HAL
open science

# Trialkoxyheptazine-Based Glyconanoparticles for Fluorescence in Aqueous Solutions and on Surfaces via Controlled Binding in Space

Monica Brachi, Paulo Henrique M. Buzzetti, Karine Gorgy, Dan Shan, Pierre Audebert, Alan Le Goff, Hong Li, R. Borsali, Serge Cosnier

## ▶ To cite this version:

Monica Brachi, Paulo Henrique M. Buzzetti, Karine Gorgy, Dan Shan, Pierre Audebert, et al.. Trialkoxyheptazine-Based Glyconanoparticles for Fluorescence in Aqueous Solutions and on Surfaces via Controlled Binding in Space. ACS Macro Letters, 2022, 11 (1), pp.135-139. 10.1021/acsmacrolett.1c00693 . hal-03736823

## HAL Id: hal-03736823
## https://hal.science/hal-03736823v1

Submitted on 22 Jul 2022

**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.

# Trialkoxyheptazine-based glyconanoparticles for fluorescence in aqueous solutions and on surfaces via controlled binding in space

Monica Brachi [a], Paulo Henrique M. Buzzetti [a], Karine Gorgy [a], Dan Shan [b], Pierre Audebert [c], Alan le Goff [a], Hong Li [d], Redouane Borsali [d] and Serge Cosnier [a*]

[a] Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France.

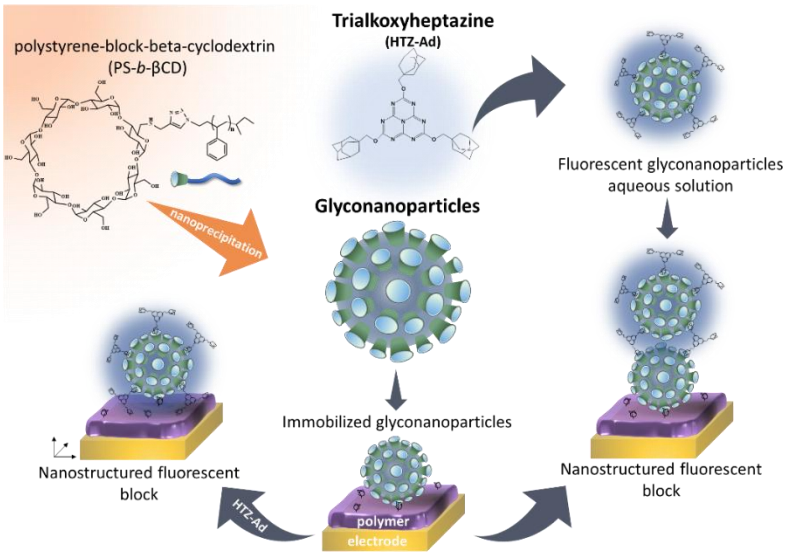
[b] School of Environmental and Biological Engineering, Nanjing University of Science and Technology, Nanjing 210094, China.

[c] PPSM, CNRS UMR 8531, ENS Cachan, 61 avenue du Président Wilson. 94235 Cachan, France.

[d] Univ. Grenoble Alpes, CNRS, CERMAV, F-38000 Grenoble, France.

KEYWORDS: fluorescent nanoparticles, nanoprecipitation, heptazine, cyclodextrin, polypyrrole, adamantane.

**ABSTRACT:** The fluorescent organic 2,5,8-tris((adamantan-1-yl) methoxy)-heptazine (HTZ-Ad) was solubilized in water by inclusion of adamantane groups into free β-cyclodextrins or cyclodextrin shell of glyconanoparticles. These glyconanoparticles with average diameters between 40 and 60 nm result from the self-assembly of polystyrene-block-β-cyclodextrin copolymer. Under UV irradiation at 365 nm, the modified nanoparticles exhibit fluorescence emission in aqueous media as well as in their adsorbed state. This constitutes the first spectroscopic characterization of a trialkoxyheptazine in aqueous medium. The specific binding of the glyconanoparticles to a surface was achieved via host-guest interactions with an electrochemically generated poly(pyrrole-adamantane) film. An interdigitated microelectrode modified with poly(pyrrole-adamantane) film and glyconanoparticles was incubated in HTZ-Ad resulting in a substrate with spatially controlled fluorescence. The same modified electrode was incubated with an aqueous suspension of glyconanoparticles previously functionalized by HTZ-Ad, resulting in a fluorescent 3D assembly.




