Arylene–ethynylene macrocycles: Privileged shape-persistent building blocks for organic materials*

Dustin E. Gross[1], Ling Zang[2], and Jeffrey S. Moore[1,‡]

[1]*Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA;* [2]*Department of Materials Science and Engineering, University of Utah, Salt Lake City, UT 84108, USA*

Abstract: This report details the advances in synthetic strategies toward arylene–ethynylene macrocycles (AEMs). After a brief description of traditional methods, we summarize recent advances based on dynamic covalent chemistry (DCC) whereby a highly active and functional group tolerant alkyne metathesis catalyst yields scalable quantities of AEMs under thermodynamic controlled reaction conditions.

*Keywords*: alkynes; alkyne metathesis; carbon; carbon-rich; depolymerization; macrocycles; explosives.

INTRODUCTION

Many factors contribute to the properties of organic materials for use in electronics (Fig. 1). These factors include scalability and processibility, which depend on synthetic methods and solubility. The latter two depend on diversity and the ability to make systematic variations to the molecular material. The sensitivity and selectivity of materials are important, which rely on processing and molecular diversity.

When considering organic materials for use in electronics, discrete molecules possess several advantages compared to their polymeric counterparts (Fig. 2) [1,2]. Macrocyclic oligomers, specifically arylene–ethynylene macrocycles (AEMs), are a class of cyclic alkyne-bridged arenes. They are shape-persistent, meaning there is minimal conformational heterogeneity. Macrocycle synthesis is also reproducible, and monodisperse products can be obtained in high purity. Furthermore, they can be constructed with an array of diverse building blocks in a systematic or modular way. This allows for the potential tuning of electronic and processibility/solubility properties. In fact, AEMs have been processed into a variety of condensed phases in our lab. These include, among others, columnar mesophases [3], nanofiber gels [4], Langmuir–Blodgett films [5], and nanoporous crystals [6]—all of which were dependent on their diverse functionality.
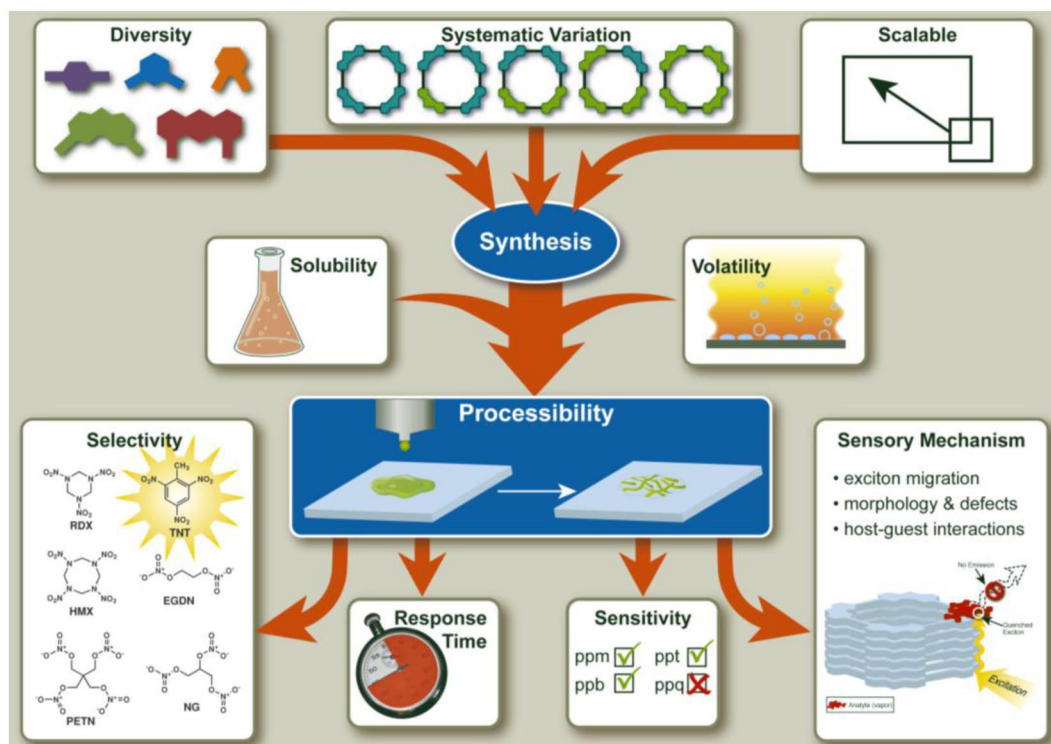
Fig. 1 Development and evaluation processes for next-generation sensory materials.

