

## 60450 - Synthetic strategies in advanced organic chemistry

### Información del Plan Docente

Academic Year	2016/17
Academic center	100 - Facultad de Ciencias
Degree	543 - Master's in Molecular Chemistry and Homogeneous Catalysis
ECTS	6.0
Course	1
Period	First semester
Subject Type	Compulsory
Module	---

### 1. Basic info

#### 1.1. Recommendations to take this course

The Knowledge of the basic concepts of Organic Chemistry is recommended: structure and reactivity of the main functional groups and chemical bond theory.

Continuous work and class attendance, especially the resolution of the proposed problems, facilitates the success in this course.

#### 1.2. Activities and key dates for the course

The *Synthetic strategies in advanced organic chemistry* course will be lectured in the first semester, like the other three compulsory subjects of the Master and the optional subjects *Fundamental methodologies in synthesis* and *Bibliographic resources and data bases*.

Throughout the course, several examinations and assignments (individually or in groups) will be made, in order to learn more deeply some issues. The dates and presentation of these works will be communicated well in advance

The practices will consist of the preparation and discussion of different synthesis protocols for organic molecules of relative complexity.

### 2. Initiation

#### 2.1. Learning outcomes that define the subject

The student must know the principles of retrosynthesis and, how to apply them to the synthesis of an organic molecule from readily accessible starting products.

The student must know the usual synthetic methods to build the carbon skeleton in organic molecules (linear chains, rings, formation of carbon-carbon bonds) and the interconversion of the most important functional groups.

The student should make use of basic organic synthetic chemistry tools, taking into account the compatibility and

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incompatibility between the functional groups.

The student must know the mechanism of the organic reactions and its relationship with issues such as: chemoselectivity, regioselectivity and stereoselectivity.

The student should be able to solve practical problems and general issues of synthetic organic chemistry.

The student must propose reasonable synthetic procedures for a relative complex organic compound, taking into account the stereochemistry of each step.

The student should be able to conduct a critical analysis of the different synthetic alternatives for the same compound and to defend the proposal synthesis.

The student should be able to conduct a critical analysis of the synthesis described in the scientific literature for a product of interest.

The student should be able to obtain information from literature sources and base data, and include that information in reports or presentations.

### 2.2.Introduction

The main objective of this course is to introduce students to the synthetic tools that allow to build an organic molecule from, more simple ones, or from starting materials that are commercial or readily accessible. This course presents, concisely, the different tools we have to address in an organic synthesis. This will require review and rearrange several concepts of Organic Chemistry in order to be applied in the resolution of a more complex synthetic route. Sometimes it will be necessary to know new reactions of special synthetic utility and, other times, the application of the reactions learned in other courses of this Master. Particular attention will be paid to the reaction mechanisms, particularly those that determine the selectivity of the process.

The course is divided into several parts, differentiated but at the same time, interconnected. The first part concerns to the study of the basic concepts of the retrosynthetic analysis, a technique for solving problems in the planning of organic syntheses. This is achieved by transforming a target molecule into simpler precursor structures (synthons). This procedure is repeated until simple or commercially available structures are reached. Then, particular attention to the construction of the carbon skeleton and the major organic functional group transformations, will be paid. Finally, a special emphasis will be on the selectivity in an organic reaction (chemoselectivity, regioselectivity, stereoselectivity), for which, an adequate use of protecting groups will be very useful.

In the last part of the course, the synthesis of more complex molecules will be studied. The students must use their creativity to apply the acquired concepts. In particular, the synthesis of natural products or other molecules of industrial interest will be proposed.

### 3.Context and competences

#### 3.1.Goals

This course constitutes one of the fundamental pillars of the Master in *Molecular Chemistry and Homogeneous Catalysis*, since it provide the knowledge needed to address the synthesis of organic molecules, a field of growing interest in chemical research. The student should be able to create a new or existing molecule using tools that provide Organic Chemistry, Organometallic Chemistry and Catalysis.

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### 3.2.Context and meaning of the subject in the degree

The course *S ynthetic strategies in advanced organic chemistry* is included in the mandatory module *Molecular Chemistry and Catalysis* and is lectured in the first quarter with a teaching load of 6 ECTS: 3 ECTS theoretical, 2,5 ECTS problem-solving and 0,5 ECTS devoted to the preparation of a practical work.

The research aimed to the preparation of organic molecules with specific properties is a field of great interest, both academically and in many chemical, pharmaceutical, cosmetic or food industry.

### 3.3.Competences

To identify the different available tools for the preparation of organic molecules

To integrate the acquired knowledge in Organic Chemistry, Organometallic Chemistry and Catalysis and apply them to solving problems related to the organic synthesis.

To design reasonable synthetic routes for the preparation of organic molecules starting from common chemicals or products easily prepared.

To assimilate and evaluate critically research findings in Molecular Chemistry and Catalysis.

To develop experimental protocols related to advanced organic synthesis.

### 3.4.Importance of learning outcomes

One of the most important challenges for a chemist is the synthesis of organic molecules (known or unknown). Learning outcomes of this course are very important because they will allow the student to propose a reasonable synthesis in the laboratory, taking into account the structural features of the molecule. They also will allow them to assess its effectiveness and the study of possible alternatives. The student will have to combine their knowledge in Organic Chemistry, Organometallic Chemistry and Catalysis, developing their ability as a researcher.

