TO MAGNIFICO RETTORE OF UNIVERSITA' DEGLI STUDI DI MILANO **ID CODE** _6386_____

I the undersigned asks to participate in the public selection, for qualifications and examinations, for the awarding of a type B fellowship at **Dipartimento di** Chimica dell'Università degli Studi di Milano

Scientist- in – charge: Prof.ssa Sattin Sara

[Laura Díaz Casado]

CURRICULUM VITAE

PERSONAL INFORMATION

Surname	Díaz Casado
Name	Laura

PRESENT OCCUPATION

Appointment	Structure
Postdoctoral Research Assistant March-2023 - present	Institute of Organic Chemistry (IQOG), CSIC, Madrid, Spain Supervisor: Dr. Juan Luis Asensio Álvarez Topic: Chemical strategies for the study of antifreeze glycopeptides: synthesis, structure and activity of non natural variants

EDUCATION AND TRAINING

Degree	Course of studies	University	year of achievement of the degree
Bachelor´s Degree	Chemistry	University Complutense of Madrid (UCM), Spain	2016
PhD	Organic Chemistry	University Complutense of Madrid (UCM), Spain	2023
MSc	Organic Chemistry	University Complutense of Madrid (UCM), Spain	2017

REGISTRATION IN PROFESSIONAL ASSOCIATIONS

Date of registration	Association	City
2019	Member of RSEQ (Real Sociedad Española de Química)	Madrid

FOREIGN LANGUAGES

Languages	level of knowledge
English	B2
Spanish	Native

AWARDS, ACKNOWLEDGEMENTS, SCHOLARSHIPS

Year	Description of award
2018	4 years-PhD Fellowship from the Ministry of Economy and Competitiveness (MINECO, Spain) 100.000€
2022	5-month extension of Training of research personnel fellowship (FPI) from the Ministry of Economy and Competitiveness (MINECO, Spain)
2022	Award a Travel Aid to attend the XIV Manuel Rico NMR School (100€). (Jaca Spain)
2023	Best Oral Presentation Award at the XXXIX Reunión Bienal de la Sociedad Española de Química de la RSEQ (150€) (Zaragoza, Spain)

TRAINING OR RESEARCH ACTIVITY

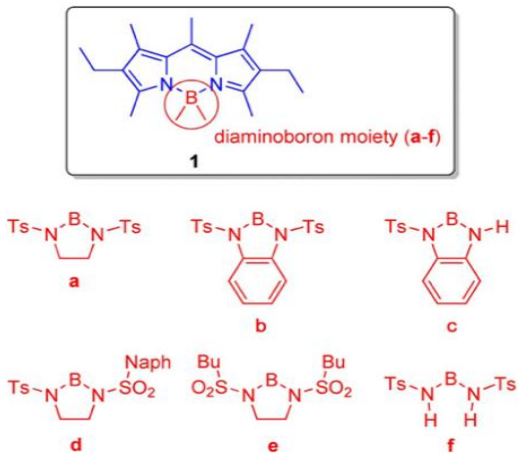


Figure 1. *N*-BODIPYs library developed.

I obtained my **university degree in Chemistry** in 2016 from University Complutense of Madrid. I had my first contact with research during my undergraduate stage through the optional subject: **research project**. This university program offered the opportunity to outstanding academic records students to begin a career in research. Thus, in 2015 I joined the group of **Prof. Cristóbal López** (Oligosaccharides and Glycosystems Group-CSIC), where I worked in the synthesis of new oligosaccharides dyes with biological applications. During this period, I learned how to work in an efficient and independent manner in a research group and acquired a multidisciplinary training in organic chemistry and carbohydrate synthesis.

Then, in 2016 I joined the group of **Prof. Santiago de la Moya** in the Complutense University of Madrid, where I worked in the synthesis of the first library of *N*-BODIPY (diaminoboron dipyrromethenes) dyes and analysed their photophysical properties (*Figure 1*). The substitutions around the nitrogen atoms, together with the multiple possibilities of derivatization patterns and straightforward synthetic access from accessible *F*-BODIPYs, make these molecules interesting scaffolds to develop improved photonic materials.

