140. *The Chemistry of Extractives from Hardwoods. Part XXXI.* 2-Acetyl-1,8-dihydroxy-3-methylnaphthalene (Musizin), a Constituent of* Maesopsis eminii.

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The heartwood of *Maesopsis eminii* contains a new phenolic compound (musizin) which can be extracted with light petroleum and has been identified as 2-acetyl-1,8-dihydroxy-3-methylnaphthalene.

Musizi is an African timber derived from the tree *Maesopsis eminii*. Although not classified as resistant, at least two well-defined phenolic compounds are present in the heartwood, a quantity of which was made available for our examination by Dr. R. H. Farmer, Forest Products Research Laboratory, Princes Risborough. The first of these (musizin) is present in the highly coloured product from extraction with boiling light petroleum. A second compound (maesopsin) can be obtained by further treatment of the wood with acetone, and will be described later. Both products appear to be concentrated in the outer heartwood zone, extraction of the inner heartwood giving no musizin and diminished yields of maesopsin.

Musizin has the molecular formula $C_{13}H_{12}O_3$. It is bright yellow and its solubility in aqueous bases and ferric chloride reaction indicate its phenolic nature. The formation of a diacetate, dibenzoate, and of a dimethyl ether with dimethyl sulphate show that there are two hydroxyl groups. Although musizin does not form carbonyl derivatives the remaining oxygen atom is part of a keto-group, since musizin dimethyl ether exhibits the infrared absorption peak at 1702 $cm.^{-1}$ of a conjugated aromatic carbonyl group. When fused with alkali musizin yields a dihydric phenol, $C_{11}H_{10}O_2$, characterised as diacetate and dibenzoate, which must therefore arise from the loss of an acetyl side-chain. The evidence is consistent with its formulation as a derivative of methylnaphthalene and confirmation was obtained by distillation of the product with zinc dust, whereupon 2-methylnaphthalene was isolated. The ultraviolet absorption of the C_{11} phenol resembles that of 1,8-dihydroxynaphthalene [1,2] and the assignment of the hydroxyl groups to the *peri*-position was endorsed by the ability of the phenol to increase the acidity of a boric acid solution,[2] the change in pH being comparable with that caused by the addition of 1,8-dihydroxynaphthalene (see Table).

Compound	pH of boric acid soln.	pH after addition	ΔpH	Compensated ΔpH
Ethanol (blank)	4·13	4·53	+0·40	—
β-Naphthol	4·11	4·50	+0·39	−0·01
Sorbitol	4·03	3·59	−0·44	−0·84
t-Butylcatechol	4·08	3·81	−0·27	−0·67
1,8-Dihydroxynaphthalene	3·96	2·02	−1·94	−2·34
Dihydroxymethylnaphthalene from alkali fusion	3·90	2·12	−1·78	−2·18

2 ml. of a 0·1M-ethanolic solution of each of the above compounds were added to 5 ml. of 0·5M-aqueous boric acid. The effect of the solvent is allowed for in the compensated ΔpH.

As with other 1,8-dihydroxynaphthalenes [2,3] reaction with diazomethane gave a monomethyl ether, and as this proved to be identical with a synthetic specimen of 1-hydroxy-8-methoxy-3-methylnaphthalene † the constitution of the product of zinc-dust distillation was thereby established as 1,8-dihydroxy-3-methylnaphthalene.

As a preliminary step in determining the position of the acetyl group, musizin was

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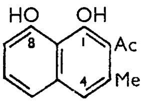
† Unpublished work by Dr. W. B. Whalley to whom the authors are indebted for a sample.

[1] Daglish, *J. Amer. Chem. Soc.*, 1950, **72**, 4859.

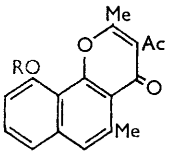
[2] Hochstein, Stephens, Conover, Regna, Pasternack, Gordon, Pilgrim, Brunings, and Woodward, *J. Amer. Chem. Soc.*, 1953, **75**, 5455.

