(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 April 2005 (21.04.2005)

PCT

(10) International Publication Number
WO 2005/035473 A2

(51) International Patent Classification[7]: C07C 31/13

(21) International Application Number:
PCT/US2004/033295

(22) International Filing Date: 8 October 2004 (08.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

10/683,472	8 October 2003 (08.10.2003)	US
60/578,781	10 June 2004 (10.06.2004)	US

(71) Applicant *(for all designated States except US)*: **UNIVERSITY OF IOWA RESEARCH FOUNDATION** [US/US]; Technology Innovation Center, Suite #214, 100 Oakdale Campus, Iowa City, IA 52242 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **MACGILLIVRAY, Leonard, R.** [CA/US]; 103 Oberlin Street, Iowa City, IA 52242 (US).

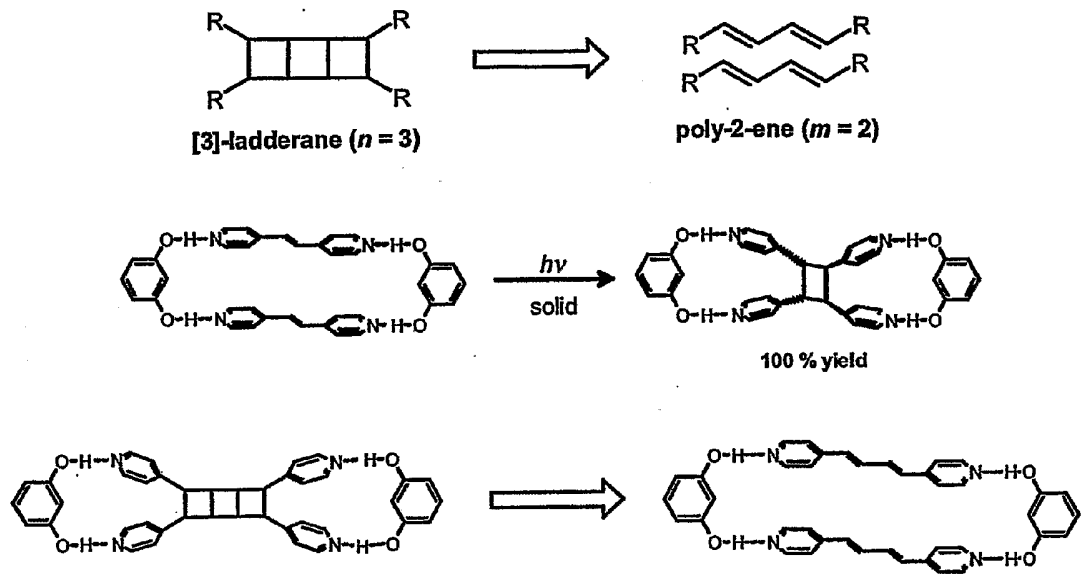
(74) Agents: **STEFFEY, Charles, E.** et al.; Schwegman, Lundberg, Woessner & Kluth, P.A., P.O. Box 2938, Minneapolis, MN 55402 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHOD FOR PREPARING LADDERANES



(57) Abstract: Ditopic molecules in the form of linear reaction templates are used to construct ladder-like hydrocarbons known as [*n*]-ladderanes (*n* = 3,5). The templates assemble and position reactant molecules in the solid state for [2+2] photodimerization. The products, which are based on recently identified naturally occurring frameworks, form stereospecifically, in gram quantities, and in quantitative yield. The control of reactivity achieved using linear templates provides a basis for the development of molecular tools, termed assemblers, that could be used to manufacture, with atomic-level precision, a wide range of products (*e.g.* molecular nanostructures) with unique properties.

WO 2005/035473 A2

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Method For Preparing Ladderanes

Priority of Invention

This application claims priority to United States Patent Application Number 10/683,472, filed 08 October 2003, and to United States Provisional Application Number 60/578,781, filed 10 June 2004.

Government Funding

The invention described herein was made with government support under CAREER Award, DMR-0133138, L.R.M. awarded by the National Science Foundation. The United States Government has certain rights in the invention.

Background of the Invention

Tools that enable picking and positioning of individual atoms and molecules for chemical reaction could have widespread applications in chemical synthesis and materials science (*e.g.* molecular nanotechnology). Such tools, or assemblers, could combine the chemical diversity of synthetic organic chemistry (*e.g.* functional groups), which is chiefly realized at the atomic level, with the ability of human engineers to fabricate objects using mechanical devices (*e.g.* robotic welders), which is chiefly realized at the macroscopic level, for the development of a universal molecular manufacturing scheme. See K. E. Drexler, *Proc. Natl. Acad. Sci. USA* **78**, 5275 (1981); K. E. Drexler, *Sci. Amer.* **285**, 74 (2001); G. M. Whitesides, *Sci. Amer.* **285**, 78 (2001); K. C. Nicolau, D. Vourloumis, N. Winssinger, P. S. Baran, *Angew. Chem. Int. Ed. Engl.* **39**, 44 (2000); S. Hecht, *Angew. Chem. Int. Ed. Engl.* **42**, 24 (2003); and K. E. Drexler, *Nanosystems. Molecular Machinery, Manufacturing and* Computation; Wiley-Interscience: New York (1992).

Owing to the superior stereo- and regiocontrol of chemical synthesis offered by assemblers, molecular manufacturing *via* molecular assemblers could provide efficient, low-cost access to molecules, and materials, with unique

molecular (*e.g.* catalytic) and bulk physical (*e.g.* mechanical) properties. Despite this realization, however, a synthetic system that enables such general 'pick-and-place' control of atoms and molecules has not been realized.

Top-down approaches, which have employed surface microscopy tips (*e.g.* STM) to position reactive sites mechanically, have had difficulties achieving atomic-level dexterity and high throughput for grabbing individual molecules and manufacturing appreciable amounts of product, respectively. See S. Hecht, *Angew. Chem. Int. Ed. Engl.* **42**, 24 (2003); V. Balzani, A. Credi, M. Venturi, *Chem. Eur. J.* **8**, 5525 (2002); D. M. Eigler and E. K. Schweizer, *Nature* **344**, 594 (1990); and S. -W. Hla, G. Meyer, K. -H. Rieder, *ChemPhysChem.* **2**, 361 (2001).

Bottom-up approaches, which have employed molecules to recognize and assemble reactive sites chemically, have had difficulties contending with structure effects of entropy and solvent of the liquid phase, which can hinder reactants molecules from achieving the necessary order for reaction. See V. Balzani, A. Credi, M. Venturi, *Chem. Eur. J.* **8**, 5525 (2002); J. -M. Lehn, *Supramolecular Chemistry*; Wiley-VCH: Weinheim (1995); T. R. Kelly, C. Zhao, G. J. Bridger, *J. Am. Chem. Soc.* **111**, 3744 (1989); and D. M. Bassani, V. Darcos, S. Mahony, J. -P. Desvergne, *J. Am. Chem. Soc.* **122**, 8795 (2000).

A [*n*]-ladderane is a molecule that consists of *n* edge-sharing cyclobutane rings (where $n \geq 2$) that define a molecular equivalent of a macroscopic ladder. See H. Hopf, *Angew. Chem.* **2003**, *115*, 2928-2931; and *Angew. Chem., Int. Ed.* **2003**, *42*, 2822-2825. Ladderanes are considered promising building blocks in optoelectronics and, very recently, have been identified in biological systems (where: $n = 3$ and 5), in the form of ladderane lipids, being integral components in the microbiological conversion of ammonium and nitrite to dinitrogen gas. See W. Li, M.A. Fox, *J. Am. Chem. Soc.* **1996**, *118*, 11752-11758; J.S.S. Damste, et al., *Nature* **2002**, *419*, 708-712; E.F. DeLong *Nature* **2002**, *419*, 676-677; and M.M.M. Kuypers, et al., *Nature* **2003**, *422*, 608-611.

In the simplest case, a *cis*-fused [*n*]-ladderane ($n = 3, 5, 7\ldots$) can be constructed by photochemical dimerization of two all-*trans*-poly-*m*-enes ($m = 2, 3, 4\ldots$). Despite the apparent simplicity of this intermolecular process, however,

such a transformation generally fails. This can be attributed to the lack of a method that overcomes the energetic cost, due to solvent and entropy effects, of organizing two polyene molecules in a suitable geometry in the liquid phase for photoreaction, although a covalent linker that holds two polyene chains in a parallel orientation for a high-yield, intramolecular photoaddition to give a [*n*]-ladderane (where: $n = 3$ and 5) has been reported. See H. Hopf, *Angew. Chem.* **2003**, *115*, 2928-2931; and *Angew. Chem., Int. Ed.* **2003**, *42*, 2822-2825; D.H. Williams, E. et al., *Chem. Commun.* **2003**, 1973-1976; M. Rekharsky, et al., *J. Am. Chem. Soc.* **2002**, *124*, 14959-14967; and H. Hopf, et al., *Angew. Chem.* **1995**, *107*, 742-744; *Angew. Int. Ed. Engl.* **1995**, *34*, 685-687.

Unfortunately, the study of these unique molecules and their properties has been hampered because existing methods for preparing ladderanes typically provide low yields and/or mixtures of products that are difficult to separate. Accordingly, there is currently a need for improved methods and intermediates that can be used to prepare ladderanes. In particular, there is a need for methods that provide improved yields of ladderanes and for methods that provide pure ladderane products as opposed to mixtures of compounds.

Summary of the Invention

The invention provides template controlled methods for preparing ladderanes. The methods of the invention allow ladderanes of high purity to be prepared in useful quantities (e.g. gram quantities). The invention also provides intermediates useful for preparing ladderanes according to the methods of the invention.

Accordingly, the invention provides a method for preparing a ladderane comprising, associating polyene molecules with a template such that the polyene molecules are properly aligned to allow for formation of the ladderane, and reacting the polyene molecules under conditions suitable to provide the ladderane.

The invention also provides a kit comprising packaging material and at least about 0.5 grams of a ladderane. In one embodiment the kit comprises at

least about 1 gram of a ladderane. In another embodiment the kit comprises at least about 2 grams or about 5 grams of a ladderane.

The invention also provides a composition comprising polyene molecules associated with a template such that the polyene molecules are properly aligned to allow for formation of a ladderane. For example, the composition can be a solid (e.g. a crystalline solid).

The invention also provides a ladderane prepared by a method of the invention, as well as a composition comprising at least about 0.5 grams of a ladderane, which composition is prepared according to a method of the invention.

The invention also provides a method for preparing a cyclobutane ring comprising, associating two or more alkene molecules with a template such that the alkene molecules are properly aligned to allow for formation of the cyclobutane ring, and reacting the alkene molecules under conditions suitable to provide the cyclobutane ring.

The invention provides a composition (e.g. a solid or a crystalline solid) comprising alkene molecules associated with a template such that the alkene molecules are properly aligned to allow for formation of a cyclobutane ring.

Brief Description of the Figures

Figure 1. Perspectives of the X-ray crystal structures of the solid-state assemblies: (a) ORTEP view of the assembly 2(5-OMe-res)·2(poly-2-ene), (b) ORTEP view of the assembly 2(5-OMeres) 2(poly-3-ene), (c) space-filling view of the packing of 2(5-OMe-res)·2(poly-2-ene), and (d) space-filling view of the packing of 2(5-OMe-res)·2(poly-3-ene). Selected interatomic distances (Å) and angles (o): O(1)···N(1) 2.761(3), O(2)···N(2)i 2.736(3), O(1)-H(1O)···N(1) 175.6(1), O(2)-H(2O)···N(2)i 172.1(1); (b) O(1)···N(1) 2.792(5), O(2)···N(3) 2.777(6), O(4)···N(2)I 2.782(6), O(5)···N(4) 2.756(6), O(1)-H(1O)···N(1) 173.6(3), O(2)-H(2O)···N(3) 173.4(3), O(4)- H(4O)···N(2) 176.6(3), O(5)-H(5O)···N(4) 175.1(3). Symmetry operator i: $-x + 1, -y, -z + 2$. It is noted that the asymmetric units of 2(5-OMe-res)·2(poly-2-ene) and 2(5-OMe-res)·2(poly-3-

ene) are occupied by two full assemblies, which are virtually identical, and one half assembly, which sits around a crystallographic center of inversion, respectively.

Figure 2. ^{1}H NMR spectra of the solid-state assemblies before and after photoreaction: (a) 2(5-OMe-res)·2(poly-2-ene) (before), (b) 2(5-OMe-res)·2(poly-2-ene) (after), (c) 2(5-OMeres) 2(poly-3-ene) (before), and (d) 2(5-OMe-res)·2(poly-3-ene) (after). Key: filled circle = olefin, cross = cyclobutane.

