

FOUR NEW ACRIDONE ALKALOIDS FROM SARCOMELICOPE DOGNIENSIS HARTLEY
(RUTACEAE)

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Abstract - Four new acridone alkaloids, 1, 3, 4 and 6 have been isolated from the leaves of Sarcomelicope dogniensis. Their structures have been elucidated by spectroscopic studies and confirmed by their synthesis, using N-desmethyiacronycine (2) as starting material.

Sarcomelicope dogniensis Hartley (Rutaceae) is a medium tree upto 12 m high recently described as endemic to the Plateau de Dogny, New Caledonia¹. In a continuation of our systematic studies of alkaloid containing plants from New Caledonia², we wish to report here the structural elucidation of four novel acridones isolated from the leaves of this species³.

(-)-Cis-1,2-dihydroxy-1,2-dihydro-N-desmethyiacronycine (1)⁴ has been obtained as a yellow amorphous compound (contents : 0.01 % from the dried plant material) ; $[\alpha]_D^{20} = -2^\circ$ (c = 0.25, MeOH). Its empirical formula has been determined by high resolution mass spectroscopy as $C_{19}H_{19}NO_5$ (Found : 341.1260 ; Calcd. : 341.1263). Its uv spectrum, λ_{max}^{MeOH} (log ϵ) : 228(4.16), 246(sh., 4.31), 260(4.41), 269(4.41), 290(4.07), 320 (sh., 3.65) and 374(3.78) is very close to that of 1,2-dihydroacronycine⁵. The ir spectrum exhibits typical absorptions at $\nu_{max} \cdot cm^{-1}$ (KBr) : 775, 1165, 1605, 1625, 1650, 2960, 3005 and 3445, the last of which indicates the presence of free alcoholic groups. The main features of the ¹H nmr spectrum

(Table I) are the signal of the NH-10 of a 9-acridone and the series of signals typical to a fused cis-3,4-dihydroxy-2,2-dimethyl-3,4-dihydro-2H-pyran system^{6,7}. These elements permitted depicting the structure of this novel alkaloid as 1. Unfortunately, the absolute configurations of the two chiral centers at C-1 and C-2 remain unknown, due to the small amount of natural product isolated. Confirmation of structure 1 could be obtained by partial synthesis. Oxidation^{7,8} of N-desmethyl-acronycine (2) ($\text{OsO}_4/\text{C}_5\text{H}_5\text{N}/20^\circ\text{C}/3\text{ h}$) leads in 95 % yield to (+)-cis-1,2-dihydroxy-1,2-dihydro-N-desmethylacronycine (1) whose chromatographic and spectral characteristics (tlc, uv, ir, ms, nmr) are identical with those of the natural product.

1-Methoxy-3-(2-methylpropanal-2-oxy)-acridin-9-one-4-carbaldehyde (3) has been obtained as a yellow amorphous solid (contents : 0.01 % from the dried plant material) ; $[\alpha]_D^{20} = 0^\circ$. Its empirical formula could be established by high resolution mass spectrometry as $\text{C}_{19}\text{H}_{17}\text{NO}_5$ (Found : 339.1095 ; Calcd.: 339.1106). The uv spectrum, $\lambda_{\text{max}}^{\text{MeOH}}$ (log ϵ) : 225(4.11), 246(4.47), 260(4.56), 275(sh., 4.38), 285(sh., 4.37), 309(4.15), 325(sh., 3.89) and 393(4.04) is close to that of acronycine⁵ and shows typical absorptions associated with a 9-acridone nucleus bearing two oxygen substituents at C-1 and C-3 and an unsaturated substituent at C-4. The ir spectrum, ν_{max} , cm^{-1} (KBr) : 780, 1160, 1610, 1625, 1640, 1655, 1745, 2950, 3000 and 3430 is consistent with a 9-acridone^{9,10} skeleton and with the presence of aliphatic and aromatic aldehyde groups. In good agreement with this statement, the ^1H nmr spectrum (Table I) exhibits one D_2O -exchangeable NH-singlet at 12.95ppm and two 1H-aldehyde singlets at 10.48 and 9.88 ppm. The aromatic signals are typical to a 1,3,4-trisubstituted 9-acridone. One 3H-singlet at 3.98 ppm and one 6H-singlet at 1.68 ppm were assigned to one OMe and one CMe_2 groups. These data suggested a structure of 1-methoxy-3-(2-methylpropanal-2-oxy)-acridin-9-one-4-carbaldehyde (3) for this novel alkaloid. Confirmation of the location of the substituents on the acridone nucleus was performed by chemical correlation. Periodic oxidation of the diol 1 ($\text{NaIO}_4/\text{MeOH}/20^\circ\text{C}/2\text{ h}$) leads in 68 % yield to the dialdehyde 3 identical with the natural product.

