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BURCHELLIN, A NEOLIGNAN FROM *ANIBA BURCHELLII**†

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Abstract—The wood of *Aniba burchellii* Kosterm. (Lauraceae) contains sitosterol, benzyl benzoate and the neolignan burchellin, for which the structure of (2*S*, 3*S*)-4-allyl-6-methoxy-3-methyl-2-piperonyl-2,3,4,7-tetrahydro-7-oxobenzofuran (XIII) is proposed.

INTRODUCTION

Aniba burchellii Kosterm. is an arboreous Lauraceae species which grows in the Amazon region. The trunk wood yielded a new compound for which the name burchellin is proposed. To the natural products chemist, its formula, $C_{18}H_{15}O_2.O_2CH_2.OCH_3$, suggests a *bis*-$C_6$-$C_3$ skeleton. Consideration of chemical shifts and coupling constants of PMR-signals (Table 1) allowed unambiguous assignment of all propanoid hydrogens, leading to the partial structures I and II. The center of insertion of the allyl-group (I) into the hexacycle R is a chiral quaternary carbon atom. The only alternative, a *sp*^{2}-carbon, would make the methylene protons doubly allylic, a situation which is in disagreement with their magnetic non-equivalence and the chemical shift of their NMR-signals. Oxidation of burchellin gave piperonylic acid. Thus, the hexacycle of the second C_6–C_3 unit (II) is a piperonyl-residue. The NMR-spectrum is consistent with this observation (τ 3·17–3·25, m, 3 arom. H; 4·03, s, O_2CH_2).

TABLE 1. PMR DATA OF BURCHELLIN

	Partial structure												
				I					II				
	R								Ar				
	$=C\underline{H}$	$=C\underline{H}$	$OC\underline{H}_3$	H^s	H^t	H^u	H^v	H^w	3H	$O_2C\underline{H}_2$	H^x	H^y	H^z
τ	4·21	4·57	6·32	7·66	7·45	4·45	4·92	4·99	3·17–3·25	4·03	4·83	7·12	8·84
Multiplicity	s	s	s	dd	dd	qt	dd	dd	m	s	d	dq	d
J (Hz)				13·0 6 8	13·0 6 8	6 8 6 8 9 5 16 5	9 5 1·5	16 5 1·5			9 5	9·5 6 9	6 9

The data were recorded on a Varian MHz NMR spectrometer in $CDLl_3$ solution, s—singlet, d—doublet, dd—double doublet, dq—double quartet, qt—quadruple triplet, m—multiplet.

At this point, all 18 carbon atoms of the skeleton have been located. In consequence, the oxygen at the α-carbon, as well as the β-carbon of the C_3-unit in II, must both be linked

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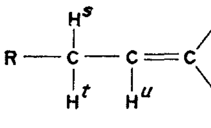
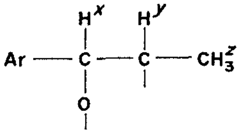
[1] O. R. GOTTLIEB and A. I. DA ROCHA, *Phytochem.* **11**, 1861 (1972).

to the hexacycle R. This comprises the group $C_6H_2O{\cdot}OCH_3$. One of its ring-carbons is linked to oxygen forming an α,β-γ,δ- or α,β-α',β'-unsaturated carbonyl (ν_{max} 1650 cm^{-1}). The maximum at 261 nm (ϵ 16 000) of burchellin's UV spectrum can be assigned to this chromophore, since the shoulder at 287 nm (ϵ 9500) must clearly be related to the piperonyl group (see e.g. safrol, λ_{max} 287 nm, ϵ 6200). Maxima in the 250–260 nm region are typical of α,β-α',β'-unsaturated carbonyls (see, e.g. III, λ_{max} 251 nm, ϵ 11 300).[2] α,β-γ,δ-Unsaturated carbonyls give rise to maxima at higher wavelength (see, e.g. IV, λ_{max} 292 nm, ϵ 4000).[3] The quaternary carbon atom of the R-group thus having been located, these data permit the expansion of the partial structure I into V.