In 2018 I obtained a highly coveted national **PhD fellowship (FPI)** from the Ministry of Science and Innovation (MICCIN, Spain) to carry out my doctoral studies in the Institute of Organic Chemistry (IQOG-CSIC, Madrid) under the supervision of **Dr. Juan Luis Asensio Álvarez and Dr. Andrés González Santana**.

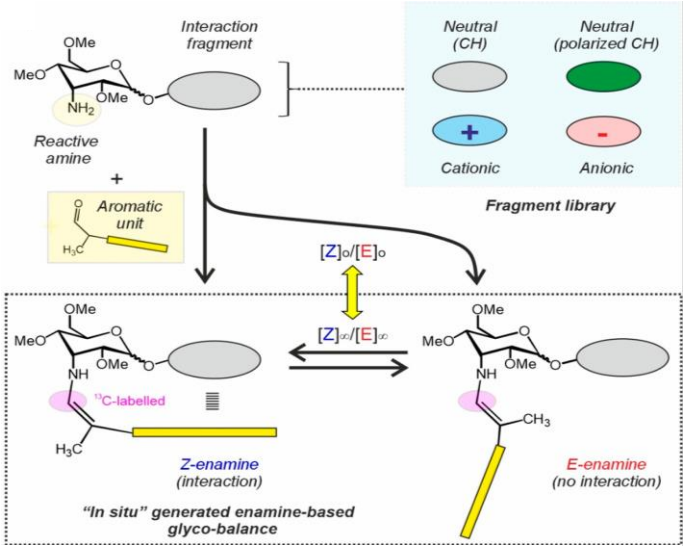


Figure 2. Schematic representation of the glycobalances generated *in situ*. Given that only the *Z*-isomer is compatible with the aromatic interaction.

The research area of the Asensio´s group lies within the Bioorganic Chemistry field, allowing me to expand my previous skills and knowledge. Specifically, the thesis project belonged to the **molecular recognition research** field and aimed to answer key questions of a fundamental and an applied character. The project goal was the systematic **study of the weak interactions** (CH/π, cation/π and anion/π) that involve aromatic systems in organic media and the precise **evaluation of their energetic contributions** by employing a novel **NMR approached based on molecular balances** (*Figure 2*).

Additionally, during this period in the IQOG, I also had the opportunity to participate in parallel projects related to **carbohydrates** and **molecular recognition of nucleic acids**.

Firstly, we addressed an experimental mechanistic study of glycosylation reactions involving glycosyl triflates was carried out. These highly reactive species are formed upon activation of common sugar donors, such as glycosyl sulfoxides or thioglycosides among others. Employing low temp. NMR, we **demonstrated that they exist as a mixture of *α*- and *β*- anomers in a fast exchange equilibrium** and both of them can participate in nucleophilic substitutions with alcohol acceptors through a continuum of **mechanisms spanning the gap between pure S_N2 and S_N1 processes** (*Figure 3*). Interestingly, chemical glycosylations with poorly nucleophilic acceptors seem to proceed with an enhanced α-selectivity, which could reflect the dominant role played in these circumstances by the minor, yet more reactive *β*-triflates or even glycosyl oxocarbenium-like species present in the reaction mixture. More recently, we focus our attention in **dissecting the mechanisms** involved in reactions with **glycosyl sulfoxides as a donor**. Reactions employing these donors are usually performed under pre-activation conditions, but an experimentally more convenient single-step protocol has also been reported, whereby activation is performed in the presence of the acceptor alcohol; yet, the nature and prevalence of the reaction intermediates formed in this more complex scenario have received minimal attention. Our efforts focused on the synthesis of different carbohydrates that incorporated a sulfoxide function in the anomeric position. Then we employed a systematic NMR-based study employing both ^{13}C-labelled and unlabelled glycosyl sulfoxide donors for the detection and monitoring of marginally populated intermediates (*Scheme 1*). The obtained results demonstrate that the formation of covalent donor/acceptor sulfonium adducts was identified as the main

