Phytochemistry, Vol. 20, No. 11, pp. 2596 2597, 1981.
Printed in Great Britain.

0031-9422/81/112596-02 $02.00/0

SPICATIN, A PROTOLIMONOID FROM *ENTANDROPHRAGMA SPICATUM*

JOSEPH D. CONNOLLY*, WILLIAM R. PHILLIPS‡, DULCIE A. MULHOLLAND† and DAVID A. H. TAYLOR†

* Department of Chemistry, University of Glasgow, Scotland, U.K.; † Department of Chemistry, University of Natal, Durban, South Africa

(*Received* 14 *April* 1981)

Key Word Index—*Entandrophragma spicatum*; Meliaceae; limonoids; spicatin; 24-hydroxygrandifoliolenone.

Abstract—The hexane extract of the timber of *Entandrophtagma spicatum* is shown to contain a new protolimonoid, spicatin, which has been identified as 24-hydroxygrandifoliolenone. The known entandrophragmin and a new ester closely related to bussein were also obtained.

INTRODUCTION

Entandrophragma spicatum is a rare mahogany growing in Ovamboland and southern Angola which has been reported [1] to contain entandrophragmin and a compound similar to bussein. We now confirm this observation, and have also isolated a protolimonoid, spicatin, which is similar to the sapelins.

RESULTS AND DISCUSSION

The ground timber of *E. spicatum* was extracted with refluxing isohexane, giving entandrophragmin (*ca* 0.2%) and a gum. Chromatography of the gum gave spicatin, which remained amorphous, and a crystalline compound spicata-2.

The mass spectrum of spicata-2 showed that it had a MW of 914; 42 units more than that of bussein (**1**) [2, 3]. The ^{1}H NMR spectrum was very similar to that of bussein, except that the resonance at δ 2.17, which has been assigned to the acetate group at C-11, was absent, and the characteristic H-11 doublet (δ 5.61 in bussein) had moved slightly up-field. This suggested that the C-11 acetate of bussein was replaced by a 2-methylbutanoate residue. In confirmation the ^{13}C NMR spectrum lacked an acetate resonance at δ 20.8 compared with that of bussein, and had four extra resonances (δ 41.3*d*, 27.0*t*, 16.0*q*, 14.0*q*). Thus, spicata-2 has the structure **2**.

The mass spectrum of spicatin showed its highest mass peak at *m/z* 526.3323, corresponding to a molecular formula $C_{32}H_{46}O_6$. The ^{1}H NMR spectrum (see Experimental) showed the characteristic resonances of a ring A α,β-unsaturated ketone, a 7α-acetoxy group and a 14,15 double bond, as in grandifoliolenone (**3**) [4]. The ^{13}C NMR spectrum was in agreement with this assignment. However, some bands were doubled suggesting the presence of stereoisomers as in turreanthin (**5**) (T. G. Halsall, personal communication). In particular, a pair of singlets at δ 97.37, 95.71 suggested the presence of a hemiketal. Acetylation of spicatin opened the hemiketal ring giving a single stereoisomer whose spectrum lacked the resonance near δ 96 and showed instead a carbonyl singlet at δ 210.8. This compound, which was also a gum, contained two new acetate groups, one primary and one secondary. There is also a tertiary hydroxyl, present in both spicatin and the derived acetate, making a total of seven oxygen atoms in spicatin. The molecular ion has therefore not been observed in the mass spectrum and the highest mass peak recorded is an anhydro derivative.

These data led us to propose the structure 24-hydroxygrandifoliolenone (**4**) for spicatin and structure **6** for the derived acetate. These structures were confirmed by periodate oxidation of spicatin and the acetate. In this way, spicatin gave the aldehydo ester (**7**) and the acetate, after esterification with diazomethane, gave the ester **8**. The spectroscopic data for these compounds are in accordance with the proposed structures.

The stereochemistry at C-23 in spicatin is unknown but in grandifoliolenone the hydroxyl has been shown to be α-oriented.

EXPERIMENTAL

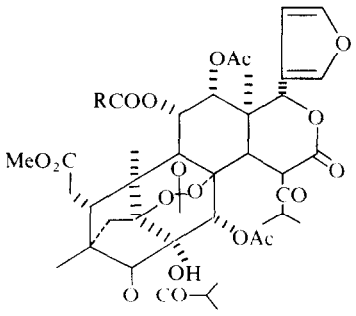
NMR spectra are determined in $CDCl_3$ with TMS as int. standard on a CFT-20 spectrophotometer.

