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Synthesis of 14,15-Epoxyandrostan-17β-yl-isoxazoles and -pyrazoles[1]

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As the key intermediates leading to the titled compounds 17β-(5-isoxazolyl)androst-14-ene(IIb) and 17β-(3-pyrazolyl)androst-14-ene(VIa) were prepared from 20-ethoxy-21-formyl-17β-pregna-14,20-diene (Ib) with hydroxylamine and hydrazine hydrate, respectively. Epoxidation of IIb with monoperphthalic acid did take place from the α-side of the Δ^{14}-double bond to yield the 14α,15α-oxido compounds (III). Reaction with N-bromoacetamide followed by treatment with alumina resulted in formation of the epimeric β-epoxides (V). Similar elaborations with the 17β-(3-pyrazolyl)-Δ^{14}-steroid gave the epimeric 14,15-epoxides (VII, IX) with success, when VIa was previously converted into the N-acetate (VIb).

As a part of our program dealing with the studies on cardiotonic steroid analogs we have previously reported the synthesis of 17-(5-isoxazolyl)-16-methyl-14,17-*cis*-androst-5-ene and 17-(3-pyrazolyl)-16-methyl-14,17-*cis*-androst-5-ene.[1] Further interest in structure–activity relationship prompted us to prepare the titled compounds including the 17β-substituted 14β, 15β-oxido steroids which fulfill the stereochemical requirements at C-14 and C-17 essential for physiological activity.[3]

The initial project was focused to the preparation of the isoxazole derivatives employing 20-ethoxy-21-formylpregna-14,20-diene (Ib) derivable from the corresponding pregn-14-en-20-one.[4] When Ib was refluxed with hydroxylamine the ring–closure did take place with ease to provide solely 17β-(5-isoxazolyl)-3β-acetoxy-5α-androst-14-en (IIb) in satisfactory yield. The mode of ring formation, namely the attached position of the isoxazole ring to the steroid nucleus, was confirmed by inspection of the ring protons in nuclear magnetic resonance (NMR) spectra.[1,5] Subsequent treatment with monoperphthalic acid furnished the 14α, 15α-epoxide (IIIb) as a single product, where the reagent would attack the Δ^{14}-double bond from the less-hindered α-side of the molecule. On the other hand the epimeric β-epoxide was synthesized starting from the same Δ^{14}-unsaturated compound through the 14,15-halohydrin. Reaction with N-bromoacetamide in aqueous acetone resulted in formation of the *trans*-bromohydrin (IVb), which on contact with alumina was readily led to the 14β,15β-epoxide (Vb) with loss of hydrogen bromide. Upon mild hydrolysis with potassium carbonate these two epimeric 14,15-oxido acetates were transformed into the desired 3-hydroxylic compounds (IIIa, Va), respectively. Preparation of Va could be attained by an alternative reaction sequence from the unsaturated aldehyde (Ia) having a free hydroxylic group at C-3. Treatment with hydroxylamine gave 17β-(5-isoxazolyl)androst-14-ene (IIa), which was then led to the β-epoxide by way of the corresponding bromohydrin (IVa).

1) This paper constitutes Part VI of the series entitled "Studies on Cardiotonic Steroid Analogs"; Part V: S. Goya, K. Shimada, J. Goto, S. Usuda, and T. Nambara, *Yakugaku Zasshi*, **90**, 537 (1970).
2) Location: *Aobayama, Sendai.*
3) Ch. Tamm, "Proceeding of the 1st International Pharmacological Meeting," Vol. 3, ed. by W. Wilbrandt, Pergamon Press, Oxford, 1963, p. 11; T. Shigei, M. Katori, H. Murase, and S. Imai, *Experientia*, **20**, 572 (1967); S. Imai, H. Murase, M. Katori, M. Okada, and T. Shigei, *Jap. J. Pharmacol.*, **15**, 62 (1965); T. Shigei and S. Mineshita, *Experientia*, **24**, 466 (1968).
4) T. Nambara, K. Shimada, and S. Goya, *Chem. Pharm. Bull.* (Tokyo), **18**, 453 (1970).
5) N.J. Doorenbos and L. Milewich, *J. Org. Chem.*, **31**, 3193 (1966).