The mode of insertion of II into V will now be considered. For steric reasons, the two linkages which extend from the propanoid group of II to the hexacycle of V must be associated with two adjoining carbons, either at α,β or at β,γ. The former alternative can be readily dismissed: The γ-carbon, being quaternary, must in this case support the methoxyl and only the α',β'-positions would remain available for the two vinylic protons. These, however, are not vicinal, since they give rise to sharp NMR-singlets (τ 4·21 and 4·57).



(I)



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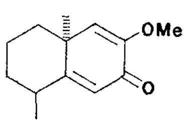

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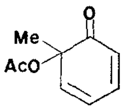

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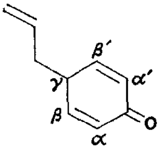

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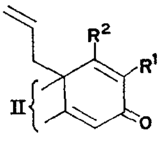
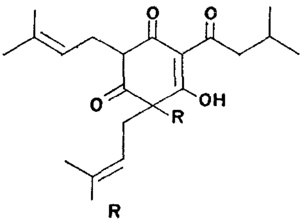
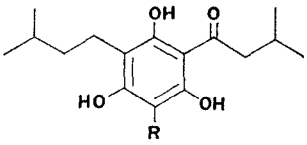


	R¹	R²
(VI) a	H	OMe
b	OMe	H



	R
(VII) a	OH
b	3,3-Dimethylallyl



	R
(VIII) a	OH
b	Isopentyl

Thus, burchellin may be accorded the partial constitution VI, in which an allyl group occupies the quaternary γ-carbon of an α,β-unsaturated ketone system, a structural unit also to be found in humulone (VIIa) and in lupulone (VIIb). Catalytic hydrogenation of these hop constituents leads not only to hydro-derivatives, but also to the hydrogenolysis products VIIIa and b.[4] It was expected, therefore, that it might be possible to transform burchellin into a considerably simpler molecule through an analogous reaction. Indeed, besides derivatives whose molecular weights were 4 (IX) and 6 mass units higher than the molecular weight of burchellin, a third reaction product appeared which had 40 mass units less than burchellin. The PMR-spectrum of this compound was uncomplicated and comparable to the spectra (Table 2) of (+)-obtusafuran (Xa)[5] and of (−)-melanoxin (XI),[6] two

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[2] D. Caine and J. B. Dawson, *Chemu. Commn.* 1232 (1970).

[3] F. Wessely and F. Sinwel, *Monatsh. Chem.* **81**, 1055 (1950).

[4] R. Stevens, *Chem. Rev.* **67**, 19 (1967).

[5] M. Gregson, W. D. Ollis, B. T. Redman, I. O. Sutherland and H. H. Dietrichs, *Chem. Commun.* 1394 (1968).

[6] B. J. Donnelly, D. M. X. Donnelly, A. M. O'Sullivan and J. P. Pendergast, *Tetrahedron* **25**, 4409 (1969).

TABLE 2. PMR DATA OF *trans*-2-ARYL-METHYL-2,3-DIHYDROBENZOFURANS

Compound		H-2	H-3	Me-3	Aryl-H	H-4	H-7	OMe	O_2CH_2	OH
Xa[5]	τ	4 90	6 4–6 9	8 63	2 63	3 30	3·53	6·20		4·77
	mult.	d	m	d	s	s	s	s		bs
	J(Hz)	8 0	—	7·0	—	—	—	—		—
XI[6]	τ	4 98	6·4–6 9	8·65	overlap		3·61			
	mult.	d	m	d	m		s			
	J(Hz)	8·5	—	7 0			—			
XIIa	τ	4 97	6·4–6·9	8 65	3·1–3 2	3·33	3·53	6 16	4 06	4 34
	mult.	d	m	d	m	s	s	s	s	bs
	J(*Hz*)	9·0	—	6 6	—	—	—	—	—	—

