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Reactions of 5α,14β-Pregn-16-en-20-one with Nucleophiles[1]

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3β,17α-Dihydroxy-5α,14β-pregnan-20-one (III) and 3β-hydroxy-5α,14β-pregn-16-en-20-one (VII) were prepared from 14β-isoandrosterone (I) by way of the 17β-ethynyl-17α-hydroxy derivative (II) in satisfactory yield. The reactivities of the nucleophilic reagents such as potassium cyanide, thioacetic acid, ethylenimine and nitromethane toward the Δ^{16}-20-ketone system in VII have been investigated. All these nucleophiles showed the β-side attack yielding the 16β-substituted derivatives, in which the configuration of the side chain at C-17 was α. These results may be ascribable to the characteristic feature of C/D-ring fusion forming the cage-like structure.

As a series of studies on cardiotonic steroid analogs we have reported the synthesis of 16-substituted 14,17-*cis*-5α-cardenolides.[3] In order to examine the effects of a variety of substituents at C-16 on the physiological activity the reactions of 14β,15β-epoxypregn-16-en-20-one with the nucleophiles have been investigated.[4] Further interest in these respects prompted us to prepare 14β-pregn-16-en-20-one and to explore its reactivities toward the nucleophilic reagents.

An initial project was directed to the development of a new synthetic route leading to 5α,14β-pregn-16-en-20-one. First, 3β-hydroxy-5α,14β-androstan-17-one (I), prepared from dehydroepiandrosterone in several steps by the method of St. André, *et al.*[5] was subjected to Grignard reaction employing ethynyl magnesium bromide. As was expected the reaction proceeded with ease to give the ethynyl derivative (IIa) as a single product. Subsequent treatment with the mercury-resin[6] was remarkably effective in promoting hydration of the acetylenic linkage to furnsih the saturated pregnanolone derivative (III) in which the presence of a chelated tertiary hydroxyl group was indicative.

Stereochemistry at C-17 was elucidated by leading to the known compound utilizing Serini reaction.[7] Reduction with lithium aluminum hydride followed by usual acetylation gave 5α,14β-pregnane-3β,17,20-triol 3,20-diacetate (IV). When refluxed with zinc granule in xylene, the 17,20-glycol 20-acetate underwent inversion of the side chain yielding 14β,17α-pregnan-20-one (V), which proved to be identical with the authentic sample prepared from the 14,16-diene (VI) by catalytic hydrogenation. This result unequivocally supported the assignment of the structure 17α-hydroxy-14β,17β-pregnan-20-one to III and hence 17β-ethynyl-17α-ol to II. It is noteworthy that the reagent would attack the 17-ketone preferentially from the less hindered β-side of a molecule due to the concave nature of C/D-*cis* fusion.[5,8]

1) This paper constitutes Part X of the series entitled "Studies on Cardiotonic Steroid Analogs"; Part IX: T. Nambara, T. Shibata, M. Mimura, and H. Hosoda, *Chem. Pharm. Bull.* (Tokyo), **19**, 954 (1971).
2) Location: *Aobayama, Sendai.*
3) T. Nambara, K. Shimada, J. Goto, and S. Goya, *Chem. Pharm. Bull.* (Tokyo), **19**, 21 (1971).
4) T. Nambara, S. Goya, J. Goto, and K. Shimada, *Chem. Pharm. Bull.* (Tokyo), **16**, 2228 (1968).
5) A.F. St.André, H.B. MacPhillamy, J.A. Nelson, A.C. Shabica, and C.R. Scholz, *J. Am. Chem. Soc.*, **74**, 5506 (1952).
6) M.S. Newman, *J. Am. Chem. Soc.*, **75**, 4740 (1953).
7) A. Serini, W. Logemann, and W. Hildebrand, *Ber.*, **72**, 391 (1939).
8) T. Nambara and J. Fishman, *J. Org. Chem.*, **26**, 4569 (1961); *idem, ibid.*, **27**, 2131 (1962); T. Nambara and K. Hirai, *Chem. Pharm. Bull.* (Tokyo), **12**, 836 (1964); T. Nambara and M. Yano, *ibid.*, **13**, 1004 (1965).

