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THE ALUMINA-CATALYZED ADDITION OF DIAZOMETHANE TO STEROIDAL KETONES

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In connection with an investigation of easy methods for the preparation of B and C-homosteroids, we studied the alumina-catalyzed (1) addition of diazomethane to several steroidal ketones. During these studies a specificity for epoxide formation was observed that was apparently a combined function of the catalyst as well as the A-B ring fusion.

The alumina-catalyzed (Woelm, neutral, activity I) reaction of 5β-androstan-17β-ol-3-one, **1**, (2) with excess distilled diazomethane in ether** resulted in a three-component mixture. Silica gel chromatography afforded a small amount of A-homo-5β-androstan-17β-ol-4-one, **2**;*** mp, 170-171° [lit. (3) mp, 172.5-173°] ; $\lambda_{max}^{CHCl_3}$ 2.76 and 5.89μ; nmr**** 0.76 and 1.08 (3H, s, angular methyl). The remaining components could not be purified but they were an epoxide and a different ketone according to infrared analysis.

When 5α-androstan-17β-ol-3-one (4) was treated in the same way, a mixture of two components resulted. The main component was isolated (50% yield) by silica gel chromatography, mp 173-174°; $\lambda_{max}^{CHCl_3}$ 2.77 (OH), 10.88 and 11.09μ (terminal epoxide); nmr, 0.76 and 0.87 (3H, s, angular methyl), 2.61 (2H, s, oxymethylene). These data support the assigned structure, **5**, an epoxide reported by Wall (5). A small amount of the second product was gotten from the

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** Prepared according to J. A. Moore and D. E. Reed, <u>Org. Syn.</u>, **41**, 16 (1961).

*** All new compounds gave acceptable analytical data for carbon and hydrogen.

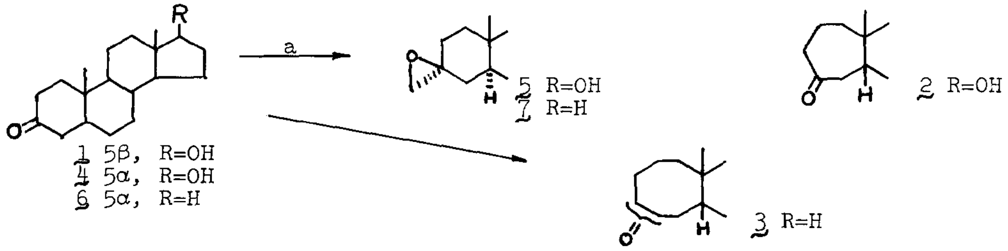
**** The nmr spectra were determined in $CDCl_3$ (internal TMS) and chemical shifts are reported in ppm (δ).

column in homogeneous but non-crystalline form and was a ketone different from starting material, probably a ring-enlarged product.

When 5α-androstan-3-one (6) was treated as above, a two-component mixture was obtained. A 30% yield of an epoxide (7, stereochemistry unknown) could be isolated, mp 96-97.5°; $\lambda_{max}^{CHCl_3}$ 11.05 and 10.85μ (terminal epoxide); nmr, 0.71 and 0.82 (3H, 2), 2.61 (2H, s, oxymethylene), as well as a small amount of the starting ketone (melting point and nmr comparisons).

To test the difference between alumina and methanol catalysis, 5α-androstan-3-one was allowed to react with diazomethane in methanol solution. A mixture of at least eight components (tlc) was obtained. None of the reaction products could be obtained pure, but ir and nmr analysis showed the presence of both ketones and epoxides. When 5β-androstan-17β-ol-3-one was treated in the same way, a complex mixture was again obtained which contained, however, a main component isolable in small quantity, mp 184-185°; $\lambda_{max}^{CHCl_3}$ 5.9μ; nmr, 0.74 and 0.90 (3H, s). The data support the structure, 3, a bis-homo-ketone.

Although selectivities of the kind observed above have been seen in a more limited way in the <u>cis</u> and <u>trans</u> decalone series (7), the marked effects reported here have not been seen heretofore and deserve further investigation.



a = CH_2N_2/Al_2O_3 b = CH_2N_2/CH_3OH

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