TABLE II

INFLUENCE OF SODIUM ACETATE, SODIUM HYDROXIDE, AND ALUMINUM CHLORIDE ON THE SPECTRA OF FLAVANONES

Compound	λ_{max}, mμ			
	C_2H_5OH[a]	NaOAc[b]	NaOH[c]	$AlCl_3$[f]
1. 7-Hydroxyflavanone	277	338	338	277
2. 7,4′-Dihydroxyflavanone (Liquiritigenin)	276	338	338	276
3. 7,3′,4′-Trihydroxyflavanone (Butin)	278	338	338	278
4. 5,7-Dihydroxyflavanone (Pinocembrin)	291	329	329	312
5. 5,7,4′-Trihydroxyflavanone (Naringenin)	290	328	328	311
6. 5,7,3′,4′-Tetrahydroxyflavanone (Eriodictyol)	289	328	328[d]	310
7. 3,5,7,3′,4′-Pentahydroxyflavanone (Taxifolin)	291	330	329[d]	314
8. 5,7-Dihydroxy-4′-methoxyflavanone (Isosakuranetin)	292	328	328	312
9. 5,3′,4′-Trihydroxy-7-methoxyflavanone	287	287	289[d]	309
10. 5,7,4′-Trihydroxy-3′-methoxyflavanone (Homoeriodictyol)	289	328	328	311
11. 5,7,3′-Trihydroxy-4′-methoxyflavanone (Hesperetin)	288	328	328	311
12. 5-Hydroxy-7,3′,4′-triacetoxyflavanone	274			303
13. Isosakuranetin 7-Rhamnoglucoside (Poncirin)	283	283	285	308
14. Eriodictyol 7-Rhamnoglucoside (Eriocitrin)	285	285	285[d]	306
15. Hesperetin 7-Rutinoside (Hesperidin)	285	285	287	308
16. Hesperetin 7-Neohesperidoside (Neohesperidin)	285	285	287	308
17. 5,4′-Dihydroxy-7-methoxyflavanone (Sakuranetin)	287	287	424[e]	310
18. Sakuranetin 5-glucoside (Sakuranin)	281	281	428[e]	281
19. Naringenin 7-glucoside (Prunin)	284	284	425[e]	308
20. Naringenin 7-rhamnoglucoside	284	284	428[e]	308

[a] Absolute ethanol. [b] Absolute ethanol saturated with fused sodium acetate. [c] 2.5 ml. absolute ethanol treated with 1 drop of 1% sodium hydroxide. [d] Solution decomposes rapidly. [e] Forms the chalcone. [f] Absolute ethanol saturated with aluminum chloride hexahydrate.

spectra of the new flavanone glycoside eriocitrin (VIII)[9] are shown. The bathochromic shift obtained with aluminum chloride shows the presence of a 5-hydroxyl group, while the lack of a shift with sodium acetate shows the presence of a sugar group at the 7-hydroxyl. The presence of free *o*-dihydroxyl groups is inferred from the instability of the compound in alkaline solution as well as from other evidence.[10]

Acknowledgment. We should like to thank Prof. L. H. Briggs for a sample of podospicatin and Dr. J. Naghski for a sample of sophoricoside. We should also like to thank Mr. Bruno Gentili for determining a number of spectra.

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(9) R. M. Horowitz and B. Gentili, *J. Am. Chem. Soc.*, 82, 2803 (1960).

(10) The compound decomposes irreversibly in alkali before chalcone formation can be observed.

[CONTRIBUTION FROM THE INSTITUTO DE QUÍMICA AGRÍCOLA, MINISTÉRIO DA AGRICULTURA]

Chemistry of Brazilian *Leguminosae*. II.[1] Isolation and Structure of Caviunin

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Caviunin, an extractive from *Dalbergianigria* (Fr. Allem.) is shown to be 5,7-dihydroxy-2′,4′,5′,6-tetramethoxyisoflavone.

