Internal Substitution of 5α-Lanostane on C-5, C-6, and C-8[1]

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Thermolysis of 3β-acetoxy-11-oxolanostan-7α-yl azidoformate gave the cyclic carbamate of 3β-acetoxy-5α-amino-11-oxolanostan-7α-ol (9%) and the corresponding 6α-amino (52%) derivative. 3β-Acetoxy-11-oxolanostan-7β-yl azidoformate gave the cyclic carbamate of 3β-acetoxy-6α-amino-11-oxolanostan-7β-ol (52%) and the corresponding 6β-amino (26%) and 8β-amino (7%) derivatives. Some features of the ^{13}C.m.r. and c.d. spectra of the above compounds and related steroids are described.

La thermolyse de l'azidoformate-7α, d'acétoxy-3β-oxo-11 lanostanyle conduit au carbamate cyclique de l'acétoxy-3β amino-5α-oxo-11 lanostanol-7α (9%) et au dérivé amino-6α (52%) correspondant. L'azidoformate-7β de l'acétoxy-3β oxo-11 lanostanyle fournit le carbamate cyclique de l'acétoxy-3β amino-6α-oxo-11-lanostanol-7β (52%) et les dérivés amino-6β (26%) et amino-8β (7) correspondants. On décrit aussi quelques caractéristiques des spectres ^{13}C.m.r. et c.d. des composés mentionnés plus haut ainsi que d'autres stéroides qui leur sont reliés. [Traduit par le journal]

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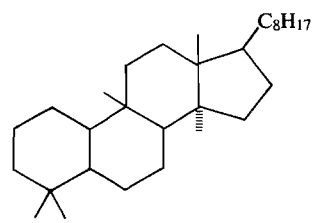
Two skeletons related to lanostane which are of exceptional interest are those of the cucurbitacins (**1**) (1) and of the fusidanes (protostanes) **2** related to probable intermediates in the biosynthesis of lanosterol (2). We attempted to produce good yields of substituted lanostanes which might be converted to compounds with these skeletons.

Attempts to produce compounds with the cucurbitane skeleton have been made by ApSimon and Rosenfeld (3), Guest and Marples (4), and Levy and Lavie (5), by the action of Lewis acids on 9α,11α-oxidolanostane derivatives. No migration of the 10-methyl group was observed. However, since we had obtained efficient migration of the 10-methyl group to C-9 during deamination of a 9α-amino-11-keto steroid (6) we hoped to extend this to deamination of 9α-amino-3β-acetoxylanostan-11-one (**3**) and 8β-amino-3β-acetoxylanostan-7-one (**4**).

Attempts to prepare a 9β,11β-oxidolanostane derivative from which the 9α-amino-11-ketone might be prepared (6) have so far failed in this laboratory (7) and in that of Marples (4).

Since approach of external reagents to the α-face of a 9,11 double bond in lanostane derivatives is somewhat impeded by the 14α-methyl group, an approach using intramolecular cyclization appeared to be one of the most promising alternatives for substituting C-9. Curran and Angier (8) had obtained a 45% yield of the oxazolidinone **5** by pyrolysis of 1-adamantanyl azidoformate, and Kreher and Kühling (9) had shown that thermal decomposition of hexahydrobenzyl azidoformate gave a 3:1 ratio of the oxazolidinone **6** and the tetrahydro-1,3-oxazin-2-one (**7**). Breslow and coworkers (10) and Lwowski (11) found that the insertion factor for different types of CH bonds was in the ratio tertiary–secondary–primary = 30:10:1. Hence we had reason to hope that the nitrene produced from the 7α-azidoformate **8**



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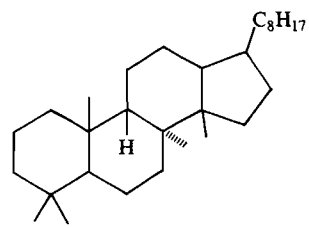

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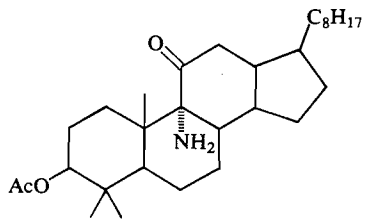
[2]NRCC Postdoctorate Fellow 1971–1972.

[3]Revision received July 26, 1973.



