Tetrahedron, 1965, Vol. 21, pp. 1215 to 1222. Pergamon Press Ltd. Printed in Northern Ireland

# SYNTHESIS OF C-NOR-D-HOMO-EPIANDROSTERONE

## STUDIES ON C-NOR-D-HOMOSTEROIDS—IV[1]

H. MITSUHASHI and N. KAWAHARA
Faculty of Pharmaceutical Sciences, School of Medicine, Hokkaido University, Sapporo, Japan

(*Received* 12 *October* 1964; *in revised form* 3 *December* 1964)

**Abstract**—The synthesis of some C-nor-D-homopregnane and androstane derivatives from hecogenin is described. Hecogenin was degraded to III which in turn was converted to Va via IV. Manganese dioxide oxidation of Va yielded XVIIIa which was reduced to C-nor-D-homo-epiandrosterone (XXVa). This latter compound possesses the epiandrosterone configuration at each of the ring junctures.

THE syntheses of C-nor-D-homosteroids have been investigated in this[2–4] and other laboratories.[5,6] Recently, Kupchan *et al.* reported the synthesis of C-nor-D-homo-testosterone acetate.[7]

In view of extensive investigations into the preparation and hormonal effects of steroids with unusual ring systems, the synthesis of C-nor-D-homosteroidal hormone analogs was a matter of some interest. The present paper describes the synthesis of C-nor-D-homo-epiandrosterone and some chemical reactins oof the intermediate compounds.

Hecogenin (I) was degraded to II which in turn was converted to the diol (III). The tosylhydrazone (IV), after pyrolytic decomposition in sodium ethyleneglycolate gave Va, m.p. 196–198°, which was reported as Vc in an earlier paper,[2] but is now formulated as a $\Delta^{12(13)}$-compound (Va) on the dasis of several oxidation products. Catalytic hydrogenation of Va with $PtO_2$ as the catalyst in acetic acid and ethanol afforded VIa, m.p. 239–240° and an unexpected product VIIa, m.p. 75°. Attempted reduction of Va in ethanol alone under the same conditions was unsuccessful. Chromic acid oxidation of VIa in 90% acetic acid gave a diketone formulated as VIII, m.p. 135–142°. Acetylation of VIIa gave a monoacetate (VIIb) while oxidation of VIIa with chromic acid in 90% acetic acid gave a monoketone formulated as IX, m.p. 45°. Both VIIa and VIIb have been derived from X by catalytic hydrogenation.[2] Chromic acid–pyridine oxidation of X and subsequent hydrogenation produced XI which proved to be identical with the nitrogen free degradation product of jervine (XII).[2] The NMR spectra of Va, Vb and VIb support a C-nor-D-homosteroid carbon

