20. *The Chemistry of Extractives from Hardwoods. Part VI.* Constituents of Muninga, the Heartwood of* Pterocarpus Angolensis, *A. : 6 : 4′-Dihydroxy-5 : 7-dimethoxy*iso*flavone (Muningin).*

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From alcoholic extracts of the heartwood of *Pterocarpus Angolensis* a new crystalline phenol, muningin, has been isolated. Through alkali fusion of the dimethyl ether, *p*-methoxyphenylacetic acid and 3 : 4 : 5-trimethoxyphenol are obtained, and the formation of *p*-ethoxyphenylacetic acid and of 4-ethoxy-3 : 5-dimethoxyphenol from the diethyl ether, with other confirmatory evidence, reveals the constitution of muningin to be 6 : 4′-dihydroxy-5 : 7-dimethoxy*iso*flavone.

Pterocarpus Angolensis is a tree of African origin which is the source of a hardwood known commercially as muninga. Only limited quantities have so far been exported but owing to its excellent general properties the timber has many potential applications in the building and furniture industries. As a wood of great natural durability it falls within the purview of our general investigations on the extractable components of resistant hardwoods and this paper gives an account of the isolation and identification of a phenolic constituent which we have termed muningin.

The genus *Pterocarpus* includes certain of the so-called insoluble redwoods, *e.g.*, red sandalwood (*P. santalinus*) and narrawood (*P. indicus*), which have already been extensively studied (see, for instance, McGookin, Robertson, and Whalley, *J.*, 1940, 787), but muninga and the very well-known commercial timbers Andaman padauk (*P. dalbergioides*) and Burma padauk (*P. macrocarpus*) have not hitherto been the subject of any chemical investigations. Unlike the padauks and the insoluble redwoods, however, muninga is not particularly conspicuous for its brilliant pigmentation, although the heartwood, which is golden- or light red-brown and streaked with lines of darker shade, is nevertheless remarkable for its handsome appearance.

The powdered timber was exhaustively extracted in succession with light petroleum, ether, boiling chloroform, and boiling ethanol. The chloroform and the alcoholic extracts afforded a pure colourless compound, m. p. 285° (decomp.), termed muningin, the total yield being 0·55% of the heartwood. Subsequently, it was found that muningin could be satisfactorily isolated with boiling ethanol, without previous treatment with other solvents, the brown-red brittle resin on crystallisation from dioxan giving 0·7% of the pure compound.

Analyses of the intensively dried specimens of muningin together with a molecular-weight determination indicated the formula $C_{17}H_{14}O_6$. Normally, the compound and its principal derivatives contain water of crystallisation in amounts corresponding to a minimum unit cell of $2M,H_2O$, a value confirmed in the case of muningin by *X*-ray crystallographic measurements for which we are indebted to Dr. S. C. Wallwork. Muningin possesses two methoxyl groups, and the formation of dimethyl and diethyl ethers, and of a diacetate and dibenzoate, denoted the hydroxylic function of two further oxygen atoms. From the appearance of a pink colour on acidifying an alcoholic solution of muningin previously reduced by sodium amalgam, a reaction which did not occur with magnesium and hydrochloric acid, the presence of a flavone or *iso*flavone nucleus was inferred and the formation of an easily hydrolysed salt when muningin was added to concentrated hydrobromic acid gave further support to this view.

The isolation of picric acid from the vigorous reaction of concentrated nitric acid with muningin, and of a mixture of dinitroanisole and 4-methoxy-3-nitrobenzoic acid from the action of this reagent on dimethylmuningin, indicated the existence of a *p*-substituted hydroxyphenyl group. No other recognisable compound was obtained from these degradations, and the easy destruction of the larger part of the molecule was again observed when a permanganate oxidation of dimethylmuningin gave *p*-anisic acid as the sole isolable product.

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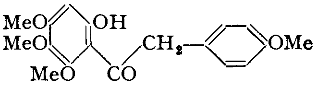
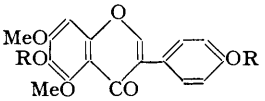
* Part V, preceding paper.