[3] Böeseken and Smitt, *Rec. Trav. chim.*, 1939, **58**, 125.

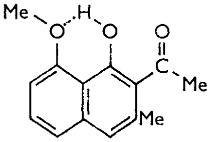
treated with alkaline hydrogen peroxide.[4] The sole isolable product was 3-hydroxyphthalic acid, whence the acetyl group is located in the ring bearing the *C*-methyl group, at either the 2- or 4-position. The marked chelation revealed by the occurrence of the carbonyl absorption peak at 1630 cm.$^{-1}$ strongly suggests that the acetyl substituent is at the 2-position adjacent to a hydroxyl group.[5] Furthermore musizin forms at low temperatures a complex with boroacetic anhydride which on decomposition with water gives a yellow monoacetate,[6] further acetylated to the diacetate. The monoacetate has the properties expected for an *o*-hydroxycarbonyl compound, gives a green colour with ferric chloride, and has infrared absorption bands at 1750 cm.$^{-1}$ (acetate carbonyl) and 1625 cm.$^{-1}$ (chelated nuclear acetyl). At higher temperatures boroacetic anhydride protects the two *peri*-hydroxyl groups and nuclear acetylation occurs. This is again apparent from the infrared absorption of the yellow crystalline product obtained on decomposition of the complex, which has bands at 1685 cm.$^{-1}$ (unchelated nuclear acetyl) and 1625 cm.$^{-1}$ (chelated nuclear acetyl), and from the formation of an *OO*-diacetate on further acetylation. Musizin is accordingly 2-acetyl-1,8-dihydroxy-3-methylnaphthalene (I).



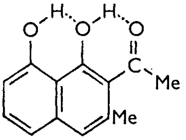
(I)



(II)



(III)



(IV)

Final proof that the acetyl side-chain is *ortho* with respect to the 1-hydroxyl group came from the preparation of the naphthopyrone (II; R = Ac) by the prolonged action of sodium acetate and acetic anhydride. Musizin is therefore a further example of the group of natural products based on 1,8-dihydroxy-3-methylnaphthalene, which include splumbagin,[7] 7-methyljuglone,[7] and diospyrol.[8] Treatment of musizin with diazomethane affords two isomeric monomethyl ethers, both of which give musizin on demethylation and musizin dimethyl ether when further methylated with methyl sulphate–potassium carbonate. However, neither product exhibits the ferric reaction nor the displacement of the infrared carbonyl absorption to 1630 cm.$^{-1}$ that would be expected for the 8-*O*-methyl isomer. In fact, the infrared carbonyl absorption of each compound (1686 and 1694 cm.$^{-1}$, respectively) is normal for an unchelated aromatic carbonyl group. The respective constitutions of the two ethers can be inferred from the action of sodium acetate and acetic anhydride. Under the conditions used to form a naphthopyrone with musizin, both compounds gave normal acetates, but at higher temperatures whereas 1-*O*-methylmusizin again yielded a normal acetate 8-*O*-methylmusizin was converted into the naphthopyrone (II; R = Me). The failure of 8-*O*-methylmusizin (III) to exhibit chelation can be attributed to hydrogen bonding between the 1-hydroxyl group and the 8-oxygen atom, an effect which may also be responsible for the characteristic monomethylation of 1,8-dihydroxynaphthalene derivatives with diazomethane. In musizin itself hydrogen bonding is possible between the two hydroxyl groups and also between the 1-hydroxyl and the acetyl substituent, as in (IV). It is noteworthy that in the methylation of musizin by diazomethane the 1-*O*-methyl isomer preponderates, which may in part be due to the activating effect of the carbonyl group.[9,10]

[4] Dieterle and Kruta, *Arch. Pharm.*, 1936, **274**, 457.

[5] Hunsberger, *J. Amer. Chem. Soc.*, 1950, **72**, 5626.

[6] Dimroth, *Annalen*, 1926, **446**, 97.

[7] R. H. Thomson, " Naturally Occurring Quinones," Butterworth's Scientific Publications, London, 1957, pp. 96, 97.