Transformation of the ethynyl derivative into 14β-pregn-16-en-20-one was then undertaken. Being refluxed in formic acid, II was converted with success into the desired pregn-16-en-20-one (VII) in 60% yield. Upon catalytic hydrogenation over palladium-on-charcoal VIIb was led to 14β,17α-pregnan-20-one (V) almost quantitatively.

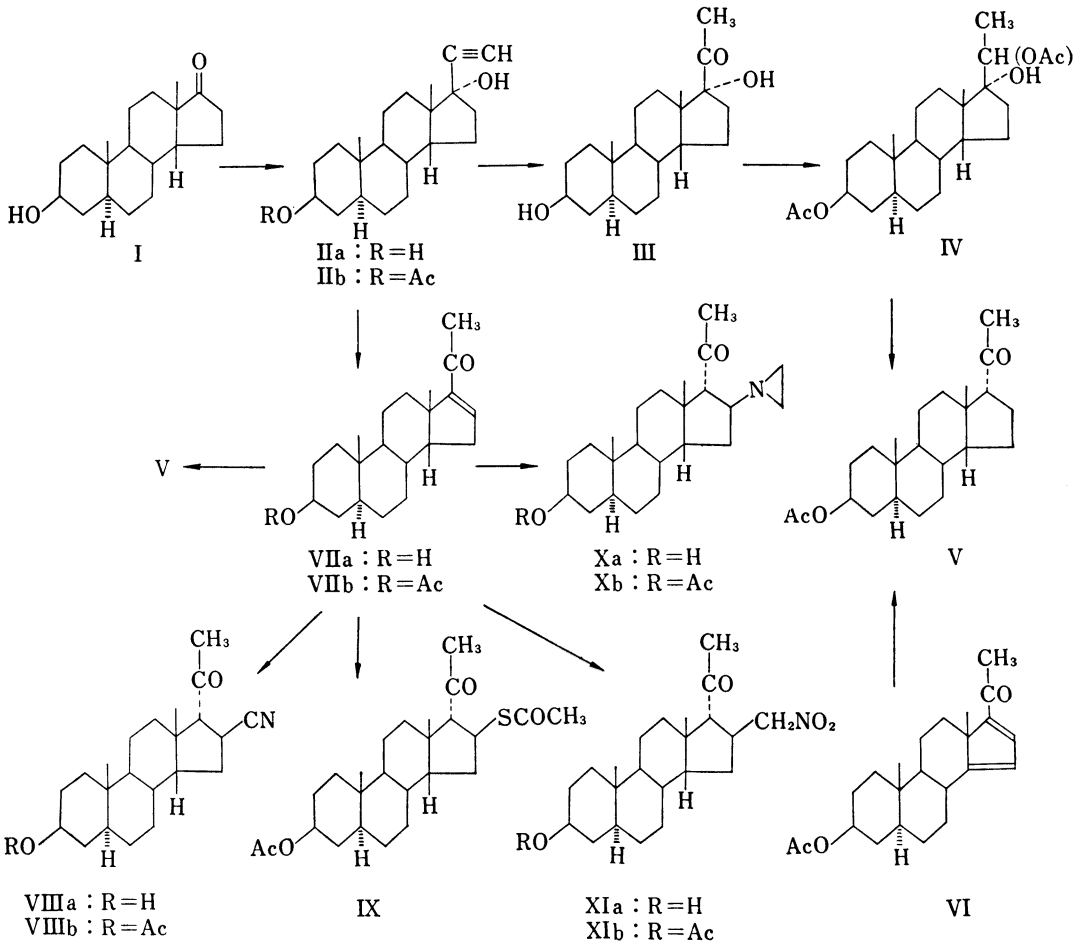


Chart 1

The reaction of cyanide with the Δ^{16}-20-ketone was first examined. When VII was boiled under reflux with potassium cyanide in aqueous ethanol, an addition product (VIII) was solely provided. As illustrated in Fig. 1, this new compound showed the negative Cotton effect. It is well documented in withe literatures that the 17β-pregnan-20-one displays the positive Cotton effect whereas the 17-epimer exhibits the negative sign.[9] Upon direct comparison this product proved not to be identical with known 16α-cyano-5α,14β,17α-pregnan-20-one.[4] Accordingly the structure of epimeric 16β-cyano-17α-pregnan-20-one could be assigned to VIII.

Additive condensation of thioacetic acid with VII was effected without catalyst to result in formation of the adduct (IX) in satisfactory yield. The α-configuration of the side-chain

9) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, 1960, p. 51; H. Mitsuhashi, T. Nomura, and M. Fukuoka, *Steroids*, **4**, 483 (1964).

at C-17 was deduced from the optical rotatory dispersion data. The *trans*-nature of C-16 and C-17 protons was indicated by the magnitude of the coupling constant and hence the configuration of C-16 substituent was deduced to be β.

