Studies on Indian Medicinal Plants. Part 77.[1] Structure and Stereochemistry of Some New Steroidal Alkaloids from *Solanum pseudocapsicum* and *Solanum giganteum* by Nuclear Magnetic Resonance Spectroscopy

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Three new stereoisomeric steroidal alkaloids, *viz.* solacapine (6), episolacapine (11), and isosolacapine (13), along with another hitherto unreported base, *O*-methylsolanocapsine (3), have been isolated from the arboreal part of *Solanum pseudocapsicum* Linn. They have been characterised as (20*S*, 22*R*, 23*S*, 25*R*)-, (20*S*, 22*R*, 23*R*, 25*R*)-, and (20*S*, 22*S*, 23*S*, 25*R*)-3β-amino-16α,23-dihydroxy-22,26-epimino-5α-cholestanes, respectively, primarily based on ^{1}H and ^{13}C n.m.r. spectra. The structures of (3), (6), and (11) could be confirmed by correlation with solanocapsine (1). Isosolacapine (13) turned out to be the first 22,26-epiminocholestane derivative encountered in nature with 22βN stereochemistry. A diagnostic down-field shift of the C-22 resonance frequency in the ^{13}C n.m.r. spectra of 22βN-22,26-epiminocholestanes by *ca.* 3 p.p.m. relative to those of the corresponding 22αN-isomers has been observed. The C-25 stereochemistry of solanogantamine (28) and isosolanogantamine (29), the stereoisomeric 3-amino solanidanes isolated from *Solanum gigantem* Jacq., has also been established.

The isolation and characterisation of two steroidal alkaloids, *viz.* solanocapsine (1) [2-6] and solacasine (2) [7], responsible for the antimicrobial activity [7,8] of *Solanum pseudocapsicum*, have been reported. A reinvestigation of the plant, undertaken in view of its antihypertensive properties,[9] led to our isolation [10] of a mixture of stereoisomeric 3-amino-16,23-dihydroxy-22,26-epiminocholestanes, intimately associated with the major alkaloid (1). The mixture has now been resolved into three new bases which we have designated solacapine (6), m.p. 286—288 °C, $[\alpha]_D$ +47.1°; episolacapine (11), m.p. 256—258 °C, $[\alpha]_D$ −41.5°; and isosolacapine (13), m.p. 238—240 °C, $[\alpha]_D$ −12.3°. Yet another new alkaloid, m.p. 183—185 °C, $[\alpha]_D$ +44.4°, characterised as *O*-methylsolanocapsine (3), has also been obtained from the same source.

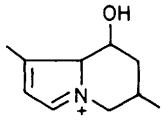
The present paper describes the structure elucidation of all the above mentioned new alkaloids as well as the determination of the C-25 stereochemistry of solanogantamine (28) and isosolanogantamine (29), the alkaloids of *S. giganteum*,[11] mainly on the basis of ^{1}H and ^{13}C n.m.r. spectral analyses.

Results and Discussion

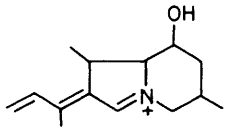
Solacapine (6), *Episolacapine* (11), *and Isosolacapine* (13).—All of them have the same molecular formula, $C_{27}H_{48}N_2O_2$ (M^+ at *m/z* 432), and exhibit almost superimposable mass spectra with slight variations in the intensities of the peaks. The alkaloids must, therefore, be stereoisomers.

The i.r. spectra of the alkaloids showed a broad absorption band in the region 3 400—3 100 cm^{-1} for NH/OH group(s). On treatment with HCHO–HCO_2H at 100 °C for 1 h, compound (13) yielded its *N,N,N'*-trimethyl derivative (14) while both (6) and (11) afforded their respective 3-*N,N*-dimethyl derivatives (7) and (12). Again, (7) could be converted into the *N,N,N'*-trimethyl derivative (8) on prolonged heating (10 h) with the same reagents. Both the trimethyl derivatives (8) and (14) on acetylation at room temperature led to the corresponding *O,O'*-diacetates (9) and (15). The structures of all the derivatives were evident from their spectral data. All the foregoing evidence demonstrated that each of the bases contains one NH_2, one NH, and two alcoholic OH functions, and that the secondary NH group of both solacapine (6) and episolacapine (11) is hindered.

That all the three alkaloids are 22,26-epiminochloestanes with an OH group in the piperidine moiety was evident [10,12] from the intense peak at *m/z* 114 (*m/z* 128 in the *N,N,N'*-trimethyl derivatives) in their mass spectra. The presence of the 3-amino group was inferred from the diagnostic [12] peaks at *m/z* 56 and 82 (*m/z* 84 and 110 in the *N,N,N'*-trimethyl and 3-*N,N*-dimethyl derivatives). On the other hand, the spectrum of isosolacapine (13) exhibited ion peaks at *m/z* 166 (26%,



a *m/z* 166

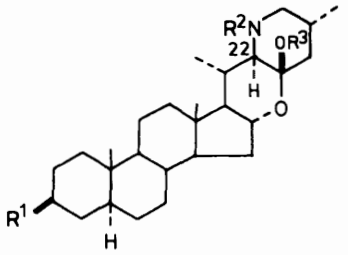


b *m/z* 220

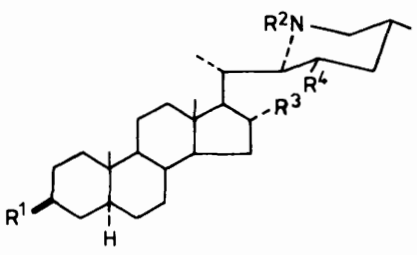
species *a*) and 220 (6%, species *b*), normally characteristic [11-13] of the solanidane skeleton with a hydroxy group in ring F. The formation of such a skeleton, by elimination of the elements of water from the molecular ion, requires the involvement of the piperidine NH and an OH group at C-16. This contention was further strengthened by the presence of the same set of peaks in the spectra of (6), (11), and their 3-*N,N*-dimethyl derivatives (7) and (12), although with much reduced intensities and their complete absence in the spectra of the *N,N,N'*-trimethyl derivatives (8) and (14), as would be expected. The observed variation in the intensities of these two peaks in the three alkaloids is presumably due to stereochemical difference at C-16 and/or C-22.

Thus, the three bases could be inferred to be 3-amino-16-hydroxy-22,26-epiminocholestanes with a hydroxy group in ring F. Their complete structures could then be deduced from n.m.r. analyses. All the ^{1}H and ^{13}C n.m.r. data discussed in the paper are given in Tables 1 and 2, respectively.