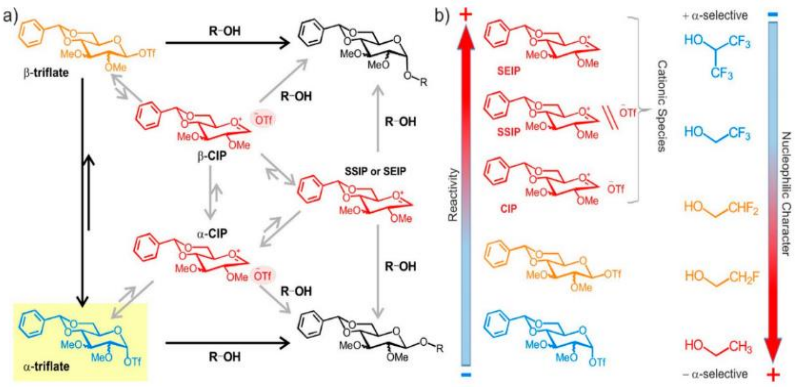
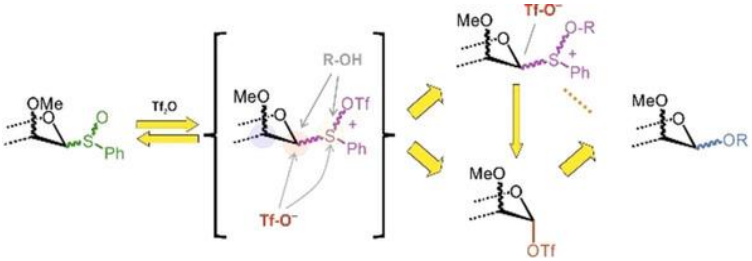


Figure 3. a) Representation of the multiple S_N2/S_N1 reaction pathways leading to the formation of α- and ß-glycosides from glycosyl triflate intermediates. CIP, SSIP, and SEIP stand for contact ion pair, solvent separated ion pair, and solvent equilibrated ion pair, respectively. (b) Reactivity gradient for the potential donor intermediates and acceptor alcohols.



Scheme 1. Triflates intermediates play a key role in glycosylation involving glycosyl sulfoxides, subsequently donor activation takes place in the presence of the acceptor alcohol

competing reaction, and thus a non-productive consumption of the acceptor that could limit the reaction yield was revealed.

In addition, I have been involved in the **design of selective ligands of DNA Duplex/Quadruplex Junctions motifs**, specifically, we have targeted the interface between DNA quadruplex and duplex regions by means of small molecules. In this communication we reported on a new pharmacophore that selectively binds with high affinity to quadruplex-duplex junctions, while presenting a poorer affinity for G-quadruplex or duplex DNA alone. Ligands complying with this pharmacophore exhibit a significant affinity and selectivity for quadruplex-duplex junctions, including the one observed in the HIV-1 LTR-III sequence. The structure of the complex between a quadruplex-duplex junction with a ligand of this family has been determined by NMR methods. According to these data, the remarkable selectivity of this structural motif for quadruplex-duplex junctions is achieved through an unprecedented interaction mode so far unexploited in medicinal and biological chemistry: the insertion of a benzylic ammonium moiety into the center of the partially exposed G-tetrad at the interface with the duplex (*Figure 4*). Further decoration of the described scaffolds with additional fragments opens up the road to the development of selective ligands for G-quadruplex-forming regions of the genome.

