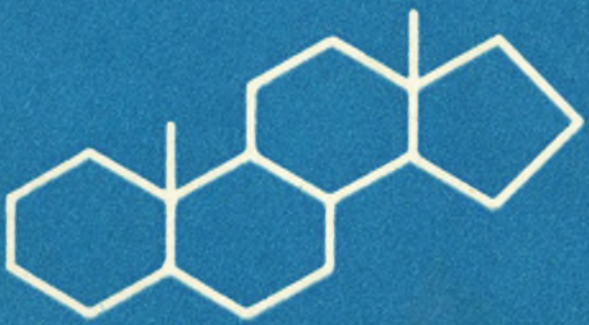
VI CONFERENCE ON ISOPRENOIDS abstracts



Toruń 14 - 18 September 1975

CUCURBITACINS OF CITRULLUS LANATUS VAR. CITROIDES AND BRYONIA DIOICA

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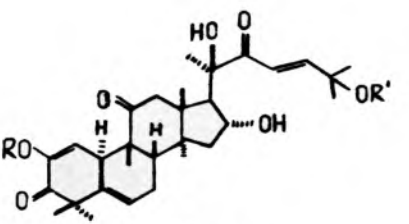
Institute for Plant Biochemistry, Research Centre for Molecular Biology and Medicine, Academy of Sciences of the GDR, Halle (Saale)

From fruit of Citrullus lanatus var. citroides in addition to cucurbitacin E (1) two glucosides were isolated which possess the structures 2-O-ß-D-glucopyranosyl-cucurbitacin I (2) and 2-O-ß-D-glucopyranosyl-cucurbitacin E (3). 2 is the third cucurbitacin glycoside which was obtained in a crystalline form.

From roots of Bryonia dioica bryoamaride (4) was received which was shown to be identical with the synthesized 23,24-dihydro-derivative of 2.



1 : R = H, R' = Ac

2 : R = ß-D-glucopyranosyl, R' = H

3 : R = ß-D-glucopyranosyl, R' = Ac

4 : R = ß-D-glucopyranosyl, R' = H, 23,24-dihydro

STEROIDAL GLYCOSIDES IN SEEDS TOMATO.

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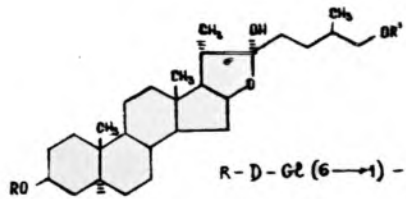
Institute of Organic Chemistry, Kirgisian Academy of Sciences, Frunze.

The glycosides tomatoside A, tomatoside B, tomatoside C have been isolated from the seeds tomato. For the genin moiety all these three glycosides have neotigogenin.

From chemical and spectral data in tomatosides the carbohydrate moiety is linked to the genin at position C_3 with an ether bond and have in addition a O-glycoside bond also at position C_{26}.



R - D - Gℓ (6⟶1) - D - Caℓ (4⟶1) - D - Gℓ

R' - D - Gℓ

NEW STEROIDAL SAPOGENINS FROM THE PLANTS OF THE GENUS ALLIUM

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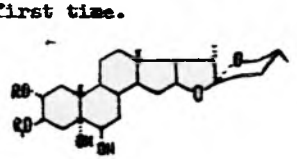
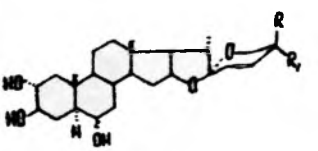
Six new spirostans, namely karatavigenin A (III), karatavigenin B (IV), 3-O-β-D-glucopyranoside of karatavigenin B (V), neoagigenin (VI), agigenin (VII) and gantogenin (VIII) have been isolated from A.karataviense and A.giganteum (Alliaceae), where they exist together with related luvigenin, diosgenin, yuccagenin, β-chlorogenin, alliogenin (I)[I] and alliogenin 3-O-β-D-glucopyranoside (II)[I].

Two naturally occurring benzoyl esters of steroidal sapogenins (III,IV) have been described for the first time.





I. R=R$_1$=H
II. R=H; R$_1$=β-D-Glc
III. R=H; R$_1$=C_6H_5CO
IV. R=C_6H_5CO; R$_1$=H
V. R=C_6H_5CO; R$_1$=β-D-Glc

VI. 6β-OH; R=CH_3; R$_1$=H
VII. 6β-OH; R=H; R$_1$=CH_3
VIII. 6α-OH; R=H; R$_1$=CH_3

I. Gorovits M.B., Khristulas F.S., Abubakirov N.K. Chem.Natur.Produc. (USSR),434, 1971.

FOUR NEW DITERPENES FROM SIDERITIS GOMERAE

A. G. González, B. M. Fraga, M. G. Hernández, F. Larruga and J. G. Luis

Department of Organic & Biochemistry, University of La Laguna; Instituto de Investigaciones Químicas, CSIC, Tenerife, Spain

From the aerial part of Sideritis gomerae Bolle four new diterpenes have been isolated and their structures determined as ent-8,13-epoxylabdan-15-al (gomeraldehyde), ent-8,13β-epoxylabdan-15-al (13-epigomeraldehyde), ent-8,13-epoxylabdan-15-oic acid (gomeric acid) and ent-8,13β-epoxylabdan-15-oic acid (epigomeric acid).

Oxidation of gomeraldehyde and its 13-epi compound by air gave gomeric acid and 13-epigomeric acid, respectively. On the other hand, $LiAlH_4$ reduction of the acids yielded the corresponding alcohols which were oxidized with CrO_3 in acetone to gomeraldehyde and 13-epigomeraldehyde, respectively.

Gomeric acid proved to be an enantiomer of the compound prepared by Fetizon & col. by oxidation of sclareol. Reduction of 13-epigomeric acid with $LiAlH_4$ gave an alcohol which was identical with that obtained by hydroboration of (-)-13-epimanoyl oxide.

THE STRUCTURE OF VERTICILLOL, A MACROCYCLIC DITERPENE FROM THE WOOD OF *SCIADOPITYS VERTICILLATA* Sieb. et Zucc. (TAXODIACEAE)

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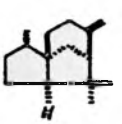
[a]Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm 70

and

[b]Forest Products Research Laboratory, P.O.B. 5604, S-114 86 Stockholm

The wood oil of *Sciadopitys verticillata* Sieb. et Zucc. (Taxodiaceae) is a rich source of terpenes[1-3]. Recently we reported the isolation and structure elucidation of a new sesquiterpene (+)-2,5-diepi-β-cedrene (1) with *trans*-fused five-membered rings[4]. The isolation of a novel macrocyclic diterpene alcohol, verticillol, has also been reported[5]. Tentative structures of this alcohol have been proposed[5,6]. The structure (2) of verticillol has now been settled. The structure elucidation, which is based on an X-ray phase structure determination of verticillol diepoxide[7] as well as chemical and spectroscopic data, will be presented.



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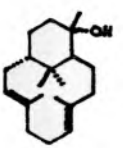

2

1. Kawamura, J., *Bull. For. Exp. Sta. Maguro*, 31, 93 (1931).
2. Sumimoto, M., *Tetrahedron*, 19, 643 (1963).
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4. Norin, T., Sundin, S., Karlsson, B., Kierkegaard, P., Pilotti, A.-M. and Wiehager, A.-C., *Tetrahedron Lett.*, 17 (1973).
5. Erdtman, H., Norin, T., Sumimoto, M. and Morrison, A., *Tetrahedron Lett.*, 3879 (1964).
6. Kaneko, C., Hayashi, S. and Ishikawa, M., *Chem. Pharm. Bull.*, 12, 1510 (1964).
7. Pilotti, A.-M. and Wiehager, A.-C., *unpublished results.*

FURANOTERPENOIDS FROM TEUCRIUM POLIUM L.

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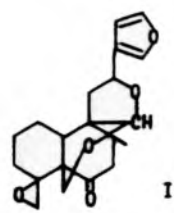
Kishinev, USSR

Some years ago C.Brieskorn and T.Pfeuffer /1/ isolated from Teucrium polium L. the diterpenoid picropoline and established its structure.

In connection with study of isoprenoids from Labiatae family we have investigated T.polium L. growing in Moldavian and North Caucasian regions and didn't find picropoline. From acetonic extract of these plants we have separated three new diterpenoids wich were named as teucrine P_1, P_2 and P_3. The structure I for major component, teucrine P_1, was established on the basis of chemical and spectroscopic data. Teucrines P_2 and P_3 were correlated with the furoacetal I. Biosynthetic pathways and ecological differences of teucrines will be discussed.



I

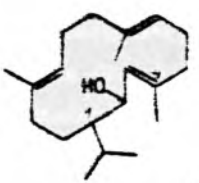
1. C.H.Briescorn, T.Pfeuffer. Chem.Ber..100. 1998 (1967).

STEREOCHEMISTRY AND SOME TRANSFORMATIONS OF CEMBRANE DITERPENOIDS

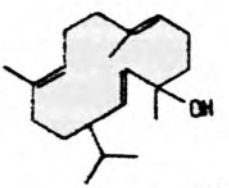
V.A.Raldugin, V.A.Pentegova

Institute of Organic Chemistry, Siberian Division of the Academy of Sciences, Novosibirsk, USSR

Rucker[1] and Patil[2] have isolated a new cembrane alkohol (1) from Commiphora mukul. We have succeeded in the partial synthesis of this compound from isocembrol (2). Action of Jones' reagent on (2) led to complex mixture of products containing the keton (3). The $C_{(3)}$-double bond in (3) possesses the trans-configuration as it determined by NOE. Reduction of (3) by $LiAlH_4$ led mainly to (1) and 2-epi-(1), each characterized by physical and spectral data.



(1)



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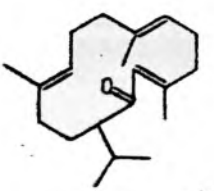

(3)

References

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NORDITERPENOIDS FROM PINACEAE AND POSSIBLE ROUTES OF THEIR FORMATION

E.N.Shmidt, N.V.Avdjukova, V.A.Pentegova

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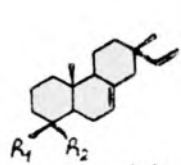
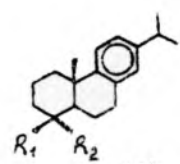
We have isolated some 18- and 19-norditerpenoids of isopimarane (1) and dehydroabietane (2) types from oleoresins of various Siberian conifers.

Oxidative degradation of the natural compounds induced by atmospheric oxygen may be by one of pathways of norditerpenoids formation. Autooxidation of (1) and (2) (a,b) leads to formation of considerable amount of norditerpenoids, which represented by $C_{(8)}$-epimeric hydroperoxides (1,2 c,d), alkonols (1,2 e,f) and hydrocarbons (1,2 k,l) with predomination of products containing equatorial oxygenated functional group[1,2].



(1)



(2)

	a	b	c	d	e	f	k	l
R_1	Me	Me	Me	OOH	Me	OH	Me	H
R_2	CHO	COOH	OOH	Me	OH	Me	H	Me

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2. idem, ibid., (2) 117 (1973).

STUDIES ON THE NEUTRAL PLANT EXTRACT CONSTITUENTS OF HOMOGYNE ALPINA (CASS.)

