Kimika Sintetiko eta Industriala Masterra

Master Amaierako Lanak *(MAL)* eskaintza

26/27 ikasturtea

- Bizkaiko Campusa
- Gipuzkoako Campusa
- Arabako Campusa

- Bizkaiko Campusa

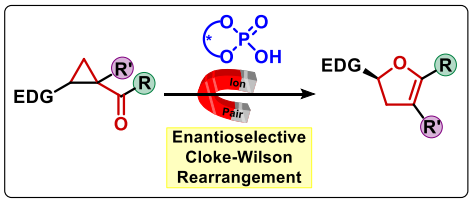
IZENBURUA:
Sintesi Asimetrikoa, Kimika Jasangarria eta Prozesu Biomimetikoak. Asymmetric Synthesis, Sustainable Chemistry and Biomimetic Processes

LABURPENA

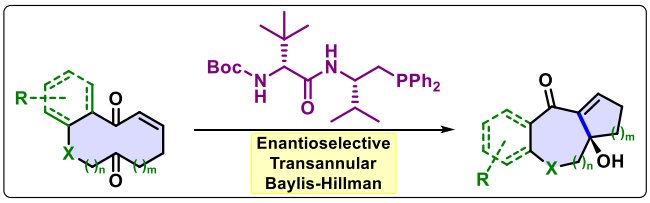
Gako-hitzak: Katalisia, Kimika Berdea, Jasangarritasuna, Farmakoen Diseinua, Produktu Naturalak, SAR azterketa, Sintesi Kimikoa, Sintesi asimetrikoa

Gizarteak etengabe eskatzen ditu ongizatea bermatzen duten farmako berriak, gaitzak arinduz, gaixotasunak prebenituz eta sendatuz, bai eta diagnostiko klinikoa eginez ere. Urtero, batez beste, 50 farmako berri onartzen dira, eta horrek oinarrizko ikerketa eskatzen du fase klinikoko ebaluaziorako hautagai berriak prestatzeko. Gure taldea entitate kimiko berrien sintesi-metodologiak garatzen ari da, estrategia jasangarriak erabiltzera bideratutako ikuspegiarekin. Konposatu berri horiek diabetesa, minbizia edo gaixotasun kardiobaskularretan parte hartzen duten diana terapeutikoen aurrean ebaluatzen dira. Birusaren aurkako jarduera duten molekulen egitura-jarduera erlazioari buruzko azterlanak ere egin dira.

Kimika Berdea eta Prozesu Jasangarriak - Sintesi Asimetrikoa - Organokatalisia

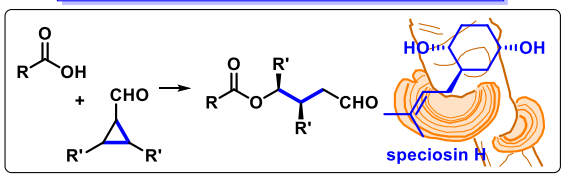


Angew. Chem. Int. Ed. **2018,** *57*, 8225-8229
Highlighted in *Synfacts*, **2018**, 868.



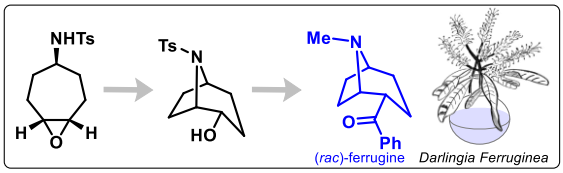
J. Am. Chem. Soc. **2019**, *141*, 9495-9499.
Catalysts **2022**, *12*, 67.

Farmakoen Diseinu et Sintesia
Egitura-Aktibitatea erlazioaren ikerketak (SAR)



Chem. Eur. J. **2018**, *24*, 8764-8768.

Prozesu Biomimetikoaks
Produktu Naturalen eta Bioaktiboen Sintesia



Angew. Chem. Int. Ed. **2020**, *59*, 6780-6784.
Org. Biomol. Chem. **2021**, *19*, 3763-3775.
Eur. J. Org. Chem. **2021**, *20*, 2855-2861.

HIZKUNTZA(K): English, Castellano, Euskera
TOKIA: Zientzia eta Tekonologia Fakultatea, UPV/EHU, Leioa (Bizkaia)
IKERKETA TALDEA: Sintesi Asimetrikoa, Kimika Iraunkorra eta Prozesu Biomimetikoak ikerketa taldea
WEBGUNEA: www.ehu.es/gsa
POSTU KOPURUA: 3
ARDURADUNA(K): José L. Vicario, Mª Luisa Carrillo, Efraím Reyes, Uxue Uria, Liher Prieto.
HARREMANETARAKO POSTA ELEKTRONIKOA: joseluis.vicario@ehu.es

IZENBURUA: 3d Metalen bidez katalizaturiko C-H aktibazioa burutzeko estrategiak. Aplikazio sintetikoak

LABURPENA

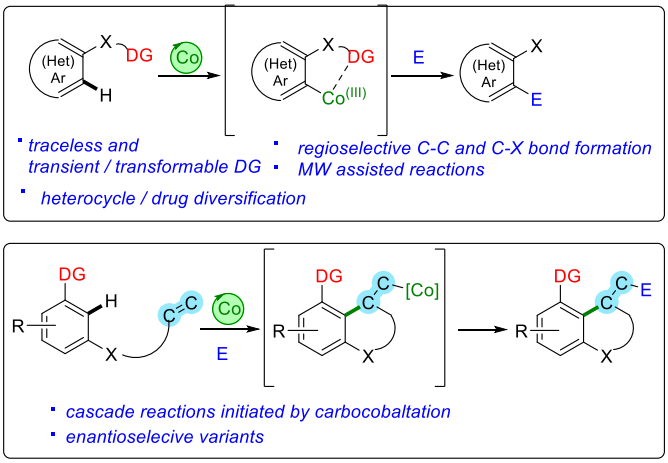
Metodologia sintetiko berritzaileen garapena ezinbestekoa da industria farmazeutikoan aktiboak izan daitezkeen molekula berrien prestakuntzarako. Hori dela eta, beharrezkoa da molekula konplexuen prestaketa modu seguru batean burutzeko metodologia sintetiko eta erreaktibotasun-patroi berriak garatzea, ingurugiroarekiko errespetua dela medio.

Metalen bidez katalizatutako C-H funtzionalizazioa funtsezko metodologia sintetiko bat da, zeinak funtzionalizatu gabeko substratuak erabiltzea ahalbidetzen duen molekula konplexuago batzuen prestaketarako. 3d trantsizio metalak, naturan ugariagoak direnak, duela gutxi hasi dira erabiliak izaten aipatutako transformazioak aurrera eramateko. Hau guztia kontuan hartuta, ekonomikoagoak diren eta toxikotasun maila baxuagoa duten metalak (Co(III), esaterako) katalizatzaile gisa erabiltzeak, aukera berriak planteatu egiten ditu erreaktibotasun eta aplikazio sintetiko berriak aurkitzeko.

Testuinguru honetan, gure proiektuen helburu orokorra C-C eta C-X loturak eratzeko metodologia efektibo eta selektiboen garapena da kobalto bidez katalizaturiko C(sp^2)-H funtzionalizazio erreakzioetan oinarrituz. Katalisi asimetrikoa ere burutu egiten da.

Talde zuzentzaileak askotan erabili egiten dira erreakzio hauen erregioselektibotasuna kontrolatzeko. Zentzu honetan, eliminatu daitezkeen talde zuzentzaileak edota talde zuzentzaile iragankorrak erabiltzeak prozedura hauen aplikagarritasuna handitu ahalko luke, farmakoen zein produktu bioaktiboen dibertsifikazioan erabili ahal izateko.

Halaber, beste talde batzuekin lankidetzan, metodologia hauen bidez lortutako egituren propietate biologikoak ebaluatu egingo dira *in vitro* zein *in silico*.



HIZKUNTZA(K): Euskara, Gaztelania, Ingelesa
TOKIA: Zientzia eta Teknologia Fakultatea, UPV/EHU (Leioa, Bizkaia)
IKERKETA TALDEA: Organometalikoak Sintesian
WEBGUNEA: https://www.ehu.eus/eu/web/oms/home
POSTU KOPURUA: 2
ARDURADUNAK: Nuria Sotomayor, Asier Carral
HARREMANETARAKO POSTA ELEKTRONIKOA: nuria.sotomayor@ehu.eus; asier.carral@ehu.eus

IZENBURUA: Adimen Artifiziala eta kimioinformatika Kimika Sintetikoan aplikatuta

LABURPENA

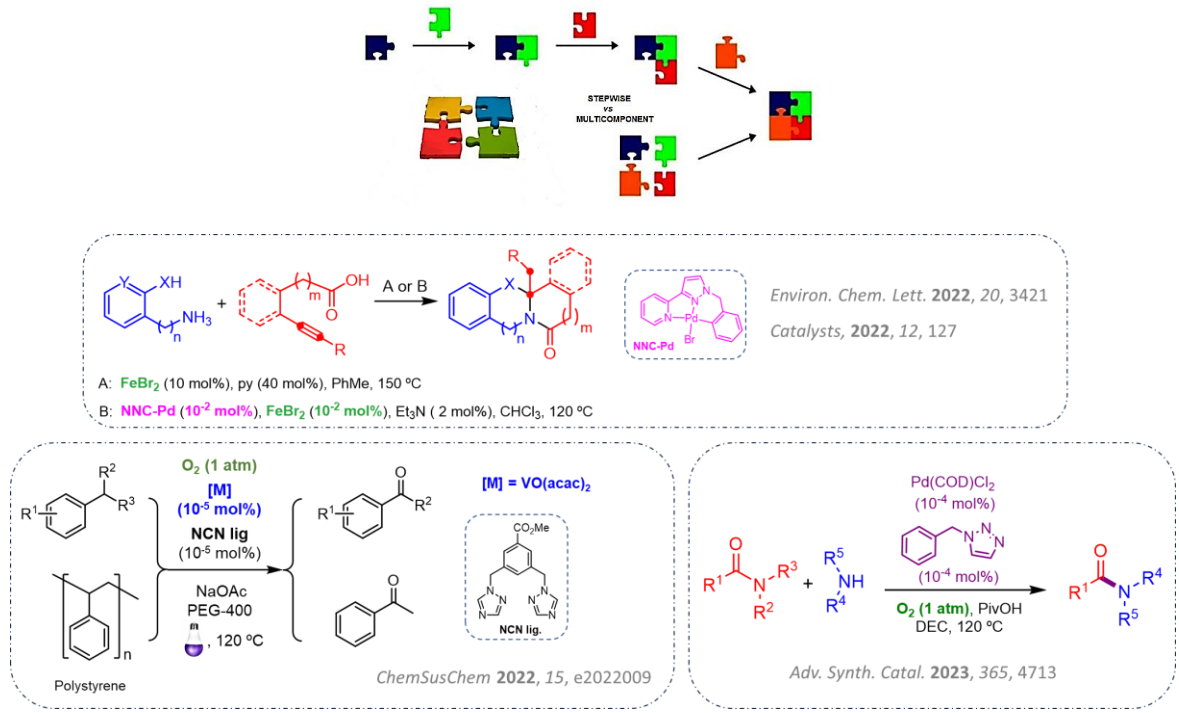
Gure Master Amaierako Lanen proiektuek eredu konputazionalen (kimio-informatikoen) garapenari heltzen diote, aurkikuntza-prozesuak, sintesi organikoa, entsegu biologikoa, garapena edota produktu kimikoen ekoizpena optimizatzeko. Besteak beste, farmakoak, katalizatzaileak, biomarkatzaileak, txertoak, nano-partikulak, bio-erregaiak eta abar. Metodologia orokorrak sistema molekularraren definizioa, egiturazko informazioaren prozesamendua eta deskribatzaile molekularren kalkulua barne hartzen ditu. Ondoren, Adimen Artifizialeko (AA) /(*Artificial Intelligence AI*) softwarea edota Ikasketa Automatikoa (IA)/ (*Machine Learning ML*) erabiltzen da eredu iragarleak aurkitzeko. Informazioa fusionatzeko teknikak (IF) erabiltzen dira, eta hainbat iturritako datuak prozesatzen dira. Aztertu beharreko sistemak honako hauek dira: molekula organikoak eta erreakzio kimikoak sintesian, proteinen egitura, erreakzio metabolikoen sare konplexuak, polimeroak, nano-partikulak, etab. Azterketa prediktiboak egiten dira propietate hobeak dituzten produktu berriak proposatzeko, eta, aldi berean, kostuak murrizten dira baliabide materialei, denborari eta laborategiko animalien erabilerari dagokienez. Gradu-prometan jaso ohi ez diren ikasketa teknika horiei buruzko prestakuntza eskaintzen diogu ikasleari. Master Amaierako lanek beste erakunde batzuekin egindako ikerketa-proiektuekin lotuta daude, hala nola PETRONOR, TEKNALIA, Biofisika, Gaiker eta abarrekin. Prestakuntza osagarria eskaintzen dugu (Europako erregulazioa eta OCED), Kimioinformatikan datuak erabiltzearekin lotuta dauden legedi eta bioetika alderdietan..

