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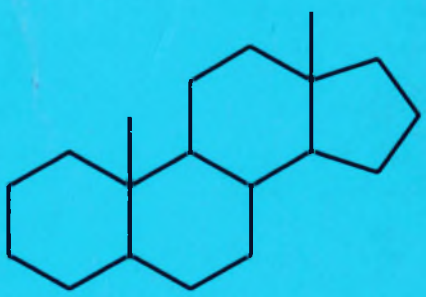
XV CONFERENCE ON ISOPRENOIDS



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Zakopane, Poland 20–25 September, 1993

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G. Vidari
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Plenary Lectures Abstracts

ISOLATION AND STRUCTURAL STUDIES ON NOVEL NATURAL PRODUCTS OF ISOPRENOID ORIGIN

ATTA-UR-RAHMAN*, M.I. CHOUDHARY and HABIB NASIR

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Karachi-75270, Pakistan
Fax Nos. (92-21) 4963373/4963124

There has been an explosive growth in NMR spectroscopy in recent years. The advent of such 1D and 2D techniques as DEPT, COSY, NOED, NOESY, 2D J-resolved, normal and long-range hetero-COSY/COLOC, 2-D INADEQUATE, HOHAHA etc. [1,2] have provided the organic chemist with powerful new tools for structure elucidation of complex natural products. Inverse measurement techniques such as HMBC and HMQC have allowed substantial enhancements of sensitivity in the heteronuclear shift correlation experiment. Some of these new methods will be presented, and their use illustrated with examples of structure elucidation of new natural products from medicinal plants.

Our work on a number of medicinal plants has recently led to the isolation and structure elucidation of a host of new natural products of isoprenoid origin. Modern techniques, particularly 2D-NMR and NOE difference measurements have been used to assign their structures and stereochemistry.

We have reported a number of steroidal alkaloids from the leaves *Buxus papillosa*. Work on the roots of this plant has resulted in the isolation and characterization of novel triterpenoides, buxapentalactone (1) and buxahejrine (2). Their structures were determined exploiting X-ray and recently developed NMR and other spectroscopic techniques.

Dihydroxypetchenol (3) was isolated from *Petchia ceylanica*, a Sri Lankan origin plant. This triterpene of ursane series contains an exocyclic double bond at C-19. In addition it contains two hydroxy groups at C-3β and C-28 positions. The structure was finalized with the help of EIMS, HREIMS, Linkscan with 2D-NMR techniques including inverse experiments such as HMBC, HMQC and HOHAHA experiments.

A new steroidal alkaloid buxidienine-A (4) was isolated from the leaves of *Buxus longifolia* of Turkish origin. The structure of buxidienine-A was determined by using 2D NMR techniques such as COSY-45°, HMQC and HMBC, etc.

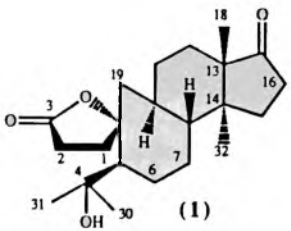
2-Dehydroxy-O_2-buxafuranamine (5), another steroidal alkaloid containing tetrahydrofuran ring was isolated from *Buxus hildebrandtii* of African origin and its structure was determined using the 1D, 2D NMR and other spectroscopic techniques.

Macroxine (6) was isolated from the leaves of *Alstonia macrophylla*. The structure was elucidated on the basis of modern spectroscopic methods.

The structure elucidation of a number of other novel compounds will also be discussed during the lecture highlighting the potential of modern 2D-NMR spectroscopic studies for structure determination of complex natural products.

References

1. Atta-ur-Rahman, Nuclear Magnetic Resonance Spectroscopy, Springer Verlag, New York (1986). Japanese translation by M. Tori and H. Hirota, Springer-Verlag, Tokyo (1988).
2. Atta-ur-Rahman, One and Two Dimensional Nuclear Magnetic Resonance Spectroscopy, Elsevier Science Publishers, Amsterdam (1989).



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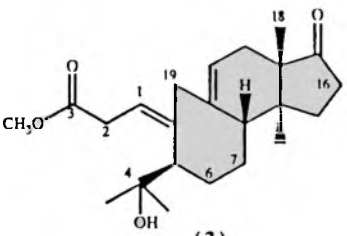

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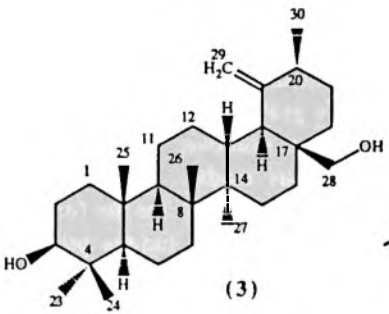

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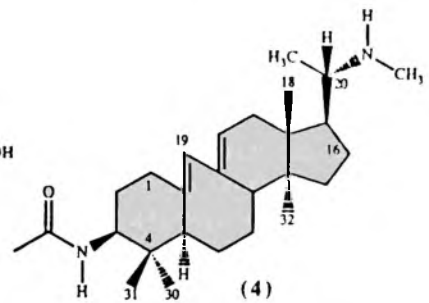

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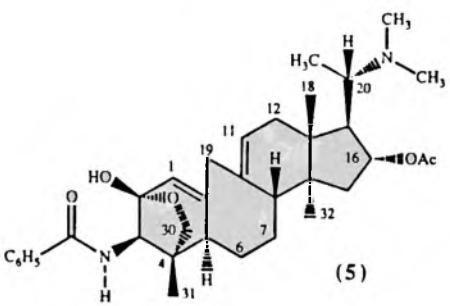

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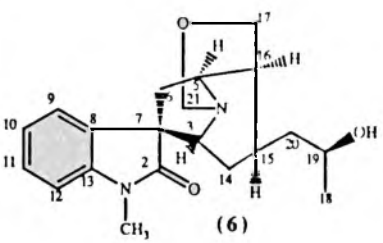
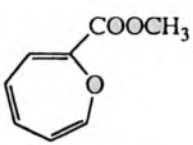


(6)

The Tremulenes, A New Type of Sesquiterpene. Structural and Biosynthetic Studies.

William A. Ayer and Elizabete R. Cruz
Department of Chemistry, University of Alberta,
Edmonton, Alberta T6G 2G2, Canada

The fungus *Phellinus tremulae* (= *Fomes igniarius* var. *populus*) causes severe heartwood rot in trembling aspen (*Populus tremuloides*), an economically important hardwood in Canada. We have studied the metabolites produced when *P. tremulae* is grown in liquid malt extract broth in the presence of DIAION HP20, a nonionic resin useful in removing nonpolar metabolites from aqueous media. In addition to 2-carbomethoxyoxepin (**1**), isolated from natural sources for the first time (Ayer and Cruz, *Tetrahedron Letters*, in press), the fungus produced several sesquiterpenes which possess the bicyclo[5.3.0]decane skeleton **2**, a new skeleton among the sesquiterpenes.



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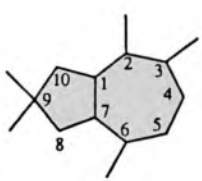

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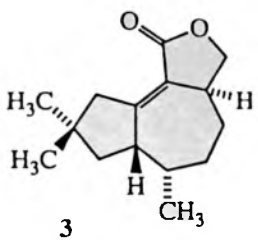


3

Tremulenolide A (**3**) is representative of these new sesquiterpenes. The structure elucidation of tremulenolide A (**3**) and several other members of this new class will be described.

The tremulanes (**2**) cannot be derived in a straightforward manner from farnesyl pyrophosphate. Biosynthetic studies utilizing singly- and doubly-labelled acetate suggest a biogenetic pathway involving condensation of isopentenyl pyrophosphate and an irregular monoterpene of the chrysanthemyl skeleton. The biosynthetic studies will be discussed.

LECTURE TITLE: Recent Progress in the Design and Testing of Chiral Adjuvants for Stoichiometric and Catalytic Asymmetric Synthesis

R. K. Boeckman, Jr.

Department of Chemistry, University of Rochester, Rochester, NY 14627, U.S.A

Efforts underway in our laboratories to design general new chiral auxiliaries and to understand the structural features which are responsible for their ability to exhibit diastereoselection in a variety of reactions will be discussed. The design criteria employed will be enumerated and the rationale for the selection of the inital camphor-derived systems will be developed. Examples of the utility of the initial auxiliaries in Diels-Alder cycloaddition, alkylation, aldol, and 2+2 cycloaddition reactions will be described. Limitations on the scope of effective use of these auxiliaries will be outlined, and a mechanistic rationale for the limitations as well as a predictive model for the sense of asymmetric induction will be proposed.

The design and preparation of a second generation group of auxiliaries will be described along with initial studies comparing these new auxiliaries with the first generation in cycloaddition and other reactions. Initial attempts to convert these auxiliaries into chiral catalysts suitable for use in cycloaddition and other reactions will be discussed if time permits.

STRUCTURAL ELUCIDATION OF NATURAL PRODUCTS

Joseph D. Cornolly.

Department of Chemistry, University of Glasgow,

Glasgow G12 8QQ, Scotland, U.K.

The structural elucidation of a range of compounds including squalene derivatives from the Meliaceae and Euphorbiaceae, methylated flavones from the Annonaceae and terpenoids from the Hepaticae and from Salvia species will be described. The use of computer assisted structural elucidation will be illustrated for some of these compounds[1].

Reference

(1) J.-M. Nuzillard and G. Massiot, *Tetrahedron*, 1991, **47**, 3655.

ISOPRENOIDS IN SYSTEMS OF CHEMICAL COMMUNICATION

Wittko Francke
Institute of Organic Chemistry
Martin-Luther-King-Platz 6
D-20146 Hamburg

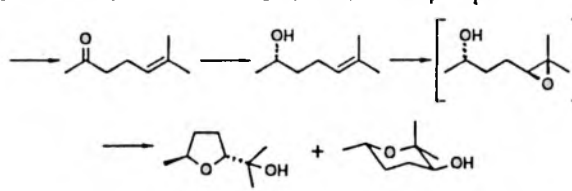
Apart from acetogenins, isoprenoids constitute the most widespread class of compounds used in chemical communication between animals. Almost all types of signals, from sex pheromones to highly potent defense substances, are found among the mevalogenins. Many of these seem to be directly sequestered from plants or represent simple transformation products thereof. It has, however, been shown that *de novo* synthesis may also take place. Sometimes associated microorganisms play an important role in the production of terpenoids: they may be involved in *de novo* synthesis as well as in secondary (or tertiary) transformations of plant-derived compounds.

The lecture will provide an overview over isoprenoids used as semiochemicals and will show close relationships in structural principles of chemical communication among many insect species.

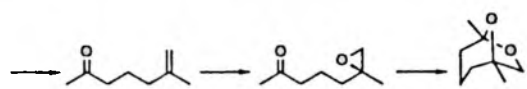
Many variations of "oxygenated isoprene" have been identified, however it is not always clear whether such iso-C_5-units represent metabolites of higher terpenes or direct derivatives of mevalonate or whether they are produced from leucine.

Monoterpenes are particularly important in systems of bark beetle communication, but they were also found in many other insect species. Distinct sequences of simple biotransformations of monoterpenes may produce volatiles which represent highly intra- or interspecific signals. This is exemplified by the stereoselective epoxidation of 6-methylhepten-2-ones in some bark beetle species:

a) *Pteleobius vittatus* start from a monoterpene precursor



b) *Dendroctonus simplex* start from a monoterpene precursor



Sesquiterpenes and diterpenes are less frequently found as insect-semiochemicals.

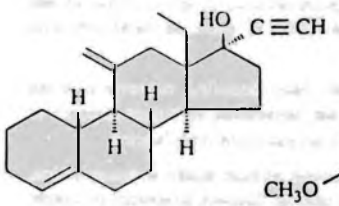
APPROACHES TOWARDS THE TOTAL SYNTHESIS OF DESOGESTREL

M.B. Groen and E.M. Groen-Piotrowska

Organon Scientific Development Group, P.O. Box 20,
5340 BH Oss, The Netherlands

Desogestrel (**1**) is a potent progestagen widely used for oral contraception. Its current production process is based on partial synthesis starting from natural steroids such as diosgenin. Starting from diosgenin the entire process involves 24 steps, including some critical reactions i.a. a high dilution intramolecular hypoiodite reaction.

Total syntheses offer an attractive alternative as the routes can be tailored towards specific structural features of **1** and, therefore, are potentially shorter than the partial synthesis used. Among the many conceivable routes leading to **1** we have focussed i.a. on intermediates having an aromatic A-ring and a functionalized C-11 position, such as **2** and **3**, as previously routes from **2** and **3** to **1** had been developed in our laboratory.



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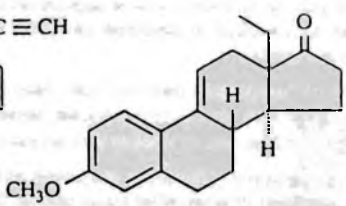

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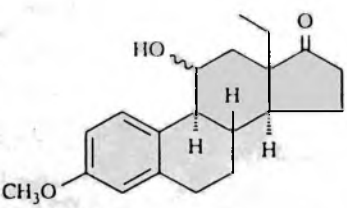

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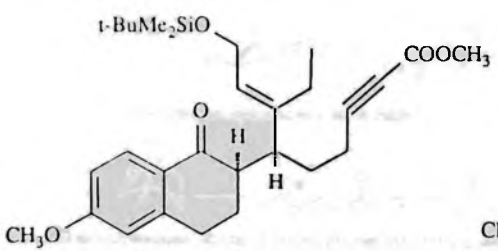
The synthesis of **3** was accomplished some years ago by a modification of the Johnson-Bartlett synthesis of estrone, which, however, suffered from some inefficient steps. Recently, we completed the synthesis of **2** by an adaptation of Mikami's strategy for the 13-methyl analogue. Key step in this synthesis is the ene-reaction of **4**, which gave the desired secosteroid **5**, along with



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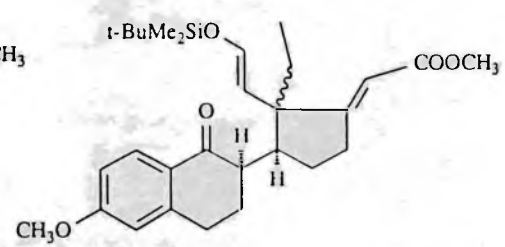


5 13 β-ethyl
6 13 α-ethyl

the 13α-isomer **6**. Compound **5** was converted in 7 steps into the relay compound **2**, using an intramolecular Wittig reaction to construct the steroid C-ring.

TRANSFORMATION OF PHYTOECDYSTEROIDS FOR ANALYTICAL AND CHEMOECOLOGICAL USE

Juraj Harmatha, Jaroslav Píš and Miloš Buděšínský

Institute of Organic Chemistry and Biochemistry,
Academy of Sciences of the Czech Republic,
166 10-Prague, The Czech Republic

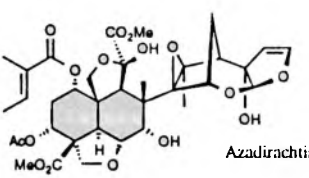
Ecdysteroids represent a widely distributed family of natural compounds occurring both in plants and invertebrates. They regulate a series of important physiological functions in insects. However, their function in plants and in the plant-insect chemical interaction is not yet enough apparent. To study this function, a range of ecdysteroid derivatives has to be prepared. In order to prepare analogues of natural ecdysteroid conjugates, a combination of protection groups was applied. Reaction of phenylboronic acid exclusively with the diol in the side chain was used for selective protection. Regioselectivity, quantitative yield as well as properties of formed boronates determined a wide use of this reaction in chemical transformation and analysis of ecdysteroids. Change of chromatographic properties of boronates was used for a simple proof of ecdysteroids by TLC or HPLC and for special separations and purifications. A rapid method was developed for determination of 20,22-hydroxyecdysteroids in biological samples based on solid-phase extraction and fast atom bombardment MS. The *in situ* acylation of hydroxyls with trichloracetylisocyanate (TAI-method) in the NMR sample tube was used for structural analysis of a series ecdysteroid derivatives.

SYNTHESIS AND CHEMISTRY OF THE INSECT ANTIFEEDANT AZADIRACHTIN

Steven V. Ley
Department of Chemistry, University of Cambridge,
Lensfield Road, Cambridge CB2 1EW

The insect antifeedant and growth disruptant Azadirachtin (1), isolated from the Neem tree *Azadirachta indica* is showing considerable promise as a new method of pest insect population control.[1] Commercial formulations of the Neem extract such as Margosan O® and Azatin® are now available.

We have been studying the synthesis of azadirachtin and related derivatives with the aim of understanding the structure activity relationships and the fundamental feeding mechanisms and perception by insects.



Azadirachtin (1)

So far we have prepared a number of derivatives of (1) and several partial structures and studied their activities.[2-6] We have also synthesised major components of (1) which we hope will eventually be useful in the total synthesis of the natural product azadirachtin. The new biological data together with recent synthetic efforts will be discussed to illustrate the current position of our research effort in this area.

1) "The Chemistry of Azadirachtin". S. V. Ley, A. A. Denholm and A. Wood, *Nat. Prod. Reports* 1993, 109.

2) For Part 11 see S. V. Ley, J. C. Anderson, W. M. Blaney, E. D. Morgan, R. N. Sheppard, M. S. J. Simmonds, A. M. Z. Slawin, S. C. Smith, D. J. Williams, *Tetrahedron* 1991, *47*, 9231.

