

# ENCYCLOPEDIA OF ENDOCRINOLOGY

by

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## SECTION I

*Classified Index of the Steroid Hormones and Related Compounds*

## VOLUME I

Introduction,  
Norestrane,  
Estrane, D-Homoestrane,  
Pyroandrostane, 18-Norandrostane,  
i-Androstane, Androstane

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## P R E F A C E

These volumes represent the first section of an Encyclopedia of Endocrinology, the purpose of which is to facilitate research in this field. The literature concerning hormones is growing at such a rapid rate that most investigators find it increasingly difficult to keep fully informed. Yet because of the manifold correlations by which the endocrine glands influence each other, and indeed most organs in the body, it is especially important to refrain from overspecialization in this science. Unlike many other disciplines, there is no contemporary handbook from which the investigator can obtain a critical and up to date evaluation of any data pertaining to endocrine literature. The subject is so vast and touches on so many fields of physiology, medicine, morphology and chemistry, that the task of preparing a handbook of this type requires the major part of a lifetime. Furthermore, the expense connected with such a venture is very great since it is technically impossible to review the immense literature on endocrines without accumulating the relevant publications in one library. Fortunately, towards the end of the last century, when endocrinology began to take shape as a separate science, Professor Stricker of Vienna established a nucleus for such a library in a small reprint collection which was carefully kept up to date by my late teacher, Professor Arthur Biedl of Prague (the author of the first reference book on hormones) and after his death by myself. It now contains approximately 150,000 reprints and abstracts. During the last ten years a detailed subject index has been prepared which places the data of the library in readily available form. As such the collection has provided our group at McGill, as well as occasional visitors from other universities, with a reasonably complete set of references on any subject pertaining to the glands of internal secretion.

It has repeatedly been suggested that the library should be made more generally available in the shape of an Encyclopedia of Endocrinology. The "Classified Index of the Steroid Hormones and Related Compounds" represents the first effort in this direction. In it an attempt is made to classify the steroids of the "hormone group" and to characterize them in accordance with their most important chemical, physical and pharmacological properties.

The loose-leaf system has been adopted in this section, and will be retained in all future parts of the handbook, since it is obviously of the utmost importance to keep these volumes up to date and the expense of publishing frequent new editions would be prohibitive. The loose-leaf folders permit the insertion of additional pages and the substitution of new sections for those which have become antiquated; hence they lend themselves well to this type of publication. It was felt, furthermore, that it would be especially desirable to present this Encyclopedia in a form which would enable every investigator and teacher to adapt it to his particular requirements. The choice of a standard type of binder — for which additional sheets are always obtainable — appears to solve this problem, since readers who wish to add personal notes to chapters which are of particular interest to them may readily do so, using

the printed pages as a basis for the classification of their data. In this manner the book may be molded into a rather personal tool of investigation.

In the case of the present volumes on steroids the provision of an abstract service is contemplated by the issuing of supplementary pages for new parent compounds and of a list of addenda to the data contained on the original pages. If, in the course of time, the data concerning a parent compound should have to be changed completely, a new page will be issued to replace the old one.

The compounds in the four volumes are numbered consecutively from 1 to 728 and new pages substituting for old ones will be issued under the same page number. Additional sheets will be given the number of the page after which they are to be inserted, followed by a decimal point and a numeral indicating the position they will take after the original page. The system is illustrated by the following example: a new page to be added after page 37 will be marked 37.1, the next inserted page 37.2 etc. It is evident that such a system of numbering is readily expandable to any number of subsequent supplemental issues, e.g. if in the above example a page should have to be inserted at a still later date between 37.1 and 37.2, it would bear the number 37.1.1.

The library numbers of each publication are used for the sake of uniformity since many publications will be quoted in different sections of the Encyclopedia. At the end of each section the references are enumerated in the order of their library numbers which means that only a small portion of the existing numbers (namely 1 to 100,000 and A1 to A59,000) will actually be used in any one section. The gaps will not be disturbing, however, since they do not interfere with orderly enumeration. References cited in future supplementary pages will, of course, bear higher numbers than those quoted in the present book; it will, therefore, be simple to add reference pages immediately following the present ones.

After completion of the entire Encyclopedia an alphabetic author index will be published, giving the full title and reference, as well as the library numbers, of all papers cited.

Great care has been taken to check all data for correctness and completeness; still, considering the vastness of the field, many disturbing errors and omissions have probably escaped attention. I shall be extremely grateful if readers will bring any such shortcomings to my attention so that they may gradually be corrected when antiquated pages are replaced by new ones.

I am especially indebted to Drs. F. L. Selye and J. S. L. Browne whose constant encouragement has been instrumental in maintaining my enthusiasm during the many years which have elapsed since I began preparing the manuscript of this Encyclopedia. I am also grateful to McGill University for supplying considerable financial aid for the maintenance and cataloguing of the reprint library.

In connection with the compilation of the present section, my greatest thanks are due to Dr. R. D. H.

Heard. By suggesting the immediate printing of this section he is chiefly responsible for initiating the publication of the Encyclopedia, a venture for whose postponement I seem always to have found a reasonable excuse. Furthermore, Drs. Heard, D. Beall and A. Odell gave me invaluable aid in checking the chemical properties of the steroids and many compounds which were missing in the original manuscript have been added from Dr. Beall's carefully prepared file. Dr. Georges Masson painstakingly checked all data concerning the pharmacology of the steroids and has helped me considerably in the preparation of the dictionary of bioassay methods. Assisted by the Misses Helen Stone and M. Romanchuk he also prepared most of the synoptic charts. Misses Helen Winter and

Helen Stone kindly re-edited the manuscript, while Misses M. Allus, P. Hart, M. Romanchuk and Mrs. D. Heller took charge of the secretarial and proofreading work.

Finally, my most sincere thanks are due to the DesBergers-Bismol Laboratories who generously sponsored the publication of the steroid section, and to Mr. A. W. T. Franks for spending much time in solving the somewhat complex problems associated with the publishing and printing of these volumes.

HANS SELYE.

Montreal, Canada

August, 1943.

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# INTRODUCTION

## CHEMICAL NOMENCLATURE AND SYSTEM OF CLASSIFICATION

The classification of the steroids in this Index is entirely based upon their chemical structure. While many such systems of classification are possible, it is obvious that no one system is completely satisfactory in all respects. The present arrangement was selected to conform primarily with the requirements of the pharmacologist. It lists all compounds as substitution products of the parent *nuclear* hydrocarbon which serves to collect, each in a group, the biologically important derivatives of androstane, estratriene, etc. and to segregate other groups of lesser pharmacological significance. From other points of view, however, it may well be more desirable to adopt a different system as, for example, that introduced by Sobotka (A34437) which is based upon the number and nature of the substituted functions. The loose-leaf nature of the catalogue makes possible the re-arrangement of the pages in accordance with any desired scheme.

A separate index page is devoted to each *parent compound* (i.e. the basic hydrocarbons or their substitution products containing one or more of the following functions: alcohols, ketones, aldehydes and acids). In bold type at the head of each page appears the systematic chemical name assigned in accordance with the system of nomenclature outlined below. In parenthesis beneath the classification name, is given the common name (where it differs from the former) and/or that assigned by the original investigator. Then follow the section headings: Isolation, Structure and Synthesis, Melting Point, Pharmacology, Remarks, Derivatives, References, under which the pertinent data are recorded; a detailed description of the arrangement of the data in these sections is given on pages 8 and 9. Under *Derivatives* are listed the reaction products commonly used in the characterization of functional groups (esters, ethers, oximes, semi-carbazones, etc.). Included also in this section are (a) enol esters, (b) nitriles and lactones, (c) oxides and (d) halo-, amino- and nitro-substitution products, all of which appear amongst the functional derivatives of the corresponding (a) saturated ketone, (b) acid, (c) unsaturated compound and (d) parent compound in which hydrogen has been replaced (e.g. 3-chloro-androstane-17-one is catalogued under androstane-17-one).

### CHEMICAL NOMENCLATURE

#### A. The Parent Hydrocarbons

All parent compounds are classified as substitution products of ten saturated *nuclear hydrocarbons* (inclusive of the angular methyl groups at C<sub>10</sub> and C<sub>11</sub>, but exclusive of alkyl substituents in other positions). These are formulated and listed (underlined on pages 3 and 4).

Mixed aliphatic and cyclic hydrocarbons are considered as alkyl-substituted derivatives of the above-mentioned basic ring structures (e.g. pregnane = 17(α)-ethyl-etiocholane; allo-pregnane = 17(α)-ethyl-androstane); this nomenclature has been adopted for convenience of classification and because it allows designation of the special relationship of side-chain to nucleus by the use of the letters α and β in the conventional manner (see section on Isomerism, pages 4 and 5).

#### B. Numeration and Nomenclature of Substituents

(a) *Nucleus.* As illustrated on page 3, the letters A, B, C. and D designate the four rings of the cyclopentanoperhydrophenanthrene skeleton and the numbers 1 to 17, the nuclear carbon atoms. The carbon atoms of the angular methyl groups at C<sub>10</sub> and C<sub>11</sub> are labelled respectively 19 and 18; while the reverse numeration is widely used, the present assignation avoids a break in the numeral sequence pertaining to estrane, the parent hydrocarbon of a larger and more important class of compounds than 18-norandrostane in which the omission (C<sub>11</sub>) now occurs.

Alcoholic and ketonic substituents in the nucleus are designated by the suffixes -ol and -one preceded by the number of the carbon atom bearing the function (i.e. androstane-3(α)-ol-17-one).

Numerical indices following the sign Δ indicate the position of double bonds in the nucleus; where the linkage extends between carbon atoms not consecutively numbered, both numbers are recorded (e.g. estrone = Δ<sup>13,14,15</sup>-estratriene-3-ol-17-one).

Etiocholane derivatives with a double bond at C<sub>1</sub> or C<sub>2</sub> are classified as androstenes.

(b) **Side-Chain.** Aliphatic side-chains, both saturated and unsaturated, are designated by the appropriate alkyl radical, the carbon atoms of which are numbered in sequence from the point of attachment. Functions substituted in the side-chain are named in accordance with the International Union Rules for the Naming of Organic Compounds (J. Amer. Chem. Soc. 55, 3905 (1933). The prefixes hydroxy, keto, aldo and carboxy (respectively alcohols, ketones, aldehydes and acids) are placed in square brackets with the name of the alkyl radical which precedes that of the nuclear hydrocarbons; in the absence of functions in the side-chain, the brackets are omitted, e.g. desoxycorticosterone = 17( $\alpha$ )-[1-keto-2-hydroxyethyl]- $\Delta^4$ -androstene-3-one; ethynyl-testosterone = 17( $\beta$ )-ethynyl- $\Delta^4$ -androstene-3-one-17( $\alpha$ )-ol).

The following alkyl radicals appear in the nomenclature:

### List of Radicals

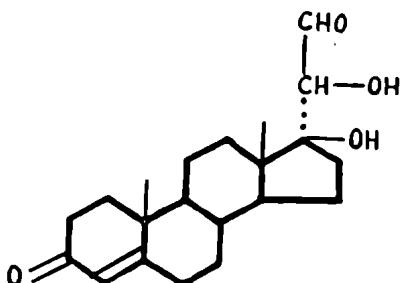
$\text{CH}_3-$	methyl
$\text{OCH}_2-$	formyl (aldo-methyl)
$\text{HOOC}-$	carboxy
$\text{CH}_2=$	methenyl
$\text{CH}_2-\text{CH}_2-$	ethyl
$\text{CH}_2=\text{CH}-$	ethylidene

$\text{CH}_2=\text{CH}-$	ethenyl
$\text{CH}\equiv\text{C}-$	ethynyl
$\text{CH}_2-\text{CH}_2-\text{CH}_2-$	propyl
$(\text{CH}_2)_2\text{CH}-$	isopropyl
$\text{CH}_2-\text{CH}=\text{CH}-$	1-propenyl
$\text{CH}_2=\text{CH}-\text{CH}_2-$	2-propenyl
$\text{CH}_2-\text{CH}_2-\text{CH}=$	propyldene
$\text{CH}_2=\text{CH}-\text{CH}_2=$	2-propenyldene
$(\text{CH}_2)_2\text{CH}=\text{CH}-$	isopropyldene
$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$	butyl
$(\text{CH}_2)_3\text{C}-$	t-butyl
$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$	pentyl
$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$	hexyl
$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_2-$	2-hexenyl
$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$	heptyl

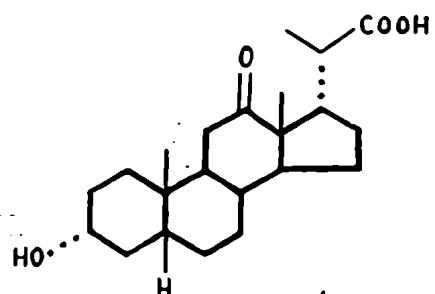
In the section listing derivatives of the parent compounds, derivatives of functions in the side-chain are indicated by numerals with indices ( $17^\alpha$ -oxime,  $16^\beta$ -acetate, etc.), the number giving the position of the alkyl radical and the index that of the substituted function.

Acid and aldehyde groups which stand in place of one or more hydrogen atoms of the nuclear carbons are designated by the prefixes carboxy- and formyl- respectively.

The following examples illustrate the nomenclature used in this index:

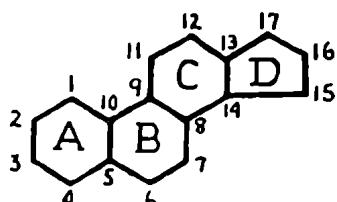


17( $\alpha$ )-[1( $\beta$ )-hydroxy-aldoethyl]- $\Delta^4$ -androstene-3-one-17( $\beta$ )-ol



17( $\alpha$ )-[1( $\beta$ )-carboxyethyl]-etiocholane-3( $\alpha$ )-ol-12-one

## THE PARENT HYDROCARBONS

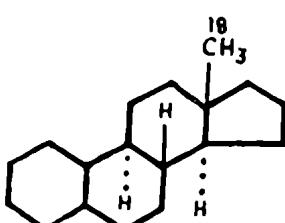


Norestrane and  
isomers of norestrane .....

No. in  
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1

Alkyl substituted norestranes and  
isomers of norestranes .....

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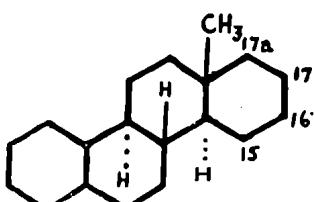


Estrane and isomers of estrane .....

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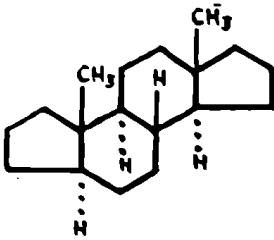
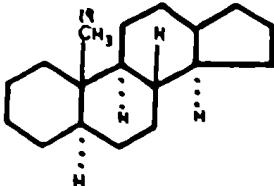
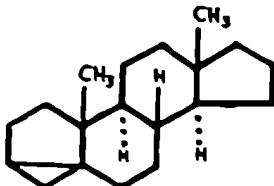
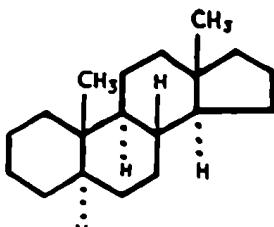
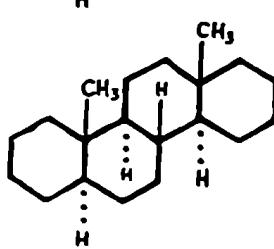
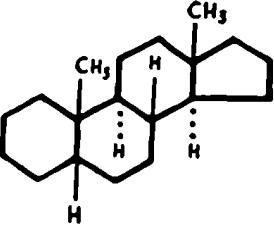
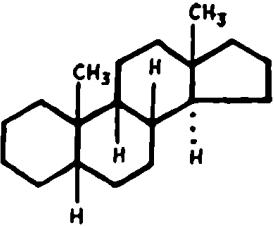


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### C. Isomerism

Outlined below are those aspects of the stereochemistry of the steroids which are especially important from a pharmacological point of view and are essential to an understanding of the nomenclature and system of classification used in this index; for a more comprehensive consideration reference should be made to the monographs of Sobotka (A34437), Fieser (A33784), Inhoffen (A56952), Strain (A57629), Reichstein and Shoppee (A58412) and others.

(a) *Nuclear Isomerism.* Consistent with the burden of evidence it is assumed that in androstanone (also pyroandrostanone and D-homoandrostanone) the substituents of each pair of adjacent asymmetric carbon atoms (i.e. 5:10, 9:10, 8:9, 8:14, 13:14) bear in space the opposite or trans relation to each other. Accordingly, the two angular methyl groups fixed at C<sub>10</sub> and C<sub>13</sub> lie on the same side of the flat plane of the molecule (arbitrarily the near side) and serve as points of reference. For representation in two dimensions (see formulae on pages

3 and 4), dotted lines are used throughout the index to denote valence bonds which project behind the plane of the paper (the trans configuration with respect to the angular methyl groups) and solid lines to indicate those which stand forward (the cis configuration).

Etiocolane differs from androstane only in the orientation about C<sub>5</sub>. Accordingly it is formulated with a solid line issuing therefrom.

Estrane is defined as the parent hydrocarbon of that isomer of estranediol which predominates on saturation of the naturally-occurring folliculoid estrone. While in all probability the configuration between rings B, C and D is that of androstane and etiocolane, the orientation of the hydrogen atoms at C<sub>5</sub> and C<sub>10</sub> is very uncertain. As nearly all members of this class (mainly the natural folliculoids) are unsaturated compounds in which ring A is benzenoid, the question of isomerism at C<sub>5</sub> and C<sub>10</sub> arises infrequently. This is also the case with D-homoestrane.

Norestrane and 18-norandrostane are the parent hydrocarbons of steroid classes in which only a limited number of saturated compounds are characterized at present. As implied by the name, norestrane should possess the same stereochemical arrangement as estrane. As the known members of the saturated norestrane series are all products of total synthesis (while those of the estrane series are derived from the natural folliculoids), the configuration of the asymmetric substituents remains unassigned. The same holds of 18-norandrostane.

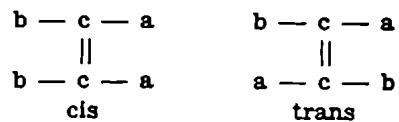
Isomerism in the nucleus is indicated by the prefixes "epi" (the opposite) and "iso". "Epi" is used when the site of the epimerization is established or assigned (e.g. urane, which is believed to differ from pregnane only in the special position of the C<sub>9</sub> hydrogen atom, is listed as 17(α)-ethyl-9-epietiocolane). When the isomerism is known to occur, but in an uncertain position, "iso" is used (e.g. isoestrane refers to any isomer of estrane in which the orientation about one or more centres of asymmetry is reversed); this is the only sense in which the prefix "iso" is employed in the classification nomenclature except when applied to side-chain radicals (see below).

(b) *Isomerism of Substituents and of the Side-chain.* For the designation of the steric arrangement of substituents at all centres of asymmetry, brackets follow the number of the substituted carbon atom. Contained therein, when the evidence justified the assignment of configuration, is the index α or β; otherwise a blank space is left for the insertion of the appropriate notation when the orientation will be determined. Use of the indices α and β was introduced by Fieser (A33784) in 1937 to denote the stereochemical relation to the rest of the molecule of the hydroxyl group at C<sub>9</sub>, which occurs in all of the sterols and bile acids and in many of the steroids of the hormone group. The β configuration was defined as that which obtains at C<sub>9</sub> in cholesterol and the sterols, and the α as that pertaining to the epimers of the sterols and to the bile acids and androsterone. In general the β epimer possesses the lower melting point, the more negative rotation, and forms an insoluble addition product with digitonin. As there is good, but not absolute, evidence that the β-hydroxyl group lies on the same side of the flat plane of the molecule as the angular methyl groups, the

terms β and cis on the one hand, and α and trans on the other, are now used synonymously. The indices α and β are also employed to distinguish stereoisomerism of the free rotation type which is encountered on substitution in the side-chain (i.e. the C17'-hydroxyl group of the pregnanediols, allo-pregnadiols and many of the steroids of the adrenal cortical series); here the configuration of the C17'-OH in the common pregnanediol from human pregnancy urine is arbitrarily referred to as α. In the present nomenclature, the convention is further extended to denote the orientation of the side-chain with respect to the nucleus. While the absolute position of the C<sub>5</sub> side-chain in the naturally occurring steroids is the subject of controversy (see Reichstein and Shoppee A58412), it is tentatively assigned the trans or α configuration in accordance with the terminology applied by Reichstein to the adrenal cortical compounds. Thus allopregnane is listed as 17(α)-ethyl-androstane and iso-allopregnane as 17(β)-ethyl-androstane. As parent hydrocarbon classes the former, 17(α)-, embraces all of the chemically stable, naturally-occurring and biologically active derivatives of allo-pregnane, while the latter, 17(β)-, includes the chemically labile, biologically less active derivatives prepared artificially.

In the structure formulae the α configuration is represented by a dotted line and the β by a solid line (the latter is also used when the configuration is undetermined).

(c) *Geometric Isomerism in Unsaturated Side-Chains.* Stereoisomerism resulting from asymmetric substitution of carbon atoms linked by a double bond (geometric or cis-trans isomerism) may occur in steroids possessing an unsaturated side-chain.



While the absolute configuration in these cases remains undetermined, blank brackets are left for its future designation (e.g. 17-[1( )-carboxymethylene]-4<sup>3</sup>-androstene-3(β)-ol cpd. 431).

(d) *Optical Isomerism.* Several steroids have now been prepared by total synthesis (e.g. equilemin). Where the racemic (dl-) product has been resolved into its optical isomerides, these are listed on the same page and designated in the conventional fashion by the prefixes d- and l-.

#### ARRANGEMENT OF PARENT COMPOUNDS

All compounds are classified as substitution products of the parent nuclear or alkyl substituted hydrocarbon containing the same number of carbon atoms. These are arranged as indicated on page 6. The alkyl derivatives of each nuclear hydrocarbon follow in order of increasing molecular size:

- 1-methyl, 2-methyl, 3-methyl, etc.
- 1-ethyl, 2-ethyl, 3-ethyl, etc.
- 1-propyl, 2-propyl, 3-propyl, etc.

Straight chain compounds precede branched chain compounds of the same size. Compounds with two or more side-chains, whether substituted on the same or different carbon atoms, are positioned according to the total number of carbon atoms contained and precede the mono-alkyl derivative of corresponding size (i.e.

1-methyl-17-ethyl-, and 17-methyl-17-ethyl precede 1-propyl).

Following each saturated parent hydrocarbon class come the corresponding unsaturated derivatives in order of increasing degree of unsaturation — i.e.

$C_{19}H_{22}$  androstane

$C_{19}H_{20}$  androstenes ( $\Delta^1$ ,  $\Delta^2$ ,  $\Delta^3$ , ..... to  $\Delta^{16}$ ).

$C_{19}H_{18}$  androstadienes ( $\Delta^{1,2}$ ,  $\Delta^{1,4}$ , ..... to  $\Delta^{1,16}$ ,  $\Delta^{2,4}$ ,

17( $\alpha$ )-ethyl-androstane

17( $\alpha$ )-ethyl-androstenes ( $\Delta^1$  to  $\Delta^{16}$ )

17( $\alpha$ )-ethyldene-androstane

17( $\alpha$ )-ethenyl-androstane

17( $\alpha$ )-ethynyl-androstane

17( $\alpha$ )-ethyl-androstadienes ( $\Delta^{1,2}$  to  $\Delta^{11,16}$ )

17( $\alpha$ )-ethyldene-androstenes ( $\Delta^1$  to  $\Delta^{16}$ )

17( $\alpha$ )-ethenyl-androstenes ( $\Delta^1$  to  $\Delta^{16}$ )

17( $\alpha$ )-ethynyl-androstenes ( $\Delta^1$  to  $\Delta^{16}$ )

17( $\alpha$ )-ethyl-androstatrienes

etc.

$\Delta^{3,5}$ , ..... to  $\Delta^{2,16}$ , etc. to  $\Delta^{14,16}$ ).  
 $C_{19}H_{20}$  androstatrienes  
 $C_{19}H_{18}$  androstatetraenes  
etc.

In the alkyl substituted hydrocarbon classes, nuclear unsaturation precedes side-chain unsaturation of the same degree. For example, under 17( $\alpha$ )-ethylan-drostan (allopregnane), the following order prevails:

(allo-pregnane)

(allo-pregnanes- $\Delta^1$  to  $\Delta^{16}$ )

( $\Delta^{11}$ -allo-pregnene)

( $\Delta^{19}$ -allo-pregnene)

(allo-pregnine-20)

(allo-pregnadlenes)

( $\Delta^{11}$ -allo-pregnadlenes- $\Delta^1$  to  $\Delta^{16}$ )

( $\Delta^{19}$ -allo-pregnadienes- $\Delta^1$  to  $\Delta^{16}$ )

(allo-pregnadienes)

(allo-pregnatrienes)

(allo-pregnatrienes)

Within each of the above mentioned parent hydrocarbon classes, both saturated and unsaturated, the arrangement is according to increasing number of oxygen atoms, the prevailing sequence of functions being: alcohols, ketones, aldehydes, acids. (As regards the position of aldehydes and acids in the index, it should be noted that the parent hydrocarbons of these functions contain an additional carbon to carbon linkage and hence are listed as alkyl substituted derivatives; e.g. 17-carboxy-androstane,  $C_{20}H_{28}O_2$ , appears under 17-methyl-androstane,  $C_{20}H_{28}$ , not under androstane  $C_{19}H_{28}$ .)

Compounds containing the same functional groups are placed in the sequence determined by the number of the carbon atoms substituted (e.g. androstane-1-ol, -2-ol, -3-ol, -4-ol, etc.).

The following outline of the classification of androstane derivatives illustrates the system according to which the derivatives of all nuclear hydrocarbons are listed in this index:

## SATURATED ANDROSTANES

### Androstane

$C_{19}H_{28}$

### Mono-oxygen cpds.

$C_{19}H_{27}O$

Mono-alcohols  
Mono-ketones

### Di-oxygen Cpds.

$C_{19}H_{26}O_2$

Diols  
Hydroxy-ketones { (a)  $\text{---OH, ---O}$  sequence  
(b)  $\text{---O, ---OH}$  sequence

Diketones

### Tri-oxygen Cpds.

$C_{19}H_{25}O_3$

Triols  
Hydroxy-ketones { OH, OH, O  
OH, O, OH  
O, OH, OH  
OH, O, O  
O, OH, O  
O, O, OH

Triketones

$C_{19}H_{24}O_3$   
etc.

## UNSATURATED ANDROSTANES

### Monenes

$C_{19}H_{26}$

### Dienes

$C_{19}H_{24}$

### Triones

$C_{19}H_{22}$

} etc.

} Each followed by their oxygen substitution products as listed under androstane.

## ALKYL SUBSTITUTED ANDROSTANES

### (Saturated and Unsaturated)

#### Mono-methyl

$C_{20}H_{28}$

1-methyl-androstane

Mono-oxygen Cpds.

$C_{20}H_{27}O$

alcohols

ketones

aldehyde (1-formyl-androstane)

Di-oxygen Cpds.

$C_{20}H_{26}O_2$

diols

hydroxy-ketones

hydroxy-aldehydes

diketones

ketoaldehydes

mono-acid (1-carboxy-androstane)

Tri-oxygen Cpds.

$C_{20}H_{25}O_3$

etc.

1-Methyl-androstenes

$C_{20}H_{26}$

1-Methylene-androstane

$C_{19}H_{26}$

1-Methyl-androstadienes

$C_{19}H_{24}$

1-Methylene-androstenes

$C_{20}H_{26}$

etc.

2-Methyl-androstane

etc.

3-Methyl-androstane

etc.

#### Di-methyl

$C_{21}H_{28}$

#### Ethyl

$C_{21}H_{26}$

#### Tri-methyl

$C_{22}H_{26}$

#### Methyl-ethyl

$C_{21}H_{27}$

#### Ethyl-methyl

$C_{21}H_{25}$

#### Propyl

$C_{21}H_{24}$

#### Iso-propyl

etc.

## PHARMACOLOGICAL NOMENCLATURE AND SYSTEM OF CLASSIFICATION

We have seen that the complicated chemical structure of the steroid molecule made it necessary to devise a rather intricate system of terminology and classification. When considering its complex pharmacological characteristics we shall find that these also require a system of orderly classification before they can be indexed or even clearly understood.

