Synthesis and insecticidal activity of new tropane alkaloids

Simone Z. Mairink[1] (PG), Luiz C. A. Barbosa[1,2] (PQ)*, Eduardo V. V. Varejão[1] (PQ), Marcelo C. Picanço[3] (PQ), Elizeu S. Farias[3] (PG)

*[1]Department of Chemistry, Universidade Federal de Viçosa, 36570-000, Viçosa, MG, Brazil. [2]Department of Chemistry, Universidade Federal de Minas Gerais, 31270-901, Belo Horizonte, MG, Brazil. [3]Department of Animal Biology, Universidade Federal de Viçosa, 36570-000, Viçosa, MG, Brazil. *correspondence to: lcab@ufmg.br*

Keywords: *oxyallyl cation,insecticide, tropane alkaloids, carbamate, Ascia monuste.*

Abstract

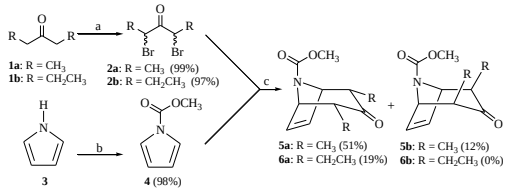
The synthesis and potential insecticidal activity of a series of new tropane-carbamates against *Ascia monuste* are reported.

Introduction

Ascia monuste (Godart) (Leptoptera) is an insect pest causative of severe defoliation in vegetable crops, which can lead up to 100% of crop losses.[1,2] Control of *A. monuste* has been done by the use of chemical insecticides, including carbamates. Tropane alkaloids constitutes an important classes of secondary metabolites implicated in plant defense, particularly against herbivore insects. In the present work, we synthesized a series of tropane derivatives presenting a carbamate group (known as highly toxic insecticides) and evaluated their insecticidal activity against *A. monuste* larvae.

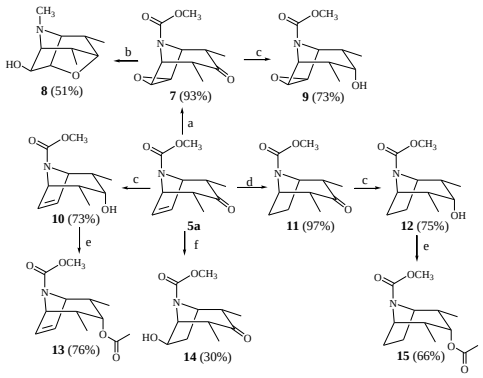
Results and Discussion

Synthesis of tropane alkaloids was carried out by cycloaddition reaction [4+3] of α,α-dibromoketone with *N*-carboxymethyl-pyrrole.[3-5] The present strategy for the preparation of tropane alkaloids with the carbamate group in its structure is depicted in Scheme 1. The synthetic approach started with obtaining α,α-dibromoketone (**2**) and *N*-carboxymethyl-pyrrole (**4**). Following, a cycloaddition reaction [4+3] between α,α-dibromoketone and *N*-carboxymethyl-pyrrole afforded the tropane alkaloids **5a**, **5b**, **6a**.



Scheme 1. (a) Br_2, HBr 48% v/v, 1.5h, r.t.; (b) NaH, THF, 24h, 50°C; (c) Cu, NaI, CH_3CN, 24h, 50°C.

Then, compound **5a** (obtained in higher yields) was subjected to a series of chemical modifications affording nine other bicyclic carbamates (Scheme 2),. Results from bioassays (Figure 1) showed that compounds **6a**, **10**, and **15** presented high activities aganist second-instar larvae of A. *monuste,* with LD_{50} of 1.01, 3.76 and 1.92 μg of substance per mg of insect, respectively.



Scheme 2. (a) *m*-CPBA, DCM, 14h r.t., 7h reflux; (b) DIBAH (10 equiv.), toluene, -78°C, 2h, r.t. 22h; (c) $NaBH_4$, EtOH, 1h reflux; (d) H_2, cat.Pd/C, ethyl acetate, 2h r.t.; (e) acetic anhydride, cat. BF_3.MeOH, DCM, 19h r.t.; (f) i) BH_3, THF, 30min 0 °C, 3h r.t., ii) H_2O_2, NaOH, 1h reflux.

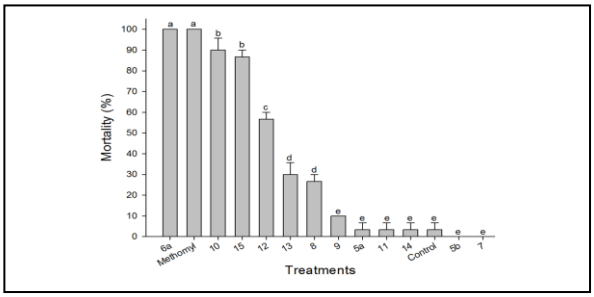


Figure 1. Contact toxicity (10 μg of compound per mg of insect). (P <0.05).

The activity of compound **6a** did not differ from that of the commercial insecticide methomyl, used as positive control.

Conclusion

Tropane alkaloids derivatives containing a carbamate group show potential for the development of novel insecticides.

Aknowledgements

To FAPEMIG, CNPq and CAPES for financial support.

[1] Liu, T. X. *Ann. Entomol. Soc. Am.* **2005**, 98, 726; [2] Picanço, M. C.; Oliveira, I. R.; Rosado, J. F.; et al. *Sociobiology* **2010**, 55, 1; [3] Mann J and Barbosa L. C. A. *J. Chem. Soc., Perkin Trans 1* **1992**, 787;[4] AJ Demuner, LCA Barbosa, DP Veloso, Química Nova **1997** 20 (1), 18-29; [5] AV Costa, LCA Barbosa, AJ Demuner, AA Silva, J. Agric. Food Chem. **1999,** 47 (11), 4807-4814