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POLYHYDROXYAGAROFURAN DERIVATIVES FROM *AUSTROPLENCKIA POPULNEA*

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Key Word Index—*Austroplenckia populnea*; Celastraceae; sesquiterpene polyol esters; dihydroagarofuran derivatives.

Abstract—The larvicidal extract of *Austroplenckia populnea* leaves gave two new polyesters of 8-oxo-1,2,3,4,9,14-hexahydroxydihydroagarofuran, a compound which is typical of Celastraceae species.

INTRODUCTION

Austroplenckia [1] is a small mainly Brazilian genus of Celastraceae [2]. Information on its chemistry is limited to the root bark of *A. populnea* which gives the antitumor agents maytenonic acid (**1**) [3] and tingenone (**2**) [4] which were also isolated from representatives of other Celastraceae genera [5]†.

As an EtOAc–hexane (1:4) extract of *A. populnea* leaves exhibited activity against the larval stages of *Strongyloides stercoralis* and hookworms, the crude extract was chromatographed in an effort to isolate the active principle. Extensive purification of a solid fraction yielded two new amorphous esters of 8-oxo-1,2,4,6,9,14-hexahydrodihydroagarofuran (**3a** and **3b**) of a type commonly found in Celastraceae [5].

RESULTS AND DISCUSSION

Structures of the two new sesquiterpenoids, small quantities of which were separated in pure form only after multiple TLC, were deduced by NMR spectrometry (Tables 1 and 2). That **3a**, the polyol ester present in larger amount, contained one benzoate and four acetate residues was indicated by its ^{1}H NMR and confirmed by its ^{13}C NMR spectrum. One of the acetate signals occurred at considerably higher than normal field (δ1.52), a fact which initially caused some confusion. Four of the acid moieties esterified secondary hydroxyls (^{1}H NMR signals at δ6.70, 5.92, 5.56 and 5.34, carbon doublets at δ79.96, 74.41-double intensity-and 68.27), the fifth esterified a primary alcohol function of type **A** (AB quartet, J = 13 Hz at δ5.07 and 4.62, carbon triplet at δ61.01). A sixth carbonyl group (carbon singlet at δ197.13) was provisionally attributed to a cyclohexanone.

Hydroxyl absorption in the IR spectrum and the absence of additional low field signals in the ^{1}H NMR spectrum indicated the presence in **3a** of a tertiary hydroxyl group. As the ^{13}C NMR spectrum contained not merely one, but three C–O singlets and the ^{1}H NMR exhibited three methyl singlets at δ1.67, 1.63 and 1.56, it was concluded that the substance was based on the

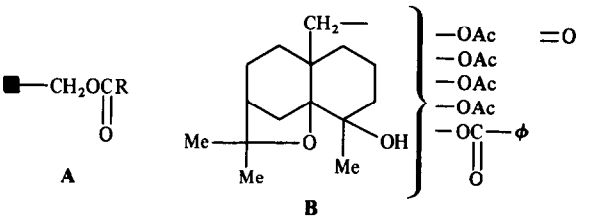


Table 1. ^{1}H NMR spectra of compounds **3a** and **3b** (270 MHz)

	3a ($CDCl_3$)	**3b** ($CDCl_3$)	**3b** (C_6D_6)
H-1	5.56 *d* (3.5)*	5.69 *d* (3.5)	6.08 *d*
H-2	5.34 *dd* (7, 3.5)	5.36 *dd* (7, 3.5)	5.65 *br dd*
H-3	2.03 *m*	2.00 (obsc.)	?
H-6	6.70 *br s*	6.69 *br s*	6.30 *br s*
H-7	3.03 *br s*	2.96 *br s*	3.39 *br s*
H-9	5.92 *s*	5.95 *s*	6.15 *s*
H-12‡	1.67 *s*†	1.60 *s*†	1.53 *s*†
H-13‡	1.63 *s*	1.56 *s*	1.19 *s*
H-14a	5.07 *d* (13)	5.11 *d* (13)	5.68 *d*
H-14b	4.62 *d* (13)	4.62 *d* (13)	4.80 *d*
H-15‡	1.56 *s*†	1.49 *s*†	1.42 *s*†
Ac‡	2.17, 2.14	2.09, 2.00	2.00, 1.70
	2.07, 1.52 *s*	2.00 *s*	1.69 *s*
H-2′,6′	8.00 *br d* (8)	7.87 *br d* (8)	8.15 *dd* (8, 3)
H-3′, 5′	7.48 *br t* (8)	in 7.17 *c*	6.75–6.95 *c*
H-4′	7.71 *br t* (8)		
H-2″		5.73 *d* (16)	5.99 *d*
H-3″		7.33 *d* (16)	7.56 *d*
H-5″, 9″		6.91 *br d* (8)	6.53 *br d*
H-6″, 8″		in 7.17 c	6.75–6.95 c
H-7″			

*Values in parenthesis are coupling constants in Hz.
†Assignments may be interchanged.
‡Intensity three protons.

