

Aspects of sustainability in chemical education - an organic chemistry teaching laboratory course for the new millennium

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Overview

Sustainability in science and technology begins when we start thinking how to solve a problem or how to turn science into technology. Chemical processes, designed and developed to have maximum efficiency, lead to sustainable chemical production. To achieve better awareness of the important issues of sustainability in chemistry within the next generation of scientists, the course content of chemistry classes must be changed to chase the mindset of the people working in science and engineering. To provide this material for organic chemistry teaching laboratory course, we have developed and collected material that allows students and teachers to consider factors relating to reactions beyond simply experimental set up, reaction mechanism and chemical yield.

Problem

Organic teaching laboratory courses are a compulsory element in university education in chemistry and other subjects. However, most curricula are still based on traditional laboratory classes in chemistry. They focus on teaching basic experimental techniques for synthesis and analysis and demonstrate potential chemical hazards. The efficiency of a chemical transformation is usually only measured by the chemical yield of the product obtained. Students often do not learn how to determine the overall efficiency of a reaction, which directly correlates with its sustainability and they are not provided with tools to increase the efficiency of a reaction. The ideas of atom efficiency and energy efficiency are rarely mentioned.

A possible solution

The ideas of the efficiency and sustainability of a reaction must be added to the content of teaching laboratory courses in organic chemistry. Within this wider scope students learn how to plan, set up, and analyze organic reactions taking their effect on the environment and humans into account. Sustainability starts with the planning of a chemical transformation. A freely accessible internet database, has been developed which provides all necessary material, covering experimental procedures, toxicity data, alternative reaction procedure and more to discuss and assess a chemical reaction in a much wider sense. The information can be adapted to a specific course. The database is currently in German only. See *More information*, below.

Background

Education in chemistry has a long history. For a long time the most important goal of chemists was to make a compound in suitable amounts and high purity from available starting materials. This biased chemical education, which had a strong focus on practical laboratory 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. In the last 20 years much more attention has been paid to the effect of chemical production and chemical compounds on the environment. This has led to one clear lesson. It is much better, less difficult and less expensive to develop from

scratch processes and compounds that are sustainable than to change an existing bad chemical process or to remove a dangerous chemical from the environment to reduce potential hazards and pollution. In order to do so, chemists, biochemists, engineers, and scientists working in drug development or constructing new materials must think about sustainability 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 laboratory 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 laboratory classes require a fresh look. Take for example the well known Beilstein test, to detect a halogen in organic compounds. To perform this test a clean copper wire is dipped into the compound to be analyzed, or a solution of it. The wire is then placed into a flame and a green or blue-green colour signals halogen content, see Figure 1. Recently the by-products of the analytical procedure were investigated in detail. The analysis showed that the Beilstein test generates in many cases considerable amounts of highly toxic dioxins. Dioxins are some of the most toxic compounds that we know on Earth. As a consequence precautions should be taken in the Beilstein test to shield the tester from the products of the test or even better, to replace the test by modern analytical techniques.



Figure 1 Performing the Beilstein test

Good and bad reactions

Of course, we cannot categorize a reaction as generally bad or good. This always depends on many parameters, *eg* 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 in addition to that chemical yield. The concept was introduced by Trost¹. To

measure the atom economy of a reaction we count the atoms of all starting materials and reagents and compare it with the number of atoms found in the desired product. Atoms of undesired side products and reaction by-products count as waste. The method allows a general measure of the efficiency of a reaction. The concept leads to the conclusion that addition reactions, for example, show better atom economy than condensation or substitution reactions, which generate stoichiometric amounts of an unwanted product, see Figure 2. While atom economy focuses on the reaction only, other measures, such as the Sheldon E factor of environmental acceptabilityⁱⁱ or a recently developed computer protocol for reaction assessmentⁱⁱⁱ, 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, Figure 3.

