STEROIDS AND RELATED NATURAL PRODUCTS. XXV

PHOTOCHEMICAL TRANSFORMATION OF 3β-NITRITO-5α-LANOSTANE[1]

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ABSTRACT

Ultraviolet irradiation of 3β-nitrito-5α-lanostane was found to follow an unusual reaction pathway and yield 2-oximo-3-oxo-3,4-seco-5α-lanostane (IV). The new aldehyde was easily converted to oxime and phenylhydrazone derivatives. Acetylating the photolysis product led to an oxime acetate (IX) which readily rearranged to 1-cyano-3,4-seco-5α-lanostane (III). Confirmation for the structural assignments was obtained from a series of proton magnetic resonance and mass spectral studies. Application of the new photochemical reaction was suggested to preparation of certain aldehydes otherwise accessible only with difficulty.

Chemical degradation of lanosterol to both 14α-methyl progesterone and 14α-methyl testosterone was previously accomplished, as part of an investigation concerned with evaluating the biological importance of 14α-methyl steroids (1). Reconstituting the triterpene-type ring A of lanosterol to one typical of the steroid hormones requires, at present, a somewhat lengthy series of synthetic steps. With eventual view to providing a greater selection of methods for reconstructing or otherwise transforming the 3β-hydroxy-4,4-dimethyl system of lanosterol, we decided to study photolytic decomposition[5] of 3β-nitrito-5α-lanostane (I*b*).

Preparation of 3β-hydroxy-5α-lanostane (I*a*) was performed essentially as previously reported (1*c*), and the required nitrite ester (I*b*) was prepared in good yield using nitrosyl chloride (5*a*) in pyridine. Although the ester proved relatively unstable (5*b*, 5*c*) rapid chromatographic purification on a Florisil column was found suitable for preparing a pure specimen. Irradiation (high-pressure mercury vapor arc lamp) of nitrite I*b* in benzene solution was performed under conditions commonly employed for the Barton reaction.[5] After approximately 40 min at 15°, spot tests (diphenylamine in concentrated hydrochloric acid) for the nitrite ester became negative. When a total of 45 min had elapsed, irradiation was terminated and the crude product was isolated. A thin-layer chromatogram of the product indicated that at least six substances were present. Partial separation of the viscous yellow oil on a column of basic alumina led to two readily predictable products in small yield: the substance expected from alkoxy radical decomposition with α-hydrogen fission (3-oxo-5α-lanostane, II) and the substance resulting from intermolecular hydrogen abstraction (alcohol I*a*). The ketone (II) was finally separated from an oily impurity (later assumed to be nitrile III) by preparative thin-layer chromatography. However, the

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[1] *For Part XXIV refer to: G. R. Pettit, A. K. Das Gupta, H. Klinger, and J. Occolowitz. Experientia, 20, 545 (1964). Contribution XXV was abstracted in part from the Ph.D. dissertation submitted by R. E. Kadunce to the Graduate School, University of Maine, May 1964.*

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[5] *Stereoselective intramolecular hydrogen abstraction by alkoxy radicals formed during photolysis of nitrites and recombination of the resulting carbon radicals with nitric oxide to form nitroso monomers, dimers, or oximes has been designated the Barton reaction (2). An interesting review of the reaction has been prepared by Nussbaum and Robinson (2) and valuable extensions have recently been described by Barton and colleagues (3). A non-cage free-radical mechanism for the transformation has been proposed (4a) and other studies (4b, 4c) related in a general way to the mechanism of photochemical reactions have recently been summarized.*

major photolysis product (1.3 g from 3.6 g of I*b*) was eventually assigned structure IV. The vitreous-like aldehyde (IV) resisted attempts at crystallization, and was further purified by successive column and preparative thin-layer chromatography on silica gel. Aldehyde IV appears to have arisen by alkoxy radical decomposition with carbon–carbon bond cleavage followed by a novel series (I*b* → IV) of transformations. While the mechanistic pathway leading to aldehyde IV is only a tentative suggestion, experiments described below provide definitive support for the structural formulation.