3) Part 12, H. C. Kolb, S. V. Ley, A. M. Z. Slawin, D. J. Williams, *J. Chem. Soc. Perkin Trans. 1*, 1992, 2735.

4) Part 13, H. C. Kolb, S. V. Ley, R. N. Sheppard, A. M. Z. Slawin, S. C. Smith, D. J. Williams and A. Wood, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2763.

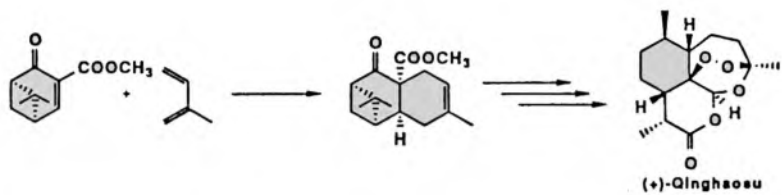
5) Part 14, S. V. Ley, H. Lovell and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1992, 1301.

6) Part 15, S. V. Ley, P. J. Lovell, A. M. Z. Slawin, S. C. Smith, D. J. Williams and A. Wood, *Tetrahedron* 1993, *49*, 1675.

A TOTAL SYNTHESIS OF THE ANTIMALARIAL NATURAL PRODUCT (+)-QINGHAOSU

Hsing-Jang Liu, Wen-Lung Yeh, and Sew Yeu Chew
Department of Chemistry, University of Alberta
Edmonton, Alberta, Canada T6G 2G2

Starting from (-)-β-pinene, an efficient total synthesis of the title antimalarial agent has been accomplished using an intermolecular Diels-Alder approach.



SYNTHETIC STUDIES ON ISOPRENOIDS AS SEMIOCHEMICALS

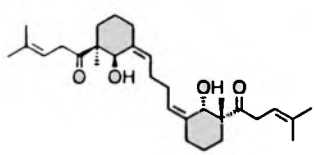
Kenji Mori

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

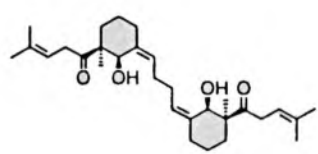
Many isoprenoids are employed as semiochemicals by various organisms. Recent examples of our synthetic studies related to chemical ecology will be discussed.

meso- and (±)-Limatulone (**1a and 1b**), the defensive triterpene metabolites of the limpet *Collisella limatula*, were synthesized. The limpet was found to produce both **1a** and **1b**.

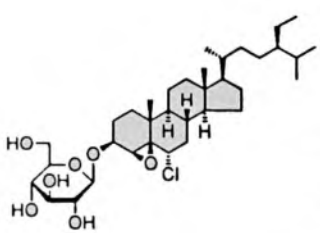
Blattellastanosides A (**2**) and B (**3**) are chlorinated steroid glucosides isolated as the aggregation pheromone of the German cockroach *Blattella germanica*. Both **2** and **3** were synthesized by starting from stigmasterol.



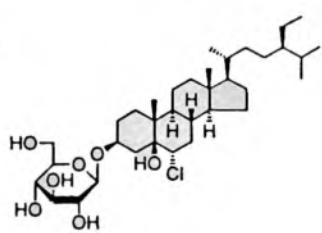
meso-Limatulone (**1a**)



(±)-Limatulone (**1b**)



Blattellastanoside A (**2**)



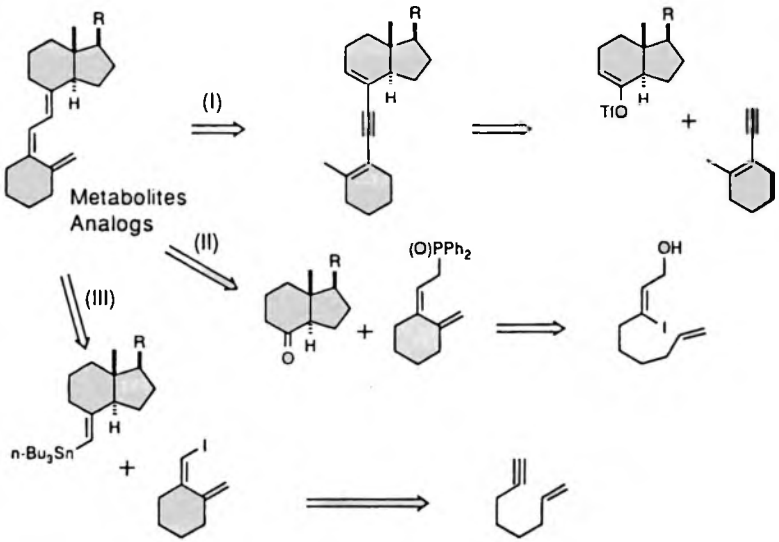
Blattellastanoside B (**3**)

SYNTHESIS OF VITAMIN D METABOLITES AND ANALOGS

Antonio Mouriño

Departamento de Química Orgánica, Facultad de Química y Sección de Alcaloides del CSIC, Universidad de Santiago de Compostela, 15706 Santiago de Compostela, Spain (FAX 34-81-595012)

The application of the dienyne approach (I) and other routes (II,III) to the synthesis of vitamin D metabolites and analogs will be presented.



CHIRAL SELECTIVITY IN ENZYME TRANSFORMATIONS AND CHIRAL CHEMODIVERSITY IN NATURE

Torbjörn Norin

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

Chiral selectivity in enzyme transformations and some aspects on the use of enzymes as a natural tool for organic synthesis will be discussed.

The molecular bases for biodiversity may be termed *chemodiversity*. Many compounds occur in Nature in both enantiomeric forms and this *chiral chemodiversity* provides useful information on the biogenesis of the compounds as well as on taxonomic and phylogenetic relationships.

Chiral chemodiversity is very pronounced among certain classes of natural products whereas other classes of compounds usually occur in only one of the enantiomeric forms. Thus triterpenoids and steroids occur in one enantiomeric forms whereas many of the lower terpenoids are present in Nature in both of their enentiomeric forms.

The chiral chemodiversity among the terpenoids will be discussed in relation to the biological functions of the compounds. The discussion will refer to recent results on the enantiomeric compositions of monoterpenes from various natural sources.[1-7]

References

1. M. Lindstrom, T. Norin, G. Birgersson and F. Schlyter, *J. Chem. Ecol.*, **15**, 541 (1989).
2. M. Lindstrom, T. Norin, J. Roersade, *J. Chromatogr.*, **513**, 315 (1990).
3. A. K. Borg-Karlson, M. Lindström, M. Persson, I. Valterova and T. Norin, *Acta Chem. Scand.*, **B47**, 138 (1993).
4. M. Lindstrom, T. Norin, I. Valterova and J. Vrkoc, *Naturwissenschaften*, **77**,134 (1990).
5. M. Lindstrom, T. Norin, K. Sjödin, *Pure and Appl. Chem.*, **62**, 1329 (1990).
6. I. Valterova, C. R. Unelius, J. Vrkoc and T. Norin, *Phytochemistry*, **31**, 3121 (1992).
7. I. Valterova, M Lindstrom, J. Vrkoc and T. Norin, *Naturwissenschaften*, **79**, 416 (1992).
8. K. Sjodin, M. Persson and T. Norin, *Phytochemistry*, **32**, 53 (1993).
9. M. Persson, A. K. Borg Karlson and T. Norin, *Phytochemistry*, in press.

TERPENE SYNTHESIS BY HOMOGENEOUS ASYMMETRIC CATALYSIS

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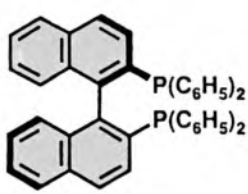
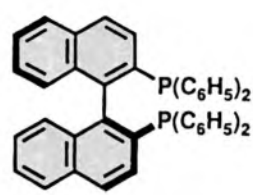
Well-designed metal complexes with chiral organic ligands can discriminate between enantiotopic atoms, groups, or faces in achiral molecules with an accuracy of 10 kJ/mol and catalyzed production of a broad array of chiral compounds of excellent enantiomeric purity. Transition metal complexes containing BINAP (2,2'-bis(diarylphosphino)-1,1'-binaphthyl), an atropisomeric C_2 chiral diphosphine, exhibit an exceptionally high chiral recognition in various homogeneous catalytic reactions, opening tremendous potential to stereoselective organic synthesis. These are not only useful for laboratory synthesis of chiral compounds but also are of industrial significance.

BINAP–Ru(II) complexes catalyze enantioselective hydrogenation of a wide variety of prochiral functionalized olefins and ketones. Geraniol and nerol are hydrogenated with substrate/catalyst mole ratio as high as 50,000 to give natural and unnatural citronellol quantitatively and in 96–99% ee. The optical purity of the products is much higher than that of the naturally occurring compounds. This method is also useful for stereoselective synthesis of the C_{15} side-chain of α-tocopherol.

Cationic BINAP–Rh(I) complexes act as catalysts of asymmetric isomerization of allylic amines to chiral enamines of high enantiomeric purity. The Rh-catalyzed hydrogen-shift reaction of geranyldiethylamine giving the citronellal enamine proceeds via an unusual nitrogen-triggered mechanism. The technical refinement has led to an innovative process working on a 9-ton scale which has been applied to (–)-menthol synthesis.



(*R*)-BINAP



(*S*)-BINAP

IDENTIFICATION AND PURIFICATION OF THE TOCOPHEROL-CYCLASE A NEW ENZYME FROM *ANABAENA VARIABILIS* (*CYANOBACTERIA*)

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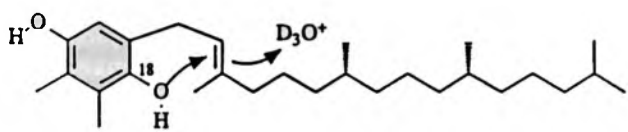
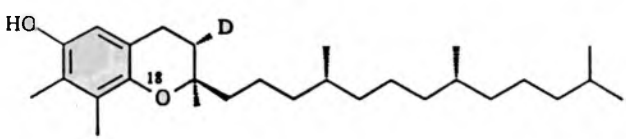
Winterthurerstrasse 190, CH-8057 Zürich

Incubation of spheroplasts of *Anabaena variabilis* (*Cyanobacteria*) with the 2,6-O-dimethyl-β-cyclodextrin complex of 2,3-dimethyl-5-phytylhydroquinone **1** revealed the presence of a new enzyme catalyzing the cyclization of the substrate to give enantiomerically pure γ-tocopherol **2**. Insight into the mechanism of this conversion was obtained by incubation of the synthetic ^{18}O-labelled precursor (4-^{18}O-*H*)-**1** with the enzyme in deuterated buffer yielding (2R,3S,4'R,8'R) (1-^{18}O,3-^{2}H$_1$)-**2**. The chirality at C(3) was determined by comparison with a synthetic deuterated sample of known absolute configuration. Accordingly the ring closure proceeds with *si*-protonation of the double bond of **1** and concomitant *re*-attack of the phenolic oxygen. Investigation of the substrate specificity with spheroplasts and purified Tocopherol-Cyclase, respectively, revealed three recognition sites at the substrate: the OH group at C(1), the (E) configuration of the double bond and the length of the lipophilic chain. The enzyme is a very hydrophobic, membrane-bound 42kD protein most likely operating without a co-factor.



(4-^{18}O-*H*)-**1**

Tocopherol-Cyclase
(*Anabena variabilis*)



(1-^{18}O,3-^{2}H$_1$)-**2**

Poster Abstracts

MONOTERPENES FROM CUBAN PINES AND THEIR ENANTIOMERIC COMPOSITION

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The Cuban pine species *Pinus caribaea* and *P. cubensis* are often heavily infested by *Dioryctria horneana*, a moth ovipositing in the resin exuded at bark injuries[1]. *P. tropicalis* and *P. maestrensis*, on the other hand, are not attacked by this pest in their natural habitat. One reason for this could be a different attractiveness of the pine species due to different compositions of the volatiles released from the resin.

Resin from the four Cuban pine species was investigated. A large series of resin samples from attacked and unattacked trees, as well as from trees growing in different localities, was analyzed by GC-MS and their composition of monoterpene hydrocarbons was determined. The enantiomeric composition of six of the chiral monoterpene hydrocarbons were determined using a two-dimensional GC system equipped with a permethylated β-cyclodextrin column[2]. The results were evaluated statistically according to an earlier investigation[3] using two methods for multivariate data analysis[4], PCA (Principal Components Analysis) and PLS-DA (Projections to Latent Structures - Discriminant Analysis).

Based on the composition of monoterpene hydrocarbons, *P. tropicalis* and *P. cubensis* formed one group separated from *P. caribaea*, while the species *P. maestrensis* was found in both groups. No significant difference was found between the attacked and unattacked *P. cubensis* trees, while the composition of volatiles of attacked *P. caribaea* trees was significantly different from that of unattacked trees.

The enantiomers (−)-α- and (−)-β-pinene, (−)-camphene, and (+)-β-pinene were important for differentiating between attacked and unattacked *P. caribaea* trees. The mean proportions of these constituents were also found to be higher in attacked than in unattacked trees.

REFERENCES:

1. Valdes E., Meba M., Martinez J.F.: Revista Forestal Baracoa *15*, 93 (1985).
2. Borg Karlson A.-K., Lindström M., Norin T., Persson M., Valterová I.: Acta Chem. Scand. *47*, 138 (1993).
3. Sjödin K., Schroeder L.M., Eidmann H.H., Norin T., Wold S.: Scand. J. For. Res. *4*, 379 (1989).
4. Wold S., Albano C., Dunn III W.J., Esbensen K., Geladi P., Hellberg S., Johansson E., Lindberg W., Sjöström M., Skagerberg B., Wikström C., Öhman J.: Intell. Instrum. and Comput. *1989*, 197.

GUAIANOLIDES FROM CREPIS PULCHRA

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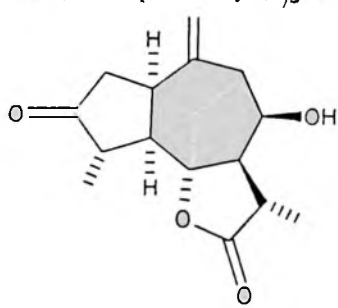
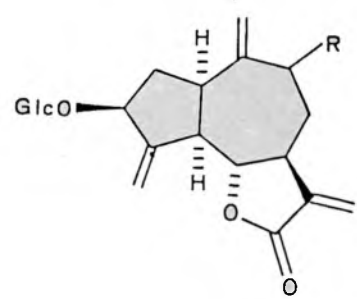
The ethanol extract of the roots of Crepis pulchra L. (Asteraceae) was repeatedly chromatographed on silica gel to afford 8-epiisoamberboin (1) and guaianolide β-D-glucopyranosides 2-4. Compounds 3 and 4 of closely related structures were separated by HPLC. With the exception of 4, they were identified by direct comparison with authentic samples. Compound 4 was characterized by comparing its spectral data with those reported in the literature.

In addition to the sesquiterpene lactones, stigmasteryl-3-O-(6'-O-palmitoyl)-β-D-glucopyranoside was isolated.



1



2 R = H vernoflexuoside

3 R = αOH macrocliniside A

4 R = βOH diaspanoside A

CONSTITUENTS OF CLADANTHUS ARABICUS

W.M. Daniewski[a], M. Gumulka[a], K. Ptaszynska[a], W. Anczewski[a], H. Grabarczyk[b], M. Wichlacz[b].

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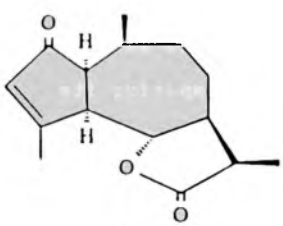
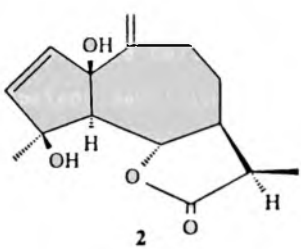
b) Department of Medicinal Plants, Academy of Medicine, 60-623 Poznan, Poland.

Multiple column chromatography and HPLC of methanol extract of aerial parts of *Cladanthus arabicus* (L.) Cass. allowed to isolate a series of compounds which included two guaianolides cladantholide (1), cladantholide B (2) and two germacranolides sintenin (3) and 11,13-dihydro-novanin (4).



1



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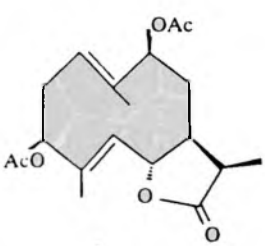
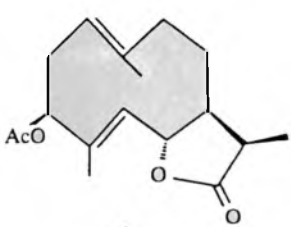


3



4

Structures of all these compounds were substantiated by extensive NMR spectroscopy. Structure of comp.1 was confirmed by X-ray investigation. Moreover the extract yielded a known coumarine "scopoletin" and a known flavonoid "artemetin".

NEW SESQUITERPENE LACTONES FROM *Montanoa tomentosa* subsp. *xanthiifolia*

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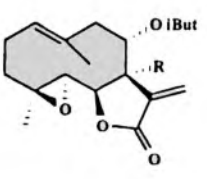
Instituto de Quimica, Circuito Exterior, Ciudad Universitaria, Coyoacán, 04510, México, D. F.

