New Steroidal Heterocycles: Synthesis and Structure of Androst-4-eno[3,2-*f*]-(*s*-triazolo[4,3-*b*]pyridazine), Androstano[17,16-*f*]-(*s*-triazolo-[4,3-*b*]pyridazines), and 2-(1,2,4-Triazol-4-ylaminomethylene)-3-(1,2,4-triazol-4-ylamino)-5α-androst-2-ene

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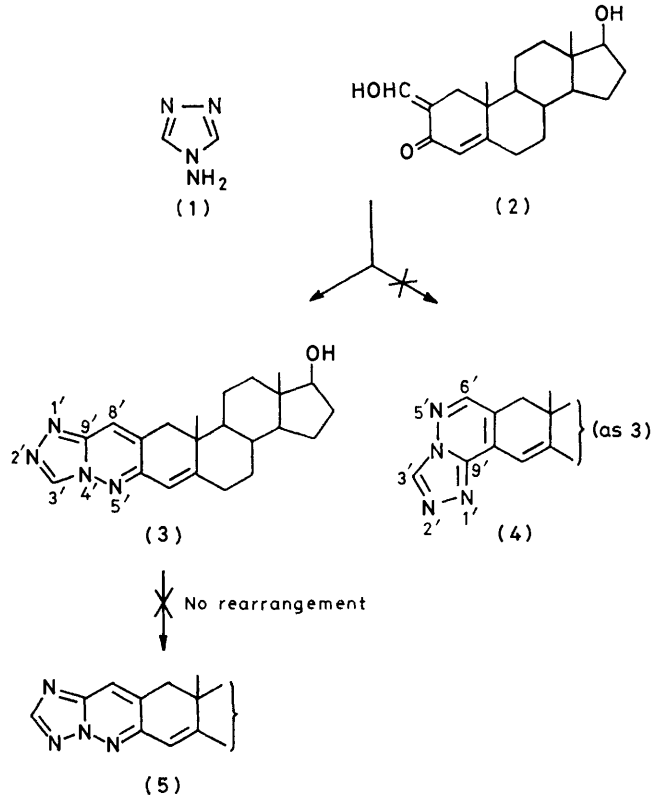
The reaction of 4-amino-1,2,4-triazole (1) with the 2-hydroxymethylene-3-oxo-Δ^4-steroid (2) and three 16-hydroxymethylene-17-oxo-steroids gave solely and in good yield androst-4-eno[3,2-*f*]-(*s*-triazolo[4,3-*b*]pyridazine) (3), the androstano[17,16-*f*]-(*s*-triazolo[4,3-*b*]pyridazines) (14) and (15), and 3-methoxyestra-1,3,5(10)-trieno[17,16-*f*]-(*s*-triazolo[4,3-*b*]pyradazine) (16) respectively. However, the reaction of 4-amino-1,2,4-triazole (1) with 2-hydroxymethylene-3-oxo-steroids without a Δ^4-double bond, under analogous conditions resulted in the formation of 2-(1,2,4-triazol-4-ylaminomethylene)-3-(1,2,4-triazol-4-ylamino)-steroids (7) and (9), also in high yield. The structures of these products were established by i.r., u.v., ^{1}H n.m.r., and ^{13}C n.m.r. spectroscopy. Chemical evidence for the mechanism of these condensation reactions is discussed. Although conditions favourable for Dimroth Rearrangement were employed, no such transformations were encountered during the synthesis of the steroidal triazolopyridazines.

As a part of our studies directed towards the development of new aza-steroids of biological interest,[1] we report the results of the reaction of 4-amino-1,2,4-triazole (1) with steroidal β-diketones.



