



Review

Aromatic micelles: toward a third-generation of micelles

By Michito YOSHIKAWA*^{1,†}  and Lorenzo CATTI*¹ 

(Edited by Keisuke SUZUKI, M.J.A.)

Abstract: Micelles are useful and widely applied molecular assemblies, formed from amphiphilic molecules, in water. The majority of amphiphiles possess an alkyl chain as the hydrophobic part. Amphiphiles bearing hydrophilic and hydrophobic polymer chains generate so-called polymeric micelles in water. This review focuses on the recent progress of “aromatic micelles”, formed from bent polyaromatic/aromatic amphiphiles, for the development of third-generation micelles. Thanks to multiple host-guest interactions, *e.g.*, the hydrophobic effect and π - π /CH- π interactions, the present micelles display wide-ranging uptake abilities toward various hydrophobic compounds in water. In addition to such host functions, new stimuli-responsive aromatic micelles with pH, light, and redox switches, aromatic oligomer micelles, saccharide-coated aromatic micelles, and related cycloalkane-based micelles were recently developed by our group.

Keywords: aromatic micelle, bent aromatic amphiphile, stimuli-responsive, host-guest interaction, water

1. Introduction

Micelles are one of the most useful molecular assemblies in our daily life, formed from amphiphilic molecules (Fig. 1a), which are mainly provided by soap and detergent. Amphiphiles generally consist of both hydrophobic and hydrophilic parts connected covalently. The structure and properties of micelles are largely affected by each of the two parts so that a wide variety of amphiphiles have been developed so far by synthetic chemists.^{1,2)} The majority of amphiphilic molecules possess linear alkyl chains as the hydrophobic part, which aggregate into roughly spherical cores through the hydrophobic effect (Fig. 1c). Anionic and cationic groups, typically used as the hydrophilic part, cover the hydrophobic cores to dissolve micelles in water. The basic properties of such alkyl chain-based micelles and their applications, *e.g.*, as dissolution, separation, preservation, and reaction tools, have been extensively studied from chemical, physical, and biological view-

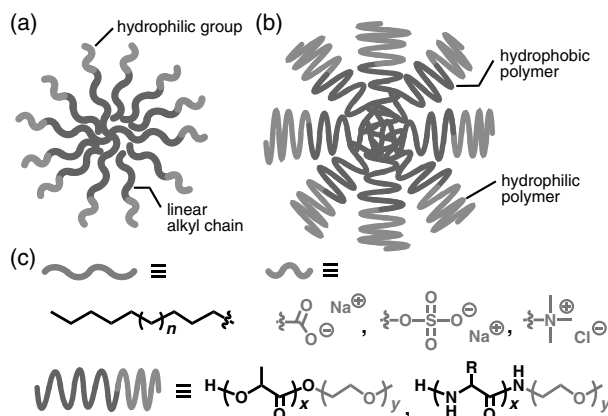


Fig. 1. (Color online) Schematic representation of (a) a conventional micelle and (b) a polymer micelle. (c) Typical amphiphilic molecules and polymers.

points.^{1–3)} In contrast, amphiphilic polymers, comprising hydrophobic and hydrophilic polymer chains, generate polymeric assemblies with spherical core-shell structures (Fig. 1b, c). As compared with conventional micelles, the polymer micelles display excellent stability against increased dilution and temperature in water, mainly due to the entropic stabilization effect. The micellar size (*i.e.*, 10–100 nm) is controllable by the choice of the polymer length. The medical application of polymer micelles

*¹ Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology, Yokohama, Japan.

† Correspondence should be addressed to: M. Yoshizawa, Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan (e-mail: yoshizawa.m.ac@m.titech.ac.jp).

(*e.g.*, drug delivery system) has been particularly investigated through the wide-ranging functionalization of the amphiphilic polymers.^{4)–6)}

2. What are “aromatic micelles”?

Unlike the two classes of micelles described above, this review focuses on the recent progress of capsular micelles with *multiple polyaromatic/aromatic panels* (Fig. 2a), reported by our group in 2013 for the first time.⁷⁾ We call these molecular assemblies “aromatic micelles” to distinguish them from the previous micelles with alkyl and polymer chains. **AA** is a bent aromatic amphiphile, developed by our group members, with two anthracene panels and two trimethylammonium groups (Fig. 2b). In water, the bent amphiphiles spontaneously and quantitatively assemble into an aromatic micelle with a spherical shell (Fig. 2c), featuring an average formula of $(\mathbf{AA})_5$ and an average core diameter of ~ 1 nm. Thanks to the combination of the hydrophobic effect and partial π - π interactions, the resultant micelles

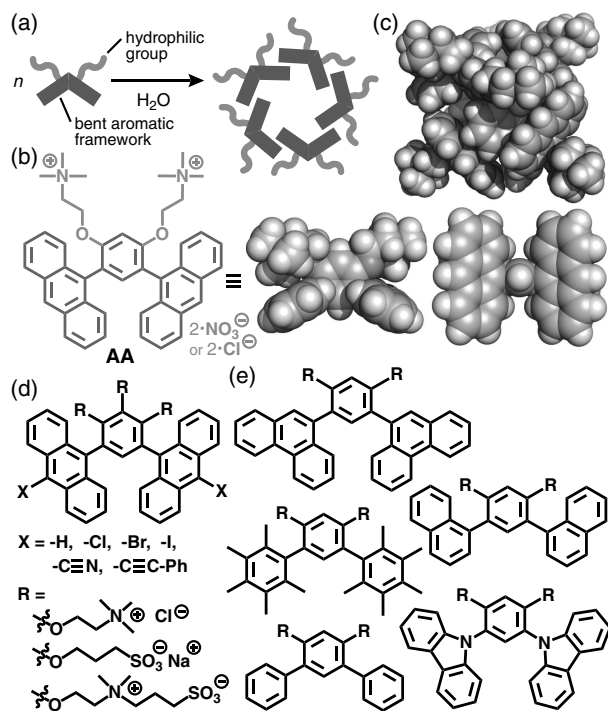


Fig. 2. (Color online) (a) Formation of an aromatic micelle from bent aromatic amphiphiles in water. (b) Anthracene-based bent amphiphile **AA** and its optimized structures (obtained by molecular mechanics (MM) calculation using forcite module, Materials Studio, Dassault Systèmes Co.). (c) Optimized structure of micelle $(\mathbf{AA})_n$. Modulation of amphiphile **AA** through (d) functionalization and (e) replacement of the anthracene panels with other panels.

