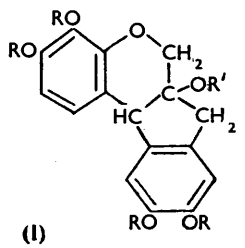
640. *Some Reactions of Hæmatoxylin.*

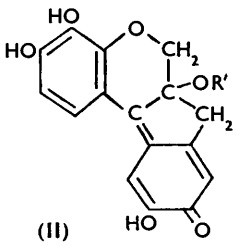
By D. J. Duff.

Hæmatoxylin has been halogenated and methylated by indirect methods, and the products have been converted into the corresponding hæmatein derivatives. Benzylidenehæmatoxylin, its sulphonic acid, and anhydrohæmatoxylone have been prepared.

Hæmatein (II; R′ = H), the colouring matter of logwood, is not present in the fresh wood, but is derived by oxidation of colourless hæmatoxylin (I; R = R′ = H).[1] Oxidising agents generally convert hæmatoxylin into hæmatein (*e.g.*, for a preparation of hæmatein in good yield by alkaline peroxide see Giles *et al.*[2]). Diazonium salts readily oxidise hæmatoxylin to hæmatein, with quantitative evolution of nitrogen; aromatic nitroso-compounds in boiling alcohol also oxidise it, no azine being formed. Halogen derivatives cannot be prepared directly, but are readily obtained by halogenation of penta-*O*-acetylhæmatoxylin (I; R = R′ = Ac) followed by hydrolysis; oxidation then yields the crystalline hæmatein derivatives.



(I)



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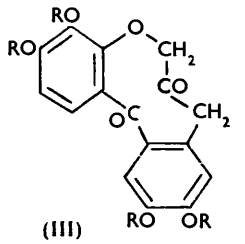

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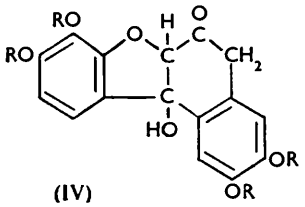

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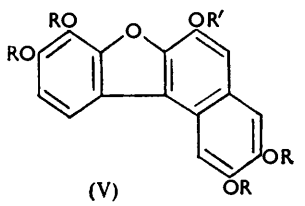

(V)

The four phenolic hydroxyl groups in hæmatoxylin are more readily alkylated than the alcoholic hydroxyl group. Thus tetra-*O*-benzylhæmatoxylin may be prepared. Methylation of this product, and removal of the benzyl residues by hydrogenation leads to the impure *O*-methylhæmatoxylin (I; R = H, R′ = Me).

Hæmatoxylin condenses readily with aldehydes; benzylidenehæmatoxylin and its sulphonic acid are described in the Experimental section.

Tetra-*O*-methylhæmatoxylin (I; R = Me, R′ = H) with chromic acid yields tetra-*O*-methylhæmatoxylone (III or IV; R = Me) (Gilbody and Perkin;[3] for a synthesis see Pfeiffer *et al.*[4]). Treatment of this with acetic anhydride, followed by hydrolysis, yields

[1] For structures see Perkin and Robinson, *J.*, 1908, **93**, 489.
[2] Arshid, Desai, Duff, Giles, Jain, and MacNeil, *J. Soc. Dyers and Colourists*, 1954, **70**, 397.
[3] Gilbody and Perkin, *Proc.*, 1899, **15**, 27.
[4] Pfeiffer, Angern, Haack, and Willems, *Ber.*, 1928, **61**, 839.

anhydrotetra-*O*-methylhæmatoxylone (V; R = Me, R′ = H), a derivative of β-naphthol.[5] Penta-*O*-acetylhæmatoxylin and chromic acid yield tetra-*O*-acetylhæmatoxylone (III or IV; R = Ac);[6] this also yields an anhydro-derivative, hydrolysed by alkali to the parent substance anhydrohæmatoxylone (V; R = R′ = H), which readily forms azo-dyes.