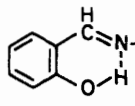
Stereochemistry at C-3 and C-5. That at least the two



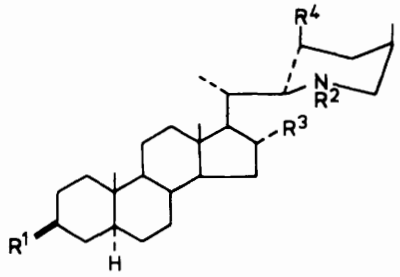
(1) $R^1 = NH_2$, $R^2 = R^3 = H$
(2) $R^1 = NH_2$, $R^3 = Me$, $\Delta^{22(N)}$
(3) $R^1 = NH_2$, $R^2 = H$, $R^3 = Me$
(4) $R^1 = NMe_2$, $R^2 = Me$, $R^3 = H$
(5) $R^1 = NMe_2$, $R^2 = R^3 = Me$



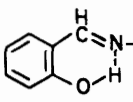
(6) $R^1 = NH_2$, $R^2 = H$, $R^3 = R^4 = OH$
(7) $R^1 = NMe_2$, $R^2 = H$, $R^3 = R^4 = OH$
(8) $R^1 = NMe_2$, $R^2 = Me$, $R^3 = R^4 = OH$
(9) $R^1 = NMe_2$, $R^2 = Me$, $R^3 = R^4 = OAc$



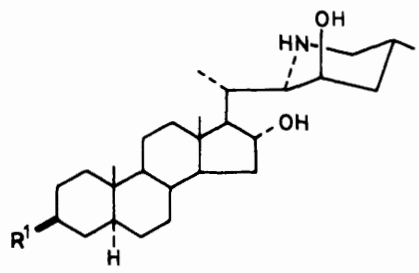
(10) R^1 = above, $R^2 = H$, $R^3 = R^4 = OH$



(13) $R^1 = NH_2$, $R^2 = H$, $R^3 = R^4 = OH$
(14) $R^1 = NMe_2$, $R^2 = Me$, $R^3 = R^4 = OH$
(15) $R^1 = NMe_2$, $R^2 = Me$, $R^3 = R^4 = OAc$



(16) R^1 = above, $R^2 = H$, $R^3 = R^4 = OH$

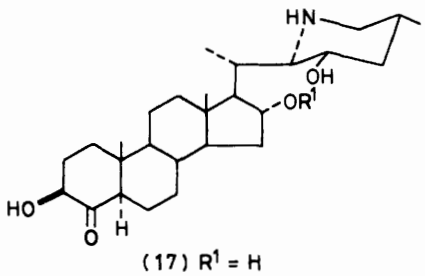


(11) $R^1 = NH_2$
(12) $R^1 = NMe_2$

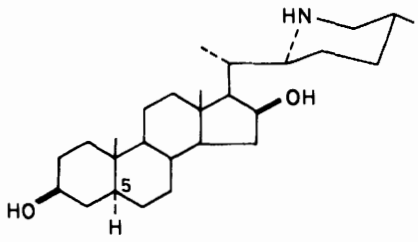
alkaloids (6) and (13) possess 3β-amino-5α-stereochemistry was evident from the c.d. spectra of their 3-*N*-salicylidene derivatives (10) and (16) which showed characteristic[14] positive Cotton effects at *ca.* 245 and 310 nm. The stereochemistry at C-3 and C-5 of all the alkaloids (6), (11), and (13) could also be deduced from the ^{13}C n.m.r. spectra of the *N*-methyl derivatives (7), (12), and (14) which exhibited chemical shifts of A- and B-ring carbons almost identical with those of *N,N,N'*-trimethylsolanocapsine (4).

Stereochemistry at C-16. The alkaloids (6), (11), and (13) and their derivatives (7), (12), and (16) showed chemical shifts of 13-Me protons (δ_H 0.67—0.76 in $CDCl_3$ and 0.71—0.76 in [$^2H_5$]pyridine) very close to those of deacetylsolaphyllidine (17).[15] It could, therefore, be inferred that as in (17), the alkaloids (6), (11), and (13) also have their 16-OH group α-orientated since a 16β-OH group would be expected to deshield significantly the 13-Me proton signal [*cf.* δ_H 0.88 in $CDCl_3$ and δ_H 1.09 in [$^2H_5$]pyridine in the spectra of tetrahydrosolasodine A (19)]. This conclusion was further borne out by the down-field ^{13}C chemical shifts of C-16 (δ_C 74.0—77.0 p.p.m.) and C-17 (δ_C 63.0—67.0 p.p.m.) of (7), (12), and (16) compared with those (δ_C 71.2 and 59.8 p.p.m. respectively) of dihydrosolasodine A (20).[16]

Location and orientation of the hydroxy group of the piperidine moiety in solacapine (6) *and episolacapine* (11). In the ^1H n.m.r. spectra of (6) and its *N,N*-dimethyl derivative (7) in $CDCl_3$, the signal for the C-23 carbinyl proton of the piper-



(17) $R^1 = H$
(18) $R^1 = Ac$



(19)
(20) Δ^5

Table 1. ^{1}H N.m.r. data [a]

