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Aza-steroids. II.[1] Enamine Reaction of Androstanones. Synthesis of 17-Acetoxy-5β-androstano[4,3-*c*]quinolizidin-2′-one[2]

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As a preliminary for the synthesis of 10-aza-steroids, enamine reaction of 3-oxo-steroids was examined. The reaction of 3-oxo-steroids with ethyl 2-piperidinoacetate (III) through intramolecular cyclization *via* their enamine, 17-acetoxy-5β-androstano-[4,3-*c*]quinolizidin-2′-one (I) and its related compound were synthesized and their conformation and configuration were examined.

A large number of aza-steroids having a bridge-head nitrogen atom have been synthesized in recent years.[4-7] As a model experiment for the synthesis of hitherto unknown 10-aza-steroids, enamine reaction of androstanone was examined and 17-acetoxy-5β-androstano[4,3-*c*]quinolizidin-2′-one [I] was synthesized (Chart 1).

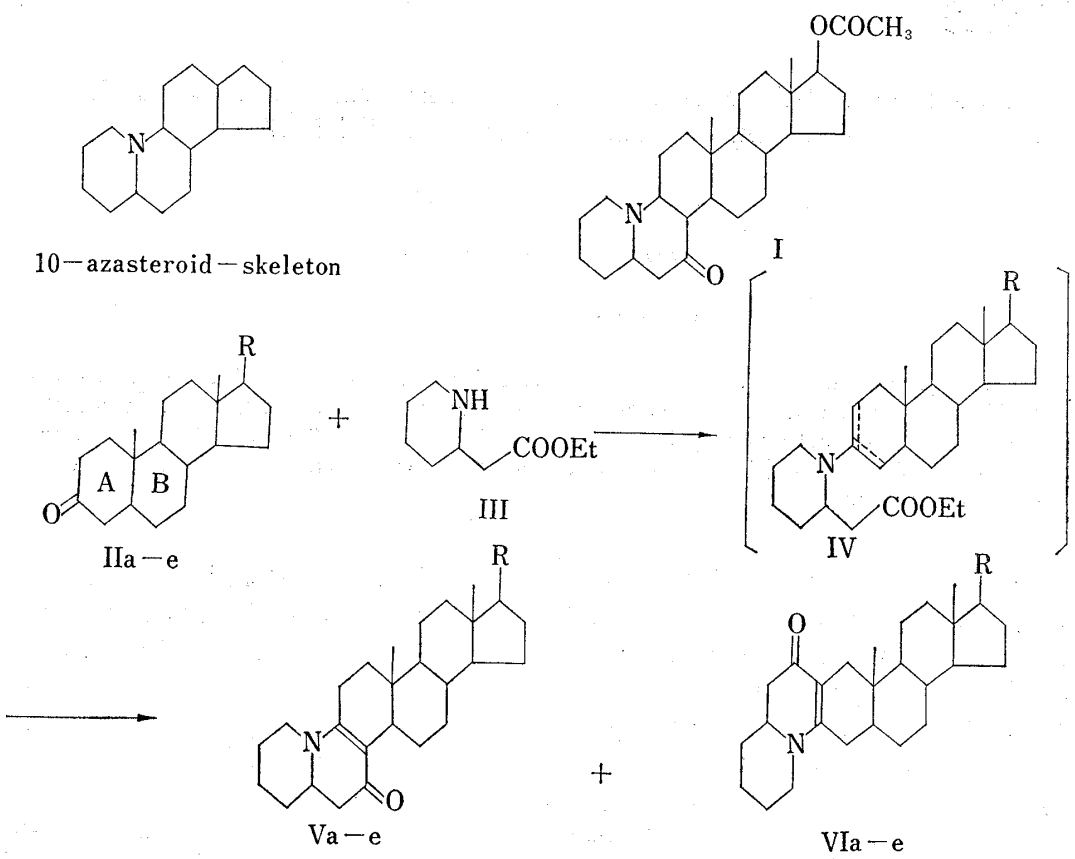
Synthesis of nitrogen-containing polycycles by the reaction of cycloalkanone and aminocarboxylic acid ester has been reported[8] and this method was applied to the reaction of steroids (II) with ethyl 2-piperidinoacetate (III).

Heating of 17-hydroxy-5β-androstan-3-one (IIa) with III, in the presence of *p*-toluenesulfonic acid or, more effectively, in the presence of trifluoroacetic acid, and cyclization by intramolecular acylation *via* the enamine (IV) afforded two kinds of vinylogous amides (Va and VIa). They were difficult to separate but acetylation to 17-acetoxy compounds (Vb and VIb) enabled their separation by column chromatography. These two compounds were structural isomers differing in the direction of cyclization, forming angular and linear structures. The structural determination of these compounds will be described later.

In a similar manner, two kinds of vinylogous amides (Vd and VId) were obtained from 17-acetoxy-5α-androstan-3-one (IId) and two kinds of vinylogous amides (Ve and VIe) from cholestan-3-one (IIe). Formation ratios of these compounds were Vb:VIb=7:5, Vd:VId =3:11, and Ve:VIe=3:10.

In general, though there are some doubts, 5β-3-ketone group in steroids mainly take the Δ^3-enol form, while 5α-3-ketone groups take the Δ^2-enol form. Attack of electrophilic reagents mainly occurs in C-4 position in the former and in the C-2 position in the latter.[9]

1) This paper forms part XXIV of "Synthesis of Quinolizine Derivatives." Part XXIII: S. Ohki and M. Akiba, *Yakugaku Zasshi*, **90**, 1193 (1970).
2) Paper presented at the 2rd Symposium on Heterocyclic Chemistry, Nagasaki, 1969, p. 147.
3) Location: *Ueno Sakuragi 1-10-19, Daito-ku, Tokyo, 110, Japan.*
4) 8-aza-steroid: R.E. Brown, D.N. Lustgarten, R.J. Stanaback, and R.I. Meltzer, *J. Org. Chem.*, **31**, 1489 (1966); A.I. Meyers and J.C. Sircar, *Tetrahedron*, **23**, 785 (1967).
5) 9-Aza-steroid: A.I. Meyers and W.N. Beverung, *Chem. Commun.*, **1968**, 877; S. Ohki and M. Akiba, *Chem. Pharm. Bull.* (Tokyo), **17**, 2484 (1969).
6) 13-Aza-steroid: W.R. Schleigh, A. Calata, and F.D. Popp, *J. Heterocyclic Chem.*, **2**, 379 (1965); A.J. Birch and G.S.R. Subbarao, *J. Chem. Soc.*, **1965**, 3007.
7) 14-Aza-steroid: E.R.H. Jones, Brit. Patent 1017700 1966 [*Chem. Abstr.*, **64**, 142 (1966)]; U.K. Pandit, K. de Jonge, G.J. Koomen, and H.O. Huismann, *Tetrahedron Letters*, **1967**, 3529.
8) A.I. Meyers and Sujan Singh, *Tetrahedron Letters*, **1967**, 5319; A.I. Meyers, A.H. Reine, and R. Gault, *J. Org. Chem.*, **33**, 698 (1968).
9) L.F. Fieser and X.A. Dominguez, *J. Am. Chem. Soc.*, **75**, 1704 (1953); A.J. Liston, *J. Org. Chem.*, **31**, 2105 (1966).