The manifold pharmacological activities of the steroids and the fact that almost any one compound possesses an apparently unpredictable combination of such activities tends to give the impression of complete lack of orderliness. It appears as though there were no correlation either between the chemical structure of a compound and its pharmacological activities, or between the various pharmacological effects themselves which a single compound may exhibit. Yet certain general laws and correlations have already been found to hold for all hormone-like steroids which have been examined up to the present time and perhaps the most fascinating, and from the practical point of view the most important, aspect of steroid hormone research today is the elucidation of such correlations. The number of steroids which could be made available by synthesis is practically endless and since their only value lies in their effectiveness as therapeutic agents, we must learn more about the structural prerequisites of their pharmacological activities in order to direct the synthetic work into profitable channels. Even a superficial perusal of this index reveals the surprising fact that only a small portion of these compounds have ever been assayed for any type of biological activity. Furthermore, with the possible exception of the most readily obtainable natural hormones (estradiol, progesterone, testosterone and desoxycorticosterone), none have been examined for all the important known hormonal effects. It is felt that from the pharmacologist's point of view the paramount task to accomplish in this index is to give a bird's-eye view of the relevant work that has been done up to date. This, it is hoped, will point out the greatest gaps which must be filled to make the picture more complete and will prevent unwarranted generalizations from personal observations on a few compounds, with disregard for the world literature. Such generalizations based on inadequate material are extremely misleading and when they are found to be incorrect tend to discredit the whole concept of the possibility to formulate rules concerning pharmaco-chemical inter-relations. The concept of the indispensability of a phenolic ring A for folliculoid activity and of a conjugated ketone group in position C, for luteoid and corticoid activity are examples of such unfounded generalizations which influenced pharmacological thought adversely, although they contained some measure of truth. Had more compounds been examined, these rules could have been expressed correctly by stating that the chemical structures mentioned are advantageous but by no means indispensable for those activities.

The literature concerning the pharmacological properties of the many steroids of the "hormone group" is not easy to find, as many of the data are hidden in postscripts and footnotes of purely chemical publications. Furthermore, the synthetic chemists who first prepared a certain compound frequently failed to give

more than a mere suggestion of the type of bioassay performed. They often speak of a compound having "estrogenic activity" without stating at what dose or in what test. At other times we find such statements as "up to 1 mg. inactive in causing vaginal cornification in the rodent". Descriptions of this type are almost completely without value as it is known that the same amount of hormone may have different effects depending upon the time over which it is administered, the solvent in which it is given, the route of administration etc. Furthermore, some compounds cause only transitory vaginal cornification no matter how large a dose is administered, so that it would have been necessary to state whether daily vaginal smears were taken and of course to indicate what species of rodent was used and whether the animals were spayed adult or immature females.

The same type of error is usually committed by the pharmacologist who obtains a compound from the chemist and describes it merely by the name which appears on the label. Such publications may be very adequate from the pharmacological point of view, but they are usually valueless in the final analysis as it is impossible to determine either the nature or the degree of purity of the preparation employed. For example, a compound merely described as "androstenediol" may be any one of a whole series of isomers depending upon the position of the double bond and the hydroxyls, as well as the steric position of the latter. It is indispensable, therefore, to identify compounds used for pharmacological purposes, by some physical constants such as their melting point, optic rotation or absorption spectrum. For a detailed discussion of steroid hormone pharmacology the reader is referred to an earlier review (A37822). Here we shall only discuss those fundamentals which are indispensable for the understanding of the data reported in this index.

### A. The Independent Actions

The basic principle according to which the pharmacological activities are classified in these volumes is that certain pharmacological actions are independent, while others are merely distinct subordinate manifestations of a single independent action. It must be clearly understood that independent actions are characterized by the fact that every one of them can be exhibited independently of any of the others; that is to say, there is no direct parallelism between the degree to which a compound exhibits the various independent actions (Selye A37822). In this sense we recognize the independent nature of the following actions: *folliculoid* (estrogenic, gynecogenic, estromimetic or follicular-hormone-like), *testoid* (androgenic, andromimetic or male hormone-like), *luteoid* (progestational, corpus luteum hormone-like), *corticoid* (adrenal cortical hormone-like), *gonadotropic* (having the ability to stimulate the gonad), *renotropic* (nephrotropic, having the ability to increase kidney size due mainly to hypertrophy of the convoluted tubules), *anti-folliculoid* (having the ability to antagonize the actions of folliculoid hormones) and *anesthetic*.

It will be noted that for those independent actions which imitate the function of an organ of internal secretion, terms are used which suggest a specific con-

nection with that particular endocrine gland. The Greek ending "-oid", which is added to the name of a gland, means "similar to" without implying that the hormone is necessarily derived from that particular gland. It merely suggests that the compound simulates its activity and this is true by definition. It would be misleading to designate hormones of the testoid type, for instance, as "testicular hormones" since such compounds are also elaborated by the adrenal cortex and probably even by ovarian and other tissues. It would be equally misleading to term them "androgenic" since the most potent natural "androgen", testosterone, causes testis atrophy in experimental animals. Thus, far from being masculinizing it is actually "demasculinizing". Similarly the so-called "estrogens" interrupt the estrous cycle in the intact rodent so that they are actually "anti-estrogenic" under ordinary circumstances of bioassay. The term "gynnecogenic" would be no more adequate for them since they cause ovarian atrophy. Hence it appears that it is unsatisfactory to designate these hormones either according to their source of origin or on the basis of one particular action on a certain target organ. It is for these reasons that preference is given to a terminology (Selye A39832, A30267) based upon the natural classification of the steroid hormone actions according to the gland whose function they simulate.

Certain actions have not as yet been sufficiently studied to make possible their accurate classification and hence they are rather arbitrarily considered as subdivisions of closely related independent activities. For instance, it is not definitely known as yet whether the mammotropic, vagina-mucifying, metrotropic, anti-Leydig cell and anti-castration cell activities are independent, or subordinate to another activity. It is extremely probable that the anti-castration and anti-Leydig cell actions are merely subordinate manifestations of folliculoid potency (Clarke and Selye A56752) but the evidence is less convincing for the mammotropic, metrotropic and vagina-mucifying actions. Provisionally however, they are all mentioned in the Index under the heading "folliculoid", but unlike other data registered there, the type of activity is specifically mentioned without abbreviation and is printed in italics.

The ability to produce nephrosclerosis or to stimulate diuresis is even more difficult to fit into a category corresponding to one of the accepted independent actions since these activities have not been adequately studied as yet. Hence they are listed under separate headings.

## B. The Subordinate Actions

We stated above that each independent action has numerous different subordinate manifestations inasmuch as it may effect a variety of target organs. Thus a folliculoid hormone, which causes vaginal cornification in the rodent, invariably — and to a degree which runs parallel with the intensity of its effect on the vagina — causes enlargement of the uterus, the oviducts, the adrenals, the nipples, hyperemia of the monkey's sex skin, atrophy of the testes etc. These latter effects are termed subordinate actions in order to emphasize that they are dependent upon and the direct consequence of a single independent action. In the same sense, the ability to stimulate the seminal vesicles, the prostate, the capon's comb etc. are subordinate to the testoid action. In the index these subordinate actions

are listed under the main heading of the independent action of which they are separate manifestations.

## C. The Potentially Subordinate Actions

There is a third type of effect which appears to be intermediate between the independent and the subordinate actions. This has been termed a "potentially subordinate" effect (Selye A37822). Two actions, which we may term A and B respectively, are potentially subordinate if A is subordinate to B — in the sense that it never occurs without the latter — while B is independent of A — inasmuch as it may occur with or without any evidence of A. For instance, no compound is known to stimulate the seminal vesicles of the rat without simultaneously increasing the weight of the prostate and preputial glands. There are compounds, however, which stimulate the latter two organs without affecting the seminal vesicles (e.g. progesterone).

Similarly among the corticoids some compounds have a particularly pronounced effect on sugar and others on salt metabolism, but all the corticoids exert a beneficial effect on life maintenance after adrenal deprivation. Hence both the sugar and the salt metabolism influencing activities are subordinate to the life-maintaining potency of the corticoids.

## ARRANGEMENT OF DATA ON A STANDARD INDEX PAGE

As previously stated, the data which characterize a compound are listed under the headings of Isolation, structure and synthesis, melting point and optic rotation, pharmacology, remarks (if they are required to illustrate special particularities concerning the compound in question), derivatives and references. The bracketed numbers in the text refer the reader to the library numbers at the bottom of the page and all bibliographical data are listed with those numbers in a special appendix at the end of volume 4 (pages 33-40).

**Isolation:** Under this heading are listed data concerning the isolation of the compound from normal or pathological body fluids or tissues. The source from which the substance was prepared is indicated first and in brackets after it are remarks specifying its nature. In this index no mention is made of the isolation of steroids following the exogenous administration of hormones and related compounds. These will be discussed with the metabolism of the hormone in future sections of the Encyclopedia in the volumes dealing with the particular gland from which the substance arises.

For the sake of convenience, synoptic charts are provided (pages 10-11) in which the naturally-occurring steroids are arranged according to the source from which they were isolated.

**Structure and Synthesis:** References to data concerning the proof of structure as well as details of methods for artificial preparation are given under this heading.

**Melting Point and Optical Rotation:** For each compound several melting points are usually given to indicate the range of the data in the literature. The optical rotations are likewise registered in this section and using the bracketed reference numbers as a guide, the corresponding rotations and melting points may readily be correlated.

**Pharmacology:** In this section data concerning each independent activity are recorded under separate head-

ings. The potentially independent and subordinate actions (for definition see page 7) are listed under the corresponding independent action. Obviously it would have been impossible to characterize the steroids pharmacologically in the space assigned to this aspect in the index if the style usually employed in pharmacological publications had been adopted. Chemistry has developed an extensive system of symbols and abbreviations, such as the structure formula, the designation of optical rotation by such symbols as  $[\alpha]_D^{25} =$ , or the designation of methyl, acetate, benzoate, *by.*, *me.*, *ac.*, *bz.* respectively and so forth. In order to permit a similarly concise presentation of pharmacological characteristics, a system has been introduced which is based on the following principles:

In order to avoid repetitions in the text the main characteristics of every commonly used bioassay method are described in a special dictionary of tests in which each of them has a serial number. This dictionary (as well as a list of the symbols and abbreviations used) will be found at the end of volume 4 (page 32). In the pharmacology section of each particular compound the serial numbers of the bioassay methods (in bold type) are followed by a brief description of the degree of activity, the capital letter used as a symbol for the species on which the experiment was performed and (in brackets) a reference to the library numbers at the bottom of the page. For instance, 27:0.05 mg. act.-G (54) means that in the sexual receptivity test on the female castrate guinea pig (which in the dictionary bears the number 27) 0.05 mg. of the compound gives a positive result and that the library number which takes 54th place at the bottom of the page should be consulted in the literature appendix for reference to the publication in which these data were described. Wherever activity is expressed in actual units this is indicated; for instance I.U. = 100 $\gamma$  (44) means the international unit equals 100 gamma by definition (not by assay on any particular species), for reference see library number (44); 29:U. = 80 $\gamma$  —C (17) means that the unit in the Tschiopp test on capons (which is described under number 29 in the dictionary of tests) equals 80 gamma, for reference see the 17th library number at the bottom of the page.

In the case of folliculoid compounds most investigators used estrone as a standard for comparison, although their bioassay techniques varied. Hence special care was taken to record the activity of estrone in the various tests. Wherever the activity of another folliculoid is expressed in estrone equivalents, the reader can thus readily compare the activity of the compound in question with that recorded for estrone under the same test number.

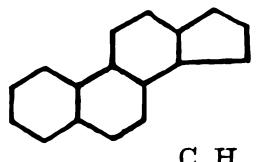
Wherever possible the degree of activity is expressed by the percentage deviation from the control in the weight of the target organ (with the standard error in brackets) per daily dose of the steroid given. Since the method of administration and all other details of the test, as well as the standard error in the control group, are described under the corresponding number in the dictionary of tests, such abbreviations remain fully descriptive. For instance, 132: s.ves. 30( $\pm 3$ )%, pta. 25( $\pm 7$ ), prep. gl. 33( $\pm 5$ )/1 mg.-R (27) means that in castrate immature rats treated according to the technic 132 a daily dose of 1 mg. of the compound increases the weight of the seminal vesicles, prostate and preputial glands by 30%, 25% and 33% respectively, see 27th library number. This manner of description obviates the necessity of creating new units for every measurable activity and gives a great deal of information in a concise manner.

For the sake of convenience synoptic charts are provided (pages 12-27) on which the pharmacological effects of all physiologically active steroids are compared.

*Remarks:* Although only comparatively few compounds require explanatory remarks, space is assigned to such on every page for the convenience of those who wish to use the index as a personal reference book and desire to add their own comments. Remarks concerning uncertainties in chemical structure or pharmacological potency are usually inserted under this heading.

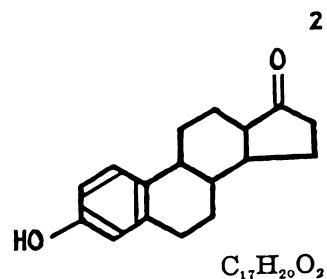
*Derivatives:* In this section are listed the melting points and optic rotations of derivatives wherever such data are recorded in the literature. Derivatives which have not been purified to any extent, but were prepared merely as intermediates in the synthesis of other compounds, are listed only in exceptional cases.



**NORESTRANE****ISOLATION:****STRUCTURE AND SYNTHESIS:****M.P.:****PHARMACOLOGY:****REMARKS:** Theoretical parent compound.**DERIVATIVES:****REFERENCES:**

$\Delta^{1,3,5:10}$ -NORESTRATRIENE-3-OL-17-ONE  
(X-norestrone, 7-hydroxy-3<sup>1</sup>-keto-1:2:3:4:9:10:11:12-octahydro-  
1:2-cyclo-pentenophenanthrene)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.: 222°: (1)

PHARMACOLOGY:

REMARKS:

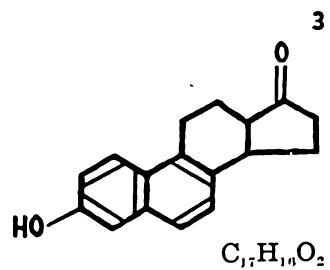
DERIVATIVES:

Me. ether 142-3°: (1)

REFERENCES:

1. A54808

$\Delta^{1,3,5:10,0,8}$ -NORESTRAPENTAENE-3-OL-17-ONE  
(X-Norequilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

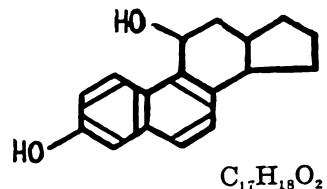
REMARKS:

DERIVATIVES:

Me. ether 116-7°: (1)  
2,4-dinitrophenyl hydrazone-me. ether 246.7°: (1)

REFERENCES:

1. 76315

**$\Delta^{1,3,5:10,6,8}$ -NORESTRAPENTAENE-3,11( )-DIOL****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

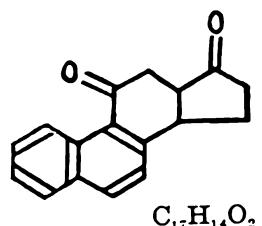
**M.P.:****PHARMACOLOGY:****REMARKS:****DERIVATIVES:**

Me. ether 141-2%; (1)

**REFERENCES:**

1. A51808

$\Delta^{1,3,5:10,6,8}$ -NORESTRAPENTAENE-11,17-DIONE



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.: 115°: (1)

PHARMACOLOGY:

REMARKS:

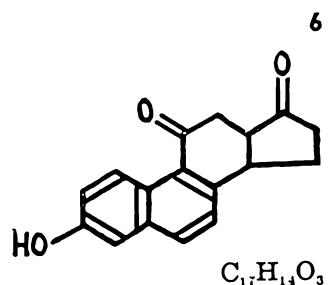
DERIVATIVES:

Semicarb.	245°: (1)
2:4-dinitrophenyl hydrazone	240°: (1)
Hydrazone	156°: (1)

REFERENCES:

1. 76315

$\Delta^{1,3,5:10,6,8}$ -NORESTRAPENTAENE-3-OL-11,17-DIONE



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

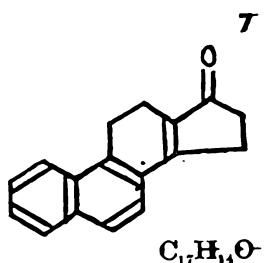
DERIVATIVES:

Me. ether 126-7°; (1)  
2-(4-dinitrophenyl) hydrazone-me. ether 243°; (1)

REFERENCES:

1. 76315

$\Delta^{1,3,5:10,6,8,13}$ -NORESTRAHEXAENE-17-ONE



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 210°: (1)

PHARMACOLOGY:

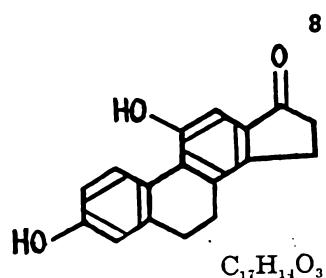
REMARKS:

DERIVATIVES:

REFERENCES:

1. A1916

*Δ*<sup>1,3,5:10,8,11,13</sup>-NORESTRAHEXAENE-3,11-DIOL-17-ONE  
(4:7-dihydroxy-3<sup>1</sup>-keto-9:10-dihydro-1:2-cyclo-pentenophenanthrene)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

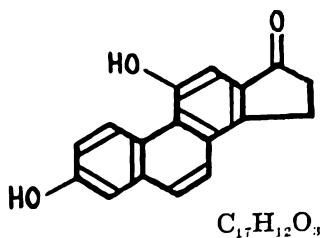
DERIVATIVES:

Dime. ether 143°: (1)  
2:4-dinitrophenyl hydrazone -dime. ether 242-3°: (1)

REFERENCES:

1. A54808

*Δ<sup>1,3,5:10,6,8,11,13</sup>-NORESTRAHEPTAENE-3,11-DIOL-17-ONE*  
*(4,7-dihydroxy-3<sup>1</sup>-keto-1:2-cyclo-pentenophenanthrene)*



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

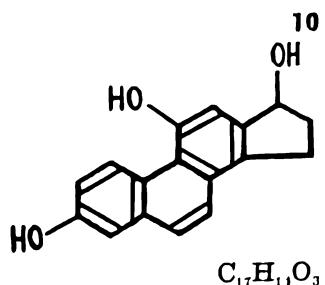
DERIVATIVES:

11-ac., 3-me. ether 241-2°: (1)  
 Dime. ether: (1)

REFERENCES:

1. A54808

$\Delta^{1,8,5:10,6,8,11,13}$ -NORESTRAHEPTAENE-3,11,17( )-TRIOL  
(4,3<sup>1</sup>,7-trihydroxy-1:2-cyclo-pentenophenanthrene)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

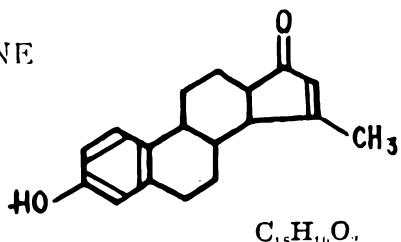
DERIVATIVES:

3-me. ether 139-40°: (1)  
3-me. ether-11-ac. 145°: (1)

REFERENCES:

1. A54808

**15-METHYL- $\Delta^{13,14;16,17}$ -NORESTRATETRAENE-3-OL-17-ONE**  
 (15-methyl-15-dehydro-N-nor-estrone)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** ca. 180°; (1)

**PHARMACOLOGY:** Folliculoid: 1: 100 $\gamma$  of impure product (probably mixture of isomerids) as act. as 0.7 $\gamma$  of estrone-R (1).

**REMARKS:** Possibly the 15-keto-17-methyl cpd. (1).

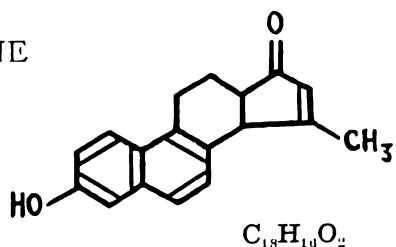
**DERIVATIVES:**

3-me. ether 181-3°; (1)  
 Oxime 185-6°; (1)

**REFERENCES:**

1. 80940

**15-METHYL- $\Delta^{1,3,5:10,6,8,15}$ -NORESTRAHEXAENE-3-OL-17-ONE  
(15-methyl-15-dehydro-X-nor-equilenin)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:** Possibly the 15-keto-17-methyl cpd. (1).

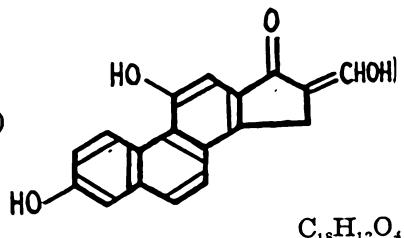
**DERIVATIVES:**

3-me. ether 116-17°: (1)

**REFERENCES:**

- 1. 80940

16-HYDROXYMETHYLENE- $\Delta^{1,3,5:10,6,8,11,13}$ -  
**NORESTRAHEPTAENE-3,11-DIOL-17-ONE**  
(4:7-dihydroxy-2<sup>1</sup>-formyl-3<sup>1</sup>-keto-1:2-cyclo-pentenophenanthrene)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

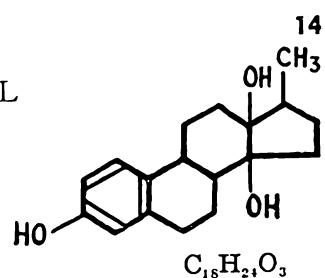
DERIVATIVES:

3,11-dime. ether 195°: (1)

REFERENCES:

1. A54808

**17( )-METHYL- $\Delta^{1,3,5:10}$ -NORESTRATRIENE-3,13( ),14( )-TRIOL  
(Retro-estratriene-triol)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 241°: (1)

PHARMACOLOGY:

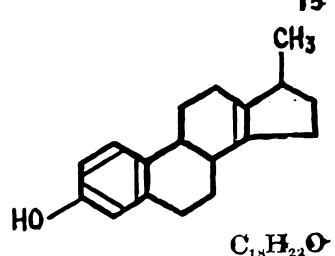
REMARKS:

DERIVATIVES:

REFERENCES:

1. A51961

**17( )-METHYL- $\Delta^{1,3,5;10,13}$ -NORESTRATETRAENE-3-OL  
(Retro-estratetraene-3-ol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: I 163°: (1)  
II 125°: (1)

I  $[\alpha]_D^{20} = -35^\circ$  (CHCl<sub>3</sub>): (1)

**PHARMACOLOGY:**

**REMARKS:** I + II isomeric, structure not assigned (1).

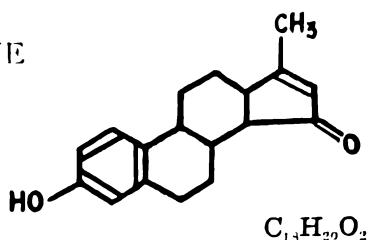
**DERIVATIVES:**

I Bz. 159°;  $[\alpha]_D^{20} = +17.8^\circ$  (CHCl<sub>3</sub>): (1)  
II Bz. 133°;  $[\alpha]_D^{20} = +69.3^\circ$  (CHCl<sub>3</sub>): (1)

**REFERENCES:**

1. A54961

**17-METHYL- $\Delta^{1,2,5,10,16}$ -MORESTRATETRAENE-3-OL-15-ONE**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

M.P.: 180°: (1)

**PHARMACOLOGY:** Folliculoid: 1: 100 $\gamma$  of impure product (probably a mixture of isomerids) as act. as 0.7 $\gamma$  of estrone-R (1).

**REMARKS:** Possibly the 15-methyl-17-keto cpd. (1).

**DERIVATIVES:**

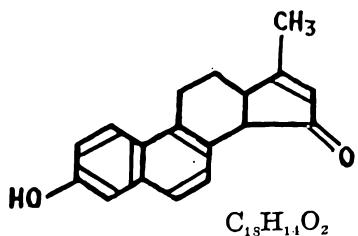
3-me. ether 181-3°: (1)

Oxime 185-6°: (1)

**REFERENCES:**

1. 80940

**17-METHYL- $\Delta^{1,9,5:10,6,8,16}$ -NORESTRAHEXAENE-3-OL-15-ONE**  
 (17-methyl-15-dehydro-nor-equilenin)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:** Possibly 15-methyl-17-keto cpd. (1).

**DERIVATIVES:**

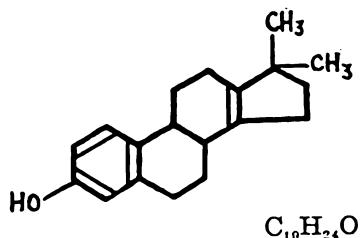
Me. ether 116-7°: (1)

**REFERENCES:**

1. 80940

18

17-DIMETHYL- $\Delta^{1,3,5:10,12}$ -NORESTRATETRAENE-3-OL.



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

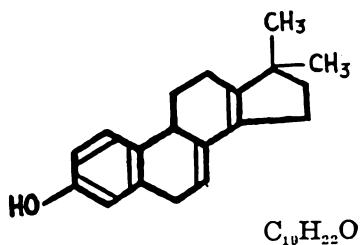
DERIVATIVES:

Me. ether (impure) 58-80% (1)

REFERENCES:

1. 53062

**17-DIMETHYL- $\Delta^{1,3,5:10,7,13}$ -NORESTRAPENTAENE-3-OL**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

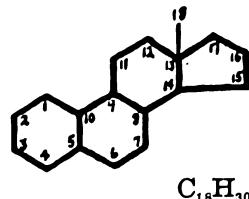
REMARKS:

DERIVATIVES:

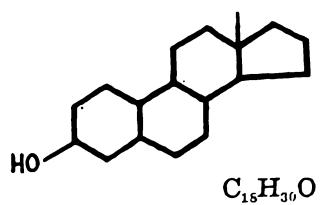
Me. ether (impure) 112-7°; (1)

REFERENCES:

1. 53862

**ESTRANE****ISOLATION:****STRUCTURE AND SYNTHESIS:****M.P.:****PHARMACOLOGY:****REMARKS:** Theoretical cpd.**DERIVATIVES:****REFERENCES:**

**ESTRANE-3( )-OL**  
**(Hexahydro-desoxy-estrone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2,3)

M.P.: I 110° (u): (1); (+ H<sub>2</sub>O) 85-95°: (1)

II 104-5°: (2,3)

III 96-100°: (3)

I  $[\alpha]_D = -2.8^\circ$  (alc.): (1)

II  $[\alpha]_D^{22} = +1.8^\circ$  (alc.): (3)

III  $[\alpha]_D^{22} = +12.3^\circ$  (alc.): (3)

**PHARMACOLOGY:**

**REMARKS:** Isomers II + III form digitonides soluble at high temperature (3).

**DERIVATIVES:**

**REFERENCES:**

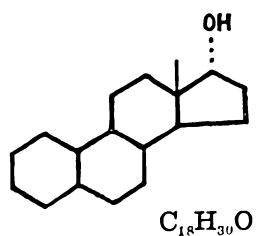
1. 18356

2. 3429

3. 34803

22

**ESTRANE-17( $\alpha$ )-OL**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 106-8°: (1)

,

PHARMACOLOGY:

REMARKS:

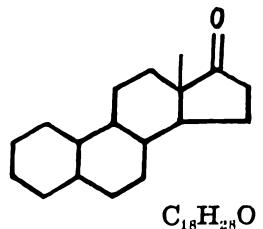
REFERENCES:

DERIVATIVES

1. 77855

**ESTRANE-17-ONE**  
**(Anhydride of hexahydro-desoxy-follicular hormone hydrate)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY:

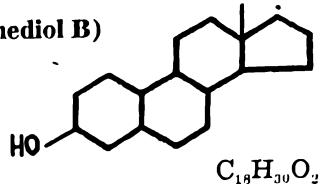
REMARKS: Structure not proved (1).

DERIVATIVES:

Semicarb. 262.5°(u) : (1) 1. 18356  
 Semicarb. of iso-estrane-17-one 278.5°(u) : (1)

REFERENCES:

**ESTRANE-3( ),17( $\alpha$ )-DIOL**  
**(Octahydro-estrone, hexahydro-desoxy-estriol, hexahydro-estradiol, estranediol B)**



**ISOLATION:**

Ur. (preg. human) : (absent 4)  
 Ur. (human ♀) : (3,4)

**STRUCTURE AND SYNTHESIS:** (1,2,3,4,5,6)

M.P.: 204-5° (u) : (2,3,4,6)  
 209-11°: (1)  
 210-1°: (6)

$[\alpha]_D^{20} = + 7.8^\circ$  (alc.) : (6)

**PHARMACOLOGY:**

**REMARKS:** Not ppt. with digitonin (3,6); a molecular cpd.  $\text{C}_{18}\text{H}_{30}\text{O}_2 \cdot \text{C}_{18}\text{H}_{30}\text{O}$  m.p. 175° has been described (2); an isomeric estranediol is also obtained on reduction of estrone m.p. 154-5°(u);  $[\alpha]_D^{10} = + 31.4^\circ$  (alc.) : (6).

