

6. Reactions of steroidal epoxides derived from 4, 5-, 5, 10- and 5, 6-enes

HORNING, E. C., THOMPSON, R. M. and LAU, S. S., Institute for Lipid Research, Baylor College of Medicine, Houston, Texas 77025, U.S.A.

Steroidal epoxides are of interest from several points of view. They may be metabolic intermediates formed from normal precursors or from steroidal drugs. Since epoxides are known to have cytotoxic, mutagenic, carcinogenic or teratogenic properties, this pathway is potentially hazardous. Routes of preparation (*m*-chloroperbenzoic acid) and separation (GC and t.l.c.), and reactions of epoxides from 4, 5-, 5, 10- and 5, 6-enes will be compared. Possible metabolic pathways involving an epoxide include the aromatization of the A-ring and the formation of 10 β -hydroxy metabolites from 19-nor-steroids.

7. Novel ⁷⁵Se-labelled steroids for use in saturation analysis

CHAMBERS, V. E. M., TUDOR, R. and RILEY, A. L. M., The Radiochemical Centre, Amersham, England

A new development in the radio-isotopic labelling of steroids for use in saturation analysis is described. For such analyses γ -emitting ⁷⁵Se-labelled steroids have proved to be novel practical alternatives to ¹²⁵I-labelled steroids. The methods for the preparation of alkylseleno- and diseleno-(⁷⁵Se) derivatives of several important steroidal hormones, including cortisol, testosterone and aldosterone are described. The structures of these compounds have been confirmed using chemical and spectroscopic techniques. The use of a ⁷⁵Se-labelled cortisol derivative in a competitive protein binding assay for cortisol is described. Some clinical results obtained with this assay are given.

8. Two novel syntheses of 18-hydroxy-deoxycorticosterone

GUZZI, U. and CIABATTI, R., Research Laboratories of Gruppo Lepetit S.p.A., Milano, Italy

18-Hydroxy-deoxycorticosterone has been synthesized by two different sequences of reactions. In both methods, the conversion of the 18-methyl to an 18-hydroxymethylene group was carried out by photolysis of the corresponding hypiodite. In one case we started from 3 β -hydroxy-5-pregnen-20-one acetate and in the other from 21-hydroxy-4-pregnene-3,20-dione acetate (DOCA). DOCA has not been used previously in the hypiodite reaction. Identity of the synthetic product with an authentic sample was demonstrated by t.l.c., n.m.r. and mass spectroscopy.

1B. Synthesis of biologically active steroids and related compounds

9. Synthesis of biologically active D-homopregnanes

ALIG, L., FUERST, A., KELLER, P. and MUELLER, M., F. Hoffmann-La Roche & Co. AG, Basle, Switzerland
KERB, U. and WIECHERT, R., Schering AG, Berlin, Germany

Various syntheses of a series of biologically active D-homopregnanes, starting from androstane derivatives, are described. The influence of the six-membered ring D on the

steric course of some reactions at C-17a and on the elaboration of various pregnane side chains has been studied. A variety of reactions in rings A, B and C of D-homosteroids and their steric implications have been investigated.

10. Synthesis of new D-homo-pregnanes

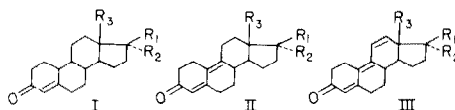
KERB, U., KIESLICH, K., PETZOLDT, K., WIECHERT, R., *FUERST, A. and *MUELLER, M., Schering AG, Berlin, Germany and *F. Hoffmann-La Roche & Cie. AG, Basle, Switzerland

The acid-promoted rearrangement of 16 α , 17 α -methylene-pregnenolone (1) provides a convenient synthesis of Δ^{17} -D-homo-pregnenolone (2), a key substance for the preparation of D-homo-progesterones and D-homo-corticoids. The ring enlargement reaction and the associated side reactions as well as the synthesis of various biologically-active D-homopregnanes from the D-homo-ketone (2) will be reported. Remarkable differences in the chemical reactivity and micro-biological 11-hydroxylation of D-homo steroids as compared to normal D-C₅ ring steroids have been observed.

11. Active steroids without a 17-hydroxyl function. Synthesis of a new class of progestomimetic agents devoid of androgenic activity

BUCCOURT, R., NEDELEC, L., GASC, J. C., ROUSSEAU, G., PHILIBERT, D. and TOURNEMINE, C., Centre de Recherches Roussel-Uclaf, Romainville, France

A new class of 19-nor steroids having an ethynyl group at C-17 but lacking the classical hydroxyl function at the same position have been prepared in three related series: the series of 19-nor testosterone I, and the dienic and trienic analogues series II and III.



- a. R₁ = H, R₂ = -C≡CH, R₃ = -CH₃
 b. R₁ = -C≡CH, R₂ = H, R₃ = -CH₃
 c. R₁ = -C≡CH, R₂ = H, R₃ = -C₂H₅

These new compounds retained the progestomimetic activity of 17 α -ethynyl 17 β -hydroxy 19-nor testosterone and lost its androgenic effect. There is one exception for compound Ia which still shows the same androgenic activity as the 17 β -hydroxy compound. Thus, in this latter case, the 17 β -hydroxyl function seems to have no physiological significance. The same phenomenon was also observed in a pure androgenic series: IIIa, with a methyl group (R₂ = CH₃) instead of the ethynyl, is a potent androgen.

12. A new class of long-acting hormonal steroid preparation: synthesis of oligomeric steroid derivatives

KUHL, H. and TAUBERT, H.-D., Abteilung für gynäkologische Endokrinologie, Zentrum der Frauenkrankheiten und Geburtshilfe, J. W. Goethe Universität, Frankfurt/Main, F. R. Germany

The synthesis of oligomeric steroid esters can be achieved by condensation of 2 or 3 steroid molecules with a dicarboxylic acid by direct esterification of the hydroxy-group