Configuration of the oxido ring of the above-mentioned compounds was tentatively deduced from the analogous reactions involving the Δ^{14}-double bond of the 17β-substituted steroid.[6] These assignments were supported by the NMR spectral evidences. It is sufficiently substantiated that as for the two epimeric 14,15-oxido compounds the 18-methyl proton of the α-epoxide resonates at higher field than that of the β-epimer.[7]

The second project was directed to the preparation of the pyrazole derivatives. Condensation of Ib with hydrazine hydrate proceeded in a similar fashion as with hydroxylamine

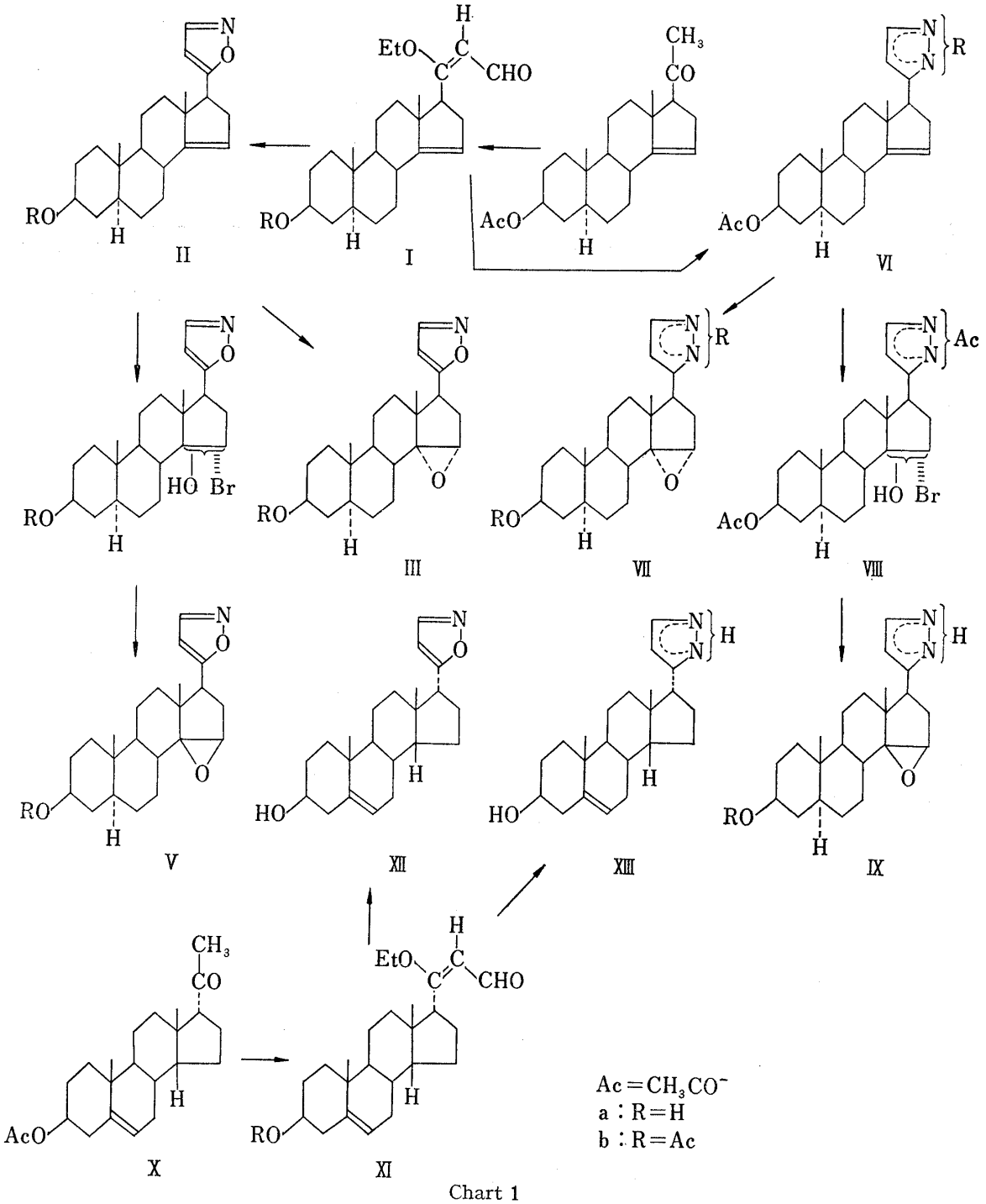

Chart 1

6) H. Ishii, *Chem. Pharm. Bull.* (Tokyo), **10**, 354 (1962); H. Hasegawa, Y. Sato, and K. Tsuda, *ibid.*, **11**, 1275 (1963).
7) K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964).

to give the 17β-(3-pyrazolyl)-Δ^{14}-steroid (VIa) as was expected. However, difficulties were encountered in the subsequent step involving epoxidation of the Δ^{14}-double bond. Being exposed to per-acid under usual conditions, VIa underwent disturbance in the pyrazole moiety yielding somewhat polar substances. The unfavorable side-reactions could be overcome with success when VIa was transformed into the pyrazole N-acetyl derivative (VIb) with the lower basicity. Thus epoxidation with monoperphthalic acid proceeded readily to give the α-epoxide (VIIb), which in turn was led to desired 17β-(3-pyrazolyl)-14α,15α-epoxyandrostane (VIIa) by alkaline hydrolysis. Reaction of VIa with hypobromous acid was again accompanied with formation of undesirable by-products, which was similarly resolved by use of the N-acetate (VIb). Treatment of VIb with N-bromoacetamide gave the 14,15-bromohydrin (VIII), which was in turn passed through an alumina column[8] to yield the β-epoxide (IXb) with simultaneous loss of hydrogen bromide and N-acetyl group. Alkaline hydrolysis under mild conditions gave finally 17β-(3-pyrazolyl)-14β,15β-epoxyandrostane (IXa) in reasonable yield.

