532. *Reduction by Dissolving Metals. Part VI. Some Applications in Synthesis.*

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By making use of the reducing properties of solutions of sodium and ethanol in liquid ammonia, (±)-compounds are synthesised corresponding to the formulæ assigned to α-, β-, and γ-curcumene, (II), (III), and (VI), piperitone (X), and carvenone (XI). *Hexœstrol di-(2-hydroxyethyl) ether* gives rise to 3 : 4-*di*-(4-*keto*cyclo*hex*-1-*enyl*)*hexane* (VIII), and the glyceryl ethers of α-œstradiol or œstrone to *œstra*-5(10)-*en*-17(β)-*ol*-3-*one* (IX). Some general conclusions are drawn as to the utility of the reagent in synthetic work.

Methods employing reduction by dissolving metals have with a few very notable exceptions been neglected during recent years in favour of catalytic methods. They have unique properties in some cases, however, and the present communication is the first of a series attempting to define some of the advantages and limitations in synthetic work of the most powerful of such methods employing alkali metal–alcohol–liquid ammonia solutions. These reagents have already been studied, chiefly from a theoretical point of view, in Parts I—V of this series (*J.*, 1944, 403; 1945, 809; 1946, 593; 1947, 102, 1642).

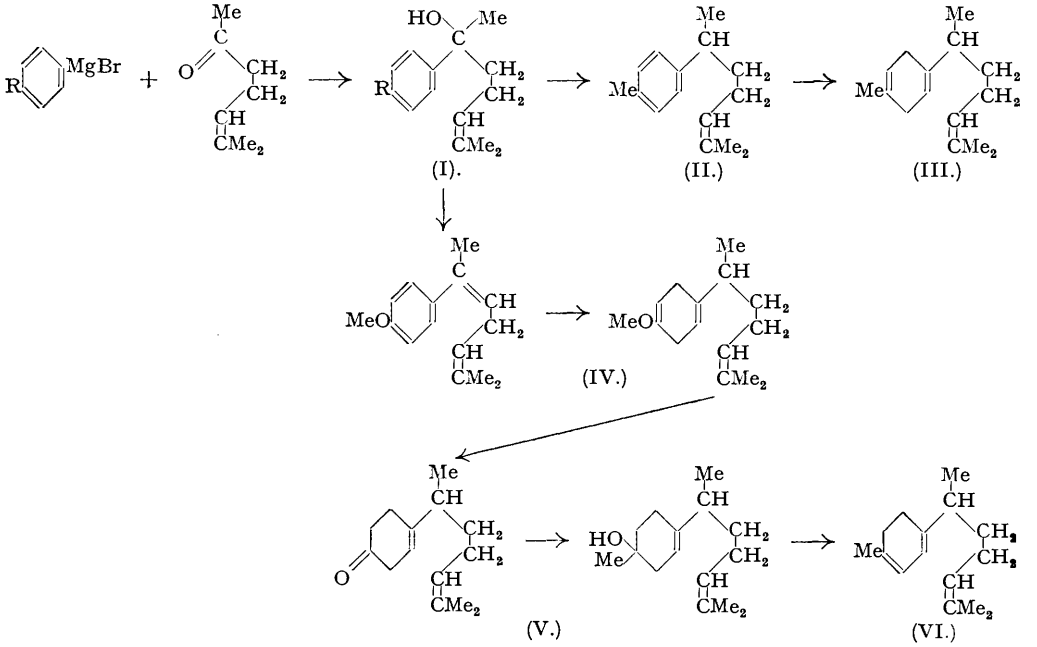
Although the reagents can be used for the reduction of ketones, esters, nitro-compounds, and other easily reducible substances, they rarely show advantages in such cases over more conventional reagents, and may be disadvantageous; *e.g.*, amides and sometimes hydrocarbons are by-products in the reduction of esters. Occasionally, advantage may result from the ease of isolation of the product from the volatile ammonia; and partly reduced compounds may be obtainable because of the low temperature, or because of the formation of stable salts which protect them from further reduction. Lack of steric hindrance, *e.g.*, in the reduction of phenyl-substituted ethylenes, and stereochemical specificity, *e.g.*, the formation of *trans*-ethylenes from acetylenes, are other characteristics. However, it is a delicate matter to crack a nut with a sledge-hammer, and inadvisable if a nut-cracker is available.