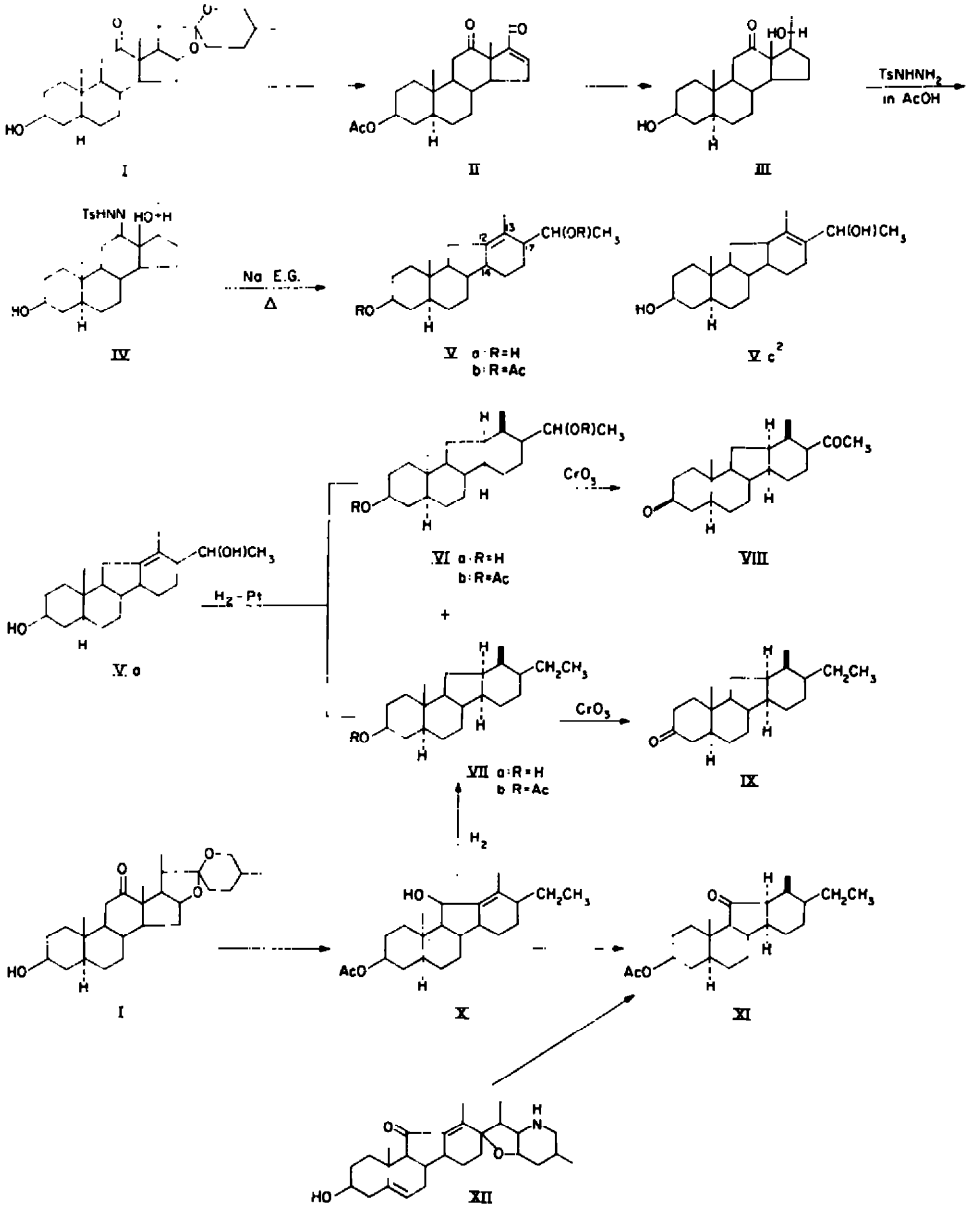
[1] Part of this work was reported at 83*rd Annual Meeting of the Pharmaceutical Society of Japan* Tokyo, Nov. 2 (1963).
[2] H. Mitsuhashi and Y. Shimizu, *Tetrahedron* **19**, 1027 (1963).
[3] H. Mitsuhashi, K. Shibata, T. Sato and Y. Shimizu, *Chem. Pharm. Bull., Tokyo* **12**, 1 (1964).
[4] H. Mitsuhashi and K. Shibata, *Tetrahedron Letters* 2281 (1964).
[5] R. Hirschmann, C. S. Snoddy, Jr., C. F. Hiskey and N. L. Wendler, *J. Amer. Chem. Soc.* **76**, 4013 (1954).
[6] J. Elks, G. H. Phillipps, D. A. H. Taylor and L. J. Wyman, *J. Chem. Soc.* 1739 (1954).
[7] S. Moris Kupchan and Seymour D. Levine, *J. Amer. Chem. Soc.* **86**, 701 (1964).

