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LIGNANS FROM *NECTANDRA TURBACENSIS**

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Key Word Index –*Nectandra turbacensis*; Lauraceae; furofuran lignans; 2-aryl-3,7-dioxa-6-oxobicyclo[3.3.0]octane.

Abstract –Bark and wood of *Nectandra turbacensis* (Lauraceae) contain, besides the known furofuran lignans (+)-sesamin, (+)-demethoxyexcelsin and (+)-piperitol, the novel (1*R*,5*R*,2*S*,6*S*)-2-(3′-methoxy-4′,5′-methylenedioxyphenyl)-6-(4″-hydroxy-3″-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane [(+)-methoxypiperitol] and (1*R*,2*S*,5*R*)-2-(3′-methoxy-4′,5′-methylenedioxyphenyl)-3,7-dioxa-6-oxobicyclo[3.3.0]octane.

INTRODUCTION

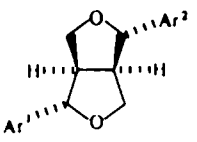
Botanical material, identified by Professor Klaus Kubitzki (Universität Hamburg) as belonging to *Nectandra turbacensis* (HBK) Nees, was collected by Dr. Hipólito F. Paulino Fo. (Universidade Estadual Paulista, Araraquara, São Paulo) in the vicinity of Humaitá, Amazonas. A sample of trunk bark was found to contain four furofuran lignans, the known (+)-sesamin (**1a**), (+)-demethoxyexcelsin (**1b**) [2] and (+)-piperitol (**1c**) [3], besides the new (+)-methoxypiperitol (**1d**). Compound **2**, belonging to the rare furolactone type [4–7], was obtained additionally, together with sitosterol, sitostenone and lichexanthone.

RESULTS

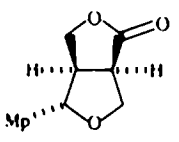
(+)-Sesamin is one of the best known 2,6-(diequatorial)-diaryl-3,7-dioxabicyclo[3.3.0]octane lignans. The reported mp 123°, $[\alpha]_D$ + 71°, NMR (^{1}H and ^{13}C) and mass spectra [2, 8, 9] are all identical with the data obtained for **1a**. The identification of **1a** was confirmed by catalytic hydrogenolysis of the isolate into (−)-dihydrocubebin (**3**) and (+)-dihydrosesamin (**4**), both obtained previously by the same process [10, 11] as well as into (−)-dehydroxycubebin (**5**), a dehydration product of **3**.

Compounds **1b** (mp 104–106°, $[\alpha]_D$ + 77°) and **1c** (mp *ca* 70°, $[\alpha]_D$ + 70°) were identified by their NMR (^{1}H and ^{13}C) and mass spectra [9] as (+)-demethoxyexcelsin (mp 101–102°, $[\alpha]_D$ + 54°) [12] and (+)-piperitol (mp 79°, $[\alpha]_D$ + 76°) [3], respectively.

* Part 83 in the series "The Chemistry of Brazilian Lauraceae". For part 82 see ref. [1]. Based in part on the Doctorate thesis presented by M. G. de C. (present address: Instituto de Ciências Exatas, Universidade Federal Rural do Rio de Janeiro, Seropédica, RJ, Brasil) to Universidade de São Paulo.



1a Ar^1 = Ar^2 = Pi
1b Ar^1 = Pi, Ar^2 = Mp
1c Ar^1 = Pi, Ar^2 = Gu
1d Ar^1 = Gu, Ar^2 = Mp



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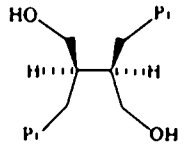

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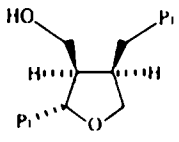

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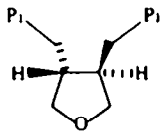

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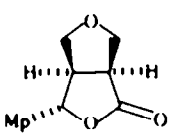

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Pi = piperonyl
Gu = guaiacyl
Mp = 3 · methoxy · 4,5 · methylenedioxyphenyl

Table 1. ^{13}C NMR data of the furofuran lignan **1d**, the furolactone **2** and the products **3**, **4** and **5** of catalytic hydrogenolysis of **1a***

