XII TH CONFERENCE ON ISOPRENOIDS

OCTOBER 4 – 11, 1987
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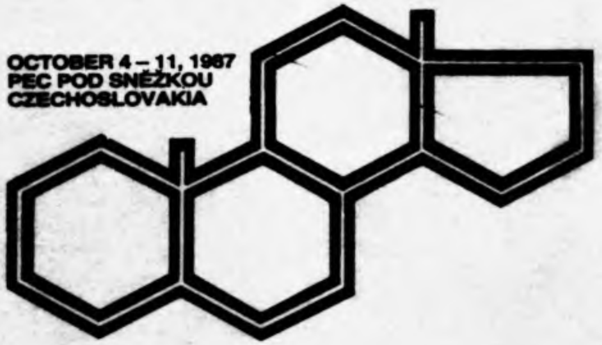

ABSTRACTS OF PAPERS

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PHOTOCHEMISTRY OF SATURATED CARBONYL GIBBERELLINS - SYNTHETIC APPLICATIONS

Günter Adam

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Photochemical reactions are a powerful tool in synthesis and modification of polyfunctionalized natural products leading as effective key steps to new structural types often unparalleled by thermal methods. This is demonstrated on reaction sequences starting from different types of carbonyl gibberellins allowing highly regio- and stereoselective transformations of such chemically sensitive diterpenoids. Thus, $n \rightarrow \pi^*$-excitation of 3-carbonyl-gibberellins lead via a Norrish I process to ring A opened gibberellins. In the gibberellin C series the photochemical ring opening is followed by a crossed intramolecular cycloaddition to highly strained oxetane intermediates useful as starting compounds for new C/D-ring substituted gibberellins. Furthermore, the photochemistry of gibberellin-6-aldehydes and a series of oxo esters will be discussed which is characterized by either Norrish II processes or intramolecular functionalization under ring closure depending on the length of the side-chain moiety at C-6. The regio- and stereoselective course of the ring closure can be explained in special cases by computerized conformational analysis of the starting carbonyl compound based on X-ray diffraction.

A NOVEL SYNTHETIC ROUTE FOR ISOPRENYLATION: SYNTHESIS OF BIOLOGICALLY ACTIVE MOLECULES

V.K. Ahluwalia

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One of the first uses perceived for 2,2-dimethylchromenes was due to their relationship to tetrahydrocannabinol. The benzopyrans were considered to be analgesics and antidepressants as well as antianxietal, antihypertensive and hypoglycemic agents. These species have been claimed to be reactivators for cytochrome reductase and antioxidants for foods and vitamin preparations. They have been cited as promising antitumor agents. Early cultures, undoubtedly used, 2,2-dimethylchromene-containing herbs such as Tzotzil, which is widely used in Mexico for treatment of diarrhea, the Chinese drug Wu-Chu-Yu, used as stimulant, carminative, beobstrunet, stomachic astringent, and anthelmintic remedy and the East African drug called wars (Wurrus or black Kamala), known to contain Rottlerines, used as a cosmetic, dye and drug. Photochromic properties have also been observed for the 2,2-dimethylchromenes.

In view of the physiological properties and the occurrence of 2,2-dimethylchromene moiety in various natural products like acetylchromenes, coumarins, flavones, isoflavones, chromones, xanthones etc., it was considered of interest to devise new methods for their synthesis.

An elegant synthesis of linear acetylchromenes viz., eupatoriochromene, encecalin, evodionol and methylevodionol has been achieved by blocking the more reactive 3-position of the appropriate polyhydroxyacetophenones with iodo group, formation of propargyl ether with 3-chloro-3-methyl-but-1-yne and subsequent thermal cyclisation accompanied by deiodination. Regiospecific introduction of C-prenyl group at less reactive 5-position has also been achieved by the reaction of the appropriate 3-iodoketones with 2-methylbut-3-ene-2-ol. The 5-prenyl ketones are also essential intermediates for the synthesis of linear acetylchromenes.

A versatile route of nuclear isoprenylation leading to the exclusive formation of 2,2-dimethylchromans has been achieved by the direct condensation of polyhydroxyacetophenones with isoprene in presence of acid. Acetylchromans, thus obtained, are dehydrogenated with DDQ to give the corresponding 2,2-dimethylchromenes. Using this method synthesis of a number of naturally occurring chromenes viz., ripariochromene-A, eupatoriochromene, encecalin evodionol, isoevodionol and methylevodionol has been effected. These chromans and chromenes are also useful intermediates for the synthesis of large number of naturally occurring compounds.

A possible mechanism has also been proposed for this reaction.

MOLECULAR REARRANGEMENTS OF NEOCLOVENE IN SUPERACIDS

T.M.Khomenko, D.V.Korchagina, J.E.Salnikov., V.I.Mamatyuk,
T.V.Rybalova, Yu.V.Gatilov, Zh.V.Dubovenko, V.A.Barkhash
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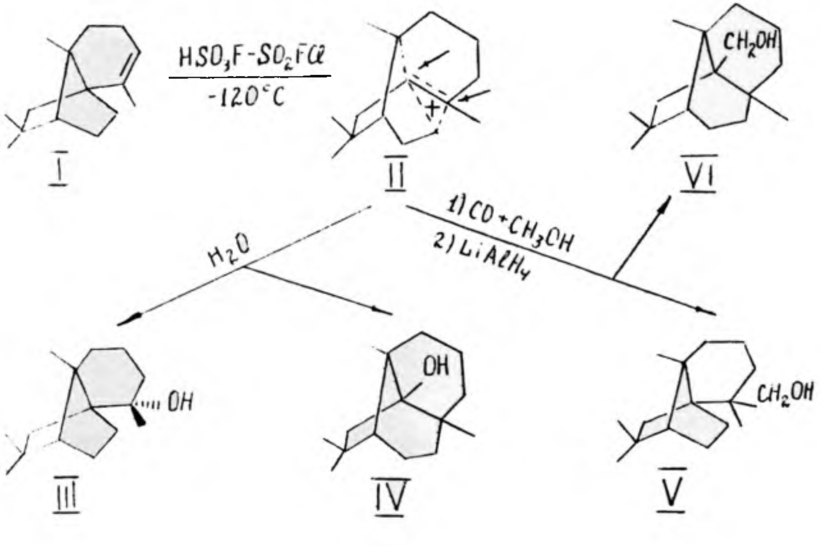
Neoclovene (I), one of the main products of acid-catalysed transformations of cariophyllene, posseses an unusual frame, but its chemistry is practically uninvestigated. We have studied for the first time molecular rearrangements of olefine (I) in superacids. Protonation of the olefine led to generation of the stable non-classic σ-delocalised carbocation (II). Interaction of the latter with nucleophiles ($CO+CH_3OH$, H_2O) gave alcohols (III-VI) whose structures were proved by the X-ray analysis (III), two-dimensional NMR spectroscopy and by comparison of the calculated and experimental values of the $Eu(fod)_3$-induced chemical shifts in the PMR spectra.



SYNTHESIS OF TERPENOIDS FROM COMPOSITAE

F. Bohlmann

Technical University, Berlin 12

The synthesis of some sesquiterpenes from Eumorphia prostata and a chiral synthesis of dehydromyopyrone is described. Furthermore a general way of preparing a large variety of elemanolides has been performed. The total synthesis of an unusual 5-methyl coumarin linked with a sesquiterpene derivative as well as the synthesis of a rearranged diterpene will be discussed which led to final confirmation of some detail in the stereochemistry.

TERPENOIDS FROM THE DEFENCE SECRETION OF OPISTHOBRANCH MOLLUSCS

Guido Cimino, Guido Sodano and Aldo Spinella

Istituto per la Chimica di Molecole di Interesse Biologico del C.N.R., Arco Felice, Napoli, Italy.

Gastropods are generally protected against predators by their shells. However, in the gastropod subclass Opisthobranchia there is an evolutionary decrease of the shell which in nudibranchs is completely lost. In spite of this the apparently unprotected opisthobranchs suffer a very low level of predation. This is due to the fact that these animals have elaborated a series of defensive strategies which include some chemicals used as allomones.

Recent studies on opisthobranchs have characterized many of the defence allomones; some of them belong to the isoprenoid classes.

We will present the results obtained studying some Mediterranean opisthobranchs with particular emphasis for structure, origin and role of the isoprenoids present in defensive secretions. Some considerations will be made about the structure--activity relationship of some molecules, with particular attention for those characterized by 1,4-dialdehydic function, which have allowed an intriguing connection between the defensive chemistry of the nudibranchs and human hot taste.

LONG-RANGE PROTON-CARBON COUPLING IN STRUCTURE ELUCIDATION. NEW COMPOUNDS FROM THE EUPHORBIACEAE

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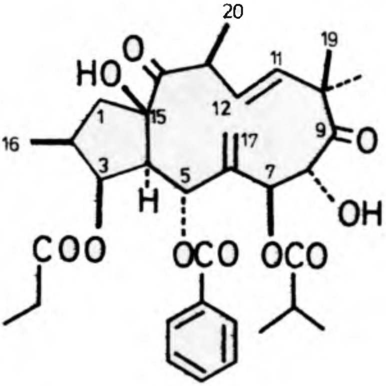
The technique of 2D long-range δ_C/δ_H correlation provides valuable structural information. Its use in the structural elucidation of enukokurin (1), a new jatrophane diterpenoid from Euphorbia lateriflora, will be described. The structures of some phorbol derivatives from E. lateriflora and some 19-hydroxyingol derivatives from E. poisonii will also be discussed.



(1)

CONSTITUENTS OF HIMALAYAN JUNIPERS

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In view of the poor quality of the Himalayan Cedarwood (*Cedrus deodora*) oil, attention has been focussed towards Juniper species of Himalayas for the better quality oil. Though *Juniperus macropoda* proved to be a rich source for the cedrol content, the genus attracted our greater attention for the occurrence of variety of organic molecules. Thus from *J. macropoda* we got interesting lignans, coumarins, acetophenones, flavonoids and their glycosides besides other reported compounds. *Juniperus pseudosabina* Hook which is very close to *J. macropoda* showed the presence of a number of very interesting diterpenoids having a labdane type of skeleton. Thus we were able to assign structures to 12 new diterpenoids. The structures assigned were based on interesting chemical reactions coupled with spectroscopic studies.

ISOPRENOIDS AS COMPOUNDS OF MANY DIVERSIFIED FUNCTIONS IN THE NATURE

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Gone are the times when isoprenoids, similarly to other "secondary metabolites" were taken as natural products mostly without any important functions. Presently, a large array of vital functions of some of their special derivatives is well known, e.g., as important plant or animal hormones or other regulators of different functions. Only in the last decades an immense amount of facts was presented, demonstrating their broad functionality in the interactions of organisms belonging to different kingdoms. They are especially important for their ecological significance, e.g., as xenochemicals (antifeedants, insect pheromones, defensive compounds, allelochemicals, etc., etc.).

An attempt will be made to summarize briefly these activities of terpenoids and steroids in a form easy to survey.

NEWER EXAMPLES OF MICROBIAL TRANSFORMATIONS OF TERPENOIDS

W.-R. Abraham, H.-A. Arfmann, B. Stumpf, P. Washausen,
K. Kieslich

Institute for Biotechnological Research, Braunschweig
Fed. Rep. Germany

Multifold investigations on biotransformations of terpenoids are already known (V. Krasnobajew; "Terpenoids" in Biotechnology ed. H.-J. Rehm and G. Reed, Verlag Chemie, Heidelberg (1984) Vol. VIa p. 97-125). Whereas former efforts tend mainly towards the elucidation of microbial degradation pathways without practically usable accumulation of intermediates, in the last fifteen years some results are reported on enzymatic conversions of representatives of this class of substrate to interesting feasibly in preparative scale (K. Kieslich; "Transformations of Terpenoids" in Progress in Essential Oil Research ed. B.J. Brunke, W. de Gruyter, Berlin (1986) p. 367-394).

This lecture describes some newer examples of microbial transformations of mono-, bi- and acyclic terpenoids. The substrates are converted by different microorganisms via epoxidation, formation of glycols or new C-C-bonds, monohydroxylation or hydration with or without partial degration to new metabolites as intermediates for further chemical synthesis.

RELATIVE AND ABSOLUTE CONFIGURATION OF ß-TURMERONE AND SOME NATURAL 1-BISABOLONES.

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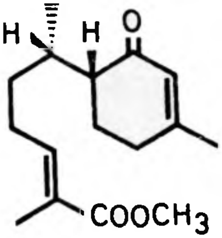
The 1-bisabolone class of sesquiterpenes represents a rapidly growing natural product family mainly found in composites. As a typical example the carboxylic ester I isolated from <u>Baeria chrysostoma</u> is shown here. Most of the family members were discovered and their structure elucidated by Bohlmann, who also gave some spectroscopic evidence regarding the relative and absolute configuration at the two adjacent chiral centres.



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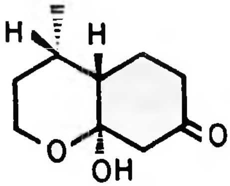

II

During the last 15 years we have synthesized some dozen natural members of this class in optically active form. From these efforts a general rule emerged for determination of the relative configuration by ^{1}H-n.m.r. spectroscopy. Moreover, we were led to the conclusion that all natural 1-bisabolones reported so far, belong to the same relative stereochemical series.

Starting from (-)-3-S-methyl-valerolactone of well established absolute configuration we synthesized the crystalline bicyclic derivative **II** and determined its relative structure by X-ray. The latter was transformed into several natural 1-bisabolones and into ß-turmerone. In this way we were able to deduce relative and also absolute configurations of these natural compounds.

NEW DEVELOPMENTS IN INSTRUMENTAL ANALYSIS OF VOLATILE TERPENES

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Essential oils represent in general rather complex multicomponent mixtures covering a wide range in concentration. Therefore, a detailed analysis of the individual oil components requires the application of modern physico-chemical methods and sophisticated instrumentation. Recent developments in this field are generally dependent on the stage of advancement of instrumentation and the skilfull combined application of individual analytical techniques. In principle the procedures to investigate such complex mixtures can be devided into two groups:

1. The mixtures to be analyzed is first separated by a chromatographic technique and subsequent identification is performed by spectroscopy. The most commonly employed analytical tool is the on-line coupling of a capillary gas chromatograph to a mass spectrometer. Some examples of advanced techniques in this field will be given to demonstrate the high efficiency and versatility of those techniques (e.g. CI with different gases, high resolution MS and mass chromatography). Furthermore, another "hyphenated technique", the coupling of a capillary gas chromatograph with a Fourier transform spectrometer (HRGC/FTIR) can provide valuable additional information, often being complementary to GC/MS data. This method has proven helpful especially for differentiating stereoisomers, determinating functional groups and detecting and analyzing overlapped gc peaks.
2. As an alternative, a completely different approach may be utilized to investigate volatile terpene mixtures: the direct spectroscopic measurement of the entire mixture by 13C NMR spectroscopy without previous chromatographic separation. The advantages and perspectives of this method are discussed by means of selected examples.

THE IMPORTANCE OF ISOPRENOIDS IN THE LIVES OF INSECTS

Jerrold Meinwald

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Isoprenoids with both conventional and unconventional structures play an important role in the chemical defense of many insect species. There are also many examples of isoprenoids serving as intraspecific or interspecific messenger substances. This lecture will open with an overview of some of the biological roles played by a variety of terpenes and steroids in the lives of insects. It will continue with more detailed discussion of the remarkable exploitation of cantharidin, one of the longestknown isoprenoids from an animal source, by a species of pyrochroid beetle. This research, in which we are collaborating with Drs. Thomas Eisner and Braden Roach, provides the first isoprenoid example of a defensive compound which is sequestered from a food source, transmitted from males to females during mating, and is subsequently incorporated into eggs, thereby rendering them distateful to predators. Evidence that cantharidin not only serves a defensive role, but also acts as an aphrodisiac pheromone for these beetles will be presented. These studies suggest that isoprenoids can play a crucial role in sexual selection, and demonstrate the closest possible relationship between chemical defense and chemical communication.

THE INTRODUCTION OF CORTICOID SIDE CHAIN INTO THE STEROIDS WITH 1,4-DIEN-3-ONE FUNCTION.

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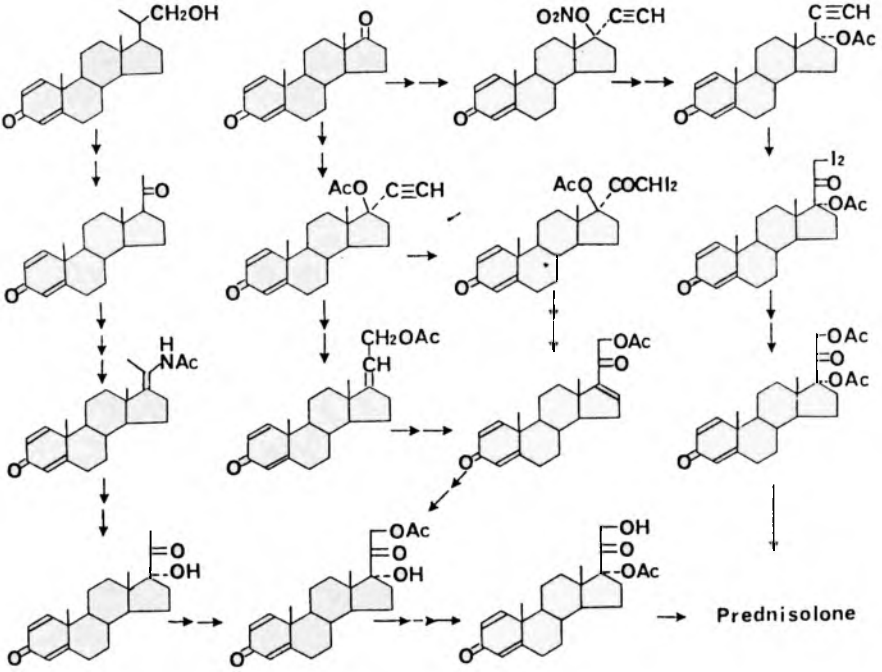
The microbial degradation of cholesterol allowed the production of 21-hydroxy-20-methylpregna-1,4-dien-3-one and androsta-1,4-diene-3,17-dione, from which various steroidal drugs such as estrone, have been produced. These steroids may be useful starting materials for prednisolone because the A ring is fully functionalized as 1,4-dien-3-one system. We present here the conversion of these starting materials into 17α,21-dihydroxypregna-1,4-diene-3,20-dione 17-acetate which is a suitable substrate for the following microbiological C-11 hydroxylation process.

The methods are summarized in the following scheme.



X-RAY DIFFRACTION TECHNIQUES IN NATURAL PRODUCTS RESEARCH

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Poland

X-Ray diffraction is the most powerful method currently available for studying molecular structure, as judged by the amount of structural information obtainable from a single determination. In natural products chemistry X-ray methods are frequently used to establish general facts about a molecule: chemical structure,stereochemistry, conformation,etc. The absolute configuration can directly be determined if the configuration of a portion of the molecule is known from other sources, or it can be assigned by means of the Bijvoet method if natural product contains a sufficient number of atoms of atomic number eight or higher to permit additional analysis of the data. Accurate structural parameters combined with molecular energy calculations provide information for interpretation of chemical activity and stability. Also present in the crystallographic literature is the information on the non-bonded or weakly-bonded intermolecular interactions. We shall make use of this information while studying environmental effects.

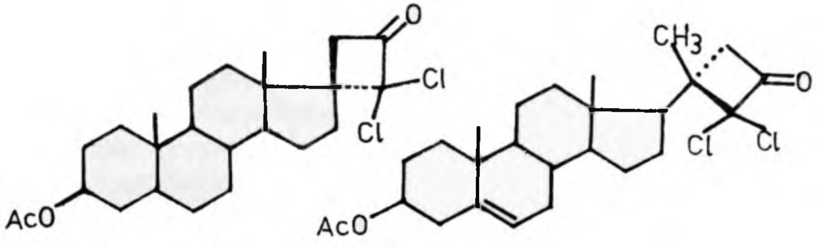
CYCLOADDITION OF DICHLOROKETENE AND METHYLENE STEROIDS

Krzysztof Błaszczyk and Zdzisław Paryzek

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

Ketenes react with alkenes to yield cyclobutanones in reactions of remarkable stereoselectivity. The stereochemical features of these reactions are consistent with an allowed ($\pi 2s + \pi 2a$) process, in which ketene acts antarafacially and the reaction has been interpreted as concerted. On the other hand, cyclobutanones are versatile intermediates in organic synthesis.

In the reaction of dichloroketene with the sterically unhindered steroid, 3-methylene-5α-cholestane, good yields of the two isomeric spiro-cyclobutanones were obtained. In the case of 17- and 20-methylene steroids, cycloadditions were regioselective and afforded one isomer of spiro-cyclobutanone **1** and **2**, respectively. Chemical and spectral evidences are presented, which allowed the assignment of the stereochemistry of cycloadducts and their reduction products.



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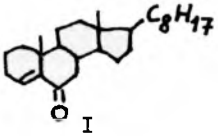
CONTRIBUTION TO PEROXYACID OXIDATION OF α,β-UNSATURATED KETONES

Václav Černý[+], Miloš Buděšínský[+], Miloš Ryba[+] and František Tureček[++]

[+] Institute of Organic Chemistry and Biochemistry,
[++] The J. Heyrovský Institute of Physical Chemistry and Electrochemistry,
Czechoslovak Academy of Sciences, Prague, Czechoslovakia

We investigated the reactivity of α,β-unsaturated ketones of the s-cis type /I and II/ and of the s-trans type /III and IV/ towards 3-chloroperbenzoic acid under standard conditions.



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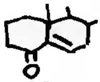

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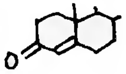

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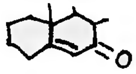

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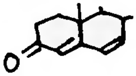
The s-cis types I and II furnish the corresponding epoxides in markedly higher yields /63% and 49%, resp./ than their s-trans counterparts III and IV /5% and 27%, resp./.

It has been generally assumed[1] that in linearly conjugated dienones the double bond more distant from the carbonyl group reacts preferentially with peroxyacid as e. g. in V → VI.



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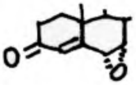

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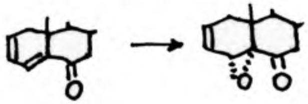

VII VIII

However, we have found that the dienone VII yields preferentially VIII. We conclude that this is due to s-cis character of the carbonyl group-adjacent double bond moiety. The rule of preferential reactivity of the double bond more distant from the carbonyl group in linearly conjugated dienones appears to be valid only for aliphatic dienones or for cyclic dienones comprising a s-trans enone moiety.

References:

1. Matthews G. J., Hassner A. in "J. Fried, J. A. Edwards: Organic Reactions in Steroid Chemistry", p. 7; Van Nostrand Reinhold Co., New York 1972.

A NOVEL REARRANGEMENT OF SOME STEROIDAL α,β-UNSATURATED PYRIDINE-N-OXIDES

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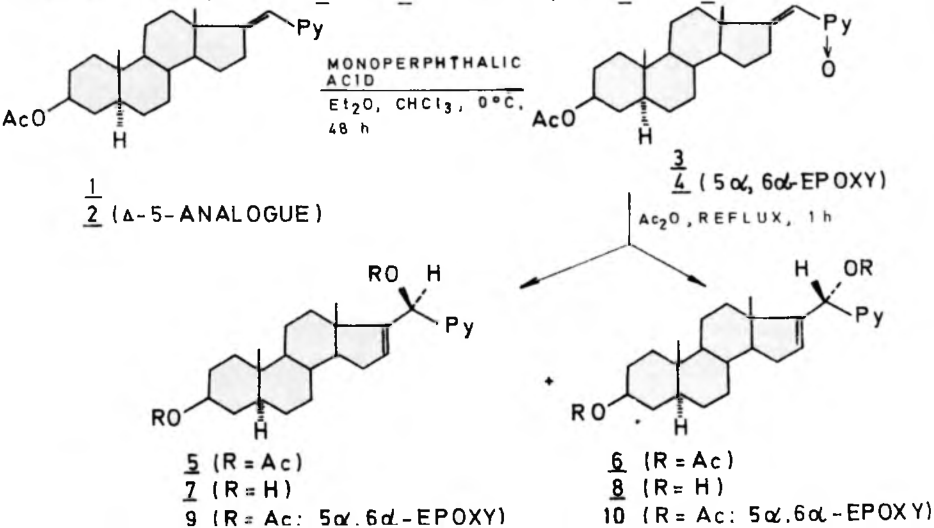
A novel rearrangement of α,β-unsaturated pyridine-N-oxides was discovered in this work. Namely, on heating 3β-acetexy-17-picolinylidene-5α-androstane-N-oxide (3) and 3β-acetoxy-5α,6α-epoxy-17-picolinylidene-androstan-N-oxide (4) in boiling Ac_2O the corresponding diastereoisomeric 20-acetoxy-17-picolyl-16-androstene derivatives (5, 6 and 9, 10) were obtained. The starting compounds 3 and 4 were prepared from 3β-acetoxy-17-picolinylidene-5α-androstane (1) and the corresponding Δ-5 analogue 2 by an oxidation with monoperphthalic acid. Diacetates 5 and 6 could not be chromatographically separated, but the corresponding diols 7 and 8 were successfully separated on a column of silicagel. Reacetylation of the separated 7 and 8 afforded pure 5 and 6.



SPIROSTANE-TYPE SAPONINS AND OTHER PHYTOSTEROIDS ACTING AS ALLELOCHEMICALS IN THE PLANT-INSECT INTERACTION

Juraj HARMATHA

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The main biologically active compound for leek-moth larvae, *Acrolepiopsis assectella*, has been isolated from the flowers of leek, *Allium porrum*, which is the specific host plant for this insect [1]. It has been identified as 3-O-([β-D-xylopyranosyl(1-3)]-[β-D-glucopyranosyl(1-2)]-[β-D-glucopyranosyl(1-4)]-[β-D-galactopyranosyl])-(25R)-5α-spirostane-2α,3β,6β-triol [2]. There are symptoms of intoxication manifested by digestive disfunctions, reduced or arrested growth and by inhibition of moulting for numerous individuals of the insect population [3]. Several other spirostane-type saponins have been tested in the same model. Digitonin displayed similar effects as the leek active compound [4]. Since saponins are known to produce a significant reduction in plasma cholesterol concentration in various animals, interference with insect development was tested. The addition of cholesterol or β-sitosterol to the diet antagonized the effect of active saponins [2,4]. The content of β-sitosterol and its derivatives in *Allium* porrum could be thus an additional factor influencing the activity of the leek active compound. The considerable difference in the quantitative content of the active saponin in the leaves and flowers may also play an important role in the maitenance of the natural equilibrium between the plant and the herbivore.

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1. J.Harmatha, B.Mauchamp, C.Arnault, K.Sláma: Biochem. Syst. Ecol. 15, 113-116 (1987).
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4. C.Arnault, B.Mauchamp: Experientia 41, 1074-1077 (1985).

1,3-DIPOLAR CYCLOADDITION OF NITRILE OXIDES TO Δ^{22}-STEROIDS: A NEW APPROACH TO THE CONSTRUCTION OF STEROID SIDE-CHAINS

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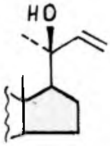
1,3-Dipolar cycloaddition of nitrile oxides to unsaturated compounds is widely used during last 10-15 years in various synthetic approaches to different classes of biologically active substances. Despite extensive studies on steroid side-chains synthesis in this period there were almost no efforts to apply the nitrile oxide approach for solving this problem. The work done by us during the recent years on the developing of methods of nitrile oxide adducts transformation in open-chain products and their application to the formation of α- and ω-chains of prostaglandins has turned out to be potentially important for synthesis of steroids possessed polyfunctional side-chains with more than 5 carbon atoms. Therefore we decided to study 1,3-dipolar cycloaddition reactions of some nitrile oxides RCNO with Δ^{22}-terminal steroids such as 1 which may be easily obtained from pregnenolone acetate by its reaction with vinylmagnesiumbromide. Nitrile oxides generated in situ from (i) hydroximic acid chlorides and triethylamine or (ii) primary nitrocompounds under the action of phenylisocyanate, reacted with double bond and yielded the isoxazolines 2 with high regio- and stereoselectivity. In some cases small amounts of 22-epimeric isoxazolines 3 and isoxazoles 4 were obtained as by-products. If the initial steroidal dipolarophile as 5 had two double bonds (obtained as a result of water elimination from 1) its reaction with nitrile oxides was rather complicated and both mono- and bis-adducts 6-8 with different regio- and stereochemistry have been obtained.

The structures of the adducts were elucidated by spectral methods and some transformations of isoxazolines were investigated. For determination of the configuration at C-22 special NMR-study using differential spectra of nuclear Overhauser effect has been developed. It was especially effective in the case of the unsaturated isoxazolines 9 and 10 obtained from corresponding 20-hydroxyisoxazolines under the action of dehydration agents.



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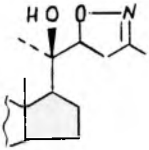
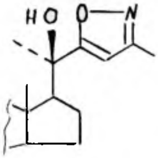


2 22R

3 22S



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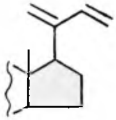

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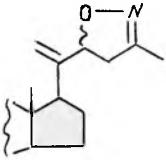

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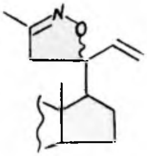

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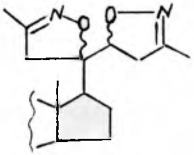

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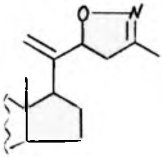


9 22R

10 22S

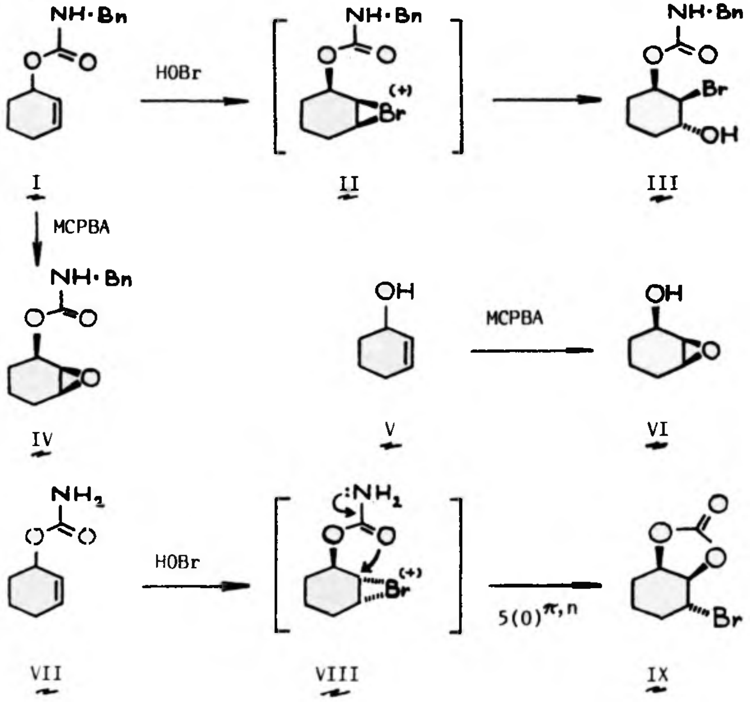
Chemical and spectral properties of the synthesized compounds will be discussed.

STERIC CONTROL OF ELECTROPHILIC ADDITIONS BY NEIGHBORING GROUPS

Pavel Kočovský

Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences, 16610 Prague 6, Czechoslovakia

The reaction of allylic carbamate I with hypobromous acid has been found to give bromohydrin III as the major product. The addition proceeds via an intermediate cis-bromonium ion (II). Similarly, epoxidation of I with m-chloroperoxybenzoic acid produces cis-epoxide IV. This behavior parallels the stereodirecting effect of an allylic hydroxyl which is well known to steer the approach of the epoxidizing reagent also from the cis-side (V → VI). The carbamate group thus appears to be an alternative to the hydroxyl in steric control of electrophilic additions. Further aspects of these effects will be discussed, namely the competition of coordination of the electrophile by the neighboring group vs. the "classical" nucleophilic neighboring group participation (compare I → III vs. VII → IX).



23,24-BISNOR-3-KETO-CHOLA-1,4-DIEN-22-OIC ACID - STARTING MATERIAL FOR STEROID SYNTHESES

B. Schönecker[a], P. Droescher[b], U. Hauschild[b] and C. Müller[b]

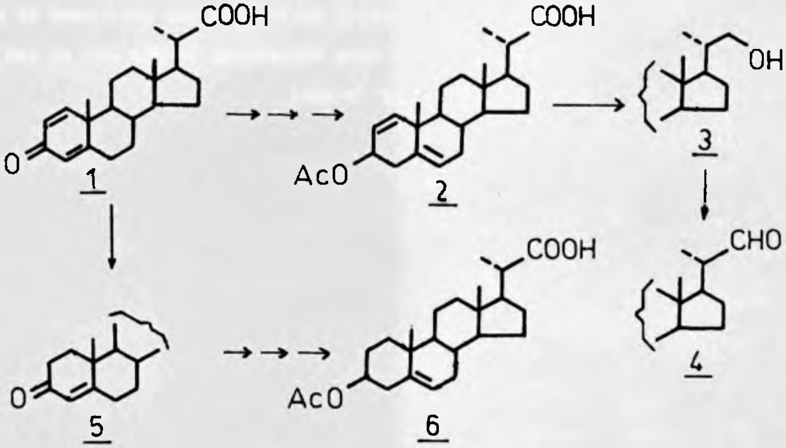
[a] Academy of Sciences of the GDR, Central Institute of Microbiology and Experimental Therapy, Jena, GDR

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

23,24-Bisnor-3-keto-chola-1,4-dien-22-oic acid (1), available by microbiological degradation of sterols , is transformed into intermediates of biologically active steroids. Deconjugation of the ring A is possible without epimerization at C-20. Reduction of the 3-keto group and acetylation after the deconjugation furnished the 23,24-bisnor-3ß-acetoxy-chola-1,5-dien-22-oic acid (2). The carboxylic acid 2 can be reduced to the 22-alcohol 3 by Ishizumia method (ClCOOEt; $NaBH_4$). Oxidation of 3 with PCC provides the aldehyde 4.

