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ARTICLE

Design and Synthesis of Covalently Tethered "IsoG-Star" as Recyclable Host for Selective Cesium Separation

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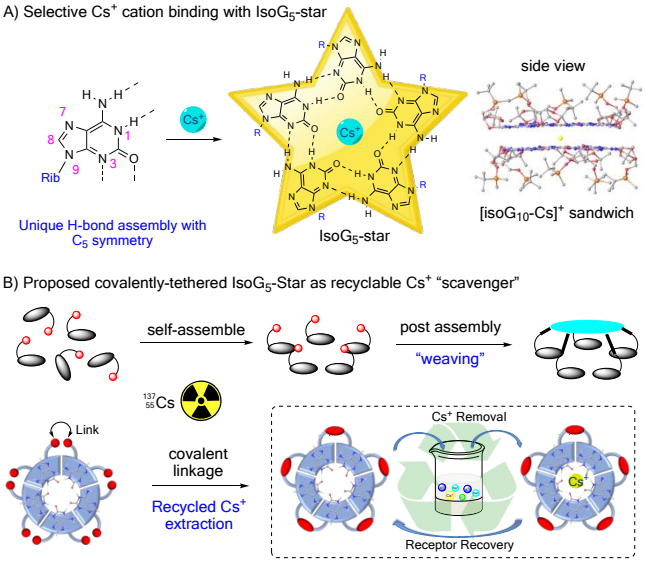
The isoguanosine self-assembled pentamer (isoG-star) has exhibited remarkable selectivity for Cs^+ binding over competing alkali and alkali earth metal cation, rendering it a promising extractor for radioactive waste ^{137}Cs separation. However, to make isoG-star a pracrtical material for Cs^+ isolation, the development of recyclable isoG-star material is required. In this study, a systematic screening of functional isoG derivatives was performed. By employing well-defined complex formation and post-assembly modification, a covalently tethered $isoG_5$-star was prepared through olefin metathesis, utilizing a designed isoG monomer. The application of this newly developed covalently linked isoG-star enabled selective Cs^+ extraction, followed by controled solvent-induced H-bond dessociation. This resulted in the creation of a recyclable Cs^+ extractor, demonstrating excellent cation selectivity and good reusability (over seven cycles) the first time. Consequently, this new supramolecular macrocycle offers a practical new platform for the treatment of radiocesium (^{134}Cs and ^{137}Cs) in an environmentally friendly and highly effective manner.

Introduction

Radiocesium ions represent significant constituents of radioactive wastewaters in nuclear power plant, necessitating efficient treatment and isolation methods for Caesium (Cs) ions.[1-3] In 2011, the Fukushima Daiichi Nuclear Power Plant (FDNPP) accident resulted in the release of substantial amounts of radiocesium (^{134}Cs and ^{137}Cs with half-lives 2.07 and 30.1 years, respectively) into the environment, further highlighted the requirement for novel systems to effectively extract Cs cation from aqueous solutions with a focus on ecological security and sustainable development.[4-7] Considering the abundant existence of Sodium (Na) and Potassium (K) cations in aqueous solutions, along with their chemical similarities, achieving selective separation of Cs^+ from such solutions can pose significant challenges.[8-11] Crown ethers and calixarenes derivatives are typical receptor for Cs^+ separation. Reinhoud and Ungaro made fundamental contribution to the hybrids of calix[4]arene and crown ethers as excellent Cs^+ selective ionophores.[12-15] Selective binding is the first part of recognition, subsequent controlled release is critical for practical application. Although certain crown ether and calixarene derivatives can selectively coordinate with Cs^+ through ion-dipole interaction or cation-π interaction, making them promising Cs^+ extractants, concerns arise regarding their limited operating pH range and poor recyclability for practical applications. Sessler and co-workers developed calix[4]pyrrole which could extract Cs^+ from aqueous phase while allowing its subsequent release by addition of K^+. Calix[4]pyrrole-containing diblock copolymers synthesis demonstrated more effective as an extractant than the corresponding free ion pair receptor.[16-21] The development of new systems exhibiting high Cs^+ binding selectivity and practical operational conditions is thus of paramount importance for environmental protection and energy sustainability.



Scheme 1. A) Cs^+ templated $isoG_5$-star pentaplex formation; **B**) Proposed covalently tethered $isoG_5$-star as recyclable Cs^+ extractor.