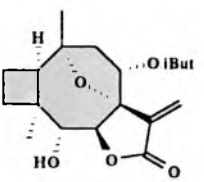
Montanoa tomentosa Cerv. (Zoapatle) has been used in Mexico since prehispanic time by the midwives to regulate the menses and induced labour and abortion. Previous chemical studies of *Montanoa* species showed that the oxepanes[1,2], kauranes[3], flavonoids[4] and sesquiterpene lactones[5-7] are the main secondary metabolites of the genus. Biologycal tests showed that the zoapatanol (oxepane) induced uterine contractions[8] and 16α-hydroxy-*ent*-kauran-19-oic acid and angeloylgrandifloric acid possesses an uteroconstrictive effect in guinea pig[9,10]

We investigated the aerial parts of *Montanoa tomentosa* subsp. *xanthiifolia* collected in Chiapas, Mexico, and obtained some known compounds as β-sitosterol, stigmasterol, taraxasterol acetate, *ent*-kauran-16-en-19-oic acid and four new sesquiterpene lactones (**1a**, **1b**, **2** and **3**), whose structures were determined by spectroscopic methods and chemical transformations. The relative stereochemistry of **1b** was corroborated by X-ray analysis.

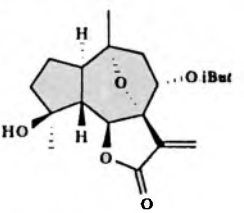
The result obtained of the treatment of **1b** with benthonic earth (Tonsil) in acetone showed that this substance can be the precursor of the compounds **2** and **3**.



1a R= H
1b R= OH



2



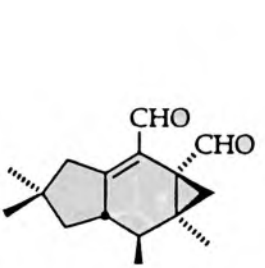
3

1. Quijano L. *et al.*, *Phytochemistry* **24**, 2741 (1985).
2. Quijano L. *et al.*, *Phytochemistry* **24**, 2337 (1985).
3. Enriquez R. G. *et al.*, *J. Chromatogr.* **258**, 297 (1983).
4. Oshima Y. *et al.*, *J. Nat. Prod.* **49**, 552 (1986).
5. Quijano L. *et al.*, *Phytochemistry* **24**, 861 (1985).
6. Seaman F. C. *et al.*, *Phytochemistry* **25**, 2663 (1986).
7. Quijano L. *et al.*, *Phytochemistry* **30**, 1947 (1991).
8. Hahn D. W. *et al.*, *Contraception* **23**, 133 (1981).
9. Lu Z. *et al.*, *J. Nat. Prod.* **50**, 995 (1987).
10. Ponce-Monter H. *et al.*, *J. Ethnopharm.* **24**, 127 (1988).

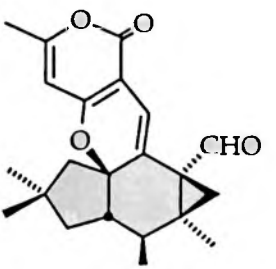
THE ISOLATION OF A NEW MERULIDIAL DERIVATIVE FROM CULTURES OF *MERULIUS TREMELLOSUS*

Mikael Jonassohn[1], Heidrun Anke[2], Olov Sterner[1] and Christer Svensson[3], Departments of [1]Organic Chemistry 2 and [3]Inorganic Chemistry 2, University of Lund (Sweden), and [2]Department of Biotechnology, University of Kaiserslautern (Germany).

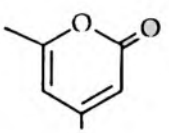
Merulidial (**1**) is a pungent, antibiotic, and mutagenic sesquiterpene containing an unsaturated dialdehyde functionality, isolated from submerged cultures of the fungus *Merulius tremellosus*. Recently it was shown that the fungus also produces the derivative **2** in approximately equal amounts. The structure of **2** was determined by spectroscopy and X-ray crystallography. In addition, the product obtained after the condensation of merulidial with the triketide **3** was in all respects identical with the isolated compound.



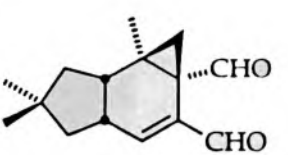
1



2



3



4

The rate of reaction of **3** with other unsaturated dialdehydes (e.g. isovelleral **4**) has also been investigated, as this may be significant for some of the biological activities that these compounds show.

ANTITUMOUR SESQUITERPENE LACTONES FROM KAZAKHSTAN PLANTS

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Scientific Industrial Introduction Small Enterprise "TABIGAT", Karaganda, 470032, Kazakhstan
Karaganda State Medical Institute
Karaganda Regional Oncology Center

Antitumour activity of 43 sesquiterpene lactones from plants of the family Asteraceae of Kazakhstan natural flora has been investigated on 12 transferring strains of animals and their drug resistant modifications.

The prospects of searching compounds of this row in species of Achillea, Artemisia, Centaurea, Chartolepis, Inula, Jurinea, Saussurea, Stizolophus, Tanacetum have been demonstrated.

At chemical modifications of the isolated germacranolides, eudesmanolides, guaianolides and pseudoguaianolides it has been determined, that the presence of α-methylene-γ-lactone, α,β-unsaturated keto-group, epoxy cycle, hydroxy-function, galoid atoms in their molecule promotes inhibition of tumour strains growth.

The data on acute and chronic toxicity, mutagenity as well as the effect of some lactones on hemogenesis and immunity are given in the paper. The preparation of rational formula of preparate usage on the basis sesquiterpene lactone is being discussed.

IZOEPOXYESTAFIATINE AND 3,4-DIHYDROXY-IZOEPOXY-ESTAFIATINE FROM ARTEMISIA SP. NOVA

Aibek Turmuchambetov, Aisha Zapolskaja-Dovnar,
Ulmeken Abdumutalieva, Koblandy Turdybekov,
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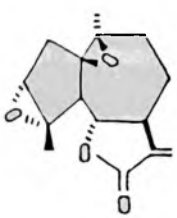
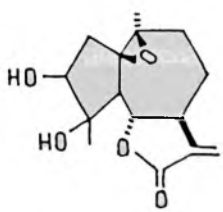
Scientific Industrial Introduction Small Enterprise
"TABIGAT", Karaganda, 470032, Kazakhstan

Two crystal substances (1) and (2) have been isolated from overground part of Artemisia sp. nova by chloroform extraction and column chromatography methods



(1)



(2)

Substance (1), $C_{15}H_{18}O_4$, m.p. 167-170°C (ethylacetate)
Substance (2), $C_{15}H_{20}O_5$, m.p. 206-208°C (ethylacetate)

On the basis of physical and chemical constants, spectral data and X-ray analysis the substance (1) has been identified as sesquiterpene lactone isoepoxyestafiatine, and the substanse (2) - 3,4-dihydroxy-izoepoxyestafiatine.

CONSTITUENTS OF LACTARIUS VELLEREUS, NEW EVIDENCE FOR THE BIOGENESIS OF 14-HYDROXYLATED LACTARANE SESQUITERPENES

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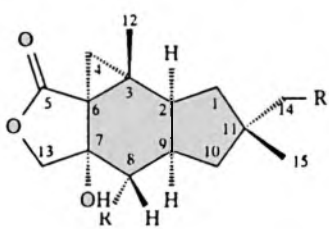
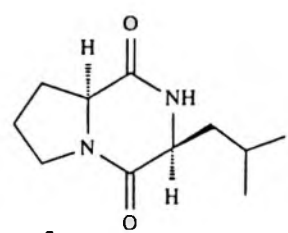
The sesquiterpenes of lactarane skeleton are derived from common precursor velutinal (marasmane skeleton). So far four 14-hydroxylated sesquiterpenes were isolated. It is unknown at which stage of the biogenesis oxidation of the 14-methyl group takes place. The isolation of the new lactone **1** (marasmane skeleton) implifies that possible oxidation of the 14-methyl group could take place at the early velutinal stage before its transformation to the final sesquiterpenes.



1. R = OH

1a.R = OAc



2.

New lactone **1** and diketopiperazine (*cyclo*-L-Pro-L-Leu) **2** were isolated from the most polar fraction of ethanolic extract of *Lactarius Vellereus*. The structure of compounds **1** and **2** were established by extensive NMR studies together with acetylation experiment.

NEW NEOCLERODANE DITERPENOIDS FROM SCUTELLARIA

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Benjamin Rodriguez, Maria Carmen de la Torre
Instituto de Quimica Organica, C.S.I.C., Juan de la Cierva 3, 28006 Madrid, Spain

Neoclerodanes are a class of diterpenoids widespread in nature: plants from different families (Verbenaceae, Labiatae, Euphorbiaceae, Compositae) are the main natural source.

Several biological proprieties were found in neoclerodanes, but their notoriety is bound essentially on the antifeedant activity against infesting insects by a group of products having a furan or hydrogenated furofuran system.

Inside the family Labiatae, the genus Scutellaria, botanically close to the genera Teucrium and Ajuga, includes some 300 species widespread in the whole world unless in South Africa, and was reported to contain some neoclerodanes.

The present communication describes the isolation and the structural elucidation of six new neoclerodane diterpenoids extracted from the species Scutellaria galericulata, Scutellaria cypria subsp. elatior and Scutellaria alpina subsp. javalambrensis.

The antifeedant activity of some of these products was also ascertained.

NEO -CLERODANE DITERPENOIDS FROM *SALVIA POLYSTACHYA*

Emma Maldonado and Alfredo Ortega

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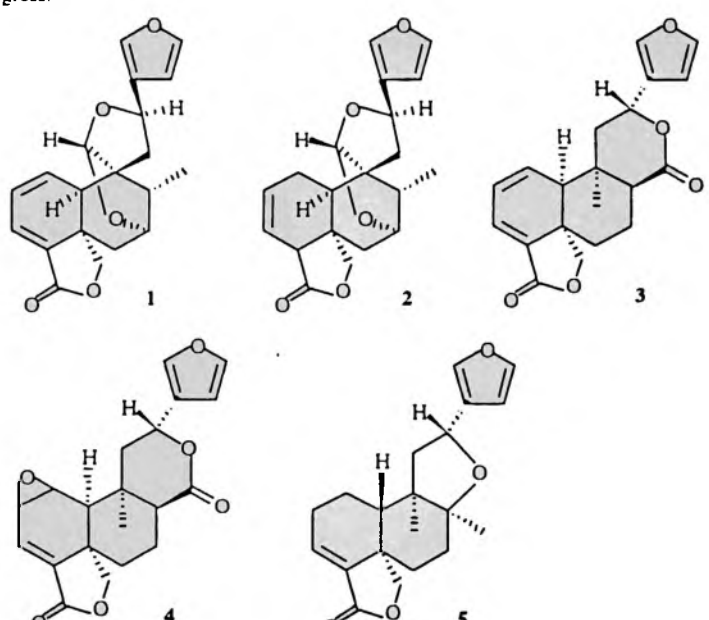
The *Salvia* genus is one of the largest genera of the *Labiatae* family. Chemically it is characterized by the presence of diterpenes, mainly with clerodane or abietane skeletons, although pimarane and labdane diterpenoids also have been isolated from these plants.

In our search for new natural compounds from *Salvia spp.*, we have analised a population of *Salvia polystachya* , a perennial shrubby species classified in the Section *Polystachyae*, subgenus *Calosphace*.

From the aerial parts of this plant the known *cis-neo*- clerodane diterpenes salvifaricine (**1**) and linearifoline (**3**) were isolated together with four new compounds, which we have named polystachynes A (**2**), B (**4**), C (**5**) and E (**6**). Structures of these diterpenes were deduced from their spectral data, except that of polystachyne E, which is actually in progress.



PHYTOECDYSTEROID DITSRIBUTION IN THE PLANTS OF THE COMPOSITAE AND CARYOPHYLLACEAE FAMILIES

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Tashkent, 700170, Kh. Abdullaev Ave. 77.

A systematic study of several species of Rhaponticum plants for ecdysteroid content has been conducted. New ecdysteroids of the C-27, C-28 and C-29 groups were isolated.

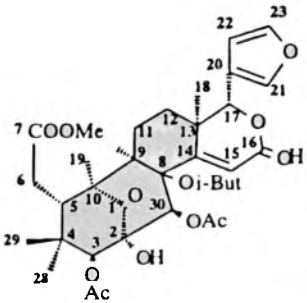
On the ground of our own experimental work and literature data we made a conclusion on the phytoecdysteroids distribution in the investigated plants and other taxonomic features.

New Constituents of Entandrophragma utile and their Antifeedant Activity

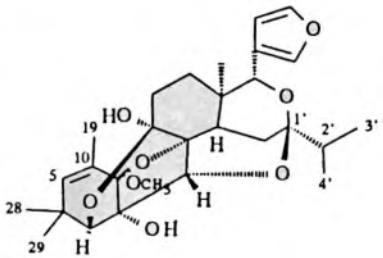
W.M. Daniewski [a], M. Gumulka [a], W. Danikiewicz [a], P. Gluzinski[a], J. Krajewski[a], E. Pankowska[a], E.Bloszyk[b], U. Jacobsson[c], T. Norin[c], F. Szafranski[d].

a) Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, 01-224 Warsaw, Poland.
b) Department of Medicinal PLants, Academy of Medicine, 60-623 Poznan, Poland.
c) Royal Institute of Technology, Department of Organic Chemistry, S-100 44 Stockholm, Sweden.
d) University of Kisangani, The Faculty of Sciences, B.P. 1665, Kisangani, Zaire.

The chloroform extract of *Entandrophragma utile* besides the already known compounds [1] afforded two new limonoids **Utilin B** and **Entilin C**. The structures of the new compounds were established by extensive NMR spectroscopy.



Utilin B (tetranortriterpenoid)



Entilin C (heptanortriterpenoid)

Structure of Utilin B was confirmed by X-ray measurement. Antifeedant activity measured against some storage pests of isolated compounds will be presented.

1. Taylor, D.A.H. Fortschr. Chem.Org. Naturst. 45, 1.

TRI-*NOR*-DAMMARANES TRITERPENOIDS AND ANTIFEEDANT *NEO*-CLERODANE DITERPENOIDS FROM *SALVIA ASPERA* (*LABIATAE*).

Francisco Guerrero, Georgina Espinosa, Rubén A. Toscano, Lydia Rodríguez-Hahn and Baldomero Esquivel.

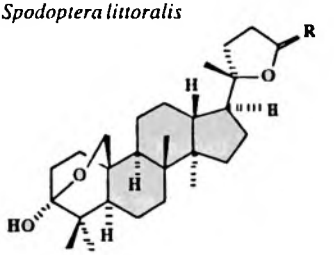
Instituto de Química de la Universidad Nacional Autónoma de México. Circuito Exterior, Cd. Universitaria, Coyoacán 04510 México D.F.

Salvia L. is the largest genus of the *Labiatae* family with over 900 species widespread all over the world. Bentham divided this genus into four subgenera: Salvia, Sclarea, Leonia and Calosphace. The phytochemical studies of Salvia spp. led to the isolation of different types of diterpenes[1]. Triterpenes of the ursane, oleanane and lupane groups are also common in the genus.

In continuation of our studies on mexican *Salvia* spp (Subgenus Calosphace) we investigated the aerial parts of *Salvia aspera* M. et G.(Section Conzattiana). From the acetonic extract of this specie we isolated two new tri-*nor*-dammarane derivatives **1** and **2**. The structure of these products were established on chemical and spectroscopic grounds. X-Ray analysis was performed on **1**. Treatment of **1**, with Jones reagent produced **2**.

This is the first report on the isolation of tri-*nor*-dammarane triterpenoids from a *Salvia* spp of the Calosphace subgenus. Dammarane triterpenoids are known only from *Salvia bicolor*[2] and *Salvia hierosolymitana*[3].

In addition three known *neo*-clerodane diterpenoids were isolated and characterized. The most abundant was identified as semiatrin and shows a significative antifeedant activity against *Spodoptera littoralis*



1 R= α and β OMe
2 R= O

References:

1.-Rodríguez-Hahn L., Esquivel B.,Cardenas J. *Trends in Organic Chemistry* **3**,99 (1992)
2.-Valverde, S., Escudero,J., López J.C. ,Rabanal R.M. *Phytochemistry* **24**, 111 (1985).
3.-Pedreros S., Rodreiguez, Benjamín, De la Torre M.C., Bruno M., Savona G., Perales A., Torres M.R. *Phytochemistry* **29**, 919 (1990).

TRITERPENE CONSTITUENTS OF THE ROOTS OF *ACANTHOTHAMNUS APHYLLUS* (CELASTRACEAE). STRUCTURAL ELUCIDATION OF THREE NEW OLEANAN TRITERPENES

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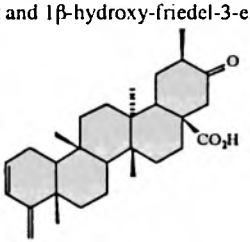
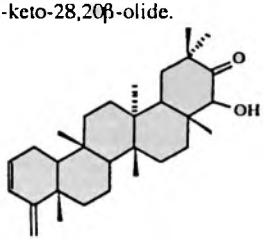
Instituto de Química de la Universidad Nacional Autónoma de México. Circuito Exterior. Cd. Universitaria, Coyoacan 04510 México D.F.

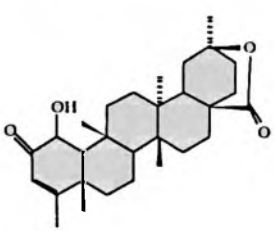
The study of the aerial parts of *Acanthothamnus aphyllus* (*Celastraceae*) led[1] to the isolation of acanthothamine a sesquiterpene alkaloid structurally related to evonine[2], which possesses a 2-epi-(R) evoninic acid residue.

