Teaching Guide
Monowave 50

Further information

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Introduction

Organic chemistry is an important part of the basic education of future chemists and constitutes the basis for further research, e.g. in the fields of drug discovery and materials science. Consequently, it is of great importance for young people to get in touch with modern techniques for efficient method development as early as possible. The pupils and students of today are the scientists of tomorrow! With this idea in mind, this comprehensive teaching guide has been prepared to support the teaching work and to enable practical experiments in a fast and safe way.

The way organic synthesis is performed in modern laboratories has probably never changed as rapidly as in the past two decades. This change is not only about new chemistry, but even more about new synthesis equipment. Oil baths and reflux condensers have been the "workhorses" in many labs for more than 100 years. A state-of-the-art laboratory requires modern and easy-to-handle instruments, such as the new Anton Paar synthesis reactor Monowave 50. With its small footprint, intuitive programming and highest safety standards it is the perfect teaching aid for organic chemistry. Many potential dangers like hot surfaces or direct contact with spilled substances after vessel breakage are avoided.

"Monowave 50 is so easy, it even works for 1st semesters."

Tim Peelen, Lebanon Valley College, PA, USA

Monowave 50 works with easy–to-handle closed vials. Hence, your synthesis can be carried out at temperatures above the solvent boiling point, shortening reaction times remarkably. Temperature control and excellent stirring ensure adequate experiment progress and obtaining the expected products.

"Sealed tube chemistry has never been easier and safer than with this device."

Prof. C. Oliver Kappe, University of Graz, Austria

With Monowave 50 contribution to green chemistry is granted. Don't waste water for refluxing systems and do not use more solvents than necessary! Employ environmentally benign and sustainable processes!

"Each chemist should have the modern and easy handling Monowave 50 reactor in his laboratory."

Prof. Thierry Besson, University of Rouen, France

Altogether, Monowave 50 simplifies synthesis and will revolutionize the way chemistry is taught to the next generation. This modern instrument features accessible for students in an easy-to-use small-scale benchtop reactor. This guide has been designed to provide you with guidelines on how to transform a reflux experiment into a high-speed closed-vessel protocol and a comprehensive collection of examples for organic synthesis. Most of the experiments herein are aimed at students who just started their chemical education whereas some of them require more advanced techniques or are multistep reactions

All experiments in this guide have been developed and tested in collaboration with the Karl-Franzens University Graz, where they are currently being taught as part of the organic chemistry curriculum. At this point, we would like to thank Prof. Oliver Kappe and his team for the fruitful collaboration and their contributions to this guide!

We hope that you will enjoy working with Monowave 50 and this Teaching Guide! If you have any questions, please contact asc_synthesis@anton-paar.com.

Contents

1. Theoretical Background

1.1 History

1.1.1 Known for More Than 100 Years: the Reflux Condenser

Among the first things that chemistry students notice about organic chemistry is that many organic reactions would proceed rather slowly without additional heating. What further complicates things is that heating of volatile, highly flammable organic solvents in open vessels does not only generate a safety risk, but will also very quickly lead to dry-off of the reaction batch. The historical solution to this problem still in use today is the reflux heating methodology utilizing water-cooled glass condensers to prevent solvent escaping into the open atmosphere.

1.1.2 Reflux Heating – the Perfect Technology?

Although reflux condensers belong to the standard inventory of most labs and can still be considered the synthetic "workhorse", the question arises whether equipment based on a technology which is more than 100 years old is still able to satisfy the needs of the fast-paced research environment in the 21st century. Today, in many competitive scientific areas, winning the fight to be the first to submit a publication or a patent can be a matter of weeks or even days.

Another important aspect is the fact that the time in educational institutions is usually limited, which makes it difficult - sometimes even impossible – for students to perform common chemical reactions which usually take several hours or even days. Furthermore environmental issues have to be considered, since reflux experiments waste a lot of water and also chemicals due to commonly used comparably large reaction flasks.

A particular weakness of the widely used reflux heating methodology is undoubtedly the accessible temperature range (being dependent on the solvent's boiling point). Thereby, the solvent choice also co-determines the reaction temperature. Choosing a low-boiling solvent for a reaction will make workup easier, but comes at the price of reduced reaction speed (Arrhenius relation: a temperature increase of 10°C doubles the reaction speed). A mostly unavoidable consequence of using the reflux heating method is that very long reaction times of between hours and days have to be accepted.

Ultimately, the boiling point limitation of traditional reflux equipment is making chemical research not only very time-consuming, but it is also setting very rigid limits to the tight schedule for the successful completion of a chemical project or students' laboratory courses.

Furthermore, reflux experiments bear some additional risks. Pressure fluctuations in the cooling water supply and/or improperly fixed equipment (an issue encountered especially when students are involved) could lead to water leakage and this could affect not only the teaching facilities but also the laboratories underneath and the equipment therein! Power shortages typically cause the involved hot plates to shut off, without any hint or clue when the necessary heating has ceased in an overnight reaction.

