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HOMOORMOSANINE-TYPE ALKALOIDS FROM *BOWDICHIA VIRGILOIDES**

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Key Word Index—*Bowdichia virgiloides*; Leguminosae; stem bark; homoormosanine-type alkaloids.

Abstract—A methanolic extract from the stem bark of the Colombian *Bowdichia virgiloides* yielded alkaloids of the ormosanine- and homoormosanine-type. Among them are the new natural products homopiptanthine and homo-18-epiormosanine, the latter exhibiting strong cytotoxic activity.

INTRODUCTION

Bowdichia virgiloides is a tree, which grows in tropical South America up to a height of 45 m [2], whereas the average height in Colombia is 6 m [3]. Its wood is used as timber and the stem bark, which is also named Cortex Alcornocco or Cortex Sebipira [2, 3], is used in folk medicine against various diseases [3, 4]. Earlier publications described lupeol as the main constituent and (−)-homoormosanine (**1**) the major alkaloid of the bark from *B. virgiloides* [5, 6]. The present report is the result of a more comprehensive phytochemical analysis with special emphasis on the alkaloidal components [7, 8].

RESULTS AND DISCUSSION

The dried bark was extracted first with petrol and then with methanol. Alkaloidal components were found exclusively in the methanol extract, from which they can be transferred into chloroform by partitioning. Successive chromatography of the chloroform extract on Sephadex LH-20 and then aluminium oxide yielded the three isomeric alkaloids **1**–**3** and a mixture of two further isomeric alkaloids (**4** and **5**), whose separation was achieved by HPLC or by CC after derivatization with formaldehyde to a mixture of the corresponding homo-alkaloids. The homo-alkaloids from **4** and **5** were found to be identical with **1** and **3**, respectively.

Whereas **1**–**3** exhibit almost identical EI mass spectra with pronounced $[M]^+$ at *m/z* 329 ($C_{21}H_{35}N_3$), their ^1H and ^{13}C NMR spectra are significantly different allowing determination of their structures using the results of a recent NMR study on homoormosanine-type alkaloids [1, 7].

Both **1** and **3** show NMR signals for the aminal protons (CH_2-24) at δ 3.38 and 3.24 ($J = 8.5$ Hz) indicative of the *trans*-orientation of H-11 and H-18 [9]. Only in **3** one proton of CH_2-10 appears as a double doublet at lowest field (δ 3.70, $J_1 = 11.5$, $J_2 = 2$ Hz) well separated from all other signals, with its geminal coupling partner at $\delta = 1.74$. The strong down-field shift together with the large difference in shift values of the geminal protons at C-10 and, in addition, the observed long range coupling of the downfield proton (on one of H_2-8) establishes the relative configuration of the methano bridge (CH_2-8) to be *cis* to the proton H-6 at the asymmetric centre [1, 7, 10]. H-6 *trans* (to C-8) compounds in the *Ormosia* series can be epimerized at C-6 by acidic hydrogenation [11]. Accordingly, (±)-**4** (available from another source) was converted to (±)-**5**, and this on treatment with formaldehyde gave (±)-homopiptanthine spectroscopically and chromatographically identical with **3**.

In **2**, the ^1H NMR signals of the aminal group exhibit a large difference in shift values and this is typical for a planar orientation of the ring system A/F/E [9]. A doublet at $\delta = 1.15$ can be assigned to H-11 and its coupling constant ($J = 10$ Hz) indicates the *trans*-orientation of H-16 to H-11. Furthermore, NOE experiments demonstrate the neighbourhood of protons at C-8, C-11 and C-18. Further evidence comes from the ^{13}C NMR data [1, 7] allowing the establishment of the structure except its absolute configuration.

From the petrol fraction besides lupeol, which constitutes the major component of the bark (up to 85% of the extract) [5, 7], we isolated β-sitosterol and as a minor component 4-hydroxy-3-methoxybenzaldehyde.

Among the isolated compounds (+)-homo-18-epiormosanine (**2**) and (−)-homopiptanthine (**3**) are new natural products. Compound **2** exhibits strong cytotoxic activity in mice embryo tissue cultures.