Since early Brazilian history, the wood of *Dalbergia nigra* (Fr. Allem.), a tree belonging to the *Dalbergiae* tribe of the *Leguminosae* family, has been a much valued article of export. The species is particularly abundant in the state of Espirito Santo, but occurs also in the neighbouring states of Bahia, Minas Gerais, Rio de Janeiro, and in São Paulo, where it is called jacarandá caviuna. In other countries, however, *Dalbergia nigra*[2] is known under different names, such as Brazilian rosewood[3]

(1) Paper I: O. R. Gottlieb and M. Taveira Magalhães, *Anais assoc. brasil. quim.*, 18, 89 (1959).

(2) An anatomical and dendrometric study of *Dalbergia nigra*, as well as a list of references to the botanical literature is given by A. de Mattos Filho and A. F. Coimbra Filho, *Arquivos do Serviço Florestal* (Rio de Janeiro), 11, 157 (1957).

(3) This name is an allusion to the red color of the heartwood and the species should not be confused with the essential oil-producing trees of the genus *Aniba* (family *Lauraceae*) which we have studied in several papers entitled, "The Chemistry of Rosewood." For the most recent article, Part VI in the series, see W. B. Mors, O. R. Gottlieb, and I. de Vattimo, *Nature*, 184, 1589 (1959).

(England), Palissandre (France) or Jacarandaholz (Germany). In spite of the economic importance of the jacarandá caviuna tree, the extractives of its wood do not seem to have previously received any attention.

Sapwood and heartwood[4] were investigated separately. The main crystalline constituent, which was found to be present in the benzene extract of the former, was a new substance which we have named caviunin. It was also obtained from the benzene extract of the heartwood, although it was there only a minor component. Work on its companion substances is now in progress.

Caviunin was easily isolated and purified through its sodium salt which is only slightly soluble in water. It formed colorless slender needles, having an empirical formula of $C_{19}H_{18}O_8$. Methoxyl determination revealed the existence of four such groups and the formation of a diacetate upon acetylation and a di-*O*-methyl ether derivative by methylation indicated the presence of two free hydroxyl groups in the molecule. Thus the formula could be written $C_{15}H_4O_2\cdot(OH)_2\cdot(OCH_3)_4$; it suggested a flavone or an isoflavone structure. The infrared spectrum supported this assumption; it showed the strong multiple absorption between 6 and 6.6 μ usually found in such systems. The ultraviolet spectrum also did not allow a clear distinction between flavone and isoflavone, as was demonstrated earlier in a variety of examples.[5] However, the intense band at 320–380 mμ, generally attributed to the chalcone chromophore of the flavones[6,7] was absent from the spectrum of caviunin.

Ready distinction between the two classes of substances is possible by mild alkaline treatment. Under such conditions flavones afford *o*-hydroxydibenzoylmethanes, whereas isoflavones yield benzyl-*o*-hydroxyphenyl ketones with the loss of one carbon atom (as formic acid).[8] Saponification of caviunin diacetate resulted in the formation of nearly three moles of acid instead of the two expected equivalents. The fact that a third mole of acid is formed would indicate an isoflavonic structure for caviunin. Furthermore, alkaline degradation, when applied to di-*O*-methylcaviunin, afforded in nearly quantitative yield a yellow crystalline substance, later shown to be II. Its empirical formula, $C_{14}H_6O_2(OCH_3)_6$, fitted the benzyl-*o*-hydroxyphenyl ketone which would be expected from di-*O*-methylcaviunin, if this, and hence also caviunin itself, were an isoflavone. The alternative possibility, *i.e.* a flavone structure for caviunin, was ruled out by the resistance of this degradation product to very vigorous alkaline treatment. β-Diketones, the corresponding degradation products of flavones, are unstable in alkali. The ultraviolet spectrum of II exhibited the three typical maxima of substituted desoxybenzoins.[8]

