

Sustainable development and "Green Chemistry"



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In a world with a continuously increasing population and limited resources the idea of a sustainable development is of major importance for the future in the 21st century. Only research and innovation will allow the development of economic and social networks and processes that fulfil the requirements of sustainability. The future has to be planned with visions, creativity and fantasy, including really new approaches and the exploration of the unknown.

Sustainability in science and technology begins when we start thinking how to solve a problem or how to turn science into technology. Chemistry, as the science of matter and its transformation, plays a central role in this process and is the bridge between physics, material sciences and life sciences. Only chemical processes, which have reached – after careful optimization – a maximum in efficiency, will lead to more sustainable products and production. Scientists and engineers, who invent, develop and optimize such processes, therefore play a key role. Their awareness, creativity and looking ahead is needed to bring reactions and chemical processes to maximum efficiency. The term "Green Chemistry" has been coined for efforts towards this goal.

Green Chemistry Mission:



To promote innovative chemical technologies that reduce or eliminate the use or generation of hazardous substances in the design, manufacture, and use of chemical products.

1 Background

Education in chemistry has a long history. For a long time the most important goal of a chemist was to make a compound in suitable amounts and high purity from available starting materials.

This biased chemical education had a strong focus on practical lab techniques and methods for compound purification. The question of how much energy is needed for a reaction and how much waste is produced was raised for industrial processes only. Although the goal for a chemist working in organic synthesis is still the same to make a compound in good yield and high purity, additional parameters must be considered in the development of new processes today. The last 20 years in which much more attention was paid to the effect of chemical production and chemical compounds on the environment have taught us one clear lesson: It is much better, less difficult and less expensive to develop processes and compounds that are sustainable from scratch than to change an existing bad chemical process or to remove a dangerous chemical from the environment to reduce potential hazard and pollution.

In order to do so, chemists, biochemists, engineers, scientists working in drug development or constructing new materials must think sustainable when they transform their ideas into products and processes. This calls for a different chemical education which teaches more than reaction mechanisms and experimental techniques. Students must learn to judge the suitability of a chemical transformation or the use of a chemical compound within a matrix of many parameters. It is not only the yield of the reaction that counts. Which starting materials are needed? Can they be made from renewable resources? Do we get toxic by-products and how can they be avoided? How much waste is generated by the process and is it energy efficient? Asking these questions at the beginning of chemical research and technology development will lead to a more efficient and sustainable use of chemistry. Asking these questions in the teaching lab course will change the way students look at a chemical reaction and prepare them much better for their professional tasks.

Not surprisingly many of the traditional methods taught in lab classes require a fresh look and new consideration. The well known Beilstein test (Figure 1), which allows to detect a halogen content in organic compounds is a nice example. To perform this test a clean copper wire is dipped into the compound to be analyzed, or a solution of it. The covered wire is then placed into a flame and a green or blue green color signals halogen content. Recently the byproducts of the analytical procedure were investigated in detail. The analysis showed that the Beilstein test generates in many cases considerable amounts of dioxins. Dioxins belong to the most toxic compounds that we know on earth. As a consequence precautions should be taken carrying out the Beilstein test to shield the experimentalist from the products of the test or – even better – to replace the test by modern analytical techniques [1].

2 Good and bad reactions

Of course, we cannot call a reaction generally bad or good. This always depends on many parameters, e.g. the scale we want to perform it on, the required purity of the product or the availability of the starting materials. However, to judge the general efficiency of a chemical transformation we can use the concept of atom economy (cf. Figure 2) in addition to the obtained chemical yield. The concept was introduced by Trost [2]. To measure the atom economy of a reaction we sum the masses of the atoms of all starting materials and reagents according to the stoichiometric equation and compare it with the sum of the masses of all atoms found in the desired product. Atoms of undesired side products and reaction by-products