## Introduction

Self-assembled nano-objects are ordered molecular aggregates with a wide range morphology formed by the spontaneous molecular organization of the constituents in solution. Particularly interesting are nano-objects derived from amphiphilic block copolymers (BCPs) due to the virtually unlimited combinations of hydrophobic and hydrophilic different blocks which allows the generation of nano-objects with tailored features and properties. [1,2] Their versatility as building blocks has attracted great attention for their potential applications in catalysis, biomaterials, biomedicine and others fields. Carbohydrates as hydrophilic block provide a route to biocompatible and bio-inspired nano-objects but remain relatively less explored, because of their tricky preparation which involves many synthesis steps. [3] We have in particular reported the synthesis of new glyconanoparticles which can be loaded in aqueous solvents with activated tetrazines via supramolecular host-guest interactions. This enables high fluorescence yields as well as the design of nanostructured arrays based on these nanoparticles.[4] However, while tetrazines are a fascinating fluorophore class with reasonable fluorescence yields [5–8] and a high redox potential

in the excited state, they also exhibit a moderate chemical stability towards nucleophilic reagents, which notably hampers their use in long-term stable sensing devices. [9] Recently, P. Audebert et al. turned their interest towards a new family of azo-fluorophores, with characteristics resembling tetrazines, but with a much better chemical stability, the heptazines. [10]

Heptazines are a family characterized by a polycyclic aromatic core, a s-heptazine (tri-s-triazine) moiety consisting of three fused s-triazine rings. The high nitrogen to carbon ratio (heptazine core: C/N = 0.85) makes them strongly electron deficient compounds. Moreover, heptazines own a much larger bandgap (3-4 eV), despite a slightly lower redox reduction potential in the fundamental state. These combined characteristics confer to their excited state outstanding oxidant properties, and make the few derivatives already prepared the best purely organic photooxidants, competitive with eg iridium or ruthenium complexes. However, because of their large aromatic core, no heptazine is soluble in water (with one single exception)[11]. Furthermore, their organization into materials is still in infancy [12–17], mainly because of the scarcity of the molecules known to date of this family.

We describe here the solubilization of our already described fluorescent tris((adamantan-1-yl)-methoxy)-heptazine (HTZ-Ad), owning a blue-violine fluorescence typical of the trialkoxyheptazine core.[18] Thanks to the formation of inclusion complexes between β-cyclodextrins (βCD) and adamantane via host-guest interactions, the transfer of the fluorescent properties of HTZ-Ad to the aqueous medium was investigated by the modification of glyconanoparticles exhibiting a shell of cyclodextrin. In addition, the specific immobilization of the glyconanoparticles by host-guest interactions was carried out on electrodes previously modified by electrogeneration of a polymer film: poly (pyrrole-adamantane) (PPY-Ad). The post-functionalization of these glyconanoparticles immobilized on the polymer surface, by tris((adamantan-1-yl)-methoxy)-heptazine then leads to materials exhibiting the photophysical properties of heptazines with in addition a spatial addressing resulting from the electropolymerization process.

## Results and discussion

2,5,8-tris((adamantan-1-yl) methoxy)-heptazine was prepared in a similar way to other trialkoxyheptazines (see experimental section). Besides the low initial solubility of heptazine in water, the presence of three adamantane groups reinforces its hydrophobic character. The inclusion of adamantane in the hydrophobic internal cavity of β-cyclodextrin (association constant around $K = 10^5$ $mol^{-1}$ L), [19] should mask this hydrophobic effect and facilitate the solubilization of HTZ-Ad in water. The solubilization of HTZ-Ad in water was therefore carried out with and without cyclodextrin, after a pretreatment of sonication and stirring overnight, and studied via the UV-vis absorption spectra of the resulting solutions (Figure 1a). HTZ-Ad showed an intense band around 260 nm and a weaker low-energy band around 318 nm. Both absorption bands were previously reported in the same region for HTZ-Ad in $CH_2Cl_2$. [18] The first more intense band can be attributed to their large aromatic core. Its

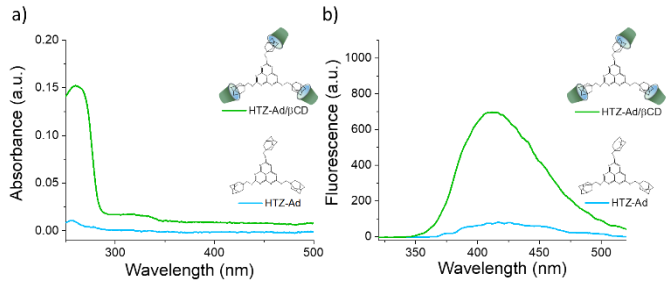



**Figure 1**. a) UV-vis absorption spectra and b) Fluorescence emission spectra in water for the supernatants of HTZ-Ad in presence or absence of βCD (HTZ-Ad/βCD equivalent ratio: 1/5).

position varies according to the electron-rich character of the exchangeable groups while the low-energy band corresponds to a transition between a natural transition orbital located on the heptazine core and the LUMO.[20] In the presence of approximately a 5-fold excess of βCD, the maximum intensities are considerably higher than that of HTZ-Ad alone. A similar phenomenon was observed measuring the fluorescence emission. All trialkoxyheptazines display a broad fluorescence emission band in the visible light region with a maximum between 408 and 412 nm in $CH_2Cl_2$ which can also be noticed for the HTZ-Ad in aqueous solution. The fluorescence emission was greatly enhanced in presence of an excess of β-cyclodextrin (Figure 1b). The increased intensities of both the absorbance and fluorescence emission in presence of βCD can thus be explained by a solubilization of HTZ-Ad after its inclusion in βCD cavities.

