New Steroidal Heterocycles: The Synthesis and Structure of Androsteno[2,3-*g*]-, Androstano[3,2-*f*]-, and Androsteno[16,17-*g*]-pyrazolo[1,5-*a*]pyrimidines

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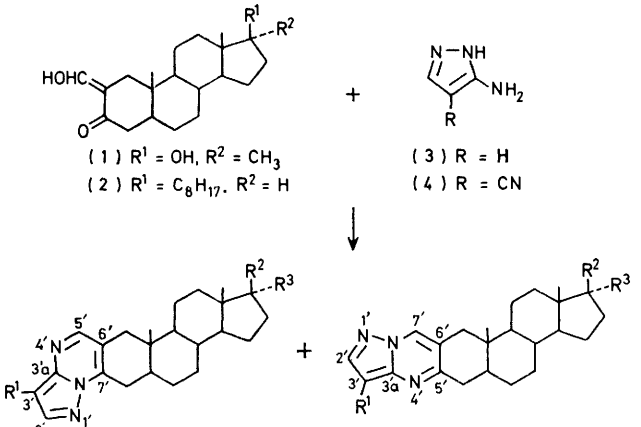
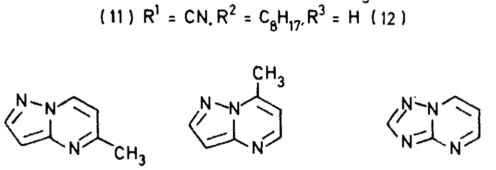
The reaction of 3-aminopyrazole and its 4-cyano-derivative with 2-hydroxymethylene-3-oxo-steroids gave a mixture of angularly fused and linearly fused products, androst-2-eno[2,3-*g*]- and androstano[3,2-*f*]-pyrazolo[1,5-*a*]pyrimidines, respectively. However, the condensation of 3-amino-4-cyano-5-cyanomethylpyrazole with 2-hydroxymethyl-3-oxo-steroids gave only angularly fused products, namely, androst-2-eno[2,3-*g*]pyrazolo[1,5-*a*]pyrimidines. The reaction of 3-aminopyrazole and its derivatives with a 2-hydroxymethylene-Δ^4-3-oxo-steroid and 16-hydroxymethylene-17-oxo-steroids also afforded only the angularly fused products, androst-2,4-dieno[2,3-*g*]- and androst-16-eno[16,17-*g*]-pyrazolo[1,5-*a*]pyrimidines, respectively. The structures of all these compounds were established by i.r., u.v., and ^{1}H and ^{13}C n.m.r. spectroscopy.

STEROIDS are known to play an important role in the animal system both from the biochemical and pharmacological standpoint.[1] In recent years particular attention has been focused on heterosteroids,[2] since several naturally occurring steroidal alkaloids are known [3] to possess significant physiological activity. A large number of synthetic steroids have been reported in which an additional heterocyclic ring system is fused with the steroid skeleton [2a,b] or a heteroatom is incorporated in the steroid nucleus.[4] In this communication we report the synthesis of several steroidal pyrazolopyrimidines.

The condensation of 3-aminopyrazole (3) with 17β-hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-





(13) (14) (15)

3-one (1) can conceivably afford 17β-hydroxy-17α-methyl-5α-androst-2-eno[2,3-*g*]pyrazolo[1,5-*a*]pyridine (5) and/or 17β-hydroxy-17α-methyl-5α-androstano[3,2-*f*]-pyrazolo[1,5-*a*]pyrimidine (6). Indeed, refluxing a solution of the steroid (1) with 3-aminopyrazole (3) in absolute alcohol overnight results in the formation of both the products (5) and (6) in 34 and 27% yield respectively. Formulation of the structures (5) and (6) is consistent with the i.r. spectra, and the molecular formula $C_{24}H_{33}N_3O$ obtained by elemental analysis and high resolution mass spectrometry. Definite assignment of these structures is made by comparison of the i.r., u.v., and ^{1}H and ^{13}C n.m.r. spectra of the two products (5) and (6) with those of 5-methylpyrazolo[1,5-*a*]pyrimidine (13) and 7-methylpyrazolo[1,5-*a*]pyrimidine (14), whose preparation and structures have been reported [5a] in a previous publication.

TABLE 1

Characteristic i.r. absorption frequencies (cm^{-1})

Compound	$\nu_{max.}$/cm^{-1}	Compound	$\nu_{max.}$/cm^{-1}
(5)	1 620, 1 530	(6)	1 625, 1 525, 1 500
(14)	1 620, 1 540	(13)	1 625, 1 535, 1 505

The i.r. spectrum of 5-methylpyrazolo[1,5-*a*]pyrimidine (13) correlates well with that of isomer (6) whilst the i.r. spectrum of 7-methylpyrazolo[1,5-*a*]pyrimidine (14) correlates with that of isomer (5). Of particular interest, in the i.r. spectra of these compounds, is the region 1 500—1 630 cm^{-1} illustrated in Table 1. The compounds (6) and 5-methylpyrazolo[1,5-*a*]pyrimidine (13) differ from the compounds (5) and 7-methylpyrazolo[1,5-*a*]pyrimidine (14) in showing an extra absorption in the region 1 500—1 505 cm^{-1}. Thus, it is inferred that the two condensation products are 17β-hydroxy-17α-methyl-5α-androst-2-eno[2,3-*g*]pyrazolo-[1,5-*a*]pyrimidine (5), m.p. 222—224°, and 17β-hydroxy-17α-methyl-5α-androstano[3,2-*f*]pyrazolo[1,5-*a*]pyrimidine (6), m.p. 186—188°.

The two products (5) and (6) are also distinguished by their u.v. spectra (Table 2). The u.v. spectra of the pyrazolopyrimidine (5) and 7-methylpyrazolo[1,5-*a*]-pyrimidine (14) are found to show similar absorptions, in contrast to the u.v. spectra of the steroid (6) and 5-methylpyrazolo[1,5-*a*]pyrimidine (13). The compounds (6) and (13) differ from the compounds (5) and (14) in exhibiting an extra $\lambda_{max.}$ in the region 228—238 nm.

