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SOLANOCASTRINE, A UNIQUE 16,23-CYCLO-22,26-EPIMINOCHOLESTANE FROM SOLANUM CAPSICASTRUM[1]

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Abstract - Solanocastrine (**1**), a novel 3-amino steroidal alkaloid, isolated from the leaves of Solanum capsicastrum Link has been characterised as 3β-amino-16,23-cyclo-23β-hydroxy-5α-H, 16ξ-H, 25βH-22,26-epiminocholestan-17(20),22(N)-diene.

In continuation of our studies[2] on the alkaloids of the leaves of S. capsicastrum Link, we isolated a unique 16,23-cyclo-22,26-epiminocholestane derivative, designated as solanocastrine (**1**), as a very minor compound. It was separated by repeated column chromatography (neutral alumina) followed by preparative TLC ($CHCl_3$:MeOH, 98:2 saturated with NH_3) of the crude alkaloid mixture obtained by hydrolysis (10% HCl-MeOH) of the methanolic extract. Herein we report the structure elucidation of the alkaloid **1**.

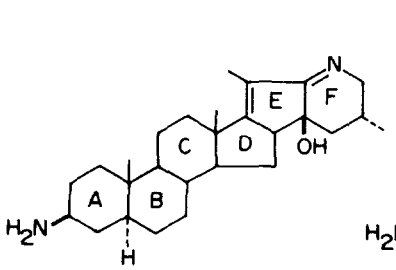
The IR spectrum of solanocastrine [$C_{27}H_{42}N_2O$, m.p. 258-260°d, $[\alpha]_D$ ± 0°($CHCl_3$); m/z (rel.intensity) 410(M^+, 47), 392(55), 382(18), 377(19), 367(6), 340(6), 214(11), 177(100) 162(17), 82(15), 56(47)] showed, besides the peaks for OH and NH_2 groups (at 3340, 3220 and 3160 cm^{-1}), a strong absorption band at 1630 cm^{-1} indicating the presence of an α,β-unsaturated C=N grouping in the molecule supported by the UV absorption maximum at 247 nm (log ε 4.06). This contention was further corroborated by the ^{13}C NMR spectrum of the alkaloid (Table 1) which exhibited three low-field singlets at δ 183.3, 169.1 and 122.6 ppm assignable respectively to C-17(C_β), C-22(C=N) and C-20(C_α). The above data allowed us also to conclude the tetrasubstituted nature of the C=C. Furthermore, the spectrum displayed signals for A and B ring carbons very close (Table 1) to those of solanocapsine (**2**), the co-occuring alkaloid, suggesting the same 3β-amino-5α-stereochemistry for **1** as well. The presence of a tertiary OH group in the alkaloid became evident from the singlet at δ 75.1 ppm.

That the tetrasubstituted double bond of the α,β-unsaturated imine moiety of **1** is located between C-17 and C-20 could be ascertained from the appearance of the 20-Me proton signal as a doublet at δ 1.79 ppm with J=2 Hz in its ^1H NMR spectrum (Table 2), the small splitting of the signal being ascribed to its allylic coupling with 16-H.

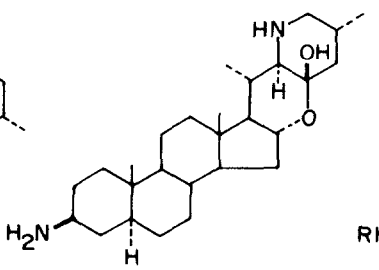
The EIMS of the alkaloid **1** showed, apart from the peaks at m/z 56 and 82 diagnostic[3] of 3-amino-5,6-dihydro steroids and intense peaks due to M^+ and M^+-H_2O, the base peak at m/z 177 (species a) compatible with the location of the tertiary OH group in either of the rings E and F. Of the two possibilities, position C-25 could be ruled out since the ^1H NMR spectrum clearly demonstrated the presence of a secondary methyl at C-25. The OH group must, therefore, be located at C-23.

Reduction of the alkaloid **1** with $NaBH_4$ or Li-liq. NH_3 yielded the dihydroderivative **3** [m.p. 242-244°, ν_{max}(KBr) 3400-3200(NH_2, NH, OH) cm^{-1}; m/z (rel.intensity) 412(M^+,21), 395 (36), 394(25), 379(11), 357(87), 337(10), 322(6), 82(36), 56(100); N,N'-diacetate (**4**), m.p. 266-268°, ν_{max}(KBr) 1650-1610(NAc) cm^{-1}; m/z 496(M^+)]. The appearance of a new doublet at δ 77.4 ppm in its ^{13}C NMR spectrum at the expense of the singlet at δ 169.1 ppm of **1** and the up-field shift of its C-17 signal by ~31 ppm with respect to that of **1** clearly suggested the reduction of C=N group with $\Delta^{17(20)}$ double bond remaining intact. Its ^1H NMR spectrum also displayed the signal for 20-Me protons as a doublet with J=2 Hz as in **1** supporting the existence of $\Delta^{17(20)}$ double bond in **3**.

