Steroids and Related Studies. Part 49.[1] 7a-Aza-B-homo[7a,7-*d*]tetrazole Analogues of Progesterone and Testosterone

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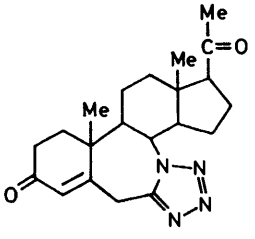
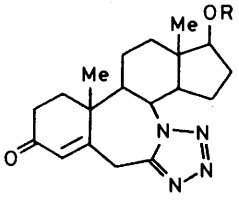
We report the syntheses of tetrazole analogues of progesterone and testosterone, namely, 7a-aza-B-homopregn-4-eno[7a,7-*d*]tetrazole-3,20-dione (1) and 3-oxo-7a-aza-B-homoandrost-4-eno[7a,7-*d*]tetrazol-17β-yl acetate (2), respectively. (25*R*)-7a-Aza-B-homospirost-5-eno[7a,7-*d*]tetrazol-3β-yl acetate (6) on Marker degradation gave 20-oxo-7a-aza-B-homopregna-5,16-dieno[7a,7-*d*]tetrazol-3β-yl acetate (7). The compound (7) on selective hydrogenation followed by hydrolysis and Oppenauer oxidation yielded (1). 7a-Aza-B-homoandrost-5-eno[7a,7-*d*]tetrazole-3β,17β-diol diacetate (13) was partially hydrolysed to the alcohol (15), which on Oppenauer oxidation gave (2).

ANALOGUES of steroid hormones possessing fused heterocyclic systems are of interest, and our laboratory is active in the area of steroidal tetrazoles. We have prepared the 7a-aza-B-homo[7a,7-*d*]tetrazole derivatives (1), and (2) and (3) of progesterone and testosterone, respectively. A preliminary communication on this work has been published.[2]



(1)

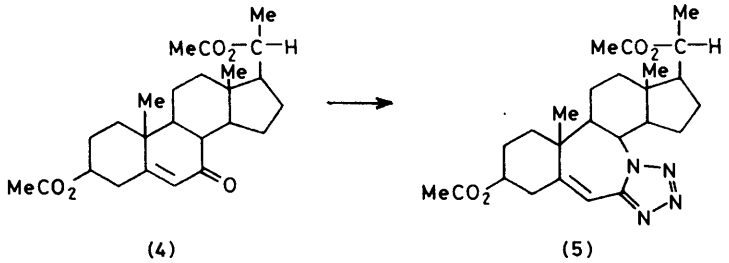


(2) R = MeCO

(3) R = H

RESULTS AND DISCUSSION

For the preparation of (1), 7-oxopregn-5-ene-3β,20β-diol diacetate (4),[3] obtained by t-butyl chromate oxidation of pregn-5-ene-3β,20β-diol diacetate,[4] was chosen as the starting material. The α,β-unsaturated ketone (4), on treatment with hydrazoic acid–boron trifluoride in chloroform, yielded the tetrazole (5). The vinylic proton signals in (4) and (5) appeared at δ 5.61 and 6.62, respectively. The structure of the tetrazole (5) was apparent from the spectra in the light of our earlier results.[5,6] The attempts at the hydrolysis of (5), and oxidation to (1), were not successful.



(4) (5)

