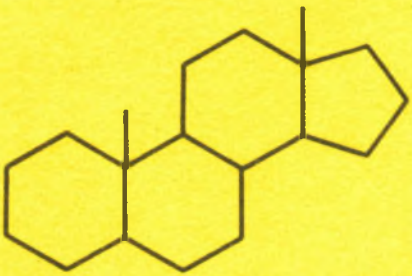
POLISH ACADEMY OF SCIENCES
INSTITUTE OF ORGANIC CHEMISTRY

ADAM MICKIEWICZ UNIVERSITY

XIII CONFERENCE ON ISOPRENOIDS



ABSTRACTS OF PAPERS

Poznań, 24—29 September, 1989

List of Plenary Lectures.

One hour

W.A. Ayer
Some New Fungal Metabolites of Isoprenoid Origin.

A. Dreiding
The title will be announced later.

M. Fetizon
The Chemistry of 1,4-Dioxene: its Application to the Syntheses of Natural Products.

P. Kocienski
Progress Towards the Immunosupressant Tsukubaenolide.

W. Kraus
Insect Feeding and Development Controlling Constituents of Meliaceae. Structure Activity Relationship and Preparative Aspects.

J.P. Kutney
Studies on Thujon Chemistry - a Chiral Synthon for the Synthesis of Natural Products and Related Compounds.

J.A. Marshall
The Synthesis of Macrocyclic Natural Products.

K. Mori
Isoprenoid Syntheses Starting from Chiral Building Bloks of Microbiological Origin.

F. Piozzi
Research on Neo-clerodane Diterpenoids.

K. Schreiber, H. Ripperger, Le Thi Quyen
Recent Results in the Chemistry of Solanum Steroid Alkaloids.

B.M. Trost
Streamlining Strategy by Enhanced Selectivity via Transition Metal Catalysed Reactions.

J. Tsuji
Palladium Catalysts as Versatile Tools for Organic Synthesis.

M.R. Uskokovic
Therapeutic Regulation of Lipids with Natural Products.

D.S. Watt, K. Kawada, M. Kim, L.A. Applegate, R.S. Gross and U. Wajcen
An Enantioselective Synthesis of Quassinoids.

Half hour

P.J. de Clercq
Synthetic Approach to Periplanone B.

C. Fehr and J. Galindo
Enantioselective Protonation of Enolates in Isoprenoid Synthesis.

B.M. Fraga
Chemical and Microbiological Synthesis of Gibberelins.

T. Frejd
Attempts Toward the Total Synthesis of Taxol and Congeners.

Ae. de Groot, J.B.P.A. Wijnberg, R.P.W. Kesselmans and L.H.D. Jenniskens
The Synthesis of Eudesmanes and their Selective Rearrangement to Guiane Sesquiterpenes.

A. Kasal
Synthesis of Antiandrogens with Unusual Steroid Skeleton.

V.A. Khripach
New Approaches to the Construction of the Steroid Side-Chains.

G. Majetich
Studies in Terpene Synthesis Based on Intramolecular Sakurai Reactions.

G.A. Molander
New Methods for Stereoselective Organic Synthesis.

M. Nishizawa
Synthetic Approach Toward Sweet Tasting Diterpene Glycosides.

U.K. Pandit
Synthetic Studies in the Field of Antitumor Alkaloids.

Z. Paryzek, J. Martynow and W. Swoboda
Reaction of Ozone with Steroidal Olefines. New Observation and Revision.

E Santaniello
Use of Biocatalysts for the Preparation of Chiral Synthons for the Synthesis of Natural Products.

W.A. Smit
A Novel Approach to the Formation of Polycyclic Framework.

Z. Tuba, S. Maho, Gy. Galik, J. Horvath and M. Marsai
Synthesis of Biologically Active Non-Hormonal Steroids (Structure and Relationship).

A.R. de Vivar
Chemical Studies of "Parthenium" and Other Species of Compositae.

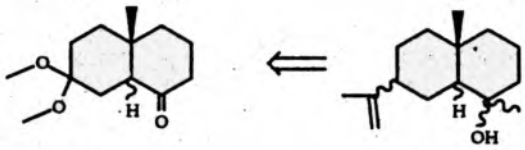
Wei-Shan Zhou
The Stereoselective Synthesis of the Brassinosteroid Side-Chain.

THE SYNTHESIS OF EUDESMANES AND THEIR SELECTIVE REARRANGEMENT TO GUAIANE SESQUITERPENES

Ae. de Groot, J.B.P.A. Wijnberg, R.P.W. Kesselmans and L.H.D. Jenniskens

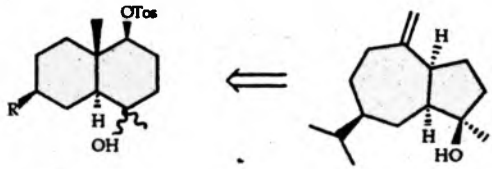
Department of Organic Chemistry, Agricultural University Wageningen
Dreijenplein 8, 6703 HB Wageningen, The Netherlands

Recently an efficient synthesis of *cis* and *trans* monoprotected perhydronaphthalenediones **1** was developed in our laboratory. The easy availability of these compunds enabled the synthesis of all possible stereoisomers of the hydroxy eudesmanes **2**. Several of these isomers were found in the defence secretions of termites.



1 **2**

With the above mentioned method for the preparation of subsituted perhydronaphthalenes at hand it was obvious to investigate their rearrangment to perhydoazulenes in order to explore the utility of this approach for the synthesis of guaianes.



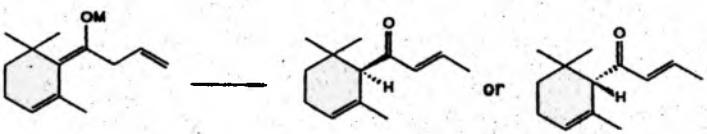
3 **4**

Solvolytic rearrangement of compounds with the general structure **3** give mixtures of double bond isomers with compounds with an endocyclic double bond as the major product. In our laboratory the selective rearrangement of compounds **3** to *cis*-fused guaianes with an exocyclic double bond, like 5-*epi*-nardol **4**, was developed.

Enantioselective Protonation in Isoprenoid Synthesis

Charles Fehr and José Galindo

We have developed new regio- and diastereoselective (E/Z) approaches to ketone enolates and studied their enantioselective protonation. The success of enantioselective protonation of enolates critically depends on the nature of the enolate, its configuration (E/Z), the metal ions, the ligands and the chiral proton source. Highest ee's were attained in the synthesis of (R)- and (S)-α-damascone (84% ee, >98% ee after purification) which are synthetically useful chiral building blocks.



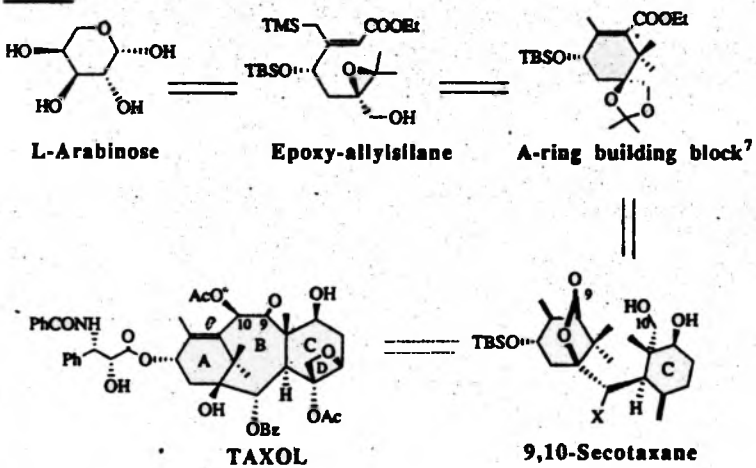
(R)-α-damascone (S)-α-damascone

ATTEMPTS TOWARDS THE TOTAL SYNTHESIS OF TAXOL AND CONGENERS.

Torbjörn Frejd, The Lund Institute of Technology, Chemical Center, P.O.B. 124, S-221 00 Lund, Sweden.

A major reason for the interest in the taxane diterpenoids is the discovery that taxol, which was isolated in small amounts from yew trees (*Taxus baccata* among others), possessed anti-leukemic and anti-tumor properties.[1] Taxol is now undergoing clinical testing. Recently, taxol derivatives have been "*semi*" synthesized by starting from taxol or bacchatin III.[2] A major step forward was the discovery that the needles of yew trees contain large amounts of 10-deacetylbacchatin III, which could be converted into taxol in good yield.[3]

Scheme.



Several ingenious attempts directed towards the "*total*" synthesis of taxanes have been made during the last decade, although taxol itself has not been synthesized.[4]

Our work is focused on the synthesis of optically active taxanes and is outlined in the Scheme. Starting with arabinose we have prepared the 9,10-secotaxane in a series of steps, which include the Sharpless asymmetric epoxidation of allylic alcohols[5] and the electrophilic ring closure of epoxy-allylsilanes[6]. We now try to find efficient ways to make the 9,10-connection as well as shorter routes to some of the important intermediates, such as the optically active epoxy-allylsilane.

References.

1. Wani, M.C.; Taylor, M.L.; Wall, M.E.; Coggon, P.; McPhail, A.T. *J. Am. Chem. Soc.* **1971**, *93*, 2325.
2. Guéritte-Voegelein, F.; Sénilh, V.; David, B.; Guenas, D.; Potier, P. *Tetrahedron* **1986**, *42*, 4451; Magri, N.F.; Kingston, D.G.I. *J. Org. Chem.* **1986**, *51*, 797-802.
3. Denis, J.-N.,Greene, A.E., Guenard, D., Gueritte-Voegelein, F., Mangatal, L. and Potier, P., *J. Amer. Chem. Soc.*, **1988**, *110*, 5917.
4. Holton, R.A., Juo, R.R., Kim, H.B., Williams, A.D., Harusawa, S., Lowenthal, R.E., and Yogai, S., *J. Amer. Chem. Soc.*, **1988**, *110*, 6558 and references cited herein.
5. Rossiter, B.E., in "*Asymmetric Synthesis*", Vol 5, pp 193, Academic Press **1985**; Finn, M.G., and Sharpless K.B., *ibid* pp 247.
6. Flemming, I.; Pearce, A. and Snowden, R.L. *J. Chem. Soc. Chem. Commun.* **1976**, 182; Armstrong, R.J.; Harris, F.L. and Weiler, L. *Can J. Chem.* **1982**, *60*, 673; Armstrong, R.J.; Weiler, L. *Can. J. Chem.* **1986**, *64*, 684; Johnson, W.S.; Newton, C. and Lindell, S.D. *Tetr. Lett.* **1986**, 6027.
7. Pettersson, L. Frejd, T., and Magnusson, G., *Tetr. Lett.*, **1987**, 28, 2753.

SYNTHESIS OF ANTIANDROGENS WITH UNUSUAL STEROID SKELETON

Alexander Kasal

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6, Czechoslovakia

The therapeutic potential of steroid antihormones[1] in general and of antiandrogens[2] in particular will be discussed. Synthetic strategies leading to various types of active analogues of androgen hormones will be presented[3]. When compared with structures of natural androgen hormones, these antiandrogens generally possess the following two features:

a) identity of one end of the molecule with that of the hormone,

b) profound structural difference of the other end of the molecule.

With these two conditions met, the analogues apparently bind to the androgen receptor in target tissues but fail to produce the change in the receptor conformation necessary for binding the DNA.

References:

1. M.K.Agarwal (ed.), Receptor Mediated Antisteroid Action, Walter de Gruyter, Berlin 1987.
2. B.R.Rao, H.J.deVoogt, A.A.Geldof, L.J.G.Gooren, F.G.Bouman, Merits and Considerations in the Use of Antiandrogens, J.steroid Biochem. 31, 731 (1988).
3. A.Kasal, Collect.Czech.Chem.Commun. 54, in press (1989).

NEW APPROACHES TO THE CONSTRUCTION OF STEROID SIDE CHAINS

V. A. Khripach

Institute of Bioorganic Chemistry, Byelorussian SSR Academy of Sciences, 220045, Minsk, Zhodinskaya, 5/2

The construction of steroid side chains is one of the key problem in the partial synthesis of numerous biologically important natural steroids (brassino- and ecdysteroids, vitamin D metabolites, withanolides, cardiac aglycons, etc.). This problem has lately drawn attention of various groups of investigators, that is due, first of all, to finding in natural sources of new types of steroidal bioregulators possessing a functionalized side chain which is shown to determine the type and level of biological activity. Among various approaches to the side chain construction one of particular interest is the use of heterocyclic intermediates containing the desired functionality in a latent form which can be realized at the corresponding stage of chemical process.

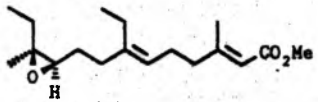
Some recent results on regio- and stereoselective synthesis of new steroidal molecules containing heterocyclic substituent (isoxazole, 2-isoxazoline and some others) into the side chain and their transformation into functionalized derivatives, analogs and precursors of natural polyhydroxysteroids such as ecdy- and brassinosteroids, will be discussed.

ISOPRENOID SYNTHESES STARTING FROM CHIRAL BUILDING BLOCKS OF MICROBIAL ORIGIN

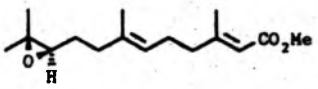
Kenji Mori

Department of Agricultural Chemistry, the University of Tokyo, Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan

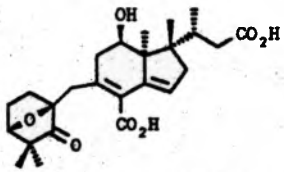
Chiral building blocks of microbial origin were extensively employed in our recent syntheses of bioactive isoprenoids such as juvenile hormones I and III, glycinoeclepin A, and others. especially our synthesis of both the enantiomers of juvenile hormones I and III revealed that the pure unnatural enantiomers were far less active than the natural ones.



(+)-JH I



(+)-JH III



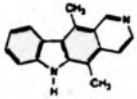
glycinoeclepin A

SYNTHETIC STUDIES IN THE FIELD OF ANTITUMOUR ALKALOIDS

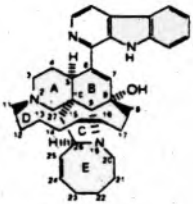
Upendra K. Pandit
Organic Chemistry Laboratory, University of Amsterdam,
Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands

The theme of antitumour natural products has been the subject of study for a number of years in our laboratory. Our current interest in this field focusses on the plant alkaloids sesbanimides and ellipticines and the recently isolated complex alkaloids (manzamines) of marine sponge origin. Synthetic studies leading to naturally occurring (+)-sesbanimide A and ellipticine, together with their analogues, will be described. Biological activity data will be presented and structure-activity relationship discussed. In the context of manzamines, progress towards the enantioselective synthesis of manzamine A will be reported.

(+)-Sesbanimide A



Ellipticine



Manzamine A

REACTION OF OZONE WITH STEROIDAL OLEFINS. NEW OBSERVATIONS AND REVISION

Zdzisław Paryzek, Jacek Martynow, and Witold Swoboda

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

Ozone, a powerful oxidizing agent, is not frequently used in steroid chemistry, besides for degradative purposes. The mechanism of reaction between alkenes and ozone seems to be well understood. The influence of the solvent used in ozonolysis was previously discussed mainly in terms of the stereochemistry of ozonides formed.

In an investigation of reactions of ozone with steroidal olefins we found the remarkable solvent effect. It appears, that the structure of the complex formed between ozone and the crowded double bond present in the triterpene depends on the polarity of the solvent. This interpretation is proposed as an explanation of the allylic oxidation, which takes place when a crowded double bond in lanost-8-ene reacts with ozone in ethyl acetate. In this case formation of an ozonide is sterically impossible. Instead, 8,9-epoxide and lanost-8-en-7-one are formed.

Interception of carbonyl/carbonyl oxide intermediate, postulated in Criegee mechanism of ozonolysis, by intramolecular nucleophilic attack of a hydroxyl group has been found in reactions of steroidal allylic alcohols.

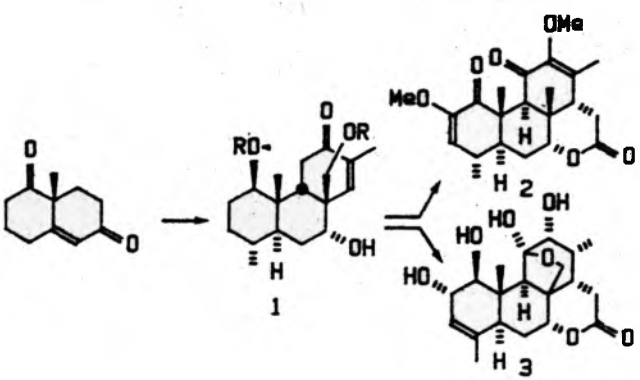
These new results enabled the revision of the structure proposed in the literature for the major product formed in ozonolysis of cholesterol carried out in participating solvents.

AN ENANTIOSELECTIVE SYNTHESIS OF QUASSINOIDS

Kenji Kawada, Moonsun Kim, Laura Anne Applegate, Raymond S. Gross, Urszula Wajcen, and David S. Watt

Department of Chemistry, University of Kentucky, Lexington, KY. 40506-0055 U. S. A.

We are developing an enantioselective synthesis of the quassinoids designed to produce for both the tetracyclic and pentacylic quassinoids in the picrasane family such as quassin (2) and chaparrin (3), respectively. This route commenced with the Wieland-Miescher ketone prepared using the Hajos-Parrish procedure and progressed to the tricylic intermediate 1. We will discuss the development of various sequences and new reagents necessary to solve problems associated with: [1] the introduction of the C-4α methyl group in a dienophile derived from the Wieland-Miescher ketone; [2] the selection of a diene necessary to construct tricyclic enones 1 which are functionalized in the C ring; [3] the oxidation of the C-11 position necessary to procure a C-11 ketone and invert the C-9β configuration; [4] the selection of the C-1 protecting group and its bearing on the C-11 oxidation process; [5] the development of new methods for closure of the D ring either as a δ-lactone or a protected δ-lactol; and [6] the manipulation of the C-8β hydroxymethyl group. We will report our progress toward various quassinoid objectives using these studies.



SYNTHESIS OF THE ALKENES BY WITTIG OLEFINATION USING LITHIUM 1,3-DIAMINOPROPANE AS A BASE.

L.Streinz and M.Romaňuk.

Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences
Flemingovo nám.2, 166 10 Prague 6,Czechoslovakia

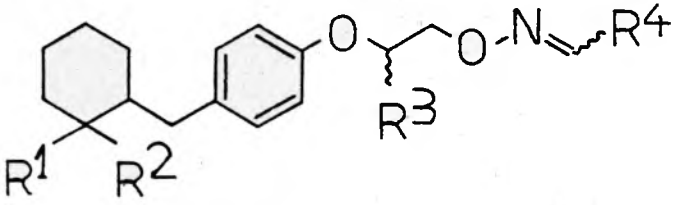
It has been found that lithium 1,3-diaminopropane can be used for generation of non-stabilized ylides from triphenyl alkylphosphonium bromides.These ylides react with aldehydes affording olefines with high Z-stereoselectivity.The role of different factors (alkyl group in the molecule of aldehyde,solvent,temperature and triphenyl alkyl phosphorane used etc.)influencing the stereoselectivity has been studied.The obtained results were applied to the synthesis of selected pheromones.

OXIME ETHERS AS POTENTIAL JUVENOIDS: THE ROLE OF THE OPTICAL ISOMERISM.

Zdeněk WIMMER and Miroslav ROMAŇUK

Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences
Flemingovo nám. 2, 166 10 Prague 6, Czechoslovakia

Recently we published a paper (1) on the synthesis of juvenoids bearing oxime ether grouping in their molecules (I; R^3 = H). The oxime ethers I (R^3 = H) exhibited promissing biological activities when tested on house fly or wax moth. Within the frame of structure-activity relationship studies, the side chain of the molecule was modified (I; $R^3 \neq H$). The racemic compounds I ($R^3 \neq H$), as well as their corresponding optically active enantiomers were synthetized and subjected to the biological studies.



I

Reference:

(1) Wimmer Z., Šaman D., Smolíková J., Romaňuk M.: Liebigs Ann. Chem. 1988, 1091.

THE SYNTHESIS OF OPTICALLY ACTIVE MIXTURE OF CHALCOGRAN DIASTEREOISOMERS WITH THE AID OF MICROORGANISMS

Eva Körblová, Bohumír Koutek, David Šaman, Aleš Svatoš, Jan Vrkoč, Petr Maloň and Miroslav Romaňuk

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague, Czechoslovakia

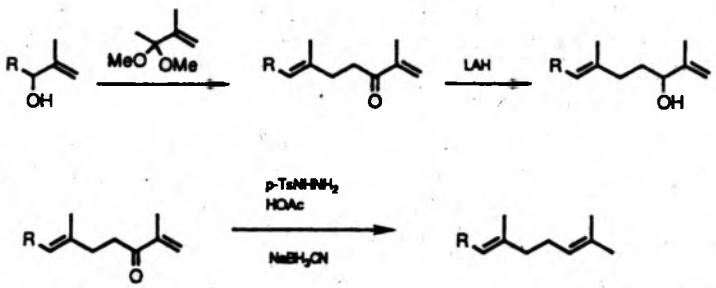
Chalcogran, 2-ethyl-1,6-dioxaspiro[4.4]nonane is a component of the aggregation pheromone of the bark beetle Pityogenes chalcographus (L). The synthesis of optically active diastereoisomeric mixture of chalcogran is described, which utilizes low temperature aldol reaction and enantioselective enzymatic reduction as the key steps.