a : series, A/B : *cis*, R=OH
b : series, A/B : *cis*, R=$OCOCH_3$ } 5β series
c : series, A/B : *trans*, R=OH
d : series, A/B : *trans*, R=$OCOCH_3$
e : series, A/B : *trans*, R=C_8H_{17} } 5α series

Chart 1

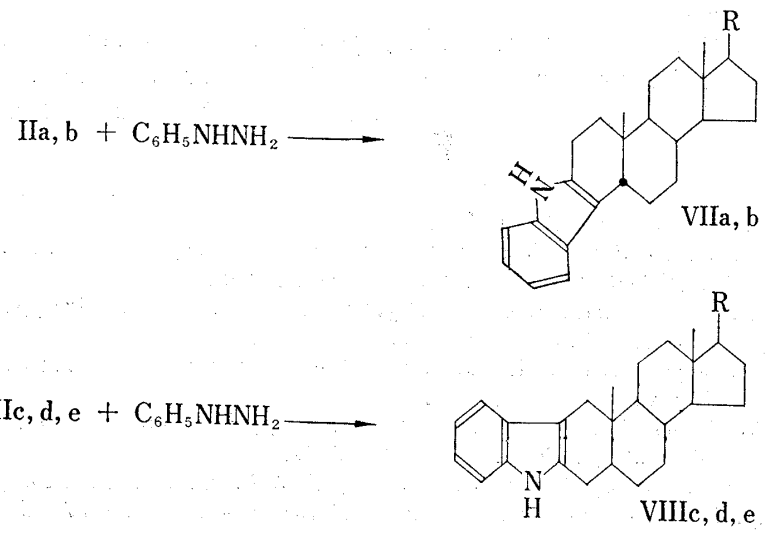
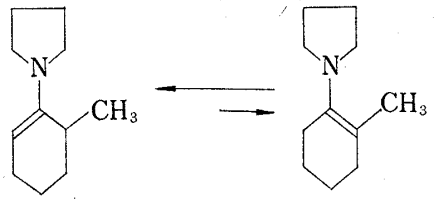


Chart 2

The direction of the double bond in the enols and enamines is not necessarily the same but, Bose and others[10] obtained Δ^3-enamine in the reaction of 5β-cholestan-3-one and pyrrolidine, and Δ^2-enamine from the 5α-series. Manhas and Mccoy[11] obtained quinolino-steroid of linear structure alone from the reaction of 5β-cholestan-3-one-pyrrolidine enamine and *o*-aminobenzaldehyde, showing the same tendency. In the synthesis of indolo-steroids by Fischer's indole synthesis, stereospecific control is made in the direction of cyclization and Doorenbos and Wu[12] obtained angular 17-hydroxy-5β-androst-3-eno[3,4-*b*]indole (VIIa) from 17-hydroxy-5β-androstan-3-one (IIa) and linear 17-hydroxy-5α-androst-3-eno[3,2-*b*]indole (VIIIc) from 17-hydroxy-5α-androstan-3-one (IIc), and also VIIIe[13] from IIe of 5α-series. In the present series of work, also, VIIb was obtained from IIb of 5β-series and VIIId from IId of 5α-series by the method of Dorée and Petrow.[14]

It is interesting that cyclization products of V and VI were produced from 5β-series, which may be understandable, but about 30% of angular structure isomers (Vd and Ve) were obtained besides those (VId and VIe) of linear structure from 5α-series (IId and IIe). Enamines, such as 2-methylcyclohexanone-pyrrolidine enamine, are known to be in the equilibrium state (IX),[15] and the enamine compound (IV) may be expected in similar equilibrium forms. For example, in the 5β-series, A form is more stable than the B form, and the equilibrium tends towards A, forming V as the main product and VI as the by-product (Chart 3). This will be reversed in 5α-series. According to the hitherto known facts, the angular structure