The timber of *Entandrophragma spicatum* (collected by J.D.C. near Ondangua; herbarium specimens are preserved at the Forest Herbarium, Oxford as DAHT 296) (5 kg) was powdered and extrd with refluxing isohexane. The extract (*ca* 200 g, still containing hexane) cryst. from toluene–cyclohexane giving entandrophragmin (10 g), mp 241°, identical with an authentic specimen. The mother liquor was chromatographed on Si gel columns, yielding spicatin, spicata-2, and impure fractions.

Spicata-2 (**2**) (1 g mp 275–280°) crystallized from MeOH or toluene cyclohexane. (Found: M$^+$ *m/z* 914, $C_{47}H_{62}O_{18}$ requires 914). ^{13}C NMR: 183.0*s*, 176.2*s*, 174.4*s*, 172.7*s*, 170.4*s*, 168.5*s*, 168.3*s*, 142.6*d*, 141.4*d*, 109.9*d*, 122.0*s*, 119.0*d*, 91.0*s*, 84.9*s*, 83.4*s*, 83.1*d*, 79.7*s*, 77.2*s*, 74.0*d*, 70.1*d*, 70.1*d*, 68.7*d*, 51.8*q*, 45.7*s*, 45.9*s*, 45.0*s*, 43.6*d*, 41.3*d*, 41.3*d*, 39.9*t*, 36.9*d*, 33.2*t*, 30.2*d*, 27.0*d*, 26.5*d*, 20.7*q*, 20.5*q*, 20.3*q*, 19.6*q*, 18.3*q*, 17.7*q*, 16.6*q*, 16.0*q*, 15.8*q*, 14.2*q*, 14.0*q*, 11.5*q*.

Spicatin (**4**). Obtained as a gum. (Found [M − 18]$^+$ *m/z* 526.3323, $C_{32}H_{48}O_6$ requires 526.3294). ^{1}H NMR δ 7.13 (1 H, *d*, *J* = 10 Hz, H-1), 5.82 (1 H, *d*, *J* = 10 Hz, H-2), 5.26 (1 H, *m*, H-15), 5.19 (1 H, *m*, H-7), 3.75 (2 H, *m*, 2 H-21), 1.92 (3 H, *s*, OAc),

‡ Senior Commonwealth Fellow, on leave of absence from Department of Chemistry, University of Ghana, Legon, Accra, Ghana.



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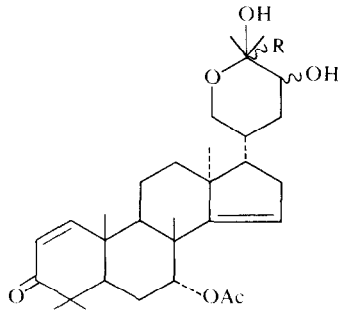

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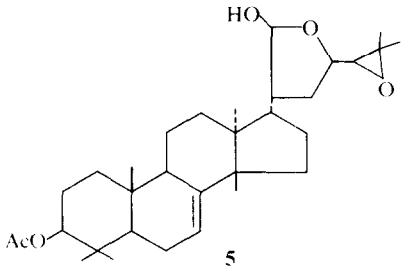
4 R = OH



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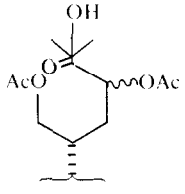

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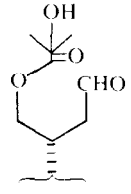

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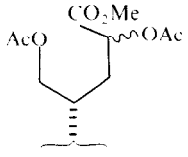

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1.4, 1.25, 1.17, 1.17, 1.05, 1.05, 1.05 (all 3 H, *s*, Me groups). ^{13}C NMR: δ 7.18 (1H, *d*, J = 10 Hz, H-1), 5.88 (1H, *d*, J = 10 Hz, H-2), 5.66 (1H, *dd*, J = 8, 4 Hz, H-24), 5.35 (1H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, H-15), 5.26 (1H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, H-7), 4.30 (1H, *dd*, J = 11, 2, H-21a), 3.95 38.5*d*, 38.4*d*, 34.8*t*, 34.5*t*, 29.6*t*, 27.1*q*, 26.9*q*, 24.3*q*, 23.9*q*, 21.0*q*, 20.8*q*, 19.8*q*, 18.8*q*, 16.6*t*.

