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THE NEOLIGNANS OF *LICARIA CANELLA**

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Key Word Index—*Licaria canella*; Lauraceae; neolignans; canellin-A; canellin-B; canellin-C; 1-allyl-4,8-dihydroxy-3,5-dimethoxy-7-methyl-6-piperonylbicyclo-[3,2,1]octane; 3a-allyl-4,5-dimethoxy-3-methyl-2-piperonyl-2,3,3a,6,7,7a-hexahydro-6-oxobenzofuran; 1-allyl-4,8-dihydroxy-5-methoxy-7-methyl-6-piperonyl-3-oxobicyclo-[3,2,1]octane.

Abstract—The trunk wood of *Licaria canella* contains, besides dillapiol and elemicin, the neolignans canellin-A, -B and -C, for which the respective structures of 1-allyl-4,8-dihydroxy-3,5-dimethoxy-7-methyl-6-piperonylbicyclo-[3,2,1]octane; 3a-allyl-4,5-dimethoxy-3-methyl-2-piperonyl-2,3,3a,6,7,7a-hexahydro-6-oxobenzofuran and 1-allyl-4,8-dihydroxy-5-methoxy-7-methyl-6-piperonyl-3-oxobicyclo-[3,2,1] octane are proposed.

INTRODUCTION

Licaria canella (Meissn.) Kosterm. is a tree which grows in the Amazon region. The trunk wood yielded sitosterol, dillapiol (1-allyl-2,3-dimethoxy-4,5-methylenedioxybenzene), elemicin (5-allyl-1,2,3-trimethoxybenzene) and three new compounds for which the names canellin-A, -B and -C are proposed.

The oxygen functions of canellin-A, $C_{21}H_{28}O_6$, were easily assigned by PMR spectrometry, warranting expansion of the formula to $C_{18}H_{18}.20H.20Me.O_2CH_2$. The C_{18}-skeleton is of the guianin (**1**) type;[2] thus, the MS contains a prominent *m/e* 162 peak attributable to **2** (Scheme), since PMR evidence accounts for all protons in the $C_{12}H_{10}O_2$ unit of the partial structure **3**. In contrast to guianin, however, here both undefined centres are fully substituted. The α-proton (τ 6·75, *d*, *J* 9·0 Hz) is coupled to one vicinal hydrogen, and the β-proton (signal analyzable in the NMR of dihydrocanellin-A: τ 7·63, apparent quintuplet, *J* apparently ≃ 8 Hz, in reality *J* 7·0 and 9·0 Hz) is coupled to four hydrogens.

Both hydroxyls have secondary alcohol functions, since two of the oxymethine proton signals suffer 1 ppm paramagnetic shifts on acetylation. One of these protons is represented by a singlet (τ 6·49) and the respective CHOH group must, consequently, be located

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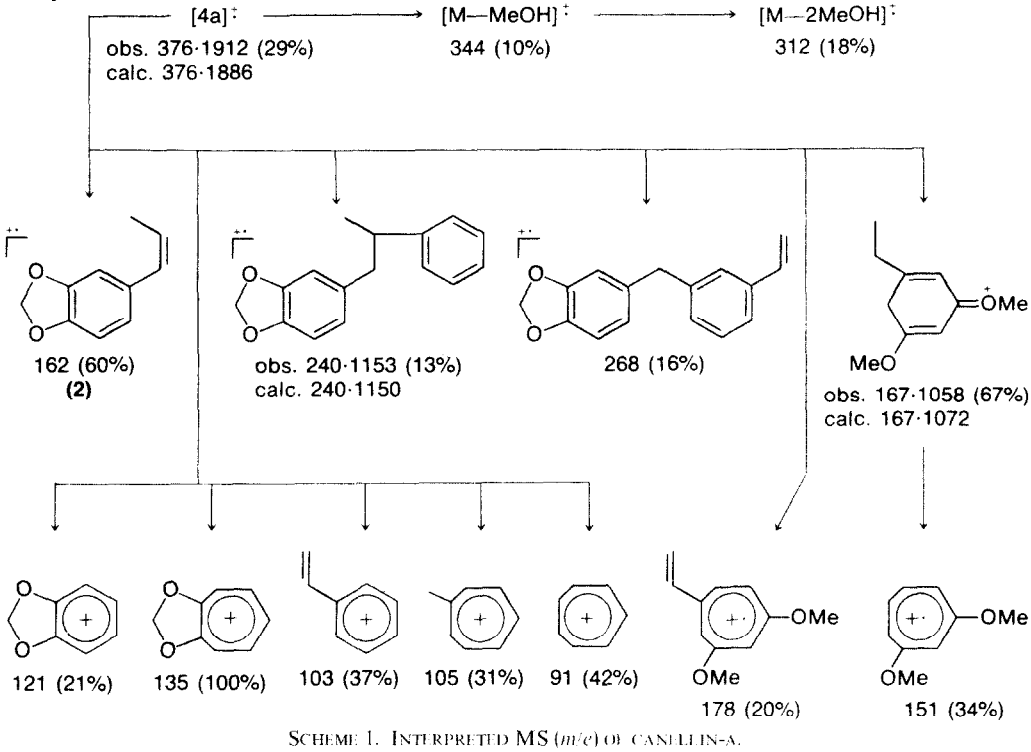
[1] FRANCA, N. C., GOTTLIEB, O. R. and PUENTES SUAREZ, A. M. (1973) *Phytochemistry* **12**, 1182.

[2] BÜLOW, M. V. von, FRANCA, N. C., GOTTLIEB, O. R. and PUENTES SUAREZ, A. M. (1973) *Phytochemistry* **12**, 1805.

between two quaternary carbons. The other proton is represented by a doublet (τ 5·97) whose coupling constant (J 6·5 Hz) reveals its axial–axial interaction with a neighbouring proton. This could, *a priori*, belong either to the CHOMe or to the CH_2 units. The oxymethine hydrogen, however, is represented by a triplet (τ 6·38, J 6·5 Hz) and is thus subject to two axial interactions, while the axial methylene hydrogen is represented by a doublet (τ 8·46, J 15·8 and 6·5 Hz) and thus vicinal to only one axial proton. This 3-carbon system must, consequently, be formulated as shown in **3**, a sequence which agrees with the observation that only the CHOMe signal (Δ −0·3 ppm), but not the CH_2 signals, is shifted on acetylation.



