Using Computers for Degradation Studies

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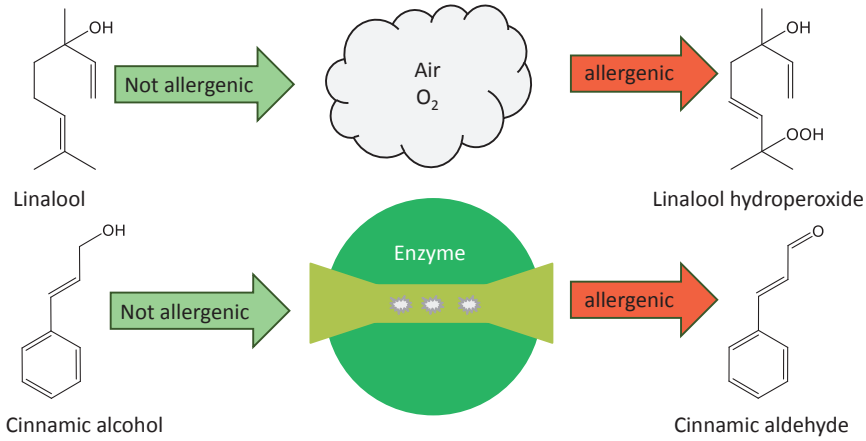
Chemical reactions typically involve synthesis and formations of products that are desirable and attractive. New synthesis pathways and catalysing agents are searched for in order to control the reactions, have higher yield, and make it economically and environmentally profitable. The opposite, the degradation reaction of a substance might well be as important. The product formed might be destroyed if it is prone for degradation and sometimes, the degradation products might even be toxic.

Skin sensitization that results in contact dermatitis is a common occupational and environmental health issue. For example, chemical fragrances are frequently used in many household products, such as detergents, perfumes, and soaps. They also occur as natural components in foodstuff. These compounds are widespread and most people come into constant contact with them in their daily life. For some people, contact with these compounds might lead to skin sensitization and allergic contact dermatitis. Sometimes, the chemical compound is not allergenic in itself, but is activated by air or by enzymes present in the skin. Once a person has become sensitized, the allergy becomes a lifelong condition.



Schematic representation of when the fragrance linalool is activated by air and cinnamic alcohol is bioactivated by an enzyme.

Whether a compound can be activated during handling and storage or by enzymes is normally not considered in the known data bases that are based on structure-activity relationship (SAR). Animal experiments are therefore made to secure the risk for exposure to allergenic compounds. But in today's society it is of utmost importance to have the possibility to replace and/or minimize animal testing with other methods when determining the biological and/or the toxically effect of a chemical compound. One such method is to use computer simulations.

There are different approaches and different methods for computational investigations. When the kinetic or the thermodynamic stability is searched for, advanced electron correlation methods, such as Density Functional Theory (DFT), are the methods of choice as reactivity and selectivity studies typically involve a focus on the potential energy surface. By theoretically calculating which energies that are necessary for a reaction to take place, and the stability of the formed compounds relative to each other, one can determine the probability for highly allergenic compounds to form when a substance is exposed to air and autoxidizes, or when it is metabolized by an enzyme (Cytochrome p450s) in the skin. It is also possible to predict if an allergenic compound is stable enough to cause contact dermatitis. And last but not least, computer simulations are used as an aid for finding the mechanistic understanding of the exact reaction route, which increases the possibilities to minimise the formation of the oxidation products that are prone to cause contact allergy.