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# STRUCTURE OF SOLANAVIOL, A NEW STEROIDAL ALKALOID FROM *SOLANUM AVICULARE*

KO KANEKO, KAZUAKI NIITSU, NAOTOSHI YOSHIDA and HIROSHI MITSUHASHI

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

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**Key Word Index**—*Solanum aviculare*; Solanaceae; steroidal alkaloid; spirosolane.

**Abstract**—A new alkaloid solanaviol ((22*R*, 25*R*)-spirosol-5-ene-3β,12β-diol) was isolated from *Solanum aviculare* in addition to solasodine as one of the main alkaloids. The structure of solanaviol was established by NMR spectroscopy, as well as by conversion into a known pregnane derivative and solasodine.

## INTRODUCTION

Solasodine (**2**) is one of the typical spirosolane alkaloids, contained as glycosides in several *Solanum* plants [1] (for instance in amounts of *ca* 1% in dried leaves of *Solanum aviculare* [2]) and it has been utilized as a starting material for the production of steroid hormones [3]. Steroidal glycoalkaloids have been generally extracted from plant material by diluted acetic acid, affording **2** after hydrolysis with hydrochloric acid. In our biogenetic studies on spirosolane and spirostane to detect alkaloids and sterols as precursors of both steroidal groups, the leaves of mature *Solanum aviculare* were extracted with ammoniacal chloroform–methanol. In addition to **2** and tomatidenol (**3a**), which was first isolated from *Solanum aviculare* in this work, solanaviol (**1a**) was isolated as the main alkaloid (the yield of **1a** was *ca* 0.05% and of **2** *ca* 0.01% in dried leaves).

## RESULTS AND DISCUSSION

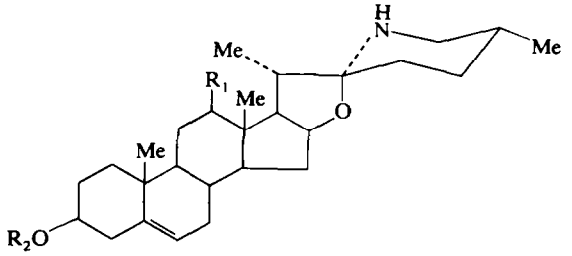
Solanaviol (**1a**), mp 229–232.5°, $[\alpha]_D$ −113° (*c* 0.97, $CHCl_3$), $C_{27}H_{43}NO_3$ (elementary analysis) afforded, by acetylation in acetic acid and hydrochloric acid [4], a monoacetate (**1b**), mp 225–229°, $\nu_{max}^{Nujol}$ 3550, 1720 $cm^{-1}$, δ 2.03 (3H, *s*). The $^1H$ NMR spectrum of **1a** displayed two singlets (3H each) at δ 0.81 and 1.04, indicative of C-18 and C-19 angular methyl groups of a normal steroidal ring system with a $\Delta^5$-double bond [5], two doublets (3H each, $J$ = 8 Hz) at 0.84 and 1.02 corresponding to two secondary methyl groups at C-21 and C-27, a signal at 4.34 (1H, *m*) for a hydrogen adjacent to the ether linkage at C-16, and a signal at 5.35 for a vinyl proton.

One of the other protons, a multiplet centered at δ 3.50, was associated with the α-hydrogen adjacent to the β-hydroxyl group at C-3 (this signal shifted downfield to δ 4.58 on acetylation), and the remaining proton appeared at 3.31 (1H, *dd*, $J$ = 12, 6 Hz) in **1b**. The MS of **1a** revealed ions at *m/e* 429 ($M^+$), 114 (base peak), and 138 (prominent peak) [6]. From these spectral data, it appeared that **1a** possessed a spirosolane skeleton with a β-equatorial hydroxyl group at C-1 or C-12 [7]. Chemical shifts of the methylene protons at C-26 (δ 2.63) and the α-hydrogen adjacent to the ether linkage at C-16 (δ 4.34) were almost the same as those in **2** (22*R*, 25*R*) but not those in **3a** (22*S*, 25*S*) [8].