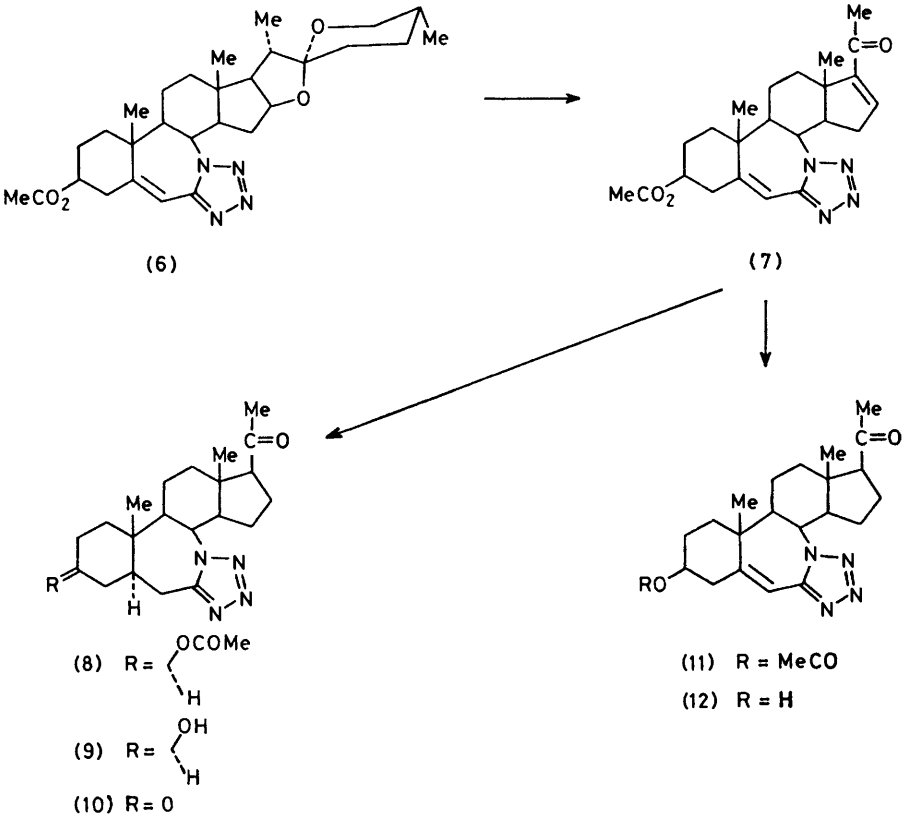
We then tried a route starting with diosgenin. This was converted into (25*R*)-7-oxospirost-5-en-3β-yl acetate,[7] and from the latter the tetrazole (6) was prepared. Marker degradation of (6) yielded 20-oxo-7a-aza-B-homopregna-5,16-dieno[7a,7-*d*]tetrazol-3β-yl acetate (7). The n.m.r. spectrum showed a singlet at δ 2.30 (3 H) for the 21-Me. The C-6 vinylic proton singlet was at δ 6.67, whereas the C-16 vinylic proton appeared as a triplet (*J* 3 Hz) at δ 6.84. The tetrazole (7), on hydrogenation over 10% palladium–charcoal, gave (8), the 5α-H and 17α-H configurations being assigned by analogy with earlier work on the hydrogenation of 5-enes [8–10] and 16-en-20-ones,[11,12] respectively. The ester (8) was hydrolysed to the alcohol (9), and the latter on Oppenauer oxidation gave the ketone (10). As expected, (10) exhibited two broad signals at δ 3.03 (d, 2 H, C-6 methylene protons) and 4.38 (m, 1 H, 8β-H).

Hydrogenation of (7) over 5% palladium–barium sulphate was selective, and led to the formation of (11). It exhibited only one vinylic proton singlet at δ 6.62, which can only be assigned to the C-6 position. On acid hydrolysis (11) gave (12), which, on Oppenauer oxidation, gave (1). The vinylic proton signal showed a corresponding shielding from δ 6.61 to 5.90 indicating that an allylic shift has occurred and the double bond was between positions 4 and 5. There also appeared a singlet at δ 4.05 integrating for two protons which could be assigned to the C-6 methylene protons.

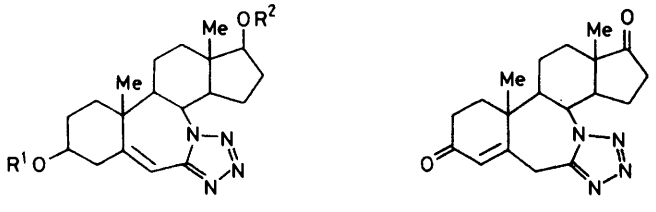
For the preparation of the androstane analogue (2), the tetrazole (13) was first prepared from 7-oxoandrost-5-ene-3β,17β-diol diacetate.[13] Acetoxy functions in (13) were hydrolysed; use of acidic or alkaline conditions led to the same product (14). No allylic shift was observed in the alkaline medium, as noted for the cholestane analogue;[5] we have no plausible explanation for this

variation. Oppenauer oxidation of the diol (14) afforded the diketone (16).

Difficulty was experienced in effecting partial hydrolysis of (13) but ultimately treatment under mild



conditions with potassium bicarbonate gave the monoacetate (15). On Oppenauer oxidation (15) gave (2) and (3) in low yields, 11.7 and 9.4%, respectively. The product (3) has evidently resulted from the Oppenauer oxidation conditions.