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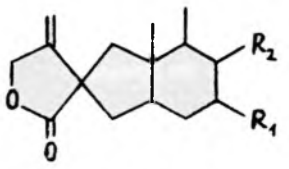
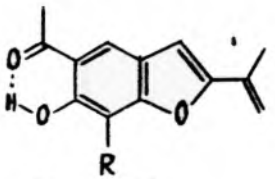
Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences, Prague 6

From the light petroleum extract of the plant Homogyne alpina three sesquiterpenic constituents with five-membered lactone ring were isolated. The first of them was identical with bakkenolid-A (I). The other two constituents, of the same bakkenolide type, have not been described so far. Both of them have an ester grouping in the molecule. Angelyl-group in the first (II) and tiglyl-group in the second (III) case. All these compounds are biogeneticaly related with the compounds of furoeremophylane type, from which their chemotaxonomic value within the Senecioneae tribe results. From the extract two further constituents were isolated and identified as euparin (IV) and methoxyeuparin (V).





I. R_1: -H ; R_2: -H

II. R_1: $-OCOC(CH_3)=CH(CH_3)$; R_2: -H

III. R_1: -H ; R_2: $-OCOC(CH_3)=CH(CH_3)$

IV. R: -H

V. R: $-OCH_3$

STRUCTURE OF HIRSUTOLIDE AND VENIDIOLIDE

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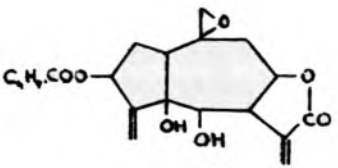
[a] Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6, Czechoslovakia

[b] Institute of Biology and Pharmacy, Academy of Medicine, Poznań, Poland

From the species Venidium hirsutum BEROL. /family Compositae/ two as yet undescribed sesquiterpenic lactones, called venidiolide and hirsutolide, were isolated[1]. For venidiolide /$C_{20}H_{26}O_7$, m.p. 58° C, $[\alpha]_D^{20}$ +38,9°/ and for hirsutolide /$C_{16}H_{20}O_5$, m.p. 110-112° C, $[\alpha]_D^{20}$ -149,6°/ the structures I and II, respectively, based mainly on the detailed analysis of their PMR spectra, were proposed.



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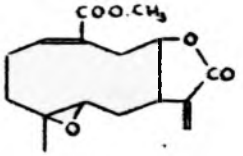

II

[1] Grabarczyk H.: Pol. J. Pharmacol. Pharm. in press.

A New Sesquiterpenic Hydroxyester from Libanotis intermedia

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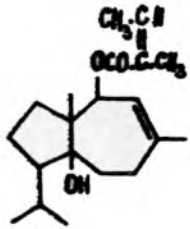
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, 166 10 Prague
[a]Biological-Pharmaceutical Institute,
Medical Academy, 60-619 Poznań

From the light petroleum extract of the fruits of Libanotis intermedia Rupr. /Umbelliferae/ a new sesquiterpenic substance of the composition $C_{20}H_{32}O_3$ m.p.46-7° and $[\alpha]_D^{20}$-198°, was isolated by silica gel chromatography. On the basis of physicochemical measurements /IR, UV, MS, NMR/ carried out with the substance and its degradation products the conclusion is that it is a hydroxyester with the probable structure:



FURTHER SESQUITERPENOIC METABOLITES OF LACTARIUS RUFUS AND LACTARIUS NECATOR

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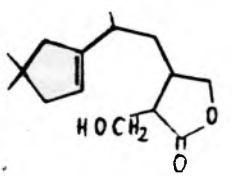
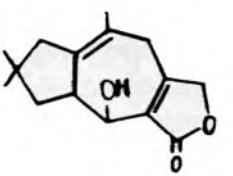
Institute of Organic Chemistry of Polish Academy of Sciences, Warsaw Poland.

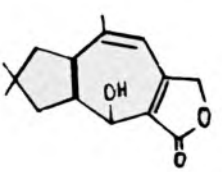
By means of HPLC a series of new sesquiterpenes was isolated. The structures of these compounds were elucidated with the aid of full chemical and spectral analyses. The structural formulae of some of them are shown below:



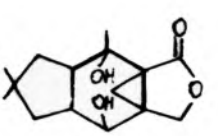
Lactaronecatorin



Deconjugated anhydro-lactarorufin A



Anhydrolactarorufin A



Lactarorufin C

ANHYDROLACTARORUFIN C

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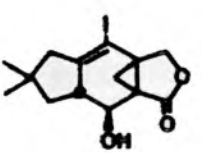
Institute of Organic Chemistry of The Polish Academy of Sciences,
ul. Kasprzaka 44, 00-961 Warszawa, Poland

and

S.Thorén

Organic Chemistry 2, The Lund Institute of Technology,
Chemical Center, Box 740, S-220 07 Lund 7, Sweden

Lactarorufin C, a sesquiterpene lactone of unknown structure from Lactarius rufus, on careful degradation gives an anhydro derivative. Combined spectral analysis and biogenetic considerations[1,2] suggest structures 1 or 2 for this compound. Computer analysis of the LIS ^{1}H-NMR spectrum indicates that 2 is the probable structure.



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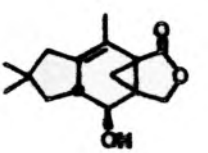


2.

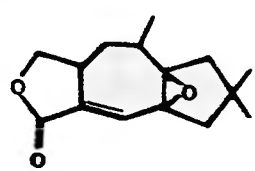
1. W.M. Daniewski and M.Kocór, Bull. Acad. Pol. Sci. Ser. Chim. 19, 555 (1971)

2. W.M.Daniewski, M.Kocór and B.Zółtowska, Ibid. 21, 785 (1973)

SESQUITERPENE STRUCTURES OF CONSTITUENTS OF LACTARIUS SCROBICULATUS SCOP.

G. Vidari, M. De Bernardi, G. Fronza[+] and P. Vita Finzi
Istituto di Chimica Organica
Università degli Studi di Pavia (Italy)
[+]Centro del CNR per le Sostanze Naturali-Politecnico-Milano

From Lactarius Scrobiculatus Scop., a toxic mushroom which grows on the mountains in the Northern regions of Italy, sesquiterpene metabolites have been isolated and studied. Some of them have new structures, with skeleton like in I[1] or II, that have been determinated mainly by spectroscopic methods (IR, MS, ^{1}H-NMR, ^{13}C-NMR). Relations with sesquiterpene compounds isolated from other Lactarius species[2,3] will be discussed.



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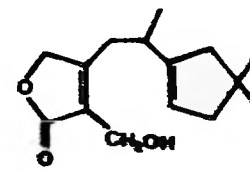

II

1. G.Vidari, L. Garlaschelli, M. De Bernardi, G. Fronza and P. Vita Finzi, Tetrahedron Letters, in press
2. W.M. Daniewski, M. Kocór and B. Zéltowska, Bull.Acad. Pol.Sci.,21, 785 (1973)
3. G. Magnusson, S. Thorén, J. Bahmen and K. Leander, Acta Chem.Scand., B28, 841 (1974)

STUDIES ON THE CHEMISTRY OF CARENES AND RELATED MONOTERPENES. THE CONFIGURATION AND CONFORMATION OF CHAMIC ACID.

Torbjörn Norin, Sture Strömberg and Michael Weber

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Chamic acid (1) and chaminic acid (2) are heartwood constituents of *Chamaecyparis nootkatentis* (Lamb.) Spach. (Yellow Cedar)[1,2]. Both acids are highly active against wood-destroying fungi[3]. Chamic acid has also a strong insecticidal activity[4]. The structures and absolute configurations of the acids have previously been elucidated[2,5] but the configuration at C(3) of chamic acid was not determined. In the present communication evidence for the C(3)-configuration of chamic acid as well as the conformation of this acid and some related car-2- and -4-enes will be discussed together with the application of a helicity rule for cisoid alkenylcyclopropane chromophores such as those of the car-2- and -4-enes.

1

2

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2. Erdtman, H., Harvey, W.E. and Topliss, J.G., *Acta Chem. Scand.*, 10, 1381 (1956)

3. Rennerfelt, E. and Nucht, G., *Svensk Botanisk Tidskrift*, 49, 419 (1955)

4. *Unpublished results*

5. Norin, T., *Arkiv Kemi*, 22, 123 (1964)

X-RAY CRYSTAL STRUCTURE ANALYSIS OF LACTARORUFINS

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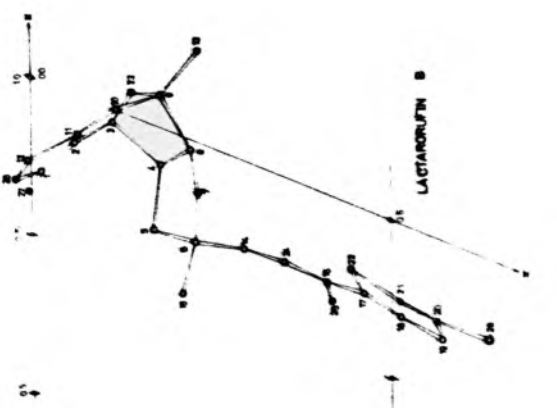
The crystal and molecular structure of lactarorufins B and C have been studied by heavy atom method, using p-bromobenzoyl derivatives.

P-bromobenzoate of lactarorufin B-3,9-ether crystalizes in the monoclinic system, space group: C2. Its unit-cell contains four molecules. The spatial structure was determined by structural x-ray analysis. The bond lengths, the intrabond angles and the dihedral angles were calculated. The two adjacent five-membered rings show envelope conformation; the six-membered ring is of half-chair conformation.

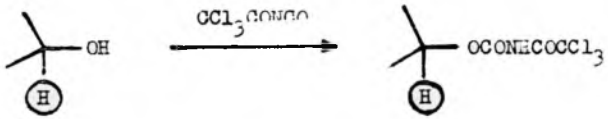


P-bromobenzoate of lactarorufin C crystalises in the trigonal system, space group : $P3_1$ or $P3_2$ with three molecules per unit-cell. The structure has been investigated by Patterson and Fourier methods.

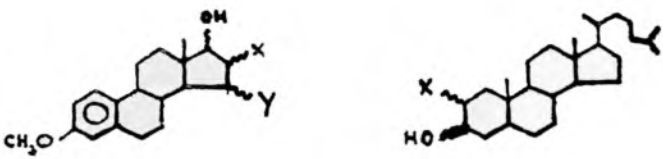
^{1}H-NMR INVESTIGATION OF SECONDARY STEROIDAL ALCOHOLS BY IN-SITU REACTION WITH TRICHLORACETYLISOCYANATE (TAI)

B. Schönecker, D. Tresselt, G. Schubert and K. Ponsold
Academy of Sciences of the GDR, Research Center for Molecularbiology and Medicine, Central Institute for Microbiology and Experimental Therapy, Jena, GDR

Steroidal alcohols react with TAI in $CDCl_3$ to trichloroacetylcarbamates. By this reaction the carbinol proton signal of a secondary steroidal alcohol suffers a downfield shift from 0,9 to 1,5 ppm.



The magnitude of this downfield shift depends on the position and the configuration of the hydroxyl group, and can also be affected by a neighbouring substituent.
The influence of several vicinal substituents is discussed. The application of this method for configurational assignments is demonstrated by 16,17-disubstituted, 15,16,17-trisubstituted and 2,3-disubstituted steroids.



X = Br, N_3
Y = H, OH

STEREOCHEMICAL INVESTIGATIONS OF STEROIDS BY CARBON-13 NMR SPECTROSCOPY

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The high sensitivity of ^{13}C chemical shifts to structural effects makes the ^{13}C-NMR spectroscopy to a powerful tool for structure elucidation of steroids. Besides the investigations on electronic substituent effects and structural changes of the steroid skeleton particulary useful results can be achieved for the stereochemistry of both the ring junction in the steroid framework and the configuration of substituents. Some basic principles of such stereochemical assignments by ^{13}C-NMR are discussed and illustrated by selected examples of substituted Δ-1,3,5(10)-östratriene, Δ-5,6-androstene and cholestane derivatives.