SCHEME 1. INTERPRETED MS (*m/e*) OF CANELLIN-A.

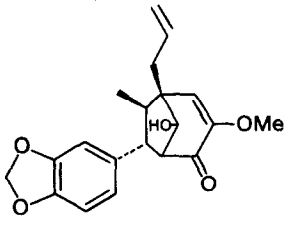
Both the remaining methoxyl and allyl groups, must be attached to non-protonated carbons. The PMR spectrum contains only the ether methine proton signal assigned above, and the allylic methylene protons (τ 7·50–7·62, m; τ 7·95, *dd*, J 9·2 and 13·5 Hz) are non-equivalent and coupled only to each other and the adjacent olefinic hydrogen.

The units of partial structure **3** can be assembled in four ways (**4**a, b; **5**a, b). The allylbenzenes, which are presumed biogenetic precursors of canellin-A, are uniformly oxygenated at the *para*-position so that the pair of alternatives **4**b and **5**a are highly improbable. By contrast, the biosyntheses of **4**a and **5**b involve reasonable metabolites, such as **6**a or **7**a, derived by oxidation of an elemicin precursor, or **6**b or **7**b, derived by oxidation of a dillapiol precursor. Radicals of type **6** are certainly formed in Lauraceae, as documented in the structures of guianan (**1**),[2] porosin (**8**)[3] and burchellin (**9**).[4] In addition, since *para*-sub-

[3] AIBA, C. J., BRAZ FILHO, R. and GOTTLIEB, O. R. (1973) *Phytochemistry* **12**, 413.
[4] ARAÚJO LIMA, O., GOTTLIEB, O. R. and TAVEIRA MAGALHÃES, M. (1972) *Phytochemistry* **11**, 2031.

stitution is favoured over *ortho*-substitution,[5] canellin-A is probably formed by coupling of **6a** or b with a radical derived from isoeugenol[6] leading to **10** or **11**, both of which would yield **4a**, rather than **5b**.

The MS fragmentation (Scheme), is, of course, consistent with either alternative. A tentative decision in favour of **4a**, with the relative stereochemistry **13a**, was reached by the following set of experiments. Treatment of canellin-A with the Jones reagent led to a mixture of ketones with carbonyls in 5-(ν_{max}1745 cm^{-1}) and 6-(ν_{max}1720 cm^{-1}) membered cycles. Since oxidation of dihydrocanellin-A failed to give a pure product, a partially protected substrate was prepared. Selective acetylation of canellin-A at the C-4 hydroxyl, diagnosed by the shift of the carbinolic proton *doublet* (Δ −1·04 ppm), led to a monoacetate. This was oxidized to give a pure ketone (**12**), which, as well as its hydrolysis product, has the carbonyl in a five-membered ring (ν_{max}1760 cm^{-1}). Oxidation of dihydrocanellin-A monoacetate also afforded a pure ketone (dihydro-**12**, ν_{max}1750 cm^{-1}). The acetate carbonyls of the mono- and di-acetates show bands at lower frequency (1735 cm^{-1}).



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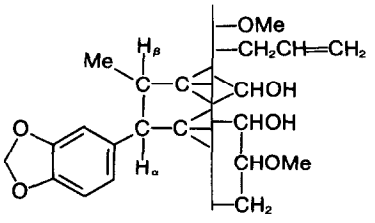

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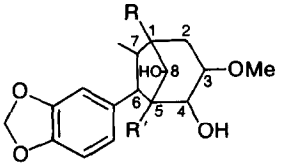
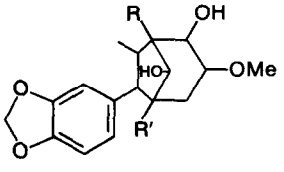
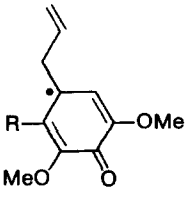


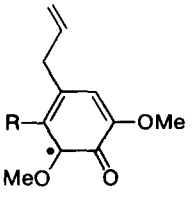
(4a) R = allyl; R′ = OMe
(4b) R = OMe; R′ = allyl



(5)



(6a) R = H
(6b) R = OH



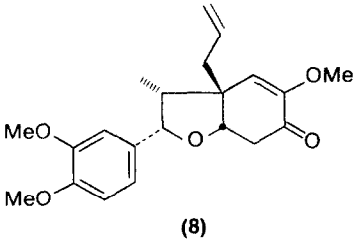
(7)

Transformation of the secondary alcohol at C-8 into a carbonyl (dihydro-**13b** → dihydro-**12**) was accompanied by two PMR phenomena. Thus, there are diamagnetic shifts of the ArH (Δ H-2′ 0·54, H-5′ 0·25, H-6′ 0·23 ppm) and the H-7 (Δ 0·50 ppm) signals, which contrasts with the virtual constancy of the H-6 (Δ −0·05 ppm) and Me-7 (Δ −0·04 ppm) signals. The *exo-endo* arrangement, which thus becomes obvious for the aryl-methyl substituents, imposes the *trans* configuration on the 6,7-bond, a fact which is consistent with the relatively large coupling $J_{6,7}$ 9·0 Hz [porosin (**8**), burchellin (**9**) and guianin (**1**), admittedly imperfect analogies, J resp. 5·4, 9·5 and 7·0 Hz] and the normal chemical shift of the Me-7 protons (τ 9·13). The *cis* configuration would place these protons into the positively shielded region above the aromatic plane [see porosin (**8**) τ 9·48]. The second PMR feature

[5] Geissman, T. A. and Crout, D. H. G. (1969) *Organic Chemistry of Secondary Plant Metabolism* p. 377. Freeman, Cooper, San Francisco.

