COURSE GUIDE
ORGANIC SYNTHESIS

1. DETAILS OF THE COURSE

1.1. Name: Organic Synthesis		
1.2 Code: 5093217	**1.3 .Plan:** Chemistry degree (2009)	**1.4.Level:** Degree
1.5 Course: 3	**1.6. Type:** Obligatory	**1.7. Semester:** 1st semester
1.9. ECTS: 9	**1.9.1.Theoretical:** 6	**1.9.2.Practical:** 3
1.10. Descriptors: Organic Synthesis, Advanced Organic Chemistry		

2. LECTURER

2.1. Name: Rodríguez García, Ignacio Manuel		
2.2. Department: Chemistry and Physics		
2.3. Field of Knowledge: Organic Chemistry		
2.4. Office: CITE I room 0.300		
2.6. Mentoring:		
2.6.1. 1st Semester: Tuesday 09:30-11:00 17:00-18:30 h Wednesday 17:00-18:30 h Thursday 12:00-13:30 h		**2.6.2. 2nd Semester:** Tuesday 17:00 - 19:00 h Wednesday 17:00 - 19:00 h Thursday 17:00 - 19:00 h
2.7. Phone: 950 015610	**2.8. E-Mail:** irodrigu@ual.es	**2.9. Virtual platform WEB CT:** Organic Synthesis Course Information Blackboard Learn
2.10. Personal Webpage: Rodríguez García		

3. DATA OF THE DEPARTMENT

3.1. Name: Chemistry and Physics			
3.2. Fields of Knowledge of the Department: Chemistry, Physics			
3.3. Director: Rodríguez Fernandez-Alba, Amadeo			
3.3.1. Office: CITE I-1.190	**3.3.2.Phone:** +34 950 015034	**3.3.3.E-Mail:** amadeo@ual.es	
3. 4. Head of Administration: Rodriguez Fuentes, Ana María			
3.4.1. Office: CITE I-2.190	**3.4.2. Phone:** +34 950 015008	**3.4.3 Fax:**	**3.4.4.E-Mail:** arodrif@ual.es

4. CONTEXT

4.1. Main objective of the course:

Organic Synthesis is one of the most powerful tool available to our civilization for the preparation of new products. The ability to make drugs, pesticides, flavorings, preservatives, plastics, insulation, textiles, paints, dyes, etc. is the result of the design and subsequent implementation by synthetic organic chemists of a series of techniques based on adequate organic chemistry reactions. This course provides an overview of the current issues and solutions, ranging from the initial rational approach to the ultimate preparation and structural design. The main objectives are:

- The understanding of the basic principles of the retrosynthetic analysis.
- The knowledge of the general methods of protection of functional groups.
- The knowledge of the main strategies of asymmetric synthesis.
- Expanding the knowledge on reactivity in organic chemistry.

These objectives can be achieved by the study of the tools for synthesis and retrosynthesis and also by solving exercises in synthesis, starting with simple cases which will progressively increase in complexity.

4.2 Previous knowledge:

The course “Organic Synthesis”, a part of the “Organic Chemistry” matter of the Fundamental Module of the Degree in Chemistry is a compulsory 9 ECTS course, 3 of which correspond to "Experimental laboratory in Organic Chemistry". The pillars of this course are the Organic Chemistry I and Organic Chemistry II also included within that matter of Organic Chemistry of the Fundamental Module and taught in the second year of the Degree. On the other hand, the Organic Synthesis is the logical basis for further courses of this matter: Enhancement of Organic Chemistry, 6 ECTS, taught in the second semester of the third year and Experimentation in Organic Chemistry, 6 ECTS, taught in the fourth year. Furthermore, a feature of modern Organic Chemistry is its interaction with other traditional areas of chemistry and other disciplines (medicine, biochemistry, materials science, etc.). Therefore, there is a close relationship between this course and other branches of chemistry as well as Biochemistry, Biological Chemistry and Materials Science. Finally, the synthesis of organic compounds at industrial level links with the matter of Chemical Engineering included in the Basic module of the Grade.

4.3. Prior conditions:

To address properly this subject is essential to have achieved a positive assessment of the competencies acquired in the courses “Organic Chemistry I” and “Organic Chemistry II”.
All the recommended bibliography or reading is mostly in English.