Due to their host-guest abilities, the attachment of cyclodextrins to inorganic nanoparticles has been developed over the past decade, for biomedical applications. Functionalized nanoparticles were thus exploited for the transport and release of drugs that formed inclusion complexes with cyclodextrin groups. [21] In particular, βCD-based glyconanoparticles are attractive nano-objects owing to their stability in aqueous medium and easy functionalization by inclusion in βCD cavities on the shell of the particles, as already reported for pyrene, [22,23] anthracene [24] and tetrazine [4] derivative compounds. With the aim to transfer HTZ-Ad in aqueous solution, we thus prepared an aqueous glyconanoparticles suspension ($GNP_{PSCD}$) from a polystyrene-block-β-cyclodextrin copolymer (PS-b-βCD) by direct nanoprecipitation. [24] After the nanoprecipitation process,

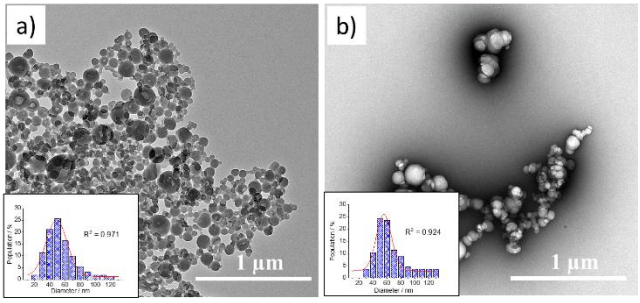



**Figure 2**. TEM images of the self-assembled a) $GNP_{PSCD}$ and b) $GNP_{PSCD}$ post-functionalized with the 2,5,8-tris((adamantan-1-yl) methoxy)-heptazine ($GNP_{PSCD\text{-}HTZ\text{-}Ad}$). Inset: respective particle size distributions fitted by a log-normal model.

spherical self-assembled nanoparticles were obtained with average diameters between 40 and 60 nm (Figure 2a). The size particle distribution was determined using ImageJ software from $GNP_{PSCD}$ TEM images and fitted by a log-normal model. These glyconanoparticles were then post-functionalized by the addition of the $GNP_{PSCD}$ suspension drop by drop in a smaller volume of HTZ-Ad in ethanol-water (70:30) v/v %. Then, after sonication and stirring overnight, the ethanol was removed from the resulting solution by dialysis against pure water. As a result of the poor solubility of HTZ-Ad in water, after one day of dialysis it was possible to separate the unreacted HTZ-Ad in the form of a solid precipitate from the rest of the nanoparticles still dispersed in the aqueous supernatant, which was collected and characterized. Figure 2b shows $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ with average diameters between 40 and 60 nm indicating that no drastic morphological change occurred after the functionalization step.

Figure 3 exhibits similar mass-weighted distributions with the appearance of three particle sizes for modified and unmodified GNPs. The smallest particle size indicates a slight decrease in the hydrodynamic radius ($R_h$) from 87 nm to 84 nm after the functionalization of GNPs. A more drastic change was observed for the second size distribution that correspond to the formation of aggregates (decrease from 312 nm to 235 nm). This phenomenon could be due to a shrinkage of the nanoparticles induced by the three adamantane groups of the heptazines which would strengthen the links between elementary micelles (with small size <20nm) which constitute the GNPs. (see also the Variation of the frequency G as a function of $q^2$ showing the diffusive motion of the nanoparticles: a) prepared from $GNP_{PSCD}$ and b) prepared from $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ (Figure S2)).