HIZKUNTZA(K): Euskara, Gaztelania, Ingelesa
TOKIA: Zientzia eta Teknologia Fakultatea, UPV/EHU (Leioa, Bizkaia)
IKERKETA TALDEA: Organometalikoak Sintesian (OMS), CHEMPTML
WEBGUNEA: https://www.ehu.eus/es/web/oms/home
https://www.ikerbasque.net/humberto-gonzalez-diaz
POSTU KOPURUA: 2
ARDURADUNAK: Sonia Arrasate, Humberto González-Díaz
HARREMANETARAKO POSTA ELEKTRONIKOA: humberto.gonzalezdiaz@ehu.eus; sonia.arrasate@ehu.eus

IZENBURUA: Erreakzionatzaile eta erreakzio-ingurune jasangarrien bidezko prozesu katalitikoen garapena

LABURPENA

Ikerketa-lan honetan, propietate biologikoengatik interesekoak diren sistema poliheterozikliko konplexuen sintesirako prozedura zuzenak garatuko dira urjauzi/cascade edo osagai-anitzezko erreakzioetan oinarritutakoak. Halaber, oxigeno molekularraren bidezko aldakuntzen bitartez nahitaezko lehengaiak eskuratuko dira. Konposatu naturalen hezurdura poliziklikoen pausu bakarrean eraikitzea ahalbidetuko duten estrategiek, toxikotasunik gabeko erreakzionatzaileak, katalizatzaileen kantitate urriak eta ingurugiroarekiko adeitsuak diren erreakzio-baldintzak erabiliko dituzte. Esate baterako, dioxigenoa bezalako oxidatzaileei lehentasuna emango zaie, eta transmetalatzaileak (ziklazioetan) edo azil kloruroak (amidazioetan) ekidingo dira. Beroketa termikoaren ordez mikrouhinen bitartezko aktibazioa arlo honetan ikertuko da, bai eta ura edo bestelako disolbatzaile jasangarrien edo disolbatzailerik gabeko erreakzioen erabilera ere.



HIZKUNTZA(K): Euskara, Gaztelania, English

TOKIA: Zientzia eta Teknologia Fakultatea, UPV/EHU

IKERKETA TALDEA: NEWSYNMETH Ikerketa taldea
WEBGUNEA: **: https://www.ehu.eus/nsm**
Dr. Raul SanMartin (google.com)
POSTU KOPURUA: 5
ARDURADUNA(K): RAUL SANMARTIN, MARÍA TERESA HERRERO, GARAZI URGOITIA
HARREMANETARAKO POSTA ELEKTRONIKOA: raul.sanmartin@ehu.eus

IZENBURUA: RECONOCIMIENTO MOLECULAR: La interacción de glicanos y gllcoproteínas con lectinas humanas en procesos patológicos: Cáncer y enfermedades virales

LABURPENA Las células eucariotas están cubiertas por una densa capa de glicanos (carbohidratos). En los últimos años se ha puesto de manifiesto la relación entre la disfunción en la biosíntesis de glicanos con la malignidad del cáncer. De hecho, la glicosilación aberrante es una característica de las células cancerosas, que usan lectinas (proteínas de unión a glicanos) de las células del sistema inmune para enmascararse y progresar. Por otra parte, los glicanos de la superficie de nuestras células también representan la primera línea de interacción en la interfaz virus-huésped. De hecho, los virus presentan lectinas en su superficie que usan como llave para colonizar las células del huésped.

El diseño racional de estrategias de prevención e intervención frente a estas patologías requiere un conocimiento detallado, idealmente a resolución atómica, del mecanismo de interacción entre los glicanos y las lectinas. Nuestras investigaciones se centran en desentrañar, a escala química, los mecanismos moleculares que dictan la especificidad de esta unión para diseñar nuevas moléculas, tanto entidades químicas como anticuerpos, que permitan tratamientos específicos y eficaces.
Utilizando técnicas integradoras de química, biología molecular y estructural (síntesis, Resonancia Magnética (RMN), cristalografía de rayos X y química computacional), hemos elucidado las interacciones a escala molecular que se dan entre anticuerpos y glicanos naturales y modificados sintéticamente con Siglecs y galectinas, lectinas relacionadas con cáncer, y lectinas de distintos virus, incluyendo coronavirus. También hemos establecido las bases para generar moléculas terapéuticas mediante síntesis química e ingeniería de proteínas.

Los 4 proyectos que se ofrecen se dirigen al estudio de las interacciones entre: **A)** *la glicoproteina CD44, asociada con una alta agresividad del cáncer, con lectinas humanas*; **B)** *anticuerpos y glicanos, naturales y sintéticamente modificados, con Siglecs*; **C)** *glicanos naturales y sintéticos, etiquetados con núcleos de ^{13}C y ^{19}F con galectina-9*; **D)** *Glicanos generados por síntesis química con lectinas del virus de la gripe A.* Estos conocimientos se usarán posteriormente para diseñar moléculas de alta afinidad que permitan combatir los procesos patológicos correspondientes.

En todos los proyectos, las personas elegidas aprenderán a aplicar un enfoque científico multidisciplinar: química sintética, biología molecular, técnicas modernas de RMN y cristalografía de rayos X para caracterizar la estructura de estas moléculas complejas y deducir su interacción con sus receptores, usando también programas de química computacional de última generación.

Referencias anteriores de los equipos investigadores relacionadas con esta propuesta:

1. https://www.who.int/news-room/fact-sheets/detail/cancer
2. *Virus: Nat Commun*. 15,**2024**,2979; *Angew Chem Int Ed* 61,**2022,**e202201432. *Nat Commun*. **2021**; 12: 5449. *J Am Chem Soc*. **2022**; 144: 424. *Angew Chem Int Ed* **2020**; 59: 23763
3. *Siglecs, glycans & cancer*: *Nat. Commun*. **2017**, 8 764. *JACS Au* **2022**, 3, 204. *Nat. Commun*. **2023**, 14, 3496. *ACS Chem. Biol*. **2024**, 19, 483. *Chem. Sci*. **2024**, DOI: 10.1039/D4SC01723D.
4. *Galectins & glycans*: *Glycobiology*. **2024**; 34: cwae002. *Pharmaceuticals*. **2022**;15:145; *Angew Chem Int Ed*. **2021**, 60:18777; *RSC Chem Biol*. **2021**;2:932; *Chem. Eur. J.* **2020**;26:15643.

HIZKUNTZA(K): ESPAÑOL, INGLÉS

TOKIA: CIC bioGUNE, Parque Científico y Tecnológico de Bizkaia, Derio (Bizkaia)

IKERKETA TALDEAK: CHEMICAL GLYCOBIOLOGY, CANCER GLYCOIMMUNOLOGY

WEBGUNEAK: https://www.cicbiogune.es/people/jjbarbero; https://www.cicbiogune.es/people/jereno

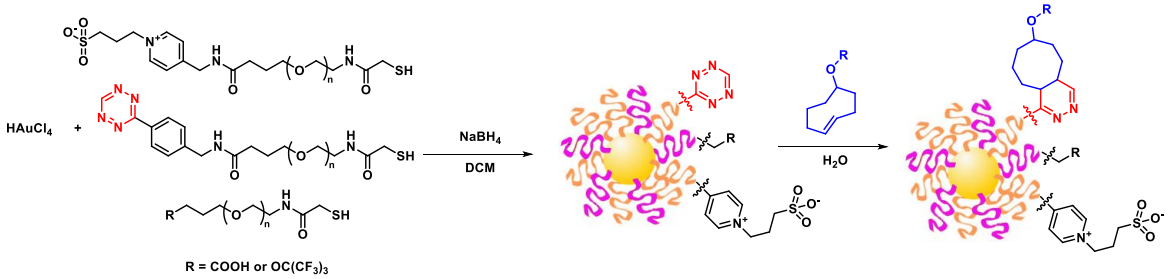
POSTU KOPURUA: 4

ARDURADUNA(K): Ana Ardá, June Ereño-Orbea, Ana Gimeno, Jesús Jimenez-Barbero, Luca Unione
HARREMANETARAKO POSTA ELEKTRONIKOA: aarda@cicbiogune.es; jereno@cicbiogune.es; agimeno@cicbiogune.es; jjbarbero@cicbiogune.es; lunione@cicbiogune.es

IZENBURUA: TCO funtzio taldea eta tetrazinaz funtzionalizaturiko urrezko nanopartikulen erreakzio boortogonalaren azterketa.

