[Chem. Pharm. Bull. 21(1) 40—46 (1973)]

UDC 547.92.04 : 547.822.3.04

Aza-steroids. III.[1] Synthesis of 17-Acetoxy-10-aza-androstan-7-one and Related Compounds[2]

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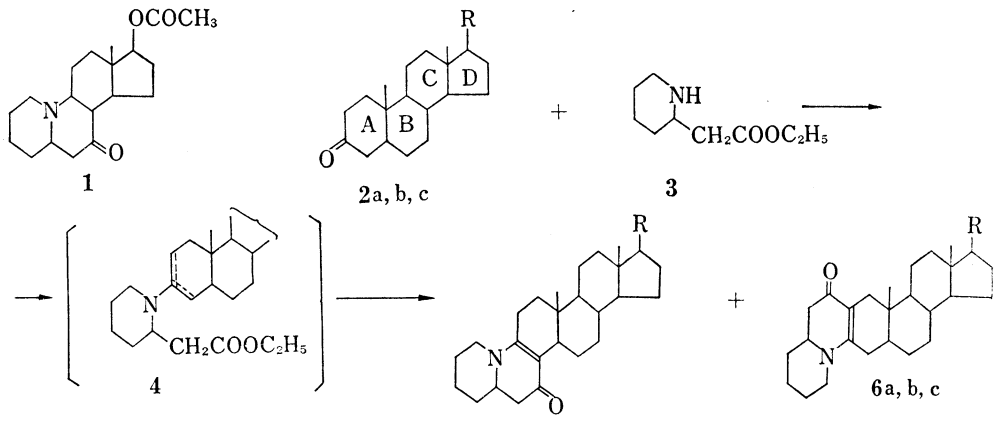
(Received May 1, 1972)

As one of the 10-aza-steroid system, 17-acetoxy-10-aza-androstan-7-one (**1**) was synthesized. Condensation of hexahydroindanone (**16**) and ethyl piperidinoacetate (**3**) gave a mixture of β-amino-enones with angular (**17**) and linear (**18**) structures. The separated **17** was reduced and then oxidized to **1**. Reaction between **3** and testosterone (**7**) mainly gave amino-dienone (**8**) of linear structure. Such a tendency was also seen in the case of tetrahydroindanone (**14**) and the amino-dienone (**19**) of linear structure was obtained solely.

As one of the 10-aza-steroid system,[4] 17-acetoxy-10-aza-androstan-7-one (**1**), and its related compounds were synthesized in the present series of experiments.

For the synthesis of **1**, the method of Meyers and others[5] for obtaining polycyclic β-amino-enones from cycloalkanone and aminocarboxylic acid ester was adopted. A similar reaction carried out earlier[1] is illustrated in Chart **1.** Condensation of androstanone (**2a** and **2b**) or cholestanone (**2c**) with ethyl piperidinoacetate (**3**) afforded β-amino-enones of angular form (**5**) and linear from (**6**), their formation ratio being 7: 5 for **5a**: **6a**, 3:11 for **5b**: **6b**, and 3:10 for **5c**: **6c**.



a : R=OH or OAc A/B=*cis*
b : R=OAc, A/B=*trans*
c : R=C_8H_{17}, A/B=*trans*

Chart 1

1) This paper forms Part XXV of "Synthesis of Quinolizine Derivatives." Part XXIV: M. Akiba and S. Ohki, *Chem. Pharm. Bull.* (Tokyo), **18**, 2195 (1970).
2) Abstr. Papers, "2rd Symposium on Heterocyclic Chemistry," Nagasaki, 1969, p. 147.
3) Location: *Ueno Sakuragi-1-chome, Taito-ku, Tokyo.*
4) Recently, the synthesis of 10-aza-steroids was reported by two groups. Ref. H.J. Wille, U.K. Pandit, and H.O. Huisman, *Tetrahedron Letters*, **1970**, 4429; D. Bertin and J. Perronnet, *Bull. Soc. Chim. France*, **1969**, 117.
5) A.I. Meyers, A.H. Reine, and R. Gault, *J. Org. Chem.*, **33**, 698 (1968).

There are still many doubtful points regarding the direction of the double bond in the 3-keton-enol and its enamine, and the direction of its nucleophilic reaction in steroids but it may be said for reaction products in general that 5β-3-ketone compounds give C-4 and C-2 substituted products, with the former predominating, and the 5α-3-ketone compounds selectively form C-2 substituted products.[6-8] Since the formation ratio of **5** and **6** is reversed in 5β series (**2a**) and 5α series (**2b** and **2c**), the above selectivity can be recognized to a certain extent, but the formation of both **5** and **6** from the 5α series differs from the general trend and is of interest.