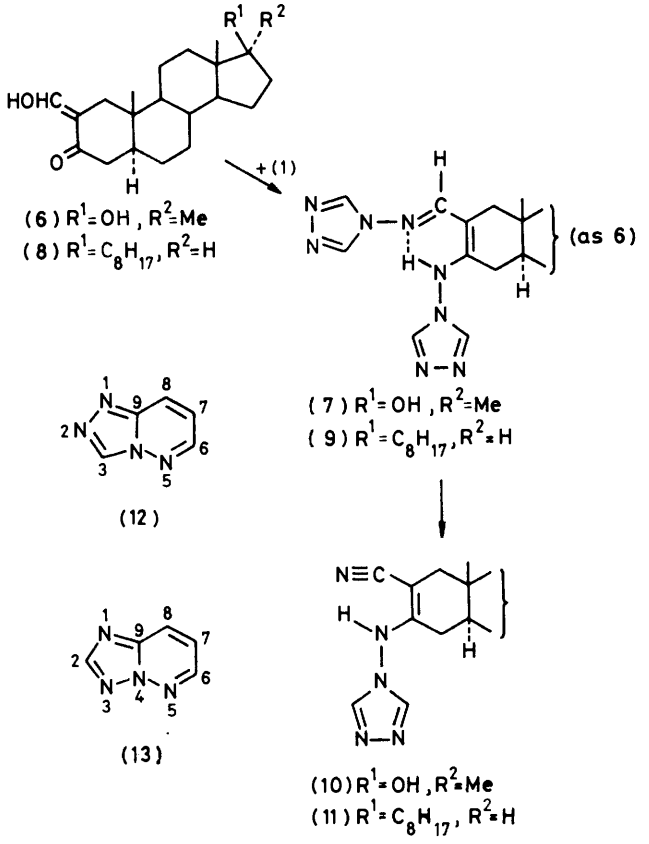
The condensation of 4-amino-1,2,4-triazole (1) with the Δ^4-unsaturated β-diketone, 17β-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (2) could conceivably afford 17β-hydroxyandrost-4-eno[3,2-*f*]-(*s*-triazolo[4,3-*b*]-pyridazine) (3) and/or 17β-hydroxyandrost-2,4-dieno-[2,3-*g*]-(*s*-triazolo[4,3-*b*]-pyridazine) (4). In fact, refluxing a solution of the steroid (2) with 4-amino-1,2,4-triazole (1) in dry toluene containing a catalytic amount of toluene-*p*-sulphonic acid for 24 h, results solely in the formation of the triazolopyridazine (3) in good yield, whose structure is discussed below.

However, under similar reaction conditions, the saturated β-diketone, 17β-hydrozy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (6) condenses with 4-amino-1,2,4-triazole (1) to give the acyclic bisanil, 17β-hydroxy-17α-methyl-2-(1,2,4-triazol-4-ylaminomethylene)-3-(1,2,4-triazol-4-ylamino)-5α-androst-2-ene (7). The elemental analysis of the bisanil (7) was consistent with its formulation as $C_{25}H_{36}N_8O$, whilst its u.v. spectrum showed $\lambda_{max.}$ (CH_3OH) at 320 nm (log ε 4.20), indicative of a highly conjugated system. The ^{1}H n.m.r. ($CDCl_3$) spectrum exhibited signals at δ 0.75 (s, 18-CH_3), 0.85 (s, 19-CH_3), 1.20 (s, 17-CH_3), 7.37 (s, N=C*H*-), 8.25 (s, triazole 2 H's), and 8.52 and 8.62 (each s, triazole, 2 H), 10.5 (s, N*H*, exchanges with D_2O). The mass spectrum failed to show a peak corresponding to the molecular ion of steroid (7), but indicated a molecular ion at 395 due to the formation of the nitrile (10), which arises from the loss of a 1,2,4-triazole fragment from the bisanil (7).

Similarly the reaction of 4-amino-1,2,4-triazole (1) with 2-hydroxymethylene-5α-cholestan-3-one (8) gave an analogous acyclic condensation product (9) in 80% yield, whose structure also followed from its analytical and spectroscopic data.

The i.r. spectrum of 17β-hydroxyandrost-4-eno[3,2-*f*]-(*s*-triazolo[4,3-*b*]pyridazine) (3) exhibited absorptions at 3 130(w), 1 630, 1 615, 1 485, 1 440, and 1 375 cm^{-1}, which closely resembled the i.r. spectra of 6-methyl- and 8-methyl-*s*-triazolo[4,3-*b*]pyridazine.[2] The ^{1}H n.m.r. ($CDCl_3$) spectrum of the condensation product (3) showed signals at δ 0.85 (s, 18-CH_3), 1.05 (s, 19-CH_3), 3.70 (t, 17-H), 6.27 (s, 4-H), 7.70 (s, 8′-H), and 8.90 (s, 3′-H), the assignment of chemical shifts to 3′-H and 8′-H being based upon the earlier studies of *s*-triazolo-[4,3-*b*]pyridazines.[2]

