$[C_6H_5CH_2]^+$ (91); CIMS (*iso*-butane, probe) 200 eV, m/z (rel.
int.): 323 $[M+1]^+$ (39), 307 (100); (Found: C, 70.7; H, 5.6; N, 8.6.
Calc. for $C_{19}H_{18}O_3N_2$: C, 70.8; H, 5.6; N, 8.7 %); ^1H NMR
(99.60 MHz, CDCl$_3$, TMS as int. std): δ 3.73 (1H, s, OH), 3.92
(3H, s, OMe), 3.93 (2H, br s, CH$_2$), 4.20 (2H, br s, CH$_2$), 7.20–7.40
(10H, m, aromatic H); ^{13}C NMR (100.40 MHz, CDCl$_3$,TMS):
δ 30.39 (Tt), 34.01 (Tt), 61.73 (Q), 126.83 (2C, Dt), 127.64 (2C, Dt),
128.49 (2C, Dd), 129.10 (2C, Dd), 129.43 (St), 129.57 (2C, Dm),
135.68 (Sm), 136.47 (Sm), 140.60 (St), 144.17 (Sm), 158.13 (St).

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^{13}C NMR SPECTRA OF 4-KETO STEROIDAL ALKALOIDS

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Abstract—Natural abundance ^{13}C NMR spectra were recorded of four naturally occurring 4-keto steroidal alkaloids,
their acetylated derivatives, and of dihydrosolaphyllidine. The assignments were made with the help of APT spectra,
based on chemical shifts arguments, and by comparison with the values reported for other steroidal alkaloids.

INTRODUCTION

As part of our investigation of the Andean flora several 4-
keto steroidal alkaloids have been isolated [1–4]. To the
best of our knowledge the literature lacks information on
the ^{13}C NMR spectra of such compounds. This paper
reports the ^{13}C NMR chemical shift assignments of
solaphyllidine (1a), deacetylsolaphyllidine (1b), deacetox-
ysolaphyllidine (2a), solamaladine (3a), their acetylated
derivatives (1c, 2b, 3b, 4), and dihydrosolaphyllidine (5).

RESULTS AND DISCUSSION

The chemical shifts of the various carbon resonances
for compounds 1–5 are listed in Table 1. The ^{13}C NMR
resonances have been assigned on the basis of chemical
shift theory and comparison with the published assign-
ments of dihydro-25-isosolafloridine, and dihydrosola-
congestidine [5]. Discrimination among carbon types
was performed by direct comparison of Proton Noise
Decoupled and APT spectra [6].

In these types of compounds quaternary carbons (C-10
and C-13) are easily distinguished from methylenes by
their lower intensity in APT conditions. The resonance of
carbon C-13 is affected by substitution at C-16. The
presence of a 16 α-acetoxy group as in 1a and 5 produces
a paramagnetic shift of 1.2 ppm, while compounds with
no substituent at C-16 (2a, 2b, 3a, 3b, and 4) show the C-
13 signal at δ 42.5.

The comparison of the quaternary carbon signals in all
alkaloids containing the 3-hydroxy-4-keto moiety (1a, 2a,
and 3a) permitted the assignment of the signal at δ 43.1 to
C-10. In the case of 1b the small difference (0.8 ppm)
could be attributed to a solvent effect. Acetylation of the
3β-hydroxy group produces a small diamagnetic shift in
all cases (1c, 2b, 3b, and 4). The presence of the carbonyl
at C-4 is responsible for shifting the C-10 resonance
about 7 ppm downfield from its normal range [5]. When
the carbonyl is reduced, as in dihydrosolaphyllidine (5),
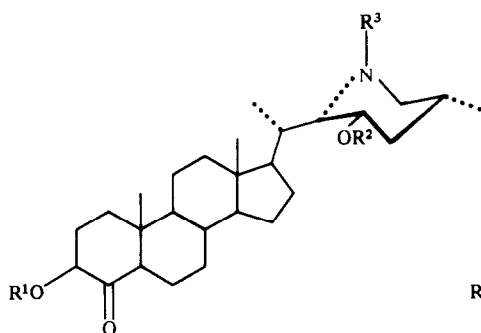C-10 appears at δ 35.5.

