45. *The Bromination of* 1 : 5-*Dihydroxy- and* 1 : 5-*Diacetoxy-naphthalene,* 5-*Methoxy*-1-*naphthol, and* 1 : 5-*Dimethoxynaphthalene.*

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Dibromination of 1 : 5-dihydroxynaphthalene, 1 : 5-diacetoxynaphthalene, 5-methoxy-1-naphthol and 1 : 5-dimethoxynaphthalene has been studied, and the orientation of the products established by oxidation either to bromohydroxynaphthaquinones or to bromomethoxyphthalic anhydrides. Thus, 1 : 5-dihydroxynaphthalene yields 2 : 6-dibromo-1 : 5-dihydroxynaphthalene; 1 : 5-diacetoxynaphthalene yields 2 : 4-*dibromo*-5-*acetoxy*-1-*naphthol*; 5-methoxy-1-naphthol yields 2 : 8-*dibromo*-5-*methoxy*-1-*naphthol*; and 1 : 5-dimethoxynaphthalene yields 4 : 8-*dibromo*-1 : 5-*dimethoxynaphthalene*.

According to Wheeler and Ergle (*J. Amer. Chem. Soc.*, 1930, **52**, 4872), bromination of 1 : 5-dihydroxynaphthalene in cold glacial acetic acid gives a mixture of dibromo- and tribromo-1 : 5-dihydroxynaphthalene. The former was stated to be the 2 : 6-dibromo-derivative, since oxidation with chromic acid removed no bromine and resulted in the formation of a dibromohydroxynaphthaquinone which formed an ester with pyroboroacetic acid and was therefore a *p*-quinone. Further, this quinone condensed with aniline with elimination of one bromine atom and formation of 6-bromo-2-anilino-5-hydroxy-1 : 4-naphthaquinone. As well as confirming these results, we have obtained further proof that the bromine atoms are in different rings and in the *o*-positions with respect to the hydroxy-groups, as oxidation of the dibromodihydroxynaphthalene monomethyl ether (III) with chromic acid gave a *dibromomethoxy*-1 : 4-*naphthaquinone* (XIV). Hence, dibromination of 1 : 5-dihydroxynaphthalene in acetic acid yields 2 : 6-dibromo-1 : 5-dihydroxynaphthalene (I), m. p. 224° (decomp.). Methylation of (I) gave 2 : 6-dibromo-1 : 5-dimethoxynaphthalene (II), m. p. 160°, and 2 : 6-dibromo-5-methoxy-1-naphthol (III), m. p. 150°

By the bromination of 1 : 5-diacetoxynaphthalene in cold glacial acetic acid, Willstätter and Schuler (*Ber.*, 1928, **61**, 362) obtained a dibromo-monoacetyl-1 : 5-dihydroxynaphthalene, m. p. 165·5°, yielding on hydrolysis a dibromo-1 : 5-dihydroxynaphthalene, m. p. 147·5°, which, without submitting any evidence, they stated to be 4 : 8-dibromo-1 : 5-dihydroxynaphthalene. This method of brominating 1 : 5-diacetoxynaphthalene in our hands led to the isolation of a *dibromo-monoacetyl*-1 : 5-*dihydroxynaphthalene* (IV), m. p. 175°, converted by hydrolysis into a dibromo-1 : 5-dihydroxynaphthalene (VII), m. p. 153°. On oxidising (IV) with chromic acid, we obtained a *monobromo*-5-*acetoxy*-1 : 4-*naphthaquinone* (XV) owing to the elimination of a bromine atom in the *p*-position to the hydroxy-group. Methylation of (IV), followed by hydrolysis of the acetyl group, gave a *dibromo*-5-*methoxy*-1-*naphthol* (VI), which was converted by oxidation with alkaline permanganate into a *dibromomethoxyphthalic anhydride* (XIX), thus proving that both the bromine atoms are in the same ring in the naphthalene nucleus. Consequently, the orientation of the bromine atoms given by Willstätter and Schuler is incorrect, and the dibromo-1 : 5-dihydroxy-

naphthalene, m. p. 153°, is actually 2 : 4-dibromo-1 : 5-dihydroxynaphthalene (VII). Methylation of (VII) gave 2 : 4-*dibromo*-1 : 5-*dimethoxynaphthalene* (VIII), m. p. 88°.