Of particular interest in the ^1H n.m.r. spectrum of compound (3) is the fact that the 8′-H singlet is broadened as a result of long-range coupling with the C-1 methylene protons. This long-range coupling was confirmed by double-resonance experiments, irradiation at the frequency of the methylene protons sharpening the broad signal of 8′-H. Similar long-range coupling has been reported in *s*-triazolo[4,3-*b*]pyridazines [2] where it was observed that the methyl group protons at either positions 8 or 7 of *s*-triazolo[4,3-*b*]pyridazine (12) are



coupled with 7-H or 8-H respectively (J = 1.2 Hz). Since coupling between the methyl protons at position 7 and 6-H has not been observed,[2] the alternative structure (4) for the condensation product is discounted since it would be expected to show a sharp singlet for 6′-H as a result of the absence of long-range coupling.

The assignment for structure (3) was further supported by ^{13}C n.m.r. evidence. The ^{13}C chemical shifts of the aromatic ring carbons of the triazolopyridazine (3) are given in the Table along with those of the two model

^{13}C N.m.r. chemical shifts of aromatic ring carbons (p.p.m.)

Compound	C-3′	C-6′	C-7′	C-8′	C-9′
(3)	137.95	150.91	130.43	119.58	143.89
(12)	139.04	146.57	121.20	124.61	143.31
(13)	152.50 (C-2)	144.55	123.04	125.92	144.05
(17)	138.03	164.67	138.41	117.43	143.99
(18)	138.31	170.34	137.52	118.68	144.05
(19)	137.38	170.14	138.42	118.76	140.33

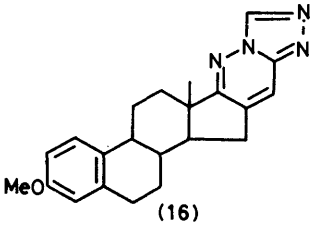
compounds *s*-triazolo[4,3-*b*]pyridazine (12) and *s*-triazolo[1,5-*b*]pyridazine (13).[3] The assignments quoted for the chemical shifts of the five carbons of the steroid (3) follow directly by analogy with the values allocated to the comparable ring system (12). It should be especially noted that the chemical shift of C-8′ (119.58 p.p.m.) in the condensation product (3) is in agreement with the chemical shift of C-8 (124.61 p.p.m.) in the triazolopyridazine (12) thus indicating a linear fusion of the steroid to the heterocyclic system. If the condensation product had the angular structure (4), the chemical shift of C-6′ would have been expected to appear in the region of 146.57 p.p.m., which is the value assigned to C-6 in the compound (12).

Isomerisation of fused *s*-triazoles by acid, base, or heat has been reported.[4] However, no such transformation was encountered during the reaction of 4-amino-1,2,4-triazole (1) with 17β-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (2) in refluxing toluene (24 h) and indeed the condensation product (3) was recovered unchanged after being heated with either formic acid for 12 h or pyridine for 3 h. *s*-Triazolo[4,3-*b*]pyridazines have been shown to resist rearrangement,[5] and the spectroscopic evidence quoted above which shows that the condensation product has structure (3), also excludes the isomeric structure (5). Reimlinger and Pieren [6] as well as Paudler and Helmic [7] have shown that, in a series of triazolopyrimidines, the triazole proton with N-4 of the triazole ring at a ring junction [as in (3)] is deshielded in comparison with the triazole proton in the isomeric series with the triazole N-1 at the ring junction [as in (5)]. If the condensation product had had structure (5), the triazole proton would have had a chemical shift comparable to that of the corresponding proton at C-2 (δ 8.38) in *s*-triazolo[1,5-*b*]pyridazine [8] (13). The low-field triazole proton in the condensation product is, in fact, observed at δ 8.90. This corresponds closely to the chemical shift of the proton at C-3 (δ 9.15) in *s*-triazolo[4,3-*b*]pyridazine (12),[2] indicating that structure (3) is correctly written with N-4 of the triazole ring occupying the bridgehead position.