CIRCULAR DICHROISM OF STEROIDAL SPIRO-2-THIAZOLIDIN-4-ONES

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Poznań

The steroid molecule served in many cases as model skeleton in circular dichroism studies. The UV transitions of chromophores placed in known positions of this basic skeleton exhibit Cotton effects of different magnitude and sign, depending on the kind of chiral perturbation. Our present studies refer to thiazolidinones which are the sulphur analogs of β- lactams. Optical activity of the electronic transitions involved is reached by building the 3 atom of the thiazolidin-4-one ring into the structure of the steroid. Three transitions could be detected in the 190 - 260 nm spectral region. The nature of these transitions is still disputable. They may be the n - π^* and π - π^* transitions of the amide grouping ,mixed with sulphur transitions . The transitions are easily detectable by the CD method, whilst the UV spectra carry only very little information in this respect. The thiazolidinone chromophore was placed in positions 3, 4, and 6 of cholestane and in position 3 of coprostane. Formation of spiro-thiazolidinones should lead, and in fact leads, to pairs of compounds where the nitrogen atom occupies the axial and equatorial position. CD spectra of about 15 samples are recorded. The synthesis and stereochemistry of these compounds is described in our preceeding papers. The structural proof rests on NMR and IR studies.

CORRELATION BETWEEN PHOTOREACTIVITY AND CRYSTAL STRUCTURE OF GIBBERELLIN ENONES

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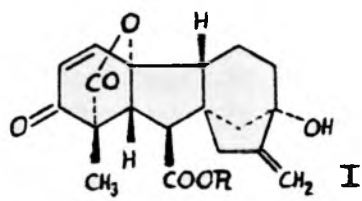
and

Central Institute for Physical Chemistry Berlin - Adlershof, Academy of Sciences of the GDR.

The photochemical behaviour of crystalline gibberellin enones of type I depends largely from the kind of the substituent R. Whereas 3-dehydro-gibberellin A_3 (R=H) upon $n \rightarrow \pi^*$ excitation of the chromophor is photodecarboxylated to the corresponding ring A phenolic acid[1] UV-irradiation of the methyl ester ($R=CH_3$) gives intermolecular [2+2] photocycloaddition leading to a main cyclobutane dimer.[2] For explanation of these striking different photochemical pathways X-ray analysis of both starting α,β-unsaturated ketones have been undertaken. In the result of these studies a clear correlation between photoreactivity and geometrical arrangement of the molecules in the crystal lattice has been found allowing the prediction of constitution and stereochemistry of the formed photodimer from all other structural possibilities.



I

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STEREOCHEMICAL STUDIES OF SOME 4,4-DIMETHYL-A-HOMOCHOLESTANE DERIVATIVES

H. Velgová, V. Černý

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Czechoslovak Academy of Sciences, Prague 6

In connection with our stereochemical studies[1] on A-homosteroids a series of 4,4-dimethyl-A-homo-5-cholestene derivatives bearing oxygen substituent at 3-position were prepared. Configuration of 3-hydroxy derivatives was established by application of the Horeau's method[2] and the benzoate rule. Stereochemistry of 2-bromo-3-hydroxy and 2-bromo-3-keto derivatives was studied by analysis of IR, NMR and CD data.

1. Velgová H., Černý V.: Coll. Czech. Chem. Commun. 39, 2476 (1974) and the previous works.

2. Horeau A.: Tetrahedron 20, 2431 (1964).

STEREOSELECTIVITY IN THE CATALYTIC HYDROGENATION AND WEITZ-SCHEFFER EPOXIDATION OF 3-OXO-Δ^4-STEROIDS

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Polish Academy of Science, Warsaw

We suggest as the working hypothesis that the stereoselectivity in both reactions is controlled by conformational equilibrium of 3-oxo-Δ^4-steroid i. e. the "half-chair"/monoplanar/ conformer of A ring gives predominantly or exclusively β-isomers and the other ones /1,2-diplanar and 1,4-diplanar/ give α-isomers. Thus the effects of the remote substituents and of the solvent on the stereoselectivity of these reactions are easily interpreted due to their influence on the conformational equilibrium.

This conclusion is based on our results concerning the reactivity and conformational properties of Δ^7-steroids and supported by a number of other authors' data.

The presented hypothesis is drawn from empirical regularities but it can be rationalised in terms of well known reaction kinetics and mechanisms. In both reactions the cyclic transition state requires the coplanarity of new formed bonds during the whole reaction course. Model studies prove that the two sides of each conformer are not equivalent in this respect.

STEREOCHEMISTRY OF MOLECULAR REARRANGEMENTS OF DISUBSTITUTED CARANES

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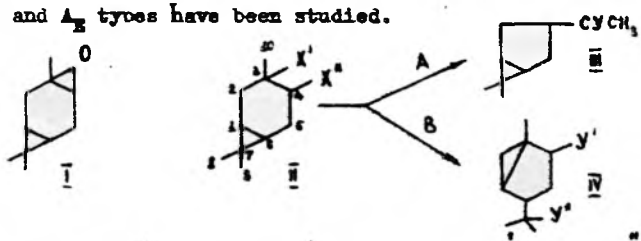
Kazan, USSR

Transformations of 3,4-disubstituted caranes in reactions of S_N, E_2 and A_E types have been studied.



Depending on the steric orientation of C_3-X' and C_4-X'' bondings /1,2/ and epoxide ring in I /3/ the bicycloheptane carbon systems of carane derivatives undergo rearrangements to bicyclononane systems of two types: III and IV. The first one (A) is caused by the sixmembered ring contraction of the carane systems with equatorial bonding C_4-X''. The second one (B) is observed in reactions of compounds with C_3-X' bondings in cis-position relatively to the cyclopropane ring.

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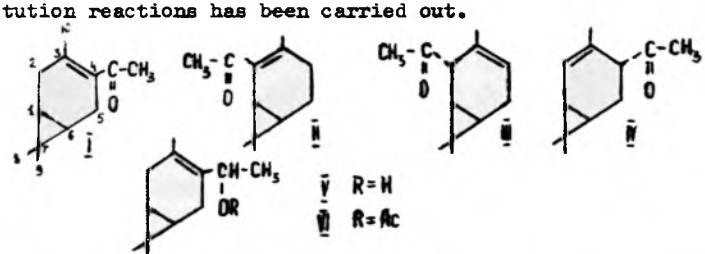
3. B.A.Arbuzov, Z.G.Isaeva, V.A. Shaihutdinov, Proc. Acad.Sci USSR. Chem. Sect., 210, 837 (1973).

SYNTHESIS AND STEREOCHEMISTRY OF THE EPOXIDE RING OPENING REACTION OF SUBSTITUTED EPOXYCARANES

B.A.Arbuzov, Z.G.Isaeva, N.D.Ibragimova
A.M.Butlerov Chemical Research Institute,
A.E.Arbusov Institute of Organic and Physical Chemistry
Kazan, USSR

The comparative study of epoxidation of substituted carenes I-VI and behavior of related epoxides in the nucleophilic substitution reactions has been carried out.



Lack of reactivity of I in the alkaline hydrogen peroxide epoxidation reactions is probably due to the reducing of conjugation in the C=C–C=O system /1,2/; II in such conditions does not react at all.

Epoxidation of ketones I-IV with peracids proceeds stereospecifically to give the isomers with trans-position of epoxide and cyclopropane rings to each other; the stereospecificity is the result of the hindered attack of the oxidant on the β-side of the double bond /3,4/.

The epoxidation of V and VI results in the formation of both possible stereoisomeric epoxides, which indicates to the certain steric effect of the substituents at 4–C–atom.

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4. B.A.Arbuzov, A.R.Vil'chinskaya, Bull. Acad.Sci USSR, Div.Chem.Sci. 1967. 954.

CHEMICAL TRANSFORMATIONS OF (-)-CIS- AND (+)-TRANS-CARANES

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Institute of Physical and Organic Chemistry of the BSSR Academy of Sciencies, Minsk, USSR

Under the influence of electrophyllic agents $Hg(OAc)_2$ and halogen hydrides the cis- and trans-carane cyclopropane ring will open stereospecifically (to 100 per cent) and regioselectively (90 to 95 per cent for $Hg(OAc)_2$ and 65 to 70 per cent for halogen hydrides) with a subsequent formation of m- and p-menthanes. In this case less stable isomers with e,a-orientation of the substituents will chiefly be formed.

The heating of caranes to temperatures of 400 to 550°C brings about their cis- and trans-isomerization as well as the opening of the cyclopropane ring. (-)-trans-Carane, p-menthene-3, cis- and trans-p-menthenes-8, cis- and trans-m-menthenes-8, p-menthene-4(8) and (+)-m-menthene-3(8), are formed from (-)-cis-carane. (+)-cis-Carane, (-)-m-menthene-3(8) and these same menthenes are formed from (+)-trans-carane.

Autooxidation of the caranes proceeds mainly by the C_3-H tertiary bond (75 to 80 per cent) and the C_4-H and C_5-H secondary bonds (20 to 25 per cent) both from α- and β-sides of the molecules with the formation of corresponding hydroperoxides.

OXIDATION OF SOME OLEFINIC MONOTERPENES WITH MANGANESE ACETATE HYDRATE AS A METHOD OF LACTONE SYNTHESIS

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Department of Organic Chemistry, Institute of Chemistry and Technology of Medicinal Products, School of Medicine, Wrocław

The growing interest in terpene lactones, which show a wide spectrum of biological activities[1-3], prompted us to synthesise lactone derivatives from olefinic monoterpenes i.e.: p-menthene, carene-3, α-pinene and bornene.

As the oxidant manganese ^{III} acetate has been used, either in the prepared hydrate form or generated "in situ" in the reaction medium. It has been found that the best results can be obtained at 110 – 130° oxidation temperature.

In all cases ca 50 % of the starting material has been recovered from the reaction mixture. The lactones were isolated by fractional disillation followed by column chromatography on silica gel.

The lactones were converted by LAH reduction into the corresponding diols.

The structure of all new compounds was established by ir and pmr spectra and microanalyses.

1) A.E.Green, J.C.Muller and G.Ourisson, Tetr.Lett.3375 (1972)
2) S.M.Kupchan, M.Maruyama, R.J.Hemingway and J.C.Hemingway, J.Org.Chem., 38, 2189 (1973)
3) P.A.Grieco, Synthesis, 67, (1975)

REACTIONS OF TOSYLATES OF MONO-TERPENOID ALCOHOLS WITH POTASSIUM t-BUTOXIDE IN APROTIC SOLVENTS

Z. Rykowski, H. Orszańska, Z. Chabudziński

Department of Organic Chemistry, Institute of Chemistry and Technology of Medicinal Products, School of Medicine, Wrocław

The trans-elimination of p-toluenesulphonic acid moiety from the tosylates of mono-terpenoid alcohols, effected with potassium t-butoxide in pyridine, DMF, or DMSO, produces unsaturated hydrocarbons in good yields. Small amounts of the corresponding alcohols are also formed; no other products were found in the reaction mixture.

This reaction is very convenient for preparation of hydrocarbons hardly accessible by other methods of preparation. Thus, cis-pinene [2] and menogene [3] can be prepared from isopinocampheol tosylate and dihydrocarveol tosylate, respectively. Other preparations are: (-)trans-p-menthene from carvomenthol tosylate, (+)trans-p-menthene from menthol tosylate, and (+)bornene-2 from borneol tosylate.

1. H. Schmidt, Ber., 80, 520 /1947/.
2. Y. Bessiére-Chrétien, J.P. Bras, Compt. rend., 268, 2221 /1969/.
3. R. Horiuchi, H. Otsuki, O. Okuda, Bull.Chem.Soc. Japan, 14, 501 /1939/.