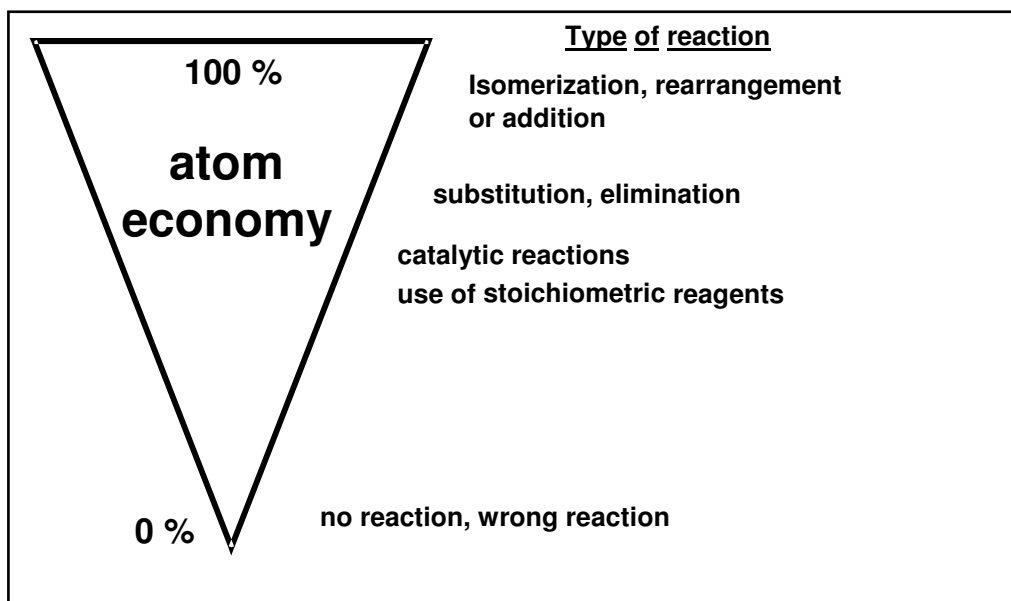


Figure 2 Classification of organic reactions by their atom economy

Environmental acceptability (E)

$$E = \frac{\text{Kg waste + unwanted byproducts}}{\text{Kg desired product(s)}}$$

	Volume of production in tons per Year	E value	
Oil refining	$10^6 - 10^8$	0.1	<div style="display: flex; align-items: center; justify-content: center;"> <div style="border-left: 1px solid black; border-right: 1px solid black; height: 100px; margin-right: 10px;"></div> <div style="display: flex; flex-direction: column; align-items: center; justify-content: center;"> <div style="color: green; font-size: 2em; margin-bottom: 5px;">↑</div> <div style="writing-mode: vertical-rl; transform: rotate(180deg); font-size: 0.8em; margin-bottom: 5px;">More optimized processes</div> <div style="color: red; font-size: 2em; margin-top: 5px;">↓</div> <div style="writing-mode: vertical-rl; transform: rotate(180deg); font-size: 0.8em; margin-top: 5px;">Higher complexity of synthesis</div> </div> </div>
commodity chemicals	$10^4 - 10^6$	< 1.5	
special chemicals	$10^2 - 10^4$	5 - 50	
drugs	$10^1 - 10^4$	25 - >100	

Figure 3 Definition of Sheldon environmental acceptability, E, and E values of industrial chemical processes

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 methene (methylene) group with a phosphonium salt (M_r 357) only a CH_2 group, with an M_r of 14, ends up in the product. The unavoidable byproduct, triphenylphosphine oxide, with a M_r of 278, one equivalent of HBr, and the base go into the waste box.

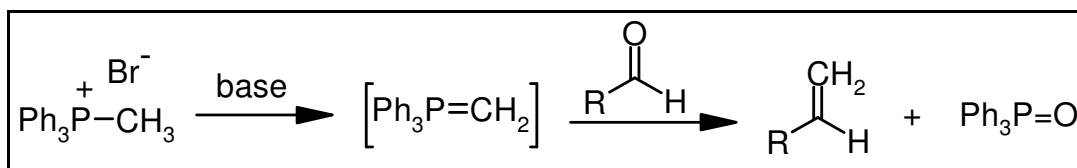


Figure 4 The Wittig olefination as an example for poor atom economy

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 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).

