

suggested by Benkeser and shown in Chart I appears to be the simplest scheme that is consistent with all observations.

We have observed that no exchange occurs between methylchlorosilane and tri-*n*-butylamine deuteriochloride in the presence of *ca.* 1 *M* tri-*n*-butylamine. This is of interest especially since Benkeser has not been able to substitute methylchlorosilane for trichlorosilane in his reactions.⁹ We are currently investigating other systems in order to sort out the factors that are and are not responsible for the success of the exchange reaction.

Acknowledgment. We are extremely grateful to Dr. Leonard Spialter for many thought-provoking discussions of this material. In addition, we wish to express our thanks to Dr. Robert A. Benkeser for sharing his results and ideas with us.

(9) R. A. Benkeser, Purdue University, personal communication, 1969.

(10) Part of this work was done while the author was a Visiting Research Associate at Aerospace Research Laboratories, Wright-Patterson Air Force Base, under University of Cincinnati Contract No. AF 33(615)2272.

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Received October 30, 1969

The Structure of Solaphyllidine, a Novel 4-Ketosteroidal Alkaloid

Sir:

We wish to report the structure of a new steroidal alkaloid isolated from the leaves and green berries of *Solanum hypomalacophyllum* Bitter,¹ a tree native to the Venezuelan Andes. The most abundant alkaloid solaphyllidine (I) was obtained pure after repeated crystallization from methanol, mp 165–170°, [α]²⁰_D –25.4° (*c* 0.887, MeOH).

methyls, an acetoxy group, and four downfield protons in addition to an OH peak.

Acetylation of I with acetic anhydride-pyridine introduced three additional acetyl groups to yield II, mp 204–206° (from isopropyl alcohol), [α]²⁰_D –25.4° (*c* 0.75, MeOH), whose mass spectrum showed a parent ion at *m/e* 615. Major fragments at *m/e* 156 and 198 and the lack of fragment *m/e* 114 indicated conversion of the C₆H₁₂NO moiety to an N,O-diacetyl derivative.

Hydrogenation of I in acetic acid solution with PtO₂ led to the dihydro base III, mp 246–248° (from acetone), [α]²⁰_D –46.5° (*c* 0.28, MeOH).

Mild hydrolysis of I with K₂CO₃-MeOH produced the diacetyl base IV, mp 272–276°, [α]²⁰_D +48.3° (*c* 0.258, MeOH). The mass spectrum of IV has a molecular ion at *m/e* 447 (C₂₇H₄₅NO₄) and the same base peak at *m/e* 114. The ir spectrum still exhibited a sharp band at 1730 cm⁻¹. It was concluded that, in addition to the original acetyl group, I must have a ketonic carbonyl group. A keto group α to the C-3 hydroxyl group³ would explain the peak at 1670 cm⁻¹ in the ir spectrum of I and the strong diamagnetic shift (0.3 ppm) shown by the C-19 methyl group of III.

Reduction of I with LiAlH₄ in ether afforded the tetraol V, C₂₇H₄₉NO₄, resulting from reduction of the carbonyl and hydrolysis of the O-acetyl group. The ir spectrum of V showed no absorption at all between 1800 and 1500 cm⁻¹. Acetylation of III with acetic anhydride-pyridine rendered a pentaacetylated derivative VI, mp 210–211° (from acetone-petroleum ether).

An X-ray diffraction analysis of a single crystal of I which contained no heavy atoms has confirmed and supplemented these observations and established the stereochemistry, except for the absolute configuration which has been assumed to be the same as that determined for cholesterol. The atoms in the unit cell were located by means of the E map computed with phase angles derived directly from structure factor magnitudes

Table I. Nuclear Magnetic Resonance Data (CDCl₃) on Solaphyllidine and its Derivatives^a

	(C-18) CH ₃	(C-19) CH ₃	(C-27) CH-CH ₃	(C-21) CH-CH ₃	(C-22) H CH C-CHNH-	(C-23) CH -CH ₂ -CH-OH	(C-3) -CO CH-CH-OH	(C-16) CH-OAc	O C-CH ₃
I	0.69	0.72	0.82	0.91	2.95	3.43	4.10	4.96	2.03
II	0.70	0.78	0.82	0.96	3.35	4.95	5.26	5.11	2.05, 2.13
III	0.75	1.01	0.82	0.91	2.93	3.40	3.63	4.87	2.01
IV	0.69	0.69	0.82	0.91	2.87	3.48	4.09	4.17	

^a Chemical shifts in δ ; TMS internal reference; I, II, IV in CDCl₃, III in CD₃OD.

