743. *Synthetic and Oxidative Studies in the Polyhydroxydiphenyl Series. Part III.*[1] 2 : 3-*Dihydroxy*-5 : 6-*dimethyldiphenyl.*

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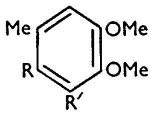
4 : 5-Dimethylveratrole has been prepared in 80% yield by a three-stage reaction from veratraldehyde, and also by treatment of 4 : 5-dichloroveratrole with methyl-lithium. With ethereal *n*-butyl-lithium it gives 13% of the 3-lithio-derivative which with carbon dioxide affords the corresponding carboxylic acid, but the expected tertiary alcohol was not obtained from reaction with *cyclo*hexanone. Ethereal 3-bromo-4 : 5-dimethylveratrole is largely debrominated by lithium or phenyl-lithium.

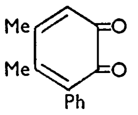
2 : 3-Dimethoxy-5 : 6-dimethyldiphenyl is formed in low yield by the crossed Ullmann reaction with 3-bromo-4 : 5-dimethylveratrole and iodobenzene. It is readily demethylated, and the resulting dihydric phenol is converted by mild oxidants into the corresponding diphenoquinone.

IN Part II [1] it was shown that 4 : 5-dichloroveratrole could not be satisfactorily metallated owing to interaction of the halogen atoms with the organolithium compound, but such a reaction is precluded in 4 : 5-dimethylveratrole and it was hoped to prepare 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl from this by a series of reactions analogous to those described in Part I.[2] The results of this work are described in the present paper.

4 : 5-Dimethylveratrole (I) was unknown until 1943, when Karrer and Schick [3] prepared it in an overall yield of 34% by the route: veratraldehyde $\longrightarrow$ 4-methylveratrole $\longrightarrow$ 6-methylveratraldehyde $\longrightarrow$ (I). The aldehydes were reduced by catalytic hydrogenation of their anils, and it was at these stages that poor yields were obtained. Consequently, other methods of effecting the change R·CHO $\longrightarrow$ $R{\cdot}CH_3$ were examined, and the Huang-Minlon [4] modification of the Wolff–Kishner reduction was found to give excellent yields at both stages. 4-Methylveratrole was converted into 6-methylveratraldehyde by the modified [5] Gattermann reaction, this procedure being superior to formylation [6] with *NN*-dimethylformamide–phosphorus oxychloride mixture. 4 : 5-Dimethylveratrole is also formed when 4 : 5-dichloroveratrole reacts with ethereal methyl-lithium, this being analogous to the formation of 4 : 5-diphenylveratrole described in Part II.[1]

(I) R = Me, R′ = H
(II) R = Me, R′ = CO_2H
(III) R = $CH_2{\cdot}CO_2H$, R′ = H
(IV) R = Me, R′ = NH_2
(V) R = Me, R′ = Ph





(VI)

Reaction of 4 : 5-dimethylveratrole with one equivalent of ethereal *n*-butyl-lithium and subsequent carboxylation afforded 13% of 4 : 5-dimethylveratrole-3-carboxylic acid (II), m. p. 120°, and 13% of 4 : 5-dimethylguaiacol; with two equivalents of butyl-lithium the yields were 15% and 32% respectively. The carboxylic acid obtained from this reaction could have been [7] the isomeric phenylacetic acid (III), but this was synthesised by Sugasawa and Sigehara [8] and had m. p. 102—104°. Further confirmation of the orientation (II) was obtained by Schmidt degradation to 3-amino-4 : 5-dimethylveratrole (IV).

The expected tertiary alcohol could not be isolated after reaction of *cyclo*hexanone with metallated 4 : 5-dimethylveratrole, the main product being an oil which

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[1] Part II, Bruce and Sutcliffe, preceding paper.
[2] *Idem, J.*, 1955, 4435.
[3] Karrer and Schick, *Helv. Chim. Acta*, 1943, **26**, 800.
[4] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[5] Adams and Levine, *ibid.*, 1923, **45**, 2373.
[6] Cf. Buu-Hoï and Lavit, *J.*, 1955, 2776.
[7] Cf. Letsinger and Schnizer, *J. Org. Chem.*, 1951, **16**, 869.
[8] Sugasawa and Sigehara, *Ber.*, 1941, **74**, 459.

on dehydration afforded a neutral compound $(C_{15}H_{20}O_2)_n$, m. p. 61·5°. Treatment of this with hydrobromic acid gave 4 : 5-dimethylcatechol, and it seemed possible that it was 4 : 5-dimethylguaiacol *cyclo*hexyl ether, $C_{15}H_{22}O_2$, but this was synthesised from 4 : 5-dimethylguaiacol and had m. p. 33°.

