The Catalytic Mechanisms of Sesquiterpene Formation in *Zea Mays* Prenylating Enzymes

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Prenyl converting or transferring enzymes are responsible for the formation or modification of naturally occurring isoprenoids. More than 60.000 different isoprenoids have been isolated from fungal, animal, microbial, and predominantly from plant resources and are thus one of the most diverse families of natural products. Approximately one half are terpenoids.[1]

The *Zea mays* sesquiterpene synthase ZmTPS10 produces a mixture of different sesquiterpenes derived from the substrate farnesyl diphosphate. These products form an efficient volatile defense signal that attracts natural enemies of maize herbivores.[2]

In order to understand the molecular basis of the catalytic mechanism including the formation of many side products, a homology model of ZmTPS10 was created using *YASARA* and *MOE*.

Docking studies of the intermediately formed farnesyl cation as well as of other intermediates were performed with *GOLD*, *PLANTS* and *GLIDE* in comparison. It is known that the allylic cation intermediates are stabilized by side chains of aromatic amino acid residues with rather high interaction energies of more than 50 kJ/mol [3] und thus essentially guide the product formation. Furthermore, a proton acceptor (Asp or Glu) is needed to terminate each reaction.

Therefore, the modeling studies should help to identify aromatic residues and putative proton acceptors in the active site. These residues could be identified and based on the docking studies accompanied by calculation of the thermodynamics for each reaction step using PM3 the formation of all products formed by ZmTPS10 can be explained. These results are nicely supported by site directed mutagenesis studies.

However, since none of the docking programs reflects the high interaction energy between the allyl cation intermediate and the surrounding aromatic residues, too many unproductive and unlikely docking arrangements were obtained which highly complicates the docking analysis. We conclude that a special parameterization of allyl cation π-interactions is required to conduct further systematic investigations of prenyl converting enzymes.

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[3] Bräuer, L., Brandt, W., Schulze, D., Zakharova, S., Wessjohann, L., *Chembiochem* **2008**, *9*, 982-992.