IX

5β—series—steroid enamine

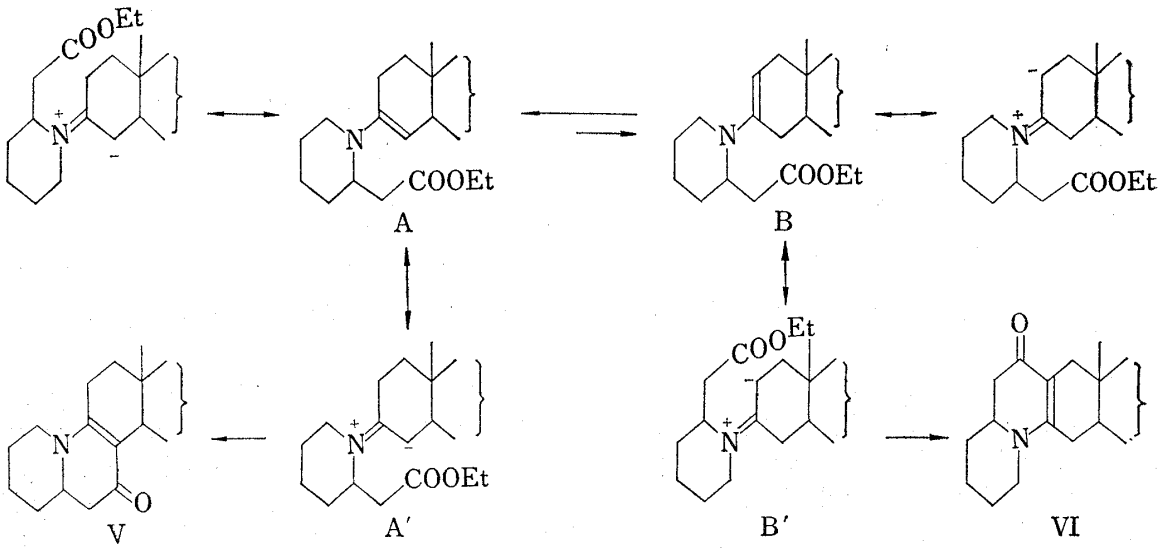


Chart 3

10) A.K. Bose, G. Mina, M.S. Mahnas, and E. Rzucidlo, *Tetrahedron Letters*, **1963**, 1467.
11) M.S. Manhas and J.R. Mccoy, *J. Chem. Soc.*(*c*), **1969**, 1419.
12) N.J. Doorenbos and M.T. Wu, *J. Med. Chem.*, **11**, 158 (1968).
13) Y. Ban and Y. Sato, *Chem. Pharm. Bull.* (Tokyo), **13**, 1073 (1965).
14) C. Dorèe and V. Petrow, *J. Chem. Soc.*, **1935**, 1391.
15) G. Stork, A. Brizzolaro, H. Landesmann, J. Szmuskovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(V) of 5α-series is likely to transit to the linear structure (VI) by a thermodynamic control, and transition of VI to V will be likely to occur in 5β-series.

However, the above hypothesis will require the establishment of a relation A′⇄V or B′⇄VI.[16] Attempts were made to effect transition of Vd and VIb respectively to VId and Vb by heating in the presence of acid but transition did not materialize. This fact seems to suggest that both A- and B-form enamine are present in equilibrium in both 5α and 5β series, and V and VI were produced from each of them.

Structural determination of angular (V) and linear structure (VI) of the products was made by comparative examination with VII and VIII whose structures had been determined already by spectroscopic and chemical means.[12–14]

In the nuclear magnetic resonance (NMR) spectra of angular (VII) and linear structure (VIII), the signals for C_1-H of the steroid are clearly different. For example, in VIIb and VIIId, the signal for C_1-H (quasi-equatorial (eq.)) in VIIId appears as one of AB type at 7.23 τ while that of C_1-H (quasi-axial (ax.)) appears at 7.70 τ by decoupling the signal at 7.23 τ (Fig. 1). This kind of absorption can not be seen in VIIb. As shown in Table I, this relation holds in VIIIe.

On the other hand, the same relationship exists between V and VI compounds synthesized in the present series of work, indicating that the former has an angular structure and the latter, a linear structure. Fig. 2 is the NMR spectrum of VIb, indicating that the signal of C_1-H_2 (quasi-eq. and-ax.), confirmed by decoupling as above, is similar to that of VIIId with greater difference in the chemical shift which is considered to be the effect of the carbonyl. This was also confirmed by the solvation effect of pyridine in VIb.

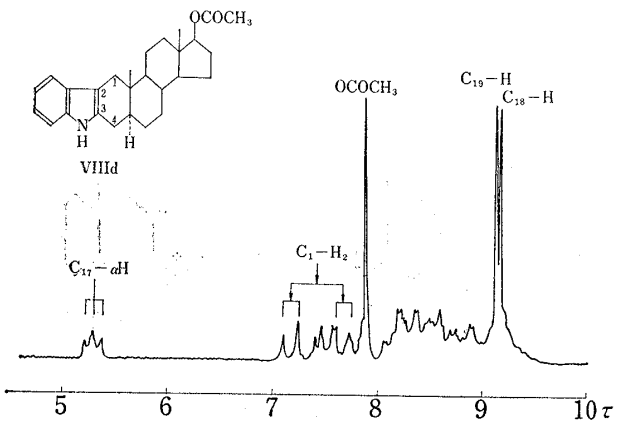


Fig. 1. NMR Spectrum of Compound (VIIId)

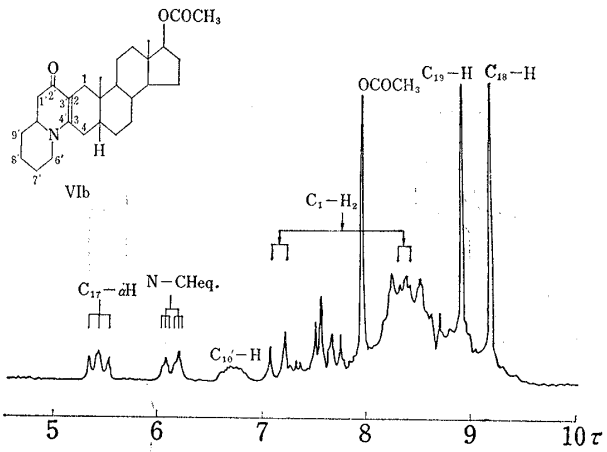


Fig. 2. NMR Spectrum of Compound (VIb)

The assignment of the signals for C_{10}'-H and N-CH_2 (eq. and ax.) in VIb was made by the following experiments: Horii and others[17] synthesized a vinylogous amide (X) from III and cyclohexanone, and obtained perhydrobenzo[*c*]quinolizinone (XIII) with all-*trans* juncture by subsequent reduction and oxidation. Oxidation of XIII by mercuric acetate gives γ-pyridone (XIV)[18] and XIV was obtained from X by the same treatment. Similar oxidation of Vb and VIb gave the corresponding γ-pyridones (XV and XVI), though in a low yield. As shown in Table II, comparison of these spectra has clarified the signals for C_{10}'-H and N-CH_2 of quinolizidione. For example, in VIb, the doublet–triplet peak at 6.16 τ was assigned to N-CH (eq.) and the multiplet peak at 6.75 τ which disappears in XVI to C_{10}'-H. A similar compound,

16) W. Sobotka, W.N. Beverung, G.G. Munoz, and A.I. Meyers, *J. Org. Chem.*, **30**, 3667 (1965).
17) Z. Horii, K. Morikawa, Y. Tamura, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **14**, 1399 (1966).
18) Z. Horii, K. Morikawa, and I. Ninomiya, *Chem. Pharm. Bull. (Tokyo)*, **17**, 846(1969).

XVII synthesized by the condensation of 2-vinylpyridine with dimedone and subsequent reduction, has been shown here as a comparative compound because the signal for C_1-H $_{(ax.)}$ appears clearly (Fig. 4).

