



# **Master in Chemical Research and Industrial Chemistry**

**NATURAL PRODUCTS CHEMISTRY**

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## **Course Guide**

2014-15

# Course Guide

## *1. Subject Description*

**Character:** Optative

**Call:** First quarter

**Credits:** 3 ECTS

### **Teaching staff:**

#### **Carlos Jiménez González**

Professor in Organic Chemistry  
Departamento de Química Fundamental,  
Facultad de Ciencias.  
Universidade da Coruña  
Lectures and tutorials

#### **Jaime Rodríguez González**

Associate Professor in Organic Chemistry  
Departamento de Química Fundamental,  
Facultad de Ciencias  
Universidade da Coruña  
Seminars

#### **Angel Rodríguez de Lera**

Professor in Organic Chemistry  
Departamento de Química Orgánica,  
Facultad de Química  
Universidade de Vigo  
Seminars and tutorials

#### **Emilio Quiñoá Cabana**

Professor in Organic Chemistry  
Departamento de Química Orgánica,

Facultad de Química

Universidade de Santiago de Compostela

Seminars and tutorials

**Language:** Spanish or English

## ***2. Status, meaning and importance of the subject in the Master degree.***

### **2.1. Module to which the subject belongs in the Master. Related subjects.**

Module 2: "*Chemical Biology*". It is mainly related to the subjects of this module.

### **2.2. Role of this subject in this module and in the Master**

This material is intended for students to acquire a thorough understanding of the Natural Products Chemistry. It starts from their applications, mainly at pharmacological level, following by the importance of their study and then, their classification from the biogenetic point of view. In order to do this, it will display the most important biogenetic routes from which originate the most abundant skeletons. Some modern techniques used today to accelerate their isolation and identification along with the use of genetic studies on new biotechnological strategies in their production is also seen.

### **2.3. Prior knowledge (recommended/required) that students must have to study the subject**

It is recommended to have previously completed the subject "Chemistry of Biomolecules".

## ***3. Learning objectives and skills to be achieved by the student with the subject***

### **3.1. Learning objectives.**

- Acquisition of advanced knowledge in the chemistry of Natural Products, from both terrestrial and marine origin.
- Learning of the most important applications, mainly as drugs and as tools in biomedical research.
- Learning of the main biogenetic routes and the main metabolites that originate.
- Learning of the modern techniques used for their isolation and identification

### **3.2. General skills.**

- Identify information from scientific literature by using appropriate channels and integrate such information to raise and contextualize a research topic
- Use the scientific terminology in English to explain the experimental results in the context of the chemical profession
- Apply correctly the new technologies of gathering and organization of the information to solve problems in the professional activity.

- The students should be able to communicate their conclusions, and the knowledge and the reasons that support them to specialists and non-specialists in a clear and unambiguous manner
- The students should apply their knowledge and ability to solve problems in new or unfamiliar environments within broader (or multidisciplinary) contexts related to their field of study.

### **3.3. Specific skills**

- Define concepts, principles, theories and specialized facts of natural products.
- Propose alternatives for solving chemical problems related to the behavior of the most important natural product.
- Apply materials and biomolecules in innovative fields of industry and chemical engineering.
- Innovate in the methods of synthesis and chemical analysis of natural products.
- Understand the chemical basis of biological processes.
- Promoting innovation and entrepreneurship in the chemical industry and in research.

### **3.4. Transversal skills**

## • 4. Contents

### 4.1. Sections

**CHAPTER 1.** Introduction to the study of natural products.

**CHAPTER 2.** Main metabolic pathways of the secondary metabolism.

**CHAPTER 3.** Metabolites derived from acetate: poliketides, fatty acids and related compounds.

**CHAPTER 4.** Metabolites derived from mevalonate: terpenes and steroids.

**CHAPTER 5.** Metabolites derived from shikimic acid.

**CHAPTER 6.** Nitrogenated natural compounds.

**CHAPTER 7.** Modern strategies for the isolation and elucidation of natural products.

### 4.2. Recommended bibliography

#### 4.2.1. Basic.

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed.", (2012) Oxford, University Press, New York.

J. Alberto Marco, "Química de los productos naturales" (2006). 1st Ed. Ed. Síntesis, Madrid.

Pilar Gil Ruiz "Productos naturales" (2002), 1st Edición. Ed. Universidad Pública de Navarra.

#### 4.2.2. Complementary.

S. D. Sarker, L. Nahar "Natural Products Isolation" (2012), 3rd Ed., Ed. Human Press, New Jersey.

J. Mann, "Secondary Metabolism" (1992), 2nd Ed. Ed. Oxford Science Publications, Oxford.

Richard B. Herbert, "The biosynthesis of secondary metabolites" (1989), 2nd Edición. Ed. Chapman and Hall, London.

Ana M. Lobo, Ana M. Lourenco, "Biossíntese de productos naturais" (2007), IST Press, Lisboa.

Paul M. Dewick, "Medicinal Natural Products. A Biosynthetic Approach", (2009) 3<sup>rd</sup>. ed., Ed. Wiley, Wiltshire.