The optically active 1-(2-furyl)-3-pentanol, the chalcogran precursor, was obtained by reduction of 1-(2-furyl)-3-pentanone with Baker's yeast or by reesterification of racemic 1-(2-furyl)-3-pentanol with trichloroethylbutyrate in the presence of pig pancreatic lipase. The enantioselectivity of these approaches will be discussed.

SYNTHESESE OF OPEN CHAIN ISOPRENOID PHEROMONE COMPONENTS

P. Baeckström and L. Li
Royal Institute of Technology, (KTH)
S-100 44 STOCKHOLM, SWEDEN

A two step iterative method has been used for constructing head to tail isoprenoid chains. The "fishtail" ending has been created by an improved method for reductive elimination of the carbonyl function with concomitant transposition of the double bond.



ACTIVE ACTINIDOLS, A PHARMACOLOGICAL PRINCIPLE IN THE THAI MEDICINAL PLANT *Ipomoea pes-caprae* (CONVOLVULACEAE).

Peter Bandaranayake,[a] Lars Bohlin,[b] Ulla Jacobsson,[a] Mikael Lindström,[a] Uthaiwan Pongpaiyoon,[b,c] Sasithorn Wasuwat[c]

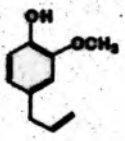
[a] Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm, Sweden.

[b] Department of Pharmacognosy, Biomedical Center, S-751 23 Uppsala, Sweden.

[c] National Institute of Scientific and Technological Research, Bangkok 10900, Thailand.

Ipomoea pes-caprae (L. R. Br.) is a plant in Thailand (thai name "phakbung tha-le"), which is used as an antidote for jelly fish stings and as an antipruritic agent. An extract (IPA) was obtained from petroleum ether extraction of a water distillate of dried leaves of the plant. This extract showed antagonistic activities.[1,2] Fractionation was monitored by using different bioassays. This technique lead to the isolation of eugenol (1) from a complex fraction, which inhibited prostaglandin synthesis. Further, two diastereomerically related compounds (2) were isolated from a fraction inhibiting ethylphenylpropiolon-induced inflammation on rat ear.

Identification of the diastereomers of 2 was performed using MS and advanced NMR techniques. The absolute configuration and relative stereochemistry have not yet been fully established. Isomers of 2 have earlier been isolated from grapes, *Vitis vinifera*,[3] and the Japanese plant *Actinidia polygama*.[4] They have been reported to show pharmacological activity.



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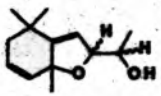


2

[1] S. Wasuwat, *Nature*, 758 (1970).

[2] U. Pongpaiyoon, L. Bohlin and S. Wasuwat, *Acta Pharm. Nord.*, 1, 41 (1989).

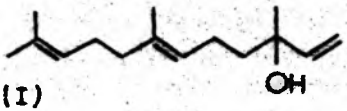
[3] E. Dimitriadis, C.R. Strauss, B. Wilson, and P.J. Williams, *Phytochemistry*, 24, 767 (1985).

[4] T. Sakan, S. Isoe, and S.B. Hyeon, *Tetrahedron Lett.*, 1623 (1967).

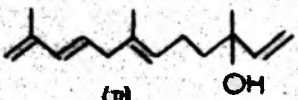
NEW SYNTHESES OF ATTRACTANTS AND JUVENOIDS BASED ON THE WOOD OIL OF PORKIENIA HODGINSHI L.

Nguyen Cong Hao, Phan Thanh Thao,
Nguyen Cuu Khoa, Nguyen Van Hung.
Institute of Chemistry. Ho Chi Minh City. SRV

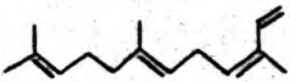
The wood oil of Pokienia Hodginshi L. is separated by distilation, column chromatography to give nerolidol (I) and Porkienol (II), Regioselective transfomation of (I) and (II) leads via 2-5 steps to some attractants of codling moth (Laspeyresia pomonella L.), cotton seed bug (Oxycarenus hyalinipennis C.) (III), red flour beetle (Tribolium castaneum) (IV), rusty grain beetles (Cryptolestes ferugineus S.) (V) and Juvenoids such as (VI) and (VII).



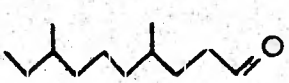
(I)



(II)



(III)



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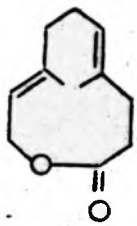
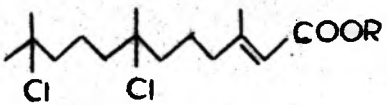
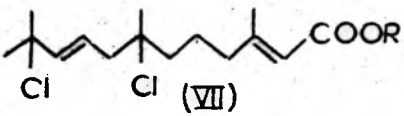


(V)



(VI)



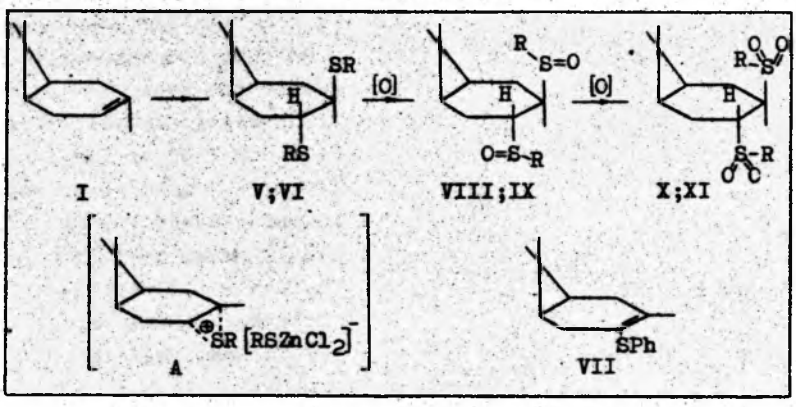
(VII)

R = CH_3 , C_2H_5

CATALYSTIC ADDITION OF DISULFIDES TO 3-CARENE

L.E.Nikitina, V.V.Plemencov, I.A.Litvinov, O.N.Kataeva
Kazan State Medical Institute named after S.V.Kurashov

The reactions of 3-carene (I) with disulfides R_2S_2 (R=CH_3(II); C_2H_5(III); C_6H_5(IV)) have been studied under Lewis acids catalysis conditions. It has been found that isomerisation (I) to n-cymol takes place in the presence of $BF_3 \cdot Et_2O$ or J_2 whereas in the presence of $CaCl_2$, $FeCl_3$, $MgCl_2$ there are no reactions. Addition products (V-VII) have been obtained by catalysis of $ZnCl_2$ reactions in the polar medium.



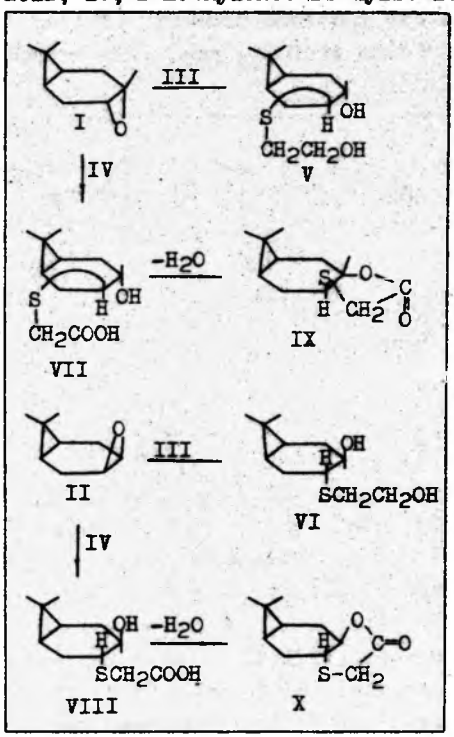
In case of 3-carene (I) interaction with disulfide (IV) only one product (VII) is isolated as a result of the formal two-steps process of addition-elimination. Bis-sulfides (V,VI) were oxidated under mild conditions to the corresponding sulfoxides (VIII,IX), which reveald hydrophyl and lipophyl properties. Sulfoxides (VIII,IX) readily oxidated to sulfones (X,XI), the compound structure (X,R=CH_3) has been identified by the method of X-ray analysis.

The mechanism of addition has been duscussed as electrophyl trans-attack of 3-carene by disulfide activated by Lewis acid (transitory state A).

3-CARENE(S) OXIDES REACTIONS WITH MERCAPTOALCOHOLS AND MERCAPTOACIDS

V.V.Plemencov, N.P.Artemova, G.Sh.Bikbulatova
Kazan State Medical Institute named after S.V.Kurashov

The trans-addition compounds with tertiary hydroxyl group (V-VIII) have been obtained by reactions of α-3,4 - epoxycarane (I) and β-3,4-epoxycarane (II) with bifunctional nucleophiles (mercaptoethanol, III; mercaptoacetic acid, IV; S-methylenecarboxyisotiourea) under basic catalysis conditions.



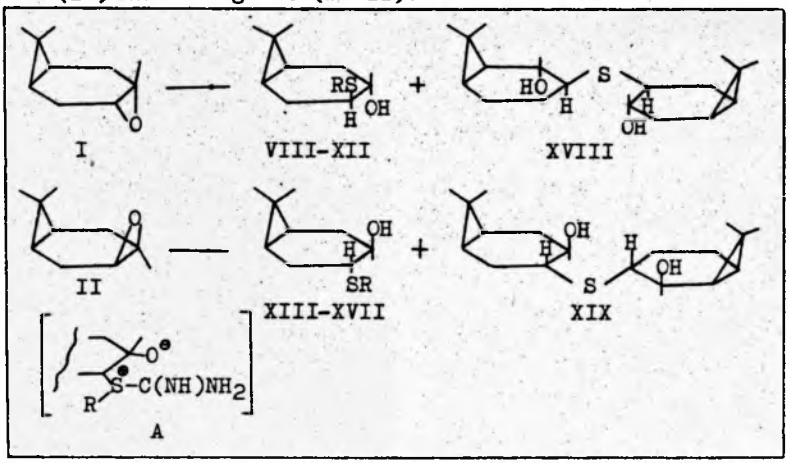
The adduct (VIII) has been found to be converted to the corresponding lactones spontaneously, while the adduct (VII) by heating. In reactions (I) and (II) with reagent (IV) under base reduced content (EtONa) small amounts of di(4 - caranyl-3-ol)sulfides have been obtained. It is assumed that their formation is due to the interaction of compounds (VII, VIII) with 3-carene oxides according to the mechanism of a synchronous attack of S-nucleophyle and H-catalysis of oxidate ring with the following elimination of methylenecarboxy group.

The structure of synthetized compounds has been proved by IR, ^{1}H NMR spectroscopy data.

REACTIONS OF 3,4-EPOXYCARANES WITH ISOTIOUREA SALTS

N.P.Artemova, G.Sh.Bikbulatova, V.V.Plemencov, I.A.Litvinov
Kazan State Medical Institute named after S.V.Kurashov

The reactions of α-3,4-epoxycarane (I) and β-3,4-epoxycarane (II) with isotiourea salts of the general formula R-S-C(NH)NH_2·HHal (R:-CH_3, III; -C_2H_5, IV; -iso-C_3H_7, V; -CH_2-CH=CH_2, VI; -CH_2-C_6H_5, VII) have been studied in the presence of bases. In all cases the reactions (I) and (II) have been shown to produce the corresponding 4-RS-carane-3-ols (VIII-XVII) as single or base products. The process of addition occurs in trans-position to the oxidate ring and in accordance with Krasusky's rule. Besides, bis-adducts (XVIII, XIX) have been isolated in the reactions (I) and (II) with reagents (V-VII).



It has been assumed that compounds (XVIII, XIX) formation is connected with a possible concurrent elimination of more stable carbonium ions (allyl and benzyl) from intermediate (A). This leads to the intermediate 4-mercaptocarane-3-ol production, which couples with the second molecule of carene oxide in the base presence.

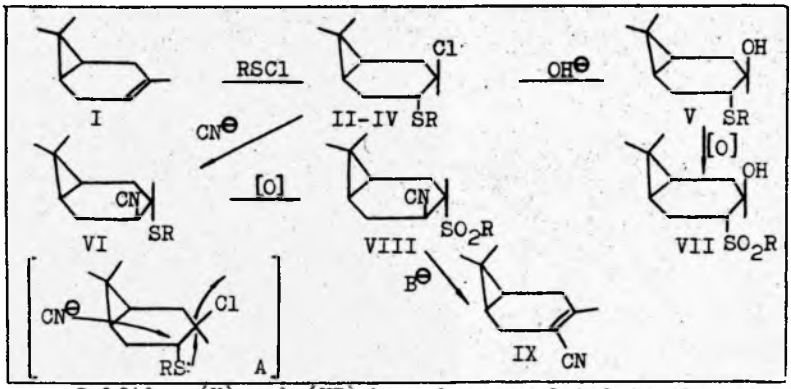
Synthetized substances structure has been proved by IR, ^{1}H NMR spectroscopy and X-ray analysis data (XVIII).

SYNTHESIS OF SULFUR-BEARING FUNCTIONAL DERIVATIVES OF CARANE BY 3-CARENE SULFENYLCHLORINATION

F.A.Bairamova, V.V.Plemencov, I.A.Litvinov
Kazan State Medical Institute named after S.V.Kurashov

4-RS-3-chlorcarane (II-IV) have been obtained using the reactions of 3-carene (I) with sulfenylhalogenids RSCl (R=Me, Et, Ph). The addition takes place according to Markovnikov's rule and it is strictly trans-stereospecific.

The reactions of β-chlorcaranylsulfides (II-IV) with bases and nucleophylic reagents have been studied. The interaction of the compound (II) with hydroxyl-anion has been shown to produce caranolsulfide (V), i.e. the substitution takes place with preservation of reactional centre configuration. The reaction between compound (II) and cyanide-anion yielded the product (VI), i.e. the substitution occurs with participation of 2 reactinal centers and with configuration reversion of both RC (A).



Sulfides (V) and (VI) have been oxydated to the corresponding sulfones (VII, VIII), sulfone (VIII) readily eliminates CH_3SO_2H forming 4-cyano-3-carene (IX).

The structure of the compound (V) has been proved by the independent synthesis, the structure of the compound (VIII) - by X-ray analysis. All compounds have been characterized using IR, ^1H NMR, ^{13}C NMR and analysis data.

RITTER REACTION OF ISOBORNEOL WITH CHLOROACETONITRILE

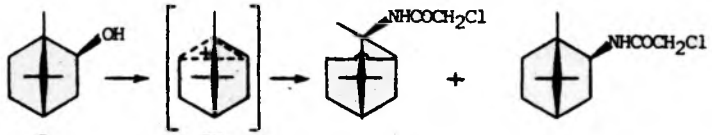
Victor Lysenkov

Institute of Physico-Organic Chemistry,

Byelorussian Academy of Sciences, Minsk, USSR

It is known that 3-aminoisocamphane and some of its N-alkyl derivatives, which have strong ganglioblocking properties, are obtained from 3-acylaminoisocamphanes which result from the condensation of camphene with nitriles of formic or polychloracetic acids[1].

We found a new approach to the synthesis of 3-acylaminoisocamphanes, based on readily accessible raw material - isoborneol (I) and chloroacetonitrile. The interaction of isoborneol (I) in acetic acid with chloroacetonitrile under 20°C can serve as an example. As a result of this interaction, 3-exo-chloroacetamidoisocamphane (III) is formed with an admixture, 8-10%, of 2-exo-chloroacetamidobornane (IV).



I II III IV

The structure of the obtained chloroacetamides (III) and (IV) is confirmed by their spectra NMR ^{1}H and ^{13}C, and also the hydrolysis of these amides up to the known 3-exo-isocamphylamine and 2-exo-bornylamine. The structure of the genetically related amides (III, IV) makes it possible to suppose that the reaction of isoborneol with chloroacetonitrile goes through the formation stage of a nonclassical ion (II).

When the amide (III) is formed from alcohol (I) the Wagner-Meerwein rearrangement occurs in an unusual direction - bornane frame → isocamphane frame. It should be noted that usually, in acid mediums bornane derivatives are formed from isocamphane derivatives and not in reverse, which is observed in this case.

Literature

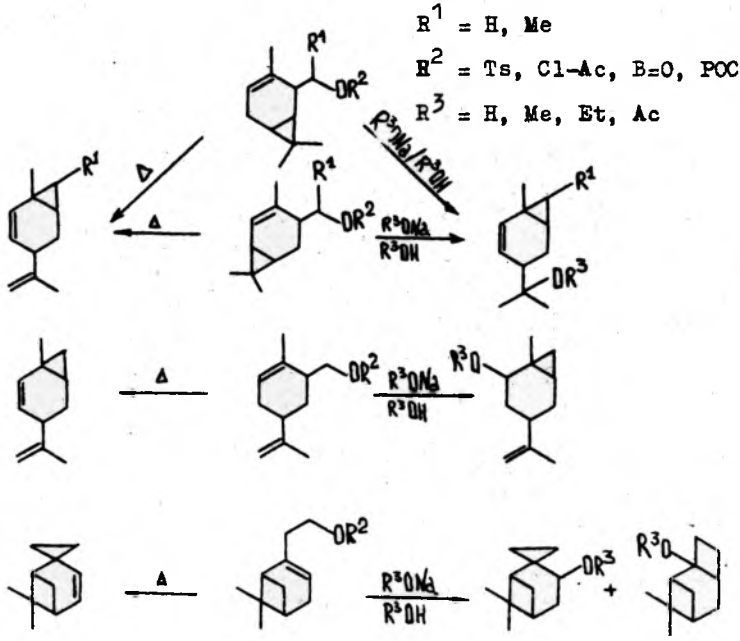
1. Kochetkov N.K., Chorlin A.J., Lopatina K.I. – J. Obsch. Chem., 1959, 29, No. 1, p. 75-81.

SMALL RING FORMATION IN REACTIONS OF TERPENE ESTERS

Vera Chuiko, Oleg Vyglazov

Institute of Physico-Organic Chemistry,
BSSR Academy of Sciences, Minsk, USSR

It has been established that in syn-elimination and nucleophilic substitution of the number of terpenoid esters of 4-oxymethyl-2-carene (1), 4-(1-oxyethyl)-2-carene (2), 2-oxymethyl-3-carene (3), 2-(1-oxyethyl)-3-carene (4), 6-oxymethyl-p-1,8-menthadiene (5), 2-(2-oxyethyl)-6,6-dimethyl-2-norpinene (6), three- and four-membered rings are formed.



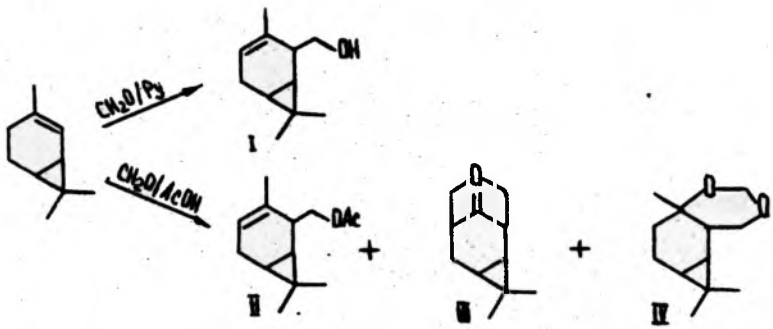
The ionic and concerted mechanisms of the reactions studied have been discussed.

2-CARENE IN THE PRINCE REACTION

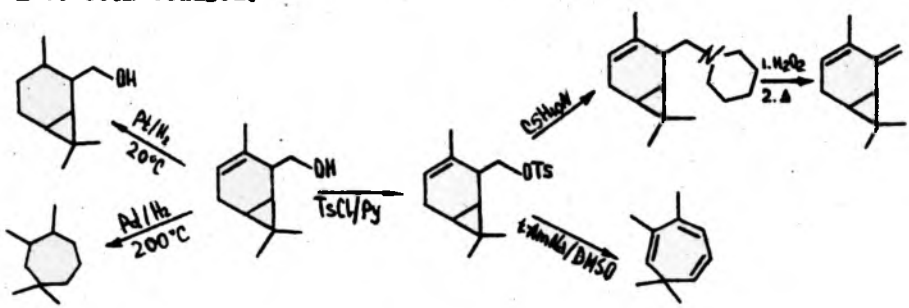
Oleg Vyglazov and Tat'yana Urbanovich

Institute of Physico-Organic Chemistry,
BSSR Academy of Sciences, Minsk, USSR

The products of thermal and acid-catalized condensation of 2-carene and formaldehyde have been investigated. Depending on the reaction conditions, homoallylic alcohol I or the mixture of ester II and ethers III and IV are the main products.



Some chemical transformations of homoallylic alcohol I have been studied.



The skeletal rearrangement mechanism of alcohol I under the conditions of vapour-phase hydrogenation and trans-elimination is discussed.