5. COMPETENCIES AND OBJECTIVES

5.1 COMPETENCIES OF THE COURSE

5.1.1. GENERAL COMPETENCIES:

- Knowledge of a second language.
- Ability of criticism and self-criticism.
- Ability to learn how to work independently.
- Ability for management and planning.

5.1.2. SPECIFIC COMPETENCIES:

- C11 Properties of aliphatic, aromatic, heterocyclic and organometallic compounds.
- C13. The main synthetic routes in organic chemistry, including the interconversion functional groups and the formation of carbon-carbon and carbon-heteroatom bonds.
- Q3. Competency to assess, explain and summarize data and chemical information.
- Q6. Skill in handling and processing computer data and chemical information
- P3. Ability for observation, monitoring and measurement of properties, events or chemical changes, and the systematic and reliable recording of documentation.
- P4. Ability to handle standard chemical instrumentation, like that used for structural elucidations and chemical separations.
- P5. Interpretation of data from observations and measurements in the laboratory in terms of its significance and the scientific theories.

5.2 GENERAL OBJECTIVES OF THE COURSE

Each student who has passed the subject of Organic Synthesis will be able, at the level of the third year in the Degree in Chemistry, to perform the following tasks:

- To plan the preparation of reports and the study time and to self-organize in a chemical laboratory to carry out the relevant experience within a reasonable time and in an efficient way.
- To conduct a comprehensive reading of scientific texts in a foreign language.
- To interpret data derived from observation and establish links with appropriate theories. Accurately identify both the fundamental and the superfluous elements in a written report or an oral presentation, either from mate students or its own.
- To organize the work and time, to meet deadlines; to prepare classes; to organize the study time. To have autonomous access to relevant information sources. To search and summarize basic bibliographical sources related to chemistry.
- To predict some fundamental properties of aliphatic, aromatic and organometallic compounds. To be able to reason the reactivity of aliphatic, aromatic and organometallic compounds. To know and justify the inorganic properties of organometallic compounds.

- To analyze what reagents would be able to react with an organic molecule on the basis of its constitution and the way they would react. To propose transformations of functional groups according to their reactivity. To propose simple synthesis of organic compounds by sequences of functional group transformations.
- To correlate the reactivity of multifunctional molecules with that of the functional groups within them. To evaluate, interpret and summarize chemical data obtained in an experimental laboratory in chemistry. To evaluate, interpret and summarize data and information obtained from different sources on chemical aspects.
- To handle chemical databases. To select information for the resolution of specific chemical problems. To prepare reports based on the results of the treatment of chemical information with the appropriate software.
- To develop protocols for the recording of data, which will guarantee the reproducibility of an experiment, conducted in the laboratory. To correlate the observed changes in the course of an experiment with the obtained results. To be able to carry out observation, monitoring and measurement of properties or chemical and / or physical changes in a certain material or reaction.
- To interpret the data obtained at the different stages of the experiments. To explain any differences between the results experimentally obtained and those expected. To prepare reports of the results with scientific rigour and conciseness.

In short, at a more specific level, the student will be able to:

- Design its own synthesis, properly planning all the phases involved in the synthetic design.
- Perform synthesis in the laboratory using conventional techniques for chemical separation, purification and structural elucidation of compounds.
- Analyze and evaluate the results obtained when performing synthesis in the laboratory, ant to propose, if necessary, the appropriate improvements.

6. CONTENTS

6.1. THEORETICAL CONTENTS:

MODULE I: SYNTHETIC DESIGN TOOLBOX

Chapter 1. Synthetic Design

- Methodology of the retrosynthetic analysis.
- Types of transformations.
- General Strategy of the retrosynthetic analysis.
- Types of synthesis.
- Inversion of the polarity of the carbonyl group (umpolung).
- Domino reactions.

Chapter 2. Stereochemical considerations of the synthetic design

- Chiral molecules with one stereogenic center.
- Chirality without stereogenic carbon.
- Chiral molecules with two or more stereogenic centers.
- Separation of enantiomers.
- Stereochemistry of the C=C and C=N double bonds.
- Stereoisomerism in cyclic structures.
- Prochirality, homotopic, enantiotopic and diastereotopic groups and faces.
- Stereochemical classification of the reactions.
- Strain and molecular mechanics.
- Conformation of acyclic molecules.
- Conformation of cyclic molecules.
- Anomeric effect.