## CHAPTER 1. Introduction to the study of natural products.

### 1. Introducción

The concept of **natural product** and its relationship to secondary metabolite will be defined. The main sources of obtaining natural products and their numerous applications that justify their study will be described. Special emphasis will be on its **pharmacological application**, mainly as the drugs because most of recently approved drugs have a direct or indirect relationship with a natural product. **Illustrative examples** of various natural products is described.

### 2. Contents

Concepts of natural product and secondary metabolite. Main natural sources. Main applications. Importance of natural products in the pharmaceutical industry. Classification and examples.

### 3. Bibliography

J. Alberto Marco, "**Química de los productos naturales**" (2006). 1st Ed. Ed. Síntesis, Madrid Chapter 1, pages 14-15.

Pilar Gil Ruiz "**Productos naturales**" (2002), 1st Edición. Ed. Universidad Pública de Navarra.

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed.", (2012) Oxford, University Press, New York.  
Chapter 51 pages 1413-1415.

Carlos Jiménez "**El papel de los productos naturales en el mercado farmacéutico actual**" Anales de Química **2013**, *109*, 134-141.

### 4. Activities

## CHAPTER 2. Main metabolic pathways of the secondary metabolism.

### 1. Introduction

This chapter describes the **general scheme of secondary metabolism** leading to the main types of natural products that allow classifying them according to the biogenetic route from which will be displayed. The mechanisms that take place at the biological level will be discussed in detail and the main strategies used to study a metabolic pathway will be shown.

### 2. Contents

General scheme of secondary metabolism, main types of natural products that originate and classification based on metabolic pathways. Main mechanisms of biological pathways. Methods of elucidation of a metabolic route.

### 3. Bibliography

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed.", (2012) Oxford, University Press, New York  
Chapter 50 pages 1381-1412.

J. Alberto Marco, "**Química de los productos naturales**" (2006). 1st Ed. Ed. Síntesis, Madrid Chapter 2, pages 27-59.

J. Mann, "**Secondary Metabolism**" (1992), 2nd Ed. Ed. Oxford Science Publications, Oxford.  
Chapter 1 pages 6-23.

#### 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

### CHAPTER 3. Metabolites derived from acetate: poliketides, fatty acids and related compounds.

#### 1. Introduction

This chapter will be focused to natural products derived from acetate which are using acetyl coenzyme A as a starting. **Polyketides, fatty acids** and **related compounds** will be studied more specifically, many of them are derived from malonyl CoA. Major metabolic biosynthetic routes will be addressed which will be illustrated with the most relevant examples.

#### 2. Contents

Metabolites derived from acetate: poliketides, fatty acids and related compounds.

#### 3. Bibliography

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed. (2012) Oxford, University Press, New York.  
Chapter 51 pages 1425-1447.

J. Alberto Marco, "**Química de los productos naturales**" (2006). 1st Ed. Ed. Síntesis, Madrid  
Chapter 3, pages 61-126.

#### 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

### CHAPTER 4. Metabolites derived from mevalonate: terpenes and steroids.

#### 1. Introduction

Natural products from acetyl coenzyme A but with a common intermediate the mevalonate CoA will be displayed: **terpenes** and **steroids**. Major routes of training which will be illustrated with examples will be most relevant for each.

## 2. Contents

Metabolites derived from mevalonate: terpenes and steroids.

## 3. Bibliography

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed. (2012) Oxford, University Press, New York.  
Chapter 51 pages 1425-1447.

J. Alberto Marco, "**Química de los productos naturales**" (2006). 1st Ed. Ed. Síntesis, Madrid  
Chapter 5, pages 171-233.

## 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

## CHAPTER 5. Metabolites derived from shikimic acid.

### 1. Introduction

The study of those natural products which have intermediate shikimic acid in common as starting material will be addressed. **Phenylpropanoids** and **flavonoids** will be studied as the main natural products where the shikimic acid is the precursor.

### 2. Contents

Biosynthetic origin of shikimic acid. Phenylpropanoids. Metabolites of mixed origin: Flavonoids.

### 3. Bibliography

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed. (2012) Oxford, University Press, New York.  
Chapter. 51 pages 1425-1447.

J. Alberto Marco, "**Química de los productos naturales**" (2006). 1st Ed. Ed. Síntesis, Madrid  
Chapter 4, pages 127-169.

Edwin Haslam, "**Shikimic Acid: Metabolism and Metabolites**" (1993), John Wiley & Sons, Chichester.

### 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

## CHAPTER 6. Natural nitrogenous compounds.

### 1. Introduction

A wide range of natural products are the nitrogenous compounds, mainly alkaloids, which have in common certain amino acid as precursors. Hence most of them are grouped according to the precursor amino acids: many aliphatic alkaloids derived primarily from the lysine and ornithine, while many aromatic alkaloids are considered derivatives of phenylalanine / tyrosine and tryptophan. Other nitrogenous compounds of diverse natural origin will be also shown.