The data were recorded on Varian 60 MHz spectrometres in $CDCl_3$ solutions, s—singlet, bs—broad singlet, d—doublet, m—multiplet.

dihydrobenzofurans which occur in species of the genus *Dalbergia* (Leguminosae). The singlets around τ 3·3 and 3·5 of all three spectra can only be assigned to the aromatic protons of the benzodihydrofuran moiety. The *para* relationship of these protons is thus clearly indicated not only for obtusafuran (Xa) and melanoxin (XI), but also for the 2,3-dihydrobenzofuran generated from burchellin. Accordingly melanoxin and the burchellin derivative should possess identical oxygenation patterns. That this is the case is shown by the similarity of their UV spectra: Melanoxin, λ_{max} 207, 233 infl., 291, 305 nm (ε 33 900, 12 000, 5350, 6300);[6] burchellin derivative, λ_{max} 207, 233 infl., 296, 305 infl. nm (ε 34 000, 12 500, 11 500, 9500).

Furthermore, while indeed the NMR-spectra of (+)-obtusafuran (Xa), (—)-melanoxin (XI) and the burchellin derivative are comparable also with respect to the chemical shifts of the proton on C-2 and the methyl group on C-3 (Table 2), the spectrum of the synthetic (±)-*cis*-2,3-dihydrobenzofuran (Xb) is different (τ 4·27 for H-2 and 9·26 for Me-3).[5] A *trans*-2,3-dihydrobenzofuran structure can therefore be assigned to the burchellin derivative. This must possess the (2*S*,3*S*)-absolute configuration of (—)-melanoxin (XI), since the ORD-data of the two compounds are closely comparable and antipodal to the data registered for (2*R*,3*R*)-obtusafuran (Table 3). Thus, the 2,3-dihydrobenzofuran derivative of burchellin can be represented by the structures XII (a or b). At this stage, however, it is

TABLE 3. ORD EXTREMA ([φ]) OF *trans*-2-ARYL-3-METHYL-2,3-DIHYDROBENZOFURANS

nm	Xa[8] (MeOH)	XI[7] (MeOH)	XIIa (dioxane)
311		−8400	−3030
312	+3150		
282	−2360		
284		+8700	
288			+10 450
261		+2040	
264	−1130		
270			+4140
240		+6830	
241			+12 750

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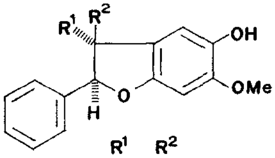
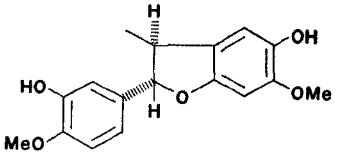
[7] D. M. X. DONNELLY, private communication (1971).

[8] B. T. REDMAN, Ph.D. Thesis, p. 96, University of Sheffield (1968).

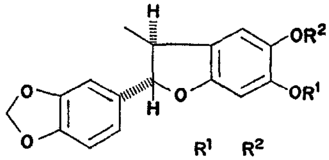
irrelevant to establish which of the alternatives is the correct one, since both point to VIb as the only structural possibility for burchellin. This can now be expanded into alternative structures XIII and XIV.



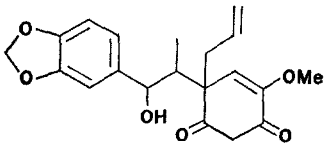
	R¹	R²
(X) a	Me	H
b	H	Me



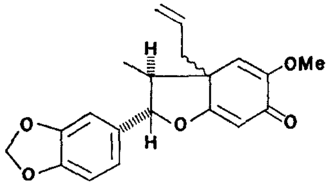
(XI)



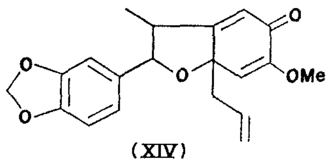
	R¹	R²
(XII) a	H	Me
b	Me	H
c	Ac	Me



(XV)



