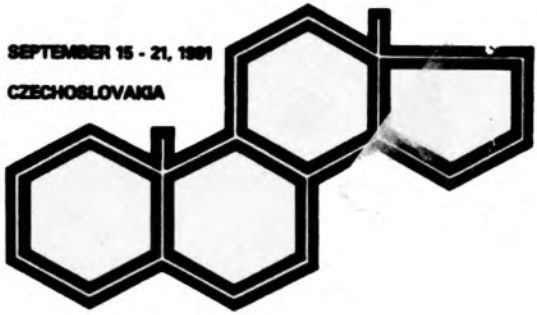
14th CONFERENCE ON ISOPRENOIDS



ABSTRACTS OF PAPERS

INSTITUTE OF ORGANIC CHEMISTRY
AND BIOCHEMISTRY
CZECHOSLOVAK ACADEMY OF SCIENCES
1991

14th CONFERENCE ON ISOPRENOIDS

Abstracts of Papers

1991

Pavel Drašar, Ivan Černý, editors

Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences

Praha

1991

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Abstracts of Plenary Lectures

RECENT ADVANCES IN THE FIELD OF TRITERPENES FROM ARALIACEAE

G. Adam[1], T. V. Sung[2], W. Steglich[3]
[1] Institute of Plant Biochemistry Halle/S., F.R.G; [2]Institute of Natural Products Chemistry, National Research Centre of SRV, Hanoi, Vietnam; [3]Institute of Organic Chemistry and Biochemistry, University Bonn, F.R.G.

Our earlier studies on the triterpenoid constituents of the Araliaceae Acanthopanax trifoliatus and Schefflera octophylla, used in East Asia as drugs in the folk medicine, have led to a series of new lupane-type triterpenes [1]. In continuation of this studies we investigated the glycoside pattern of Schefflera octophylla leading to the isolation and structural elucidation of six new triterpene glycosides of the lupane and ursane series, respectively, all bearing a sugar side-chain moiety at postion 28. Two of them were shown to be bisdesmosidic triterpene saponins with sugar chains at positons 3 and 28. Remarkable is also the detection of a new sulphated triterpene glycoside in this plant. The structural elucidation of this glycosides and further constituents on the basis of spectroscopic data, especially 2D NMR experiments, as well as chemical transformations will be discussed.

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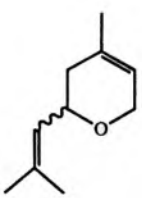
2. T. V. Sung, W. Steglich, G. Adam, Phytochemistry in press.

STRUCTURAL STUDIES BY NMR.

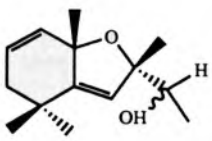
Ulla Jacobsson
Department of Organic Chemistry
Royal Institute of Technology
S–100 44 Stockholm, Sweden

The developments of NMR magnets (60 → 600 MHz), electronics and software have provided a remarkable creation of new and sophisticated NMR techniques during the last decade. Computer-controlled pulse sequences have resulted in a wealth of ingenious procedures – well hidden behind smart acronyms.

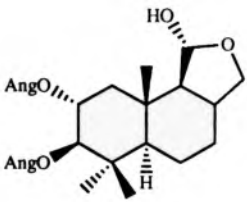
Useful and successful experiments from our own research will be illustrated through some examples, *e.g.*



Neroloxide
Neuroleon nostras



Actinidol
Ipomoea pes-caprae



Polygodin A
Polygonum glabrum

STEREOELECTRONIC EFFECTS IN MEDIUM-SIZE RING ISOPRENOIDS: NEW REARRANGEMENTS OF THE GERMACRANE SKELETON.

Giovanni Appendino

Dipartimento di Scienza e Tecnologia del Farmaco, C.so Raffaello 31, I-10125 Torino (Italy).

Germacrane derivatives represent one of the most abundant classes of sesquiterpenes. Their cyclodecane skeleton is biogenetically derivable from the simple intramolecular cyclization of farnesyl-PP; therefore these compounds also represent one of the most elementar classes of sesquiterpenes.

The skeletal rearrangements of germacranes afford compounds of the eudesmane-, guaiane- and elemane-type. These rearrangements require acid catalysis or pyrolytic conditions. Detailed studies of these reactions confirmed the biogenetic relevance of these reactions.

As part of an investigation on stereoelectronic effects in medium-size ring isoprenoids (1, 2), we observed some new rearrangements of the germacrane skeleton involving, besides the carbocyclic ring, also the isopropyl side-chain.

A new series of radical and photochemical rearrangements is also presented, discussing mechanism, stereoelectronic requirements and biogenetic relevance of these reactions.

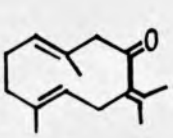
1. G. Appendino,M.G.Valle and P. Gariboldi, J. Chem. Soc., Perkin Trans. 1, 1363 (1986)
2. G. Appendino, P. Tettamanzi and P. Gariboldi, J. Chem. Soc., Perkin Trans. 1, 2139 (1990).

BIOMIMETIC TRANSFORMATIONS OF GERMACRADIENES

Elena Tsankova and Valentin Enev

Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

The present lecture describes some approaches to the biomimetic olefin cyclisation of germacradienes carried out with natural germacrone 1 and its derivatives 2-5 by treatment with a variety of electrophiles, such as $BF_3.Et_2O$, TMSO-Tf, $Hg(OAc)_2$ and $Pb(OAc)_4$. In most of the cases the transannular cyclisation proceeded highly regio- and stereoselectively yielding eudesmanes and guaianes with defined stereochemistry of the ring annelation. Some of the reactions are assumed to involve carbocation intermediates which undergo molecular rearrangement leading to the products 6-9 with new carbon skeletons. The biogenetic-type conversion of 2 to 10 was also achieved. The mechanism of the described reactions will be discussed.



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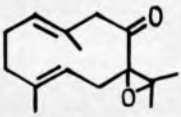

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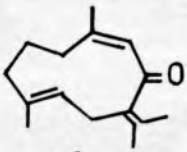

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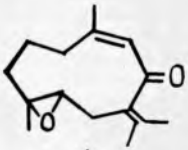

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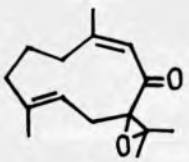

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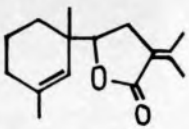

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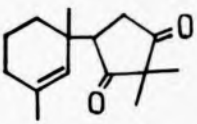

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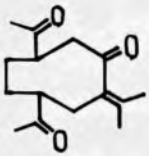

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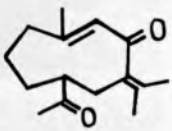

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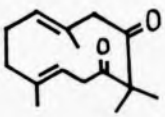


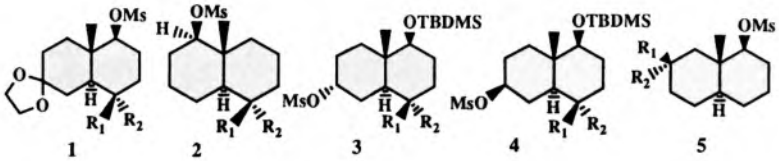
10

BASE INDUCED AND DIRECTED REACTIONS OF PERHYDRONAPHTHALENE-1,4-DIOL MONOSULFONATE ESTERS IN THE SYNTHESIS OF SESQUITERPENES.

L.H.D. Jenniskens, R.V.A. Orru, J.B.P.A. Wijnberg and Ae. de Groot
Department of Organic Chemistry,Agricultural University,
Dreijenplein 8, 6703 HB, Wageningen, The Netherlands.

It has been demonstrated that the base induced and directed rearrangement of substituted *trans* - perhydronaphthalene-1,4-diol monosulfonate estersis an effective route to *cis* - perhydro-azulene systems*. Further investigations have revealed that in apolar solvents like benzene or toluene the dissociation of sulfonate esters can be induced by an electron donating alcoholate, even when it is located at a distance of four bonds. This situation of a sulfonate leaving group and an electron donating alcoholate can be created in a perhydro-naphthalene system in several ways as shown in compounds **1-5**. It has appeared that the reactions of these compounds strongly depend on the regio- and stereochemistry of the alcoholate and mesyl groups. Sofar the following reactions have been observed.

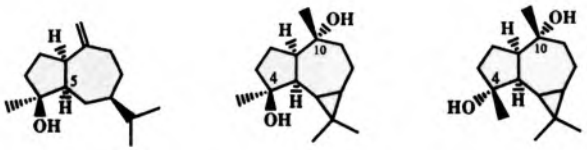
-- a rearrangement to a perhydroazulene system in **1**
-- a homo fragmentation reaction in **2**
-- a regioselective elimination in **3**
-- a homo fragmentation or a regioselective elimination in **4**
-- a rearrangement followed by fragmentation or elimination in **5**



1 **2** **3** **4** **5**

R_1=OH, R_2=CH_3 R_1=CH_3, R_2=OH

These reactions have been applied in the total syntheses of sesqui-terpenes like 5-epi nardol and allo-apoaromadendrene-4b,10a or 4a,10a-diol.



5-epinardol 4b,10a- and 4a,10a- alloaromadendane

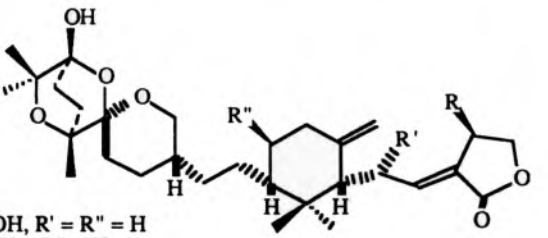
*J.B.P.A. Wijnberg, L.H.D. Jenniskens, G.A. Brunekreef and Ae. de Groot, J. Org. Chem. **55**, 941 (1990)

NEW TRITERPENES METABOLITES FROM *TRICHOLOMA SAPONACEUM*

Maria De Bernardi[a], Luigi Garlaschelli[a], Giorgio Mellerio[b], Giovanni Vidari[a] and Paola Vita-Finzi[a]
[a]Dipartimento di Chimica Organica dell'Università degli Studi, Via Taramelli 10, 27100 Pavia, Italy
[b]Centro Grandi Strumenti dell'Università degli Studi, Via Taramelli 10, 27100 Pavia, Italy

During our studies on Basidiomycetes metabolites looking for new biologically active compounds we carried out on the crude extracts antifungal, antibacterial and cytotoxic tests.[1]

Since the AcOEt extract of *Tricholoma saponaceum* showed a strong inhibition of the growing of P388 leukemia cells although no antibacterial activity, we undertook a chemical studies of this mushroom. By chromatographic methods we isolated the two main constituents that we named saponaceolide A (I)[1,2] and saponaceolide B (II)[2]. These products are responsible of the strong antitumor activity of the mushroom and show a characteristic unprecedented molecular skeleton as reported in the following formula. The molecules are constituted by thirty carbon atoms and therefore can be considered triterpenes although the assumed biosynthesis pathway involves two C_{15} units.



I R = OH, R' = R" = H
II R = R' = R" = H
III R = R' = OH, R" = H
IV R = R" = OH, R' = H

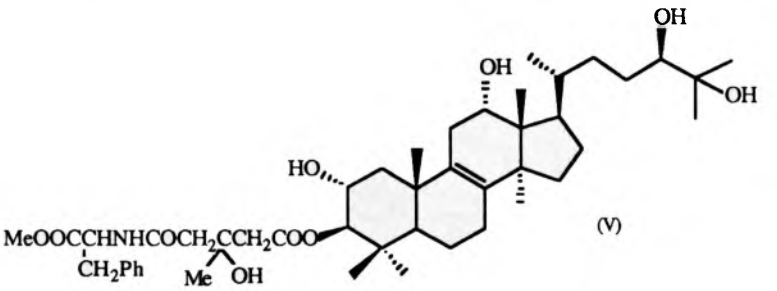
Recently other two saponaceolides C (III) and D (IV) have been isolated from the same *Tricholoma saponaceum* extract. Their structures have been elucidated by spectroscopic methods. Saponaceolide C show cytotoxic activity in the *Artemia salina* test.

The relative configuration of the secondary allylic carbinol in (III) has been established also by molecular calculation (MM2). By chemical correlation with L-erithrulose

the absolute configuration of saponaceolide A has been determined.

From the same extract, in the more polar chromatographic fractions three new depsipeptides were isolated. These compounds show a lanostane skeleton and can be considered derivatives of fasciculol B, a triterpene that we previously isolated from *Naematoloma sublateritium*.

The most characteristic feature of these triterpenes, as reported for (V), is the depsipeptide chain constituted by the amide of the 3-hydroxy,3-methylglutaric acid with aminoacids as phenylalanine and phenylserine. To our knowledge this is the first example in Nature of this kind of depsipeptides.



(V)

Interesting enough is the lacking of these triterpenes in other Tricholoma species, as for instance *Tricholoma virgatum*, whose most important and characteristic metabolites are indole derivatives.

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TOTAL SYNTHESIS OF QUASSIN. A QUEST FOR SELECTIVITY

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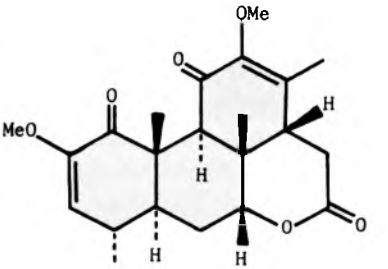
Department of Chemistry, University of New Brunswick
Bag Service #45222, Fredericton, New Brunswick, Canada E3B 6E2

The total synthesis of d,l-quassin **1** will be described. The chosen strategy consists of the establishment of a rigid framework



1

on which the desired configuration could be established at crucial C-atoms. The synthetic sequence includes an orientation reversal in a Diels-Alder addition by Lewis acid catalysts, the use of a highly selective quaternary base for HCN elimination and an unusual regioselective introduction of the two diosphenol groups of quassin. No conventional blocking group was used for any of the five (formal) carbonyl groups in the course of the synthesis.

APPLICATIONS OF DIOXIRANE OXIDATIONS IN STEROID CHEMISTRY

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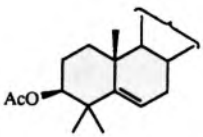
Department of Chemistry, The Unversity of Technology,
Loughborough, Leics. LE11 3TU, U.K.
K H Baggaley
SmithKline Beecham Pharmaceuticals, Brockham Park,
Betchworth, Surrey, RH3 7AJ.

The use of dioxiranes (1) in a wide variety of oxidation processes is now well known.[1,2] We have recently shown[3] that important mechanistic information may be obtained by an examination of selected dioxirane-mediated steroid oxidations (e.g. 2→3). These and further results in this area will be discussed.

(1)



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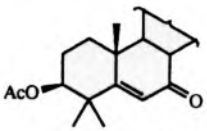

(3)

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3. B. A. Marples, J. P. Muxworthy and K. H. Baggaley, *Tetrahedron Lett.*, 1989, *32*, 533.

THE FASCINATING STEROID RECEPTORS

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Retired Head Organic Chemistry R&D Laboratories Organon
Floraliastraat 2, 5384 GP Heesch, the Netherlands

Most of the biological actions of the steroids are mediated by intracellular receptors regulating gene expression. For that reason, medicinal chemists have tried, even at times when little was known about these proteins, to develope models of these receptors to generate ideas for new interesting steroids and to rationalize structure-activity relations.

In the 1960's, steroid chemists assumed that only a part of the steroid molecule interacted with the receptor and discussions centred upon the exact location of the interacting site. Was it the α-face or the β-face, ring A or ring D ? Interesting examples of these discussions can be found in the book "Mechanism of action of the steroid hormones" edited by C.A.Villee and L.L. Engel, Pergamon 1961, and in later reviews.

Further research demonstrated that the binding of a steroid agonist induces a series of conformational changes of the receptor protein. As a result of these changes, the steroid becomes surrounded by the receptor. This model made it possible to rationalize many confusing data but it proved difficult to explain the action of steroid antagonists. However, all steroid antagonists, known at that time, were in effect partial agonists so it was assumed that this was characteristic for the steroids. True steroid antagonists were developed later.

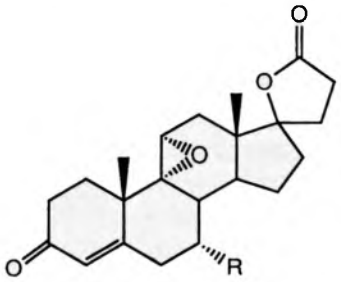
In recent years, the rapid development of molecular biology produced a wealth of interesting and detailed information on the structure and function of these steroid receptors. This helped to explain the action of steroid antagonists. Many further questions remain, but already now the available knowledge provides the synthetic chemists with a number of interesting working hypotheses which can be tested. This may lead to novel steroid drugs.

SEARCH FOR SELECTIVE ALDOSTERONE ANTAGONISTS. EFFECT OF CONFORMATION ON RECEPTOR BINDING

Jaroslav Kalvoda, Urs Joss, Jürgen Grob, Michel Biollaz, Steven Whitebread and Peter Wieland

Pharmaceuticals Division, Ciba-Geigy Ltd., CH-4002 Basel, Switzerland

The overall conformation of the steroid molecule has been altered by the introduction of additional double bonds and/or epoxides in various positions of the skeleton, and the effect of these changes on binding to aldosterone and sex-hormone receptors has been studied. A unique discriminatory influence was exerted by an epoxy function in 9α,11 position, permitting the synthesis of highly selective aldosterone antagonists of type **1**.



1a R= $COOCH_3$ (CGP 30 083)
1b R= $SCOCH_3$ (CGP 33 033)

SELECTED ECOLOGICALLY RELEVANT MOLECULES FROM MEDITERRANEAN OPISTHOBRANCHS

Guido Cimino, Vincenzo Di Marzo, Angelo Fontana, Margherita Gavagnin, Aldo Spinella and Rosa Rita Vardaro
Istituto per la Chimica di Molecole di Interesse Biologico del CNR, Via Toiano n. 6, 80072 Arco Felice, Napoli, Italia

Many defensive allomones have been characterized from opisthobranch molluscs living in different geographical areas [1-3]. In this communication we will present results recently obtained studying population of opisthobranchs from Italian and Iberian coasts. The studies have been directed to clarify: 1) the chemical structure of potential allomones; 2) their anatomical distribution in the molluscs; 3) their origin; 4) their biological functions.

It has been observed that the defensive molecules can be obtained either by diet upon other invertebrates or by *de novo* biosynthesis. In both cases many molluscs are able to transfer the toxic allomones in protected sections of their mantle. Very often the biosynthetic pathways display multifunctional roles leading to related compounds selectively distributed in the tissues of the animals and exhibiting specific biological activities.

1) Faulkner D. J., Nat. Prod. Report **7**, 269 and previous reports.

2) Karuso P. In "Biorganic Marine Chemistry" ed.Springer-Verlag, Berlin-Heidelberg 1987, pp.31-60.

3) Cimino G. and Sodano G. Chemical Scirpta **29**, 289, 1989.

TRANSFORMATION OF HAJOS - PARISH ENEDION INTO A - FRAGMENT OF PRECURSOR OF VITAMIN D_3

Andrzej R. Daniewski and Wanda Wojciechowska

Institute of Organic Chemistry Polish Academy of Sciences

01 - 224 Warsaw, Kasprzaka 44/52

A new approach to A - fragment of precursor of vit. D_3 **2** starting from Hajos - Parish enedione **1** will be presented.

1 **2**

SEPARATION OF THE TOAD POISON BUFADIENOLID BY SEPHADEX LH-20

Yoshiaki KAMANO* and Machiko TOZAWA**

*Department of Biological Sciences, School of Science, Kanagawa University, No. 2946 Tsuchiya, Hiratsuka, Kanagawa, 259-12, JAPAN

**Department of Chemistry, The Jikei University, School of Medicine, 8-3-1 Kokuryo, Chofu, Tokyo, 182, JAPAN

The steroidal bufadienolides are distinguished by a 5-substituted 2-pyrone ring at the 17β- position. The Chinese toad venom preparation Ch'an Su (Senso) is the most useful source of bufadienolides. By the use of a variety of bufadienolides isolated from Ch'an Su, our thirty year (sice 1961) efforts provided the progress and development in the chemical[1], analytical[2] and biological[3] investigation of toad poison bufadienolides.