1.2 How Can We Accelerate Chemical Transformations?

1.2.1 Reaction Rates, Activation Energy and the Arrhenius Law

When two reactants, A and B, are combined to form a product P, the following reaction equation can be written:

$$A + B \rightarrow P$$

Since both A and B are needed to form P, this type of reaction can be called a *bimolecular reaction*. If we now want to quantify the reaction speed of the reaction above, or, to be more precise, the *reaction rate* **r**, we would typically use the following equation:

$$r=\frac{d[P]}{dt}=k(T)\times[A]\times[B]$$

On a molecular level, the two reactants need to meet in the reaction mixture and their kinetic energy needs to be high enough to overcome the activation energy barrier. Thus, the formation rate of product P depends on the concentration of **A**, the concentration of **B** (the more A and B molecules are present, the more likely they will meet) and a reaction rate constant **k** which is a function of the temperature **T** (this represents the kinetic energy of the reactants).

Now, let us have a look at the reaction energy. Figure 1.1 shows an energy diagram of a chemical reaction. G is the free energy of a given substance. If the free energy of the products is lower than the free energy of the educts, the reaction is energetically favored meaning that this reaction will take place spontaneously provided that the activation energy barrier can be overcome. E_a, the activation energy can be seen as an energetic barrier which needs to be overcome in order for the reaction to proceed. Therefore, some chemical reactions need to be heated up in order to take place.

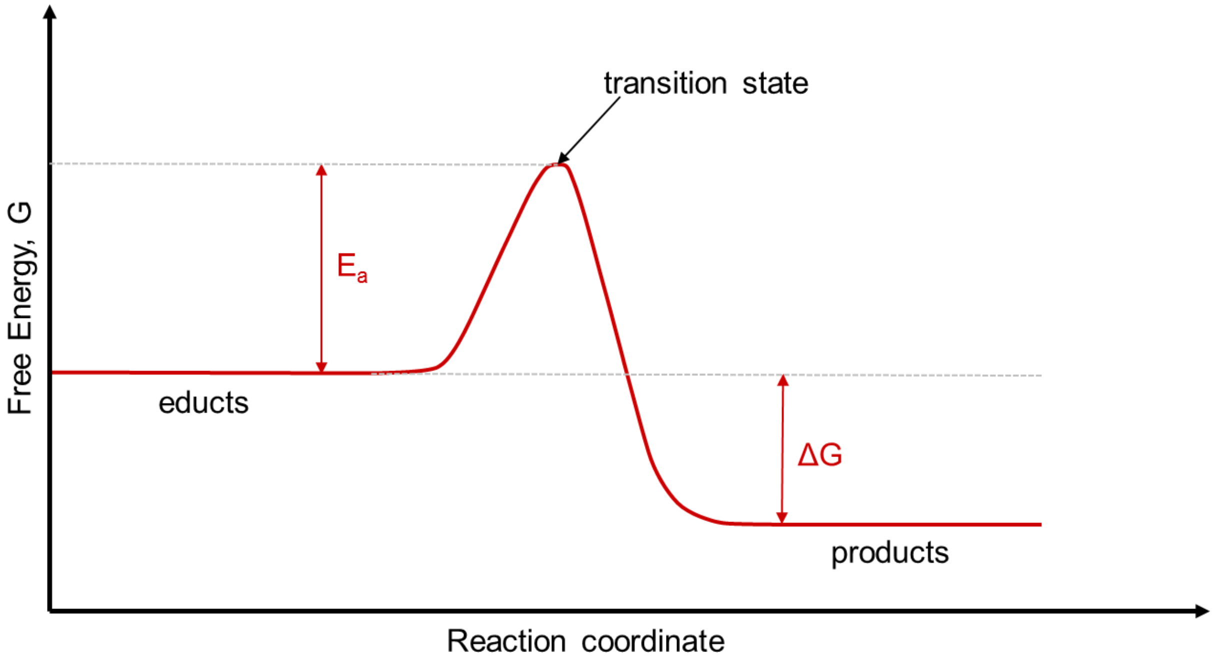

Figure 1.1 Reaction energy and activation energy

There is a relationship between the reaction rate constant k and the reaction temperature. To describe this relationship, the Arrhenius Law is used.

$$\text{Arrhenius Law} \qquad k=A\times e^{-E_a/RT}$$

k = rate constant (quantifies the speed of a chemical reaction)
A = pre-exponential factor
E_a = activation energy
R = universal gas constant
T = reaction temperature

E_a and k are different for every chemical reaction and this is the reason why some reactions already take place at room temperature or even temperatures below 0°C whereas others need to be heated to high temperatures. Reaction times can be calculated as a function of the reaction temperature using a simplified version of the Arrhenius equation.

Keep in mind:

Rule of Thumb: 10°C temperature increase = 2-fold rate acceleration

Example:

If a reaction would take eight hours at 80° C heating up to 90°C (10°C temperature increase) would reduce the reaction time by 50%. Upon further heating, the reaction time can be further reduced, so that at 140°C, it takes only 8 minutes instead of 8 hours to complete this reaction.