Experimental

Monobromohæmatein.—Penta-*O*-acetylbromohæmatoxylin[7] (5 g.) was warmed with alcohol (25 c.c.) and 40% aqueous sodium hydroxide (10 c.c.) until dissolved. An equal volume of water was added, then 10-vol. hydrogen peroxide (10 c.c.). After a few minutes the solution was acidified with hydrochloric acid; the red *bromohæmatein* precipitated was collected, dried, and recrystallized from aqueous alcohol, forming red leaflets (1·8 g.), which shrink with charring at *ca.* 300°, but do not melt below 360° (Found: C, 48·0; H, 3·6; Br, 19·4; loss at 100°, 5·9. $C_{16}H_{11}O_6Br,H_2O$ requires C, 48·4; H, 3·3; Br, 20·2; H_2O, 4·5%).

Dibromohæmatein.—Penta-*O*-acetylhæmatoxylin (25 g.) in glacial acetic acid was treated with bromine (5·5 c.c.), the temperature being allowed to rise. After 2 hr. the solution was diluted with alcohol and poured into dilute sulphurous acid. The precipitate was dried and recrystallised from alcohol, then from acetone with addition of alcohol and water, forming needles of impure penta-*O*-acetyldibromohæmatoxylin (5 g.), m. p. 232—234° (Found: Br, 25·5. Calc. for $C_{26}H_{22}O_{11}Br_2$: Br, 23·9%). Hydrolysis and oxidation yielded *dibromohæmatein* as red leaflets, which char at *ca.* 250° but do not melt below 360° (Found: C, 41·0; H, 2·9; Br, 33·0; loss at 100°, 4·2. $C_{16}H_{10}O_6Br_2,H_2O$ requires C, 40·4; H, 2·5; Br, 33·6; H_2O, 3·8%).

Chlorohæmatein.—A slow stream of chlorine was passed through a solution of penta-*O*-acetylhæmatoxylin (10 g.) in acetic acid. *Penta-O-acetylchlorohæmatoxylin* (8·5 g.) separated as needles, m. p. 194° (Found: Cl, 6·55. $C_{26}H_{23}O_{11}Cl$ requires Cl, 6·50%). The product (5 g.) was hydrolysed and oxidised to chlorohæmatein (2·2 g.), lustrous red leaflets (from aqueous acetone) which shrink at *ca.* 300° but do not melt below 360° (Found: C, 55·2; H, 3·9; Cl, 9·6; loss at 100°, 6·75. Calc. for $C_{16}H_{11}O_6Cl,H_2O$: C, 54·5; H, 3·7; Cl, 10·1; H_2O, 5·1%).

Chlorotetra-O-methylhæmatoxylin.—(*a*) Tetra-*O*-methylhæmatoxylin (10 g.) was chlorinated in acetic acid, and the *product* isolated by addition of dilute sulphurous acid and recrystallised from alcohol as needles, m. p. 149—150° (Found: C, 61·5; H, 5·6; Cl, 9·1. $C_{20}H_{21}O_6Cl$ requires C, 61·2; H, 5·9; Cl, 9·0%).

(*b*) Penta-*O*-acetylchlorohæmatoxylin (10 g.) was mixed with warm alcohol, and 40% w/w aqueous potassium hydroxide (20 c.c.) and dimethyl sulphate (15 c.c.) were added alternately in portions. When the reaction subsided, the product was isolated in the same way as product (*a*), forming needles, m. p. 166—168° (Found: C, 61·5; H, 5·7; Cl, 8·7%), apparently an *isomer* of product (*a*).

Hydrolysis and methylation of penta-*O*-acetylbromohæmatoxylin yielded bromotetra-*O*-methylhæmatoxylin, colourless needles, m. p. 187—188°, identical with the product prepared by Pfeiffer *et al.*[8] from tetra-*O*-methylhæmatoxylin.

Tetra-O-benzylhæmatoxylin.—Perkin, Pollard, and Robinson[6] reported the preparation of this product without details; they described it as amorphous, but giving a crystalline acetyl derivative, m. p. 112°. The following method gave good results. Hæmatoxylin (30 g.) and benzyl chloride (50 c.c.) in methanol (250 c.c.) were brought to the b. p. under reflux, while nitrogen was passed through the solution to agitate it and maintain an inert atmosphere. Sodium hydroxide (16 g.) in methanol (250 c.c.) was dropped in during about 3 hr. Refluxing was continued for 1 hr. more, then the solvent was distilled off. The oily residue was dissolved in ether and washed with dilute alkali, water, and dilute sulphurous acid. The ethereal layer was separated and evaporated and the residue was steam-distilled to remove benzyl chloride. The residual *ether* solidified under cold water. It was dried and crystallised from acetone as needles (29 g.), m. p. 120°, rising to 130—140° on repeated recrystallisation (Found: C, 80·0; H, 5·95. $C_{44}H_{38}O_6$ requires C, 79·8; H, 5·7%).

