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Arylene Ethynylene Macrocycles: From Molecular Hosts to Components of High-Performance Supramolecular Architectures

Merry K. Smith and Ognjen Š. Miljanić*

Supramolecular chemistry of conjugated and conformationally rigid arylene ethynylene macrocycles (AEMs) has been the subject of increasing recent interest. AEMs are suited to function as supramolecular building blocks and hosts for small molecular guests thanks to their well-defined, non-collapsible central cavities and the potential for long range ordering through intermolecular π-stacking. Their syntheses are highly modular—albeit typically lengthy—allowing access to a great structural variety of AEM candidates for applications as carbon-rich mesogens and ligands in liquid crystals, nanoporous solids, molecular electronics, and chemical sensors. In this perspective, we highlight our recent work on the inclusion complexes and porous materials constructed from AEMs. Through this prism, we reflect on the recent advances and the remaining challenges in the supramolecular chemistry of AEMs.

Introduction

Inspired in part by the discoveries of graphene and fullerenes, chemistry of carbon-rich macromolecules has enjoyed a renaissance in recent years. Particularly promising examples of carbon-rich macrocycles are shape-persistent rings formally prepared from arylene and ethynylene subunits: arylene ethynylene macrocycles (AEMs).[1] On account of their capability for self-assembly and intermolecular recognition, AEMs are attractive targets for remarkably diverse applications in supramolecular chemistry,[2] as liquid crystals, chemical sensors, optoelectronic materials, and nanoporous solids.

Characterized by repeating structural units, conformationally rigid backbones, and shape-persistent central cavities, AEMs can serve as both mesogenic building blocks in complex higher order aggregates and versatile chemical hosts for atomic and molecular guests.[1b,2] Conformational rigidity of AEMs is provided by aromatic moieties linked directionally with ethynyl spacers; their structures have limited rotational degrees of freedom, resulting in well-defined central cavities. Their tuneable, modular syntheses have been reviewed,[1,2b,3] and have led to enormous structural diversity within the AEM family, including examples with a variety of cavity geometries and sizes, as well as with different chemical functionalities—both on the inside of the cavities and outside of them.

