Thiele Acetylation of Quinones. Part III.[1] *p*-Benzoquinones with Bromo- and Methoxy-substituents

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The three monobromo-monomethoxy-*p*-benzoquinones have been prepared; they all undergo Thiele acetylation. The entering acetoxy-group is found *ortho* or *para* to the bromine atom in each of the triacetates, and never *ortho* to the methoxy-group.

Thiele acetylation of the three isomeric dibromo-monomethoxy-*p*-benzoquinones and the three monobromo-dimethoxy-*p*-benzoquinones has been studied. Of these six compounds the only two which undergo the reaction are 2,6-dibromo-3-methoxy- and 2-bromo-5,6-dimethoxy-*p*-benzoquinone.

EARLY studies by Erdtman [2] on Thiele acetylation reactions, catalysed by concentrated sulphuric acid, showed that 2-methoxy- and 2,3-dimethoxy-quinone † undergo the reaction to give 1,2,4-triacetoxy-5-methoxy- and 1,2,4-triacetoxy-5,6-dimethoxy-benzene respectively, whereas 2,5- and 2,6-dimethoxyquinone do not undergo the reaction. We have confirmed these results and also find that neither the latter two quinones nor 2,3,5-trimethoxyquinone undergo Thiele acetylation even in the presence of perchloric acid, which generally behaves as a much more powerful catalyst than sulphuric acid. The present paper describes the preparation and study of the Thiele acetylation of all the possible di- and tri-substituted quinones containing both bromo- and methoxy-groups.

The three isomers, (1), (2), and (3), of monobromo-monomethoxyquinone can be made by Dakin oxidation of the corresponding bromovanillin followed by oxidation with ferric chloride of the hydroquinones thus formed. The only previously known isomer, 2-bromo-5-methoxy-quinone (2), had been made [3] by oxidation of 1-bromo-2,4-dimethoxybenzene with peracetic acid, but it is conveniently made by the similar oxidation of 1-bromo-2,4,5-trimethoxybenzene. Although the product contains a small amount of 2,5-dimethoxyquinone, the latter is both insoluble and unreactive under Thiele acetylation conditions. Oxidative demethylation of 1-bromo-2,4,5-trimethoxybenzene with nitric acid in ethanol does not take place (*cf.* ref. 4), 2,4,5-trimethoxy-1-nitrobenzene being formed instead.

The bromo-methoxyquinones (1), (2), and (3) readily undergo Thiele acetylation with boron trifluoride as catalyst. The structure of the triacetate (4; R = Ac) obtained from quinone (1) was shown by hydrolysis and methylation, which gave the bromo-ether (4; R = Me). An attempted synthesis of this compound by bromination of 1,2,4,5-tetramethoxybenzene gave only the oxidation product, 2,5-dimethoxyquinone. However, further bromination of the bromo-ether (4; R = Me) gave 1,4-dibromo-2,3,5,6-tetramethoxybenzene, identical with the compound prepared by reduction and methylation of 2,5-dibromo-3,6-dimethoxyquinone. Further confirmation of the structure of compound (4; R = Me)

† Throughout this paper the name quinone refers to *p*-benzoquinone.

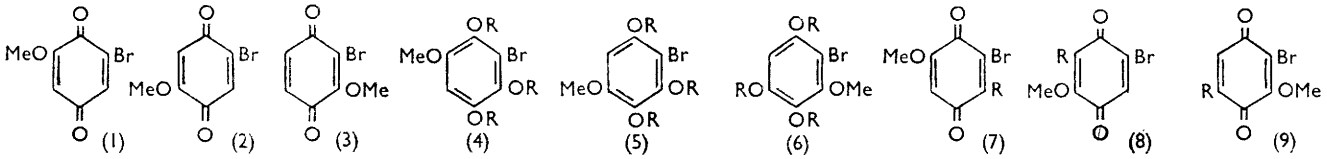
[1] Part II, J. M. Blatchly, J. F. W. McOmie, and J. B. Searle, preceding paper.

[2] H. Erdtman, *Proc. Roy. Soc.*, 1933, **143**, 177.

[3] H. Davidge, A. G. Davies, J. Kenyon, and R. F. Mason, *J. Chem. Soc.*, 1958, 4569.

[4] J. M. Blatchly and J. F. W. McOmie, *J. Chem. Soc.*, 1963, 5311.

was provided by its oxidation with nitric acid in ethanol, which gave 2-bromo-3,6-dimethoxyquinone (7; R = OMe). The latter compound had been made by Lindberg [5] but the experimental details for the last step in the synthesis were inadvertently omitted from the publication. We repeated the synthesis using details supplied by Lindberg and, with his permission, the missing details are given in the appendix to the Experimental section.



