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NEOLIGNANS FROM *ANIBA TERMINALIS**

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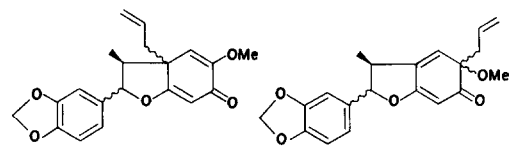
Key Word Index—*Aniba terminalis*; Lauraceae; tetrahydrooxobenzofuran neolignans; benzofuran neolignan.

Abstract—A benzene extract of the trunk wood of *Aniba terminalis* (Lauraceae) contained besides benzyl benzoate, benzyl salicylate, *d*,l-camphor and sitosterol, (2*S*,3*S*,3a*R*)- and (2*R*,3*S*,3a*S*)-3a-allyl-5-methoxy-3-methyl-2-piperonyl-2,3,3a,6-tetrahydro-6-oxobenzofurans, which may be responsible, through sequential rearrangements of the Cope, retro-Claisen and Claisen types, and finally dehydrogenation, for the formation of the co-occurring (2*S*,3*S*,5*S*)- and (2*R*,3*S*,5*R*)-5-allyl-5-methoxy-3-methyl-2-piperonyl-2,3,5,6-tetrahydro-6-oxobenzofurans, the (2*S*,3*S*)-6-*O*-allyl-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran, the (2*S*,3*S*)- and (2*R*,3*S*)-7-allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonyl-2,3-dihydrobenzofuran and the 7-allyl-6-hydroxy-5-methoxy-3-methyl-2-piperonylbenzofuran.

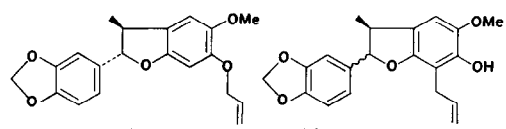
INTRODUCTION

Neolignans of structural types **1**, **2**, **3** and **4** co-occur in the C_6H_6-extract of an *Aniba* sp. [1]. The opinion that all four represent natural products originating from an isoeugenol–eugenol oxidative dimer (type **1**) by successive *in vivo* rearrangements was based on the stability of derivatives belonging to types **1** and **2** under extraction conditions. Additional evidence stems from the fact that in *Aniba terminalis* representatives of these same types are accompanied by **5**. Dehydrogenation of 2,3-dihydrobenzofurans would not be expected to occur during manipulation of the plant or extract, and a reasonable rationalization of the biosynthetically unusual placement of the allyl substituent in **5** involves a sequence of reactions in which **2**, **3** and **4** would function as intermediates.



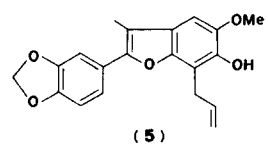
(1a) α-piperonyl, β-allyl
(1b) β-piperonyl, α-allyl
(1c) α-piperonyl, α-allyl

(2a) α-piperonyl, β-allyl
(2b) β-piperonyl, α-allyl



(3)

(4a) α-piperonyl
(4b) β-piperonyl



(5)

RESULTS AND DISCUSSION

The NMR features of dihydrobenzofuran neolignans are well known [1–4]. The structures of the compounds belonging to types **1**–**4** were thus deduced with ease. The particular dienone systems of **1** and **2** were further characterized by

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IR and UV spectra (ν_{max} 1645 and 1685 cm^{-1} respectively; λ_{max} 285 and 314 nm respectively). The relative position of the *O*-allyl and *O*-methyl substituents in **3** was inferred from considerations concerning the biogenesis of the compound. Analogous evidence, also decisive for structural assignments in the case of compounds **4** and **5**, was partially confirmed by determining NMR spectral modifications due to acetylation in the latter case. Constancy of position of the aromatic proton singlet established the *meta*-relationship of H and OH, while diamagnetic shifts of the CH_2–CH= and OMe resonances established the *ortho*-relationship of the allyl and the methoxyl to the hydroxyl. Placement of the lone aromatic hydrogen at C-4, rather than the C-7 position, seemed in better accord with its relatively low field NMR signal, while placement of the methoxyl at C-5, rather than the more hindered C-7 position, seemed in better accord with its relatively high field NMR signal. The spectrum of **5** was of course simpler than the spectra given by compounds belonging to types **1**–**4**. Selective conjugation with the furan system separated all piperonyl H-resonances, while the C–Me was represented by a sharp singlet at appropriately low frequency.

