1D. Structure, conformation and configuration

23. Reassignment of absolute configuration of 19-substituted 19-hydroxysteroids

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Since opposite stereomechanisms of estrogen biosynthesis in the human placenta were reported concerning the second hydroxylation of the C-19, we independently studied the absolute configuration and conformation of 19-^{2}H- and 19-CH_3-19-hydroxysteroids. [19proS$_{Our}$-^{2}H]-19-OH-4-androstene-3,17-dione (I), the assignment given to the major product of NaB^2H_4 reduction of 4-en-3-on-19-al system, was transformed to [19proS$_{Our}$-^{2}H]-5-androstene-3β,17β,19-triol triacetate (II) by enol acetylation followed by reduction and acetylation. [19proS$_{Our}$-^{2}H] II was analyzed by 300 MHz NMR and MS to have a stereochemistry (19-H_2 at σ 3·98 and 4·50, J_{AB}12Hz; H at σ 3·98 predominantly labelled) identical to [19proR$_{Skinner}$-^{2}H] II, the assignment given to the major product of NaB^2H_4 reduction of 5-en-3β-ol-19-al. The major [19S$_{Our}$] and minor [19R$_{Our}$] 19-CH_3-5-androsten-3β,17β,19-triol (III) were obtained from 3β,17β-diacetoxy-5-androsten-19-al (IV) by CH_3Li reaction. The structure of [19R$_{Our}$] III was determined by X-ray direct methods to be 19R with a conformation of the CH_3 over the B-ring.[19S$_{Our}$] III was identical in all respects to [19R$_{Caspi}$] III, the assignment given to the major product of CH_3Li reaction of IV. For these reasons we propose that previous assignments of the absolute configuration of 19-substituted 19-OH-steroids be reversed. (Research supported by USPHS HD-04945 and CA10906 and Amer. Can. Soc. Award PRA-72).

24. Comparative analysis of glucocorticoid conformations

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X-Ray analysis of cortisol and its 9α-halogenated derivatives has revealed significant differences in their A-ring conformations. With the exception of 9α-chlorocortisol, the A-ring orientations parallel the glucocorticoid activities reported by Fried. The A-ring in 9α-fluorocortisol has a half-chair conformation and is bent underneath the plane of the B, C, and D-rings to a much greater extent than is the A-ring in cortisol which has a sofa conformation. This conformational change, which may be related to close intramolecular non-bonded contacts between the 9α-fluorine and the α-axial hydrogens, causes the overall molecular shape to resemble 6α-methylprednisolone and dexamethasone in which the C1–C2 bond is unsaturated. The A-ring orientations in 9α-chloro and 9α-bromocortisol are very similar to that seen in cortisol itself, and the strain associated with the larger halogens appears to be alleviated in other ways such as flattening of the B and C-rings. It should be noted that in contrast to the A-ring variation, the orientation of the C-17 side chain is invariant with atoms C-20 and C-21 being *cis* coplanar and C-20 situated over the D-ring on the side of C-13. (Research supported by USPH Research Grant No. CA-10906).

25. Structure-activity relationship of 14α,17α-alkylidenedioxy-corticoids

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14α, 17α-alkylidenedioxy-corticosterone 21-esters are a new series of corticoids with low systemic and high local activity. For structure-activity correlations we used ΔR_M-values of reversed phase t.l.c., which correlated well with lipophylicity. We applied the method of multiple regression analysis to find a correlation between local activity and lipophylicity. Variation of the 21-ester-moiety did not give a simple relationship. Introduction of Taft's steric parameter was necessary to obtain a good correlation. Variation of the alkylidenedioxy group yielded a complex equation indicating a correlation of activity with lipophylicity and the length of the alkylidenedioxy group.

26. Steroidal glycosides in Yucca filifera

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The desert plant *Yucca filifera* grows abundantly in large areas of northern México. The seeds contain in high yield a mixture of glycosides which afford on hydrolysis sarsasapogenin as the only aglycone. The glycoside mixture could be separated into two components which we have called filiferin A and filiferin B (separated by column chromatography on silica gel). Filiferin A is formed by 1 ml of galactose and 1 mol of a pentose, attached in that order to C-3 of sarsasapogenin. The sugars were isolated from the hydrolysis mixture by column chromatography on silica gel. Galactose was fully characterized by glc of its TMS derivative and by its osazone. The experimental data indicate that the pentose might be ribose. The most abundant glycoside, filiferin B consists of 1 mol of galactose and 1 mol of glucose joined to C-3 of the sapogenin.