(+)-1-Hydroxy-1,2-dihydro-N-desmethylacronycine (4) has been obtained as light yellow prisms from methanol, mp $212-214^\circ\text{C}$ (contents : 0.01 % from the dried plant material) ; $[\alpha]_D^{20} = +4^\circ$ ($c = 0.25$, MeOH). The empirical formula could be established by high resolution mass spectrometry as $\text{C}_{19}\text{H}_{19}\text{NO}_4$ (Found : 325.1301 ;

Calcd. : 325.1313). The uv spectrum, $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ) : 227(4.11), 247(sh., 4.35), 260(4.48), 269(4.49), 291(4.07), 315(sh., 3.68), 321(sh., 3.62) and 374(3.72) is very similar with that of 1,2-dihydroacronycine. The ir spectrum, $\nu_{\text{max.}}$ cm^{-1} (KBr) : 765, 1165, 1605, 1625, 1650, 2960, 3010 and 3450 shows the characteristic absorptions of a 9-acridone system^{9,10} and of a free OH-group. The ^1H nmr spectrum (Table I) exhibits in addition to the signals of a 1,3,4-trisubstituted 9-acridone, the signals associated with a fused 4-hydroxy-2,2-dimethyl-3,4-dihydro-2H-pyran system⁶. These elements permitted depicting the structure of this new alkaloid as 4. Nevertheless, the absolute stereochemistry at C-1 remains unknown, due to the small amount of natural product at our disposal. The structure of this alkaloid was finally confirmed by its synthesis from N-desmethyiacronycine (2). In a first step, hydroxybromination^{8,11} of 2 (N-bromosuccinimide/50 % aqueous THF/0°C/3 h) led in 47 % yield to (+)-trans-hydroxy-1-bromo-2-dihydro-1,2-N-desmethyiacronycine (5). This bromohydrin could then be smoothly debrominated using tributyltinhydride-reduction^{11,12} (Bu_3SnH /2,2'-Azabis(2-methylpropionitrile)/Toluene/Reflux under Ar/1 h). This latter reaction leads in 80 % yield to (+)-1-hydroxy-1,2-dihydro-N-desmethyiacronycine (4) whose chromatographic and spectral characteristics (tlc, uv, ir, ms, nmr) are identical with those of the natural product.

1-Oxo-1,2-dihydro-N-desmethyiacronycine (6) has been isolated as a yellow amorphous solid (contents : 0.02 % of the dried plant material) ; $[\alpha]_{\text{D}}^{20} = 0^\circ$. Its empirical formula has been determined by high resolution mass spectrometry as $\text{C}_{19}\text{H}_{17}\text{NO}_4$ (Found : 323.1154 ; Calcd. : 323.1157). The uv spectrum, $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ) : 227(3.71), 245(3.92), 260(4.01), 275(sh., 3.93), 280(3.94), 310(3.59), 326(sh., 3.25) and 384(3.57) and the ir spectrum, $\nu_{\text{max.}}$ cm^{-1} (KBr) : 780, 1160, 1615, 1630, 1645, 1655, 2940, 3000 and 3415 showed diagnostic absorptions of a 9-acridone nucleus⁹. The ^1H nmr spectrum (Table I) exhibits in the aromatic region the signals associated with a 1,3,4-trisubstituted 9-acridone skeleton. In the aliphatic region, one 3H-singlet at 4.06 ppm, one 2H-singlet at 2.83 ppm and one 6H-singlet at 1.56 ppm could be assigned to one OMe and to the protons of a $\text{Ar-CO-CH}_2\text{-C}(\text{CH}_3)_2\text{-O-Ar}$ system. These elements permitted depicting the structure of this novel acridone as 6. Confirmation of this structure was obtained by its synthesis from the benzylic alcohol 4. Chromic oxidation^{13,14} of (+)-1-hydroxy-1,2-dihydro-N-desmethyiacronycine (4) (Pyridinium chlorochromate/anh. CH_2Cl_2 /20°C/3 h) leads in 68 % yield to 1-oxo-1,2-dihydro-N-desmethyiacronycine (6) identical