EXPERIMENTAL

I.r. spectra were obtained for potassium bromide discs. N.m.r. spectra (60 MHz) were recorded for solutions in deuteriochloroform containing tetramethylsilane as internal reference. T.l.c. was carried out on silica gel G (E. Merck) and plates were developed by exposure to iodine vapour, and ceric sulphate solution (2 g in 100 ml of 10% v/v sulphuric acid), followed by heating at 150 °C. Anhydrous sodium sulphate was employed as the drying agent.

7a-*Aza*-B-*homopregn*-5-*eno*[7a,7-d]*tetrazole*-3β,20β-*diol Diacetate* (5).—A solution of 7-oxopregn-5-ene-5β,20β-diol diacetate (4) [3] (1.0 g) in dry chloroform (20 ml) was added slowly during 4 h to a mixture of boron trifluoride–ether complex (1 ml) and hydrazoic acid (6—8%) in chloroform (20 ml) maintained at 0 °C. After addition was complete, the reaction mixture was set aside at room temperature (20—25 °C) for 24 h. It was then washed successively with aqueous sodium bicarbonate (10%) and water, dried, and solvent removed to leave a brown residue (0.7 g), which was crystallised from acetone to furnish the *product* (5) (0.6 g, 68.9%), m.p. 223—224 °C; $\lambda_{max.}$ (EtOH) 242 nm (log ε 4.08); $\nu_{max.}$ 2 907, 2 857, 1 733, 1 667, 1 511, 1 466, 1 449, 1 370, and 1 242 cm^{-1}; δ 0.80 (3 H, s), 1.27 (3 H, s), 2.03 (3 H, s), 2.05 (3 H, s), 4.25 (1 H, m), 4.85 (2 H, m), and 6.62 (1 H, s) (Found: C, 66.05; H, 7.77; N, 12.54. $C_{25}H_{36}N_4O_4$ requires C, 65.76; H, 7.95; N, 12.27%).

(25R)-7a-*Aza*-B-*homospirost*-5-*eno*[7a,7-d]*tetrazol*-3β-*yl Acetate* (6).—A solution of (25*R*)-7-oxospirost-5-en-3β-yl acetate [7] (10.0 g) in dry chloroform (200 ml) was added during 4 h to a mixture of hydrazoic acid in chloroform (200 ml) and boron trifluoride–ether complex (10 ml) cooled to 0 °C. The reaction mixture was set aside for 20 h at room temperature (25—30 °C). It was then washed successively with aqueous sodium bicarbonate (10%) and water, dried, and the solvent removed. The brown residue (8.1 g) was purified on a column of alumina (100 g) in benzene, then crystallised from methanol to yield the *product* (6) (6.1 g, 56.2%), m.p. 245—247 °C; $\lambda_{max.}$ (EtOH) 242 nm (log ε 4.16); $\nu_{max.}$ 2 891, 2 849, 1 724, 1 667, 1 499,

1 466, 1 449, 1 366, 1 239, 926, and 901 cm^{-1}; δ 0.93 (3 H, s), 1.33 (3 H, s), 2.09 (3 H, s), 3.46 (2 H, m), 4.50 (3 H, m), and 6.68 (1 H, s) (Found: C, 68.43; H, 8.41; N, 10.75. $C_{29}H_{42}N_4O_4$ requires C, 68.20; H, 8.29; N, 10.97%).