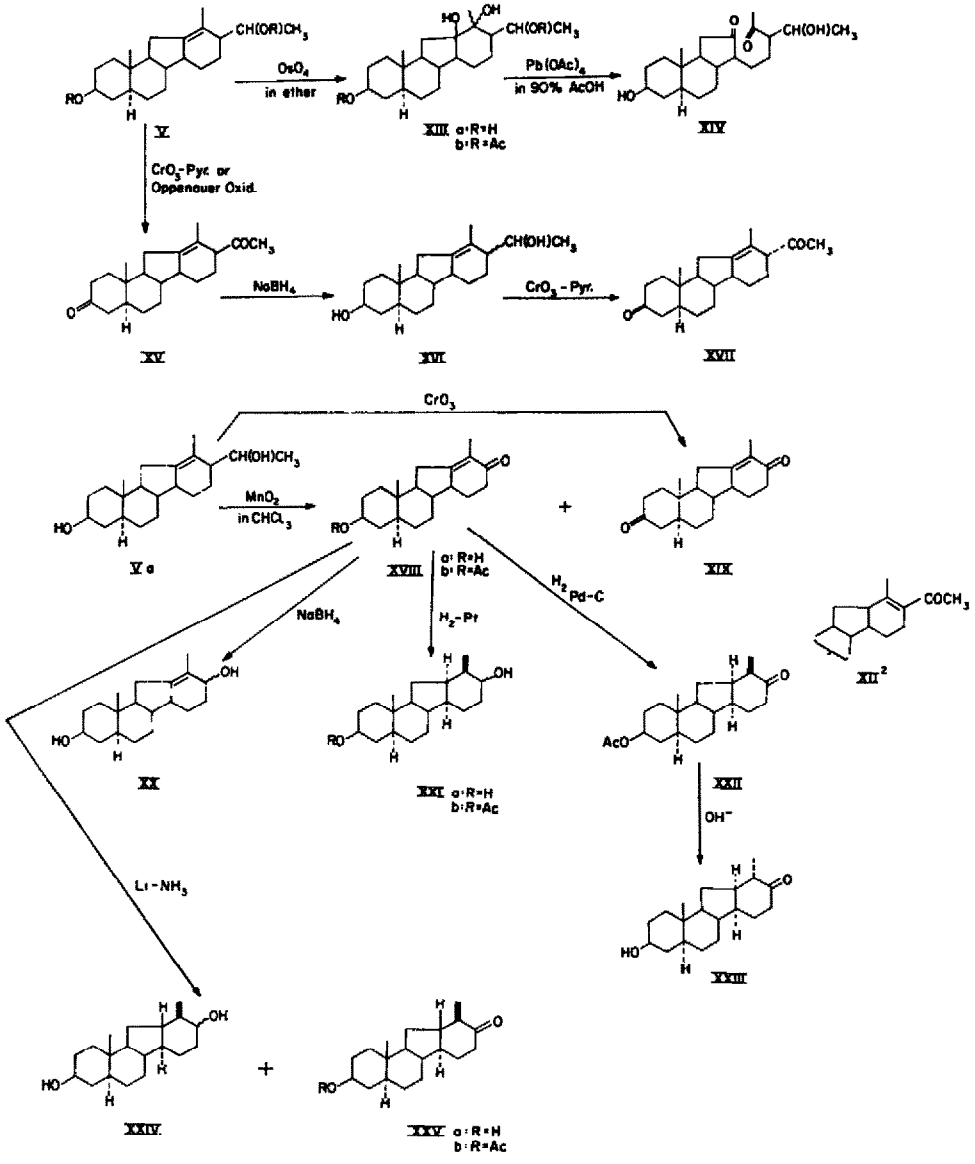
skeleton. Oxidation of Vb with osmium tetroxide in ether containing pyridine afforded, after decomposition of the initially formed osmate ester, a tetrol (XIIIa), m.p. 199–202°, which gave a diacetate (XIIIb), m.p. 109–113° with acetic anhydride and pyridine. During lead tetraacetate oxidation of XIIIa in 90% acetic acid, 1·1 moles of the reagent was consumed, which indicates that XIIIa has only one glycol group per molecule. Acetaldehyde could not be detected as a product of oxidation. The IR spectrum of the oxidation product (XIV) showed bands for an aliphatic ketone (1700 $cm^{-1}$) and a five membered ring ketone (1733 $cm^{-1}$). Both Oppenauer oxidation or chromic acid–pyridine oxidation of Va gave a diketone (XV) m.p. 122–125° which showed no selective UV absorption. A small quantity of yellow oil also formed during the oxidation could not be purified, but showed a UV maximum at 247 m$\mu$. Several attempts to prepare the $\Delta^{13(17)}$-20-one type from XV by treatment with alkali and acid, afforded only intractable mixtures. Contrary to results in the previous paper,[2] the $\alpha,\beta$-unsaturated ketone described as (XII)[2] could not be prepared. This phenomenon is of interest in that a double bond *exo* to a 5-membered ring is more stable than the 13-ene-20-one. Sodium borohydride reduction of XV, in 90% methanol containing a small quantity of sodium hydroxide, produced XVI which was a mixture of epimers at C-20. This mixture (XVI) was oxidized with chromic acid–pyridine to XVII, m.p. 116–122°. There is little possibility of a carbon skeleton rearrangement during these reactions. The m.p. and IR spectra of XV and XVII were distinctly different. The ORD curves of XV and XVII (Fig. 1), after subtraction of the effect of the C-3 keto group are exactly opposite. These results indicate that the reaction sequence of XV to XVII occurred with epimerization of the C-17 side chain from the axial to the more stable equatorial configuration.