In order to confirm the inclusion of HTZ-Ad in the βCD cavity of the $GNP_{PSCD}$, fluorescence emission spectra were acquired from the post-functionalized $GNP_{PSCD}$ aqueous suspension. Figure 4a shows almost negligible fluorescence emission for the $GNP_{PSCD}$ while a strong fluorescence emission at $\lambda_{em.}$ = 420 nm was observed for the $GNP_{PSCD\text{-}HTZ\text{-}Ad}$. This drastic difference clearly corroborates the successful inclusion of adamantyl groups inside the cyclodextrin cavity and hence the attachment of HTZ-Ad to the periphery of the nanoparticles. In addition, the aqueous suspensions of unmodified and modified particles were deposited on a glass support and

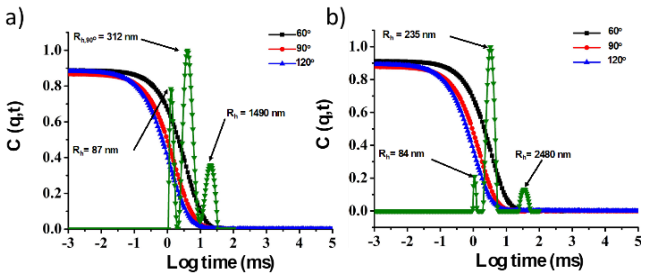



**Figure 3**. Auto-correlation functions and size distributions measured using dynamic light scattering for the scattering angles shown: a) unmodified $GNP_{PSCD}$. b) modified $GNP_{PSCD}$.

adsorbed by simple evaporation of the solvent. Fluorescence microscopy images, carried out with a filter DAPI with $\lambda_{ex.}$ = 340 - 380 nm and $\lambda_{em.}$ = 450 - 490 nm, demonstrate no fluorescence emission for $GNP_{PSCD}$ (Figure 4b and c). In contrast, a bright fluorescence emission was observed for the post-functionalized particles $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ that perfectly reflects the shape of the deposit. (Figure 4d and e).

With the aim to confer through nanoparticles, fluorescence properties to conductive surfaces with little respect to their shape and size, the latter were modified by electropolymerization of a pyrrole-adamantane (Figure S3). The resulting film combines the advantages of the electrochemical addressing of polymer films with those of host-guest interactions with $GNP_{PSCD}$. To illustrate this spatial localization of the nanoparticles, a microelectrode of a pair of interdigitated gold electrodes was modified by electrogeneration of a poly(pyrrole-adamantane) film followed by immersion in $GNP_{PSCD}$ aqueous suspension overnight. As previously reported for poly(pyrene-adamantane) and poly(pyrrole adamantane) films, the polypyrrole film is able to anchor the $GNP_{PSCD}$ via the βCD-adamantyl inclusion complex. [25,26] It is expected that the majority of βCD groups on the $GNP_{PSCD}$ shell are not involved in the interaction with the underlying film and are therefore available for post-functionalization. Then, the resulting interdigitated gold electrodes were modified either directly by HTZ-Ad or by $GNP_{PSCD\text{-}HTZ\text{-}Ad}$. Regarding HTZ-Ad approach, the electrode/PPY-Ad/$GNP_{PSCD}$ substrate was immersed in a 0.66 mg $mL^{-1}$ HTZ-Ad solution (EtOH/ Milli-Q water (70:30) v/v %) for 1 hour and then washed with a EtOH/Milli-Q water solution. Figure 5c

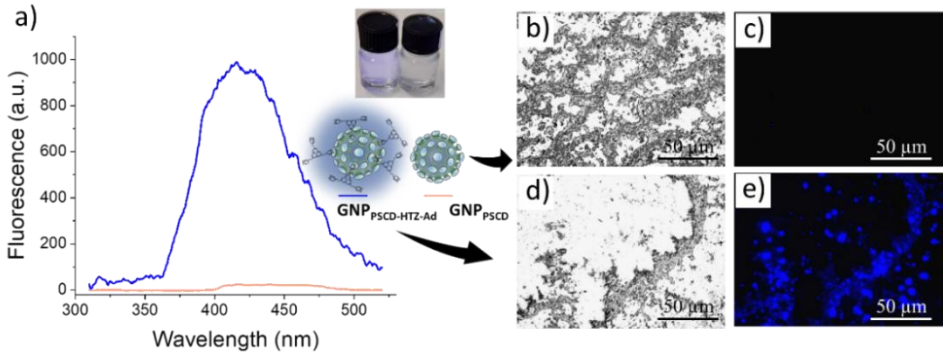



**Figure 4.** a) Fluorescence emission spectra of $GNP_{PSCD}$ and $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ aqueous suspensions and the glyconanoparticles aqueous suspensions under UV irradiation at 365 nm (λ = 365 nm); inset. Brightfield and fluorescence images of $GNP_{PSCD}$ (b and c) and $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ (d and e) aqueous suspensions adsorbed onto a glass substrate.