After hydrogenation of the 1-double bond of 1 the known 23,24-bisnor-3ß-acetoxy-chol-5-en-22-oic acid (6) is available by analogous reactions as described.

The possibilities of further selective reactions are discussed.



STEROLS FROM SOME LEPIOTACEAE

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80138 NAPOLI - Italy

In recent years attention has been focused on the mushrooms for their very important role in our dietary and for their pharmacological, taxonomic and economic interest (1-5).

By modern cultivation method it has been shown that by growing mushrooms is possible obtain nutritious and delicious food.

The connaissance of the chemical composition of mushrooms being of taxonomic significance is interesting because might provide an index of quality and flavour charateristics above all in relation to investigations and evaluations of new cultivable species.

In the present paper were reported the results obtained from the investigation of three species of Agaricales of the family of Lepiotaceae, namely Lepiota cristata (A. & S. ex Fr.) Kumme, L. procera Scop. ex Fr. and L. rhacodes Vitt. The isolation and purification of sterols was performed as previously described (1); the structures were determined by GLC and on the basis of spectral data (I.R., U.V., M.S. and ^{1}H-NMR).
The results are shown in Table I.

Table I

Sterol composition of Lepiotaceae (%)

	L. cristata	L. procera	L. rhacodes
Cholesterol	3.3	3.5	4.2
Ergosta-5,7-dien-3β-ol	8.8	10.3	9.5
Fungisterol	10.3	6.9	8.4
Ergosta-7,22-dien-3β-ol	6.2	8.2	9.9
Ergosterol	68.4	65.8	63.6
Brassicasterol	1.3	2.6	1.8
24-methylencholesterol	T	0.8	1.3
Fucosterol	T	0.3	T
Undetermined	4.7	1.6	1.3

T= Traces

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CHEMISTRY AND STRUCTURE-ACTIVITY RELATIONSHIPS OF NEUROMUSCULAR BLOCKING AGENTS

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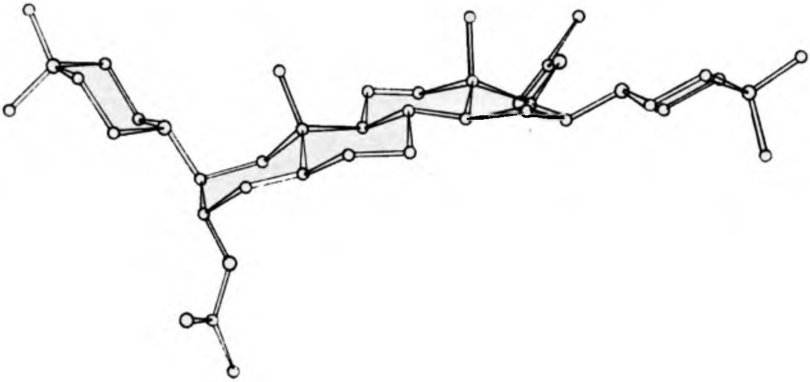
A series of quaternary ammonio steroids having androstane skeletons have been synthetised some of which possessed high neuromuscular blocking activity. One of the series 2β,16β-bis-/4',4'-dimethyl-1'-piperazino/-3α,17β-diacetoxy-5α-androstane dibromide, /Pipecuronium bromide, ARDUAN^{R}/ /I/ has proved to be clinically useful agent of medium duration of action without side effects.



The crystal and molecular structure of /I/ has been determined by a single crystal X-ray analysis and by spectrometric methods IR, NMR and MS.

The molecular geometry of /I/ has been compared with the geometry of pancuronium bromide /2β,16β-dipiperidino-3α,17β-diacetoxy-5α-androstane dimethobromide/ which potency may be associated with the rigidity of the molecule and in particular with the geometries of two acetylcholine-like fragments.

The preparation of these and related ammonio steroids and structure-activity relationships within the series are discussed too.

APPROACHES TO THE SYNTHESIS OF LINEATIN

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

Dedicated to Professor Holger Erdtman on his 85th birthday.

Lineatin is a pheromone component for the bark beetle *Trypodendron lineatum.* Based on the Skattebøl synthesis,[1] lineatin is presently manufactured at high cost and used in lures. The commercial value and the intriguing structure of this odd monoterpenoid makes new synthetic approaches of interest.

An account of our efforts towards the synthesis of lineatin will be presented.

Lineatin

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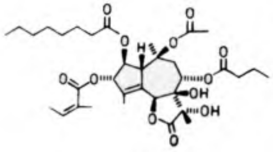
[1] L. Skattebøl and Y. Stenström, *Acta Chem. Scand.*, B 39, 291 (1985).

STRUCTURE OF THAPSIGARGIN AND CELL STABILIZING PROPERTIES OF OXYGENATED SESQUITERPENE LACTONES

S. Brøgger Christensen,[1)] Peter Moldt,[1)] Ole Thastrup,[1)] and M. Holub [2)]
1) Department of Chemistry BC, The Royal Danish School of Pharmacy, DK-2100 Copenhagen, Denmark and 2) Institute of Organic Chemistry and Biochemistry Czechoslovak Academy of Sciences, Prague, Czechoslovakia.

The guaianolide, thapsigargin, has been characterized as the major skin irritating principle in the umbelliferous plant Thapsia garganica.[1] Based on the X-ray structure of the epoxide 2, and on chemical and ^{1}H NMR spectroscopic investigations, including NOE experiments, the structure of thapsigargin was established as 1.[2,3] A later study has questioned this structure and instead suggested the structure 3.[4] This conclusion was mainly based on the formation of an isopropylidene derivative by reacting debutanoylthapsigargin with 2,2-dimethoxypropane, a reaction which was considered a proof for cis disposed 7 and 8 hydroxy groups. ^{13}C NMR spectroscopic studies have revealed that the acetal carbon of the isopropylidene derivative is built into a six-membered ring. Thus, we suggest the structure 4 for the isopropylidene derivative. CD spectroscopic investigations of debutanoylthapsigargin and a partly hydrogenated derivative establish the S configuration of C3. Based on these results and on the X-ray structure of 2 we conclude the correct formula of thapsigargin to be that of 1. This conclusion is further confirmed by comparison with trilobolide, the structure of which has been established by X-ray crystallography.[5]

The ability of Tg potently to activate cells involved in the immune system [6] has prompted us to screen a number of oxygenated sesquiterpene lactones for their effects on peritoneal rat mast cells. None of the compounds were found to be potent activators, but two of the lactones (5,6) were potent Tg-antagonists having IC_{50} values of 8 and 25 µM, respectively. A similar antagonist activity was also demonstrated in human platelets.



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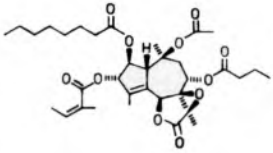

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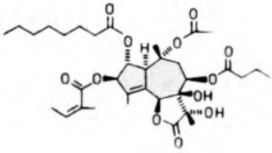

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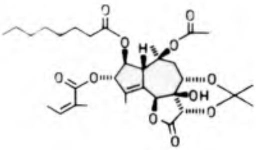

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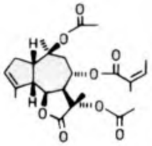

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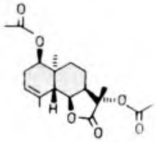

6

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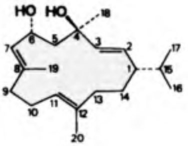
CEMBRANOID DERIVED TOBACCO FLAVOUR CONSTITUENTS

Curt Enzell and Inger Wahlberg

Research Department, Swedish Tobacco Co, Stockholm, Sweden

Dedicated to Professor Holger Erdtman on his 85th birthday

Tobacco, a chemically most closely examined plant, contains cembranoids as major constituents, the predominant representatives being (1*S*,2*E*,4*R*,6*R*,7*E*,11*E*)- and (1*S*,2*E*,4*S*,6*R*,7*E*,11*E*)-2,7,11-cembratriene-4,6-diol (1 and 2).



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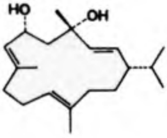

2

Initial pre- and post-harvest transformations of these two major constituents (1,2), involving mainly oxidation of double bonds and rearrangement reactions, account for the formation of the more than fifty C_{20} cembranoids encountered in tobacco to date. Some of these serve as intermediates and suffer further reactions with the formation of degraded cembranoids. These possess irregular isoprenoid skeletons, containing an isopropyl group and consisting of 19 to 8 carbon atoms. The major biogenetic pathways, assigned on the basis of stereostructural knowledge and biomimetic synthesis, will be discussed along with the chemistry and flavour properties of some of the about sixty degraded tobacco cembranoids presently known.

NEW SYNTHON FOR THE CONSTRUCTION OF Z ISOPRENOID CHAIN

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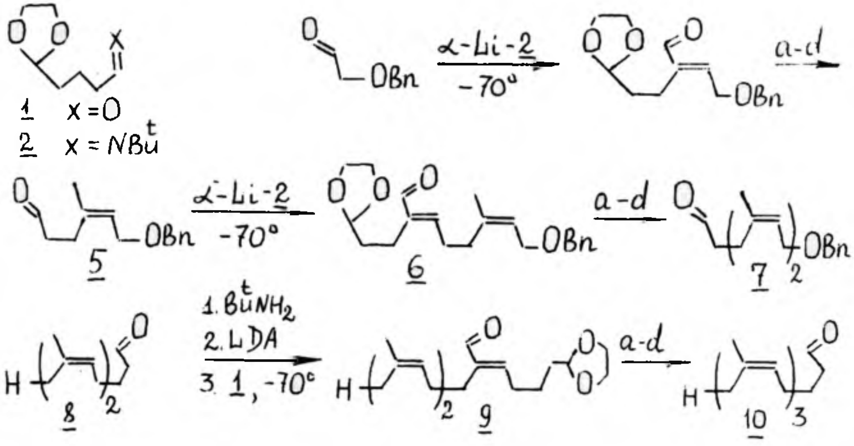
N.D.Zelinsky Institute of Organic Chemistry,
Academy of Sciences, Moscow, U.S.S.R.

5-Ethylenedioxypentanal (I) and respective imine 2 were found to be useful building blocks for five-carbon elongation of linear isoprenoid chain with simultaneous, highly stereoselective generation of Z trisubstituted C=C bond.

Application of 2 for elongation of "head" fragment of isoprenoid molecule is illustrated here by the conversion of benzyloxy acetaldehyde (3), via acetals 4 and 6, into aldehydes 5 and 7 - the known products of selective oxydative degradation of neryl and (Z,Z)-farnesyl benzyl ethers, respectively. Similar elongation of the "tail" moiety of (Z,Z)-trishomofarnesal (8) using I leads via intermediate acetal 9 to its Z isoprenolog IO. Stereochemical purity of E disubstituted acroleins 4,6,9 and corresponding Z olefins thus prepared exceeds 95%.



a. SBH; b. Py·SO$_3$, c. LAH, d. H$_3$O$^⊕$

BIOOXIDATION OF α-PINENE BY METHYLOTROPHIC BACTERIA

Günter Haufe, Marina Dörre, Lutz Weber,
Hans-Dieter Repp and Ulrich Stottmeister

Sektion Chemie, Karl-Marx-Universität, Leipzig
Institut für Biotechnologie, Akademie der Wissenschaften
der DDR, Leipzig

Oxygenated mono- or bicyclic monoterpenes are used as flavours and pheromones, respectively. The synthesis of such compounds using exclusively chemical methods is often not easy accomplished. Usually many step syntheses and/or expensive reagents are necessary.

The stereoselective introduction of oxygen functionalities by microbial methods is therefore a good alternative. In the literature some methods for the monohydroxylation of terpenes are already reported. Unfortunately long fermentation times and working under sterile conditions are usually needed.

We have tested some acidophilic and neutrophilic methylotrophic bacteria in respect to their ability for the monooxygenation of α-Pinene in shaking cultures and by laboratory fermentation. The methanol grown Acetobacter species as well as the (non specified) neutrophilic strains are able to oxidize this terpene. In very short fermentation time (10 to 20 min) the products of autoxidation, mainly trans-Verbenol and Verbenone were produced by Acetobacter methanolicus MB 58 at a pH-optimum of 3.8 to 4.5. Minor components cis-Verbenol, trans-Pinocarveol and trans-Sobrerol were identified in some cases using ^{13}C NMR techniques and capillary gas chromatography. The product ratio can be influenced by variation of the reaction conditions. Nitrogen limitation and addition of glucose or gluconic acid have been shown to be profitable in respect to the selectivity of the transformation.

COMPONENTS IN ROOTS OF ANGELICA SYLVESTRIS L.

Jaroslav Kopecký, Jan Toman, David Šaman,
Ladislav Novotný and Juraj Harmatha

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

Roots of Angelica sylvestris L. contain in addition to fatty acids, steroids, flavonoids and monoterpenoids, also coumarins and furocoumarins.

We isolated furocoumarins imperatorin (I) and ostruthol (II) and sequiterpenic ketoalkohol bisabolangelone[1] (VI), which has a strong insect feeding deterrent activity against some storage pests [2]. So far these compounds were not described in roots of Angelica sylvestris. Further archangelin (III), isoimperatorin (IV) and oxypeucedanin (V) were found.

The analysis of petroletheric extract was carried out by RP HPLC C18 and isolation by column chromatography on silicagel. The structure of isolated compounds was confirmed by spectroscopic methods (^{1}H and ^{13}C NMR, MS, IR).

References:

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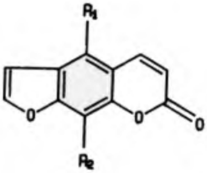
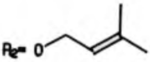
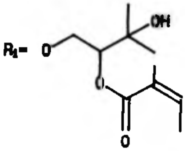
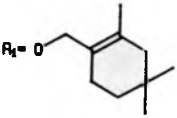
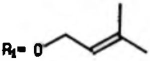
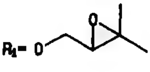
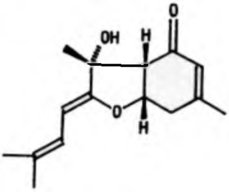


I	R_1= H	
II		R_2= H
III		R_2= H
IV		R_2= H
V		R_2= H



VI

CLAISEN AND PHOTO AZA CLAISEN REARRANGEMENTS IN TERPENOID SYNTHESIS

W. KRAUS, R.BAYER, U.BENKHOFF, J.BUHLERT, and B.VOGLER
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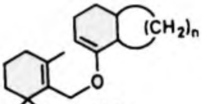
D-7000 Stuttgart 70
West Germany

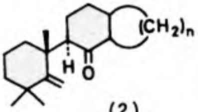
B-seco terpenoids of type (2) have been found to show insect antifeedant activity. We report on synthetic pathways using Claisen and the new photo aza Claisen rearrangement leading to the basic skeleton of these systems.

Claisen rearrangement of enol ethers (1) gives compounds (2) which can be isomerized to (3). The stereochemistry of the reaction products will be discussed in detail.

Irradiation of the vinylogous amides (4) leads to the formation of compounds (5) in a new type of reaction which we call a photo aza Claisen rearrangement. Scope and limitations of this new photo reaction will be discussed.



(1)



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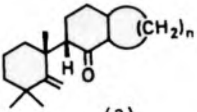

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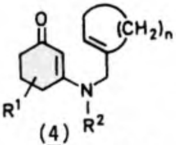

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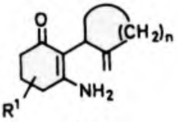

(5)

$R^1, R^2 = H, CH_3$

CYCLODEXTRIN AS A STATIONARY PHASE FOR THE GC SEPARATION OF MONOTERPENE HYDROCARBON ENANTIOMERS.

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Dedicated to Professor Holger Erdtman on his 85th birthday

Cyclodextrin, dissolved in a formamide matrix, can be used for GC separation of the enantiomers of α- and β-pinene, as demonstrated by Koscielski *et al.*[1]. Recently we reported a further development of this method where we have separated several other monoterpene hydrocarbon enantiomers such as limonene, camphene, 2-carene and 3-carene.[2] The method is also used for the study of the enantiomeric composition of these monoterpenes in the frontal gland secretion of the peruvian termite *Nasutitermes ephratae*. Studies of the enantiomeric composition in spruce, *Picea abies* L. Karst and pine, *Pinus sylvestris* are now in progress. The genetic and biogenetic significance of the enantiomeric compositions will be discussed.

1. Koscielski, T., Sybilska, D. and Jurczak, J., *J. Chromatography* **280** (1983) 131-134.
2. Lindström, M., Norin, T. and Roeraade, J., submitted.

^{13}C NMR DATABASIS OF SESQUITERPENE LACTONES AND THE POSSIBILITIES OF STRUCTURAL INTERPRETATION OF THEIR ^{13}C NMR SPECTRA

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High sensibility of present FT NMR spectrometers and the new experimental techniques enable the measurement of ^{13}C NMR of natural substances even in milligram amounts. The consequence of this is also the growing number of completely analysed ^{13}C NMR spectra of sesquiterpene lactones. Till the end of 1986, on the basis of published papers and their own measurements, the authors succeeded in gathering ^{13}C NMR data of more than 900 compounds of this type. A databasis has been created which contained values of chemical shifts and multiplicities of ^{13}C signals together with informations on the structure of the substances and on their plant origin. Programs have been formed for automatic identity determination of the compounds studied with any lactone contained in the databasis and for automatic identification of ester in the sesquiterpene lactone molecule. Other programs enable the choise of compounds according to the selected structural features (type of skeleton, type and position of the subsituent), according to the plant origin, or to the values of chemical shifts, respectively. Critical evaluation of the gathered data made it possible to correct a number of erroneous structural assignment of signals and to formulate more general conclusions for structural ^{13}C NMR spectra analysis of newly isolated sesquiterpene lactones.

NEW ROUTES TO THE NON-RACEMIC INSECT PHEROMONES FROM (+)-β-CITRONELLENE

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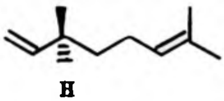
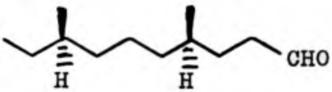
of Sciences, Moscow, the USSR

(+)-β-Citronellene (I), easily available from (+)-α-pinene as a technical-grade product with optical purity within 40-70%, is a good starting material for the synthesis of many chiral insect pheromones. Thus, (R,R)-4,8-dimethyldecanal (II), its stereoisomers and functionally modified analogues were prepared from the mono- and bifunctial chirons of types (III,IV, m+n=3), all obtainable from (I) in a few steps, by use of the organocuprate or Wittig coupling reactions.

Another example of synthetic utility of (I) is its incorporation as a whole unit into the molecule of (2RS, 3S, 7RS)-diprionyl acetate (V) which was achieved in six steps via the the easily available intermediate (VI).



(I)



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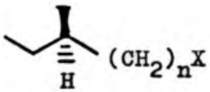

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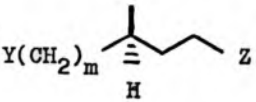

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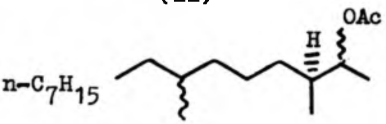

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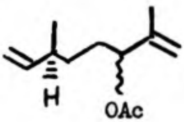

(VI)

STEREOSELECTIVE TRANSFORMATIONS IN THE RING "A" OF (-)-α-MUUROLENE

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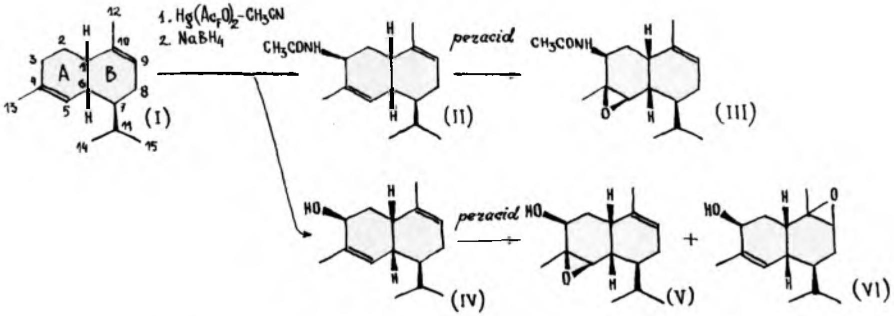
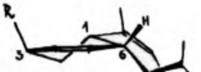
The (-)-α-muurolene (I) molecule has two trisubstituted double bonds with almost the same reactivity, which complicates the stereo- and regioselective functionalisation of the molecul. It was found however that the reaction of compound (I) with mercury-II trifluoroacetate gives only the 3β-substituted derivatives - amide (II) and alcohol (IV). Introduction of a polar 3β-substituent provides the high stereoselectivity of epoxidation of the 4,5-double bond: the reaction leads to the formation of 4,5-epoxides (III, V) exclusively with β-configuration of the epoxy-group. It is noteworthy that epoxidation of amide (II) gives no monoepoxide at the 9,10-double bond, whereas the reaction of alcohol (IV) leads to a considerable formation of stereoisomeric epoxides (VI).



As shown by the ^1H and ^{13}C NMR-spectroscopy, α-muurolene (I) and its 3β-derivatives (II) and (IV) exist in solution in conformation (VII), 3β-substituent having pseudoaxially orientation.



(VII)

Asymmetric Epoxidation of Allylic Alcohol by the Modified Sharpless Reagent

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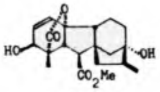
345 Lingling Lu, Shanghai, China

An efficient method for the asymmetric epoxidation of allylic alcohol using Sharpless reagent [Ti(OiPr)$_4$, (+)- or (-)-diethyl tartrate (DET) and tert-butyl hydroperoxide (TBHP)] is extremely useful in the synthesis of chiral compounds. In application of this efficient method for synthesis of insect pheromone in our laboratery, we discovered that addition of a catalytic amount of calcium hydride and silica gel to the Sharpless reagent can greatly reduce the reaction time. For example, the reaction time of (Z)-2-tridecen-1-ol in presence of 5-10 mol% equivalent of calcium hydride and 10-15 mol% equivalent of silica gel with the Sharpless reagent can be reduced from 96 hrs to 8 hrs, while both chemical and optical yield of the epoxide product remain unchanged. The reaction time of dl-1-tridencen-3-ol in the presence of 5-10 mol% equivalent of calcium hydride and 10-15% mol equivalent of silica gel with the Sharpless reagent via kinetic resolution can be reduced from 360 hrs to 25 hrs. Similar results were obtained from our experiments with the epoxidation of nine allylic alcohols.

In order to extend the scope of the modified method, we further investigated the asymmetric epoxidation of various substrats. In the epoxidation of the homoallylic alcohol, similar chemical and optical yield were obtained in comparison with Sharpless method, but the reaction time was greatly reduced. In kinetic resolution of racemic allylic alcohol, the steric hindrance in β-carbon seemed to be of no influence and the reaction time was also reduced. The modified Sharpless reagent could reduce the oxidation time of sulfide to sulfoxide with excellent chemical yield, but the optical yield was much lower than that obtained by Kagan's modified method. Compared with the results of Sharpless method, lower optical yield was also observed from the kinetic resolution of racemic β-thioalcohol and β-aminoalcohol.

In the epoxidation of methyl gibberellate 1 using Sharpless reagent, the starting material was not completely consumed even after 30 days, while epoxidation could be accomplished within 30 hrs in 81% yield by our modified Sharpless reagent at -40 °C and the reaction was regiospecific, that is the epoxidation takes place only on the tertiary allylic alcohol moiety, not on the secondary allylic alcohol one, e.g. 2. When the temperture rose to -20 °C or 0 °C, the epoxidation of 1 with modified Sharpless reagent not only took place on the tertiary allylic alcohol but also on the secondary allylic alcohol to give 3. After acetylation of C_{13}-hydroxy of 1, the epoxidation of 4 at 0 °C with modified Sharpless reagent selectively took place on $C_{1,2}$ double bond giving 1,2-epoxy compound 5. So the polyhydroxy methyl gibberellate (GA_8) 6 could be prepared conveniently by cleavage of epoxide 5 (1 → 4 → 5 → 6), while preparation of 6 using classical procedure needed 9-10 steps.



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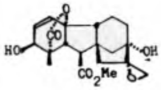

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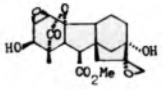

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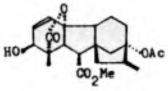

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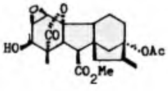

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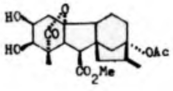

6

This modified Sharpless reagent could also be adapted for epoxidation of allylic alcohol in using the catalytic amount of $Ti(OiPr)_4$ and DET, which was recently discovered by Sharpless and his co-worker.

^{29}Si NMR SPECTRA OF SOME TRIMETHYLSILYLOXY STEROIDS

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Institute of Organic Chemistry and Biochemistry[a] and Institute of Chemical Process Fundamentals[b], Czechoslovak Academy of Sciences, Prague, Czechoslovakia

The ^{29}Si and ^{13}C NMR spectra of a series of trimethylsilyloxy steroids were measured and the chemical shifts found were correlated with structural patterns of the substrates. The chemical shifts were found to depend on the nature of the parent hydroxy group both in terms of the degree of geminal substitution (i.e. primary, secondary or tertiary hydroxy group) and conformational characteristic (axial or ecquatorial ones). The usefulness of the ^{29}Si NMR spectroscopy for structure determination of steroidal alcohols was expected in cases where more common NMR techniques (^{1}H, ^{13}C NMR) do not give sufficient information, particularly in establishing the structure of tertiary hydroxy derivatives.

MASS SPECTROMETRY OF EPOXYSTEROIDS

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

Epoxysteroids, however, have a significant importance as reactive intermediates in both the synthesis and metabolism of this group of compounds, only a few of them have been studied by mass spectrometry.

As a continuation of our earlier study [1] in this field, this work deals with the effect of positional isomerism on the EI fragmentation of a series of epoxyandrostanes possessing an oxiran ring in various positions of A or D rings of the steroidal skeleton. The results obtained from the LRP and HRP mass spectra, as well as from low energy and metastable ion (B/E and B^2/E scan) spectra have been compared with the mass spectrometric behaviour observed for analogous epoxy derivatives bearing a keto or a hydroxy group at C_{17}-position.

The comparison reveals that the epoxy function has a characteristic fragmentation directing role for all of these compounds. The fragmentation routes depend highly on the position of the oxiran ring, leading to mass spectra characteristic of the positional isomerism. This feature was found to be valid both for unsubstituted and for 17-substituted epoxy-steroids, too.

Since most of the α- and ß-epoxides result in different mass spectra, they also can be well distinguished by this method.

Accordingly, mass spectrometry enables us to obtain detailed structural information for this type of compounds.

[1] M.Mák, J.Tamás and Z.Tuba: Adv. Mass Spectrom. 1985, (B) 1333.

A VECTOR METHOD OF REPRESENTING ENZYMIC REACTIONS IN THE $K_m'V'$ COORDINATES AND ITS PROPERTIES

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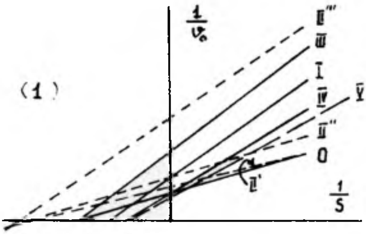
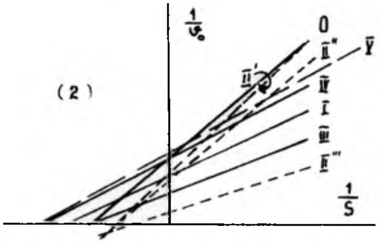
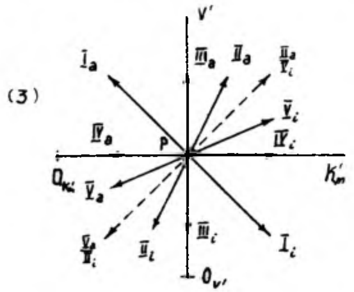
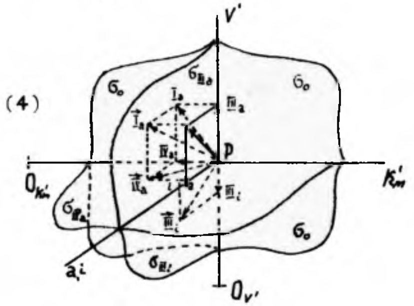
The papers [1-3] show the possibility of existence within the framework of the scheme by Michaelis-Menten of five (I_i to $\overline{V}_i$) types of inhibition (Fig.1, lines $\bar{I}$ to $\overline{V}$) and five (I_a to $\overline{V}_a$) types of activation (Fig.2, lines I to $\overline{V}$) of enzymes. Taking into account the type $\overline{II}_i$ inhibition degenerating into three subtypes $\overline{II}_i'$, $\overline{II}_i''$, $\overline{II}_i'''$ (Fig.1, lines II', $\overline{II}''$, $\overline{II}'''$) and the type $\overline{II}_a$ activation into three subtypes $\overline{II}_a'$, $\overline{II}_a''$, $\overline{II}_a'''$ and also considering the initial type (Figs.1,2, lines 0) it makes the set of 15 types of enzymic reactions. The classification of these types is suggested. The works [2,3] describe the 2-dimensional (Fig.3) and the spatial (Fig.4) $K_m'V'$coordi-









nates suitable for the diagram (Fig.3) and vector (Fig.4) representations of these reactions. Both coordinates are constructed by crossing the horisontal axis $0K'_m$ (for the values of effective Michaelis constants K'_m revealing in the presence of an inhibitor i or an activator a) and the vertical axis $0V'$ (for the values V' of the reactions) in point $P(K^\circ_m, V^\circ)$, where K°_m and V° are the parameters of the initial (neither inhibited nor activated) reaction. One of the consequences of the vector representation of enzymic reactions states that the ratio of the positive difference of the projection coordinates for any spatial vector in the semi-axis $P_{a,i}$ to that of its projection on the plane σ_0, multiplied by the last member in this difference is an equation to calculate the respective constant K_i or K_a. Thus, for instance, it is seen from Fig.4 that the positive differences of the vectors $\overrightarrow{P\overline{III}_i}$ projection coordinates for (non-competitive enzyme inhibition) in the semi-axis $P_{a,i}$ will be $i-0$, and in the plane σ_0 (semi-axis $P0_{V'}$ to be more exact) $V^\circ - V'$ because here $V' < V^\circ$. Therefore, the equation for the inhibition constant shall be here $\frac{i-0}{V^\circ - V'} \cdot V' = \frac{i}{V^\circ/V' - 1} = K_{\overline{III}_i}$ which completely coincides with the known equation [4]. Similarly, the other equations were obtained: $K_{I_a} = \frac{a}{K^\circ_m V'/K'_m V^\circ - 1}$, to be used in the case of lines I and 0, Fig.2; $K_{\overline{II}_a} = \frac{a}{K'_m V'/K^\circ_m V^\circ - 1}$, in the case of lines $\overline{II}'$, $\overline{II}''$ or $\overline{II}'''$ and 0, Fig.2; $K_{\overline{III}_a} = \frac{a}{V'/V^\circ - 1}$, lines $\overline{III}$ and 0, (Fig.2); $K_{\overline{IV}_a} = \frac{a}{K^\circ_m/K'_m - 1}$, lines $\overline{IV}$ and 0, Fig.2 and $K_{\overline{V}_a} = \frac{a}{K^\circ_m V^\circ/K'_m V' - 1}$ lines $\overline{V}$ and 0, Fig.2. The same way $K_{I_i} = \frac{i}{K'_m V^\circ/K^\circ_m V' - 1}$, lines I and 0, Fig.1; $K_{\overline{II}_i} = \frac{i}{K^\circ_m V^\circ/K'_m V' - 1}$, lines $\overline{II}'$, $\overline{II}''$, $\overline{II}'''$ and 0, Fig.1 and $K_{\overline{V}_i} = \frac{i}{K'_m V'/K^\circ_m V^\circ - 1}$, lines $\overline{V}$ and 0, Fig.1. The equations for $K_{\overline{III}_i}$ (see above) and $K_{\overline{IV}_i} = \frac{i}{K'_m/K^\circ_m - 1}$ constants calculation are well known [4].

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ХИМИЧЕСКИЕ СДВИГИ ЯДЕР ^{13}C И СТРУКТУРА ПРОИЗВОДНЫХ МЕНТАНА, ПИНАНА, ФЕНХАНА И ИЗОКАМФАНА

Виктор Лысенков

Институт Физико-органической химии Академии Наук БССР, Минск, СССР

Измерены химические сдвиги ядер ^{13}C и определена относительная конфигурация 62 монотерпеноидов, являющихся производными ментана, пинана, фенхана и изокамфана.

Определено влияние 22 заместителей на химические сдвиги ядер ^{13}C циклогексанового кольца, а для некоторых из соединений ряда ментана определена конфигурация предпочтительных ротамеров изопропильной группы.