The failure of 3-lithio-4 : 5-dimethylveratrole to react in the expected manner with *cyclo*hexanone may be due to steric hindrance, though the low concentration of the lithio-compound could also be a contributing factor, and consequently attempts were made to prepare lithiodimethylveratrole by reactions involving halogen–metal interchange.

3-Iodo-4 : 5-dimethylveratrole could only be obtained from the amine (IV) from which the 3-bromo- and the 3-chloro-derivative were also prepared. The 3-bromo-compound was, however, more conveniently obtained by treatment of 4 : 5-dimethylveratrole with one equivalent of bromine; with two equivalents in the presence of a halogen carrier, 3 : 6-dibromo-4 : 5-dimethylveratrole was formed.

Reaction of 3-bromo-4 : 5-dimethylveratrole with one equivalent of ethereal phenyl-lithium and subsequent carboxylation afforded, unexpectedly, 78% of 4 : 5-dimethylveratrole and an unidentified carboxylic acid. When an ethereal solution of the bromo-compound was refluxed with lithium metal and then carboxylated, the products were 4 : 5-dimethylveratrole, 4 : 5-dimethylveratrole-3-carboxylic acid, and 4 : 5-dimethylguaiacol. No reaction occurred in benzene solution, nor did the compound react with magnesium. With two equivalents of ethereal phenyl-lithium, and subsequent carboxylation, 3 : 6-dibromo-4 : 5-dimethylveratrole also suffered debromination, giving the acid (II); with lithium metal, only a trace of acidic material was formed, the main product being 3-bromo-4 : 5-dimethylveratrole.

Owing to the failure to obtain good yields of 3-lithio-4 : 5-dimethylveratrole, the Ullmann reaction with a mixture of 3-bromo-4 : 5-dimethylveratrole and iodobenzene was attempted, and this afforded the required diphenyl (V) in low yield, together with 2 : 3 : 2′ : 3′-tetramethoxy-5 : 6 : 5′ : 6′-tetramethyldiphenyl. An attempt was made to prepare dimethoxydimethyldiphenyl (V) by the reaction of 4 : 5-dichloro-3-phenylveratrole [1] with two equivalents of ethereal methyl-lithium, but, in contrast to 4 : 5-dichloroveratrole itself, only one chlorine atom was replaced. The orientation of the product is being investigated. When the reaction was conducted in higher-boiling solvents the diphenyl suffered extensive decomposition.

2 : 3-Dihydroxy-5 : 6-dimethyldiphenyl was obtained by demethylation of its dimethyl ether (V), and on oxidation with silver oxide in ether or sodium iodate in aqueous ethanol it afforded 5 : 6-dimethyl-2 : 3-diphenoquinone (VI), which showed similar solubility properties to those of the parent 2 : 3-diphenoquinone.[2] The quinone was obtained by iodate oxidation as an amorphous powder which, in contrast to 5 : 6-dichloro-2 : 3-diphenoquinone,[1] adsorbed considerable quantities of water. Like the dichlorodiphenoquinone, the compound (VI) is unaffected by long storage at 20° with 2% aqueous sodium carbonate, sodium hydrogen carbonate, or disodium hydrogen phosphate, but when boiled with these aqueous bases it forms a dark mass which dissolves only partially. It is readily soluble, with decomposition, in 2% aqueous sodium hydroxide.

These differences between 5 : 6-dichloro- and 5 : 6-dimethyl-2 : 3-diphenoquinone suggest that, in the presence of aqueous bases, the former decomposes smoothly to soluble products whereas the latter both decomposes and polymerises. Such a polymerisation may be due to activation of the 4-position by the adjacent methyl group, or to participation of methyl groups in a chain-forming process. The marked instability of tetramethyl-1 : 2-benzoquinone [9] supports the second view.

