EXPERIMENTAL WORK

The melting points reported are uncorrected. Most of the elemental and spectral analyses were performed through Professor W. B. Whalley, University of London. Some of the elemental and optical rotations were performed by Dr. F. B. Strauss, Microanalytical Laboratories, Oxford, U.K., Central Drug Research Institute, Lucknow, and Australian Microanalytical Services CSIRO, University of Melbourne. The optical rotations were measured in chloroform. Plates for TLC were prepared with silica gel G acc. to Stahl (E. Merck) and activated at 110°C for 30 min. The plates were developed by exposure to iodine vapours. Thionyl chloride and dioxan were purified before use. Anhydrous sodium sulphate was utilised as drying agent.

17-OXIMINO-5-ANDROSTEN-3ß-YL ACETATE (11)

A solution of sodium acetate trihydrate (31.0 g) and hydroxylamine hydrochloride (12.3 g) in water (150 ml) was added to a refluxing solution of 17-oxo-5-androsten-3ß-yl acetate (10) (12.5 g) in aldehyde free ethancl (385 ml).
After 4 hr, the refluxing solution was gradually diluted with water (385 ml) and allowed to cool. The separated crystals were filtered, washed with 30% aqueous ethanol (60 ml), and allowed to dry. The product so obtained was crystallised (MeOH); yield 12.8 g (98%), mp 183-184° (lit93 162-163°, dil MeOH).

17-OXO-17a-AZA-D-HOMO-5-ANDROSTEN-3β-YL ACETATE (12)

A mixture of thionyl chloride (10 ml) and dioxan (50 ml) was added dropwise to a stirred solution of 17-oximino-5-androsten-3β-yl acetate (11) (20.0 g) in thiophene-free benzene (350 ml) at 15°. The reaction mixture was stirred for further 15 min at 20°. Water (45 ml) was added to the cooled reaction mixture which was then basified by addition of dilute solution of ammonia (90 ml). The organic layer was separated and the aqueous part extracted with chloroform (4 x 50 ml). The combined organic layer was washed with water, dried, and the solvent removed under reduced pressure. The brownish semi-crystalline residue obtained was crystallised (MeOH); yield 12.8 g (64%), mp 292-293° (lit65 289-292°).

3β-HYDROXY-17a-AZA-D-HOMO-5-ANDROSTEN-17-ONE (13)

A solution of 17-oxo-17a-aza-D-homo-5-androsten-3β-yl acetate (12) (11.0 g) in methanol (165 ml) containing potassium hydroxide (2.3 g) was refluxed for 70 min. The reaction mixture was acidified with glacial acetic acid (2.3 ml) and concentrated to induce crystallisation. The separated crystals were washed
with 40% aqueous methanol (45 ml) and crystallised (MeOH); yield 9.6 g (99.7%), mp 295-298°C (lit65 295-297°C).

**Anal.:**

IR (KBr): 3400, 3250, 1660 and 1650 cm⁻¹

Calcd for C₁₉H₂₉NO₂: C, 75.20; H, 9.63; N, 4.62. Found: C, 74.61; H, 9.45; N, 4.55.

17a-AZA-D-HOMO-4-ANDROSTENE-3,17-DIONE (14)

A solution of 3β-hydroxy-17a-aza-D-homo-5-androsten-17-one (13) (7.2 g) in cyclohexanone (72 ml), dioxan (300 ml) and dry toluene (255 ml), was slowly distilled as a solution of aluminium iso-propoxide (7.2 g) in toluene (36 ml) was added gradually. Distillation was continued for 2 hr as more toluene (180 ml) was added and 480 ml of the distillate collected. The reaction mixture was then refluxed for 4 hr, allowed to stand overnight at room temperature and filtered. The filtrate was steam-distilled until complete removal of organic solvents was effected. The aqueous suspension was extracted with chloroform (4 x 50 ml). The combined chloroform extracts were washed with water, dried, and the solvent removed under reduced pressure. The light yellow semicrystalline residue was crystallised (EtOAc); yield 5.7 g (79.7%), mp 262-264°C (lit⁶₅ 261-263°C).

**Anal.:**

UV max (MeOH): 240 nm (ε 16,200) (lit⁶₅ 240 nm, ε 16,600).

Calcd for C₁₉H₂₇NÖ₂: C, 75.75; H, 8.97; N, 4.65. Found: C, 75.72; H, 9.09; N, 4.49.
A solution of potassium carbonate (3.38 g) in water (96 ml) was added to a vigorously stirred solution of 17α-aza-D-homo-4-androstene-3,17-dione (14) (4.7 g) in 90% aqueous tert-butanol (360 ml), immediately followed by addition of sodium metaperiodate solution (65 ml; 24 g in 300 ml water) and then potassium permanganate solution (6 ml; 0.8%). Stirring of the mixture was continued and the periodate solution was added at the rate of 13 ml/min during the first 10 min and 3.5 ml/min during the next 30 min. The potassium permanganate solution was added when necessary to maintain the purple colour. The mixture was stirred for another 2 hr, treated with sodium metabisulphite to complete disappearance of purple colour, acidified with ice-cold 50% sulphuric acid, diluted with water (150 ml), and extracted with chloroform (8 x 100 ml). The chloroform extract was washed with sodium metabisulphite solution (120 ml; 5%) and water (3 x 100 ml), dried, and the solvent removed under reduced pressure to give white fluffy residue. This was taken in potassium hydroxide solution (50 ml; 10%); washed with solvent ether, and filtered. The clear solution was acidified with cold 10% sulphuric acid. The separated fine needles were filtered, washed with water, dried in a vacuum desiccator, and crystalised (MeOH); yield 3.8 g (79.5%), mp 266-268° (lit63 266-267°).
Anal.