Our studies describe *Ormosia* type-alkaloids in *Bowdichia* species for the first time and thereby corroborate the occasionally contested botanical assignment of the genus *Bowdichia* to the tribus Sophoreae [12]. The occurrence of (−)-**4** besides (−)-**5** [and (−)-**1** besides (−)-**3**] is interesting from a biosynthetic point of view as (−)-**5** constitutes the 6-*epi* diastereomer of (+)-**4**.

*Part 36 in the series 'Constituents of Tropical Medicinal Plants'. For part 35 see ref. [1].

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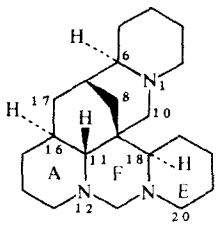

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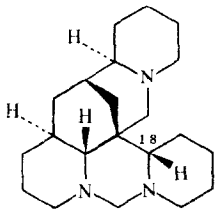

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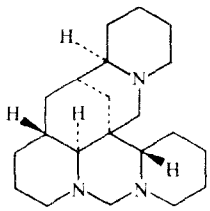

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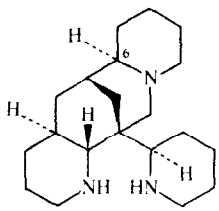

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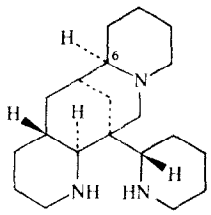

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EXPERIMENTAL

Plant material. Bark of *B. virgiloides* Humboldt, Bonpland et Kunth (local names Alcornoque and Algarrobo) was collected in August 1982 and October 1984 at the edges of the rivers Manacacias and Meta, respectively (Departamento Meta, Colombia); voucher specimens are kept under nos 8205 and 8414 at our herbarium in Erlangen.

General. Mps: uncorr. IR were taken in KBr. NMR: see [1]. MS were obtained by EI at 70 eV. TLC was performed on precoated plates (Nano plates Sil-20 UV, Macherey–Nagel) using cyclohexane–diethylamine (9:1); detection with Dragendorff's reagent [13].

Extraction and chromatography. Pulverized bark (1.6 kg) was extracted with petrol and then with MeOH at room temp.; the yield was 20 g petrol extract and 280 g MeOH extract (=ext. A). Ext. A was redissolved in MeOH–H_2O (1:1) and extracted with $CHCl_3$ yielding 6.4 g $CHCl_3$ fr. (=ext. B). Chromatography of ext. B over Sephadex LH-20 with petrol–EtOAc–MeOH (3:4:3) yielded 1.81 g alkaloid-containing fraction (=fr. A). Fr. A was repeatedly chromatographed over aluminium oxide (Woelm, basic and later neutral) using EtOAc–MeOH, cyclohexane–MeOH or petrol–Me_2CO, which yielded compounds **1** (*ca* 0.02% dry bark), **2** (*ca* 0.01%), **3** (*ca* 0.0006%) and a mixt. of **4** and **5**. Sepn of **4** (*ca* 0.004% dry bark) and **5** (*ca* 0.001%) was achieved by HPLC (Nucleosil RP18, MeOH). A part of the mixt. was treated with HCHO–HOAc [6] to convert the alkaloids into their homoderivatives.

Homoormosanine (**1**). Colourless crystals (189 mg), mp 126–128°; TLC: R_f 0.6, orange; $[\alpha]_D^{21} -9°$ ($CHCl_3$; *c* 1.0); spectral properties identical with published data [1, 6].

Homo-18-epiormosanine (**2**). Colourless crystals (96 mg), mp 93–95°; TLC: R_f 0.73, orange; $[\alpha]_D^{21} +6°$ ($CHCl_3$; *c* 1.03); IR ν_{max} cm^{-1}: 2925, 2845, 2780, 2740; MS *m/z* (≧50) (rel. int. ≧20%): 329 (100 $[M]^+$), 246 (92), 231 (67), 163 (29), 162 (20), 150 (28), 149 (31), 148 (26), 98 (55), 96 (30), 84 (65), 55 (31); for other data see ref. [1].

Homopiptanthine (**3**). Colourless crystals (5 mg), mp 184–185°; TLC: R_f 0.69, orange; $[\alpha]_D^{21} -40°$ ($CHCl_3$; *c* 0.32); IR ν_{max} cm^{-1}: 2920, 2845, 2760; MS *m/z* (≧50) (rel. int. ≧20%): 329 (83 $[M]^+$), 328 (30), 247 (22), 246 (84), 245 (33), 233 (25), 232 (24), 231 (100), 217 (21), 205 (21), 164 (28), 163 (62), 162 (46), 150 (59), 149 (63), 148 (54), 136 (47), 134 (37), 110 (22), 98 (63), 96 (32), 84 (44); for other data see ref. [1].

