FARNESYLTRANSFERASE INHIBITORS AS NOVEL AGENTS AGAINST LEISHMANIASIS

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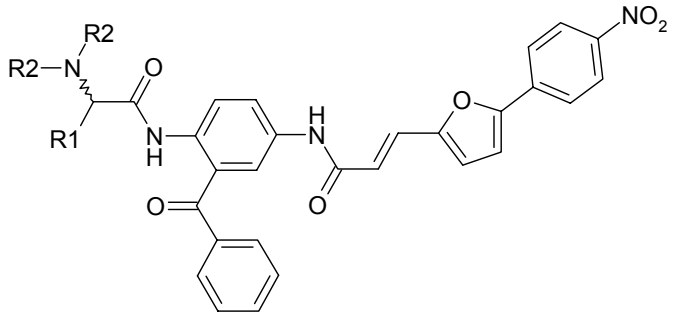
Leishmania species are protozoan parasites for which adequate chemotherapies are not available. Because the presently used antimony compounds show significant toxic side effects novel agents are urgently needed.
Farnesyltransferase (FTase) catalyzes the posttranslational modification of numerous proteins which are involved in the intracellular signal transduction. FTases have been found in different pathogenous protozoa including *Leishmania* [1]. Therefore, FTase inhibitors are interesting candidates for new drugs against *Leishmania* parasites.
We tested a series of benzophenone based farnesyltransferase inhibitors against *Leishmania mexicana*.



R1 = aryl, alkyl
R2 = H, heterocycle, alkyl

Some of our derivatives showed excellent activity in the nanomolar range and high selectivity.

[1] Bruckner, F. S.; Eastman, R. T.; Nepomuceno-Silva, J. L.; Speelmon, E. C.; Myler, P. J.; Van Voorhis, W. C.; Yokoyama, K.; *Mol. Biochem. Parasit*. **2002**, *122*, 81 – 183.