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APARISTHMAN, METHYL 1-(3-FUROYLMETHYL)-4a-HYDROXY-1,2-DIMETHYL-2,3,4,4a,5,8,9,9a-OCTAHYDRO-1H-BENZOCYCLOHEPTENE-6-CARBOXYLATE, A SEVEN MEMBERED RING DITERPENOID FROM *APARISTHMIUM CORDATUM*

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Key Word Index—*Aparisthmium cordatum*; Euphorbiaceae; rearranged clerodane diterpenoid; aparisthman.

Abstract—A new diterpenoid, aparisthman, with a rearranged clerodane skeleton has been isolated from the bark of *Aparisthmium cordatum*. Its molecular structure has been investigated by spectroscopic means and by X-ray analysis.

INTRODUCTION

Aparisthmium cordatum (Juss.) Bail., known in the State of Pará (Northern Brazil) as 'ariquena queimosa', is a medium sized tree which is native to the North Brazilian coastal region. To our knowledge it has no popular use, but there is a close botanical relationship to genus *Alchornea*. The latter has been intensively investigated because of its use in traditional African medicine [1].

The benzene extract of the bark of *A. cordatum* yielded two new furan diterpenoids as well as a triterpenoid acid of unknown structure. The isolation and investigation of the structure of aparisthman (1) is reported.

RESULTS AND DISCUSSION

Aparisthman (1) has the molecular formula $C_{21}H_{28}O_5$. Its IR spectrum is consistent with the presence of a hydroxyl group (3570 cm^{-1}), two conjugated carbonyl groups (1690 and 1670 cm^{-1}) and a furan ring (3130, 1510, 875 cm^{-1}) [2]. The presence of the furan ring was also indicated by the slightly positive Ehrlich-test [3].

The conjugation of the keto group (C-12) to the furan ring follows from the NMR downfield shifts of the ^{1}H and ^{13}C signals for the furan ring. Similar shifts were observed for chettaphanin-I [4] and for derivatives of teumassilin [5] and of sciadin [6].

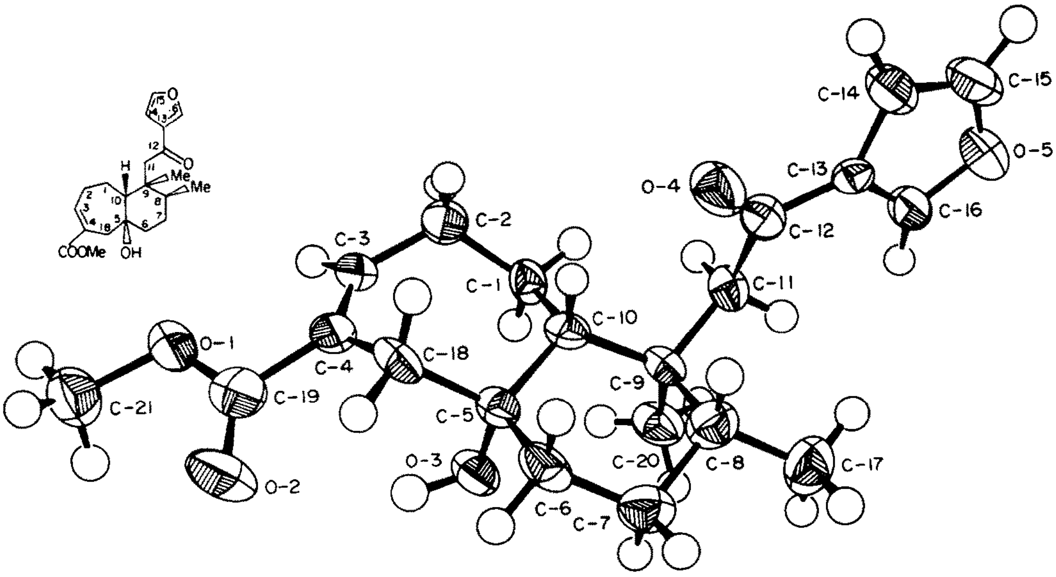

Fig. 1. The X-ray model of Aparisthman (1). The thermal ellipsoids are the 50% probability surfaces, the sizes of the H-spheres and the enantiomorph are chosen arbitrarily. The numbering scheme was taken from other diterpenoids of the clerodane series for easier comparison.

The ^{1}H NMR spectrum of **1** additionally shows signals of a tertiary methyl group at δ0.87 (*s*), a secondary methyl group at δ0.90 (*d*), a methyl ester at δ3.70 (*s*) and a multiplet at δ7.25, which by double resonance experiments was assigned to the β-hydrogen (H-3) of the α,β-unsaturated ester.