Figure 1: The classical Beilstein test

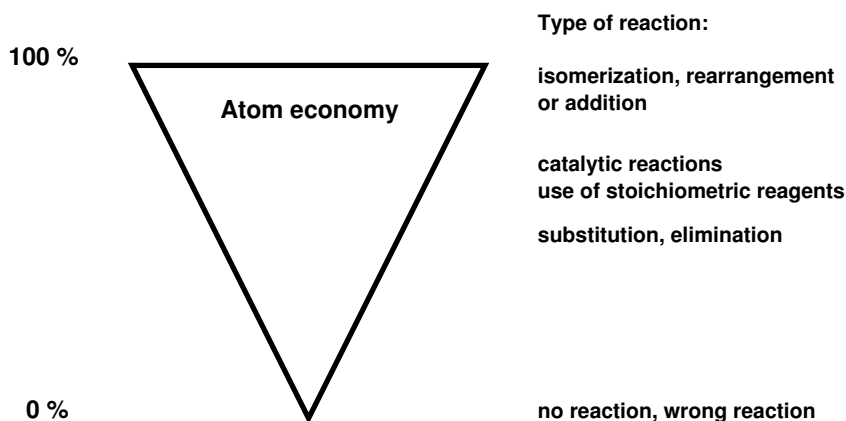


Figure 2: Classification of organic reactions by their atom economy

count as waste. The method gives a general measure of the efficiency of a reaction. The concept leads to the conclusion that e.g. addition reactions show better atom economy than condensation or substitution reactions, which generate stoichiometric amounts of an unwanted product.

While atom economy focuses on the reaction only, other measures, such as the Sheldon factor E (Figure 3) of environmental acceptability [3] or a recently developed computer protocol for reaction assessment [4], take solvents, energy consumption and toxicity of chemicals into account. If established chemical production processes are analyzed by these methods, not unexpectedly, a correlation between environmental acceptability and production scale is noticed.

The most prominent example of an important organic reaction that has in some cases a low atom economy is the Wittig olefination (Figure 4). In the conversion of a carbonyl group into a methylene group with a phosphonium salt (molecular weight 357 g/mol) only a CH_2 group with the molecular weight of 14 g/mol ends up in the product. The unavoidable byproduct triphenylphosphine oxide with a molecular weight of 278 g/mol, one equivalent of HBr and the base go into the waste box.

This does not mean that the Wittig reaction is a bad reaction! The reaction is one of the most valuable and powerful tools in organic synthesis to selectively create double bonds from carbonyl compounds. However, if used on a large scale one has to think about recycling of the phosphine oxide (which is done in industry) or develop alternative procedures (such as alkene metathesis).

3 A case for Sherlock Holmes

Let's turn to real case examples from the organic chemistry teaching lab. The conversion of carbonyl groups into acetals is on the agenda of most lab classes. The protection procedure