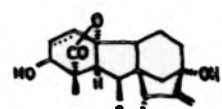
CHEMICAL TRANSFORMATIONS OF GIBBERELLINS AND THE SEARCH FOR STRUCTURE-ACTIVITY RELATIONSHIP

E.P.Serebryakov, N.S.Kobrina, L.M.Suslova and V.F.Kucherov

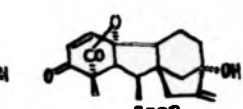
(Zelinsky Institute for Organic Chemistry, theUSSR Academy of Sciences, Moscow-II7334)

Gibberellins A_1 and A_3 when treated with neutral manganese dioxide undergo oxidative decarboxylation to (Ia,b) or oxidative lactonization to (IIa,b). 3-Dehydro-GA_3 (IIIa) or its methyl ester (IIIb) easily react with nucleophiles to give the adducts of type (IV), where R=H or Me and X is a nucleophile residue. The use of p-methoxyphenacyl esters of GA_3 and its derivatives as a convenient photosensitive protection of the carboxyl group allows to obtain the products of O-alkylation (Va,b,c) and other compounds with free COOH group. The results of bioassays (on dwarf pea, lettuce and cucumber) of compounds thus obtained are compatible with the assumption that gibberellins can bind to some particular sites of the corresponding receptors in the plant.

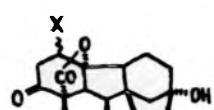
Ia (from GA_1)
Ib, Δ^4 (from GA_3)



IIa (from GA_1)
IIb (from GA_3), Δ^4



IIIa R=H
IIIb R=Me



IV

Va R=Me, R'=H
Vb R=H, R'=Me
Vc R=R'=Me

SYNTHETIC TRANSFORMATION OF RESIN ACIDS. OXIDATION OF ABIETIC AND 7-KETODEHYDRO-ABIETIC DERIVATIVES

M.I.Goryaev, F.S.Sharipova, L.K.Tikhonova

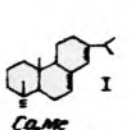
(Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR, Alma-Ata, USSR).

To obtain reactivity groups of a molecule of abietic and dehydroabietic acids certain reactions of their oxidation have been studied.

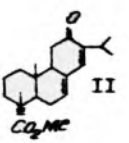
Oxidation of methyl abietate (I) with chromic acid in an acetic medium at 80°C produces the mixture of 7-ketomethyldehydroabietate (Va), 12-ketomethylabietate (II), 6,12-diketomethylabietate (III) and the product of a further reaction (II), compound IV. Oxidation of the (I) with chromic acid in an acetic medium at 0°C resulted in the mixture of II, III and V.

Oxidation with potassium permanganate in pyridine at 0°C produces the mixture of (I) and (II).

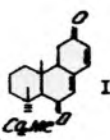
Oxidation of 12-R-7-ketomethyldehydroabietate (V a,b,c,d) with chromic acid in an acetic medium results in Δ-diketones (VI). Oxidation of the (V a-e) with oxygen in the presence of tertiary potassium butylate produces ketoenollactones (VII).



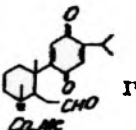
I



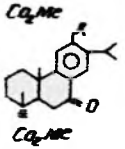
II



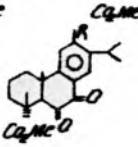
III



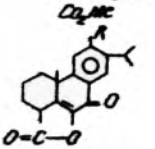
IV



V a R=H
b R=Br
c R=OCOCH$_3$
d R=NH$_2$
e R=OH



VI



VII a R=H
b R=Br
c R=OCOCH$_3$
d R=NH$_2$
e R=OH

SYNTHESIS AND REACTIONS OF 5,7-CYCLO-B-HOMOCHOLESTANES

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Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences, Prague 6

The synthesis of 5,7-cyclo-B-homocholestanes substituted in position 4 was carried out and their chemical behaviour discussed with respect to the participation of the cyclopropane ring.

AUTO-OXIDATION OF 3α,5-CYCLO-5α-CHOLESTAN-6-ONE AND 3α,5-CYCLO-5α-CHOLESTAN-7-ONE

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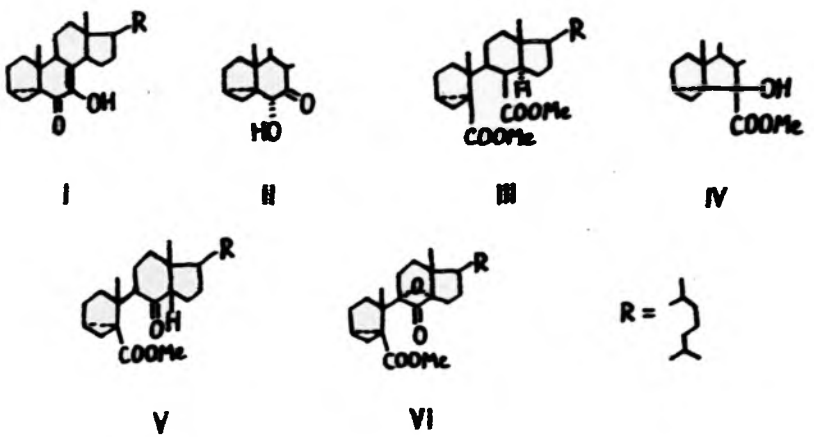
Czechoslovak Academy of Sciences, Prague 6

Auto-oxidation of both starting compounds in tert-butyl alcohol in the presence of potassium tert-butoxide gave, after separating the reaction mixture into acidic and neutral components and isolating the acids as methyl esters, the substances I - VI. Formation of an oxetanone (VI) from a ketone (V) in the course of an auto-oxidation process has been observed for the first time. The diosphenol I is a precursor of V, whereas V gives rise to VI. The compound II is a precursor of III, IV, V and VI. Compounds III and IV are not formed from I. Mechanistic implications of these facts are briefly discussed.



I II III IV

V VI

SYNTHESIS OF LACTONES BY OPPENAUER OXIDATION

L. Eignerová and A. Kasal.
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague 6.

Oppenauer oxidation of 3β-dimethylamino-5-pregnen-18,20α-diol yields 3β-dimethylamino-20α-hydroxy-5-pregnen--18-oic acid lactone which was believed[1] to be a product of intramolecular hydride shift in the 18,20-dicarbonyl intermediate. In order to verify this hypothesis we prepared and oxidized a number of analogous 18,20-dioxygenated derivatives. Product distribution indicates that two main mechanisms jointly contribute to the lactone formation: one of them may be classified as gradual oxidation of the primary hydroxy group without any change of the oxidation state at the carbon $C_{(20)}$, whereas the other one involves formation and subsecuent stereospecific intramolecular reduction of the corresponding 20-keto derivative. The possible reaction mechanism is discussed.

1. R. Bellon, Brit. 917,447 /Chem. Abstr. 59, 1716 (1963)/.

SIMMONS-SMITH METHYLENATION OF STEROIDAL DOUBLE BONDS

J. Pajkoš, J. Joska, L. Kohout
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague 6

Simmons-Smith methylenation of the 4,5 and 5,6-double bonds in the normal as well as in the B-norsteroid series has been investigated. The results will be discussed in detail.

Synthesis of Some Bis-Amino-Androstanes and Pregnanes.

Z. Tuba M. Marsei

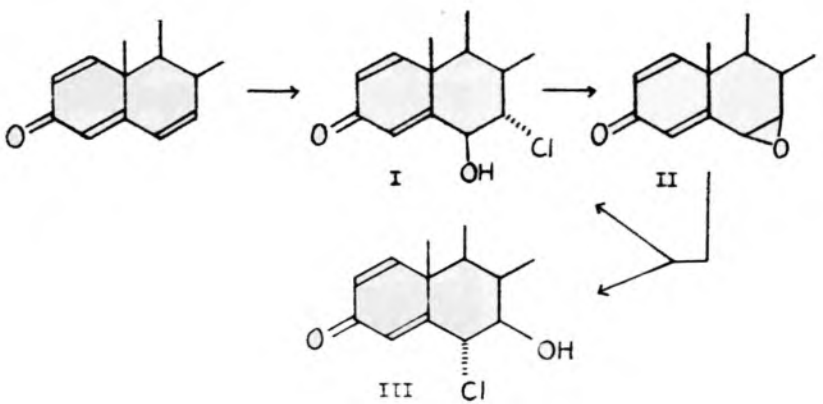
A new synthesis of the 2,16-bis-amino-androstane and pregnane derivatives is presented. The bis-quaternary salts of the synthetised amino-compounds possess a potent neuromuscular blocking activity.

In the studies some attention has been paid to the connection of the chemical structure and the biological activity too.

SYNTHESIS OF SOME STEROIDAL UNSATURATED 6β,7β-EPOXIDES AND THEIR REACTIONS

M.Kocór and A.Kurek
Institute of Organic Chemistry
Polish Academy of Sciences ,Warsaw

6β-Hydroxy-7α-chloro-3-keto-1,4-dienes (I) were produced in moderate yields by the action of chloramine T or N-hexachloromelamine on the corresponding trienones. The chlorohydrines I on treatment with alkali gave the title compounds II in good yields. The cleavage of the oxirane ring of II by hydrochloric acid or lithium chloride led to the formation of the chlorohydrines I and to the diequatorial chlorohydrines III in the ratio 4:1 . The structures of the new compounds I were proved by their conversion into acetates and the oxidation to the 3,6-diketo-1,4--dienes (IV). The mechanism of the trans-diequatorial oxirane ring cleavage will be discussed .



REACTION OF 2,3,5-TRIPHENYLTETRAZOLIUM CHLORIDE /TTC/ WITH 21-HYDROXY-20-KETOSTEROIDS

J. Jasiczak and M. A. Smoczkiewicz

Department of General and Analytical Chemistry
Institute of Goods Science, Academy of Economics
Poznań, Poland

The oxidation products of steroids with an α-ketol group /desoxycorticosterone/ and dihydroxyacetone group /prednisolone/ are studied. As oxidizer, 2,3,5-triphenyltetrazolium chloride TTC was applied.

The process is found to lead to the respective glyoxal groups which, in the reaction medium applied, undergo essentially an intramolecular Cannizarro rearrangement reaction to the respective hydroxyacid groups. From the glyoxal derivatives under continued action of TTC, the respective ketoacid /if the glyoxal derivative arose from desoxycorticosterone/ and 17-ketosteroid /if the glyoxal derivative arose from prednisolone/ was isolated. A mechanism of these red-ox processes is proposed.

The oxidative properties of TTC with regard to corticosteroids are compared to those of standard oxidizers: HIO_4, $NaBiO_3$, $Cu/OAc/_2$, CrO_3, and the experimental conditions are established for the use of TTC in the preparative oxidation of the side chain of corticosteroids.

STABILITY OF STEROIDAL 5,6-DIHALOGENO SUBSTITUENTS TOWARDS GRIGNARD'S REAGENT

H. Salwa, T. Ryznar and R. Jaworska
Institute of Pharmaceutical Industry, Warsaw

The behaviour of 5,6-dihalogeno substituents of 5,6-dihalogeno-3-acetoxy-pregnan-20-ethyleneketals towards Grignard's reagent was examined.
The results were helpful in the subsequent synthesis of 5-bromo-6β-fluoro-3β,17α-dihydroxy-5α-pregnan-20-on.