LABURPENA: Azken urteotan, urrezko nanopartikulak interes handia hartu dute euren propietate optiko eta elektronikoengatik, eta horren ondorioz, hainbat arlotan erabiltzen hasi dira (materialen zientzian, biomedikuntzan eta katalisian, besteak beste).[1] Haien aplikazio egokirako, nanokristalaren berezko propietateez gain, funtsezkoa da nanopartikulak inguratzen dituzten ligandoak egoki aukeratzea, koloide-egonkortasuna eta dagokion disolbatzaileetan disolbagarritasuna hobetzeko, eta, oso garrantzitsua dena, gainazala kimikoki funtzionalizatzeko nanopartikulak helburu espezifikoetara (targeting) zuzendu ahal izateko. Ildo horretan, gure ikerketa-taldeak esperientzia handia dauka urrezko nanopartikulen sintesi eta funtzionalizazioan, haien tamaina eta egonkortasuna kontrolatuz, eta hainbat arlotan metodologia berriak garatzea ahalbidetzen duten ligando espezifikoak sartuz.[2] Proiektu honetan, tetrazinan oinarritutako ligandoak sintetizatzea eta urrezko nanopartikuletan kokatzea planteatzen da, eta, ondoren, ingurune urtsuan, TCO (*trans*-ziklooktenoa) taldeekin duten erreakzio bioortogonala aztertzea. Erreakzio honetan interesa handitu da azken urteotan, izan ere, in vitro zein in vivo sistemetan oso selektiboa eta biobateragarria baita.

Multidisziplinar den proiektu honek, sintesi organikoa eta materialen zientzia fusionatzen ditu, eta lortutako emaitzak zelula-kultiboetan eta/edo animalia-ereduetan aplikatuko dira. Proiektuan inkorporatzen den ikasleak ligandoak prestatuko ditu sintesi organikoaren bidez, eta, ondoren, urrezko nanopartikulak funtzionalizatzeko erabiliko ditu. Era berean, erreakzio bioortogonalaren bideragarritasuna aztertuko du eta beharrezko parametroak optimizatuko ditu.



Eskema 1. Urrezko nanopartikula funtzionalizatuen sintesia eta ondorengo TCO erreakzioaren azterketa.

HIZKUNTZA(K): GAZTELAINA, INGELESA
TOKIA: Instituto Biofisika (CSIC, UPV/EHU), Leioa, Bizaia
IKERKETA TALDEA: FluoroNanoTools Laboratory
WEBGUNEA: https://www.biofisika.org/en/research/fluoronanotools-laboratory
POSTU KOPURUA: 1
ARDURADUNAK: Mónica Carril, Galder Llorente
HARREMANETARAKO POSTA ELEKTRONIKOA: monica.carrilg@ehu.eus

[1] (a) Johannsmeier, S.; Heeger, P.; Terakawa, M.; Kalies, S.; Heisterkamp, A.; Ripken, T.; Heinemann, D. Gold nanoparticle-mediated laser stimulation induces a complex stress response in neuronal cells. *Sci. Rep.* **2018**, *8*, 6533 (b) Chiang, M.-C.; Yang, Y.-P.; Nicol, C. J. B.; Wang, C.-J. Gold Nanoparticles in Neurological Diseases: A Review of Neuroprotection. *Int. J. Mol. Sci.* **2024**, *25*, 2360. (c) Damnjanovic, R.; Bazard, P.; Frisina, R. D.; Bhethanabotla, V. R. Hybrid Electro-Plasmonic Neural Stimulation with Visible-Light-Sensitive Gold Nanoparticles. *ACS Nano* **2020**, *14*, 12345-12354. (d) Paviolo, C.; Stoddart, P. R. Gold Nanoparticles for Modulating Neuronal Behavior. *Nanomaterials* **2017**, *7*, 92.

[2] For example, see: (a) Atabakhshi-Kashi, M.; Carril, M.; Mahdavi, H.; Parak, W. J.; Carrillo-Carrion, C.; Khajeh, K. In Vitro Cellular Uptake Studies of Self-Assembled Fluorinated Nanoparticles Labelled with Antibodies. *Nanomaterials* **2021**, *11*, 1906. (b) Arango, J. M.; Padro, D.; Blanco, J.; Lopez-Fernandez, S.; Castellnou, P.; Villa-Valverde, P.; Ruiz-Cabello, J.; Martin, A.; Carril, M. Fluorine Labeling of Nanoparticles and In Vivo 19F Magnetic Resonance Imaging. *ACS Appl. Mater. Interfaces* **2021**, *13*, 12941–12949. (c) Padro, D.; Cienskowski, P.; Lopez-Fernandez, S.; Chakraborty, I.; Carrillo-Carrion, C.; Feliu, N.; Parak, W. J.; Carril, M. Toward Diffusion Measurements of Colloidal Nanoparticles in Biological Environments by Nuclear Magnetic Resonance. *Small* **2020**, *16*, 2001160. (d) Michelena, O.; Padro, D.; Carrillo-Carrión, C.; del Pino, P.; Blanco, J.; Arnaiz, B.; Parak, W. J. Novel Fluorinated Ligands for Gold Nanoparticle Labelling with Applications in 19F-MRI. *Chem. Commun.* **2017**, *53*, 2447–2450.

IZENBURUA: Exploring the photochemistry of aryl sulfoxides: towards angular polycyclic aromatic hydrocarbons.

LABURPENA: The precursor approach is a powerful strategy for accessing insoluble or unstable polycyclic aromatic hydrocarbons through the synthesis of accessible molecular precursors, eventually converted in situ into functional materials in response to specific stimuli (e.g., heat, light).[1,2] In this sense, this project investigates aryl sulfoxide derivatives as photoactivable precursors for the preparation of large angular acenes, an interesting family of molecules with potential application as semiconductor in electronics (Figure 1). Our strategy is based on the light induced SO-extrusion of thiepine *S*-oxides, which forces the seven-membered ring contraction to give the fully conjugated acene.[3] This reaction can be carried out both in solution and in solid state, involving green processing techniques to evaluate the film formation of the material precursors. Thus, the project will encompass research in multi-step synthesis, methodology and photochemistry of conjugated aryl sulfoxides. Eventually, the final compounds will be study in the solid state, with the aim of implementing them in electronic devices as organic semiconductors.

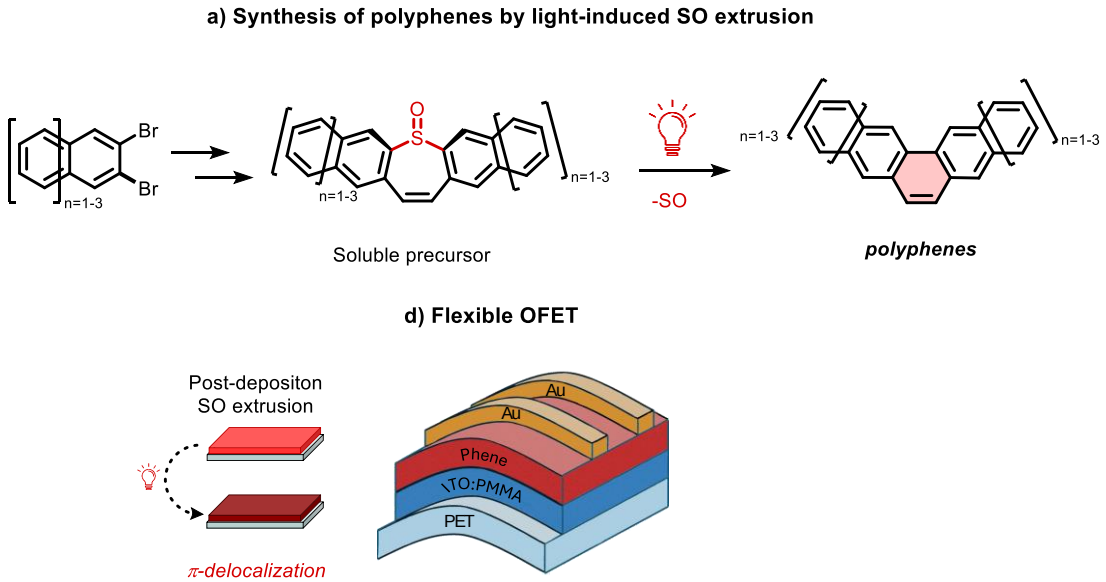


Figure 1. a) Synthetic strategy for the preparation of angular acenes (polyphenes). b) Transistor architecture implementing an organic semiconductor.

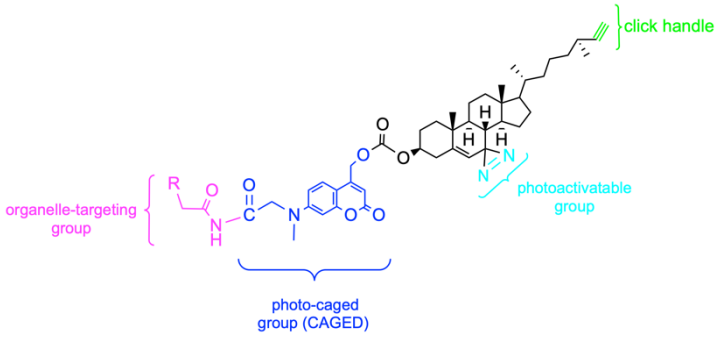
[1] A. Okba, P. Simón Marqués, K. Matsuo, N. Aratani, H. Yamada, G. Rapenne, C. Kammerer, "Synthesis of π-conjugated polycyclic compounds by late-stage extrusion of chalcogen fragments" *Beilstein J. Org. Chem.* **2024**, *20*, 287–305.
[2] P. Simón Marqués, S. Pérez-Domínguez, N. Bréfuel, S. Ueno, N. Saffon-Merceron, H. Yamada, L. Malaquin, C. Kammerer, **2025**, DOI: 10.26434/chemrxiv-2025-b8p41-v2.
[3] P. Simón Marqués, A. Okba, N. Bréfuel, S. Ueno, N. Saffon-Merceron, N. Ratel-Ramond, K. Matsuo, G. Rapenne, N. Aratani, C. Kammerer, H. Yamada, "Light-Induced SO Extrusion from Tribenzothiepine *S* -oxides: A Precursor Approach to the Triphenylene Core" *Chem Eur J* **2025**, e02655.

HIZKUNTZA(K): GAZTELAINA, INGELESA
TOKIA: Edificio Martina Casiano, BCMaterials, UPV/EHU, Leioa (Bizkaia)
IKERKETA TALDEA: Advanced functional materials and surfaces
WEBGUNEA: https://www.bcmaterials.net/en
POSTU KOPURUA: 2
ARDURADUNAK: Pablo Simón Marqués, Isabel Moreno Benítez
HARREMANETARAKO POSTA ELEKTRONIKOA: pablo.simon@bcmaterials.net

IZENBURUA: Kolesterol-proteina interakzioak zelula bizietan aztertzeko kolesterolaren analogo tetrafuntzionalen diseinua eta sintesia

LABURPENA:
Kolesterola zelula eukariotoen mintzetako funtsezko lipidoa da, eta prozesu garrantzitsuak erregulatzen ditu, hala nola mintz plasmatikoaren antolaketa, organuluen arteko komunikazioa eta zelula-seinalizazioa. Gainera, lipido honek zeregin erabakigarria du hainbat giza gaixotasunetan, hala nola minbizian; izan ere, mintzen antolaketa, zelula-seinalizazioa eta gaixotasunaren hasieran eta progresioan inplikatutako proteinen funtzioa modula ditzake. Hala ere, zelula bizietan kolesterolaren eta proteinen arteko interakzio espezifikoen identifikazio zuzena erronka handia da oraindik, bereziki interakzio horiek iragankorrak direnean, testuinguru azpizelularraren menpe daudenean edo metodo biokimiko konbentzionalen bidez detektatzeko zailak direnean.

