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CHROMONES AND LIMONOIDS FROM *HARRISONIA ABYSSINICA*

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Key Word Index—*Harrisonia abyssinica*; Simaroubaceae; chromones; alloptaeroxylin; peucenin; *O*-methylalloptaeroxylin; limonoids; obacunone; atalantolide.

Abstract—Examination of the roots of *Harrisonia abyssinica* yielded three known chromones, alloptaeroxylin, peucenin, *O*-methylalloptaeroxylin and two known limonoids, obacunone and atalantolide. The co-occurrence of chromones and limonoids is unusual in Simaroubaceae and therefore renders the taxonomic position of *Harrisonia* uncertain.

INTRODUCTION

Recently, Kubo *et al.*[1] isolated a limonoid, harrisonin(**1**) from the root bark of an African sample of the medicinal plant *Harrisonia abyssinica* Oliv. This was taxonomically interesting because limonoids had only been found previously in the Meliaceae[2], Rutaceae[2] and Cneoraceae[3]. Since *H. abyssinica* is in the Simaroubaceae, it seemed worthwhile to investigate a west African collection of this plant.

RESULTS AND DISCUSSION

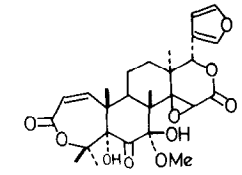
Hot hexane extraction of the roots of *H. abyssinica* followed by CC on Si gel furnished five compounds (A–E). Compound A had yellow crystals mp 151–153°, M^+ 258 analysing for $C_{15}H_{14}O_4$. The presence of a chromone nucleus was indicated[4] by the IR and UV spectra. The ^1H NMR spectrum showed the presence of 2,2-dimethylchromen and 2-methylchromone systems[4]. Compound A was identified as alloptaeroxylin[4, 5] (**2**) and not the related isomer, spatheliachromen, by the detailed analysis of the IR, UV, ^1H NMR and mass spectral data and the mp. This identification was further confirmed by both the spectral data and mp 144–145° of the acetate[4]. Alloptaeroxylin was first isolated from the timber of *Ptaeroxylon obliquum*.

Compound B mp 210–212°, M^+ 260 was also found to be a chromone. The UV spectrum suggested the presence of a 5,7-dihydroxy-2-methylchromone system[6]. The ^1H NMR showed that it lacked a 2,2-dimethylchromen nucleus but contained a methyl group adjacent to a double bond. This was highly reminiscent of a 3,3-dimethylallyl fragment. Detailed analysis of the spectral data confirmed compound B as peucenin (**3**) [7, 8].

The ^1H NMR spectrum of compound E, mp 155–157° was similar to that of compound A except for the presence of a three proton singlet at δ 3.80 in the former. The mass spectrum of E had M^+ at 272, showing that E was a methyl ether of compound A. A study of the ^1H NMR and mass spectra revealed that compound E was indeed the chromone, *O*-methylalloptaeroxylin (**4**)[4, 9] first isolated from the heartwood of *Cedrelopis grevei*.

The IR spectrum of compound C, mp 229–231°, M^+ 484 had the typical bands for a β-substituted furan at ν_{max} cm^{-1}: 1502 and 875, for OH at 3450 and a series of CO bands at 1735, 1710 and 1645, the last band being due to an α, β-unsaturated CO. The ^1H NMR spectrum (Varian, T-60, $CDCl_3$, δ-scale) confirmed the presence of a β-substituted furan by multiplets at δ 7.40 (2H) and 6.38 (1H). It further established that compound C was a limonoid[2] with five tertiary C–Me groups absorbing as singlets at δ 2.02, 1.80, 1.41, 1.38 and 0.65; a COOMe as a singlet at δ 3.53 (3H) and OH group at δ 4.22 (1H, lost on deuteration). Two of the five C–Me groups absorbing at δ 2.02 and 1.80 were ascribed to two methyl groups at a double bond, suggesting a seco-limonoid. The presence of a ring D epoxy lactone moiety was revealed by the characteristic H–15 and H–17 singlets at δ 4.23 and 5.48 respectively. The ^1H NMR also had two protons of a conjugated double bond absorbing as two AB doublets at δ 6.31 (J = 12.5 Hz) and 5.57 (J = 12.5 Hz). This large coupling constant (> 10 Hz) for H–1 and H–2 combined with their chemical shifts showed that compound C belonged to the obacunone-type[10] limonoids with seco-ring A of the methyl obacunoate (**5**) rather than the gedunin-type (**6**)[11]. Detailed comparison of the ^1H NMR spectrum of compound C with that published for the revised structure (**7**) of atalantolide[12] confirmed that compound C is **7**.