At the outset, photolytic transformation of nitrite I*b* was not expected to follow a predictable reaction pathway and any firm assumption concerning composition of the product(s) seemed premature. Shortly after the photolysis product was found consistent with empirical formula $C_{30}H_{53}NO_2$, Robinson and colleagues (6) reported conversion of certain nitrite esters (adjacent to a tertiary-carbon atom) to the corresponding hydroxamic acids. Thus, it appeared that an initially formed alkoxy radical underwent ring fission to give a tertiary-carbon radical which then combined with nitric oxide yielding a tertiary-nitroso aldehyde (such as V) with eventual formation of hydroxamic acid VI (2). An infrared (neat) study of the photolysis product showed stretching absorption at 3 395, 1 710, and 1 670 cm^{-1} and on this basis hydroxamic acid structure VI did not appear likely[6]. Also, the product gave a negative iron(III) chloride test, and attempts to prepare a crystalline lactam derivative by reduction with a variety of reagents including zinc – acetic acid[7] and Raney nickel (9) were unsuccessful. Furthermore, an infrared examination of substance IV in chloroform solution revealed free hydroxyl stretching at 3 630 cm^{-1} and bonded hydroxyl absorption at 3 330 cm^{-1} characteristic of an oxime grouping (10). Absence[8] of infrared absorption in the 2 700 cm^{-1} region typical of aldehyde carbon–hydrogen stretching delayed recognition of this functional group until detection by a proton magnetic resonance (p.m.r.) investigation.

In carbon tetrachloride solution a p.m.r. spectrum of oxime IV exhibited, in addition to high-field skeletal responses, signals at 2.50 (two protons), 9.05 (one proton) and 9.63 (one proton) δ. The low-field response at 9.05 δ was undiminished by treating the solution with deuterium oxide (12*a*); however, the signal at 9.63 δ was absent. The oxime proton of androstane derivative VII*a* (prepared for comparison purposes), in the same solvent, emerged at 8.75 δ and also disappeared on exposure to deuterium oxide. Similar observations were noted in both cases using deuterochloroform as solvent. The signals at 9.05 and 9.63 δ were, therefore, assigned to aldehyde (12*b*) and oxime (12*c*) protons, respectively.

Presence of the aldehyde group was further substantiated by conversion of substance IV to dioxime VIII*a* using hydroxylamine in pyridine solution (13). Infrared carbonyl absorption was absent in the product and a p.m.r. signal for the oxime proton appeared at 7.54 δ. Treating the dioxime with nickel(II) chloride in ethanol gave a deep orange precipitate indicative of a vicinal *anti* dioxime (13*a*).

An attempt at confirming respective assignment of positions C-2 and C-3 for the oxime and aldehyde groups was next undertaken. Aldehyde IV was allowed to react with excess phenylhydrazine in ethanol (14) as the first step in a sequence directed at obtaining the corresponding osotriazole (15). The crystalline phenylhydrazone derivative, which separated from solution as the reaction progressed, was assigned structure VIII*b*. Results of elemental and mass spectral analyses were consistent with a monophenylhydrazone structure (VIII*b*). Interestingly, a p.m.r. spectrum of the hydrazone suggested two different

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[6] *An infrared and ultraviolet study of hydroxamic acids has recently been reported (7).*

[7] *We are grateful to Dr. C. H. Robinson (6b) for providing us with unpublished details of his experience with the cyclic hydroxamic acid → lactam reduction reaction (8).*

[8] *The mono-2,4-dinitrophenylhydrazone derivative of glyoxal also lacks absorption in the aldehyde region (11).*

environments for the C-1 methylene group protons as two distinct signals corresponding to one proton each were evident[9] at 2.58 and 2.78 δ. The five aromatic-type protons emerged at 6.67–7.15 δ and signals corresponding to one proton each appeared at 7.61 (oxime or amino proton) and 7.78 (C-3 proton) δ. The signal at 7.61 δ disappeared in the presence of deuterium oxide. No further attempt at preparing a diphenylhydrazone derivative was made when a series of experiments (IV → III) beginning with acetylation of oxime IV were shown to reflect 2,3-positioning of the oxime and aldehyde groups.

Allowing oxime IV to react with acetic anhydride – pyridine at room temperature led to a crystalline monoacetyl derivative corresponding to empirical formula $C_{32}H_{55}NO_3$. An infrared spectrum of the acetate (IX) displayed carbonyl absorption at 1 790 (acetate) and 1 715 (aldehyde) cm^{-1}. Confirmation for assignment IX was obtained by evaluating the acetate's p.m.r. spectrum. In addition to responses expected for the hydrocarbon skeleton, three significant peaks were observed: three acetyl protons at 2.15, two methylene protons at 2.54, and one aldehyde proton at 9.31 δ. No change in the p.m.r. response occurred when the solution was treated with deuterium oxide. Nearly identical infrared and p.m.r. spectra were observed in the acetyl regions employing an authentic sample of oxime acetate VII*b*.[10]