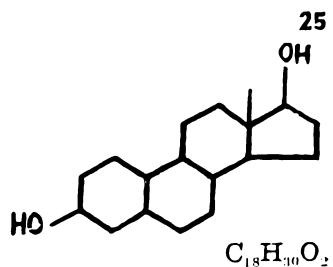
**DERIVATIVES:**

Diac. 160°: (3,4)

**REFERENCES:**

1. 8041
2. 73728
3. A17994
4. 71843
5. 18356
6. 34803

**ESTRANE-3( ),17( )-DIOL**  
**(Estranediol A)**



**ISOLATION:**

Ur. (preg. human) : (absent 2)  
 Ur. (human ♀) : (2)

**STRUCTURE AND SYNTHESIS:** (1,2)

M.P.: 242°: (2)

**PHARMACOLOGY:**

**REMARKS:** Not ppt. with digitonin (1,2).

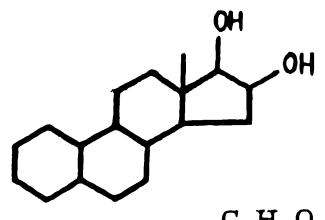
**DERIVATIVES:**

Diac. 160°: (1,2)

**REFERENCES:**

1. 71843
2. A17994

**ESTRANE-16( ),17( )-DIOL**  
**(Hexahydro-desoxy-follicular hormone hydrate; Iso-hexahydro-**  
**desoxy-follicular hormone hydrate)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** I 153°: (1)  
 II 162°: (1)

I  $[\alpha]_D = -12.2^\circ$  (alc.): (1)

**PHARMACOLOGY:**

**REMARKS:**

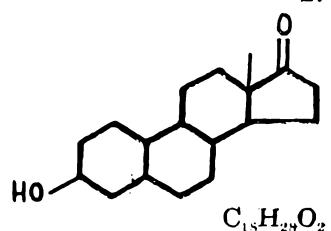
**DERIVATIVES:**

I diac. 84°:  $[\alpha]_D = -37.6$  (alc.): (1)  
 II diac. 131°: (1)

**REFERENCES:**

1. 18356

**ESTRANE-3(17)-OL-17 ONE**  
**(Hexahydro-estrone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:** I + II isomers (1).

**DERIVATIVES:**

Semicarb.-I  $255^\circ$ ;  $[\alpha]_D^{20} = +46^\circ$  (alc.): (1)

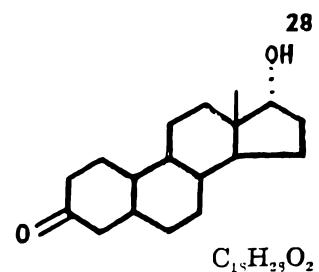
Semicarb.-II  $255^\circ$ ;  $[\alpha]_D^{22} = +77.2^\circ$  ( $\text{CHCl}_3 + \text{alc.}$ ): (1)

2:4-dinitrophenyl hydrazone  $105-110^\circ$ : (1)

**REFERENCES:**

1. 34803

**ESTRANE-3-ONE-17( $\alpha$ )-OL**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** 102-4°: (1)

**PHARMACOLOGY:**

**REMARKS:**

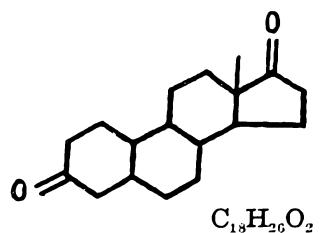
**DERIVATIVES:**

Br. (non-crystalline): (1)

**REFERENCES:**

1. 77855

**ESTRANE-3,17-DIONE**  
**(Estranedione A + B)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2)

M.P.: I (Estranedione A) : 124°: (1,2)

II (Estranedione B) : 170°: (2,3)

III                    { 148°: (1)  
                       { 144-6° and 179-80°: (4)

**PHARMACOLOGY:**

**REMARKS:** Isomerism possibly at C<sub>6-10</sub> (1); I + III not ppt. with digitonin (1,3).

**DERIVATIVES:**

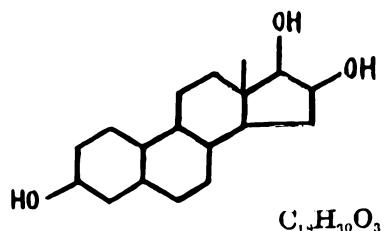
Br.-III 170-2°: (4)

**REFERENCES:**

1. 71843
2. A17994
3. 73728
4. 77855

**ESTRANE-3( ),16( ),17( )-TRIOL  
(Hexahydro-estriol)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2,3)

M.P.: 268°: (2,4)

255-6°(u): (1,3)

PHARMACOLOGY:

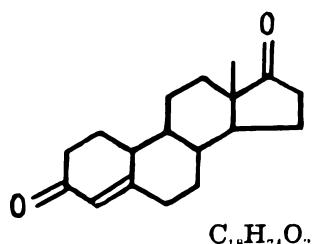
REMARKS:

DERIVATIVES:

Triac. 135°: (1)

REFERENCES:

1. 3930
2. 7967
3. 3429

**$\Delta^4$ -ESTRENE-3,17-DIONE****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)

M.P.: 146-8°: (1)

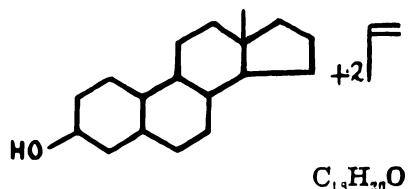
**PHARMACOLOGY:**

REMARKS: Position of double bond uncertain (1).

**DERIVATIVES:****REFERENCES:**

1. 77855

*Δ<sup>1</sup>-ESTRADIENE-3(17)-OL*  
*(Dihydrodesoxoestrone)*



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** 129°: (1)

**PHARMACOLOGY:** Folliculoid: Test?: "physiologically inert": (1).

**REMARKS:**

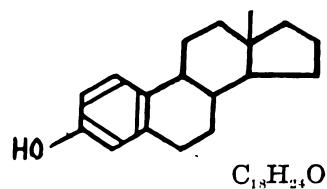
**DERIVATIVES:**

Bz. 166-7°: (1)

**REFERENCES:**

1. 3930

$\Delta^{1,3,5:10}$ -ESTRATRIENE-3-OL  
(Desoxy-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2,3,4,5,6)

M.P.: 134° (u): (2,5,6)

132-3.5° (u): (3)

135.5-7°: (5)

133-4.5°: (4)

$[\alpha]_D = +86-91^\circ$  (alc.): (2)

$[\alpha]_{5463} = +107-12^\circ$  (alc.): (2)

$[\alpha]_D = +77^\circ$  (alc.): (5)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

Me. ether 76.5°;  $[\alpha]_D = +81^\circ \pm 5^\circ$ ;  $[\alpha]_{5463} = +100^\circ \pm 4^\circ$  (alc.): (1,2)

Bz. 173.5°:

3-bz.-17-Cl 158°;  $[\alpha]_D^{23} = +16.6^\circ$  (CHCl<sub>3</sub>):

3-bz.-17-iso-Cl. 198°;  $[\alpha]_D^{23} = +56.8^\circ$  (CHCl<sub>3</sub>):

REFERENCES:

1. 3930

2. 18356

3. 7967

4. 1605

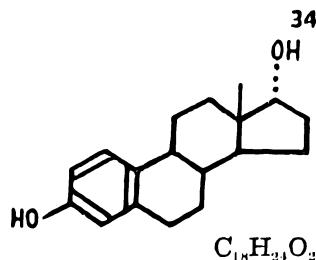
5. A30454

6. 3429

7. A54961

$\Delta^{1,3,5,10}$ -ESTRATRIENE-3,17( $\alpha$ )-DIOL

( $\alpha$ -Estradiol; dihydrofollicular hormone; dihydroxyestrin; dihydrotheelin; dihydromenformon)



ISOLATION:

Ov. (pig):	(2,36,4)
Ur. (preg. mare):	(5)
Ur. (preg. human):	(14,27,35)
Placenta (human):	(37)
Te. (horse):	(38,39)

STRUCTURE AND SYNTHESIS: (1,3,4,6,7,8,10,11,12,13,15,19,24,42)

Microbial synthesis:	(1,49)
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M.P.: 170°:	(6)
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173°(u):	(2)
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174-5°(u):	(10,15)
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[ $\alpha$ ] <sub>D</sub> <sup>25</sup> = + 82° (dioxane):	(10)
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174-5°:	(7)
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[ $\alpha$ ] <sub>D</sub> = + 80° (dioxane):	(7,9)
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176-7°(u):	(9,11)
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[ $\alpha$ ] <sub>D</sub> = + 81° (alc.):	(3)
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178°:	(?)
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[ $\alpha$ ] <sub>D</sub> <sup>18</sup> = + 78° (alc.):	(11,13)
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PHARMACOLOGY:

Folliculoid: I.Bz.U. = 0.1 $\gamma$  of 3 mono-bz. (52); **5,22,14B**: ca. 2  $\times$  as act. as estrone-M (9); **9**: as act. as estrone-M (9); **16**: ca. 2  $\times$  as act. as estrone-R (9); **18**: 2  $\times$  as act. as estrone-G (9); **8**: < than 3  $\times$  as act. as estrone-R (9); **17A**: 20  $\times$  as act. as estrone-R (9); **6**: 1.6  $\times$  as act. as estrone-R (2); **1**: free cpd. and 3 mono-bz. 12  $\times$  and 6  $\times$  as act. as estrone respectively-R (3,34); **9,16,22**: dose per os/dose by injection = 40-45/1-M (9,53); **22**: 3 mono-bz. ca. 5-6  $\times$  as act. as estrone-M, and 3-4  $\times$  as act. as estrone-R (9); **22**: diac. and di-bz. ca. 2.5  $\times$  and ca. 150  $\times$  less act. than estrone-M (9); **62?**: ratio of act. free cpd./3-bz. = 20/13-15-M (13); **23**: threshold dose of free cpd. = 0.4 $\gamma$ , diac. = 0.5 $\gamma$ , 3-ac.-17 pr. = 0.6 $\gamma$ , dipr. = 0.75 $\gamma$ , di-n-butyrate = 3.5 $\gamma$ , di-isobutyrate = 6 $\gamma$ , di-n-valerate = 7 $\gamma$ , di-n-hexanoate = 8 $\gamma$ , di-n-octanoate = 10 $\gamma$ , di-n-decanoate = 25 $\gamma$ , dipalmitate = 27 $\gamma$ , 3-bz.-17-ac. = 4 $\gamma$ , 3-bz.-17 pr. = 4 $\gamma$ , 3-bz.-17-n-butyrate = 9 $\gamma$ , 3-bz.-17-n-valerate = 17 $\gamma$ , 17-bz.-3-ac. = 8 $\gamma$ , 17-bz.-3 pr. = 28 $\gamma$ , 17-bz.-3-n-butyrate = 45 $\gamma$  and dibz. = 125 $\gamma$ -R (22); **24**: free cpd. 2  $\times$ , diac. 13.4  $\times$ , 3-ac-17 pr. 27.4  $\times$ , dipr. 55.8  $\times$ , di-n-decanoate 120  $\times$ , and 3-bz. 11.8  $\times$  as act. as estrone-R (22); **23,24**: "di-esters have on the whole more intense and more prolonged effects than are attained even with the best estrone esters"-R (22); **3**: free cpd., diac., bz. and dipr. 3, 1.1, 2 and 0.7  $\times$  as act. as estrone-M (26); **60**: act-B (60); **28**: U. = 0.02 $\gamma$ -M (46); **118**: 100 $\gamma$ /day act.-R (61); **5**: free cpd. and 3-bz. ca. 2.5 and 2  $\times$  as act. as estrone-M (11); **65A**: 3.5-4  $\times$  as act. as estrone, 1/4 as act. as stilbestrol-R (28); **139**: *Metrotropic act.*: 1 $\gamma$  as act. as 20 $\gamma$  of estrone-R (56); **140**: *Metrotropic act.*: 1 $\gamma$  as act. as 12 $\gamma$  of estrone-R (57); **19**: free cpd. -70% /0.5 $\gamma$ ; monobz. -67%/0.5 $\gamma$ ; and diac. -68%/0.5 $\gamma$  -R (9); **20**: free cpd. 200%/0.5 $\gamma$ ; monobz. 450%/0.5 $\gamma$  and diac. 210%/0.5 $\gamma$  -R (9); **20**: free cpd. 36%/0.2 $\gamma$ ; 120%/0.5 $\gamma$ ; 165%/2 $\gamma$ ; mono-bz. 107%/0.5 $\gamma$ ; 220%/2 $\gamma$ ; 230%/6 $\gamma$ ; dibz. 100%/2 $\gamma$ ; 57%/6 $\gamma$ ; diac. 7%/0.5 $\gamma$ ; 185%/2 $\gamma$ ; 3-me. ether 21%/3 $\gamma$  -  $\delta$  /cR (55); **141**: even large doses of free cpd. have a transient effect, diac. and 3-bz. in that order show increasingly prolonged act. without loss of intensity; 3-bz.-17-ac. shows prolonged act. with a slight loss of intensity, dibz. and 17-me. ether have a very low intensity-C (58); **130**: S/L = 50 for free cpd. and 160 for bz.-M (54); **Test?**: 5-10 $\gamma$  dime. ether; < 2.5 $\gamma$ -17-me. ether; ca. 100 $\gamma$ -17-p-toluenesulphate and 4-5 $\gamma$  of Na. derivative of 3-me. ether as act. as 2 $\gamma$  of estrone-R (48); **8**: glucoside 4-6  $\times$  as act. as free cpd.-R (41); **Test?**: glucoside in divided doses 6  $\times$  as act. as free cpd.-M (41); **Test?**: glucoside in divided doses as act.

or less than free cpd. - R (41); Test $\gamma$ : 2.5 $\gamma$  of me. ether act; 5  $\times$  as act. as estrone-Species? (43); **25**: threshold dose-free cpd. < 0.03 $\gamma$  and bz. < 0.3 $\gamma$ -M (50); **9A**: 60 $\gamma$  of triacetylglucuronic acid or its me. ether-3 bz. act.-M (17); **74B**: glucoside orally 16-18  $\times$  less act. than bz. parenterally -Woman (47); **74B**: Bz. less act. than diph.-Woman (30); **22**: 17-carbethoxyester, 17-succinate, 17-sulphate, 17-pr., 17-ac., 17-butyrate more act., 17-phthalic acid ester, 17-diallylac., 17-bz., 17-stearate, 3-pr.-17-bz. and 3-bz.-17-pr. less act. than 3-bz.-M (23); **22**: Dose necessary to produce positive result in 75-100% of the animals are 0.4 $\gamma$  of 3-bz., 0.3 $\gamma$  of 17-succinate, 0.2 $\gamma$  of 17-carbethoxyester, 0.3 $\gamma$  of 17-sulphate, 0.4 $\gamma$  of 17-butyrate, 0.3 $\gamma$  of 17-pr. and 0.5 $\gamma$  of 17-ac.; 17-bz. inact.-R (23); **5**: Duration of estrus, after injection of 1 $\gamma$  of free cpd. increases in following order: pr., ac., free cpd., diallylac., carbethoxy-ester, and bz.; stearate inact.-M (23); **110**: Metrotropic act.: free cpd. 30%/ $0.01\gamma$ , 100%/ $0.02\gamma$ , 220%/ $0.06\gamma$ ; bz. 210%/ $0.07\gamma$ , 240%/ $0.14\gamma$ ; vag. opening: free cpd. 40%/ $0.01\gamma$ , 63%/ $0.02\gamma$ , 100%/ $0.06\gamma$ ; bz. 25%/ $0.07\gamma$ , 100%/ $0.14\gamma$ -R (72); **128A**: Metrotropic act.:  $63(\pm 10)\%$ / $0.1\gamma$ ,  $586(\pm 38)\%$ / $0.5\gamma$ ,  $444(\pm 3)\%$ / $2\gamma$ ,  $478(\pm 30)\%$ / $5\gamma$ ,  $485(\pm 39)\%$ / $10\gamma$ -R (62). **74B**: Parentally 2-3 mg./week of bz. act. in relieving menopausal symptoms; ca. 1-2 mg./week of bz. followed by withdrawal bleeding; monopr. and diph. have almost the same act. but free cpd. slightly less act. and of shorter duration-Human (67); **30**: 500 $\gamma$  act.-C (70); **74B**: Parentally bz. and diph. ca. equally act. and ca. 3  $\times$  as potent as estrone in relieving menopausal symptoms and causing vag. cornification-Woman (68,69); **128A**: Anti-castration cell act. o- + / $0.1\gamma$ ; + + / $0.5\gamma$ ; + + + / $10\gamma$ -R (62); **132**: Anti-castration cell act. + + + /2 mg.-R (63); **142**: Anti-castration cell act. = + + + / $0.1\gamma$  of 3-bz.- $\delta$ /c +  $\alpha$ /c R (64); **39B**: Metrotropic act.: 5  $\times$  as act. as estrone-R (65); **2**: 5-10  $\times$  as act. as estrone-M (10).

Luteoid: **46**: 500 $\gamma$  inact.-Rb. (45).

Corticoid: **47A**: up to 10 mg. of bz. inact.-R (33); **119**: 0.5-12.5 $\gamma$ /day of 17-pr. inact.-R (29).

Gonadotropic: **21**: up to 7.6 mg. inact.-X (31).

Renotropic: 300 $\gamma$ /day for 21 days inact.-♀ R (66).

Anesthetic: **11**: U = > 20 mg., bz. inact. at 20 mg.-R (32,44); **127**: U = 2 mg., bz. inact. at 7 mg.-Fish (44); **127**: Diph. inact. at 7 mg.-Fish (73).

REMARKS: Ppt. with digitonin (12).

#### DERIVATIVES:

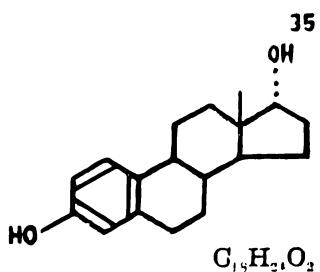
3-ac.	136.5-7.5°: (20,40)
17-ac.	215-7.5°: (20)
Diac.	127°: (3,9,11)
3-bz.	195°; $[\alpha]_D = + 60^\circ$ (dioxane): (3,9,11,13,24)
Dibz.	168-9°: (11); 170°, 145°, 160°: (9)
3-ac.-17-bz.	161-1.5°: (22)
3-ac.-17-pr.	113°: (22)
3-pr.	124-5°(u): (1,20)
3-me. ether	97-8°: (11,13)
m-Bromo-bz.	155-6°(u): (2)
Di- $\alpha$ -naphthoate	195-6°(u): (2)
17-glucuronide	191-4°(u): (17,21)
3-bz.-17-glucuronide	189-91°(u); $[\alpha]_D = 0$ : (21)
3-bz.-triacytetylglucuronic acid me. ester	188-91.5°; $[\alpha]_D^{20} = + 9.2^\circ$ ( $\text{CHCl}_3$ ): (17)
3-t-butylac	127-9°: (51)
3,17-di-t-butylac	98-100°: (51)
Diph.	104-5°: (20)
Di-n-butyrate	64-5°: (20)
Di-iso-butyrate	100.5-1.5° (18)
Di-n-valerate	(oil): (20)
Di-n-hexanoate	(22)

#### REFERENCES:

1. 7505S	23. 71506
2. 61656	24. A9603
3. 68703	25. A19948
4. 32442	26. A35939
5. 32872	27. A30457
6. A33730	28. A36620
7. 8042	29. A38216
8. 8041	30. 81413
9. 31727	31. 75731
10. 34803	32. A36741
11. 69136	33. A31765
12. A17993	34. A9910
13. A31088	35. A30457
14. A34396	36. A54226
15. 73728	37. A32842
16. A38517	38. A54224
17. 75026	39. A35662
18. 69521	40. 83023
19. 53602	41. A38987
20. A2305	42. A39626
21. 74172	43. A56240
22. A15264	44. A38070

Di-n-octanoate	(22)	45. A50335	00. A38054
Di-n-decanoate	(oil) : (20)	46. A002	01. A31650
Di-palmitate	63-5° : (18)	47. A50871	02. A50752
3-bz.-17-ac.	172-3° : (20)	48. A54750	03. A37513
3-bz.-17-pr.	167-7.5° : (20)	49. 75738	04. A320
3-bz.-17-n-butyrate	128.5-9° : (20)	50. A18182	05. 66604
3-bz.-17-n-valerate	133-3.5° : (18)	51. 75053	06. A31120
3-pr.-17-bz.	165-6° : (18)	52. A30508	07. A37564
3-n-butyrate-17-bz.	141.5-2° : (18)	53. 75101	08. 82852
3-palmitate	69-71° : (20)	54. A38063	09. 78012
17-pr.	198-200° : (20)	55. 52700	10. 73572
17-n-butyrate	166.5-7° : (20)	56. A19148	11. A58196
3-n-butyrate	98-9° : (18)	57. 71906	12. A35275
3-stearate	78-9° : (18)	58. 68721	13. 100000
17-me. ether	213.5-4.5° : (48)	59. 75618	
3-bz.-17-me. ether	165.5-6.5° : (48)		
17-n-hexanoate	128-9° : (50)		
17-n-octanoate	117.5-8.5° : (50)		
3-trimethyl-ac.	178-80° : (51)		
3,17-bis-trime.-ac.	174-6° : (51)		
17-iso-butyrate	183-3.5° : (18)		
17-n-valerate	144-5° : (18)		
17-caprinate	112-2.5° : (18)		
17-bz.	92.5-4° : (18)		
17-me. carbonic acid ester	216.5-8° : (18)		
17-et. carbonic acid ester	171-2° : (18)		
3,17-di-et. carbonic acid ester	138-9° : (18)		
3-furoyl	(16)		
Glucoside	(41,47)		
Na. derivative of me. ether	95-7° : (48)		
Dime. ether	161-2° : (48)		
3-me. ether-17-ac.	103.5-4.5° : (48)		
3-me. ether-17-bz.	131-2° : (48)		
3-me. ether-17-p-toluenesulphonate	160-1° : (48)		
17-p-toluenesulphonate	171-2° : (48)		
17-me. ether-3-p-toluenesulphonate	124.5-5.5° : (48)		
Di-p-toluenesulphonate	172-3° : (48)		
3-bz.-17-p-toluenesulphonate	184-5° : (48)		
2,4-dibr.	215.5-6.5° : (71)		
3-n-valerate	ca. 58-60° : (50)		
3-n-hexanoate	ca. 46-61° : (50)		
3-n-octanoate	ca. 48-53° : (50)		
3-n-decanoate	59-60° : (50)		

$\Delta^{1,3,5(10)}$ -8-EPIESTRATRIENE-3,17( $\tau$ ) DIOL.  
(iso-estradiol; 8-epi-estradiol)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 181°(u); (1)

$[\alpha]_D = +18^\circ$  (dioxane); (1)

PHARMACOLOGY: Folliculoid: 1: U. = 0.3 $\gamma$  of free cpd. and 0.5-0.8 $\gamma$  of 3-bz., equivalent to 0.1 and 0.22 $\gamma$  of  $\alpha$ -estradiol and it's 3-bz.-R. (1).

REMARKS:

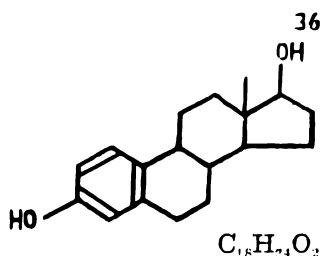
DERIVATIVES:

3-bz. 190°(u);  $[\alpha]_D = +9.5^\circ$  (dioxane); (1)

REFERENCES:

1. A9603

$\Delta^{1,3,5:10}$ -ESTRATRIENE-3,17( $\beta$ )-DIOL  
( $\beta$ -estradiol)



ISOLATION: Ur. (preg. mare): (5,8,10)

STRUCTURE AND SYNTHESIS: (1,2,3,4,6,7,11,12)

M.P.: 215° (u): (7)

220-3°: (1)

216-8° (u): (3)

222-4° (5,8)

$[\alpha]_D^D = +54^\circ$  (dioxane): (1)

$[\alpha]_D^{18} = +56.7^\circ$  (alc.): (3,6)

$[\alpha]_D^{25} = +56^\circ$  (alc.): (5)

PHARMACOLOGY: Folliculoid: Test?: 4  $\times$  as act. as estrone; probably impure sample—Species? (1,13) **1**: act. of "synthetic" free cpd. and bz. ca. 30% and 15% that of estrone; act. of free cpd. from mare's urine about 5-10% that of estrone-R (1,5,8); **3**: Metrotropic act. of "synthetic" free cpd. 7.5, of urinary free cpd. 5, of 3-bz. 10-20 and diac. 0.1% that of estrone-M (9); **5**: "synthetic" free cpd. ca. 10  $\times$  less act. than estrone-M (3,6).

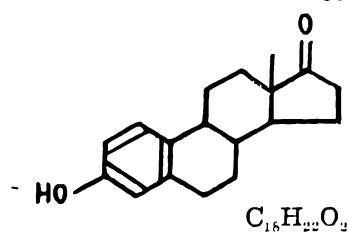
REMARKS: Not ppt. with digitonin (11,12); comparatively high folliculoid act. of cpd. obtained by reduction of estrone probably due to contamination with 17( $\alpha$ ) isomerid (1).

DERIVATIVES:

Diac.	139-41.5°: (1,3,4,5,6)
3-me. ether	109-10°: (6)
3-bz. (3 forms)	{ I 63°: (5) II 153°: (5) III 158°: (5)
3-bz.	156-7°: (1,3,4,6)

REFERENCES:

1. 68703
2. A33730
3. 69136
4. A9603
5. A9910
6. A34088
7. 73728
8. A17877
9. A35939
10. A38095
11. 68846
12. 69136
13. A33730

$\Delta^{1,3,5,10}$ -ESTRATRIENE-3-OL-17-ONE(Estrone;  $\alpha$  or  $\beta$  follicular hormone; theelin; keto-hydroxy-estrin)

## ISOLATION:

Ur. (preg. mare):	(2,3,22)
Ur. (preg. human):	(2,3,6,17,21,25,26,52,53)
Ur. (stallion):	(21,42)
Ur. (bull):	(51)
Ur. (preg. mare as sulphate):	(43,44)
Ur. ( $\delta$ human):	(54)
Placenta (human):	(56)
Te. (horse):	(31,57,58)
Ad. (cattle):	(59)
Palm kernels:	(60)

## STRUCTURE AND SYNTHESIS: (2,3,4,5,7,8,9,11,12,13,14,18,19,20,23,27,29,63,66,67)

M.P.: 254.5-5° (u):	(3,5,11)	$[\alpha]_D^{32} = +159^\circ$ (alc.):	(20)
258-9°:	(50)		
254°; 256°; 259°:	(1)	$[\alpha]_D^{20} = +158.5-68^\circ$ ( $CHCl_3$ ):	(2,21)
254-7°:	(7)		
259-61.5° (u):	(20,65)	$[\alpha]_{5401} = +188^\circ$ (alc.):	(8)
262°:	(42)		
	(67)	$[\alpha]_D = +170^\circ$ (dioxane):	(69)

## PHARMACOLOGY:

**Folliculoid:** I. U. = 0.1 $\gamma$  (62); **5:** U. = 0.1-0.17 $\gamma$ -M (11,73,77,100); **1:** U. = 1 $\gamma$ -R (74); **140:** U. = 0.3 $\gamma$ -R (75); **65A:** threshold dose = 0.2 $\gamma$  for *metrotropic act.* and 0.35 $\gamma$  for vag. cornification-R (10); **65B:** threshold dose = 1.0 $\gamma$  for *metrotropic act.* and 0.5 $\gamma$  for vag. cornification-R (10); **22:** U. = 0.1 $\gamma$ -M (3,77,96); **14A:** U. = 0.1 $\gamma$ -M (77); **8:** U. = 1.6 $\gamma$ -R (77); **9:** U > 40-66 $\gamma$ -R (77); **9,16,22:** Dose per os/dose s.c. = 10/1-M (77,79); **17A:** U. = 1 $\gamma$ -R (77); **18:** act.-G (3,77); **25:** threshold dose > 0.8 $\gamma$ -M (40); **5:** U. = 0.1-0.083 for bz. and 2 $\gamma$  for oxime; semicarb. and me. ether inact. (dose?) -M (11,73); **1,8,14A:** act. increased 1.5-5  $\times$  by giving subdivided doses-M,R (11,21,88); **9,22:** oral dose = 40  $\times$  s.c. dose-R (2); **141:** Even large doses of free cpd. and ac. have only a transient effect; bz. shows prolonged act. without change in minimum effective dose; 100 $\gamma$  of me. ether inact.-C (72); **19:** -76%/ $1\gamma$ -R (77); **20:** 1 $\gamma$  inact.-R (77); **20:** free cpd. 57%/ $2\gamma$ , 107%/ $6\gamma$ , 93%/ $10\gamma$ ; bz. 14%/ $2\gamma$  and ac. 65%/ $2\gamma$ - $\delta$ /c R (78); **118:** 30 $\gamma$ /day act.-R (90); **130:** S/L = 260 for free cpd., 230 for butyrate, 500 for caproate and 60 for me. ether-M (80); **24:** If *metrotropic act.* of free cpd. is taken as 1, ac. = 1.4, pr. = 1.9, n-butyrate = 2.9, iso butyrate = 5, n-valerate = 6.5, n-hexanoate = 10.5, n-octanoate = 14.1, n-decanoate = 6.9, laurate = 3.2 and bz. = 8.6-R (28); **60:** act.-B (86); **28:** U. = 0.06 $\gamma$ -M (87); **7:** U. = 1.08 $\gamma$ -R (89); **Test?:** 10 $\gamma$  of p-aminophenyl ether in oil produces estrus in more than 50% of the animals; 450 $\gamma$  of phenyl-ether-p-azocasein in water inact. but 830 $\gamma$  act; "on the basis of its estrone content the conjugate is about 1/10 as act. as estrone p-aminophenyl ether"-R (71); **Test?:** threshold dose of  $\beta$ -naphthoate = 1-2.5 $\gamma$  with "prolonged period of estrus although the onset is delayed", diethylaminoethyl ether up to 1000 $\gamma$  inact.-R (36); **23:** threshold values for free cpd. = 0.7 $\gamma$ , ac. = 0.85 $\gamma$ , pr. = 0.85 $\gamma$ , n-butyrate = 1.25 $\gamma$ , iso-butyrate = 1.5 $\gamma$ , n-valerate = 3.5 $\gamma$ ,

n-octanoate = 4 $\gamma$ , n-decanoate = 6 $\gamma$ , laurate = 35 $\gamma$ , palmitate = 75 $\gamma$ , stearate = 75 $\gamma$ , and bz. = 3 $\gamma$ , from the butyrate upwards the duration of estrus is increased; the duration attains its maximum with n-hexanoate and n-octanoate-R (28); **76**: *Metrotropic act.* 900%/ $5\gamma$ , 1100%/ $15\gamma$ ; more act. if same total amount given on alternate days-Rb. (81); **5**: 10 $\gamma$  of Na sulphate ester as act. s.c. (in oil or water) as per os; quinidine sulphate ester as act. as Na sulphate ester; of pyridinium sulphate ester in oil 1 $\gamma$ , in water 2 $\gamma$ , and orally 3 $\gamma$  have threshold act.; sulphate and its derivatives have no more prolonged act. than free cpd.; 400 $\gamma$  of sulphonic acid derivative and 120 $\gamma$  of its dime. ester inact.-M (39); **2**: Cl-formate 1/10 as act. as free cpd.; carbonic acid ester and et. carbonic acid ester more act. than free cpd.-M (32); **22**: bz., pr., stearate, carbethoxy-ester less act., while diallylac. and ac. ca. as act. or more act. than free cpd.-M (101); **22**: Ac. ca. as act. as free cpd.-R (101); **5**: duration of estrus after injection of 1 $\gamma$  of free cpd. increases in following order: pr., ac., free cpd., diallylac., carbethoxy-ester and bz.; stearate inact.-M (101); **110**: *Metrotropic act.* free cpd. 53%/ $0.14\gamma$ , 160%/ $0.21\gamma$ , 675%/ $0.39\gamma$ ; bz. 0.14 $\gamma$  inact., 50%/ $0.28\gamma$ ; vag. opening: free cpd. 30%/ $0.14\gamma$ , 100%/ $0.21\gamma$ - $0.39\gamma$  bz. 0.14 $\gamma$ - $0.28\gamma$  inact.-R (16). **128A**: *Metrotropic act.* 40.7 ( $\pm 4$ )%/ $0.01\gamma$ , 526 ( $\pm 17$ )%/ $1\gamma$ -R (91); **30**: 500 $\gamma$  act.-C (95); **Test?**: 15 $\gamma$  of me. ether as act. as 2 $\gamma$  of free cpd.-R (68); **Test?**: 2.5 $\gamma$  of me. ether as act. as 0.5 $\gamma$  of free cpd.-Species? (15); **Test?**: Me. ether in M has an act. of 200,000 M.U./gm. (S5), and in the rat of 20,000 R.U./gm. (82); **8**: glucoside somewhat > act. than free cpd.-R (55); **Test?**: in subdivided doses, glucoside 5  $\times$  as act. as free cpd. in M, but 1/2 as act. as free cpd. in-R (55); **74B**: 0.4 mg. of Na. sulphate 3  $\times$  daily per os act.-Woman (64,99,97,98); **74B**: 5-10 mg./week parentally act. in relieving menopausal symptoms-Woman (93); **128A**: *Anti-castration cell act.*- $0.01\gamma$ , + + +/ $1\gamma$ -R (91); **142**: *Anti-castration cell act.* = + + +/ $50\gamma$  -  $\delta$  /c R (92).