TABLE I.[a] NMR Spectrum of Angular and Linear Structure

Compound	$C_{(1)}$-H (quasi-eq.)	$C_{(1)}$-H (quasi-ax.)	Δ[b](Hz)	$C_{(18)}$-H	$C_{(19)}$-H	C_1-H-gemHz	$OCOCH_3$
VIIId	7.23	7.70	47	9.20	9.19	15	7.93
VIIIe	7.25	7.70	45	9.30	9.20	15	—
VIIb	—	—	—	9.25	8.90	—	8.03
VId	7.375	8.325	95	9.22	9.32	15.5	8.00
VIe	7.375	8.275	90	9.35	9.35	15.5	—
VIb	7.185	8.385	120	9.22	8.96	16.2	8.00
	(6.84)	(8.24)	(140)	(9.25)	(9.00)	(16.2)	(8.05)
Vd	—	—	—	9.21	9.32	—	7.98
Ve	—	—	—	9.35	9.35	—	—
Vb	—	—	—	9.22	8.97	—	7.97
	—	—	—	(9.17)	(9.00)	—	(7.97)
XV	—	—	—	9.33	9.12	—	8.12
XVI	6.81	8.01	120	9.23	8.90	17.5	8.00

a) measured in $CDCl_3$; chemical shift in τ value Values in parentheses measured in C_5D_5N.
b) Δ=[$C_{(1)}$-H (quasi-ax.)−$C_{(1)}$-H (quasi-eq.)] (Hz)

X

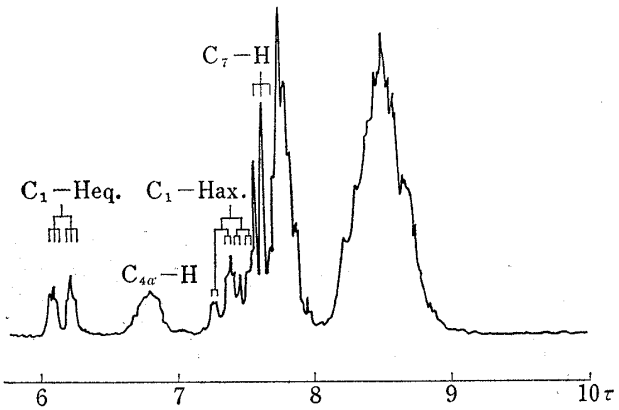
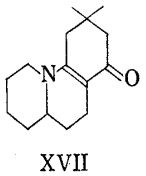


Fig. 3. NMR Spectrum of Compound (X)



XVII

Fig. 4. NMR Spectrum of Compound (XVII)

TABLE II.[a] NMR Spectrum of 6*a*,10*a*-Dehydro-6-oxo-perhydrobenzo[*c*]-quinolizine (X) and its Related Compound

	Vb	Vd	Ve	VIb	VId	VIe	X	XIV	XV	XVI	XVII
C_1-Heq.							6.17	6.18			6.05
C_6'-Heq.	6.16	6.17	6.16	6.16	6.16	6.16			6.27	6.15	
C_1-Hax.							7.40	6.18			7.15
C_6'-Hax.	7.40	7.20	7.20	—	—	—			6.27	6.15	
C_{4a}-H							6.80				6.90
C_{10}'-H	7.00	6.65	6.65	6.75	6.92	6.92					