The reagents would appear to be of greatest use where their combination of power and specificity can be brought into play, notably in the reduction of benzene rings to the dihydro-derivatives, and in the hydrogenolysis of certain benzyl and allyl alcohols. The following syntheses of α-, β-, and γ-curcumene, (II), (III), and (VI) respectively, illustrate some points of interest.

The specific reduction of a conjugated system (even an aromatic one) without that of an isolated double bond makes possible reduction of the benzene ring without touching the side chain; and the fact that hydrogenolysis of the *alcohol* (I; R = Me) to α-curcumene (II) proceeds

far more readily than the reduction of the ring, permits the isolation of α-curcumene almost uncontaminated by (±)-β-*curcumene* (III). In any case, traces of (III) can be re-oxidised to (II) by means of lead tetra-acetate, which is a smooth reagent for converting αδ-dihydrobenzenes into benzenes (Criegee, *Annalen*, 1930, **481**, 236; Birch, unpublished work). The reduction of α-curcumene (II) to β-curcumene (III) recalls the formation of γ-terpinene from *p*-cymene (Part I, *loc. cit.*), and can be accomplished by a large excess of reducing agent. The positions assigned to the added hydrogen atoms follow from the orientation rules already enunciated (Part I) and confirmed by all subsequent work.

Reduction of the alcohol (I; R = OMe) would result chiefly in hydrogenation of the aromatic ring without removal of the hydroxyl group, because benzyl alcohols are hydrogenolysed only to a minor extent if they contain a powerful electron-donor group in the *p*-position (Birch, unpublished work). Accordingly, it was necessary to dehydrate the compound, and it was then possible to reduce the resulting double bond because of its conjugation with the aromatic ring. Reduction of the ring in the product and acid hydrolysis then gave the ketone (V). This is formulated as βγ-unsaturated because of its lack of a light-absorption maximum in the



range 2200—2800 A. (cf. the formation of 4-methyl*cyclo*hex-3-enone from *p*-tolyl methyl ether, Part III, *loc. cit.*).

In all these compounds, natural and synthetic, the position of the side-chain double bond in a propenyl or *iso*propylidene group is subject to the usual uncertainty with terpenes. In the synthetic substances it depends on the constitution of the methylheptenone employed, which is probably mostly the *iso*propylidene derivative.

Sesquiterpene.	B. p.	n_D.	Derivatives, m. p. Nitrosate.	Nitrol-benzylamine.
α-Curcumene, (−)-natural *	137°/17 mm.	1·4989/20°	101°	104—105°
(±)-synthetic *	134°/16 mm.	1·5002/20°	114	—
(±)-synthetic †	140°/19 mm.	1·5014/20°	115—116	75
			Trihydrochloride.	
β-Curcumene, (−)-natural *	142°/19 mm.	1·491/20°	84—85°	
(±)-synthetic †	142—143°/18 mm.	1·4937/21°	66—67	
			U.V. Absorption.	
γ-Curcumene, (+)-natural ‡	94°/3 mm.	1·4975/25°	2670 A. ($\varepsilon_{max.}$ 3500) (*cyclo*hexane)	
(±)-synthetic †	135°/15 mm.	1·4956/20°	2650 A. ($\varepsilon_{max.}$ 2900) (methanol)	