Найдено, что для атома C^8 цис-пинана и его производных с заместителями в положениях 2,3 и IO характерен химический сдвиг, равный 23,5±0,3 м.д., а для атома C^8 транс-пинана и его производных с заместителями в положениях 3 и IO - 20,I±0,2 м.д. Определено влияние различных заместителей на величины экранирования ядер ^{13}C замещённых 6,6-диметилбицикло/3,I,I/гептанов, цис- и транс-пинанов. Найдено, что терпеноиды ряда цис-пинана существуют предпочтительно в конформации "связанная ванна", терпеноиды ряда транс-пинана - в конформации "связанное кресло", а производные 2,3-дидегидро-6,6-диметилбицикло/3,I,I/гептана - в конформации с плоским фрагментом $C^1-C^2-C^3-C^4-C^5$.

Определены эффекты заместителей на ядрах ^{13}C эпимерных изокамфанов. Показано, что использование химических сдвигов ядер ^{13}C эндо- и экзо-изокамфанов для расчёта химических сдвигов ядер ^{13}C их монозамещённых производных приводит к значительно более точным результатам, чем использование для этой цели таковых 2,2-диметилнорборнана и других моно- и дизамещённых норборнанов.

ELECTROCHEMICAL METHOXYLATION OF SOME BICYCLIC TERPENES

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Institute of General Food Chemistry, Technical University of Łódź - POLAND

In order to continue our investigation on electrochemical transformation of terpenoids a series of experiments involving electrochemical anodic methoxylation of bicyclic terpene hydrocarbons (α-pinene, β-pinene, 3-carene) was performed. The attempts were carried out in methanol on Pt-anode in the presence of sodium p-toluenosulfonate as a supporting electrolyte. It was found that the substrate hydrocarbons disappeared after 2.0-2.5 F/mol had been delivered and the product consisted mainly of mono- and dimethoxy derivatives. In case of α-pinene methoxylation the dominated compononts was a mixture of two isomers of 6,8-dimethoxy-p-menth-1-ene. The individual compounds were isolated by column chromatography and their structure determined on the basis of spectral data. Some of the synthesized methoxy derivatives are interesting from the perfumery's poind of view.

DETERMINATION OF THE ABSOLUTE CONFIGURATION OF SECONDARY ALCOHOLS BY MODIFIED HOREAU'S METHOD USING HPLC

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Czechoslovak Academy of Sciences, 166 10 Prague,
Czechoslovakia

We have modified Horeau's method[1,2] for the determination of the absolute configuration of the alcohols for HPLC analysis. The method is very sensitive and the absolute configuration of the alcohols can be determined on the nmoles level quantities. The method was checked in a series of terpenoid and steroidal alcohols of known absolute configuration. The method was used for the determination of the absolute configuration of some defense diterpenes of termites. The influence of experimental conditions on the course of the determination will be discussed.

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2. Gilbert J.D., Brooks C.J.: Anal. Lett. 6, 639 (1973).

SYNTHESIS AND BIOTRANSFORMATION OF GLUTAMIC ACID AND GLYCINE ESTERS OF CORTEXOLONE

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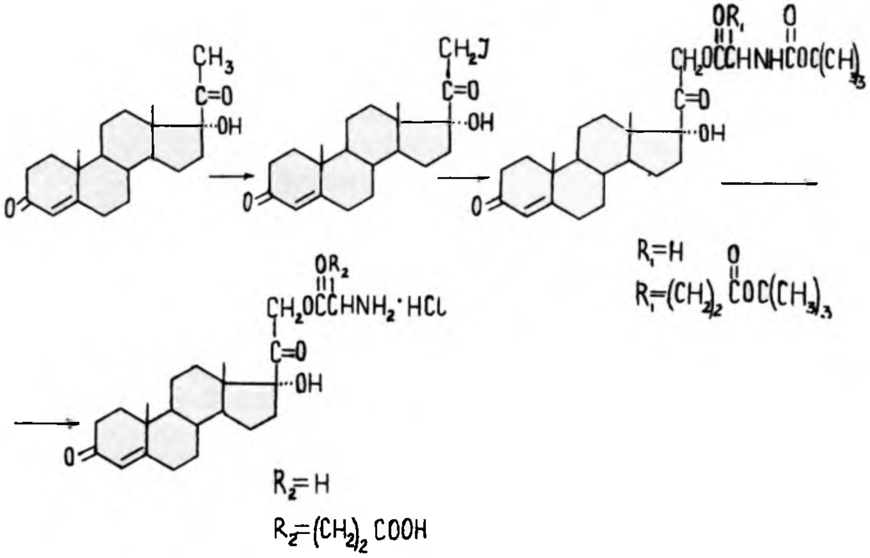
S.Ordjonikidze All-Union Research Chemical-Pharmaceutical Institute, Moscow, USSR

21-Cortexolone esters with glycine and glutamic acid have been obtained by the interaction of 21-iodo hydroxyprogesterone derivative with potassium salts of corresponding amino acids N-terminal of which is protected by tertiary-butyloxicarbonic group (Boc). Protection hydrolysis was carried out with HCl solution in dioxan; high yields of cortexolone esters with hydrochloride of the amino acids in question have been obtained in this case.

Microbiological transformation of the compounds obtained has been studied with the culture <u>Curvularia</u> <u>lunata</u>.



THE INFLUENCE OF SUBSTITUENTS ON THE REDUCTION OF CARBONYL GROUP AT C-3 IN 5α- AND 5β-DIHYDRODERIVATIVES OF TESTOSTERONE AFFECTED BY APHANOCLADIUM ALBUM

J.Dmochowska-Gładysz, T.Kołek, A.Siewiński

Institute of Fundamental Chemistry, Agricultural University of Wrocław, Poland

In our studies on the application of microorganisms as in vitro models for investigating the metabolism of steroids, we have found that the Aphanocladium album strain reduces stereospecifically testosterone and some of its derivatives to respective 3α-allyl alcohols. The reduction is hindered by the presence the following substituents: CH_3 at C-4, OAc at C-17 and OH at C-19.

Now, we present the effect of the same substituents on the reduction of carbonyl group at C-3 in a series of 5α- and 5β-dihydro-derivatives of testosterone. We have found that the reduction takes place with good yields (substrate was not isolated) and the ratio 3α : 3β depends on the kind of substituent, as shown in Table 1.

Table 1. The results of reduction of carbonyl groups in 5α- and 5β-dihydro-testosterone derivatives

Substrate	ratio 3α :3β
17β-hydroxy-4α-methyl-5α-androstan-3-one, 1	3β only
17β-hydroxy-4β-methyl-5β-androstan-3-one, 2	1 : 1
17β,19-dihydroxy-5α-androstan-3-one, 3	1 : 1
17β,19-dihydroxy-5β-androstan-3-one, 4	3β only
17β-acetoxy-5α-androstan-3-one, 5	4 : 1
17β-acetoxy-5β-androstan-3-one, 6	3α only

The carbonyl group at C-3 in acetates of 1 and 2 was found not to be reduced. Clearly, the simultaneous presence of methyl group at C-4 and acetyl one at C-17 totally inhibited the previously observed reduction of carbonyl group.

GLUCOSYLATION OF STEROID COMPOUNDS BY ENZYME PREPARATIONS FROM OAT SEEDLINGS

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Young oat leaves contain two UDP-glucose dependent glucosyltransferases which catalyze the formation of steroid 3-β-D-monoglucosides: a membrane-bound enzyme specific for phytosterols and a soluble (cytosolic) enzyme with a quite different specificity pattern [Kalinowska, Wojciechowski, Phytochem. 25, 2525 (1986) and 26, 353 (1987)].

In the present work the latter enzyme has been partly purified by $(NH_4)_2SO_4$ fractionation, acetone precipitation and gel filtration on Sephadex G-100 and its specificity studied in detail using a wide range of steroid substrates. The highest activity was found with nuatigenin (3β,26-dihydroxy,22,25-epoxy-furost-5-en), however some other steroid sapogenins were also glucosylated: isonuatigenin (45% activity as compared with nuatigenin), chlorogenin (30%), diosgenin (12%), tigogenin (8%), sarsasapogenin (6%). Typical sterols (sitosterol, cholesterol, stigmasterol, cholestanol) were very poor substrates (less than 2% activity with nuatigenin). The enzyme could glucosylate solanidine (38%) and tomatidine (55%) as well as a number of pregnane or androstane derivatives: pregnenolone (35%), androstenolone (15%), androstanol (8%). The above specificity pattern strongly suggests that the physiological function of the enzyme is the formation of nuatigenin 3-monoglucoside which reaction is the first step in the biosynthesis of oat saponins - avenacosides A and B.

INVESTIGATION ON DEACETYLASE FROM HELIANTHUS ANNUUS

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Previous studies have shown that crude enzymatic preparation (supernatant 16000 x g) obtained from sunflower seeds catalyse the deacetylation of tetraacetylglucosides of abscisic acid, gibberelins and oleanolic acid. During the hydrolysis of these compounds the ester-glycoside bond was not splitted.

It was shown that enzymatic activity of deacetylase is not present in shoots and roots of H. annuus.

The present study was aimed at closer characterization of the enzyme, in particular of its substrate specificity.

It was shown that the enzyme catalysed the deacetylation of pentaacetylglucose and tetraacetylglucosides of cholesterol and pregnenolone but not tetraacetylglucosides of aromatic compounds: p-hydroxybenzoic acid, β-naphthol and quercetin. Acyl esters of β-naphthol and cholesterol with long fatty acids were not hydrolyzed.

These observations shown that deacylase from sunflowers seeds splittes specifically acetyl moieties bound to glucose. When acetylated glucose is bound in glycoside the character of aglycone influences the reaction. In glycoside with aliphatic polycyclic aglycone reaction is proceeding efficiently, but it is completely inhibited when aglycone is aromatic. The esters of long fatty acids i.e. palmitic are not hydrolyzed irrespectively of alcohol rest being aliphatic or aromatic.

SOLASODIN PRODUCTION IN CULTURE TISSUE OF SOLANUM LACINIATUM AIT.

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Alma-Ata,USSR

Alkaloid solasodin obtained from aboveground part of Solanum Laciniatum Ait. is important initial raw for synthesis of different species of steroid hormones produced in pharmaceutical industry.

At present time there is information of obtaining of culture tissues of Solanum laciniatum Ait. but only in two reports (Hosoda ,Otasawa,1979;Chandler,Dods,1983)the fact of alkaloid solasodin formation is stated.

The aim of present work was getting of passage culture of cells of S.laciniatum Ait. and study of influence of some factors on formation of steroid alkaloides in callus tissue. Callus tissues were cultivated during four weeks on nutritive media containing naphtylacetic acid (NAA),different concentrations of 2,4-dichlorophenoxyacetic acid (2,4-D) or in media, containing 2,4-D and kinetin.NAA was added into medium in concentration 1mg/l and 2mg/l.Action of kinetin was checked by its addition (0,5mg/l) to nutritive medium containing 2,4-D (1mg/l).It was revealed that growth of callus tissues in medium containing NAA;2,4D-2;2,4D-1,kinetin-0,5 was lower in comparison with media containing 2,4D-1.Sosubstitution of 2,4D - NAA and addition of kinetin or concentration increase of 2,4D in nutritive media do not have positive effect on callus growth.Solasodin content producing in account on per retort was appropriate to growth of callus tissues but alkaloid concentration in cultivated tissues with 2,4D was higher in comparison with ones grown on nutrient media containing NAA;2,4D-2;2,4D-1,kinetin-0,5.At cultivation of callus tissues in light and in darkness it was shown that increase of solusodin synthesis in darkness in callus cultures grown on nutritive media at addition of 2,4D-1,kinetin-0,5 takes place. However similar regularities were not **observed** at cultivation of tissues in media with 2,4D-1.Obtained data are affirmed by investigations of Chandler and Dods (1983).

Suspension cultures of Solanum laciniatum Ait.were obtained from loose uniform callus.It was discovered that for successful growth of suspension cultures medium of Murashige and Skoog at addition of 2,4D and 3% sucrose is necessary.

14,15-DIDEHYDROAJUGAREPTANSIN, A NEW CLERODANE DITERPENE FROM MICROPROPAGATED *Ajuga reptans*.

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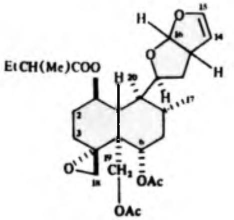
Barcelona-08034. Spain.

In the context of our ongoing interest in the study of the preparation of bioactive molecules via *in vitro* cell and tissue cultures, we have studied the production of insect antifeedant clerodane diterpenes by *Ajuga reptans* micropropagated in test tubes, after finding the adequate balance of phytohormones and nutrients brought in the cell culture system.

Extraction and separation of the desired compounds was carried out following the procedure previously described for the whole plant investigation, resulting in the isolation of a 0.1 % (based on dry weight of plant) of ajugareptansin (I) and a 0.01 % of the so far elusive title compound (II).



14,15-Didehydroajugareptansin, II
Ajugareptansin, I (14-15
single bond)

BIOTRANSFORMATION OF 2-(4-METHOXYBENZYL)-1-CYCLOHEXANONE BY PLANT TISSUE CULTURES

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Plant cells cultured in vitro can be used not only for production but also for biotransformation of various compounds. For the transformation substances of both natural and synthetic origin may be utilized as substrates. For study of the biotransformation of compounds strange to the plant cells we used 2-(4-methoxybenzyl)-1-cyclohexanone, a model compound of the dicyclic juvenoid skeleton.
We utilized Digitalis lanata, Solanum aviculare, and Dioscorea deltoidea suspension cultures, both free and immobilized in alginate gel, for our experiments.
Reaction which prevailed in all tested cell cultures was stereospecific reduction of keto group following by glucosylation of the resulting alcohols. Further minor products were isolated and identified.

BIOTRANSFORMATION OF 2-(4-METHOXYBENZYL)-1-CYCLOHEXANONE BY SACCHAROMYCES CEREVISIAE[1]

Zdeněk WIMMER, Miloš BUDĚŠÍNSKÝ, Tomáš MACEK, Aleš SVATOŠ,
David ŠAMAN, Soňa VAŠÍČKOVÁ and Miroslav ROMAŇUK

Institute of Organic Chemistry and Biochemistry,
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2-(4-Methoxybenzyl)-1-cyclohexanone, a model compound of the dicyclic juvenoid skeleton, was a subject of a biotransformation reaction carried out by yeast cells of Saccharomyces cerevisiae. Reaction kinetics and reaction course were studied within the incubation period of 8 days. Two diastereoisomeric alcohols, cis-(1S,2S)-(+)- and trans-(1S,2R)-(+)-2-(4-methoxybenzyl)-1-cyclohexanol in optical purity of at least 91.6 + 1.0 % and 97.5 + 1.0 %, respectively, were found to be the only products of the biotransformation reaction. Their absolute configuration was determined by the combination of the following methods:

a) by ^{1}H, ^{13}C and ^{19}F NMR of their MTPA esters;

b) by their chemical correlation with the known respective enantiomers of cis- and trans-hexahydro-2(3H)benzofuranone.

Reference:

1. Wimmer Z., Buděšínský M., Macek T., Svatoš A., Šaman D., Vašíčková S., Romaňuk M.: Coll. Czech. Chem. Commun., in press.

ENZYMIC ENANTIOSELECTIVE HYDROLYSIS OF 1,2-DIOL DIACETATES

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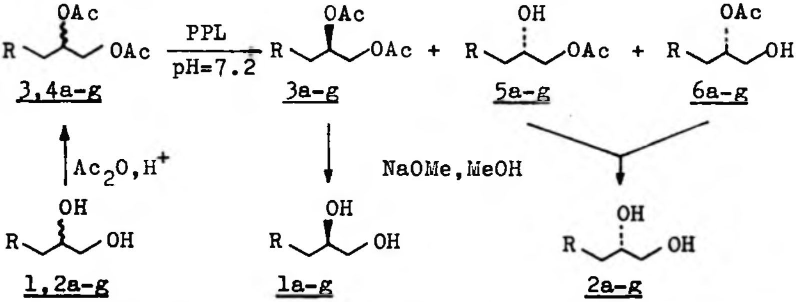
Chiral 1,2-glycols can be used as building blocks in the syntheses of many important molecules e.g. several fungicides, prostacyclin analogues, pheromones or β-blockers. Therefore, a general procedure having ability to prepare them has real importance. This paper describe a pig pancreatic lipase /PPL/ enzyme mediated kinetic resolution of 1,2-diols by enantioselective hydrolysis of their diacetates.



1-6	a	b	c	d	e	f	g
R	H	CH_3	CH_2CH_3	$/CH_2/_3CH_3$	Cl	OCH_3	$OCH_2C_6H_5$

Dependence of the enantioselectivity and the ratio of 5 to 6 on the type of the R group and conversions used is also discussed.

THE FIRST BIOMIMETIC CONVERSION OF AN EPOXYGERMACRONE INTO HUMULENONE

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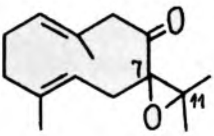
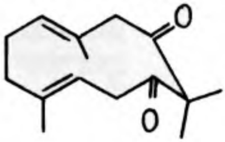
Upon treatment with $BF_3.Et_2O$ 7,11-epoxygermacrone, 1, was readily converted into an 11-membered ring compound, 2, in 75% yield. Two selinane ketoalcohols, 3 and 4, were isolated as minor products (total yield 15%). The structures of the products 2 - 4 were deduced from their spectral data. The formation of the humulene triketone 2 was assumed to include a rearrangement, typical for α,β-epoxyketones, thus accounting for the ring enlargement. To our knowledge, this is the first example of a biogenetic type in vitro conversion of a germacrane skeleton to a humulane skeleton.



1



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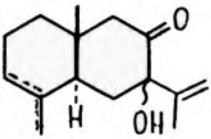

3 $\Delta^{3,4}$

4 $\Delta^{4,15}$

BIOTRANSFORMATIONS BY MEANS OF ORCHDS' TISSUE CULTURES

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In our last paper[1] we studied the possibility of the transformations of isoprenoids by the following orchids: Cymbidium 'Saint Pierre', Epidendrum ochraceum and Dendrobium phalaenopsis. We found that menthyl acetate was hydrolyzed with small enantioselectivity, and steroid coumpounds were transformed in traces only.

Now we have found that these tissue cultures enantioselectively hydrolyze acetates of shikimic acide analogues /benzyl alcohol, /±/-1-phenyletanol, /±/-1-[2-naphtyl]ethanol, /±/-1-[1-naphtyl]ethanol, /±/-2-phenylbutanol, cinnamonyl alcohol, methyl salicylate, methyl vanilinate, methyl 2,5-dihydroxybenzoate and methyl 3,4,5-trihydroxybenzoate/ with the yield 20-100%.

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1. A.Mironowicz, K.Krasiński, K.Kukułczanka, A.Siewiński: Transformations of Isoprenoids by Orchids in Tissue Cultures, Phytochemistry 1987 in press.

ENANTIOSELECTIVE OXIDATION OF CERTAIN TERPENIC ALCOHOLS AND THEIR ACETATES WITH ARMILLARIELLA MELLEA

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In our investigations, we have noticed that the Armillariella mellea fungus, a parasite of our woodlands, was capable of selective oxidizing components of coniferous tree resin /terpenic hydrocarbons and their oxygen-containing derivatives/. The oxidation occured only for certain compounds depending on their structure.

For transformations of this type, we made the following observations on the enantioselectivity of oxidation /hydroxylation/ of (±)α-terpineol and (±)menthyl acetate. Oxidation of (±) α-terpineol proceeded faster with enantiomer 4S. It took place via allyl hydroxylation and epoxidation of double bond; (-)trans-sobrerol and (+)1,2,8-p-menthantriol were the main products. The allyl hydroxylation proceeded only when the first hydroxy group was present in substrate (α-terpineol); no hydroxylation was observed for limonene.
In (±) menthol acetate, hydrolysis of ester and hydroxylation at C-8 were found to occur simultaneously. These transformations proceeded faster for enantiomer 1R,3R,4S; (-)3,8-menthandiol was formed.

It was also found that Armillariella mellea oxidized verbenol to verbenone and trans-sobrerol to hydroxycarvotanacetone. Trans-sobrerol monoacetate underwent a partial hydrolysis and hydroxylation; 3,6,8-p-menthantriol was found among the products. Menthol, cis-carveol and cis-carveol acetate were found resistant against Armillariella mellea.

1. B. Draczyńska-Łusiak, A.Siewiński, A.Rymkiewicz, A.Zabża, A.Leufvèn, J.Basic Microbiol. 8, 487 1985 .
2. B. Draczyńska-Łusiak, Thesis, Agricultural Academy, Wrocław 1986 .

ENANTIOSELECTIVE HYDROLYSIS OF ACETATES OF RACEMIC MONOTERPENIC ALCOHOLS WITH SPIRODELA OLIGORRHIZA

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In our previous works, we found that the water plant: Spirodela oligorrhiza was capable of hydrolysing esters of alcohols - derivatives of androstane [1] and racemic aliphatic-aromatic esters of derivatives of shikimic acid [2]. In the same conditions, the plant oxidized secondary alcohols to respective ketones. For the shikimic acid derivatives, the reaction proceeded enantioselectively.

Now, we present the results obtained for the third group of compounds: esters of selected racemic monoterpenic alcohols, namely, (±) menthol (1), (±) borneol (2), (±)trans-2-hydroxy-trans-dihydropinol (3), (±) cis-2-hydroxy-trans-dihydropinol (4), and (±)trans-2-hydroxy-cis-dihydropinol (5). Acetates 1, 3, 4, and 5 were found to be hydrolysed enantiospecifically; alcohols R formed faster than S ones.

Hydrolysis of acetates 1 and 2 proceeded at the concentration of substrates ranging from 0.2 - 1 g/dm^3. The lack of light hindered the reaction.

1. E.Tłomak, P.Pawłowicz, W.Czerwiński, A.Siewiński, Phytochemistry (1986) 25(1), 61
2. P.Pawłowicz, A.Siewiński, ibid. 1987 26 4, 1001

NEW CARDIAC GLYCOSIDES AND AGLYCONES

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Of late years we isolated from plants five new cardenolides and established their structures:

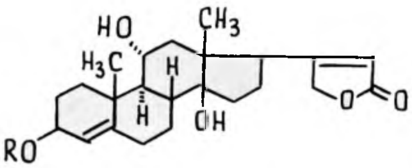
Δ^4-Anhydrosarmentogenin or 3β,IIα,I4-trihydroxy-I4β-card-4,20(22)dienolide (I) was obtained from glycosides II and III; $C_{23}H_{32}O_5$, m.p. 296-302°, $[\alpha]_D^{20}$ 26,2° (in Py). It is rather a rare case of finding natural cardenolide with isolated double bond. The structure of the genin (I) has been established on the basis of spectral data and chemical transformations. For confirmation of the correct presented structure I we carried out counter-synthesis of Δ^4-anhydrosarmentogenin using bipindogenin as an initial substance.

Δ^4-Anhydrosarmentogenin-rhamnoside, $C_{29}H_{42}O_9$, m.p.268-275°, $[\alpha]_D^{20}$-38,2° (in Chf - MeOH). It is 3β-O-α-L-rhamnopyranosyl-IIα,I4-dihydroxy-I4β-card-4,20(22)dienolide (II). The glycosides II and III were isolated from Cheiranthus allioni hort.

Δ^4-Anhydrosarmentogenin-rhamnosyl-glucoside, $C_{35}H_{52}O_{I4}$, $[\alpha]_D^{20}$-44,I° (in MeOH). It is 3β-O-α-L-rhamnopyranosyl-4'-O-β-D-glucopyranosyl-IIα,I4-dihydroxy-I4β-card-4,20(22)dienolide (III).

Glucoacovenoside B (IV) was isolated from Acocanthera venenata G.Don.; $C_{38}H_{58}O_{I5}$, m.p. 269-275/300-304°, $[\alpha]_D^{20}$-69,8° (in MeOH). It is Iβ-O-acetyl-3β-O-α-L-(3-O-methyl)talomethylopyranosyl-4'-O-β-D-glucopyranosyl-I4-hydroxy-5β,I4β-card-20(22)enolide.

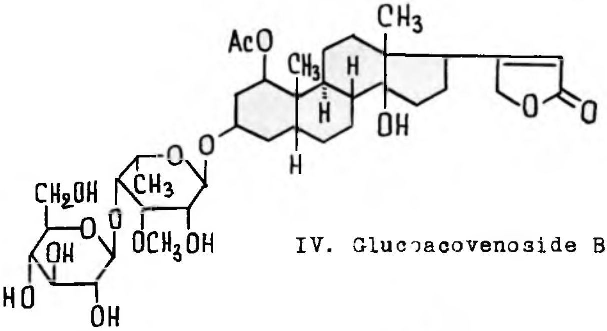
Bipindogenin-allomethylosyl-glucoside (V) was isolated from Erysimum repandum L.; $C_{35}H_{54}O_{I5}$, m.p. 207-2II°, $[\alpha]_D^{2I}$-I8,0° (in Chf - MeOH). It is 3β-O-β-D-allomethylopyranosyl-O-β-D-glucopyranosyl-5,IIα,I4-trihydroxy-5β,I4β-card-20(22)enolide.



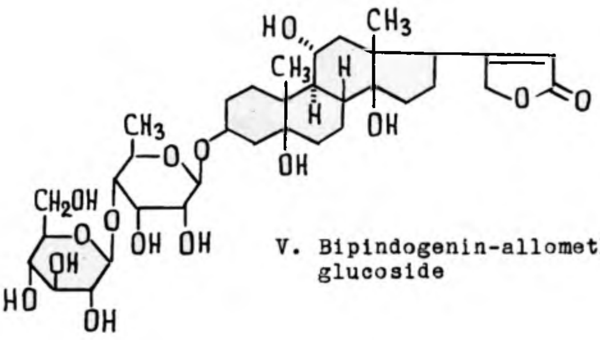
I. R = H. Δ^4-Anhydrosarmentogenin

II. R = α-L-Rha. Δ^4-Anhydrosarmentogenin-rhamnoside

III. R = α-L-Rha-4'-O-β-D-Glu. Δ^4-Anhydrosarmentogenin-rhamnosyl-glucoside



IV. Glucoacovenoside B



V. Bipindogenin-allomethylosyl-glucoside

STEROID GLYCOSIDES OF DIOSCOREA DELTOIDEA PLANTS AND SUSPENSION CULTURES FROM DIOSCOREA DELTOIDEA

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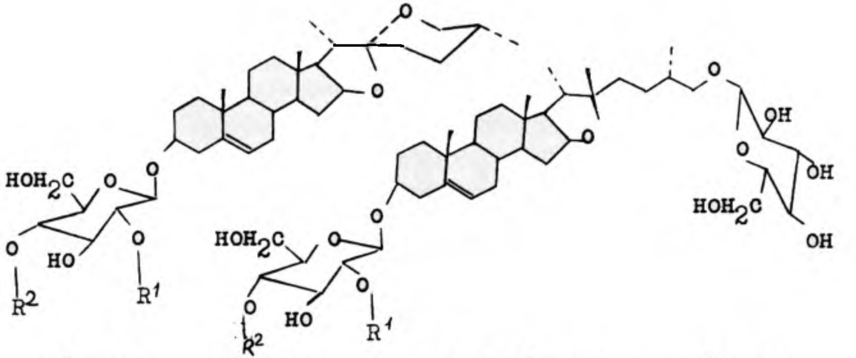
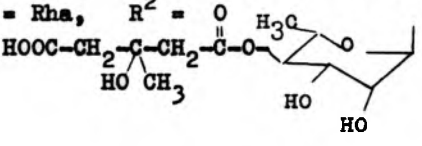
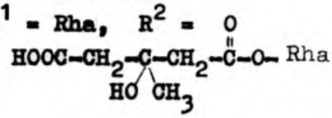


I R^1 = Rha, R^2 = Glc
II R^1 = H, R^2 = Glc
IV R^1 = Rha, R^2 = Rha
V R^1 = Rha, R^2 =



III R^1 = Rha, R^2 = Glc
VI R^1 = R^2 = Rha
VII R^1 = Rha, R^2 =


$HOOC-CH_2-C(OH)(CH_3)-CH_2-C(=O)-O-$ Rha

Plant steroid glycosides (saponins) are used in the pharmaceutic industry as the main source for production of steroid hormones: androgenes, estrogenes, and corticosteroids. Diosgenin obtained from steroid glycosides of Dioscorea deltoidea rhizomes is the most convenient substance to the pharmaceutical purpose. During our study of the plant steroid constituents we have compared the composition of the steroid glycosides in the leaves and rhizomes of Dioscorea deltoidea Wall. From rhizomes of D. deltoidea plants two new oligospirostanosides deltonin (1), mp 293-297°, $[\alpha]^{23}_{546}$ -98,7° (c 1,0; Py);

diosgenin 3-O-ß-D-glucopyranosyl-(1→4)-ß-D-glucopyranosid (II), mp 271-273°, $[\alpha]^{20}_{546}$ -83,8° (c 0,5; Py) and oligofurostanosid deltosid (III), mp 243-247°, $[\alpha]^{23}_{546}$ -63,0° (c 0,5; MeOH) have been isolated. A known oligospirostanosid dioscin (IV), mp 284-285°, $[\alpha]^{23}_{546}$ -114,0° (c 0,5; EtOH) and new acid oligospirostanosid deltofolin (V), mp 207-208°, $[\alpha]^{23}_{546}$ -64,4° (c 0,5; EtOH) have been isolated from the leaves of D. deltoidea plants. In the underground parts the dioscin and deltofolin usually present as the corresponding oligofurostanosides protodioscin (VI) and protodeltofolin (VII), which accumulate in special epidermal cells-idioblasts. The detection and estimation of content oligofurostanosid in the leaves have based on color reaction with Ehrlich's reagent. Therefore it has been shown that the leaf steroid glycosides stand in marked contrast to the rhizome glycosides.

The composition of steroid glycosides in suspension cultures from D. deltoidea has been studied by HPLC method. Analysis have been performed with LKB model liquid chromatograph on a Ultropac Lichrosorb RP C_{18} column with detection at 207 nm; elution has been carried out with 25% acetonitrile in water. The presence of protodioscin and deltosid in ratio 16:10 in water extracts of suspension cultures was observed by HPLC method. As a result of fermentation by ß-glucosidase from cell of suspension cultures dioscin (III), mp 284-285°, $[\alpha]^{10}_{546}$ -106,5° (c 5,0; Py) and deltonin (I), mp 296°, $[\alpha]^{10}_{546}$ - -90,8° (c 5,0; Py) has been isolated. Thus in suspension cultures from D. deltoidea the characteristic steroid glycoside of rhizome (deltosid) and leaves (protodioscin) have been formed. This indicated to the totipotency of Dioscorea cells in vitro. Content of steroid glycoside in D. deltoidea leaves was usually about 1% on dry wt and in suspension culture - to 10% on dry wt of cells. The structures of new oligofurostanosides have been determinated by spectroscopic methods (^{13}C-n.m.r., IR, mass-spectrometry) and some chemical transformation (total and partial hydrolysis, permethylation). Thus D.deltoidea suspension cultures are the good source of biological active oligofurostanosides and diosgenin.

STEROIDS OF SPIROSTANE AND FUROSTANE ROWS FROM COLLECTIVE FRUITS OF ALLIUM CEPA, ALLIUM SUVOROVII, ALLIUM STIPITATUM.

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M.B.Gorovits, N.K.Abubakirov.

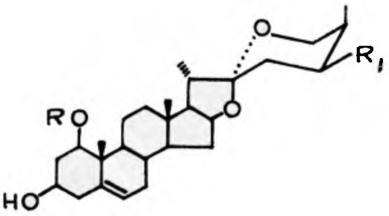
Institute of the Chemistry of Plant Substances of the
Uzbek SSR Academy of Sciences. Tashkent. USSR.

Besides the known (25S)-ruscogenin(I), six new compounds: genin from the spirostane row - cepagenin(II), spirostanol glycosides - alliospirosides A(III), B(IY), C(Y), D(YI) and furostanol glycoside - alliofuroside A(YII), were isolated from collective fruits of onion (Allium cepa L.).

Collective fruits of Allium suvorovii Rgl. and Allium stipitatum Rgl. (cultivated together) are the source of 5 spirostanol genins: diosgenin(YIII), yuccagenin(IX) and alliogenin(X) which are known compounds; anzurogenins A(XI) and B(XII) have not been described earlier.

Anzurogenin B(XII) is the first representative of spirostan row natural genins, which has a ring A in the boat conformation thanks to the presence of C-2 - C-5 oxygen linkage.

The structures of enumerated steroids were proved by chemical transformations and spectral data.



