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Studies on Indian Medicinal Plants. Part XLVIII*. Novel 3-Amino-solanidanes from *Solanum giganteum*

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Two more novel 3-amino-solanidanes, *viz.* solanogantamine (2a) and iso-solanogantamine (2b) have been isolated apart from solanogantine (1) from the leaves of *Solanum giganteum*. Spectroscopic and chemical evidence leading to their structure elucidation along with the details of the work on 1 are presented.

In continuation of our search[1] for antihypertensive agents[2,3] from *Solanum* species, we investigated *S. giganteum* Jacq. The isolation and structure determination of a major alkaloid, solanogantine (1), a novel 3-amino-solanidane, from this plant has already been reported from this laboratory in a preliminary communication[4]. We now report the experimental details of this work along with the isolation and structure elucidation of two more new 3-amino-solanidanes, designated as solanogantamine (2a) and iso-solanogantamine (2b). The former has also been isolated by us as the major alkaloid from *S. vegum* (unpublished work).

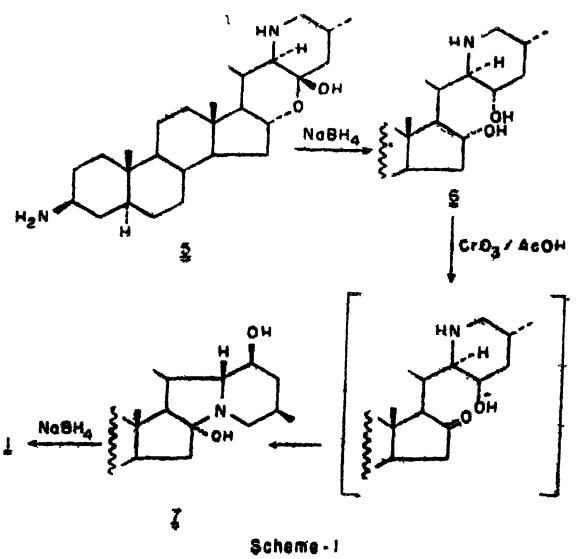
Acid hydrolysis of the total glycosidic bases of *S. giganteum* yielded a mixture of three alkaloids from which solanogantine (1), solanogantamine (2a), $C_{27}H_{46}N_2O$, m.p. 180°, $[\alpha]_D$+35° ($CHCl_3$) and iso-solanogantamine (2b), $C_{27}H_{46}N_2O$, m.p. 252-254°, $[\alpha]_D$+31° ($CHCl_3$) were obtained pure by chromatography over alumina.

The structure of solagantine (glass) was established as 1 mainly on the basis of the analysis of the PMR spectra of its N,N-dimethyl (3) and N,O-diacetyl (4) derivatives through which it was characterized. It was further confirmed by the partial synthesis of the alkaloid from solanocapsine (5) as follows : Sodium borohydride reduction of 5 yielded [22*R*:23*S*:25*R*]-3β-amino-16α, 23-dihydroxy-22,26-epimino-5α-cholestane (6) which on selective oxidation afforded the carbinolamine(7) through the 16-oxo intermediate ; sodium borohydride reduction of 7 thereafter furnished solanogantine (Scheme 1), identical in all respects with the natural product[4].

Both the new bases, *viz.* solanogantamine (2a) and iso-solanogantamine (2b) formed the corresponding N,N-dimethyl (8a and 8b), N-acetyl (9a and 9b) and N,O-diacetyl (10a and 10b) derivatives. Attempted oxidation of the alcoholic function of the free bases or their N-acetyl derivatives with CrO_3/AcOH, however, did not lead to any isolable product.