Oxidation of Steroidal 5-En-7-ones with Hydrogen Peroxide in Alkaline Medium

by Teresa Kołek and Irena Małunowicz
Institute of General Chemistry, Academy of Agriculture, Wrocław

The oxidation of steroidal 5-en-7-ones with hydrogen peroxide in alkaline medium leads always to the formation of 5,6α-epoxy-7-ketones, independently of the substitution pattern of ring A. Under slightly more drastic conditions these epoxides underwent easily oxidative ring cleavage, yielding 6-nor-5-oxo-5,7-seco-7-carboxylic acids.
4,4-Dimethyl- and 6-methyl-5en-7-ketones gave under these conditions stable 5,6α-epoxy-7-ketones resistant to further oxidation.
The structures of such obtained epoxides and acids were established by means of IR, PMR and ORD.

SYNTHESIS OF STEROID SULPHONATES BY PHASE TRANSFER CATALYSIS

S. SCHWARZ and (Mrs.) G. WEBER

VEB Jenapharm, Bereich Forschung und Entwicklung,
DDR - 69 Jena, Otto-Schott-Str. 13

Sulphonate 6 - active estrogenic principle of the depot-contraceptively acting drug DEPOSISTON ® - as well as the highly antifertile acting esters 3 - 5 can be synthesized easily and in high yields by using phase transfer catalysed (PTC) esterification of 1 or 2 with the corresponding sulphonylchlorides 7 - 9.

PTC technique allows the totally selective esterification of the phenolic hydroxyl group in the compounds 1 and 2.

Conventional means of esterification reveal unsatisfactory results, especially regarding the preparation of the amido-sulphonates 3 - 5.[1)]

The mechanism of PTC esterification is to be discussed. It was especially investigated in the case of the reaction of 1 with 9 by means of labelling with deuterium.

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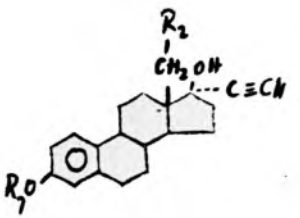
1) S. SCHWARZ, G. WEBER, M. SCHREIBER
Pharmazie 30, 7 (1975)

S. SCHWARZ, G. WEBER
Z. Chem. 10, 299 (1970)



1: R_1 = H; R_2 = H
2: R_1 = H; R_2 = CH_3
3: R_1 = SO_2-$N(C_2H_5)_2$; R_2 = H
4: R_1 = SO_2-$N(C_2H_5)_2$; R_2 = CH_3
5: R_1 = SO_2-N⬠; R_2 = H
6: R_1 = SO_2-$CH(CH_3)_2$; R_2 = H

R-SO_2Cl

7: R = $N(C_2H_5)_2$
8: R = N⬠
9: R = $CH(CH_3)_2$

NEIGHBOURING GROUP PARTICIPATION DURING THE OXIDATION OF STEROID TOLUENE-p-SULPHONATES WITH DIMETHYL SULPHOXIDE--SODIUM HYDROGEN CARBONATE.

Gy.Schneider and I.Weisz-Vincze

Institute of Organic Chemistry József Attila University, Szeged, Hungary.

The oxidation of 3β-acetoxy-16-p-tolylsulphonyloxymethyl--androst-5-en-17-acetates with dimethyl sulphoxide in the presence of sodium hydrogen carbonate gives the corresponding 16-aldehyde derivatives.

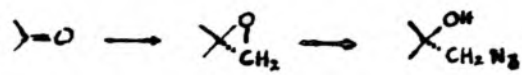
Under similar conditions, it is the cyclic carbonates exclusively that is formed from 3β-acetoxy-16-p-tolylsulphonyloxymethyl-androst-5-en-17-ols with cis hydroxyl function on the D ring. The oxidation is taken place if a hydroxyl group with trans function is present beside the p-tolylsulphonyloxymethyl group.

The formation of a cyclic carbonate is a typical neighbouring group participation. We propose the $\left[(OH\text{-}HCO_3^-)\text{-}6\right]$ symbol to characterise this process.

A NEW SYNTHESIS OF FORMYL STEROIDS

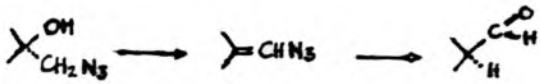
L. Hübner and K. Ponsold
Academy of Sciences of the GDR, Research Center for Molecularbiology and Medicine, Central Institute for Microbiology and Experimental Therapy, Jena, GDR

Vicinal azido alcohols I in the estratriene-, androstane-, and 19-norandrostane-series were synthesized starting from ketones according the following scheme:



I

With acid anhydrides acylated I could be obtained, while reaction with mesylchloride leads to dehydration.
The so formed stable vinylazides II were treated with triphenylphosphine giving formyl steroids III in high yields.



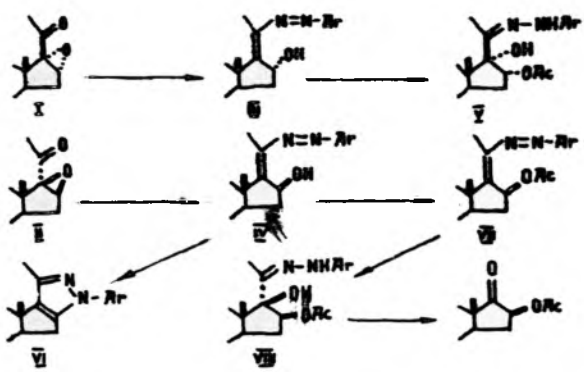
I II III

SYNTHESIS AND TRANSFORMATIONS OF ISOMERIC 20-ARYLAZOPREGNA-5,17 (20)- DIENE- 3 β,16- DIOLS

Skorova, A.V., Kamernitzky, A.V., Pavlova-Grishina, N.S.

N.D.Zelinsky Institute of Organic Chemistry, the USSR Academy of Sciences, Moscow

The reaction of both 16α, 17α-(I) and 16β, 17β- oxide (II) of dehydropregnenolone with p-nitrophenylhydrazine in the presence of small amounts of acids gives rise to the isomeric 20p-nitrophenylazopregna- 5,17(20)- dien - 3β,16-diols (III) and (IV). Azoolefin (III) when treated with sodium acetate gives 20-hydrazone 16-acetate of 16α,17α- diol (V), while the azoolefin (IV) under the same conditions gives only pyrazole (VI). However, the 16-acetate of IV (VII) yields 20-hydrazone 3,16-diacetate of 17α-pregn - 5-en- 3β,16β,17β- triol- 20-one (VIII). This reaction apparently proceeds by intermediacy of an orthoacetate. The structure of (VIII) was proved by spectral methods and by degradation of the side chain.

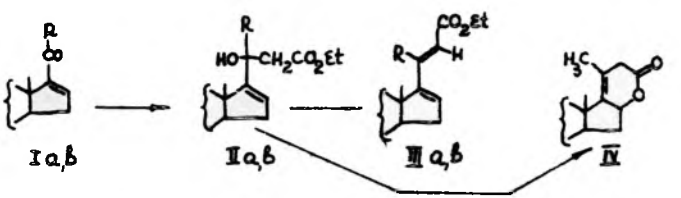


SYNTHESIS OF THE ESTERS OF NOR- AND DINORCHOLA - 5,16,20(22)-TRIENOIC ACIDS

Kamernitzky, A.V., Kryvoruchko, V.A., Litvinovskaja, R.P., Reshetova, I.G.

N.D.Zelinsky Institute of Organic Chemistry, the USSR Academy of Sciences, Moscow

Reformatsky reaction of dehydropregnenolone acetate (Ia) and 3β- acetoxyandrosta-5,16-diene- 17β-carbaldehyde (Ib) affords the acetates of carbethoxydiols (IIa,b) in good yield. Dehydratation of the latter with $POCl_3$-pyridine gives the corresponding carbethoxydienes (IIIa,b), which can be used as intermediates for the synthesis of polyhydroxysteroids. From the carbethoxydiol acetate (IIa) both E and Z- isomers about the $\Delta^{20(22)}$- bond could be obtained, but carbethoxydiol acetate (IIb) gives only E-isomer. Diene (IIIb) was also prepared by the Wittig-Wadworth-Horner condensation of (Ib) with $(C_2H_5O_2)P(O)CH_2COOC_2H_5$ and by dehydrohalogenation of the Δ^{16}-20- chloro-steroid which was obtained from (IIb) with $SOCl_2$. Treatment of hydoxysteroid (IIa) with $SOCl_2$ yielded lactone (IV).

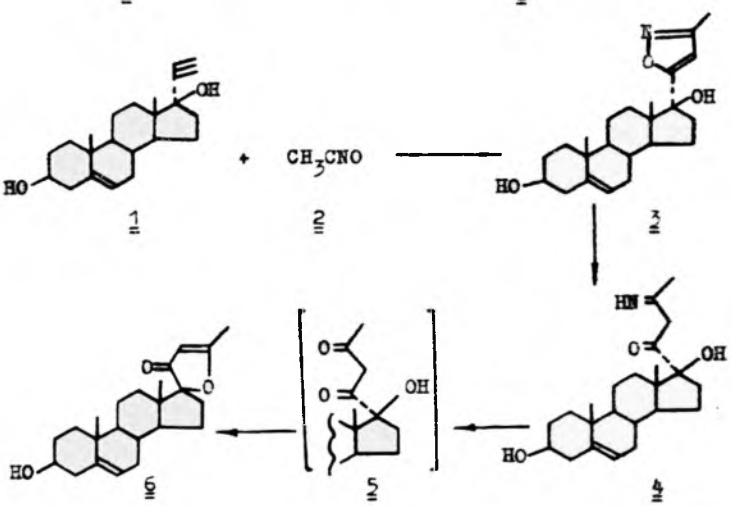


a. R = CH_3
b. R = H

NOVEL SYNTHESIS OF ANDROSTANE-17-SPIRO-2'-FURANE DERIVATIVES

A. A. Akhrem, F. A. Lakhvich and V. A. Khripach
Institute of bioorganic Chemistry, Byelorussian
Academy of Sciences, Minsk

A simple synthesis of 17-spirofurane steroid derivatives has been developed on the basis of adducts 1,3-dipolar addition of nitrile oxides to a triple bond of steroid acetylene alcohols. Thus, for example, isoxasol 3, obtained in 90% yield from ethynyldiol 1 and acetonitrile oxide 2 in situ, during hydrogenation in ethanol on Ni/Re undergoes reductive cleavage of the N-O bond to form iminoketone 4 in high yield. Hydrolysis of the latter yields spirofuranone 6 clearly via intermediate formation of β-diketone 5. The reaction hydrogenation proceeding in acetic acid allows conversion of isoxasol 3 to spirofuranone 6 to be achieved in one step with quantitative yield. The total spirofuranone 6 yield approaches 90% based on 1.



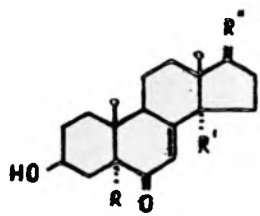
1 2 3 4 5 6

SYNTHESIS OF RUBROSTERONE ANALOGS

G.M. Segal and Zh.S. Sydykov

Shemyakin Institute of Bioorganic Chemistry, USSR Academy of Sciences, Moscow, USSR

Synthetic routes were worked out to 2-deoxyanalogs of rubresterone of type (I), which are possible metabolites of natural 2-deoxyecdysones. Some 5α-hydroxy-6-ketosteroids were shown to rearrange in A-homo-B-norsteroids under alkaline conditions.