I. $R = R_I = H$

II. $R = H$, $R_I = OH$

III. $R = S_I$, $R_I = H$

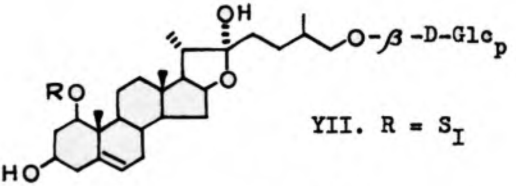
IY. $R = S_2$, $R_I = H$

Y. $R = S_I$, $R_I = OH$

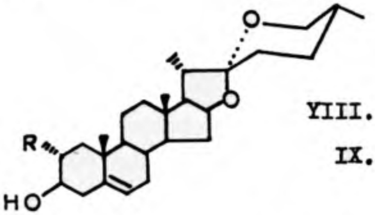
YI. $R = S_2$, $R_I = OH$

$S_I = \alpha\text{-L-Rha}_p \xrightarrow{2} \alpha\text{-L-Ara}_p$

$S_2 = \alpha\text{-L-Rha}_p \xrightarrow{2} \beta\text{-D-Gal}_p$

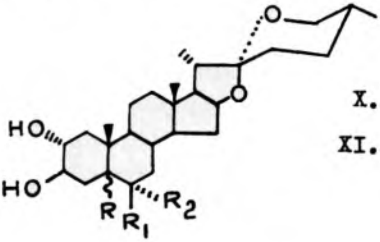


YII. R = S_I



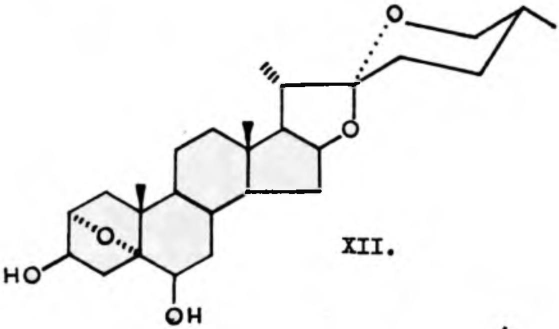
YIII. R = H

IX. R = OH

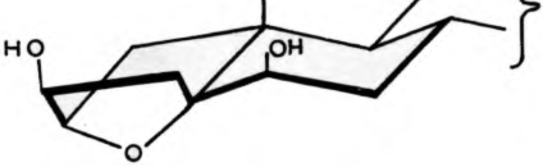


X. R = α-OH, R_I = OH, R_2 = H

XI. R = β-OH; R_I, R_2 = (=O)



XII.



STEROIDAL CONSTITUENTS OF THE HORSE-CHESTNUT'S BARK

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The horse-chestnut, Aesculus hippocastanum L., and other species of Hippocastanaceae, as Aesculus Indica Colebr, for a long time is employed in the traditional folk medicine of some countries.

The extractive preparations of A. hippocastanum are numerous and they have been and are used in terapy (decoction, infusion, medicated wine, ointment, tincture, etc.) as astringent, light anti feverish, anti diarrhoic, anti hemorragic, anti hemmorroidal and antiseptic (1-3).

In the seeds, pericarpe and bark were detected coumarins (4,5), saponins (4,6,7), flavonoids (8), plastquinons (9) and tannins (4).

This report deal with the presence of sterols in the A. hippocastanum's bark. For this study barks of 2-3 years were collected, crushed and made into powder form. The powdered material was extracted with petrol ether three times for 7-8 hr. The ethereal solution was evaporated under reduced pressure and the obtained material was saponified with KOH 10% in EtOH 70% for 2 hr. at reflux under N_2. EtOH was removed and the solution was added with H_2O/Et_2O; the ethereal mojety was anhydrified on anhydrous Na_2SO_4 and then evaporated in vacuo. The residue was applied to a Si gel column and sterol fraction was recovered and after acetylated and purified in the usual manner (10).

The structures of acetyl sterols were determined by G.L.C. on Sigma 115 Perkin-Elmer equipped with an F.I.D. and Silica-gel capillary column OV-30 3% and on the basis of spectral data (I.R., U.V., M.S. and ^{1}H-NMR).

The results are reported in table I.

TABLE I

Steroidal composition of the horse-chestnut's bark (%)

Cholesterol	0.9
Campesterol	1.9
Stigmasterol	16.5
β-sitosterol	57.2
Δ^7-campesterol	2.3
Spinasterol	15.4
Undetermined	5.8

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CYCLOARTANE METHYLSTEROIDS AND THEIR GLYCOSIDES FROM ASTRAGALUS ORBICULATUS AND ASTRAGALUS TRAGACANTHA

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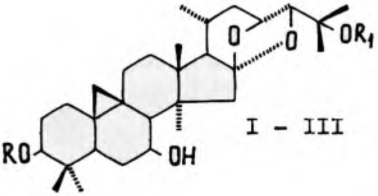
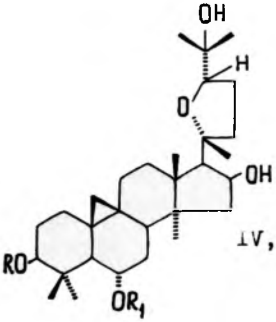
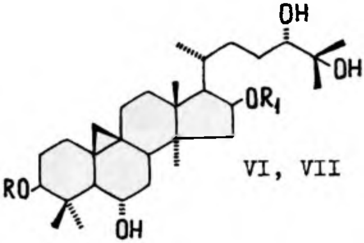
We have investigated two plant species of Astragalus genus (Leguminosae) on the content of cycloartane methylsteroids. Cycloorbigenine (I) and 2 its glycosides - cycloorbicosides A (II) and G (III) were isolated from A. orbiculatus and their structures were elucidated. Besides known cyclosiversigenine (IV) and cyclosiversioside F (V) new methylsteroids cyclocantogenine (VI) and its glycoside - cyclocantoside D (VII) were found in Astragalus tragacantha.



I - III



IV, V



VI, VII

I. $R=R_1=H$
II. $R=\beta$-D-Xylp, $R_1=H$
III. $R=\beta$-D-Xylp, $R_1=\beta$-D-Glcp
IV. $R=R_1=H$
V. $R=\beta$-D-Xylp, $R_1=\beta$-D-Glcp
VI. $R=R_1=H$
VII. $R=\beta$-D-Xylp, $R_1=\beta$-D-Glcp

STEROIDAL ALKALOIDS FROM KOROLKOWIA SEWERZOWII

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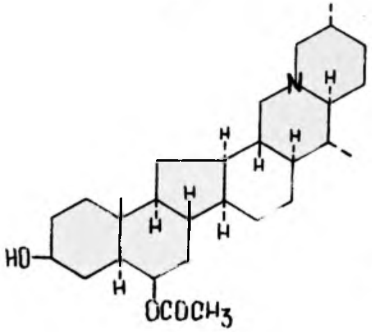
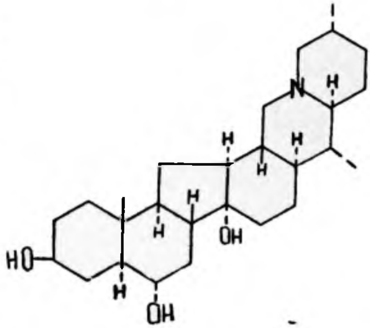
The plants of genera Korolkowia Sewerzowii are mainly occured at the Middle Asia region. Alkaloid content (3,7-0,3%) is due to the vegetation period, field groun and plant organs, as it was found. 28 new compounds bearing on typical, C-nor-D- homosteroidal and new tyre steroidal alkaloids were isolated from that genera plant.

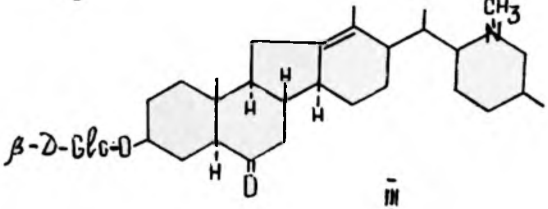
The physiological activity alkaloids have been found among their. The structures of 3 new steroidal alkaloids (acetylsevedine I , sevedamine II , korsemine III)are discussed.



I



II



III

ISOLATION AND IDENTIFICATION OF PHYTOECDYSONES FROM BLECHNUM SPICANT (L).

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The distribution of phytoecdysones, the plant analogues of insect moulting hormones, is in the plant kingdom widespread. At present more than 60 different phytoecdysteroids have been isolated and characterized. Such substances may play an important role in the plant-insect interaction.

From the methanolic extract of the aerial part of the plant α-ecdysone and ecdysterone were isolated and identified. In the more polar n-butanol-water extract glycosidic derivatives of phytoecdysones were detected by means of HPLC and DA-UV detection. Their structure and bioactivity are studied.

ACAULIN: A SESQUITERPENOID WITH A NEW CARBON SKELETON FROM THE MEDITERRANEAN ALCYONACEAN ALCYONIUM ACAULE

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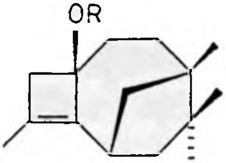
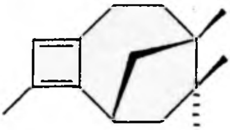
The apparently unprotected alcyonaceans (Octocorallia) have elaborated for their survival a series of defensive strategies which include the use of terpenoids as allomones against predators (1). Until now chemical studies have been performed mainly on tropical alcyonaceans. This is due to the fact that the distribution of alcyonaceans is primarly in tropical seas, while in more temperated waters they are not common.

In the Mediterranean sea there are only a few species of alcyonaceans: *Alcyonium palmatum*, *Alcyonium coralloides* and *Alcyonium acaule*. Chemical works have been reported for *Alcyonium palmatum* and *Alcyonium coralloides*, which possess some sesquiterpenoids (2,3). We now report the results obtained studying the terpenoidic fraction of *Alcyonium acaule*.

From the diethyl-ether solubles from the acetone extract of the alcyonacean the major metabolite, acaulin (1) $C_{17}H_{26}O_2$, was isolated by a series of chromatographic steps.



1 R=Ac
2 R=H



3

All the ^{1}H- and ^{13}C-chemical shifts of 1 were assigned on the basis of the data obtained by DEPT sequence, ^{1}H-^{1}H homo-correlation, direct and long-range hetero-correlation. These data, along with those collected studying some simple derivatives(2,3) of 1, led to suggest the structure 1 as the most probable one.

The suggested carbon skeleton of 1 is unique among the natural sesquiterpenoids. Two of the three isoprene units seem to be linked tail to tail. However, it is likely that during the biosynthesis there has been a methyl rearrangement.

Now studies are in progress in order to valuing the biological activities of acaulin 1.

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   J. Nat. Prod.; 47,877-878 (1984)

DITERPENOID CONSTITUENTS OF HELIANTHUS MOLLIS AND THEIR INSECT DETERRENT ACTIVITY

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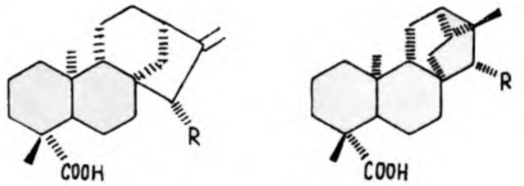
In looking for antifeedants of Compositae family we investigated the extract of Helianthus mollis. Besides the known sesquiterpene lactone desacetyleupasserin[1] which had a moderate deterrent activity we isolated a series of diterpenoic acids:



R= H, OAng

The free acids isolated as a mixture had a very strong antifeedant activity especially against the larvae of Trogoderma granarium (IV class). The acids were separated and identified as their methyl esters which had much lower activity.

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THE STRUCTURES OF NEW GUAIANOLIDES OF SOME SPECIES OF THE CENTAUREA AND CHARTOLEPSIS GENUSES

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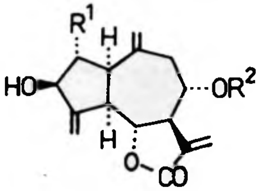
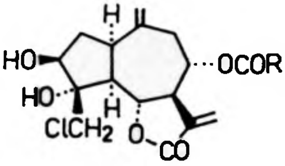
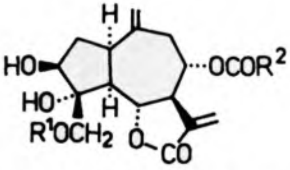
Analysing four species of the genus Centaurea and four species of the genus Chartolepsis we have isolated and identified nine guaianolides described earlier as components of other plants species. In addition to these described guaianolides we have isolated, identified and clarified the structures - including the relative and absolute configuration - mainly on the basis of a detailed analysis of the ^{1}H NMR spectra and by means of CD, of further eleven guaianolides which we called cebelins A (I), B (II), C (III), E (IV), F (V), G (VI), H (VII), I (VIII), K (IX), pterocaulin (X) and 15-deoxyrepin (XI).



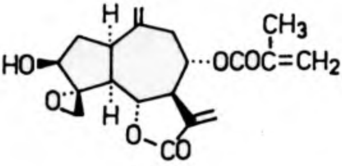
I: $R^1 = OCOC(CH_3)C_2H_5$; $R^2 = H$
II: $R^1 = OCOCH(CH_3)_2$; $R^2 = H$
V: $R^1 = H$; $R^2 = CO.C(CH_3)=CH.CH_2OH$
XI: $R^1 = H$; $R^2 = CO.\underbrace{C(CH_3).CH_2}_{O}$



III: $R = C(CH_2OH)=CH_2$
IV: $R = C(CH_3)=CH_2$
IX: $R = CH(CH_3)_2$



VI: $R^1 = COCH_3$; $R^2 = C(CH_2OH)=CH_2$
VII: $R^1 = COCH_3$; $R^2 = C(CH_3)=CHCH_2OH$



VIII

ABSOLUTE STEREOCHEMISTRY OF DISIDEIN AND OF TWO RELATED HALOGENATED SESTERTERPENOIDS. TWO-DIMENSIONAL NMR STUDIES AND X-RAY CRYSTAL STRUCTURE

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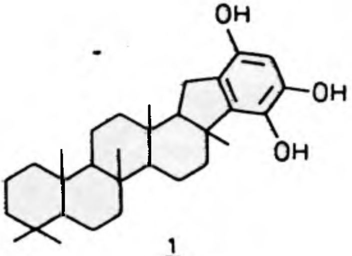
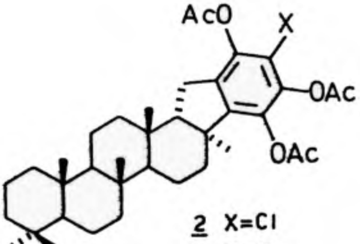
Sesterterpenoids showing the carbon skeleton of scalarane are frequently present in Porifera of the order Dictyoceratida[1]. Disidein (1) is until now the unique scalarane sesterterpenoid condensed with a hydroxyhydroquinone moiety. Its structure was suggested[2] in 1975 without stereochemical implications. Further studies on Disidea pallescens have given, in addition to Disidein, two new closely related halogenated sesterterpenoids, isolated as triacetate (2, 3). All the ^{1}H- and ^{13}C-NMR chemical shifts of Disidein triacetate (4) were assigned by two-dimensional experiments.

Treatment of 4 with chlorine and bromine afforded 2 and 3, respectively. The X-ray diffraction analysis on compound 3 showed unambiguously the complete stereochemistry and the configuration of all these molecules. Disidein triacetate (4) possesses a weakly analgesic activity in the tail-click[3] test on mice.



1



2 X=Cl
3 X=Br
4 X=H

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RAMOSMIN, A NEW CHROMENOCHALCONE FROM CROTALARIA RAMOSISSIMA.

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India.

Crotalaria ramosissima is a wood plant whose floral parts exude a gummy yellow substance. One of the components of the gummy exudate is a new chalcone, Ramosmin. It analysed for $C_{21}H_{20}O_6$, optically inactive and gave a dark brown ferric reaction. Its UV data suggested that it was a chalcone. Infrared spectral data of the compound indicated the presence of hydroxyl groups and an α,β-unsaturated keto function, characteristic of a chalcone. Its PMR spectrum suggested the presence of a dimethyl chromene ring system. The PMR data was further suggestive of the substitution pattern in ramosmin.

The molecular ion at m/z 368 in its mass spectrum supported the molecular formula obtained from elemental analysis. The fragmentation pattern conclusively proved that the A-ring, has a dimethyl chromene ring and a 2'-hydroxy function. The B-ring contained the remaining two hydroxyls and a methoxyl group. The positions of the substituents have been assigned on the basis of the coupling pattern of its PMR spectrum. Based on chemical and the ^{13}C NMR spectral data ramosmin has been assigned the structure 2,4-dimhydroxy-5-methoxy 2'-hydroxy 6'', 6'''-dimethyl pyrano (2'', 3'', 4',3') chalcone.

ISOLATION AND SYNTHESIS OF A NEW PRENYLATED CHALCONE FROM CROTALARIA MEDICAGINEA.

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Department of Chemistry, Kakatiya University, Warangal-506 009
(A.P.) INDIA

A new isoprenylated chalcone besides β-sitosterol and two pyrrolizidine alkaloids viz., supinidine methyl ether and heliotridine methyl ether has been isolated from the roots of *Crotalaria medicaginea*.

The new compound $C_{25}H_{28}O_4$ (M^+ 392) answered the colour reactions for chalcones and gave a positive ferric reaction. Its PMR spectrum revealed the presence of p-substituted phenyl ring with A_2B_2 pattern of signals, two isopentenyl groups and 2'-OH function. The mass spectral fragmentation pattern gave evidence to the existence of 4-OH substituted B-ring and 3',5'-di-C-prenylated 2',4'-dihydroxy A-ring. Attached proton technique confirmed this further. Oxidation of the chalcone gave p-hydroxy benzoic acid.

The structure of the new chalcone has been proved by its unambiguous synthesis: prenylation of resacetophenone using prenyl bromide in presence of methanolic KOH gave 3,5-di-C-prenylated resacetophenone which on condensation with p-hydroxy benzaldehyde afforded a chalcone identical with the one isolated from the natural source.

Thus the new chalcone has been assigned the structure 3',5'-di-C-prenyl 2',4',4-trihydroxy chalcone.

NEW TYPES OF DITERPENES FROM COMPOSITAE

C. Zdero

Technical University, Berlin 12

The structure elucidation of several diterpenes and derived compounds from an Australian *Myriocephalus* species will be discussed. Furthermore the isolation of some unique diterpenes from *Corymbium villosum* and its chemotaxonomic relevance will be discussed.

SESQUITERPENE LACTONES OF THE SUBTRIBE CENTAUREINEAE

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and Miloš Buděšínský[b]

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[b]Institute of Organic Chemistry and Biochemistry,
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In the species classified in the lower taxa of the subtribe Centaureineae (family Compositae) the presence of sesquiterpene lactones was studied. It has been found that the sesquiterpene lactones are important chemotaxonomical characters of the mentioned subtribe. The occurrence of sesquiterpene lactones and their structures in the genera, subgenera, sections and species of the subtribe Centaureineae facilitate their identification and their correct classification in the systematics of the mentioned subtribe.

SESQUITERPENE LACTONES OF Cephalophora aromatica (HOOK) SCHRADER AND THEIR DETERRENT ACTIVITY. THE STEREOSTRUCTURE OF GEIGERININ AND HYMENORATIN. REVISION OF THE STEREOSTRUCTURE OF LINIFOLIN A.

Włodzimierz M. Daniewski[a], Wojciech Kroszczyński[a], Elżbieta Błoszyk[b], Aleksandra Dudek[c], Zofia Kosturkiewicz[c], Urszula Rychlewska[c], Jan Nawrot[d], Miloš Buděšínský[e], Soňa Vašíčková[e] and Miroslav Holub[e]

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[b]Department of Medicinal Plants, Academy of Medicine, Poznań, Poland

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[d]Institute of Plant Protection, Poznań, Poland

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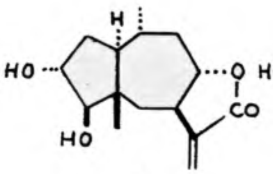
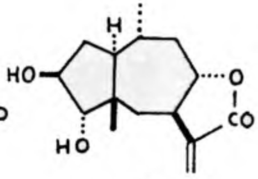
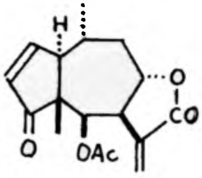
From the mentioned species the authors isolated a series of sesquiterpene lactones described earlier (helenalin, aromatin, aromaticin, mexicanin I and linifolin A) and a new one geigerinin (I). The stereostructure of compound I has been solved and checked by X-ray structural analysis. On this basis the stereostructure of hymenoratin (II) has been deduced. The stereostructure of linifolin A is revised in the sense of formula III. The feeding deterrency of mexicanin I, geigerinin, 11,13-dihydrogeigerinin, a mixture of aromatin and aromaticin and helenalin as a standard was examined against selected insect storage pest. All the substances mentioned - with the exception of 11,13-dihydrogeigerinin - showed feeding deterrent activity.



I



II



III

TRITERPENOIDES OF ASTRAGALUS QUISQUALIS BUNGE

L.A.Kholzineva, A.A.Savina and I.Romero Maldonado

All-Union Reseach Institute of Medicinal Plants, Moscow, USSR.
Institute of Chemical Physics of the AS of the USSR, Moscow.

Five cycloartane type triterpenoid glycosides, the quisvalozides A,B,E,F and G were isolated from the herb of A. quisqualis Bunge. The structure of the quisvalozide B (I) was elucidated.

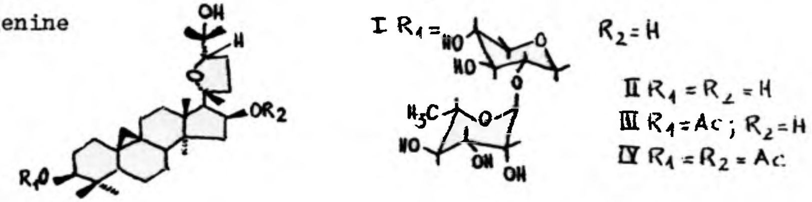
The acidic hydrolysis of (I) with 0,5% H_2SO_4 in MeOH yielded an earlier unknown aglycone, the quisvagenine (II). The cycloartane nature of (II) was determinated from the ^1H NMR spectrum (0,34 ppm and 0,59 ppm, d, J= 4,39 Hz) and the ^{13}C NMR spectrum (30,6 ppm, t, J= 150,0 Hz). These signals are belonging to the methylenic group of the cyclopropane at the C-9,19 position. The presence in the mass-spectrum of (II) of fragment ion peaks with m/z= 143 (100%) and m/z= 144 (100%) for his deuterium derivate is typical for the cycloartanes with α-methyl, α'-oxyizo-propyltetrahydrofuran mojety at C-17. The etheric character of the oxygen function in this fragment was confirmed by the undisplayed triplet at 3,77 ppm in the ^1H NMR spectrum of (II) on acetylation. The presence of two secondary OH-groups at C-3 and C-16 was determinated by comparison of the ^1H NMR spectra of (II) and its mono- (III) and diacetates (IV): δ_{H-3}= 3,29 ppm, dd (II), 4,54 ppm, dd (III, IV); δ_{H-16}= 4,67 ppm, dt (II,III), 5,38 ppm, dt (IV); and also by the data of the ^{13}C NMR spectrum of (II): δ_{C-3}= 78,77 ppm, d, J= 146,1 Hz; δ_{C-16}= 73,48 ppm, d, J= 146,1 Hz.

The formation of (III) simultaneously with (IV) may be explained by the spacial hindrance of the secondary OH-group at C-16 on acetylation of (II). The β-configuration of the OH-groups at C-3 and C-16 was determinated by the difference in in the molecular rotations III-II (+139,2°) and IV-III (+178,3°). The OH-group at C-3 is equatorial (J= 11,47 Hz and 4,39 Hz). The C-20(R) and C-24(S) configuration of the substituents was established from the ^{13}C NMR spectrum of (II) (δ_{C-24}= 81,56 ppm), as it is known that a value of δ_{C-24} for the 20(R), 24 (S) configuration is 81,6 ppm and for the 20(S), 24(R)-85 ppm.

Thus, the structure of (II) is to be 20(R), 24(S)-epoxy-cycloartan, 3β, 16β, 25-triol.

We suggest a new parameter for the determination of the configuration of the substituents at C-20 and C-24: the difference of the chemical shifts of C-20 and C-24 ($\Delta\delta_{20-24}$). For 20(R), 24(S) configuration this value should be 5,5-5,6 ppm and for 20(S), 24(R) - 1,7 ppm.

By the spectral analysis of (I) and its penta-(V, where R = H) and hexaacetates (VI, where R = Ac) the structure of a new glycoside, the quisvalozide B, was assigned as the 3-O--[α-L-rhamnopiranosil(1→2)]-O-β-D-xylopyranoside of quisvagenine



I R$_1$ = … R$_2$=H

II R$_1$ = R$_2$ = H

III R$_1$=Ac; R$_2$=H

IV R$_1$ = R$_2$ = Ac

The quisvalozides E,F and G on acidic hydrolysis yield a mixture of aglycones with prevalence of the siversigenine, a well-knowed artifact of the cyclosiversigenine.

ABSCISIC ACID EXTRACTIONS WITH ORGANIC SOLVENTS FROM AQUEOUS SOLUTIONS

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Institute of Biology, UFA 450054 U.S.S.R.

Our investigations were carried out for the extractions of abscisic acid (ABA) from aqueous solutions with sulfoxides (I), tributylphosphate (II), ethers (III), esters (IV), alcohols (V), aliphatic (VI), aromatic (VII), and chlororganic (VIII) solvents.

(I), (II), (IV), and (V) were found the most effective extragents for ABA. However, (IV) should be considered the most selective one. In the homologous series of extragents, e.g. esters, the distribution coefficients of ABA vary antibatically to the extragent molecular weights, butyl acetate being the most appropriate ABA extragent.

The bilogarythmic method was employed to determine the compositions of ABA extracted complexes with (I), (II), (III), (IV), and (V). The concentration constants of extraction were calculated and the quantitative description was given for the ABA distribution in the wide range of varied concentrations of components and of the process parameters.

According to the data obtained, the optimal conditions were selected to provide effective ABA concentrating both during the extraction stage and with further reextraction of the phytohormone. With the distribution regime selected, phenols may be removed from ABA in the course of ABA reextractions from butyl acetate with $NaHCO_3$ aqueous solution.

Experimental results with the ABA extractions from model aqueous solutions were confirmed by ABA extractions from the aqueous residues obtained after evaporation of the maize alcohol extracts. To decrease the amount of the interphase formed, proteins were first precipitated by the introduction of 30% $Al_2(SO_4)_3$ into the solution and by further making pH= 6-7.

ABA extractions with butyl acetate and the subsequent re-extraction with $NaHCO_3$ make it quite possible to avoid completely the extract evaporation stages thus simplifying the operative problems of isolation.

SESQUITERPENE LACTONE GLYCOSIDES FROM CREPIS TECTORUM

Wanda Kisiel

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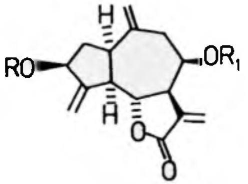
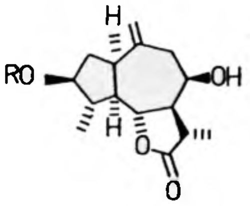
Silica gel column chromatography of the ethanol extract of the roots of Crepis tectorum L. (Compositae) afforded five sesquiterpene lactone glycosides. The comparison (TLC, mmp, IR) of the glycosides, their aglycones and acetyl derivatives with authentic samples allowed to identify four compounds represented by formulae.



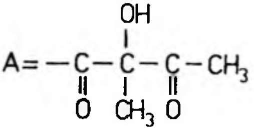
R=Gl R$_1$=H

R=Gl R$_1$=A

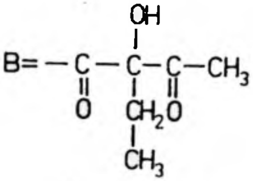
R=Gl R$_1$=B



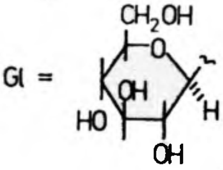
R=Gl



$A = -C(=O)-C(OH)(CH_3)-C(=O)-CH_3$



$B = -C(=O)-C(OH)(CH_2CH_3)-C(=O)-CH_3$



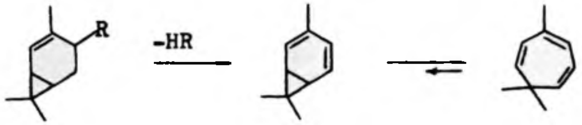
INTERRELATIONSHIP BETWEEN THE CARANE AND TRIMETHYLCYCLOHEPTANE TERPENOIDS

Edward Manukov and Vera Chuiko

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

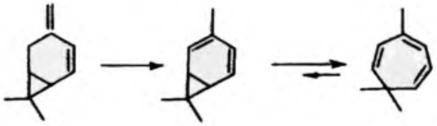
The presence of the 1,1,4-trimethylcycloheptane skeleton terpenoids in essential oils and turpentine asks for the insight into their genesis. The relationship between terpenoids of the carane and trimethylcycloheptane series seems to be based on the dynamic equilibrium of valent tautomers, 2,4-caradiene and 3,7,7-trimethyl-1,3,5-cycloheptatriene. The use of this equilibrium opens new possibilities in the synthesis of the cycloheptane terpenoids. The tautomeric equilibrium is almost totally shifted towards a monocyclic molecule. Therefore, the preparation of seven-membered cycle compounds is actually reduced to obtaining the corresponding caradiene from available terpenoids of the carane series.

The 2-carene and its derivatives having a double bond in the required position can be used as starting materials for the synthesis of hydrocarbons. The second double bond is formed upon dehydrogenation of 2-carene or elimination of its functional derivatives.

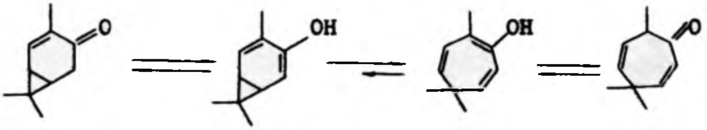


where R= H,
Hal,OH,
OTs

The formation of 2,4-caradiene occurs also upon isomerization of 3(10),4-caradiene having transoid dienic system.



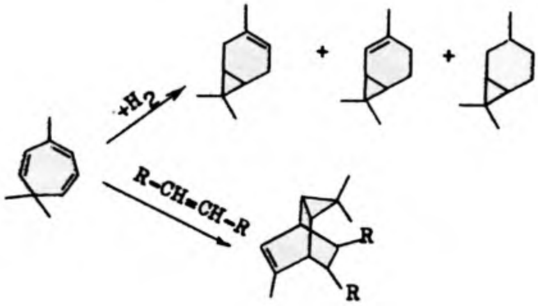
The oxygen derivatives of cycloheptane terpenoids were also obtained from the carane ones using valent tautomerism. In so doing, one of double bonds in the bicyclic molecule was formed in the process of enolization.



Thus, in this case transformation of carane structure into cycloheptane one is effected by several tautomeric transformations (cascade).

All the above reactions were also carried out with homologues of the carane series terpenoids.

In turn, the 1,1,4-trimethylcycloheptane derivatives can react to give carane derivatives. Thus, the hydrogenation of 3,7,7-trimethyl-1,3,5-cycloheptatriene produces 2- and 3-carenes, cis- and trans-caranes, while condensation with dienophiles results in caradiene adducts.



SESQUITERPENES WITH A NEW SKELETON FROM *Polygonum glabrum.*

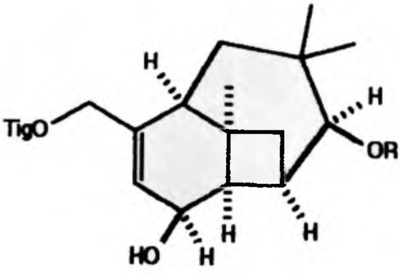
Ulla Jacobsson and Abdel K. Muddathir

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

Dedicated to Professor Holger Erdtman on his 85th birthday.

The Sudanese plant *Polygonum glabrum* Willd. has been used as anthelmintic agent in traditional medicine.[1] The bioactive principle has been isolated from the methanol/water extract of the leaves. Further separation by reversed phase chromatography gave four closely related compounds.

The structural elucidation was mainly based on extensive one- and two-dimensional NMR studies. Evaluation of the NMR-data implies the new sesquiterpenoid skeleton **1**. The four compounds show varying composition in the side chain R. One of the compounds is presently subjected to X-ray analysis.



1

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[1] A.K. Muddathir, G. Balansard, P. Timon-David, A. Babadjamian, A.K. Yagoub and M.J. Julien, *J. Pharm. Pharmacol.*, **39**, 296 (1987).

NEW SESQUITERPENOIC LACTONE OF MARASMANE SKELETON FROM LACTARIUS VELLEREUS

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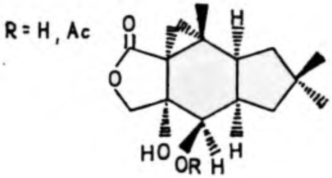
a) Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland.

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

The HPLC chromatogram of dihydroxy-compounds fraction of Lactarius vellereus showed that it was a very complicated mixture. Further investigation led to the isolation and structure elucidation of a series of sesquiterpenes of marasmane skeleton[1]. Now the isolation and structure elucidation of a new dihydroxy sesquiterpenoic lactone from this fungi will be presented.



The structure of $7\alpha,8\beta$-dihydroxy-marasmane-5,13-lactone was substantiated by two dimensional ^{1}H and ^{13}C NMR spectroscopy of its monoacetyl derivative.

1. W.M. Daniewski, W. Kroszczynski, P. Skibicki, M. DeBernardi, G. Fronza, G. Vidari, P. Vita-Finzi, Phytochemistry, in press.

NEW LACTARANE SESQUITERPENES FROM *LACTARIUS SCROBICULATUS* SCOP. (BASIDIOMYCETES)

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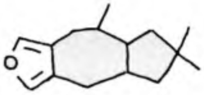
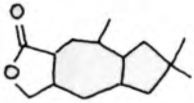
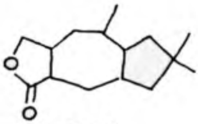
In the last years studies on the metabolites of *Lactarius* mushrooms (Russulaceae, Basidiomycetes) have been growing in order either to find products with new structures or to understand their biosynthesis and their biological activities.

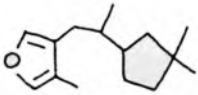
Pursuing our research in this field we analyzed some fractions of medium polarity obtained by extraction of *Lactarius scrobiculatus* Scop.