20-*Oxo*-7a-*aza*-B-*homopregna*-5,16-*dieno*[7a,7-d]*tetrazol*-3β-*yl Acetate* (7).—In a sealed tube compound (6) (5.0 g) and acetic anhydride (40 ml) were heated in an oil-bath at 200 ± 10 °C for 2 h. The cooled mixture was poured into water and the supernatant liquid was decanted. The brown oily residue was washed with water, dissolved in glacial acetic acid (50 ml), and treated with chromium trioxide (1.75 g) in 90% acetic acid (40 ml), with the temperature being kept below 15 °C. The mixture was stirred occasionally during 2 h at room temperature, and ethanol (10 ml) was added to destroy the excess of chromium trioxide. The reaction mixture was diluted with water, the precipitate was extracted with benzene–ether (1 : 1), and the extract was washed successively with saturated aqueous sodium hydrogencarbonate and water, dried, and evaporated. The residue was taken up in glacial acetic acid (40 ml), refluxed for 2 h, cooled, diluted with water, and the precipitate extracted with benzene–ether (1 : 1). The extract was again washed successively with saturated aqueous sodium hydrogencarbonate and water, dried, and evaporated. A sticky residue was obtained which was purified by passage through alumina (100 g) in dry benzene. Crystallisation from acetone–methanol gave the *product* (7) (2.26 g, 56.2%), m.p. 225 °C; $\lambda_{max.}$ (EtOH) 241 nm (log ε 3.94); $\nu_{max.}$ 2 933, 1 736, 1 672, 1 600, 1 515, 1 445, 1 370, 1 325, and 1 250 cm^{-1}; δ 1.11 (3 H, s), 1.21 (3 H, s), 2.05 (3 H, s), 2.30 (3 H, s), 4.36—5.17 (centred at 4.76, 2 H, br m), 6.67 (1 H, s), and 6.84 (1 H, t, *J* 3 Hz) (Found: C, 67.51; H, 7.30; N, 13.59. $C_{23}H_{30}N_4O_3$ requires C, 67.29; H, 7.37; N, 13.65%).

20-*Oxo*-7a-*aza*-B-*homo*-5α-*pregnano*[7a,7-d]*tetrazol*-3β-*yl Acetate* (8).—To a solution of 20-oxo-7a-aza-B-homopregna-5,16-dieno[7a,7-*d*]tetrazol-3β-yl acetate (7) (0.2 g) in absolute alcohol (20 ml) was added 10% palladium–charcoal [14] (0.07 g), and the mixture was shaken under hydrogen at 25 lbf in^{-2} for 2 h. The solution was filtered and the solvent removed to afford a residue, which on crystallisation from methanol yielded rhombic-shaped crystals of the *product* (8) (0.11 g, 54.6%), m.p. 205—207 °C; $\nu_{max.}$ 2 907, 1 733, 1 718, 1 531, 1 447, 1 433, 1 381, 1 364, and 1 250 cm^{-1}; δ 0.76 (3 H, s), 1.23 (3 H, s), 2.03 (3 H, s), 2.18 (3 H, s), 2.96 (2 H, d), and 4.05—4.99 (centred at 4.52, 2 H, br m) (Found: C, 66.74; H, 8.24; N, 13.52. $C_{23}H_{34}N_4O_3$ requires C, 66.66; H, 8.40; N, 13.53%).

3β-*Hydroxy*-7a-*aza*-B-*homo*-5α-*pregnano*[7a,7-d]*tetrazol*-20-*one* (9).—To a refluxing solution of 20-oxo-7a-aza-B-homo-5α-pregnano[7a,7-*d*]tetrazol-3β-yl acetate (8) (0.1 g) in 95% ethanol (4 ml) was added 6N hydrochloric acid (0.6 ml) and the reaction refluxed for 2.5 h. The reaction mixture was then concentrated, poured into ice-cold water, and the product extracted with chloroform (4 × 50 ml). The extract was washed with water, dried, the solvent was distilled off, and the residue (0.09 g) so obtained was crystallised from acetone–light petroleum (b.p. 60—80 °C) to afford the *product* (9) (0.08 g, 89.0%), m.p. 267—269 °C; $\nu_{max.}$ 3 350, 2 933, 1 695, 1 658, 1 520, 1 500, 1 440, 1 421, and 1 346 cm^{-1}; δ 0.75 (3 H, s), 1.20 (3 H, s), 2.18 (3 H, s), 2.96 (2 H, d), 3.66 (1 H, m), and 4.35 (1 H, m) (Found: C, 67.73; H, 9.03; N, 14.76. $C_{21}H_{32}N_4O_2$ requires C, 67.63; H, 8.66; N, 15.04%).