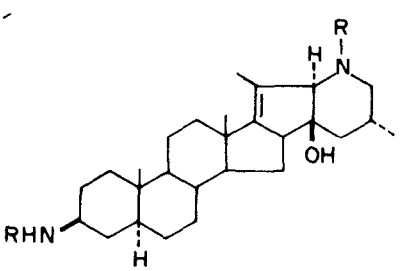
The alkaloid on treatment with $HCHO-HCO_2H$ at 100° for 2 hr furnished the keto-N,N,N',N'-tetramethyl derivative (**5**) [amorphous, λ_{max}(EtOH) 247 nm (logϵ 3.97); m/z (rel. intensity) 484(M^+, 3), 466(1), 182(2), 181(2), 135(3), 128(2), 110(11), 105(10), 98(7), 84(34), 58(100)] which could be reduced by $NaBH_4$ to the diol (**6**) [m/z 486 (M^+)]. The F ring opened structure **5** was indeed supported by (i) the strong band at 1700 cm^{-1} for five membered α,β-unsaturated ring ketone in its IR spectrum, (ii) the most intense peak at m/z 58(species b) almost certainly arising out of the cleavage of the bond between C-25 and C-26 in its mass spectrum and (iii) a new ^{13}C NMR signal at δ 213.7 ppm for an α,β-unsaturated carbonyl carbon. The formation of **5** could presumably be explained by hydrolysis of



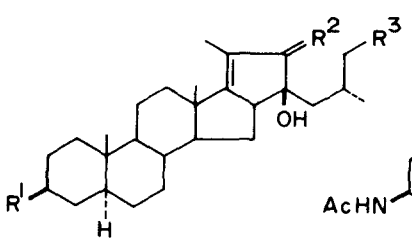
1



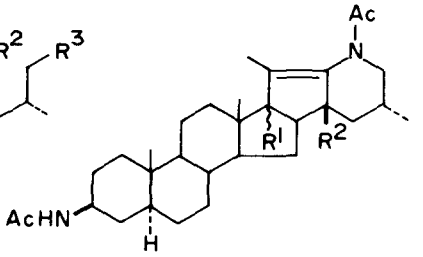
2



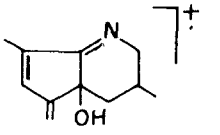
3 R = H
4 R = Ac



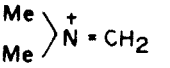
5 $R^1 = R^3 = NMe_2$, $R^2 = O$
6 $R^1 = R^3 = NMe_2$, $R^2 = \langle^{H}_{OH}$
7 $R^1 = R^3 = NH_2$, $R^2 = O$
9 $R^1 = R^2 = NHAc$, $R^2 = O$



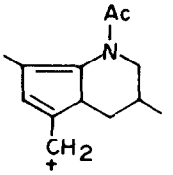
8 $R^1 = OAc$, $R^2 = OH$
10 $R^1 = R^2 = H$



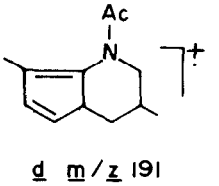
g m/z 177



b m/z 58



c m/z 204



d m/z 191

Table 1. ^{13}C chemical shifts[a] (δ ppm from TMS) of solanocastrine (**1**) and its derivatives.

Carbon	**1**	**2**[b]	**3**	**5**	**8**	carbon	**1**	**2**[b]	**3**	**5**	**8**
1	37.9	37.2	37.6	37.7	37.2	17	183.3	60.6	152.4	183.0	103.3
2	31.2	31.6	31.5	24.7	28.5	18	15.9	13.5	16.4	15.7	15.4
3	51.3	50.7	51.0	64.0	48.9	19	12.3	12.1	12.2	12.2	12.2
4	37.9	38.9	39.0	31.1	35.9	20	122.6	32.8	124.5	124.2	129.1
5	45.8	45.4	45.5	45.6	45.3	21	9.1	15.0	12.5	8.1	11.7
6	28.4	28.4	28.6	28.9	28.8	22	169.1	68.4	77.4	213.7	144.9
7	33.7	32.1	32.6	31.5	31.8	23	75.1	95.7	78.5	75.9	79.3
8	35.7	34.7	35.8	35.8	35.0	24	41.4	45.9	41.5	47.4	45.1
9	54.7	54.6	54.7	54.7	54.4	25	29.3	30.1	31.0	26.2	27.7
10	35.5	35.4	35.5	35.8	35.4	26	54.7	54.6	52.0	68.1	48.9
11	20.8	20.2	20.7	20.7	20.8	27	20.3	18.6	18.9	22.0	19.2
12	35.3	38.9	35.3	34.5	35.2	NMe_2	-	-	-	41.8	-
13	43.0	41.5	41.8	44.5	48.4	$N'Me_2$	-	-	-	45.0	-
14	56.8	54.6	58.2	54.3	50.4	NAc &	-	-	-	-	21.3,21.8,
15	21.3	28.2	21.4	21.6	26.4	OAc	-	-	-	-	23.5,169.1, 169.6
16	55.1	73.8	49.7	51.8	52.8						

a The spectra were recorded in $CDCl_3$. b Data incorporated from ref. 4.

