Limonoids from *Xylocarpus moluccensis* (Lam.) M. Roem

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Xyloccensins A, B, D, and F, obtained from *Xylocarpus moluccensis*, are derivatives of methyl meliacate containing a 1,8-hemiacetal group. A similar hemiacetal forms spontaneously in a model compound. Xyloccensin E is phragmalin triacetate. Fruit of *Xylocarpus mekongensis* has also been examined; this plant is probably a variety of *Xylocarpus granatum*.

EXTRACTION of seeds or timber of *Xylocarpus moluccenis* (collected on the Tanzanian coast near Tanga; herbarium specimens DAHT 276 in the Forest Herbarium, Oxford) has given seven substances, xyloccensins A—F and methyl angolensate, in varying proportions.

The xyloccensins were found to be limonoid esters, similar to those obtained in our earlier work. Although esters of different alcohols were readily separated by chromatography, the alcohols occurred as mixtures of isobutyrates and α-methylbutyrates, as is common with limonoids (*cf.* bussein[1]), and these are difficult to separate. Xyloccensin E was obtained as a pure substance; the others were isolated only as mixed esters. In the absence of pure compounds, the mixed esters were characterised by the low-field region of the ^{1}H n.m.r. spectrum where the esters of isobutyric and α-methylbutyric acids show only minor differences.

Xyloccensin E was identical with a specimen of phragmalin triacetate (1) kindly supplied by Professor Arndt.[2] Xyloccensin A [δ_H 5.05 (s), 5.15 (d, *J* 10 Hz), 5.6 (d, *J* 4.5 Hz), and 6.05 (s)] showed its highest mass peak in the mass spectrum at *m/e* 670.3322, corresponding to the bis-α-methylbutyrate $C_{37}H_{50}O_{11}$. The ^{13}C n.m.r. spectrum showed the characteristic bands of an αβ-unsaturated lactone similar to carapin (2) [δ_C 160.1 (s, C-14), 117.6 (d, C-15), 164.8 (s, C-16), and 81.6 (d, C-17)],[3] and the ^{1}H n.m.r. spectrum showed bands indicating a CHOR·CH·CHOR system, not further coupled, as anticipated for a 3,30-dioxygenated methyl meliacate derivative [3-H, δ 5.15 (*J* 10 Hz); 2-H (in C_6D_6–$CDCl_3$), δ 1.95; 30-H, δ 5.6 (*J* 4.5 Hz)]. The ^{13}C n.m.r. spectrum did not show the ketonic carbonyl signal expected for C-1; the presence of four nuclear methyl groups showed that the ring A bridge characteristic of phragmalin was not present either. The molecule contains two more oxygen atoms, one as a tertiary hydroxy-group, the other as an ether. The ^{13}C n.m.r. spectrum shows a singlet at δ 107.7, suggesting an acetal carbon atom, and a singlet at δ 81.6, suggesting a tertiary hydroxy-group or ether. If we assume that a normal limonoid skeleton is present, these observations are uniquely explained by the presence of a 1,8-hemiacetal. The stereochemistry of the hemiacetal requires that the oxygen at C-8 be α-oriented, the 2-H,30-H coupling requires that the oxygen at C-30 be α-oriented, and the 2-H,3-H coupling requires that the oxygen at C-3 be β-oriented. These are also the configurations found in all related limonoids so far described.[4] We therefore propose the structure (3) for xyloccensin A. In the rare cases, all so far partially synthetic, where a 1-hydroxy-group occurs, the 1,2-coupling constant is much lower, 1-H resonating as a broad singlet.[5] A further example is the reduction product of 8β-hydroxycarapin (see later).

The structures of xyloccensins B, D, and F readily follow. The mass spectra showed that B had two hydrogen atoms more than A, D one oxygen more than A, and F two hydrogens more than D. In the magnetic resonance spectra, B [δ_H 5.13 (d, *J* 10 Hz), 5.26 (s), and 6.16 (d, *J* 4 Hz)] did not show the bands characteristic of an unsaturated lactone; instead the shifts observed for C-17 [76.4(d)] and C-16 [169.8(s)] suggested a dihydro-derivative;[3] as the spectra are otherwise similar to those of A we conclude B is 14,15-dihydro-A. There is no direct evidence of the configuration at C-14; it is probable that the ring junction is *cis*- as in phragmalin and swietenine.

