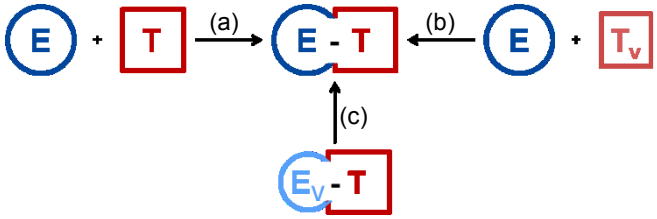
Abstract

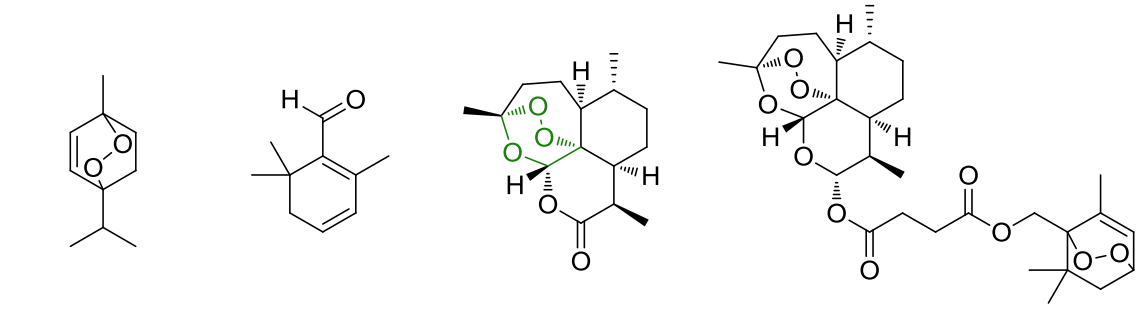
In this thesis three synthetic pathways were examined to generate dyads with endoperoxide and trioxane motif, depicted in the scheme below. Pathway (a) studies the covalent linkage of the endoperoxide (E) and trioxane (T) in a terminal step. The second concept (pathway (b)) investigates the synthesis of ET-dyads by peroxyacetalisation of an endoperoxide with suitable hydroxy hydroperoxides (T_V). The approach of pathway (c) is the synthesis of ET-dyads by photooxygenation of 1,2,4-trioxanes with appropriate side chains (E_V-T) to introduce the endoperoxide motif. The key step of each route is the dye sensitized photooxygenation with singlet oxygen to obtain endoperoxides ([4+2]-addition) or hydroxy hydroperoxides (Schenck-ene reaction).



E = endoperoxide
T = 1,2,4-trioxane
E_V = precursor of the endoperoxide
T_V = precursor of the 1,2,4-trioxane

Scheme i General reaction scheme of dyads.

The substances used for each pathway are on the one hand derived from the natural products ascaridole (E) and safranal (E_V) and on the other hand from artemisinin (T) and synthetic 1,2,4-trioxanes (T). The design of ET-dyads could not be realized by pathway (a) and (b). The ET-dyad, depicted in Scheme ii, could be synthesized by photooxygenation of a diene with an appropriate side chain, and therefore pathway (c) has been established as the best one. By this way the approach of new potential drugs against malaria is possible.



ascaridole (E) safranal (E_V) artemisinin (T) ET-dyad

1,2,4-trioxane (T)

Scheme ii Key substances and synthesized ET-dyad.