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Molecular self-assembly is a prevalent process in nature that gives rise to various receptors, providing a powerful approach for designing selective ionophores.[22-24] Guanosine (G) rich nucleic acids are recognized for their ability to coordinate alkali and alkaline earth cations through the formation of Hydrogen-bonded G_4-quartet motif.[25-33] This rigid macrocyclic structure exhibits a high binding affinity towards K^+, Sr^{2+}, and Ba^{2+}.[34-39] However, despite its structural reversibility, the H-bonding supramolecular architecture lacks flexibility and tends to maintain a fixed size to maximize H-bonding interactions. Consequently, the G_4-quartet demonstrates no binding affinity towards Cs^+ due to a size mismatch. Interestingly, the structure isomer of G, known as isoguanosine (isoG, also referred to as 2-hydroxy-adenosine) features a larger H-bond donors and acceptors angle (108° for isoG compare to 90° in G-quartet), leading to the formation of a pentameric assembly, $isoG_5$, in contrast to the tetrameric G_4-quartet.[40-46] With the significantly larger central core, the $isoG_5$ exhibits strong binding towards Cs^+ (radii=174 pm) with high affinity and excellent selectivity over Na^+ and K^+ (**Scheme 1A**).[47-50] Although self-assembly is a powerful tool for creating supramolecular scaffold, it faces challenges as a stable molecular host due to non-covalent bond dissociation, limiting its practical applications. To address these limitations and improve the binding affinity (minimizing entropy penalty associated with self-assembly) and practical usability (recyclability), we have directed our efforts towards the development of the first covalently tethered $isoG_5$-star through post-assembly supramolecular modification (**Scheme 1B**).

In theory, covalently tethered supramolecular scaffold can be achieved through two approaches: A) covalent linkage of a monomer to a template or B) post-assembly modification. The first approach offers greater synthetically accessibility, allowing for easy functional group modification.[51-54] However, it requires precise template design to ensure the formation of self-assembly with optimal non-covalent binding, which can be challenging. On the other hand, the post-assembly modification approach ensures the formation of a supramolecular assembly with strong non-covalent interaction, similar to the self-assembled process. However, it requires compatible synthetic methods and appropriate linkage design to ensure the proper weaving of supramolecular scaffold without disrupting the non-covalent binding. Nonetheless, in either approach, the availability of good synthetic handles and the establishment of effective self-assembly are critical factors.

To evaluate different building blocks in the formation of $isoG_5$-star, various isoG derivatives were synthesized and applied in the Cs^+ binding experiments (**Figure 1A**). Typically, the purine C-8 and N-9 positions provide potential synthetic sites without disrupting H-bond formation. Non-sugar isoG derivatives **1a-1d** were synthesized and subjected to evaluate Cs^+ binding.[55] While these compounds were able to effectively extract from aqueous solution, analysis using NMR and MS revealed the presence of complex reaction mixtures with no clear detection of isoG-star formation (**Figure S1, S2**). This outcome is attributed to the formation of various stacking isomers. Further investigation revealed that the structure of isopropylidene modified isoG **2a** could form a stable decamer

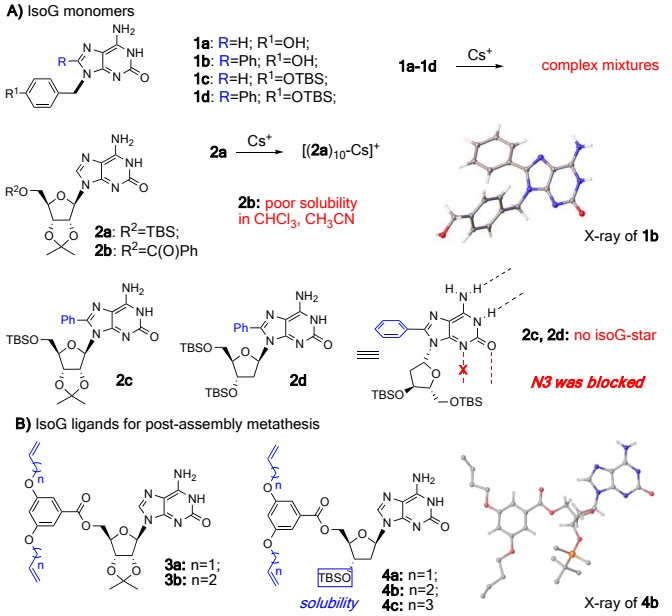

Figure 1. (A) Non-sugar IsoG derivatives **1** and 8-phenyl-isoG derivatives **2**; (B) IsoG ligand **3** and **4** for post-assembly weaving.