C	1d	2	3	4	5
1,1'	135.6; 132.4	133.5 *s*;	134.3	134.0 *s*; 136.9 *s*	134.0
2,2'	99.7; 108.5	99.7 *s*;	107.8	106.1 *d*; 107.8 *d*	108.0
3,3'	148.7; 146.5	143.4 *s*;	147.4	146.7 *s*; 147.6 *s*	147.5
4,4'	134.2; 145.0	134.9 *s*;	145.6	145.7 *s*; 147.6 *s*	145.8
5,5'	143.2; 114.1	149.6 *s*;	109.2	108.0 *d*	108.9
6,6'	105.4; 118.5	105.7 *d*;	121.7	118.9 *d*; 121.2 *d*	121.3
7,7'	85.4	85.7 *d*; 177.8 *s*	35.7	82.7 *d*; 33.0 *t*	39.1
8,8	54.0; 53.6	45.6 *d*; 48.0 *d*	44.1	52.4 *d*; 42.1 *d*	46.5
9,9'	71.3	69.6 *t*; 69.8 *t*	60.1	60.5*t*; 72.7 *t*	73.1
OMe	55.5; 56.3	56.4 *q*;	—		—
O_2CH_2	101.0	101.3 *t*	100.6	100.8 *t*	100.7

* In order to facilitate spectral comparisons lignans are considered to be oxidative dimers of two cinnamyl alcohol units, the two aliphatic C_3-chains of which are numbered, starting from the aryls, 7, 8, 9 and 7', 8', 9' [2].

The elementary formula $C_{21}H_{22}O_7$ for **1d** was determined by a combination of low resolution mass spectrometry and NMR C and H counts. Trivial spectral analysis disclosed the presence of two methoxyls and one methylenedioxyl accounting for the three carbons in excess of the basic C_{18}-lignan skeleton. These oxy-groups are substituents of two aryls identified with guaiacyl (IR ν_{max} 3450 cm^{-1}; ^1H NMR δ6.8–6.85, 3ArH) and 3-methoxy-4,5-methylenedioxyphenyl (^1H NMR δ6.55, *s*, 2ArH) units. The mass spectrum with the base peak at *m/z* 179 (100%) and another prominent peak at *m/z* 151 (94%) is consistent with this identification. Both aryl groups must be equatorial since the NMR signals due to the aliphatic part of **1d** are closely comparable with the analogous signals of the known compounds **1a**, **1b** and **1c** [9]. With identical relative configurations having thus been verified for **1a**, **1b**, **1c** and **1d**, the fact that all four compounds are dextrorotatory indicates their common absolute configuration and establishes the structure **1d** for the novel compound designated (+)-methoxypiperitol.

The elementary formula $C_{14}H_{14}O_6$ for **2** was determined by a combination of low resolution mass spectrometry and NMR C and H counts. The mass spectral peaks at *m/z* 179 (80%) and 165 (100%), as well as the ^1H NMR signals for aromatic OMe (δ3.91, *s*), O_2CH_2 (δ5.97, *s*) and for two practically identical protons (δ6.51, 6.53, both *dd*, J = 2 and 0.5 Hz) indicated again the existence of a 3-methoxy-4,5-methylenedioxyphenyl ($C_8H_7O_3$) unit. This leaves $C_6H_7O_3$ for the aliphatic part of the molecule. Two of the three oxygens belong to a γ-lactone (IR ν_{max} 1780 cm^{-1}) and the third one to an ether as shown in **2**. The key NMR feature concerns the H-1 signal. Not being benzylic, carbinolic or vicinal to a carbonyl, H-1 gives a signal at relatively high field (δ3.09). Furthermore H-1, occupying a central position on the aliphatic part, gives rise to a strongly split multiplet (*dddd*, J = 7, 9, 7 and 2 Hz). The coupling constants suggest the existence of hydrogens at the vicinal positions C-2 (J = 7 Hz), C-5 (J = 9 Hz) and C-8 (axial, J = 7 Hz; equatorial, J = 2 Hz). The geminal coupling of H-8_{ax} and H-8_{eq} is evidenced by J = 10 Hz. H-5 is represented by a *ddd*. One of the couplings (J = 9 Hz) is due to interaction with H-1 (see above). The additional couplings of J = 9 and 4 Hz are due to the vicinal axial and equatorial hydrogens at position C-4. Here the geminal coupling of H-4_{ax} and H-4_{eq} is expressed by J = 9 Hz. This evidence leads to the alternative structural proposals **2** and **6**. Both support the aryl group at position C-2, a plausible assignment also in view of the relatively large chemical shift (δ4.59) of the doublet representing H-2, which is both benzylic and carbinolic in nature. All possible decoupling experiments were performed and corroborate the proposals. A decision in favour of structure **2** was reached considering the chemical shifts of the methylene protons. For compound **6** similar values would be expected for both methylenes, while in the case of **2** the carbinolic protons at C-8 are part of a lactone system and are represented by signals at lower field (δ4.33, 4.50) than the carbinolic protons at C-4 (δ4.19, 4.35).