Assignment of these structures is further supported by ^{1}H n.m.r. spectroscopy. The ^{1}H n.m.r. spectrum of 17β-hydroxy-17α-methyl-5α-androst-2-eno[2,3-*g*]pyrazolo-[1,5-*a*]pyrimidine (5) shows signals at δ 0.82 (s, 18-CH_3), 0.90 (s, 19-CH_3), 1.25 (s, 17-CH_3), 6.60 (d, *J* 2 Hz, 3′-H), δ 8.0 (d, *J* 2 Hz, 2′-H), and 8.15 (s, 5′-H), whilst the ^{1}H n.m.r. spectrum of 17β-hydroxy-17α-methyl-5α-androstano[3,2-*f*]pyrazolo[1,5-*a*]pyrimidine (6) shows signals at δ 0.85 (s, 18-CH_3), 0.92 (s, 19-CH_3), 1.25 (s, 17-CH_3), 6.50 (d, *J* 2 Hz, 3′-H), 8.00 (d, *J* 2 Hz, 2′-H) and 8.37 (s, 7′-H). A number of authors have attempted to show that for related nitrogen heterocycles, an emperical correlation exists between the chemical shifts and the electron densities. However, it has been pointed out that the observed chemical shifts are not a very reliable measure of π-electron density. Nevertheless, available spectral evidence from related azoloazines with bridgehead nitrogen [6] postulates a higher δ value for the proton at position 7′ in the steroid (6) compared with the δ value for the proton at position 5′ in the steroid (5). The chemical shift of 7′-H (δ 8.37) in the steroid (6) is observed at a higher value than the chemical shift of 5′-H (δ 8.15) in the steroid (5), and this further supports the structural assignment of the two compounds (5) and (6).

TABLE 2

Characteristic u.v. absorption wavelengths (nm)

Compound	λ/nm	log ε	Compound	λ/nm	log ε
(5)	232	4.60	(6)	209	4.41
				235	4.66
	317	3.40		238	4.66
				287	3.27
(14)	228	4.64	(13)	207	4.40
				229	4.65
	278	3.27		232	4.66
	318	3.28		280	3.23

The striking difference in the ^{1}H n.m.r. spectra of compounds (5) and (6) is the fact that the signal for the 7′-H of the compound (6) is broadened due to a small long-range coupling with the protons at C-1 whereas the 5′-H of the compound (5) gives a sharp singlet because of the absence of any long-range coupling. This long-range coupling between the C-1 protons and 7′-H possibly arises because of the higher bond order of the 6′–7′ bond [7] and was confirmed by double resonance experiments. Similar long-range coupling has been reported [6a] in *s*-triazolo[1,5-*a*]pyrimidines where it was observed that the methyl group protons at either position 6 or 7 of *s*-triazolo[1,5-*a*]pyrimidine (15) are coupled with the 7- or 6-H respectively (*J ca.* 0.4—1 Hz). Coupling between the methyl protons at position 5 and 6-H has not been observed.[6a]

The assignments of structures (5) and (6) are finally confirmed by ^{13}C n.m.r. evidence. The ^{13}C chemical shifts of the aromatic ring carbons of the pyrazolopyrimidines (5) and (6) are given in Table 3. The assignments quoted for the chemical shifts of the five carbons of the steroids (5) and (6) follow directly by analogy with the values allocated to the model compounds (13) and (14).[5] The chemical shift of C-5′ (δ 150.85 p.p.m.) in the condensation product (5) is found to be in good agreement with the chemical shift of C-5 (δ 148.58 p.p.m.) in 7-methylpyrazolo[1,5-*a*]pyrimidine (14), confirming an angular fusion of the steroid to the heterocyclic system, whilst the chemical shift of C-7′ (δ 133.10 p.p.m.) in the condensation product (6) agrees well with the chemical shift of C-7 (δ 134.43 p.p.m.) in 5-methylpyrazolo[1,5-*a*]-pyrimidine (13), confirming a linear fusion of the steroid to the heterocyclic system.

Under analogous reaction conditions, the condensation of 3-aminopyrazole (3) with 2-hydroxymethylene 5α-cholestan-3-one (2) gave 5α-cholest-2-eno[2,3-*g*]- (7) and 5α-cholestano[3,2-*f*]-pyrazolo[1,5-*a*]pyrimidine (8) whilst reaction of 3-aminopyrazole (3) with 2-hydroxymethylene-5α-spirostane-3,11-dione (16) gave 11-oxo-5α-spirost-2-eno[2.3-*g*]- (17) and 11-oxo-5α-spirostano-[3,2-*f*]-pyrazolo[1,5-*a*]pyrimidine (18).

Similarly the reaction of 3-amino-4-cyanopyrazole (4) with 2-hydroxymethylene-3-oxo-steroids (1) and (2) gave 17β-hydroxy-3′-cyano-17α-methyl-5α-androst-2-eno[2,3-*g*]- (9) and 17β-hydroxy-3′-cyano-17α-methyl-5α-androstano[3,2-*f*]- (10), and 3′-cyano-5α-cholest-2-eno-[2,3-*g*]- (11) and 3′-cyano-5α-cholestano[3,2-*f*]-pyrazolo-[1,5-*a*]pyrimidine (12), respectively.

TABLE 3

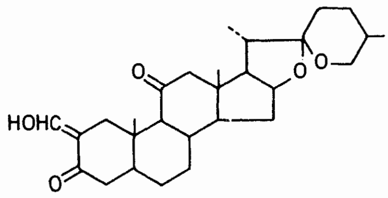
^{13}C Chemical shifts of steroidal pyrazolo[1,5-*a*]pyrimidines [δ (p.p.m.)]

Compound	C-2′	C-3′	C-3′a	C-5′	C-6′	C-7′	Other
(5)	143.68	96.68	147.70	150.85	115.62	142.96	
(6)	144.48	94.73	147.61	158.98	117.38	133.10	
(9)	146.53	82.67	148.89	154.28	119.10	145.17	CN, 112.99
(10)	147.19	80.85	148.73	163.94	120.66	134.14	CN, 113.18
(13)	145.01	95.68	148.30	158.90	108.74	134.43	
(14)	144.39	96.97	148.91	148.58	107.42	146.13	
(21)	149.11	82.12	149.20	154.62	119.71	145.24	CN, 114.43; CH_2CN 111.63
(24)	143.98	96.08	148.83	149.00	110.48	149.00	C-4, 110.73; C-5, 162.33
(37)	144.71	96.04	149.38	147.06	120.06	157.01	C=O, 170.54

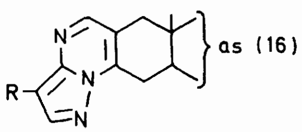
It was observed that the angularly fused product was again the major product when 3-aminopyrazole (3) was replaced by its 4-cyano-derivative (4). In one particular example, the reaction of 3-amino-4-cyanopyrazole (4) with 2-hydroxymethylene-5α-spirostane-3,11-dione (16), only the angularly fused product, 11-oxo-3′-cyano-5α-spirost-2-eno[2,3-*g*]pyrazolo[1,5-*a*]pyrimidine (19) was isolated.

