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Guidelines for the Basic practical course in Organic Chemistry in the module "Synthesis Lab Course"

and the practical course

Organic analysis in module "Structure Elucidation of Organic Compounds" of the Implementing Regulations of June 25, 2019

1. Eligibility requirements and goals

According to the current model study plan chemistry Bachelor, the organic-chemical basic lab course is attended by students in the 3rd semester. The lab course process "Basic practical course in Organic Chemistry" and "Organic analysis" will be explained in a preliminary discussion, to which you will be invited via Stud.IP and by email.

Regular and active participation in the compulsory lectures "Organic experimental Chemistry I and II" and the associated exercises is desirable. Use the lecture-free time after the 2nd semester to theoretically prepare for the lab course by familiarizing yourself with the content of the "Organikum".

The aim of the organic-chemical basic course is to impart the basic working methods of organic-chemical laboratory practice as well as practical knowledge of the most important reaction types and substance classes. In addition to the preparative work in the "Basic practical course in Organic Chemistry" you will carry out wet analytical separations in the course "Organic analysis". You should learn to work with small amounts and to expand your general knowledge of the subject matter.

2. Organization

Please register for the lab course BEFORE the practical course starts in Stud.IP. Information on this can be found in Stud.IP. The preliminary meeting takes place around a week before the start of the lab course. The appointment is announced via Stud.IP and by email.

The obligatory safety seminar usually takes place after the preliminary discussion (see under 4.). **Participation is compulsory** and must be confirmed by your signature. No lab course without a safety seminar! Please find out about the date in good time!

The assignment to the assistants takes place after the safety seminar. You sign in for your lab cabinet with glass ware before the lab course starts. Taking over the lab space will be supervised by the assistants and Mr. M. Spillner. The lab cabinet is handed in at the end of the lab course. Complaints about the equipment should be directed to Mr. M. Spillner. The appointment for the handover of the lab cabinet must be agreed with Mr. Spillner. Participation in the lab course will not be confirmed if the correct lab cabinet handover has not taken place within 4 weeks after the end of the practical course. The students are responsible for procuring the lab coat and protective goggles. Goggles for people who wear glasses can be borrowed if required.

You carry out the preparative work in your lab course room. The opening times of the lab course rooms will be determined at the preliminary meeting, they are expected to be:

Monday	**1:00 p.m. to 6:00 p.m.**
Tuesday	**8:00 a.m. to 6:00 p.m.**
Wednesday	**1:00 p.m. to 6:00 p.m.**
Thursday	**1:00 p.m. to 6:00 p.m.**
Friday	**8:00 a.m. to 5:00 p.m.**

The responsible supervisor opens the hall. If there are no students present up to 15 minutes after the hall has opened, the hall will be closed for this shift. In addition, the lab course is closed during special events such as the institute seminar or GDCh lectures.

Your presence during opening hours **is compulsory**; in the event of illness, please notify your assistant and submit a medical certificate.

10 weeks are planned for the implementation of the lab course. **If the lab course is cancelled, it will be counted as a failed attempt for the examination unit!**

The chemicals are issued by the central chemical warehouse on the order form with the signature of the responsible assistant.

Colloquia are integrated into the experimental work, in which you demonstrate knowledge of the theoretical background of the preparations. The colloquia must be submitted to the assistants at certain intervals. A corresponding list will be published at the beginning of the lab course. Repeat colloquia take place after one week at the latest. **If the candidate fails twice, an acceptance test is carried out by Prof. Wilhelm.** The colloquia are based on the book:

- **Organikum: Organisch-chemisches Grundpraktikum, 24. Aufl., Wiley-VCH, Weinheim 2015**

The “Organikum” is an lab course and not a textbook. Recommended, accompanying Textbooks are:

- Organic Chemistry, P. Y. Bruice, Pearson Studium, München 2010.
- Solomons' Organic Chemistry, T. W. G. Solomons, C. B. Fryhle, S. A. Snyder, Wiley & Sons, New York 2017
- Organische Chemie, K. P. C. Vollhardt, N. E. Shore, VCH, Weinheim 2005.
- Organische Chemie, H. Hart, L. E. Craine, D. J. Hart, Wiley- VCH, Weinheim 2007.
- Organische Chemie, ein praxisbezogenes Lehrbuch, G. Jeromin, Harry Deutsch, Frankfurt am Main 2006.
- Lehrbuch der Organischen Chemie, W. Walter, W. Francke, S. Hirzel, Stuttgart 2004.

