IN VITRO ANTI-LEISHMANIAL AND ANTI-TRYPANOSOMAL ACTIVITY OF HYDRAZONES, PYRAZOLES, PYRAZOLO[1,5-*A*]-PYRIMIDINES AND PYRAZOLO[3,4-*B*]-PYRIDINE, SYNTHESIZED FROM 6-SUBSTITUTED-3-FORMYLCHROMONES.

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Between the functionalized chromones, 3-formylchromone is a highly reactive synthon used in many reactions due to the presence of electron-deficient centers at C-2, C-4 and the C-3 formyl group. Reaction of the -CHO group with nitrogenated nucleophiles such as hydrazine and aminopyrazole derivatives have led to the formation of a variety of molecules that have been studied in detail for being of interest to drug discovery. Chromone-3-carboxyaldehydes react with aromatic primary hydrazines mainly at the formyl group by a straight forward 1,2-addition to form the corresponding hydrazone, but when the reaction is submitted to prolonged heating, a pyrazole-type structure is produced by a 1,4-addition reaction accompanied by pyrone ring-opening followed by recyclization and proton transfer. On the other hand, reaction of 3-formylchromone with equimolar quantities of aminopyrazole derivatives have shown to afford mainly pyrazolo[1,5-*a*]-pyrimidines, formed by the above-mentioned cyclization process of an imine intermediate.

Led by the biological and pharmacological relevance of the 3-formylchromone derivatives and it's interesting chemistry, in this work we present the synthesis of a series of pyrazoles (**4a-c**), hydrazones (**5a-c**), pyrazolo[1,5-*a*]-pyrimidines (**6a**, **6b**) and one pyrazolo[3,4-*b*]-pyridine (**7**) and the report on their *in vitro* anti-leishmanial and anti-trypanosomal activity. Chemical results showed that the formation of regioisomer **7** may arise from an imine intermediary that undergoes 1,4-addition at C-2 by attack of C-4' from the pyrazole instead of the nitrogen atom N-2'. To the best of our knowledge, this is the first report regarding formation of pyrazolo[3,4-*b*]-pyridines by intramolecular attack of an sp^2 carbon atom.

The *in vitro* studies were performed against strains of *Leishmania mexicana* (bel 21) and *Tripanosoma cruzi* (DM28). Compounds **5a** and **5b** showed activity at micromolar level and good selectivity index (SI) with IC_{50} values of 6.3 (SI = 3.4) and 15 (SI = 1.9) μM for *L. Mexicana* and 4.1 (SI = 5.2) and 10 (SI = 3) μM for *T. cruzi* respectively. From the above-mentioned, compounds **5a** and **5b** may be considered for further chemical modifications in order to increase their activity as potential antiparasitic agents.