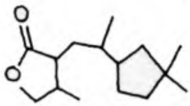
The mushrooms have been extracted with acetone at -20°C in order to avoid rearrangements. Previously the less polar fractions have 'been considered and the structure of a number of products determined. They show a sesquiterpenoid structure with one of the following skeleton: furolactarane (I), 5-lactaranolide (II), 13-lactaranolide (III) or seco-lactarane (IV-V) (1-3).


(I)

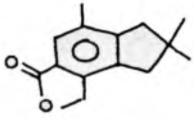

(II)


(III)

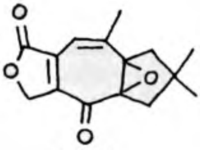

(IV)


(V)

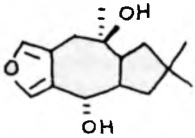
Here we report the structure of five new products (VI-X) determined by spectroscopic methods and chemical correlations.
Furthermore two dimers of the marasmane (X) have been identified.



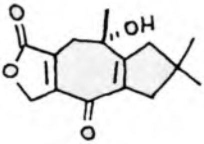
(VI)



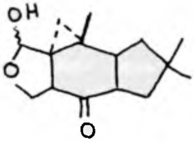
(VII)



(VIII)



(IX)



(X)

The structures will be discussed and framed in the already known Lactarius metabolites.

References
1. G. Vidari, L. Garlaschelli, M. De Bernardi, G. Fronza and P. Vita-Finzi - Tetrahedron Letters, 1773 (1975).
2. M. De Bernardi, G. Fronza, G. Vidari and P. Vita-Finzi - Chim. Ind. **58**, 177 (1976).
3. R. Battaglia, M. De Bernardi, G. Fronza, G. Mellerio, G. Vidari and P. Vita-Finzi - J. Nat. Product, **43**, 319 (1980).

C_{30} - COMPOUNDS FROM TRICHOLOMA SAPONACEUM (BASIDIOMYCETES)

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Giuseppina Gatti[c], Giovanni Vidari[a] and Paola Vita-Finzi[a]

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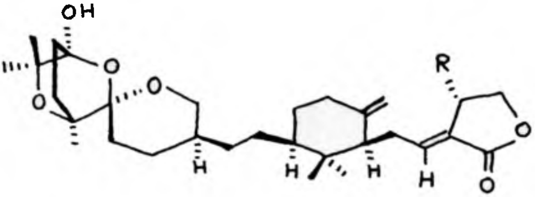
The genus *Tricholoma* (Basidiomycetes) includes a number of species which are almost not studied from a chemical point of view. Some species are edible and others are considered toxic.
Tricholoma saponaceum is a widespread mushroom in the Italian woods during the autumn and is considered not edible for the bad taste.

Preliminary tests on the antitumor activity of the total extracts of several *Tricholoma* species indicated that *T. saponaceum* is highly active *in vitro* (P-388).
From the AcOEt extract of this mushroom three C-30 products have been isolated: two new saponaceolides A e B (I-II) and the triterpene acid (III).
Saponaceolides show a skeleton never found before in nature.

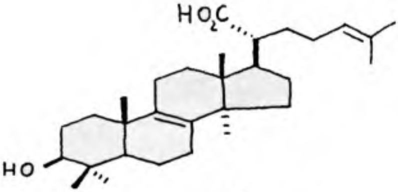


I R = H

II R = OH

Their structure has been established by spectroscopic methods, including the X rays diffractometric analysis for II.
These metabolites show a noteworthy antitumor activity *in vitro*.
Since these structures have never been found before, their biosynthesis will be discussed.

The triterpene acid (III) shows a lanostane skeleton and has previously been isolated only from the mushroom *Trametes odorata*[1].



III

Reference

1. T.G. Halsall, R. Hodges and G.C. Sayer, J.Chem.Soc., 1959, 2036.

THE STRUCTURE PECULIARITIES OF SESQUITERPENE LACTONES OF KAZAKHSTAN PLANTS

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Kazakh Academy of Sciences, Karaganda, U.S.S.R.

The sesquiterpene lactones of germacrane,eudesmane,guaiane and pseudoguaiane types have been isolated from the plants of Asteraceae family of Kazakhstan flora. Most of them are non-linear on structure,containing exometylene group,conjugated with carbonyl of γ-lactone.

Epoxy,hydroxy,acetyl,ketone groups are the most typical of the functional groups. The presence of the residues of crotonic (in incaspin) and acrylic (in cepseudin) acids in the structure of sesquiterpene lactones has been determined for the first time.

The research conducted evidences about correspondence of sesquiterpene lactones of indicated structural types to the representatives of the definite genuses of Asteraceae family.

Thus germacranolides and guaianolides have been isolated from the species of genus Achillea L., section Absinthium DC. subgenus Artemisia L. and genus Centaurea L. Eudesmanolides and pseudoguaianolides have been detected in the plants of genus Inula L. The sesquiterpene lactones of eudesmane type with saturated lactone ring generally are typical for the representatives of subgenus Seriphidium (Bess.) Rouy. genus Artemisia L.

CONSTITUENTS FROM THE TRIBE LIABEAE

Jasmin Jakupovic

Institute of Organic Chemistry, TU Berlin 12, Germany

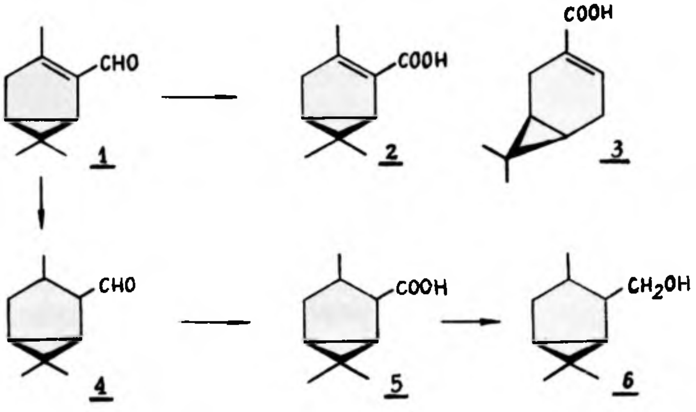
The investigation of a further *Ferreyanthus* species afforded eleven new eudesmanolides, three rearranged lactones and a dimeric sesquiterpene lactone. A *Liabum* species gave further new guaianolides. The chemotaxonomy of the tribe is discussed.

NEW OPTICALLY ACTIVE DERIVATIVES OF 3,6,6-TRIMETHYLBICYCLO-[3.1.0]HEXANE

Mirosław Walkowicz and Jerzy Podlejski

Institute of Organic and Physical Chemistry,
Technical University, Wrocław, Poland
Institute of General Food Chemistry,
Technical University, Łódź, Poland

Optically active bicyclic aldehyde 1 containing ten carbon atoms was synthesized from (+)-3-carene via keto aldehyde. Mild oxidation of 1 afforded unsaturated acid 2 which can be considered as analog of isochamic acid 3. Catalytic hydrogenation of 1 led to saturated aldehyde 4 which, oxidized in alkaline medium, yielded a mixture of two stereoisomeric acids 5. Reduction of this mixture with $LiAlH_4$ led to a mixture of corresponding alcohols 6 which had interesting odor properties.

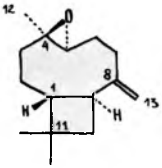


STRUCTURE AND CONFORMATION OF DIHYDROCARYOPHYLLENE EPOXIDE IN SOLUTION.

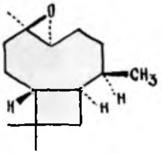
A.V.Tkachov, O.V.Toropov, G.E.Salnikov, V.A.Pentegova

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

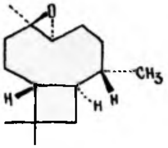
Caryophyllene oxide (I), a wide-spread sesquiterpenoid, undergoes the catalytic hudration to give the dihydro-derivative, which has already been known for 40 years but whose stereochemistry has not yet been cleared out. We carried out hydration of epoxide (I) on the platinum catalist in the aqueous methanol to obtain a mixture of dihydroepoxides (II) and (III) in the 4:1 ratio. The main product with m.p.66-67°C was obtained by crystallisation of the raw material from chloroform-acetonitrile.



(I)



(II)



(III)

Stereochemistry and conformation of the main product (II) of hydration were established in the following way:

1) the conformation analysis of the nine-membered cycle has been carried out using "stage-by-stage and fragment-by-fragment" approach, and a conformation has been chosen that matches the ^{1}H NMR spectrum best;
2) for the chosen conformation with two alternative orientations of methyl at the C^{8} atom, the molecular mechanics calculations have been carried out, which gave the corrected bond lengths, bond and torsion angles further used to calculate the spin-spin coupling constants $^{3}J_{H-H}$;
3) on the basis of all hydrogen chemical shifts found from the

two-dimensional spectrum and using the calculated spin-spin coupling constants, there were calculated the splitting parameters of hydrogen signals in the ^1H NMR spectra; it appeared that the calculated parameters are in the best agreement with the experimental ones in the case of β-orientation of methyl at C^8 atom (structure II);

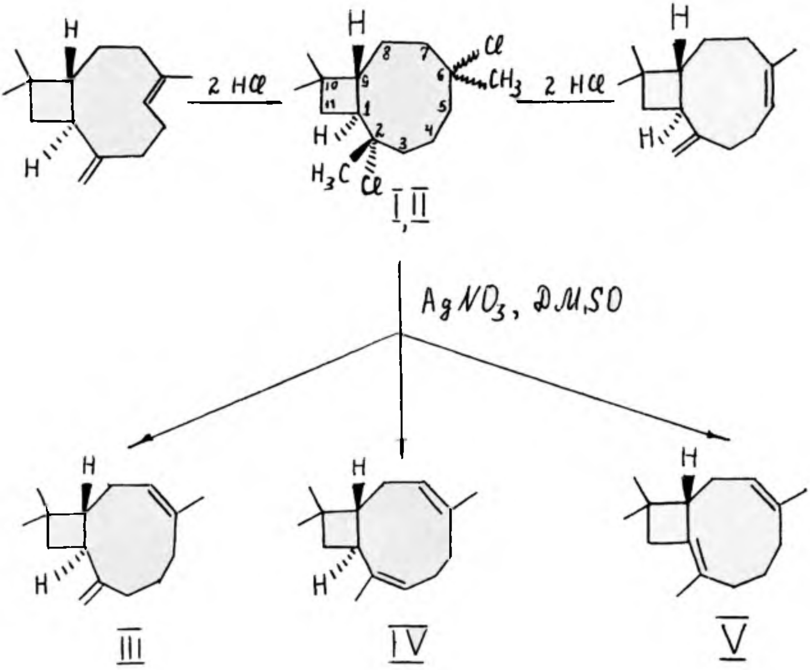
4) the structure and conformation thus found were confirmed by the comparison of the calculated and experimental values of hydrogen chemical shifts induced by small additions of the shift-reagent (+0.1 mole/mole $Yb\,fod_3$).

STRUCTURE AND DEHYDROCHLORINATION OF CARIOPHYLLENE DIHYDROCHLORIDES

T.M.Khomenko, D.V.Korchagina, I.Yu.Bagryanskaya, Yu.V.Gatilov, A.V.Tkachev, Zh.V.Dubovenko, V.A.Barkhash

Institute of Organic Chemistry, Novosibirsk, USSR

Previously it has been reported that dehydrochlorination of cariophyllene dihydrochloride by $AgNO_3$-DMSO leads to a complex mixture of products of unknown structures[1]. We have isolated from this mixture three new dienes with cariophyllane frame, whose structures and stereochemistry were established chemically and by ^{1}H and ^{13}C NMR.



The starting "cariophyllene dihydrochloride" with m.p. 69-70 °C [2] was regarded earlier as an individual compound in which case the configuration of chiral centres has not been ascertained. We have found the ^{13}C NMR spectrum of the crystalline product to contain two sets of signals, each having about 15 signals, which indicates a mixture of two compounds. The crystalline and molecular structures of the dihydrochlorides were established by the X-ray structure analysis. Dihydrochlorides (I) and (II) happened to differ from each other only by configuration of the C-CI bond at C^6. The same mixture of dihydrochlorides is formed from isocariophyllene.

1. G.Mehta, Indian J. Chem., 9, 559 (1971).
2. J.L.Simonsen, D.H.R.Barton, The terpenes, vol. III, 1952.

THE NEW TYPE OF DITERPENOID ALKALOIDS-ZERACONINE AND ITS N-OXIDE.

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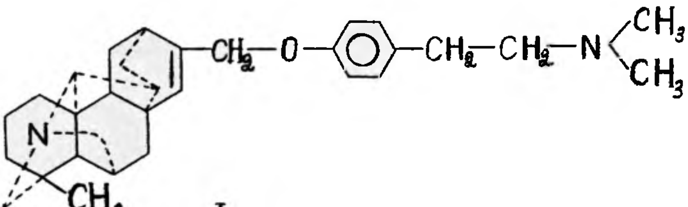
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent, USSR.

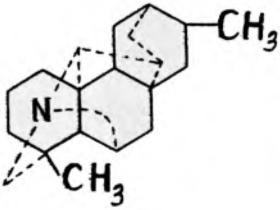
Zeraconine (I) and its N-oxide has been isolated from Aconitum zeravschanicum. I has the content $C_{30}H_{40}ON_2$, m.p. 130-131°C, M^+444.

The structure I has been established on the basis of spectral results and by obtaining dihydrodesoxynominine (II) and the known alkaloid gordenine (III) after hydrogenolysis of the I.

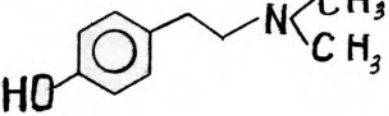
Zeraconine is the first diterpenoid alkaloid being ether of diterpenoid and phenolic derivative.



I



II



III

WITHANOLIDE - LIKE PLANT STEROIDS FROM BROWALIA GRANDIFLORA

Bogumiła Rozkrutowa

Polish Academy of Sciences, Institute of Pharmacology,
Department of Phytochemistry, Cracow, Poland

In search of biologically active substances in plants of Solanaceae family, Browalia grandiflora Grah. has been examined. This species is a well known tropical plant. It was experimentally cultivated in Poland's geoclimatic conditions. The culture was established from seeds supplied by Botanical Garden in Bordeaux, France. Two crystalline substances of the withanolide group were isolated. By physico-chemical methods they were identified as nicandrenone and withaferin A which are known as biologically active compounds.

ANTIMICROBIAL PROPERTIES OF THE ESSENTIAL OIL FROM MELALEUCA LEUCADENDRON

O. Motl[a], J. Preslová[b], T.T. Xuyen[c] and K. Stránský[a]

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

[b]Institute of Hygiene and Epidemiology, Prague

[c]Cho Ray Hospital, Ho Chi Min, Vietnam

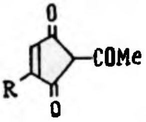
The essential oil from the leaves of Melaleuca leucadendron, freed of phenolic components, displays distinct antimicrobial properties. The screening of the distillation fractions by testing on reference strains of Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa showed that the highest activity was in higher boiling fractions containing linalool and terpinen-4-ol. A lower activity was also found in further newly identified components guaiol among them. It is highly probable that melalimol of Melaleuca linariifolia essential oil - mentioned in literature (cf. Gildemeister, Hoffmann, Die ätherischen Öle, Vol. III.b, p. 352) is identical with guaiol.

2-ACETYLCYCLOPENT-4-EN-1,3-DIONES AS A USEFUL SYNTHONS IN TOTAL STEROID SYNTHESES. SYNTHESIS OF AROMATIC 16-ACETYL-15,17-DIKETO-STEROIDS

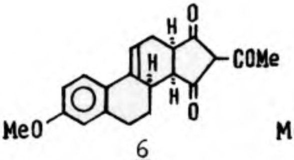
Vjacheslav L. Novikov, Olga P. Shestak and Nadezda N. Balanyova

Pacific Institute of Bioorganic Chemistry, Far East Scientific Centre, Academy of Sciences, Vladivostok-22, U.S.S.R.

Cyclopentenoid triacylmethanes possessing a high dienofilic activity in thermal [4+2]-cycloaddition reactions have been of interest for the preparation of various polycyclic ketones including natural ones. Unfortunately, possibilities for synthetic use of compounds 1-3 were limited due to low efficiency of methods for their obtaining [1].



1:R=H; 2:R=Me;
3:R=Cl;4:R=Br



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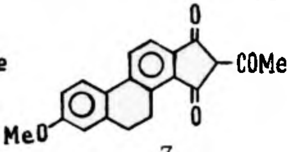

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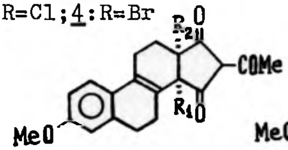
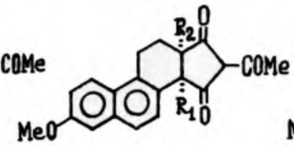
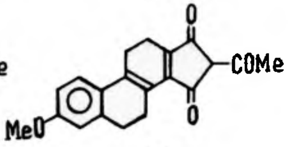


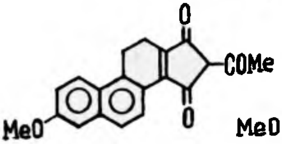
8:R_1=Me,R_2=H;
9:R_1=H, R_2=Me



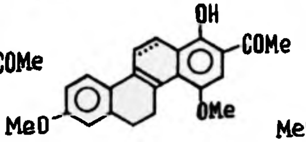
10:R_1=Me,R_2=H;
11:R_1=H, R_2=Me



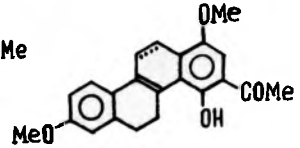
12



13



14:11,12-dehydro-
16:11,12-dihydro-



15:11,12-dehydro-
17:11,12-dihydro-

We have improved the method for synthesis of cyclopentenoid β,β'-triketones involving acylation of maleic anhydrides with isopropenylacetate and prepared the compounds 1-4 in 40-72% yields. Triketones 1-4 easily reacted with 6-methoxy-1-vinyl-3,4-dihydronaphthalene 5. Interaction of 1 with 5 in benzene under 20°C gave 6 in 51% yield. The latter on the treatment with DDQ under 25°C was converted into 7 in 26% yield. Reaction of 2 with 5 in boiling benzene led to formation of a mixture of ortho-adducts 8 (40% yield) and 10 (19%) and metha-adducts 9 (13%) and 11 (7%).

Condensation of both 3 and 4 with 5 in benzene under 80°C afforded a mixture of adducts 12 (25-28%) and 13 (22-28%). Hydrolysis of triketones 6-13 with boiling hydrochloric acid gave the corresponding 15,17-diketones in moderate yields. In the case of 6 this process has been accompanied double-bond migration to the 8(9)-position.

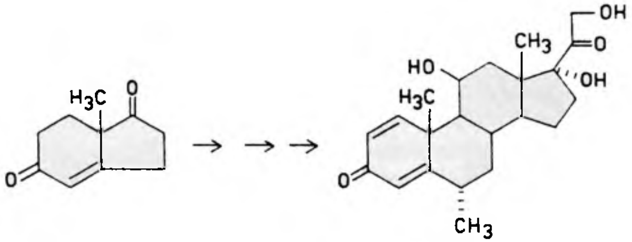
Steroidal triketones having $\Delta^{13(14)}$-bond can be transformed into the corresponding chrysenes by the treatment of CH_2N_2. Thus, reaction of 7 and 12 with CH_2N_2 yielded a mixture of isomers 14,15 and 16,17, respectively, in moderate yields (32-46%).

[1]. Nilsson M. - Acta Chem. Scand.,1964,v.18,N2,p.441-446.

TOTAL SYNTHESIS OF 6α-METHYLPREDNISOLONE

Andrzej Robert Daniewski and Emilia Piotrowska
Institute of Organic Chemistry, Polish Academy of Sciences
01-224 Warsaw, Poland

Starting from chiral endione (1), the title compound (2) was obtained.



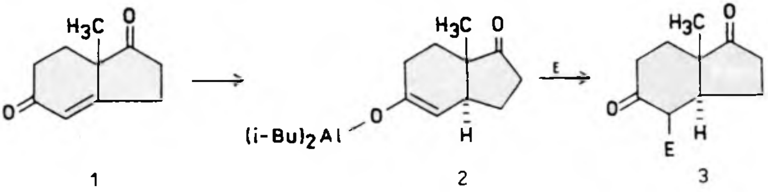
1 2

The sequence of the reactions was considerably shortened by the two stereoselective reductive alkylations steps.

AN EFFICIENT TOTAL SYNTHESIS OF ESTROGENS

Andrzej Robert Daniewski and Jarosław Kiegiel
Institute of Organic Chemistry, Polish Academy of Sciences
01-224 Warsaw, Poland

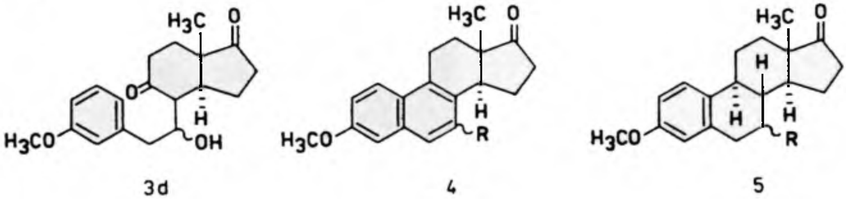
The stereoselective reduction of endione (1) with DIBAH mediated by t-butylcopper gave the aluminum enolate (2), which was trapped by various active electrophiles (Scheme 1).



$E = H^+$, NBS, $CH_2{=}CH{-}CH_2Br$, m-$CH_3OC_6H_4CH_2CHO$, m-$CH_3OC_6H_4CH_2COCl$

Scheme 1

The product 3d (diastereoisomeric mixture at C-7, 1 : 1) proved to be an useful substrate for synthesis of estrogens 4 and 5 (Scheme 2).



R = H, OH

R = H, αOH, βOH

Scheme 2

SIDE-CHAIN CONSTRUCTION IN 17-OXOSTEROIDS
17-(HYDROXYACETYL)-Δ^{16}-STEROIDS

A.M. van Leusen, D. van Leusen, J. Moskal and E. van Echten

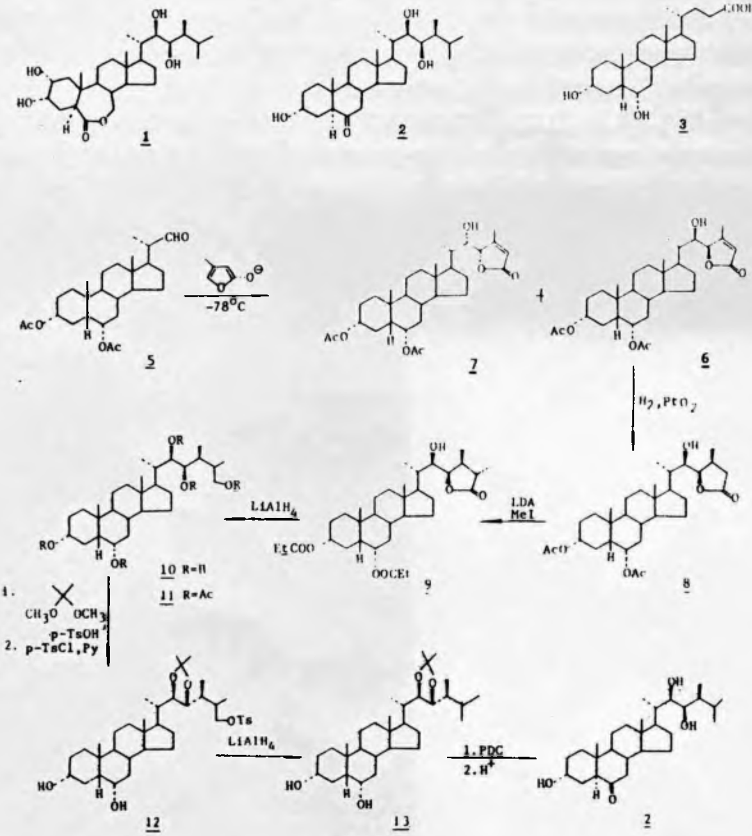
Department of Organic Chemistry, Groningen University,
Groningen, The Netherlands

We have developed an efficient method for introduction of the 17-hydroxyacetyl side-chain of corticosteroids in 17-oxosteroids. In a stepwise process, the C-20 carbonyl is introduced via a masked formaldehyde molecule, in the form of tosylmethyl isocyanide (TosMIC), followed by the C-21 hydroxymethyl in the form of formaldehyde as such. The merits of this methods are compared with other approaches.

STEREOSELECTIVE SYNTHESIS OF TYPHASTEROL FROM HYODEOXYCHOLIC ACID

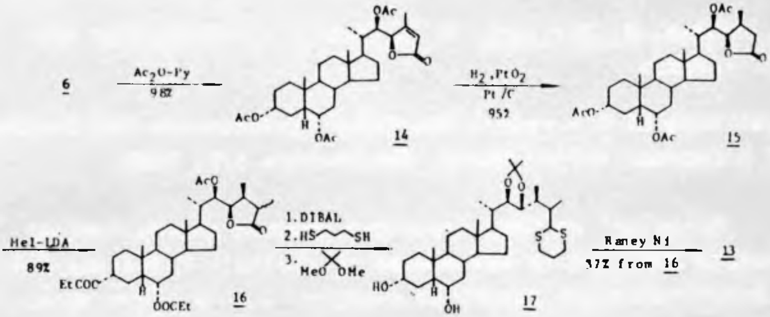
WEI-SHAN ZHOU* and WEI-SHENG TIAN
Shanghai Institute of Organic Chemistry, Academia Sinica
345 LingLing Lu, Shanghai, China

Since the discovery of novel plant-growth hormone brassinolide 1 in 1979, a number of new brassinosteroids in other higher plant have been isolated and identified. A simple analogue of brassinolide, typhasterol 2, isolated from cat-tail pollen (Typha latifolia L.) represents the first example of 2-deoxy--brassinosteroid plant-growth hormone. Although syntheses of brassinolide and its analogues have been achieved by several research groups from stigmasterol or ergosterol as starting material, the syntheses of them starting from hyodeoxycholic acid 3 have not yet been reported. Now we wish to report the synthesis of natural typhasterol 2 starting from 3.



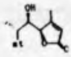
Scheme I

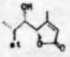
An improved route for the synthesis of 13 was achieved from 6 through the following sequence of reaction: 6→14→15→16→17→13 in 30% overall yield from 6. The result is much better than that obtained from the above route: 6→8→9→10→12→13 in 7% overall yield from 6.

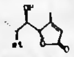


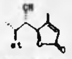
Scheme 2

The most suitable reaction temperature i.e. -78°C was found in the aldol reaction of steroidal aldehyde 5 with the anion of 3-methyl 2-butenolide 4, giving a mixture of (22R, 23R)-6 and (22S,23S)-7 in a ratio of 70:30 in 98.7% yield, as shown in Tab. 1 .

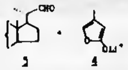

(22R,23R)-6


(22S,23S)-7


(22R,23S)-6'


(22S,23R)-7'

Tab.1 Result of the Aldol reaction of 5 with 4

No:	Reactants	Temp (°C)	Time (hr.)	The percentage of products				Yield (%)
				5	6	7	8	
1	 5 + 4	-100	8	76	24			43
2		-78	10.5	70	30			98.7
3		-50	8	52	28	13	7	87
4		-20	6	45	32	15	8	85
5		0	7	24	33	31	12	52.7

A NEW DATA ON CIS-HYDROXYLATION OF 2,4-DIENE-6-KETOSTEROIDS

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

Recently[1] we have described unusual stereochemical results obtained in the course of cholesta-2,4-diene-6-one cis-hydroxylation reactions studies. It has been shown that only $2\alpha,3\alpha$-diol without any β-substituted derivatives are formed in a good yield under typical conditions for Δ^2-bond β-cis-hydroxylation (I_2-AgOAc-$AcOH_{aq}$). Opposite result was observed when the conditions for α-cis-hydroxylation were used. In this case only $2\beta,3\beta$-hydroxylated products were obtained. Then we have suggested that both sterical and electronic factors effected on the direction of cis-hydroxylation when Δ^2-bond was conjugated with Δ^4-6-ketofunction. These results along with their theoretical importance proved to be very useful in practical aspect since they opened a new efficient way to $2\alpha,3\alpha$-diols without employment OsO_4, very expensive and toxic reagent.

Now we report some new data on cis-hydroxylation of 2,4-diene-6-ketosteroids in order to clarify the scale of applicability and mechanism of such reactions. A number of 2,4-diene-6-ketosteroids with different substituents in D-cycle were used as substrates for hydroxylation in Woodward's method conditions. For estimation of electron density distribution effect on structure and yields of reaction products some derivatives on 6-ketofunction were synthesized. In most cases $2\alpha,3\alpha$-diols as major products were obtained in good yields.

---

[1] A.A.Akhrem, F.A.Lakhvich, V.A.Khripach, N.V.Kovganko, Zhurn. Org. Khim., 1983, v. 19, N 6, p. 1249.

PHOTOCHEMICAL REACTIONS OF STEROID-6-KETONES

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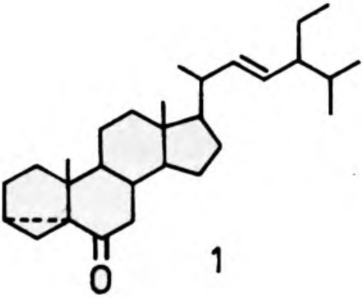
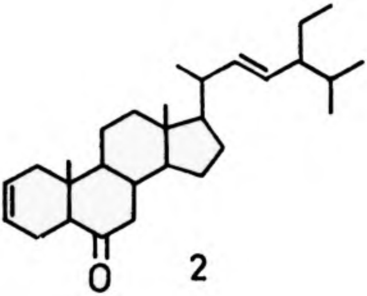
Institute for Plant Biochemistry of the Academy of Sciences of the GDR, 4050 Halle/Saale, GDR

In connection with investigations on brassinosteroids we have investigated the photoreactivity of (24S)-ethyl-3α,5-cyclo-5α-cholest-22E-en-6-one (1) and (24S)-ethyl-5α-cholesta-2,22E-dien-6-one (2) as key intermediates in brassinosteroid synthesis.

Irradiation of (24S)-ethyl-3α,5-cyclo-5α-cholest-22E-en-6-one (1) in benzene and dioxane led under valence isomerization to a mixture of the corresponding Δ^3-6-ketone and Δ^4-6-ketone as main products. In the presence of water the latter compound underwent photoaddition leading to the 4α-hydroxy-6-ketone compound. Whereas photolysis of (24S)-ethyl-5α-cholesta-2,22E-dien-6-one (2) gave a complex reaction pattern, irradiation in acetic acid as a solvent led to a direct photoaddition of HOAc to the Δ^2-double bond.



1



2

A STUDY ON PHOTOCHEMICAL DECOMPOSITION OF CRYSTALLINE PREDNISOLONE

Ryszard Glinka

Institute of Technology and Chemistry of Drugs,
Medical Academy, Lódz, Poland

Prednisolone, a cross-conjugated corticoid, is very well known in the European Pharmaceopoea.

Investigation have already been published showing that crystalline prednisolone is unstable (J. Reisch, Y. Topalogh, G. Henhel, Acta Pharm. Techn., in press). According to thin-layer chromatography prednisolone gives two products on irradiation after 3 h and 3 photoproducts after 24 h. After 48 h irradiation it is decomposed to 50%. Thus, it is assumed that steroidal dienones with a 11β-hydroxy group are unstable.

In this work prednisolone was exposed to UV light for 48 h (Heraeus Quarz Lampengesellschaft, Hanau Typ KTFU-Hg, Q300, 300 Watt). After 3, 6, 24, 36 and 48 h the sample was submitted to thin-layer chromatography (Kieselgel 60 F_{254}) using a mixture of dichloromethane, ether, methanol and water (77:15:8:1,2) as eluent.

After 48 h exposure time the chromatogram showed 12 photoproducts with h R_f between 20 and 67.

This investigation shows that prednisolone is decomposed to about 1% only.

Preparative column chromatography gave the same result (Kieselgel 60 Gr. A.C. Merck - solvent mixture toluene - ethyl acetate 6:4). About 1% photoproducts could be isolated after 48 h exposure of prednisolone to UV light.

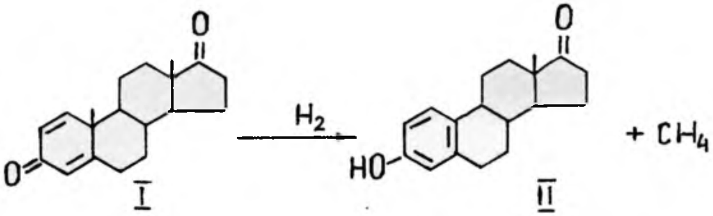
High performance liquid chromatography showed that after 48 h exposure of prednisolone only 1% was decomposed.

The results of this investigation indicate that after 48 h irradiation of crystalline prednisolone it is decomposed only to 1%. TLC and HPLC show that there are 12 compounds in the mixture of photoproducts.

THE STRUCTURE OF BY-PRODUCTS OF ANDROST-1,4-DIEN-3,17-DIONE PYROLYTIC AROMATIZATION

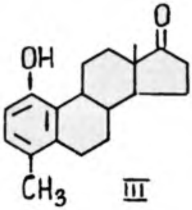
E.M.Dolginova, K.F.Turchin, Yu.I.Laz'yan, G.S.Grinenko
S.Ordjonikidze All-Union Research Chemical-Pharmaceutical Institute, Moscow, USSR

Pyrolytic aromatization of androst-1,4-dien-3,17-dione (I) is a promising procedure for the industrial production of estrone (II). The process is effected as a continuous one by mixing the solution (I) in xylene with the flow of a preheated kerosene serving as a heat-transfer agent and a hydrogen donor by the following scheme:

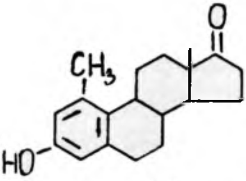


Given optimal conditions found by us (pyrolysis temperature 600-610°C, pressure 3-5 atm., time of contact 0.5 sec.) the yield of the II is 70-72%, extraneous material content - 3-5%.