* Simonsen *et al.*, *loc. cit.* † This paper. ‡ Batt and Slater, *loc. cit.*

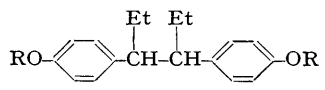
The structures (II) and (III) assigned to α- and β-curcumene on the basis of evidence from degradations and a synthesis of (±)-α-curcumene, appear to be firmly established (Rao and Simonsen, *J.*, 1928, 2496; Carter, Copp, Rao, Simonsen, and Subramanian, *J.*, 1939, 1504; Carter, Simonsen, and Williams, *J.*, 1940, 451). Nevertheless, the natural compounds are optically active, so that their derivatives and those of the (±)-synthetic compounds are not identical. The general resemblance is evident however (see Table). A partial synthesis of optically active β-curcumene could be carried out by reduction of the natural α-curcumene.

The assigned disposition of the conjugated double bonds in γ-curcumene (Batt and Slater, this vol., p. 838), although probably correct, is not quite certain. It is favoured by the close resemblance between the natural and synthetic compounds (see Table), and could probably be determined definitely by the method of Alder and Rickert (*Ber.*, 1937, **70**, 1364).

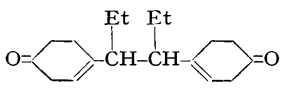
In default of (±)-compounds from natural sources, it may be possible to racemise the optically active curcumenes by the action of potassium amide in liquid ammonia (cf. Part V and unpublished work) because the asymmetric carbon atom in each case possesses a hydrogen in an allyl or benzyl position. Comparisons of infra-red absorption spectra should in any case be decisive.

The reduction of α-curcumene (II) to β-curcumene (III) illustrates one of the chief difficulties, *viz.*, slow reaction because of insolubility in ammonia. With reductions not requiring alcohol this limitation is often not serious, but in the presence of alcohol, as here, evolution of gaseous hydrogen is an important competing reaction, and a large excess of reducing agent is necessary. That reduction does take place indicates that hydrocarbons up to $C_{(15)}$ can react despite a comparatively unfavourable substitution of the benzene ring (cf. Birch, *Faraday Soc. Discussion*, 1947, **2**, 249). The presence of oxygen in a molecule often increases solubility, and (IV) can be reduced without undue difficulty.

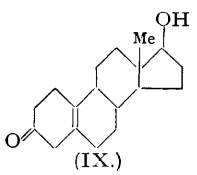
An example of extreme insolubility is hexœstrol dimethyl ether (VII; R = Me), which has not so far been reduced despite repeated attempts under varying conditions and with mixed solvents. The high solubility of alcohols in liquid ammonia led to the expectation that 2-hydroxyethyl or glyceryl ethers would be more soluble than the methyl ethers. *Hexœstrol di-(2-hydroxyethyl) ether* (VII; R = CH_2·CH_2·OH) is fairly soluble and readily reduced (cf. Birch and Mukherji, *Nature*, 1949, **163**, 766), giving, after acid hydrolysis, 3 : 4-*di*-(4-*keto*-cyclo*hex*-1-*enyl*)*hexane* (VIII). The constitution of this as the βγ-unsaturated ketone was demonstrated by its lack of an absorption maximum in the range 2200—2800 A. The glyceryl ether of α-œstradiol or œstrone by the same treatment gave rise to what is probably *œstra*-5(10)-*en*-17(β)-*ol*-3-*one* (IX). These ketones are being tested for androgenic activity.



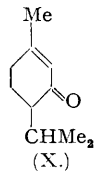
(VII.)



(VIII.)



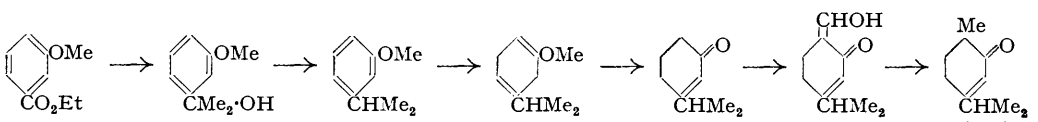
(IX.)



(X.)