The known burchellin (**1a**) differs stereochemically from the *A. terminalis* constituent **1b**. While, with reference to the aryl substituent, the allyl group of **1b** is again *trans*-oriented (CH_2, $\tau < 7{\cdot}6$ [1]), the methyl is *cis*-oriented (τ 9·47). From the two configurational alternatives, which could be formulated on this evidence, **1b** was chosen on grounds of the nearly antipodal ORD curves of **1a** and **1b**. Burchellin (**1a**), as characterized by a *trans*-methyl resonance (τ 8·84), and another compound tentatively identified with 3a-*epi*-burchellin (**1c**) (Me τ 8·73, CH_2 $\tau > 7{\cdot}6$), were present in substantial amounts, (35 and 10% respectively), in a less pure sample of **1b**.

Since a 2,3-*trans* geometry must prevail in **2a** (Me τ 8·75), it represents most probably the Cope-rearrangement product of burchellin (**1a**). In agreement with this supposition, its ORD curve is different from the curves of (5*R*)-allyl derivatives [1]. The isolate contained about 10% of a 2,3-*cis* derivative (Me τ 9·38), probably **2b**, the Cope product of **1b**. In contrast, **3** was obtained in pure form. Significantly, NMR (Me τ 8·67) and ORD data showed this compound to belong to the (2*S*,3*S*)-2-aryl-3-methyl series of 2,3-dihydrobenzofurans [1,2]. Product **4** was again a 1:1·2 mixture of **4a** (Me τ 8·67) and **4b** (Me τ 9·19). The absolute stereochemical assignments in the formulae were based solely on the probable interrelationship of *A. terminalis* constituents of the *trans*-(**1a** → **2a** → **3** → **4a**) and the *cis*-(**1b** → **2b** → **4b**) series.

The leaves of this species [5] contain 4-methoxyparacotoin [6], in addition to benzyl benzoate and benzyl salicylate.

EXPERIMENTAL

Isolation of the constituents. Trunk wood (2 kg) of *Aniba terminalis* Ducke (voucher specimens INPA. Manaus, Herbaria Bot. 42206, Chem. 5/73) from the Ducke Forest Reserve, Manaus, Amazonas, gave a C_6H_6-extract (15 g) which was chromatographed on Si gel (500 g) to give the following fractions with the indicated eluants: A_1 and A_2 (C_6H_6), A_3 and A_4 (C_6H_6–EtOAc, 9:1). A_5 (C_6H_6–EtOAc. 7:3). A_1 (4 g) was composed of aliphatic esters. A_2 (2·2 g) was rechromatographed on Si gel to yield benzyl benzoate, benzyl salicylate, and a 3-component mixture which was separated by PLC (SiO_2, C_6H_6) into **5** (15 mg) and a 2-component mixture. This was separated, again by PLC (SiO_2, C_6H_6–$CHCl_3$, 99:1), into the less polar **3** (30 mg) and the more polar **4** (25 mg). A_3 (0·9 g) in $CHCl_3$ pptd. upon addition of MeOH, a solid which was crystallized from MeOH to give sitosterol (50 mg). A_4 (1·9 g), upon heating, gave sitosterol (600 mg) in the residue and *d*,l-camphor (100 mg) in the sublimate. A_5 was separated by PLC (SiO_2, Et_2O) into the less polar **1b** (40 mg) and the more polar **2** (50 mg).

(2R,3S,3aS)-3a-*Allyl*-5-*methoxy*-3-*methyl*-2-*piperonyl*-2,3,3a,6-*tetrahydro*-6-*oxobenzofuran*. (**1b**) viscous oil (M^+ found: 340·1314; $C_{20}H_{20}O_5$ requires: 340·1310). UV λ_{max}^{EtOH} nm (log ϵ): 257, 285 (4·24, 3·96). IR ν_{max}^{film} (cm^{-1}): 1645, 1611, 1472, 1241, 1163, 1041, 941. NMR ($CDCl_3$, τ): 3·25 (*m*, 3ArH), 4·03 (*s*, O_2CH_2), 4·0–4·3 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·15 (*s*, H-4), 4·50 (*s*, H-7), 4·77 (*d*, *J* 2·4 Hz, H-2), 4·75–4·95 (*m*, $CH_2CH{=}C\underline{H}_2$), 6·38 (*s*, OMe-5), 7·15–7·45 (*m*, $C\underline{H}_2CH{=}CH_2$ and H-3), 9·47 (*d*, *J* 7·0 Hz, Me-3). MS (*m/e*): 341 (25%) $M^+ + 1$, 340 (100) M^+, 320 (20), 299 (70), 267 (28), 239 (20), 211 (10), 177 (25), 162 (35), 161 (18), 150 (12), 149 (22), 135 (30), 131 (15), 121 (13), 106 (16). ORD (c 3 mg/100 ml. MeOH, 240–400 nm): $[\phi]_{400} -1150$, $[\phi]_{360}^{pk} -900$, $[\phi]_{317}^{tr} -10850$, $[\phi]_{304}$ 0, $[\phi]_{293}^{pk} +6700$, $[\phi]_{275}^{tr} +2700$.