The presence of a tertiary hydroxyl was confirmed by a singlet at δ70.2 in the ^{13}C NMR spectrum and because **1** resisted acetylation under normal conditions (Ac_2O–pyridine, room temp.).

Aparisthman crystallizes in the non-centrosymmetric orthorhombic space group of $P2_12_12_1$, with $a = 7.550(2)$, $b = 12.752(3)$, $c = 19.713(4)$ Å, $D_x = 1.26$ g/cm^3 and, therefore, $z = 4$. A model of the molecular structure was derived by X-ray crystallographic analysis (Fig. 1), the final (mean) discrepancy index being $R = 4.5\%$ for 829 reflections against 235 free variables of the arbitrarily chosen enantiomorph. The bond lengths and bond angles are given in Table 1. There are no other than van der Waals intermolecular interactions.

As can be seen from **1**, aparisthman posesses a rearranged clerodane type skeleton [7], in which the angular methyl group (C-18) of the clerodanes is included in a seven-membered ring. From the CD curve there is some indication of the configuration of **1** as shown in Fig. 1, but further work is in progress by either synchroton or X-ray multiple reflection experiments. Compound **1** shows a negative band at 223 nm composed of contributions of the α,β-unsaturated carboxylate ester and the conjugated carbonyl furan system. A similar negative Cotton effect has been observed for methyl hardwickiate and methyl barbascoate [8].

Table 1. Bond lengths (Å) and angles (°), with estimated standard deviations in parentheses

Bond lengths		Bond angles	
O-1–C-19	1.329 (9)	C-2–C-1–C-10	117.3 (6)
O-1–C-21	1.440 (9)	C-1–C-2–C-3	113.9 (7)
O-2–C-19	1.190 (9)	C-2–C-3–C-4	122.7 (7)
O-3–C-5	1.461 (8)	C-3–C-4–C-18	123.4 (7)
O-4–C-12	1.219 (11)	C-3–C-4–C-19	120.9 (7)
O-5–C-15	1.353 (14)	C-18–C-4–C-19	115.6 (7)
O-5–C-16	1.363 (11)	C-6–C-5–C-10	111.3 (6)
C-1–C-2	1.537 (11)	C-6–C-5–C-18	107.3 (6)
C-1–C-10	1.529 (11)	C-10–C-5–C-18	112.5 (6)
C-2–C-3	1.499 (11)	C-6–C-5–O-3	107.7 (6)
C-3–C-4	1.316 (13)	C-10–C-5–O-3	109.8 (5)
C-4–C-18	1.502 (11)	C-18–C-5–O-3	108.1 (5)
C-4–C-19	1.497 (11)	C-5–C-6–C-7	113.3 (6)
C-5–C-6	1.518 (11)	C-6–C-7–C-8	110.6 (6)
C-5–C-10	1.550 (11)	C-7–C-8–C-9	111.7 (6)
C-6–C-7	1.514 (11)	C-7–C-8–C-17	108.9 (6)
C-7–C-8	1.537 (11)	C-9–C-8–C-17	115.3 (6)
C-8–C-9	1.559 (11)	C-8–C-9–C-10	111.3 (6)
C-8–C-17	1.527 (11)	C-8–C-9–C-11	107.7 (6)
C-9–C-10	1.550 (9)	C-8–C-9–C-20	109.9 (6)
C-9–C-11	1.543 (10)	C-10–C-9–C-11	112.1 (6)
C-9–C-20	1.577 (10)	C-10–C-9–C-20	110.8 (6)
C-11–C-12	1.524 (12)	C-11–C-9–C-20	104.8 (6)
C-12–C-13	1.456 (12)	C-1–C-10–C-5	113.3 (6)
C-13–C-14	1.414 (13)	C-1–C-10–C-9	112.2 (6)
C-13–C-16	1.345 (13)	C-5–C-10–C-9	114.9 (6)
C-14–C-15	1.339 (15)	C-9–C-11–C-12	119.2 (6)
C-18–C-5	1.529 (10)	C-11–C-12–C-13	118.0 (8)
		C-11–C-12–O-4	121.9 (7)
		C-13–C-12–O-4	120.2 (8)
		C-12–C-13–C-14	125.5 (8)
		C-12–C-13–C-16	128.7 (8)
		C-14–C-13–C-16	105.8 (7)
		C-13–C-14–C-15	107.2 (8)
		C-14–C-15–O-5	110.1 (8)
		C-13–C-16–O-5	110.4 (8)
		C-4–C-18–C-5	116.7 (6)
		C-4–C-19–O-1	113.1 (7)
		C-4–C-19–O-2	123.4 (7)
		O-1–C-19–O-2	123.5 (7)
		C-19–O-1–C-21	116.7 (6)
		C-15–O-5–C-16	106.5 (7)

EXPERIMENTAL

Mp: uncorr.; ^{1}H NMR (100 MHz) and ^{13}C NMR (20 MHz): $CDCl_3$, TMS as internal standard. The plant materials were collected in March 1984 in Terra Alta (Pará, Brazil) and identified by Dr. Paulo B. Cavalcante (Museu P. E. Goeldi, Belém-Pa, Brazil).