All books can be borrowed from the ZB's textbook collection.

The following textbook cannot be borrowed from the ZB, but it offers you an in-depth look at the various reaction mechanisms in organic chemistry.

- Organic Mechanisms: Reactions, Stereochemistry and Synthesis, R. Bruckner, Springer, Berlin 2010.

3. Course

Basic practical course in Organic Chemistry: Approximately one week before the start of the lab course, the preliminary discussion including the obligatory safety seminar takes place (see under 4.). The appointment is announced via Stud.IP and by email. **This is a compulsory course; no lab course can be carried out without safety instruction.** The lab space will be taken in the lab room you will be assigned to (room B 206 or A 318) takes place before the lab course begins and is supervised by Mr. M. Spillner and the assistants. The lab cabinet is handed in at the end of the lab course.
In a one-day preliminary course in the 1st week of the lab course (appointment by arrangement and by email), you will learn the experimental basics of synthetic organic chemistry.

After the safety seminar, the respective assistant will take the safety colloquium (0th colloquium). If this is successfully passed, the date for the first block colloquium of the first part of the synthesis may be set. On the other hand, the three basic operations (preliminary course experiments) can be carried out at the beginning of the lab course.

After the basic operations there are 4 synthesis parts, each of which is experimentally processed after passing a colloquium (3 preparations per block). The colloquia must be submitted to the assistants at certain intervals up to the respective deadline. In addition, colloquia are held in German or English with the respective assistant. A corresponding list will be published at the beginning of the lab course. A colloquium must be arranged on weekdays **at least 24 hours before the deadline**. A **cancellation must be made no later than 24 hours before the appointment**, otherwise it is considered failed. If a colloquium is not passed or if the student does not attend a seminar without a valid,

verifiable reason, the assistant will set a repeat date. **If the candidate fails twice, an acceptance test is carried out by Prof. Wilhelm.** The successful third attempt at the colloquium is graded 4.0. **If, however, proof of expertise cannot be provided in the third colloquium, the lab course is considered not passed for safety reasons and must be repeated in the next semester.** A part of the synthesis is completed when the preparations and the corresponding protocols have been handed in to your assistant. From the 3rd colloquium onwards, all previous protocols must also be graded. Only then can the next part of the synthesis be started by taking the colloquium. The content of the colloquium can be found in the appendix (see list of keywords, point 10). The colloquia and the protocols are censored internally. The resulting lab course grade is included in the module grade.

The working instructions for the preparations come from various lab course books, including English ones. This means your entry into technical English, which you will have to familiarize yourself with while studying chemistry.

The first submission, as well as the corrections, of the protocols must take place every 14 days after the synthesis has been passed. (See point 6.)

The entrance colloquia and the protocols are censored internally. The resulting lab course grade is included in the module grade.

Organic analysis: The Basic practical course in Organic Chemistry is followed by a wet-analytical separation of two and three substances. After the two-substance analysis has been passed, the three-substance analysis is carried out. Various test and detection reactions are available to identify the organic two- and three-component mixtures. These are based on the following book, which is available in both lab rooms and can be borrowed from the ZB:

- Die Technik der organischen Trennungsanalyse, H. Laatsch, Georg Thieme Verlag, Stuttgart 1988.

In addition to this, you can also consult the book „Organikum: Organisch-chemisches Grundpraktikum, 24. Aufl., Wiley-VCH, Weinheim 2015: *Kapitel E: Identifizierung organischer Substanzen*“.

