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POLYCATIONIC ORGANIC SALTS - SYNTHESES AND INVESTIGATIONS

by

JaimeLee Iolani Cohen

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

2001

This manuscript has been read and accepted by the Graduate Faculty in Chemistry in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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ABSTRACT

Polycationic Organic Salts - Syntheses and Investigations

by

JaimeLee Iolani Cohen

Advisor: Professor Robert Engel

A variety of polyammonium and polyphosphonium organic salts have been prepared. This work has involved the synthesis and investigations of these polycationic species based on several structural categories including "strings," "rings," cyclodextrin derivatives, DMAP, pyridine, and imidazolium derivatives. It has been demonstrated that several applications for these newly prepared materials exist. These include their capabilities as antibacterials, their use as antihydrophobic agents, their interaction with DNA, host/guest binding capabilities with a variety of biologically significant organic anions, as well as their conversion to ionic liquids. Most recently, work has been directed toward the preparation of a new category of ionic liquids - *Liquid Ionic Phosphates,* referred to as LIPs. These materials are particularly intriguing and have potential applications for batteries, non-aqueous polar reaction media, "green" extractive processes, and as catalysts.

Dedicated to my children Tiffany Leilanipolihenamakamaekui'iamenapua'a'alahenohenowili'iamemailelauli'i Cohen and Joshua Kahanapukahi Cohen.

ACKNOWLEDGEMENTS

I would first like to thank the two most important people in the world...my two wonderful children, T and Josh! Their love has enabled me to accomplish my dream. Of course, my husband, Michael, and my in-laws, Selma and Jerry, for their understanding.

I'm so happy that I have finally been able to make my parents, James and Shelley Asao proud of me! Dad, you lectured Jarisse and me on countless occasions, "Be a professional so you can be your own boss." Mom, you prayed for us everyday. I guess the combination of lecturing and prayers worked...Jarisse is now a District Attorney and I will be a Professor of Organic Chemistry. Wow! Who would've thought?!

I am most grateful to The Kamehameha Schools, Queensborough Community College, Queens College, and The Graduate School and University Center of The City University of New York. Specifically, I would like to thank a few VIPs (*V*ery *I*mportant *P*rofessors/*P*eople): Fred Kramer, John Riggle, Paris Svoronos, Patricia Allaire, Neville Parker, Claude Brathwaite, Thomas Strekas, Klaus Grohmann, Gerald Koeppl, David Locke, A.D. Baker, and Herman Zieger, who have guided me to this point.

I am most appreciative to the Department of Chemistry and Biochemistry of Queens College, LS-AMP, and PFF of the ACS and NSF for their financial support throughout the years.

To my friends in our research group, especially Valbona, Sharon, Marie, Chris and Amir, thanks for making work fun!

And last, but never least, my mentor and soon-to-be "colleague", Robert Ralph Engel. It is all too common and typical to say, "thank you for your patience, understanding, and guidance..." However, you, of all people, know how uncommom and atypical I am! Not only did I learn from you *how* to learn, but you taught me how important imagination, hard-work, and determination are. I will soon be an educator and mentor myself; I've learned by your example how to do so most effectively. After having me around for 4 1/2 years, I do believe that you now deserve that sabbatical! "You done good, kid!"

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phosphoric acid

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Statement of Problem

The intent of the present project has been the preparation and investigation of several series of polycationic salts with particular structural topologies, polyammonium and polyphosphonium salts. Structural limits for facile syntheses were to be explored, along with the examination of potential applications for the particular salts. The investigations of particular applications were to include interactions with biologically related systems as well as non-biological systems. Finally, the intent was also to investigate the possibilities for conversion of the parent polycationic salts into room temperature ionic liquids.