The orientations of the triacetates (5 and 6; R = Ac) from the quinones (2) and (3) respectively were proved to be as shown by catalytic reduction, when both triacetates yielded 2,3,5-triacetoxyanisole. Attempts to hydrolyse and methylate these two Thiele acetylation products failed in one case (5; R = Ac) and gave only a low yield of bromo-ether (6; R = Me) in the other (6; R = Ac). This is most probably due to rapid 1,4-elimination of hydrogen bromide in alkaline solution from the intermediates (5 and 6; R = H). Asp and Lindberg [6] have noted that 2-bromo-3,5-dimethoxyhydroquinone rapidly decomposes to 2,6-dimethoxyquinone. The expected elimination product in the present work, 2-hydroxy-6-methoxyquinone, is known to polymerise in alkaline solution.[7]

Since there is no reported instance of an acetoxy-group entering *ortho* to a methoxy-group during Thiele acetylation, only two of the three isomeric dibromomethoxyquinones, namely (8 and 9; R = Br) might be expected to give triacetoxybenzenes. We have found that quinone (8; R = Br) does indeed undergo Thiele acetylation, even with the mildest catalyst, boron trifluoride, whereas quinones (7 and 9; R = Br) both fail to undergo the reaction even with perchloric acid as catalyst.

The preparation and proof of structure of the three isomeric dibromo-1,2,4-trimethoxybenzenes were described in Part II.[1] Oxidative demethylation of two of the isomers [formulae (3) and (5) in Part II] with nitric acid in ethanol gave the quinones (7 and 8; R = Br) in 62 and 11% yields, respectively. Reaction of the third isomer, 3,6-dibromo-1,2,4-trimethoxybenzene, with nitric acid gave the 5-nitro-derivative, and the desired quinone (9; R = Br) was made in two steps from 2,5-dibromovanillin. We obtained quinone (7; R = Br) as a yellow solid, m.p. 187—189°, whereas when it was previously [8] prepared by the same method (and incorrectly thought to be 2,5-dibromo-3-methoxyquinone) it was described as red crystals, m.p. 172°. In order to prove that no migration of bromine had occurred during the oxidation, a number of experiments were carried out. The quinone (7; R = Br) was reduced by sulphur dioxide and the resulting hydroquinone was oxidised back to the quinone. The hydroquinone was also methylated to give 5,6-dibromo-1,2,4-trimethoxybenzene, from which it had been obtained by nitric acid oxidation as already mentioned. The structure of the hydroquinone was proved by showing that it could be obtained by addition of hydrogen bromide to both 2-bromo-5-methoxy- and 2-bromo-6-methoxy-quinone. In an attempt to prepare unambiguously a sample of 5,6-dibromo-1,2,4-trimethoxybenzene, methyl 2,3,6-trimethoxybenzoate was brominated, but the main product was 2,3,5-tribromo-6-hydroxyquinone instead of the desired dibromo-ester.

The dimethoxy-quinones (7 and 9; R = OMe) have previously been reported not to undergo Thiele acetylation catalysed by sulphuric acid.[5] Quinone (7; R = OMe) fails to undergo the reaction in presence of boron trifluoride [4] and we now report that perchloric acid is also ineffective as the catalyst.

The previously unknown isomer, 2-bromo-5,6-dimethoxyquinone, was prepared as follows. Bromination of 2,3,4-trimethoxyacetophenone by *N*-bromosuccinimide in acetic acid gave the 5-bromo-derivative. This, on oxidation with peracetic acid (Baeyer-Villiger reaction) gave 1-acetoxy-5-bromo-2,3,4-trimethoxybenzene. Hydrolysis of the latter followed by oxidation gave the desired quinone. Thiele acetylation of the quinone was sluggish; the yields of triacetate after 24 hr. at 45—50° were 6·5, 37, and 11·5% with boron trifluoride, concentrated sulphuric acid, and 72% perchloric acid respectively as catalysts.

The n.m.r. spectra of many of the compounds prepared are recorded in the Experimental section.

EXPERIMENTAL

2-Bromo-6-methoxyquinone (1).—Hydrogen peroxide (30%; 2·5 ml.) in water (20 ml.) was added to a solution of 5-bromovanillin [9] (3·1 g.) in 4% aqueous sodium hydroxide (20 ml.). After 15 min., concentrated hydrochloric acid (5 ml.) was added, followed by hydrated ferric chloride (4 g.) dissolved in a small volume of water. The precipitate was collected and recrystallised twice from methanol, giving the *quinone* (2 g., 69%) as yellow-orange needles, m.p. 161—162° (Found: C, 39·1; H, 2·3. $C_7H_5BrO_3$ requires C, 38·7; H, 2·3%).

[5] B. Lindberg, *Acta Chem. Scand.*, 1952, **6**, 1048, and personal communication.
[6] L. Asp and B. Lindberg, *Acta Chem. Scand.*, 1950, **4**, 1192.
[7] T. R. Seshadri, *Rev. Pure Appl. Chem.* (*Australia*), 1951, **1**, 192.
[8] H. W. Dorn, W. H. Warren, and J. L. Bullock, *J. Amer. Chem. Soc.*, 1939, **61**, 144.
[9] R. L. Shriner and P. McCutchan, *J. Amer. Chem. Soc.*, 1929, **51**, 2193.