EXPERIMENTAL

Reactions with organolithium compounds were conducted under oxygen-free nitrogen. Solutions in organic solvents were dried with sodium sulphate. The term (c) indicates that crystallisation was effected by cooling of the solution, prepared at room temperature, in solid

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[9] Smith and Hac, *J. Amer. Chem. Soc.*, 1934, **56**, 477.

carbon dioxide-acetone. Absorption spectra were measured in dioxan in a Unicam S.P. 500 spectrophotometer. M. p.s are corrected.

4-*Methylveratrole*.—Veratraldehyde (183 g.), potassium hydroxide pellets (200 g.), 90—95% hydrazine hydrate (145 c.c.), and diethylene glycol (1·4 l.) were heated under reflux (3 l. flask) on a boiling-water bath with frequent shaking until all the hydroxide had dissolved (30 min.); the aldehyde hydrazone separated as a pale yellow solid. The temperature (liquid) was then gradually raised. Decomposition of the hydrazone, indicated by evolution of nitrogen and considerable frothing, commenced at 95°, and during the subsequent heating regular shaking was necessary in order to break the foam; at 125° the froth rapidly subsided. After being refluxed (135°) for 3 hr. the solution was cooled and added to cold water (2·5 l.), and the oil was extracted with light petroleum (b. p. 60—80°). The extract was washed with 5% hydrochloric acid, then water and dried, and the solvent was removed. Distillation of the residue gave 4-methylveratrole (160 g., 96%), b. p. 60°/0·2 mm., m. p. 22·5° (Karrer and Schick [3] gave m. p. 21—22°).

6-*Methylveratraldehyde*.—(*a*) A rapid stream of dry hydrogen chloride was passed into a stirred mixture of powdered zinc cyanide (200 g.), 4-methylveratrole (160 g.), and dry benzene (1 l.) cooled in ice. After 3 hr., benzene (500 c.c.) and then, during 20 min., anhydrous aluminium chloride (175 g.) were added, and a slower passage of hydrogen chloride was continued at 0° for 20 min. and then at 40—45° for 1 hr. The mixture was cooled and added to ice-cold 10% hydrochloric acid (2·5 l.), and the suspension was stirred and refluxed for 1½ hr. After cooling, the benzene phase was separated, washed successively with water, 10% aqueous sodium hydroxide, and water, and dried. Removal of the solvent and distillation of the residue gave the aldehyde, b. p. 110—111°/0·2 mm., needles (158 g., 84%) [from benzene-light petroleum (b. p. 60—80°)], m. p. 74° (lit.,[3,10] 75°, 76°).

(*b*) Freshly distilled phosphorus oxychloride (41 c.c.) was added during 30 min. to a stirred mixture of 4-methylveratrole (53·5 g.) and *NN*-dimethylformamide (30 g., b. p. 151—152°). After being heated on the water-bath for 7 hr., the solution was poured into cold water (500 c.c.), an excess of 10% aqueous sodium hydroxide was added, and the solid which separated was extracted with benzene, the extract being washed with 5% hydrochloric acid and water, and dried. Removal of the solvent, distillation, and crystallisation as under (*a*) gave the aldehyde (41 g., 65%), m. p. 72—73°.

4 : 5-*Dimethylveratrole* (I).—(*a*) 6-Methylveratraldehyde (160 g.) was reduced with potassium hydroxide pellets (160 g.), 90—95% hydrazine hydrate (120 c.c.), and diethylene glycol (1·2 l.) as described for 4-methylveratrole; decomposition of the hydrazone commenced at 110°, but the foam did not subside until the reflux temperature (140°) was reached. Refluxing was continued for 3½ hr. 4 : 5-Dimethylveratrole (146 g., 99%), obtained by distillation, had b. p. 60°/0·2 mm., m. p. 42·5°. Crystallisation (c) from light petroleum (b. p. 40—60°) gave needles, m. p. 43° (Karrer and Schick [3] give m. p. 43·5°).