A case for Sherlock Holmes

Let us turn to real case examples from the organic chemistry teaching laboratory. The conversion of carbonyl groups into acetals is included in most laboratory classes. The protection procedure 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 laboratory 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 a isolated chemical yield of product of 80 - 90 % depending on the experimental skill of the operator, reaction B yields the acetal in only 55 - 65 % yield. In textbooks 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 simply disappeared! Like a detective we can search for hidden pathways and unwanted outlets, and indeed it is possible to trap carbon dioxide evolving from the reaction and to detect propanone in the aqueous reaction phase. Now the case becomes much clearer. These are good hints to a severe side reaction of our starting material. Using our knowledge of organic reaction mechanisms the unwanted pathway is easily discovered. The β -keto ester is hydrolyzed under the acidic reaction conditions to give a β -keto carboxylic acid. These compounds are known to split off carbon dioxide if heated. In our reaction this leads to carbon dioxide and propanone. This reaction sequence, which competes with the acetalization, consumes approximately half of the starting material, so that the reason for 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 the first things to try.

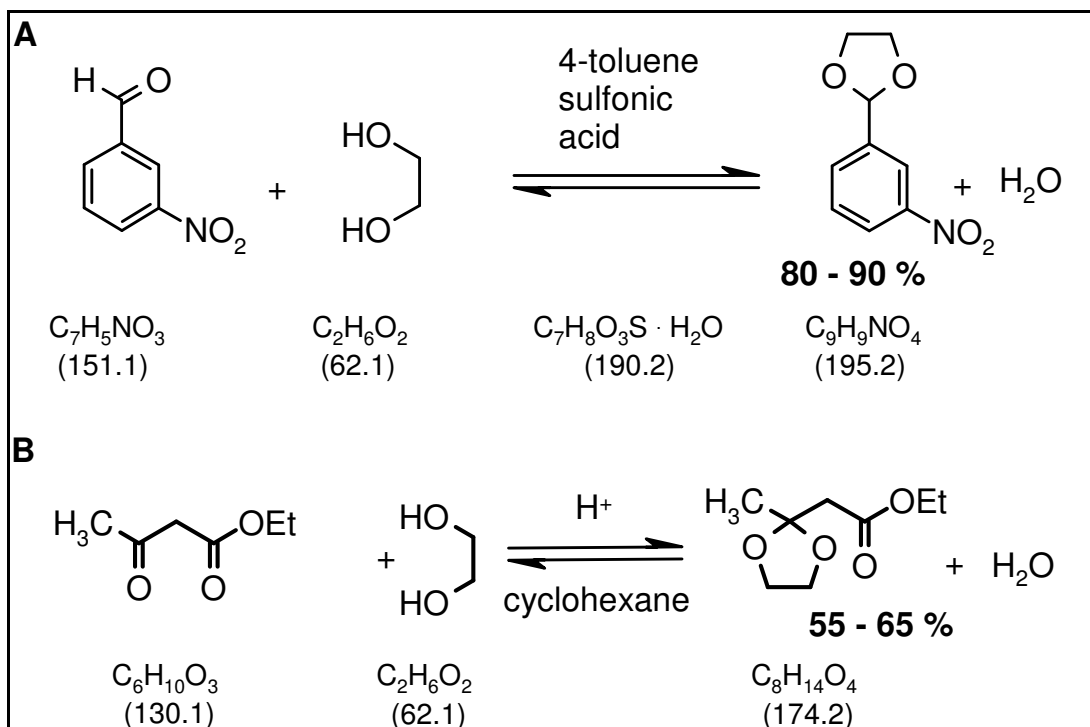


Figure 5 Two classical reactions from the organic teaching laboratory

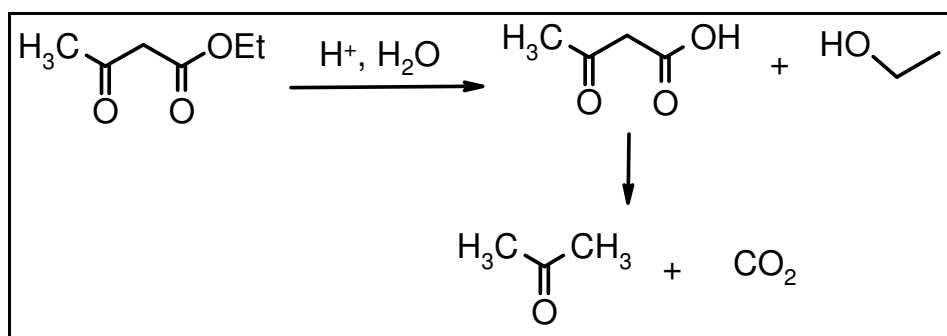
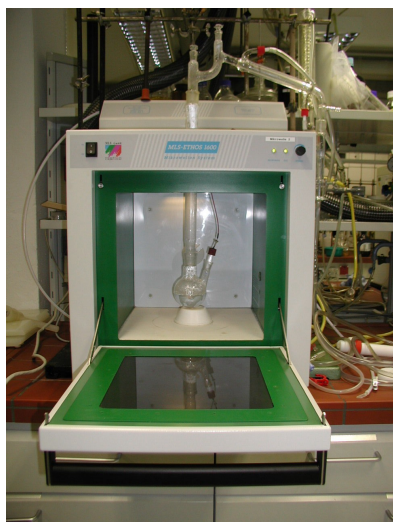


Figure 6. . . . but B has a competing reaction pathway leading to 'invisible' by-products.

Energy matters

Let us go back to reaction A. The chemistry of this process gives the desired product in high yield and purity. But there are several ways in which 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? Although we expect the same product to be produced in all cases, the energy consumption for the same amount of material varies significantly. Figure 7 shows the three experimental set ups and the measured energy consumption for reaction and work up for all three cases. The microwave oven clearly wins the competition. However it should be noted that, at present, microwave ovens cannot be used on an industrial scale.



microwave



oil bath



heating mantle

Energy consumption of the syntheses

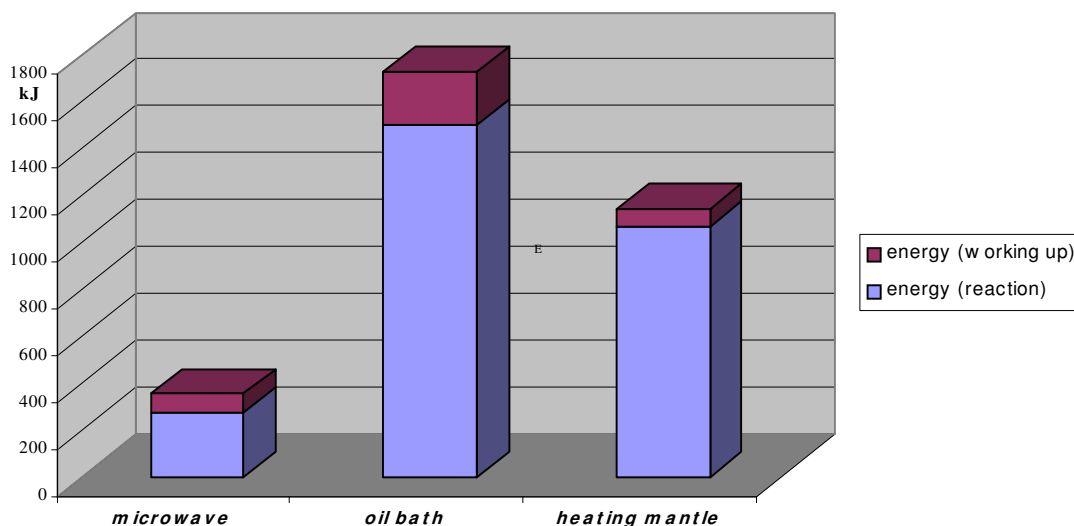
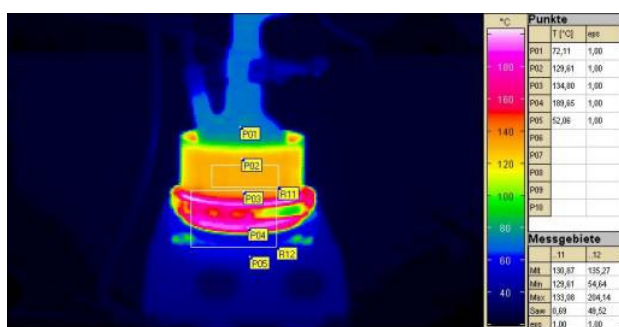