In the synthesis of 10-aza-steroid system, as will be described later, it would be necessary to control the direction of acylcyclization towards the formation of an angular form and, in order to find condition for it, some experiments were added to the foregoing model experiments.

Johnson and others[9] stated that the reaction of Δ^4-3-oxo-steroids and secondary amines gives a linear-conjugated 3-amino-3,5-dienes so that selective intramolecular acylation to C-4 can be expected in the reaction of **3** with Δ^4-3-oxo-steroids. Therefore, reaction of testosterone (**7**) and **3**, in the presence of trifluoroacetic acid, was carried out, and β-amino-enone (**8**) of linear form was obtained as the main product, with a minute amount of **9**. The nuclear magnetic resonance (NMR) spectrum of **8** showed AB-type absorption of C-1 methylene proton in the steroid portion at 7.00 and 8.17 τ, as a quartet (J=16.2 Hz), indicating **8** to have a linear structure.[1] The infrared (IR) spectrum of **8** exhibited absorptions at 1618 and 1538 cm^{-1}, and its ultraviolet (UV) spectrum showed absorption at 270 and 386 mμ for conjugated β-amino-enone. Catalytic reduction of **8** over platinum oxide catalyst for absorption of 1 mole of hydrogen, followed by acetylation, gave a compound which was entirely identical with the known **6a**,[1] thereby proving the structure of **8**. This latter hydrogenation indicates that the attack occurred preferentially from the β-side. The NMR spectrum of **9** exhibited a vinyl proton at C-6 position of the steroid as a triplet (J=7.75 Hz) at 3.44 τ. The absorption for a conjugated β-amino-enone appeared at 1621 and 1546 cm^{-1} in its IR spectrum and at 255 and 364 mμ in its UV spectrum. The structure of **9** was presumed from these spectral evidences but was not proved due to the small amount available.

The foregoing results differed somewhat from expectations but it seems more appropriate to consider that the contribution of the cross-conjugated 3-amino-2,4-diene system was rather great in this reaction, resulting in the majority undergoing cyclization to the linear structure. In order to examine this point, the UV and NMR spectra of the pyrrolidine- (**10**), morpholine- (**11**), and piperidine-dienamines (**12**) of **7** were comparatively examined

Table I. Enamines of Teststerone

	Method[a]	mp (°C)	UV (λ_{max}^{EtOH} mμ)	NMR spectrum (τ)	
				C_4-H,	C_6-H
Pyrrolidine-dienamine (**10**)	A, B	135—142 (decomp.)	281	5.20 (s)	4.95 (t)
Morpholine-dienamine (**11**)	B, C	187—195 (decomp.)	263	4.82 (s)	4.80 (t)
Piperidine-dienamine (**12**)	B, C	—	263	4.83 (s)	4.75 (t)

a) A: Heated and refluxed for 30 min in abs. MeOH.
B: Refluxed for 48—60 hr in abs. toluene with dehydration. Catalytic amount of p-TSOH used.
C: Refluxed for 24—48 hr in abs. toluene with dehydration. Catalytic amount of trifluoroacetic acid used.

6) A.J. Liston, *J. Org. Chem.*, **31**, 2105 (1966).
7) A.K. Bose, G. Mina, M.S. Manhas, and E. Rzucidlo, *Tetrahedron Letters*, **1963**, 1467.
8) A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935); L.F. Fieser and X.A. Dominguez, *J. Am. Chem. Soc.*, **75**, 1704 (1953).
9) J.J. Johnson, M.E. Herr, J.C. Babcock, A.E. Fonken, J.E. Stafford, and F.W. Heyl, *J. Am. Chem. Soc.*, **78**, 430 (1955).

(Table I). Their absorption were simillar to the absorption of exocyclic dienamines of the $\Delta^{1,8a}$-2-octalone system reported by Firrell and Hickmott,[10] suggesting the **10**, **11**, and **12** take the 3-amino-3,5-diene system. Such discrepancies are now being examined. There are difference in the absorption of **10** and those of **11** and **12**, especially the shift of C-4 proton in the steroid portion to a higher mangetic field which indicates the increased electron density in this region and a higher nucleophilic activity may be expected.[9]

Based on the foregoing experiments, condensation reaction was carried out between **3** and 1-hydroxy-8-methyl-4,5,6,7-*cis*-8,9-hexahydroindan-5-one (**15**), the reduction product of 1-hydroxy-8-methyl-5,6,7,8-tetrahydroindan-5-one[11] (**13**), or its acetylated compound (**16**) and **1** was synthesized as shown in Chart 2. The use of the *cis* compounds (**15**, **16**) followed the example of the formation of **5a** from **2a**

