

## UČNI NAČRT PREDMETA / COURSE SYLLABUS

<b>Predmet:</b>	IZBRANA POGLAVJA IZ HETEROCIKLIČNE KEMIJE
<b>Course Title:</b>	SELECTED TOPICS IN HETEROCYCLIC CHEMISTRY

Študijski program in stopnja Study Programme and Level	Študijska smer Study Field	Letnik Academic Year	Semester Semester
DR Kemijske znanosti, 3. stopnja	/	1.	1. in 2.
Doctoral programme in Chemical Sciences, 3 <sup>rd</sup> Cycle	/	1 <sup>st</sup>	1 <sup>st</sup> and 2 <sup>nd</sup>

Vrsta predmeta / Course Type:

izbirni/Elective

Univerzitetna koda predmeta / University Course Code:

KZ309

Predavanja Lectures	Seminar Seminar	Vaje Tutorial	Klinične vaje Work	Druge oblike študija	Samost. delo Individual Work	ECTS
30	30	/	/	30	60	5

Nosilec predmeta / Lecturer:

prof. dr. Jurij Svete /Dr. Jurij Svete, 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:**

Študent s soglasjem mentorja med spodaj navedenimi temami v izbere tiste, ki so najrelevantnejše za njegovo raziskovalno delom. Nosilec predmeta in vodja študija poskrbita, da obseg študentovega dela ustreza 5 KT. Če je izvajalcev več, izvajanje koordinira nosilec.

- Sinteza in uporaba heterociklov v stereoselektivni organokatalizi. 5- in 6-členski heterocikli in njihovi kondenzirani analogi kot pomembna skupino katalizatorjev v asimetrični organokatalizi. Sinteze *N*-heterocikličnih karbenov (NHC-jev), derivatov prolina in imidazolidinonov ter njihova uporaba v stereoselektivnih pretvorbah z ustreznimi

**Content (Syllabus outline):**

From the topics listed below the student selects (in agreement with the supervisor) those that are most relevant to his research work. The course- and the study-leader take care that the student's workload corresponds to 5 credits. In case of multiple teachers, the performance is coordinated by the course leader.

- Synthesis and application of heterocycles in stereoselective organocatalysis. 5- and 6-membered heterocycles and their fused analogues as an important group of catalysts in stereoselective organocatalysis. Synthesis of *N*-heterocyclic carbenes (NHC's), proline derivatives, and imidazolidinones and their applications in stereoselective transformations

katalitski cikli/načini aktivacije substrata. (U. Grošelj)

- Diels–Alderjeva reakcija kot temeljna metoda tvorbe novih C–C vezi v heterociklični kemiji.

Uporaba alkenov (maleimidi, maleinanhidrid itd.) in alkinov kot dienofilov ter heterocikličnih sistemov (furani, tiofeni, 2H-piran-2-oni, 2-piridoni, kumarini itd.) kot dienov v Diels–Alderjevih reakcijah. Sinteze heterocikličnih sistemov s pomočjo cikloadicij: (benzo)izoindoli, indoli, oksabiciklo[2.2.2]okteni, dianhidridi biciklo[2.2.2]okt-7-en tetrakarboksilnih kislin itd. in s tem povezana vprašanja regio- ter stereoselektivnosti. Priprava pomembnih spojin: derivati taksola, boskalida, talidomida itd. Izboljšanje tovrstnih sintez z uporabo sodobnih pristopov: uporaba mikrovalov, visokih tlakov (do 18 kbar), vode idr. neškodljivih topil itd. (K. Kranjc)

- Moderni pristopi v sintezi heterocikličnih spojin. Heterociklizacije, transformacije obročev, molekulske premestitve, regio- in stereoselektivne ciklizacije, sinteza nasičenih sistemov. Modularni pristop k sintezi obročnih sistemov. Sintezni gradniki za pripravo heterociklov, modularni pristop k načrtovanju sinteze obročev, kontrola kemo-, regio- in stereoselektivnosti. Sinteza funkcionaliziranih heterociklov: sinteza s funkcionalizacijo obroča, sinteza s funkcionalizacijo gradnikov. Kombinatorna sinteza heterociklov. Sinteze in pretvorbe alkil 3-(dimetilamino)propenoatov in sorodnih enamionov; od heterociklov do naravnih spojin. Reakcije z nukleofili in elektrofili, cikloadicije. Aplikacije v sintezi heterocikličnih sistemov, funkcionaliziranih heterociklov, in sintezi naravnih spojin in njihovih analogov. (J. Svete)

combined with respective catalytic cycles/activation modes of substrates will be presented. (U. Grošelj)

