dilution with water, it was neutralized with sodium bicarbonate and extracted with ether. The ether layer was washed with sodium bicarbonate solution and water, and dried over anhydrous sodium sulfate. The residue (215 mg.) after removal of the solvent was recrystallized from methanol-water or chromatographed over alumina (ether eluate) and gave 152 mg. (76%) of IVA, m.p. 169–173°, analytical sample, m.p. 173–175.5°, $[\alpha]_D^{20}$ −35° ($CHCl_3$), λ_{max}^{EtOH} 239 mμ (log ε 4.0), identical in all respects with an authentic specimen.

Anal. Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.45; H, 9.11.

In a continuous operation from solasodine (IA) (1 g.) using 3.8 mole equiv. of acetic anhydride for the acetylation and without purification or isolation of the intermediates, an over-all yield of 65% of IVA, m.p. 169–173° was obtained.

A small amount of the lactone and a second component presumably the 3,5-diene were often detected by infrared spectra in these oxidations.

Oxidation of IIIB to 3β-acetoxy-5α-pregn-16-en-20-one (IVB). A solution of chromic anhydride (146 mg., 2 mole equiv.) in 10 ml. of 80% aqueous acetic acid was added over a period of 15 min. to a stirred solution of 365 mg. of IIIB in 16 ml. of acetic acid while cooling (10–20°). After stirring for 1 hr. at room temperature, the reaction mixture was worked up as described above for IVA and 285 mg. of oxidation product was obtained. Purification of the crude product by recrystallization from methanol-water or chromatography on alumina gave 206 mg. (79%) of IVB, m.p. 163–166°, analytical sample m.p. 165–167°, $[\alpha]_D^{20}$ +42° ($CHCl_3$), λ_{max}^{EtOH} 239 mμ (log ε 3.98). It agreed in all properties with an authentic sample.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.58.

In a continuous operation from tomatidine (IB), analogous to solasodine, an over-all yield of 68% of IVB was obtained.

Oxidation of IIIC *to 3β-acetoxy-5α-pregn-16-en-20-one* (IVB). A solution of chromic anhydride (90 mg., 2 mole equiv.) in 7 ml. of 80% aqueous acetic acid was added over a period of 15 min. to a stirred solution of IIIC (230 mg.) in 8 ml. of acetic acid while cooling. After stirring for 1 hr. the reaction mixture was worked up in a manner similar to that described above for IVA. The crude product (188 mg.) was chromatographed over alumina; the fraction eluted with ether gave 123 mg. (75%) of IVB, m.p. 163–166°, identical in all respects with an authentic specimen.

Solasodine (IA) *from* VIA. A solution of 100 mg. of VIA in 20 cc. of 10% methanolic potassium hydroxide was refluxed for 12 hr. After partial concentration of the volume and addition of water, the product was collected and dried. Upon crystallization from aqueous methanol or chromatography over alumina (Grade II eluted with 2% methanol in ether), 61 mg. (80%) of IA, m.p. 199–202°, was obtained, identical in every respect with an authentic specimen of solasodine.

Tomatidine (*IB*) *from VIB.* Tomatidine was obtained from VIB in the same manner as described above for solasodine.

BETHESDA 14, MD.

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

The Chemistry of the Spiroaminoketal Side Chain of Solasodine and Tomatidine. II.[1] Chemistry of 3β,16β-Diacetoxy-20-(2′-Δ$^{2'}$-*N*-acetyl-5′-methyltetrahydropyridyl)-5-pregnene

YOSHIO SATO AND NOBUO IKEKAWA[2]

Received September 24, 1959

The chemistry and the manifold interrelationship of the acetylated tetrahydropyridyl pregnenes and the diacetylaminofurostadiene derivative obtained in the treatment of solasodine with acetic anhydride are discussed.