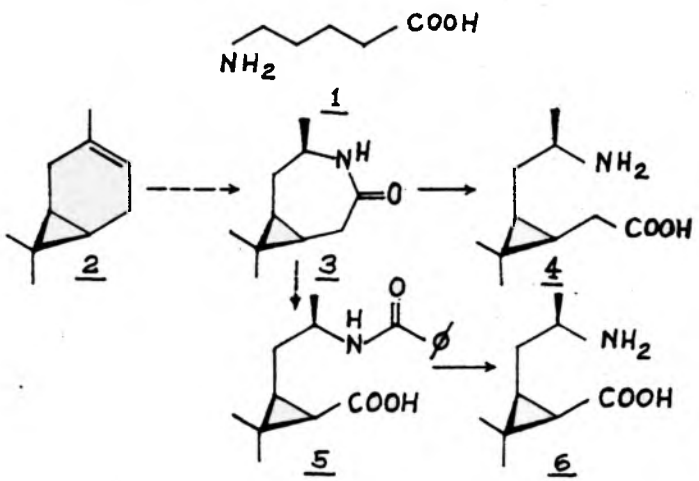
TWO NEW GABA ANALOGS FROM (+)-3-CARENE

Mirosław Walkowicz and Sławomir Janicki

Institute of Organic and Physical Chemistry
Technical University, Wrocław, Poland

We have synthesized two new analogs of known inhibitory neurotransmitter, γ-aminobutyric acid (GABA) (1) with three centers of chirality. We started from (+)-3-carene (2) and after known three-step synthesis we obtained (-)-4-caranone oxime in good yield. Then, using TosCl in acetone and aq. NaOH, we rearranged the oxime to lactame 3. This lactame after alkaline hydrolysis gave amino acid 4. The same lactame after benzoylation and hydroxymethylenation by means of NaH and HCOOEt and after alkaline oxidation of the intermediate gave amido acid 5. This amide after alkaline hydrolysis gave the second title compound, amino acid 6.

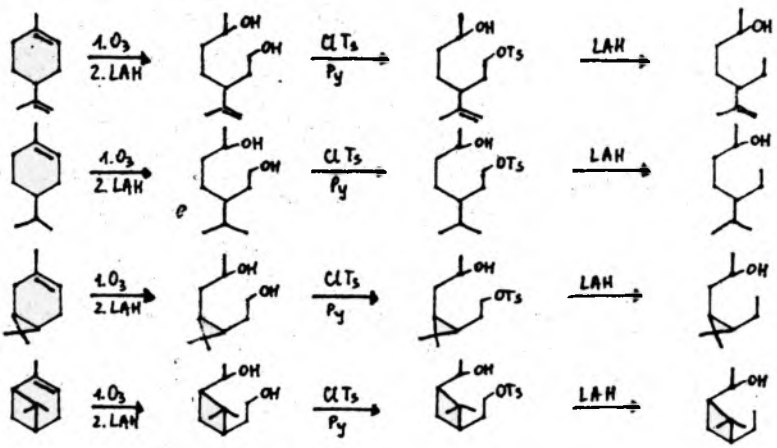
Structures of all compounds were confirmed by the IR, ^{1}H NMR and ^{13}C NMR spectra.



SYNTHESIS OF SECONDARY MONOTERPENE ALCOHOLS

Jerzy Podlejski, Magdalena Sikora
Institute of General Food Chemistry
Technical University, Łódź, Poland

Investigating possibility of utilization of terpene hydrocarbons in synthesis of odour compounds Kulesza and coworkers /1/ have obtained from limonene, 1-p-menthene, 3-carene and alfa-pinene, four primary alcohols with interesting odour properties: 3-isopropenyl-1-heptanol, 3-isopropyl-1-heptanol, 1-/2-hydroxyethyl/-3,3-dimethyl-2-propylocyclopropane and 1-ethyl-3-/2-hydroxyethyl/-2,2-dimethylocyclobutane.
We have undertaken research on synthesis of secondary alcohols from the same hydrocarbons. At first corresponding diols were obtained by ozonolysis and $LiAlH_4$ reduction. Primary hydroxyl group in diols was selectively esterified by means of p-toluenesulphonyl chloride and then monotosylate was reduced with $LiAlH_4$ yielding following 4 secondary alcohols: 2-hydroxy-5-isopropenylheptan, 2-hydroxy-5-isopropylheptan, 1-/2-hydroxypropyl/-3,3-dimethyl-2-ethylcyclopropane, 1-ethyl-3-/1-hydroxyethyl/-2,2-dimethylcyclobutane /see scheme/:



Structures of secondary alcohols obtained were determined by GLC, ^1H-NMR, IR and MS method and their odour properties were described.

1. Kulesza J. and coworkers - Riechstoffe Aromen Körperpflegemittel 26, 278 /1976/

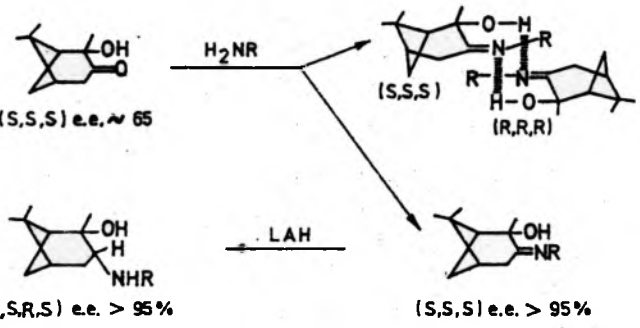
2α-HYDROXY -3α-[N-ALKYL(ARYL)] PINANOAMINES.

The nature of some Schiff bases of 2α-hydroxypinan-3-one and its derivatives. Crystal structure of racemic 2α-hydroxy -2,6,6-trimethylbicyclo [3.1.1] hepta-3-ylidenaminobenzene.

Stanisław Wojciech Markowicz[*], *Janina Karolak-Wojciechowska*[**], *Witold Kwiatkowski*[*]

[*]*Institute of Organic Chemistry,* [**]*Institute of General Chemistry, Technical University ,90-924 Łódź, Żwirki 36 Poland*

Some Schiff bases of 2α-hydroxypinan-3one, being precursors of 2α-hydroxy-3α-[N-alkyl(aryl)]pinanoamines were obtained in two forms: solid form (racemate) and liquid form (optically pure). As it appeared from crystallographic studies of the racemic form in the solid state there are intramolecular-H-bonded dimers.



Structural research was performed within the framework of the Polish Ministry of Education programme R.P.II.10. The remaining studies were financed by CPBP 01.13.2.5 programme and by Pharmaceutical Plant "Polfa" Pabianice.

Markowicz S.W.(1987), XII Conference on Isoprenoids, Pec, Czechoslovakia, Oct 4-11, Abstract 164, Preliminary comm. dedicated to Prof. S. Valenta on the occasion of his 60th anniversary. Markowicz S.W., Karolak-Wojciechowska J., Kwiatkowski W.,(1988) J. Crystallogr. Spectrosc. Res. 18,(3),335-345, Karolak-Wojciechowska J., Kwiatkowski W., Markowicz S.W., J. Crystallogr. Spectrosc. Res.,(1988) in press, and references cited therein.

SYNTHESIS AND REACTIONS OF α,β-UNSATURATED TERPENE AMINES AND TOLUENOSULFONAMIDES

Iwona WYŻLIC and Arkadiusz UZAREWICZ

Institute of Chemistry, Nicolaus Copernicus University, 87-100 Toruń, Poland

Toluenosulfonamidation of terpenes such as /+/- and /-/-2-pinenes, /-/-2/10/-pinene, /+/-3-carene and /+/-limonene by imidoselenium compounds gave α,β-unsaturated toluenosulfonamides which were reduced by sodium in ammonia to the corresponding amines. We have demonstrated that toluenosulfonamidation-reduction of these terpenes provides a highly efficient route to optically active α,β-unsaturated terpene amines.

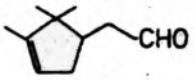
Hydroboration-oxidation of these toluenosulfonamides and amines produced hydroxy-toluenosulfonamides and amino-alcohols, respectively. Coordination compounds /$RNH_2 \cdot BH_3$/ were formed in the first step of the reaction of amines with borane. Their structures were determined by mass spectrometry. It is shown that the amino group in amines is more reactive toward borane than the double bond. However, the double bond of toluenosulfonamides reacts more readily with borane than the toluenosulfonamide group.

Mechanism of the hydroboration reaction of α,β-unsaturated toluenosulfonamides and amines is proposed.

SYNTHESIS AND REACTIONS OF FENCHOLENALDEHYDE

K. Schulze and H. Uhlig
Sektion Chemie der Karl-Marx-Universität Leipzig, DDR

Rearrangements of α-pinene oxide with acid or base catalysts are well known. Homogeneous reactions with Lewis acids such as $ZnBr_2$ give α-campholenaldehyde (1) and with $Al(i\text{-}PrO)_3$ the isomeric aldehyde 2 via trans-pinocarveol and bromoisofenchol. We discuss the mechanism of these two rearrangements. The aldehyde 2 is formed by a fenchane rearrangement therefor we call it fencholenaldehyde.



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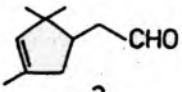

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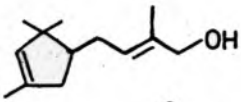

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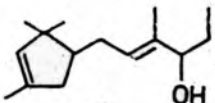


4

α-Campholenaldehyde besides some other reactions, is used for the synthesis of fragrance compounds with sandal wood odor. Very few was known about fencholenaldehyde. We have synthesized many fencholenaldehyde derivatives e.g. 3 and 4 and compared them with the analogeous campholen derivatives. They have fruity, woody, musk and only in some cases sandal wood odor.

BIOTRANSFORMATION OF LIMONENE BY SOLANUM AVICULARE AND DIOSCOREA DELTOIDEA FREE AND IMMOBILIZED PLANT CELLS

T. Vanek, T. Macek, I. Valterova, S. Vasickova, K. Stransky and K. Ubik.
Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences
Flemingovo nam.2, 166 10 Praha 6, Czechoslovakia

The biotransformation of monoterpenes verbenol and verbenone by suspension cultures of Solanum aviculare was recently studied in our laboratory (1). In this paper we described the biotransformation of limonene by Solanum aviculare and Dioscorea deltoidea. Free cells incubated in medium according to Murashige and Skoog, supplemented by naphtaleneacetic acid and kinetin (2), transformed at pH 5.7 limonene to carvone, cis-carveol, trans-carveol and other minor products. The maximal yield was achieved at temperature 27° C after 6 days. The effect of different immobilization methods on this reaction has been investigated. The immobilized biocatalyst was prepared by binding the cells to polyphenyleneoxide (3), by entrapping them into the matrix of alginate, carrageenan (4) and pectate gels (5) and by permeation into polyurethane foam (6). Cells immobilized into polyurethane foam yielded the same results as the free cells, while the results obtained when using other binding methods differred in the ratio of the main products obtained. The structures of products were determined using GC-MS and GC-IR.

(1) T. Vanek, T. Macek, K. Ubik, K. Stransky (1988), Abstr. 14th IUB Congress, Prague, Vol. 5, FR:587, p.190

(2) T. Macek (1988), in: Biotechnology in Agriculture and Forestry, Y.P.S. Bajaj, ed., Springer Verlag Berlin, Heidelberg, New York, Tokyo, Vol. 7, p. 443

(3) T. Macek, T. Vanek, B. Sisova, V. Jirku, I. Benes, V. Kubanek, B. Veruovic (1985), Proc. 16th FEBS Meeting, Yu. A. Ovchinnikov, ed., VNU Science Press, Utrecht, Holland, Part C, Lecture Sect. Biotechnol. p. 197

(4) P. Brodelius,K. Nilsson (1980), FEBS Lett 103, 93

(5) T. Vanek, R. Vankova, T. Macek (1988), Immobilization of plant cells and protoplasts into pectate gel. Czechoslovak patent, P.V. 5942-88

(6) K. Lindsey, M.M. Yeoman (1984), J. Exp. Bot. 35, 1684

TRANSFORMATION OF SOME MONOTERPENIC ESTERS BY ARMILLARIELLA MELLEA.

B.Draczyńska-Łusiak, A.Siewiński, Cz.Wawrzeńczyk
Inst.of Fundamental Chemistry, Agricultural University of Wroclaw.

In our earlier studies* on thy ability of Armillariella mellea species to transform some terpenic compounds, we found thet this organism is able to hydrolise some terpenic esters (e.g.menthyl and sobrelyl acetates). We have observed that the hydrolysis was followed by additional hydroxylation in terpenic skeleton to obtain respective diols and hydroxyesters. No hydroxylation was observed when an alkohol was used as a substrate.

Now, we examine the pathways of the transformation of other simple monotetrpenic alkohols acetates as: (±) citronellyl, (±) E and Z isomers of 3,7-dimethyl-4-octene-1-yl, geranyl and farnesyl acetates by Armillariella mellea.

In all cases the hydrolysis was the main reaction but we also identified in the postreaction mixture the presence of respective diols. Transformations of (±) citronellyl acetate and (±) 3,7-dimethyl-4-octene-1-yl acetate was enantioselective.

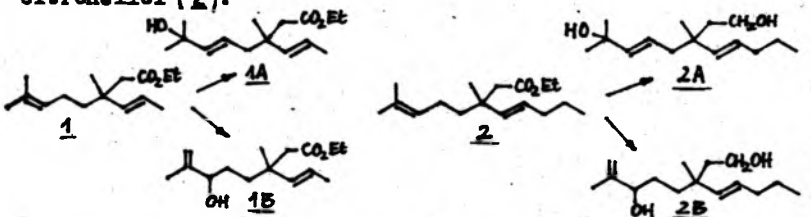
*/ B.Draczyńska-Łusiak, Thesis 1986 Agricultural University of Wroclaw.

TRANSFORMATIONS OF 3-ALKENYLSUBSTITUTED DERIVATIVES OF CITRONELLIC ACID BY SPIRODELA OLIGORRHIZA

P. Pawłowicz, C. Wawrzeńczyk, A. Siewiński

Department of the Fundamental Chemistry, Agricultural University of Wrocław

In our previous paper [1] we reported the preliminary results of transformation of 3-alkenyl substituted esters of citronellic acid by Spirodela oligorrhiza. Now we present some further details connected with the structures of the products of the transformations of ethyl ester 1 and 3-(1-pentenyl)--citronellol (2).



Two hydroxyesters 1A (49%) and 1B (35%) were isolated as the products of the transformation of ester 1. Diols 2A (59%) and 2B (41%) were formed in the transformation of alcohol 2.

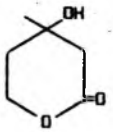
[1] P.Pawłowicz, C. Wawrzeńczyk, A. Siewiński; International Symposium on Endocrynological Frontiers of Insect Ecology, Szklarska Poręba 1987

STUDIES ON A NEW CHEMOENZYMATIC SYNTHESIS OF CHIRAL MEVALONOLACTONE

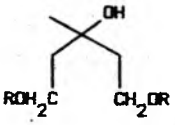
P. Ferraboschi, P. Grisenti, E. Santaniello
Dipartimento di Chimica e Biochimica Medica
Università di Milano - Italy

We have studied new approaches to the synthesis of (R)- and (S)-mevalonolactone (1, MVL) utilizing chemical or enzymatic methods for the introduction of the chirality at C-3.

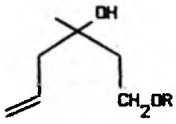
The enzymatic hydrolysis of diesters of the prochiral triol (2) proceeded with very low enantioselectivity; lipases and acylcholinesterases hydrolyzed esters of enediol (3) with a maximum 65% ee.



(1)



(2)



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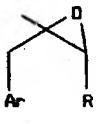

(4)

The enzymatic resolution of the epoxyesters (4, R=COOR', CH_2COR') catalyzed by pig liver esterase (PLE) or lipases may constitute a valid alternative to the above enzymatic hydrolyses and are under current investigation.

Also the preparation of the chiral epoxyalcohol (4, R=CH_2OH) has been studied. The corresponding allyl alcohol has been epoxidized under the Sharpless conditions efficiently and with high ee. The best chemical conversion of the epoxyalcohol (4, R=CH_2OH) to MVL (1) has also been investigated and now we are able to prepare MVL (1) in 40% yields from the epoxyalcohol (4, R=CH_2OH).

SYNTHESIS OF 12-DIMETHYLSILASQUALENE AND ITS TERMINAL EPOXIDES

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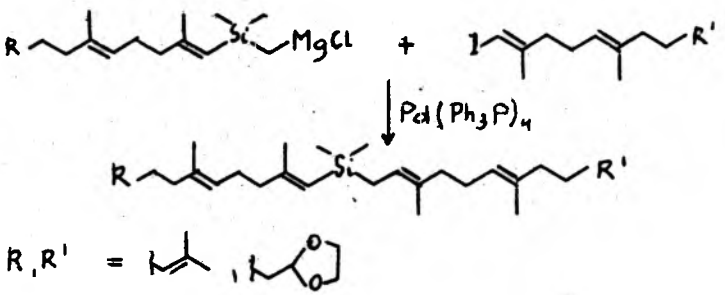
b. Department of Chemistry, State University of New York, Stony Brook, N.Y. 11794, USA

12-dimethylsilasqualene, 2,3-epoxy-12-dimethylsilasqualene and 2,3epoxy-13-dimethylsilasqualene were obtained from geranylacetone in multistep syntheses. The coupling reaction of corresponding Grignard compounds and vinuyl iodides [1/] was applied as a key step in these syntheses:



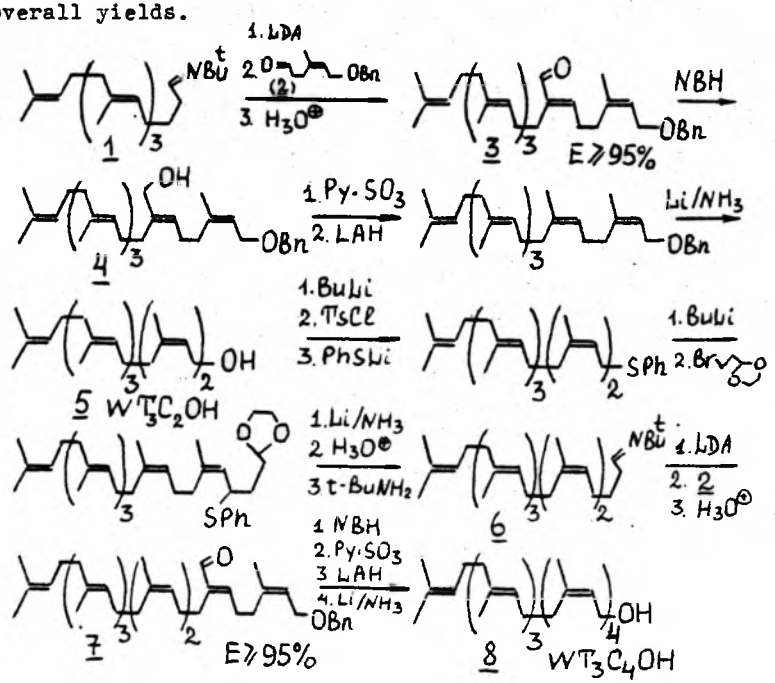
The final epoxides were obtained from reactions of corresponding dimethylsilasqualenoid aldehydes with diphenylsulfonium isopropylide. Silasqualene and its epoxides were checked as inhibitors of oxidosqualene cyclase from pig liver.

1. G.D. Prestwich, C.Wawrzeńczyk, Tetrahedron Letters, 30, 403 (1989)

TOTAL SYNTHESIS OF HEXAPRENOL WT_3C_2OH AND OCTAPRENOL WT_3C_4OH

N.Ya.Grigorieva, O.A.Pinsker, A.M.Moiseenkov
N.D.Zelinsky Institute of Organic Chemistry,
Academy of Sciences, Moscow, U.S.S.R.

The title polyprenols were isolated recently from fruits of Serenoa repens (Bart.) Small (Palmae) employed for the treatment of functional disorders related to prostate hypertrophy. The compounds have been synthesized according to developed by us earlier "blockwise" approach using highly stereoselective cross-aldol coupling of the aldimine I and 6 with the aldehyde 2 on key steps. Stereospecific transformation of intermediate (E)-acroleins 3 and 7 into respective target polyprenols 5 and 8 is accomplished via corresponding allylic alcohols like 4 in high overall yields.



TOWARDS UNDERSTANDING OF RELACTONIZATION PROCESS- QUANTUM-CHEMICAL AND MOLECULAR MECHANICS APPROACH

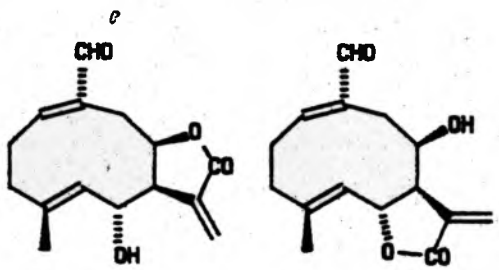
G.Sroczyńska, A.Popiel, J.Komasa, J.Rychlewski and U.Rychlewska

Department of Chemistry, A.Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland

Naturally occuring sesquiterpene lactone Schkuhriolide (I) undergoes relactonization to its *allo* isomer (II) upon strong alkaline treatment and subsequent acidification[1]. To study the nature of this process we used semiempirical: MNDO and CNDO/2, and molecular mechanics MM2 methods. The relative energy differences between both isomers were calculated for X-ray[2,3] and optimized geometries. These energy differences are relatively small, suggesting that relactonization is rather kinetically than thermodynamically driven.

