Phytochemistry, Vol. 20, No. 11, pp. 2547–2552, 1981.
Printed in Great Britain.

0031-9422/81/112547-06 $02.00/0

CHLORINATED WITHANOLIDES FROM *WITHANIA SOMNIFERA* AND *ACNISTUS BREVIFLORUS*

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(*Received* 16 *February* 1981)

Key Word Index—*Withania somnifera*; *Acnistus breviflorus*; Solanaceae; chlorowithanolides; steroidal lactones; X-ray structure.

Abstract—The structure of a new chlorinated withanolide isolated from the hybrid plants of *Withania somnifera*, chemotypes III (Israel) by Indian I, is established as the chlorohydrin of withanolide D (6α-chloro-4β,5β,20α_F-trihydroxy-1-oxo-22*R*-witha-2,24-dienolide). Two other known chlorinated withanolides had been isolated from different sources and additional data are provided, including the X-ray diffraction study of 4-deoxyphysalolactone (chlorohydrin of withanolide E). All available data are used for comparative analysis of the six known chlorinated withanolides. The origin of the chlorine atom in these compounds in the plants has been determined by carrying out a simple reaction of withanolide D with NaCl on silica gel.

INTRODUCTION

Halogenated compounds are not very widespread in nature. During our studies on the withanolides, the steroidal lactones occurring naturally in different plants of the Solanaceae family, three chlorinated withanolides **1a**, **2** and **3a** were obtained. One of them, **1a**, turned out to be a new compound, for which a structure elucidation is provided. Having in our hands three chlorowithanolides out of the six so far known, it seemed appropriate to make a detailed study of the group, collect the scattered information and add appropriate data concerning these rather unusual naturally occurring chlorocompounds.

The five chlorinated withanolides reported to date are: jaborosalactones C (**4**) and E (**5**) from *Jaborosa intergrifolia* [1]; 6α-chloro-5β-hydroxywithaferin A (**3a**), from *Withania frutescens* [2]; physalolactone (**6**) [3], and quite recently 4-deoxyphysalolactone (**2**) [4], both from *Physalis peruviana*. We now make a new addition to this list of 6α-chloro-5β-hydroxywithanolide D (**1a**) isolated from the hybrids of *Withania somnifera* Dun. chemotypes III (Israel) by Indian I [5]. Compound **2** is also isolated from the same plant species but a different chemotype collected from the mid-coastal plain of Israel (around Yavne), and compound **3a** from *Acnistus breviflorus* Griseb. Complete spectral data are provided for these three compounds. Furthermore, the X-ray analysis of compound **2** provides the first such analysis of a chlorinated withanolide. The origin of the chlorine atom in these compounds has been assigned to the mineral NaCl which is present in sizeable amounts in these plants.

RESULTS AND DISCUSSION

In order to determine unequivocally the location of the chlorine in the chlorowithanolides and enable a study of the conformational changes due to the presence of such an atom on the rest of the molecule, an X-ray analysis of one of these compounds was carried out. Compound **2** was chosen for this purpose since it was the best model in our hands, and also because the parent epoxide **8** was subjected to a similar study. The stereoscopic view of the crystallographically derived structure of **2** is shown in Fig. 1.