display relatively high stability and very narrow size distribution. The physical properties and host ability of micelle $(\mathbf{AA})_n$ can be readily tuned by the functionalization of the anthracene/phenylene rings (Fig. 2d) and the replacement of the anthracene panels with other aromatic ones (*e.g.*, phenanthrene, naphthalene, and carbazole; Fig. 2e).^{8)–16)}

Importantly, despite strong self-assembling properties, aromatic micelle $(\mathbf{AA})_n$ can efficiently incorporate various hydrophobic dyes into the dynamic cavities in water, through multiple host-guest interactions, *e.g.*, the hydrophobic effect and π - π /CH- π interactions (Fig. 3a). The uptake ability of the present micelle is much higher than that of previous alkyl-based micelles, *e.g.*, from sodium dodecyl sulfate (SDS) and dodecyltrimethylammonium chloride (DTAC). Fluorescent dyes such as Nile red and dicyanomethylenepyran derivative,^{7),17)}

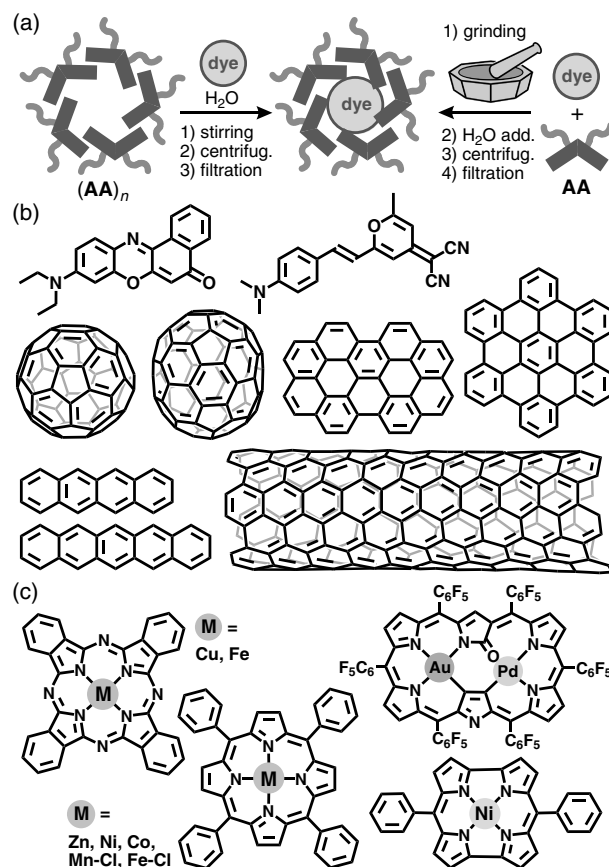


Fig. 3. (Color online) (a) Schematic representation of the incorporation of hydrophobic compounds (*e.g.*, dyes) by aromatic micelle $(\mathbf{AA})_n$ in water. (b) Representative fluorescent dyes, nanocarbons, and (c) metal-complexes incorporated by aromatic micelles.

nanocarbons such as fullerenes, nanographenes, and carbon nanotubes (Fig. 3b),^{18)–20)} and π -conjugated metal-complexes such as metal-phthalocyanines, metal-porphyrins, *N*-confused Au(III)/Pd(II)-oxohexaphyrin, and Ni(II)-norcorroles (Fig. 3c)^{21)–26)} were incorporated by the aromatic micelle in water, through a simple stirring or grinding protocol. The solid-state grinding of mixtures of **AA** and highly hydrophobic compounds by hand enhances the formation of aqueous host-guest composites.

On the basis of the characteristic structures and superior host capabilities of (**AA**)_{*n*} and its derivatives,^{27),28)} for the development of third-generation micelles with unique functions in water, this review describes the recent achievements with our aromatic micelles as follows: (i) stimuli-responsive aromatic micelles, (ii) aromatic oligomer micelles, (iii) saccharide-coated aromatic micelles, and (iv) related cyclohexyl/adamantyl-based micelles. Related aromatic capsules, tubes, and bowls with coordination and/or covalent bonds have been focused on in our previous reviews.^{29)–32)}

3. Stimuli-responsive aromatic micelles

Development of stimuli-responsive molecules, supramolecules, and polymers has been one of the most active research fields in recent chemistry.^{33)–35)} However, the investigation of an ideal combination of stimuli-responsiveness and host-guest interactions is still ongoing. The incorporation of small pH-, light-, and redox-responsive switches into bent aromatic amphiphiles would be expected to develop highly stimuli-responsive aromatic micelles with both guest uptake and release functions in water.

To construct a pH-responsive aromatic micelle, we replaced the two anthracene panels of **AA** with protonable acridine panels, yielding bent amphiphile **AcA** (Fig. 4a).³⁶⁾ In a manner similar to **AA**, self-assembly of **AcA** formed a capsular micelle with a narrow size-distribution and displayed wide-ranging host abilities toward hydrophobic dyes in neutral water. Importantly, addition of HCl aq. was shown to induce the disassembly of micelle (**AcA**)_{*n*} via the protonation-induced electrostatic repulsion and increased hydrophilicity of **AcA** (Fig. 4a). Disassembly of the micelle resulted in the quantitative release of the incorporated dyes, as evidenced by UV-visible (UV-vis) and NMR spectroscopy. Straightforward re-assembly of the micelle could be achieved through deprotonation via addition of NaOH aq. It is noteworthy that the assembly-disassembly of (**AcA**)_{*n*} was repeated more than ten times without any