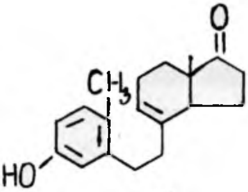
Inconsistent data on the structure of by-products of thermal dealkylation I are found in the literature. As admixtures to estrone we have isolated and characterized 1-hydroxy-4-methylestra-1,3,5(10)-trien-17-one (III); 3-hydroxy-1-methylestra-1,3,5(10)-trien-17-one (IV) and 3-hydroxy-9,10-secoandrosta-1,3,5(10)8-tetraen-17-one (V). The structure of the above compounds is proposed on the basis of the IR, NMR and mass-spectroscopy data, while for the compounds III and IV it is also confirmed by an alternate synthesis with dienone-phenol rearrangement.



III



IV



V

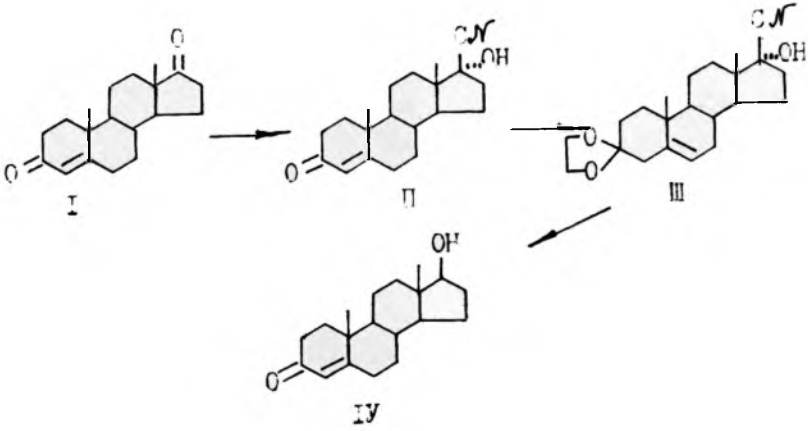
The optimal conditions for thermal 19-demethylation are shown to require somewhat severe conditions for the pyrolysis process, otherwise the amount of admixtures - products of dienone-phenol rearrangement - tends to increase.

SYNTHESIS OF TESTOSTERONE FROM ANDROST-4-ENE-3,17-DIONE - THE SITOSTEROL'S MICROBIOLOGICAL CLEAVAGE PRODUCT

V.A.Andryushina, L.S.Morosova, G.S.Grinenko

S.Ordjonikidze All-Union Research Chemical-Pharmaceutical Institute, Moscow, USSR

To develop a unified scheme for the production of hormonal preparations from androst-4-ene-3,17-dione(AD), we have synthesized testosterone through the 17α-hydroxy-3,3-ethylenedioxyandrost-5-ene-17β-carbonitril - the key intermediate in the synthesis of corticoids and hestagens from AD. This method involves the preparation of the 17β-cyanohydrine (II) and its ketalization with the formation of carbonitril (III). Carbonitril (III), while being treated with potassium hydroxide and sodium borohydride in the presence of calcium chloride, undergoes simultaneously dehydrocyanation and reduction with the formation of testosterone (IV) seaturing high yield and quality.



SYNTHESIS OF 3β-HYDROXY-22-PHENYLSULFONYL-23,24-BISNORCHOLA-5,7-DIENES

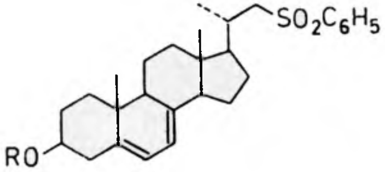
Eberhard Schrötter, Elfi Landmann, Hans Schick

Central Institute of Organic Chemistry of the Academy of Sciences of the GDR, Berlin, German Democratic Republic

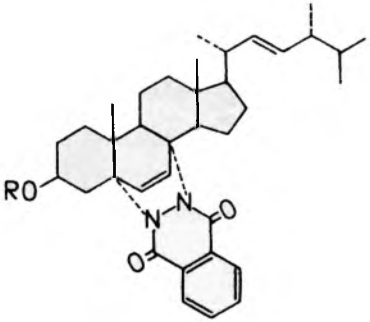
Bruno Schönecker, Ulrich Hauschild

VEB Jenapharm, Division of Research, Jena, German Democratic Republic

Ether and ester of 3β-hydroxy-22-phenylsulfonyl-23,24-bisnorchola-5,7-dienes 1 (R = Tetrahydropyranyl, Benzoyl)



1



2

were synthesized from the aza-Diels-Alder-adducts 2, obtained from ergosterol derivatives and 1,4-dihydrophthalazine-1,4-dione, by ozonisation of the 22,23-double bond, reduction of the ozonide to the 22-alcohol, tosylation, replacement of the tosyloxy group by bromine, reaction with sodium benzene sulfonate, and removal of the diene protective group.
In comparison with procedures described in the literature (1) this route affords the steroid intermediate 1 in a significantly improved overall yield.

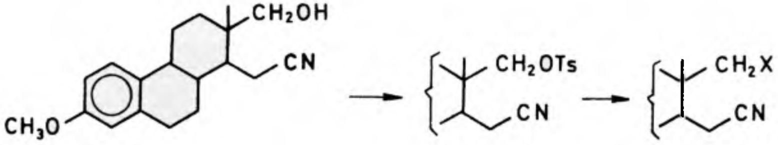
(1) H. Takayama, S. Yamada, M. Ohmori, Europ. Pat. 45 524

SYNTHESIS AND ESTROGENIC ACTIVITY OF SOME NEW 16,17-SECO-ESTRONE DERIVATIVES

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

[1]Pharm. and Chem. Ind. "Galenika", Institute for Research and Development, 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

The following new D-seco-estrone derivatives have been synthesized according to the scheme:



1 2 3

a) X = Cl
b) X = Br
c) X = J

By an action of p-toluenesulphonyl chloride in pyridine on the earlier synthesized[1] seco-cyanoalcohol 1, at room temperature, p-toluenesulphonate ester 2 was obtained in a 70% yield. Reaction of tetrabutylammonium halides with 2, in methyl ethyl ketone, afforded the corresponding 17-halogeno-derivatives 3a-c. The structures of compounds 3a-c were firmly established by analyzing their ^{1}H-NMR-spectra, especially the AB-quartets of the C_{17}-methylene group. The new D-seco-estrone derivatives have been submitted to residual estrogenic activity determination using the uterotropic method.

[1] D. Miljković, J. Petrović, J. Org. Chem., 42, 2101 (1977).

SYNTHESIS AND BIOLOGICAL ACTIVITY OF STEROIDAL 2'-DEOXY-GALACTOSI

J. Petrović, Dj. Čanadi, J. Csanàdi, D. Miljković

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In a continuation of our study directed towards synthesis of 2'-deoxy-glycosides in phytosterol and cholesterol series, with a final aim of producing new antineoplasmatic compounds, we prepared new cholesteryl and stigmasteryl α- and β-2'-deoxy-galactosides. An influence of different reaction conditions on the yield and ratio of empiric steroidal 2'-deoxy-galactosides has been studied. Optimal conditions involved an action of 2-deoxy-3,4,6-tri-O-acetyl-galactopyranosyl chloride upon cholesterol or stigmasterol in nitromethane, in presence of $Hg(CN)_2$ as a catalyst. Under these conditions, the main product (α-anomer) could be isolated by direct crystallization, whereby the β-anomer was obtained by subsequent column chromatography of the mother liquor.

Some of these derivatives, in acetylated and deacetylated form, were tested for a possible cytostatic activity.

SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME STEROIDAL THIAZOLES

Pavel **DRAŠAR**, Vladimír **POUZAR**, Ivan **ČERNÝ**,
George R. **PETTIT***, and Miroslav **HAVEL**

Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences, 166 10 Praha CSSR, and
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Heterocyclic steroidal derivatives containing sulphur and nitrogen atoms in the side chain ring represent a group of compounds with continuous importance from the synthetic as well as biological point of view.

Generally, in the synthesis of steroidal thiazoles the Hantzsch reaction was used leading to the 17β-[4-(1,3-thiazolyl)]androstane type of compound with a variety of steroidal skeletons as well as the substituent in position on $C_{2'}$ of the respective thiazole moiety.

Steroid skeletons used in this laboratory are inter alia 5-androsten-3-oles, 4-androsten-3-ones, 21-nor-5-pregnen-3-oles. Substituents in position 2 of thiazole moiety are e.g. amino, formamido, alkoxycarbonyl, alkylamino, alkoxycarbonylmethyl, alkyl or aryl.

Among those thiazoles no compound was found with antibacterial activity on an Escherichia coli culture. Some of them represented interesting level of the inhibition of incorporation of protein and/or nucleic acids ^{14}C components into Ehrlich ascites carcinoma cells, inhibition activity on Na^+,K^+-ATPase (rat brain), and growth inhibition of NCI's cell-line screening system derived from murine lymphocytic leukemia (P388).

This study is a continuation of a series of papers[1,2] and is now in progress.

REFERENCES

1. Drašar P., Pouzar V., Černý I., Smolíková J., Havel M.: Collection Czech. Chem. Commun. 49, 1039 (1984).

2. Drašar P., Pouzar V., Černý I., Havel M.: Collection Czech. Chem. Commun. 49, 1051 (1984).

REACTIONS OF 3α,5α-CYCLO-6β-METHOXY-14β-ANDROSTAN-17-ONE

Ivan Černý, Vladimír Pouzar, Pavel Drašar and Miroslav Havel

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

Using the title ketone as a starting compound the reactions leading to construction of a side chain in position 17 of CD-cis steroid were compared.

The first reaction sequence under study consisted of the methylenation with triphenylphosphonium methylide, subseqent hydroboration, and alkaline hydrogen peroxide oxidation of the formed boranes. The alternative ways in question were based on boron trifluoride etherate - sodium borohydride treatment of the 16,17-epoxides. The epoxides were prepared from the corresponding exomethylene derivative by the oxidation with metachloroperbenzoic acid, or by the iodoacetoxylation with iodine - silver acetate followed by the subsequent epoxide closure. Finally the epoxides were prepared directly from the starting ketone by the addition of dimethylsulfoxonium methylide in dimethyl sulfoxide.

The resulting 20-hydroxyderivatives were analysed by the HPLC after the cleavage of 3α,5α-cyclo protecting group and benzoylation. The authentic sample of 17α-derivative was prepared from 3β-acetoxy-pregna-5,14,16-trien-20-one.

SENSITIZED BEAN INTERNODE BIOASSAYS FOR BRASSINOSTEROIDS

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During the course of our investigations into the structure activity relationship of brassinosteroids, we used and sensitized two different bean internode bioassays. These bioassays are based either on the enhancement of auxin-induced curvature of plant organs, or on the stimulation of organ elongation.

Inversion of the bean first internode sections increases the sensitivity of bioassay to IAA 1000 times. High sensitivity to auxin was closely related to the elevated sensitivity to 24-epibrassinolide (24-BR). Optimalization of the second bean internode bioassay increases its sensitivity to 24-BR by factor of 100. With respect to the double phasic response of the internode curvature, and in some cases also of the internode elongation to brassinosteroids, the estimation of their biological activities must be based on testing of broad range doses of substances under the test. Activities of different brassinosteroids are not always parallel in the two bioassays. This difference is probably a result of the interference of externally applied brassinosteroids with endogenous fytohormones. The development of a new bioassay and the relationships between the chemical structure and biological activity of several brassinosteroids will be presented.

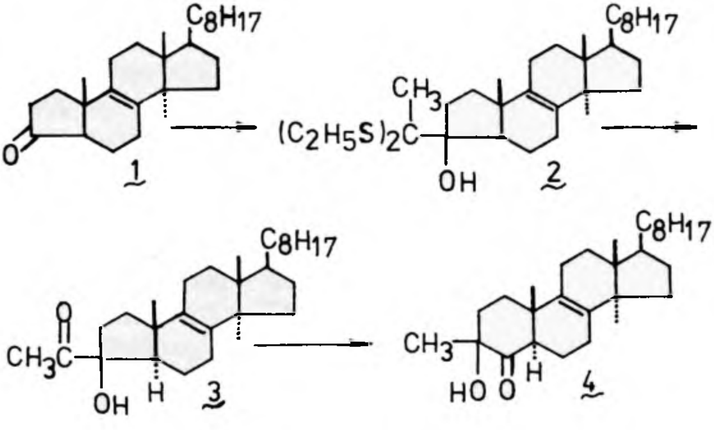
RING A EXPANSIONS OF ACYLOINS DERIVED FROM 14α-METHYL-A-NOR-CHOLESTAN-3-ONE

Jacek Martynow and Zdzislaw Paryzek

Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland

A great deal of work has been reported (mainly by Kirk's group) on acyloin rearrangement of 17-hydroxy-20-oxo pregnane derivatives, while the study of similar reaction of 3-acetyl-3-hydroxy-A-nor steroids has not been undertaken.

The acid catalyzed ring expansion of acyloin 3 obtained from 1 via 2 resulted in a rather unexpected migration of C(2) - C(3) bond. Thus formation of the six membered ketol 4 was observed. Spectral and chemical evidences support this structure. The results of the rearrangement of the 5β isomer of 3 and of 5β-7,9(11)-diene analogue will also be described.



REACTION OF OZONE WITH HINDERED DOUBLE BONDS IN LANOSTANE DERIVATIVES

Jacek Martynow and Zdzisław Paryzek

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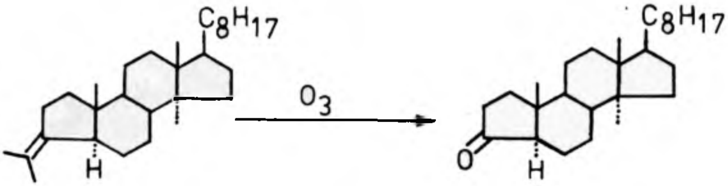
Retropinacolic rearrangement of 5α-lanostan-3β-ol under the action of PCl_5 gives ring A contracted isopropylidene compound 1. Ozonolysis of 1 is a good method of the synthesis of 14α-methyl-A-nor-cholestan-3-one 2. Similar sequence of reactions has frequently been described for penta- and tetracyclic triterpenes. However, ozonolysis reaction is more complicated, when an additional double bond in position 8,9 of the lanostane skeleton is present. This highly hindered double bond in several lanostane derivatives was found susceptible to oxidation with ozone and these reactions were dependent on the polarity of the solvent used in the reaction. For example, reaction of 3β-acetoxy-5α-lanost-8-ene with ozone gave 8α,9α-epoxide in methylene chloride, while 3β-acetoxy-5α-lanost-8-en-7-one, an allylic oxidation product, was the main compound formed in ethyl acetate. In hexane, 8,9-double bond was innert toward ozone under similar conditions.

The apparent influance of the solvent polarity on the reactions under study is explained in terms of the structure of the initial complex formed between ozone and the reacting olefin.



1

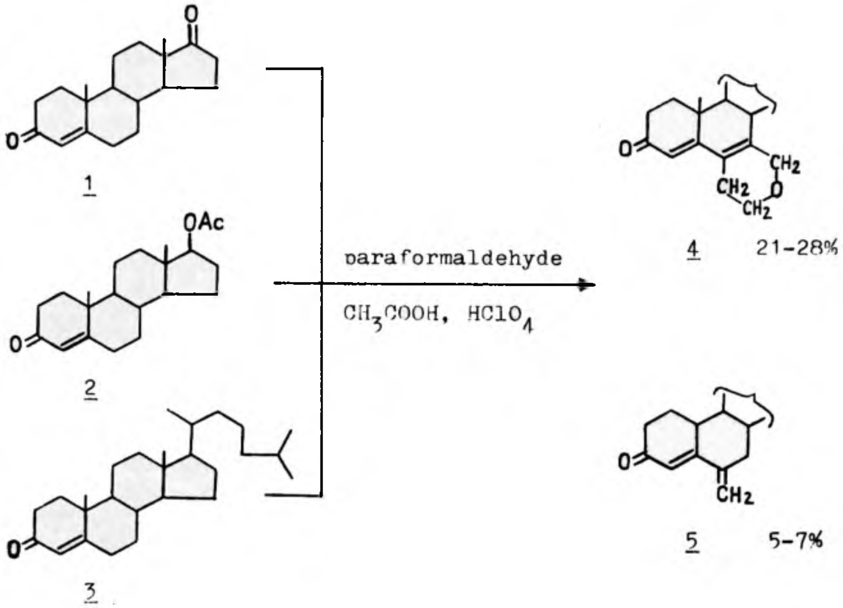
2

REACTIONS OF STEROIDAL 4-ENE-3-ONES AND A 4,6-DIENE-3-ONE WITH FORMALDEHYDE UNDER ACIDIC CONDITIONS

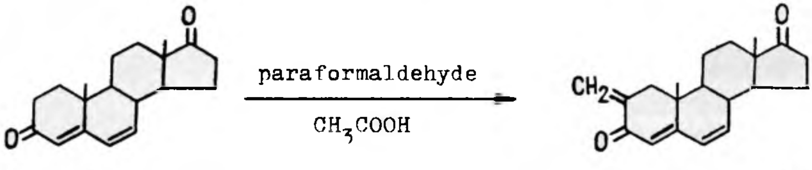
B. Osipowicz, L. Jabłoński, S. Mejer

Department of Fundamentals of Chemistry, Agricultural
University, Wrocław, Poland

Steroidal 4-ene-3-ones 1,2,3 formed with paraformaldehyde under acidic conditions the corresponding derivatives 4 containing dihydropyrane ring, and small amounts of 6-methylene-4-ene-3-ones 5. In a separate experiment we established that from pure 6-methylene-4-ene-3-one 5 and paraformaldehyde also the product 4 was formed.



4,6-Androstadien-3-17-dione 6 gave with paraformaldehyde 2-methylene derivative 7 in fair yield.



6

7 74%

The reactions proceeded most likely through the addition of protonated formaldehyde to the enols of the starting unsaturated ketones.

THE INTRAMOLECULAR CYCLIZATION OF STROIDAL α-EPOXY-KETO-ALDEHYDES TO ACETALS

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02-093 Warszawa, ul. L. Pasteura 1, Poland

The reaction of α-epoxy-diols 1, 2 and 3 with lead tetraacetate in various solvents (benzene, chloroform and methanol) in the presence of acetic acid led to respective α-epoxy-keto-aldehydes 4, 5 and 6. Compounds 4, 5, 6 underwent intramolecular cyclization under quite mild acid conditions, including chromatography on silica gel, to give respecitve acetals 7, 8, 9 and 10. Similar cyclization may occur on heating above the melting point. The acetal 10 treated with BF_3-etherate in benzene underwent a further intramolecular rearrangement to give two isomeric acetals 11 and 12.

The structure of acetals was determined on the basis of ^{1}H-NMR and ^{13}C-NMR spectra (including NOE experiment). Additional proof for the structures was achieved by a comparison of ^{1}H-NMR and ^{13}C-NMR spectra of 7, 9, 10, 11 and 12 labelled with deuterium in C-3 and C-7 position, respectively.

The simplest mechanism wchich explains this cyclization is a nucleophilic attack by the carbonyl group concerted with epoxide bond rupture leading to acetals bridged structures (Scheme 2). The details of the stereochemical courses of the intramolecular acetalization will be discussed.

It appears that reported cyclization is a not isolated case since a formation of cyclic acetal derivatives during the oxidation of steroidal triols have been previously described.[1]

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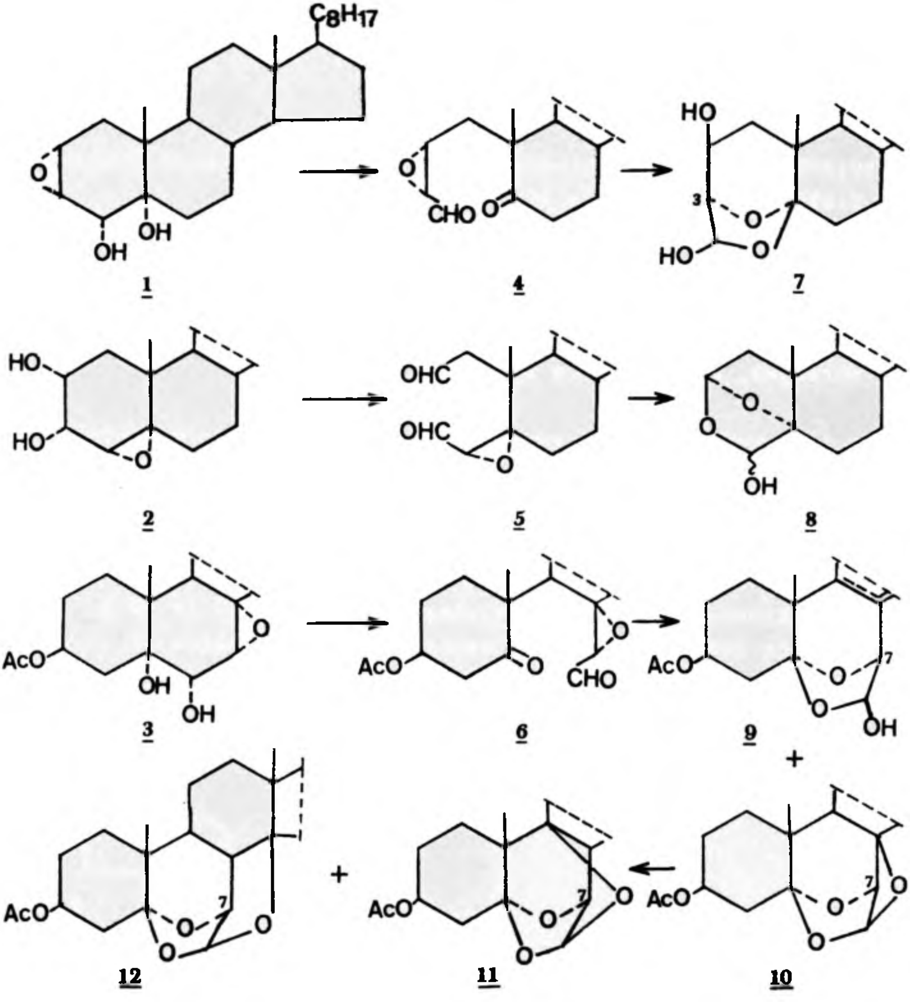
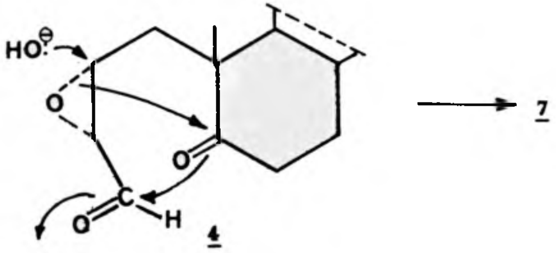
1. L. F. Fieser, T. Goto and K. Bhattacharyya, J.Am.Chem.Soc., **82**, 1700 (1960).

Scheme 1



Scheme 2



THE RINGS CD FRAGMENT FOR THE SYNTHESIS OF VITAMIN D_3 RELATIVES

Jacek W. Morzycki

Institute of Chemistry, University of Warsaw - Białystok Branch,
15443 Białystok, Al. 1-Maja 11/4, Poland

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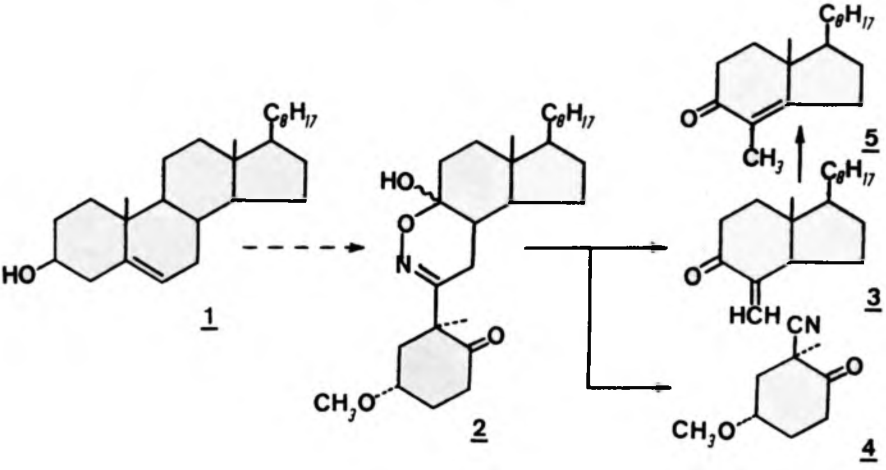
02093 Warszawa, ul. Pasteura 1, Poland

An improved method of synthesis of the precursor of vitamin D_3 relatives, 8-methylene-des-AB-cholestan-9-one (3), from cholesterol is presented. The starting material 1 was transformed to 2 in 7 steps in 40 % yield. On treatment with acids in a nonpolar solvent compound 2 undergoes the fragmentation to 3 and 2-cyano-4-methoxy-2-methylcyclohexanone (4) in 75 % yield. In the case of prolonged heating of 3 with acids it isomerizes to s-trans-enone 5 by the hydride migration from C-14 to C-7. The utility of s-cis-enone 3 in vitamin D_3 chemistry was shown.

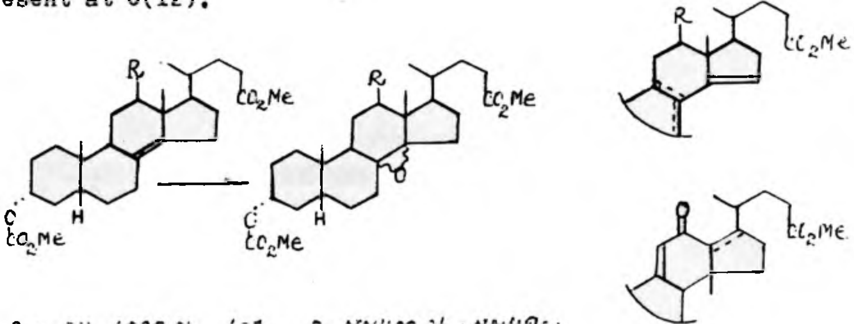


THE USE OF CHOLANIC ACID DERIVATIVES FOR DIRECTED I8(I3→I4) REARRANGEMENT

I.G.Reshetova , A.V.Kamernitzky, V.G.Levy, S.V.Chernov, E.I. Chernoburova

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

Synthesis of 8,I4α- and 8,I4β-epoxides of 5β-cholanic acid derivatives bearing substituents at C(I2) such as O,α-OH $-OCO_2H$,-OAc, II-eneacetoxy-, N-carbethoxy- or N-tosylhydrazone starting from cholic acid have been elaborated. Lewis and proton acid catalyzed rearrangements of these epoxides have been studied. The nature of the substituent at C(I2) affects both the stereochemistry of 8(I4)-double bond oxidation and the course of acid-catalyzed epoxide cleavage. Rather unexpectedly it has been found that the derivatives of α-8,14-epoxides in cholanic acid series are able to undergo rearrangement with I3,I4-methyl group shift provided keto group is present at C(I2).



$R = \alpha OH; \alpha OCO_2Me, \alpha OAc, =O; NNHCO_2Et, NNHTs;$

STUDY OF THE 17α-HYDROPEROXY-16α-METHYL-PREGNANE PROPERTIES

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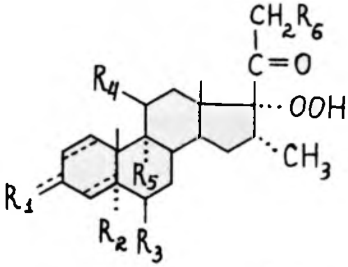
A series of 17α-hydroperoxy-16α-methyl-pregnanes (I-VII) which may be used to yield biologically active corticosteroids has been synthesized.



I : $R_1=\beta OAc$; R_2R_3 = double bond; $R_4=R_5=R_6=H$;
II : $R_1=\beta OAc$; $R_2=R_3=R_4=R_5=R_6=H$;
III : $R_1=\beta OAc$; R_2R_3 = double bond; $R_4=R_5=H$; $R_6=OAc$;
IV : $R_1=O$; Δ^4-double bond; $R_3=R_4=R_5=H$; $R_6=OAc$;
V : $R_1=O$; $\Delta^{1,4}$-double bonds; $R_3=R_5=H$; $R_4=R_6=OAc$;
VI : $R_1=O$; $\Delta^{1,4}$- double bonds; $R_3=H$; $R_4=OH$; $R_5=F$; $R_6=OAc$;
VII : $R_1=O$; $\Delta^{1,4}$-double bonds; $R_3=H$; $R_4=R_6=OAc$; $R_5=F$.

The stability of hydroperoxides has been studied. The latter appeared to be stable in the form of crystals and in solutions at temperatures from 20° to 80°C. However in acid and alkaline media, in the presence of the transitional metal salts as well as under the conditions of the ordinary acetylation, hydroperoxides easily decompose forming the products of androstane series and a small quantity of 17α-hydroxypregnanes. Conditions for a complete decomposition of hydroperoxides have been found, the reaction products have been isolated and characterized.

Biological activity of the compounds I-VII has been studied.

NEW SYNTHESIS OF STEROIDAL TETRAHYDROOXAZIN-2-ONES

László Hackler and Gyula Schneider

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Szeged, Hungary

It is well known that primary and secondary tosylates can be oxidized into the corresponding carbonyl derivatives in DMSO/NaHCO$_3$ system, *via* a carbonic acid half-ester. When a hydroxy-group is atteched in an favourable steric position to the neighbouring carbon atom, a cyclic carbonate is formed and oxidation does not occur.

On the basis of the above mechanism, it can be expected that in the presence of a primary or secondary amino group in an appropriate steric position in the vicinity of tosyl group, the reaction will yield tetrahydrooxazin-2-one or its N-substituted derivatives.

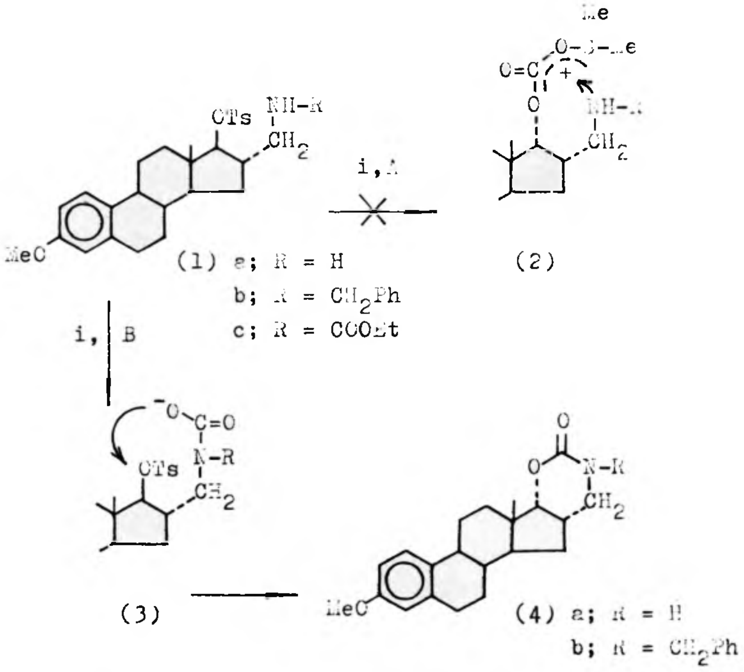
Thus, 16α-aminomethyl- and 16α-benzylaminomethyl-3-methoxy-17β-tosyloxyestra-1,3,5(10)-triene (1a-b) are transformed to the corresponding tetrahydrooxazin-2-ones (4a-b) in excellent yield in DMSO/NaHCO$_3$ system at 100 °C in 120 min.

Two reaction mechanism can be considered (Scheme).

In path A, the 17β-tosyloxy group is replaced by the HCO$_3^-$ ion *via* inversion, and the carbonic acid half-ester formed is stabilized by the DMSO solvent. This unstable intermediate (2) undergoes cyclization with the amino function to tetrahydrooxazin-2-one (4a-b). However, since 17β-tosylates are not oxidized under similar conditions, another mechanism was regarded.

In path B, the formation of free carbaminic acid (3) was assumed in the DMSO/NaHCO$_3$ system, and its cyclization *via* intramolecular catalysis yields the corresponding tetrahydrooxazin-2-one.

In order to verify this assumption, 16α-ethoxycarbonyl-aminomethyl-17β-tosyloxy-3-methoxyestra-1,3,5(10)-triene (<u>1c</u>) was heated in DMSO in the presence of NaOH, hydrolysed to the free carbaminic acid (<u>3a</u>) and then transformed to <u>4a</u> in an intramolecular reaction.



i, DMSO-$NaHCO_3$

(Scheme)

A fast cyclisation process yielding a homogeneous product is typical of neighbouring group participation; these reaction can be classified as $(R-NH-COO^{-}-6)$ according to the notation introduced by Winstein.

NEW TYPE OF ANTIJUVENILE HORMONE AGENTS AND THEIR POSSIBLE MODE OF ACTION

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[a]Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, Czechoslovakia
[b]Institute of Entomology, Czechoslovak Academy of Sciences, České Budějovice, Czechoslovakia
[c]Institute for Research, Production and Application of Radioisotopes, Prague, Czechoslovakia

Synthesis of some of the biologically active aromatic terpenoid ethers and compounds structurally similar to precocenes, the structure-activity (on insects and mites) relation and the mode of their action as determined from radiobioassay, will be discussed.

