NJC

Accepted Manuscript

This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/njc

NJC

RSCPublishing

PAPER (FOCUS)

Guanosine and isoGuanosine derivatives in supramolecular devices

Cite this: DOI: 10.1039/xoxxoooooox

Valentina Abet[a]* and Raphaël Rodriguez[b]

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

www.rsc.org/

Guanosine and isoguanosine derivatives can self-assemble by means of hydrogen-bonding, π-π and cation-dipole interactions, yielding supramolecules that have found broad applications in diverse areas, such as material science, medicinal chemistry or nanotechnology. This article reviews the different self-organized architectures generated by guanosine and isoguanosine scaffolds and reports on recent examples of their use in the preparation of functional devices.

1. Introduction

Molecular self-assemblies are predominant in Nature and are involved in many fundamental biological processes reliant on protein function and storage of the genetic material. For instance, self-organized systems include quaternary structures of proteins and the formation of double helical DNA as a result of self-recognition of two single-stranded oligonucleotides. The intermolecular forces that drive these events are dominated by hydrophobic, van der Waals as well as π-π interactions and hydrogen bonding.[1] Base pairing within a long DNA polymer is specifically dictated by the self-complementarity of Watson-Crick hydrogen bond networks that provide the fidelity required for proper packaging of DNA, thereby enabling processes of replication and transcription to take place. These elegant processes used by Nature have attracted considerable interest among the scientific community and prompted the design of bio-inspired supramolecular structures. Hydrogen bond-mediated self-assembly of natural and synthetic nucleobases is thus becoming a powerful tool for generating (nano)structures and materials with predictable physicochemical properties, based on the selective self-recognition between functionalized small molecules.[2] Such self-assembled supramolecular systems present a valuable feature that is the ability to respond to an external pressure through exchanging and rearranging their molecular components, thanks to the reversible nature of non-covalent interactions that hold them together.[3] This dynamic feature allows the preparation of functionalized architectures, whose physical characteristics can be tuned and controlled by a variety of external *stimuli* including light, pH, temperature and magnetic field.

Guanosine (G) and isoguanosine (isoG) represent versatile multiple hydrogen bonding units, where isoG is a non-natural nucleobase isomer of G with transposed carbonyl and amino groups. Over the past twenty years, broad applications of guanosine-related derivatives have emerged, spanning from structural biology to medicinal chemistry through material chemistry and nanotechnology.[4] Herein, supramolecular self-assembly of G- and isoG-containing molecules are discussed, followed by a review on their use as powerful scaffolds employed in nanotechnological applications.

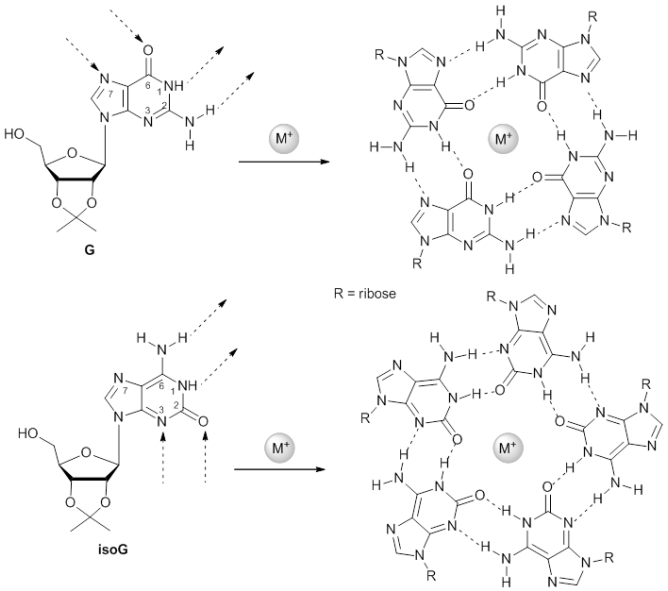
2. Self-assembly of guanosine derivatives

Guanosine self-assembly has been observed since the 19th century, as Bang reported that guanylic acid formed gel at concentrated solution.[5] It was only in 1962 that Gellert and co-workers proposed that the bases in such gels were organized in tetrameric structure.[6] This G-quartet (Scheme 1), formed in water in the presence of Na^+ or K^+ ions, is a macrocycle made up of four guanines with the complementary Watson-Crick (N^1H and N^2H) and Hoogsteen (O^6 and N^7) edges hydrogen bonded and the metal sited in the central cavity.[7] These structures pile up, due to π-π interactions between the aromatic planes and cation-dipole interactions, providing columnar architectures that at certain concentration can reach a length of 8-30 nm.[8] Similarly, in nature guanosine-rich DNA and RNA sequences self-assemble in four-stranded structures known as G-quadruplexes.[9]

Lipophilic guanosine derivatives can self-assemble even in organic solvents in the presence of alkali metal ions,[10] giving rise to polymeric columnar aggregates of G-quartets which form liquid-crystalline phases, as revealed by Polarizing Optical Microscopy (POM) and X-ray measurements.[11] Alternatively, in absence of cations, similar lipophilic guanosine derivatives self-assemble into linear ribbon-like supramolecular architectures that have been detected both in solution by NMR spectroscopy and ESI-MS,[12] and at the solid state by single-crystal X-ray diffraction.[13] Two types of ribbons with different hydrogen-bonding patterns, and so a different symmetry, were observed (Figure 1): ribbons A, which are characterized by cyclic N^2H-O^6 and the N^1H-N^7 hydrogen bonds, and ribbons B, thermodynamically more stable, which are characterized by N^1H-O^6 and N^2H-N^3 hydrogen bonds.