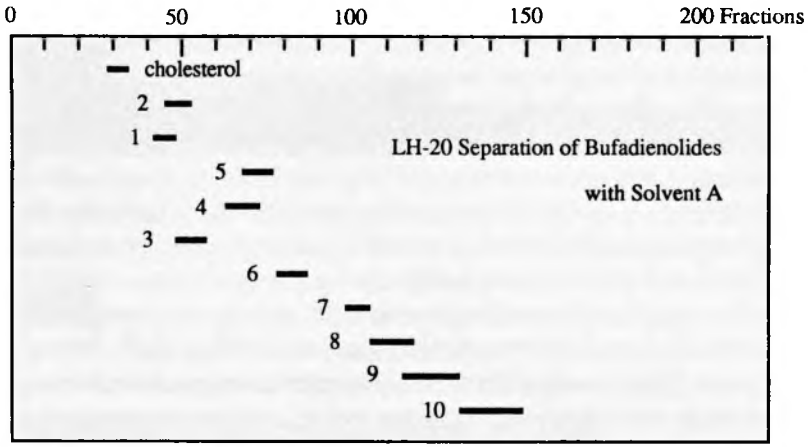
Recently we found that isolation of bufadienolides from Ch'an Su by column chromatography on Sephadex LH-20 was much more better than the case of use of silica gel. The result led us to do the systematic examination on separation of bufadienolides by use of sephadex LH-20.

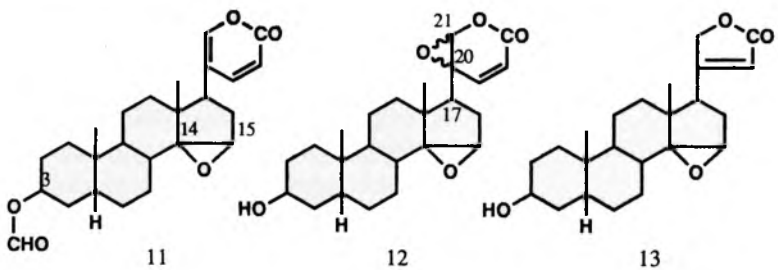
As the samples, the major 10 bufadienolides; cinobufagin(1), resibufogenin(2), cinobufotalin(3), bufotalin(4), bufalin(5), telocinobufagin(6), desacetylcinobufagin(7), desacetylbufotalin(8), gamabufotalin(9) and desacetylcinobufotalin(10) were chosen. To the bufadienolide mixture, cholesterol was added as a standard compound. The column of 2.2cmφx48cm or 2.5cmφx67cm was used. As solvent for developement, the following four solvents were selected after some examination; (A) n-hexane-CH_2Cl_2-CH_3OH (4:5:1), (B) n-hexane-EtOAc-CH_3OH (4:5:1), (C) n-hexane-toluene-CH_3OH (3:2:1), and (D) n-hexane-CH_2Cl_2-acetone (4:3:3).

The chromatography have been done quickly by the simple method. Each separation was excellent. All compounds could be separated perfectly by use of combination of four solvents (as an example, separation with solvent A was figured). Extended separation of many bufadienolide derivatives including cardenolide provided the similar good result. Based on these results, the relationship between structure and chromatographic elution was discussed, and the order of elution was summarized. (a) bufadienolide>cardenolide, (b) 5β–H > 5α–H, (c) 14β–H > 14α–H (epoxide is same, too), (d) 19-CH_3 > 19-CHO, (e) 3-OAc > 3-CO > 3β–OH > 3α–OH, (f) suberate > succinate, (g) 14β–OH,15α–Cl > 14β–Cl,15α–OH, (h) 16β-O-ester > 3β-O-ester, (i) 5β–OH > 16β–OH > 11α–OH, (j) 3-CO > Δ^4-3-CO > $\Delta^{1,4}$-3-CO > 3β–OH.

A summary of these results will be outlined, in addition to identification of interesting compounds such as resibufogenin 3-formate (11)(mp. 226-228°C), 20,21-epoxyresibufogenin (12)(mp. 126-128°C) and 14,15β-epoxy-14-deoxy-digitoxigenin (13)(mp. 230-233°C) were isolated from Ch'an Su.

Finally, the benefit of separation by sephadex LH-20 may be discussed.





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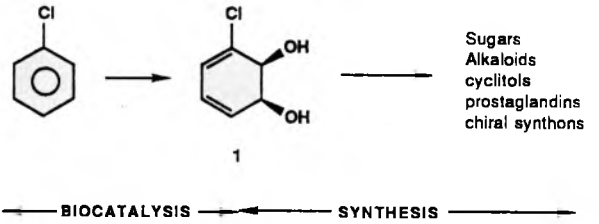
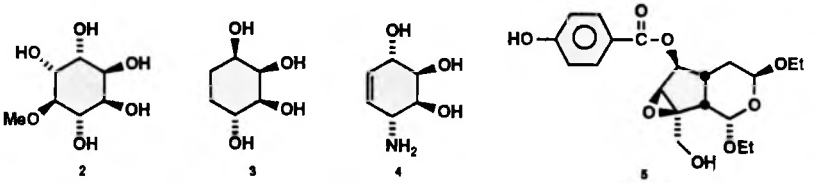
BIOCATALYSIS, SYMMETRY, AND STRAIN IN THE SYNTHESIS OF OXYGENATED COMPOUNDS: PINITOL, SPECIONIN, AND OTHER NATURAL PRODUCTS

T. Hudlicky, T. Tsunoda, F. Rulin, M. Natchus, H. Luna, H. Olivo.

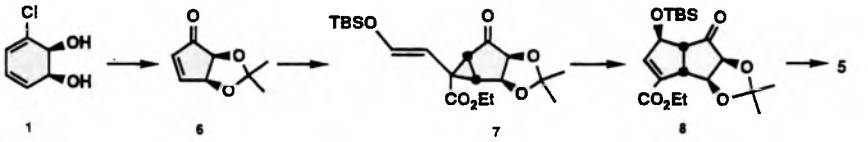
Microbial degradation of halogenated aromatic compounds provides convenient chiral synthons such as **1** in preparatively useful amounts and in >99% ee.



The diols such as **1** may be efficiently transformed to a wide array of complex natural products in completely stereo- and enantiocontrolled manner. The total synthesis of (+)- and (-)-Pinitol **2**, several cyclitols such as **3** and **4**, and the antifeedant monoterpene specionin **5** will be presented.



The guiding principles for the synthesis of **2**, **3**, and **4** and their enantiomers are considerations of latent symmetry in the synthetic intermediates and exploitation of efficient synthetic transformations leading to enantiodivergent preparation of these targets. In the synthesis of **5** a low-temperature vinylcyclopropane rearrangement is utilized to take advantage of strain as a driving force.



The details of the synthesis of **6** from **1**, and the generation and rearrangement of **7** to **8**, en route to specionin **5** will be disclosed.

The environmental aspects of this methodology in the context of cost-effective disposal of chlorinated aromatic waste by biocatalysis will also be presented.

RECENT STRATEGIES FOR THE CONVERSION OF DESOXYCHOLIC ACID INTO CORTICOIDS

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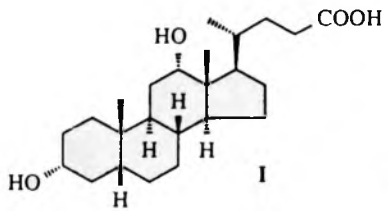
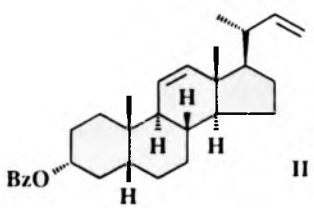
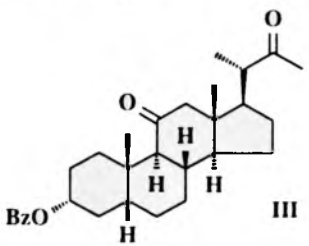
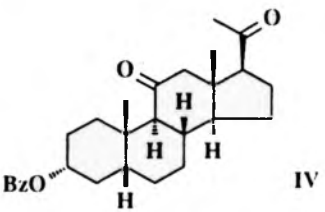
One of the historical routes for industrial access to corticoids is based on the process developed by American Merck Company [Sarrett & Kendall] beginning with desoxycholic acid. Using the same starting material, we embarked on some improvements to that multistep scheme.









*First desoxycholic acid (**I**) is transformed into the relay diene **II**, which subsequently on the action of PDC and iodine simultaneously is functionalized to the dicetone **III** in 87 % yield. The latter, after selectively having formed a single regio- and stereoisomeric enolacetate, on treatment with ozone releases compound **IV**, a well known intermediate of the Sarrett and Kendall sequence in nine steps, only.*

ENANTIOSELECTIVE TERPENE SYNTHESIS ——— PINTHUNAMIDE AND STYPOLDIONE

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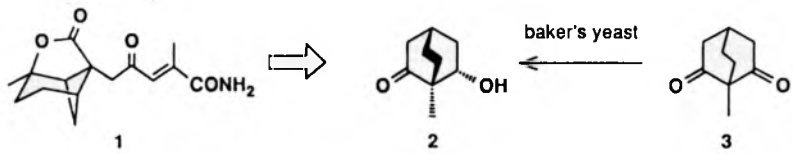
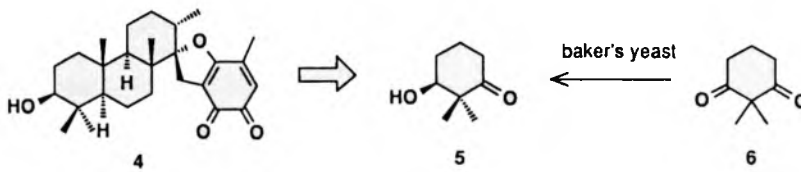
Pinthunamide(**1**) is a tricyclic sesquiterpene amide produced by a fungus, *Ampulliferina* sp., and accelerates the root growth of lettuce seedlings by 150% at a dose of 300 mg/l.[1] We synthesized **1** by starting from a bridged ketol **2**, which was prepared by reducing diketone **3** with baker's yeast.[2]



1 2 3

Stypoldione(**4**) is an ichthyotoxic and cytotoxic diterpene with a spiro-*o*-benzoquinonefuran C_7 unit isolated from a brown alga, *Stypopodium zonale*.[3] We synthesized **4** by starting from a ketol **5**, which was prepared by reducing diketone **6** with baker's yeast.[4]



4 5 6

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UNUSUAL ECDYSTEROIDS IN THE MOLTING OF CRAYFISH AND PLANTHOPPERS

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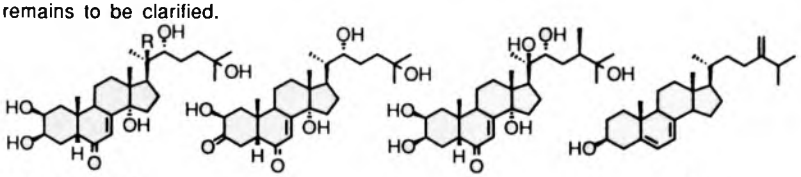
The active and most commonly occurring molting hormone is 20-hydroxyecdysone (**1**, R=OH) derived from ecdysone (**1**, R=H). It is also currently accepted that ecdysteroids other than 20-hydroxyecdysone function as molting hormones during the developing life stages of *Arthropoda*.

3-Dehydroecdysone. Large quantities of the ecdysteoid 3-dehydroecdysone (**2**) rather than ecdysone were found to be biosynthesized in the Y-organs *in vitro*, molting glands in crayfish, *Procambarus clarkii*. The compound **2** was characterized by immunological and spectroscopic methods. In the present *in vitro* experiments, **2** was neither the descendant nor the precursor of ecdysone. Molting has been correlated with distinct peaks of 20-hydroxyecdysone in the hemolymph, even when ecdysone biosynthesis in the Y-organs was not active and **2** was the only distinct product. Although the physiological role of **2** in molting is yet unclear, the ketoreductase activity is assumed to be involved.

Makisterone A. A phytoecdysteroid makisterone A (**3**) is the only known insect molting hormone not synthesized from cholesterol. The presence of **3** in some *Hemiptera* and *Hymenoptera* insects was found and shown the evidence, that certain insects could utilize dietary C_{28} phytosterols as precursors for their molting hormone, without conversion to cholesterol (Kaplanis et al. 1975). We found that ergosta-5,7,24(28)-trien-3β-ol (**4**) met the sterol requirment of some *Homoptera* insects, the planthoppers (*Nilaparvata lugens* Stal and *Laodelphax striatellus* Fallen), which associate with the intracellular yeastlike symbiotes. The compound **4** was provided from their symbiotes and utilized as the precursor for the host's major molting hormone **3**. The determination of true molting hormone activity, that is implicated in other ecdysteroids, is difficult and remains to be clarified.



(**1**) R=H or OH (**2**) (**3**) (**4**)

GUAIANOLIDES FROM CREPIS SP.

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Department of Phytochemistry, 31-343 Kraków, Poland

The genus Crepis belongs to the tribe Lactuceae of the Compositae family. Only a small number of plants of the tribe have been studied so far. Lactucin-like guaianolides seem to be characteristic constituents at least for ten genera. However, they are absent in plants of the genus Crepis.

From these plants new structurally related C-3 and C-8 oxygenated guaianolides and their glycosides have been isolated, among them 8-epidesacylcynaropicrin, its 3-β-D-glucopyranoside and a series of esters of the latter with rare plant acids, e.g. 3-(4-hydroxyphenyl)-lactic acid. Known sesquiterpene lactone glycosides, e.g. ixerin F, glucozaluzanin C and its 11β,13-dihydroderivative, have been also identified. All the compounds can be derived from zaluzanin C. They frequently have C-8 β- or C-9 α-hydroxyl groups.

Members of this series of guaianolides occur in the three other genera of the tribe: Andryala, Ixeris and Prenanthes. The genera are all characterized by the presence of 8-epidesacylcynaropicrin or its glucopyranoside and the lack of lactucin-like guaianolides.

These results may be of chemotaxonomic significance, although much more work has to be done on the Lactuceae.

SOME BIOGENETIC-TYPE TRANSFORMATIONS OF SESQUITERPENE LACTONES

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A variety of sesquiterpene lactones have been prepared *via* transannular cyclizations of *trans*,*trans*-1(10),4-germacradienolides (or their monoepoxides), which create sigma bonds regio- and stereospecifically (1,2). Although accumulated results permit the generalization that these reactions require a chair-like transition states, only few reports on transannular reactions of the geometric isomers of germacrolides exist.

Some biogenetic-type rearrangements of germacrolides performed in our laboratory, and acid induced transformations of the heliangolide 15-hydroxy-acetylleptocarpin (3) and the melampolide schkuhriolide, will be presented. These acid catalyzed reactions yielded products of functional groups transformations, rearrangements and transannular cyclizations, and the course of the reactions are dependent on the reaction conditions. No evidence was obtained of direct C(1)C(10)-C(4)C(5) transannular interaction of the above mentioned sesquiterpene lactones.

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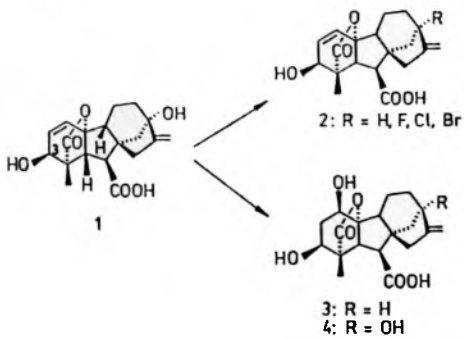
Abstracts of Short and Poster Communications

NEW SYNTHETIC PATHWAYS TO 13-DEOXYGENATED GIBBERELLIN PHYTOHORMONES GA_7 AND GA_{54} AS WELL AS 13-HALOGENATED ANALOGS

Brunhilde Voigt and Günter Adam
Institute of Plant Biochemistry, Halle/S., O-4050, FRG

From the hirtherto known 79 native gibberellins /1/ 13-deoxygenated members have specific biological activity /2/ and are therefore of special interest. We report about a new 5 step synthesis of the important phytohormone GA_7. As starting material GA_3 (1) was used which is the only one member of the gibberellin family readily available in large scale via a biotechnological process. Key reaction is the synthesis of 3-acetoxy-13-chloro-GA_7-7-phenacyl ester followed by removing the 13-chloro- and the phenacyl group in one step with tri-n-butylstannane.

For biological investigations also the hirtherto unknown 13-fluoro-, -chloro- and -bromo analogs of GA_7 (2) were synthesized and their structure determined by spectroscopic data. Furthermore, a new reaction sequence to the scarce gibberellin GA_{54} (3) via GA_{55} (4) /3/ was developed.



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/2/ R.P. Pharis, S.B. Rood (Edit.), Plant Growth Seubstances 1988, Springer, Berlin-Heidelberg 1990, 604
/3/ B. Voigt, G. Adam, unpublished results

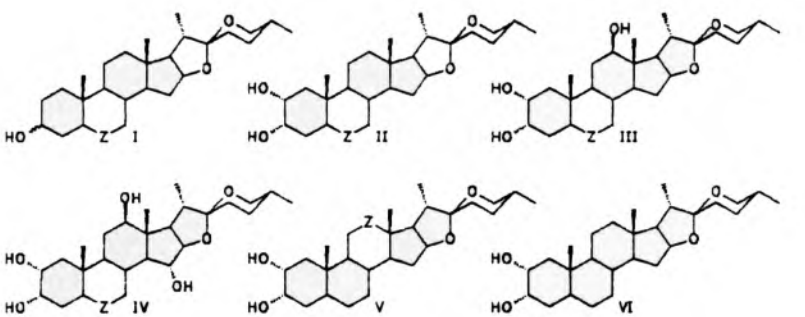
SYNTHESIS OF NEW BRASSINOSTEROID ANALOGS WITH SPIROSTAN SIDE CHAIN

V.Marquardt[1], G.Adam[1], E.Alonso[2], F.Coll[2], A.Porzel[1]

[1] Institute of Plant Biochemistry, Weinberg 3, Halle/S. O-4050, Germany
[2] University of Habana, Cuba

In regard to structure- activity relationships of brassinosteroids we were interested in the synthesis of spirostan analogs with modifications in the steroidal skeleton. The starting compounds diosgenin, isochiapagenin, bahamgenin , hecogenin and tigogenin were available by extraction of plant material of *Dioscorea* or *Solanum bahamense*, respectively, followed by chromatographic separation.

The reaction sequence included isomerization step, CrO_3 - oxydation, rearrangement procedures, hydroxylation with OsO_4 / NMMNO and Baeyer- Villiger oxidation. The synthesized analogs I - VI, (with Z= -C(=O)-; -O-C(=O)- or -(O=)C-O-) were characterized by spectroscopic methods and tested in the rice lamina inclination test, a specific assay for brassinosteroid activity.

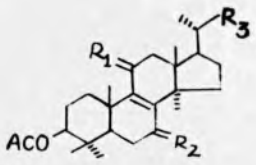


NEW TRITERPENOIDS. SYNTHESIS OF BIOLOGICALLY ACTIVE LANOSTEROL ANALOGS WITH MODIFIED SIDE-CHAIN.

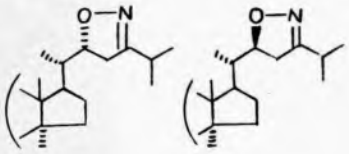
Rajesh K. Thaper, Irina G. Reshetova and Aleksey V. Kamernitsky

Zelinsky Inst. of Org. Chem., USSR Acad. of Sciences, 47-Leninsky Prospect, Moscow B-334.