Oxime acetate IX derived from photolysis product IV proved quite labile and purification required mild procedures. Recognition of the unusual stability properties of acetate IX opened a path to the most compelling structural evidence for aldehyde IV and its transformation products. When the acetate was chromatographed in hexane–benzene solution on silica gel and elution delayed until the following day, the product was nitrile III. The distinctive nitrile infrared stretching frequency at 2 350 cm^{-1} and absence of carbonyl-type absorption provided the first indication that oxime IX had been converted to a nitrile. In accordance with structure III the lowest-field signal in the nitriles p.m.r. spectrum appeared at 2.25 δ. Elemental analytical data for the nitrile corresponded to empirical formulas $C_{30}H_{53}N$ or $C_{29}H_{51}N$. Definite selection of the formula (III) representing loss of one carbon atom was possible when mass spectral examination of the nitrile yielded a molecular ion at m/e 413. Formation of the nitrile with loss of one carbon atom indicated a type of "second-order Beckmann" rearrangement (16) arising from an α-oximino aldehyde structure, thereby eliminating a ketone formulation for the photolysis product. In addition, facile formation of the nitrile[11] by simply absorbing oxime acetate IX on silica gel suggested an *anti* configuration for the photolysis product (IV). Basic hydrolysis of *syn* oxime acetates having an adjacent oxygen substituent results in saponification with relatively little rearrangement (17).

In summary, photochemical transformation of 3β-nitrito-5α-lanostane (I*b*) was found to follow a novel reaction pathway leading to aldehyde IV.[12] The preceding experiments suggest that the new photochemical reaction may provide a useful synthetic avenue to certain α-oximino aldehydes and derivatives, e.g. α-amino acids, otherwise accessible only with difficulty.

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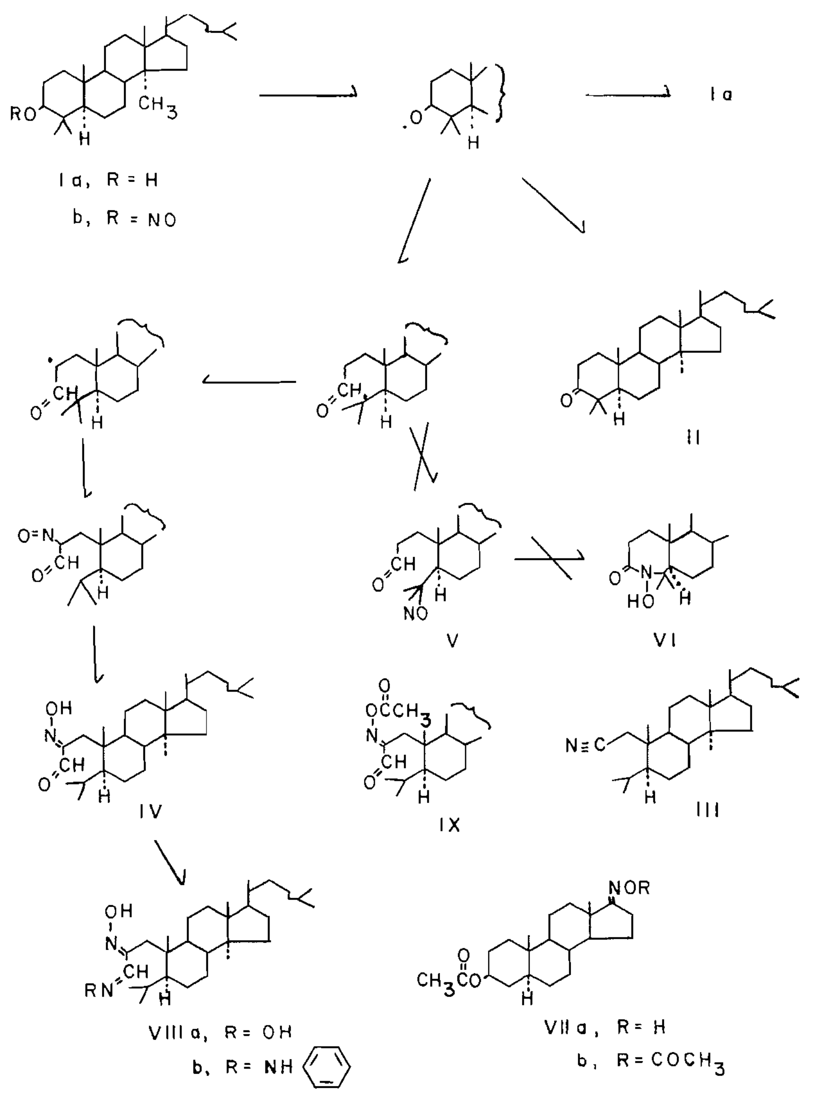
[9] *Appearance of a partially resolved or distinct C-1 methylene doublet in p.m.r. spectra of the photolysis product and derivatives may be due, in part, to asymmetry of the adjacent C-10 position (see e.g. ref. 12d).*