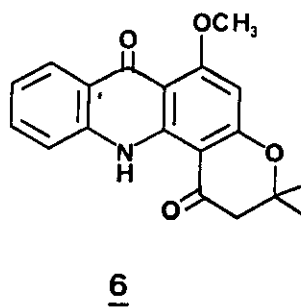
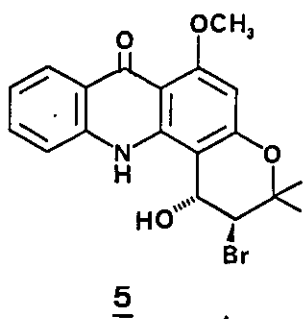
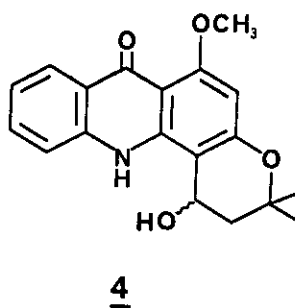
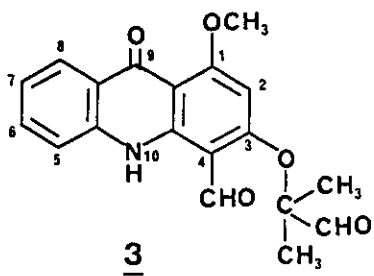
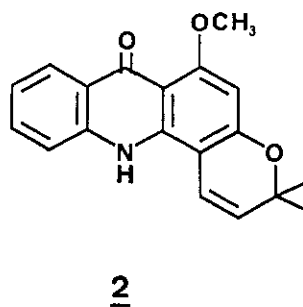
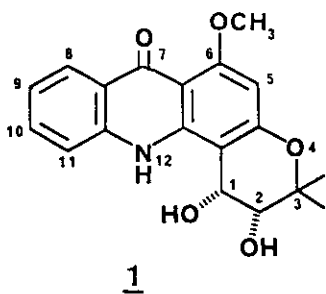


Table I : ^1H nmr spectra of acridones 1, 3, 4 and 6

H	<u>1</u> ^a	<u>4</u> ^a	<u>6</u> ^b	H	<u>3</u> ^b
H-1A	5.02 d:5	5.08 q:6, tr. to t:6 by D ₂ O	-	CHO-4	10.48 s
OH-1B	5.33 br.s.D ₂ O exch.	5.97 d:6, D ₂ O exch.	-		
H-2A	3.68 d:5	2.14 dd:14,6	2.83 s (2H)	-OCMe ₂ CHO	9.88 s
H-2B	-	2.04 dd:14,6			
OH-2B	3.40 br.s.D ₂ O exch.	-	-		
Me-3A	1.32 s	1.43 s	1.56	-OCMe ₂ CHO	1.68
Me-3B	1.38 s	1.34 s	s (6H)		s (6H)
H-5	6.11 s	6.11 s	6.16 s	H-2	5.89 s
OMe-6	3.78 s	3.77 s	4.06 s	OMe-1	3.98 s
H-8	8.09 dd:8,1.5	8.07 dd:8,1.5	8.43 dd:8,1.5	H-8	8.41 dd:8,1.5
H-9	7.17 td:8,1.5	7.17 td:8,1.5	7.30 td:8,1.5	H-7	7.33 td:8,1.5
H-10	7.62 td:8,1.5	7.61 td:8,1.5	7.64 td:8,1.5	H-6	7.66 td:8,1.5
H-11	7.61 dd:8,1.5	7.81 dd:8,1.5	7.37 dd:8,1.5	H-5	7.40 dd:8,1.5
NH-12	10.26 br.s.D ₂ O exch.	10.35 br.s.D ₂ O exch.	12.90 br.s.D ₂ O exch.	NH-10	12.95 br.s.D ₂ O exch.

a : in CD₃SOCD₃b : in CDCl₃

with the natural product.

All the novel acridone alkaloids isolated from the leaves of Sarcomelicope dogniensis result from an oxidation of the dimethylpyran ring of N-desmethyl-acronycine¹⁵⁻¹⁷. This latter compound and acronycine itself are the major alkaloids of the plant. From a chemotaxonomic point of view, these results are in full agreement with the recent botanical revision of Hartley¹, since all the Sarcomelicope species so far studied are characterized by the presence of acronycine and acronycine-derived alkaloids.

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3. The plant material has been collected on the Plateau de Dogny (New Caledonia) in November 1983. Herbarium samples (Pusset-Chauvière 705) are held in the herbaria of the Centre ORSTOM de Nouméa.
4. The semi-trivial nomenclature used in this paper is that generally used for acronycine derivatives, i.e., 6-hydroxy-3,12-dihydro-3,3,12-trimethyl-7H-pyrano[2,3-c]acridin-7-one is known as noracronycine, whereas 3,12-dihydro-3,3-dimethyl-6-methoxy-7H-pyrano[2,3-c]acridin-7-one is known as N-desmethyl-acronycine.
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