

Reduction of Furanoheliangolides

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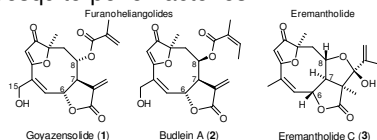
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INTRODUCTION

Furanoheliangolides and eremantholides (*figure 1*) are natural sesquiterpene lactones that show a number of interesting biological activities, e.g. trypanocidal, anti-inflammatory, anti-tumor, etc.

Figure 1. Sesquiterpene Lactones



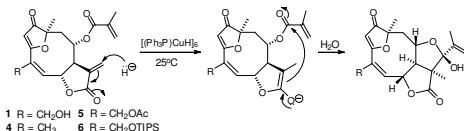
We have recently described a method for transforming furanoheliangolides (found in larger amounts in plants) into eremantholides using Stryker's reagent.^{1,2}

In this work we explore an interesting aspect regarding the stereochemistry of these compounds. There are no eremantholides, in nature, with relative stereochemistry *cis* between the substituent's of positions C₇ and C₈. We have then decided to investigate if eremantholides could be prepared from *cis* substituted at C₇ - C₈ furanoheliangolides such as budlein A (2).

RESULTS AND DISCUSSION

We have found that many furanoheliangolide (including 1 and derivatives 4, 5 and 6) can be reduced with Stryker's reagent in a reasonably selective way: despite the large number and variety of reducible functions present on these molecules, the addition of hydride to the α -methylene-lactone system followed by cyclization, as shown in *scheme 1*, was consistently a preferable path.

Scheme 1.

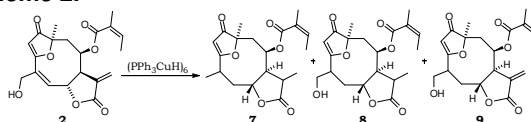


Substrates containing oxygenated functions at C₁₅ (such as 1, 5 and 6) gave also some products of reduction of the $\alpha,\beta,\gamma,\delta$ -unsaturated furanone, but eremantholides were always obtained with yields between 30 to 50% in all cases of *scheme 1*.

However, when we treated budlein A (2) with Stryker's reagent under the same conditions, no

eremantholide was formed at all. As shown in *scheme 2*, only reduced products were formed, and no cyclization occurred.

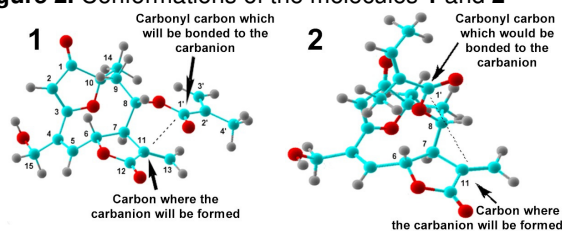
Scheme 2.



By using molecular models or molecular mechanics computer programs we can see that, due to a peculiar conformation of the 9-membered ring, the vicinity relationship of the groups attached to carbons C₇ and C₈ is opposite to what we usually expect from examination of planar structural formulas: the *trans* disposed groups (as in cases of *scheme 1*) are nearer to each other than the *cis* disposed groups (as in case of *scheme 2*).

In *figure 2* are depicted the more stable conformations of the molecules of goiazensolide (1) and of budlein A (2).

Figure 2. Conformations of the molecules 1 and 2



In this picture we can see that the carbon atoms that should be connected to form eremantholides are at a favourable distance for (1), but are very far apart from each others in structure 2.

CONCLUSION

We can conclude that only *trans*-substituted at C₇ and C₈ furanoheliangolide can give eremantholides, because the *cis* configuration determines a conformation where the groups that connect to each others are maintained far apart.

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REFERENCES

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