Sessler and co-workers demonstrated that attaching a bulky group to the guanine C^8 position of lipophilic G-derivatives resulted in a conformationally constrained nucleoside, which adopts a *syn*-glycosidic bond conformation both in the solid state and solution, thus preventing ribbon formation.[14] Such molecules self-assemble into an "empty" G-quartet without the assistance of cation templation.

New Journal of Chemistry Accepted Manuscript



Scheme 1. Assembly of guanosine (G) and isoguanosine (isoG) in the presence of metal ions (M^+).

3. Self-assembly of isoguanosine derivatives

Like guanosine, isoguanosine also self-organizes around alkali ions into discrete hydrogen-bonded assemblies: the relative orientation of hydrogen-bond donor and acceptor groups favors the formation of a planar cyclic pentamer (Scheme 1).[15] The crystal structure of a Cs^+-templated decamer formed form 5'-*t*-butyldimethylsilyl-2',3'-*O*-isopropylidene-substituted isoG unambiguously showed that two C_5-symmetric pentamers stack in a sandwich-like structure with a central 10-coordinated cesium ion.[16] Pentamer self-assembly is mediated by 15 hydrogen bonds: 10 correspond to those between N^1H-O^2 and N^6H-N^3, while 5 are formed between the N^6 of a monomer and the $O^{2'}$ of the ribose of the neighboring molecule. In contrast to guanosine, the ribose and the hydrogen bond acceptors (O^2 and N^3) are located together on the lower edge of the purine residue; sugar-base hydrogen bonds are so allowed, thus facilitating the self-assembly process. Diffusion NMR studies and MS experiments provided solid evidence that D_5-symmetric decameric species are the only assemblies formed in solution.[17]

4. Applications of self-assembled G- and isoG-based systems

4.1. Ion extractants and artificial ion channels

The synthesis of calixarenes, crown ethers and other covalent ionophores that present a structure with a prebuilt binding site requires considerable efforts in order to fix the molecule in the correct conformation. In contrast, self-assembled ionophores based on non-covalent interactions can be prepared more easily and efficiently. In addition, these dynamic structures offer the possibility to reverse the assembly by changing some parameter, such as solvent, temperature or pH. Davis and co-workers described the self-assembled decamer formed from the isoG derivative **1** (Scheme 2) as a highly selective cesium ionophore.[16] Indeed compound **1** can extract $^{137}Cs^+$ from water to chloroform with high affinity and selectivity. Moreover, in a competition experiment, the self-assembled isoG **1** is able to quantitatively remove bound Cs^+ ions from a calix[4]arene-crown ether. In a related study, isoG **1** and its corresponding guanosine analogue **2** self-organize around $^{226}Ra^{2+}$

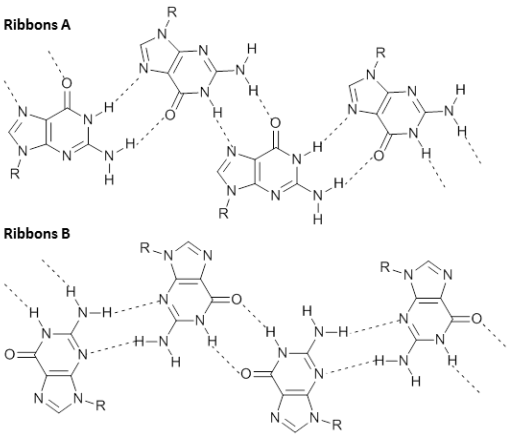
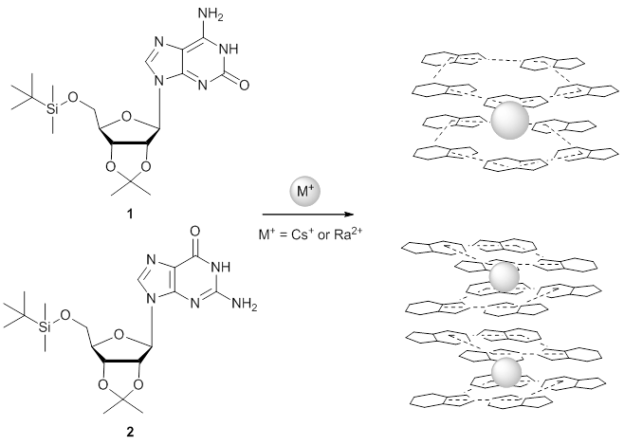


Figure 1. Different ribbons structures formed by self-assembly of lipophilic G-derivatives.

ions in decameric and hexadecameric structures respectively, exhibiting high selectivities even in the presence of million fold excess of alkali cations (Scheme 2).[18] These examples show the potential of G and isoG supramolecular self-assembly to construct highly selective ion receptors for the decontamination of radioactive wastes.



Scheme 2. Decamer formed from isoG **1** in presence of Cs^+ or Ra^{2+} and hexadecamer formed from G **2** in presence of Ra^{2+}.[16,18]

Davis and co-workers also described the preparation of a "unimolecular" G-quadruplex by combining non-covalent synthesis and post-assembly modifications.[19] The starting material was a guanosine derivative that carries two allyl ether moieties suitable for olefin metathesis to covalently link two neighboring G monomers within the assembly. Thus, after allowing the system to self-assemble around K^+ as a D_4-symmetric hexadecamer, olefin metathesis was performed using Grubb's second generation catalyst, yielding a product which was apparently trapped into a channel-like structure that consents the transport of Na^+ ions across phospholipid bilayer membranes, as demonstrated by ^{23}Na NMR spectroscopy.