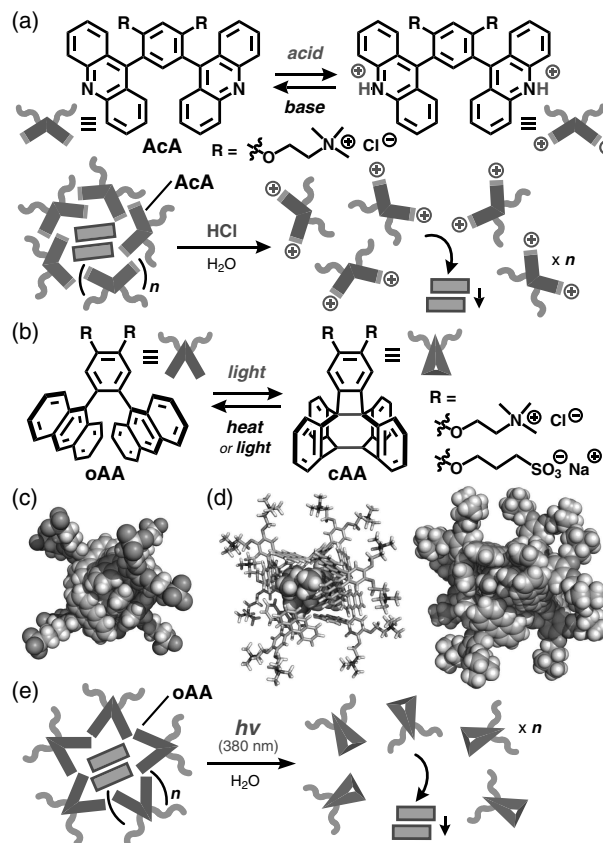


Fig. 4. (Color online) (a) pH-responsive bent amphiphile **AcA** and its aromatic micelle with guest releasing ability upon acid addition. (b) Photo-responsive bent amphiphile **oAA** and the optimized structures (MM calculation) of (c) aromatic micelle (**oAA**)_{*n*} and (d) its host-guest composite including Nile red. (e) Guest releasing ability of micelle (**oAA**)_{*n*} upon light irradiation.

decomposition, which even allowed the re-inclusion of released dyes.

Anthracene is known to undergo a [4+4]-photocyclization reaction under light irradiation. Despite featuring two anthracene panels, original amphiphile **AA** shows neither intra- nor intermolecular photocyclization ability, due to spatial separation of the panels and shielding by the hydrophilic side-chains, respectively. Changing the anthracene connectivity from *meta* to *ortho* yielded *ortho*-dianthrylbenzene-based bent amphiphile **oAA**, which is converted to the closed form (**cAA**) by quick and quantitative intramolecular [4+4]-photocyclization in water upon irradiation at 380 nm (Fig. 4b).³⁷⁾ Importantly, the cyclization was shown to be partially and quantitatively reversible via irradiation at lower wavelength (287 nm) and heating (160 °C, microwave), respectively. Switching between the assembled and dis-

assembled states could be repeated five times without any sign of decomposition. Photo-responsive micelle (**oAA**)_n allowed the water-solubilization of a wide-range of hydrophobic dyes such as Nile red, fullerene, and phthalocyanines via the narrow binding pocket of **oAAs** (Fig. 4c, d). The disassembly ability of the guest-loaded micelles upon light irradiation was subsequently utilized for the quantitative release of the guests into water (Fig. 4e), as evidenced by UV-vis analysis. Furthermore, the photo-induced release of fluorescent dyes from the micelle demonstrated drastic increase of their partially quenched emission ($\Delta\Phi_F = \sim 60\text{--}70\%$).

By attaching redox-active phenothiazine panels to the *meta*-phenylene spacer, we were able to synthesize novel bent amphiphile **PTA** with reversible oxidation and reduction properties (Fig. 5a).³⁸ In water, **PTA** quantitatively self-assembled into an aromatic micelle with ~ 2 nm in average diameter, as confirmed by dynamic light scattering (DLS), DOSY NMR, and atomic force microscopy (AFM) analyses. Both electrochemical and chemical oxidation of redox-responsive micelle (**PTA**)_n could reversibly transform its neutral framework into oligo(radical cation) ones with moderate stability in sharp contrast to unstable phenothiazine radicals, in water (Fig. 5b), as revealed by UV-vis and electron spin resonance (ESR) analyses. Rapid and quantitative reformation of the neutral micelle was achieved upon simple addition of the Zn powder. The uptake of hydrophobic dyes by the micelle and subsequent chemical oxidation generated an intriguing radical host-guest composite. UV-vis investigation indicated conversion of up to 36% of the phenothiazine panels into radical cations in the host-guest composites. In addition, chemical oxygenation of the sulfur atoms into sulfones on **PTA** with NaClO induced the disassem-

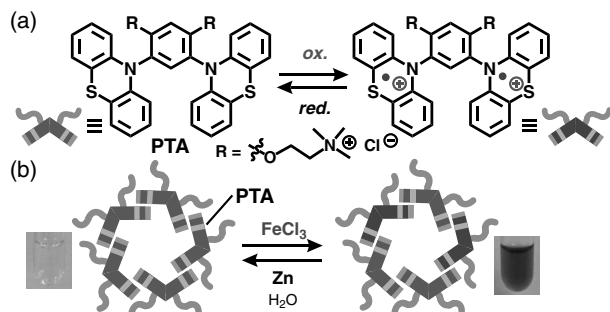


Fig. 5. (Color online) (a) Redox-responsive bent amphiphile **PTA** and (b) its aromatic micelle capable of reversibly forming a radical micelle upon oxidation.

sembly of the micelle and subsequent release of encapsulated guests into water.³⁸

4. Aromatic oligomer micelles

Covalent cross-linking of amphiphiles into dimers and oligomers is an important strategy to improve the stability of their assemblies and control assembly morphologies through variation of the cross-linking positions.^{39,40} While there have been several reports on amphiphilic oligomers containing several polyaromatic panels, extensive self-stacking into columnar structures is limiting their host functions and applications.⁴¹

The connection of two **AAs** has been studied by our group using different rigid spacers.^{42–44} For the development of a highly stable aromatic oligomer micelle with adequate host ability, we covalently connected three **AA** molecules alternately with two flexible hydrophilic chains in a linear fashion (Fig. 6a, b).⁴⁵ Obtained amphiphilic trimer **AT** quantitatively assembled into aromatic oligomer micelle (**AT**)₂ ($d_{av} = 1.8$ nm) upon dissolution in water, as revealed by the combination of NMR, DLS, AFM, and molecular modeling studies. Notably, **AT** displayed a more than 300 times lower critical micelle