IR (KBr): 3258, 1710, 1692, 1687 and 1605 cm$^{-1}$
Calcd for C$_{18}$H$_{27}$N$_2$O$_4$: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.16; H, 8.72; N, 4.63.

5-OXIMINO-17-OXO-17a-AZA-D-HOMO-3,5-SECO-4-NORANDROSTAN-3-OIC ACID (16)

A mixture of 5,17-dioxo-17a-aza-D-homo-3,5-seco-4-norandrostane-3-oic acid (15) (1.0 g), hydroxylamine hydrochloride (0.45 g) and potassium hydroxide (1.4 g) in ethanol (45 ml) and water (30 ml), was refluxed for 2 hr. After acidification with glacial acetic acid, the solution was concentrated in vacuum to about half of the volume and diluted with water (100 ml). The separated fine needles were filtered and dried. The product was crystallised (MeOH); yield 0.85 g (80.7%), mp 245-247° (lit$^6$ 247-248°).

Anal.

IR (KBr): 3460, 3208, 1700 and 1640 cm$^{-1}$
Calcd for C$_{18}$H$_{28}$N$_2$O$_4$: C, 64.26; H, 8.39; N, 8.33. Found: C, 64.03; H, 7.92; N, 8.72.

4,17a-DIAZA-D-HOMO-5α-ANDROSTANE-3,17-DIONE (9)

Strong solution of ammonia was added dropwise to formic acid (3 ml; 98%) till the mixture just became alkaline. A suspension of 5,17-dioxo-17a-aza-D-homo-3,5-seco-4-norandrostane-3-oic acid (15) (2.0 g) in nitrobenzene (10 ml) was added to
the ammonium formate solution, previously brought to 165° in
an oil bath. The reaction mixture was occasionally stirred
during 20 hr at 180-200°, cooled, washed gently with water,
added ethanol (20 ml) and concentrated hydrochloric acid (5 ml),
and refluxed the mixture for 2 hr. It was steam-distilled to
remove nitrobenzene. The residual part was extracted with
chloroform (8 x 50 ml). The combined organic layer was washed
with 2% sodium carbonate solution and water, and dried. The
solvent was distilled to leave an amorphous residue which was
crystallised (CHCl₃-Me₂CO); yield 0.6 g (31%), mp >330°.

Anal.:  
IR (KBr): 3175 and 1655 cm⁻¹  
Calcd for C₁₈H₂₈N₂O₂: C, 71.01; H, 9.27; N, 9.20. Found:  
C, 71.12; H, 9.38; N, 9.11.

4,17a-DIAZA-D-HOMO-5α-ANDROSTANE (17)

PROCEDURE A

Sodium metal (1.2 g) was added in small portions to a
refluxing solution of 4,17a-diaza-D-homo-5α-androstane-3,17-
dione (9) (0.15 g) in 1-pentanol (24 ml). The mixture was
refluxed till the sodium metal had reacted, cooled to room
temperature, and water (20 ml) was added. The solvent was
removed by steam distillation and residual part extracted with
chloroform (5 x 25 ml). The organic layer was washed with
water and dried. The solvent was removed to leave a solid
residue, which was crystallised (Me₂CO); yield 0.07 g (51%),
mp 174-175°.

Anal.:
IR (KBr): 3285 cm⁻¹
[α]D⁰ + 10.13° (c 1.23)
Calcd for C₁₈H₃₂N₂: C, 78.20; H, 11.67; N, 10.13. Found: C, 77.99; H, 11.78; N, 10.22.

PROCEDURE B

Sodium metal (12.0 g) was added slowly to a refluxing solution of 5-oximino-17-oxo-17a-aza-D-homo-5,5-seco-4-nor-androstan-3-cic acid (16) (1.2 g) in 1-pentanol (300 ml). The refluxing was continued till sodium metal had completely reacted. The reaction mixture was cooled to room temperature, water (50 ml) was added, and the mixture steam-distilled to remove pentanol. The residual solution was cooled, the separated material filtered, washed with water, and dried. It was picked up with hot acetone, filtered and allowed to crystallise. Recrystallised (Me₂CO); yield 0.55 g (56%), mp 174-175°.

Anal.:
IR (KBr): 3285 cm⁻¹
Calcd for C₁₈H₃₂N₂: C, 78.20; H, 11.67; N, 10.13. Found: C, 78.05; H, 11.75; N, 10.49.

4,17a-DIMETHYL-4,17a-DIAZA-D-HOMO-5α-ANDROSTANE (18)

A mixture of formic acid (6 ml), formalin (6 ml) and 4,17a-diaza-D-homo-5α-androstan-3-one (17) (0.1 g) was refluxed for
8 hr. The reaction mixture was cooled, poured into ice-cold water (25 ml), and made alkaline with dilute solution of ammonia. The mixture was extracted with chloroform (4 x 25 ml). The combined chloroform layer was washed with water (25 ml), dried, and the solvent removed. The residue was crystallised (Me₂CO); yield 0.09 g (81.7%), mp 162-163°.

**Anal.:**

**IR (KBr):** 2850 cm⁻¹

**NMR (CDCl₃):** δ 0.80 (s,3H), 0.90 (s,3H), 2.14 (s,3H) and 2.18 ppm (s,3H)

[α]D²³ - 1.1° (c 0.35)

Calcd for C₁₀H₁₈N₂: C, 78.88; H, 11.92; N, 9.20. Found: C, 79.08; H, 12.07; N, 9.54.

