# **776.** *Biphenylenes. Part V.*[1] *Some Di- and Tetra-methoxybiphenylenes.*

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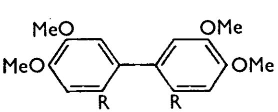
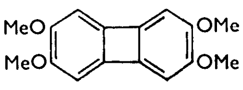
Convenient syntheses of 2,3,6,7-tetramethoxybiphenylene and 2,7-dimethoxy-1,3,6,8-tetramethylbiphenylene are described, together with an improved preparation of 2,7-dimethoxybiphenylene. The Ullmann reaction of 4-bromo-5-iodoveratrole has given, in addition to 2,2'-dibromo-4,5,4',5'-tetramethoxybiphenyl, 2,3,6,7-tetramethoxydibenzofuran and traces of 2,3,6,7-tetramethoxybiphenylene.

Certain polymethoxybiphenylenes may be readily obtained by the following general method. Suitably orientated methoxybiphenyls undergo direct iodination in positions 2- and 2'-, and the resulting di-iodobiphenyls are then converted into biphenylenes by heating them with cuprous oxide, as described in Parts I [2] and II [3] of this series.



(I)



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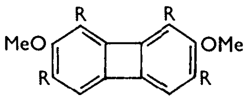
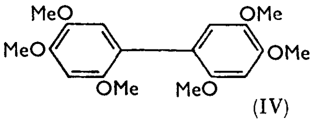


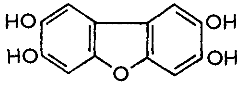
(III)

The synthesis of 2,3,6,7-tetramethoxybiphenylene (II) is a particularly favourable example. 3,4,3',4'-Tetramethoxybiphenyl (I; R = H), obtained from 4-iodoveratrole by an Ullmann reaction, gave with iodine and iodic acid a 67% yield of 2,2'-di-iodo-4,5,4',5'-tetramethoxybiphenyl (I; R = I) which when heated with cuprous oxide gave 2,3,6,7-tetramethoxybiphenylene (II).

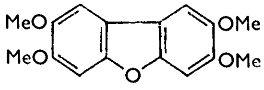
The method has been extended to the preparation of 2,7-dimethoxy- (III; R = H) and 2,7-dimethoxy-1,3,6,8-tetramethyl-biphenylene (III; R = Me). The starting material for the former, 3,3'-dimethoxybiphenyl, was obtained by deamination of the commercially available 3,3'-dimethoxybenzidine; that for the latter was obtained by reduction and methylation of 3,5,3',5'-tetramethyldiphenoquinone. Iodination of 3,3'-dimethoxybiphenyl gave not more than a 30% yield of 2,2'-di-iodo-5,5'-dimethoxybiphenyl; nevertheless, this series of reactions leading to 2,7-dimethoxybiphenylene is much more convenient than the lengthy synthesis described by Lothrop.[4] The iodination of 3,3'-dimethoxybiphenyl also yielded 9% of 4,4'-di-iodo-3,3'-dimethoxybiphenyl.



(IV)



(V)



(VI)

Attempts have been made to prepare 2,3,6,7-tetramethoxybiphenylene (II) directly from veratrole derivatives. Bromination of 4-iodoveratrole gave 4-bromo-5-iodoveratrole, identical with the product obtained from 4-amino-5-bromoveratrole by replacement of the amino-group with iodine. Attempts to produce compound (II) by dimerisation of a benzyne intermediate [5] were unsuccessful: *e.g.*, 4-bromo-5-iodoveratrole failed to react with magnesium under a variety of conditions. Reaction of 4-bromo-5-iodoveratrole

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[1] Part IV, Baker, McOmie, Preston, and Rogers, *J.*, 1960, 414.

[2] Baker, Boarland, and McOmie, *J.*, 1954, 1476.

[3] Baker, Barton, and McOmie, *J.*, 1958, 2658.

[4] Lothrop, *J. Amer. Chem. Soc.*, 1942, **64**, 1698.

[5] Heaney, Mann, and Millar, *J.*, 1957, 3930.

with copper bronze in nitrobenzene gave, in addition to the expected 2,2'-dibromo-4,5,4',5'-tetramethoxybiphenyl (I; R = Br), small amounts of 2,3,6,7-tetramethoxybiphenylene (II) and 2,3,6,7-tetramethoxydibenzofuran (VI). The only previous report of biphenylene formation in an Ullmann reaction using copper is by Ward and Pearson [6] who obtained small amounts of 2,3:6,7-dibenzobiphenylene by prolonged reaction of 2,3-dibromonaphthalene with copper bronze in dimethylformamide. In the present work, reaction of 4-bromo-5-iodoveratrole with copper bronze in dimethylformamide gave the biphenyl (I; R = Br) and starting material.

