SYNTHETIC APPROACHES TO POLIFUNCTIONALIZED PERHYDRINDANES

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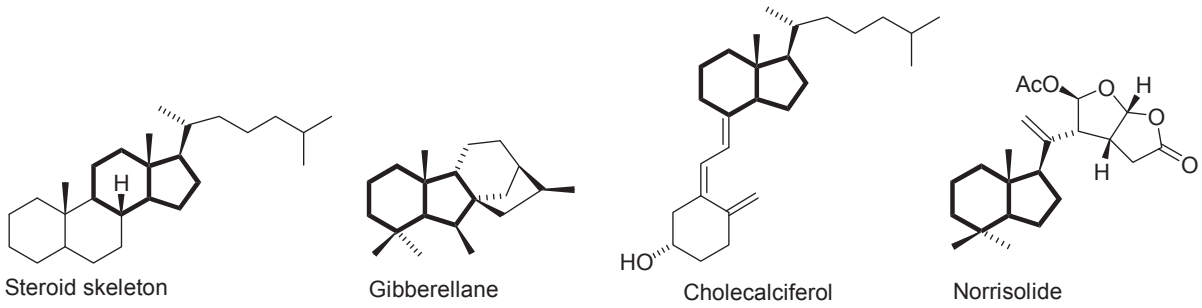
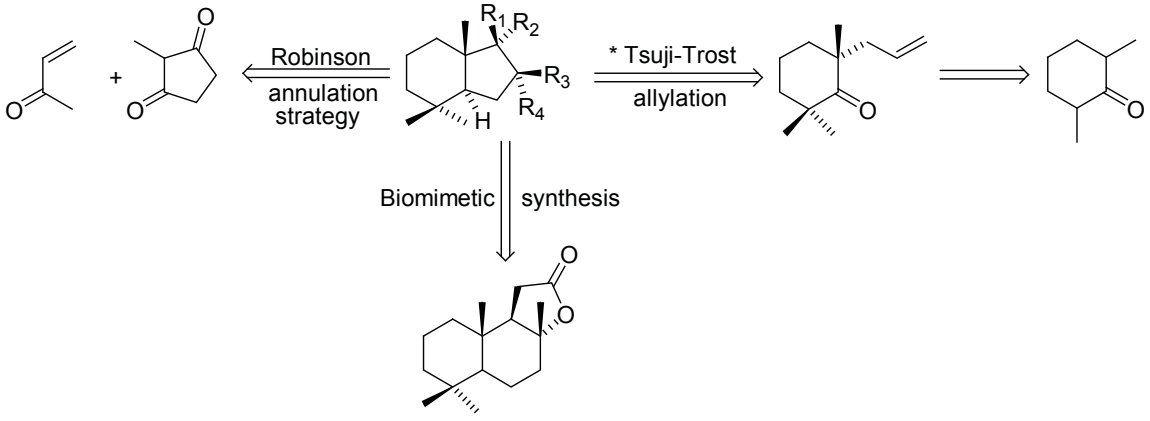
Abstract: The current communication represents an extended abstract of the presentation delivered on the joint Moldo-Italian seminar "New frontiers in natural product chemistry", held in the Institute of Chemistry, Academy of Sciences of Moldova on 31 September. An overview of the synthetic methods oriented to the synthesis of functionalized terpenic perhydrindanes is provided. Different synthetic strategies are considered, including those based on biomimetic approach. The array of obtained new structures can serve as leads in structure-activity studies as well as useful building blocks towards other perhydrindanes.

Introduction

The perhydrindane fragment represents a structural motif broadly found in natural products frequently connected to relevant biological activities. The incorporation of this substructure in the certain molecule can be of two distinct fashions: as a part of a condensed polycyclic system (steroids, giberellins) or as a "stand alone" fragment (vitamine D, rearranged spongiane diterpenoids).



The "stand alone" disposal of perhydrindane moiety is inevitable accompanied by a certain degree of functionalization, and due to the inconveniences connected to the use of this fragment from natural sources, considerably efforts have been undertaken to access functionalized perhydrindanes by synthesis. Different strategies have been reported in the literature, the most proeminent ones are depicted in scheme 1.

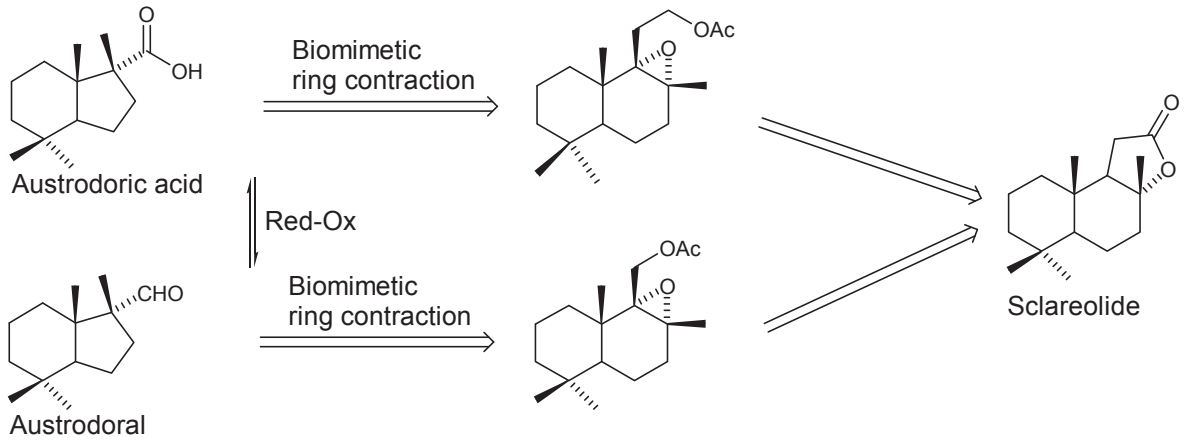


Scheme 1

The current communication presents an outline of synthetic procedures based on different strategies and elaborated in our research group for the synthesis of B-ring functionalized perhydrindanic core.