(2S,3S,3aR)-3a-*Allyl*-5-*methoxy*-3-*methyl*-2-*piperonyl*-2,3,3a,6-*tetrahydro*-6-*oxobenzofuran* (**1a**) *ex A. burchellii* Kosterm. [2]. ORD (c 25·8 mg/100 ml. MeOH, 230–400 nm): $[\phi]_{400} +1200$, $[\phi]_{353} +1450$, $[\phi]_{311}^{pk} +9350$, $[\phi]_{290}$ 0, $[\phi]_{286} -7350$, $[\phi]_{248}^{pk} -850$.

(2S,3S,5S)-5-*Allyl*-5-*methoxy*-3-*methyl*-2-*piperonyl*-2,3,5,6-*tetrahydro*-6-*oxo*-*benzofuran* (**2**). Viscous oil (M^+ found: 340·1311; $C_{20}H_{20}O_5$ requires: 340·1310. UV λ_{max}^{EtOH} nm (log ϵ): 236, 289, 314 (4·21, 3·97, 3·84). IR ν_{max}^{film} (cm^{-1}): 1681, 1645, 1610, 1493, 1253, 1190, 1000, 939. NMR ($CDCl_3$, τ): 3·30 (*br s*, 3ArH), 3·94 (*d*, *J* 3·0 Hz, H-2), 4·03 (*s*, O_2CH_2), 4·2–4·6 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·54 (*s*, H-4), 4·91 (*s*, H-7), 4·9–5·1 (*m*, $CH_2CH{=}C\underline{H}_2$), 6·9–7·2 (*m*, H-3), 7·00 (*s*, OMe-5), 7·58 (*d*, *J* 6·6 Hz, $C\underline{H}_2CH{=}CH_2$), 8·75 (*d*, *J* 7·2 Hz, Me-3). MS (*m/e*):

341 (25%) M^+ +1,340 (100) M^+, 310 (10), 301 (16), 300 (59), 280 (16), 270 (13), 221 (13), 216 (10), 215 (10), 179 (22), 177 (13), 175 (13), 165 (13), 162 (15), 161 (10), 154 (11), 150 (13), 149 (27), 141 (10), 137 (15), 135 (65), 131 (13), 128 (10), 121 (10), 119 (11), 115 (11), 109 (10), 106 (10), 105 (11), 103 (15). ORD (3 mg/100 ml, MeOH, 245–400 nm): $[\phi]_{400}$ +1600. $[\phi]_{340}$ +3150, $[\phi]^{DK}_{290}$ +15400, $[\phi]^{tr}_{280}$ +12200, $[\phi]^{DK}_{274}$ +13800, $[\phi]_{250}$ 0, $[\phi]_{245}$ −12200.

(2S,3S)-6-O-*Allyl*-5-*methoxy*-3-*methyl*-2-*piperonyl*-2,3-*dihydrobenzofuran* (**3**). Viscous oil (M^+ found: 340·1309; $C_{20}H_{20}O_5$ requires: 340·1310). UV λ^{EtOH}_{max} nm (log ϵ): 234, 294, 325, 340 (4·37, 4·24, 3·96, 3·31). IR ν^{film}_{max} (cm^{-1}): 1592, 1486, 1256, 1116, 936. NMR ($CDCl_3$, τ): 3·1–3·3 (*m*, 3ArH), 3·42 (*s*, H-4), 3·65 (*s*, H-7), 3·7–4·2 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·05 (*s*, O_2CH_2), 4·5–4·9 (*m*, $CH_2CH{=}C\underline{H}_2$), 5·09 (*d*, *J* 8·0 Hz, H-2), 5·55 (*d*, *J* 4·5 Hz, OCH_2), 6·26 (*s*, OMe-5), 6·5–7·0 (*m*, H-3), 8·67 (*d*, *J* 7·0 Hz, Me-3). MS (*m/e*): 340 (9%) M^+, 204 (20), 179 (13), 175 (13), 165 (46), 161 (52), 159 (19), 149 (16), 138 (31), 135 (62), 123 (18), 122 (20), 121 (37), 120 (18), 119 (100), 105 (49). ORD (c 3 mg/100 ml, MeOH. 235–400 nm): $[\phi]_{400}$ +1350, $[\phi]^{tr}_{321}$ −5900, $[\phi]_{301}$ 0, $[\phi]^{DK}_{297}$ +10400, $[\phi]_{280}$ 0, $[\phi]^{DK}_{244}$ +20150, $[\phi]_{237}$ 0.