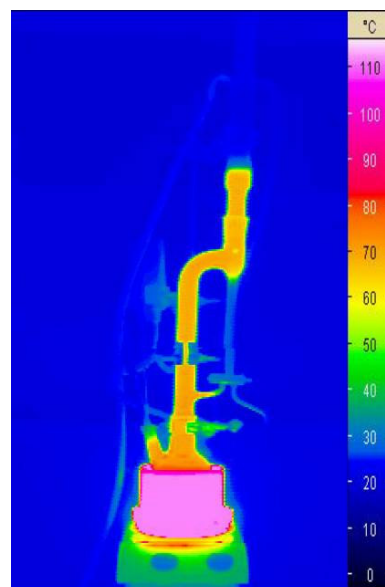
Figure 7 Three ways to get the reaction done, but different energy bills to pay

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

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



oil bath



heating mantle

Figure 8 Infrared pictures make energy emissions visible

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

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 on 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 laboratory classes, is an illustrative example. The nitration of methylbenzene (toluene) yields several reaction products in different amounts. The careful analysis of the crude product mixture reveals that besides the *ortho*- and *para*-substitution products, as expected from the selectivity rules of electrophilic aromatic substitution, considerable amounts of other products are formed. Their relative amounts vary with reactions conditions, but a reaction yielding a single substitution product is hard to achieve. Standard work-up 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, the desired ones and the unwanted ones, into account, because they all have been produced and humans are exposed to them.

The measurement of the overall effect of a chemical compound on humans and the environment is difficult. A reasonable estimate is the effect factor, which is derived from a variety of toxicity data, but also considers how a compound is distributed in the environment and how long it withstands degradation. Figure 9 shows all compounds used in and produced by the reaction with colour-coded effect factors to allow an easy detection of dangerous components. The data to do such an assessment for any kind of reaction are provided as background material on the web pages of our project, see *More information*, below. However, data is not available for all compounds 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 this material everybody who takes an organic chemistry teaching laboratory course will be able to estimate the potential chemical hazard of a reaction.

