COURSE DATA

DATA SUBJECT

Code: 44707
Name: Advanced organic synthesis
Cycle: Master's Degree
ECTS Credits: 4
Academic year: 2025-26

STUDY (S)

Degree	Center	Acad. year	Period
2226 - Master's degree in Organic Chemistry	Facultat de Química	1	Annual

SUBJECT-MATTER

Degree	Subject-matter	Character
2226 - Master's degree in Organic Chemistry	Advanced organic synthesis	COMPULSORY

COORDINATION

VILA DESCALS CARLOS

SUMMARY

The subject Organometallic reagents in synthesis, together with asymmetric catalysis, constitute the Advanced Organic Chemistry subject. It intends to cover the most relevant methods in organic synthesis, with a equilibrated balance between classical methodologies, still valid nowadays as efficient methods for the preparation of organic compounds, and the new methods that were incorporated to organic synthesis in the last decades.

In this context, the application of organometallic in organic synthesis will be addressed initially, paying special attention to the transition metal derived organometallics, since in the last decades the reactions with those metals have witnessed a spectacular development. The consolidation of homogeneous catalysis in industrial applications played a crucial role as a mechanism of feedback in basic research in this field. The development of new catalysts that adapt initial academic methodologies to strategic products from an industrial point of view is a tendency observed frequently in scientific publications, showing the synthetic potential of those methodologies that progressively are incorporated to the repertoire of methods in organic synthesis.

The subject Asymmetric synthesis and catalysis deals with the synthesis and enantioselective catalysis, an important and intense area of current research. Its understanding requires the combination of all the relevant disciplines in organic chemistry (reactivity/structure, kinetics, molecular recognition, stereochemistry and of course, organic synthesis).

For the pharmaceutical industries, the preparation of enantiomerically pure compounds (EPC) is a very attractive area from an economical point of view, as S. Ley indicated in *Chem. Med. Chem* . **2007** , *2*, 768, and for this reason, generates highly qualified work (every year, in *Chemical and Engineering News*, published by the American Chemical Society, appears articles dedicated to this area of research and business). The interest of the chemical-pharmaceutical industries in the synthesis and asymmetric catalysis is easy to understand, since a lot of useful properties of organic compounds are associated to its chirality, or in other words, therapeutic properties of a lot of drugs are inherent of each enantiomer, since biological systems (enzymes and proteins, etc..) of living organisms are able to identify differentially each of the members of two enantiomers. Therefore, each enantiomer is able to induce different biochemical responses. Is important to point out that American FDA and its equivalent in Europe demand strict biological tests of the activity of each enantiomer and the current regulation only permits to patent enantiomerically pure compounds.

PREVIOUS KNOWLEDGE

RELATIONSHIP TO OTHER SUBJECTS OF THE SAME DEGREE

There are no specified enrollment restrictions with other subjects of the curriculum.

OTHER REQUIREMENTS

Essential:
They are essential requirements: basic knowledge in advance organic chemistry and basic organic synthesis.

Recommendable:
They are recommendable requirements: basic knowledgte in organometallic chemistry (transtion metals), inorganic chemistry (coordination chemistry) and kinetics.

For an ideal situation of the subject synthesis and asymmetric catalysis, is convenient that students have studied previously, the subjects organic synthesis and organometallic reagents in synthesis

COMPETENCES / LEARNING OUTCOMES

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Be able to access to information tools in other areas of knowledge and use them properly.

Capacidad para utilizar los conocimientos adquiridos para el diseño y realización de síntesis eficaces de productos con valor añadido.

Competencias de gestión tales como la capacidad para la planificación y gestión de tiempo y recursos, así como para dirigir y tomar decisiones.

Conocer y saber aplicar la reactividad de los compuestos organometálicos en síntesis orgánica.

Poseer habilidades sociales, un buen nivel de comunicación oral y escrita, así como capacidad para trabajar en equipo y con personas de diferentes procedencias.

Profundizar en los principios de la síntesis y catálisis asimétrica.

Saber participar en debates y discusiones, dirigirlos y coordinarlos y ser capaces de resumirlos y extraer de ellos las conclusiones más relevantes y aceptadas por la mayoría.

Ser capaces de valorar la necesidad de completar su formación científica, en lenguas, en informática, asistiendo a conferencias o cursos y/o realizando actividades complementarias, autoevaluando la aportación que la realización de estas actividades supone para su formación integral.

Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.

Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.

Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.

Students should demonstrate self-directed learning skills for continued academic growth.

Students should possess and understand foundational knowledge that enables original thinking and research in the field.

Use different presentation formats (oral, written, slide presentations, boards, etc.) to communicate knowledge, proposals and positions.

DESCRIPTION OF CONTENTS

1. Introduction

Electronic configuration of the metal and the complex. Saturated and insaturated complexes. MO diagrams of octaedric complexes, tetraedric and square planar. Nature and bonding type in transition metal complexes. High and low spin complexes.

2. Types of reactions and mechanism with organometallics from transition metals

Ligand exchange. Oxidative addition/reductive elimination. Transmetalation. Insertion/desinsertion. Nucleophilic and electrophilic attack of coordinated ligands to transtion metals.

