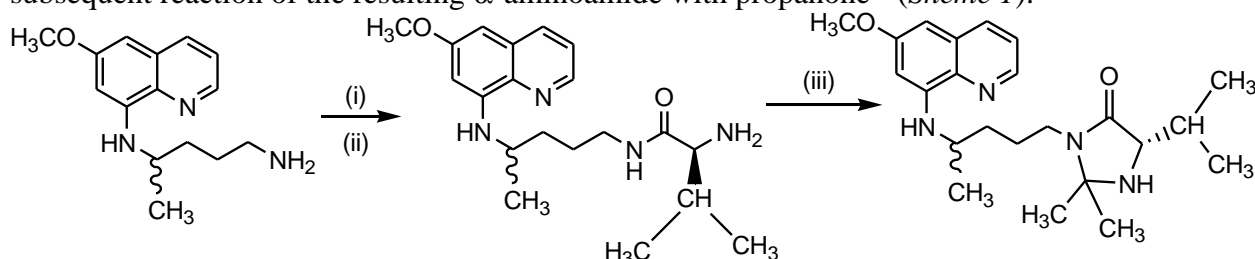


FUNGICIDAL ACTIVITY OF IMIDAZOLIDIN-4-ONES OF THE ANTI-MALARIAL PRIMAQUINE

The 5-Isopropyl-3-[4-(6-methoxy-quinolin-8-ylamino)-pentyl]-2,2-dimethyl-imidazolidin-4-one (ValPQacet) was synthesized through acylation of the anti-malarial primaquine with α -valine and subsequent reaction of the resulting α -aminoamide with propanone¹ (Scheme 1).



Scheme 1. Synthetic route for the formation of the ValPQacet: (i) DCCl, HOBt, N^{α} -BocVal-OH; (ii) TFA, Na_2CO_3 ; (iii) propanone in refluxing methanol, TEA, molecular sieves.

Imidazolidin-4-ones of the anti malarial primaquine are being synthesized to develop new variants in order to improve more effective treatments against malaria². Recently it has been observed that primaquine derivatives could have effect in a new kind of yeast³. To study the fungicidal activity against *Candida albicans*, *Candida tropicalis*, *Issatchenkia orientalis*, *Sacharomyces cerevisiae*, the ValPQacet was put in the form of the hydrochloride salt. The minimal inhibitory concentration (MIC) could be determined for all yeast in the concentration range assayed. Also was determined MIC's of primaquine hydrochloride salt for all yeast, and this shows that the parent drug is less active than our compound. Further studies are being performed to determine viability and cellular injury with this drugs.

¹ P. Gomes, M. J. Araújo, M. Rodrigues, N. Vale, Z. Azevedo, J. Iley, P. Chambel, J. Morais and R. Moreira, *Tetrahedron*, 2004, **60**, 5551.

² Maria João Araújo, Joana Bom, Rita Capela, Catarina Casimiro, Paula Chambel, Paula Gomes, Jim Iley, Francisca Lopes, José Morais, Rui Moreira, Eliandre de Oliveira, Virgílio do Rosário, and Nuno Vale; *J. Med. Chem.*, 2005, **48**, 888-892.

³ Thomas E. Goodwin, Carole J. Boylan, William L. Current, John C. Byrd, Clint B. Edwards, Danny A. Fuller, Jennifer L. Green, Christine D. Larocca, Kevin D. Raney, Ashley S. Ross and W. Andrew Tucker, *Bioorganic & Medicinal Chemistry Letters*, 2000, **10**, 2205-2208.