Attribute	Polymer	Discrete Molecule
Solution processible	✓	✓
Modular	✓	☐
Homogeneity	mixture	✓
Solid state order	glassy semi-xtl	✓
Trace solvent/impurities	high	low
Batch-to-batch reproducibility	low	high

Fig. 2 Comparison of discrete molecules and polymers for use in organic electronics.

SYNTHETIC APPROACHES TOWARD ARYLENE–ETHYNYLENE MACROCYCLES

Traditionally, AEMs have been synthesized under kinetically controlled conditions (Figs. 3A,B) [7–15]. The most commonly used reactions to attain these macrocycles are palladium-catalyzed Sonogashira couplings [16] or copper-catalyzed Glaser-type couplings [17,18], to form arylene–ethynylene or arylene–butadiyne connections, respectively. One of the caveats of this method is that the reaction is

irreversible, and overshooting the target cyclooligomerization length is a problem (Fig. 3E). In this case, polymerization competes with macrocyclization and low yields are generally attained [19,20]. A way around this has been to build up the oligomers sequentially then connect the ends of the difunctionalized oligomers in a final macrocyclization step (Fig. 3B) [21,22]. However, this requires multiple coupling/deprotection reactions, and the final cyclization step is not always high-yielding. Another approach has been to use a template-directed synthesis, which has shown an increase in macrocycle yield [23,24]. Select examples of these methods shown in Fig. 3 are highlighted below.
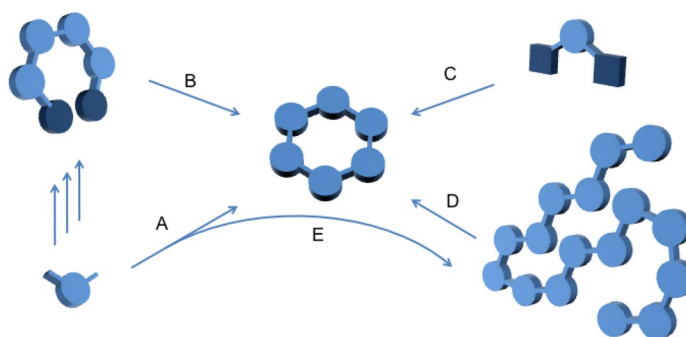
Fig. 3 Pathways to AEMs: (A) kinetic cyclooligomerization; (B) kinetic macrocyclization; (C) dynamic cyclooligomerization; (D) dynamic depolymerization cyclooligomerization; and (E) overshooting or polymerization.

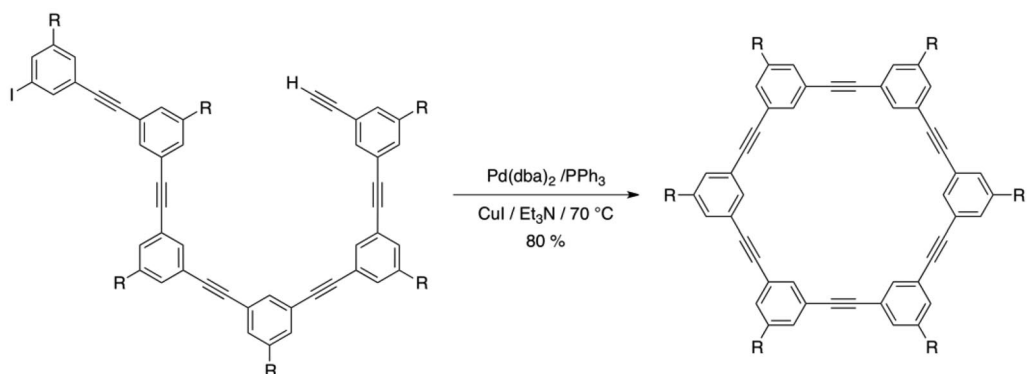## Irreversible cyclooligomerization (method A)