Conclusive support for structure (3) rather than the isomeric structure (5) again comes from ^{13}C n.m.r. spectroscopy. One major difference between the carbon atom C-2 of *s*-triazolo[1,5-*b*]pyridazine (13) and the carbon atom C-3 of *s*-triazolo[4,3-*b*]pyridazine (12) is that C-2 of pyridazine (13) is bonded to two ring nitrogens whereas C-3 of pyridazine (12) is bonded to a ring nitrogen and the bridgehead nitrogen. For nitrogen heterocyclic systems, the carbons bonded to nitrogen atoms are known to be appreciably deshielded relative to benzene while β-carbons are shielded.[9] Nitrogen atoms at bridgehead positions, however, have little deshielding effect on the adjacent carbon atoms owing to the significant delocalisation of the lone pair of electrons.[10] Thus the chemical shift of C-2 in pyridazine (13) occurs further downfield (152.5 p.p.m.) as compared to the chemical shift of C-3 in pyridazine (12) which occurs at 139.04 p.p.m. In the ^{13}C n.m.r. spectrum of the steroidal triazolopyridazine

(3), the chemical shift of C-3′ was found to be 137.95 p.p.m., consistent with the structure (3).

The condensation reaction of 4-amino-1,2,4-triazole (1) was successfully extended to 16-hydrozymethylene-17-oxo steroids. Thus the condensation of (1) with



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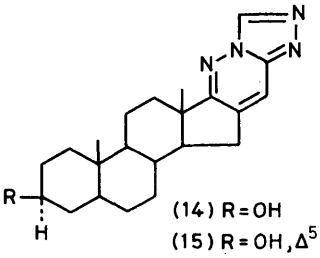
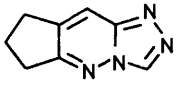


(14) R = OH
(15) R = OH, Δ^5
(18) R = OAc
(19) R = OAc, Δ^5



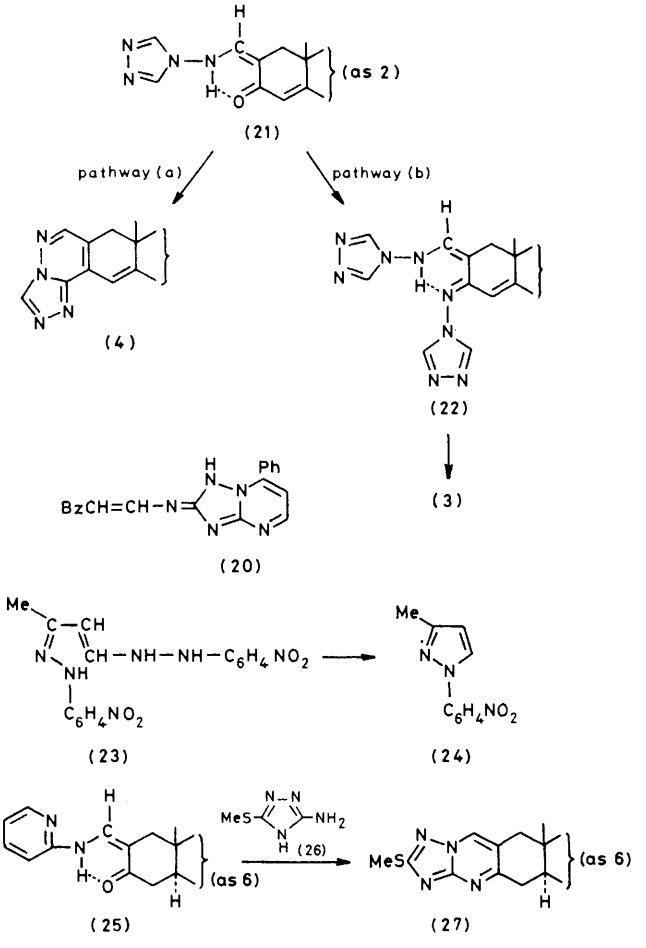
(17)

3β-hydroxy-16-hydroxymethylene-5α-androstan-17-one, 3β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one, 16-hydroxymethylene-3-methoxyestra-1,3,5(10)-trien-17-on, and 2-hydroxymethylenecyclopentanone under analogous reaction conditions gave 3β-hydroxy-5α-androstano[17,16-*f*]-(*s*-triazolo[4,3-*b*]pyridazine) (14), 3β-hydroxyandrost-5-eno[17,16-*f*]-(*s*-triazolo-[4,3-*b*]-pyridazine) (15), 3-methoxyestra-1,3,5(10)-trieno[17,-16-*f*]-(*s*-triazolo[4,3-*b*]pyridazine) (16), and 6,7-dihydro-8*H*-cyclopenta[*d*]-*s*-triazolo[4,3-*b*]pyridazine (17) respectively. Acetylation of the sterols (14) and (15) gave the corresponding acetyl derivatives, (18) and (19).