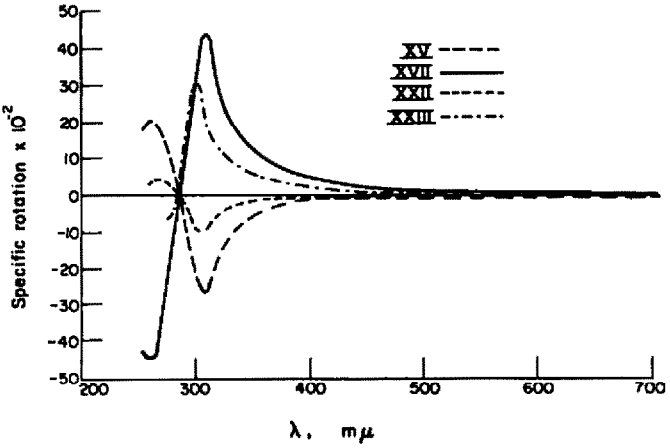
Active manganese dioxide oxidation of Va gave XVIIIa, an oil, which was characterized as its acetate (XVIIIb), m.p. 163–165°, $\lambda_{max}^{EtOH}$ 247 m$\mu$ ($\varepsilon$ = 18100) and XIX, m.p. 134–141°, $\lambda_{max}^{EtOH}$ 247 m$\mu$ ($\varepsilon$ = 15200). The UV data suggest the presence of an $\alpha,\beta$-unsaturated keto system in both products. Compound XIX also was formed from chromic acid oxidation of Va in 90% acetic acid. These results indicate that cleavage of C-17-20 bond has occurred—an interesting phenomenon in comparison with the usual manganese dioxide oxidation. As XIX is identical with (XII)[2], described in the previous paper,[2] the structure (XII)[2] has to be corrected to XIX. Sodium borohydride reduction of XVIIIb gave XX, m.p. 152–161°. Catalytic hydrogenation of XVIIIb with $PtO_2$ in ethanol and acetic acid afforded XXIb. Catalytic hydrogenation of XVIIIb with Pd-C as the catalyst in ethanol afforded XXII, m.p. 122–127°, which was deacetylated to XXIII, m.p. 149–155° by refluxing in 5% methanolic potassium hydroxide solution. The ORD curves of XXII and XXIII are shown in Fig. 1. These data and examination of molecular models of the ketones show that the C-18 Me group has epimerized to the more stable equatorial configuration under the above conditions. Reduction of XVIIIb with a solution of lithium in liquid ammonia gave a diol (XXIV) and a monoketone (XXVa), m.p. 221–222°. Alkaline treatment of XXVa with 5% methanolic potassium hydroxide gave only starting material, therefore this serves as evidence for the presence of an equatorial C-18-Me in XXVa. Thus structure XXVa must be expressed as (a) or (b). However, structure (a) has already been assigned to compound XXIII. Therefore structure XXVa must be expressed as (b). The mass spectrum of XXVa shows $M^+$ 290, the value required by the epiandrosterone system.

a b

On the basis of experience with the steroids encountered in this work the C-nor-D-homosteroid system proved to be generally more difficult to obtain crystalline than the normal steroid derivatives.




CH(OR)CH3
OsO4
in ether
Pb(OAc)4
in 90% AcOH
CH(OH)CH3
XIII a:R=H
b:R=Ac
XIV
V
CrO3-Pyr or
Oppenauer Oxid.
COCH3
NaBH4
CrO3-Pyr.
XV
XVI
XVII
CrO3
MnO2
in CHCl3
Va
XVIII
a:R=H
b:R=Ac
XIX
H2-Pr
H2
Pd-C
NaBH4
XII2
XX
XXI a:R=H
b:R=Ac
XXII
OH⁻
XXIII
Li-NH3
XXIV
XXV a:R=H
b:R=Ac


XV
XVII
XXII
XXIII
Specific rotation x 10⁻²
50
40
30
20
10
0
-10
-20
-30
-40
-50
200
300
400
500
600
700
λ, mμ

## EXPERIMENTAL

All m.p.s (except mix. m.p.) were measured on the Kofler Hot Stage Microscope and are uncorrected. For identification purposes, homogeneity tests were used and in order to follow the course of reactions, use was made of thin-layer chromatography on $Al_2O_3$ (Aluminumoxide G nach Stahl). The spots were developed by $I_2$ vapour and conc. $H_2SO_4$. The NMR spectra were taken on a Nihon Denshi JNMC-60 (60Mc) in the indicated solvents using tetramethylsilane as internal reference. The UV spectra were measured in EtOH on a Shimadzu Self-Recording UV-Spectrophotometer "RS-27". The IR spectra were taken in a Shimadzu IR Spectrophotometer type IR. The ORD spectra were determined on a Nippon Bunko ORD/UV-5 in MeOH solution. Active $MnO_2$ was prepared in accordance with the reported method.* Compounds II, III, IV and Va,b were prepared from hecogenin (I) by methods previously described.[2] NMR: Va ppm (pyridine); 0·71 (19-Me, singlet), 1·21 (21-Me, doublet, J = 6·6 c/s), 1·67 (18-Me, singlet); Vb ppm ($CDCl_3$); 0·74 (19-Me, singlet), 1·03 (21-Me, doublet, J = 6·6 c/s), 1·59 (18-Me, singlet), 1·97 (acetyl).