$[(\mathbf{2a})_{10}Cs]^+$. However, the introduction of a benzyl group at the 5'-position, serving as a potential synthetic handle, significantly reduced solubility in organic solvents. Modification of the C-8 position with a phenyl group gave compounds **2c** and **2d**, both of which exhibited good solubility in organic solvents. However, despite their favourable solubility properties, neither of these compounds was able to form isoG-star. The *X-ray* crystal structure of **2c** and **2d** revealed the configuration is energetically favored by avoiding repulsion.[49] As a result, the O5' was placed close to N3, blocking the critical H-bonding in $isoG_5$ formation. Armed with this mechanistic understanding, our research focused on exploring the isopropylidene modified isoG derivatives **3a-b**, and the 2'-deoxy isoG derivatives **4a-4c** with the intention of striking a balance between solubility and H-bonding formation (**Figure 1B**).

With the incorporation of longer ester chain, both compounds **3a** and **3b** exhibited improved solubility compared to **2b**. Treatment of isoG **3a** in $CDCl_3$ solution with CsCl and $NaBPh_4$ (in an aqueous solution) resulted in one sets of signals in ^1H NMR. The proton integration between isoG ligand and anion was 10:1. Both N1-H (at 13.60 ppm) and N6-H_A (at 11.02 ppm) protons displayed clear downfiled shifts, indicating the foramtion $[(\mathbf{3a})_{10}Cs]^+(BPh_4^-)$ and successful extraction of Cs^+ into the organic layer. Interestingly, $BARF^-$ anion led to the formation of a different Cs^+ complex, $[(\mathbf{3a})_5Cs]^+(BARF^-)$, with 5:1 integration ratio, suggesting a specificl role of the BARF anion in this assembly. Additionally, isoG **3b,** with one extra carbon on the side chain, could also form similar Cs^+ complexes, $[(\mathbf{3b})_{10}Cs]^+(BPh_4^-)$ and $[(\mathbf{3b})_5Cs]^+(BARF^-)$. The detailed NMR spectra are provided in **Figure S3, S4**.

Following isoG-star formation, we proceeded with the supramolecular weaving process in an attempt to covalently link the isoG-star through olefin metathesis. Both the decamer and pentamer from **3a** and **3b** were treated with Hoveyda-Grubbs-II (HG-II) catalyst, and the reaction process was monitored by MALDI-TOF. Subsequent analysis through NMR and MS confirmed the occurrence

of metathesis when treating $[(\mathbf{3a})_{10}Cs]^+(BPh_4^-)$ and $[(\mathbf{3a})_5Cs]^+(BARF^-)$ with HG-II. However, a mixture of oligomers was observed, and the desired formation of pentameric isoG$_5$-star did not materialize. Our hypothesis is that the ester linker might not be sufficiently long to establish a connection with neighboring isoG units. As expected, treating $[(\mathbf{3b})_{10}Cs]^+$ with HG-II led to the detection of the alkene-linked cyclic isoG$_5$ by MALDI-TOF with MW of 2829.15. However, the resulting cyclic structure showed very poor solubility in $CHCl_3$, pacipitating from the reaction mixture, which makes it unsuitable for the proposed Cs^+ extraction application.

To address the solubility issue, we investigated the metathesis reaction with 2'-deoxy isoG derivatives **4a-4c**. **Figure 2A** illustrates the treatment of deoxy isoG **4a** and **4b** in $CDCl_3$ solution with CsCl and NaBARF aqueous solution, leading to the formation of simple complexes exhibiting a single set of signals in ^{1}H NMR. Diffusion NMR experiments deoxy isoG derivatives confirmed the presence of C5-symmetric decamer with the formula $[(\mathbf{4a})_{10}Cs_2]^{2+}(BARF^-)_2$ and $[(\mathbf{4b})_{10}Cs_2]^{2+}(BARF^-)_2$. This finding establishes that the enhanced $CDCl_3$ solubility of these deoxy-isoG derivatives enables effective Cs^+ extraction into the organic layer through straightforward procedures. Moreover, it is notaworthy that these deoxy-isoG derivatives can also form isoG-star structures with both Na^+ and K^+. To assess the binding selectivity of these alkene-modified isoG compounds, extrations of Cs^+ in the presence of competing Na^+ and K^+ were performed. The summarized results are presented in **Figure 2B** and **2C**.