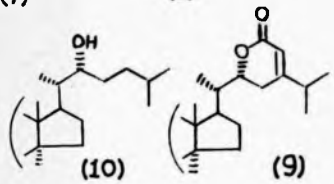
In our laboratory it was shown that additional alkyl (hydrophobic) groups present in the steroid molecule play very important role for hydrophobic bonding which dertermines the biological activity. Lanosterol, possessing three additional methyl groups and cheaply available was, therefore, choosen for chemical and biological investigation aimed at the elucidation of the role of additional methyls on the biological activity arising due to functionalisation of the molecule. In the oxidation of Δ^{24}-double bond of lanosterol by Lemieux-von Rudloff reagent we discovered the formation of keto acids (2) and (3) in addition to 24-nor acid (1). Terminal olefins (4), (5) and (6) obtained from them serve as reactive intermediates for the reconstruction of side-chain with desired functions. 1,3-dipolar cycloaddition reaction of (4) with i-Pr. nitrile-oxide gave 22R and 22S isoxazoline derivatives (7) and (8) futher transformed in two or three steps into bioligically active analogue of deoxyantheridiol (9) and antitumour agent inotodiol (10).



(1) $R_1 = R_2 = H$; $R_3 = CH_2CO_2H$
(2) $R_1 = R_2 = O$; $R_3 = CH_2CO_2H$
(3) $R_1 = H$; $R_2 = O$; $R_3 = CH_2CO_2H$
(4) $R_1 = R_2 = H$; $R_3 = CH{=}CH_2$
(5) $R_1 = R_2 = O$; $R_3 = CH{=}CH_2$
(6) $R_1 = H$; $R_2 = O$; $R_3 = CH{=}CH_2$



(7) (8)



(10) (9)

Synthesis of new cholesterol derivatives

Zsuzsa Szendi, Irén Vincze, György Dombi*, Frederick Sweet#

Department of Organic Chemistry, Attila József University
Szeged, Dóm tér 8., H-6720
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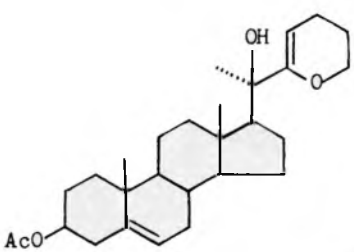
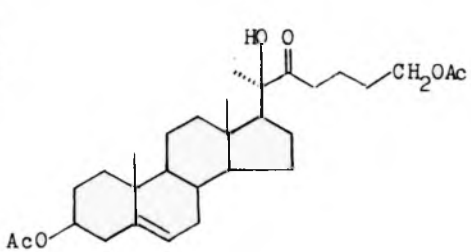
# Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri 63110, USA

Pregnenolone 3-acetate was condensed with 3,4-[2H]dihydropyran to 20R-[6'-(3',4'-[2'H]dihydropyranyl)]-pregn-5-en-3β,20-diol 3-acetate (**1**). Acid-catalyzed opening of the dihidropyranyl-ring at C-20 in (**1**) and acetylation provided 20R-27-norcholest-5-en-22-one-3β,20,26-triol 3,26-diacetate (**2**)[1,2].

In present work (**2**) was transformed to give new cholesterol analogs. Dehydration involving the 20-hydroxy group and also Wolff-Kishner reduction of (**2**) were investigated.
Rather than a simple reduction, the starting material (**2**) underwent a base-catalyzed 1,5-hydride shift and then the product was reduced. Treatment of (**2**) with anhydrous ethanolic HCl resulted in Michael addition of ethanol.



(**1**)



(**2**)

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2., Zs. Szendi, F. Sweet : Novel Synthesis of Cholesterol Analogs: Condensation of Pregnenolone with Dihydropyran or Dihydrofuran Steroids 56 1991.(in press)

8-ISO-D-HOMO-ESTRATRIENE-17ß-OL - A NOVEL SIMPLE METHOD FOR ITS PREPARATION VIA 14ß,15ß-METHYLENE STEROIDS

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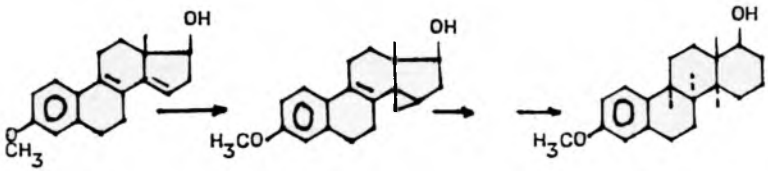
A new simple way for the preparation of d-homo-steroids starting from 3-methoxy-estra-1,3,5(10),8,14-pentaene-17ß-ol (Pentaenol) will be described. We have found that under Simmon-Smith reaction conditions a selective methylenation under participation of the 17ß-hydroxy group takes place (34 % yield).



Parallel to this synthesis we started from 3-methoxy-14ß,15ß-methylene-estra-1,3,5(10)-triene-17ß-ol / 1 / and got the same product after an electrochemical methoxylation in position 9 and acid cleavage of methanol.
The cyclopropano-compound acts like d-homopentaenol. After catalytic hydrogenation an opening of the cyclopropan appears and then a hydrogenation from the α-face gave 8-iso-d-homo-estra-1,3,5(10)-triene-17ß-ol.

Lit. / 1 / R. Prousa, B. Schönecker, D. Tresselt and K. Ponsold; J. prakt. Chem. 328 (1986) 1, 55 - 70

STRUCTURE AND STEREOSPECIFIC SUPERACIDIC CYCLIZATION OF GERANYLGERANIC AND BICYCLOGERANYLGERANIC ACIDS AND THEIR ESTERS

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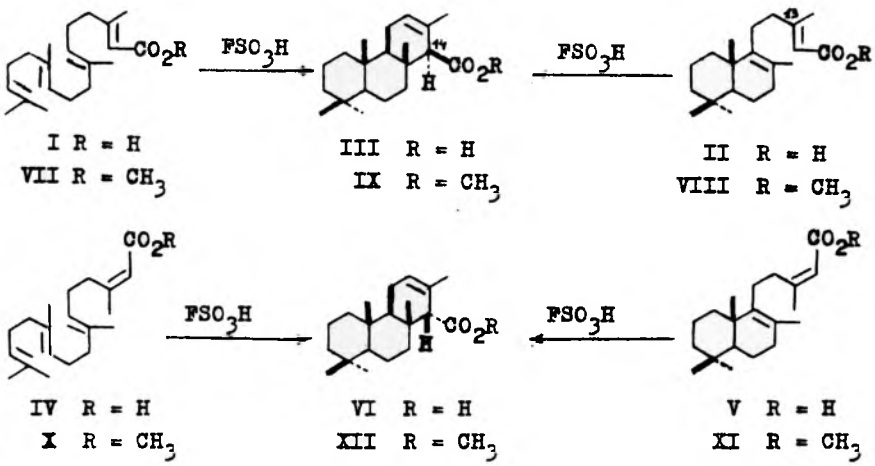
It has been revealed that on fluorosulfonic acid treatment in 2-nitropropane the E,E,E-geranylgeranic and 13E-bicyclogeranylgeranic acids (I) and (II) affords the 14R-isoagath-12-en-15-oic acid (III) in 86-92% yelds. Under the same conditions Z,E,E-geranylgeranic (IV) and 13Z-bicyclogeranylgeranic (V) acids give 14S-isoagath-12-en-15-oic acid (VI) in 81-87% yelds.

The cyclization of esters (VII) and (VIII) leads to isoagathanic compound (IX) (92-95%), and the cyclization of esters (X) and (XI) - the isoagathanic ester (XII) (85-91%).

Thus it was demonstrated that the superacidic cyclization of geranylgeranic and bicyclogeranylgeranic acids and their esters represents an efficient structure selective and stereospecific way for preparing the isoagathanic diterpenoids.



I R = H
VII R = CH_3

III R = H
IX R = CH_3

II R = H
VIII R = CH_3

IV R = H
X R = CH_3

VI R = H
XII R = CH_3

V R = H
XI R = CH_3

SUPERACIDIC CYCLIZATION OF 13E,17E- AND 13E,17Z-BICYCLOGERANYLFARNESIC ACIDS AND THEIR ESTERS - AN EFFICIENT STRUCTURE AND STEREOSPECIFIC WAY TO SCALARANE SESTERTERPENOIDS

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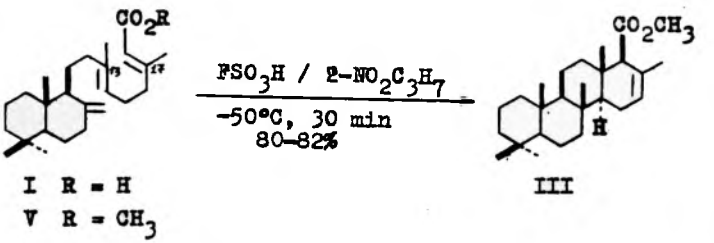
Institute of Chemistry, the SSR Moldova Academy of Sciences,
277028, Kishinev, USSR

The scalarane esters (I) and (II) have been prepared in 74-80% yelds on fluorosulfonic acid cyclization of 13E,17E- and 13E,17Z-bicyclogeranylfarnesic acids (III) and (IV) respectively and subsequent methylation of reaction products.

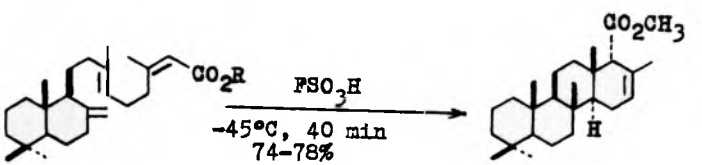
The methyl esters (V) and (VI) give on the cyclization under the same conditions the tetracyclic compounds (I) and (II) in 78-82% yelds.

Thus, the superacidic cyclization of bicyclogeranylfarnesic acids and their esters represents a convenient and efficient structure and stereospecific route to the tetracyclic scalarane sesterterpenoids.



I R = H
V R = CH_3

III



II R = H
VI R = CH_3

IV

EFFECTIVENESS OF ANTIFEEDANTS OF PLANT ORIGIN IN PROTECTION OF PACKAGING MATERIALS AGAINST RHIZOPERTA DOMINICA Fabr.

Elżbieta Błoszyk [a*], Juraj Harmatha [b] and Bohdan Drożdż [a]

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ABSTRACT

Over one hundred plant secondary metabolites of sesquiterpene, lignan, coumarin, rotenoide, and other various structural types were tested for their feeding deterrent activity against selected species of storage pest insects.[1] The effect of some of plant antifeedants on survival, reproduction and morphogenesis of the selected species of storage pest insects was also described. Attempt for their practical use has also been introduced. Recently results have shown that few of sesquiterpenes, rotenone and juglone were very useful in the protection of selected packaging materials from perforation by Rh. dominica and Sitophilus granarius beetles[2].

Nine compounds with a high deterrent activity were used for impregnating three different kinds of packaging materials for foodstuffs to protect them from the invasion of Rh. dominica Fabr. beetles. Among the 9 compounds tested, 3 are sesquiterpenes (bisaboloangelon, bakkenolide A and 6α OH-2,3 dihydroaromaticin), 1 is tropolonic derivative (β-thujaplicin), 3 are lignan and related phenylpropanoids (pinoresinol, piperonylbutoxide and safrol), and 2 are aliphatic compounds (1-triakontanol, 3-nitropropionic acid). The examined sesquiterpenes and 3-nitropropionic acid were

isolated from different plant species of Asteraceae, Apiaceae and Fabaceae families. The remaining ones were prepared by chemical transformations of native compounds or they were commercially obtained from Sarsyntex.

The following packaging materials for foodstuffs were examined: wrapping parchment paper [A], usual wrapping paper for flour [B], polyethylene sheeting of a small density [C]. The compounds have been applied to material at dose of 200 $\mu g/cm^2$.

It was found that the least number of heavy damages (perforations) was observed in the case, when safrol and bisaboloangelon were used for impregnation of the materials B and C. On the contrary, the weakest protective action on the chosen materials was displayed by piperonylbutoxide and bakkenolide "A"

The size of the surfaces damaged by beetles was the smallest after the application of piperonylbutoxide (experiments with materials B and C), β-thujaplicin (only experiment with material B), safrol (experiment with material A), and 6α-OH-2,3-dihydroaromaticin (experiment with material C). On the other hand, the largest damages to the selected material surface caused by Rh. dominica beetles ware observed after the use of bakkenolide "A" (in each kind of material), safrol (in experiments with materials B and C). The applied antifeedants did not fully protect packaging materials from damages. One of the possible reasons of that might be a specific behaviour of beetles. Perforation of material in that case was not related to food uptaking, but was rather a protecting impulse.

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2) E. Błoszyk, J. Nawrot, J. Harmatha, B. Drożdż and Z. Chmielewicz: J. Appl. Ent. 110, 96 (1990).

THE USE OF SOLID PHASE EXTRACTION FOR AN EFFICIENT ISOLATION OF SOME PHYTOECDYSTEROIDS.

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Institute of Organic Chemistry and Biochemistry,
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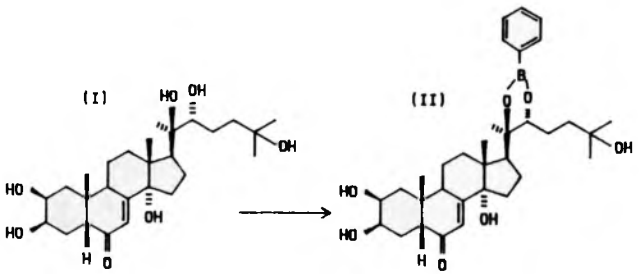
Czechoslovakia

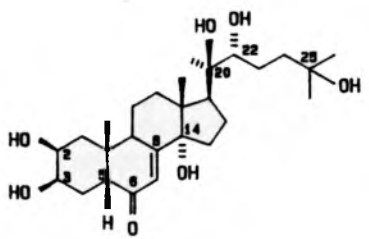
Phenylboronic acid (dihydroxyphenylborane) is used for the protection of 1,2 and 1,3 diols. It forms cyclic esters, which are usually unstable under protic conditions. In the case of 20-hydroxyecdysone (I) (insect molting hormone), which contains two diol systems, only one of them can react with the phenylboronic acid, producing phenylboronate (II). This ester is surprisingly stable in protic conditions and the deprotection requires oxidative spliting of C-B bond by hydrogen peroxide. Conditions for preparing the ester (II) and the methods for the deprotection are discussed. This experience is extended for a solid supported phenylboronic acid with the aim to simplify isolation of ecdysteroids possessing diol system in position 20,22 from plant sources. Several methods for the recovery of 20-hydroxyecdysone (I) from the solid supported reagent was used. Special attention has been paid to non-destructive conditions of cleavage to regenerate the reagent.



PHENYLBORONIC ACID A VERSATILE DERIVATIZATION AGENT FOR CHROMATOGRAPHY OF ECDYSTEROIDES

Jaroslav Píš and Juraj Harmatha
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, CS-166 10 Prague 6,
Czechoslovakia

Ecdysteroids represent a large family of steriod compounds widespread among invertebrates and plants. They control the development and reproduction in invertebrates. Up to now more than 100 compounds of this type are known. They differ in the number and position of hydroxy groups, and in the substitution of the present hydroxy groups. Several different chromatographic systems were used both for TLC and HPLC of the ecdysteroides. Now we wish to report a simple method for determination of the presence of the free diol system in position 20,22. This method consists in the reaction of ecdysteroids on the starting zone of the TLC plate with phenylboronic acid (dihydroxyphenyl borane). The presence of 20,22 diol group is recognized from the difference of R_F values of the treated spot and of the reference spot corresponding to the same sample.



20-HYDROXYECDYSONE

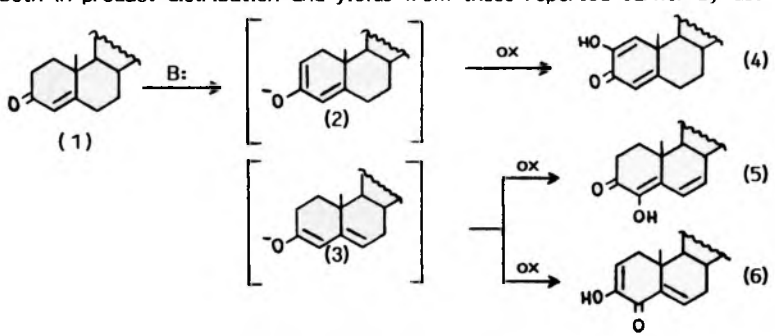
OXIDATION OF ENONE STEROIDS BY TETRAZOLIUM SALTS IN APROTIC MEDIA

Jan Jasiczak

Institute of Commodity Sciences, AE, 60 967 Poznań, Poland

Our earlier studies on the redox reaction between oxidizers with reversible redox potentials and enone or α-ketol steroids led in strong protic media showed that the alkaline medium transformed respective enone or α-ketol group of the steroids into the thermodynamic activ form. The presence of their form determined the further cours of the oxidation[1,2].

In the present communication, we report the results of a comparative study on these same oxidation of enone steroids in aprotic media. As the results outlined below indicate, the course of these oxidations differs substantially both in product distribution and yields from those reported earlier by us.



It is noteworthy, that diosterols (5) and (6) result from the oxygenation of thermodynamic active form (3), enol (4) requires the intermediacy of the thermodynamically less stable but kinetically favored active form (2).
The trapping of the kinetic dienolate (2) in aprotic media is by no means new, its application to oxidative processes in general and to the synthesis of enol (4) has until now, to the best of our knowledge, been unreported.

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Unusual Sesquiterpene lactones From Old World Vernonia

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Institute of Organic Chemistry, Technical University,
1000 Berlin 12

From V. zanzibarensis four unusual glaucolides have been isolated all being dilactones related to brachycalyxolide. A further dilactone obviously was formed by intramolekular nucleophilic attack. V. holstii gave several new so-called cistifolides while in V. grandis vernodalin derivatives and 19-hydroxy glaucolide A cooccur. Structures were elucidated by high field NMR spectroscopy.

NOVEL NEOCLERODANE DITERPENOIDS FROM TEUCRIUM OLIVERIANUM

Maurizio Bruno, Maria Carmen de la Torre, Abdallah A. Omar, Franco Piozzi, Benjamin Rodriguez and Giuseppe Savona

Department of Organic Chemistry, University of Palermo, Palermo, Italy; Instituto de Quimica Organica, C.S.I.C., Madrid, Spain; College of Agriculture, King Saud University, Buriedah, Saudi Arabia.

Continuing our chemotaxonomical investigation of the genus Teucrium (family Labiatae), we have examined Teucrium oliverianum (Ging. ex Benth.) R.Br., a species growing in Saudi Arabia where it is used in folk medicine for the treatment of diabetes.

We report here on the isolation and structural determination of eight new neoclerodane diterpenoids, teucrolivins A-H. It is interesting to remark that teucrolivin F is the second tetranor-neoclerodane found in nature. Teucrolivin G and teucrolivin H have novel structures, showing a very unusual 2,6-dioxabicyclo-[2,2,1]-heptane system.

ALTERATION OF STEROL DEGRADATIVE ABILITY OF MYCOBACTERIA BY IN VIVO GENETIC RECOMBINATION

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Institute for Drug Research, P.O.Box 82, Budapest, Hungary

Nowadays microbial conversion of the readily available plant sterols into 17-keto-androstane derivatives is the most commonly used way to obtain useful intermediates of steroid drug synthesis (1). In the 1970s, microbial strains which selectively remove the side chain of sterols were prepared by mutagenic treatments of different species of sterol degrading mycobacteria (2, 3). We found recently that in vivo genetic recombination carried out by spheroplast fusion provides another possibility to develop genetically modified mycobacterium strains for application in microbial transformation of sterols (4). Now we report that electrofusion is also a useful genetic technique for the modification of steroid degradative ability of mycobacteria. Using the latter method we obtained mycobacterium strains which produce a wide variety of sterol transformation products with partially degraded side chains, by recombination of a strain converting sterols into 26-oic acid derivatives and another strain removing the sterol side chain to a high degree. For the analysis of steroids in the fermentation broths of recombinant strains we have worked out an efficient HPLC method using 25 sterol degradation products as standards. The details and performance of the HPLC method will also be presented.

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SYNTHESIS OF B-CAMPHOLENE COMPOUNDS BY REARRANGEMENTS

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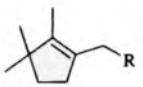
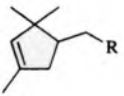
Sektion Chemie der Universität Leipzig
O-7010 Leipzig, Germany

The β-campholene structure (A), found in some natural compounds, is of interest for fragrance and insekticide chemistry. In contrast to the well known α-campholene (B) and fencholene compounds (C) only a few is known about β-campholene derivatives.