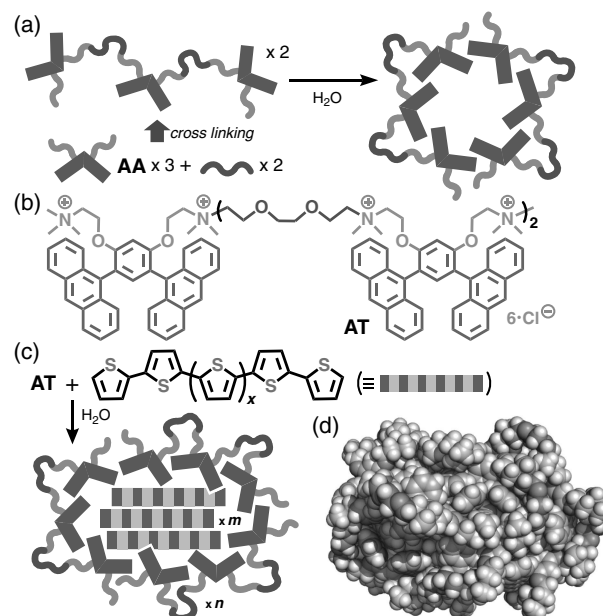


Fig. 6. (Color online) (a) Formation of an aromatic oligomer micelle from amphiphilic trimers in water. (b) Amphiphilic trimer **AT** bearing three bent aromatic amphiphiles **AA**. (c) Formation of host-guest composites from **AT** and oligothiophenes in water and (d) the optimized structure (MM calculation).

concentration (cmc; $<3\ \mu\text{M}$) than **AA**, indicating superior stability of the oligomer micelle against high dilution. The assembled structure was found to be stable even at elevated temperature ($130\ ^\circ\text{C}$) and in the presence of excess organic solvent (60% methanol), due to the polyaromatic chelate effect. Isothermal titration calorimetry (ITC) experiments revealed that the high stability of $(\mathbf{AT})_2$ is driven by large enthalpic stabilization based on efficient π -stacking interactions and the hydrophobic effect.

Despite such tight self-stacking, $(\mathbf{AT})_2$ showed enhanced uptake abilities relative to $(\mathbf{AA})_n$ and selectively encapsulated unsubstituted oligothiophenes (≥ 4 -mer) with high efficiency (Fig. 6c). Multiple oligothiophenes (*e.g.*, quinquethiophene) were incorporated as small stacks, yielding ellipsoidal host-guest composites seamed by hydrophilic chains (Fig. 6d). Encapsulation furthermore induced large changes in the fluorescent properties of the oligothiophenes. Importantly, **AT** also allowed the solubilization of otherwise insoluble, unsubstituted polythiophenes, which could be subsequently released onto glass substrates via a casting and washing protocol.⁴⁵⁾

5. Saccharide-coated aromatic micelles

Saccharide clusters are key biological structures that can interact selectively with protein surfaces through weak yet multipoint interactions.^{46),47)} Mimicking such bio-clusters with artificial constructs (*e.g.*, dendrimers, metal nanoparticles, vesicles, and metal-organic frameworks), providing strong and/or colorful emission properties, would result in valuable tools for non-covalent cell labeling and protein sensing.⁴⁸⁾ However, strong emission from artificial saccharide clusters is often hampered by aggregation-caused quenching (ACQ) or the heavy metal effect.

Access to a new micellar saccharide cluster was achieved by replacing the ionic hydrophilic side-chains of **AA** with three non-ionic mannose residues (Fig. 7a).⁴⁹⁾ The synthesized amphiphile **MA** formed a well-defined spherical micelle ($\sim 2\ \text{nm}$ in diameter), thoroughly coated by multiple mannose units, in water (Fig. 7b). The stability of micelle $(\mathbf{MA})_n$ against dilution is ~ 50 -fold higher than that of $(\mathbf{AA})_n$, which likely results from the lack of electrostatic repulsion between the hydrophilic side-chains. Interestingly, $(\mathbf{MA})_n$ exhibited moderate blue fluorescence ($\Phi_F = 19\%$), whose intensity is ~ 20 times higher than that of $(\mathbf{AA})_n$, implying restricted π -stacking interactions between the anthracene panels due to the sterically demanding saccharide groups.

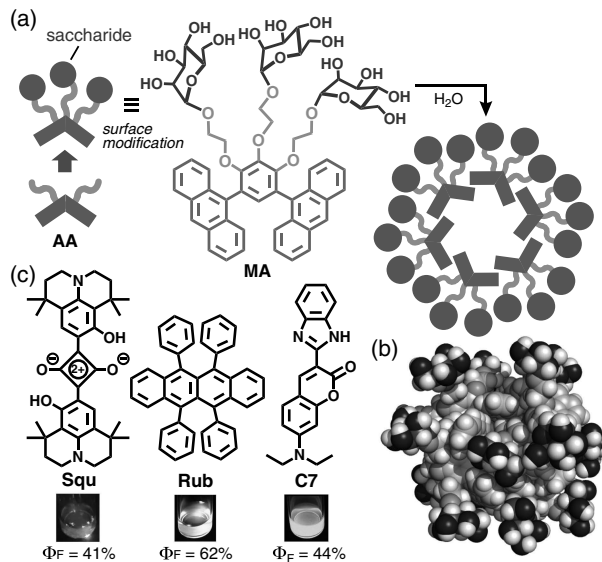


Fig. 7. (Color online) (a) Formation of a saccharide-coated aromatic micelle from bent amphiphiles **MA** with three mannose groups in water and (b) the optimized structure (MM calculation) of $(\mathbf{MA})_n$. (c) Fluorescent dyes loaded by the micelle, and the photographs and emission quantum yields of the corresponding host-guest complexes.

The emission color of the present micelle could be readily altered by loading of various fluorescent dyes into the cavity, using a simple grinding protocol. As indicated by UV-vis, DLS, and fluorescence analyses, the resultant micelles containing squaraine (**Squ**), rubrene (**Rub**), and coumarin 7 (**C7**) were shown to display strong red, yellow, and green emission, respectively, with quantum yields up to 62% (Fig. 7c). The unusually high guest-emission arises from suppression of ACQ by the non-ionic and bulky mannose side-chains.

Biofunctionality of micelle $(\mathbf{MA})_n$ as an artificial saccharide cluster was unequivocally demonstrated by its selective interactions with mannose-binding protein concanavalin A (ConA). Addition of $(\mathbf{MA})_n$ to a clear aqueous solution of ConA led to gradual aggregation via non-covalent cross-linking, as indicated by UV-vis turbidity analysis. Importantly, interactions of fluorescent dye-loaded micelle $(\mathbf{MA})_n$ with ConA were likewise demonstrated without disassembly of the host-guest structure. In contrast, no interactions were observed with a galactose-binding protein, emphasizing the specificity of the observed phenomenon.

