



**HAL**  
open science

## Synthesis and chelation study of a fluoroionophore and a glycopeptide based on an aza crown iminosugar structure

Alexandra Bordes, Ana Poveda, Nathalie Fontelle, Ana Ardá, Jérôme Guillard, Yi Bin Ruan, Jérôme Marrot, Shuki Imaeda, Atsushi Kato, Jérôme Désiré, et al.

► **To cite this version:**

Alexandra Bordes, Ana Poveda, Nathalie Fontelle, Ana Ardá, Jérôme Guillard, et al.. Synthesis and chelation study of a fluoroionophore and a glycopeptide based on an aza crown iminosugar structure. Carbohydrate Research, 2021, 501, pp.108258. 10.1016/j.carres.2021.108258 . hal-04336072

**HAL Id: hal-04336072**

**<https://hal.science/hal-04336072v1>**

Submitted on 12 Apr 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Title :** Synthesis and Chelation Study of a Fluoroionophore and a Glycopeptide based on an Aza Crown Iminosugar Structure

**Authors names and affiliations :**

Alexandra Bordes,<sup>a</sup> Ana Poveda,<sup>b</sup> Nathalie Fontelle,<sup>a</sup> Ana Ardá,<sup>b</sup> Jérôme Guillard,<sup>a</sup> Yi Bin Ruan,<sup>c</sup> Jérôme Marrot,<sup>d</sup> Shuki Imaeda,<sup>e</sup> Atsushi Kato,<sup>e</sup> Jérôme Désiré,<sup>a</sup> Juan Xie,<sup>c\*</sup> Jesús Jiménez-Barbero,<sup>b,f,g\*</sup> Yves Blériot<sup>a\*</sup>

<sup>a</sup> *Université de Poitiers, IC2MP, UMR CNRS 7285, Equipe "Synthèse Organique", Groupe Glycochimie, 4 rue Michel Brunet, 86073 Poitiers cedex 9, France*

*e-mail: [yves.bleriot@univ-poitiers.fr](mailto:yves.bleriot@univ-poitiers.fr)*

<sup>b</sup> *CICbioGUNE, Parque Tecnológico de Bizkaia, Derio-Bizkaia 48160, Spain*

*e-mail: [jjbarbero@cicbiogune.es](mailto:jjbarbero@cicbiogune.es)*

<sup>c</sup> *Université Paris-Saclay, ENS Paris-Saclay, CNRS, Photophysique et Photochimie Supra- et Macromoléculaires (PPSM), , 4 avenue des sciences 91190 Gif-sur-Yvette, France.*

*e-mail : [joanne.xie@ens-cachan.fr](mailto:joanne.xie@ens-cachan.fr)*

<sup>d</sup> *Institut Lavoisier de Versailles, UMR-CNRS 8180, Université de Versailles, 45 avenue des États-Unis, 78035 Versailles Cedex, France*

<sup>e</sup> *Department of Hospital Pharmacy, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan*

<sup>f</sup> *IKERBASQUE, Basque Foundation for Science, 48009 Bilbao, Spain*

<sup>g</sup> *Dept. Organic Chemistry II, Faculty of Science and Technology, University of the Basque Country, 48940 Leioa, Spain*

**Corresponding author :**

Yves Blériot, *Université de Poitiers, IC2MP, UMR CNRS 7285, Equipe "Synthèse Organique", Groupe Glycochimie, 4 rue Michel Brunet, 86073 Poitiers cedex 9, France*

[yves.bleriot@univ-poitiers.fr](mailto:yves.bleriot@univ-poitiers.fr)

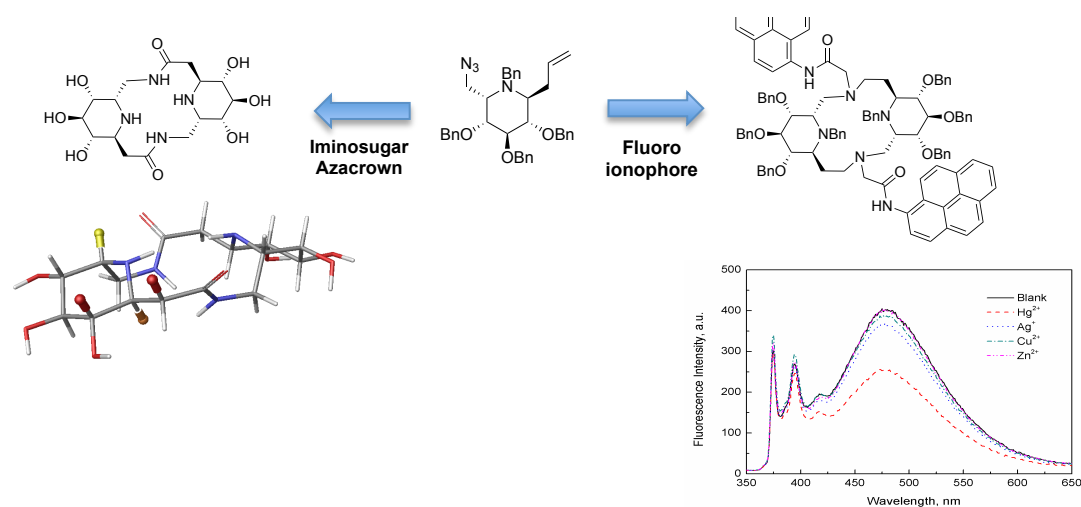
**Highlights**

- First synthesis of fluoroionophore based on an iminosugar scaffold
- The fluoroionophore shows selectivity for Hg<sup>++</sup> cations
- First synthesis of iminosugar azacrown (ISAC) with amide pending arms
- Introduction of amide arms abolishes the chelation properties observed for ISAC with amine arms

## Abstract

Capitalizing on a recently reported iminosugar-based aza-crown (ISAC) accessed by a double Staudinger azaWittig coupling reaction, we have expanded the structural diversity of this new family of sweet cyclam analogs. Replacement of the two secondary amines linking the iminosugar units by two amide bonds obtained a cyclodimerization with BOP and DIPEA led to a macrocycle that did not demonstrate efficient  $\text{Zn}^{2+}$  chelation unlike the parent ISAC. Introduction of two pyrene moieties on the secondary amines of the parent ISAC yielded a new fluoroionophore that selectively binds  $\text{Hg}^{2+}$  in methanol.