Figure 3. ORTEP perspectives of the ladderanes: (a) [3]-ladderane and (b) [5]-ladderane. Symmetry operator ii: -x+2, -y, -z+1. It is noted that the asymmetric units of the [3]-ladderane and [5]-ladderane are occupied by two full ladderanes, which are virtually identical, and one half ladderane, which sits around a crystallographic center of inversion, and an included benzene, respectively.

Figure 4. Illustrates the structure of [3]-ladderane and [5]-ladderane.

Figure 5. Illustrates the synthesis and retro-synthesis of [3]-ladderane and [5]-ladderane using resorcinol templates.

Figure 6. X-ray crystal structure of complex **1** prepared in Example 5: ball-and-stick views of (a) tetranuclear assembly and (b) hydrogen-bonded array. Color scheme: Zn = yellow, Cl = gray; C = blue; O = red; N = green; C = blue; H = black.

Figure 7. Overlay views of complex **1** (blue) and complex **2** formed in Example 6 (green): (a) tetranuclear assembly and (b) hydrogen-bonded array.

Figure 8. Spectra of complex **1** and complex **2**: (a) emission spectra (290 nm excitation) (inset: microscope images of fluorescence of single crystals of complex **1** and complex **2** at 40X mganifcation) and (b) confocal fluorescencfe microscopy data comparing ratios of intensitites at 510 nm and 480 nm (blue = complex **1**; green = complex **2**). Each ratio image taken for a 10 μm x 30 μm cross section ~ 12 μm from crystal surface. Cross section is ~ 1 μm thick. Spatial resolutions: 50 nm in xy-plane and ~ 1 μm along z-axis.

Figure 9. Shows a perspective view of the crystal structure of complex **3** prepared in Example 8.

Figure 10. Shows a perspective view of the crystal structure of complex **4** prepared in Example 8.

Detailed Description

That a [*n*]-ladderane may serve a target of a linear template synthesis is realized by a retrosynthetic analysis of the ladderane framework (Figure 5). A single-step construction of a [*n*]-ladderane, which is composed of *n* linearly fused cyclobutane units, can be achieved by cross-linking two identical all-*trans*-poly-*m*-enes (*m* = 2, 3, 4....) *via* intermolecular [2+2] photodimerizations. Such a transformation has not been reported. This may be attributed to the lack of a suitable method to organize two polyenes, in either solution or the solid state, in a position favorable for ladderane formation. See Mehta, M. B. et al., *J. Org. Chem.* **59**, 6131 (1994); R. W. Warrener, et al., *J. Am. Chem. Soc.* **116**, 3645 (1994); W. Li and M. A. Fox, *J. Am. Chem. Soc.* **118**, 11752 (1996); and H. Hopf, H. Greiving, P. G. Jones, P. Bubenitschek, *Angew. Chem. Int. Ed. Engl.* **34**, 685 (1995).

Templates

Template molecules (e.g. ditopic molecules in the form of linear reaction templates) can be used to construct [*n*]-ladderanes (see Figure 4). For related discussions see S. Anderson, H. L. Anderson, In *Templated Organic Synthesis*; F. Diederich, P. S. Stang, Eds.: Wiley-VCH: New York, pp. 1-38 (2000); G. R. Desiraju, *Science* **278**, 404 (1997); J. L. Atwood, L. J. Barbour, A. Jerga, *Science* **296**, 2367 (2002); G. Mehta, M. B. Viswanath, A. C. Kunwar, *J. Org. Chem.* **59**, 6131 (1994); and R. W. Warrener, G. Abbenante, C. H. L. Kennard, *J. Am. Chem. Soc.* **116**, 3645 (1994). For example, the linear templates can operate by positioning the two poly-*m*-enes (e.g. *m* = 2 or 3), *via* hydrogen bonds for ultraviolet- (UV) induced [2+2] cycloaddition reactions. See G. M. J. Schmidt, *Pure Appl. Chem.* **27**, 647 (1971). By using the organized, solvent-free environment of the solid state as the medium for reaction, the effects of entropy and solvent that have made intermolecular interactions of the bottom-up approach difficult to control in the liquid phase can be circumvented. See T. R.

Kelly, C. Zhao, G. J. Bridger, *J. Am. Chem. Soc.* **111**, 3744 (1989); and D. M. Bassani, V. Darcos, S. Mahony, J. -P. Desvergne, *J. Am. Chem. Soc.* **122**, 8795 (2000).

The template can be any inorganic molecule (e.g. a transition metal complex), organic molecule (e.g. a polyol, a poly-ether, or a polyamine), solid support, or assembly of inorganic and/or organic molecules or ions held together by non-covalent bonds (e.g. a coordination complex) that is capable of associating with the polyenes or alkenes such that the double bonds are properly aligned to allow for formation of cyclobutane rings (e.g. a ladderane). In one embodiment the template comprises an aromatic ring. In another embodiment the template comprises an aromatic ring that is 1,3 substituted with groups capable of associating with the polyene molecules (e.g. a 1,3-substituted phenyl ring or a 1,3-substituted naphthyl ring). In another embodiment the template comprises comprises a 1,3-dihydroxy substituted phenyl ring or a 1,3-dihydroxy substituted naphthyl ring

In a preferred embodiment the template is resorcinol (1,3-dihydroxybenzene) or a substituted resorcinol. For example, the template can be resorcinol substituted with one or more (e.g. 1, 2, or 3) (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkyl, (C_1-C_6)alkanoyl, (C_1-C_6)alkanoyloxy, (C_1-C_6)alkoxycarbonyl, cyano, halo, hydroxy, nitro, carboxy, trifluoromethyl, trifluoromethoxy, methylenedioxy, aryl, heteroaryl, aryl(C_1-C_6)alkyl, heteroaryl(C_1-C_6)alkyl, aryl(C_1-C_6)alkanoyl, heteroaryl(C_1-C_6)alkanoyl, or NRR, wherein each R is independently (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkyl, (C_1-C_6)alkanoyl, (C_1-C_6)alkanoyloxy, (C_1-C_6)alkoxycarbonyl, and wherein each aryl or heteroaryl is optionally substituted with one or more (e.g. 1, 2, 3, or 4) (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkyl, (C_1-C_6)alkanoyl, (C_1-C_6)alkanoyloxy, (C_1-C_6)alkoxycarbonyl, cyano, halo, nitro, carboxy, trifluoromethyl, trifluoromethoxy, methylenedioxy, or NRR.

In another embodiment, the template can comprise an association of metal ions. Certain metal ions (e.g. metal cations) are known to be attracted to each other by forces that are weaker than most covalent or ionic bonds but

stronger than van der Waals bonds. See for example P. Pyykko, *Chem Rev.*, **1997**, *97*, 597-636. Such metal ion assemblies can operate as templates that position polyene or alkene molecules for cycloaddition reactions. In one specific embodiment of the invention, the template comprises an assembly of two or more metal cations. In another specific embodiment the template comprises an assembly of two or more transition metal cations. In another specific embodiment the template comprises an assembly of two or more silver or gold ions. It will be appreciated that such poly metal cation assemblies will also comprise suitable counter ions. The nature of the counter ions is not critical provided the resulting assembly is capable of orienting the alkene molecules for cycloaddition reaction. For example, the counter ions may be carboxylates, (e.g. acetates and triflates), sulfonates, or halides, or mixtures thereof. The polyene containing molecules can associate with the metal ions of the metal cation assemblies by ionic bonds, or other non-covalent bonds (e.g. dipole-dipole interactions, hydrogen bonds, van der Waals interactions, or coordination)

The following definitions are used, unless otherwise described: halo is fluoro, chloro, bromo, or iodo. Alkyl, alkoxy, alkenyl, alkynyl, etc. denote both straight and branched groups; but reference to an individual radical such as "propyl" embraces only the straight chain radical, a branched chain isomer such as "isopropyl" being specifically referred to. Aryl denotes a phenyl radical or an ortho-fused bicyclic carbocyclic radical having about nine to ten ring atoms in which at least one ring is aromatic. Heteroaryl encompasses a radical attached via a ring carbon of a monocyclic aromatic ring containing five or six ring atoms consisting of carbon and one to four heteroatoms each selected from the group consisting of non-peroxide oxygen, sulfur, and N(X) wherein X is absent or is H, O, $(C_1$-$C_4)$alkyl, phenyl or benzyl, as well as a radical of an ortho-fused bicyclic heterocycle of about eight to ten ring atoms derived therefrom, particularly a benz-derivative or one derived by fusing a propylene, trimethylene, or tetramethylene diradical thereto. The term "alkene" includes compounds having one or more carbon-carbon double bonds. In one specific embodiment of the invention, "alkene" is a compound having a chain of atoms that includes one carbon-carbon double bond.

Specific and preferred values listed below for radicals, substituents, and ranges, are for illustration only; they do not exclude other defined values or other values within defined ranges for the radicals and substituents

Specifically, (C_1-C_6)alkyl can be methyl, ethyl, propyl, isopropyl, butyl, iso-butyl, sec-butyl, pentyl, 3-pentyl, or hexyl; (C_3-C_6)cycloalkyl can be cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; (C_1-C_6)alkoxy can be methoxy, ethoxy, propoxy, isopropoxy, butoxy, iso-butoxy, sec-butoxy, pentoxy, 3-pentoxy, or hexyloxy; (C_2-C_6)alkenyl can be vinyl, allyl, 1-propenyl, 2-propenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1,-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1- hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, or 5-hexenyl; (C_2-C_6)alkynyl can be ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, 1-pentynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 1- hexynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, or 5-hexynyl; (C_1-C_6)alkanoyl can be acetyl, propanoyl or butanoyl; (C_1-C_6)alkoxycarbonyl can be methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, pentoxycarbonyl, or hexyloxycarbonyl; (C_2-C_6)alkanoyloxy can be acetoxy, propanoyloxy, butanoyloxy, isobutanoyloxy, pentanoyloxy, or hexanoyloxy; aryl can be phenyl, indenyl, or naphthyl; and heteroaryl can be furyl, imidazolyl, triazolyl, triazinyl, oxazoyl, isoxazoyl, thiazolyl, isothiazoyl, pyrazolyl, pyrrolyl, pyrazinyl, tetrazolyl, pyridyl, (or its N-oxide), thienyl, pyrimidinyl (or its N-oxide), indolyl, isoquinolyl (or its N-oxide) or quinolyl (or its N-oxide).

A specific resorcinol that can be used as a template according to the methods of the invention is resorcinol, orcinol [5-methylresorcinol], 4-ethylresorcinol, 4-hexylresorcinol, olivetol [5-pentylresorcinol], 4-cyclohexylresorcinol, 4-benzylresorcinol, 4-chlororesorcinol, 4-bromoresorcinol, 4,6-dichlororesorcinol, 4,6-dibromoresorcinol, 4,6-di-*tert*-butylresorcinol, 4,6-di-(1,1-diphenylethyl)resorcinol, 3,5-dihydroxybenzaldehyde, 5-cyanoresorcinol, 5-acetylresorcinol, 5-methoxyresorcinol, 5-carboxymethylresorcinol, 1,3-dihydroxynaphthalene, 4,6-dibromo-5-carboxymethylresorcinol, 2,4,6-trihydroxybenzaldehyde (phloroglucinaldehyde), methyl 2,4-6-trihydroxyphenyl ketone, ethyl 2,4-6-trihydroxyphenyl ketone, propyl 2,4-6-trihydroxyphenyl ketone, butyl 2,4-6-

trihydroxyphenyl ketone, pentyl 2,4-6-trihydroxyphenyl ketone, hexyl 2,4-6-trihydroxyphenyl ketone, or phenyl 2,4-6-trihydroxyphenyl ketone.

Association Between Templates and Polyenes and Alkenes

According to the methods of the invention, the polyene molecules or alkenes can be "associated" to the template molecules by any suitable attractive force, such as, for example, ionic bonds, or other non-covalent bonds (e.g. dipole-dipole interactions, hydrogen bonds, van der Waals interactions, or coordination). The term "associated" does not include covalent bonding between the polyene molecules or alkene molecules and the template.