1 R = NH_2, R = H 3 R = NMe_2, R = H 4 R = NHAc, R = Ac

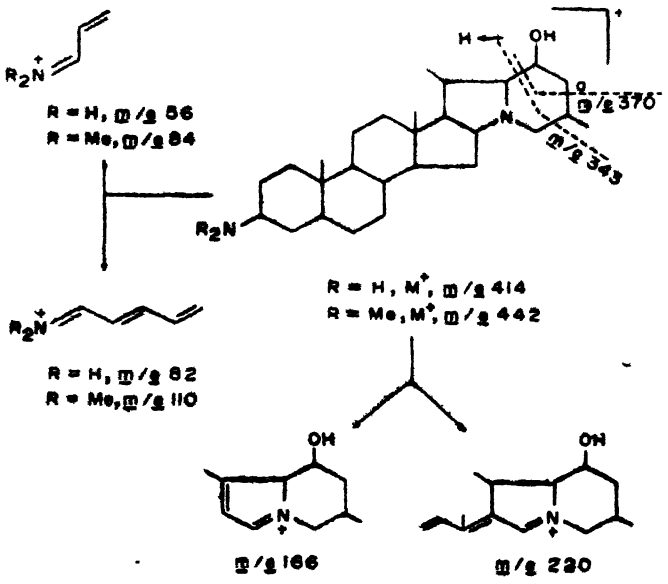


Scheme - 1

The mass-spectra of 2a and 2b and their dimethyl and diacetyl derivatives were almost superimposable with those of solanogantine and its corresponding derivatives indicating that the three bases 1, 2a and 2b are stereoisomeric. The two new alkaloids and their

*For Part XLVII, see T. Fujii, S. Yoshifuji, S. Minami, S. C. Pakrashi and E. Ali, *Heterocycles*, 1977, 8, 175.

dimethyl derivatives showed diagnostic fragmentation[4,5] for 3-amino-solanidanes with a hydroxy group at ring E or F. Furthermore, the characteristic fragments at *m/e* 370 and 343 indicated the presence of the hydroxy group at C-23 as in solanogantine (Scheme 2).



Scheme-2

Nitrous acid deamination of **2a** produced the diol **11** as the major product (65%) along with the acetate **12** (17%) and an olefin **13** (10%), whereas **2b** afforded the same olefin (**13**) in 70% yield. It was therefore apparent that the NH_2 group is equatorial in **2a** and axial in **2b** and that these two compounds differ only in respect of their C-3 stereochemistry. Finally, the epimeric nature of **2a** and **2b** at C-3 as well as their common 5α configuration could also be confirmed by the CD spectra (Table 1) of their salicylidene derivatives **14a** and **14b** that showed characteristic Cotton effects for 3β- and 3α-amino-5α-steroids[6] respectively.

TABLE 1—CD DATA (MeOH) OF THE SALICYLIDENE DERIVATIVES **14a** AND **14b**.

Compound	λ (nm)	[θ]
14a	251	+6750
	313	+3050
	400	+720
14b	251	−5290
	313	−3120
	400	−860

The axial orientation of the C-23 OH group in the two compounds were inferred from the PMR spectra (Table 2) which showed the carbinyl proton signal as a broadened singlet ($W_{1/2}$, 7-9 Hz).