Table 2. ^{1}H chemical shifts[a] (δ ppm from TMS) of solanocastrine (**1**) and its derivatives.

Compd.	10-Me	13-Me	20-Me	25-Me	3-H	22-H	26-Heq	26-Hax	Others
1	0.79s	0.95s	1.79d(2)	0.98d(6)	2.56br	-	3.66dd (14,4)	3.21dd (14,9)	2.78dd(10,2)
2[b]	0.73s	0.77s	0.93d(6)	0.83d(6)	-	-	3.02br d (9)	-	2.65m
3	0.79s	0.88s	1.76d(2)	0.88d(6)	2.62m ($W\frac{1}{2}$=23)	3.11s	3.20br d (13)	2.91br d (13)	-
4	0.80s	0.94s	1.63d(2)	1.05d(6)	3.72m ($W\frac{1}{2}$=22)	-	3.16m	3.16m	1.93,2.15(NAc x 2)
5	0.80s	1.01s	1.71d(2)	0.86d(7)	-	-	-	-	2.27,2.31(NMe_2x 2)
6	0.78s	0.82s	1.64d(2)	0.89d(7)	-	4.30s	-	-	2.27,2.32(NMe_2x 2)
8	0.80s	0.95s	1.52s	0.92d(7)	3.72m ($W\frac{1}{2}$=24)	-	4.14dd (12,4)	3.14dd (12,4)	2.07(OAc),2.02,1.93 (NAcx2),5.24d(CONH)
9	0.82s	1.05s	1.75d(2)	1.00d(6)	3.72m ($W\frac{1}{2}$=23)	-	-	-	2.00,1.93(NAcx2),2.80· 3.30m(?),5.30d,6.00 t-like(CONHx2)

a The spectra were taken in $CDCl_3$. Figures in the parentheses are the coupling constants in Hz. b Ref.4.

C=N group to the ketoamine (**7**) followed by methylation.

Acetylation of the alkaloid with Ac_2O-Py at room temp. for 20 hr yielded a N,N',O-triacetate (**8**) [m.p. 194-196°, ν_{max}(KBr) 1730(OAc), 1630(NAc) cm^{-1}; λ_{max}(EtOH) 225 nm (logϵ 3.44); m/z 494(M^+- AcOH)] as the major product besides a minor N,N'-diacetate (**9**) [m.p. 164-166°, ν_{max}(KBr) 1700(α,β-unsaturated five membered ring ketone), 1655-1640(NAc) cm^{-1}; λ_{max}(EtOH) 248 nm (logϵ 3.63), m/z 512(M^+)]. The acetates **8** and **9** could apparently be derived from the respective 1,4 and 1,2 addition of Ac_2O molecule to the α,β-unsaturated imine moiety.

The triacetate (**8**) on hydrogenation in presence of 10% pd/c and $HClO_4$ yielded **10** [m/z 480(M^+), 465(M^+- CH_3), 437(M^+- CH_3CO), 204(species c), 191(species d), 162(c-42), 149(d-42), 120, 118] in which both the 17-OAc and 23-OH groups were hydrogenolysed confirming thereby the structure of **8**. The strong ion peaks at m/z 204 (species c) and 191 (species d) in the EIMS of **10** clearly demonstrated a direct linkage between C-16 and C-23 in the alkaloid **1**.

A comparison of the ^{13}C NMR spectra revealed that C-25 of both **1** (δ 29.3 ppm) and its dihydro derivative (**3**) (δ 31.0 ppm) resonated close to that of solanocapsine (**2**) (δ 30.1 ppm) indicating that 23-OH and 25-Me groups of **1** should have the same β and α orientations respectively as in **2**. This conclusion was also supported by (i) the up-field shift of C-15 signal of **1** and **3** by ~7 ppm due its γ_g interaction with 23-OH group and (ii) the close chemical shift of 25-Me carbon of **1** (δ 20.3 ppm) and **3** (δ 18.9 ppm) with that of **2** (δ 18.6 ppm). A small difference in the chemical shifts of C-24 to C-27 carbons of **1** and **3** when compared with those of **2** is not unexpected in view of the double bond(s) present in the E/F ring system of the former. The ^1H chemical shift of 25-Me protons of **3** at δ 0.88 ppm which is close (Table 2) to that of **2** (0.83 ppm) also corroborated the assigned orientation of 23-OH and 25-Me groups. The stereochemistry at C-16 could not, however, be established from the available data.

Based on the above evidences, solanocastrine could be assigned 3β-amino-16,23-cyclo-23β-hydroxy-5α-H, 16β-H, 25β-H-22, 26-epiminocholestan-17(20), 22(N)-diene structure(**1**). It thus represents a new class of steroidal alkaloid with a novel C-C linkage between C-16 and C-23 in a 22, 26-epiminocholestane skeleton.

References

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