In order to compare the biological activity the synthesis of the 17α-substituted 14β-androstane derivatives was then carried out. In the manner as mentioned above 14β,17α-pregn-5-en-20-one (X) was first converted into corresponding 20-ethoxy-21-formyl-14β,17α-pregna-5,20-diene (XIa, b) without epimerization at C-17.[9] Condensation of the unsaturated aldehyde with hydroxylamine and hydrazine gave 17α-(5-isoxazolyl)-14β-androst-5-ene and 17α-(3-pyrazolyl)-14β-androst-5-ene (XII, XIII), respectively.

Recently, Mineshita, *et al.* reported that the furanosteroids, in which the furan ring is linked to C-17 of the steroid nucleus with 3-position, exhibit the cardiotonic activity to almost the same degree as the cardenolides.[10] This finding is of particular interest in suggesting that the unsaturated lactone ring at C-17 is not necessarily essential for physiological potency and can be substituted by the isosteric hetero ring. It is hoped that the 14,17-*cis*-steroids thus prepared may also possess the cardiotonic activity and in addition the result of biological assay may throw light on the significance of oxygen atom attached to C-21.

Experimental[11]

17β-(5-Isoxazolyl)-3β-acetoxy-5α-androst-14-ene (IIb)——To a solution of 3β-acetoxy-20-ethoxy-21-formyl-5α,17β-pregna-14,20-diene (Ib) (150 mg) in AcOH (5 ml) were added $NH_2OH \cdot HCl$ (50 mg) and AcONa (150 mg) and the resulting solution was allowed to stand at 70° for 1.5 hr. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with 5% $NaHCO_3$, H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (10:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.33) was eluted with AcOEt. Recrystallization of the eluate from MeOH gave IIb (80 mg) as colorless prisms. mp 107—109°. $[\alpha]_D^{18}$ 0° (c=0.11). *Anal.* Calcd. for $C_{24}H_{33}O_3N$: C, 75.16; H, 8.67; N, 3.65. Found: C, 74.94; H, 8.70; N, 3.73. NMR (4% solution in $CDCl_3$) δ: 0.65 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 1.92 (3H, s, 3β-OCOCH_3), 4.55 (1H, m, 3α-H), 5.15 (1H, m, 15-H), 5.87 (1H, m, 4′-H), 7.95 (1H, d, J=3 cps, 3′-H).

