

UČNI NAČRT PREDMETA / COURSE SYLLABUS

Predmet:	USMERJENA ORGANSKA SINTEZA S KEMIJO ZDRAVIL
Course Title:	TARGET ORIENTED ORGANIC SYNTHESIS WITH MEDICINAL CHEMISTRY

Študijski program in stopnja Study Programme and Level	Študijska smer Study Field	Letnik Academic Year	Semester Semester
MAG Biokemija, 2. stopnja	/	2.	4.
USP Biochemistry, 2 nd Cycle	/	2 nd	4 th

Vrsta predmeta / Course Type: izbirni strokovni / Elective Professional

Univerzitetna koda predmeta / University Course Code: BI2113

Predavanja Lectures	Seminar Seminar	Vaje Tutorial	Klinične vaje Work	Druge oblike študija	Samost. delo Individual Work	ECTS
30	15	30 LV	/	/	75	5

Nosilec predmeta / Lecturer: prof. dr. Marijan Kočevar / Dr. Marijan Kočevar, Full Professor

Jeziki / Languages:

Predavanja / Lectures: slovenski / Slovenian

Vaje / Tutorial: slovenski / Slovenian

Pogoji za vključitev v delo oz. za opravljanje študijskih obveznosti:

Študent oz. kandidat mora imeti predmet opredeljen kot študijsko obveznost.

Prerequisites:

The course has to be assigned to the student.

Vsebina:

Pristopi k usmerjeni sintezi organskih spojin. Uvod. Sinteza spojin za določen namen. Klasične metode sinteze. Oblikovanje biološko aktivnih spojin na osnovi znanih struktur receptor-ligand in uporaba molekularnega modeliranja. Kombinatorialna sinteza.

Retrosintezna analiza. Transformi, inverzija polarnosti (Umpolung), sintoni in sintezni ekvivalenti.

Kemijske metode preoblikovanja organskih spojin. Uvod v selektivno in stereoselektivno sintezo. Zaščitne skupine. Homogena in heterogena kataliza. Asimetrična indukcija in metode, ki bazirajo na uporabi učinkovitih kiralnih pomožnikov (chiral auxiliaries) v stereoselektivni sintezi. Druge metode v

Content (Syllabus outline):

Approach to the directed organic synthesis. **Introduction.** Synthesis of the target compounds. Conventional synthetic methods. Design of biologically active compounds on the basis of the known structure receptor-ligand (enzyme-active compound) and the application of molecular modelling. Combinatorial synthesis.

Retrosynthetic analysis. Basic principles of retrosynthetic analysis: transforms, inversion of polarity (Umpolung), synthons and synthetic equivalents.

Chemical methods of the design of organic compounds. Introduction to selective and stereoselective synthesis. Protecting groups. Homogeneous and heterogeneous catalysis.

selektivni sintezi. Sinteza s pomočjo encimov. Uporaba prehodnih elementov v organskih reakcijah. Mehanizmi v selektivni sintezi. Specifične reakcije za tvorbo različnih kemijskih vezi. Uporaba molekularnega modeliranja v sintezi in racionalno preoblikovanje spojin. Primeri sintez nekaterih učinkovin, npr. antibakterijskih in drugih sredstev.

Osnove kemije biološko aktivnih spojin.

Strukturne lastnosti organskih spojin in odnos med strukturo in lastnostmi (npr. aktivnostjo). Struktura spojin v kristalni obliki in struktura v raztopini. Strukturni odnosi na relaciji receptor-ligand. Kvalitativna in kvantitativna zveza med strukturo in lastnostjo. Določanje strukture organskih spojin v raztopini.

Laboratorijske vaje. Tvorba različnih tipov vezi: C-C (Diels-Alderjeva reakcija), C-H (hidrogeniranje vezi C=C), C-O (epoksidacija), primer uvedbe zaščitne skupine, primeri iz zelene kemije, večstopenjska sinteza.

Asymmetric induction and methods based on the application of chiral auxiliaries. Other methods of selective synthesis. Enzymatic reactions and the application of transition metals in organic reactions. Mechanisms in selective synthesis. Specific reactions for the formation of individual chemical bonds. The application of molecular modeling in the synthesis and rational design of the molecule. Synthesis of some biologically compounds (for example antibacterials).

Fundamentals of the synthesis of the biologically active compounds. Structural properties of organic compounds and the relation between the structure and the property (for example biological activity). Structure of the compound in the crystalline form and in solution. Structural relation receptor-ligand. Qualitative and quantitative structure-property relationship. Structure determination of organic compounds in the solution.

Laboratory courses. Formation of different types of bonds: C-C (Diels-Alder reaction), C-H (hydrogenation of the C=C double bond), C-O (epoxidation), introduction of the protecting group, green chemistry, multistep synthesis.