† In these articles the species is referred to by its older name [2] *Plenckia populnea* Reiss in Mart.

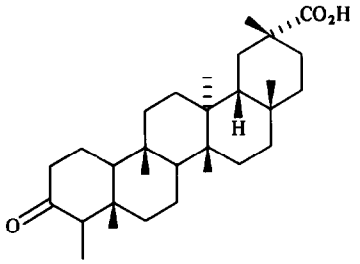
Table 2. ^{13}C NMR spectrum of compound **3a** (67.89 MHz, $CDCl_3$)*

C-1	68.27 *d*	C-11	69.78
C-2	74.41 *d*	C-12	29.27 *q*
C-6	74.41 *d*	C-13	25.15 *q*
C-3	41.99 *t*	C-14	61.01 *t*
C-4	85.16	C-15	24.54 *q*
C-5	93.31	C-1′	128.93
C-7	64.91 *d*	C-2′, 6′	129.85 *d*
C-8	197.13	C-3′, 5′	128.71 *d*
C-9	79.66 *d*	C-4′	133.66 *d*
C-10	52.63	Ac	21.32, 21.21, 20.59, 20.31 *q*

*Unmarked signals are singlets.

dihydroagarofuran skeleton **B** typical of the sesquiterpene polyol esters and sesquiterpene polyol ester alkaloids found in other Celastraceae [5]. The remaining three carbon signals, a triplet, a doublet and a singlet, corroborated this deduction [6, 7].

The distribution of ketone and ester groups over rings A and B and the stereochemistry were dictated by the chemical shift, multiplicities and coupling constants deduced by spin decoupling experiments. Thus the chemical shifts of H-7 and C-7 indicated that the ketone group was located on C-8. H-6 at δ6.70 under the C-6 ester function almost invariably present in compounds of this type was only weakly coupled to equatorial H-7 and hence axial and β-orientated in the absolute configuration depicted in the formula.



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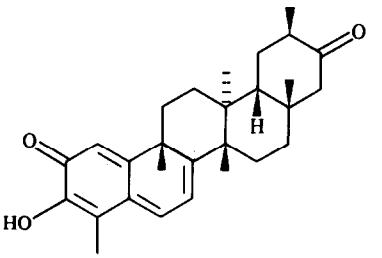

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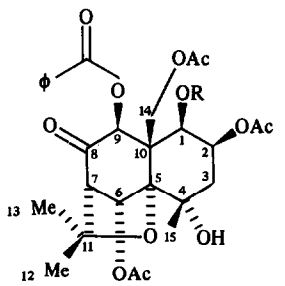
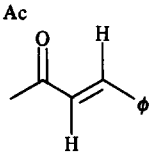
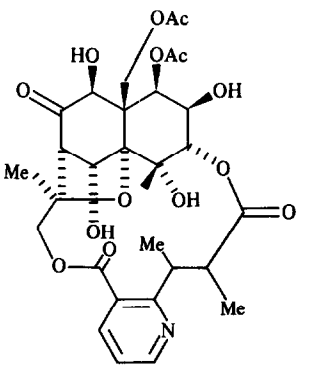


3a R = Ac

3b R =





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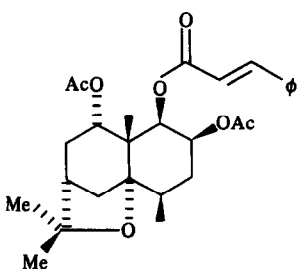

5

Reference has already been made to the unusual diamagnetic shift of one of the acetate methyl signals (δ1.52). Previous workers [8–11] have drawn attention to this phenomenon which arises when an equatorially orientated acetate on C-1 is shielded by an aromatic ester on C-9. Consequently the benzoate ester was placed on C-9 and two of the four acetates on C-1 and C-6. As the axial H-1 at δ5.56 was vicinally coupled to another low-field proton at δ5.36 ($J_{1,2}$ = 3.5 Hz) and the latter was significantly coupled to only one of the protons at C-3 ($J_{2,3}$ = 7 Hz), H-2, under the third acetate, was equatorial and α. That the fourth acetate was on C-14 rather than on C-12 was deduced by comparing the chemical shifts and coupling constants of H-14a,b with literature values in compounds acylated in C-14 [12] and both C-12 and C-14 [13].

The stereochemistry assigned to the benzoate on C-9 is based on measurement of NOE difference spectra. Irradiation in the methyl region (specifically at δ1.63) produced a 20% increase in the intensity of the H-9 signal. Conversely, irradiation at the frequency of H-9 produced a 27% enhancement in the intensity of the H-1 signal and a small, but signficant (3%) increase in the methyl signal at δ1.63. Hence H-9 (and H-1) are axial and α and the δ1.63 signal is that of H-13. Similar information has been used for assigning the stereochemistry of evonine (**4**) [13].