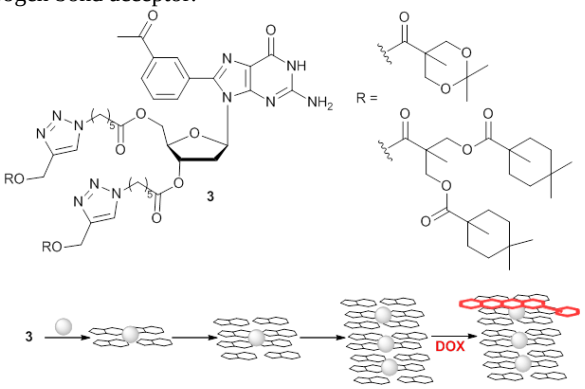
4.2. Self-assembled dendrimers

Dendrimers are tree-branched macromolecules composed by a central core, an inner shell (the dendritic branches) and an outer shell highly dense in functional groups.[20] A rational combination of these components can lead to compounds with specific physicochemical properties. As a result, dendrimers have found widespread applications including drug delivery, catalysis or nanotechnology.[21] The complex structure of these molecules makes their synthesis difficult and expensive. An alternative strategy include the self-

New Journal of Chemistry Accepted Manuscript

 This journal is © The Royal Society of Chemistry 2012

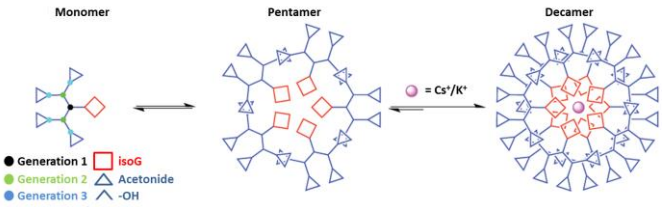
assembly approach: dendritic macromolecules can be generated through the self-organization of small monomers by means of non-covalent interactions, such as hydrogen bonding. Resulting compounds are known as self-assembled dendrimers (SADs).
Rivera and co-workers prepared dendronized guanosine derivatives (**3**, Scheme 3) embedded with an extended aromatic surface, through functionalization of C^8 with a phenyl ring carrying an additional hydrogen bond acceptor.[22]



Scheme 3. Dendronized G-derivatives self-assemble into tetramers, which further stack to octamers and then form hexadecameric structures. Addition of doxorubicin (DOX) results in the formation of a host-guest complex.[22e]

This substitution forces the building blocks into the *syn*-glycosidic conformation, thus prohibiting formation of ribbons, thereby providing a larger aromatic surface for π-π interactions between stacked G-quartets. This introduced four additional hydrogen bond per quartet involving the exocyclic N^2 amino hydrogen in the hydrogen bond system. These derivatives form hexadecameric self-organized structures in the presence of potassium ions in both organic and aqueous media under a wide variety of conditions, furnishing discrete, well-defined, chiral and thermally stable SADs. It has been shown that such assemblies can serve as thermo-, photo- and metallo-responsive scaffolds, which can be exploited for the purpose of drug delivery.[23] In particular, Rivera's group synthesized 8-(*m*-ethoxycarbonylphenyl)-2'-deoxyguanosine derivatives, which in a K^+-containing aqueous solution self-assembled into discrete hexadecamers. Upon addition of doxorubicin to the medium, such assemblies further self-organized into microglobules, therefore encapsulating the drug within the resulting suprastructure. These SADs represent an attractive and complementary strategy to polymer-based systems for drug encapsulation at biocompatible temperatures.

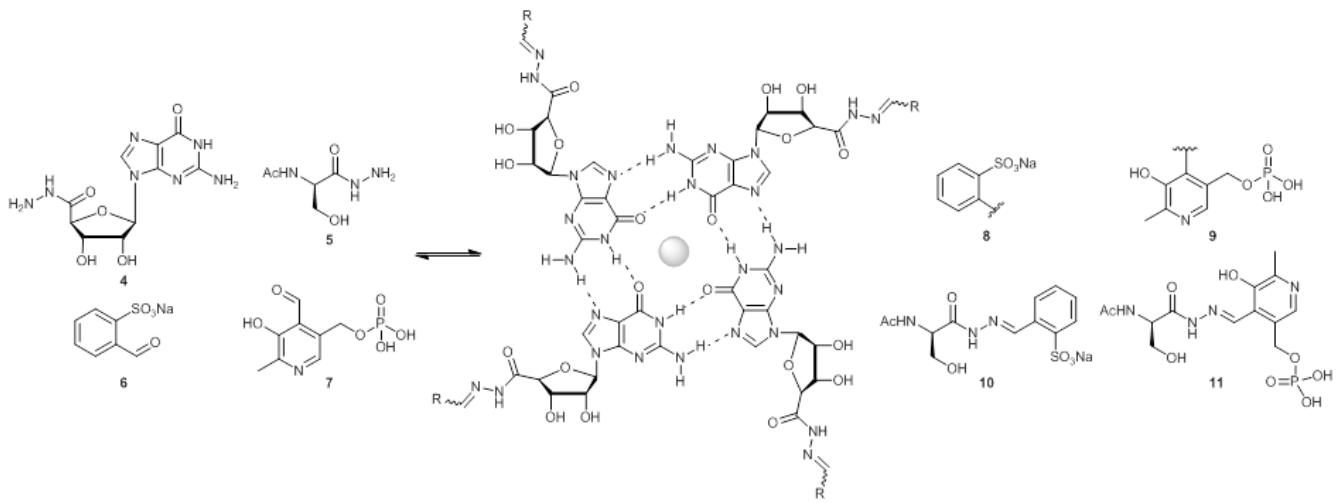
More recently, Abet and co-workers described the rapid and versatile preparation of isoguanosine-containing dendritic small molecules, or nucleodendrimers (ND), diverse in size, polarity, stability, geometry and peripheral functionalities, that readily self-assemble into pentameric structures in polar solvents (Scheme 4).[24] Addition of alkali metals promotes the formation of stable decameric architectures, with a preference for cesium ions over other cations. The authors reported that co-incubation of guanosine- and isoguanosine-containing nucleodendrons results in the formation of decameric structures in absence of added salts. Further analysis of the mixture indicated that guanosine derivatives facilitate the formation of, but are not involved in, the self-assembled system, as there are no evidences of hybrid G/isoG nucleodentritic species, evocating a molecular crowding situation previously reported for G-quadruplex nucleic acids.[25] This dynamic system could in principle be used to produce multifunctional heterodendrimers with tunable physicochemical properties just by strategically mixing isoguanosine dendritic derivatives.



