2 were prepared because of their potential as irreversible progesterone antagonists. The 13β,16β bridge was constructed by intramolecular alkylation of the C-16 enolate anion from 3-methoxy-13β-(3'-tosyloxypropyl)gona-3,5-dien-17-one, the latter being obtained *via* Birch reduction of both aryl groups of **1**. The 11β,13β bridge was constructed by Prins cyclization of 17β-acetoxy-3-methoxy-13β-(3'-oxopropyl)gona-1,3,5(10),9(11)-tetraene (**3**), itself obtained *via* Birch reduction of only the side chain aryl group of **1**. The *in vitro* binding affinities of 11β,13β- and 13β,16β-propano derivatives of 17α-ethynyl-17β-hydroxygon-4-en-3-one for the cytosol receptor protein were 22% and 1.3% relative to progesterone.

7. Conjugate addition of organocopper reagents to steroidal polyenones

RAO, P. N. and PETERSON, D. M., Department of Organic and Biological Chemistry, Southwest Foundation for Research and Education, San Antonio, TX 78284, U.S.A.

Introduction of a 7α-methyl function and a Δ^{14}-double bond into 19-nortestosterone enhances androgenic activity to 1000 × testosterone in the chick comb assay. 7α-Methyl-14-dehydro-19-nortestosterone was prepared from 7α-methylestrone which in turn was obtained from dehydroisoandrosterone. An early step in the synthesis involves conjugate addition of copper-catalyzed methyl Grignard reagent to 17-ethylenedioxyandrosta-4,6-diene-3,17-dione, resulting in a mixture of 7α- and 7β-methyl isomers in the ratio of 2:1; separation of the 7α-isomer is laborious. In contrast, conjugate addition of lithium dimethylcuprate to 17β-acetoxyestra-4,6-dien-3-one, a 19-norsteroid, yields only the 7α-methyl adduct. In this light one would also expect 17β-acetoxyestra-4,6,14-triene to undergo "normal" conjugate addition to form a 7α-methyl adduct. Contrary to expectation, the conjugate addition yielded the 7β-methyl adduct *exclusively*. The steric factors responsible for the 7β-methyl adduct from a Δ^{14}-steroid can be explained by X-ray crystal data obtained on a variety of Δ^{14}-steroids.

8. Identification of natural spirolactones in man

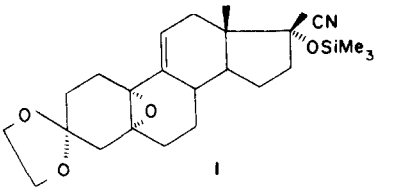
GENARD, P., PALEM, M., EECHAUTE, W. and VAN CAUWENBERGE, H., Medecine A, University of Liege, Hôpital de Bavière, Liège, Belgium

The extract of a urinary pool of normal man without treatment was analysed by Gas Liquid Chromatography (GLC) with electron capture detection using an OV_{17} 3%—6 feet column. The chromatogram shows two peaks with a retention time (R_T) of 26.4 and 41.2 min, respectively. The ^1H and ^{13}C n.m.r. spectra of the purified compound with R_T value of 41.2 indicates a steroid molecule with a spirolactonic structure similar to that of Spironolactone or Canrenone, and with two O-atoms localized on carbon 6 and 7 respectively as an hydroxyl group or as a methoxy group. Mass spectrometry of this compound confirms the n.m.r. data. Finally the preliminary results also indicate a spirolactonic structure for the compound with R_T of 26.4 min

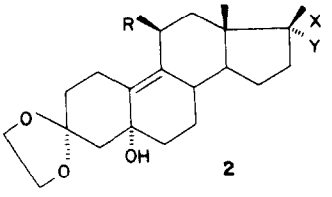
9. Regional- and stereo-specific synthesis of 11β-substituted 19-nor-steroids

TEUTSCH, G., BELANGER, A. and PHILIBERT, D., Centre de Recherches, Roussel-Uclaf, 93310-Romainville, France