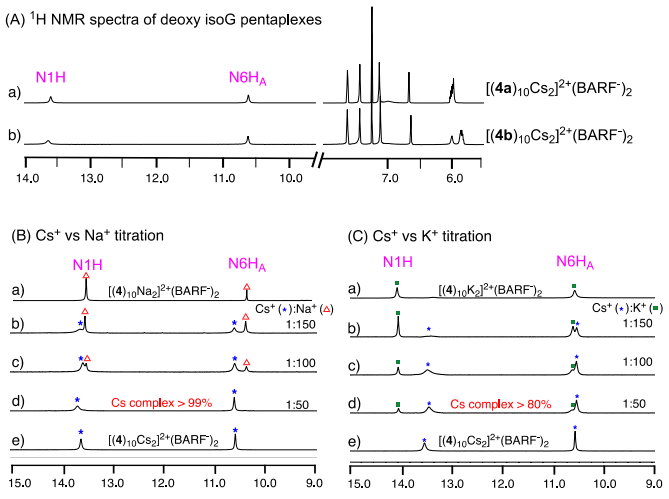

Figure 2. (A) Self-assembly experiments of **4a** and **4b**: a) ^{1}H NMR spectrum of $[(\mathbf{4a})_{10}Cs_2]^{2+}(BARF^-)_2$ in $CDCl_3$, b) ^{1}H NMR spectrum of $[(\mathbf{4b})_{10}Cs_2]^{2+}(BARF^-)_2$ in $CDCl_3$. B) ^{1}H NMR experiments of **4b** with Cs^+ and Na^+ mixture at 25°C in $CDCl_3$, (a) $[(\mathbf{4})_{10}Na_2]^{2+}(BARF^-)_2$, Cs^+ : Na^+ molar ratio of : (b) 1:150, (c) 1:100, (d) 1:50, (e) $[(\mathbf{4})_{10}Cs_2]^{2+}(BARF^-)_2$. The concentrations of Cs^+ in aqueous solution are the same in all cases. (C) ^{1}H NMR experiments of **4b** with Cs^+ and K^+ mixture at 25°C in $CDCl_3$, (a) $[(\mathbf{4b})_{10}K_2]^{2+}(BARF^-)_2$, Cs^+ : K^+ molar ratio of (b) 1:150, (c) 1:100, (d) 1:50, (e) $[(\mathbf{4b})_{10}Cs_2]^{2+}(BARF^-)_2$. The concentrations of Cs^+ in aqueous solution are the same in all cases. The portion of the spectra shows the region of the N1H and N6H$_A$ peaks.

As anticipated, ^{1}H NMR spectra demonstrated excellent Cs^+ cation binding selectivity over Na^+ and K^+ cations. At a Cs^+/Na^+ ratio of 1:50, deoxy isoG **4b** formed over 99% Cs^+ complex with minimal Na^+ complex formation observed. Slightly reduced Cs^+ selectivity was observed when treating **4b** with a large excess of K^+, resulting in 80% Cs^+ complex formation with a 1:50 Cs^+/K^+ mixture. Other alkaline earth metal cations (Mg^{2+}, Ca^{2+}, and Ba^{2+}) were applied to investigate their influence on the selectivity of Cs^+. Nearly zero amount of Mg^{2+}, Ca^{2+}, Ba^{2+} was extracted in the competition experiments with a 1:100 Cs^+/alkaline earth metal ions mixture separately. Remarkably, at a Cs^+/Mg^{2+} ratio of 1:150, Cs^+ complex is still dominant in solution. Slightly reduced Cs^+ selectivity was observed when treating **4b** with a large excess of Ca^{2+}, resulting in 90% Cs^+ complex formation with a 1:150 Cs^+/Ca^{2+} mixture (Figure S9-S11).

Remarkably, the resulting Cs^+ complexes derived from isoG **4b** remain stable even at very low concentration (0.0001 M) with no significant dissociation. Variable-temperature NMR (VT-NMR) experiments confirmed that these Cs^+ complexes maintained stability even at elevated temperature (55 °C, see dilution and VT NMR in **Figure S8**). These results strongly support the potential of using deoxy isoG **4** as a new host for Cs^+ extraction even in the presence of excess of Na^+ and K^+ cations.

