UNIWERSYTET GDAŃSKI

Course title
Synteza związków biologicznie czynnych/Synthesis of biologically active compounds

ECTS code
13.3.0448

Name of unit administrating study
Faculty of Chemistry

Studies

Field of study	Type	Form	
Chemistry	Master	Full-time studies	

Teaching staff
Prof. dr hab. Piotr Rekowski, prof. dr. hab. Franciszek Kasprzykowski, dr hab. Janusz Madaj, dr hab. Jarosław Ruczyński, dr hab. Elżbieta Jankowska, dr Justyna Siemaszko-Fiertek

Forms of classes, the realization and number of hours

A. Forms of classes, in accordance with the UG Rector's regulations
lecture, laboratory classes

B. The realization of activities
In-class learning

Number of hours
lecture 30 h, laboratory classes 90 h

ECTS credits
classes 120 h
Tutorial classes 20 h
Student's own work 135 h
TOTAL: 275 h - 11 ECTS

The academic cycle
2019/2020 winter semester

Type of course
obligatory

Language of instruction
Polish

Teaching methods

Lecture with multimedia presentation
Laboratory experiments

Form and method of assessment and basic criteria for evaluation or examination requirements

A. Final evaluation, in accordance with the UG study regulations
Course completion (with a grade), exam

B. Assessment methods

- determining the final grade based on partial grades received during the semester
- written exam with open questions

C. The basic criteria for evaluation or exam requirements

Lecture:
• positive assessment of each of the three partial written examinations consisting of 5-10 open questions covering the issues listed in the course content; answers to questions will require solutions to tasks related to the recorded learning outcomes; the scale of grades will be adapted to the scoring range of the assessed written papers. The final grade will be the average of the grades for partial exams.

Laboratory exercises:
Partial assessments cover:
• quality and organization of experimental work,
• theoretical preparation for exercises (oral answer before starting the exercise),
• three written reports presenting the performed experiments and obtained results as well as their analysis .

	• determining the final grade based on partial grades received during the semester • written exam with open questions (tasks)

Required courses and introductory requirements

courses in organic chemistry, biochemistry, physical chemistry, chemical spectroscopy
possession of knowledge, skills and competences arising from the above subjects (listed in formal requirements)

Aims of education

• familiarizing students with all issues listed in the lecture program content,
• to familiarize students with the names used in the chemistry of peptides, sugars, and chiral compounds
• familiarizing students with the basic methods: peptide bond synthesis, organic asymmetric synthesis, glycoamine conjugate synthesis
• teaching students how to design peptide synthesis
• chemical tripeptide synthesis by solid support method (Merrifield method)
• acquaintance with methods of determining the structure of the oligo- or polysaccharide part of a glycopeptide or glycoamino acid
• introduction to methods of O-glycosidic bond formation and oligosaccharide synthesis
• familiarizing students with the importance of optical isomerism for the biological activity of organic compounds;
• providing students with knowledge about the construction of optically active compounds and methods for determining optical purity, as well as methods for obtaining such compounds through the separation of racemic mixtures (compounds), asymmetric synthesis or using biotechnological methods.
• acquaint students with the methods of synthesis and / or separation of racemic mixtures / compounds.

Course contents

A. Problems of the lecture:

Part I (Peptide synthesis) will be devoted to the chemical synthesis of peptides, including such issues as: the chemical structure of protein amino acids; peptide bond; amino, carboxyl, alcohol, guanidine, thiol, imidazole, indole, amide function protecting groups; putting on and taking off covers from the mentioned groups and advantages and disadvantages of the discussed protective groups; prevention of adverse reactions and processes during the use of protective groups; methods of peptide bond synthesis: azide, anhydride, active esters, carbodiimide, phosphorus and uronium compounds, tactics and strategy for chemical peptide synthesis; tactics for the synthesis of Boc / Bzl and Fmoc / t-Bu (Trt); solid support peptide synthesis (Merrifield synthesis); racemization during peptide synthesis, carrier resins;

Part II (Synthesis of structure and properties of the sugar part of glycoconjugates) will cover such issues as: definitions of glyconjugates, in particular glycoamino acids and glycopeptides, structure of a simple sugar molecule, instability factors, equilibrium state in solution, methods of glycoside formation (O- and N -), methods of selective blocking and removal of hydroxyl groups, anomeric effect and its effects, qualitative analysis of the sugar part of a glycoamino acid or glycopeptide, selected methods of Can-N bond formation and methods of purification of formed compounds.

Part III (Organic Asymmetric Synthesis) covers the following topics: Optical Isomerism. The importance of optical isomerism for the biological activity of compounds. Chirality. Center, axis and plane of asymmetry. Enantiomers and diastereomers. Racemic mixture, racemic compound, solid racemic solution, meso isomer and their physicochemical properties. Optical purity of chemical compounds. Enantiomeric and diastereomeric excess. Methods for determining the optical purity of compounds: polarimetry, NMR

methods (using Mosher's reagent and derivatives of this reagent, chiral chemical shift inducing reagents, chiral solvents). Determination of optical purity by isotope dilution. Chromatographic techniques in determining the optical purity of compounds and preparative separation enantiomers. Chromatography of diastereomers. Liquid and gas chromatography on chiral phases. Types of chiral phases and the scope of their application. Methods of obtaining optically active compounds. Methods of separation of racemic mixtures / compounds: formation of diastereomeric compounds, kinetic separation of racemic mixtures / compounds. The use of enzymes to separate racemic mixtures / compounds. Asymmetric synthesis. The use of a chiral auxiliary group. Oppolzer sultam and its application in asymmetric synthesis. The use of chiral metal-containing catalysts, organocatalysts and enzymes in asymmetric synthesis. Biotechnological methods for obtaining optically active compounds and comparison of these methods with chemical synthesis. Oxidation of allyl alcohols by the Sharpless method. Asymmetric synthesis of cyanohydrin. Asymmetric synthesis of amino acids by the Strecker method using organocatalysts and metal-containing catalysts. The use of enzymes in asymmetric synthesis. The use of microorganisms to obtain optically active compounds.