4,17α-DIMETHYL-4,17α-DIAZA-D-HOMO-5α-ANDROSTANE DIMETHIODIDE (HS-342) (8)

Methyl iodide (0.4 ml) was added to the refluxing solution of 4,17α-dimethyl-4,17α-diaza-D-homo-5α-androstane (18) (0.1 g) in absolute ethanol (2 ml). The mixture was refluxed for 1 hr, cooled, and poured into dry solvent ether (50 ml). The precipitated yellow material was filtered and crystallised (MeOH-Me₂CO); yield 0.16 g (82.7%), mp 293-295°.

**Anal.:**

Calcd for C₂₂H₄₂I₂N₂: I, 43.19; N, 4.76. Found: I, 42.69; N, 4.69.
PROCEDURE A

A solution of 17-oxo-17a-aza-D-homo-5-androsten-3β-yl acetate (12) (3.0 g) in dioxan (200 ml) was added to the refluxing suspension of lithium aluminium hydride (1.0 g) in dioxan (100 ml). The refluxing was continued for 48 hr, water (6 ml) added carefully, and refluxed for further 1 hr. The reaction mixture was filtered while hot and solvent removed under reduced pressure. The residue was taken in 20% hydrochloric acid and filtered. The filtrate was made alkaline with 20% sodium hydroxide solution, and the precipitate filtered. The product was crystallised (MeOH); yield 1.7 g (67.6%), mp 231-233° (lit65 231-233°).

Anal.:
IR (KBr): 3400, 3250, 1680 cm⁻¹
[α]D²⁵ = 98.6° (c 2.0)
Calcd for C₁₉H₃₁NO: N, 4.84. Found: N, 4.52.

PROCEDURE B

Sodium metal (6.0 g) was added slowly to the refluxing solution of 17-oxo-17a-aza-D-homo-5-androsten-3β-yl acetate (12) (1.5 g) in 1-pentanol (120 ml). The reaction mixture was refluxed till the sodium metal had reacted, cooled to room temperature, and diluted with water (50 ml). Solvent was steam-distilled and solid residue filtered. The product
was taken in 20% hydrochloric acid, filtered, and made alkaline with 20% sodium hydroxide solution. The resultant precipitate was filtered and crystallised (MeOH); yield 0.85 g (67.6%), mp 232-233° (lit65 231-233°).

**Anal.:**
IR (KBr): 3400, 3250 and 1680 cm⁻¹
Calcd for C₁₉H₃₁NO: N, 4.84. Found: N, 4.30.

17α-METHYL-17α-AZA-D-HOMO-5-ANDROSTEN-3ß-OL (21)

A mixture of formalin (36 ml), formic acid (36 ml) and 17α-aza-D-homo-5-androsten-3ß-ol (20) (1.2 g) was refluxed for 6 hr. The reaction mixture was cooled, diluted with water (100 ml), made alkaline with dilute ammonia, and extracted with chloroform (3 x 50 ml). The chloroform layer was washed with water, dried, and solvent removed to leave a solid residue. The product was crystallised (Me₂CO); yield 0.62 g (49.3%), mp 172-174°.

**Anal.:**
IR (KBr): 3250, 2900, 2820 and 2730 cm⁻¹
NMR (CDCl₃): δ 0.83 (s, 3H), 0.96 (s, 3H), 2.20 (s, 3H) and 5.34 ppm (1H)
[α]D<sup>20</sup> - 64.2° (c 1.46)
Calcd for C₂₀H₃₃NO: C, 79.15; H, 10.96; N, 4.62. Found: C, 79.48; H, 11.10; N, 4.44.
17α-METHYL-17α-AZA-D-HOMO-5-ANDROSTEN-3β-YL ACETATE (22)

A mixture of acetic anhydride (0.3 ml) and 17α-methyl-17α-aza-D-homo-5-androsten-3β-ol (21) (0.3 g) was heated at 100° for 2 hr. The reaction mixture was cooled, poured into water, made alkaline with 10% potassium hydroxide solution and extracted with solvent ether (5 x 50 ml). The ether layer was washed with water, dried, and solvent removed. The material obtained was crystallised (Me₂CO); yield 0.25 g (73%), mp 140-143°.

Anal.:  
IR (KBr): 2948, 2790, 1736 and 1252 cm⁻¹  
NMR (CDCl₃): 0.82 (s, 3H), 0.97 (s, 3H), 2.01 (s, 3H), 2.20 (s, 3H) and 5.37 ppm (1H)  
Calcd for C₂₂H₃₅N₂O₂: N, 4.05. Found: N, 4.36.

17α-METHYL-17α-AZA-D-HOMO-5-ANDROSTEN-3β-OL METHIODOIDE  
(HS-308) (23)

Methyl iodide (0.1 ml) was added to the refluxing solution of 17α-methyl-17α-aza-D-homo-5-androsten-3β-ol (21) (0.1 g) in absolute ethanol (2 ml). The reaction mixture was refluxed for 0.5 hr, cooled, and poured into dry solvent ether. The precipitated yellow material was filtered, and crystallised (EtOH-EtOAc); yield 0.1 g (68%), mp 238-242°.

Anal.:  
17a-METHYL-17a-AZA-D-HOMO-5-ANDROSTEN-3β-YL ACETATE METHIODIDE (HS-433) (24)

Methyl iodide (0.2 ml) was added to the refluxing solution of 17a-methyl-17a-aza-D-homo-5-androsten-3β-yl acetate (22) (0.15 g) in dry acetone (25 ml). The reaction mixture was refluxed for 2 hr, concentrated to about 10 ml, cooled, and poured into dry solvent ether (50 ml). The precipitated material was filtered. The product was crystallised (Me₂CO); yield 0.2 g (94.4%), mp 274-276°.

Anal.:
Calcd for C₂₃H₃₈I₂N₂O₂: C, 56.67; H, 7.80; I, 26.08; N, 2.87.
Found: C, 56.94; H, 7.84; I, 26.36; N, 2.92.