SYNTHESIS OF 3,3a-PROPANO CANTHINE DERIVATIVES

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Research Institute of Pharmacy and Biochemistry,
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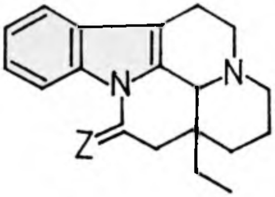
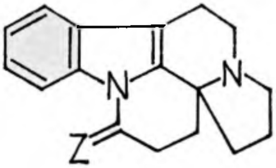
Monoterpenoid indole alkaloids of eburnane type (I) represent the attractive synthetic targets mainly because of their potent pharmacological properties. As a continuation of our efforts in this field we report on a new synthesis of analogs of these bases (II). The crucial step of the synthesis consists in the Pictet-Spengler-like formation of indolizino/8,7-b/indole intermediates.



I



II

SYNTHESIS OF SUSPENSOLIDE, A NOVEL MACROLIDE COMPONENT FROM CARIBBEAN FRUIT FLY (*ANASTREPHA SUSPENSA* (LOEW)) VOLATILES

M. A. Battiste and R. L. Wydra*

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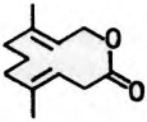
Gainesville, USA

J. H. Tumlinson and T. Chuman

Insect Attractants, Behavior, and Basic Biology
Research Laboratory, Agric. Res. Serv., USDA,
Gainesville, USA

Suspensolide (1), a 11-membered lactone, was found recently to be a major component of male Caribbean fruit fly (*Anastrepha suspensa* (Loew)) volatiles.

In this communication, the six step synthesis of the title compound, starting from easily available mesityl oxide will be presented. Spectral properties of suspensolide and its (3Z,8E)-isomer will also be discussed.



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* On leave from Faculty of Chemistry, A. Mickiewicz University, Poznan, Poland

SYNTHESIS OF (E)- 3,7-DIMETHYL-2,7-OCTADIENYL PROPANOATE USING ISOPRENE AS A STARTING MATERIAL.

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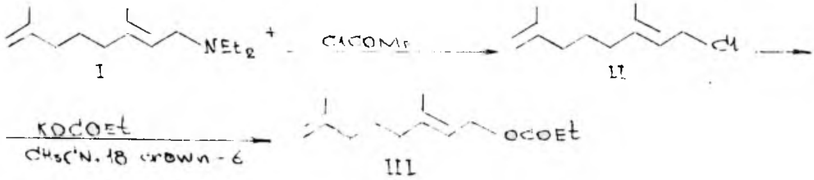
1 All-Union Institute of Biological Control,Kishinev,USSR

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

The synthesis of the title compound, the sex pheromone component of the San Jose scale, was carried out by palladium catalyzed telomerization of isoprene with diethyl amine :

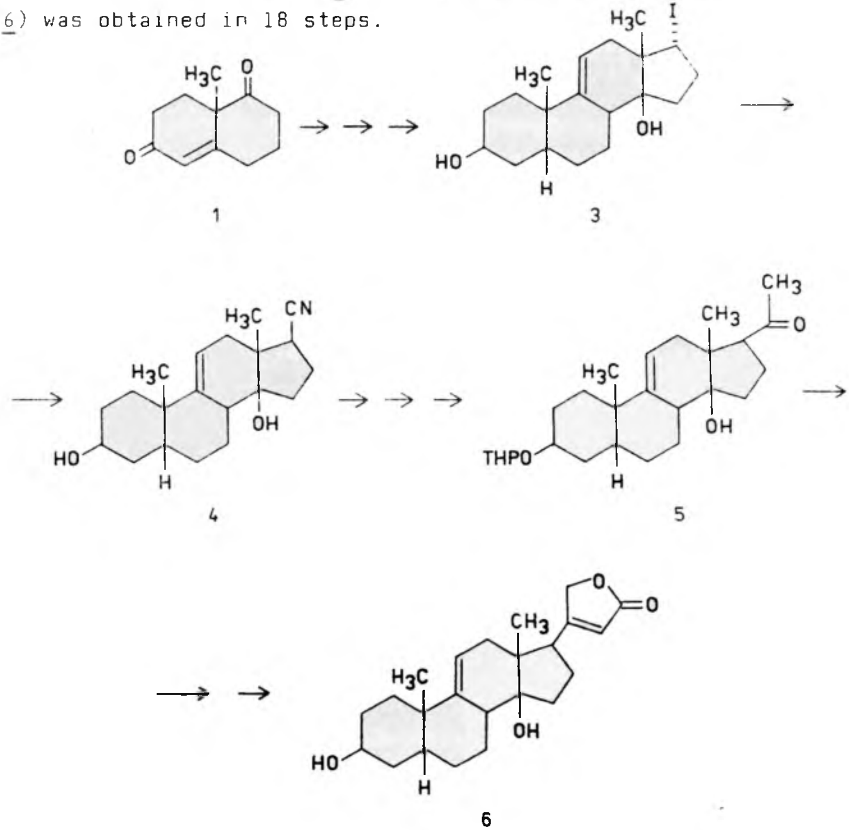


Amine I was converted into chloride II by treatment with excess of methylchlorformiate. This chloride was acetylated by potassium propanoate to give the product III.

TOTAL SYNTHESIS OF 9,11-DEHYDRODIGITOXIGENIN

A. R. Daniewski, M. Kabat, M. Masnyk, J. Wicha and
W. Wojciechowska
Institute of Organic Chemistry, Polish Academy of Sciences
01-224 Warsaw, Poland

Starting from ketone (1) the 9,11-dehydrodigitoxigenin (6) was obtained in 18 steps.



One of the crucial steps was free radical substitution of the iodine atom in 3 with the nitrile group. The configuration at C-17 was proved by transformation of 4 into lactone and by an equilibration of 5 to the termodynamically more stable 17α-methyl ketone.

FACILE METHOD FOR THE SYNTHESIS OF 3,3-DIMETHYLGLUTARIC ACID

Jerzy Podlejski
Institute of General Food Chemistry
Technical University of Łódź

3,3-Dimethylglutaric acid 1 is a convenient starting material for the preparation of 4,4-dimethyl-cyclopentanone and 1,1-dimethylcyclopentadiene-2,4. A few synthetic aproaches to 1 heve been reported up to date.

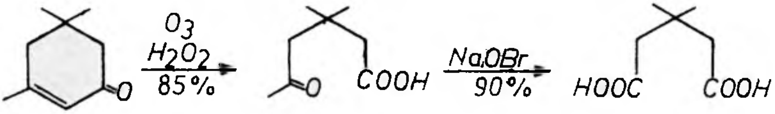
The acid 1 is obtained by:

i. condensation of aceton with cyanacetamide followed by hydrolysis of the resultant 5-carbamyl-3-cyjano-4,4-dimethyl-6-amino-2-piperidone[1]

ii. reaction of sodium diemethylmalonate with mesityl oxide and oxidation of the resultant 5,5 dimethylcyclohexadienone-1,3.[2]

iii. condensation of aceton with ethyl cyanoacetate and subsequent hydrolysis of the resultant dicyanimide[3].

We wish to present a new and simple method for the synthesis of 1 based on easyly available isoforon as a starting material. The method is shown in the following scheme.



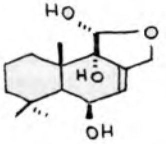
1. F.B. Thole, I.F. Thorpe, J.Chem.Soc., 99, 422 /1911/
2. Organic Synthesis coll Vol.2 200 /1943/, 31 40
3. Arthur J.Vogel - Preparatyka Organiczna - 891, WNT, W-wa 1964.

ENANTIOSPECIFIC SYNTHESIS OF BIOLOGICALLY ACTIVE DRIMANE SESQUITERPENES FROM UVIDIN A.

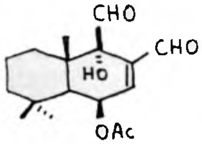
Luigi Garlaschelli[a], Giovanni Vidari[a] and Giorgio Mellerio[b]

[a] Department of Organic Chemistry; [b] Laboratory of Mass Spectrometry - The University of Pavia - V.le Taramelli, 10 - 27100 PAVIA - ITALY

Many drimane sesquiterpenes, isolated from plants and mushrooms, exhibit interesting biological properties[1]. Pereniporin A (**1**)[2] shows antimicrobial and cytotoxic activity in vitro and is a plant growth inhibitor; cinnamodial (**2**)[3,4] exhibits strong antifeedant activity. Neither of these compounds has been obtained so far by total or partial enantioselective synthesis. Moreover, the absolute configuration of pereniporin A is based only on biosynthetic considerations[2]. In this communication we describe the synthesis of the compounds **1-2** and the related sesquiterpene 3, cinnamosmolide[3], from uvidin A (**4**)[5]. The latter drimane has known absolute configuration and contains various functionalities on ring B, particularly the oxygenated functions at C-6 and C-11 which offer obvious advantages for the synthesis of the highly oxygenated sesquiterpenes **1-3**.



(1)



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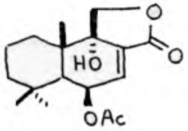

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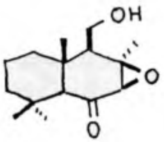

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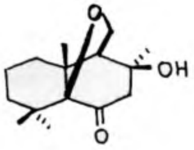

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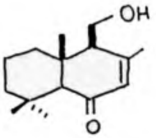
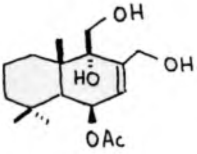


(6)

During the preliminary studies we discovered an interesting rearrangement of uvidin A which led to compound **5**, having new tricyclic carbon skeleton. The possible mechanism of this reaction will be discussed. Deepoxidation of uvidin A (**4**), with the recently introduced system Ph_3P. I_2 in moist CH_3CN[6], led, in quantitative yields, to the enone **6** which was then converted in few steps and good overall yields into the triol **7**. The same compound **7**, with identical optical rotation, could be obtained from cinnamodial **(2)**, not by direct reduction, but in few steps and only after protection of the tertiary OH as SEM derivative. During these reactions the boronate **8** has been prepared and then converted into pereniporin A (1).



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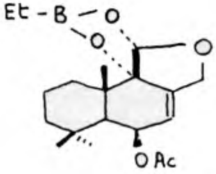

(8)

Selective oxidations of triol **7** yielded cinnamodial (2) and cinnamosmolide (3), respectively, which have physical and spectroscopic data identical with those reported in literature.

References

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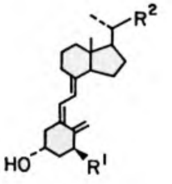
5. M. De Bernardi, G. Mellerio, G. Vidari, P. Vita-Finzi and G. Fronza, J. Chem. Soc., Perkin I **1980**, 221.
6. L. Garlaschelli and G. Vidari, Gazz. Chim. It., accepted for publication (1987).

SIDE CHAIN MODIFIED ANALOGUES OF VITAMINS D
NOVEL SYNTHETIC APPROACH

Andrzej Kutner[a], Kato L. Perlman, Heinrich K. Schnoes and Hector F. DeLuca[b]

[a]Institute of Pharmaceutical Industry, Warszawa, Poland
[b]University of Wisconsin-Madison, Madison, Wisconsin

The general method was developed for the preparation of side chain modified analogues of vitamin D_2 and D_3 of potential therapeutic activity. The synthesis involved the use of the hitherto unknown key intermediates, vitamin D - type C-22 aldehydes 1 (R^1 = H or OH; R^2=CHO). The intermediates 1 were prepared in good yield from easily available 22,23-bisnor-5-cholenic acid by means of consecutive protection of both functional groups and 5,7-diene formation followed by the triene system elaboration and final DIBAL-H reduction of the resulting C-22 vitamin D ester. 1α-Hydroxyl was introduced by the method previously developed in this[b] laboratory. The retention of natural 20S configuration of 1 was proved by 270 MHz ^{1}H-NMR and chromatographic methods. Coupling of aldehydes 1 with side chain fragments bearing a sulfone function gave after usual dehydroxy-desulfonylation vitamin D_2 analogues 2 (C_{22}-C_{23} double bond). Grignard-type condensation of 1 with side chain fragment provided some new vitamin D_3 analogues 2 (C_{22}-C_{23} single bond). Protection of the triene system of 1 at the coupling step was found not to be necessary.



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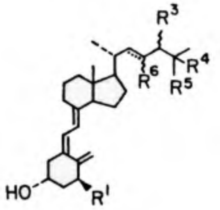


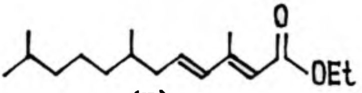
2

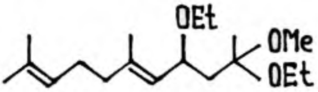
A NEW SYNTHESIS OF HYDROPRENE

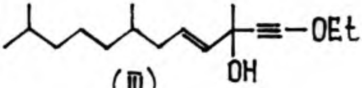
G.V.Kryshtal , E.P.Serebryakov , L.A.Yanovskaya, G.M.Zhdankina

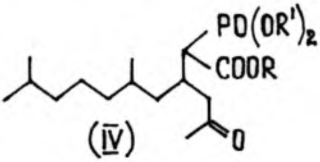
Institute of Organic Chemistry, the USSR Academy of Sciences, Moscow, the USSR

A six-step synthesis of ethyl 3,7,11-trimethyl-2,4-dodecadienoate (hydroprene, I) from citral based on the acetal condensation and subsequent hydrogenation of the intermediate alcoxy ketal (II) is described, the final step of which involves the formation and rearrangement of acetylenic carbinol (III). The overall yield of (I) is 31%


(I)


(II)


(III)

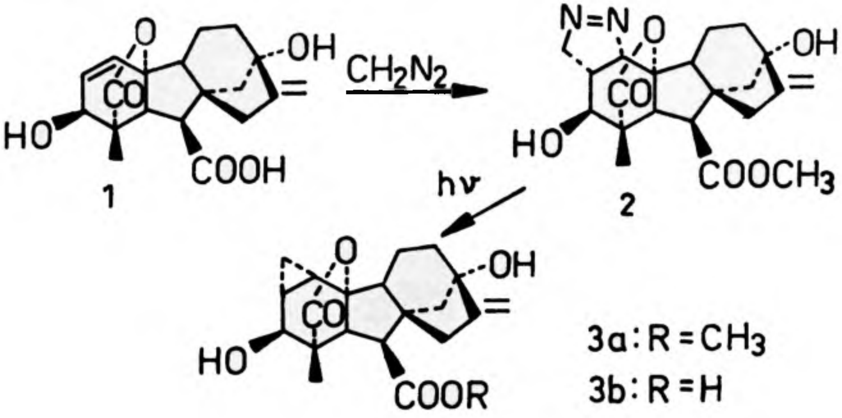

(IV)

The hydrogenation of (II) under different conditions and the formation of the Michael adducts of type (IV) is also reported.

SYNTHESIS OF METHYLENE GIBBERELLINS VIA PYRAZOLINE PRECURSORS

Brunhilde Voigt, Alfred Preiss and Günter Adam
Institute for Plant Biochemistry of the Academy of Sciences
of the GDR, 4050 Halle/Saale, GDR and
Leo Kutschabsky
Institute for Molecular Biology of the Academy of Sciences
of the GDR, 1115 Berlin-Buch, GDR

Continuing our investigations on synthesis of new gibberellin analogs for structure-activity relationships we prepared methylene gibberellins of structural type 3. Thus, long-termed reaction of GA_3 (1) with diazomethane yielded the pyrazoline ester 2, the structure of which was established by spectroscopic methods including NMR data and X-ray diffraction. Irradiation of 2 ($\lambda > 300$ nm) in acetonitrile afforded under loss of nitrogen the 1α,2α-methylene-gibberellin 3a and after hydrolysis the free acid 3b, representing a gibberellin analog of high biological activity.

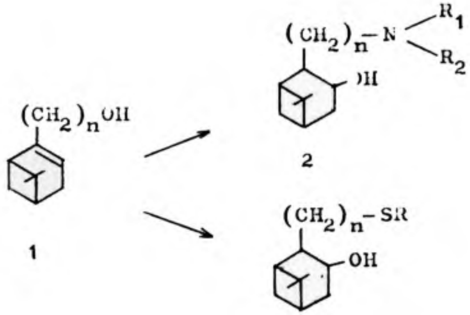


SYNTHESES OF SOME TERPENE HYDROXYAMINES AND HYDROXYSULFIDES AS REAGENTS FOR ASYMMETRIC REDUCTION OF KETONES

L.Borowiecki, A.Kazubski, E.Reca

Institute of Chemistry, N.Copernicus University,
Toruń, Poland

Syntheses of some terpene hydroxyamines /2/ and hydroxysulfides /3/ from myrtenol /1, n=1/ and nopol /1, n=2/ are presented.



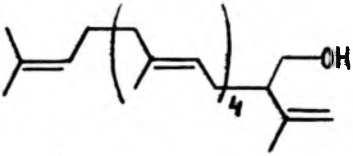
Preparation of borane-2 and borane-3 complexes and its use in asymmetric reduction of acetophenone is described.

SYNTHESIS OF (±)-ULMOPRENOL

V.A. Koptenkova, V.V. Veselovsky, A.M. Moiseenkov

N.D. Zelinsky Institute of Organic Chemistry,
Academy of Sciences, Moscow, U.S.S.R.

The title compound - irregular plant hexaprenol 1 [1] - has been prepared in several steps starting from geranylgeranyl bromide and sulfur containing building blocks 2 and 3 .



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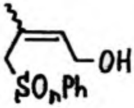

2: n = 2 (E)
3: n = 0 (Z)

References:

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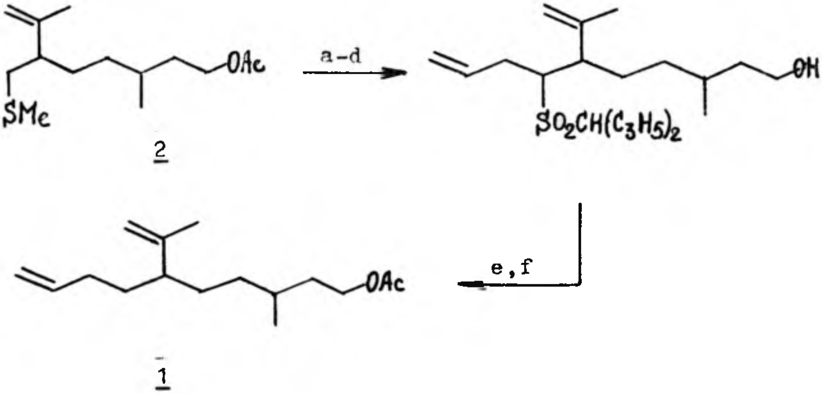
SYNTHESIS OF 6-ISOPROPENYL-3-METHYL-9-DECEN-1-YL ACETATE - A COMPONENT OF THE CALIFORNIA RED SCALE PHEROMONE

Vladimir A. Dragan and Vladimir V. Veselovsky

N.D. Zelinsky Institute of Organic Chemistry,
Academy of Sciences, Moscow, U.S.S.R.

The hydroxy sulfide 2, readily available from citronellol, was converted into the title compound (±)-1 in ~ 30% overall yield.



[a] MCPBA, [b] LAH, [c] ^{n}BuLi, [d] C_3H_5Br, [e] Na/NH_3, [f] Ac_2O/Py.

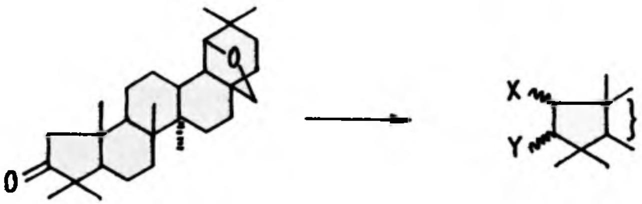
STEREOCHEMISTRY AND REARRANGEMENTS OF A-NOR TRITERPENOIDS

Jiří Klinot[a], Jiří Rozen[a], Jiří Liška[a], Alena Forgáčová[a]
Miloš Buděšínský[b] and Alois Vystrčil[a]

[a] Department of Organic Chemistry, Charles University,
[b] Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague, Czechoslovakia

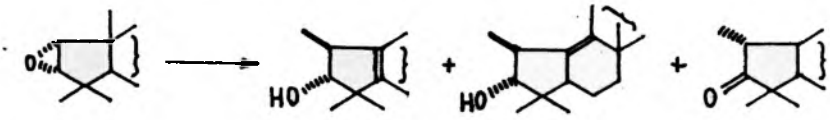
Some A-nor-derivatives of 19β,28-epoxy-18α-oleanane with substituents at C(2) and C(3) (II) were prepared from ketone I. Proton NMR and IR spectra show that the 2α- and 3β-bonds at the five-membered ring A are pseudoaxial whereas the 2β- and 3α-bonds are pseudoequatorial.

Reactions of epoxide III with acids or boron trifluoride etherate are accompanied with rearrangement of 10β-methyl group. Unsaturated alcohols IV and V and ketone VI are formed. The structure and configuration of compounds IV-VI was deduced from chemical transformations and ^1H NMR, ^{13}C NMR, IR, UV and mass spectra.



I

II X, Y = H, OH, Br, =O



III IV V VI

ACYLATION REACTION OF α-PINENE

Péter Vinczer[1], Zoltán Juvancz[1], Mária Kajtár-Peredy[1],
Lajos Novák[2] and Csaba Szántay[1,2]

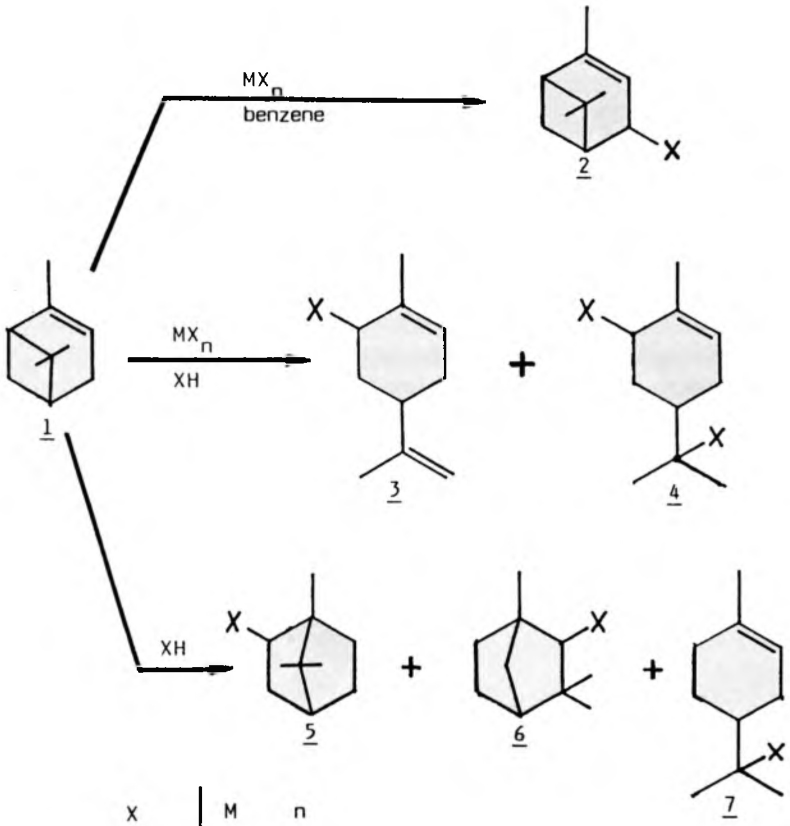
[1]Central Research Institute for Chemistry of the Hungarian Academy of Sciences, P.O.Box 17, Budapest, H-1525 HUNGARY
[2]Institute for Organic Chemistry, Technical University, P.O.Box 91, Budapest, H-1521 HUNGARY

α-Pinene is a useful starting material for the synthesis of terpene-derivatives. The acylation of α-pinene was studied with reagents whose valence states may change during the process.

These reagents can

- acylate the unsaturated ring of α-pinene in allylic position (1 ⟶ 2) in neutral conditions,
- open up the saturated ring of α-pinene and then acylate the unsaturated ring in the other allylic position (1 ⟶ 3+4) in acidic solution.

The ring cleavage of α-pinene is acid catalyzed reaction and gives different products (3 - 7). The formation of these compounds, namely the mechanism of the reaction will be discussed.



X	M	n
$\mathrm{CH_3\underset{\underset{O}{\|}}{C}O}$	Pb	4
	Hg	2
	PhI	2
$\mathrm{C_2H_5\underset{\underset{O}{\|}}{C}O}$	Pb	4

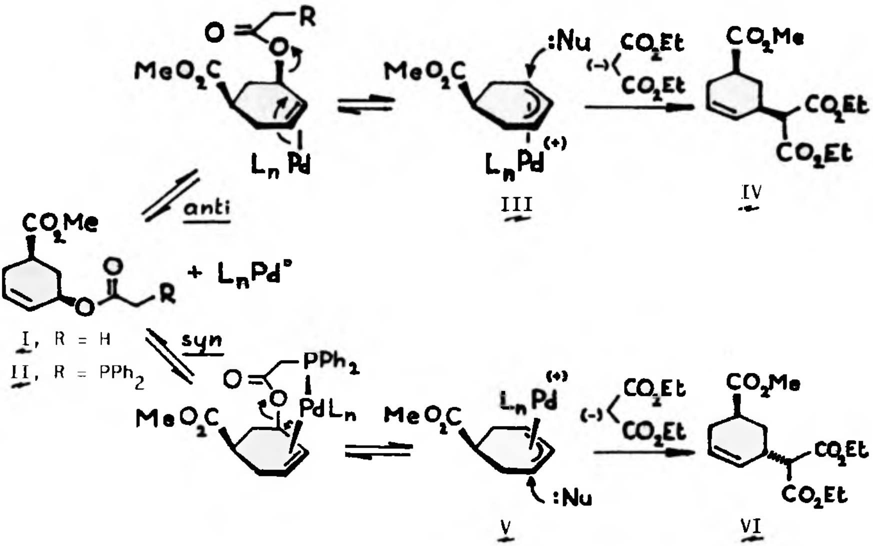
AN OBSERVATION OF SYN-ANTI DICHOTOMY IN THE FORMATION OF π-ALLYL PALLADIUM COMPLEXES

Ivo Starý and Pavel Kočovský

Institute of Organic Chemistry and Biochemistry
Czechoslovak Academy of Sciences, 16610 Prague 6, Czechoslovakia

Formation of the π-allyl palladium complexes from allylic acetates has been known to proceed stereoselectively via an *anti*-mechanism (**I**→**III**). Following reaction with stabilized C-nucleophiles leads to **IV** as the sole product, again via an *anti*-mechanism.

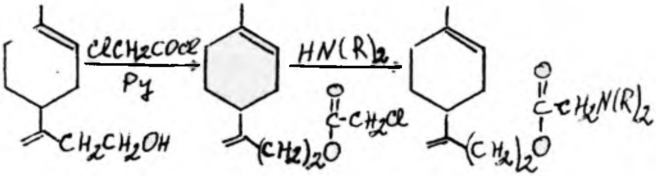
We have found that the *syn*-pathway may be forced by pre-coordination of the Pd(0) reagent with a part of the leaving group (e.g. $-PPh_2$ as in **II**). This pre-complexation steers the approaching Pd from the cis-side which results in the *syn*-mechanism and formation of the intermediate complex **V**. Following reaction with lithium diethyl malonate affords **VI** via an ordinary *anti*-mechanism. On catalytic reaction the ester **II** thus gives a mixture of **IV** and **VI** in a 1.4 : 1 ratio, which reflects the competition of *anti*- and *syn*-pathways of formation of the π-allyl palladium complexes **III** and **V**.

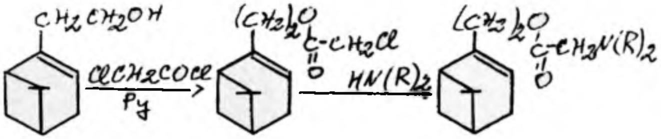


SINTHESIS OF THE MONOCHLOROACETATES AND AMINOESTERS OF 9-HYDROXYMETHYL-1,8(10)-P-MENTHADIENE AND NOPOL

Georgi Y.Papanov, K.N.Tomova and P.Y.Malakov
University of Plovdiv, 4000 Plovdiv,Bulgaria

Acylation of 9-hydroxymethyl-1,8(10)-p-menthadiene and nopol with monochloroacetylchloride gives their monochloroacetates(3,4), from which different aminoesters have been synthesized by reactions with secondary amines.





MECHANISTIC CONSIDERATIONS ON RED-OX REACTION BETWEEN OXIDIZERS WITH REVERSIBLE RED-OX POTENTIALS AND SOME ISOPRENOIDS

Jan Jasiczak

Institute of Commodity Sciences, Academy of Economics,
Marchlewskiego 146/150, 60 967 Poznań, Poland

In our earlier papers[1-2] we have described new reaction of oxidation of isoprenoids with α-ketol or enone groups with thermodynamically reversible red-ox potentials. We found that, in one-step reactions, it is possible to obtain high yields of the respective steroid hydroxyacids as well as keto and hydroxy isoprenoid derivatives.

In the present communication, we report the results of a comparative study on the alternative reaction mechanisms of oxidation of α-ketol and enone isoprenoids on the basis of kinetic and chemical data.

1. J.Jasiczak, M.A.Smoczkiewicz: SYNTHESIS, 1981, 804;
TETRAHEDRON LETT., 1985, 5221.
2. J.Jasiczak: J.ORG.CHEM. /in press/.

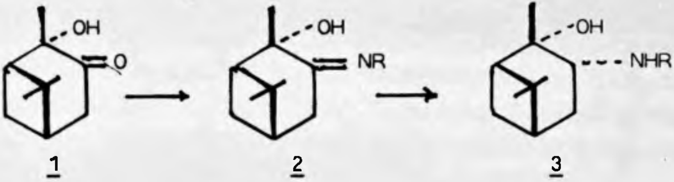
2α-HYDROXY-3α-(N-ALKYL)AMINOPINANES AND 2α,10-DIHYDROXY-3α-(N-ALKYL)AMINOPINANES

Stanisław Wojciech Markowicz

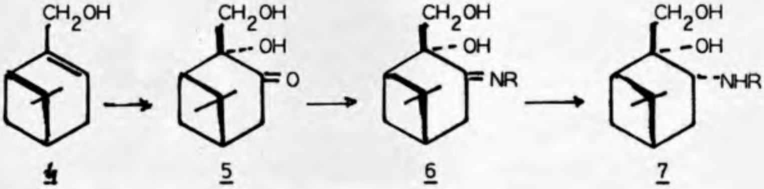
Institute of Organic Chemistry, Technical University
ul.Żwirki 36, 90-924 Łódź, Poland

2α-Hydroxypinan-3-one (1) is known as an excellent chiral auxiliary, accessible in both enantiomeric forms^{1,2}. In this communicate the utility of 1 for the preparation of 2α-hydroxy-3α-(N-alkyl)aminopinanes (3)^{3} - potential chiral chemical reagents is presented.

The aminoalcohols 3 were obtained in 70% yields from the corresponding Schiff's bases 2 by reduction with NaBH$_4$.



Oxidation of myrtenol (4) gives 2α,10-dihydroxypinan-3-one (5) (as a major product) which is transformed in the similar way to 2α,10-dihydroxy-3α-(N-alkyl)aminopinanes (7).



The aminoalcohols 3 and 7 give the crystalline diastereomeric salts, suitable for optical resolution of chiral carboxylic acids. Additionally, these aminoalcohols afford chiral complexes with NaBH$_4$ as well as chiral Lewis acid.

References: 1) S.Yamada et al.,Chem.Pharm.Bull.,26,803 (1978)
2) Ph.Viallefont et al.,Tetrahedron Lett.,25,1789 (1984); 3) 2α-Hydroxy-3-aminopinane was first obtained by Z.Chabudziński et al., Pol.J.Chem.,52,1721 (1978).

EVIDENCE FOR THE EXISTENCE OF A TERTIARY NONCLASSICAL CARBENIUM ION IN THE FORMATION OF TRICYCLIC γ-LACTONES

Vassil Vassilev and Blagoy Blagoev

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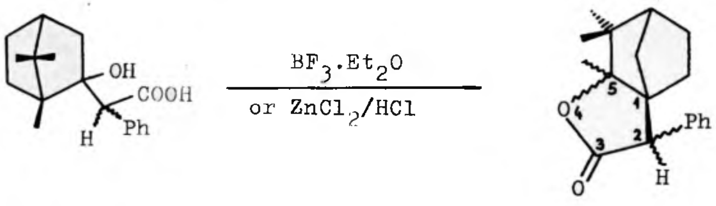
1040 Sofia, Bulgaria

The diastereoisomeric β-hydroxy acids 1, obtained by the addition of the phenylacetic acid magnesium reagent to (+)-camphor, are converted under the action of acid reagents into the tricyclic γ-lactones 2.



1

2

The configuration of the γ-lactones at C5 depends upon the acid reagent used. The stereochemistry of the products indicates the existence of a tertiary nonclassical carbenium ion.