Thanks to their versatile syntheses, AEMs may be constructed in a variety of shapes. Considering phenyl subunits as vertices and ethynylene linkers as edges, macrocycle geometry can be tuned based on arene substitution pattern. We will focus our discussion of AEMs on those employing vertices with a single arene ring, which can classified as *ortho*-AEMs (linkers 60° apart), *meta*-AEMs (120°), *para*-AEMs (180°), and hybrid-AEMs (Figure 1). Each class demonstrates notably different supramolecular properties, with both cavity size and chemical substituents impacting the mesogenic properties, hosting capabilities, and crystal packing motifs of the macrocycles. This perspective highlights our recent work in the supramolecular chemistry of AEMs, and uses it as a starting point to discuss both their limitations and future outlook in materials applications. Our objective is not a comprehensive review of AEM chemistry and syntheses, as several have been published recently.[1,2]
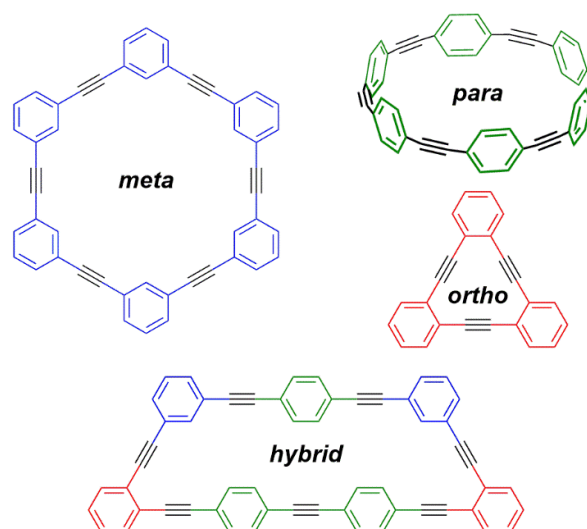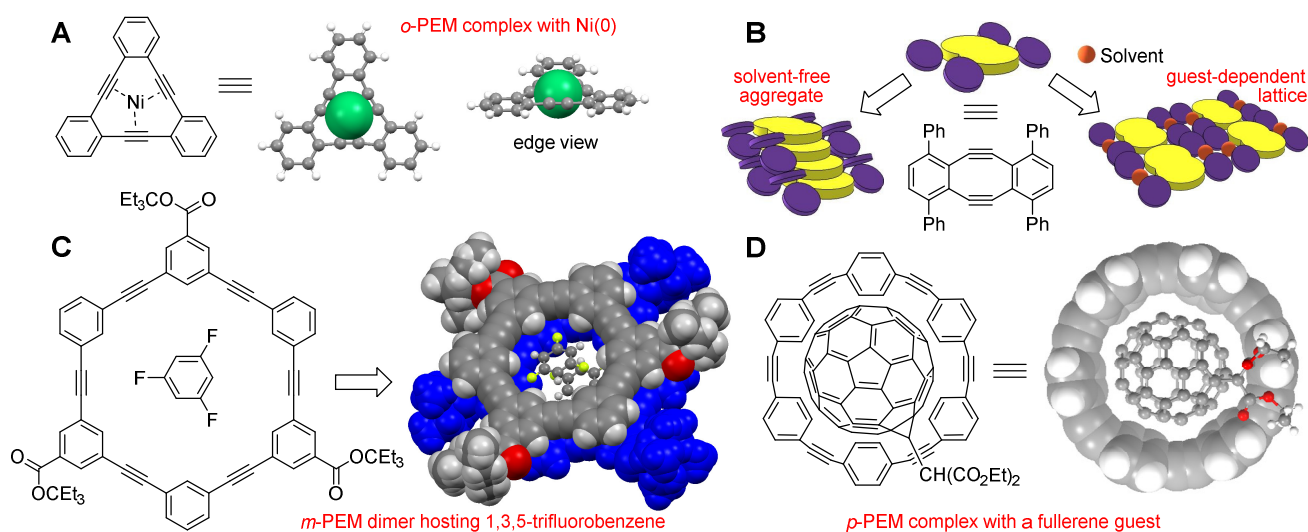

Fig. 1 Examples of the four geometric categories of AEMs (*ortho*-linkages are shown in red, *meta*- in blue, and *para*- in green).

*Department of Chemistry, University of Houston, 112 Fleming Building, Houston, Texas 77204-5003, USA. E-mail: miljanic@uh.edu

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Fig. 2 Examples of the hosting properties of a series of AEMs including **A**—an *o*-AEM hosting a Ni(0) atom in its central cavity, **B**—a representation of the guest (orange sphere) dependent crystallization an *o*-AEM (yellow core with purple phenyl substituents), **C**—an *m*-AEM dimer embracing two molecules of 1,3,5-trifluorobenzene, with the blue structure equivalent to the structure coloured by element, and **D**—*p*-AEM hosting a fullerene derivative in its central cavity.

AEMs as Supramolecular Hosts

Attractive for its potential in chemical sensing and electronics, molecular hosting is largely dependent on central cavity sizes of the AEM in question, which is directly influenced by their *ortho*, *meta*, or *para*-linkage geometry. First synthesized in 1966,[4] the smallest members of the AEM family feature arene vertices *ortho*-connected with ethynylene linkers (Figure 1). The most common examples of *ortho*-AEMs (*o*-AEMs) feature three phenyl vertices; they are planar and triangular in shape. Complexation chemistry of these compounds has been extensively studied, since the seminal communication by Youngs et al. which reported a trigonal *o*-AEM neatly hosting a Ni(0) atom in its central cavity (Figure 2A).[5] This inclusion complex is of interest in molecular electronics, due to the desirable coordination between a soft donor atom and a conjugated acceptor. Complexes of the parent *o*-AEM with Cu(I)[6] and Co(0)[7] have also been characterized (although their geometries are different from Ni(0) complex). Larger metals, such as Ag(I), cannot fit into the center of a single macrocycle and thus form a sandwich complex wherein the metal is squeezed between two macrocycles.[8] Methoxy-substituted *o*-AEMs similarly hosted a Ni(0) atom, although the electron-withdrawing substituents altered the crystal structure from the slipped-stacked herringbone packing of the non-functionalized *o*-AEM/Ni(0) complex to a hydrogen-bonded layered.[9]