From the roots of this plant we isolated and characterised the methylen-quinones pristimerin, tingenon and 22β-hydroxytingenon frequently found in the roots of plants of the *Celastraceae*[2]. The known oleanane triterpenes germanicon, 21β-hydroxy-oleanolic acid and the friedelan triterpene 3β-hydroxy-2-keto-29-oic acid, were also found in this study.

Three new friedelan triterpenes were isolated and their structures deduced on spectroscopic evidence as 2,4(23)-friedeldien-20-keto-28-oic acid, 2,4(23)-friedeldien-21-hydroxy-20-one and 1β-hydroxy-friedel-3-en-2-keto-28,20β-olide.







References:

1.- Sánchez A.A., Cardenas J., Soriano-Garcia M, Toscano R., Rodríguez-Hahn L. *Phytochemistry* **25**, 2647 (1986).

2.- Bruning R. Wagner, H. *Phytochemistry* **17**, 1821 (1978)

COMPARATIVE STUDY ON THE STEAM DISTILLATION - CO_2 EXTRACTION OF THE VOLATILE CONSTITUENTS OBTAINED FROM *MENTHA PIPERITA* L. LEAVES

F. Senatore* and E. Reverchon°

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°Dipartimento di Ingegneria Chimica ed Alimentare, Università degli Studi di Salerno Ponte Don Melillo, 84084 Fisciano (Sa) - Italy.

We examined the yield and composition of extracts obtained by steam distillation (SD) and supercritical fluid extraction (SFE). The extraction of natural matters using supercritical gases represents a major and wide field of application of this technique. Treatment of products at low temperatures with physiologically safe solvents, such as CO_2, offers particular advantages: no organic solvent residues, storage stability and purity. The essential oil of the *Mentha piperita* L. leaves was obtained using SD and SFE extraction with different parameters of temperature and pressure to compare the influence of extraction technique on the composition and flavour of the essential oil. The SFE extracts shows better fragrance with respect to that obtained from hydrodistillation.

CONSTITUENTS OF *CRITHMUM MARITIMUM* L. ESSENTIAL OIL

Felice Senatore

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Crithmum maritimum L. is an herbaceous, perennial plant that occurs in wild state in coastal sections of Mediterranean countries. The succulent leaves are used in folk medicine for their carminative, diuretic and vermifuge properties. The essential oil extracted by steam distillation from plants growing in Campania shows a composition different from that of other plants examined by other Authors. This variety could represent another chemiotype.

LACTONES AS MIMICS OF THE ACETATE FUNCTION IN PHEROMONE-BASED ATTRACTION

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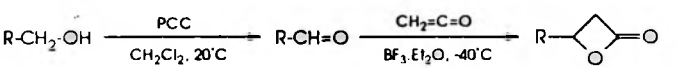
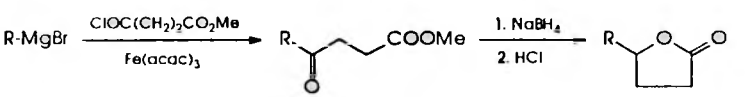
In the search for new biorational pesticides based on semiochemicals, we concentrated ourselves on synthesis of lactone analogues of the Oriental fruit moth (*Cydia molesta*) and the European corn borer (*Ostrinia nubilalis*) sex pheromones.

Five-membered enol-lactones bearing a halogen at the vinylic position are known[1] to be mechanism-based inactivators (suicide inactivators) of serine hydrolases. Similarly, ynenol lactones are featured as suicide inactivators of serine proteinase. It is also known that simple β-propiolactone is a powerful alkylating agent proposed to alkylate even sulphidic sulphur in methionine. We expect that due to their alkylating properties even the more simple 4- and 5-membered lactones could exhibit similar inhibition effects.

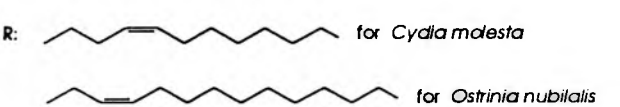
The synthesis of 4-membered lactones is based on a cycloaddition of ketene on corresponding aldehyde[2] (Reaction 1). The 5-membered lactones have been prepared by reduction of suitable ketoesters followed by lactonisation. The ketoesters had been synthesized by Fe(acac)$_3$ catalyzed coupling of alkenylmagnesiumbromides with methoxycarbonylpropionylchloride[3] (Reaction 2).



Reaction 1



Reaction 2



References:

1. Grant A.K., Katzenellenbogen J.A.: *J.Am.Chem.Soc.* **103**, 5459 (1981).
2. Noels A.F., Herman J.J., Teyssié P.: *J.Org.Chem.* **41**, 2527 (1976).
3. Cardellicchio C., Fiandanese V., Marchese G, Ronzini L.: *Tetrahedron Lett.* **28**, 2053 (1987).

PREPARATION OF *E*-ALKENES USING LITHIUM AND 1,3-DIAMINOPROPANE

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The Czech Republic

We report here a new and convenient method for the preparation of (E)-alkenes by a new selective reducing system, lithium in 1,3-diaminopropane. This system enables the preparation of (E)-olefins from acetylenes in high purity. We found that the reduction of 1,2-dialkylacetylenes by lithium in 1,3-diaminopropane has many advantages over commonly used reduction in liquid ammonia or reduction in 1,2-diaminoethane. The reaction does not require a high excess of solvent and proceeds fast enough under mild conditions (low or room temperature). THF can be used as a cosolvent. The system is apparently capable of reducing triple bonds to saturated carbon chains, but it is possible to stop the reaction in the first reduction stage by controlling the reaction conditions. In the experimets various compounds containing a triple bond and/or an aromatic ring were used as reduction substrates. The reduction yielded 68-98% of the corresponding (E)-alkenes while the presence of (Z)-isomers was less than 1.5%.

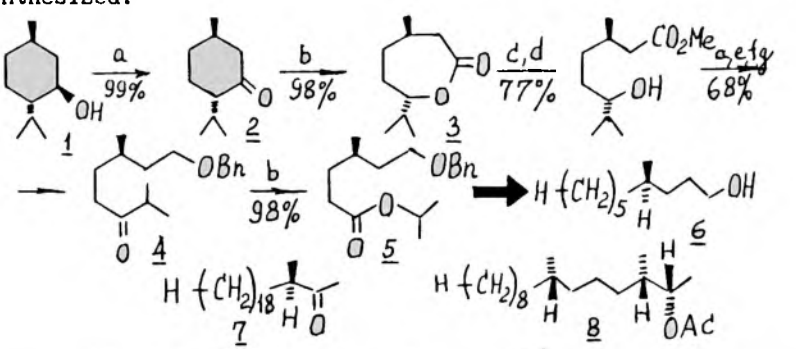
ENANTIOSPECIFIC SYNTHESIS OF CHIRAL PHEROMONES, BASED ON OXIDATION RING OPENING PRODUCT IN L-(-)-MENTHOL

V.N.Odinokov*, G.Yu.Ishmuratov**, R.Ya.Kharisov**, M.P.Yakovleva**, R.L.Safiullin**, G.A.Tolstikov**

*Institute of Petrochemistry and Catalysis, Bashkirian Academy of Sciences

**Institute of Organic Chemistry, Ural Department of the Russian Academy of Sciences

The paper describes an effective approach to the synthesis of insect chiral pheromones, starting from an available natural compound L-(-)-menthol (1). Decane sulfoperacid (DSPA) was used as a new oxiditing agent at principal steps of the synthetic procedure, i.e. at those of oxidative breakage of (-)-(1R,4S)-menthone (2) and acyclic ketone (4). The peracid provides for regioselective transformation of (2) and (4) into a lactone (3) and an ester (5), respectively, in high yields. Proceeding from the ester (5) having the (R)-configuration, optically pure sex pheromones for Tenebrio molitor, Blatella germanica and Neodiprion sertifer, (6), (7) and (8), respectively, were synthesized.



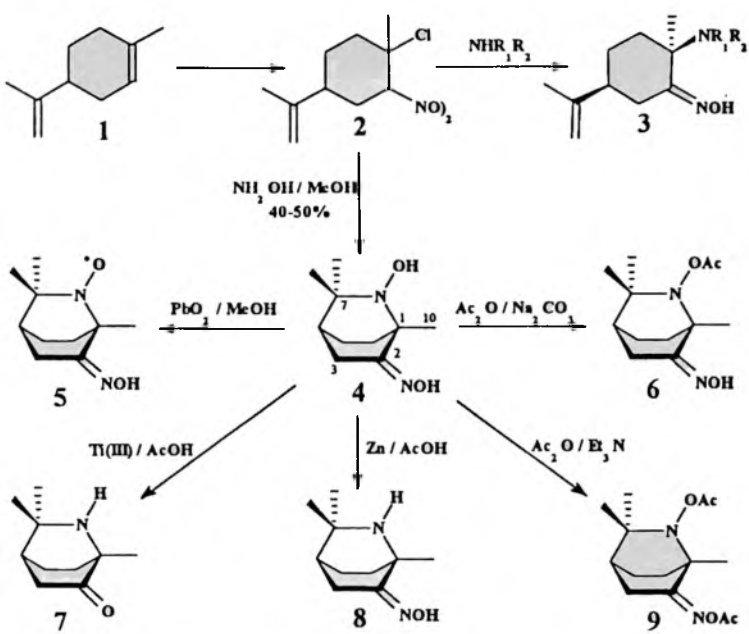
Reagent and conditions: a, PCC, CH_2Cl_2, 22°C, 2ч; b, DSPA, MeCN, 22°C, 0.5ч; c, KOH, MeOH, 22°C, 4ч; d, MeOH, TsOH, 22°C, 48ч; e, $(CH_2OH)_2$, TsOH, PhH, 80°C, 30ч; f, DIBAH, PhMe-Et_2O, -15°C, 1.5ч; g, BuCl, KOH, DMSO, 22°C, 20ч.

NEW BICYCLIC NITROGEN-CONTAINING DERIVATIVES OF LIMONENE .

Stanislav A. Bakunov, Andrey M. Chibirjaev,
Alexey Yu. Denisov, Alexey V. Tkachev

Novosibirsk Institute of Organic Chemistry
Novosibirsk 630090 , Russia

Dimeric nitroso chloride **2** derived from monoterpene hydrocarbon limonene **1** is known to react easily with primary and secondary amines to give α–amino oximes **3**. We have found that treatment of nitroso chloride **2** with NH_2OH results in the formation of unusual bicyclic compound **4**. The structure of the compound obtained was determined by NMR-spectroscopy (INADEQUATE, selective INADEQUATE; $^3J_{C^7\text{-}C^{10}}$ = 2.1 Hz). Based on the new α-hydroxylamino oxime **4**, a number of interesting bicyclic derivatives of limonene **5-9** have been synthesized.



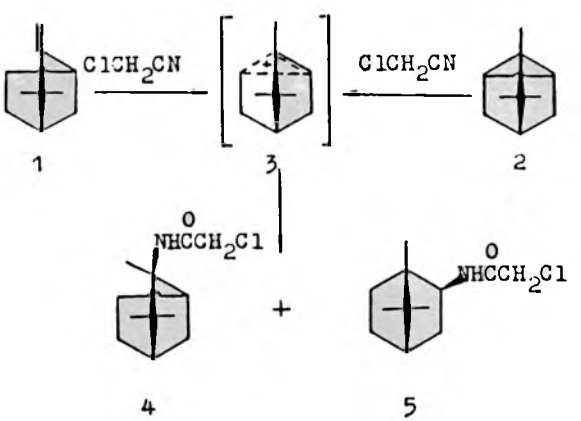
RITTER REACTION OF CAMPHENE AND TRICYCLENE WITH CHLOROACETONITRILE

Victor Lysenkov

Institute of Physical Organic Chemistry
Academy of Sciences of the Republic of Belarus
13 Surganov Street, Minsk 220603, Republic of Belarus

It is known that 3-aminoisocamphane and some of its N-alkyl derivatives, which have strong ganglioblocking properties, are obtained from 3-acylaminoisocamphanes.

We found a new approach to the synthesis of 3-acylaminoisocamphanes based on readily accessible raw material - camphene (1), tricyclene (2) and chloroacetonitrile. Mixture of 3-exo-chloroacetamidoisocamphane (4) and 2-exo-chloroacetamidobornane (5) is formed with high yield as a result of interaction camphene (1) and/or tricyclene (2) with chloroacetonitrile.



Forming amides ratio (4/5) depends on the reaction conditions essentially.

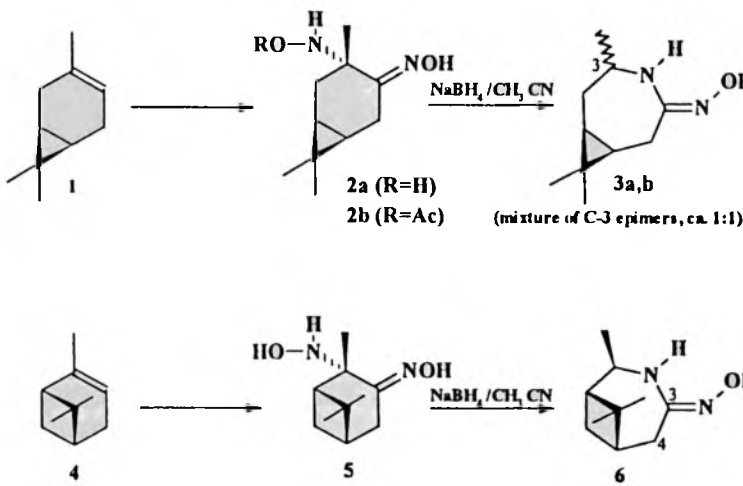
The structure of the obtained amides (4) and (3) is confirmed by their NMR ^{1}H and ^{13}C.

SYNTHESIS OF NEW AZA-DERIVATIVES OF α-PINENE AND 3-CARENE.

Pavel A. Petukhov, Alexey Yu. Denisov, Alexey V. Tkachev

Novosibirsk Institute of Organic Chemistry
Novosibirsk 630090 , Russia

Treatment of oximes of 3-(N-hydroxy)-aminocaran-4-one **2a** and 3-[N-(O-acetyl)-hydroxy]-aminocaran-4-one **2b** with sodium borohydride in boiling acetonitrile gave *ca.* 1:1 mixture of epimeric cyclic amidooximes **3a,b**. The reaction of α–pinene derivative **5** resulted in the only isomer **6**, whose configuration based on comparison of calculated and experimental NMR parameters. Z-Configuration of the oxime moiety in the aza-derivatives synthesized seems to be more preferable due to the anomeric effect. This was confirmed for **6** by NMR spectroscopy: experimental value of the carbon-carbon coupling constant $^1J_{C^3\text{-}C^4}$ is 51.5 Hz, while calculated ones are 51-53 Hz and 43-44 Hz for Z- and E- isomer respectively.



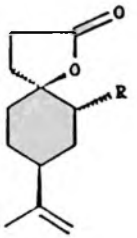
The rearrangement found is a simple and convenient synthetic route to the new aza-derivatives of 3-carene **1** and α–pinene **4**.

SYNTHESIS OF LACTONES WITH THE LIMONENE SYSTEM

Edyta PARUCH and Czesław WAWRZENCZYK

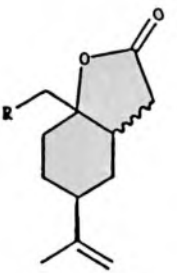
Institute of Fundamental Chemistry,
Agricultural University, Wrocław, Poland

Terpene and sesquiterpene lactones are widely occuring natural products. They usually exhibit specific biological activity. One of the most interesting group among them are the lactones with anti-feeding activity against insects. Being interested in the synthesis of new antifeedants we obtained two types of γ-lactones (1 and 2) with the limonene system in their structure.



R = -H or -J

1



2

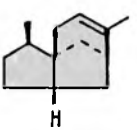
The spirolactones 1 were obtained in a six step synthesis from S-(-)-limonene. The lactones 2, as a mixture of diastereoisomers were prepared in five step synthesis from S-(-)-perillaldehyde. The key step of these syntheses, lactone ring closure, has been carried out by iodolactonization (J_2, $NaHCO_3$) of corresponding γ,δ-unsaturated acids.

SUPERACID REARRANGEMENTS OF α-CEDREN TO TRICYCLIC COMPOUNDS

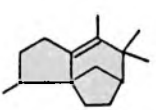
M.P.Polovinka, D.V.Korchagina, V.A.Barkhash.

Institute of Organic Chemistry, Siberian Branch of the Russia Academy of Sciences,
630090, Novosibirsk, Russia.

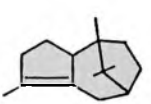
For the first time α-cedren (I) were transformed in superacid to tricyclic hydrocarbons with natural zizaane (II) and patchoulane (III) types of skeleton. Their structures were determined on the basis of ^{1}H and ^{13}C NMR date and also the 2D spectrum of ^{13}C-^{13}C correlation based on biquantum coherency (2D-INADEQUATE).