TFM honen helburua kolesterolaren analogo tetrafuntzional berrien diseinua eta sintesia izango da, zelula-organulu desberdinetan gertatzen diren interakzio horiek aztertzeko: mintz plasmatikoan, mitokondrietan eta erretikulu endoplasmatikoan. Zundek lau elementu funtzional izango dituzte: 1) talde alkino bat, ondoren click kimikaren bidez deribatizatzeko; 2) fotoentrekrutzamendurako talde bat, erradiazio ultramorearen (UV) ondoren lipidoaren eta hurbileko proteinen artean lotura kobalentea sortzea ahalbidetuko duena; 3) CAGED motako talde babesle fotoaktibagarri bat, zundaren aktibazioa kontrolatzeko; eta 4) zuzentze azpizelularrerako talde bat, analogoaren metaketa intereseko organuluan faboratzeko.



1. eskema. *Kolesterolaren analogo tetrafuntzionalen diseinua, zelula-organuluetan kolesterol–proteina interakzioak aztertzeko.*

Proiektu multidiziplinarra da, eta kimika organiko sintetikoa, kimika analitikoa eta zelula-biologia kimikoa uztartzen ditu. Hautatutako pertsonak molekulen sintesi multietapan, purifikazioan eta karakterizazioan parte hartuko du, kromatografia, HPLC, masa-espektrometria eta EMN bezalako teknikak erabiliz. Lortutako analogoak ondoren zelula bizietan probatuko dira, haien inkorporazioa, kokapen azpizelularra eta UV bidezko irradiatzearen eta click kimikaren ondoren kolesterolari lotutako proteinak harrapatzeko duten gaitasuna ebaluatzeko.

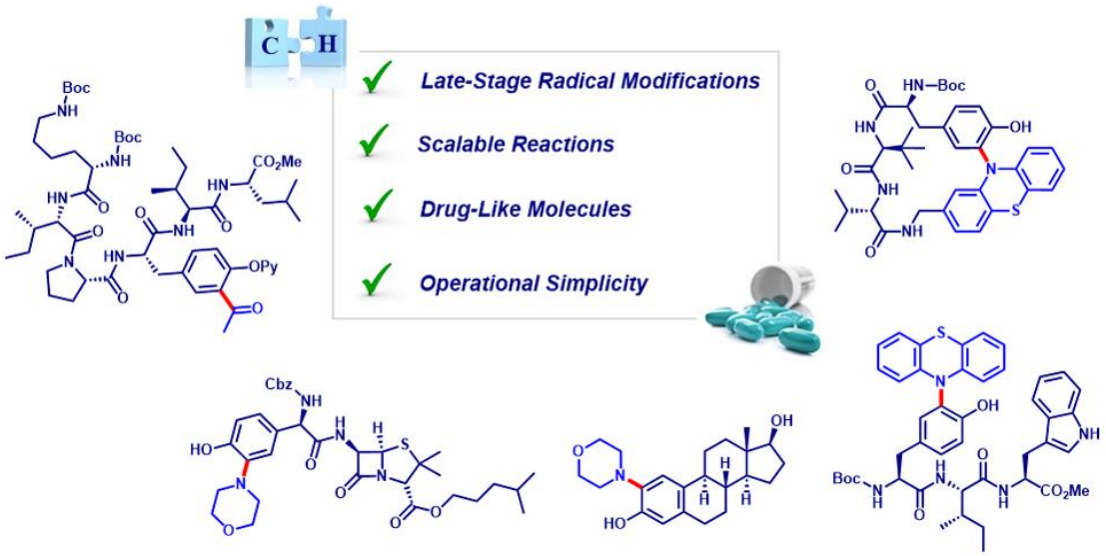
HIZKUNTZAK: EUSKERA, GAZTELANIA ETA INGELESA
TOKIA: BIOKIMIKA ETA BIOLOGIA MOLEKULARREKO SAILA ETA BIOFISIKA INSTITUTUA, UPV/EHUKO CAMPUSA
IKERKETA TALDEA: CHEMICAL CELL BIOLOGY
WEBGUNEA: HTTPS://WWW.BIOFISIKA.ORG/EN/ABOUT/PEOPLE/XABIER-CONTRERAS-GOMEZ
POSTU KOPURUA: 1
ARDURADUNAK: XABIER CONTRERAS
POSTA ELEKTRONIKOA: xabier.contreras@ehu.eus

- Gipuzkoako Campusa

IZENBURUA: Metalek katalizatutako C–H funtzionalizazioa

LABURPENA:

C–H funtzionalizazioa egungo kimikaren arlo gorikoenen artean kokatzen da. Izan ere, bestela erreakzionatzeko gai ez diren C–H loturak eraldaketa kimikoetarako talde funtzional arruntzat hartzeko aukera dakar, eta honek sintesi kimikoak diseinatzeko garaian iraultza bat suposatu du kimika organikoaren baitan. Geure ikerketa taldearen helburuak medikuntzaren esparruan garrantzia duten konposatuen eraikuntzarako metalek katalizatutako C–H funtzionalizazio erreakzio berritzaile eta jasangarrien garapenean datza. ***Lanaren helburua katalisi metalikoaren ebaluazioa egitea izango da, peptidoak aldatzeko tresna praktiko gisa***. Proiektu honetan zehar, ikaslea peptidoen sintesia barne hartzen duen kimika organiko klasikora ohituko da, baita C–H loturak aktibatu ondorengo eraldaketa organometaliko modernoetara ere.



HIZKUNTZA(K): Euskera, Ingelesa, Gaztelania
TOKIA: Joxe Mari Korta Zentroa, Donostia
IKERKETA TALDEA: Katalisi Jasangarria: Metodoak eta Konputazioa
WEBGUNEA: https://www.ehu.eus/eu/web/qbbm/arkaitz-correa
POSTU KOPURUA: 1
ARDURADUNA: Arkaitz Correa
HARREMANETARAKO POSTA ELEKTRONIKOA: arkaitz.correa@ehu.eus

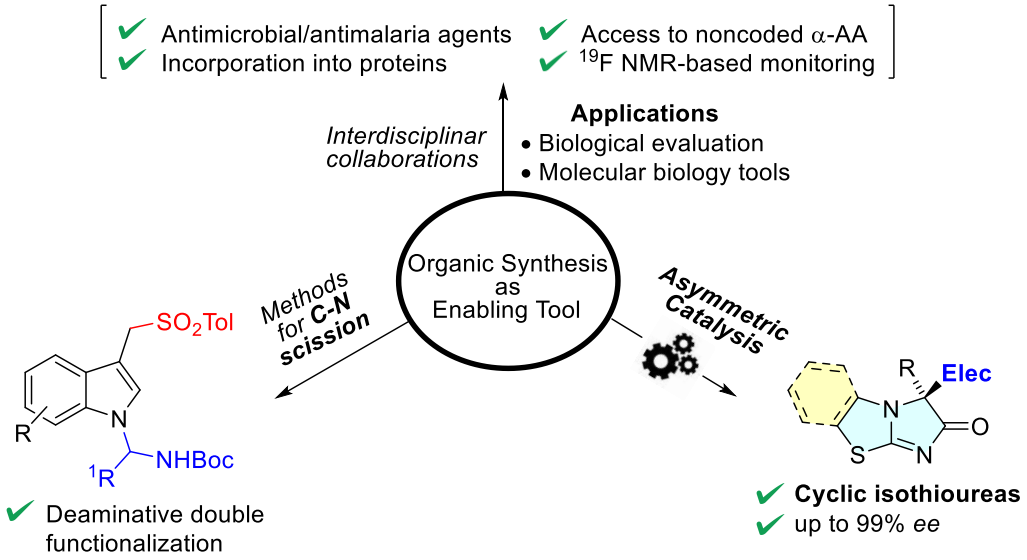
IZENBURUA: Organic synthesis and asymmetric catalysis: from new methods to applications

LABURPENA:

Gure laborategian bi ikerketa-lerro nagusi ditugu gaur egun: (i) Aminen deaminazio prozesu batean oinarritutako sintesi-bide berrien azterketa (amina tertziarioak *feedstock* moduan), eta (ii) katalizatzaile kiral berrien garapena katalisi asimetrikoan erabili ahal izateko.

Sintesi organikoa tresna ahaltsua dugu molekula berriak diseinatu eta prestatzeko, azken batean beste ikerketa-esparru batzuetan ekarpen baliotsuak egin ahal dutenak, esaterako kimika medizinalaren esparruan (molekula terapeutiko berrien aurkikuntza) edo biologia molekularrean. Ikuspuntu honi jarraituz, zenbait lankidetza martxan ditugu aktibitate biologikoaren ebaluazioan, egiturazko biologian edo biologiari zuzendutako EMN teknologietan adituak diren nazioarteko espezialistekin.

Master ikasleak aukera izango du gai hauetan sakontzeko eta esperientzia praktikoa lortzeko.



HIZKUNTZAK: Euskera, Gaztelania, Ingelesa

LEKUA: Kimika Fakultatea, Donostia-San Sebastián

IKERKETA TALDEA: Katalisi asimetrikoa eta sintesi kimikoa

WEB GUNEA: https://www.ehu.eus/eu/web/gicas/hasiera

PLAZA KOPURUA: 2

ARDURADUNAK: Iñaki Ganboa, Aitor Landa, Mikel Oiarbide

HARREMANETARAKO E-MAILAK: a.landa@ehu.eus, mikel.oiarbide@ehu.eus

IZENBURUA: RATIONAL DRUG DESIGN USING COMPUTATIONAL TOOLS

LABURPENA

In silico drug design has become a powerful tool to help understand drug–ligand interactions, thereby reducing the number of potential synthetic combinations. Actually, the use of computational techniques such as docking, molecular dynamics simulations, and the prediction of absorption, distribution, metabolism, excretion, and toxicity (ADMETox) properties allows the recognition of the relevant interactions between candidate compounds and their targets, thus providing key information for structural optimization before moving on to experimental validation. In fact, the use of these tools significantly reduces the time required for drug discovery, as well as the costs and risks associated with the subsequent stages of clinical development

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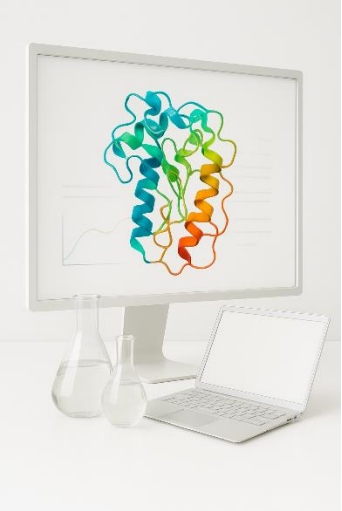


TOKIA: Kimika Fakultatea, Donostia, UPV/EHU. Joxe Mari Korta Zentroa

IKERKETA TALDEA: Kimika Bioorganikoa eta Modelizazio Molekularraren Ikerketa taldea (QuiBioSupraMM)

WEBGUNEA: https://www.ehu.eus/eu/web/qbmm/hasiera

POSTU KOPURUA: 1

ARDURADUNAK: FERNANDO P. COSSÍO, NEREA ALBERRO, ABEL DE COZAR

HARREMANETARAKO POSTA ELEKTRONIKOA: fp.cossio@ehu.eus; nerea.alberro@ehu.eus, abel.decozar@ehu.es

IZENBURUA: THEORETICAL STUDY OF DNA INTERACTION WITH POLYELECTROPHILIC COMPOUNDS OF POSSIBLE ANTITUMOUR ACTIVITY.