Polyenes of any length can be used in the methods of the invention, provided they are capable of forming ladderanes. In one embodiment, the polyene molecules comprise about 3-20 double bonds. In another embodiment, the polyene molecules comprises 3-10 double bonds. In yet another embodiment, the polyene molecules comprises 3-6 double bonds. In yet another embodiment, the polyene molecules comprise only *trans* double bonds. In yet another embodiment, the polyene molecules comprise only *cis* double bonds. In yet another embodiment, the polyene molecules comprise a mixture of *cis* and *trans* double bonds. The polyenes or alkenes can be branched or unbranched and they can include other functionality such as rings, heteroatoms and substituents, provided the other functionality does not interfere with the association of the polyenes or alkenes with the templates or with the reaction to form cyclobutane rings. Typically the polyene or alkene molecules comprises from about 6 to about 40 carbon atoms. In one embodiment, the polyene or alkene molecules comprises from about 6 to about 30 carbon atoms. In another embodiment the polyene or alkene molecules comprises from about 6 to about 20 carbon atoms.

In one embodiment, each polyene or alkene is terminally substituted with a group that is capable of associating with the template. For example, each group can independently comprises an amino nitrogen, a thiol, an alcohol, or a carboxylic acid.

In one embodiment, each polyene or alkene is terminally substituted with a pyridine ring (e.g. a 4-pyridine ring).

Typically, according to the methods of the invention, the polyene or alkene double bonds will be aligned within about 3.2 to 4.5 Angstroms of each other in order to facilitate formation of the cyclobutane ring(s). In one particular embodiment, the polyene or alkene double bonds are aligned within less than about 4.2 Angstroms of each other.

Reaction

The reaction of the polyenes or alkenes can be carried out under any conditions that are suitable to allow for the formation of the cyclobutane rings. Typically, the reaction is carried out in a solid state (e.g. a crystalline state). The reaction can be initiated using any suitable means. For example, the reaction can conveniently be initiated with an energy source, such as heat or light.

Specific Embodiments

The following specific embodiments are for illustration only; they are not limiting and they do not exclude other embodiments described herein.

In one specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) associating two polyene molecules with a template, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

In another specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) associating two polyene molecules with a template comprising two hydroxyl groups, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

In another specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) associating two polyene molecules that each comprise an amino nitrogen with a template comprising two hydroxyl groups, 2) forming a solid comprising the template and the polyene molecules,

wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

In another specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) associating two polyene molecules that each comprise a pyridine ring with a template comprising a 1,3-dihydroxy substituted phenyl ring, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

In another specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) combining polyene molecules that comprise a pyridine ring with template molecules that comprise a 1,3-dihydroxy substituted phenyl ring in a solvent, 2) allowing a crystalline solid that comprises the template molecules and the polyene molecules to form, wherein the polyene molecules are properly aligned within the crystalline solid to allow for formation of the ladderane, and 3) irradiating the solid under conditions suitable to provide the ladderane.

In another specific embodiment, the invention provides a method for preparing a ladderane comprising, 1) associating two or more polyene molecules with a template comprising an assembly of metal ions (e.g. silver ions), 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

In another specific embodiment, the ladderane is an [n]-3, [n]-4, [n]-5, [n]-6, [n]-7, [n]-8, [n]-9, [n]-10, [n]-11, or [n]-12 ladderane.

In another specific embodiment, the polyene is 1,4-bis(4-pyridyl)-1,3-butadiene or 1,6-bis(4-pyridyl)-1,3,5-hexatriene.

In another specific embodiment, the polyene comprises all *cis* double bonds.

In another specific embodiment, the polyene comprises all *trans* double bonds.

In another specific embodiment, the polyene comprises a mixture of *cis* and *trans* double bonds.

In another specific embodiment, the template is 1,3-dihydroxybenzene.

In another specific embodiment, the template comprises an assembly of metal ions (e.g. wherein two or more metal ions are attracted to each other by forces that are weaker than a covalent or ionic bond but stronger than a van der Waals bond).

In another specific embodiment, the template comprises an assembly of two or more metal cations.

In another specific embodiment, the template comprises an assembly of two or more transition metal cations.

In another specific embodiment, the template comprises an assembly of two or more gold ions.

In another specific embodiment, the template comprises an assembly of two or more silver ions.

Example 6 illustrates the formation of a cyclobutane ring by the cyclization of two alkenes that are associated with an organo-metallic template that comprises two metal atoms. Example 8 illustrates the formation of a cyclobutane ring from two alkenes that are associated with a metal cation assembly. Although the products of Examples 6 and 8 are cyclobutanes, these Examples illustrate the use of additional templates to properly align double bond containing molecules (alkenes or polyenes) for cycloaddition reactions.

Additionally, Examples 6 and 8 illustrate the preparation of novel cyclobutane compounds as well as novel methods and novel intermediates useful for preparing such compounds. Such compounds, methods, and intermediates are also embodiments of the invention. Accordingly, the invention also provides a method for preparing a cyclobutane ring comprising, associating (as described herein) two or more alkene molecules with a template (as described herein) such that the alkene molecules are properly aligned to allow for formation of the

cyclobutane ring, and reacting the alkene molecules under conditions suitable to provide the cyclobutane ring.

In another specific embodiment, the invention provides a method for preparing a cyclobutane comprising, 1) associating two or more alkene molecules with a template, 2) forming a solid comprising the template and the alkene molecules, wherein the alkene molecules are properly aligned within the solid to allow for formation of the cyclobutane, and 3) reacting the alkene molecules under conditions suitable to provide the cyclobutane.

In another specific embodiment, the invention provides a method for preparing a cyclobutane comprising, 1) associating two or more alkene molecules with one or more organo-metallic templates that each comprise two metal atoms, 2) forming a solid comprising the template(s) and the alkene molecules, wherein the alkene molecules are properly aligned within the solid to allow for formation of the cyclobutane, and 3) reacting the alkene molecules under conditions suitable to provide the cyclobutane.

In another specific embodiment, the invention provides a method for preparing a cyclobutane comprising, 1) associating two or more alkene molecules with a template that comprises an assembly of metal ions, 2) forming a solid comprising the template(s) and the alkene molecules, wherein the alkene molecules are properly aligned within the solid to allow for formation of the cyclobutane, and 3) reacting the alkene molecules under conditions suitable to provide the cyclobutane.

In another specific embodiment, the invention provides a composition (e.g. a solid or a crystalline solid) comprising alkene molecules associated with a template such that the alkene molecules are properly aligned to allow for formation of a cyclobutane ring.

In another specific embodiment, the invention provides a solid prepared by associating two or more alkene molecules with a template such that the alkene molecules are properly aligned in the solid to allow for formation of a cyclobutane.

In another specific embodiment, the invention provides complex **1**, **2**, **3**, or **4** as described hereinbelow.

Examples

The invention will now be illustrated by the following non-limiting Examples.

Ladderanes were prepared by co-crystallization of a template molecule (e.g. resorcinol), with an all-*trans*-bis(4-pyridyl)poly-*m*-ene (4-pyr-poly-*m*-ene) to produce a four-component molecular assembly, 2(resorcinol)·2(4-pyr-poly-*m*-ene) (Figure 5), wherein each resorcinol positioned, by way of two O-H···N hydrogen bonds, two polyenes for [2+2] photoreaction. The two polyenes were positioned by the templates such that the carboncarbon double (C=C) bonds of the olefins were parallel and separated by less than about 4.2 Å, a position suitable for reaction. See G. M. J. Schmidt, *Pure Appl. Chem.* **27**, 647 (1971). UV-irradiation of the solid produced the [*n*]-ladderane, the C=C bonds reacting to form the fused cyclobutane framework.

In a typical experiment, one equivalent of the template 5-methoxyresorcinol (5-OMe-res), was co-crystallized with an equimolar amount of a a poly-*m*-ene (*m* = 2 or 3), from ethanol. Single-crystals of 2(5-OMe-res)·2(4-pyr-poly-*m*-ene) suitable for X-ray analysis formed within the ethanolic solution within a period of approximately one day.

Single-crystal X-ray structure analyses of 2(5-OMe-res)·2(poly-2-ene) and 2(5-OMeres) 2(poly-3-ene) revealed that the templates organized each polyene in a position for intermolecular [2+2] photodimerization favorable for ladderane formation. In each case, the templates and the polyenes formed four-component molecular assemblies held together by four O-H···N hydrogen bonds (Figure 1) wherein the templates oriented the polyenes in a parallel arrangement, the average separation between the stacked C=C bonds ranging from 3.78-3.82 Å in 2(5-OMe-res)·2(poly-2-ene) and from 3.69-3.97 Å in 2(5-OMeres) 2(poly-3-ene). Nearest-neighbor assemblies of each solid packed antiparallel such that the olefins of the hydrogen-bonded assemblies are the sole C=C bonds organized to undergo reaction.

To evaluate the reactivity of the solid-state assemblies, powdered crystalline samples of 2(5-OMe-res)·2(poly-2-ene) and 2(5-OMe-res)·2(poly-3-

ene) were subjected to UV-irradiation (broadband Hg lamp). As evidenced by 1H NMR spectroscopy (solvent: DMSO-*d6*), the [3]- and [5]-ladderanes formed stereospecifically and in quantitative yield (Figure 2). Each ladderane is characterized by the complete disappearance of the olefinic protons and the emergence of cyclobutane protons in the 3.0 - 4.3 ppm range. The three fused cyclobutane rings of the [3]-ladderane produced two broad signals at 3.49 and 4.30 ppm (ratio: 1:1), while the five fused cyclobutane rings of the [5]-ladderane produced three broad signals at 3.12, 3.29, and 4.26 ppm (ratio: 1:1:1). To confirm the structures of the ladderanes, the reactions were repeated in gram quantities. The templates were then separated from each product *via* solvent extraction. Single crystals of each product were grown, during a period of approximately three days, by way of slow solvent evaporation from benzene.

Single-crystal X-ray structure analyses confirm the structures of the ladderanes (Figure 3). Each product consists of an *exo,exo*-fused cyclobutane framework with ends functionalized with four 4-pyridyl groups. The C-C bond distances and C-C-C bond angles of the cyclobutane units compare well to both calculated and experimentally related structures. See M. A. Miller and J. M. Schulman, *J. Mol. Struct.* **163**, 133 (1988).

The ladderanes appear to form within 2(5-OMe-res)·2(poly-2-ene) and 2(5-OMeres) ·2(poly-3-ene) by way of stepwise [2+2] photodimerizations. 1H NMR spectra obtained 24 and 48 hours into each reaction reveal that lower-order ladderanes form during the generation of each final product. Thus, a product consistent with a single cycloaddition (*i.e.* '[1]-ladderane') precedes the [3]-ladderane while products consistent with single and double cycloadditions (*i.e.* [3]-ladderane) precede the [5]-ladderane. Such stepwise reactions may occur either randomly or by way of a 'zipper' process in each solid.

Thus, templates can be used to construct [*n*]-ladderanes ($n = 3$ or 5). The templates operate (e.g. in the solid state) by positioning (e.g. by way of hydrogen bonds) polyenes suitable for [2+2] photodimerizations. The ladderanes can be formed in gram quantities and quantitative yield.

All crystal data were measured on a Nonius Kappa CCD single-crystal X-ray diffractometer at liquid nitrogen temperature. After anisotropic refinement of

all non-hydrogen atoms, aromatic, methine, and hydroxyl hydrogen atoms were placed in idealized positions and allowed to ride on the atom to which they are attached. All crystallographic calculations were conducted using SHELXL-97 locally implemented on an IBM compatible pentium-based PC (G.M. Sheldrick, SHELXL-97, Program for Refinement of Crystal Structure, University of Göttingen, Göttingen, Germany, **1997**.).

Example 1 Preparation of 2(5-OMe-res)·2(poly-2-ene)

4-Pyr-poly-2-ene was prepared according to a literature procedure (see P. Carsky, et al., *Liebigs Ann. Chem.* **1980**, 291-304). 5-OMe-res was commercially available. Co-crystals of 2(5-OMe-res)·2(poly-2-ene) were obtained by evaporation of a solution of 0.058 g of 4-pyr-poly-2-ene (0.28 mmol) and 0.039 g of 5-OMe-res (0.28 mmol) in 3.0 mL of hot methanol. ^{1}H NMR of 2(5-OMe-res)·2(poly-2-ene) before irradiation (300 MHz, DMSO-d_6): $\delta = 9.15$ (br. s, 2H), 8.54 (dd, 4H), 7.50 (dd, 4H), 7.40 (dd, 4H), (dd, 4H), 5.82 (br. t, 1H), 5.78 (br. d, 2H), 3.61 (s, 3H). Crystal data for 2(5-OMe-res)·2(poly-2-ene): monoclinic, P 2_1/c, $a = 9.182(5)$ Å, $b = 13.381(5)$ Å, $c = 15.122(5)$ Å, $\beta = 106.712(5)^\circ$, $V = 1779.5(13)$ Å^3, $Z = 4$, $\rho_{calc} = 1.300$ g/cm^3, $R_1 = 0.0441$ for 2324 reflections with $I > 2\sigma(I)$.