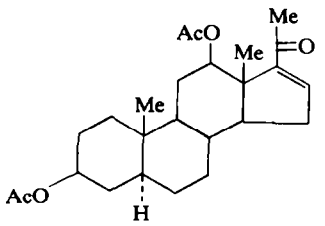
Comparison of the corresponding peaks of C-20, C-23 and C-26 in the $^{13}C$ NMR spectra of **1a**, **2** and **3b** indicated that those in **1a** were nearly the same as in **2** and differed from those of tomatidine (**3b**) [9], as shown in Table 1. The resonance of the C-18 methyl group shifted upfield (Δ δ = −6 ppm) because of γ-gauche interaction with β-equatorial hydroxyl group at C-12, and the two carbons at C-11 (Δ δ = + 10.5 ppm) and C-13 (Δ δ = + 5.5 ppm) shifted downfield because of the β-effect with the equatorial hydroxyl group at C-12, so that it seems reasonable to conclude that the second hydroxyl group in **1a** had a β-equatorial configuration at C-12. In the light of these spectral data, **1a** was assumed to be (22*R*, 25*R*)-spirosol-5-ene-3β,12β-diol.

In order to confirm the structure of **1a**, its conversion to a known pregnane derivative was performed. Compound **1a** was reduced with $PtO_2$ to dihydrosolanaviol (**4a**) which was acetylated in acetic anhydride/pyridine to the *O,O,N*-triacetate (**4b**) and oxidized with $CrO_3$ by the method of Sato [3] to the pregnane derivative **5**. The physical constants of **5** agreed well with those of 3β,12β-diacetoxy-5α-pregn-16-en-20-one which was prepared from hecogenin [10], and the mp of **5** was not depressed by admixture with an authentic specimen of 3β,12β-diacetoxy-5α-pregn-16-en-20-one.

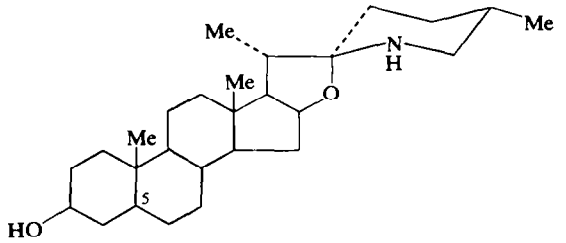
Finally, **1b** was oxidized with $CrO_3$ to solanavione-3-acetate (**6**), which was reduced by the Wolff–Kishner reduction [11] to **2**. The physical constants of **2** agreed well with those of solasodine, and the mp of **2** was not



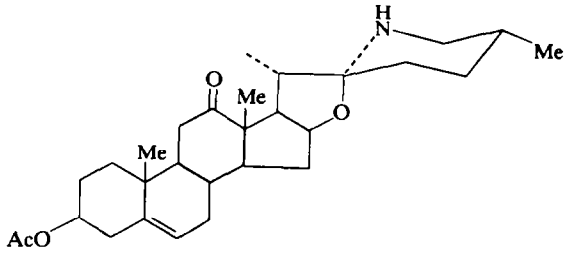
**1a** $R_1 = OH$, $R_2 = H$
**1b** $R_1 = OH$, $R_2 = Ac$
**2** $R_1 = R_2 = H$



