

# The chemistry of Brazilian Lauraceae. LXV. 5, 7, 8, 3', 4', 5' - Hexamethoxyflavone from an *Aniba* species

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## Abstract

*Aniba* species (Lauraceae) are characterized by the presence of neolignans or of 6-aryl (or 6-styryl)-2-pyrone. Flavonoids occur either together with pyrones or, in rare cases, as predominant micromolecular type. The branch wood of an *Aniba* species from Marapí, Parú do Oeste River, near Tiriós (Pará State), constitutes such a case. It contains 5,7,8,3',4',5'-hexamethoxyflavone, obtained for the first time from a natural source.

## INTRODUCTION

One of the chemosystematically significant results of our studies on the genus *Aniba* (family Lauraceae) (for the previous part of the series see Dias *et al.*, 1981) concerns the neat dichotomy between neolignan *versus* pyrone containing species (Gottlieb & Kubitzki, 1981). Not once both types of compounds have yet been reported for a single species. This fact is apparently associated with reduction in biosynthetic capability. Allylphenols and propenylphenols, the oxidative coupling of which leads to neolignans, are end products of the shikimate pathway (see Fig. 5 in Gottlieb, 1980). Blocking of reaction steps would imply the availability of cinnamates as biosynthetic starting materials for pyrones, benzophenones and flavonoids. Indeed, these latter groups or micromolecules do occur together, as in *A. rosaeodora* Ducke and *A. duckei* Kosterm. (now merged under the former binomial by Kubitzki, 1982), as well as in *A. coto* (Rusby) Kosterm. and *A. pseudocoto* (Rusby) Kosterm. (the validity of the latter binomial being questioned by Kubitzki, 1982) (Gottlieb, 1972, and references cited therein). In rare cases species which use cinnamates as starting material for

the synthesis of secondary metabolites may even accumulate flavonoids to the apparent exclusion of pyrones. This phenomenon has been noted so far only once for *A. riparia* (Nees) Mez which was reported to contain, besides a relatively large proportion of tri-O-methylgalangin (1a) (Franca *et al.*, 1976), lesser quantities of izalpinin (1b), di-O-methylpinocembrin (2a), pinostrombin (2b), flavokawin-B (3) and 3-hydroxy-5,7-dimethoxyflavanone (4) (Fernandes *et al.*, 1978). All these flavonoids possess 5,7-dioxygenated A-rings and unsubstituted B-rings. Except for pinocembrin (2c), which was isolated from *A. rosaeodora* (Gottlieb & Mors, 1958), all are strongly O-methylated.

## RESULTS

The botanical material with which the present report is concerned, registered under number 14952 in the Herbarium of EMBRAPA, Pará, was collected from a tree growing at Marapí, Parú do Oeste River, near Tiriós (Pará State). Professor Klaus Kubitzki, Hamburg University, albeit unable to identify the material conclusively on account of its sterile condition, suggested that it should either belong to *Aniba burchelli* Kosterm. or to a new species.

An extract of branch wood failed to yield burchellin (Lima *et al.*, 1972) and related neolignans (Alvarenga *et al.*, 1977). Compound 5 was isolated instead. Its structural elucidation was based on the molecular formula  $C_{21}H_{22}O_8$ , determined by high resolution mass spectrometry. Analysis of the proton nuclear magnetic resonance spectrum allowed this formula to be expanded to  $C_{15}H_4(OMe)_6$  which, together with the infrared and ultraviolet

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spectra, suggested the existence of a basic flavone skeleton. Indeed, the typical H-3 singlet was registered at  $\delta$  6.60. The three additional yet undefined protons were represented by two singlets: one at  $\delta$  6.93, which can only stand for two symmetrical H-2' and H-6', and one at  $\delta$  6.36, which can only stand for H-6,  $\delta$  6.80 being typical for H-8 on a 5,6,7-trimethoxylated flavone (Henrick & Jefferies, 1964). 5,6,7,3',4',5'-Hexamethoxyflavone differs from the compound in question also on account of its melting point (152-154° (Braz Filho & Gottlieb, 1971) versus 120-121° for 5).

