VIRTUAL DOCKING EXPERIMENTS ON PLEUROMUTILIN DERIVATIVES FUNCTIONALIZED IN POSITION 13

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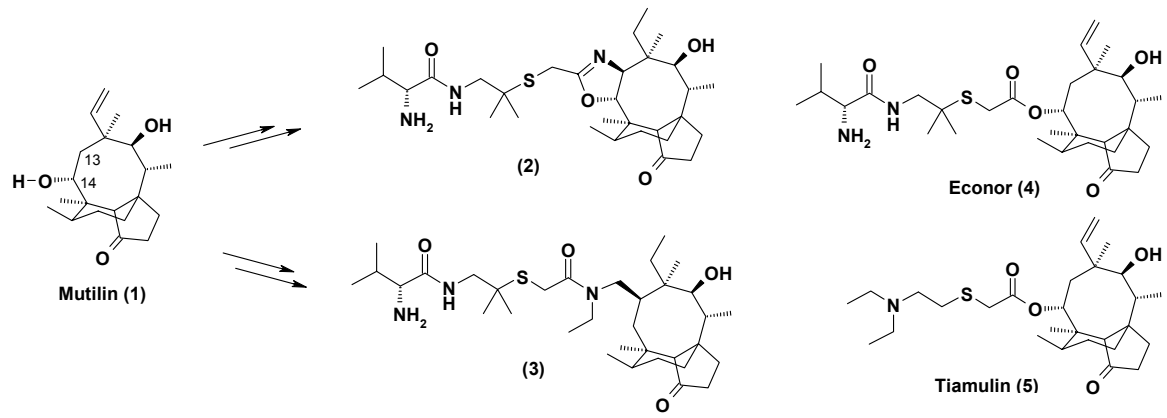
The emergence of multiple resistance in bacteria demands for new antibiotic classes for human application. Pleuromutilins are a class of antibiotics solely used in veterinary medicine so far, containing a tricyclic scaffold with a unique anellation of 5, 6 and 8 membered rings.

Here we present synthesis and docking experiments of two example compounds (2,3) of our research program concerning new substitution patterns at the tricyclic skeleton of pleuromutilin derivatives. These substances represent different orientation or transposition of the C14-side chain of Econor (4) and are realized via a multiple-step synthesis starting from mutilin (1) using different hydride shifts [1].



We performed our virtual docking experiments [2] on the basis of a recently published X-ray structure of the 50S ribosomal subunit of *Deidococcus radiodurans* co-crystallized with Tiamulin (5) [3]. The docking studies elucidate the weak antimicrobial activities of (2) and (3). Alterations in substrate orientation and hydrogen bonding of (2) and (3) at the binding site will be discussed in comparison to their parent compound Econor.

[1] Berner H.; Vyplel, H.; Schulz, G. *Monatshefte für Chemie* **1983**, 114, 501.
[2] MOE Software, Computational Chemistry Group.
[3] Schlünzen, F.; Pyetan, E.; Fucini, P.; Yonath, A.; Harms, J.M. *Molecular Microbiology* **2004**, 54, 1287.