Scheme 4. Schematic representation of dynamic ND formation.[24]

4.3. Dynamic polymers

Dynamic covalent chemistry (DCC)[26] is a powerful tool in supramolecular chemistry, since it allows the amplification of selected compounds from a dynamic combinatorial library (DCL) of building blocks, following exposure to an external template able to engage supramolecular interactions with specific members of the library. In 2005, Lehn and co-workers reported on the preparation of dynamic hydrogels based on the stacking and cross-linking of G-quartets formed by a guanosine hydrazyde (**4**, Scheme 5) that can be covalently modified on the sugar sidechain.[27] Reaction of **4** with various aldehydes in the presence of metal cations affords highly viscous thermally reversible hydrogels by acylhydrazone bond formation. The authors demonstrated that the equilibrium of a DCL composed of 2 hydrazides and 2 aldehydes that can yield 4 different acylhydrazones is shifted towards the formation of product **9**, being the one which forms the most stable hydrogel at this temperature. Hydrogels derived from low-molecular weight compounds may have



Scheme 5. Dynamic combinatorial library of acylhydrazones **10** and **11** and G-quartets based acylhydrazones **8** and **9**.[27]

New Journal of Chemistry Accepted Manuscript

broad applications in medicinal chemistry, as recently demonstrated by Rowan and co-workers. In this study, the authors described that 8-methoxy-2',3',5'-tri-*O*-acetylguanosine acts as a non-toxic to cell injectable G-based hydrogelator that could be used for tissue engineering purposes.[28] Functional hydrogels formed by co-incubation of G and 8-bromoG in a potassium salt medium have been shown to control the diffusion and release of small molecules, thus unambiguously demonstrating a potential biomedical application for this kind of device.[29]

The self-assembly of octadecyl-guanine derivatives on highly oriented pyrolytic graphite has been studied by Spada and co-workers by scanning tunneling microscopy, thus providing a direct evidence at the sub-nanometer scale of the structure operating at the surface.[30] Hydrogen bonded ribbons in such molecules naturally self-organize and are converted into G-quartet architectures upon addition of K^+ picrate, then reversed to nanoribbons after incubation with [2.2.2]cryptand. Subsequent addition of trifluoromethanesulfonic acid to protonate the cryptand releases potassium cations to allow G-quartet motifs formation. This *in situ* reversible assembly between two highly ordered supramolecular structures at the surface of graphite can open new avenues towards the generation of nanopatterned responsive architectures.

4.4 Guanosine self-assembly in nanosized materials

Self-assemblies mediated by dynamic supramolecular interactions have been extensively used for the synthesis of functional devices with nanometer dimensions, including oligomeric or polymeric structures or monodisperse nanoparticles.[31] Remarkably, the reversible nature of the supramolecular bonds, which can readily be formed or broken in response to an external trigger, confers unique properties that can hardly be accomplished with irreversible covalently bonded molecules.

For example, a long-range amplification of G-quartet-based supramolecular architectures into macroscopic polymeric functional films has been reported by Barbiou and co-workers in 2007.[32] The authors efficiently synthesized bisiminoboronate guanosine derivatives (**12**, Scheme 6), which self-assemble after addition of K^+ ions, generating G-quartet-encoded polymeric films containing cross-linked arrays of G-quartets interconnected by the polytetrahydrofurane linker. The authors also investigated the transport properties of such materials, demonstrating that membranes made up of G-quartets stabilized by K^+ templating ions show an increased conductivity compared to the nontemplated ones, indicating that G-quadruplexes enables directional transport events.

Zimmerman and co-workers described the formation of a supramolecular polymer blend of poly(butyl)methacrylate(PMBA) and polystyrene (PS), two documented immiscible polymers, driven by the self-assembly between appended guanosine-ureas (UG) and 2,7-diamido-1,8-naphtyridines (DAN).[33] When the UG-PMBA and DAN-PS derivatives (**13** and **14**, Figure 2) were mixed, the hydrogen bond network formed by UG and DAN connected PS and PMBA coils at the molecular level, allowing the generation of colorless and transparent films with no evidence of phase separation. This result underscores the importance of high-affinity and high-fidelity heterocomplexation in the creation of new supramolecular polymeric architectures.