TABLE 2—PMR DATA* OF *S. giganteum* ALKALOIDS AND THEIR DERIVATIVES

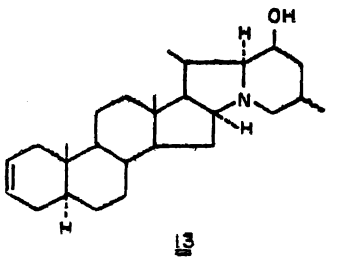
Sl. No.	Compound	18−Me & 19−Me	21−Me & 27−Me	26−H eq.	23−H	16−H	22−H	3−H	Others
1.	Solanogantamine (**2a**) (90 MHz)	0.80 0.85	0.94 d (6) 1.17 d (6)	2.70 d (11)	3.75 ($W_{\frac{1}{2}}$=7)	—	—	—	2.87 m (?)
2.	Iso-solanogantamine (**2b**) (90 MHz)	0.78 0.85	0.93 d (6) 1.17 d (7)	2.70 d (11)	3.75 ($W_{\frac{1}{2}}$=7)	—	—	3.22 ($W_{\frac{1}{2}}$=8)	2.57 m (?)
3.	Dimethyl-solanogantamine (**8a**) (270 MHz)	0.76 0.86	0.95 d (7) 1.18 d (7)	2.69 d (11)	3.77 ($W_{\frac{1}{2}}$=9)	—	—	—	2.26 (N Me_2) 2.75 m (?)
4.	Dimethyl-isosolanogantamine (**8b**) (270 MHz)	0.81 0.85	0.93 d (7) 1.17 d (7)	2.69 d (11)	3.75 ($W_{\frac{1}{2}}$=9)	—	—	—	2.31 (NMe_2) 2.75 m (?)
5.	Diacetyl-solanogantamine (**10a**) (100 MHz)	0.80 0.90	0.93 d (6) 1.13 d (6)	2.67 d (11)	5.03 ($W_{\frac{1}{2}}$=7)	—	—	3.70 m	1.93 (NAc) 2.02 (OAc) 2.80 m (?) 5.40 (N H)
6.	Dimethyl-solanogantine (**3**) (270 MHz)	0.78	0.88 d (7) 1.01 d (7)	2.78 d (10)	3.51 ($W_{\frac{1}{2}}$=23)	3.69 m	2.25 m	—	2.30 (N Me_2)
7.	Diacetyl solanogantine (**4**) (100 MHz)	0.80	0.83 d (7) 0.86 d (7)	2.78 d (10)	4.64 d d d (10,9,4)	3.64 m	2.61 dd (10,6)	3.64 m	1.93 (NAc) 2.01 (OAc)
8.	Dihydroleptinidine diacetate[7] (100 MHz)	0 83 0.86	—	2.5−3.0 m	5.07 ($W_{\frac{1}{2}}$=6)	2.5−3.0 m	—	4.68 m (10,5)	2.00 (OAc) 2.04 (OAc)

* In $CDCl_3$. Chemical shifts are in δ units and the coupling constants and the line widths are in Hz.



a = 3β b = 3α

2, R = NH_2, R′ = H
8, R = NMe_2, R′ = H
9, R = NHAc, R′ = H
10, R = NHAc, R′ = Ac
11, R = βOH, R′ = H
12, R = βOAc, R′ = H
14, R = −N=CH- (HO-phenyl), R′ = H
15, R = βOAc, R′ = Ac



13

It has already been shown by us[4] that in N,N-dimethyl solanogantine (3), 22-H, which is *trans* to the nitrogen lone pair, resonates at δ 2.25 and the signal at δ 3.69 must be assigned to the *cis* related 16-H. Since the PMR spectra of the dimethyl derivatives (8a and 8b) of the new bases did not exhibit any signal downfield to δ 3.00, it must be assumed that both 22-H and 16-H are *trans* to the lone pair of electrons on nitrogen as in the normal solanidanes. Furthermore, the signals for two protons in the δ 2.5−2.9 region, one of which must be assigned to 26-H (eq), are similar to that of 5α-solanidane and dihydroleptinidine derivatives[7]. The above evidence coupled with the observed facile mercuric acetate oxidation of both the bases established the stereochemistry of the two alkaloids at the D/E/F ring junctures to be the same as that of solanidine.

Thus, the structure and stereochemistry of solanogantamine and iso-solanogantamine can be represented by **2a** and **2b** respectively except the orientation of the methyl group at C-25, unequivocal assignment of which was not possible from the data available with us at present.

Had **2a** an equatorial methyl group at C-25, the derived diol **11** would be expected to be identical with dihydroleptinidine. An authentic specimen of the latter being not available, we are unable to either confirm or eliminate such a possibility. The IR spectrum of dihydroleptinidine (obtained through the courtesy of Dr. H. Ripperger[7]) is apparently not identical with that of **11** and a comparison of the physical constants of dihydroleptinidine and its diacetate with those of **11** and **15** (Table 3) also did not allow us to arrive at a definite conclusion.

