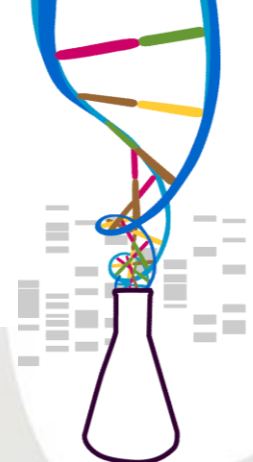


Ad Futurum: DEL XVII AL XXI: PROYECTANDO NUESTRA TRADICIÓN HACIA EL FUTURO

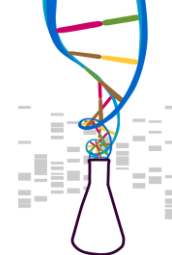


1608

2010

**1ª JORNADA
SECTORIAL: 16/02/11
L3: BIOMEDICINA Y
DESARROLLO DE FÁRMACOS**

**VICENTE GOTOR FERNÁNDEZ (INVESTIGADOR RAMÓN Y CAJAL)
GRUPO DE BIOORGÁNICA DE LA UNIVERSIDAD DE OVIEDO**



Coordinador / investigador responsable: Vicente Miguel Gotor Santamaría

Número de miembros: 28

Dirección postal: Avenida Julián Clavería s/n. Facultad de Química

Tel: 985 103448

E-mail: vgs@uniovi.es

Web: www.unioviedo.es/bioorganica

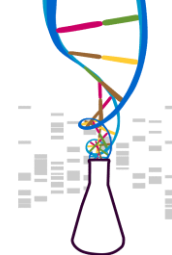
Bioorganic Research Group (Universidad de Oviedo)



Since its creation in **1988**, our group carries out research and training activities in the field of organic synthesis, employing enzymes as **biocatalyst** for the preparation of high added value compounds with application in **pharmaceutical and synthetic chemistry**.

Facts:

- ◆ Near 300 publications (30 in 2010)
- ◆ 42 Doctoral Thesis (3 in 2010)
- ◆ Multiple national and international collaborations (industry & academia)



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Bioorganic Research Group (Universidad de Oviedo)

Composition starting 2011

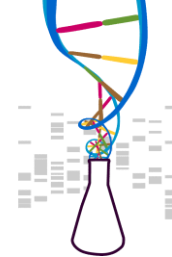
1 Full Professor: **Vicente Gotor**

5 Professors: Francisca Rebolledo, Miguel Ferrero, Ramón Liz, Rosario Brieva, Susana Fernández

5 Senior scientists: Vicente Gotor-Fernández, Iván Lavandera, Eduardo Busto, Gonzalo de Gonzalo, Cristina Rodríguez

2 Technicians: Manuel Ascariz, Lara Fernández

15 Ph. D. students (Spain, Brazil, France, Germany and Poland)



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Líneas de investigación principales (General overview)

Organic chemistry: Alcohols, amines, amides, carbamates, carboxylic acids, esters, sulfoxides...

Enzymes:

Hydrolases: esterases, lipases...

Oxidoreductases: alcohol dehydrogenases, Baeyer-Villiger monooxygenases...

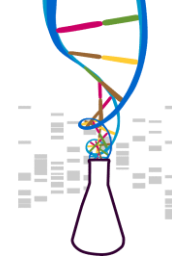
Lyases: Nitrile hydratases, oxynitrilases....

Applied Biocatalysis: pharmaceuticals

Natural products: nucleosides, nucleotides and vitamin D₃ analogues

Enzymatic promiscuity: discovery of new activities

Supramolecular chemistry: polyamine complexes



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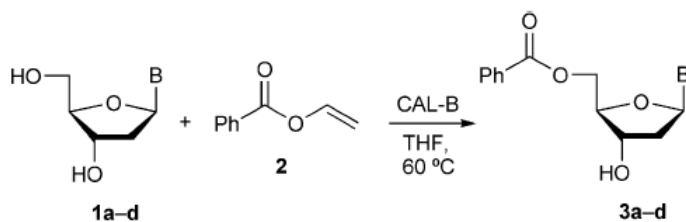
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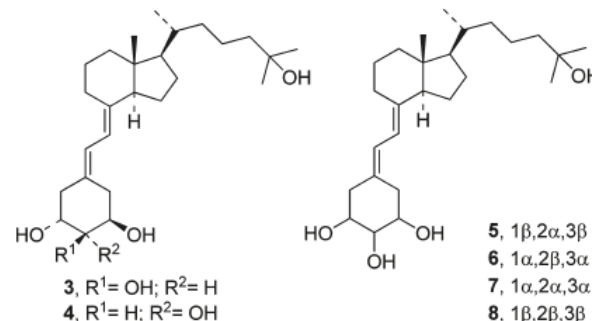
Líneas de investigación principales (More in depth-1)

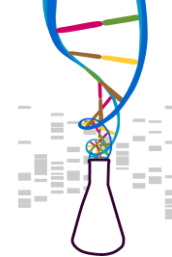
Natural products:

- ◆ Synthesis of $1\alpha,25$ -dihydroxyvitamin D_3 selectively modified by chemical or enzymatic methods in the A-ring (conformationally restricted *cis*-structures, amine derivatives...)
- ◆ Synthesis of 25-hydroxyvitamin D_3 with high affinity for the vitamin D binding protein
- ◆ Synthesis of quinic and shikimic acid derivatives as precursors of A-ring vitamin D_3 analogues
- ◆ Enzymatic resolution of racemates and α/β anomeric mixtures of nucleosides
- ◆ Chemoenzymatic synthesis of oligonucleotide precursors and azasugar nucleosides



a, B = T; b, B = C^{Bz}; c, B = A^{Bz}; d, B = G^{Ibu}





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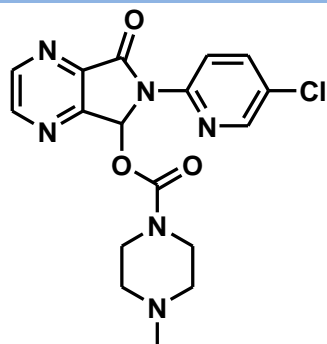
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Líneas de investigación principales (More in depth-2)

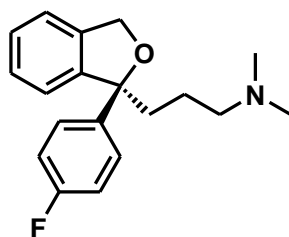
Chemoenzymatic synthesis of pharmaceuticals:

- (i) synthesis of adequate racemic or prochiral intermediates
- (ii) lipase-catalyzed stereoselective transformations
- (iii) final chemical synthesis of APIs



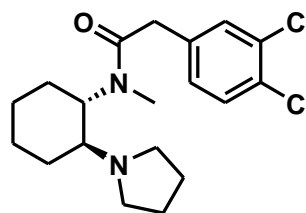
(S)-Zopiclone

Tetrahedron: Asymmetry
2002, 13, 2577-2582
2003, 14, 429-438



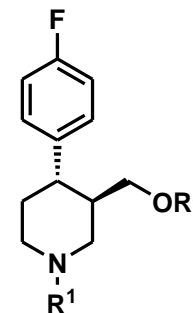
(S)-Citalopram

Tetrahedron: Asymmetry
2004, 15, 341-345



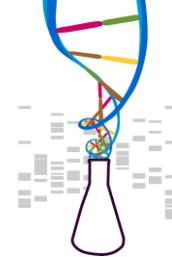
U-50,488

Chem. Eur. J.
2004, 10, 5788-5794



(-)-Paroxetine analogues

J. Org. Chem. **2001**, 66, 8947-8953
J. Org. Chem. **2003**, 68, 3333-3336
Tetrahedron: Asymmetry **2003**, 14, 1725-1731



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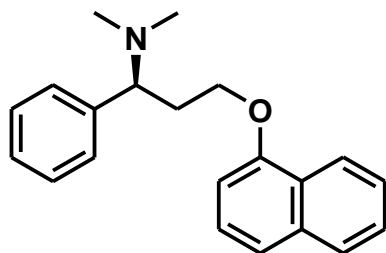
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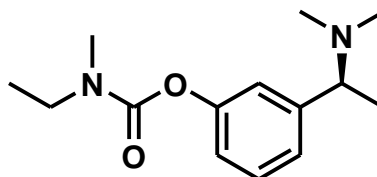
Líneas de investigación principales (More in depth-2)

Chemoenzymatic synthesis of pharmaceuticals:

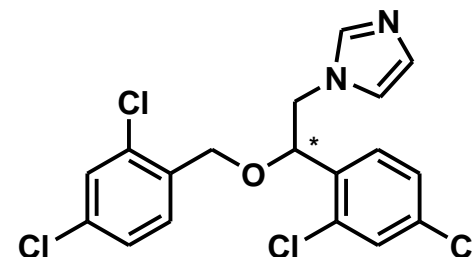
- (i) synthesis of adequate racemic or prochiral intermediates
- (ii) lipase or oxidoreductases catalyzed stereoselective transformations
- (iii) final chemical synthesis of APIs
- (iv) biological evaluation



(S)-Dapoxetine



(S)-Rivastigmine



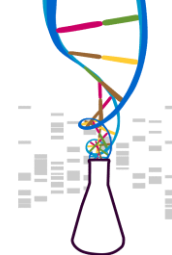
(S) and (R)-Miconazole

Tetrahedron: Asymmetry **2006**, 17, 860-866

J. Org. Chem. **2009**, 74, 5304-5310

J. Org. Chem. **2011** in press

Adv. Synth. Catal. **2010**, 352, 395-406



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Proyectos, contratos, patentes... en desarrollo o realizados

◆ **11 Projects with industry since 1989**

◆ **Active participation in scientific programmes:**

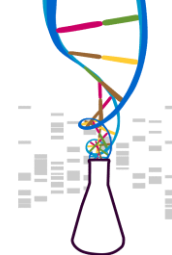
(I) National. Química Sostenible. Procesos biocatalíticos para la preparación de productos de alto valor añadido. Aplicaciones en organocatalisis y en síntesis de fármacos (Plan Nacional I+D+i; Ministerio Ciencia e Innovación)

(II) Mixed sponsorship. Resoluciones cromatogáficas y enzimáticas aplicadas a la obtención de compuestos enantiopuros de interés farmacológico (Plan Nacional I+D+i; Ministerio Ciencia e Innovación, Proyecto TRACE)

(III) European networks.