(XIII) Burchellin

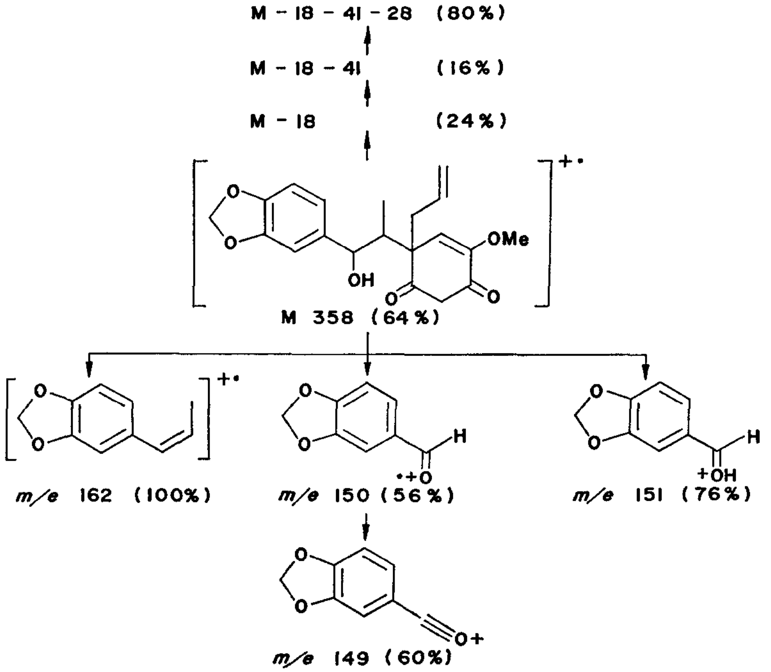


(XIV)

Burchellin is stable in *N*-methanolic KOH solution at reflux temperature, but under more vigorous conditions (4 N methanolic KOH), it is transformed into a crystalline derivative. This is not a degradation product, since in acid solution it reverts to a product which is chromatographically indistinguishable from the starting material. Indeed, its molecular weight is 18 mass units higher than that of burchellin. The IR spectrum reveals the presence of hydroxyl (ν_{max} 3350 cm^{-1}) and of two carbonyls, one in saturated environment (ν_{max} 1715 cm^{-1}) and one conjugated to a double bond (ν_{max} 1658 cm^{-1}). These results can best be rationalized in terms of the formation of XV, which points to XIII as the correct structure of burchellin, and to XIIa as the structure of the derived 2,3-dihydrobenzofuran.

NMR spectral data confirm the formulation XV for the hydrolytic product. While the signals due to the hydrogens of the piperonyl and the allyl portions of its molecule are present in the same form as in the NMR spectrum of burchellin itself, the doublet due to the benzylic proton shows now a much reduced coupling constant (*J* 5·6 Hz against 9·5 Hz, see H^x in Table 1), typical of vicinal coupling in open chains. Furthermore, in comparison with the spectrum of the original burchellin (Table 1), the chemical shift of this signal (τ 5·30), as well as of the C-methyl doublet (τ 8·69, *J* 7·4 Hz), suffered substantial alterations, indicating that structural modifications must have taken place at these sites. The clearest evidence, however, refers to the aliphatic ring of structure XV, which is associated in the NMR spectrum with three sharp singlets at τ 4·70 ($=C\underline{H}$), 6·43 ($=C-OC\underline{H}_3$) and 7·02 ($CO.C\underline{H}_2.CO$). The equivalence of the methylene protons which thus becomes apparent, demonstrates the conformational mobility which the ring gained upon opening of the tetrahydrofuran unit of burchellin.