a) measured in $CDCl_3$; chemical shift in τ value

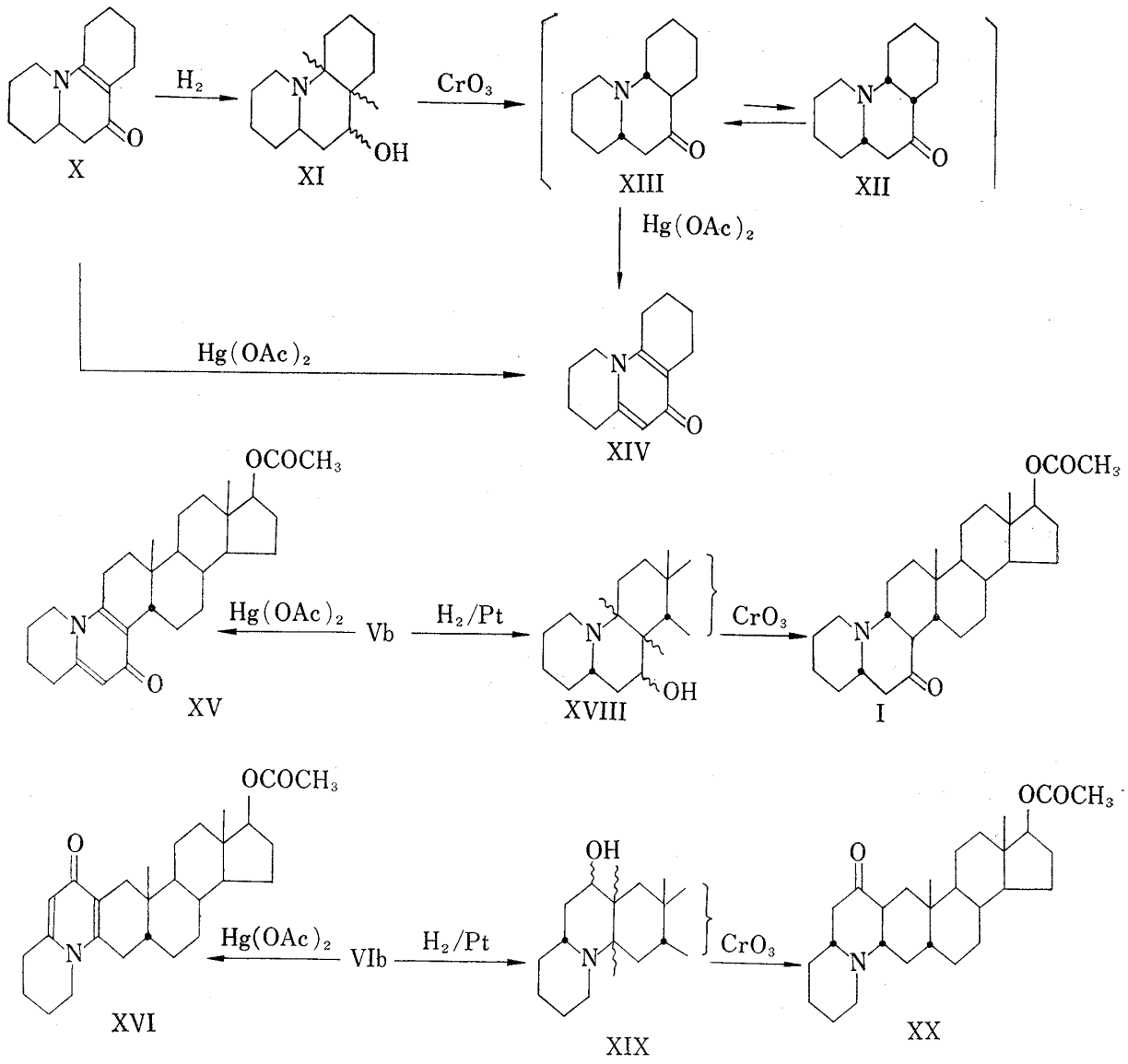


Chart 4

The shift of C_{19}-H in Vb and VIb is in a lower magnetic field than that of C_{19}-H in ordinary steroids, while those in Vd, Ve, VId, and VIe are in a higher magnetic field. This is probably due to the strong effect of magnetic anisotropy of –Ċ=Ċ–C=O of vinylogous amide. Consequently, steric structures of these compounds will be D form for Vb, C form for VIb, B form for Vd and Ve, and A form for VId and VIe (Eig. 5).

In cyclization to vinylogous amides, there must have been formed the compounds with angular methine proton (C_{10}'-H) of the quinolizidine ring in β-configuration and α-configuration but only one kind was actually obtained. Determination of this configuration was considered to be difficult and the steric structure of A, B, C, and D forms was indicated by β-configuration alone.

Infrared (IR) and ultraviolet (UV) absorption spectra of V and VI are given in Table III. IR spectra exhibits two bands of strong intensity at 6.0—7.5 μ, corresponding to α,β-unsaturated β-aminoketone.[19] The absorption at 333—341 mμ in the UV spectra corresponds to the characteristic absorption of >N–C=C–C=O chromophore.[16,20]

19) G.O. Dudek, *J. Org. Chem.*, **30**, 548 (1965).
20) F. Bohlmann and O. Schmidt, *Ber.*, **97**, 1354 (1964); F. Bohlmann, E. Winterfeldt, O. Schmidt, and W. Reusche, *ibid.*, **94**, 1774 (1961).

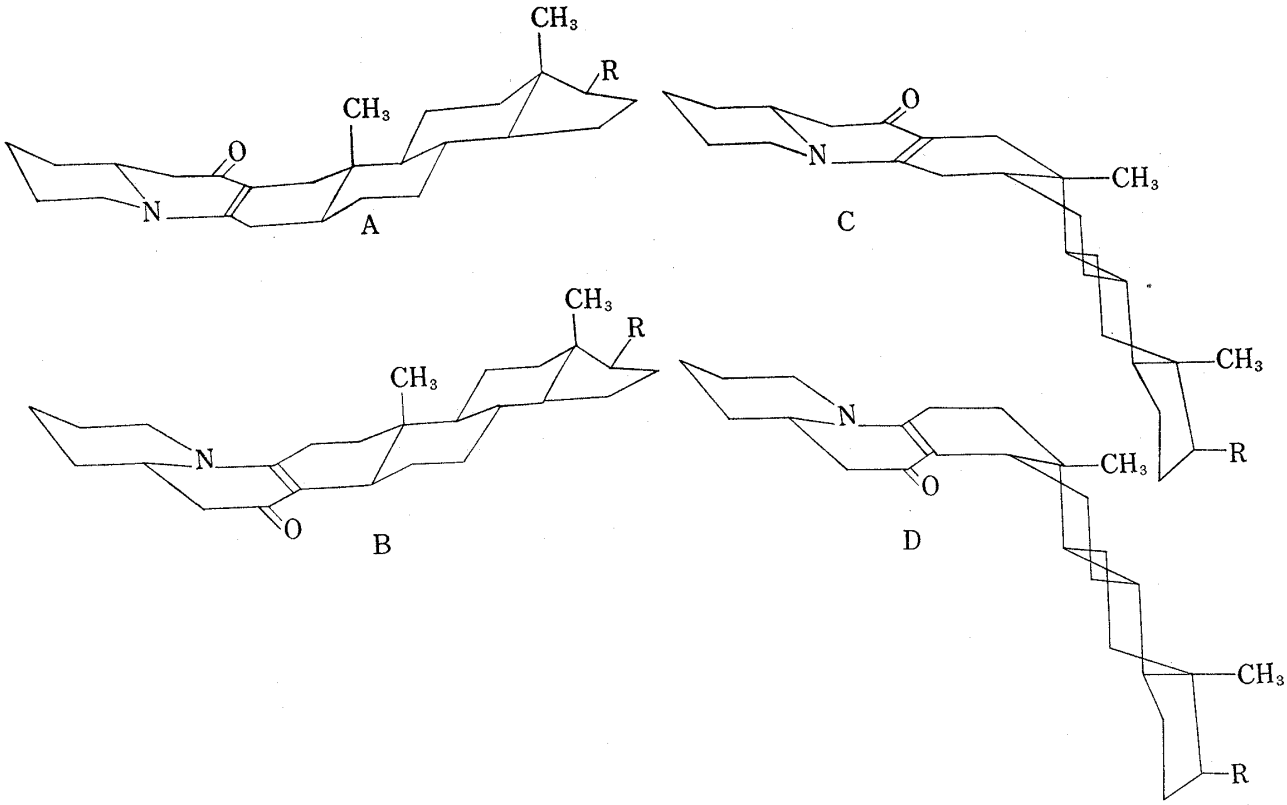


Fig. 5. Steric Structure of Vinylogous Amide (V and VI)

TABLE III. IR and UV Spectrum of Compound (V and VI)

	UV λ_{max}^{EtOH} mμ	IR ν_{max}^{KBr} cm^{-1}	
Vb	332	1626 (s)	1550 (s)
Vd	340	1626 (s)	1570 (s)
Ve	340	1631 (s)	1565 (s)
VIb	336	1610 (m)	1553 (s)
VId	334	1645 (s)	1580 (s)
VIe	334	1635 (s)	1567 (s)

Catalytic reduction of Vb over platinum dioxide in acetic acid to the alcohol compound (XVIII) and its oxidation with chromium trioxide in acetic acid gave quinolizidinone (I) as an unity. IR spectrum of I exhibited *trans*-quinolizidine band. Horii and others[21] obtained a more stable *trans* compound (XIII) by the same oxidation of XI, while they obtained a mixture of the *cis* (XII) and *trans* (XIII) compounds by oxidation with chromium trioxide and pyridine. From these examples and the possibility of the β-side attack of hydrogen for D-form, the compound obtained as an unity is considered to be I having the configuration shown in Chart 4. Similarly, the isomer (XX) of I was obtained as an unity from VIb.