Addition of nitromethane was effected by the catalysis of tetraethylammonium hydroxide to furnish 16β-nitromethyl-17α-pregnan-20-one (XI) in reasonable yield. Configurational assignments at C-16 and C-17 were similarly rationalized on the basis of the rotatory dispersion curve and nuclear magnetic resonance spectra.

Reaction with ethylenimine employing triethylamine as catalyst also proceeded with relative ease to give the 16-aziridinyl derivative (X). The adduct showed the negative Cotton effect indicating the α-configuration of the side chain at C-17. In this case, however, the coupling constant was not definitive to determine the stereochemistry at C-16. The analogous reactions mentioned above indicate the assignment of the β-configuration to C-16 substituent, though we can offer no ready explanation for the small coupling constant other than to propose a conformational deformation of ring D. As was shown in Table I, C-17 proton of 16,17-*trans*-substituted pregnan-20-ones resonates at the lower field than that of the parent compound, while the existence of the *cis*-substituent at C-16 exerts no significant influence on the chemical shift of C-17 proton. These data may be helpful to assume the orientation of the aziridinyl group to be β rather than α.

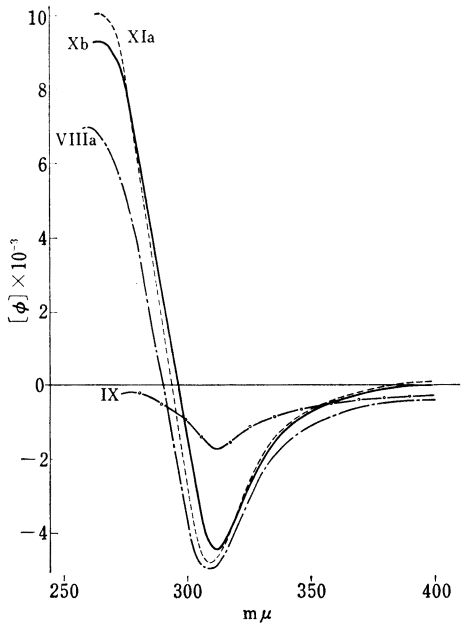


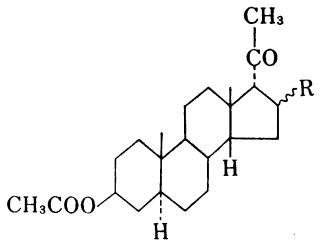
Fig. 1. Optical Rotatory Dispersion Curves of 16β-Substituted 5α, 14β, 17α-Pregnan-20-ones in Methanol

The attempt for condensation with the alcohol, *i.e.* methanol and benzyl alcohol, in the presence of alkaline catalyst resulted in failure because of the remarkably less reactivity.