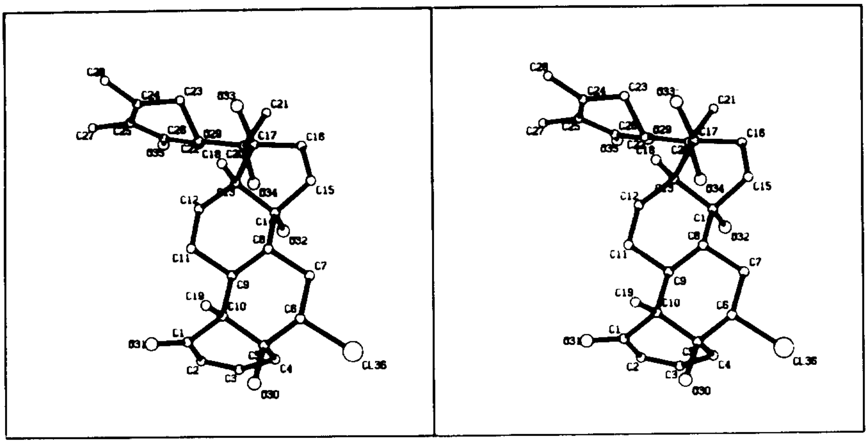
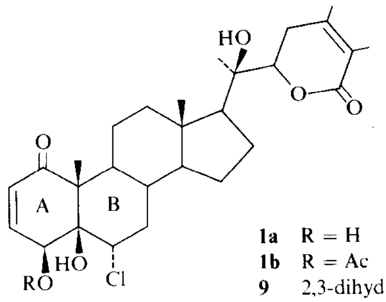


Fig. 1. Stereoscopic view of compound **2**.

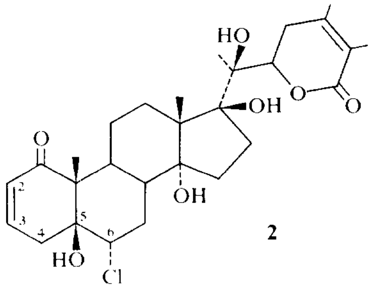
X-ray analyses have been carried out before on withaferin A [7], withanolide E (**8**) [8] and two derivatives [4, 9]. Comparing these analyses with that of compound **2** one can see that ring A is mostly flat, carbons 1, 2, 3, 4 and 5 being almost in one plane, with C-10 below it, while in the parent epoxide **8**, only carbons 1, 2 and 3 were considered as coplanar. Concerning ring B it is in this case a real chair and not a half chair like in **8**. The rest of the molecule has the same conformation.

A clear insight into the configurational influence on the pattern of ^{1}H NMR (Table 1) in the AB rings system of the chlorinated compounds could be obtained by comparing the 4-H and 4-OH derivatives as seen in **2** and **1a**. For a better evaluation the respective pairs of epoxy compounds were also compared, namely withanolide E (**8**) and withanolide D (**7**). Values of the different coupling constants were obtained by decoupling all the protons in turn.

The geminal coupling constant of the two 4-H in **2**, as well as in **8** is rather large (*ca* 20 Hz). We have previously analysed the reasons which may govern such a value [10, 11]; they are due first to the presence of the orbital system of the 2-en-1-one function, and secondly to the orientation of the electronegative substituent at C-5. The maximum effect is obtained when the angle (ϕ_1) formed by the *p* orbitals and the plane (*P*) that bisects the Hα–C(4)–Hβ group is 90°. Also a large effect is obtained when the angle (ϕ_2) existing between the C(5)–O bond and the plane *P* is 90°. The observed angles for the two compounds analysed by X-ray are $\phi_1 = 77°$, $\phi_2 = 104°$, $J = 19.7$ Hz for **2**, and $\phi_1 = 55°$, $\phi_2 = 10°$, $J = 18$ Hz for **8**.



1a R = H
1b R = Ac
9 2,3-dihydro, R = Ac



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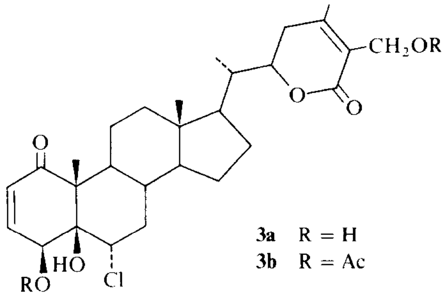
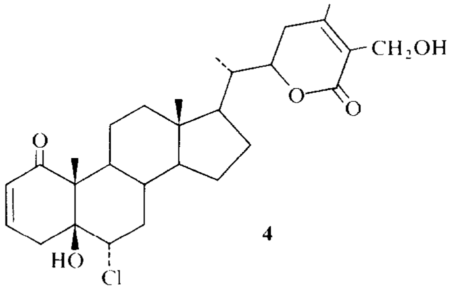