(2S,3S)- and (2R,3S)-7-*allyl*-6-*hydroxy*-5-*methoxy*-3-*methyl*-2-*piperonyl*-2,3-*dihydrobenzofuran* (**4**a and **4**b respectively). Viscous oil. IR ν^{film}_{max} (cm^{-1}): 3450, 1611, 1490, 1253, 1128, 946, 848. NMR ($CDCl_3$, τ) signals common to **4**a and **4**b: 3·1–3·3 (*m*, 3ArH), 3·57 (*br s*, H-4), 4·10 (*s*, O_2CH_2), 3·9–4·4 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·47 (*s*, OH-6), 4·95–5·15 (*m*, $CH_2CH{=}C\underline{H}_2$), 6·20 (*s*, OMe-5), 6·66 (*d*, *J* 6·0 Hz, $C\underline{H}_2CH{=}CH_2$); signals due to **4**a: 4·93 (*d*, *J* 8·0 Hz, H-2), 6·5–7·0 (*m*, H-3), 8·67 (*d*, *J* 7·0 Hz, Me-3); signals due to **4**b: 4·76 (*d*, *J* 8·0 Hz, H-2), 5·7–6·2 (*m*, H-3), 9·19 (*d*, *J* 7·0 Hz, Me-3). MS (*m/e*): 340 (8%) M^+, 179 (10), 175 (100), 161 (42), 149 (23), 135 (12), 121 (23), 119 (33), 105 (27).

7-*Allyl*-6-*hydroxy*-5-*methoxy*-3-*methyl*-2-*piperonylbenzofuran* (**5**). Prisms, mp 125–127° (petrol) (M^+ found: 338·1140; $C_{20}H_{18}O_5$ requires: 338·1154). UV λ^{EtOH}_{max} nm (log ϵ): 250, 290, 337 (3·83, 4·06, 4·44). IR ν^{KBr}_{max} (cm^{-1}): 3448, 1651, 1616, 1503, 1475, 1429, 1380, 1350, 1228, 1130, 1048, 915, 861. NMR (CCl_4, τ): 2·76 (*dd*, *J* 9·2, 1·5 Hz, H-6′), 2·78 (*d*, *J* 1·5 Hz, H-2′), 3·13 (*d*, *J* 9·2 Hz, H-5′), 3·23 (*s*, H-4), 3·5–4·1 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·00 (*s*, O_2CH_2), 4·20 (*s*, OH-6), 4·65–5·05 (*m*, $CH_2CH{=}C\underline{H}_2$), 6·07 (*s*, OMe-5), 6·32 (sec. split *d*, *J* 6·0 Hz, $C\underline{H}_2CH{=}CH_2$), 7·64 (*s*, Me-3). MS (*m/e*): 338 (14%) M^+, 258 (13), 167 (39), 150 (73), 149 (100), 113 (17), 112 (10), 105 (17). *Acetate*, needles mp 112–114° (MeOH). NMR (CCl_4, τ): 2·83 (*dd*, *J* 8·4, 1·5 Hz, H-6′), 2·86 (*d*, *J* 1·5 Hz, H-2′), 3·18 (*d*, *J* 8·4 Hz, H-5′), 3·23 (*s*, H-4), 3·8–4·4 (*m*, $CH_2C\underline{H}{=}CH_2$), 4·00 (*s*, O_2CH_2), 4·7–5·1 (*m*, $CH_2CH{=}C\underline{H}_2$), 6·17 (*s*, OMe-5), 6·47 (sec. split *d*, *J* 6·0 Hz, $C\underline{H}_2CH{=}CH_2$), 7·64 (*s*, Me-3), 7·77 (*s*, MeCO). MS (*m/e*): 381 (9%) M^+ +1, 380 (41) M^+, 339 (23), 338 (100), 295 (14), 173 (40), 167 (14), 149 (64), 148 (17), 147 (87), 135 (11).

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