In the present series of work, reaction of aminocarboxylic ester with androstanones was examined and synthesis of 10-aza-steroid will be reported subsequently.

Experimental[22]

Reaction of 3-Oxo-steroids and Ethyl 2-Piperidinoacetate——1) 17-Acetoxy-5β-androst-3-eno[4,3-*c*]-[3′,4′]dehydroquinolizidin-2′-one (Vb) and 17-Acetoxy-5β-androst-2-eno[3,2-*b*]-[3,′4′]dehydroquinolizidin-2′-

21) Z. Horii, K. Morikawa, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1472 (1968).
22) All melting points are uncorrected. NMR spectra were recorded at 100 Mcps, using tetramethylsilane as internal standard.

one (VIb): A solution of 200 mg of 17-hydroxy-5β-androstan-3-one (IIa) and 120 mg of ethyl 2-piperidinoacetate (III) dissolved in 10 ml of abs. toluene, with a small amount of *p*-TsOH as a catalyst, was heated for 30 hr in N_2 stream, with continuous removal of H_2O. Toluene was distilled off under a reduced pressure and the residue was purified by silica gel chromatography to afford 58 mg of a mixture of vinylogous amides (Va and VIa). Since their separation seemed impossible, this mixture was dissolved in 1 ml of Ac_2O–pyridine, allowed to stand over-night at room temperature, and Ac_2O and pyridine were distilled off under a reduced pressure, leaving 50 mg of a mixture of Vb and VIb. This mixture was submitted to thin-layer chromatography and a small amount of Vb and VIb was obtained.

The same reaction was carried out on a solution of 102 mg of 17-acetoxy-5β-androstan-3-one (IIb) and 106 mg of III dissolved in 5 ml of abs. xylene and 42 mg of a mixture of Vb and VIb was obtained in 15.3% yield. The use of trifluoroacetic acid as a catalyst in place of *p*-TsOH in the reaction of 1 g of IIb and 520 mg of III dissolved in 20 ml of abs. xylene gave 446 mg of a mixture (yield, 29.3%). This mixture was purified by column chromatography, using benzene–acetone mixture (10:3), and 259 mg of Vb was obtained from the initial fraction and 187 mg of VIb from the second fraction. Vb was recrystallized from hexane–acetone to colorless plates, mp 221—223°. *Anal.* Calcd. for $C_{28}H_{41}O_3N$: C, 76.49; H, 9.40; N, 3.19. Found: C, 76.18; H, 9.30; N, 2.95. UV λ_{max}^{EtOH}: 332 mμ. IR ν_{max}^{KBr} cm^{-1}: 1739 (ester), 1626, 1550 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 6.16 (1H, d-t, J=12.3, C_6'–$H_{eq.}$), 7.00 (1H, m, C_{10}'–H), 7.40 (1H, m, C_6'–$H_{ax.}$), 7.97 (3H, s, $OCOCH_3$), 9.00 (3H, s, C_{19}–H), 9.17 (3H, s, C_{18}–H). Mass Spectrum *m/e*: 439 (M^+).

VIb was recrystallized from hexane–acetone to colorless needles, mp 229—231°. *Anal.* Calcd. for $C_{28}H_{41}O_3N$: C, 76.49; H, 9.40; N, 3.19. Found: C, 76.49; H, 9.35; N, 3.42. UV λ_{max}^{EtOH}: 336 mμ. IR ν_{max}^{KBr} cm^{-1}: 1739 (ester), 1610, 1553. NMR ($CDCl_3$) τ: 6.16 (1H, d-t, J=12.25, C_6'–$H_{eq.}$), 6.75 (1H, m, C_{10}'–H), 7.185 (1H, J=16.2, C_1–$H_{quasi-eq.}$), 8.00 (3H, s, $OCOCH_3$), 8.39 (1H, J=16.2, C_1–$H_{(quasi-ax.)}$), 8.96 (3H, s, C_{19}–H), 9.22 (3H, s, C_{18}–H), Mass Spectrum *m/e*: 439 (M^+), 177 (M^+-262) ($C_{19}H_{27}O_3N$).

2) 17-Acetoxy-5α-androst-3-eno[4,3-*c*]-[3′,4′]dehydroquinolizidin-2′-one (Vd) and 17-Acetoxy-5α-androst-2-eno[3,2-*b*]-[3′,4′]dehydroquinolizidin-2′-one (VId): A solution of 500 mg of 17-acetoxy-5α-androstan-3-one (IId) and 260 mg of III dissolved in 15 ml of abs. xylene, in the presence of a small amount of trifluoroacetic acid was heated for 40 hr and the reaction mixture was treated as above. The product mixture was submitted to column chromatography, the column was eluted with benzene–acetone mixture (5:1), and 110 mg (14.5%) of VId and 30 mg (3.9%) of Vd were obtained.

VId was recrystallized from hexane–acetone to colorless powder, mp above 300°. *Anal.* Calcd. for $C_{28}H_{41}O_3N$: C, 76.49; H, 9.40; N, 3.19. Found: C, 76.02; H, 9.44; N, 3.16. UV λ_{max}^{EtOH}: 334 mμ. IR ν_{max}^{KBr} cm^{-1}: 1645, 1580 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 6.16 (1H, d-t (J=12.25), C_6'–$H_{eq.}$), 6.92 (1H, m, C_{10}'–H), 7.375 (1H, C_1–H_2 gem (J=15.5), C_1–$H_{(quasi-eq.)}$), 8.00 (3H, s, $OCOCH_3$), 8.325 (1H, C_1–H_2 gem (J=15.5), C_1–$H_{(quasi-ax.)}$), 9.22 (3H, s, C_{18}–H), 9.32 (3H, s, C_{19}–H).

