



SIMPOSIO NACIONAL DE QUÍMICA ORGÁNICA  
CÓRDOBA - ARGENTINA 2021



### Estimados colegas,

Como comunicáramos en la segunda circular de esta XXIII SINAQO, aprovechando los desafíos y oportunidades que nos brinda esta situación tan particular, hemos decidido incluir en el marco de las actividades virtuales del SINAQO, tres Ciclos de Conferencias denominados XXIII SINAQO - Virtual Opening Meetings (VOMs). A continuación, les hacemos llegar el programa y detalles del **XXIII SINAQO - 1st Virtual Opening Meeting: From Basic Organic Chemistry to Health Applications - 1ra VOM Desde la Química Orgánica Básica a las Aplicaciones en Salud**, a realizarse el día 24 de junio del corriente:

**8:55 - 9:00 am (ARG time):** Opening Remarks

**9:00 - 9:40 am (ARG time):** Conference Dr. Hideaki Shirota (Department of Chemistry, Chiba University, Japan), Moderator: Dra. Lydia Bouchet

**9:40 - 10:20 am (ARG time):** Conference Dr. Marcelo Calderón ( Polymat - Basque Center for Macromolecular Design and Engineering / University of the Basque Country), Moderator: Dra. Lydia Bouchet

**10:20 - 11:00 am (ARG time):** Conference Dr. Diego Muñoz-Torrero ( Faculty of Pharmacy and Food Sciences, University of Barcelona), Moderator: Dra. Lydia Bouchet

**11:00 am (ARG time):** Closing Remarks and 2nd VOM presentation

¡Esperamos contar con su participación!!!

Cordialmente,

**Comisión Organizadora  
XXIII SINAQO**



## HEAVY ATOM SUBSTITUTION EFFECTS ON LIQUID PROPERTIES OF IONIC LIQUIDS

**Hideaki Shiota & Masatoshi Ando**

*Department of Chemistry, Chiba University*

*1-33 Yayoi, Inage-ku, Chiba 263-8522, JAPAN*

E-mail: [shiota@faculty.chiba-u.jp](mailto:shiota@faculty.chiba-u.jp)

### Key Words: Ionic Liquid, Heavy Atom Substitution, Viscosity

Room temperature ionic liquids (ILs) are molten salts at ambient temperatures. ILs are very unique, because they are non-volatile at standard ambient conditions and show relatively high electrical conductivities. One of the most fascinating features in the ILs is their property control. By tuning the combination of cation and anion, the properties of ILs can be varied as desired. Accordingly, the basic science and application for ILs are getting more attentions in these ten to twenty years.<sup>1</sup>

A unique feature of ILs compared (neutral) molecular liquids is heavy atom substitution effect of ion species on liquid properties, such as viscosity.<sup>2</sup> For example, the viscosities at 297 K of 1-butyl-3-methylimidazolium-based ILs with the anions of  $[\text{PF}_6]^-$ ,  $[\text{AsF}_6]^-$ , and  $[\text{SbF}_6]^-$  are 290 cP, 228 cP, and 134 cP, respectively.<sup>3</sup> This trend of the viscosities in these ILs to the molecular weights of the anion species is opposite to that in common solvents (e.g., 0.224 cP in  $(\text{C}_2\text{H}_5)_2\text{O}$  and 0.422 cP in  $(\text{C}_2\text{H}_5)_2\text{S}$ ). This similar unique feature was observed in other ILs.<sup>2</sup>

Recently, our group has successfully synthesized novel phosphonium-based ILs, whose cations having thioether functional groups.<sup>4</sup> Unlike the other ILs, thioether group substituted phosphonium-based ILs show larger viscosities than the respective ether group substituted phosphonium-based ILs, e.g., 91.6 cP in triethyl[2-(ethylthio)ethyl]phosphonium bis(fluorosulfonyl)amide and 35.6 cP in triethylethoxyethylphosphonium bis(fluorosulfonyl)amide. In this talk, I will review typical heavy atom substitution effects on the liquid properties of ILs, and then discuss the distinguished features in the phosphonium-based IL together with the respective control ILs. Some spectroscopic observations by low-frequency vibrational spectroscopic techniques will also be discussed.

### Acknowledgments:

This work was supported by JSPS KAKENHI (19K05382), Takahashi Industrial and Economic Research Foundation, and Marubun Research Promotion Foundation.