Following the confirmaiton of Cs^+ binding selectivity, excellent solubility, and good complex stability, we investigated the possiblity of forming covalently-linked isoG-star using these deoxy-isoG derivatives **4a** - **4c**. Complexes derived from these compounds were

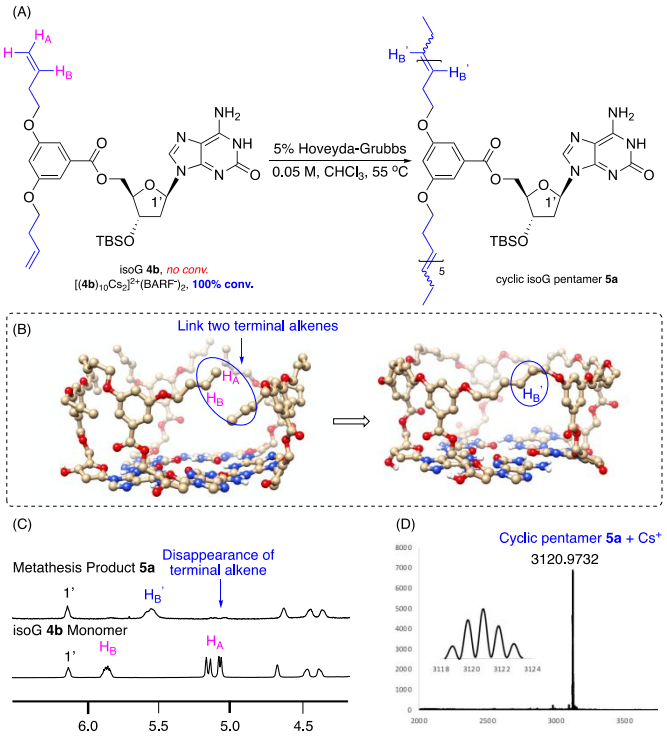

Figure 3. Chemical structure, model and characterizations of cyclic doxy isoG pentamer **5a**. (A) Macrocyclization process through olefin metathesis; (B) Computational model of cyclic pentamer; (C) ^{1}H NMR spectra of deoxy isoG **4b** monomer and metathesis product cyclic doxy isoG pentamer **5a** in DMSO; (D) MALDI-TOF spectrum showing the effective extraction of Cs^+ from aqueous phase.

treated with HG-II catalyst, and the metathesis reactions were monitored using NMR and MALDI-TOF. As depicted in **Figure 3A**, both isoG ligand and the Cs^+ complex $[(\mathbf{4})_{10}Cs_2]^{2+}(BARF^-)_2$) were treated with HG-II catalyst (5 mol%). Interestingly, no olefin metathesis products were observed while reacting with monomer **4**, likely due to the catalyst being quenched by the purine moiety. In the presence of the complex $[(\mathbf{4})_{10}Cs_2]^{2+}(BARF^-)_2$, the metathesis reaction was observed with complete consumption of the terminal olefin within 8 h in $CHCl_3$ at 55 °C. Monitoring the process with MALDI-TOF sugested the formaiton of isoG trimer and tetramer with allyl ether **4a**, indicating the chain length was not sufficient enough to accommodate the $isoG_5$-pemtermer cyclization, leading to compelx dissociation after pentamer formation. With a longer linker, the desired cyclic pentamer was successfully observed with m/z = 3120.9732, consistent with convalently linked cyclic $isoG_5$ containing one Cs cation ($C_{145}H_{195}N_{25}O_{35}Si_5Cs^+$, **Figure 3D**). The overall yield was over 90%, giving the cyclic deoxy isoG pentamer **5a** as the dominant product. Compound **5a** could be readily purified through column chromatography, with no terminal olefin signals observed in ^1H NMR. Similar cyclic isoG-pentamer structures were observed with **4c**, the ligand contianing even longer chain. However, complex NMR was received, likely due to the overly flexible side arms.