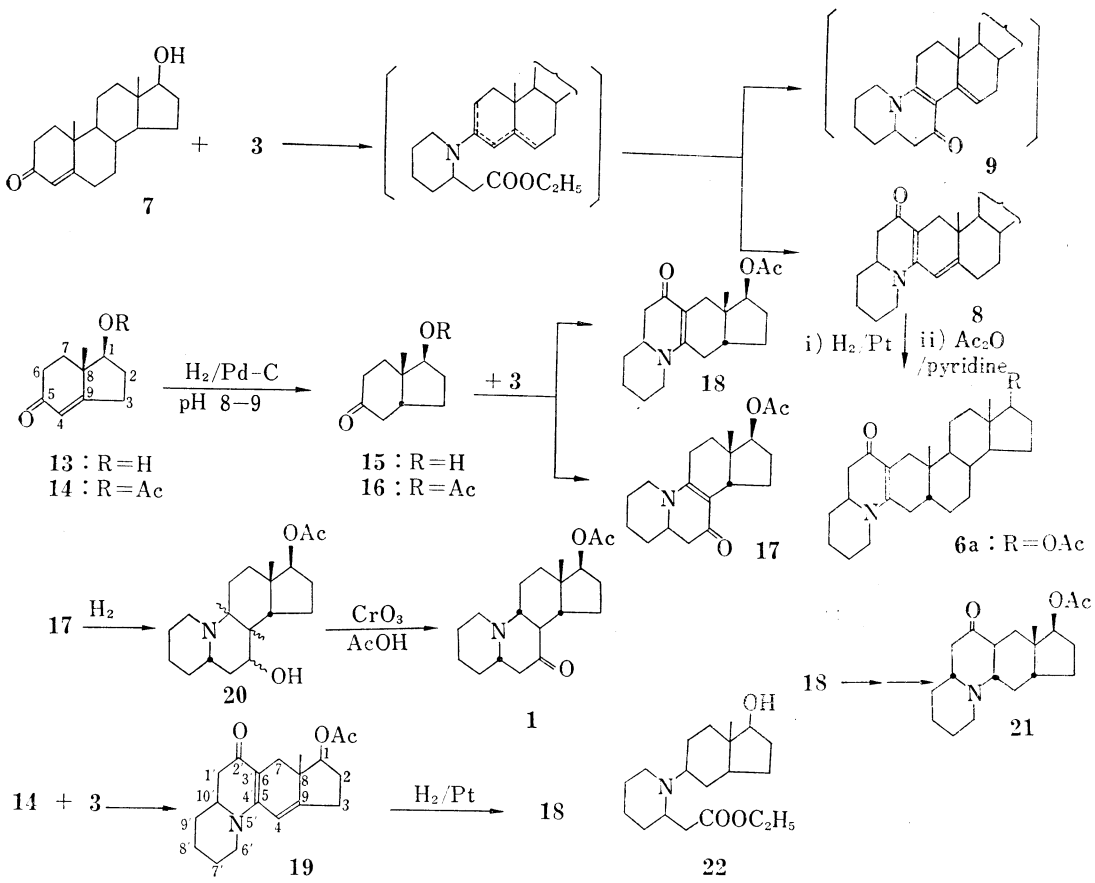


Chart 2

The ethanolic solution of **13** was adjusted to pH 8—9 and submitted to catalytic reduction over palladium-carbon catalyst, giving the *cis* compound (**15**) as an unity. In this case, reduction in a neutral solution gives a mixture of *cis* and *trans* compounds. The NMR spectrum of the acetylated compound (**16**) shows an ABX-type signal for $C_{(4)}$-$H_{(eq)}$ in the indanone portion at around 7.5 τ, which had shifted to a lower magnetic field. The same signal appears

10) N.F. Firrell and P.W. Hickmott, *J. Chem. Soc.*, **1969**, 293.
11) C.B.C. Boyce and J.S.W. Hurrt, *J. Chem. Soc.*, **1960**, 4547.