## DISCUSSION

Thus still another *Aniba* species in which so far neither neolignans nor pyrones could be located, contains a flavonoid in its trunk wood. The compound (5), the first flavone to be described for an *Aniba*, has a surprisingly high oxidation level. Tri-oxygenated cinnamate derived B-rings have not been reported previously for pyrones, benzophenones or flavonoids from *Aniba*. In contrast, *Aniba* species of the neolignan group contain either di-oxyphenyl or tri-oxyphenyl substituted neolignans and the feature is thus of clear systematic importance (Fernandes *et al.*, 1978). Furthermore, the acetate derived ring is oxygenated at C-8. Extra A-ring oxygenation of flavonoids can occur at C-6 or at C-8; the former mode characterizing compounds from species of the relatively advanced subclass Asteridae (*sensu* Cronquist, 1968) and the latter mode characterizing the relatively primitive angiosperms belonging, e.g., to the Ranunculaceae, Papaveraceae (Harborne, 1977) and, as shown in the present paper, Lauraceae. The per-methylation of the novel compound 5 is in line with the fact that most micromolecules from *Aniba* species are strongly O-methylated.

While 5,7,8,3',4',5'-hexamethoxyflavone was not reported previously as a natural product, four less fully O-methylated derivatives of 5,7,8,3',4',5'-hexahydroxyflavone were isolated from *Gardenia* (Rubiaceae) species (Wollenweber & Dietz, 1981). The structure of 5,3'-dihydroxy-7,8,4',5'-tetramethoxyflavone, attri-

buted in the review by Wollenweber & Dietz (1981) to a compound from *Lychnophora affinis* Gardn. (Asteraceae) has recently been revised to 5,3'-dihydroxy-3,7,4',5'-tetramethoxyflavone (Le Quesne *et al.*, 1979). Interest in such highly oxygenated flavonoids was stimulated by observations that some of them showed activity versus the KB cell culture (Edwards *et al.*, 1979). Our compound from *Aniba* should, consequently, also be submitted to pharmacological testing.

## EXPERIMENTAL

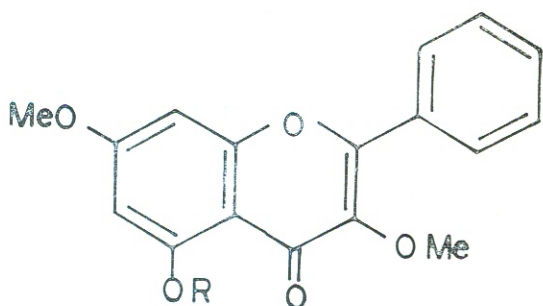
*Isolation of the flavone.* Powdered branch wood (1.8 kg) was percolated with light petrol. The extract (350 mg) was separated by preparative TLC (Si gel, C<sub>6</sub>H<sub>6</sub>-AcOEt 4:1) into a more polar fraction (200 mg) and a less polar fraction (100 mg). The latter was purified by repeated TLC (Si gel, C<sub>6</sub>H<sub>6</sub>-AcOEt 6:4) to 5,7,8,3',4',5'-hexamethoxyflavone (8 mg).

5,7,8,3',4',5'-Hexamethoxyflavone, mp 120-121° (C<sub>6</sub>H<sub>6</sub>) (Found: 402.1394; C<sub>21</sub>H<sub>22</sub>O<sub>8</sub> requires: 402.1315). UV  $\lambda_{\text{max}}^{\text{MeOH}}$  nm: 235, 266, 316 (9800, 6030, 12100). IR  $\nu_{\text{max}}^{\text{KBr}}$  cm<sup>-1</sup>: 1629. <sup>1</sup>H NMR (60 MHz, CCl<sub>4</sub>)  $\delta$ : 6.93 (s, H-6'), 6.60 (s, H-3), 6.36 (s, H-6), 3.95 (s, OCH<sub>3</sub>), 3.92 (s, OCH<sub>3</sub>, OCH<sub>3</sub>), 3.88 (s, OCH<sub>3</sub>), 3.80 (s, OCH<sub>3</sub>, OCH<sub>3</sub>). MS m/z (rel. int.): 402 (9), 388 (5), 387 (19), 343 (7), 151 (9), 145 (20), 113 (9), 69 (100), 57 (5).