[6] Gottlieb, O. R. (1972) *Phytochemistry* **11**, 1537.

is the large paramagnetic shift of the high field (Δ 0·10 ppm), which contrasts with the low field (Δ 0·02 ppm) methoxy signal. The former signal must thus be correlated with the bridgehead methoxyl situated in the plane of the introduced carbonyl. The high field but not the low field signal is sensitive to change of solvent. Thus, on changing from $CDCl_3$ to CCl_4 solutions of canellin-A and its derivatives this signal is shifted to even higher field (**4**a: Δ 0·14 ppm, dihydro-**13**b: Δ 0·06 ppm). Formation of a D-bridge between the basic aryl group and the solvent molecule is possible, evidently, only in $CDCl_3$.[7] The fact that the heightened magnetic anisotropy of the aryl group in CCl_4 produces additional shielding of methoxyl is taken as an indication that these groups are vicinal and excludes structure **5**b as a viable alternative.



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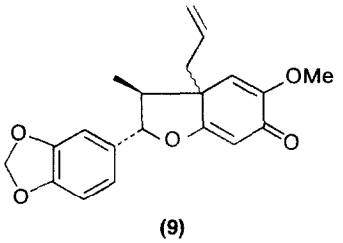

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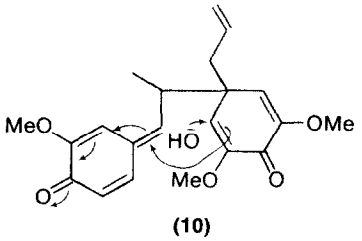

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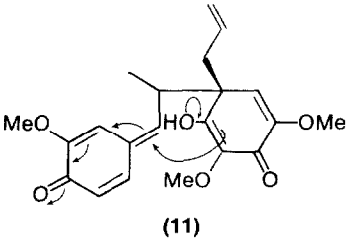


(11)

Acetylation of the hydroxyl at C-4 leaves the ArH and H-7 signals unaffected, but causes significant shifts of the H-6 (Δ −0·40 ppm) and H-3 (Δ −1·00 ppm) signals. The modified group must thus occupy the *endo* face of the molecule and, since the proton at C-4 is axial, as shown by its axial axial interaction (J 6·5 Hz) with the neighbouring H-3, the 6-membered ring occurs in the chair conformation. The equatorial conformation of the acetoxyl is consistent with the relative resistance of **7** to hydrolysis which requires hot 5% aq. NaOH. The PMR spectrum of the resulting alcohol showed, besides the expected changes, the carbinolic proton signal with an unexpectedly small J (*ca* 2 Hz) and the OMe-5 signal at an unexpectedly high field (τ7·20). These facts probably reflect a retroaldol-aldol equilibrium. The consequent inversion at C-4 pushes the H-4 into the equatorial position (hence diminishing $J_{H-3,H-4}$) and the methoxyl over the aryl group (hence increasing τ_{OMe}). Finally, acetylation of the hydroxyl at C-8 shifts the H-7 signal (Δ −0·29 ppm), but leaves the signals due to the protons of the 6-membered ring unaltered. Its orientation towards the 5-membered ring is, consequently, indicated. Only in this configuration would it be able to contribute towards the molecular asymmetry caused by the aryl group and portrayed by the slight non-equivalence of the methylenedioxy protons (AB system, τ 4·11 and 4·12). This non-equivalence would be expected to be enhanced through substitution of the C-8 carbinol by a carbonyl and this is indeed the case (AB system, τ 4·19 and 4·21).

[7] LASZLO, P. (1964) *Bull. Soc. Chim. France* 2658.

TABLE 1. 220 MHz PMR SPECTRA OF POROSIN (**8**) AND OF CANELLIN-B (**14**) IN $CDCl_3$

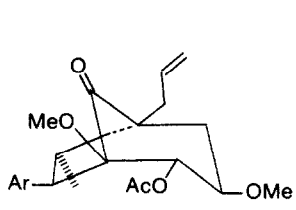
	(**8**)			(**14**)		
		Mult.	*J* (Hz)		Mult.	*J* (Hz)
ArH	3·07	*d*	8·0			
ArH	3·17	*dd*	8·0, 2·0	3·23–3·32	*m*	
ArH	3·24	*d*	2·0			
O_2CH_2	—			4·09	*s*	
$CH{=}CH_2$	3·94–4·15	*m*		4·05–4·23	*qd*	16·0, 10·0, 8·5, 6·5
H-4	4·41	*s*		—		
$=CH_2$	4·60–4·72	*m*		4·73–4·84	*m*	
H-2	4·11	*d*	5·4	4·95	*d*	10·0
H-7a	5·98	*dd*	12·0, 5·0	5·97	*dd*	12·0, 5·5
2 ArOMe	6·10	*s*		—		
ROMe	6·38	*s*		6·30	*s*	
ROMe	—	s		6·45	s	
CH–CH=	7·31	*dd*	14·5, 7·0	7·40	*dd*	15·0, 6·5
CH–CH=	7·44	*dd*	14·5, 7·0	7·55	*dd*	15·0, 8·5
H-3	7·4	*m*		7·93	*dq*	10·0, 7·0
H_{eq}-7	7·78	*dd*	12·0, 5·0	7·52	*dd*	12·0, 5·5
H_{ax}-7	8·08	*t*	12·0	8·24	*t*	12·0
Me-3	9·48	*d*	7·5	8·96	*d*	7·0

The bisarylpropanoid nature of canellin-B was inferred by the formula $C_{21}H_{24}O_6$, determined by high resolution MS, and expanded to $C_{18}H_{16}O_2.O_2CH_2.2OMe$ after inspection of the PMR spectrum. This showed additionally that canellin-B (ν_{max}1660 cm^{-1}) is of the porosin (ν_{max}1667 cm^{-1}, **8**)[3] type (Table 1). With the exception that the two aromatic methoxy signal in porosin are replaced by a O_2CH_2 signal, and that its H-4 singlet is replaced by a signal due to an enolic methoxyl, all spectral features are duplicated, and must, consequently be interpreted in an analogous manner, leading to structure **14** for canellin-B. In contrast to the situation in porosin where the multiplicity of the pertinent PMR signals indicate the relative locations of the functions on the aliphatic 6-membered ring, in the case of canellin-B structure **15** has to be considered as a valid, albeit less probable, alternative. The stereochemistry of the 2,3-bond constitutes an additional difference between the two neolignans. Clearly *cis* in porosin ($J_{H-2,H-3}$ 5·4 Hz), where the Me group (τ 9·48) falls into the shielded region above the aryl group, it is *trans* in canellin-B ($J_{H-2,H-3}$ 10·0 Hz, τ_{Me} 8·96). The MS is compatible with the proposed structures, revealing the expected facile loss of an allyl radical ($[M-C_3H_5]^+$ 100%, $[M-C_3H_5-CO]^+$ 84%) and cleavage of the heterocycle ($[CH_2O_2C_6H_3CH{=}CHMe]^+$ 90%).