The condensation of 3-amino-4-cyano-5-cyanomethylpyrazole (20) with 2-hydroxymethylene-3-oxo-steroids

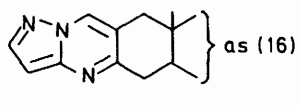
(1) and (2) afforded only the angularly fused products, 17β-hydroxy-3′-cyano-2′-cyanomethyl-17α-methyl-5α-androst-2-eno[2,3-*g*]- (21) and 3′-cyano-2′-cyanomethyl-5α-cholest-2-eno[2,3-*g*]-pyrazolo[1,5-*a*]pyrimidine (22).



(16)



(17) R = H
(19) R = CN



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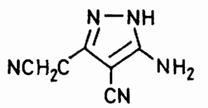

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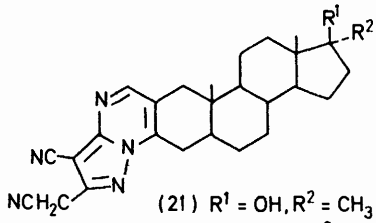
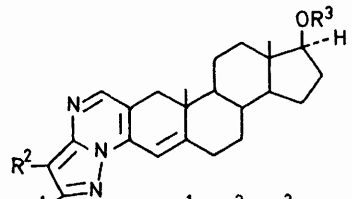


(21) R^1 = OH, R^2 = CH_3
(22) R^1 = C_8H_{17}, R^2 = H

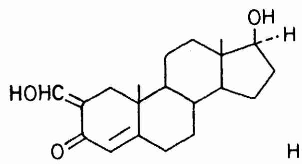


(24) R^1 = R^2 = R^3 = H
(25) R^1 = H, R^2 = CN, R^3 = H
(26) R^1 = CH_2CN, R^2 = CN, R^3 = H
(27) R^1 = H = R^2, R^3 = $COCH_3$
(28) R^1 = H, R^2 = CN, R^3 = $COCH_3$

These products were again identified by spectroscopic methods.

The condensation of 17β-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (23) with aminopyrazoles (3), (4), and (20), under analogous reaction conditions, also gave only the angularly fused products, 17β-hydroxyandrosta-2,4-dieno[2,3-*g*]- (24), 17β-hydroxy-3′-cyanoandrosta-2,4-dieno[2,3-*g*]- (25), and 17β-hydroxy-3′-cyano-2′-cyanomethylandrosta-2,4-dieno[2,3-*g*]-pyrazolo[1,5-*a*]pyrimidine (26), respectively. The 17β-acetoxy-derivatives (27) and (28) were obtained by acetylation of the steroids (24) and (25), respectively, using acetic anhydride in pyridine.

The reaction of 3-aminopyrazole (3) with 3β-hydroxy-16-hydroxymethylene-5α-androstan-17-one (29) gave 3β-hydroxy-5α-androst-16-eno[16,17-*g*]pyrazolo[1,5-*a*]pyrimidine (33). The i.r. spectrum of this product exhibited absorptions at 1 600, 1 545, and 1 510 cm^{-1} in the region 1 500—1 630 cm^{-1}, these compare well with the absorption in the i.r. spectrum of 17β-hydroxy-17α-methyl-5α-androstano[3,2-*f*]pyrazolo[1,5-*a*]pyrimidine (6) and thus it was predicted that the condensation product had the linear structure (32). However, the condensation product was actually shown to have the angular structure (33) from a consideration of its u.v. and ^{1}H and ^{13}C n.m.r. spectra. Similarly the condensation of 3-aminopyrazole (3) with either 3β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (30) or 16-hydroxymethylene-3-methoxyoestra-1,3,5(10)-trien-17-one (31) again gave only the angularly fused condensation products, 3β-hydroxyandrost-5,16-dieno-[16,17-*g*]- (34) and 3-methoxyoestra-1,3,5(10),16-tetraeno[16,17-*g*]-pyrazolo[1,5-*a*]pyrimidine (41), respectively. The compounds, 3β-hydroxy-3′-cyano-5α-androst-16-eno-[16,17-*g*]- (35), 3β-hydroxy-3′-cyanoandrosta-5,16-dieno-



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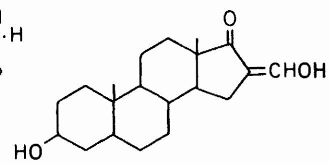
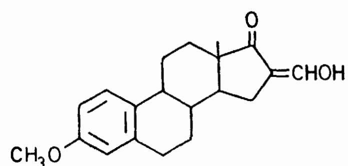


(29) 5α–H
(30) Δ^5



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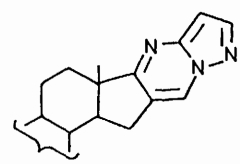
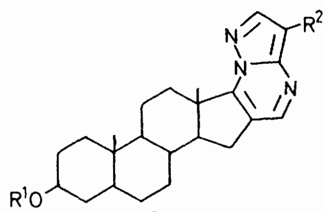
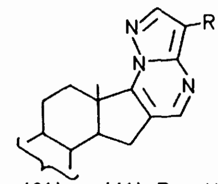

as (29) (32)



(33) R^1 = R^2 = H
(34) Δ^5, R^1 = R^2 = H
(35) R^1 = H, R^2 = CN
(36) Δ^5, R^1 = H, R^2 = CN
(37) R^1 = $COCH_3$, R^2 = H
(38) Δ^5, R^1 = $COCH_3$, R^2 = H
(39) R^1 = $COCH_3$, R^2 = CN
(40) Δ^5, R^1 = $COCH_3$, R^2 = CN



as (31) (41) R = H
(42) R = CN

[16,17-*g*]- (36), and 3′-cyano-3-methoxyoestra-1,3,5(10),-16-tetraeno[16,17-*g*]-pyrazolo[1,5-*a*]pyrimidine (42) were obtained by the reaction of 3-amino-4-cyanopyrazole (4) with 16-hydroxymethylene-17-oxo-steroids (29)—(31), respectively. The sterols (33)—(36) were acetylated using acetic anhydride in pyridine to give the corresponding 3β-acetyl derivatives (37)—(40).