17β-(5-Isoxazolyl)-3β-hydroxy-5α-androst-14-ene (IIa)——A solution of Ia (150 mg) in AcOH (3 ml) was treated with $NH_2OH \cdot HCl$ (50 mg) and AcONa (60 mg) in the same manner as described in IIb. The crude product obtained was submitted to the preparative TLC using benzene–AcOEt (4:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.50) was eluted with AcOEt. Recrystallization of the eluate from MeOH gave IIa (130 mg) as colorless leaflets. mp 178—179°. $[\alpha]_D^{19}$ +29.5° (c=0.10). *Anal.* Calcd. for $C_{22}H_{31}O_2N$: C, 77.37; H, 9.15; N, 4.10. Found: C, 77.19; H, 9.21; N, 4.35. NMR (4% solution in $CDCl_3$) δ: 0.70 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 3.50 (1H, m, 3α-H), 5.25 (1H, m, 15-H), 6.05 (1H, m, 4′-H), 8.15 (1H, d, J=2 cps, 3′-H).

8) P. Hofer, H. Linde, and K. Meyer, *Helv. Chim. Acta*, **45**, 1041 (1962).
9) T. Nambara, K. Shimada, and S. Goya, *Chem. Pharm. Bull.* (Tokyo), **18**, 617 (1970).
10) T. Mineshita, R. Hirota, S. Kimoto, M. Uno, and Y. Uemura, *Ann. Rept. Shionogi Res. Lab.*, **18**, 94 (1968).
11) All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ unless otherwise specified. NMR spectra were obtained on Hitachi Model H-60 spectrometer at 60 Mc using tetramethylsilane as an internal standard. Abbreviation used s=singlet, d=doublet, and m=multiplet.

17β-(5-Isoxazolyl)-3β-acetoxy-14α,15α-epoxy-5α-androstane (IIIb)——To a solution of IIb (34 mg) in ether (2 ml) was added an ethereal solution of monoperphthalic acid (20 mg/ml, 1 ml) and the resulting solution was allowed to stand at 4° for 24 hr. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was washed with 5% $Na_2S_2O_3$, H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (9:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.30) was eluted with AcOEt. Recrystallization of the eluate from AcOEt gave IIIb (12 mg) as colorless prisms. mp 176—177°. $[\alpha]_D^{22}$ +20.0° (c=0.15). *Anal.* Calcd. for $C_{24}H_{33}O_4N$: C, 72.15; H, 8.33; N, 3.51. Found: C, 72.50; H, 8.47; N, 3.43. NMR (4% solution in $CDCl_3$) δ: 0.63 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 1.98 (3H, s, 3β-$OCOCH_3$), 3.49 (1H, s, 15β-H), 4.65 (1H, m, 3α-H), 5.86 (1H, m, 4′-H), 8.06 (1H, d, J=3 cps, 3′-H).

17β-(5-Isoxazolyl)-3β-hydroxy-14α,15α-epoxy-5α-androstane (IIIa)——To a solution of IIIb (30 mg) in MeOH (5 ml) was added 5% K_2CO_3 (1 ml) and the resulting solution was allowed to stand at room temperature for 5 hr. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (4:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.33) was eluted with AcOEt. Recrystallization of the eluate from MeOH gave IIIa (20 mg) as colorless prisms. mp 181—183°. $[\alpha]_D^{19}$ +27.9° (c=0.14). *Anal.* Calcd. for $C_{22}H_{31}O_3N$: C, 73.91; H, 8.74; N, 3.92. Found: C, 74.19; H, 8.90; N, 3.85. NMR (4% solution in $CDCl_3$) δ: 0.65 (3H, s, 18-CH_3), 0.83 (3H, s, 19-CH_3), 3.52 (1H, s, 15β-H), 3.52 (1H, m, 3α-H), 5.92 (1H, m, 4′-H), 8.12 (1H, m, 3′-H).