Aside from revealing replacement of one of the four acetates of **3a** by a *trans*-cinnamate, the ^{1}H NMR spectrum of the second polyol ester **3b** was essentially identical with that of **3a**, with coupling constants and most chemical shifts (Table 1) indicating identical stereochemistry. As the three acetate frequencies resonated in the normal range (δ2.00–2.10) and as the H-1 signal had experienced a distinct paramagnetic shift while the frequencies of H-2, H-6, H-9 and H-14a,b had remained constant, the cinnamate was placed on C-1, with the benzoate remaining on C-9 and equatorial. In this arrangement the mutual anisotropic effects of the two aromatic moieties should result in significant diamagnetic shifts. This is seen if the frequencies of the benzoate of **3b** are compared with those of **3a** and if the frequencies of the cinnamate of **3b** are compared with those reported for the cinnamate in ester **5** derived from isocelorbicol [14].

EXPERIMENTAL

Leaves of *Austroplenckia populnea* (Reiss. in Mart.) Lundell, (6.5 kg) were collected by Dr. Hermógenes de Freitas Leitão Filho in Morro das Camisinhas, Pocos de Caldas, Minas Gerais State, Brasil, in March 1983. As an extract of the leaves with hexane–EtOAc (5:1) exhibited larvicidal activity against *Strongyloides stercoralis* and hookworm [15], the material was extracted with this solvent combination. The crude extract (192 g) was dissolved in 2.2 l. of EtOH, diluted with H_2O, filtered and evaporated at red. pres. The residue was extracted with $CHCl_3$; the washed and dried extract on evaporation afforded 18 g of gum which was chromatographed over 200 g of silica gel, 400 ml fractions being eluted with hexane–EtOAc containing increasing proportions of EtOAc as follows. Fr. 1–10 (20:1); Fr. 10–14 (17:1); Fr. 15–20 (14.3:1); Fr. 21–23 (12.5); Fr. 1; 24–25 (11.1:1); Fr. 26–27 (10:1); Fr. 28–29 (9:1); Fr. 30–31, (8.3:1); Fr. 32–33 (7.1:1), Fr. 36–37 (6.6:1); Fr. 38–39 (6.25:1); Fr. 40–41 (5.9:1); Fr. 42–59 (5.5:1); Fr. 60–61 (5:1); Fr. 62–64 (3.3:1); Fr. 65 (EtOAc), and Fr. 66–67 (EtOH). Fr. 65 afforded 2.7 g of gum which was further purified by TLC ($CHCl_3$–EtOAc, 17:1). Elution of the major spot with $CHCl_3$ gave 1.6 g of a resinous mixture (NMR spectrum). Portions of this material were further purified by multiple TLC first with $CHCl_3$–MeOH (19:1) and then with C_6H_6–EtOAc (1:1) to give eventually small quantities of pure **3a** and **3b** as amorphous solids which resisted attempts at crystallization. Separation was monitored by ^{1}H NMR spectrometry; the intermediate fractions recovered from the TLC plates consisted of mixtures of **3a** and **3b** as well as at least one other related substance. The ^{1}H NMR spectra of **3a** and **3b** are listed in Table 1; the ^{13}C NMR spectrum of **3a** is given in Table 2. Other data were as follows. Compound **3a**: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2545, 1740, 1372, 1270, 1210, 1055, 935, 795 and 730; MS (positive CI) *m/z*: 604 $(M)^+$; MS (EI, low resoln) *m/z* (rel. int.): 544 $[M - C_2H_4O_2]^+$ (0.55), 502 (1.19), 484 (0.22), 482 (0.21), 442 (0.26), 422 (0.19), 394 (0.24), 380 (0.92), 362 (0.32), 343 (0.27), 320 (0.42), 302 (0.31), 281 (0.09), 260 (0.99), 218 (12.1), 137 (2.5), 131 (8.4) 105 (100).

Compound **3b**: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 1740, 1635, 1600, 1452, 1375, 1345, 1315, 1250, 1060, 1030, 1055, 1013, 965, 870, 710 and 672; MS (positive CI) *m/z*: 692 $(M)^+$; MS (EI, low resoln) *m/z* (rel. int.): 692 $[M]^+$ (0.07), 675 (0.05), 632 (0.33), 590 (0.52), 570 (0.26), 544 (0.27), 530 (0.10), 502 (0.14), 484 (0.40), 398 (0.21), 382 (0.37), 367 (0.39), 362 (0.37), 351 (0.37), 320 (0.60), 302 (0.62), 291 (0.61), 289 (0.60), 284 (0.98), 281 (0.87), 263 (0.91), 260 (1.46), 232 (1.36), 218 (11.10), 165 (2.46), 157 (2.77), 137 (2.21), 131 (81), 105 (100).

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