Bromination of 5-methoxy-1-naphthol in carbon tetrachloride with 1 mol. of bromine gave a *monobromo-5-methoxy-1-naphthol* (IX), m. p. 95°, which, on further bromination with 1 mol. of bromine, yielded a dibromo-5-methoxy-1-naphthol (X), m. p. 130°. The latter was converted by oxidation with chromic acid into a *dibromo-5-methoxy*-1 : 4-*naphthaquinone* (XVII), and by oxidation with permanganate into a *monobromomethoxyphthalic anhydride* (XVIII). Both oxidations establish that the bromine atoms are in different rings of the naphthalene nucleus and, since compound (X) is not identical with 2 : 6-dibromo-5-methoxy-1-naphthol (III), it must be 2 : 8-*dibromo-5-methoxy-1-naphthol*, methylation of which gave 2 : 8-*dibromo*-1 : 5-*dimethoxynaphthalene* (XI), m. p. 84°.

Finally, from the bromination of 1 : 5-dimethoxynaphthalene in carbon tetrachloride with 2 mols. of bromine, a dibromo-1 : 5-dimethoxynaphthalene, m. p. 187°, was isolated. Since this compound is not identical with any of the three isomeric dibromo-1 : 5-dimethoxynaphthalenes (II), (VIII) and (XI), it is clearly 4 : 8-*dibromo*-1 : 5-*dimethoxynaphthalene* (XII).

Experimental.

2 : 6-*Dibromo*-1 : 5-*dihydroxynaphthalene* (I).—To a solution of 1 : 5-dihydroxynaphthalene (20 g.) in glacial acetic acid (700 c.c.) at 80°, a solution of bromine (39 g.) in glacial acetic acid (50 c.c.) was added during 30 mins. (Wheeler and Ergle, *loc. cit.*). On standing, pale green needles (29 g.; 73%) separated, which, when recrystallised from glacial acetic acid, formed colourless needles, m. p. 224° (decomp.) (Found : C, 37·9; H, 2·3; Br, 50·2. Calc. for $C_{10}H_6O_2Br_2$: C, 37·75; H, 1·9; Br, 50·3%). On acetylation with acetic anhydride in pyridine, the diacetate, which recrystallised from chloroform–ether in colourless needles, m. p. 225°, was obtained.

2 : 6-*Dibromo*-1 : 5-*dimethoxynaphthalene* (II).—The compound (I) (1 g.) was dissolved in sodium hydroxide solution (10 c.c., 2·5%) and warmed to 60°. Excess of methyl sulphate was added and, after shaking for 10 mins., the precipitate was collected and recrystallised three times from alcohol, forming colourless needles, m. p. 160°.

2 : 6-*Dibromo-5-methoxy-1-naphthol* (III).—When the alkaline filtrate from (II) above was acidified with hydrochloric acid, a white precipitate separated; recrystallised twice from alcohol, it formed colourless needles, m. p. 150°.

2 : 4-*Dibromo-5-acetoxy-1-naphthol* (IV).—Bromine (7 g.) in glacial acetic acid (12 c.c.) was added dropwise during 30 mins. to a solution of 1 : 5-diacetoxynaphthalene (5 g.) in cold glacial acetic acid (180 c.c.) (compare Willstätter and Schuler, *loc. cit.*). After 16 hrs., 2 : 4-*dibromo-5-acetoxy-1-naphthol* separated as a crystalline solid (3·8 g.; 48%), which was recrystallised from benzene, forming colourless prisms, m. p. 175° (Found : C, 40·5; H, 2·15; Br, 43·95. $C_{12}H_8O_3Br_2$ requires C, 40·0; H, 2·2; Br, 44·4%). Acetylation with acetic anhydride in pyridine gave 2 : 4-dibromo-1 : 5-diacetoxynaphthalene, which crystallised from alcohol in long, pale yellow needles, m. p. 131°, and which Willstätter and Schuler erroneously regarded as the 4 : 8-isomeride.

2 : 4-*Dibromo-5-acetoxy-1-methoxynaphthalene* (V).—To a solution of 2 : 4-dibromo-5-acetoxy-1-naphthol (3 g.) in methyl alcohol (20 c.c.) and ether (25 c.c.) cooled to — 15°, was added an ethereal solution of diazomethane, prepared by the interaction of potassium hydroxide solution (10 c.c., 50%) and nitrosomethylurea (5 g.). After 3 hrs., the evolution of nitrogen having ceased, the solution was concentrated to half volume; 2 : 4-*dibromo-5-acetoxy-1-methoxynaphthalene* separated as a crystalline solid (2 g.; 64%), which was recrystallised from carbon tetrachloride, forming colourless needles, m. p. 121° (Found : C, 41·6; H, 2·7. $C_{13}H_{10}O_3Br_2$ requires C, 41·7; H, 2·7%).