## 4.Evaluation

The continuous assessment of this course is based on the following activities, weighted as indicated:

1.- Control questions and problem solving tests (40%).

2.- Elaboration of a supervised individual or team-based written practical work on the development of a detailed synthetic protocol of a complex organic compound (10%).

3.- Written exam to be held during the global exams period. This exam will consist in the resolution of several synthetic problems (50%).

The final grade will be the best of the following:

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Mark 1 = 0,40 x control tests + 0,10 x mark of practical work + 0,50 x mark of written exam

Mark 2 = Qualification of the written exam

The number of official examination calls per registration and their use will be subjected to the statements of the *Regulation of Permanence in Master Studies and [Regulation of the Learning Assessment](#)*. The latest document will also regulate the general design and scoring criteria of the assessment activities, as well as the exam schedules and timetable for the post-examination review.

### 5.Activities and resources

#### 5.1.General methodological presentation

1.- Interactive lectures (3 ECTS).

2.- Seminars and problem-solving sessions (2,5 ECTS).

3.- Practical work: development of an experimental synthetic protocol (0,5 ECTS).

#### 5.2.Learning activities

Training activity focused on acquisition of advanced knowledge in advanced organic synthesis. This activity includes 30 hours of interactive lectures.

Training activity of seminars and problem solving sessions. This activity includes 25 classroom hours in which students, individually or in small groups, will solve practical cases.

Tutoring. Students will have 3 hours per week for individualized tutoring.

#### 5.3.Program

The lecture topics to be covered are as follows:

##### **Chapter 1 . *The bases of retrosynthetic analysis .***

The retrosynthetic analysis. Disconnections. The synthon concept. Electrophile synthons. Nucleophile synthons. Synthetic equivalents. Type of transformations. Financial considerations in the retrosynthetic analysis. Starting products

##### **Chapter 2 . *Formation of simple Carbon-Carbon bonds .***

Carbanions of type d 1 . Carbanions of type d 2 : synthesis from enolates. Alkylation. Alkylation of compounds with active methylenes. Alkylation of 1,3-dicarbonyl compounds. Aldolic condensation. Michael type additions. Carbanions of type d: syntheses from organometallic compounds: organolithium and organomagnesium compounds. Organocuprates. Substitutions, additions and conjugate additions. Coupling reactions catalysed by palladium. Reactions with p-allyl palladium complexes.

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### Chapter 3 . *Formation of multiple carbon-carbon bonds .*

Alkene syntheses. Elimination reactions. Condensation of carbonyl compounds with ylide and other carbanions. Syntheses mediated by metallic carbenes, metathesis reactions. Alkyne syntheses. Elimination reactions. Condensation reactions.

### Chapter 4 . *Formation of cyclic compounds .*

Baldwin's rules. Cyclopropanes: Carbene additions. Cyclopentanes. Cyclohexanes and cyclohexenes: cycloadditions [4+2]. Robinson annelation. Ring closing metathesis (RCM).

### Chapter 5 . *Protecting groups in organic synthesis .*

Orthogonal groups. Protection of hydroxyl groups: formation of ethers, esters, diols. Protection of carboxylic acids: esters. Protection of amine groups: amide, carbamate and substituted amines. Protection of carbonyl groups: acetal, thioacetal and enol derivatives.

### Chapter 6 . *Oxidations and reductions .*

Alcohol oxidations. Oxidations with Cr (VI), Oxidations with RuO<sub>4</sub> . Oxidations with DMSO. Oxidations with hypervalent iodine. Other oxidations.

Alkene oxidations. Dihydroxylation of alkenes. Epoxidation of alkenes. Oxidative cleavage of alkenes and glycols.

Baeyer-Villiger oxidation.

Catalytic hydrogenation. Hydrogenations in absence of hydrogen. Reductions with metallic hydrides of group III (B, Al). Reductions with active metals. Deoxygenation of carbonyl compounds. Other reductions.

## 5.4.Planning and scheduling

The information about schedules, calendars and exams is available at the websites of the Sciences Faculty, <https://ciencias.unizar.es/calendario-y-horarios> , and the Master, <http://masterqmch.unizar.es> .

The students will be provided with different scholar material either at reprography or through the University's web tool: <https://moodle2.unizar.es/add> .

## 5.5.Bibliography and recommended resources

- Zweifel, G. S.; Nantz, M. H. Modern Organic Synthesis. An Introduction. - 2nd. ed. W. H. Freeman and Company, 2006.
- Borrell Bilbao, José I. Síntesis orgánica / José I. Borrell Bilbao, Jordi Teixidó Closa, José Luís Falcó. - 2º ed. Madrid : Síntesis, 2003
- Mackie, Raymond K. Guidebook to organic synthesis / Raymond K. Mackie, David M. Smith and R. Alan Aitken. - 3rd ed. Harlow, England : Prentice Hall, 1999
- Wyatt, P.; Warren, S. Organic Synthesis: Strategy and Control. Wiley, 2007
- Warren, Stuart. Diseño de síntesis orgánica: introducción programada al método del sintón / S. Warren; versión

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española de D. Armesto Vilas . - [1a. ed. española] Madrid : Alhambra, 1983

- Chiara Chiron and Russell J. Thomas. Exercises in Synthetic Organic Chemistry. Oxford University Press, 1 st Ed, New York, 1997

**Recommended web-sites :** <http://www.organic-chemistry.org/>