Xyloccensin D [δ_H 4.85 (s), 4.90 (s), 5.63 (s), and 6.15 (s)] had a second hydroxy-signal in the ^{1}H n.m.r. spectrum. Since it shows the resonances ascribed to 3-H and 30-H as singlets, not doublets, and is otherwise spectrally similar to A, we conclude that D is 2-hydroxy-A.

In a similar way F [δ_H 4.88 (s), 5.18 (s) and 6.21 (s)] showed the signals expected for a saturated lactone, similar to B, and the 3-H and 30-H signals corresponding to a 2-hydroxy-compound, like D. It is therefore 2-hydroxy-B.

Xyloccensin C, $C_{37}H_{50}O_4$ [δ_H 4.86 (s), 5.28 (s), and 5.75 (s)] was only obtained from one early batch of seed. Unfortunately insufficient remained for a ^{13}C n.m.r. spectrum, and we have not been able to assign a structure to this compound.

Synthetic models of xyloccensin A have been obtained by the oxidation of carapin (2) or mexicanolide (4) with selenium dioxide. The oxidation of mexicanolide (4) gives several products and some of these apparently suffer further oxidation, as the overall conversion with 1 mol. equiv. of oxidising agent is small. Three products were isolated: the diene 8,9-didehydrocarapin,[6] a compound $C_{27}H_{32}O_8$, m.p. 190—192°, $[\alpha]_D$ +114°, containing one more oxygen atom, and an isomer of the latter, isolated in small amount and not obtained crystalline.

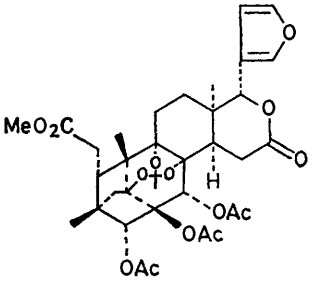
Oxidation of carapin (2) proceeds cleanly and in much higher yield and conversion, only the compound of m.p.

[1] R. Hanni and Ch. Tamm, *J.C.S. Chem. Comm.*, 1972, 1253.
[2] R. R. Arndt and W. H. Barschers, *Tetrahedron*, 1972, **28**, 2333.
[3] D. A. H. Taylor, *J.C.S. Perkin I*, 1974, 437.
[4] *Cf.* H. R. Harrison, O. Hodder, C. W. L. Bevan, D. A. H. Taylor, and T. G. Halsall, *Chem. Comm.*, 1970, 1388.
[5] E. K. Adesogan, D. A. Okorie, and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1970, 205.
[6] D. A. H. Taylor and F. W. Wehrli, *J.C.S. Perkin I*, 1973, 1599.

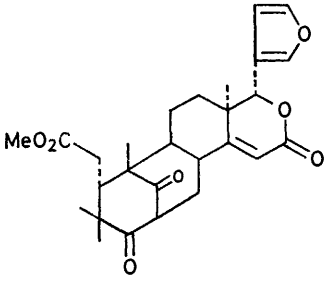
190—192°, being isolated. The ^{1}H n.m.r. spectrum of this compound shows the presence of the carapin double bond [15-H, δ 6.16 (s), 17-H δ 5.16 (s) at 30 °C] and a tertiary hydroxy-group. As the 15-H resonance is a singlet, it is an obvious suggestion that the compound is 8-hydroxycarapin. There is however evidence against this, as the compound cannot be dehydrated. With thionyl chloride in pyridine it readily yields a stable chloro-compound, which is hydrolysed to the original alcohol with silver nitrate in dimethyl sulphoxide. There is no apparent reason why the allyl alcohol 8-hydroxycarapin should not undergo dehydration readily to give 8,9-didehydrocarapin.

This problem was solved by examination of the ^{13}C n.m.r. spectrum of the product, which showed a signal for only one ketonic carbonyl group and in place of the other an acetal carbon signal at δ 108.6, a signal for tertiary carbon bearing oxygen was also seen, at δ 81.7. It follows that 8-hydroxycarapin forms an internal hemiacetal, as in the xyloccensin series.