The reaction of solasodine (I) with acetic anhydride[3] (three hours boiling) leads to the formation of a gummy resinous mass which is presumably a mixture of 26-aminodiacetyl-5,20(22)-furostadien-3β-ol acetate[4] (III), Δ$^{22(23)}$ tetrahydropyridylpregnene derivative IIA and the probable isomeric Δ$^{20(22)}$ piperidylpregnene derivative IIB. Upon chromatography[3] of this mixture on alumina, III is readily deacetylated and emerges from the column as 26-acetylamino-5,20(22)-furostadien-3β-ol acetate (VIa). It can be reconverted to the original hitherto unisolated crystalline aminodiacetyl derivative III by treatment with acetic anhydride and pyridine. The degradation of VIa to 3β-acetoxy-5,16-pregnadien-20-one has been described in the foregoing paper.[1] Compounds IIA and IIB, which are eluted from the column as an amorphous mixture, are assigned their structures from considerations of spectroscopic and chemical data. The mixture exhibits an ultraviolet absorption band at 236 mμ (log ε, 3.95) consistent with the assignment of an α,β-unsaturated acetylamino function.[5,6] The infrared spectrum reveals the

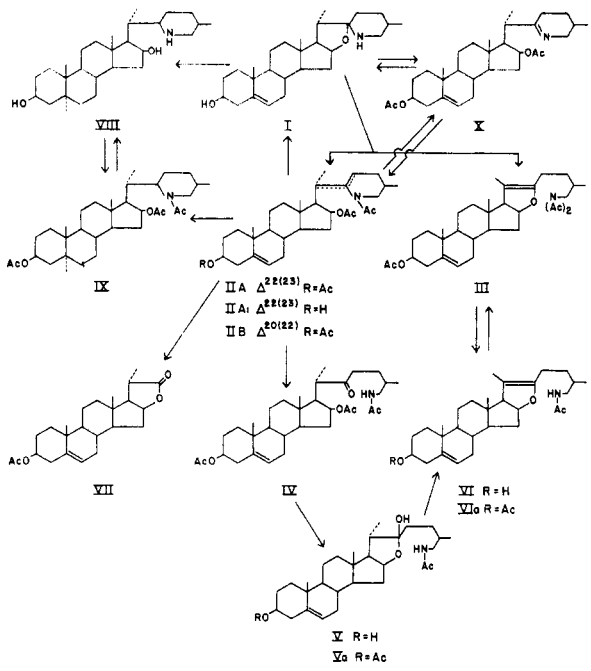
(1) Part I, Y. Sato, N. Ikekawa, and E. Mosettig, *J. Org. Chem.*, **25**, 783 (1960).

(2) Visiting Scientist, National Institutes of Health.

(3) Y. Sato, H. G. Latham, Jr., and E. Mosettig, *J. Org. Chem.*, **22**, 1496 (1957).

(4) *Cf.* Y. Sato, A. Katz, and E. Mosettig, *J. Am. Chem. Soc.*, **74**, 538 (1952). Compound III has never been directly isolated from the reaction mixture. It is assumed that the reaction proceeds in the same manner as with tomatidine where the corresponding 26-aminodiacetyl derivative can be directly crystallized from the reaction mixture. The chemistry of these related tomatidine derivatives will be discussed in a forthcoming publication.

(5) G. Rosenkrantz, O. Mancera, F. Sondheimer, and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956).



presence of an ester (5.78 μ) and a probable unsaturated tertiary amide (5.98, 6.07 μ) group.[6] Hydrolysis of this mixture with hydrochloric acid in acetic acid proceeds readily to yield the acetylamino ketone IV in good yields. The ease of hydrolysis of Δ^2-tetrahydropyridines is well known.[7] Another component in varying amounts (3–10%), along with the mixture of IIA and IIB and pure VIa, has been obtained from this chromatography.[1] It has been identified as IV and therefore considered as arising primarily from the mixture IIA and IIB as the result of hydrolysis taking place in the alumina column. A small amount of IV may have been present originally as a very rapid chromatography yields about 3% of IV. Compound IV displays the following absorption bands: $\lambda_{max}^{CHCl_3}$ 2.94 μ (N-H), 5.80 μ (OAc and CO), 6.0, 6.62 μ (HN-Ac), $\lambda_{max}^{CS_2}$ 5.75 μ (OAc), 5.83 μ (CO); $\lambda_{max}^{C_2H_5OH}$ 286 mμ (log ϵ, 1.85) and behaves chemically as expected. When IV is subjected to hydrolysis with methanolic alkali, hemiketal formation between the C-16 hydroxyl and C-22 carbonyl takes place and the compound, 26-acetylamino-3β,22-dihydroxy-5-furostene (V) is obtained. Hemiketalization of this type has been observed in the reduction of 5,6-dihydrokryptogenin diacetate[8] with Raney nickel. The 3-acetate of diol V (Va) has also been prepared by treating solasodine diacetate with hydrochloric acid in dioxane.[9] When V is refluxed briefly with acetic acid, it is converted into the pseudo derivative, 26-acetylamino-5,20-(22)-furostadien-3β-ol (VI), which is identical with the 3-alcohol of pseudodiacetylsolasodine (VIa) obtained from *O,N*-diacetylsolasodine.[1]