Example 2 Preparation of 2(5-OMe-res) 2(poly-3-ene)

4-Pyr-poly-3-ene was prepared according to a literature procedure (see P. Carsky, et al., *Liebigs Ann. Chem.* **1980**, 291-304). Co-crystals of 2(5-OMe-res)·2(poly-3-ene) were obtained in a manner similar to that described in Example 1 using 0.030 g of 4-pyr-poly-3-ene (0.13 mmol) and 0.018 g of 5-OMe-res (0.13 mmol). ^{1}H NMR of 2(5-OMe-res)·2(poly-3-ene) before irradiation (300 MHz, DMSO-d_6): $\delta = 9.16$ (br. s, 2H), 8.52 (dd, 4H), 7.46 (dd, 4H), 7.33 (m, 2H), 6.72 (m, 4H), 5.82 (br. t, 1H), 5.79 (br. d, 2H), 3.61 (s, 3H). Crystal data for 2(5-OMe-res)·2(poly-3-ene): triclinic, $P\bar{1}$, $a = 9.081(3)$ Å, $b = 21.143(4)$ Å, $c = 21.308(18)$ Å, $\alpha = 87.92(4)^\circ$, $\beta = 79.47(6)^\circ$, $\gamma = 78.91(2)^\circ$, $V =$

3947(4) Å^3, $Z = 2$, $\rho_{calc} = 1.260$ g/cm^3, $R_1 = 0.0891$ for 6150 reflections with $I > 2\sigma(I)$.

Example 3 Irradiation of 2(5-OMe-res)·2(poly-2-ene) to Provide [3]-Laddarane.

A finely ground sample of 2(5-OMe-res)·2(poly-2-ene) was placed between two pyrex plates and irradiated with a 500 W Hg lamp. The sample was turned in eight hour intervals to ensure uniform irradiation over a period of 120 hours to provide the [3]-ladderane in 100 % conversion. ^{1}H NMR of irradiated 2(5-OMe-res)·2(poly-2-ene) (300 MHz, DMSO-d_6): $\delta = 9.16$ (br. s, 4H), 8.26 (dd, 8H), 7.04 (dd, 8H), (br. t, 2H), 5.78 (br. d, 4H), 4.30 (br. s, 4H), 3.61 (s, 6H), 3.49 (br. s, 4H). Stirring of the irradiated solid with 1M KOH solution, followed by extraction with methylene chloride and evaporation of the organic phase, yielded the [3]-ladderane as a white solid in 85 % yield. Crystal data for the [3]-ladderane: triclinic, P $\bar{1}$, $a = 12.534(5)$ Å, $b = 12.583(5)$ Å, $c = 14.787(5)$ Å, $\alpha = 100.388(5)^\circ$, $\beta = 106.555(5)^\circ$, $\gamma = 89.945(5)^\circ$, $V = 2195.7(14)$ Å^3, $Z = 2$, $\rho_{calc} = 1.260$ g/cm^3, $R_1 = 0.0647$ for 4018 reflections with $I > 2\sigma(I)$. The structure was determined to be a rotational twin, the twinning law being a two-fold rotation about the (0, 1, 1) reciprocal lattice direction.

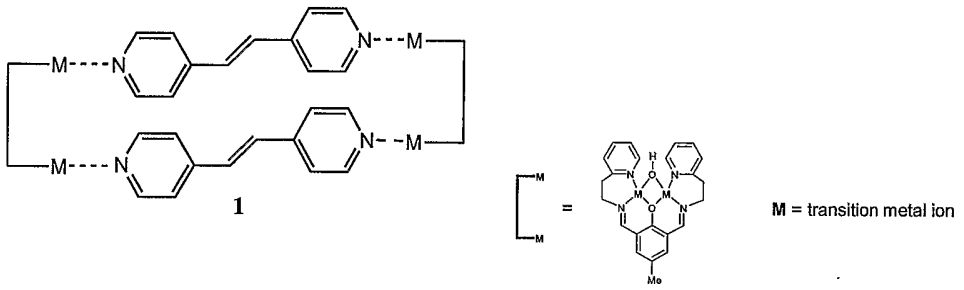
Example 4 Irradiation of 2(5-OMe-res)·2(poly-3-ene) to Provide [5]-Laddarane.

A finely ground sample of 2(5-OMe-res)·2(poly-3-ene) was placed between two pyrex plates and irradiated with a 500 W Hg lamp. The sample was turned in eight hour intervals to ensure uniform irradiation over a period of 72 hours to provide the [5]-ladderane in 100 % conversion. ^{1}H NMR of irradiated 2(5-OMe-res)·2(poly-3-ene) (300 MHz, DMSO-d_6): $\delta = 9.15$ (br. s, 4H), 8.25 (dd, 8H), 7.02 (dd, 8H), (br. t, 2H), 5.78 (br. d, 4H), 4.27 (br. s, 4H), 3.61 (s, 6H), 3.27 (br. s, 4H), 3.12 (br. s, 4H). Stirring of the irradiated solid with 1M KOH solution, followed by extraction with methylene chloride and evaporation

of the organic phase, yielded the [5]-ladderane as a white solid in 85 % yield. Crystal data for the [5]-ladderane·2(benzene): monoclinic, $P\,2_1/c$, $a = 9.475(2)$ Å, $b = 15.048(3)$ Å, $c = 12.235(2)$ Å, $\beta = 95.95(3)°$, $V = 1735.0(6)$ Å^3, $Z = 4$, $\rho_{calc} = 1.196$ g/cm^3, $R_1 = 0.0438$ for 1625 reflections with $I > 2\sigma(I)$.

The procedures described in examples 1-4 were readily scaled up to give the ladderanes in gram quantities. Single crystals of the [3]-ladderane were grown from ethanol, while single crystals of [5]-ladderane were grown from benzene yielding a 1:2 benzene solvate.

Example 5 Preparation of Representative Complex of the Invention (Complex **1**)



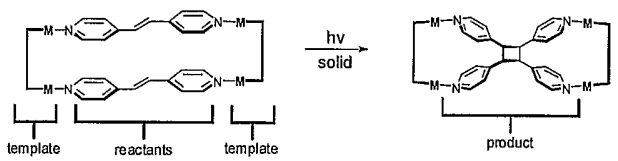
Ditopic LH was synthesized from condensation of 2-hydroxy-5-methyl-isophthalaldehyde (0.84 g) with 2-aminoethyl-pyridine (1.24 g) (1:2 ratio) in MeOH (15 mL) (Visinescu, D. et al., *Inorg. Chem. Commun.* **2002**, 5, 42). Dissolution of $Zn(ClO_4)_2·6H_2O$ (0.37 g) and $LiOH·H_2O$ (0.03 g) in H_2O (5 mL) (2:3 ratio) produced a yellow solution. Diffusion of a MeOH solution (10 mL) of 4,4'-bpe (0.90 g) into the aqueous Zn(II) and Li(I) solution (ratio: 4:2:3) resulted in precipitation of a light-yellow crystals of $[Zn_4L_2(OH)_2(4,4'\text{-bpe})_2](ClO_4)_4·4H_2O$ **1** (where: LH = 2,6-bis[N-(2-pyridylethyl)formimidoyl]-4-methylphenol) over a period of two weeks (yield: 76%), as illustrated below.

A view of the crystal structure of **1** (Figure 8; X-ray data for **1**: triclinic, space group P $\bar{1}$, $\alpha = 10.7509(11)$, $b = 10.9233(11)$, $c = 18.558(2)$, $\alpha = 97.531(5)°$, $\beta = 101.758(5)°$, $\gamma = 110.933(5)°$, $U = 1942.7(4)$Å^3 for $Z = 1$ and $R = 0.046$) reveals that two dinuclear $[Zn_2L(OH)]^{2+}$ units assemble with two molecules of 4,4'-bpe to form a tetranuclear rectangular assembly, $[Zn_4L_2(OH)_2(4,4'\text{-bpe})_2]^{4+}$, sustained by four Zn-N bonds [Zn-N (Å): Zn(1)-N(5)

2.090(3), Zn(2)-N(6)a 2.105(3) (a: -x+1,-y+2,-z+2)] (Figure 8a). Each metal [Zn···Zn (Å): Zn(1)-Zn(2) 3.135(1), Zn(1)-Zn(2)a 13.542] adopts a square pyramidal geometry where the pyridyl N- atoms of 4,4'-bpe occupy the apical positions while the remaining sites are occupied by a single O- and two N-atoms of L and a single O-atom of a μ_2-OH^- ion. Each assembly is surrounded by two ClO_4^- ions, one which lies disordered across two sites A and B (occupancies: (A) 0.53, (B) 0.47), and two water molecules that assemble with the OH^- ligand to form a 1D hydrogen-bonded array with cavities filled by four ClO_4^- ions and four water molecules [O···O (Å): O(2)···O(11) 2.888(5), O(11)···O(12) 2.804(6), O(11)···O(4) 2.787(5), O(12)···O(8A) 3.03(1), O(12)···O(7)b 3.063(8), (b: -x+1,-y+1,-z+2)] (Figure 8b). In this arrangement, the C=C bonds of the assembly lie parallel and separated by 3.64 Å. This geometry conforms to the topochemical postulate of Schmidt for [2+2] photoreaction (Schmidt, G.M.J. *Pure Appl. Chem.* **1971**, 27, 647). C=C bonds of nearest-neighbor assemblies lie offset and separated by 9.82 Å such that the C=C bonds of the polygonal assembly are the sole olefins organized for reaction.

Example 6 Preparation of Representative Complex of the Invention (Complex **2**)

Exposure of either single crystals or a powdered crystalline sample of complex **1** to UV radiation, using either a broadband or a 419 nm Hg lamp (Enkelmann, V. et al., *J. Amer. Chem. Soc.* **1993**, 115, 10390), for a period of 5 hours resulted in dimerization of 4,4'-bpe to give *rctt*-tetrakis(4-pyridyl)cyclobutane (4,4'-tpcb) complex **2** in 100% yield as illustrated below.



1 **2**

The reaction occurs *via* a single-crystal-to-single-crystal (SCSC) transformation (Enkelmann, V. et al, *Amer. Chem. Soc.* **1993**, 115, 10390) that

exhibits a red shift in fluorescence (Tyson, D. S. et al., *J. Am. Chem. Soc.* **2002**, 124, 4562; Pistolis, G. et al., *Chem. Mater.* **2002**, 14, 790) from blue to green.

The identity of 4,4'-tpcb in **2** was confirmed by ^{1}H NMR spectroscopy. Optical microscopy revealed the transparency and shape of the single crystals exposed to the 419 nm UV source (Enkelmann, V. et al., *J. Amer. Chem. Soc.* **1993**, 115, 10390) remained intact during the photoreaction, which suggested the reaction occurred *via* a SCSC transformation.

A single-crystal X-ray diffraction analysis of photoreacted **1** (X-ray data for **2**: triclinic, space group P $\bar{1}$, a = 10.9644(11), b = 11.2922(11), c = 17.6367(18), α = 96.933(5)°, β = 101.342(5)°, γ = 113.218(5)°, U = 1919.4(3)Å3 for Z = 1 and R = 0.044) confirmed the solid-state reaction occurred *via* a SCSC transformation (Figure 9). Overlay views of **1** and **2** reveal that the olefins dimerized to give 4,4'-tpcb (Figure 9a). In this arrangement, 4,4'-tpcb lies within **2** such that the pyridyl groups, which adopt a unsymmetrical boat conformation and lie inclined by approximately 12° with respect to the basal planes of the metals, interact with the Schiff-base complex within a tetranuclear assembly, similar to **1**, sustained by four Zn-N bonds (Zn-N (Å): Zn(1)-N(5) 2.094(3), Zn(2)-N(6) 2.106(3). To accommodate 4,4'-tpcb, the distances between the metals within and between the Schiff-base ligands have slightly increased and decreased, respectively [Zn···Zn (Å): Zn(1)-Zn(2) 3.182(1), Zn(1)-Zn(2)c 13.36 (c: -x+1, -y+1, -z+1)], while the hydrogen-bonded array has undergone a slight deformation, the most significant being a 1.15 Å displacement of the ordered ClO_4^- ion toward the center of each inclusion cavity (Figure 9b).