Compd.	Solvent [b]	13-Me	10-Me	20-Me	25-Me	16-H	23-H	22-H	26-H$_{eq}$	Others
(1)	A	0.77	0.73	0.93d (6)	0.83d (6)	4.45m			3.02br d (9)	2.65m
	B	0.73	0.73	1.18d (6)	0.77d (6)	4.80m			3.10br d (9)	2.70m
(3)	A	0.77	0.72	0.96d (6)	0.80d (6)	4.03m			3.00dd (12, 4)	3.11 (OMe), 2.60m
	B	0.70	0.73	1.12d (6)	0.72d (6)	4.17m			3.00dd (12, 4)	3.17 (OMe), 2.63m
(4)	A	0.77	0.77	0.97d (6)	0.81d (6)	4.44m			2.87br d (10)	2.42 (N′Me), 2.27 (NMe$_2$)
	B	0.75	0.78	1.13d (6)	0.76d (6)	4.83m			2.97br d (10)	2.70 (N′Me), 2.27 (NMe$_2$)
(5)	A	0.75	0.75	0.93d (6)	0.80d (6)	4.07m			2.86br d (12)	3.11 (OMe), 2.37 (N′Me), 2.25 (NMe$_2$)
(6)	A	0.70	0.78	0.92d (7)	0.85d (7)	4.17m	3.50ddd (10, 10, 4)	2.57dd (10, 4)	2.89br d (12)	
	B	0.71	0.71	1.15d (7)	0.72d (7)	4.40m	3.82ddd (10, 10, 4)	2.98dd (10, 4)		
(7)	A	0.70	0.75	0.92d (7)	0.85d (7)	4.18m	3.49ddd (10, 10, 4)	2.57dd (10, 4)	2.88br d (12)	2.26 (NMe$_2$),
(8)	A	0.72	0.75	1.15d (7)	0.83d (7)	4.04m	3.90m		2.66br d (12)	2.42 (N′Me), 2.26 (NMe$_2$)
(9)	A	0.68	0.76	1.03d (6)	0.83d (6)	4.85m	4.60m		2.70br d (10)	2.30 (N′Me), 2.26 (NMe$_2$), 2.02 and 2.06 (OAc)
(11)	B	0.74	0.70	1.41d (7)	0.72d (7)	4.43m	4.14m ($w_{1/2}$ 8 Hz)	3.00m ($w_{1/2}$ 6 Hz)		
(12)	A	0.67	0.75	1.12d (7)	0.82d (7)	4.04m	3.96m ($w_{1/2}$ 6—9 Hz)	2.68m ($w_{1/2}$ 8 Hz)	3.04br d (12)	2.26 (NMe$_2$)
(13)	A	0.75	0.75	1.02d (7)	1.20d (7)	3.88m	4.06m ($w_{1/2}$ 7 Hz)	2.84m ($w_{1/2}$ 6 Hz)	2.22br d (10)	
(14)	A	0.76	0.71	1.09d (7)	1.17d (7)	4.20m	4.03m			2.38 (N′Me), 2.27 (NMe$_2$)
(15)	A	0.76	0.72	1.00d (7)	1.17d (7)	4.86m	5.40m ($w_{1/2}$ 8 Hz)		2.72br d (12)	2.18 (N′Me), 2.32 (NMe$_2$), 2.02 (OAc)
(16)	A	0.76	0.84	1.03d (7)	1.20d (7)	3.90m	4.06m ($w_{1/2}$ 2 Hz)	2.84m ($w_{1/2}$ 6 Hz)	2.22br d (10)	8.36 (=CH−), 6.78—7.40 (Ar−H)
	B	0.76	0.76	1.18d (7)	1.34d (7)	4.20m	4.24m	2.90m ($w_{1/2}$ 6 Hz)	2.40br d (10)	8.48 (=CH−), 6.85—7.50 (Ar−H)
(17) [c]	A	0.69	0.69	0.91	0.82	4.17	3.48			
(19)	A	0.88	0.80	1.03d (7)	0.82d (7)	4.40m			2.98br d (12)	3.60m (3-H)
	B	1.09	0.83	1.08d (7)	0.72d (7)	4.60m			2.98br d (12)	3.84m (3-H)
(22) [d]	A	0.68	0.79	1.03d (7)	0.96d (6)	4.10m			2.73d	3.59m (3-H)
(28)	A	0.85	0.80	0.94d (6)	1.17d (6)		3.75m ($w_{1/2}$ 6 Hz)		2.70br d (10)	2.87m
	B	0.97	0.78	1.00d (6)	1.43d (6)		3.98m ($w_{1/2}$ 6 Hz)		2.77br d (10)	2.53m, 3.10m
(29)	A	0.85	0.78	0.93d (6)	1.17d (6)		3.75m ($w_{1/2}$ 6 Hz)		2.70br d (10)	2.55m, 3.22m
	B	1.02	0.74	0.98d (6)	1.43d (6)		3.97m ($w_{1/2}$ 6 Hz)		2.76br d (10)	2.50m, 3.38m
(30)	A	0.83	0.83	0.92d (7)	0.82d (7)				2.86br d (9)	3.70m (3-H), 2.70m
	B	0.93	0.83	0.96d (7)	0.83d (7)				2.90br d (9)	3.83m (3-H), 2.60m

[a] Chemical shifts are expressed on the δ scale from $SiMe_4$. Figures in parentheses are coupling constants in Hz. [b] A = $CDCl_3$, B = [$^2H_5$]pyridine. [c] Ref. 15. [d] Ref. 19.

idine moiety was observed at δ_H 3.50 as a doublet of a double doublet with J 10, 10, and 4 Hz. The corresponding signal of (11) in [$^2H_5$]pyridine and its *N*,*N*-dimethyl derivative (12) in $CDCl_3$ appeared at δ_H 4.14 and 3.96, respectively, as unresolved multiplets having $w_{\frac{1}{2}}$ 6—9 Hz. The secondary OH group in the piperidine moiety must, therefore, be equatorial in (6) and axial in (11). That it is located at C-23 in both the alkaloids was evident from the multiplicity of the 22-H signal

Table 2. ^{13}C N.m.r. data [a]

