COURSE DATA

Data Subject	
Code	44706
Name	Organic synthesis
Cycle	Master's degree
ECTS Credits	4.0
Academic year	2023 - 2024

Study (s)

Degree	Center	Acad. year	Period
2226 - Master's degree in Organic Chemistry	Faculty of Chemistry	1	Annual

Subject-matter

Degree	Subject-matter	Character
2226 - Master's degree in Organic Chemistry	2 - Organic synthesis	Obligatory

Coordination

Name	Department
DEL POZO LOSADA, CARLOS	325 - Organic Chemistry

SUMMARY

This course together with Advanced Organic Synthesis aims to cover the most relevant synthetic methods with a proper balance between the classic methodologies that are in force as effective methods for the preparation of organic compounds, and the new methods that have been incorporated into the baggage of the organic synthesis in recent decades.

In this sense, the most significant oxidation methods of various types of organic molecules are initially discussed, paying special attention, for their importance in organic synthesis, to alcohols and olefins. Both the classical oxidation methods and the most modern and current ones are incorporated in both the racemic and chiral version. The methods of reduction in both heterogeneous and homogeneous phase are approached in second place with the idea that the student acquires the widest possible knowledge in this important field both from an industrial and fundamentally academic point of view.

Radical chemistry is another key point that will be studied. A detailed knowledge of the reactions of abstraction and radical additions will allow the student to incorporate a different but significant aspect within the context of the current organic synthesis. The generation and reactions of carbenes and nitrenes will also be studied. Other aspects to consider is the use of protective groups. The incompatibility of functional groups in the synthesis of complex molecules has persisted over time. The use of protective groups partially solves most of these problems. In this section we will study the main protective groups and their usefulness in the synthesis of more complex molecules, especially considering their usefulness in the synthesis of peptides.

In the second part of the subject, the principles of retrosynthetic analysis are introduced as a fundamental tool in the design of organic synthesis. The C-X and C-C disconnections of one and two groups are developed, with special emphasis on the concepts of natural polarity and inverted polarity. The main synthetic methods of forming C-C bonds associated with the disconnections considered are developed

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

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

Other requirements

Essentials:
Essential requirements: basic knowledge of advanced Organic Chemistry and basic Organic Synthesis.

Recommended:
Recommended requirements: basic knowledge of Kinetics, Chemical Thermodynamics and pharmaceutical chemistry.

COMPETENCES (RD 1393/2007) // LEARNING OUTCOMES (RD 822/2021)

2226 - Master's degree in Organic Chemistry

- 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.
- Be able to access to information tools in other areas of knowledge and use them properly.
- 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.
- Poseer habilidades sociales, un buen nivel de comunicación oral y escrita, así como capacidad para trabajar en equipo y con personas de diferentes procedencias.
- Competencias de gestión tales como la capacidad para la planificación y gestión de tiempo y recursos, así como para dirigir y tomar decisiones.
- 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.
- Profundizar en el conocimiento de la síntesis orgánica.
- Conocer los métodos disponibles para la generación de los distintos tipos de enlaces así como para la interconversión de grupos funcionales.

LEARNING OUTCOMES (RD 1393/2007) // NO CONTENT (RD 822/2021)

The results to be achieved in this subject are summarized in the following points:

- That the student acquires the fundamental principles on which the organic synthesis is based.

- That the student knows the resources available for the generation of the different types of bond as well as for the interconversion of functional groups

- That the student knows the different protective groups and acquires criteria for their selection.

- That the student acquires an overview of the methodologies, their historical evolution and their adaptation to the new demands of today's society. In a more specific way: that you can use the knowledge acquired in the design of effective synthesis of products with added value.

- Replace toxic reagents with others that are less dangerous to human health and less polluting (SDG 3-health and well-being and SDG 6-clean water and sanitation).

- Design synthetic sequences according to the principles of green chemistry with the principles of energy saving, selectivity and atomic efficiency, decreasing waste production (SDG 12-production and responsible consumption).

- Select affordable starting products to turn them into high value-added products (SDG 9-industry, innovation and infrastructure and SDG 12-responsible production and consumption).

- Design syntheses that facilitate the recovery, reuse and recycling of chemical reagents and solvents avoiding their discharge into the atmosphere or water (SDG 12-responsible production and consumption).

DESCRIPTION OF CONTENTS

1. Oxidation in synthesis

Changes in the oxidation states of organic molecules: Concept of oxidation number. Oxidation of alcohols: Chromium and manganese reagents, oxidation with dimethyl sulfoxide via alkoxysulfonium salts, hypervalent iodine reagents, oxoammonium ions, Oppenauer oxidation. Oxidation of alkenes: Epoxidation with peracids, hydroperoxides and dioxyranos. Dihydroxylation of alkenes with osmium tetroxide. Oxidation of ketones: Baeyer-Villiger reaction. Allylic oxidation: selenium dioxide and chromic oxide. Biological oxidation methods

2. Reduction in Synthesis

Introduction. Homogeneous and heterogeneous catalytic hydrogenations of alkenes and other functional groups. Reduction with metals in solution: Birch reaction, reduction and reductive coupling of carbonyl compounds. Reductions with metal hydrides: Chemoselectivity in the reduction of carbonyl compounds. Meerwein-Pondorf-Verley reduction. Reductions through diacenes: Wolf-Kishner reaction, Shapiro reaction. Other reducing agents: Samarium iodide. Transfer of hydride of biological origin.

