62. *The Catalytic Hydrogenation of Diosphenol.*

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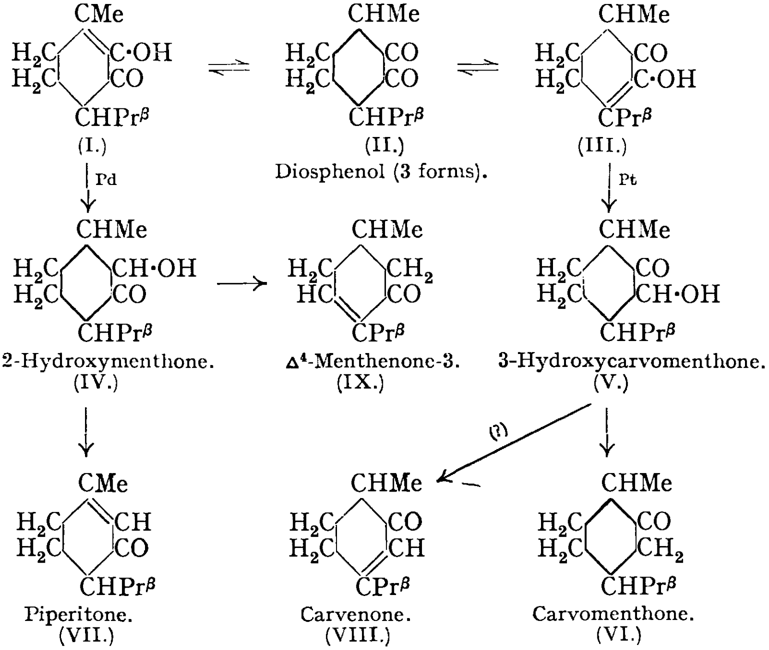
DIOSPHENOL exists in three tautomeric forms : (I) has been shown by the work of Semmler and McKenzie (*Ber.*, 1906, **39**, 1158) to correspond to the familiar solid crystalline diosphenol having m. p. 83°; and Wallach (*Annalen*, 1919, **418**, 36; 1924, **437**, 148) has obtained evidence suggesting the independent existence of the other two forms (II and III).

It would appear probable that suitably arranged catalytic hydrogenation of (I) would yield either 2-hydroxymenthone (IV) or *p*-menthan-2 : 3-diol. The first catalytic hydrogenation of diosphenol (I), carried out by Cusmano and Boccucci (*Gazzetta*, 1923, **53**, 649) with a platinum-black catalyst, gave a mixture of stereoisomeric forms of a keto-alcohol with a small quantity of a crystalline solid which they considered to be the derived diol, *p*-menthan-2 : 3-diol. The keto-alcohol was shown to possess the constitution (V) of 3-hydroxycarvomenthone, since it was converted through the corresponding bromo-ketone into carvomenthone (VI), which was characterised as the oxime. To explain the production of (V) these authors suggested that the equilibrium between the three forms of diosphenol is a labile one, and that the form (III) is hydrogenated with the greatest ease, with the production of (V), the ethylenic linkage only being reduced. In the present investigation, colloidal palladium was used as the catalyst, and easy access was gained to a keto-alcohol, termed dihydrodiosphenol, which could possess either of the constitutions (IV) and (V).



(I.) (II.) (III.) Diosphenol (3 forms).

2-Hydroxymenthone. (IV.)

Δ⁴-Menthenone-3. (IX.)

3-Hydroxycarvomenthone. (V.)

Piperitone. (VII.)

Carvenone. (VIII.)

Carvomenthone. (VI.)

Now it might be anticipated that sulphonic esters of a keto-alcohol of the constitution (IV) might decompose on pyrolysis with the production of piperitone (VII), while those of (V) would yield carvenone (VIII). When, however, the *d*-camphor-10-sulphonate of the present keto-alcohol was dry-distilled, the product had the physical properties neither of piperitone or carvenone nor of a mixture of the two :

	Piperitone.	Carvenone.	Product.
n_D	1·4845 (20°) 1·4825 (25°)	1·48245 (20°)	1·4729 (25°)
B. p.	110°/15 mm.	108°/12 mm.	90—97°/10 mm.

