Phytochemistry, 1973, Vol. 12, pp. 1805 to 1808. Pergamon Press. Printed in England.

GUIANIN: A NEOLIGNAN FROM *ANIBA GUIANENSIS**

MARIA VITTORIA VON BÜLOW, NIDIA CAVALCANTI FRANCA, OTTO RICHARD GOTTLIEB and AURA MARIA PUENTES SUAREZ†

Laboratório de Produtos Naturais da Fundação de Amparo à Pesquisa do Estado de São Paulo, Instituto de Química, Universidade de São Paulo, Brasil

(*Received* 5 *December* 1972. *Accepted* 23 *January* 1973)

Key Word Index—*Aniba guianensis*; Lauraceae; benzyl benzoate, benzyl salicylate; *O*-methyleugenol; *O*-methylisoeugenol; neolignan; guianin; 1-allyl-8-hydroxy-3-methoxy-7-methyl-4-oxo-6-piperonylbicyclo-[3,2,1]oct-2-ene.

Abstract—The wood of *Aniba guianensis* Aubl. (Lauraceae) contains benzyl benzoate, benzyl salicylate, sitosterol, *O*-methyleugenol, *O*-methylisoeugenol and the neolignan guianin for which the structure of 1-allyl-8-hydroxy-3-methoxy-7-methyl-4-oxo-6-piperonylbicyclo[3,2,1]oct-2-ene (VI) is proposed.

Aniba guianensis Aubl. is an arboreous Lauraceae species which grows in the Amazon region. The trunk wood yielded *O*-methyleugenol, *O*-methylisoeugenol, benzyl benzoate, benzyl salicylate, sitosterol and a new compound for which the name guianin is proposed. The formula $C_{18}H_{16}O \cdot OH \cdot O_2CH_2 \cdot OCH_3$, suggesting a *bis*-$C_6 \cdot C_3$ skeleton, and the PMR spectrum, showing features reminiscent of burchellin (I)[2] and of porosin (II),[3] classified the compound as a neolignan.[4] Electron bombardment cleaves guianin cleanly into two radical ions. The structure III was assigned to one of the fragments, *m/e* 162, in view of previous experience with burchellin (I).[2] This indicates the existence of the constitutional moiety IV in guianin. Indeed, the 220 MHz PMR spectrum contains evidence for the piperonyl group (τ 3·34, *d*, *J* 8·0 Hz [1H]; τ 3·47, *d*, *J* 8·0 [1H]; τ 3·49, *s* [1H]; τ 4·18, *s* [2H]) and the methyl group (τ 8·77, *d*, *J* 7·0 Hz [3H]) linked to a tertiary carbon atom. The proton at this centre gives rise to a quintuplet (τ 7·78, *J* 7·0 Hz, rel. peak int. 1:4:6:4:1), thus revealing vicinality not only to the benzylic proton, but also to a quaternary carbon atom. The benzylic proton can only be associated with the triplet (*J* 7·0 Hz) at τ 6·45 of the PMR spectrum, and must, consequently, be situated in the vicinity of a further tertiary centre.

The undefined quaternary and tertiary centres of III must, of course, belong to the additional $C_6 \cdot C_3$ unit which gives rise in the mass spectrometer to the second major fragment ion, *m/e* 180·0813 ($C_{10}H_{12}O_3$ requires: 180·0786). The hexacycle of this unit contains an α,β-unsaturated ketone (ν_{max}^{KBr} 1681 cm^{-1}) which sustains only one isolated olefinic proton. The corresponding PMR singlet, occurring at relatively low field (τ 3·90),

* Part XXIV in the series "The Chemistry of Brazilian Lauraceae". For Part XXIII see Ref. 1. Sponsored by Instituto Nacional de Pesquisas da Amazônai, Conselho Nacional de Pesquisas, Manaus.

† Multinational Program in Chemistry, Organization of American States, graduate fellow, 1971–2.

[1] LEÃO DA SILVA, M., SOARES MAIA, J. G., ANDRADE DA MATA REZENDE, C. M., and GOTTLIEB, O. R. (1973) *Phytochemistry* **12**, 471.