## Graphical abstract



## Keywords

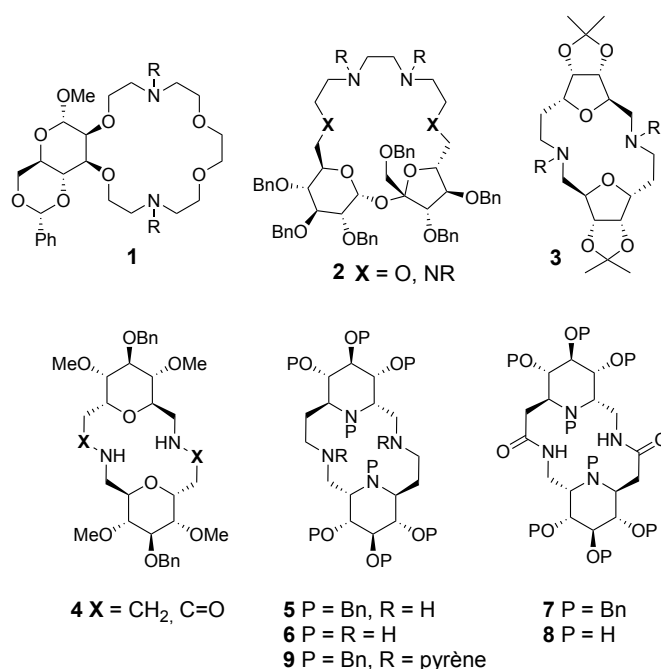
Iminosugar, ionophore, macrocycle, NMR analysis

## Acknowledgements

YB acknowledges financial support from the European Union (ERDF) and "Région Nouvelle Aquitaine". J.J.B. thanks the European Research Council for financial support (ERC-2017- AdG, Project Number 788143-RECGLYC-ANMR). J.J.B. also thanks Agencia Estatal Investigación of Spain, AEI (Grant RTI2018-094751-B-C21, a Juan de la Cierva contract to A.F., and the Severo Ochoa Excellence Accreditation (SEV-2016- 0644).

## Introduction

Aza-crown ethers and cyclams are important molecular receptors for molecular or ionic recognition studies that find applications notably in analytical chemistry as well as nuclear medicine.<sup>1,2</sup> The inherent chirality of carbohydrates is very suitable for the design of chiral receptors and ligands for asymmetric synthesis or chemosensors. Accordingly, chiral aza-crown ethers incorporating various carbohydrate motifs have received much attention in recent years<sup>3,4</sup> and demonstrated biological, environmental, and medical properties. Here are some representative examples (Figure 1) in which a pyranose **1**,<sup>5</sup> a disaccharide **2**,<sup>6</sup> two furanoses **3**<sup>7</sup> or two pyranoses **4**<sup>8</sup> have been used to delineate a macrocycle. Depending on the size of the macrocycle and/or the number of oxygen and nitrogen donor atoms, different guests have been accommodated, including ammonium cations,<sup>6</sup> alkali metal cations,<sup>9</sup> and transition metal cations, such as cadmium(II), mercury(II), and copper(II) using a fluorescent sensor.<sup>10,11</sup> Very recently, we disclosed the synthesis of the first amine-linked iminosugar macrocycles **5** and **6** (Scheme 1), coined iminosugar-aza-crowns (ISACs), obtained by dimerization of an iminosugar-based aminoaldehyde by reductive amination.<sup>12</sup> Alternative dimerization of a related iminosugar-based amino acid through amide bonds formation is of interest to generate more rigid cavities that may lead to exquisite specificity of recognition and catalyst.<sup>13,14,15</sup> Herein we report the synthesis, conformational analysis and complexation study of such cyclic C2-symmetric glycopeptides **7** and **8** as well as the study of a fluorescent ISAC **9** bearing two pyrenyl arms (Figure 1).



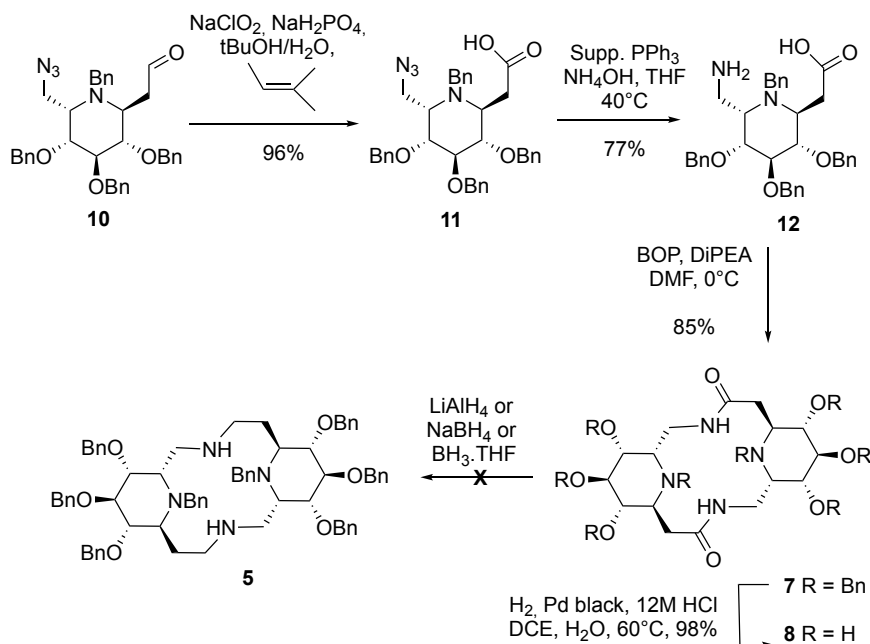
**Figure 1:** Structure of known **1-5** and new **6-9** diazasugar-based macrocycles