DISCUSSION

The bark of Amazonian trees is usually overgrown by lichens and ideally these should be carefully scraped off in order to avoid the presence of compounds such as lichexanthone in the bark extract. However, in the present work this was not done but it was observed that a sample of trunk wood yielded all the compounds mentioned above with the expected exception of lichexanthone.

A mechanism for the transformation here exemplified by **1d** → **2** has been proposed [2] and the furolactone **2** may be an artifact.

EXPERIMENTAL

Isolation of the constituents. Dry trunk bark was reduced to powder (1.5 kg) and extracted successively with hexane and $CHCl_3$ in a Soxhlet apparatus. The hexane soln was concd to a small vol. Lichexanthone crystallized overnight and was separated by filtration. The filtrate was evapd. The residue (5.5 g) was partitioned between hexane and MeOH–H_2O (9:1). The top layer was evapd. The residue (2.95 g) gave crystalline **1a**, separated by filtration from fatty oil. The methanolic layer was evapd. The residue (2.44 g) was submitted to flash chromatography (silica gel, CH_2Cl_2–EtOAc mixtures of gradually increasing polarity). The resulting fractions were separated by prep. TLC

(silica gel) into **1a**, **1b**, **1c**, **1d** and **2**. The original $CHCl_3$ soln was submitted to the same process. The top (hexane) layer yielded **1a**, sitosterol, sitostenone and lichexanthone. The methanolic layer yielded **1a**, **1b**, **1c**, **1d** and **2**. The trunk wood was submitted to an analogous procedure and yielded **1a**, **1b**, **1c**, **1d** and **2**. Total quantities obtained from the bark: **1a** (320 mg), **1b** (110 mg), **1c** (130 mg), **1d** (250 mg), **2** (100 mg), sitosterol (10 mg), sitostenone (20 mg), lichexanthone (170 mg). Total quantities obtained from the wood: **1a** (300 mg), **1b** (50 mg), **1c** (60 mg), **1d** (180 mg), **2** (30 mg), sitosterol (80 mg).

Identification of known compounds. Compounds **1a** [8, 9, 12], **1b** [12], **1c** [3], sitosterol, sitostenone and lichexanthone [13] were identified by comparison of mp, $[\alpha]_D$ and spectra with analogous data registered in the lit.

(+)-Sesamin (**1a**). Compound **1a** (100 mg) in $CHCl_3$–MeOH (1:1, 30 ml) and 5% Pd–C (20 mg) was hydrogenated (24 hr). The mixture was filtered through a small column of silica gel. The soln was evapd and the residue was separated by prep. TLC (silica gel, C_6H_{14}–EtOAc 9:1) into **3** (50 mg), **4** (17 mg) and **5** (15 mg).

