Synthesis of 16,17-Pyrazolo-fused Derivatives of A-Homo-steroidal Ring A Lactams

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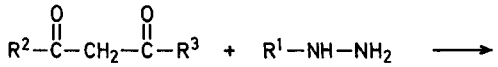
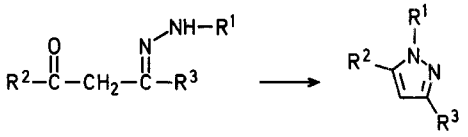
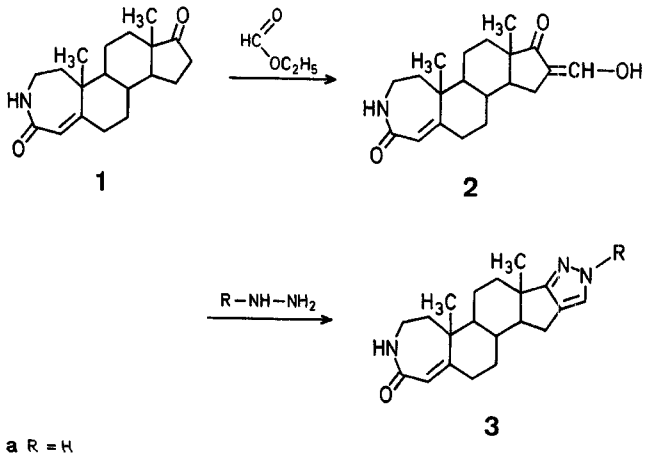
Pyrazoles are best synthesized from 1,3-dicarbonyl compounds and hydrazines.





Pyrazole-fused steroids have been reported to possess biological activity[1,2,3]. On the other hand, certain steroidal lactams possess antitumor activity[4,5]. As part of our studies on the synthesis of new azasteroids of biological interest[6,7] we report here the preparation of 4-oxo-3-aza-A-homo-4α-androsteno[16,,17-*c*]pyrazoles according to the following scheme.



a R = H
b R = CH_3
c R = C_6H_5

16-Hydroxymethylene-4,17-dioxo-3-aza-A-homo-4α-androstene (2): A mixture of 3-aza-A-homo-4α-androstene-4,17-dione[8] (**1**; 3.29 g, 10 mmol), dry benzene (70 ml), and ethyl formate (5 ml) is stirred in an ice bath for 30 min and then at room temperature for 120 h. The solvent is evaporated under reduced pressure and to the residue is added cold water (100 ml). The mixture is acidified with dilute hydrochloric acid and extracted with chloroform (3 × 100 ml). Drying with sodium sulfate and evaporation of the solvent affords the crude 16-hydroxymethylene derivative **2** in 95% yield. The product is purified by column chromatography on silica gel using chloroform as eluent; yield: 1.5 g (45%); m.p. 269–270°C (ethyl acetate).

$C_{20}H_{27}NO_3$	calc.	C 72.97	H 8.20	N 4.25
(329.4)	found	72.66	8.22	4.08

I.R. (KBr): ν = 1700 (CO); 1650 cm^{-1} (NH—CO).

4-Oxo-3-aza-A-homo-4α-androsteno[16,17-*c*]pyrazoles (3); General Procedure:

To a solution of 16-hydroxymethylene-4,17-dioxo-3-aza-A-homo-4α-androstene (**2**; 1.974 g, 6 mmol) in toluene (50 ml) is added 80% hydrazine (0.4 ml, 6.5 mmol) or a substituted hydrazine (6 mmol). The resultant solution is refluxed for 4–17 h (see Table), then evaporated to dryness in yacuo. The residue is purified by column chromatography on alumina using chloroform/methanol (98/2) as eluent.

Table. 4-Oxo-3-aza-A-homo-4α-androsteno[16,17-*c*]pyrazoles (**3**) prepared

3	Reaction Time [h]	Yield [%]	m.p. [°C]	Molecular Formula[a]	U.V.(CH_3OH) λ_{max} (ε)
a	9	83	288–289°	$C_{20}H_{27}N_3O$ (325.45)	225 (22570)
b	27	84	269–270°	$C_{21}H_{29}N_3O$ (339.5)	225 (29250)
c	4	72	268–270°	$C_{26}H_{31}N_3O$ (401.5)	225 (25970)

[a] The microanalyses showed the following maximum deviations from the calculated values: C ±0.40, H ±0.30, N ±0.39.

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