Corticoid: 50 $\gamma$  toxic in adrx.-R (61).

Gonadotropic: **21** : up to 10 mg. inact.-X (45).

Anesthetic: **11** : U. = > 20 mg.-R (46); **127** : U. = > 7.0 mg.-Fish (94).

**REMARKS:** Three crystal forms: rhombic metastable m.p. 254°; monoclinic metastable m.p. 256° and rhombic stable m.p. 259° (1).

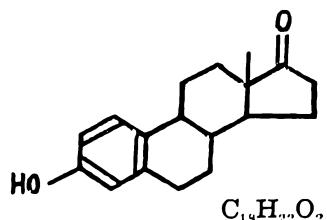
#### DERIVATIVES:

			REFERENCES:
Ac.	126°:	(3,7,11,14)	1. 19842
Bz.	217.5°; $[\alpha]_D = + 120^\circ$ (dioxane):	(2,3,11,20,33,42)	2. 20456
Oxime	233°; 230°(u):	(7,11,21,33)	3. 2693
Br.-bz.	221.5-3°:	(49)	4. 27614
3-me. ether	168.5-9.5°; $[\alpha]_{540} = + 171^\circ$ (CHCl <sub>3</sub> ):	(2,8,19,82,84)	5. 18356
Oxime-me. ether	182-7°:	(8)	6. 2651
Semicarb.-me. ether	267°:	(12)	7. 1925
17-me.-carbinol-me. ether	95-100°(impure):	(19)	8. 3225
Semicarb.	259-60°; $[\alpha]_D = + 164.5^\circ$ (dioxane):	(48)	9. 3425
	266-7° (+H <sub>2</sub> O):	(69)	10. A36020
	257-8°:	(12,20,21,30)	11. 3929
Carboxymethoxime	188°(u):	(50)	12. 3930
Di- $\alpha$ -naphthoate	200.5-2°:	(49)	13. 7665
Quinoline	not sharp:	(5)	14. 8052
n-butyrate	101-2.5°:	(34)	15. A56240
Pr.	134-5.5°:	(34)	16. A35275
Valerate	100-1°:	(34)	17. 14470
Caprinato	71-1.5°:	(34)	18. A17993
Capronate	94.5-5°:	(35)	19. 53062
Iso-butyrate	120-1°:	(35)	20. 63715
Octanoate	70-1°:	(36)	21. 19991
Laurate	70°:	(36)	22. 67353
Stearate	82°:	(35)	23. 1006
Palmitate	76°:	(34)	24. 1605
Sulphonic acid	210°:	(39)	25. 2S23
Dimethyl ester-sulphonic acid	197° + 207°:	(30)	26. 2804
2:4 dinitrophenylhydrazone	278-80°:	(71)	27. 8011
			28. A14800
			29. 27615
			30. 7967
			31. A55010
			32. 34802
			33. A9603
			34. A2365
			35. 69521
			36. A18260
			37. A33920
			38. 34803
			39. A32289
			40. 75616
			41. 53758
			42. 29398
			43. 67193
			44. 78183
			45. 75731
			46. A36744
			47. 82713
			48. A30454
			49. 64056
			50. A31396
			51. 75332
			52. 23927
			53. A34616
			54. 72388

Me. carbonic acid ester	127°:	(32)	55. A38087	70. 75101
Et. carbonic acid ester	115°; $[\alpha]_D^{24} = +114^\circ$ (dioxane):	(32)	56. A19019	80. A38663
Cl-formate	101-2°:	(32)	57. A35062	81. 67358
Diet. amide-Cl-formate	194-5°:	(32)	58. A54224	82. A1916
Neutral carbonic acid ester	247°:	(32)	59. A31251	83. 75626
Allyl-ether	108-9°:	(35)	60. 14785	84. A34088
Allyl-bz.	155-60°:	(35)	61. 38816	85. 63634
Cinnamyl-ether	149°:	(35)	62. A30596	86. A39054
Diethylaminomethylether	76-7°:	(36)	63. 43053	87. A692
Diethylaminoethylether·HCl	190-1°:	(36)	64. A57068	88. 1917
$\alpha$ -naphthoate	200-2°:	(65)	65. A56887	89. 1928
$\beta$ -naphthoate	262-4°:	(36)	66. A54807	90. A240
3-ac.-17-cyanhydrin			67. A56095	91. A56752
	151-3°; $[\alpha]_D^{24} = +27.6^\circ \pm 2^\circ$ (dioxane):	(47)	68. A54750	92. 70000
17 epimer-3-ac.-17-cyanhydrin	170-1°; $[\alpha]_D^{20} = +15.4^\circ \pm 2^\circ$ (dioxane):	(47)	69. 2226	93. A37564
3,17-diac.-cyanhydrin	231-3°; $[\alpha]_D^{24} = +25.5^\circ \pm 2^\circ$ (dioxane):	(47)	70. 75953	94. 100000
17 epimer-3,17-diac.-cyanhydrin	233-5°; $[\alpha]_D^{20} = +11.6^\circ \pm 2^\circ$ (dioxane):	(47)	71. A54645	95. 73572
K-sulphate ester	233-42°:	(44)	72. 68721	96. 2664
Na. sulphate ester (+H <sub>2</sub> O)	228-30°; $[\alpha]_D^{20} = +110^\circ$ :	(39,43)	73. 69136	97. A57071
Semicarb.-Na. sulphate ester (+H <sub>2</sub> O)	258-60°:	(39)	74. 68703	98. A57070
Pyridinium sulphate ester	173-5°; $[\alpha]_D^{23} = +84.1^\circ$ :	(39)	75. 71906	99. A57069
Quinine sulphate ester	168-70°:	(39)	76. A57982	100. 2665
Quinidine sulphate ester (+3 H <sub>2</sub> O)	167-70°:	(39)	77. 31727	101. 71506
Diet. carbamate	194-5°:	(32)	78. 52700	
Picrate		(76)		
7-Cl-3-monobz.	247-8°:	(37)		
Triacetyl glucuronic acid me. ester				
	225.5-8°; $[\alpha]_D^{25} = +57.1^\circ$ (CHCl <sub>3</sub> ):	(83)		
p-nitrophenyl ether	192-4°:	(71)		
p-aminophenyl ether	166.5-8.5°:	(71)		
p-aminophenyl ether-picrate	ca. 160°:	(71)		
p-aminophenyl ether semicarb.	ca. 295°:	(71)		
p-aminophenyl ether-2,4 dinitrophenylhydrazone	238-40°:	(71)		
p-acetylaminophenyl ether	170°+202-4°:	(71)		
Azoproteins		(71)		
Et. carbamate-p-aminophenyl ether	163-5°:	(71)		
Carbamate-p-aminophenyl ether	210-2°:	(71)		
Tetraacetyl glucoside		(55)		
Azobenzene-4-carboxylate	226-7.5°:	(65)		
p-nitrobenzyl ether	176.5-8.5°:	(71)		
p-nitrobenzyl ether-semicarb.	273-5°:	(71)		
Br.-ac.	133-47°:	(23)		
Mono-Br.-me. ether	191-3°:	(63)		
Trimethylac.	154-6°:	(70)		
t-butylac.	148-50°:	(70)		

38

$\Delta^{1,8,5:10}$ -ISOESTRATRIENE-3-OL-17-ONE  
(Estrone-a)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1,2)

M.P.: 214-4.5°: (1)

PHARMACOLOGY: Folliculoid: Test?: "No estrogenic act." at  $3.2\gamma$  or less; slight act. at  $100\gamma$ ;  $250\gamma$  as act. as  $1\gamma$  of estrone- $\beta$  /c R (1).

REMARKS: Synthetic stereoisomer of estrone (1); cpd. m.p. 210° (2) assigned the 14-epi structure may be identical?

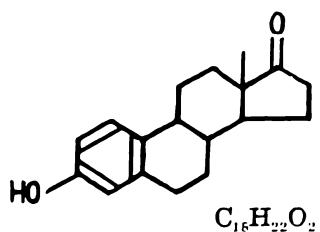
DERIVATIVES:

Bz. 175-6°: (1)  
Me. ether 81.5-2° and 101.5-2.5°: (1)

REFERENCES:

1. A56995
2. A54807

$\Delta^{1,3,5:10}$ -8-EPIESTRATRIENE-3-OL-17-ONE  
(Iso-estrone; 8-epi-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 247°: (1)

$[\alpha]_D^{20} = +94^\circ$  (dioxane) : (1)

PHARMACOLOGY: Folliculoid: 1: U. = 2 $\gamma$  of free cpd. and 3 $\gamma$  of bz. equivalent to 0.83 $\gamma$  and 1.3 $\gamma$  of estrone and it's bz.-R (1).

REMARKS:

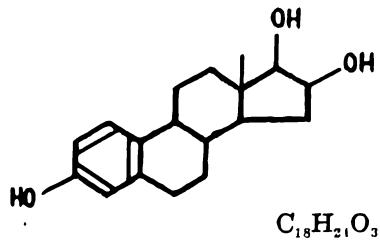
DERIVATIVES:

Bz. 196°;  $[\alpha]_D^{20} = +61^\circ$  (dioxane) : (1)  
Semicarb. 270°(u) : (1)

REFERENCES:

1. A9603

$\Delta^{1,3,5,10}$ -ESTRATRIENE-3,16( ),17( )-TRIOL  
**(Estriol, follicular hormone hydrate; trihydroxy estrin; theelol)**



**ISOLATION:**

Ur. (preg. human):	(1,2,7,9,13,28)
Ur. (preg. human as glucuronide):	(15)
Placenta (human):	(29)
Pussy-willows:	(22)

**STRUCTURE AND SYNTHESIS:** (1,2,3,5,6,7,9,11,12,25,27,30)

M.P.: 279.5-80.5°(u): (3,9,10)  
 273°(u); 282-3°: (4)  
 264-6°(u): (2)  
 275-6°: (1,5)

$[\alpha]_{5461}^{22} = + 41.9^\circ$  (pyridine): (3,9)  
 $[\alpha]_{5461} = + 76^\circ$  (alc.): (9);  $+ 80^\circ$ : (3)  
 $[\alpha]_D = + 64^\circ$  (alc.): (3)  
 $[\alpha]_{5461} = + 38.5^\circ$  (pyridine): (1,2)

**PHARMACOLOGY:**

**Folliculoid:** **28**: ca. 20  $\times$  less act. than estrone-M (20); **5,14A**: 1/4—1/5 as act. as estrone-M (1,3); **10**: ca. 1/2 as act. as estrone-R (28); **5**: free cpd. ca. 100  $\times$  and triac. ca. 10  $\times$  less act. than estrone-M (10); **7**: s.c. 6-7  $\times$  and orally ca. 3.5  $\times$  as act. as estrone-R (28); **10**: in oil ca. 90  $\times$  and in water 250  $\times$  less act. than estrone-R (31); **7**: ca. 4  $\times$  as act. as estrone-R (31); **4**: Na glucuronide s.c. ca. 29  $\times$  and orally ca. 2  $\times$  less act. than free cpd.-M (14,17); **4**: ca. 1/2 as act. as estrone-M (32); **139**: *Metrotropic act.* only slight increase in uterine weight without accumulation of uterine fluid-R (33); **3**: *Metrotropic act.* 60% that of estrone-M (34); **65A**: threshold dose s.c. for *metrotropic act.* and for vag. cornification = 0.05 $\gamma$ -R (8); **65B**: Threshold dose per os for *metrotropic act.* = 0.05 $\gamma$  and for vag. cornification = 0.25 $\gamma$ -R (8); **16**: dose per os/dose s.c. = 3/1-M (35); **130**: S/L = 2000-M (36); **30**: 500 $\gamma$  inact.-C (40); **20**: s.ves. 28%/2 $\gamma$ , 36%/10 $\gamma$ - $\delta$ /c R (37); **18**: act.-G (38); **74B**: "20,000 to 40,000 oral units"/week of glucuronide per os necessary to cause withdrawal bleeding-Human (39); **110**: *Metrotropic act.* 30%/0.55 $\gamma$ , 55%/5.5 $\gamma$ , 70%/16.5 $\gamma$ ; vag. opening: 60%/0.55 $\gamma$ , 100%/5.5 $\gamma$ -16.5 $\gamma$ -R (41).

**Luteoid:** **27**: up to 0.8 mg. inact.-G (21).

**Gonadotropic:** **21**: 4 mg. of Na glucuronide inact.-X (23).

**Anesthetic:** **11**: U. > 20 mg.-R (24).

**REMARKS:**

**DERIVATIVES:**

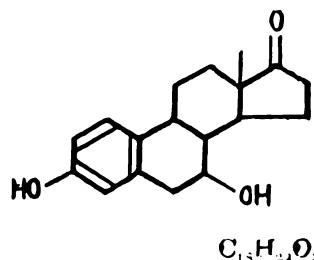
Mono-me. ether	$\left\{ \begin{array}{l} 169^\circ; [\alpha]_D = + 34.7^\circ \text{ (pyridine)} : \\ 162.4^\circ \text{ (u)}; [\alpha]_D = + 30^\circ \text{ (pyridine)}; [\alpha]_{5461} = + 65^\circ \text{ (alc.)} : \end{array} \right. \quad (1)$
Oxime-mono-me. ether	$\left\{ \begin{array}{l} 159.60^\circ; [\alpha]_D = + 65.3^\circ \text{ (alc.)} : \\ 183.7^\circ \text{ (u)} : \end{array} \right. \quad (9)$
Mono-bz.	225°: (26)
Triac.	$\left\{ \begin{array}{l} 126^\circ; \left\{ \begin{array}{l} [\alpha]_D = - 19^\circ \text{ (CHCl}_3\text{)} : \\ [\alpha]_D = 0^\circ \text{ (pyridine or alc.)} : \end{array} \right. \\ 120.2^\circ \text{ (u)} : \end{array} \right. \quad (3,6,7)$
Diac.-mono-me. ether	140.2°: (2,12)

Mono-Br.-me. ether	200-3°;	(30)
Glucuronide	193-7°;	(16,18)
Na-salt-glucuronide (+½ Me OH)	305°; $[\alpha]_{5461}^{28} = -28.2^\circ$ ;	(14,16,17)
Na-salt-glucuronide (-1½ H <sub>2</sub> O)	256°;	(17)

## REFERENCES:

- |           |           |            |            |            |
|-----------|-----------|------------|------------|------------|
| 1. 1917   | 9. 3225   | 17. 67192  | 25. 18356  | 33. A19148 |
| 2. 2171   | 10. 3929  | 18. 18414  | 26. A34396 | 34. A35939 |
| 3. 7173   | 11. 7665  | 19. 3930   | 27. 8041   | 35. 75101  |
| 4. 7967   | 12. S052  | 20. A692   | 28. 1928   | 36. A38663 |
| 5. 1926   | 13. 3569  | 21. A7923  | 29. A54227 | 37. 52700  |
| 6. 1927   | 14. 69S13 | 22. A54225 | 30. 43053  | 38. 29399  |
| 7. 1667   | 15. 55949 | 23. 75731  | 31. 35085  | 39. A37564 |
| S. A36620 | 16. A7927 | 24. A36744 | 32. 29862  | 40. 73572  |
|           |           |            |            | 41. A35275 |

$\Delta^{1,3,5;10}$ -ESTRATRIENE-3,7(10)-DIOL-17-ONE  
(7 $\beta$ -hydroxy-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 265-7°: (1)

$[\alpha]_D^{25} = +134.5^\circ$  (dioxane): (1)

PHARMACOLOGY: Folliculoid: Test?: 1/300 as act. as estrone-R (1).

REMARKS:

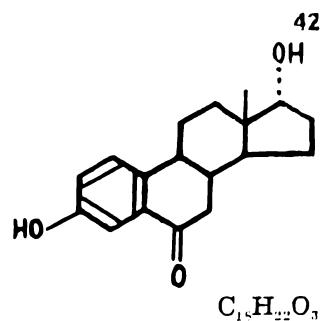
DERIVATIVES:

Diac. 122-3° and 131-1.5°: (1)  
3-bz. 181°: (12)

REFERENCES:

1. A30454
2. A33920

$\Delta^{1,3,5:10}$ -ESTRATRIENE-3,17( $\alpha$ )-DIOL-6-ONE  
(6-keto- $\alpha$ -estradiol)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 283°: (1)

$[\alpha]_D^{23} = +4^\circ$  (alc.): (1)

PHARMACOLOGY: Folliculoid: Test?: 1/4 as act. as  $\alpha$ -estradiol-R (1).

REMARKS:

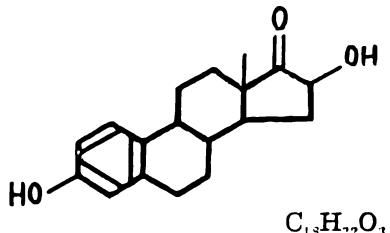
DERIVATIVES:

Diac. 173-5°: (1)  
Semicarb. 280-320°: (1)

REFERENCES:

1. A32846

*Δ<sup>1,3,5,10</sup>-ISOESTRATRIENE-3,16( )-DIOL-17-ONE*  
*(16-hydroxy-iso-estrone)*



**ISOLATION:**

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:** Rings C-D configuration presumably cis (1).

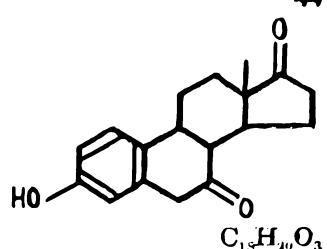
**DERIVATIVES:**

3-me. ether 167°: (1)

**REFERENCES:**

1. A54807

$\Delta^{1,3,5(10)}$ -ESTRATRIENE-3-OL-7,17-DIONE  
(7-keto-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 212-2.5°: (1)

$[\alpha]_D^{22} = +167^\circ$  (dioxane): (1)

PHARMACOLOGY:

**Folliculoid:** Test?: 1/300 as act. as estrone-R? (1); **3:** much less act. than estrone-M (2).

**Anesthetic:** **11:** U. = > 20 mg.-R (3).

REMARKS:

DERIVATIVES:

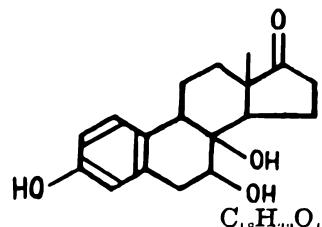
Dioxime	252-3°: (1)
Disemicarb.	> 295°: (1)
Enol diac.	171.5°: (1)

REFERENCES:

1. A30454
2. A35939
3. A36744

$\Delta^{1,3,5:10}$ -ESTRATRIENE-3,7( ),8( )-TRIOL-17-ONE  
(Equilin-glycol)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2)

M.P.: 246-8°; 250-2°; 255-6°: (2)  
210-6°: (2)  
245°(u): (1)

$[\alpha]_D^{23} = +139^\circ$  (dioxane) (m.p. 251°): (2)  
 $[\alpha]_D^{23} = +135^\circ$  (dioxane) (m.p. 214-20°): (2)

PHARMACOLOGY:

Folliculoid: **1**: 0.5 mg. of ac. inact.-R (1).

Testoid: **32**: 2 mg. of ac. slightly act.-C (1).

REMARKS: Differences in m.p. ascribed to crystal polymorphism. Identical reactions (2).

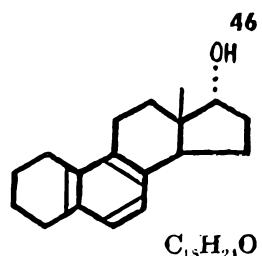
DERIVATIVES:

Diac.     $\begin{cases} 214^\circ(\text{u}): & (1) \\ 211.5-2^\circ; [\alpha]_D^{26} = +92^\circ(\text{alc.}): & (2) \end{cases}$

REFERENCES:

1. A9603
2. A30454

$\Delta^{5,10,6,8}$ -ESTRATRIENE-17( $\alpha$ )-OL



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2,3)

M.P.: 148°: (1,2)  
144-6°: (3)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

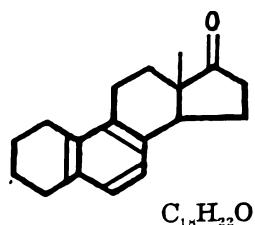
Ac. 104°: (1,2,3)

REFERENCES:

1. 70100
2. 73582
3. 77849

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$\Delta^{5,10,6,8}$ -ESTRATRIENE-17-ONE



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 107-9°; (1)

PHARMACOLOGY:

REMARKS:

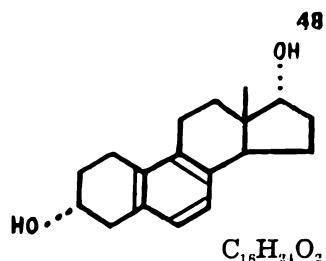
DERIVATIVES:

Oxime 203-5°; (1)

REFERENCES:

1. 77849

$\Delta^{5:10,6,8}$ -ESTRATRIENE-3( $\alpha$ ),17( $\alpha$ )-DIOL  
(3 epi-hexahydro-equilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2,3)

M.P.: 181°: (2)

172°(u): (1)

191-3°: (3)

$[\alpha]_D = + 68^\circ$  (alc.): (3)

PHARMACOLOGY: Folliculoid: 1: U. = 120-150 $\gamma$ -R (2); Test?: 20 $\gamma$  inact.-♀ /c M (3).

Testoid: 29: 2 mg./day inact.-C (2); 31: 100 $\gamma$ /day inact.-C (3).

REMARKS: Cpd. of (1) possibly possesses 3 $\beta$  configuration (4).

DERIVATIVES:

Mono-bz. 195°: (1)

Diac. 128-9.5°: (3)

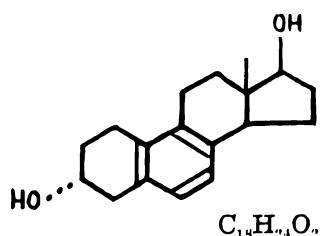
REFERENCES:

1. 72930

2. 73582

3. 74170

4. A36229

$\Delta^{5,10,6,8}$ -ESTRATRIENE-3( $\alpha$ ),17( $\beta$ )-DIOL

## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1,2)

M.P.: 179°: (1)

181-3°: (2)

 $[\alpha]_D = +31^\circ$  (alc.): (2)PHARMACOLOGY: Folliculoid: Test?: "as slightly act. as" 3( $\alpha$ ), 17( $\alpha$ ) epimer-  $\varphi$  /c M (2).Testoid: 31: "as slightly act. as" 3( $\alpha$ ), 17( $\alpha$ ) epimer-C (2).

## REMARKS:

## DERIVATIVES:

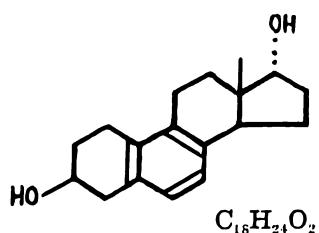
Diac. 90-1.5°: (2)

## REFERENCES:

1. 72930
2. 74170

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$\Delta^{5:10,6:8}$ -ESTRATRIENE-3( $\beta$ ).17( $\alpha$ )-DIOL  
(Hexahydro-equilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,3)

M.P.: 166.5°: (1)

166.8°: (2)

168.8.5°: (3)

$[\alpha]_D = -16^\circ$  (alc.): (2)

$[\alpha]_D^{23} = -5^\circ \pm 4^\circ$  (alc.): (3)

PHARMACOLOGY: Folliculoid: 1: U. = ca. 250 $\gamma$ -R (1); Test?: 20 $\gamma$  inact.-♀/c M (2).

Testoid: 31: 100 $\gamma$ /day inact.-C (2).

REMARKS: Not ppt. with digitonin (3).

DERIVATIVES:

Diac. 115-6°: (1,3)

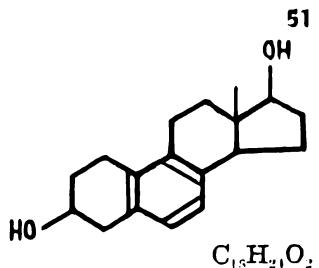
Diac. 117-8°: (2)

REFERENCES:

1. 73582

2. 74170

3. A36229

$\Delta^{5,16,17,18}$ -ESTRATRIENE-3( $\beta$ ),17( $\beta$ )-DIOL.

## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1)

M.P.: 171-3°: (1)

[ $\alpha$ ]<sub>D</sub> = -49° (alc.): (1)

## PHARMACOLOGY:

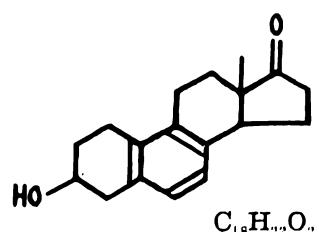
## REMARKS:

## DERIVATIVES:

Diac. 146-7°: (1)

## REFERENCES:

1. 74170

$\Delta^{5:10,6,8}$ -ESTRATRIENE-3( $\beta$ )-OL-17-ONE

ISOLATION: Ur. (preg. mare) : (4,5)

STRUCTURE AND SYNTHESIS: (1,2,3,4,5)

M.P.: 138-9.5°: (4,5)

$[\alpha]_D = + 59^\circ$  (alc.) : (4,5)

PHARMACOLOGY:

REMARKS: Not ppt. with digitonin (4); cpd. designated as "folliculosterone" m.p. 248-8.5°;  $[\alpha]_D^{18} = + 162^\circ$  ( $\text{CHCl}_3$ ) whose pharmacol. act. parallels those of estrone has been assigned this structure (1,2,3); however this is held in question (4,6).