6. Cycloalkane-based micelles

In contrast to linear alkanes, which are essential

subunits of natural and artificial amphiphiles, cyclic alkanes are far less explored as substitutes and their influence on host-guest interactions remains mostly unclear.⁵⁰⁾ The higher rigidity and directionality of cycloalkanes compared to linear alkanes are expected to significantly alter the host functions (*e.g.*, uptake efficiency and selectivity) of the corresponding micellar structures. Incorporating such semi-rigid parts into a bent amphiphile represents a new design principle for alkane-based micelles, which also differs from oligocyclic steroid-based amphiphiles reported previously.⁵¹⁾

As the first attempt into this direction, we replaced the anthracene panels on **AA** with two cyclohexyl groups to create amphiphile **CHA** (Fig. 8a), obtained in only four steps starting from pyrogallol.⁵²⁾ Dissolution of **CHA** in water was shown to yield spherical micelles (**CHA**)_n (*d*_{av} = 2.3 nm), composed of twelve amphiphile molecules in

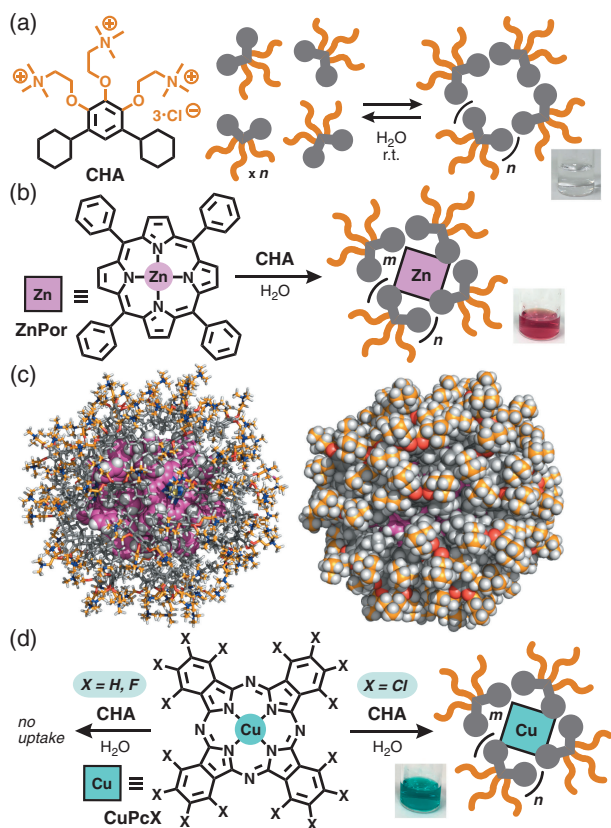


Fig. 8. (a) Cyclohexane-based bent amphiphile **CHA** and the formation of its capsular micelle in water. (b) Multiple uptake of **ZnPor** by micelle (**CHA**)_n in water and (c) the optimized structure (MM calculation) of the host-guest composite. (d) Substituent-selective uptake of **CuPcX** (X = H, F, and Cl).

average. The cmc of **CHA** was found to be ~ 170 times higher than that of **AA**, mainly due to the absence of π - π interactions. Unexpectedly, micelle (**CHA**)_n displayed unusual uptake ability toward various large metal-complexes in water. For instance, subjecting **CHA** and bulky Zn(II)-tetraphenylporphyrin (**ZnPor**) to a grinding-based uptake protocol gave rise to a clear purple solution, displaying characteristic porphyrin-based absorption bands (Fig. 8b). The uptake efficiency of **CHA** was increased by 2.5- and 6.7-fold, as compared to that of **AA** and SDS, respectively, due to favorable interactions between the cyclohexyl groups and non-planar **ZnPors**. The combination of the NMR and DLS (*d*_{av} = 3.8 nm) data with molecular modeling indicated the formation of spherical host-guest composite (**CHA**)₄₅•(**ZnPor**)₉ (Fig. 8c). Furthermore, in stark contrast to previous micelles (**AA**)_n and (SDS)_n, the substituent-dependent uptake of planar Cu(II)-phthalocyanines (**CuPcX**) was demonstrated by (**CHA**)_n in water. While (**CHA**)_n could solubilize perchlorinated **CuPcCl** with high efficiency upon encapsulation by a grinding protocol, no encapsulation was observed using non-substituted **CuPcH** or perfluorinated **CuPcF**, even under various uptake conditions (Fig. 8d).

Replacement of the aromatic panels with aliphatic units was expected to improve guest emission even upon incorporation, as verified using trinuclear Au(I)-complex **AuPz** (Fig. 9a). Solid-state **AuPz** displays strong red emission based on intermolecular Au(I)-Au(I) interactions, upon irradiation at 290 nm. The interactions are lost upon dissolution, resulting in complete emission quenching. The treatment of **AuPz** with **CHA** facilitated the successful uptake of (**AuPz**)_m in a stacked fashion, by the micelle cavity (Fig. 9b). Importantly, strong red emission was observed from the clear aqueous solution of (**CHA**)_n•(**AuPz**)_m in more than 30% quantum yield upon irradiation under air, indicating the presence of

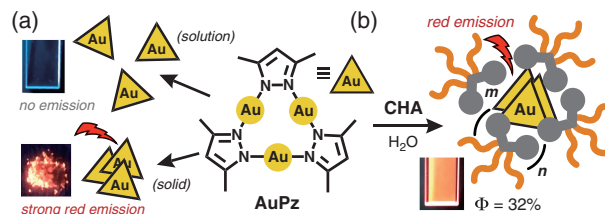


Fig. 9. (a) Emission properties of trinuclear Au(I)-complex **AuPz** in solution and in the solid state, and (b) uptake-induced solution-state emission of **AuPz** by cyclohexane-based micelle (**CHA**)_n in water and the photograph.

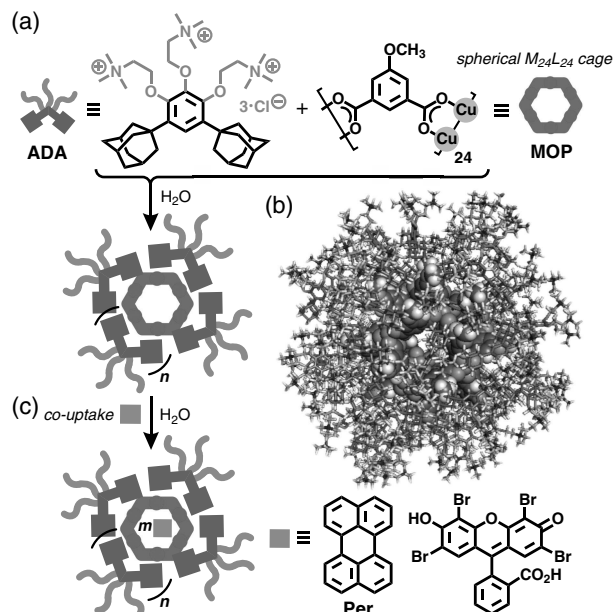


Fig. 10. (Color online) (a) Efficient uptake of metal-organic polyhedra (MOP) by adamantane-based bent amphiphile **ADA** in water and (b) the optimized structure (MM calculation) of the host-guest composite. (c) Efficient co-uptake of MOP and fluorescent dyes by adamantane-based micelle $(\text{ADA})_n$ in water.

intermolecular Au(I)-Au(I) interactions in the cavity, even in solution.