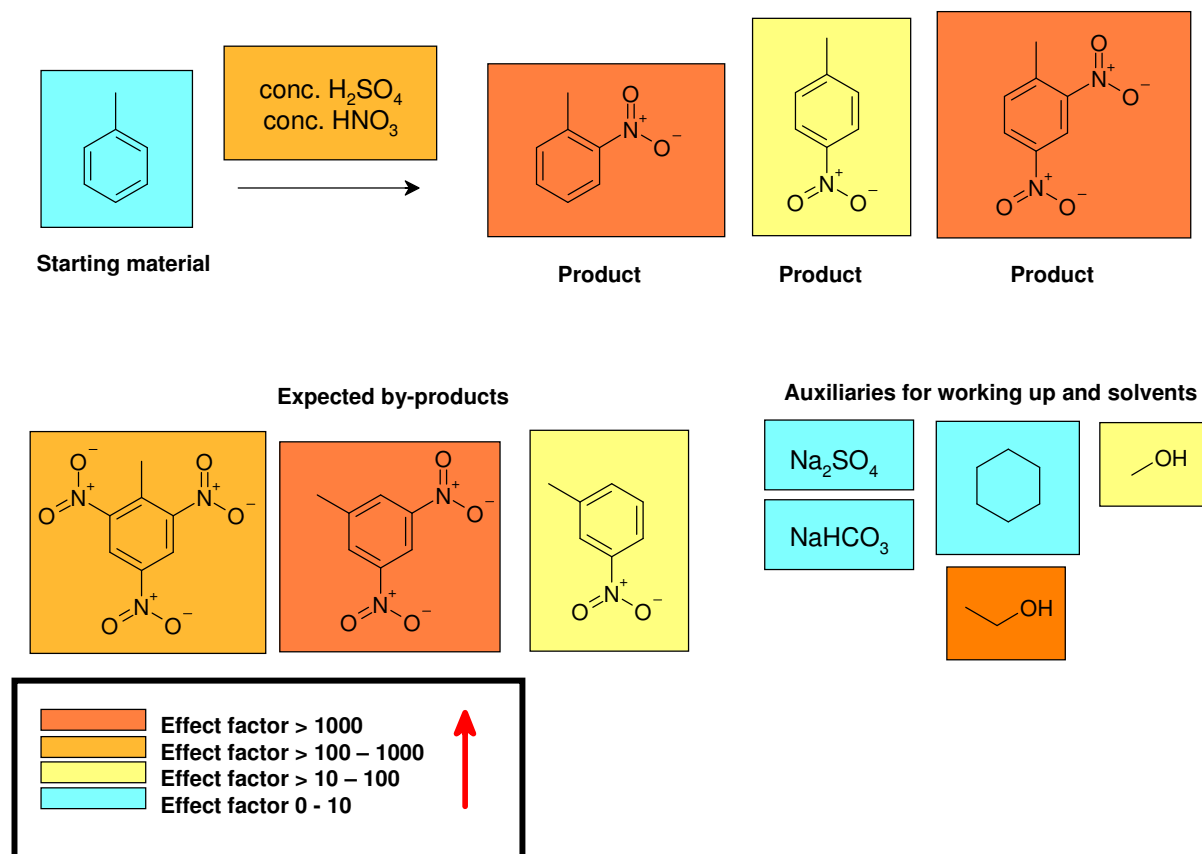


Figure 9 Nitration of methylbenzene (toluene) with compound effect factor encoded by colours

The effect of a chemical reaction on the environment does not end at the door of the laboratory, but in teaching laboratory courses it is like this due to the small amounts of chemicals and waste involved. To extend the view from time to time can provide new insights and teach interesting lessons. The exercise starts at the reaction itself. We then extend 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 the identification of problems and opportunities for improvement and synergies.

