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ISOFLAVONES OF THE HEARTWOOD OF *DALBERGIA RETUSA*

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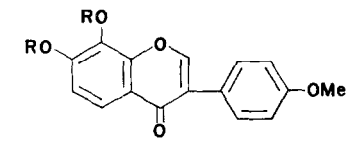
Key Word Index—*Dalbergia retusa*; Leguminosae; 7,8-dihydroxy-4′-methoxyisoflavone; 7-hydroxy-8,4′-dimethoxyisoflavone.

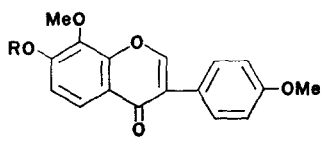
Abstract—Ether extracts of the heartwood *Dalbergia retusa* yield two crystalline isoflavones, identified by degradation, spectra, and synthesis as 7,8-dihydroxy-4′-methoxyisoflavone (retusin) and 7-hydroxy-8,4′-dimethoxyisoflavone (8-*O*-methylretusin).

INTRODUCTION

THE HEARTWOOD of the Panamanian tree, *Dalbergia retusa* (cocobolo), is extremely resistant to attack by marine boring organisms.[1] In addition to the quinone pigments which are described in a related paper, ether extracts of the heartwood yield major quantities of a colorless, crystalline phenol, $C_{16}H_{12}O_5$, m.p. 249°, now called *retusin* and identified as 7,8-dihydroxy-4′-methoxyisoflavone Ia, and minor amounts of a second colorless phenol,



(I a) R = H
(I b) R = Me
(I c) R = CH_3CO



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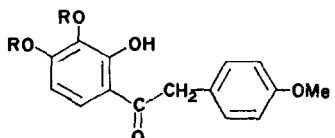

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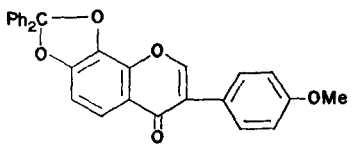
(III b) R = Me



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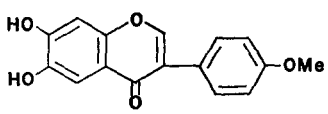

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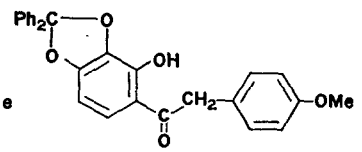
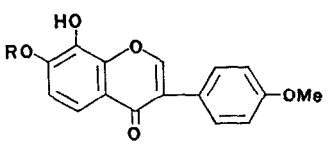
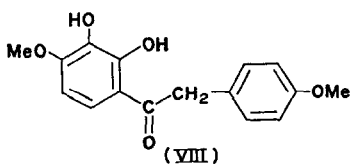


(VI)



(VII a) R = $PhCH_2^-$
(VII b) R = Me



(VIII)

[1] C. R. SOUTHWELL and J. D. BULTMAN, *Biotropica* **3**, 81 (1971).

$C_{17}H_{14}O_5$, m.p. 221°, shown to be the 8-*O*-methyl derivative IIa of retusin. These isoflavones, which constitute approximately 1% of the weight of the heartwood, appear to be the first 7,8,4′-trioxygenated isoflavones reported from plant sources.

Dalbergia is in the Leguminosae, and a number of different isoflavones have been detected in other species of this genus. These include biochanin-A, genistein, caviunin, and 7-*O*-methyltectorigenin, which occur free or as *O*- or *C*-glycosides in various parts of *D. lanceolaria*,[2] *D. sissoo*,[3,4] *D. paniculata*[5] and *D. nigra*.[6,7] 5-Deoxyisoflavones have also been detected in some species. These include formononetin from the heartwood of *D. baroni*[8] and *D. barretoana*,[9] 7,4′-dimethoxyisoflavone from *D. violaceae*,[10] and ψ-baptigenin and formononetin, which co-occur with biochanin-A and caviunin in the heartwood of *D. spruceana*.[10] *Machaerium villosum*, which is closely related to *Dalbergia*, contains daidzein, formononetin, isoformononetin, 7,4′-dihydroxy-3′-methoxyisoflavone, and 7,3′,4′-trihydroxyisoflavone.[11] Oliveira *et al.*[12] very recently reported that 5-deoxyisoflavones (structures unspecified) occur in five other *Dalbergia* species, viz. *D. obtusa*, *D. frutescens*, *D. cearensis*, *D. ecastophyllum* and *D. volubilis*.