TABLE 3 – PHYSICAL CONSTANTS OF DIOL **11**, DIHYDROLEPTINIDINE AND THEIR ACETATES.

Compound	m.p.	$[\alpha]_D$ ($CHCl_3$)	Ref
11	215–216°	+40.4°	
Dihydroleptinidine	215°	+32°	8
	221–224°	+31.3°	9
15	212–214°	+8.5°	
Diacetyldihydroleptinidine	222–223°	+2.95°	8
	229–232°	+0.9°	9

Further work to establish the stereochemistry at the C-25 centre of both **2a** and **2b** is in progress and will be reported elsewhere in due course.

Experimental

All m.p.s were determined in open capillaries in a sulphuric acid bath and are uncorrected. IR spectra were recorded as Nujol mull in a Perkin-Elmer Infracord-137 spectrophotometer. Optical rotations are in $CHCl_3$, measured in a Hilger-Watts M-511 photoelectric polarimeter. PMR spectra were taken in $CDCl_3$ with TMS as internal standard. Mass spectra were recorded in a Hitachi RMU-6L instrument. TLCs were done on silica gel with the solvent system C_6H_6:EtOAc (2:8) saturated with ammonia. Column chromatographies were done over neutral alumina.

Isolation of the alkaloids. Dried leaves of *Solanum giganteum* (2 kg) were defatted with light petrol and extracted with alcohol in a Soxhlet apparatus for 30 hr. The extract was concentrated and the glycosides precipitated with excess of ether. The separated glycoside mixture was hydrolysed with 2*N* ethanolic HCl under reflux for 8 hr. Conventional work-up afforded the crude mixture of alkaloids as a gum (2 g) which on repeated chromatography afforded solanogantine (**1**, 0.3 g)[4] as glass. *m/e* 414 (M^+, 18), 399 (3), 370 (3), 355 (2), 343(3), 220(21), 166(100), 82(15), 56(20); *solanogantamine* (**2a**, 0.55 g), crystallised from methanol-acetonitrile in plates, m.p. 180°, $[\alpha]_D$ +35°; ν_{max} 3325(sh), 3130, 2400-2700 cm^{-1}; *m/e* 414 (M^+, 15), 399(3), 370(2), 355(2), 343(3), 220(23), 166(100), 82(16), 56(25); (Found: C, 78.43, H, 11.06; N, 6.50. Calcd. for $C_{27}H_{46}N_2O$: C, 78.20; H, 11.18; N, 6.76%.) and iso-solanogantamine (**2b**, 0.15 g) crystallised from chloroform-petroleum ether in flakes, m.p. 252-254°; $[\alpha]_D$ +31°; ν_{max} 3200, 2400-2700 cm^{-1}; *m/e* 414 (M^+, 20), 399(3), 370(3), 355(2), 343(3), 220(23), 166(100), 82(14), 56(18); (Found: C, 78.35; H, 11.15; N, 6.60. Calcd. for $C_{27}H_{46}N_2O$: C, 78.20; H, 11.18; N, 6.76%).

N,N-Dimethyl-solanogantine (**3**). Solanogantine (**1**, 0.15 g) was dissolved in 98% formic acid (2 ml) and treated with 40% formaldehyde solution (4 ml). The mixture was heated on a steambath for 1 hr. Conventional work-up, chromatography and crystallisation from aqueous acetone yielded **3** (14 mg) as

needles, m.p. 111-112°; $[\alpha]_D$+41.3°; *m/e* 442 (M^+, 30), 427(5), 398(3), 37 (4), 220(23), 166(94), 110(30) and 84(100).

N,N-Dimethyl-solanogantamine (8a). Methylation of solanogantamine (2a, 0.3 g) under similar condition followed by chromatography over alumina and crystallisation from methanol yielded 8a (0.15 g); m.p. 207-210°; $[\alpha]_D$+50°; *m/e* 442 (M^+, 29), 427(5), 398(4), 371(4), 220(21), 166(92), 110(29) and 84(100).