Example 7 Fluorescence of Complex **1** and Complex **2**

Illumination of complex **1** and complex **2** at room temperature with UV energy reveals that complex **2** exhibits a remarkably different fluorescence emission than complex **1** (Figure 10). Specifically, excitation of complex **1** at 290 nm gives blue emission at 464 nm while similar excitation of complex **2** gives green emission at 520 nm (Figure 10a). Illumination of cleaved crystals of complex **1** and complex **2** using a handheld UV lamp demonstrates that the emissions are propagated from the bulk, an observation confirmed by laser

scanning confocal fluorescence microscopy which reveals a consistent difference in fluorescence between complex **1** and complex **2**, as determined by comparing ratios of the fluorescence at 480 nm and 510 nm (Figure 10b), at different depths in each single-crystalline solid.

Example 8 Preparation of Representative Complexes of the Invention (Complexes **3** and **4**) Using A Metal Cation Assembly Template

Agentophilic forces, in the form of Ag···Ag interactions, were used to guide stacking of olefins in the dinuclear complex $[Ag_2(4\text{-stilbz})_4][CO_2CF_3]_2$ **3** (where: 4-stilbz = *trans*-1-(4-pyridyl)-2-(phenyl)ethylene) in a geometry suitable to undergo a regiocontrolled head-to-head [2+2] photodimerization in the solid state in 100% yield. The reaction occurs *via* a single-crystal-to-single-crystal (SCSC) transformation that, in addition to C-C bond making, involves breaking and formation of Ag···Ag and Ag···C interactions, respectively. Remarkably, the breaking and formation of the forces are accompanied by a 1.15 Å movement and approximately 90° rotation of the Ag(I) and carboxylate ions, respectively, which results in the dinuclear complex being converted into a one-dimensional (1D) coordination network.

Interactions between closed-shell d^{10} metal ions are being used increasingly to construct supramolecular assemblies that exhibit rich host-guest, photophysical, and electrical properties. Both solid-state and liquid-phase data have established that such forces are prevalent, particularly in the absence of structural influences of bridging ligands, at distances shorter than the sum of the van der Waals radii. Thus, for the Ag(I) ion, Ag···Ag or argentophilic forces are evoked at separations < 3.4 Å, although separations < 3.8 Å have been cited. Importantly, these distances fall within the distance criterion of Schmidt for a [2+2] photodimerization in a solid.

Reaction of a solution of $AgCO_2CF_3$ in ethanol with 4-stilbz afforded large colorless plates of **3** upon slow evaporation. The formulation of **3** was confirmed *via* ^1H NMR spectroscopy, as well as powder and single-crystal X-ray diffraction data.

Perspective views of **3** are shown in Figure 9. The metal and organic components have assembled to form a discrete dinuclear complex held together by a Ag···Ag force (Ag···Ag distance (Å): 3.41). In this arrangement, the primary coordination sphere of the Ag(I) ion is based on a T-shaped geometry that involves two transoid N-atoms of two 4-pyridyl groups of two olefins [Ag-N distances (Å) and angles (°)]: Ag(1)-N(1) 2.161, Ag(1)-N(2) 2.149, N(1)-Ag-N(2) 166.9) and a single O-atom of a carboxylate ion [Ag-O distance (Å) and angles (°)]: Ag(1)-O(1) 2.600, O(1)-Ag-N(1) 94.5, O(1)-Ag-N(2) 96.5). The two olefins that span the Ag···Ag interaction lie approximately parallel, the pyridine units participating in offset, face-to-face π-π forces (pyridine centroid-centroid distances (Å): 3.60). The carboxylate group is twisted approximately orthogonal to the stacked olefins such that each -CF_3 group points away from the center of the complex. As a consequence of the assembly process, the carbon-carbon double (C=C) bonds, which adopt a criss-cross arrangement, are separated by 3.82 Å (C···C distances (Å): C(6)···C(19) 3.82, C(6)···C(20) 3.71, C(7)···C(20) 4.15, C(7)···C(19) 4.06). This separation distance conforms to the distance criterion of Schmidt for [2+2] photoreaction in a solid. The complex self-assembles to form 1D quadruple π-stacked arrays, which are canted at approximately 60°, with nearest-neighbor olefins offset and separated by 4.26.

To test whether the olefins of **3** are photoactive, **3**, in the form of either single crystals or a powdered crystalline sample, was exposed to UV radiation (either a 419 nm or broadband Hg lamp) for a period of approximately 24 hours. A ^{1}H NMR spectrum of photoreacted **3** demonstrates, as revealed by the complete disappearance of the olefinic protons and the emergence of cyclobutane protons, that the olefins reacted to give 4-pyr-ph-cb in 100% yield. Optical microscopy revealed that the transparency and shape of the single crystals remained intact during the photoreaction, which suggested that the reaction occurred *via* a SCSC transformation.

An X-ray diffraction analysis of the single crystal of photoreacted **3** confirms that the reaction occurred *via* a SCSC transformation. As shown in Figure 10, the olefins of **3** have reacted to give 4-pyr-ph-cb in [Ag(4-pyr-ph-

cb)][CO_2CF_3] **4** in quantitative yield. The cyclobutane ring of **4** adopts two orientations in the solid, an observation consistent with the C=C bonds undergoing a pedal-like change in conformation in **3** prior to the photoreaction.

The generation of the photoproduct of **4** is accompanied by major repositioning of the Ag(I) and carboxylate ions. Specifically, the two Ag(I) ions of each complex have moved 2.3 Å away from each other (Ag···Ag distance: 5.74Å) in a direction approximately parallel to the newly formed C-C bonds. Despite such movement, however, the Ag-N (Ag-N distances (Å): Ag(1)-N(1) 2.178, Ag(1)-N(2) 2.192) and Ag-O (Ag-O distance (Å): Ag(1)-O(1) 2.421) bonds have remained intact in **4**. Each Ag(I) ion now assumes an approximate trigonal planar coordination geometry (X-Ag-X angles (°): N(1)-Ag-N(2) 145.8, N(1)-Ag-O(1) 97.4, N(2)-Ag-O(1) 109.2), with each metal ion lying 0.3 Å out of the plane of the two N- and single O-donor atoms, while each carboxylate ion is now oriented approximately perpendicular to the pyridyl groups. This orientation is consistent with each carboxylate ion undergoing an approximate 90° rotation in the solid.

An important consequence of the movement displayed by the ions is that Ag···C forces, which lie at the far end of the typical range (Ag···C(phenyl) distances (Å): Ag(1)···C(24) 2.88, Ag(1)···C(25) 2.67), have formed between each repositioned Ag(I) ion and a *para*-carbon atom of a phenyl group of a neighboring complex. The Ag···C forces serve to link adjacent stacked complexes of **3** into a 1D extended structure. Thus, the photoreaction has, in effect, forced the Ag···Ag interactions to break and Ag···C forces to form in **4** which, in turn, has resulted in the discrete complex of **3** being converted into a 1D coordination network.

All publications, patents, and patent documents are incorporated by reference herein, as though individually incorporated by reference. The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within the spirit and scope of the invention.

CLAIMS

What is claimed is:

1. A method for preparing a ladderane comprising, associating two or more polyene molecules with a template such that the polyene molecules are properly aligned to allow for formation of the ladderane, and reacting the polyene molecules under conditions suitable to provide the ladderane.

2. The method of claim 1 where the polyene molecules and the template are associated by dipole-dipole interactions or by van der Waals forces.

3. The method of claim 1 where the polyene molecules and the template are associated by coordination.

4. The method of claim 3 where the polyene molecules and the template are associated by hydrogen bonds.

5. The method of any one of claims 1-4 wherein each of the polyene molecules comprises 3-20 double bonds.

6. The method of any one of claims 1-4 wherein each of the polyene molecules comprises 3-10 double bonds.

7. The method of any one of claims 1-4 wherein each of the polyene molecules comprises 3-6 double bonds.

8. The method of any one of claims 1-7 wherein each polyene comprises only *trans* double bonds.

9. The method of any one of claims 1-8 wherein each polyene independently comprises from about 6 to about 40 carbon atoms.

10. The method of any one of claims 1-8 wherein each polyene independently comprises from about 6 to about 30 carbon atoms.

11. The method of any one of claims 1-8 wherein each polyene independently comprises from about 6 to about 20 carbon atoms.

12. The method of any one of claims 1-11 wherein each polyene is terminally substituted with a group that is capable of associating with the template.

13. The method of claim 12 wherein each group independently comprises an amino nitrogen, a thiol, an alcohol, or a carboxylic acid.

14. The method of claim 13 wherein each group comprises an amino nitrogen.

15. The method of claim 14 wherein each group is a pyridine ring.

16. The method of claim 15 wherein each group is a 4-pyridine ring.

17. The method of any one of claims 1-16 wherein the template is an inorganic molecule, an organic molecule, a solid support, or an assembly comprising organic or inorganic molecules or ions, or a mixture thereof, held together by non-covalent bonds.

18. The method of any one of claims 1-16 wherein the template is an inorganic molecule.

19. The method of any one of claims 1-16 wherein the inorganic molecule is a transition metal complex.

20. The method of any one of claims 1-16 wherein the template is an organic molecule.

21. The method of claim 20 wherein the organic molecule is a polyol, a poly-ether, or a polyamine.

22. The method of claim 20 wherein the organic molecule comprises an aromatic ring.

23. The method of claim 22 wherein the aromatic ring is 1,3 substituted with groups capable of associating with the polyene molecules.

24. The method of claim 22 wherein the organic molecule comprises a 1,3-substituted phenyl ring or a 1,3-substituted naphthyl ring.

25. The method of claim 22 wherein the organic molecule comprises a 1,3-dihydroxy substituted phenyl ring or a 1,3-dihydroxy substituted naphthyl ring.

26. The method of claim 22 wherein the organic molecule is resorcinol, orcinol, 4-ethylresorcinol, 4-hexylresorcinol, olivetol, 4-cyclohexylresorcinol, 4-benzylresorcinol, 4-chlororesorcinol, 4-bromoresorcinol, 4,6-dichlororesorcinol, 4,6-dibromoresorcinol, 4,6-di-*tert*-butylresorcinol, 4,6-di-(1,1-diphenylethyl)resorcinol, 3,5-dihydroxybenzaldehyde, 5-cyanoresorcinol, 5-acetylresorcinol, 5-methoxyresorcinol, 5-carboxymethylresorcinol, 1,3-dihydroxynaphthalene, 4,6-dibromo-5-carboxymethylresorcinol, 2,4,6-trihydroxybenzaldehyde, methyl 2,4-6-trihydroxyphenyl ketone, ethyl 2,4-6-trihydroxyphenyl ketone, propyl 2,4-6-trihydroxyphenyl ketone, butyl 2,4-6-trihydroxyphenyl ketone, pentyl 2,4-6-trihydroxyphenyl ketone, hexyl 2,4-6-trihydroxyphenyl ketone, or phenyl 2,4-6-trihydroxyphenyl ketone.

27. The method of any one of claims 1-16 wherein the template comprises an assembly of metal ions.

28. The method of claim 27 wherein two or more metal ions of the assembly are attracted to each other by forces that are weaker than a covalent or ionic bond but stronger than a van der Waals bond.

29. The method of any one of claims 1-16 wherein the template comprises an assembly of two or more metal cations.

30. The method of any one of claims 1-16 wherein the template comprises an assembly of two or more transition metal cations.

31. The method of any one of claims 1-16 wherein the template comprises an assembly of two or more gold ions.

32. The method of any one of claims 1-16 wherein the template comprises an assembly of two or more silver ions.

33. The method of any one of claims 1-32 wherein each double bond of one polyene is aligned within about 3.2 to about 4.5 Angstroms of a double bond on another polyene to allow for formation of the ladderane.

34. The method of any one of claims 1-32 wherein each double bond of one polyene is aligned within less than about 4.2 Angstroms of a double bond on another polyene to allow for formation of the ladderane.

35. The method of any one of claims 1-34 wherein the reacting is carried out in a solid state.

36. The method of any one of claims 1-35 wherein the reacting is carried out by treating the polyenes with light or heat or a combination thereof.

37. A method for preparing a ladderane comprising, 1) associating two or more polyene molecules with a template, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

38. A method for preparing a ladderane comprising, 1) associating two or more polyene molecules with a template comprising two hydroxyl groups, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

39. A method for preparing a ladderane comprising, 1) associating two polyene molecules that each comprise an amino nitrogen with a template comprising two hydroxyl groups, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

40. A method for preparing a ladderane comprising, 1) associating two polyene molecules that each comprise a pyridine ring with a template comprising a 1,3-dihydroxy substituted phenyl ring, 2) forming a solid comprising the template and the polyene molecules, wherein the polyene molecules are properly aligned within the solid to allow for formation of the ladderane, and 3) reacting the polyene molecules under conditions suitable to provide the ladderane.