Some of the first examples of AEMs were obtained by Stephens–Castro couplings of iodo functionalized copper arylacetylide monomers. For example, the synthesis of a *meta*-phenylene–ethynylene cyclic hexamer was accomplished in low yield by six successive coupling steps in one pot (Fig. 4) [20]. The low yield was attributed to overshoot products, that is, the polymerization competes with macrocyclization.
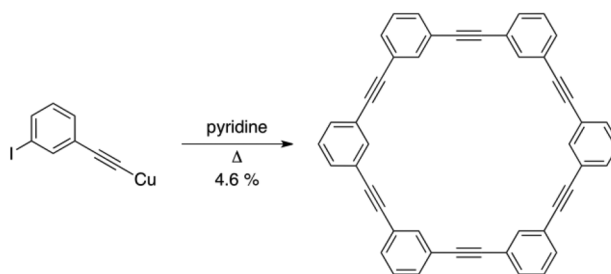
Fig. 4. Kinetic cyclooligomerization [20].
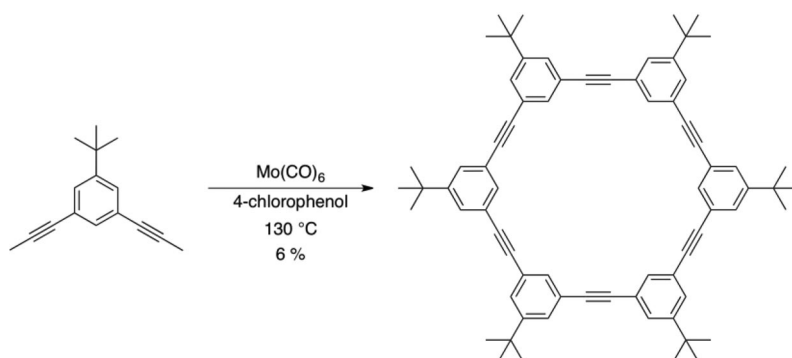
Macrocyclization (method B)

Overall yields are improved when using a stepwise method such as that shown in Fig. 5. Whether the final synthetic step involves a single connection or a case where two partial cycles are connected (not shown), higher yields are generally obtained. This method works best under high-dilution or pseudo-high-dilution conditions. Like method A above, it also has the potential to overshoot the target and form kinetically trapped products.

Fig. 5 Kinetic macrocyclization [21,22].

Cyclooligomerization using alkyne metathesis (method C)

The pursuit of macrocycles using reversible reactions, which give the molecules an opportunity to self-correct (a concept known as "dynamic covalent chemistry") [25,26], has great potential. Alkyne metathesis among other techniques has the ability to undergo reversible reactions and will be the focus for the remainder of this manuscript. Initial evidence of cyclooligomerization via alkyne metathesis was provided by Bunz and co-workers while exploring alkyne metathesis to construct arylene–ethynylene polymers. They found that the synthesis of *meta*-phenylene–ethynylene cyclic hexamer was possible by using a dipropynyl functionalized monomer and an "instant catalyst", molybdenum hexacarbonyl and phenol (Fig. 6) [19]. Unfortunately, the macrocycle was obtained in low yield, likely owing to the fact that the reaction is not under dynamic equilibrium when using these conditions.

Fig. 6 Metathetic cyclooligomerization [19].