Encouraged by the intriguing properties of $(\text{CHA})_n$, we next designed amphiphile **ADA**, composed of two adamantyl groups linked by a *meta*-phenylene (Fig. 10a).⁵³ The properties of adamantane are similar to those of cyclohexane yet the structural rigidity resembles that of anthracene. Adamantane-based micelle $(\text{ADA})_n$ was spontaneously and quantitatively generated in water from **ADA** at high concentration (~ 70 mM). The DLS and DOSY analyses confirmed the formation of spherical micelles $(\text{ADA})_n$ with an average core diameter of 2.5 nm, suggesting the main composition to be $(\text{ADA})_{16}$. Micelle $(\text{ADA})_n$ displayed wide-ranging host abilities toward medium-size to huge spherical compounds (*i.e.*, approximately 0.6 to 3 nm), such as adamantane, diamantane, fullerenes, and metal-organic polyhedra (**MOP**) in water, unlike previous micelles (*i.e.*, $(\text{AA})_n$, $(\text{CHA})_n$, and $(\text{SDS})_n$). Among them, **MOP** is a notoriously insoluble, huge cage with a diameter of ~ 3 nm, composed of 24 Cu(II) ions and 24 isophthalates (Fig. 10a). The product structure of 1:1 host-guest composite $(\text{ADA})_n \cdot \text{MOP}$ ($n = \sim 40$) was confirmed

by UV-vis, DLS, molecular modelling, and FT-IR analyses (Fig. 10b).

Taking advantage of the open cavity of **MOP**, the formation of ternary core-shell structures could be achieved in water using medium-sized fluorescent dyes. Subjecting a mixture of **ADA**, **MOP**, and perylene (**Per**) to a grinding protocol afforded a clear solution including $(\text{ADA})_n \cdot \text{MOP} \cdot (\text{Per})_m$ (Fig. 10c). Accommodation of **Per** in the **MOP** cavity was indicated by DLS and fluorescence analyses, which showed an identical size to $(\text{ADA})_n \cdot \text{MOP}$ and emission bands different from free **Per** and $(\text{ADA})_n \cdot (\text{Per})_m$, respectively. The efficient formation of a similar ternary composite was achieved using eosin Y. It is noteworthy that other alkane-based amphiphiles such as **CHA** and SDS were not suitable for the co-uptake, likely due to occupation of the cage cavity by the less-bulky hydrophobic groups.

7. Conclusion

This review focused on the recent achievements with aromatic micelles in our group. For the development of stimuli-responsive aromatic micelles, two anthracene panels on the original, bent aromatic amphiphile **AA** were replaced by other panels with *meta* and redox switches as well as rearranged from *meta* to *ortho* connectivity for photo-responsiveness. The resultant aromatic micelles displayed efficient uptake and release abilities for a wide range of hydrophobic compounds in water. Simple cross-linking of **AA** with hydrophilic spacers led to an aromatic oligomer micelle with high thermal and dilution stability as well as selective uptake ability for oligothiophenes. Furthermore, replacement of the hydrophilic groups on **AA** with saccharides generated a new aromatic micelle with an outer saccharide shell, capable of selectively binding to specific proteins. Strong and colorful emission of the so-called sugar nanocluster was demonstrated upon simple uptake of fluorescent dyes. As a new class of derivatives, bent amphiphiles with two non-aromatic groups, *i.e.*, cyclohexyl and adamantyl groups, also yielded capsular micelles with unique host abilities in water. Therefore, the present progress enriched the functions and utility of our aromatic micelles. We believe that, through further investigation from the viewpoint of synthetic, analytical, material, and biological nanotools, the present micelles would become third-generation micelles, differing from conventional and polymer micelles, in the near future.

Acknowledgements

The authors would like to express their sincere appreciation to all of our group members and collaborators, whose names appear in the original papers. The research project on “aromatic micelles” was supported by JSPS KAKENHI, Support for Tokyo Tech Advanced Researchers (STAR), Research Grants in the Natural Sciences (The Mitsubishi Foundation), and Sasakawa Scientific Research Grant.