Chapter 3. Protecting groups in organic synthesis

- Concept and characteristics of protecting groups.
- Protection of the hydroxyl group.
- Protection of the carbonyl group.
- Protection of diols.
- Protection of carboxylic acids.
- Protection of the amino group.
- Protection of multiple bonds.

MODULE II: FUNCTIONAL GROUP MANIPULATION TOOLBOX

Chapter 4. Reactivity of π-carbon-carbon bonds

- Oxymercuration-reduction.
- Hydroboration.
- Epoxidation and azidirination.
- Dihydroxylation.
- Degradation of C=C double bonds.
- Palladium-catalysed oxidation of alkenes.

Chapter 5. Oxidation

- Oxidation of alcohols.
- Allylic oxidation of alkenes.
- Oxidation of ketones and aldehydes.

Chapter 6. Reduction

- Catalytic hydrogenation.
- Reduction by dissolving metals.
- Group III hydride-transfer reagents.
- Reductions with soluble metals.
- Reductive deoxygenation of carbonyl compounds.

MODULE III: C-C BOND FORMATION TOOLBOX

Chapter 7. Formation of carbon-carbon bonds via enolates

- Generation of carbanions by deprotonation.
- Regioselectivity and stereoselectivity in the formation of enolates.
- Alkylation of enolates.
- Generation and alkylation of dianions.
- Influence of the solvent in the alkylation of enolates.
- Oxygen versus carbon alkylation.
- Alkylation of carbon nucleophiles by conjugate addition.
- Aldol addition and related reactions.
- Nitrogen analogs of enols and enolates.
- Addition reactions to imines and iminium ions.
- Acylation of carbanions.

Chapter 8. Pericyclic reactions

- The Diels-Alder cycloaddition reaction.
- 1,3-Dipolar cycloaddition reactions.
- [3,3]-Sigmatropic rearrangements.
- [3,2]-Sigmatropic rearrangements.

Chapter 9. Formation of carbon-carbon π-bonds

- β-elimination reactions.
- Pyrolytic *syn*-eliminations.
- Synthesis of alkenes from hydrazones.
- Stereodefined synthesis of alkenes from alkynes.
- The Wittig and related reactions.
- Alkene metathesis.

Chapter 10. Formation of carbon-carbon bonds via organometallic reagents

- Preparation and properties of organomagnesium and organolithium reagents.
- Reactivity of organomagnesium and organolithium reagents.
- Organozincates.
- Copper organometallic intermediates.
- Reactions with palladium organometallic intermediates.
- Alkene metathesis.

6.2. PRACTICAL CONTENTS:

MODULE IV. LABORATORY EXPERIMENTAL TECHNIQUES

Organic synthetic reactions

- Setting the reaction: use of the scale and volumetric measurement devices.
- Stoichiometric calculations.
- Monitoring the reaction. Thin layer chromatography.
- Work-up of the reaction. Calculations on the crude weight.

Isolation and purification of the product of an organic synthetic reaction

- Liquid liquid extraction.
- Gravity filtration.
- Filtration under reduced pressure.
- Crystallization.
- Distillation.
- Evaporation of solvent in the rotatory evaporator.

Interpretation of the results of a reaction

- Calculation of the yield of the reaction.
- Reaction product characterization: spectroscopy, melting point, boiling point.

7. METHODOLOGY

7.1 Methodology for the treatment of the theoretical contents :

The THEORY GROUP classes are always interactive lessons, in which the lecturer presents the subject with the aid of audiovisual materials, and at the same time, opens the door to the participation of the students in order to enrich the lecture. In this way, the students are randomly requested to answer the questions thrown by the lecturer or by addressing their own questions to the lecturer or to their own fellow mates. Theoretical-type contents are always followed by practical examples.

7.2 Methodology for the treatment of practical content:

There are two types of PRACTICE GROUP classes, those addressed to the practice of problem solving which take place in the classroom and those addressed to practice experimental skills, which take place in the laboratory.

There are collections of problems available in the course web page. At the conclusion of each Theory Group session, the lecturer will specify the problems that must be solved to exercise the contents exposed in that class. An independent work of the problems in advance to the CLASROOM PRACTICE GROUP class designed for their solution is critical for the successful learning of the student. Acquiring the skills to solve problems can only be achieved by the student work prior to the discussion in groups or with the lecturer.