α-Œstradiol glyceryl ether is much more strongly adsorbed on alumina than (IX) and the substances are therefore easily separated. This strong adsorption is probably due to the extra hydroxyl groups, and should therefore be displayed by similar compounds. With the lower molecular-weight compounds the hydroxylated ethers have the advantage of a boiling point high in comparison with that of the ketone produced in the acid hydrolysis, thus permitting ready purification of this ketone by distillation. Thymyl methyl ether has already been reduced (Part I, *loc. cit.*) and the hydrolysis product shown to contain (±)-piperitone (X), but it was difficult to isolate the ketone in a state of purity. This was easily accomplished from the reduction product of thymyl 2-hydroxyethyl or glyceryl ether. Carvenone (XI) was similarly prepared from carvacryl 2-hydroxyethyl ether.

Another synthesis of carvenone is as follows :



(XI.)

Reduction of the ring is facilitated in this case by the presence of only one alkyl group, and the formyl derivative can be isolated in a state of purity because of the solubility in water of its sodium salt.

Other aspects of the subject, including the protection of active groups and the use of the reagents in the examination of some natural products, will be considered in a later publication.

Experimental.

2-p-*Tolyl*-6-*methylhept*-5-*en*-2-*ol* (I; R = Me).—To the Grignard reagent from *p*-bromotoluene (20 g.) in ether (150 c.c.) was added methylheptenone (from citral, purified over the bisulphite compound, 15 g.) with ice-cooling. The mixture was decomposed with aqueous ammonium acetate, and the ethereal layer separated, dried, and distilled. A fore-run and a higher boiling residue were rejected; the *carbinol* (I; R = Me) (12·5 g.) distilled as a colourless, somewhat viscous oil, b. p. 110°/0·35 mm., with a sweet odour (Found : C, 82·2; H, 9·4. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%).

(±)-*α-Curcumene*.—A mixture of the above carbinol (8·5 g.), ethyl alcohol (10 g.), and ether (20 c.c.) was stirred into ammonia (300 c.c.), and sodium (5 g.) added gradually. The mixture was cautiously decomposed with water (200 c.c.), and the product (II) collected with ether, dried (K_2CO_3), and distilled over sodium. It was a colourless oil (6 g.), b. p. 140°/19 mm., n_D^{21} 1·5014 (Found : C, 88·9; H, 10·9. Calc. for $C_{15}H_{22}$: C, 89·1; H, 10·9%). Treated for a short time with lead tetra-acetate in acetic acid, it was recovered unchanged. The nitrosate was obtained as tiny colourless needles (from chloroform–alcohol), m. p. 115—116°; the *nitrolpiperidine* formed colourless needles (from alcohol), m. p. 129—130° (Found : C, 76·2; H, 10·1. $C_{20}H_{32}ON_2$ requires C, 76·0; H, 10·1%); and the *nitrolbenzylamine* formed colourless needles (from alcohol), m. p. 75° (Found : C, 77·9; H, 8·4. $C_{22}H_{30}ON_2$ requires C, 78·1; H, 8·9%). The best derivative for characterisation appears to be the nitrolpiperidine.

(±)-*β-Curcumene* (III).—(±)-α-Curcumene (5 g.) was reduced with sodium (5 g.) and alcohol (15 g.) in ammonia (300 c.c.). The product (4·6 g.) had b. p. 141—143°/18 mm. and n_D^{21} 1·4945. It still contained α-curcumene, since it gave rise to the nitrolpiperidine in small yield. The reduction was repeated, sodium (10 g.), alcohol (25 g.), and ammonia (400 c.c.) being used, and the (±)-*β-curcumene* (4 g.) had b. p. 142—143°/18 mm. and n_D^{21} 1·4937 (Found : C, 88·6; H, 11·5. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%). The *trihydrochloride* was prepared according to Simonsen and his co-workers (*loc. cit.*) as clusters of elongated prisms from a little chilled light petroleum (b. p. 40—60°); m. p. 66—67° (Found : Cl, 33·8. $C_{15}H_{27}Cl_3$ requires Cl, 34·0%).