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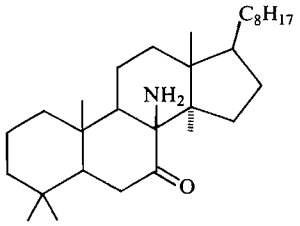

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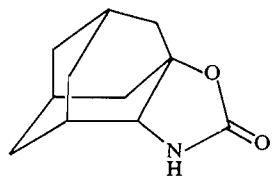

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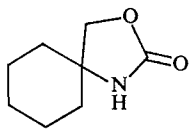

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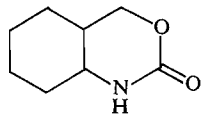

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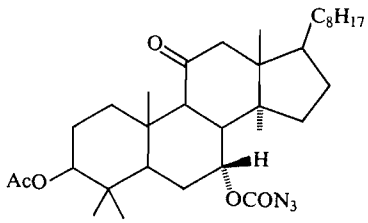

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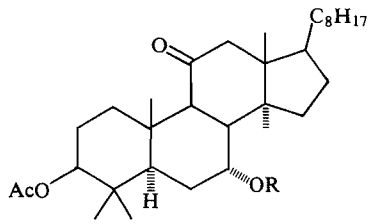
would preferentially attack the 5α- and 9α-CH bonds.[4]

Dihydrolanosterol was converted via 3β-acetoxy-7,11-dioxolanost-8-ene to a mixture of 3β-acetoxy-11-oxolanostan-7α-ol (**9**, R = H) and the corresponding 7β-alcohol (12*a*, 13). Phosgene converted the alcohols to the chloroformates, then sodium azide in dimethyl formamide transformed these to the desired azidoformates.

A solution of the 7α-azidoformate **8** in carbon tetrachloride in a sealed tube was maintained at 140–142° for 2 h. By this time the azide group had disappeared (i.r.) and a mixture of at least five products had formed. These were separated by column chromatography and preparative t.l.c., and the four major components characterized. The main product (52%) clearly arose from insertion into the 6α-CH bond. Its i.r. spectrum (ν_{max} ($CHCl_3$) 1760 cm^{-1}) was characteristic of an oxazolidinone. In addition a new low-field hydrogen (δ 3.83; triplet, $J_{5,6}$ = 10.6 Hz; $J_{6,7}$ = 5 Hz) was present in its p.m.r. spectrum and the coupling constants were as expected for a 6α orientation. Hence we assign it structure **10**. Its ^{13}C.m.r. spectrum is described below.



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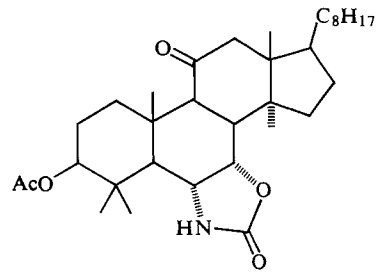

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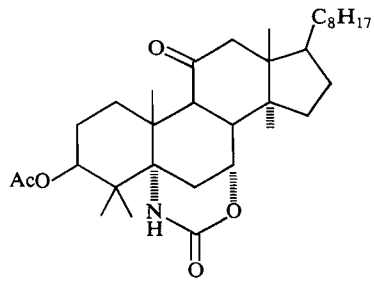

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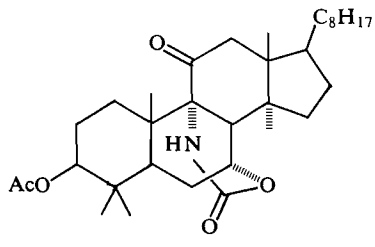

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[4]The only related work for lanostane skeleton seems to be functionalization of C-32 (14α-methyl) by photolysis of the 7α-nitrite or action of lead tetraacetate–iodine on the 7α-alcohol (12).

TABLE 1.

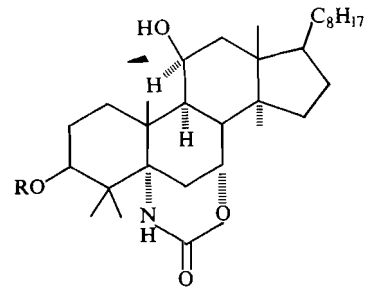
Compound	ν_{max}*	ε	c.d. (Δε)	δ† C-11	δ† C-3
23 (R = $NHCOCH_3$)	295	46	+0.80	204.8	73
23 (R = $NHCOOCH_3$)	296	44	+0.86	205.4	73
23 (R = H)	301	25	+0.18	210.9	73
11	296	30	+1.33	211.0	74.9
9 (R = $CONH_2$)	295	39	+0.60	208.6	80.5
9 (R = H)	302	27	+0.43		
3β-Acetoxy-11-keto lanostane	301	25	+0.43		

*In dioxane.
†In $CDCl_3$; ^{13}C.m.r. signal relative to TMS = 0.