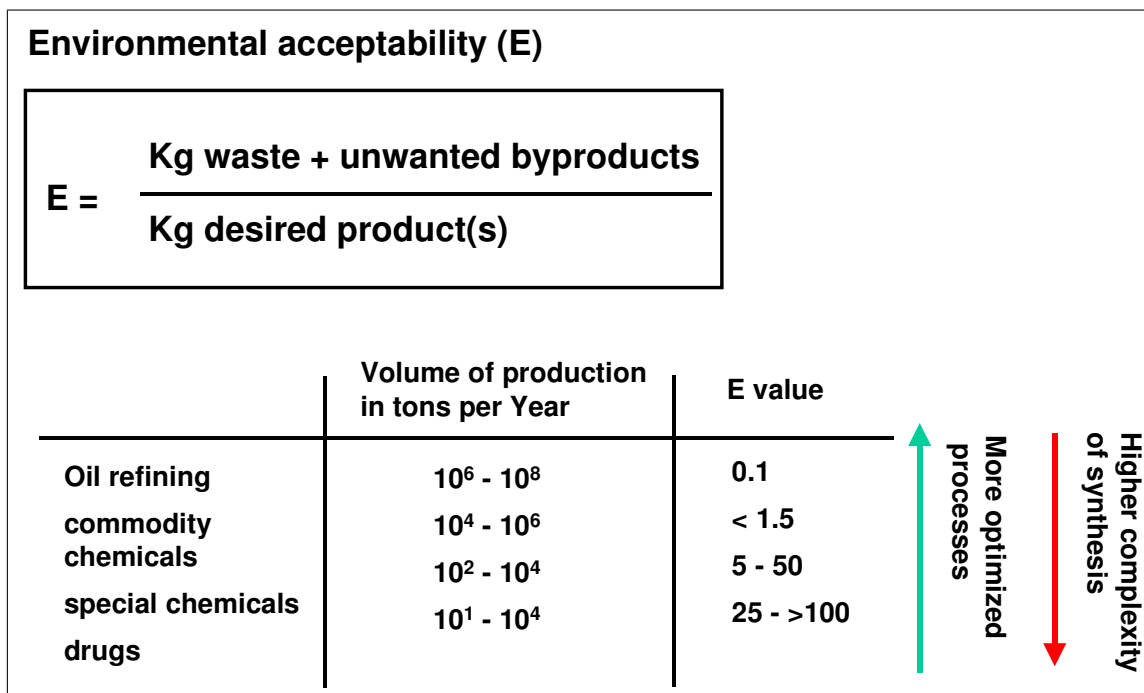


Figure 3: Definition of Sheldon's environmental acceptability E and E values of industrial chemical processes

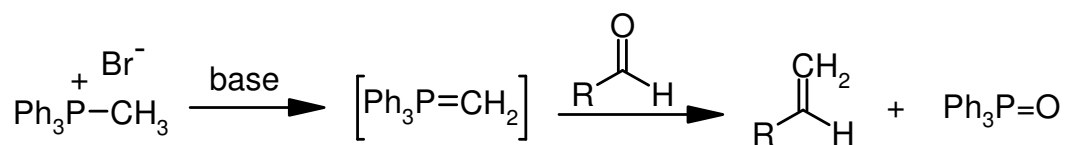


Figure 4: The Wittig olefination as an example for poor atom economy

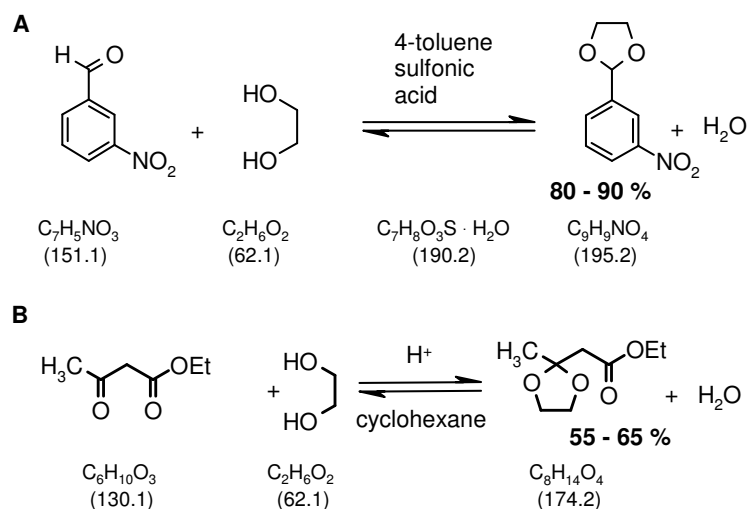


Figure 5: Two classical reactions from the organic teaching lab ...

is of general importance in organic synthesis, it nicely illustrates the reactivity of carbonyl groups and introduces the use of apparatus, such as the Dean Stark trap, to remove water from the reaction mixture to shift a chemical equilibrium. The two reactions shown in Figure 5 are found in many manuals for practical lab courses. Both reactions are fine from their atom economy: Only one equivalent of water is produced. The method of water removal, the choice of catalyst and the work up procedures may strongly influence the overall efficiencies. But there is a more striking difference between the two reactions: While reaction A gives an isolated chemical yield of product of 80 to 90 % depending on the experimental skill of the operator, reaction B yields the acetal in only 55 to 65 %. In all inspected textbooks around the globe that cite the experiments the yields of reaction B are significantly lower compared to A. So there must be a chemical reason for the difference.