Treatment of 5α,10α-epoxy $\Delta^{9(11)}$-steroids with lithium organocuprates or copper I catalyzed Grignard reagents, leads to exclusive 11β-substitution (**1** → **2**). Dehydration of the intermediate allylic alcohol and simultaneous unmasking of the 3-keto function affords the novel 11β alkyl, alkenyl or aryl 3-keto-$\Delta^{4,9}$ dienones (**3**) which can be further transformed by known procedures to the corresponding ring A aromatic steroids (**4**). The mechanism of 11β-alkylation will be discussed. Cytosolic receptor affinities will be briefly presented.



1



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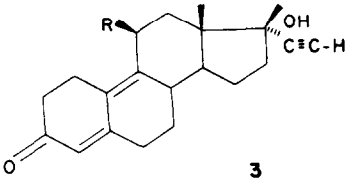

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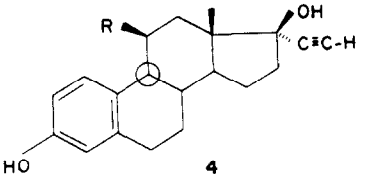


4

(a) X = CN
Y = $OSiMe_3$

(b) X = OH
Y = C≡C-H

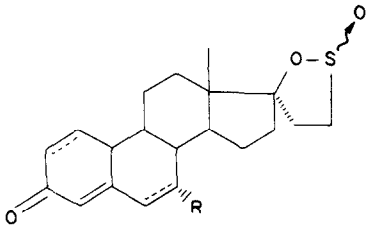
10. Sultine analogues of spirolactones

NEDELEC, L., TORELLI, V., ROUSSEAU, G., ALLAIS, A., PHILIBERT, D., FOURNEX, R. and AZADIAN-BOULANGER, G., Centre de Recherches Roussel-Uclaf, 93310-Romainville, France

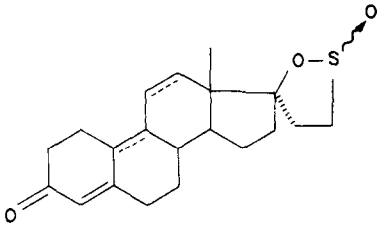
New structural analogues of the antimineralocorticoid spirolactones, where the carbonyl group of the 17β lactonic ring has been replaced by a sulphinyl group, have been synthetised from 17,20-epoxysteroids.

The resulting spirosultines (**1**) and (**2**), each of which existing in two diastereoisomeric forms, have been studied systematically *in vitro* for their ability to bind to hormonal receptors and *in vivo* for their aldosterone antagonising properties in rats. All spirosultines of type (**1**) bind moderately to mineralocorticoid receptors. As in spirolactone series diuretic potencies and hormonal side effects depend largely on the nature of the substituents in different pos-

itions of the steroid nucleus. The 19-nor spirosultines of type **2** are mainly characterized by their strong affinity for the progestin receptor. In the Clauberg test, the trienic derivative appears to be a very potent progestomimetic agent with few other hormonal effects.



I



2

11. New 13-substituted gonenes

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13β-formyl-gonenes generated from 18-iodo-19-norpregnene-20-one derivatives by a novel reaction sequence, served as precursors in the synthesis of a series of 13-substituted gonenes, consisting of 13-vinyl, 13-ethynyl and 13-difluoromethyl analogues of norethisterone and ethynylestradiol. The different steric requirements for the alkyl substituent on C(13) in these two groups are reflected by the biological activity of the individual compounds. On the whole, the biological profile of the new gestagens compares favourably with that of the corresponding mother compounds, whereas in the estrogenic group the activity is generally less pronounced.