References

- Moroi, Y. (1992) *Micelles: Theoretical and Applied Aspects*. Plenum, New York.
- Myers, D. (2006) *Surfactant Science and Technology*. 3rd ed. Wiley, Hoboken.
- Dwars, T., Paetzold, E. and Oehme, G. (2005) Reactions in micellar systems. *Angew. Chem. Int. Ed.* **44**, 7174–7199.
- Alexandridis, P. and Lindman, B. (2000) *Amphiphilic Block Copolymers: Self-Assembly and Applications*. Elsevier, Amsterdam.
- Kataoka, K., Harada, A. and Nagasaki, Y. (2001) Block copolymer micelles for drug delivery: design, characterization and biological significance. *Adv. Drug Deliv. Rev.* **47**, 113–131.
- Miyata, K., Nishiyama, N. and Kataoka, K. (2012) Rational design of smart supramolecular assemblies for gene delivery: chemical challenges in the creation of artificial viruses. *Chem. Soc. Rev.* **41**, 2562–2574.
- Kondo, K., Suzuki, A., Akita, M. and Yoshizawa, M. (2013) Micelle-like molecular capsules with anthracene shells as photoactive hosts. *Angew. Chem. Int. Ed.* **52**, 2308–2312.
- Suzuki, A., Kondo, K., Akita, M. and Yoshizawa, M. (2013) Atroposelective self-assembly of a molecular capsule from amphiphilic anthracene trimers. *Angew. Chem. Int. Ed.* **52**, 8120–8123.
- Kondo, K., Suzuki, A., Akita, M. and Yoshizawa, M. (2014) Micellar polyaromatic capsules: enhanced emissive properties through shell-functionalization. *Eur. J. Org. Chem.* **2014**, 7389–7394.
- Okazawa, Y., Kondo, K., Akita, M. and Yoshizawa, M. (2015) Polyaromatic nanocapsules displaying aggregation-induced enhanced emissions in water. *J. Am. Chem. Soc.* **137**, 98–101.
- Okazawa, Y., Kondo, K., Akita, M. and Yoshizawa, M. (2015) Well-defined aqueous nanoassemblies from amphiphilic *meta*-terphenyls and their guest incorporation. *Chem. Sci.* **6**, 5059–5062.
- Matsumoto, A., Jono, K., Akita, M. and Yoshizawa, M. (2017) Side-chain-directed dispersion of MoS₂ nanosheets by V-shaped polyaromatic compounds. *Chem. Asian J.* **12**, 2889–2893.
- Lin, H.-S., Okawa, S., Ma, Y., Yotsumoto, S., Lee, C., Tan, S. *et al.* (2020) Polyaromatic nanotweezers on semiconducting carbon nanotubes for the growth and interfacing of lead-halide perovskite crystal grains in solar cells. *Chem. Mater.* **32**, 5125–5133.
- Ito, K., Nishioka, T., Akita, M., Kuzume, A., Yamamoto, K. and Yoshizawa, M. (2020) An aromatic micelle with bent pentacene-based panels: encapsulation of perylene bisimide dyes and graphene nanosheets. *Chem. Sci.* **11**, 6752–6757.
- Kudo, K., Ide, T., Kishida, N. and Yoshizawa, M. (2021) Preparation of a multicarbazole-based nanocapsule capable of largely modulating guest spectroscopic properties in water. *Angew. Chem. Int. Ed.* **60**, 10552–10556.
- Yamashina, M., Suzuki, H., Kishida, N., Yoshizawa, M. and Toyota, S. (2021) Synthesis of azaylide-based amphiphiles by staudinger reaction. *Angew. Chem. Int. Ed.* **60**, 17915–17919.
- Sartin, M.M., Kondo, K., Yoshizawa, M., Takeuchi, S. and Tahara, T. (2017) Local environment inside a novel aromatic micelle investigated by steady-state and femtosecond fluorescence spectroscopy of an encapsulated solvatochromic probe. *Phys. Chem. Chem. Phys.* **19**, 757–765.
- Kondo, K., Akita, M., Nakagawa, T., Matsuo, Y. and Yoshizawa, M. (2015) A V-shaped polyaromatic amphiphile: solubilization of various nanocarbons in water and enhanced photostability. *Chem. Eur. J.* **21**, 12741–12746.
- Origuchi, S., Kishimoto, M., Yoshizawa, M. and Yoshimoto, S. (2018) A supramolecular approach to preparation of nanographene adlayers using water-soluble molecular capsules. *Angew. Chem. Int. Ed.* **57**, 15481–15485.
- Catti, L., Narita, H., Tanaka, Y., Sakai, H., Hasobe, T., Tkachenko, N.V. *et al.* (2021) Supramolecular singlet fission of pentacene dimers within polyaromatic capsules. *J. Am. Chem. Soc.* **143**, 9361–9367.
- Kondo, K., Akita, M. and Yoshizawa, M. (2016) Solubility switching of metallo-phthalocyanines and their larger derivatives upon encapsulation. *Chem. Eur. J.* **22**, 1937–1940.
- Omagari, T., Suzuki, A., Akita, M. and Yoshizawa, M. (2016) Efficient catalytic epoxidation in water by axial N-ligand-free Mn-porphyrins within a micellar capsule. *J. Am. Chem. Soc.* **138**, 499–502.
- Kai, T., Kishimoto, M., Akita, M. and Yoshizawa, M. (2018) Encapsulation-induced emission enhancement (EIEE) of Eu(III)-complexes by aromatic micelles in water. *Chem. Commun.* **54**, 956–959.
- Wang, Y., Kai, H., Ishida, M., Gokulnath, S., Mori, S., Murayama, T. *et al.* (2020) Synthesis of a black dye with absorption capabilities across the visible-to-near-infrared region: a MO-mixing approach via heterometal coordination of expanded porphyrinoid. *J. Am. Chem. Soc.* **142**, 6807–6813.
- Yoshimoto, S., Hashiguchi, S., Maruyama, Y., Origuchi, S., Katagiri, Y. and Yoshizawa, M. (2022) Nanoreactor functions of a water-soluble molecular capsule for electrochemical reactions of Fe-porphyrins and phthalocyanines. *Electrochem.*