The most shielded methine is C-25 on the side chain.
The resonance of C-25 appears at δ 30–31 in all com-
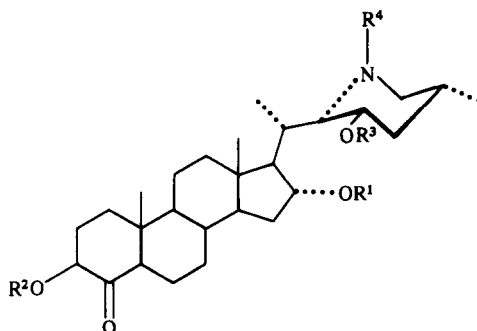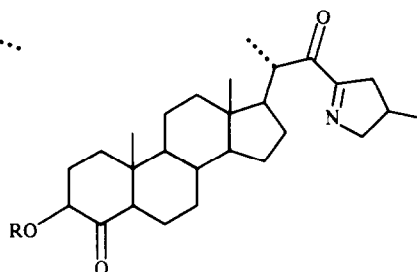
1a R¹ = Ac, R², R³, R⁴ = H
1b R¹, R², R³, R⁴ = H
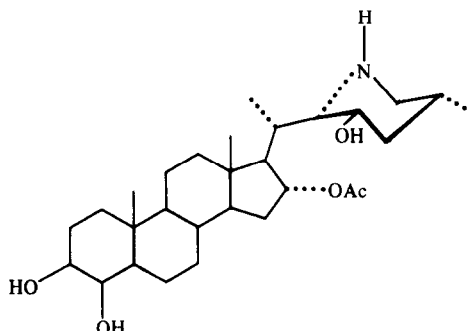1c R¹, R², R³, R⁴ = Ac

2a R¹, R², R³ = H
2b R¹, R², R³ = Ac

3a R = H
3b R = Ac
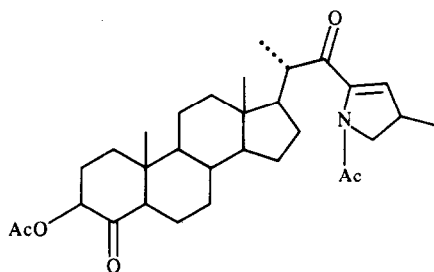
4

5

pounds, except in compound **4** where C-25 is next to a double bond. Since the C-27 methyl is equatorial in the investigated 4-keto-steroidal alkaloids [1] there is a good correlation with the sapogenins [7] which show the C-25 resonance at δ 30 in the (25R)-configuration but at δ 27 in the (25S)-epimers.

The methine carbon resonances are in line with the values reported in the literature for steroidal alkaloids. The C-9 signal shows very little variation (δ 53.6 to 54.3); on the other hand C-14 is affected by substitution at C-16 and shows a wider range (δ 51.7 to 53.5). The C-20 resonance appears around δ 35 with the exception of solamaladine and related alkaloids which have a carbonyl next to it. Acetylation helped in the assignment of

the C-17 and C-22 signals. As expected the presence of a ketone group at C-4 affects strongly the magnetic environment of C-5 shifting its resonance downfield by around 12 ppm.

In compounds **2a** and **3a** carbons C-2, C-11, C-12, C-15 and C-16 showed resonances very similar to those reported for dihydrosolacongestidine [5]. There is also a close correspondence for the methylene signals of carbons at the steroid nucleus between **1b** and dihydro-25-isosolafloridine B [5]. On the other hand C-6 in all 4-keto-steroidal alkaloids showed an upfield shift of 7 ppm which is to be expected considering the position of this carbon relative to the diamagnetic field induced by the carbonyl at C-4.