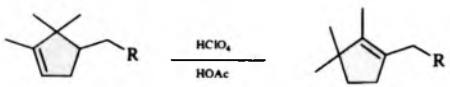
(A)

(B)



(C)

Since the end of the last century [1] the hydrolysis of camphor oxime to a mixture (1:1) of α- and β-campholene nitril was the only preparative method forβ-campholene compounds.
We have found a new synthesis of β-campholene esters from camphor or camphor oxime via β-dihydrocampholene lactone [2].
Gardenas and Kane [3] rearranged α- to β-campholene compounds with phosphoric acid. Now we want to report on our results of the rearrangement of α- to β-campholene derivatives with perchloric acid.



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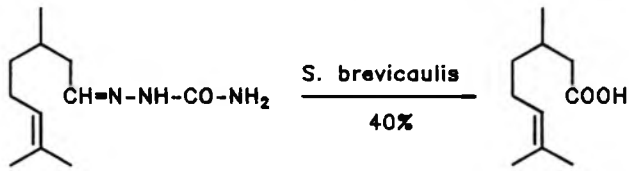
Microbial Transformation of Substituted Terpenoids by fungi

Günter Haufe, Marina Dörre, Holger Hofmann, Lutz Weber and Igor A. Parshikov

Fachbereich Chemie, Universität Leipzig, Germany and
Chemistry Department, State University of Moscow, USSR

The biotransformation of monoterpenic hydrocarbons has often some disadvantages connected to their volatility and insolubility in water. In many cases it is profitable to use derivatives bearing hydrophilic substituents.

We present a study on microbial transformation of terpenic semicarbazones using fungi. Treating the semicarbazones of citronellal, α- and β-campholene aldehyde with Penicillium simplicissimum KM 16 and Scopulariopsis brevicaulis, respectively, mainly oxidation yielding the corresponding carboxylic acids has been obtained.



On the other hand carvone semicarbazone has been only hydrolyzed to yield the parent ketone. In contrast the transformation of myrcenal semicarbazone gave a cyclized compound by partial degradation of the carbon skeleton.

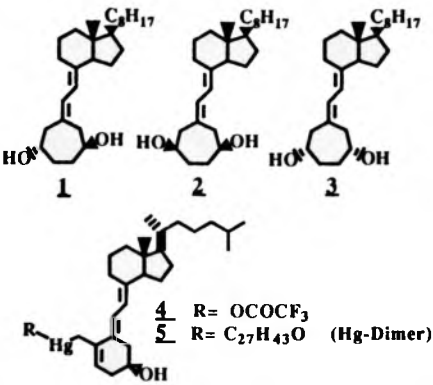
ON THE BEHAVIOUR OF THE VITAMIN D TRIENE SYSTEM TOWARDS MERCURY-SALTS

Wolfgang Reischl and Hermann Kalchhauser

Department of Organic Chemistry, University of Vienna, Vienna, Austria

In our continuous search for selective transformations of the vitamin D triene system, we drew our attention towards reacting the conjugated polyene system with mercury salts. Our hope was that a simple hydroxymercuration procedure would give a convenient entry towards C-10 functionalized derivatives of vitamin D.

Treatment of vitamin D with mercury(II)acetate in THF/water resulted after reduction with sodiumborohydride in a poor conversion (20-30%) to a mixture of more polar compounds. Structural eludicidation revealed A-ring rearrangedseven membered ring analogs **1**-**3** (ratio **1**:**2**:**3** = 5 : 1 : 1) instead of the expected 10-hydroxy isomers of vitamin D as the outcome of this reaction. Attempts to improve the yield of the seven membered ring analogs failed. Some insight into the mechanism of this rearrangement could be gained by using sodium-borodeuteride as the reducing agent. Incorporation of one deuterium atom at the position of a hydroxyl group bearing C-atom was found, showing clearly that structures having a carbonyl fuction are intermediates in this rearrangement.



By treatment of vitamin D with mercury(II)trifluoroacetate in dry THF a totally different reaction occurs. In a clean and quantitative reaction a compound of type **4** or **5** is formed, which is perfectly stable for several hours in solution. Attempts to isolate this product failed.The cross structure of this seco-steroid could be easily established by one- and two dimensional NMR experiments. Arguments accounting for structure **4** as well as for structure **5** (Hg-dimer) including Hg-NMR results will be presented.

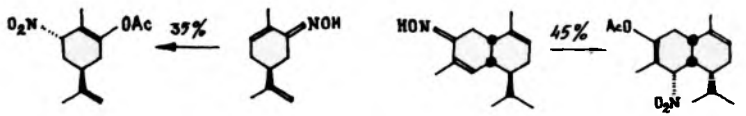
Treatment of this mercury intermediate with various oxidising agents gives rise to 1-hydroxilated products. An alternative route for C-1 hydroxylations of vitamin D via this mercury intermediate will be presented.

THE NITROSATION OF CERTAIN α,β-UNSATURATED TERPENIC OXIMES: A NOVEL REARRANGEMENT OF THE CARANE SKELETON.

Andrey M. Chibirjaev, Alexey Yu. Denisov,
Alexey V. Rukavishnikov, Alexey V. Tkachev

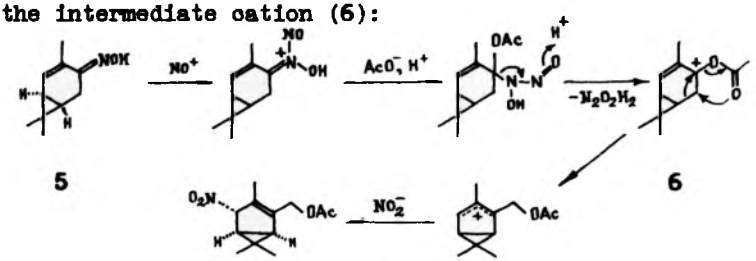
Novosibirsk Institute of Organic Chemistry,
Novosibirsk 630090 USSR

Reaction of the α,β-unsaturated terpenic oximes of limonene (2) and muurolene (3) series with $NaNO_2$-AcOH results in the formation of the corresponding nitro acetates (1) and (4) with the same carbon skeleton in satisfactory yields:



1 2 3 4

In case of the carane derivative (5) the rearrangement product (7) is obtained in 45% yield. The formation of the unusual product (7) is assumed to be due to the rearrangement of the intermediate cation (6):



5 6 7

Structure elucidation and stereochemical studies of the resultant nitro acetates (1), (4), and (7) [IR, UV, MS, NMR: *INADEQUATE, LRJMD*] show the attachment of NO_2^--group from less hindered side of allylic cation at the last step of the reaction.

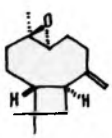
ATTEMPTS OF CONFORMATIONAL ANALYSIS OF NATURAL MEDIUM RING EPOXIDES - CARYOPHYLLENE-4β,5α-EPOXIDE AND HUMULENE-6,7-EPOXIDE.

Yury V. Gatilov, Alexey V. Tkachev,
Dina V. Korchagina, Alexey Yu. Denisov.

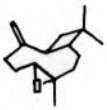
Novosibirsk Institute of Organic Chemistry,
Novosibirsk 630090 USSR

Natural occurring epoxy sesquiterpenoids caryophyllene-4β,5α-epoxide (1) and humulene-6,7-epoxide (4) possess a reasonably high conformation mobility of the carbocyclic fragment, just as their parent hydrocarbons caryophyllene and humulene. The epoxy compounds are supposed to be conformational counterparts of the hydrocarbon analogues.

We have analyzed in detail the ^{1}H NMR spectra of the oxide (1) ($^3J_{HH}$ values, NOE, 2D-NOESY) and have found the epoxide to exist in solution (at least, in $CDCl_3$ and C_6D_6) as *ca* 1:1 mixture of two conformers βα (2) and αα (3) which undergo fast interconversion ($\Delta H^{\neq}$[βα→αα]=7.0 kcal/mol according to the molecular mechanics calculations). These results agree with the molecular mechanics calculations using the MM2 program with the new parameterization for the epoxy group [1]. At the same time, for caryophyllene itself the ratio of the above conformational isomers is 25:1 [2].



1

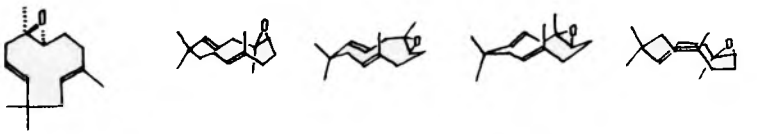


2

3

As for humulene oxide (4), 4 conformational isomers are possible: **CT**, **CC**, **TC**, and **TT**. The analysis of ^{1}H and ^{13}C NMR spectra of humulene epoxide (4) (^{13}C NMR spectral data at

temperatures between +25 and -100°C, 2D-NOESY, NOE, $^3J_{HH}$ values) shows **CT** to be a single conformation existing in the solution. This result agrees with the data of numerous chemical experiments on transannular cyclizations of humulene oxide (**4**) where product stereochemistry suggests **CT** to be the starting conformation for these cyclizations. It should be noted that the **CT** conformation was predicted to be the most stable form of humulene molecule [3]. Though the molecular mechanics method (**MM2**, with parameters of ref. [1] or with those proposed by Yury V.Gatilov) favours the **TC** conformation for epoxy humulene (**4**).



4	**CT**	**CC**	**TC**	**TT**
		$\Delta\Delta H^\circ_f$ (kcal/mol)		
MM2 + [1]	1.1	1.0	0.0	2.8
Yu.V.Gatilov [4]	0.5	0.6	0.0	2.0
humulene [3]	0.0	0.2	1.1	3.6

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[4] Unpublished parameterization for the epoxide ring.

ABOUT CEPSEUDIN STRUCTURE, A SESQUITERPENE LACTONE FROM CENTAUREA PSEUDOMACULOSA

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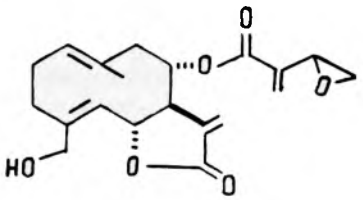
Institute of Organic Synthesis and Coal Chemistry
of the Kazakh Academy of Sciences
Karaganda, U. S. S. R.

Cepseudin (I) - a new sesquiterpene lactone, $C_{20}H_{24}O_6$, mp 200 °C (decomp.; from ethanol), $[\alpha]_D^{18}$ + 70°(c 0.006: acetone) has been isolated from above the ground part of Centaurea pseudomaculosa Dobrocz.

This paper reports about investigation of the cepseudin (I) structure.

The comparison of the data of NMR, C^{13} NMR -spectra with such data for costunolide, cnicin, salonitenolide permitted to suggest trans-, trans - germacradienolide. Structure for the molecule (I) H' - H' and C - H' - correlations on COSY spectra have given the same results.

On the base of the results obtained the structure 15 -hydroxy - 8α- [18(19) - epoxyethyl] -acryloxy -germacr - 1(10),4(5),11(13) -trien -6,12 - olide(I) has been suggested for cepseudin.



(I)

ELECTROFILLE CYCLIZATION OF TRANS, TRANS-GERMACRADIENOLIDE, HANPHYLLIN

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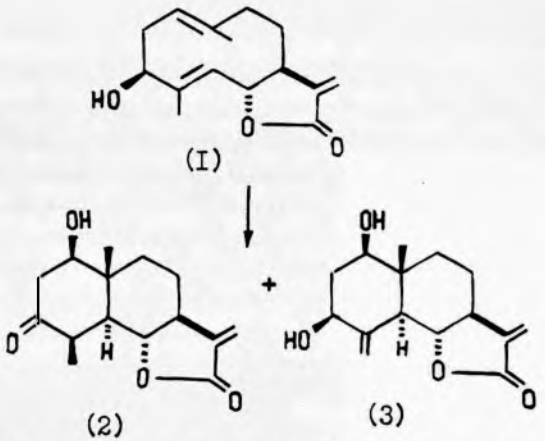
Karaganda, U. S. S. R.

The data of electrofille cyclization of trans-, trans - germacradienolide hanphyllin (1), isolated from Achillea nobilis L. are reported in this paper.

Two crystal compounds (2) and (3) are obtained by interaction of [1] with MCPBA in chloroform.



(2), $C_{15}H_{20}O_4$, mp 187 - 189° C (ethylacetate),

$[\alpha]_D^{18}$ + 46° (c 0.015; chloroform).

(3), $C_{15}H_{20}O_4$, mp 188 - 190° C (ethylacetate),

$[\alpha]_D^{18}$ + 30° (c 0.001; chloroform).

On the basis of obtained physical and chemical constants and spectral data (IR-, NMR-, mass-) compound (2) has been indentified as epimer trans- eudesmanolide artecalin and the structure 1β-hydroxy -3- keto-1,4,5,7α(H), 6β(H) -eudesm- 11 (13)- en-6,12-olide, (3) proved has been suggested for it, but (3) proved to be identical to ridentin-B.

GAIGRANIN AND SPATULIN FROM GAILLARDIA GRANDIFLORA

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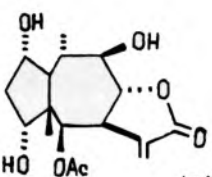
Karaganda, U.S.S.R.

From above the ground part of Gaillardia grandiflora Hort., cultivated in the Karaganda Botanical Garden the sum of lactones has been obtained by chloroform extraction with subsequent processing of the crude substances by the mixture of ethanol-water (2:1) and isolation of filtrate by chloroform. Then two crystal compounds (1) and (2) have been isolated from this sum of lactones by column chromatography on silicagel.

Compound 1 .$C_{17}H_{24}O_7$ .M+ 340. mp 187-189° C (benzene-ether .1:1), proved to be a new sesquiterpene lactone and it was named gaigranin. The data of IR - spectrum testify about availability of hydroxyl groups, of γ- lactone ring, of ether function in its structure. The presence the maximum in UV - spectrum in the field of 215 nm (E 3894) is typical for α-methylene γ-lactone presence in the structure (1). H'- H' and C - H'correlation on COSY permitted to suggest for the structure 2α, 4α,9β-trihydroxy - 6β-acetoxy - 1,7α(H),8,10β(H) -pseudoguai - 11(13) -en -8,12 - olide(1) for gaigranin



(I)

Compound 2 .$C_{19}H_{26}O_8$, M+382, mp 261-262°C (acetone -petroleum ether), according to physical and chemical constants and spectral data (IR-, NMR-, mass-) has been identified as a sesquiterpene lactone of pseudoguaiane type - spatulin. The conformation of cycles in molecule of spatulin has been determined according to the data of X-Ray analysis and the structure of 2α,4α- dihydroxy - 6β,9β-diacetoxy - 1α,7α(H), 8β,10β(H) -pseudoguai -11(13)-en-8,12 -olide has been confirmed for it.

ARGRACIN, A NEW SESQUITERPENE LACTONE FROM ARTEMISIA GRACILESCENS

Sergazy Adekenov, Aibek Turmukhambetov
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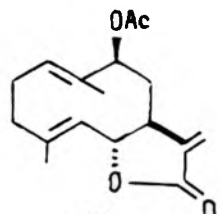
of the Kazakh Academy of Sciences

A colourless crystal substance of $C_{17}H_{22}O_4$ composition mp 210 - 212°C(ethanol, decomposition) has been isolated from above the ground part of Artemisia gracilescens Krasch et Iljin collected during flowering phase in Karaganda region of Kazakhstan by means of acetone extraction followed by chromatography of the obtained resin on column with silicagel of type at sum/carrier ratio 1:20 and by benzene-ether (9:1) mixture elution. This substance proved to be a new sesquiterpene lactone and it was called argracin. The data of (IR-, mass, NMR-) spectra characterize argracin molecule structure as germacradienolide one which is similar to costunolide and its derivatives structure.

The correlation of the NMR spectrum data of argracin to those given in literature [1] identified its chemical shifts to those of acetate haagenolide. This fact allows to suggest the structure of 9β -acetoxy- 6β ,7∝(H)-germacr-1(10), 4(5), II(13) - trien -6, 12-olide (1) for the molecule of argracin.



(I)

[1] Kisiel W. A new germacranolide from Zinnia Haageana // Phytochemistry 1978, v.17, N6, pp 1059-1060

DEHYDRATION OF 17α- AND 17β-HYDROXYCYANOANDROSTENES

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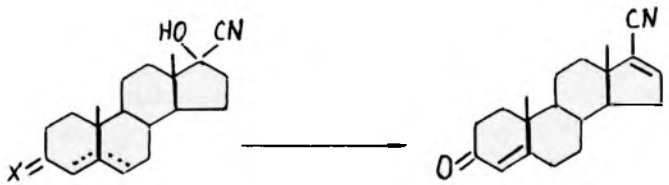
In an effort to work out rational ways for the synthesis of 16-dehydropregnanes on the basis of androst-4-en-3,17-dion (AD), dehydration of isomeric 17α- and 17β-hydroxycyanoandrostenes (I,II,a,b) has been studied. The compounds I and II had been used by us previously in the synthesis of 17-oxyprogesterone from AD.



I 17α-OH, 17β-CN III

II 17β-OH, 17α-CN

a X=O, Δ^4- double bond

b X= O, O, Δ^5-double bond

To obtain 16-dehydro-17-carbonitrile III, thionyl chloride and phosphorus oxychloride in pyridine at different temperature were used.

On exposure of the compound IIa to thionyl chloride at a temperature ranging from 45 to 65 C, the splitting off of 17-hydroxyl was found to occur to a small extent while 17β-hydroxy-17α-cyano-3-chlorandrosta-3,5-diene appeared to be the main product of the reaction.

The action of phosphorus oxychloride in pyridine on the compounds Ia and IIa (on boiling) led to their rapid transformation irrespective of the 17-hydroxyl orientation, however, the desired product III was formed with a low

yield (30-50%) because of a side reaction occuring at 3-keto-group to form a mixture of polar products (according to the data of TLC, IR, and PMR spectroscopy). In the case of IIa, the process of interaction at 3-keto-group was prevailing.

The use of the ethylene ketal protection of the 3-keto-group of isomeric cyanohydrines (Ib, IIb) allowed us to prevent the side reaction to occur. In this case, dehydration with phosphorus oxychloride ran smoothly and after hydrolysis, the desired 16-dehydro-17-carbonitrile III was obtained with a yield 80-85% from cyanohydrine Ib with pseudo-axial 17β-hydroxyl.

3α,11α-DIHYDROXY-5α-PREGNAN-20-ONE 11-HYDROGEN SUCCINATE AS A HAPTEN FOR RIA OF 3α-HYDROXY-5α-PREGNAN-20-ONE

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Czechoslovak Academy of Sciences, Prague, Czechoslovakia.

3α-Hydroxy-5α-pregnan-20-one, a major metabolite of progesterone, is one of the most potent ligands of γ-aminobutyric acid receptor complex in the central nervous system. The compound is thought to have an important role in the response of the CNS to stress, and therefore the need has arisen to develop a radioimmunoassay for its measurement. Two routes will be presented leading to a hapten posessing a spacer in the position 11α: the key step in the first is microbial hydroxylation of 3α-hydroxy-5α-pregnan-20-one. The key step of the second route consists of the chemical conversion of the Δ^4-3-oxo grouping of 11α-hydroxyprogesterone to 3α,11α-dihydroxy-5α--pregnan-20-one. Selective acylation of the equatorial 11α--hydroxy group of the 3α,11α-dihydroxy derivative will be discussed.

SYNTHESIS OF SOME BORNANE DERIVATIVES. STERILIZATION OF GRAIN CROPS AND SUNFLOWER ANTHERS - NOVEL APPLICATION AREA OF TERPENOIDS

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High yields of the 2-exo-bornane derivatives (1) of a general formula

1

where: A = exo-OCH, exo-$OCCF_3$, exo-$OCCCl_3$, exo-$OCCH_2Cl$, exo-$OCCH_2Br$, exo-$OCC(CH_3)_3$, exo-OCH_2CH_2Cl, exo-$OCH(CH_2Cl)_2$, exo-Ph, have been prepareted from camphene and corresponding electrophilic agents.

