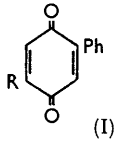
1013. *Thiele Acetylation of 2-Phenyl-1,4-benzoquinone and its 5-Methoxy-derivative.*

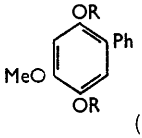
By J. M. Blatchly and J. F. W. McOmie.

The products from Thiele acetylation of 2-phenyl-1,4-benzoquinone and its 5-methoxy-derivative have been shown to be 2,4,5-triacetoxybiphenyl and 2,3,6-triacetoxy-4-methoxybiphenyl, respectively. Three other similar quinones did not undergo Thiele acetylation.

2-Phenyl-1,4-benzoquinone (I; R = H) undergoes Thiele acetylation by acetic anhydride and boron trifluoride, to give a triacetoxybiphenyl. The latter was converted by hydrolysis, oxidation, and then methylation into a methoxy-derivative of phenylbenzoquinone, but the orientation of the substituent was not determined.[1] We have repeated this work and have shown that the final product of this sequence of reactions is 5-methoxy-2-phenyl-1,4-benzoquinone (I; R = OMe). Hence Thiele acetylation of the original quinone had given 2,4,5-triacetoxybiphenyl. An authentic sample of the 5-methoxyquinone was made by the reduction of 4,5-dimethoxy-2-nitrobiphenyl [2] and oxidation of the resulting amine. The same quinone (I; R = OMe) was formed in low yield by addition of methanol to phenylbenzoquinone (I; R = H) in the presence of zinc chloride. Phenylation of 2-methoxy-1,4-benzoquinone with diazotised aniline did not, however, give the quinone (I; R = OMe) but an isomer thereof, which must therefore be the 3-methoxy- or the 6-methoxy-2-phenylquinone, although similar phenylation [3] of toluquinone yielded 5-methyl-2-phenyl-1,4-benzoquinone.



(I)



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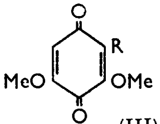
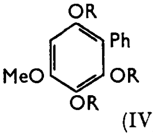


(III)



(IV)

Thiele acetylation of 5-methoxy-2-phenyl-1,4-benzoquinone (I; R = OMe) proceeded very slowly and gave the triacetate (IV; R = Ac). The orientation of this was demonstrated by hydrolysis and methylation, which gave the tetramethoxybiphenyl (IV; R = Me), identical with the product made by a crossed Ullmann synthesis between iodobenzene and 1-bromo-2,3,4,6-tetramethoxybenzene.

Oxidative demethylation of the tetramethoxybiphenyl (IV; R = Me) with nitric acid yielded 3,5-dimethoxy-2-phenyl-1,4-benzoquinone (III; R = Ph). Similarly, 1-bromo-2,3,4,6-tetramethoxybenzene gave the quinone (III; R = Br). These two quinones failed to undergo Thiele acetylation when treated with acetic anhydride and boron trifluoride at 30° for 50 and 24 hours, respectively. Under similar conditions 5-methoxy-2-*o*-methoxyphenyl-1,4-benzoquinone [4] was converted into a tar.

Experimental

5-*Methoxy*-2-*phenyl*-1,4-*benzoquinone* (I; R = OMe).—(*a*) A mixture of 5-hydroxy-2-phenyl-1,4-benzoquinone [1] (I; R = OH) (0·48 g.), methanol (5 ml.), and boron trifluoride–ether complex (3 drops) was kept at room temperature for 10 days. The orange-yellow quinone (0·4 g., 78%) separated as needles, m. p. 199—200° (lit.,[1] 199—200°).

(*b*) Stannous chloride dihydrate (4·8 g.) in concentrated hydrochloric acid (10 ml.) was added to a suspension of 4,5-dimethoxy-2-nitrobiphenyl [2] (1·8 g.) in warm ethanol (20 ml.). The mixture was boiled under reflux for 15 min.; then it was cooled and an excess of 10% aqueous sodium hydroxide was added. The 2-amino-4,5-dimethoxybiphenyl was collected in ether, and after removal of the solvent it was at once dissolved in concentrated hydrochloric

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[1] Fieser, *J. Amer. Chem. Soc.*, 1948, **70**, 3165.