[10] *The oxime acetate signal of substance VIIb appeared with a shoulder at approximately one-half height which may indicate a mixture of anti and syn isomers.*

[11] *Significant amounts of nitrile-containing products have been obtained by Beckmann rearrangement of unconjugated oximes using p-toluenesulfonyl chloride in pyridine (18).*

[12] *Although several examples of irradiation-induced cleavage of a triterpene ring A have been recorded (19), the presently described reaction appears to follow a unique course. The experimental results used in support of structure IV, however, do not necessarily exclude a reaction sequence involving ring B (cf. 20, p. 584). Final support for the structural assignments must now await correlation with a substance of established structure.*



EXPERIMENTAL

Melting points were determined employing a Kofler melting point apparatus. Introduction to the experimental section of a previous contribution (1*c*) concerned with oxidation of 3β-acetoxy-5α-lanostane provides a brief description of several reagents and techniques (e.g. silica gel t.l.c.) employed below. The acetic anhydride, pyridine (from potassium hydroxide), and all solvents were redistilled. In addition, diethyl ether was further purified by filtration through a column of activated alumina. Acid-washed alumina (Merck, Rahway), neutral alumina (E. Merck, AG., Darmstadt, Germany), basic alumina (Aluminum Company of America F-20), silica gel (0.05–0.20 mm, E. Merck), and Florisil (100 mesh) were employed as column chromatographic adsorbents. Fluorescent silica gel (HF 254, average particle size 5–25 μ, E. Merck) was employed for one preparative thin-layer chromatogram, which contained a substance fluorescent under ultraviolet light. The photolysis experiments were performed using a Hanovia high-pressure mercury arc lamp (Englehard Hanovia, Inc., 200 W) with a Pyrex filter sleeve (E. H., Inc., No. 516-27-116). All new substances are colorless unless otherwise noted.

The p.m.r. spectra were obtained using a Varian Associates Model A-60 n.m.r. spectrometer. Each solvent contained approximately 10% w/v of sample and enough tetramethylsilane was added to standardize the instrument. The scanning rate (from low to high field) was 120 c.p.s./min and measurements are reported in δ (p.p.m.) units with respect to TMS. The optical rotation (chloroform solution) and infrared measurements and elemental analyses were provided by Drs. Hill, Janssen, and Bernhardt (1*c*). Mass spectral determinations were performed using a direct inlet technique.

3β-Hydroxy-5α-lanostane (Ia)

A specimen (45 g) of 3β-acetoxy-7,11-dioxo-5α-lanostane was converted to 3β-hydroxy-5α-lanostane as previously described (1*c*). The crude product (37.4 g) was dissolved in 1:1 benzene–hexane and absorbed on 750 g of acid-washed alumina. Elution with the same solvent gave a sample (8.5 g) of alcohol I*a* melting at 172–175°. Further elution with benzene gave a pure sample (12.5 g) which after recrystallization from chloroform–methanol melted at 173–175°; $[\alpha]_D^{20}$ +34.8 (*c*, 1.1); reported (21) m.p. 171–172°, $[\alpha]_D$ +35°.

3β-Nitrito-5α-lanostane (Ib)

Method A

A solution of nitrosyl chloride (2 ml) in pyridine (20 ml) was added dropwise (over 1 h) to a solution of alcohol I*a* (4.0 g) in dry benzene (50 ml) and pyridine (25 ml). After stirring the mixture one additional hour, the brown solution was diluted with water and extracted with benzene. The combined benzene extract was washed with cold dilute hydrochloric acid, washed with water, dried, and concentrated *in vacuo*. A thin-layer chromatogram (3:17 ethyl ether – hexane mobile phase) indicated that the product contained a small quantity (less than 10%) of starting alcohol. A solution of the residue in petroleum ether was chromatographed on Florisil (90 g) and eluted with the same solvent to yield 3.6 g of nitrite ester I*b* melting at 122–126°. Two recrystallizations from hexane afforded an analytical sample melting at 123.5–126.5°; $[\alpha]_D^{20}$ +28.9° (*c*, 2.35); ν_{max}^{KBr} 1 640, 1 595, and 800 cm^{-1}.