R = H, OH

R' = H, OH

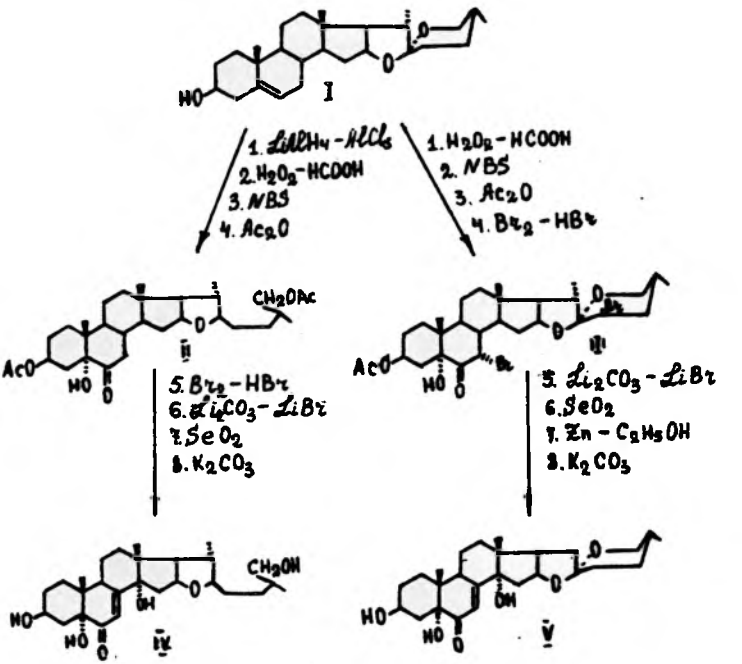
R'' = 

SYNTHESES OF ECDYSONE ANALOGS ON THE BASIS OF STEROIDAL SAPOGENINS

I.L.Novoselskaya, M.B.Gorovits, N.K.Abubakirov

Institute of the Chemistry of Plant Substances, Academy of Sciences of Uzbek SSR, Tashkent, USSR

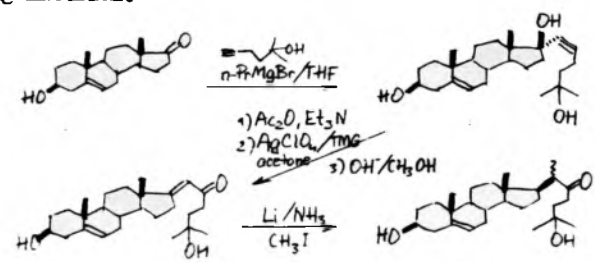
Starting from diosgenin (I) we have synthesised two analogs of ecdysone: (25R)-5α-spirost-7-en-3β,5,14α-triol-6-one (V) and (22R,25R)-5α-furost-7-en-3β,5,14α,26-tetraol (IV).



SYNTHESIS OF OXYGENATED STEROL SIDE CHAIN

M.Kocór and A.Cieplak
Institute of Organic Chemistry
Polish Academy of Science,Warsaw

The diastereomeric mixture of 20R and 20S 3β,25-dihydroxy-cholest-5-en-22-ones has been obtained on relatively short and efficient way using androstenolone as the starting material.



This product is a suitable intermediate for the synthesis of ecdysone and hydroxylated D_3 vitamine type compounds.

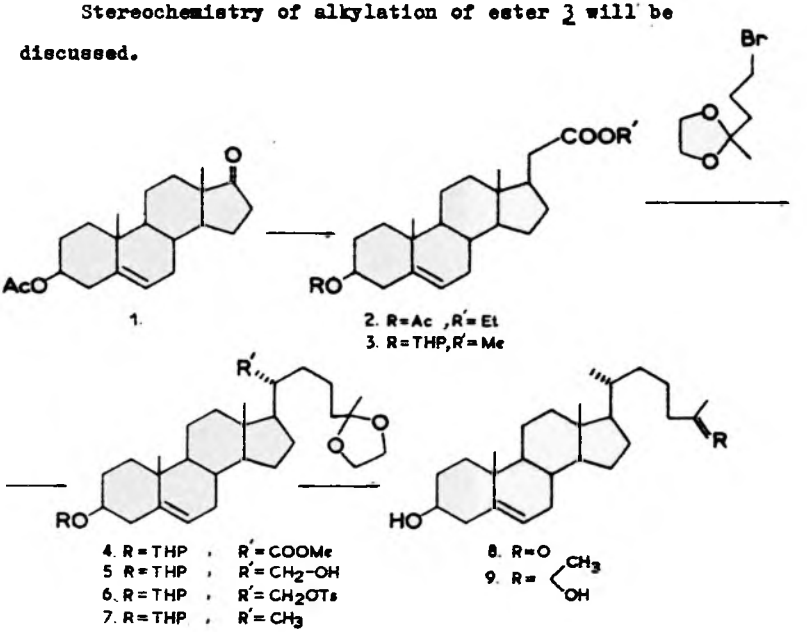
Synthesis of 25-Hydroxycholesterol from Androstenolone Acetate

J. Wicha, K. Bal

Institute of Organic Chemistry of the Polish Academy of Sciences

Androstenolone acetate 1 was transformed to ethyl 3β-acetoxy-5-pregnen-21-oate 2 by Reformatsky reaction with ethyl bromoacetate, followed by dehydration and selective hydrogenation. Ester 2 was converted to its tetrahydropyranyl-methyl derivative 3. Alkylation of 3 with 2-methyl-2-(3′-bromopropyl)-1,3-dioxolane gave 27-nor-cholestane derivative 4. Intermediate 4 was reduced to 7 via alcohol 5 and tosyl ester 6. Acid hydrolysis of 7 gave 27-nor-25-oxocholest-5-ene-3β-ol 8, which on treatment with methyl magnesium iodide furnished the title compound 9.

Stereochemistry of alkylation of ester 3 will be discussed.



CONTROLLED PRENOL HOMOLOGATION

J. S. Baran, B. S. Pitzele and D. H. Steinman

Searle Laboratories, Skokie Ill., U.S.A.

Polyprenols such as dolichol, bactoprenol and betulaprenol, which function as carriers of glycosyl groups in glycoprotein biosynthesis, are examples of natural substances made of sequential E or Z isoprene units. An approach to their synthesis was developed which allows controlled prenol homologation. The synthesis involves the novel γ-alkylation of the dianion derived from but-2-ynoic acid with an isoprenyl bromide 1 to yield 2. Stereoselective addition of a methyl group to the methyl ester of 2 or its thiol adduct 3, followed by reduction of the ester group with AlH_3 yielded the desired E or Z prenol. In this manner nerol and E-E or Z-Z farnesol were obtained in >91% purity.

1 RBr 2 $R\text{-}CH_2C{\equiv}CCOOH$ 3 $RCH_2C(S\phi){=}CHCOCH_3$

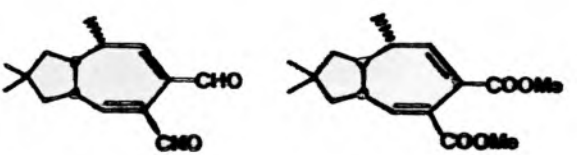
A SYNTHETIC APPROACH TOWARDS THE VELLERAL SKELETON

J.Froborg, G.Magnusson and S.Thorén

Organic Chemistry 2, The Lund Institute of Technology,

Chemical Center, Box 720, S-220 07 Lund 7, Sweden

We have undertaken a synthesis of velleral (1)[1], a C_{15}-dialdehyde from Lactarius vellereus and L. pergamenus. An investigation has now been made of steps in a sequence leading to the diester 2. Compound 2 appears to be a synthon of value for the synthesis of other sesquiterpenes from basidiomycetes[2].



1 2

1. G.Magnusson, S.Thorén and T.Drakenberg, Tetrahedron 29, 1631 (1973)

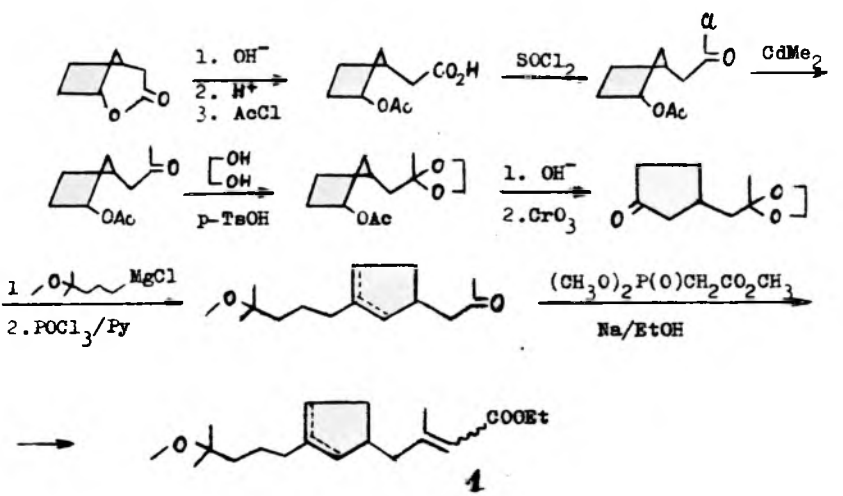
2. G.Magnusson and S.Thorén, Acta Chem. Scand. 27, 2396 (1973)

JUVENILE HORMONE ANALOGUES. SYNTHESIS OF 4-[3-(4-METHOXY-4-METHYLPENTYL)-CYCLOPENTENYL]-3-METHYLCROTONIC ACID ETHYL ESTER

W. Biernacki, W. Sobótka, M. Kocór

Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw

In search for new bioanalogues of the juvenile hormones (JH), an unsaturated ester 1 with a cyclopentene ring was synthesized according to the following reaction scheme:

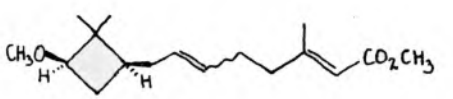


The cyclopropene ring can be regarded as an optional model system of a fixed conformation of the JH ethyl group at C-7 with its methyl attached to C-5.

THE SYNTHESIS OF POSSIBLE JUVENILE HORMONE BIOANALOGUE WITH CYCLOBUTANE RING

R. Sterzycki, W. Sobótka, M. Kocór
Institute of Organic Chemistry,
Polish Academy of Sciences, Warsaw

The compound /I/ was synthesized to investigate its activity as juvenile hormone bioanalogue.



I

The natural products from monoterpene group: geraniol and /1R,5R/-pinene were used to obtain the C_7 and C_8 synthons. In the last stage of multistep synthesis these synthons were combined in the Wittig reaction, forming the central C-7 double bond.

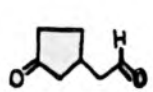
APPROACH TO THE SYNTHESIS OF JH ANALOGUE WITH AN ALICYCLIC RING.

M. Kozłowska and W. Sobótka

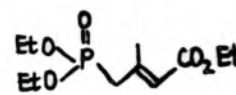
Institute of Organic Chemistry, Polish Academy of Sciences,

00-961 Warsaw, Poland

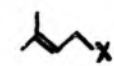
An attempt of the total synthesis of the juvenile hormone analogue with the five-membered ring at the position C_7-C_9 by combining synthons 1, 2 and 3 will be reported. Compounds 1, 2 and 3 were prepared in multistep transformations from cyclopentadiene, 3,3-dimethyl acrylic acid and isoprene respectively.