The mass spectrum of the hydrolytic product also favours the previous deductions. Fragmentation into the oxonium ion of *m/e* 151 (Scheme 1), to be expected for this bicyclic compound (XV), is of course not observed during the electron bombardment of the tricyclic burchellin (XIII) itself. Practically with the exception of the peak at *m/e* 162 however, the



SCHEME 1. INTERPRETED MASS SPECTRUM OF THE HYDROLYTIC PRODUCT (XV) OF BURCHELLIN (XIII).

mass spectrum of burchellin was not specially helpful for the structural analysis of this compound. The rearrangements which seem to account for some of its major peaks (Scheme 2) could only be formulated with confidence after elucidation of the structure by other means.

Plant products based on a carbon skeleton having two *n*-propyl-benzene residues linked at the β-positions are termed lignans. In burchellin (XIII), as well as in other natural compounds,[9] the two residues are not linked through the β-positions. It is proposed to designate this novel class of bis-arylpropanoids as neolignans.[9]

EXPERIMENTAL

Isolation of the constituents of Aniba burchellii. The powdered trunk wood (5 kg) was continuously extracted with benzene. The filtered benzene solution was evaporated and the residue (35 g) extracted with light petroleum. The insoluble portion was filtered through silica and crystallized from MeOH, yielding burchellin (XIII, 250 mg). The light petroleum soluble portion was chromatographed on silica, yielding benzyl benzoate (5 g) and sitosterol (150 mg).

Burchellin (XIII), white crystals, m.p. 154–156° (MeOH) (Found: C, 70·15; H, 5·92; OMe 9·56. $C_{20}H_{20}O_5$ requires: C, 70·57; H, 5·92; 1 OMe, 9·12%). ν_{max} ($CHCl_3$, cm^{-1}): 1650, 1615, 1502, 1490, 1448, 1382, 1360, 1250, 1160, 1037, 934. λ_{max} (EtOH, nm): 213, 261, 287 sh (ϵ20 250, 16 000, 3500). ORD (dioxane, c 0·083, 600–290 nm, c 0·028, 290–240 nm): $[\phi]_{589}$ −395, $[\phi]_{400}$ −395, $[\phi]_{380}$ −1630, $[\phi]_{367}$ −4390, $[\phi]_{358}$ −2170, $[\phi]_{353}$ −2615, $[\phi]_{348}$ 0, $[\phi]_{340}$ +6460, $[\phi]_{320}$ +27 080, $[\phi]_{304}$ +45 085, $[\phi]_{296}$ +20 370, $[\phi]_{293}$ 0, $[\phi]_{280}$ −36 405, $[\phi]_{266}$ −43 065, $[\phi]_{260}$ −37 590, $[\phi]_{248}$ 0.

Oxidation of burchellin. To XIII (30 mg) in acetone (5 ml) a saturated solution of $KMnO_4$ in acetone was added dropwise at room temp. until a pink colour persisted. Sodium dithionite was then added and the mixture filtered. Evaporation of the solvent and sublimation of the residue under reduced pressure gave piperonylic acid (4 mg), m.p. and m.m.p. 229–231°.

Hydrogenation of burchellin. (a) XIII (100 mg) in EtOH (20 ml) was added to prehydrogenated PtO_2