It has been disclosed that the nucleophiles so far examined undergo the Michael-type condensation with Δ^{16}-20-ketone system yielding 16β-substituted 17α-pregnan-20-ones. It is to be noted that the reactivity of Δ^{16}-20-ketone system of VII toward nucleophiles is somewhat less than that of the 14β,15β-epoxy derivative.[4] Although no plausible explanation is now available, it may probably be due to the conformational difference in ring D. It is sufficiently substantiated that the access of the reagent would favor the front-side of the 14β-steroid molecule since the geometry of *cis*-jointed rings C/D is such as to constitute a cage-like structure. The present results are fairly in accord with many instances previously reported. With respect to the stereochemistry at C-17 the orientation of hydrogen must be affected by equilibration under the reaction condition and may be expected to be β. The steric interaction with C-16 substituent would also favor the α-orientation of the side-chain at C-17. In actual fact 17α-pregnan-20-one derivatives were exclusively produced.

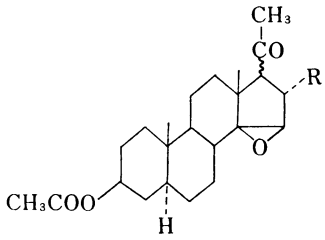
Further studies on the development of an alternative route leading to the desired 14β, 17β-pregnan-20-ones having a variety of substituents at C-16 are being conducted in our laboratory and will be reported in near future.

Table I-a. Chemical Shifts of C-17, C-18 and C-21 Protons in 16-Substituted 5α, 14β, 17α-Pregnan-20-ones



Compound			Chemical shift (δ) ppm[a]		
R	Configuration of 16-H		17-H	18-H	21-H
H		V	2.65	1.22	2.14
CN	β		2.76	1.20	2.22
CN	α	VIIIb	3.08	1.32	2.22
$SCOCH_3$	α	IX	3.11	1.13	2.29
	α	Xb	3.00	1.26	2.21
CH_2NO_2	α	XIb	2.63	1.26	2.15

Table I-b. Chemical Shifts of C-17 Protons in 16α-Substituted 14β, 15β-Epoxy-5α-pregnan-20-ones



Compound		Chemical shift (δ) ppm[a]
R	Configuration of 17-$COCH_3$	17-H
H	α	2.63
OCH_3	α	2.60
$OCH_2C_6H_5$	α	2.70
OH	α	2.50
$OCOCH_3$	α	2.73
CN	α	2.63
$SCOCH_3$	β	3.05

a) All the spectra were measured in $CDCl_3$ using tetramethylsilane as an internal standard.

Experimental[10]

17β-Ethynyl-5α,14β-androstane-3β,17α-diol (IIa)——A stream of purified acetylene gas was bubbled through anhydrous tetrahydrofuran (THF) (200 ml) at room temperature for 2 hr. Without interrupting the acetylene stream, EtMgBr in ether (3 N, 38 ml) was slowly added and the passage of acetylene was continued for 3 hr. Then a solution of 3β-hydroxy-5α,14β-androstan-17-one (I) (2.5 g) in anhydrous THF (50 ml) was added and refluxed for 1 hr. The resulting solution was poured into a cold saturated NH_4Cl solution and extracted with AcOEt. The organic phase was washed with 5% HCl, H_2O and dried over anhydrous Na_2SO_4. After usual work-up the residue obtained was chromatographed on Al_2O_3 (50 g). Elution with benzene and recrystallization of the eluate from MeOH gave IIa (1.5 g) as colorless needles. mp 209—210°. $[\alpha]_D^{24}$ +35.0° (c=0.14). *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.35; H, 10.15. NMR (4% solution in $CDCl_3$) δ: 0.78 (3H, s, 19-CH_3), 1.09 (3H, s, 18-CH_3), 2.50 (1H, s, -C≡CH), 3.55 (1H, m, 3α-H).