4. Safety instructions

Attendance is compulsory for the safety seminar. Information is provided about the operating instructions according to §20 GefStoffV[1], lists of carcinogenic and teratogenic hazardous substances, and for female students about possible employment restrictions and dangers for employees of childbearing potential and nursing mothers when handling hazardous substances. This information is posted in detail in the lab course rooms. Unless already done in other lab courses, the laboratory regulations of the Clausthal University of Technology are distributed.

[1] Section 20 of the Hazardous Substances Ordinance (GefStoffV)

Even those who did an lab course in the previous semester **must take part in the safety seminar again in the following semester**.

Thoroughly acquaint yourself about the standard equipment for organic-chemical reactions in the Organikum. All equipment must be checked by the supervising assistant before commissioning.
If you are absent (lunch or library), ongoing experiments must be supervised by a student.

Before the experiment, present your signed operating instructions to the supervising assistant. This includes the reaction equation [starting material(s) and product(s) and by-products, if known, but without mechanism], as well as H-, P- and possibly EUH-phrases[2] for the compounds used (if known). You can find the template for the operating instructions at: https://www.ioc.tu-clausthal.de/fileadmin/user_upload/Spezielle_Betriebsanweisung_OC-GP_Leer.docx

Example operating instructions for the synthesis of 1-bromobutane can be found at: https://www.ioc.tu-clausthal.de/fileadmin/user_upload/Spezielle_Betriebsanweisung_OC-GP_1-Brombutan.pdf

Operating instructions must be visibly always attached to the front window of the fume hood during the experiment.

The batch size of the synthesis is to be dimensioned in such a way that, in the case of the literature yield, either 10 g of a liquid or 5 g of a solid can be expected. The experiments are to be recorded in writing in the form of a laboratory journal. An exemplary representation of a laboratory journal entry can be found under: https://www.ioc.tu-clausthal.de/fileadmin/user_upload/Beispiel_Laborjournaleintrag.pdf.

5. Personal protective equipment

Personal protective equipment consisting of: a lab coat, protective goggles with side protection and closed, slip-resistant shoes is required for the laboratory lab course. Wearers of glasses must wear over goggles with side protection, as contact lenses are forbidden in the laboratory!

Scarfs or headgear (e.g. headscarves) may only be worn inside the laboratory if they are made of pure cotton (100%) and fit tightly to the head. This serves to minimize the risk in the event of a fire and to reduce possible contamination with chemicals.

The lab coat must be long, long-sleeved and made of cotton or cotton blends (cotton content at least 35%). In addition, it must always remain closed within the hall. The smock must be worn inside the lab course room, while outside smocks are prohibited. This is to keep the chemical contamination of public places as low as possible: e.g. toilets.

Disposable nitrile or latex gloves generally only serve as splash protection. Many chemicals can diffuse into the gloves within a short time and therefore no longer offer

[2] H = GHS hazard phrases; P = GHS precautionary phrases; EUH = European Union hazard phrases

adequate protection for the wearer. Thus, you should be informed in advance about the correct selection of gloves and their area of application. For example, thick gloves must be worn for the KOH / iso-propanol bath.

Gloves may not be worn outside of the lab course halls. They are to be taken off when operating the rotary evaporator, computers, taps, doorknobs, drawers, cupboards, measuring devices, scales, etc. as well as when doing paperwork.

6. Protocols

A protocol with self-drawn molecules and self-written texts must be made for each preparation. The ChemBioDraw Ultra program should be used to represent the molecules and mechanisms. This can be downloaded from the following link: https://doku.tu-clausthal.de/doku.php?id=lizenzen_und_software:campus_software:chemoffice The completed protocols of the completed preparations must be presented to your assistant at least 24 hours before the respective colloquium. Protocols for a part of the synthesis must be submitted by the next colloquium and must be graded for the next colloquium.