Alongside but separate from the development of synthetic methods for macrocycles, alkyne metathesis catalysts have also evolved (see Fig. 7 for a rough timeline) [27–32] beginning in the mid-1970s with the work of Mortreux [33] (similar to that used above by Bunz) to the pioneering work of Schrock [34–36] and more recent advances by the groups of Cummins [37,38], Fürstner [39–41], Johnson [42,43], and Bunz [31,44,45]. Recently, we reported a reductive recycle strategy to synthesize a highly active alkyne metathesis catalyst [46,47]. Using 4-nitrophenol as a ligand, cross-metathesis under thermodynamically controlled equilibrium can be achieved at room temperature. More recently, following our own work [48,49] and that of Furstner [40], we have found that triphenylsilanol is a superior ligand for metathesis.
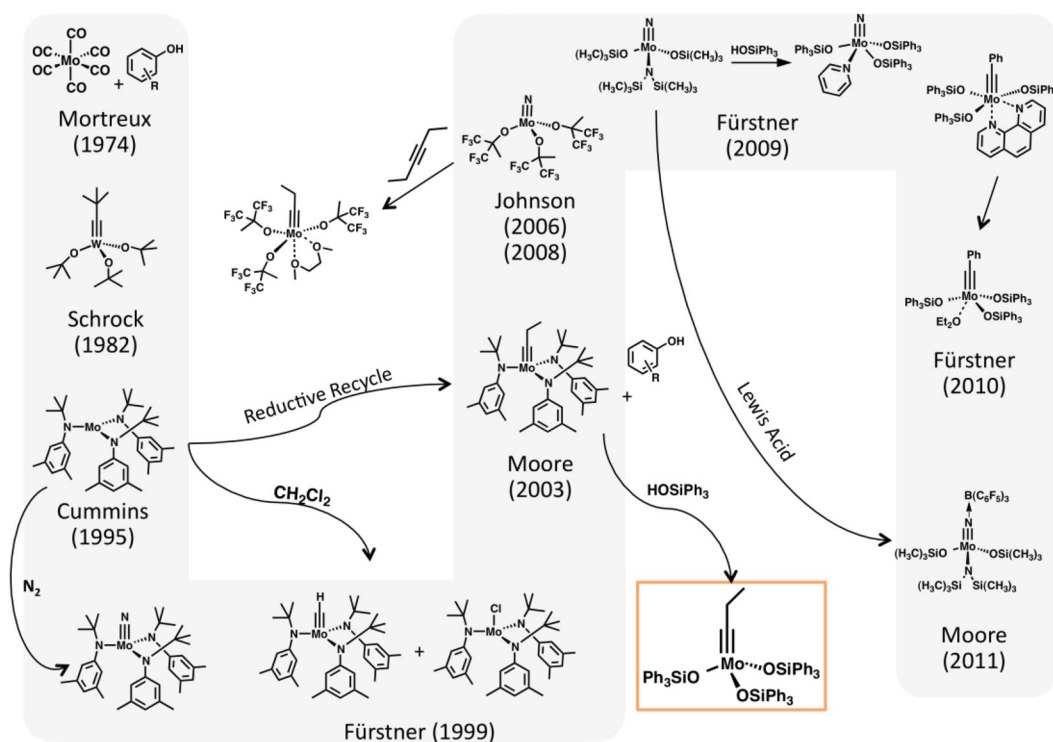
Fig. 7 Evolution of alkyne metathesis catalysts.

ACYCLIC DIYNE METATHESIS MACROCYCLIZATION (ADIMAC)