We believe that the mechanism of the condensation of the aminotriazole (1) with steroidal β-diketones is correctly represented as passing through a bisanil of type (22). Initially there appears to be two possible sites for the condensation of the 4-amino-group of triazole (1) with the Δ^4-2-hydroxymethylene-3-oxo-steroid (2). However, it seems more likely that the amino-group of (1) would first react with the 2-formyl group to give the 3-oxo-2-anil (21) by analogy with the reaction of β-oxo-acetals with aniline [11] and the isolation of 2-(2-benzoyl-vinylimino)-5-phenyl-*s*-triazolo[1,5-*a*]pyrimidine (20) as a by-product during the reaction between 3,5-diamino-1,2,4-triazole and β,β-dimethoxypropiophenone.[12] However, direct cyclisation [by pathway (a)] of the β-oxo-anil (21) would result in the formation of 17β-hydroxyandrost-2,4-dieno[2,3-*g*]-(*s*-triazolo[4,3-*b*]pyrid-azine) (4), which obviously is at variance with the correct structure (3) of the product obtained.

Thus it is clear that some other intermediate must interpose between the oxo-anil (21) and the final condensation product (3), and the condensation of the oxo-anil (21) with another molecule of the triazole (1) to give a bisanil (22) furnishes just such an intermediate [pathway (b)]. The bisanil (22) then spontaneously undergoes a cyclisation to form 17β-hydroxyandrost-4-eno[3,2-*f*]-(*s*-triazolo[4,3-*b*]pyridazine) (3). It was of interest to observe that the bisanils (7) and (9), which were the sole products obtained from the reaction of 4-amino-1,2,4-triazole (1) with the β-dioxo-steroids (6) and (8) respectively, could not be cyclised.

Support for the route outlined in pathway (b) comes from a study of the reaction of *p*-nitrophenylhydrazine with 4-methoxybut-3-en-2-one,[12] in which an attempt to condense 1 mol of the hydrazine with the methoxy-vinyl ketone produced the bishydrazone (23) which, when heated, cyclised to the known 3-methyl-1-*p*-nitrophenylpyrazole (24), with the loss of 1 mol of *p*-nitrophenylhydrazine. We have also observed a similar sequence of reactions during the condensation of 17β-hydroxy-17α-methyl-2-(2-pyridylaminomethylene)-5α-androstan-3-one (25) and 3-amino-5-methylthio-1,2,4-triazole (26) to yield 17β-hydroxy-17α-methyl-2′-methyl-thio-5α-androstano[3,2-*f*]-(*s*-triazolo-[1,5-*a*]pyrimidine) (27).



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, unless otherwise stated, on a Perkin-Elmer 157G spectrometer. ^{1}H N.m.r. spectra were recorded in deuteriated chloroform using tetramethylsilane as an

internal standard on Nuclear Magnetic Resonance Ltd EM 360 (60 MHz) or Varian HA 100 (100 MHz) spectrometers. Mass spectrometry was carried out on AEI MS 902 instrument. ^{13}C N.m.r. spectra were obtained in deuteriochloroform 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 °C.

All the starting steroidal β-diketones were prepared by the known literature routes.

17β-*Hydroxyandrost*-4-*eno*[3,2-f]-(s-*triazolo*[4,3-b]*pyridazine*) (3).—A solution of 17β-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (2) (0.316 g, 1×10^{-3} mol), 4-amino-1,2,4-triazole (1) (0.126 g, 1.5×10^{-3} mol), and toluene-*p*-sulphonic acid (20 mg) in dry toluene (30 ml) was refluxed overnight. After cooling, the reaction mixture was evaporated *in vacuo* to dryness and the residue chromatographed over alumina (activity II) using chloroform as the eluant to give the title compound (3) (0.138 g, 37%). Recrystallisation from ethanol gave yellow crystals, m.p. 243—245 °C, $\lambda_{max.}$ 243, 250, and 288 nm (log ε 4.40, 4.42, and 3.95), $\nu_{max.}$ 3 590 (OH), 1 630, 1 615, 1 485, 1 440, and 1 375 cm^{-1}; δ 0.85 (s, 3 H, 18-CH_3), 1.05 (s, 3 H, 19-CH_3), 3.70 (t, 1 H, 17-H), 6.27 (s, 1 H, 4-H), 7.70 (s, 1 H, 8′-H), 8.90 (s, 1 H, 3′-H) (Found: C, 72.25; H, 7 8; N, 14 95%; M^+, 364.225 7. $C_{22}H_{28}N_4O$ requires C, 72.48; H, 7.68; N, 15.37%; *M*, 364.226 00).