The **synthesis protocol** contains:

- Name of the preparation in the correct IUPAC nomenclature (see the IUPAC guidelines, OC library).
- Reference of the work specification.
- Concrete reaction equation including the mechanism. Enter the molecular weight under the formula for the starting materials and the product.
- Experiment description of the actual course, i.e., your own observations - sensibly in the past tense with quantities in g or ml **and** (m)mol.
- Characterization of the product, i.e., melting point, boiling point and, for comparison, the corresponding data from the literature.
- The yields achieved in grams and percent of theory and literature.

An example protocol can be found at: http://www.ioc.tu-clausthal.de/studium/praktikum/.

A complete **analysis protocol** contains:

- a description of the preliminary tests
- qualitative analysis
- and the identification of the individual substances.
- The comparative data from the literature must also be given.

Plagiarism: In the case of clear plagiarism, the synthesized product is not recognized, and a penalty product must be synthesized. The protocol must then be submitted in handwritten form!

7. Handing in the preparations

Finished preparations are handed over to the responsible assistant. A label attached to the preparation jar contains the following information legibly and written in pencil: Name of the student and the product, yield, physical data with comparative data from the literature.

The purity requirements are: n_D = ± 0.001; mp. (≤100 °C) ± 3 °C, mp. (≥100 °C) ± 3%.

Required yield ≥ 50% of the literature yield.

8. Completion of the practical work

Please vacate your workplace immediately after you have finished the experimental activity. At the end of the lab course, there is a **joint cleaning of the lab room**. Subsequently, the proper lab cabinet handover takes place with Mr. M. Spillner. Glass appliances that break during the lab course must be replaced by the student. This should be done before the cabinet is handed in.

The courses “Basic practical course in Organic Chemistry” and “Organic analysis” are over when **all protocols have been graded** and are available to your assistant as a **PDF file**.

9. Final colloquium

To complete the module “Synthesis Lab Course”, a 45-minute examination is taken with Prof. Wilhelm.

To complete the module “Structure Elucidation of Organic Compounds” there is a written exam for the lecture “Structure elucidation of organic compounds”.

10. Key point list of the most important topics for the "Basic practical course in Organic Chemistry"

The colloquia are based on the content of the book "Organikum".

Safety colloquium (0th colloquium)

Safety:

- Laboratory dress code, lab coat + goggles + gloves
- Behaviour in lab
- Safety installations
- Danger symbols, H-/P- and EUH-phrases

Laboratory technique:

- Pumping unit, types of vacuum pumps
- Construction of standard apparatuses (distillation, refluxing, …)
- Solvents
    - Types of Solvents (protic, aprotic, polar, non-polar)
    - Drying, drying agents
    - Waste disposal
- Heating, cooling
    - Heating mediums, heating apparatuses
    - Cooling baths, cryostats
- Purification of substances
    - Extraction
    - Recrystallisation
    - Distillation (standard pressure, vacuum, column, steam)
    - Sublimation
    - Identification of melting point, boiling point and refractive index

Basic operations (GO): Procedures are available in Studip!

- BO 1: Fractional distillation
- BO 2: Recrystallization
- BO 3: Use of the separating funnel and the rotary evaporator

1st colloquium

Basics:

- Nomenclature, common names
- Functional groups
- Conformation
- Configuration (*E*, *Z*, *cis*, *trans*, *syn*, *anti*)
- Types of isomerism, isomers, enantiomers, racemate, CIP priority rules
- Bond theories, types of hybridization, bond angles and lengths
- Acid and base theories, especially Lewis theory, pH, pK_a, pK_b
- Catalysis, catalyst, activation energy
- Le Chatelier
- Energy schemes

Radical substitution:

- What is a radical
    - Formation
    - Stability
    - Reactivity
- • Initiators
    - BPO
    - AIBN

- Radical chain reaction
    - Initiation, propagation and termination reactions
- Inhibitors
- Halogenation with elemental halogen, NBS
- Chlorination with sulfuryl chloride
- Sulfochlorination