1,4-*Diacetoxy*-2-*bromo*-6-*methoxybenzene*.— 5-Bromovanillin (3·1 g.) was oxidised as before and then more 4% aqueous sodium hydroxide (20 ml.) was added together with acetic anhydride (5 ml.) and the mixture was shaken for 10 min. The product was collected in ether and recrystallised from petroleum (b.p. 40—60°) to give the *diacetoxy-compound*, m.p. 80—81° (Found: C, 43·65; H, 3·7. $C_{11}H_{11}BrO_5$ requires C, 43·6; H, 3·7%).

Thiele Acetylation of 2-*Bromo*-6-*methoxyquinone*.—The quinone (1 g.) in acetic anhydride (15 ml.) and 40% boron trifluoride in acetic acid (0·5 ml.) were kept for 16 hr. at 35°. Dilution of the mixture with water (200 ml.) gave 1,2,4-*triacetoxy*-3-*bromo*-5-*methoxybenzene* (IV; R = Ac) which, after two recrystallisations from methanol, formed prisms (1·5 g., 90%), m.p. 140° (Found: C, 43·4; H, 3·8. $C_{13}H_{13}BrO_7$ requires C, 43·2; H, 3·6%).

The triacetoxy-compound (3·8 g.) in methanol (20 ml.) and dimethyl sulphate (20 ml.) was treated dropwise with potassium hydroxide (20 g.) in water (20 ml.). The mixture was then boiled for 5 min., and diluted with water (200 ml.). The precipitate gave 1-*bromo*-2,3,5,6-*tetramethoxybenzene* (IV; R = Me) (2·3 g., 78%) as needles, m.p. 67—68° (from aqueous methanol) (Found: C, 43·5; H, 4·8. $C_{10}H_{13}BrO_4$ requires C, 44·3; H, 4·7%).

Bromination of 1,2,4,5-*Tetramethoxybenzene*.—Bromine (0·65 g.) in chloroform (10 ml.) was added to the tetramethoxybenzene (0·8 g.) in the same solvent (10 ml.). Analysis of the yellow product (0·3 g.) showed that it was a mixture (*ca.* 4 : 1) of 2,5-dimethoxy- and 2-bromo-3,6-dimethoxy-quinone. The mixture was recrystallised from aqueous acetic acid (1 : 1) and gave 2,5-dimethoxyquinone as yellow crystals, m.p. 300° (decomp.) (lit.,[3] 300° decomp.).

1,4-*Dibromotetramethoxybenzene*.—(*a*) The foregoing bromotetramethoxybenzene (0·48 g.) in acetic acid (10 ml.) was treated with bromine (0·21 g.) and pyridine (5 drops). After 0·5 hr. at room temperature, orange needles (0·27 g.; m.p. 119—120°) separated. They had a faint bromine-like odour, and gave back starting material when recrystallisation from methanol was attempted. The analysis suggests a 2 : 1 molecular complex of the bromoether and bromine (Found: C, 34·7; H, 3·9. Calc. for $C_{10}H_{13}BrO_4,\frac{1}{2}Br_2$: C, 33·6; H, 3·6%). Subsequent attempts to prepare the complex failed, as in every case bromination occurred and long needles of the dibromoether eventually separated. After dilution of the mixture the solid was collected and recrystallised from methanol. The purified product (0·57 g., 92%) had m.p. 134—135°.

(*b*) Sodium dithionite was added to 2,5-dibromo-3,6-dimethoxyquinone (1·14 g.)[10] in 50% aqueous methanol (10 ml.) until a colourless solution was obtained; then dimethyl sulphate (5 ml.) and (dropwise) potassium hydroxide (5 g.) in water (5 ml.) were added. Dilution of the mixture and recrystallisation gave the dibromo-compound (0·9 g., 72%), m.p. 134—135°, alone and mixed with material from (*a*) (lit.,[11] 133°) (Found: C, 33·9; H, 3·6. Calc. for $C_{10}H_{12}Br_2O_4$: C, 33·7; H, 3·4%).

2-*Bromo*-3,6-*dimethoxyquinone* (7; R = OMe).—1-Bromo-2,3,5,6-tetramethoxybenzene (0·51 g.) was dissolved in ethanol (1·5 ml.) and 35% nitric acid (1·5 ml.) was added. After 10 min. at 35°, the mixture was cooled to 0°, and the precipitated quinone gave orange needles, m.p. 135° (from methanol), alone or mixed with an authentic specimen[5] (see appendix).