41. A method for preparing a ladderane comprising, 1) combining polyene molecules that comprise a pyridine ring with template molecules that comprise a

1,3-dihydroxy substituted phenyl ring in a solvent, 2) allowing a crystalline solid that comprises the template molecules and the polyene molecules to form, wherein the polyene molecules are properly aligned within the crystalline solid to allow for formation of the ladderane, and 3) irradiating the solid under conditions suitable to provide the ladderane.

42. The method of any one of claims 37-41 wherein the ladderane is an [n]-3, [n]-4, [n]-5, [n]-6, [n]-7, [n]-8, [n]-9, [n]-10, [n]-11, or [n]-12 ladderane.

43. The method of any one of claims 37-41 wherein the polyene is 1,4-bis(4-pyridyl)-1,3-butadiene or 1,6-bis(4-pyridyl)-1,3,5-hexatriene.

44. The method of any one of claims 37-41 wherein the template comprises a 1,3-dihydroxybenzene.

45. The method of any one of claims 37-43 wherein the template comprises an assembly of metal ions.

46. The method of claim 45 wherein the template comprises an assembly of two or more silver ions.

47. A ladderane prepared by the method of any one of claims 1-46.

48. A composition comprising polyene molecules associated with a template such that the polyene molecules are properly aligned to allow for formation of a ladderane.

49. The composition of claim 48 that is a solid.

50. The composition of claim 49 which is a crystalline solid.

51. A solid prepared by associating two or more polyene molecules with a template such that the polyene molecules are properly aligned in the solid to allow for formation of a ladderane.

52. A kit comprising packaging material and at least about 0.5 grams of a ladderane.

53. The kit of claim 52 which comprises at least about 1 gram of a ladderane.

54. The kit of claim 52 which comprises at least about 2 grams of a ladderane.

55. The kit of claim 52 which comprises at least about 5 grams of a ladderane.

56. A composition comprising at least about 0.5 grams of a ladderane, which composition is prepared according to the method claim 1.