- BIOTRAINS: A European Biotechnology training network for the support of chemical manufacturing. Marie Curie Initial Training Networks (European Union)

- BIONEXGEN, Developing the next generation of biocatalysts for industrial chemical synthesis . FP7 Knowledge Based BioEconomy projects (European Union)



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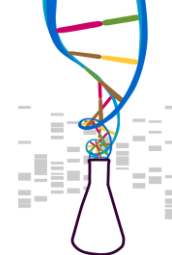
Colaboraciones con empresas, centros tecnológicos, redes...

Industry

- EntreChem (spin-off Universidad de Oviedo)
- Novozymes
- Farmhispania S. A.
- Amano Enzyme Europe
- Rolabo Outsourcing S. L

European networks

- University of Manchester (UK)
- Juelicch Institute (Germany)
- Technical University of Denmark
- University of Stuttgart (Germany)
- Leibnitz Institute (Germany)
- BASF (Germany)
- University of York(UK)
- Lund University (Sweden)
- University of Graz (Austria)
- TU Dortmund (Germany)
- Lentikats (Czech Republic)
- ACIB (Austria)
- University of Basel (Switzerland)
- Delft University of Technology (The Netherlands)
- Academy of Sciences of the Czech Republic
- The University College of London (UK)
- Royal Institute of Technology (Sweden)
- CLEA Technologies (The Netherlands)



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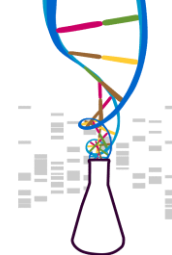
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Competencias y capacidades tecnológicas más relevantes

- ◆ Excellent background in organic synthesis for the development of efficient routes to interesting high-added value compounds
- ◆ Great experience in enzymatic methods for the development of chemo- and regioselective processes. Avoidance of protection and deprotection steps
- ◆ High expertise in the synthesis of vitamin D₃ analogues, nucleosides and pharmaceuticals
- ◆ Use of enzymatic reactions for stereoselective processes: amidation, reduction, carbamoylation, hydrolysis, transesterifications....
- ◆ Resolution of racemic mixtures or desymmetrization of prochiral compounds by means of easily scalable lipase-catalyzed reactions using commercially available hydrolases
- ◆ Development of oxidation-reduction processes and continuously incorporating new biocatalysts in our processes



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Desarrollo: intereses, objetivos, proyectos futuros

◆ **Profile:**

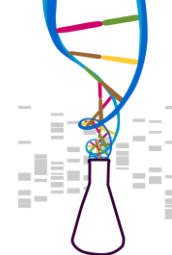
- **Synthetic chemists: organic and enzymatic reactions**
- **Chemoselective, regioselective or stereoselective transformations**

◆ **Interest:**

- **Pharmaceuticals**
- **Discovery of new enzymatic sources and activities with synthetic purposes**
- **Open for collaborations mainly in the field of biological evaluation**

◆ **Future plans:**

- **Interaction with industry and academic partners**
- **Activity in national and international networks involved in multidisciplinary scientific areas**
- **Publication of scientific research: articles, reviews, book chapters, patents, doctoral thesis....**



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LIBRE PARA DESTACADOS, IMÁGENES, LOGOS...

Current collaborations:

Industry

- EntreChem - <http://www.entrechem.com>
- Novozymes - <http://www.novozymes.com>
- Amano Enzyme Europe - <http://www.amano-enzyme.co.jp>
- Farmhispania S. A. - <http://www.farmhispania.com/>
- Rolabo Outsourcing S. L. - <http://www.rolabo.com/>

Academia

- Instituto Universitario de Biotecnología de Asturias - <http://www.unioviedo.es/IUBA/>
- Prof. Carlos Cativiela - <http://www.unizar.es>
- Prof. Santiago V. Luis - <http://www.uji.es>
- Dr. Ignacio Alfonso - <http://www.iqac.csic.es>
- Dr. Victor M. Sanchez-Pedregal - <http://web.usc.es>
- Dr. Wolfgang Kroutil - <http://biocatalysis.uni-graz.at/>
- Prof. Marco Fraaije - www.rug.nl



**OPEN MIND FOR NEW
COLLABORATIONS!!!!!!!**