*Catalytic hydrogenation of the diol* (Va)

(i) Platinum oxide (100 mg) was pre-reduced in acetic acid (10 ml) and EtOH (8 ml) and the diol (Va; 450 mg) in acetic acid (10 ml) and EtOH (10 ml) was added. Hydrogen up-take stopped after 10·5 hr (35 ml at 10°), at which time 1 mole equiv. had been taken up. The catalyst was filtered off and the solution evaporated to dryness under red. press. The residue was diluted with water, and extracted with ether. The ethereal solution was washed with water, 5% $NaHCO_3$ solution, water and dried ($Na_2SO_4$). Evaporation of the solution yielded a product which recrystallized from MeOH to give needles (VIa; 150 mg, 33%), m.p. 239–240°. (Found: C, 78·79; H, 11·36. $C_{21}H_{36}O_2$ requires: C, 78·69; H, 11·32%). Acetylation of VIa with acetic anhydride in pyridine at room temp afforded a diacetate (VIb), m.p. 99–100°, $\nu_{max}^{Nujol}$ 1740 $cm^{-1}$(acetyl). NMR, ppm ($CDCl_3$); 0·79 (19-Me, singlet), 0·74 (18-Me, doublet, J = 5·4 c/s), 1·17 (21-Me, doublet, J = 6·0 c/s), 1·97 (acetyl, singlet).

(ii) The reduction of the diol (Va; 1·12 g) was repeated under the same conditions as above, and recrystallization from MeOH gave needles (VIa; 336 mg). The combined mother liquors from (i) and (ii) were evaporated to dryness to give 1·1 g yellow oil which was dissolved in benzene and chromatographed on $Al_2O_3$ (42 g). Elution with $CHCl_3$ yielded a colourless oil (740 mg) which was rechrogmatoraphed on $Al_2O_3$ (25 g). Elution with benzene gave waxy crystals (VIIa; 628 mg, 40%), m.p. about 75°. Acetylation of VIIa gave a colourless oil (VIIb), $\nu_{max}$ 1740 $cm^{-1}$ (acetyl).

*Chromic acid oxidation of* VIa

Compound VIa (52 mg) in 90% acetic acid (7 ml) was treated with a solution of $CrO_3$ (50 mg) in 90% acetic acid at room temp and after 16 hr, the excess oxidant was destroyed with MeOH. The reaction mixture was taken up in ether and washed with water, $NaHCO_3$ solution and water respectively and dried. After evaporation of solvent, the residue was crystallized from MeOH to give VIII (23 mg), m.p. 135–142°, $\nu_{max}^{Nujol}$ 1715 $cm^{-1}$(C=O). (Found: C, 79·42; H, 10·24. $C_{21}H_{32}O_2$ requires: C, 79·70; H, 10·19%).

*Chromic acid oxidation of* VIIa

Compound VIIa (486 mg) was dissolved in 90% acetic acid (15 ml) and added to a solution of $CrO_3$ (200 mg) in 90% acetic acid (15 ml). After standing 16 hr at room temp, the excess oxidant was destroyed with MeOH. The reaction mixture was extracted with ether and the ethereal solution washed with water, $NaHCO_3$ solution, and water respectively and dried. The residual yellow oil (446 mg), after evaporation of solvent, was chromatographed on $Al_2O_3$(15 g). Elution with n-hexane gave waxy crystals (IX; 321 mg), m.p. 43–48°, $\nu_{max}^{Nujol}$ 1715 $cm^{-1}$(C=O). (Found: C, 83·30; H, 11·22. $C_{21}H_{34}O$ requires: C, 83·38; H, 11·33%). ORD: $[\phi]_{301}^{peak} = +2422$, $[\phi]_{295}^{trough} = -3826$, a = +62.5 ($\times 10^2$).

*Osmium tetroxide oxidation of* Vb *to* XIIIa

Compound Vb (1·1 g) was dissolved in anhydrous ether (30 ml) and anhydrous pyridine (1·4 ml) and $OsO_4$ (0·96 g) in anhydrous ether (26 ml) was added. After standing for 103 days at 25°, the

* Attenburrow, T. Cameron *et al.*, *J. Chem. Soc.* 1094 (1952).

solvent was removed *in vacuo*. The black residue was dissolved in EtOH and hydrolysed by refluxing with a solution of $Na_2SO_3$ for 4 hr. The precipitate was filtered and washed with hot EtOH. The combined EtOH solutions were diluted with water, concentrated *in vacuo* and extracted with ether, the ether solution was dried ($Na_2SO_4$) and evaporated to dryness. The residue was crystallized from MeOH to yield XIIIa (260 mg), m.p. 199–202°, $\nu_{max}^{Nujol}$ 3300 $cm^{-1}$(OH, broad). (Found: C, 71·82; H, 10·33. $C_{21}H_{36}O_4$ requires: C, 71·55; H, 10·32%). The above tetrol (XIIIa, 50 mg) was warmed with pyridine (2 ml) and acetic anhydride (1 ml) for 30 min on a waterbath. After pouring into ice-water, the mixture was extracted with ether and treated according to the usual procedures. Recrystallization of the product from ether gave a diacetate (XIIIb; 50·6 mg), m.p. 109–113°, $\nu_{max}^{Nujol}$ $cm^{-1}$: 3500, 3600 (OH), 1730 (acetyl). (Found: C, 68·66; H, 9·21. $C_{25}H_{40}O_6$ requires: C, 68·77; H, 9·24%).