Further support for structures IIA and IIB has been derived from the synthesis of the crystalline compound IIA (m.p. 166–169°) through another route, *i.e.*, by allowing pesudosolasodine B[3] (X) to stand at room temperature with acetic anhydride in the presence of pyridine. The original mixture, when seeded with IIA thus obtained, yielded a fair amount of crystalline IIA. The samples from these two sources were identical in all respects and gave identical transformation products (I, IIA1, and IV). The $\Delta^{20(22)}$-isomer[10] has not been obtained as yet in crystalline form.

Although the above data do not preclude the alternate $\Delta^{20(22)}$ position for the site of unsaturation in IIA, the Δ^2-tetrahydropyridine structure is favored and is provisionally assigned to IIA on the basis of the recognized greater stability of the endocyclic double bond as compared with an exocyclic bond.[11] Chromic acid oxidation of IIA and IIB in aqueous 80% acetic acid did not permit a decision between IIA and IIB, as both pregnadienolone (3β-acetoxy-5,16-pregnadien-20-one) and the lactone, 3β-acetoxy-16β-hydroxy-5-bisnorcholenic 22→16-lactone (VII) were obtained from the amorphous mixture as well as from pure IIA. It is of interest to note that oxidation of IIA conducted under anhydrous conditions (sodium dichromate–benzene–acetic acid) yielded no identifiable product. Thus in aqueous media hydrolysis to the ketone precedes oxidation.

The catalytic reduction and subsequent alkaline hydrolysis of the amorphous mixture, IIA and IIB yields tetrahydrosolasodine identical with an authentic specimen prepared from the direct catalytic reduction of solasodine. Of some interest in this reduction is the resinous nature of the triacetyltetrahydrosolasodine[12] (IX) as compared with the

(6) R. Griot and T. Wagner-Jauregg, *Helv. chim. Acta*, **42**, 121, 605 (1959).

(7) A. Lipp, *Ann.*, **289**, 173 (1896); A. Lipp and E. Widnmann, *Ber.*, **38**, 2471 (1905).

(8) H. Hirschmann and F. B. Hirschmann, *Tetrahedron*, **3**, 243 (1958).

(9) Y. Sato and N. Ikekawa, *J. Org. Chem.*, Part III.

(10) The fact that the hydrolysis of the amorphous mixture yields IV in high yields and the good agreement of the elemental analysis[1] with formulas IIA and IIB point strongly to a mixture of isomers. The ultraviolet absorption band and extinction coefficient of the oil remaining after removal of IIA do not differ appreciably from the original mixture. Although the infrared spectra are practically identical some subtle differences, notably in the C—H stretching and deformation vibration regions are observed. Differences in the respective specific rotations are more pronounced (−3° to −36°). Attempts at obtaining homogeneous IIA by acid catalyzed isomerization of the amorphous mixture failed. IIA is also stable in boiling acetic anhydride. Thus IIA and IIB are not in equilibrium.

(11) R. B. Turner and R. H. Garner, *J. Am. Chem. Soc.*, **80**, 1424 (1958).

(12) This is probably due to contamination by the C-22 epimer arising from the reduction of the mixture IIA and IIB. The reduction of solasodine to tetrahydrosolasodine (VIII) probably proceeds stereospecifically because of the rigid spatial configuration of the spiroaminoketal side chain.

crystalline triacetyl derivative[13] prepared from I via VIII.

Finally it is of interest to note that the treatment of IIA or the amorphous mixture with acetic acid or with hydrogen chloride gas in ether-benzene solution affords pseudosolasodine B (X).

EXPERIMENTAL[14]

3β,16β-Diacetoxy-20-(2′-Δ²′-N-acetyl-5′-methyltetrahydropyridyl)-5-pregnene (IIA) *and the 3-alcohol* (IIA1) *from* IIA *and the amorphous mixture.* The preparation and properties of the original amorphous substance are described in Part I of this series. The crystalline compound (IIA) was prepared in the following manner. A solution of 150 mg. of pseudosolasodine B[3] (X) in 5 ml. of pyridine and 2 ml. of acetic anhydride was allowed to stand for 20 hr. at room temperature. It was then poured on ice water and extracted with ether. The residue from the ethereal extract was chromatographed on alumina. Elution with ether yielded 127 mg. of the unsaturated triacetyl derivative, m.p. 166–169° (ether-hexane); $[\alpha]_D^{20}$ +97° ($CHCl_3$); $\lambda_{max}^{C_2H_5OH}$ 236 mμ (log ε, 3.93).