Potassium permanganate oxidation of caviunin yielded asaronic acid (2,4,5-trimethoxybenzoic acid) which was identified by direct comparison with an authentic sample. This compound could only have arisen from ring B of the isoflavone, since ring A, fused to the oxygen heterocycle, would be expected to suffer deep seated degradation under the conditions of the reaction. It was already known that carbon atom 2 of the heterocyclic ring was not substituted by an oxygen function, since, when this carbon atom was lost in the degradation of di-*O*-methylcaviunin (Ic) to the hexamethoxybenzyl *o*-hydroxyphenyl ketone (II), all oxygen atoms of the original molecule were still preserved. Thus the allocation of three methoxy groups to ring B, leaves for the remaining methoxyl and two hydroxyls only positions 5,6,7, and 8 of ring A.

The hexamethoxybenzyl *o*-hydroxyphenyl ketone (II) was very stable, even towards rather vigorous treatment with aqueous alkali. Fusion with alkali had to be employed to effect further cleavage. In this way homoasaronic acid (2,4,5-trimethoxyphenylacetic acid) (IV) and antiarol (3,4,5-trimethoxyphenol) (IIIb) were obtained. The former was identified by comparison with an authentic sample and by degradation to asaronic acid. The formation of a phenylacetic acid (besides a phenol) in this reaction is characteristic of isoflavones and was considered additional proof of such a structure for caviunin. Antiarol (IIIb) was identified by direct comparison with an authentic sample. Its formation through cleavage of di-*O*-methylcaviunin assigns to the three oxygen functions of ring A in caviunin the positions 5, 6, and 7.

Only one of the phenolic hydroxyls of caviunin was readily attacked by diazomethane. Resistance to methylation, together with a positive ferric chloride test and sparing solubility in aqueous alkali are indicative of a conjugated chelate system. Such a system would arise through hydrogen bonding in compounds of the *o*-hydroxy acetophenone type. One of the hydroxyls has, therefore, to be placed in position 5. This fact, together with the conclusion of the preceding paragraph, indicated that caviunin is a phenol with an unsubstituted *para*-position. A positive Gibbs test,[9] performed on mono-*O*-methylcaviunin, confirmed this finding.

(4) Wood samples were secured through the courtesy of Serviço Florestal and Jardim Botânico, both of the Ministério da Agricultura, Rio de Janeiro, and identified as *Dalbergia nigra* (Fr. Allem.), respectively, by Dr. Paulo Agostinho de Matos Araújo and Dr. Armando de Mattos Filho. They had been collected in the vicinity of Rio de Janeiro.

(5) F. Sondheimer and A. Meisels, *Tetrahedron*, 9, 139 (1960).

(6) K. Venkataraman in L. Zechmeister's *Progress in the Chemistry of Organic Natural Products*, Vol. 17, pp. 1–64, Springer Verlag, Wien (1959).

(7) W. K. Warburton, *Quart. Rev.*, 8, 70 (1954).

(8) For pertinent discussion and references see P. Crabbé, P. R. Leeming, and C. Djerassi, *J. Am. Chem. Soc.*, 80, 5258 (1958).

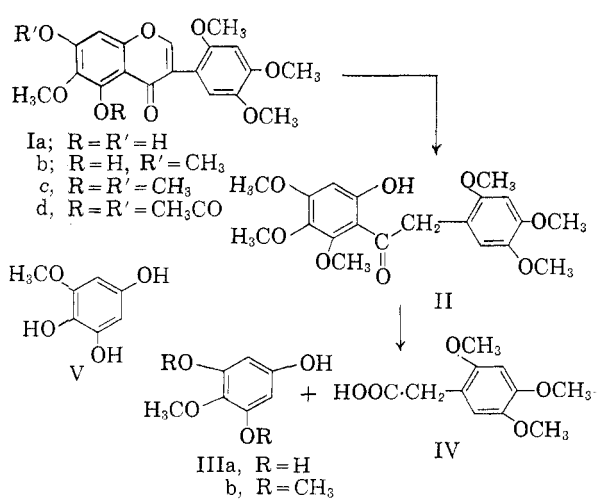
(9) F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, 563 (1957).