### $Pb(OAc)_4$ *oxidation of* XIIIa

A N/25 $Pb(OAc)_4$ acetic acid solution (20 ml) was added to a solution of the tetrol (XIIIa; 54 mg) in 70% acetic acid (10 ml). The mixture, in a closed flask, was allowed to stand for 3 hr at room temp in the dark. The gas in the flask, which was driven into a solution of 2,4-dinitrophenylhydrazine, did not produce the 2,4-dinitrophenylhydrazone of acetaldehyde. Ethylene glycol (1%, 15 ml) and water (50 ml) was added and the oxidation solution then kept for 1 hr in the dark at room temp. After most of the solvent had been removed *in vacuo*, water was added and the mixture extracted with ether. The ether extracts were washed with $NaHCO_3$ solution, water and dried. The residue failed to crystallize after evaporation of the solvent. The IR spectrum showed an aliphatic (1700 $cm^{-1}$) and a five membered ketone (1733 $cm^{-1}$).

#### *Titration*

A N/25 $Pb(OAc)_4$ acetic acid solution (10 ml) was added to the tetrol (17·65 mg, 0·05 mmole) in 70% acetic acid (5 ml). After standing at room temp in the dark, an aliquate was taken each hr, with the results as shown below:

| Time | 28 min | 60 min | 19 hr | 43 hr | 142 hr |
|---|---|---|---|---|---|
| Consumed moles $Pb(OAc)_4$ | 0·6 | 1·01 | 1·0 | 1·04 | 1·10 |

### *Oppenauer oxidation of* Va

Aluminium isopropoxide (1·2 g) in anhydrous toluene (30 ml) was added to a solution of Va (1 g) and cyclohexanone (13 ml) in anhydrous toluene (150 ml). The toluene was evaporated before 70 ml and after 30 ml of the reagent had been added. The solution was refluxed for 4 hr. After cooling, dil. HCl was added and the solution extracted with ether. The residual solution after removal of the ether was steam distilled and then extracted with ether. After removal of the solvent, the residual oil (1·0 g) was chromatographed on $Al_2O_3$ (30 g). The residues from the benzene eludents were crystallized from ether to give XV, 353 mg, m.p. 122–125°, and elution with ether yielded a multicomponent mixture (507 mg) which could not be purified.

### *Chromic acid oxidation of* Va

To a solution of $CrO_3$ (700 mg) in pyridine (10 ml), Va (715 mg) in pyridine (15 ml) was added with ice-cooling, and the resulting mixture allowed to stand for 27 hr at 28°. After addition of water, the solution was extracted with ether. The organic layer was washed with dil. HCl, water and dried. After evaporation of the solvent, the residue (644 mg) was chromatographed on $Al_2O_3$ (25 g). Elution with benzene yielded XV which crystallized from ether (279 mg) and was confirmed as XV, by m.p. and IR spectra, $\nu_{max}^{Nujol}$ $cm^{-1}$: 1718, 1703(C=O), UV; no selective absorption. (Found: C, 80·28; H, 9·68. $C_{21}H_{30}O_2$ requires: C, 80·21; H, 9·62%). ORD: $[\phi]_{306}^{trough} = -8540$, $[\phi]_{361}^{peak} = +6280$, $a = -148$ ($\times 10^3$). The product (152 mg) eluted with ether showed a strong absorption at 247 m$\mu$ but it was not apparent whether the bands were those of a $\Delta^{13(18)}$-17-one or a $\Delta^{15(17)}$-20-one type

system, but the IR spectrum ($CHCl_3$) indicated that it was probably the latter. Attempted purification by chromatography failed.

*Sodium borohydride reduction of* XV

A solution of $NaBH_4$ (510 mg) and a small quantity of NaOH in aq. MeOH was added to a solution of XV (426 mg) in MeOH (38 ml). The mixture was then allowed to stand for 16 hr at 28°. After the solution was acidified with dil. acetic acid, most of the solvent was removed *in vacuo*, and water added. The ether extracts were washed with water, $NaHCO_3$ solution, water and dried. Evaporation of the solvent gave crystals which were recrystallized from MeOH to give a mixture of crystals (epimers), (XVI, 245 mg), m.p. 160–163°, 178–184°, $\nu_{max}^{Nujol}$ 3250 $cm^{-1}$(broad). (Found: C, 79·20; H, 10·65. $C_{21}H_{34}O_3$ requires: C, 79·19; H, 10·76%).