Canellin-C, $C_{20}H_{24}O_6$, is also a bisarylpropanoid, since functional analysis establishes the partial structure $C_{18}H_{17}O.2OH.OMe.O_2CH_2$. The undefined oxygen in this formula, however, is not part of an ether, but of a carbonyl function in saturated environment (ν_{max}1720 cm^{-1}), and thus the compound could be a structural analogue of canellin-A (**4a**), rather than of canellin-B (**14** or **15**). Indeed, comparison of the PMR spectra (Table 2) clearly favours this. The significant difference reveals replacement of the methoxymethine at position 4 in canellin-A (**4a**) by the carbonyl in canellin-C. This fact rationalizes the appearance of the C-4 oxymethine signal as a singlet and of the C-2 methylene signals at lower field. Alternatives to structure **16a**, which thus is tentatively proposed for canellin-C, could not be disproved, due to lack of material.

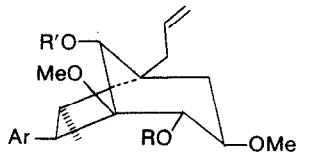
The relationship between canellins A and C extends to their stereochemistry. While the hydroxyl at C-8 of guianin (**1**)[2] is acetylated with ease, only the 4-*O*-acetyl derivatives (**13b**,

16b) result upon treatment of the two canellins with Ac_2O/C_6H_5N at room temp. Attack of the hydroxyl at C-8 seems to be hindered by the proximity of the aryl group, the *exo*-attachment of this group being evident, additionally, by the non-equivalence of the methylenedioxy protons. The benzylic hydrogens at C-6 are thus *endo* oriented in the canellins A and C, the diamagnetic shift of the respective signal upon passing from A to C being due to shielding by the carbonyl of the latter cmpd.

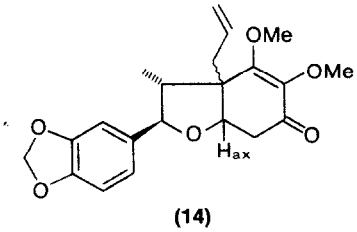


(12)

Ar = piperonyl



(13)	R	R'
a	H	H
b	Ac	H
c	Ac	Ac



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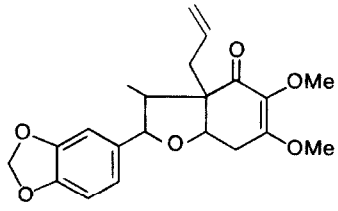
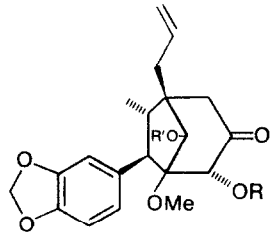


(15)



(16a) R = H; R' = H
(16b) R = Ac; R' = H
(16c) R = Ac; R' = Ac

EXPERIMENTAL

Isolation of the constituents of Licaria canella. A tree at the Ducke Forest Reserve, Manaus, identified by the botanist William Rodrigues (Herbarium sample INPA, Manaus, 21.230) gave a trunk wood sample (5 kg) which was dried, powdered, and extracted successively with C_6H_6 and with EtOH. The C_6H_6 soln., after conc. and standing at room temp., pptd. a solid (6 g) which was separated by filtration, washed with Et_2O and recrystallized from C_6H_6 to give canellin-A (**5a**, 9·2 g). The filtrate was evaporated to give an oily residue (13 g), which was chromatographed on silica. The following fractions were eluted, in order, with the indicated solvents: A_1 and A_2 (C_6H_6), A_3 (C_6H_6–$CHCl_3$ 19:1), A_4 (C_6H_6–$CHCl_3$ 1:4), A_5 ($CHCl_3$), A_6 and A_7 ($CHCl_3$–MeOH 99:1). A_1 (0·55 g) oily aliphatic esters. A_2 (2·5 g) was purified by vacuum distillation to give dillapiol (b.p.$_{10mm}$ 160–161°). A_3 (0·22 g) was a mixture present also in previous and subsequent fr. A_4 (0·92 g) was fractionated in part (0·10 g) by preparative TLC (SiO_2, C_6H_6–AcOEt 4:1) into elemicin (59 mg) and sitosterol (30 mg). A_5 and A_6 (1·56 g) was a complex mixture containing elemicin, sitosterol and canellin-A from which the latter cmpds. were separated by preparative TLC (SiO_2, $CHCl_3$–MeOH 19:1). A_7 (5·4 g) was crystallized repeatedly from C_6H_6 to give a total of 2·5 g of canellin-A. The mother liquors were evaporated and part (0·7 g) of the oily residue was chromatographed on florisil. The following products were eluted, in order, with light petrol–Et_2O mixtures of indicated composition: aliphatic esters (17:3), canellin-A (0·3 g, 4:1, canellin-C (40 mg, 4:1), canellin-B (0·12 g, 1:1), aliphatic material (0:100). Only a small fraction of the EtOH extract of the wood was eluted from a silica column by C_6H_6 ctg. up to 2% EtOH. This was shown, by TLC, to be composed chiefly of the compounds already isolated from the C_6H_6 extract.

Dillapiol (1-allyl-2,3-dimethoxy-4,5-methylenedioxybenzene). B.p.,[8] IR[9] and PMR[9] spectra as required by lit. MS (*m/e*) 222 (100%) M, 207 (20), 177 (59), 175 (12), 149 (47), 134 (13), 133 (15), 121 (41), 119 (11), 117 (11), 107 (14), 106 (47), 105 (21), 103 (11).