Proton acceptor affinity of the hydroxyl groups of the two isomers was estimated by means of the electrostatic potential maps, calculated at the CNDO/2 level. The results well mirror different hydrogen bonding pattern observed in the crystal structures of (I) and (II).

The geometry of the intermediate product based on MNDO and MM2 methods is postulated.



(I) (II)

[1] Z.Samek, M.Holub, E.Bloszyk, B.Drożdż, Z.Chem.,19,449(1979)
[2] U.Rychlewska, J.Chem.Soc.Perkin II,1641(1982)
[3] U.Rychlewska, Acta Cryst.C39,1303(1983)

VERIFICATION OF STEREOSTRUCTURES OF GUAIANOLIDE SESQUITERPENE LACTONES: BADKHYSIN AND ISOBADKHYSIN BY X-RAY CRYSTALLOGRAPHY

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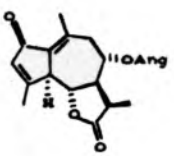
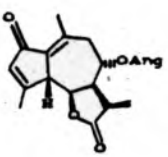
b) Institute of Botany, Azerbaijan Academy of Sciences, 370073 Baku, USSR

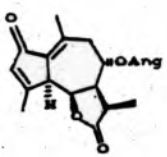
Badkhysin (1), a sesquiterpene lactone isolated from roots of Ferula oopoda, was initially assigned the stereostructure (Ia)[1]. A new interpretation of ^{1}H NMR data revised its structure to (I)[2] which we now confirm on grounds of X-ray analysis. We also establish the stereostructure of isobadhysin (II), thus providing evidence that isomerization of (I), induced by alkali treatment, takes place at C(5) carbon atom.



(Ia)



(I)



(II)

1. S.V. Serkerov, Khim. Prir. Soedin., 510 (1980)
2. U. Rychlewska, D.J. Hodgson, M. Holub, M. Buděšinský, Z. Smitalová, Coll. Czechosl. Chem. Commun. 50, 2607 (1985)

ISOLATION AND STRUCTURE OF FURANTRIOL A NEW SESQUITERPENE FROM LACTARIUS MITISSIMUS

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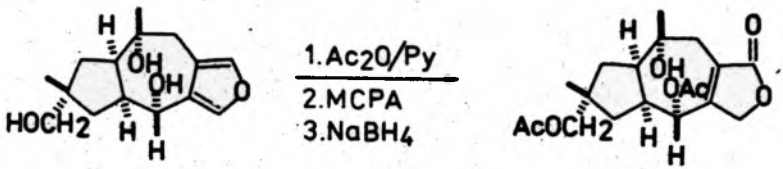
Institute of Organic Chemistry, of Polish Academy of Sciences, 01-224 Warsaw, Poland.

By multiple column chromatography as well as preparative HPLC furantriol (1) a new sesquiterpene was isolated from the ethanolic extract of Lactarius mitissimus. The structure of 1 was established by spectroscopic studies especially ^{1}H and ^{13}C NMR. The transformation of 1 into lactarorufin B whose structure was established by X-ray [1], confirmed our assignments unambigously.



1 2

1. M. Bogucka-Ledóchowska, A. Heapel, Z. Dauter, A. Könitz, E. Borowski, W.M. Daniewski and M. Kocór. Tetrahedron Letters, 1976, 2267.

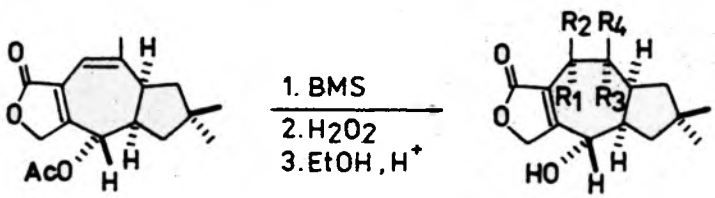
CHEMICAL CORELATION OF LACTARORUFIN A WITH LACTARORUFIN E

Włodzimierz M. Daniewski[a], Maria Gumułka[a], Katarzyna Ptaszyńska[a], Piotr Skibicki[a], Ulla Jacobsson[b] and Torbjorn Norin[b].

a) Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland.

b) Department of Organic Chemistry, Royal Institute of Technology, S-100-44 Stockholm, Sweden.

The hydroboration of anhydrolactarorufin A (1), followed by oxidation and hydrolysis afforded a mixture of dihydroxy sesquiterpenes which was separated by preparative HPLC to give 3-epi-lactarorufin D (2a), lactarorufin E (2b), lactarorufin A (2c) and 3-epi-lactarorufin E (2d). The structures were substantiated by high field ^{1}H NMR spectroscopy which included decoupling experiments and NOEDS investigations. Stereochemistry of the hydroboration reaction will be discussed.



1 2

2 a. R_1=OH ; R_2=R_3=H ; R_4=CH_3 (3-epi-lactarorufin D)

2 b. R_1=R_4=H ; R_2=OH ; R_3=CH_3 (lactarorufin E)

2 c. R_1=R_2=H ; R_3=OH ; R_4=CH_3 (lactarorufin A)

2 d. R_1=R_3=H ; R_2=OH ; R_4=CH_3 (3-epi-lactarorufin E)

COMPARATIVE STUDIES OF FURANDIOL OXIDATION INTO LACTONES BY MEANS OF NBS AND MCPBA

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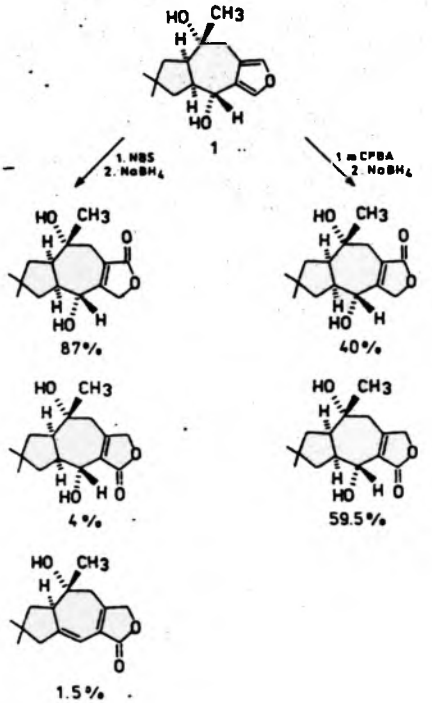
a) Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland.
b) Department of Organic Chemistry, Royal Institute of Technology, S-100-44 Stockholm, Sweden.

The furandiol (1) a sesquiterpene present in all ethanolic extracts of mushrooms of Lactarius family is an important intermediate in biogenesis of lactones of lactarane skeleton. In studying the antifeedant activity of these lactones it was important to find the deterent activity of lactones with the carbonyl group at C-13 of the lactarane skeleton. Such compounds can be obtained by oxidation of 1 by NBS or MCPA. The reactior course and its products will be discussed.

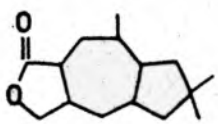


ANTIFEEDANT ACTIVITY OF SESQUITERPENES OF LACTARIUS ORIGIN

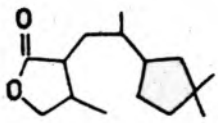
Włodzimierz M. Daniewski[a], Maria Gumułka[a], Katarzyna Ptaszynska[a], Piotr Skibicki[a], Bohdan Drożdż[b], Elżbieta Błeszyk[b] and Sture Stromberg[c].

a) Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland.
b) Department of Medicinal Plants, Academy of Medicine, Poznań, Poland.
c) Department of Organic Chemistry, Royal Institute of Technology, S-100-44 Stockholm Sweden.

Antifeedant activity, as a part of chemical defense system of mushrooms of Lactarius family will be discussed. Structure activity relationship will be presented. The sesquiterpenes of the following skeletons were investigated: lactarane (1), secolactarane (2), isolactarane (3), marazmane (4) and 13-nor-marazmane (5).



1



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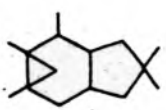

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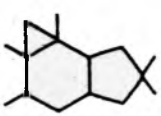

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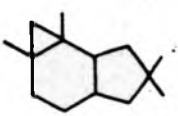
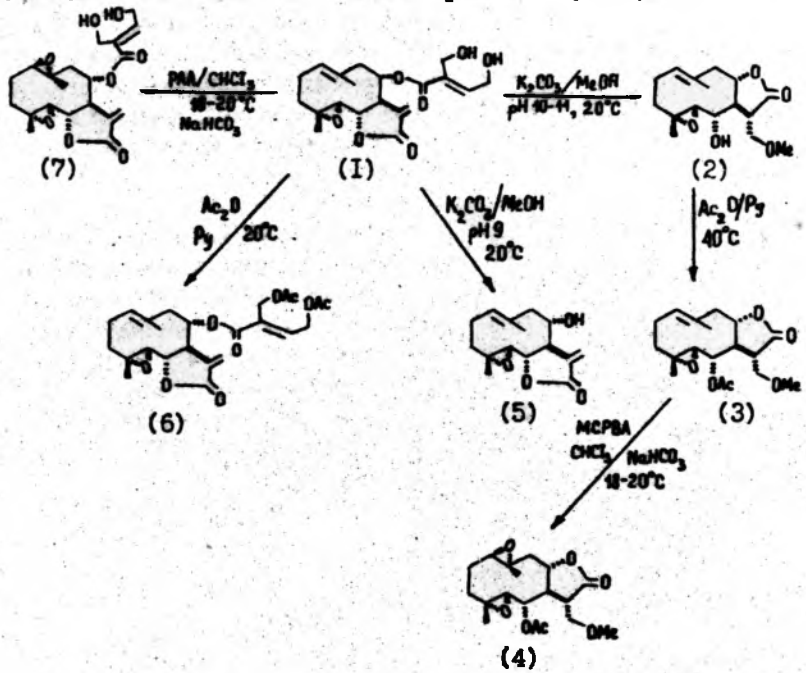


5

CHEMICAL MODIFICATION OF THE SESQUITERPENE LACTONE, STIZOLICIN

S.M.Adekenov, N.M.Gafurov
Institute of Organic Synthesis and Coal Chemistry
of the Kazakh Academy of Sciences
Karaganda, U.S.S.R.

The following derivatives (2),(3),(4),(5),(6) and (7) have been obtained by chemical modification (acylation, hydrolysis, epoxidation) of the trans,trans-germacranolide,stizolicin (1),isolated from Stizolophus balsamita (Lam.)Cass.ex Takht. and S.coronopifolius (Lam.)Cass.



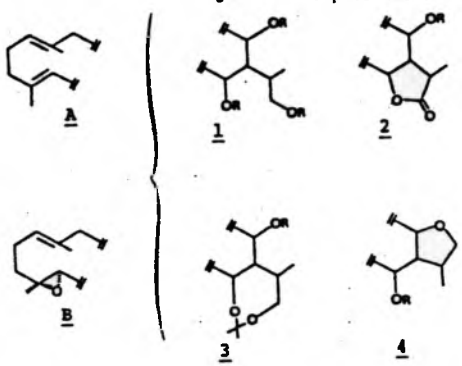
The structures of the synthesized compounds have been determined according to the data of IR-,UV-,NMR-,mass-spectra and X-ray analysis.

REMARKABLE STEREOSELECTIVITY IN THE ALLYLIC OXIDATION OF MEDIUM-SIZE DIOLEFINS AND EPOXYOLEFINS

Giovanni Appendino, Roberto Vola, Patrizia Lusso
Dipartimento di Scienza e Tecnologia del Farmaco, TORINO (Italia)
Pierluigi Garboldi
Dipartimento di Scienze Chimiche, CAMERINO (Italia).

The stereochemical outcome of the allylic oxidation (SeO_2, TBHP) of a set of structurally related germacradienes (1a--4a) and epoxygermacranes (1b--4b) was investigated. In all cases chemo- and regioselectivity of the reaction were the same (attack at the 1,10 double bond, oxidation of the allylic methyl), but remarkable differences were observed as regards stereoselectivity, since the oxidation of compounds 2a,b occurred with inversion of configuration of the 1,10 double bond, whereas in all other cases the reaction took place with ritention of configuration of the double bond.

Transannular interaction between the endocyclic double bonds affected only the rate of the reaction, that was much slower in the epoxy olefins than in their corresponding diolefins. Remarkable differences of reactivity within the set of compounds investigated were also observed as regards electrocyclic and electrophilic-induced reactions of the double bond(s). Preliminary attempts to rationalize these data on stereo-electronic grounds are presented.

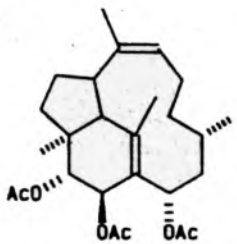


TRINERVITANE DERIVATIVES FROM THE FRONTAL GLAND SECRETION OF Nasutitermes nigriceps TERMITE SOLDIERS

Irena Valterová, Miloš Buděšínský and Jan Vrkoč

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague, Czechoslovakia

Frontal gland secretion of termites from the subfamily Nasutitermitinae is known to contain monoterpene hydrocarbons and polyoxygenated diterpenes with bi-, tri-, and tetracyclic skeletons. Recently, we investigated in detail the composition of the defense secretion of Nasutitermes nigriceps termite soldiers from Mexico. Eight monoterpene hydrocarbons were found in the volatile fraction. In the non-volatile fraction, five compounds with the tricyclic trinervitane skeleton were present. The determination of the structure of a new triacetate (I) is discussed. The composition of the non-volatile fraction differs from that of the secretion of the same species collected in Peru and Panama.



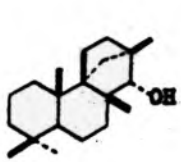
I

ISOMERIZATION OF (1S,2S,7S,10R,11S,12S)-2,6,6,10,12-PENTAMETHYLTETRACYCLO[10.2.1.$0^{1,10}$.$0^{2,7}$]PENTADECAN-11-OL ON PHOSPHORUS OXYCHLORIDE DEHYDRATION

N.D.Ungur, A.N.Barba, S.T.Malinovsky, P.F.Vlad

Institute of Chemistry, Moldavian SSR Academy of Sciences, 277028, Kishinev, USSR

It has been shown that phosphorus oxychloride dehydration of (1S,2S,7S,10R,11S,12S)-2,6,6,10,12-pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]pentadecan-11-ol (I) one of the products of the acidic cyclization of a range of labdane diterpenoids gives a mixture of three hydrocarbons: the known (1R,2S,7S,10S,11R,12S,13S)-2,6,6,10,12-pentamethylpentacyclo[10.2.1.$0^{1,10}$.$0^{2,7}$.$0^{11,13}$]pentadecane (II) /1/ and the new (1R,2S,7S,10S,11S)-2,6,6,10,12-pentamethyltetracyclo[9.2.2.$0^{1,10}$.$0^{2,7}$]pentadeca-12(13)-en (III) and (1R,2S,7S,10S,11S)-2,6,6,10-tetramethyl-12-methylenetetracyclo[9.2.2.$0^{1,10}$.$0^{2,7}$]pentadecane (IV) with a new carbon skeleton. The structure and stereochemistry were elucidated on the basis of chemical transformations and confirmed by X-ray analysis.



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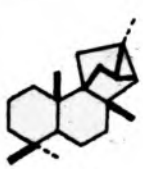
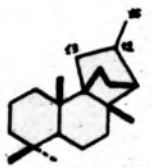


II



III $\Delta^{12(13)}$
IV $\Delta^{12(16)}$

/1/ P.F.Vlad, N.D.Ungur, A.N.Barba, S.T.Malinovsky, Yu.A.Simonov, T.I.Malinovsky, Khim. Prirod. Soed. 203 (1988).

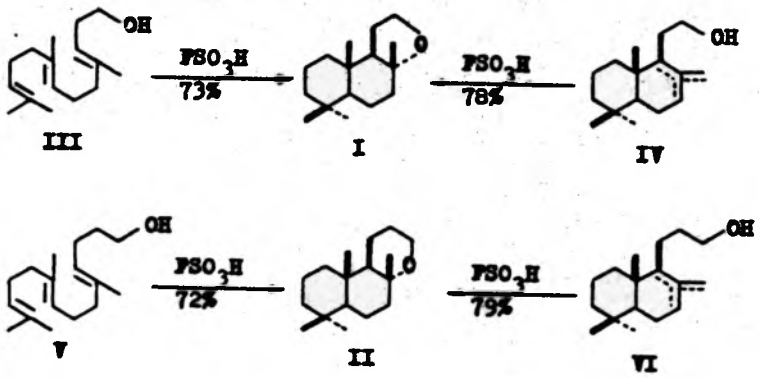
SYNTHESIS OF AMBROX AND HOMOFIXATEUR

N.D.Ungur, V.B.Perutsky, P.F.Vlad

Institute of Chemistry, Moldavian SSR Academy of Sciences, 277028, Kishinev, USSR

Ambrox (3a,6,6,9a-tetramethyl-trans-perhydronaphto-[2,1-b]furan) (I) and homofixateur (4a,7,7,10-tetramethyl-trans-perhydronaphto[2,1-b]pyran (II), two very important compounds for parfumeria, have been synthesized either by superacidic cyclisation of E,E-homofarnesol (III) or of the mixture of isomeric bicyclohomofarnesols (IV) and E,E-bishomofarnesol (V) or the mixture of isomeric bicyclobishomofarnesols (VII), correspondinly.

It was shown, that the cyclisation of alcohols (III)-(VI) with fluorosulfonic acid in 2-nitropropane at -80°C represented an efficient structural - selective and stereospecific method for preparing ambrox (I) and homofixateur (II).



MICROBIAL ESTERIFICATION OF ABIETIC ACID

Jerzy Szykuła, Józef Orpiszewski, Cezary Hebda
Institute of Organic and Physical Chemistry, Technical University, 50-370 Wrocław, Poland

Elżbieta Szulkowska-Wojaczek, Jan Marek
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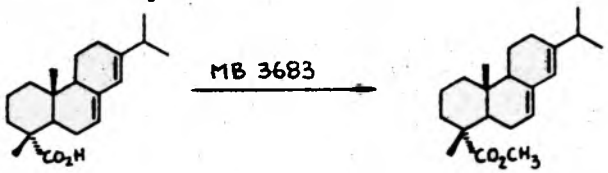
Abietic acid (1), the main acidic component of tall oil resins has high toxicity towards fish when present in the pulp mill effluent [1] . Also during the manufacturing tall oil sterols, some residual resin acids are transferred to the waste water.

In the course of the studies on tall oil, we examined the ability of some strains of Mycobacteria degradating the sterols side chain to convert abietic acids.

It was found that the strain Mycobacterium MB 3683 transforms abietic acid to its methyl ester (2) quantitatively, during 120 hr at the concentration of 200 mg/l at 30°C. Some factors influencing the reaction course were studied.



1 2

Preliminary biological test towards fry carp (Cyprinus carpio) showed no toxicity of methyl abietate at 5 mg/l during 96 hr whereas similar dose of abietic acid was lethal during 4 hr.

[1] *J.P.Kutney,E.Diaitriadis,G.M.Hewitt,M.Singh,B.R.Worth*, Helv.Chim.Acta 65, 661 (1982).

FAB-MS OF QUATERNARY SALTS OF SOME AMINOANDROSTANES

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[2]Chemical Works of Gedeon Richter Ltd., Budapest, Hungary

In our earlier paper we have shown the electron ionization (EI) mass spectra of some mono- and bis-quaternary salts formed by alkylation of 2- and/or 16-(4'-methyl-1-piperazino) androstane derivatives with various alkyl halides.

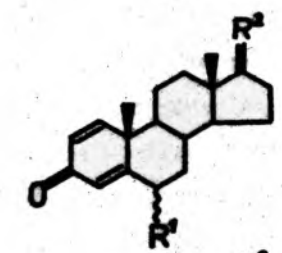
This work deals with the applicability of the recently developed fast atom bombardment mass spectrometry (FAB-MS) to these salts in comparison with the EI-MS results. FAB technique, producing ions from salts dissolved in glycerol matrix and bombarding the surface of the mixture with high energy neutral particles, leads to unique information about the mass of the cation (C) and the number of the quaternary centers. For example their mass spectra exhibit C^+ ions for the mono-, C^{++} ions for the bis-quaternary salts. In the latter case $C^{++}A^-$ cluster ions can also be observed. The fragmentation provides direct information about the quaternary alkyl-group(s) and for bis- or higher quaternary salts also about the quality of the anions. The EI-MS spectra, however, are more suitable to characterize the structure of the basis of the salt molecules. Consequently, it can be ascertained that the two methods provide complementary informations about the structure of this type of compounds.

STEROIDS ON BIOTECHNOLOGICAL BASIS. A NOVEL APPROACH TO 6-FLUORO ANDROSTANE- AND 6-FLUORO BISNORCHOLANE DERIVATIVES AS INTERMEDIATES IN THE SYNTHESIS OF FLUORO CORTICOIDS.

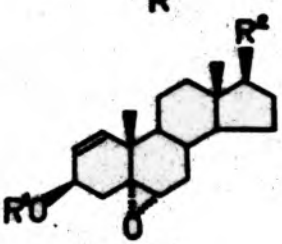
S. Ring, M. Wentzke, H. Stopsack, S. Schwarz
Division of Research, VEB Jenapharm, DDR-6900 Jena
German Democratic Republic

The products of the microbial sterol degradation 1 and 2 can be used as starting materials for the synthesis of the 6-fluoro steroids 3 and 4. Key intermediates in the preparation of the derivatives 3 and 4 are the epoxides 5 and 6, which were obtained from the steroids 1 and 2 in 5 steps each. Opening of the epoxide rings in compounds 5 and 6 by $BF_3.Et_2O$ and regeneration of the 1,4-dien-3-one structure gave the title compounds 3 and 4.

