Phytochemistry, 1980, Vol. 19, pp. 1859–1860. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0801-1859 $02.00/0

CECILIN, A 1-BENZYL-β-CARBOLINE FROM *ANIBA SANTALODORA**

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(*Received* 5 *November* 1979)

Key Word Index—*Aniba santalodora*; Lauraceae; benzyl benzoate, 1-*p*-hydroxybenzyl-6-methoxy-β-carboline; cecilin.

Abstract—The trunk wood of *Aniba santalodora* (Lauraceae) contains benzyl benzoate and a novel alkaloid, 1-*p*-hydroxybenzyl-6-methoxy-β-carboline.

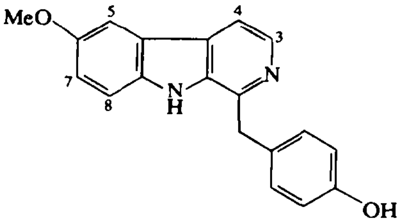
INTRODUCTION

Wood of *Aniba santalodora* Ducke, 'louro umiri', a lauraceous tree from the Manaus region of Amazonas State, Brazil, upon solvent extraction yielded an oily constituent, identified as benzyl benzoate, and a crystalline substance called cecilin.

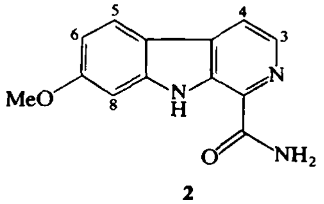
RESULTS AND DISCUSSION

The structural proposal **1** for cecilin was based on its ^{1}H NMR spectrum which shows an AA'BB' system at τ 2.82 and 3.35 (shifted to τ 2.56 and 2.96 in cecilin acetate) characteristic of a 4-hydroxyphenyl group, a singlet (τ 5.67) for the benzylic protons, the typical H-3, H-4 doublets (τ 1.78 and 2.04, $J = 5$ Hz) of the carboline unit, a singlet (τ 6.13) for the methoxyl, besides two doublets (τ 2.22, $J = 2.0$ and 2.47, $J = 8.5$ Hz) and one double-doublet (τ 2.79, $J = 2.0$ and 8.5 Hz) assigned respectively to H-5, H-8 and H-7. The only alternative assignment compatible with these multiplicities and coupling constants was ruled out by comparison of the chemical shifts with those of H-8 (τ 2.66, $J = 2.1$ Hz), H-5 (τ 1.88, $J = 8.6$ Hz) and H-6 (τ 3.13, $J = 2.1$ and 8.6 Hz) for the model compound **2** (in the same DMSO-solvent [2]).

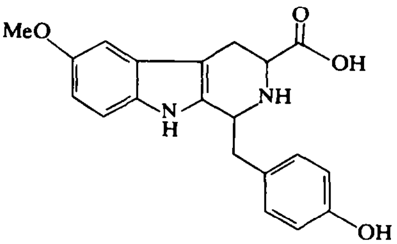
The structural proposal for cecilin was confirmed by a two-step synthesis involving condensation of (±)-5-methoxytryptophan with *p*-hydroxyphenylpyruvic acid [3] to **3** and concomitant oxidation/decarboxylation of this intermediate to **1**. The condensation procedure was adapted from procedures described for mechanistically analogous reactions of tryptophans or tryptamines with phenylacetic aldehydes [4–6] and of tryptamines with phenylpyruvic acid [7]. The aromatization procedure has been used previously for similar purposes [8, 9].



1



2



3

While benzyl benzoate has been isolated from most *Aniba* species [10], tryptophan-derived alkaloids, such as 2-*N*-methyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline from *Nectandra megapotamica* (Sprg.) Chod. et Hassl. [11], are very rare in Lauraceae. The common alkaloids of this family, and the genus *Aniba* is no exception [12], are derived from phenylalanine [13].

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[*] Part LX in the series "The Chemistry of Brazilian Lauraceae". For Part LIX see ref. [1].

Cecilin (**1**) is of mixed biosynthetic origin, deriving from both these aromatic amino acids. A recent review on β-carboline alkaloids does not report a single representative of this type [14], such derivation is therefore a rare feature indeed for a natural product.