*Chromic acid oxidation of* XVI

The above diol (XVI; 130 mg) in pyridine (3 ml) was added with ice-cooling to a solution of $CrO_3$ (150 mg) in pyridine (2 ml). The mixture was then allowed to stand for 40 hr at 28°. After addition of water, the solution was extracted with ether, the ether layer washed with dil. HCl, water and dried. Evaporation of the solvent gave material which recrystallized from MeOH in needles (XVII; 32 mg), m.p. 116–122°, $\nu_{max}^{Nujol}$ 1710 $cm^{-1}$(C=O), m.m.p. of XV and XVII; 86–110°. ORD: $[\phi]_{307}^{peak} = +14740$, $[\phi]_{263}^{trough} = -14740$, a = +295 (×10³).

*Chromic acid oxidation of* Va *to* XIX

Compound Va (217 mg) in 90% acetic acid (15 ml) was added to a solution of $CrO_3$ (188 mg) in 90% acetic acid (15 ml). After being left overnight at room temp, the excess oxidant was destroyed with MeOH. The solution was concentrated under red. press., diluted with water and extracted with ether. The ethereal layer was washed with water, $NaHCO_3$ solution and water and dried ($Na_2SO_4$). After evaporation of the solvent, the residue (188 mg) was chromatographed on $Al_2O_3$ (6 g). The residue from the benzene eludents was crystallized from MeOH to give XIX (86 mg), m.p. 134–141°. (Found: C, 79·80; H, 9·21. $C_{19}H_{26}O_2$ requires: C, 79·69; H, 9·15%). $\lambda_{max}^{EtOH}$ 247 mμ (ε = 15200), $\nu_{max}^{Nujol}$ $cm^{-1}$: 1704 (isolate C=O), 1650, 1640 (α,β-unsaturated ketone).

*Manganese dioxide oxidation of* Va

Compound Va (3 g) was heated under reflux in $CHCl_3$ (300 ml) with active $MnO_2$ (30 g) for 10 hr. After cooling, the $MnO_2$ was filtered off and the $CHCl_3$ solution evaporated to dryness. The residue was chromatographed on $Al_2O_3$ (75 g). The residue from the fractions (129 mg) eluted with benzene showed a strong UV absorption at 247 mμ and was crystallized from MeOH to give XIX, m.p. 134–141°. The residue after removal of solvent (XVIIIa; 676 mg) from the 50% benzene–$CHCl_3$ eludents were warmed on a steam bath for 30 min with pyridine and acetic anhydride. After pouring into ice-water, the mixture was extracted with ether and treated according to the usual procedures. Recrystallization of the product from MeOH gave prisms (XVIIIb; 288 mg), m.p. 163–165°, $\lambda_{max}^{EtOH}$ 247 mμ (ε = 18100). (Found: C, 76·39; H, 9·17. $C_{21}H_{30}O_3$ requires: C, 76·32; H, 9·15%). $\nu_{max}^{Nujol}$ $cm^{-1}$: 1730 (acetyl), 1655 (C=O), 1640 (C=C). The 2,4-dinitrophenylhydrazone prepared from the residue of the 50% benzene–$CHCl_3$ eludents was recrystallized from MeOH, m.p. 258–262°, $\lambda_{max}^{EtOH}$ mμ: 258 (ε = 14300), 388 (ε = 24700). (Found: C, 64·02; H, 6·82; N, 11·65. $C_{25}H_{32}O_5N_4$ requires: C, 64·08; H, 6·88; H, 11·96). The residue from the ether eludents gave prisms (13 mg), m.p. 244–253°, UV $\lambda_{max}^{EtOH}$ mμ: 231 (ε = 1320), 268 (ε = 759), 272 (ε = 650), 277 (ε = 733). (Found: C, 80·32; H, 9·57. $C_{21}H_{30}O_2$ requires : C, 80·21; H, 9·62%.) The UV data and elemental analysis indicated that aromatization of the D-ring had occurred, but further investigation was abandoned due to the shortage of material.

*Sodium borohydride reduction of* XVIIIb *to* XX

Compound XVIIIb (21 mg) in MeOH was treated with a solution of $NaBH_4$ (30 mg) in aq. MeOH (3 ml) at room temp for 15 hr. Dil. acetic acid was added to the reaction mixture which was diluted with water and concentrated to dryness *in vacuo*. The residue was distributed between water and ether. The organic layer was separated and washed with water, and dried ($Na_2SO_4$). Evaporation of the solvent gave crystals, which were recrystallized from MeOH–ether to give XX (10 mg), m.p. 152–161°, $\nu_{max}^{Nujol}$ 3350 $cm^{-1}$ (OH).