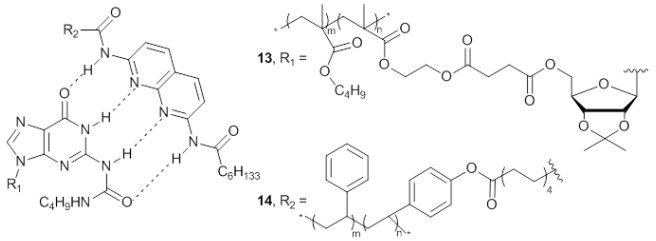
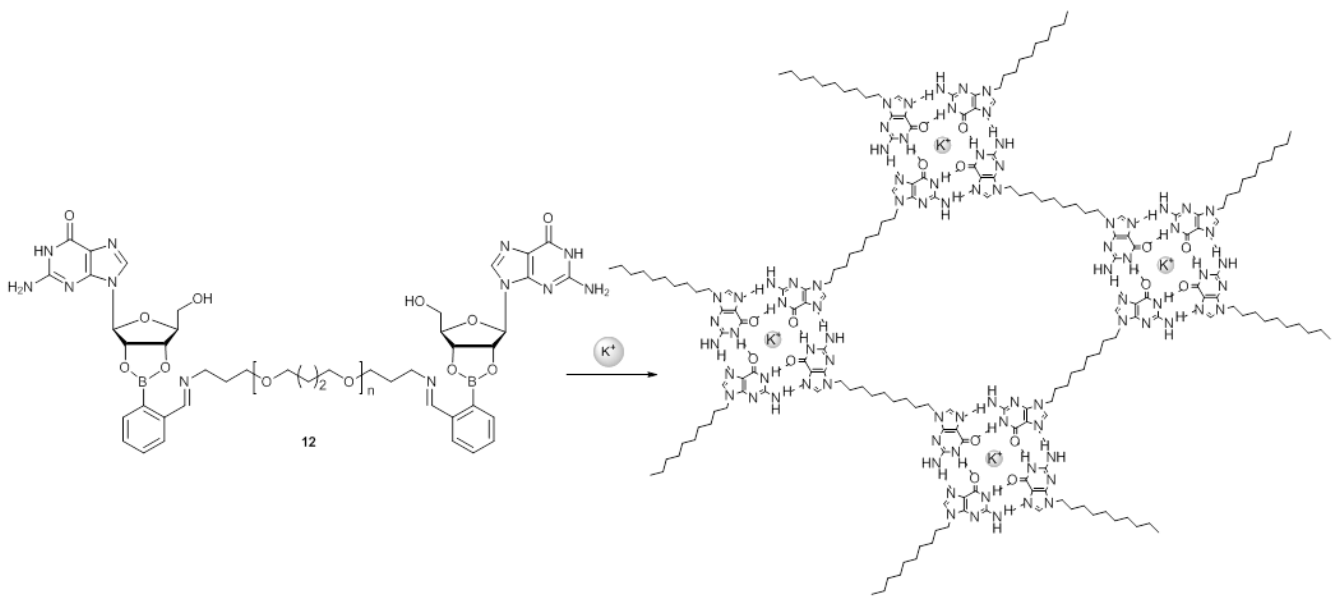


Figure 2. Formation of a strong complex between UG-PMBA (**13**) and DAN-PS (**14**).[33]

Araki and co-workers reported the preparation of micrometer-sized giant vesicles, by hydrogen bond-directed supramolecular self-assembly of guanosine derivatives that carry a rigid phenyl unit within the alkyl chain of extended oxyethylene units.[34] A 2D-hydrogen bonding network is formed in between the guanosine moieties, while the oxyethylene residues are located on the surface of the sheet assemblies, thus enhancing the hydrophilicity of the system. These vesicles are highly stable in water and under thermal or mechanical stress, and highly resistant to the permeation of water or other substances. The addition of hexadecyltrimethylammonium chloride, a cationic surfactant, induces an effective destruction of the vesicles. This dynamic response is the direct manifestation of the reversible nature of the intermolecular interactions, constituting the major advantage of self-assembled supramolecular materials.

The supramolecular synthesis of disk-shaped organic nanoparticles



Scheme 6. The cation-templated self-assembly of bisiminoboronate guanosine **12** into polymeric membrane films.[32]

New Journal of Chemistry Accepted Manuscript

 This journal is © The Royal Society of Chemistry 2012

comprising oligo(*p*-phenylene-vinylene) oligomers capped with a guanosine or a guanine moiety (**15**-**17**, Figure 3) has been studied by different techniques in solution, solid state and on surface, in both the absence and the presence of alkaline salts.[35] When no salt is added, these π-conjugated molecules self-organize in hydrogen bonded oligomeric architectures in which the G-quartet structure is predominant. In contrast, upon addition of Na^+ or K^+ salts, discrete self-assembled nanoparticles made up of exactly eight functional molecules, highly stable to temperature and concentration changes, are formed selectively and quantitatively. These results show how the guanosine scaffold imparts stability to the assembly and limits its growth to a well-defined arrangement, a behavior that may allow its use in the construction of discrete nano-objects.