The derived acetate (**6**) was prepared with Ac_2O–pyridine. ^{1}H NMR: δ 7.18 (1 H, *d*, J = 10 Hz, H-1), 5.88 (1 H, *d*, J = 10 Hz, H-2), 5.66 (1 H, *dd*, J = 8, 4 Hz, H-24), 5.35 (1 H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, H-15), 5.26 (1 H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, H-7), 4.30 (1 H, *dd*, J = 11, 2, H-21a), 3.95 (1 H, *dd*, J = 11, 5, H-21b), 2.08, 2.07, 1.97 (all 3 H, *s*, OAc), 1.45, 1.40, 1.18, 1.15, 1.07, 1.07, 1.03 (all 3 H, *s*, Me groups). ^{13}C NMR: 210.8*s*, 204.0*s*, 170.7*s*, 170.3*s*, 169.6*s*, 159.3*s*, 157.6*d*, 125.6*d*, 119.2*d*, 77.3*s*, 74.8*d*, 73.6*d*, 65.8*t*, 56.0*d*, 46.8*s*, 46.3*d*, 44.2*s*, 42.9*s*, 39.9*s*, 38.8*d*, 36.5*d*, 34.7*t*, 34.3*t*, 31.5*t*, 27.7*q*, 27.3*q*, 27.3*q*, 27.0*q*, 23.9*t*, 21.1*q*, 20.9*q*, 20.6*q*, 20.6*q*, 19.5*q*, 18.8*q*, 16.8*t*.

Periodate oxidation of spicatin. A soln of spicatin (**4**) (77 mg) in MeOH (10 ml) was stirred at room temp. for 48 hr with sodium metaperiodate (excess), after which H_2O was added. $CHCl_3$ extrd a gum (60 mg) which showed two spots on TLC. Prep. TLC gave the major band as a gum (32 mg) which was the aldehydo ester (**7**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1668, 1600. ^{1}H NMR: δ 9.74 (1 H, *bs*, CHO); 7.11 (1 H, *d*, J = 10 Hz, H-1); 5.83 (1 H, *d*, J = 10 Hz, H-2); 5.31 (1 H, *m*, H-15); 5.21 (1 H, *m*, H-7); 4.42 (1 H, *dd*, J = 12, 3 Hz, H-21b); 3.98 (1 H, *dd*, J = 12, 6 Hz, H-21a); 1.92 (3 H, *s*, OAc); 1.37, 1.37, 1.13, 1.11, 1.04, 1.02, 1.02 (all 3 H, *s*, Me groups). ^{13}C NMR: 204.5*s*, 201.1*d*, 177.3*s*, 170.0*s*, 159.2*s*, 157.9*d*, 125.6*d*, 118.9*d*, 74.6*d*, 72.1*s*, 67.3*t*, 54.6*d*, 46.5*s*, 46.2*d*, 45.5*t*, 44.2*s*, 42.8*s*, 39.8*s*, 38.4*d*, 35.0*t*, 34.2*t*, 33.7*d*, 27.3*q*, 27.3*q*, 27.3*q*, 27.1*q*, 23.8*t*, 21.2*q*, 21.1*q*, 19.6*q*, 19.0*q*, 16.7*t*.

Periodate oxidation of the derived acetate. The acetate (80 mg) was oxidized as above. Sodium bicarbonate isolated an acid fraction which was methylated with CH_2N_2. Purification by TLC gave the ester (**8**) as a gum (20 mg). MS m/z: 600 [M]$^+$, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1668, 1600. ^{1}H NMR: δ 7.15 (1 H, *d*, J = 10 Hz, H-1); 5.85 (1 H, *d*, J = 10 Hz, H-2); 5.30 (1 H, *m*, H-15); 5.20 (1 H, *m*, H-7); 4.15 (2 H, *m*, 2 H-21); 3.73 (3 H, *s*, CO_2Me); 2.08, 2.05, 1.92 (all 3 H, *s*, OAc). ^{13}C NMR: 204.6*s*, 171.1*s*, 170.8*s*, 170.4*s*, 170.1*s*, 159.1*s*, 158.1*d*, 125.6*d*, 119.1*d*, 74.6*d*, 71.6*d*, 65.4*t*, 55.4*d*, 52.4*q*, 46.6*s*, 46.2*d*, 44.2*s*, 42.7*s*, 39.8*s*, 38.5*d*, 35.6*d*, 34.7*t*, 34.0*t*, 32.2*t*, 27.4*q*, 27.1*q*, 23.8*t*, 21.2*q*, 21.2*q*, 20.9*q*, 20.7*q*, 19.5*q*, 19.0*q*, 16.8*t*.

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