HISTORICAL

INTRODUCTION

For some years chemists have been concerned with polyammonium organic salts. These intriguing compounds are highly charged, water-soluble, organic species that serve as models for the investigation of biological supramolecular interactions, modify solubilities of organic materials as antihydrophobic agents, act as ion exchange agents and find use as polyelectrolytes. With the great developing interest in this field, the preparation of new ion exchange dendrimers, polyammonium "strings" and polymers, polycationic macrocycles (paracylophanes and related structures), modified cyclodextrin derivatives and non-aqueous ionic liquids have been investigated by our laboratory. Multiple cationic sites (ammonium and phosphonium) are located within the covalent structure of each of the species, with associated "free-floating" anions. For some of the materials a variety of aspects have already been investigated, including molecular topology, biochemical interactions, antibacterial effects, solubility enhancement, and host/guest binding interactions.

DENDRIMERS

Previous work in our laboratory included syntheses and studies of

polycationic dendrimers, compounds incorporating multidimensional elements of repetitive symmetry, reminiscent of the symmetry of fractals. In past years others have investigated a wide range of macromolecular and supramolecular structures looking toward the possible application of such species. [1-3]

Dendrimers incorporate four fundamental structural components: 1) a core or foundation site for the diverging branches of the cascade or dendrite structure; 2) one or more branching arms emanating from the core site, each incorporating a further branch point; 3) extension units between the core and branch sites and between branch sites, and 4) a terminal functionality for each of the branches, including a reactive site that allows continued systematic elaboration of the dendritic structure (Figure 1).

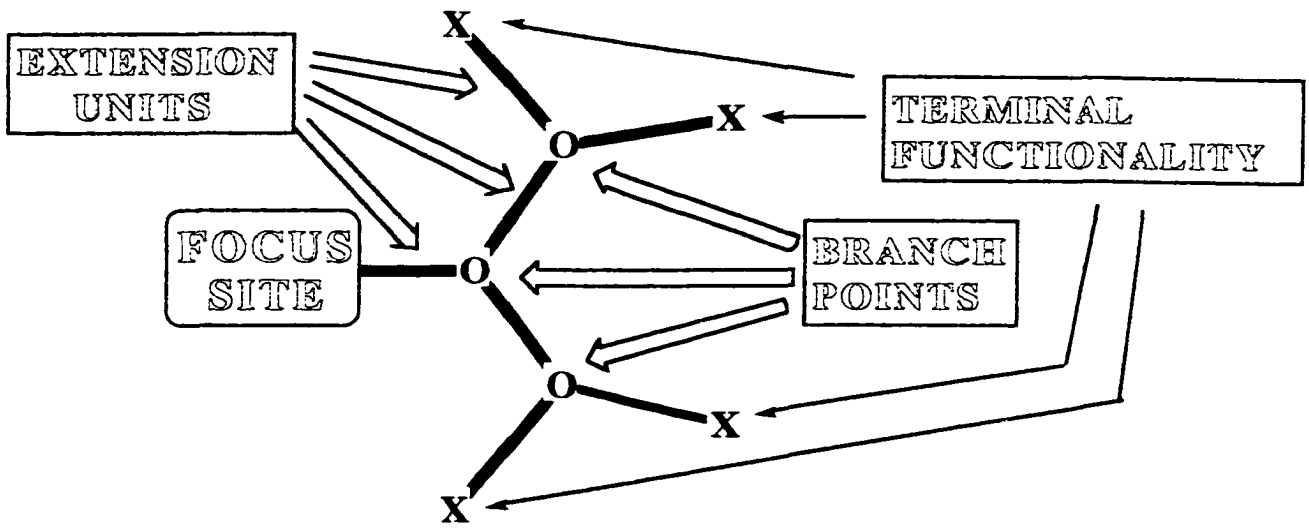


Figure 1

General structure of dendrimers - In addition to a focus site, dendrimeric structures contain branch points, extension units linking branch points, and terminal functionality.