The 2-exo-bornane derivatives (1) can be used for highly efficent sterilization (98-100%) of anthers of a broad range of crops, while preserving a high settability (75-98%) of seads in open pollination [1].

LITERATURE

1. Patent USA N 4,966,756.

NEW CARDENOLIDE GLYCOSIDES

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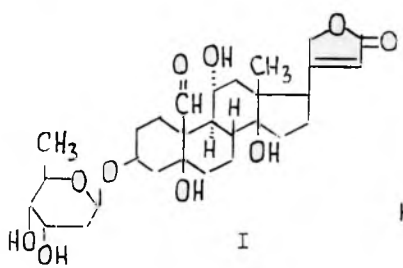
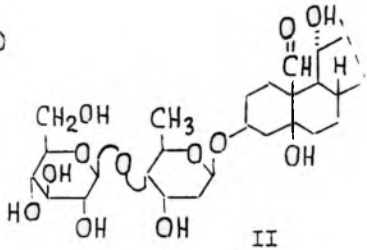
Erysimum contractum Somm. et Lev., f.Brassicaceae is a new sourse of cardiac glycosides which has not been previously studied. We have determined that sum of cardenolide glycosides in this plant makes up 3.2%; main components: erysimosid (1.26%), erysimin (0.22%) and a new glycoside E.cn.5 (0.45%). Seven components have been isolated in pure crystalline state: erysimin, erysimosid, strophanthidin, erycordin, glucocanescein and two new glycosides - E.cn.4 and E.cn.5.

The chemical structure of the new glycosides was determined by chemical and spectral methods. One of them, E.cn.4, $C_{29}H_{42}O_{10}$, m.p.141-145°C, $[\alpha]_D^{20} = +16.0 \pm 2^o$ (MeOH), presents itself: 3β-O-β-D-digitoxopyranosyl-5,11α,14-trihydroxy-19-oxo-5β,14β-card-20(22)enolide (I); its semi-trivial name is nigrescigenin-digitoxoside; the second one is E.cn.5, $C_{35}H_{52}O_{15}$, m.p.169-174°C, $[\alpha]_D^{20} = -2.6 \pm 2^o$ (MeOH), 3β-O-β-D-digitoxopyranosyl-5,11α,14-trihydroxy-19-oxo-5β,14β-card-20(22)enolide (II); its semi-trivial name is nigrescigenin-digilanidobioside.

Relatively high cardiac glycosides content in the species of Erysimum under research makes it perspective for practical use.



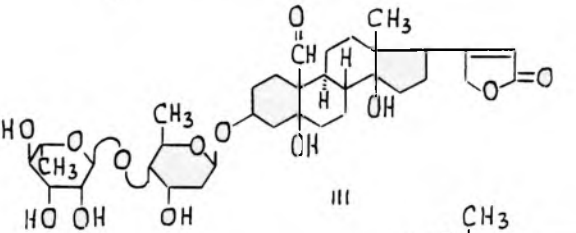
I



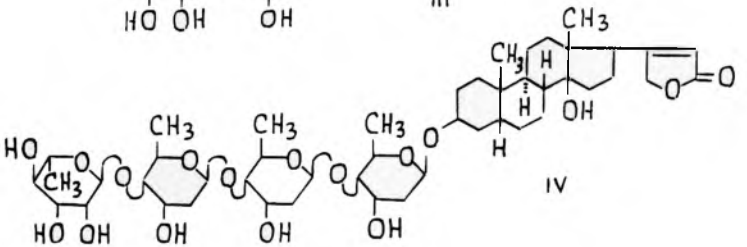
II

It is known that the monoglycosides which contain L-rhamnose are biologically more active compared with analogous glycosides with sugar units of D-series. It was interesting to know if this regularity remains when L-rhamnose is remoted from aglycone and is end-line unit in di-, tri- and tetraglycosides. There are no natural glycosides of such structure. Therefore in order to clarify the question we synthesized the following new glycosides: erysimin-L-rhamnoside (III), $C_{35}H_{52}O_{13}$; $[\alpha]_D^{20} = -16{,}0 \pm 3^\circ$ (MeOH);

digitoxin-L-rhamnoside (IV), $C_{47}H_{74}O_{17}$, m.p.169-170/255-261°; $[\alpha]_D^{21} = -20.1 \pm 2^\circ$ (MeOH).



III



IV

In both compounds (III,IV) L-rhamnose is in pyranose form and is linked by α-glycosidic bond.

It was determined that biological activity of the compound III and IV is 1.4 times more than the activity of erysimoside and purpureaglycoside A correspondingly. The last two glycosides are analogous to III and IV correspondingly and are distinguished only by presence of D-glucose as an end-line sugar unit. We think that explanation of this fact may be given on the basis of conformational differences of the compounds.

OXIDATION PRODUCTS OF OLEANOLIC ACID DERIVATIVES

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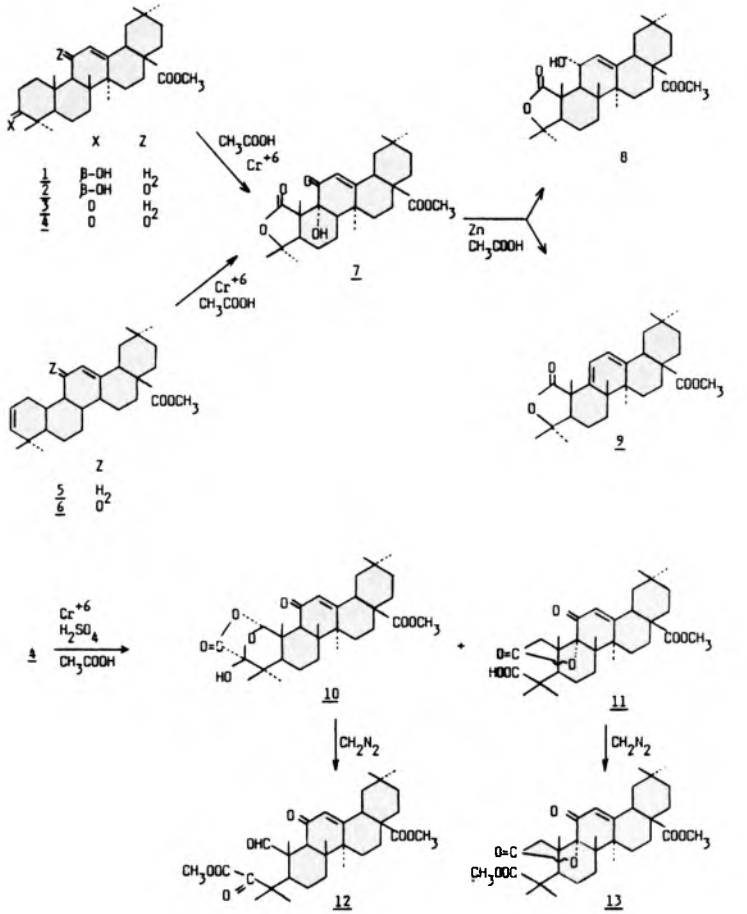
Compound 7 was isolated as the final oxidation product of the oleanolic acid derivatives 1-6 with sodium bichromate in glacial acetic acid. Compound 7 when treated with zinc dust in acetic acid gives compds. 8 and 9.

Oxidation of compound 4 with chromium trioxide or sodium bichromate in glacial acetic acid with some drops of conc. sulphuric acid provides a mixture of compounds 10 and 11 . The first one is transformed into compound 12 , the second one into the methyl ester by the treatment with diazomethane.

The structures of compounds 7-13 were confirmed on the base of spectral data.


X Z
1 β-OH H2
2 β-OH O
3 O H2
4 O O
CH3COOH
Cr+6
COOCH3
7
Zn
CH3COOH
8
9
Z
5 H2
6 O
Cr+6
CH3COOH
4
Cr+6
H2SO4
CH3COOH
10
11
CH2N2
12
13

AN UNUSUAL EFFECT PRODUCED BY SOME HYDROTROPES UPON DISTRIBUTION OF LAPPACONITINE FROM NATURAL EXTRACTS

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Lappaconitine (1), i.e. 1α, 14α,16β-trimethoxy-4-(N-acetylanthranoloxy)-8,9-dioxy-N-ethyl-18-noraconane , is usually isolated via water-alcohol extraction followed by concentration of the extract (evaporation) to its aqueous residue, and further interphase distribution in a liquid-liquid system. The aqueous residues can contain a small amount of ethanol, the effect of the latter upon extraction of (1) being unknown. For the first time, we obtained data on the dependence of distribution constants of (1) in model aqueous solutions and natural extracts, under introduction of such hydrotropes as ethanol (2), 1,3-butane diol (3), glycine (4), and urotropine (5). In the presence of the hydrotropes, extraction behaviour of the model systems obeys general regularities described elsewhere, which is revealed in antibate changes of distribution coefficients with hydrotrope concentration. However, an unusual effect was observed in an experimental series with natural extracts. After introduction of the first portion of (5), the distribution coefficients of (1) increase, reach their maxima, and then decrease. The values and positions of maximum points depend on the nature of plant extracts of (1) and the conditions of their preparation. The observed effect can be rationalyzed in terms of competing intermolecular interactions of the hydrotropes with water soluble species existing in natural extracts. It would be of interest to note that the coefficients of distribution of (1) from natural extracts are essentially lower than those from model systems, and that the coefficients depend appreciably on the preparation procedure of the extracts. This is most likely due to the formation of non-extractable complexes of (1) with natural hydrotropes.

NEW SESQUITERPENE LACTONES FROM THE ACHILLEA GENUS

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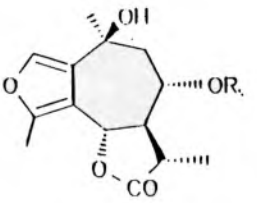
Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

In addition to flavonoids, unsaturated amides and acetylenic compounds, sesquiterpenic lactones[1] (guaianolides, germacranolides, eudesmanolides) also belong among characteristic components of the Achillea genus[2]. Their presence is not only characteristic of individual species but it also influences considerably the character of their essential oils. In connection with a broader investigation of Mongolian species[3], sesquiterpenic lactones of the so far undescribed type were isolated from the above-ground parts of Achillea millefolium compl. Their structures, I and II, with the primary skeleton of 3-oxaguaianolide, were determined on the basis of their IR, MS and principally ^{1}H and ^{13}C NMR spectra.



I R = $COCH_3$

II R = $COC(CH_3)=CHCH_3$

References:

1. F.C. Seaman: Bot.Rev. 48, 121 (1982).
2. F.C. Schandler, S.N. Hooper, M.J. Harvey: Economic Botany 36, 203 (1982).
3. O.Motl, G.Ochir, K.-H. Kubeczka: Flavour Frag. J. 5, 153 (1990).

APPLICATION OF MOLECULAR MODELING TECHNIQUES TO THE STUDY OF NATURAL PRODUCTS

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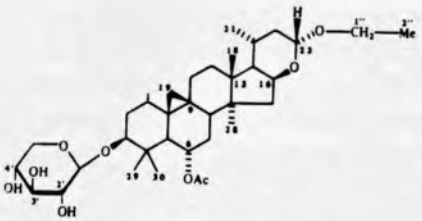
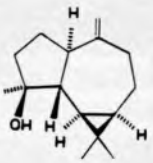
Over the past several years there has been a steadly evolving use of molecular modeling as a tool in many research fields. Concerning the natural products, this technique can be used both for structure elucidation of extractive components, and analysis of metabolites and, in general, investigation of the potential energy surfaces which provides information about the conformations accessible to the molecules.

In the stereochemical elucidation of natural products the presence of conformationally flexible systems may invalidate stereochemical assignements attributed by correlation between dihedral angles and $^3J_{H-H}$ coupling constants. In these cases conformational analysis using molecular modeling techniques can be quite helpful. Specific examples of this approach in the isoprenoids field is the structure elucidation of some metabolites from Astragalus tomentosus and Baccharis semiserrata, in particular the stereochemical assignemet of C-6, C-23 in

(-) tomentoside 1[1] and of C-1, C-5 in (+) spatulenol 2. Dihedral angles calculated for the minumum energy conformations have been introduced in the Karplus' equation modified by Haasnoot[2].



1



2

Both force-field (MMPMI[3]) and semi-empirical methods (AM1[4]) have been used.

The semiempirical method AM1 has been also used to study metabolic intermediates related to biotransformations.

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3. Serena Software, Box 3076, Bloomington, USA.
4. Quantum Chemistry Program Exchange n. 527, Indiana University, USA

2α-HYDROXY-3α-[N-ALKYL(ARYL)]-PINANOAMINES III. CONVENIENT CHIRAL LIGANDS IN ASSYMMETRIC SYNTHESIS

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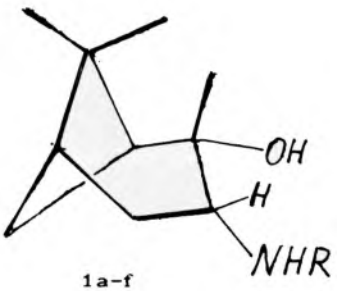
Easy accessible from (+) or (-) α-pinene optically pure hydroxyamines **1a-f** were tested in several, typical asymmetric syntheses affording products >80% e.e.



1a-f

	R
1a	nPr
1b	iPr
1c	nBu
1d	CH_2CH_2OH
1e	C_6H_{11}
1f	C_6H_5

Hydrogenation of acetophenone with complex of $LiAlH_4$ and **1f** gave carbinol (91% e.e.). Alkylation of 2-cyclohexenone by cuprates in the presence of **1f** yielded 3-alkylcyclohexanones in 81-85% e.e.

Analogs of hydroxyamines **1** obtained from nopol were found useful for asymmetric addition of lithium enolates to benzaldehyde affording condensation products in high e.e.

REFERENCES: S.W.Markowicz, Conference on Isoprenoids XII, **1987**; ibid. XIII, **1989**; S.W.Markowicz, J.Karolak-Wojciechowska, W.Kwiatkowski, J.Crystallogr.Spectrosc.Res.-**1989**, 19, 535-545; ibid. 893-903; J.W.Ap Simon, T.Lee Collier, Tetrahedron **1986**, 42, 5157-5254; K.Tomioka, Synthesis **1990**, 541-549 and references cited therein.

The financial support of this work by Technical University of Łódź and by Pharmaceutical Plant "Polfa" Pabianice is gratefully acknowledged.

TRANSFORMATION OF CAR-3-ENE TO THF AND THP DERIVATIVES

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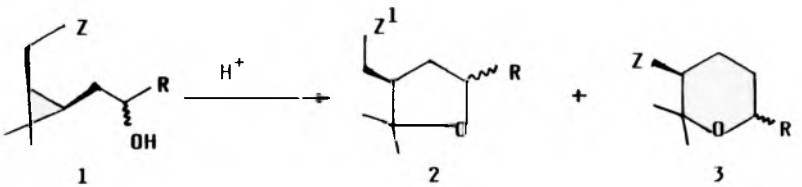
Institute of General Food Chemistry, Technical
University of Łódź, 90-924 Łódź, Poland

Tetrahydrofuran and tetrahydropyran system is largely spreaded in natural products, olfactory substances and therapeutic agents. We have developed an original method for transformation of 3-substituted 2,2-dimethylcyclopropaneethanols (easily available from car-3-ene) into THF and THP derivatives of the determined absolute configuration of the molecule. Depending on the character of the substituent, two-directional opening of the cyclopropane ring occurs selectively when a solution of sulfuric acid is used as a catalyst



1 2 3

1a: Z = Et
1b: Z = COMe
1c: Z = $COHMe_2$

2a: Z^1 = n-Pr
2b: Z^1 = CH_2COMe
2c: Z^1 = $CHCHMe_2$

3a: Z = Et
3b: Z = COMe
R = H, Me

Three different mechanisms have been proposed to explain the proton participation in the creation of the transition state, the role of the substituent, the direction of the cyclopropane ring opening and the product composition. This type of transformations occur with the retention of configuration of the chiral carbon atoms.
Stereochemistry of the THP derivatives is also discussed.

HYDROBORATION OF VARIOUS Δ^5 CHOLESTANES

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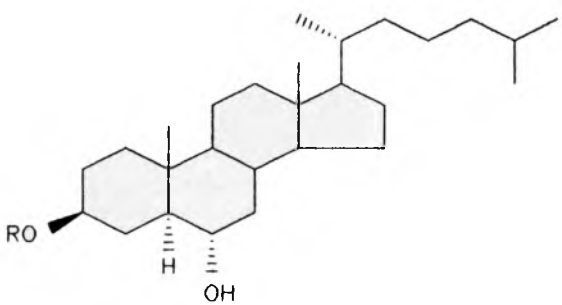
Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague, Czechoslovakia

Selectively protected 5α-cholestane-3β,6α-diols are useful precursors for syntheses of sulfated steroid derivatives (e.g. hydroxy sulfates and glycoside sulfates).

We prepared five diols of this type with various protective groups in the position 3β. In all cases (except of the acetyl derivative) good yields of the products were obtained. These results are at variance with literature[1].



R = MOM, THP, TXDMS, Piv, Ac, H

Literature

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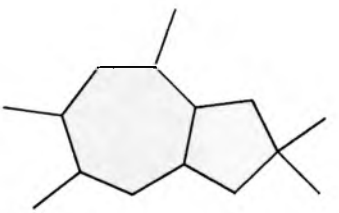
ANTIFEEDANT ACTIVITY OF SESQUITERPENES OF LACTARIUS ORIGIN

Włodzimierz M. Daniewski[a], Maria Gumułka[a], Katarzyna Ptaszyńska[a], Piotr Skibicki[a], Elżbieta Błoszyk[b] and Bohdan Drożdż[b].

a) Institute of Organic Chemistry Polish Academy of Sciences 01-224 Warsaw, Poland.
b) Chair of Medicinal Plants, Academy of Medicine, Poznan, Poland.

Antifeedant activity of several sesquiterpenes of lactarane skeleton using storage pests *Tribolium confusumv* Duv., *Trogoderma granarium* Ev. *and Sitophilus granarius* L. was investigated. The sesquiterpenes were isolated from various Lactarius species, or some of them were modified chemically in order to check the structure activity relationship. Activity of several furans, lactones and hydroxylactones was determined. The number, the position as well as the stereochemistry of substituents played an important role.



Lactaran

NEW SESQUITERPENES OF LACTARAN SKELETON FROM LACTARIUS VELLEREUS

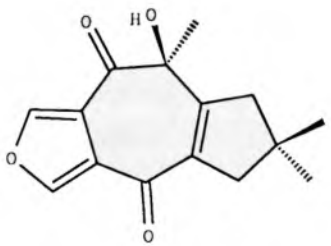
Włodzimierz M. Daniewski, Maria Gumułka, Katarzyna Ptaszyńska, Piotr Skibicki, Janusz Krajewski and Przemysław Gluziński.

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

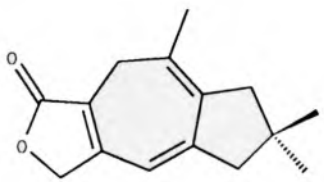
From the non polar fraction of the ethanolic extract of *Lactarius vellereus* three new sesquiterpenes have been isolated:

1. 5,13-oxy-3β-hydroxy-lactara-2(9),5,7(13)-trien-4,8-dione
2. 13-hydroxy-lactara-2,6,8-trien-5-oic-acid γ-lactone,
3. 5-hydroxy-lactara-6,8-dien-13-oic-acid γ-lactone.

The structures of these compounds were substantiated with the aid of ^{1}H and ^{13}C NMR spectroscopy. Structure of compound 1 was confirmed by single crystal X-ray method.[1]



1



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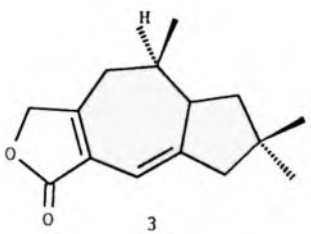


3

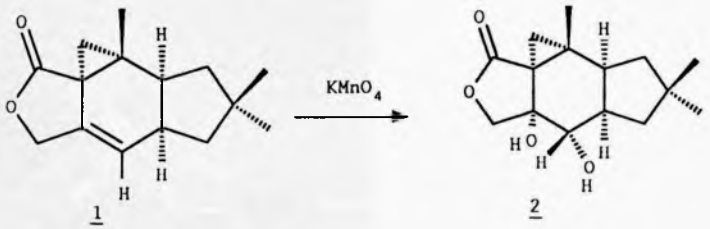
1. W.M. Daniewski, M. Gumułka, P. Skibicki, J. Krajewski, and P. Gluziński, Phytochemistry 30, 1326, (1991).