Vd was recrystallized from hexane–acetone to colorless powder, mp above 300°. *Anal.* Calcd. for $C_{28}H_{41}O_3N$: C, 76.49; H, 9.40; N, 3.19. Found: C, 76.58; H, 9.39; N, 3.18. UV λ_{max}^{EtOH}: 340 mμ. IR ν_{max}^{KBr} cm^{-1}: 1626, 1570. NMR ($CDCl_3$) τ: 6.17 (1H, d-t, C_6'–$H_{eq.}$), 6.65 (1H, m, C_{4a}–H), 7.20 (1H, m, C_6'–$H_{ax.}$), 7.98 (3H, s, $OCOCH_3$), 9.21 (3H, s, C_{18}–H), 9.32 (3H, s, C_{19}–H).

3) 5α-Cholestan-3-eno[4,3-*c*]-[3′,4′]dehydroquinolizidin-2′-one (Ve) and 5α-Cholestan-2-eno[3,2-*b*]-[3′,4′]-dehydroquinolizidin-2′-one (VIe): The reaction of 500 mg of 5α-cholestan-3-one (IIe) and 252 mg of III afforded 150 mg (20.6%) of VIe, mp 242—243°, and 45 mg (6.2%) of Ve, mp 237—239°. *Anal.* Calcd. for $C_{34}H_{55}ON$ (VIe): C, 82.70; H, 11.23; N, 2.84. Found: C, 82.88; H, 11.16; N, 3.01. UV λ_{max}^{EtOH}: 334 mμ. IR ν_{max}^{KBr} cm^{-1}: 1635, 1567. NMR ($CDCl_3$) τ: 6.16 (1H, d-t, C_6'–$H_{eq.}$), 6.75 (1H, m, C_{10}'–H), 7.375 (1H, C_1–$H_{quasi-eq.}$), 8.275 (1H, C_1–$H_{(quasi-ax)}$), 9.35 (3H, s, C_{18}–H), 9.35 (3H, s, C_{19}–H). Ve: *Anal.* Calcd. for $C_{34}H_{55}ON$: C, 82.70; H, 11.23; N, 2.84. Found: C, 82.46; H, 11.13; N, 2.79.

17-Acetoxy-5β-androst-3-eno[3,4-*b*]indole[12] (VIIb)——A solution of 400 mg of phenylhydrazine dissolved in 2 ml of AcOH was added to a solution of 200 mg of IIb dissolved in 6 ml of AcOH and the mixture was heated on a water bath for 20 min. The tetrahydrocarbazole compound (VIIb) crystallized out when the reaction mixture was cooled and was recrystallized from MeOH–H_2O to yellow needles, mp 231—232°. Yield, 185 mg (71.9%). *Anal.* Calcd. for $C_{27}H_{35}O_2N$: C, 79.96; H, 8.70; N, 3.45. Found: C, 80.25; H, 8.21; N, 3.45. NMR ($CDCl_3$) τ: 2.2—3.0 (4H, m, aromatic proton), 5.53 (1H, t (J=7.5), C_{17}–H), 8.03 (3H, s, $OCOCH_3$), 8.90 (3H, s, C_{19}–H), 9.25 (C_{18}–H).

17-Acetoxy-5α-androst-2-eno[3,2-*b*]indole[12] (VIId)——Treatment of the reaction in the same way as for VIIb gave yellow needles, mp 275—277°. *Anal.* Calcd. for $C_{27}H_{35}O_2N$: C, 79.96; H, 8.70; N, 3.45. Found: C, 79.47; H, 8.21; N, 3.47. NMR ($CDCl_3$) τ: 2.27—2.90 (4H, m, aromatic proton), 5.33 (1H, t (J=7.5), C_{17}–H), 7.23 (1H, C_1–$H_{(quasi-eq.)}$), 7.70 (1H, C_1–$H_{(quasi-ax.)}$), 7.93 (3H, s, $OCOCH_3$), 9.19 (3H, s, C_{19}–H), 9.20 (3H, s, C_{18}–H).

4a-5;6a-10a-Didehydro-perhydrobenzo[*c*]quinolizine (XIV)——To a solution of 90 mg of 6a,10a-dehydro-6-oxo-perhydrobenzo[*c*]quinolizine (X) dissolved in 4 ml of 35% aq. AcOH, 140 mg of $Hg(OAc)_2$ and 146 mg of EDTA were added and the mixture was heated on a water bath of 60—65° for 4 hr with stirring. When cooled, the reaction mixture was basified with Na_2CO_3, extracted with benzene, and the benzene layer was dried over Na_2SO_4. The yellow oil left after evaporation of benzene was purified through Al_2O_3 chromato-

graphy and 78 mg (89.1%) of a liquid was obtained. Picrate: mp 226—228°, which agreed with the value recorded in literature.[18] *Anal.* Calcd. for $C_{19}H_{20}O_8N_4$: C, 52.78; H, 4.66; N, 12.96. Found: C, 52.89; H, 4.83; N, 12.74. IR $\nu_{max}^{liq.\ film}$ cm^{-1}: 1629, 1565 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 3.73 (1H, s, vinyl proton), 6.18 (2H, t (J=7.5), C_1–H_2), 7.25 (2H, t (J=7.0), C_4–H_2).

17-Acetoxy-5β-androst-3-eno[4,3-*c*]-[6′,7′,8′,9′]tetrahydro-2′*H*-quinolizine-2′-one (XV)——To a solution of 100 mg of 17-acetoxy-5β-androst-3-eno[4,3-*c*]-[3′,4′]dehydroquinolizidin-2′-one (Vb) dissolved in 10 ml of 35% AcOH, 73 mg of $(AcO_2)Hg$ and 84 mg of EDTA were added and the mixture was heated for 6 hr with stirring as in the foregoing case. The same treatment as above afforded 47 mg (47.0%) of viscous oil. Picrate: mp 150—151° (recrystallized from EtOH). *Anal.* Calcd. for $C_{34}H_{42}O_{10}N_4$: C, 61.25; H, 6.35; N, 8.40. Found: C, 61.24; H, 6.70; N, 8.61. IR $\nu_{max}^{liq.\ film}$ cm^{-1}: 1721 ($OCOCH_3$), 1613, 1560, 1527 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 3.93 (1H, s, vinyl proton), 5.50 (1H, t (J=7.5), C_{17}–H), 6.27 (2H, t (J=5.0), C_6'–H_2), 7.35 (2H, t (J=7.0), C_9'–H_2), 8.12 (3H, s, $OCOCH_3$), 9.12 (3H, s, C_{19}–H), 9.33 (3H, s, C_{18}–H).