Originally reported more than 10 years ago [1,2,3] the preparation of polyamine dendrimers elaborated to large generations (Scheme 1) consists of reiterative sequential Michael addition of acrylonitrile to each of several N-H linkages available, followed by reduction to new amino groups at the termini.

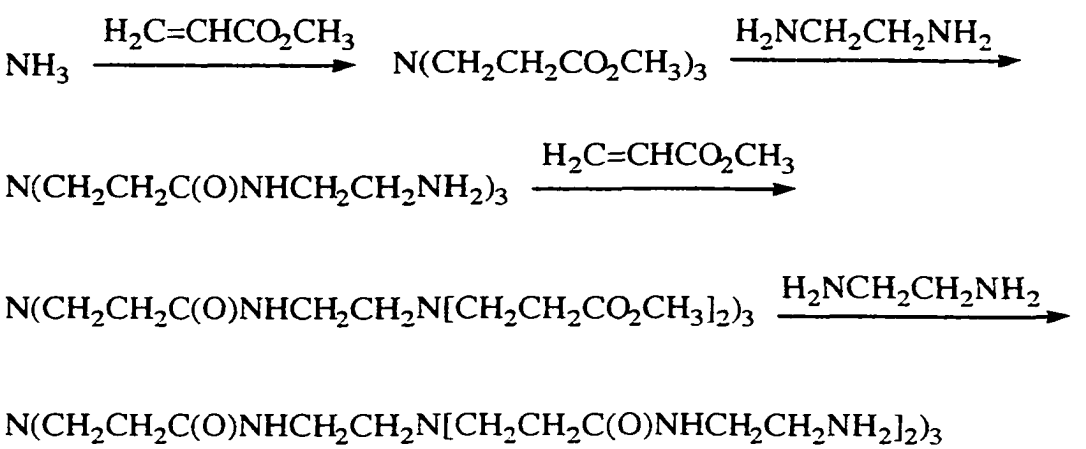
$$RNH_2 \xrightarrow{H_2C=CHCN} RN(CH_2CH_2CN)_2 \xrightarrow[CoCl_2]{NaBH_4} RN(CH_2CH_2CH_2NH_2)_2$$

$$\xrightarrow{H_2C=CHCN} RN(CH_2CH_2CH_2N[CH_2CH_2CN]_2)_2 \xrightarrow[CoCl_2]{NaBH_4}$$

$$RN(CH_2CH_2CH_2N[CH_2CH_2CH_2NH_2]_2)_2$$

Scheme 1

The construction of PAMAM (polyamidoamine) dendrimers has also been accomplished in a similar manner. [4-8] Starting with an amino or ammonia core, exhaustive Michael addition of methyl acrylate generates an esteric product upon which ester-amide interchange is performed with ethylenediamine. The new termini are "R-NH_2" sites upon which exhaustive Michael addition may again be performed for continued elaboration of the dendrimer (Scheme 2).



Scheme 2

Efforts by co-workers in this laboratory were directed toward incorporating cationic ammonium and phosphonium sites within the covalent dendrimeric structure. Nitrogen has the potential of serving as a branch point of a dendrimer structure while bearing four carbon substituents and a positive charge. Triethanolamine was used as the

fundamental building block for the construction of such ammonium dendrimers. Upon alkylation of triethanolamine with an ordinary haloalkane, a "balloon" type structure could be generated, expanding in three directions from the core and from each of the branch points (Figure 2).