[8] Loder, Mongolsuk, Robertson, and Whalley, *J.*, 1957, 2233.

[9] Geissman and Hinreiner, *J. Amer. Chem. Soc.*, 1951, **73**, 782.

[10] Haber, Nikuni, Schmid, and Yagi, *Helv. Chim. Acta*, 1956, **39**, 1654.

EXPERIMENTAL

Unless otherwise stated melting points are uncorrected and light petroleum (b. p. 60—80°) was used; ether solutions were washed with water and dried over magnesium sulphate.

Musizin.—The comminuted heartwood (2·5 kg.) of *Maesopsis eminii* was extracted for 18 hr. with boiling light petroleum in a continuous-return apparatus. The solution obtained was evaporated to a red powder (16 g.) which was dissolved in ether (1600 ml.) and extracted with 5% aqueous sodium carbonate (500 ml.). The aqueous extracts on acidification deposited a bright yellow solid (6·4 g.) which crystallised from light petroleum in yellow needles of *musizin*, m. p. 164—165° (evac. tube) (Found: C, 72·1; H, 5·5. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%); $\lambda_{max.}$ in light petroleum, 219, 266, 402 mμ (log ε 4·17, 4·39, 3·68); infrared band in chloroform at 1630 cm.$^{-1}$ which was not displaced on dilution of the sample. Musizin was insoluble in aqueous sodium hydrogen carbonate, soluble in sodium carbonate, and gave a green colour with ferric chloride solution; its solution in hot methanol rapidly discoloured and on cooling dark brown crystals were obtained.

With boiling acetic anhydride and pyridine musizin afforded a *diacetate*, m. p. 189—190° (Found: C, 67·7; H, 5·3. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%) [$\lambda_{max.}$ in ethanol 225, 286, and 324 mμ (log ε 4·82, 3·80, 3·13)], obtained as prisms from ethanol or acetic acid, and with boiling benzoyl chloride–pyridine *a dibenzoate*, m. p. 187—188° (Found: C, 76·5; H, 4·9. $C_{27}H_{20}O_5$ requires C, 76·4; H, 4·8%), was obtained which crystallised from ethanol as fine needles.

Musizin Dimethyl Ether.—Musizin (2 g.) and dimethyl sulphate (6 ml.) in boiling acetone (150 ml.) were stirred with anhydrous potassium carbonate (20 g.) for 2 hr. The solution was then filtered, concentrated, and treated with concentrated ammonia and the product, precipitated with water, was collected in ether. Evaporation of the ether solution gave a brown syrup which was purified by filtering a benzene solution through alumina. The filtrate afforded a colourless syrup (1·65 g.) which crystallised from light petroleum as prisms of *musizin dimethyl ether*, m. p. 77—81° [Found: C, 73·5; H, 6·6; OMe, 24·4%; *M* (Rast), 289. $C_{15}H_{16}O_3$ requires C, 73·7; H, 6·6; OMe, 25·4%; *M*, 244]; infrared band in carbon tetrachloride at 1702 cm.$^{-1}$. Repeated crystallisation did not narrow the melting range.

The dimethyl ether (0·5 g.) was heated with pyridinium chloride (1·5 g.) for 30 min. at 200—210°.[11] The melt was digested with water; the precipitated solid when recrystallised from light petroleum gave musizin (0·28 g.), m. p. 162—163° (evac. tube).