Carbon	(1) [b]	(3)	(4)	(6) [c]	(7)	(8) [c,d]	(12)	(13)	(14)	(16)	(16) [e]	(20) [f]	(21) [f]	(22) [f]	(28)	(29)	(30) [g]
1	37.2	37.1	37.4	36.8	37.6	37.2	37.6	37.6	37.5	37.3	38.3	37.3	37.0	37.0	36.9	31.4	37.1
2	31.6	31.5	24.4	30.8	24.6	23.8	24.7	31.6	24.6	30.1	30.3	31.6	31.4	31.5	31.3	29.0	31.6
3	50.7	50.7	63.9	50.0	63.2	63.7	64.0	50.8	63.3	68.3	68.3	71.7	71.2	71.2	50.9	45.8	71.3
4	38.9	38.8	30.9	37.6	30.8	30.3	31.0	37.9	31.0	36.7	36.9	42.3	38.3	38.3	39.2	36.2	38.3
5	45.4	45.3	45.6	44.8	45.5	45.3	45.5	45.2	45.5	45.0	45.0	141.0	44.9	44.9	45.6	39.2	45.0
6	28.4	28.3	28.8	27.9	28.9	28.4	28.9	28.5	28.9	28.7	28.8	121.6	28.7	28.7	28.6	28.7	28.8
7	32.1	32.2	31.8	31.2	31.8	31.4	31.8	32.2	31.9	31.9	32.2	31.9	31.8	31.9	32.1	32.2	32.3
8	34.7	34.6	34.8	34.5	35.2	34.8	35.2	34.9	35.0	35.2	35.3	31.4	35.2	35.3	35.2	35.4	35.4
9	54.6	54.5	54.8	53.7	54.3	54.0	54.1	53.9	54.1	54.2	54.3	50.2	54.3	54.3	54.5	54.6	54.6
10	35.4	35.3	35.7	34.8	35.6	35.2	35.6	35.2	35.6	35.5	35.5	36.5	35.5	35.5	35.5	36.4	35.6
11	20.2	20.1	20.3	20.2	20.8	20.4	20.6	20.7	20.8	20.9	21.1	20.9	21.1	21.0	20.8	20.5	21.1
12	38.9	39.0	39.2	39.6	40.2	39.9	39.6	39.0	40.2	38.1	38.3	40.2	40.4	40.2	39.5	39.7	40.2
13	41.5	41.5	41.9	43.5	44.2	44.2	44.5	45.7	44.9	46.0	46.0	42.7	45.2	44.6	41.3	41.4	40.6
14	54.6	54.5	54.8	53.1	53.6	53.3	53.5	53.5	53.3	53.8	54.1	54.4	54.6	53.7	57.3	57.5	57.4
15	28.2	27.9	28.3	34.3	34.8	34.2	34.2	34.3	33.7	34.6	35.5	35.7	35.4	34.7	32.4	32.2	33.5
16	73.8	73.5	73.7	73.7	74.2	75.0	74.9	76.5	76.1	76.9	76.7	71.2	75.2	75.4	69.3	69.5	69.0
17	60.6	60.9	61.9	63.0	64.0	62.9	63.3	66.8	66.2	67.0	67.3	59.8	64.6	63.0	62.1	62.2	63.3
18	13.5	13.3	13.6	12.6	13.7	13.0	13.4	13.1	13.5	13.4	13.6	13.5	13.5	13.8	16.6	16.7	17.1
19	12.1	12.0	12.2	11.3	12.7	11.6	12.2	12.1	12.3	12.4	12.4	19.4	12.3	12.3	12.2	11.3	12.4
20	32.8	32.6	23.6	31.5	33.2	25.2	37.6	37.3	37.0	37.0	37.1	35.9	39.8	38.3	30.4	30.6	36.7
21	15.0	15.1	15.3	13.2	14.3	15.0	17.8	15.9	17.8	16.3	16.6	19.2	19.6	15.9	18.6	18.7	18.3
22	68.4	68.3	69.5	62.7	64.2		63.3	66.2	69.1	66.4	66.7	62.8	64.6	61.4	78.8	78.9	74.7
23	95.7	97.9	97.2	67.0	68.3	67.8	67.2	64.1	64.0	64.9	64.5	27.4	31.8	22.4	66.6	66.8	29.3
24	45.9	46.0	47.5	42.1	43.2	43.7	42.7	40.3	42.8	40.6	40.9	33.7	34.3	30.4	37.1	37.1	31.1
25	30.1	30.3	30.9	30.0	30.5	32.4	25.4	25.4	27.9	25.5	26.5	31.5	31.4	26.9	26.8	26.9	31.3
26	54.6	54.5	62.5	51.6	52.0	62.9	54.1	51.3	60.1	51.4	52.1	54.5	53.5	51.6	58.5	58.6	60.2
27	18.6	18.4	18.5	17.8	18.7	18.0	19.0	20.0	20.8	20.2	20.5	19.5	19.4	16.6	22.0	22.2	19.5
OMe		54.5															
NMe_2			41.6		41.7	40.7	41.8		41.8								
N'Me			35.9			38.7			37.0								

[a] Unless otherwise stated, the spectra were recorded in $CDCl_3$ and the chemical shifts expressed on the δ scale from $SiMe_4$. [b] Based on T_1 measurement and multiplicities in the SFORD spectra, the recently reported [16] assignments for C-15 and C-25 have been reversed. [c] Spectra recorded in $CDCl_3$–CD_3OD (3 : 1). [d] Spectrum recorded at 60 °C. [e] Spectrum recorded in [$^2H_5$]pyridine. [f] Data incorporated from ref. 16. [g] Data incorporated from ref. 23.

which appeared as a double doublet with J 10 and 4 Hz in (6) and (7) and as unresolved multiplet with $w_{\frac{1}{2}}$ 6—8 Hz in (11) and (12).

Complete structure of solacapine (6) *and episolacapine* (11). The foregoing evidence, therefore, settled the stereochemistry of (6) and (11) at all the centres except C-22 and C-25; these could, however, be established by their correlation with solanocapsine (1). Thus, sodium borohydride reduction of the masked carbonyl group of (1) yielded solacapine (6) as the major and episolacapine (11) as the minor product.

The structures of solacapine (6) and episolacapine (11) could, therefore, be deduced to be (20*S*, 22*R*, 23*S*, 25*R*)- and (20*S*, 22*R*, 23*R*, 25*R*)-3β-amino-16α,23-dihydroxy-22,26-epimino-5α-cholestane, respectively.

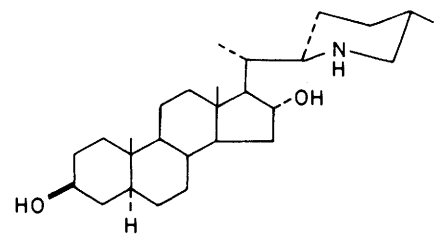
Location and orientation of the hydroxy group of the piperidine moiety in isosolacapine (13). That the hydroxy group of the piperidine moiety in (13) is axially orientated was evident from the nature of the one-proton signal at δ_H 4.06 (in $CDCl_3$) which appeared as an unresolved multiplet having $w_{\frac{1}{2}}$ 7 Hz in the ^1H n.m.r. spectra of both (13) and its 3-*N*-salicylidene derivative (16). Of the two possible locations of the hydroxy group, *viz.* C-23 and C-24, the latter position could be ruled out from the following considerations. The ^{13}C n.m.r. spectrum of (13) exhibited a C-25 signal at δ_C 25.4 p.p.m. which is at a higher field than those reported [16] for compounds devoid of any hydroxy substitution in the piperidine moiety. Thus, both dihydrosolasodine A (20) and dihydro-25-isosolafloridine A (21) with an equatorial 25-Me showed the signal at δ_C *ca.* 31.5 p.p.m. while in dihydro-25-isosolafloridine B (22), having an axial methyl, C-25 resonated at δ_C 26.9 p.p.m. Since introduction of an axial hydroxy group at C-24 would be expected to further deshield the C-25 signal the hydroxy group in isosolacapine (13) must be located at C-23.

