) w, 868 (868) w 854 (854) w, 836 (834) w, 806 (803) w, 797 (794) w, 769 (765) w, 740 (740) w.

Piperitone. Liquid : 3571 s, 3367 w, 2967 s, 2899 s, 2755 w, 2681 w, 2532 w, 1667 s, 1637 s, 1443 s, 1377 s, 1351 s, 1314 s, 1289 i, 1269 i, 1253 s, 1209 s, 1196 i, 1174 s, 1149 i, 1134 s, 1104 s, 1075 w, 1047 i, 1024 s, 991 s, 966 m, 927 s, 894 s, 875 s, 851 s, 818 s, 789 s, 761 s.

Acetylated α- *and* β-*dipiperitone* (β in paretheses). Powder form : 2950 (2941) s, 2882 s ——, 1718 (1724) s, 1664 (1653) s, 1616 s (1608 m), 1451 s (1447 m), 1427 s ——, —— 1379 m, 1360 (1355) s, 1318 (1319) m, —— 1284 m, 1255 (1247) s, 1224 (1220) s, 1178 (1171) m, 1145 m (1143 i), —— 1127 i, 1115 (1100) w, 1104 (1100) w, 1086 vw ——, 1054 w ——, 1036 s (1026 w), 1018 s (1010 m), 1007 s ——, 964 (962) m, 937 (938) m, 918 (916) w, 897 (896) w, 873 (880) w, 858 (869) w, 825 m, (821 w), 804 m (806 w), 769 (769) w, 740 w (751 m).

Lithium aluminium hydride reduction product of α-*dipiperitone.* Nujol mull : 3521 w, 1290 w, 1239 w, 1178 w, 1130 w, 1059 i, 1036 w, 1005 w, 974 m, 962 w, 938 m, 892 w, 775 w, 760 w.

Raney nickel reduction product of α-dipiperitone. Liquid: 3195 w, 2915 s, 1460 s, 1381 s, 1368 s, 1292 w, 1266 w, 1244 w, 1218 w, 1182 i, 1168 s, 1116 w, 1100 vw, 1072 vw, 1032 2, 994 m, 971 w, 952 w, 920 m, 902 vw, 866 m, 852 m.

Phenol from α-dipiperitone by dehydrogenation with bromine. Nujol mull over the whole range, and powder where the Nujol interfered: 3289 s, 3185 s, 2933 s, 1629 s, 1456 s, 1418 s, 1335 m, 1366 s, 1381 s, 1311 w, 1253 m, 1222 w, 1182 w, 1151 w, 1122 w, 1081 w, 1056 m, 1035 w, 1010 m, 985 m, 964 w, 946 w, 926 w, 905 w, 889 w, 851 w, 836 w, 812 w, 801 w, 774 m, 740 w.

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