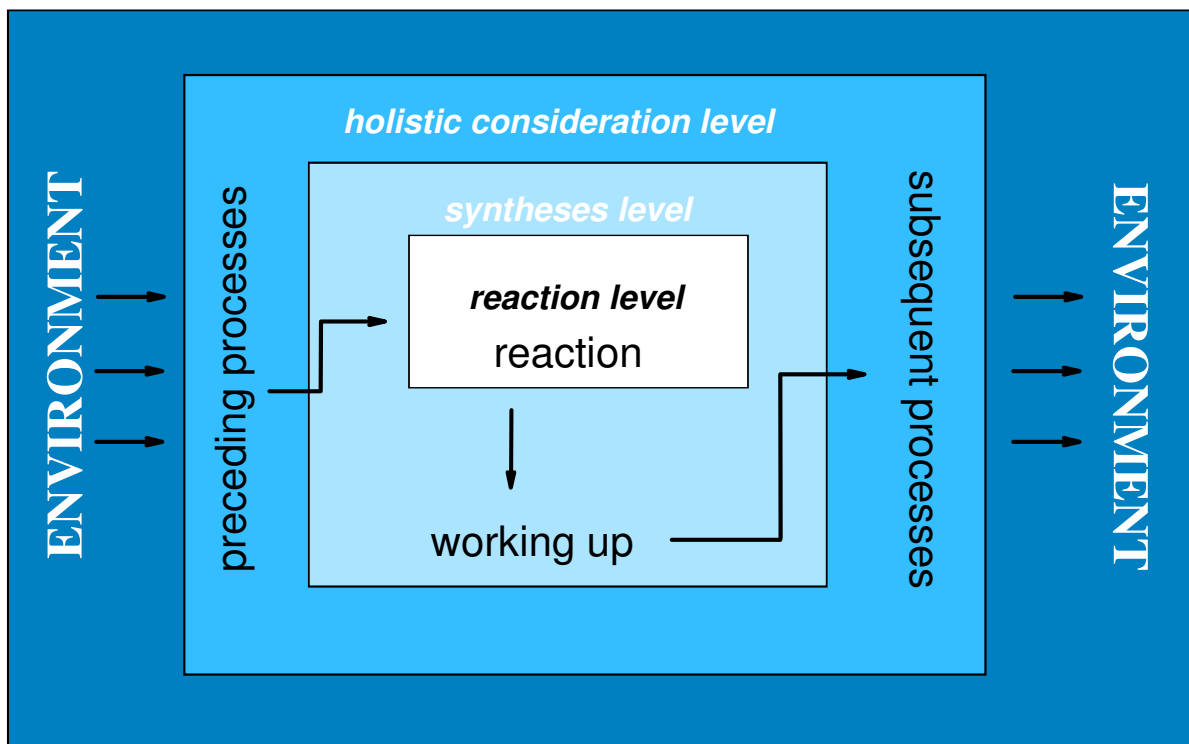


Figure 10 Assessment of the effect of a reaction on the environment

Some help from nature

Enzymatic transformations 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 laboratory course and we provide several reliable protocols for experiments in our database. At a first glance biotransformations appear as perfect sustainable chemistry, but quite often this is wrong. In particular for the production of larger quantities of product the work up from aqueous reaction mixtures can generate huge energy bills. Some 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 the highest sustainability.

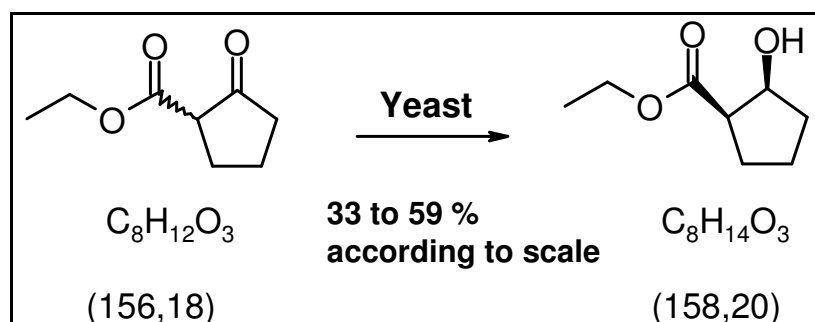


Figure 11 Biotransformation for the teaching laboratory: dynamic enantioselective reduction of a β -keto ester

More information

To allow a better coverage of all the issues of sustainability in chemical education we are developing a database, which will contain approximately 100 laboratory experiments. Beside a detailed experimental protocol, safety guidelines and analytical data a variety of additional material is provided that addresses the aspect of sustainability. The material can be individually adapted to any type of organic chemistry teaching laboratory course or used for projects in and outside the classroom. All material is available free on the internet. Progress of the project, which will be completed by the year 2004, can be followed at <http://www.uni-regensburg.de/Uni/Agenda21/OCPraktikum/umwelt-home.htm> (Accessed October 2002)

This web page gives more information about the ongoing project. 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

- ⁱ B. M. Trost, *Science*, **1991**, *254*, 1471.
- ⁱⁱ Sheldon, *Chem. Tech.* **1994**, *24*, 38.
- ⁱⁱⁱ M. Eisen, J. Metzger, unpublished.