Structural and Docking Studies of β-lapachone Derivatives

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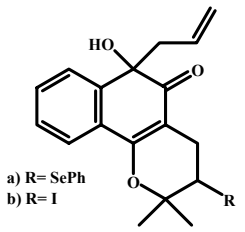
As it was shown that β-lapachone is active against *Trypanosoma cruzi* and that its 3-allyl derivative is not inactivated in blood, thus suppressing tripomastigote infectivity, compounds (a) and (b) were synthesized and studied. **T**he pentahydro-5-oxaphenanthrene moieties of both structures are almost identical, rms deviation of the superposition of the 14 atoms being 0.052 Å. Molecules are packed in a same ladder fashion through OH...O, CH...O and CH...π (in (a)) interactions.



a) R= SePh
b) R= I

Docking studies were carried out with DOCK3.5 [1,2], for (a) and (b) and their dione analogs modelled based on the crystal structures, in the active site (AS) and the interface site (IS) of human gluthathione and *T. cruzi* trypanothione reductases (GR and TR). For the modelled dione ligands, it was possible to choose a preferred orientation in each site with total energies of *ca* -20 kcal/mol in TR-AS, -28 kcal/mol in TR-IS and GR-AS and -30 kcal/mol in GR-IS. On the other hand, docking studies with (a) and (b) did not show any preferred orientation. These results are in agreement with the showed trypanocidal activity, *in vitro,* of the dione derivatives and the inactivity of (a) and (b).

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