NEW SESQUITERPENES OF MARASMANE SKELETON FROM LACTARIUS VELLEREUS

Włodzimierz M. Daniewski, Maria Gumułka, Katarzyna Ptaszynska, Piotr Skibicki, Janusz Krajewski and Przemysław Gluziński.

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

Thorough examination of ethanolic extract of *Lactarius vellereus* allowed to isolate two new sesquiterpenes of marasmane skeleton:
13-hydroxy-marasm-7-en-5-oic-acid γ-lactone (1) and 7α,8α,13-trihydroxy-marasman-5-oic-acid γ-lactone (2). Structures of Compounds 1 and 2 were substantiated by ^{1}H and ^{13}C NMR spectroscopy. Compound 1 was oxidised with $KMnO_4$ and gave 2. The structure of 2 was confirmed by single crystal X-ray diffraction method.

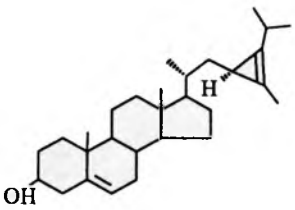


1 2

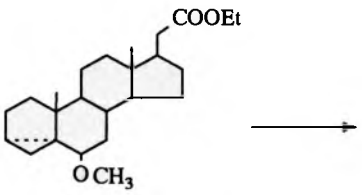
TOWARDS CALYSTEROL SYNTHESIS. METHOD FOR CONSTRUCTION OF CYCLOPROPENE-CONTAINING SIDE CHAIN.

Alicja Kurek-Tyrlik, Kazimierz Minksztym, Andrzej Zarecki and Jerzy Wicha
Institute of Organic Chemistry, Polish Academy of Sciences,
01-224 Warszawa, ul. Kasprzaka 44, Poland

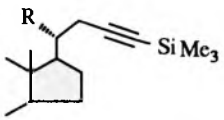
Calysterols[1-4] (1), closely related sterols of marine origin, have not been synthesized till now.



1 (23H-Isocalysterol)

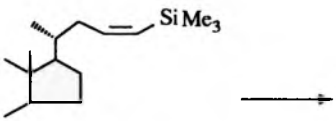


2

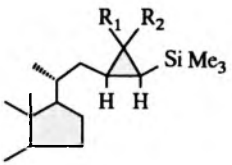


3 R=COOEt

4 R=CH_3

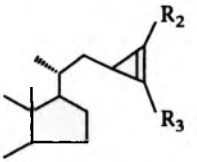


5



6 R_1=R_2=Br

7 R_1=Br R_2=alkyl



8 R_2=alkyl R_3=H

9 R_2=alkyl R_3=alkyl

In this communication we present an approach to the synthesis of calysterols **9** starting from ester **2**[5] *via* its alkylation product **3** and the acetylenic derivative **4**, as the key intermediate. Reduction of the triple bond to Z-olefin **5**, dibromocarbene addition[6] to the latter resulting in dibromocyclopropanes **6**, afforded, after further monoalkylation[7], bromoalkylcyclopropanes **7**. Fluoride-ion promoted elimination of trimethylsilyl bromide[8] from **7** generated cyclopropenes **8** which were finally alkylated to **9**.

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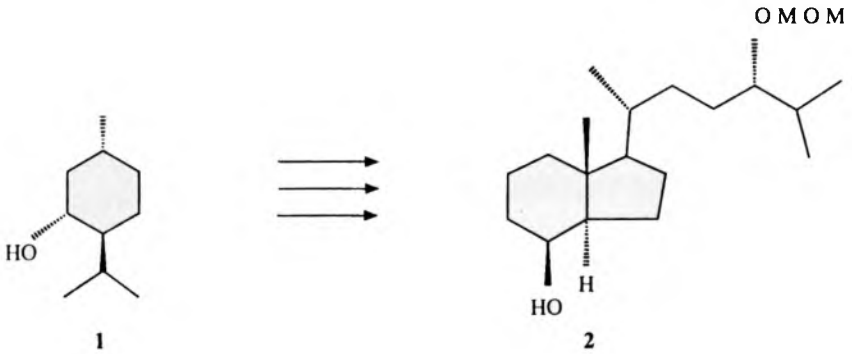
TRANSFORMATION OF MENTHOL INTO CD-FRAGMENT OF VITAMIN

Andrzej Robert Daniewski and Tadeusz Warchol

Institute of Organic Chemistry, Polish Academy of Sciences

01-224 Warsaw, ul. Kasprzaka 44/52

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



1 **2**

EFFICIENT SYNTHESIS OF 25-HYDROXY-VITAMIN D_3 AND ITS 26,27-HOMOLOGUES

B. Schönecker[a], R. Prousa[a], E. Schrötter[b], H. Schick[b], P. Droescher[c], R. Fischer[d], D. Walther[d], M. Reichenbächer[d], S. Gliesing[d]

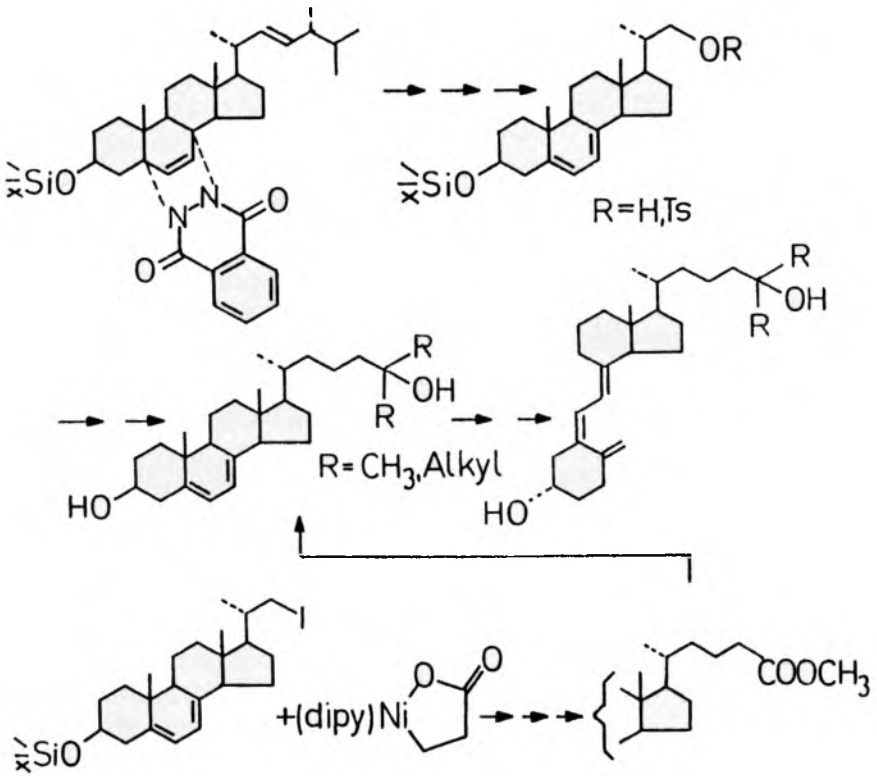
[a]Institute of Microbiology and Experimental Therapy, Jena, O-6900, FRG; [b]Central Institute of Organic Chemistry, Berlin, O-1199; [c]Jenapharm GmbH, Jena, O-6900; [d]Friedrich Schiller University Jena, O-6900

In continuation of our work on the synthesis of vitamin D_3 metabolites / 1 / and analogues with different biological activities we looked for an efficient and convenient synthesis of 25-hydroxyvitamin D_3. Our further interest was directed at the synthesis of C_{25} carboxylic esters / 2 /, which should be useful intermediates in the synthesis of 26,27-homologues and of deuterated and tritiated compounds.

The phthalazine-1,4-dione Diels-Alder adduct of 3-O-tert-butyldimethylsilylergosterol was synthesized from ergosterol. Ozonolysis of the side chain double bond and deprotection of the 5,7-diene system with $LiAlH_4$ gave the 22-alcohol in a total yield of 50 % from ergosterol. Tosylation of the 22-alcohol, coupling with the Grignard compound of 4-chloro-2-methyl-2-/(trimethylsilyl)oxy/butane and desilylation of the 3ß- and the 25-functions furnished 25-hydroxy-7-dehydrocholesterol. This compound and 26,27-homologues are also obtainable in good yields by reaction of the 22-iodide with a nickel-acycle as a new d^3 synthon, esterification of the C_{25} carboxylic acid, Grignard reaction and desilylation.

UV irradiation of the unprotected provitamins using a suitable filter solution, separation of the photoisomers by flash-chromatography on silver-impregnated silica gel and recycling of the reversible photoisomers gave the vitamins

in satisfactory yields after thermal isomerization of the previtamins.



Literature

/ 1 / Schrötter, E.; Schönecker, B.; Hauschild, U.; Droescher, P.; Schick, H.; Synthesis 1990, 193

/ 2 / Schönecker, B.; Walther, D.; Fischer, R.; Nestler, B.; Bräunlich, G.; Eibisch, H.; Droescher, P.; Tetrahedron Letters /London/ 31 (1990) 1257

NEW STEREOSELECTIVE ROUTE TO ISOPRENOIDS WITH 1,3-DIENIC UNITS VIA HYDROALUMINATION OF ENYNE ALCOHOLS.

A.P.Khrimian, O.A.Gharibian, G.M.Makarian, G.A.Panosyan and Sh.O.Badanian

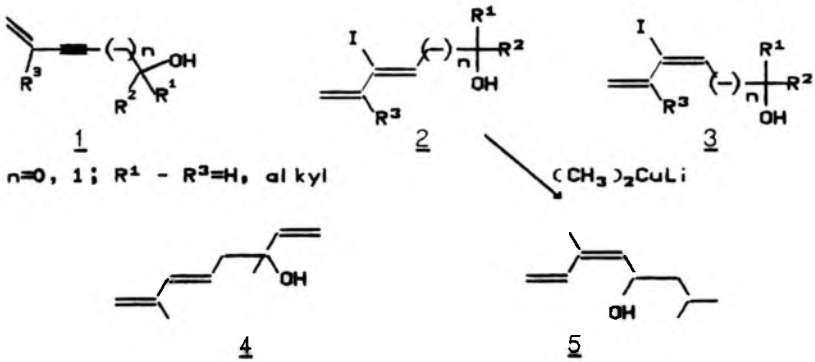
Institute of Organic Chemistry Armenian Academy of Sciences, Kamo 167-a 375094. Yerevan, Armenia, USSR.

LAH hydroalumination of enyne α- and β-alcohols 1 with the next substitutive methylation of iododienols 2 and 3 having been studied as a potential approach to isoprenoids afforded:

1. An easy access to substrates with 2-methyl-1,3-dienic moiety, e.g. (±)-hotrienol 4.

2. Unusual cis-stereoselectivity (2:3 - 15:80) of iodine cleavage of the intermediate trans-aluminate formed from enynols 1 with the number of substituents nearby the triple bond ($R^3=CH_3$, n=0, R^1 and R^2=alkyl).

3. Nearly full inversion (90-95 %) of configuration under carbodeiodination of trans-iododienols 2. This new cis-favoured methylation has been used for synthesis of terminal 3-methyl-1,3-dienic monoterpenes, e.g. cis-tagetol 5.



1 2 3

n=0, 1; R^1 - R^3=H, alkyl

4 5

Processes details and mechanistic pathways to compounds 2-5, as well as configurational assignment of 2 and 3, using NOE and J-resolved 2D-NMR spectroscopy will be discussed.

TEO NEW DIGLYCOSIDES FROM EPIGUNUM AURITUM

Qi-Duan Jin an Quang-Zhang Mu
(Laboratory of Phytochemistry, Kunming Institute of Botany, Chines Academy of Sciences, Kunming 650204)

ABSTRACT Two new oligoglycosides designated as epigeoside A and B have been isolated from the dried rhizomes of Epigynum auritum(Apocy-naceae). Spectroscopic and chemical evidence are consistent with the structure(+)-catechin-3-O-β-D-glucopyranosyl-(1⟶4)-α-L-rhamnopyranoside A and (+)-catechin-3-O-β-D-glucopyranosyl-(1⟶6)-β-D-glucopyranoside B.

Epigeoside A mp 147-151°C, $[\alpha]_D^{20}$ +18.5°, $C_{27}H_{34}O_{15}$. Fabms of intact epigeoside A produced a protonated molecular ion at m/z 599(M + 1)$^+$and ions at m/z 436(M + 1 - glucose)$^+$, 285(M + 1 - glucose - rhamnose)$^+$. The Uv spectrun showed absorptions at 227 and 280nm . Its IR spectrum showed the presence of a hydroxy group(3400cm^{-1}) and an aromatic ring(1625, 1580 and 1520cm^{-1}). Confimation of the diglycoside structure of compound A and configuration of sugar was provided by the ^{1}H NMR(400MHz) spectrum of A, which indicated the presence of (+)catechin as aglycone moiety at 5.80-7.10(5H, m, aromatic), 4.10(1H, ddd, J=12, 10, 5Hz, 3β—H), 4.70(1H, d, J=10Hz, 2α—H). The large coupling constant indicated an axial coupling of H—1 of β-D-glucopyranoside and the small coupling constant indicated an equatorial coupling of H—1 of α-L-rhamnopyranoside, respectively. The ^{13}C NMR spectrum of compound A provided also satisfactory informations of the structure of the aglycone with fifteen carbon signals and that of the sugar moiety with twelve carbon signals.

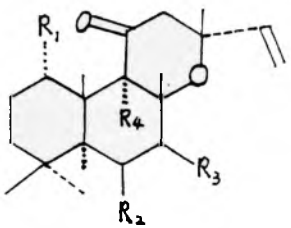
Epigeoside B mp. 156-159.5°C , $[\alpha]_D^{20}$ +19.4°, $C_{27}H_{34}O_{16}$. Fabms of intact epigeoside B produced a protonated molecular ion at m/z 615 (M + 1)$^+$and ion at m/z 552(M +1 - glucose)$^+$and 298(M + 1 - glucose -glucose)$^+$ the Uv and IH spectra of compound B were similar to those of A. ^{1}H NMR and ^{13}C NMRspectra of compound B were slightly different those of compound A. For the sugar moieties, in the ^{1}H NMR two anomeric proton signals appeared at 4.25(1H, d, J=7.8Hz) and 4.45(1H, d, J=7.6 Hz), these large coupling constants indicated a diaxial coupling of H—1 to H--2 of -D-glucopyranoside. The two anomeric carbon signals appeared at 98.2 and 104.3ppm, the up-field signal was assignad to the anomeric carbon of the inner D-glucose linked to the C—OH of (+)catechin.

THE CHEMICAL CONSTITUENTS FROM COLEUS FORSKOHLII BRIQ NATIVE TO YUNNAN CHINA

Qi-Duan Jin and Quang-Zhang Mu
(Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204)

ABSTRACT We have isolated from Coleus forskohlii Briq.(Labaitae) native to Yunnan China three diterpenoids(compounds I. II. III.). two of which(compounds I. II.) are new compounds, but III is kown compound. The structures of I. II. and III were deduced on the basis of chemical and spectral evidence as 1α, 6β, 7β-triacetoxy-8,13-epoxy-9α-hydroxy-14-en-11-one(i.e. 1, 6-diacety-forskolin); 1α,7β-diacetoxy-8, 13-epoxy-6β-, 9α-dihydroxy-14-en-11-one(i. e. 1-acety-forskolin) and 6β-acetoxy-8,13-epoxy-1α, 7β, 9α-trihydrxy-14-en-one(i.e. isoforskolin), and the structure of III is similar to isoforskolin which Indian scholar has isolated from Coleus forskohlii Briq. native to India.

The structures are as follows:



I. $R_1=R_2=R_3=OAc$, $R_4=OH$

II. $R_1=R_3=OAc$, $R_2=R_4=OH$

III. $R_1=R_3=R_4=OH$, $R_2=OAC$

The pharmacological study showed that three compounds display interesting blood pressure lowering, cardioactive, glaucoma, asthma, and thrombosis properties. The clinical study is under progress in traditional medicine.

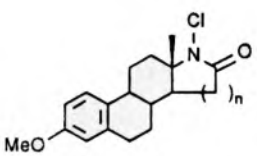
THE CHEMISTRY OF SOME NOVEL N-CHLOROAZASTEROIDS

J.W. Morzycki[a], T.G. Back[b], J.H.-L. Chau[b], B.P. Dyck[b], P.L. Gladstone[b] and E.K.Y. Lai[b]

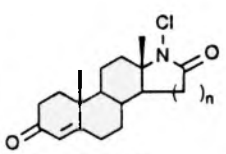
(a) Institute of Chemistry, University of Warsaw, Bialystok Branch, 14-443 Bialystok, Poland; (b) Department of Chemistry, University of Calgary, Calgary, Alberta, Canada, T2N 1N4.

N-Chloroazasteroids are novel reactive mimics of natural steroid hormones that produce N-S (sulfenamide) derivatives with model thiols.[1] Since thiol groups play a vital role in the recognition and binding of steroid hormones by their receptors,[2] such N-chloro compounds have potential value as affinity labels and antagonists of steroid hormones by forming covalent bonds with the corresponding active sites. Our work[1,3] has focused principally on various azasteroids with nitrogen atoms in ring A or D, as these regions are especially crucial for binding. This paper will describe the preparation of several novel N-chloro-17-aza- and N-chloro-17a-aza-D-homoazasteroids (e.g. 1 and 2), as well as a new synthetic approach to 17-azasteroid lactams.[4]

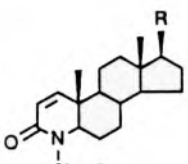
Furthermore, N-chloroazasteroids are also of interest as inhibitors of enzymes that recognize them as substrates. Δ^1-4-Azasteroids are known to be potent transition state inhibitors of 5α-reductase,[5] an enzyme implicated in the development of prostatic hypertrophy. The N-chloro derivatives 3 are potential irreversible inhibitors of this enzyme. The preparation and properties of a series of such compounds will be described.



1 n= 1,2



2 n= 1,2



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SYNTHESIS OF 12-ALKYL- AND 12-ALKENYL-19-NORPREGNANES

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Organon International Scientific Development Group
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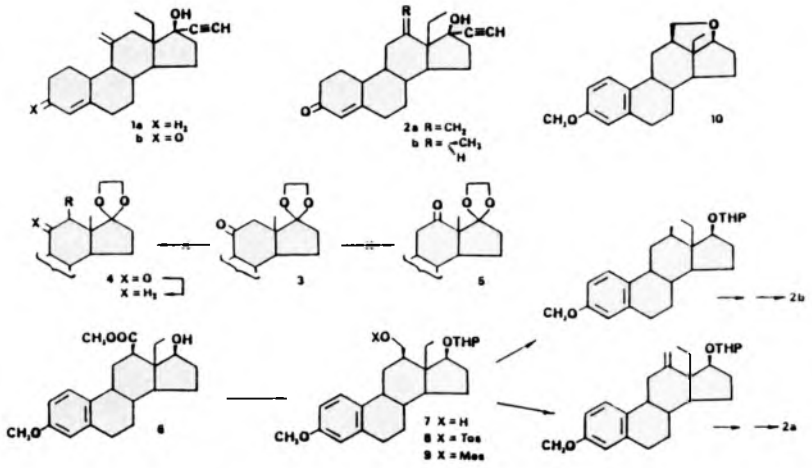
The 11-methylene compound Desogestrel 1a is known to be a very potent progestagen. In order to investigate the effect of a shift of the 11-methylene group to the 12-position the corresponding pregnanes 2 were prepared via total synthesis, after attempts to alkylate 11-ketones (3 → 4) or to effect a carbonyl shift (3 → 5) had failed. Key intermediates 6 were prepared according to a known[1] procedure. After reduction of the 12-carboxylate to the alcohol 7 the tosylate 8 could either be reduced to the 12β-methyl group or eliminated (via the iodide) to the 12-metylene. Attempted elimination of the corresponding mesylate 9, however, afforded the epoxymethano compound 10 as the sole identifiable product. Finally, Birch reduction and ethynylation gave the desired pregnanes 2 as racemic mixtures.