Compound D, mp 230–231°, M^+ 454 had bands in the IR spectrum characteristic of the presence of a limonoid skeleton. The ^1H NMR spectrum showed five tertiary C–Me groups but there were no vinylic



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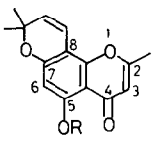
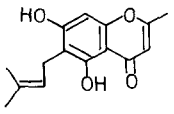


2 R=H
4 R=Me



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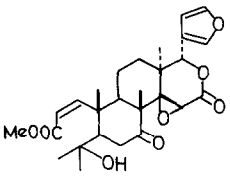

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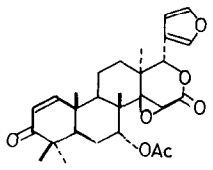

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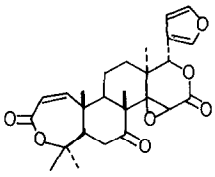

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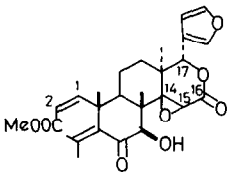

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methyl groups, suggesting that compound D was not a seco-ring A limonoid. It further confirmed the presence of a ring D epoxy lactone system of the obacunone type. Compound D was identified as obocunone (**8**)[10].

The co-occurrence of limonoids and chromones in *H. abyssinica* is most unusual, having only been previously found in Cneoraceae[3] and in *Spathelia sorbifolia*[4], which is now placed in the Rutaceae. However *H. abyssinica* does not contain the characteristic ceneorins[13] which occur in Creoraceae. The chromones have also previously been found in Ptaeroxylaceae[5], a small family closely related to the Meliaceae[14]. In the light of this new evidence, the taxonomic position of *Harrisonia* is not clear. It is now being re-examined by F. White and C. B. T. Styles at Oxford. [Taylor, D. A. H., personal communication]. The chemical differences between the west and east African samples are also noteworthy, with obacunone and atalantolide being replaced by harrisonin in the east African plant. Whether the chromones found in the west African samples occur in east African samples has yet to be determined.

EXPERIMENTAL

Mps are uncorr. IR spectra were in Nujol, UV spectra in EtOH and ^{1}H NMR spectra were recorded in $CDCl_3$ with TMS as int. standard, chemical shifts being expressed in δ units. Si gel refers to Merck kieselgel 60 (70–230 mesh ASTM). UV and IR spectra agreed with lit. data.

Harrisonia abyssinica. Plant material was collected at Ilaro, Ogun State, Nigeria and identified by the Forestry Research Institute of Nigeria, Ibadan. A herbarium specimen No. FH1 96258 is filed with the Federal Department of Forestry Research, Ibadan, Nigeria.

Extraction of the roots. Dried roots of *H. abyssinica* (1.0 kg) were milled and extracted with boiling hexane. The extract was concd. to a gummy solid which was dissolved in C_6H_6 and chromatographed on a column of Si gel eluting with increasing percentages of Et_2O–hexane. Hexane–Et_2O (4:1) eluted alloptaeroxylin (**2**) as yellow needle-like crystals mp 151–153°, (0.30 g) (lit.[5] mp 150–152°). ^{1}H NMR: ($CDCl_3$) δ 12.73 (1H, *s*, ArOH, lost on deuteration), 6.62 (1H, *d*, J = 10 Hz), 6.20(1H, *s*, H–6), 5.98 (1H, *s*, H–3), 5.57(1H, *d*, J = 10 Hz), 2.20(3H, *s*, Me), 1.43(6H, *s*, 2 Me); MS *m/z* 258[M]$^+$; 244, 243, 121. (Found: C, 69.70; H, 5.54; $C_{15}H_{14}O_4$ requires: C, 69.75; H, 5.50%.) Hexane–Et_2O (7:3) fractions gave peucenin (**3**) mp 210–212° (0.06 g) (lit.[8] mp 212–214°). ^{1}H NMR: ($CDCl_3$) δ 6.30 (1H, *s*, H–8), 5.95(1H, *s*, H–3), 5.30(1H, *t*, J = 8 Hz), 3.42(2H, *d*, J = 8 Hz), 2.34(3H, *s*, Me), 1.82(3H, *s*, Me), 1.78(3H, *s*, Me); MS *m/z* 260[M]$^+$, 245, 217, 205 (base peak), 192, 115. (Found: C, 69.05; H, 6.30; $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%.) Hexane–Et_2O (3:2) eluates furnished atalantolide (**7**) mp 229–231° (0.092 g) (lit.[12] 230–231°). ^{1}H NMR: ($CDCl_3$) δ 7.40 (2H, *m*, α-furan H), 6.38(1H, *m*, β-furan H), 6.31(1H, *d*, J = 12.5 Hz, H–1), 5.57(1H, *d*, J = 12.5 Hz, H–2), 5.48(1H, *s*,H–17), 4.80(1H, *d*, J = 3 Hz becomes a singlet with D_2O, H–7), 4.23(1H, *s*, H–15), 4.22(1H, *d*, J = 3 Hz lost on deuteration, OH), 3.53(3H, *s*, COOMe), 3.39(1H, *m*, H–9), 2.02(3H, *s*, Me), 1.80(3H, *s*, Me), 1.41 (3H, *s*, Me) 1.38(3H, *s*, Me), 0.65(3H, *s*, Me), MS *m/z* 484[M]$^+$, 466, 451, 438, 361 (base peak), 343. (Found: C, 66.84, H, 6.60; $C_{27}H_{32}O_8$ requires: C, 66.93; H, 6.66%.) Hexane–Et_2O (3:7) eluted obacunone (**8**) mp 230–231° (0.15 g) (lit.[10] 229–231°). ^{1}H NMR δ 7.40 (2H, *m*, α-furan H), 6.56 (1H, *d*, J = 12 Hz), 6.38(1H, *m*, β-furan H), 5.95(1H, *d*, J = 12 Hz), 5.48(1H, *s*, H–17), 3.65(1H, *s*, H–15), 1.48(6H, *s*, 2 Me), 1.44(3H, *s*, Me), 1.23(3H, *s*, Me), 1.10(3H, *s*, Me). MS *m/z* 454[M]$^+$, 439, 331 (base peak). Found: C, 68.79; H, 6.73; $C_{26}H_{30}O_7$ requires: C, 68.68; H, 6.66%.) Hexane–Et_2O (1:4) yielded crystals of *O*-methylalloptaeroxylin (**4**) mp 155–157° (1.8 g) (lit.[9] 155–157°). ^{1}H NMR δ 6.65(1H, *d*, J = 10 Hz), 6.24(1H, *s*) 5.95(1H, *s*), 5.52(1H, *d*, J = 10 Hz), 3.88(3H, *s*, ArOMe), 2.22(3H, *s*, Me), 1.40(6H, *s*, 2Me). MS *m/z* 272[M]$^+$, 257 (base peak), 243 228, 227, 217, 202. (Found: C, 70.68; H, 6.04; $C_{16}H_{16}O_4$ requires: C, 70.6; H, 5.9%.)

