TWO NEW SESQUITERPENE-ESTER ALKALOIDS FROM MAYTENUS MYRSINOIDES REISS. (CELASTRACEAE)

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Abstract - Two new alkaloids belonging to the dihydroagarofuran series, maymyrsine (1) and acetylmaymyrsine (2) have been isolated from the fruits of Maytenus myrsinoides Reiss. Their structures have been elucidated by M.S., ^{1}H NMR and X-ray diffraction analysis.

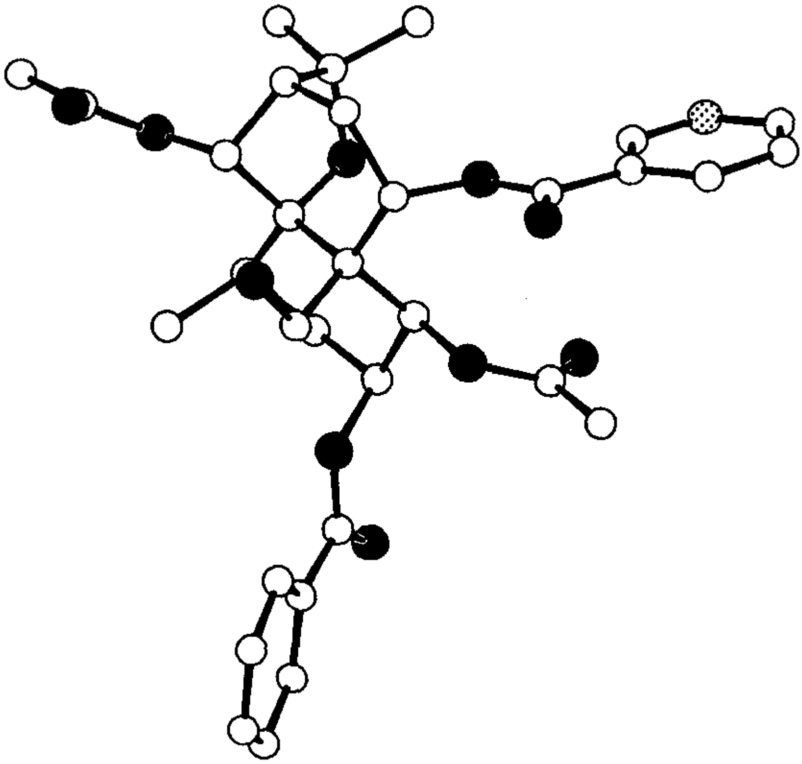
Maytenus myrsinoides Reiss. (Celastraceae) is a small tree growing throughout Guyana[1] and the northeastern region of Brazil[2]. In a continuation of our studies of alkaloid containing plants from French Guyana[3], we wish to report here the structural elucidation of two new alkaloids isolated from the fruits of this species[4] and named maymyrsine and acetylmaymyrsine.

Maymyrsine (1) has been obtained as colourless prisms from ethanol, mp 185-187°C, $[\alpha]_D$ = +93° ($CHCl_3$, C=1) (contents : 0.14 % from the dried plant material). The molecular formula has been established by high resolution mass spectrometry as $C_{32}H_{37}NO_{10}$ (Found : 595.2426 ; Calcd. : 595.2417). Substantial fragmentation ions suggested the presence of nicotinate (m/z = 124 and 106), benzoate (m/z = 105) and acetate (m/z = 43) units in the structure. In good agreement with these statements, the U.V. spectrum showed typical absorptions at λ_{max}^{EtOH} nm (log ε) : 230(4.13), 258 (sh., 3.51), 265(3.55), 271 (sh., 3.47) and 282 (sh., 3.06)[5] and the I.R. spectrum at ν_{max}^{KBr} cm^{-1} = 725, 750, 1245, 1285, 1600, 1730, 1760, 2945 and 3400-3600, the last of which indicated the presence of a free alcoholic hydroxyl group. Moreover, the

^{1}H N.M.R. spectrum exhibits the characteristic signals of one nicotinate and one benzoate in the aromatic region and of two acetate groups (two 3H singlets at δ = 1.45 and 1.73 ppm). Maymyrsine was thus a tetraester of a $C_{15}H_{26}O_5$ sesquiterpene pentaol belonging to the dihydroagarofuran[5,6,7] series as shown by a 6H-singlet at δ = 1.39 ppm ($-O-C(CH_3)_2-$) and a 3H-doublet (J = 7Hz) at δ = 1.26 ppm ($CH_3-CH<$) on the ^{1}H N.M.R. spectrum and by the fragmentations at m/z = 580, 553, 520, 431 and 308 typical to this series[5]. The presence of a strong fragment at m/z = 202 instead of m/z = 233 generally encountered in the M.S. of Celastraceous alkaloids[5] indicated the existence of a free primary alcoholic function at C-15. The oxygenation pattern on the dihydroagarofuran skeleton (C-1 eq., C-2 ax., C-6 eq. and C-9 ax.) has been determined by ^{1}H N.M.R., using double irradiation experiments (Table I). Unfortunately, the nature of the esterificating acids on these four positions could not be elucidated on N.M.R. basis because the ring effects created by benzoate and nicotinate groups are quite similar[8].

We therefore decided to elucidate the structure by X-ray analysis. The crystals are monoclinic, space group $P2_1$ with a = 14.058(7), b = 8.652(5), c = 13.606(7) A and β = 108.37(7)° ; Z = 2, V = 1570 A^3, d_x = 1.18. The experimental data were collected with a Philips 4-circle diffractometer, using graphite monochromated Cu K radiation (λ = 1.5418 A). From 3170 measured independent reflexions, the intensities of 2584 of them were significant ($I > 3\sigma(I)$). The crystal structure was solved using local Direct Methods programs[9]. All hydrogen atoms but 3 were located from Fourier-differences syntheses. The refinement was performed using the large blocks least-squares method[10] to a discrepancy factor of 6.3 %. The identification of the nitrogen atom was made by interchanging the diffusion factors of C and N in the possible positions. A water molecule was included in the refinement with half occupation factor. The figure shows a perspective view of the molecule.