(*b*) To methyl-lithium, from methyl iodide (15·5 c.c.) and lithium (4 g.), in ether (150 c.c.) stirred at 0° was added during 45 min. 4 : 5-dichloroveratrole [1] (20·7 g.) in ether (150 c.c.), and the resulting grey suspension was stirred at 0° for 1 hr., at 20° for 1 hr. and then refluxed for 3 hr. After cooling, the mixture was decomposed at 0° with water (100 c.c.) and acidified with 10% hydrochloric acid, and the ethereal phase was separated, washed with water, and dried. Removal of the solvent and distillation of the dark residue gave a colourless oil, b. p. 58—60°/0·2 mm., from which, by crystallisation (c) from light petroleum (b. p. 40—60°), 4 : 5-dimethylveratrole (11 g., 66%) was obtained as needles, m. p. 40—41°.

4 : 5-*Dimethylguaiacol and* 4 : 5-*Dimethylveratrole*-3-*carboxylic Acid* (II).—*n*-Butyl-lithium, from *n*-butyl bromide (32 c.c.) and lithium (4·7 g.), in ether (150 c.c.) was added during 1 hr. to a stirred solution of 4 : 5-dimethylveratrole (40 g.) in ether (250 c.c.) at 0°, and stirring was continued at 0° for 1 hr. and then at 20° for 5 hr. The grey suspension was added to solid carbon dioxide (300 g.) and ether (100 c.c.), the mixture was decomposed with water (250 c.c.) and basified with 10% aqueous sodium hydroxide and the phases were separated. The ether solution, after being washed with water and dried, afforded, by distillation and crystallisation (c) of the distillate from light petroleum (b. p. 40—60°), 4 : 5-dimethylveratrole (17·5 g., 44%), m. p. 42° The aqueous phase was acidified at 10—15° with concentrated hydrochloric acid and extracted with ether. The extract was washed with water and dried, the solvent was removed and the residue distilled to give : (1) an oil, b. p. 48—50°/0·2 mm.; (2) a sublimate (bath-temp. 100°/0·2 mm.); and (3) a yellow viscous oil, b. p. 136°/0·15 mm., which solidified. Fractions (1) and (2) were combined and stirred with an excess of 5% aqueous sodium hydrogen

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[10] Perkin and Weizmann, *J.*, 1906, **89**, 1649; Gattermann, *Annalen*, 1907, **357**, 370.

carbonate, and the solid (4·8 g., 13%) was collected and crystallised (c) from light petroleum (b. p. 40—60°) to give the *guaiacol* as blades, m. p. 68·5° (Found: C, 70·9; H, 7·7. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). With dimethyl sulphate in aqueous sodium hydroxide, this afforded 4 : 5-dimethylveratrole, m. p. and mixed m. p. 43°, and on demethylation with 48% hydrobromic acid gave 4 : 5-dimethylcatechol (87%), needles [from light petroleum (b. p. 80—100°)], m. p. 86—87° undepressed on admixture with dimethylcatechol prepared[3] directly from 4 : 5-dimethylveratrole. Fraction (3) was extracted with 5% aqueous sodium hydrogen carbonate, the extract was slowly acidified at 10—15° with 10% hydrochloric acid, and the solid was collected, washed with water, and dried *in vacuo*; it had m. p. 61—66°, but, on being rubbed, the melt solidified and then had m. p. 116—118°. The anhydrous acid was obtained by refluxing this hydrate with light petroleum (b. p. 100—120°) under an azeotropic water-separator. Recrystallised from light petroleum (b. p. 80—100°), 4 : *5-dimethylveratrole-3-carboxylic acid* (6·4 g., 13%) formed spikes, m. p. 120° (Found: C, 63·0; H, 6·6. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