2-p-*Methoxyphenyl*-6-*methylhepta*-2 : 5-*diene* (IV).—To the Grignard reagent from *p*-bromoanisole (40 g.) in ether (200 c.c.) was added methylheptenone (27 g.) in ether (50 c.c.) with ice-cooling. The mixture was heated under reflux on the steam-bath for 2 hours and decomposed with aqueous ammonium acetate. The ether layer was dried (K_2CO_3) and distilled under reduced pressure in the presence of a crystal of iodine. The distillate was washed with sodium thiosulphate solution and redistilled, giving the *diene* (IV) as a colourless, viscous oil with a sweet odour (37 g.), b. p. 160—161°/13 mm. (Found : C, 82·6; H, 9·4. $C_{15}H_{20}O$ requires C, 83·3; H, 9·2%).

6-(4-*Keto*cyclo*hexenyl*)-2-*methylhept*-2-*ene* (V).—The above heptadiene (13 g.) was reduced in ammonia (750 c.c.) with sodium (18·4 g.) and alcohol (55 g.). The product gave two fractions : (i) b. p. 125—135°/13 mm. (3 g.), and (ii) b. p. 148—155°/13 mm. Fraction (i) redistilled mostly at 120—122°/13 mm., and is probably 6-cyclo*hexenyl*-2-*methylhept*-2-*ene* (Found : C, 87·1; H, 12·9. $C_{14}H_{24}$ requires C, 87·5; H, 12·5%). Fraction (ii) was heated on the steam-bath with aqueous sulphuric acid (30 c.c., 5%) for 30 minutes, and the product taken up in ether and converted into the derivative with sodium bisulphite. This was well washed with ether and decomposed with cold sodium hydroxide solution (5%). The 6-(4-*keto*cyclo*hexenyl*)-2-*methylhept*-2-*ene* (5·5 g.) was taken up in ether, dried (K_2CO_3), and distilled; b. p. 150—152°/13 mm. (Found : C, 81·3; H, 10·6. $C_{14}H_{22}O$ requires C, 81·5; H, 10·7%). The *semicarbazone* crystallised as prisms from dilute methanol, m. p. 114° (Found : C, 68·0; H, 10·0; N, 15·0. $C_{15}H_{25}ON_3$ requires C, 68·4; H, 9·5; N, 15·9%).

(±)-*γ-Curcumene*.—To the Grignard reagent from methyl iodide (14 g.) in ether (50 c.c.) was added the above ketone (9·8 g.) with ice-cooling. After an hour, the mixture was heated under reflux for 30 minutes, decomposed with aqueous ammonium acetate, and the ether layer separated and dried (K_2CO_3). Distillation gave 6-(4-*hydroxy*-4-*methyl*cyclo*hexenyl*)-2-*methylhept*-2-*ene* as a colourless, rather viscous oil (8 g.), b. p. 147—148°/10 mm. (Found : C, 81·0; H, 12·2. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). It was dehydrated in two ways.

(i) Thionyl chloride (freshly distilled over linseed oil, 3·6 g.) was slowly added to the carbinol (4·5 g.) dissolved in dry pyridine (9·5 g.) cooled in ice. The mixture was left for 8 hours, decomposed with ice and dilute hydrochloric acid, and the oil collected with ether, dried (K_2CO_3), and distilled. The (±)-*γ-curcumene* was a colourless, terpene-smelling oil (1·8 g.), b. p. 135°/15 mm., n_D^{20} 1·4956, $\lambda_{max.}$ 2650 A., $\varepsilon_{max.}^{mol.}$ 2900 (Found : C, 88·0; H, 12·1. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%).

(ii) The carbinol (3 g.) was heated at 175—185° for 15 minutes with 2 moles of phthalic anhydride (cf. Schinz and Schäppi, *Helv. Chim. Acta*, 1947, **30**, 1483). The product (2·5 g.) had b. p. 132°/13 mm. and n_D^{20} 1·4850 (Found : C, 87·8; H, 12·0%).