57. The composition of claim 54 which comprises at least about 1 gram of a ladderane.

58. The composition of claim 54 which comprises at least about 2 grams of a ladderane.

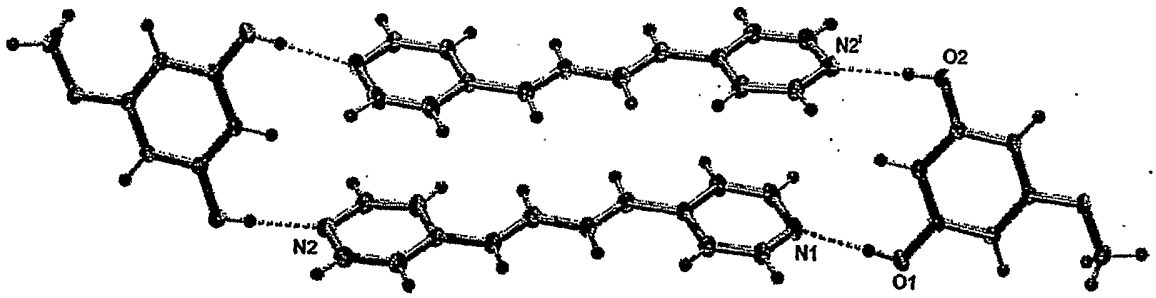


Figure 1a

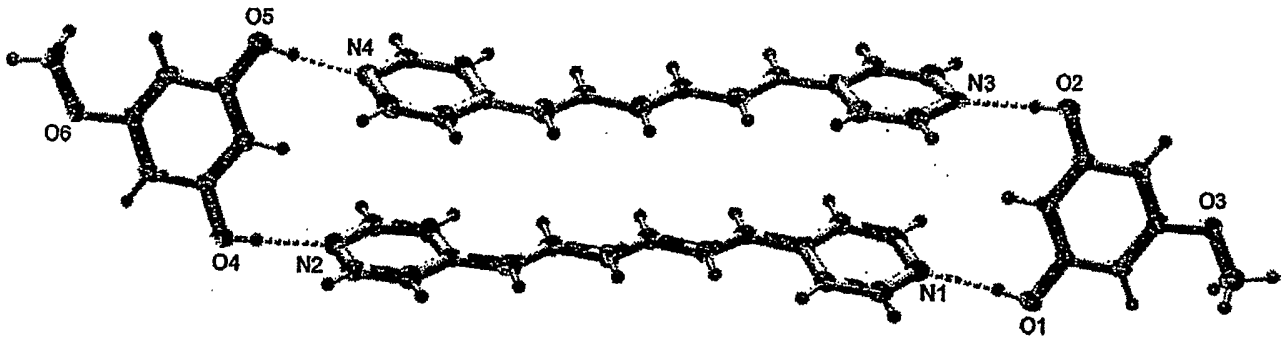


Figure 1b

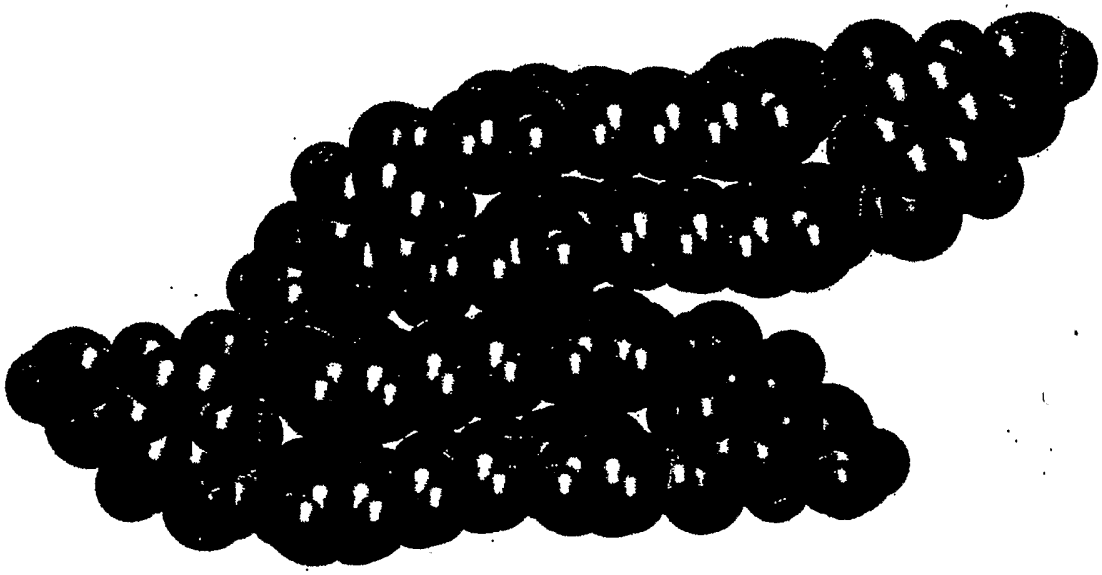


Figure 1c

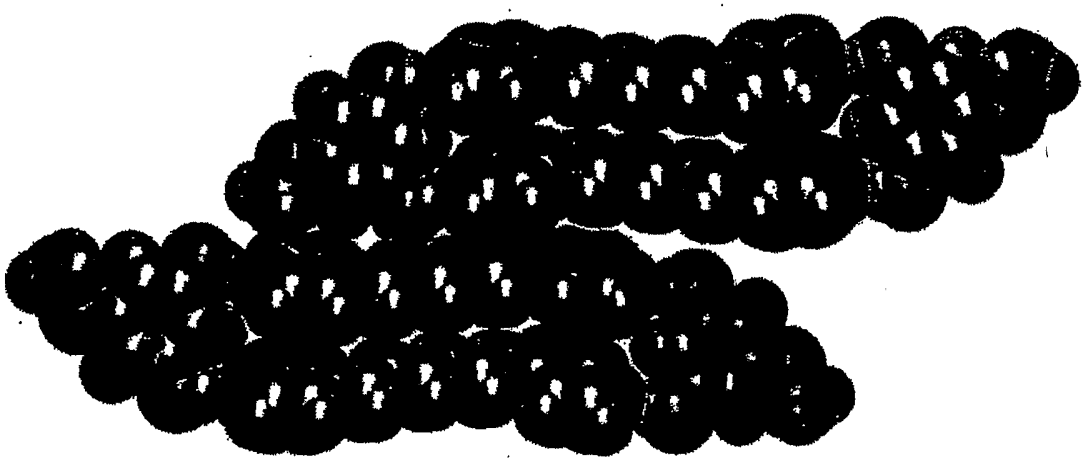


Figure 1d

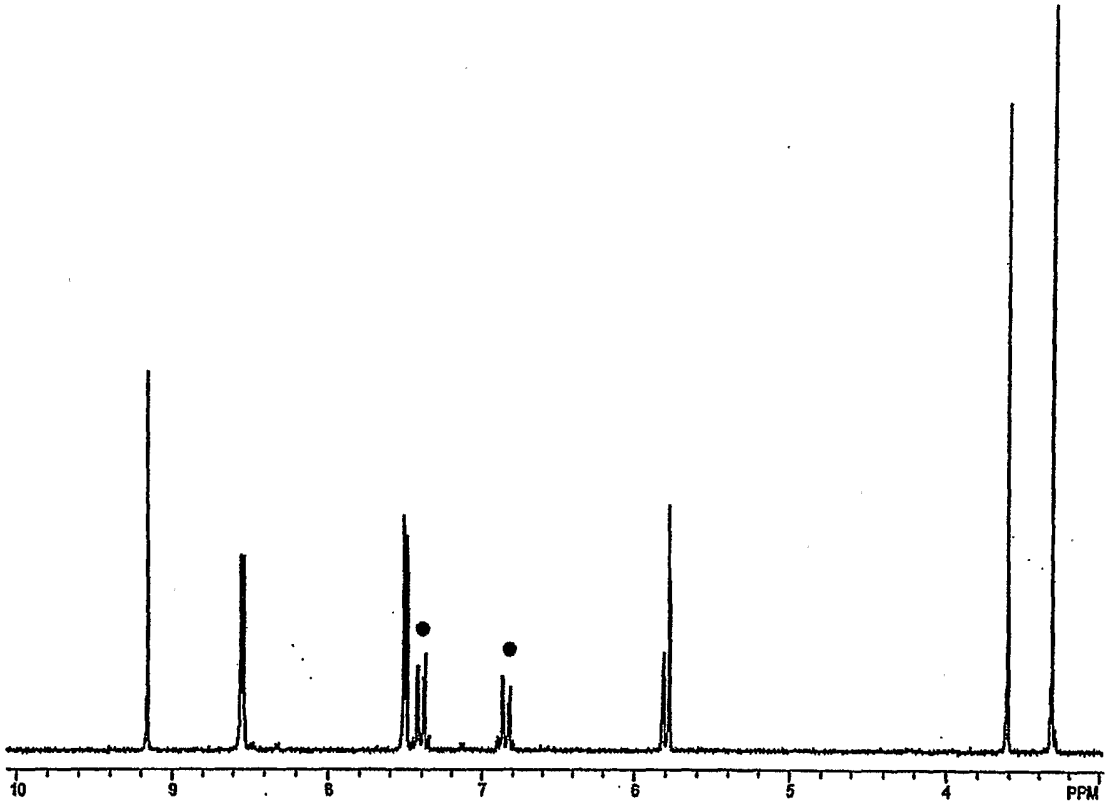


Figure 2a

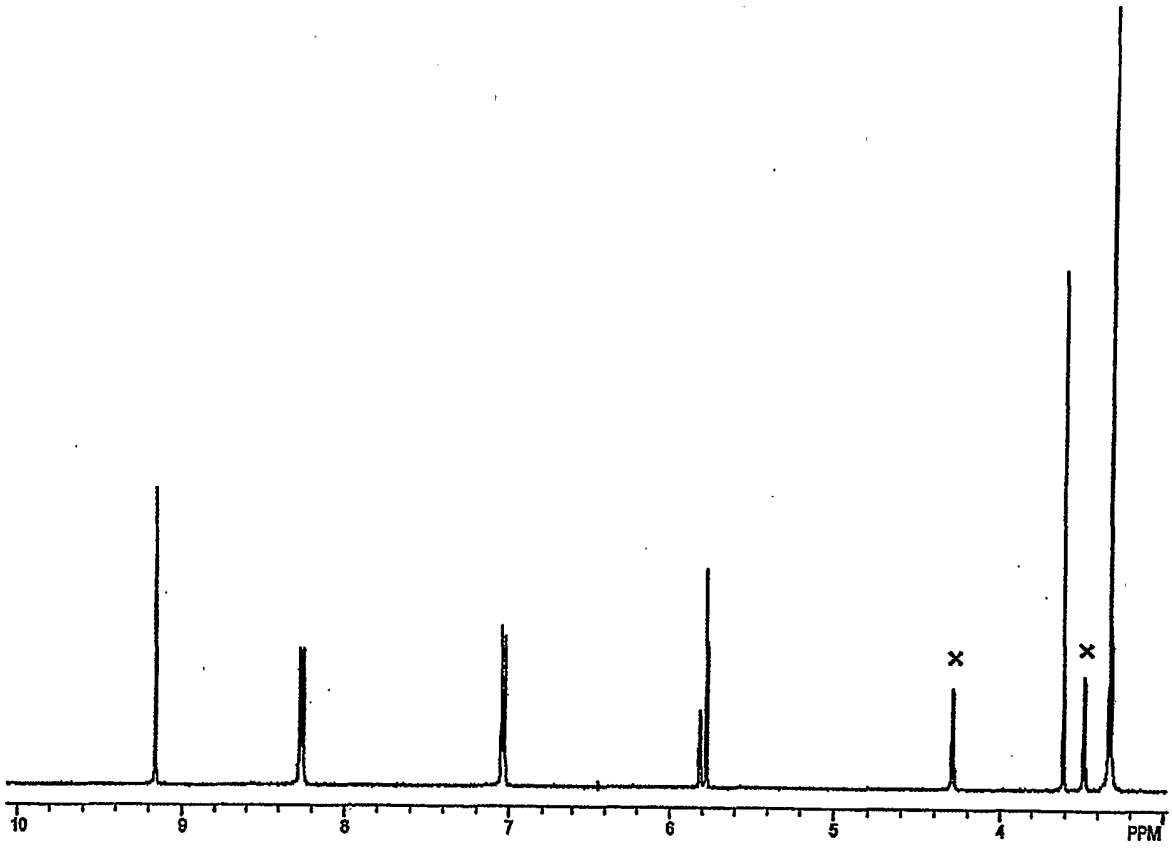


Figure 2b

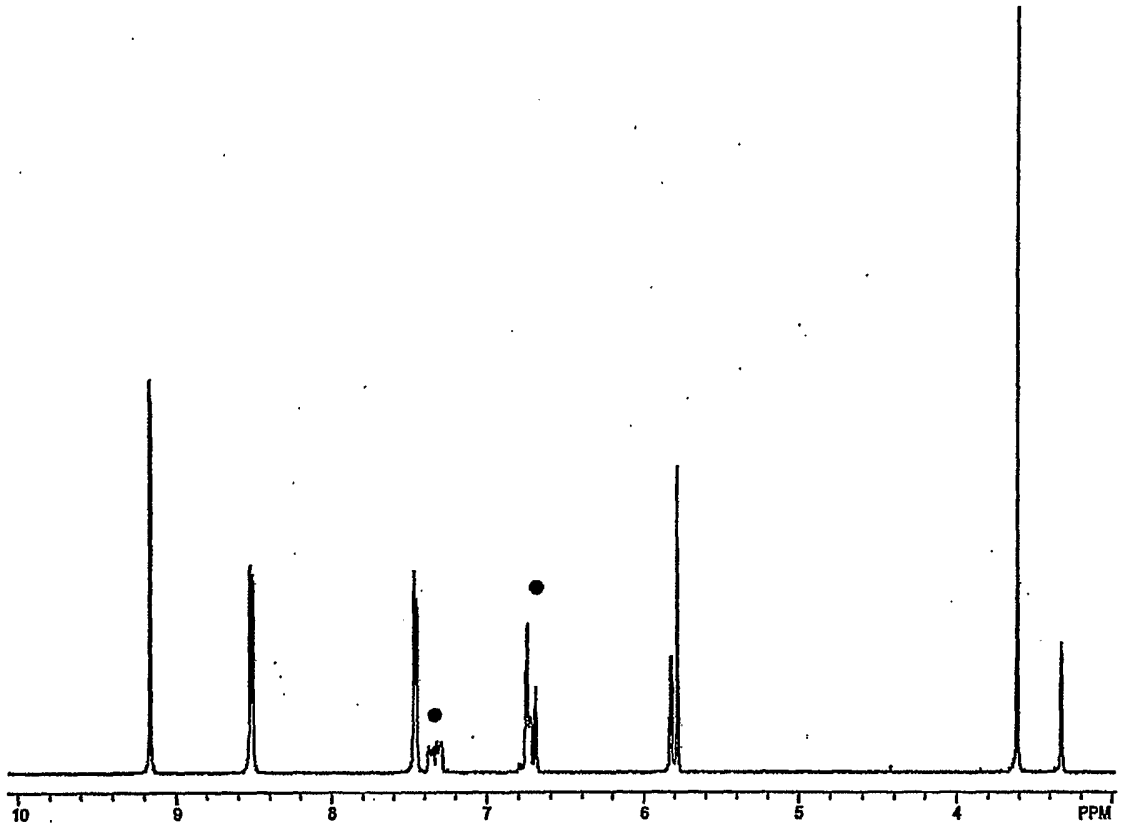


Figure 2c

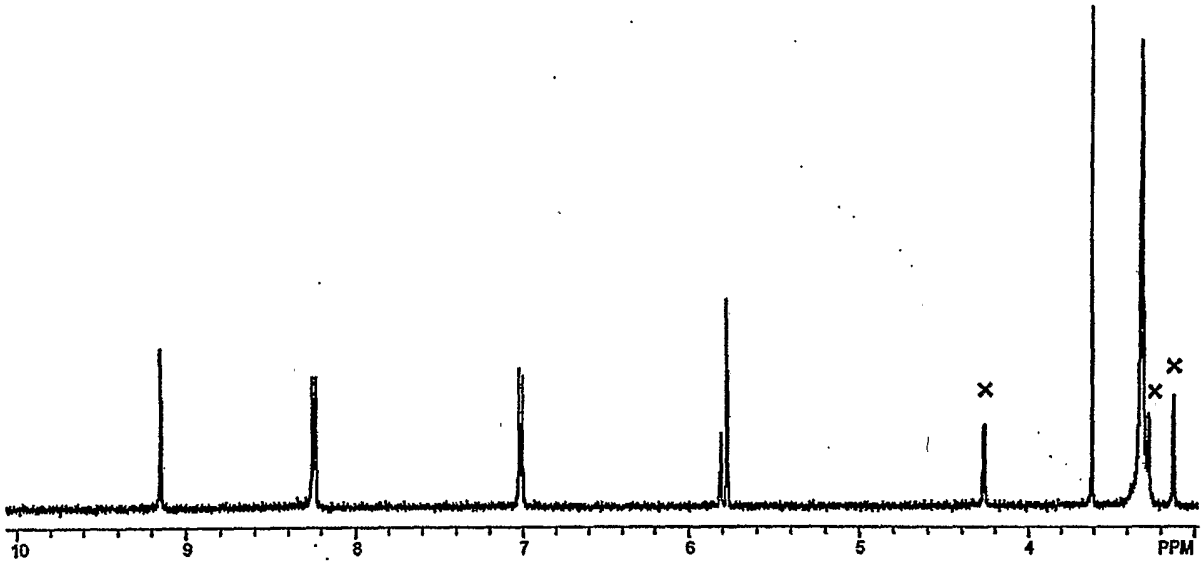


Figure 2d

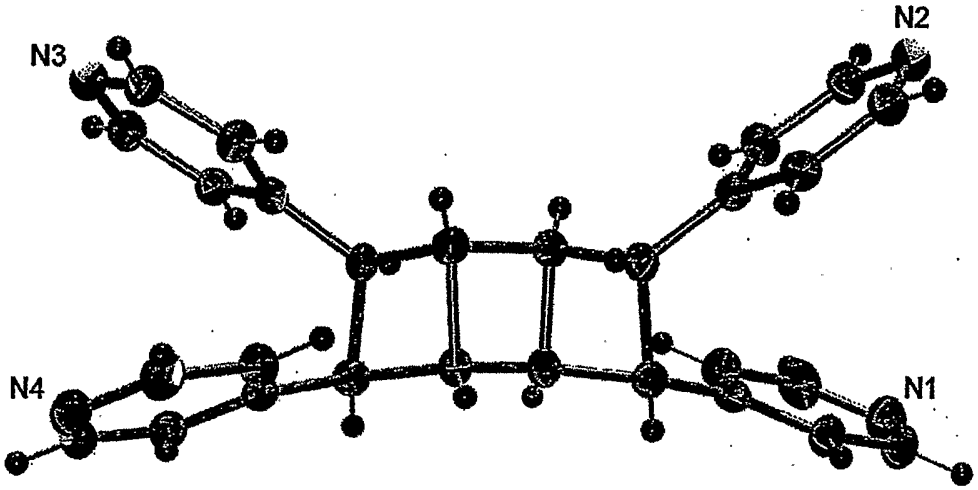


Figure 3a

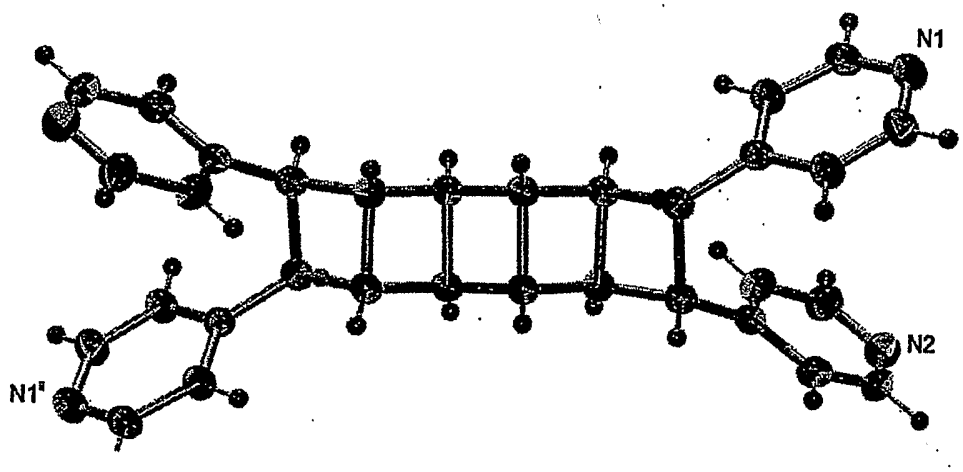
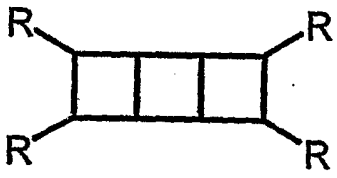
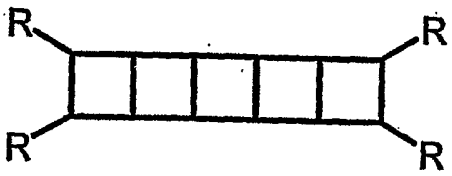