3. Carbon-carbon and carbon-heteroatom bond formation by means of cross coupling reactions. Pd, Ni and Fe catalysis.

Kumada, Negishi, Stille, Suzuki, Hiyama, Sonogashira, Buchwald-Hartwig reactions and analogues. Heck reaction. Tsuji-Trost reaction and analogues. Interesting synthetic applications.

4. Reactions of transition metal complexes with insaturated ligands.

Reactions with carbon monoxide. Reactions with carbenes. Metathesis reactions. Reactions with alkenes and dienes. Cycloaddition reactions. Interesting synthetic applications.

5. Photoredox catalysis

Synthetic applications of visible-light photoredox catalysis. C-C and C-heteroatom (B, O, N, P, S, F, Cl, Br, I) bond formation reactions. Mechanistic considerations

6. Catalysis with Au complexes

Cycloisomerization reaction of enynes and analogues. Nucleophilic addition reactions: alcoholes, amines, amides, aryls. Oxidation reactions.

7. Current challenges in transition metal catalysis

Reagent functionalization with transition metals. C-H activation reactions. Substituion of organometallic reagents

8. Sterochemistry. Introdution to the synthesis and asymmetric catalysis

Basic stereochemistry. Chirality. Prochirality. Asymmetric induction. Cutin-Hammett principle.

9. Access to enantiomerically pure compounds (EPC)

Methods to access EPC. Racemic mixture resolution by means of physical methods. Racemic mixture resolution by means of chemical methods. De-racemization ¿Viedma¿ of racemic mixtures.

10. Asymmetric synthesis.

Basic principles of asymmetric synthesis. Diastereoselective synthesis, Chiral auxiliaries.

11. Kinetic resolutions and de-racemizations.

Simple kinetic resolutions (KR). Parallel kinetic resolutions (PKR). Kinetic dynamic de-racemization (DKR). Enantioconvergent de-racemizations (ECP). Cyclic de-racemization (CycD). Asymmetric kinetic dynamic transformations (DYKATT I y II).

12. Asymmetric catalysis

Basic principles of asymmetric catalysis. Multiplication of chirality. Non linear effects (NLE). Amplyfication of chirality. Mono-, by- and multifunctional catalysis.

13. Enantioselective catalysis.

Organocatalysis: basic principles. HOMO activation through chiral enamines. LUMO activation through chiral insaturated iminium salts. SOMO activation. Counter-ion activation.

WORKLOAD

PRESENCIAL ACTIVITIES

Activity	Hours
Theory	20,00
Seminar	20,00
Total hours	**40,00**

NON PRESENCIAL ACTIVITIES

Activity	Hours
Attendance at other activities	0,00
Individual or group project	10,00
Independent study and work	40,00
Preparation of lessons	0,00
Preparation for assessment activities	10,00
Resolution of case studies	0,00
Total hours	**60,00**

TEACHING METHODOLOGY

The subject is formulated in a manner that the student is the principal actor of its own learning. From the beginning of the course, students will have the whole didactic material necessary and the teaching will be structured in the following manner:

• Master classes (in person): In those classes will be directed to discuss with the students the most complicated aspects or those where the students have more difficulties in the previous study of the teaching material provided. Those classes will be complemented with personal study.

• Seminars.- In the seminars the specific application of the acquired knowledge of the students during the master classes will be carried out. The students have to work with the problems previously. Their resolution will be take place alternatively for the professor and for the students, either in group or individually.

• Written assignment.- Additionally, when the teacher will consider it, some assignments will be proposed, normally related to the study of a practical case, connected with one of the themes of the program, that will be detailed in a scientific publication.

EVALUATION

The assessment of the course will be carried out continuously by the professor throughout the academic term and will consist of the following components:

Direct evaluation by the professor. 10% of the final grade will come from the professor¿s direct assessment during theoretical and problem-solving classes, as well as in tutorials. This evaluation will consider various aspects, including:

- Attendance and clear, well-reasoned participation in discussions.
- Problem-solving and raising of relevant questions.
- Critical thinking.

Assessment of the student¿s work. 20% of the final grade will be based on the completion and submission of exercises that will be sent by the professor through the Virtual Classroom or via email. These exercises must be completed by students either individually or in groups, at the professor¿s discretion. The student or group must send their answers through the indicated channel (Virtual Classroom or email) within the period set by the professor.

Exams and written tests. 70% of the final grade will be obtained from the results of written tests, which will take place during designated periods. Students must achieve a minimum of 5 out of 10 on each written exam in order to have the other components of the grade counted.

- Traditional-style exams covering both theoretical questions and problem-solving, along with content related to the subject. These questions and problems will require students to connect different concepts from various topics within the course, or if deemed appropriate by the professor, from other related subjects.
- Non-attendance-based exams, in which the professor directly hands out or sends via email a series of questions to be solved by students, either individually or in groups, at the professor¿s discretion. The student or group must submit their answers via the same channel and within the deadline set by the professor.

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