17β-(5-Isoxazolyl)-3β-acetoxy-14β,15β-epoxy-5α-androstane (Vb)——To a solution of IIb (50 mg) dissolved in acetone (5 ml) and H_2O (1 ml) was added N-bromoacetamide (20 mg) and stirred for 2 hr at room temperature. The reaction mixture was extracted with ether and washed with 5% Na_2SO_3, H_2O and dried over anhydrous Na_2SO_4. The crude bromohydrin (IVb) (50 mg) thus obtained was chromatographed on Al_2O_3 (500 mg). The eluates with benzene–AcOEt (1:1) were collected and submitted to the preparative TLC using benzene–AcOEt (9:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.30) was eluted with AcOEt–acetone (1:1) and recrystallization of the eluate from MeOH gave Vb (12 mg) as colorless leaflets. mp 240—243°. $[\alpha]_D^{17}$ 0° (c=0.13). *Anal.* Calcd. for $C_{24}H_{33}O_4N$: C, 72.15; H, 8.33; N, 3.51. Found: C, 72.05; H, 8.39; N, 3.61. NMR (4% solution in $CDCl_3$) δ: 0.80 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 2.00 (3H, s, 3β-$OCOCH_3$), 3.55 (1H, s, 15α-H), 4.60 (1H, m, 3α-H), 6.15 (1H, d, J=3 cps, 4′-H), 8.10 (1H, m, 3′-H).

17β-(5-Isoxazolyl)-3β-hydroxy-14β,15β-epoxy-5α-androstane (Va)——i) In the same manner as described in Vb, IIa (45 mg) was treated with N-bromoacetamide (21 mg). The crude bromohydrin (IVa) (40 mg) thus obtained was chromatographed on Al_2O_3 (300 mg). The eluates with AcOEt were collected and submitted to the preparative TLC using benzene–AcOEt (4:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.33) was eluted with AcOEt. Recrystallization of the eluate from acetone gave Va (20 mg) as colorless leaflets. mp 200—202°. $[\alpha]_D^{16}$ 0° (c=0.15). *Anal.* Calcd. for $C_{22}H_{31}O_3N$: C, 73.91; H, 8.74; N, 3.92. Found: C, 74.04; H, 8.70; N, 3.88. NMR (4% solution in CCl_4) δ: 0.80 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 3.55 (1H, s, 15α-H), 3.55 (1H, m, 3α-H), 6.15 (1H, d, J=3 cps, 4′-H), 8.11 (1H, d, J=3 cps, 3′-H).

ii) In the same manner as described in IIIa, Vb (30 mg) was treated with K_2CO_3 in aq. MeOH. On usual work-up the crude product obtained was submitted to the preparative TLC using benzene–AcOEt (4:1) as developing solvent. The corresponding spot was eluted with AcOEt and recrystallization of the eluate from acetone gave Va (20 mg) as colorless leaflets. mp 200—202°. Mixed mp measurement on admixture with the sampled obtained in i) and physical data comparison showed the identity of two samples.

17β-(3-Pyrazolyl)-3β-acetoxy-5α-androst-14-ene (VIa)——To a solution of Ib (50 mg) in AcOH (3 ml) was added $NH_2NH_2 \cdot H_2O$ (20 mg), and the resulting solution was allowed to stand at 70° for 1.5 hr. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with 5% $NaHCO_3$, H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (9:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.33) was eluted with AcOEt. Recrystallization of the eluate from acetone gave VIa (30 mg) as colorless prisms. mp 178°. $[\alpha]_D^{22}$ −14.4° (c=0.10). *Anal.* Calcd. for $C_{24}H_{34}O_2N_2$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.46; H, 9.07; N, 7.63. NMR (4% solution in CCl_4) δ: 0.63 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 1.95 (3H, s, 3β-$OCOCH_3$), 4.55 (1H, m, 3α-H), 6.17 (1H, m, 15-H), 5.95 (1H, m, 4′-H), 7.35 (1H, m, 5′-H).