I



II

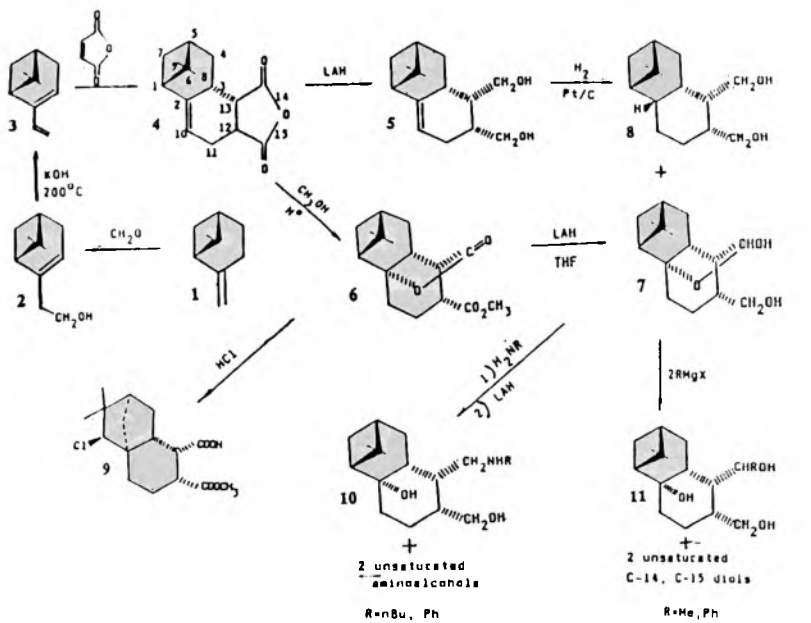


III

NEW TRICYCLIC CHIRAL AUXILIARIES OBTAINED FROM β-PINENE. CRYSTAL AND MOLECULAR STRUCTURE OF A TETRACYCLIC LACTON AND LACTOL WITH THE PINANE SKELETON.

S.W.Markowicz* and J.Karolak-Wojciechowska**

**Institute of Organic Chemistry, **Institute of General and Ecological Chemistry, Technical University of Łodz*, ul Żwirki 36, 90-924 Łodz, Poland.



Tetracyclic anhydride **4**, available from β-pinene **1** by nopol **2** and nopadiene **3**, can be purified by crystallization and then used as a precursor of optically pure chiral auxiliaries. To reach this goal the diol **5** was obtained and next, the derivatives of major product of esterification of **4** - lacton **6** were synthetized. Reaction of lacton **6** with LAH in THF led to lactol **7** and saturated diol **8**. Lactol **7** was transformed in to 1,4 diols **11** with a new C-14 chiral center and 1,4 aminoalcohols **10**. Structures of lacton **6** and lactol **7** were determined by the X-ray method.

References: J. Karolak-Wojciechowska, S. W. Markowicz, *J. Cryst. Spekt. Res.*, **23**, 33, (1993), and cited ref.

C5-CONFIGURATION IN A-HOMO-B,19-DINOR-STEROIDS. A CORRECTION

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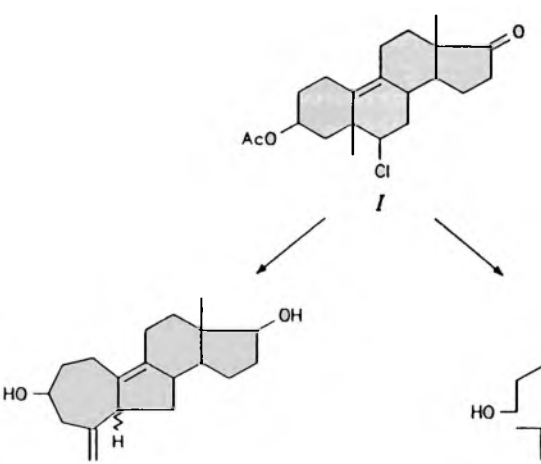
Institute of Organic Chemistry and Biochemistry,
166 10 Prague 6, The Czech Republic.

Solvolysis of Westphalen - type compounds (e.g., I) was reported to yield corresponding A-homo-B,19-dinor-steroids (e.g., II and III); structure assignment was based on chemical correlation and indirect evidence. X-Ray diffraction of two products of hydrogenation of diene II cast doubts at the reported α-configuration of hydrogen in position 5.

Detailed NMR study of compounds II and III, particularly, complete assignment of all proton and carbon signals and interproton NOE's, prove that the 5-hydrogen occupies the α-configuration even before the hydrogenation, thus structures IIa and IIIa are to be corrected to IIb and IIIb.



I

IIα 5β–H (wrong)
IIb 5α–H (correct)

IIIα 5β–H (wrong)
IIIb 5α–H (correct)

BRASSINOSTEROID ANALOGUES WITH CHOLESTANE SIDE CHAIN

Ladislav Kohout[1] and Miroslav Strnad[2]

[1] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 166 10 Prague 6

[2] Institute of Experimental Botany, Academy of Sciences of the Czech Republic, 772 00 Olomouc

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

Synthesis of new brassinolide analogues with cholestane side chain will be described and their biological activities in the second beam internode bioassay[2] will be given.

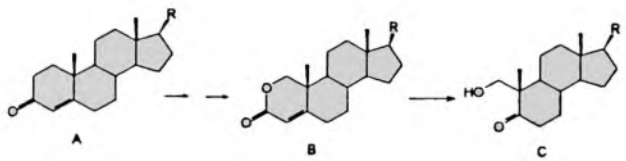
References:

1. Grove M.D. et al.: Nature (London) 281, 261 (1979).
2. Mandava N.B.: Ann. Rev. Plant Physiol. Plant Mol. Biol. 39, 23 (1988).
3. Mitchell J. W. et al.: Agriculture Handbook No. 36, p. 36, US Government Printing Office, Washington D.C., 1968.

OZONOLYSIS OF 2-OXA-3-OXO-Δ^4-ANDROSTANES

Karlheinz KOCKERT and Friedrich W. VIERHAPPER

Department of Organic Chemistry
University of Vienna, Vienna, Austria



As starting materials for the synthesis of steroids carbon labelled at positions 2,3 and 4 in the A-ring, 1,5-seco-steroids (C) were prepared from commercially available 3-oxo-Δ^4-steroids (A). Best results were obtained by ozonolysis of 2-oxa-3-oxo-Δ^4-androstanes (B, R=OtBu).

Conditions for both the ozonolysis of B and the subsequent hydrolysis of the intermediately formed ring-opened esters were carefully optimized.

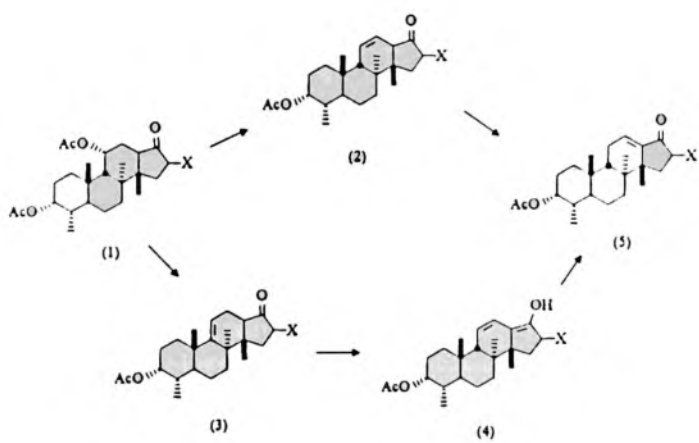
Reaction parameters (time, temperature, solvents etc.) and distribution of products will be presented.

FURTHER INVESTIGATIONS INTO THE ELUSIVE MECHANISM OF ACID AND BASE CATALYSED ELIMINATION OF ETHANOIC ACID FROM AN 18-NOR-11-α-ACETOXY-9β-ANDROSTAN-17-ONE

William S. Murphy and Andrzej Zarecki

Department of Chemistry, University College Cork, Ireland

Treatment of (1) with acetic acid or pyridine at elevated temperatures effects elimination of acetic acid molecule and formation of a conjugated ketone (5). Murphy and Cocker[1] challenged the mechanism proposed by Diassi at al.[2] [(1) → (2) → (5)] with the proposal of the initial formation of the $\Delta^{9,11}$- androstane (3) rather than the $\Delta^{11,12}$- androstane (2) which rapidly rearranged to the corresponding Δ^{12}-isomer [(1) → (3) → (4) → (5)] under the conditions. A further series of experiments to elucidate this mechanism will be presented - such as an investigation of the dienol acetate derived from the $\Delta^{9,11}$-androstane, comparison of the 13α- with the 13β-series, demand for 17-oxo- functionality, a detailed re-investigation of the deuteration experiments of Murphy and Cocker [1]



1) W. S. Murphy and D. Cocker, J. Chem. Soc. Perkin Trans. I, 1977, 2565
2) P. A. Diassi, G. W. Krakower, I. Bacso and H. Ann Van Dine, Tetrahedron, 1966, 22, 3459

NOVEL EFFECTIVE STEREOSELECTIVE EPOXIDATION OF ALLYL- AND HOMOALLYL ALCOHOLS BY H_2O_2 WITH CHLORAL HYDRATE AS A CATALYST

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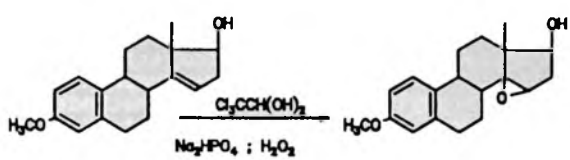
Beutenbergstr.11 HA 07708 Jena, Germany

Introduction of epoxids into the steroid sceleton via olefinic double bonds is a synthetic tool in organic chemistry. It is one prerequisite to prepare vicinal substituted compounds.
A lot of catalysts can be used in chemical as well as in biological systems for this reaction in the presence of H_2O_2.
Epoxidation with participation of neighbouring groups is known from reactions of allyl- or homo-allyl- alcohols or appropriate urethanes with peracids.[1] With highly active peracids the selectivity is not as high as in case of H_2O_2 and a catalyst like hexachloro- or hexafluoro-acetone[2] or m-nitro-trifluoracetophenone.
Until now, aldehydes were not used for epoxidation because of their easy oxidation into the corresponding acids or rearrangement into esters by Baeyer-Villinger or Dacin reaction.
We could indicate that aldehydes which are able to form hydrates can be used for epoxidation in catalytical and equimolar amounts, respectively.
In the presence of H_2O_2 hydroperoxide anion was added to the carbonyl group, and this intermediate product is able to epoxidize olefinic double bonds in a different manner.
One of the best catalyst in this series was found to be chloral hydrate which is non-toxic and very cheap.

Isolated olefinic double bonds are nearly inert whereas conjugated double bonds, allyl- and homoallyl alcohols are very reactive and give epoxides of excellent yields. The selectivity was found to be better than with peracids.
This reaction behaviour of chloral hydrate and H_2O_2 to allyl- and homoallyl-alcohols seems to be especially attributed to the neighbouring group participation of the reagent with the substrate via hydrogen bonding.



Stereoselective epoxidations were likewise found by reaction of tert. allyl- and tert. homoallyl-chromic acid esters.

[1] K.Ponsold, G.Schubert, M.Wunderwald and D.Tresselt ; J.pract.Chem. 3233 (1981) 819-828

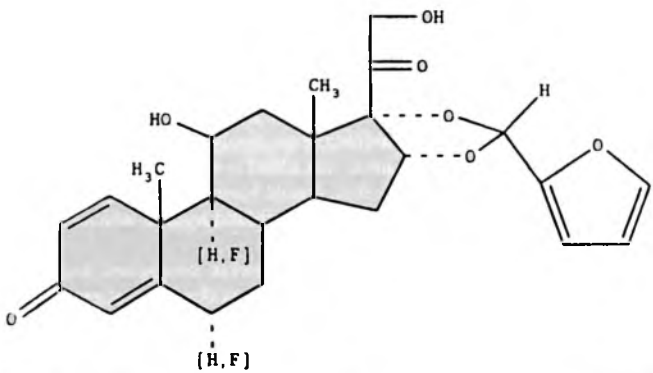
[2] C.T.Ratcliffe, C.V.Hardin, L.R.Anderson and W.B.Fox; J.Chem.Soc., Chem.Comm. (1971) 784

NEW GLUCOCORTICOIDS WITH THE PRONOUNCED IMMUNOSUPPRESSIVE PROPERTIES

Teresa Uszycka-Horawa*, Barbara Trzpil*, Grzegorz Grynkiewicz**

* INFARM Ltd.] Poland, 01-793 Warsaw
**Pharmaceutical Research Institute.] 8 Rydygiera Street

A new group of 16α-hydroksyprednisolone derivatives of a general formula I was synthesized.



Our previous experience indicated that the configuration of new stereogenic center, introduced with an acetal function, may be crucial for biological activity. Consequently, stereoselective acetalization procedure was developed, allowing to obtain both: 22R and 22S stereoisomers without resort to tedious separation by crystallization or chromatography. New compounds were characterized by analytical and spectral methods and for one pair of C-22 epimers an absolute configuration was established by the X-ray crystallography. Pharmacological study confirmed considerable difference in activity of epimeric furfuryl acetals. 22R epimer ([H,F] = H, R_1 - $COCH_3$) was found to exhibit pronounced immunosuppressive properties.

STABILITY OF ORGANOSILICON PROTECTING GROUPS ON 17β-HYDROXYL GROUP OF ANDROSTENE DERIVATIVES

Ivan Černý, Pavel Drašar, and Vladimír Pouzar

Institute of Organic Chemistry and Biochemistry ASCR, Flemingovo n. 2, 166 10 Prague, Czech Republic

For the use in complex synthesis we needed versatile protection of the 17β-hydroxy group, compatible with other functions present in intermediates (acetates, hemisuccinates, etc.). Taking into account that in the final step of indirect method of hemisuccinate preparation the tetrabutylammonium fluoride (TBAF) splitting of protecting 2-(trimethylsilyl)ethyl group takes place, we focused our attention to organosilicon hydroxyl protection, from which we awaited the very mild protection with the possibility of accomplishing both deprotections in one step.

Initial experiments with thexyldimethylsilyl (TxDMS) and t-butyldimethylsilyl (TBDMS) groups revealed their unawaited stability against TBAF and even in acidic medium. We prepared corresponding trimethylsilyl (TMS) and isopropyldimethylsilyl (IPDMS) model derivatives and compared the behavior of all these groups in TBAF and acidic medium.

The results shows extremely quick splitting of TMS group in both medium, however, this group remains unstable to base and this limits its broader use. In all respect the best group for our use is IPDMS group, not only for its easy splitting but also for quick introduction, which compensates relatively difficult availability of starting reagents for protection.

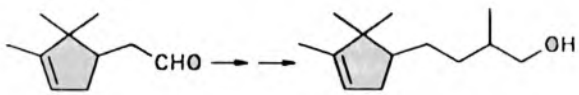
	TMS	IPDMS	TBDMS	TxDMS
TBAF/r.t	<5'	2 h	>48 h	>48 h
TBAF/50°	-	-	15 h	>24 h
H^+	<5'	10'	6 h	>24 h

THE SYNTHESIS OF "HOMO"-BRAHMANOL® - A CONTRIBUTION FOR THE INVESTIGATION OF STRUCTURAL RELATIONS BETWEEN SANDALWOOD-FLAVOURS

K. Beutmann, K. Wyßuwa, K. Schulze

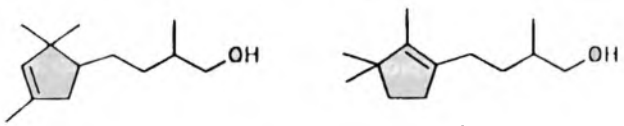
Fachbereich Chemie der Universität Leipzig, Germany

The synthesis of sandalwood-flavours, resulting from α-campholenic aldehyde (**1**), has an old tradition at the University of Leipzig [1]



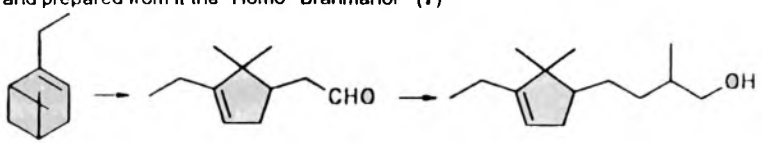
1 **2**

During the last decade we investigated the correlation between structure and odour of this flavours. Besides the well known Brahmanol® (**2**) it was possible to prepare the isomeric fencholenic (**3**) and the isomeric ß-campholenic (**4**) substances [2, 3]



3 **4**

We found that the compounds **3** and **4** possess a woody but no sandalwood note. Now we are interested in giving a more detailed statement about the influence of the methyl group at the ring on the fragrance of these compounds. This should be possible by the replacement of this methyl group by an longer alkyl group. So we concerned with the homologous campholenic and fencholenic derivatives. First we used ethylapopinene (**5**) for the synthesis of the ethyl-α-campholenic aldehyde (**6**) and prepared from it the "Homo"-Brahmanol® (**7**)



5 **6** **7**

We want to report on this synthesis and on attempts to prepare the isomeric fencholenic compound

[1] M. Muhlstadt, G. Feustel, M. Herrmann, W. Dollase DD 68 936 (20.9.69), C. A. 1970, 72, 125 008
[2] H. Uhlig, M. Muhlstädt, K. Schulze, Miltitzer Berichte **1985**, 23
[3] K. Schulze, A.-K. Habermann, H. Uhlig, K. Wyßuwa, J. Prakt. Chemie, in press

A New Approach to the Synthesis of Iridolactones

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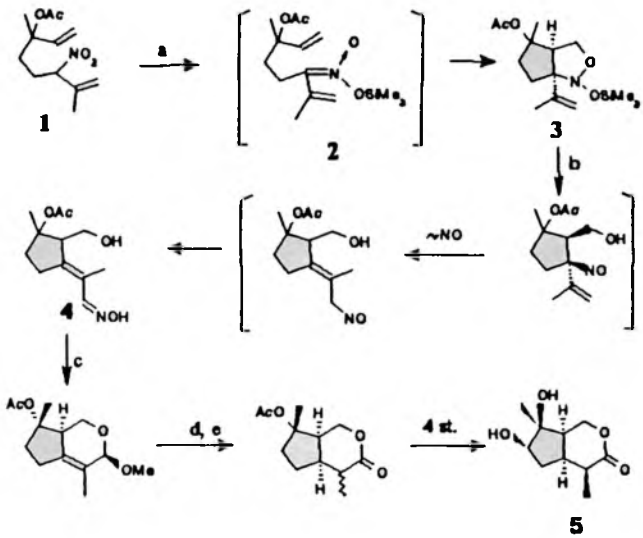
N.D. Zelinsky Institute of Organic Chemistry,
Russian Academy of Sciences, Moscow, Russia

Efficient route to the construction of iridoids was elaborated using as a key step an intramolecular 1,3-dipolar cycloaddition of the silylnitronate **2** generated *in situ* from the nitroolefin **1**. Transformation of isoxazolidine **3** into oximes **4** involved an unprecedented 1,3-tertiary to primary allylic shift of nitrosogroup. Conversion of **4** into the target structure **5** was carryed out *via* a sequence of routine steps.