The next most abundant nitrogen-containing product was a tetrahydro-1,3-oxazinone (ν_{max} ($CHCl_3$) near 1690 cm^{-1}). It gave no low-field p.m.r. signals other than the ones for the 3- and 7-hydrogens, since it was the product of attack on C-5 or C-9. We had anticipated that the u.v. spectrum would distinguish these, since the nπ* transition for ketone carbonyls with axial electronegative substituents such as methoxyl, halogen, and azide (6, 14) groups is at wavelength longer and of higher intensity than that of the unsubstituted ketone. Since the unknown product and 3β-acetoxy-11-ketolanostane had very similar absorption (Table 1) it appeared that the compound has structure **11**. On the other hand c.d. evidence appeared to demand the alternate structure **12** with a 9α substituent (see below). However its ^{13}C.m.r. (see below) was consistent with the 5-substituted structure, and chemical transformations confirmed that it was indeed **11**.

The compound was very resistant to acid or alkaline hydrolysis. Meerwein's reagent converted it to an imino ether. Treatment of this ether with base only hydrolyzed the 3-acetoxy group, while acid hydrolysis gave back the tetrahydrooxazinone. The tetrahydrooxazinone was inert to nitrosyl chloride or dinitrogen tetroxide, so direct deamination was not possible. Hence an indirect proof of structure was used.

Sodium borohydride reduced the ketone carbonyl and hydrolyzed the 3-acetoxy group. The resulting diol was transformed by pivaloyl chloride into a monopivaloyloxy derivative. Dehydration of this with thionyl chloride – pyridine gave a trisubstituted olefin without disturbing the cyclic urethane group. It must therefore have structure **14**, proving the intermediates to be **13** (R = H or pivaloyl) and the original tetrahydrooxazinone to be **11**.



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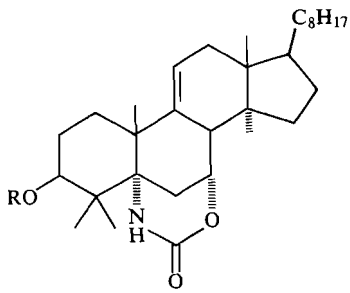

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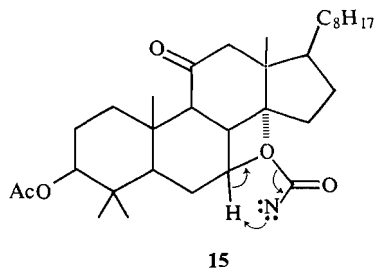

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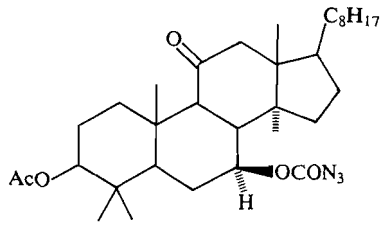
The third product characterized was the simple urethane of the 7α-alcohol, presumably formed by abstraction of hydrogen from other molecules by the *triplet* state of the nitrene. The fourth product was 3β-acetoxylanosta-7,11-

dione. It seems likely that this arose by thermal fragmentation of the nitrene as illustrated in **15**.

The yield of **11** was roughly 9%. Hence other factors were overriding the discrimination factor mentioned earlier. It seems certain that the azide decomposition to nitrene and the insertion of the nitrene into saturated CH bonds are independent events. Hence the observations of Breslow and co-workers (10) regarding the reaction of ethyl azidoformate with 2-methylbutane imply that ethoxycarbonyl nitrene survives numerous collisions with primary CH bonds before it reacts. Thus in the lanostane cases the *nitrene* rotamer ratios are large factors in determining which CH bonds will be attacked. A family of rotamers roughly represented by **16** must be the most highly populated one. This would account for the relatively high yield of 6α-substituted product. This also has the potential of giving insertion into the 5-CH bond, but the low yield of **11** despite the tertiary nature of the hydrogen, indicates that approach to the CH bond is impeded by the 4α-methyl group and the 6α-hydrogen.

A second family of rotamers represented by **17** does not participate to any extent, since it would permit insertion into the 5- and 9-CH bonds with equal facility.