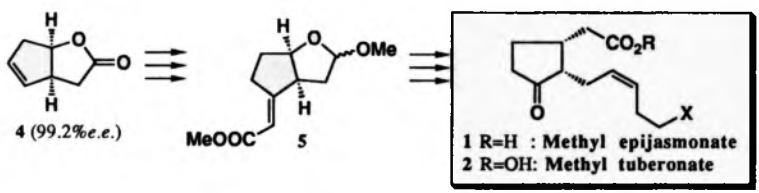
1) Tohma et al, Chem.Pharm.Bull. 35(1987),585; 36(1988),4284

ENANTIOSELECTIVE SYNTHESIS OF BIOREGULATORS (ANTHERIDIC ACID AND JASMONATES).

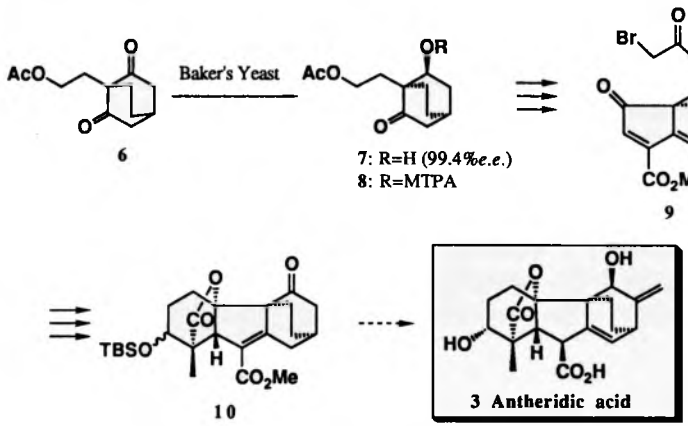
Takeshi KITAHARA.* Masahiro MIYAKE, Tunehiro NISHI and Kenji MORI
Department of Agricultural Chemistry
The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku,Tokyo 113,
JAPAN

It is one of very important tasks to solve the mechanism of regulating life cycles of living organisms in studying biological phenomena. Substances related to these phenomena are usually available in only very minute amount from natural sources and sometimes it is very hard even to determine their structures. Chiral synthesis is particularly indispensable for the precise biological evaluation of those bioactive natural products and their analogs by supplying sufficient amounts of pure materials.

We have been studying the synthesis of bioactive molecules in optically active forms from this standpoint. We discuss here our recent work on the enantioselective synthesis of several bioregulators with phytohormonal activities, methyl epijasmonate **1** and methyl tuberonate **2** (potato tuber inducing factors) and antheridic acid **3** (antheridium inducing factor of fern) in optically pure forms. Both the enantiomers of Jasmonate Analogs was synthesized starting from 2-oxabicyclo[3.3.0]octan-3-one **4** and its antipode. The rigid bicyclic system was effectively utilized for stereoseletive introduction of methoxycarbonylmethyl side chain *via* **5**.



Synthesis of (+)-antheridic acid **3** was started from the chiral building block **7** with bicyclo[2.2.2]octan-2-one system, which was obtained in high yield by asymmetric reduction of symmetrical bridged diketone **6** with baker's yeast. The desired stereochemistry was confirmed by X-ray analysis of the crystalline (*S*)-MTPA ester **8**. Starting from **7**, pentacyclic lactone **10** with antheridane skeleton was synthesized via intramolecular Reformatsky reaction of **9** and the synthesis of **3** is now towards the end.



6 9 10

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SYNTHESIS OF (2S,3S,7S)-3,7-DIMETHYLPENTADEC-2-YLACETATE AS THE SEX PHEROMONE OF RED-HEADED PINE SAWFLY (Neodiprion lekontei) AND ITS (2R,3S,7S)-ENANTIOMER, PROCEEDING FROM (R)-(+)-PULEGONE

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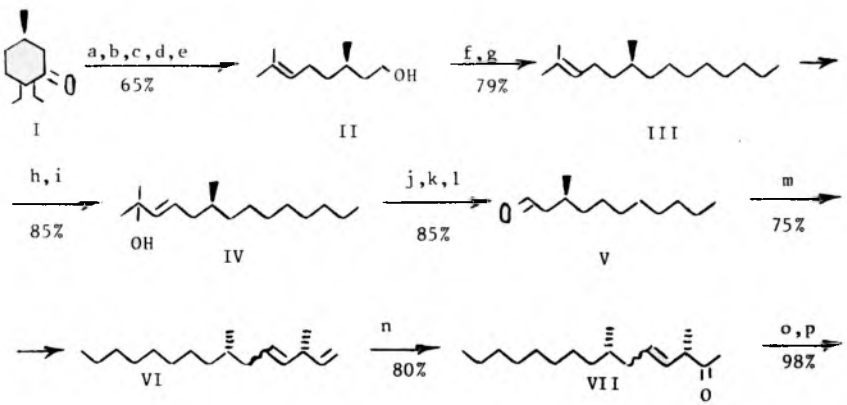
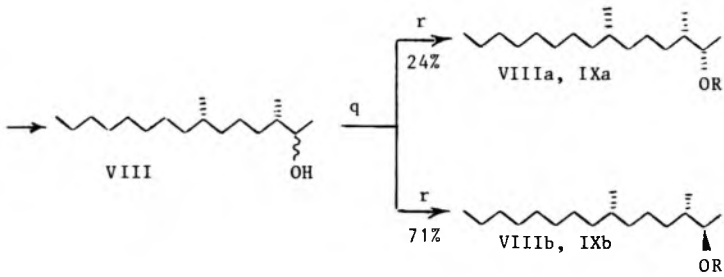
Institute of Organic Chemistry, Ural Department of the USSR Academy of Sciences, Ufa, SU-450054, U.S.S.R.

Starting from (R)-(+)-pulegone (I), (S)-(-)-4-methylundecanal (V) was synthesized via intermediates (II-IV). Olefination of (V) with (2R-methyl-3-butenylidene)triphenylphosphorane resulted in 3,7-dimethyl-branched pentadecadiene (VI). Catalyzed by $PdCl_2$, diene (VI) was oxidized with O_2. The oxidation was selective for the terminal double bond to give ketone (VII) with (S,S)-configuration of its asymmetric centres. As it had been expected, hydride reduction of ketone (VII) was diastereoselective. This was followed by hydration of double bond to lead to a mixture of erithro- (VIIIa) and threo- (VIIIb) isomeric alcohols (VIII) that were subsequently separated by HPLC. Acetylation of the alcohols (VIIIa) and (VIIIb) gave the title pheromone (2S,3S,7S)-3,7-dimethylpentadec-2-ylacetate (IXa) and its (2R,3S,7S)-enantiomer (IXb).





R = H(VIIIa, VIIIb), Ac(IXa, IXb)

Reagents: a) HCl, b) 40% KOH, c) H_3O^+, d) CH_2N_2, e) i-Bu_2AlH, f) TsCl/Py,
g) $C_6H_{13}MgCl/CuJ$, h) Ph_2Se_2/H_2O_2, i) t-BuOOH, j) O_3/CH_2Cl_2,
k) Me_2S/MeOH, l) 10% HCl, m) $BrPh_3P$  , n-BuLi/THF,
n) $O_2/PdCl_2$-CuCl, THF-H_2O, o) $NaBH_4$, p) H_2-Pt, q)HPLC,
r) Ac_2O/Et_3N/DMAP .

ENZYMATIC HYDROLYSIS OF CORTICOSTEROIDAL ESTERS

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Some corticosteroidal esters are resistant because of steric reasons to usual hydrolysing reagents in mild conditions. More drastic methods are not possible in the presence of sesitive groups such as dihydroxyacetone chain. We have paid attention especially to hydrolysis of 11β, 17α,21-triacetate of prednisolone, 21-tetrahydrophthalate of prednisolone and 21-pivalate of flumethasone. Several enzymatic preparations obtained from plants (oat and sunflower), fungi (Curvularia lunata, Curvularia tuberculata, Aspergillus oryzae) and bacteria (Pseudomonas aeruginosa, Aeromonas hydrophila) have been investigated.

DIENONE - PHENOL REARRANGEMENT OF 6α - AND 6ß-METHYL 3,17-DIOXO-ANDROSTA-1,4-DIENE

Thomas Henkel[1], Sven Ring[2], Andrea Porzel[3], Dieter Klemm[1], and Sigfrid Schwarz*[2]

[1]Friedrich Schiller University, Institute of Organic and Polymer Chemistry, D- 0-6900 Jena

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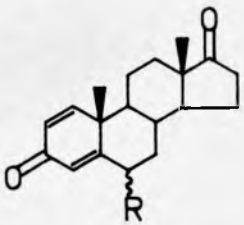
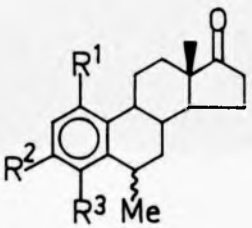
[3]Institute of Plant Biochemistry, D- 0-4020 Halle

In connection with a synthesis of methyl prednisolone from ADD (1) via the 6-methyl derivatives 2 and 3 /1/ the dienone-phenol rearrangement of the compounds 2 and 3 was studied with regard to the products formed and the temperature dependence /2/.



1: R=H
2: R=ß-Me
3: R=α-Me



4: R^1=Me; R^2=OAc; R^3=H; 6ß-Me
5: R^1=Me; R^2=H; R^3=OAc; 6α-Me
6: R^1=OAc; R^2=H; R^3=Me; 6α-Me
7: R^1=Me; R^2=OAc; R^3=H; 6α-Me

Rearrangement of 6ß-Me ADD (2) gave mainly the meta product 4 besides the para compounds 5 and 6. Transformation of 6α-Me ADD (3) lead to the para compounds 5 and 6 in equal yields, whereas the meta products 4 and 7 were formed in a minor amount.
6ß-Me ADD (2) was transformed much faster than 6α-Me ADD (3) or ADD (1) at room temperature. The higher the reaction temperature the lower was the rate difference between the transformation of 2 and 3.

The results can be interpreted on the basis of a generally accepted mechanism of the dienone-phenol rearrangement /3/.

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/3/ R. H. Shapiro in "Steroid Reactions", edit. C. Djerassi, Holden-Day Inc. San Francisco 1963, p. 371

K.-F. Wedemeyer in "Methoden der Organischen Chemie (Houben-Weyl)", Georg Thieme Verlag Stuttgart 1976, Vol. VI/1c, Part 2, pp. 759-783

THE INTRODUCTION OF FLUORINE INTO C-6 POSITION OF 17α-HYDROXY-20-KETOPREGNANES. SYNTHESIS OF 6α-FLUOROCORTEXOLONE.

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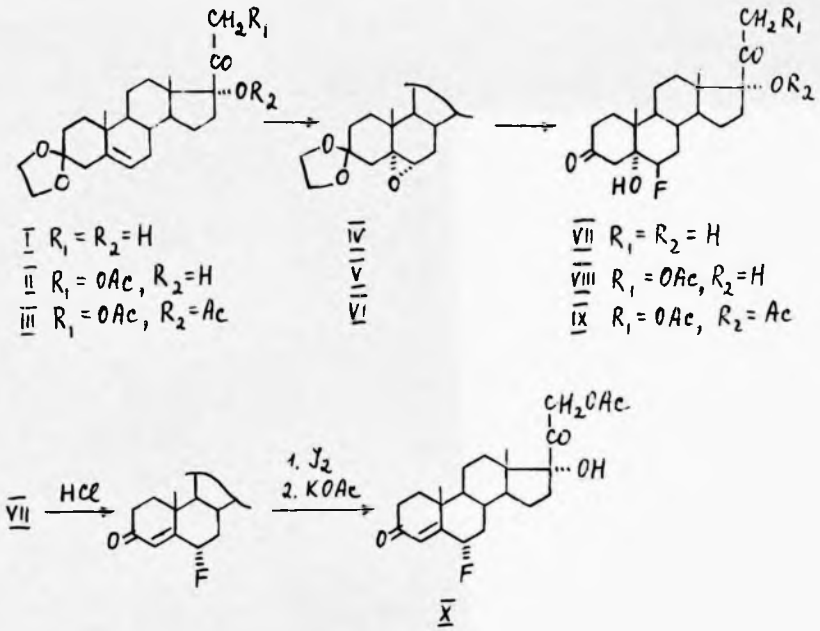
All-Union Research Chemical-Pharmaceutical Institute,
119815 Moscow, Zubovskaya 7, USSR

To work out the approaches to the synthesis of 6-fluorated corticosteroids based on androstendione (AD), a product of microbiological oxidation of sitosterol, we have studied the possibility of fluorine introduction at various stages of the synthesis, namely, into the molecule of 3-ethylene ketal 17α-hydroxyprogesterone (I) and into cortexolone esters of which the synthesis from AD has been sufficiently studied.



To this end the method of opening of 5α,6-epoxides with 70% aqueous hydrogen fluoride obtained by oxidation of the corresponding ethylene ketals (I-III) has been used. Stereoselectivity of the epoxidation process has been studied using different peracids. In case of the compaund (IV), the *trans*-diaxial opening of oxides occured with a quantitative yield while the formation of fluorohydrins (VIII,IX) was accompanied with side reactions of D-homoannulation and hydrolysis of 21-acetoxy group. This allowed us to make the conclusion about the efficiency of the primary introduction of fluorine into 20-ketopregnene (I) with a subsiquent transfer to 6α-fluorocortexolone through dehydration, epimerization of fluorine, iodization and acetoxylation.

SIMPLE CONVERSION OF ALDEHYDES TO 1,1-DICHLOROALKANE AND -1-ALKENE DERIVATIVES

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[a]Central Research Institute for Chemistry
1525 Budapest, P.O.Box 17, HUNGARY

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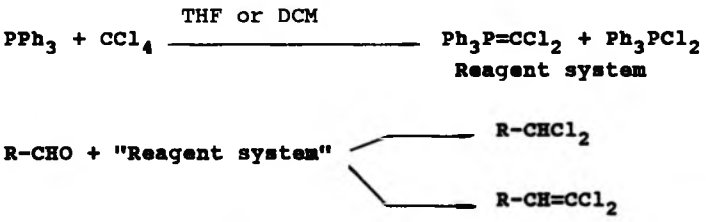
1,1-Dichloroalkanes and 1,1-dichloro-1-alkenes are useful starting materials for the formation of terminal acetylenic bond. With the reagent system, (PPh_3/CCl_4 in appropriate solvent), the reaction affords saturated or unsaturated dichloro-derivatives depending on the solvent used.



This method can be used conveniently for the preparation of pheromones in large scale.

LIGHT-INDUCED CAROTENOGENESIS IN NEUROSPORA CRASSA: STEPS OF THE SIGNAL TRANSDUCTION MECHANISM.

T.A.Belozerskaya, N.N.Levina, T.V.Potapova, M.S.Kritsky
A.N.Bach Institute of Biochemistry USSR Academy of Sciences, Moscow, USSR.

Blue light sensitive photoreceptor mechanism in the cells of N.crassa provides for the regulation of carotenoid biosynthesis via expression of albino genes: al-1, al-2, al-3 and the gene white collar 1 (wc-1) concedered to have a damage in photoregulation process. It has been shown that the blue light signal transduction chain includes two transient photoelectric reactions of the plasma membrane: the input resistance change on the 2 - 5 min of illumination and plasma membrane hyperpolarization with the maximum on the 25th min of illumination. Those photoelectric reactions of the plasma membrane may be mediated by changes in the cyclic AMP system. Mutant strains of N.crassa with impaired synthesis of the soluble and particulate enzyme activities catalyzing phytoene formation and dehydrogenation differ significantly in their electrical parameters (membrane potential (MP), input resistance and electrical coupling coefficient (K_{ec}) from the same parameters of the wild type strain. The albino mutations block photoelectrical reactions of the N.crassa plasma membrane. MP value of the wc-1 mutant was about 1,3 times lower and the K_{ec} between the cells was 2,5 times lower than those of the wild type strain. The mutant wc-1 lacked the ability to respond to light by shifts in the electrical properties of its plasma membrane. Those facts suggest that the relationship exists in N.crassa between the functional properties of the cell membranes and the photosensory transduction chain leading to carotenoid biosynthesis in the N.crassa cells.

STEROLS IN CAROTENOIDLESS MUTANTS OF NEUROSPORA CRASSA

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A.N.Bach Institute of Biochemistry of the USSR Academy of Sciences, 33 Leninsky Prospekt, Moscow, 117071, USSR

Sterols and carotenoids play an important role in control of the membrane properties as well as in regulation of growth cycle and reproduction of fungi. To reveal a relationship between metabolism of the two groups of prenyl lipids we have compared the composition of sterols in a wild type strain R2 of N.crassa and in some mutants defective in different reactions of carotenoid biosynthesis. The mutants R133 (albino-3), R184 (albino-2) and R200 (albino-1) are lacking respectively prenyl transferase, phytoene synthase and phytoene desaturase reactions and are incapable to produce carotenoids in response to photoinduction.

The N.crassa mycelium was cultivated in a shaken liquid culture in Vogel medium in the dark. Lipids were extracted by acetone and then hydrolyzed with KOH in MeOH. Sterols were isolated from an unsaponified fraction by TCL on Silufol with EtOAc-hexane (1:1) and estimated by GLC using 3% OW17 column at the temperature 235^{o}C. The sterols content was estimated by comparison of their peak areas with that of preadded standard.

Two main compounds - ergosterol and fecosterol - are present in sterol fraction of a wild type and of all three mutants and one more unidentified sterol has been found in al-2 and al-3 cells. The sterol content increases during mycelial aging: in all the strains it increases from about 30 μg/g dry wt in the 24 hrs cultures up to 90-130 μg/g dry wt in the 48hrs ones. After 72hrs al-1 mycelium shows a difference in the sterol content with a wild type (220 μg/g dry wt against 430 μg/g dry wt in wild type cells).

Induction of coloured carotenoid biosynthesis by illumination of the dark grown 48 hrs wild type mycelium is accompanied by a two fold increase of sterol content. Under the same illumination conditions some increase of sterol content is observed in al-1 cells, but not in the al-2 or in al-3 mutants.

Incorporation of [2-^{14}C]-mevalonate into the sterol fraction of cell free extracts was studied. to estimate the rate of sterol biosynthesis in wild type and mutant cells. In this experiment 20 hrs dark grown cultures were examined. After 2 hrs incubation with [2-^{14}C]-mevalonate the radioactivity of sterol fraction in the extracts from wild type cells times exceeded three - four times that in the al-1 cells.

It can be concluded that a relationship between sterol and carotenoid biosynthetic pathways can be revealed in N.crassa under the conditions when carotenoid formation is blocked due to genetic lesions or is activated by light. Genetic impairment of carotenoid metabolism influences the content, composition and rate of biosynthesis of sterols. It can be assumed that some components both of phytoene formation and phytoene desaturation steps may play roles in the control of sterol pathway.