- Diels–Alder reaction as the fundamental method for the construction of new C–C bond in heterocyclic chemistry. Use of alkenes

(maleimides, maleic anhydride etc.) and alkynes as dienophiles as well as various heterocyclic systems (furans, thiophenes, 2H-pyran-2-ones, 2-pyridones, coumarins etc.) as dienes in Diels–Alder reactions. Synthesis of heterocyclic systems with the use of cycloadditions: (benzo)isoindoles, indoles, oxabicyclo[2.2.2]octenes, dianhydrides of bicyclo[2.2.2]oct-7-ene tetracarboxylic acids etc. and the issues of regio- and stereoselectivity of these transformations. Preparation of important compounds: derivatives of Taxol, Boscalid, Thalidomide etc. Improvement of such syntheses by the application of modern approaches: use of microwaves, high pressure (up to 18 kbar), water and other non-toxic solvents etc. (K. Kranjc)

- Modern approaches in the synthesis of heterocyclic compounds. Heterocyclizations, ring transformations, molecular rearrangements, regio- in stereoselective cyclizations, synthesis of saturated systems. Modular approach to the ring synthesis. Building blocks, modular approach to the ring synthesis, chemo- regio- and stereo-control. Synthesis of functionalized heterocycles. Combinatorial synthesis of heterocycles. Synthesis and transformations of alkyl 3-(dimethylamino)propenoates and related enamionones; from heterocycles to natural products. Reactions with nucleophiles and electrophiles, cycloadditions. Applications in the synthesis of heterocyclic systems, functionalized heterocycles, and natural products and their analogues. (J. Svete)

### Temeljna literatura in viri / Readings:

Izbrana poglavja iz monografij: / Selected chapters from monographies:

- J. A. Joule, K. Mills: Heterocyclic Chemistry, 5th Edition, Wiley-Blackwell, 2010. (ISBN 978-1-405-13300-5).

- Eicher, T.; Hauptmann, S.: The chemistry of heterocycles, 2nd completely revised and enlarged edition. Wiley-VCH, Weinheim, 2003. (ISBN: 978-3-527-30720-3).
- Hudlický, T.; Reed, J. W.: The way of synthesis. Evolution of design and methods for natural products. Wiley-VCH, Weinheim, 2007. (ISBN: 978-3-527-31444-7).
- Sankararaman, S.: Pericyclic reactions – a textbook. Reactions, applications and theory. Wiley-VCH, Weinheim, 2005. (ISBN: 3-527-31439-3).
- A. Berkessel, H. Gröger: Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis. Wiley-VCH, Weinheim, 2005. (ISBN: 9783527305179).
- A. Padwa, W. H. Pearson: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products, John Wile & Sons, Inc., Hoboken, New Jersey, 2003. (ISBN 0-471-28061-5).
- *Handbook of Combinatorial Chemistry, Drugs, Catalysts, Materials*. Ed. by K. C. Nicolau, R. Hanco, W. Hartwig, Volume 2, Wiley-VCH, Weinheim, 2002. (ISBN 3-527-30509-2)
- Pregledni članki z izbranih področij: / Review articles on selected topics:
- Stanovnik, B.; Svete, J., Synthesis of Heterocycles from Alkyl 3-(Dimethylamino)propenoates and Related Enaminones. *Chemical Reviews (Washington, DC, United States)* **2004**, 104, (5), 2433-2480.
- Kranjc, K.; Kočevar, M., Regio- and stereoselective syntheses and cycloadditions of substituted 2H-pyran-2-ones and their fused derivatives. *Arkivoc*, **2013**, (i), 333–363.
- Seayad, J.; List, B. Asymmetric organocatalysis. *Org. Biomol. Chem.* **2005**, 3, 719-724.