[8] KARRER, W. (1958) *Konstitution und Vorkommen der organischen Pflanzenstoffe*. Birkhäuser, Basel.
[9] SØRENSEN, J. S. and SØRENSEN, N. A. (1969) *Aust. J. Chem.* **22**, 758.

TABLE 2. 220 MHz PMR SPECTRA OF CANELLIN-A (**4a**) AND-C (**16**) IN $CDCl_3$ (IN PRESENCE OF D_2O: *a d*, *J* 6·5 Hz, *b* ABSENT)

	(**4a**)			(**16**)		
		Mult.	*J* (Hz)		Mult.	*J* (Hz)
ArH-2′	3·05	*s*		3·12	*s*	
ArH-6′	3·25	*d*	8·0	3·37	*s*	
ArH-5′	3·36	*d*	8·0			
O_2CH_2	4·11, 4·12	AB syst.	indet.	4·14, 4·15	AB syst.	indet.
$CH{=}CH_2$	4·00–4·20	*m*		4·02–4·22	*m*	
$=CH_2$	4·85–5·00	*m*		4·83–4·95	*m*	
H-4	5·97	*dd*[a]	8·5, 6·5	5·65	*s*	
H-3	6·38	*t*	6·5	—		
H-8	6·49	*s*		5·92	*s*	
OH-4	6·52[b]	*d*	8·5	6·23[b]	br.s	
OMe	6·60	*s*		—		
OMe	6·78	*s*		6·72	*s*	
OH-8	7·55[b]	*s*		7·58[b]	*s*	
H-6	6·75	*d*	9·0			
H-7						
CH–CH=	7·50–7·62	*m*		7·40–7·65	*m*	
H_{eq}-2	8·14	*d*	15·8			
H_{ax}-2	8·46	*dd*	15·8, 6·5			
CH–CH=	7·95	*dd*	13·5, 9·2	7·96	*dd*	13·9
Me-7	9·13	*d*	7·0	9·23	*d*	7·0

Elemicin (5-allyl-1,2,3-trimethoxybenzene). B.p. as required by lit.[8] IR ν_{max}^{film} (cm^{-1}): 1640, 1590, 1460, 1420, 1330, 1240, 1180, 1125, 1010, 980, 915, 825. PMR ($CDCl_3$, 60 MHz, τ): 3·58 (*s*, two ArH), 3·77–4·33 (*m*, $CH{=}CH_2$), 4·77–5·10 (*m*, $CH{=}CH_2$), 6·17 (*s*, 3 OMe), 6·67 (*d*, *J* 6·0 Hz, $ArCH_2$). PMR (CCl_4, τ): 6·23 (*s*, 2 OMe), 6·33 (*s*, OMe). PMR (C_6H_6, τ): 6·20 (*s*, OMe), 6·50 (*s*, 2 OMe). MS (*m/e*): 208 (100%) M, 193 (69), 177 (19), 165 (15), 150 (15), 135 (11), 134 (11), 133 (35), 124 (10), 121 (10), 119 (10), 118 (27), 115 (11).

Canellin-A (**8a**). Colourless prisms, m.p. 144·5–145° (C_6H_6). M found 376·1912; calcd. for $C_{21}H_{28}O_6$ 376·1886. UV λ_{max}^{EtOH} (nm): 228, 282 (ε 5600, 4400). IR ν_{max}^{KBr} (cm^{-1}): 3500, 1504, 1480, 1460, 1372, 1240, 1230, 1087, 1040, 995, 930, 920, 890, 850, 840, 816. PMR ($CDCl_3$, Table 2) (CCl_4, 60 MHz, τ): 3·14 (ArH-2′), 3·35 (ArH-6′), 3·40 (ArH-5′), 4·12 (O_2CH_2), 4·00–4·35 ($CH{=}CH_2$), 4·80–5·20 ($CH{=}CH_2$), 6·08 (CHOH), 6·43 (CHOMe), 6·70 (CHOH), 6·60 (OMe), superimp. (ArCH), 6·92 (OMe), 7·50–8·50 (2 CH_2, CHMe), 9·18 ($CHCH_3$). MS (*m/e*): 376 (29%) M, 344 (9), 312 (18), 271 (13), 268 (16), 240 (13), 225 (13), 199 (10), 178 (21), 167 (66), 165 (13), 162 (60), 161 (16), 153 (13), 151 (33), 149 (24), 147 (13), 145 (13), 141 (10), 139 (13), 137 (26), 136 (16), 135 (100), 134 (13), 133 (16), 131 (16), 129 (10), 128 (13), 127 (10), 125 (13), 123 (10), 122 (10), 121 (21), 119 (10), 117 (18), 115 (25), 109 (13), 107 (18), 105 (31), 104 (21), 103 (37), 95 (18), 93 (27), 91 (42). ORD (MeOH, 400–225 nm, *c* 12·4 mg/100 ml): $[\phi]_{400}$ −600, $[\phi]_{350}$ −909, $[\phi]_{300}$ −1666, $[\phi]_{250}$ −3181, $[\phi]_{240}^{tr}$ −4242, $[\phi]_{230}$ −1212, $[\phi]_{225}$ 0.