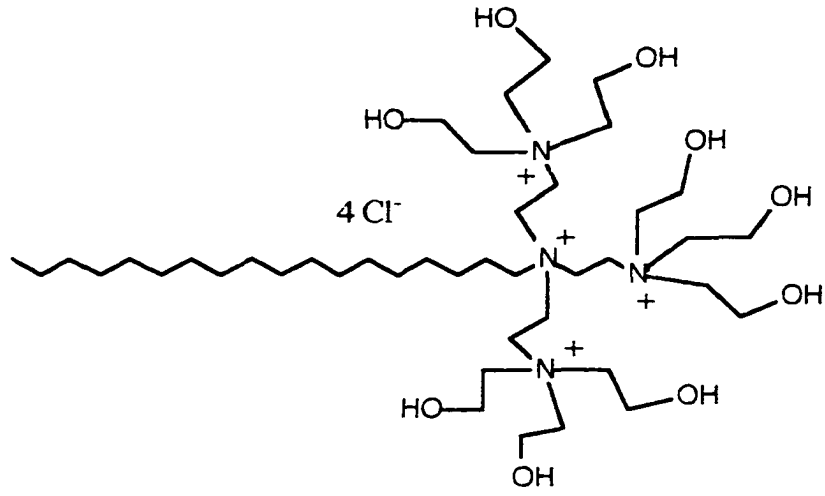


Figure 2

Example of a "balloon" dendrimer - The ammonium sites are branch points about the focus site (long alkyl chain) with ethylene units as the extension units and terminal hydroxyl groups.

Similarly, initial alkylation of the triethanolamine core with 2-chloroethanol allows the construction of a "star" type dendrimer with spherical symmetry, capable of being elaborated in four directions from the core with each branch point being capable of expanding in three directions (Figure 3). [9,10]

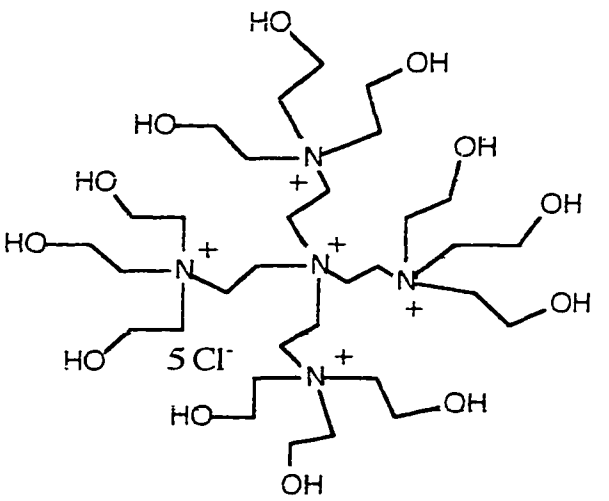


Figure 3

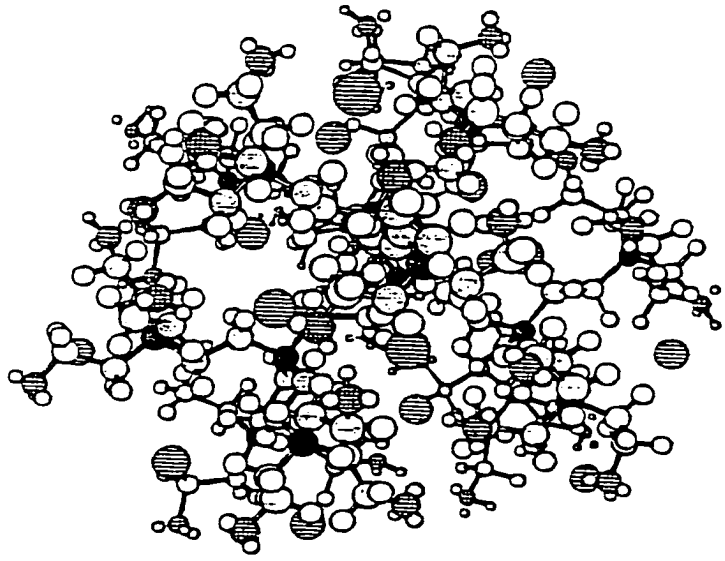
Example of a "star" dendrimer - The central ammonium ion site is the focus site, with ethylene units as extension units, additional ammonium ion sites as branch points, and hydroxyl groups as the termini.