It is evident that the substituents on the pyrazole nucleus as well as the β-dicarbonyl structure of the steroid markedly influence the course of the condensation of 3-aminopyrazoles with steroidal β-keto-aldehydes. Thus the condensation of 3-aminopyrazole (3) with 2-hydroxymethylene-3-oxo-steroids gives a mixture of linearly and angularly fused products. However the reaction of 3-amino-4-cyano-5-cyanomethylpyrazole (20) with 2-hydroxymethylene-3-oxo-steroids leads exclusively to the formation of angularly fused products. The reaction of 3-aminopyrazoles (3), (4), and (20) with 2-hydroxymethylene-Δ^4-3-oxo- and 16-hydroxymethylene-17-oxo-steroids always affords the angularly fused products. The condensation of 3-aminopyrazoles with steroidal β-ketoaldehydes proceeds by the mechanism similar to the one reported in our previous publication.[5b]

EXPERIMENTAL

M.p.s were determined on Gallenkamp apparatus and are uncorrected. The u.v. spectra were taken in methanol on a Unicam SP 800 spectrometer. I.r. spectra were recorded in bromoform on a Perkin-Elmer 157G spectrometer. ^{1}H N.m.r. spectra were recorded in deuteriated chloroform using tetramethylsilane as an internal standard on a Nuclear Magnetic Resonance Ltd. EM 360 (60 MHz) or a Varian HA 100 (100 MHz) spectrometer. Mass spectrometry was carried out on AEI MS902 instrument. ^{13}C N.m.r. spectra were obtained in deuteriated chloroform solutions on a Varian CFT-20 n.m.r. spectrometer operating at 20–80 MHz in the Fourier-transform mode at a probe temperature of 30°.

All the starting steroidal β-ketoaldehydes were prepared by the known literature methods.

General Procedure for the Condensation Reactions.—A solution of the steroidal β-ketoaldehyde (1.5×10^{-3} mol) and 3-aminopyrazole (3) or its derivative (4) or (20) (2×10^{-3} mol) in absolute alcohol (30 ml) was refluxed overnight. The mixture was evaporated to dryness *in vacuo*. The residue was chromatographed over alumina (activity II; 50 g) and the crude products thus obtained were recrystallised from suitable solvents.

17β-Hydroxy-17α-methyl-5α-androst-2-eno[2,3-g]- (5) *and 17β-Hydroxy-17α-methyl-5α-androstano*[3,2-f]*-pyrazolo-*[1,5-a]*pyrimidine* (6). Source. 17β-Hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (1) and 3-aminopyrazole (3). General. Alumina chromatography (eluant ether–ethyl acetate, 3 : 7). *Compound* (5) was recrystallised from ethanol as long needles (34%), m.p. 222—224°, $\nu_{max.}$ 3 590 (OH), 1 620, 1 530, 1 445, and 770 cm^{-1} (Found: C, 75.7; H, 8.7; N, 10.9%; M^+, 379.261 508. $C_{24}H_{33}N_3O$ requires C, 75.95; H, 8.75; N, 11.1%; *M*, 379.262 349). *Compound* (6) was recrystallised from ethanol as light brown crystals (27%), m.p. 186—188°, $\nu_{max.}$ 3 590 (OH), 1 625, 1 530, 1 500, 1 440, 1 405, and 765 cm^{-1} (Found: C, 75.75; H, 8.85; N, 10.95%; M^+, 397.261 132).

5α-Cholest-2-eno[2,3-g]- (7) *and 5α-Cholestano*[3,2-f]*-pyrazolo*[1,5-a]*pyrimidine* (8).—Source. 2-Hydroxymethylene-5α-cholestan-3-one (2) and 3-aminopyrazole (3). General. Alumina chromatography (eluant ether). *Compound* (7) was recrystallised from ethanol as crystals (35%), m.p. 165—167°, $\lambda_{max.}$ 283 and 317 nm (log ε 4.59 and 3.19), $\nu_{max.}$ 1 620, 1 530, 1 450, 1 440, 795, and 770 cm^{-1}, δ 0.70, 0.80, 0.84, and 0.90 (Me), 6.62 (1 H, d, *J* 2 Hz, 3′-H), 8.02 (1 H, d, *J* 2 Hz, 2′-H), and 8.20 (1 H, s, 5′-H) (Found: C, 80.75; H, 10.1; N, 9.05%; M^+, 461.376 241. $C_{31}H_{47}N_3$ requires C, 80.65; H, 10.25; N, 9.1%; *M*, 461.376 980). *Compound* (8) was recrystallised from ethanol as long yellow needles (18%), m.p. 138—140°, $\lambda_{max.}$ 206, 229, 233, and 280 nm (log ε 4.33, 4.76, 4.74, and 3.56), $\nu_{max.}$ 1 620, 1 530, 1 500, 1 465, 1 450, 1 405, and 765 cm^{-1}, δ 0.70, 0.80, 0.84, and 0.90 (Me), 6.47 (1 H, d, *J* 2 Hz, 3′-H), 7.98 (1 H, d, *J* 2 Hz, 2′-H), and 8.32 (1 H, s, 7′-H) (Found: C, 80.4; H, 10.35; N, 8.85%; M^+, 461.376 241).

17β-Hydroxy-3′-cyano-17α-methyl-5α-androst-2-eno-[2,3-g]- (9) *and 17β-Hydroxy-3′-cyano-17α-methyl-5α-androstano*[3,2-f]*-pyrazolo*[1,5-a]*pyrimidine* (10).—Source. 17β-Hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (1) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant ether–ethyl acetate, 2 : 3). *Compound* (9) was recrystallised from ethanol as crystals (24.7%), m.p. 246—248°, $\lambda_{max.}$ 206, 226, and 315 nm (log ε 3.91, 4.55, and 3.66), $\nu_{max.}$ 3 600 (OH), 2 220 (CN), 1 620, 1 535, 1 465, 1 440, 1 365, and 755 cm^{-1}, δ 0.84 (3 H, s, 18-H_3), 0.90 (3 H, s, 19-H_3), 1.24 (3 H, s, 17-H_3), 8.28 (1 H, s, 2′-H), and 8.42 (1 H, s, 5′-H) (Found: C, 73.95; H, 7.85; N, 13.5%; M^+, 404.256 375. $C_{25}H_{32}N_4O$ requires C, 74.2; H, 8.0; N, 13.85%; *M*, 404.256 774). *Compound* (10) was recrystallised from acetone to give crystals (18.5%), m.p. 212—215°, $\lambda_{max.}$ 207, 235, 240, and 315 nm (log ε 4.05, 4.66, 4.66, and 3.33), $\nu_{max.}$ 3 590 (OH), 2 220 (CN), 1 630, 1 510, 1 460, 1 440, 1 405, and 755 cm^{-1}, δ 0.82 (3 H, s, 18-H_3), 0.90 (3 H, s, 19-H_3), 1.22 (3 H, s, 17-H_3), 8.22 (1 H, s, 2′-H), and 8.42 (1 H, s, 7′-H) (Found: C, 74.85; H, 7.9; N, 13.6%; M^+, 404.257 598).