RESULTS

Retusin contains one methoxyl and two phenolic hydroxyl groups. In accord with the proposed isoflavone structure it reacts slowly with Mg–HCl to give a red–brown solution, and its UV spectrum[13] in ethanol shows a single λ_{max} of high intensity at 261 nm (E 3·3 × 10^4) with only an inflection of low intensity at 308 nm (E 6·53 × 10^3). Retusin forms a di-*O*-methyl derivative (m.p. 151°), which is hydrolyzed by alcoholic KOH to yield a deoxybenzoin, subsequently identified as IIIb.

Retusin rapidly reduces ammoniacal $AgNO_3$, gives a brilliant green color with ethanolic $FeCl_3$, and its λ_{max} undergoes an 8 nm bathochromic shift on addition of boric acid–sodium acetate.[13] Oxidation of retusin with conc HNO_3 yields traces of a compound, which, on the basis of its m.m.p., appears to be 3-nitroanisic acid. These data indicate location of the methoxyl at the 4′ position in the *B* ring, and an *ortho*-orientation of the two hydroxyls in the *A* ring. The presence of the *ortho*-dihydroxyl grouping was chemically confirmed by the facile formation of a crystalline diphenylmethylene derivative-IV, when retusin was heated briefly[14] with α,α-dichlorodiphenylmethane.

In the presence of ethanolic sodium acetate the λ_{max} of retusin undergoes a pronounced bathochromic shift (16 nm) to 277 nm, indicating[13] location of one hydroxyl at position 7, and, therefore, the other at position 8, as in Ia, or at position 6, as in texasin V. Since the

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[4] A. BANERJI, V. V. S. MURTI and T. R. SESHADRI, *Indian J. Chem.* **4**, 70 (1966).
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[12] A. B. DE OLIVEIRA, O. R. GOTTLIEB, W. D. OLLIS and C. T. RIZZINI, *Phytochem.* **10**, 1863 (1971).
[13] L. JURD, in *The Chemistry of Flavonoid Compounds* (edited by T. A GEISSMAN), 107, Pergamon Press, Oxford (1962).
[14] L. JURD, *J. Org. Chem.* **27**, 872 (1962).

spectral and other reported properties of texasin[15] (m.p. 285–287°) and its di-*O*-methyl derivative[16] (m.p. 174–175°) distinctly differ from those of retusin, the latter can only be formulated as the 7,8-dihydroxyisoflavone derivative Ia. The NMR spectra of retusin derivatives fully confirm this structure. Thus, the 100 MHz spectrum of retusin diacetate (m.p. 166–167°) in $CDCl_3$ shows the protons at C_2 as a singlet at δ7·94, and the protons at positions 3′ (5′), 2′ (6′), and 6 as *ortho*-coupled doublets ($J = 9{\cdot}0$ Hz) at δ6·96, 7·47 and 7·25, respectively. The proton at C_5, *ortho*- to the carbonyl group, occurs well downfield as a doublet ($J = 9{\cdot}0$ Hz) at δ8·20. The structure IIIb was assigned to the deoxybenzoin formed by alkaline hydrolysis of di-*O*-methylretusin on the basis of, (a) its intense, wine-red ferric reaction, (b) its formation of a monomethyl derivative (m.p. 54°), and (c) its 100 MHz spectrum in $CDCl_3$. The latter showed the presence of the three methoxyls as 3H singlets at δ3·77, 3·87, and 3·89, the benzylic methylene as a 2H singlet at δ4·15, and the protons at positions 6, 3′ (5′), 2′ (6′), and 5 as *ortho*-coupled doublets ($J = 9{\cdot}0$ Hz) at δ6·47 (1H), δ6·85 (2H), δ7·18 (2H), and δ7·61 (1H), respectively. The chelated hydroxyl appears downfield as a singlet at δ12·55.