Neither muningin nor dimethylmuningin showed carboxylic reactions, but on mild alkaline hydrolysis of the methyl ether formic acid was liberated, and the resulting crystalline product readily formed a semicarbazone. These results clearly established the *iso*flavone character of muningin and, when, as a result of a sodium hydroxide fusion of dimethylmuningin, *p*-methoxyphenylacetic acid and antiarol (3 : 4 : 5-trimethoxyphenol) were obtained, it was evident that the primary product of hydrolysis consisted of 2-hydroxy-4 : 5 : 6-trimethoxyphenyl 4-methoxybenzyl ketone (I), and that dimethylmuningin was therefore the 5 : 6 : 7 : 4′-tetramethoxy*iso*flavone (II; R = Me). A resynthesis of the latter from the ketone (I), ethyl formate, and sodium confirmed this interpretation.

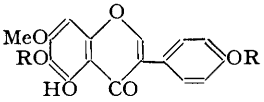
(I)

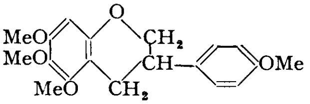




(II)

(III)





(IV)

Only the relative distribution of the hydroxy- and methoxy-groups at the 5-, 6-, 7-, and 4′-positions in muningin now remained to be elucidated. It is obvious from the oxidation results already quoted that one of the two hydroxyl groups occupies the 4′-position. Moreover, since muningin does not give a ferric reaction, the 5-substituent, which if phenolic would take part with the adjacent carbonyl in co-ordination complex formation, cannot be unmethylated. Hence the second hydroxyl group must be located at either the 6- or the 7-position. Its precise orientation became apparent from the degradation of muningin diethyl ether by alkali fusion, the formation of *p*-ethoxyphenylacetic acid and 4-ethoxy-3 : 5-dimethoxyphenol leading to 6 : 4′-dihydroxy-5 : 7-dimethoxy*iso*flavone (II; R = H) as the structure of the natural product. For comparison we prepared 4-ethoxy-3 : 5-dimethoxyphenol by a method which is an improvement over that of Bogert and Ehrlich (*J. Amer. Chem. Soc.*, 1919, **41**, 798).

It was now possible to assign complete structures to certain demethylation and reduction products obtained earlier in the investigation. For example, the phenol obtained by heating muningin with a mixture of hydrobromic and acetic acids proved to have lost only one of the two methoxyl groups and, in view of the well-recognised effect of the carbonyl group on the stability of *o*-alkyloxy substituents, it may reasonably be concluded that this derivative is 5 : 6 : 4′-trihydroxy-7-methoxy*iso*flavone (III; R = H). When this compound was methylated under mild conditions the relatively unreactive 5-hydroxyl group was unaffected, the product being 5-hydroxy-6 : 7 : 4′-trimethoxy*iso*flavone (III; R = Me) identical with tectorigenin dimethyl ether (Shriner and Stephenson, *J. Amer. Chem. Soc.*, 1942, **64**, 2737).

Dimethylmuningin was reduced catalytically to a dihydro-derivative, evidently the corresponding *iso*flavanone, which afforded both an oxime and a 2 : 4-dinitrophenylhydrazone. The *iso*flavanone was further reduced by the Clemmensen reagent, but the boiling hydrochloric acid, unlike the mixture of hydrobromic and acetic acids, was without action on the 5-methoxyl group and the product is therefore regarded as 5 : 6 : 7 : 4′-tetramethoxy*iso*flavan (IV).

EXPERIMENTAL

Muningin.—The muninga used in these experiments was provided by the Forest Products Research Laboratory, and was made available through the generous assistance of the Director of the Laboratory and of Dr. W. P. K. Findlay.