3′-Cyano-5α-cholest-2-eno[2,3-g]- (11) *and 3′-Cyano-5α-cholestano*[3,2-f]*-pyrazolo*[1,5-a]*pyrimidine* (12).—Source. 2-Hydroxymethylene-5α-cholestan-3-one (2) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant ether–ethyl acetate, 1 : 1). *Compound* (11) was recrystallised from acetone to give light yellow crystals (51%), m.p. 207—209°, $\lambda_{max.}$ 232, 279, and 314 nm (log ε 4.58, 3.73, and 3.77), $\nu_{max.}$ 2 220 (CH), 1 625, 1 535, 1 465, 1 440, 1 375, and 775 cm^{-1}, δ 0.70, 0.80, 0.82, 0.88, and 0.95 (Me), 8.27 (1 H, s, 2′-H), and 8.42 (1 H, s, 5′-H) (Found: C, 78.95; H, 9.55; N, 11.55%; M^+, 486.373 134. $C_{32}H_{46}N_4$ requires C, 78.95; H, 9.55; N, 11.5%; *M*, 486.372 229). *Compound* (12) was recrystallised from acetone to give yellow crystals (17%), m.p. 214—217°, *m/e* 486 (M^+), $\nu_{max.}$ 2 220 (CN), 1 630, 1 550, 1 505, 1 460, 1 405, and 750 cm^{-1}, δ 0.70, 0.80, and 0.90 (Me), 8.25 (1 H, s, 2′-H), and 8.45 (1 H, s, 7′-H) (Found: C, 78.65; H, 9.4; N, 11.6%).

11-Oxo-5α-spirost-2-eno[2,3-g]- (17) *and 11-Oxo-5α-spirostano*[3,2-f]*-pyrazolo*[1,5-a]*pyrimidine* (18).—Source. 2-Hydroxymethylene-5α-spirostane-3,11-dione (16) and 3-aminopyrazole (3). General. Alumina chromatography (eluant ether–ethyl acetate, 3 : 1). *Compound* (17) was restallised from acetone as crystals (40%), m.p. 243—245°, $\lambda_{max.}$ 207, 227, and 314 nm (log ε 4.33, 4.62, and 3.96), $\nu_{max.}$ 1 700 (CO), 1 620, 1 530, 1 450, 1 380, 1 350, and 770 cm^{-1}, δ 0.78 (3 H, s, 18-H_3), 1.04 (3 H, s, 19-H_3), 6.63 (1 H, d, *J* 2 Hz, 3′-H), 8.05 (1 H, d, *J* 2 Hz, 2′-H), and 8.20 (1 H, s, 5′-H) (Found: C, 73.7; H, 8.25; N, 7.95%; M^+, 503.312 372. $C_{31}H_{41}N_3O$ requires C, 73.9; H, 8.2; N, 8.35%; *M*, 503.314 775). *Compound* (18) was recrystallised from ethanol as yellow crystals (27%), m.p. 270—272°.

$\lambda_{max.}$ 208, 231, 280, and 316 nm (log ε 4.22, 4.70, 3.57, and 3.53), $\nu_{max.}$ 1 695 (CO), 1 620, 1 500, 1 445, 1 405, 1 380, and 765 cm^{-1}, δ 0.78 (3 H, s, 18-H_3), 1.02 (3 H, s, 19-H_3), 6.45 (1 H, d, *J* 2 Hz, 3'-H), 7.96 (1 H, d, *J* 2 Hz, 2'-H), and 8.35 (1 H, s, 7'-H) (Found: C, 73.5; H, 8.2; N, 8.2%; M^+, 503.312 836).

11-*Oxo*-3'-*cyano*-5α-*spirost*-2-*eno*[2,3-g]*pyrazolo*[1,5-a]-*pyrimidine* (19).—Source. 2-Hydroxymethylene-5α-spirostane-3,11-dione (16) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant ethyl acetate) gave *compound* (19) which was recrystallised from methanol to give yellow crystals (45%), m.p. 288—290°, $\lambda_{max.}$ 207, 227, and 314 nm (log ε 4.33, 4.62, and 3.96), $\nu_{max.}$ 2 220 (CN), 1 700 (CO), 1 540, 1 450, 1 385, 1 370, and 755 cm^{-1}, δ 0.76 (3 H, s, 18-H_3), 1.02 (3 H, s, 19-H_3), 8.26 (1 H, s, 2'-H), and 8.42 (1 H, s, 5'-H) (Found: C, 72.45; H, 7.65; N, 10.35%; M^+, 528.310 046. $C_{32}H_{40}N_4O_3$ requires C, 72.7; H, 7.65; N, 10.6%; *M*, 528.310 024).

17β-*Hydroxy*-3'-*cyano*-2'-*cyanomethyl*-17α-*methyl*-5α-*androst*-2-*eno*[2,3-g]*pyrazolo*[1,5-a]*pyramidine* (21).—Source. 17β-Hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (1) and 3-amino-4-cyano-5-cyanomethylpyrazole (20). General. After cooling the reaction mixture to room temperature, *compound* (21) was obtained directly as crystals (71%), m.p. 265—267°, $\lambda_{max.}$ 207, 232, and 313 nm (log ε 4.07, 4.65, and 3.76), $\nu_{max.}$ 3 600 (OH), 2 220 (CN), 1 625, 1 535, 1 490, 1 440, 1 405, 1 380, and 760 cm^{-1}, δ 0.85 (3 H, s, 18-H_3), 0.90 (3 H, s, 19-H_3), 1.25 (3 H, s, 17-H_3), 4.05 (2 H, s, 2'-CH_2CN), and 8.40 (1 H, s, 5'-H) (Found: C, 72.95; H, 7.55; N, 15.7%; M^+, 443.269 215. $C_{27}H_{33}N_5O$ requires C, 73.1; H, 7.5; N, 15.8%; *M*, 443.268 497).