Anal. Calcd. for $C_{33}H_{49}O_5N$: C, 73.43; H, 9.15. Found: C, 73.10; H, 9.24.

When the amorphous mixture IIA and IIB (130 mg.) dissolved in ether-hexane was seeded with crystalline IIA thus obtained, it afforded 82 mg. of a crystalline substance (heavy columns, m.p. 120–150°) which when twice recrystallized from the same solvent melted at 165–168° (22 mg.). This agreed in every respect (melting point, mixture melting point, rotation and infrared spectrum) with IIA obtained from X.

The mother liquor yielded an amorphous matter, $[\alpha]_D^{20}$ −36° ($CHCl_3$), $\lambda_{max}^{C_2H_5OH}$ 236 mμ (log ε, 3.94) which exhibited infrared spectra bands similar to but not identical with IIA.

The *3-alcohol* IIA1, of amorphous IIA and IIB was prepared by hydrolysis with 2% methanolic potassium hydroxide (30 min. refluxing). The product was chromatographed over alumina and the substance was eluted with ether-methanol (0.5%) collected as the 3-hydroxy compound, m.p. 192–196° (acetone-hexane), $[\alpha]_D^{20}$ +107° ($CHCl_3$), $\lambda_{max}^{CHCl_3}$ 2.77, 2.90 μ (hydroxyl); 5.78 μ (acetoxyl); 5.98, 6.08 μ (unsaturated tertiary amide).

Anal. Calcd. for $C_{31}H_{46}O_4N$: C, 74.95; H, 9.34. Found: C, 74.66; H, 9.31.

The mild alkaline hydrolysis of IIA in the above manner yielded IIA1 identical with IIA1 from amorphous IIA and IIB.

On the other hand the vigorous alkaline hydrolysis of IIA (10% potassium hydroxide in methanol for 12 hr.) produced the starting material solasodine (I) as in the case of amorphous mixture.[1]

3β,16β-Diacetoxy-26-acetylamino-5-cholesten-22-one (IV). A solution of 285 mg. of the amorphous mixture of IIA and IIB, 8 ml. of acetic acid, and 1.5 ml. of 4*N* hydrochloric acid was allowed to stand at room temperature for 45 min. After addition of excess water and partial neutralization with sodium bicarbonate solution, the precipitate was collected, dried, and crystallized from acetone-hexane. The compound (plates, 220 mg.) melted 168–171°. An analytical sample recrystallized from the same solvent pair melted 175–178°, $[\alpha]_D^{20}$ +9° ($CHCl_3$) and possessed the infrared and ultraviolet spectra bands as described in the text. An attempt to form the oxime with hydroxylamine hydrochloride in the presence of potassium acetate in methanol failed.

Anal. Calcd. for $C_{33}H_{51}O_6N$: C, 71.06; H, 9.22; N, 2.51. Found: C, 70.94; H, 8.96; N, 2.59.

IIA also yielded IV when hydrolyzed in the same manner with the above reagents. When IV thus obtained was compared with the sample, m.p. 175–178°, obtained from the chromatography (ether-2% methanol eluate) of the reaction mixture[1] of solasodine with acetic anhydride, it agreed in properties (melting point and infrared spectrum) with the latter.

26-Acetylamino-5-furostene-3β,22-diol (V). One hundred milligrams of the 22-oxo derivative IV was dissolved in 10 ml. of 2% methanolic potassium hydroxide and refluxed for 1.5 hr. After removal of the methanol *in vacuo*, water was added to the residue and the compound taken up in chloroform. The substance recovered from the chloroform phase was crystallized from acetone-hexane, m.p. 119–122°, $[\alpha]_D^{20}$ −55° ($CHCl_3$), $\lambda_{max}^{CHCl_3}$ 2.78, 2.90 μ (OH, NH), 5.99, 6.58 μ (HNAc).

Anal. Calcd. for $C_{29}H_{47}O_4N$: C, 73.52; H, 10.00. Found: C, 73.78; H, 10.22.