(i) The powdered heartwood (1600 g.) which is sharply demarcated and easily distinguished from the pale sapwood, was first extracted with cold light petroleum (3 × 1 l.) and then with cold ether (12 × 5 l.), the respective extracts consisting of a yellow oil (10·8 g., 0·68%) and a dark red resin (89·4 g., 5·6%). This was followed by digestion with quantities of boiling chloroform (6 × 1 l.) until further treatment no longer extracted coloured material. Crystalline solid separated during concentration of the combined chloroform solutions and, when the evaporated extract (48·7 g., 3·04%) was refluxed with methanol (100 c.c.), a microcrystalline solid (5·6 g.) was deposited after the mixture had been left at 0°. From this, muningin was obtained, by crystallisation from dioxan (charcoal), in colourless minute hexagonal plates, m. p. 285° (decomp.).

After chloroform extraction the timber was exhausted by boiling ethanol (3 × 5 l.). When the solvent had been evaporated the friable red-brown product (135 g.) remaining was refluxed with methanol (300 c.c.) and set aside at 0°. This afforded a crystalline solid (5 g.) which on recrystallisation (dioxan; charcoal) gave muningin (4 g., 0·25%) of m. p. 285° (decomp.); the total yield was 0·55%. Finally, the wood was digested with hot water, and the black amorphous extract (17 g., 1·05%) treated with 10% hydrochloric acid. Evaporation of the filtered acid solution and crystallisation of the residue from aqueous alcohol yielded potassium chloride (4·8 g.).

(ii) The powdered wood (6200 g.) was treated in batches (*ca.* 500 g.) for 6 hours with hot ethanol in a percolator. The combined extracts were evaporated to dryness and the residue (1150 g.) refluxed with methanol (1100 c.c.). After 12 hours at 0° the crude *muningin* (49 g.) was collected, and recrystallised from dioxan (charcoal), thus affording the pure compound (43·5 g., 0·7%), m. p. 285° (decomp.) (Found: C, 63·4, 63·1; H, 5·0, 4·8. $C_{17}H_{14}O_6,\frac{1}{2}H_2O$ requires C, 63·2; H, 4·6. Found, in a specimen dried in a vacuum at 150°: C, 64·8; H, 4·3. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5%). Muningin is only very sparingly soluble in ether, chloroform, or ethanol, and slightly soluble in dioxan, ethanol, acetone, or acetic acid. It dissolves in aqueous sodium hydroxide to deep yellow solutions which become red on being warmed. It gives a deep red colour with sulphuric acid containing a trace of nitric acid. Prolonged treatment with sodium amalgam in alcohol is necessary before a pink colour is produced on acidification.

OO-*Diacetylmuningin*.—Muningin (0·1 g.) and fused sodium acetate (0·2 g.) were refluxed for 1 hour with acetic anhydride (2 c.c.), and the mixture was poured into water. Crystallisation of the precipitated product from acetic acid or ethanol gave *diacetylmuningin* (0·1 g.), as silky needles, m. p. 232—233° (Found, in a specimen dried in a vacuum at 110°: C, 61·7, 61·8; H, 4·7, 4·6. $C_{21}H_{18}O_8,\frac{1}{2}H_2O$ requires C, 61·9; H, 4·7%).

OO-*Dibenzoylmuningin*.—The oily product obtained by shaking a solution of muningin (0·1 g.) in 2N-sodium hydroxide (10 c.c.) with benzoyl chloride (0·2 g.) was thoroughly washed with water and dissolved in ethanol. *Dibenzoylmuningin* (0·12 g.) separated in long needles, m. p. 180° (Found: C, 70·2; H, 4·6. $C_{31}H_{22}O_8,\frac{1}{2}H_2O$ requires C, 70·1; H, 4·3. Found, in a specimen dried in a vacuum at 110°: C, 71·7; H, 4·6. $C_{31}H_{22}O_8$ requires C, 71·4; H, 4·2%).