3'-*Cyano*-2-*cyanomethyl*-5α-*cholest*-2-*eno*[2,3-g]*pyrazolo*-[1,5-a]*pyrimidine* (22).—Source. 2-Hydroxymethylene-5α-cholestan-3-one (2) and 3-amino-4-cyano-5-cyanomethylpyrazole (20). General. Alumina chromatography (eluant chloroform) gave *compound* (22) which was recrystallised from ethanol to give a solid (28%), m.p. 260—262°, $\lambda_{max.}$ 208, 231, and 311 nm (log ε 4.05, 4.48, and 3.69), $\nu_{max.}$ 2 220 (CN), 1 620, 1 540, 1 490, 1 460, 1 440, 1 400, 1 380, and 755 cm^{-1}, δ 0.70, 0.80, 0.84, and 0.90 (Me), 4.06 (2 H, s, 2'-CH_2CN), and 8.44 (1 H, s, 5'-H) (Found: C, 76.4; H, 8.9; N, 12.85%; M^+, 525.382 049. $C_{34}H_{47}N_5$ requires C, 77.65; H, 9.0; N, 13.35%; M^+, 525.383 128).

17β-*Hydroxyandrosta*-2,4-*dieno*[2,3-g]*pyrazolo*[1,5-a]-*pyrimidine* (24).—Source. 17β-Hydroxy-2-hydroxymethyleneandrost-4-en-3-one (23) and 3-aminopyrazole (3). General. Alumina chromatography (eluant ethyl acetate) gave *compound* (24) which was recrystallised from acetone to give yellow crystals (72%), m.p. 230—232°, $\lambda_{max.}$ 209, 235sh, 242, and 370 nm (log ε 3.89, 4.48, 4.57, and 3.98), $\nu_{max.}$ 3 595 (OH), 1 630, 1 590, 1 520, 1 460, and 770 cm^{-1}, δ 0.80 (3 H, s, 18-H_3), 1.00 (3 H, s, 19-H_3), 3.66 (1 H, m, 17-H), 6.56 (1 H, d, *J* 2 Hz, 3'-H), 7.00 (1 H, s, 4-H), 8.05 (1 H, d, *J* 2 Hz, 2'-H), and 8.18 (1 H, s, 5'-H) (Found: C, 75.8; H, 8.15; N, 11.5%; M^+, 363.231 059. $C_{23}H_{29}N_3O$ requires C, 76.0; H, 8.05; N, 11.55%; *M*, 363.231 050).

17β-*Hydroxy*-3'-*cyanoandrosta*-2,4-*dieno*[2,3-g]*pyrazolo*-[1,5-a]*pyrimidine* (25).—Source. 17β-Hydroxy-2-hydroxymethyleneandrost-4-en-3-one (23) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant chloroform) gave *compound* (25) which was recrystallised from ethanol to give yellow crystals (53%), m.p. 258—260°, $\lambda_{max.}$ 209, 239, 251, 313, and 364 (log ε 4.18, 4.50, 4.25, 3.59, and 3.94), $\nu_{max.}$ 3 600 (OH), 2 220 (CN), 1 630, 1 595, 1 530, 1 480, 1 375, and 760 cm^{-1}, δ 0.82 (3 H, s, 18-H_3), 1.04 (3 H, s, 19-H_3), 3.68 (1 H, t, 17-H), 6.98 (1 H, s, 4-H), 8.26 (1 H, s, 2'-H), and 8.40 (1 H, s, 5'-H) (Found: C, 75.95; H, 7.2; N, 14.3%; M^+, 388.225 263. $C_{24}H_{28}N_4O$ requires C, 74.2; H, 7.3; N, 14.45%; *M*, 388.226 300).

17β-*Hydroxy*-3'-*cyano*-2'-*cyanomethylandrosta*-2,4-*dieno*-[2,3-g]*pyrazolo*[1,5-a]*pyrimidine* (26).—Source. 17β-Hydroxy-2-hydroxymethyleneandrost-4-en-3-one (23) and 3-amino-4-cyano-5-cyanomethylpyrazole (20). General. Alumina chromatography (eluant chloroform) gave *compound* (26) which was recrystallised from acetone as yellow crystals (23%), m.p. 268—270°, $\nu_{max.}$ 3 590 (*OH*), *2 220* (CN), 1 630, 1 595, 1 530, 1 490, 1 380, and 925 cm^{-1}, δ 0.85 (3 H, s, 18-H_3), 1.05 (3 H, s, 19-H_3), 3.70 (1 H, m, 17-H), 4.10 (2 H, s, 2'-CH_2CN), 7.02 (1 H, s, 4-H), and 8.50 (1 H, s, 5'-H) (Found: C, 72.9; H, 6.8; N, 16.25%; M^+, 427.235 968. $C_{26}H_{29}N_5O$ requires C, 73.0; H, 6.85; N, 16.4%; *M*, 427.237 198).

3β-*Hydroxy*-5α-*androst*-16-*eno*[16,17-g]*pyrazolo*[1,5-a]*pyrimidine* (33).—Source. 3β-Hydroxy-16-hydroxymethylene-5α-androstan-17-one (29) and 3-aminopyrazole (3). General. Alumina chromatography (eluant ethyl acetate) gave *compound* (33) which was recrystallised from acetone as fine crystals (91%), m.p. 240—241°, $\lambda_{max.}$ 236 and 327 nm (log ε 4.51 and 3.38), $\nu_{max.}$ 3 590 (OH), 1 600, 1 545, 1 510, 1 455, 1 345, and 775 cm^{-1}, δ 0.90 (3 H, s, 18-H_3), 1.18 (3 H, s, 19-H_3), 3.65 (1 H, m, 3-H), 6.70 (1 H, d, *J* 2 Hz, 3'-H), 8.15 (1 H, d, *J* 2 Hz, 2'-H), and 8.45 (1 H, s, 5'-H) (Found: C, 75.35; H, 8.65; N, 11.85%; M^+, 365.245 445. $C_{23}H_{31}N_3O$ requires C, 75.55; H, 8.55; N, 11.5%; *M*, 365.246 700).