### References:

- 1- *Ionic Liquids in Synthesis*; 2 ed.; Wasserscheid, P.; Welton, T.; Eds.; Wiley-VCH: Weinheim, **2008**.
- 2- *Ionic Liquids: Theory, Properties, New Approaches*, Shiota, H.; Fukazawa, H.; Alexander Kokorin, Ed. (InTech: Rijeka, Croatia) **2011**, 201–224 (Chapter 9).
- 3- Shiota, H.; Nishikawa, K.; Ishida, T. *J. Phys. Chem. B* **2009**, *113*, 9831-9839.
- 4- Shiota, H.; Takahashi, K.; Ando, M.; Kakinuma, S. *J. Chem. Eng. Data* **2019**, *64*, 4701-4707 (Special Issue on Celebrating Our High Impact Authors).

## BIODEGRADATION AS KEY FEATURE TO CROSS BIOLOGICAL BARRIERS: DESIGN OF SENSITIVE LINKERS TO YIELD MUCOSE- AND TUMOR-PENETRATING NANOGELS

Marcelo Calderón<sup>a,b</sup>

<sup>a</sup>POLYMAT and Applied Chemistry Department, Faculty of Chemistry, University of the Basque Country UPV/EHU, Paseo Manuel de Lardizabal 3, 20018 Donostia-San Sebastián, Spain.

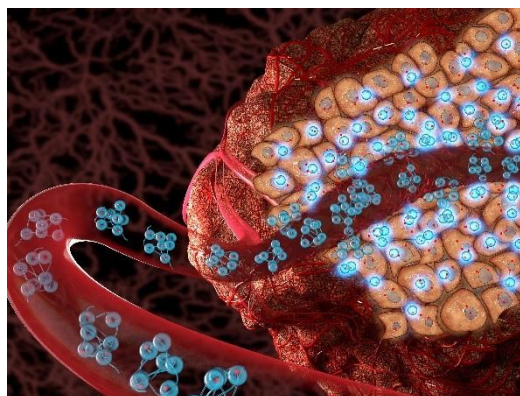
<sup>b</sup>IKERBASQUE, Basque Foundation for Science, 48013 Bilbao, Spain.

E-mail: [marcelo.calderon@polymat.eu](mailto:marcelo.calderon@polymat.eu). Homepage: [www.polymat.eu](http://www.polymat.eu)

### Keywords: drug delivery, polymeric nanocarriers, smart nanogels

The term nanogel (NG) refers to nanometer-sized crosslinked polymeric networks that reveal intrinsic properties ideal for biomedical applications, i.e. high water content, soft nature, cell and tissue compatibility, and excellent water dispersability/solubility. Therefore, NGs are commonly developed as drug carriers that can shrink, swell or be degraded, expelling or absorbing large amounts of water, selectively releasing their cargo in response to environmental stimuli. We have developed synthetic procedures that allow to use dendritic polyglycerols (dPG) as multifunctional anchoring points for the coupling of bioactives through redox- or enzyme-sensitive linkers, and for the synthesis of environmentally responsive NGs. As example, we have developed matrix metalloproteinase (MMP)-sensitive peptide-crosslinked nanogels (pNGs) with beneficial size shrinking property for deep tumor penetration (see figure).

The intrinsic reporter moiety of the crosslinker was exploited to study the degradation of pNGs with different compositions and their tumor penetration.<sup>1</sup> Moreover, we prepared several thermoresponsive NGs and nanocapsules (NCs) as drug delivery systems based on dPG as a macro-crosslinker and different thermoresponsive polymers. Their synthesis, characterization, and potential application for topical drug delivery will be discussed.<sup>2</sup> Here, the synthesis, characterization, and potential application in topical protein delivery of thermo- and redox-responsive NGs is presented. The delivery of proteins such a Etanercept,<sup>3</sup> will be discussed as anti-inflammatory treatment in several skin/mucose related diseases.



### Acknowledgments:

The author gratefully acknowledges financial support from IKERBASQUE- Basque Foundation for Science, MINECO project RTI2018-099227-B-I00, and Diputación Foral de Gipuzkoa project 2020-GAIX-000004-01.