17β-Ethynyl-5α,14β-androstane-3β,17α-diol 3-Acetate (IIb)——Usual treatment of IIa with Ac_2O and pyridine followed by recrystallization from acetone–hexane gave IIb as colorless prisms. mp 128—130°. $[\alpha]_D^{22}$ +22.2° (c=0.11). *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.25; H, 9.70. IR ν_{max}^{KBr} cm^{-1}: 3260 (-C≡CH), 1730 (C=O). NMR (4% solution in $CDCl_3$) δ: 0.80 (3H, s, 19-CH_3), 1.10 (3H, s, 18-CH_3), 2.00 (3H, s, 3β-$OCOCH_3$), 2.50 (1H, s, -C≡CH), 4.65 (1H, m, 3α-H).

3β,17α-Dihydroxy-5α,14-βpregnan-20-one (III)——To an ethanolic solution (6 ml) of IIa (200 mg) were added H_2O (0.6 ml) and Hg-Dowex 50[6] (1.2 g) and refluxed for 5 hr. The reaction mixture was filtered and the filtrate was diluted with AcOEt, washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up the crystalline product was obtained. Recrystallization from aq. MeOH gave III (120 mg) as colorless plates. mp 200—202°. $[\alpha]_D^{16}$ 0° (c=0.10). *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.13; H, 10.09. IR ν_{max}^{KBr} cm^{-1}: 1698 (C=O). NMR (4% solution in $CDCl_3$) δ: 0.78 (6H, s, 18- and 19-CH_3), 2.24 (3H, s, 21-CH_3), 3.55 (1H, m, 3α-H). ORD (c=0.12, MeOH) $[\alpha]^{18}$ (mμ): +76.4° (400), +619.5° (315) (peak), 0° (297), −390.4° (282) (trough).

Transformation of III into 3β-Acetoxy-5α,14β,17α-pregnan-20-one (V)——To a solution of III (40 mg) in anhydrous THF (4 ml) was added $LiAlH_4$ (25 mg) and refluxed for 3 hr. To this solution was added moistened ether to decompose the excess reagent and acidified with 10% HCl. The organic phase was separated, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of solvent the crystalline product obtained was acetylated with Ac_2O and pyridine. On usual work-up 5α,14β-pregnane-3β,17,20-triol 3,20-diacetate (IV) was obtained as an oily product. To a solution of IV in xylene (4 ml) was added granulated Zn (800 mg) and refluxed under a stream of N_2 for 12 hr. The reaction mixture was filtered and the filtrate was evaporated. An oily residue obtained was subjected to preparative thin-layer chromatography (TLC) on Silica gel H using benzene–AcOEt (100:1) as developing solvent. The adsorbent of the zone corresponding to *Rf* 0.80 was eluted with AcOEt and recrystallization of the eluate from acetone–hexane gave V (34 mg) as colorless plates. mp 109—111°. Mixed melting point on admixture with the authentic sample[11] showed no depression and infrared spectra of two samples were identical in every respect.

3β-Hydroxy-5α,14β-pregn-16-en-20-one (VIIa)——A solution of IIa (900 mg) in formic acid (30 ml) was refluxed for 1.5 hr. After evaporation of solvent an oily residue obtained was dissolved in a solution of KOH (600 mg) in 90% aq. dioxane (20 ml) and stirred at room temperature overnight. The reaction mixture was diluted with $CHCl_3$, washed with 5% HCl, H_2O and dried over anhydrous Na_2SO_4. After usual work-up the residue obtained was chromatographed on Al_2O_3 (30 g). Elution with ether and recrystallization of the eluate from acetone–hexane gave VIIa (540 mg) as colorless leaflets. mp 126—128°/144—146°. $[\alpha]_D^{21}$ +89.7° (c=0.12). *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.43; H, 10.25. UV λ_{max}^{EtOH} mμ (ε): 242 (10300). IR ν_{max}^{KBr} cm^{-1}: 1660 (conjugated C=O), 1600 (C=C). NMR (4% solution in $CDCl_3$) δ: 0.79 (3H, s, 19-CH_3), 1.24 (3H, s, 18-CH_3), 2.24 (3H, s, 21-CH_3), 3.55 (1H, m, 3α-H), 6.60 (1H, t, J=2.3 cps, 16-H).