Anal. Calcd. for $C_{30}H_{52}NO_2$: C, 78.40; H, 11.62; N, 3.05. Found: C, 78.02; H, 11.45; N, 3.16.

In later experiments, a 5-min addition period for the nitrosyl chloride (at ice-bath temperature) and a 1/2 h period at room temperature was found satisfactory. In general, the nitrite ester proved sensitive and rapid isolation and purification proved desirable.

Method B

Samples of the nitrite ester suitable for the photolysis reaction were prepared as follows. Nitrosyl chloride was passed into a pyridine (40 ml) solution of alcohol I*a* (4.0 g) at −10°. Stirring and addition of gaseous nitrosyl chloride was continued until the reaction mixture retained a pale-brown color. The solution was allowed to warm to room temperature and after 1/2 h was poured into ice water (200 ml) .The solid product was collected, washed with cold water, and dissolved in hexane, and the resulting solution was washed with cold dilute hydrochloric acid and water. Removal of solvent (*in vacuo* at room temperature) gave 3.7 g (87%) of the nitrite ester.

2-Oximo-3-oxo-3,4-seco-5α-lanostane (IV)

A solution of the nitrite ester (I*b*, 3.6 g) in dry benzene (250 ml under nitrogen) was cooled (10–15°) and irradiated for 45 min. Spot tests (diphenylamine in concentrated hydrochloric acid) for the nitrite group became negative after 40 min. The fluorescent green solution was concentrated *in vacuo* at room temperature to a viscous yellow oil. A hexane solution of the residue was chromatographed on basic alumina (70 g). One fraction eluted with hexane–benzene (1:1) afforded a viscous yellow oil (0.6 g). A 0.09-g sample of the oil was further purified using preparative thin-layer chromatography (8:1 hexane – ethyl ether mobile phase). By this means a 0.04-g specimen of *3-oxo-5α-lanostane* (II), m.p. 130–134°, was isolated.[13] The next most abundant component (0.02 g) was an oily nitrile (λ_{max}^{Nujol} 4.44 μ) later assumed to correspond with degradation product III. The fractions eluted with 3:2 to 1:4 hexane–benzene corresponded to the principal photolysis product. A thin-layer chromatogram (5:1 hexane – ethyl ether mobile phase) indicated that these fractions (IV, 1.3 g) represented a nearly pure substance. Continued elution with benzene gave an oily fraction (0.04 g) which was not investigated further, while the fractions eluted with benzene – ethyl ether and with ethyl ether afforded another 2.7 g of viscous oil. The latter fractions were combined and rechromatographed on acid-washed alumina (60 g). The fraction (0.64 g, m.p. 160–170°) eluted with hexane–benzene (3:1) was recrystallized from chloroform–methanol and identified[13] as *3β-hydroxy-5α-lanostane (21)*.

When attempts to crystallize the principal photolysis product (1.3 g) proved unsuccessful, the photolysis reaction was repeated. As with the example noted above, a thin-layer chromatogram (9:1 hexane – ethyl acetate mobile phase) indicated that the crude product was composed of at least six components. Chromatographic separation of the viscous yellow oil was repeated employing neutral alumina with hexane, benzene, and chloroform solvent systems. Essentially the same observations were made. The following procedure, however, was used to obtain a pure specimen of oxime IV.

The reaction was again repeated and the product was chromatographed on 100 g of neutral alumina. Elution with 99:1 to 9:1 hexane – ethyl acetate yielded 1.6 g corresponding principally to 3-ketone II, lesser quantities of 3β-alcohol I*a*, and a small quantity of the nitrile (III) accompanied by a trace of nitrite ester (I*b*). Continued elution with 9:1 hexane – ethyl acetate to ethyl acetate gave 1.5 g of oxime IV. The oxime was rechromatographed on silica gel (45 g) and elution with 99:1 to 19:1 hexane – ethyl acetate removed