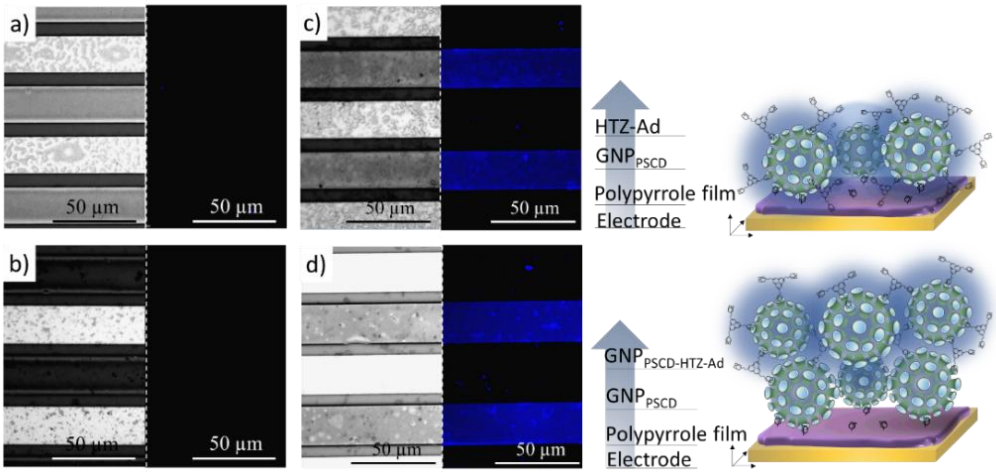



**Figure 5.** Brightfield and fluorescence images of the a) electrode/PPY-Ad after incubation with HTZ-Ad; b) electrode/PPY-Ad/$GNP_{PSCD}$; c) electrode/PPY-Ad/$GNP_{PSCD}$/HTZ-Ad and d) electrode/PPY-Ad/$GNP_{PSCD}$ /$GNP_{PSCD\text{-}HTZ\text{-}Ad}$ substrates and the respective building block schemes for c and d.

shows that the fluorescence emission occurs only on the microelectrode previously coated with the polymer. This demonstrates the availability of βCD groups of $GNP_{PSCD}$ immobilized on the polymer film, for a host-guest interaction with HTZ-Ad. This also highlights the efficiency of electrochemical addressing of fluorescence. A similar result of spatial resolution with a bright fluorescence emission localized only on the modified microelectrode, was obtained after immersing an electrode/PPY-Ad/$GNP_{PSCD}$ in the $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ aqueous suspension (Figure 5d). This fluorescence results from the interaction between βCD groups of the $GNP_{PSCD}$ immobilized on the polymer surface and the free adamantly group of HTZ-Ad anchored on the $GNP_{PSCD\text{-}HTZ\text{-}Ad}$. HTZ-Ad acts thus as a bridge between two nanoparticles. Moreover, it should be emphasized that no fluorescence was observed on an electrode/PPY-Ad/$GNP_{PSCD}$ without the post-modification by HTZ-Ad or $GNP_{PSCD\text{-}HTZ\text{-}Ad}$ (Figure 5b). In addition, no fluorescence was recorded with another control based on an electrode / PPY-Ad immersed in the HTZ-Ad solution (EtOH/ Milli-Q water (70:30) v/v %) for 1 hour without the incubation with $GNP_{PSCD}$, thus confirming the importance of specific CD-adamantane interactions (Figure 5a). These results show the possibility to spatially control the immobilization of glyconanoparticles on surfaces coated by polymers by exploiting the inclusion properties of β-cyclodextrins and the multidirectional availability of the adamantane groups of HTZ-Ad.

## Conclusion

We have demonstrated that the near insolubility of 2,5,8-tris((adamantan-1-yl) methoxy)-heptazine in water can be counterbalanced in the presence of an excess of β-cyclodextrins via the formation of inclusion complex between cyclodextrins and adamantane groups thus allowing the first spectroscopic characterization of a trialkoxyheptazine in aqueous medium. This nice outcome could be a future opening for water splitting and possible other photocatalytic routes in water medium. This interaction was then explored for the post-functionalization of glyconanoparticles resulting from the self-assembly of polystyrene-block-β-cyclodextrin copolymer system. The obtained nanoparticles exhibited fluorescent properties in aqueous media as well as after their adsorption on a glass surface. In addition, an eco-friendly approach of functionalizing surfaces by heptazine has been illustrated by modifying conductive surfaces with a poly(pyrrole-adamantane) film and exploiting the host-guest interactions between adamantane and cyclodextrin. Fluorescence imaging clearly shows that the immobilized glyconanoparticles are able to bind in water both free heptazine derivative and heptazine functionalized nanoparticles and hence can be used for building nanostructured fluorescent materials.

## Supporting Information

Experimental details, synthesis of heptazine derivative and polystyrene-block-β-cyclodextrin copolymer, preparation and characterization of glyconanoparticles, SEM data, electropolymerisation process and DLS data.