Stereochemistry of isosolacapine (13) *at* C-22 *and* C-25. With an axial hydroxy group at C-23, isosolacapine may then be represented by any of the three possible stereoisomeric structures (13), (24), and (25), the fourth one (11) being already assigned to episolacapine.*

Now, a comparison of the ^1H chemical shifts of the 25-Me protons of solacapine (6), episolacapine (11) and its *N*,*N*-dimethyl derivative (12), and tetrahydrosolasodine A (19) in $CDCl_3$ and [$^2H_5$]pyridine revealed that when the 25-Me group is equatorial, the presence or orientation of the OH group at C-23 has no effect either on its resonance frequency (δ_H 0.82—0.85 in $CDCl_3$ and 0.72 in [$^2H_5$]pyridine) or the pyridine-induced up-field shift thereof. On the other hand, in the case of isosolacapine (13) and its 3-*N*-salicylidene derivative (16), the 25-Me signal was not only deshielded (δ_H 1.20 in $CDCl_3$) but also it suffered significant (0.14 p.p.m.) pyridine-induced down-field shift. This could be explained only by assuming a *syn*-1,3-diaxial relationship between the 23-OH and 25-Me groups. This conclusion received additional support from the up-field shift of the C-24 and C-26 signals by *ca.* 2.5 p.p.m. as well as the down-field displacement of the C-27 signal by 1 p.p.m. (δ effect) in the ^{13}C n.m.r. spectrum of (13) relative to (12). The structure (25) for isosolacapine could thus be eliminated.

Though it is difficult to distinguish between the other two

* Structures with the bulky steroid moiety in the axial configuration need not be considered because of their high conformational instability.



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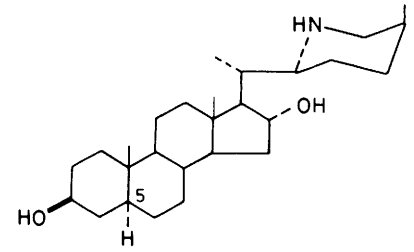

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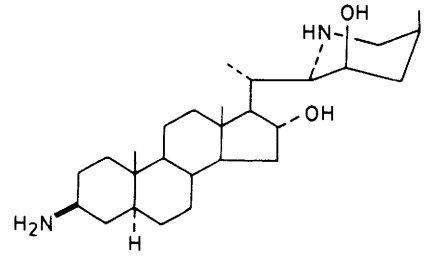
(23) Δ^5



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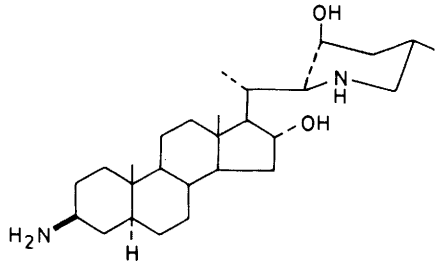

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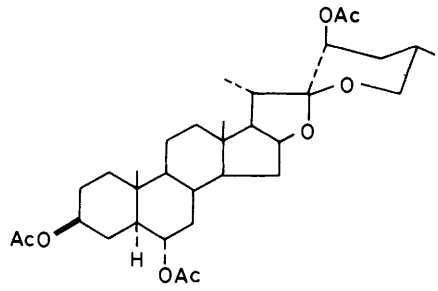

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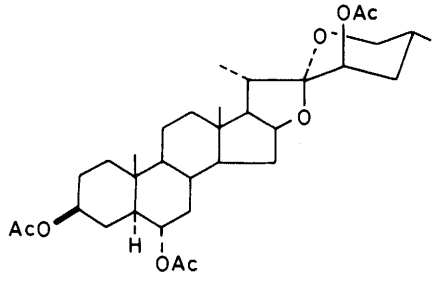


(27)

possibilities, isosolacapine could reasonably be assigned the structure (13) having 22βN (22*S*) stereochemistry from the following considerations. (i) A comparison of the ^{13}C n.m.r. spectrum of isosolacapine (13) with that of *N,N*-dimethylepisolacapine (12) showed that despite the same stereochemistry at both C-16 and C-23 (axial OH), the signals for C-17 and C-22 were deshielded by 3.5 and 2.9 p.p.m. respectively in (13). Since similar down-field shifts were observed [16] in dihydro-25-isosolafloridine A (21) having 22βN stereochemistry, compared with its 22αN-isomer (22), it could be presumed that isosolacapine also has 22βN stereochemistry. Incidentally, deshielding of the C-22 signal by 3.3 p.p.m. was also noted earlier [17] for the 22βO-spirostane derivative hispigenin acetate (26) *vs.* its 22αO-isomer, solaspigenin acetate (27). The deshielding of C-22 by *ca.* 3 p.p.m. therefore appears to distinguish the 22βN-epiminocholestanes and 22βO-spirostanes from their 22αN or 22αO epimers. (ii) The relatively slow rate of methylation of the piperidine NH (*vide supra*) of (6) and (11) could not have been dependent upon the orientation of the OH group at C-23 or C-16 since (6) and (11) are 23-epimers and all three alkaloids (6), (11), and (13) possess the same 16α-OH group. The only other factor responsible for this could be the involvement of the nitrogen lone pair in strong intramolecular hydrogen bonding with 16-OH. Molecular models indeed showed that in their preferred conformation (*vide infra*), the 16α-OH hydrogen atom of (6) and (11) can come close to the equatorially orientated nitrogen lone pair to facilitate intramolecular hydrogen bonding which is not feasible in the 22βN-compounds. Hydrogen bonding between the piperidine NH and 16-OH groups has recently been proposed [18] for deacetylmuldamine (23).

Based on the above observations, isosolacapine could be represented by (20*S*, 22*S*, 23*S*, 25*R*)-3β-amino-16α,23-dihydroxy-22,26-epimino-5α-cholestane (13). Thus, isosolacapine represents the first member of the naturally occurring 22,26-epiminocholestanes with 22βN (22*S*) stereochemistry.