(1*R*,5*R*,2*S*,6*S*)-2-(3′-*Methoxy*-4′,5′-*methylenedioxyphenyl*)-6-(4″-*hydroxy*-3″-*methoxyphenyl*)-3,7-*dioxabicyclo*[3.3.0]*octane* [(+)-*methoxypiperitol*, **1d**]. viscous oil, $[\alpha]_D$ + 59° (*c* 1.0; $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450 (OH), 1530, 1450 (Ar), 1280, 1060 (COC). UV λ_{max}^{MeOH} nm: 280, 230 (ε 4400, 11900). ^1H NMR (60 MHz, $CDCl_3$): δ 3.05 (*m* H-1, H-5), 3.73 3.85 (*m* H-4_{eq}, H-8_{eq}), 3.87, 3.90 (*s*, 2OMe), 4.07 4.4 (*m*, H-4_{ax}, H-8_{ax}), 4.7 (*d*, *J* = 5 Hz, H-2, H-6), *ca* 5.8 (OH), 5.95 (*s*, O_2CH_2), 6.55 (*s*, H-2′, H-6′), 6.8 6.85 (*m*, H-2″, H-5″, H-6″). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 386 [M]$^+$ (5), 203 (13), 191 (24), 189 (15), 179 [MpCO]$^+$ (100), 165 [$MpCH_2$]$^+$ (35), 161 (33), 152 (41), 151 [Mp]$^+$, [GuCO]$^+$ (94), 137 [$GuCH_2$]$^+$ (50), 135 [$PiCH_2$]$^+$ (89), 123 [Gu]$^+$ (70), 121 [Pi]$^+$ (77). *Acetate*, viscous oil. IR ν_{max}^{film} cm^{-1}: 1760 (ArOAc), 1520, 1440 (Ar), 1230, 1080 (COC). ^1H NMR (60 MHz, $CDCl_3$): δ 2.27 (*s*, OAc), 3.05 (*m*, H-1, H-5), 3.75–3.95 (*m*, H-4_{eq}, H-8_{eq}), 3.85, 3.90 (2*s*, 2OMe), 4.07 4.4 (*m*, H-4_{ax}, H-8_{ax}), 4.6 4.8 (*m*, H-2, H-6), 5.95 (*s*, O_2CH_2), 6.5 (*s*, H-2′, H-6′), 6.7–6.8 (*m*, H-2″, H-5″, H-6″). MS *m/z* (rel. int.): 428; [M]$^+$ (61), 386 (37), 207 (21), 191 (42), 179 [MpCO]$^+$ (100), 165 [$MpCH_2$]$^+$ (66), 151 [Mp]$^+$, [GuCO]$^+$ (94), 137 [$GuCH_2$]$^+$ (50), 135 [$PiCH_2$]$^+$ (20), 123 [Gu]$^+$ (10), 121 [Pi]$^+$ (6). *Methyl ether*, viscous oil. IR ν_{max}^{film} cm^{-1}: 1540, 1450 (Ar), 1280, 1070 (COC). ^1H NMR (60 MHz, $CDCl_3$): δ 3.05 (*m*, H-1, H-5), 3.7 3.9 (*m*, H-4_{eq}, H-8_{eq}), 3.87 (*s*, 3OMe), 4.1–4.4 (*m*, H-4_{ax}, H-8_{ax}), 4.75 (*d*, *J* = 4 Hz, H-2, H-6), 5.95 (*s*, O_2CH_2), 6.53 (*s*, H-2′, H-6′), 6.86 (*s*, H-2″, H-5″, H-6″). MS *m/z* (rel. int.): 400 [M]$^+$ (17), 208 (10), 203 (12), 191 (32), 179 (100), 165 (68), 151 (70), 149 (31), 135 (13), 121 (9).

(1*R*,2*S*,5*R*)-2-(3′-*Methoxy*-4′,5′-*methylenedioxyphenyl*)-3,7-*dioxa*-6-*oxobicyclo*[3.3.0]*octane* (**2**). Viscous oil, $[\alpha]_D$ + 64° (*c* = 0.6; $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1780 (δ-lactone), 1500, 1440 (Ar), 1150, 1100 (COC). UV λ_{max}^{MeOH} nm: 283, 230 (ε 3400, 9700). ^1H NMR (300 MHz, $CDCl_3$): δ 3.09 (*dddd*, *J* = 9, 7, 7, 2 Hz, H-1), 4.19 (*dd*, *J* = 9, 4 Hz, H-4_{eq}), 3.43 (*ddd*, *J* = 9, 9, 4 Hz, H-5), 3.91 (*s*, OMe), 4.33 (*dd*, *J* = 10, 2 Hz, H-8_{ax}), 4.35 (*dd*, *J* = 9, 9 Hz, H-4_{ax}), 4.50 (*dd*, *J* = 10, 7 Hz, H-8_{eq}), 4.59 (*d*, *J* = 7, H-2), 5.97 (*s*, O_2CH_2), 6.51, 6.53 (two *dd*, *J* = 2, 0.5 Hz, H-2′, H-6′). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 278 [M]$^+$ (69), 193 (20), 179 (80), 165 (100), 135 (18). CD (*c* 10^{-4} g/ml MeOH): $[\theta]_{320}$ + 800, $[\theta]_{230}$ + 4700.

(8*R*,8′*R*)-8,8′-*Bis*-(3′,4′-*methylenedioxybenzyl*)-*tetrahydrofuran* (**5**). Viscous oil, $[\alpha]_D$ − 37° (*c* 1.0; $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1500, 1450 (Ar), 1250, 1050 (COC). ^1H NMR (60 MHz, $CDCl_3$): δ 2 2.35 (*m*, H-8, H-8′), 2.51 (*m*, 2H-7, 2H-7′) 3.55 (*dd*, *J* = 8, 5 Hz, H-9_{ax}, H-$9'_{ax}$), 3.90 (*dd*, *J* = 8, 5 Hz, H-9_{eq}, H-$9'_{eq}$), 5.95 (*s*, $2CH_2O_2$), 6.5–6.8 (*m*, 6ArH). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 340 [M]$^+$ (25), 136 [PiMe]$^+$ (100), 135 [$PiCH_2$]$^+$ (10), 122 [PiH]$^+$ (2).

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