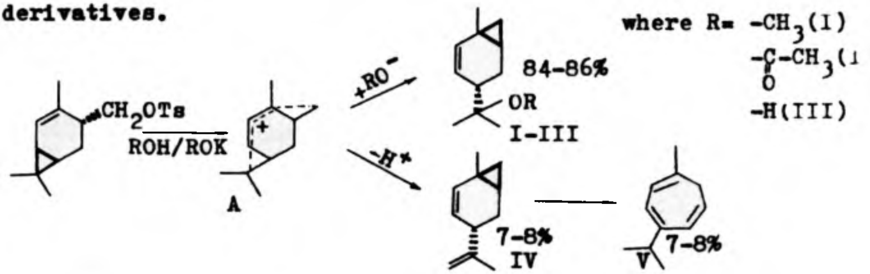
SKELETAL REARRANGEMENT OF THE CARANE STRUCTURE DURING SOLVOLYSIS OF TRANS-4-TOSYLOXYMETHYL-2-CARENE

Oleg Vyglazov and Edward Manukov

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

Terpenoids of carane series are convenient models used to study different skeletal rearrangements involving a cyclopropane ring. In particular, the rearrangements observed in solvolysis are due to interaction between the cyclopropane ring (CPR) and an evolving electron-deficient site.

Acetolysis, methanolysis and hydrolysis of trans-4-tosyloxymethyl-2-carene have been found to be accompanied by the opening of a gem-dimethylcyclopropane ring and closing of a new three-membered carbocycle. Similar rearrangements have not been previously observed in the solvolysis of carane derivatives.



The selective skeletal rearrangement is accounted for by the formation of an intermediate homopentadienyl ion A. The latter is formed as a result of interaction through space between the charged site, double bond and gem-dimethylcyclopropane ring. The nucleophylic attack against atom C^7 gives I-III products. Hydrocarbon IV is formed as a result of stabilization of an intermediate ion A upon ejection of a proton from the CPR methyl group. A futher isomerization of hydrocarbon IV via a norcaradiene intermediate leads to the substituted cycloheptatriene V.

FORMATION OF 3-CARENE IN REACTIONS OF MENTHANE ALCOHOLS ESTERS

Vera Chuiko and Oleg Vyglazov

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BSSR Academy of Sciences, Minsk, USSR

Thermal decomposition of boric esters of 4-hydroxymethyl-2-carene did not lead to the expected 4-methylene-2-carene but gave 1-methyl-4-isopropenylbicyclo/4.1.0/hept-2-ene as a primary product. Thus, the skeletal rearrangement accompanied by opening the gem-dimethylcyclopropane ring and closing a new three-membered carbocycle was observed. A new three-membered cycle involves a carbon atom separating the ester group from a six-membered cycle.

The molecules of α-terpineol and silveterpineol esters have a similar arrangement of a functional group and six-membered cycle. Therefore, the pyrolysis of boric esters of these menthane alcohols was studied. The reaction was carried out at 180-200°C. The product of α-terpineol monoborate decomposition was a mixture containing dipentene and terpinolene (in 40%), other menthadienes (in 0.1-3.0%) and 1.3% of 3-carene. The formation of dipentene and terpinolene is the most probable pathway of reaction in terms of current theories. The other menthadienes are products of retransformations of the above hydrocarbons.

The presence of 3-carene in the reaction mixture indicates the possibility of γ-elimination under pyrolysis conditions. Since the reaction seems to be concerted it is postulated that there is transition state with orbital interaction both through bond abd through space.

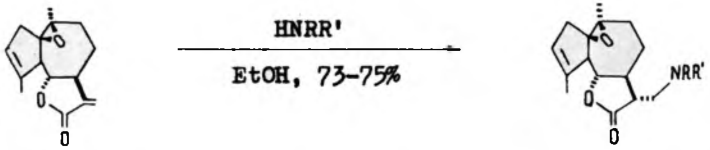
Silveterpineol borate pyrolysis occurs similarly. The pyrolysate contains 1.5% of 3-carene.

CHEMICAL TRANSFORMATIONS OF SOME SESQUITERPENE LACTONES

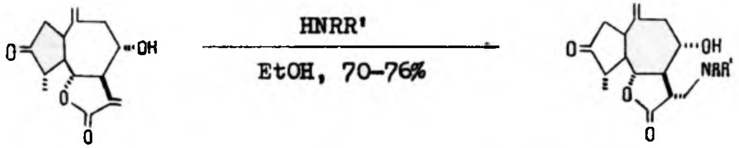
S.M.Adekenov, K.A.Aituganov

Institute of Organic Synthesis and Coal Chemistry,
Kazakh Academy of Sciences, Karaganda, U.S.S.R.

The heteroatom containing derivatives of the sesquiterpene lactones of arglabin (1) and grosshemin (2), isolated from Artemisia glabella Kar.et Kir. and Chartolepis intermedia Boiss. have been synthesized.



NRR'= $N(CH_2)_4O$, $HNCH_2COONa$, $HNCH(COONa)CH_2C_6H_5$



NRR'= $HNCH_2COONa$, $HNCH(COONa)CH_2C_6H_5$

The structures of the synthesized compounds have been determined according to the data of IR-,UV-,PMR-spectra.

STEREOCHEMISTRY OF DEHYDRATION OF (-)-(1S,3R,4R,6R)-3,4-CARANEDIOL ACETATE

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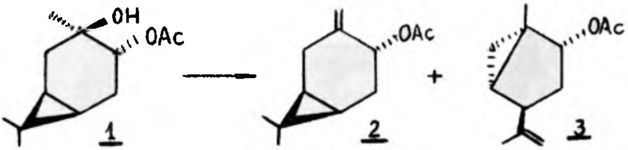
Institute of Organic and Physical Chemistry,
Technical University, Wrocław, Poland

Known reaction of dehydration of 3,4-caranediol acetate 1 leads to a mixture of unsaturated acetates, whose main components are carenol acetate 2 and acetate 3 formed in the relation near 1:1.



Modification of the dehydration process allowed to change its course towards formation of product of intramolecular rearrangement, acetate 3. The best results above 90% of 3 were achieved by the application of a pyridine-dioxane mixture as a solvent in the presence of lithium perchlorate which, when applied in oxygen solvent, favors a reaction running through ionic intermediates. A mechanism of the reaction was proposed. By the application of this method, bicyclic compounds, analogs of thujane derivatives, can be obtained from acetate 1 in high yields.

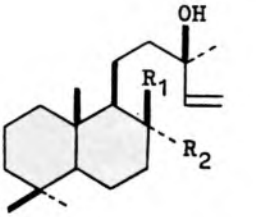
SUPERACIDIC CYCLIZATION OF SOME ALLYLIC LABDANE ALCOHOLS WITH HYDROXY GROUP AT C_{13}

P.F.Vlad[a], N.D.Ungur[a], A.N.Barba[a], D.V.Korchagina[b],
I.Yu.Bagrianskaya[b], Yu.V.Gatilov[b], V.P.Gatilova [b]
and V.A.Barkhash[b]

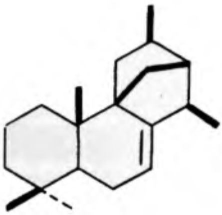
[a] Institute of Chemistry, Moldavian SSR Academy of sciences, 277028, Kishinev, USSR

[b] Institute of Organic Chemistry, Siberian Branch of the USSR Academy of Sciences, 630090, Novosibirsk, USSR

The allylic labdane diterpene alcohols with hydroxy group at C_{13} manool (I), sclareol (II) and others on fluorosulfonic acid treatment gave a mixture of two tetracyclic hydrocarbons having new carbon skeletons - (1R,2S,7S,11S,12R,13R)-2,6,6,11,13-pentamethyltetracyclo $[10.2.1.0^{2,11}.0^{3,8}]$pentadeca-9-ene (III) and (1S,2R,11S,12R,15R)-2,7,7,11,15-pentamethyltetracyclo $[10.2.1.0^{2,11}.0^{3,8}]$pentadeca-3(8)-ene (IV). Their structures and stereochemistry were determined on the basis of spectral data and X-ray analysis.



I $R_1+R_2=CH_2$
II $R_1=CH_3;R_2=OH$



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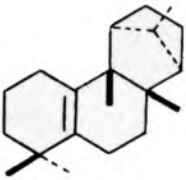


IV

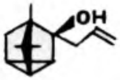
DEHYDRATION OF SOME TERTIARY ISOCYCLENIC ALCOHOLS

M.WEŁNIAK

Institute of Chemistry, N.Copernicus University,
Toruń, Poland

The course of dehydration of the tertiary isocyclenic alcohols 1 - 4 was studied under various conditions / $SOCl_2$/Py, PCl_5/benzene, $HClO_4$/THF or CH_3COOH/H_2SO_4 /.

1



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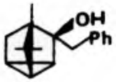


4

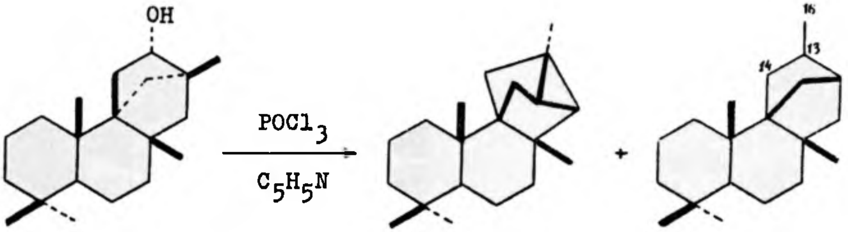
The structure of obtained compounds was confirmed by IR, ^1H NMR and ^{13}C NMR spectroscopies as well as by elemental microanalyses. Proposed mechanisms will be presented.

THE PRODUCTS OF (1R,2S,7S,10S,12S,13S)-2,6,6,10,12-PENTAMETHYLTETRACYCLO $[10.2.1.0^{1,10}.0^{2,7}]$PENTADECAN-13-OL DEHYDRATION

N.D.Ungur[a], P.F.Vlad[a], A.N.Barba[a], S.T.Malinovski[a],
Yu.A.Simonov[b], T.I.Malinovski[b]

[a] Institute of Chemistry,
[b] Institute of applied phisics, Moldavian Academy of Sciences,
277028, Kishinev, USSR

The phosphorus oxychloride dehydration of (1R,2S,7S,10S,12S,13S)-2,6,6,10,12-pentamethyltetracyclo $[10.2.1.0^{1,10}.0^{2,7}]$pentadecan-13-ol (I), the electrophilic cyclization product of a range of labdane diterpene alcohols, yields a mixture of hydrocarbons (II) - (IV) having new carbon skeletons. Their structure and stereochemistry were determined on the basis of chemical transformations, spectral data and for the last two compounds by X-ray analysis.



I

II

III - $\Delta^{13(14)}$

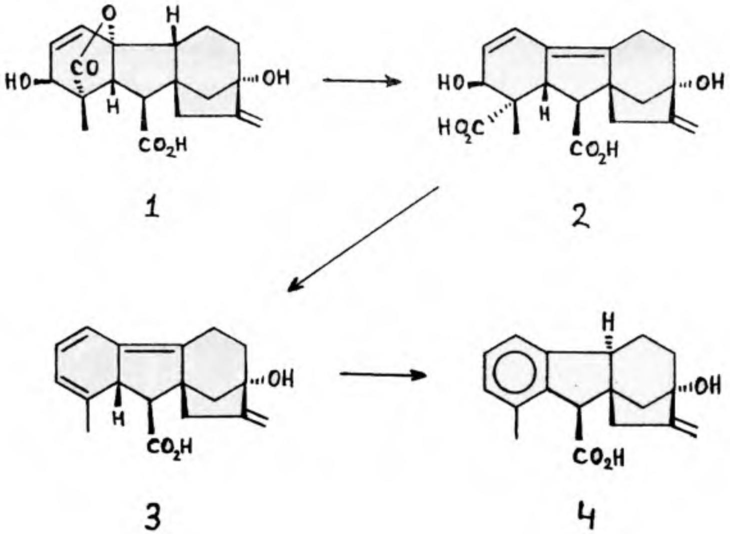
IV - $\Delta^{13(16)}$

EVIDENCE ON THE UNSTABLE TRIENE FORMATION IN THE PROCESS OF GIBBERELLIN A_3 AROMATISATION

N.A.Pankrushina, A.V.Tkachov, A.G.Druganov and V.A.Pentegova

Institute of Organic Chemistry, Siberian Division of
the USSR Academy of Sciences, Novosibirsk 90, USSR

It is shown that upon decomposition of gibberellin A_3 (1) in water, a highly active triene (3) is formed via gibberellenic acid (2). The triene (3) was obtained as a mixture with allogibberic acid (4) (1:2).



STUDIES ON STRUCTURE AND SYNTHESIS OF ARTEANNUIN AND RELATED COMPOUND

XXII. THE REGIOSELECTIVE SYNTHESIS OF ARTEANNUIN D

ZHOU Wei-Shan* XU Shi-Jie and ZHANG Lian
Shanghai Institute of Organic Chemistry, Academia Sinica
345 Lingling Lu, Shanghai, China

Arteannuin D (1) coexists with arteannuin (2), which is an antimalarial principal, in Chinese herbal medicine, Aetemisia annua. L. In this paper we wish to report the regioselective synthesis of 1.

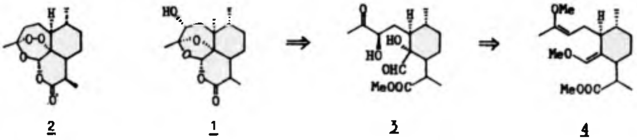
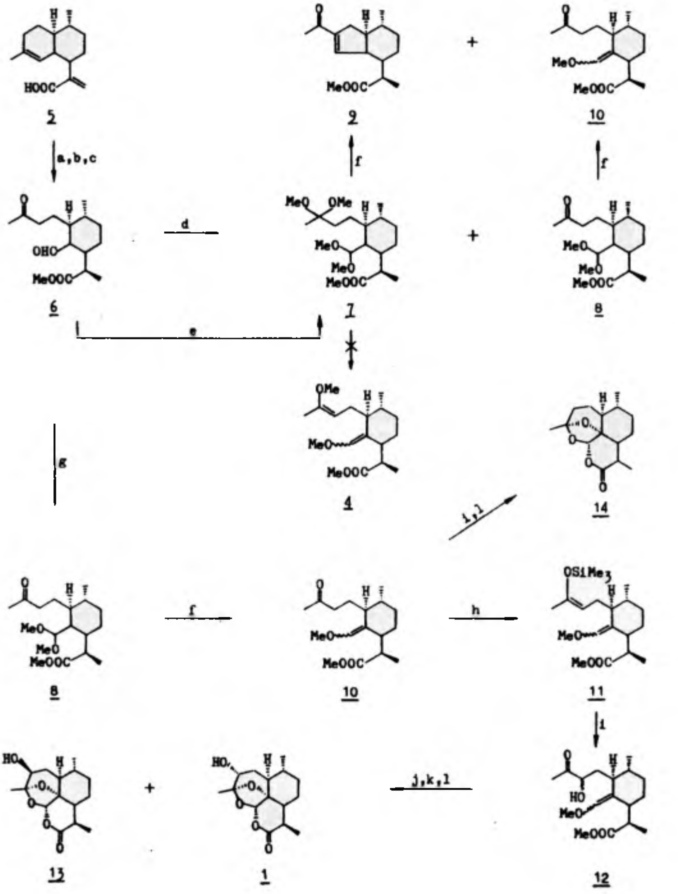


Fig. 1

The aldehyde-ketone 6 obtained from arteannuinic acid 5 was treated with 1 eq. trimethyl orthoformate in methanol in the presence of a catalytic amount of p-TsOH to provide 7 and 8 in 86% yield in the ratio of 1 to 1, and with 2 eq. of the orthoformate in the same condition to give only 7 in the yield of 88%. However, pyrolysis of 7 in xyiene did not give the intermediate 4 , but gave 9 and 10 in the yields of 34% and 30%, respectively. Similarly, pyrolysis of 8 gave 10 in 60% yield.

We turn to synthesize 1 by using enol-silyl ether 11 as a key intermediate obtained from 6 through the following sequence of reactions: 6→8→10→11. Trimethylsilyl enol ether 11 was hydroxylated with N-methyl morpholine N-oxide (NMMO) and a catalytic amount of OsO_4 to give the C_3-OH product 12 regioselectively in an overall yield of 52% in two steps. After protection of C_3-OH of 12 by acetylation it was hydroxylated with a stoichiometric amount of OsO_4 followed by cyclization with 10% potassium carbonate to give a mixture of arteannuin D (1) and its C_3-OH isomer 13 in 59% yield in a retio of 3:2, which after column chromatography gave arteannuin D (1), m.p. 190-192 °C, whose spectral data were identical with those reported in literature. 10 on hydroxylation with a catalytic amount of OsO_4 and NMMO followed by treatment with 10% K_2CO_3 gave the deoxyarteannuin 14.

Scheme



Reagents: a, CH_2N_2; b, $NaBH_4$, $NiCl_2\cdot 6H_2O$; c, O_3, Me_2S; d, 1 eq. $HC(OMe)_3$, MeOH, p-TsOH;
e, 2 eq. $HC(OMe)_3$, MeOH, p-TsOH; f, Xylene, p-TsOH, Δ; g, 1 eq. $HC(OMe)_3$, 1% HCl;
h, Me_3SiI, $(Me_3Si)_2NH$; i, NMMO, cat OsO_4; j, Ac_2O/Py; k, OsO_4; l, 10% K_2CO_3

INDEX OF AUTHORS

SUPPLEMENTARY ABSTRACTS

BIOLOGICAL ACTIVE ISOPRENOIDS ISOLATED RECENTLY FROM MEXICAN MEDICINAL PLANTS.

X.A. Domínguez.

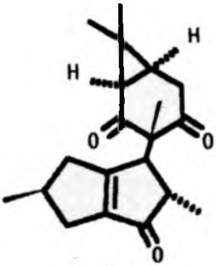
Laboratorio de Fitoquímica, Departamento de Quimica, ITESM
Sucursal de Correos "J" Monterrey, N. L. C.P. 64849 MEXICO

Mexican native flora has more than 20,000 species of Fanerogams. For more than three thousand years the different Indian nations that lived in Mexico accumulated a wide knowledge on the most common diseases and the most adequate plants to cure them. Their knowledge survived the Spanish Conquest and the destruction of most of their scholars and codices. Since their first arrival to Mexico, the Spaniards were astounded by the great number of medicinal plants sold in Technochtitlan Markets and the great ability of their physicians to cure their sick people. Even Hernan Cortez recommended to the Emperor Charles V to substitute his court physicians by Aztec ones. Between 1547 to 1585, the Spanish frair. Bernardino de Sahagun wrote his "General History of the Things of New Spain", one of the three best sources of information about the Aztecs knowledge of bioactive plants and the diseases healed with them. The second XVI century source is the Martin Cruz-Juan Badianus, two Xochimilca Indians "Libellus de Medicinalibus Indorum Herbs" a beautiful pictured codex dated 1552. The third source was the book written in 1570-1575 by Francisco Hernández, personal physician to the king Philip II of Spain, who on his orders, personally collected medicinal plants and information on their uses, all around central Mexico.

Those books and the oral tradition on mexican medicinal plants, still available in the indigen towns and in the folk names for them, has given to mexican and foreign scientists the clues to look for their bioactive compounds. A good case of the above, is the excellent Aztec knowledge on the activity of Montanoa tomentosa infusions as abortive and as an oxytocic, calling the plant "Cihuapathli" from "cihua" woman and "pathtli", medicine. Recent work on the water extracts of this plant yielded two new diterpenols, zoapatanol and montanol, both abortives and oxytocics.

Using those XVI century books as a guide, we have studied several dozens of mexican medicinal plants. Among them the "gualulo" Jatropha dioica var. sessiliflora. From which several years ago, we isolated a new diterpentrione, riolozatrione (I) with a new ring system, the riolozane.

Further studies of this plant, yielded us two other bioactive compounds; the known jatropholone-A (II) and the new one, 3,4-epoxyjatrophatrione-7,12,14 (III) whose structure was elucidated on basis of its chemical and spectroscopic behavior, particularly, ^{1}H and ^{13}C-NMR mono and bidimensional, to be discussed[4].



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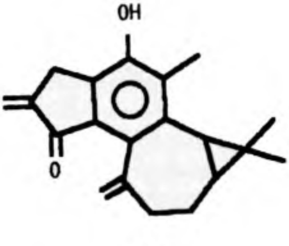

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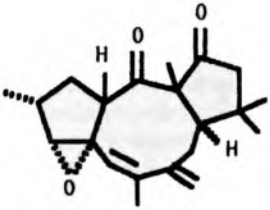
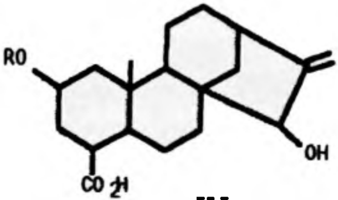


III

The hiedpele (Drymaria arenaroides) a medicinal and toxic plant, contains as bioactive principles glucosides of an ent-kaurene nor-terpenoid (IV)[5]. Its structure elucidation and also the structure of other isoprenoids isolated from two other mexican folk medicinal plants will be discussed.



IV b R = glc Nb_glc^1 - ^{2}glc

IV a R = glc.

1.- Levine and 27 collaborators; J. Am. Chem. Soc. 101, 3404 (1979).
2.- Dominguez, Cano, Franco, Villarreal, Watson and Zabel, Phytochemistry, 19, 2478 (1980)
3.- Purushothaman and Chandrasekharan, Tetrahedron Lett, 979 (1979).
4.- Dominguez, Villarreal, Howard, Jakupovic, Scott, Sánchez, paper submitted for publication.
5.- Vargas, Dominguez, Acuña, Hostettmann, paper submitted for publication.

The economical help from CONACYT Mexico research grant PCECBNA-031053 is acknowledged.

STRUCTURE AND CHEMISTRY OF SESQUITERPENE LACTONES FROM HELIANTHEAE (ASTERACEAE)

Nikolaus H. Fischer and Francisco A. Macias
Department of Chemistry
Louisiana State University
Baton Rouge, LA 70803, U.S.A.

Recent phytochemical studies of members of the tribe Heliantheae (Asteraceae) will be presented. Chemical analysis of Lecocarpus darwinii, L. lecocarpoides and L. pinnatifidus, all endemics of the Galapagos Islands (Ecuador), provided melampolides which are structurally very similar to sesquiterpene lactones found in the genus Acanthospermum of the subtribe Melampodiinae. The structures of the new sesquiterpene lactones were elucidated by high field ^1H NMR, ^{13}C NMR and 2D-correlations. The taxonomic significance of the chemical findings of the three rare Lecocarpus species will also be discussed.

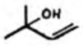
PHEROMONES AND RELATED CHEMICAL SIGNALS OF ISOPRENOID NATURE — SYNTHESES AND STRUCTURE/ACTIVITY RELATIONSHIPS

Torbjörn Norin

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

Dedicated to Professor Holger Erdtman on his 85th birthday.

2-Methyl-3-buten-2-ol (**1**), *cis*-verbenol (**2**) and ipsdienol (**3**) are important isoprenoid constituents of the aggregation pheromone of the spruce bark beetle (*Ips typographus*, Coleoptera: Scolytidae). Synthetic aspects and molecular features of the biological action of these pheromone constituents will be discussed. Similar studies on the pheromone constituents, *e.g.* (2*S*, 3*S*, 7*S*)-diprinyl acetate (**4**), of the pine saw-fly (*Neodiprion sertifer*, Hymenoptera) will be presented. These studies demonstrate the importance of synthetic strategies which provide products of very high isomeric and enantiomeric purity. Strategies, which offer the possibility to tailor structurally related compounds are also of importance for investigations on structure/activity relationships in pheromone research.



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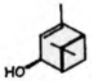

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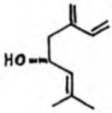

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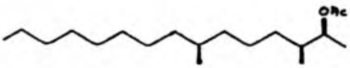
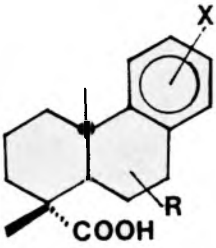


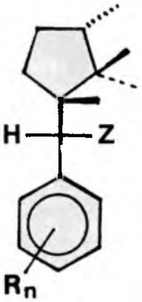
4

Günther SNATZKE: Applications of CD to the Structure Elucidation of Isoprenoidal Natural Products.

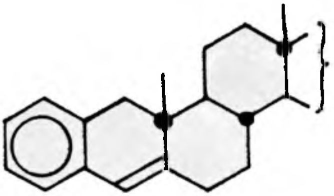
Abstract

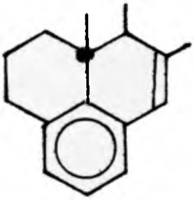
With D. Cambie, K. Netzke, and J. Schulte: The CD of the benzene chromophore depends strongly on the substitution pattern of the aromatic system. This is shown with examples derived from mono- and diterpenoids. Mere replacement of a methyl group by the neopentyl moiety can change the sign of the CD within the -band!



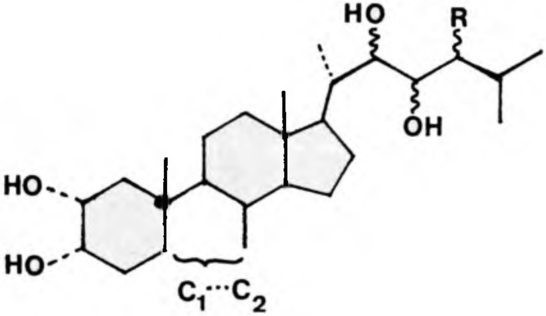


With G. Hoffmann, J. Schulte, and P. Pant: Several steroidal styrenes with rigid structure have been prepared and it could be shown, that CRABBE's original rule for the inherently twisted styrene chromophore has to be inverted.

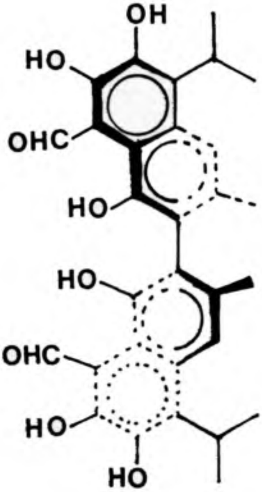




With N. Ikekawa: From the CD of the in-situ complexes of bis-glycols of brassicasterol type the stereochemistry of both glycols can be determined even in presence of keto groups.



With Hung L.: By application of the exciton theory to gossypol it was found that the (+)-enantiomer has P-configuration.



NEW METHODS IN ECDYSTEROID SYNTHESIS

Peter Welzel[a], Udo Hedtmann[a], Kurt Hobert[a], and Zenka Milkova[b]

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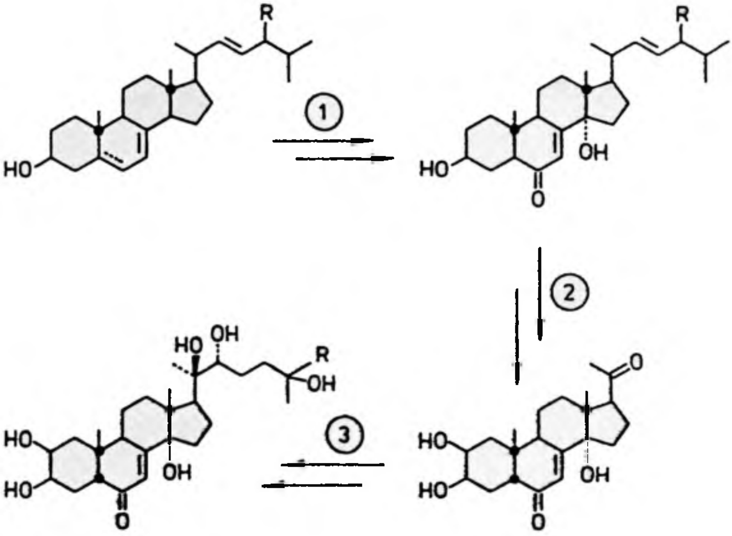
Postfach 102148, D-4630 Bochum (FRG)

[b] Bulgarian Academy of Sciences, Institute of Organic Chemistry
1113 Sofia (Bulgaria)

Results obtained on the basis of the synthetic plan shown below will be described.



THE NUMBERING OF REGULAR TERPENES: AN APPEAL FOR A UNIFIED SYSTEM

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Adoption of a unified system for the numbering of regular terpenes is proposed to avoid literature ambiguity or contradiction, as shown by selected examples.

DISTINCTION BETWEEN Z and E ISOMERS OF UNSATURATED ACETATES BY CHEMICAL IONIZATION

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There is a constant interest in mass spectrometric analysis of long chain unsaturated esters, acetates and related compounds. This is partly due to the need of structure identification of insect pheromones.

Z and E isomers of long chain unsaturated acetates - the pheromone components of Lepidopteras - have been studied by isobutane chemical ionization. Though both $[M-H]^+$ and adduct $[M+X]^+$ ions $[X(m/z) = 39,43,57]$ are minor peaks in the spectra their abundance ratio is characteristically higher for the Z than for E isomers, therefore the isomer pair can be distinguished and identified by mass spectrometry alone.

This method is interesting not only for mass spectrometrist but also for pheromone research. The method is straightforward does not require special instrumentation, sample derivatization or purification and can be coupled to GC.

SYNTHESIS OF HIGHLY UNSATURATED INSECT PHEROMONES

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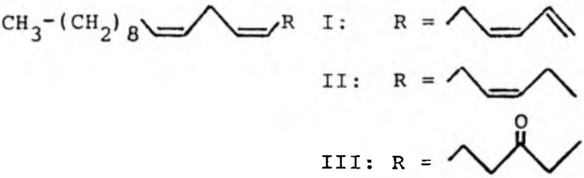
We elaborated a simple, stereocontrolled route for the synthesis of polyene type compounds, wich are pheromone components of geometrid moth, e.g. "*Operophtera brumata*" (I), "*Boarmia selenaria*" (II), "*Boarmia rhomboidaria*" (III).



We synthetized these pheromones from derivatives of 2-butyn-1,4-diol *via* acetylenic compounds, using a stereocontrolled reduction of triple bonds.

$$R''O\text{-}CH_2\text{-}C{\equiv}C\text{-}CH_2\text{-}X \xrightarrow{R'\text{-}C{\equiv}CH} R''O\text{-}CH_2\text{-}C{\equiv}C\text{-}CH_2\text{-}C{\equiv}C\text{-}R' \longrightarrow$$

$$\xrightarrow{R'''\text{-}Z} R'''\text{-}CH_2C{\equiv}C\text{-}CH_2\text{-}C{\equiv}C\text{-}R' \longrightarrow I,\ II,\ III$$

STEREOSTRUCTURES OF NATIVE COMPOUNDS RELATED TO 2β-ANGELOYLOXY-8α-(2'-METYL)BUTYRYLOXY-10β,11α-DIACETOXYSLOV-3-ENOLIDE (ARCHANGELOLIDE)

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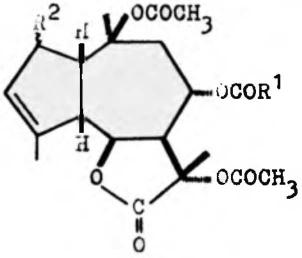
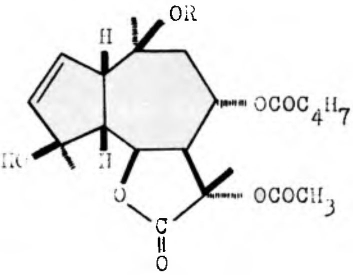
Stereostructures of the four sesquiterpene lactones 2β-angeloyloxy-8α-(2'-metyl)butyryloxy-10β,11α-diacetoxyslov-3-enolide (archangelolide; I), 2α-hydroxy-8α-angeloyloxy-10β,11α-diacetoxyslov-3-enolide (II), 4β-hydroxy-8α-angeloyloxy-10β,11α-diacetoxyslov-2-enolide (III) and 4β,10β-dihydroxy-8α-angeloyloxy-11α-acetoxyslov-2-enolide (IV) isolated from species of Umbelliferae family[1-3] were established on the basis of a detailed study of the ^{1}H-NMR spectra, CD spectra and chemical correlation with 3α-angeloyloxy-10β,11α-diacetoxyslov-3-enolide (V)[4]. The products of hydrogenation and hydrogenolysis of substances mentioned were studied.



I : $R^1 = C_4H_9$;
$R^2 = \beta\text{-}OCOC_4H_7$
II: $R^1 = C_4H_7$; $R^2 = \alpha\text{-}OH$
V : $R^1 = C_4H_7$; $R^2 = H$



III: R = $COCH_3$

IV: R = OH

References

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2. Smítalová Z., Buděšínský M., Šaman D., Vašíčková S., Holub M.: Collect. Czech. Chem. Commun. 49, 852 (1984).
3. Smítalová Z., Buděšínský M., Šaman D., Holub M.: Collect. Czech. Chem. Commun. 51, 1323 (1986).
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COMPARISON OF BETULINIC ACID PRODUCTION IN VITRO IN AGROBACTERIUM INDUCED TUMOURS AND CALLUS CULTURES OF SOLANUM AVICULARE FORST.

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In order to improve the ability of plant cells to produce secondary metabolites in vitro the possibility of increasing the level of their differentiation was studied. Tumour cells of "Crown Gall" or "Hairy Root" type are obtained after transformation induced by Agrobacterium tumefaciens and Agrobacterium rhizogenes, respectively.

A large set of tumour cultures induced by 5 different bacterial mutants (shooter, rooter, wild type etc.) from Solanum aviculare Forst. was analysed in order to compare the effect of plasmid genes coding for auxin and cytokinine on the secondary metabolic pathways. In the case of the above mentioned model species we earlier investigated in nearly 200 callus cultures the levels of accumulation of steroidal glycoalkaloids of solasodine (normally present in native plant) and of the triterpenic betulinic acid (not found in native plant). Now we are studying the accumulation of these secondary metabolites in amorphous and differentiating tumour cultures and comparing it with that in callus cultures derived from the same plant species.

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SUPPLEMENT

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