Phytochemistry, Vol. 21, No. 8, pp. 2083–2085, 1982.
Printed in Great Britain.

0031–9422/82/082083–03\$03.00/0

SOLANOLIDE, A STEROID LACTONE SAPOGENIN FROM *SOLANUM HISPIDUM**

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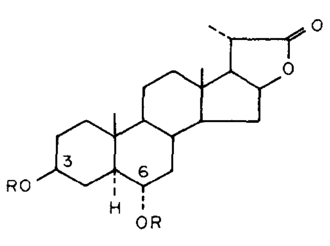
(*Revised received* 1 *December* 1981)

Key Word Index—*Solanum hispidum*; Solanaceae; sapogenin; 3*β*, 6*α*, 16*β*-trihydroxy-5*α*-pregnane-20*S*-carboxylic acid (22, 16)-lactone; ^{1}H NMR; ^{13}C NMR.

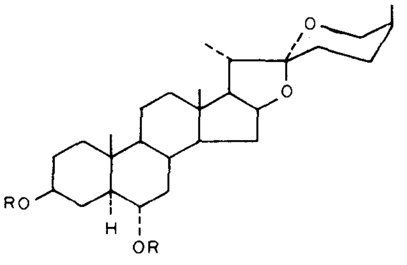
Abstract—Solanolide, a new C_{22} steroid lactone sapogenin isolated from the leaves of *Solanum hispidum* Pers., has been characterized as 3*β*, 6*α*, 16*β*-trihydroxy-5*α*-pregnane-20*S*-carboxylic acid (22, 16)-lactone from ^{1}H and ^{13}C NMR analyses and correlation with neochlorogenin.

Recently we have reported the isolation of a number of new spirostane saponins and sapogenins from the leaves [1, 2] and seeds [3] of *Solanum hispidum*. We now report another new C_{22} steroid sapogenin, designated as solanolide, from the leaves of this plant.

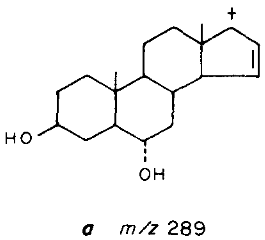
Solanolide (**1**), $C_{22}H_{34}O_4$ (M^+ at *m/z* 362), mp 252–254°, $[\alpha]_D - 28°$ ($CHCl_3$; *c* 0.5), was isolated as fine needles (MeCN) upon acidification of the alkali-soluble part of the crude aglycone mixture [1] obtained by Smith degradation of the major dirhamnoside fraction of the leaf extract. The yield was very poor (1.5% based on the crude aglycone). It could not be methylated with MeOH–HCl or with Me_2SO_4–NaOH indicating the absence of any free phenolic hydroxyl or carboxyl group. That it was a lactone became evident from its IR spectrum (KCl) which showed a strong absorption band at 1760 cm^{-1} for a five-membered lactone, besides a broad band between 3500 and 3100 cm^{-1} for hydroxy group(s). Its mass spectrum exhibited intense peaks at *m/z* 344 $[M - H_2O]^+$, 329 $[344\text{–}Me^{\cdot}]^+$, 326 $[344 - H_2O]^+$, 311 $[326 - Me^{\cdot}]^+$, 289 $[M - C_3H_5O_2^{\cdot}]^+$, 271 $[289 - H_2O]^+$, 264 $[M - C_5H_6O_2^{\cdot}]^+$, 246 $[M - H_2O - C_5H_6O_2^{\cdot}]^+$, 231 $[246 - Me^{\cdot}]^+$ and 213 $[231 - H_2O]^+$ indicating the presence of two hydroxyl groups in the molecule. The remaining two oxygen atoms form part of the lactone ring. The location of the



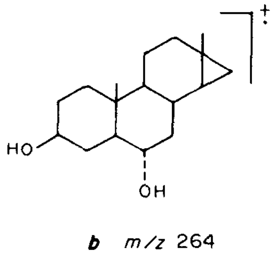
1 R = H
2 R = Ac
3 3, 6 – diketo



4 R = H
5 R = Ac



a *m/z* 289



b *m/z* 264

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*Part 66 in the series, "Studies on Indian Medicinal Plants". For Part 65 see Ali, E., Bagchi, D. and Pakrashi, S. C. *Phytochemistry* (1982) **21**, 243.

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Table 1. ^{1}H NMR spectral data (δ) of solanolide (**1**) and its derivatives*

Compound	19-Me	18-Me	21-Me	16-H	20-H	3-H	6-H	OAc
1	0.84	0.75	1.31 *d* (7)	4.98 *ddd* (7, 7, 4)	2.59 *q* (7)	3.52 *m*	3.52 *m*	—
1†	0.82	0.71	1.24 *d* (7)	4.90 *ddd* (7, 7, 4)	2.65 *q* (7)	3.86 *m*	3.63 *ddd* (10, 10, 4)	—
2	0.91	0.75	1.31 *d* (7)	4.97 *ddd* (7, 7, 4)	2.58 *q* (7)	4.68 *m*	4.68 *m*	2.02
3	0.96	0.78	1.31 *d* (7)	4.94 *ddd* (7, 7, 4)	—	—	—	—

*Spectra were recorded in $CDCl_3$. The values in parentheses are the coupling constants in Hz.
†Spectrum recorded in pyridine-d_5.