### References:

- 1- Nagel, G.; Sousa-Herves, A.; Wedepohl, S.; Calderón, M. *Theranostics* **2020**, *10*, 91.
- 2- Tiwari, N.; Sonzogni, A. S.; Calderón, M. *Nanomedicine (Lond.)* **2019**, *14*, 2891.
- 3- Charbaji, R.; Kar, M.; Theune, L. E.; Bergueiro, J.; Eichhorst, A.; Stumpff, F.; Calderón, M.;\* Hedtrich, S.\* *Small* **2021**, 2007963.

## LA COMPLEJIDAD ESTRUCTURAL COMO RECURSO PARA EL TRATAMIENTO DE LA ENFERMEDAD DE ALZHEIMER

Diego Muñoz-Torrero

Laboratory of Medicinal Chemistry, Institute of Biomedicine (IBUB) – Drug and Target Discovery

Faculty of Pharmacy and Food Sciences. University of Barcelona.

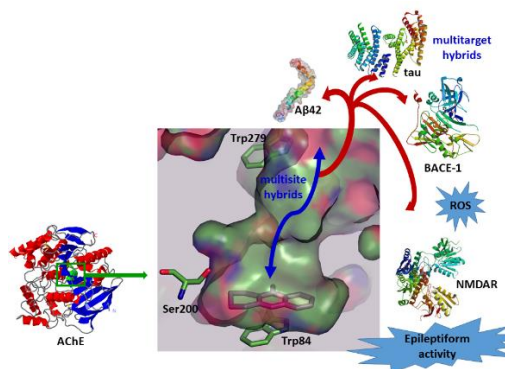
Av. Joan XXIII, 27-3108028-Barcelona (Spain)

E-mail: [dmunoztorrero@ub.edu](mailto:dmunoztorrero@ub.edu)

**Palabras clave:** Hibridación molecular; Reacciones multicomponente; Compuestos multidiana.

En diseño de fármacos, la optimización de compuestos modelo (*hits*, *leads*) suele implicar el mantenimiento o la disminución del nivel de complejidad estructural inicial, ya que se asume que únicamente las moléculas sencillas van a tener propiedades fisicoquímicas y farmacocinéticas adecuadas para su uso como fármacos (*drug-like properties*). Sin embargo, en ocasiones el diseño de compuestos estructuralmente más complejos que los modelos iniciales puede resultar beneficioso en el perfil farmacológico de estos análogos, sin comprometer su eficacia *in vivo*.

En esta ponencia se van a presentar ejemplos de diseño de candidatos a fármacos contra la enfermedad de Alzheimer, en los que se ha recurrido a la complejidad estructural mediante el uso de reacciones multicomponente y técnicas de hibridación molecular para conseguir notables aumentos de potencia o efectos frente a múltiples dianas involucradas en esta enfermedad.<sup>1-3</sup>



### Agradecimientos:

The author gratefully acknowledges financial support from Ministerio de Ciencia, Innovación y Universidades (MCIU), Agencia Estatal de Investigación (AEI) and FEDER (SAF2017-82771-R) and Generalitat de Catalunya (2017SGR106).

### Referencias:

- 1- Di Pietro, O.; Viayna, E.; Vicente-García, E.; Bartolini, M.; Ramón, R.; Juárez-Jiménez, J.; Clos, M. V.; Pérez, B.; Andrisano, V.; Luque, F. J.; Lavilla, R.; Muñoz-Torrero, D. *Eur. J. Med. Chem.* **2014**, *73*, 141–152
- 2- Di Pietro, O.; Pérez-Areales, F. J.; Juárez-Jiménez, J.; Espargaró, A.; Clos, M. V.; Pérez, B.; Lavilla, R.; Sabaté, R.; Luque, F. J.; Muñoz-Torrero, D. *Eur. J. Med. Chem.* **2014**, *84*, 107–117.
- 3- Viayna, E.; Coquelle, N.; Cieslikiewicz-Bouet, M.; Cisternas, P.; Oliva, C. A.; Sánchez-López, E.; Ettchetto, M.; Bartolini, M.; De Simone, A.; Ricchini, M.; Rendina, M.; Pons, M.; Firuzi, O.; Pérez, B.; Saso, L.; Andrisano, V.; Nachon, F.; Brazzolotto, X.; García, M. L.; Camins, A.; Silman, I.; Jean, L.; Inestrosa, N. C.; Colletier, J.-P.; Renard, P.-Y.; Muñoz-Torrero, D. *J. Med. Chem.* **2021**, *64*, 812–839.