in the NMR spectrum of **2a** (R=OAc) and, since such a signal is not observed in **2b** of the 5α series, **15** was assumed to be a *cis* compound. Hara and others[12] also observed a similar behavior in this kind of protons. Heating of **15** and **3** in the presence of trifluoroacetic acid unexpectedly gave the reduction product (**22**) of the enamine in 40% yield. This is similar to the formation of 2-N-hexamethyleneiminobicyclo[2.2.1]heptane by the reaction of norcamphor and hexamethyleneimine reported by Cook and others.[13] In contrast, the reaction of **16** and **3** afforded the expected angular form β-amino-enone (**17**) and its linear form (**18**), their formation ratio being 4: 3 for **17**:**18**. Both **17** and **18** exhibited two strong absorption bands in the region of 1667—1538 cm^{-1} in their IR spectra, showing absorption for a typical β-amino-α,β-unsaturated ketones.[14] Their UV spectra showed absorption of 2,3-dihydro-γ-pyridone >N–C=C–C=O chromophore[15] at 336 mμ. In order to discriminate which of these compounds was angular and which linear, NMR spectrum of $C_{(7)}$-methylene proton in the indanone portion was compared in accordance with the example of discrimination between **5** and **6**. In the case of **17** and **18**, however, the signals were too complicated for facile discrimination and an attempt was made to do it through their mass spectra. Both **17** and **18** have the molecular formula of $C_{19}H_{27}O_3N$ and their mass spectra show *m/e* 317 (M^+), indicating them to be structural isomers but their fragmentation peaks are vastly different, the peak of *m/e* 177 ($C_{11}H_{15}ON$) appearing very strong in **18** while such is not observed in **17**. The same is also seen in the known **6**. On the other hand, the peak intensity of 317 (M^+) of **17** is much greater than that of **18**. This fact suggests that a retro-Diels-Alder reaction has taken place, as shown in Chart 3, and this fact seems to have confirmed the structure of **17** and **18**.

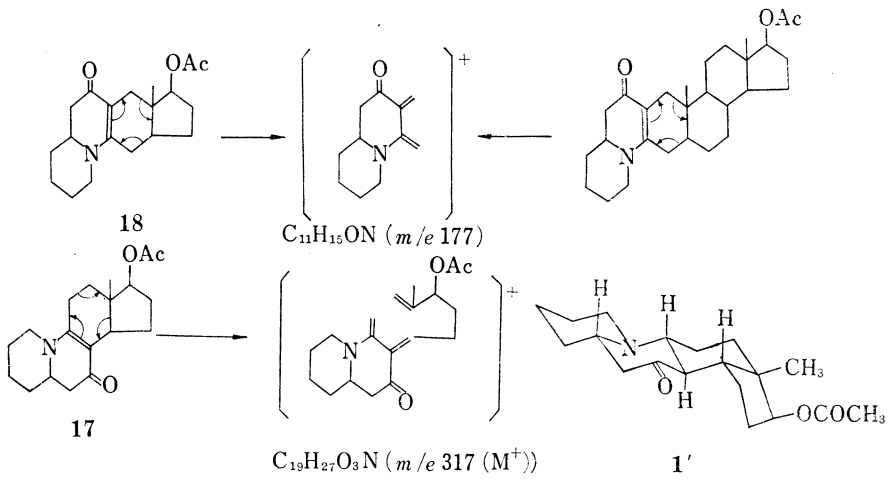


Chart 3

Condensation of the 1-acetylated compound (**14**) of **13** and **3** proceeded as in the case of **7** and **3**, and the dienone compound (**19**) of linear structure was obtained as a single product of mp 192—193°. The NMR spectrum of **19** showed signals for the $C_{(7)}$-methylene proton in the indanone portion as an AB-type quartet at 3.79 τ, and absorptions for β-amino-α,β-unsaturated ketone appeared at 1610 and 1527 cm^{-1} in its IR spectrum and at 263 and 384

12) K. Oka, Y. Ike, and S. Hara, *Tetrahedron Letters*, **1969**, 4543.
13) A.G. Cook, W.C. Meyer, K.E. Ungrodt, and R.H. Muelier, *J. Org. Chem.*, **31**, 14 (1966).
14) N.H. Cromwell, F.A. Miller, A.R. Johnson, R.L. Franck, and D.J. Wallace, *J. Am. Chem. Soc.*, **71**, 3337 (1949); G.D. Dudek, *J. Org. Chem.*, **30**, 548 (1965).
15) F. Bohlmann, E. Winterfeldt, O. Schmidt, and W. Reusche, *Ber.*, **94**, 1774 (1961); F. Bohlmann and O. Schmidt, *ibid.*, **97**, 1354 (1964).

mμ in its UV spectrum. Catalytic reduction of **19** over platinum oxide to absorb 1 mole of hydrogen gave a product which agreed entirely with **18**. Consequently attack of hydrogen occurred specifically from the β-side.

Catalytic reduction of **17** over platinum oxide to the alcohol compound (**20**) and its oxidation with chromium trioxide gave 17β-acetoxy-10-aza-androstan-7-one (**1**) whose IR spectrum showed absorption for Bohlmann's *trans*-quinolizidine.[16] Since 2-oxo-perhydrobenzo-[*c*]quinolizine ring,[17] corresponding to the A–B–C ring of **1**, easily takes the all-chair, all-*trans* steric structure and since hydrogenation proceeds from the β-side, there is a strong possibility that this compound takes the steric structure represented by formula **1'**.