With active catalysts in hand, alkyne metathesis of acyclic diynes was pursued. As expected, a mixture of oligomers and macrocycles was observed. To drive the equilibrium toward macrocyclic products, leaving groups were installed that could be removed either by volatilization or precipitation (Fig. 8) [50]. These leaving-group byproducts have functionalities such as methyl/ethyl or benzoyl biphenyl to yield 2-butyne/3-hexyne or bis(benzoylbiphenyl)-acetylene byproducts, which could be removed from the reaction mixture by vacuum or precipitation methods, respectively. This process allows the reaction mixture to be entropically driven to macrocycle products. Unfortunately, vacuum-driven methods suffer from scalability owing to catalyst pseudo-poisoning [47,50]. However, when using leaving groups that result in byproducts that precipitate from the reaction, high yields of the most thermodynamically stable macrocycle are obtained even on a multigram scale. The dynamic nature of this process was confirmed by mixing two macrocycles having different monomer units in the presence of the molybdenum alkylidyne catalyst [51]. The resulting mixture was shown to contain hybrid macrocycles as a result of monomer scrambling. In a separate experiment, a *meta*-phenylene–ethynylene polymer was treated with catalyst, which resulted in the formation of short oligomers and macrocycles [52].
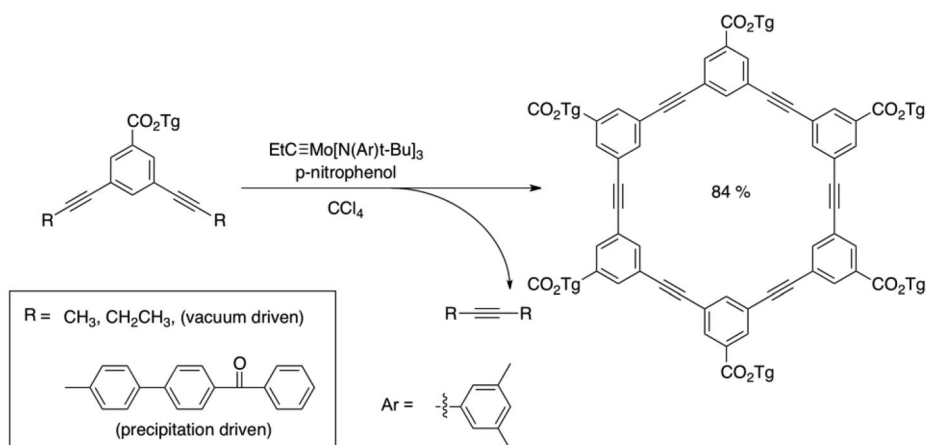
Fig. 8 Acyclic diyne metathesis macrocyclization.

ALKYNE METATHESIS DEPOLYMERIZATION MACROCYCLIZATION (DPMAC)

With the understanding that the ADIMAC is under thermodynamic control and that potential reaction intermediates are in fact polymeric in nature, we envisioned that the starting point for the final macrocyclization step could be initiated from an arylene–ethynylene polymer. The success of this transformation relies on the favorable entropy of such a process, as well as, intra- vs. intermolecular reactions (i.e., the greater tendency of geometrically restricted oligomers to cyclize intramolecularly rather than react intermolecularly).

Macrocyclic depolymerization has the advantage of having no leaving group byproducts because the sp–sp^2 single bond is formed in the polymerization step; therefore, the only necessary transformation is scrambling of the sp–sp (C–C triple) bonds. The logistics of the reaction are more facile than the precipitation or vacuum methods because no filtration of precipitated byproduct nor reduced pressure are needed, respectively. The starting polymer only requires simple monomers, dihalides and dialkynes (i.e., **1** and **2**, respectively), common intermediates in the synthesis of previous ADIMAC monomers. Overall the process is atom economical; from monomer-to-polymer-to-macrocycle, the only loss is HX. In contrast, the stoichiometric byproducts account for greater than 2/3 of the starting mass in some cases of ADIMAC. This is important from the perspective of scalability.

To demonstrate this technique, carbazolylethynylene polymers **3** were synthesized from the requisite dihalides and dialkynes (Fig. 9). The polymers, which were isolated by simple precipitation, had molecular weights (M_n) near 7 kDa and degrees of polymerization near 20, based on calibration using polystyrene standards. Without any further purification, the polymers were subjected to alkyne metathesis conditions to afford good yields of carbazole tetracycles **4** [53].