Hexœstrol Di-(2-*hydroxyethyl*) *Ether*.—Hexœstrol (8·5 g.) was heated under reflux with sodium hydroxide solution (400 c.c., 5%) until it went into solution. The hot, turbid solution was heated with ethylene chlorohydrin (5 moles) at about 80° for an hour. The cold solution was extracted with chloroform, the extract dried (K_2CO_3), and the solvent removed. The residue was a white solid which, crystallised three times from benzene, gave colourless plates (6 g.), m. p. 90—91°, of the *ether* (Found : C, 73·4; H, 7·9. $C_{22}H_{30}O_4$ requires C, 73·7; H, 8·4%).

3 : 4-*Di*-(4-*keto*cyclo*hexenyl*)*hexane*.—The above ether (4·5 g.) was dissolved in alcohol (36 g.), and the mixture added to liquid ammonia (450 c.c.) to give a clear solution. Sodium (12 g.) was added in small pieces as rapidly as was practicable with vigorous stirring. After the blue colour had disappeared,

the pasty mass was decomposed cautiously by addition of water (250 c.c.), and the thick oil taken up in chloroform. The solvent was removed under reduced pressure and the residue heated under reflux with sulphuric acid (100 c.c., 5%) for 30 minutes. The product was taken up in ethyl acetate and chromatographed on alumina; the least adsorbed fraction, showing a bluish fluorescence in ultra-violet light, formed the major portion of the material From it 3 : 4-*di*-(4-*keto*cyclo*hexenyl*)*hexane* was crystallised by the addition of light petroleum (b. p. 40—60°) to a solution in ether. It formed colourless elongated prisms, m. p. 132—133° (shrinks about 120°) (Found : C, 78·6; H, 9·9. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·5%). The absence of any marked light absorption in the region 2000—2800 A. indicated that it is not the $\alpha\beta$-unsaturated ketone. No crystalline compound could be obtained from the later, gummy fractions of the chromatogram. After being left with a 3% solution of sodium in ethanol under nitrogen for 8 hours the crystalline solid was converted into a glass evidently containing $\alpha\beta$-unsaturated ketone, $\varepsilon_{mol.}$ 6500 at λ 2200 A. Since this work was done, Ungnade and Tucker (*J. Amer. Chem. Soc.*, 1949, **71**, 1381) have published the preparation of the *meso*- and (±)-$\alpha\beta$-unsaturated diketones, which were obtained as glasses with absorption in the region 2250—2350 A. and weaker absorption at 2800—2850 A.

Œstra-5(10)-*en*-17(β)-*ol*-3-*one*.—α-Œstradiol (m. p. 173°; 480 mg.) was dissolved in the minimum amount of boiling ethanol and added to a solution of sodium hydroxide (2·5 g.) in water (50 c.c.). α-Chlorohydrin (6 g.) was then added, and the solution heated to 80° for 30 minutes under nitrogen. Sodium hydroxide (2·5 g.) in a little water and α-chlorohydrin (6 g.) were then added, and heating continued for 15 minutes. After cooling, the solution was acidified with acetic acid, extracted with chloroform, and the solvent evaporated. The product was a white solid (430 mg.), m. p. 175—180°. A small portion was crystallised from ethyl acetate–light petroleum (b. p. 40—60°) to give *α-œstradiol* 3-(1-*glyceryl*) *ether* as clumps of colourless needles, m. p. 184—185° (Found : C, 72·3; H, 8·6. $C_{21}H_{30}O_4$ requires C, 72·8; H, 8·6%).