Nucleophilic substitution:

- S_N1 & S_N2 reactions
- Mechanisms
- Side reactions
- When is which mechanism preferred?
- Solvent effects, structure effects, leaving groups
- Walden inversion, racemization, inversion
- Sideproducts
- Ambident nucleophiles
- Phase-transfer catalysts
    - Crown ethers, ammonium salts
- Halides from alcohols and alcohols from halides
    - $POCl_3$, PCl_5, $SOCl_2$, SO_2Cl_2
    - Shifting reaction equilibria
- Ether formation
    - Acid etherification, ether cleavage
    - Williamson ether synthesis
- Finkelstein reaction
- Production of methyl ethers
- Wagner-Meerwein rearrangement

Elimination:

- α, β-elimination
- E_1, E_2 and E_1cB elimination
- Influencing factors
    - Electronic effects
    - Steric effects
    - Solvent and temperature effects
    - Cumulated, conjugated double bonds
- • Direction of elimination
    - Thermodynamic or kinetic control ...
    - Zaitsev, Hofmann product
- • syn-, anti-elimination
- • Hofmann degradation, elimination from quaternary ammonium salts
- • Dehydration

2nd colloquium

Addition to non-activated C-C multiple bonds:

General:

- Electronic structure and geometry of alkenes and alkynes
- Isolated, conjugated and cumulated double bonds

Addition reactions:

- Possibilities of addition:
  - Electrophilic addition
  - Nucleophilic addition
  - Radical addition
- Mechanism of electrophilic addition
  - influencing factors. e.g. substituents, conformation ...
  - Markovnikov rule
  - syn and anti addition (bromonium ion)
- Halogen addition, comparison of halogens
- Epoxidation
  - Peroxo compounds
  - Prilezhaev reaction
  - Ring opening reactions (ethylene glycol)
- Hydroxylation
  - Osmium tetroxide and potassium permanganate
  - *cis diols*
- Hydroboration and subsequent reaction of the boranes

Cycloadditions:

- General
  - Pericyclic reactions
- [2+1] cycloadditions
  - Simmons-Smith reaction
  - Singlet and triplet carbenes
- [4+2] cycloadditions
  - Diels-Alder reaction
    - *endo* rule (Alder rule)
    - Diene und dienophile
    - Reversibility e.g. cracking of dicyclopentadiene
- Heterogeneously catalysed hydrogenation
  - Raney nickel
  - Pd/C
  - Surface quality
  - Lindlar catalysis

Electrophilic and nucleophilic substitution on aromatics:

General:

- Definition of an aromatic system
  - Monocyclic and polycyclic aromatic hydrocarbons
  - Common carbocyclic and heterocyclic aromatic and non-aromatic compounds
  - Common names
- Electrophilic aromatic substitution
  - Mechanism
    - π- complex
    - σ-complex
    - Substituent effects
    - Direction of the second substitution
    - *Ipso* substitution
  - Nitration and reagents
    - nitryl cation

    - Sulphonation and reagents
    - Halogenations
        - Lewis acid catalysis
        - “SSS” rule (“Siedehitze, Sonne, Seitenkette”, meaning high heat, light, side chain) →side-chain directing parameter
        - “KKK” rule (“Kälte, Katalysator, Kern”, meaning cold, catalyst, core ring) →core-ring directing parameter
    - Friedel-Crafts alkylation
    - Friedel-Crafts acylation
    - Gattermann reaction
    - Vilsmeier–Haack reaction
    - Hydroxymethylation
    - Blanc reaction
    - Kolbe–Schmitt reaction
        - Salicylic acid
- Nucleophilic aromatic substitution
    - Meisenheimer complex
    - Differences from electophilic aromatic substitution
    - Chichibabin reaction
    - Aryne
        - Definition
        - Formation
        - Reactions

Oxidation:

- Definition
- Oxidation numbers of carbon compounds
- Oxidizing agents
    - DDQ, Chloranil….
    - Potassium permanganate…
- Oxidation with sodium hypochlorite
- Swern oxidation
- Chromium compounds e.g. PCC
- Quinones
    - Properties
    - Uses
- Oxidation with C-C cleavage
    - Glycol cleavage
- Oxidation of C-C multiple bonds
- Haloform reaction (unicorn reaction)

Hetero-analogous Carbonyl Compounds:

- Reduction of nitro compounds to amines, intermediate stages, oxidation numbers (Bechamp reduction)
- Formation and reactions of diazonium salts
    - Sandmeyer reaction
    - Balz-Schiemann reaction

3rd colloquium

Addition reactions of carbonyl compounds:

- Carbonyl compounds (definition, formation, properties)
- Reaction of carbonyl compounds with bases, e.g. nucleophilic additions, electrophilic substitutions
    - Influences of substituents
    - Catalysis options
- Reactions of carbonyl compounds with heteroatom nucleophiles
- Formation of hydrates, hemiacetals, acetals and thioacetals
- Reactions with amino compounds
    - Imine (Schiff bases)
    - Ammonolysis and aminolysis
    - Carboxylic acids
- Esterification and saponification
    - Fats / fatty acids / soaps
- Reaction and production of acid chlorides and acid amides
    - Phosgene and carbonic acid derivatives ...
- Addition to nitriles and isocyanates
- Formation and reaction of orthoesters, xanthates, ketenes
- Carbon nucleophiles / CH-acidic compounds
- Reaction of carbonyl compounds with CH-acidic compounds
- Carbon nucleophiles / CH-acidic compounds
    - Deprotonation at the α-carbon
- Tautomerism
- Substituent effects
- Reduction of carbonyl groups
    - Wolff–Kishner reduction
    - Bouveault–Blanc reduction
    - Clemmensen reduction
    - Reduction with complex hydrides ($LiAlH_4$, $NaBH_4$)
- Synthesis of cyanohydrins
    - Strecker synthesis
- Ethynylation
- Aldol reaction and condensation
    - Methylene and carbonyl compounds
    - Claisen-Schmidt reaction
- Acyloin condensation
- Stetter reaction (Stetter umpolung)
- Wittig reaction
    - cis / trans selectivity
- (Wittig) -Horner-Emmons reaction (Horner-Wadsworth-Emmons)
    - cis / trans selectivity
- Knoevenagel condensation
- Mannich reaction
- Ester condensation
    - Dieckmann ester condensation
- Reactions of enamines
- Knorr synthesis

4th colloquium

Further reactions of carbonyl compounds:

- Meerwein-Ponndorf-Verley reduction
  - Shifting the equilibrium (see Oppenauer oxidation)
- Oppenauer oxidation
- Cannizzaro reaction
  - Crossed cannizzaro reaction
- Benzilic acid rearrangement
- Leuckart-Wallach reaction
  - Formation of the educt
- Grignard reaction
  - Prerequisites for the reaction
  - Schlenk equilibrium
  - Polarity reversal
  - Stoichiometry
  - Wurtz reaction
  - Grignard reduction
- Normant reagents
- Rearrangements on nitrogen
  - Hofmann, Lossen, Curtius rearrangement
  - Schmidt, Beckmann rearrangement
  - Intermediate stages (isocyanate, nitrene, etc.)
- Baeyer–Villiger oxidation

Vinylogous carbonyl compounds:

- Definition of the principle of vinylogy
- Pearson's HSAB concept
- Acid and base catalyzed reactions on vinylogous systems
- Addition of amines
- Addition of water, alcohol, thiols ...
- Michael addition
- Stork enamine alkylation
- Robinson annulation
- Addition of acid amides
- Substitution reactions

Vinylogous electron-donating compounds:

- Alkylation of carbonyl compounds
- Hard and soft alkylating reagents
- Halogenation of carbonyl compounds
- Acylation and alkylation of enamines