The product (29 g.) was methylated by refluxing in dry benzene (300 c.c.) with powdered sodium methoxide (4·5 g.) and methyl iodide (12 c.c.) for 3 hr. The solution was filtered, benzene distilled off, and the residue recrystallised from acetone, forming needles (25·5 g.), softening about 60°, m. p. 120° (decomp.), of *tetra-O-benzyl-O-methylhæmatoxylin* (Found: C, 80·0; H, 5·95. $C_{45}H_{40}O_6$ requires C, 79·9; H, 5·9%).

[5] Perkin and Robinson, *J.*, 1909, **95**, 381.
[6] Perkin, Pollard, and Robinson, *J.*, 1937, 49.
[7] Buchka, *Ber.*, 1884, **17**, 683.
[8] Pfeiffer, Doring, Kobs, and Werner, *J. prakt. Chem.*, 1938, **150**, 199.

O-Methylhæmatoxylin.—The last ether (4 g.) and palladium oxide (0·2 g.) in ethyl acetate (100 c.c.) absorbed 500 c.c. of hydrogen in 4 hr. at room temperature. Removal of solvent left a reddish amorphous powder which was not obtained crystalline (m. p. 75—82°) (Found: OMe, 7·75. Calc. for $C_{16}H_{11}O_6$·OMe: OMe, 9·8%).

Oxidation with alkaline peroxide yielded impure *O*-methylhæmatein, a dark reda morphous powder, with tinctorial properties very similar to those of hæmatein. The substance does not melt below 360° (Found: C, 64·0; H, 5·4; OMe, 7·6. Calc. for $C_{16}H_9O_6$·OMe: C, 64·8; H, 4·5; OMe, 9·85%).

Benzylidenehæmatoxylin.—Hæmatoxylin (6 g.), alcohol (25 c.c.), water (25 c.c.), hydrochloric acid (2 c.c.), and benzaldehyde (1 c.c.) were mixed and boiled under reflux for 1 hr. On cooling, benzylidenehæmatoxylin (3 g.) separated. It forms colourless prisms (from alcohol), becoming red at 240°, then black and apparently melting with decomposition at 270°. The analysis suggests that the substance is the *pentahydrate*; it is unchanged at 100° (Found: C, 59·5; H, 5·5. $C_{39}H_{32}O_{12}$,$5H_2O$ requires C, 59·9; H, 5·4%).

Sodium Benzylidenehæmotoxylinsulphonate.—Hæmatoxylin (3 g.), sodium *o*-formylbenzenesulphonate (1 g.), hydrochloric acid (2 c.c.), and water (20 c.c.) were refluxed for 1 hr. The oily *product*, after drying, crystallised from alcohol as red-tinted leaflets (0·9 g.) (Found: S, 3·9; Na, 2·7. $C_{39}H_{27}O_{15}SNa$ requires S, 4·05; Na, 2·9%).

Anhydrohæmatoxylone.—Penta-*O*-acetylhæmatoxylin is oxidised by chromic acid to tetra-acetylhæmatoxylone [6] (Found: C, 58·9; H, 4·2. Calc. for $C_{24}H_{20}O_{11}$: C, 59·5; H, 4·1%). Heating this with acetic anhydride and sodium acetate gave *penta-O-acetylanhydrohæmatoxylone*, needles, m. p. 258° (Found: C, 61·3; H, 4·0. $C_{26}H_{20}O_{11}$ requires C, 61·3, H, 3·9%), hydrolysed by aqueous-alcoholic alkali to *anhydrohæmatoxylone*, yellowish granules (from dioxan), darkening between 80° and 300°, but not melting below 360° (Found: C, 65·1; H, 3·4. $C_{16}H_{10}O_6$ requires C, 64·5; H, 3·4%).

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