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[13] *Identity was established by mixture melting point determination and infrared spectral comparison (in potassium bromide) with an authentic sample.*

approximately 0.1 g of less polar impurities. The next fraction eluted with 19:1 hexane – ethyl acetate weighed 1.15 g and was found by thin-layer chromatography (9:1 hexane – ethyl acetate mobile phase) to represent pure product (IV, 31% yield). However, attempts to crystallize the vitreous solid were unsuccessful. An analytical specimen was prepared by preparative thin-layer chromatography on silica gel HF 254 (4:1 cyclohexane – ethyl ether mobile phase), and the desired zone was identified using an ultraviolet lamp. In this case, the plate was first eluted with methanol (and reactivated at 110°) to remove some impurities. The oxime was eluted from the silica gel with chloroform, and the solution was filtered, concentrated to dryness *in vacuo*, treated with pentane, and finally evaporated in high vacuum to yield a colorless foam. Purity was reconfirmed by a thin-layer chromatogram but attempts to crystallize the product were again unsuccessful. A p.m.r. spectrum of the oxime in CCl_4 exhibited responses at 0.11, 0.74, 0.80, 0.84, 0.89, 1.15–1.47 (complex and broad), 2.50 (two methylene protons), 9.05 (one aldehyde proton) and 9.63 (one oxime proton) δ. After shaking the carbon tetrachloride solution with deuterium oxide for 15 min, the peak at 9.63 δ disappeared. The infrared spectrum displayed absorption at: $\nu_{\max}^{\mathrm{KBr}}$ 3 300 (broad), 1 700 (broad), 1 470, 1 450, 1 392, 1 370, and 1 200 cm^{-1}. Results of elemental analyses were consistent with the oxime structure.

Anal. Calcd. for $C_{30}H_{53}NO_2$: C, 78.37; H, 11.62; N, 3.05; O, 6.96. Found: C, 77.95; H, 11.48; N, 3.16; O, 7.35.

3-Oxo-5α-lanostane (II)

To a solution of 3β-hydroxy-5α-lanostane (2.0 g) in acetone (150 ml) at room temperature was added excess 8 *N* chromium trioxide reagent (22). When oxidation appeared complete, the remaining chromium trioxide was reduced with methyl alcohol and the mixture was filtered through Celite and concentrated to approximately 10 ml. After dilution with water, the product was collected and recrystallized from hexane to yield 1.43 g melting at 132–133°, $[\alpha]_D^{20}$ +25.4° (*c*, 7.29); reported (21) m.p. 127–128° and $[\alpha]_D$ +27°.

P.m.r. Chemical Shifts of 3β-Acetoxy-17-oximo-5α-androstane (VIIa) and 3β-Acetoxy-17-acetoximino-5α-androstane (VIIb)

Oxime VII*a* (23): p.m.r. in CCl_4 solution 0.80, 0.84, 1.19, 1.61, 1.88 (three acetate protons), 2.34 (broad, C-3 proton), and 8.75 (one oxime proton which disappears in the presence of deuterium oxide); in $CDCl_3$ solution 0.84, 0.88, 1.23–1.82 (complex), 1.97, 2.11 (three acetate protons), 2.44 (broad, C-3 proton), and 8.64 (one oxime proton which disappears in the presence of deuterium oxide). Oxime acetate VII*b* (16, 23): in CCl_4 solution 0.84, 0.94, 1.22–1.72 (broad and complex), 1.88 (3-acetate), 2.0–2.02 (oxime acetate), and 2.42 (broad, C-3 proton).

2,3-Dioximo-3,4-seco-5α-lanostane (VIIIa)

The dioxime derivative (VIII*a*, 0.06 g) obtained (0.08 g hydroxylamine hydrochloride, 1 ml pyridine, for 12 h at room temperature) from 0.08 g of the mono-oxime IV was purified by preparative thin-layer chromatography (3:1 hexane – ethyl ether mobile phase). Recrystallization from chloroform–hexane gave a pure sample melting at 168–171°: p.m.r. in $CDCl_3$ solution gave responses at 0.46, 0.78, 0.89, 0.99, 1.15–1.50 (complex and broad), 2.58 (two methylene protons) and 7.54 (broad, oxime proton, disappears in the presence of deuterium oxide) δ; $\nu_{\max}^{\mathrm{Nujol}}$ 3 570, 959, 935, and 885 cm^{-1}.

Anal. Calcd. for $C_{30}H_{54}N_2O_2$: C, 75.89; H, 11.47; N, 5.90. Found: C, 75.73; H, 11.49; N, 6.26.