3-*Amino*-4 : 5-*dimethylveratrole* (IV).—Sodium azide (1·6 g.) was added during 30 min. to a stirred mixture of 4 : 5-dimethylveratrole-3-carboxylic acid (4·2 g.), chloroform (50 c.c.), and concentrated sulphuric acid (40 c.c.) at 20—21°. After 30 minutes' further stirring at this temperature the mixture was added to ice (150 g.), the chloroform layer was removed, and the aqueous phase was basified, below 20°, with 40% aqueous sodium hydroxide. The solid, separated by benzene extraction, gave, on distillation, the *amine* (3·4 g., 94%), b. p. 90°/0·1 mm., which solidified (m. p. 75°) and, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded needles, m. p. 75·5° (Found: C, 66·3; H, 8·2; N, 7·8. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3; N, 7·7%). The β-*naphthol azo-derivative* formed red blades with a golden reflex (from butan-1-ol), m. p. 171° (Found: C, 71·3; H, 5·9; N, 8·5. $C_{20}H_{20}O_3N_2$ requires C, 71·4; H, 6·0; N, 8·3%).

Reaction of Metallated 4 : 5-*Dimethylveratrole with* cyclo*Hexanone*.—4 : 5-Dimethylveratrole (50 g.) in ether (200 c.c.) was metallated, as described above, with *n*-butyl-lithium, from *n*-butyl bromide (42 c.c.) and lithium (6·2 g.) in ether (200 c.c.), and to the suspension was added at 0° during 1 hr. *cyclo*hexanone (51 c.c.) in ether (100 c.c.). After being stirred at 0° for 3 hr. and at 20° for 12 hr., the mixture was decomposed at 0° with water (250 c.c.) and acidified with concentrated hydrochloric acid. The ethereal phase was separated, washed with 5% aqueous sodium hydroxide (acidification of the washings gave 11·8 g. of dimethylguaiacol), then with water, and dried. Removal of the solvent and distillation of the residue gave: (1) a fore-run of *cyclo*hexanone; (2) an oil, b. p. 56—60°/0·2 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded dimethylveratrole (22 g.); and (3) a yellow viscous oil (11·1 g.), b. p. 130—132°/0·15 mm., from which no crystalline material could be obtained. Redistillation of the last gave: (4) an oil (0·4 g.), b. p. up to 129°/0·2 mm., which was discarded, (5) a yellow viscous oil (9·3 g.), b. p. 129—135°/0·2 mm., and (6) a yellow residue, which on trituration with light petroleum (b. p. 40—60°) gave a solid (33 mg.). Recrystallised from light petroleum (b. p. 100—120°) this formed needles, m. p. 186° (Found: C, 78·3; H, 10·1%). Fraction (5) was dehydrated by refluxing, under an azeotropic water-separator, for 30 min. with toluene (80 c.c.) and anhydrous oxalic acid (2 g.). The mixture was cooled and filtered, the filtrate was washed with water and dried, and the solvent was removed. Distillation of the residue afforded a yellow oil (7 g.), b. p. 126—129°/0·2 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), gave a solid (3·9 g.); recrystallisation (c) from methanol afforded needles, m. p. 61·5° (Found: C, 77·5; H, 8·8%). On being refluxed for 6 hr. with 48% hydrobromic acid (25 c.c.), this compound (1 g.) yielded 4 : 5-dimethylcatechol (0·1 g.). The solvent was removed from the light petroleum mother-liquors, and the residue was dehydrogenated with chloranil (5 g.) in xylene (25 c.c.). After being refluxed for 8 hr., the solution was cooled and filtered from tetrachloroquinol, and the filtrate was washed with 10% aqueous sodium hydroxide, then water, and dried. Removal of the solvent and distillation gave a yellow oil, b. p. 106—134°/0·04 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded needles (60 mg.), m. p. 57·5—58·5° (Found: C, 78·4; H, 8·6%).

4 : 5-*Dimethylguaiacol* cyclo*Hexyl Ether*.—4 : 5-Dimethylguaiacol (6·1 g.) in ether (20 c.c.) and alcohol (20 c.c.) was added to a solution of sodium (1 g.) in ethanol (15 c.c.), the suspension was shaken for 20 min., and the sodium salt (5·5 g.) was collected, washed with ether, and dried *in vacuo*. A portion (1·8 g.), finely powdered, was stirred and refluxed for 150 hr. with *cyclo*hexyl bromide (1·5 c.c.) in dry xylene (50 c.c.), the suspension was cooled and filtered, and the filtrate was washed with 5% aqueous sodium hydroxide, then with water, and dried. Removal of the solvent and distillation gave a viscous oil, b. p. *ca.* 150°/0·03 mm., which, on crystallisation

(c) first from methanol and then from light petroleum (b. p. 40—60°), afforded the *ether* (0·35 g., 15%) as prisms, m. p. 33° (Found: C, 77·3; H, 9·3. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%).