3β-Acetoxy-5α,14β-pregn-16-en-20-one (VIIb)——Usual treatment of VIIa with Ac_2O and pyridine followed by recrystallization from MeOH gave VIIb as colorless leaflets. mp 170—171°. $[\alpha]_D^{23}$ +77.5° (c=0.14). *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.07; H, 9.65. NMR (4% solution in $CDCl_3$) δ: 0.82 (3H, s, 19-CH_3), 1.27 (3H, s, 18-CH_3), 2.03 (3H, s, 3β-$OCOCH_3$), 2.27 (3H, s, 21-CH_3), 4.65 (1H, m, 3α-H), 6.64 (1H, t, J=2.3 cps, 16-H).

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10) All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ unless otherwise stated. Rotatory dispersion curves were obtained on JASCO Model ORD/UV-5 recorder. Infrared spectral measurements were run on JASCO Model IR-S spectrometer. Nuclear magnetic resonance spectra were run on Hitachi Model H-60 spectrometer at 60 Mc; the chemical shifts are quoted as ppm downfield from $(CH_3)_4Si$ used as an internal standard. Abbreviation used s=singlet, d=doublet, t=triplet, and m=multiplet.

11) Pl.A. Plattner, L. Ruzicka, H. Heusser, and E. Angliker, *Helv. Chim. Acta*, **30**, 385 (1947).

Hydrogenation of VIIb——A solution of VIIb (10 mg) in EtOH (5 ml) was shaken with 5% Pd/C (10 mg) under a stream of H_2 at room temperature for 2 hr. After removal of catalyst by filtration the filtrate was concentrated to give the crystalline product. Recrystallization from acetone-hexane gave V (8 mg) as colorless plates. mp 108—111°. Mixed melting point on admixture with the authentic sample[11] showed no depression.

3β-Hydroxy-16β-cyano-5α,14β,17α-pregnan-20-one (VIIIa)——To an ethanolic solution (10 ml) of VIIa (or VIIb) (100 mg) was added an aq. solution (2 ml) of KCN (50 mg) and refluxed for 3 hr. The reaction mixture was extracted with $CHCl_3$, washed with H_2O and dried over anhydrous Na_2SO_4. After usual work-up the residue obtained was subjected to preparative TLC on Silica gel G using benzene-AcOEt (5:1) as developing solvent. The adsorbent of the zone corresponding to *Rf* 0.50 was eluted with AcOEt and recrystallization of the eluate from aq. MeOH gave VIIIa (75 mg) as colorless plates. mp 204—206°. $[\alpha]_D^{24}$ −19.6° (c=0.15). *Anal.* Calcd. for $C_{22}H_{33}O_2N$: C, 76.92; H, 9.68; N, 4.08. Found: C, 77.01; H, 9.83; N, 3.93. IR ν_{max}^{KBr} cm^{-1}: 2235 (C≡N), 1690 (C=O). NMR (4% solution in $CDCl_3$) δ: 0.78 (3H, s, 19-CH_3), 1.32 (3H, s, 18-CH_3), 2.22 (3H, s, 21-CH_3), 3.08 (1H, d, J=9 cps, 17β-H), 3.55 (1H, m, 3α-H). ORD (c=0.11, MeOH) $[\alpha]^{15}$ (mμ): −113° (400), −620° (330), −1324° (308) (trough), 0° (290), +1859° (261) (peak).