While *o*-AEM's central cavity can accommodate just a single atom, larger guest species—that reside outside of AEM cavities—may still associate with the AEM. Hisaki, Miyata, and co-workers have shown that tetraphenyl-substituted two-vertex *o*-AEM oval cocrystallizes with a series of solvents, leading to superstructures which accommodated solvent molecules in intermolecular voids (Figure 2B).[10] The crystal engineering of π-conjugated molecules is of great importance to molecular electronics, and these subtleties of crystal structure dependence on host/guest interactions promise to provide critical information in the fabrication of nanoscale electronic devices. The syntheses of *o*-AEMs are steadily improving with several high-yielding (>50%) routes reported,[1a,11] although catalyst costs associated with alkyne metathesis continue to limit their practical applications.

Hosting properties of AEMs change as the central cavity diameter increases in *meta*- or *para*-connected systems (Figure 1). As the cavity size increases in *m*-AEMs, kinetically-controlled cyclooligomerizations and couplings become less efficient, and give way to higher-yielding thermodynamically-controlled synthetic strategies. In the dynamic synthesis of AEMs from *meta*-vertex subunits, hexameric *meta*-AEMs (*m*-AEMs) are the most enthalpically favoured products, which has led to an extensive family of hexagonal *m*-AEMs.[1a] Based on the hosting behaviour of related *o*-AEMs, *m*-AEMs should function as versatile molecular hosts. Indeed, hosting properties of *m*-AEMs can be predicted based on cavity size and substituents, as shown by Höger and Morrison, who used simulations to predict a molecular guest (an aryl species tetra-substituted with ethynyl-spaced amines) that would associate with their amphiphilic *m*-AEMs.[12] Through NMR studies, they found the complementary coordination to be reversible and tuneable, with binding strength varying with substituent's steric bulk. Recently, our group crystallographically characterized coordination complexes of *m*-AEMs with a series of oligofluorobenzenes (example shown in Figure 2C).[13] Computational analysis of these complexes—which are

isostructural, regardless of the fluoroarene used—suggested that their association in the solid state is dominantly entropic in character, as the included structure leaves less empty space in the crystal.

The class of non-hybrid AEMs with the largest central cavity diameters (up to 1.74 nm) are those featuring *para*-connectivity between aromatic subunits (Figure 1).[14] These unusual, bracelet-shaped compounds have been shown to complex xylenes[14] and fullerenes (Figure 2d).[15] *Para*-AEMs (*p*-AEMs) differ significantly from their *o*-AEM and *m*-AEM analogs in shape. While *o*- and *m*-AEMs are typically planar and rigid, the considerable ring strain in *p*-AEMs forces them into a somewhat flexible, non-planar barrel shape, with average bond angles of the sp carbons ranging from 164 ° to 169 °.[14] Conformationally reminiscent of carbon nanotubes, *p*-AEMs are not only efficient molecular hosts for large aromatic molecules, but also useful in the study of π-conjugation on curved compound surfaces.