During the Classroom Practice Group class, the teacher will solve only some of the most challenging exercises, allowing the students to make a public resolution of some exercises of their own choice. Alternatively, work groups of three or four people will be organized with the aim of doing some group work for the resolution of exercises or sharing solution proposals.

The aim of the LABORATORY PRACTICE GROUP classes is to obtain a good training in the practice of experimental techniques. In advance of the laboratory session, students should study the experiments and techniques to be developed through the information provided at the course webpage, in addition to the use of specific literature. At the beginning of the laboratory session, the student must present the lecturer a schematic summary of the tasks to be performed that day. This scheme will not be marked by the lecturer, but failing to provide it will prevent from any practical work during the lab session. A laboratory notebook (the *lab book*) must be fulfilled, following the indicated guidelines, while the experiment is being developed. Later, as homework, the students will answer in writing a series of questions related to the experiment, answers that will be handed to the teacher at the beginning of the next laboratory session. At the conclusion of the period of laboratory practice classes, the complete lab book will be delivered to the lecturer.

7.3 Innovation in education activities

Links to animations of the main reaction mechanisms presented in the theory group classes are available in the course web page. These are interactive animations, whose visualization is highly illustrative of the process from a three-dimensional point of view.

Video-tutorials illustrating the different experimental techniques that will be developed in the laboratory are also available in the course web page. It is important to visualize these videos before doing any experimental work in order to get a more close idea on haw to do the experimental work.

7.3 Workload of the student (calculated by number of hours)

WORKING HOURS OF THE STUDENT

7.3.1. IN-CLASS HOURS (with professor)

TEACHING ACTIVITY		NO. HOURS	NO. OF GROUPS	TEACHING HOURS (in ECTS)
CLASS of theory (THEORY GROUP ACCORDING TO OD)		26.0		
CLASS OF PRACTICAL TRAINING (PRACTICE GROUPS ACCORDING TO OD)	Laboratory	22.5		
	Problems	19.0		
	Informatics			
	Field			
	Other			
OTHER TEACHING ACTIVITIES	Seminars			
	Group Tutoring			
	Other			
SUBTOTAL IN-CLASS HOURS		67.5		
HOURS FOR TESTS AND EXAMS		4.0		

7.3.2 . AUTONOMOUS WORKING HOURS (not in-class, estimated)

HOURS OF PREPARATION FOR ACTIVITIES AND WORK (theory)	84.0		
HOURS OF PREPARATION FOR ACTIVITIES AND WORK (practice)	42.0		
HOURS OF STUDY FOR TESTS AND EXAMS	31.5		
OTHER			
SUBTOTAL AUTONOMOUS WORKING HOURS	*157.5*		
TOTAL WORKING HOURS		***STUDENT***	***TEACHER***
		225	

8. BIBLIOGRAPHY OF THE COURSE

8.1 Mandatory Reading:

1. *Modern Organic Synthesis: An Introduction* 2nd Ed. G.S. Zweifel, M.H. Nantz, P. Somfai; John Wiley & Sons Inc. Hoboken, 2017.
2. *Stereochemistry* D.G. Morris; Wiley-Royal Society of Chemistry, Cambridge, 2001.
3. *Modern methods of organic synthesis* 4th Ed. W. Carruthers, I. Coldham; Ed. Cambridge University Press, Cambridge, 2004.
4. *Advanced Organic Chemistry Part B: Reaction and Synthesis* 5th Ed. R.J. Sundberg, F.A. Carey; Ed. Springer, New York, 2007.
5. *Organic chemistry: an intermediate text* R. V. Hoffman. Wiley Interscience, Hoboken, New Jersey, 2004.
6. *Síntesis orgánica* J.L. Borrel, J. Teixidó, J.L. Falcó; Síntesis, Madrid, 1999.
7. *Experimental organic chemistry* 3rd Ed. P. B. Cranwell, L. M. Harwood, C. J. Moody; John Wiley & Sons Inc. Hoboken, 2017.