Interestingly the analysis of the crude reaction products of A and B by techniques, such as nuclear magnetic resonance (NMR) or gas chromatography (GC) clearly show in both cases a clean reaction. Only the desired product and traces of unreacted starting material could be detected. In reaction B some material must have been simply disappeared! Like a detective we can search for hidden pathways and unwanted outlets, and indeed it is possible to trap CO_2 evolving from the reaction and to detect acetone in the aqueous reaction phase (Figure 6). Now the case becomes much clearer. These are good hints to a severe side reaction of our starting material. Using our knowledge on organic reaction mechanisms the unwanted pathway is easily discovered. The SS-keto ester is hydrolyzed under the acidic reaction conditions to give a SS-keto carboxylic acid. These compounds are known to split off CO_2 if heated. In our reaction this leads to CO_2 and acetone. This reaction sequence, which competes with the acetalization, consumes approximately half of the starting material, thus the reduced yield of the desired product becomes obvious. Now that we have spotted and understood the problem, we can start thinking how to do better and turn the reaction into a more efficient process. Another catalyst, different reaction conditions or another solvent may be first things to try.

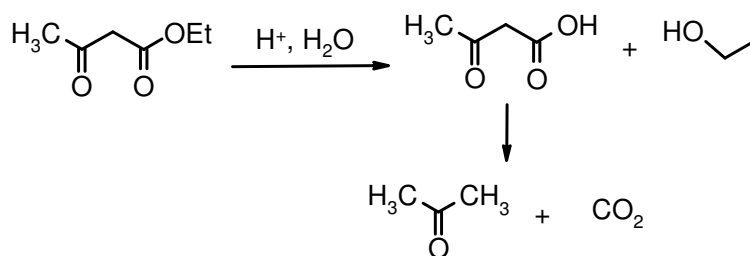


Figure 6: ... but B has a competing reaction pathway leading to "invisible" byproducts.

4 Energy matters!

Let's go back to reaction A. The chemistry of this process is working fine giving the desired product in high yield and purity. But there are several ways how to set up the reaction experimentally. Does it make any difference if we heat our reaction vessel with an oil bath, if we use a heating mantle or a microwave oven? It surely does! Although we expect the same product produced in all cases the energy consumption per amount of material varies significantly. Figure 7 shows the three experimental setups and the measured energy consumption for reaction and work up for all three cases. The microwave oven clearly wins the competition.

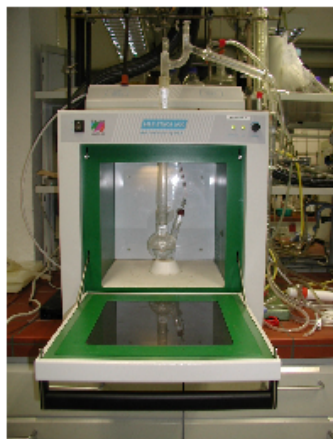
But there are other parameters which define the energy demand of a reaction and which are usually not recognized at the first glance. Several organic solvents can be used in reaction A to give the same product, but their heat capacity contributes to the energy demand. So this might be a parameter to be considered if the reaction should be performed on large scale.

Loss of energy can be detected by infrared pictures. Figure 8 shows the pictures of experimental setups of reaction A with oil bath and heating mantle. This explains why in these setups so much more energy is needed for heating compared to a microwave oven. Insulating parts of the apparatus may reduce energy loss and the success can be monitored by infrared pictures and changes in the energy uptake.