OO-*Dimethylmuningin* (II; R = Me).—(i) A mixture of muningin (1 g.) and potassium carbonate (2 g.) was heated under reflux for 10 hours with acetone (100 c.c.) containing methyl iodide (5 c.c.). The filtered solution was then evaporated, and the residue washed with water and crystallised from methanol. *Dimethylmuningin* (0·84 g., 81%) separated in prisms, m. p. 176° [Found: C, 65·2; H, 5·4%; unit cell, 678. $C_{19}H_{18}O_6,\frac{1}{2}H_2O$ requires C, 64·8; H, 5·4%; unit cell, 693. Found, in a specimen dried in a vacuum at 50°: C, 66·3; H, 5·2; OMe, 37·8%; *M* (Rast), 324. $C_{15}H_{10}O_2(OMe)_4$ requires C, 66·6; H, 5·3; OMe, 36·2%; *M*, 342].

(ii) A solution of muningin (1 g.) in 2N-sodium hydroxide was shaken for 2 hours at room temperature with methyl sulphate (2 c.c.). Crystallisation of the precipitate from methanol gave the dimethyl ether (0·7 g., 68%), m. p. and mixed m. p. 175—176°.

OO-*Diethylmuningin* (II; R = Et).—Prepared by the ethyl iodide–potassium carbonate method, *diethylmuningin* (yield 67%) crystallised from ethanol in needles, m. p. 156° (Found: C, 67·9; H, 6·1. $C_{21}H_{22}O_6$ requires C, 68·1; H, 5·9%).

Nitric Acid Oxidation of Muningin and of Dimethylmuningin.—Addition of concentrated nitric acid (5 c.c.) to muningin (0·5 g.) caused a vigorous reaction. The mixture was then warmed on a steam-bath for 15 minutes and poured into water (20 c.c.). Ether-extraction isolated a product which was completely soluble in aqueous sodium hydrogen carbonate and on crystallisation from alcohol had m. p. 120° alone or mixed with a specimen of picric acid.

Dimethylmuningin (0·4 g.) was warmed with concentrated nitric acid (5 c.c.) on a steam-bath for 30 minutes and the liquid then poured into water (20 c.c.). The resulting solution was extracted with ether (3 × 10 c.c.), and the combined extracts were washed with aqueous sodium hydrogen carbonate. Evaporation of the dried ethereal layer gave a pale yellow oil which crystallised from light petroleum in colourless needles, m. p. 84—86°. After recrystallisation the product (0·03 g.) had m. p. 87°, undepressed by 2 : 4-dinitroanisole prepared by the method of Meldola, Woolcott, and Wray (*J.*, 1896, **69**, 1330).

The bicarbonate solution was acidified, and then yielded to ether a pale yellow solid which crystallised from water in colourless needles (0·12 g.), m. p. 185—187° undepressed by an authentic specimen of 4-methoxy-3-nitrobenzoic acid.

Oxidation of Dimethylmuningin with Potassium Permanganate.—No reaction occurred when dimethylmuningin (0·5 g.) dissolved in cold acetone (50 c.c.) was treated with powdered potassium permanganate, but warming the mixture under reflux yielded a copious precipitate and the addition of reagent was continued until a slight excess remained. The precipitate was collected and digested with boiling water (2 × 10 c.c.), and the resulting solution filtered and acidified The light brown solid thus obtained crystallised from water in colourless long needles (0·13 g.), m. p. and mixed m. p. with *p*-anisic acid, 187°. The acetone filtrate was also examined but contained no organic compound.

Alkaline Hydrolysis of Dimethylmuningin.—Dimethylmuningin (1 g.) was heated under reflux for 30 minutes with ethanol (50 c.c.) containing potassium hydroxide (2 g.). When the solution was made slightly acid with dilute sulphuric acid and the alcohol distilled, an oil separated which was collected in ether. Further concentration of the aqueous solution gave an acid distillate which rapidly precipitated silver from Tollens's reagent. Distillation of the dried ethereal extract afforded a yellow viscous syrup (0·82 g.), b. p. 190—200° (bath-temp.)/1 mm. which crystallised from light petroleum in colourless plates, m. p. 73° (Found : C, 64·6; H, 5·7. $C_{18}H_{20}O_6$ requires C, 64·9; H, 6·0%). The product, *6-hydroxy-2 : 3 : 4-trimethoxyphenyl 4-methoxybenzyl ketone* (I), gave a green ferric reaction. It formed a *semicarbazone* which separated from aqueous ethanol in needles, m. p. 181° (Found : N, 10·9, 11·0. $C_{19}H_{23}O_6N_3$ requires N, 10·8%).

