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

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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 10β-hydroxy metabolites from 19-nor-steroids.

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

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A new development in the radio-isotopic labelling of steroids for use in saturation analysis is described. For such analyses γ-emitting ^{75}Se-labelled steroids have proved to be novel practical alternatives to ^{125}I-labelled steroids. The methods for the preparation of alkylseleno- and diseleno-(^{75}Se) 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 ^{75}Se-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

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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 hypoiodite. In one case we started from 3β-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 hypoiodite 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

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KERB, U. and WIECHERT, R., Schering AG, Berlin, Germany

Various syntheses of a series of biologically active D-homo-pregnanes, 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-homo-steroids 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 16α, 17α-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-homo-pregnanes from the D-homo-ketone (2) will be reported. Remarkable differences in the chemical reactivity and microbiological 11-hydroxylation of D-homo steroids as compared to normal D-C_5 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

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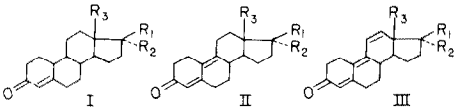
A new class of 19-nor steroids having an ethinyl group at C-17 but lacking the classical hydroxyl function at the same position have been prepared in three related series: the series of 19-nor testosterone I, and the dienic and trienic analogous series II and III.



a $R_1 = H, R_2 = -C\equiv CH, R_3 = -CH_3$
b $R_1 = -C\equiv CH, R_2 = H, R_3 = -CH_3$
c $R_1 = -C\equiv CH, R_2 = H, R_3 = -C_2H_5$

These new compounds retained the progestomimetic activity of 17α-ethinyl 17β-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 17β-hydroxy compound. Thus, in this latter case, the 17β-hydroxyl function seems to have no physiological significance. The same phenomenon was also observed in a pure androgenic series: IIIa, with a methyl group ($R_2 = CH_3$) instead of the ethinyl, is a potent androgen.

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

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