The structure of retusin was also confirmed synthetically. Thus, alkaline hydrolysis of IV, the α,α-diphenylmethylene derivative of retusin, gave a crystalline deoxybenzoin VI. Acid hydrolysis of VI then gave a crystalline trihydroxydeoxybenzoin, m.p. 157°. This trihydroxy compound was considered to be IIIa, although a substance of this structure had previously been synthesized by BF_3 catalyzed condensation of 4-methoxyphenylacetic acid with pyrogallol and was reported[17] to melt at 145–146°. Repetition of this synthesis gave a trihydroxydeoxybenzoin, m.p. 157°, identical in all respects with the product from retusin. The structure of the synthetic product as IIIa was established by its formation of a di-*O*-methyl derivative, identical with the deoxybenzoin IIIb from di-*O*-methyl retusin, and by its formation of a triacetate (m.p. 126°), whose NMR spectrum showed the presence of three acetyl groups, a benzylic methylene group, and six *ortho*-coupled protons. Reaction of synthetic IIIa with ethyl orthoformate[17] gave 7,8-dihydroxy-4′-methoxyisoflavone, which was identical with the natural product.

The second, minor phenol, m.p. 221°, from *Dalbergia retusa* contains two methoxyl and one hydroxyl groups, and on methylation it gives di-*O*-methyl retusin Ib. The λ_{max} of this new isoflavone in ethanol (256 nm) shifted to 270 nm on the addition of sodium acetate, indicating the location of the free hydroxyl at position 7 as in structure IIa. The 100 MHz NMR spectrum of the acetate (m.p. 124°) of this isoflavone showed the proton at C_6 as an *ortho*-coupled doublet at δ7·11, and an upfield shift (relative to retusin diacetate) of the C_5 proton doublet to δ8·04. The structure of this isoflavone as 8-*O*-methylretusin was confirmed by its synthesis from 7,8-diacetoxy-4′-methoxyisoflavone Ic. Selective benzylation[18] of Ic and alkaline hydrolysis of the product gave 7-benzyloxy-8-hydroxy-4′-methoxyisoflavone VIIa. This was methylated and then catalytically hydrogenolyzed to yield 7-hydroxy-8,4′-dimethoxy-isoflavone IIa, identical in all respects with the natural product.

Further confirmation of the structure of the above isoflavone was provided by the synthesis of the isomeric 8-hydroxy-7,4′-dimethoxy-isoflavone VIIb, by (a) selective methylation of 7,8-diacetoxy-4′-methoxyisoflavone and (b) in good yield by reaction of the deoxybenzoin VIII with $POCl_3$ and dimethylformamide. The properties of VIIb (m.p.

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203–204°; diacetate, m.p. 154–155°) differ markedly from those of the natural isoflavone IIa, and its λ_{max} in ethanol (260 nm) does not shift in the presence of sodium acetate.