Reagents: a - BSA; b - $KF \cdot 2H_2O$; c - $Tl(NO_3)_3$/ $HClO_4$/MeOH; d - CrO_3/dl. H_2SO_4; e - $NiCl_2 \cdot 6H_2O/NaBH_4$

SYNTHESIS OF TRICYCLIC FURANOSESQUITERPENOIDS RELATED TO PALLESCENSIN A

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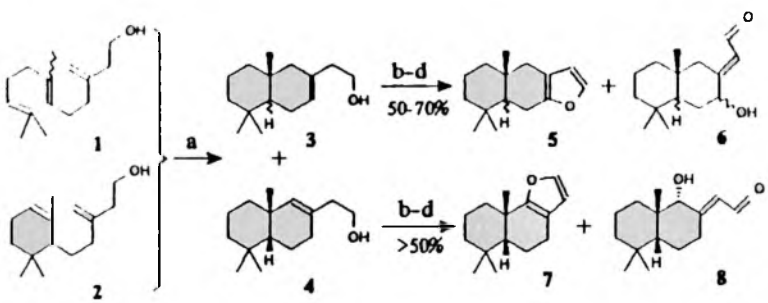
N. D. Zelinsky Institute of Organic Chemistry, Russian Acedemy of Sciences, Moscow. Fax:(095)135-53-28

Cationic cyclization of the *E*- and *Z*-isofarnesols **1** containing α-isoprenoid unit with *exo*methylene group leads smoothly to the regio- and stereoisomeric octalins **3** and **4** in ratios *trans*-**3**/*cis*-**3**/**4**≈80:15:5 and *trans*-**3**/*cis*-**3**/**4**≈10.70.20, respestively. Sesquiterpene **2** under treatment $F_3B \cdot OEt_2$ in CH_2Cl_2 gives the same compounds in ratio *trans*-**3**/*cis*-**3**/**4**≈20:60:20. Thus obtained alcohols were transformed futhur to tricyclic furanosesquiterpenoids **5** and **7** related to the metabolites of some marine organisms, and *E*-oxyaldehydes **6** and **8**.



Reagents and conditions: a — $F_3B \cdot OEt_2$/hexane(emulsion) or CH_2Cl_2, 0→25°, >60% for **1**, ~40% for **2**; b — MCPBA/CH_2Cl_2, 0°; c — $CrO_3 \cdot 2Py/CH_2Cl_2$, 25°; d — SiO_2, 25°.

1

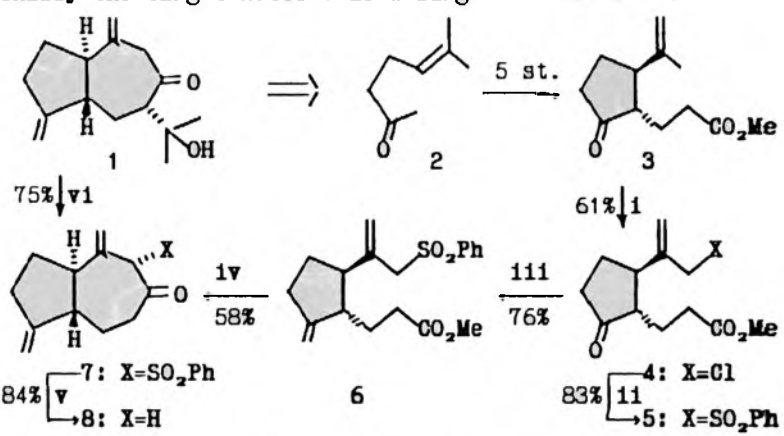
APPROACH TO THE SYNTHESIS OF GUAIANE SESQUITERPENE

B. T. Zhuzbaev, V. V. Veselovsky, S. M. Adekenov and A. M. Moiseenkov

Institute of Organic Synthesis and Coal Chemistry of the National Academy of Sciences, 470061 Karaganda, Kazakhstan
N. D. Zelinsky Institute of Organic Chemistry Academy of Sciences, 117913 Moscow, Russia

A stereocontrolled synthesis of the guaiane-type hydroazulenoid 1 starting from the cyclopentane derivative 3 readily available from metylheptenone 2 is reported.

Chlorination of the 3 under the conditions developed [1] gave the chloride 4 which was converted smoothly to the sulfone 5. Alkenation of the 5 led to the diene 6. Heptaannulation of the key 6 followed by desulfonylated gave ketone 7. Aldol condensation of the latter with acetone gave finally the target ketol 1 as a single stereoisomer.



i, SO_2Cl_2/Py; ii, $PhSO_2Na$; iii, $CH_2Br_2/TiCl_4/Zn$; iv, $NaN(SiMe_3)_2$; v, Al(Hg); vi, LDA, $ZnCl_2$, $(CH_3)_2CO$

LITERATURE

1. V. V. Veselovsky, B. T. Zhuzbaev, S. M. Adekenov et.al. Izv. Akad. Nauk SSSR, Ser. Khim., 1992, 658.

A Short Synthesis of Gastrolactone

C. Rikard Unelius and Torbjörn Norin

Royal Institute of Technology, Department of Organic Chemistry,

S-100 44 Stockholm, Sweden, and

Gastrolactone (I) has been isolated from the larval defense secretion of the chrysomelid beetle *Gastrophysa cyanea*.[1] Gastrolactone has been synthesized by Jones and Blum in more than ten steps in 4 % overall yield from carvone.[2] Here we would like to report a four step syntesis from citral according to the scheme below. The key step is a enal-enamine [2+4]-cycloaddition (Fig 1).[3]

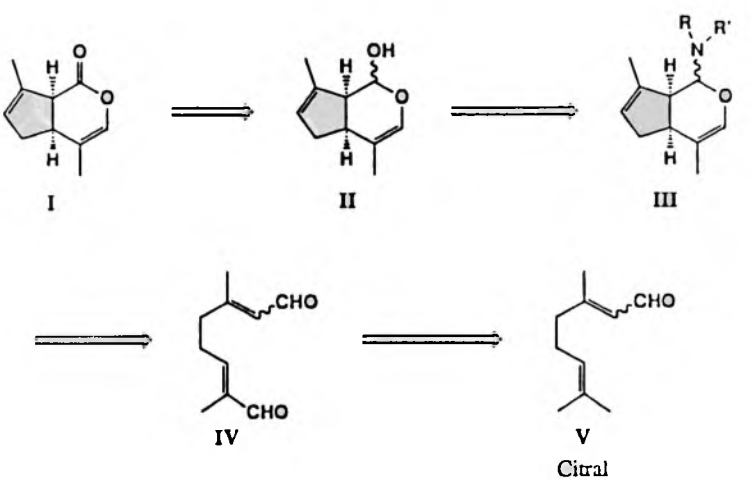


Fig. 1.

The synthesis gives, so far, a racemic product. Attempts to perform the cycloaddition in a stereoselective manner by use of a chiral amine will soon be executed and might be reported on the conference.[4]

(1) Blum, M. S.; Wallace, J. B.; Duffield, R. M.; Brand, J. M.; Fales, H. M.; Sokoloski, E. A. *J. Chem. Ecol.* **1978**, *4*, 47-53.

(2) Jones, T. H.; Blum, M. S. *Tetrahedron Lett.* **1981**, 22, 4373-6.

(3) Schreiber, S. L.; Meyers, H. V.; Wiberg, K. B. *J. Am. Chem. Soc.* **1986**, *108*, 8274; Daniewski, W.M. and Gumulka, M. Unpublished results.

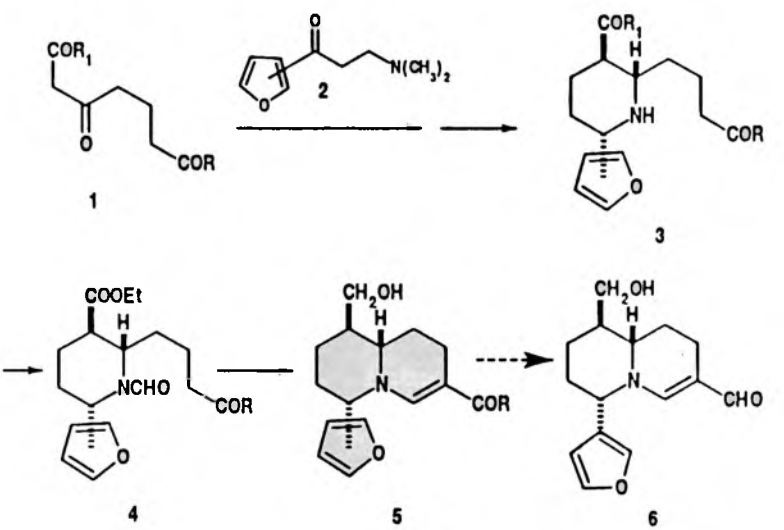
(4) Schreiber, S. L.; Meyers, H. V. *J. Am. Chem. Soc.* **1988**, *110*, 5198-5200.

SYNTHETIC STUDIES OF *NUPHAR* ALKALOID – NUPHACRISTINE

Jerzy Szychowski and Krystyna Wojtasiewicz

Department of Chemistry, Warsaw University

Nuphacristine (**6**), an alkaloid isolated from *Nuphar luteum* is probably biosynthetic precursor of dimeric sulfur-containing *Nuphar* alkaloids. Continuing our studies directed toward the total synthesis of these dimeric alkaloids we chose nuphacristine as synthetic precursor. A general idea of study was one pot formation of all chiral centers by reductive aminocyclization.

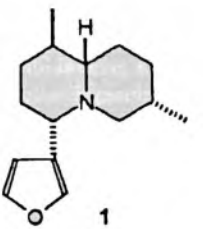


Starting from diethyl 3-oxopimelate (**1** R = R_1 = OEt) conditions of regioselective aminolysis for both ester groups (**1** R or R_1 = 1-piperydyl) were found. After condensation with Mannich base (**2**), reductive aminocyclization step gave compound (**3**) with desired stereochemistry (in case of R = 1-piperydyl a yield was unsatisfactory). The selective reduction of the carboethoxyl group in the piperidine ring unexpectedly could be completed after formylation of nitrogen atom (**4** R = OEt). Otherwise the reduction involves the ester group in the side chain. Cyclization of (**4**) to (**5**) is being currently investigated.

GENERAL APPROACH TO THE SYNTHESIS OF NUPHAR ALKALOIDS.

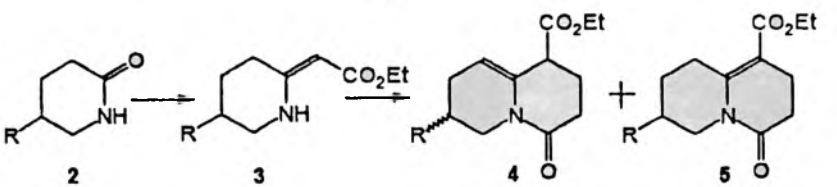
Jacek Nowacki, Department of Chemistry, University of Warsaw, L.Pasteura 1, 02-093 Warsaw, Poland.

The majority of Nuphar alkaloids incorporate in their structures uniformly substituted (positions 1,4 and 7) quinolizidine ring system, like the simple representative - deoxynupharidine **1**.



1

Consequently, development of a general approach to the synthesis of this group of compounds seems to be a worthwhile objective. Synthesis of the promising key intermediates **4** and **5**, suitable for elaboration into a variety of Nuphar alkaloids, involved acryloil chloride annelation of cyclic vinylogous uretanes **3** derived via lactim ethers from 2-piperidone derivatives **2**.



2 3 4 5

R= -H; -CH_3; -OAc; -CO_2Et; -OAc, -CH_3

Investigation of the synthetic potential of the enamidoester moiety and conversions of the functions on carbon 7 of dehydroquinolizidones **4** and **5** afforded highly advanced precursors of the most known to date C-15 Nuphar alkaloids, as well as lupinine, epilupinine and a number of novel piperidine and quinolizidine derivatives. The stereo-chemical aspects and synthetic scope of this methodology will be discussed.

SYNTHESIS OF SOME EPITESTOSTERONE ANALOGUES

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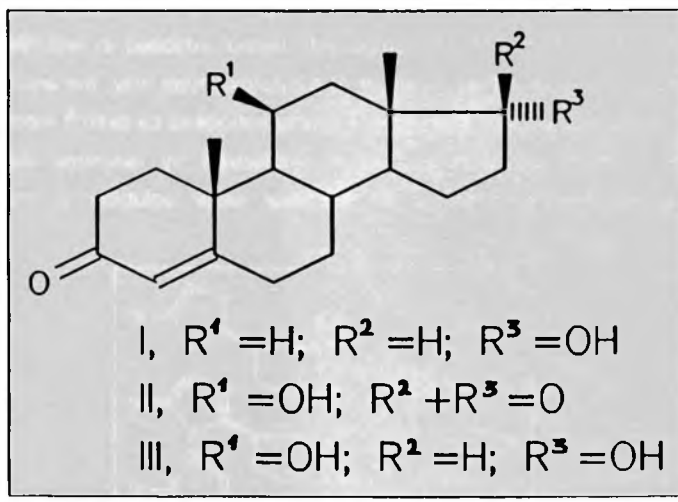
Academy of Sciences of the Czech Republic, 166 10 Prague 6

11ß-Hydroxyandrost-4-ene-3,17-dione (II) was converted into a potential metabolite of epitestosterone (I) - 11ß,17α-dihydroxyandrost-4-en-3-one (III) in 5 steps, including inversion of configuration of a 17ß-hydroxy group. The inversion was not feasible in the preparation of the other analogues, where the 17α-hydroxy group was introduced first and only then the rest of the molecule was worked out.



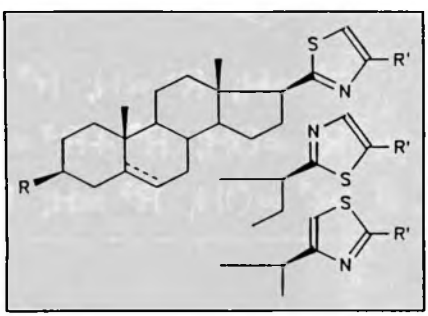
SYNTHESIS AND THE INITIAL BIOLOGICAL EVALUATION OF STEROIDAL THIAZOLES AND THEIR SMALL CONJUGATES

URBANSKÝ Marek, ČERNÝ Ivan, POUZAR Vladimír, and DRAŠAR Pavel

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Flemingovo 2, CZ-166 10 Praha 6

Steroidal thiazoles are known for their close relationship to cardiac steroids of bufadienolide and cardenolide type. Also, they represent a typical example between the above type of activity and antimetabolic activity, postulated by Kamano. Hence, a broader biological screening has been initiated where steroids were tested on their antimicrobial, antimetabolic, Na^+,K^+-ATPase inhibitory, antiviral, and anti-HIV activities i.a. The first cummulative results of the screening show that there are several compounds among steroidal thiazoles exhibiting antimetabolic and Na^+,K^+-ATPase inhibitory activity. Some of the compounds tested exhibited in anti-HIV screen a remarkable biological activity, however of a cytotoxic type only; the anti-HIV activity was in several compounds moderate in concentrations of ca $5x10^{-5}$ mol/l.

Steroidal thiazoles studied were synthesized by reactions described in literature[1,2]. They were tested as for their water solubility in the form of hemisuccinates.