The emergence of hybrid AEMs (h-AEMs), including those AEMs incorporating heterocyclic aromatic linkers, has further expanded the host/guest chemistry of AEMs. A pervasive challenge in the use of large AEMs as effective supramolecular hosts is the strength of guest binding. Guest association is based on weak intermolecular interactions: dispersion forces, hydrogen bonding, and halogen bonding. The guest affinity of h-AEMs may be tuned by employing heterocyclic vertices within the cavity, providing pre-programmed host/guest binding sites. This was accomplished by Abe, Inouye and co-workers, who incorporated alternating 3,5- and 2,6-pyridylene vertices into an *m*-AEM hexagon; supplying binding sites for a saccharide guest while overcoming unfavourable local dipole interactions in the cyclization step.[16] In another example from Schlüter et al., terpyridine-containing h-AEM hexagons were found to host three ordered molecules of benzene in their crystal structure.[17] Preparation of AEMs with predesigned binding sites may be taken a step further in the future with incorporation of moieties capable of engaging in dynamic covalent chemistry with target guests.

Self-Association of AEM through π-Stacking and Solvophobic Interactions

Non-covalent long-range interactions of molecules are essential in the preparation of advanced organic materials, including liquid crystals, molecular wires, gels, and thin films. AEMs of different sizes and topologies are well suited to form versatile supramolecular architectures on account of their propensity for π-stacking and solvophobic aggregation between macrocycles. Furthermore, thanks to AEMs' modular syntheses, a wide variety of substituted derivatives is synthetically accessible.

Substitution of small *o*-AEMs can have a dramatic impact on their packing in the solid state. For example, although typically non-porous once crystallized, with judicious choice of
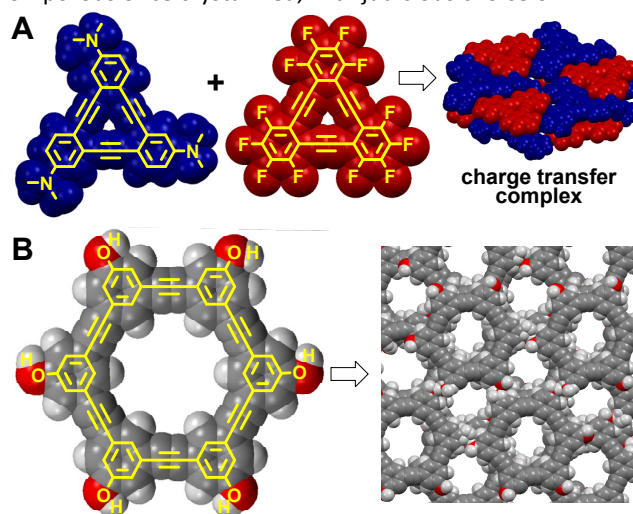
Fig. 3 Examples of AEM supramolecular architectures: **A**—Self-assembled charge transfer complex between two *o*-AEM derivatives. Donor compound is shown in blue, acceptor in red. **B**—Crystallization of a hexahydroxy-substituted *m*-AEM results in a layered solid with an open-channel topology.

substituents, *o*-AEMs have been shown to crystallize with open channels.[18] In a study by Tobe et al., functional groups were utilized to tune both the HOMO/LUMO energies and the crystal packing of triangular *o*-AEMs, which were employed as donor/acceptor molecular building blocks in the preparation of a bimolecular charge transfer material (Figure 3A).[19]

Substituent effect and macrocycle geometry also considerably impact the larger AEMs. For example, barrel-shaped parent *p*-AEMs crystallize in a non-porous conformation,[11] possibly reflecting the inability to effectively connect the individual molecules in the solid as they lack a planar π-surface area. On the other hand, planar *m*-AEMs are capable of constructing supramolecular architectures with large voids. Moore and co-workers synthesized a hexa-phenolic *m*-AEM hexagon that crystallizes as a permanently porous solid, thanks to the hydrogen bonding between hydroxyl groups and extended π-stacking.[20] The subunits align in hexagonally packed 2D layers, which stack on top of each other so that open channels are retained through the crystalline solid (Figure 3B).