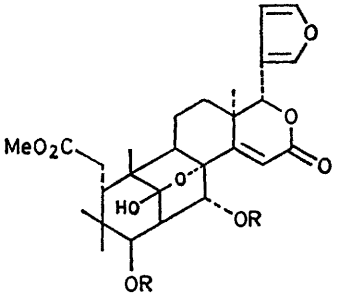
Reduction of the hemiacetal with borohydride gives two products, in amounts depending on conditions. In one the ketone only is reduced, in the other the ketone and lactone carbonyl groups are both reduced. The proton vicinal to the new alcoholic hydroxy-group in both these compounds resonates as a broad singlet (δ 3.5), and the new hydroxy-group is sterically hindered to acetylation. Both these observations are highly unlikely for a 3-hydroxy-compound, but fit the presence of an alcohol, and hence of the original ketonic carbonyl group, at C-1 as the 1-H,2-H coupling is known to be small.[5] Thus the hemiacetal group extends from C-3 to C-8, and not from C-1 to C-8 as in xyloccensin. Consideration of the formation by oxidation of carapin suggests that the hydroxy-group should be β-oriented, as the α-side of the molecule is hindered. A model shows that a 1,8β-epoxide link is impossible, and only a 3,8β-epoxide can be formed. Similarly, with the 8α-hydroxy-group, as in the xyloccensins, only a 1,8α-ether linkage can be formed. The hemiacetal is therefore to be represented by structure (5).



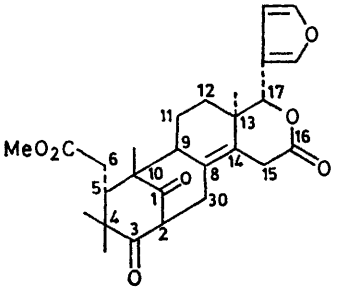
(1)



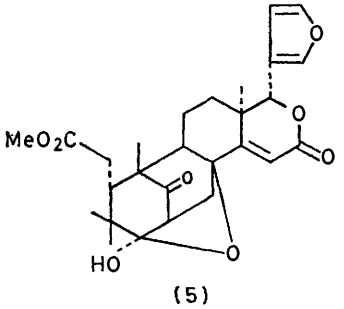
(2)



(3)
R = COPr^i or COBu^i



(4)



(5)

This structure explains the fact that the ^1H n.m.r. spectrum of the acetal is temperature dependent, the 15-H signal in particular shifting downfield with increased temperature. This can now be seen to depend on the presence of the hydroxy-ketone tautomer, in which the hydroxy-group at C-8 is close to H-15. This temperature dependence has not been noticed in the spectra of the xyloccensins, which have a different acetal ring.

We assume that the minor product from the oxidation of mexicanolide [15-H δ 6.05 (s); 17-H δ 5.15 (s)] is the 1,8α-hemiacetal, directly analogous to the xyloccensins, but we have no direct proof of this. It may be formed by allylic rearrangement of a 15-hydroxy 8(14)-ene during the reaction.

The hemiacetal of 8β-hydroxycarapin has been isolated by one of us (J. D. C.) as a natural product from *Cedrela glaziovii* C. DC. Xylocarpin,[7] from *Xylocarpus granatum* is closely related to the xyloccensins, being the 8,30α-epoxide corresponding to xyloccensin B. Humilin, from *Swietenia humilis*,[8] is 2-hydroxyxylocarpin, thus corresponding to xylocarpin F.

We have also examined the seed of *Xylocarpus mekongensis*, collected by Mr. J. S. Bond near Tanga (Herbarium specimens are held by Dr. B. T. Styles of the Forest Herbarium, Oxford). This is a rare plant on the East African coast, similar to *X. granatum*, but having the small fruit typical of *X. moluccensis*, which has been considered as possibly a hybrid of these two species. We found the seed similar to that of *X. granatum*,[7] containing xylocarpin, and it seems most probable that East African specimens of *X. mekongensis* are a small-fruited variety of *X. granatum*.

EXPERIMENTAL

Proton noise-decoupled ^{13}C n.m.r. spectra were obtained for solutions in deuteriochloroform with a Varian C.F.T.20 or XL 100 spectrophotometer; off-resonance decoupled spectra were used to aid assignments. ^1H N.m.r. spectra were obtained with a Varian A 56/60 or HA100 spectrophotometer, for solutions in deuteriochloroform, with Me_4Si as internal standard.