N,N-Dimethyl-iso-solanogantamine (8b). Iso-solanogantamine (2b, 75 mg) was methylated by the same procedure as mentioned above to give 8b (42 mg), crystallised from methanol in flakes, m.p. 200-203°; $[\alpha]_D$+41°; *m/e* 442 (M^+, 27), 427 (5), 398(3), 371(4), 220(21), 166(95), 110(29) and 84(100).

N,O-Diacetyl-solanogantine (4). Solanogantine (0.1 g) was acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml) at room temp. for 2 hr to furnish 4 (60 mg), crystallised from acetone in prisms, m.p. 219-221° dec., $[\alpha]_D$+27.2°, ν_{max}3200, 1725, 1640, 1550, 1255 cm^{-1}; *m/e* 498 (M^+, 2), 455 (2), 438(100), 423(5), 262(12), 208(5), 162(11) and 158(40).

N-Acetyl-(9a) *and N,O-diacetyl* (10a) *solanogantamine.* To a solution of 2a (0.12 g) in pyridine (2 ml) was added acetic anhydride (1 ml) at room temp. and allowed to stand for 1 hr. Excess reagent was removed under reduced pressure and the residue chromatographed to afford N-acetyl-solanogantamine (9a, 105 mg), crystallised from acetone in prisms; m.p. 258-260°; $[\alpha]_D$+28°; ν_{max}3275, 1650, 1590, 1570 cm^{-1}; *m/e* 456 (M^+, 8), 220(24) and 166 (100).

Compound 9a (25 mg) on further acetylation at room temp for 40 hr afforded N,O-diacetyl-solanogantamine (10a, 18 mg), crystallised from dilute acetone in fine needles, m.p. 229-231°; $[\alpha]_D$+11°; ν_{max}3460, 3200, 1725, 1715, 1660, 1635, 1550, 1230, cm^{-1}; *m/e* 498 (M^+, 2), 455(5), 438(100), 423(6), 262(12), 208(5), 162 (10) and 148 (42).

N-Acetyl-(9b) *and N,O-diacetyl-*(10b) *iso-solanogantamine.* Compounds 9b and 10b were obtained from 2b in a similar way as mentioned above. 9b, m.p. 257-259° (from acetone); $[\alpha]_D$+35.5°; ν_{max}3180, 1625, 1545 cm^{-1}; *m/e* 456 (M^+, 9), 220(25), 166(100); 10b, *m/e* 498 (M^+, 2), 438(100), 423(5), 262(13), 208(5), 162(12) and 148(45).

N-Salicylidene derivatives 14a and 14b. To a solution of the base 2a or 2b (25 mg) in ethanol (10 ml) was added two drops of salicylaldehyde and then refluxed for 30 min. The salicylidene derivatives crystallised out on concentration of the reaction mixture. 14a, m.p. 227-229°; *m/e* 518 (M^+) and 14b, m.p. 114°-116°; *m/e* 518 (M^+).

Deamination of solanogantamine with nitrous acid. A solution of solanogantamine (2a, 60 mg) in 50% acetic acid (2 ml) was treated with $NaNO_2$ (200 mg) and kept at room temp for 18 hr. The mixture was diluted with water, basified with ammonia and extracted with chloroform. The product on chromatography yielded the *olefin* 13 (6 mg, 10%), m.p. 167-168°; *m/e* 397 (M^+, 100), 382(10), 220(38), 166(98); the acetate 12 (10 mg, 17%), m.p. 193-196°; ν_{max}3400, 1730, 1223 cm^{-1}; *m/e* 457 (M^+, 31), 220(17), 166(100); and the *diol* 11 (40 mg, 65%), m.p. 215-216°; ν_{max}3400 cm^{-1}; *m/e* 415 (M^+, 76), 400(33), 384(8), 371 (17), 370(18), 356(17), 344(26), 342(18), 328(15), 314(16), 220(67), 166(100). *Diacetate* (15); crystallised as needles from methanol, m.p. 212-214°; $[\alpha]_D$+8.5°; *m/e* 499 (M^+).