Having successfully prepared cyclic-isoG **5a**, aqueous extraction experiments to evaluate its Cs^+ extraction capabilities were performed. As expected, these covalently linked isoG-star effectively extract Cs^+ from the aqueous solution, forming Cs^+ complexes in $CHCl_3$. The formation of new complexes was confirmed by ^{133}Cs NMR that 25 ppm and 53 ppm signals clearly proved the coordination between Cs^+ and cyclic pentamer product. In recyclebility experiment, protic solvent MeOH can disrupt the H-bond in deoxy isoG pentamer and cause the decomposition of isoG complex. Upon treating the complex MeOH, complex dissociation occurred, resulting in the release of Cs^+. The fact that cyclic pentamer **5a** is not soluble in MeOH led it starts to precipitate from solution. The receptor itself can be regenerated after filtration. In this way, Cs^+ can be released or storage in another container by adding MeOH solvent, giving $C145H195N25O35Si5Na^+$ and $C145H195N25O35Si5K^+$ on MALDI-TOF. The resulting recycled cyclic isoG **5a** could be reapplied for Cs^+ extraction by dissolving it in $CHCl_3$ and reacting it with Cs^+ containing aqueous solution. Remarkably, this process was performed multiple cycles (7 times) without losing Cs^+ selectivity and binding affinity (**Figrue 4**). The detailed results for each cycle were provided in **Figure S14**. Furthermore, the pH influence on Cs^+ selective extraction was investigated, showing effective extraction of Cs^+ between pH=1 and pH=14. The effective pH range covers a broad region, making cyclic deoxy isoG pentamer widely applicable ionophores. To the best of klnowledge, this is the first covalently-linked isoG-star that has been synthesized, and its ease of operation for effective Cs^+ extraction demonstrates its potential as a promising solution for the treatment of radioactive Cs^+ waste.

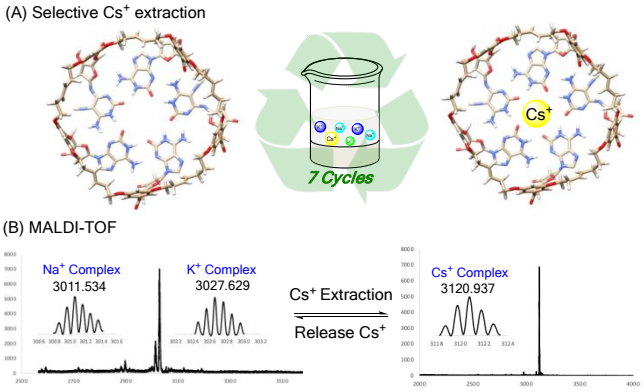

Figure 4. Selective Cs^+ extraction by cyclic pentamer **5**. (A) 7 cycles extraction without significant efficiency decrease; (B) MALDI-TOF spectra of Cs^+ extraction and release.

Conclusion

In summary, we have successfully developed the first covalently linked isoG-star through olefin metathesis with selected deoxy-isoG derivatives. The resulting cyclic isoG-star has demonstrated exceptional performance in Cs^+ extraction and separation with ease of operation and excellent recyclability. This breakthrough not only offers a novel material for potential Cs^+-containing radioactive nuclear waste treatment, but also introduces a new strategy for the preparation of extra-large macrocycles through post-assembly modification. We anticipate that this strategy will be applicable in the development of new supramolecular hosts, and our ongoing investigations in the laboratory are currently exploring its potential applications.

Author Contributions

M.L. conducted the experiments, performed the characterization, and analyzed the results and data; Y.H. analyzed the results and data; L.W. solved and refined the crystal structures; X.S. conceived the original idea, set research directions, and designed the experiments.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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References