Similar treatment of 18 gave the compound (**21**). The mass spectra of both **1** and **21** show *m/e* 319 (M^+), while their NMR spectra show methyl signals at 9.05 and 9.06 τ, having shifted to a lower magnetic field than that of $C_{(18)}$-H in ordinary steroids. This is possible only when the carbonyl at C-7 and the methyl group take a configuration allowing them to be in the same plane. Such an example can be seen in the $C_{(19)}$-H signal in the steroid portion of **6b**.[1] Johnson and others[18] determined the configuration of $C_{(9)}$-H in veratramine and jervine by the same means. Consequently, $C_{(8)}$-H in **1** takes the α-configuration and the formula **1'** is endorsed.

Experimental[19]

Reaction of Testosterone and Ethyl 2-Piperidinoacetate——A solution of 500 mg of testosterone (**7**) and 260 mg of ethyl 2-piperidinoacetate (**3**) dissolved in 10 ml of abs. xylene, added with a small amount of trifluoroacetic acid, was heated for 56 hr in N_2 stream, removing H_2O formed by the reaction. The reaction mixture was cooled, xylene was evaporated in a reduced pressure, and the residue was separated by silica gel chromatography, using benzene–acetone mixture (3:1). The initial fraction afforded 29 mg (4.2%) of 17-hydroxyandrosta-3,5-dieno[4,3-*c*][3',4']dehydroquinolizidin-2'-one (**9**) as a viscous substance. Its crystallization was difficult. UV λ_{max}^{EtOH}: 255, 364 mμ. IR ν_{max}^{KBr}: 3640 (-OH), 1621, 1546 (=N-C=C-C=O) cm^{-1}. NMR ($CDCl_3$) τ: 3.44 (t, 1, J=7.75 Hz, $C_{(6)}$-H), 6.04 (d-t, 1, J=12.25 Hz, $C'_{(6)}H_{eq}$), 6.35 (t, 1, J=7.75 Hz, $C_{(17)}$-H), 6.70 (m, 1, $C'_{(10)}$-H), 9.08 (s, 3, $C_{(19)}$-H), 9.23 (s, 3, $C_{(18)}$-H).

From the second fraction, 125 mg (18.0%) of 17-hydroxyandrosta-2,4-dieno[3,2-*c*][3',4']dehydroquinolizidin-2'-one (**8**) was obtained as yellow crystals and recrystallized from hexane–acetone as yellow needles, mp 254—256°. *Anal.* Calcd. for $C_{26}H_{39}O_2N$: C, 78.94; H, 9.43; N, 3.54. Found: C, 78.87; H, 9.76; N, 4.16. UV λ_{max}^{EtOH}: 270, 386 mμ. IR ν_{max}^{KBr}: 3497 (-OH), 1618, 1536 (=N-C=C-C=O) cm^{-1}. NMR ($CDCl_3$) τ: 4.05 (s, 1, $C_{(4)}$-H), 6.0 (b-t, 1, J=12.25 Hz, $C'_{(6)}$-H_{eq}), 6.83 (t, 1, J=7.75 Hz, $C_{(17)}$-H), 6.70 (m, 1, $C'_{(10)}$-H), 7.00 (d, 1, J=16.2 Hz, $C_{(1)}$-$H_{quasi-eq}$), 8.17 (d, 1, J=16.2 Hz, $C_{(1)}$-$H_{quasi-ax}$), 9.10 (s, 3, $C_{(19)}$-H), 9.22 (s, 3, $C_{(18)}$-H).

17-Acetoxy-5β-androst-2-eno[3,2-*c*][3',4']dehydroquinolizidin-2'-one[1] (**6a**: **R=OAc**)——A solution of 100 mg of **8** dissolved in 5 ml of EtOH was submitted to catalytic reduction over 20 mg of PtO_2 at ordinary pressure. After absorption of 1 mole of H_2, the catalyst was filtered off, the filtrate was evaporated, and white powdery residue was recrystallized from EtOH to 58 mg of the alcohol compound (**6a**: R=OH), mp 235—237°. *Anal.* Calcd. for $C_{26}H_{39}ON$: C, 78.54; H, 9.89; N, 3.52. Found: C, 78.16; H, 9.97; N, 3.47. UV λ_{max}^{EtOH}: 336 mμ. IR ν_{max}^{KBr}: 1610, 1553 cm^{-1}. NMR ($CDCl_3$) τ: 6.06 (d-t, 1, J=10.0 Hz, $C'_{(6)}$-H), 6.38 (t, 1, J=7.75 Hz, $C_{(17)}$-H), 6.75 (m, 1, $C'_{(10)}$-H), 7.04 (d, 1, J=16.2 Hz, $C_{(1)}$-$H_{quasi-eq}$), 8.98 (s, 3, $C_{(19)}$-H), 9.30 (s, 1, $C_{(18)}$-H). The difference in the chemical shift between $C_{(19)}$-H and $C_{(18)}$-H of 0.32 indicates that C-5 position is in β-configuration.