## Results and discussion

### 1. Iminosugar azacrown linked by amide bonds

#### 1.1 Synthesis of C-2 symmetric iminosugar azacrown **8**

A range of C-2 symmetric glycopeptides have been synthesized either by solid phase<sup>16</sup> or solution phase<sup>17,18</sup> peptide synthesis from a sugar amino acid (SAA) precursor. Using a similar methodology, the corresponding iminosugar amino acid was synthesized as follows. Iminosugar azidoaldehyde **10**, easily available from the corresponding C-allyl iminosugar,<sup>19</sup> was oxidized to the azidoacid **11**. Conversion of the azide group into the amine with supported PPh<sub>3</sub> and NH<sub>4</sub>OH provided the iminosugar-based aminoacid **12**. While solution phase peptide coupling with EDC and HOBt furnished the expected glycopeptide **7** in modest 32% yield, cyclodimerization of **12** using BOP and DIPEA under diluted conditions in DMF<sup>14</sup> provided macrocycle **7** in excellent 85% yield. Its hydrogenolysis under classical conditions furnished the glycopeptide **8**. Attempts to convert **7** into **5** through reduction of the amides either with NaBH<sub>4</sub>, BH<sub>3</sub>.THF or LiAlH<sub>4</sub> failed (Scheme 1).

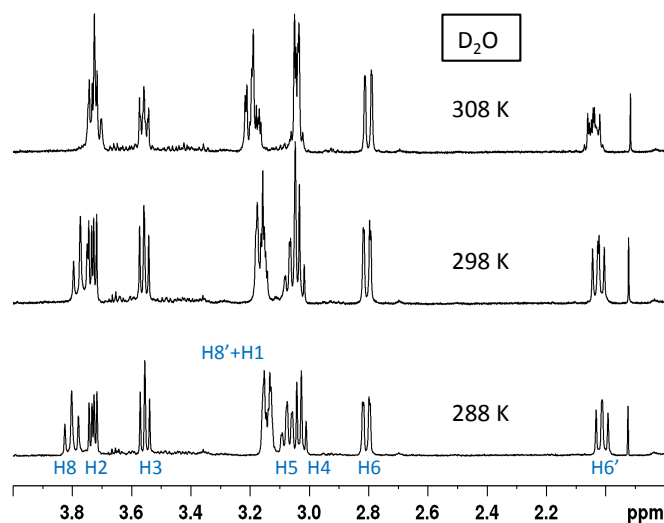


**Scheme 1:** Synthesis of ISAC **8**

#### 1.2 Study of the stability and geometry of ISAC **8**

The geometry in water of ISAC **8** was then studied through extensive NMR analysis, supported by molecular modeling protocols. The relative simplicity of its <sup>1</sup>H NMR spectrum associated with the presence of only one set of sugar protons confirmed its C2 symmetry in the chemical shift NMR time scale. Both iminosugar rings adopts the typical <sup>4</sup>C<sub>1</sub>-type chair geometry with equatorial OH groups as deduced from the large coupling constants (J<sub>1,2</sub>, J<sub>2,3</sub>, J<sub>3,4</sub> ≥ 9.0 Hz, see SI). The stability of ISAC **8** was then evaluated in D<sub>2</sub>O

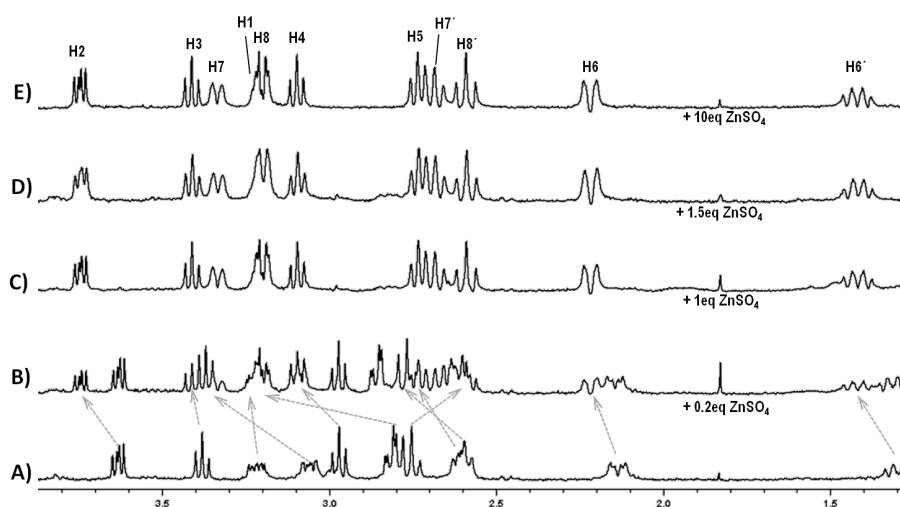
and DMSO at various temperatures. Only slight changes in the chemical shifts of the exchangeable protons were observed upon heating, evidencing the existence of intramolecular hydrogen bonds (Figure 2).



**Figure 2:**  $^1\text{H}$  NMR study of the structure and stability of ISAC **8** at 1mM in  $\text{D}_2\text{O}$  at 288, 298 and 308K.

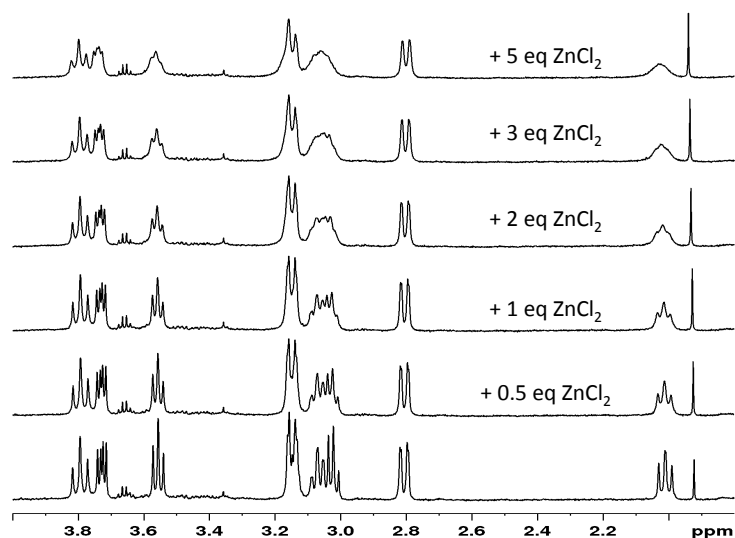
### 1.3 Study of the ability of ISACs **6** and **8** to chelate $\text{Zn}^{2+}$