EXPERIMENTAL

Isolation of retusin Ia *and* 8-O-*methyl retusin* IIa. Sawdust of *Dalbergia retusa* heartwood (2500 g) was extracted continuously with low boiling petroleum for 2 days, and then with ether for 2 days. The residue (253 g) obtained on evaporation of the ether extract was heated with benzene (2 × 500 ml) and the undissolved, cream-colored crystalline residue was collected (25·0 g). TLC on silicic acid showed that this residue consisted chiefly of retusin, contaminated with a small quantity of 8-*O*-methylretusin. The residue was dissolved in warm acetone (1 l.), concentrated to 300 ml, diluted with EtOAc (500 ml) and reconcentrated to 600 ml. On cooling, crude retusin separated as cream-colored crystals (m.p. 243–245°) (16·0 g). Concentration of the EtOAc filtrate yielded further quantities of retusin (5·7 g). The EtOAc filtrate was then passed through a short column of silicic acid impregnated with boric acid. Evaporation of the filtrate gave chromatographically homogenous 8-*O*-methylretusin (1·07 g). 8-*O*-Methylretusin was also obtained from the petroleum extract of the wood. The orange solid which separated from the extract was heated with ether (250 ml) and filtered. The ether extract was evaporated and the residue was dissolved in a minimal volume of hot benzene. 8-*O*-Methylretusin slowly crystallized on standing (0·53 g).

Retusin. Recrystallized from acetone–MeOH and from acetone alone *retusin* Ia separated as colorless, glistening prisms, m.p. 249° (Found: C, 67·8; H, 4·39; MeO–, 10·8. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·26; 1 MeO–10·9). *Retusin diacetate* (Ic) crystallized from acetone–MeOH as colorless, glistening needles, m.p. 166–167° (0·25 g) λ_{max}^{EtOH} 257 nm (Found: C, 65·2; H, 4·36; MeO–, 8·41. Calc. for $C_{20}H_{16}O_7$: C, 65·2; H, 4·38; 1 MeO–, 8·43).

*Di-*O-*Methylretusin* Ib. Methylation of retusin with Me_2SO_4–K_2Co_3–Me_2Co for 2 hr gave a solid which was crystallized from acetone–MeOH to yield *di-*O-*methylretusin* Ib as thick, colorless needles, m.p. 151° (1·8 g) (Found: C, 69·4; H, 5·09; MeO–, 29·7. Calc. for $C_{18}H_{16}O_5$: C, 69·2; H, 5·16; 3 MeO–, 29·8). 100 MHz NMR spectrum in $CDCl_3$–3H, *S*, δ3·84; 6H, *S*, δ4·00; 1H, *d*, δ6·95, J = 9·0 Hz; 2H, *d*, δ7·05, J = 9·0 Hz; 2H, *d*, δ7·50, J = 9·0 Hz; 1H, *S*, δ7·98; 1H, *d*, δ8·03, J = 9·0 Hz. Ethylation of retusin gave *di-*O-*ethyl-retusin* from MeOH as colorless, soft needles, m.p. 110° (Found: C, 70·5; H, 5·92. Calc. for $C_{20}H_{20}O_5$: C, 70·6; H, 5·92). 100 MHz spectrum in $CDCl_3$: 3H, *t*, δ1·44, J = 7·0 Hz; 3H, *t*, δ1·51, J = 7·0 Hz, 3H, *S*, δ3·82; 4H, *q*, δ4·23, J = 7·0 Hz; 1H, *d*, δ6·94, J = 9·0 Hz; 2H, *d*, δ7·04, J = 9·0 Hz; 2H, *d*, δ7·52, J = 9·0 Hz; 1H, *S*, δ7·99; 1H, *d*, δ8·01, J = 9·0 Hz.

*Alkaline hydrolysis of di-*O-*methylretusin.* Di-*O*-methylretusin (0·80 g) was heated under reflux with EtOH (80 ml) and 10% aq. KOH (8·0 ml) for 1 hr. The product was recrystallized from acetone–MeOH to yield 4-*methoxybenzyl* 2-*hydroxy*-3,4-*dimethoxyphenyl ketone* IIIb as long, colorless needles, m.p. 122–123° (0·52 g), which gave an intense wine-red color with alcoholic $FeCl_3$ (Found: C, 67·6; H, 6·01; MeO–, 30·6. Calc. for $C_{17}H_{18}O_5$; C, 67·5; H, 6·00; 3 MeO–, 30·8). Methylation of IIIb gave 4-*methoxybenzyl* 2,3,4-*trimethoxyphenyl ketone*, glistening, brittle needles from petroleum, m.p. 54°, which did not give a color with alcoholic $FeCl_3$ (Found: C, 68·2; H, 6·46. Calc. for $C_{18}H_{20}O_5$: C, 68·3; H, 6·37). 100 MHz spectrum in $CDCl_3$: 3H, *S*, δ3·78; 6H, *S*, δ3·88; 3H, *S*, δ3·95; 2H, *S*, δ4·21; 1H, *d*, δ6·68, J = 9·0 Hz; 2H, *d*, δ6·84, J = 9·0 Hz; 2H, *d*, δ7·16, J = 9·0 OHz; 1H, *d*, δ7·46, J = 9·0 Hz.