Orientation of the piperidine ring in the alkaloids. Comparison of the ^{13}C chemical shifts of C-20 and C-21 of *N,N*-dimethylsolacapine (7) and *N,N*-dimethylepisolacapine (12) with those of dihydro-25-isosolafloridine B (22) revealed that the equatorial 23-OH group of (7) exerted a γ_g effect on C-20 by *ca.* 5 p.p.m. On the other hand, the axial OH group of (12) produced a deshielding δ effect on C-21 by *ca.* 2.0 p.p.m. through a *syn*-1,3-diaxial-type interaction. The presence of such an interaction was also supported by the down-field shift of the resonance frequency of the 20-Me protons {δ_H 1.12 in (12) *vs.* δ_H 1.03 in (22) [19] in $CDCl_3$ and δ_H 1.41 in (11) in [$^2H_5$]pyridine}. From these observations it could be concluded that, in the preferred conformation, the plane of the piperidine ring of solacapine (6) and episolacapine (11) is perpendicular to that of the androstane moiety as in solaphyllidine (18).[15] No definite conclusion could, however, be drawn about the orientation of the piperidine ring in isosolacapine (13) from the available data.

O-*Methylsolanocapsine* (3).—The mass spectrum of *O*-methylsolanocapsine (3), $C_{28}H_{48}N_2O_2$ (M^+ at *m/z* 444), showed that the principal peaks differ from those of solanocapsine (1) by an additional 14 mass units. On methylation

with HCHO–HCO_2H, it formed *N,N,N′,O*-tetramethylsolanocapsine (5) and *N,N,N′*-trimethylsolanocapsine (4).

The ^1H n.m.r. spectrum of (3) showed, *inter alia*, a three-proton singlet at δ_H 3.11, assignable to an OCH_3 group. That it is the *O*-methyl derivative of (1) became apparent from its ^{13}C n.m.r. spectrum which exhibited very close chemical shifts for all the carbons to those of (1) except C-23 which was deshielded by 2.2 p.p.m. The structure was finally confirmed by its direct comparison with the methyl ether prepared from (1).

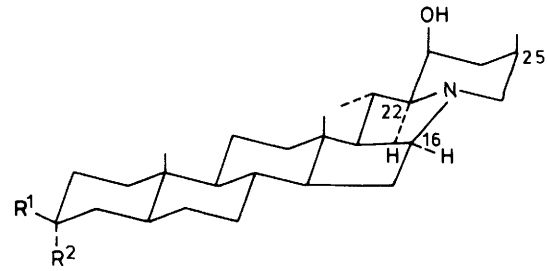
The effect of methylation of the piperidine NH of solanocapsine on the ^{13}C chemical shifts deserves special mention. Thus, the N′-Me group of (4) exerted a strong γ_g effect on C-20 by 9.2 p.p.m., indicating its axial orientation. This was also corroborated by the ^{13}C chemical shift at δ_C 35.9 p.p.m. and pyridine-induced down-field shift (by 0.28 p.p.m.) of the ^1H signal of the N′-Me group. The expected γ_g effect of such an N′-Me group on C-25 was, however, not observed. Moreover, the unusually weak β effect on C-22 (1.1 p.p.m.) as well as deshielding of C-17, C-23, and C-24 by 1.5 p.p.m. were contrary to expectation. Nevertheless, these observations may be explained by assuming geometrical deformation [17,20] of ring F induced by outward bending of the N′-Me and 23-OH groups to relieve partially the steric strain arising out of the *syn*-1,3-diaxial interaction between them.

Incidentally, the signal for the 20-Me protons of solanocapsine (1) and its *O*-methyl- (3) and *N,N,N′*-trimethyl- (4) derivatives experienced significant (0.16—0.25 p.p.m.) pyridine-induced down-field shifts. The 16β-H signal of (3) also suffered a similar unexpected shift of 0.14 p.p.m. The reason for such down-field shifts is not readily understood. However, many spirostanes without any OH function in the C–D–E–F ring system are also reported [21] to exhibit pyridine-induced deshielding of their 20-Me proton signals.

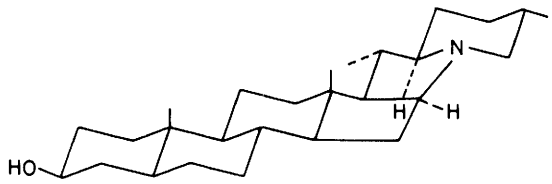
Stereochemistry of Solanogantamine (28) *and Isosolanogantamine* (29) *at* C-25.—It has already been shown [11] that compounds (28) and (29) are C-3 epimers with an axial hydroxy group at C-23 in a 16αH,22αH,5α-solanidane skeleton. Both of them exhibited ^1H n.m.r. signals at δ_H 1.17 and 0.93 in $CDCl_3$ for two secondary methyls (20-Me and 25-Me) but precise assignments were not possible due to the non-availability of the chemical-shift data of these two methyl protons for such solanidanes. We therefore examined the ^1H n.m.r. spectrum of demissidine (30) which, though devoid of the 23-OH group, possesses the same stereochemistry at all the ring junctures as in the two epimers under discussion.

The spectrum of (30) in $CDCl_3$ showed three-proton doublets at δ_H 0.92 and 0.82 assigned, respectively, to 20-Me and 25-Me protons in analogy with spirostane sapogenins [21,22] and other *Solanum* alkaloids [15] of known stereochemistry, along with those already discussed in this paper. Therefore, the signal at δ_H 0.93 could be ascribed to 20-Me in (28) and (29) since the introduction of an axial OH group at C-23 of demissidine is not expected to affect its chemical shift. The other signal, at δ_H 1.17, then (necessarily) had to be assigned to the 25-Me protons. The down-field shift of this signal by 0.35 p.p.m. in relation to that in (30) indicated that the 25-Me group must be axial in both (28) and (29). This contention was further supported by the significant pyridine-induced down-field shift of the same methyl proton signal by 0.26 p.p.m., in agreement with its *syn*-1,3-diaxial relationship with the 23-OH group.

^{13}C N.m.r. data also independently corroborated the assigned structure and stereochemistry. Thus, the close correspondence of the chemical shifts of all the carbons except those in ring A supported their C-3 epimeric nature. Again,



(28) $R^1 = NH_2$, $R^2 = H$
(29) $R^1 = H$, $R^2 = NH_2$



(30)

the shielding of the α-carbon (C-3) and γ-carbons (C-1 and C-5) by 5—6 p.p.m. and the β-carbons (C-2 and C-4) by 2—3 p.p.m. in (29) with respect to those of (28) was in excellent accord with the proposed [11] axial and equatorial orientations of the 3-NH_2 groups in (29) and (28), respectively. The displacement of the signals of E- and F-ring carbons in relation to those of demissidine (30) [23] was also in excellent agreement with the axial nature of both 23-OH and 25-Me groups in (28) and (29). Thus, the up-field shift of C-20 signal by *ca.* 6 p.p.m. through the γ_g effect clearly demonstrated the presence of an axial 23-OH group in both the alkaloids. On the other hand, the up-field shift of the C-26 signal by *ca.* 1.7 p.p.m. and the down-field shift of the C-27 signal by *ca.* 2.5 p.p.m. allowed unequivocal assignment of axial orientation to the 25-Me group. The observed deshielding of C-27 could be ascribed to the δ effect of the 23-OH group through a *syn*-1,3-diaxial interaction.