The differences in energy consumption for laboratory experiments are insignificant in their absolute numbers. The aim of such experiments is therefore not the reduction of energy needed in lab classes, but to make everybody working in science and engineering aware of these issues, that really make a difference on the large scale.

5 Tell me: Are you dangerous?

Working with chemicals always implies a potential hazard for humans and the environment. Everybody using chemicals in her or his professional life should therefore be able to handle hazardous compounds safely, to retrieve information about toxicity and to assess the implications of a reaction or a compound for the environment from these data. Using, understanding and interpreting toxicity data must be an essential part of chemical education. The following reaction, again a very typical example from organic chemistry textbooks and frequently performed in lab classes, is an illustrative example. The nitration of toluene yields several



microwave



oil bath



heating mantle

Energy consumption of the syntheses

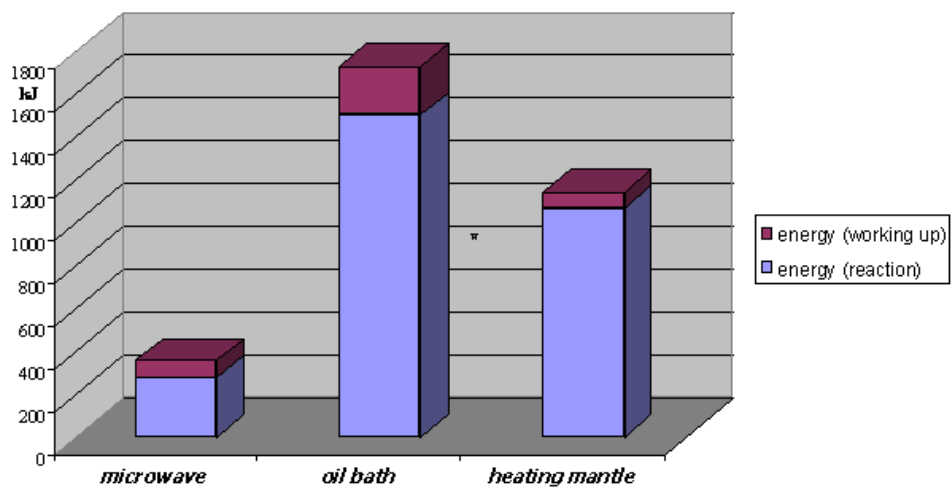
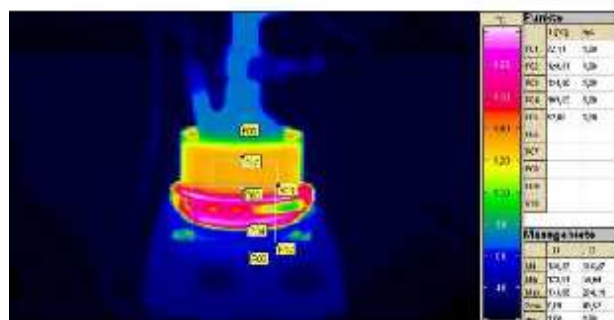
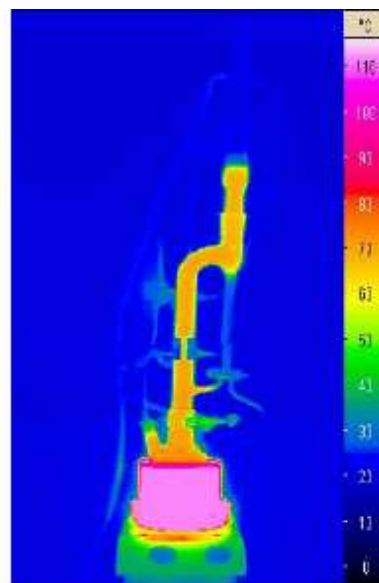


Figure 7: Three ways to get the reaction done, but different energy bills to pay!