17β-*Hydroxy*-17α-*methyl*-2-(1,2,4-*triazol*-4-*ylamino-methylene*)-3-(1,2,4-*triazol*-4-*ylamino*)-5α-*androst*-2-*ene* (7).—This compound was prepared in the manner described above except that two equivalents (0.168 g) of 4-amino-1,2,4-triazole (1) were used for one equivalent (0.332 g) of steroid (6) and the product was eluted over alumina using 10% methanol in chloroform. Recrystallisation from methanol–benzene gave a white solid (78%), m.p. 200—202 °C, *m/e* 395 ($M^+ - 69$), $\lambda_{max.}$ 208 and 320 nm (log ε 3.95 and 4.20), $\nu_{max.}$ (Nujol) 3 400 (OH), 3 100 (NH), 1 630, 1 555, 1 500, 1 460, 1 375, 1 190, and 1 060 cm^{-1}; δ 0.75 (s, 3 H, 18-CH_3), 0.85 (s, 3 H, 19-CH_3), 1.20 (s, 3 H, 17-CH_3), 7.37 (s, 1 H, N=C*H*–), 8.25 (s, triazole 2 H's), 8.52 and 8.62 (each s, triazole 2 H's), and 10.5 (s, N*H*, exchanges with D_2O) (Found: C, 64.3; H, 7.55; N, 23.95; $C_{25}H_{36}N_8O$ requires C, 64.65; H, 7.76; N, 24.13%).

2-(1,2,4-*Triazol*-4-*ylaminomethylene*)-3-(1,2,4-*triazol*-4-*ylamino*)-5α-*cholest*-2-*ene* (9).—The title compound was prepared from 2-hydroxymethylene-5α-cholestan-3-one (0.414 g, 1×10^{-3} mol) following the procedure described for (7). Recrystallisation from ethanol–chloroform gave fine crystals (80%), m.p. 244—245 °C (decomp.), *m/e* 477 ($M^+ - 69$), $\lambda_{max.}$ 207 and 321 nm (log ε 4.01 and 4.21), $\nu_{max.}$ (Nujol) 3 110 (NH), 1 630, 1 570, 1 460, 1 380, and 1 060 cm^{-1} (Found: C, 69.65; H, 9.2; N, 20.15. $C_{32}H_{50}N_8$ requires C, 70.28; H, 9.22; N, 20.50%).

3β-*Hydroxy*-5α-*androstano*[17,16-f]-(s-*triazolo*[4,3-b]-*pyridazine*) (14).—This compound was prepared from 3β-hydroxy-16-hydroxymethylene-5α-androstan-17-one (0.318 g, 1×10^{-3} mol) and 4-amino-1,2,4-triazole (1) (0.126 g, 1.5×10^{-3} mol) in the manner described for compound (3). Recrystallisation from acetone gave white needles (78%), m.p. 287—289 °C (decomp.), $\lambda_{max.}$ 215 and 291 nm (log ε 4.27 and 3.56); $\nu_{max.}$ 3 590 (OH), 1 515, 1 415, and 1 375 cm^{-1}; δ 0.90 (s, 3 H, 18-CH_3), 1.10 (s, 3 H, 19-CH_3), 3.60 (m, 1 H, 3-H), 7.80 (s, 1 H, 8′-H), and 8.95 (s, 1 H, 3′-H) (Found: C, 71.85; H, 8.3; N, 15.2%; M^+, 366.241 198. $C_{22}H_{30}N_4O$ requires C, 72.08; H, 8.25; N, 15.30%; *M*, 366.241 949).

