Semi-synthetic kaurenoic acid derivatives and their antifungal activity against *Colletotrichum lindemunthianum*.

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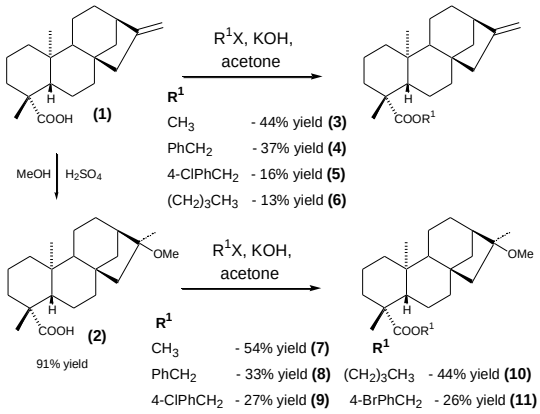
Keywords: *antifungal activity, Colletotrichum lindemunthianum, diterpenes, kauranes.*

Introduction

Kaurane type diterpenes are known to be found in several plant families. Among them, kaurenoic acid is the major component of a considerable number of species in Asteraceae and Euphorbiaceae families. This compound is related to biological activities such as anti-tumor, anti-inflammatory, antibacterial and antifungal, among others.[1] Furthermore, one can take into account that structural modifications can lead to more active and more selective compounds. So, the structural modification of an active natural product can furnish new promising compounds. One of the world's most economically relevant problems is related to some phytopathogenic agents which cause losses in agriculture. According to our research interests, this work's goal is to modify the original structure of kaurenoic acid and evaluate the antifungal activity of the derivatives against the phytopathogenic fungus *Colletotrichum lindemunthianum*.

Results and Discussion

The isolation of kaurenoic acid **(1)** from a commercial sample of *Mikania glomerata* was firstly undertaken. Then, **1** was transformed into the 16-methoxy kaurenoic acid **(2)**. Both compounds were, then, submitted to the esterification reactions, as shown on scheme 1. Five different alkyl halides and a total of nine ester derivatives were achieved (**3**-**11**). All compounds were identified and characterized by the use of ^{1}H and ^{13}C NMR experiments results, with the use of 2D NMR in some cases. The group of compounds (**1** to **11**) was assayed *in vitro* against two strains of *C. lindemunthianum* fugi. This specie is responsible for causing anthracnose in bean crops, leading to several losses in this kind of culture. All biological assays were performed with a unique concentration for all assayed substance (500 $\mu g.mL^{-1}$). They were tested against two different strains of the fungus and the results were detected as: **N** - the fungus did not grow or **Y** – the fungus did grow. The promising samples are those which result in not growing both strains of the fungus. They can be used in further antifungal evaluations.



Scheme 1. Reactions that led to the production of kaurenoic acid derivatives.

Table 1. Antifungal assays results.

Compound:	**1**	**2**	**5, 6, 7, 10**	**3, 4, 8, 9**	**11**
Growing of Strains 65/89	N Y	Y N	Y Y	N Y or Y N	N N

The observation of the results can firstly show that the conversion of **1** in **2**, caused no effect in the activity. Compound **2** has similar result as the natural product (**1**). Four of the obtained esters (**5**-**7** and **10**) are less active than **1**, while four others (**3**, **4**, **8** and **9**) displayed the same level of activity of **1**. On the other hand, compound **11** displayed a better activity and can be considered promising to future activity evaluations.

Conclusions

The results prove that structural modification can lead to more active compounds indeed. Compound **11** presented a promising activity and will be further investigated.

Acknowledgements

FAPESP, CAPES, CNPq.

[1] Uchôa, P. K. S. et al, *Quím. Nova,* **2013**; *36*: 6; 778-782.
[2] De Carvalho *et al. Phytochemistry* **1997**.
[3] Cechinel Filho, V. et al, *Quím. Nova,* **1998**; *21*: 1; 99-105.