The formation of 2,3,6,7-tetramethoxydibenzofuran (VI) is somewhat surprising, it is probable that the hetero-ring oxygen is derived from the solvent. When the reaction time was increased no tetramethoxybiphenylene (II) could be isolated, but the amount of 2,3,6,7-tetramethoxydibenzofuran (VI) increased; very little of the biphenyl (I; R = Br) was then isolated. The structure of the dibenzofuran (VI) was confirmed by independent synthesis. The known 2,4,5,2',4',5'-hexamethoxybiphenyl (IV), prepared by the oxidative coupling of two molecules of 1,2,4-trimethoxybenzene,[7] undergoes demethylation with concomitant ring closure when boiled with aqueous hydrogen bromide. The resulting 2,3,6,7-tetrahydroxydibenzofuran (V) was methylated to give the ether (VI).

## EXPERIMENTAL

2,2'-*Di-iodo*-4,5,4',5'-*tetramethoxybiphenyl* (I; R = I).—Iodic acid (6 g.) in water (20 ml.) was added during 20 min. to a refluxing solution of 3,4,3',4'-tetramethoxybiphenyl [8] (20 g.) and iodine (16 g.) in acetic acid (400 ml.). After 2 hr. the solution was poured into water containing a little sodium hydrogen sulphite, and the solid was collected and dried. After chromatography on a short silica gel column in benzene, the 2,2'-*di-iodo*-4,5,4',5'-*tetramethoxybiphenyl* was obtained as microcrystals (26 g.), m. p. 183—183·5° after recrystallisation from benzene [Found: C, 36·6; H, 3·4; OMe, 23·45. $C_{12}H_4I_2(OMe)_4$ requires C, 36·5; H, 3·0; OMe, 23·6%].

2,3,6,7-*Tetramethoxybiphenylene* (II).—The above di-iodo-compound (2 g.) was powdered with cuprous oxide (20 g.) and heated at 330—360° ($\frac{1}{4}$ hr.), the method described previously [2,3] being used. Towards the end of the reaction the pressure was reduced to 50 mm. to facilitate volatilisation of the product. This was chromatographed in benzene on silica gel to give 2,3,6,7-*tetramethoxybiphenylene* as yellow plates (0·32 g., 31%), m. p. 211—212° from light petroleum (b. p. 60—80°) [Found: C, 70·8; H, 5·8; OMe, 45·6. $C_{12}H_4(OMe)_4$ requires C, 70·6; H, 5·8; OMe, 45·6%], $\lambda_{max.}$ (in EtOH) 248, 257, 393 mμ (log ε 4·79, 4·90, 4·26, respectively).

A similar experiment with 2,2'-dibromo-4,5,4',5'-tetramethoxybiphenyl gave the biphenylene (4%) and starting material (63%).

2,2'-*Di-iodo*-5,5'-*dimethoxybiphenyl*.—Iodic acid (1·7 g.) in water (4 ml.) was added dropwise to a stirred solution of 3,3'-dimethoxybiphenyl [9] (5 g.) and iodine (4·7 g.) in acetic acid (50 ml.) at 100°. The mixture was stirred at 100° for 2 hr., then poured into water containing sodium hydrogen sulphite. The product was chromatographed in benzene on silica gel. The eluate yielded material which was crystallised from light petroleum (b. p. 60—80°). The first fractions yielded 4,4'-di-iodo-3,3'-dimethoxybiphenyl, m. p. and mixed m. p. with authentic material [10] 184—186°; later fractions gave 2,2'-di-iodo-5,5'-dimethoxybiphenyl (3·3 g.), m. p. 141—141·5° [Found: C, 36·6; H, 2·9; OMe, 13·5. $C_{12}H_6I_2(OMe)_2$ requires C, 36·1; H, 2·6; OMe, 13·3%].

2,7-*Dimethoxybiphenylene* (III; R = H).—The above di-iodo-compound (1 g.) was heated with cuprous oxide (10 g.) as in the preparation of (II) above. The product, a yellow oil, was chromatographed in benzene on silica gel, giving 2,7-*dimethoxybiphenylene* (0·19 g., 42%), m. p. 106—108° and starting material (0·37 g.). Recrystallisation from n-pentane gave yellow plates, m. p. 107·5—109° (Lothrop [4] gives m. p. 107—108°), $\lambda_{max.}$ (in EtOH) 245, 254, 360 mμ (log ε 4·37, 4·92, 4·96, respectively).