Temeljna literatura in viri / Readings:

- C. Stowell, *Intermediate Organic Chemistry*, J. Wiley, New York, 2. izdaja, 1994, 334 str. / pages (deli knjige; 55%).
- P. J. Kocienski, *Protecting Groups*, Georg Thieme Verlag, Stuttgart, popravljena izdaja, 2000, 260 str./ pages (deli knjige, 15%)

Dodatna literatura: / Supplementary reading:

- *Asymmetric Synthesis*, ed. R. A. Aitken and S. N. Kilenyi, Blackie Academic and Professional, London, 1994, 233 str. (deli knjige, 15%)
- J. Clayden, N. Greeves, S. Warren, P. Wothers, *Organic Chemistry*, Oxford University Press, Oxford, 2nd ed. 2012. (deli knjige) / (Parts only).
- Članki iz literature / Papers from the journals.

Cilji in kompetence:

Cilj predmeta je, da se študent se seznani s pristopom k sintezi spojin, ki bi naj služile določenemu namenu, s poudarkom na sintezi biološko aktivnih spojin oz. zdravil ter z osnovami interakcij med ligandi in receptorji.

Objectives and Competences:

Understanding of the rational analysis and the use of methods and reagents for the synthesis of the target organic molecules, with the emphasis on the synthesis of biologically active compounds for medicinal chemistry.

Poudarek je na kompetentnem razvijanju sposobnosti analize literaturnih virov in racionalne rabe metod in reagentov za sintezo organskih molekul.

Understanding basic principles of receptor-ligand interactions.
Analysis of literature sources and the ability to apply rational design and reagents in the synthesis of organic compounds.

Predvideni študijski rezultati:

<u>Znanje in razumevanje</u> Študent se nauči retrosintezne analize in pretvorb nekaterih funkcionalnih skupin.
<u>Uporaba</u> Študent se nauči pravilnega načrtovanja sintez različnih organskih spojin (npr. zdravil).
<u>Refleksija</u> Zavedanje, da je osnova za načrtovanje sintez organskih spojin natančen študij posameznih reakcijskih stopenj.
<u>Prenosljive spretnosti</u> Pri predmetu se študenti z reševanjem znanih in neznanih problemov izurijo v uporabi znanja in analitičnega razmišljanja ter spoznajo nekatere nove laboratorijske tehnike.

Intended Learning Outcomes:

<u>Knowledge and Comprehension</u> Understanding retrosynthetic analysis and transformation of some functional groups.
<u>Application</u> To learn rational analysis and the design of the target organic molecule, with the emphasis on the synthesis of biologically active compounds.
<u>Analysis</u> Understanding that detailed studies of individual reaction steps represent fundamentals for the rational design of organic compounds.
<u>Skill-transference Ability</u> Students obtain the expertise for analytical thinking by solving known and unknown problems, and are introduced with some novel laboratory techniques.

Metode poučevanja in učenja:

Predavanja, seminarji in laboratorijske vaje.

Learning and Teaching Methods:

Lectures, seminars and practical training.

Načini ocenjevanja:

Kolokvij iz vaj
Seminar
Pisni in ustni izpit

Delež (v %) /

Weight (in %) **Assessment:**

Laboratory tutorial colloquium
Seminar
Written and oral examination

Reference nosilca / Lecturer's references:

- KRIVEC, Marko, GAZVODA, Martin, KRANJC, Krištof, POLANC, Slovenko, **KOČEVAR, Marijan**. A way to avoid using precious metals: the application of high-surface activated carbon for the synthesis of isoindoles via the Diels-Alder reaction of 2H-pyran-2-ones. Journal of organic chemistry, ISSN 0022-3263, 2012, vol. 77, no. 6, str. 2857-2864, doi: 10.1021/jo3000783. [COBISS.SI-ID 35801349].

- CIMPEANU, Valentin, **KOČEVAR, Marijan**, PÂRVULESCU, Vasile I., LEITNER, Walter. Preparation of rhodium nanoparticles in carbon dioxide induced ionic liquids and their application to selective hydrogenation. Angewandte Chemie, ISSN 1433-7851. [Print ed.], 2009, vol. 48, no. 6, str. 1085-1088, doi: 10.1002/anie.200803773. [COBISS.SI-ID 30100997].

- KRANJC, Krištof, PERDIH, Franc, **KOČEVAR, Marijan**. Effect of ring size on the exo/endo selectivity of a thermal double cycloaddition of fused pyran-2-ones. Journal of organic chemistry, ISSN 0022-3263, 2009, vol. 74, no. 16, str. 6303-6306, doi: 10.1021/jo9011199. [COBISS.SI-ID 30678277].

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