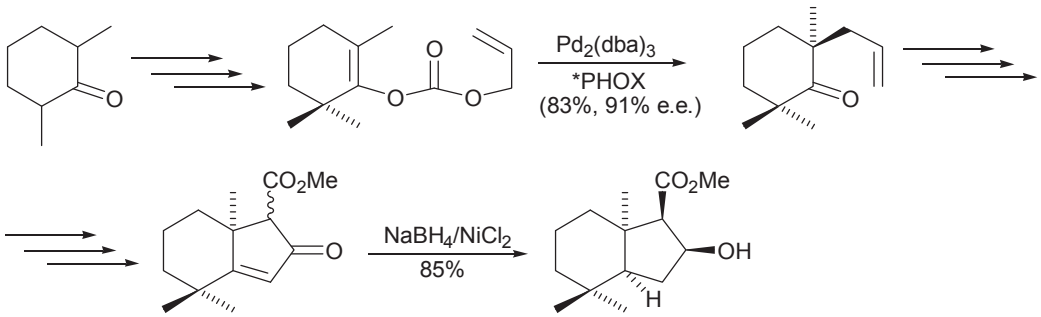
Biomimetic strategy. The biomimetic strategy in retrosynthetic analysis of perhydrindanic natural products relies on a ring contraction process. Potential substrates are drimanes or homodrimanes, easily accessible from commercial sclareolide. We have used this strategy for the successful synthesis of austrodoral and austrodoric acid - two compounds

of marine origin, isolated by Gavagnin and coworkers from the dorid nudibranch *Austrodoris Kerguelenensis* [1]. The key transformation was a ring contraction of suitable functionalized drimanic or homodrimanic epoxides (scheme 2) [2,3].



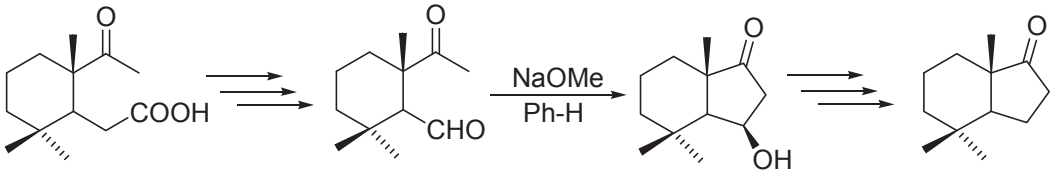
Scheme 2

Tsuji-Trost enantioselective allylation strategy. This strategy has been reported previously by several authors and we have adapted it in order to get a deeper functionalisation of the B-ring. Accordingly, the carboxymethyl group has been introduced by a formylation protocol. The double bond on the A-B junction was selectively reduced by nickel boride to provide the cis-fused perhydrindane (scheme 3).



Scheme 3

Intramolecular aldol strategy. The starting material represents the known keto-acid, readily available from sclareolide (scheme 4). The synthetic sequence leading to bicyclic structure includes a oxidative decarboxylation which lead to a primary iodide. Substitution of the iodine for hydroxyl group and Jones oxidation led to the keto-aldehyde, which underwend a smooth intramolecular aldol condensation to provide the functionalized perhydrindane. Further deoxigenation led to the known saturated ketone, used previously for the synthesis of important rearranged spongian terpenes of marine origine [4].



Scheme 4

Conclusions. A whole series of new B-ring functionalized terpenic perhydrindanes have been synthesized using different synthetic strategies. The obtained compounds will be further involved in chemical modification and activity testing studies.

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Dr. Veaceslav Kulcitki was born in 1969. He graduated from Moldova State University in 1992 and obtained the Ph.D. degree in 1998 from the Institute of Chemistry, Moldova Academy of Sciences, under the supervision of Professor P. F. Vlad and Dr. Sci. N. Ungur. He was a postdoctoral fellow with Professor Guido Cimino (ICB, Naples, Italy) and Professor Oliver Reiser (Regensburg University, Germany) being involved in different projects connected to natural products and synthetic organic chemistry. He is the author of more than 70 publications, including review articles, book chapters and two patents. Dr. Kulcitki has been appointed Associated Professor in 2006 and holds currently the position of a senior scientific researcher at the Institute of Chemistry, Moldova Academy of Sciences. His research interests include synthesis of natural products by biomimetic approaches, including electrophilic cyclisations and molecular rearrangements.

References

[1]. Gavagnin, M.; Carbone, M.; Mollo, E.; Cimino, G. *Tetrahedron Lett.* **2003**, *44*, 1495–1498.
[2]. Kulcitki, V.; Ungur, N.; Gavagnin, M.; Carbone, M.; Cimino, G. *Tetrahedron Asymm.,* **2004**, *15* (3), 423-428.
[3]. Kulciţki, V.; Ungur, N.; Gavagnin, M.; Carbone, M.; Cimino, G. *Eur. J. Org. Chem.,* **2005**, (9), 1816–1822.
[4]. Brady, T.P.; Kim, S.H.; Wen, K.; Theodorakis, E.A. *Angew. Chem.,Int. Ed.,* **2004**, *43*, 739-749.