Reaction of 1-*Bromo*-2,4,5-*trimethoxybenzene with Nitric Acid*.—Nitric acid (35%; 7 ml.) was added to the bromo-compound (2 g.) dissolved in ethanol (7 ml.). The mixture was kept at 35° for 3 min. (no further reaction after 3 hr.) and the solid (0·92 g., 53%) which separated gave 2,4,5-trimethoxy-1-nitrobenzene as yellow needles, m.p. 126—127° (from ethanol) (lit.,[12] 128°) (Found: C, 50·6; H, 5·4. Calc. for $C_9H_{11}NO_5$: C, 50·7; H, 5·2%).

2-*Bromo*-5-*methoxyquinone* (2).—(*a*) 6-Bromovanillin[13] (7·1 g.) was treated in the same way as the 5-isomer and gave the quinone (1·7 g., 58%), m.p. 190—191° (lit.,[3] 190—191°).

(*b*) A solution of 1-bromo-2,4,5-trimethoxybenzene (8 g.) in 20% peracetic acid (40 ml.) containing concentrated sulphuric acid (0·4 g.) was kept at room temperature for 4 days. The bright yellow crystals (2·6 g.) which separated were used in Thiele acetylations without purification. During a Thiele reaction only 0·1 g. of 2,5-dimethoxybenzoquinone [m.p. 300° (decomp.)] remained unchanged and undissolved, so that the yield of the desired quinone (2) was 2·5 g. (36%).

Thiele Acetylation of 2-*Bromo*-5-*methoxyquinone*.—The quinone (1·7 g.) in acetic anhydride (20 ml.) and 40% boron trifluoride in acetic acid (0·5 ml.) were kept for 2 days at 45°. Dilution of the mixture with water and recrystallisation of the precipitated product from methanol gave 1,2,4-*triacetoxy*-3-*bromo*-6-*methoxybenzene* (0·93 g., 33%) as granules, m.p. 119—120° (Found: C, 43·15; H, 3·6. $C_{13}H_{13}BrO_7$ requires C, 43·2; H, 3·6%). Hydrolysis and attempted methylation of the triacetoxy-compound gave no isolable product.

Catalytic Reduction of 1,2,4-*Triacetoxy*-3-*bromo*-6-*methoxybenzene*.—The procedure was the same as that used for the 5-bromo-isomer (see later); the same amount of catalyst was used for 0·8 g. of the bromo-compound. The re-acetylated reduction product was contaminated with starting material, showing that more catalyst should have been used. Five recrystallisations of the product from ethanol gave crystals (0·36 g.), m.p. 86—90°. These were further purified by chromatography on silica gel with chloroform–benzene (1 : 9) as eluant, thereby giving 2,3,5-triacetoxyanisole (0·13 g.) (from ethanol), m.p. 89·5—90·5, mixed m.p. 90—91·5° with an authentic sample. Robinson and Vasey[14] gave the m.p. of 2,3,5-triacetoxyanisole as 105°, but the compound almost certainly exists in two polymorphic forms. After 6 months a sample of the anisole, made by reduction and acetylation of 2-hydroxy-6-methoxyquinone, melted partly at 91—92° and partly at 104—105°.

2-*Bromo*-3-*methoxyquinone* (3).—2-Bromovanillin[13] (3·1 g.) was oxidised in the same way as 5-bromovanillin. The crude product (2 g.) gave the *quinone* as orange blades, m.p. 98—99° [from petroleum (b.p. 60—80°)], which decomposed after a few days when kept exposed to light (Found: C, 39·0; H, 2·2. $C_7H_5BrO_2$ requires C, 38·7; H, 2·3%).

1,4-*Diacetoxy*-2-*bromo*-3-*methoxybenzene*.—The method was the same as that for the 6-methoxy-isomer. The *diacetoxybenzene* formed needles (from methanol), m.p. 75—

[10] O. Diels and R. Kassebart, *Annalen*, 1937, **530**, 51.
[11] G. B. Marini-Bettolo and F. S. Trucco, *Gazzetta*, 1943, **73**, 300.
[12] H. Gilman and J. R. Thirtle, *J. Amer. Chem. Soc.*, 1944, **66**, 858.
[13] L. C. Raiford and W. C. Stoesser, *J. Amer. Chem. Soc.*, 1927, **49**, 1077.
[14] R. Robinson and C. Vasey, *J. Chem. Soc.*, 1941, 660.

76° (Found: C, 43·65; H, 3·7. $C_{11}H_{11}BrO_5$ requires C, 43·6; H, 3·7%).

Thiele Acetylation of 2-Bromo-3-methoxyquinone.—The quinone (1·4 g.) in acetic anhydride (15 ml.) and 40% boron trifluoride in acetic acid (1 ml.) were kept for 8 hr. at 35°. The product, obtained on dilution of the mixture with water, was twice recrystallised from methanol and gave 1,2,4-*triacetoxy*-5-*bromo*-6-*methoxybenzene* (6; R = Ac) as granules (0·83 g., 36%), m.p. 115—116° (Found: C, 43·1; H, 3·6. $C_{13}H_{13}BrO_7$ requires C, 43·2; H, 3·6%).