2-Oximo-3-phenylhydrazono-3,4-seco-5α-lanostane (VIIIb)

Phenylhydrazine hydrochloride (0.53 g) in water (8 ml) was added to a stirred solution of oxime IV (0.75 g) in ethanol (30 ml). After approximately 3 h at room temperature, a crystalline product began to separate. Eighteen hours later, the mixture was cooled and the solid was collected and washed with methanol: yield 0.62 g (62%), m.p. 158–160°. An analytical specimen (pure as evidenced by thin-layer chromatography using 7:3 hexane – ethyl acetate as mobile phase) recrystallized from acetone–methanol as pale-yellow crystals, m.p. 169–170°; p.m.r. spectrum in $CDCl_3$ solution 0.65, 0.80, 0.90, 0.99, 1.18, 1.52, 2.58 (one proton), 2.78 (one proton), 6.67–7.15 (five aromatic protons), 7.61 (one proton which disappears in the presence of deuterium oxide) and 7.78 (one C-3 proton); $\nu_{\max}^{\mathrm{KBr}}$ 3 200, 1 600, 1 560, 1 510, 1 490, 1 470, 1 380, 1 250, 1 230, 1 160, 970, and 930 cm^{-1}. The mass spectral data (M^+ at 549 with a calculated mass of 549) and elemental analyses were also consistent with structure VIII*b*.

Anal. Calcd. for $C_{36}H_{59}N_3O$: C, 78.63; H, 10.82; N, 7.64; O, 2.91. Found: C, 78.74; H, 10.70; N, 7.78; O, 2.79.

2-[O-Acetyloximo]-3-oxo-3,4-seco-5α-lanostane (IX)

A solution of oxime IV (0.60 g) in acetic anhydride (4 ml) and pyridine (8 ml) was allowed to stand at room temperature 15 h. The mixture was poured into ice water containing excess sodium bicarbonate and allowed to stand 1 h. A hexane extract of the aqueous mixture was washed with water and concentrated *in vacuo* (after drying) at room temperature to a viscous yellow oil (0.52 g) which melted at 104–115°, following crystallization from hexane. Three recrystallizations from hexane – ethyl ether yielded a pure sample melting at 117–119°; $[\alpha]_D^{20}$ +37.5° (*c*, 0.48); p.m.r. spectrum in CCl_4 solution 0.71, 0.75, 0.80, 0.84, 1.14–1.45 (complex and broad), 2.15 (three acetyl protons), 2.54 (two methylene protons), and 9.31 (one aldehyde proton which remains unchanged in the presence of deuterium oxide) δ; $\nu_{\max}^{\mathrm{KBr}}$ 1 790, 1 715, 1 470, 1 370, 1 220, and 1 160 cm^{-1}.

Anal. Calcd. for $C_{32}H_{55}NO_3$: C, 76.59; H, 11.05; N, 2.79; O, 9.57. Found: C, 77.08; H, 11.18; N, 2.70; O, 9.12.

The oxime acetate was found sensitive and purification was achieved more easily by avoiding heat, light, and the atmosphere. In earlier experiments, an analytical sample prepared following four recrystallizations from hexane melted at 120–123° and exhibited $[\alpha]_D^{20}$ +35.8° (*c*, 0.36). Found: C, 76.74; H, 11.24; N, 2.33; O, 9.88.

1-Cyano-3,4-seco-5α-lanostane (III)

A solution of oxime acetate IX (0.14 g) in 4:1 hexane–benzene was added to a column of silica gel. After approximately 20 h the column was eluted with the same solvent. Removal of solvent *in vacuo* yielded an oil (0.09 g) which solidified, m.p. 83–87°, upon trituration with methanol. Recrystallization from methanol afforded pure needles melting at 85–87°; $[\alpha]_D^{20}$ +42.4° (*c*, 0.24); p.m.r. in CCl_4 solution gave signals at 0.15, 0.69, 0.72, 0.83, 1.05–1.55 (complex and broad) and 2.25 (partially masked doublet) δ; $\nu_{\max}^{\text{Nujol}}$ 2 350 and 1 400 cm^{-1}.

Anal. Calcd. for $C_{29}H_{51}N$: C, 84.26; H, 12.35; N, 3.39. Found: C, 84.52; H, 12.21; N, 3.40.

A mass spectrum of the nitrile exhibited a molecular ion at 413 (calcd. mol. wt. 413).