High-resolution mass spectrometry indicated the molecular formula of I to be C₂₉H₄₇NO₅. The base peak at *m/e* 114 suggested a hydroxytetrahydropyridinium ion.² Fragments at *m/e* 447 (*M* – 42) and *m/e* 429 (*M* – 60) and ir bands at 1255 and 1730 cm⁻¹ suggested the presence of an O-acetyl group. A hydroxyl band at 3430 cm⁻¹ and a small band at 1670 cm⁻¹ were also present. The 100-Mc nmr spectrum (Table I) showed the presence of two tertiary C-methyls, two secondary

using the symbolic addition procedure for noncentrosymmetric crystals.^{4,5}

The space group is P2₁2₁2₁ with four molecules in the unit cell with *a* = 15.24, *b* = 10.32, and *c* = 17.50 Å. Independent reflections (2600) were recorded with Cu K α radiation by the multiple-film, equinclination Weissenberg technique and their intensities were estimated visually. Initial phases for the E_{*hki*} were obtained by means of a sum of angles formula⁵ and were

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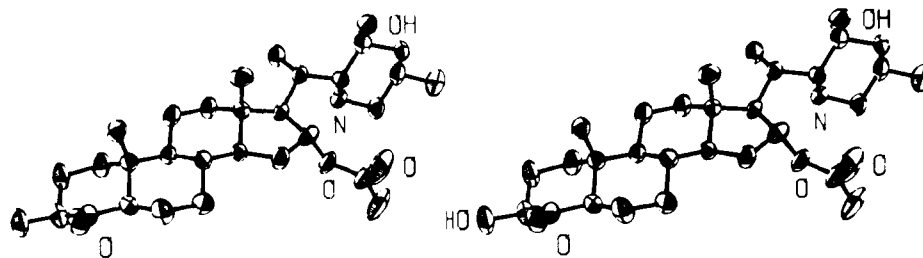


Figure 1. Stereodrawing of the configuration of solaphyllidine as determined by X-ray analysis. The drawing was made by a computer program prepared by C. K. Johnson, Oak Ridge National Laboratory. The picture should be viewed with a three-dimensional viewer for printed stereophotographs (commercially available, e.g., from Hubbard Scientific Co. Northbrook, Ill.).

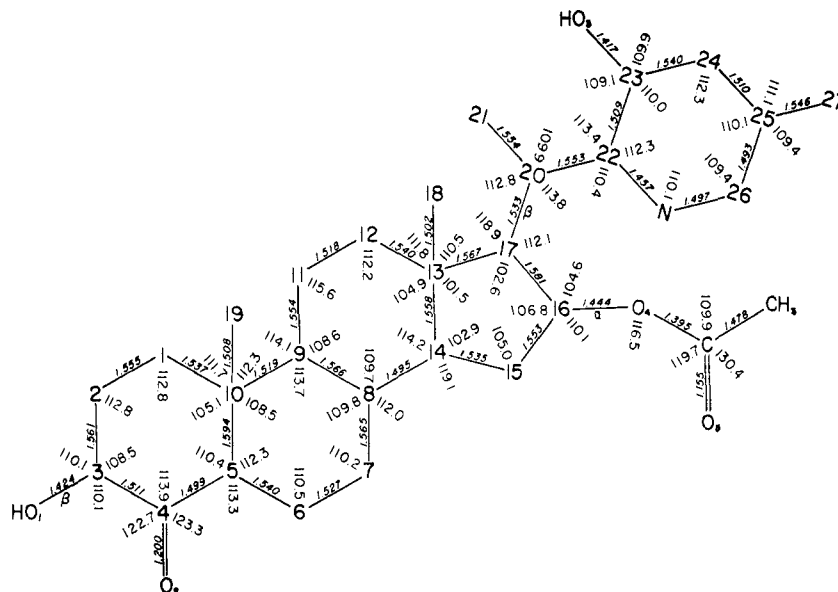
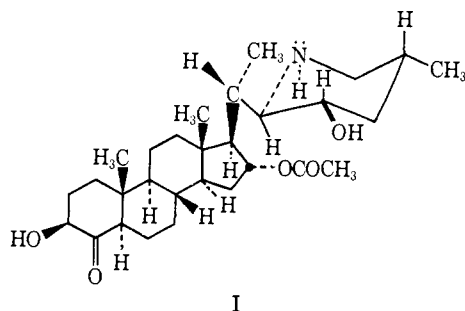


Figure 2. Bond lengths and angles of solaphyllidine. Additional angles are: 5-10-19, 109.2°; 1-10-9, 109.8°; 12-13-17, 115.3°; 14-13-18, 112.2°.

based on three phases assigned to specify the origin and four phases assigned symbols of unknown value, one of which determined the enantiomorph. In the course of phase determination, relationships occurred among all the symbols so that values could be assigned to them, except for one which was determined to have a value either $+\pi/2$ or $-\pi/2$. Of the two E maps computed, one revealed the positions of the C, N, and O atoms. Thirty-two of the 51 hydrogen atoms were found in a difference map. The total number of atoms to be found included one molecule of CH_3OH which cocrystallized with the steroid. Refinement of the structural parameters resulted in an *R* factor of 9.9%.

Solaphyllidine (I) is completely extended with ring junctions A/B, B/C, and C/D all *trans*. The average planes of the O-acetyl group and the 3-hydroxy-5-methylpiperidyl group are nearly perpendicular to the average plane of the steroid nucleus (Figure 1). Rings



A, B, C, and E are in the chair conformation even though ring A is a substituted cyclohexanone. Ring D has the β -envelope conformation with atom C(13) 0.68 Å out of the plane of the other four atoms. The asymmetric centers are 22R, 23S (eq), and 25R (eq). Bond lengths and angles are illustrated in Figure 2.

Solaphyllidine is a new possible intermediate in the (still hypothetical) chain of events that leads to the biosynthesis of solanum and veratrum alkaloids.^{6,7} In addition to batrachotoxin,⁸ samandarine,⁹ and veratrobasin,¹⁰ solaphyllidine is a new steroidal alkaloid for which exact X-ray data have now become available.

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Received October 1, 1969