17a-METHYL-17a-AZA-D-HOMO-4-ANDROSTEN-3-ONE (25)

A solution of 17a-methyl-17a-aza-D-homo-5-androsten-3β-ol (21) (0.5 g) in cyclohexanone (5 ml) and toluene (45 ml) was slowly distilled as aluminium iso-propoxide (0.5 g) in toluene (2.5 ml) was added. Distillation was continued for 0.5 hr as 10 ml of distillate was collected. The mixture was refluxed for 2.5 hr and then allowed to stand for 12 hr. It was filtered to remove an orange coloured precipitate, filtrate steam-distilled, and the residue extracted with chloroform (4 x 50 ml). The combined chloroform extracts were washed with water, dried, and solvent removed. The residue was crystallised (Me₂CO); yield 0.35 g (70.4%), mp 172-173°.
UV max (EtOH): 240 nm (ε 16,980)
IR (KBr): 2938, 2858, 2810, 2728, 1670 and 1620 cm⁻¹
NMR (CDCl₃): δ 0.87 (s, 3H), 1.15 (s, 3H), 2.20 (s, 3H) and 5.70 ppm (1H)
[α]D° + 94.2° (c 1.43)

Calcd for C₂₀H₃₁NO: C, 79.67; H, 10.37; N, 4.65. Found: C, 79.81; H, 10.87; N, 4.62.

17α-METHYL-17α-AZA-D-HOMO-4-ANDROSTEN-3-ONE METHIODIDE (HS-316) (26)

Methyl iodide (0.1 ml) was added to the refluxing solution of 17α-methyl-17α-aza-D-homo-4-androsten-3-one (25) (0.1 g) in absolute ethanol (2 ml). The reaction mixture was refluxed for 0.5 hr. The mixture was cooled, poured into dry solvent ether (50 ml), filtered, and the resulting solid material crystallised (Me₂CO); yield 0.11 g (74.7%), mp 264–265°.


3-PYRROLIDINO-17α-AZA-D-HOMO-3,5-ANDROSTADIEN-17-ONE (27)

Freshly distilled pyrrolidine (0.5 ml) was added to a well shaken boiling solution of 17α-aza-D-homo-4-androstene-3,17-dione (14) (1.2 g) in methanol (20 ml). The yellow needles which crystallised out on cooling, were filtered,
washed with methanol, and dried in a vacuum desiccator; yield 1.35 g (94.5%), mp 320-325°C; dec (lit71 320-324°C; dec).

**Anal.:**

UV max (MeOH): 275 nm (E 16,000)

Calcd for C_{23}H_{34}N_{2}O: N, 7.90. Found: N, 7.46.

3β-PYRROLIDINO-17α-AZA-D-HOMO-5-ANDROSTEN-17-ONE (28)

Sodium borohydride (2.0 g) was added to a stirred suspension of 3-pyrrolidino-17α-aza-D-homo-3,5-androstadien-17-one (27) (2.5 g) in methanol (50 ml) during 6 hr. The mixture was stirred for further 10 hr, filtered into ice-cold water (400 ml), and extracted with chloroform (6 x 50 ml). The combined organic layer was washed with water, dried, and the solvent removed under reduced pressure to leave a solid residue. The product so obtained was crystallised (MeOH-Me₂CO); yield 1.7 g (67.5%), mp 285-290°C; dec (lit71 279-283°C; dec).

**Anal.:**

IR (KBr): 3155, 3050, 2930, 2780 and 1660 cm⁻¹

NMR (CDCl₃): δ 0.99 (s, 3H), 1.16 (s, 3H), 5.32 (1H) and 6.61 ppm (1H, disappeared on deuterium exchange)

Calcd for C_{23}H_{36}N_{2}O: C, 77.50; H, 10.10; N, 7.80. Found: C, 77.74; H, 10.36; N, 7.65.

3β-PYRROLIDINO-17α-AZA-D-HOMO-5-ANDROSTEN-17-ONE METHIODIDE (HS-311) (29)

Methyl iodide (0.2 ml) was added to the refluxing solution of 3β-pyrrolidino-17α-aza-D-homo-5-androsten-17-one
(28) (0.5 g) in absolute ethanol (5 ml). The mixture was refluxed for 1 hr, cooled, poured in dry solvent ether (50 ml), and precipitate filtered. The product was crystallised (EtOH-Me$_2$CO); yield 0.45 g (64.6%), mp 317-318°.

**Anal.:**

Calcd for C$_{24}$H$_{39}$IN$_2$O: C, 57.76; H, 7.82; I, 25.47; N, 5.61.
Found: C, 57.91; H, 8.17; I, 25.08; N, 5.46.

**3p-PYRROLIDINO-17a-AZA-D-HOMO-5-ANDROSTENE (30)**

Sodium metal (4.0 g) was added slowly to the refluxing solution of 3p-pyrrolidino-17a-aza-D-homo-5-androsten-17-one (28) (1.0 g) in 1-pentanol (80 ml). The mixture was refluxed till sodium metal had completely reacted. The reaction mixture was cooled to room temperature, water (100 ml) added, and 1-pentanol removed by steam distillation. The aqueous layer was extracted with chloroform (3 x 50 ml), the chloroform part washed with water, dried, and solvent removed under reduced pressure. The residue was crystallised (Me$_2$CO); yield 0.6 g (62.4%), mp 168-172°.