6 : 8-*Dibromo-5-methoxy-1-naphthol* (VI).—A suspension of compound (V) (0·9 g.) in aqueous sodium hydroxide (30 c.c., 10%) was refluxed for 2 hrs. until a clear solution was obtained. Water (200 c.c.) was added, and the solution acidified with hydrochloric acid. After 16 hrs., 6 : 8-*dibromo-5-methoxy-1-naphthol* separated as a colourless solid (0·7 g.; 92%), which was recrystallised from aqueous methyl alcohol, forming colourless needles, m. p. 112° (Found : C, 39·45; H, 2·55. $C_{11}H_8O_2Br_2$ requires C, 39·8; H, 2·4%).

2 : 4-*Dibromo*-1 : 5-*dihydroxynaphthalene* (VII).—2 : 4-Dibromo-5-acetoxy-1-naphthol (1 g.) was hydrolysed by dissolving it in aqueous sodium hydroxide (100 c.c., 0·4%) and leaving the deep brown solution overnight in a vacuum desiccator. Excess of hydrochloric acid was then added, and the precipitated 2 : 4-dibromo-1 : 5-dihydroxynaphthalene recrystallised from acetone; it formed colourless needles, m. p. 153°.

2 : 4-*Dibromo*-1 : 5-*dimethoxynaphthalene* (VIII).—An ethereal solution of diazomethane, prepared by the action of potassium hydroxide solution (12 c.c., 50%) on nitrosomethylurea (4 g.), was added to a well-cooled solution of compound (VII) (2 g.) in ether (50 c.c.). After 16 hrs., the solution was concentrated and allowed to cool. 2 : 4-*Dibromo*-1 : 5-*dimethoxynaphthalene* separated; after crystallising twice from methyl alcohol, it formed colourless needles, m. p. 88° (0·1 g.; 4·6%) (Found : C, 41·9; H, 2·8; Br, 45·65. $C_{12}H_{10}O_2Br_2$ requires C, 41·6; H, 2·9; Br, 46·25%).

2-*Bromo-5-methoxy-1-naphthol* (IX).—Bromine (4·6 g.) in carbon tetrachloride (10 c.c.) was added to a solution of 5-methoxy-1-naphthol (5 g.) in carbon tetrachloride (100 c.c.) at 70°. After 18 hrs., the colourless

solution was concentrated and allowed to cool. 2-*Bromo*-5-*methoxy*-1-*naphthol* separated in pale yellow crystals (2·4 g.; 33%), which, when recrystallised twice from ligroin, formed colourless needles, m. p. 95° (Found : C, 51·9; H, 3·6; Br, 31·3. $C_{11}H_9O_2Br$ requires C, 52·2; H, 3·55; Br, 31·6%).

2 : 8-*Dibromo*-5-*methoxy*-1-*naphthol* (X).—Bromine (18·2 g.) in carbon tetrachloride (20 c.c.) was added to a solution of 5-methoxy-1-naphthol (10 g.) in carbon tetrachloride (250 c.c.) at 70°. After 16 hrs., the solution was boiled (charcoal), concentrated to 100 c.c., and allowed to cool. 2 : 8-*Dibromo*-5-*methoxy*-1-*naphthol* separated in yellow prisms, m. p. 130° (10·8 g.; 57%) (Found : C, 40·9; H, 2·7; Br, 48·0. $C_{11}H_8O_2Br_2$ requires C, 39·8; H, 2·4; Br, 48·2%). Acetylation with acetic anhydride in boiling pyridine yielded 2 : 8-*dibromo*-1-*acetoxy*-5-*methoxynaphthalene*, colourless needles, m. p. 133° (Found : C, 41·45; H, 2·7. $C_{13}H_{10}O_3Br_2$ requires C, 41·7; H, 2·7%).