3β-*Hydroxyandrost*-5,16-*dieno*[16,17-g]*pyrazolo*[1,5-a]-*pyrimidine* (34).—Source. 3β-Hydroxy-16-hydroxymethyleneandrost-5-en-17-one (30) and 3-aminopyrazole (3). General. Alumina chromatography (eluant chloroform) gave *compound* (34) which was recrystallised from alcohol as long needles (84%), m.p. 248—249°, $\lambda_{max.}$ 206, 234, and 330 nm (log ε 3.99, 4.58, and 3.53), $\nu_{max.}$ 3 595 (OH), 1 600, 1 545, 1 510, 1 455, 1 370, and 755 cm^{-1}, δ 1.12 (3 H, s, 18-H_3), 1.25 (3 H, s, 19-H_3), 3.55 (1 H, m, 3-H), 5.45 (1 H, t, 6-H), 6.70 (1 H, d, *J* 2 Hz, 3'-H), 8.15 (1 H, d, *J* 2 Hz, 2'-H), and 8.40 (1 H, s, 5'-H) (Found: C, 75.8; H, 8.1; N, 11.95%; M^+, 363.229 650. $C_{23}H_{29}N_3O$ requires C, 76.0; H, 8.05; N, 11.55%; *M*, 363.231 050).

3β-*Hydroxy*-3'-*cyano*-5α-*androst*-16-*eno*[16.17-g]*pyrazolo*-[1,5-a]*pyrimidine* (35).—Source. 3β-Hydroxy-16-hydroxymethylene-5α-androstan-17-one (29) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant chloroform) gave *compound* (35) which was recrystallised from ethanol as crystals (40%), m.p. 316—318° (decomp.); $\nu_{max.}$ 3 590 (OH), 2 220 (CN), 1 610, 1 555, 1 520, and 770 cm^{-1}, δ 0.92 (3 H, s, 18-H_3), 1.18 (3 H, s, 19-H_3), 4.70 (1 H, m, 3-H), 8.30 (1 H, s, 2'-H), and 8.55 (1 H, s, 5'-H) (Found: C, 73.7; H, 7.9; N, 14.15%; M^+, 390.242 024. $C_{24}H_{30}N_4O$ requires C, 73.8; H, 7.75; N, 14.35%; *M*, 390.241 949).

3β-*Hydroxy*-3'-*cyanoandrosta*-5,16-*dieno*[16,17-g]*pyrazolo*-[1,5-a]*pyrimidine* (36).—Source. 3β-Hydroxy-16-hydroxymethyleneandrost-5-en-17-one (30) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant chloroform) gave *compound* (36) which was recrystallised from ethanol to give light yellow crystals (38%), m.p. 308—311° (decomp.), $\lambda_{max.}$ 207, 233, and 322 nm (log ε 4.12, 4.54, and 3.82), $\nu_{max.}$ 3 590 (OH), 2 220 (N), 1 610, 1 540, 1 520, 1 370, and 770 cm^{-1}, δ 0.92 (3 H, s, 18-H_3), 1.20 (3 H, s, 19-H_3), 3.70 (1 H, m, 3-H), 8.42 (1 H, s, 2'-H), and 8.65 (1 H, s, 5'-H) (Found: C, 74.05; H, 7.25; N, 14.4; M^+, 388.223 760. $C_{24}H_{28}N_4O$ requires C, 74.2; H, 7.25; N, 14.45%; *M*, 388.226 309).

3-*Methoxyoestra*-1,3,5(10),16-*tetraeno*[16,17-g]*pyrazolo*-[1,5-a]*pyrimidine* (41).—Source. 16-Hydroxymethylene-3-methoxyoestra-1,3,5(10)-trien-17-one (31) and 3-aminopyrazole (3). General. *Compound* (41) crystallised out as needles upon cooling the reaction mixture (98%), m.p. 203—205° (decomp.), $\nu_{max.}$ 1 600, 1 545, 1 510, 1 495, 1 455, 1 345, 775, and 755 cm^{-1}, δ 1.20 (3 H, s, 18-H_3), 3.74 (3 H, s, 3-OCH_3), 6.62—6.78 (3 H, m, 3'-, 2-, and 4-H), 7.20 (1 H, d, 1-H), 8.06 (1 H, d, *J* 2 Hz, 2'-H), and 8.33 (1 H, s, 5'-H) (Found: C, 76.65; H, 7.15; N, 12.0%; M^+, 359.198 064. $C_{23}H_{25}N_3O$ requires C, 76.85; H, 7.0; N, 11.8%; *M*, 359.199 752).

3'-*Cyano*-3-*methoxyoestra*-1,3,5(10),16-*tetraeno*[16,17-g]-*pyrazolo*[1,5-a]*pyrimidine* (42).—Source. 16-Hydroxymethylene-3-methoxyoestra-1,3,5(10)-trien-17-one (31) and 3-amino-4-cyanopyrazole (4). General. Alumina chromatography (eluant chloroform) gave *compound* (42) which was recrystallised from ethanol–chloroform to give crystals (53%), m.p. 255—257°, $\nu_{max.}$ 2 220 (CN), 1 610, 1 520, 1 500, and 955 cm^{-1}, δ 1.22 (3 H, s, 18-H_3), 3.76 (3 H, s, 3-OCH_3), 6.70—6.88 (2 H, m, 2- and 4-H), 7.30 (1 H, d, 1-H), 8.32 (1 H, s, 2'-H), and 8.58 (1 H, s, 5'-H) (Found: C, 74.75; H, 6.3; N, 14.65%; M^+, 384.195 502. $C_{24}H_{24}N_4O$ requires C, 74.95; H, 6.3; N, 14.6%; *M*, 384.195 001).

17β-*Acetoxyandrosta*-2,4-*dieno*[2,3-g]*pyrazolo*[1,5-a]*pyrimidine* (27).—A solution of 17β-hydroxyandrosta-2,4-dieno-[2,3-*g*]pyrazolo[1,5-*a*]pyrimidine (24) (400 mg, 1.11 × 10^{-3} mol) in pyridine (25 ml) containing a few drops of acetic anhydride was refluxed for 2 h. The solvent was evaporated *in vacuo* and the residue taken up in chloroform. The chloroform solution was washed with water, 5% hydrochloric acid, saturated sodium hydrogencarbonate solution, and water again before being dried ($MgSO_4$) and was evaporated to dryness. The residue was chromatographed over alumina. Elution with chloroform gave 17β-*acetoxy-androsta*-2,4-*dieno*[2,3-g]*pyrazolo*[1,5-a]*pyrimidine* (27) which was recrystallised from acetone as yellow crystals (290 m, 65%), m.p. 185—187°, $\lambda_{max.}$ 206, 242, and 374 nm (log ε 4.08, 4.54, and 3.77), $\nu_{max.}$ 1 715 (C=O), 1 625, 1 585, 1 520, 1 455, 1 420, 1 370, 1 355, 1 245, 1 035, 895, 860, and 770 cm^{-1}, δ 0.84 (3 H, s, 18-H_3), 1.00 (3 H, s, 19-H_3), 2.04 (3 H, s, 17-$OCOCH_3$), 4.62 (1 H, t, 17-H), 6.58 (1 H, d, *J* 2 Hz, 1 H, 3'-H), 7.00 (1 H, s, 4-H), 8.00 (1 H, d, *J* 2 Hz, 2'-H), and 8.20 (1 H, s, 5'-H) (Found: C, 74.2; H, 7.7; N, 10.55%; M^+, 405.239 142. $C_{25}H_{31}N_3O_2$ requires C, 74.05; H, 7.7; N, 10.35%; *M*, 405.241 614).