17-Acetoxy-5β-androst-2-eno[3,2-*c*]-[6′,7′,8′,9′]tetrahydro-2′*H*-quinolizine-2′-one (XVI)——To a solution of 100 mg of vinylogous amide (VIb) dissolved in 10 ml of AcOH, 73 mg of $Hg(AcO)_2$ and 84 mg of EDTA were added and the mixture was heated at 60—65° for 6 hr with stirring. The reaction mixture was treated as above and 41 mg (41.0%) of a viscous oil was obtained. Recrystallization from hexane–acetone gave needles, mp 285—287°. Picrate: mp 260—263° (from EtOH). *Anal.* Calcd. for $C_{34}H_{42}O_{10}N_4$: C, 61.25; H, 6.35; N, 8.40. Found: C, 60.87; H, 6.30; N, 6.50. IR ν_{max}^{KBr} cm^{-1}: 1634 ($OCOCH_3$), 1630, 1572, 1541 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 3.77 (1H, s, vinyl proton), 5.50 (1H, t (J=7.5), C_{17}–H), 6.15 (2H, t (J=5.0), C_6'–H_2), 6.81 (1H, d, C_1–$H_{(quasi-eq.)}$), 7.23 (2H, t (J=7.0), C_9'–H_2), 8.00 (3H, s, $OCOCH_3$), 8.01 (1H, d, C_1–$H_{(quasi-ax.)}$), 8.90 (3H, s, C_{19}–H), 9.23 (3H, s, C_{18}–H).

9-Dimethyl-7-oxo-1,2,3,4,5,6-hexahydrocyclohexano[1,2-*c*]quinolizine (XVII)——To 15 ml of an equivalent mixture of abs. toluene and abs. benzene, 0.033 g of metallic Na was added, the mixture was stirred while adding 2 g of dimedone and 0.76 g of 2-vinylpyridine, and the mixture was refluxed for 2 hr, during which time the colorless liquid changed to a red solution. When cooled, unreacted dimedone precipitated as crystals which were removed by filtration. The filtrate was dissolved in 10% HCl, the HCl layer was basified with K_2CO_3, and extracted with benzene. The extract was dried over Na_2SO_4 and evaporation of benzene gave 1.3 g (40.0%) of 1-[β-(2-pyridyl)ethyl]dimedone as crystals. Its recrystallization gave a product melting at 105—107°. Picrate: mp 90—95° (from EtOH). *Anal.* Calcd. for $C_{21}H_{22}O_9N_4$: C, 53.16; H, 4.67; N, 11.81. Found: C, 52.84; H, 5.11; N, 11.68.

1-[β-(2-Pyridyl)ethyl]dimedone was submitted to reductive cyclization by dissolving 1.3 g of it in 32 ml of abs. EtOH, 8 ml of Raney–Ni in EtOH was added, and submitted to hydrogenation in an autoclave at 70°, 11 atmosphere. After absorption of a theoretical volume of H_2, hydrogenation was continued until UV absorption of pyridine disappeared and that at 320 mμ appeared. The catalyst was filtered off, the solvent was evaporated, and 0.64 g (51.7%) of XVII was obtained as white crystals which melted at 92° after recrystallization from AcOEt. *Anal.* Calcd. for $C_{15}H_{23}ON$: C, 77.20; H, 9.92; N, 6.60. Found: C, 76.89; H, 10.04; N, 6.04. IR ν_{max}^{KBr} cm^{-1}: 1626, 1580 (>N–C=C–C=O). NMR ($CDCl_3$) τ: 6.05 (1H, d-t (J_{AB}=12.5, J_{AX}=2.5), C_1–$H_{eq.}$), 7.15 (1H, d-q-q (J_{AB}=12.5, J_{BX}=10.5, J_{BY}=2.5), C_1–$H_{ax.}$), 6.90 (1H, m, C_{4a}–H), 7.63 (2H, t (J=6.3), C_6–H_2), 7.75 (2H, s, C_8–H_2), 7.81 (2H, s, C_{10}–H_2), 8.93 (6H, s, C_9–Me).

17-Acetoxy-5β-androstano[4,3-*c*]quinolizidin-2′-one (I)——A solution of 105 mg of Vb dissolved in 3 ml of AcOH was submitted to catalytic reduction with 20 mg of PtO_2 at an ordinary pressure. After absorption of H_2, the catalyst was filtered off and the filtrate was neutralized with $NaHCO_3$ by which crystals precipitated. These crude crystals (XVIII) exhibited the Bohlmann band in its IR spectrum. Without further recrystallization, the crude crystals were dissolved in 1.5 ml of AcOH, 50 mg of CrO_3 was added, and the mixture was allowed to stand overnight at room temperature. A small volume of H_2O was then added, basified cautiously with $NaHCO_3$, and the mixture was extracted with benzene. The extract was dried over Na_2SO_4, benzene was evaporated, and the residue was purified by silica gel chromatography, from which 20 mg (18.9%) of crystals, showing one spot on thin-layer chromatogram, was obtained. Recrystallization from MeOH–acetone gave needles, mp 265—267°. *Anal.* Calcd. for $C_{28}H_{43}O_3N$: C, 76.15; H, 9.81; >C=O N, 3.17. Found: C, 75.94; H, 10.01; N, 3.00. IR ν_{max}^{KBr} cm^{-1}: 2762 (Bohlmann band), 1733 (ester), 1715 (>C=O), Mass Spectrum *m/e*: 441 (M^+).

17-Acetoxy-5β-androstano[3,2-c]quinolizidin-2′-one (XX)——In a similar manner as the reaction for I, 100 mg of VIb was submitted to the reaction and after treatment as above and 17 mg (16.0%) of crystals, showing one spot on thin-layer chromatogram, was obtained. Recrystallization from acetone gave colorless needles, mp 263°. *Anal.* Calcd. for $C_{28}H_{43}O_3N$: C, 76.15; H, 9.81; N, 3.17. Found: C, 75.94; H, 9.99; N, 3.14. IR ν_{max}^{KBr} cm^{-1}: 2793, 2755 (Bohlmann band), 1742 (ester), 1712 (>C=O). Mass Spectrum *m/e*: 441 (M^+).

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