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Synthesis of Tribenzo-1,4,7-triazacyclononene “N3-CTV” (Cyclophane family) and Derivatives as Supramolecular Scaffolds

A toolbox of supramolecular derivatives useful for organic- and opto-electronic materials.

Contact

Loyola University Chicago
1032 W. Sheridan Road
Chicago, IL 60660
Angelica Vaca
Interim Research Services
Director (773) 508-2480
avaca1@luc.edu

Inventors

Daniel P. Becker, Ph.D.
Andria M. Panagopoulos, Ph.D.
Marion R. Lutz, Jr.

Field

Fine Chemicals
Qualitative/Quantitative ion analysis
Drug delivery vehicles & diagnostics
Materials science
Catalysis

Technology

Supramolecule scaffold and derivatives that can be solubilized in water and tuned for host-guest specificity.

Key Features

- ▲ Conformationally flexible binding site
- ▲ Binding site modified by peripheral substituents
- ▲ Soluble in aqueous and non-aqueous solvents
- ▲ Attachment to solid support/resin systems

Key Benefits

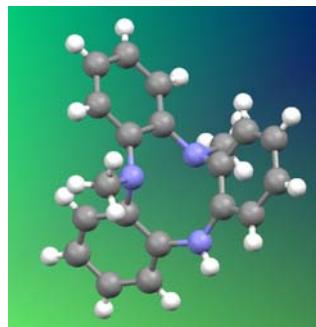
Patent contains broad coverage for composition of matter as well as for synthetic routes for parent compound and numerous derivatives.

Supramolecular compounds

Supramolecular chemistry involves the formation of complex molecular entities that have the capacity to participate in specific molecular recognition of guest molecules and finds commercial application over a wide range of analytical methodologies, materials science and medical diagnostics end uses. This results from their principal characteristic of being able to form non-covalent molecular complexes with a variety of ionic and non-ionic moieties in aqueous and non-aqueous solution. A commonly employed scaffold in supramolecular chemistry is the trimeric crown-shaped molecule cyclotrimeratrylene (CTV) that is useful for its unique functionality and targeted capacity for guest-host recognition and binding stability. CTV has been studied extensively for its capability of binding a number of smaller organic and organometallic guests within its bowl-shaped cleft and has been used as a building block enabling the construction of more complex cryptophanes. The new N3-CTV derivatives employ three nitrogen atoms in the cyclononene core to dramatically enhance the versatility of CTV. General applications of N3-CTV include use as a transition-metal ligand, qualitative and quantitative analysis of metal and non-metallic ions in solution, encapsulation of drugs, environmental analysis, catalysis, magnetic resonance, medical diagnostic imaging and optoelectronic applications.

Synthesis of Tribenzo-1,4,7-triazacyclononene (N3-CTV) and derivatives

The inventors have claimed the composition of matter of the new supramolecular scaffold designated as N3-CTV and its derivatives and have developed a new, patented, synthetic route to the family of compounds. Derivatives may be easily prepared with enhanced water solubility over the commonly-employed CTV (cyclotrimeratrylene). The binding site or cavity, containing 3 nitrogens in a 9-membered ring, can produce pH-dependent binding and conformational properties which can be important in modulating its binding properties. The derivative compounds lend themselves to attachment to solid substrates/resins via alkylation, ester or amide formation.



X-Ray crystal structure of N3-CTV

N3-CTV supramolecule and its derivatives provide enhanced functionality as a family of compounds

The popular supramolecular scaffold CTV (cyclotrimeratrylene) is insoluble in water. Replacement of the three apical methylenes of CTV with nitrogen atoms significantly enhances water solubility and also provides manifold

<p>Stage of Development</p> <ul style="list-style-type: none"> ▲ Basic synthesis route for key compound completed ▲ Substantial work on yield improvement ▲ Synthetic work on derivatives limited ▲ Functionality data for compounds needs development <p>Status</p> <p>Seeking a sponsored research and/or licensing partner</p> <p>Patent Status</p> <p>Provisional Status</p>	<p>functionalization possibilities. Addition of substituents to its three benzene rings can be employed to fine tune binding characteristics, thereby greatly broadening its potential applications. This may also include biomedical applications such as drug delivery. These properties are not routinely found in the class of materials recognized as supramolecules. Further, derivatives of N3-CTV can allow one to produce host-binding sites/cavities that are tailored to specific guest ions or substrate size or polarity. This flexibility, derived from a parent material, is quite rare among this class of materials. Addition of apical substituents can allow for covalent binding to solid support systems and resins.</p> <p>N3-CTV supramolecule derivatives for organic and optoelectronic materials.</p> <p>In related work, the researchers at Loyola University have developed a novel apex-modified cyclotrimeratrylene (CTV) derivative with an attached thiolane-containing lipoic acid linker. This was directly patterned onto gold substrates via dip-pen nanolithography (DPN). The addition of a dithiolane-containing linker to the apex of CTV provides a molecule that can adhere to a gold surface with its bowl-shaped cavity directed away from the surface, thereby providing a surface-bound CTV host that can be used for the directed assembly of guest molecules.</p> <p>Exposure of the CTV microarrays to C60 in toluene resulted in the directed assembly of predesigned, spatially controlled, high-density microarrays of C60 [<i>Nanotechnology</i>, 2011, <i>22</i>, 275611]. With its unique structure, physical, and electronic properties, C60 (buckminsterfullerene) has demonstrated potential for the development of organic electrical and optical devices. It is an excellent electrical conductor at the nanoscale, a good thermal conductor and is one of the strongest materials known, being 100 times stronger than steel but one-sixth the weight. The molecular recognition capabilities of this CTV template toward C60 provides proof-of-concept that supramolecular CTV scaffolds can be directly patterned onto surfaces providing a foundation for the development of organic electronic and optoelectronic materials.</p> <p>By controlling the spatial distribution of organic molecules on a surface by directed molecular binding, these materials will potentially allow for the development of new nano-optical, nanoelectronic, and/or nanoelectrochemical systems (NEMS).</p> <p>Opportunity</p> <p>Loyola University Chicago is seeking a sponsored research and/or licensing partner.</p>
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