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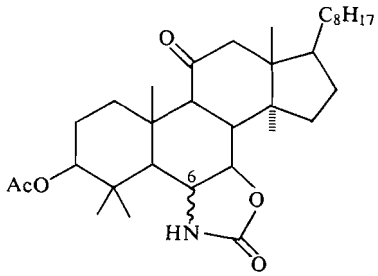

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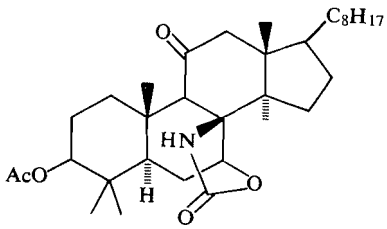
a 6α-amino

b 6β-amino



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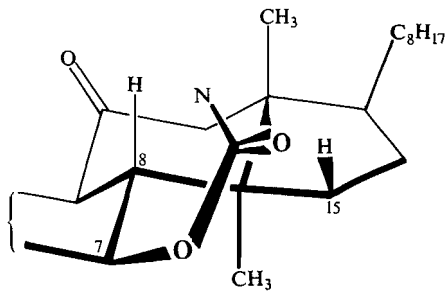

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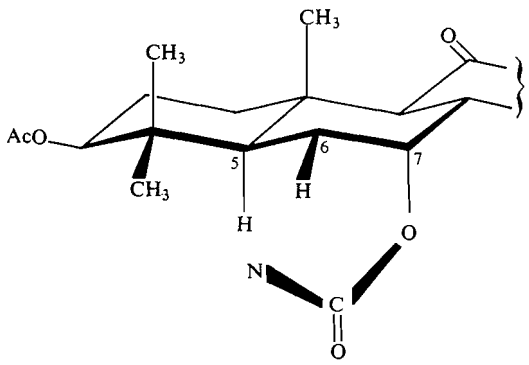

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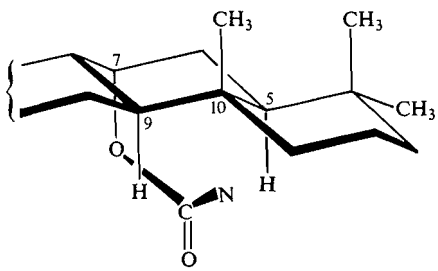

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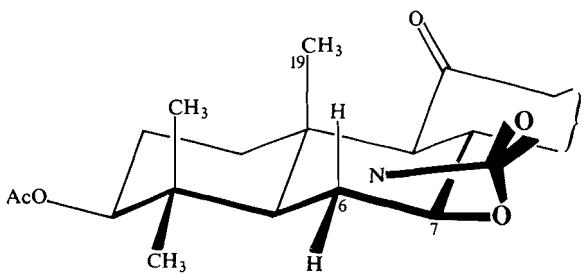

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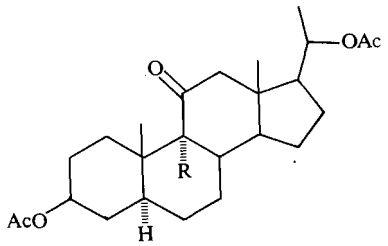

23

Photolysis of the 7α-azidoformate in methylene chloride appeared to give a more complex mixture than the thermolysis, hence this was not pursued further.

In a manner analogous to that for the 7α isomer, 3β-acetoxy-11-oxolanostan-7β-ol was converted to the azidoformate **18**. Thermolysis at 140° converted this to a mixture of at least three compounds. Again, products of insertion into the C-6 hydrogen bonds (**19**) predominated (78%) with the ratio of 6α to 6β insertion being at least 2:1. The 6α isomer was identified by the fact that the axial 6β-hydrogen and the 7α-hydrogen gave rise to two triplets with $J = 10$ centered at δ 3.65 and 3.99 in its p.m.r. spectrum. The product of insertion into the C-8–hydrogen bond (**20**) was only formed in 7% yield.

The product ratios are again accounted for on the basis of nitrene rotamers and non-bonded repulsion in the transition state. Examination of models showed that only rotamer **21** enables formation of a three-center cyclic transition state for insertion into the C-8—H bond. Because of repulsive interaction with the 15β hydrogen this rotamer is unfavorable, hence the low yield of **20**. Rotamer **22** appears to be the only one permitting close-enough approach to the 6-hydrogens for insertion. To account for the higher percentage of insertion into the 6α-CH bond we suggest that repulsive interaction of the β-hydrogen with C-19, as the transition state for insertion develops, raises its energy relative to that of the 6α case.