Catalytic hydrogenation (EtOH, Pd/C) of **8a** gave *dihydrocanellin*-A, colourless needles, m.p. 181–182°; IR ν_{max}^{KBr} (cm^{-1}): 3480, 1610, 1500, 1480, 1440, 1380, 1246, 1234, 1097, 1087, 1036, 990, 930, 880, 835, 815, 760. PMR ($CDCl_3$, 220 MHz, τ): 3·05 (*s*, ArH-2′), 3·25 (*d*, *J* 8·0 Hz, ArH-6′), 3·36 (*d*, *J* 8·0 Hz, ArH-5′), 4·11 and 4·12 (O_2CH_2), 5·95 (*dd*, *J* 6·5 and 8·5 Hz, CHOH), 6·37 (*t*, *J* 6·5 Hz, CHOMe), 6·47 (*s*, CHOH), 6·51 (*d*, *J* 8·5 Hz, OH), 6·60 (*s*, OMe), 6·74 (*d*, *J* 9·0 Hz, ArCH), 6·78 (*s*, OMe), 7·55 (*s*, OH), 7·63 (apparent quintuplet, $J \sim 8$ Hz, CHMe), 8·12 (*d*, *J* 15·8 Hz, $CH_{ax}H_{eq}$), 8·38–8·48 (*m*, $CHCH_2$–Me), 8·44 (*dd*, *J* 6·5 and 15·8 Hz, $CH_{ax}H_{eq}$), 8·57–8·68 (*m*, CH–CH_2–Me and CH_2–CH_2–Me), 9·05 (*t*, *J* 6·5 Hz, CH_2–CH_2–CH_3), 9·13 (*d*, *J* 7·0 Hz, $CHCH_3$). MS (*m/e*): 379 (20%) M + 1, 378 (100%) M, 346 (25), 328 (13), 314 (52), 308 (13), 296 (27), 289 (17), 285 (13), 271 (20), 270 (42), 267 (10), 252 (10), 251 (37), 243 (10), 242 (25), 232 (29), 225 (25), 213 (10), 199 (10), 178 (37), 169 (10), 167 (33), 163 (10), 162 (42), 151 (25), 149 (17), 139 (50), 135 (54), 123 (13), 121 (13), 115 (10), 109 (20), 107 (15), 105 (15), 103 (15), 97 (13), 95 (15), 93 (15), 91 (20).

Oxidation of **8a** with Jones reagent and purification of the reaction product in $CHCl_3$ by passage through silica gave a chromatographically pure amorphous solid. IR ν_{max}^{KBr} (cm^{-1}): 3500 (broad), 1750 inf., 1720, 1640, 1500, 1490, 1440, 1525, 1100, 1040. PMR showed this to be a mixture.

Canellin-A *monoacetate* (**13b**) and derivatives. Treatment of **13a** with Ac_2O–C_5H_5N (room temp., overnight) gave **13b**, purified by passage through silica (C_6H_6–AcOEt 8:2), m.p. 50–52° (*n*-C_6H_{14}). M found 418·1997; calcd. for $C_{23}H_{30}O_7$ 418·1992. IR ν_{max}^{KBr} (cm^{-1}): 3530, 1735, 1640, 1500, 1480, 1450, 1370, 1245, 1095, 1036, 930. PMR

(CCl_4, 60 MHz, τ): 3·17 (*s*, ArH-2′), 3·33 (*d*, *J* indet., ArH-6′), 3·40 (*d*, *J* indet., ArH-5′), 4·17 (*s*, O_2CH_2), 4·00–4·30 (*m*, $CH{=}CH_2$), 4·80–4·96 (*m*, $CH{=}CH_2$), 5·08 (*d*, *J* 6·5 Hz, CHOAc), 6·17 (*t*, *J* 6·5 Hz, CHOMe), 6·38 (*d*, *J* indet., ArCH), 6·48 (*s*, CHOH), 6·72 (*s*, OMe), 6·98 (*s*, OMe), 7·49–7·80 (*m*, CHMe, $CH_2CH{=}CH_2$ and $CH_{ax}H_{eq}$), 7·87 (*s*, CHOAc), 8·20–8·42 (*m*, $CH_{ax}H_{eq}$), 9·10 (*d*, *J* 7·0 Hz, $CHCH_3$).

Oxidation of canellin-A monoacetate with Jones reagent and purification of the reaction product in C_6H_6–Me_2CO 95:5 by passage through silica gave **12** as oil. M found 416·1829. $C_{23}H_{28}O_7$ requires 416·1835. IR ν_{max}^{KBr} (cm^{-1}): 1750, 1730 infl., 1510, 1490, 1450, 1380, 1240, 1105, 940. PMR ($CDCl_3$, 60 MHz, τ): 3·45–3·58 (*m*, 3 ArH), 4·12 (*s*, O_2CH_2), 4·05–4·30 (*m*, $CH{=}CH_2$), 4·87 (*d*, *J* indet., CHOAc), 4·85–5·20 (*m*, $CH{=}CH_2$), 6·20 (*t*, *J* 6·5 Hz, CHOMe), 6·32 (*d*, *J* 9·0 Hz, ArCH), 6·67 (*s*, OMe), 6·80 (*s*, OMe), 7·82 (*d*, *J* indet., $CH_{ax}H_{eq}$), 7·87 (*s*, OCOMe), 7·75–8·05 (*m*, CHMe and CH_2–$CH{=}CH_2$), 8·40 (*dd*, *J* 16·0 and 6·5 Hz, $CH_{ax}H_{eq}$), 8·97 (*d*, *J* 7·0 Hz, $CHCH_3$).

Hydrolysis of **12** (30 mg) in EtOH (2 ml) was performed with 5% aq. NaOH (10 ml) (50°, 20 min.). The mixture was acidified and extd. with $CHCl_3$. The $CHCl_3$ soln. was dried and evaporated. The residue was separated by preparative TLC (SiO_2, C_6H_6–AcOEt 1:1) into starting material and a more polar chromatographically pure amorphous solid (10 mg). IR ν_{max}^{KBr} (cm^{-1}): 3450, 1750, 1500, 1490, 1445, 1375, 1250, 1095, 1045, 930, 860. PMR (CCl_4, 60 MHz, τ): 3·40–3·52 (*m*, 3 ArH), 4·08 (*s*, O_2CH_2), 4·00–4·23 (*m*, $CH{=}CH_2$), 4·85–5·20 (*m*, $CH{=}CH_2$), 5·60 (*d*, *ca* 2 Hz, CHOH), 6·45·6·60 (*m*, CHOMe), 6·57 (*s*, OMe), 6·70 (*d*, *J* 9·0 Hz, ArCH), 7·20 (*s*, OMe), 7·30 (*s*, OH; disapp. with D_2O), 7·75–8·05 (*m*, CHMe, CH_2–$CH{=}CH_2$ and $CH_{ax}H_{eq}$), 8·40 (*dd*, *J* 16·0 and 6·5 Hz, $CH_{ax}H_{eq}$), 8·97 (*d*, *J* 7·0 Hz, $CHCH_3$). MS (*m/e*): 374 (25%) M, 334 (20), 333 (100), 287 (12), 241 (18), 211 (15), 210 (18), 199 (10), 197 (20), 183 (20), 165 (75), 163 (12), 162 (50), 153 (18), 151 (20), 149 (40), 139 (10), 137 (12), 135 (65), 117 (20), 113 (48), 111 (20), 109 (10), 107 (10).