3-*Iodo*-4 : 5-*dimethylveratrole*.—3-Amino-4 : 5-dimethylveratrole (0·72 g.) in concentrated hydrochloric acid (4 c.c.) and water (6 c.c.) was diazotised at 0° with 20% aqueous sodium nitrite, and to the orange solution was added potassium iodide (0·9 g.) in water (1 c.c.). After 1 hr. at 20° the mixture was heated on the water-bath until nitrogen evolution ceased and the *iodo-compound*, which separated as an oil, was worked up in the usual way. It had b. p. 90°/0·2 mm., and separated from methanol (c) as ill-defined crystals (0·7 g., 60%), m. p. 63·5° (Found: C, 41·4; H, 4·4; I, 43·4. $C_{10}H_{13}O_2I$ requires C, 41·1; H, 4·5; I, 43·5%).

3-*Chloro*-4 : 5-*dimethylveratrole*.—3-Amino-4 : 5-dimethylveratrole was diazotised as described for the preceding compound. Treatment of the solution with cuprous chloride and working up in the usual manner afforded the *chlorodimethylveratrole* (75%), b. p. 68°/0·15 mm., m. p. 21° (Found: C, 60·2; H, 6·7; Cl, 18·0. $C_{10}H_{13}O_2Cl$ requires C, 59·9; H, 6·5; Cl, 17·7%).

3-*Bromo*-4 : 5-*dimethylveratrole*.—(*a*) Diazotisation of 3-amino-4 : 5-dimethylveratrole (0·72 g.) in concentrated sulphuric acid (0·6 c.c.) and water (5 c.c.), treatment with cuprous bromide, and working up as usual gave the *bromodimethylveratrole*, b. p. 80°/0·2 mm., needles [from methanol (c)], m. p. 31° (Found: C, 49·2; H, 5·3; Br, 32·0. $C_{10}H_{13}O_2Br$ requires C, 49·0; H, 5·3; Br, 32·6%).

(*b*) Bromine (24 g.) in glacial acetic acid (150 c.c.) was added during 1¼ hr. to 4 : 5-dimethylveratrole (24·9 g.) in glacial acetic acid (150 c.c.) stirred at 10°. Stirring at 10° was continued for 45 min., and the solvent was then removed at 30—40°/20 mm. The residue, dissolved in light petroleum (b. p. 60—80°), was washed with 5% aqueous sodium hydroxide, with water, and dried, and the solvent was removed. Distillation of the residue gave an oil, b. p. 78—82°/0·15 mm., from which, by crystallisation (c) first from light petroleum (b. p. 40—60°) and then from methanol, the bromo-compound (24 g., 65%) was obtained as needles, m. p. 30·5° undepressed on admixture with material prepared by method (*a*) (Found: Br, 33·1%).

3 : 6-*Dibromo*-4 : 5-*dimethylveratrole*.—Bromine (16 g.) in glacial acetic acid (75 c.c.) was added during 30 min. to a stirred solution of 4 : 5-dimethylveratrole (8·3 g.) and iodine (0·2 g.) in glacial acetic acid (50 c.c.) at 20°. After being stirred at 20° for 5 hr. the mixture was worked up as described for the preceding compound, giving the *dibromodimethylveratrole* (10·7 g., 62%), b. p. 82—83°/0·03 mm., blades (from methanol), m. p. 79° (Found: C, 37·2; H, 3·6; Br, 48·9. $C_{10}H_{12}O_2Br_2$ requires C, 37·0; H, 3·7; Br, 49·4%).