The proton-decoupled ^{13}C.m.r. spectrum of **11**, in comparison with those of 9-substituted steroidal molecules (**23**, R = $NHCOCH_3$ or $NHCOOCH_3$) supported the 5-substituted structure. In the models an upfield shift of *ca.* 5 p.p.m. was noted for the carbonyl carbon, relative to the corresponding 11-ketone with no substituent on C-9 (Table 1) (see ref. 15). In contrast the carbonyl of **11** had no such displacement (Table 1). A 5 p.p.m. upfield shift of C-3 in the spectrum of **11** was observed. This too is more consistent with substitution on C-5 rather than on the more remote C-9.

As mentioned above, the c.d. spectrum of **11** corresponded well with that of the 9α-amido-11-ketopregnane models **23** (Table 1). However we now must conclude that the presence of the acylamino group on C-5 in a positive octant is the source of the sizeable positive ΔΔε for **11**.

The failure to obtain the 9-substituted derivative and the low yield of the 8-substituted one, discourages this approach to cucurbitanes and protostanes. However substitution of C-9 from an 11α-azidoformate remains an interesting possibility.

Experimental

Infrared spectra were taken on a Perkin-Elmer model 257 grating spectrophotometer, with chloroform as solvent; p.m.r. spectra were determined using a Varian A-60-A spectrometer using deuteriochloroform as solvent and TMS as internal reference; ^{13}C.m.r. spectra were obtained using a Varian XL-100 Fourier transform spectrometer using external TMS in deuteriochloroform as reference; u.v. spectra were recorded using a Cary model 11 spectrophotometer and o.r.d–c.d. spectra on a Durrum-Jasco model ORD-5 spectropolarimeter, all in 95% ethanol. Thin-layer chromatography was done using silica gel. Rotations were for solutions in chloroform with concentrations near 10 g/l.

Materials

Crude lanosterol (Sigma Chemical Co.) was converted into 3β-acetoxylanostan-7,11-dione, which was reduced catalytically to 3β-acetoxy-11-oxolanostan-7α-ol (12) or with sodium borohydride, to 3β-acetoxy-11-oxolanostan-7β-ol (12).

3β-Acetoxy-11-oxolanostan-7α-yl Chloroformate

3β-Acetoxy-11-oxolanostan-7α-ol (153 mg) was dissolved in 15 ml of benzene. To this was added 108 mg of phosgene–pyridine complex (16) and the mixture stirred at room temperature for 25 min. The benzene solution was washed three times with cold water, dried with sodium sulfate, and evaporated. The 167 mg of oily residue crystallized in the presence of *n*-pentane. Two recrystallizations from *n*-hexane gave 130 mg of the chloroformate: m.p. 128–132°; ν_{max} 1770, 1726, and 1700 cm^{-1}; $[\alpha]_D$ +21°.

Anal. Calcd. for $C_{33}H_{53}O_5Cl$: C, 70.12; H, 9.45; Cl, 6.30. Found: C, 70.29; H, 9.60; Cl, 6.13.

3β-Acetoxy-11-oxolanostan-7α-yl Azidoformate (8)

To a solution of 472 mg of 3β-acetoxy-11-oxolanostan-7α-yl chloroformate in 30 ml of dimethylformamide was added 800 mg of sodium azide. The mixture was stirred for 3 h at 50 °C, 5 ml of water was then added and the product extracted into benzene. The benzene layer was washed three times with water, dried over magnesium sulfate and evaporated. The 474 mg of residue was recrystallized from methanol. The azidoformate had m.p. 123–125°; ν_{max} 2185, 2135, 1720, and 1700 cm^{-1}; $[\alpha]_D$ +2°.

Anal. Calcd. for $C_{33}H_{53}O_5N_3$: C, 69.32; H, 9.34; N, 7.35. Found: C, 69.45; H, 9.70; N, 7.07.

*Thermolysis of 3β-Acetoxy-11-oxolanostan-7α-yl Azidoformate (**8**)*

A solution of 905 mg of **8** in 50 ml of carbon tetrachloride in a sealed tube was maintained at 140–142° for 1 h, 45 min. The cooled solution was washed with sodium bicarbonate solution, dried over magnesium sulfate, and distilled. The residual oil was adsorbed onto a column of 120 g of neutral alumina, grade III. The column was eluted with benzene, benzene–ether mixtures, ether, and ether–methanol mixtures. The main products are listed in the order of their emergence:

3β-Acetoxylanostan-7,11-dione

The crude fraction (47 mg) after purification by t.l.c. gave 40 mg m.p. 216–218° (lit. (12) 223–224°). Its i.r. and n.m.r. spectra were identical with those of authentic 3β-acetoxylanostan-7,11-dione.