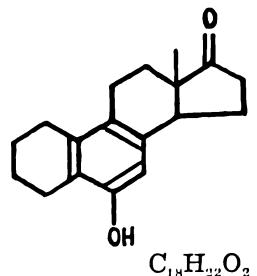
DERIVATIVES:

Ac.	158°(u) :	(4,5)
Oxime	195-7° :	(4,5)
Bz.	196-8°(u) :	(4)
Semicarb.	pure:	(4)

REFERENCES:

1. 67662
2. 67663
3. A15311
4. A36229
5. 81023
6. 73582

$\Delta^{5:10,6,8}$ -ESTRATRIENE-6-OL-17-ONE  
(6-hydroxy-1,2,3,4-tetrahydro-17-equilenone)



## ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form 150-0.5°: (1)

PHARMACOLOGY: Folliculoid: Test?: "Failed to induce the estrus response in ovariectomized rats in doses as high as 1000 $\gamma$ " (1).

## REMARKS:

## DERIVATIVES:

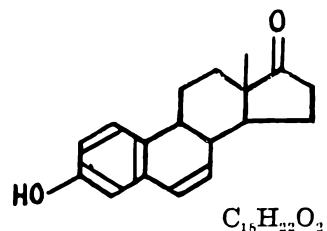
Me. ether- $\alpha$ -form 118-8.5°: (1)  
Me. ether- $\beta$ -form 108-9°: (1)

## REFERENCES:

1. A56997

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$\Delta^{1,3,5:10,6}$ -ESTRATETRAENE-3-OL-17-ONE  
( $\Delta^6$ -isoequilin)



## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1)

M.P.: 265-6°: (1)

 $[\alpha]_D^{24} = +150^\circ$  (dioxane): (1)PHARMACOLOGY: Folliculoid: 3: *metrotropic act.* ca. 1/13 that of estrone-M (2).

## REMARKS:

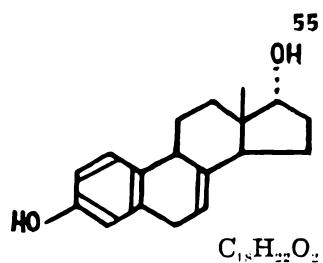
## DERIVATIVES:

Bz. 202°: (1)  
Ac. 140-1°: (1)

## REFERENCES:

1. A33920
2. A35939

$\Delta^{1,2,5,16,7}$ -ESTRATETRAENE-3,17( $\alpha$ )-DIOL.  
(17( $\alpha$ )-dihydro-equillin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 174.5-6°: (1)

$[\alpha]_D = +220^\circ$  (dioxane) : (1)

PHARMACOLOGY: Folliculoid: **22**: ca. 2  $\times$  as act. as equilin-M (1); **3**: *Metrotropic act.* 100% more than estrone and 90% more than equilin-M (2); **14A**: ca. 3  $\times$  as act. as estrone; monobz. ca. 2  $\times$  less act. than free cpd.-R (3,4).

REMARKS:

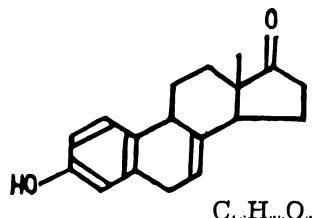
DERIVATIVES:

Dibz. 175-5.5°;  $[\alpha]_D = +120^\circ$  (dioxane) : (1)  
Bz.: (4)

REFERENCES:

1. 29400
2. A35939
3. 72048
4. A9603

$\Delta^{1,3,5:10,7}$ -ESTRATETRAENE-3-OL-17-ONE  
(Equilin)



ISOLATION: Ur. (preg. mare) : (3,5,6,7,8,9,10)

STRUCTURE AND SYNTHESIS: (1,2,3,6,8,10)

M.P.: 238-40°: (6,8,10)  
236-7.5°(u) : (3)

$[\alpha]_D^{15} = +308^\circ$  (dioxane) : (3,6,8,10)  
 $[\alpha]_D^{25} = +325^\circ$  (alc.) : (8)

PHARMACOLOGY:

**Folliculoid:** **12**: ca. 2/3 as act. as estrone-M (3); **12**: ca. 4/3 as act. as estrone-R (3); **13**: *metrotropic act.* 112%/0.075 $\gamma$ -R (3); **17A**: as act. as estrone-R (3); **19**: Te.: 85%/0.75 $\gamma$ -R (3); **20**: s.ves.: 1000%/15 $\gamma$ -R (3); **18**: as act. as estrone-G (3); **1**: U. = 2-3 $\gamma$  equivalent to 0.83 $\gamma$  of estrone-R (1); **2**: "as act. as follicle hormone"-M (7); **3**: slightly more *metrotropic* than estrone-M (11); **55**: vag. cornification-R (12); **14A**: s.c. 1-1.5 $\gamma$  as act. as 0.83 $\gamma$  of estrone-R (4); **14B**: per os 40 $\gamma$  as act. as 60 $\gamma$  of estrone-M (4); **1**: 1/7 as act. as estrone-R (10); **7**: 1/3 as act. as estrone-R (10); **10**: "Equilin is approximately 75% as act. as standard theelin when injected in aqueous 10% alc. containing 0.5% Na<sub>2</sub>CO<sub>3</sub>; when injected without the addition of 0.5% Na<sub>2</sub>CO<sub>3</sub>, equilin is approximately 30% as act. as standard theelin"-R (8); **30**: 500 $\gamma$  inact. 1000 $\gamma$  slightly act.-C (13); **110**: *Metrotropic act.* 85%/0.17 $\gamma$ , 130%/0.35 $\gamma$ , 330%/0.5 $\gamma$ ; vag. opening: 70%/0.17 $\gamma$ , 90%/0.35 $\gamma$ , 100%/0.5 $\gamma$ -R (14).

**Anesthetic:** **11**: 20 mg. inact.-R (12).

**REMARKS:** "Hippulin" [C<sub>18</sub>H<sub>26</sub>O<sub>2</sub>; m.p. 233°  $[\alpha]_D = +128^\circ$  (dioxane);  $[\alpha]_D = +145^\circ$  (me. alc.); which in tests **1** and **7** is as act. as equilin, was isolated from preg. mare's urine and is isomeric (5,10).

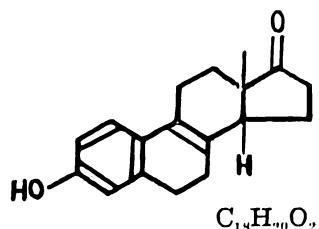
DERIVATIVES:

Me. ether	160.5-1.5°: (2)
Me. ether-me. carbinol	132-9°: (2)
Bz.	196-7°: (8,10)
Semicarb.	265-7°: (10)
Oxime	221-3°: (10)

REFERENCES:

1. A9603
2. 53662
3. 53758
4. 72048
5. 7351
6. 2226
7. 31517
8. 34942
9. 67353
10. 2227
11. A35039
12. A36744
13. 73572
14. A35275

$\Delta^{1,5,5;10,5}$ -**14-EPIESTRATETRAENE-3-OL-17-ONE**  
 (Iso-equilin A; 14-epi- $\Delta^5$ -equilin)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

M.P.: 231°: (1)

$[\alpha]_D^{25} = +222^\circ$  (alc.): (1)

**PHARMACOLOGY:** Folliculoid: 1: 1/5 as act. as estrone-R (1).

**REMARKS:**

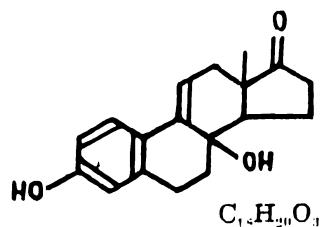
**DERIVATIVES:**

Semicarb. (+½H₂O) 230°: (1)  
 Ac. 83-95°: (1)

**REFERENCES:**

1. A18346

*Δ<sup>13</sup>*-ESTRATETRAENE 3,8(10)-DIOL-17-ONE  
 (14-epi-*Δ<sup>13</sup>*-8-hydroxy-equilin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 204°: (1)

PHARMACOLOGY:

REMARKS:

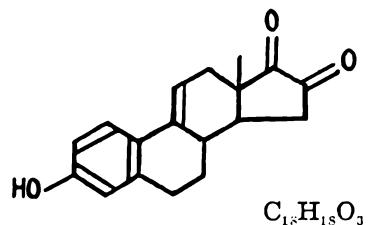
DERIVATIVES:

Ac. oil: (1)

REFERENCES:

- 1. A18346

$\Delta^{1,3,5:10,0:11}$ -ISOESTRATETRAENE-3-OL-16,17-DIONE  
 ( $\Delta^{0:11}$ -16-keto-iso-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2)

Total Synthesis: (1,2)

M.P.:

PHARMACOLOGY:

REMARKS: Presumably 14-epi (1,2).

DERIVATIVES:

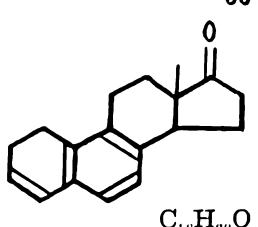
3-me. ether: (1)

REFERENCES:

1. A54831
2. A54807

60

$\Delta^{9,5:10,6,9}$ -ESTRATETRAENE-17-ONE



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2)

M.P.: 114-5°: (1,2)

PHARMACOLOGY:

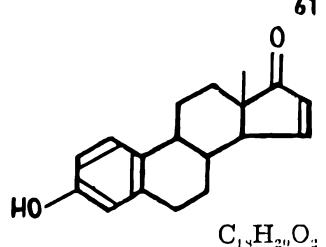
REMARKS:

DERIVATIVES:

REFERENCES:

1. A36229
2. A54246

$\Delta^{1,3,5:10,15}$ -ISOESTRATETRAENE-3-OL-17-ONE  
(Dehydro-iso-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.: 244-5°: (1)

PHARMACOLOGY:

REMARKS: Probably 14-epi (1).

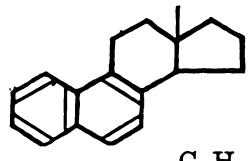
DERIVATIVES:

Phenylhydrazone (no m.p. given): (1)

REFERENCES:

1. A54807

$\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE  
(Equilenane)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 73-5°; (1)

PHARMACOLOGY:

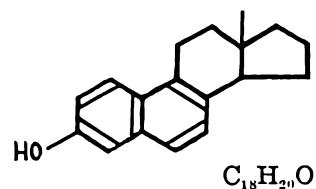
REMARKS:

DERIVATIVES:

REFERENCES:

1 77849

$\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL  
 (3-hydroxy- $\Delta^{1,3,5:10,6,8}$ -estrappaene; 17-desoxo-equilenin)



## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1)

## M.P.:

## PHARMACOLOGY:

## REMARKS:

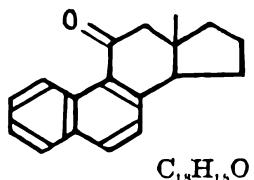
## DERIVATIVES:

Me. ether 121-2°; (1)  
 Me. ether-picrate 128-9°; (1)

## REFERENCES:

1. 28864

$\Delta^{10,5-10,6\beta}$ -ESTRAPENTAENE-11-ONE  
(11-equilenone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 156-8°: (1)

PHARMACOLOGY:

REMARKS:

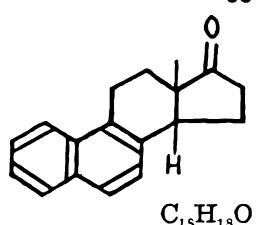
DERIVATIVES:

REFERENCES:

1. 77849

65

$\Delta^{1,3,5:10,0,8}$ -ESTRAPENTAENE-17-ONE  
(Desoxy-equilenin; 17-equilenone; desoxy-iso-equilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.: dl  $\alpha$  form 100-1°: (1)  
dl  $\beta$  form 188.5-9.5°: (1)

PHARMACOLOGY: Folliculoid: Test?  $\alpha$  and  $\beta$  forms "500 $\gamma$  inact. on estrus"-♀ /c R (1).

REMARKS: Rings C-D epimers; configuration unassigned (1).

DERIVATIVES:

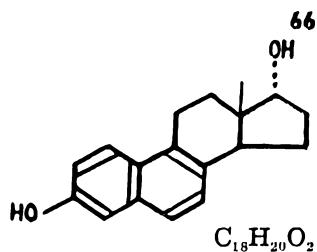
$\alpha$  picrate 109.5-10.5°: (1)  
 $\beta$  picrate not formed: (1)

REFERENCES:

1. A54247

$\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3,17( $\alpha$ )-DIOL  
( $\alpha$ -dihydro-equilenin)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2,3,5)

M.P.: 248°: (1,3)  
251-3°: (4)  
245°(u): (2)

PHARMACOLOGY: Folliculoid: Test?: "250 R.U. per mg." "... 1/12 as act. as estrone" (3);  
Test?: "ca. 1.5 $\gamma$ /I.U."-M (4,6); **14A**: ca. 1/12-1/24 as act. as estrone-R (7).

REMARKS: Not ppt. with digitonin (3).

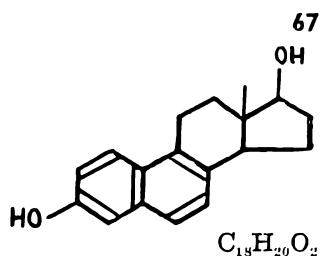
DERIVATIVES:

Mono-bz. 215°: (1,3)  
Diac. 126°: (1,3,5)

REFERENCES:

1. 70100
2. A9603
3. A17993
4. 74170
5. 73582
6. 29400
7. 72048

$\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3,17( $\beta$ )-DIOL  
( $\delta$ -follicular hormone;  $\beta$ -17-dihydro-equilenin)



ISOLATION: Ur. (preg. mare) : (3,5,7,9)

STRUCTURE AND SYNTHESIS: (1,2,3,4,7)

M.P.: 215°: (1,4)

217-8°: (8,10)

215-7°: (3,5)

$[\alpha]_D^{25} = -5^\circ$  (dioxane) : (3)

PHARMACOLOGY:

Folliculoid: 1: 1/10 as act. as estrone-R (3,5); Test?: > 4 $\gamma$ /I.U.-M (8); 3: Metrotropic act. 6% that of estrone-M (6); 55: slight vag. cornification with 20 mg.-R (10).

Anesthetic: 11: U. > 20 mg.-R (10).

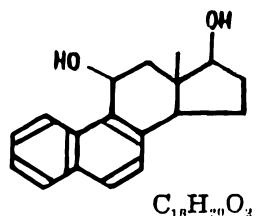
REMARKS: Not ppt. with digitonin (4); misprinted as  $\beta$ -17-dihydro-equilin by 10).

DERIVATIVES:

Di-p-nitro-bz.	251-2°:	(3)
3-bz.	204°:	(1,3,4)
Picrate	ca. 170°:	(3)
Diac.	115-7°:	(3)

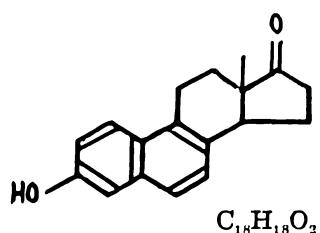
REFERENCES:

- |           |            |
|-----------|------------|
| 1. 70100  | 6. A35939  |
| 2. A9603  | 7. 32872   |
| 3. A9910  | 8. 74170   |
| 4. A17993 | 9. 66744   |
| 5. A17877 | 10. A36744 |

**$\Delta^{13,14(15)}$ -ESTRAPENTAENE-11( ),17( )-DIOL****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)**M.P.:** 209-12°: (1)**PHARMACOLOGY:****REMARKS:****DERIVATIVES:****REFERENCES:**

1. 77849

$\Delta^{1,9,10,16,17}$ -ESTRAPENTAENE-3-OL-17-ONE  
(Equilenin)



ISOLATION: Ur. (preg. mare) : (7,8,14)  
Ur. (human ♀) : (absent 7)

STRUCTURE AND SYNTHESIS: (1,3,4,5,6,10,15)  
Total Synthesis: (15)

M.P.:

d. 258-9°(vac.) :	(2,8,15)	d. $[\alpha]_D^{10} = + 87^\circ$ (dioxane) :	(8,15)
d. 256° :	(3,5)	d. $[\alpha]_D^{25} = + 89^\circ$ (alc.) :	(2,5)
l. 258-9°(vac.) :	(15)	l. $[\alpha]_D^{30} = - 85^\circ$ (dioxane) :	(15)
dl. 276-8°(vac.) :	(15)	dl. $[\alpha]_D^{30} = 0^\circ$ (dioxane) :	(15)
dl. 180° (+ benzene) :	(15)		

PHARMACOLOGY:

Folliculoid: **2**: ca. as act. as estrone-M (6); **1**: 12-20  $\times$  less act. than estrone-R (8); **14A**: ca. 1/20-1/30 as act. as estrone-R (13); **1**: ca. 1/6 as act. as estrone-R (9); Test?: amount required to produce estrus in more than 50% of the rats tested = 30 $\gamma$  of d-form and 400 $\gamma$  of l-form, these amounts are equivalent to 1 $\gamma$  of estrone (15,16); **55**: moderate vag. cornification with 20 mg.-R (12); **110**: *Metrotropic act.*: 0.17 $\gamma$  inact., 25%/0.35 $\gamma$ , 50%/0.5 $\gamma$ , 70%/0.8 $\gamma$ , 150%/1 $\gamma$ ; vag. opening: 0.17 $\gamma$ -0.35 $\gamma$  inact., 20%/0.5 $\gamma$ , 80%/0.8 $\gamma$ , 100%/1 $\gamma$ -R (17).

Anesthetic: **11**: U. > 20 mg.-R (12).

REMARKS: The naturally occurring hormone is the d- $\beta$ -form (15).

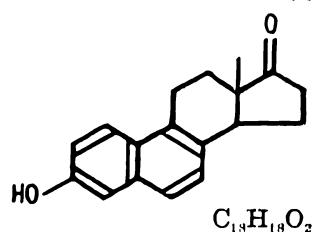
DERIVATIVES

Picrate d.	205-8°:	(6,7)
Me. ether-semicarb. d.	273-5°(u) :	(1,7)
Styphnate d.	213-5°:	(7)
Ac.-picrate d.	106-7°:	(7)
Oxime d.	249-50°:	(8)
Mono-br. d.	225-7°:	(8)
3-oxyacetic acid d.	233-6°:	(11)
Me. ester-3-oxyacetic acid d.	180-2°:	(11)
Ac. { d.	156-7°:	(8,15)
{ dl.	159.5-60°(vac.) :	(15)
Bz. { d.	222.5-3°(vac.) :	(2,8,9,15)
{ dl.	248.5-9.5°(vac.) :	(15)
Me. ether { d.	193.5-4°(vac.) :	(1,7,15)
{ dl.	185-6.5°(vac.) :	(15)
Trinitrobenzene complex d.	205.5-7°(vac.) :	(15)
l-menthoxy ac. d.	174-4.5°(vac.) ; $[\alpha]_D^{30} = + 18^\circ$ (benzene) :	(15)
d-menthoxy ac. l.	174.5-5°(vac.) ; $[\alpha]_D^{30} = - 16^\circ$ (benzene) :	(15)

REFERENCES:

1. 28864
2. A17993
3. A17994
4. 53662
5. 55131
6. 31517
7. 7505
8. 7351
9. A9910
10. A18346
11. 77849
12. A36744
13. 72048
14. 2227
15. A54232
16. A54235
17. A35275

$\Delta^{1,3,5:10,6,8}$ -14-EPIESTRAPENTAENE-3-OL-17-ONE  
(14-epi-equilenin; isoquillenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2,3)

Total Synthesis: (3)

M.P.: d. 262°: (2)	d. $[\alpha]_D^{30} = +160^\circ$ (alc.): (2)
d. 257-8°: (3)	d. $[\alpha]_D^{29} = +147^\circ$ (dioxane); $+173^\circ$ (alc.): (3)
l. 257-8°: (3)	l. $[\alpha]_D^{28} = -147^\circ$ (dioxane); $-162^\circ$ (alc.): (3)
dl. 223-4° (vac.): (3)	dl. $[\alpha]_D = 0^\circ$ (dioxane): (3)

PHARMACOLOGY: Folliculoid: Test?: "amount required to produce estrus in more than 50% of the rats tested > 500 $\gamma$  of d-and l-forms" (3); dl-form inact. at 500 $\gamma$  (4).

REMARKS: Cpd. designated as  $\alpha$ -form (3).

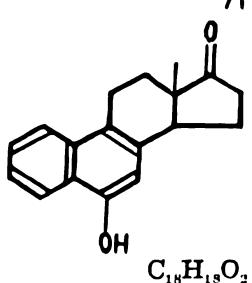
DERIVATIVES:

Me. ether d.	118.5-9.5° (vac.): (3)
Me. ether dl.	127-7.5° + 130° (vac.): (3)
Ac. d.	126-7.5° + 146-7° (vac.); $\begin{cases} [\alpha]_D^{22} = +129.4^\circ \text{ (alc.)} : (3) \\ [\alpha]_D^{24} = +137^\circ \pm 7^\circ \text{ (alc.)} : (2,3) \end{cases}$ 4. A54235
Ac. dl.	159-60° (vac.): (3)
Trinitrobenzene complex dl.	186-7° (vac.): (3)

REFERENCES:

1. 28864
2. A18346
3. A54232
4. A54235

$\Delta^{1,3,5;10,6,8}$ -ESTRAPENTAENE-6-OL-17-ONE  
(6-hydroxy-17-equilenone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form 240-2°(vac.): (1)  
dl.  $\beta$ -form 171.5-2.5°(vac.): (1)

PHARMACOLOGY: Folliculoid: Test?: up to 500 $\gamma$  of  $\alpha$  or  $\beta$  forms inact.-? /c R (1).

REMARKS: dl.  $\alpha$  and  $\beta$  = cis and trans forms (1).

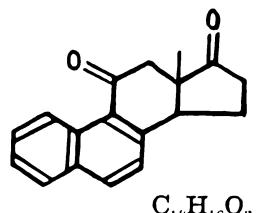
DERIVATIVES:

6-me. ether- $\alpha$  form 147.5-9°(vac.): (1)  
6-me. ether- $\beta$  form 112-3°(vac.): (1)

REFERENCES:

1. A54233

$\Delta^{1,3,5;10,6,8}$ -ESTRAPENTAENE-11,17-DIONE  
( $\beta$  desoxy-11-keto-equilenin)



ISOLATION: Ur. (preg. mare); (1)

STRUCTURE AND SYNTHESIS: (2)

M.P.: 212-4°: (1)

PHARMACOLOGY:

REMARKS: Artefact due to oxidation during isolation from urine (2).

DERIVATIVES:

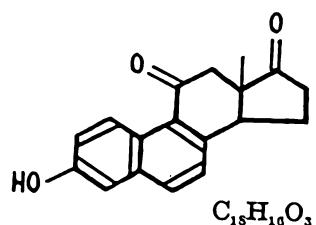
Mono-semicarb. 255-60°: (1)

REFERENCES:

- 1. 76880
- 2. 77849

$\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-11,17-DIONE  
(11-keto-equilenin)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

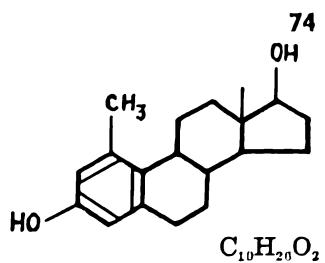
DERIVATIVES:

Ac. 195-7°; (1)  
Mono-semicarb. 238-41°; (1)

REFERENCES:

1. 77849

**1-METHYL- $\Delta^{1,3,5:10}$ -ESTRATRIENE-3,17( )-DIOL  
(1-methyl-estradiol)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2)

M.P.:

PHARMACOLOGY: Folliculoid: Test?: 1 mg. inact.-Species? (1,2).

REMARKS:

DERIVATIVES:

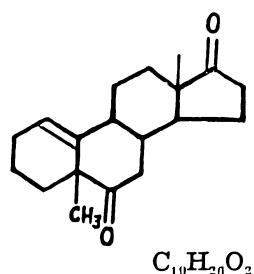
Diac.: (1)

REFERENCES:

1. A39626
2. A55236

**5( )-METHYL- $\Delta^{1:10}$ -ESTRENE-6,17-DIONE**

**ISOLATION:**



**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 215-6°: (1)

$[\alpha]_D^{10} = +21^\circ$  (CHCl<sub>3</sub>): (1)

**PHARMACOLOGY:**

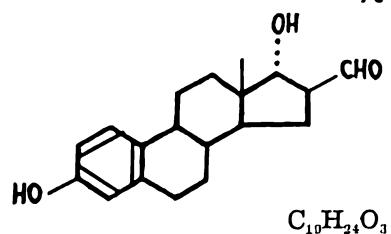
**REMARKS:** Structure uncertain (1).

**DERIVATIVES:**

**REFERENCES:**

1. 80945

16( )-FORMYL- $\Delta^{1,3,5:10}$ -ESTRATRIENE-3,17( $\alpha$ )-DIOL  
 (Formyl-estradiol)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 218-9°: (1)

PHARMACOLOGY: Folliculoid: 5?: 200,000 M.U./gm. (1).

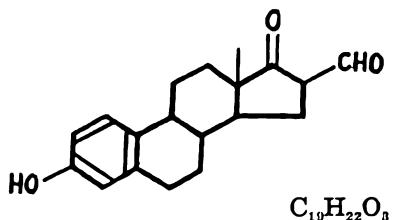
REMARKS:

DERIVATIVES:

REFERENCES:

1. A34088

**16( )-FORMYL- $\Delta^{1,3,5:10}$ -ESTRATRIENE-3-OL-17-ONE  
(Formyl-estrone)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY: Folliculoid: 5: Me. ether 1/10 as act. as estrone me. ether-M (1,2).

REMARKS:

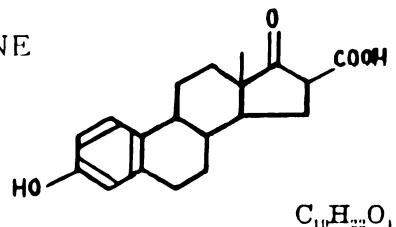
REFERENCES:

Me. ether 172°: (1,2)

DERIVATIVES:

1. A34088
2. A1916

**16( )-CARBOXY- $\Delta^{1,8,5:16}$ -ISOESTRATRIENE-3-OL-17-ONE  
(16-carbhydroxy-iso-estrone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

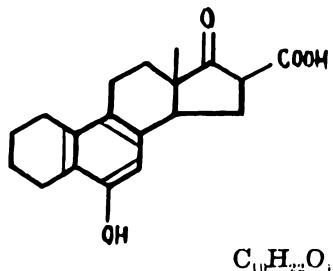
**REMARKS:**

**DERIVATIVES:**

dl. Me. ether-me. ester (mixture of stereoisomers) oil: (1) 1. A56995

**REFERENCES:**

**16( )-CARBOXY- $\Delta^{5;10,6,9}$ -ESTRATRIENE-6-OL-17-ONE  
(6-hydroxy-16-carbohydroxy-1,2,3,4-tetrahydro-17-equilenone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:**  $\alpha + \beta$  forms rings C-D isomers (1).