Isolation of Xyloccensins.—Extractions of seed and of timber gave similar results, except that more product was isolated from the seed. The relative amounts of the compounds isolated varied; the results described are from an early sample of seed which contained xyloccensin C, but no B. Minced seed of *Xylocarpus moluccensis* (175 g) was thoroughly extracted with refluxing 2-methylpentane. A precipitate (4.2 g) settled from the cooled extract. This was chromatographed over silica gel; elution with ether–petroleum ether gave successively: *xyloccensin A* (24 mg), m.p. 221—223° (from methanol) (Found M^+, 670.332 2. $C_{37}H_{50}O_{11}$ requires M, 670.335 23) δ_H 6.05 (s, 15-H), 5.60 (J 4.5 Hz, 30-H), 5.05 (s, 17-H), and 5.15 (J 10 Hz, 3-H), δ_C 164.8 (C-16) 160.1 (s, C-14), 117.6 (d, C-15), 107.7 (s, C-1), 81.6 (d, C-17), 87.6 (s, C-8), 76.5 (d, C-3), 74.4 (d, C-30), and 53.5 (d, C-2); methyl angolensate (100 mg), identical with an authentic sample; *xyloccensin C* (80 mg), m.p. 280° (from methanol) (Found: C, 66.5; H, 7.5%; M^+, 670.338 9. $C_{37}H_{50}O_{11}$ requires C, 66.2; H, 7.5%; M, 670.335 23), δ_H 4.86 (s), 5.28 (s), and 5.75 (s); *xyloccensin D* (150 mg), m.p. 212—215° (from methanol) (Found: M^+, 686.328 2. $C_{37}H_{50}O_{12}$ requires M, 686.330 1), δ_H 6.15 (s, 15-H), 5.63 (s, 30-H), 4.90 (s, 17-H), and 4.85 (s, 3-H), δ_C 163.1 (s, C-16), 158.3 (s, C-14), 118.6 (d, C-15), 108.9 (s, C-1), 87.2 (d, C-17), 80.6 (s, C-8), and 75.4 (d, C-30), xyloccensin E (40 mg), m.p. 212—215° (from methanol), identical with a sample of phragmalin triacetate; and *xyloccensin F* (100 mg), m.p. 237—239° (Found: M^+, 688.343 8. $C_{37}H_{52}O_{12}$ requires M, 688.345 83), δ_H 6.21 (30-H), 4.88 (s, 3-H), and 5.18 (s, 17-H), δ_C 169.8 (s, C-16), 107.0 (s, C-1), 82.1 (s, C-8), 80.1 (d, C-3), 76.9 (d, C-17), 75.5 (d, C-30), 63.2 (s, C-14), and 36.1 (t, C-15).

Xyloccensin B, only obtained from one sample of wood, had m.p. 154—160° (from methanol), M^+ 672, δ_H 6.16 (d, J 4Hz, 30-H), 5.26 (s, 17-H), and 5.13 (d, J 10 Hz, 3-H), δ_C 169.8 (s, C-16), 106.6 (s, C-1), 82.2 (s, C-8), 76.4 (d, C-17), 75.1 (d, C-30), 73.3 (d, C-3), 63.8 (d, C-14), and 36.3 (t, C-15).

Extraction of Xylocarpus mekongensis *Seed.*—The minced seed (224 g) was extracted with hot 2-methylpentane, giving a precipitate (1.07 g), which was chromatographed over silica gel. Ether–hexane eluted xylocarpin (150 mg), identical with a sample obtained from *Xylocarpus granatum*.[7]

Oxidation of Carapin.—Carapin (20 g) and selenium dioxide (2.5 g) were refluxed for 3 h in glacial acetic acid (150 ml). The cold solution was filtered and evaporated and the residue in methylene chloride filtered through a column of alumina. The residue crystallised from methanol to give *8β-hydroxycarapin 3,8-hemiacetal* (5) (12.1 g), m.p. 190—192°, $[\alpha]_D$ +114.5 (in $CHCl_3$). The m.p. was increased by the presence of traces of residual carapin (Found: C, 67.0; H, 6.8%; M^+, 484. $C_{27}H_{32}O_8$ requires C, 66.9; H, 6.65%; M, 484), δ_H 6.61 (s, 15-H) and 5.16 (s, 17-H), δ_C 212.9 (C-1), 165 (s, C-16), 166.5 (s, C-14), 118.6 (d, C-15), 108.6 (s, C-3), 81.1 (d, C-17), 81.7 (C-8), and 53.5 (d, C-2).