The ability of ISAC **8** to chelate  $\text{Zn}^{2+}$  was then examined by NMR and compared to that of ISAC **6** that has been previously shown to bind  $\text{Cu}^{2+}$  and  $\text{Cd}^{2+}$  metal cations.<sup>12</sup> As already observed for  $\text{Cu}^{2+}$  and  $\text{Cd}^{2+}$  (Figure 3) with **6**, the formation of a zinc-bound macrocycle takes place in slow exchange in the chemical shift time scale. Moreover, the conformation of **6** does not change much upon binding as the coupling constants are very similar in the free state and when bound to  $\text{Zn}^{2+}$ , suggesting a preorganization in the free state and an interesting interplay between preorganization and flexibility.



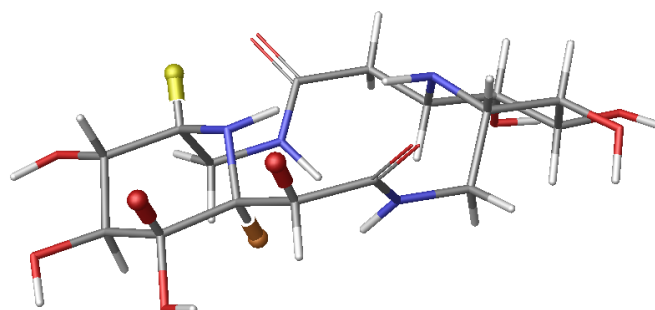
**Figure 3:** Study by  $^1\text{H}$  NMR of the complexation of  $\text{ZnSO}_4$  by ISAC **6**. A)  $^1\text{H}$  NMR spectrum of ISAC **6** at 1mM in  $\text{Na}_2\text{CO}_3/\text{NaHCO}_3$  buffer at pH=11 in  $\text{D}_2\text{O}$  and 298K. B)-E)  $^1\text{H}$  NMR spectra of ISAC **6** upon increasing additions of  $\text{ZnSO}_4$  (0.2, 1, 1.5 and 10 equivalents). The arrows indicate the shifts of the  $^1\text{H}$  resonances upon binding to Zn(II).

The results obtained with ISAC **8** were strikingly different. Unlike ISAC **6**, neither changes in chemical shifts nor new NMR signals were observed upon addition of increasing amounts of  $\text{ZnCl}_2$ . This fact supports the existence of a weak interaction between ISAC **8** and  $\text{Zn}^{2+}$  (Figure 4).



**Figure 4:** Study by  $^1\text{H}$  NMR of the complexation of  $\text{ZnCl}_2$  by ISAC **8**. A)  $^1\text{H}$  NMR spectrum of ISAC **8** at 1mM in  $\text{Na}_2\text{CO}_3/\text{NaHCO}_3$  buffer at pH=11 in  $\text{D}_2\text{O}$  and 298K. B)-E)  $^1\text{H}$  NMR spectra of ISAC **8** upon increasing additions of  $\text{ZnCl}_2$  (0.2, 1, 1.5 and 10 equivalents).

Conformation of ISAC **8** in the presence of  $\text{ZnCl}_2$  was studied by NMR and strongly suggests a macrocycle where the piperidines adopt a  $^4\text{C}_1$  chair conformation and in which the C=O groups of the amide bonds point outside the cavity delineated by the four amines (Figure 5 and SI).



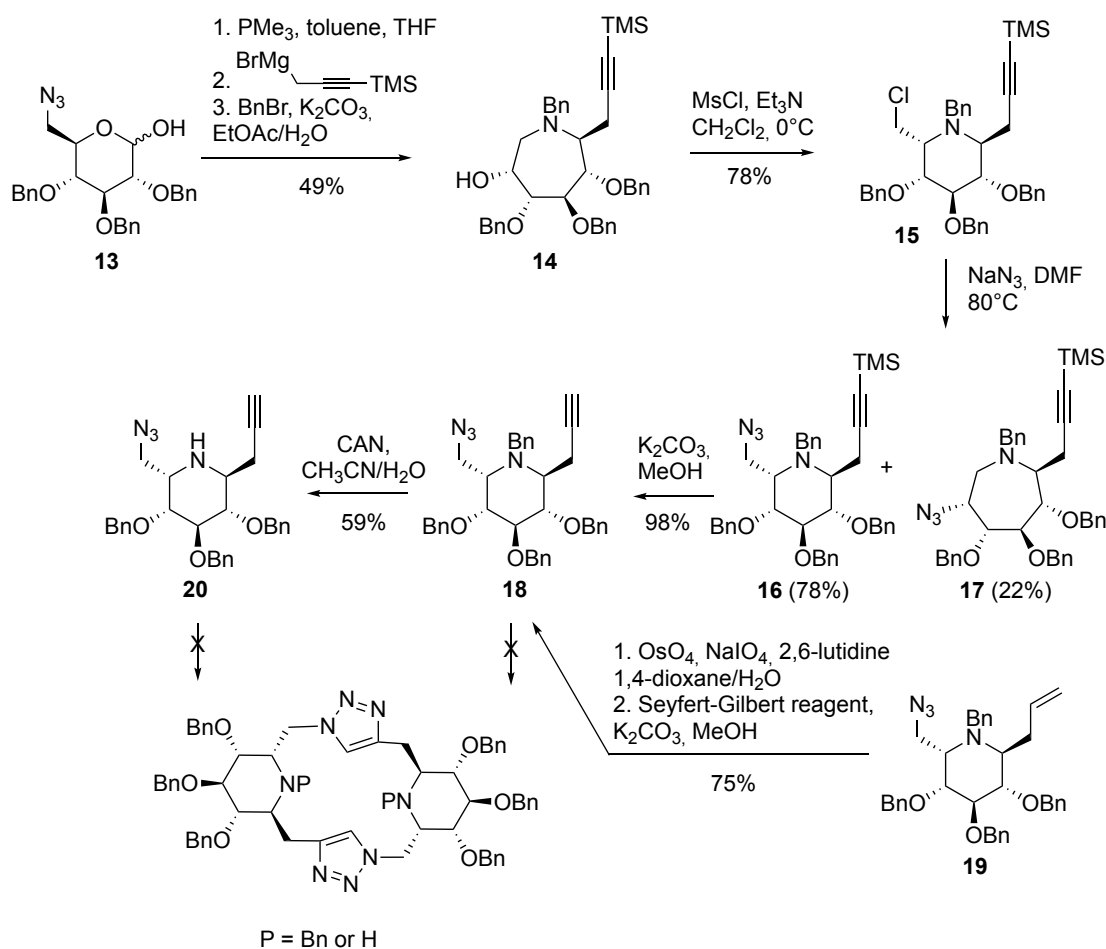
**Figure 5:** Possible conformation for ISAC **8** in the presence of ZnCl<sub>2</sub> according to NMR data; the <sup>1</sup>H that are the more affected/ broadened by the addition of ZnCl<sub>2</sub> are highlighted.