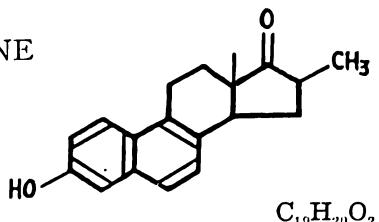
**DERIVATIVES:**

Me. ether-me. ester { dl.  $\alpha$ -form 146-7°(vac.) : (1)  
dl.  $\beta$ -form 129.5-30°(vac.) : (1)

**REFERENCES:**

1. A56997

**16( )-METHYL- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
(16-methyl-equilenin)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

M.P.: dl.-form 261.5-3° (vac.): (1)

**PHARMACOLOGY:**

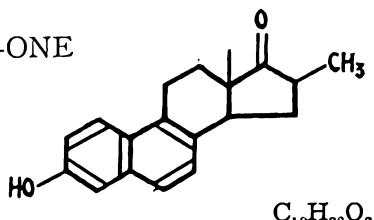
**REMARKS:**

**DERIVATIVES:**

**REFERENCES:**

1. A54235

**16( )-METHYL- $\Delta^{1,3,5:10,6,8}$ -ISOESTRAPENTAENE-3-OL-17-ONE  
(16-methyl-iso-equilenin)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

**M.P.:** dl-form 183-4° (vac.) : (1)

**PHARMACOLOGY:**

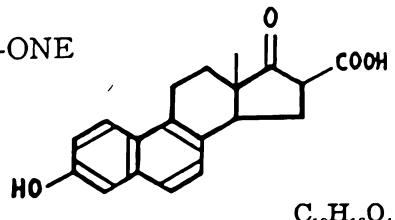
**REMARKS:**

**DERIVATIVES:**

**REFERENCES:**

1. A54235

**16( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
(16-carbhydroxy-equilenin)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

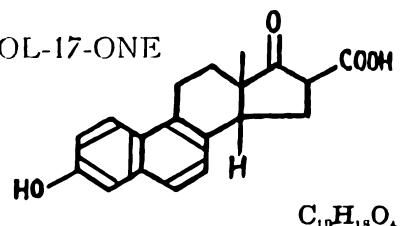
**DERIVATIVES:**

Me. ether-me. ester dl. 181-2° (vac.): (1)

**REFERENCES:**

1. A54232

**16( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -14-EPIESTRAPENTAENE-3-OL-17-ONE  
(16-carbhydroxy-iso-equilenin)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:**

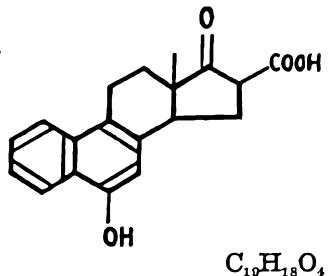
**DERIVATIVES:**

Me. ether-me ester dl. 149-9.5°; 152.5-3.5° (vac.): (1)

**REFERENCES:**

- 1. A54232

**16( )-CARBOXY- $\Delta^{1,3,5;10,0,8}$ -ESTRAPENTAENE-6-OL-17-ONE  
(6-hydroxy-16-carbhydroxy-17-equilenone)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

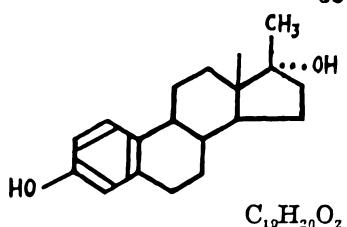
REMARKS:  $\alpha$  and  $\beta$  forms are rings C-D epimers; structure not assigned (1).

DERIVATIVES:

Me. ether-me. ester dl.  $\alpha$ -form 151-2°(vac.): (1) 1. A54233  
dl.  $\beta$ -form 140-1°(vac.): (1)

REFERENCES:

**17(β)-METHYL- $\Delta^{1,3,5;10}$ -ESTRATRIENE-3,17(α)-DIOL  
(17-methyl-estradiol)**



## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1)

M.P.:

**PHARMACOLOGY:** Folliculoid: Test?: ca. as act. as estradiol-Species? (3).

**REMARKS:**

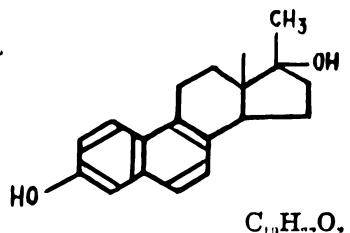
## **DERIVATIVES:**

Picrate-17-aminomethyl-3-ac. 233-4°: (1)  
3-me. ether 95-100° (impure): (2)

## **REFERENCES:**

1. 82713
  2. 53662
  3. A55236

**17( )-METHYL- $\Delta^{1,3,5(10),6,8}$ -ESTRAPENTAENE-3,17( )-DIOL  
(3,17-dihydroxy-17-methyl-estra  $\Delta^{1,3,5(10),6,8}$ -pentene)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

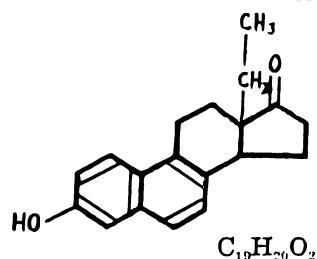
DERIVATIVES:

3-me. ether d. 133-3.5°; (1,2)

REFERENCES:

1. 53662
2. A54232

**18( )-METHYL- $\Delta^{1,8,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
(3-hydroxy-19-methyl-17-equilenone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form 219-20° (vac.) : (1)  
dl.  $\beta$ -form 251-5° (vac.) : (1)

**PHARMACOLOGY: Folliculoid: Test?:** dl.-racemic mixture of  $\alpha$  form "failed to induce the estrus response when injected in doses as high as 500 $\gamma$ . On the other hand the  $\beta$ -racemic mixture proved to be active in 100 $\gamma$  doses. In as much as dl.-equilenin required about 60-70 $\gamma$  to give the response in rats under the same conditions, it is evident that substitution of an ethyl group for the angular methyl group has not resulted in any materially decreased activity"- ♀/c R (1,2); dl.  $\alpha$ -form inact. at 1000 $\gamma$  and dl.  $\beta$ -form act. at 100 $\gamma$  in test in which 1 $\gamma$  of estrone act.- ♀/c R (2).

**REMARKS:**  $\alpha$ -form probably corresponds to dl.-isoequilenin (i.e. 14-epi) : (1).

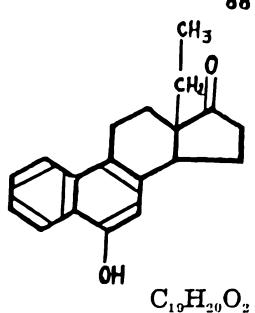
**DERIVATIVES:**

3-me. ether dl.  $\alpha$ -form 124.5-5.5° (vac.) : (1)  
3-me. ether dl.  $\beta$ -form 171-3° (vac.) : (1)

**REFERENCES:**

1. A54234
2. A54235

**18( )-METHYL- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-6-OL-17-ONE  
(6-hydroxy-19-methyl-17-equilenone)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form 206-8°(vac.); (1)  
dl.  $\beta$ -form 121.5-3°(vac.); (1)

PHARMACOLOGY: Folliculoid: Test?: Both dl.  $\alpha + \beta$  forms inact. up to 1000 $\gamma$  "in ovariectomized rat" (1).

REMARKS: Rings C-D epimers; configuration not assigned (1).

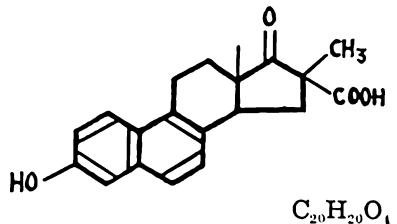
DERIVATIVES:

6-me. ether dl.- $\alpha$ -form 142°: (1)  
6-me. ether dl.- $\beta$ -form 75-6°: (1)

REFERENCES:

1. A54233

**16( )-METHYL-16( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
(16-methyl-16-carbhydroxy-equilenin)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

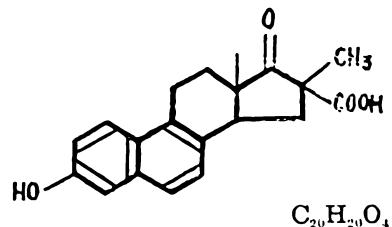
Me. ether-ene ester dl. 163-4° (vac.): (1)

REFERENCES:

1 A54235

16( )-METHYL-16( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -  
**ISOESTRAPENTAENE-3-OL-17-ONE**  
 (16-methyl-16-carbhydroxy-iso-equilenin)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)  
 Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

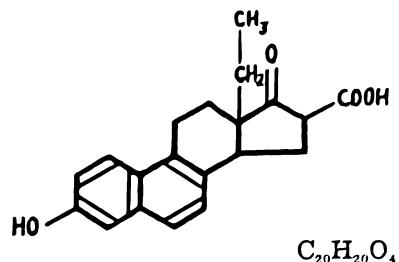
DERIVATIVES:

Me. ether-me. ester dl. 145.5-7° (vac.); (1)

REFERENCES:

1. A54235

16( )-CARBOXY-18-METHYL- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
 (3-hydroxy-16-carbhydroxy-19-methyl-17-equilenone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
 Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

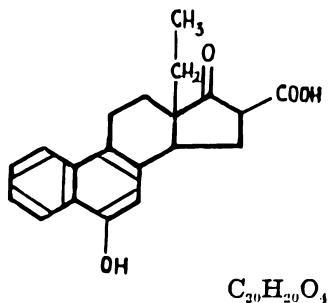
Me. ester-me. ether { dl.  $\alpha$ -form 137-8°(vac.) : (1)  
 { dl.  $\beta$ -form 167-8.5°(vac.) : (1)

REFERENCES:

1. A54234

16( )-CARBOXY-18-METHYL- $\Delta^{1,3,5(10),6,8}$ -  
**ESTRAPENTAENE-6-OL-17-ONE**  
(6-hydroxy-16-carbhydroxy-19-methyl-17-equilenone)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

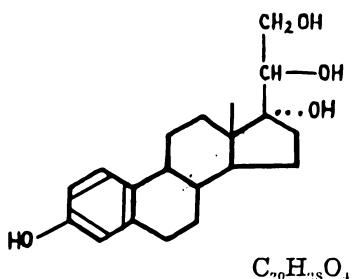
REMARKS:  $\alpha + \beta$  forms are rings C-D isomers; structure not assigned (1).

DERIVATIVES:

Me. ester-me. ether { dl.  $\alpha$ -form 161-2° (vac.) : (1)      1. A54233  
dl.  $\beta$ -form 118-20° (vac.) : (1)

REFERENCES:

**17( )-[1( ),2-DIHYDROXYETHYL]- $\Delta^{1,3,5:10}$ -ESTRATRIENE-3,17( $\alpha$ )-DIOL  
(Dihydroxy-ethenyl-estradiol)**



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 207-8°(u): (1)

PHARMACOLOGY: Folliculoid: **14A,14B**: 10 $\gamma$  inact. s.c. or per os-R (1).  
Corticoid: **15**: 5 mg. inact.-Cat (1).

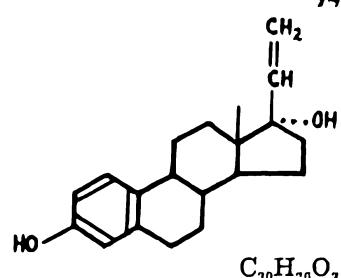
REMARKS:

DERIVATIVES:

REFERENCES:

1. 72048

**17(β)-ETHENYL- $\Delta^{1,8,9;10}$ -ESTRATRIENE-3,17(α)-DIOL  
(17-ethenyl-estradiol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 148-50°(u): (1)

[ $\alpha$ ]<sub>D</sub> = + 57.3°(dioxane): (1)

**PHARMACOLOGY:** Folliculoid: **14A**: 1/5-1/6 as act. as estradiol-R (1); **14B**: ca. as act. as estradiol-R (1).

**REMARKS:**

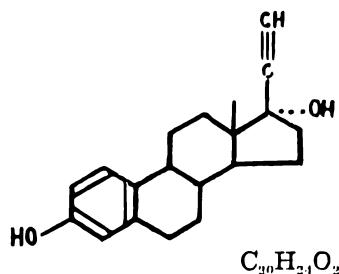
**DERIVATIVES:**

Bz. 160-2°(u): (1)

**REFERENCES:**

1. 72048

**17(β)-ETHYNYL- $\Delta^{1,8,5:10}$ -ESTRATRIENE-3,17(α)-DIOL  
(17-ethynyl-estradiol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,3)

M.P.: 145-6°(u): (1,3)

$[\alpha]_D = +1.8^\circ$  (dioxane): (1,3)

**PHARMACOLOGY:**

**Folliculoid:** **14A:** as act. as estradiol-R (1,3); **14B:** 3γ as act. as 50γ of estradiol-R (1,3); **74B:** 0.05 mg./day orally act. in menopausal women (4); **74B:** "Extraordinarily act. by mouth"-Human (6); **74B:** 0.5-1.0 mg./day orally act. in menopause-Human (7,8); **128A:** *Anti-castration cell act.*: + + /0.1γ; + + + /0.5γ-R (5). **128A:** *Metrotropic act.* 437( $\pm 40$ )%/0.1γ, 611( $\pm 32$ )%/0.5γ, 603( $\pm 48$ )%/5γ-R (5).

**Anesthetic:** **11:** U. = 10 mg.-R (2); **127:** U. = 1 mg.-Fish (2).

**REMARKS:**

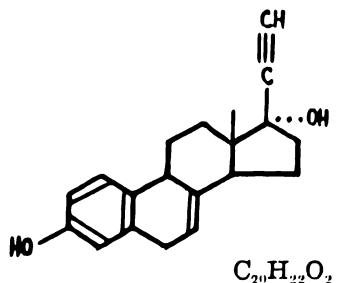
**DERIVATIVES:**

Bz. 200-2°(u): (1)

**REFERENCES:**

1. 72048
2. A38070
3. 70997
4. A57476
5. A56752
6. A37564
7. A37075
8. A55061

**17(β)-ETHYNYL- $\Delta^{1,3,5(10),7}$ -ESTRATETRAENE-3,17(α)-DIOL  
(17-ethynyl-dihydro-equilin)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** 179° (u) : (1)

**PHARMACOLOGY:** Folliculoid: **14A**: as act. as estradiol-R (1); **14B**: 2γ as act. as 50γ of estradiol-R (1).

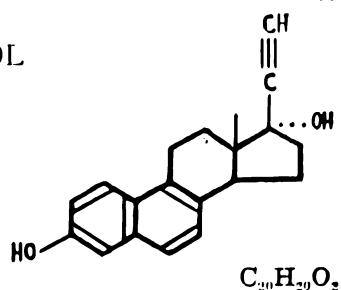
**REMARKS:**

**DERIVATIVES:**

**REFERENCES:**

- 1. 72048

**17(β)-ETHYNYL- $\Delta^{1,3,5(10),6,8}$ -ESTRAPENTAENE-3,17(α)-DIOL  
(17-ethynyl-dihydroequilenin)**



**ISOLATION:**

M.P.: 179°(u): (1)

**PHARMACOLOGY:** Folliculoid: **14A**: 5 $\gamma$  as act. as 0.1 $\gamma$  of estradiol-R (1).

**REFERENCES:**

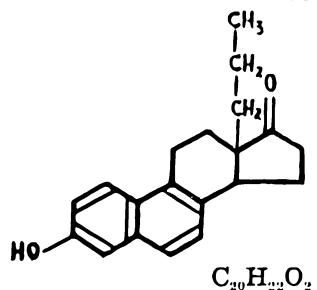
**DERIVATIVES:**

Bz. 225°(u): (1)

**REFERENCES:**

1. 72048

**18-ETHYL- $\Delta^{1,3,5:10,16,18}$ -ESTRAPENTAENE-3-OL-17-ONE  
(3-hydroxy-19-ethyl-17-equilenone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

**M.P.:**  $\alpha$ -form 153-4°(vac.): (1)  
 $\beta$ -form 236-7°(vac.): (1)

**PHARMACOLOGY:** Folliculoid: Test?: 250 $\gamma$  of dl.  $\alpha$ -form or 25 $\gamma$  of dl.  $\beta$ -form as act. as 1 $\gamma$  of estrone- $\alpha$ /c R (1).

**REMARKS:**  $\alpha + \beta$  forms rings C-D isomers (1).

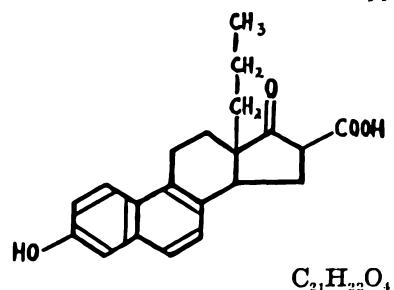
**DERIVATIVES:**

Me. ether { dl.  $\alpha$ -form 103.5-4.5°(vac.): (1)  
dl.  $\beta$ -form 148.5-9.5°(vac.): (1)

**REFERENCES:**

1. A54235

**16-CARBOXY-18-ETHYL- $\Delta^{1,3,5;10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
(3-hydroxy-16-carbhydroxy-19-ethyl-17-equilenone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)  
Total Synthesis: (1)

**M.P.:**

**PHARMACOLOGY:**

**REMARKS:**  $\alpha + \beta$  forms rings C-D isomers (1).

**DERIVATIVES:**

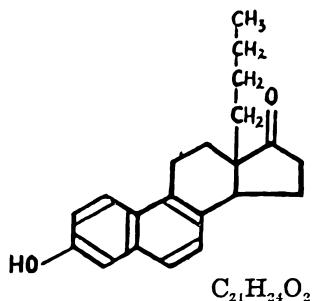
Me. ether-me. ester { dl.  $\alpha$ -form 135-6°(vac.) : (1)  
{ dl.  $\beta$ -form 172.5-3.5°(vac.) : (1)

**REFERENCES:**

1. A54235

100

**18-PROPYL- $\Delta^{1,3,5:10,0,8}$ -ESTRAPENTAENE-3-OL-17-ONE**  
**(3-hydroxy-19-propyl-17-equilenone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form (not crystalline): (1)  
 dl.  $\beta$ -form 191-2° (vac.): (1)

**PHARMACOLOGY:** Folliculoid: Test?: dl.  $\beta$ -form inact. at 1000 $\gamma$  in test in which 1 $\gamma$  of estrone act.-♀/c R (1).

**REMARKS:**  $\alpha + \beta$  forms rings C-D isomers (1).

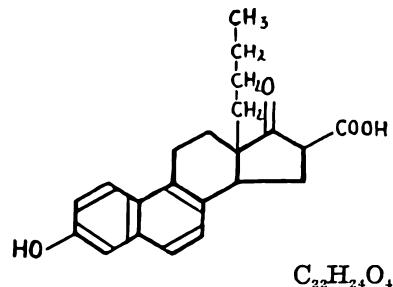
**DERIVATIVES:**

Me. ether { dl.  $\alpha$ -form 93.4° (vac.) and 104-5° (vac.): (1)  
 { dl.  $\beta$ -form 141-2°: (1)

**REFERENCES:**

1. A54235

16( )-CARBOXY-18-PROPYL- $\Delta^{1,3,5:10,6,8}$ -ESTRAPENTAENE-3-OL-17-ONE  
 (3-hydroxy-16-carbhydroxy-19-n-propyl-17-equilenone)



## ISOLATION:

Total Synthesis: (1)

M.P.:

## PHARMACOLOGY:

REMARKS:  $\alpha + \beta$  forms rings C-D isomers (1).

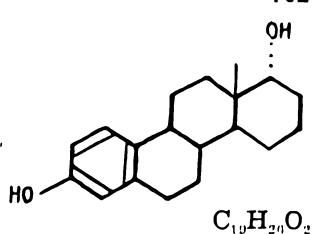
## DERIVATIVES:

Me. ether-me. ester { dl.  $\alpha$ -form 115.5-6.5°: (1)  
 } dl.  $\beta$ -form 153-4°(vac.): (1)

## REFERENCES:

1. A54235

*Δ<sup>1,3,5:10</sup>-D-HOMOESTRATRIENE-3,17a(α)-DIOL*  
*(D-homo-α-estradiol)*



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 232-5-3°: (1)

$[\alpha]_{\text{D}}^{22} = +87.6^\circ \pm 2^\circ$  (dioxane): (1)

PHARMACOLOGY: Folliculoid: **23**: U. = 20-25γ, about 1/30 as act. as estrone-R (1).

REMARKS: C<sub>17a</sub> configuration uncertain; not ppt. with digitonin (1).

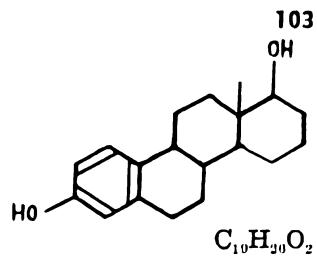
DERIVATIVES:

Diac. 165-6°: (1)

REFERENCES:

1. 82713

$\Delta^{1,8,5:10}$ -D-HOMOESTRATRIENE-3,17 $\alpha$ ( $\beta$ )-DIOL  
(D-homo- $\beta$ -estradiol)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY: Folliculoid: **23**: U. = 20-25 $\gamma$ , about 1/30 as act. as estrone-R (1).

REMARKS: Uncertain which of two isomerids is 17 $\alpha$ ( $\alpha$ ) but only m.p. 232-33 cpd. has been prepared and assayed.

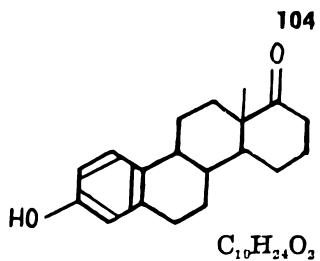
DERIVATIVES:

REFERENCES:

1. 82713

104

$\Delta^{1,8,5:10}$ -D-HOMOESTRATRIENE-3-OL-17a-ONE  
(D-homo-estrone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: 269°: (1)

$[\alpha]_D^{25} = +27.5^\circ \pm 2^\circ$  (dioxane): (1)

PHARMACOLOGY: Folliculoid: 23: U. = 20 $\gamma$ ; 1/30 as act. as estrone-R (1).

REMARKS:

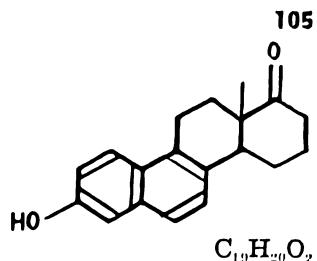
DERIVATIVES:

Ac.	130-1°; $[\alpha]_D^{25} = +30^\circ$ (dioxane): (1)	1. 81742
Oxime	221-2°: (1)	2. 82713
Me. ether	138.5-9.5°: (2)	

REFERENCES:

1. 81742
2. 82713

$\Delta^{1,3,5;10,6,8}$ -D-HOMOESTRAPENTAENE-3-OL-17a-ONE  
(D-homo-equilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1,2)  
Total Synthesis: (1,2)

M.P.: dl-form 232-3°(vac.): (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

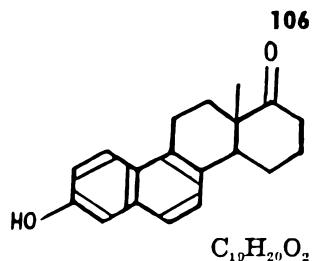
Me. ether { dl. 212-3°: (2)  
          { dl. 213-4°(vac.): (1)  
Semicarb.-me. ether dl. { 244-6°: (1)  
          { 245°: (2)

REFERENCES:

1. A54235
2. A58294

106

$\Delta^{1,3,5:10,6,8}$ -D-HOMOISOESTRAPENTAENE-3-OL-17a-ONE  
(D-homo-iso-equilenin)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.: dl. form 239-40°(vac.): (1)

PHARMACOLOGY:

REMARKS:

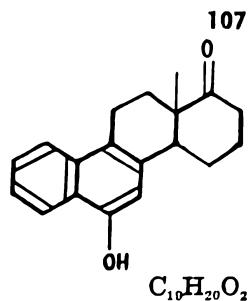
DERIVATIVES:

Me. ether dl. 125-6°: (1)

REFERENCES:

1. A54235

$\Delta^{1,9,5;10,6,8}$ -D-HOMOESTRAPENTAENE-6-OL-17a-ONE  
(6-hydroxy-D-homo-17a-equilenone)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.: dl.  $\alpha$ -form      227-9°(vac.) : (1)  
dl.  $\beta$ -form      223-5°(vac.) : (1)  
dl.  $\alpha + \beta$ -form 193-202°(vac.) : (1)

PHARMACOLOGY: Folliculoid: Test?: 1 mg. of  $\alpha$  or  $\beta$  forms inact.-♀/c R (1).

REMARKS: Rings C-D epimers, configuration not assigned (1).

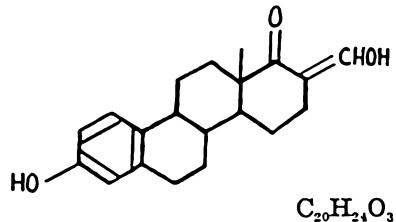
DERIVATIVES:

6-me. ether { dl.  $\alpha$ -form 131-2.5°(vac.) : (1)  
                  { dl.  $\beta$ -form 142-3°(vac.) : (1)

REFERENCES:

1. A54233

**17-HYDROXYMETHYLENE- $\Delta^{1,3,5:10}$ -D-HOMOESTRATRIENE-3-OL-17a-ONE  
(17-hydroxymethylene-D-homoestrone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.:

**PHARMACOLOGY:**

**REMARKS:**

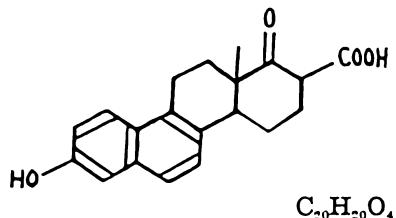
**DERIVATIVES:**

Me. ether 195-7<sup>1</sup>; (1)

**REFERENCES:**

1. 82713

17( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -D-HOMOESTRAPENTAENE-3-OL-17a-ONE  
 (17-carbhydroxy-D-homo-equilenin)



## ISOLATION:

STRUCTURE AND SYNTHESIS: (1)  
 Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

## DERIVATIVES:

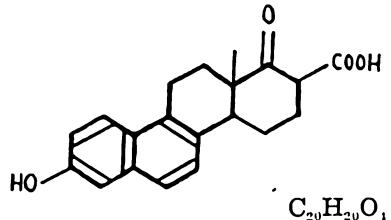
Me. ether-mc. ester dl. 158-60° (vac.): (1)

## REFERENCES:

1. A54235

17( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -D-HOMOISOESTRAPENTAENE-3-OL-17a-ONE  
 (17-carbhydroxy-D-homoisoequilenin)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

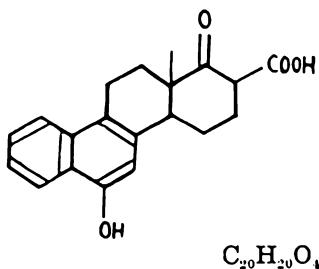
Me. ether-me. ester dl. 133-5° (vac.); (1)

REFERENCES:

1. A54235

17( )-CARBOXY- $\Delta^{1,3,5:10,6,8}$ -D-HOMOESTRAPENTAENE-6-OL-17 $\alpha$ -ONE  
(6-hydroxy-D-homo-17-carbhydroxy-17 $\alpha$ -equilenone)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)  
Total Synthesis: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

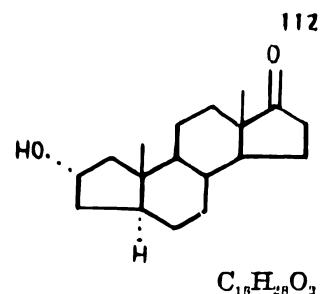
DERIVATIVES:

D-methyl ether-methyl ester (dl.  $\alpha$ -form 152-4° (vac.); (1)  
(dl.  $\beta$ -form 150-1° (vac.); (1)

REFERENCES:

1. A54233

**PYROANDROSTANE-2( $\alpha$ )-OL-17-ONE  
(Pyroandrostosterone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** 124°: (1)

**PHARMACOLOGY:**

**REMARKS:** Not ppt. with digitonin (1).

**DERIVATIVES:**

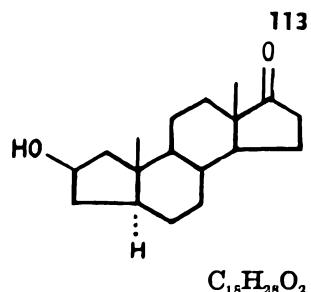
Semicarb. 250°: (1)  
Ac. 102°: (1)

**REFERENCES:**

1. 70098

113

**PYROANDROSTANE-2( $\beta$ )-OL-17-ONE  
(Pyro-iso-androsterone)**



ISOLATION:

M.P.:

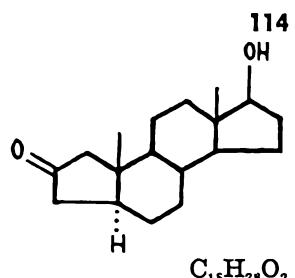
PHARMACOLOGY:

REMARKS: Ppt. with digitonin (1).

DERIVATIVES:

REFERENCES:

1. 70098

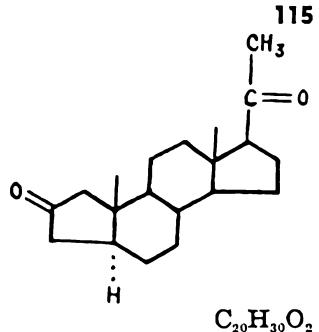
**PYROANDROSTANE-2-ONE-17( )-OL****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)**M.P.:** 197°; (1)**PHARMACOLOGY:****REMARKS:****DERIVATIVES:**

Semicarb. 238°; (1)

**REFERENCES:**

L. 70098

**17( )-[1-KETOETHYL]-PYROANDROSTANE-2-ONE  
(Pyroallopregnandione)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 180°; (1)

**PHARMACOLOGY:**

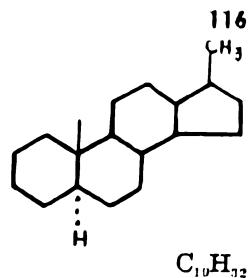
**REMARKS:**

**DERIVATIVES:**

**REFERENCES:**

1. 70006

17( )-METHYL-13-NORANDROSTANE  
(Pseudo-androstane)



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.: oil: (1)

PHARMACOLOGY:

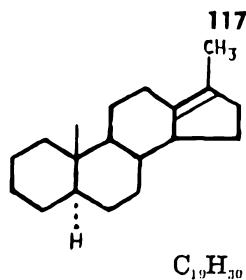
REMARKS: Structure uncertain (1).