3a R = H
3b R = Ac



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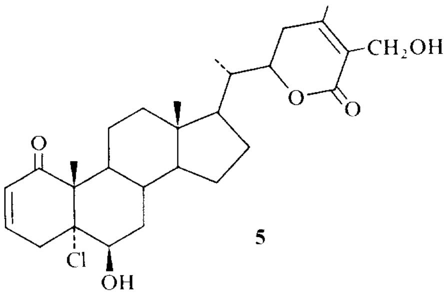

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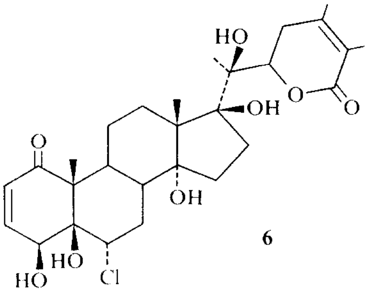

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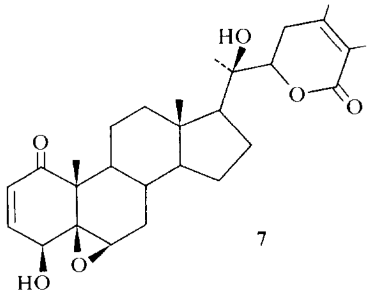

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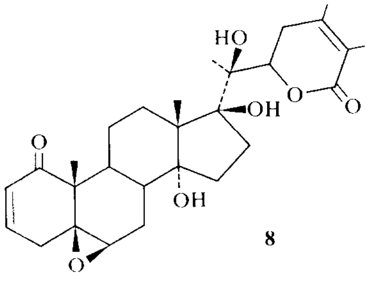

8

Table 1. ^{1}H NMR signals of relevant protons in chlorinated withanolides

						Methyl groups				
Compound	2-H	3-H	4-H	6-H	22-H	18	19	21	27, 28	
1a	6.00	6.47	5.08	4.44	4.18	0.81	1.22	1.25	1.87, 1.94	
	dd (10.0–1.9)	*dd* (10.0–2.5)	*m*	*dd* (12.3–5.3)	*dd* (13.2–3.5)	*s*	*s*	*s*		
1b	6.05	6.28	6.27	4.34	4.19	0.85	1.27	1.25	1.88, 1.95	4β-OAc 2.15
	dd (10.0–2.0)	*dd* (10.0–2.4)	*d* (1.8)	*dd* (9.9–4.6)	*dd* (13.1–2.7)	*s*	*s*	*s*		
2	5.99	6.77	3.03 4α-H	4.33	4.79	1.06	1.22	1.41	1.85, 1.92	
	dd (10.0–1.6)	*dq* (10.0–5.2–2.3)	*bdd* (19.7–2.3)	*dd* (9.1–7.6)	*dd* (10.0–6.0)	*s*	*s*	*s*		
			2.52 4β-H							
			(*bdd* 19.7–5.0)							
3a	6.02	6.48	5.05	4.40	4.40	0.69	1.27	0.98	2.04	27-H 4.40 *m*
	dd (10.3–1.9)	*dd* (10.3–2.3)	*m*	*m*	*m*	*s*	*s*	*d* (6.5)		
3b	6.07	6.30	6.26	4.35	4.41	0.69	1.28	0.98	2.06	27-OAc 2.16
	dd (9.9–1.8)	*dd* (9.9–2.0)	*t* (2.4)	*dd* (12.9–5.0)	*dt* (13.2–2.6)	*s*	*s*	*d* (6.7)		4β-OAc 2.09
										27-H 4.89 *d* (2.4)
9	—	—	6.08	4.36	4.19	0.84	1.18	1.25	1.88, 1.95	
			dd (11.3–5.5)	*dd* (12.8–4.0)	*dd* (13.6–2.9)	*s*	*s*	*s*		

Chemical shifts are in δ units; coupling constants (in Hz) are in parentheses.