*Carbamate of 3β-Acetoxy-11-oxolanostan-7α-ol (**9**, R = $CONH_2$)*

Crude weight 58 mg. T.l.c. purification followed by recrystallization from methanol gave a product with m.p. 235–240°. It had ν_{max} 3540, 3430, 1725, 1700, and 1585 cm^{-1}; ν_{max} 293 nm (ε 51); p.m.r. signals at δ 5.29 (broad singlet, 7β-H), 5.07 (s, NH), 4.69 (t, 3α-H); ^{13}C.m.r. signals at 208.6 (C-11), 171.1 (3β-O*C*OCH$_3$), 155.9 (O*C*ONH), 80.5 (C-3), and 72.0 (C-7) p.p.m.; $[\alpha]_D$ +18°.

Anal. Calcd. for $C_{33}H_{55}NO_5$: C, 72.62; H, 10.16; N, 2.57. Found: C, 72.78; H, 9.97; N, 2.50.

*Cyclic Carbamate of 3β-Acetoxy-6α-amino-11-oxolanostan-7α-ol (**10**)*

The 478 mg needed only recrystallization from ethanol – methylene chloride to give **9** m.p. 258–262°. It had ν_{max} 3500, 3300, 1760, 1735, and 1702 cm^{-1}; p.m.r. signals at δ 6.76 (s, NH), 4.60 (d, J = 5 Hz, 7β-H), 4.44 (t, J = 7 Hz, 3α-H), 3.83 (broad q, J_1 = 10 Hz, J_2 = 5 Hz, 6β-H); ^{13}C.m.r. signals at 210.6 (C-11), 170.7 (3β-OCOCH$_3$), 158.9 (OCONH), 79.4 (C-7), and 55.8 (C-6); $[\alpha]_D$ +27°.

Anal. Calcd. for $C_{33}H_{53}O_5N$: C, 72.89; H, 9.82; N, 2.58. Found: C, 72.73; H, 10.00; N, 2.53.

*Cyclic Carbamate of 3β-Acetoxy-5α-amino-11-oxolanostan-7α-ol (**11**)*

The crude product (119 mg) was purified by preparative t.l.c. followed by recrystallizations from acetone and ethanol – methylene chloride. It then gave a single spot on t.l.c. and gave sharp spectra. However its m.p. still had the range 278–292° unaltered on further recrystallization. It had ν_{max} 3340, 1725, and 1690 cm^{-1}; λ_{max} 296 nm (ε 34); and p.m.r. signals at δ 5.87 (s, NH), 5.10 (broad, 3α-H), 4.67 (broad singlet, 7β-H); $[\alpha]_D$ +18°. It gave ^{13}C.m.r. signals at 211.0 (C-11), 170.6 (3β-O*C*OCH$_3$), 153.6 (O*C*ONH), 74.9 (C-3), 74.4 (C-7), and 64.2 (C-5) p.p.m.

Anal. Calcd. for $C_{33}H_{53}O_5N$: C, 72.84; H, 9.82; N, 2.58. Found: C, 72.69; H, 9.98; N, 2.49.

In a larger run the yields were: **9**, 7%; **10**, 50%; **11**, 9%.

*3β-Acetoxy-11-oxolanostan-7β-yl Azidoformate (**18**)*

Phosgene was bubbled into a solution of 1.34 g of 3β-acetoxy-11-oxolanostan-7β-ol and 0.8 ml of pyridine in 70 ml of benzene for 1.5 h. The reaction mixture was washed three times with water, dried over magnesium sulfate, then the solvent removed under reduced pressure. The crude chloroformate was dissolved in 6 ml of dry dimethylformamide. After addition of 1.3 g of sodium azide the mixture was heated at 55–60° for 4 h. Water was added to the cooled solution, the product extracted into benzene, and the benzene washed three times with water. The benzene layers gave 1.53 g of crude crystalline azidoformate. After recrystallization from acetone–methanol it had m.p. 141–146°; ν_{max} 2185, 2135, 1725, and 1705 cm^{-1}; $[\alpha]_D$ +34°.

Anal. Calcd. for $C_{35}H_{53}O_5N_3$: C, 69.32; H, 9.34; N, 7.35. Found: C, 69.14; H, 9.51; N, 7.32.

*Thermolysis of **18***

A solution of 720 mg of **18** in 50 ml of carbon tetrachloride in a sealed tube was kept at 140–142° for 70 min. It was then washed with sodium bicarbonate solution, dried, and distilled. The residue was given a preliminary purification by chromatography on alumina (activity III), then separated into two main fractions by preparative t.l.c. The one with higher R_f was rich in oxazolidinone **20** while the more polar one contained a mixture of the two epimeric oxazolidinones **19**. These were separated by fractional crystallization from methanol – methylene chloride and ethanol–chloroform mixtures.