17β-(3-Pyrazolyl)-3β-acetoxy-5α-androst-14-ene N-Acetate (VIb)——A solution of VIa (70 mg) in pyridine (2 ml) and Ac_2O (1 ml) was heated at 80° for 30 min. The resulting solution was diluted with ether, washed with 5% HCl, 5% $NaHCO_3$ and H_2O, and dried over anhydrous Na_2SO_4. On usual work-up the yellow product obtained was not crystallized and therefore submitted to further elaboration without purification. NMR (4% solution in $CDCl_3$) δ: 0.65 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 1.95 (3H, s, 3β-$OCOCH_3$), 2.62 (3H, s, N–$COCH_3$), 4.60 (1H, m, 3α-H), 5.20 (1H, m, 15-H), 6.17 (1H, d, J=3 cps, 4′-H), 8.07 (1H, d, J=3 cps, 5′-H).

17β-(3-Pyrazolyl)-3β-acetoxy-14α,15α-epoxy-5α-androstane N-Acetate (VIIb)——In the same manner as described in IIIb, VIb (49 mg) was treated with monoperphthalic acid (25 mg). On usual work-up the yellow oily product obtained was submitted to further elaboration without purification. NMR (4% solution in $CDCl_3$) δ: 0.59 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 1.95 (3H, s, 3β-$OCOCH_3$), 2.60 (3H, s, N-$COCH_3$), 3.38 (1H, s, 15β-H), 4.60 (1H, m, 3α-H), 6.08 (1H, d, J=3 cps, 4′-H), 8.05 (1H, d, J=3 cps, 5′-H).

17β-(3-Pyrazolyl)-3β-hydroxy-14α,15α-epoxy-5α-androstane (VIIa)——To a solution of VIIb (45 mg) in MeOH (5 ml) was added 5% K_2CO_3 (1 ml) and the resulting solution was refluxed for 1 hr. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (3:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.20) was eluted with AcOEt. Recrystallization of the eluate from acetone gave VIIa (20 mg) as colorless prisms. mp 198—200°. $[\alpha]_D^{16}$ −11.1° (c=0.09). *Anal.* Calcd. for $C_{22}H_{32}O_2N_2$: C, 74.12; H, 9.05; N, 7.86. Found: C, 74.07; H, 9.29; N, 8.05. NMR (4% solution in $CDCl_3$) δ: 0.60 (3H, s, 18-CH_3), 0.80 (3H, s, 19-CH_3), 3.50 (1H, s, 15β-H), 3.50 (1H, m, 3α-H,), 6.00 (1H, d, J=3 cps, 4′-H), 6.55 (1H,m, N-H), 7.45 (1H, d, J=3 cps, 5′-H).

17β-(3-Pyrazolyl)-3β-acetoxy-14β,15β-epoxy-5α-androstane (IXb)——In the same manner as described in IVb, VIb (50 mg) was treated with N-bromoacetamide (20 mg). The crude bromohydrin (VIII) (50 mg) was chromatographed on Al_2O_3 (500 mg). The eluates with AcOEt were collected and submitted to the preparative TLC using benzene–AcOEt (7:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.20) was eluted with AcOEt. On usual work-up IXb (30 mg) was obtained as yellow oily product. NMR (4% solution in CCl_4) δ: 0.70 (3H, s, 18-CH_3), 0.87 (3H,s, 19-CH_3), 1.95 (3H, s, 3β-$OCOCH_3$), 3.47 (1H, s, 15α-H), 4.60 (1H, m, 3α-H), 5.80 (1H, m, 4′-H), 7.21 (1H, m, 5′-H), 9.10 (1H, m, N-H).