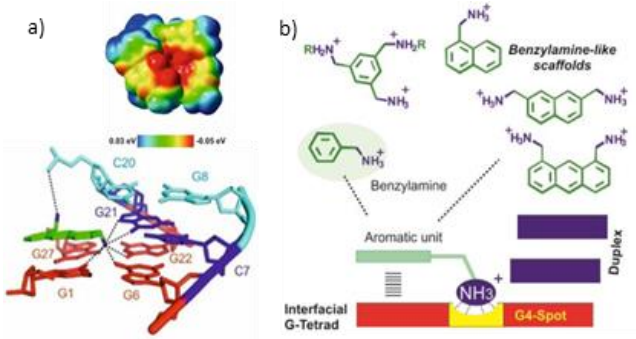


Figure 4. a) Unusual electrostatic potential of G-tetrads at the interface with a duplex in quadruplex–duplex junctions. b) Proposed binding mode for a benzylamine-like pharmacophore targeting the G4 spot.

Finally, I performed binding screens based on the **development of new NMR methodologies for the identification of DNA/RNA ligands in compound libraries**. We explored the scope and limitations of a strategy that makes use of a binding indicator previously unexploited by NMR: the perturbation of the ligand reactivity caused by complex formation. This approach was first done on a ligand mixture in the presence of a nucleic acid receptor. By employing a reductive amination reaction with ^{12}C-FMA (formaldehyde), only the unprotected groups were methylated; then, we removed the receptor with via enzymatic digestion and in the last step, the reaction mixture was methylated in this case with ^{13}C-FMA to increase the sensitivity of the best binders (*Figure 5a*). The subtraction of the corresponding HSQC spectra in presence and in absence

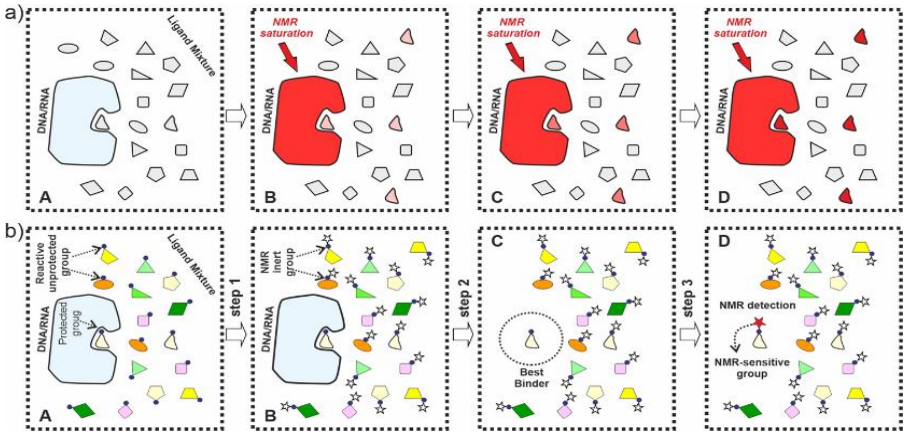


Figure 5. a) STD-NMR experiment commonly used for the identification of binders. Upon saturation of the receptor signals, magnetisation is transferred to the ligands. b) Strategy for a reactivity-based screening protocol. The expected decrease in ligand reactivity associated to complex formation is exploited to preferentially label the best binders within a mixture of candidates.

of the receptor reveals the best binders within mixtures of significant complexity, providing a conceptually different reactivity-based alternative within NMR screening methods (*Figure 5b*).
Currently, I have continued working as a Postdoctoral research assistant in the group of Dr. Juan Luis Asensio, again at the Institute of Organic Chemistry (IQOG) in Madrid. Here, I am involved in several projects that tackle **synthesis and functionalization of carbohydrates and cyclodextrins**. The extensive work carried out in the first years of my professional career proves that I have a well-rounded scientific background in Bioorganic Chemistry that will give me a great prospect to construct a future independent career.