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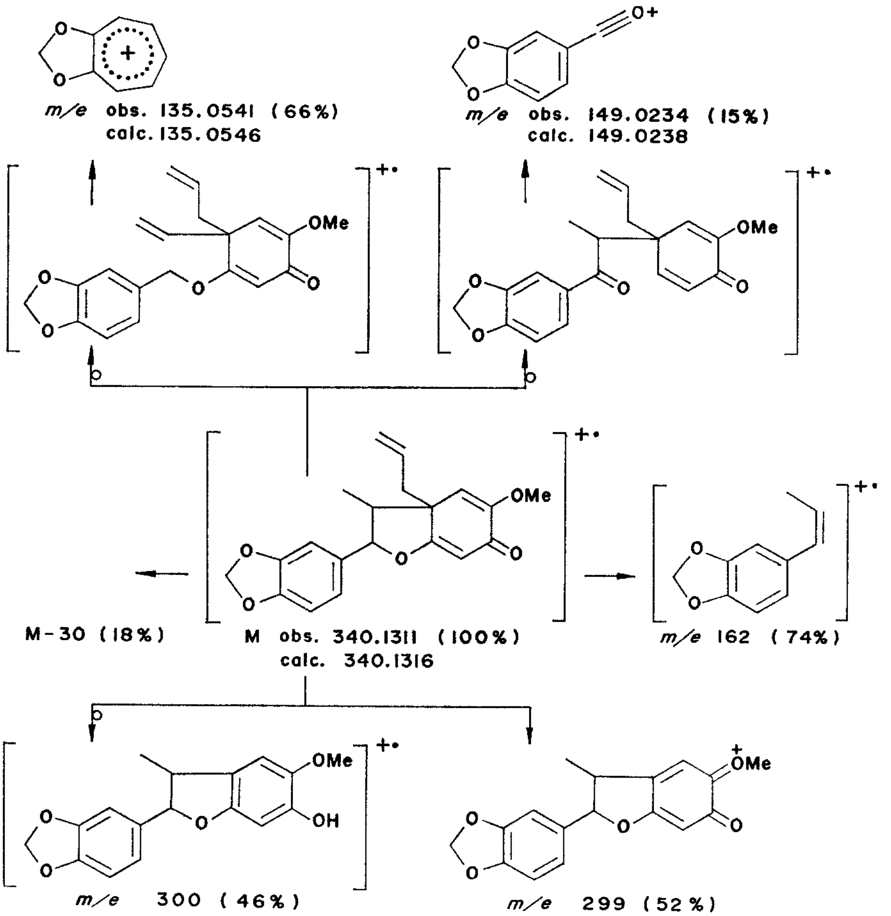
[9] O. R. GOTTLIEB, *Phytochem.* **11**, 1537 (1972).



Scheme 2. Interpreted mass spectrum of burchellin (XIII).

(20 mg) in EtOH (10 ml), and treated with excess H_2. The reaction mixture was chromatographed on silica. Successive elution with benzene, benzene–EtOAc 95:5 and benzene–EtOAc 9:1 gave respectively fractions A, B and C. Evaporation of the eluate A, and recrystallization of the residue (20 mg) from light petroleum gave XIIa. Evaporation of the eluates B and C afforded residues which were shown, by mass spectrometry, to be mixtures respectively of hexahydroburchellin-tetrahydroburchellin (35 mg) and tetrahydroburchellin-burchellin (25 mg). The predominant tetrahydroderivative (IX) was separated by fractional recrystallization from EtOH.

(2*S*,3*S*)-2,3-*Dihydro-6-hydroxy-5-methoxy-3-methyl-2-piperonylbenzofuran* (XIIa), white crystals, m.p. 94–96°. ν_{max} ($CHCl_3$, cm^{-1}): 3510, 1621, 1486, 1462, 1439, 1332, 1242, 1210, 1152, 1112, 1037, 997, 939, 857, 828 cm^{-1}. MS: M 300 (100%), *m/e* (%) 285 (15), 267 (10), 257 (12), 253 (5), 239 (19), 165 (34), 163 (5), 160 (6), 152 (7), 149 (7), 146 (5), 134 (17), 132 (6), 115 (5), 77 (8), 69 (9). ORD (dioxane, c 0·052, 600–230 nm): $[\phi]_{589}$ +175, $[\phi]_{450}$ +200, $[\phi]_{334}$ 0, $[\phi]_{320}$ −1635, $[\phi]_{311}$ −3030, $[\phi]_{304}$ −2975, $[\phi]_{302}$ 0, $[\phi]_{300}$ +1260, $[\phi]_{296}$ +5405, $[\phi]_{288}$ +10 450, $[\phi]_{280}$ +6615, $[\phi]_{270}$ +4145, $[\phi]_{260}$ +4915, $[\phi]_{250}$ +8365, $[\phi]_{241}$ +12 750, $[\phi]_{230}$ +3345.

