Preparation of New Prenylated (*E*)-Chalcones

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INTRODUCTION

Chalcones comprise one of the main classes of natural products, and their structure is an interesting scaffold for different chemical modifications, including the functional group interconversions.[1,2] Among the different groups that are correlated to bioactivity of chalcones, the side prenyl chains seem to be related to plasmatic membrane anchorage. For this reason, we have synthesized a series of 20 new *O*-prenylated chalcones, including isoprenylated, geranylated and farnesylated derivatives. In addition, these compounds were evaluated as antifungal agents.

RESULTS AND DISCUSSION

The (*E*)-chalconic building block preparation was carried out by Claisen-Schmidt aldol reaction, under basic or acid catalysis, generating monohydroxylated chalcones (Figure 1).

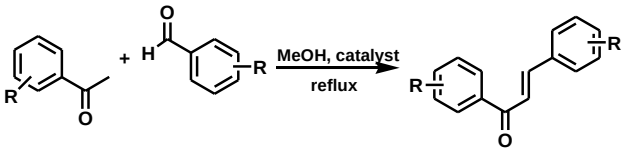

Figure 1. Preparation of *(E)*-chalconic building blocks (catalyst = H_2SO_4 or NaOH; R = H or hydroxyl)

For preparation of the prenylated (*E*)-chalcone derivatives was used alkylation reactions with terpenyl bromides in alkaline medium, and reflux (Figure 2).

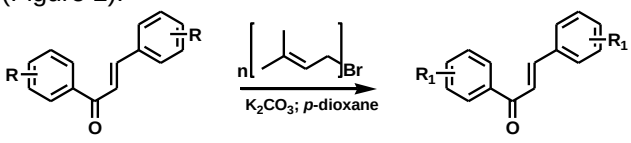

Figure 2. Preparation of prenylated *(E)*-chalcones [R=H or hydroxyl; R_1= H, isoprenyl (n = 1), geranyl (n = 2) or farnesyl (n = 3)]

In general, the preparation of the monohydroxylated chalcones demonstrated yields between 56% and 86%, and the prenylated chalcones were obtained in satisfactory yields (57%-92%). Despite the formation of the designed *O*-prenylated chalcones, some *C*-prenylated derivatives as byproducts from Claisen rearrangements were detected, requiring additional purification steps, including Column Chromatography and Preparative Thin Layer Chromatography.

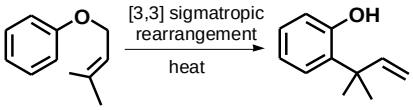

Figure 3. Conversion from *O*-prenylated chalcone to *C*-prenylated chalcone via Claisen rearrangement

3-*O*-Geranyl-chalcone (**1**) and 3-*O*-farnesyl chalcone (**2**) demonstrated potent antifungal activity against *Paracoccidioides* species, exhibiting MIC values ranging from 0.48 to 3.90 µg.mL^{-1}.

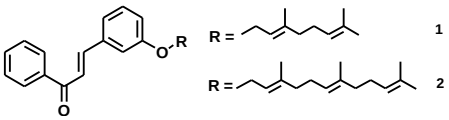

Figure 4. Antifungal 3-*O*-prenylated chalcones

CONCLUSION

In conclusion, the current work described the preparation of 20 new chalcones with satisfactory yields. Among these, 3-*O*-prenylated compounds (**1** and **2**) showed potent anti-*Paracoccidioides* activity.

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REFERENCES

[1] Chetana, B. P.; Mahajan, S. K.; and Survana, A. K., *J. Sci. Res.* **2009**, *1*, 11.
[2] Dong, X.; Chen, J.; Jiang, C.; Liu, T. and Hu, Y. *Arch. Pharm. Chem. Life Sci.* **2009**, 342, 428.