The product was characterised as the oxime, an ethereal solution of which was washed with dilute sulphuric acid in order to remove any piperitone oxime (Read, Smith, and Bentivoglio, J., 1922, **121**, 582) and any carvenone oxime (Wallach, *Annalen*, 1893, **277**, 125). From the acid washings, only 17·6% of the total oximation product was recovered, and this was shown to be essentially *dl*-piperitone α-oxime by comparison with an authentic specimen. The ethereal solution yielded the remainder of the oximation product, which was shown to be identical with the oxime of *dl*-Δ^4-menthenone-3 (IX); this oxime (nitrosomenthene) was synthesised from *dl*-Δ^3-menthene through the nitrosochloride (cf. Richtmann and Kremers, *Amer. Chem. J.*, 1896, **18**, 765) for purposes of comparison. Furthermore, the physical properties of *dl*-Δ^4-menthenone-3 (IX) ($n_D^{20°}$ 1·4733, b. p. 95—97°/12 mm.) agree well with those of the pyrolysis product, of which it formed over 80%. Since the virtual dehydration of dihydrodiosphenol has led to the exclusive production of unsaturated ketones having the keto-group in the 3-position, it follows that the dihydrodiosphenol itself must have possessed the constitution (IV).

A keto-alcohol having the constitution (IV) now advanced for dihydrodiosphenol has apparently been prepared previously by Kötz, Blendermann, Rosenbusch, and Sirringhaus (*Annalen*, 1913, **400**, 71), by the chlorination of 1-methyl-4-*iso*propyl*cyclo*hexan-3-one-4-carboxylic ester, followed by hydrolysis of the product and elimination of carbon dioxide. These authors record only the b. p. of their keto-alcohol, which is somewhat higher than that observed for dihydrodiosphenol (IV). Furthermore, it was not found possible to dehydrate this keto-alcohol (Kötz, Blendermann, Mähnert, and Rosenbusch, *ibid.*, p. 76) to the expected menthenone (VII) (piperitone). Again, Semmler and McKenzie (*loc. cit.*) have obtained a keto-alcohol from *p*-menthan-2 : 3-diol (formed when diosphenol is reduced with sodium and alcohol), by partial oxidation, and this could have either of the constitutions (IV) and (V). The physical properties of the various keto-alcohols (IV) and (V) which have been described are given in the following table :

	B. p.	n_D.	*d.*	M. p. semicarb.
a	234°	—	—	225° 180—181
b	139/17 mm.	—	—	—
c	105—115/13 mm.	1·4616	0·968 (20°)	200
d	108—115/12 mm.	1·4648 (25°)	0·9915 (25°)	210—211

a, C. and B. (*loc. cit.*); b, K., B., R., and S. (*loc. cit.*); c, S. and McK. (*loc. cit.*); d, present writers.

In order to establish still further that dihydrodiosphenol is 2-hydroxymenthone (IV), an attempt was made to hydrogenate the *p*-toluenesulphonate of diosphenol, but this did not succeed under the conditions employed. An attempt to reduce the keto-group in *p*-toluenesulphonyldihydrodiosphenol also failed. It was felt that a more convenient route to 2-hydroxymenthone (IV) (dihydrodiosphenol) would be by the reduction of piperitone oxide catalytically. The beautifully crystalline product was, however, distinct from dihydrodiosphenol; it had the formula $C_{10}H_{18}O_2$, and may be 1-hydroxymenthone. A crystalline substance obtained similarly from *dl*-carvenone oxide was probably 4-hydroxycarvomenthone.