Therefore these observations suggest that aminated arms are required to generate an efficient di-cation binder. As the aim of this strategy is to develop new iminosugar-based macrocycles for chelation studies devoided of glycosidase inhibition potency, the two ISACs **6** and **8** were further assayed on a panel of twenty-one glycosidases. Satisfyingly and as expected regarding the structure of these dimeric iminosugars in which the iminosugar unit is sterically hindered by the other unit, neither **6** nor **8** did demonstrate significant glycosidase inhibition at 1 mM concentration (see SI).

## 2. Attempted synthesis of an ISAC linked by triazole arms

A convenient alternative to amide bonds to link sugar units in sugar-based macrocycles is the use of triazoles exploiting click chemistry. Several groups have reported such cyclic oligosaccharides in which the glycosidic bond has been replaced by a triazole moiety.<sup>21,22,23</sup> To generate a cyclic iminosugar dimer displaying two triazole-based tethers requires the introduction of azide and alkyne moieties of the iminosugar scaffold in a trans relationship to avoid intramolecular cyclization. Introduction of the alkyne moiety was performed as follows. Known azidolactol **13**<sup>24,25</sup> was first converted to a crude bicyclic hemiaminal under Staudinger-azaWittig conditions<sup>26</sup> that was subsequently opened by silylated propargyl organomagnesium bromide, synthesized according to literature<sup>27</sup> to afford azepane **14** as a single diastereoisomer in 49% yield over three steps after N-benylation. The introduction the azide function started with the ring contraction of **14** with mesyl chloride to furnish, in a stereoretentive manner, the chloropiperidine **15** in 78% yield. The chlorine atom was displaced with sodium azide to produce the expected azidopiperidine **16** (78%) along with the corresponding azidoazepane **17** (22%). Removal of the silyl protecting group under slightly basic conditions yielded the target piperidine-based azidoalkyne **18**. Compound **18** was also efficiently obtained from known azidoallyl derivative **19**<sup>19</sup> though alkene oxidative cleavage with OsO<sub>4</sub>/NaIO<sub>4</sub> combination followed by olefination with the Seyfert-Gilbert reagent.<sup>29</sup> Azidoalkyne **18** was then submitted to several click chemistry conditions including conditions that proved successful for the synthesis of iminoglycoconjugates from *N*-benzyl iminosugars.<sup>30</sup> Unfortunately, whatever the conditions used (CuI, DIPEA, toluene; CuSO<sub>4</sub>, sodium ascorbate, methanol or EtOAc/H<sub>2</sub>O; [(CH<sub>3</sub>CN)<sub>4</sub>Cu]PF<sub>6</sub>, CH<sub>2</sub>Cl<sub>2</sub>) over a range of temperatures, no trace of expected dimer was detected by TLC or MS. Application of the same click conditions to the NH free azidoalkyne **20**, obtained by removal of the *N*-benzyl group with CAN, were also unsuccessful.



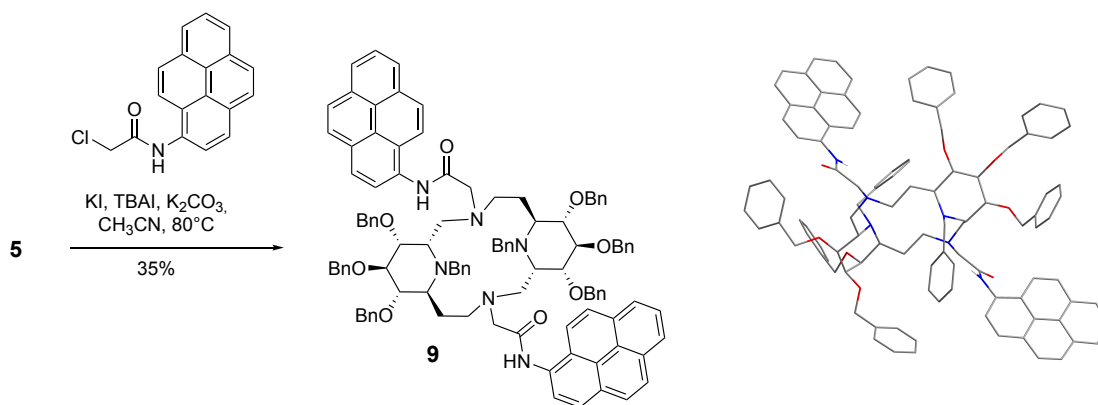


**Scheme 2:** Synthesis of iminosugar-derived azidoalkynes **18** and **20** and attempts to produce the corresponding cyclic dimers