**Anal.:**

IR (KBr): 3250 cm$^{-1}$

NMR (CDCl$_3$): δ 0.96 (s, 3H), 1.03 (s, 3H) and 5.31 ppm (1H)

[α]$_D^{20}$ - 67.6° (c 1.68)

Calcd for C$_{23}$H$_{38}$N$_2$: C, 80.64; H, 11.18; N, 8.18. Found: C, 80.19; H, 11.27; N, 8.38.
17a-METHYL-3g-PYRROLIDINO-17a-AZA-D-HOMO-5-ANDROSTENE (31)

A mixture of formic acid (15 ml), formalin (15 ml) and 3β-pyrrolidino-17α-aza-D-homo-5-androstene (30) (0.5 g) was refluxed for 8 hr. The reaction mixture was cooled, poured into ice-cold water (50 ml), and made alkaline with dilute ammonia. The aqueous layer was extracted with chloroform (3 x 50 ml). The chloroform layer was washed with water, dried, and solvent removed under reduced pressure. The solid residue was crystallised (Me$_2$CO); yield 0.3 g (57.6%), mp 160-164°.

Anal.:
IR (KBr): 2900 and 2760 cm$^{-1}$
NMR (CDCl$_3$): δ 0.84 (s, 3H), 0.97 (s, 3H), 2.20 (s, 3H), and 5.31 ppm (1H)
Mass: M$^+$ 356
[α]$_D^{20}$ -55.1° (c 1.34)
Calcld for C$_{24}$H$_{40}$N$_2$: C, 80.83; H, 11.31; N, 7.86. Found: C, 80.64; H, 11.42; N, 7.53.

17a-METHYL-3β-PYRROLIDINO-17a-AZA-D-HOMO-5-ANDROSTENE DIMETHIODIDE (CHANDONIUM IODIDE) (HS-310) (19)

Methyl iodide (0.2 ml) was added to boiling solution of 17α-methyl-3β-pyrrolidino-17α-aza-D-homo-5-androstene (31) (0.15 g) in absolute ethanol (2 ml). The mixture was refluxed for 10 min. The separated material was filtered, washed with dry solvent ether (25 ml) and dried. The residue was crystallised
Anal.
Calcd for C_{26}H_{46}I_{2}N_{2}: C, 48.72; H, 7.18; I, 39.65; N, 4.37.
Found: C, 48.64; H, 7.27; I, 39.30; N, 4.38.

17β-HYDROXY-5-OXO-3,5-SECO-4-NORANDROSTAN-3-OIC ACID (33)

A solution of potassium carbonate (0.56 g) in water (16 ml) was added to a vigorously stirred solution of 17β-acetoxy-4-androsten-3-one (1.0 g) in 90% aqueous tert-butanol (60 ml), immediately followed by sodium metaperiodate (10 ml; 4 g in 50 ml water) and then potassium permanganate solution (1 ml; 0.8%). Stirring of the mixture was continued and the sodium metaperiodate solution added at a rate of 2.2 ml/min during the first 10 min and 0.6 ml/min during the next 30 min. The permanganate solution was added when necessary to maintain the purple colour. The reaction mixture was stirred for another 2 hr, treated with sodium metabisulphite to complete disappearance of purple colour. The resulting mixture was concentrated to about 65 ml under reduced pressure, cooled to 4°, acidified with cold 50% sulphuric acid, and extracted with solvent ether (3 x 50 ml). The combined ether layer was washed with sodium metabisulphite solution (4%) till free from iodine, washed with water, dried, and solvent removed. The residue was picked up in 10% sodium hydroxide solution, filtered, acidified with cold 50% sulphuric acid, and extracted with solvent ether (3 x 50 ml). The combined ether extracts were washed with water, dried, and solvent removed. The residue so
obtained was crystallised (Me₂CO); yield 0.25 g (26.7%), mp 206-209° (lit 206.5-207°).

**Anal.:**

IR (KBr): 3380, 1712 and 1700 cm⁻¹

NMR (CDCl₃): ð 0.81 (s, 3H), 1.12 (s, 3H) and 4.54 ppm (1H, disappeared on deuterium exchange)

Calcd for C₁₈H₂₈O₄: C, 70.10; H, 9.15. Found: C, 69.76; H, 9.36.

17ß-HYDROXY-5-OXIMINO-3, 5-SECO-4-NORANDROSTAN-3-OIC ACID

A mixture of 17ß-hydroxy-5-oxo-3, 5-seco-4-norandrostan-3-oic acid (33) (0.2 g), potassium hydroxide (0.4 g) and hydroxylamine hydrochloride (0.12 g) in ethanol (12 ml) and water (8 ml), was refluxed for 2 hr. After acidification with glacial acetic acid, the solution was concentrated under reduced pressure, water (20 ml) added, and allowed to crystallise. The fine needles of the oxime were collected and recrystallised (EtOH-H₂O); yield 0.12 g (57.2%), mp 200-204° (lit 199-202°).

**Anal.:**

IR (KBr): 3680, 3500, 3250, 1730, 1705 and 1660 cm⁻¹

Calcd for C₁₈H₂₉NO₄: C, 66.84; H, 9.04; N, 4.33. Found: C, 66.68; H, 8.74; N, 4.15.

4-AZA-5ß-ANDROSTAN-17ß-OL (34)

Sodium metal (8.0 g) was added slowly to the refluxing solution of 17ß-hydroxy-5-oximino-3, 5-seco-4-norandrostan-3-
oic acid (1.0 g) in 1-pentanol (200 ml). The reaction mixture was refluxed till sodium metal had reacted. The resulting solution was cooled, and steam-distilled to remove 1-pentanol. The solid residue was filtered, dried, taken in acetone, filtered, and concentrated to crystallise. Recrystallisation (Me$_2$CO); yield 0.65 g (75.7%), mp 205-207° (lit$^{73}$ 202-203°).

Anal.:  
IR (KBr): 3226 cm$^{-1}$  
NMR (CDCl$_3$): $\delta$ 0.73 (s, 3H) and 0.91 ppm (s, 3H)  
Mass: M$^+$ 277  
Calcd for C$_{16}$H$_{31}$NO: C, 77.92; H, 11.26; N, 5.05. Found: C, 77.95; H, 11.17; N, 5.18.