The epimerization of 6β-fluoro 1,4-dien-3-one steroids into the corresponding 6α-fluoro compounds proved to be a crucial step. Compounds 3 and 4 are intermediates in the synthesis of corticoids with fluorine in position 6.



1: R^1 = H; R^2 = O
2: R^1 = H; R^2 = α-H, β-CH(Me)CH_2OH
3: R^1 = F; R^2 = O
4: R^1 = F; R^2 = α-H, β-CH(Me)CH_2OH



5: R^1 = Ac; R^2 = OAc
6: R^1 = Ac; R^2 = CH(Me)CH_2OH

EPIMERIC 17-HYDROXYDERIVATIVES OF 14β-ANDROST-5-EN-3β-OL ACETATE.

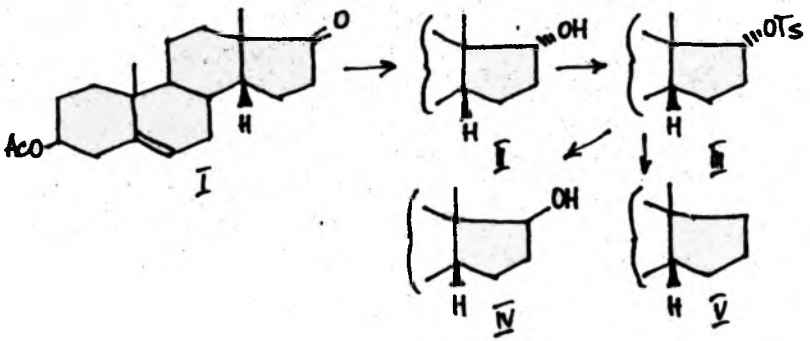
Ivan ČERNÝ, Vladimír POUZAR, Pavel DRAŠAR and Miroslav HAVEL

Institute of Organic Chemistry and Biochemistry Czechoslovak Academy of Science, 166 10 Prague, Czechoslovakia

The aim of our work is to prepare and to prove the structure of the title epimeric derivatives designed for glycosylation experiments in CD-cis steroids.

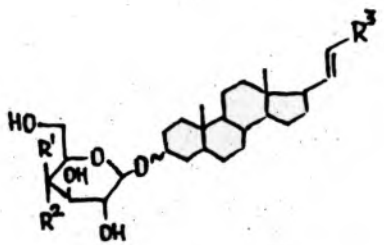
As a starting compound we used 3β-acetoxy-14β-androst--5-en-17-one (I), available in seven steps from dehydroepiandrosterone. Sodium borohydride reduction of I yielded stereoselectively 14β-androst-5-en-3β,17α-diol 3-acetate (II) in nearly quantitative yield. Epimerisation on C-17 was accomplished in two steps: tosylation with tosyl chloride in pyridine gave 17-O-tosyl derivative III, which was then reacted with sodium nitrite in hexamethyl phosphoric triamide (HMPA). This reaction takes 4 h of heating on 90°C for completion and gives only moderate yield of target 14β--androst-5-en-3β,17β-diol 3-acetate (IV).

To prove the structure we compared the ^{1}H and ^{13}C NMR spectra of epimers II and IV with the spectrum of parent deoxy derivative V, prepared from tosylate III by treating with sodium iodide and zinc in 1,2-dimethoxyethane.



GLYCOSIDES OF STEROIDS WITH THREE-CARBON SIDE CHAIN IN THE POSITION 17β

H. Chodounská, V. Pouzar, P. Drašar, and M. Havel
Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Flemingovo 2, 166 10 Prague 6, Czechoslovakia



R^1, R^2 = OH, H or H, OH; R^3 = CN, $COOCH_3$, or $COOCH_2CH_3$

In the program of a search for steroid conjugates with reduced lipophilicity there have been prepared 3β-D-galactosides and glucosides from the parent 3α or 3β steroidal alcohols with the 17β unsaturated, three carbon side chain. Tetra-O-acetyl-α-D-gluco- and galactopyranosyl bromides were used as the glycosylation reagents in the reaction[1] catalyzed by silver silicate. The glycosides were isolated after saponification of reaction products (without isolation of the acetates), to achieve higher overall yields, and characterized as the unprotected tetrols. Their structure was confirmed by ^{1}H NMR spectra (200 MHz) of the tetraacetates prepared by acetylation.

These conjugates are being examined for their biological activity as the evaluation of parent steroid aglycons faced an unsatisfactory solubility *in media* used for biological testing.

Reference: 1. Paulsen H., Lockhoff O.: Chem. Ber. *114*, 3102 (1981).

Some notes on reductive deoxygenation of steroidal alcohols

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Various experimental methods have been applied to achieve the transformation of steroidal alcohols into their deoxy derivatives. In a search for the most universal technique the substrates were chosen which were both sterically hindered and prone to rearrangement, i.e. 6β-hydroxy-5β-methyl-19-nor-9-pregnene derivatives.

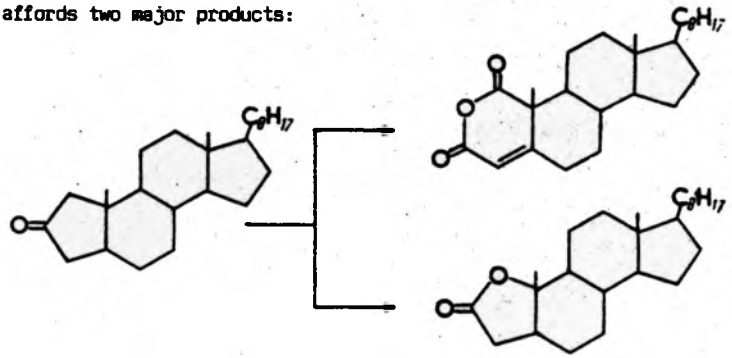
A set of transformations of these compounds and their reactive derivatives is presented (i.e. deoxygenation via mesylates, acetates, thiobenzoates etc.). Special attention was given to reactions having radical intermediate mechanism. Deoxygenated products will be used for the synthesis of analogues of progestins with modified biological activity. Structure of these compounds was verified by physical methods including X-ray diffraction.

REACTIONS OF STEROIDAL FIVE-MEMBERED KETONES WITH BEZENESELENINIC ANHYDRIDE

Jacek W. Morzycki and Jolanta Mudź

Institute of Chemistry, University of Warsaw, Białystok Branch, Poland

Cyclic six-membered ketones are smoothly dehydrogenated in high yield using benzeneseleninic anhydride generated in situ by oxygen atom transfer from iodoxybenzene, $PhIO_2$, to catalytic amounts of diphenyl diselenide. The same procedure has been used for oxidation of steroidal five-membered ketones. However the reactions require higher temperature and a longer reaction time. The oxidation of five-membered ketones is much more complex than in case of steroidal 3-ketones and other six-membered ketones.* For example the oxidation of A-nor-cholestanone affords two major products:



Some intermediates have also been isolated and the mechanism of the reaction will be discussed.

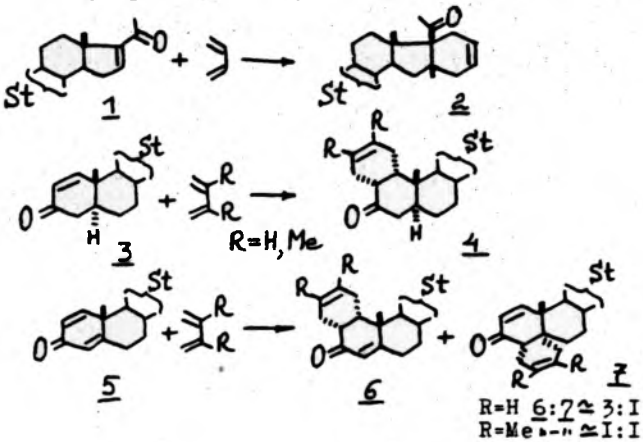
*D.H. Barton, C.R.A. Godfrey, J.W. Morzycki, W.B. Motherwell, S.V. Ley, J. Chem. Soc., Perkin Trans. I, 1982, 1947.

LEWIS ACID CATALYSIS AT HIGH PRESSURE: NEW METHODOLOGY FOR REALIZATION OF STERICALLY HINDERED DIELS-ALDER REACTIONS

I.Levina, A.Kamernitzky, L.Kulikova, B.El'yanov, E.Gonikberg.
N.D.Zelinsky Institute of Organic Chemistry, Academy of Sciences , Moscow, U.S.S.R.

Diels-Alder reaction of sterically hindered and non-reactive under conventional conditions conjugated steroidal ketones like 1,3,5 is now possible to perform using the combination of Lewis acid catalysis and high pressure technique. Thus, [4+2]cycloaddition of buta-1,3-diene with 16-methyl-16-dehydropregnenolone acetate 1 was found to give quantitatively the ketone 2 in the presence of catalytic amount of $AlCl_3$ at 14 kbar. Similarly, starting from (2,3-dimethyl)buta-1,3-diene and Δ^1-3-keto-5α-pregnanes 3, the cycloadducts 4 were obtained. Easily separable mixture of two monoadducts 6 and 7 was prepared from $\Delta^{1,4}$-3-ketones 5 in this way. It should be noted that the separate use of either high pressure technique or Lewis acid catalysis was proved to be ineffective in all above cases.

The structures of all the compounds synthesized were confirmed by spectral (NMR, MS) methods.



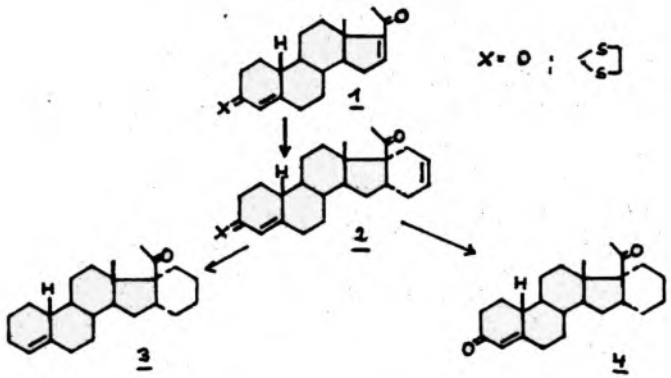
SYNTHESIS OF PROGESTAGENIC ACTIVE 16α,17α-CYCLOHEXANO-19-NOR-PROGESTERONE DERIVATIVES STARTING FROM 19-NOR-TESTOSTERONE

H. Kasch

Central Institute of Microbiology and Experimental Therapy Jena of the Academy of Sciences of the GDR

From previous work / 1 / we know that the progestagenic activity of progesterone can be increased by an additional 16α,17α-carbocycle. The same effect could be observed in the 19-nor-series / 2 /. Here we want to present a new way of a formal total synthesis of 16α,17α-cyclohexano-19-nor-progesterone derivatives 3 and 4 in which the carbocycle was introduced at the end of the reaction sequence.

Starting from 19-nortestosterone the acetyl group was build up via the unsaturated nitrile by Grignard reaction.



1 was transformed by Lewis acid catalyzed Diels-Alder reaction with butadiene into the 16α,17α-cyclohexeno compound 2. The Δ^4-3-keto-group doesn't act under this conditions as a dienophile. The cyclohexeno products 2 were transformed into 3 und 4.

This work was a part of a cooperation between the Steroid departments of the Central Institute of Organic Chemistry in Moscow and the Institute of Microbiologie in Jena.

Literature:

/ 1 / A.V.Kamernitzki, I.S.Levina et al.; J.Steroid Biochem. 16.61 (1982)

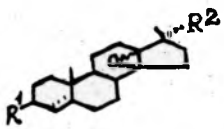
/ 2 / H.Kasch; publication in press

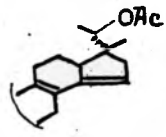
THE SYNTHESIS AND REARRANGEMENTS OF I3(I4)-EPOXY-I7β-METHYL-PREGNANES

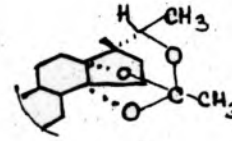
I.G.Reshetova, E.I.Chernoburova, V.S.Bogdanov, A.V.Kamernitzky

N.D.Zelinsky Institute of organic chemistry USSR Academy of Sciences, Moscow, USSR

The possibility of functionalization at C(I4) steroids was investigated on the example of series of I3(I4)-epoxy-I7β-methyl-I7α-pregnanes. Latter were prepared by Wagner-Meerwein rearrangement of normal 3,20-diacetoxy-, 3,20-diketo-pregnanes and followed by epoxidation of Δ^{I3}-double bond. Configuration of oxides was established by the study of NMR ^{I3}C, ^{I}H spectras. Treatment of the epoxides with $BF_3.Et_2O$ in CH_2Cl_2 or in benzene afforde the steroid olefines or the cyclisation products (ortoethers type, involving acetoxy group of side chain) depending upon the configuration of epoxide ring.







R^I=OAc, 5αH; R^2=C-CH_3OAc, I3α; I3β;

R^I=O; Δ^4; R^2=$COCH_3$; R^I=O; 5αH; R^2=$COCH_3$, I3α.

NOVEL D-HOMO STEROID DERIVATIVES

Evgenija Djurendić[1], Katarina Gaši[2], Ljubica Medić-Mijačević[2], Dušan Miljković[1]

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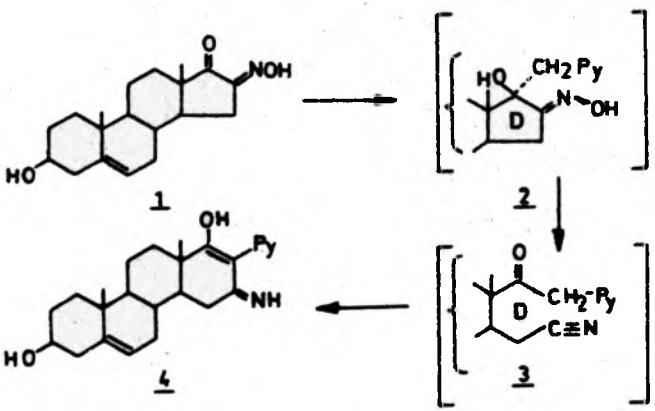
[2]Pharmaceutical and Chemical Industry "Galenika" 11000 Belgrade, Yugoslavia

A novel type of cyclization of some D-seco-5-androstene has been found, whereupon new D-homo steroid system is formed. Namely, on heating 3β-hydroxy-16,17-seco-16-nitrile-17-keto-17-picolyl-5-androstene (3)[1] with KOH in ethylene glycol at 160°C D-homoderivative 4 was obtained in a moderate yield. The needed reaction sequence, from dehydro-epi-androsterene to 3, we have successfully modified.



Structure elucidation of 4, together with a possible mechanism of its formation, will be discussed.

1. D. Miljković, K. Gaši, Bull. Soc. Chim. Belgrade 46,263(1981).

SYNTHESIS OF 6 ξ,17β-DIHYDROXY-7-OXIMINO-3-METHOXYESTRA-1,3,5(10)-TRIENE

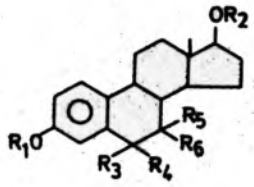
V. Pejanović[1], J. Petrović[2], J. Hranisavljević[3] and D. Miljković[2]

[1]Pharamaceutical and Chemical Industry "GALENIKA", Belgrade, Yugoslavia

[2]Institute of Chemistry, Faculty of Sciences, University of Novi Sad, Yugoslavia

[3]Institute of General and Physical Chemistry, University of Belgrade, Yugoslavia

Oxidation of 3,17β-dipropionoxy-estra-1,3,5(10)-triene with CrO_3 in CH_2Cl_2 in presence of 3,5-dimethylpyrazole afforded 3,17β-dipropionoxy-6-oxo-estra-1,3,5(10)-triene (1) and 3-hydroxy-17β-propionoxy-estra-1,3,5(10)-triene (2)



1: $R_1=R_2=C(=O)CH_2CH_3$; $R_3,R_4=O$; $R_5=R_6=H$

2: $R_1=R_5=R_6=H$; $R_2=C(=O)CH_2CH_3$; $R_3,R_4=O$

3: $R_1=R_2=R_5=R_6=H$; $R_3,R_4=O$

4: $R_1=CH_3$; $R_2=R_5=R_6=H$; $R_3,R_4=O$

5a,b: $R_1=CH_3$; $R_2=H$; $R_3,R_4=O$; $R_5,R_6=N\text{-}OH$

6: $R_1=CH_3$; $R_2=H$; $R_3=H$ (or OH); $R_4=OH$ (or H), $R_5,R_6=N\text{-}OH$

in a total yield of 30%. Compounds 1 and 2 were saponified to diol 3 which was subsequently converted to 3-methyl ether 4. By an action of n-amyl nitrite upon 4 in t-BuOH in presence of K-O-Bu-t, syn (5a) - and anti (5b) - oximes were obtained. Finally, sodium borohydride reduction of 5b afforded a single reduction product 6.

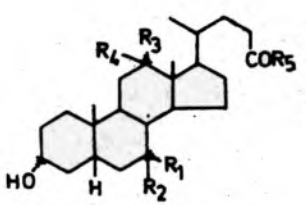
A NOVEL PREFERENTIAL 12α-HYDROXYL MONO-OXIDATION IN CHOLIC ACID DERIVATIVES

K. Kuhajda[1], J. Hranisavljević[2] and D. Miljković[1]

[1]Institute of Chemistry, Faculty of Sciences, University of Novi Sad, Yugoslavia

[2]Institute of General and Physical Chemistry, University of Belgrade, Yugoslavia

It has been known for many years that in cholic acid derivatives, 7α-hydroxyl-mono-oxidation can be successfully carried out in one step by using NBS under slightly alkaline conditions (1 → 4; 70% yield)[1]. Thus, it has been generally accepted that the reactivity order in selective oxidation of cholic acid derivatives is 7 > 12 > 3.



1: $R_1=R_3=R_5=OH$; $R_2=R_4=H$

2: $R_1=R_3=OH$; $R_2=R_4=H$; $R_5=-OCH_3$

3: $R_1=R_3=OH$; $R_2=R_4=H$; $R_5=-NH_2$

4: $R_1=O$; $R_3=OH$; $R_4=H$; $R_5=OH$

5: $R_1=OH$; $R_2=H$; $R_3=O$; $R_5=-NH_2$

6: $R_1=OH$; $R_2=H$; $R_3=O$; $R_5=OH$

Now, we wish to report that the order of selective mono-oxidation in cholic acid derivatives can be drastically changed (12 > 7 > 3) if one starts with cholic acid amide (3), where a neighbouring side chain participation takes place inducing an enhanced reactivity of 12α-hydroxyl function (3 → 6, 70% yield)[2].

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1. L.Fieser: S.Rajagopalan, J.Amer.Chem.Soc., 71, 3935, (1949).

2. K.Kuhajda, J.Hranisavljević, D.Miljković, applied for a Yugoslav Patent.

A NOVEL PREPARATION METHOD OF STABLE 21-SUCCINYLCORTICOSTEROIDS SODIUM SALTS

Maria K.Łypacewicz, Teresa Wasiak, Jadwiga Smolińska
Institute of Pharmaceutical Industry, Warszawa, Poland

A new method of preparation of the title compounds has been found. The salts were obtained in the reactions of steroid 21-hemisuccinates with sodium salts of organic or inorganic acids, possessing pK_1 higher than pK_1 of the steroid substrate. The reactions was carried out in organic or aqueous-organic solution.

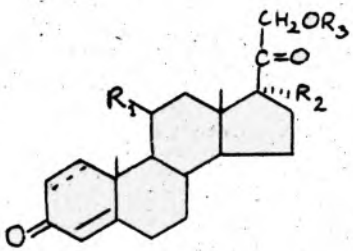
Spectroanalytical data of sodium succinates of prednisolone, 6α-methylprednisolone and hydrocortisone, compounds of great therapeutic importance, are discussed.

TETRAHYDROPHTHALIC ESTERS OF CORTICOSTEROIDS

Wojciech Kroszczyński, Maria K.Łypacewicz, Jadwiga Smolińska and Teresa Wasiak

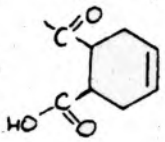
Institute of Pharmaceutical Industry, Warszawa, Poland

Tetrahydrophthalic esters of corticosteroids have been synthesized. Different systems of solvents were used for HPLC in order to analyse the resulting mixtures of products. Methods of preparative separation and spectro-analytical data of the isolated products are described.



R_1, R_2, R_3 = H; OH; OAc

or



STUDIES ON ACETYLATION OF PREDNISOLONE

Teresa Uszycka-Horawa, Wojciech Kroszczyński
Institute of Pharmaceutical Industry, Warszawa, Poland

Prednisolone 17-α, 21-diacetate /I/ is an important pharmaceutical product, obtained from prednisolone in several steps. Mother liquors of the final compound and of intermediates are relatively complex mixtures. Attempts to optimalize yields and purity of I were monitored by TLC and HPLC. Syntheses of some standards were necessary. Significant amounts of 11-acetyl derivatives were detected in products of acetylation. The transformation of 11β-OH group /usually considered as resistant to acylation/ is in agreement with earlier observations of Gardi.