Reaction of 3-*Bromo- and* 3 : 6-*Dibromo*-4 : 5-*dimethylveratrole with Phenyl-lithium*.—3-Bromo-4 : 5-dimethylveratrole (2·45 g.) in ether (20 c.c.) was added during 10 min. to a stirred solution of phenyl-lithium, from bromobenzene (2·3 g.) and lithium (0·2 g.), in ether (15 c.c.) stirred at 0°. After being stirred at 20° for 6 hr. the brown mixture was added to solid carbon dioxide (25 g.), water (50 c.c.) and 10% aqueous sodium hydroxide (20 c.c.) were added, and the phases were separated. The ethereal phase, after being washed with water and dried, afforded, by distillation, 4 : 5-dimethylveratrole (1·3 g., 78%), m. p. 41—42°. The aqueous phase was acidified with 10% hydrochloric acid, the liberated resin was taken up in ether, and the ethereal solution was extracted with 5% aqueous sodium hydrogen carbonate; acidification of this extract with 10% hydrochloric acid gave a resin, from which, by distillation and crystallisation of the distillate (b. p. *ca.* 180°/0·2 mm.) from light petroleum (b. p. 100—120°), a carboxylic acid (0·2 g.) was obtained as prisms, m. p. 168·5° (Found: C, 71·9; H, 6·3%).

When 3 : 6-dibromo-4 : 5-dimethylveratrole (3·24 g.) was similarly treated, with twice the quantity of phenyl-lithium, the products were: (1) a neutral compound which separated (c) from methanol as rhombic plates (30 mg.), m. p. 159—161° after sintering at 147° (Found: C, 87·6; H, 6·0%); (2) benzoic acid (0·5 g.); (3) 4 : 5-dimethylveratrole-3-carboxylic acid (0·25 g.), m. p. and mixed m. p. 119°; and (4) a carboxylic acid which crystallised from xylene as prisms (0·26 g.), m. p. 235—237° (Found: C, 59·6; H, 5·4%).

Reaction of 3-*Bromo- and* 3 : 6-*Dibromo*-4 : 5-*dimethylveratrole with Lithium*.—3-Bromo-4 : 5-dimethylveratrole (1·22 g.) in ether (10 c.c.) was refluxed with lithium wire (0·2 g.) for 3 hr., the suspension was cooled and filtered, and the filtrate was added to solid carbon dioxide (20 g.). The mixture was decomposed with water (25 c.c.), 10% aqueous sodium hydroxide (10 c.c.) was added, and the phases were separated and worked up as before, giving: (1) 4 : 5-dimethylveratrole (0·4 g., 48%), m. p. 41—42°; (2) 4 : 5-dimethylguaiacol (5 mg., 0·4%), m. p. 67—68°; and (3) 4 : 5-dimethylveratrole-3-carboxylic acid (35 mg., 3%), m. p. 118°.

Similar treatment of 3 : 6-dibromo-4 : 5-dimethylveratrole (1·62 g.) with lithium wire (0·4 g.) gave 3-bromo-4 : 5-dimethylveratrole (0·2 g., 17%), m. p. 29—30°; 0·3 g. (19%) of starting material was recovered.

In both cases, the lithium wire remained almost unchanged.

2 : 3-*Dimethoxy*-5 : 6-*dimethyldiphenyl* (V) *and* 2 : 3 : 2′ : 3′-*Tetramethoxy*-5 : 6 : 5′ : 6′-*tetramethyldiphenyl*.—3-Bromo-4 : 5-dimethylveratrole (1·22 g.) and iodobenzene (2·5 g.) were stirred together at 225° whilst activated [11] copper bronze (4 g.) was added during 10 min. The temperature was kept for 15 min. at 225°, raised during 10 min. to 280°, held for 20 min. at 280°, and finally raised during 5 min. to 350°. The cooled mixture was extracted with boiling light petroleum (b. p. 60—80°), the solvent was removed from the extract, and the residue was distilled giving: (1) a fore-run of iodobenzene; (2) an oil (0·85 g.), b. p. 70—72°/0·05 mm., which, crystallised from methanol, gave diphenyl; and (3) a yellow viscous oil (0·45 g.), b. p. 100—150°/0·05 mm., which largely solidified. This was triturated with cold light petroleum (3·5 c.c., b. p. 40—60°); the sparingly soluble solid (147 mg.) was collected [filtrate (A)] and crystallised from methanol, to give *tetramethoxytetramethyldiphenyl* as platelets, m. p. 133° (Found: C, 72·3; H, 7·7. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%). Light absorption: $\lambda_{max.}$ 284 mμ (log ε 3·65). The filtrate (A) was cooled to −75°, and the solid (65 mg.) was collected and crystallised (c) from light petroleum (b. p. 40—60°), to yield *dimethoxydimethyldiphenyl* as prisms, m. p. 64·5—65·5° (Found: C, 79·4; H, 7·4. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·4%). Light absorption: $\lambda_{max.}$ 284 mμ (log ε 3·36).