3β-Acetoxy-16β-cyano-5α,14β,17α-pregnan-20-one (VIIIb)——Usual treatment of VIIIa with Ac_2O and pyridine followed by recrystallization from aq. MeOH gave VIIIb as colorless needles. mp 175—177°. $[\alpha]_D^{24}$ −17.4° (c=0.14). *Anal.* Calcd. for $C_{24}H_{35}O_3N$: C, 74.76; H, 9.15; N, 3.63. Found: C, 75.01; H, 9.24; N, 3.47. NMR (4% solution in $CDCl_3$) δ: 0.79 (3H, s, 19-CH_3), 1.33 (3H, s, 18-CH_3), 2.01 (3H, s, 3β-$OCOCH_3$), 2.22 (3H, s, 21-CH_3), 3.08 (1H, d, J=9 cps, 17β-H), 4.65 (1H, m, 3α-H).

3β-Acetoxy-16β-acetylthio-5α,14β,17α-pregnan-20-one (IX)——To a solution of VIIb (100 mg) in THF (2 ml) was added AcSH (0.1 ml) and allowed to stand at room temperature for 3 days. The reaction mixture was extracted with ether, washed with 5% $NaHCO_3$, H_2O and dried over anhydrous Na_2SO_4. After usual work-up the crystalline product obtained was subjected to preparative TLC on Silica gel HF using benzene-AcOEt (40:1) as developing solvent. The adsorbent of the zone corresponding to *Rf* 0.35 was eluted with ether and recrystallization of the eluate from acetone-hexane gave IX (35 mg) as colorless needles. mp 139—141°. $[\alpha]_D^{24}$ −8.0° (c=0.12). *Anal.* Calcd. for $C_{25}H_{38}O_4S$: C, 69.09; H, 8.81. Found: C, 69.24; H, 8.70. IR ν_{max}^{KBr} cm^{-1}: 1730, 1715, 1692 (C=O). NMR (4% solution in $CDCl_3$) δ: 0.78 (3H, s, 19-CH_3), 1.13 (3H, s, 18-CH_3), 2.02 (3H, s, 3β-$OCOCH_3$), 2.07 (3H, s, 16β-$SCOCH_3$), 2.29 (3H, s, 21-CH_3), 3.11 (1H, d, J=10 cps, 17β-H), 4.45 (1H, m, 16α-H), 4.65 (1H, m, 3α-H). ORD (c=0.12, MeOH) $[\alpha]^{15}$ (mμ): −86° (400), −402° (312) (trough), −51° (278) (peak). The adsorbent of the zone corresponding to *Rf* 0.45 was eluted with ether. Recrystallization of the eluate from MeOH gave unchanged VIIb (55 mg) as colorless leaflets.

3β-Hydroxy-16β-(1′-aziridinyl)-5α,14β,17α-pregnan-20-one (Xa)——To a solution of VIIa (50 mg) were added ethylenimine (1 ml) and $(Et)_3N$ (2 drops) and allowed to stand at room temperature for 20 hr. Upon evaporation of solvent the crystalline product was obtained. Recrystallization from acetone gave Xa (45 mg) as colorless prisms. mp 195—197°. $[\alpha]_D^{24}$ +25.6° (c=0.14). *Anal.* Calcd. for $C_{23}H_{37}O_2N$: C, 76.83; H, 10.37; N, 3.90. Found: C, 76.62; H, 10.31; N, 4.26. NMR (4% solution in $CDCl_3$) δ: 0.77 (3H, s, 19-CH_3), 1.26 (3H, s, 18-CH_3), 2.21 (3H, s, 21-CH_3), 3.00 (1H, d, J=7 cps, 17β-H), 3.55 (1H, m, 3α-H).