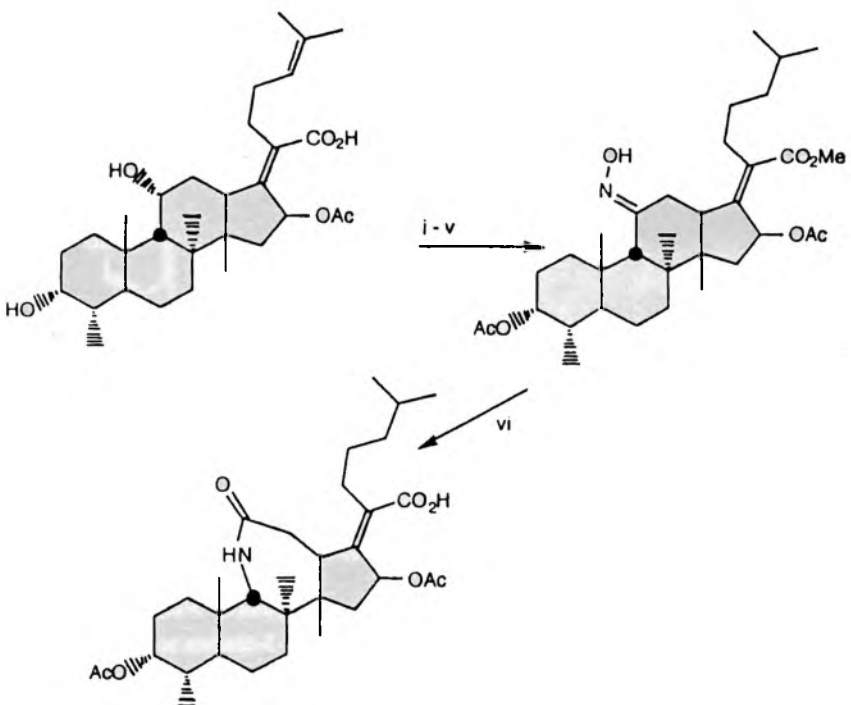
References:

1. Urbanský M., Drašar P.: Synth. Commun. 23, 829 (1993).
2. Drašar P., Tureček F., Havel M.: Collect. Czech. Chem. Commun. 46, 2906 (1981).

FIRST SYNTHESIS OF A 9β-C-HOMO-AZASTEROL

*William S. Murphy * and Basil Sarsam*
Chemistry Department University College Cork Ireland

Investigation of the Beckmann rearrangement of oximes derived from fusidic acid have been investigated for two reasons : (i) , as an entry into novel aza-steroids with potential biological activity and (ii) , determine whether the uncommon 9β -steroids with ring B constrained in a boat conformation , undergo normal rearrangement . The result of rearrangement of the 11-E- oxime is outlined in the Scheme below .The structure of the lactone has been confirmed by high field nmr and X- ray crystallography . Results of the Beckmann rearrangement of rings A and D lactones will also be presented .



Reagents : i , CH_2N_2 ,quant. ii, H_2, Pd° , quant. ; iii , Ac_2O -py, RT, 16 h, quant.; iv , PDC - CH_2Cl_2 - RT , 24 h. quant. ; v, $NH_2OH.HCl$ - KOAc , MeOH , Δ , 30 h, quant. ; vi , TsCl-py , RT,13 d ,81%

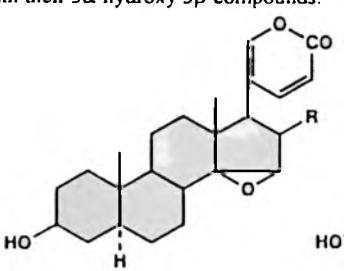
SYNTHESIS OF SOME 5α–H-BUFADIENOLIDES

Machiko Tozawa[1], Pavel Drasar[2] and Yoshiaki Kamano[3]

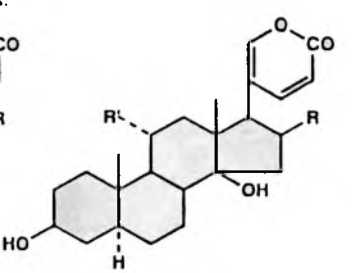
1. Department of Chemistry, The Jikei University, School of Midicine; 8-3-1, Kokuryou , Chofu Tokyo, 182, JAPAN
2. Institute of Organic Chemistry and Biochemistry, Academy of Sciences of Czech Republic, CS-166 10 Praha 6, CZECH REPUBLIC
3. Department of Biological Sciences, School of Science, Kanagawa University; 2946 Tsuchiya, Hiratsuka, Kanagawa, 259-12, JAPAN

The research was undertaken to prepare the 5α-H isomers of natural bufadienolides, owing to the aim of further biological investigation. The preparation of 5α–H-cinobufagin(**1**) was already reported by the means of $LiBH_4$ reduction of Δ^4-3-keto derivative in pyridine[1)] by using similar method as Stache et al.[2)].

In this report, reduction of Δ^4-3-keto derivatives of resibufogenin, bufalin, bufotalin and gamabufotalin with $LiBH_4$ in pyridine at 0°C afforded the aimed 5α–H isomers (**2**,**3**,**4** and **5**) of resibufogenin, bufalin, bufotalin and gamabufotalin in good yield, together with their 3α-hydroxy 5β-compounds.



R=$OCOCH_3$; (**1**)
R=H ; (**2**)



R=R'=H : (**3**)
R=$OCOCH_3$, R'=H ; (**4**)
R=H, R'=OH ; (**5**)

In the connection with the results of $LiBH_4$ pyridine reduction of Δ^4-3-keto derivatives of above mentioned bufadienolides, reduction of cholest-4-en-3-one was achieved under the same condition and by KBH_4, $NaBH_4$, $LiAl[OC(CH_3)_3]_3H$ at several temperature.

1) Y.Kamano, P.Drasar, G.R.Pettit, M.Tozawa; *Coll.Czech.Chem.Commun.*, **52**, 1325 (1987)

2) U.Stache, K.Radscheit, W.Fritsch, W.Haede, H.Kohl, H.Ruschig; *Liebigs Ann.Chem.*, **750**, 149 (1971)

A STEROID ZIRKONOCENE TEMPLATE SYNTHESIS

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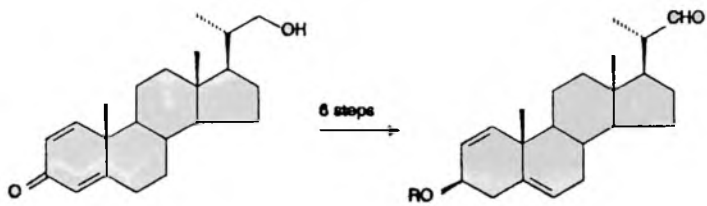
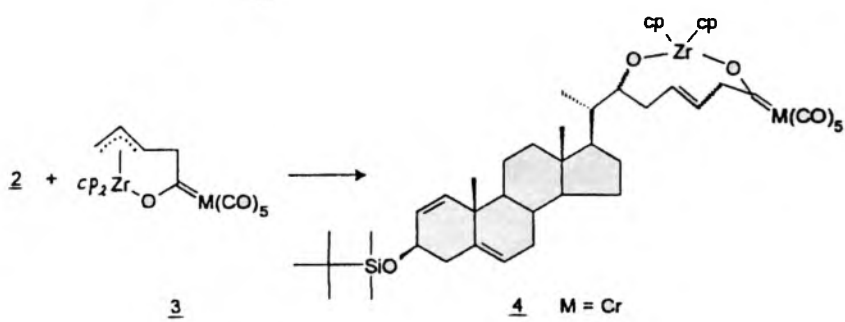
As part of a program for the synthesis of steroids with new side chains we are interested in the utilization of recently developed transition metal complexes as starting materials for stereoselective organometallic template reactions.

A number of steroid model compounds as substrates have been prepared. Starting with compound 1 we developed an efficient six step approach to the 3-protected 3β-hydroxypregna-1,5-diene-20-carbaldehyde 2, a C_{22}-steroid with potential importance in the synthesis of vitamin D analogues.



1 2 55% overall yield

The reaction of (π-allyl)zirconoxycarbene complexes 3 with steroid carbonyl compounds as 2 results in the formation of so far unknown chiral nine-membered metallacyclic ring systems 4.



3 4 M = Cr

SYNTHESIS OF 2β,25-DIHYDROXYVITAMIN D_3

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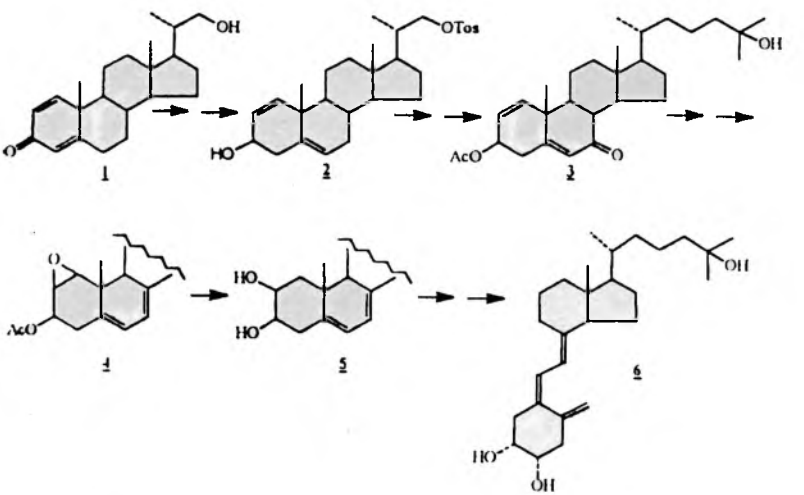
2β,25-Dihydroxyvitamin D_3 (6), an isomer of the biologically important vitamin D metabolite 1α,25-dihydroxyvitamin D_3, has been synthesized from (20S)-20-hydroxymethyl-pregna-1,4-diene-3-one (1) in thirteen steps.



Compound 2, suitable for C-C coupling reactions, is available in three steps from 1. The further key compound 3, which is to be obtained by allylic oxidation, represents a new steroid type, possessing a protected 3β-oxygen function and the 1,5-diene-7-oxo system. The 1β,2β-epoxy group has been introduced by HOBr addition and cyclization. After introduction of the 5,7-diene system reduction with $LiAlH_4$ gave the provitamin 5. Irradiation and thermal isomerization furnished the desired dihydroxyvitamin D isomer 6.

STEREOSELECTIVE SYNTHESES AND BIOLOGICAL ACTIVITIES OF (22*R*)- AND (22*S*)-22-METHYL-1α,25-DIHYDROXYVITAMIN D_3, ACTIVE VITAMIN D_3 ANALOGS WITH FIXED SIDE CHAIN CONFORMATION

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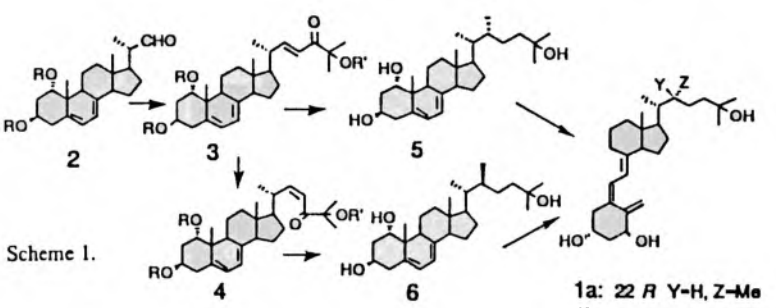
Two new active vitamin D_3 analogs, (22*R*)- and (22*S*)-22-methyl-1α,25-dihydroxyvitamin D_3 (**1a** and **1b**), were synthesized from 1α-hydroxylated C(22)-steroid **2** (Scheme 1). The vitamin D analogs (**1a** and **1b**), whose side chains are conformationally rigid, were designed to study the stereochemical structures required to bind to the receptor (VDR) for 1α,25-dihydroxyvitamin D_3 (**1c**) and to serum vitamin D binding protein (DBP). According to force-field calculations, the active vitamin D_3 (**1c**) adopts the anti and gauche(+) conformations with respect to the dihedral angle at C(17-20-22-23) with nearly equal distribution. In the 22-methylated analogs, **1a** and **1b**, however, the side chain conformations are restricted with more than 90% population in the gauche(+) and the anti forms, respectively. Either the (22*R*)- or (22*S*)-methylated steroidal side chain was constructed with high stereoselectivity (>97%) via a kinetically controlled conjugate addition of Me_2CuLi to (22*E*)- or (22*Z*)-22-ene-24-one (**3** or **4**), respectively, as a key step. The abilities of the two analogs, **1a** and **1b**, to bind to pig intestinal VDR were 1/50 and 1/3, respectively, and those to rat serum DBP were 1/200 and 2/3 respectively. The results suggest that the side chain conformation of the active vitamin D_3 (**1c**) best fitted to VDR and DBP is the same C(17-20-22-23) anti form.



Scheme 1.

1a: 22 *R* Y=H, Z=Me

1b: 22 *S* Y=Me, Z=H

1c: Y=Z=H

Yamamoto, K., et al. *Tetrahedron Lett* 1992, 33, 7521-7524; *J. Org. Chem.* 1993 ,58, 2530-2537.

NOVEL 2-HYDROXY- AND 2-ALKOXY-ANALOGS OF 1α, 25-DIHYDROXY- 19-NOR- VITAMIN D_3

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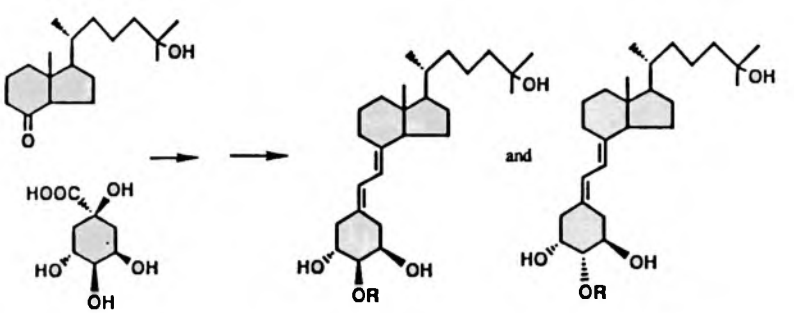
1α, 2α, 25-Trihydroxy-19-nor-vitamin D_3, 1α, 2β, 25-trihydroxy-19-nor-vitamin D_3 and their alkoxy analogs were prepared efficiently in a convergent synthesis starting with (-)-quinic acid and a Windaus-Grundmann type ketone. Configurations of the A-ring fragment substituents were determined by ^1H, ^1H COSY 2D spectra and ^1H NOE difference spectroscopy.

The new analogs exhibited an interesting biological profile, with potential for the treatment of osteoporosis.



NOVEL CONCURRENT SYNTHESIS OF SIDE-CHAIN ANALOGUES OF VITAMINS D_2 AND D_3

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Solvay Duphar B.V., P.O. Box 2, 1380 AAWeesp, Holland

A novel synthetic method was developed for the concurrent synthesis of both series of vitamins D_2 and D_3. The method was conceived as a part of our program of the evaluation of the vitamin D analogue with a highly specific activity profile. The method is illustrated by the preparation of analogues of 25-hydroxycholecalciferol with the extended side chain, i.e. 24,24-Dihomo- and (22E)-22-dehydro-24,24-dihomo-25-hydroxycholecalciferols. The new analogues were also designed in order to verify the hypothesis of the possible involvement of the side chain double bond and more specifically, C-22 and C-23 carbons, in the deactivating metabolism of synthetic analogues of vitamins D. The present method allows for the convenient preparation of vitamin D_2 and D_3 analogues from the same synthetic intermediates i.e. C-22 aldehyde of phenyltriazolinedione adduct of previtamin D and a side-chain alkyl sulfone. The key steps in this synthesis involve the Julia coupling of the vitamin D synthon with the side-chain sulfone followed by Barton radical deoxygenation of the C-22 alcohol or dehydroxy- desulfonylation of the respective ß-hydroxysulfone. The absolute configurations at C-22 and C-23 of the intermediate ß-hydroxysulfones were tentatively assigned by ^{1}H NMR. The vicinal coupling constants of H-22 and H-23 were compared with the respective values calculated for the least energy conformers obtained by molecular mechanics modeling.

1. A. Kutner, M. Chodyński, S.J. Halkes, J. Brugman, Bioorg. Chem. 1993, in press.
2. A. Kutner, J. Choliński, M. Chodyński, S.J. Halkes, Bioorg. Med. Chem. Lett., 1993, in press.

A Total Synthesis of the C/D Rings - Side Chain Fragment of Vitamin D and Sterols, Using Mukaiyama - Michael Conjugated Addition

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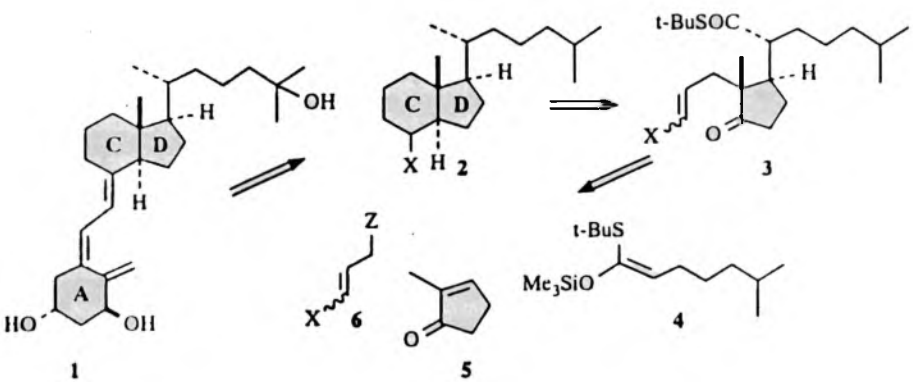
Vitamin D and sterol C\D - side chain fragment **2** was synthesised from ketene acetal **4** derived from 6-methylheptanoic acid, 2-methylcyclopent-2-en-1-one **5** and allyl methyl carbonate, using the Mukaiyama-Michael conjugate addition and Tsuji alkylation as the key steps.