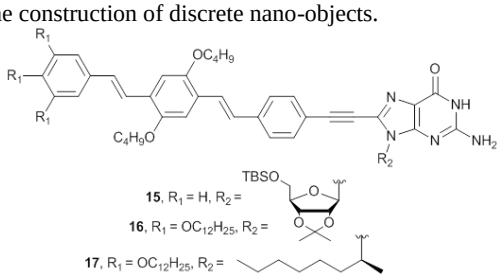


Figure 3. Structure of the oligophenylenevinylene-guanine molecules.[35]

4.5. Intramolecular synthetic G-quartets

Naturally occurring G-quartets have recently attracted a great deal of attention for their ability to arise intra- or intermolecularly from G-rich DNA and RNA oligonucleotides.[36] The discovery of quadruplex-forming sequences in key regions of chromosomes or mRNA raised the possibility to interfere with the corresponding cellular events by the stabilization of the G-quadruplexes with small ligands, which are currently considered promising anti-cancer agents.[9]

In 2008, Sherman and co-workers introduced a new class of compounds, the Template-Assembled Synthetic G-Quartets or TASQ, which are guanine-linked cavitands that spontaneously form G-quartets in both organic[37] and aqueous media[38] and even in absence of cations, as the guanosine self-assembly is facilitated by the pre-organized structure of the cavitand. This synthetic model of G-quadruplex-DNA has been used as a probe for interactions with potential anticancer ligands, thus demonstrating its applicability as a tool for the development of novel binders or as a screening technology device for the detection of G-quadruplex interacting compounds within a library of small molecules.

Monchaud and co-workers reported on a novel series of synthetic G-quartets, the DOTASQ and ^{PNA}DOTASQ (Figure 4), whose structure is based on the formation of an intramolecular G-quartet templated by the water-solubilizing DOTA macrocycle (with DOTA: 1,4,7,10-tetraazacyclododecane-*N*,*N*',*N*'',*N*'''-tetraacetic acid).[39] These molecules were designed to interact with G-quadruplexes according to a nature-inspired *like likes like* approach, based on the association between two G-quartets, one being native (G-quadruplex DNA) and the other one artificial (ligand). DOTASQ was able to bind to quadruplex-DNA only when a metal (terbium) was inserted in its cavity. Metal coordination (with the four ring nitrogen atoms and the four carbonyl oxygen atoms) indeed favors the closed conformation over the open one, thus placing the guanine moieties on the same side of the ring and so allowing G-quartet formation and quadruplex-DNA recognition. In ^{PNA}DOTASQ the guanine arm is substituted by a PNA-monomer. It is noteworthy that these assemblies are based on guanine as opposed to guanosine derivatives where the sugar moiety was replaced by hydrophilic linkers, the resulting TASQ being surrounded by four protonable primary amines, a structural feature that increase water solubility and G-quadruplex affinity.[40] Here, the interaction of the small molecule with a quadruplex-DNA favors synthetic G-quartet folding (Figure 4b). In contrast, a duplex-DNA does not allow this TASQ arrangement, thereby ensuring a high level of quadruplex selectivity. The ability of ^{PNA}DOTASQ to interact selectively with DNA- and RNA-quadruplexes has also been studied, as well as its catalytic activity in peroxidase-like hemin-mediated oxidation, thus demonstrating that such compounds are versatile biotechnological tools.[41]

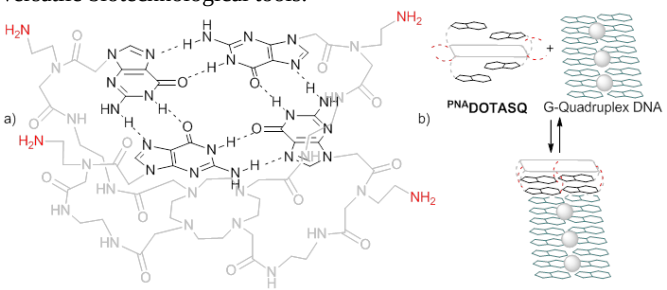


Figure 4. a) Closed conformation of ^{PNA}DOTASQ; b) G-quadruplex recognition principle.[39]

5. Conclusions

Self-organization of G- and isoG-derivatives can be controlled by the rational design of subunits and by modulating the physicochemical conditions into which a given system is allowed to evolve. Over the past decade, guanosine analogues have been extensively used in material science and nanotechnology, as their supramolecular assemblies allow for the preparation of functional architectures with predictable properties including ion channels, hydrogels and noncovalent polymers among others. Great efforts are recently being devoted towards the use of guanosine-containing small molecules as enhancing agents for DNAzyme processes[41,42] or as probes for the detection of important signalling molecules.[43] Given that G-quadruplexes appear to be involved in biological processes, in particular in those associated with telomere maintenance, transcription and translation,[40,44] G-quartets-derived systems may constitute useful tools for the design of new anticancer drugs as well as for the selection of the best DNA or RNA binder.

Surprisingly, not so many applications based on isoguanosine-derived molecules have yet emerged. The astonishing stability and cation-selectivity exhibited by isoG analogues open the way towards new applications. The development of such derivatives for the preparation of materials with tunable physicochemicals properties still holds great promise.

Acknowledgements

We thank the Centre National de la Recherche Scientifique for generous funding.

Notes and references

[a]*Institut Curie, UMR 176, Campus Universitaire, Bat. 110-112, 91405, Orsay, France;* [b]*Institut de Chimie des Subtances Naturelles, Centre National de la Recherche Scientifique, Avenue de la Terrasse, Bat. 27, Gif-sur-Yvette, France.*

Email: valentina.abet@curie.fr

1 R. R. Sinden, *DNA Structure and Function*, Academic Press, Inc. New York, 1994.

New Journal of Chemistry Accepted Manuscript

2 a) S. Sivakova, S. J. Rowan, *Chem. Soc. Rev.*, 2005, **34**, 9; b) J. L. Sessler, C. M. Lawrence, J. Jayawickramarajah, *Chem. Soc. Rev.*, 2007, **36**, 314; c) M. Fathalla, C. M. Lawrence, N. Zhang, J. L. Sessler, J. Jayawickramarajah, *Chem. Soc. Rev.*, 2009, **38**, 1608.