The indophenol chromophore was found at 680 mμ.

At this stage only the relative position of a hydroxy and a methoxy group on C-6 and C-7 remained to be established. Alkaline degradation of caviunin was used to settle this question. In contradistinction to its di-*O*-methyl ether, caviunin afforded easily, by refluxing with aqueous alkali, 2,4,5-trimethoxyphenylacetic acid (IV), originating, as before, from ring B, and a phenol, m.p. 184–186°, identified as iretol, 2,4,6-trihydroxyanisol (IIIa) (lit.[10] m.p. 186°). 2,3,5-Trihydroxyanisol (V), which would have arisen from this degradation if the methoxyl and hydroxyl had the alternative orientation in caviunin, has a reported[11] m.p. of 119–125°; it readily yields a colored quinone, which was not obtained from our product.

From these facts the structure of 5,7-dihydroxy-2′,4′,5′,6-tetramethoxyisoflavone (Ia) was assigned to caviunin.

According to a recent review,[6] only thirteen isoflavones, excluding those containing additional ring systems, have so far been isolated from plants. Although, as stated, these belong to widely different families, the isoflavone skeleton seems to be rather typical of the *Leguminosae-Papilionatae*. This phytochemical regularity is accentuated further, if the results of the present research are added to the reviewer's findings. The parent plants of both substances, cabreuvin [3′,4′,7-trimethoxyisoflavone; the isolation of which from *Myroxylon balsamum* (L.) Harms and *Myrocarpus fastigiatus* (Fr. Allem.) was reported in the previous paper of this series[1]] and caviunin here presented belong to this subfamily. Thus twelve out of the fifteen known naturally occurring simple isoflavones were found in *Papilionatae* species.[12]



This relationship between taxonomy and chemistry is emphasized by the fact that almost all known isoflavonoids which contain additional furan or pyran rings, are also found in leguminous plants. The majority of substances in this latter group is oxygenated in position 2′, osajin and pomiferin being exceptions, since they occur in the family *Moraceae* and are unsubstituted in position 2′. Oxygenation in position 2′ is comparatively rare among the flavonoids[13]; it is interesting that *Dalbergia nigra* which contains caviunin, the new 2′-substituted isoflavone described in the present paper, belongs to the same tribe *Dalbergiae* of the *Papilionatae*, as do the genera *Derris*, *Dipteryx*, *Piscidia*, *Tephrosia*, *Mundulea* in which the majority of 2′-oxygenated isoflavonoid structures seem to be concentrated.

Irigenin,[10] the aglucon of iridin which occurs in *Iris* and *Belamcanda* species (*Iridaceae* family) was up to now the only known natural derivative of the hexahydroxyisoflavone skeleton. The difference between caviunin and irigenin is the presence of a 2′-methoxyl in the former, as opposed to a 3′-hydroxyl in the latter.

EXPERIMENTAL[14]

Extraction procedure. (a) *From sapwood.* The white sapwood of *Dalbergia nigra* was reduced to sawdust and 1.22 kg. were then extracted exhaustively with benzene in a Soxhlet apparatus. After concentration, small quantities of basic and acidic materials were removed from the benzene solution with dilute hydrochloric acid and concentrated sodium bicarbonate solutions respectively. Upon addition of concentrated sodium carbonate solution (or 3% sodium hydroxide solution) a sodium salt precipitated which was separated by centrifugation and washed with water and benzene. A suspension of the white mass in water was acidified and extracted with chloroform. Evaporation of the solvent yielded 750 mg. of slightly yellow, crystalline crude caviunin (Ia), melting between 185–191°. The aqueous alkaline extraction and wash solutions were united, extracted with benzene to remove suspended organic material, and acidified. Chloroform extraction removed an oil. Its ethanol solution, by slow evaporation, afforded an additional amount of 250 mg. of crystals, m.p. 185–190°.