Convergent Synthesis of Isocalysterol Homologue

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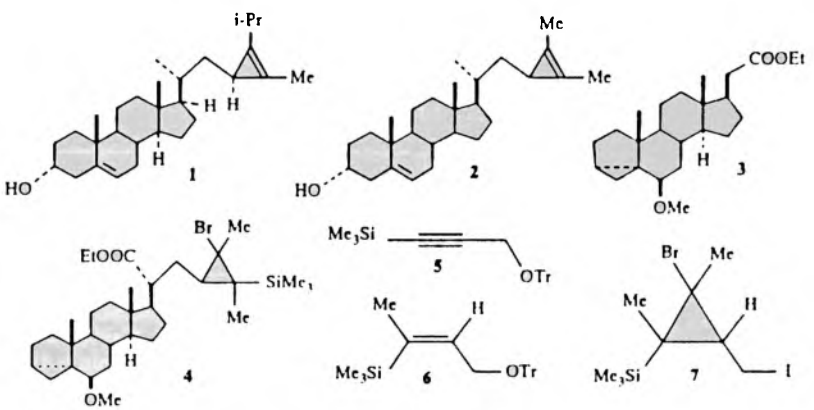
Institute of Organic Chemistry, Polish Academy of Sciences

In a program of research aimed on the synthesis of isocalysterol (**1**, Scheme 1) and related cyclopropene - containing marine sterols, 27,28-dinor homologue **2** has been synthesised. The synthesis involves alkylation of ester **3** with iodide **7** and further transformation of the alkylation product **4**. Iodide **7** was prepared from the propargyl alcohol derivative **5** *via* vinylsilane **6** and the corresponding dibromocyclopropane.



Tr = CPh_3

STRUCTURE ACTIVITY RELATIONSHIPS: PREPARATION AND OLFACTIVE PROPERTIES OF (-)-THIOAMBROX COMPARED WITH (-)-AMBROX

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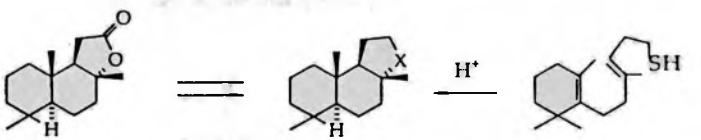
(-)-Ambrox® ((-)-1a, [1], [2]), a key compound in perfumery for its persistent amber scent [3], is compared in terms of volatility, lipophilicity, dipolar moment, accessible polar surface [4], hydrogen bond acceptor and electronic density [5] with the (-)-thio analogue ((-)-1b), which possesses similar olfactive profile but with a higher threshold value.



(+)-Sclareolide

(-)-1a X = O
rac or (-)-1b X = S

X	R_f[1]	R_t[2]	Rt[3]	Rt[4]	bp [°C]	APS[5]	→ μ[6]	log (P)[7]	threshold [8]
O	0.32	6.5	2.07	1.64	314.6	12.1	2.90	4.0	0.3
S	0.64	0.9	4.14	2.90	347.9	34.9	3.66	≥ 5.4	170

1) TLC, SiO_2 60 F254 0.025 cm, cyclohexane; 2) HPLC, Nucleosil 50-5, cyclohexane/AcOEt 98:2, 2 ml/min. 350 bars, in [min.]; 3) GC, Carbowax Chrompac CPwax 52 CB 10 m, 0.25 mm, 160°C 1 min., 5°C/min. in [min.]; 4) GC Silicon Chrompac CPSil 5CB 10 m, 0.25 mm, 160°C 1 min, 5°C/min. in [min.]; 5) Accessible Polar Surface for a probe radius = 1.4 A [5] in [A^2]; 6) Dipole moment mesured in dioxane in [Db]; 7) partition coefficient octanol/water; 8) Detection of the typical and clean amber note in [ppb].

References

[1] registered trade name of *Firmenich SA*;
[2] M. Stoll, M. Hinder, *Helv. Chim. Acta*, 1950, *33*, 1251;
[3] G. Ohloff, Riechstoffe und Geruchssinn, Die molekulare Welt der Düfte, Springer Verlag Heidelberg, 1990;
[4] B. Winter, *Helv. Chim. Acta*, 1989, *72*, 1278;
[5] F. Mohamadi, N. Richards, W. Guida, R. Liskamp, M. Lipton, C. Canfield, G. Chang, T. Hendrickson, W.C. Still, *J. Comput. Chem.*, 1990,*11*, 440;

2-SUBSTITUTED CYCLOHEXANOLS: A SURVEY OF ENZYME MEDIATED SYNTHESIS OF CHIRAL COMPOUNDS

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Flemingovo náměstí 2, 166 10 Prague 6, Czech Republic

This contribution summarizes the results achieved during the investigation focused on a preparation of all possible enantiomers of 2-(4-hydroxybenzyl)-1-cyclohexanol, which has been used in a synthesis of biologically active insect juvenile hormone analogs (JHAs). During this research, a demand for biological screening of all respective enantiomers of several promising JHA structures derived from the above identified alcohol has increased. Enzymatic ways using microorganisms, plant cell cultures and even pure enzymes to prepare the compounds requested have been studied.

The early stage of the research has been focused on a reduction of 2-(4-methoxybenzyl)-1-cyclohexanone by either *Saccharomyces cerevisiae* (Wimmer et al., 1987; 1992) or by *Solanum aviculare* cell cultures (Vaněk et al., 1989), respectively, followed by liberating the aromatic hydroxy group by a chemical way. The *cis*-(1S,2S)- and *trans*-(1S,2R)-2-(4-methoxybenzyl)-1-cyclohexanols have been achieved with different optical purity depending on an enzyme source used.

Later, a porcine pancreatic lipase (PPL) mediated hydrolysis of the racemic respective *cis*- and *trans*-2-(4-methoxybenzyl)-1-cyclohexyl acetates and the racemic respective *cis*- and *trans*-2-(4-tetrahydropyranyloxybenzyl)-1-cyclohexyl acetates has been employed, and has resulted in a synthesis of the opposite enantiomers (i.e. *cis*-(1R,2R)- and *trans*-(1R,2S)-alcohols), while the *cis*-(1S,2S)- and *trans*-(1S,2R)-enantiomers have been found in a form of their optically active acetates.

All enzymatic reactions used in the research have been performed in aqueous media. Satisfactory optical purity of the compounds desired has been determined in most cases, while satisfactory yield has not been achieved with the PPL mediated hydrolysis of the above identified acetates. Therefore, the attention has recently been focused on performing the PPL mediated hydrolysis of acetates in non-aqueous media.

References:

Vaněk T., Wimmer Z., Macek T., Šaman D., Svatoš A., Romaňuk M. (1989) *Biocatalysis* **2**, 265-272.

Wimmer Z., Buděšínský M., Macek T., Svatoš A., Šaman D., Vašíčková S., Romaňuk M. (1987) *Coll. Czech. Chem. Commun.* **52**, 2326-2337.

Wimmer Z., Vaněk T., Macek T., Šaman D., Svatoš A. (1992) *Enzyme Microb. Technol.* **14**, 197-202.

METABOLISM OF TESTOSTERONE AND ITS DERIVATIVES IN THE CULTURE *Absidia coerulea*

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The strain *Absidia coerulea* was used to transform testosterone and its derivatives to obtain some information about hormones metabolic pathways.

The substrates were: testosterone, androstendione, 1-dehydrotestosterone, 17α-methyltestosterone, 17α-methyl--1-dehydrotestosterone and progesterone. All of them were hydroxylated by the strain used. Position of hydroxylation depended on the structure of the substrate: testosterone, androstendione and 1-dehydrotestosterone were transformed to 14α-hydroxy-derivatives; 17α-methyltestosterone was transformed to 6-dehydro- and 7α-hydroxy- derivatives, and 17α-methyl-1-dehydrotestosterone was hydroxylated at C-11 forming 11β-hydroxy-17α-methyl-1-dehydrotestosterone. The main product obtained after transformation of progesterone was 7α,14α-dihydroxyprogesterone.

MICROBIAL DEGRADATION OF PLANT STEROL SIDE CHAINS BY A RECOMBINANT MYCOBACTERIUM SP. STRAIN

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About 10 years ago the time was ripe for the development of genetic manipulation on mycobacteria, with many applied objectives. The first is medical, stimulated by the fact that mycobacteria are responsible for two of the world's most important bacterial human diseases, tuberculosis and leprosy, as well as widespread animal infections. The second is utility of various non-pathogenic mycobacteria in the field of industrial bioconversion of steroids. From the eighties the industrial synthesis of the majority of steroid drugs is based on the microbial transformation products obtained by the removal of the side chain of the cheap and readily available sitosterol (*1*).

In recent years our group has isolated recombinant strains after spheroplast fusion which can bioconvert the different plant sterols (ergosterol, stigmasterol, sitosterol, campesterol) into new transformation products having partially degraded side chain (*2*). The structures of the new 26-oxygenated compounds were elucidated by UV, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy (*3*).

REFERENCES

1. Kieslich, K.: J. Basic. Microbiol. *25*, 461 (1985).
2. Jekkel, A., Csajági, É., Ilkőy, É., Ambrus, G.: J. Gen. Microbiol. *135*, 1727 (1989).
3. Horváth, Gy., Ilkőy, É., Jekkel, A. and Ambrus, G.: Proc. of the 5th Symp. on the Analysis of Steroids (1993).

MICROBIAL TRANSFORMATION OF SITOSTEROL BY A MUTANT *MYCOBACTERIUM* SP. STRAIN

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The microbial transformation of sterols and various steroid intermediates, is an important expedient as a source of commercial supply of the steroid drugs (*1*). A variety of microorganisms is capable of utilising sterols for growth as a sole carbon source (*2*). We investigate the use of mycobacteria for the degradation of sterol compounds (*3,4*). We used a new method of mycobacterial lysis for application in mutagenic treatment. This method applies rapid chemical pre-treatment of bacteria with sodium dodecyl sulphate (SDS) that remove the outer layer in the tripartite structure of the cell envelope. Our procedure makes the bacteria susceptible to nitrosoguanidine. Two Mycobacterium mutants have been identified which degrade sitosterol and campesterol only partially and both of them accumulate the same new degradation product of 23,24-dinorcholane side chain as the main product, during the fermentation process.

REFERENCES

1. Charney, W. and Herzog, H.C.: Microbial transformation of steroids. A handbook. Academic Press, New York and London (1967).
2. Iida, M., Tsuyuki, K., Kitazawa, S., and Iizuka, H.: Production of 20-(carboxy-pregna-1,4-dien-3-one from sterols by mutants of *Rhodococcus* sp. J. Ferment. Technol. *65*, 525-529 (1987).
3. Jekkel, A., Csajági, É., Ilkőy, É. and Ambrus, G.: Genetic Recombination by Spheroplast Fusion of Sterol-transforming *Mycobacterium* Strains. Journal of General Microbiology *135*, 1727-1733 (1989).
4. Ambrus, G., Ilkőy, É., Horváth, Gy., Podányi, B., Böcskei, Zs., Gyürky, S. and Jekkel, A.: Novel Intermediates of Microbial Side Chain Degradation of Sitosterol. Tetrahedron Letters, Vol. 33. No. 36., pp. 5267-5268 (1992)

HYDROXYLATION OF 4-EN-3-OXO STEROIDS BY *Fusarium culmorum*

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Institute of Fundamental Chemistry, Agricultural University, Wrocław, Poland.

The strain of *Fusarium culmorum* proved to be efficient in hydroxylation of some of 4-en-3-oxo steroids. All the used substrates underwent complete transformation usually to one main product.

The substrates were 4-en-3-oxo steroids which differ in substituents at C-17; i.e. 17β: -OH, $-OCOCH_3$, $-OCOC_2H_5$, $-COCH_3$, or 17-oxo group. It was observed that stereochemistry and the position of hydroxyl group introduced (6β, 12β, 15α or 15β) slightly depended on substituents at C-17.

SESQUITERPENE BIOSYNTHESIS IN HAIRY ROOT CULTURE OF LACTUCA VIROSA: INFLUENCE OF THE NUTRIENT MEDIA

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Polish Academy of Sciences, 31-343 Krakow, Poland

Hairy root culture of Lactuca virosa was derived from "in vitro" grown, aseptic plantlets infected with Agrobacterium rhizogenes strain LBA 9402. The axenic roots obtained were cultivated in MS medium with macronutrients reduced by a half on a gyrotory shaker (110 r.p.m.) in the dark and were subcultured every two weeks. Genetic transformation was proved by rifampicin resistance of the tissue, as well as by opine biosynthesis.

Six nutrient media: MS (1), $^1/_4$ MS (2), MS medium with macronutrients of half-strenght (3), GB, (4), MS + 10 mg/l GA_3 + 2.25 µg/l BAP (5) and MS + 10 mg l GA_3 + 10µg l BAP (6), were examined to establish their influence on biomass increment and sesquiterpene lactone biosynthesis. All cultures were harvested three weeks after inoculation.

The biomass increment was the best in cultures grown in medium 1. Media 4 and 6 gave unsatisfactory results, although in the case of medium 4, a fresh weight was the highest one.

The cultures were capable of synthesizing sesquiterpene lactones characteristic of the intact plant e.g. dihydrolactucin, jacquinelin, lactulide A, lactuside A and jacquinelin glycoside. However, remarkable differences in their HPLC profiles (RP HPLC, Nova-Pak C8 cartridge, solvent system: MeOH-H_2O, 35:65, isocratic mode, flow rate: 2ml/min) were observed.

The well growing cultures contained sesquiterpene lactones mainly in glycosidic form. Aglycones predominated in the cultures showing poor biomass increment.

SYNTHESES AND CONFORMATIONAL ANALYSIS OF THE 10- AND 13-HYDROXYDERIVATIVES OF CEMBRENE

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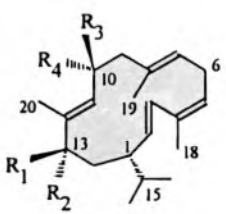
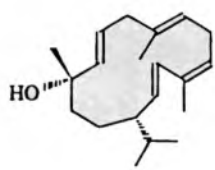
Conformational analysis of 10- and 13-hydroxycembrenes (2)–(5) was performed by using NMR methods and molecular mechanics calculations. The final results revealed that conformational states of all investigated compounds in solution are characterized by the same orientation of double bonds with respect to the average plane of the macrocycle. The alcohols (2), (5) are conformationally homogeneous and their solution structures correspond to crystal structure of cembrene (1), which as was shown previously to be retained in solution. In the case of alcohols (3) and (4) additional conformational flexibility in C(8)-C(11) molecular fragment appears. These facts are in agreement with pseudoequatorial orientation of hydroxyl group in "cembrene-like" conformation for alcohols (2), (5) and pseudoaxial hydroxyls for alcohols (3), (4).





6

1 $R_1 = R_2 = R_3 = R_4 = H$
2 $R_1 = OH$, $R_2 = R_3 = R_4 = H$
3 $R_2 = OH$, $R_1 = R_3 = R_4 = H$
4 $R_3 = OH$, $R_2 = R_3 = R_4 = H$
5 $R_4 = OH$, $R_1 = R_2 = R_3 = H$
7 $R_3 + R_4 = O$, $R_1 = R_2 = H$

The 13-hydroxyderivatives (2), (3) were prepared according to previously published procedure of regioselective SeO_2/t-BuOOH oxidation of cembrene (1). The 10-hydroxycembrenes (4), (5) were synthesized from alcohol (6), which was known to be the product of photooxidation of cembrene (1), by PCC oxidation to ketone (7) followed by reduction with $LiAlH_4$. Since cembranoids (5) and (7) are natural compounds, this transformation is a biomimetic synthesis as well.

CONFORMATIONAL STUDY OF α-SUBSTITUTED CARANONE-4

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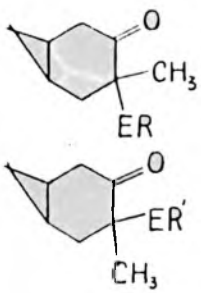
Kazan, Russia

Synthesis and investigation of conformational behavior of α-subsituted caranones-4 in solution have been made. The derivatives of cyclohexanon and aceton with the same substitution have been used as a model substances.

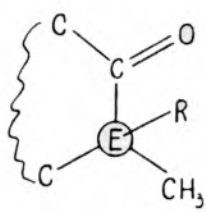
The application of complex of experimental and calculation methods made it possible to obtain correct data concerning the molecular conformations and dynamics of their interconversion.

Conformational analysis was carried out using dipole moments method, Kerr effect, and X-ray diffraction. Molecular mechanics was used in addition to experimental methods.



ER=OH, OCH_3, SCH_3, SPh

ER'=OH, OCH_3



It was established, that for the most compounds the axial conformers are favour and for them along C-E bond the structure is realised, in wich E-R bonds is parallel to carbonyl group.

DERIVATIZATION REACTIONS IN MASS SPECTROMETRY OF ECDYSTEROIDS

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The ecdysteroids represent natural steroids widespread in several groups of plants and invertebrates. Structural variability of them is derived from insect molting hormone ecdysone. The structural analysis of ecdysteroids is usually accomplished by spectral methods especially ^{1}H NMR, IR and MS. Because of their low concentration in biological material only limited amount of compound is usually available for measurment. Mass spectrometry, the method which requires only sub-milligramme amounts of compound to be analyzed, can furnish important structural informations. In order to gain more informations different ionization methods have been employed. Fast atom bombardment (FAB) and electron impact (EI) mass spectrometry appear to be the best combination of such methods the former giving mostly information about molecular weight the latter some structural information arising from extensive fragmentation. Further information were obtained using derivatization carried out directly in FAB matrix. The formation of cyclic boronates and deuterium exchange give the best results. An application boronate formation in crude plant extracts will also be discussed.

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