3β-*Hydroxyandrost*-5-*eno*[17,16-f]-(s-*triazolo*[4,3-b]*pyridazine*) (15).—Treatment of 3β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (0.316 g, 1×10^{-3} mol) with 4-amino-1,2,4-triazole (1) (0.126 g, 1.5×10^{-3} mol) in the manner described for the preparation of compound (3), followed by recrystallisation from ethanol, gave the title compound as white needles, (83%), m.p. 245—247 °C, $\lambda_{max.}$ 215 and 291 nm (log ε 4.28 and 3.50); $\nu_{max.}$ 3 590 (OH), 1 510, 1 450, 1 430, and 1 375 cm^{-1}, δ 1.07 (s, 3 H, 18-CH_3), 1.10 (s, 3 H, 19-CH_3), 3.55 (m, 1 H, 3-H), 5.40 (t, 1 H, 6-H), 7.80 (s, 1 H, 8′-H), and 8.90 (s, 1 H, 3′-H) (Found: C, 72.25; H, 7.7; N, 15.0%; M^+, 364.224 701. $C_{22}H_{28}N_4O$ requires C, 72.48; H, 7.75; N, 15.38%; *M*, 364.226 300).

3-*Methoxyestra*-1,3,5(10)-*trieno*[17,16-f]-(s-*triazolo*-[4,3-b]*pyridazine*) (16).—The title compound was obtained in 85% yield from 16-hydroxymethylene-3-methoxyestra-1,3,5(10)-trien-17-one (0.312 g, 1×10^{-3} mol) and 4-amino-1,2,4-triazole (1) (0.126 g, 1.5×10^{-3} mol) by the procedure described for the preparation of compound (3). It was recrystallised from ethanol to give white needles, m.p. 232—234 °C, $\nu_{max.}$ 1 605, 1 500, 1 450, and 1 375 cm^{-1}; δ 1.15 (s, 3 H, 18-CH_3), 3.80 (s, 3 H, 3-OCH_3), 6.65—7.30 (3 H, 1-H, 2-H, 4-H), 7.80 (s, 1 H, 8′-H), and 8.90 (s, 1 H, 3′-H) (Found: C, 73.6; H, 6.65; N, 15.2%; M^+, 360.193 466. $C_{22}H_{24}N_4O$ requires C, 73.29; H, 6.76; N, 15.55%; *M*, 360.195 001).

6,7-*Dihydro*-8H-*cyclopenta*[d]-(s-*triazolo*[4,3-b]*pyridazine*) (17).—This compound was prepared from 2-hydroxymethylenecyclopentanone (0.9 g, 8×10^{-3} mol) and 4-amino-1,2,4-triazole (1) (1.0 g, 1.2×10^{-2} mol) by the method described for the preparation of compound (3). Recrystallisation from benzene gave white crystals (60%), m.p. 139—140 °C, $\lambda_{max.}$ 219 and 296 nm (log ε 4.64 and 3.51); $\nu_{max.}$ 3 140, 1 545, 1 510, 1 445, 1 420, and 1 380 cm^{-1}; δ 2.35 (m, 2 H, 7-H's), 3.00 (m, 4 H, 6-H's and 8-H's), 7.85 (s, 1 H, 9-H), and 9.00 (s, 1 H, 3-H) (Found: C, 59.85; H, 5.05; N, 35.0%; M^+ 160.074 115. $C_8H_8N_4$ requires C, 60.00; H, 5.00; N, 35.00%; *M*, 160.074 892).

3β-*Acetoxy*-5α-*androstano*[17,16-f]-(s-*triazolo*[4,3-b]-*pyridazine*) (18).—A solution of compound (14) (0.2 g, 5.4×10^{-4} mol) in dry pyridine (20 ml) containing a few drops of acetic anhydride was refluxed for 2 h. After cooling, the solution was evaporated to dryness *in vacuo*. The residue was taken up in chloroform, washed with 5% hydrochloric acid solution, water, and finally with saturated sodium chloride solution. The chloroform solution was dried ($MgSO_4$), evaporated to dryness *in vacuo*, and the residue recrystallised from ethanol to give the title compound (0.136 g, 61%), m.p. 311—313 °C (decomp.), $\lambda_{max.}$ 214 and 293 nm (log ε 4.28 and 2.50); $\nu_{max.}$ 1 715 (CO), 1 515, 1 445, and 1 350—1 365 cm^{-1}; δ 0.92 (s, 3 H, 18-CH_3), 1.10 (s, 3 H, 19-CH_3), 2.02 (s, 3 H, 3-$OCOCH_3$), 4.70 (m, 1 H, 3-H), 7.80 (s, 1 H, 8′-H), and 9.00 (s, 1 H, 3′-H) (Found: C, 70.45; H, 7.85; N, 13.5%; M^+, 408.251 875. $C_{24}H_{32}N_4O$ requires C, 70.54; H, 7.83; N, 13.71%; *M*, 408.252 512).