*Cyclic Carbamate of 3β-Acetoxy-6α-amino-11-oxolanostan-7β-ol (**19a**)*

This had m.p. 268–276°; ν_{max} 3440, 1758, 1730, and 1705 cm^{-1}; p.m.r. signals at δ 6.58 (s, NH), 4.40 (t, J = 8 Hz, 3α-H), 3.99 (t, J = 10 Hz, 7α-H), 3.65 (t, J = 10 Hz, 6β-H); $[\alpha]_D$ +54°.

Anal. Calcd. for $C_{35}H_{53}O_5N$: C, 72.89; H, 9.82; N, 2.58. Found: C, 72.88; H, 10.02; N, 2.51.

*Cyclic Carbamate of 3β-Acetoxy-6β-amino-11-oxolanostan-7β-ol (**16b**)*

This had m.p. 307–313°; ν_{max} 3460, 1755, 1730, and 1705 cm^{-1}; p.m.r. signals at δ 5.78 (s, NH), 4.60 (t, J = 8 Hz, 3α-H), 4.32 (multiplet, 6α- and 7α-H); $[\alpha]_D$ +90°.

Anal. Calcd. for $C_{35}H_{53}O_5N$: C, 72.89; H, 9.82; N, 2.58. Found: C, 72.74; H, 9.99; N, 2.50.

*Cyclic Carbamate of 3β-Acetoxy-8β-amino-11-oxolanostan-7β-ol (**20**)*

The 45 mg of product was recrystallized from methanol – methylene chloride to give **17**, m.p. 315–320°. It had ν_{max} 3490, 1755, 1730, and 1715 cm^{-1}; p.m.r. signals at δ 5.34 (s, NH), 4.67 (t, J = 7 Hz, 3α-H), 4.42 (t, J = 8 Hz, 7α-H); $[\alpha]_D$ +46°.

Anal. Calcd. for $C_{33}H_{53}O_5N$: C, 72.89; H, 9.82; N, 2.58. Found: C, 72.67; H, 9.68; N, 2.37.

*Partial Hydrolysis of **11***

A solution of 203 mg of carbamate **11** and 115 mg of potassium hydroxide in 5 ml of ethanol and 0.5 ml of dioxane was refluxed for 15 min. After dilution with water, the mixture was extracted with chloroform. The 190 mg of crystalline product melted at 245–248° and gave n.m.r. signals at δ 6.70 (NH), 4.58 (7β-H), 3.86 (3α-H); ν_{max} 3600–3100, 3450, 1705, 1685 cm^{-1}. This is consistent with the 3β-hydroxy-11-keto carbamate.

*11β-Hydroxy-3β-pivalate (**13**) (R = pivaloyl)*

A solution of 100 mg of the 3β-hydroxy-11-keto car-

bamate in 2 ml of methanol was refluxed gently while 95 mg of sodium borohydride was added in 15-mg portions over a period of 16 h.

The reaction mixture was diluted with water then extracted with chloroform. The dried ($MgSO_4$) chloroform layers gave 96 mg of product giving one spot on a t.l.c. plate (chloroform–ethanol, 10:1). This was dissolved in 2 ml of pyridine, 0.2 ml of pivaloyl chloride added then the mixture left for 18 h at room temperature. After addition of ice water, the product was extracted into benzene. The benzene solution was washed with dilute hydrochloric acid, sodium bicarbonate solution, then with water, dried ($MgSO_4$), and distilled. The residue was purified by preparative t.l.c. (10:1 chloroform–ethanol) giving 70 mg of crystalline solid. After recrystallization from methanol – methylene chloride it had m.p. 302–312° and gave one spot on a t.l.c. plate (10:1 $CHCl_3$—EtOH). It had ν_{max} 3605, 3440, 1725, and 1690 cm^{-1} and gave n.m.r. signals at δ 5.40 (NH), 4.85 (3α-H), 4.56 (7α-H), and 4.29 (11α-H).

Anal. Calcd. for $C_{36}H_{61}NO_5$: C, 73.55; H, 10.46; N, 2.38. Found: C, 73.51; H, 10.74; N, 2.33.

