

## SYNTHESIS OF C<sub>6</sub> AND C<sub>7</sub> FUNCTIONALIZED DRIMANES FROM LARIXOL AND SCLAREOL

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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 30 September. An overview of the synthetic methods oriented to the synthesis of C<sub>6</sub> and C<sub>7</sub> functionalized euryfurans is provided.

### Introduction

Sesquiterpene euryfuran **1** was isolated from several marine organisms such as nudibranches *Hypselodoris californiensis* and *H. Porterae* [1], sponges *Dysidea herbacea* [2] *Euryspongia* species [1] and, from a new genus of a Pacific sponge of the family *Thorectidae* [3]. This natural product has attracted much interest due to its antitumor activity<sup>3</sup> and its potential as synthetic intermediate [4].

Several semisynthetic routes and total synthesis of euryfuran **1** have been published [5-15]. This compound was used as starting material for the syntheses of others natural drimane sesquiterpenes [7-10,16,17].

We will like to report our preliminary results on the syntheses of C<sub>6</sub> and C<sub>7</sub> functionalized euryfurans starting from the abundantly available labdanic diterpenes larixol **2** and sclareol **3**. The side chains of these two labdanes was removed by oxidation to the corresponding 14,15-bisnorlabd-13-ones **4** and **5**, which were transformed by known methods in dienes **6** and **14** [18-20] (Figure 1).

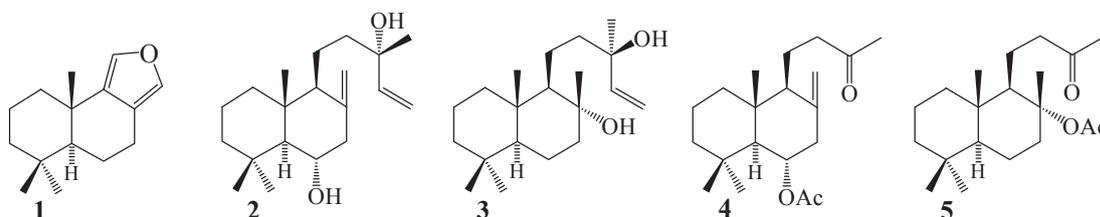


Figure 1

### Results and discussion

Diene **6** is an interesting starting material for the synthesis of several C<sub>6</sub> functionalized drimanes. The diene moiety in **6** was submitted to photooxygenation to give the endoperoxide **7** in high yield, which was converted into acetoxyfuran **8** by treatment with FeSO<sub>4</sub>. The acetate **8** was hydrolyzed and oxidized to 6-ketofuran **13** in an overall yield of 68%. The same 6-ketofuran **13** was obtained *via* a slightly different sequence of the same transformations of the intermediates **10**, **11** and **12** in 72% overall yield (Figure 2).

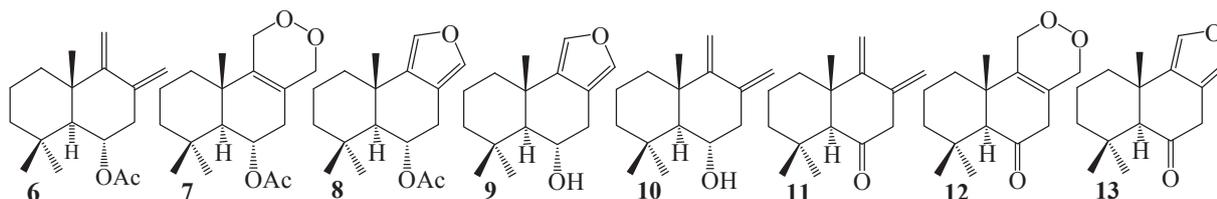
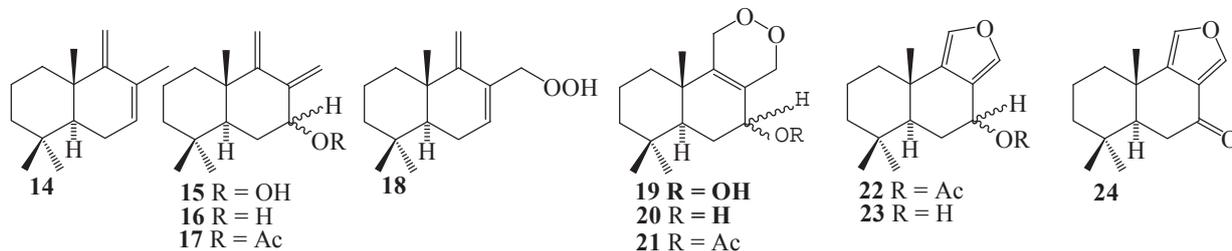


Figure 2

The known endocyclic drim-7,9(11)-diene **14** is a suitable starting material for synthesis of  $C_7$  functionalized drimanes [19,20,22-26]. It is known that olefins with allylic hydrogens give unsaturated hydroperoxydes in the ene-reaction with singlet oxygen [27]. The photooxygenation of diene **14** also shows this ene-reaction to hydroperoxide (**15**) as the main reaction. A 1,4-cycloaddition of singlet oxygen to the exocyclic diene and a rearrangement are responsible for the formation of the two by-products **18** and **19** (Figure 3).



**Figure 3**

The main product **15** was submitted to reduction with thiourea and acetylation to give a mixture of the  $C_7$ -acetates **17**, which was photooxidized to the acetoxyperoxydes **21** (Figure 3) [28]. The reduction of **21** with ferrous sulphate followed by saponification of the acetate and oxidation gave the 7-ketofuran **24** in 23.4% overall yield. The structures of compounds **19** and **21** were confirmed by X rays analysis. The same compound **24** in 8.7% overall yield was also obtained from side product **19** after reduction of the  $C_7$ -peroxide with thiourea, treatment of resulted 7-hydroxyperoxydes **20** with ferrous sulphate and oxidation of the  $C_7$ -hydroxy group (Figure 3).

### Conclusions

Breakdown of the side chain of (+)-larixol **2** or (+)-sclareol **3** gives an easy access to an exocyclic diene **6** and an endocyclic diene **14** respectively. These two dienes **6** and **14** are excellent starting materials for the syntheses of ring B functionalized drimanes, as it was proved by present syntheses of 6-ketoeuryfuran **13** and of 7-ketoeuryfuran **24**, in respectively 68% and 23.4%.

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