Isolation of aparisthman (**1**). Dried and powdered bark (3 kg) of *A. cordatum* was extracted with MeOH (8 l.) for 72 hr at 60°. The solvent was evaporated and the residue (600 g) mixed with 1.5 kg silica gel (Merck no. 60) and 20 g Na_2SO_4 (dry). This mixture was extracted (Soxhlet) for 48 hr with 3 l. of C_6H_6. The C_6H_6 extract was concd under vacuum yielding a gum (185 g), which was subjected to CC over silica gel (4 kg, Merck no. 60). Elution (*n*-hexane–CH_2Cl_2 gradient) gave **1**, 4 g after crystallization from *n*-hexane–EtOAc (2:1). Mp 140–142°; $[\alpha]_D^{20} = -80.8°$ (*c* 1.0; $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3570, 3130, 3020, 2950, 2850, 1690, 1670, 1650, 1560, 1510, 1440, 1395, 1355, 1290, 1250, 1195, 1150, 1120, 1095, 1050, 1000, 945, 930, 875, 835, 815, 790, 775, 765, 735; ^{13}C NMR ($CDCl_3$): δ21.1 (*t*, C-1), 28.2 (*t*, C-2), 145.6 (*d*, C-3), 131.2 (*s*, C-4), 70.2 (*s*, C-5), 41.5 (*t*, C-6)^{a}, 26.7 (*t*, C-7), 36.9 (*d*, C-8), 42.6 (*s*, C-9), 52.5 (*d*, C-10), 45.8 (*t*, C-11), 194.7 (*s*, C-12), 129.2 (*s*, C-13), 108.5 (*d*, C-14), 143.9 (*d*, C-15), 146.6 (*d*, C-16), 16.9 (*q*, C-17)^{b}, 42.4 (*t*, C-18)^{a}, 168.5 (*s*, C-19), 16.5 (*q*, C-20)^{b}, 51.7 (*q*, C-21);^{a,b} assignments may be interchanged. ^{1}H NMR ($CDCl_3$): δ7.98 (1H, *s*, H-16), 7.41 (1H, *m*, H-15), 7.25 (1H, *m*, H-3), 6.74 (1H, *m*, H-14), 3.70 (3H, *s*, OMe), 2.75 (2H, *s*, H-11), 2.55–1.16 (13H), 0.90 (3H, *d*, H-17), 0.87 (3H, *s*, H-20). (Found: C, 69.95; H, 7.86; $C_{21}H_{28}O_5$ requires C, 69.97; H, 7.83%.)

X-ray analysis. A clear and colourless disphenoidal crystal of $0.2 \times 0.2 \times 0.3$ mm^3 in dimensions, which showed perfect and symmetrical extinction in polarized light, was used to collect X-ray data on a Hilger & Watts 4-circle diffractometer. The instrument was reconstructed in order to fulfil the mechanical and software requirements of the XTL diffractometer and structure determination package of Syntex Analytical Instr. Corp. The lattice parameters were refined from the setting angles of 25 $^{+}h^{+}k^{+}l$-reflections. 1056 symmetrically independent reflections were measured in the $2\theta/\omega$ flexible scan mode using Nb-filtered Mo K_α-radiation. The correction for background was applied by a special algorithm following the method described by Lehmann and Larsen [11]. The solution of the structure by MULTAN [12] was straightforward when the 5-membered furan ring was inserted as an *a priori* known molecular fragment. For the subsequent refinement of the molecular model the programmes of the X-ray [9] system were employed on the UNIVAC 1100/61 computer of the HRZ of the University of Frankfurt/M. Only intensities with $I > 3\sigma\ (I)$ were admitted in the least squares process, being weighted as structure factors by $W = (\text{maxfct.}\ (2\sigma(F), 0.01/F/))^{-1}$ within the conventions of the X-ray programme package. While the heavy atoms were refined anisotropically, the hydrogen atoms were allocated to precalculated positions with isotropic temp. coefficients. The data is deposited at the Cambridge Crystallographic Data Centre.

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