(b) *From heartwood.* The dark red heartwood was reduced to sawdust and 2.67 kg. were extracted exhaustively with benzene in a Soxhlet apparatus. Upon concentration of the benzene solution a crystalline mass settled out and was removed by filtration. By a series of fractional crystallizations from acetone this could be separated into two components, one less soluble, called J-1, as red crystals, m.p. 186–187° (dec., variable depending upon rate of heating) and another, J-2, as yellow needles, m.p. 112–113°. Upon addition of dilute hydrochloric acid to the benzene solution a dark brown mass precipitated which was taken up in chloroform. From both organic solutions basic and acidic material was removed by further extractions with dilute hydrochloric acid

(10) G. de Laire and F. Tiemann, *Ber.*, 26, 2015 (1893).

(11) R. Robinson and C. Vasey, *J. Chem. Soc.*, 660 (1941).

(12) Since this paper was completed, several other natural isoflavones were described. *Cf.* L. H. Briggs and T. P. Cebalo, *Tetrahedron*, 6, 145 (1959); T. B. H. McMurry and C. Y. Theng, *J. Chem. Soc.*, 1491 (1960).

(13) A. J. Birch in L. Zechmeister's *Progress in the Chemistry of Organic Natural Products*, Vol. 14, pp. 186–216, Springer Verlag, Wien (1957).

(14) Melting points were taken on a Kofler hot-stage microscope. Ultraviolet absorption spectra were performed with a Beckman model DU spectrophotometer. Infrared spectral measurements were recorded on a Perkin Elmer Infracord model 137 double beam spectrometer.

and concentrated sodium bicarbonate solutions. Upon treatment with concentrated sodium carbonate solution and working up of the precipitate as described under (a), 450 mg. of crude caviunin (Ia) were obtained.

Caviunin (Ia). Two recrystallizations of crude caviunin from ethanol provided white slender needles, m.p. 191–193°,[15] $[\alpha]_D$ 0° (*c* 1.0, chloroform). The substance sublimed unchanged. With alcoholic ferric chloride a violet color passing into dark green was observed. Infrared bands (in Nujol mull) occured *inter al.*, at 2.95, 6.00, 6.15, 6.30, 6.56, 8.25, 10.35, and 12.08 μ. The ultraviolet absorption spectrum in 95% ethanol solution (neutral and acidic conditions) exhibited maxima at 263 mμ (log ϵ 4.37) and 297 mμ (log ϵ 4.25), minima at 245 mμ (log ϵ 4.23) and 282 mμ (log ϵ 4.15). Upon addition of alkali the maxima were shifted to higher wavelength: λ_{max} 271 mμ (log ϵ 4.32) and 339 mμ (log ϵ 4.14); λ_{min} 254 (log ϵ 4.17) and 315 mμ (log ϵ 4.05).

Anal. Calcd. for $C_{19}H_{18}O_8$: C, 60.96; H, 4.85; 4 OCH_3, 33.16. Found: C, 61.23; H, 4.98; OCH_3, 32.95.

7-O-Methylcaviunin (Ib). Caviunin (Ia) (150 mg.) in ether solution was left overnight in presence of excess diazomethane. After evaporation, crystalline material, m.p. 181–186°, remained. Recrystallization from boiling ethanol afforded yellow needles, m.p. 185.5–187.5°. The ferric chloride test was positive. A blue-green color, λ_{max} 680 mμ was obtained with 2,6-dichlorobenzoquinone when the Gibbs test was performed according to the procedure of King, King, and Manning[9] in borate buffered solution of *p*H 9.3. The ultraviolet absorption spectrum in 95% ethanol solution (unchanged by acid) was practically identical with that of caviunin: λ_{max} 265 mμ (log ϵ 4.40) and 295 mμ (log ϵ 4.27); λ_{min} 246 mμ (log ϵ 4.24) and 283 mμ (log ϵ 4.20). In alkaline solution: λ_{max} 275 mμ (log ϵ 4.31) and 370 mμ (log ϵ 3.60); λ_{min} 255 mμ (log ϵ 4.19); and 332 mμ (log ϵ 3.30).