B. Problems of laboratory exercises:

Part I. Peptide synthesis: chemical synthesis of tripeptide on solid support with Fmoc / But tactics using trityl resin, chromatographic analysis of tripeptide after synthesis (HPLC), mass spectrum analysis (MS-MALDI-TOF).

Part II Synthesis of glycoamino acid conjugates: synthesis of 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride sugar substrate; sugar derivative coupling reaction with N-9-fluorenylmethoxycarbonyl-L-serine benzyl ester, chromatographic analysis obtained after synthesis of glycoamino acid conjugate (TLC).

Part III Asymmetric organic synthesis: solution synthesis in racemic amino acid derivatives; separation of racemic amino acids using enzymes (α-chymotrypsin, papain); separation of racemic amino acids using diastereomeric salts, determination of the degree of optical purity of separated compounds by the polarimetric method.

Bibliography of literature

Literature required to pass the course

A. Literature required for the final passing of classes (passing the exam):

Part I.

A.1. used during classes:

Monographic materials prepared by the lecturers

A.2. studied independently by the student:

Shwan Doonan, "Peptides and Proteins" PWN, Warsaw 2007.
H.-D. Jakubke, H. Jeschkeit, "Amino acids, peptides, proteins", PWN, Warsaw, 1989.
A. Kołodziejczyk "Natural organic compounds", PWN, 2003.

Part II

A.1. used during classes:

Monographic materials prepared by the lecturers

A.2. studied independently by the student:

Fundamentals of Chemistry of Carbohydrates, Świderski J., Strusiński J., Temeriusz A., 1973.
Fundamentals of Sugar Chemistry, Wiśniewski A., Madaj, J., 1997.

Part III

A.1. used during classes:

Monographic materials prepared by the lecturers

A.2. studied independently by the student:

Jakubke H, Jeschkeit H. J., "Amino acids, peptides, proteins", PWN, Warsaw, 1989.
Sparrow J .T. (ed.), "Preparation and elements of organic synthesis", PWN, Warsaw, 1983.

A. Extracurricular readings B. Supplementary literature
Jacek Gawroński, Krystyna Gawrońska, Karol Kacprzak, Marcin Ślub "Contemporary organic synthesis. Selection of experiments ", PWN, Warsaw, 2004.
and other textbooks discussing the issues presented in the lectures

A.

Knowledge

1. Names amino acid derivatives, peptides and their derivatives
2. Lists protective groups and those used in peptide synthesis
3. Characterizes methods of peptide bond formation
4. Illustrates the principles of solid-peptide synthesis
5. Shows the state of equilibrium of simple sugar in solution
6. Lists ways to activate the anomeric carbon atom
7. Lists the effects of the anomeric effect in mono-, oligo- and polysaccharides
8. Lists ways of forming O- and N-glycosidic bond with amino acids
9. Describes the conditions of optical isomerism and its role in interactions with biological objectives.
10. Presents the basic methods for determining optical purity and understands the sources of errors in measuring the purity of each of these methods.
11. Gives examples of optically active compounds having an asymmetry center, asymmetry axis and asymmetry plane.
12. Lists, compares and characterizes basic methods for determining optical purity of compounds. Identifies error sources specific to each method.
13. Distinguishes between a racemic compound, a racemic mixture and a meso compound.
14. Has general knowledge about the basic methods of obtaining optically active compounds and the scope of their application.
15. Defines the basic concepts related to the determination of optical purity of chemical compounds
16. Explains the principles of polarimeter operation

Skills

1. Uses chemical terminology to the extent necessary for the presentation (in written and oral form) of the course content
2. Designs peptide synthesis in a schematic form
3. Anticipates the possibility of some adverse reactions during peptide synthesis
4. Proposes methods for determining the structure of the sugar part in glycopeptide and glycoamino acid
5. Draws conclusions from the fragmentation of MS alditoli obtained after hydrolysis and reduction of the high molecular sugar portion of the glycopeptide
6. Suggests O- and N-glycosidic linking of sugar and amino acid
7. Performs the synthesis of amino acid derivatives and performs their characterization
8. Separates the racemic mixture of amino acids
9. Measures the specific rotation of isolated compounds and analyzes the results of conducted experiments
10. Performs calculations of enantiomeric (diastreomeric) excess based on the provided experimental data.

Social competence

1. Appreciates the need for teamwork skills through discussion and consultation
2. Is aware of the need for critical analysis of own work, shows creativity in the search for alternative solutions
3. Demonstrates responsibility in laboratory work (including for work tools entrusted to him, generally available apparatus and laboratory equipment)

4. Appreciates the need to continually expand knowledge and practical skills
5. Be careful when handling chemicals