PROJECT ACTIVITY

Year	Project
2018-2020	"Studies on molecular recognition of glycosides: molecular bases and optimization of bioactive compounds" Ministry of Economy and Competitiveness (MINECO, Spain) PI: Dr. Juan Luis Asensio Álvarez.
2020-Present	"Design and synthesis of molecular balances based on carbohydrate/aromatic models, analysis of cation/π, anion/π and CH/π interactions. Synthesis of aromatic systems with isotopic labeling." Ministry of Economy and Competitiveness (MINECO, Spain) PI: Dr. Juan Luis Asensio Álvarez (2020-present).

CONGRESSES AND SEMINARS

Date	Title	Place
2024	7th Iberian Carbohydrate Meeting **Oral communication**: "Illuminating a Solvent-dependent Hierarchy for Aromatic CH/π Complexes with Dynamic Covalent Glyco-Balances"	Sitges, Spain
2023	Autumn GERMN NMR Day **Attended**	Madrid, Spain
2023	XXXIX Reunión Bienal de la Sociedad Española de Química de la RSEQ **Oral communication and poster presentation**: "Binding-driven reactivity attenuation enables NMR identification of selective drug candidates for nucleic acid targets"	Zaragoza, Spain
2022	Summer School in Biomedical Glycoscience (RSEQ) **Poster presentation:** "Dissecting the essential role of anomeric ß-Triflates in glycosylation reactions"	Jaca, Spain
2022	Scientific conference of the Institute of Organic Chemistry (IQOG) **Oral communication:** "Design of molecular balances for the quantification of aromatic interactions"	Madrid, Spain
2021	RESQ Symposium (Real Sociedad de Química) **Poster presentation:** "De Novo Design of Selective Quadruplex-Duplex Junction Ligands and Structural Characterisation of their Binding Mode: Targeting the G4 Hot-Spot"	Online
2021	VII Young Researchers Symposium	Online

	Poster presentation: "De Novo Design of Selective Quadruplex-Duplex Junction Ligands and Structural Characterisation of their Binding Mode: Targeting the G4 Hot-Spot"	
2021	European Chemical Biology Symposium **Attended**	Online
2019	Workshop on Biomedical Glycoscience **Attended**	San Sebastián, Spain
2018	One day Symposium: Research in Carbohydrates **Attended**	Sevilla, Spain
COURSE		
2022	XIV "Manuel Rico" NMR Summer School (24 h)	Jaca, Spain

PUBLICATIONS

Articles in reviews
Díaz-Casado L., Villacampa A., Corzana F., Jiménez-Barbero J., Gómez A.M., González A., Asensio J.L. ¨**Illuminating a Solvent-dependent Hierarchy for Aromatic CH/π Complexes with Dynamic Covalent Glyco-Balances**¨ *JACS Au*, **2024**, DOI: 10.1021/jacsau.3c00592
Díaz-Casado L., González A., Gómez-Pinto I., Villacampa A., Corzana F., Jiménez-Barbero J., González C., Asensio J.L. ¨**Binding-driven reactivity attenuation enables identification of selective drug candidates: an innovative NMR-based screening strategy for Nucleic Acid targets**¨ *Commun Chem.* **2022**, *5*, 137. DOI: 10.1038/s42004-022-00755-8
González A., **Díaz-Casado L**., Montalvillo L., Jiménez-Moreno E., Mann E., Asensio J.L. ¨**Aromatic Interactions in Glycochemistry: From Molecular Recognition to Catalysis**¨ *Curr. Med. Chem*. **2022**, *29*, 1208. DOI: 10.2174/0929867328666210709120216
Díaz-Casado L., Serrano-Chacón I., Montalvillo L., Corzana F., Bastida A., González C., Asensio J.L. ¨**De Novo Design of Selective Quadruplex-Duplex Junction Ligands and Structural Characterisation of Their Binding Mode: Targeting the G4 Hot-Spot**¨ *Chem. Eur. J.*, **2021**, *27*, 6204. DOI: 10.1002/chem.202005026
González A., Montalvillo L., **Díaz-Casado L.**, Mann E., Jiménez-Barbero J., Gomez A.M., Asensio J.L. ¨**Single-Step Glycosylations with ^{13}C-Labelled Sulfoxide Donors: A Low-Temperature NMR Cartography of the Distinguishing Mechanistic Intermediates**¨ *Chem. Eur. J.* **2021**, 27, 2030. DOI: 10.1002/chem.202003850
González A., Montalvillo L., **Díaz-Casado L.**, Corzana F., Merino P., Cañada J.F., Jiménez-Osés G., Jiménez-Barbero J., Gomez A.M., Asensio J.L. ¨**Dissecting the Essential Role of Anomeric ß-Triflates in Glycosylation Reactions**¨ *J. Am. Chem. Soc.* **2020**, 142, 28, 12501. DOI: 10.1021/jacs.0c05525
Ray C., **Díaz-Casado L.**, Avellanal E., Bañuelos J., Cerdán L., García-Moreno I., Moreno F., L. Maroto B., López-Arbeloa I., de la Moya S. ¨**N-BODIPYs Come into Play. Smart Dyes for Photonic Materials**¨ *Chem. Eur. J.* **2017**, *23*, 9383. DOI: 10.1002/chem.201701350