8.2 Recommended Reading:

1. *Advanced Organic Chemistry Part A: Structure and Mechanism.* 5th Ed. R.J. Sundberg, F.A. Carey; Ed. Springer, New York, 2007.
2. *March's advanced organic chemistry: reactions, mechanisms, and structure* 7th Ed. M.B. Smith; John Wiley & Sons, Hoboken, 2013.
3. *Organic synthesis - Strategy and Control* P. Wyatt, S. Warren; Wiley, Chichester, 2007.
4. *Organic synthesis: The disconnection approach* 2nd Ed. S. Warren; Wiley & Sons, London, 2008.
5. *Organic Synthetic Methods* J. R. Hanson; Royal Society of Chemistry, Cambridge, 2002.
6. *Name Reactions: A Collection of Detailed Reaction Mechanisms* J.J. Li; Ed. Springer (5ª Ed.), Berlin, 2014.
7. *Strategic applications of Named Reactions in Organic Synthesis* L. Kürti, B. Czakó; Ed. Elsevier, Burlington, 2005.
8. *Solutions manual for Modern organic synthesis: an introduction* M. H. Nantz, H. Palandoken; Ed. Freeman, New York, 2006.
9. *Síntesis orgánica: resolución de problemas por el método de la desconexión* M. Cardá; Ed. Publicacions de la Universitat Jaume I, Castelló de la Plana, 1996.
10. *Técnicas experimentales en síntesis orgánica* M. A. Martínez Grau, A. G. Csákÿ; Ed. Síntesis, Madrid, 1998.
11. *Organic Synthesis*. M. Smith; 4th Ed. Academic Press, New York, 2011.

1.3 Web addresses:

http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/intro1.htm
(Virtual Textbook of Organic Chemistry)

9 EVALUATION SYSTEM

9.1 Aspects and/or criteria:

This course has two alternative of evaluation systems: a continuous evaluation system or a single examination system.

9.2 Modalities and instruments:

Assessment instruments

- Progress report.
- Tests, exercises, problems.
- Observations of the process.
- Final assessment of reports, works and projects.
- Final tests (whether written or oral).

Monitoring mechanisms:

- Attendance to tutorials.
- Attendance and participation in seminars.
- Access to the virtual platform.
- Participation in communication tools (e mails, discussion forums).
- Submitting classroom activities.
- Submitting of tutorial activities.
- Submitting of virtual platform activities.

9.3 Marking system:

CONTINUOUS EVALUATION SYSTEM: The student must carry out the activities proposed by the lecturer, actively participating in them. The activities to be evaluated are listed below along with the weighting used for the rating:

Part A. Blocks I to III. Organic Synthesis toolbox.

This part deals with the general competencies "Ability to learn how to work independently", as well as specific competencies "Properties of aliphatic, aromatic, heterocyclic and organometallic compounds" and "The main synthetic routes in organic chemistry, including the interconversion functional groups and the formation of carbon-carbon and carbon-heteroatom bonds". Their assessment is carried out considering:

- Student participation in classes, seminars and tutorials: 10%
- Regular checks: 50%
- Final examination to be held on the date set by the Faculty of Experimental Sciences in the February call (a minimum rating of 4 is required): 40%

Part B. Block IV. LABORATORY EXPERIMENTAL TECHNIQUES.

In addition to the student autonomous work, the activities of this section are developed in the laboratory, being mandatory the attendance to all sessions. In this part the general competencies "Knowledge of a second language", "Ability of criticism and self-criticism " and "Ability for management and planning" as well as the specific competencies "Competency to assess, explain and summarize data and chemical information", "Skill in handling and processing computer data and chemical information", "Ability for observation, monitoring and measurement of properties, events or chemical changes, and the systematic and reliable recording of documentation", "Ability to handle standard chemical instrumentation, like that used for structural elucidations and chemical separations" and "Interpretation of data from observations and measurements in the laboratory in terms of its significance and the scientific theories" Their assessment is carried out considering:

- Work in the laboratory: 30%
- Laboratory notebook and results report: 40%
- Questions to be solved in autonomous working hours: 30%

To pass the course, a minimum grade of 5 out of 10 in each of the two sections, A and B is required. The final grade will be the result of the following weighting: Part A 75% and Part B 25%

SINGLE EXAMINATION SYSTEM.

It will be applied in all extraordinary and ordinary calls for those students who do not benefit from continuous assessment. It will consist of a written exam on the date fixed by the Faculty of Experimental Sciences.