Acetylmaymyrsine (2) has been obtained as a colourless amorphous solid, $[\alpha]_D^{20}$= +92° ($CHCl_3$, C=1)(contents : 0.44 % from the dried plant material). The molecular formula has been established by high resolution mass spectrometry as $C_{33}H_{36}NO_{11}$ (Found : 637.2492 ; Calcd. : 637.2523). The U.V. spectrum : λ_{max}^{EtOH} nm (log ε) = 230(4.12), 258 (sh. 3.51), 265(3.54), 271 (sh. 3.47), 282 (sh. 3.06) is very similar to that of maymyrsine. The I.R. spectrum differs from that of maymyrsine by the absence of typical OH absorption at 3400-3600 cm^{-1}. The ^{1}H N.M.R. spectrum (Table I) is also closely related to that of maymyrsine but exhibits the signals of three acetate



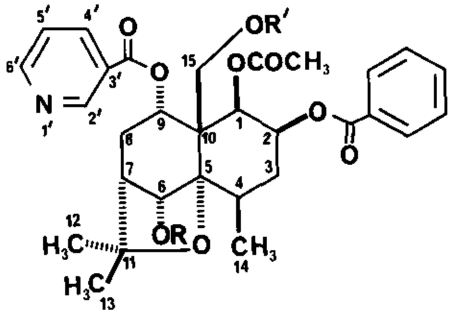
groups (three 3H singlets at δ = 1.35, 1.61 and 1.91 ppm). Downfield shifts of $H\text{-}15_a$ and $H\text{-}15_b$ (4.52 and 5.72 instead of 4.13 and 4.62 ppm) and a strong shielding by 1,3-diaxial interaction of the signal of H-6ax. (6.10 instead of 6.51 ppm) clearly indicate that this second alkaloid is the acetic ester of maymyrsine at the C-15 position. Furthermore, acetylation of maymyrsine 1 (Ac_2O/C_5H_5N/48 h) leads to acetylmaymyrsine 2 in almost quantitative yield.

Maymyrsine and acetylmaymyrsine are novel alkaloids related to a new $C_{15}H_{26}O_5$ sesquiterpene pentaol. From a chemotaxonomic point of view, it is interesting to note that two structurally related sesquiterpene alkaloids had been previously isolated ; cathedulin E8 from Catha edulis Forsk. (Celastraceae)[7] and salacinin C from Salacia brachypoda Peyr. (Hyppocrateaceae)[5]. This emphasizes the chemical *homogeneity of the family Celastraceae and its close relationship with Hippocrateaceae*[11,12].

TABLE I

[1]H N.M.R. spectra of maymyrsine (400 MHz) and acetylmyrsine (270 MHz) C_6D_6,TMS, δ (ppm).

	Maymyrsine 1	Acetylmaymyrsine 2
Me-14	1.26, 3H, d, J=7Hz	1.14, 3H, d, J=7Hz
Me-12 and Me-13	1.39, 6H, s	1.30 and 1.32, 2x3H, s
Ac	1.45 and 1.73, 2x3H, s	1.35, 1.61 and 1.91, 3x3H, s
H-3(ax.)	1.65, 1H, dd, J=17Hz, J'=1Hz	not individualized
H-4(eq.)	2.28, 1H, qdd, J=7Hz, J'=6Hz, J"= 1Hz	2.17, 1H, qdd, J=7Hz, J'=6Hz, J"= 1Hz
H-3(eq.)	2.46, 1H, ddd, J=17Hz, J'=6Hz, J"= 3Hz	2.39, 1H, ddd, J=17Hz, J'=6Hz J"= 3Hz
H-8(eq.)	2.67, 1H, ddd, J=16Hz, J'=7Hz, J"= 3Hz	2.51, 1H, ddd, J=16Hz, J'=7Hz J"= 3Hz
H-15_a	4.13, 1H, d, J= 13Hz	4.52, 1H, d, J=13Hz
H-15_b	4.62, 1H, d, J=13Hz	5.72, 1H, d, J=13Hz
H-9(eq.)	5.94, 1H, d, J=7Hz	5.83, 1H, d, J=7Hz
H-1(ax.)	6.12, 1H, d, J=3.5Hz	6.14, 1H, d, J=3.5Hz
H-2(eq.)	6.20, 1H, dd, J=3.5Hz, J'=3Hz	6.24, 1H, dd, J=3.5Hz, J'=3Hz
H-6(ax.)	6.51, 1H, s	6.10, 1H, s
Nicotinoyl H-5'	6.78, 1H, dd, J=8Hz, J'=5Hz	6.73, 1H, dd, J=8Hz, J'=5Hz
Benzoyl	7.15-7.37, 5H, m	7.12-7.38, 5H, m
Nicotinoyl H-4'	8.17, 1H, dt, J=8Hz, J'=1.5Hz	8.30, 1H, dt, J=8Hz, J'=1.5Hz
Nicotinoyl H-6'	8.38, 1H, dd, J-5Hz, J'=1.5Hz	8.44, 1H, dd, J=5Hz, J'=1.5Hz
Nicotinoyl H-2'	8.63, 1H, d, J=1.5Hz	8.53, 1H,d, J=1.5Hz



1 R = $COCH_3$ R' = H

2 R = $COCH_3$ R' = $COCH_3$

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