### 2. Contents

Aliphatic alkaloids: derivates from lysine and ornithine. Aromatic alkaloids: derivates from phenylalanine/tyrosine and tryptophan. Other estructural frameworks. Biosynthesis of non ribosomal peptides.

### 3. Bibliography

Jonathan Clayden, Nick Greeves, Stuart Warren "Organic Chemistry 2nd. Ed. (2012) Oxford, University Press, New York.  
Chapter 51 pages 1414-1425.

J. Alberto Marco, "Química de los productos naturales" (2006). 1st Ed. Ed. Síntesis, Madrid  
Chapter 4, pages 236-275.

### 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

## CHAPTER 7. Modernas estrategias de aislamiento e identificación

### 1. Introduction

Once the main types of natural products were studied, we will proceed to know in detail the methods used for isolation and identification. It will start for the traditional methods for isolation and identification to follow by the most modern strategies used today to accelerate this process, (dereplication techniques). The advances on genetic studies are allowing not only predict in some cases the natural products they produce but also perform transformations on them.

### 2. Contents

Traditional methods. Dereplication techniques. Biotechnology strategies based on genetic studies: Genome mining, recombinant biosynthesis and combinatorial biosynthesis.

### 3. Bibliography

S. D. Sarker, L. Nahar "Natural Products Isolation" (2012), 3rd Ed., Ed. Human Press, New Jersey.

### 4. Activities

The student will have to perform the exercises related to the chapter indicated by the teacher and deliver them on the date indicated on the calendar of activities of the subject (the student should keep a copy of submitted work). During the seminar, students will solve these exercises on the blackboard.

Those students who have particular difficulty with the exercises performed in this area should contact the hours of tutoring with the teacher to receive the necessary support.

## 5. - Methodological guidelines and ECTS credits assignment.

### 5.1. ECTS credits assignment.

CLASSROOM WORK	HOURS	PERSONAL WORK	HOURS
Lectures in large groups	12	independent, individual or in a group study	29
Interactive class in small groups (Seminars)	7	Oral presentation of papers and exercises proposed by the teacher	21
Interactive class in very reduced groups (Tutorials)	2	Preparation of oral presentations, resolution of proposed exercises. Library work or similar.	4
<b>Total classroom work hours</b>	<b>21</b>	<b>Total personal work hours</b>	<b>54</b>
<b>Total hours</b>			<b>75</b>

### 5.2. Training activities in the classroom

A) *Lectures in large groups* ("L" in the timetable): It will be held 12 sessions of lectures in one group where the theoretical contents of the course will be associated with illustrative examples. It will consist mainly in PowerPoint presentations. Copies of these presentations will be available for the students in advance via the virtual campus of the course. This will allow the students to study ahead the contents of the course and to facilitate the monitoring of explanations.

B) *Interactive class in small groups (Seminars, "S" in the timetable)*: 7 sessions in small group seminars where students will present the work proposed by the professor followed by a discussion section. Students will have in advance the proposed exercises and papers via the virtual campus of the course. Attendance at these classes is mandatory.

D) *Interactive class in very reduced groups (Tutorials, "T" in the timetable)*: Tutoring scheduled by the professor and coordinated by the Centre. It will be 2 hours per student and will involve the supervision of proposed work, clarifying doubts, etc. Attendance at these classes is mandatory.

### 5.3. Recommendations for the study of the course

- Lecture attendance is more than recommended.

- It is essential to keep the study of course up to date.
- After the reading of a chapter in the reference manual, it is useful to summarize the key points (see summary of important concepts in the Reference Manual).
- Reading the specific biography for each chapter is encouraged for a better understanding of the key concepts.



12-13							
13-14							
16-20							

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## 6. Evaluation

### 6.1. Evaluation procedure

The evaluation of this course will be done by means of the continuous assessment and completion of a final exam. Access to the exam will be conditioned on the participation in at least 80% of the mandatory classroom teaching activities (seminars and tutorials). Continuous assessment (N1) will be 40% of the qualification and will consist of two components: interactive class in small groups (seminars) and interactive class in very small groups (tutorials). Seminars and tutorials include the following: resolution of exercises and practical cases (15%), realization of homework and reports (10%), oral presentations [(papers, reviews and practical cases), 10%] and oral questions during the course (5%).

The final exam (N2) will cover all the contents of the course.

The student's score will result of applying the following formula:

$$\text{Final score} = 0.4 \times N1 + 0.6 \times N2$$

N1 and N2 are the marks corresponding to the continuous assessment (0-10 scale) and the final exam (0-10 scale), respectively.

The repeaters will have the same system of class attendance than those who study the course for first time.

### 6.2. Recommendations

The students should review the theoretical concepts introduced in each chapter using the reference manual and the material provided by the professor. Those students, which have significant difficulties when working the proposed activities, should contact with the professor during the tutorials, in order to analyze the problem and to receive the necessary support.

The professor will analyze with those students who do not successfully pass the evaluation, and so wish, their difficulties in learning the course content. Additional material (questions, exercises, tests, etc..) to strengthen the learning of the course might be also provided.