A Synthetic Approach to the 9(10 → 19)*abeo*-Androstane System

By F. KOHEN, L. K. LALA, W. VAN BEVER, and R. E. COUNSELL*

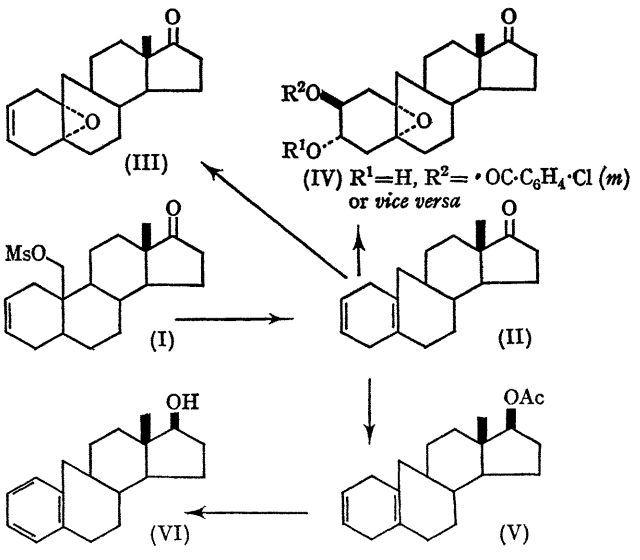
(*Laboratory of Medicinal Chemistry, College of Pharmacy, The University of Michigan, Ann Arbor, Michigan* 48104)

Summary Solvolysis of 19-hydroxy-5α-androst-2-en-17-one methanesulphonate in pyridine gives 9(10 → 19)*abeo*-androsta-2,5(10)-dien-17-one as a major product.

IN the course of studies on the synthesis of C-19 radioactively labelled steroids, we examined the solvolysis products of 19-hydroxy-5α-androst-2-en-17-one methanesulphonate (I).[1]

When a solution of (I) in pyridine was heated under reflux, a mixture of steroidal olefins was produced, and t.l.c. on silica gel G impregnated with silver nitrate indicated the presence of one major and one minor product. Chromatography of the reaction mixture on alumina (Activity II) yielded a crystalline product (II) (25%), an oily product (10%),† and starting material (45%).

The major product (II) had an analysis which corresponded to the molecular formula $C_{19}H_{26}O$. The intense end-absorption in the u.v. spectrum indicated the presence of nonconjugated double bonds as well as a highly substituted double-bond. The n.m.r. spectrum showed one angular methyl group corresponding to C-18, at δ 0·97.



† Because of lack of material, we have not yet studied this product further.

This indicated that C-19 had become part of the steroid nucleus. The presence of two vinyl protons at δ 5·6 (m) and the absence of cyclopropyl protons suggested that the suspected additional double bond was tetra-substituted. This was substantiated by the formation of a monoepoxide (III), which still showed two vinyl hydrogens at δ 5·6 and the absence of methine hydrogens attached to a carbon bearing an oxygen function.

Treatment of (III) with an excess of *m*-chloroperoxybenzoic acid gave a product formulated as (IV), *m/e* 458. Reduction of (II) with $LiAlH_4$ and subsequent acetylation gave a crystalline acetate (V).

There are several Wagner–Meerwein rearrangement products of (I) that would account for the results. Structure (II), however, was confirmed by the mass spectrum‡ and chemical transformation into an aromatic steroid. Dehydrogenation of (V) with Pd–C (5%) in ethylene glycol solution gave (VI), *m/e* 270 (M^+), λ_{max} (EtOH) 278 (ε 400), 274sh (ε 370), and 269 nm. (ε 460), ν_{max} (KBr) 2·98 μ-(hydroxy), and n.m.r. spectrum showed four aromatic hydrogens at δ 6·85 (s) and four benzylic hydrogens at δ 2·76.[2]

Thus the solvolysis of 19-substituted steroids[1] offers another approach to 9(10→19)*abeo*-steroid derivatives and complements the route developed by Kupchan and his co-workers[3] which involves Wolff–Kishner reduction of 9β,19-cyclo-11-oxo-steroids.

This study was supported by grants from the National Cancer Institute, U.S. Public Health Service, and from the American Cancer Society.

(*Received, January 27th*, 1969; *Com.* 111.)

‡ We thank Dr. P. Klimstra and G. D. Searle and Company for the mass spectral analyses.

[1] R. E. Counsell, G. W. Adelstein, P. D. Klimstra and B. Smith, *J. Medicin. Chem.*, 1966, **9**, 685.
[2] Compare with the n.m.r. spectrum of tetralin, "Varian Spectra Catalog", No. 577.
[3] S. M. Kupchan, E. Abushanab, K. T. Shamasundra, and A. W. Bly, *J. Amer. Chem. Soc.*, 1967, **89**, 6327.