Table 1.1 Reaction time as a function of reaction temperature

Reaction Temperature	80° C	90° C	100° C	110° C	120° C	130° C	140° C	150° C	160° C
Reaction Time	8 h	4 h	2 h	1 h	30 min	15 min	8 min	4 min	2 min

1.2.2 The Catalytic Effect

Basically catalysts reduce the activation energy ($E_{a,cat}$, see Figure 1.2) for a given chemical reaction so that less free energy is needed to reach the transition state. The energy difference ΔG between starting materials and products is not changed. This effect can be so pronounced that some reactions do even not take place in their uncatalyzed form!

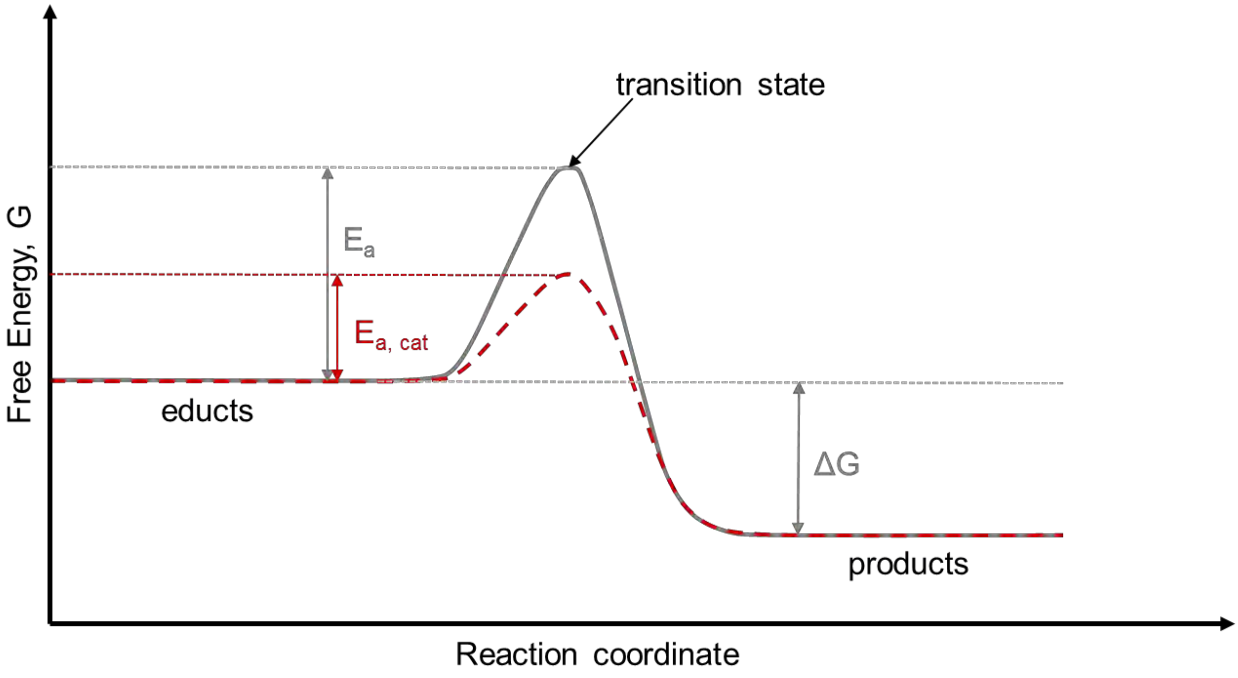

Figure 1.2 Effect of catalysts

Since there are many different chemical reactions, it is impossible to generalize how catalysts work. Indeed, there are various mechanisms for catalysis ranging from chemical bond polarization over chemisorption of reactants to dissociation of reagents. While the catalyst participates in the reaction, it is not consumed and can be recovered from the reaction mixture afterwards. Therefore, while catalysts are very helpful to facilitate certain chemical reactions, an additional purification step is needed and they could also act as an impurity in the product.

As mentioned in Chapter 1.2.1, heating up chemical reactions is another method to accelerate them. So much so, that in some cases reactions, which require catalysis at room or reflux temperature, can be performed at higher temperatures without the use of catalysts at all!

1.3 Superheating in Closed Vessels

Why and how are we able to shorten the reaction times and increase our efficiency using Monowave 50? In fact, Monowave 50 works under sealed vessel conditions. If the reaction vessels are sealed, the reaction mixture can reach temperatures far above the boiling point of the used solvent(s), which leads to dramatically reduced reaction times (from several hours down to a few minutes!).

According to the Arrhenius law (Chapter 1.2.1) the simplest way of increasing the rate of a reaction is to increase the temperature, a strategy that is usually limited by the boiling point of the used solvent. If, however, a reaction mixture is heated inside a hermetically sealed reaction vessel, no solvent vapor can escape and theoretically, any reaction temperature can be realized. This method is often referred to as “superheating” of a solvent and requires the use of reinforced reaction vessels because of the built-up pressure. In a closed vessel, the pressure of the trapped liquid heated to a temperature above the boiling point equals the vapor pressure.

Keep in mind:

Only closed vessel systems provide reaction enhancement due to superheating above the boiling point of the used solvent(s).