The complete structure and stereochemistry of solanogantamine and isosolanogantamine could, thus, be represented as (16αH,22αH,25αH)-3β-amino- and 3α-amino-23β-hydroxy-5α-solanidane (28) and (29), respectively.

Experimental

All m.p.s were taken in open capillaries in a sulphuric acid bath and are uncorrected. Neutral alumina was used for column chromatography unless otherwise stated. ^1H N.m.r. spectra were measured at 100 MHz and ^{13}C n.m.r. spectra were recorded at 25 MHz on Varian XL-100 and Jeol FX-100 instruments and the chemical shifts are expressed on the δ scale from $SiMe_4$ as internal standard. Mass spectra were recorded in a Hitachi RMU-6L instrument at 70 eV using a direct-inlet system while a Perkin-Elmer spectrophotometer (Model 177) was used for the i.r. spectra in Nujol. Optical rotations were determined in a Perkin-Elmer polarimeter (Model 141) and c.d. spectra were recorded in methanol solution on a JASCO J-20A spectropolarimeter. Light petroleum refers to that fraction boiling in the range 60—80 °C.

Isolation of Alkaloids.—The defatted powdered arboreal part (7 kg) of *S. pseudocapsicum* was extracted (Soxhlet) with ethanol for 24 h, the extract was concentrated (1 l) and

poured into stirred 2M AcOH (6 l). The mixture was shaken with $CHCl_3$ (2 l) and filtered. The aqueous phase of the filtrate was basified with aqueous NH_3 and extracted with $CHCl_3$ (1 l). The organic layer was washed with water, dried (anhydrous Na_2SO_4), and evaporated to dryness under reduced pressure.

Isolation of O-*methylsolanocapsine* (3). The crude alkaloid mixture (50 g) was chromatographed. Elution with 10—20% $CHCl_3$ in light petroleum afforded *O*-methylsolanocapsine (3) (1 g), which crystallised as fine needles (MeOH–MeCN), m.p. 183—185 °C; $[\alpha]_D$ +44.4° (*c* 0.63 in $CHCl_3$); $\nu_{max.}$ 3 100—3 500 cm^{-1}; *m/z* 444 (M^+, 6%), 443 (0.8), 429 (16), 412 (100), 397 (8), 384 (6), 342 (8), 179 (10), 171 (72), 144 (7), 139 (24), 112 (23), 111 (34), 84 (12), 82 (16), and 56 (22).

Further elution with 25—40% $CHCl_3$ in light petroleum gave mainly solanocapsine (1) (10 g), purified by repeated crystallisations as fine flakes ($CHCl_3$–light petroleum), m.p. 208 °C. Continued elution with 50% $CHCl_3$ in light petroleum to pure $CHCl_3$ yielded a gum (5 g) which was partially purified by extraction with acetate buffer (pH 4.6) from $CHCl_3$ solution. The regenerated base (1 g) was then chromatographed.

Isolation of solacapine (6), *episolacapine* (11), *and isosolacapine* (13). Elution with 40% $CHCl_3$ in light petroleum (0.5 l) furnished isosolacapine (13) as a viscous oil which could be crystallised (0.2 g) as fine needles (MeOH–MeCN), m.p. 238—240 °C; $[\alpha]_D$ −12.3° [*c* 0.73 in $CHCl_3$–MeOH (1 : 1)]; $\nu_{max.}$ 3 000—3 300 cm^{-1}; *m/z* 432 (M^+, 0.1%), 431 (0.1), 414 (3), 399 (0.6), 397 (0.8), 319 (3), 302 (0.2), 291 (0.2), 220 (6), 166 (26), 156 (11), 142 (8), 141 (13), 114 (100), 84 (8), 82 (15), 70 (18), and 56 (28).

Continued elution with the same solvent (0.6 l) gave solacapine (6) as a solid, which crystallised (0.15 g) as fine needles (MeOH–$CHCl_3$), m.p. 286—288 °C; $[\alpha]_D$ +47.1° [*c* 0.68 in $CHCl_3$–MeOH (1 : 1)]; $\nu_{max.}$ 3 100—3 400 cm^{-1}; *m/z* 432 (M^+, 0.1%), 431 (0.1), 414 (0.5), 399 (0.4), 397 (0.2), 319 (2), 302 (0.7), 291 (0.4), 220 (2), 166 (4), 156 (4), 142 (4), 141 (7), 114 (100), 84 (9), 82 (13), 70 (17), and 56 (13).

Further elution with 40—50% $CHCl_3$ in light petroleum (0.4 l) afforded episolacapine (11), which crystallised (7 mg) as shining prisms (MeOH–$CHCl_3$), m.p. 258—260 °C; $[\alpha]_D$ −41.5° [*c* 0.41 in $CHCl_3$–MeOH (1 : 1)]; $\nu_{max.}$ 3 000—3 400 cm^{-1}; *m/z* 432 (M^+, 0.2%), 431 (0.2), 414 (1), 399 (5), 397 (1), 319 (3), 302 (0.3), 291 (0.2), 220 (2), 166 (4), 156 (10), 142 (5), 141 (8), 114 (100), 82 (6), 70 (12), and 56 (17).

Methylation of Alkaloids.—To a solution of the appropriate alkaloid in 85% HCO_2H (0.5—1 ml) was added 40% aqueous HCHO (1—2 ml) and the mixture was heated on a steam-bath for 1 h (unless otherwise stated), cooled, diluted with water (10 ml), basified with aqueous NH_3 and extracted with chloroform. The crude product was purified by chromatography and crystallisation.

N,N,N′-*Trimethylisosolacapine* (14) *from isosolacapine* (13). Isosolacapine (13) (50 mg) yielded compound (14) (40 mg) as fine needles (MeOH–Me_2CO), m.p. 200—201 °C; *m/z* 474 (M^+, 0.5%), 473 (1), 456 (2), 330 (5), 186 (2), 185 (1.5), 155 (3), 128 (100), 110 (18), 98 (22), and 84 (39).