The *acetate* Va of the above diol V prepared in the usual manner (acetic anhydride-pyridine-room temperature, 15 hr.) and chromatographed on alumina (elution with 3% methanol in ether) yielded plates (aqueous acetone) m.p. 152–155°; $\lambda_{max}^{CHCl_3}$ 2.81 μ (OH); 2.92 μ (N—H); 5.80 μ (OAc); 6.00, 6.63 μ (HNAc). Its spectrum agreed with that of the substance obtained from the treatment of diacetylsolasodine with 2*N* hydrochloric acid in dioxane.[9]

26-Acetylamino-5,20(22)-furostadien-3β-ol (VI). The diol V (40 mg.) was refluxed with 3 ml. of acetic acid for 30 min. The acid was removed *in vacuo* and the residue crystallized from acetone-hexane. It melted at 185–190°.

Anal. Calcd. for $C_{29}H_{45}O_3N$: C, 76.44; H, 9.95. Found: C, 76.29; H, 10.01.

VI *from 26-acetylamino-5,20(22)-furostadien-3β-ol acetate* (VIa). The diacetylpseudo derivative VIa[1] (50 mg.) was refluxed with 5 ml. of 2% methanolic potassium hydroxide for 1 hr. and the solvent was removed. After the addition of water, it was extracted with methylene chloride. The solvent was then removed and the residue crystallized from acetone-hexane. The compound, $[\alpha]_D^{20}$ −27.3° ($CHCl_3$), melted at 186–190°. It was identical in respect to melting point and infrared spectrum with VI obtained from the treatment of V with acetic acid.

26-Aminodiacetyl-5,20(22)-furostadien-3β-ol acetate (III) *from* VIa. *O,N*-Diacetylpseudosolasodine (VIa, 80 mg.) was dissolved in pyridine (1 ml.) and acetic anhydride (1 ml.) and refluxed for 3 hr. The reaction product was poured on ice water and collected. The compound, twice crystallized from aqueous methanol (plates), melted at 89–90°, $[\alpha]_D^{20}$ −23° ($CHCl_3$), $\lambda_{max}^{C_2H_5OH}$ 218 mμ (log ε, 4.09), $\lambda_{max}^{CS_2}$ 5.75, 8.06 μ (3-OAc); 5.86 μ (N—Ac_2), 5.97 μ (C=C—O—).

Anal. Calcd. for $C_{33}H_{49}O_5N$: C, 73.43; H, 9.15. Found: C, 73.23; H, 9.28.

3β-Acetoxy-16β-hydroxy-5-bisnorcholenic 22 → 16-lactone (VII). A solution of chromic acid (300 mg. chromium trioxide in 15 ml. 80% acetic acid) was added dropwise to a solution (15 ml. acetic acid) containing 350 mg. of amorphous IIA and IIB while stirring. After the addition of the oxidant, the stirring was continued for another 2 hr. Water and a small amount of sodium sulfite were then added and the mixture extracted with ether. The residue recovered from the ether extract was refluxed with ethanolic potassium hydroxide (3%) for 2 hr. and the solvent was removed. Water was added to the residue and the mixture was extracted with ether. The ether soluble fraction, after acetylation in the conventional manner, yielded 41 mg. of a neutral fraction which was subjected to chromatography on alumina.

(13) L. H. Briggs and T. O'Shea, *J. Chem. Soc.*, 1654 (1952).

(14) Melting points were taken on the Kofler block and are uncorrected. Micro analyses were performed by the Institute's Analytical Service Laboratory under the direction of Dr. W. C. Alford. The infrared spectra were taken on the Model 21 Perkin Elmer Infrared Spectrometer by Messrs. H. K. Miller and R. T. Brown. Neutral Woelm alumina, grade 1, was used in the chromatography, unless otherwise noted.

From the benzene eluate, 17 mg. of impure 3β-acetoxy-5,16-pregnadien-20-one were obtained, which yielded 6 mg. of the pure specimen. The aqueous layer from the ether extract was acidified with hydrochloric acid and reextracted with ether. This after acetylation yielded 143 mg. of crude lactonic material which was chromatographed on acidic alumina. From the ether eluate, 30 mg. of lactone VII, m.p. 212–215° (from acetone-hexane), was obtained, which was identical (melting point, mixture melting point, infrared spectrum) with an authentic specimen prepared from another source.[9]

Tetrahydrosolasodine (VIII) *from amorphous mixture.* The amorphous mixture (177 mg.) was dissolved in 6 ml. of acetic acid and reduced catalytically with 94 mg. of platinum oxide. In about 30 min. the consumption (2 moles) of hydrogen ceased. Although the tetrahydro derivative was chromatographed, it refused to crystallize,[12] $[\alpha]_D^{29}$ +24° ($CHCl_3$).