4′-*Methoxy*-7,8-*diphenylmethylenedioxyisoflavone* IV. An intimate mixture of retusin (1·42 g) and α,α-dichlorodiphenylmethane (1·45 g; 1·2 mol equiv.) was heated in an oil bath to 210°. The mixture was maintained at this temp. until the evolution of HCl gas ceased (5 min). MeOH (20 ml) was added to the cooled reaction mixture and the undissolved crystalline product was collected (2·02 g). Recrystallized from acetone–MeOH 4′-*methoxy*-7,8-*diphenylmethylenedioxyisoflavone* IV was obtained as glistening, slightly brown colored, needles, m.p. 198° (Found: C, 77·6; H, 4·53. Calc. for $C_{29}H_{20}O_5$: C, 77·7; H, 4·50).

4-*Methoxybenzyl* 2-*hydroxy*-3,4-*diphenylmethylenedioxyphenyl ketone* VI. A solution of IV (1·0 g) in EtOH (100 ml) and 10% aq. KOH (10·0 ml) was heated under reflux for 2 hr. The solid product was recrystallized from acetone–MeOH to give VI as glistening, slightly brown plates, m.p. 146° (0·81 g). With alcoholic $FeCl_3$ VI gives an intense red color (Found: C, 76·7; H, 5·10. Calc. for $C_{28}H_{22}O_5$: C, 76·7; H, 5·06).

4-*Methoxybenzyl* 2,3,4-*trihydroxyphenyl ketone* IIIa. (a) A solution of 4-methoxybenzyl 2-hydroxy-3,4-diphenylmethylenedioxyphenyl ketone VI (0·4 g) in HOAc (2·0 ml) was treated with 2 drops of conc. HCl and heated at 100° for 5 min. The solution was slowly diluted with H_2O and a layer of benzene was added. After cooling, the crystalline product was collected and recrystallized successively from aq. MeOH and from acetone–benzene. IIIa separated as glistening, almost colorless, brittle prisms, m.p. 157°, undepressed with the synthetic product prepared in (b) (0·12 g) (Found: C, 65·9; H, 5·22; MeO–, 11·2. Calc. for $C_{15}H_{14}O_5$: C, 65·7; H, 5·15; 1 MeO–, 11·3). (b) A solution of pyrogallol (6·0 g) and 4-methoxyphenylacetic acid (12 g) in $CHCl_3$ (40 ml) was cooled in an ice bath and saturated with BF_3, and the mixture kept at room temp. for 2 days. The product crystallized from aq. MeOH to give slightly brown needles, m.p. 156° (7·0 g). Recrystallized from acetone–benzene synthetic IIIa separated as glistening, colorless prisms, m.p. 157° (Found: C, 66·0; H, 5·29; MeO–, 11·3. Calc. for $C_{15}H_{14}O_5$: C, 65·7; H, 5·15, MeO–, 11·3). 100 MHz spectrum in $CDCl_3$:

3H, *S*, δ3·87; 2H, *S*, δ4·21; 1H, *d*, δ6·47, J = 9·0 Hz; 2H, *D*, δ6·86, J = 9·0 Hz; 2H, *d*, δ7·26, J = 0·9 Hz; 1H, *d*, δ7·35, J = 9·0 Hz. Mixed with IIIa from (a), the product migrates as a single substance on silicic acid TLC (R_f 0·33 in Me_2CO–$CHCl_3$ 1:10; 0·24 in benzene–EtOH, 9:1). Acetylation gave *4′-methoxybenzyl 2,3,4-triacetoxyphenyl ketone* from MeOH as colorless, brittle needles, m.p. 126° (Found: C, 63·1; H, 5·19. Calc. for $C_{21}H_{20}O_8$: C, 63·0; H, 5·04). 100 MHz spectrum in $CDCl_3$: 9H, *S*, δ2·28; 3H, *S*, δ3·77; 2H, *S*, δ4·12; 2H, *d*, δ6·86, J = 9·0 Hz; 2H, *d*, δ7·12, J = 9·0 Hz; 1H, *d*, δ7·20, J = 9·0 Hz; 1H, *d*, δ7·74, J = 9 Hz. Methylation of synthetic IIIa with CH_2N_2 in Et_2O and crystallization of the oily product from MeOH (×3) gave long colorless needles, m.p. and m.m.p. with IIIb, 122°. Mixed with IIIb the product migrated as a single substance on silicic acid TLC (R_f 0·56 in Et_2O–petroleum, 2:1, 0·72 in benzene–EtOH, 9:1).

7,8-*Dihydroxy-4′-methoxyisoflavone*. Synthetic 4-methoxybenzyl-2,3,4-trihydroxyphenylketone IIIa (1·0 g) was heated under reflux with pyridine (2·0 ml), piperidine (4 drops), and ethyl *ortho*formate 17 (1·0 ml) for 7 hr. The product was collected and recrystallized successively from aq. MeOH and acetone–EtOAc to give 7,8-*dihydroxy-4′-methoxyisoflavone* as colorless, brittle prisms, m.p. and m.m.p. with retusin, 248–249° (0·32 g). The synthetic isoflavone reduced $AgNO_3$, gave a brilliant green color with $FeCl_3$, and migrated as a single substance on silicic acid TLC when mixed with retusin (R_f 0·14 in benzene–EtOH, 9:1; 0·82 in $CHCl_3$–MeOH, 4:1, 0·16 in acetone–$CHCl_3$, 1:10). Acetylation gave 7,8-*diacetoxy-4′-methoxyisoflavone*. This separated from acetone–MeOH as colorless needles, m.p. and m.m.p. with retusin diacetate, 166–167°. A mixture with natural retusin diacetate migrated as a single substance on silicic acid TLC (R_f 0·24 in Et_2O–petroleum, 2:1; 0·67 in benzene–EtOH, 9:1). (Found: C, 65·3; H, 4·54. Calc. for $C_{20}H_{16}O_7$: C, 65·2; H, 4·38.) The NMR spectrum in $CDCl_3$ was identical with that of retusin diacetate.

8-*O*-*Methylretusin* IIa. Recrystallized several times from acetone–MeOH 8-*O*-methylretusin separated as colorless brittle prisms, m.p. 221°. It did not reduce $AgNO_3$ and it did not give a color with $FeCl_3$. (Found: C, 68·5; H, 4·75; MeO–, 20·3. Calc. for $C_{17}H_{14}O_5$: C, 68·45; H, 4·73; 2 MeO–, 20·8.) Acetylation of 8-*O*-methylretusin gave the *acetate IIb*, which crystallized from MeOH as colorless needles, m.p. 124–125°, λ_{max}^{EtOH} 256 nm. (Found: C, 67·3; H, 4·80. Calc. for $C_{17}H_{16}O_6$: C, 67·05; H, 4·75.) 100 MHz spectrum in $CDCl_3$: 3H, *S*, δ2·38; 3H, *S*, δ3·83; 3H, *S*, δ4·10; 2H, *d*, δ6·95, J = 9·0 Hz; 1H, *s*, δ7·11, J = 9·0 Hz; 2H, *d*, δ7·48, J = 9·0 Hz; 1H, *S*, δ8·02; 1H, *d*, δ8·04, J = 9·0 Hz. 8-*O*-Methylretusin was methylated in the usual way; the product crystallized from MeOH as long colored needles, m.p. and m.m.p. with di-*O*-methylretusin, 151°. The NMR spectrum and R_f values (0·78 in benzene–EtOH, 9:1; 0·49 in Et_2O–petroleum, 2:1) were identical with those of di-*O*-methylretusin.