### 3. Fluoroionophore based on an iminosugar azacrown scaffold

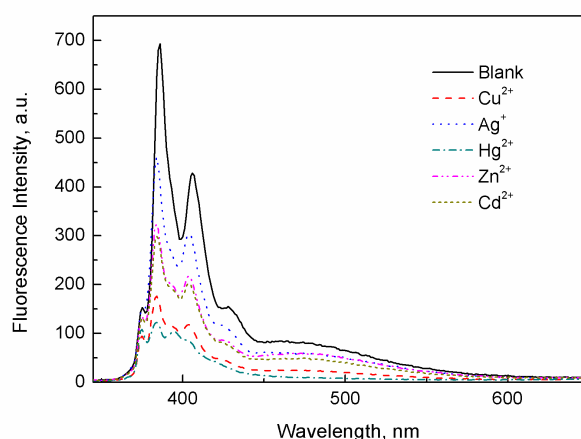
#### 3.1 Synthesis of a fluorophoric iminosugar azacrown **9**

The disappointing results obtained with the strategy consisting in modifying the arms connecting the two iminosugar units forced us to turn our attention to another structural modification that could advantageously modify the properties of the ISAC structure. Combination of macrocyclic ionophores with fluorophore moieties has been often used in the preparation of fluorescent sensors and a significant number of derivatives have been developed.<sup>31</sup> Amongst the wide range of fluorophores that have been reported in the literature, introduction of a pyrene moiety as the signalling unit to examine the chemosensing properties by fluorescence is well-adapted.<sup>32,33,34</sup> The fluorescence enhancement can be attributed to the photoinduced electron transfer triggered by the complexation of the metal ion. In order to develop a fluoroionophore derived from ISAC **6**, compound **5** was treated with an excess of *N*-(1-pyrenyl)-chloroacetamide to provide in 70% yield the protected fluorescent ISAC **9** which crystal structure was solved and fully confirmed the structure (Scheme 3). Interestingly, here, one piperidine adopts a  ${}^4C_1$  conformation with pseudoequatorial orientation of the benzyloxy groups while the other piperidine adopts a  ${}^1C_4$  conformation with pseudoaxial orientation of the benzyloxy groups.



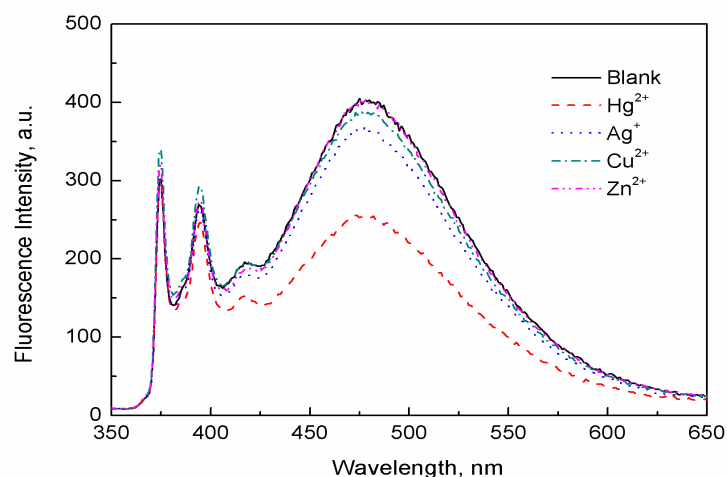
### 3.2 Study of the chemosensor properties of ISAC 9

The chemosensor properties of ISAC 9 were studied by fluorescence measurement. The conditions of observation of the monomer and excimer bands were optimized leading to the use of a 5 mM concentration of ISAC 9 with excitation at 341 nm. While methanol/water (1:1) allowed the best observation of the excimer band, methanol, dichloromethane and acetonitrile proved to be the best solvents to observe the monomer band (see SI). Study of the monomer band of 9 in acetonitrile in the presence of various cations ( $\text{Cu}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Hg}^{2+}$ ,  $\text{Zn}^{2+}$  and  $\text{Cd}^{2+}$ ) was performed (Figure 6). Interestingly, while ISAC 6 has proved to bind  $\text{Zn}^{2+}$  and  $\text{Cd}^{2+}$ ,<sup>12</sup> introduction of two pyrene moieties on the iminosugar ring nitrogens changed the chemosensor properties of the corresponding ISAC 9 that demonstrated some selectivity towards  $\text{Cu}^{2+}$  and  $\text{Hg}^{2+}$  cations and only weak chelation of  $\text{Zn}^{2+}$  and  $\text{Cd}^{2+}$ . This result suggests the arm amine functions as handles to tune the chemosensor properties of these ISACs.



**Figure 6:** Fluorescence spectra of ISAC 9 in the presence of various metal ions in MeCN;  $[\text{M}^{n+}] = 0.2 \text{ mM}$ ,  $[\mathbf{9}] = 5 \text{ mM}$ ,  $\lambda_{\text{ex}} = 341 \text{ nm}$ .

A second study of the excimer band in methanol/water (1:1) in the presence of  $\text{Cu}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Zn}^{2+}$  (at 0.2 mM concentrations) and  $\text{Hg}^{2+}$  (at 40 mM concentration) demonstrated a significant selective fluorescence quenching of compound **9** in the presence of  $\text{Hg}^{2+}$  ion. Interestingly, ISAC **9** exhibits a similar complexation profile as the pyrenylacetamide-functionalized cyclam<sup>23</sup> (Figure 7).



**Figure 7:** Fluorescence spectra of ISAC **9** in the presence of various metal ions in MeOH/H<sub>2</sub>O (v/v= 1:1); [ $\text{M}^{n+}$ ] = 0.2 mM, [ $\text{Hg}^{2+}$ ] = 40 mM, [**9**] = 5 mM,  $\lambda_{\text{ex}}$  = 341 nm.