1. Y. H. Koo, Y. S. Yang and K. W. Song, *Prog. Nucl. Energy*, 2014, **74**, 61-70.
2. J. L. Wang, S. T. Zhuang and Y. Liu, *Coord. Chem. Rev.*, 2018, **374**, 430-438.
3. J. L. Wang and S. T. Zhuang, *Reviews in Environmental Science and Bio-Technology*, 2019, **18**, 231-269.
4. G. Katata, M. Chino, T. Kobayashi, H. Terada, M. Ota, H. Nagai, M. Kajino, R. Draxler, M. C. Hort, A. Malo, T. Torii and Y. Sanada, *Atmospheric Chemistry and Physics*, 2015, **15**, 1029-1070.
5. K. Saito, I. Tanihata, M. Fujiwara, T. Saito, S. Shimoura, T. Otsuka, Y. Onda, M. Hoshi, Y. Ikeuchi, F. Takahashi, N. Kinouchi, J. Saegusa, A. Seki, H. Takemiya and T. Shibata, *J. Environ. Radioact.*, 2015, **139**, 308-319.
6. M. Andoh, Y. Nakahara, S. Tsuda, T. Yoshida, N. Matsuda, F. Takahashi, S. Mikami, N. Kinouchi, T. Sato, M. Tanigaki, K. Takamiya, N. Sato, R. Okumura, Y. Uchihori and K. Saito, *J. Environ. Radioact.*, 2015, **139**, 266-280.
7. B. C. Russell, I. W. Croudace and P. E. Warwick, *Anal. Chim. Acta*, 2015, **890**, 7-20.
8. R. D. Shannon, *Acta Crystallographica Section A*, 1976, **32**, 751-767.
9. Y. W. Chen and J. L. Wang, *Nucl. Sci. Tech.*, 2016, **27**.
10. Y. A. Yin, J. Hu and J. L. Wang, *Environmental Progress & Sustainable Energy*, 2017, **36**, 989-996.
11. R. J. Ellis, B. Reinhart, N. J. Williams, B. A. Moyer and V. S. Bryantsev, *Chem. Commun.*, 2017, **53**, 5610-5613.
12. A. Casnati, F. Sansone, J.-F. Dozol, H. Rouquette, F. o. Arnaud-Neu, D. Byrne, S. Fuangswasdi, M.-J. Schwing-Weill and R. Ungaro, *J. Inclusion Phenom.Macrocyclic Chem.*, 2001, **41**, 193-200.
13. A. Casnati, A. Pochini, R. Ungaro, F. Ugozzoli, F. Arnaud, S. Fanni, M.-J. Schwing, R. J. M. Egberink, F. de Jong and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1995, **117**, 2767-2777.
14. L. A. J. Chrisstoffels, F. de Jong, D. N. Reinhoudt, S. Sivelli, L. Gazzola, A. Casnati and R. Ungaro, *J. Am. Chem. Soc.*, 1999, **121**, 10142-10151.
15. R. Ungaro, A. Casnati, F. Ugozzoli, A. Pochini, J.-F. Dozol, C. Hill and H. Rouquette, *Angew. Chem. Int. Ed*, 1994, **33**, 1506-1509.
16. T. A. Hanna, L. H. Liu, A. M. Angeles-Boza, X. D. Kou, C. D. Gutsche, K. Ejsmont, W. H. Watson, L. N. Zakharov, C. D. Incarvito and A. L. Rheingold, *J. Am. Chem. Soc.*, 2003, **125**, 6228-6238.
17. T. G. Levitskaia, L. Maya, G. J. Van Berkel and B. A. Moyer, *Inorg. Chem.*, 2007, **46**, 261-272.
18. I. V. Kolesnichenko and E. V. Anslyn, *Chem. Soc. Rev.*, 2017, **46**, 2385-2390.
19. S. K. Kim, H. G. Lee, G. I. Vargas-Zuniga, V. M. Lynch, C. Kim and J. L. Sessler, *Chem. Eur. J.*, 2014, **20**, 11750-11759.
20. S. K. Kim, G. I. Vargas-Zuniga, B. P. Hay, N. J. Young, L. H. Delmau, C. Masselin, C. H. Lee, J. S. Kim, V. M. Lynch, B. A. Moyer and J. L. Sessler, *J. Am. Chem. Soc.*, 2012, **134**, 1782-1792.
21. X. Chi, G. M. Peters, C. Brockman, V. M. Lynch and J. L. Sessler, *J. Am. Chem. Soc.*, 2018, **140**, 13219-13222.
22. J. T. Davis, S. Tirumala, J. R. Jenssen, E. Radler and D. Fabris, *J. Org. Chem.*, 1995, **60**, 4167-4176.
23. H. Piotrowski, K. Polborn, G. Hilt and K. Severin, *J. Am. Chem. Soc.*, 2001, **123**, 2699-2700.
24. M. Debnath, S. Chakraborty, Y. P. Kumar, R. Chaudhuri, B. Jana and J. Dash, *Nat. Coummun.*, 2020, **11**.
25. F. Fuhrman, G. Fuhrman, R. Nachman and H. Mosher, *Science*, 1981, **212**, 557-558.