1



2



3

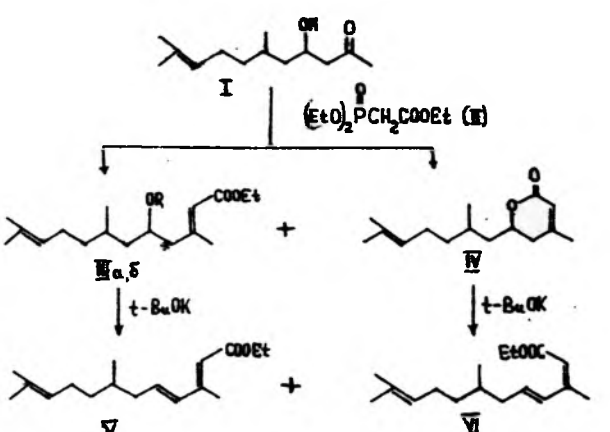
X = Cl, Br

THE MODIFIED WITTIG REACTION OF SESQUITERPENOID β-HYDROXYKETONES

M.Z.Krimer and V.I.Spektor

Institute of Chemistry, Moldavian Academy of Sciences,
Kishinev, USSR

The interaction of β-hydroxycitronellylacetone (I) with triethylphosphonoacetate (II) has been studied in the conditions of the modified Wittig reaction. It has been found that the result of this reaction is the formation of ethyl 5-hydroxy-3,7,11-trimethyl-trans-2,10-dodecadienoate (IIIa) and α,β-unsaturated δ-lactone (IV). The hydroxy ester (IIIa) was acetylated to the corresponding acetoxy ester (IIIb). The latter and lactone (IV) on treatment with potassium t-butoxide in THF at room temperature followed by treatment with diazoethane in ether have produced ethylesters of 3,7,11-trimethyl-trans-2, trans-4,10-dodecatrienoic (V) and 3,7,11-trimethyl-cis-2,trans-4,10-dodecatrienoic (VI) acids. The hydrogenated analogue of I reacts with the phosphonate II in the same manner.

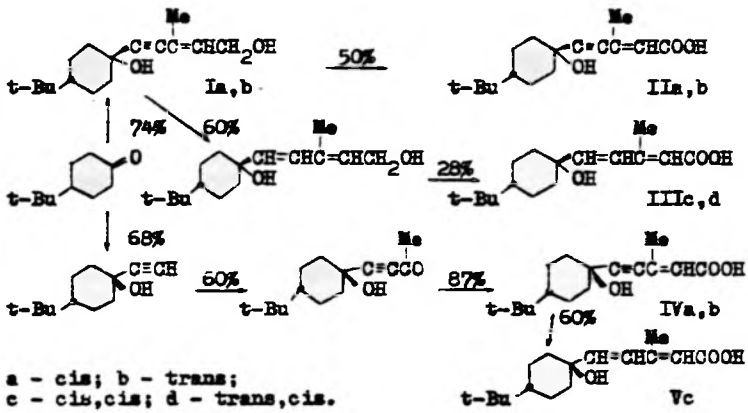


THE SYNTHETIC INVESTIGATIONS IN THE SERIES OF ABSCISIC ACID ANALOGUES

N.S.Wulfson, V.B.Berzin, L.G.Isaeva, E.M.Koff, V.I.Kefeli.

Shemyakin Institute of Bioorganic Chemistry and Timiryazev Institute of Plant Physiology, USSR Academy of Sciences, USSR, Moscow.

For determination of the influence of mutual steric relations between pentadiene side chain and cyclohexane ring in abscisic acid and its biological activity, some model hydroxy acids (II-V) with fixed conformation were synthetised by the following scheme:



a - cis; b - trans;
c - cis,cis; d - trans,cis.

The methyl esters of IIa,b were obtained in a good yields by two steps stereospecific oxydation of isomeric diols Ia,b. Under other conditions the conversion of I in to II was unsuccessful. Preliminary biological testing showed the presence of abscisic acid activity in compound IV and V.

CATALYTIC REDUCTION OF 17α,20; 20,21-BISMETHYLENE-DIOXY-19-NORPREGNA-1,3,5(10),9(11)-TETRAEN-3-YL METHYL ETHER

J. Zjawiony and H. Zając
Institute of Organic Chemistry, Technical University,
Żwirki 36, Łódź, Poland

Catalytic reduction of steroidal p-methoxystyrenoid systems is known[1] to afford stereospecifically hydrogenated derivatives of natural (9α) configuration. Hydrogenation of the title compound led unexpectedly to the formation of 17α,20; 20,21-bismethylenedioxy-19-nor-9β-pregna-1,3,5(10)-trien-3-yl methyl ether (31%), 17α,20; 20,21-bismethylenedioxy-19-nor-9α-pregna-1,3,5(10)-trien-3-yl methyl ether (21%), 17α,20; 20,21-bismethylene-19-nor-5ξ,9ξ,10ξ-pregnane (42%) and 17α,20; 20,21-bismethylenedioxy-19-nor-5ξ,9ξ,10ξ-pregnan-3ξ-ol (5%). The structure of the products was deduced from spectroscopic data and from chemical transformations.

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[1] H.J. Keereman, D. Van der Sijde and A.F. Marx, Recl. Trav. Chim. Pays-Bas 91, 1095 (1972 and ref. cit. therein.

SEARCH FOR A NOVEL ROUTE TO THE TOTAL SYNTHESIS OF STEROIDS

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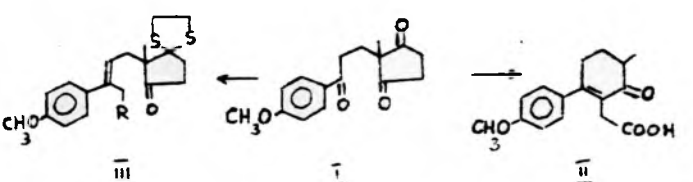
Institute of Organic Chemistry, Technical University, Żwirki 36, Łódź, Poland

2-methyl-2(3-p-methoxyphenyl-3-oxopropyl)cyclopentadion-1,3 (I) was synthesized in excellent yield in a two-step reaction from anisole. (I) was found to cyclodehydrate easily under acidic conditions into a compound which rearranges in alkaline media into known[1] unsaturated ketoacid (II); this can be utilized in the total synthesis of steroids. The triketon (I) affords conveniently an ethylendithioketal which reacts regioselectively with Grignard reagent to give, following dehydration, an unsaturated derivative (III). The last compounds is a suitable intermediate for final elaboration of the steroid skeleton.



III I II

[1] D.K. Banerjee, K.M. Sivanandaiah, J. Indian. Chem. Soc., 38, 652 (1961)

STUDIES ON 8,14-SECO-STEROIDS

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The stereospecific reduction of the keto group in 1 and 2 respectively provides the basis for a total synthesis of gonanes being epimeric at C-13.

Reduction of 1 by complex hydrides results in a (1 : 2,7) mixture of diols 3 and 4, whereas reduction of the derivatives 5 and 6 by $NaBH_4$ in MeOH yields nearly quantitatively the corresponding 14β-alcohols 7 and 8 (steric approach control).

Performing the reduction of 1 by $NaBH_4$ under conditions of phase transfer catalysis effects a preferential formation of the 14α-isomer (3 : 4 = 1,4 : 1). MEERWEIN-PONNDORF-VERLEY-reduction of 1 offers the method of choice for synthesizing 3 in preparative scale (3 : 4 = 4 : 1).

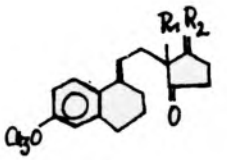
In addition, compound 3 is accessible by microbial transformation of seco-dion 13[1].

3 and 4 are extremely sensitive to acids: Under mild acidic conditions the double bond changes into position 8 (→ 9, 10)[2], and furthermore 3 is transformed into the 9,14-ether 11. Under stronger acidic conditions 4 rearranges within an intramolecular redox reaction into compound 12[3].

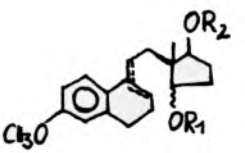
1) l.c. F. W. KUNSTMANN, A. SCHUBERT and S. SCHWARZ, DDR-Patent 64 054 (5. 10. 68; DDR Appl. 9. 11. 67)

2) l.c. G. LANGBEIN and S. SCHWARZ, J. Chem. 1975, in progress

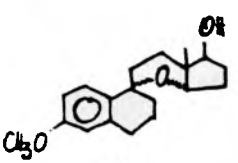
3) After having concluded this experimental part, LAHR et al. reported about the same reaction (Tetrahedron Letters 1974, 3271).



1: R_1 = CH_3; R_2 = α-H, β-OH
2: R_1 = C_2H_5; R_2 = α-H, β-OH
3: R_1 = CH_3; R_2 = α-H, β-OSi-$(CH_3)_3$
6: R_1 = CH_3; R_2 = α-H, β-OCOC_6H_4-pC_6H_5
12: R_1 = CH_3; R_2 = O



3: R_1 = R_2 = H; 14α; $\Delta^{9(11)}$
4: R_1 = R_2 = H; 14β; $\Delta^{9(11)}$
7: R_1 = H; R_2 = $Si(CH_3)_3$; 14β; $\Delta^{9(11)}$
8: R_1 = H; R_2 = CO-C_6H_4-pC_6H_5; 14β; $\Delta^{9(11)}$
9: R_1 = R_2 = H; 14α; Δ^{8}
10: R_1 = R_2 = H; 14β; Δ^{8}



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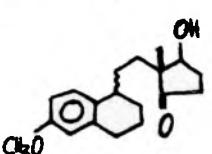

12

A NEW VARIANT IN SYNTHESIS OF 1,4-DIHYDRO-ESTRADIOL-3-METHYLETHER

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The reductions of 8-denydro-estradiol-3-methylether 1 and estradiol-3-methylether 2 to 1,4-dihydro-estradiol-3-methylether 3 by the method of Birch are important reaction steps in the industrial totalsynthesis of 19-norsteroids. Therefore it is useful to connect both reductions in a convenient an economical way to a single step.

A modified procedure is described by RZHEZNIKOW, ANANCHENKO and TORGOV[1] using potassium and lithium in a single reduction step of D-homo-8-denydro-estradiol-3-methylether to the 1,4-dihydro-derivatives.

Another variant for reducing 1 to 3 has been investigated. 1 can be hydrogenated in a single step to 3 under special conditions using sodium in the presence of an alconol in a strict stereochemical manner.

By this modified process 1,4-dihydro-estradiol-3-methylether can be synthesized in high yields from 1 economizing starting material and working hours to a high degree.

A probable mechanism of this modified reaction will as well be discussed.

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1) V. M. RZHEZNIKOW, S. N. ANANCHENKO and I. V. TORGOV Izvest. Akad. Nauk SSSR Otdel. Khim. Nauk 465 (1962)

NEW TOTAL SYNTHESIS OF ESTRONE

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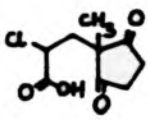
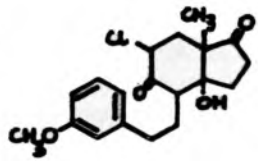
The easily accesible racemic acid 1 was resolved into enantiomers with (-)-ephedrine, and then it was transformed in a series of reactions into optically active tricyclic chlorodiketone 2. The removal of chlorine from 2 followed by cyclisation with acids yielded the known pentaene 4 in optically pure (-) form. The stereochemical course of the formation of 2 and 4 will be discussed.



1



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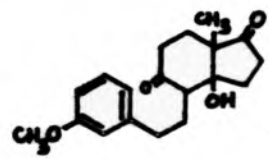
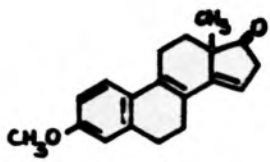


3



4

SYNTHESIS OF 14-HYDROXYESTRADIOLS AND 14-HYDROXY-19-NORTESTOSTERONES

S.N. Ananchenko, A.O. Lailiev and K.K. Koshoev

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A synthetic procedure was worked out for preparation of isomeric 17α and 17β 3-hydroxy- and 3-methoxy-14β-hydroxyestradiols of type (I). We have studied the effect of substitution at C_3 of the secosteroids (I) on the yield and the stereochemistry of the cyclisation products. Birch reduction of isomeric 14β-hydroxyestradiol methyl ethers gave corresponding 14β-hydroxy-19-nortestosterones.