- Commun. **135**, 107218.
- 26) Liu, S.-Y., Kishida, N., Kim, J., Fukui, N., Haruki, R., Niwa, Y. *et al.* (2022) Realization of stacked-ring aromaticity in a water-soluble micellar capsule. *J. Am. Chem. Soc.* **144**, doi: 10.1021/jacs.2c08795. (in press)
 - 27) Kondo, K., Klosterman, J.K. and Yoshizawa, M. (2017) Aromatic micelles as a new class of aqueous molecular flasks. *Chem. Eur. J.* **23**, 16710–16721.
 - 28) Yoshizawa, M. and Catti, L. (2019) Bent anthracene dimers as versatile building blocks for supramolecular capsules. *Acc. Chem. Res.* **52**, 2392–2404.
 - 29) Yoshizawa, M. and Klosterman, J.K. (2014) Molecular architectures of multi-anthracene assemblies. *Chem. Soc. Rev.* **43**, 1885–1898.
 - 30) Yoshizawa, M. and Yamashina, M. (2017) Coordination-driven nanostructures with polyaromatic shells. *Chem. Lett.* **46**, 163–171.
 - 31) Yazaki, K., Catti, L. and Yoshizawa, M. (2018) Polyaromatic molecular tubes: from strategic synthesis to host functions. *Chem. Commun.* **54**, 3195–3206.
 - 32) Catti, L., Sumida, R. and Yoshizawa, M. (2022) Aqueous polyaromatic receptors for biomolecules with high selectivity. *Coord. Chem. Rev.* **460**, 214460.
 - 33) Qu, D.-H., Wang, Q.-C., Zhang, Q.-W., Ma, X. and Tian, H. (2015) Photoresponsive host-guest functional systems. *Chem. Rev.* **15**, 7543–7588.
 - 34) Wang, W., Wang, Y.-X. and Yang, H.-B. (2016) Supramolecular transformations within discrete coordination-driven supramolecular architectures. *Chem. Soc. Rev.* **45**, 2656–2693.
 - 35) Blanco-Gómez, A., Cortón, P., Barravecchia, L., Neira, I., Pazos, E., Peinador, C. *et al.* (2020) Controlled binding of organic guests by stimuli-responsive macrocycles. *Chem. Soc. Rev.* **49**, 3834–3862.
 - 36) Kishimoto, M., Kondo, K., Akita, M. and Yoshizawa, M. (2017) A pH-responsive molecular capsule with an acridine shell: catch and release of large hydrophobic compounds. *Chem. Commun.* **53**, 1425–1428.
 - 37) Catti, L., Kishida, N., Kai, T., Akita, M. and Yoshizawa, M. (2019) Polyaromatic nanocapsules as photoresponsive hosts in water. *Nat. Commun.* **10**, 1948.
 - 38) Satoh, Y., Catti, L., Akita, M. and Yoshizawa, M. (2019) A redox-active heterocyclic capsule: radical generation, oxygenation, and guest uptake/release. *J. Am. Chem. Soc.* **141**, 12268–12273.
 - 39) Zana, R. (2002) Dimeric and oligomeric surfactants. Behavior at interfaces and in aqueous solution: a review. *Adv. Colloid Interface Sci.* **97**, 205–253.
 - 40) Dekker, M. (2003) Gemini Surfactants, Synthesis, Interfacial and Solution-Phase Behavior, and Applications. CRC Press, New York.
 - 41) Li, W., Kim, Y. and Lee, M. (2013) Intelligent supramolecular assembly of aromatic block molecules in aqueous solution. *Nanoscale* **5**, 7711–7723.
 - 42) Suzuki, A., Kondo, K., Sei, Y., Akita, M. and Yoshizawa, M. (2016) A fluorescent molecular capsule with a flexible polyaromatic shell for detecting monoterpene compounds in water. *Chem. Commun.* **52**, 3151–3154.
 - 43) Jono, K., Suzuki, A., Akita, M., Albrecht, K., Yamamoto, K. and Yoshizawa, M. (2017) A polyaromatic molecular clip that enables the binding of planar, tubular, and dendritic compounds. *Angew. Chem. Int. Ed.* **56**, 3570–3574.
 - 44) Nishioka, T., Kuroda, K., Akita, M. and Yoshizawa, M. (2019) A polyaromatic gemini amphiphile that assembles into a well-defined aromatic micelle with higher stability and host functions. *Angew. Chem. Int. Ed.* **58**, 6579–6583.
 - 45) Tsuchida, Y., Aratsu, K., Hiraoka, S. and Yoshizawa, M. (2021) An aromatic oligomer micelle: large enthalpic stabilization and selective oligothiophene uptake. *Angew. Chem. Int. Ed.* **60**, 12754–12758.
 - 46) Mammen, M., Choi, S.-K. and Whitesides, G.M. (1998) Polyvalent interactions in biological systems: implications for design and use of multivalent ligands and inhibitors. *Angew. Chem. Int. Ed.* **37**, 2754–2794.
 - 47) Varki, A., Cummings, R.D., Esko, J.D., Stanley, P., Hart, G.W., Aebi, M. *et al.* (2017) *Essentials of Glycobiology*. 3rd ed. CSH Press, New York.
 - 48) Delbianco, M., Bharate, P., Varela-Aramburu, S. and Seeberger, P.H. (2016) Carbohydrates in supramolecular chemistry. *Chem. Rev.* **116**, 1693–1752.
 - 49) Narita, H., Catti, L. and Yoshizawa, M. (2021) An aromatic micelle-based saccharide cluster with changeable fluorescent color and its protein interactions. *Angew. Chem. Int. Ed.* **60**, 12791–12795.
 - 50) Tadros, T.F. (2005) *Applied Surfactants: Principles and Applications*. Wiley-VCH, Weinheim.
 - 51) di Gregorio, M.C., Travaglini, L., Giudice, A.D., Cautela, J., Pavel, N.V. and Galantini, L. (2019) Bile salts: natural surfactants and precursors of a broad family of complex amphiphiles. *Langmuir* **35**, 6803–6821.
 - 52) Hanafusa, M., Tsuchida, Y., Matsumoto, K., Kondo, K. and Yoshizawa, M. (2020) Three host peculiarities of a cycloalkane-based micelle toward large metal-complex guests. *Nat. Commun.* **11**, 6061.
 - 53) Katagiri, Y., Tsuchida, Y., Matsuo, Y. and Yoshizawa, M. (2021) An adamantane capsule and its efficient uptake of spherical guests up to 3 nm in water. *J. Am. Chem. Soc.* **143**, 21492–21496.

(Received Oct. 28, 2022; accepted Nov. 15, 2022)

Profile

Michito Yoshizawa was born in Saitama in 1974. He received his bachelor and master degrees from Tokyo University of Agriculture and Technology in 1997 and Tokyo Institute of Technology in 1999, respectively. He received his Ph.D. from Nagoya University in 2002 under the supervision of Professor Makoto Fujita. After a JSPS postdoctoral fellow and an Assistant Professor in the Fujita group at The University of Tokyo, he has been an Associate Professor at Chemical Resources Laboratory (2008–2016) and Laboratory for Chemistry and Life Science, Institute of Innovative Research (2016–2020), Tokyo Institute of Technology. He was promoted to a Professor in 2020. His scientific contributions are recognized with Inoue Research Award for Young Scientists (2003), Chemical Society of Japan Award for Young Chemists (2007), Young Scientist Prize from MEXT (2010), Thomson Reuters Research Front Award (2012), Nagase Science Technology Foundation Award (2015), Teshima Memorial Research Award (2020), and Inoue Prize for Science (2021). He was a Visiting Professor at University of Strasbourg in 2006, 2014, and 2022. His research interests focus on the development of functional polyaromatic nanospaces.



Profile

Lorenzo Catti was born in 1989 in Bavaria, Germany. He received his bachelor and master degrees in organic chemistry from Technical University of Munich. From 2013 to 2017 he conducted his Ph.D. research under the supervision of Professor Konrad Tiefenbacher (Technical University of Munich/University of Basel). In 2017 he was awarded the JSPS postdoctoral fellowship and joined the Yoshizawa group at Tokyo Institute of Technology. In 2020 he moved to the WPI-NanoLSI of Kanazawa University to work as a Specially Appointed Assistant Professor under the supervision of Professor Shigehisa Akine and Professor Mark MacLachlan. He then returned to Tokyo Institute of Technology as an Assistant Professor in 2021. His research interests include molecular recognition in water, supramolecular catalysis, and photoresponsive systems.