The triacetoxy-compound (0·5 g.) was hydrolysed and methylated as for the 3-bromo-5-methoxy-isomer. The product (80 mg.), m.p. 69—70°, was shown to be 1-bromo-2,3,4,6-tetramethoxybenzene by mixed m.p. (69—70°) with an authentic sample (lit.,[4] 72°) and not 1-bromo-2,3,5,6-tetramethoxy benzene (m.p. 67—68°); mixed m.p. <50°.

Catalytic Reduction of 1,2,4-Triacetoxy-5-bromo-6-methoxybenzene.—Palladium chloride (0·071 g.) was added to ethanol and stirred at 30° overnight, then activated charcoal (1·0 g.) was added, and nitrogen (oxygen-free) was passed through the mixture. A solution of sodium borohydride (0·4 g.) in ethanol (10 ml.) was added, the mixture was stirred for 1 hr. and anhydrous sodium acetate (0·2 g.) and a solution of the triacetoxybenzene (0·25 g.) in ethanol (5 ml.) were added. The nitrogen was replaced by an atmosphere of hydrogen and the mixture was stirred for 24 hr. The hydrogen was then replaced by nitrogen, and acetic acid (5 ml.) was added. The catalyst was filtered off under nitrogen, and the filtrate was evaporated. Ether extraction gave a phenolic oil which was acetylated by acetic anhydride (3 ml.) containing a trace of perchloric acid thereby giving 2,3,5-triacetoxyanisole (0·14 g., 72%) as needles, m.p. 91·5—92°, mixed m.p. 91—93° (Found: C, 55·2; H, 4·9. Calc. for $C_{13}H_{14}O_7$: C, 55·3; H, 5·0%).

Thiele Acetylation of 2,6-Dibromo-3-methoxyquinone.—The quinone (see later) (25 mg.) in acetic anhydride (1 ml.) and 40% boron trifluoride in acetic acid (0·1 ml.) were kept for 32 hr. at 50°. Dilution with water and recrystallisation of the solid from ethanol gave 1,2,4-*triacetoxy*-3,5-*dibromo*-6-*methoxybenzene* (8 mg., 29%) as needles, m.p. 136—140° (Found: C, 35·1; H, 2·7. $C_{13}H_{12}Br_2O_7$ requires C, 35·5; H, 2·75%).

Attempted Thiele Acetylation of 2,5-Dibromo-3-methoxy- and 2,3-Dibromo-5-methoxy-quinone.—The 2,5-dibromo-isomer was recovered unchanged when boron trifluoride, concentrated sulphuric acid, or perchloric acid was used as catalyst in acetic anhydride at room temperature. With perchloric acid at 65° for 3 hr. or 130° for 5 hr. slow decomposition of the quinone occurred. The 2,3-dibromo-quinone was recovered in high yield with all three catalysts, *e.g.* with perchloric acid at 20° for 8 days or at 50° for 3 days, 76% of the quinone was recovered.

Action of Nitric Acid on 3,5-, 3,6-, and 5,6-Dibromo-1,2,4-trimethoxybenzene.—(*a*) Concentrated nitric acid (0·25 ml.; *d* 1·42) was added to 3,5-dibromo-1,2,4-trimethoxybenzene (0·1 g.). The solid dissolved with evolution of nitrogen dioxide. The mixture was heated to 60° for 1 min., cooled, and diluted with water. The resulting oil gave crystals of 2,6-*dibromo*-3-*methoxyquinone* (8; R = Br) (0·01 g., 11%) as red plates, m.p. 126—128·5° (from ethanol) (Found: C, 28·45; H, 1·3. $C_7H_4Br_2O_3$ requires C, 28·4; H, 1·4%).

(*b*) Similar treatment of the 3,6-dibromo-isomer (0·2 g.) yielded a solid which was sublimed at 50°/0·1 mm. to give 3,6-*dibromo*-1,2,4-*trimethoxy*-5-*nitrobenzene* (0·1 g., 44%) as an orange powder, m.p. 82—86° (Found: C, 29·05; H, 2·5; N, 3·8. $C_9H_9Br_2NO_5$ requires C, 29·1; H, 2·5; N, 3·8%).

The nitro-compound, m.p. 127°, obtained by Dorn *et al.*[8] and assumed to be 3,6-dibromo-1,2,4-trimethoxy-5-nitrobenzene, must in fact be 5,6-dibromo-1,2,4-trimethoxy-3-nitrobenzene, since the compound which it gives on reduction and deamination is now known to be 5,6-dibromo-1,2,4-trimethoxybenzene (*cf.* ref. 1).