## Conclusions

Two iminosugar azacrowns bearing either fluorescent appendages or incorporating amide bonds have been described. Preliminary chemosensor studies on the fluorescent ISAC **21** demonstrate selectivity towards  $\text{Hg}^{2+}$  ions unlike the undecorated ISAC **6**, suggesting that further structural modification of the aminated arms could control the chelation properties of these molecules. Work is now in progress to access the geometry of the **21**- $\text{Hg}^{2+}$  complex. In parallel, the first example of a C<sub>2</sub> symmetric iminoglycopeptide **8** has been reported and generated from an iminosugar amino acid precursor by solution phase peptide coupling. Replacement of the aminated arms by amide bonds abolishes the  $\text{Zn}^{2+}$  complexation observed for the parent ISAC **6** suggesting a distinct geometry for the **8**- $\text{Zn}^{2+}$  complex.

## Conflicts of interest

“There are no conflicts to declare”.

## References

- 1 L. Fabbrizzi, A Lifetime Walk in the Realm of Cyclam, in: R. M. Izatt (Eds.), *Macrocyclic and Supramolecular Chemistry*, John Wiley & Sons, Ltd, Chichester, UK, 2016, pp. 165–199.
- 2 X. Liang and P. J. Sadler, Cyclam complexes and their applications in medicine, *Chemical Society Reviews*, 33 (2004) 246-266. <http://xlink.rsc.org/?DOI=b313659k>.
- 3 M. A. Potopnyk and S. Jarosz, Nitrogen-Containing Macrocycles Having a Carbohydrate Scaffold, in *Advances in Carbohydrate Chemistry and Biochemistry*, Elsevier, 2014, vol. 71, pp. 227–295. <https://linkinghub.elsevier.com/retrieve/pii/B9780128001288000030>
- 4 J. Xie and N. Bogliotti, Synthesis and Applications of Carbohydrate-Derived Macrocyclic Compounds, *Chemical Reviews*, 114 (2014) 7678–7739. <https://pubs.acs.org/doi/10.1021/cr400035j>
- 5 M. Pietraszkiewicz, P. Safariski and J. Jurczak, High-pressure approach to the synthesis of novel chiral cryptands derived from methyl 4,6-*O*-benzylidene- $\alpha$ -D-manno-, - $\alpha$ -D-galacto-, and - $\alpha$ -D-gluco-pyranoside, *J. Chem. Soc., Chem. Commun.*, (1983) 1184-1184. <https://doi.org/10.1039/C39830001184>
- 6 B. Lewandowski and S. Jarosz, Chiral recognition of  $\alpha$ -phenylethylamine by sucrose-based macrocyclic receptors, *Chemical Communications* (2008) 6399-6401. <http://xlink.rsc.org/?DOI=b816476b>
- 7 Y.-C. Hsieh, J.-L. Chir, W. Zou, H.-H. Wu and A.-T. Wu, Convenient approaches to synthesis of furanoid sugar-aza-crown ethers from C-ribosyl azido aldehyde via a reductive amination/amidation, *Carbohydrate Research*, 344 (2009) 1020–1023. <https://linkinghub.elsevier.com/retrieve/pii/S0008621509001049>
- 8 M. Ménand, J.-C. Blais, J.-M. Valéry and J. Xie, De Novo Synthesis of Sugar-Aza-Crown Ethers via a Domino Staudinger Aza-Wittig Reaction, *The Journal of Organic Chemistry*, 71 (2006) 3295–3298. <https://pubs.acs.org/doi/10.1021/jo052489q>
- 9 P. Bakó, K. Vízvárdi, S. Toppet, E. Van der Eycken, G. J. Hoornaert and L. Töke, Synthesis, extraction ability and application in asymmetric synthesis of azacrown ethers derived from D-glucose, *Tetrahedron*, 54 (1998) 14975–14988. <https://linkinghub.elsevier.com/retrieve/pii/S0040402098009387>
- 10 Y.-C. Hsieh, J.-L. Chir, S.-T. Yang, S.-J. Chen, C.-H. Hu and A.-T. Wu, A sugar-aza-crown ether-based fluorescent sensor for Cu<sup>2+</sup> and Hg<sup>2+</sup> ions, *Carbohydrate Research*, 346 (2011) 978–981. <https://linkinghub.elsevier.com/retrieve/pii/S0008621511001224>
- 11 Y.-C. Hsieh, J.-L. Chir, H.-H. Wu, P.-S. Chang and A.-T. Wu, A sugar-aza-crown ether-based fluorescent sensor for Hg<sup>2+</sup> and Cu<sup>2+</sup>, *Carbohydrate Research*, 344 (2009) 2236–2239. <https://linkinghub.elsevier.com/retrieve/pii/S0008621509004042>
- 12 A. Bordes, A. Poveda, T. Troadec, A. Franconetti, A. Ardá, F. Perrin, M. Ménand, M. Sollogoub, J. Guillard, J. Désiré, R. Tripiet, J. Jiménez-Barbero and Y. Blériot, Synthesis, Conformational Analysis, and Complexation Study of an Iminosugar-Aza-Crown, a Sweet

Chiral Cyclam Analog, *Organic Letters*, 22 (2020) 2344–2349.  
<https://pubs.acs.org/doi/10.1021/acs.orglett.0c00503>

13 S. A. W. Gruner, V. Truffault, G. Voll, E. Locardi, M. Stöckle and H. Kessler, Design, Synthesis, and NMR Structure of Linear and Cyclic Oligomers Containing Novel Furanoid Sugar Amino Acids, *Chemistry - A European Journal*, 8 (2002) 4365–4376.  
<http://doi.wiley.com/10.1002/1521-3765%2820021004%298%3A19%3C4365%3A%3AAID-CHEM4365%3E3.0.CO%3B2-U>

14 E. Locardi, M. Stöckle, S. Gruner and H. Kessler, Cyclic Homooligomers from Sugar Amino Acids: Synthesis, Conformational Analysis, and Significance, *Journal of the American Chemical Society*, 123 (2001) 8189–8196.  
<https://pubs.acs.org/doi/10.1021/ja010181k>

15 T. K. Chakraborty, P. Srinivasu, E. Bikshapathy, R. Nagaraj, M. Vairamani, S. K. Kumar and A. C. Kunwar, Cyclic Homooligomers of Furanoid Sugar Amino Acids, *The Journal of Organic Chemistry*, 68 (2003) 6257–6263.  
<https://pubs.acs.org/doi/10.1021/jo034586u>