*3β-Pivaloyloxy-5α-lanost-9(11)-ene-5α(N),7α(O)-carbamate (**14**)*

The 3β-pivaloyloxy-11β-hydroxy carbamate (**13**) (R = pivaloyl) (65 mg) was dissolved in 0.5 ml of pyridine and the solution cooled to 5 °C. After addition of 0.03 ml of thionyl chloride the mixture was left at 5 °C for 15 min. After dilution with ice water the product was extracted into benzene, the benzene layers washed with water, dilute acid, sodium bicarbonate solution, and water, dried and distilled. The 64 mg of crystalline product after one recrystallization from ethanol had m.p. 282–288°; $[\alpha]_D$ +25°; and ν_{max} 3440, 3040, 1725, and 1700 cm^{-1}. It gave n.m.r. signals at δ 5.48 (NH), 5.42 (11-H), 4.83 (3α-H), 4.65 (7β-H).

Anal. Calcd. for $C_{36}H_{59}NO_4$: C, 75.88; H, 10.44; N, 2.46. Found: C, 75.76; H, 10.51; N, 2.39.

*3β,20β-Diacetoxy-9α-methoxycarbon-amido-5α-pregnan-11-one (**23**, R = NHCOOCH$_3$)*

A mixture of 126 mg of 3β,20β-diacetoxy-9α-aminopregnane-11-one (6), 1 ml of methyl chloroformate, and 3 ml of pure chloroform was refluxed gently for 5 days. The solution was taken to dryness under reduced pressure, the residue dissolved in methylene chloride, and the solution filtered through a short column of neutral alumina (Activity I). The 160 mg of crystalline product was recrystallized repeatedly to give a m.p. 228–230°; $[\alpha]_D$ +71°; ν_{max} 3450, 1730, and 1505 cm^{-1}. It gave p.m.r. signals at δ 5.38 (NH), 4.90 (broad, 2H, C*H*OAc), 3.83 (OCH_3), 2.1 (6H, OAc); and ^{13}C.m.r. signals at 205.4 (C-11); 170.8 and 170.5 (3β- and 20β-O*C*OCH$_3$); 156.2 (N-*C*OCH$_3$); 72.9 and 72.4 (C-3 and C-20); and 66.8 (C-9) p.p.m.

Anal. Calcd. for $C_{27}H_{41}NO_7$: C, 65.96; H, 8.41; N, 2.85. Found: C, 65.89; H, 8.51; N, 2.56.

*3β,20β-Diacetoxy-9α-acetamido-5α-pregnane-11-one (**23**, R = NHCOCH$_3$)*

A solution of 86 mg of 3β,20β-diacetoxy-9α-aminopregnan-11-one (6) in 1.3 ml of acetic anhydride was heated at 130° for 2h. The product crystallized from the hot solution. After cooling, 83 mg of crystals were collected by filtration. These were recrystallized from ethanol – methylene chloride to give the *N*-acetyl derivative, m.p. 324–332°; $[\alpha]_D$ +67°; ν_{max} 3450, 1725, 1682, and 1505 cm^{-1}. It gave p.m.r. signals at δ 6.02 (NH), 4.76 broad (3α- and 20α-H), 2.13 ($NCOCH_3$), 2.05 ($OCOCH_3$), 1.20 (C-19), and 0.61 (C-18); and ^{13}C.m.r. signals at 204.8 (C-11); 170.9, 170.0, 169.7 (3β- and 20β-O*C*OCH$_3$ and *N*-*C*OCH$_3$); 73.1 and 72.4 (C-3 and C-20); 67.0 (C-9) p.p.m.

Anal. Calcd. for $C_{27}H_{41}NO_6$: C, 68.18; H, 8.69; N, 2.94. Found: C, 68.06; H, 8.82; N, 3.01.

*3β-Acetoxy-11-oxolanostan-7α-yl Carbamate (**9**, R = CONH$_2$)*

Aqueous ammonia (28%, 0.5 ml) was added to a stirred ice-cold solution of 3β-acetoxy-11-oxolanostan-7α-yl chloroformate in 1 ml of tetrahydrofuran. After 3 h at 0° water was added and the product extracted into chloroform. The 99 mg of crystalline product was recrystallized from methanol giving the carbamate with m.p. 237–240° and ν_{max} 3540, 3435, 1725, 1700, 1585, and 1400 cm^{-1}. It gave n.m.r. signals at δ 5.17 (7β-H), 5.04 (NH_2), and 4.58 (3α-H).

Anal. Calcd. for $C_{33}H_{55}NO_5$: C, 72.62; H, 10.16; N, 2.57. Found: C, 72.69; H, 10.22; N, 2.61.

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