Dimethylmuningin was resynthesised when the ketone (I) (1·7 g.) was shaken for 6 hours at 0° with anhydrous ethyl formate (30 c.c.) containing powdered sodium (0·5 g.) and then left overnight in a refrigerator. The mixture was poured on ice and vigorously stirred to evaporate the excess of ethyl formate, the product being isolated by ether-extraction. Crystallised from methanol, the *iso*flavone (0·35 g., 20%) had m. p. and mixed m. p. 175°.

Degradation of Dimethylmuningin by Alkali Fusion.—A mixture of dimethylmuningin (2 g.), sodium hydroxide (5 g.) and water (2 c.c.) in a copper tube fitted with an air-condenser was heated for 45 minutes at 220° (oil-bath). When cold, the product was dissolved in water which was acidified with hydrochloric acid, and the solution extracted with ether (4 × 50 c.c.). The ethereal extract, when washed with sodium hydrogen carbonate solution and dried, gave on evaporation a reddish product crystallising from benzene in long colourless needles (0·31 g., 29%), m. p. 147° alone or mixed with a specimen of antiarol prepared by the method of Chapman, Perkin, and Robinson (*J.*, 1927, 3028) (Found : C, 58·7; H, 6·4. Calc. for $C_9H_{12}O_4$: C, 58·7; H, 6·5%). It gave pale yellow-green colour with ferric chloride, and its acetate had the recorded m. p. of 74°.

The bicarbonate washings of the ethereal extract were acidified and shaken with ether. Evaporation of the dried ethereal solution gave an oil which crystallised from light petroleum in colourless plates (0·45 g., 47%) consisting of *p*-methoxyphenylacetic acid, m. p. and mixed m. p. 85—86°.

Alkali Degradation of Diethylmuningin.—Diethylmuningin (1 g.), sodium hydroxide (5 g.) and water (2 c.c.), treated as described for the dimethyl ether, gave, from the ethereal extract, colourless needles, m. p. 118°, consisting of 4-ethoxy-3 : 5-dimethoxyphenol (Found : C, 60·9; H, 7·1. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). Acidification of the bicarbonate washings and ether extraction gave *p*-ethoxyphenylacetic acid (Warmer, *Annalen*, 1902, **322**, 149), m. p. and mixed m. p. 84°.

4-Ethoxy-3 : 5-dimethoxyphenol.—The preparation of this phenol by Bogert and Ehrlich's method (*loc. cit.*) is unsatisfactory at the final stage, *viz.*, diazotisation, etc., of the 4-ethoxy-3 : 5-dimethoxyaniline. It is more conveniently obtained by the following adaptation of the Chapman, Perkin, and Robinson synthesis (*loc. cit.*). 2 : 6-Dimethoxyquinol (1 g.) was dissolved in 10% aqueous sodium hydroxide (25 c.c.) containing a trace of sodium dithionite, and the solution shaken with ethyl sulphate (1·4 c.c., 2 mols.) for 1 hour. After extraction with ether, the solution was acidified and the brown oil collected with ether and crystallised from light petroleum. Further crystallisation from water, which was attended by considerable loss, gave 4-ethoxy-3 : 5-dimethoxyphenol in needles (0·22 g., 19%), m. p. 118°, alone or mixed with a specimen obtained from diethylmuningin.