*Catalytic hydrogenation of* XVIIIb *to* XXIb

Compound XVIIIb (130 mg) was shaken with $PtO_2$ (100 mg) in acetic acid (5 ml) and EtOH (5 ml) under an $H_2$ atm. for 4 hr 40 min. The catalyst was filtered off and the solvent evaporated to dryness under red. press. The residue was diluted with water and extracted with ether. The ether phase was washed with water, $NaHCO_3$ solution and water. After the ethereal solution was dried ($Na_2SO_4$), evaporation of the solvent gave a colourless oil which behaved as a pure substance (XXIb; 97 mg) on chromatography ($Al_2O_3$), $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3600 (OH), 1740 (acetyl). A solution of XXIb (42 mg) in 3 ml of 5% methanolic KOH was refluxed for 30 min. After the reaction mixture was treated according to the usual procedures, the product crystallized from ether-isopropylether in needles (XXIa), m.p. 148–164°, $\nu_{max}^{Nujol}$ 3350 $cm^{-1}$ (OH). (Found: C, 78·36; H, 10·96. $C_{19}H_{32}O_2$ requires: C, 78·03; H, 11·03%.)

*Catalytic hydrogenation of* XVIIIb *to* XXII

Compound XVIIIb (200 mg) in EtOH (15 ml) was hydrogenated in the presence of prereduced 5% Pd–C (100 mg). The hydrogenation was stopped after 1 mole equiv. $H_2$ had been absorbed (11 hr). After the catalyst had been filtered off and washed with EtOH, the filtrate was concentrated. The residue was crystallized from MeOH to give plates (XXII; 170 mg), m.p. 122–127°, $\nu_{max}^{Nujol}$ $cm^{-1}$: 1710 (C=O), 1730 (acetyl). ORD: $[\phi]_{304}^{trough} = -3788$, $[\phi]_{266}^{peak} = +1232$, $a = -50{\cdot}2$ ($\times 10^2$).

*Hydrolysis of* XXII *to* XXIII

Compound XXII (150 mg) was hydrolysed by refluxing with 5% methanolic KOH (4 ml) for 1 hr To this solution, after cooling, water was added and the MeOH removed *in vacuo*. After extraction with ether, the ether solution was washed with water and dried ($Na_2SO_4$). Evaporation of solvent gave a residue which was crystallized from MeOH to give needles (XXIII; 62 mg), m.p. 149–155°, $\nu_{max}^{Nujol}$ $cm^{-1}$: 3500 (OH), 1700 (C=O), (Found: C, 78·21; H, 10·27. $C_{19}H_{30}O_2$ requires: C, 78·57; H, 10·41%.) ORD: $[\phi]_{300}^{peak} = +8738$, $a = +87{\cdot}4$ ($\times 10^2$).

Li-*liquid* $NH_3$ *reduction of* XVIIIb

Compound XVIIIb (304 mg) in absolute ether (30 ml) and dry dioxane (30 ml) was added with stirring during 1 min to a solution of Li (400 mg) in liquid $NH_3$ (125 ml), and the mixture stirred for 0·5 min. Ammonium chloride (3 g) was added and after the $NH_3$ had evaporated overnight, water was added and the product isolated with ether and washed with water and dried. After evaporation, the residue (300 mg) which showed 3 spots on thin-layer chromatography ($Al_2O_3$) and no selective UV absorption was chromatographed on $Al_2O_3$ (9 g). Elution with ether gave material which crystallized from ether to afford XXIV, m.p. 72–78°, $\nu_{max}^{Nujol}$ 3500 $cm^{-1}$ (OH, broad). (Found: C, 75·86; H, 10·93. $C_{19}H_{32}O_2 \cdot \frac{1}{2}H_2O$ requires: C, 75·70; H, 11·03%.) The residue from the MeOH eludents was crystallized from MeOH–ethyl acetate to give XXVa, m.p. 221–222°, $\nu_{max}^{Nujol}$ $cm^{-1}$: 3400 (OH, broad), 1685 (C=O). (Found: C, 78·46; H, 10·31. $C_{19}H_{30}O_2$ requires: C, 78·57; H, 10·41%.) Compound XXVa was warmed on a water bath for 30 min with pyridine and acetic anhydride. After pouring into ice-water, the mixture was extracted with ether and treated according to the usual procedures. Recrystallization of the product from MeOH gave the monoacetate (XXVb), m.p. 223–224°, $\nu_{max}^{Nujol}$ $cm^{-1}$: 1727 (acetyl), 1677 (C=O). (Found: C, 75·39; H, 9·50. $C_{21}H_{32}O_3$ requires: C, 75·86; H, 9·70%.)

*Acknowledgements*—We wish to express our thanks to Dr. K. Takeda, Director of Shionogi Laboratory for the starting materials and Prof. T. Irie (Hokkaido University), for kindly permitting us to use their spectrometer. We are also indebted to Mr. S. Shimokawa (Hokkaido University) for NMR measurement.