In compound **8** the vicinal coupling constant existing between the 3-H and the gem-protons at C-4 is 2.3 Hz with the 4β-H axial, and 5 Hz with the 4α-H equatorial. The conversion of the 5β,6β-epoxide to the 6α,5β-chlorohydrin **2** interchanges the respective configurations of the two protons at C-4. The 2.3 Hz value is now due to the coupling of 3-H with 4α-H (ax) and the 5 Hz with the 4β-H (eq). A similar change takes place when the epoxide **7** is converted to the chlorohydrin **1a**, when the 4α-H equatorial in the former becomes axial in the latter. The respective values are thereby $J = 5$ and 2.3 Hz. Such an effect has been associated [12] with the fact that rings A and B with a 5β,6β-epoxide ring are fused in a way approaching a cholestane-type structure which, following the epoxide opening, assumes the all-chair coprostane type conformation.

The allylic coupling constant between 2-H and 4-H is also worth reporting. The variation of allylic coupling constant in relation to stereochemistry is well documented [13]. In the chlorinated withanolide **2** the allylic coupling constant $J = 1.6$ Hz of the 2-H is mainly due to the 4α-H (ax), as expected from the angle formed between the plane H-C(2)-C(3)-H and the direction of this proton having a value of 59°. In withanolide D (**7**) the allylic coupling of 2-H with 4α-H which is equatorial is too small to be recorded. However, in **1a** this coupling constant becomes 1.9 Hz, the 4α-H being axial.

Concerning the 19-Me resonance in **1a** (or **3a**), the value (δ 1.22) is a result of upfield shift by 0.22 ppm compared to **7**, since in the former both deshielding groups (5β,6β-epoxide the 4β-OH axial) are absent.

The chemical shift of 4α-H in **1a** is at a fairly low field (δ 5.08) and can be explained by analysing the influence of a 4β-OH group on its geminal proton. Comparing **8** and **7**, this OH group induced a change of this proton from δ 1.80 to 3.75 ($\Delta = 1.95$). Going from **2** to **1**, again the change was from δ 3.0 to 5.08 ($\Delta = 2.08$).

Interesting deductions could be made in the ^{13}C NMR in relation to the configurational changes taking place in the AB rings system of the chlorinated and non-chlorinated compounds. Comparing **1a**, **2** and **3a** (all having a 5β-OH group) to the epoxides **7** and **8** (Fig. 2), one observes for C-19 a shielding of about 7 ppm due to the γ-effect. Inversely, this 5β-OH γ-effect is lost for the C-7 as seen when comparing **1a** (39.1) to **7** (31.0) and **2** (31.6) to **8** (26.4). This can be accounted for by the fact that the 7β-H becomes equatorial in the chlorinated **1a** and **2** and thereby does not transmit the γ-effect. Concerning C-6, the usual position expected for a CH–Cl group is 45–60. The observed low value of 66 in **1a**, **2** and **3a** is therefore due to a β-effect of the 5-OH. It is noteworthy that this C-6 is not influenced by the 4β-OH present in both **1a** and **3a**, as is the case when one compares **7** to **8**: 61.9 against 64.5. As for the C-4, comparing **2** (34.5) to **8** (33.1) no sizeable change is observed, and the γ-effects are due to the Cl and O, transmitted through the equatorial 4β-H and axial 4α-H respectively. Ultimately, in compounds **1a** and **7** the lower values for C-4 (66.6 compared to 69.9) are due to the different relative orientations of the 5-oxygens as discussed above, and which produce different β-effects (see Table 2).

