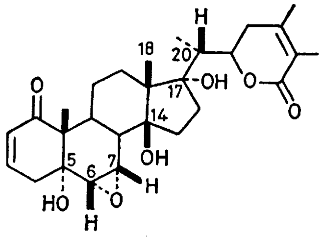
Novel Occurrence of 14β-Hydroxy-group on a Withanolide Skeleton; *X*-Ray Crystal and Molecular Structure of 14β-Hydroxywithanone

By S. Sarma Nittala, Felix Frolow, and David Lavie*

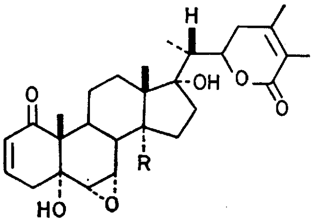
(*Departments of Organic Chemistry and Structural Chemistry, The Weizmann Institute of Science, Rehovot, Israel*)

Summary 14β-Hydroxywithanone (**1**), the first example of a 14β-substitution among withanolides, was isolated from *Withania somnifera* and its structure established by *X*-ray analysis.

The steroidal lactones of the withanolide group isolated from *Withania* and other genera of the Solanaceae family exhibit remarkable structural variations.[1] We now report the isolation, from hybrids of *W. somnifera*, of 14β-hydroxywithanone (**1**), the first example in this series of a 14β-substitution, which thereby produces a *cis*-fusion of the rings C and D.



(1)



(2) R = H
(3) R = OH

Compound (**1**), $C_{28}H_{38}O_7$ ($M^+ - H_2O$) 468·2478, m.p. 280 °C (EtOAc), $[\alpha]_D$ +36·7° ($CHCl_3$–MeOH 4: 1) gave ^1H n.m.r. ($CDCl_3$, 270 MHz) signals which indicated a withanone (**2**)-type substitution with a 5α-hydroxy-6α,7α-epoxy system[2,3] and a 14-OH group. However, the signals assigned to 7-H (β, eq) and 18-Me at δ 3·78 (dd, J 3·8 and 1·6 Hz) and 1·16 (s), respectively, were at too low-field to be due to these protons situated in the usual skeleton. Also, the C-20 methine proton, normally submerged in the high-field region, could be easily recognised in the ^1H n.m.r. spectrum of (**1**) at δ 2·67 (m). Hence, an *X*-ray crystal structure analysis of the compound was carried out.

Crystal data: (**1**), $C_{28}H_{38}O_7$, triclinic, space group $P1$, a = 6·456(3), b = 7·387(1), c = 13·572(1) Å, α = 77·75(1), β = 86·94(2), γ = 73·35(2)°, Z = 1. Intensities of 2599 reflections (2486 classed as observed) were measured ($\theta \leqslant 25°$) on a CAD-4 diffractometer with Mo-K_α radiation. The structure (Figure) was solved by direct methods and refined to R 0·053.†

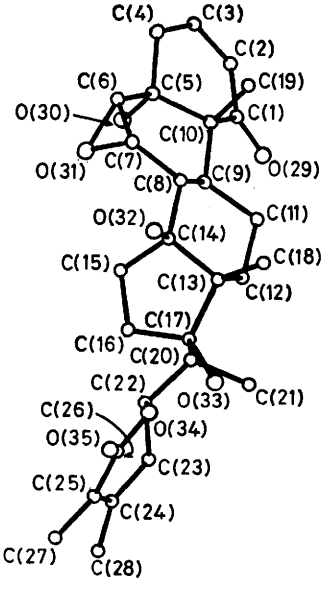


Figure. *X*-Ray crystal structure of compound (**1**).

---

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

A second new compound from the same plant, established as the epimeric 14α-hydroxywithanone (**3**), $C_{28}H_{38}O_7$, M^+ 486·2587, m.p. 250 °C ($CHCl_3$–MeOH), $[\alpha]_D$ +29·75° ($CHCl_3$–MeOH 4:1) exhibited the normal absorption features in its ^1H n.m.r. spectrum [δ 3·32 (dd, J 4 and 1 Hz, 7-H) and 0·97 (s, 18-Me)].

Compounds (**1**) and (**3**) were isolated during a re-examination of the hybrid plants resulting from the cross of two chemotypes, Indian I and chemotype III (Israel) of *Withania somnifera*.[3] The yield of (**3**) was about eight times less than that of (**1**). Biogenetically, withanone (**2**) may first undergo an enzymatic C-14 hydroxylation to give (**3**), with retention of configuration, followed by inversion, possibly *via* a C-14 carbonium ion. A side product of this process could be the Δ^{14} compounds reported earlier.[4]

Cardanolides and bufanolides are, so far, the only other known natural aglycones having a *cis*-fusion of the rings C and D.

We thank Mr. Arieh Abraham for carrying out the hybridisations and the Deutscher Akademischer Austauschdienst for a scholarship (to S. S. N., on leave of absence from Andhra University, Waltair, India).

(*Received, 28th October* 1980; *Com.* 1158.)

---

[1] E. Glotter, I. Kirson, D. Lavie, and A. Abraham in 'Bioorganic Chemistry,' ed. E. E. van Tamelen, Vol. II, Academic Press, New York, 1978, pp. 57—95.

[2] I. Kirson, E. Glotter, D. Lavie, and A. Abraham, *J. Chem. Soc. C*, 1971, 2032.

[3] I. Kirson, A. Abraham, and D. Lavie, *Isr. J. Chem.*, 1977, **16**, 20.

[4] A. Abraham, I. Kirson, D. Lavie, and E. Glotter, *Phytochemistry*, 1975, **14**, 189.