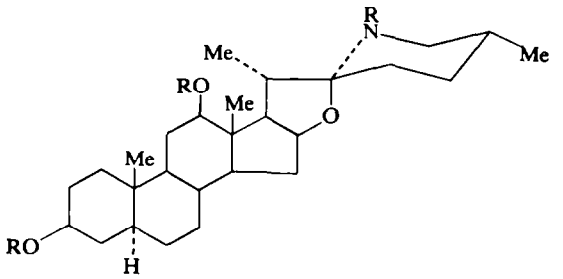
**5**



**3a** $\Delta^5$
**3b** 5α-H



**6**



**4a** R = H
**4b** R = Ac

Table 1. $^{13}C$ NMR chemical shifts of **1a**, **2**, and **3b***

| Carbon No. | **1a** | **2**† | **3b**† | Carbon No. | **1a** | **2**† | **3b**† |
|---|---|---|---|---|---|---|---|
| 1 | 37.2 | 37.3 | 37.0 | 15 | 31.7§ | 32.1 | 32.6 |
| 2 | 31.5‡ | 31.7 | 31.5 | 16 | 78.9 | 79.0 | 78.5 |
| 3 | 71.6 | 71.5 | 71.0 | 17 | 62.4 | 62.9 | 62.0 |
| 4 | 42.1 | 42.3 | 38.2 | 18 | 10.5 | 16.4 | 16.9 |
| 5 | 140.9 | 140.9 | 44.9 | 19 | 19.3 | 19.3 | 12.3 |
| 6 | 121.5 | 121.3 | 28.6 | 20 | 41.7 | 41.3 | 43.0 |
| 7 | 31.8§ | 32.1 | 32.3 | 21 | 14.6 | 15.2 | 15.8 |
| 8 | 30.5 | 31.5 | 35.0 | 22 | 98.5 | 98.4 | 99.3 |
| 9 | 49.7 | 50.2 | 54.4 | 23 | 34.2 | 34.1 | 26.6 |
| 10 | 36.7 | 36.7 | 35.5 | 24 | 30.4 | 30.3 | 28.6 |
| 11 | 31.4‡ | 20.9 | 21.1 | 25 | 31.5‡ | 31.5 | 31.0 |
| 12 | 79.7 | 40.0 | 40.2 | 26 | 47.7 | 47.7 | 50.2 |
| 13 | 46.0 | 40.5 | 40.9 | 27 | 19.3 | 19.3 | 19.3 |
| 14 | 55.1 | 56.6 | 55.8 | | | | |

*The solvent was $CDCl_3$; ppm from TMS.
†See ref. [9].
‡§These values may be reversed.

depressed by admixture with the authentic specimen of solasodine.

The mature *Solanum aviculare* plant contains **2** and **1a** as the main alkaloids, but **1a** does not occur in etiolated seedling and callus of this plant. Therefore, it seems most reasonable to conclude that **1a** is a metabolite of **2** in *Solanum aviculare*.

## EXPERIMENTAL

*Plant material. Solanum aviculare* Forst. f. was cultivated in the Experimental Station for Medicinal Plant Studies, Hokkaido University. Plants were harvested in the early autumn.

*Extraction and separation of alkaloids.* Dried and powdered leaves (4.5 kg) were extracted with ammoniacal $CHCl_3$–MeOH. The glycosidic part (552 g) was refluxed with N HCl in MeOH for 6 hr. Resulting crude alkaloid (9.2 g) was purified by chromatography on a column of 270 g of $Al_2O_3$ and the column was eluted consecutively with $C_6H_6$, $Et_2O$–$C_6H_6$, $CHCl_3$, and MeOH to give fractions containing solasodine (**2**) (515 mg) and tomatidenol (**3a**) (44 mg) (from $Et_2O$–$C_6H_6$ (1:9) fraction), and the new alkaloid, **1a** (2.3 g) (from $Et_2O$–$C_6H_6$ (1:4) fraction).