7a-*Aza*-B-*homo*-5α-*pregnano*[7a,7-d]*tetrazole*-3,20-*dione* (10).—A solution of 3β-hydroxy-7a-aza-B-homo-5α-pregnano[7a,7-*d*]tetrazol-20-one (9) (0.4 g) in dioxan (50 ml) was added to a mixture of dry toluene (50 ml) and cyclohexanone (4 ml) from which 5-ml bulk had been distilled off. The distillation was continued and a solution of aluminium isopropoxide (1.0 g) in dry toluene (20 ml), followed by more toluene (25 ml), was added dropwise during 1 h. After distilling off toluene (25 ml), the mixture was refluxed for 1 h and then set aside overnight at room temperature. It was then filtered, the filtrate steam-distilled, and the aqueous suspension was extracted with chloroform (3 × 100 ml). The combined chloroform extracts were washed with water, dried, and solvent removed to give a solid (0.18 g), which on crystallisation from methanol afforded the *product* (10) (0.25 g, 62.8%), m.p. 223—225 °C; $\nu_{max.}$ 2 907, 1 727, 1 709, 1 531, 1 466, 1 439, 1 389, and 1 359 cm^{-1}; δ 0.79 (3 H, s), 1.42 (3 H, s), 2.18 (3 H, s), 3.03 (2 H, d), and 4.38 (1 H, m) (Found: C, 67.96; H, 8.15; N, 14.64. $C_{21}H_{30}N_4O_2$ requires C, 68.08; H, 8.16; N, 15.12%).

20-*Oxo*-7a-*aza*-B-*homopregn*-5-*eno*[7a,7-d]*tetrazol*-3β-*yl Acetate* (11).—To the solution of 20-oxo-7a-aza-B-homopregna-5,16-dieno[7a,7-*d*]tetrazol-3β-yl acetate (7) (0.2 g) in absolute alcohol (50 ml) was added 5% palladium–barium sulphate catalyst [14] (0.4 g), and the mixture was shaken under hydrogen at 30 lbf in^{-2} for 7 h. The solution was filtered, and the solvent removed to afford a residue, which on crystallisation from methanol yielded the *product* (11) (0.12 g, 60.3%), m.p. 189—190 °C; $\lambda_{max.}$ (MeOH) 241 nm (log ε 4.03); $\nu_{max.}$ 2 924, 1 736, 1 710, 1 667, 1 511, 1 473, 1 443, 1 355, and 1 259 cm^{-1}; δ 0.82 (3 H, s), 1.30 (3 H, s), 2.05 (3 H, s), 2.20 (3 H, s), 4.27 (1 H, m), 4.76 (1 H, m), and 6.62 (1 H, s) (Found: C, 66.78; H, 7.87; N, 13.63. $C_{23}H_{32}N_4O_3$ requires C, 66.99; H, 7.77; N, 13.58%).

3β-*Hydroxy*-7a-*aza*-B-*homopregn*-5-*eno*[7a,7-d]*tetrazol*-20-one (12).—To a refluxing solution of 20-oxo-7a-aza-B-homopregn-5-eno[7a,7-*d*]tetrazol-3β-yl acetate (11) (0.2 g) in 95% ethanol (10 ml) was added 6N hydrochloric acid (2 ml) and the solution refluxed for 2.5 h. The reaction mixture was then concentrated, poured into water, and extracted with chloroform (3 × 50 ml). The extract was washed with water, dried, and solvent distilled off to furnish a residue (0.17 g) which, on crystallisation from acetone–light petroleum (b.p. 60—80 °C), afforded the needles of the *product* (12) (0.14 g, 77.8%), m.p. 279—281 °C; $\lambda_{max.}$ (MeOH) 242 nm (log ε 4.07); $\nu_{max.}$ 3 356, 2 976, 1 727, 1 695, 1 550, 1 534, 1 482, 1 372, and 1 093 cm^{-1}; δ 0.82 (3 H, s), 1.35 (3 H, s), 2.20 (3 H, s), 3.75 (1 H, m), 4.28 (1 H, m), and 6.61 (1 H, s) (Found: C, 67.81; H, 8.39; N, 15.02. $C_{21}H_{30}N_4O_3$ requires C, 68.08; H, 8.16; N, 15.12%).