3 J. M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, Germany, 1995.

4 a) J. T. Davis, *Angew. Chem. Int. Ed.*, 2004, **43**, 668; b) J. T. Davis, G. P. Spada, *Chem. Soc. Rev.*, 2007, **36**, 296; c) S. Lena, S. Masiero, S. Pieraccini, G. P. Spada, *Chem. Eur. J.*, 2009, **15**, 7792; d) M. Franceschin, *Eur. J. Org. Chem.*, 2009, 2225.

5 I. Bang, *Biochem. Z.*, 1910, **26**, 293.

6 M. Gellert, M. N. Lipsett, D. R. Davies, *Proc. Natl: Acad. Sci. USA*, 1962, **48**, 2013

7 T. J. Pinnavaia, C. L. Marshall, C. M. Mettler, C. L. Fisk, H. Todd Miles, E. D. Becker, *J. Am. Chem. Soc.*, 1978, 3625.

8 a) S. L. Forman, J. C. Fettinger, S. Pieraccini, G. Gottarelli, J. T. Davis, *J. Am. Chem. Soc.*, 2000, **122**, 4060; b) A. Wong, R. Ida, L. Spindler, G. Wu, *J. Am. Chem. Soc.*, 2005, **127**, 6990.

9 a) S. Neidle, S. Balasubramanian, *Quadruplex Nucleic Acids*, Royal Society of Chemistry, London, Cambridge, 2006; b) S. Balasubramanian, L. H. Hurley, S. Neidle, *Nat. Rev. Drug Discov.*, 2011, **10**, 261.

10 a) G. Gottarelli, S. Masiero, G. P. Spada, *J. Chem. Soc. Chem. Commun.*, 1995, 2555; b) J. T. Davis, S. Tirumala, J. Jenssen, E. Radler, D. Fabris, *J. Org. Chem.*, 1995, **60**, 4167.

11 S. Pieraccini, G. Gottarelli, P. Mariani, S. Masiero, L. Saturni, G. P. Spada, *Chirality*, 2001, **13**, 7.

12 G. Gottarelli, S. Masiero, E. Mezzina, S. Pieraccini, J. P. Rabe, P. Samori, G. P. Spada, *Chem. Eur. J*,. 2000, **6**, 3242.

13 T. Giorgi, F. Grepioni, I. Manet, P. Mariani, S. Masiero, E. Mezzina, S. Pieraccini, L. Saturni, G. P. Spada, G. Gottarelli, *Chem. Eur. J.* 2002, **8**, 2143.

14 J. L. Sessler, M. Sathiosatham, K. Doerr, V. Lynch, K. A. Abboud, *Angew. Chem. Int. Ed.*, 2001, **11**, 3018.

15 J. C. Chaput, C. Switzer, *Proc. Natl. Acad. Sci. USA*, 1999, **96**, 10614.

16 M. Cai, A. L. Marlow, J. C. Fettinger, D. Fabris, T. J. Haverlock, B. A. Moyer, J. T. Davis, *Angew. Chem. Int. Ed.*, 2000, **39**, 1283.

17 T Evan-Salem, L. Frish, F. W. B. van Leeuwen, D. N. Reinhhoudt, W. Verboom, M. S. Kaucher, J. T. Davis, *Chem. Eur. J.*, 2007, **13**, 1969.

18 F. W. B. van Leeuwen, W. Verboom, X. Shi, J. T. Davis, D. N. Reinhoudt, *J. Am. Chem. Soc.*, 2004, **126**, 1675.

19 M. S. Kaucher, W. A. Harrell, Jr., J. T. Davis, *J. Am. Chem. Soc*,. 2006, **128**, 38.

20 a) G. R. Newkome, C. N. Moorefield, F. Vögtle, *Dendritic Molecules: Concepts, Synthesis, Perspectives*, WILEY-VCH, Weinheim, Germany, 1986; b) J. M. J. Fréchet, D. A. Tomalia, *Dendrimers and Other Dendritic Polymers*, Wiley, Chichester, U.K., 2001.

21 a) M. Denise, D. Astruc, *Coord. Chem. Rev.*, 2006, **250**, 1965; b) B. Helms, E. W. Meijer, *Science*, 2006, **313**, 929; c) A. M. Caminade, A. Ouali, M. Keller, J. P. Majoral, *Chem. Soc. Rev.*, 2012, **41**, 4113.

22 a) M. Garcia-Arriaga, G. Hobley, J. M. Rivera, *J. Am. Chem. Soc.*, 2008, **130**, 10492; b) J. E. Betancourt, J. M. Rivera, *Org. Lett.*, 2008, **10**, 2287; c) J. E. Betancourt, M. Martin-Hidalgo, V. Gubala, J. M. Rivera, *J. Am. Chem. Soc.*, 2009, **131**, 3186; d) J. E. Betancourt, J. M. Rivera, *J. Am. Chem. Soc.*, 2009, **131**, 16666; e) J. M. Rivera, M. Martin-Hidalgo, J. C. Rivera-Rios, *Org. Biomol. Chem.*, 2012, **10**, 7562.

23 a) J. E. Betancourt, C. Subramani, J. L. Serrano-Velez, E. Rosa-Molinar, V. M. Rotello, J. M. Rivera, *Chem. Commun.*, 2010, **46**, 8537; b) M. Martin-Hidalgo, J. M. Rivera, *Chem. Commun.*, 2011, **47**, 12485; c) J. M. Rivera, D. Silva-Brenes, *Org. Lett.*, 2013, **15**, 2350.