In another example, we showed for the first time productive metathesis of 1,3-butadiynes by depolymerization of a carbazolylbutadiyne polymer. The resulting products were a mixture of carbazole tetracycles (**4b**, **6a–e**) with varying amounts of alkyne bridging units (Fig. 10). This is the first example of catalytic metathesis activity on a 1,3-butadiyne system.
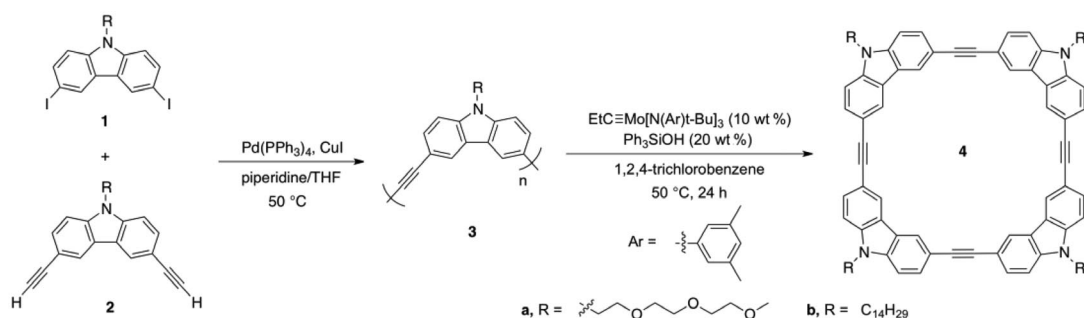
Fig. 9 Synthesis of AEMs from readily available monomers via depolymerization macrocyclization.
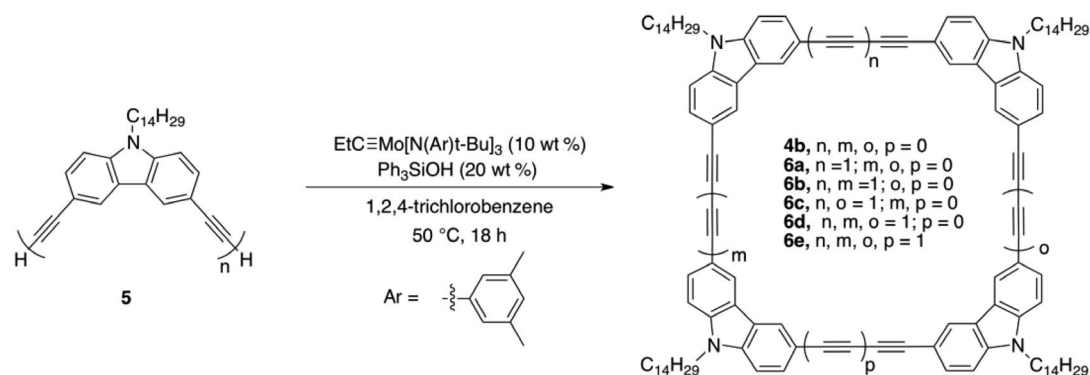

**Fig. 10** Depolymerization of a carbazolylbutadiyne polymer.

SENSORY MATERIALS FOR EXPLOSIVES DETECTION

Macrocycles of type **4** have been found to form fluorescent nanofibril structures. Upon solution-based processing, the molecules become organized with optimal π–π stacking in cooperation with the side-chain association [4]. This favorable π–π stacking facilitates the 1D growth of molecular assembly (Fig. 11). Specifically, sensory material from fluorescent nanofibril films has been developed from an alkoxycarbonyl-substituted carbazole-based tetracycle. Upon exposure to oxidizing agents such as nitroaromatics the fluorescence is quenched [54]. The mechanism of sensing is likely due to interaction of explosive vapors in the nanoporous morphology formed within the film. This results in a disruption of the long-range exciton migration through the nanofibers (Fig. 12).