LABURPENA:

The application of DNA-targeting compounds represents a prevalent strategy in cancer treatment. Two prominent families of such compounds, nitrogen mustards, and cisplatin derivatives, have been developed for this purpose. Their mechanism of action relies on second-order SN2 nucleophilic reactions, wherein DNA, typically guanine, acts as a nucleophile and attacks the electrophilic chemotherapeutic agent, displacing the leaving group.

Despite the well-characterized binding modes between chemotherapeutic agents and DNA, computational studies leveraging quantum mechanics calculations and modeling can provide a deeper understanding of these interactions. These studies offer critical insights that are invaluable for the design of novel chemotherapeutic agents.
The proposed research will involve conducting computational calculations (DFT, ONIOM, docking, etc.) using a DNA model currently under development by our research group alongside polyelectrophilic compounds synthesized in our laboratory

HIZKUNTZA(K): Euskera, ingelesa, gaztelania

TOKIA: Kimika Fakultatea, Donostia, UPV/EHU. Joxe Mari Korta Zentroa

IKERKETA TALDEA: Kimika Bioorganikoa eta Modelizazio Molekularraren Ikerketa taldea

(QuiBioSupraMM)

WEBGUNEA: https://www.ehu.eus/eu/web/qbmm/hasiera

POSTU KOPURUA: 1

ARDURADUNAK: FERNANDO P. COSSÍO, IVÁN RIVILLA, NEREA ALBERRO

HARREMANETARAKO POSTA ELEKTRONIKOA: fp.cossio@ehu.eus; ivan.rivilla@ehu.es, nerea.alberro@ehu.eus

IZENBURUA: SYNTHESIS AND CHARACTERISATION OF RADIOMETRIC SENSORS OF BARIUM CATIONS (2+) CATIONS FOR USE IN NEUTRINO-FREE DOUBLE-DECAY EXPERIMENTS

LABURPENA:

The main goal is to synthesize novel fluorescent heterocycles that exhibit shifts in their emission spectra in the presence of Ba^{2+} cations. These compounds will be designed with optimized photophysical properties to achieve high quantum yields and signal-to-noise ratios, which are essential for facilitating Xe to Ba^{2+} reactions in neutrinoless double beta decay experiments.

For more information, see Rivilla I, Aparicio B, et al. "Fluorescent bicolor sensor for low-background neutrinoless double β decay experiments." Nature. 2020 Jul;583(7814):48-54. doi: 10.1038/s41586-020-2431-5.

HIZKUNTZA(K): Euskera, ingelesa, gaztelania

TOKIA: Kimika Fakultatea, Donostia, UPV/EHU. Joxe Mari Korta Zentroa

IKERKETA TALDEA: Kimika Bioorganikoa eta Modelizazio Molekularraren Ikerketa taldea

(QuiBioSupraMM)

WEBGUNEA: https://www.ehu.eus/eu/web/qbmm/hasiera

POSTU KOPURUA: 1

ARDURADUNAK: FERNANDO P. COSSÍO, IVÁN RIVILLA, NEREA ALBERRO

HARREMANETARAKO POSTA ELEKTRONIKOA: fp.cossio@ehu.eus; ivan.rivilla@ehu.es, nerea.alberro@ehu.eus

IZENBURUA: PALADIO-LIGANDOEN DISEINUA

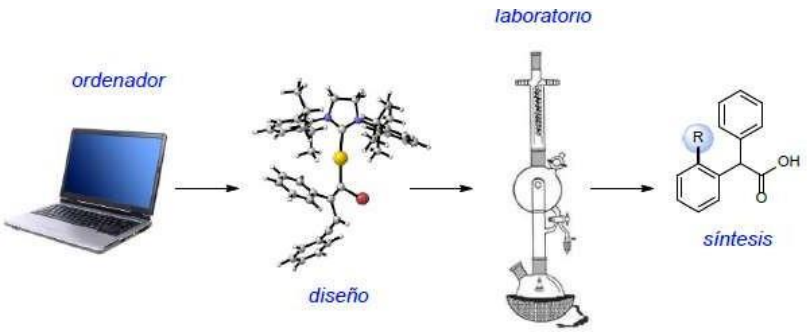
LABURPENA

Sintesi Organiko eta Kimika Konputazionala arloen arteko lan bat eskaintzen da, Katalisi Jasangarri Taldean garatzen ari garen proiektu baten barruan. Gure taldea Kimika Fakultatean dago, eta Korta ikerketa-zentroan (Tolosa hiribidea) kokatzen da.
Paladio, Nikel edo Rhodio bezalako trantsizio metalekin lotzen diren ligandoak diseinatzea, eta sortutako konplexuak erreakzio sintetiko modernutan erabiltzea dira gure helburua.
Metodo horiek oso interesgarriak dira molekulen sintesirako, gero jarduera biologikoagatik, farmazeutikoagatik, etab. interesa daukatelako molekula horiek.

Proiektuak bi alderdi ditu:

- DISEINUA: Ordenagailua erabiliz, konplexu aktiboenak sortuko dituzten ligandoak bilatuko dira. Horretarako punta-puntako softwarea erabiliko da (Gaussian, Molden, etab.), UPV/EHU-n dagoen superkonputazio zerbitzuak ematen dituen programak eta aukerak direla medio.
Zati teoriko honetan, kalkulu software-a erabiltzen zerotik ikasiko da, eta beraz, EZ da beharrezkoa aldez aurretik kimika teorikoko edo konputazioko ezagutzak izatea.

- SINTESIA: Hasiera batean, kalkuluen bidez, arrazionalki aurrez diseinatutako ligandoak prestatuko dira laborategian esperimentalki, sekuentzia sintetiko sinpleak erabiliz. Ondoren, ligando horiek erreakzio katalitiko interesgarrietan erabiliko dira. Prozesuan zehar, banatze-teknikak eta teknika espektroskopiko berrienak ikasiko dira. Ikaslearen asmoen arabera, alderdi teorikoan edo esperimentalean jarriko da azpimarra. Beraz, TFM lan bat, soilik esperimentala, soilik teorikoa, edo bien nahasketa bat egin daiteke. Hori guztia, taldeko beste lankideekin batera, kolaborazioan garatu daiteke.



HIZKUNTZA(K): EUSKARA, CASTELLANO, ENGLISH
TOKIA: KORTA ERAIKINA. KIMIKA FAKULTATEA, DONOSTIA
IKERKETA TALDEA: KATALISI JASANGARRIA: METODOAK ETA KONPUTAZIOA
WEBGUNEA: https://www.ehu.eus/es/web/qbbm/home
POSTU KOPURUA: 2
ARDURADUNA(K): ENRIQUE GOMEZ BENGOA, ROSA M. LOPEZ, MAIALEN SAGARTZAZU
HARREMANETARAKO POSTA ELEKTRONIKOA: enrique.gomez@ehu.eus

IZENBURUA: Catalytic generation of planar chirality

LABURPENA

Planar chirality is one of the most fascinating expressions of chirality, which is exploited by nature to lock three-dimensional chiral conformations and, more recently, by chemists to create new chiral reagents, catalysts, and functional organic materials. Nevertheless, the shortage of procedures able to induce and secure asymmetry during the generation of these unique chiral entities has dissuaded chemists from exploiting their structural properties. We try to mitigate this scarcity by designing unconventional procedures devoted to conquering three-dimensional complexity making use of the three pillars of asymmetric catalysis: Biocatalysis, Metal Catalysis and Organocatalysis.
The proposed TFMs will cover fundamental aspects in organic chemistry, e.g. the design and optimization of new reagents and catalytic systems, from accessible simple molecules, and the elucidation of the reaction mechanisms through experimental and computational studies.
Depending on the student´s preferences, emphasis will be placed on the experimental or in the theoretical approach to carry out a purely experimental, purely theoretical TFM work, or a mix of both approaches *(It is NOT necessary to have previous knowledge of theoretical chemistry or computer science).*

HIZKUNTZA(K): EUSKARA, CASTELLANO, ENGLISH
TOKIA: KORTA ERAIKINA. KIMIKA FAKULTATEA, DONOSTIA
IKERKETA TALDEA: KATALISI JASANGARRIA: METODOAK ETA KONPUTAZIOA
WEBGUNEA: https://www.ehu.eus/es/web/qbbm/home
POSTU KOPURUA: 2
ARDURADUNA(K): ENRIQUE GOMEZ BENGOA, ROSA M. LOPEZ, MAIALEN SAGARTZAZU
HARREMANETARAKO POSTA ELEKTRONIKOA: enrique.gomez@ehu.eus

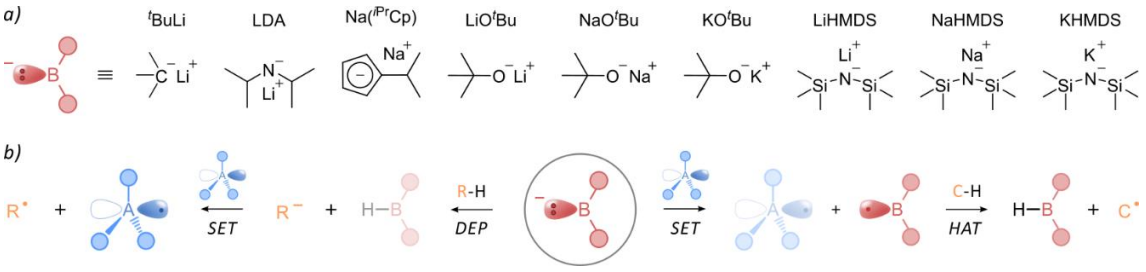
IZENBURUA: Unlocking direct C-H activation with radical pairs

LABURPENA:

Saturated hydrocarbons represent the most abundant carbon feedstocks, yet their chemical valorisation is severely limited by the intrinsic inertness of aliphatic C–H bonds, which are strong, non-polar, and difficult to differentiate selectively. Conventional functionalization strategies therefore rely on pre-functionalization or harsh oxidative conditions, increasing synthetic inefficiency and waste. **Radical-based approaches to direct C–H activation** offer a compelling alternative, as open-shell intermediates enable C–H cleavage under comparatively mild conditions while providing access to reactivity patterns inaccessible to closed-shell pathways [1]. By allowing selective hydrogen-atom abstraction and subsequent functionalization without pre-installed handles, radical C–H activation not only improves step and atom economy but also reframes C–H bonds as programmable reaction sites for the late-stage and sustainable upgrading of saturated hydrocarbons**.**

In our group, we combine experimental and computational strategies to advance radical-based chemistry. In particular, we have recently shown that nitrobenzene is an ideal platform to implement radical-based chemistry via single electron transfer processes from anionic species.[2,3] Crucially, nitroaromatics induce the formation of potent hydrogen-atom transfer (HAT) species, opening the door to direct C–H activation under remarkably simple conditions. After HAT from a saturated hydrocarbon, the resulting carbon-centered radicals are primed to engage with the persistent nitrobenzene radical, providing an ideal reaction partner for subsequent radical cross-coupling reactions. This dual reactivity unlocks C–H activation via HAT and C(sp^3)–C(sp^2) bond formation in one pot, allowing C(sp^2) functionalization to occur concomitantly with radical generation. As such, nitrobenzene serves not only as a C–H activation trigger but also as a built-in radical acceptor, unifying activation and functionalization within a single radical manifold.

