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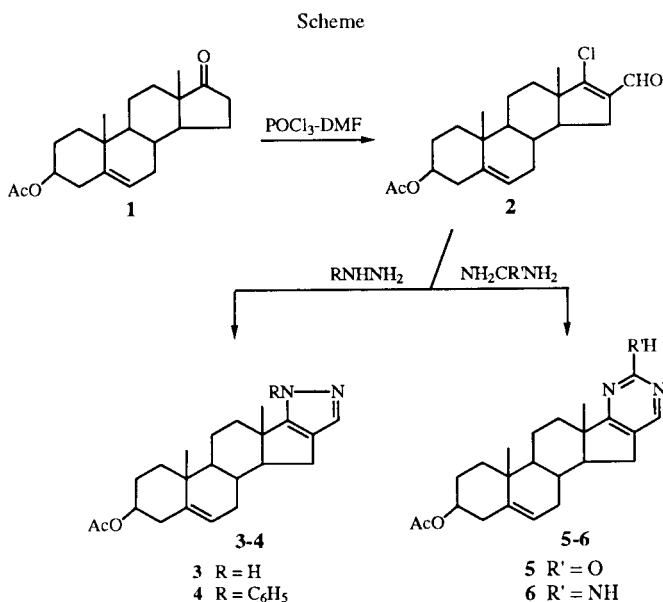
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The Vilsmeier-Haack reaction of 3 β -acetoxyandrost-5-en-17-one (1) with phosphorous oxychloride and dimethylformamide gave 3 β -acetoxy-17-chloro-16-formylandrosta-5,16-diene (2). Reaction of 2 with hydrazine and phenylhydrazine provided substituted 5-androsteno[17,16-*d*]pyrazoles 3 and 4 respectively. Similarly, condensation of 2 with urea and guanidine hydrochloride revealed the formation of the corresponding substituted pyrimidines 5 and 6 respectively.

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Heterocyclic steroids with pyrazole or pyrimidine ring fused in different positions of steroidal ring system are endowed with useful biological activities [2], consequently their preparation and further transformations are of importance [3]. In continuation of our work on heterosteroids [4], we now report a new synthesis of steroidal pyrazole and pyrimidine derivatives from Vilsmeier-Haack reaction product of a steroidal ketone.

The Vilsmeier-Haack reaction [5] of 3 β -acetoxyandrost-5-en-17-one (1) with phosphorus oxychloride and dimethylformamide gave 3 β -acetoxy-17-chloro-16-formylandrosta-5,16-diene (2). The ir spectrum of 2 showed a characteristic absorptions at 1700 (CHO) and 760 cm⁻¹ (C-Cl) and the ¹H nmr showed a broad singlet at δ 9.9 for CHO proton.



Reaction of 3 β -acetoxy-17-chloro-16-formylandrosta-5,16-diene (2) with hydrazine and phenylhydrazine revealed the formation of substituted 5-androsteno[17,16-*d*]pyrazoles 3 and 4 respectively. The structure of 3 and 4 is supported by the ¹H nmr downfield signal for the

pyrazole ring proton at δ 8.9. The ¹H nmr of 3 showed a broad singlet at δ 7.6 for the NH proton whereas the nmr of 4 showed a multiplet in the region of δ 7.2-7.6 for the aromatic protons.

The reaction of 2 with urea gave pyrimidine derivative 5, whose ¹H nmr showed a singlet at δ 8.92 for the pyrimidine ring proton and a broad singlet at δ 7.4 for the OH proton. Similarly, condensation of 2 with guanidine hydrochloride gave the corresponding substituted 2-aminopyrimidine 6. The ¹H nmr of 6 revealed a singlet at δ 9.05 for the pyrimidine ring proton and a broad singlet at δ 4.4 for the NH₂ protons which disappeared upon treatment with deuterium oxide.

EXPERIMENTAL

Melting points are uncorrected. The infrared spectra were recorded as potassium bromide pellets using Perkin-Elmer 137 spectrometer. The uv spectra were obtained in 95% ethanol on Beckmann DB spectrometer. The ¹H nmr spectra were obtained in deuteriochloroform on a varian FT-80 or on a Varian XL 200 spectrometer with TMS as the internal standard. Chemical shifts are given in ppm (δ).

3 β -Acetoxy-17-chloro-16-formylandrosta-5,16-diene (2).

A solution of 3 β -acetoxyandrost-5-en-17-one (1) (1 g, 3 mmoles) in chloroform (20 ml) was added dropwise to a cold mixture of phosphorus oxychloride (5 ml) and dimethylformamide (5 ml). The mixture was allowed to attain room temperature and then refluxed under nitrogen for 4 hours. The mixture was concentrated *in vacuo* and then poured onto ice and extracted with ether. The ether extract was concentrated and recrystallized from methanol-acetone to give 0.71 g of 2 as a colorless solid (62%), mp 145-147°; ir: ν max 1735 (acetate C=O), 1700 (CHO), 1250 (C-O), 760 (C-Cl) cm⁻¹; ¹H nmr: δ 9.9 (s, 1H, CHO), 5.36 (m, 1H, C₆-H), 4.60 (m, 1H, W_{1/2} = 12 Hz, H-3 α), 2.15 (s, 3H, CH₃COO), 1.18 (s, 3H, C₁₉-H₃), 0.80 ppm (s, 3H, C₁₈-H₃).