24 V. Abet, R. Evans, F. Guibbal, S. Caldarelli, R. Rodriguez, *Angew. Chem. Int. Ed.*, 2014, **53**, 4862.

25 S.-I. Nakano, D. Miyoshi, N. Sugimoto, *Chem. Rev.*, 2014, **114**, 2733.

26 I. Huc, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA*, 1997, **94**, 2106.

27 N. Sreenivasachary, J.-M. Lehn, *Proc. Natl. Acad. Sci. USA*, 2005, **102**, 5938.

28 a) L. E. Buerkle, Z. Li, A. M. Jamieson, S. J. Rowan, *Langmuir*, 2009, **25**, 8833; b) L. E. Buerkle, H. A. von Recum, S. J. Rowan, *Chem. Sci.*, 2012, **3**, 564; c) A. E. Way, A. B. Korpusik, T. B. Dorsey, L. E. Buerkle, H. A. von Recum, S. J. Rowan, *Macromolecules*, 2014, **47**, 1810.

29 R. Nath Das, Y. Pavan Kumar, S. Pagoti, A. J. Patil, J. Dash, *Chem. Eur. J.*, 2012, **18**, 6008.

30 A. Ciesielski, S. Lena, S. Masiero, G. P. Spada, P. Samori, *Angew. Chem. Int. Ed.*, 2010, **49**, 1963.

31 a) J. M. Lehn, *Chem. Soc. Rev.*, 2007, **36**, 151; b) J. A. Thomas, *Chem. Soc. Rev.*, 2007, **36**, 856.

32 C. Arnal-Herault, A. Pasc, M. Michau, D. Cot, E. Petit, M. Barboiu, *Angew. Chem. Int. Ed.*, 2007, **46**, 8409.

33 T. Park, S. C. Zimmerman, *J. Am. Chem. Soc.*, 2006, **128**, 11582.

34 a) I. Yoshikawa, J. Sawayama, K. Araki, *Angew. Chem. Int. Ed.*, 2008, **47**, 1038; b) J. Sawayama, I. Yoshikawa, K. Araki, *Langmuir*, 2012, **26**, 8030.

35 D. Gonzalez-Rodriguez, P. G. A. Janssen, R. Martin-Rapun, I. De Cat, S. De Feyter, A. P. H. J. Schenning, E. W: Meijer, *J. Am. Chem. Soc.*, 2010, **132**, 4710.

36 G. W. Collie, G. N. Parkinson, *Chem. Soc. Rev.*, 2011, **40**, 5867.

37 M. Nikan, J. C. Sherman, *Angew. Chem. Int. Ed.*, 2008, **47**, 4900.

38 G. A. L. Bare, B. Liu, J. C. Sherman, *J. Am. Chem. Soc.*, 2013, **135**, 11985.

39 a) L. Stefan, A. Guedin, S. Amrane, N. Smith, F. Denat, J.-L. Mergny, D. Monchaud, *Chem. Commun.*, 2011, **47**, 4992; b) R. Haudecoeur, L. Stefan, F. Denat, D. Monchaud, *J. Am. Chem. Soc.*, 2013, **135**, 550.

40 .R. Rodriguez, S. Müller, J. A. Yeoman, C. Trentesaux, J.-F. Riou, S. Balasubramanian, *J. Am. Chem. Soc.*, 2008, **130**, 15758.

41 R. Haudecoeur, L. Stefan, D. Monchaud,. *Chem. Eur. J.*, 2013, **19**, 12739.

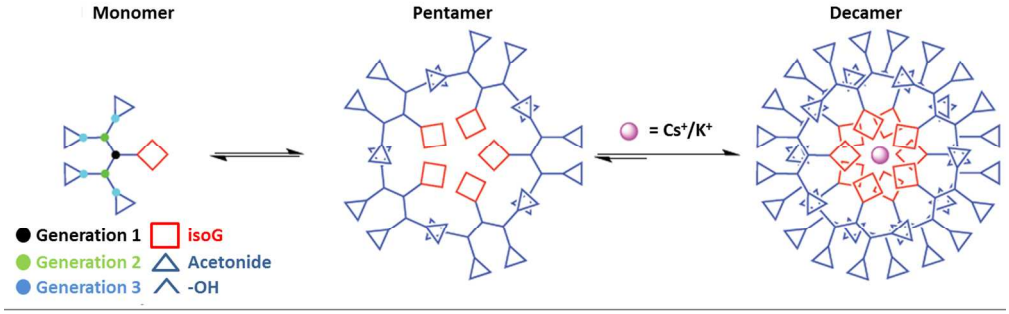
42 B. T. Roembke, J. Wang, S. Nakayama, J. Zhou, H. O. Sintim, *RSC Adv.*, 2013, **3**, 6305.

43 S. Nakayama, I. Kelsey, J. Wang, K. Roelofs, B. Stefane, Y. Luo, V. T. Lee, H. O. Sintim, *J. Am. Chem. Soc.*, 2011, **133**, 4856.

44 R. Rodriguez, K. M. Miller, J. V. Forment, C. R. Bradshaw, S. Britton, T. Oelschlaegel, M. Nikan, B. Xhemalce, S. Balasubramanian, S. P. Jackson, *Nat. Chem. Biol.*, 2012, **8**, 301.

New Journal of Chemistry Accepted Manuscript

 This journal is © The Royal Society of Chemistry 2012



252x83mm (150 x 150 DPI)

New Journal of Chemistry Accepted Manuscript