Based on this, you will design, synthesise and characterise radical pairs derived from nitroaromatics and anionic species, aimed at achieving direct C-H activation of saturated compounds. Handling these radical species requires inert conditions, so you will also earn experience working with a glovebox and Schlenk lines.



References:

[1] Z. Lu et al., *Nature*, **2023**, 619, 514–520.
[2] S. A. Balahoju et al., *ACS Omega* **2025**, 10, 22, 23798–23807
[3] S. A. Balahoju et al., https://doi.org/10.26434/chemrxiv.15002430/v1

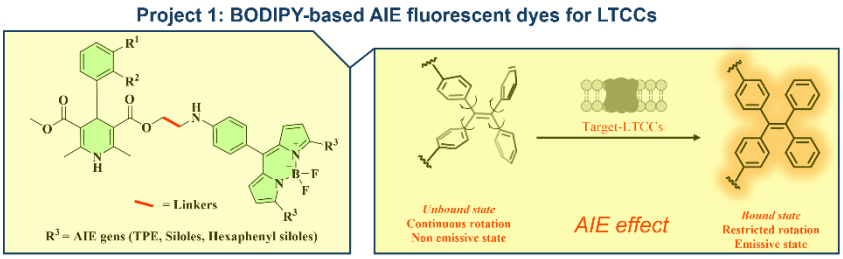
HIZKUNTZA(K): CASTELLANO, ENGLISH
TOKIA: KIMIKA FAKULTATEA, DONOSTIA
IKERKETA TALDEA: ORGANIC RADICALS GROUP
WEBGUNEA: www.danielreta.com
POSTU KOPURUA: 2
ARDURADUNA(K): Daniel Reta
HARREMANETARAKO POSTA ELEKTRONIKOA: daniel.reta@ehu.eus

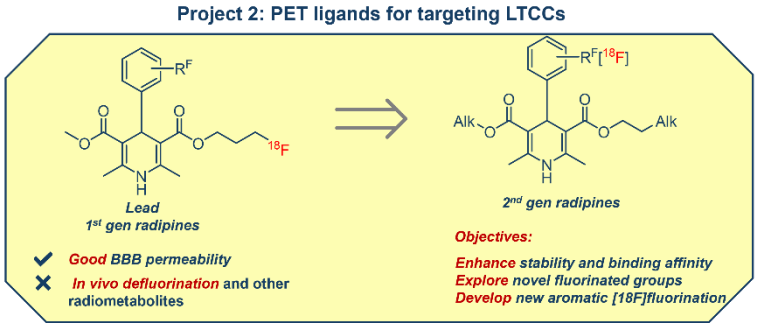
IZENBURUA: Aggregation induced emission small molecule fluorescent ligands & positron emission tomography radiotracers for studying L-type calcium channels from cells to in vivo

LABURPENA

L-type calcium channels (LTCCs) are transmembrane proteins that regulate key electrophysiological processes, in the cardiovascular as well as central nervous system. Altered LTCC expression or activity is associated with a wide range of diseases, including cardiovascular diseases, neurodegenerative and neuropsychiatric disorders, as well as addiction. Despite being successfully used as therapeutic targets to treat cardiovascular diseases, we still lack bioimaging toolkits able to effectively interrogate these ion channels in the brain, in vivo. Our recent far-red emitting fluorescent ligands have been successfully used in live-cell imaging, but due to moderate selectivity, increased background fluorescence was observed. On the other hand, brain-permeable radiotracers for positron emission tomography have not been reported yet. We offer two TFM topics as part of ongoing projects that aim to fill these missing gaps in LTCC research.

In the project 1 the Master's candidate will develop aggregation-induced emission (AIE)-based small molecule fluorescent ligands. AIE fluorophores dissipate energy when in solution due to their continuous rotation. On the other hand, restricted movements in biological systems, such as binding to receptors, lead to fluorescence emission. This unique "turn-on" behaviour makes AIEgens highly attractive candidates for developing high contrast light up fluorescent probes to overcome previous drawbacks observed with our fluodipines. The candidate will carry out organic synthesis related to the synthesis of BODIPY-based AIE dyes and their amide coupling to the pharmacophore of choice being the 1,4-DHP core. For this a thorough training in organic synthesis is envisaged, including reaction setup, purification techniques (flash column, PTLC, HPLC) and characterization (NMR, HR-MS, MALDI) of small molecules. In addition to this, the candidate will define the spectrofluorometric properties of the novel fluorescent ligand and assist initial experiments in cells using TIRF microscopes, recently installed at CIC biomaGUNE.





Project 2 will focus on the development of positron emission tomography (PET) tracers for the in vivo imaging of LTCC-related in the brain. Current drugs targeting LTCCs are used to treat cardiovascular disorders, and, due to peripheral side effects, it is complicated to translate them toward CNS-related indications. In addition, the lack of molecular imaging tools able to evaluate brain penetration and target engagement in vivo considerably hampers the development of CNS-selective LTCC modulators. Starting from a lead PET ligand candidate recently developed in our group (*unpublished results*), displaying improved BBB permeability and preferential targeting of cerebral LTCCs over cardiac LTCCs, the candidate will contribute to the development of next-generation PET tracers for CNS imaging applications. The candidate will carry out organic synthesis related to the preparation of [^{18}F]labelled 1,4-dihydropyridine (1,4-DHP) derivatives and their corresponding radiolabelling precursors. For this, a thorough training in organic synthesis and radiochemistry is envisaged, including reaction setup, purification techniques (flash chromatography, PTLC, semi-preparative HPLC) and characterization (NMR, LC-MS, HR-MS and radio-HPLC) of small molecules and radiotracers. In addition to this, the candidate will assist in the physicochemical and biological evaluation of the developed PET ligands, including lipophilicity measurements, metabolic stability studies and preliminary in vitro experiments. The student will also participate and have access to the unique radiolabelling, including the cyclotron.

REFERENCES:

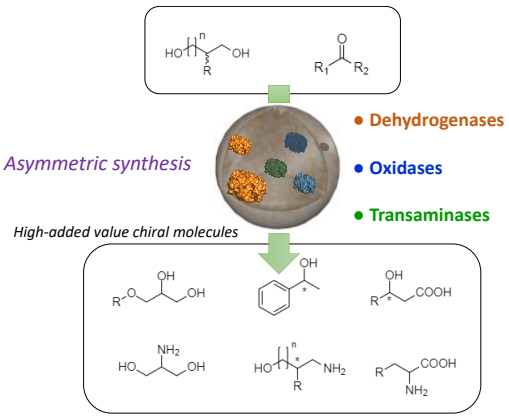
Striessnig et al., *Pharmacol Rev,* **2015**, 67, 821-870 DOI
Ismalaj et al., *J Med Chem* ***2024***, 67, 18038-18052 DOI
Liu et al., *Angew Chem Int Ed,* **2020**, 59, 9868-9886 DOI
Wang et al.,. *Frontiers Chem* **2019,** 7, 712 DOI
Crouzel et al., Nucl Med Biol, 1998, 25, 339-342 DOI
Liang et al., Nature Comm, 2023, 14, 3257 DOI

HIZKUNTZA(K): Gaztelania, English
TOKIA: CIC BiomaGUNE, Guipuzkoako Zientzia eta Teknologia Parkea, Donostia
IKERKETA TALDEA: MOLECULAR AND FUNCTIONAL IMAGING
Wegunea: https://www.cicbiomagune.es/org/research-associate-detail?nid=43003
POSTU KOPURUA: 2
ARDURADUNA(K): Ermal Ismalaj
HARREMANETARAKO POSTA ELEKTRONIKOA: eismalaj@cicbiomagune.es

IZENBURUA: SÍNTESIS BIOCATALÍTICA DE AMINOALCOHOLES Y AMINOÁCIDOS QUIRALES CON INTERÉS EN QUÍMICA FINA

LABURPENA

La síntesis enantoselectiva de aminoalcoholes es fundamental en el contexto de la química industrial ya que estas moléculas forman parte del esqueleto de muchos compuestos de alto valor añadido, como fármacos, fitosanitarios, aditivos alimentarios y polímeros, entre muchos otros (ver figura). En este proyecto de máster se buscará el desarrollo de métodos enzimáticos para la valorización de residuos agrícolas y plásticos en compuestos de alto valor añadido (p.e fármacos y aditivos) mediante transformaciones enzimáticas enantioselectivas. Las enzimas nos permitirán llevar a cabo esquemas sintéticos complejos (multietapa) en condiciones acuosas y temperaturas y presión ambientes, lo que nos permitirá aumentar la sostenibilidad tanto medioambiental como económica de estos procesos. Para lograr este objetivo, llevaremos a cabo el cribado y selección de diferentes enzimas (oxidorreductasas, tranferasas, hidrolasas), la inmovilización de estas en soportes sólidos para aumentar su estabilidad y mejorar su procesabilidad, y el desarrollo de métodos analíticos (espectrofotométricos y cromatográficos) para la identificación de los productos y la cuantificación de la productividad y selectividad de los biocatalizadores. El objetivo final del trabajo de final de master desarrollar un sistema multi-enzimático heterogéneo (inmovilizado) capaz de sintetizar aminoalcoholes con una alta productividad y estabilidad operacional.