Anal. Calcd. for $C_{20}H_{20}O_8$: C, 61.85; H, 5.19; 5 OCH_3, 39.95. Found: C, 61.53; H, 5.13; OCH_3, 39.70.

5,7-Di-O-methylcaviunin (Ic). Caviunin was dried at 70° *in vacuo* and 250 mg. were dissolved in 15 ml. of acetone (dried over freshly ignited potassium carbonate). Purified dimethyl sulfate (0.3 ml.) and 0.8 g. of the ignited potassium carbonate were added. After the mixture had been heated for 14 hr. under reflux, 0.2 ml. of dimethyl sulfate and 0.4 g. of potassium carbonate were added and reflux time brought to a total of 40 hr. After cooling, the reaction mixture was treated with water and extracted with chloroform. Upon evaporation of the solvent white crystals, m.p. 152.5–153.5°, remained. By recrystallization from methanol the m.p. rose to 154.5–155.5°. The ferric chloride test was negative. The infrared spectrum in Nujol mull showed the absence of hydroxyl functions, λ_{max}, *inter al.*, at 6.09, 6.25, 7.83, 8.28, 8.70, 8.87, and 9.67 μ.

Anal. Calcd. for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51; 6 OCH_3, 46.27. Found: C, 62.62; H, 5.70; OCH_3, 45.10.

5,7-Di-O-acetylcaviunin (Id). Caviunin was dried at 70° *in vacuo* and 50 mg. was dissolved in a mixture of dry pyridine (1 ml.) and acetic anhydride (1 ml.). After 8 min. boiling and cooling to room temperature, water was added and the mixture extracted with chloroform. The organic solution was washed with dilute hydrochloric acid and sodium hydroxide solutions. Evaporation of the chloroform and recrystallization from cyclohexane-benzene 2:1 afforded 26.3 mg. of white crystals, m.p. 198–200°. The ferric chloride test was negative. The infrared spectrum showed the absence of hydroxyl functions and absorption maxima at 5.8 μ (ester) and 6.2 μ (α,β-unsaturated ketone), *inter al.*

Anal. Calcd. for $C_{23}H_{22}O_{10}$: C, 60.26; H, 4.84. Found: C, 59.97; H, 4.80. The substance (3.772 mg.) was refluxed with *N* methanolic sodium hydroxide during 90 min. The volatile acids were distilled and, upon titration, consumed 2.09 ml. 0.01 *N* sodium hydroxide, equivalent to 0.706 mg. CH_3CO— (calcd. for $2CH_3CO$—) and 0.131 mg. HCO— (calcd. by difference). Theoretically 0.238 mg. HCO— are available by decomposition of the isoflavone.

2,4,5-Trimethoxybenzyl 2-hydroxy-4,5,6-methoxyphenyl ketone (II). To 150 mg. of 5,7-di-*O*-methylcaviunin (Ic) 10 ml. of water were added and a slow current of nitrogen was passed through the mixture. After 5 ml. of a 10% aqueous sodium hydroxide solution had been admitted, the mixture was refluxed for 100 min., cooled to room temperature and the yellow solution extracted with chloroform. Upon evaporation of the solvent 145 mg. of crystalline material, m.p. 128.5–131°, was obtained. Recrystallization from methanol afforded pure 2,4,5-trimethoxybenzyl 2-hydroxy-4,5,6-methoxyphenyl ketone (II), yellow crystals, m.p. 129.5–131°. The ferric chloride test was positive. The same product (II) was obtained when 150 mg. of 5,7-di-*O*-methylcaviunin (Ic) were refluxed for 16 hr. under nitrogen with 10 ml. of a 22% aqueous solution of potassium hydroxide. Infrared bands (in Nujol mull) occurred *inter al.*, at 6.22, 8.28, 8.67, 9.10, and 9.62 μ. The ultraviolet absorption spectrum in 95% ethanol solution exhibited maxima at 220 mμ (log ϵ 4.19), 285 mμ (log ϵ 4.08) and 332 mμ (log ϵ 3.56); minima at 253 mμ (log ϵ 3.53) and 318 mμ (log ϵ 3.51). In alkaline solution λ_{max} 232 mμ (log ϵ 4.12), 285 mμ (log ϵ 3.70) and 353 mμ (log ϵ 3.47); λ_{min} 270 mμ (log ϵ 3.60) and 312 mμ (log ϵ 3.25).