EXTRACTIONS OF PREDNISOLONE AND HYDROCORTISONE WITH OXYGEN CONTAINING SOLVENTS FROM AQUEOUS SOLUTIONS

E.L.Smol'skaya and N.L.Egutkin

Institute of Chemistry, Bashkirian Research Centre,
USSR Acad.Sci. Ural Department, Ufa, SU-450054

Extractions of prednisolone (I) and hydrocortisone (II) with aliphatic alcohols, ethers, esters, chloroform, and methylene chloride have been studied. The extractivity of those solvents towards I and II has been shown to grow in the series: ethers < methylene chloride < chloroform < esters < alcohols.

Among the solvents investigated, pentanol has been found to show the highest extractivity; prednisolone is somewhat better extracted with that as well as with other alcohols than hydrocortisone, the distribution coefficients being 86 and 62, respectively. However, extractions with ethers and esters give similar extractions constants for I and II, while prednisolone is extracted somewhat worse as compared to hydrocortisone. The coefficient of distribution into chloroform and methylene chloride are appreciably lower for I than for II; thus $P_{d(I)} = 4.0$ and $P_{d(II)} = 6.6$ in extractions with chloroform.

With the growing molecular weight of solvents-homologs, the distribution coefficients for I and II have been established to decrease regularly due to the packing effect. The bilogarythmic method has been applied to estimate the composition of the extracted complexes formed for the homologous series of solvents; with alcohols, the solvation number q=3. Extractions of I and II with esters have been found to give a mixture of tri- and tetra-solvates. The obtained results have enabled to calculate the concentration constants of extraction to provide thus for the quantitative description of interphase distribution for I and II.

SYNERGIC EXTRACTION OF HYDROCORTISONE AND PREDNISOLONE WITH MIXED SOLVENTS

N.L.Egutkin

Institute of Chemistry, Bashkirian Research Centre,
USSR Acad.Sci. Ural Department, Ufa, SU-450054

The distribution coefficients of hydrocortisone (I) and prednisolone (II) have been observed positively deviated from the additivity in extractions of corticosteroids from aqueous solutions with mixed solvents based on aliphatic alcohols (III) [C_4-C_{10}] with chloroform (IV) or methylene chloride (V).

Despite slightly different structures of (I) and (II), the patterns of synergic effects therewith differ appreciably. The most distinct synergic effects are revealed in extractions of hydrocortisone to give its highest distribution coefficient in the synergic maximum region, that 2-3 times exceeding the coefficient of distribution into the most effective component of the mixed solvent. However, the distribution coefficient is increased no more that 1.2-1.4 times in extraction of prednisolone.

Of interest is that the extraction of (I) with mixed butyl acetate (VII) and (III) gives the synergic effect; quite the reverse, the distribution coefficients are observed negatively deviated from the additivity with (II).

Small synergic effects are peculiar also for extractions of (I) and (II) with mixed chloroform and diethyl ether in a 3:1 volume ratio.

In addition to high distribution coefficients, the extractions of (I) and (II) with mixtures as (III-IV) and (III-V) are characterized by the relatively fast distribution of the emulsions formed.

Accounting for the obtained results, diagrams have been plotted to enable the estimation of the extraction rate for (I, II) in different extraction modes with synergic mixtures.

The nature of synergic effects has been viewed in terms of the formation of mixed extractable complexes, the changed self-association of (III), and the concurrent intermolecular reactions between the extragent compounds. It has been shown that with the growing electron-donor ability of a mixed extragent component the synergic effect is reduced as much as it is inverted into the antagonistic one, which has been rationalized within the prevailing interactions $S_1+S_2 \rightleftharpoons S_1 \cdot S_2$.

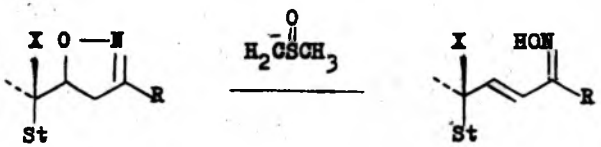
UTILITY OF 20-ISOXAZOLINYLSTEROIDS FOR THE CONSTRUCTION OF STEROIDS WITH MODIFIED SIDE CHAINS

V.Khripach, R.Litvinovskaya, A.Baranovsky, E.Ermolenko

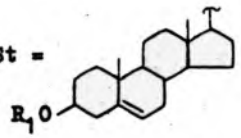
Institute of Bioorganic Chemistry, Byelorussian SSR Academy of Sciences, 220600, Minsk, ul.Zhodinskaya, 5/2

In the present work a new approach to the synthesis of steroid side chains has been described. It includes 1,3-dipolar cycloaddition of nitrile oxides to the corresponding steroidal olefines followed by ring opening of the 20-isoxazolinylsteroids (I,II) under highly basic conditions.

α,β-Unsaturated ketoximes (III,IV) were obtained using DMSO-anion as the base.

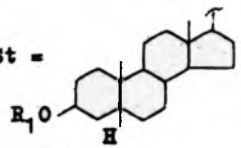


I(II) III(IV)

I,III St =  , X=OH

R= CH_3, $CH(CH_3)_2$

R_1= H, Ac

II,IV St =  , X=H

The spectral properties of synthesised compounds will be discussed.

SYNTHESIS AND SOME CYCLOADDITION REACTIONS OF STEROIDAL NITRILE OXIDE

Khripach V. A., Zhabinskiy V. N.

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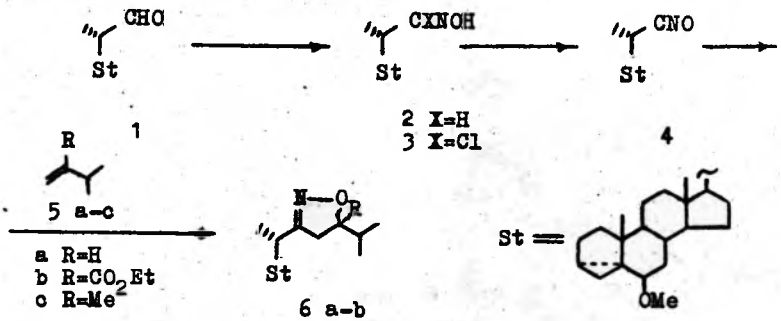
Recently, we reported a new approach to the synthesis of polyfunctional steroid side chains containing more than 5 carbon atoms via 1,3-dipolar cycloaddition of nitrile oxides to terminal steroidal olefins or acetylenes followed by chemical transformation of cycloadducts under hydrogenation conditions.

Here we report an alternative variant of this approach based on the reactions of the steroidal nitrile oxide 4 (first example in steroid series) with the simple alkenes 5 as dipolarophiles.



The oxime 2, prepared by the usual method from the aldehyde 1, was chlorinated with N-chlorosuccinimide to give the hydroximic acid chloride 3. The nitrile oxide 4 obtained by treatment of 3 with a base proved to be relatively stable (T1/2 ~ 10 h). Its reaction with the alkenes 5 a,b gave the isoxasolines 6 a,b. All attempts to obtain the cycloadducts of 4 with the trisubstituted alkene 5 c containing unactivated double bond was unsuccessful.

The potentials of the approach considered for the regio- and stereoselective steroid side chains synthesis will be discussed.

BRASSINOSTEROIDS

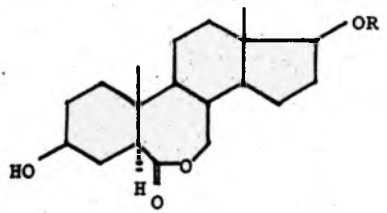
Kohout L.[+] and Strnad M.[++]

[+] Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, 166 10 Prague 6

[++] Institute of Experimental Botany, Czechoslovak Academy of Science, 772 00 Olomouc, Czechoslovakia

Brassinolide[1] is the only plant hormone with steroid type skeleton. Many types of brassinolide-like compounds - brassinosteroids - were synthesized[2].

Brassinosteroid I with new types of side chain



(I)

with the biological activity in the second bean internode bioassay[3] and their synthesis will be given.

References:

1. Grove M.D. et al.: Nature (London) 281, 261 (1979).
2. for summary - see e.g. Adam G. et al.: Zeitschrift für Chemie 27, 41 (1987).
3. Mitchell J.W. et al.: Agriculture Handbook No. 36, p. 36, US Government Printing Office, Washington D.C. 1968.

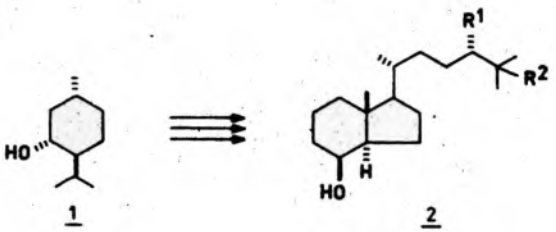
A STUDIES ON TRANSFORMATION OF MENTHOL INTO CD-FRAGMENT OF VITAMIN D

Andrzej Robert Daniewski and Tadeusz Wartchol

Institute of Organic Chemistry, Polish Academy of Sciences

01-224 Warsaw, ul. Kasprzaka 44/52, Poland

A new approache to CD-fragment of vitamin D (2), starting from menthol (1) will be presented.



1 2

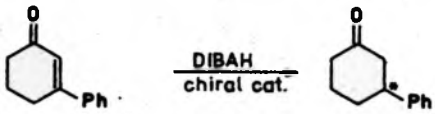
THE ASYMMETRIC CONJUGATE REDUCTION OF α,β-UNSATURATED KETONES

Andrzej Robert Daniewski and Anna Prugar

Institute of Organic Chemistry, Polish Academy of Sciences

01-224 Warsaw, ul Kasprzaka 44/52, Poland

The reduction of 3-phenylcyclohexenone (1) to 3-phenylcyclohexanone (2) by di.sobutylaluminum hydride in the presence of the chiral catalyst will be presented.



1 2

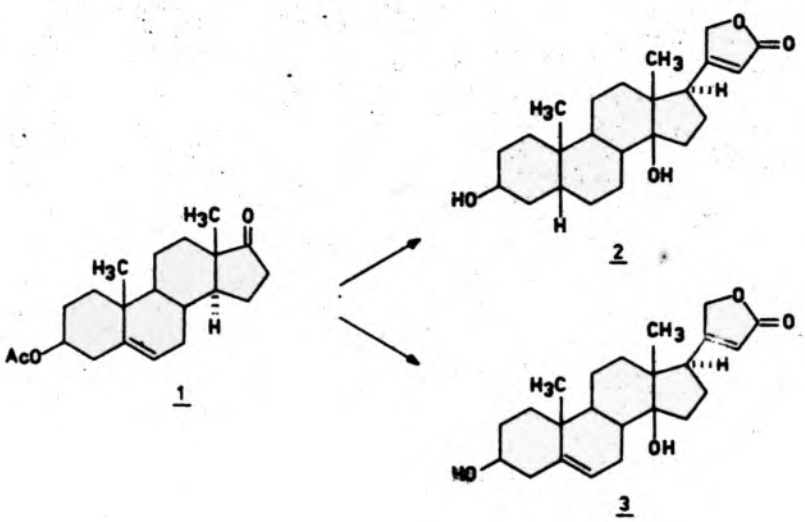
THE SYNTHESIS OF DIGITOXIGENIN AND XYSMALOGENIN

Andrzej Robert Daniewski, Marek Michał Kabat, Marek Masnyk, Wanda Wojciechowska and Jerzy Wicha

Institute of Organic Chemistry, Polish Academy of Sciences

01-224 Warsaw, ul. Kasprzaka 44/52, Poland.

The convertion of 3-hydroxy-5-androsten-17-one acetate (1) into digitixigenin (2) and xysmalogenin (3) will be presented.

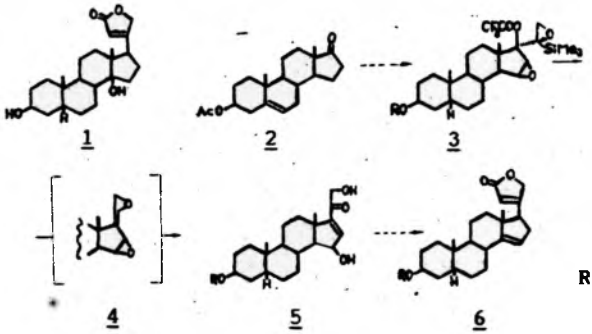


SYNTHESIS OF DIGITOXIGENIN FROM 3β-ACETOXY-ANDROST-5-EN-17-ONE INVOLVING ALLENE OXIDE FOR CONSTRUCTION OF PREGNANE SIDE CHAIN

Marek M. Kabat

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, 01-224 Warszawa, Poland

A partial synthesis of digitoxigenin 1 from 3β-acetoxy-androst-5-en-17-one 2 is reported. The key compound of this synthesis, pregnane 5, was obtained in one pot reaction from the di-epoxide 3 by the formation of an unstable allene oxide 4 and its reaction with water. The hydrogenation of the double bond in 5 followed by the reaction with Ph_3P-C-C-O and the elimination of 15β-OH afforded anhydro-digitoxigenin 6.



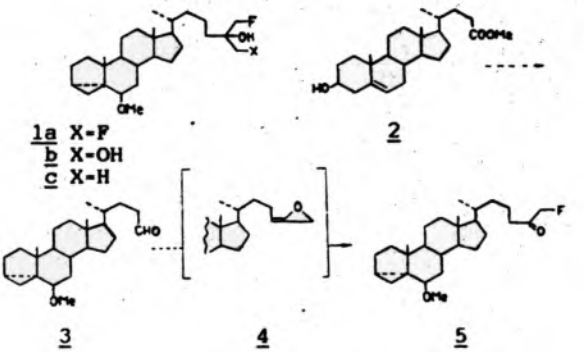
1 2 3 4 5 6

SYNTHESIS OF 26,27-DIFLUORO-25-HYDROXY, *(25R,S)*-27-FLUORO-25,26-DIHYDROXY-, AND *(25R,S)*-26-FLUORO-25-HYDROXY-, CHOLESTEROL DERIVATIVES FROM METHYL 3β-HYDROXY-5-CHOLENOATE

Marek M. Kabat

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, 01-224 Warszawa, Poland

25-Hydroxy cholesterol derivatives 1a-c - precursors of 25-OH vitamin D_3 analogues with a fluorine atom(s) introduced at some of metabolic positions (C-26 and/or C-27) - were obtained from methyl 3β-hydroxy-5-cholenoate 2. The key intermediate, fluoroketone 5, was formed in four steps from aldehyde 3 (60% yield) in the reaction sequence which involved the synthesis of allene oxide 4 and its opening by a tetrabutylammonium fluoride trihydrate (TBAF $3H_2O$). Reaction of 5 with trimethylsulfoxonium iodide followed by a cleavage of the oxirane ring with TBAF $3H_2O$ afforded 1a and 1b. Compound 1c was formed by a Grignard reaction of 5 with MeMgI.



1a X-F
b X-OH
c X-H

2

3 4 5

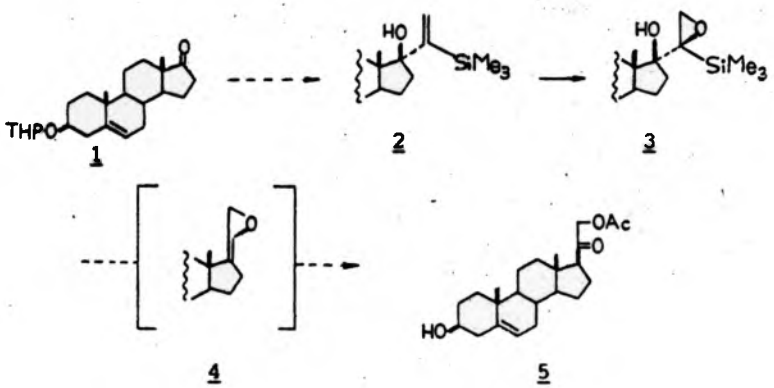
A NOVEL APPROACH TO PREGNANES. SYNTHESIS OF 5-PREGNEN-3β,21-DIOL-20-ONE 3-ACETATE FROM 3β-(TETRAHYDROPYRAN-2'-YLOXY)-ANDROST-5-EN-17-ONE *VIA* ALLENE OXIDE

Marek M. Kabat and Jerzy Wicha

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, 01-224 Warszawa, Poland

The synthesis of 21-acetoxy pregnenolone 5 from 3β-(tetrahydropyran-2`-yloxy)-androst-5-en-17-one 1 *via* allene oxide is reported. Addition of 1-lithio-1-trimethylvinyl silane to the carbonyl group of 1 and oxidation of the allylic double bond in 2 afforded epoxy-silane 3. Transformation of 3 into pregnane compound was prepared by the formation of the key intermediate 4 and its reaction with AcOK.

Some chemical properties of epoxy-silane 3 were studied.



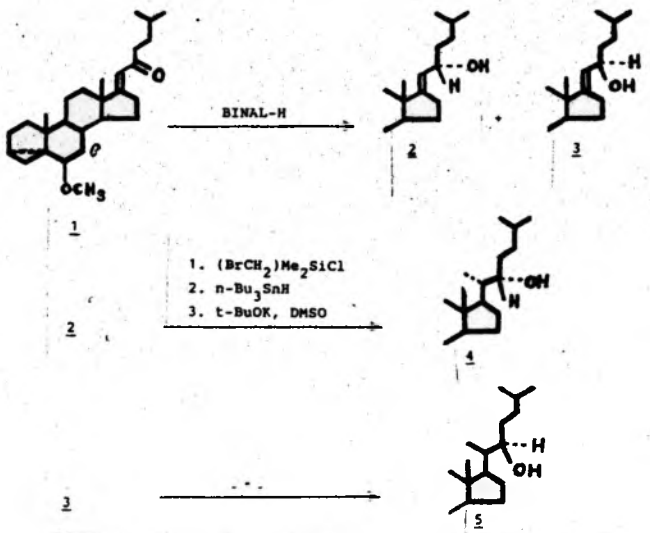
1 2 3 4 5

SYNTHESIS OF (20S,22S) AND (20R,22R) 22-HYDROXYCHOLESTEROL DERIVATIVES FROM 17-OXOANDROSTANES. CHIRALITY TRANSFER IN METHYLATION OF ALLYLIC ALCOHOLS VIA FREE-RADICAL INTERMEDIATES

Alicja Kurek-Tyrlik, Jerzy Wicha and Andrzej Zarecki

Institute of Organic Chemistry of the Polish Academy of Sciences, Kasprzaka 44, 01-224 Warszawa, Poland

Ketone 1, prepared from androstane derivatives, undergoes reduction with the (R) or (S) Noyori reagent to alcohols 2 and 3, respectively, with high diastereoselectivity.
Free-radical methylation of allylic alcohols 2 and 3 by the method of Nishiyama[1] and Stork[2] proceeds with complete regio- and diastereoselectivity to give the corresponding cholestane derivatives, 4 and 5.



1. H. Nishiyama, T. Kitajima, M. Matsumoto, K. Ito, J. Org. Chem., 1984, 49, 2299
2. G. Stork, M. J. Sofia, J. Am. Chem. Soc., 1986, 108, 6826

SYNTHESIS AND BIOLOGICAL EVALUATION OF 24-HOMOLOGATED 22E-DEHYDRO ANALOGUES OF 1α,25-DIHYDROXYCHOLECALCIFEROL

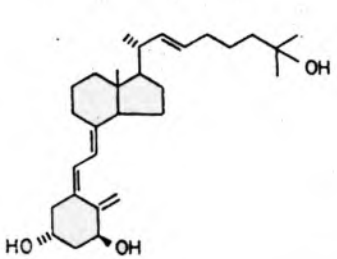
K. Perlman, A. Kutner[a], J. Prahl, C. Smith, M. Inaba, H.K. Schnoes, and H. F. DeLuca

University of Wisconsin-Madison, Department of Biochemistry, Madison WI 53706, USA; [a]Institute of Pharmaceutical Industry, Rydygiera 8, 01-793 Warszawa, Poland

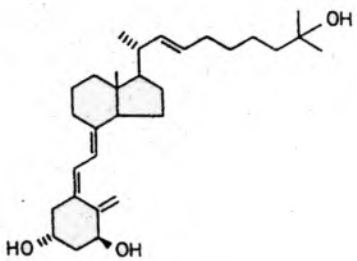
Based on the previously developed synthetic startegy[1] there have been synthesized two novel synthetic analogues 1 and 2 of $1,25\text{-}(OH)_2D_3$. Comparing to the structure of the natural vitamin D hormone both new analogues have C-22 double bond and the extended aliphatic side chain. The key step of the synthesis was the condensation of the vitamin D C-22 aldehyde synthon with the respective protected sulfone of the side chain fragment.

Homologation of Δ^{22} analog of $1,25\text{-}(OH)_2D_3$ by two or three carbons has resulted in the ten-fold increase or one-half reduction, respectively, of the activity in stimulating the differentiation of human promyelocytic HL-60 cells. Homologation also causes a progressive drop (ca ten-fold with each carbon atom added) in in vivo calcium mobilization activity.

Synthetic aspects of the preparation of the title analogues as well as some details of the first practical separation of both main biological activities of vitamin D analogues will be discussed.