DERIVATIVES:

REFERENCES:

1. 75739

**17-METHYL- $\Delta^{13:17}$ -NORANDROSTENE  
(Pseudo-androstene)**



ISOLATION:

M.P.: oil: (1)

$[\alpha]_D^{10} = -25^\circ$  (alc.): (1)

**PHARMACOLOGY:**

**REMARKS:** Structure uncertain (1).

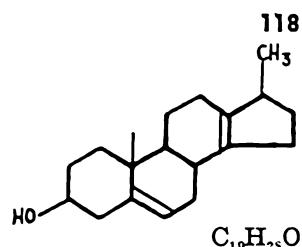
DERIVATIVES:

REFERENCES:

1. 75739

118

**17( )-METHYL- $\Delta^{5,13}$ -NORANDROSTADIENE-3( $\beta$ )-OL  
(Retro-androstadiene-3-ol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.:

**PHARMACOLOGY:**

**REMARKS:**

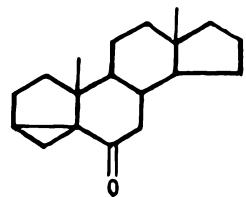
**DERIVATIVES:**

3-ac - 75°;  $[\alpha]_D^{25} = +68^\circ$  (alc.) (1)

**REFERENCES:**

1. A54981

**i-ANDROSTANE-6-ONE**  
*(i-androstane-6-one)*



ISOLATION:

C<sub>19</sub>H<sub>28</sub>O

STRUCTURE AND SYNTHESIS: (1)

M.P.: 122-2.5°: (1)

[α]<sub>D</sub> = +34.5° (alc.): (1)

PHARMACOLOGY:

REMARKS:

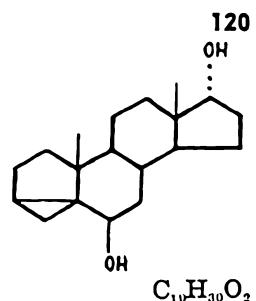
DERIVATIVES:

REFERENCES:

1. A50838

120

i-ANDROSTANE-6( ),17( $\alpha$ )-DIOL



ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY:

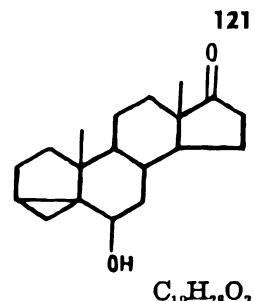
REMARKS:

DERIVATIVES:

6-mc-ether-17-tosylate 124°; ( $\alpha$ )<sup>25</sup> = + 23.5° (CHCl<sub>3</sub>): (1) 1. 60135

REFERENCES:

**i-ANDROSTANE-6( )-OL-17-ONE**  
**(i-androstan-6-ol-17-one)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 136-8°: (1)

$[\alpha]_D^{20} = +122^\circ$  (alc.): (1)

**PHARMACOLOGY:**

**REMARKS:**

**DERIVATIVES:**

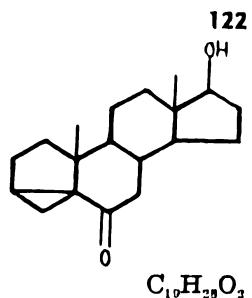
Ac. 113-4°;  $[\alpha]_D^{20} = +117^\circ$  (alc.): (1)  
 Semicarb. 237-40°: (1)

**REFERENCES:**

1. A50838

122

**i-ANDROSTANE-6-ONE-17( )-OL**  
**(i-androstane-6-one-17( )-ol)**



ISOLATION:

M.P.:

PHARMACOLOGY:

REMARKS:

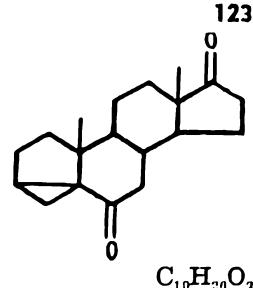
DERIVATIVES:

Ac. 109-10°: (1)

REFERENCES:

1. A50838

**i-ANDROSTANE-6,17-DIONE**  
**(i-androstane-6,17-dione)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 182-3°: (1)

$[\alpha]_D^{20} = +113^\circ (\text{CHCl}_3)$ : (1)

**PHARMACOLOGY:** Testoid: Physiologically inact. (1).

**REMARKS:**

**DERIVATIVES**

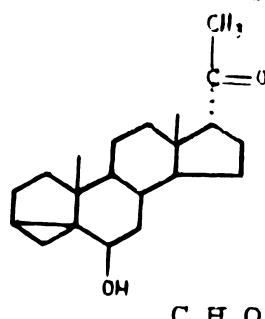
Dioxime 269-71°: (1)

**REFERENCES:**

1. A50838

**17(20)-[1-KETOETHYL]-*5*-ANDROSTANE-6(*β*)-OL  
(1-pregnene-6 $\beta$ -ol)**

**ISOLATION:**



**STRUCTURE AND SYNTHESIS:** 12

**M.P.:**

**PHARMACOLOGY:**

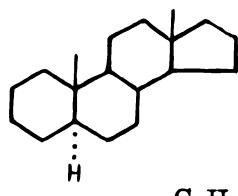
**REMARKS:**

**DERIVATIVES:**

Me. ether 124-5°;  $[\alpha]_D^{20} = +132^\circ$  ( $\text{CHCl}_3$ ): (1) 1. 69135  
2. A32422

**REFERENCES:**

**ANDROSTANE**  
(Ethy-allo-cholane)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,3,4)

M.P.: 49-50°(u): (1)  
49-51°: (4)  
51-2.5°: (5)

**PHARMACOLOGY:**

**Folliculoid:** **128C:** 2 mg./day inact.-R (8); **128A:** 2 mg./day no *metrotropic* and no *anti-castration cell act.*-R (8).

**Luteoid:** **46:** 50 mg. inact.-Rb. (6).

**Anesthetic:** **11:** 10 mg. inact.-R (7); **127:** 7 mg. inact.-Fish (7).

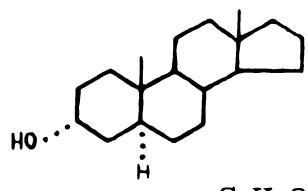
**REMARKS:**

**DERIVATIVES:**

17-Amino.HCl 345°: (2)

**REFERENCES:**

- |          |           |
|----------|-----------|
| 1. 32388 | 5. 83020  |
| 2. 35147 | 6. A56335 |
| 3. A8217 | 7. A38070 |
| 4. 63691 | 8. A56752 |

ANDROSTANE-3( $\alpha$ )-OL

## ISOLATION:

## STRUCTURE AND SYNTHESIS: (1)

M.P.:

**PHARMACOLOGY:** Testoid: **29**: 1 mg./day of 17-amine act.-C (2); **31**: 17-amine in 1% solution in oil definitely act.-C (2); Test?: 17-amine "has comparatively slight act. on s.ves."-Species? (3).

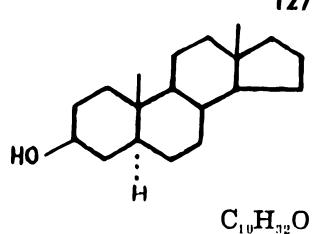
## REMARKS:

## DERIVATIVES:

17-amine       $187\text{-}8^\circ$ :      (2)  
17-amine.HCl  $340^\circ$ : (1);  $365^\circ$ : (2)

## REFERENCES:

1. 35147
2. A31549
3. A33511

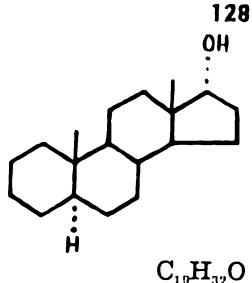
**ANDROSTANE-3( $\beta$ )-OL****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)

M.P.: 148°; (1)

**PHARMACOLOGY:****REMARKS:****DERIVATIVES:****REFERENCES:**

1. 80054

**ANDROSTANE-17( $\alpha$ )-OL**  
**(androstane-17 trans-ol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2,3,5)

M.P.: 166°: (1)

164-6°: (3)

158-9°: (5)

163-4°: (6)

**PHARMACOLOGY:** Luteoid: **46**: I.U. = 80 mg.-Rb. (4).

**REMARKS:**

**DERIVATIVES:**

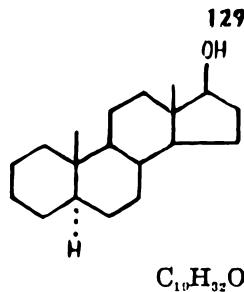
Ac. 75-6°: (5)

**REFERENCES:**

- |          |           |
|----------|-----------|
| 1. 35147 | 4. A56335 |
| 2. 78246 | 5. A50838 |
| 3. 79003 | 6. 75739  |

129

**ANDROSTANE-17( $\beta$ )-OL**  
(androstan-17-cis-ol)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 152-3°: (1)

**PHARMACOLOGY:**

**REMARKS:**

**DERIVATIVES:**

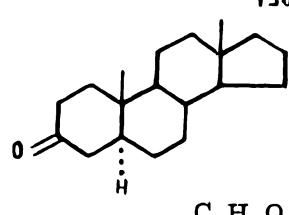
Hexahydrobz. 138-9°: (1)

**REFERENCES:**

1. 75739

130

**ANDROSTANE-3-ONE**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1)

M.P.: 97-8°: (1)

**PHARMACOLOGY:**

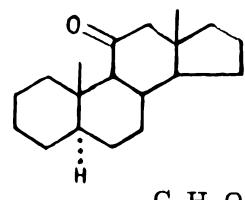
**REMARKS:**

**DERIVATIVES:**

Semicarb. 238-40°: (1)

**REFERENCES:**

1. A8219

**ANDROSTANE-11-ONE****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)

M.P.: 52°: (1)

**PHARMACOLOGY:**

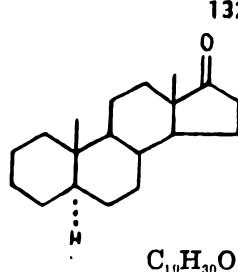
**REMARKS:** Forms no semicarb. (1).

**DERIVATIVES:****REFERENCES:**

1. A8217

## ANDROSTANE-17-ONE

## ISOLATION:



## STRUCTURE AND SYNTHESIS: (1,2,6,9,11)

M.P.: 122°(u): (1)  
 121-2°: (2,3,6)  
 117-9°: (9)

PHARMACOLOGY: Testoid: **29**: U. = 500 $\gamma$  of  $3\alpha$  or  $3\beta$ -Cl-C (7,8); **29**: 2 mg. of  $3\beta$ -Cl inact.-C (4);  
**31**: 1% sol. of  $3\beta$ -Cl act.  $\beta$ -C (4); Test?:  $3(\alpha)$ -Br. inact.-C (10).

## REMARKS:

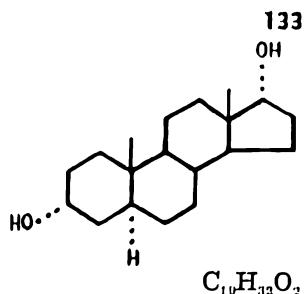
## DERIVATIVES:

Semicarb.	$\left\{ \begin{array}{ll} 263-6^\circ(\text{u}): & (1) \\ 275-7^\circ: & (2) \\ 284-5^\circ: & (9) \end{array} \right.$
$3(\beta)$ -Cl.	128°: (1,4,7)
$3(\alpha)$ -Cl.	$\left\{ \begin{array}{ll} 173^\circ: & (1) \\ 172-4^\circ: & (6) \\ 170-1^\circ(\text{u}): & (5) \end{array} \right.$
$3(\alpha)$ -Cl. semicarb.	279-81°(u): (5)
$3(\beta)$ -Cl. semicarb.	268-9°: (7)
$3(\alpha)$ -Br.	163-4°: (4)

## REFERENCES:

1. 32388
2. 30818
3. 63691
4. 31644
5. 34804
6. 80929
7. 30097
8. 30098
9. 83009
10. A33511
11. A54806

**ANDROSTANE-3( $\alpha$ ),17( $\alpha$ )-DIOL**  
(Dihydroandrosterone; androstadiol; 3 cis 17 transandrostadiol)



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2,3,4)

M.P.: 223°: (2)  
221° (u): (1)  
219-22°: (3)  
218-20°: (13)

$[\alpha]_D^{23} = +12.6^\circ$ : (1)

**PHARMACOLOGY:**

**Testoid:** **29**: I.U. = 20 $\gamma$ -C (6); **29**: I.U. = 25 $\gamma$ -C (15); **68**: I.U. = 33 $\gamma$ -C (8); **29**: I.U. = 25-30 $\gamma$  of 3-ac.; 35-40 $\gamma$  of 3-pr.; 50 $\gamma$  of 3-n-butyrate; 300 $\gamma$  of 3-bz.; 30 $\gamma$  of diac.; 100 $\gamma$  of dipr.; > 1 mg. of 3-palmitate; > 1 mg. of 17-bz.-C (15); **32A**: U. = 45-50 $\gamma$ -C (1); **32B**: 20-24 $\gamma$  as act. as 45-50 $\gamma$  in test **32A-C** (1); **32A**: U. = 60-70 $\gamma$  of diac.-C (1); **29**: U. = 15-20 $\gamma$  of free cpd., 3-ac. and diac.-C (2,4,14,31); **32A**: U. = 50-60 $\gamma$  of free cpd., 3-ac., and diac.-C (2); **121**: U. = 21 $\gamma$  of "androstanediol"-R (29); **59**: U. = 2.4 $\gamma$  locally, 165 $\gamma$  intramuscularly, and 25000 $\gamma$  per os-C (24); **29**: 3-mono-succinate less act. than free cpd.; 17-monobz. inact. at 1 mg./day-C (27); **29**: U. = 250 $\gamma$  of di-succinate-C (14); and 50-60 $\gamma$  of 3-mono-succinate-C (5); **33**: U. = 0.3 mg.-R (7); **32A**; **33**: R.U./C.U. = 5-6/1 (7); **63**: U. = 0.6-1 $\gamma$ -C (28,33); **80**: U. = 200 $\gamma$ -M (33); **29**; **32A**: ca. 5  $\times$  more act. than androsterone-C (1,27); **37A**; **45**: 3-4  $\times$  more act. than androsterone-R (14,48); **45**: s.ves. 210% / 100 $\gamma$ , 430% / 200 $\gamma$ ; pta. 0/100 $\gamma$ , 225% / 200 $\gamma$ -R (4,14,31); **37A**: s.ves. 130% / 150 $\gamma$ , 330% / 250 $\gamma$ ; 1000% / 1 mg.; pta. 160% / 150 $\gamma$ ; 250% / 250 $\gamma$ ; 700% / 1 mg.-R (8); **29**: Among 3 monoesters intensity of act. decreases and duration of act. increases with length of aliphatic acid chain, but 3-palmitate much less act.-C (15); **45**: 3-pr. and 3-n-butyrate somewhat more act. than free cpd.; bz. and dipr. much less act.-R (15); **43**: practically all esters especially 3-n-butyrate more act. than free cpd.-R (15); **31**: ca. as act. as androsterone-C (23); **121**: "androsterone-diol" more act. on s. ves. than on pta. "return to normal of secondary sexual organs"-R (19); **44**: "androstane-diol bz." s.ves.: 50% / 250 $\gamma$ , 83% / 750 $\gamma$ ; pta.: 0/250 $\gamma$ , 60% / 750 $\gamma$ -R (32).

**Folliculoid:** **38**: "androstane-diol" mitogenic and mucifying on vag.-R (9); **39A**: "androstane-diol" 1-2.5 mg./day act.-R (10); **68**: "androstane-diol" 1 mg./day exerts strong *metrotropic, mammatropic* and *anti-castration* cell act. also slight *vag. mucifying* act.-R (17); **51**: *vag. mucifying* and *metrotropic* act. of "androsterone-diol" > than that of "androsterone"-R (19,20); **73**: 1 mg./day of "androstane-diol" inact.-C (25); **142**: *Anti-castration cell act.:* "androstane-diol" up to 10 mg. inact.-R (30).

**Anti-folliculoid:** **120**: "androstane-diol" inhibits vag. cornification-R (9).

**Luteoid:** **46**: 20 mg. of "androstane-diol" inact.-Rb. (21); **86A**: 12 mg. of "androstane-diol" inact.-Rb. (26); **124**: "androstane-diol" does not maintain pregnancy-M (35).

**Gonadotropic:** **21**: 10 mg. of "cis-androstane-diol" act.-X (18,22).

**Anesthetic:** **11**: U. > 10 mg. of 3-bz.-R (11); **11**: U. = ca. 10 mg. of free cpd.-R (34); **127**: U. = 2 mg.-Fish (34).

REMARKS: References to pharmacological act. which fail to indicate steric position of C<sub>17</sub>-OH are quoted with this cpd.

## DERIVATIVES:

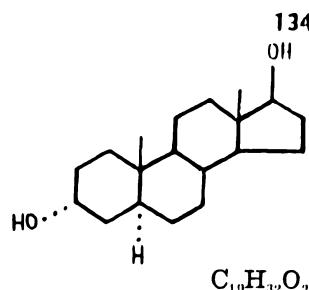
3-ac.	183°:	(2)
17-ac.	191-2°:	(12)
Diac.	162-3°; [α] <sub>D</sub> <sup>23</sup> = + 12.5°:	(1,2,3)
17-bz.	203-4°:	(12)
3-ac.-17-bz.	198-9°:	(12)
1/2-succinate	226°:	(16)
3-mono-succinate	207-8°:	(5)
3,17-disuccinate	139-40°:	(4)
3-n-butyrate	124-5°:	(15)
Dipr.	122°:	(15)
3-palmitate	ca. 40°:	(15)
3-pr.	120-1°:	(15)

## REFERENCES:

1. 53442	13. 35417	25. 69323
2. 32022	14. 56241	26. A2959
3. 79639	15. 70023	27. A33511
4. 51129	16. 82661	28. A2569
5. 33338	17. 38576	29. 38925
6. 69949	18. 75731	30. 70000
7. 55960	19. 54550	31. 31735
8. 56092	20. 54552	32. A15269
9. 72100	21. 67357	33. 63734
10. 55720	22. 66025	34. 100000
11. A36744	23. 71314	35. A36553
12. 34805	24. 75101	

**ANDROSTANE-3( $\alpha$ ),17( $\beta$ )-DIOL  
(3-cis-17-cis androstandiol)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 227-8°: (1)

PHARMACOLOGY: Testoid: 29: I.U. = ca. 350 $\gamma$ -C (1); 45: 1 mg./day inact. on s.ves. and pta.-R (1).

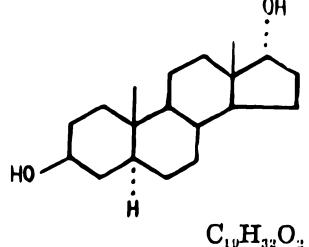
REMARKS: References to pharmacological act. which fail to indicate steric position of C<sub>17</sub>-OH are quoted under the heading of Androstane-3( $\alpha$ ), 17( $\alpha$ )-diol.

DERIVATIVES:

REFERENCES:

- 1. 69949

**ANDROSTANE-3( $\beta$ ),17( $\alpha$ )-DIOL**  
**(Iso-androstanediol-trans; 3-trans-17-trans-androstanediol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,4,5,11,13,14,15,18)

Microbial Synthesis: (15)

M.P.: 168°: (4,5)

163-4°(u): (11,13)

162-4°: (1,14)

$[\alpha]_D^{20} = +4.2^\circ$  (alc.): (11,15)

**PHARMACOLOGY:**

**Testoid:** **29**: I.U. = 500-550 $\gamma$ -C (2,4,10); **32A**: U. = ca. 1 mg. of "isoandrostandiol"-C (11,12); **31**: U. = ca. 4 $\gamma$ -C (3); **29**: U. = 350-370 $\gamma$ -C (4,5); **33**: U. = ca. 1.3 mg. of "isoandrostandiol"-R (12); **32A,33**: C.U./R.U. = 1-C, R (12); **33**: U. = 750 $\gamma$ -R (16); **63**: U. = 4-10 $\gamma$ -C (17,20); **45**: s.ves.: 50% / 200 $\gamma$ , pta.: 200% / 200 $\gamma$ -R (5,10); **80**: 500 $\gamma$  inact.-M (20).

**Luteoid:** **46**: 50 mg. inact.-Rb. (19).

**Gonadotropic:** **21**: up to 10 mg. of "trans androstanediol" inact.-X (7,8).

**Anesthetic:** **11**: U. = ca. 10 mg.-R (19); **127**: U. > 7 mg.-Fish (19).

**REMARKS:** References to pharmacological act. which fail to indicate steric position of 17-OH are quoted on this page. Not ppt. with digitonin (11).

**DERIVATIVES:**

Diac.	127-8°; { $[\alpha]_D = +4.9^\circ$ (alc.): (1,4,11,12,14)
	{ $[\alpha]_D^{14} = -1^\circ \pm 1^\circ$ (acetone): (1)
17-ac.	147-8°(u): (9)
3-ac.-17-hexahydrobz.	134-5°: (2)
17-hexahydrobz.	168°: (2)

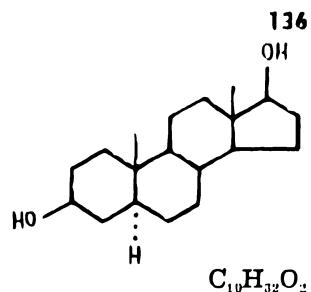
**REFERENCES:**

1. 79638
2. 69949
3. 71314
4. 54129
5. 56783
6. A38941
7. 75731
8. 66925
9. 60172
10. 56241
11. 55952
12. 55960
13. 75059
14. 69401
15. 69403
16. A9540
17. A2569
18. 78847
19. 100000
20. 63734

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**ANDROSTANE-3( $\beta$ ),17( $\beta$ )-DIOL  
(3-trans-17-cis-androstanediol)**

**ISOLATION:**



**STRUCTURE AND SYNTHESIS:** (1,2,3)

M.P.: 213.5-4.5°: (3)

**PHARMACOLOGY:**

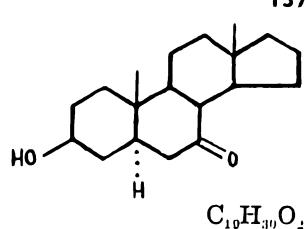
**REMARKS:**

**DERIVATIVES:**

Diac.	147-7.5°: (3)
17-hexahydrobz.	208.5-9.5°: (1)
3-ac.-17-hexahydrobz.	(oil): (1)
17-1/2-succinate	225.5-6.5°: (2)

**REFERENCES:**

1. 69949
2. 82661
3. 59165

**ANDROSTANE-3( $\beta$ )-OL-7-ONE****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)

M.P.: 131°: (1)

 $[\alpha]_D = -69^\circ$ : (1)

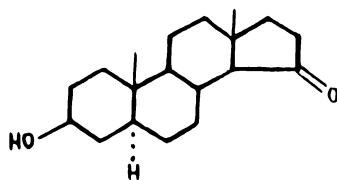
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**PHARMACOLOGY:****REMARKS:****DERIVATIVES:**

Ac. 110-3°: (1)

**REFERENCES:**

1. 80054

**ANDROSTANE-3(β)-OL-15-ONE**

ISOLATION: Ur. (preg. mare): (1,2,3)

## STRUCTURE AND SYNTHESIS: (1,3)

M.P.: 187-7.5°: (3)

 $[\alpha]_D^{25} = -160^\circ$  (dioxane): (3)

## PHARMACOLOGY:

REMARKS: Ketone group may be at C<sub>10</sub>, although C<sub>15</sub> is more probable (1).

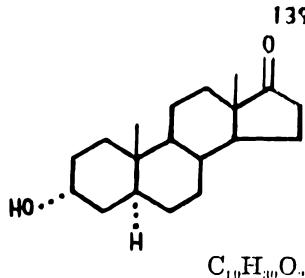
## DERIVATIVES:

Oxime 194-5°: (3)  
 Bz. 206-8°: (3)

## REFERENCES:

1. 80054
2. A56972
3. 76961

**ANDROSTANE-3( $\alpha$ )-OL-17-ONE**  
(Androsterone, cis-androsterone)



ISOLATION:	Ur. (♂ human):	(6,7,10,47,49)
	Ur. (♀ human):	(36,46)
	Ur. (preg. cow):	(14)
	Ur. (bull):	(14)
	Ur. (preg. human):	(15)
	Ur. (♂ /c human):	(48)
	Ur. (♀ /c human):	(37,43)
	Ur. (♀ human with breast cancer):	(71)
	Ur. (hysterectomized human):	(51)
	Ur. (♀ human with adrenal tumor):	(26,52)
	Ur. (human with Leydig cell tumor- as Na sulphate ester):	(39,57)
	Ur. (ox):	(42)

STRUCTURE AND SYNTHESIS: (12,4,5,8,11,12,13,37,40,50,56)

M.P.: 185-5.5°: (50)

182-3°: (2,8,37,40)

178°: (6)

177-8°(u): (3,9)

180-1.5°: (7)

$[\alpha]_D^{25} = +94.6^\circ$  (alc.): (2)

$[\alpha]_D^{25} = +96^\circ$  (alc.): (7)

$[\alpha]_D^{15} = +87.8^\circ \pm 1.5^\circ$  (dioxane): (50)

$[\alpha]_{D,461}^{15} = +107.3^\circ \pm 1.5^\circ$  (dioxane): (50)

**PHARMACOLOGY:**

**Testoid:** I.U. = 100 $\gamma$ -(44); **29:** U. = 70 $\gamma$ -C (53); **31:** U. = 0.7 $\gamma$ -C (59); **32A:** U. = 150-200 $\gamma$ -C (10,31); **41:** U. = 500 $\gamma$ -C (33); **33:** U. = 1 mg.-R (31); **32B:** U. = 44-50 $\gamma$ -C (10); **63:** U. = 2 $\gamma$ -C (66,74); **29:** U. = 60-80 $\gamma$  of 1/2 succinate and 80-100 $\gamma$  of Na succinate-C (17); **29:** U. = ca. 100 $\gamma$  of ac.-C (54); **32A:** U. = 150-170 $\gamma$  of ac.-C (60); **43:** 2 mg. of ac., pr., n-butyrate and bz. inact.-R (54); **137:** at low dose level bz. as act. as free cpd., but > act. at high dose level-C (16); **137:** 200 $\gamma$ /day of bz. inact., but with 1 mg./day irregular and protracted act.-C (17); **32B:** oxime less act. than free cpd. (U. > 900 $\gamma$ ) but act. prolonged-C (60); **45:** free cpd.: s.ves. 43%/200 $\gamma$ ; 870%/1000 $\gamma$ , pta. 28%/200 $\gamma$ , 510%/1000 $\gamma$ ; ac.: s.ves. inact./500 $\gamma$ , pta. 25%/500 $\gamma$ ; pr.: s.ves. inact./500 $\gamma$ , 57%/1000 $\gamma$ , pta. 16%/500 $\gamma$ , 40%/1000 $\gamma$ ; n-butyrate: s.ves. 14%/500 $\gamma$ , 80%/1000 $\gamma$ , pta. 12%/500 $\gamma$ , 45%/1000 $\gamma$ ; bz.: s.ves. inact./500 $\gamma$ , 14%/1000 $\gamma$ , pta. 9%/500 $\gamma$ , 16%/1000 $\gamma$ -R (54,62); **37A:** free cpd.: s.ves. 71%/600 $\gamma$ , 210%/1000 $\gamma$ , 230%/1500 $\gamma$ , 360%/2000 $\gamma$ , pta. 160%/600 $\gamma$ , 340%/1000 $\gamma$ , 540%/1500 $\gamma$ , and 570%/2000 $\gamma$ -R (21,22); **106:** s.ves. 38%/125 $\gamma$ , pta. 120%/125 $\gamma$ -R (72); **81:** masculinizes ♀ chick (34); **29:** among the esters the act. increases in duration and decreases in intensity in proportion to the length of the chain-C (54); **32A,33:** R.U./C.U. = 5/1-C, R (31); **121:** U. 170 $\gamma$ -R (68); **59:** U. = 3 $\gamma$  by local application, 500 $\gamma$  by i.m. injection and 4500 $\gamma$  per os-C (69); **138B:** act.-R (64); **128:** prep. gl. 62( $\pm$ 15)%/0.1 mg., 176( $\pm$ 26)%/1 mg.-R (73); **132:** s.ves. 40( $\pm$ 18)%/0.1 mg., pta. 244( $\pm$ 9)%/0.1 mg.-R (77).

**Folliculoid:** **3:** *Metrotropic* act. < 0.01% that of estrone-M (30); **39A:** 1 mg./day inact.-R (23); **7:** 1 mg. inact.-R (24); **81:** feminizes ♂ chick (34); **66:** at 1 mg./day slight *anti-castration* cell act. but no *mammotrophic*, *metrotrophic* or vag. act.-R (32); **67:** act. in aqueous but not in oily sol.-G (35); **39B:** less act. on uterus and vag. than "androsterone-diol"-R (61); **58:** vag. opening and cornification with 10 mg./day-M (63); **39B:** no vag. cornification with 15 mg./day-R (25); **62:** up to 5 mg./day inact.-M (67); **128A:** up to 1 mg./day not *metrotropic*-R (73); **142:** *Anti-castration* cell act. inact./1 mg.-R (70); **128A:** *Anti-castration* cell act. 0 - +/1 mg.-R (73).