4-METHYL-4-AZA-5α-ANDROSTAN-17β-OL (35)  

Sodium borohydride (0.08 g) was added in small portions over a period of 0.5 hr, to solution of 4-aza-5α-androstan-17β-ol (34) (0.2 g) and formalin (0.5 ml) in methanol (10 ml). The mixture was poured into water (50 ml) and extracted with chloroform (4 x 25 ml). The chloroform layer was washed with water, dried, and solvent removed. The solid residue was crystallised (Me$_2$CO); yield 0.19 g (90%), mp 176-177°.

Anal.:  
IR (KBr): 3226, 2941, 2857, 2809 and 2750 cm$^{-1}$  
NMR (CDCl$_3$): $\delta$ 0.73 (s, 3H), 0.96 (s, 3H) and 2.16 ppm (s, 3H)  
Mass: M$^+$ 291  
[α]$_D^{25}$ + 18.58° (c 1.88)
Calcd for C\textsubscript{19}H\textsubscript{33}NO: C, 78.29; H, 11.41; N, 4.81. Found: C, 78.06; H, 11.23; N, 4.94.

4-METHYL-4-AZA-5α-ANDROSTAN-17β-YL ACETATE (36)

A mixture of 4-methyl-4-aza-5α-androstan-17β-ol (35) (0.2 g) and acetic anhydride (0.2 ml) was heated at 100° for 2 hr. The reaction mixture was cooled, poured into ice-cold water (50 ml), made alkaline with 10% potassium hydroxide solution and extracted with solvent ether (4 x 25 ml). The combined ether extract was washed with water, dried, and solvent removed by distillation. The material was crystallised (Me\textsubscript{2}CO); yield 0.19 g (83.3%), mp 143-145°.

Anal.: 
IR (KBr): 2940, 2850, 2780, 1732 and 1255 cm\textsuperscript{-1} 
NMR (CDCl\textsubscript{3}): δ 0.78 (s,3H), 0.96 (s,3H), 2.02 (s,3H) and 2.15 ppm (s,3H) 
[α]\textsubscript{D}\textsuperscript{25} - 28.28° (c 0.88) 
Calcd for C\textsubscript{21}H\textsubscript{35}N\textsubscript{2}O\textsubscript{2}: C, 75.63; H, 10.58; N, 4.20. Found: C, 76.10; H, 10.32; N, 4.60.

4-METHYL-4-AZA-5α-ANDROSTAN-17β-OL METHIODIDE (HS-419) (37)

Methyl iodide (0.1 ml) was added to the refluxing solution of 4-methyl-4-aza-5α-androstan-17β-ol (35) (0.2 g) in absolute ethanol (2 ml). The reaction mixture was refluxed for 1 hr, cooled, poured into dry solvent ether, and precipitated material filtered. Yellow product was crystallised (MeOH-Me\textsubscript{2}CO); yield 0.23 g (77%), mp 285-286°.
Anal.:  
Calcd for C_{20}H_{36}INO: C, 55.42; H, 8.38; I, 29.27; N, 3.23.  
Found: C, 55.51; H, 8.17; I, 28.90; N, 3.15.

4-METHYL-4-AZA-5α-ANDROSTAN-17β-YL ACETATE METHIODIDE  
(HS-435) (38)

Methyl iodide (0.2 ml) was added to boiling solution of  
4-methyl-4-aza-5α-androstan-17β-yl acetate (36) (0.15 g) in  
dry acetone (25 ml). The reaction mixture was refluxed for  
2 hr, concentrated to about 10 ml, cooled, and poured into  
dry solvent ether (50 ml). The precipitated material was  
collected and crystallised (Me_2CO); yield 0.18 g (84%), mp  
288-290°.

Anal.:  
Calcd for C_{22}H_{38}INO_2: C, 55.58; H, 8.00; I, 26.73; N, 2.94.  
Found: C, 55.63; H, 7.99; I, 26.58; N, 2.91.

3β-HYDROXY-5-ANDROSTEN-17-ONE

A solution of 3β-acetoxy-5-androsten-17-one (1.0 g) in  
methanol (15 ml) containing potassium hydroxide (0.2 g) was  
refluxed for 1 hr. The reaction mixture was acidified with  
glacial acetic acid, concentrated to about 10 ml, cooled, and  
poured into ice-cold water. The precipitated material was  
filtered and dried. Crystallised from benzene-petroleum ether;  
yield 0.9 g (100%), mp 144-146° (lit 148°).
4-ANDROSTENE-3,17-DIONE

A solution of 3\(\beta\)-hydroxy-5-androsten-17-one (0.8 g) in cyclohexanone (10 ml) and toluene (90 ml) was slowly distilled as aluminium iso-propoxide (1.0 g) in toluene (5 ml) was added. Distillation was continued for 0.5 hr as 20 ml of distillate were collected. The mixture was refluxed for 2 hr, allowed to stand for 12 hr, filtered to remove an orange coloured precipitate, and the solvents removed by steam distillation. The aqueous suspension was extracted with solvent ether (4 x 50 ml). The organic layer was washed with water, dried, and solvent distilled off. Crystallisation (hexane) of the residue gave the product; yield 0.55 g (69.4%), 169-171° (lit\(^95\) 168-170°).