7a-*Aza*-B-*homopregn*-4-*eno*[7a,7-d]*tetrazole*-3,20-*dione* (1).—A solution of 3β-hydroxy-7a-aza-B-homopregn-5-eno-[7a,7-*d*]tetrazol-20-one (12) (0.2 g) in dioxan (25 ml) was added to a mixture of dry toluene (25 ml) and cyclohexanone (3 ml) from which 5-ml bulk had been distilled off. The distillation was continued and a solution of aluminium isopropoxide (0.5 g) in dry toluene (10 ml), followed by more toluene (25 ml), was added dropwise during 1 h. After distilling off toluene (25 ml), the mixture was refluxed for 2 h and set aside overnight at room temperature. It was then filtered and the filtrate steam-distilled. The aqueous suspension was extracted with chloroform (4 × 50 ml), washed with water, and dried. Removal of the solvent gave a solid (0.18 g) which was purified by passage through alumina (25 g) in dry benzene, and crystallisation from methanol gave the *product* (1)

(0.08 g, 40.2%), m.p. 204—207 °C; $\lambda_{max.}$ (MeOH) 235 nm (log ε 4.77); $\nu_{max.}$ 2 933, 2 857, 1 709, 1 685, 1 616, 1 536, 1 462, 1 439, 1 389, and 1 359 cm^{-1}; δ 0.82 (3 H, s), 1.28 (3 H, s), 2.20 (3 H, s), 4.05 (2 H, s), 4.59 (1 H, br m), and 5.90 (1 H, s) (Found: C, 67.93; H, 8.39; N, 15.01. $C_{21}H_{28}N_4O_2$ requires C, 68.45; H, 7.66; N, 15.21%).

7a-*Aza*-B-*homoandrost*-5-*eno*[7a,7-d]*tetrazole*-3β,17β-*diol Diacetate* (13).—A solution of 7-oxoandrost-5-ene-3β,17β-diol diacetate [13] (4.0 g) in dry chloroform was added to a mixture of boron trifluoride–ether complex (3 ml) and hydrazoic acid–chloroform (150 ml) during 4 h at 0 °C, and the reaction was set aside at room temperature (30—35 °C) for 20 h. It was then washed successively with aqueous sodium hydrogencarbonate (10%) and water, dried, and the brown residue (3.5 g) after removal of the solvent was crystallised from acetone–methanol to yield the *product* (13) (2.85 g, 63.2%), m.p. 249—251 °C; $\lambda_{max.}$ (EtOH) 242 nm (log ε 4.21); $\nu_{max.}$ 2 882, 1 724, 1 667, 1 504, 1 466, 1 449, 1 370, and 1 248 cm^{-1}; δ 0.95 (3 H, s), 1.27 (3 H, s), 2.05 (6 H, s), 4.36 (1 H, m), 4.74 (2 H, m), and 6.62 (1 H, br s) (Found: C, 64.04; H, 7.30; N, 13.57. $C_{23}H_{32}N_4O_4$ requires C, 64.46; H, 7.53; N, 13.08%).

Alkaline Hydrolysis of the Diacetate (13).—A solution of the diacetate (13) (2.2 g) in methanol (60 ml) containing potassium hydroxide (1.2 g) was refluxed for 2 h. The reaction mixture was acidified with glacial acetic acid, concentrated to 5 ml, poured into ice-cold water, and then set aside at room temperature for 24 h. The precipitate was collected, dried, and crystallised from methanol to afford 7a-*aza*-B-*homoandrost*-5-*eno*[7a,7-d]*tetrazole*-3β,17β-*diol* (14) (1.7 g, 95.9%), m.p. 266—268 °C; $\lambda_{max.}$ (EtOH) 244 nm (log ε 4.30); $\nu_{max.}$ 3 322, 2 924, 2 841, 1 667, 1 511, 1 475, 1 445, and 1 389 cm^{-1} (Found: C, 66.15; H, 8.19; N, 16.83. $C_{19}H_{28}N_4O_2$ requires C, 66.25; H, 8.19; N, 16.27%).

Acid Hydrolysis of the Diacetate (13).—To a refluxing solution of the diacetate (13) (0.5 g) in ethanol (30 ml) was added 6N hydrochloric acid (2 ml), and the mixture refluxed for 8 h. The reaction mixture was concentrated to slight turbidity and set aside overnight. The separated crystalline material was collected, washed with a little ice-cold ethanol, dried, and crystallised from methanol to give the *product* (14) (0.2 g, 49.8%), m.p. 266—267 °C; $\lambda_{max.}$ (EtOH) 245 nm (log ε 4.30); $\nu_{max.}$ 3 322, 2 924, 2 841, 1 667, 1 511, 1 475, 1 445, and 1 389 cm^{-1} (Found: C, 66.75; H, 8.08; N, 16.12. $C_{19}H_{28}N_4O_2$ requires C, 66.25; H, 8.19; N, 16.27%).