Deamination of iso-solanogantamine with nitrous acid. A solution of 2b (10 mg) in 50% acetic acid (2 ml) was treated with $NaNO_2$ (50 mg) and kept at room temp for 18 hr. Conventional work-up and crystallisation from methanol afforded the olefin 13 (7 mg, 70%) as fine needles, m.p. 166-167°; identical (IR, m.m.p.) with the olefin obtained from solanogantamine.

Mercuric acetate oxidation of the alkaloids 1, 2a, *and* 2b. Solutions of the alkaloids in 50% acetic acid were heated on a steam-bath with 5 eqv. of mercuric acetate. Crystals of Hg(I) acetate started separating immediately in all the cases.

Synthesis of solanogantine (1)

(a) *[22R, 23S, 25R]-3β-amino-16α, 23-dihydroxy-22, 26-epimino-5α-cholestane* (6) *from solanocapsine*(5).

A solution of 5 (3 g) in ethanol (30 ml) was treated with $NaBH_4$ (3 g) and the reaction mixture was kept at room temp for 12 hr. It was diluted with water (100 ml) and the separated solid was filtered, washed, dried and crystallised from ethanol to furnish the diol 6 (2.0 g, yield 66%) as colourless needles, m.p. 286-288°; *m/e* 432 (M^+, 0.2), 114(100), 82(14), 56(14); (Found: C, 74.67; H, 11.08; N, 6.52. $C_{27}H_{48}N_2O_2$ requires: C, 74.95; H, 11.18; N, 6.48%).

(b) *Carbinolamine* (7) *from* 6. A solution of CrO_3 (0.75 g) in glacial acetic acid (25 ml) was added portionwise with stirring to a solution of 6 (2 g) in the same solvent (15 ml) at room temp and the reaction mixture allowed to stand for 20 hr. It was then diluted with water (100 ml), cooled, basified with ammonia and extracted with chloroform to get the carbinolamine (7, 1.8 g) as an amorphous material, *m/e* 430 (M^+). It was used as such without further purification.

(c) *Solanogantine* (1) *from* 7. A solution of 7 (1.8 g) in ethanol (25 ml) was treated with $NaBH_4$ (2 g) at room temp for 20 hr. Usual work-up afforded 1 (1.5 g) which on acetylation yielded the N,O-diacetyl derivative 4 (0.8 g), m.p. 219-221°, identical (m.m.p., TLC, IR, MS) with the N,O-diacetyl-solanogantine.

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References

1. B. ALI, A.K. CHAKRAVARTY, S.C. PAKRASHI, K. BIEMANN and C. E. HIGNITE, *Tetrahedron*, 1977, 33, 1371.
2. M. L. DHAR, M. M. DHAR, B. N. DHAWAN, B. N. MEHROTRA and C. ROY, *Indian J. Exp. Biol.*, 1968, 6, 232.
3. D S. BHAKUNI, M.L DHAR, M M. DHAR, B.N. DHAWAN and B. N. MEHROTRA, *Indian J. Exp. Biol.*, 1969, 7, 250.
4. S. C. PAKRASHI, A. K. CHAKRAVARTY and E. ALI, *Tetrahedron Letters*, 1977, 645.
5. H. BUDZIKIEWICZ, C. DJERASSI and D. WILLIAMS, "Structure Elucidation of Natural Products by Mass-spectrometry", Holden-Day, San-Francisco, Vol. 2, 1964, p. 5.
6. H. RIPPERGER, K. SCHREIBER, G. SNATZKE and K. POUSOLD, *Tetrahedron*, 1969, 25, 827.
7. K. SCHREIBER and H. RIPPERGER, *Chem. Ber.*, 1967, 100, 1381.
8. R. KUHN and I. LÖw, *Chem. Ber.*, 1961, 94, 1096; 1962, 95, 1748.
9. H. RIPPERGER and K. SCHREIBER, *Chem. Ber.*, 1969, 102, 4080.