oil bath



heating mantle

Figure 8: Infrared pictures make energy emissions visible

reaction products in different amounts. The careful analysis of the crude product mixture reveals that besides the ortho- and para-substitution products, which are expected from the selectivity rules of electrophilic aromatic substitution, considerable amounts of other products are formed. Their relative amounts vary with reaction conditions, but a reaction yielding a single substitution product is hard to achieve. Standard workup procedures allow the separation and purification of single compounds. However, for our assessment of potential hazards of a reaction we have to take all reaction products into account, the desired ones and the unwanted, because they all are being produced and humans are exposed to them.

The measurement of the overall effect of a chemical compound on humans and the environment is difficult. An effect factor model, which is derived from a variety of acute and chronic toxicity data, enables us to assess the comparative risk of chemicals and mixtures, even if some of the toxicity data have not been determined. We use the model of the TRGS 440 [5] which is officially to be used for assessing the relative hazard of chemicals in the workplace. In addition we widen our assessment by also considering how easy a compound is distributed in the environment, how long it withstands degradation and how strongly it affects e.g. aquatic life. Figure 9 shows compounds used in and produced by the investigated reaction with color coded effect factors to allow an easy detection of dangerous components. Data on which such an assessment for any kind of reaction is based is provided as background material on the web pages of our project. However, not for all compounds data are available and new compounds have not been tested. For these cases we have to look for structural elements that may signal dangerous properties. Such structure-toxicity relationships are provided and discussed in examples. With these material everybody who took an organic chemistry teaching lab course