(*c*) Similar treatment of the 5,6-dibromo-isomer (2·5 g.) gave 2,3-dibromo-5-methoxyquinone (7; R = Br) (1·4 g., 62%) as a yellow powder, m.p. 187—189° (lit.,[8] red crystals, m.p. 172°) (Found: C, 28·3; H, 1·3. Calc. for $C_7H_4BrO_3$: C, 28·4; H, 1·4%).

2,3-Dibromo-5-methoxyhydroquinone.—Sulphur dioxide was bubbled through a suspension of 2,3-dibromo-5-methoxyquinone (0·5 g.) in ethanol (10 ml.) and water (10 ml.). The initial black precipitate of the quinhydrone slowly redissolved to give a pale yellow solution. This was evaporated to dryness under reduced pressure and the residue was crystallised twice from aqueous ethanol to give the hydroquinone (0·25 g., 50%) as fluffy, yellow needles, m.p. 134—145° (decomp.) (the m.p. depends on rate of heating) [lit.,[8] m.p. 155° (decomp.)] (Found: C, 28·2; H, 2·0. Calc. for $C_7H_6Br_2O_3$: C, 28·2; H, 2·0%).

Treatment of the hydroquinone (0·6 g.) with dimethyl sulphate and alkali gave 5,6-dibromo-1,2,4-trimethoxybenzene (0·35 g., 53%), m.p. and mixed m.p. 99—100°. Oxidation of the hydroquinone (0·5 g.) by silver oxide (1 g.) in acetone (5 ml.) gave 2,3-dibromo-5-methoxyquinone (0·47 g., 95%), m.p. and mixed m.p. 189—190°.

Addition of Hydrogen Bromide to 2-Bromo-6-methoxy- and to 2-Bromo-5-methoxy-quinone.—(*a*) A mixture of 2-bromo-6-methoxyquinone (1 g.) in acetic acid (20 ml.) and 45% hydrogen bromide in acetic acid (1 ml.) was stirred at 20° for 5 min. The solution was filtered and diluted with water. The precipitate was recrystallised twice from water to give 2,3-dibromo-5-methoxyhydroquinone (0·85 g., 62%), m.p. 141—143° (decomp.) (Found: C, 28·3; H, 2·1. Calc. for $C_7H_6Br_2O_3$: C, 28·2; H, 2·0%). The i.r. spectrum was identical to that of the hydroquinone made in the preceding experiment.

(*b*) A mixture of 2-bromo-5-methoxyquinone (0·2 g.) in acetic acid (4 ml.) and 45% hydrogen bromide in acetic acid (0·25 ml.) was kept for 2 days. Addition of water gave a grey-black precipitate (0·9 g.) which was chromatographed on silica gel with benzene-petroleum (b.p. 60—80°) as eluant. Successive fractions contained 2,3-dibromo-5-methoxyquinone (0·4 g.), 2-bromo-5-methoxyquinone (0·045 g.), and finally (with benzene as eluant) 2,3-dibromo-5-methoxyhydroquinone (0·34 g.). These compounds were characterised by their i.r. spectra.

2,5-Dibromo-3-methoxyquinone (9; R = Br).—2,5-Dibromovanillin [15] (1·95 g.) in N-potassium hydroxide (15 ml.) and 3% hydrogen peroxide (20 ml.) was heated on a steam-bath for 10 min. with shaking. The solution was cooled and acidified with N-hydrochloric acid (1 ml.). The hydroquinone was collected in ether then dissolved in water (25 ml.) and oxidised with sodium dichromate (1·8 g.) in 2N-sulphuric acid (10 ml.). The product was collected in benzene and sublimed at 100°/0·1 mm. to give 2,5-*dibromo*-3-*methoxyquinone* (1·15 g., 62%) as orange plates, m.p. 119—120° (Found: C, 28·65; H, 1·4. $C_7H_4O_3Br$ requires C, 28·4; H, 1·5%).

2,3,5-Tribromo-6-hydroxyquinone.—Bromine (1·75 g.) in

[15] L. C. Raiford and W. C. Stoesser, *J. Amer. Chem. Soc.*, 1928, **50**, 2560.

acetic acid (10 ml.) was added to methyl 2,3,6-trimethoxybenzoate (1·92 g.) in acetic acid (25 ml.) and the mixture was kept at 50° for 8 hr. and then at 100° for 9 hr. The solution was then poured into an excess of aqueous sodium hydrogen carbonate and was extracted with ether. The extract (0·1 g.) was shown by t.l.c. to contain at least nine substances and was discarded. The aqueous solution was acidified and extracted with ether to give a solid (2·08 g.), which on sublimation at 120°/0·1 mm. gave 2,3,5-tribromo-6-hydroxyquinone (0·56 g., 18%) as a deep red powder, m.p. 204—206° (lit.,[16] 210°) (Found: C, 20·9; H, 0·4; Br, 66·2. Calc. for $C_6HBr_3O_3$: C, 20·0; H, 0·3; Br, 66·4%).