16 F. El Oualid, G. A. van der Marel, H. S. Overkleeft and M. Overhand, Alkylated Sugar Amino Acids: A New Entry toward Highly Functionalized Dipeptide Isosters, *Organic Letters*, 6 (2004) 3167–3170. <https://pubs.acs.org/doi/10.1021/ol048750r>

17 J. F. Billing and U. J. Nilsson, Cyclic peptides containing a  $\delta$ -sugar amino acid—synthesis and evaluation as artificial receptors, *Tetrahedron*, 61 (2005) 863–874.  
<https://linkinghub.elsevier.com/retrieve/pii/S0040402004018964>

18 N. Singh, P. S. Kandiyal, P. K. Shukla, R. S. Ampapathi and T. K. Chakraborty, Conformational studies of glycosylated cyclic oligomers of furanoid sugar amino acids, *Tetrahedron*, 72 (2016) 5671–5678.  
<https://linkinghub.elsevier.com/retrieve/pii/S0040402016307293>

19 M. Mondon, N. Fontelle, J. Désiré, F. Lecornué, J. Guillard, J. Marrot and Y. Blériot, Access to l- and d-Iminosugar C-Glycosides from a d-gluco-Derived 6-Azidolactol Exploiting a Ring Isomerization/Alkylation Strategy, *Organic Letters*, 14 (2012) 870–873.  
<https://doi.org/10.1021/ol203385w>

21 K. D. Bodine, D. Y. Gin and M. S. Gin, Synthesis of Readily Modifiable Cyclodextrin Analogues via Cyclodimerization of an Alkynyl–Azido Trisaccharide, *Journal of the American Chemical Society*, 126 (2004) 1638–1639.  
<https://pubs.acs.org/doi/10.1021/ja039374t>

22 S. Jarosz, B. Lewandowski and A. Listkowski, Towards Sucrose Macrocycles with Higher Symmetry via a ‘Click Chemistry’ Route, *Synthesis*, 2008 (2008) 913–916.  
<http://www.thieme-connect.de/DOI/DOI?10.1055/s-2008-1032198>

23 A. Singh, V. Khatri, S. Malhotra and A. K. Prasad, Sugar-based novel chiral macrocycles for inclusion applications and chiral recognition, *Carbohydrate Research*, 421 (2016) 25–32. <https://linkinghub.elsevier.com/retrieve/pii/S0008621515003900>

- 24 T. K. Chakraborty, S. Ghosh, S. Jayaprakash, J. A. R. P. Sharma, V. Ravikanth, P. V. Diwan, R. Nagaraj and A. C. Kunwar, Synthesis and Conformational Studies of Peptidomimetics Containing Furanoid Sugar Amino Acids and a Sugar Diacid, *The Journal of Organic Chemistry*, 65 (2000) 6441–6457. <https://pubs.acs.org/doi/10.1021/jo000408e>
- 25 G. Gradnig, G. Legler and A. E. Stütz, A novel approach to the 1-deoxynojirimycin system: Synthesis from sucrose of 2-acetamido-1,2-dideoxynojirimycin, as well as some 2-N-modified derivatives, *Carbohydrate Research*, 287 (1996) 49–57. <https://linkinghub.elsevier.com/retrieve/pii/0008621596000651>
- 26 M. Zoidl, B. Müller, A. Torvisco, C. Tysoe, M. Benazza, A. Siriwardena, S. G. Withers and T. M. Wrodnigg, Concise synthesis of C-1-cyano-iminosugars via a new Staudinger/aza Wittig/Strecker multicomponent reaction strategy, *Bioorganic & Medicinal Chemistry Letters*, 24 (2014) 2777–2780. <http://www.sciencedirect.com/science/article/pii/S0960894X14002960>
- 27 H. P. Acharya, K. Miyoshi and Y. Kobayashi, Mercury-Free Preparation and Selective Reactions of Propargyl (and Propargylic) Grignard Reagents, *Organic Letters*, 9 (2007) 3535–3538. <https://pubs.acs.org/doi/10.1021/ol071397f>
- 29 S. Müller, B. Liepold, G. H. Roth, H. J. Bestmann, *Synlett*, 8 (1996) 521–522.
- 30 C. Nicolas, F. Engo-Ilanga, C. Cocaud and O. Martin, En Route to Novel Furanoside Mimics through Stereoselective Zinc-Mediated Propargylation of N-Benzyl Glycofuranosylamines Using Ultrasound Activation, *Synlett*, 26 (2014) 187–192. <http://www.thieme-connect.de/DOI/DOI?10.1055/s-0034-1379551>
- 31 H. G. Loehr and F. Voegtle, Chromo- and fluoroionophores. A new class of dye reagents, *Accounts of Chemical Research*, 18 (1985) 65–72. <https://doi.org/10.1021/ar00111a001>
- 32 J. H. Kim, A.-R. Hwang and S.-K. Chang, Hg<sup>2+</sup>-selective fluoroionophore of p-tert-butylcalix[4]arene-diaza-crown ether having pyrenylacetamide subunits, *Tetrahedron Letters*, 45 (2004) 7557–7561. <https://linkinghub.elsevier.com/retrieve/pii/S004040390401857X>
- 33 S. H. Kim, J. S. Kim, S. M. Park and S.-K. Chang, Hg<sup>2+</sup>-Selective OFF–ON and Cu<sup>2+</sup> - Selective ON–OFF Type Fluoroionophore Based upon Cyclam, *Organic Letters*, 8 (2006) 371–374. <https://pubs.acs.org/doi/10.1021/ol052282j>
- 34 J. Xie, M. Ménand, S. Maisonneuve and R. Métivier, Synthesis of Bispyrenyl Sugar-Aza-Crown Ethers as New Fluorescent Molecular Sensors for Cu(II), *The Journal of Organic Chemistry*, 72 (2007) 5980–5985. <https://pubs.acs.org/doi/10.1021/jo070315y>

**Declaration of interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:



Click here to access/download

**Supporting File**

Supporting information Cyclam II BLERIOT.pdf