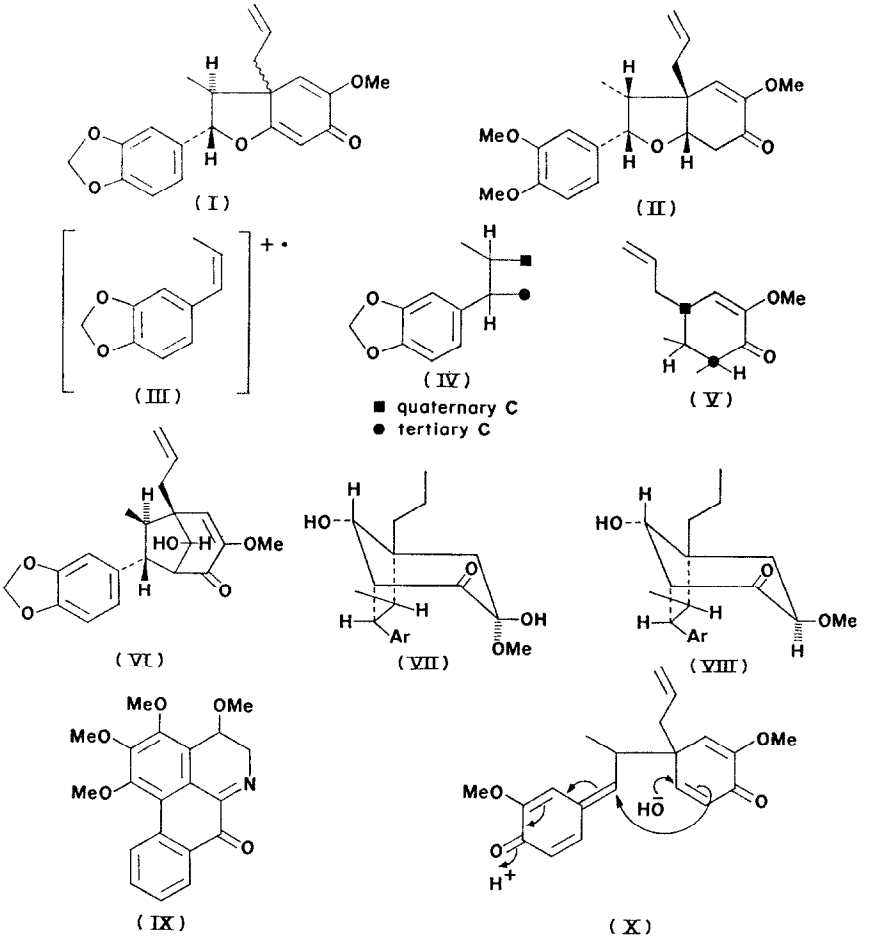
[2] AIBA, C. J., BRAZ FILHO, R. and GOTTLIEB, O. R. (1973) *Phytochemistry* **12**, 413.

[3] ARAÚJO LIMA, O., GOTTLIEB, O. R. and TAVEIRA MAGALHÃES, M. (1972) *Phytochemistry* **11**, 2031.

[4] GOTTLIEB, O. R. (1972) *Phytochemistry* **11**, 1537.

places the proton at the β-position, implying the presence of the enolic methoxyl (τ 6·38, *s*) at the α-position and the existence of a quaternary C-atom at the γ-position. An allyl group is inserted at this chiral centre, the PMR signals due to the methylene (τ 7·36, *dd*, *J* 14·0 and 7·0 Hz; τ 7·60, *dd*, *J* 14·0 and 7·0 Hz) and vinyl (τ 4·05–4·25, *m*; =CH; τ 4·68–4·87, *m*, $=CH_2$) protons showing comparable chemical shifts, and identical multiplicities and coupling constants in the PMR spectra of burchellin (I),[2] of porosin (II)[3] and of guianin.

While the structural moiety V, which thus emerges, clearly defines the quaternary centre indicated in IV, two alternatives for the definition of the tertiary C-atom are offered. The proton of this centre, however, gives rise to a PMR doublet at such a low field (τ 6·81, *J* 7·0 Hz), that it must be located in the anisotropically deshielded region vicinal to the carbonyl system.



