

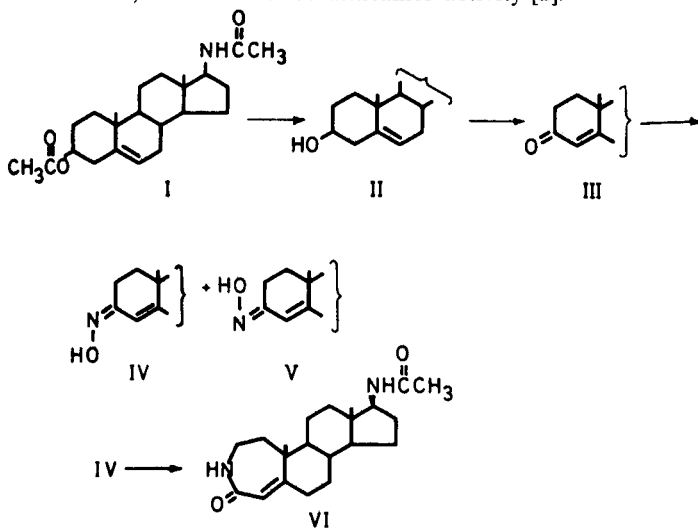
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A synthetic approach for the preparation of 17 β -acetamido-3-aza-A-homo-4 α -androst-4-one is described.*J. Heterocyclic Chem.*, **21**, 927 (1984).

The biological action of steroidal lactams, characterized by the -CONH- group, may be structurally specific and therefore more prolonged. These properties may be a result of the multiple interaction of such a group with similar groups present in proteins and nucleic acids. When cultures of human leukemia cells were treated with 3 β -hydroxy-13 α -amino-13,17-seco-5 α -androst-17-oin-13,17-lactam, an increased proliferating activity was exhibited [1]. On the other hand 3,17 α -diaz-A,D-bishomoandrost-4 α -ene-4,17-dione showed antitumor activity [2].



Thus it was found of interest to effect the synthesis of steroidal lactam containing a second -CONH- group out of the steroid nucleus, namely 17 β -acetamido-3-aza-A-homo-4 α -androst-4-one (VI) and tested it for biological activity.

Beckmann rearrangement of pregnenolone oxime form-

ed the 17 β -acetamido-derivative I [3]. The latter after hydrolysis and Oppenauer oxidation produced the ketone III, in 40% yield, mp 240-242°; ir (potassium bromide): ν max 3340 (NH), 1650 (CO), 1610 cm^{-1} (C=C); nmr (deuteriochloroform): δ 6.65 (C=CH), 5.35 (NH), 3.90 (17 β -H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{31}\text{NO}_2$: C, 56.59; H, 9.42; N, 4.25. Found: C, 56.22; H, 9.50; N, 4.10.

Treatment of III with hydroxylamine hydrochloride in a mixture of pyridine-ethanol produced the corresponding ketoximes IV and V.

The general trend is that *syn*-oxime IV of α,β -unsaturated ketoximes undergo the facile rearrangement to lactam, while *anti*-isomers V resist the rearrangement under similar conditions [4].

Beckmann rearrangement of unresolved 17 β -acetamido-4-androst-3-one oxime with thionyl chloride in dioxane [4] produces lactam VI in 32% yield, mp 236-238° (ethyl acetate); ir (potassium bromide): 3250 (NH), 1625 cm^{-1} (CO); nmr (deuteriochloroform): δ 6.48 (NH), 5.78 (C=CH), 5.36 (NHCOCH₃), 3.85 (17 α -H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_2$: C, 73.25; H, 9.30; N, 8.13. Found: C, 73.50; H, 9.50; N, 7.90.

Under similar reaction conditions the 4-pregnen-3-one dioxime produces compound VI in 25% yield after column chromatography.

REFERENCES AND NOTES

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