Elaboration of these "star" and "balloon" dendrimers were performed in a stepwise manner, initially activating the terminal hydroxyl groups by conversion to tosylate esters followed by displacement with triethanolamine.

Changing the terminal functionality modified the solubility of the polyammonium dendrimers. For example, with hydroxyl groups at the termini, significant water solubility (and hydroscopic character) was maintained throughout the elaboration to higher generation stages (incorporating up to 40 positive charges in an individual molecule). At

the same time, moderate solubility in "organic" solvents such as acetonitrile was maintained at a level sufficient to allow measurement of NMR spectra. Acylation of the terminal hydroxyl groups results in a negligible decrease in water solubility and organic solubility increases significantly. [11] In addition, molecular modeling of the "star" and "balloon" dendrimers indicated that the "free-floating" anions (chloride, fluoride, and nitrate) were associated with the surface of the dendrimer structure rather than being intercalated within the cationic arms (Chem 3D+™). A representation of the modeled dendrimer species is illustrated in Figure 4 for the second generation "star" dendrimer derived from triethanolamine.

(a)



(b)

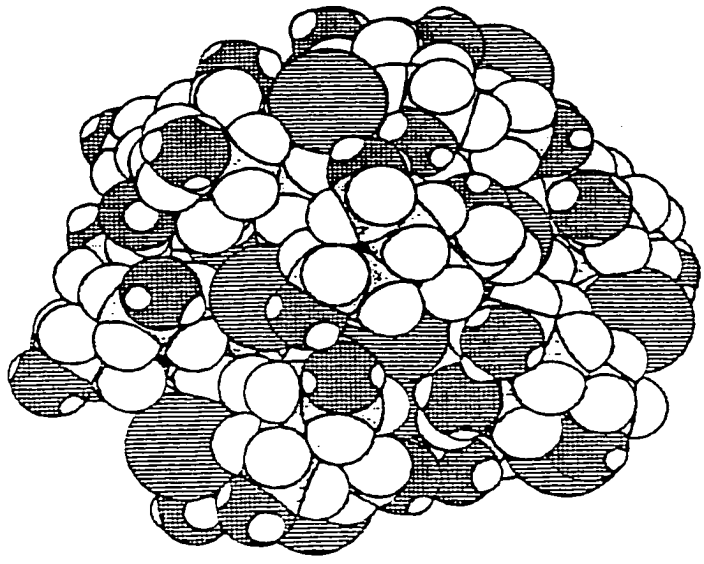
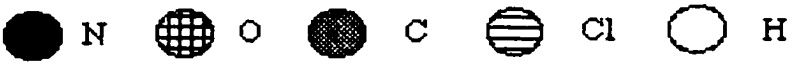


Figure 4

Modeled second generation "star" dendrimer - Chem 3D+™ energy-minimized (local minimum) views of the second-generation "star" polyammonium dendrimer