This alcohol compound was dissolved in 0.5 ml each of Ac_2O and pyridine, and the mixture was allowed to stand for 3 hr at room temperature. The solvent was evaporated under a reduced pressure and the residue was purified through silica gel chromatography to 48 mg (43.1%) of the acetoxy compound (**6a**: R=OAc). Recrystallization from hexane–acetone gave colorless crystals of mp 229—230°, showing no depression on admixture with **6a** (R=OAc) obtained earlier.[1] Their IR and NMR spectra were in complete agreement, and both gave the same thin-layer chromatogram.

1β-Acetoxy-8-methyl-5,6,7,8-tetrahydroindan-5-one (**14**)——A solution of 2.01 g of 1β-hydroxy-8-methyl-5,6,7,8-tetrahydroindan-5-one[11] (**13**) dissolved in a mixture of 2 ml each of pyridine and Ac_2O was

16) F. Bohlmann, *Angew. Chem.*, **69**, 641 (1957).
17) Z. Horii, K. Morikawa, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1472 (1968).
18) D.M. Bailey, D.P.G. Hamon, and W.S. Johnson, *Tetrahedron Letters*, **1963**, 555.
19) All melting point are uncorrected. NMR spectra were recorded at 100 Mcps, using tetramethylsilane as internal standard.

allowed to stand overnight at room temperature, the solvent was evaporated under a reduced pressure, and the residue was purified by silica gel chromatography, affording 1.4 g (62.7%) of viscous yellow oil (**14**). UV λ_{max}^{EtOH}: 230 mμ (α,β-unsaturated ketone). IR $\nu_{max}^{Liq.film}$: 1647, 1735, 1300, 1050 cm^{-1}. NMR ($CDCl_3$) τ: 4.12 (s, 1, $C_{(4)}$-H), 5.13 (t, 1, J=7.75 Hz, $C_{(1)}$-H), 7.88 (s, 3, $OCOCH_3$), 8.80 (s, 3, $C_{(8)}$-CH_3).

1β-Hydroxy-8-methyl-4,5,6,7-*cis*-8,9-hexahydroindan-5-one (15)——A solution of 1.5 g of **13** dissolved in 20 ml of EtOH was adjusted to pH 8—9 with a small quantity of KOH and submitted to catalytic reduction over 1% Pd-C at ordinary pressure. After 1 mole of H_2 was absorbed, the catalyst was filtered off, the filtrate was evaporated, and the residue was purified through silica gel chromatography (benzene:acetone=5:1) to 1.32 g (87.9%) of yellow oil which showed only one spot in thin-layer chromatography and only one peak in gas-liquid chromatography. IR $\nu_{max}^{Liq.film}$: 3404 (-OH), 1709 (>C=O) cm^{-1}: There was no absorption at 242 mμ in its UV spectrum.

1β-Acetoxy-8-methyl-4,5,6,7-*cis*-8,9-hexahydroindan-5-one (16)——A solution of 1.2 g of **15** dissolved in a mixture of 5 ml each of abs. pyridine and Ac_2O was allowed to stand overnight at room temperature, the solvent was evaporated under a reduced pressure, and the residue was purified through silica gel chromatography (eluted only with benzene) to 1.05 g (70.0%) of colorless viscous liquid which showed only one spot in thin-layer chromatography and only one peak in gas-liquid chromatography. *m/e* calcd. for $C_{12}H_{18}O_3$: 210.125574. Found: 210.126337. IR $\nu_{max}^{Liq.film}$: 1739 ($OCOCH_3$), 1711 (>C=O) cm^{-1}. NMR ($CDCl_3$) τ: 5.05 (q, 1, J=3 Hz, $C_{(1)}$-H), 7.95 (s, 3, $OCOCH_3$), 8.84 (s, 3, $C_{(8)}$-CH_3).

A solution of 288 mg of **13** dissolved in 4 ml of abs. EtOH was submitted to catalytic reduction over 1% Pd-C and the reaction mixture was treated as above. Purification through silica gel chromatography afforded 200 mg (69%) of a mixture which showed two close spots in thin-layer chromatography. According to the result of gas-liquid chromatography, the ratio of *cis* and *trans* compounds is 3:2, which agrees with the ratio of CH_3 signal and of -$OCOCH_3$ in NMR spectrum. NMR ($CDCl_3$) of 1β-acetoxy-8-methyl-4,5,6,7-*trans*-8,9-hexahydroindan-5-one shows 8.05 (s, 3, $OCOCH_3$) and 8.96 (s, 3, CH_3) τ.