Oxidation of Mexicanolide.—Mexicanolide (20 g), selenium dioxide (2.5 g), and acetic acid (150 ml) were refluxed for 3 h. The cooled solution was filtered and evaporated under vacuum. Crystallisation from methanol gave mexicanolide (3.05 g). The residue was dissolved in methanol, made slightly alkaline, and stored overnight to destroy the remaining mexicanolide, which was otherwise difficult to separate. The product was chromatographed over neutral alumina (elution with methylene chloride–pentane). The first fractions crystallised to give 8,9-didehydrocarapin (0.35 g), m.p. 238—240° (from methanol), identical with an authentic sample. Subsequent fractions gave 8β-hydroxycarapin 3,8-hemiacetal (4.5 g) identical with that described above. ^1H N.m.r. spectroscopy of the mother liquor from the 8β-hydroxycarapin hemiacetal showed that it contained a mixture of this and one other principal component. Repeated chromatography gave 8α-hydroxycarapin 3,8-hemiacetal (250 mg) as a gum which did not crystallise, δ_H 6.06 (s, 15-H) and 5.51 (s, 17-H). Similar results were obtained with dioxan as solvent in the oxidation.

Action of Thionyl Chloride on 8β-Hydroxycarapin 3,8-Hemiacetal.—The hemiacetal (220 mg) and thionyl chloride (0.5 ml) were kept in pyridine (10 ml) overnight at −5 °C. Dilution with water and extraction with methylene chloride gave a chloro-ether (174 mg), m.p. 248—260° (from methanol), δ_C 110.75 (C-3) and 84.95 (C-8) (Found: C, 64.9; H, 6.5. Calc. for $C_{27}H_{31}ClO_7$ requires C, 64.5; H, 6.2%).

Hydrolysis of the Chloro-ether.—The chloro-ether (100 mg)

[7] D. A. Okorie and D. A. H. Taylor, *J. Chem. Soc.*[(C), 1970, 211.

[8] D. A. Okorie and D. A. H. Taylor, *Phytochemistry*, 1971, **10**, 469.

and silver nitrate (100 mg) in dimethyl sulphoxide (10 ml) were heated on a steam-bath for 2 h. Dilution with water and extraction with methylene chloride gave the hemiacetal (5), identical with the original sample. The use of ethanol or acetic acid as solvent gave the corresponding ethyl ether and acetate respectively; dimethylformamide gave the original hemiacetal.

Reduction of 8β-*Hydroxycarapin* 3,8-*Hemiacetal.*—(*a*) *Mild conditions.* The hemiacetal (215 mg) in methanol (4 ml) and methylene chloride (2 ml) was treated with sodium borohydride (100 mg) in water (0.5 ml) at 0 °C. After 0.5 h the solution was worked up as usual; crystallisation gave the dihydro-derivative (178 mg), m.p. 145—148° (from methylene chloride–toluene), δ_H 6.34 (15-H), 5.10 (17-H), and 3.5br (s, 3-H), M^+ 486.

(*b*) *Vigorous conditions.* The hemiacetal (270 mg) in methylene chloride (6 ml) and methanol (6 ml) was treated with sodium borohydride (70 mg) in water (0.5 ml). After 2 h at room temperature the product was isolated as usual.

Crystallisation gave the very soluble tetrahydro-derivative (147 mg), m.p. 136—140° (from methylene chloride–toluene), δ_H 5.90 (d, *J* 3 Hz, 15-H), 4.83 (d, *J* 3 Hz, 16-H), 4.46 (s, 17-H), and 3.4br (s, 3-H), δ_C 148.8 (C-14), 121.9 (C-15), 107.2 (C-8), 96.6 (C-16), 82.5(C-3), 82.0 (C-8), and 75.2 (C-17), M^+ 488.

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