*Solanaviol* (**1a**). The compound from the $Et_2O$–$C_6H_6$ (1:4) fraction was crystallized from $Me_2CO$–hexane and recrystallized from $Me_2CO$ to colourless plates, mp 229–232.5°; $[\alpha]_D$ −113° (*c* 0.97, $CHCl_3$); MS *m/e*: 429 ($M^+$), 414, 411, 138, 125, 114 (base peak), 113; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3400, 1050, 965, 955, 875, 865; $^1H$ NMR ($CDCl_3$): δ 0.81 (3H, *s*), 0.84 (3H, *d*, *J* = 8 Hz), 1.02 (3H, *d*, *J* = 8 Hz), 1.04 (3H, *s*), 2.63 (2H, *m*), 3.50 (2H, *m*), 4.34 (1H, *m*), 5.35 (1H, *m*); $^{13}C$ NMR (see Table 1). (Calc. for $C_{27}H_{43}NO_3$: C, 75.48; H, 10.09; N, 3.26. Found: C, 75.47; H, 10.09; N, 3.21%).

*Solanaviol-3-acetate* (**1b**). Solanaviol (**1a**) was acetylated with HOAc and conc HCl to **1b**. Crystallization of **1b** from aq. MeOH gave colourless plates, mp 225–229°; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3550, 1720, 1030, 980, 975, 905, 890; $^1H$ NMR ($CDCl_3$): δ 0.81 (3H, *s*), 0.84 (3H, *d*, *J* = 7 Hz), 1.03 (3H, *d*, *J* = 7 Hz), 1.06 (3H, *s*), 2.03 (3H, *s*), 2.64 (2H, *m*), 3.31 (1H, *dd*, *J* = 12, 6 Hz), 4.31 (1H, *m*), 4.58 (1H, *m*), 5.39 (1H, *m*).

*Dihydrosolanaviol* (**4a**). A soln of **1a** (256.4 mg) in HOAc was stirred with $PtO_2$ (256 mg) and the mixture was worked up in the usual way to afford **4a**. Crystallization of **4a** from $Me_2CO$ gave 134.2 mg of colourless plates, mp 131–135°/216–219.5°; MS *m/e*: 431 ($M^+$), 416, 413, 138 (base peak), 114, 113; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3400, 1040, 980, 960, 895, 880; $^1H$ NMR ($CDCl_3$): δ 0.78 (3H, *s*), 0.83 (3H, *s*), 0.86 (3H, *d*, *J* = 7 Hz), 1.11 (3H, *d*, *J* = 7 Hz), 2.66 (1H, *m*), 3.29 (1H, *dd*, *J* = 12, 6 Hz), 3.61 (1H, *m*), 4.30 (1H, *m*).

*3β, 12β-Diacetoxy-5α-pregn-16-en-20-one* (**5**). A soln of **4a** (99.7 mg) in 3 ml Py and 0.9 ml $Ac_2O$ was refluxed for 2 hr and poured into ice $H_2O$, followed by addition of $NaHCO_3$ and NaCl. After 1 hr, **4b** was collected and dried (125.1 mg). Compound **4b** was dissolved in 5 ml HOAc and refluxed for 30 min. When cooled, a soln of $CrO_3$ (49 mg in 3.6 ml 80% HOAc) was added dropwise during 10 min, while cooling in a water bath. The reaction mixture was stirred for 1 hr at room temp., then $H_2O$ and a small amount of $NaHSO_3$ were added. The mixture was extracted with $Et_2O$. The $Et_2O$ extract (111.1 mg) was dissolved in 15 ml HOAc and refluxed for 5 hr. After removal of excess HOAc, the reaction mixture was neutralized with $NaHCO_3$ and extracted with $Et_2O$. The $Et_2O$ extract was purified by TLC and gave 18.2 mg (19%) of **5**. Crystallization of **5** from aq. MeOH gave colourless needles, mp 135–138.5°; MS *m/e*: 416 ($M^+$), 373, 356, 341, 313, 296, 281, 253, 147, 135, 43 (base peak); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1720, 1670, 1585, 1260, 1210; $^1H$ NMR ($CDCl_3$): δ 0.87 (3H, *s*), 1.02 (3H, *s*), 2.02 (3H, *s*), 2.11 (3H, *s*), 2.23 (3H, *s*), 4.67 (1H, *m*), 5.02 (1H, *dd*, *J* = 11, 5 Hz), 6.63 (1H, *m*); UV $\lambda_{max}^{EtOH}$ nm: 233 (log ε 4.10). The mp of **5** was not depressed by admixture with an authentic specimen of 3β,12β-diacetoxy-5α-pregn-16-en-20-one.