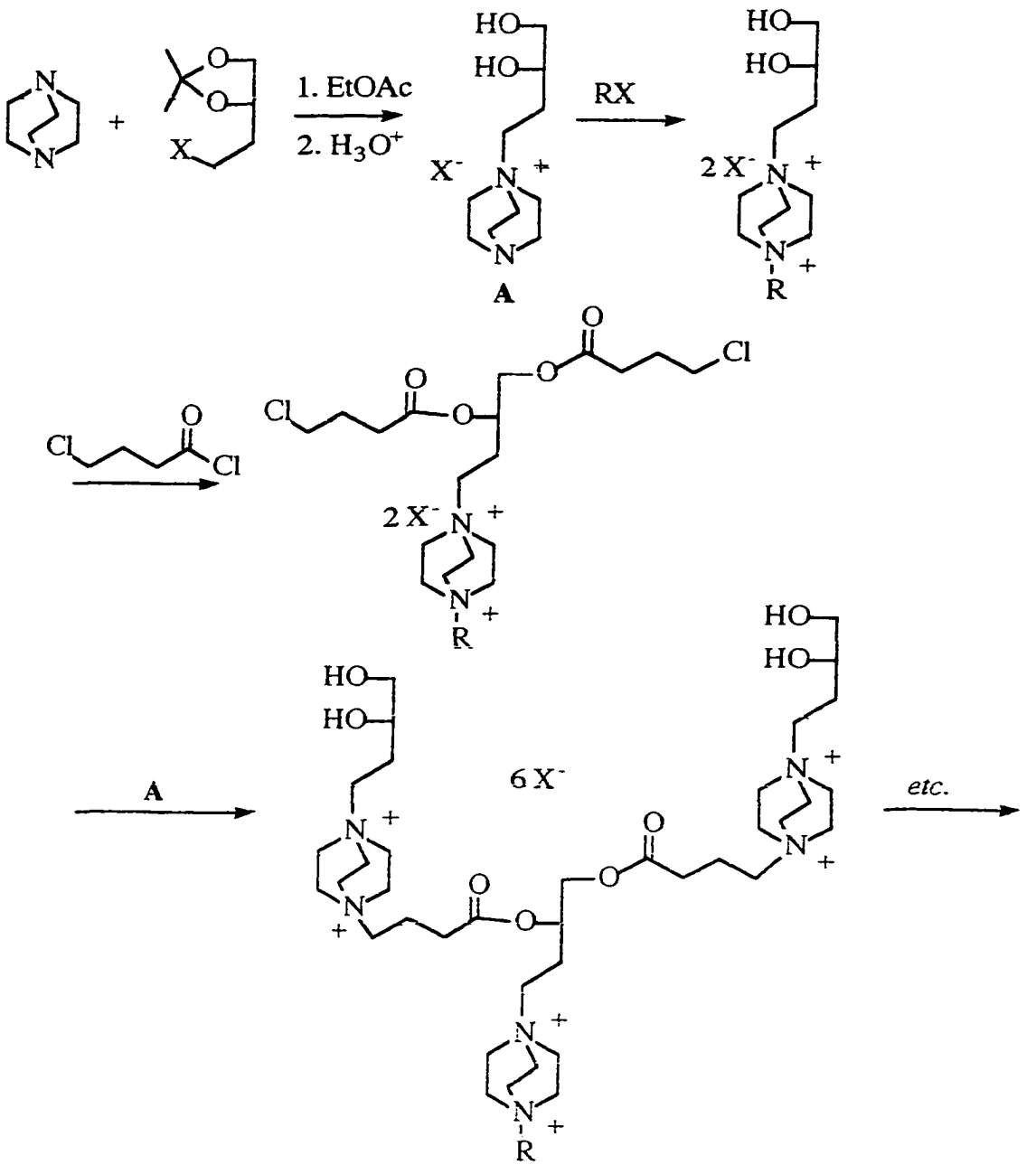
based on triethanolamine - (a) Ball-and-stick presentation showing the distortions of the internal N-C-C and C-C-H bond angles of the covalent structure; (b) Space-filling presentation indicating location of the chloride anions at the surface of the covalent structure. Atom types are as shown below.



Dendrimers derived from triethanolamine incorporate multiple charged sites that are located in close proximity to each other within the covalent structure. In effect, since the anions do not have sufficient space within the arms of the dendrimer to stabilize these charges, the interior of the covalent structure becomes distorted and undergoes facile cleavage (Hofmann-type elimination) to relieve this strain. As a result, although these materials can be purified for analyses, they decompose within a short period of time, a few months even when stored below 0°.

Further efforts in this laboratory concerned with the syntheses of ammonium dendrimers focused on the preparation of *chiral* ammonium dendrimers. [12,13] Incorporated as components of the extension units were quaternary ammonium sites. The use of 1,4-diazabicyclo[2.2.2]octane (dabco) with quaternization of both of its nitrogen centers provided the cationic sites for the dendrimer. This was achieved at one end with a derivative of (*S*)-1,2,4-butanetriol. The

(*S*)-1,2,4-butanetriol provided the stereogenic branch point for the newly prepared chiral dendrimer. Shown in Scheme 3 is the general approach for the synthesis of this series of compounds.