2 : 8-*Dibromo*-1 : 5-*dimethoxynaphthalene* (XI).—Methyl sulphate (2 g.) was added to a solution of compound (X) (1 g.) in aqueous sodium hydroxide (200 c.c., 0·125%) a few drops at a time, with shaking between the additions. The solution was warmed to 30° and shaken for 30 mins., and the dark coloured precipitate (1 g.; 96%) collected; after recrystallising three times from methyl alcohol, 2 : 8-*dibromo*-1 : 5-*dimethoxynaphthalene* was obtained in colourless needles, m. p. 84° (Found : C, 40·8; H, 3·2; Br, 46·6. $C_{12}H_{10}O_2Br_2$ requires C, 41·6; H, 2·9; Br, 46·25%).

4 : 8-*Dibromo*-1 : 5-*dimethoxynaphthalene* (XII).—Bromine (8·5 g.) in carbon tetrachloride (10 c.c.) was added during 15 mins. to a solution of 1 : 5-dimethoxynaphthalene (5 g.) in carbon tetrachloride (120 c.c.) at 70°. After refluxing for 30 mins., the solution was concentrated to 50 c.c. and allowed to cool. 4 : 8-*Dibromo*-1 : 5-*dimethoxynaphthalene* separated; after crystallising twice from carbon tetrachloride, it formed colourless leaflets, m. p. 187° (2 g.; 22%) (Found : Br, 46·3. $C_{12}H_{10}O_2Br_2$ requires Br, 46·25%).

2 : 6-*Dibromo*-5-*hydroxy*-1 : 4-*naphthaquinone* (XIII).—A solution of chromium trioxide (20 g.) in water (20 c.c.) was added to a suspension of 2 : 6-dibromo-1 : 5-dihydroxynaphthalene (10 g.) in cold glacial acetic acid (200 c.c.) (Wheeler and Ergle, *loc. cit.*). A vigorous reaction occurred and the temperature rose to 85°; after 10 mins., the solution was cooled. The brown crystalline solid which separated was recrystallised, first from alcohol and then from acetic acid; it formed dark red needles, m. p. 202° (1·3 g.; 12·5%) (Found : Br, 47·95. Calc. for $C_{10}H_4O_3Br_2$: Br, 48·2%).

6-*Bromo*-2-*anilino*-5-*hydroxy*-1 : 4-*naphthaquinone*.—Aniline (1·5 g.) was added to compound (XIII) (0·5 g.) in absolute alcohol (70 c.c.). After refluxing for 5 mins., the solution was allowed to cool; dark lustrous prisms (0·4 g.; 77%) then separated. These were twice recrystallised from alcohol, forming dark red prisms, m. p. 249° (Found : Br, 23·4. Calc. for $C_{16}H_{10}O_3NBr$: Br, 23·25%).

2 : 6-*Dibromo*-5-*methoxy*-1 : 4-*naphthaquinone* (XIV).—2 : 6-Dibromo-5-methoxy-1-naphthol (0·95 g.) was suspended in cold glacial acetic acid (10 c.c.), and a solution of chromium trioxide (2 g.) in water (6 c.c.) added. The mixture was stirred rapidly and warmed to 80°; a vigorous reaction occurred. The crystalline solid (0·4 g.; 40%) which separated on cooling, crystallised from alcohol in bright yellow needles, m. p. 177° (Found : Br, 45·8. $C_{11}H_6O_3Br_2$ requires Br, 46·25%).

2-*Bromo*-5-*acetoxy*-1 : 4-*naphthaquinone* (XV).—Chromium trioxide (5 g.), dissolved in water (10 c.c.), was added to a suspension of 2 : 4-dibromo-5-acetoxy-1-naphthol (5 g.) in cold glacial acetic acid (20 c.c.). The temperature rose to 40°; after the vigorous reaction had subsided, the solution was boiled and then allowed to cool. The deposited crystals (1·5 g.; 37%) were washed with ligroin and dried; 2-*bromo*-5-*acetoxy*-1 : 4-*naphthaquinone* crystallised from alcohol in bright yellow needles, m. p. 158° (Found : Br, 27·3. $C_{12}H_7O_4Br$ requires Br, 27·1%).

2-*Bromo*-5-*methoxy*-1 : 4-*naphthaquinone* (XVI).—A solution of chromium trioxide (5 g.) in water (10 c.c.) was added to a suspension of 2-bromo-5-methoxy-1-naphthol (2 g.) in cold glacial acetic acid (25 c.c.). After 10 mins., the solution was cooled and diluted with water and the crystalline 2-*bromo*-5-*methoxy*-1 : 4-*naphthaquinone* (0·9 g.; 43%) which separated was recrystallised twice from alcohol, forming bright yellow needles, m. p. 134° (Found : Br, 29·8. $C_{11}H_7O_3Br$ requires Br, 29·95%).