7-*Benzyloxy*-8-*hydroxy*-4′-*methoxyisoflavone* VIIa. A mixture of 7,8-diacetoxy-4′-methoxyisoflavone (2·0 g), $PhCH_2Cl$ (2·1 ml), KI (1·0 g), K_2CO_3 (5 g) and dry acetone (15 ml) was heated under reflux for 16 hr. The product crystallized from acetone–MeOH to give colorless needles, m.p. 160–163° (1·7 g). Mild alkaline hydrolysis gave a solid which was crystallized successively from acetone–MeOH and from acetone alone. VIIa was obtained as glistening, colorless prisms, m.p. 213–214° (1·08 g), λ_{max}^{EtOH} 262 nm, unchanged on addition of NaOAc. (Found: C, 73·8; H, 4·92. Calc. for $C_{23}H_{18}O_5$: C, 73·8; H, 4·85.)

7-*Benzyloxy*-8,4′-*dimethoxyisoflavone*. VIIa was methylated to yield 7-*benzyloxy*-8,4′-*dimethoxyisoflavone* as colorless, fluffy needles from Me_2CO–MeOH m.p. 135° (0·80 g). (Found: C, 74·2; H, 5·31. Calc. for $C_{24}H_{20}O_5$: C, 74·2; H, 5·19.) 100 MHz spectrum in $CDCl_3$: 3H, *S*, δ3·84; 3H, *S*, δ4·03; 2H, *S*, δ5·27; 2H, *d*, δ6·96; J = 9·0 Hz; 1H, *d*, δ7·08, J = 9·0 Hz; 7H, *m*, δ7·28–7·56; 1H, *s*, δ7·99; 1H, *d*, δ8·00, J = 9·0 Hz.

7-*Hydroxy*-8,4′-*dimethoxyisoflavone* IIa. 7-Benzyloxy-8,4′-dimethoxyisoflavone (0·70 g) was dissolved in tetrahydrofuran (10 ml) and hydrogenated at atmospheric pressure over a 5% Pd-C. 1 mol equiv. of hydrogen was absorbed. The filtered solution was evaporated and the residue was crystallized from acetone–benzene. 7-*Hydroxy*-8,4′-*dimethoxyisoflavone* separated as glistening, colorless prisms, m.p. and m.m.p. with 8-*O*-methylretusin, 221°. Mixed with 8-*O*-methylretusin it migrated as a single substance on silicic TLC (R_f 0·45 in benzene–EtOH, 9:1 0·18 in Et_2O–petroleum, 2:1). (Found: C, 68·4; H, 4·79; MeO–, 20·6. Calc. for $C_{17}H_{14}O_5$: C, 68·45; H, 4·73; 2 MeO– 20·8.) λ_{max}^{EtOH} 256 nm; $\lambda_{max}^{EtOH-NaOAc}$ 270 nm. 7-*Acetoxy*-8,4′-*dimethoxyisoflavone* separated as colorless needles, m.p. and m.m.p. with 8-*O*-methylretusin acetate, 124–125°. Mixed TLC with 8-*O*-methylretusin acetate on silicic acid, R_f 0·56 in Et_2O–petroleum, 2:1, 0·85 in benzene–EtOH, 9:1. (Found: C, 67·1; H, 4·81. Calc. for $C_{19}H_{16}O_6$: C, 67·05; H, 4·75.) NMR spectrum was identical with that previously described for 8-*O*-methylretusin acetate.