To gain more insight into this sensing phenomenon, a systematic study was undertaken to analyze the effect of side chain on solid-state packing. The hope was to shed light on the bulk properties as it is directly related to their functional applications. A series of macrocycles containing different side chains were synthesized using the above alkyne metathesis methods [6]. In the case of these single-crystalline X-ray diffraction studies, the results indicate that face-on aromatic π–π interactions predominate in carbazole tetracycles containing *n*-alkyl side chains up to C_9 in length (Fig. 13). In contrast, macrocycles with C_{10} or longer side chains lead to a completely different packing arrangement, involving π-alkyl-π stacking. In another case when triethylene glycol (Tg) side chains were used, there is phase segregation of polar side chains and nonpolar macrocycle framework [55]. What was originally thought of as an opportunity to improve solubility turns out to play a key role in solid-state morphology. The diversity of these materials is clearly evident, and packing ability is highly dependent on their side-chain substituents.
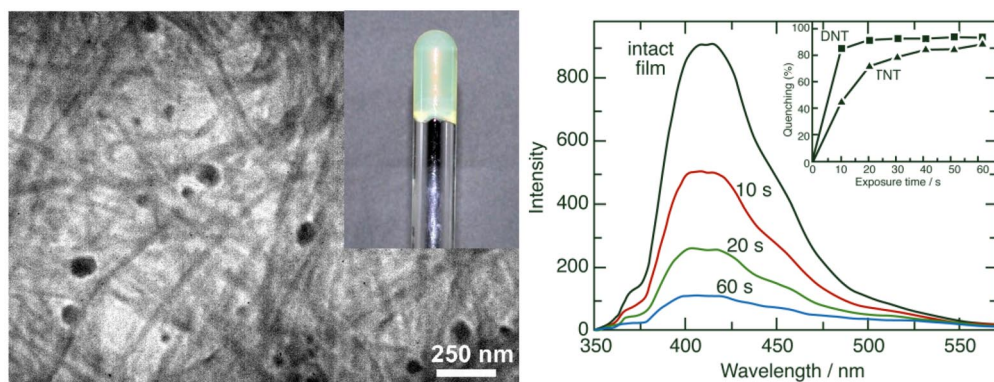
Fig. 11 (a) Nanofiber formation from macrocycle **4** R = $CO_2C(CH_3)_2n$-$C_{12}H_{25}$. (b) Fluorescence spectra of a 90-nm-thick nanofibril film fabricated on glass from the coplanar tetracycle AEM upon exposure to saturated vapor of TNT (5 ppb) at different times. Inset shows a time course of quenching for TNT and DNT. Reproduced from refs. [4,54].
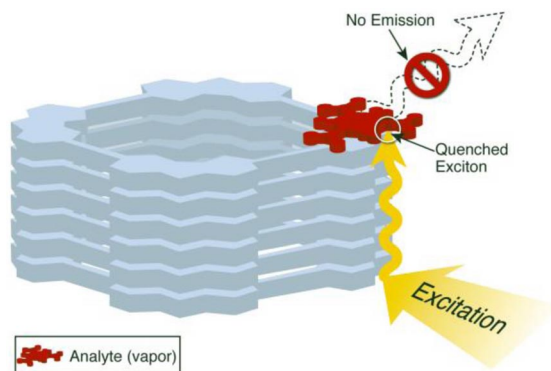
Fig. 12 Proposed mechanism of explosives sensing in carbazole tetracycle-based nanofibers (depicted in light blue).
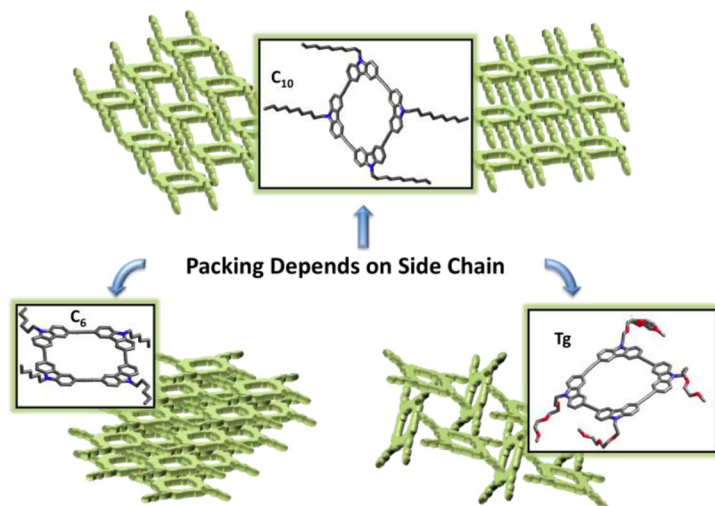
Fig. 13 Illustration of molecular packing of carbazole tetracycles [6].

CONCLUSION

Alkyne metathesis has been shown to be a valuable tool for the synthesis of AEMs. Through the use of DCC it is possible to drive reactions to their thermodynamic products while avoiding the irreversibility of kinetic processes. It has enabled the scalable synthesis of numerous AEMs. These materials show potential as sensory materials for explosives detection. The scope of the depolymerization technique is now being applied to diverse monomer units and copolymers to achieve easy access to a library of AEMs with systematic variation.

ACKNOWLEDGEMENTS

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