# AUTHOR INFORMATION

Corresponding Author

*** Serge Cosnier** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* orcid.org/0000-0002-8290-4374; serge.cosnier@univ-grenoble-alpes.fr

Authors

**Monica Brachi** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* https://orcid.org/0000-0003-1749-648X

**Paulo Henrique M. Buzzetti** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* orcid.org/0000-0003-1074-054X

**Karine Gorgy** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* orcid.org/0000-0001-6176-4803

**Dan Shan** - *School of Environmental and Biological Engineering, Nanjing University of Science and Technology, Nanjing 210094, China;* orcid.org/ 0000-0002-2965-8610

**Pierre Audebert -** *PPSM, CNRS UMR 8531, ENS Cachan, 61 avenue du Président Wilson. 94235 Cachan, France;* orcid.org/ 0000-0001-9943-7808

**Alan le Goff** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* orcid.org/0000-0002-6765-5859

**Hong Li** - *Univ. Grenoble Alpes, CNRS, CERMAV, F-38000 Grenoble, France ;* orcid.org/0000-0002-3060-1400

**Redouane Borsali** - *Univ. Grenoble Alpes, CNRS, CERMAV, F-38000 Grenoble, France.* orcid.org/0000-0002-7245-586X

**Serge Cosnier** - *Univ. Grenoble Alpes, DCM UMR 5250, F-38000 Grenoble, France. CNRS, DCM UMR 5250, F-38000 Grenoble, France;* orcid.org/0000-0002-8290-4374

### Author Contributions

Conceptualization, Karine Gorgy, Alan le Goff, Pierre Audebert and Serge Cosnier; validation, Karine Gorgy Pierre Audebert and Serge Cosnier; formal analysis, Monica Brachi, Paulo Henrique M. Buzzetti and Karine Gorgy, investigation, Monica Brachi, Paulo Henrique M. Buzzetti and Karine Gorgy; data curation, Monica Brachi and Paulo Henrique M. Buzzetti, DLS experiments Hong Li; writing - original draft preparation, Monica Brachi, Paulo Henrique M. Buzzetti, Pierre Audebert and Serge Cosnier; writing - review and editing Karine Gorgy, Pierre Audebert, Alan le Goff, Redouane Borsali, Dan Shan and Serge Cosnier; visualization, Monica Brachi and Paulo Henrique M. Buzzetti; supervision, Karine Gorgy, Pierre Audebert, Alan le Goff, Redouane Borsali and Serge Cosnier; project administration, Serge Cosnier; funding acquisition, Serge Cosnier and Redouane Borsali.

### Funding Sources

The authors thank the French National Research Agency for post-doc funding (ANR NanoFueCell-18-CE09-0022), the Labex Arcane and CBH-EUR-GS (ANR-17-EURE-0003) and the Sino-French international research network IRN CNRS 876.

## ACKNOWLEDGMENT

This work was supported by the French National Research Agency (ANR-18-CE09-0022) and the Labex Arcane and CBH-EUR-GS (ANR-17-EURE-0003). The authors also gratefully acknowledge the support from the Institut Carnot PolyNat (CARN 0007-01) and the Sino-French international research network IRN CNRS 876 “New nanostructured materials and biomaterials for renewable electrical energy sources”. The authors thank Dr Laurent Galmiche for its contribution to the synthetic work.

## ABBREVIATIONS

HTZ-Ad, 2,5,8-tris((adamantan-1-yl) methoxy)-heptazine; BCPs, block copolymers; βCD, β-cyclodextrin; PS-b-βCD, polystyrene-block-β-cyclodextrin copolymer; $GNP_{PSCD}$, polystyrene-block-β-cyclodextrin glyconanoparticles; $GNP_{PSCD\text{-}HTZ\text{-}Ad}$, 2,5,8-tris((adamantan-1-yl) methoxy)-heptazine functionalized polystyrene-block-β-cyclodextrin glyconanoparticles; PY-Ad, pyrrole-adamantane and PPY-Ad, poly(pyrrole-adamantane).

## REFERENCES

(1) Zepon, K. M.; Otsuka, I.; Bouilhac, C.; Muniz, E. C.; Soldi, V.; Borsali, R. Self-Assembly of Oligosaccharide-b-PMMA Block Copolymer Systems: Glyco-Nanoparticles and Their Degradation under UV Exposure. *Langmuir* **2016**, *32* (18), 4538–4545. https://doi.org/10.1021/acs.langmuir.6b00212.

(2) Zepon, K. M.; Otsuka, I.; Bouilhac, C.; Muniz, E. C.; Soldi, V.; Borsali, R. Glyco-Nanoparticles Made from Self-Assembly of Maltoheptaose- Block -Poly(Methyl Methacrylate): Micelle, Reverse Micelle, and Encapsulation. *Biomacromolecules* **2015**, *16* (7), 2012–2024. https://doi.org/10.1021/acs.biomac.5b00443.