Anal. Calcd. for $C_{20}H_{24}O_8$: C, 61.21; H, 6.17; 6 OCH_3, 47.44. Found: C, 61.05; H, 6.04; OCH_3, 47.13.

Iretol (IIIa) *and homoasaronic acid* (IV). To 150 mg. of caviunin 10 ml. of water were added and a slow current of nitrogen was passed through the mixture. After 5 ml. of a 10% aqueous solution of potassium hydroxide had been admitted, the mixture was refluxed for 3 hr. After cooling to room temperature, the current of nitrogen was replaced by one of carbon dioxide which was allowed to pass until saturation of the solution. Ether (free from peroxides) extraction afforded 39 mg. of oily material which was only slightly soluble in chloroform. After several days crystals slowly started to appear. These were separated and purified by vacuum sublimation providing colorless crystals of iretol (IIIa), m.p. 184–186° (lit.[10] m.p. 186°). The substance is not very stable.

Anal. Calcd. for $C_7H_8O_4$: C, 53.84; H, 5.16; 1 OCH_3, 19.88. Found: C, 53.33; H, 5.20; OCH_3, 19.98.

The aqueous solution was acidified and extracted again with ether. Upon evaporation of the solvent a cream colored solid remained which, by vacuum sublimation, afforded white crystals of 2,4,5-trimethoxyphenylacetic acid (IV), melting partially above 70°, recrystallizing and melting finally at 84–87° (lit.[16,17] m.p. 87°). A sample of 2,4,5-trimethoxyphenylacetic acid which was synthetized by hydrolysis of 2,4,5-trimethoxyphenylacetonitrile[18] showed the same melting behavior and did not depress the melting point of the degradation product IV.

Anal. Calcd. for $C_{11}H_{14}O_5 \cdot H_2O$: C, 54.09; H, 6.60; 3 OCH_3, 38.12. Found: C, 54.36; H, 6.55; OCH_3, 37.92.

Upon oxidation of the degradation product IV with alkaline potassium permanganate (by the procedure outlined under the heading "Asaronic acid"), 2,4,5-trimethoxybenzoic acid, m.p. and mixture m.p. with an authentic sample 144–145.5°, was obtained. The infrared spectra of both samples were superimposable. Nitration yielded 1-nitro-2,4,5-trimethoxybenzene, m.p. 128–130° (lit.[16] m.p. 129°).

Antiarol (IIIb) *and homoasaronic acid* (IV). 2,4,5-Trimethoxybenzyl 2-hydroxy-4,5,6-methoxyphenyl ketone (II) (145 mg.), 5% methanolic potassium hydroxide solution (3 ml.) and water (0.5 ml.) were heated slowly to 180° in a platinum crucible. The temperature was maintained at

(15) During several melting point determinations of caviunin samples a second melting point followed at 197–198°.

(16) S. Takei, S. Miyajima, and M. Ono, *Ber.*, **65**, 288 (1932).

(17) The literature records also different melting points, which is due, probably, to the existence of hydrates; *cf.* ref. 18.

(18) A. Robertson and G. L. Rusby, *J. Chem. Soc.*, 1371 (1931).

180° during 15 min. After cooling to room temperature, the product was taken up in water and washed with chloroform. The aqueous solution was saturated with carbon dioxide and again extracted with chloroform. Upon evaporation of the solvent an oily mass remained which was submitted to vacuum sublimation at 120°, 0.005 mm. Two resublimations yielded colorless crystals of antiarol (IIIb) (5 mg.), m.p. 144–146° (lit.[3] m.p. 145.5–146°). Identity with an authentic sample was established by mixture melting point determination and by infrared spectral comparison; λ_{max} (in Nujol mull) 3.03, 6.16, 12.16, and 12.84 μ.