Partial Alkaline Hydrolysis of the Diacetate (13).—Potassium hydrogencarbonate (0.25 g) was added to a solution of the diacetate (13) (0.5 g) in methanol (75 ml), and the reaction was set aside at room temperature (25—28 °C) for 24 h. It was then acidified with dilute acetic acid, concentrated, diluted with water, and extracted with chloroform (4 × 50 ml). The combined chloroform extract was washed with water, dried, and the solvent removed to give a solid residue (0.45 g), which on t.l.c. showed one major and two minor spots. The residue was dissolved in chloroform–methanol (1 : 1) (20 ml) and mixed with alumina (10 g). The alumina was warmed slightly, with shaking, to evaporate off the solvent and then activated at 80 °C, and loaded on a column of activated alumina (90 g) in benzene. Elution with chloroform (2 × 25 ml) yielded the unreacted diacetate (13) (0.01 g), and further elution with chloroform–methanol (100 : 0.2; 20 × 25 ml) yielded a solid residue (0.36 g), which was crystallised from acetone–light petroleum (b.p. 60—80 °C) to yield 3β-*hydroxy*-7a-*aza*-B-*homoandrost*-5-*eno*[7a,7-d]*tetrazol*-17β-*yl acetate* (15) (0.32 g, 70.9%), m.p. 254—255 °C; $\lambda_{max.}$ (MeOH) 241 nm (log ε 4.14); $\nu_{max.}$ 3 279, 2 907, 1 745, 1 669, 1 515, 1 449, 1 431, 1 381, 1 355, 1 307, and 1 258 cm^{-1}; δ 0.93 (3 H, s), 1.32 (3 H, s), 2.06 (3 H, s), 2.83 (1 H, br s, D_2O exchangeable), 3.79 (1 H, m), 4.28 (1 H, m), 4.75 (1 H, m), and 6.58 (1 H, s) (Found: C, 65.15; H, 7.84; N, 14.45. $C_{21}H_{30}N_4O_3$ requires C, 65.26; H, 7.82; N, 14.50%).

7a-*Aza*-B-*homoandrost*-4-*eno*[7a,7-d]*tetrazole*-3,17-*dione* (16).—7a-Aza-B-homoandrost-5-eno[7a,7-d]tetrazole-3β,17β-diol (14) (1.5 g) and cyclohexanone (15 ml) were added to a mixture of dry toluene (150 ml) and dioxan (60 ml). The mixture was refluxed till the solid material completely dissolved and then distillation was started. When 15 ml had been distilled off, a solution of aluminium isopropoxide (1.5 g) in dry toluene (15 ml) was added dropwise during 30 min. After distilling off another 50 ml, the mixture was refluxed for 4 h, cooled, filtered, and the residue washed with toluene (30 ml). The combined organic layer was steam-distilled, and on cooling a crystalline material appeared. This was filtered, washed with water, dried, and crystallised from acetone–light petroleum (b.p. 60—80 °C) to yield the *product* (16) (0.5 g, 33.7%), m.p. 266—268 °C; $\lambda_{max.}$ (EtOH) 240 nm (log ε 4.18); $\nu_{max.}$ 2 899, 2 857, 1 739, 1 675, 1 621, 1 538, 1 460, 1 399, 1 376, and 1 351 cm^{-1}; δ 1.09 (3 H, s), 1.19 (3 H, s), 4.05 (2 H, s), 4.73 (1 H, m), and 5.90 (1 H, s) (Found: C, 66.67; H, 7.21; N, 16.60. $C_{19}H_{24}N_4O_2$ requires C, 67.03; H, 7.11; N, 16.46%).