5,17-DIOXO-3,5-SECO-4-NORANDROSTAN-3-OIC ACID

A solution of potassium carbonate (2.2 g) in water (60 ml) was added to a vigorously stirred solution of 4-androstene-3,17-dione (3.8 g) in 90% aqueous tert-butanol (230 ml), immediately followed by sodium metaperiodate solution (35 ml; 15.2 g in 190 ml) and then potassium permanganate solution (3.8 ml; 0.8%). Stirring of the mixture was continued and the periodate solution was added at the rate of 8 ml/min during the first 10 min and 2.5 ml/min during the next 30 min. The potassium permanganate solution was added when necessary to maintain the purple colour. The mixture was stirred for another 2 hr, treated with sodium metabisulphite to remove permanganate colour, and tert-butanol was removed under reduced pressure. The aqueous portion was
cooled to 4°, acidified with sulphuric acid, and extracted with chloroform (5 x 50 ml). The combined chloroform layer was washed with 5% sodium metabisulphite solution till free from iodine and then washed with water, dried, and solvent removed to yield an oily residue (3.1 g). The latter was picked up in 10% potassium hydroxide solution, washed with solvent ether, and filtered. The filtrate was acidified with ice-cold 50% sulphuric acid, and extracted with chloroform (5 x 50 ml). The chloroform extracts were washed with water, dried, and solvent removed under reduced pressure to give residue (2.3 g, mp 100-105°), which could not be crystallised.

5,17-DIOXIMINO-3,5-SECO-4-NORANDROSTAN-3-OIC ACID (39)

A mixture of 5,17-dioxo-3,5-seco-4-norandrostan-3-oic acid (2.3 g), hydroxylamine hydrochloride (1.0 g) and potassium hydroxide (3.1 g) in ethanol (100 ml) and water (60 ml), was refluxed for 2 hr. The reaction mixture was acidified with glacial acetic acid, diluted with water (100 ml), and concentrated till a turbidity appeared. The turbidity was removed by adding ethanol (2 ml) and allowed to crystallise; yield 2.05 g (81.4%), mp 214-216°.

**Anal.**

IR (KBr): 3350, 3180, 1690, 1673 and 1650 cm⁻¹

Calcd for C₁₆H₂₈N₂O₄: C, 64.26; H, 8.39; N, 8.33. Found: C, 63.98; H, 8.51; N, 8.28.
**17β-AMINO-4-AZA-5α-ANDROSTANE (40)**

Sodium metal (20 g) was added in small portions to a refluxing solution of 5,17-dioximino-3,5-seco-4-norandrostan-3-oic acid (39) (3.0 g) in 1-pentanol (500 ml). The refluxing was continued till the sodium metal had reacted. The reaction mixture was cooled to room temperature, water (100 ml) added, and steam-distilled to remove organic solvent. The aqueous layer was filtered to collect the material, dried, taken in petroleum ether, filtered, and allowed to crystallise; yield 1.6 g (64.9%), mp 155-157°.

**Anal.:**

IR (KBr): 3390, 3300, 2950 and 1615 cm\(^{-1}\)

NMR (CDCl\(_3\)): δ 0.63 (s, 3H), 0.90 (s, 3H) and 1.53 ppm (Disappeared on deuterium exchange)

\([\alpha]_D^{25} + 39.93° (c 3.24)\)

Calcd for C\(_{18}H_{32}N_2\): N, 10.13. Found: N, 10.29.

**17β-ISOPROPYLIDENEAMINO-4-AZA-5α-ANDROSTANE (41)**

Sodium-pentanol reduction of 5,17-dioximino-3,5-seco-4-norandrostan-3-oic acid (39) (2.0 g) and crystallisation of the residue from acetone yielded 17β-isopropylideneamino-4-aza-5α-androstane; yield 0.55 g (25.9%), mp 155-157°.

**Anal.:**

IR (KBr): 3460, 3280, 1690 and 1583 cm\(^{-1}\)

NMR (CDCl\(_3\)): δ 0.82 (s, 3H), 0.89 (s, 3H), 1.79 (s, 3H) and 1.97 ppm (s, 3H)

4-METHYL-17β-DIMETHYLAMINO-4-AZA-5α-ANDROSTANE (42)

**PROCEDURE A**

Sodium borohydride (0.96 g) was added in small portions, over a period of 0.5 hr, to the stirred solution of 17β-amino-4-aza-5α-androstane (40) (0.8 g) and formalin (3.5 ml) in methanol (40 ml). The reaction mixture was poured into water (100 ml) and extracted with solvent ether (5 x 50 ml). The ether extract was washed with water, dried, and solvent removed. The product so obtained, was crystallised (Me₂CO); yield 0.95 g (100%), mp 153-155°.

**Anal.:**

IR (KBr): 2950, 2780 and 2730 cm⁻¹

NMR (CDCl₃): δ 0.80 (s, 3H), 0.95 (s, 3H), 2.16 (s, 3H) and 2.21 ppm (s, 6H)

Mass: $M^+$, 318

Calcld for $\text{C}_{21}\text{H}_{38}\text{N}_2$: C, 79.18; H, 12.03; N, 8.80. Found: C, 79.38; H, 12.36; N, 8.89.

**PROCEDURE B**

Sodium borohydride (0.12 g) was added in small portions, over a period of 0.5 hr, to the stirred mixture of 17β-isopropylideneamino-4-aza-5α-androstane (41) (0.1 g) and formalin (0.2 ml) in methanol (10 ml). The mixture was poured into cold
water and extracted with solvent ether (4 x 50 ml). The extract was washed with water, dried, and solvent removed. The residue was dissolved in 10% hydrochloric acid (10 ml), washed with solvent ether, filtered, made alkaline with 10% potassium hydroxide solution, and extracted with solvent ether (4 x 25 ml). The combined extracts were washed with water, dried, and solvent removed to get a yellow residue. The material obtained was crystallised (MeCN); yield 0.07 g (69.6%), mp 154-155°.