8-*Hydroxy*-7,4′-*dimethoxyisoflavone* VIIb. (a) A mixture of 7,8-diacetoxy-4′-methoxyisoflavone (1·1 g), MeI (2·0 ml), K_2CO_3 (5 g) and Me_2CO (20 ml) was heated under reflux for 24 hr. The filtered solution was evaporated to give an oily product which consisted of a mixture of methylated and unreacted material. It was dissolved in MeOH (5 ml) and hydrolyzed by heating with 10% aq. NaOH (5 ml) for 10 min. H_2O was added, the solution was acidified, and the crude product was extracted with Et_2O. The ethereal solution was extracted twice with 5% aq. borax. Acidification of the borax extract gave 7,8-dihydroxy-4′-methoxyisoflavone. The ethereal solution, after removal of the dihydroxyisoflavone with borax, was evaporated to a crystalline solid. Recrystallized from MeOH 8-*hydroxy*-7′4-*dimethoxyisoflavone* was obtained as glistening, cream-colored needles, m.p. 203–204°, R_f 0·42 (benzene–EtOH, 9:1). (Found: C, 68·5; H, 4·91; MeO–, 20·9. Calc. for $C_{17}H_{14}O_5$: C, 68·45; H, 4·73; 2 MeO–, 20·8.) Acetylation gave 8-*acetoxy*-7,4′-dimethoxyisoflavone. as long, colorless needles from MeOH, m.p. 154°, λ_{max}^{EtOH} 251 nm. (Found: C, 67·2; H, 4·81. Calc. for $C_{19}H_{16}O_6$: C, 67·0; H, 4·75.) 100 MHz spectrum in $CDCl_3$: 3H, *S*, δ2·43; 3H, *S*, δ3·85; 3H, *S*, δ3·98; 2H, *d*, δ6·97,

J = 9·0 Hz; 1H, *d*, δ7·09, J = 9·0 Hz; 2H, *d*, δ7·49, J = 9·0 Hz; 1H, *S*, δ7·91; 1H, *d*, δ8·19, J = 9·0 Hz. (b) A solution of 3-methoxycatechol (6·0 g) and 4-methoxyphenyl-acetic acid (12·0 g) in ice-cold $CHCl_3$ (40·0 ml) was saturated with BF_3 and allowed to stand at room temp. for 2 days. H_2O (300 ml) and Et_2O (100 ml) were added and the crystalline solid was collected. The ether–$CHCl_3$ layer was evaporated and the residue was crystallized from aq. MeOH. This crystalline product was combined with the above crystalline product and recrystallized from acetone–MeOH. 4-*Methoxybenzyl* 2,3-*dihydroxy*-4-*methoxyphenyl ketone* VIII was thereby obtained as brittle, cream-colored prisms, m.p. 137° (12·0 g). (Found: C, 66·6; H, 5·61; MeO–, 21·6. Calc. for $C_{16}H_{16}O_5$: c, 66·7; H, 5·59; 2 MeO–, 21·5.) The *diacetate* of VIII crystallized from MeOH as colorless needles, m.p. 136–137°. (Found: C, 64·5; H, 5·49. Calc. for $C_{20}H_{20}O_7$: C, 64·5; H, 5·41.) VIII was converted into the isoflavone by adaptation of the method of Kagal *et al.*[19] VIII (2·88 g) was added to a solution of $POCl_3$ (1·8 ml) in *N,N*-dimethylformamide (5·0 ml) and the mixture was heated on a steam-bath for 1·5 hr. H_2O was added and the product was crystallized from acetone–MeOH. 8-*Hydroxy*-7,4′-*dimethoxyisoflavone* was obtained as colorless needles, m.p. and m.m.p. with product from (a), 203–204°. (1·6 g). The product formed a *monoacetate*, m.p. and m.m.p. with the acetate of the product from (a), 154–155°.

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[19] S. A. KAGAL, P. M. NAIR and K. VENKATARAMAN, *Tetrahedron Letters* 593 (1962).