Oppenauer Oxidation of 3β-*Hydroxy*-7a-*aza*-B-*homoandrost*-5-*eno*[7a,7-d]*tetrazol*-17β-*yl Acetate* (15).—The monoacetate (15) (0.6 g) was dissolved in dry toluene (50 ml) and cyclohexanone (8 ml) and added to dry toluene (50 ml) from which 10-ml bulk had been distilled off. The distillation was continued and a solution of aluminium isopropoxide (1.5 g) in dry toluene (30 ml) was added dropwise during 30 min. After distilling off more toluene (50 ml), the mixture was refluxed for 1 h, set aside at room temperature for 12 h, then filtered and the filtrate steam-distilled. The aqueous suspension was extracted with chloroform (4 × 50 ml), and the combined chloroform extracts were washed with water, dried, and solvent removed to give a solid (0.35 g), which showed two spots on t.l.c. (ethyl acetate–hexane, 4 : 1). The material was chromatographed over alumina (30 g) in dry benzene. Elution with solvents of increasing polarity was carried out; fractions (10 × 50 ml) obtained with chloroform–methanol (100 : 0.1) yielded a solid (0.08 g), which was crystallised from acetone–hexane to obtain 3-*oxo*-7a-*aza*-B-*homoandrost*-4-*eno*[7a,7-d]*tetrazol*-17β-*yl acetate* (2) (0.07 g, 11.7%), m.p. 251—253 °C; $\lambda_{max.}$ (MeOH) 234 nm (log ε 4.10); $\nu_{max.}$ 2 907, 1 736, 1 684, 1 616, 1 529, 1 460, 1 429, 1 361, and 1 250 cm^{-1}; δ 1.02 (3 H, s), 1.19 (3 H, s), 2.10 (3 H, s), 4.05 (2 H, s), 4.73 (2 H, m), and 5.90 (1 H, br s) (Found: C, 65.58; H, 6.69; N, 14.36. $C_{21}H_{28}N_4O_3$ requires C, 65.60; H, 7.34; N, 14.57%). Further elution with chloroform–methanol (100 : 0.5; 6 × 50 ml) yielded a solid residue (0.06 g), which on crystallisation from acetone–light petroleum (b.p. 60—80 °C) afforded 17β-*hydroxy*-7a-*aza*-B-*homoandrost*-4-*eno*[7a,7-d]*tetrazol*-3-*one* (3) (0.05 g, 9.41%), m.p. 252—254 °C; $\lambda_{max.}$ (MeOH) 235 nm (log ε 4.07); $\nu_{max.}$ 3 425, 2 933, 1 689, 1 616, 1 515, 1 449, 1 437, 1 389, and 1 342 cm^{-1}; δ 0.96 (3 H, s), 1.08 (3 H, s), 3.79 (1 H, m), 4.04 (2 H, br s), 4.73 (1 H, m), and 5.92 (1 H, br s) (Found:

C, 66.36; H, 7.64; N, 16.05. $C_{19}H_{26}N_4O_2$ requires C, 66.64; H, 7.65; N, 16.36%).

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REFERENCES

[1] Part 48; H. Singh, T. R. Bhardwaj, and D. Paul, *J.C.S. Perkin I*, 1979, 2451.
[2] H. Singh, K. K. Bhutani, R. K. Malhotra, and D. Paul, *Experientia*, 1978, **34**, 557.
[3] J. P. Kutney and C. Gletsos, *Steroids*, 1966, **7**, 67.
[4] W. Klyne and E. Miller, *J. Chem. Soc.*, 1950, 1972.
[5] H. Singh, R. K. Malhotra, and N. K. Luhadiya, *J.C.S. Perkin I*, 1974, 1480.
[6] H. Singh, R. B. Mathur, and P. P. Sharma, *J.C.S. Perkin I*, 1972, 990.
[7] H. Singh and S. Padmanabhan, *Indian J. Chem.*, 1969, **7**, 1084.
[8] R. L. Augustine and E. Reardon, *Org. Prep. Proc.*, 1969, **1**, 107.
[9] J. H. Pierce, H. C. Richards, C. W. Shoppee, R. J. Stephenson, and G. H. R. Summers, *J. Chem. Soc.*, 1955, 694.
[10] C. W. Shoppee, B. D. Agashe, and G. H. R. Summers, *J. Chem. Soc.*, 1957, 3107.
[11] J. Attenburrow, J. E. Connett, W. Graham, J. F. Oughton, A. C. Ritchie, and P. A. Wilkinson, *J. Chem. Soc.*, 1962, 4547.
[12] C. Djerassi, H. Martinez, and G. Rosenkranz, *J. Org. Chem.*, 1951, **16**, 1278.
[13] K. Heusler and A. Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284.
[14] A. I. Vogel, 'Practical Organic Chemistry,' E.L.B.S., London, 1971, p. 951.