[2] Blatchly, McOmie, and Watts, *J.*, 1962, 5085.

[3] Brassard and l'Écuyer, *Canad. J. Chem.*, 1959, **37**, 1505; Hoegerle and l'Écuyer, *ibid.*, 2068.

[4] Blatchly, McOmie, and Thatte, *J.*, 1962, 5090.

acid (0·6 ml.)–water (90 ml.). This solution was cooled to 6—9° and chromium trioxide (3·6 g.) in water (120 ml.) was added. The mixture was warmed to 60° to dissolve the precipitated green imino-chromate and then allowed to cool. Three hours later the quinone was collected by filtration, a further amount being obtained by extraction of the mixture with chloroform. The combined crops were recrystallised from methanol, giving the quinone (0·45 g., 30%), m. p. and mixed m. p. with the quinone made by Fieser's method [1] 199—200° (Found: C, 72·4; H, 4·75. Calc. for $C_{13}H_{10}O_3$: C, 72·9; H, 4·7%).

(*c*) 2-Phenyl-1,4-benzoquinone (2·0 g.) and anhydrous zinc chloride (3·0 g.) in methanol (15 ml.) were boiled under reflux for 6 hr. The deep-red mixture was allowed to cool and 2 days later the brown solid was collected. Recrystallisation from methanol (charcoal) gave the 5-methoxyquinone (0·05 g., 4·5%), m. p. and mixed m. p. 198—200°. When boron trifluoride–acetic acid complex was used in place of zinc chloride, a compound, m. p. 162—163°, was obtained in low yield. Its structure has not been elucidated.

Phenylation of 2-*Methoxy*-1,4-*benzoquinone*.—Sodium nitrite (1·75 g.) in water (5 ml.) was added to aniline (2·3 g.) in concentrated hydrochloric acid (6·2 ml.) below 5°. The solution obtained was added to a stirred suspension of 2-methoxy-1,4-benzoquinone (3·8 g.) in water (250 ml.) containing hydrated sodium acetate (10·2 g.), at a rate which kept the temperature below 30°. Stirring was continued for 5 hr. and the mixture was kept at room temperature until evolution of nitrogen ceased (2 days). The solid was collected and recrystallised several times from ethanol (charcoal) and then benzene–acetone, giving 3- or 6-*methoxy*-2-*phenyl*-1,4-*benzoquinone* as yellow plates (50 mg.), m. p. 194—195° (mixed m. p. with 5-methoxy-2-phenyl-1,4-benzoquinone, *ca.* 180°) (Found: C, 73·2; H, 4·9. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%).

2,5-*Diacetoxy*-4-*methoxybiphenyl* (II; R = Ac).—The 5-methoxyquinone (100 mg.), suspended in boiling methanol (5 ml.), was reduced by addition of sodium dithionite (85 mg.) in water (5 ml.). The colourless solution was diluted with water and the quinol was extracted with ether. After removal of the ether, the yellow oil was boiled with acetic anhydride (5 ml.) and sodium acetate (50 mg.) for 30 min. The mixture was cooled, then poured into water, and the solid was collected. Recrystallisation from methanol gave the *diacetate* (55 mg.) as needles, m. p. 138—139° (Found: C, 68·4; H, 5·5. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

2,4,5-*Trimethoxybiphenyl* (II; R = Me).—2,4,5-Triacetoxybiphenyl [1] (100 mg.) in methanol (1 ml.) and dimethyl sulphate (1 ml.) was treated dropwise with sodium hydroxide (0·84 g.) in water (1 ml.) during 20 min. Sodium dithionite (5 mg.) was added to prevent aerial oxidation. Thirty minutes later, water (5 ml.) was added and the white precipitate was collected by filtration. It was sublimed under reduced pressure, then recrystallised from light petroleum (b. p. 60—80°), giving the 2,4,5-*trimethoxybiphenyl* (33 mg.) as granular crystals, m. p. 88° (Found: C, 73·9; H, 6·9. $C_{15}H_{16}O_3$ requires C, 73·7; H, 6·6%).