12. A quantum mechanical study on hormonal steroids

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In the so-called hormonal steroids there are some phenomenological problems:

—chemical similarity, but different biological activity (sex steroids and their antagonists);

—a difference in the chemical structure (artificial sex steroids) but a similarity with the biological activity of natural sex steroids;

—a different quantitative scale in biological activity (oestradiol, oestrone, oestriol and others). The focus of the present study has been centered on methods allowing the evaluation of these kinds of bio-active molecules at the level of quantum mechanical parameters. For this purpose our modification and extension of the Hückel LCAO-MO method has been used. The parameters of a molecular diagram and the comparison between the energy in the initial and first excited state have been considered in the light of the possibility that the receptors recognize quantum mechanical level parameters.

13. Molecular relaxation of methyl groups in hormonal steroids

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A theoretical expression for molecular relaxation due to methyl group rotation in some hormonal steroids has been worked out on the basis of quantum statistical mechanical methods. Special attention has been focused on quantum tunnelling in molecular processes underlying all double-minimum relaxation phenomena. The high temperature minimum is attributed to the classical reorientations of a group and the low temperature one to tunnelling disturbed by an interaction with the matrix. Our rate expression is of the form:

$$3\gamma^4\hbar^2/20nr^6[J(w_0) + 4J(2w_0)]$$

with

$$J(w) = R_e\int_0^{\infty} dt\, f(t)\exp(-iwt)$$

and

$$f(t) = \langle \exp[2i\theta(o)]\exp[-2i\theta(t)]\rangle$$

The spectral density $J(w_0)$ is obtained from stochastic properties.

14. Phytoecdysones of the plants of Labiatae and Compositae families

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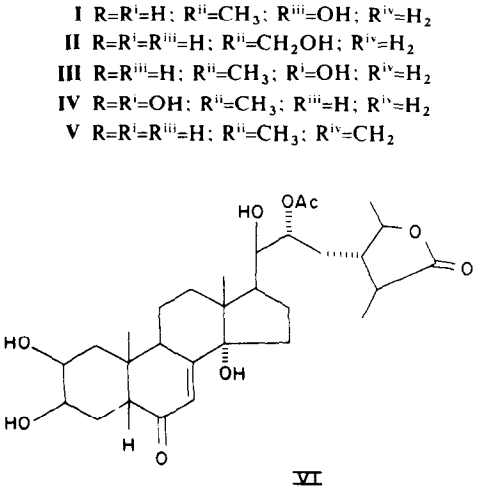
Phytoecdysones of some of the plants growing in Mid-Asia have been investigated. Along with the known ecdysones ecdysterone, cyasterone, ajugalactone and ajugasterone B new ecdysones turkesterone (I), $C_{27}H_{44}O_8$, and 22-acetylcyasterone (VI), $C_{31}H_{46}O_9$, have been isolated from Ajuga turkestanica (Rgl) Brig. (Labiatae). Ecdysterone, viticosterone E and previously unknown phytoecdysone sogdisterone (II), $C_{27}H_{44}O_8$, have been found by studying Serratula sogdiana Bge. (Compositae). In addition to the ecdysterone, new phytoecdysones integristerone A (III), $C_{27}H_{44}O_8$, integristerone B (IV), $C_{27}H_{44}O_9$, and 24(28)-dehydromakisterone A (V), $C_{28}H_{44}O_7$, have been isolated from Rhaponticum integrifolium C. Winkl (Compositae). The isolated compounds offer MH-activity.

I $R=R^{i}=H$; $R^{ii}=CH_3$; $R^{iii}=OH$; $R^{iv}=H_2$
II $R=R^{i}=R^{iii}=H$; $R^{ii}=CH_2OH$; $R^{iv}=H_2$
III $R=R^{iii}=H$; $R^{ii}=CH_3$; $R^{i}=OH$; $R^{iv}=H_2$
IV $R=R^{i}=OH$; $R^{ii}=CH_3$; $R^{iii}=H$; $R^{iv}=H_2$
V $R=R^{i}=R^{iii}=H$; $R^{ii}=CH_3$; $R^{iv}=CH_2$



VI