The work now described affords the first passage from menthone to piperitone (the diosphenol used being prepared entirely from menthone); opens a new route from menthone to Δ^4-menthenone-3; and discloses the important fact that diosphenol may be used as a " turn-table " between the menthone and the carvomenthone series. Since diosphenol is a natural product, the last fact may have an interesting biological significance (cf. *Chemical Reviews*, 1930, **7**, 42). It seems possible that a species producing diosphenol could lead to other species producing either carvomenthone or menthone, or their respective congeners. Thus, in the genus *Pycnanthemum*, it has been shown that while *P. incanum* and *P. lanceolatum* are almost morphologically identical—and therefore presumably descended from a common near ancestor—the essential oils of the two species differ profoundly. The oil of the former contains 90% of pulegone; that of the latter has only a trace of pulegone, and consists mainly of carvacrol (Miller, *Thesis*, Minnesota, 1918; cf. Gortner, " Outlines of Biochemistry," New York, 1929, 670—1). The results of the present work point to the possible descent of these two species from a common ancestral species which produced diosphenol.

The authors are grateful to Mr. R. E. Lishmund, B.Sc., Department of Natural Philosophy, United College, University of St. Andrews, for measuring the ultra-violet absorption spectra of some of the ketones to which reference has been made above. The following table gives the positions of the heads of the absorption bands and the molecular extinction coefficients :

	Max.	Mol. ext. coeff.		Max.	Mol. ext. coeff.
Diosphenol	2715 Å.	11,000	Carvomenthone	2845 Å.	22·2
Dihydrodiosphenol	2745	128·25	Piperitone	3180	49·5
Menthone	2870	23·8	Carvenone	3119	49

The most notable feature is the five-fold increase in the intensity of the absorption of menthone occasioned by the introduction of the hydroxyl group in dihydrodiosphenol. Also, while menthone possesses greater general absorption in the extreme ultra-violet than carvomenthone, the reverse is the case with piperitone and carvenone. The very intense absorption of diosphenol is, of course, due to its being an enolised ketone.

EXPERIMENTAL.

Catalytic Hydrogenation of Diosphenol to Dihydrodiosphenol.—The diosphenol used was prepared by the method of Asahina and Mituhori (*J. Pharm. Soc. Japan*, **1922**, 255) by the oxidation of menthone with ferric chloride in 50% acetic acid solution. The yields of diosphenol obtained were small (12—13%), and a considerable amount of the menthone was recovered (26—27%); the deficit represents the proportion of a black tarry by-product. The diosphenol was purified by distillation in a vacuum, followed by crystallisation from absolute alcohol. Colourless needles, m. p. 82°.

Pure crystalline diosphenol (39·4 g.) was mixed with a quantity of ether insufficient for complete solution and shaken in hydrogen at approx. 3 atm. with a solution of gum arabic (0·5 g.) and palladium chloride (0·3 g.) in water (220 c.c.). The theoretical amount of hydrogen was absorbed in a few hours. The product was removed in steam and the steam distillate was extracted with ether. The extract was washed twice with dilute sodium hydroxide solution (*ca.* 2*N*) to remove any unchanged diosphenol, and was then dried over anhydrous sodium sulphate and fractionated. The crude product (39 g.) was further distilled in a vacuum : a colourless limpid oil (35·5 g.) was obtained, b. p. 108—115°/12 mm., $n_D^{18.5°}$ 1·4668, $n_D^{25°}$ 1·4648, $d_{4°}^{25°}$ 0·9915. Hence, $[R_L]_D = 47{\cdot}34$ (calc., 47·7). The *p*-toluenesulphonyl derivative was analysed.

Dihydrodiosphenol Semicarbazone.—Dihydrodiosphenol (3·25 g.) was allowed to react with a slight excess of semicarbazide hydrochloride (2·4 g.) and sodium acetate crystals (3 g.) in aqueous alcohol (*ca.* 35 c.c.) for 6 days; the crystalline separation (2·6 g.) was then filtered off and washed well with rectified spirit. The mother-liquors and washings were added to water and extracted with chloroform; when dried and fractionated, this extract yielded a stiff syrup (2·17 g.), which partly crystallised when kept. The solid (2·6 g.), when crystallised from rectified spirit, had m. p. 210—211° (decomp.), and this was unaltered by further recrystallisation.