Catalytic hydrogenation (EtOH, Pd/C) of **13b** and purification of the reaction product by filtration through silica gave chromatographically pure dihydro-**13b** as amorphous solid. M found 420·2141; calcd. for $C_{23}H_{32}O_7$ 420·2148. IR ν_{max}^{KBr} (cm^{-1}): 3450, 1730, 1600, 1480, 1360, 1235, 1090, 1031, 960, 935. PMR ($CDCl_3$, 220 MHz, τ): 3·06 (*s*, ArH-2′), 3·22 (*d*, *J* 8·0 Hz, ArH-6′), 3·33 (*d*, *J* 8·0 Hz, ArH-5′), 4·12 (*s*, O_2CH_2), 4·97 (*d*, *J* 6·5 Hz, CHOAc), 6·08 (*t*, *J* 6·5 Hz, CHOMe), 6·34 (*d*, *J* indet., ArCH), 6·36 (*s*, CHOH), 6·72 (*s*, OMe), 6·92 (*s*, OMe), 7·52–7·66 (*m*, CHMe), 7·56 (*s*, OH), 7·83 (*s*, OCOMe), 8·14 (*d*, *J* 15·8 Hz, $CH_{ax}H_{eq}$), 8·35–8·47 (*m*, CH_2CH_2Me), 8·40 (*dd*, *J* 6·5 and 15·8 Hz, $CH_{ax}H_{eq}$), 8·56–8·68 (*m*, CH_2–CH_2–Me and CH_2–CH_2–Me), 9·04 (*d*, *J* indet., $CHCH_3$), 9·06 (*t*, *J* 6·5 Hz, CH_2CH_3). PMR (CCl_4, 60 MHz, τ): 3·20 (ArH-2′), 3·32 (ArH-6′), 3·38 (ArH-5′), 4·13 (O_2CH_2), 5·08 (CHOAc), 6·18 (CHOMe), 6·40 (ArCH), 6·46 (CHOH), 6·72 (OMe), 6·98 (OMe), 7·5–8·0 ($CH_{ax}H_{eq}$, CHMe, OCOMe, OH), 8·2–8·8 ($CH_{ax}H_{eq}$, CH_2CH_2Me), 8·9–9·2 (2 Me).

Oxidation of dihydrocanellin-A monoacetate with Jones reagent and purification of the reaction product in C_6H_6–Me_2CO 95:5 by passage through silica and preparative TLC gave chromatographically pure dihydro-**12** as amorphous solid. IR ν_{max}^{KBr} (cm^{-1}): 1750, 1730 inf., 1510, 1490, 1420, 1380, 1240, 1100, 1038, 930, 805. PMR (CCl_4, 220 MHz, τ): 3·43 (*d*, *J* 8·0 Hz, ArH-6′), 3·57 (*d*, *J* 8·0 Hz, ArH-5′), 3·60 (*s*, ArH-2′), 4·18 (*s*, O_2CHH), 4·20 (*s*, O_2CHH), 4·92 (*d*, *J* 6·5 Hz, CHOAc), 6·20 (*t*, *J* 6·5 Hz, CHOMe), 6·39 (*d*, *J* 9·0 Hz, ArCH), 6·70 (*s*, OMe), 6·82 (*s*, OMe), 7·87 (*d*, *J* indet., $CH_{ax}H_{eq}$), 8·10 (*ca* quint., apparent *J* *ca* 8 Hz, CHMe), 8·41 (*dd*, *J* 6·5 and 15·8 Hz, $CH_{ax}H_{eq}$), 8·63–8·88 (*m*, CH_2CH_2–Me and CH_2CH_2Me), 8·99 (*d*, *J* 7·0 Hz, $CHCH_3$), 9·10 (*t*, *J* 6·5 Hz, CH_2CH_3). MS (*m/e*): 418 (100%) M, 318 (21), 315 (11), 289 (16), 196 (19), 182 (18), 181 (11), 165 (12), 162 (57), 153 (36), 149 (15), 141 (14), 140 (11), 135 (23), 85 (11), 55 (20), 45 (10), 43 (87), 41 (11).

Canellin-A *diacetate* (**13c**) and derivatives. Treatment of **13a** with Ac_2O–C_5H_5N (60°, 2 hr) gave a mixture which was separated by column chromatography (SiO_2, light petrol.–AcOEt 4:1 into the *monoacetate* (**13b**, 2nd fraction) and the *diacetate* **13c**, colourless prisms, m.p. 118–120° (light petrol). IR ν_{max}^{KBr} (cm^{-1}): 1735, 1500, 1470, 1360, 1240, 1100, 1032, 935, 918, 805. PMR ($CDCl_3$, 60 MHz, τ): 3·01 (*s*, ArH-2′), 3·24 (*d*, *J* indet., ArH-6′), 3·31 (*d*, *J* indet., ArH-5′), 4·12 (*s*, O_2CH_2), 4·22–4·58 (*m*, $CH{=}CH_2$), 4·85–5·00 (*m*, $CH{=}CH_2$), 4·87 (*d*, *J* indet., CHOAc), 4·97 (*s*, CHOAc), 6·07 (*t*, *J* 6·5 Hz, CHOMe), 6·23 (*d*, *J* 9·0 Hz, ArCH), 6·70 (*s*, OMe), 6·98 (*s*, OMe), 7·50–7·98 (*m*, CHMe and CH–$CH{=}CH_2$), 7·77 (*s*, OCOMe), 7·87 (*s*, OCOMe), 8·08 (*d*, *J* 15·8 Hz, $CH_{ax}H_{eq}$), 8·13–8·40 (*m*, CH–$CH{=}CH_2$), 8·32 (*dd*, *J* 6·5 and 15·8 Hz, $CH_{ax}H_{eq}$), 9·04 (*d*, *J* 7·0 Hz, $CHCH_3$).