x-*Chloro*-y-*methyl*-2 : 3-*dimethoxydiphenyl*.—To methyl-lithium, from methyl iodide (2 g.) and lithium (0·2 g.), in ether (10 c.c.) stirred at 0° was added during 5 min. 5 : 6-dichloro-2 : 3-dimethoxydiphenyl [1] (1·42 g.) in ether (15 c.c.). The mixture was stirred at 0° for 1 hr., refluxed for 6 hr., and decomposed at 0° with water (20 c.c.), and the ethereal phase was separated, washed with water, and dried. Removal of the solvent and distillation of the residue gave an oil (1·1 g.), b. p. 109—110°/0·04 mm., which solidified and, on crystallisation from methanol, afforded the *diphenyl* as rhombic plates, m. p. 92·5° (Found: C, 68·6; H, 5·6; Cl, 13·4. $C_{15}H_{15}O_2Cl$ requires C, 68·6; H, 5·7; Cl, 13·5%). Light absorption: $\lambda_{max.}$ 288 mμ (log ε 3·36).

2 : 3-*Dihydroxy*-5 : 6-*dimethyldiphenyl*.—A mixture of 2 : 3-dimethoxy-5 : 6-dimethyldiphenyl (0·48 g.), powdered anhydrous aluminium chloride (1 g.), and dry chlorobenzene (10 c.c.) was refluxed for 3 hr., cooled, and added to 15% hydrochloric acid (40 c.c.). After being stirred vigorously for 30 min., the mixture was extracted with ether, the extract was washed with water and dried, and the solvent was removed. Trituration of the residue with a little cold light petroleum (b. p. 40—60°) and sublimation of the insoluble material at 145°/0·02 mm. gave a colourless solid (0·36 g., 85%) from which, by crystallisation from light petroleum (b. p. 80—100°), the *dihydroxydiphenyl* was obtained as needles, m. p. 171·5—172·5° (Found: C, 78·4; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). Light absorption: $\lambda_{max.}$ 291 mμ (log ε 3·46). Its *diacetate* formed rhombic plates, m. p. 111°, from aqueous ethanol (Found: C, 72·6; H, 6·0; Ac, 28·3. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0; Ac, 28·9%).

5 : 6-*Dimethyl*-2 : 3-*diphenoquinone* (VI).—(*a*) Silver oxide,[12] from silver nitrate (0·25 g.), and anhydrous sodium sulphate (0·5 g.) were suspended in ether (6 c.c.), and 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl (54 mg.) in ether (6 c.c.) was added. After being shaken at 20° for 20 min. the suspension was filtered and the red filtrate was cooled to −75°; the *quinone* (44 mg., 83%) separated as deep red plates with a golden reflex, m. p. 109—110° after sintering at 105° (Found: C, 78·9; H, 5·7. $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7%). Light absorption: $\lambda_{max.}$ 410 mμ (log ε 3·30).

(*b*) To a stirred solution of 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl (54 mg.) in ethanol-water (5 c.c. each) at 20° was added all at once sodium iodate hydrate (110 mg.) in water-ethanol (5 c.c., 2·5 c.c.). After 1½ hr. the solid was collected, washed with 50% aqueous ethanol, then water, and dried *in vacuo*. The orange-brown product (15 mg.), m. p. 104—106° after sintering at 100°, was spectroscopically almost identical with the quinone prepared by method (*a*). Light absorption $\lambda_{max.}$ 410 mμ (log ε 3·28).

One of us (J. M. B.) thanks the International Wool Secretariat for financial assistance.

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[*Received, May 22nd, 1956.*]

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