p-*Toluenesulphonyldihydrodiosphenol.*—A solution of dihydrodiosphenol (11 g.) and a slight excess of *p*-toluenesulphonyl chloride (12·6 g.) in dry pyridine (50 c.c.) was after a few days poured into water and steam-distilled to remove unesterified oil and pyridine. A dried ethereal extract of the residue, when fractionated, yielded a colourless syrup (18·5 g.), which partly crystallised. Recrystallisation from rectified spirit furnished colourless crystals (8·6 g.), m. p. 106—107° (Found : C, 63·2; H, 7·5. $C_{17}H_{24}O_4S$ requires C, 62·9; H, 7·4%). The mother-liquors furnished a non-crystallising and very viscid syrup. The *ester* was sparingly soluble in alcohol and in ethyl acetate, from which solvents it could be obtained in a beautifully crystalline condition.

d-Camphor-10-sulphonyldihydrodiosphenol, prepared from dihydrodiosphenol (10 g.) and *d*-camphor-10-sulphonyl chloride (17·2 g.) precisely as described above in the case of the *p*-toluenesulphonyl derivative, was a non-crystallising viscous syrup (20·5 g.), $[\alpha]_D^{18°} + 22{\cdot}1°$ (*c* 1·75, chloroform).

Thermal Decomposition of d-*Camphor*-10-*sulphonyldihydrodiosphenol.*—The above derivative (19 g.) decomposed in a vacuum at about 150° (bath-temperature), giving a colourless turbid distillate; this was dissolved in ether, washed with water, and dried. The brown acidic still-residue was submitted to an ether–water separation and the ether extract was dried. The two ethereal extracts furnished respectively 5·43 and 2·1 g. of oil. When these were united and distilled in a vacuum, 5·8 g. of a clear, colourless, mobile oil with a distinctive odour passed over at 90—97°/10 mm., and had $n_D^{25°}$ 1·4729. This product (5·7 g.) was oximated by the method of Read, Smith, and Bentivoglio (J., 1922, **121**, 586). An ethereal solution of the oily product was washed twice with dilute sulphuric acid, once with water, and then dried over sodium sulphate. The sulphuric acid washings were carefully neutralised with sodium hydroxide solution and a crystalline precipitate (0·50 g.) was obtained. The filtrate from this material yielded a viscous syrup (0·59 g.) on extraction with ether. The solid obtained from the acid washings was recrystallised from absolute alcohol and then from light petroleum, after filtration. Crystals were obtained having the appearance of those of *dl*-piperitone α-oxime, m. p. 115—116°; mixed m. p. with an authentic sample (m. p. 112—113°) was 112—114°. A second fraction was obtained which also did not depress the m. p. of an authentic sample of *dl*-piperitone α-oxime.

The above ethereal extract, when separated from the dilute sulphuric acid, dried, and fractionally distilled, furnished a colourless viscid syrup (5·11 g.), which crystallised rapidly and completely. This product was readily soluble in all the common solvents; crystallisation from aqueous alcohol gave felted tufts of needles, m. p. 64—65°; light petroleum gave better-developed crystals, m. p. 65·5—66·5° (Found: C, 71·6; H, 9·8. Calc. for $C_{10}H_{17}ON$: C, 71·9; H, 10·1%). The substance was also volatile in steam. The benzoyl derivative was an oil. The above oxime corresponds closely to the description of the oxime of *dl*-Δ^4-menthenone-3 in the literature, and this oxime was now synthesised by the method of Richtmann and Kremers (*Amer. Chem. J.*, 1896, **18**, 765) for purposes of comparison.

dl-Δ^3-Menthene was prepared by Robertson's method (Read and Reid, J., 1928, 1492; cf. Milobedzki and Kolitowska, *Rocz. Chem.*, 1926, **6**, 67) by the action of phosphorus trichloride on *dl*-menthol. After two fractionations in a vacuum the hydrocarbon was refluxed for 3 hours with sodium and then distilled from the metal; b. p. 60·5°/12 mm., $n_D^{17·6°}$ 1·4525. By the method of Richtmann and Kremers (*loc. cit.*), *dl*-Δ^3-menthene nitrosochloride was isolated as a fine white crystalline powder, m. p. 118—119°. This was boiled under reflux with 10% excess of 10% ethyl-alcoholic potassium hydroxide for 2 hours. The product was filtered, and the cake (potassium chloride) washed with alcohol. The filtrate and the washings were added to much water, whereby an oil was precipitated which soon crystallised. The *dl*-Δ^4-menthenone-3 oxime was filtered off, washed with dilute alcohol (*ca.* 25%), and dried: m. p. 62·5—65°, which was not depressed (63—66°) on admixture with the oxime (m. p. 65·5—66·5°) obtained as described above. The solidified melts were remelted, and the following m. p.'s were observed: *dl*-Δ^4-menthenone-3 oxime, 64·5—65·5°; mixed, 64·5—66°.