The crude material obtained above (400 mg.) was dissolved in warm ethanol (15 c.c.) and added to ammonia (400 c.c.) followed by sodium (3 g.). After the colour had disappeared, water (75 c.c.) was added, and the ammonia evaporated, finally by boiling. The solution was neutralised to methyl-orange by addition of hydrochloric acid (5%), and a further amount of acid added to give a 5% concentration of hydrogen chloride. Ethyl acetate (50 c.c.) was added, and the solution vigorously shaken until all the suspended solid had gone into solution. The ethyl acetate was separated, and the aqueous solution again extracted with ethyl acetate (50 c.c.). The combined extracts were dried (K_2CO_3), and the solvent removed under reduced pressure. The residual gum solidified, but was difficult to purify. It was chromatographed on alumina in ethyl acetate solution. The substance carried through the column, which is probably *œstra*-5(10)-*en*-17(β)-*ol*-3-*one*, formed large prisms on evaporation of the solvent. Elution of the column with alcohol gave another substance, which on crystallisation from ethyl acetate–light petroleum (b. p. 40—60°) had m. p. 183—184°, undepressed by the starting material. Œstra-5(10)-en-17(α)-ol-3-one crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as large colourless prisms (105 mg.), m. p. 181—182° (Found : C, 78·7; H, 9·7. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·5%). It reacted with 2 : 4-dinitrophenylhydrazine in cold alcoholic sulphuric acid to produce a derivative as orange flat plates, m. p. 162—163°, converted by boiling with alcoholic sulphuric acid into a dark red crystalline solid, m. p. 180—183° after previous softening.

The reaction of œstrone with α-chlorohydrin as above gave a crystalline solid which was not closely investigated, but which on reduction as above gave the same ketone, m. p. 181—182°, together with some α-œstradiol glyceryl ether, m. p. 184—185°.

Thymyl 2-Hydroxyethyl Ether (cf. Boyd and Marle, *J.*, 1914, **105**, 2134).—Thymol (20 g.) was dissolved in the minimum amount of sodium hydroxide solution (10%) at about 80°, and to the solution was added ethylene chlorohydrin (32 g.) in about 5-g. portions alternating with an approximately equivalent amount of aqueous sodium hydroxide (20%). Ether extraction and distillation gave thymyl 2-hydroxyethyl ether as a viscous oil (25 g.), b. p. 154—158°/0·7 mm. (Found : C, 74·4; H, 9·2. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·3%). Boyd and Marle (*loc. cit.*) give m. p. 53—54°, but the above did not solidify after being kept for a short time.

Thymyl 1-Glyceryl Ether.—Thymol (15 g.) was treated as above with glycerol monochlorohydrin (35 g.) (cf. Boyd and Marle, *J.*, 1912, **101**, 312). Thymyl 1-glyceryl ether (20 g.) distilled at 198—202°/20 mm. and solidified on cooling. It crystallised as needles from light petroleum (b. p. 60—80°); m. p. 56° (Found : C, 69·4; H, 8·9. Calc. for $C_{13}H_{20}O_3$: C, 69·6; H, 8·9%) (Boyd and Marle, *ibid.*, give m. p. 57°).

Carvacryl 2-Hydroxyethyl Ether.—Prepared from carvacrol in the same way as the corresponding thymyl compound, carvacryl 2-hydroxyethyl ether was a viscous oil, b. p. 153—155°/12 mm., which solidified; m. p. 50° (Found : C, 74·0; H, 9·2. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·3%) (Boyd and Marle, *loc. cit.*, give m. p. 51—52°).

Piperitone.—(A) Thymyl 2-hydroxyethyl ether (22 g.) in alcohol (30 g.) was added to liquid ammonia (350 c.c.) and reduced with sodium (15 g.). The resulting 2-(2-*hydroxyethoxy*)-4-*methyl*-1-iso*propyl*-cyclo*hexa*-1 : 4-*diene* distilled as a viscous oil, b. p. 150—152°/10 mm. (Found : C, 73·2; H, 10·1. $C_{12}H_{20}O_2$ requires C, 73·5; H, 10·2%). This substance (17·5 g.) was heated under reflux with hydrochloric acid (5%) for 20 minutes and the resulting piperitone (14 g.) had b. p. 112°/15 mm. (Found : C, 79·0; H, 10·8. Calc. for $C_{10}H_{16}O$: C, 79·0; H, 10·4%). It gave a 2 : 4-dinitrophenylhydrazone as orange-red needles (from benzene–alcohol), m. p. 116°, undepressed by the authentic piperitone derivative.