The *acetate* (XIIc) was obtained from XIIa as white crystals, m.p. 95–100° (light petroleum). ν_{max} ($CHCl_3$, cm^{-1}): 1760, 1625. λ_{max} (EtOH, nm): 208, 237, 306. NMR (60 MHz, $CDCl_3$, τ): 3·1–3·2, m, 3H arom.; 3·25 and 3·46, singlets, 2H arom.; 4·06, s, $O_2C\underline{H}_2$; 4·95, d, *J* 9·0 Hz, Ar–C$\underline{H}$–O; 6·16, s, $OC\underline{H}_3$; 7·66, s, $C\underline{H}_3CO$. MS: M 342 (51%), *m/e* (%) 300 (100), 285 (18), 267 (11), 239 (15), 165 (25), 160 (5), 153 (5), 135 (15), 77 (5), 69 (5), 43 (8).

Tetrahydroburchellin (IX), white crystals, m.p. 158–160° (EtOH). ν_{max} ($CHCl_3$, cm^{-1}): 1692. λ_{max} (EtOH, nm): 206, 274 (ϵ 39 200, 29 600). NMR (220 MHz, $CDCl_3$, τ): 3·20–3·33, m, 3H arom.; 4·06, s, $O_2C\underline{H}_2$;

4·55, s, $=C\underline{H}$; 4·98, d, *J* 10·0 Hz, $Ar{-}C\underline{H}(CH)O{-}$; 6·43, dd, *J* 5·5 and 2·0 Hz, $-C\underline{H}(CH_2)O-$; 6·48, s, $=C{-}OC\underline{H}_3$; 7·53, dd, *J* 14·5 and 2·0 Hz, $=CH{-}CH\ \underline{H}eq{-}CO$; 8·0–8·9, m, 5$\underline{H}$; 8·94, d, *J* 6·5 Hz, $=CH{-}C\underline{H}_3$; 9·08, t, *J* 7·0 Hz, $-CH_2{-}C\underline{H}_3$. MS: M 344 (3%), *m/e* (%) 315 (31), 288 (23), 274 (100), 260 (31), 259 (31), 245 (11), 231 (20), 219 (11), 189 (11), 177 (34), 164 (23), 161 (20), 151 (23), 137 (27), 133 (11), 129 (11), 128 (11), 123 (11), 112 (10), 104 (11), 77 (14), 69 (14), 54 (11), 41 (11).

Treatment of burchellin with alkali. XIII (100 mg) in 4 N KOH/MeOH (20 ml) was heated under reflux (4 hr, N_2). The solvent was evaporated under vacuum. The residue was taken up in benzene and chromatographed over silica. Elution with benzene–EtOAc (9:1) gave a product which was recrystallized from light petroleum–Et_2O yielding XV (45 mg), white crystals, m.p. 158–160°. ν_{max} ($CHCl_3$, cm^{-1}): 3380, 1715, 1658 cm^{-1}. λ_{max} (EtOH, nm): 216, 244, 268. NMR (60 MHz, $CDCl_3$, τ): 3·28, 3$\underline{H}$ arom.; 4·07, s, $O_2C\underline{H}_2$; 3·9–4·4, m, $-CH_2{-}C\underline{H}{=}CH_2$; 4·69, s, $=CH$; 4·7–5·0, m, $-CH_2{-}CH{=}C\underline{H}_2$; 5·30, d, *J* 5·6 $\underline{H}$z, $Ar{-}C\underline{H}$ $({=}CH)$ OH; 6·43, s, $OC\underline{H}_3$; 7·02, s, $-COC\underline{H}_2CO$; 7·4–8·0, m, $-C\underline{H}_2{-}CH{=}CH_2$ and $=CH{-}C\underline{H}{-}CH_3$; 8·69, d, *J* 7·0 Hz, $=CH{-}C\underline{H}_3$.

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Key Word Index—Aniba burchelli; Lauraceae; benzyl benzoate; sitosterol; burchellin; neolignan.