(3) Otsuka, I.; Osaka, M.; Sakai, Y.; Travelet, C.; Putaux, J. L.; Borsali, R. Self-Assembly of Maltoheptaose-Block-Polystyrene into Micellar Nanoparticles and Encapsulation of Gold Nanoparticles. *Langmuir* **2013**, *29* (49), 15224–15230. https://doi.org/10.1021/la403941v.

(4) Gross, A. J.; Haddad, R.; Travelet, C.; Reynaud, E.; Audebert, P.; Borsali, R.; Cosnier, S. Redox-Active Carbohydrate-Coated Nanoparticles: Self-Assembly of a Cyclodextrin-Polystyrene Glycopolymer with Tetrazine-Naphthalimide. *Langmuir* **2016**, *32* (45), 11939–11945. https://doi.org/10.1021/acs.langmuir.6b03512.

(5) Gong, Y. H.; Miomandre, F.; Méallet-Renault, R.; Badré, S.; Galmiche, L.; Tang, J.; Audebert, P.; Clavier, G. Synthesis and Physical Chemistry of S-Tetrazines: Which Ones Are Fluorescent and Why? *European J. Org. Chem.* **2009**, No. 35, 6121–6128. https://doi.org/10.1002/ejoc.200900964.

(6) Clavier, G.; Audebert, P. S -Tetrazines as Building Blocks for New Functional Molecules and Molecular Materials. *Chem. Rev.* **2010**, *110* (6), 3299–3314. https://doi.org/10.1021/cr900357e.

(7) Miomandre, F.; Lépicier, E.; Munteanu, S.; Galangau, O.; Audibert, J. F.; Méallet-Renault, R.; Audebert, P.; Pansu, R. B. Electrochemical Monitoring of the Fluorescence Emission of Tetrazine and Bodipy Dyes Using Total Internal Reflection Fluorescence Microscopy Coupled to Electrochemistry. *ACS Appl. Mater. Interfaces* **2011**, *3* (3), 690–696. https://doi.org/10.1021/am100980u.

(8) Guermazi, R.; Royer, L.; Galmiche, L.; Clavier, G.; Audebert, P.; Hedhli, A. Synthesis and Characterization of New Fluorinated Tetrazines Displaying a High Fluorescence Yield. *J. Fluoresc.* **2016**, *26* (4), 1349–1356. https://doi.org/10.1007/s10895-016-1822-3.

(9) Miomandre, F.; Audebert, P. 1,2,4,5-Tetrazines: An Intriguing Heterocycles Family with Outstanding Characteristics in the Field of Luminescence and Electrochemistry. *J. Photochem. Photobiol. C Photochem. Rev.* **2020**, *44*, 100372. https://doi.org/10.1016/j.jphotochemrev.2020.100372.

(10) Audebert, P.; Kroke, E.; Posern, C.; Lee, S. H. State of the Art in the Preparation and Properties of Molecular Monomeric S‐Heptazines: Syntheses, Characteristics, and Functional Applications. *Chem. Rev.* **2021**, *121* (4), 2515–2544. https://doi.org/10.1021/acs.chemrev.0c00955.

(11) Saplinova, T.; Bakumov, V.; Gmeiner, T.; Wagler, J.; Schwarz, M.; Kroke, E. 2,5,8-Trihydrazino-s-Heptazine: A Precursor for Heptazine-Based Iminophosphoranes. *Zeitschrift fur Anorg. und Allg. Chemie* **2009**, *635* (15),

2480–2487. https://doi.org/10.1002/zaac.200900311.

(12) Luebke, R.; Weseliński, Ł. J.; Belmabkhout, Y.; Chen, Z.; Wojtas, Ł.; Eddaoudi, M. Microporous Heptazine Functionalized (3,24)-Connected Rht-Metal-Organic Framework: Synthesis, Structure, and Gas Sorption Analysis. *Cryst. Growth Des.* **2014**, *14* (2), 414–418. https://doi.org/10.1021/cg401802s.

(13) Dang, Q. Q.; Zhan, Y. F.; Wang, X. M.; Zhang, X. M. Heptazine-Based Porous Framework for Selective CO2 Sorption and Organocatalytic Performances. *ACS Appl. Mater. Interfaces* **2015**, *7* (51), 28452–28458. https://doi.org/10.1021/acsami.5b09441.

(14) Kailasam, K.; Mesch, M. B.; Möhlmann, L.; Baar, M.; Blechert, S.; Schwarze, M.; Schröder, M.; Schomäcker, R.; Senker, J.; Thomas, A. Donor–Acceptor-Type Heptazine-Based Polymer Networks for Photocatalytic Hydrogen Evolution. *Energy Technol.* **2016**, *4* (6), 744–750. https://doi.org/10.1002/ente.201500478.