Alkali Fusion of Musizin.—Musizin (2 g.), sodium hydroxide (3 g.), potassium hydroxide (3 g.), and water (6 ml.) were fused at 200—210° under a stream of nitrogen, and the melt was kept at this temperature for 15 min. Water was added to the cooled mixture, and the solution obtained was acidified, precipitating a brown solid which was collected in ether solution. Evaporation of the ether solution afforded a red solid which crystallised from water as feathery buff-coloured crystals (1 g.), m. p. 135—138°. Recrystallisation from light petroleum (b. p. 80—100°) gave almost colourless crystals of 1,8-*dihydroxy*-3-*methylnaphthalene*, m. p. 140—141° (Found: C, 75·5; H, 5·8. $C_{11}H_{10}O_2$ requires C, 75·8; H, 5·8%); $\lambda_{max.}$ in ethanol 231, 307, 322, 336 mμ (log ε 4·83, 3·87, 3·92, 4·01). 1,8-Dihydroxynaphthalene, prepared by alkali fusion of sodium 8-hydroxynaphthalene-1-sulphonate, had $\lambda_{max.}$ 227, 305, 320, 335 mμ (log ε 4·73, 3·83, 3·87, 3·96).

By the action of boiling acetic anhydride and pyridine a *diacetate*, m. p. 117—118° (Found: C, 69·9; H, 5·6. $C_{15}H_{14}O_4$ requires C, 69·7; H, 5·5%), was obtained which crystallised from light petroleum, and boiling benzoyl chloride and pyridine gave needles from ethanol of a *dibenzoate*, m. p. 192° (Found: C, 78·4; H, 4·8. $C_{25}H_{18}O_4$ requires C, 78·5; H, 4·7%).

Zinc-dust Distillation of 1,8-*Dihydroxy*-3-*methylnaphthalene.*—An intimate mixture of the dihydroxymethylnaphthalene (0·32 g.) and purified zinc dust (15 g.)[2] was put in a tube and covered with a further 15 g. of zinc dust. With a current of hydrogen passing through it, the tube was gradually heated to red heat. The distillate was purified by passing a solution in light petroleum through alumina. The evaporated eluate gave 2-methylnaphthalene (0·06 g.), m. p. 25—28° (picrate, m. p. 114—115° undepressed by an authentic sample of 2-methylnaphthalene picrate, m. p. 115—116°).

Methylation of 1,8-*Dihydroxy*-3-*methylnaphthalene.*—Excess of diazomethane in ether (30 ml.) was added to a solution of the dihydroxymethylnaphthalene (0·4 g.) in ether (20 ml.) which

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[11] Prey, *Ber.*, 1941, **74**, *B*, 1219.

was then kept at 0° for 1 hr. Evaporation of the solvent afforded an orange oil which was purified by chromatography in light petroleum on silica. First fractions yielded crystals (0·22 g.), m. p. 85—90°, which discoloured on exposure to the air. Recrystallisation from light petroleum gave needles of 1-*hydroxy*-8-*methoxy*-3-*methylnaphthalene*, m. p. 92—93° (Found: C, 76·5; H, 6·3. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). This compound did not depress the melting point of a synthetic sample, m. p. 91—93°, kindly supplied by Dr. W. B. Whalley.[12] The compound was insoluble in cold or hot aqueous sodium hydroxide but dissolved in aqueous ethanolic sodium hydroxide.

Oxidation of Musizin by Alkaline Hydrogen Peroxide.—Musizin (1 g.) was dissolved in aqueous sodium hydroxide (40 ml.; 2N), and hydrogen peroxide (20 ml.; 100 vol.) was added. After the initial reaction had subsided the mixture was heated at 100° for 30 min. The solution was acidified and extracted with ether, the extracts yielding a yellow syrup which was chromatographed in benzene–ether (20 : 1) on silica. Elution by benzene–ether (10 : 1) gave 3-hydroxyphthalic acid (0·21 g.), m. p. 168—169° (evac. tube) resolidifying and melting again at 200—201° (Found: C, 52·5; H, 3·3. Calc. for $C_8H_6O_5$: C, 52·7; H, 3·3%). 3-Hydroxyphthalic acid has recorded m. p. 166—167° and the anhydride m. p. 199—201°.[13]

Methylation of the 3-hydroxyphthalic acid isolated in this work and of a sample of crude dimethyl 3-hydroxyphthalate kindly supplied by Prof. A. W. Burgstahler [14] gave identical samples of dimethyl 3-methoxyphthalate, m. p. 75—76°.