## ACKNOWLEDGEMENTS

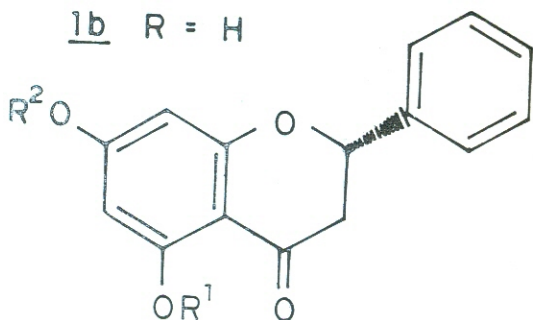
This work was supported by grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico, Financiadora de Estudos e Projetos and Fundação de Amparo à Pesquisa do Estado de São Paulo; as well as by a CNPq research fellowship to M. Y. and a CAPES-PICD graduate fellowship (to S.H.C.). The authors are indebted to Dr. Paul M. Baker, NPPN, Universidade Federal do Rio de Janeiro, for MS.

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1a R = Me

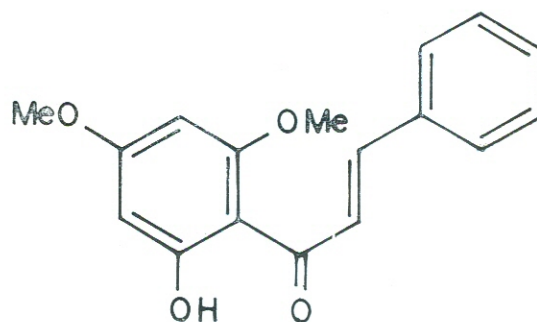
1b R = H



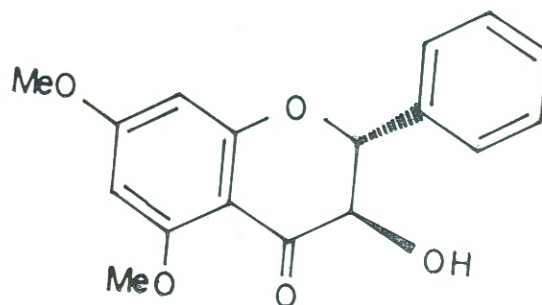
2a R<sup>1</sup> = R<sup>2</sup> = Me

2b R<sup>1</sup> = H, R<sup>2</sup> = Me

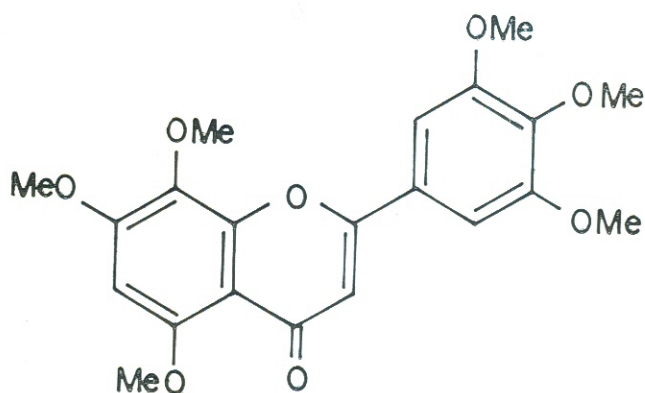
2c R<sup>1</sup> = R<sup>2</sup> = H



3



4



5

#### SUMMARY

Espécies de *Aniba* (Lauraceae) são caracterizadas pela presença de neolignanas ou de 6-aryl-(ou 6-estiril-) 2-pironas. Flavonoides ocorrem seja juntos com pironas, seja, em raros casos, como tipo micromolecular predominante. A madeira dos ramos de uma espécie de *Aniba* coletada em Marapi, no alto rio Paru do Oeste, nas proximidades de Tiriós (Pará), constitui um caso desta índole. Contém 5,7,8,3',4',5'-hexametoxiflavona, obtida pela primeira vez de fonte natural.

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