1



2

1. A. Kutner, K. Perlman, A. Lago, R. R. Sicinski, H. K. Schnoes, H. F. DeLuca, J. Org. Chem. 53, 3450 (1988).
2. K. Perlman, A. Kutner, J. Prahl, C. Smith, M. Inaba, H. K. Schnoes, H. F. DeLuca, in preparation.

ON THE CHEMISTRY OF VITAMIN D TRIENE SYSTEM - RING OPENING REACTIONS OF VITAMIN D MONO-OXIRANES

Wolfgang Reischl

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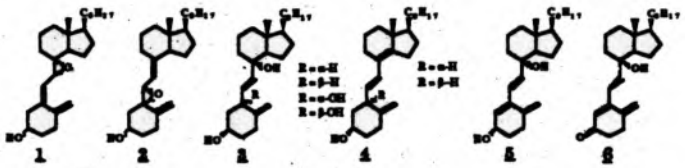
The chemistry of vitamin D is still a field of continuing interrest for producing analogs to study the mode of action of this steroid hormone [1]. Whereas most of the modifications have been made in the side chain or in ring A, little is known about the chemistry of the triene part of vitamin D besides thermal and photochemical isomerisations [2]. The present paper will focus on the synthesis of analogs with double bond shifted and/or partially oxidised triene system.

The easily accessible vitamin D mono-oxiranes **1** and **2** [3] were investigated towards oxirane ring opening. Treatment of **1** with hydride reagents gives rise to allylic alcohols of type **3** with predominate deconjugation of the polyene, which in turn could be further transformed to analogs with the overall structure **4**. Hydrolysis of **1** and **2** under acidic conditions produces allylic diols of type **5**.



A different type of ring opening reaction occurs, if the mono-oxiranes are treated with LiBr/HMPA complex in benzene. Starting from **1** the resulting product **5** is closely related to **6**, a metabolite of vitamin D produced by phagocytic cells (M1, HL-60) [4].

The stereo- and regiochemical outcome of the above transformations as well as modell studies will be discussed.

References:

[1] A. W. Norman; Vitamin D: the Calcium Homeostatic Steroid Hormone, Academic: New York, 1979

[2] T. Kametani, H. Furuyama; Medical Res. Rev. 7, 147 (1987)

[3] C. Kratky, W. Reischl, E. Zbiral; Monatsh. Chem. 115, 145 (1984);

W. Reischl, H. Bernhard, C. Kratky, E. Zbiral; Monatsh. Chem. 116, 831 (1985)

[4] T. Hayashi, S. Yamada, C. Miyaura, H. Tanaka, K. Yamamoto, E. Abe, H. Takayama, T. Suda; Febs. Lett. 218, 200 (1987)

CARBON-CARBON COUPLING REACTIONS WITH ORGANONICKEL COMPLEXES

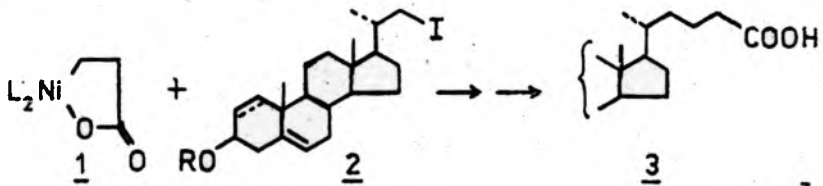
B. Schönecker[a], H. Eibisch[a], D. Walther[b], R. Fischer[b], B. Nestler[b], G. Bräunlich[b], P. Droescher[c]

[a] Academy of Sciences of the GDR, Central Institute of Microbiology and Experimental Therapy, Jena, GDR

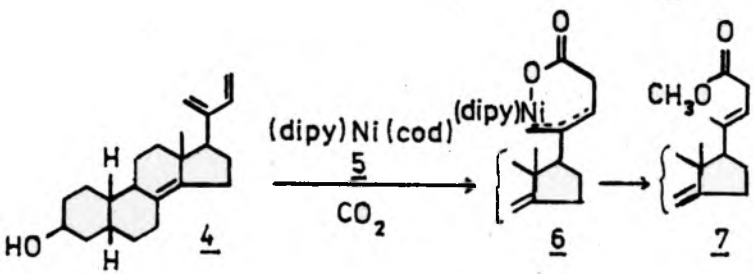
[b] Friedrich Schiller University Jena, Department of Chemistry, Jena, GDR

[c] VEB Jenapharm, Division of Research and Development, Jena, GDR

We have found that the easily available nickel complexes of the structure 1[1] react as propionic acid donor synthons with alkyl iodides after addition of MnI_2. The reaction is useful for the synthesis of C_{25} carboxylic acids of steroids (3) from C_{22} iodides (2).



Further studies provided the first example of a steroidal η^3-allyl nickel carboxylate complex 6, obtained by reaction of a steroidal 1,3-diene, a nickel(0) complex (5) and CO_2. Protonation, hydrolytic cleavage and reaction with CH_2N_2 furnished the ß,γ-unsaturated methyl carboxylate 7.



1) E. Uhlig, G. Fehske, B. Nestler; Z. Anorg. Allg. Chem. 465 (1980) 151

ENZYMATIC SYNTHESIS OF A VITAMIN D_3 SIDE CHAIN BUILDING BLOCK

Eberhard Schrötter, Judith Weidner, Hans Schick
Central Institute of Organic Chemistry of the Academy of Sciences of the GDR, Berlin,

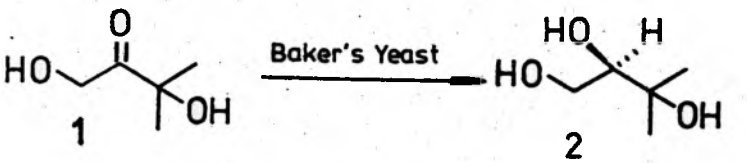
Barbara Häfner
VE Research Center of Biotechnology, Berlin

Peter Droescher
VEB Jenapharm, Division of Research

Bruno Schönecker
Central Institute of Microbiology and Experimental Therapy, Jena

For the construction of the side chain of (24R)-24,25-dihydroxyvitamin D_3 (R)-3-methyl-1,2,3-butanetriol 2 is needed as a precursor.

The hitherto known line of synthesis (Takayama et al., Europ. Pat. 45 524) is based upon D-Mannitol. It includes 7 steps, some of which are complicated and expensive. The total yield amounts to 17 % related to D-mannitol.



The presented procedure starts from the industrial large scale product 2-methyl-3-butyn-1-ol. Using known methods prochiral 3-methyl-1,3-dihydroxy-2-butanone 1 is prepared in 5 steps and reduced by means of baker's yeast with an enantiomeric excess of 90 %. The chemical yield of this step is 73 %, the total yield amounts to 26 % related to 2-methyl-3-butyn-1-ol.

Following the proposed procedure the called vitamin D_3 building block is obtained in a simple manner with a higher overall yield.

SYNTHESIS OF C/D-trans STEROID GLYCOSIDES DIFFERING IN THE GEOMETRY OF A/B RING JUNCTION - EFFECT ON THE BIOLOGICAL ACTIVITY

J. Weiland, W. Schönfeld and K.R.H. Repke
Academy of Sciences of the GDR
Central Institute of Molecular Biology, Berlin-Buch, GDR

Statement of problem

Hormonal C/D-trans steroids such as progesterone and chlormadinol acetate (CMLA) have been known to depress cardiac contractility. We have discovered, however, that glycosides of CMLA enhance contractility, although glycosidation results in lowering of the apparent Gibbs energy ($\Delta G^{0\prime}$) of interaction with the target enzyme of cardiotonic steroid action, the Na^+/K^+ transporting ATPase (1).

The purpose of the present study has been to explore the possibilities whether the geometry of the junction of the rings A and B predictably determines the yield of synthesis and the negative or positive effect on biological activity.

Procedures

Glycosides of C/D-trans steroids differing in A/B ring junction (A/B-cis, A/B-trans, Δ^4, Δ^5, and $\Delta^{4,6}$ representatives) and in substitution on C-6 or C-17 have been prepared by using an optimized Koenigs-Knorr method. Their biological activity has been estimated in the Na/K-ATPase assay and quantified by the $\Delta G^{0\prime}$ value (1).

Conclusions

The yield of glycosidation is essentially determined by the presence or absence of the double bond neighbouring 3β-OH. The effect of glycosidation on the $\Delta G^{0\prime}$ quantity is a function of the spatial disposition of the sugar moiety in the glycosides. Conjugates of hormonal steroids may be viewed as candidates for the much-sought-after endogenous digitalis.

(1) J. Weiland, K. Schwabe, D. Hübler, W. Schönfeld and K.R.H. Repke; J. Enzyme Inhibition 2, 31-36 (1987).

BIOTRANSFORMATIONS OF 2α,3α-DIHYDROXY-5α-CHOLESTAN-6-ONE

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Institute of Plant Biochemistry, Academy of Sciences of the GDR, Weinberg 3, DDR-Halle/Saale, 4050

H. Böhme, S. Dänhardt, C. Hörhold
Central Institute of Microbiology and Experimental Therapy, Academy of Sciences of the GDR, Beutenbergstr. 11, DDR-Jena, 6900

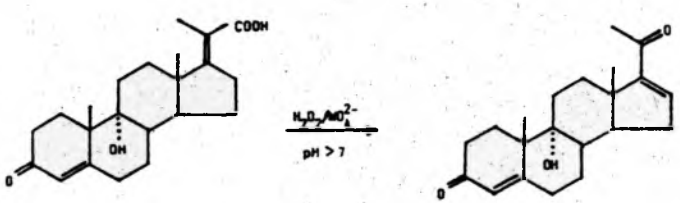
Microbial transformations of A/B-modified steroids with sterol side-chain moiety open new pathways to intermediates useful for brassinosteroid synthesis. In model experiments wie investigated biotransformations of 2α,3α-dihydroxy-5α-cholestan-6-one with Mycobacterium vaccae leading to 2α,3α,6α-trihydroxy-5α-cholestan-6-one and 2α-hydroxy-androst-4-en-3,17-dione in a yield of 40 and 25 %, respectively. Fermentation procedure, isolation as well as structural elucidation, including 2D-NMR-spectroscopy, will be described.

CATALYTIC OXIDATIVE DECARBOXYLATION OF 17(20)-DEHYDRO-23,24-DINORCHOLAN-22-OIC ACIDS

A. Toró, I. Pallagi, N. Makk and G. Ambrus
Institute for Drug Research, Budapest, Hungary

Partial microbial side chain cleavage of sitosterol into 23,24-dinorcholane derivatives is a promising way to obtain starting materials for corticosteroid syntheses.

We transformed 9α-hydroxy-3-oxo-4,17(20)-dinorcholadien-22-oic acid (1), the known sitosterol degradation product, in a one step reaction into 9α-hydroxy-4,16-pregnadiene-3,20-dione (2) by a tungstate (or molibdate) catalized novel oxidative decarboxylation.



1 2

Application of this reaction for decarboxylation of several 17(20)--dehydro-23,24-dinorcholan-22-oic acids prepared by chemical modification of compound 1 afforded some well-known 16-dehydro-20-oxo--pregnanes used as steroid synthesis intermediates in the past decades, and some new 16-unsaturated-20-oxo-pregnanes which are more suitable for the synthesis of corticosteroid drugs. In the presentation we suggest a mechanism for the new decarboxylation reaction.

NOVEL MICROBIAL DEGRADATION PRODUCTS OF SITOSTEROL

É. Ilkóy, A. Jekkel, Gy. Horváth, B. Podányi and G. Ambrus
Institute for Drug Research, Budapest, Hungary

In our experiments carried out for studying genetic recombination between sterol transforming Mycobacteria by spheroplast fusion we obtained two genetically modified strains which degraded sitosterol into transformation products representing the initial stages of the side chain degradation pathway. One of these strains produced 4--stigmasten-3-one, 3-oxo-1,4-stigmastadien-26-oic acid methyl ester, 3-oxo-4-stigmasten-26-oic acid and its methyl ester, the other strain accumulated 9α-hydroxy-3-oxo-23,24-dinor-4-cholen-22-oic acid methyl ester, 9α-hydroxy-27-nor-4-cholestene-3,24-dione, 3-oxo-stigmasten-26--oic acid methyl ester, 9α-hydroxy-3-oxo-4,24(25)-stigmastadien-26--oic acid and its methyl ester from β-sitosterol. 24(25)-Unsaturated 26-oic acid derivatives are new transformation products, which could be fitted into the microbial degradation pathway of sitosterol elucidated by Sih and coworkers. The structures of degradation products were determined by UV-, IR-, ^{1}H-NMR-, ^{13}C-NMR and mass spectroscopic methods. The E-geometry of the 24(25) double bond in the Δ24(25)-26-oic acid derivatives was determined by heteronuclear NOE measurement resulting in the intensity enhancement of C-26 carbon upon irradiation of 28--methylene protons. Transformation of campesterol by the above mentioned strains are also discussed in the presentation.

20-ISOSTEROLS FROM MACOMA BALTHICA

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81-967 Sopot, Poland

Marine organisms are a rich source of new sterols with unexpected structural features. Almost all of them possess the "natural" R-configuration at C-20.

Macoma balthica - a bivalve mollusc wide-spread in the Baltic Sea - has been intensively investigated in our laboratory for its sterol content and composition. C_{26}+C_{29} 4-desmethyl-Δ^5-sterols and C_{26}+C_{29} 4-desmethylstanols were the major sterols of Macoma balthica. Among the minor components a fraction of "unnatural" 20-isosterols was detected. Their structure was elucidated by GC and GC-MS measurements. The main constituent - (20S)-cholest-5-en-3β-ol was isolated by reversed phase HPLC and characterized by ^{1}H NMR.

It is a first isolation of a serie of 20-isosterols corresponding to the "natural" (20R)-sterols from the natural sources.

CONFORMATIONAL ANALYSIS OF PLANT STEROLS AND PENTACYCLIC TRITERPENOIDS: BIOSYNTHETIC AND FUNCTIONAL IMPLICATIONS.

W. David Nes[1] and Jane F. Griffin[2]

[1]Plant and Fungal Lipid Research, Plant Physiology Research Unit, Russell Research Center, 950 College Station Road, Athens, GA 30613 and [2]Medical Foundation of Buffalo, Inc., Buffalo, NY 14203.

Sterols and substances which mimic them (pentacyclic and tetracyclic triterpenoids) are ubiquitous constituents of crop plants at some point in their life history. However, all sterols and sterol-like molecules are not structurally or functionally equivalent throughout plant ontogeny even though they share similar amphipathic properties which make them suitable membrane inserts. As part of a cooperative USDA/Medical Foundation study we examined the solution (determined by NMR) and solid state (determined by X-ray crystallography) properties of several naturally-occurring sterols and triterpenoids synthesized by tracheophytes. The biosynthetically important 9β,19-cyclopropyl sterols eg., cycloartenol 1, were found to be pseudoplanar or flat analogous to lanosterol, cholesterol and sitosterol. The sterol-like pentacyclic triterpenoids such as tetrahymanol, motiol 2 and friedelin 3 were also demonstrably flat. For 1, 2, and 3 the trans-syn configuration at the ring junction which natural product chemists have determined to place the molecule into a conformationally bent system is shown to be erroneous. Evidence is given that the molecules orient into 3-dimensionally flat polycyclic systems by one or more of the rings becoming twist-boat through the squalene-oxide cyclization process. Molecular modeling indicates interconversion of boat into chair conformers unlikely. Through incubations of the titled compounds with sterol auxotrophs and interference of phytosterol biosynthesis using transition state inhibitors (N-steroids) synthesized at the Russell laboratory, we have also demonstrated a causal relationship between the biosynthetic inclusion of select molecular groupings (eg., C-24 alkyl group, tilt and H-bonding capabilities of the 3-OH group and 3 dimensional flatness) with the occurrence of these compounds in plant maturation and reproduction.

THE SYNTHESIS OF SPIRO-STEROIDS FROM STEROIDAL SPIRO-CYCLOBUTANONES

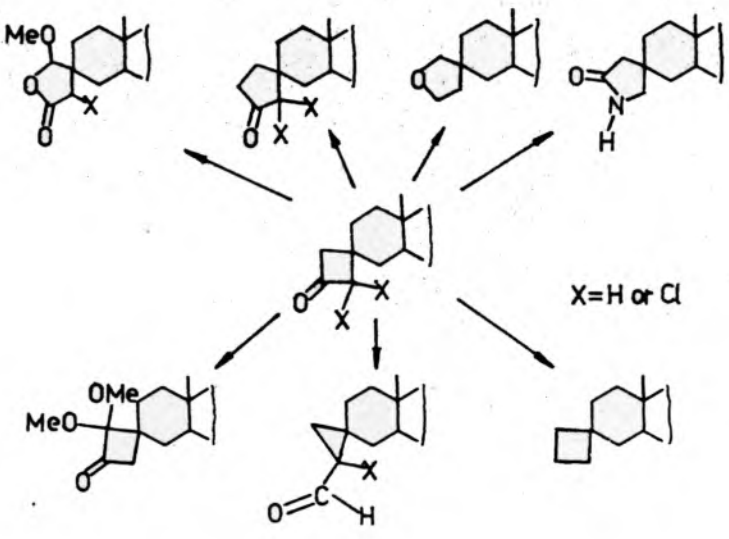
Krzysztof Błaszczyk and Zdzisław Paryzek

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

Steroidal spiro-cyclobutanones were prepared by the reaction of egzomethylene steroids with dichloroketene. The stereochemistry of cycloadducts was established.

In this communication the chemical transformations of cyclobutane spiro-steroids are presented.

The following scheme summarizes the reactions of (3R)-spiro-[(5α-cholestane)-3,1'-(2',2'-dichloro-3'-oxocyclobutane)], the major cycloaddition product obtained from 3-methylene-5α-cholestane, leading to other types of spiro-cholestanes.



A NEW 4-DEMETHYLATION OF DIHYDROLANOSTEROL VIA A BAMFORD - STEVENS REACTION

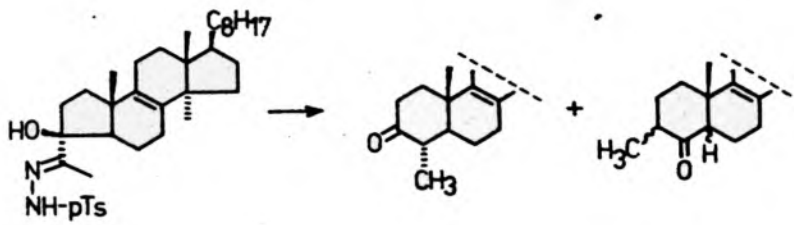
Jacek Martynow and Zdzisław Paryzek

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

The existing methods of 4-monodemethylation of triterpenes often result in low overall yield of the required product. In our search for an alternative method, ring expansions of suitably constructed A-nor-steroids have been studied. Sulfur-, oxygen-, and nitrogen-based ring expansions were examined. This communication reports on the nitrogen-based approach.

The 14α-methyl-A-nor-5α-cholest-8-en-3-one, obtained from dihydrolanosterol in five steps, was transformed to the tosylhydrazone. This, in a Bamford - Stevens reaction, gave a mixture of 6-membered α-methyl ketones, from which 4α,14α-dimethyl-5α-cholest-8-en-3-one was isolated in about 30% yield. The other products were the isomeric 3-methyl-4-oxo-cholestenes. The stereochemistry of α-methylketones was established on the basis of spectral analysis (1-H and 13-C NMR, CD). This was supported by equilibration studies and by the synthesis on an independent route.

An unusual, ring B inverted, conformation have been found for 3β,14α-dimethyl-5β-cholest-8-ene-4-one.



CARBOCATIONIC REARRANGEMENTS OF 9,11-EPOXY-4β-DIMETHYLLANOSTANES

Jacek Martynow and Zdzisław Paryzek

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

The skeletal rearrangements of 9,11-epoxy-lanostanes resulted in formation of compounds with cucurbitane or protostane skeleton, depending on the structural features of the substrate.

In continuation of our work on skeletal rearrangements of triterpenes, the importance of 1,3-diaxial interaction between 4β- and 19β-methyl groups in C-9 carbocation rearrangements has been studied.

The 4α,14α-dimethyl-5α cholest-8-ene-3-one was transformed into the following epoxides: 3β-acetoxy-9β,11β-epoxy-4β-demethyl-5α-lanostan-7-one, 9β,11β-epoxy-4β-demethyl-5α-lanostane-3,7-dione, and 9α,11α-epoxy-4β-demethyl-5α-lanostan-3-one.

The rearrangements of the above mentioned epoxides afforded a series of new 4α,14α-dimethyl-19(10→9β)abeo-cholestanes.

The structures of compounds were established on the basis of their spectral properties and chemical interconversions within this new family of steroids.

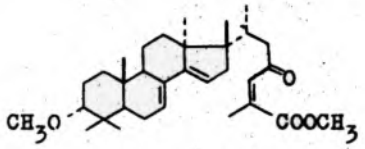
The mechanistic aspects of the rearrangements will also be discussed.

NEW REARRANGED LANOSTANOIDS FROM NEEDLES OF SIBERIAN FIR (ABIES SIBIRICA L.).