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REFERENCES

1. (*a*) G. R. Pettit and P. Hofer. Helv. Chim. Acta, **46**, 2142 (1963).
   (*b*) G. R. Pettit and P. Hofer. J. Chem. Soc. 4439 (1963).
   (*c*) G. R. Pettit, D. S. Alkalay, P. Hofer, and P. A. Whitehouse. Tetrahedron, **20**, 1745 (1964).
2. A. L. Nussbaum and C. H. Robinson. Tetrahedron, **17**, 35 (1962).
3. M. Akhtar *et al.* J. Am. Chem. Soc. **86**, 3394 (1964); **86**, 1528 (1964).
4. (*a*) M. Akhtar and M. M. Pechet. J. Am. Chem. Soc. **86**, 265 (1964).
   (*b*) H. E. Zimmerman and S. Somasekhara. J. Am. Chem. Soc. **85**, 922 (1963).
   (*c*) H. E. Zimmerman and D. I. Schuster. J. Am. Chem. Soc. **83**, 4486 (1961).
5. (*a*) L. J. Beckham, W. A. Fessler, and M. A. Kise. Chem. Rev. **48**, 319 (1951).
   (*b*) N. Kornblum and E. P. Oliveto. J. Am. Chem. Soc. **69**, 465 (1947).
   (*c*) K. Freudenberg and H. Biller. Ann. **510**, 230 (1934).
6. (*a*) P. Kabasakalian and E. R. Townley. J. Org. Chem. **27**, 3562 (1962).
   (*b*) C. H. Robinson *et al.* J. Am. Chem. Soc. **83**, 1771 (1961).
7. O. Exner and B. Kakáč. Collection Czech. Chem. Commun. **28**, 1656 (1963).
8. J. A. Moore and J. Binkert. J. Am. Chem. Soc. **81**, 6029 (1959).
9. R. M. Jipson, F. H. Pettit, C. G. Skinner, and W. Shive. J. Org. Chem. **28**, 1425 (1963).
10. A. Palm and H. Werbin. Can. J. Chem. **31**, 1004 (1953).
11. The Sadtler Standard Spectra. Sadtler Research Laboratories, Philadelphia. No. 8470. 1960.
12. (*a*) H. M. Fales and A. V. Robertson. Tetrahedron Letters, 111 (1962).
    (*b*) L. M. Jackman. Nuclear magnetic resonance spectroscopy. Pergamon Press, N.Y. 1959. p. 62.
    (*c*) G. J. Karabatsos, R. A. Taller, and F. M. Vane. J. Am. Chem. Soc. **85**, 2327 (1964).
    (*d*) G. M. Whitesides *et al.* J. Am. Chem. Soc. **87**, 1058 (1965).
13. (*a*) D. H. R. Barton and J. M. Beaton. J. Am. Chem. Soc. **83**, 4083 (1961).
    (*b*) C. V. Banks. Record Chem. Progr. **25**, 85 (1964).
14. S. P. Findlay. J. Org. Chem. **21**, 644 (1956).
15. L. Mester, E. Moczar, and J. Parello. Tetrahedron Letters, 3223 (1964). R. M. Hann and C. S. Hudson. J. Am. Chem. Soc. **66**, 735 (1944).
16. A. Hassner and I. H. Pomerantz. J. Org. Chem. **27**, 1760 (1962). A. R. Ferris, G. S. Johnson, and F. E. Gould. J. Org. Chem. **25**, 1813 (1960). A. H. Blatt. Chem. Rev. **12**, 215 (1933).
17. R. P. Barnes and A. H. Blatt. J. Am. Chem. Soc. **57**, 1330 (1935).
18. R. T. Conley and R. J. Lange. J. Org. Chem. **28**, 210 (1963). L. Mangoni and M. Belardini. Tetrahedron Letters, 921 (1963). G. H. Whitham. Proc. Chem. Soc. 271 (1959).
19. P. de Mayo and S. T. Reid. Quart. Rev. London, **15**, 393 (1961). D. H. R. Barton, J. F. McGhie, and M. Rosenberger. J. Chem. Soc. 1215 (1961). D. Arigoni *et al.* Proc. Chem. Soc. 306 (1959).
20. J. Karliner, H. Budzikiewicz, and C. Djerassi. J. Am. Chem. Soc. **87**, 580 (1965).
21. W. Voser *et al.* Helv. Chim. Acta, **33**, 1893 (1950).
22. K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon. J. Chem. Soc. **39** (1946).
23. R. D. H. Heard, M. T. Ryan, and H. I. Bolker. J. Org. Chem. **24**, 172 (1959).