Table 1 ^{13}C NMR chemical shifts of compounds **1a**, **1b**, **1c**, **2a**, **2b**, **3a**, **3b**, **4** and **5**

C	1a	1b	1c	2a	2b	3a	3b	4	5
1	35.7	35.3	35.9	35.5	36.0	35.5	35.8	35.9	37.1
2	32.6	32.2	28.4	32.2	28.5	32.4	28.4	28.5	32.3
3	74.5	74.1	76.0	74.6	76.1	74.3	76.0	76.1	74.7
4	212.1	211.5	205.1	212.5	205.0	211.8	205.8	205.1	72.3
5	56.8	55.8	57.3	56.7	57.3	56.5	57.2	57.3	49.1
6	21.5	21.1	21.4	21.5	21.7	21.5	21.5	21.7	25.7*
7	30.2	30.0	30.1	30.1	30.1	30.1	30.1	30.2	25.8*
8	32.1	32.8	32.6	33.1	34.1	34.9	34.9	35.0	32.2
9	54.3	53.6	54.2	54.2	54.3	54.1	54.1	54.3	55.2
10	43.1	42.3	42.6	43.1	42.5	43.1	42.8	42.9	35.5
11	20.1	20.2	20.0	20.0	20.2	20.0	20.0	20.2	20.4
12	40.1	40.8	39.7	39.7	39.7	39.6	39.6	39.8	40.2
13	43.7	43.8	43.5	42.5	42.5	42.8	42.5	42.5	43.7
14	53.5	53.1	53.4	51.7	52.4	52.3	52.3	52.2	54.0
15	34.5	35.3	34.5	23.8	23.9	24.3	24.3	24.3	34.6
16	79.6	73.5	79.4	27.3	27.9	27.2	27.4	27.7	80.1
17	58.4	63.5	58.8	56.4	56.1	55.1	55.2	55.5	58.4
18	12.7	13.6	12.8	11.6	11.7	12.4	12.3	12.2	12.7
19	13.3	13.3	13.1	13.4	13.5	13.7	13.5	13.5	14.6
20	34.6	34.3	34.9	34.9	35.1	42.6	42.6	46.7	35.0
21	13.8	13.9	13.5	12.1	12.5	16.0	16.6	17.3	13.2
22	64.9	63.7	61.7	64.8	61.7	203.1	203.6	198.0	65.0
23	67.9	67.0	70.4	66.5	70.7	173.4	173.8	143.8	67.7
24	44.0	43.6	39.9	42.6	39.8	41.6	41.5	129.3	43.8
25	31.7	30.6	31.8	29.8	32.6	30.9	30.9	35.9	31.5
26	54.4	52.7	54.2	51.9	54.0	69.6	69.6	56.9	54.4
27	18.8	19.0	18.4	18.2	18.5	19.8	20.0	19.0	18.8
3 Ac			169.9*		169.9*		169.9*	169.8	
			21.0*		20.9*		20.6	20.5	
16Ac	170.5		170.2						170.9
	21.4		21.4						21.4
23Ac			169.8*		169.6*				
			20.5*		20.4*				
N–Ac			170.0*		169.9*			168.4	
			21.0*		20.9*			22.8	

* Can be exchanged.

Carbon C-1 appears at δ 35.3–35.7 but in dihydrosolaphyllidine (**5**), which has no carbonyl at C-4, the C-1 resonance is found at a normal value of δ 37.1. Acetylation of these compounds produced the expected diamagnetic shifts on the β-carbons, which were used diagnostically to assign C-2, C-15, and C-24.

The methyl carbon resonances were always found upfield and were readily discriminated from methines in APT spectra. Carbons C-18 and C-19 are usually the most shielded and their signals appear at δ 12–13. The C-21 resonance is affected by the nature of the side chain and substitution at C-16, it varies from δ 12.1 in deacetoxysolaphyllidine (**2a**) to 17.3 in O,N-diacetylsolamaladine (**4**). The C-27 signal appears between δ 18.2 and 20.0 depending on the structure of the side chain.

0.15 M; tube size, 5 mm. TMS was used as int. standard PND (proton noise decoupled) and APT (attached proton test) spectra were recorded for all compounds.