*Solanavione-3 acetate* (**6**). A soln of $CrO_3$ (54.3 mg in 10 ml 90% HOAc) was added dropwise over a period of 15 min to a stirred soln of **1b** (124.3 mg) in 5 ml HOAc while cooling in a water bath, and the mixture was stirred at this temp. for 15 min. $H_2O$ and a small amount of $NaHSO_3$ were added to the reaction mixture, which was made alkaline with $NaHCO_3$ and extracted with $Et_2O$. The product was purified by chromatography on an $Al_2O_3$ column. Elution with $Et_2O$–$C_6H_6$ (1:19) gave 44.7 mg of **6** and 49 mg of **1b**. Crystallization of **6** from MeOH gave colourless plates, mp 198–204°; MS *m/e*: 469 ($M^+$), 138, 125, 114 (base peak), 113; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3700, 1730, 1710, 1260, 1220, 1040, 980, 970, 900, 880; $^1H$ NMR ($CDCl_3$): δ 0.84 (3H, *d*, *J* = 6 Hz), 1.04 (3H, *d*, *J* = 7 Hz), 1.12 (3H, *s*), 1.13 (3H, *s*), 2.03 (3H, *s*), 2.59 (2H, *m*), 4.21 (1H, *m*), 4.59 (1H, *m*), 5.44 (1H, *m*).

*Wolff–Kishner reduction of* **6**. Wolff–Kishner reduction of **6** (109.1 mg) in the presence of $H_2NNH_2 \cdot 2HCl$ (10 mol equiv.) gave **2** (47.4 mg), which crystallized from $Me_2CO$ to colourless plates, mp 199–201°; $[\alpha]_D$ −103.4° (*c* 0.70, $CHCl_3$); MS *m/e*: 413 ($M^+$), 138, 114 (base peak), 113; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3400, 1050, 970, 960, 890, 870; $^1H$ NMR ($CDCl_3$): δ 0.82 (3H, *s*), 0.84 (3H, *d*, *J* = 7Hz), 0.96 (3H, *d*, *J* = 7 Hz), 1.00 (3H, *s*), 2.64 (2H, *m*), 3.45 (1H, *m*), 4.26 (1H, *m*), 5.30 (1H, *m*). (Calc. for $C_{27}H_{43}NO_2$: C, 78.40; H, 10.48; N, 3.39. Found: C, 78.58; H, 10.45; N, 3.28%). The mp of **2** was not depressed by admixture with an authentic specimen of solasodine.

*Tomatidenol* (**3a**). Elution of the $Al_2O_3$ column in the chromatography of the hydrolysed crude alkaloid with $Et_2O$–$C_6H_6$ (1:9) gave a mixture of **2** and **3a**. Compound **3a** was purified by TLC. Crystallization of **3a** from $Me_2CO$ gave colourless plates, mp 235.5–240°, $[\alpha]_D$ −39.5° (*c* 0.258, $CHCl_3$); MS *m/e*: 413 ($M^+$), 138, 125, 114 (base peak), 113; IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3350, 1065, 980, 970, 910, 890; $^1H$ NMR ($CDCl_3$): δ 0.86 (3H, *s*), 0.87 (3H, *d*, *J* = 6 Hz), 1.01 (3H, *d*, *J* = 7 Hz), 1.03 (3H, *s*), 2.78 (2H, *m*), 3.50 (1H, *m*), 4.14 (1H, *m*), 5.36 (1H, *m*). (Calc. for $C_{27}H_{43}NO_2$: C, 78.40; H, 10.48; N, 3.39. Found: C, 78.38; H, 10.55; N, 3.32%). The mp of **3a** was not depressed by admixture with an authentic specimen of tomatidenol.

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