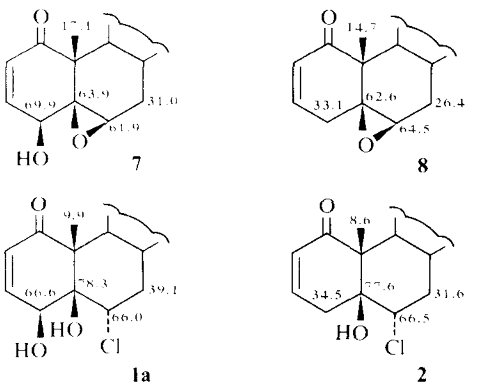

Fig. 2. Comparison of ^{13}C NMR data in rings A and B of chlorowithanolides (Table 2) and the parent epoxides **7**, **8** [14].

Finally, the new compound **1a** was submitted to heating under reflux with AcONa in AcOH and withanolide D (**7**) was obtained quantitatively. When **7** was treated with 32 % aq. HCl solution, the chlorohydrin **1a** was obtained, both compounds being identical (undepressed mixture mp, identical NMR and superimposable IR spectra).

The occurrence of six chlorinated withanolides induced us to seek and suggest a source for the chlorine atom in these compounds. Interestingly, in all of them the system involving the chlorine is a 6,5-chlorohydrin with an inverted configuration implying a diaxial opening of the epoxide usually present at this location. Furthermore, during our studies in the various species of this Solanaceae family we always encountered sizeable quantities of NaCl. We therefore thought that this mineral could be the origin of the chlorine and the cause of epoxide opening. This idea was tested experimentally by using withanolide D (**7**) as substrate. It was absorbed in EtOH solution on a mixture of silica gel–NaCl (2:1), and the dried powder was heated under vacuum at 100° for 24 hr. The reaction products were eluted from the inorganic carriers with EtOAc through a column and a product obtained in 10 % yield was identified as the chlorohydrin **1a**. The identification of the other products in this reaction will be described in a subsequent publication.

On this basis one could explain why in most, if not all, cases when an epoxide is present in major quantity, it is

Table 2. ^{13}C NMR spectral data for compounds **1a**, **2** and **3a**

	1a	**2**	**3a**		**1a**	**2**	**3a**
1-C	201.1	206.8	200.2	15-C	23.5	30.2	23.9
2-C	127.7	127.0	127.6	16-C	21.9	37.6	27.2
3-C	143.1	144.5	143.0	17-C	54.4	87.4	57.3*
4-C	66.6	34.5	66.6	18-C	13.7	20.6	11.8
5-C	78.3	77.6	78.6	19-C	9.9	8.6	9.9
6-C	66.0	66.5	66.0	20-C	80.7	78.8	38.7
7-C	39.1	31.6	39.0	21-C	20.6	19.0	13.3
8-C	34.5	39.1	35.0	22-C	80.7	81.0	78.2
9-C	45.7	37.3	45.8	23-C	31.3	32.3	29.8
10-C	55.7	55.7	55.3	24-C	149.3	152.0	152.9
11-C	22.5	22.9	22.7	25-C	121.8	121.3	125.7
12-C	39.2	34.5	39.3	26-C	165.6	167.8	166.9
13-C	43.1	54.9	43.1	27-C	12.5	12.2	57.3
14-C	57.2	82.2	57.2*	28-C	20.5	20.6	20.0

* Refer to interchangeable data.

Measurements were made on a Bruker WH-90 spectrometer at 22.63 MHz.

associated with a minor quantity of its chlorohydrin. Withanolide D (7), withanolide E (8), withaferin A, Jaborosalactone A, and 4β-hydroxywithanolide E are thus considered as the biogenetic parents of the chlorowithanolides 1–6, respectively. This association in the plant of chlorohydrin with its parent epoxide is not unique, and has been observed for example in a sesquiterpene [15].

The compounds isolated from different laboratories were not considered as artefacts. For confirmation, withanolide D (7) was submitted to the same extraction conditions and combination of solvents, and no trace of the corresponding chlorohydrin (1a) was detected. Moreover, during our experimental work the extracts before chromatography were carefully washed with water. These chlorowithanolides have to be therefore considered as naturally occurring, and presumably in the plant the process should be mediated by appropriate enzymes.