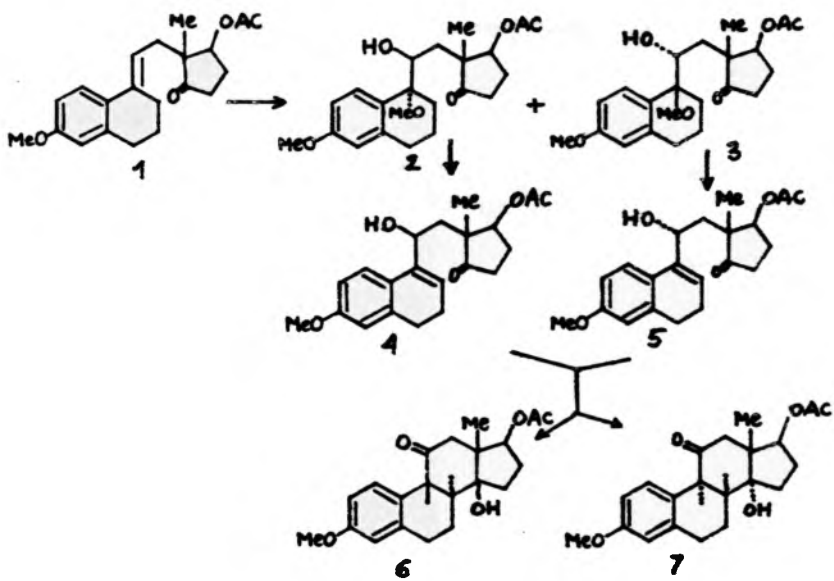
R = H, CH_3

Total Synthesis of Optically Active Derivatives of 8-Isoestrone Oxidized at C-11 and C-14.

P.Aweryn, A.R.Daniewski and M.Kocór

Institute of Organic Chemistry, Polish Academy of Sciences, Warszawa 00961, Poland

The optically active 3-methoxy-17β-acethoxy-8,14-secoestra-1,3,5(10),9(11)-tetraen-14-one 1 was converted in a series of reactions presented below into the compounds 6 and 7. The best yields of the intermediates 4 and 5 were obtained with MCPBA as oxidant in the presence of pyridine N-oxide as buffer and in methanol as solvent. The cyclisation of the mixture of 4 and 5 with Meerwein reagent ($Et_3O^+BF_4^-$) gave the tetracyclic compounds 6 and 7 in 40% overall yield (with respect to 1).



MICROBIAL OXYGENATION OF 6β-METHOXY-3α,5-CYCLO-5α-ANDROSTAN-17-ONE WITH RHIZOPUS NIGRICANS

Ž. Procházka and Huynh Kim Thoa
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague 6

The title compound was submitted to microbial transformation with Rhizopus nigricans under conditions which do not cause isomerization of the i-steroid and the products were isolated and their structure investigated.

MICROBIAL OXYGENATION OF B-NORSTEROIDS

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Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague 6
and
Research Institute for Pharmacy and Biochemistry,
Prague 9

Microbial hydroxylation of 17α,21-dihydroxy-B-nor-4-pregnene-3,20-dione and 3β,17α,21-trihydroxy-B-nor-5-pregnen-20-one with the fungus Beauveria bassiana was investigated. A series of products of this biotransformation was isolated and their structure determined.

MICROBIOLOGICAL OXIDATION OF PHYTOECDYSONES

Luigi Canonica, Bruno Danieli

Istituto di Chimica Organica della Facoltà di Scienze
Università degli Studi di Milano

The high insect moulting hormone ectivity of unusually ring hydroxylated phytoecdysones like muristerone A led us to study the microbiological oxidation of some ecdysones.

Crustecdysone, makisterone A and muristerone A are not affected by the whole cells of Curvularia lunata, Rhizopus arrhizus and Rhizopus nigricans, whereas they are rapidly transformed by the lysed cells.

Suprisingly enough, the transformation is not an hydroxylation, but in every case it is a 20,22 side-chain cleavage to afford the corresponding pregnane derivative. This compound can be in turn degradated to a 17-keto steroid. In these conditions ecdysone is not affected. The biological implications and the possible mechanism of these degradations of general interest are discussed.

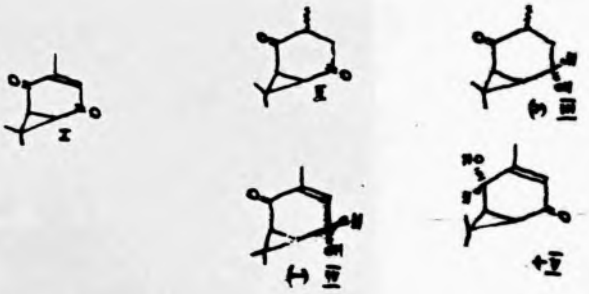
MICROBIOLOGICAL REDUCTION OF CAR-3-EN-2,5-DIONE BY RHODOTORULA MUCILAGINOSA

A.SIEWIŃSKI, A.ZABZA, W.PECZYŃSKA-CZOCH, A.SZEWCZUK

Academy of Agriculture, Wrocław; Technical University of Wrocław; Institute of Immunology and Experimental Ther. of Polish Academy of Science, Wrocław

The products of microbiological transformation by Rhodotorula mucilaginosa of car-3-en-2,5-dione /I/ were investigated. Compound I appears to be an interesting substrate, because of its not commonly encountered structure /two carbonyl groups conjugated with an unsaturated bond and also with a cyclopropane ring/. Therefore there exist different possibilities of reduction of both carbonyl groups or $\Delta^{3,4}$-double bond.

The results of our studies suggest that two pathways are possible for carendion /I/ transformation /Scheme 1./. The one of these involves first, the reduction of $\Delta^{3,4}$-double bond with formation of saturated diketone II, which is further reduced to the ketoalcohol III. The second pathway yields directly the allylic alcohol on C-2 /IV/ or on C-5 /V/ without prior reduction of the double bond. Small variations of yields of the products /III-V/ suggest that there is not much preference of either of the two pathways.



Scheme 1

GIBBERELLINS OF APPLE SEEDS

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Institute of Botany, the University of Warszawa, Poland

Dormant apple seeds contain three gibberellins : A_4, A_7 and A_9[1]. It was earlier demonstrated that during the removal of dormancy only the content of gibberellin A_4 undergoes marked changes[2].

In order to answer the question whether the process of gibberellin biosynthesis is involved in the observed changes, the experiments were performed using labelled gibberellin biosynthesis precursor - ^{14}C-2- mevalonic acid and an inhibitor of gibberellin biosynthesis - AMO-1618. It was shown that the embryos isolated from seeds submitted to cold stratification and cultured for several days are able to synthesize gibberellin A_4.

The results obtained indicate the correlation between the ability of embryos to synthetize GA_4 and the depth of embryonal dormancy.

The comparison of the changes in GA_4 content, the intensity of GA_4 biosynthesis and of the changes in germination ability of embryos isolated after different time of seeds after-ripening allows to conclude that biosynthesis of GA_4 is one of the factors involved in the removal of embryonal dormancy of apple seeds.

1. Sińska I.,Lewak St., Gaskin P. and MacMillan J., Planta, 114, 359 /1973/

2. Sińska I.and Lewak St., Physiol.Vég., 8, 661 /1970/

NEW REARRANGEMENTS OF LANOSTANE DERIVATIVES THE SYNTHESIS OF CUCURBITANE SKELETON

Z. Parvzek[a] and O.E. Edwards[b]

The cucurbitacins constitute an important group of tetracyclic triterpenoids of plant origin. Attempts to synthesize the cucurbitane skeleton /19(10→9β)-abeo-lanostane/ have failed so far.

Our approach to a cucurbitane is based on acid-catalysed rearrangement of 9,11-functionalized lanostane derivatives.

3β-acetoxy-9α-hydroxylanost-n-11-on treated with p-toluenesulfonic acid in benzene furnished a C-nor-D-homo compound, while under Westphalen rearrangement conditions 19-methyl migration occured affording 3β-acetoxy-5α-cucurbit-1/10/-ene-11-one and 3β-acetoxycucurbit-5/10/-ene-11-one. These structures were elucidated using spectral methods /CD, ^{13}C nr. shift reagent/ and were confirmed by chemical transformations. Finally, the correlation between these compounds and a natural cucurbitacin derivative was achieved.

a/ Institute of Chemistry, A. Mickiewicz University, Poznań,
b/ Division of Biochemistry, National Research Council, Ottawa, Canada.

ENZYMIC FORMATION OF TRITERPENE GLYCOSIDES BY CELL-FREE PREPARATIONS FROM CALENDULA OFFICINALIS SEEDLINGS

Z. Wojciechowski

Department of Biochemistry, Warsaw University, 02-089 Warsaw

We have previously shown / Phytochem. 6,69, 1967 / that six structurally related oleanolic acid glycosides occur in C.officinalis the most complex of which was 3β[4'-glucosyl-(3'-galactosyl-)]-glucuronoside,28-glucoside of oleanolic acid. In present study using cell-free enzymic preparations from C.officinalis seedlings we were able to demonstrate that the biosynthesis of these compounds proceeds by way of stepwise elongation of the sugar chain. The first step in this process is the synthesis of oleanolic acid 3β-D-glucuronoside from oleanolic acid and UDP--glucuronate. The corresponding enzyme is present in microsomes and seems to be highly specific for both oleanolic acid and UDP-glucuronate. Moreover, the formation of more complex glycosides by succesive addition of galactose and glucose to oleanolic acid 3β-D-glucuronoside / in positions 3' and 4' respectively / took place when cell-free preparations were incubated with UDP--galactose or UDP-glucose. The corresponding glycosyltransferases seem to be localized within the Golgi complex. The glucosylation of 17-COOH in oleanolic acid 3β-D-glucuronoside also could be demonstrated. This step is catalyzed by an enzyme present in the cytosol fraction.

THE SITES OF BIOSYNTHESIS OF OLEANOLIC ACID GLYCOSIDES IN CALENDULA OFFICINALIS

ZOFIA KASPRZYK AND WIRGINIA JANISZOWSKA
Institute of Biochemistry, University of Warsaw
02-089 Warszawa, Al. Żwirki i Wigury 93

The intracellular localization and the biosynthesis of oleanolic acid glycosides, derivatives of 3-glucuronoside /5 compounds/[1] and derivatives of 3-glucoside /5 compouds/[2] were investigated in the leaves of Calendula officinalis.

The conventional methods of fractiobation were used for obtaining of the subcellular fractions, 2-^{14}C-mevalonate for labelling and GLC for determination of oleanolic acid in individual glycosides as well as in oleanolic acid precursors. It was shown that the cyclization of squalene to β-amyrin, the oxidation of the latter to oleanolic acid and at least first glycosylations procede in the microsomal fraction. All the derivatives of 3-glucuronoside are then accumulating in the membranes fractions at first in the fraction of mitochondria and Golgi apparatus and with some delay in the fractions of chloroplasts and cell wall and cell membranes. The derivatives of 3-glucoside of oleanolic acid are all biosynthetized in the microsomal fraction and the final products of their transformation - pentaglycosides are selectively accumulating one, serving as a transport form, in the postmicrosomal supernatant and the second one in fraction of cell wall and cell membrane.

1. Z.Kasprzyk and Z.Wojciechowski, Phytochem. /1967/, 6, 69
2. Z.Wojciechowski, A.Jelonkiewicz-Konador, M.Tomaszewski, J.Jankowski and Z.Kasprzyk. Phytochem. /1971/ 10, 1121

Author Index