3β-*Acetoxyandrost*-5-*eno*[17,16-f]-(s-*triazolo*[4,3-b]*pyridazine*) (19).—Treatment of (15) (0.20 g, 5.4×10^{-4} mol) in the above-described manner, followed by recrystallisation from methanol, gave white needles (67%), m.p. 293—295 °C, $\nu_{max.}$ 1 720 (CO), 1 510, 1 450, 1 430, and 1 375 cm^{-1}; δ 1.15 (s, 6 H, 18-CH_3 and 19-CH_3), 2.07 (s, 3 H, 3-$OCOCH_3$), 4.65 (m, 1 H, 3-H), 5.50 (t, 1 H, 6-H), 7.85 (s, 1 H, 8′-H), and 9.00 (s, 1 H, 3′-H) [Found: C, 70.0; H, 7.3; N, 13.35%; M^+, 346 ($M - 60$). $C_{24}H_{30}N_4O$ requires C, 70.93; H, 7.38; N, 13.79%; *M*, 406].

17β-*Hydroxy*-17α-*methyl*-2-(2-*pyridylaminomethylene*)-5α-*androstan*-3-*one* (25).—A solution of 17β-hydroxy-2-hydroxymethylene-17α-methyl-5α-androstan-3-one (0.31 g, 9.1 × 10^{-4} mol) and 2-aminopyridine (0.093 g, 9.9 × 10^{-4} mol) in pyridine (5 ml) was set aside at room temperature overnight. The pyridine solution was evaporated to dryness *in vacuo* and the residue taken up in chloroform, washed with 5% hydrochloric acid solution and saturated sodium chloride solution and the chloroform solution dried ($MgSO_4$) and evaporated to dryness. The crude product was then purified by chromatography over alumina using ethyl acetate as the eluant and recrystallised from methanol to give yellow crystals (45%), m.p. 106—107 °C (lit.,[13] 102—104 °C), $\lambda_{max.}$ 235, 292, and 353 nm (log ε 3.69, 3.57, and 4.13); $\nu_{max.}$ 3 600 (OH), 1 640 (CO), 1 595, 1 545, 1 475, 1 440, and 1 415 cm^{-1}; δ 0.80 (s, 3 H, 18-CH_3), 0.85 (s, 3 H, 19-CH_3), 1.25 (s, 3 H, 17-CH_3), 6.70—7.00 (m, 2 H, pyridine ring 3-H and 5-H), 7.50 (dd, 1 H, pyridine ring, 4-H), 7.87 (d, 1 H, *J* 11.5 Hz, NH–C*H*=C), 8.30 (d, 1 H, pyridine ring, 6-H) and 11.97 (d, 1 H, *J* 11.5 Hz, N*H*).

17β-*Hydroxy*-17α-*methyl*-2′-*methylthio*-5α-*androstano*-[3,2-f]-(s-*triazolo*-[1,5-a]*pyrimidine*) (27).—A solution of 17β-hydroxy-17α-methyl-2-(2′-pyridylaminomethylene)-5α-androstan-3-one (25) (0.408 g, 1 × 10^{-3} mol) and 3-amino-5-methylthio-1,2,4-triazole (26) (0.150 g, 1.15 × 10^{-3} mol) in dry toluene (50 ml) was refluxed for 72 h. After cooling, the reaction mixture was evaporated to dryness *in vacuo* and the residue chromatographed over alumina. Elution with ethyl acetate, followed by recrystallisation from ethanol, gave white crystals of the title compound (0.265 g, 65%), m.p. 207—209 °C, $\lambda_{max.}$ 212, 227, 237, and 315 nm (log ε 4.40, 4.40, 4.43, and 4.03); $\nu_{max.}$ 3 600 (OH), 1 620, 1 510, 1 440, 1 415, 1 345, 965, 930, and 770 cm^{-1}; δ 0.78 (s, 3 H, 18-CH_3), 0.88 (s, 3 H, 19-CH_3), 1.22 (s, 3 H, 17-CH_3), 2.66 (s, 3 H, 2′-SCH_3), and 8.32 (s, 1 H, 7′-H) (Found: C, 67.3; H, 8.2; N, 13.35%; M^+, 426.245 320. $C_{24}H_{34}N_4OS$ requires C, 67.57; H, 8.04; N, 13.14%; *M*, 426.246 147).

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