The degradation product IIIb was treated with boiling acetic anhydride and anhydrous sodium acetate. Crystallization from ethanol afforded colorless prisms of *O*-acetylantiarol, m.p. 73–74° (lit.[19] 74°).

The above aqueous solution was now acidified with dilute hydrochloric acid and extracted with ether. Evaporation of the solvent afforded a crystalline mass which was purified by three vacuum sublimations to yield colorless crystals of homoasaronic acid (IV), melting partially at 78°, resolidifying and melting finally at 84–87° (lit.[16] m.p. 87°). Identity of this product was established as outlined above.

Asaronic acid. A solution of caviunin (Ia) (90 mg.) in 5 ml. of 3% aqueous sodium hydroxide was treated at 50° with small portions of potassium permanganate solution until the consumption of the oxidant subsided. The excess permanganate was reduced with sodium sulfite, the precipitate separated by filtration and washed with 3% sodium hydroxide solution. The combined filtrates were acidified and extracted with chloroform. The organic layer was washed with concentrated sodium bicarbonate solution. This yielded, after acidification and extraction with chloroform, 40 mg. of a slightly yellow solid which was washed with a little ethanol. Vacuum sublimation afforded white crystals of asaronic acid, m.p. 144–145° (lit.[16] m.p. 144–145.5°). Identity with an authentic sample of 2,4,5-trimethoxybenzoic acid was established by mixture melting point determination and infrared spectral comparison; λ_{max} (in Nujol mull), *inter al.*, 5.80, 6.00, 7.77, 8.23, 9.26, and 9.80 μ. Nitration yielded 1-nitro-2,4,5-trimethoxybenzene,[16] m.p. and mixture m.p. with an authentic sample 128–130°.

Oxidation of caviunin (Ia) with alkaline hydrogen peroxide[20] also yielded asaronic acid.

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RIO DE JANEIRO, BRAZIL

(19) E. Chapmann, A. G. Perkin, and R. Robinson, *J. Chem. Soc.*, 3028 (1927).

(20) O. A. Stamm, H. Schmid, and J. Büchi, *Helv. Chim. Acta*, 41, 2006 (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY, BRISTOL, AND THE DEPARTMENT OF ORGANIC CHEMISTRY, UNIVERSITY OF BRISTOL]

Synthesis of Isoflavones. Part III.[1] Caviunin

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The synthesis of caviunin (5,7-dihydroxy-2′,4′,5′,6-tetramethoxyisoflavone) using the ethoxalylation method is described.

At the suggestion of Dr. Gottlieb and Dr. Magalhães, whose interest we are pleased to acknowledge, we have investigated the synthesis of caviunin whose determination of structure is described in the preceding paper.[2] Of the various methods which are available for the synthesis of isoflavones,[3] the method due to Baker and Ollis[4] involving the reaction of benzyl *o*-hydroxyphenyl ketones with ethoxalyl chloride is particularly suitable for the synthesis of isoflavones bearing several hydroxyl groups.

Caviunin is one of the more unusual types of isoflavone in that it is a derivative of 5,7-dihydroxy-6-methoxyisoflavone. This class includes tectorigenin (I), irigenin (II), and podospicatin[5] (III) as well as caviunin (IV). Previously the synthesis of isoflavones in this class has presented some difficulty but recently it was shown that the ethoxalylation method could be used for the synthesis of tectorigenin and irigenin.[6] By a similar method, the followed synthesis of caviunin has been achieved.

Hoesch condensation of iretol and 2,4,5-trimethoxybenzyl cyanide yielded the benzyl *o*-hydroxyphenyl ketone (VII). This ketone was treated with ethoxalyl chloride in pyridine solu-

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