Functional Materials Based on AEMs

Informed by the supramolecular properties of their analogues, AEMs are now prepared with increasingly predictable supramolecular properties in mind. Designer h-AEMs have provided libraries of unprecedented AEM shapes and substituent patterns, including an unusual molecular rod, the aromatic backbone of which is shown in Figure 1 (hybrid AEM example). This h-AEM series was prepared by Mayor and co-workers for the fabrication of self-assembled, single
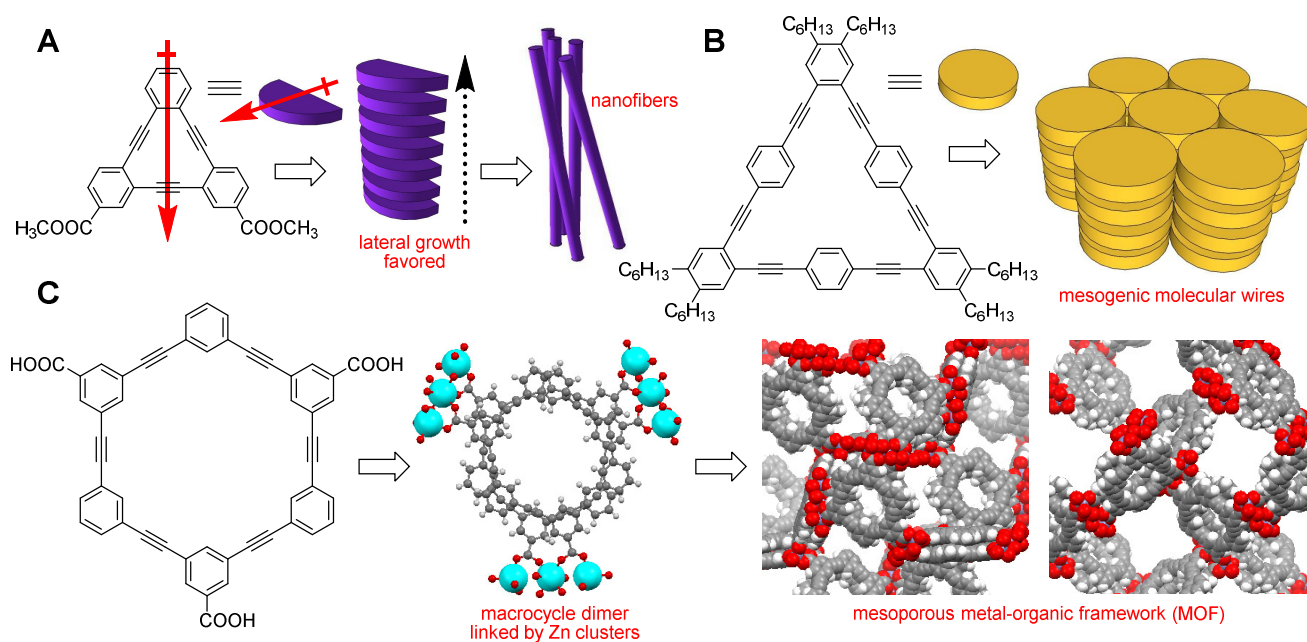
Fig. 4 Functional materials constructed from AEMs. **A**—Nanofiber self-assembly from boomerang-shaped polar *o*-AEM subunits. **B**—h-AEM discotic mesogen and its self-assembly into photoconductive molecular wires. **C**—Carboxylate-functionalized *m*-AEM reacts with Zn (cyan) to form a mesoporous metal-organic framework (MOF). The view shown on the left highlights the pre-programmed central cavities in the MOF crystal structure, while the view on the right highlights the 3D pores extending through the lattice.

molecule electrodes.[21]

Progress in these 'programmable' applications is reflected in recent reports of advanced organic materials constructed from each of the four classes of AEMs introduced in Figure 1. Hisaki, Miyata, and co-workers have shown that directionally-substituted *o*-AEMs can be used to prepare a host of crystalline supramolecular nanofibers.[22] Conventionally, van der Waals interactions between flexible substituents are employed to drive nanofiber assembly, but in this case, the authors used polar functional groups to enforce a dipole moment in the *o*-AEM unit, driving 1D assembly through dipole-dipole interactions (Figure 4A). Lateral elongation was favored, as hypothesized, producing supramolecular nanofibers with a high degree of crystallinity. Further study revealed a HOMO/LUMO gap in the appropriate range for high-performance optoelectronic materials. In the realm of optoelectronics, the traditional liquid crystal structure of a rigid aromatic core flanked with flexible alkyl moieties can be mimicked by substituted AEMs. In 2010, Zhao and co-workers employed a trigonal h-AEM compound as a discotic mesogen for the preparation of liquid crystalline, size-consistent microwires (Figure 4B) with excellent photoconductivity.[2b]