*5 : 6 : 4′-Trihydroxy-7-methoxy*iso*flavone* (III; R = H).—When muningin (1 g.) was dissolved in a mixture of hydrobromic acid (15 c.c.; *d* 1·5) and acetic acid (5 c.c.) a yellow precipitate—presumably the hydrobromide—immediately separated. The mixture was heated, whereupon the precipitate dissolved to be followed shortly afterwards by the separation of the *trihydroxy*-compound (0·88 g.) which crystallised from acetic acid or ethanol in clusters of prisms, m. p. 258° (decomp.) (Found : C, 62·1, 61·8; H, 4·4, 4·4; OMe, 9·2. $C_{15}H_9O_5\cdot OMe,\frac{1}{2}H_2O$ requires C, 62·1; H, 4·2; OMe, 9·2%). The *iso*flavone gave a deep green colour with ferric chloride.

*5-Hydroxy-6 : 7 : 4′-trimethoxy*iso*flavone* (III; R = Me).—The foregoing compound (0·1 g.), potassium carbonate (1 g.), methyl iodide (2 c.c.), and acetone (50 c.c.) were refluxed for 10 hours and the product was worked up in the usual way. When crystallised from ethanol 5-hydroxy-6 : 7 : 4′-trimethoxy*iso*flavone (0·09 g.) formed needles, m. p. 186° (lit., 188°) (Found : C, 64·6; H, 5·2. Calc. for $C_{18}H_{16}O_6,\frac{1}{2}H_2O$: C, 64·2; H, 5·0%). It is very sparingly soluble in methanol, insoluble in aqueous sodium hydroxide, and gives a deep green ferric reaction.

When methylation was effected with methyl sulphate and potassium carbonate in boiling acetone for 30 hours, the product (yield 56%) was muningin dimethyl ether, m. p. and mixed m. p. 176°.

Dihydromuningin Dimethyl Ether (*5 : 6 : 7 : 4′-Tetramethoxy*iso*flavanone*).—Dimethylmuningin (0·8 g.) in ethanol (40 c.c.), in a catalytic reduction over palladised charcoal (0·1 g.), absorbed 55 c.c. of hydrogen (theory, 56·2 c.c.) in 35 minutes. When the solution was filtered and concentrated to 5 c.c., the iso*flavanone* (0·62 g., 77%) crystallised in rosettes of needles, m. p. 147—148° (Found : C, 65·9; H, 5·6. $C_{19}H_{20}O_6$ requires C, 66·2; H, 5·8%). In warm ethanolic 2 : 4-dinitrophenylhydrazine sulphate, this gave deep red rods of the *2 : 4-dinitrophenylhydrazone*, m. p. (after crystallisation from ethanol) 165—166° (Found : C, 56·3; H, 4·7; N, 9·9. $C_{25}H_{24}O_9N_4,\frac{1}{2}H_2O$ requires C, 56·3; H, 4·7; N, 10·5. Found, in a specimen dried in a vacuum at 100° : C, 57·6; H, 4·7. $C_{25}H_{24}O_9N_4$ requires C, 57·2; H, 4·6%). The *oxime* crystallised from ethanol in rhombic plates, m. p. 193° (Found : C, 63·2, 63·4; H, 6·2, 6·2; N, 4·0. $C_{19}H_{21}O_6N$ requires C, 63·4; H, 5·9; N, 3·9%).

*5 : 6 : 7 : 4′-Tetramethoxy*iso*flavan* (IV).—Amalgamated zinc dust (5 g.) was covered with acetic acid (15 c.c.) and dihydromuningin dimethyl ether (0·3 g.) added. The mixture was gently refluxed for 8 hours with the occasional addition of concentrated hydrochloric acid (total, 10 c.c.). The product was extracted from the cooled solution by ether which when washed with water, dried, and evaporated gave the iso*flavan* (0·22 g.), crystallising from methanol as a microcrystalline powder, m. p. 95—96° (Found : C, 69·1; H, 6·5. $C_{19}H_{22}O_5$ requires C, 69·0; H, 6·7%). The *iso*flavan was insoluble in aqueous sodium hydroxide and gave a negative ferric reaction.

One of the authors (A. J. W.) is indebted to the Department of Scientific and Industrial Research for the award of a Maintenance Grant.

THE UNIVERSITY, NOTTINGHAM. [*Received, September 17th, 1951.*]