17β-(3-Pyrazolyl)-3β-hydroxy-14β,15β-epoxy-5α-androstane (IXa)——In the same manner as described in VIIa, IXb (45 mg) was treated with K_2CO_3 in aq. MeOH. On usual work-up the residue obtained was submitted to the preparative TLC using benzene–AcOEt (3:1) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.20) was eluted with AcOEt. Recrystallization of the eluate from MeOH gave IXa (20 mg) as colorless leaflets. mp 232°. $[\alpha]_D^{16}$ +25.7° (c=0.27). *Anal.* Calcd. for $C_{22}H_{32}O_2N_2$: C, 74.12; H, 9.05; N, 7.86. Found: C, 73.96; H, 8.98; N, 7.76. NMR (4% solution in $CDCl_3$) δ: 0.73 (3H, s, 18-CH_3), 0.85 (3H, s, 19-CH_3), 3.56 (1H, s, 15α-H), 3.56 (1H, m, 3α-H), 5.50 (1H, m, N-H), 5.98 (1H, m, 4′-H), 7,40 (1H, m, 5′-H).

3β-Acetoxy-20-ethoxy-21-formyl-14β,17α-pregna-5,20-diene (XIb)——To a solution of 3β-acetoxy-14β, 17α-pregn-5-en-20-one (X)[12] (300 mg) in ethyl orthoformate (5 ml) was added a few drops of 70% $HClO_4$ dropwise under ice-cooling over a period of 20 min. After addition of several drops of pyridine to decompose the perchlorate, the resulting solution was extracted with ether. The organic layer was washed with cold 5% HCl, 5% $NaHCO_3$ and H_2O, successively. On usual work-up the crude product obtained was recrystallized from MeOH to give XIb (200 mg) as colorless prisms. mp 168—170°. $[\alpha]_D^{24}$ +124.9° (c=0.16). *Anal.* Calcd. for $C_{26}H_{38}O_4$: C, 75.32; H, 9.24. Found: C, 75.13; H, 9.04.

3β-Hydroxy-20-ethoxy-21-formyl-14β,17α-pregna-5,20-diene (XIa)——To a solution of XIb (200 mg) in MeOH (10 ml) was added 5% K_2CO_3 (2 ml) and the resulting solution was refluxed for 1 hr. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4. On usual work-up the yellow product obtained was not crystallized and therefore submitted to further elaboration without purification.

17α-(5-Isoxazolyl)-3β-hydroxy-14β-androst-5-ene (XII)——A solution of XIa (150 mg) in AcOH (3 ml) was treated with $NH_2OH \cdot HCl$ (50 mg) and AcONa (60 mg) in the same manner as described in IIb. The crude product obtained was submitted to the preparative TLC using benzene–AcOEt (3:2) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.67) was eluted with AcOEt. Recrystallization of the eluate from MeOH gave XII (120 mg) as colorless needles. mp 198—200°. $[\alpha]_D^{27}$ +34.8° (c=0.10). *Anal.* Calcd. for $C_{22}H_{31}O_2N$: C, 77.37: H, 9.15: N, 4.10. Found: C, 77.59; H, 9.27; N, 4.08. NMR (4% solution in $CDCl_3$) δ: 0.98 (3H, s, 19-CH_3), 1.08 (3H, s, 18-CH_3), 3.50 (1H, m, 3α-H), 5.40(1H, m, 6-H), 5.98 (1H, d, J=3 cps, 4′-H), 8.12 (1H, d, J=3 cps, 3′-H).

17α-(3-Pyrazolyl)-3β-hydroxy-14β-androst-5-ene (XIII)——A solution of XIa (150 mg) in AcOH (3 ml) was treated with $NH_2NH_2 \cdot H_2O$ (1 ml) in the same manner as described in VIa. The crude product obtained was submitted to the preparative TLC using benzene–AcOEt (3:2) as developing solvent. The adsorbent corresponding to the spot (*Rf* 0.17) was eluted with AcOEt. Recrystallization of the eluate from acetone gave XIII (120 mg) as Colorless leaflets. mp 237—240°. $[\alpha]_D^{27}$ +57.7° (c=0.17). *Anal.* Calcd. for $C_{22}H_{32}ON_2$: C, 77.60; H, 9.47; N, 8.23. Found: C, 77.66; H, 9.61; N, 8.30.

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12) Pl.A. Plattner, H. Heusser, and A. Segre, *Helv. Chim. Acta*, 31, 249 (1948).