1β-Acetoxy-8-methyl-7,8-dihydroindano[6,5-*c*][3′,4′]dehydroquinolizidin-2′-one (19)——A few drops of trifluoroacetic acid was added to a solution of 1.4 g of **14** and 1.1 g of **3** dissolved in 10 ml of abs. xylene and the mixture was refluxed for 70 hr. The reaction mixture was treated as before and purified through silica gel chromatography to 205 mg (9.9%) of yellow crystals. Recrystallization from hexane–acetone gave a product melting at 192—193°. *Anal.* Calcd. for $C_{19}H_{25}O_3N$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.26; H, 7.95; N, 4.67. UV λ_{max}^{EtOH}: 255, 364 mμ. IR ν_{max}^{KBr}: 1733 ($OCOCH_3$), 1610, 1527 (=N-C=C-C=O) cm^{-1}. NMR ($CDCl_3$) τ: 3.90 (s, 1, $C_{(4)}$-H), 5.09 (q, 1, J=7.75 Hz, $C_{(1)}$-H), 6.02 (d-t, 1, J=15.0 Hz, $C'_{(6)}H_{eq}$), 6.75 (m, 1, $C_{(10)}$-H), 6.98 (d, 1, J=17.5 Hz, $C_{(7)}$-$H_{quasi-eq}$), 7.93 (s, 3, $OCOCH_3$), 8.15 (d, 1, J=17.5 Hz, $C_{(7)}$-$H_{quasi-ax}$), 9.05 (s, 1, $C_{(8)}$-CH_3).

5-[1-(2-Ethoxycarbonylmethyl)piperidinyl]-1β-hydroxy-8-methyl-4,5,6,7-*cis*-8,9-hexahydroindane (22)——To a solution of 168 mg of the ketol (**15**) dissolved in 3 ml of abs. toluene, a solution of 171 mg of **3** dissolved in 2 ml of abs. toluene was added, followed by a small quantity of trifluoroacetic acid, and the mixture was heated in N_2 stream for 48 hr, with constant removal of water formed. When cooled, 10% HCl was added to the mixture, the toluene layer was separated, and dried over Na_2SO_4. Toluene was evaporated and the unreacted ketol was recovered. The HCl solution was neutralized with Na_2CO_3, rendered alkaline, and extracted with benzene. The benzene layer was dried over Na_2SO_4, evaporated, and the residue was purified through silica gel chromatography to 65 mg (40.1%) of yellow oil. Picrate: mp 182—185° (recrystallized from EtOH). *Anal.* Calcd. for $C_{25}H_{36}O_{10}N_4$: C, 54.34; H, 6.57; N, 10.14. Found: C, 54.54; H, 6.43; N, 9.98. IR $\nu_{max}^{Liq.film}$: 3448 (-OH), 1733 (-COOEt) cm^{-1}. NMR ($CDCl_3$) τ: 5.97 (q, 2, J=7.5 Hz, $COOCH_2$-CH_3), 6.85 (broad, 1, $C_{(1)}$-OH), 8.78 (t, 3, J=7.5 Hz, $COOCH_2CH_3$), 9.03 (s, 3, $C_{(8)}$-CH_3), 5.98 (q, 2, J=7.5 Hz, $COOCH_2CH_3$), 6.85 (broad, 1, $C_{(1)}$-OH), 8.78 (t, 3, J=7.5 Hz, $COOCH_2CH_3$), 9.03 (s, 3, CH_3). From the slight chemical shift difference of the signal for $COOCH_2CH_3$ in its NMR spectrum, this product was assumed to be an epimeric mixture at C-5, the ratio being approximately 1:1.