3β-Acetoxy-16β-(1′-aziridinyl)-5α,14β,17α-pregnan-20-one (Xb)——Usual treatment of Xa with Ac_2O and pyridine followed by recrystallization from acetone-hexane gave Xb as colorless needles. mp 160—160.5°. $[\alpha]_D^{21}$ +22.5° (c=0.13). *Anal.* Calcd. for $C_{25}H_{39}O_3N$: C, 74.77; H, 9.79; N, 3.49. Found: C, 75.05; H, 9.89; N, 3.77. IR ν_{max}^{KBr} cm^{-1}: 1730, 1702 (C=O), 1035 (C-N). NMR (4% solution in $CDCl_3$) δ: 0.78 (3H, s, 19-CH_3), 1.26 (3H, s, 18-CH_3), 1.99 (3H, s, 3β-$OCOCH_3$), 2.21 (3H, s, 21-CH_3), 3.00 (1H, d, J=7 cps, 17β-H), 4.65 (1H, m, 3α-H). ORD (c=0.13, MeOH) $[\alpha]^{18}$ (mμ): 0° (400), −1115° (311) (trough), 0° (296), +2321° (266) (peak).

3β-Hydroxy-16β-nitromethyl-5α,14β,17α-pregnan-20-one (XIa)—— To a solution of VIIa (150 mg) in THF (4 ml) were added nitromethane (2 ml) and 10% aq. solution of $(Et)_4NOH$ (0.4 ml) and refluxed for 8 hr. The resulting solution was diluted with AcOEt, washed with H_2O and dried over anhydrous Na_2SO_4. After usual work-up an oily residue obtained was subjected to preparative TLC on Silica gel HF using hexane-AcOEt (2:3) as developing solvent. The adsorbent of the zone corresponding to *Rf* 0.60 was eluted with AcOEt and recrystallization of the eluate from acetone-hexane gave XIa (40 mg) as colorless plates. mp 173—174°. $[\alpha]_D^{24}$ −3.5° (c=0.14). *Anal.* Calcd. for $C_{22}H_{35}O_4N$: C, 69.99; H, 9.35; N, 3.71. Found: C, 70.25; H, 9.37; N, 3.69. IR ν_{max}^{KBr} cm^{-1}: 1690 (C=O), 1552 (N-O). NMR (4% solution in $CDCl_3$) δ: 0.77 (3H, s, 19-CH_3), 1.26 (3H, s, 18-CH_3), 2.15 (3H, s, 21-CH_3), 2.63 (1H, d, J=10 cps, 17β-H), 3.55 (1H, m, 3α-H), 4.22 (2H, d, J=7 cps, 16β-CH_2NO_2). ORD (c=0.19, MeOH) $[\alpha]^{18}$ (mμ): +61° (390), 0° (384), −1271° (309) (trough), 0° (293), +2654° (264) (peak). The adsorbent of the zone corresponding to *Rf* 0.70 was eluted with AcOEt. Recrystallization of the eluate from acetone-hexane gave unchanged VIIa (52 mg) as colorless leaflets.

3β-Acetoxy-16β-nitromethyl-5α,14β,17α-pregnan-20-one (XIb)——Usual treatment of XIa with Ac_2O and pyridine followed by recrystallization from acetone-hexane gave XIb as colorless plates. mp 167—168°. $[\alpha]_D^{24}$ −5.1° (c=0.10). *Anal.* Calcd. for $C_{24}H_{37}O_5N$: C, 68.70; H, 8.89; N, 3.34. Found: C, 68.86;

H, 8.82; N, 3.78. NMR (4% solution in $CDCl_3$) δ: 0.79 (3H, s, 19-CH_3), 1.26 (3H, s, 18-CH_3), 2.00 (3H, s, 3β-$OCOCH_3$), 2.15 (3H, s, 21-CH_3), 2.63 (1H, d, $J=10$ cps, 17β-H), 4.22 (2H, d, $J=7$ cps, 16β-CH_2NO_2), 4.65 (1H, m, 3α-H).

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