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A REVISION OF THE STRUCTURES OF THREE LIMONOIDS

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Key Word Index—Limonoids; ^{13}C NMR spectra; IR spectra.

Abstract—Three limonoids, two from *Aphanamixis polystacha* and one from *Trichilia prieuriana*, have been found to have ^{13}C NMR spectra at variance with the assigned structures. Alteration of the position of certain lactone rings gives structures which agree with the spectra.

The group of limonoids related to prieurianin is rapidly growing and more than 20 are now known. In the course of compiling a collection of the ^{13}C NMR spectra of these compounds, we have discovered a discrepancy. The structure of prieurianin acetate (**1**) is securely based on an X-ray crystal structure determination [1]. In this compound there are only two tertiary oxygen functions, and it is easy to assign the singlet resonance at δ 84.6 to C-4. In *Aphanamixis rohituka* 2 acetate [2], which was believed only to differ from **1** by having an acetoxy group at C-15 in place of the ketone, C-4 resonates at δ 88.4. While this discrepancy was not noted originally when few comparison substances were known, it now appears quite striking. Other compounds with a similarly low field resonance for C-4 are the closely related rohituka substance 1 [2], differing only in the substituent at C-12, *Trichilia prieuriana* substance D_5 [3], to which the structure **2** was assigned, the hydrolysis products with a γ-lactone ring similar to PM_2 (**3**) [3], in which C-4 resonates at δ 87.3, and dregeanin, now believed to have the structure **4** [4], in which it is at δ 88.6.

The deduction is clear, that the low field position of the C-4 resonance depends on it being in a γ-lactone ring. This requires that the structures of rohituka substances 1 and 2 are revised to **5** and **6** respectively, while that of prieuriana substance D_5 is revised to **7**. It should be possible to detect signals for the γ-lactone ring in the IR spectrum. In the hydrolysis products similar to PM_2 the lactone vibration frequency is 1790 cm^{-1}, while in D_5 it is 1775 cm^{-1}. Although of a lower frequency, this is well in the range accepted for a γ-lactone.

This new formulation explains four observations that were previously difficult to accommodate. The first is the very existence and relative stability of these compounds, which survived extraction with refluxing hexane and isolation by chromatography, whereas a hydroxy ester such as **2** would be expected to lactonize very readily in solution.

The second is the fact that borohydride reduction of prieurianin does not give rohituka compound 2. Only one reduction product has been obtained [MacLachlan, L. K. and Taylor D. A. H., unpublished results], and although this could of course be the 15-epimer of the natural compound, there seems to be more difference between the two compounds than can be accounted for in this way. In particular while rohituka compound 2 has the C-4 resonance at δ 88.4, as already mentioned, in the acetate of prieurianin reduction product it is in the normally expected position of δ 84.9.

The third is the strange hydrolysis result of dregeanin and related compounds [3]. It was shown that dregeanin (**4**) and D_5 (**7**) gave the same complex set of hydrolysis products, while two other compounds, the related 7,29 lactone which is *Guarea thompsonii* substance B [3], and its 1,2 anhydro derivative D_4 [3], give only one of these products.

It is known that dregeanin methanolyses very readily [Okorie, D. A. and Taylor, D. A. H., unpublished results], probably due to the presence of the eight-membered lactone ring [5]. Thus the first stage