N,N-*Dimethylsolacapine* (7) *from solacapine* (6). Solacapine (6) (50 mg) yielded compound (7) (30 mg) as stout needles (MeOH–Me_2CO), m.p. 273—276 °C; $\nu_{max.}$ 3 200—3 300 cm^{-1}; *m/z* 460 (M^+, 1%), 459 (0.5), 442 (14), 347 (22), 330 (11), 277 (5), 262 (5), 220 (1), 166 (4), 156 (14), 142 (4), 141 (7), 114 (82), 110 (48), and 84 (100).

N,N-*Dimethylepisolacapine* (12) *from episolacapine* (11). Episolacapine (11) (20 mg) gave compound (12) (13 mg) as fine needles (MeOH–Me_2CO), m.p. 242—244 °C; *m/z* 460 (M^+, 0.5%), 459 (0.5), 442 (3), 347 (15), 330 (5), 277 (4), 262 (5), 220 (2), 166 (6), 156 (10), 142 (8), 141 (11), 114 (100), 110 (34), and 84 (88).

N,N,N′-*Trimethylsolacapine* (8) *from* N,N-*dimethylsolacapine* (7). *N,N*-Dimethylsolacapine (7) (20 mg) on being heated with HCO_2H (0.5 ml) and 40% aqueous HCHO (1 ml) on a steam-bath for 10 h furnished compound (8) (14 mg) as prisms (MeOH–Me_2CO), m.p. 228—230 °C; $\nu_{max.}$ 3 050—3 300 cm^{-1}; *m/z* 474 (M^+, 1%), 473 (3), 456 (2), 330 (6), 186 (2), 185 (2), 170 (8), 155 (4), 128 (100), 110 (28), 98 (12), and 84 (42).

O,O′-*Diacetyl*-N,N,N′-*trimethylisosolacapine* (15) *from* N,N,N′-*trimethylisosolacapine* (14). Compound (14) (45 mg) was acetylated with Ac_2O–pyridine at room temperature for 24 h. The excess of reagent was removed under reduced pressure and the product, on chromatography over silica gel, yielded the diester (15) (15 mg) as shining flakes (Me_2CO–water), m.p. 147—149 °C; *m/z* 558 (M^+, 8%), 543 (5), 516 (26), 498 (17), 483 (6), 456 (43), 438 (10), 170 (21), 110 (100), and 84 (90).

O,O′-*Diacetyl*-N,N,N′-*trimethylsolacapine* (9) *from* N,N,N′-*trimethylsolacapine* (8). Compound (8) (20 mg) was acetylated as above and the product was chromatographed over silica gel to give the diester (9) (12 mg) as fine needles (Me_2CO–water), m.p. 162—163 °C; *m/z* 558 (M^+, 0.3%), 543 (0.4), 516 (0.3), 498 (2), 483 (3), 456 (7), 438 (4), 170 (40), 110 (100), and 84 (85).

N,N,N′,O-*Tetramethyl*- (5) and N,N,N′-*trimethylsolanocapsine* (4) *from* O-*methylsoloancapsine* (3). *O*-Methylsolanocapsine (3) (80 mg) yielded compound (5) (40 mg) as shining needles ($CHCl_3$–Me_2CO), m.p. 195—197 °C; *m/z* 486 (M^+, 40%), 471 (100), 454 (77), 185 (69), 184 (47), 170 (7), 110 (30), and 84 (78), and compound (4) (20 mg) as prisms ($CHCl_3$–Me_2CO), m.p. 220—222 °C; *m/z* 472 (M^+, 2%), 454 (8), 171 (4), 156 (8), 128 (15), 126 (12), 111 (100), 110 (16), 98 (62), and 84 (64).

N-*Salicylidenesolacapine* (10) *from Solacapine* (6).—A solution of solacapine (6) (15 mg) in ethanol (1 ml) was refluxed with two drops of salicylaldehyde for 30 min and cooled. The separated solid, on crystallisation from $CHCl_3$–EtOH, furnished compound (10) (10 mg) as shining prisms, m.p. 265—267 °C; *m/z* 536 (M^+); c.d. ($\Delta\varepsilon$) 307 (0.70) and 246 nm (1.68).

N-*Salicylideneisosolacapine* (16) *from Isosolacapine* (13).—Compound (16) prepared as above, was obtained as shining prisms, m.p. 242—244 °C; *m/z* 536 (M^+); c.d. ($\Delta\varepsilon$) 305 (0.55) and 245 nm (1.30).

Solacapine (6) *and Episolacapine* (11) *from Solanocapsine* (1).—A solution of solanocapsine (1) (3 g) in ethanol (30 ml) was treated with $NaBH_4$ (3 g) at room temperature and the mixture was left for 12 h. It was then diluted with water (100 ml) and the separated solid was filtered off, washed, and dried. Crystallisation from MeOH–$CHCl_3$ gave solacapine (6) (1.5 g) as fine needles, m.p. 286—288 °C.

The mother liquor, on repeated chromatography and fractional crystallisation from the same solvent, yielded episolacapine (11) (50 mg) as shining prisms, m.p. 258—260 °C, along with a further crop of solacapine (6) (0.5 g). Both compounds were identical in all respects (mixed m.p., i.r., t.l.c., m.s.) with the corresponding natural products.

O-*Methylsolanocapsine* (3) *from Solanocapsine* (1).—Dry HCl gas was passed through a solution of solanocapsine (1) (0.3 g) in dry MeOH (20 ml) for 2 h and the reaction mixture was kept overnight at room temperature. Usual work-up gave an oily product which, on crystallisation from aqueous

MeOH, afforded compound (3) (0.27 g) as fine needles, m.p. 183—185 °C, identical (mixed m.p., i.r., t.l.c.) with the natural product.

Tetrahydrosolasodine A (19) *from Solasodine*.—Solasodine (1 g), dissolved in glacial AcOH (25 ml) containing few drops of conc. HCl, was hydrogenated over PtO_2 (100 mg) for 24 h and the mixture was then filtered. The filtrate was diluted with water (100 ml), basified with aqueous NH_3, and extracted with $CHCl_3$. The product was crystallised to give compound (19) (0.7 g) as prisms (MeOH), m.p. 288—290 °C; *m/z* 417 (M^+).

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