(B) As above, thymyl glyceryl ether (12 g.), alcohol (15 g.), and sodium (7 g.) in ammonia (200 c.c.) being used, piperitone (4·6 g.), b. p. 116°/20 mm., was obtained.

Carvenone.—(A) Carvacryl 2-hydroxyethyl ether was reduced as for the thymyl ether to give carvenone (67%), b. p. 105°/10 mm. (Found : C, 78·8; H, 10·4. Calc. for $C_{10}H_{16}O$: C, 79·0; H, 10·6%). The 2 : 4-*dinitrophenylhydrazone* formed bright red needles (from ethyl acetate–alcohol), m. p. 165° (Found : C, 57·5; H, 5·8. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·0%). The semicarbazone had m. p. 198—200° (Wallach, *Ber.*, 1895, **28**, 1960, gives m. p. 200—201°).

(B) The action of methylmagnesium iodide in the standard manner on ethyl 3-methoxybenzoate

gave rise to 3-methoxyphenyldimethylcarbinol, b. p. 130—132°/12 mm. (Found : C, 72·2; H, 8·3. Calc. for $C_{10}H_{14}O_2$: C, 72·4; H, 8·4%) (cf. Béhal and Tiffeneau, *Bull. Soc. chim.*, 1908, **3**, 316). Reduction of the carbinol (15 g.) with sodium (5·5 g.) and alcohol (15 g.) in ammonia (300 c.c.) produced 3-methoxy*iso*propylbenzene (11 g.), b. p. 93°/12 mm. (Found : C, 79·9; H, 9·5. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·3%).

m-Methoxy*iso*propylbenzene (11 g.) was reduced with sodium (9 g.) and alcohol (25 g.) in ammonia (300 c.c.) to give 1-*methoxy*-5-iso*propyl*cyclo*hexa*-1 : 4-*diene*, b. p. 93—94°/14 mm. (Found : C, 78·9; H, 10·7. $C_{10}H_{16}O$ requires C, 79·0; H, 10·4%). This diene was hydrolysed by boiling with dilute hydrochloric acid (50 c.c., 5%) for 30 minutes, and the 3-isopropyl*cyclo*hex-2-enone (8·5 g.) distilled; b. p. 102—104°/20 mm. (Found : C, 77·8; H, 10·2. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised as dark red needles (from ethyl acetate), m. p. 155° (Found : C, 56·4; H, 5·6. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7%).

This ketone was methylated through the formyl derivative. Ketone (5 g.) was slowly added with stirring and ice-cooling to a mixture of dry sodium ethoxide (from sodium, 1·0 g.) and ether (40 c.c.) with ethyl formate (3 g.). A yellow solid rapidly separated. After 2 hours, ice and water were added, the dark red aqueous layer separated and acidified, and the oil taken up in ether. Distillation gave a pale yellow oil, b. p. 136°/17 mm. (3·2 g.). This was added to an ice-cold solution of sodium (0·6 g.) in alcohol (10 c.c.), followed by methyl iodide (6 g.). After being left for an hour the mixture was heated under reflux until the red colour had disappeared (about 2 hours). A solution of sodium hydroxide (5 g.) in water (25 g.) was then added, and refluxing continued for an hour. The mixture was poured into water (50 c.c.), and the oil taken up in ether and distilled; b. p. 112—114°/20 mm. (Found : C, 79·1; H, 10·5. Calc. for $C_{10}H_{16}O$: C, 79·0; H, 10·4%). It gave a 2 : 4-dinitrophenylhydrazone, m. p. 165°, undepressed by the derivative obtained in the method (A).

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