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[6] Pearson, *Chem. and Ind.*, 1960, 899; Ward and Pearson, *J.*, 1961, 515.
[7] Erdtman, *Proc. Roy. Soc.*, 1934, *A*, **143**, 191.
[8] Ritchie, *J. Proc. Roy. Soc. New South Wales*, 1945, **78**, 134; *Chem. Abs.*, 1946, **40**, 876.
[9] Kornblum, *Org. Synth.*, 1941, **21**, 31.
[10] Pfeiffer, Schmitz, and Inoue, *J. prakt. Chem.*, 1929, **121**, 75.

*4,4′-Dihydroxy-3,5,3′,5′-tetramethylbiphenyl.*—3,5,3′,5′-Tetramethyldiphenoquinone [11] (20 g.) and sodium dithionite (40 g.) were ground together and added in portions to a mixture of ethanol (200 ml.) and water (100 ml.) at 80°. When reduction was complete (*ca.* 5 min.) the solution was cooled and diluted, and the white solid collected. The yield was quantitative; the material was methylated without further purification. A sample crystallised from methanol had m. p. 220—221° (lit.,[12] m. p. 220—221°).

*4,4′-Dimethoxy-3,5,3′,5′-tetramethylbiphenyl.*—Dimethyl sulphate (50 ml.) and 20% aqueous sodium hydroxide (30 ml.) were added in portions to a stirred solution of 4,4′-dihydroxy-3,5,3′,5′-tetramethylbiphenyl (40 g.) in ethanol (400 ml.) and 20% aqueous sodium hydroxide (10 ml.). The solution was stirred for a further ½ hr. and the solid collected (42 g.). *4,4′-Dimethoxy-3,5,3′,5′-tetramethylbiphenyl* separated from methanol in prisms, m. p. 99—99·5° [Found: C, 79·6; H, 8·1; OMe, 23·2. $C_{16}H_{16}(OMe)_2$ requires C, 80·0; H, 8·2; OMe, 22·9%].

*2,2′-Di-iodo-4,4′-dimethoxy-3,5,3′,5′-tetramethylbiphenyl.*—Iodic acid (4 g.) in water (3 ml.) was added during 10 min. to a stirred refluxing solution of 4,4′-dimethoxy-3,5,3′,5′-tetramethylbiphenyl (10 g.) and iodine (8 g.) in acetic acid (100 ml.). The solution was refluxed for 5 hr., cooled, and poured into water containing sodium hydrogen sulphite. The solid was collected (14·2 g.) and crystallised from ethanol, giving *2,2′-di-iodo-4,4′-dimethoxy-3,5,3′,5′-tetramethylbiphenyl* as prisms, m. p. 179·5—180° [Found: C, 41·6; H, 4·0; OMe, 11·2. $C_{16}H_{14}I_2(OMe)_2$ requires C, 41·4; H, 3·8; OMe, 11·9%].

*2,7-Dimethoxy-1,3,6,8-tetramethylbiphenylene* (III; R = Me).—The above di-iodo-compound (5 g.) was heated with cuprous oxide (50 g.) as in the preparation of (II) above. The condensates from four such experiments were chromatographed in benzene on silica gel (20 × 2 cm.) with benzene–light petroleum (b. p. 60—80°) as eluent, giving starting material (10·1 g.) and *2,7-dimethoxy-1,3,6,8-tetramethylbiphenylene* (1·43 g., 28%), m. p. 112—113°. Crystallisation from n-pentane gave pale yellow needles, m. p. 116—116·5° [Found: C, 80·7; H, 7·5; OMe, 23·6. $C_{16}H_{14}(OMe)_2$ requires C, 80·6; H, 7·5; OMe, 23·2%], $\lambda_{max.}$ (in EtOH) 253, 263, 337 (shoulder), 351, 372 mμ (log ε 4·67, 3·46, 3·79, 3·93, respectively).

*4-Bromo-5-iodoveratrole.*—(*a*) 4-Iodoveratrole (26 g.) in acetic acid (25 ml.) was stirred and treated with bromine (17 g.) in acetic acid (20 ml.) at <30°. After ½ hr. the mixture was stirred with water (300 ml.) and treated with sodium hydrogen sulphite. The solid *4-bromo-5-iodo*veratrole crystallised from aqueous ethanol as needles, m. p. 98—100° (33 g., 95%). Further crystallisation gave material of m. p. 102·5—104° [Found: C, 28·2; H, 2·45; OMe, 18·4. $C_6H_2BrI(OMe)_2$ requires C, 28·0; H, 2·3; OMe, 18·1%].