Similarly, treatment of compounds (25) and (33)—(36) with acetic anhydride in pyridine gave the corresponding acetyl derivatives (28) and (37)—(40).

17β-*Acetoxy*-3'-*cyanoandrosta*-2,4-*dieno*[2,3-g]*pyrazolo*-[1,5-a]*pyrimidine* (28) was recrystallised from ethanol as yellow crystals (54%), m.p. 235—237°, $\nu_{max.}$ 2 220 (CN), 1 720 (C=O), 1 628, 1 595, 1 520, 1 575, 1 370, and 760 cm^{-1}, δ 0.86 (3 H, s, 18-H_3), 1 04 (3 H, s, 19-H_3), 2.04 (3 H, s, 17-$OCOCH_3$), 4.62 (1 H, m, 17-H), 6.96 (1 H, s, 4-H), 8.26 (1 H, s, 2'-H), and 8.40 (1 H, s, 5'-H) (Found: C, 72.3; H, 6.95; N, 12.8%; M^+, 430.237 711. $C_{26}H_{30}N_4O_2$ requires C, 72.5; H, 7.05; N, 13.0%; *M*, 430.236 863).

3β-*Acetoxy*-5α-*androst*-16-*eno*[16,17-g]*pyrazolo*[1,5-a]-*pyrimidine* (37) was recrystallised from ethanol to give needles (61%), m.p. 264—265°, $\lambda_{max.}$ 235 and 330 nm (log ε 4.58 and 3.56), $\nu_{max.}$ 1 720 (CO), 1 600, 1 545, 1 510, 1 460, and 775 cm^{-1}; δ 0.90 (3 H, s, 18-H_3), 1.16 (3 H, s, 19-H_3), 2.00 (3 H, s, 3-$OCOCH_3$), 4.68 (1 H, m, 3-H), 6.63 (1 H, d, *J* 2 Hz, 3'-H), 8.04 (1 H, d, *J* 2 Hz, 2'-H), and 8.33 (1 H, s, 5'-H) (Found: C, 73.8; H, 8.15; N, 10.35%; M^+, 407.254 023. $C_{25}H_{33}N_3O_2$ requires C, 73.65; H, 8.15; N, 10.3%; *M*, 407.257 263).

3β-*Acetoxyandrosta*-5,16-*dieno*[16,17-g]*pyrazolo*[1,5-a]-*pyrimidine* (38) was recrystallised from ethanol as long needles (85%), m.p. 229—231°, $\lambda_{max.}$ 206, 234, 284, and 331 nm (log ε 3.84, 4.57, 3.16, and 3.33), $\nu_{max.}$ 1 720 (CO), 1 600, 1 545, 1 510, 1 460, 1 445, and 775 cm^{-1}, δ 1.12 (3 H, s, 18-H_3), 1.20 (3 H, s, 19-H_3), 2.02 (3 H, s, 3-$OCOCH_3$), 4.60 (1 H, m, 3-H), 5.42 (1 H, t, 6-H), 6.64 (1 H, d, *J* 2 Hz, 3'-H), 8.06 (1 H, d, *J* 2 Hz, 2'-H), and 8.34 (1 H, s, 5'-H) (Found: C, 74.15; H, 7.6; N, 10.65%; M^+, 405.239 518. $C_{25}H_{31}N_3O_2$ requires C, 74.05; H, 7.7; N, 10.35%; M^+, 405.241 614).

3β-*Acetoxy*-3'-*cyano*-5α-*androst*-16-*eno*[16,17-g]*pyrazolo*-[1,5-a]*pyrimidine* (39) was recrystallised from ethanol as crystals (58%), m.p. 335—337°, $\lambda_{max.}$ 207, 234, and 323 nm (log ε 4.11, 4.50, and 3.81), $\nu_{max.}$ 2 220 (CN), 1 720 (CO), 1 610, 1 550, 1 520, 1 365, and 755 cm^{-1}, δ 0.92 (3 H, s, 18-H_3), 1.18 (3 H, s, 19-H_3), 2.02 (3 H, s, 3-$OCOCH_3$), 4.70 (1 H, m, 3-H), 8.32 (1 H, s, 2'-H), and 8.56 (1 H, s, 5'-H) (Found: C, 72.35; H, 7.45; N, 12.9%; M^+, 432.253 011. $C_{26}H_{32}N_4O_2$ requires C, 72.2; H, 7.45; N, 12.95%; *M*, 432.252 512).

3β-*Acetoxy*-3'-*cyanoandrosta*-5,16-*dieno*[16,17-g]*pyrazolo*-[1,5-a]*pyrimidine* (40) was recrystallised from ethanol as crystals (59%), m.p. 298—300° (decomp.), $\lambda_{max.}$ 208, 239, and 324 nm (log ε 4.07, 4.49, and 3.75), $\nu_{max.}$ 2 220 (CN), 1 720 (CO), 1 610, 1 550, 1 520, 1 380, and 950 cm^{-1}, δ 1.12 (3 H, s, 18-H_3), 1.22 (3 H, s, 19-H_3), 2.02 (3 H, s, 3-$OCOCH_3$), 4.58 (1 H, m, 3-H), 5.45 (1 H, t, 6-H), 8.32 (1H, s, 3'-H), and 8.58 (1 H, s, 5'-H) (Found: C, 72.4; H, 7.0; N, 13.5%; *m/e* 370. $C_{26}N_{30}N_4O_2$ requires C, 72.5; H, 7.05; N, 13.0%; $M^+ - CH_3CO_2H$, 370).

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