EXPERIMENTAL

Mps were measured on a Fischer–Johns apparatus and are uncorr. Optical rotations were determined in $CHCl_3$. IR spectra were recorded with KBr pellets; UV spectra were recorded for EtOH solns; ^1H NMR spectra were determined on a Bruker WH 270 instrument for ~1% solns in $CDCl_3$, containing TMS as int. standard. Liquid CC was done over Si gel G 60, using hexane–EtOAc mixtures as eluant. Analytical TLC was carried out using chromatoplates (50 × 75 mm, Si gel F_{254}), and prep. TLC using chromatoplates, 200 × 200 × 2 mm, Si gel 60 F_{254}. Mass spectra were determined under the direction of Dr. Z. Zaretskii. Analyses, of the samples dried under vacuum at 70° for 8 hr, were performed in the microanalytical laboratory of our Institute by Mr. R. Heller. X-Ray single-crystal analysis was made using three-dimensional intensity data collected on an Enraf–Nonius CAD-4 diffractometer.

*6α-Chloro-4β,5β,20α$_F$-trihydroxy-1-oxo-*22R*-witha-*2,24*-dienolide* (**1a**). Dry leaves (3.3 kg) of the hybrid plants (by cross pollination) of *Withania somnifera* chemotypes III (Israel) by Indian I (Delhi), grown in our experimental plots were extracted in the usual way [5]. The crude residue in $MeOH–H_2O$ (1:1) after initial washing with hexane was extracted with $CHCl_3$ instead of Et_2O. This extract was thoroughly washed with H_2O to remove soluble inorganic minerals; the resulting residue (73 g) in Me_2CO was adsorbed on Si gel (225 g) and was chromatographed over a bed of the same carrier (1.8 kg). Gradient elution was done with hexane–EtOAc mixtures and 1 l. fractions were collected. Compound **1a** was obtained from fractions 69 and 70 when the eluant composition was 50:50. The compound was purified by prep. thick layer chromatography. Mp 245–247° (EtOAc); $[\alpha]_D$ +19.8° (c 0.3); UV λ_{max}: 216 nm (ε 10 500); IR ν_{max} cm^{-1}: 3420, 1700 and 1685; MS (LR) m/z (rel. int.): 470 $[M - HCl]^+$ (1), 345 $[M - 125 - HCl]^+$ (51), 327 $[M - 125 - HCl - H_2O]^+$ (52), 309 $[M - 125 - HCl - 2H_2O]^+$ (32). MS (HR) m/z (rel. int.): 425.2065 $[C_{27}H_{32}O_2\ {}^{37}Cl]$ (1.8), 423.2060 $[C_{27}H_{32}O_2\ {}^{35}Cl]^+$ (2.9), 365.1664 $[C_{21}H_{28}O_3\ {}^{37}Cl]^+$ (13.5), 363.1692 $[C_{21}H_{28}O_3\ {}^{35}Cl]^+$ (34.6). (Found: C, 66.04; H, 7.90. $C_{28}H_{39}O_6Cl$ requires C, 66.46; H, 7.57%. MW 506.5.)

*4β-Acetoxy-6α-chloro-5β,20α$_F$-dihydroxy-1-oxo-*22R*-witha-*2,24*-dienolide* (**1b**). Compound **1a** (50 mg) was acetylated with Ac_2O pyridine at room temp. for 24 hr. The crude acetate **1b** (45 mg) cryst. from EtOAc, mp 232–235°; $[\alpha]_D$ +36.8° (c 0.3); UV λ_{max}: 216 nm (ε 11 400); IR ν_{max} cm^{-1}: 3400, 1735, 1705 and 1685. MS (LR) m/z (rel. int.) 548 $[M]^+$ (0.1), 423 $[M - 125]^+$ (13), 363 $[M - 125 - AcOH]^+$ (30), 327 $[M - 125 - AcOH - HCl]^+$ (12). MS (HR) m/z (rel. int.): 550.2534 $[M]^+$ $(C_{30}H_{41}O_7\ {}^{37}Cl)$ (0.8), 548.2556 $[M^+]$ $(C_{30}H_{41}O_7\ {}^{35}Cl)$ (1.6), 365.1664 $[C_{21}H_{28}O_3\ {}^{37}Cl]^+$ (13.5), 363.1692 $[C_{21}H_{28}O_3\ {}^{35}Cl]^+$ (34.6). (Found: C, 65.26; H, 7.85. $C_{30}H_{41}O_7Cl$ requires C, 65.75; H, 7.54%. M 548.5.)