26. J. T. Davis and G. P. Spada, *Chem. Soc. Rev.*, 2007, **36**, 296-313.
27. D. Jiang and F. Seela, *J. Am. Chem. Soc.*, 2010, **132**, 4016-4024.
28. Q. Cheng, J. Gu, K. R. Compaan and H. F. Schaefer III, *Chem. Eur. J.*, 2012, **18**, 4877-4886.
29. S. A. Ingale, P. Leonard, Q. N. Tran and F. Seela, *J. Org. Chem.*, 2015, **80**, 3124-3138.
30. H. Zhao, H. Feng, J. Liu, F. Tang, Y. Du, N. Ji, L. Xie, X. Zhao, Z. Wang and Q. Chen, *Biomaterials*, 2020, **230**, 119598.
31. V. Gubala, J. E. Betancourt and J. M. Rivera, *Org. Lett.*, 2004, **6**, 4735-4738.
32. J. E. Betancourt, M. Martín-Hidalgo, V. Gubala and J. M. Rivera, *J. Am. Chem. Soc.*, 2009, **131**, 3186-3188.
33. M. Garcia-Arriaga, G. Hobley and J. M. Rivera, *J. Org. Chem.*, 2016, **81**, 6026-6035.
34. F. W. B. van Leeuwen, W. Verboom, X. Shi, J. T. Davis and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 2004, **126**, 16575-16581.
35. Y. He, Y. Zhang, M. Liu, K. Zhao, C. Shan, L. Wojtas, H. Guo, A. Ding and X. Shi, *Cell Rep. Phys. Sci.*, 2021, **2**, 100519.
36. Y. He, Y. Zhang, L. Wojtas, N. G. Akhmedov, D. Thai, H. Wang, X. Li, H. Guo and X. Shi, *Chem. Sci.*, 2019, **10**, 4192-4199.
37. D. González-Rodríguez, J. L. J. van Dongen, M. Lutz, A. L. Spek, A. P. H. J. Schenning and E. W. Meijer, *Nat. Chem.*, 2009, **1**, 151-155.
38. Y. He, M. J. Liu, S. Teng, L. Wojtas, G. X. Gu and X. D. Shi, *Chin. Chem. Lett.*, 2022, **33**, 4203-4207.
39. X. Shi, J. C. Fettinger and J. T. Davis, *Angew. Chem. Int. Ed.*, 2001, **40**, 2827-2831.
40. M. Cai, X. Shi, V. Sidorov, D. Fabris, Y.-f. Lam and J. T. Davis, *Tetrahedron*, 2002, **58**, 661-671.
41. J. T. Davis, *Angew. Chem. Int. Ed.*, 2004, **43**, 668-698.
42. T. Ding, F. Tang, G. Ni, J. Liu, H. Zhao and Q. Chen, *RSC Advances*, 2020, **10**, 6223-6248.
43. M. Meyer and J. Sühnel, *J. Phys. Chem. A*, 2003, **107**, 1025-1031.
44. J. Gu, J. Wang and J. Leszczynski, *J. Comput. Chem.*, 2007, **28**, 1790-1795.
45. J. Gu, J. Wang and J. Leszczynski, *Chem. Phys. Lett.*, 2007, **445**, 243-245.
46. H. Zhao, A. H. Schäfer and F. Seela, *ChemPlusChem*, 2017, **82**, 826-833.
47. X. Shi, J. C. Fettinger, M. Cai and J. T. Davis, *Angew. Chem. Int. Ed.*, 2000, **39**, 3124-3127.
48. M. Cai, A. L. Marlow, J. C. Fettinger, D. Fabris, T. J. Haverlock, B. A. Moyer and J. T. Davis, *Angew. Chem. Int. Ed*, 2000, **112**, 1339-1341.
49. M. Liu, Y. He, C. Shan, L. Wojtas, I. Ghiviriga, O. Fathalla, Y. Yan, X. Li and X. Shi, *Chem. Sci.*, 2021, **12**, 7569-7574.
50. T. Evan-Salem, L. Frish, F. W. van Leeuwen, D. N. Reinhoudt, W. Verboom, M. S. Kaucher, J. T. Davis and Y. Cohen, *Chem. Eur. J.*, 2007, **13**, 1969-1977.
51. A. Ashcraft, K. X. Liu, A. Mukhopadhyay, V. Paulino, C. Liu, B. Bernard, D. Husainy, T. Phan and J. H. Olivier, *Angew. Chem. Int. Ed.*, 2020, **59**, 7487-7493.

52. V. Paulino, K. X. Liu, V. Cesiliano, I. Tsironi, A. Mukhopadhyay, M. Kaufman and J. H. Olivier, *Nanoscale*, 2023, **15**, 4448-4456.
53. F. K. Metze, I. Filipucci and H. A. Klok, *Angew. Chem. Int. Ed.*, 2023, DOI: 10.1002/anie.202305930.
54. M. S. Kaucher, W. A. Harrell and J. T. Davis, *J. Am. Chem. Soc.*, 2006, **128**, 38-39.
55. W. B. Lu, S. Sengupta, J. L. Petersen, N. G. Akhmedov and X. D. Shi, *J. Org. Chem.*, 2007, **72**, 5012-5015.