HIZKUNTZA(K): CASTELLANO E INGLES

TOKIA: CIC BIOMAGUNE

IKERKETA TALDEA: BIOCATALISIS HETEROGÉNEA

WEBGUNEA:https://flg802.wixsite.com/flopezgallego

POSTU KOPURUA: 1

ARDURADUNA: FERNANDO LÓPEZ GALLEGO

HARREMANETARAKO POSTA ELEKTRONIKOA: flopez@cicbiomagune.es

IZENBURUA: **Síntesis Metalocajas Multifuncionales como Estabilizadores de Cuadruplexes de Guanina**

LABURPENA

*Las **metalacajas (MCgs) son ensambles metal-orgánicos**, su **potencial como sistemas de liberación de fármacos (DDS)** o como vehículos para agentes de imagen, junto con la incorporación de múltiples centros metálicos, los posiciona como metalofármacos o profármacos con mayor bioactividad que sus análogos monometálicos a dosis equivalentes.*[1] *Nuestro grupo está interesado en desarrollar MCgs con verdadero potencial terapéutico y diagnóstico.*[2] *Además, el uso de bloques constructores funcionales, por ejemplo, con actividad biológica, terapéutica o de imagen intrínsecas, transfiere estas propiedades únicas al ensamblaje global, abriendo nuevas modalidades terapéuticas.*[3]

En este contexto, hemos desarrollado MCgs basadas en porfirinas de oro(III)[4] *cuya incorporación mejora las propiedades fotofísicas y medicinales, generando plataformas capaces de, además de actuar como DDS, ser fotosensibilizadores para PDT y estabilizantes de cuadruplexes de guanina (G4s). Este tipo de **estructuras de ADN no canónicas**, juegan papeles importantes en los procesos de división celular y **han sido identificadas como dianas terapéuticas en el tratamiento del cáncer**.*[5] *El desarrollo de estabilizadores selectivos para estas estructuras es, por tanto, de gran relevancia, y las MCgs representan una alternativa atractiva en esta dirección.*

*En este proyecto, **se sintetizarán nuevas metalocajas fotoactivas (Figura 1), diseñadas para interactuar selectivamente con estructuras de ADN no canóico**. Las estructuras elegidas presentarán actividad como fotosensibilizadores y sistemas liberadores de fármacos. Los estudiantes participantes en el proyecto adquirirán experiencia en la síntesis de sistemas metal-orgánicos, desarrollarán capacidades en la evaluación de las propiedades espectroscópicas de los sistemas obtenidos y aprenderán técnicas analíticas aplicables a la evaluación de interacciones supramoleculares entre las metalocajas y las estructuras de DNA. Se requiere experiencia básica en síntesis e interés por la química supramolecular y medicinal.*

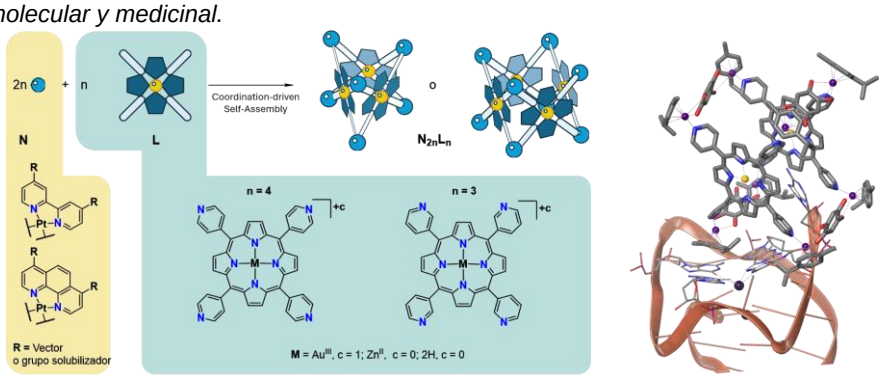


Figura 1. Representación esquemática de los sistemas a sintetizar y estructura optimizada de la interacción de una metalacaja con un G4

Referencias

1. *Xu, D., Li, Y., Yin, S. & Huang, F. Strategies to address key challenges of metallacycle/metallacage-based supramolecular coordination complexes in biomedical applications. Chemical Society Reviews 53, 3167–3204 (2024).*
2. *Willnhammer, N. et al. Post-assembly modification of Pt(II) metallacages provides an open door to medicinal applications. Cell Reports Physical Science 7, (2026).*
3. *Moreno-Alcántar, G. & Casini, A. Bioinorganic supramolecular coordination complexes and their biomedical applications. FEBS Letters 597, 191–202 (2023).*
4. *Rodíguez-Prieto, T. et al. A Golden Touch in the Design of Multifunctional Porphyrin Metallacages: Host–Guest Chemistry for Drug-Target Interactions. CCS Chemistry 6, 1662–1671 (2024).*
5. *Balasubramanian, S., Hurley, L. H. & Neidle, S. Targeting G-quadruplexes in gene promoters: a novel anticancer strategy? Nat Rev Drug Discov 10, 261–275 (2011).*

HIZKUNTZA(K): CASTELLANO E INGLES
TOKIA: CIC BIOMAGUNE
IKERKETA TALDEA: SUPRAMOLECULAR INORGANIC BIOSYSTEMS

WEBGUNEA: **WWW.CICBIOMAGUNE.ES**

POSTU KOPURUA: 3

ARDURADUNA: GUILLERMO MORENO ALCÁNTAR

HARREMANETARAKO POSTA ELEKTRONIKOA: gmorenoalcantar@cicbiomagune.es

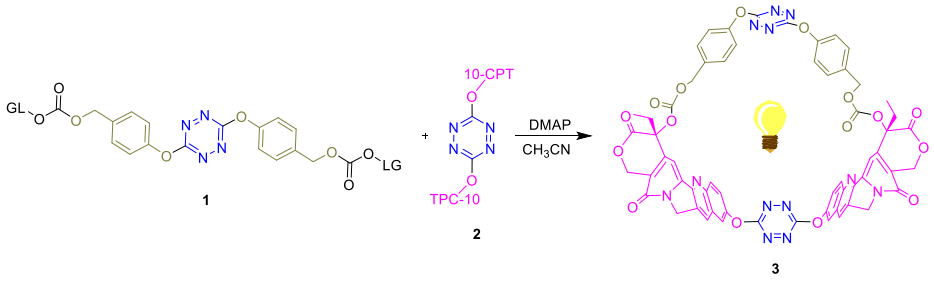
- Arabako Campusa

IZENBURUA: Tetrazine-based dual self-immolative systems as releasers of TopI inhibitor.

LABURPENA:

This Final Master's Thesis project aims to explore the development of novel dual-action prodrugs through the synthesis of tetrazine-based self-immolative systems. These systems are designed to release Topoisomerase I (TopI) inhibitors—such as camptothecin (CPT) derivatives—upon activation by intracellular triggers like hydrogen sulfide (H_2S), a stimulus overexpressed in certain tumor environments.
The project integrates multiple areas of medicinal chemistry: organic synthesis of tetrazine derivatives, preparation of self-immolative linkers, molecular docking studies, and biological evaluation. Once the prodrug is assembled, its capacity to protect the drug from premature degradation and selectively release it under tumor-like conditions will be evaluated.

The student will acquire advanced experimental skills in synthetic organic chemistry (including multistep synthesis and purification), gain experience in analytical techniques (NMR, MS, HPLC), and perform in vitro biological assays (TopI inhibition, cytotoxicity in human cancer cell lines such as A-549, SKOV3, HTC-116, and the non-cancerous MRC-5 line). Additionally, computational chemistry tools will be used to support the rational design of the self-immolative systems



HIZKUNTZA(K): Euskara, Gaztelania, Ingelesa
TOKIA: Farmazia Fakultatea, UPV/EHU, Vitoria-Gasteiz
IKERKETA TALDEA: Sintesi Organikoa Medikuntza-Kimikan
WEBGUNEA: www.ehu.eus/eus/web/pfq/hasiera
POSTU KOPURUA: 2
ARDURADUNA: Concepción Alonso Pérez, Endika Martín Encinas
HARREMANETARAKO POSTA ELEKTRONIKOA: endika.martin@ehu.eus

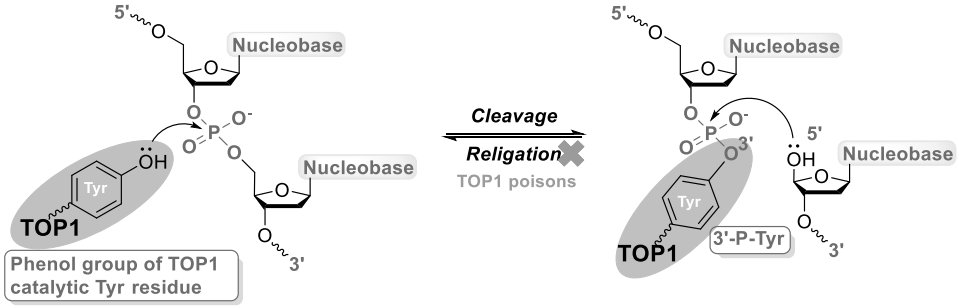
IZENBURUA: Design and synthesis of heterocyclic enzyme inhibitors with anticancer, antileishmanial and antibacterial activity.

LABURPENA:

This TFM project focuses on the design and synthesis of novel heterocyclic compounds as enzyme inhibitors with potential biological activity in three areas of major therapeutic interest: cancer, leishmaniasis and bacterial infections. The project is based on the strategic modification of heterocyclic cores known to interact with key enzymes involved in cell proliferation, parasite survival or bacterial resistance.

The student will be involved in the rational design of small molecules, multistep organic synthesis, purification, and complete characterization using analytical techniques such as NMR, MS, IR, and HPLC. Biological evaluation will include in vitro screening assays in collaboration with specialized research groups, aiming to assess cytotoxicity, enzymatic inhibition, and antimicrobial activity.

This multidisciplinary project combines medicinal chemistry, synthetic organic chemistry, and drug discovery. It is particularly suitable for students interested in the early stages of drug design and the development of new therapeutic agents aligned with global health challenges



HIZKUNTZA(K): Euskara, Gaztelania, Ingelesa
TOKIA: Farmazia Fakultatea, UPV/EHU, Vitoria-Gasteiz
IKERKETA TALDEA: Sintesi Organikoa Medikuntza-Kimikan
WEBGUNEA: www.ehu.eus/eus/web/pfq/hasiera
POSTU KOPURUA: 2
ARDURADUNA: Concepción Alonso Pérez, María Fuertes Sánchez
HARREMANETARAKO POSTA ELEKTRONIKOA: maria.fuertes@ehu.eus

IZENBURUA: Synthesis of novel cinnoline-phosphonate hybrids through Pd-catalyzed coupling of allenes and diazobenzenes

LABURPENA

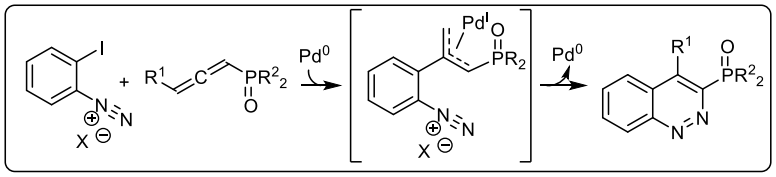
The practice of polypharmacology is not a new concept, but the approaches adopted to administer two or more bioactive entities for the treatment of a disease have evolved over time. The current form of polypharmacology is gaining popularity in the form of hybrid molecules (multi-ligand approach) through the development of molecular entities capable of modulating multiple targets. Over the last few decades, the synthesis of hybrid molecules by combining different biologically relevant moieties has been steadily increasing, along with their evaluation as pharmacological agents.[1]

In this regard, cinnolines are an important class of bicyclic diazines that have emerged as versatile and pharmacologically valuable scaffolds, which enables diverse chemical functionalization and precise modulation of biological interactions across multiple therapeutic areas.[2] Moreover, It is well known that structural modifications of active molecules involving the introduction of phosphorated functionalities, very often results in increased (or new) activities. Due to the stability of its P-C bond and their chemical similitude to phosphate ester and anhydride metabolites, phosphonate derivatives show an assorted biological activity and, consequently, they have found numerous applications in medicine and agrochemistry.[3]

Typical approaches for the synthesis of cinnolines involve the Richter cyclization as well as the related Widman–Stoermer and Borsche–Herbert reactions.[4] Interestingly, t**here are not precedents in the literature regarding the use of allenes** in the synthesis of cinnolines while, in the other hand, **there is not a general method described so far for the synthesis of phosphorated cinnolines**.

