# Synthesis of Pimarane-type Diterpenes from Constituents of Copaiba Oil.

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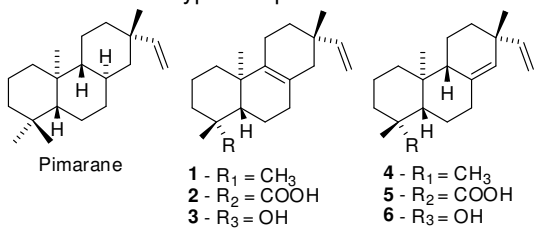
## INTRODUCTION

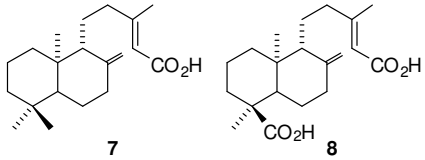
Pimarane-type diterpenes, such as pimara-8,15-diene (**1**) and pimaradienoic acid (**5**) (*figure 1*), are mainly isolated from conifer oleoresin. This class of compounds has shown interesting biological activities, e.g. analgesic, anti-tumor, anti-inflammatory, vasorelaxant, antimicrobial activities, anti-Alzheimer and antioxidant effects.[1] Due to the importance of this class, several research groups have already proposed total synthesis of those substances.

**Figure 1.** Pimarane-type diterpenes




Thus, we decided to study the synthesis of these compounds from two main constituents of Copaiba oil, copalic acid (**7**) and *ent*-agathic acid (**8**) (*figure 2*).

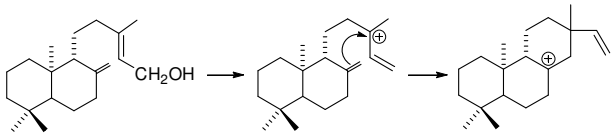
**Figure 2.** Constituents of Copaiba oil




## RESULTS AND DISCUSSION

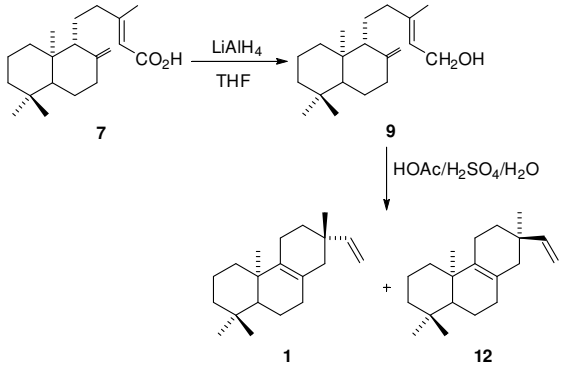
Considering the structures of the compounds in *figures 1* and *2*, we see that the pimaranes could be obtained from derivatives of the acids **7** and **8** (e.g. compound **9**) (*scheme 1*), through an acid catalyzed elimination for formation of carbocation **10** and subsequent rearrangement with cyclization to produce **11**. The elimination of a proton could give the pimaranes systems (*figure 1*).

**Scheme 1.**




We started our studies with the copalic acid (**7**). Firstly it was reduced with $LiAlH_4$ in THF to its corresponding alcohol (copalol **9**), with a yield of 90% (*scheme 2*). Subsequently the copalol (**9**) was treated with a solution containing acetic acid, sulphuric acid and water at 50ºC,[2] quenching the reaction right after complete consumption of starting material. As shown in *scheme 2*, we can obtain the pimara-8,15-diene (**1**) and its epimer **12**, with yields of 32% and 28% respectively.

**Scheme 2.**




## CONCLUSION

The acid catalyzed rearrangement of the more abundant copalol-type structures can produce pimarane-type diterpenes with reasonable yields. We intend to realize an extensive study of several reaction conditions in order to obtain better yields and, if possible, some others structures as compound **5**.

## ACKNOWLEDGEMENTS

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## REFERENCES

[1] Jung, H. A. et al. *Arch Pharm Res* **2009**, *32*, 1399-1408.
[2] .McCreadie, T. et al. *J. Chem. Soc.* **1971**, 312-316.