Ormosanine (**4**). Colourless crystals (2.4 mg), mp 172–173°; TLC: R_f 0.39, orange; $[\alpha]_D^{21} -11°$ ($CHCl_3$; *c* 0.12); MS *m/z* (≧50) (rel. int. ≧10%): 317 (28 $[M]^+$), 234 (26), 233 (10), 219 (44), 151 (32), 98 (35), 96 (11), 84 (100).

Piptanthine (**5**). Colourless crystals (1.6 mg), mp 137–140°; TLC: R_f 0.39, orange; $[\alpha]_D^{21} -19°$ ($CHCl_3$; *c* 0.10); MS *m/z* (≧50) (rel. int. ≧10%): 317 (29 $[M]^+$), 234 (52), 233 (11), 219 (14), 191 (10), 151 (22), 98 (38), 96 (13), 84 (100), 56 (14).

Isomerization of (±)-**4**. Racemic ormosanine (20 mg) was stirred under H_2 in HOAc (5 ml) in the presence of PtO_2 (50 mg) at room temp. and 760 Torr for 48 hr. After work-up the residue was treated with HCHO–HOAc according to ref. [6]. CC of the reaction mixt. yielded 9 mg (±)-**1** and 4 mg (±)-**3** identical with natural **1** and **3** in all chromatographic and spectroscopic properties.

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VENECURINE, AN INDOLE ALKALOID FROM CURARE

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Key Word Index—Venezuelan curare; quaternary indole alkaloid; venecurine; 2D-NMR.

Abstract—A new quaternary indole alkaloid, venecurine, has been isolated by chromatographic techniques from a curare obtained from the Hoti tribe of Venezuela. Elucidation of its structure is based mainly on 2D-NMR studies.

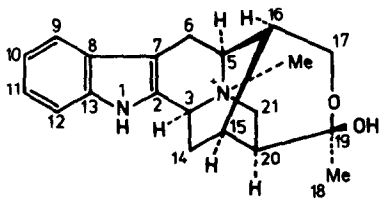
INTRODUCTION

In a preliminary TLC screening of some South American curares we encountered a sample that appeared not to contain any of the known dimeric curarizing alkaloids. The sample originated from the Hoti, a small tribe who inhabit the mountainous border region between the Venezuelan States of Bolivar and Amazonas north of the Rio Ventuari region where curares are prepared from the *Strychnos* genus of the *Loganiaceae* family [1]. They do not use the bow and arrow, but for hunting small animals rely on the blowpipe and unpoisoned or curare-poisoned darts. The southern Hoti make their own curare, part of which is destined for external trade, while the northern Hoti obtain theirs from another tribe, the E'niepa (= Panare) [2].

The present communication reports the isolation and structure determination of a new quaternary monomeric indole alkaloid (**1**), to which we have given the trivial name venecurine, from the above-mentioned sample of curare.

RESULTS AND DISCUSSION

The major alkaloid afforded a grey coloration with 1% ceric sulphate in 10% aqueous sulphuric acid. Its UV spectrum showed the characteristic chromophore of an unsubstituted indole alkaloid and was similar to that of macusine B. No shifts were detected in either basic or acidic solution. The FAB mass spectrum showed a $[M]^+$ at *m/z* 325, corresponding to the elemental composition $C_{20}H_{25}N_2O_2$, which gives an unsaturation number of 10. A strong peak at *m/z* 324 $[M-1]^+$, of the elemental composition $C_{20}H_{24}N_2O_2$ (calc.: 324.1837; found: 324.1823), was observed in the EI mass spectrum. Characteristic fragments of a sarpagan skeleton were observed at



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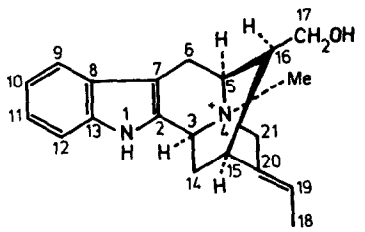

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