3. Radicals, carbenes and nitrenes

General aspects: Stability of radicals, characteristics of radical reactions. Methods of generating radicals. Radical substitution reactions: Halogenation, autooxidation, reductions with tributyltin hydride. Radical addition reactions: Radical hydrohalogenation of alkenes, addition of acyl radicals. Intramolecular H transfer reactions: Hoffman-Loefler reaction, nitrite photolysis (Barton reaction). Tandem and cascade radical reactions. Radical transposition and fragmentation reactions. Carbenes: electronic structure and generation of carbons. Cyclopropanation reactions. C-H bond insertion reactions. Wolf transposition. Nitrenes: electronic structure and generation of nitrenes. Nitrite addition and insertion reactions. Reactions through electron deficient nitrogen: Curtius transposition, Hofmann transposition, Beckmann transposition.

4. Protecting groups

Characteristics of the protective groups. Methods of protection / deprotection of functional groups. Orthogonal protection. Temporary protection. Protective groups in peptide synthesis

5. Retrosynthetic analysis. C-X disconnections

Basic concepts: Disconnection, interconversion of functional groups, synthon, reagent. Disconnections in aromatic compounds: the order of events. C-X disconnections of a group: in alcohols and derivatives, in carboxylic acids and derivatives. C-X disconnections of two groups: Compounds 1,3-, 1,2 and 1,1-difunctionalized

6. One-group C-C disconnections.

1,1- Disconnections : synthesis of alcohols and synthesis of carbonyl compounds. 1,2- disconnections: Synthesis of alcohols and synthesis of carbonyl compounds. 1,3- disconnections: synthesis of carbonyl compounds

7. Two groups C-C disconnections: Odd relations

Disconnections in 1,3-difunctionalized compounds: -hydroxycarbonyl compounds and 1,3-dicarbonyl compounds. Disconnections in 1,5-dicarbonyl compounds

8. Two groups C-C disconnections: Even relations

Disconnections in 1,2-difunctionalized compounds. Disconnections in 1,4-difunctionalized compounds. Disconnections in 1,6-difunctionalized compounds. Reconnection

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	20,00	100
Seminars	20,00	100
Study and independent work	40,00	0
Preparation of evaluation activities	10,00	0
Preparation of practical classes and problem	10,00	0
TOTAL	**100,00**	

TEACHING METHODOLOGY

The subject is structured as follows:

• Theoretical classes (face-to-face) .- The classes will be devoted to discussing with students the most complicated aspects or those in which they had more difficulty in the previous study of the material provided. These classes are complemented by study time and autonomous work.

• Problem classes.- In these classes the specific application of the knowledge that students have acquired in the theory classes will be carried out. Students must have previously worked on the problems that are going to be solved. The resolution of these problems will be carried out alternately by the teacher or by the students, either in a group, or individually.

• Works.- An additional possibility, which will be optionally carried out by the teacher, will be the realization of a work related to any of the themes of the program and described in a scientific publication

EVALUATION

The evaluation of the subject will be carried out continuously by the teacher throughout the course and will consist of the following sections.

- **Direct teacher evaluation**. 15% of the mark will come from the direct evaluation of the teacher in the theoretical and problem classes and in the tutorials. In this evaluation, different aspects will be taken into account, including:

- Assistance and reasoned and clear participation in the discussions.

-Resolution of problems and questioning.

-Critical spirit.

-Delivery of exercises or works.

- **Evaluation of the work done by the student**. Both the content and the form will be taken into account. This section will correspond to 25% of the final grade.

- **Exams and written tests**. 60% of the mark will be obtained from the results of the written tests.

- Face-to-face exams of traditional style, both theoretical and problem issues, and content related to the subject. These questions and problems will be of such a nature that they force the student to relate different aspects that appear in different subjects of the subject or also, if the teacher considers it appropriate, in different subjects of the subject.

- Non-face-to-face exams in which the teacher delivers directly, or sends by email, a series of questions that must be resolved by the students, either individually or in groups, at the discretion of the teacher. The student / group must send the answers to the teacher through the same channel mentioned above and within the period established by the teacher.

REFERENCES

Basic

- Organic Chemistry . Clayden, J., Greeves, N., Warren, S., Wothers, P. Oxford University Press, Oxford, 2000
- Advanced Organic Chemistry: Part B: Reaction and Synthesis Carey, F. A.; Sundberg, R. J. 5th edition, 2008.
- Modern Methods of Organic Synthesis. Carruthers, W.; Coldham, I. Cambridge University Press. 2004.
- Organic Synthesis. The Disconnection Approach. Warren, S., Wyatt, P., 2nd edition, 2008, Wiley

Additional

- Protective Groups, Kociensky, P.J. Georg Thieme Verlag Sttutgart New York 2000
- Síntesis Totales. Retrosíntesis y Mecanismos. Carda, M., Falomir, E., Universitat Jaume I, Castellón, 2008.
- The Logic of Chemical Synthesis. Corey, E. J., Wiley, New York, 1989.