Reaction of Ethyl 2-Piperidinoacetate and 1β-Acetoxy-8-methyl-4,5,6,7-*cis*-8,9-hexahydroindan-5-one——A solution of 550 mg of **3** and 540 mg of **16** dissolved in 10 ml of abs. xylene, added with a small quantity of trifluoroacetic acid, was treated as above. The product was fractionally purified through silica gel chromatography. The initial fraction eluted with benzene–acetone mixture (10:1) gave 143 mg (17.4%) of 1β-acetoxy-8-methyl-6,7,8,9-tetrahydroindano[5,5-*c*][3′,4′]dehydroquinolizidin-2′-one (17-acetoxy-10-azaandrost-8-en-7-one) (**17**) as viscous orange oil. *m/e* Calcd. for $C_{19}H_{27}O_3N$: 317.199. Found: 317.197. UV λ_{max}^{EtOH}: 336 mμ. IR $\nu_{max}^{Liq.film}$: 1736 ($OCOCH_3$), 1623, 1560 (=N-C=C-C=O) cm^{-1}. NMR ($CDCl_3$) τ: 5.13 (d, 1, J=4.0 Hz, $C_{(1)}$-H), 6.16 (d-t, 1, J=15.0 Hz, $C'_{(6)}$-H_{eq}), 7.72 (m, 1, $C'_{(10)}$-H), 7.98 (s, 3, $OCOCH_3$), 9.10 (s, 3, $C_{(8)}$-CH_3).

The second fraction eluted with benzene–acetone mixture (5:1) afforded 107 mg (13.1%) of 1β-acetoxy-8-methyl-4,7,8,9-tetrahydroindano[6,5-*c*][3′,4′]dehydroquinolizidin-2′-one (**18**) as viscous yellow oil. *m/e* Calcd. for $C_{19}H_{27}O_3N$: 317.199. Found: 317.197. UV λ_{max}^{EtOH}: 336 mμ. IR $\nu_{max}^{Liq.film}$: 1733 ($OCOCH_3$), 1637, 1565 cm^{-1}. NMR ($CDCl_3$) τ: 5.15 (d-d, 1, J=4.0 Hz, $C_{(1)}$-H), 6.12 (d-t, 1, J=15.0 Hz, $C'_{(6)}$-H_{eq}), 7.65 (m, 1, $C'_{(10)}$-H), 7.99 (s, 3, $OCOCH_3$), 9.09 (s, 3, $C_{(8)}$-CH_3).

A solution of 50 mg of **19** dissolved in 2 ml of EtOH was submitted to catalytic reduction over 10 mg of PtO_2. After absorption of 1 mole of H_2, the catalyst was filtered off, the solvent was evaporated, and

the residue was purified through silica gel chromatography to 23 mg (46%) of **18**. Its IR and UV spectra, and *Rf* value in thin-layer chromatography agreed with those of **18**.

1-Acetoxy-8-methylperhydroindano[5,4-*c*]quinolizidin-2′-one(17-Acetoxy-10-aza-androstan-7-one)(1)——A solution of 100 mg of the vinylogous amide (**17**) dissolved in 3 ml of AcOH was submitted to catalytic reduction over 20 mg of PtO_2. After absorption of H_2, the catalyst was filtered off, 50 mg of CrO_3 was added to the filtrate, and the mixture was allowed to stand for 24 hr at room temperature. A small quantity of water was added to this mixture which was carefully neutralized and further rendered weakly alkaline with $NaHCO_3$, and extracted with benzene. The benzene layer was dried over Na_2SO_4, the solvent was evaporated, and the yellow oily residue was purified through silica gel chromatography to 15 mg (14.5%) of viscous yellow oil. *m/e*: Calcd. for $C_{19}H_{29}O_3N$: 319.214711. Found: 319.216423. IR $\nu_{max}^{Liq.film}$: 2770 (Bohlmann band) cm^{-1}, 1729 ($OCOCH_3$), 1715 (>C=O) cm^{-1}. NMR ($CDCl_3$) τ: 5.13 (d, 1, $C_{(1)}$-H), 6.60 (m, 1, $C'_{(6)}$-H_{eq}), 8.02 (s, 3, $OCOCH_3$), 9.05 (s, 3, $C_{(8)}$-CH_3).

The same reaction was carried out on **17** and 12.9% of 1-acetoxy-8-methylperhydroindano[6,5-*c*]quinolizidin-2′-one (**18**) was obtained as a viscous oil. *m/e* Calcd. for $C_{19}H_{29}O_3N$: 319.214711. Found: 319.217364. IR $\nu_{max}^{Liq.film}$: 2770, 2740, 1736, 1721 cm^{-1}. NMR ($CDCl_3$) τ: 5.16 (d, 1, $C_{(1)}$-H), 6.60 (m, 1, $C'_{(6)}$-H_{eq}), 8.02 (s, 3, $OCOCH_3$), 9.06 (s, 3, $C_{(3)}$-CH_3).

Acknowledgement The author gratefully acknowledge the help of Dr. K. Oka and Mr. T. Ono for the measurement of NMR spectra and thank Mrs. Y. Baba, Miss S. Suzuki, and Mr. A. Wakamatsu of this College for elemental analyses. Thanks are also due to Mr. H. Satoh of Hitachi Naka Works for the exact mass measurement using Hitachi RMU-7 mass spectrometer. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education.