5-Bromo-2,3,4-trimethoxyacetophenone.—A mixture of 2,3,4-trimethoxyacetophenone [17] (21 g.) and *N*-bromosuccinimide (19 g.) in acetic acid (100 ml.) and acetic anhydride (5 ml.) was boiled under reflux for 1 hr. The cooled mixture was poured into water and the product was collected in ether. After being distilled at 112—115°/0·3 mm. the product solidified (m.p. 46—48°) and was then recrystallised from light petroleum to give the bromoacetophenone (15·75 g., 54·5%) as needles, m.p. 52·5—53° (Found: C, 45·7; H, 4·55. Calc. for $C_{11}H_{13}BrO_4$: C, 45·8; H, 4·5%).

The position of the bromine atom is shown by a comparison of the n.m.r spectrum of the bromo-compound with that of the unbrominated acetophenone; this shows that the nuclear hydrogen atom *meta* to the acetyl group has been replaced (see end of Experimental section). Mannich and Hahn [18] had previously brominated 2,3,4-trimethoxyacetophenone with bromine and sodium acetate in acetic acid but had not established the position of the bromine atom. We repeated the experiment and showed that the product was identical with 5-bromo-2,3,4-trimethoxyacetophenone, by mixed m.p. and by the identity of the i.r. and n.m.r. spectra of the two compounds.

2-Bromo-5,6-dimethoxyquinone (8; R = OMe).—The bromo-acetophenone just described (5·8 g.) in acetic acid (5 ml.) was added dropwise to a stirred solution of 36—40% peracetic acid (6·5 ml.) in acetic acid (1·1 ml.) containing anhydrous sodium acetate (0·12 g.). The mixture was stirred for 19 hr. at 42—45°, then a dilute solution of sodium hydrogen sulphite was added to reduce the excess of peracid. The whole mixture was then poured into water and the product was collected in ether. Removal of the ether left 1-acetoxy-5-bromo-2,3,4-trimethoxybenzene (5·7 g.) as an oil. This and potassium hydroxide (5 g.) in ethanol (3 ml.) and water (30 ml.) were boiled under reflux for 3 hr. The cooled mixture was acidified with dilute hydrochloric acid and the oily product (3·7 g.) was collected in ether. The crude material was dispersed in vigorously stirred hot water and oxidised by addition of sodium dichromate (3 g.) in 2N-sulphuric acid (20 ml.). After 1 hr., the cooled solution was extracted with ether; the extract, on evaporation, left a red oil. After two recrystallisations from petroleum (b.p. 30—40°) the *quinone* (1·2 g.) (24% overall yield) was obtained as orange crystals, m.p. 69—71° (Found: C, 39·3; H, 2·8. $C_8H_7BrO_4$ requires C, 38·9; H, 2·85%). The compound gradually decomposes on exposure to light [$\lambda_{max.}$ (ethanol) 208 and 289 mμ (log ε 4·01 and 3·85)].

Thiele Acetylation of 2-Bromo-5,6-dimethoxyquinone.—A mixture of the quinone (0·5 g.), acetic anhydride (8 ml.), and concentrated sulphuric acid (0·5 ml.) was kept at 45—50° for 24 hr. During the reaction the flask was wrapped in aluminium foil to protect the quinone from decomposition by light. The mixture was poured into water and the product was collected in ether. It was chromatographed in methylene chloride on a thick-layer silica gel plate. The orange oil was seeded with a crystal of pure triacetate which had been obtained in another experiment by distillation at 164—168°/0·5 mm. The solid was recrystallised twice from aqueous methanol and gave 1,2,4-*triacetoxy-3-bromo-5,6-dimethoxybenzene* (0·295 g., 37%), m.p. 74·5—75·5° (Found: C, 42·8; H, 3·85. $C_{14}H_{15}BrO_8$ requires C, 43·0; H, 3·9%), $\lambda_{max.}$ (ethanol) 216 and 270 mμ (log ε 4·00 and 2·69).

In similar experiments but on half the scale, and with 40% boron trifluoride in acetic acid (0·2 ml.) or 72% perchloric acid (0·3 ml.) in place of sulphuric acid as catalyst, the yields were 6·5 and 11·5% respectively.

Hydrolysis and methylation of the triacetate gave *1-bromo-2,3,4,5,6-pentamethoxybenzene*, m.p. 104·5—105·5° (from di-isopropyl ether) (Found: C, 43·4; H, 4·5. $C_{11}H_{15}BrO_5$ requires C, 43·0; H, 4·9%).