**Luteoid:** **49**: inact.-Rb. (20); **46**: up to 50 mg. inact.-Rb. (38,53); **27**: 0.8 mg. inact.-G (27).

**Corticoid:** **53B**: impure preparation inact.-R (65).

**Anti-folliculoid:** **129**: Hyp. - 30( $\pm 1$ )% /2 mg.; Ad. + 13.4( $\pm 9$ )% /2 mg.; Te. + 53.5( $\pm 8$ )% /2 mg.-R (75).

**Gonadotropic:** **21**: 10 mg. act.-X (28); **122**: 15 mg./day inact.-R (25); **138A**: 0.5-2.5 mg./day act.-R (64).

**Anesthetic:** **11**: U. = 4.5 mg.-R (29); **127**: U. = 0.25 mg.-Fish (76).

**REMARKS:** Not ppt. with digitonin: (55).

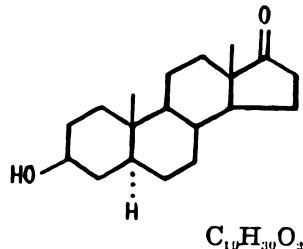
#### DERIVATIVES:

Ac.	165°; $[\alpha]_D^{20} = +86^\circ$ : (1,2,6,9,17,50)
Oxime	214-5°: (2,14)
Bz.	178-8.5°: (45)
Ac.-oxime	ca. 215°: (2); 272-3°: (62)
Ac.-semicarb.	284-5°: (2,5,8,19)
Semicarb.	274-5°: (2,10)
½-succinate	185-5.5°: (17)
Alkaline salts-½-succinate:	(18)
Neutral oxalate	149°: (2)
Na.-sulphate ester	144°: (39,57)
Na.-sulphate ester (+H <sub>2</sub> O):	188-92°: (39,57)
Pr.	151-2°: (2)
Tetra-acetyl-β-glucoside	154° and 179-81°: (41)
β-glucoside	228-9°: (41)
Oxalic acid addition product not formed:	(40)
Phenylhydrazone	153-4°: (10)
Thiosemicarb.	250-5°: (10)
n-butyrate	102-3°: (54)

#### REFERENCES:

1. 32388	27. A7923	53. A56335
2. 30098	28. 75731	54. 70023
3. 53442	29. A36744	55. A32421
4. 32021	30. A35939	56. A54806
5. 32589	31. 55960	57. A57511
6. 3429	32. 38576	58. 54129
7. 52699	33. A30100	59. 71314
8. 55133	34. 71207	60. 32389
9. 75059	35. A15263	61. 54552
10. 30225	36. A19775	62. A33511
11. 53441	37. 76419	63. 58875
12. 78598	38. 67357	64. 69957
13. 70093	39. S2380	65. 76576
14. 75332	40. S3021	66. A2569
15. 73729	41. S3022	67. 31122
16. 56093	42. 75573	68. 38925
17. 33338	43. A37253	69. 75101
18. 64621	44. A36596	70. 70000
19. 69947	45. 32022	71. A57666
20. 29442	46. 76319	72. A37407
21. 52584	47. 76320	73. A56752
22. 56092	48. A33793	74. 63734
23. 55720	49. A36219	75. A37637
24. 55958	50. S3506	76. 100000
25. 68772	51. A37254	77. A38071
26. 81144	52. A35703	

**ANDROSTANE-3(β)-OL-17-ONE**  
**(Iso-androsterone; trans-androsterone)**



**ISOLATION:** Ur. (cancerous ♂ and ♀ human): (14)  
 Ur. (♂ human): (9,14)  
 Ur. (♀ human): (9,14)  
 Ur. (♀ human with ad. tumor): (20, absent 6)  
 Ur. (preg. mare): (21)

**STRUCTURE AND SYNTHESIS:** (1,2,3,4,5,8,9,17,19)  
 Microbial Synthesis: (5)

M.P.: 174-5°: (12)  
 170-1° (u): (3,5,9,17)  
 176-7°: (4,19)

$[\alpha]_D^{20} = +87.5^\circ$  (me. alc.): (1)  
 $[\alpha]_D^{20} = +78^\circ$  (alc.): (9)  
 $[\alpha]_D^{15} = +81.1^\circ \pm 1^\circ$  (dioxane): (19)  
 $[\alpha]_{5461}^{15} = +100.6^\circ \pm 1^\circ$  (dioxane): (19)

**PHARMACOLOGY:**

**Testoid:** **36:** I.U. = ca.  $700\gamma$ -C (12,23); **32A:** U. =  $1400\gamma$ -C (16); **29:** U. =  $500\gamma$ -C (2); **36:** U. =  $625\gamma$ -C (11); **63:** U. =  $15-20\gamma$ -C (24,27); **33:** U. = ca. 4 mg.-R (16); **45:** 1 mg. inact. on s.ves. and pta-R (23); Test?: orally act. but less than s.c.-C (2); **32A,33:** R.U./C.U. = 4/1-C, R (16); **80:** U. = 1 mg.-M (27).

**Luteoid:** **46:** at 50 mg. slight act. if any-Rb. (26).

**Gonadotropic:** **21:** 10 mg. inact.-X (13).

**Anesthetic:** **11:** U. = 4.5 mg.-R (15).

**REMARKS:** Identity of cpd. from mare's urine doubtful (21); ppt. with digitonin (10).

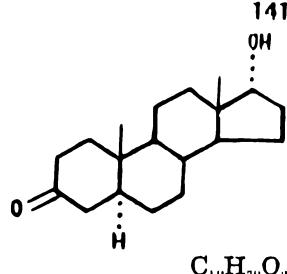
**DERIVATIVES:**

Ac.	96-7°:	(2,6)
Bz.	219-20°:	(9,25)
Oxime	185-6°:	(2,7)
$\beta$ -glucoside (+H <sub>2</sub> O)	216-7°:	(10)
Semicarb.	261-2°: (2,6); 282-3°:	(23)
Semicarb.-bz.	251-3°:	(25)
Semicarb.-3-ac.	272-3°:	(2,7)
Tetraacetyl- $\beta$ -glucoside	191-2°:	(18)
Oxalic acid adduct.	139-40°:	(17)
5-Cl.:		(22)

**REFERENCES:**

1. 30097	11. 52584	21. A56972
2. 30098	12. 56092	22. A50839
3. 53441	13. 75731	23. A33511
4. 55132	14. A37378	24. A2569
5. 75059	15. A36744	25. 32022
6. 73562	16. 55960	26. 100000
7. 78868	17. 83021	27. 63734
8. 78849	18. 83022	
9. 80906	19. 83506	
10. A15412	20. A35705	

**ANDROSTANE-3-ONE-17( $\alpha$ )-OL  
(trans-dihydrotestosterone)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2,3,7,8)

M.P.: 181.5-2.5°: (2)

178°(u): (3,7)

180-1°: (1)

179-80°: (8)

$[\alpha]_D^{20} = +32.4^\circ$  (alc.): (1)

**PHARMACOLOGY:** Testoid: **29**: I.U. = 20 $\gamma$  of free cpd., 25-30 $\gamma$  of formate, ac., and pr., 60-70 $\gamma$  of n-butyrate and 200 $\gamma$  of n-valerate-C (6,9); **29**: U. = ca. 15 $\gamma$ -C (1,5); **32A**: U. = 50 $\gamma$ -C (3,4); **29**: intensity of act. increases and duration of act. decreases with length of aliphatic acid chain-C (6); **45**: relative act. of various esters same as that of testosterone esters but quantitatively smaller; the n-valerate is most act.-R (6); **45**: s.ves. 157%/50 $\gamma$ , 325%/100 $\gamma$ , 600%/200 $\gamma$ ; pta. 63%/50 $\gamma$ , 150%/100 $\gamma$ , 240%/200 $\gamma$ -R (6,9).

**REMARKS:** Whenever steric position of - OH not stated pharmacological data relating to more highly act. isomer given here.

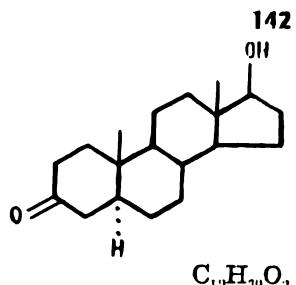
**DERIVATIVES:**

17-ac.	156-7°(u); 158°: (3,6,7)	1. 34805
Hexahydro-bz.	164-5°: (2)	2. 69949
Oxime	209°(u): (3)	3. 55952
Semicarb.	237-43°(u): (3)	4. 55960
Formate	141-2.5°: (6)	5. 56783
Pr.	121-2°: (6)	6. 70023
n-butyrate	91° and 101°: (6)	7. 60172
n-valerate	103°: (6)	8. 82661
1/2-succinate	160° + 168.5°: (8)	9. A33511
Ac.-2-Br.	177-8°: (7)	10. 72715
2-Br.	180-1°: (7,10)	
Bz.	199-200°: (1)	

**REFERENCES:**

**ANDROSTANE-3-ONE-17( $\beta$ )-OL  
(Cis-dihydrotestosterone)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 179.5-80°: (1)

PHARMACOLOGY: Testoid: **29**: I.U. = ca. 300 $\gamma$  of free cpd. and ca. 1 mg. of bz.-C (1); **45**: 1-2 mg. inact. on s.ves. and pta.-R (1).

REMARKS: Whenever steric position of — OH not stated, pharmacological data relating to less act. isomer given here.

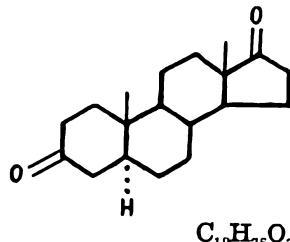
DERIVATIVES:

Ac. 150-1°: (1)  
Hexahydro-bz. 137.5-8°: (1)

REFERENCES:

1. 69949

## ANDROSTANE-3,17-DIONE



ISOLATION: Te. (pig): (4)

STRUCTURE AND SYNTHESIS: (1,3,6,7,8,9)

M.P.: 128-9°: (2,3,6)	$[\alpha]_D^{20} = +111^\circ$ (alc.) : (1)
133° (u): (1)	$[\alpha]_D^{20} = +107.1^\circ \pm 2^\circ$ (acetone); $[\alpha]_{5461}^{20} = +132.5^\circ \pm 2^\circ$ (acetone): (21)
132-3° (u): (5,21)	$[\alpha]_D^{18} = +113.5^\circ \pm 2^\circ$ ( $CHCl_3$ ); $[\alpha]_{5461}^{18} = +138^\circ \pm 2^\circ$ ( $CHCl_3$ ): (21)
133-4°: (7,9)	$[\alpha]_D^{14} = +100.4^\circ$ (alc.): (9)

## PHARMACOLOGY:

**Testoid:** **29:** I.U. = 120-130 $\gamma$ -C (14,24); **29:** U. = ca. 100 $\gamma$ -C (13,14,15); **32A:** U. = 250-400 $\gamma$ -C (5,11,12); **33:** U. = ca. 0.7 mg.-R (12); **32A,33:** R.U./C.U. = 2-3/1-C, R (12); **45:** s.ves. 107%/200 $\gamma$ , 115%/500 $\gamma$ , pta. 56%/200 $\gamma$ , 160%/500 $\gamma$ -R (14,24).

**Folliculoid:** **67:** act.-G (19); **142:** *Anti-castration cell act.* + +/0.5 mg.-R (25).

**Luteoid:** **46:** I.U. > 80 mg.-Rb. (22).

**Gonadotropic:** **21:** up to 10 mg. inact.-X (17).

**Anesthetic:** **11:** U. = 7.5 mg.-R (18); **11:** 2-Br. inact. at 20 mg.-R (16).

## REMARKS:

## DERIVATIVES:

2-Br.	213-4°:	(10)
5-Cl.	179°:	(23)
5-Cl-2-br.	156°:	(23)
Pyridinium Br. (+H <sub>2</sub> O)	ca. 315°:	(26)
Diet. acetal	121-3°; $[\alpha]_D^{20} = +75.6^\circ$ :	(27)
3-enol ether	105-6°; $[\alpha]_D^{20} = +126^\circ$ (dioxane):	(27)

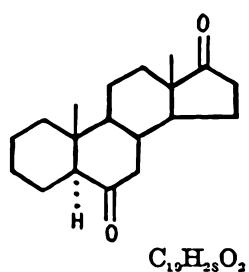
## REFERENCES:

1. 55952      15. 31735
2. 35147      16. A38070
3. A6243      17. 75731
4. A32425      18. A36744
5. 53441      19. A15263
6. 69401      20. A37486
7. A19373      21. 83506
8. 73729      22. A56335
9. 78847      23. A50839
10. 60172      24. A33511
11. 32389      25. 70000
12. 55960      26. 73581
13. 56271      27. A58075
14. 54129

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**ANDROSTANE-6,17-DIONE**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 134-5°; (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

Dioxime: 288-90°; (1)  
3-Br: 184°; (1)

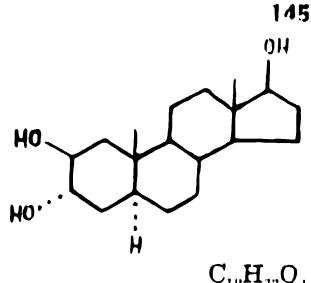
REFERENCES:

1. A50838

145

**ANDROSTANE-2( $\beta$ ),3( $\alpha$ ),17( $\beta$ )-TRIOL**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 264°: (1)

PHARMACOLOGY:

REMARKS: Not ppt. with digitonin (1).

DERIVATIVES:

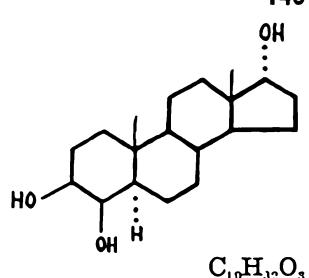
Triac. 188°: (1)

REFERENCES:

1. 75894

**ANDROSTANE-3( $\beta$ ),4( $\beta$ ),17( $\alpha$ )-TRIOL**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 260-1°: (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

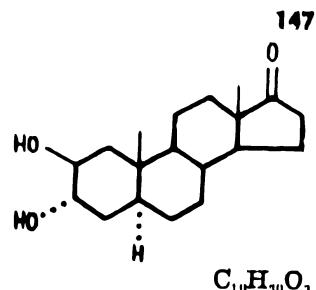
Prilec - 22253.5° - (1)

REFERENCES:

1 69945

**ANDROSTANE-2( ),3( $\alpha$ )-DIOL-17-ONE  
(2-hydroxy androsterone)**

**ISOLATION:**



**STRUCTURE AND SYNTHESIS:** (1)

**M.P.:** 195-8°; (1)

**PHARMACOLOGY:**

**REMARKS:** Not ppt. with digitonin (1).

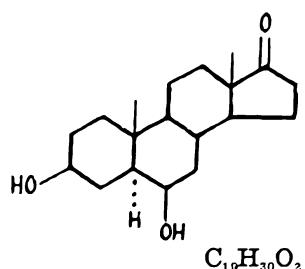
**DERIVATIVES:**

**REFERENCES:**

1. 75894

**ANDROSTANE-3( $\beta$ ),6( $\beta$ )-DIOL-17-ONE  
(6-hydroxy-iso-androsterone)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 205°: (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

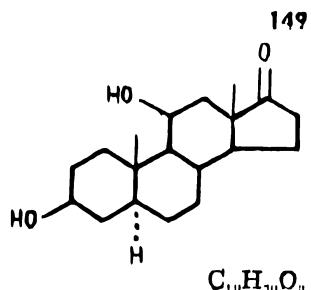
Diac.-semicarb. 222°: (1)

REFERENCES:

1. 78243

**ANDROSTANE-3(3),11(1)-DIOL-17-ONE**  
 (Reichstein's monoketone 236°)

ISOLATION: Ad.: (1)



STRUCTURE AND SYNTHESIS: (1,2,3,4,6)

M.P.: 236°: (3,5)  
 234.5°: (6)       $[\alpha]_{D}^{20} = +81.3^\circ \pm 2^\circ$  (dioxane);  $[\alpha]_{D}^{20} = +104.9^\circ \pm 2^\circ$  (dioxane); (6)  
 $[\alpha]_{D}^{20} = +84.5^\circ \pm 3^\circ$  (alc.); (3)

PHARMACOLOGY: Testoid: 31: U. = ca. 20 $\gamma$ , about 1/30 as act. as androsterone-C (3).

REMARKS: Ppt. with digitonin (3).

DERIVATIVES:

Diac.	154-6°:	(2)
3-ac.	230-1°:	(1,2)
3:5 dinitrobz.	257-8°:	(4)
Semicarb.	317-22°:	(3)

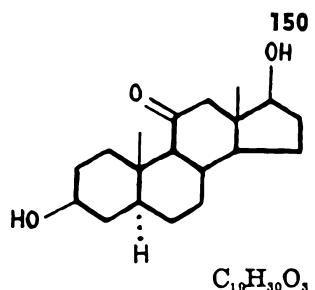
REFERENCES:

1. A19374
2. A8217
3. 63692
4. 63691
5. 81702
6. 83506

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ANDROSTANE-3( ),17( )-DIOL-11-ONE

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 247-8°: (1)

PHARMACOLOGY:

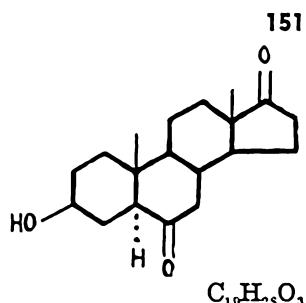
REMARKS:

DERIVATIVES:

Diacetate: 162-3°: (1)

REFERENCES:

1 AS217

**ANDROSTANE-3( )-OL-6,17-DIONE****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)**M.P.:****PHARMACOLOGY:****REMARKS:****DERIVATIVES:**

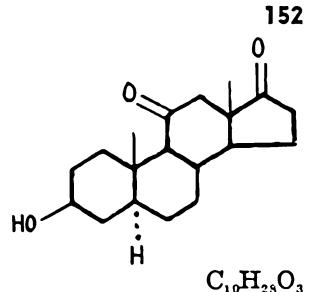
Ac - 197-S - (1)

**REFERENCES:**

1 A50838

**ANDROSTANE-3( $\beta$ )-OL-11,17-DIONE  
(11-keto-androsterone)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.: 166.5-8°; (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

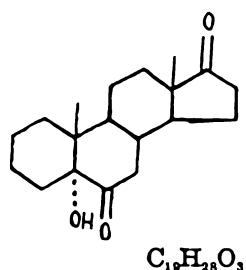
Ac. 162.5-3.5 (12)

REFERENCES:

1. AS217
2. 83506

**ANDROSTANE-5( $\alpha$ )-OL-6,17-DIONE**

ISOLATION:



STRUCTURE AND SYNTHESIS:

M.P.: 225-8°: (1)

PHARMACOLOGY:

REMARKS:

DERIVATIVES:

Ac - 187°: (1)

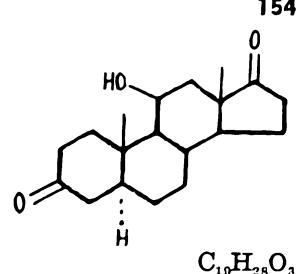
REFERENCES:

1. 80945

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## ANDROSTANE-3,17-DIONE-11( )-QL

ISOLATION:



STRUCTURE AND SYNTHESIS (2,4)

M.P.: ca. 225°: (4)

 $[\alpha]_D^{18} = +100.3^\circ \pm 3^\circ (\text{CHCl}_3)$ : (4)

PHARMACOLOGY:

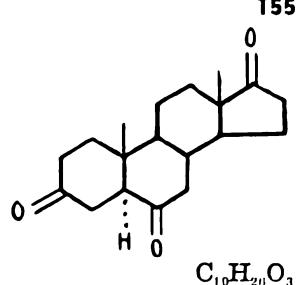
REMARKS: Cpd. of m.p. 160° and 178° (1,2,3) to which this structure had been assigned proved to be androstane-3,11,17-trione samples of varying purity (4).

## DERIVATIVES:

Dioxime 254-6°: (4)

## REFERENCES:

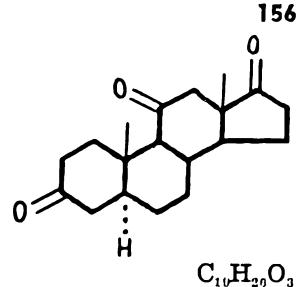
1. 63692
2. A33510
3. A9077
4. S1702

**ANDROSTANE-3,6,17-TRIONE****ISOLATION:****STRUCTURE AND SYNTHESIS:** (1)**M.P.:** 191-2°: (1)**PHARMACOLOGY:****REMARKS:****DERIVATIVES:****REFERENCES:**

1. A58120

**ANDROSTANE-3,11,17-TRIONE**  
 (dihydro-adrenosterone)

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2,3,4,5,6,7,8)

M.P.: 178-80°: (1)

176.5-8°: (2)

179-81°: (3)

182-3°: (6)

$[\alpha]_{D}^{25} = +191^\circ \pm 1.5^\circ$  (alc.): (3)

$[\alpha]_D^{12} = +152.8^\circ \pm 5^\circ$  (acetone): (6)

PHARMACOLOGY: Testoid: 31: U. =  $2\gamma$ -C (2).

REMARKS: Had originally been assigned structure of androstane-3,17-dione-11-ol (2,5,8) but this was proven to be erroneous (7).

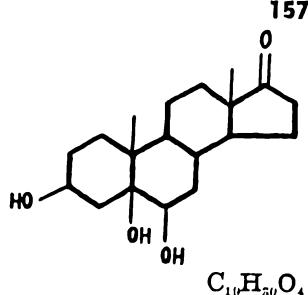
DERIVATIVES:

Dioxime 274-6°: (2)

REFERENCES:

1. A8217
2. 63692
3. 72169
4. 63691
5. A33510
6. S3506
7. S1702
8. A9077

**ANDROSTANE-3( $\beta$ ),5( $\beta$ ),6( $\beta$ )-TRIOL-17-ONE  
(androstane-17-one-3( $\beta$ ),5,6(cis)-triol)**



**ISOLATION:**

**STRUCTURE AND SYNTHESIS:** (1,2,3,4,5,6)

M.P.: 243-5.5°: (1)  
243.5-4°: (5)

$[\alpha]_D^{20} = +79.5^\circ$  (acetone) : (1)

**PHARMACOLOGY:**

**REMARKS:** 5-OH probably cis to 10-CH<sub>3</sub>, (1,3) but listed here and not among etiocholanes since cpd. is described as "androstan" derivative.

**DERIVATIVES:**

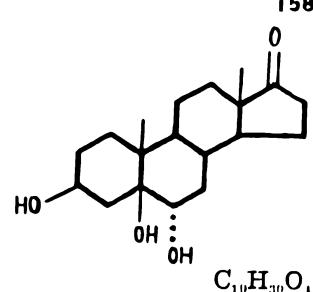
3,6-diac. { 248.5-9°:  
{ 253-4°;  $[\alpha]_D^{20} = +63.3^\circ$  (acetone) : (3) (6)

**REFERENCES:**

1. 78698
2. 80945
3. 81156
4. A54241
5. A58119
6. A58121

**ANDROSTANE-3(β),5(β),6(α)-TRIOL-17-ONE**  
**(androstane-17-one-3(β),5,6 (trans) triol)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2,4)

M.P.: 295-5°: (1)  
 298-300°: (5)

PHARMACOLOGY:

REMARKS: 5-OH probably cis to 10-CH<sub>3</sub>, (3), but listed here and not among etiocholanes since cpd. is described as an "androstan" derivative.

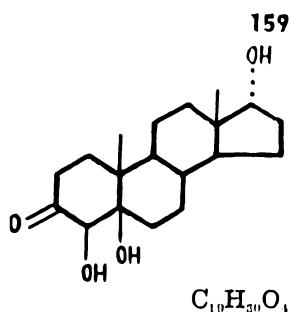
DERIVATIVES:

3,6-diac.	215-7°; $[\alpha]_D^{20} = 0^\circ$ (acetone):	(3,4)	1. 78698
3-ac.	234-5°:	(3)	2. A18098
3,5-diac.	202.5-4°; $[\alpha]_D^{20} = +22.7^\circ$ (acetone):	(4)	3. S1156
Triac.	184-5°; $[\alpha]_D^{20} = -8.2^\circ$ (acetone):	(4)	4. A36674
6-ac.	276-7°; $[\alpha]_D^{24} = +23.6^\circ$ (me. alc.):	(4)	5. A15412
3-glucoside	ca. 285° (impure):	(5)	6. 80°45
3-bz.	262-4°:	(6)	
3-ac.	231-2°; $[\alpha]_D^{10} = +33.5^\circ$ (CHCl <sub>3</sub> ):	(6)	

REFERENCES:

1. 78698
2. A18098
3. S1156
4. A36674
5. A15412
6. 80°45

## **ANDROSTANE-3-ONE-4( ),5( ),17( $\alpha$ )-TRIOL**



## ISOLATION:

STRUCTURE AND SYNTHESIS: (1)

M.P.:

**PHARMACOLOGY:** Testoid: 63: 200 $\gamma$ /day of ac. inact.-C (1).

**Folliculoid:** 62: 2 mg./day of ac. inact.-M (1).

**REMARKS:**

## DERIVATIVES:

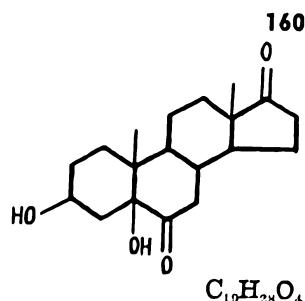
17-ac.  $185.8^\circ$  (u);  $[\alpha]_{D}^{21} = +35.7^\circ$  ( $\text{CHCl}_3$ ): (1)  
 4,17-diac.  $220.2^\circ$  (u): (1)

## REFERENCES:

1. 72717

**ANDROSTANE-3( $\beta$ ),5( $\alpha$ )-DIOL-6,17-DIONE**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,2)

M.P.: 296-8°: (1)  
282-4°: (2)

PHARMACOLOGY:

REMARKS: 5-OH probably  $\beta$  (2), but listed here since cpd. is described as "androstane" derivative.

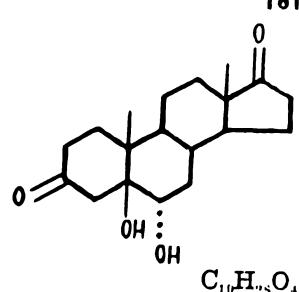
DERIVATIVES:

Dioxime	245-7°:	(1) 1. 80945
3-ac.	{ 210-1°: { 197.5-9°; $[\alpha]_D^{28} = +17^\circ$ (acetone): (2)	(1) 2. S1156 (2)
3-bz.	256-7°:	(1)
3-tosylate	133°:	(1)

REFERENCES:

**ANDROSTANE-3,17-DIONE-5(3),6( $\alpha$ )-DIOL**  
**(androstane-3,17-dione-5,6 trans -diol)**

ISOLATION:



STRUCTURE AND SYNTHESIS:

M.P.:

PHARMACOLOGY:

REMARKS: 5-OH probably  $\beta$  (2) in this series, but listed here since cpd. was described as an "androstane" derivative.

DERIVATIVES:

6-ac. 219-20.5°;  $[\alpha]^{20}_D = + 44.6^\circ$  (acetone): (1)

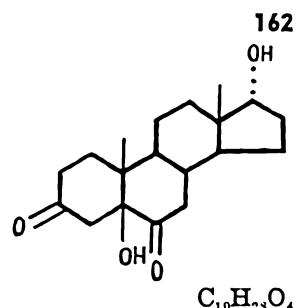
REFERENCES:

1. A36674
2. S1156

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**ANDROSTANE-3,6-DIONE-5( ),17( $\alpha$ )-DIOL  
(androstenedione-3,6-diol-5,17)**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1)

M.P.:

PHARMACOLOGY:

REMARKS:

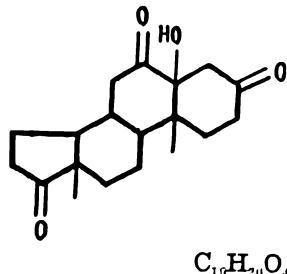
DERIVATIVES:

$\text{L} \cdot \text{ac} = 239.41$ ;  $[\alpha]_D^25 = -29.9^\circ \pm 1.2^\circ$  (acetone); (1) 1-60173

REFERENCES:

**ANDROSTANE-3,6,17-TRIONE-5( $\beta$ )-OL**

ISOLATION:



STRUCTURE AND SYNTHESIS: (1,3,4,5)

M.P.: 248-9° (u): (1,3)  
249.5-50.5°: (4)

$[\alpha]_D^{22} = + 54.6^\circ$  (acetone): (2,3)  
 $[\alpha]_D^{22} = + 62.2^\circ$  (acetone): (1,4)

PHARMACOLOGY:

REMARKS: 5-OH probably  $\beta$  but listed here since cpd. was described as an "androstane" derivative.

## DERIVATIVES:

## REFERENCES:

1. 78698
2. A34408
3. 60173
4. A36674
5. A58118