Anal. Calcd. for C₂₂H₂₉O₃Cl: C, 70.11; H, 7.76. Found: C, 70.20; H, 7.88.

3 β -Acetoxy-5-androsteno[17,16-*d*]pyrazole (3).

A solution of 3 β -acetoxy-17-chloro-16-formylandrosta-5,16-diene (2) (0.5 g, 1.32 mmoles) and hydrazine hydrate (0.65 g,

10.56 mmol) in methanol (30 ml) was refluxed with 2-3 drops of acetic acid for 5 hours. The mixture was concentrated *in vacuo* and then poured onto ice. The resulting precipitate was filtered, washed with water and recrystallized from methanol to give 0.28 g of **3** as a colorless solid (60%), mp 138-140°; ir: ν max 3395 (NH), 1740 (acetate C=O), 1645 (C=N), 1250 (C-O) cm^{-1} ; uv: λ_{max} 220 nm (ϵ 6000); ^1H nmr: δ 8.90 (s, 1H, 3'-H of the pyrazole ring), 5.40 (m, 1H, C₆-H), 4.56 (m, 1H, $W_{1/2}$ = 12 Hz, H-3 α), 2.12 (s, 3H, CH₃COO), 1.15 (s, 3H, C₁₉-H₃), 0.80 ppm (s, 3H, C₁₈-H₃).

Anal. Calcd. for C₂₂H₃₀N₂O₂: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.68; H, 8.42; N, 7.98.

1'-Phenyl-3 β -acetoxy-5-androsteno[17,16-*d*]pyrazole (**4**).

To a solution of **2** (0.6 g, 1.54 mmol) in methanol (40 ml) was added phenylhydrazine (1.38 g, 12.73 mmol) and acetic acid (2 drops) and the mixture was refluxed for 6 hours. The solid product obtained was crystallized from methanol-acetone (9:1) to give 0.41 g of **4** as a colorless solid (58%), mp 149-151°; ir: ν max 1735 (acetate C=O), 1640 (C=N), 1590 (C=C), 1250 (C-O) cm^{-1} ; ^1H nmr: δ 8.92 (s, 1H, 3'-H of the pyrazole ring), 5.38 (m, 1H, C₆-H), 4.6 (m, 1H, $W_{1/2}$ = 12 Hz, H-3 α), 2.12 (s, 3H, CH₃COO), 1.18 (s, 3H, C₁₉-H₃), 0.80 ppm (s, 3H, C₁₈-H₃).

Anal. Calcd. for C₂₈H₃₄N₂O₂: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.0; H, 7.88; N, 6.62.

2'-Hydroxy-3 β -acetoxy-5-androsteno[17,16-*e*]pyrimidine (**5**).

To a solution of **2** (0.75 g, 1.99 mmol) in methanol (50 ml) was added urea (0.96 g, 15.92 mmol) and the mixture was refluxed with 2 drops of piperidine for 10 hours. The mixture was concentrated under reduced pressure and the residue poured onto ice. The precipitated product was filtered off and crystallized from methanol to give 0.44 g (58%) of **5** as a colorless solid, mp 182-184°; ir: ν max 3500 (OH), 1735 (acetate C=O), 1630 (C=N), 1250 (C-O) cm^{-1} ; uv: λ_{max} 264 nm (ϵ 7200); ^1H nmr: δ 8.96 (s, 1H, 4'-H of the pyrimidine ring), 5.40 (m, 1H, C₆-H), 4.54 (m, 1H, $W_{1/2}$ = 12 Hz, H-3 α), 2.12 (s, 3H, CH₃COO), 1.16 (s, 3H, C₁₉-H₃), 0.82 ppm (s, 3H, C₁₈-H₃).

Anal. Calcd. for C₂₃H₃₀N₂O₃: C, 72.22; H, 7.91; N, 7.32. Found: C, 72.34; H, 7.98; N, 7.4.

2'-Amino-3 β -acetoxy-5-androsteno[17,16-*e*]pyrimidine (**6**).

A mixture of **2** (0.5 g, 1.32 mmol), methanol (40 ml), guanidine hydrochloride (1 g, 10.56 mmol) and sodium acetate (0.87 g, 10.56 mmol) was refluxed for 10 hours. The mixture was concentrated *in vacuo* and the residue poured onto ice. The precipitate which formed was filtered, washed with water and crystallized from methanol to give 0.30 g (59%) of **6** as a colorless solid, mp 161-163°; ir: ν max 3380, 3220 (NH) 1740 (acetate C=O), 1635 (C=N), 1250 (C-O) cm^{-1} ; uv: λ_{max} 258 nm (ϵ 6300); ^1H nmr: δ 9.05 (s, 1H, 4'-H of the pyrimidine ring), 5.42 (m, 1H, C₆-H), 4.58 (m, 1H, $W_{1/2}$ = 12 Hz, H-3 α), 2.12 (s, 3H, CH₃COO), 1.17 (s, 3H, C₁₉-H₃), 0.81 ppm (s, 3H, C₁₈-H₃).

Anal. Calcd. for C₂₃H₃₁N₃O₂: C, 72.41; H, 8.19; N, 11.01. Found: C, 72.32; H, 8.27; N, 11.18.

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