A part of the triacetate (64 mg.) was therefore hydrolyzed in methanolic potassium hydroxide (10%) for 3 hr. and the product crystallized from aqueous methanol. It formed prisms, m.p. 288–292°, $[\alpha]_D^{29}$ −8.7° ($CHCl_3$), identical in respect to melting point and infrared spectrum with an authentic specimen of tetrahydrosolasodine obtained from the direct reduction of solasodine.[15]

Conversion of IIA *and the amorphous mixture into pseudosolasodine B* (X). (a) The amorphous mixture (225 mg.) was refluxed with 15 ml. of acetic acid for 3 hr. The acetic acid was removed *in vacuo* and the residue chromatographed on alumina. The fraction eluted with ether (175 mg.) crystallized from methanol as plates, m.p. 184–191°, and agreed in properties (melting point and infrared spectrum) with an authentic specimen[3] prepared from the interaction of a solution of zinc chloride-acetic anhydride-acetic acid with solasodine.

Anal. Calcd. for $C_{31}H_{47}O_4N$: C, 74.81; H, 9.52. Found: C, 74.58; H, 9.43.

The treatment of IIA in the same manner also gave X in good yields.

(b) A solution of 130 mg. of amorphous IIA and IIB in 20 ml. of benzene-ether (1:1) containing hydrogen chloride gas (slow bubbling for *ca.* 5 min.) was allowed to stand overnight at 5°. The product was chromatographed on alumina. The ether eluate (45 mg.) proved to be X.

BETHESDA 14, MD.

(15) H. Rochelmeyer, *Arch. Pharm.*, **277**, 329 (1939).

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

The Chemistry of the Spiroaminoketal Side Chain of Solasodine and Tomatidine. III.[1] The Reaction of *O,N*-Diacetylsolasodine in Acidic Media

YOSHIO SATO AND NOBUO IKEKAWA[2]

Received September 24, 1959

The isomerization of *O,N*-diacetylsolasodine in nonpolar media forms the pseudo derivative, 26-acetylamino-5,20(22)-furostadien-3β-ol acetate in good yields. Aqueous or alcoholic acidic media promote the formation of C-22 substituted 26-acetylaminofurostene derivatives. The chemistry of the 22-hemiketal and alkoxyketals is discussed.

In the course of our investigations of the acid-catalyzed isomerization of the diacetates of the steroidal alkaloids, tomatidine, and solasodine[1] several interesting new compounds were obtained from the treatment of these diacetyl derivatives with mineral acid in polar solvents. In the presence of aqueous hydrochloric acid in dioxane[3] diacetylsolasodine (I) yields, along with the known pseudo compound II,[1] the 22-hydroxyl derivative III. This structure was deduced from the proposed course of the pseudomerization reaction (VIII→IX→X) and confirmed by spectroscopic and chemical data.

The infrared spectrum of III is characterized by the appearance of a hydroxyl absorption (2.78 μ) in addition to to the normal acetoxy (5.78 μ) and secondary amide function (2.90, 5.98, 6.60 μ). As would be expected III is readily converted into the pseudo derivative II by treatment with acetic acid. Structure III is further supported by the preponderant formation of the C-22 methoxy derivative IV when methanol is used as solvent in place of dioxane in its preparation from diacetylsolasodine. When ethanol is employed in place of methanol, the ethoxy derivative V is obtained, which can be converted to the methoxyl compound IV by allowing it to stand in a solution of methanol and acetic acid. The process is easily reversed (IV→V) by employing ethanol and acetic acid. By mild treatment with 80% acetic acid, these alkoxy derivatives IV and V are transformed into the hydroxyl compound III which, in turn, is readily reconverted into IV or V with acetic acid and the appropriate alcohol. More vigorous treatment with acetic acid converts compounds IV and V directly into II. This series of transformations parallels the sequence of reactions which Hirschman and Hirschman have found for the C-22 ketals obtained from kryptogenin.[4]

(1) For Part I and II see *J. Org. Chem.*, **25**, 783 (1960).

(2) Visiting Scientist, National Institutes of Health.

(3) Hydrochloric or perchloric acid (60%) in acetic acid also acts similarly.[1]

(4) H. Hirschman and F. B. Hirschman, *Tetrahedron*, **3** 243 (1958).