2,3,6-*Triacetoxy*-4-*methoxybiphenyl* (IV; R = Ac).—Boron trifluoride in acetic acid (5 drops of 40% solution) was added to a solution of 5-methoxy-2-phenyl-1,4-benzoquinone (250 mg.) in acetic anhydride (50 ml.) at 40°. After having been kept at 40—50° for 150 hr., the mixture was diluted with water (200 ml.), and the precipitate was collected. It was extracted with cold methanol–water (9 : 1; 10 ml.), leaving unchanged quinone (165 mg.). Evaporation of the methanol solution gave the crude compound (115 mg.), m. p. 128—130°, which crystallised from ethanol, giving the pure *triacetate*, m. p. 134° (Found: C, 63·6; H, 4·6. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%).

2,3,4,6-*Tetramethoxybiphenyl* (IV; R = Me).—(*a*) 2,3,6-Triacetoxy-4-methoxybiphenyl (115 mg.) in methanol (1 ml.) and dimethyl sulphate (1·2 ml.) was treated dropwise with sodium hydroxide (1 g.) in water (1 ml.) during 20 min. After 30 min. more, the mixture was diluted with water and the solid was collected. It was sublimed under reduced pressure, then recrystallised from methanol, giving the tetramethoxybiphenyl (45 mg., 51%) as needles, m. p. 92°.

(*b*) 1-Bromo-2,3,4,6-tetramethoxybenzene (5·0 g.), iodobenzene (4·6 g.), and copper bronze (3·9 g.) were stirred together at 220—240° for 2 hr. The product was extracted with methanol and, after being treated with charcoal, the extract yielded 2,3,4,6-*tetramethoxybiphenyl* (0·8 g., 16%) as needles, m. p. 93° alone and 92—93° when mixed with the material from (*a*) (Found: C, 70·0; H, 6·9. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%).

1-*Bromo*-2,3,4,6-*tetramethoxybenzene*.—Bromine (7·8 g.) in acetic acid (20 ml.) was added gradually to a stirred solution of 1,2,3,5-tetramethoxybenzene [5] (9·9 g.) in acetic acid (25 ml.).

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[5] Baker, *J.*, 1941, 662.

The almost colourless solution was poured into water (600 ml.), and the bromo-compound was collected and recrystallised twice from methanol. The compound (6·5 g.) then had m. p. 72° (lit.,[6] 72—74°).

Reaction of 1-*Bromo*-2,3,4,6-*tetramethoxybenzene with Nitric Acid.*—35% Nitric acid (7 ml.) was added to a solution of 1-bromo-2,3,4,6-tetramethoxybenzene (2·2 g.) in ethanol (7 ml.) at 35°. After 10 min. at this temperature the mixture was cooled to 0° and the product (0·75 g.) was collected. Recrystallisation from methanol gave 2-bromo-3,5-dimethoxy-1,4-benzoquinone as orange-red needles, m. p. 148° (lit.,[7] 148°).

3,5-*Dimethoxy*-2-*phenyl*-1,4-*benzoquinone* (III; R = Ph).—2,3,4,6-Tetramethoxybiphenyl (350 mg.) and ethanol (1 ml.) were treated with 35% nitric acid (1 ml.) and warmed to 35° for 10 min. The solid rapidly dissolved, to give an orange solution which, on cooling, deposited the quinone, m. p. 110°. Recrystallisation from methanol–water (9 : 1) gave the *quinone* (220 mg., 70%) as red needles, m. p. 112° (Found: C, 68·8; H, 5·05. $C_{14}H_{12}O_4$ requires C, 68·9; H, 4·95%). The quinone did not undergo Thiele acetylation when treated with boron trifluoride and acetic anhydride at 30° for 50 hr.

2,5-*Diacetoxy*-4,6-*dimethoxybiphenyl.*—Reduction and acetylation of the above quinone in the same way as for the 5-methoxyquinone gave 2,5-*diacetoxy*-4,6-*dimethoxybiphenyl* as granular crystals, m. p. 98—99° (Found: C, 65·65; H, 5·6. $C_{18}H_{18}O_6$ requires C, 65·4; H, 5·5%).

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King's School, Bruton (J. M. B.).
The University, Bristol (J. F. W. McO.).

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[6] Bargellini and Madesani, *Gazzetta*, 1931, **61**, 684.
[7] Levine, *J. Amer. Chem. Soc.*, 1926, **48**, 797.