Hydrochlorination of withanolide D (7). Powdered withanolide D (**7**) (100 mg) was triturated with 32% aq. HCl (2.0 ml) for 10 min, and was poured into H_2O (100 ml). The product after extraction with $CHCl_3$ and thick layer chromatography, yielded compound **1a** (50 mg) and unreacted 7 (45 mg), identical with authentic samples by mmp, IR and NMR spectra.

Compound 7 from **1a**. The chlorohydrin **1a** (50 mg) dissolved in glacial AcOH (15 ml) was refluxed at 120° for 12 hr, with dry NaOAc (50 mg) and was poured into H_2O (100 ml). The product obtained from its $CHCl_3$ extract (45 mg) cryst. from EtOAc and was found to be identical with withanolide D (mmp, IR and NMR spectra).

*4β-Acetoxy-6α-chloro-5β,20α$_F$-dihydroxy-1-oxo-*22R*-witha-*24*-enolide* (**9**). Compound **1b** (30 mg) was hydrogenated over 5% $Pd–CaCO_3$ in absolute EtOH, the 2,3-dihydro-derivative **9** crystallized from EtOAc, mp 226–228°; $[\alpha]_D$ 0° (c 0.15); UV λ_{max} nm: 212 (ε 4200 *sh*) and 232 (ε 4100); IR ν_{max} cm^{-1}: 3460, 1735, 1725 and 1713. MS (LR) m/z (rel. int.): 456 (0.1) and 454 (0.2) $[M - AcOH - 2H_2O]^+$, 427 (0.3) and 425 (0.1) $[M - 125]^+$, 367 (0.2) and 365 (0.6) $[M - 125 - AcOH]^+$, 331 (5) and 329 (15) $[M - 125 - 2H_2O - AcOH]^+$, 313 (9) and 311 (18) $[M - 125 - 3H_2O - AcOH]^+$. MS (HR): no genuine pairs of peaks were observed.

*6α-Chloro-5β,14α,17β,20α$_F$-tetrahydroxy-1-oxo-*22R*-witha-*2,24*-dienolide* (**2**). Dry leaves (1.75 kg) of *Withania somnifera* collected near the village of Yavne (mid-coastal plain of Israel) yielded after the usual extraction procedure [16] a residue (25 g) which was adsorbed on Si gel (80 g) and chromatographed over the same gel (600 g); 24 fractions of 500 ml each being collected. Fraction 13 (0.37 g) upon rechromatography yielded **2** (0.14 g). Mp 224–225° (EtOAc); $[\alpha]_D$ +82.5° (c 0.3); UV λ_{max}: 224 nm (ε 14 300); IR ν_{max} cm^{-1}: 3400, 1680 and 1670. MS m/z (rel. int.): 504 $[M - H_2O]^+$ (0.5), 486 $[M - 2H_2O]^+$ (0.5), 381 (3.5) and 379 (7) $[M - 125 - H_2O]^+$, 169 (40), 125 (80). (Found: C, 62.83; H, 7.76. $C_{28}H_{39}O_7Cl.\frac{1}{2}H_2O$ requires C, 63.21; H, 7.33%. MW 522.5). Crystal data: crystals of **2** are orthorhombic, space group $P\,2_12_12_1$, $a = 11.091$ (1), $b = 11.544$ (1), $c = 22.406$ (2) Å, $Z = 4$. Intensities of 2652 reflections (2510 classed as observed) were measured ($\theta \leq 25°$) using Mo-K_α radiation. The structure was solved by direct methods and refined to $R = 0.045$.