Figure 3b

Figure 4

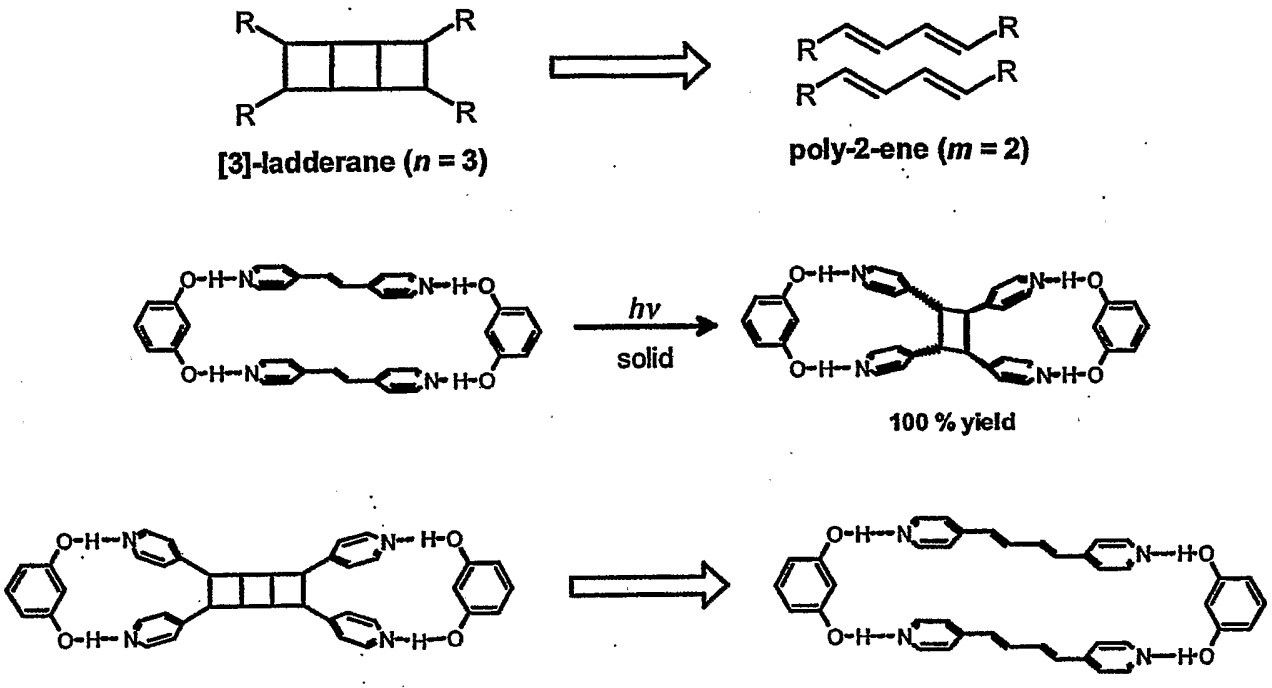


[3]-ladderane
n = 3

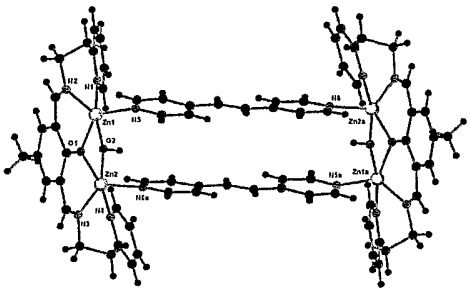


[5]-ladderane
n = 5

Figure 5



a)



b)

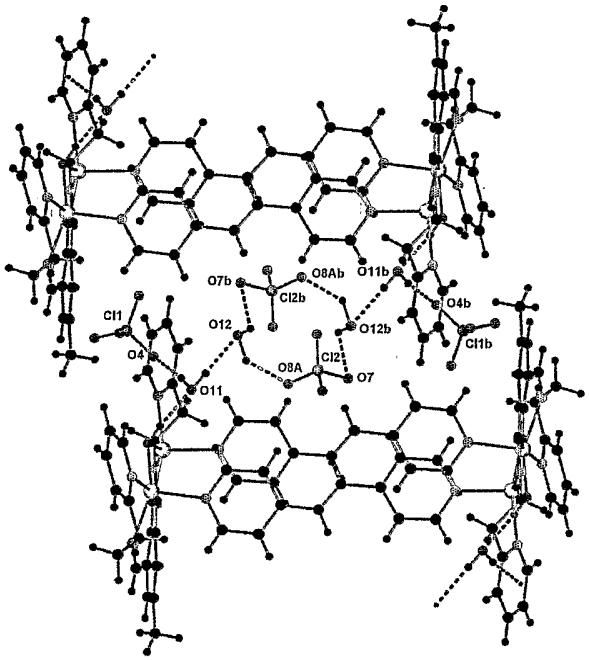
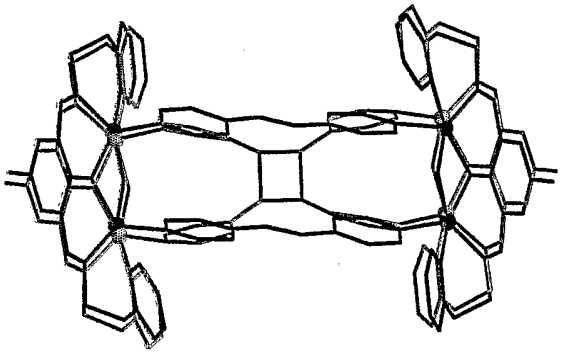


Figure 6

a)



b)

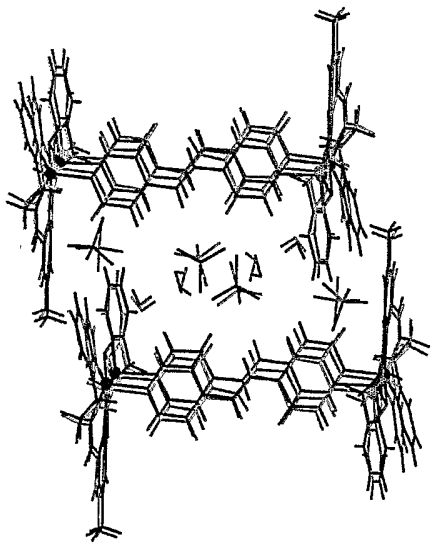
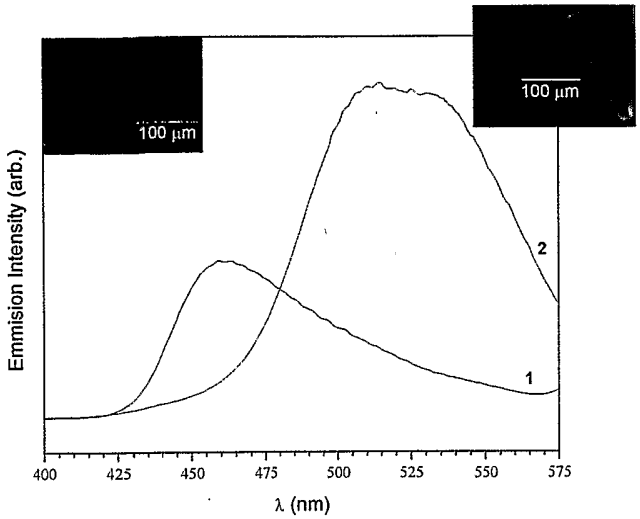


Figure 7

a)


100 µm
100 µm
Emmision Intensity (arb.)
2
1
400
425
450
475
500
525
550
575
λ (nm)

b)

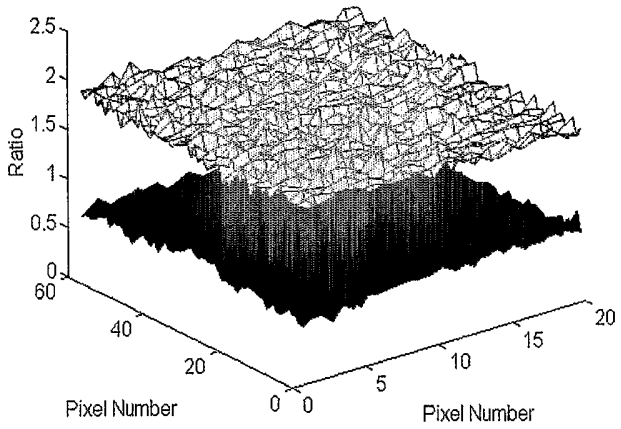

Ratio
2.5
2
1.5
1
0.5
0
60
40
20
0
Pixel Number
0
5
10
15
20
Pixel Number

Figure 8

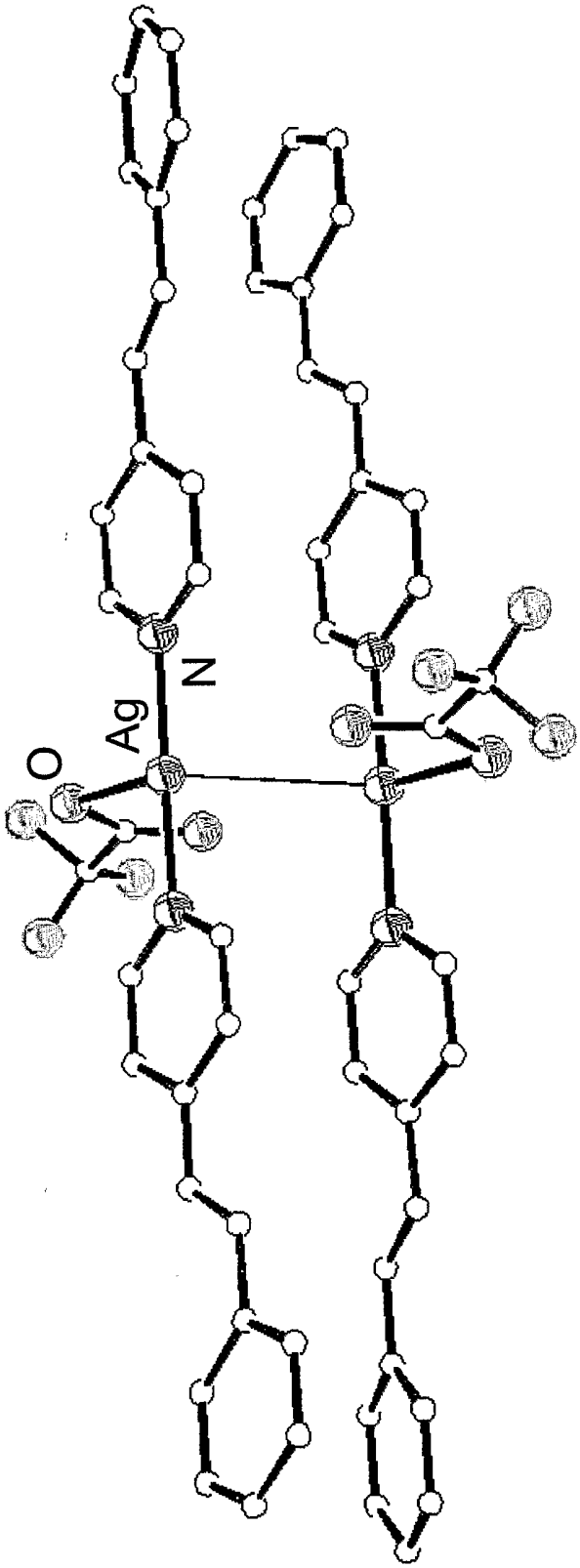


Figure 9

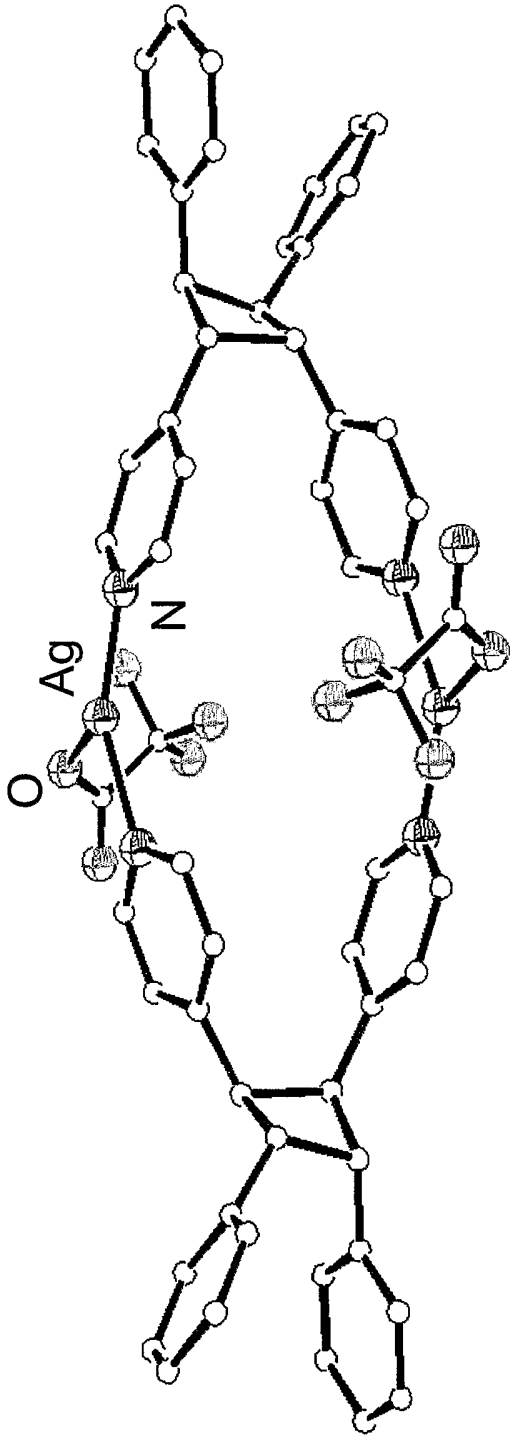


Figure 10