Action of Boroacetic Anhydride on Musizin.—(*a*) *At* 45—50°.[6] Musizin (0·5 g.), boroacetic anhydride (0·5 g.), and acetic anhydride (3 ml.) were heated at 45—50° for 90 min. The mixture was kept at room temperature overnight and then hydrolyzed by pouring it into hot water. The precipitate was collected and leached with boiling light petroleum (b. p. 80—100°) leaving a red residue. The filtered petroleum solution, on cooling, gave yellow needles (0·11 g.) of 8-O-*acetylmusizin*, m. p. 128—129° (Found: C, 69·7; H, 5·4. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%). The compound gave a green colour with ferric chloride in methanol and displayed intense infrared bands in chloroform at 1750 and 1625 cm.$^{-1}$. A weak band at 1685 cm.$^{-1}$ was attributed to impurity. The red petroleum-insoluble residue, after hydrolysis by ethanol, afforded unchanged musizin.

Acetylation of the above monoacetate by boiling acetic anhydride and pyridine gave musizin diacetate, m. p. 182—185°, after two recrystallisations from ethanol; mixed m. p. with authentic sample 186—189°.

(*b*) *At* 100°. A mixture of musizin (0·5 g.) boroacetic anhydride (0·5 g.), and acetic anhydride (2·5 ml.) was heated to 100° during 45 min., and kept thereat for another 75 min. before being decomposed with boiling water. After the mixture had cooled, a greenish-yellow solid was filtered off and repeatedly extracted with boiling light petroleum (b. p. 80—100°). The concentrated extract, on cooling, afforded yellow plates (0·21 g.) of a C-*acetylmusizin*, m. p. 204—205° (Found: C, 69·3; H, 5·3. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%); infrared bands in chloroform at 1685 and 1625 cm.$^{-1}$. The compound gave a green colour with ferric chloride.

C-Acetylmusizin (0·10 g.) treated with boiling acetic anhydride and pyridine for 10 min. afforded a *diacetate* (0·09 g.), m. p. 168—169° (Found: C, 66·7; H, 5·2. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%), as blades from ethanol.

Naphthopyrone Derivative of Musizin.—Musizin (0·2 g.), fused sodium acetate (0·5 g.), and acetic anhydride (5 ml.) were boiled under reflux for 18 hr., and the mixture was then poured on crushed ice. The solid obtained was recrystallised from acetic acid and then ethanol to give cream-coloured needles of the *naphthopyrone derivative* (II; R = Ac), m. p. 198—199° (Found: C, 70·3; H, 5·2. $C_{19}H_{16}O_5$ requires C, 70·4; H, 5·0%); $\lambda_{max.}$ in ethanol 225, 251, 304, 339, 354 mμ (log ε 4·90, 4·93, 3·80, 3·64, 3·64). Under the above conditions 1,8-dihydroxynaphthalene gave its normal diacetate, m. p. 151—153°.

Musizin Monomethyl Ethers.—A solution of musizin (3 g.) in ether was treated with excess of diazomethane in ether at 0°, and the solution was allowed to warm to room temperature during 1 hr. before being evaporated to dryness. The red syrup obtained, which crystallised on cooling, was extracted with light petroleum (b. p. 40—60°) (3 × 60 ml.) leaving a colourless residue (0·52 g.). Evaporation of the combined petroleum extracts gave red crystals (2·65 g.)

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[12] W. B. Whalley, unpublished work.

[13] Miyasita, *J. Pharm. Soc. Japan*, 1940, **60**, 506.