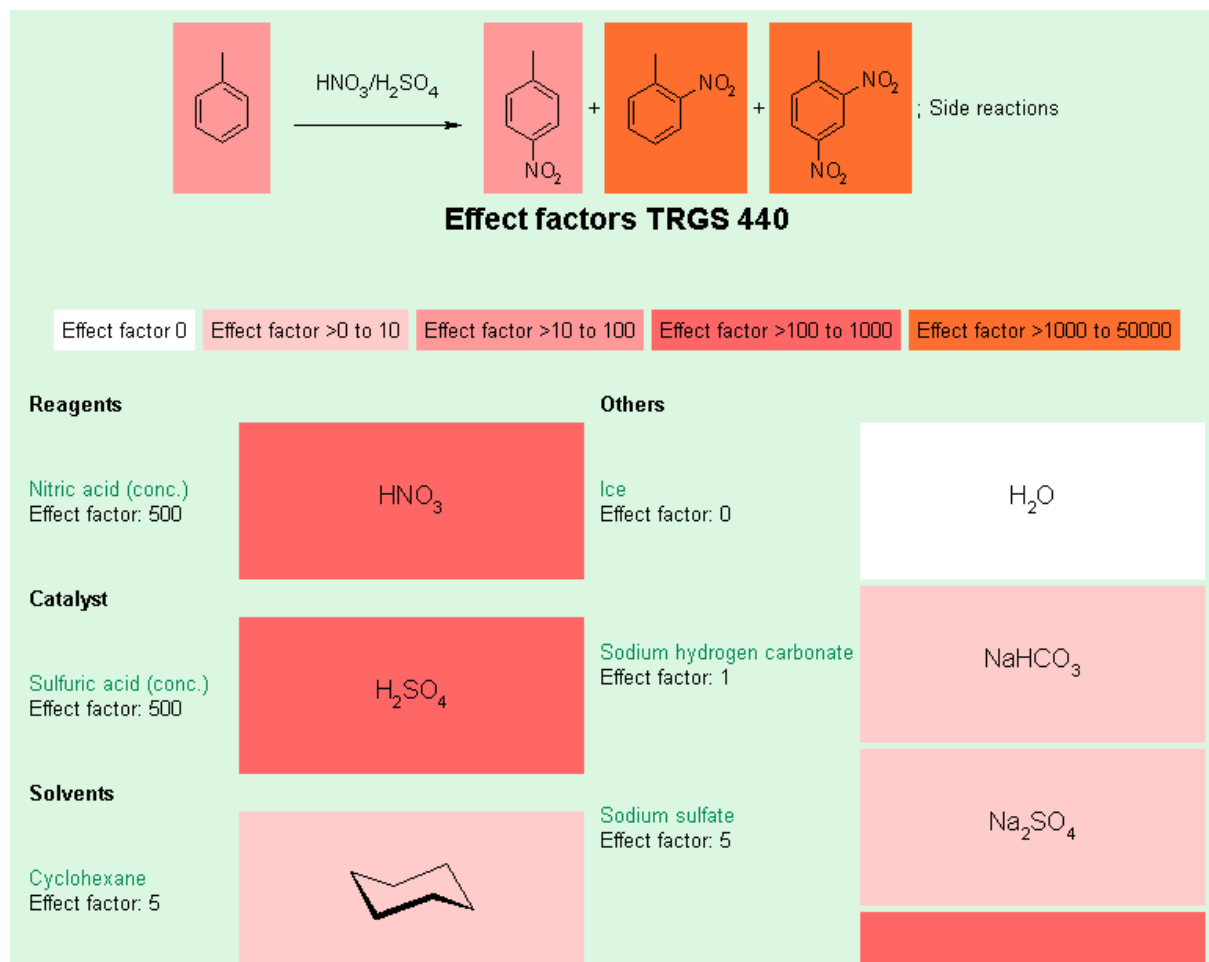


Figure 9: Nitration of toluene with compound effect factors encoded by colors

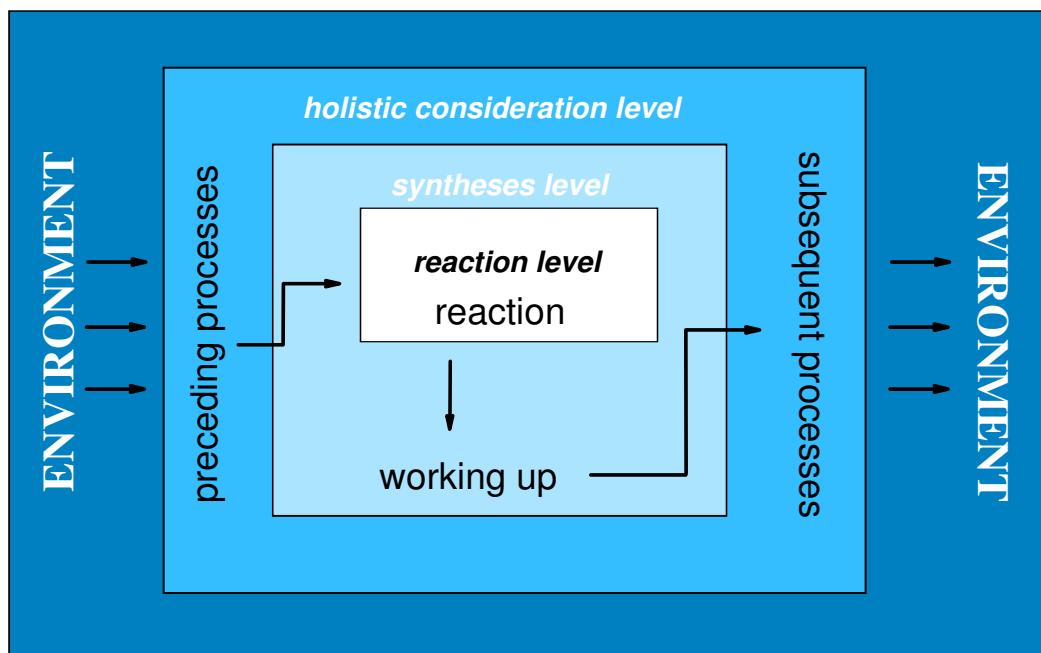


Figure 10: Assessment of the effect of a reaction on the environment

will be able to estimate the potential chemical hazard of a reaction.

