Leishmaniasis is one of the most important neglected tropical diseases, endemic in around 100 countries, with more than 350 million people living at risk of infection and over 20000 deaths estimated annually. Leishmaniasis, caused by protozoa of the genus Leishmania, can manifest as tegumentary or visceral leishmaniasis, the latter being fatal if untreated. The currently available drugs are not only expensive and toxic, but are beginning to lose efficacy due to the increasing of parasitic resistance. Thus, the design of novel, efficient and safer drugs is of uttermost importance. The natural peroxide artemisinin (1) and its derivatives have shown good efficacy against parasites such as Plasmodium, and are widely used for the malaria treatment. Some synthetic peroxides, i.e. tetraoxanes (2) or trioxolanes (3), are now considered valid anti-malarials. Much less is known about the anti-leishmanial properties of peroxides. We recently proposed a novel family of synthetic simple 1,2-dioxanes (4) as potential anti-malarials [1]. Here we report our studies on the synthesis and the anti-leishmanial bioactivity of a selected group of 1,2-dioxanes [2]. 13 compounds showed a good in vitro inhibitory activity on L. donovani promastigotes (IC_{50} range = 1.6 - 16.4 µM). Moreover, the 6 compounds exhibiting the best selectivity index proved to be active also against L. tropica, L. major and L. infantum promastigotes and against L. donovani amastigotes, highlighting their potential as hits for lead optimization.