OTHER INFORMATION

PROFESSIONAL EXPERTISE

- **Multi-step synthesis** of complex organic molecules involving functional group transformation.
- Optimization of synthetic methods using inert-handling techniques, conventional and microwave reaction setups.
- **Isotopic labelling** with ^{13}C reagents in order to facilitate NMR detection of reaction intermediates.
- Mono- and bidimensional **NMR analysis**, including variable temperature NMR and reaction kinetics.
- Experience in NMR (Nuclear Magnetic Resonance, Bruker 600 MHz), Infrared Spectroscopy (PerkinElmer FT-IR) and UV-Visible Spectroscopy (Carry series 100 UV-Vis. Spectrometer)
- Experience in HRMS and HPLC purification.
- Experience in chemical literature searches using SciFinder, Reaxys and Web of Science.
- Operating Systems-M.S. Office Package with an excellent PowerPoint presentation skill, MestReNova, TopSpin, ChemBioDraw, Pymol, CorelDRAW, Derive and Origin.
- Problem-solving skills, attention to detail, collaborating with cross-functional teams and a commitment to staying current with science advancements.

TEACHING ACTIVITIES:

09/2021-present Supervision of a PhD student
Group of Dr. Juan Luis Asensio, Institute of Organic Chemistry (IQOG, CSIC), Madrid, Spain

03/2019-07/2019 Supervision of an undergraduate student
Group of Dr. Juan Luis Asensio, Institute of Organic Chemistry (IQOG, CSIC), Madrid, Spain

OTHER SKILLS:

Ability to work on multiple projects under minimal supervision. Excellent organizational skills, experimental planning and problem solving. Extensive experience writing reports and documenting experiments, presenting data at laboratory or departmental meetings, seminars and scientific conferences.

I am a talented young researcher with outstanding expertise at the interface between chemistry and biology a multidisciplinary training. I gained a solid background of organic chemistry which was further expanded during my undergraduate, PhD and Postdoc period. During this time, I also gained an expertise in bioorganic chemistry including carbohydrate and aromatic chemistry and nuclear magnetic resonance (NMR) spectroscopy. This multidisciplinary training has led to the formation of an independent, versatile and creative researcher whose learning capacity speaks for itself and is demonstrated by her research outputs. The proposed research is an excellent fit, as I have ample experience in the areas this proposal will have high demands of (organic chemistry and NMR structural analysis) from my post-graduate and current postdoctoral work.

Declarations given in the present curriculum must be considered released according to art. 46 and 47 of DPR n. 445/2000.

The present curriculum does not contain confidential and legal information according to art. 4, paragraph 1, points d) and e) of D.Lgs. 30.06.2003 n. 196.

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Place and date: _____Madrid (Spain)_____, _____06/02/2024_____