The pulse conditions for PND spectra were the following: pulse width, 4 sec; flip angle, 30°; adquisition time, 0.817 sec; spectral width, 5 kHz; data points, 8000. For APT spectra the following parameters were used: pulse width, 11 sec (90° pulse); adquisition time, 0.974 sec; spectral width, 4202 Hz; data points, 8000; time delay ($\tau = 1/J$), 7.2 msec; pulse delay, 1.1 sec.

The isolation of all compounds has been described elsewhere [1–4]. Alkaloids **1a**, **1b**, and **2a** were purified by prep. TLC on silica gel plates. Solamaladine (**3a**) and diacetylsolamaladine (**4**) were obtained pure by recrystallization from MeOH. The acetates **1c** and **2b** were purified by silica gel CC.

EXPERIMENTAL

^{13}C NMR spectra were recorded at 20.0 MHz Fourier mode. The spectra were determined in CDCl$_3$ except for **1b** (DMSO-d_6) and **5** (CDCl$_3$ + one drop of MeOH). The concn was *ca*

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SIMPLEXINE (14-HYDROXY-4-METHOXY-13,14-DIHYDRONORSECURININE): AN ALKALOID FROM *PHYLLANTHUS SIMPLEX*

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Abstract—From the whole plant of *Phyllanthus simplex* (Fam. Euphorbiaceae), two securinegia alkaloids, simplexine (1) and phyllanthine (2) have been isolated and their structures elucidated on the basis of spectroscopic data.

INTRODUCTION

Phyllanthus simplex's common Indian names are 'Bhuiaveli' in Marathi and 'Uchchiyusirika' in Telgu. Its fresh leaves are used as a wash for itch in children [1]. The plant has not been chemically investigated before. Our present investigation of the whole plant led to the isolation of a new alkaloid, the structure of which has been established as 1.

RESULTS AND DISCUSSION

The alkaloid 1 showed a UV absorption at 255 nm and IR absorptions at 3622 cm^{-1} (OH), 1800 cm^{-1} (five-membered ring lactone), 1117 cm^{-1} (–OMe) and 1773 cm^{-1} (C=O) and 1642 cm^{-1} (olefinic bond). Its mass spectrum showed a molecular ion peak at m/z 251 and a base peak at m/z 207. On the basis of the mass and ^{1}H NMR spectra of this alkaloid, the position of a –OMe group in the ring A at C-4 and the position of a hydroxyl group in the ring C at C-14 were established. The mass fragmentation at m/z 68 confirmed the presence of a five-membered ring in the alkaloid. The fragment at m/z 100 showed the –OMe group is present in the ring A and the fragment at m/z 56 established the isolation of –OMe at C-4. This is further confirmed by its ^{1}H NMR spectrum which showed a singlet at $\delta 3.22$ corresponding to 3 protons for –OMe. Further it shows a one-proton triplet at $\delta 5.67$ due to the olefinic proton at C-11–C-12 coupled with two allylic protons at C-13 suggesting that the hydroxyl group in the alkaloid is located at C-14. Further

a multiplet at $\delta 4.48$ was observed that corresponds to 1H, ($>$CHOH), and an exchangeable (in D$_2$O) proton at $\delta 2.48$ shows the presence of the additional oxygen as a secondary hydroxyl function in the alkaloid. The peak at m/z 207 was assigned to the ion formed by loss of CH$_2$=CHOH. The peak at m/z 44 indicated that the ion at 207 was not due to the loss of CO$_2$. Therefore, the position of the hydroxyl group could only be assigned at C-14–OH in the ring C of the alkaloid. From all these spectral data, the structure of a new alkaloid is established as simplexine (14-hydroxy-4-methoxy-13,14-dihydronorsecurinine) (1). Earlier, dihydronorsecurinine was isolated from *Securinegia virosa* [2].

Alkaloid 2 showed a UV absorption at 256 nm, characteristic of the securinine type skeleton and its IR spectrum showed absorption at 1775 cm^{-1} (six-membered ring lactone), 1118 cm^{-1} (–OMe) and 1642 cm^{-1} (C=O) [3]. Its ^{1}H NMR and mass spectra were also found to be the same as earlier reported for phyllanthine [4]. From the

1

2