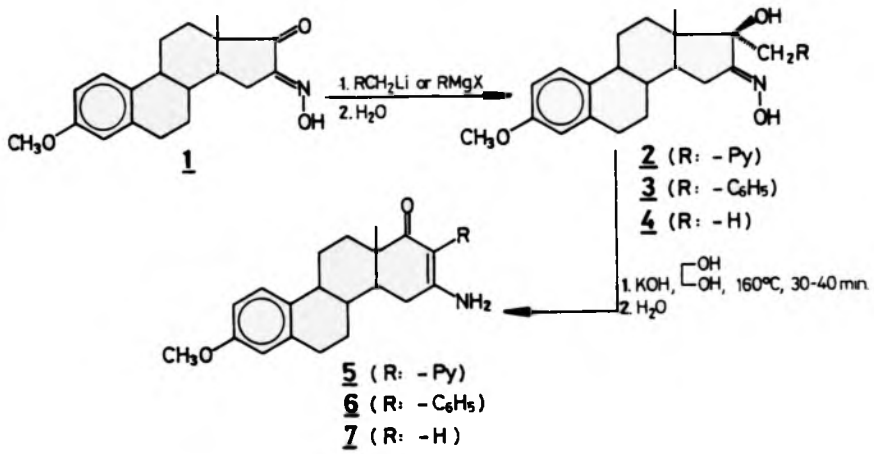
A NEW ROUTE TO D-HOMO-ESTRONE DERIVATIVES

Evgenija Djurendić[1], Ljubica Medić-Mijačević[2], Katarina Gaši[1], Dušan Miljković[1], Slobodanka Stanković[3]

1. Institute of Chemistry, Faculty of Sciences, 21000 Novi Sad, Yugoslavia
2. Pharmaceutical and Chemical Industry "Galenika" 11000 Belgrade, Yugoslavia
3. Institute of Physics, Faculty of Sciences, 21000 Novi Sad, Yugoslavia

A new synthetic route to D-homo estrone derivatives was achieved starting from oximino ketone 1[1]. Addition of α-picolyl-lithium, benzyllithium and methyl magnesium-iodide to the 17-oxo-group of 1, followed by "one-pot" fragmentation-cyclization reaction of the obtained intermediates 2, 3 and 4[2] (Scheme 1.) afforded D-homo estrone derivatives 5, 6 and 7.

The structures of newly synthesized compounds were confirmed by spectroscopic data and X-ray structural analysis.



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SYNTHESIS AND BECKMANN FRAGMENTATION REACTION OF 3-METHOXY-6α,17β-DIHYDROXYESTRA-1,3,5(10)-TRIENE-7-ONE OXIME

Vjera Pejanović[1], Dušan Miljković[2], Julijana Petrović*[2], János Csanádi[2] and Slobodanka Stanković [3]

[1]Pharmaceutical and Chemical Industry "Galenika", 11000 Belgrade, 29. Novembra 111, Yugoslavia
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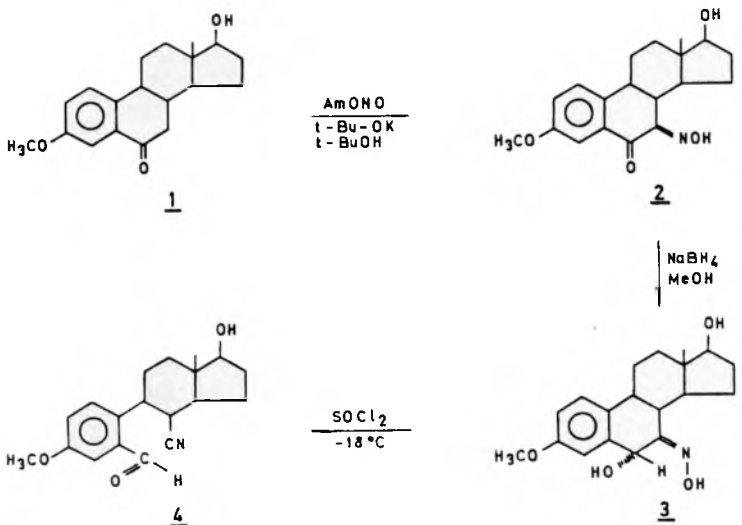
3-Methoxy-17β-hydroxyestra-1,3,5(10)-triene-6-one (1, Scheme 1) was firstly converted to the corresponding 7-oximino derivative 2, and then reduced with $NaBH_4$ to 6α-hydroxy-7-oximino derivative 3. X-Ray structural analysis revealed syn-geometry for 3. The Beckmann fragmentation reaction was performed by an action of $SOCl_2$ on 3, whereby seco-cyanoaldehyde 4 was obtained, instead of the expected seco-oxo-iso-cyanide[1], most likely through a six-membered cyclic O,O,N-sulfite intermediate.



Scheme 1

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HIGH-PRESSURE LIQUID CHROMATOGRAPHY ANALYSIS OF OX BILE CONJUGATES, ACIDS AND AMIDES IN MIXTURES

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Insitute of Chemistry, Faculty of Sciences, University of Novi Sad,21000 Novi Sad, Trg Dositeja Obradovića 3, Yugoslavia

During various stages of ox bile processing,complex mixtures of numerous bile acid derivatives can be formed. In our study on ammonolysis of conjugated ox bile acids, a complex mixture containing unreacted glyco- and tauro-conjugates of cholic and deoxycholic acids, free bile acids, as well as unsubstituted amides of cholic and deoxycholic acids were formed. So far, several high pressure liquid chromatography methods for determination of solely conjugated bile acids[1,2] and/or free bile acids[3] in their mixtures have been described. On contrary, similar data do not exist in the literature for bile acid amides.

In this work determination of the individual constituents in the complex ammonolysis mixtures have been successfully performed. Optimal conditions involve Novopac-C-18 column and the mobile phase consisting methanol-water-acetate buffer, pH = 4.3.

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TERPENOIDS IN TWO PERUVIAN ASTERACEAE

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** Shanghai Institue of Pharmaceutical Industry, Beijing Road 1320, Shanghai, People's Republic of China

In continuation of our studies on peruvian medicinal plants (1-3) we studied terpenoidic fraction of two Asteraceae, *Diplostephium foliosissimum* Blake and *Tessaria integrifolia* R. et P. The first plant is used to calm intestinal and gastric pains and to cure hypotension; the other as an antipyretic, a cholagogue and an hepatical riactivator.

Terpenoidic fraction was isolated in usual manner (4) and consitutents were determined by GLC and GC/MS methods.

The triterpenoidic fraction shows tetra- and pentacyclic triterpenes. Between tetracyclic compounds Δ^5 sterols in *D. foliosissimum* are approximatively a quarter of the total terpenoidic fraction, whereas in *T. integrifolia* they are present in very low amounts.

Pentacyclic compounds were α– and β–amyrin, bauerenol and 3-oxo-urs-12-en-24-oic acid, but they are present in low amounts.

Other terpenoidic compounds are constituted by mono- and sesquiterpenes, present in greater amount in *T. integrifolia*.

References

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3) D'Agostino M., De Feo V., De Simone F., Pizza C. (1990) *Fitoterapia* **61**, 477.

4) Senatore F., De Simone F., Dini A., Ramundo E., Basso F. (1990) *Riv. Ital. Sost. Grasse*, **LXVII**, 503.

STEROL CONTENTS IN TWO *LATHYRUS* SPP. SEEDS

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** Dipartimento di Produzione Vegetale, Facoltà di Agraria, via N. Sauro,85 - 85100 Potenza, Italy

Among the cultivated herbaceous plants, the grain Leguminosae represents a large food source. Nevertheless, except for peanut, soya or bean, only few researches have been conducted on other Leguminosae.

In this paper, as a continuation of our previous investigations on Leguminosae (1-4), we report on the sterol contents of two Papilionaceae native to Europe: *Lathyrus sativus* L. (cicerchia) and *Lathyrus cicera* L. (mocho), both formerly widely cultivated in Southern Italy for human consumption and animal feed.

Sterol extraction, separation and purification were accomplished as previously described (4). Identification of sterols was performed by GLC and GC/MS analyses.

C_{29} sterols are the principal sterols with lesser amounts of C_{27} and C_{28} sterols. β–sitosterol predominates, the second most abundant sterol was stigmasterol. Also low amounts of β–amyrin were detected.

References

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ENANTIOSELECTIVE SYNTHESIS OF (−)-MINTLACTONE AND (+)-ISOMINTLACTONE

Miguel Carda and J. Alberto Marco

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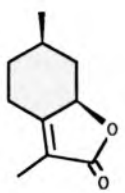
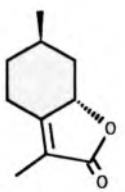
The essential oil of *Mentha piperita* L. (peppermint oil) is one of the most important commercial flavoring materials and is produced in many countries. Its chemical composition has been thoroughly investigated, more than 300 components having been reported. Among the minor constituents, (−)-mintlactone **1** and (+)-isomintlactone **2** were isolated from a sample of American peppermint oil.[1]



1



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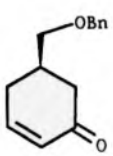
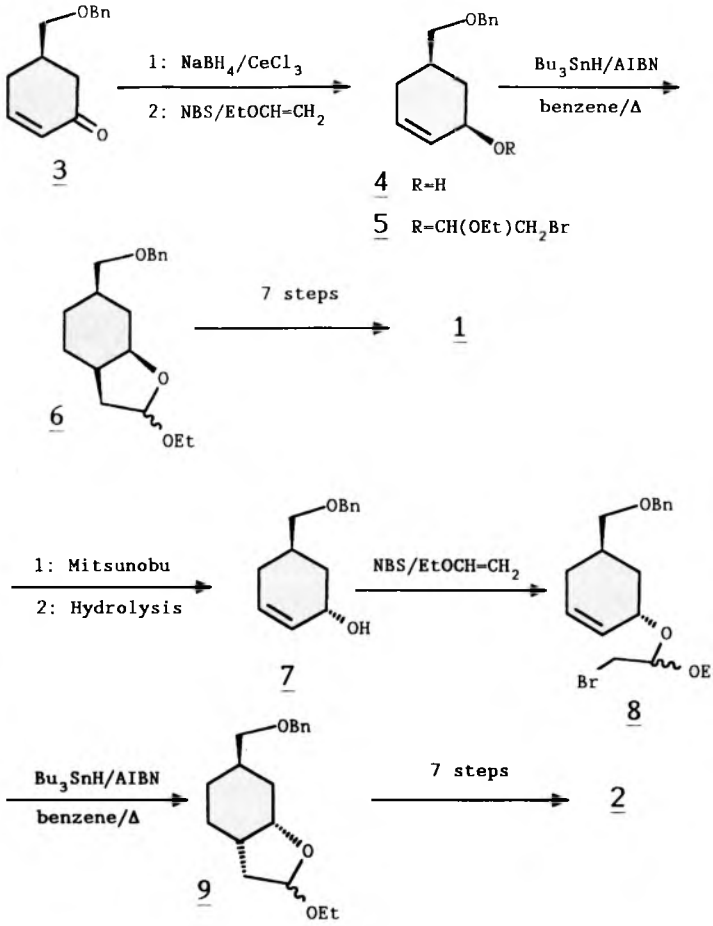


3

Before their first description as natural products, these compounds had been reported among the products formed during photoooxidation of menthofurane.[2,3] Racemic **1** was also an intermediate in a total synthesis of menthofurane.[4] Very recently, a nonselective synthesis of racemic **1** and **2** has been published.[5] We now wish to report the first stereodirected synthesis of optically active **1** and **2**, using the chiral enone **3**[6] as the starting material. The key step in each synthesis was a stereoselective, radical mediated ring closure, **5** → **6** and **8** → **9**.



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PHYTOECDYSTEROID PRODUCTION AND ACCUMULATION IN *AJUGA REPTANS* L. *IN VIVO* AND *IN VITRO* CULTURES

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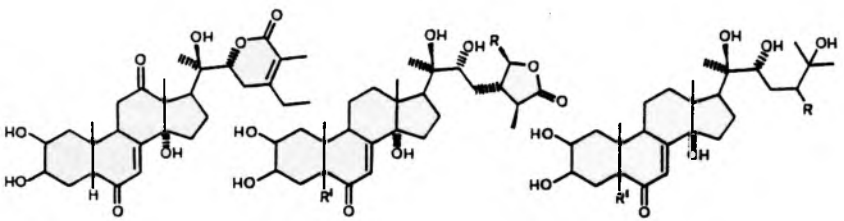
The phytoecdysteroids produced by *Ajuga reptans* (Labiatae) have been described earlier, as well as their efficient HPLC determination (1-3). Recently, we became interested in the possibility of obtaining these metabolites from cultured material, and thus, phytoecdysteroid production and accumulation in *A.reptans* have been studied in plant substrates of either *in vivo* or *in vitro* origin. The relationship of phytoecdysteroid relative concentration with growing conditions and source of tissue are discussed.



ajugalactone (AJL)

cyasterone (CY) R=Me,R'=H
29-norcyasterone (29NC) R=R'=H
sengosterone (SG) R=Me,R'=OH
29-norsengosterone (29NS) R=H,R'=OH

8-ecdysone (20E) R=R'=H
sakisterone A R=Me,R'=H
polypodine B (520E) R=H,R'=OH

The ratio of C_{28} /C_{29} phytoecdysteroids was established amongst the major compounds (29NS+29NC/CY+AJL) representing an averageof 92% of the total content. This ratio was found to be <1 in all types of leaves from wild material, slightly higher than 1 in the roots of wild plants, and in the range from 3 to 5 in greenhouse and *in vitro* propagated plants. Micropropagated plants had an extremely low content in leaves, whereas that in roots was the highest detected in our experiments. Callus cultures obtained from leaves completely lost their capacity to produce ecdysteroids.

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ISOLATION AND STRUCTURAL INVESTIGATION OF RHAPONTICUM CARTHAMOIDES SEEDS PHYTOECDYSTEROIDS

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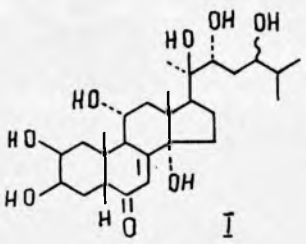
It has been reported earlier that Rh.carthamoides roots are a rich source of ecdysteroids (1). In the present work there are given the results of Rh.carthamoides seeds phytoecdysteroids investigation.

Air-dried Rh.carthamoides seeds were extracted with mathanol. After the corresponding treatment on column chromatography on silica gel alongside with the known ecdysteroids - ecdysteron, 2-desoxyecdysteron, 24(28)-dehydromakysteron A and 20,22-monoacetonide of ecdysteron there have been isolated 2 new ecdysteroids which have been named rapisterons B(I), C(II).

The structure of new ecdysteroids has been proved on the basis of physical-chemical methods of the investigation with the use of 2D corelation NMR spectroscopy (2D-cosy) $^{1}H - ^{1}H$ and $^{1}H - ^{13}C$.



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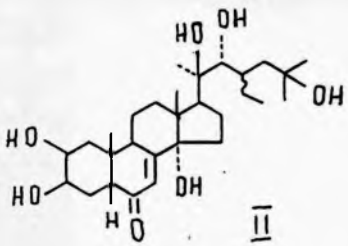

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BRASSINOSTEROIDS

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

Synthesis of new brassinosteroids and their biological activities in the second bean internode bioassay[3] will be given.

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BIOTRANSFORMATION OF MONOTERPENES BY FREE AND IMMOBILIZED PLANT CELL CULTURES.

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The utilization of plant cell cultures for the production and biotransformation of secondary metabolites has been studied extensively.
For biotransformation experiments both natural (e.g. digitoxigenine[1]) and synthetic substances (e.g. 2-(4-methoxybenzyl)-1-cyclohexanone[2]) were used. In this contribution the results concerning the biotransformation of the whole range of monoterpenes (Tab. 1.) by cell cultures of *Solanum aviculare* and *Dioscorea deltoidea* have been presented.

Table 1. Monoterpenes used as a starting compounds

SUBSTRATE	PLANT CELL CULTURES	
	Solanum aviculare	*Dioscorea deltoidea*
cis-verbenol	+	
trans-verbenol	+	
verbenone	+	
thujol	+	+
thujone	+	+
isothujol	+	+
neothujol	+	+
neoisothujol	+	+
(-)-limonene	+	+
(+)-*delta*-3-karene	+	+
(-)-*alfa*-pinene		+
citronellal	+	

For these experiments both free and immobilized plant cells were used. The a immobilization methods included entrapment into the gells (alginate, carrageenane and pectate[3]), immobilization to the polyurethane foam and covalent coupling on the surface the solid carrier[4]. The effect of various immobilization techniques on the course of biotransformation reaction has been evaluated and discussed.

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SYNTHESIS OF 17β-(2'-THIAZOLYL)-ANDROST-5-ENE DERIVATIVES

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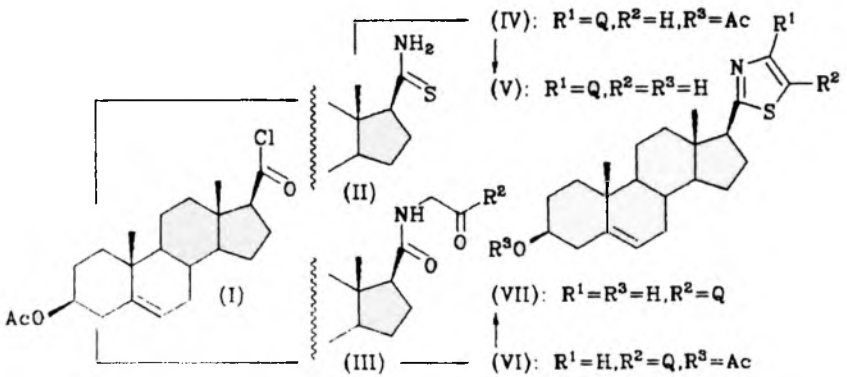
The thiazole ring attached to the steroidal skeleton has aroused great interest due to the biological properties. Since only 2'-substituted 17β-(4'-thiazolyl)-androstenes have appeared in the literature we decided to prepare steroids linked in the 17β-position to the 2'-carbon atom of the thiazole moiety. Starting from 3β-acetoxyandrost-5-ene--17β-carboxylic acid chloride (I) we prepared thiocarboxamide (II) which underwent condensation with bromoacetone, bromoacetophenone, and bromoacetic acid esters yielding 4'-substituted 17β-(2'-thiazolyl)-androst-5-en-3β--ol acetates (IV). Acylation of aminoacetone, aminoacetophenone, and glycine esters by (I) led to the amides (III). Cyclization of (III) under heating with phosphorus pentasulfide in dioxane afforded isomeric 5'-substituted 2'--thiazolyl derivatives (VI). Alkaline hydrolysis of acetates (IV) and (VI) gave alcohols (V) and (VII).



Q = Me,Ph,MeO,EtO,PrO

COMPLETE ANALYSIS OF PROTON NMR SPECTRA OF CORTISOL 21-GLUCURONIDE AND ITS METHYL ESTER TRIACETATE

Ivan Černý and Miloš Buděšínský

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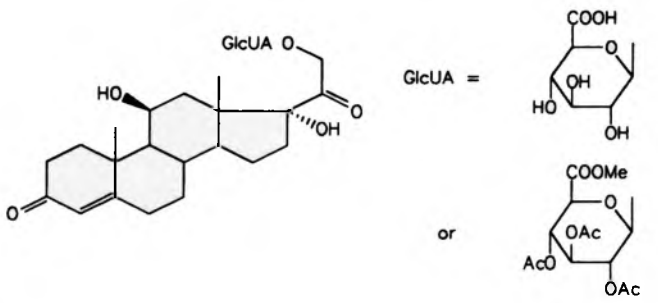
Recently the high field ^{1}H-NMR spectrometers in connection with modern 2D-NMR techniques made possible to assign all protons in ^{1}H-NMR spectra of some steroid derivatives[1]. We have used this attempt for proving the structure of synthetic[2] cortisol glucuronide and its protected derivative. From 1D- and 2D-^{1}H-NMR spectra at 500 MHz the complete sets of proton chemical shifts and interproton coupling constants were obtained and compared with published data of parent cortisol.



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SYNTHESIS OF STIGMASTEROL AND SITOSTEROL CONJUGATES

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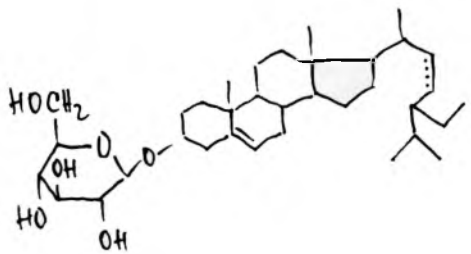

It has been reported recently[1] that the mixture of acetylated glucosides of sitosterol and stigmasterol showed interesting biological activity, i.a. cardiotonic.

Using Paulsen[2] glycosylation method there were prepared both compounds representing biological interest. The compounds were submitted to testing in the form of peracetates as well as with the free carbohydrate moieties. For the sake of comparison of the biological properties with the other type of common conjugates there were synthesized also sodium salts of sulphates of both sterols.

The structure has been confirmed by the ^{1}H-NMR and IR spectroscopy.

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