[14] Eliel, Burgstahler, Rivard, and Haefele, *J. Amer. Chem. Soc.*, 1955, **77**, 5092.

which were purified by filtration first of an ether solution and then of a light-petroleum solution through alumina. The eluted solid was recrystallised from aqueous methanol to give needles of 1-O-*methylmusizin* (0·93 g.), m. p. 73—74° (Found: C, 72·7; H, 6·2; OMe, 12·9. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1; OMe, 13·5%); infrared bands in chloroform at 3360 and 1694 cm.$^{-1}$. The recrystallisation mother liquors yielded more monomethyl ether (0·66 g.), m. p. 65—70°. The solid, insoluble in light petroleum, was purified by chromatography of an ether solution on alumina and recrystallisation from aqueous methanol, giving needles of 8-O-*methylmusizin* (0·42 g.), m. p. 109—110° (Found: C, 72·8; H, 6·1; OMe, 13·3%); infrared bands in chloroform at 3360 and 1686 cm.$^{-1}$. Neither compound gave a colour with ferric chloride, but each dissolved in aqueous sodium hydroxide to give a yellow solution.

Demethylation and Methylation of the Monomethyl Ethers of Musizin.—8-*O*-Methylmusizin (0·2 g.) and pyridinium chloride (0·7 g.) were heated at 200—210° for 15 min. The dark green melt was digested with water, and the green precipitate recrystallised from light petroleum to give greenish-yellow needles of musizin (0·12 g.), m. p. 162—164°. Similar treatment of 1-*O*-methylmusizin also afforded musizin, m. p. 162—164°, in the same yield.

A mixture of 1-*O*-methylmusizin (0·11 g.), potassium carbonate (1 g.), acetone (10 ml.), and dimethyl sulphate (0·3 ml.) was boiled for 2 hr. The filtered solution was evaporated and treated with aqueous ammonia. The residual syrup, isolated with ether, was dissolved in benzene and filtered through a column of alumina. The eluted syrup crystallised from light petroleum in prisms of musizin dimethyl ether (0·09 g.), m. p. 76—78° undepressed by an authentic sample. Similar methylation of 8-*O*-methylmusizin also gave musizin dimethyl ether, m. p. 80—83°, in quantitative yield. The infrared spectrum of the product obtained was in each case identical with that of musizin dimethyl ether.

Acetates of the Monomethyl Ethers of Musizin.—1-*O*-Methylmusizin (0·2 g.), sodium acetate (0·5 g.), and acetic anhydride (7·5 ml.) were boiled under reflux for 18 hr. and then poured into water. The solid obtained was collected in ether and recrystallised from light petroleum, giving prisms of 8-O-*acetyl*-1-O-*methylmusizin* (0·14 g.), m. p. 97—98° (Found: C, 71·0; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). Under the same conditions 8-*O*-methylmusizin (0·2 g.) gave 1-O-*acetyl*-8-O-*methylmusizin* (0·15 g.) (from light petroleum), m. p. 110—111° depressed to 80—83° by starting compound (Found: C, 70·9; H, 5·9%).

8-*O*-Methylmusizin (0·11 g.), fused sodium acetate (0·25 g.), and acetic anhydride (2 ml.) were heated at 190° in a sealed tube for 5 hr. The mixture was then decomposed by water, and the product was extracted into ether. The evaporated solution gave a syrup which was dissolved in light petroleum. The filtered petroleum solution was evaporated and the partially crystalline mass crystallised from methanol, forming pale yellow needles of the *naphthopyrone* (II; R = Me) (0·016 g.), m. p. 172—174° (Found: C, 72·8; H, 5·3. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%); $\lambda_{max.}$ in ethanol 242, 317, 364 mμ (log ε 4·64, 3·80, 3·94), $\lambda_{infl.}$ 214—220, 234—238, 262—268, 352—355 mμ (log ε 4·44, 4·62, 4·40, 3·91). The mother liquors from the methanol recrystallisation were evaporated to a syrup which was leached with hot light petroleum. On cooling of the petroleum solutions, 1-*O*-acetyl-8-*O*-methylmusizin (0·023 g.), m. p. 105—107°, crystallised. Recrystallisation gave material, m. p. 110—111° undepressed by an authentic sample.

Treatment of 1-*O*-methylmusizin (0·20 g.) under these conditions gave only 8-*O*-acetyl-1-*O*-methylmusizin (0·134 g.), m. p. 93—96° (raised to 97—98° by recrystallisation).

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