#### Cilji in kompetence:

Poglabljeno poznavanje izbranih področij organske kemije. Kandidat se seznanja z modernimi metodami organske in heterociklične kemije, kar ga usposobi za samostojno reševanje problemov iz tega področja dejavnosti.

#### Objectives and Competences:

Advancement of knowledge on selected topics and methods in organic and heterocyclic chemistry, which is basic for student ability to solve practical problems in the field of organic chemistry.

#### Predvideni študijski rezultati:

##### Znanje in razumevanje

Študent nadgradi in poglobi svoje znanje na naslednjih področjih:

- sinteze heterocikličnih sistemov s posebnim poudarkom na modernih pristopih
- pretvorbe heterocikličnih sistemov, s posebnim poudarkom na modernih pristopih
- pomen in uporaba heterocikličnih spojin v organski (sintezni) kemiji, medicinski kemiji, kemiji materialov in biokemiji.

##### Uporaba

Poznavanje heterociklične kemije je eden od temeljev organske kemije, zlasti v sintezni organski kemiji, kjer služijo heterocikli mnogokrat kot reaktivni intermediati. To

#### Intended Learning Outcomes:

##### Knowledge and Comprehension

The student upgrades and deepens the knowledge on:

- syntheses of heterocyclic systems with emphasis on modern approaches
- transformations of heterocyclic systems with emphasis on modern approaches
- relevancy and applications of heterocyclic compounds in organic (synthetic) chemistry, medicinal chemistry, material science, and biochemistry

##### Application

The knowledge of heterocyclic chemistry belongs to fundamentals of organic chemistry, especially in synthetic organic chemistry, where heterocyclic compounds are frequently used as

<p>znanje je poleg tega uporabno še vrsti drugih s kemijo povezanih področij, predvsem biokemiji in farmaciji, kemiji kompleksov z anorganskimi ioni, itd.</p>	<p>reactive intermediates. This knowledge is also essential in other chemistry related fields, such as biochemistry, pharmacy, coordination chemistry, etc.</p>
<p><u>Refleksija</u> Predmet je osnova za delo na ostalih področjih kemije predvsem nekaterih predmetov izbirnega sklopa organske kemije in biokemije. Posebnega pomena je tovrstno znanje za delo v kemijski in farmacevtski industriji.</p>	<p><u>Analysis</u> Knowledge of heterocyclic chemistry is required for practical work in other areas of chemistry. It is also useful if not a prerequisite for elective courses from various specialized topics in organic chemistry. This knowledge is of vital importance for those working in chemical and pharmaceutical industry.</p>
<p><u>Prenosljive spretnosti</u> Znanje heterociklične kemije zagotavlja zaradi prisotnosti heteroatomov v organskem skeletu najširše strukturne in reakcijske možnosti na celotnem področju kemije.</p>	<p><u>Skill-transference Ability</u> Due to presence of heteroatoms in organic structure, the knowledge of heterocyclic chemistry gives wide structural and reaction possibilities within the whole area of chemistry.</p>

**Metode poučevanja in učenja:**

Predavanja in seminarji.

**Learning and Teaching Methods:**

Lectures, seminars.

**Načini ocenjevanja:**

Ustni izpit.

Delež (v %) /

Weight (in %)

**Assessment:**

100 %

Oral examination.

**Reference nosilca / Lecturer's references:**

Petek, N.; Štefane, B.; Novinec, M.; **Svete, J.** Synthesis and biological evaluation of 7-(aminoalkyl)pyrazolo[1,5-*a*]pyrimidine derivatives as cathepsin K inhibitors. *Bioorganic chemistry*, **2019**, *84*, 226-238.

Grošelj, U.; **Svete, J.** [3 + 2] Cycloadditions of azomethine imines. *Organic reactions, Volume 103*, Evans, P. A., Weinreb, S. M. Eds., *Chapter 2*, J. Aubé, Ed.; Hoboken: John Wiley & Sons, **2020**, *103b*, 529-930.

Petek, N.; Erjavec, B.; Slapšak, D.; Gaber, A.; Grošelj, U.; Požgan, F.; Ričko, S.; Štefane, B.; Klemenčič, M.; **Svete, J.** 2-Acyl-1-aryl-6,7-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole derivatives : versatile fluorescent probes with remarkably large Stokes shift. *Dyes and pigments*, **2022**, *201*, 110224.