*6α-Chloro-4β,5β,27-trihydroxy-1-oxo-*22R*-witha-*2,24*-dienolide* (**3a**). Dry leaves (12 kg) of *Acnistus breviflorus*, the seeds of which were collected in Argentina and the plants grown in our experimental plot, yielded after the extraction procedure adopted for the above hydrid plants of *W. somnifera* a residue (90 g), which was adsorbed on Si gel (300 g) and chromatographed over the same gel (2.6 kg). Fractions of 1 l. were collected and compound **3a** was obtained from fractions 53–69 (hexane–EtOAc, 40:60) and purified by crystallization (0.32 g). Mp 277–280° (EtOAc); $[\alpha]_D$ +37.4° (c 0.4); UV λ_{max} 215 nm (ε 8500); IR ν_{max} cm^{-1}: 3400, 1690 and 1680. MS (LR) m/z (rel. int.): 508 (0.8) and 506 (1.6) $[M]^+$, 490 (0.3) and 488 (0.1) $[M - H_2O]^+$, 472 (0.7) and 470 (3.0) $[M - 2H_2O]^+$, 454 (0.8) and 452 (1.0) $[M - 3H_2O]^+$, 426 (3.5) and 424 (10.6), 257 (19.5) $[M - HCl - 125 - O]^+$. MS (HR) m/z (rel. int.): 508.2413 $[M]^+$ (3.5) $[C_{28}H_{39}O_6\ {}^{37}Cl]+$, 506.3927 (6.4) $[C_{28}H_{39}O_6\ {}^{35}Cl]$, 425.2271 $[C_{24}H_{36}O_4\ {}^{37}Cl]^+$ (40.4), 423.2288 $[C_{24}H_{36}O_4\ {}^{35}Cl]^+$ (100). (Found: C, 66.11; H, 7.82. $C_{28}H_{39}O_6Cl$ requires C, 66.46; H, 7.57%. MW 506.5.)

*6α-Chloro-4β,27-diacetoxy-5β-hydroxy-1-oxo-*22R*-witha-*2,24*-dienolide* (**3b**). Compound **3a** (50 mg) was acetylated with

Ac_2O–pyridine at room temp. for 24 hr. The crude diacetate **3b** (47 mg) crystallized from EtOAc, mp 245–247°; $[\alpha]_D$ +40.8° (*c* 0.2); UV λ_{max}; 215 nm (ε 10 800); IR ν_{max} cm^{-1}: 3400, 1735, 1712 and 1685. MS (LR) *m/z* (rel. int.): 592 (2%) and 590 (4.3) $[M]^+$, 550 (4.7) and 548 (11.9) $[M - COCH_2]^+$, 465 (20) $[M - 125]^+$, 428 (21.3) $[M - 126 - HCl]^+$, 368 (10.9) $[M - 126 - HCl - AcOH]^+$, 285 (10.4) $[M - 126 - 151 - H_2O]^+$, 123 (100). MS (HR) *m/z* (rel. int.): 409.2137 (1.4%) $[C_{27}H_{32}O\ ^{37}Cl]$, 407.2108 (2.8) $[C_{27}H_{32}O^{35}Cl]$, 349.1789 (0.9) $[C_{21}H_{28}O_2\ ^{37}Cl]^+$, 347.1798 (3.2) $[C_{21}H_{28}O_2\ ^{35}Cl]^+$. (Found: C, 64.85; H, 7.52%. $C_{32}H_{43}O_8Cl$ requires C, 65.14; H, 7.35%. MW 590.5.)

Acknowledgements—We thank Mr. Arieh Abraham, Agricultural Research Organization, Volcani Center, Bet Dagan, for carrying out the hybridizations, Dr. I. Kirson for fruitful discussions and Dr. H. E. Gottlieb for contributing in the spectral interpretations. S.S.N. (on leave of absence from Andhra University, Waltair, India) acknowledges a scholarship from the Deutscher Akademischer Austauschdienst.

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