These data lead to constitution VI for guianin. The secondary nature of the alcohol function is confirmed upon comparison of the PMR spectra of the natural compound and of its acetate. The carbinolic proton signal, suffering a paramagnetic shift from 6·02 to 4·86 (Δ 1·16 ppm) is easily identified. It consists substantially of a singlet. Coupling of the carbinolic proton to the vicinal methine proton is thus quite inefficient, and indeed, this

methine proton signal was already indicated above to be a doublet. A Dreiding model of V shows that the dihedral angle between the H–C–C–H unit involving a carbinolic proton oriented towards the hexacycle is about 82°. For such an arrangement, the Karplus equation[5] gives indeed J_{vic} 0. The hydroxyl must, consequently, be oriented towards the pentacycle, probably *cis* to the benzylic proton, whose PMR triplet suffers a diamagnetic shift from 6·45 to 6·63 (Δ 0·18 ppm) upon acetylation. An identical number of bonds separates the hydroxyl from the benzylic proton and the methylene protons of the allyl group. It is thus not surprising that an analogous shift from 7·36 to 7·53 (Δ 0·17 ppm) occurs also with the double quartet representing one of these methylene protons. The double quartet representing the other methylene proton is shifted to a considerably lesser extent from 7·60 to 7·66 (Δ 0·06 ppm).

The *trans* relationship between the vicinal aryl and methyl substituents is suggested by the chemical shift of the methyl protons (τ 8·77). In analogy with 2-aryl-3-methyl-2,3-dihydrobenzofurans,[2,3] the *cis* relationship, in which the C–Me group falls into the magnetically protected region above the aromatic system, would be expected to lead to a signal at about τ 9·3. The relative stereochemistry shown in VI is thus tentatively proposed for guianin.

Since catalytic hydrogenation of VI should take a predictable course, leading to the epimeric tetrahydroderivatives VII and VIII, this reaction was performed on guianin to collect additional evidence for the structural proposal. The reaction product gave PMR singlets due to methylenedioxy (τ 4·12 and 4·08, rel. int. 2:1) and methoxy (τ 7·31 and 6·81, rel. int. 2:1) protons, and should thus be composed of VII and VIII in the proportion 2:1. Addition of hydrogen from the β-side of the hexacycle is clearly favoured over addition from the sterically hindered α-side. β-Addition forces the methoxyl into the α-axial situation in which the vicinal carbonyl is able to exert maximal anisotropic shielding on its protons. The respective chemical shift value of τ 7·31 is consistent with this deduction. A signal at even higher field (τ 7·96) has been reported for the protons of the aliphatic methoxyl of dihydroimenine (IX).[6]

Additional information, derived from the PMR spectrum of the tetrahydroguianin mixture, concerned the methyl groups which had been formed through addition of hydrogen to the terminal vinyl group of guianin (VI). As expected, they give rise to a 1:2:1 triplet (J 7·0 Hz) at an identical chemical shift value (τ 8·70). In contradistinction, the doublets due to the ring C-methyl protons appeared a slightly different field, around τ 9, for VII and VIII.

In *Aniba guianensis*, isoeugenol and eugenol seem to be metabolized along two routes. Either they are inactivated by transformation into the corresponding methyl ethers, or they suffer intermolecular oxidative coupling to a quinone methide.[4] Erdtman postulated that such intermediates might add water,[7] a reaction which, occurring as indicated (X), would lead to a guianin type.

EXPERIMENTAL

For experimental techniques see Ref. 2.

Isolation of the constituents of A. guianensis. The EtOH extract of the wood (13·5 kg) was extracted with C_6H_6. The benzene was evaporated and the residue (60 g) was chromatographed on silica (400 g). The

[5] KARPLUS, M. (1963) *J. Am. Chem. Soc.* **85**, 2870.

[6] GLICK, M. D., COOK, R. E., CAVA, M. P., SRINIVASAN, M. KUNITOMO, J. and DA ROCHA, A. I. (1969) *Chem. Commun.* 1217.

[7] ERDTMAN, H. (1933) *Biochem. Z.* **258**, 177; (1933) *Ann. Chem.* **503**, 283; (1968) in *Recent Advances in Phytochemistry* (MABRY, T. J., ALSTON, R. E. and RUNECKLES, V. C., eds.), Vol. 1, p. 13, Appleton-Century-Crofts, New York.

following compounds were eluted in order with the indicated solvents: mixture of benzyl benzoate and benzyl salicylate (C_6H_6), benzyl salicylate (C_6H_6), mixture of *O*-methyleugenol and iso-*O*-methyleugenol (C_6H_6–$CHCl_3$ 9:1), sitosterol (C_6H_6–$CHCl_3$ 6:4), guianin (728 mg, $CHCl_3$). The mixtures were resolved by preparative GLC.