The effect of a chemical reaction on the environment does not end at the door of the lab, although in the teaching lab courses we mostly pretend it that way due to the small amounts of chemicals and waste involved. To extend the view (Figure 10) from time to time can provide new insights and teach interesting lessons. The exercise starts with the reaction itself. We then widen the scope to be considered step by step. How have our starting materials been made? Can we trace them back to renewable resources? What happens to our waste? From where do we get the energy needed for the reaction and how is it generated? What was necessary to produce our reaction apparatus? Finally we will end up with a complete picture how our reaction interacts with the environment. In most cases it will be difficult to determine all parameters in exact measures, but even rough estimates allow to identify problems and opportunities for improvement and synergies.

6 Some help from nature

Enzymatic transformations (e.g. Figure 11) are an established part of the repertoire of modern organic synthesis. They impress by their mostly very high selectivities and increasing commercial availability facilitates practical applications. Therefore, biotransformations should be part of every organic chemistry lab course and we provide several reliable protocols for experiments in our database. At first glance biotransformations appear as perfectly sustainable chemistry, but quite often this is wrong. In particular for the production of larger product quantities the work up from aqueous reaction mixtures can generate huge energy bills. Some

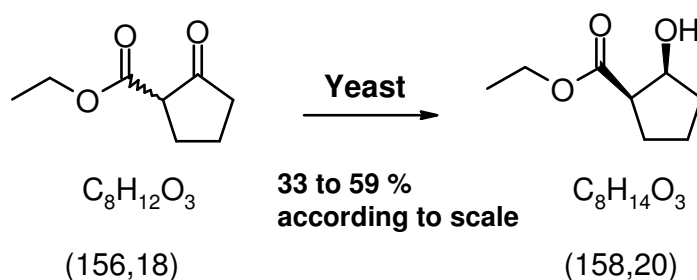


Figure 11: Biotransformation for the teaching lab: dynamic enantio-selective reduction of a SS-keto ester

enzymes can be used in organic solvents to resolve this problem, but scope and selectivity may be restricted. The selectivity of a reaction is an important parameter, but it has to be balanced with other parameters to achieve maximum efficiency in chemical transformation. This has to be considered with biotransformations, too. The comparison of enzymatic reactions with catalytic processes of modern organic synthesis is always worth a try in the search for the process with highest sustainability.

7 More information

To allow a better coverage of all the issues of sustainability in chemical education our **team** developed a database, which will contain approx. 100 laboratory experiments. Besides a detailed experimental protocol, safety guidelines and analytical data a variety of additional material is provided that addresses the different aspects of sustainability. The material can be individually adapted to any type of organic chemistry teaching lab course or used for projects in and outside the classroom. All material is **available** for free in the internet. The project, which is a joint effort of seven German universities, is financed by the Deutsche Bundesstiftung Umwelt (German Environmental Foundation). This support is gratefully acknowledged.

References

- [1] B. M. Scholz-Boettcher, M. Bahadir, and H. Hopf. *Angew. Chem.*, 104:477–479, *Angew. Chem., Int. Ed. Engl.*, 31, 443–444, 1992.
- [2] B. M. Trost. *Angew. Chem. Int. Ed. Engl.*, 34:259 – 281, 1995.
- [3] R. Sheldon. *Chemtech*, 24(3):38 – 47, 1994.
- [4] M. Eissen and J. O. Metzger. Environmental performance metrics for daily use in synthetic chemistry. *Chem. Eur. J.*, 8(16):3580 – 3585, 2002.
- [5] F. Kalberlah and H. Wriedt. *Bewertung und Fortentwicklung der Gesetzgebung: Anwendbarkeit der TRGS 440*. Schriftenreihe der BAuA.

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