Considering this gap in the research field and with the aim of developing new synthetic strategies for biologically valuable phosphorated heterocyclic compounds, **the general objective of this Master's Thesis** will be the development of a **new general synthetic methodology for the synthesis of phosphorus-containing cinnolines** through a Pd-catalyzed coupling of phosphorated allenes and aromatic diazocompounds, which are readily available starting materials as described in Scheme 1.

The fact that the starting materials in this project can be easily synthesized from commercially available substrates makes this project ideal not only for the training of master's students, but also for the rapid generation of publishable results within a short period of time.



Scheme 1. General objective. Synthesis of phosphorated cinnolines from azocompounds and phosphorated allenes.

References

1) Shaveta, Mishra, S.; Singh, P. Hybrid molecules: The privileged scaffolds for various pharmaceuticals. *Eur J Med Chem.* **2016**, *124*, 500.

2) *a)* Nafie, M. S.; Fahmy, S. A.; Kahwash, S. H.; Diab, M. K.; Dawood K. M.; Abbas, *RSC Adv*. **2025**, *15*, 5597. *(b)* Szumilak M.; Stanczak, A. *Molecules* **2019**, *24*, 2271.

3) Kafarski, P. In: Contemporary Topics about Phosphorus in Biology and Materials. IntechOpen, **2019**.

4) *(a)* Vinogradova O. V.; Balova, I. A. *Chem. Heterocycl. Compd*. **2008**, *44*, 501 *(b)* Leonard, N. J. *Chem. Rev.* **1945**, 37, 269.

HIZKUNTZA(K):, gaztelania, ingelesa, euskara

TOKIA: Kimika Organikoa I Saila. Farmazia Fakultatea, EHU, (Vitoria-Gasteiz)

IKERKETA TALDEA: Sintesi Organikoa Kimika Medikoan (OSMC)

WEBGUNEA: https://www.ehu.eus/eu/web/pfq/hasiera

POSTU KOPURUA: 1

ARDURADUNA(K): JAVIER VICARIO (ORCID: 0000-0002-8976-0991**),), JESÚS M. DE LOS SANTOS (ORCID:** 0000-0003-1315-4263)

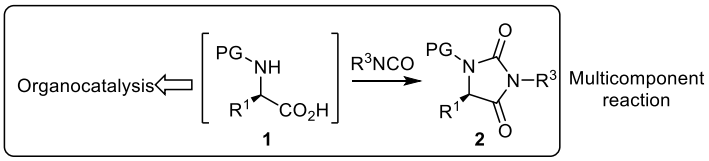
HARREMANETARAKO POSTA ELEKTRONIKOA: javier.vicario@ehu.eus / jesus.delossantos@ehu.eus

IZENBURUA: Organocatalyzed Enantioselective Multicomponent Reactions for the Design of Hybrid Molecules with a Hydantoin Core

LABURPENA

The practice of polypharmacology is not a new concept, but the approaches adopted to administer two or more bioactive entities for the treatment of a disease have evolved over time. The current form of polypharmacology is gaining popularity in the form of hybrid molecules (multi-ligand approach) through the development of molecular entities capable of modulating multiple targets. Over the last few decades, the synthesis of hybrid molecules by combining different biologically relevant moieties has been steadily increasing, along with their evaluation as pharmacological agents. [1]

In this regard, it is well known that hydantoin derivatives possess exceptional pharmacological characteristics and exhibit a broad spectrum of activities against, for example, cancers, microbial infections, metabolic diseases, and epilepsy.[2] In this context, one of the simplest methods for the modification of the hydantoin skeleton consists of the Urech-Read reaction, in which an α-amino acid derivative reacts with an isocyanate to give a urea that subsequently undergoes intramolecular cyclization.



Scheme 1. General objective. Urech-Read reaction of α-aminoacids **1** generated *in situ.*

The in situ generation of α-amino acids **1** in the presence of isocyanates is a very suitable method for the development of multicomponent methodologies leading to hydantoin derivatives **2**. These types of multicomponent strategies, where three or more compounds react simultaneously to yield a new molecular entity, are highly valuable in organic chemistry due to the various advantages that they offer if compared to classical sequential reactions.[3]

Depending on the origin of the α-amino acids **1** (R^1), hybrids derived from different molecular entities can be obtained. Specifically, the Organic Synthesis in Medicinal Chemistry research group (OSMC) at the Faculty of Pharmacy of Vitoria-Gasteiz has successfully used this strategy for the preparation of γ-lactam derivatives as well as hybrids that feature a hydantoin core along with a second unit of tetrahydroquinoline, phosphonate, or indole.[4]

With the aim of expanding the synthetic utility of this protocol, **the general objective of this Master's Thesis** will be the development of new asymmetric multicomponent reactions, through the generation of new α-amino acid derivatives **1** using organocatalytic methodologies, which in the presence of isocyanates would lead to the enantioselective formation of hydantoin derivatives **2**.

References

1) Shaveta, Mishra, S.; Singh, P. Hybrid molecules: The privileged scaffolds for various pharmaceuticals. *Eur J Med Chem.* **2016**, *124*, 500.
2) Cho, S.; Kim, S.-H.; Shin, D. Recent applications of hydantoin and thiohydantoin in medicinal Chemistry. *Eur J Med Chem.* **2019**, *164*, 517.
3) Zhu, J.; Wang, Q.; Wang, M.-X. *(Eds.) Multicomponent Reactions in Organic Synthesis,* Wiley-VCH, Weinheim, 2015.
4) Some research of the group in MCR: a) del Corte, X.; Maestro, A.; Vicario, J.; Martínez de Marigorta, E.; Palacios, F. Brönsted-Acid-Catalyzed Asymmetric Three-Component Reaction of Amines, Aldehydes, and Pyruvate Derivatives. Enantioselective Synthesis of Highly Functionalized γ-Lactam Derivatives. *Org. Lett.* **2018**, *20*, 317. b) del Corte, X.; López-Francés, A.; Maestro, A.; Martínez de Marigorta, E.; Palacios, F.; Vicario, J. Brönsted Acid Catalyzed Multicomponent Synthesis of Phosphorus and Fluorine-Derived γ-Lactam Derivatives. *J. Org. Chem.* **2020**, *85*, 14369. c) López-Francés, A.; del Corte, X.; Serna-Burgos, Z.; de los Santos, J. M.; de Cózar, A.; Vicario, J. Chiral Self-Recognition in a Bispericyclic Cyclodimerisation Reaction of 1-Azadienes. *Org. Chem. Front.* **2023**, *10*, 6103.

HIZKUNTZA(K):, gaztelania, ingelesa, euskara

TOKIA: Kimika Organikoa I Saila. Farmazia Fakultatea, EHU, (Vitoria-Gasteiz)

IKERKETA TALDEA: Sintesi Organikoa Kimika Medikoan (OSMC)

WEBGUNEA: https://www.ehu.eus/eu/web/pfq/hasiera

POSTU KOPURUA: 1

ARDURADUNA(K): JAVIER VICARIO (ORCID: 0000-0002-8976-0991**), XABIER DEL CORTE (ORCID:** 0000-0002-6973-0912).

HARREMANETARAKO POSTA ELEKTRONIKOA: javier.vicario@ehu.eus JAVIER VICARIO (ORCID: 0000-0002-8976-0991**), XABIER DEL CORTE (ORCID:** 0000-0002-6973-0912).

IZENBURUA: Design and synthesis of high added-value organic materials for electrochemical storage

LABURPENA:
Organic Chemistry provides a vast chemical space for the development of materials, offering numerous possibilities for addressing global challenges. The scientific community has increasingly focused its attention on organic materials as solutions for these challenges, especially in the context of the energy transition. Organic materials play a crucial role in various technologies, including electric vehicles through lithium batteries and in the integration of renewable energy via Na-ion and redox flow batteries. The inherent tunability of organic compounds, achieved through rational design of their structure, enables the development of materials with specific properties such as voltage stability, solubility, and thermal stability.

Organic materials are utilized in several key applications:

- **Flame retardants or additives** in electrolyte formulations for the safe operation of next-generation lithium batteries.[3]
- **Active materials** in organic batteries, providing a sustainable alternative to critical raw materials like vanadium and cobalt.
- **Fluorine-free ionically conductive salts** for sustainable Na-ion batteries that can operate effectively at low temperatures.
- **Plasticizers** in safe, solid electrolytes for non-flammable, high-capacity lithium metal batteries, designed to meet the growing global energy demand.

This project will focus on the design and synthesis of high-performance organic materials to improve the efficiency, sustainability, and safety of electrochemical storage devices.

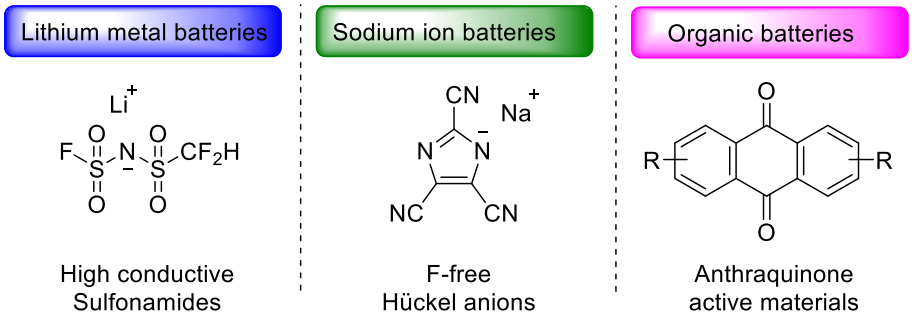


Figure 1. Schematic illustration of CIC energiGUNE developed materials for Lithium metal batteries; Sodium -ion batteries and Organic flow batteries, respectively.

HIZKUNTZA(K): English, Castellano, Euskara
TOKIA: CIC energiGUNE, Parque Tecnológico de Álava (Vitoria-Gasteiz)
IKERKETA TALDEA: Organic and Hybrid materials
WEBGUNEA: **www.cicenergigune.com**
POSTU KOPURUA: 1
ARDURADUNA: Eduardo Sánchez / María Martinez
HARREMANETARAKO POSTA ELEKTRONIKOA: esanchez@cicenergigune.com

[3] Q. Lixin et al. *Nature Materials* **2022**, *21*, 455–462.