(*b*) 4-Acetamido-5-bromoveratrole [13] (2 g.) and hydrochloric acid (10 ml.) were refluxed for 5 min. The crystalline suspension was diluted with water (10 ml.), cooled, and diazotised at 3—5° with sodium nitrite (0·5 g.) in a little water. The resulting solution was added with stirring to potassium iodide (2 g.) in 10% sulphuric acid (10 ml.). After 1 hr. the mixture was warmed on the water bath and treated with sodium hydrogen sulphite. The tarry product was collected in methylene chloride and purified by crystallisation from aqueous ethanol and then from light petroleum (b. p. 60—80°) to give colourless needles, m. p. 96—98° (0·6 g., 24%). Further crystallisation gave 4-bromo-5-iodoveratrole, m. p. and mixed m. p. with a sample prepared by method (*a*) 102—104°.

*Ullmann Reaction of 4-Bromo-5-iodoveratrole.*—The halide (20 g.) in nitrobenzene (20 ml.) was stirred in a bath at 220—230° whilst copper bronze (20 g.) was added in portions (¼ hr.). After a further ¼ hr. the solution was cooled and filtered. The nitrobenzene was removed by steam distillation and the residue fractionated, to give starting material (5·1 g.), b. p. 100—115°/0·09 mm., and a viscous amber oil (3·8 g.), b. p. 170—190°/0·005 mm. The latter crystallised from light petroleum (b. p. 60—80°), giving *2,2′-dibromo-4,5,4′,5′-tetramethoxybiphenyl* (2·8 g., 30%) as colourless needles, m. p. 154—158°. The pure substance has m. p. 160—161° (Found: C, 43·9; H, 3·7. $C_{16}H_{16}Br_2O_4$ requires C, 44·4; H, 3·7%). The mother liquors gave material which was fractionally crystallised from ethanol and light petroleum (b. p. 60—80°), giving *2,3,6,7-tetramethoxydibenzofuran* (VI) (0·2 g.) as very pale yellow needles, m. p. 167—168° (Found: C, 67·0; H, 5·4. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%), $\lambda_{max.}$ (in EtOH) 224, 251, 326 mμ (log ε 4·57, 4·32, 4·52, respectively), and 2,3,6,7-tetramethoxybiphenylene (II), yellow plates, m. p. 208—210° (0·02 g.). The mixed m. p. of the latter with a sample of compound

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[11] Moore and Waters, *J.*, 1952, 2432.

[12] Auwers and von Markovits, *Ber.*, 1905, **38**, 226.

[13] Simonsen and Rau, *J.*, 1918, **113**, 782; Jones and Robinson, *J.*, 1917, **111**, 903.

(II) above showed no depression and the ultraviolet spectra were identical. This biphenylene was obtained in two out of five such experiments. When the reaction time was increased to 4 hr., 2,2′-dibromo-4,5,4′,5′-tetramethoxybiphenyl (0·4 g.) and 2,3,6,7-tetramethoxydibenzofuran (VI) (1·4 g.) were obtained.

*2,2′-Dibromo-4,5,4′,5′-tetramethoxybiphenyl* (I; R = Br).—Bromine (1·62 g.) in acetic acid (2·5 ml.) was added dropwise to a solution of 3,4,3′,4′-tetramethoxybiphenyl (1·37 g.) in acetic acid (10 ml.) kept below 25°. After several hours water (100 ml.) was added and the white solid collected (1·98 g.). Two crystallisations from benzene gave 2,2′-dibromo-4,5,4′,5′-tetramethoxybiphenyl as colourless needles, m. p. and mixed m. p. 157—159°.

*2,3,6,7-Tetramethoxydibenzofuran* (VI).—2,4,5,2′,4′,5′-Hexamethoxybiphenyl [7] (2 g.) was refluxed with 48% hydrobromic acid (20 ml.) for 3 hr. The grey solid was collected, washed, and suspended in dimethyl sulphate (10 ml.). 20% Sodium hydroxide solution (30 ml.) was added during 20 min. with rapid stirring. After refluxing for 1 hr. the solution was diluted and filtered. The solid dibenzofuran (1·5 g.), m. p. 161—164°, crystallised from light petroleum (b. p. 60—80°) as very pale yellow needles, m. p. and mixed m. p. 167—168°.

We thank the Department of Scientific and Industrial Research for the award of a Studentship to M. L. W.

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[*Received, April 4th,* 1961.]