Catalytic hydrogenation (EtOH, Pd/C) of **13** and purification of the reaction product by filtration through silica gave dihydro-**13c** as a colourless solid. IR ν_{max}^{KBr} (cm^{-1}): 1735, 1600, 1500, 1480, 1360, 1250, 1230, 1095, 1038, 935, 795. PMR ($CDCl_3$, 220 MHz, τ): 3·00 (*s*, ArH-2′), 3·23 (*d*, *J* 8·0 Hz, ArH-6′), 3·33 (*d*, *J* 8·0 Hz, ArH-5′), 4·10 (*s*, O_2CH_2), 4·90 (*d*, *J* 6·5 Hz, CHOAc), 4·97 (*s*, CHOAc), 6·07 (*t*, *J* 6·5 Hz, CHOMe), 6·31 (*d*, *J* 9·0 Hz, ArCH), 6·72 (*s*, OMe), 6·99 (*s*, OMe), 7·76 (*s*, OCOMe), 7·76–7·91 (*m*, CHMe), 7·86 (*s*, OCOMe), 8·08 (*d*, *J* 15·8 Hz, $CH_{ax}H_{eq}$), 8·33 (*dd*, *J* 6·5 and 15·8 Hz, $CH_{ax}H_{eq}$), 8·30–8·42 (*m*, CH–CH_2–Me), 8·67–8·84 (*m*, CH–CH_2–Me and CH_2–CH_2–Me), 9·08 (*d*, *J* 7·0 Hz, $CHCH_3$), 9·15 (*t*, superimp., CH_2–CH_3).

Canellin-B (**14**). Oil, M found 372·1587; calcd. for $C_{21}H_{24}O_6$ 372·1573. UV λ_{max}^{MeOH}(nm): 239 *sh*., 278 (ε 6000, 16500). IR ν_{max}^{film} (cm^{-1}): 1660, 1640, 1500, 1485, 1260, 1155, 1115, 940, 865, 790. PMR: Table 1. Ms (*m/e*): 372 (46%) M, 342 (15), 332 (20), 331 (100), 304 (14), 303 (84), 301 (13), 271 (32), 241 (18), 239 (17), 211 (15), 209 (14), 190 (15), 181 (15), 165 (19), 163 (16), 162 (90), 161 (18), 153 (11), 149 (15), 141 (11), 136 (10), 135 (50), 132 (10), 131 (15), 129 (12), 128 (13), 121 (14), 115 (30), 107 (12), 105 (16), 104 (35), 103 (32), 101 (13), 95 (14), 91 (32). ORD (MeOH, 400–235 nm, *c* 2·0 mg/100 ml): $[\phi]_{400}$ +5300, $[\phi]_{345}^{pk}$ +16100, $[\phi]_{325}$ 0, $[\phi]_{302}$ −46400, $[\phi]_{275}$ 0, $[\phi]_{260}^{pk}$ +12500, $[\phi]_{235}$ 0.

Canellin-C (**16a**). Oil, M found 360·1590, calcd. for $C_{20}H_{24}O_6$ 360·1573. IR ν_{max}^{film} (cm^{-1}): 3500, 1720, 1590, 1495, 1460, 1260, 1240, 1150, 1100, 1040, 990, 930. PMR: Table 2. MS (*m/e*): 360 (14%) M, 287 (37), 279 (10), 270 (10), 187 (20), 167 (10), 162 (15), 151 (10), 149 (40), 135 (15), 129 (10), 121 (15), 119 (35), 117 (15), 111 (12), 109 (12), 97 (22), 95 (22), 91 (25), 88 (12), 86 (75), 85 (18), 84 (100), 83 (35), 82 (10), 81 (20), 79 (12), 77 (12), 73 (12), 71 (20), 69 (20), 67 (11), 60 (11), 57 (30), 56 (11), 55 (30), 49 (10), 47 (15), 45 (10), 43 (28), 41 (30).

Canellin-C *monoacetate* (**16b**). Treatment of **16a** with Ac_2O–C_5H_5N (room temp., overnight) gave **16b**, purified by preparative TLC (SiO_2, C_6H_6–AcOEt 8:2). IR ν_{max}^{film} (cm^{-1}): 3500, 1738, 1725, 1500, 1640, 1485, 1450, 1370, 1250, 1100, 1040, 990, 940. PMR (60 MHz, $CDCl_3$, τ): 3·20 (*s*, ArH), 3·37 (*s*, 2 ArH), 4·14 (*s*, O_2CH_2), 3·95–4·28 (*m*, $\underline{CH}$=CH_2), 4·53 (*s*, H-4), 4·75–5·10 (*m*, CH=CH_2), 5·85 (*s*, H-8), 6·82 (*s*, OMe), 7·40–7·82 (*m*, H-6, H-7, $C\underline{H}$–CH=, 2 H-2), 7·62 (*s*, OH), 7·77 (*s*, OCOMe), 7·99 (*dd*, *J* 14·9 Hz, $\underline{CH}CH$=), 9·22 (*d*, *J* 7·0 Hz, Me).

Canellin-C *diacetate* (**16c**). Treatment of **16a** with Ac_2O–C_5H_5N (60°, 2 hr.) gave **16c**. PMR ($CDCl_3$, 220 MHz, τ): 3·17 (*s*, ArH), 3·35 (*s*, 2 ArH), 4·13 (*s*, O_2CH_2), 4·00–4·25 (*m*, $\underline{CH}$=CH_2), 4·40 (*s*, CHOAc), 4·50 (*s*, CHOAc), 4·85–4·98 (*m*, CH=$C\underline{H}_2$), 6·85 (*s*, OMe), 7·75 (*s*, OCOMe), 7·94 (*s*, OCOMe), 7·26–7·65 (*m*, H-6, H-7, $C\underline{H}$–CH=, 2 H-2); 7·95 (*dd*, $C\underline{H}$–CH=), 9·20 (*d*, *J* 7·0 Hz, Me). MS (*m/e*): 444 (35%) M, 402 (100), 384 (25), 361 (10), 342 (12), 324 (15), 310 (10), 301 (20), 288 (40), 287 (20), 284 (30), 283 (18), 270 (15), 257 (60), 256 (15), 162 (45), 161 (15), 151 (40), 149 (45), 135 (45), 103 (20), 91 (15), 43 (100).

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