2 : 8-*Dibromo*-5-*methoxy*-1 : 4-*naphthaquinone* (XVII).—A suspension of 2 : 8-dibromo-5-methoxy-1-naphthol (3 g.) in cold glacial acetic acid (40 c.c.) was vigorously stirred, and a solution of chromium trioxide (6 g.) in water (12 c.c.) added rapidly. The temperature rose to 40°, the suspended solid dissolved, and in a few minutes dark coloured crystals (2 g.; 64%) separated. Recrystallisation from alcohol gave 2 : 8-*dibromo*-5-*methoxy*-1 : 4-*naphthaquinone* in dark reddish-brown needles, m. p. 199° (Found : C, 38·2; H, 1·8; Br, 45·8. $C_{11}H_6O_3Br_2$ requires C, 38·15; H, 1·75; Br, 46·25%).

Oxidation of 2 : 8-*Dibromo*-5-*methoxy*-1-*naphthol with Permanganate. Isolation of* 5-*Bromo*-6-*methoxyphthalic Anhydride* (XVIII).—A solution of 2 : 8-dibromo-5-methoxy-1-naphthol (40 g.) in aqueous sodium hydroxide (60 g. of sodium hydroxide in 1330 c.c. of water) was heated to the b. p. in 30 mins., during which time potassium permanganate (120 g.) was added in portions. After boiling for 15 mins., the residual permanganate was destroyed with sodium sulphite, and manganese dioxide filtered off and extracted with boiling water (1000 c.c.). Hydrogen peroxide (150 c.c., 100 vol.) was added to the united filtrate and extract, and the solution concentrated to 500 c.c. After cooling and acidification with hydrochloric acid, the product was extracted with ether (450 c.c.), the extract dried over sodium sulphate, and the solvent removed. The residual yellow oil set to a solid (14 g.) when left overnight in a vacuum desiccator. The solid was covered with ether (100 c.c.); the undissolved residue (6 g.), when recrystallised three times from glacial acetic acid, gave 5-*bromo*-6-*methoxyphthalic anhydride* (4 g.) in colourless needles, m. p. 212° (Found : C, 42·4; H, 2·1; Br, 31·3.

$C_9H_5O_4Br$ requires C, 42·0; H, 1·95; Br, 31·1%). It was insoluble in water, did not react with sodium bicarbonate solution, and gave the fluorescein test when fused with resorcinol.

5-Bromo-6-methoxyphthalanil.—A solution of aniline (0·2 g.) in acetic acid (5 c.c.) was added to a solution of 5-bromo-6-methoxyphthalic anhydride (0·5 g.) in boiling glacial acetic acid (10 c.c.), and the mixture refluxed for 5 mins. and allowed to cool. The *phthalanil*, when recrystallised twice from glacial acetic acid, formed colourless needles, m. p. 232° (0·5 g.; 77%) (Found: C, 54·5; H, 2·85; N, 4·8. $C_{15}H_{10}O_3NBr$ requires C, 54·2; H, 3·0; N, 4·2%).

Oxidation of 6 : 8-*Dibromo-5-methoxy-1-naphthol with Permanganate. Isolation of* 3 : 5-*Dibromo-6-methoxyphthalic Anhydride* (XIX).—A solution of 6 : 8-dibromo-5-methoxy-1-naphthol (21 g.) in aqueous sodium hydroxide (60 g. of sodium hydroxide in 800 c.c. of water) was oxidised with potassium permanganate (63 g.), the conditions and method of isolation of the product being similar to those in the case of compound (XVIII) above. The solid (15 g.) was covered with ether (50 c.c.); the undissolved residue, when recrystallised twice from ether, gave 3 : 5-*dibromo-6-methoxyphthalic anhydride* (2·8 g.) in long, colourless, prismatic needles, m. p. 140° (Found: C, 32·7; H, 1·55; Br, 47·85. $C_9H_4O_4Br_2$ requires C, 32·15; H, 1·2; Br, 47·6%), with similar properties to those of compound (XVIII).

3 : 5-*Dibromo-6-methoxyphthalanil* crystallised from glacial acetic acid in long colourless needles, m. p. 191° (Found: C, 43·8; H, 2·3; N, 3·8; Br, 38·65. $C_{15}H_9O_3NBr_2$ requires C, 43·8; H, 2·2; N, 3·4; Br, 38·9%).

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