EXPERIMENTAL

Isolation of constituents. Air-dried, ground trunk wood (4 kg), obtained from a sample collected between km 14 and 19 of the Manaus–Itacoatiara road and identified by the botanist Dr. William A. Rodrigues, was percolated with EtOH. The solvent was evapd and the residue (400 g) extracted with petrol in a Soxhlet apparatus. The solvent was evapd and the residue (20 g) chromatographed on Si gel. Elution with $CHCl_3$ and $CHCl_3$–MeOH (19:1) gave respectively benzyl benzoate and a product which, when recrystallized from EtOH, gave cecilin.

Cecilin (**1**), mp 224–228° dec. (EtOH) (Found: C, 75.20; H, 5.15; N, 9.79. $C_{19}H_{16}O_2N_2$ requires: C, 74.98; H, 5.30; N, 9.20%). λ_{max}^{EtOH} (nm): 232, 248 sh, 293 sh, 299, 355, 380 sh. (22 700, 17 650, 10 950, 15 200, 3650, 3650). $\lambda_{max}^{EtOH+NaOH}$ (nm): 238, 248 sh, 299, 355, 380 sh (21 100, 15 950, 10 950, 3000, 3000). ν_{max}^{KBr} (cm^{-1}): 3400, 3230, 1605, 1580, 1450, 1210, 810. ^{1}H NMR (DMSO-d_6, 100 MHz): τ 0.8 (*br s*, NH), 1.78 (*d*, $J = 5$ Hz, H-3), 2.04 (*d*, $J = 5$ Hz, H-4), 2.22 (*d*, $J = 2$ Hz, H-5), 2.47 (*d*, $J = 8.5$ Hz, H-8), 2.79 (*dd*, $J = 8.5$ and 2 Hz, H-7), 2.82 and 3.85 (AA'BB' system, $J = ca$ 8.5 Hz), 5.67 (*s*, CH_2), 6.13 (*s*, OMe). MS (*m/e*): 304 (100%) M^+, 303 (72), 302 (5), 290 (5), 289 (22), 260 (4), 259 (4), 210 (4), 195 (14), 152 (9), 140 (4), 130 (7). *Acetate* ^{1}H NMR (DMSO-d_6, 100 MHz): τ 2.56 and 2.96 (AA'BB' system, $J = ca$ 8.5 Hz), 5.83 (*s*, CH_2), 6.12 (*s*, OMe), 7.78 (*s*, OAc). MS (*m/e*): 346 (95%) M^+, 331 (6), 304 (42), 303 (93), 289 (23), 260 (13), 210 (4), 195 (25), 167 (7), 140 (7), 107 (4), 43 100).

Synthesis of **1**. (±)-5-Methoxytryptophan (0.5 g) and *p*-hydroxyphenylpyruvic acid (0.5 g) in a mixture of M H_2SO_4 (2.5 ml), H_2O (8 ml) and EtOH (5 ml) were heated under reflux (22 hr). After evapn of EtOH and addition of 18 M NH_4OH (3 ml) and active charcoal, the mixture was boiled (30 min), cooled, diluted with NH_4OH (1.5 ml), filtered, washed with Et_2O, concd and kept at 0° (24 hr). Successive crops of crystals, mp 230–232°, 210–220°, 202–205°, mixtures of stereoisomers of **3**, were combined (0.24 g) and used directly in the next step. To a boiling soln of **3** (0.21 g) in H_2O (35 ml) were added 10% aq. $K_2Cr_2O_7$ (7 ml) and HOAc (1.2 ml). After reflux (30 min) and cooling aq. Na_2SO_3 was added. The mixture was made alkaline with aq. $NaHCO_3$ and extracted with Et_2O. The Et_2O soln was dried and evapd. The residue was crystallized from $CHCl_3$–MeOH–hexane to **1** (30 mg), indistinguishable by mmp and spectra from the natural product.

Acknowledgements—This work was supported through financial aid by FINEP (to the group at Universidade Federal de Minas Gerais), and through fellowships by CAPES (to L.M.G.A.) and CNPq (to R.B.F. and J.R. de S.). The authors are grateful to Dr. Paul M. Baker, NPPN, Universidade Federal do Rio de Janeiro, for the 100 MHz ^{1}H NMR spectra and MS.

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