N.M.R. Spectra of Quinones.—(*a*) 2-Methoxy-: τ($CDCl_3$) 3·36 (H-5, H-6, unresolved dd), 4·12 (H-3, unresolved d), and 6·23 (OMe), $J_{5,6}$ <1·5 c./sec. (*b*) 2,3-Dimethoxy-: τ($CDCl_3$) 3·33 (H-5, H-6) and 5·92 (OMe). (*c*) 2,5-Dimethoxy-: τ($F_3C{\cdot}CO_2H$) 4·02 (H-3, H-6) and 6·10 (OMe). (*d*) 2,6-Dimethoxy-: τ($F_3C{\cdot}CO_2H$) 3·90 (H-3, H-5) and 6·08 (OMe). (*e*) 2,3,5-Trimethoxy-: τ($CDCl_3$) 4·37 (H-6) and 5·98, 6·12, and 6·25 (3 OMe). (*f*) 2-Bromo-3-methoxy-: τ($CDCl_3$) 3·32 (H-6, d), 3·48 (H-5, d), and 5·87 (OMe), $J_{5,6}$ 10·0 c./sec. (*g*) 2-Bromo-5-methoxy-: τ($CDCl_3$) 2·98 (H-3), 4·07 (H-6), and 6·25 (OMe), $J_{3,6}$ 0 c./sec. (*h*) 2-Bromo-6-methoxy-: τ($CDCl_3$) 3·02 (H-3), 4·03 (H-5), and 6·32 (OMe), $J_{3,5}$ 2·15 c./sec. (*i*) 2,3-Dibromo-5-methoxy-: τ($CDCl_3$) 4·00 (H-6) and 6·22 (OMe). (*j*) 2,5-Dibromo-3-methoxy-: τ($CDCl_3$) 2·71 (H-6), and 5·86 (OMe). (*k*) 2,6-Dibromo-3-methoxy-: τ($CDCl_3$) 3·03 (H-5) and 5·88 (OMe). (*l*) 2-Bromo-5,6-dimethoxy-: τ($CDCl_3$) 2·98 (H-3) and 6·02 and 6·08 (2 OMe).

N.M.R. Spectra of Other Compounds.—(*a*) 1,2,4-Triacetoxy-6-methoxybenzene: τ($CDCl_3$) 3·56 (H-3, H-5), 6·32 (OMe), 7·78 (OAc), and 7·82 (2 OAc). (*b*) 1,4-Diacetoxy-2,6-dimethoxybenzene: [19] τ($CDCl_3$) 3·79 (H-3, H-5), 6·30 (OMe), 7·76 (OAc), and 7·80 (OAc). (*c*) 1,4-Diacetoxy-3-bromo-2,6-dimethoxybenzene: [6] τ($CDCl_3$) 3·47 (H-5), 6·18 (OMe), 6·25 (OMe), and 7·6 (2 OAc). (*d*) 5-Bromovanillin: [9] τ($CF_3{\cdot}CO_2H$) 2·26 (H-6, d), 2·50 (H-2, d), and 5·95 (OMe), $J_{2,6}$ 1·9 c./sec. (*e*) 2-Nitrovanillin: [15] τ($CF_3{\cdot}CO_2H$) 2·18 (H-6, d), 2·67 (H-5, d), and 5·92 (OMe), $J_{5,6}$ 8·4 c./sec. (*f*) 1,2,4-Triacetoxy-3-bromo-5,6-dimethoxybenzene: τ($CDCl_3$) 6·18 and 6·21 (2 OMe) and 7·68, 7·72, and 7·74 (3 OAc). (*g*) 2,3,4-Trimethoxyacetophenone: τ($CDCl_3$) 2·53 (H-6, d), 3·37 (H-5, d), 6·10, 6·17, and 6·20 (3 OMe), and 7·46 (Ac), $J_{5,6}$ 9·0 c./sec. (*h*) 5-Bromo-2,3,4-trimethoxyacetophenone: τ($CDCl_3$) 2·39 (H-6), 6·10 (2 OMe), 6·15 (OMe), and 7·46 (Ac).

APPENDIX

2-Bromo-3,6-dimethoxyquinone (7; R = OMe) (B. Lindberg).—An excess of diazomethane in ether was added to a solution of 2-bromo-3,6-dihydroxyquinone in ether. After

[16] J. Thiele and K. Jaeger, *Ber.*, 1901, **34**, 2837.
[17] N. P. Zapevalova and M. M. Koton, *Zhur. obshchei Khim.*, 1959, **29**, 2900 (*Chem. Abs.*, 1960, **54**, 12,036).
[18] C. Mannich and F. L. Hahn, *Ber.*, 1911, **44**, 1551.
[19] F. Mauthner, *J. prakt. Chem.*, 1937, **147**, 287.

10 sec. the excess was destroyed by addition of acetic acid. The ethereal solution was washed with aqueous sodium hydrogen carbonate, dried ($CaCl_2$) and then concentrated to dryness. The residue gave the *quinone* as yellowish-red needles (75%), m.p. 134—135° (from ethanol) (Found: C, 38·9; H, 2·85. $C_8H_7BrO_4$ requires C, 38·9; H, 2·9%).

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