Guianin (V). Needles, m.p. (189–90° (C_6H_6–$CHCl_3$). M: Found 342·1563. $C_{20}H_{20}O_5$ requires: 342·1467. λ_{max}^{EtOH} (nm). 235, 265 (ε 8600, 10 300). ν_{max}^{KBr} (cm^{-1}). 3460, 1681, 1626, 929. PMR (220 MHz, $CDCl_3$, τ): 3·34 (*d*, *J* 8·0 Hz, ArH–5); 3·47 (*d*, *J* 8·0 Hz, ArH–6); 3·49 (*s*, ArH–2); 3·90 (*s*, CH=COMe); 4·18 (*s*, O_2CH_2); 4·05–4·25 (*m*, CH=CH_2); 4·68–4·87 (*m*, CH=CH_2); 6·02 (*s*, CHOH); 6·38 (*s*, OCH_3); 6·45 (*t*, *J* 7·0 Hz, ArCH); 6·81 (*d*, *J* 7·0 Hz, CHCO); 7·36 (*dd*, *J* 7·0 and 14·0 Hz, CH–CH=CH_2); 7·60 (*dd*, *J* 7·0 and 14·0 Hz; CH–CH=CH_2); 7·59 (*s*, OH); 7·78 (quintuplet, *J* 7·0 Hz, CHMe); 8·77 (*d*, *J* 7·0 Hz, CH_3). MS: M 342 (100%), *m/e* (%) 314 (5), 311 (3), 309 (3), 301 (3), 297 (3), 283 (10), 271 (8), 240 (5), 181 (8), 180 (28), 179 (20), 178 (6), 177 (7), 176 (7), 175 (12), 167 (6), 165 (12), 164 (18), 163 (20), 162 (95), 161 (15), 152 (10), 151 (11), 149 (14), 147 (10), 140 (12), 135 (12), 131 (16), 121 (12), 119 (12), 117 (17), 115 (10), 113 (12), 108 (12), 106 (17), 104 (12), 103 (12), 102 (18). The *acetate* was obtained (Ac_2O, pyridine, room temp., 15 hr) as crystals, m.p. 124–5° (EtOH). ν_{max}^{KBr} (cm^{-1}). 1739, 1692, 1613, 1227, 1142, 1081, 928. PMR (220 MHz, $CDCl_3$, τ). 3·35 (*d*, *J* 8·0 Hz, ArH–5); 3·47 (*d*, *J* 8·0, ArH–6); 3·49 (*s*, ArH–2); 3·90 (*s*, CH=COMe); 4·18 (*s*, O_2CH_2); 4·1–4·3 (*m*, CH=CH_2); 4·77–4·95 (*m*, CH=CH_2); 4·86 (*s*, CHOAc); 6·39 (*s*, OCH_3); 6·63 (*t*, *J* 7·0 Hz, ArCH); 6·77 (*d*, *J* 7·0 Hz, CHCO); 7·53 (*dd*, *J* 7·0 and 14·0 Hz, CH–CH–CH_2); 7·66 (*dd*, *J* 7·0 and 14·0 Hz, CH–CH=CH_2); 7·89 (*s*, $OCOCH_3$); 8·77 (*d*, *J* 7·0 Hz, CH_3). MS. M 384 (100%), *m/e* (%) 323 (87), 308 (35), 283 (62), 282 (100), 239 (27), 179 (30), 177 (47), 162 (47), 161 (72). The *tetrahydroguianins* were obtained (H_2, Pd–C, EtOH) as crystals, m.p. 157–73°. ν_{max}^{film} (cm^{-1}): 3485, 1721. MS. M 346 (15%), *m/e* (%) 330 (100), 179 (83), 162 (99), 149 (67), 135 (88).

Acknowledgement—The authors are indebted to Professor E. Wenkert, Indiana University, Bloomington, Ind., U.S.A., for the MS and the PMR.