**Anal.**:

IR (KBr): 2950, 2778 and 2720 cm\(^{-1}\)

NMR (CDCl\(_3\)): 0 0.80 (s, 3H), 0.95 (s, 3H), 2.16 (s, 3H) and 2.21 ppm (s, 6H)

Mass: M\(^+\), 318

\[\alpha\]\(^{25}\)_D + 40.54° (c 0.37)

Calcd for C\(_{21}\)H\(_{38}\)N\(_2\): C, 79.18; H, 12.03; N, 8.80. Found: C, 78.75; H, 11.76; N, 8.56.

**4-METHYL-17β-DIMETHYLAMINO-4-AZA-5α-ANDROSTANE DIMETHIODIDE (HS-467) (32)**

Methyl iodide (0.2 ml) was added to the boiling solution of 4-methyl-17β-dimethylamino-4-aza-5α-androstane (42) (0.05 g) in absolute ethanol (5 ml). The refluxing was continued for 2 hr, concentrated to about 2 ml, cooled, and poured into dry solvent ether (25 ml). The precipitated material was filtered, washed with dry solvent ether, and crystallised (Me\(_2\)CO-MeOH); yield 0.03 g (31.7%), mp 284-285°.
A solution of 4-aza-5α-cholestan-3-one (44) (0.78 g) in chloroform (10 ml) was added dropwise with stirring to a cooled (0-10°) Vilsmeier-Haack reagent prepared from dimethylformamide (0.44 g) and phosphorus oxychloride (0.77 g). The reaction mixture was heated for 6 hr at boiling point. After cooling, the solvent was removed and the yellow residue was treated with ice-cold water. The mixture was neutralised with 5% sodium bicarbonate solution and extracted with chloroform (3 x 20 ml). The chloroform extract was washed with water, dried and solvent removed to leave a yellow residue. The material obtained was crystallised (EtOH); yield 0.17 g (20%), mp 233-235°.

**Anal.:**

UV max (EtOH): 304 nm (ε 23,440)

IR (KBr): 3290, 1630, 1558 and 1490 cm⁻¹

NMR (CDCl₃): δ 0.69 (s, 3H), 0.93 (s, 3H), 4.68 (1H, disappeared on deuterium exchange) and 9.74 ppm (s, 1H)

Mass: M⁺, 433

[α]D²⁰ + 78.5° (c 0.97)

Calcd for C₂₇H₄₄ClNO: C, 74.63; H, 10.13; Cl, 8.17; N, 3.22.

Found: C, 75.14; H, 10.21; Cl, 7.90; N, 3.16.
3β-ACETOXY-17-CHLORO-17a-AZA-D-HOMO-5,16-ANDROSTADIEN-16-ALDEHYDE (46)

A solution of 17-oxo-17a-aza-D-homo-5-androsten-3β-yl acetate (12) (0.34 g) in chloroform (10 ml) was added dropwise while stirring at 0-10° to the Vilsmeier-Haack reagent prepared from dimethylformamide (0.22 g) and phosphorus oxychloride (0.38 g). The reaction mixture was refluxed for 6 hr. After removal of the solvent, the residue was treated with cold water. The resulting solution was neutralised with 5% sodium acetate solution and extracted with chloroform (3 x 25 ml). The chloroform extract was washed with water, dried, and solvent removed to leave a yellow residue, which was crystallised from acetone-methanol. Recrystallisation from the same solvent afforded the product; yield 0.07 g (18%), mp 252-254°.

Anal.:
UV max (EtOH): 302 nm (ε 26, 300)
IR (KBr): 3145, 1734, 1626, 1550 and 1466 cm⁻¹
NMR (CDCl₃): δ 1.02 (s,3H), 1.12 (s,3H), 2.04 (s,3H), 4.61 (1H), 5.20-5.52 (2H, on deuterium exchange collapsing to 1H signal, δ 5.30-5.50) and 9.68 ppm (s,1H)
Mass: M⁺, 391
[α]D²⁰ - 141.0° (c 1.06)
Calcd for C₂₂H₃₀ClNO₃:  C, 67.43; H, 7.66; Cl, 9.08; N, 3.57.
Found: C, 67.76; H, 7.81; Cl, 8.59; N, 3.24.

17a-METHYL-3,17a-DIAZA-A,D-BISHOMO-4a-ANDROSTENO[3,4-d]TETRAZOLE (48)

A solution of hydrazoic acid in chloroform was freshly prepared:
sodium azide (10 g) was dissolved in water (25 ml), cooled to -5°C, stirred vigorously and chloroform (50 ml) added. Concentrated sulphuric acid (9.3 ml) was added dropwise to the cooled and stirred mixture during 0.5 hr. The mixture was stirred for another 0.5 hr below 0°C, and the chloroform layer was separated and dried.

To the chloroform solution of hydrazoic acid (10 ml) kept at 0°C, was added freshly distilled boron trifluoride etherate (0.15 ml). A solution of 17α-methyl-17α-aza-D-homo-4-androsten-3-one (25) (0.25 g) in chloroform (10 ml) was added in parts to this mixture during 5 hr and the mixture was shaken after every addition. The reaction mixture was allowed to stand for 20 hr at room temperature, washed with 5% sodium bicarbonate solution till free from acid, and then with water. The chloroform layer was dried, and removal of solvent gave solid residue. Crystallisation (Me₂CO) yielded 0.13 g (45%) of the product, mp 238-240°C.

Anal.:  
UV max (EtOH): 243 nm (ε 16,660)  
IR (KBr): 2940, 2870, 2790, 1652, 1528, 1440 and 1320 cm⁻¹  
NMR (CDCl₃): δ 0.87 (s, 3H), 1.21 (s, 3H), 2.19 (s, 3H), 4.50 (m, 2H) and 6.52 ppm (1H)  
[α]D²⁵ + 40.69° (c 0.49)  