p-Toluenesulphonyldiosphenol, prepared by the action of *p*-toluenesulphonyl chloride on diosphenol in dry pyridine, was readily soluble and was obtained crystalline by deposition from ethyl acetate and alcohol; m. p. 76°. When the ester (1·5 g.), dissolved in methanol (150 c.c.), was shaken in hydrogen at 3 atm. with 10 g. of a 2% palladinised calcium carbonate catalyst for an hour, it was recovered unchanged.

Attempted Catalytic Reduction of p-*Toluenesulphonyldihydrodiosphenol to* 2-p-*Toluenesulphonyloxymenthol*-3.—Owing to the sparing solubility of *p*-toluenesulphonyldihydrodiosphenol in absolute alcohol, a mixture of absolute alcohol (145 c.c.), ethyl acetate (15 c.c.), and ether (70 c.c.) was used to dissolve the ester (6·7 g.). The solution was shaken in hydrogen at 3 atm. with an active Adams's platinum oxide catalyst for 2·5 hours, but the starting material was recovered entirely unchanged. Reduction with sodium and alcohol removed the sulphonyl group, as anticipated.

Catalytic Reduction of dl-*Piperitone Oxide.*—*dl*-Piperitone oxide was prepared by the method of Kötz and Hoffmann (*J. pr. Chem.*, 1925, **110**, 121), 4*N*-alkali (cf. Weitz and Scheffer, *Ber.*, 1921, **54**, 2336) being used instead of *N*/4. The oxide (13·9 g.) was dissolved in methanol (200 c.c.) and shaken in hydrogen at 3 atm. with a 2% palladinised calcium carbonate catalyst (15 g.). When the pressure no longer fell, the product (13·1 g.) was isolated; it crystallised partly on standing. The above treatment was repeated with fresh catalyst (12 g.). The total absorption of hydrogen exceeded 2 atoms per molecule but was less than 4. When the final crude product (12·7 g.) was fractionated in a vacuum, two fractions were obtained: (*a*) a menthone-smelling colourless oil (5·2 g.), b. p. to 125°/14 mm., $n_D^{14°}$ 1·4570; (*b*) a colourless viscous oil (7·1 g.), b. p. mainly 137—139·5°/14 mm., $n_D^{14·5°}$ 1·4695. This fraction, which was odourless, crystallised spontaneously with evolution of heat. After being pressed on a porous tile, the substance separated from light petroleum (b. p. 60—80°) in well-developed crystals, m. p. 88·5—90·5°, softening from 86·5°; this m. p. was unaltered after repeated crystallisation (Found: C, 70·6; H, 10·4. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·6%).

Catalytic Reduction of dl-*Carvenone Oxide.*—*dl*-Carvenone, from dihydrocarvone, was converted into the oxide as in the case of piperitone. *dl*-Carvenone oxide, when hydrogenated under the conditions noted above for piperitone oxide, yielded a product which was readily separated into two fractions when fractionally distilled in a vacuum: (*a*) a carvomenthone fraction, b. p. to 125°/16 mm., $n_D^{18°}$ 1·4582; (*b*) a colourless, rather viscid oil, b. p. 137—142°/16 mm., $n_D^{18°}$ 1·4710. When the second fraction was mixed with light petroleum and placed in the ice-chest, large well-developed prisms were deposited in a few hours. Recrystallisation from light petroleum furnished beautiful needles, m. p. 72·5—74°, softening from 71° (Found: C, 70·6; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%).

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