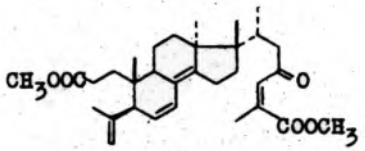
S. Shevtsov, V. Raldugin

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

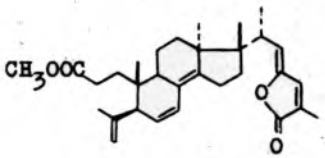
Three new triterpene compounds have been isolated from the acid moiety of the ether extract of needles of siberian fir (Abies sibirica L.) after methylation and silicagel chromatography, which have a rearranged carbon skeleton of lanostane. The structures and stereochemistry of methyl ether of new lanostanoids (1 - 3) have been established by physico-chemical methods (IR, UV, PMR, MS) and chemical correlations.



(1)



(2)



(3)

The precursors of compounds (2) and (3) are apparently 3,4-seco-lanostanoids found earlier in the needles /1/.

/1/.Raldugin V.A., Shevtsov S.A. e.a., Xhim.Prirod.Soedin., 824 (1988).

NEW DERIVATIVES OF OLEANOLIC ACID

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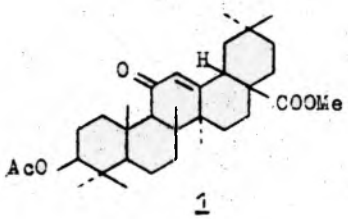
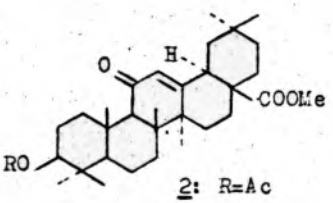
By treating 1 with HBr or 3 with Ac_2O the known triterpene 2 together with a new compound of the formula 4 has been obtained.

Hydrolysis of 2 (KOH/EtOH) gave also two products, the expected known triterpene 3 and the new product 5.

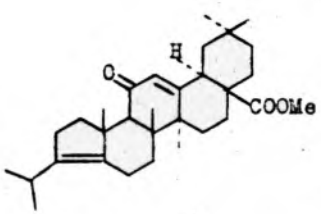
The structure of 4 and 5 was elucidated by means of UV, IR, ^1H-, ^{13}C-NMR and MS spectra analysis. The structure of 5 has been confirmed by x-ray study.



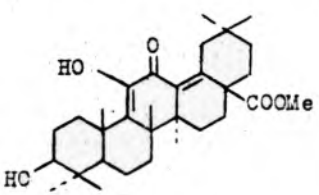
1



2: R=Ac
3: R=H



4



5

ISOLATION AND STRUCTURAL INVESTIGATION OF PHYTOECDYSTEROIDES OF RHAPONTICUM AND SILENE GENUS.

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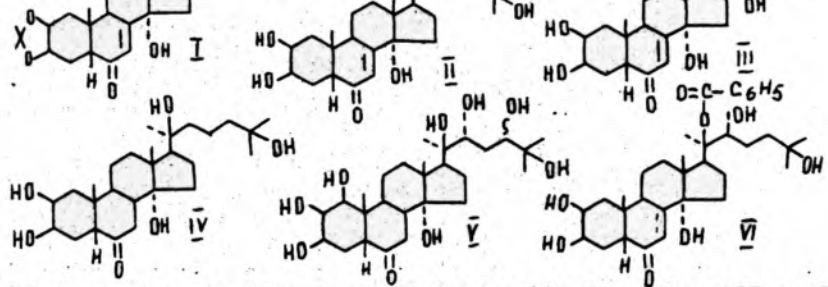
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent, USSR.

From the roots with Rhaponticum carthamoides (Willd) Iljin (family Compositae) rhizomes 8 ecdysteroides have been isolated: of them known earlier-2-desoxyecdysterone, ecdysterone, polipodine B, integristerone A and 24(28)-dehydromakisterone A; and new ecdysteroids-ecdysterone-2,3-monoacetonide (I), ecdysterone-20,22-monoacetonide (II) and rapisterone (III)/1/.

From the overground part Silene nutans L. family Caryophyllaceae the new ecdysteroides have been obtained at the reversedphase columns/2/ by means of higly effective liquid chromatography: 22-desoxyecdysterone (IV)/3/ and nusilsterone (V)/4/ (known ecdysterone and polipodine B).

New phytoecdisteroid-ecdysteron-20-O-benzoate has been isolated from the whole plant Silene tatarica (L) Pers/5/.



/1/. Baltaev U.A., Abubakirov N.K. Khimija prirod. soedin. 1987, N5, 681.

/2/. Baltaev U., Belov Yu.P., Chumachenco M.N., Abubakirov N.K. Khimija prirod. soedin. 1984, N3, 322.

/3/. Baltaev U., Bashkes Ya.V., Darmograi V.N., Belov Yu.P., Abubakirov N.K. Khimija prirod. soedin. 1985, N1, 62.

/4/. Baltaev U., Bashkes Ya.V., Abubakirov N.K. Khimija prirod. soedin. 1985, N4, 522.

/5/. Baltaev U.A., Darmograi V.N., Abubakirov N.K. Khimija prirod. soedin. 1987, N6, 850.

SAPONINS OF ELEUTHEROCOCCUS SENTICOSUS MAXIM. ROOTS

Ewa Segiet-Kujawa[1/], Macki Kaloga[2/]

1. Institute of Medicinal Plants, 61-707 Poznań, Poland
2. Institute of Pharmaceuthical Biology, Free University-Berlin, 1000 Berlin 33.

Methanolic extract of E.senticosus roots was purified by reextraction with petroleum ether, ethyl ether and n-butanol. Butanol soluble fraction was chromatographed over silica gel column. Elution with gradient of $CHCl_3$- CH_3OH-H_2O yielded phenolic glycosides[1/] and saponins. Crude saponin fractions containing Saponin E1 and Saponin E2 in the ratio 85 : 15 was purified on Safadex LH 20. Separation of both saponins was achieved by rotatory TLC. Acid hydrolysis of both saponins gave the same aglicon which was identified by HR MS, H^1NMR, C^{13}NMR as primulagenin A. Spectroscopic study of Saponin E1 / H^1NMR, C^{13}NMR, +FABMS, -FABMS/ showed that genuine aglicon has the structure of protoprimulagenin A and allowed to determine the structure of sugar moiety.

1. E.Segiet-Kujawa, Third International Conference on Chemistry and Biotechnology of Biologically Active Natural Products, vol. 4. , 432, 1985, Sofia, Bulgaria.

NEW NATURAL AND SEMI-SYNTHETIC CARDIAC GLYCOSIDES AND AGLYCONES

I.F.Makarevich, A.I.Pavlij, I.S.Terno, S.I.Makarevich, N.V.Kovganko, N.T.Novokhatskaya

All-Union Research Institute of Drug Chemistry and Technology. Kharkov, USSR

From seeds of Cheiranthus allioni hort. we have isolated new cardiac glycoside, $C_{41}H_{64}O_{19}$, m.p.132-135°, $[\alpha]_D^{20}$ = -22,2±2°(MeOH). Its aglycone is cannogenol. The carbohydrate component of the glycoside consists of D-gulomethilose and of two units of D-glucose. The sequence and sites of links of the carbohydrate units were determined by partial hydrolysis and by identification of the hydrolysis products. And the configurations of glycosidic bonds were determined according to the data of NMR spectrums. As a result the structure of the glycoside which we named glucoericordin has been ascertained as: cannogenol-3β-O-β-D-gulomethilopyranosyl-4' -O-β-D-glucopyranosyl-4'' -O-β-D-glucopyranoside.

From seeds of Strophanthus kombe Oliv. we have isolated new cardiac aglycone (S-3), $C_{23}H_{32}O_7$, m.p. 288-289°, $[\alpha]_D^{20}$63,2±2°(Chf-MeOH-Py). On the basis of chemical and physical research we have established that it is 17α-cardenolide which has angular aldehyde group, two tertiary and two secondary hydroxyl groups. One of the secondary hydroxyl groups is equatorial and the other is axial. As a whole new aglycone has been characterized as: 1α,3β,5,14-tetrahydroxy-19-oxo-5β,14β,17α-card-20(22)enolide and we consider this structure to be the most preferable.

Besides, new cardiac glycoside has been synthesized (all in five stages): strophanthidin-3β-O-α-L-rhamnosyl-4'-O-α-L-rhamnoside, $C_{35}H_{52}O_{13}$, m.p.124-126°, $[\alpha]_D^{20}$ -24,0± 2° (MeOH). Biological activity of the glycoside (LD_{100}) is 0,42-0,43 mg per kg of pigeon, which is lower as compared with biological activity of corresponding monoglycoside convallatoxin.

ENZYMIC GLUCOSYLATION OF STEROIDAL SAPOGENINS IN TWO *ASPARAGUS* SPECIES

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Dept. of Biochemistry, Warsaw University, 02-089 Warsaw, Al. Żwirki i Wigury 93, Poland

UDPG-dependent glucosyltransferases which efficiently glucosylate steroidal sapogenins of the spirostane type to their 3-O-monoglucosides have been isolated from two species belonging to the genus Asparagus: A. plumosus and A. officinalis. Enzymes present in these two plants share many common properties: they occur mainly in the soluble (cytosolic) fraction, show similar pH and temperature optima and are similarly affected by a number of various enzyme effectors. However, their specificity patterns with respect to various spirostanols are quite different. The enzyme from A. officinalis is specific for 5β-H compounds (the non-planar steroid nucleus) such as sarsasapogenin (the aglycone of saponins of A. officinalis) or its 25R--epimer, smilagenin, while for the enzyme from A. plumosus yamogenin (the aglycone of saponins of A. plumosus), its 25R-epimer, diosgenin and tigogenin, i.e. compounds with the Δ^5 or 5α-H structure (the planar steroid nucleus) are the best substrates. It means that there is evident correlation between specificity of glucosyltransferase present in each species and the type of steroidal sapogenins produced by these plants. This strongly indicates that the studied enzymes are specifically involved in the formation of sugar chains at C-3 during the biosynthesis of steroidal saponins. The enzyme from A. plumosus which efficiently glucosylates free yamogenin is unable to glucosylate 26-monoglucoside of the furostanol form of yamogenin. It clearly speaks against the hypothesis (see e.g. Tal et al., Biochem. J., 219, 619, 1984) according to which 26-glucosidic derivatives of sapogenins (in their furostanol form, i.e. with the ring F opened) are biogenetic precursors of steroidal saponins of the spirostane type.

CONTENT AND METABOLIC CHARACTERISTIC OF STEROLS IN *KALANCHOE DAIGREMONTIANA*

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Warsaw University, Dept. of Biochemistry, 02-089 Warsaw, Al. Żwirki i Wigury 93, Poland
*Plant Physiology Research Unit, USDA, Athens, GA, USA
**Drexel University, Philadelphia, PA, USA

Both 24α- and 24β-isomers of 24-alkyl-sterols have been isolated from *Kalanchoe daigremontiana* (Crassulaceae). 24β-Ethyl-25(27)-dehydrocholesterol (clerosterol) and 24β-ethyl-22,25(27)-bisdehydrocholesterol (22-dehydroclerosterol) consisted ca. 95% of total sterols present in leaves while in roots these two sterols made less than 5% of total sterols. 24α- and 24β-Ethylcholesterol (63%), 24α- and 24β-methylcholesterol (19%), as well as 24α- and 24β-ethyl-22-dehydrocholesterol (10%) were found to be the main sterols in roots. Intermediate patterns of sterol composition were observed in stems and flowers of *Kalanchoe* as major sterols of both leaves and roots were present in these organs in considerable amounts.

Apart from the 8 above mentioned sterols, 8 further Δ^5-sterols, which were usually present only in trace amounts, have been identified in *Kalanchoe*. Among them two very rare sterols, i.e. 24-dimethyl-22,25(27)-dehydrocholesterol and 24-methylene-25-methylcholesterol were detected.

Time-course labelling experiments have shown that the most rapidly synthesized and metabolized sterols in *Kalanchoe* are cholesterol and 24-methylenecholesterol. After 72 hours of feeding specific radioactivities of these sterols were 3-times and 15-times higher, respectively, than those of other sterols.

BIOLOGICAL ACTIVITIES OF OLEANOLIC ACID GLYCOSIDES FROM CALENDULA OFFICINALIS

Wirginia Janiszowska[1], Marian Jurzysta[2], Zofia Kasprzyk[1]

[1]Institute of Biochemistry, University of Warsaw, 02-089 Warszawa, al.Żwirki i Wigury 93, Poland

[2]Institute of Soil Sciences and Plant Cultivation, Dept. of Biochemistry and Physiology of Crop Plants, 24-100 Puławy, Poland

Hemolytic index and % of inhibition of Trichoderma viride growth were determined for oleanolic acid and its glycosides isolated from Calendula officinalis flowers and roots. The following compounds were tested: oleanolic acid (OL), its monoglycosides, i.e. 3-O-glucoside (I) and 3-O-glucuronide (F) and the mixtures of glycosides derived from I (MGlc) as well as from F (MGlcUA). The compounds unsufficiently soluble in water were before determination sonificated. The following results were obtained:

-inhibition of Trichoderma viride growth: OL - 8% (5 mg/ml), I- 32% (5 mg/ml), F - 54% (5 mg/ml), MGlc - 24% (5 mg/ml) and 43% (10 mg/ml), MGlcUA - 54% (5 mg/ml).

-hemolytic index: OL - 0, I- 70000, F- 25000, MGlc - 2000, MGlcUA - 20000.

The above results indicate that oleanolic acid glycosides are active in hemolysis and in inhibition of Trichoderma viride growth. However, differences in these activities are observed between I and F and their derivatives. OL is active only in inhibition of T.viride growth but completely inactive in hemolysis. The greatest hemolytic index is observed for I obtained synthetically.

BIOSYNTHESIS OF STEROID GLYCOSIDES IN Dioscorea deltoidea CELL SUSPENSIONS

I.S.Vasilyeva, V.A.Paseshnichenko
A.N.Bach Institute of Biochemistry, USSR Academy of Sciences, Moscow, U.S.S.R.

Dioscorea cell cultures are a potential source of diosgenin and steroid glycosides. The sterol fraction of the cell suspension of Dioscorea deltoidea st. IFR DM-0.5 contained sitosterol, campesterol, stigmasterol and cholesterol. The amounts of the sterols varied from 3.5 mg dry wt (exponential growth) to 0.35 mg/g dry wt (during degradation). The steroid glycoside fraction of the D.deltoidea cell suspension contained only steroid glycosides of the furostanol type such as protodioscin, deltoside and Δ^5--furosten-3β,22,26-triol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl-26-O-β-D-glucopyranoside (protobioside). The levels of oligofurostanosides in the D.deltoidea cells varied from 36.7 mg/g wt at the exponential growth to 141.0 mg/g during degradation. In the D.deltoidea cell suspension /2-^{14}C/-acetate was converted to phytosterols and oligofurostanosides. After 2.5 h incubation of the D.deltoidea cell suspension with /2-^{14}C/-acetate the incorporation of the label into sterols was 3.7, 4.5 and 0.011% at the exponential, stationary and during degradation respectively, while the incorporation of the label into oligofurostanosides was 0.39, 0.71 and 0.16%, respectively. In all the experiments, protobioside had a higher specific activity than prototriosides (deltoside and protodioscin). The specific activity of protobioside was 75.9×10^6; 33.6×10^6 and 19.7×10^6 dpm/mmol at the exponential, stationary phases and during degradation, respectively.

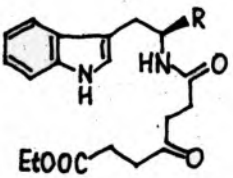
The specific activity of deltoside was higher than that of protodioscin (9.8×10^6 and 5.3×10^6 dpm/mmol at the stationary growth, respectively. The results obtained indicate that protobioside is an intermediate in the biosynthesis of prototriosides. Deltoside and protodioscin are synthesized from the common precursor.

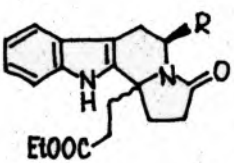
SYNTHESIS OF 3,3a-PROPANO CANTHINE ANALOGS

Josef HÁJÍČEK

Research Institute of Pharmacy and Biochemistry
Kouřimská 17, CS-13060 Prague 3

The eburnane/canthine bases attract considerable attention of synthetic chemists mainly because of their potent pharmacological activities. We report here on further chemistry of 3,3a-propano analogs of canthinones. The crucial step of the synthesis involves Pictet-Spengler type cyclization of oxo-tryptamide (1→2). An approach to asymmetric synthesis of this class of compounds will also be presented (3→4).





1 R = H
3a R = COOMe
3b R = $CONH_2$

2 R = H
4a R = COOMe
4b R = $CONH_2$

GLUCOSYLATION OF STEROIDAL ALKALOIDS BY GLUCOSYLFRANSFERASE FROM POTATO (*SOLANUM TUBEROSUM*) PLANTS

Jan Zimowski and Ireneusz Dziekoński

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Partialy purified glucosyltransferase catalyzing the synthesis of solanidine 3-monoglucoside (γ-chaconine) has been obtained from *Solanum tuberosum* leaves. It shows optimal activity at pH 6.8 and is activated by β-mercapthoethanol. This glucosyltransferase uses uridine diphosphoglucose as the sugar donor. Except solanidine, some other steroidal alkaloids are glucosylated by this enzyme, however, at distinctly lower rate. The relative glucosylation rates with respect to solanidine (100%) are: 85% for the saturated analoque of solanidine, demisidine, 76% for tomatidine and 70% for solasodine. This glucosyltransferase is able to glucosylate also steroidal sapogenins of the spirostane type, such as ruatigenin (51%), isoruatigenin (49%), hecogenin (46%), diosgenin (19%) or ruscogenin (16%). Typical phytosterols are poor glucose acceptors for this enzyme. The relative glucosylation rates for sitosterol, stigmasterol or campesterol make only 18%, 9% and 6%, respectively.

Our results strongly indicate that the above described enzyme participate *in vivo* in the initiation of sugar chain synthesis during the formation of α-chaconine - the glycoalkaloide of potato plant.

The enantiomeric composition of the monoterpene hydrocarbons in the volatile part of termite defence secretions.

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Many of the specific phases of termite life are chemically based. Morphologically specialized soldier caste of termite societies undertake the colony defense. Soldiers of the most advanced subfamily of the higher termites (Nasutitermitinae) can project the sticky frontal liquid for a distance with very high precision, and physical contact with the enemy can be totally avoided[1]. Chemical studies of African, Australian and South American genera indicate species specific features of the defense secretions[2] The biosynthetic ability of the soldiers to produce *de novo* both monoterpenes and diterpenes have been demonstrated[3].

In this study we have used a GC column packed with α-cyclodextrin in a water/formamide matrix[4] in a simple multi dimensional GC system to determine the enantiomeric composition of the monoterpene hydrocarbons in soldier termites from different colonies of the termites *Nasutitermes nigriceps*, *N. ephratae*, and *Velocitermes velox*..

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ABSTRACTS WHICH ARRIVED AFTER EDITION OF THE BOOK

STEROLS FROM *LEONURUS CARDIACA* L. OF DIFFERENT GEOGRAPHIC AREAS

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More studies show that different climatic and environmental conditions and latitudes may influence both qualitatively and quantitatively the contents of metabolites in plants.

Previous papers reported the different contents of flavonoid glycosides, alkaloids, fatty acids and aminoacids in some plants and outlined the phytogeographic implication of these effects (1-3).

No studies are carried out in this field on the steroidal content effects.

In this study we have examined the possible variations of sterol contents between the *Leonorus cardiaca* L. (motherwort) growing in different climatic and latitude conditions, in Poland and in Italy, 53°N and 43°N, respectively.

Preliminary results show that the quantitative sterols content is not affected by different environmental conditions. Also the qualitative contents were quite similar.

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EFFECTS OF FERTILIZER TREATMENTS ON STEROL CONTENT OF CHICK-PEA (*Cicer arietinum* L.) SEEDS.

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As a continuation of our previous investigations on some Leguminosae (1-5), this paper deals with the extent of qualitative and quantitative variability in the sterol content of three chick-pea populations (Bianco and Nero di Rutigliano, Rosso di Cassano) widely cultivated in the Apulia region, Southern Italy, submitted to different fertilization treatments with N-P-K nutrients.

Sterol extraction, separation and purification were accomplished as previously described (6); identification of each sterol, as acetyl ester, was performed by GLC analysis and ^{1}H-MNR and MS spectra examination.

The experimental data show some appreciable variations in the total sterol content, although no significant differences were observed between the control and treated chick-pea composition.

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STEROL CONTENTS IN SOME SAPROPHYTIC BASIDIOMYCETES

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As a continuation of previous researches on the chemical constituents of Basidiomycetes (1-4), this communication deals with sterol content of five saprophytic mushrooms, three Strophariaceae [*Stropharia aeruginosa* (Curtis ex Fr.) Quél., *S. coronilla* (Bull. ex Fr.) Quél. and *S. semiglobata* (Batsch. ex Fr.) Quél.] and two Thelephoraceae [*Stereum gausapatum* (Fr.) Fries and *S. rugosum* (Pers. ex Fr.) Fries].

The sterol fractions of the unsaponifiable material were isolated as previously described (1).

Sterol separation and identification, as acetylderivatives, was carried out by GLC and on the basis of their ^{1}H-NMR, MS and U.V. Spectra.

Sterol mixtures were mainly constituted of C_{28} sterols with ergosterol as the principal sterol. Lesser amounts of C_{27} and C_{29} sterols were also detected.

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