(15) Zambon, A.; Mouesca, J. M.; Gheorghiu, C.; Bayle, P. A.; Pécaut, J.; Claeys-Bruno, M.; Gambarelli, S.; Dubois, L. S-Heptazine Oligomers: Promising Structural Models for Graphitic Carbon Nitride. *Chem. Sci.* **2016**, *7* (2), 945–950. https://doi.org/10.1039/c5sc02992a.

(16) Mir Sayed, S.; Deng, L. L.; Lin, B. P.; Yang, H. A Room-Temperature Heptazine Core Discotic Liquid Crystal. *Liq. Cryst.* **2017**, *44* (14–15), 2175–2183. https://doi.org/10.1080/02678292.2017.1371343.

(17) Bala, I.; Gupta, S. P.; Kumar, S.; Singh, H.; De, J.; Sharma, N.; Kailasam, K.; Pal, S. K. Hydrogen-Bond Mediated Columnar Liquid Crystalline Assemblies of C3-Symmetric Heptazine Derivatives at Ambient Temperature. *Soft Matter* **2018**, *14* (30), 6342–6352. https://doi.org/10.1039/c8sm00834e.

(18) Le, T.; Galmiche, L.; Masson, G.; Allain, C.; Audebert, P. A Straightforward Synthesis of a New Family of Molecules: 2,5,8-Trialkoxyheptazines. Application to Photoredox Catalyzed Transformations. *Chem. Commun.* **2020**, *56* (73), 10742–10745. https://doi.org/10.1039/d0cc05118g.

(19) Chen, G.; Jiang, M. Cyclodextrin-Based Inclusion Complexation Bridging Supramolecular Chemistry and Macromolecular Self-Assembly. *Chem. Soc. Rev.* **2011**, *40* (5), 2254–2266. https://doi.org/10.1039/c0cs00153h.

(20) Ehrmaier, J.; Huang, X.; Rabe, E. J.; Corp, K. L.; Schlenker, C. W.; Sobolewski, A. L.; Domcke, W. Molecular Design of Heptazine-Based Photocatalysts: Effect of Substituents on Photocatalytic Efficiency and Photostability. *J. Phys. Chem. A* **2020**, *124* (19), 3698–3710. https://doi.org/10.1021/acs.jpca.0c00488.

(21) Cutrone, G.; Casas-Solvas, J. M.; Vargas-Berenguel, A. Cyclodextrin-Modified Inorganic Materials for the Construction of Nanocarriers. *Int. J. Pharm.* **2017**, *531* (2), 621–639. https://doi.org/10.1016/j.ijpharm.2017.06.080.

(22) Gross, A. J.; Chen, X.; Giroud, F.; Travelet, C.; Borsali, R.; Cosnier, S. Redox-Active Glyconanoparticles as Electron Shuttles for Mediated Electron Transfer with Bilirubin Oxidase in Solution. *J. Am. Chem. Soc.* **2017**, *139* (45), 16076–16079. https://doi.org/10.1021/jacs.7b09442.

(23) Hammond, J. L.; Gross, A. J.; Giroud, F.; Travelet, C.; Borsali, R.; Cosnier, S. Solubilized Enzymatic Fuel Cell (SEFC) for Quasi-Continuous Operation Exploiting Carbohydrate Block Copolymer Glyconanoparticle Mediators. *ACS Energy Lett.* **2019**, *4* (1), 142–148. https://doi.org/10.1021/acsenergylett.8b01972.

(24) Carrière, M.; Buzzetti, P.; Gorgy, K.; Mumtaz, M.; Travelet, C.; Borsali, R.; Cosnier, S. Functionalizable Glyconanoparticles for a Versatile Redox Platform. *Nanomaterials* **2021**, *11* (5), 1162. https://doi.org/10.3390/nano11051162.

(25) Holzinger, M.; Bouffier, L.; Villalonga, R.; Cosnier, S. Adamantane/β-Cyclodextrin Affinity Biosensors Based on Single-Walled Carbon Nanotubes. *Biosens. Bioelectron.* **2009**, *24* (5), 1128–1134. https://doi.org/10.1016/j.bios.2008.06.029.

(26) Haddad, R.; Holzinger, M.; Villalonga, R.; Neumann, A.; Roots, J.; Maaref, A.; Cosnier, S. Pyrene-Adamantane-β-Cyclodextrin: An Efficient Host-Guest System for the Biofunctionalization of SWCNT Electrodes. *Carbon N. Y.* **2011**, *49* (7), 2571–2578. https://doi.org/10.1016/j.carbon.2011.02.049.