Table 2. ^{13}C Chemical shifts* of solanolide (**1**) and its derivatives

Carbon no.	**1**†	**2**‡	**3**‡	**5**§
1	38.2	36.8	33.0	36.8
2	32.1	27.0	37.1‖	27.1
3	70.8	72.8	210.5	73.0
4	33.2	28.2	36.9‖	28.4
5	52.5	48.4	57.4	48.5
6	68.3	71.6	207.7	72.0
7	42.5	37.6	46.3	37.8
8	33.9	33.4	37.2‖	33.7
9	54.2	53.4	53.4	53.6
10	36.5	36.6	41.0	36.6
11	20.8	20.4	21.0	20.9
12	37.9	38.0	37.7‖	39.8
13	41.7	41.7	42.1	40.5
14	54.4	54.1	54.6	55.9
15	33.5	32.9	32.8	31.6
16	82.6	82.3	82.1	80.6
17	58.9	58.8	58.8	61.9
18	13.8	13.7	13.8	16.4
19	13.6	13.2	12.6	13.3
20	36.2	36.0	36.0	42.1
21	17.9	17.8	17.9	14.3
22	180.9	180.8	180.7	109.6
$\underline{C}$OMe	—	170.3	—	170.5
		170.5		170.7
CO$\underline{C}H_3$	—	21.1	—	21.3
		21.3		21.4

*Spectra were recorded in a Jeol FX-100 spectrometer at 25.05 MHz. Conditions for measurements were: data points, 8K; spectral width, 6 KHz, repetition time, 1.0 or 1.2 sec; flip angle, 25–40°. The chemical shifts expressed on the δ scale using TMS as internal standard. The assignments were based on the SFORD spectra, low-power noise-modulated decoupled spectra and selective proton decoupled spectra (where applicable) as well as the chemical shifts of 5α-spirostanols and their acetates[10].
†Spectrum recorded in pyridine-d_5.
‡Spectra taken in $CDCl_3$.
§Chemical shifts included from Ref. [10].
‖The closely lying peaks may be interchanged.

lactone chromophore in the terminal E ring was evident from the formation of ions at m/z 289 (species **a**) and 264 (species **b**) by the expulsion of $C_3H_5O_2$ and $C_5H_6O_2$ radicals respectively from the molecular ion. The peak at m/z 264 appears to be diagnostic for the lactones of the solanolide type since the peak at m/z 289 could also be obtained from the spirostane derivatives with two hydroxy groups in the androstane moiety[1, 2].

Acetylation of **1** with Ac_2O–pyridine at room temperature afforded a diacetate (**2**), mp 250–252°, $[\alpha]_D -46°$ ($CHCl_3$; c 0.5), IR ν_{max}^{KCl} cm^{-1}: 1770 (lactone), 1725 and 1250 (acetate); m/z 446 $[M]^+$, 386 $[M-AcOH]^+$, 371 $[386-Me^{\cdot}]^+$, 344 $[386-C_2H_2O]^+$, 326 $[386-AcOH]^+$ and 311 $[326-Me^{\cdot}]^+$. On oxidation with Kiliani reagent, **1** yielded a diketone (**3**), mp 248–250°, $[\alpha]_D -45°$ ($CHCl_3$; c 0.4), IR ν_{max}^{KCl} cm^{-1}: 1760 (lactone), 1700 (six-membered C=O); m/z 358 $[M]^+$, 343, 329 and 205, indicating that both the hydroxy groups of **1** are secondary ones and are located in six-membered rings.

The ^{1}H NMR chemical shifts (Table 1) of the C-19 methyl protons of solanolide (**1**) and its acetate (**2**) were found to be very close to those of a co-occurring sapogenin, viz. neochlorogenin (**4**) and its acetate (**5**)[1], respectively. Since the chemical shifts of angular methyl protons are dependent[4, 5] on the position and orientation of the hydroxyl group in the androstane moiety, it can be presumed that solanolide possesses the same 3β, 6α-dihydroxy-5α-androstane ring system which was also supported by the multiplicity of the signals for H-3 (broad multiplet whose $W_{1/2}$ could not be measured correctly) and H-6 (*ddd*, $J = 10, 10, 4$ Hz). The presence of only one secondary methyl group resonating at somewhat lower field (δ 1.31, $J = 7$ Hz) indicated that Me-21 must be adjacent to the lactone carbonyl. Additional support for the substitution pattern in the A/B ring was also obtained from the spectrum of **3** which showed the expected chemical shift (δ 0.96) for the C-19 methyl group of such a 3, 6-diketo-5α-steroid[1, 2].

The above conclusions were also borne out by the ^{13}C NMR spectra (Table 2) of solanolide (**1**) and its derivatives (**2** and **3**). Thus, the chemical shifts for the A and B ring carbons of solanolide acetate (**2**) were in excellent agreement with the values found[10] for the 3β,6α-diacetoxy-spirostane sapogenin (**5**). The chemical shifts for the same carbons of the diketone (**3**) also corresponded with the calculated[11] values (C-1, 38.2; C-2, 37.3; C-4, 35.8; C-5, 58.1; C-7, 46.6; C-8, 38.0; C-9, 54.1 and C-10, 41.1) within ± 1 ppm, a deviation in reasonable agreement with the proximity of the two carbonyl functions. On the other hand, considerable differences in the resonance frequencies of C-15–C-17 and C-20–C-22 of **1–3** compared to those of **5** reflected the location of the lactone chromophore in the E ring.

Finally, the structure of the compound was established as 3β, 6α, 16β-trihydroxy-5α-pregnane-$20S$-carboxylic acid (22, 16)-lactone (**1**) by its correlation with neochlorogenin (**4**). Thus, neochlorogenin acetate (**5**) on oxidation with nitric acid[6] in Et_2O–$CHCl_3$ (4 : 1) at room temperature yielded a product exactly identical (mp, mmp, IR, TLC) with solanolide (**1**).

Only two other lactones of this type have so far been reported[6–9] from other *Solanum* species.

Acknowledgement—We are indebted to the Council of Scientific and Industrial Research, New Delhi, for a Junior Research Fellowship to B.D.

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