In the realm of porous solids, our group has recently prepared the first example of a metal organic framework (MOF) utilizing shape-persistent macrocycles as ligands.[2d] When Zn(II) was reacted with a triacid *m*-AEM, a crystalline MOF with 86% void volume was produced. The incorporation of the AEM 'pre-programs' a 8.6 Å-wide central cavity into the framework, and also may serve as a highly specific host for substituted benzene derivatives. The results were tempered by the relatively low stability of the prepared MOF and by the low yielding final

cyclization step (21%) in the synthesis of the poorly soluble *m*-AEM ligand,[13] again highlighting synthetic challenges in AEM utility. However, the MOF-formation proceeded in high yields (76%),[2d] suggesting that once synthetic issues are overcome, AEMs may be useful components of organic frameworks. This AEM-based MOF is an example of the scope of potential applications of AEMs which utilize their unique structural characteristics to develop novel materials—in spite of synthetic difficulties.

Conclusions

The works featured herein serve as tangible examples of both the exciting outlook and practical limitations of AEM chemistry in materials applications. Versatile hosting of metal ions,[5-8] aryl derivatives,[13–17] saccharides,[14] and fullerenes[15,16] speaks to AEM potential in chemical sensing, while laying the foundation for the preparation of molecularly resolved host/guest coordination materials. Weak binding interactions may be overcome by the introduction of heterocyclic binding sites, or by the use of electron donating or withdrawing substituents to modulate AEM electronics. Structural versatility of AEMs also allows their utilization in the formation of complex supramolecular architectures, including liquid crystalline wires and fibers,[2b,22] and nanoporous solids.[2d,18,19] Their syntheses may be lengthy and often low-yielding, but their remarkable properties will continue to inspire creative synthetic solutions.

Despite the practical challenges of AEM incorporation into devices, there is still plenty of room to probe, define, and optimize the relationship between the structure and supramolecular function of AEMs, and to use this insight in the

realization of high-performance molecular electronic devices and unique organic materials.

Acknowledgements

Author Biographies

Merry K. Smith graduated from Trinity College in 2009 with a BS in Chemistry. She went on to earn her PhD in Chemistry from Wesleyan University in 2014, where she performed research under the supervision of Prof. Brian Northrop. Currently, she is a postdoctoral scholar in the group of Prof. Ognjen Miljanić at the University of Houston (UH).

Ognjen Š. Miljanić was born in Belgrade, then Yugoslavia, in 1978. He holds a Diploma (2000) from the University of Belgrade, and a PhD (2005) from the University of California at Berkeley. Between 2005 and 2008, he was a postdoctoral scholar at UCLA. He started his independent career at the UH in 2008, where he is presently an Associate Professor of Chemistry. He is a 2013 Cottrell Scholar, a recipient of NSF CAREER and UH Research and Teaching Excellence awards, and a father of three.

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Graphical Abstract
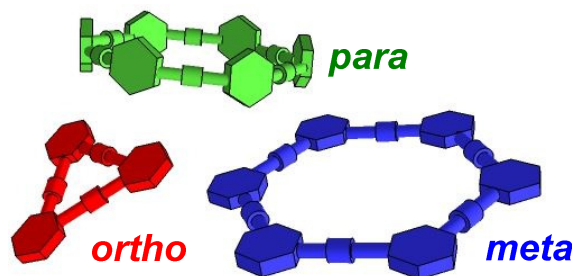
This perspective highlights the recent utilization of arylene ethynylene macrocycles as supramolecular synthons—and speculates on what future may hold.