Scheme 3

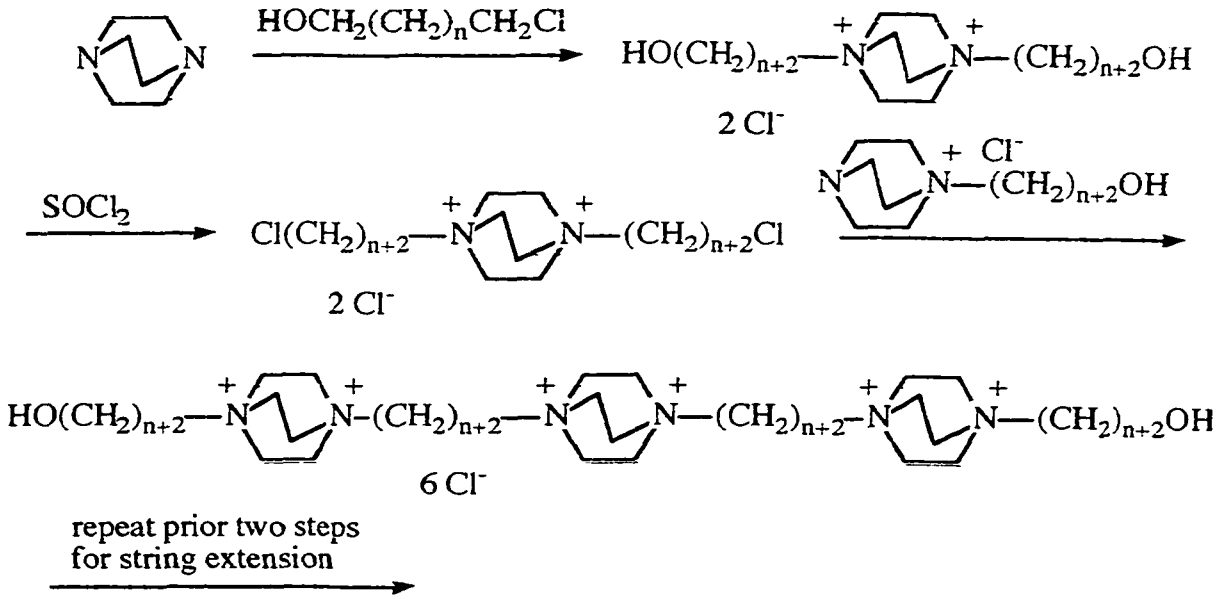
Using this approach, a series of chiral polyammonium dendrimers have been synthesized bearing up to 14 ammonium ion sites and 7 defined stereogenic sites in the covalent structure. [14]

Interestingly, the optical rotation under standard conditions of measurement does not change significantly upon increasing the number of stereogenic sites. Seebach, et al [15] have also observed this phenomenon with the synthesis of a chiral *non-ionic* dendrimer. The simultaneous introduction of a significant increase in mass of the dendrimer with the introduction of new stereogenic centers results in a dilution of the optical effect. In addition, no conformational chirality would appear to be present.

POLYAMMONIUM STRINGS

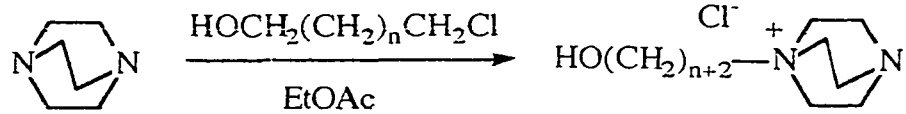
The construction of polycationic "string" species has also been accomplished. The rationale for these syntheses derived from consideration of potential interactions of such species with the polyanionic groove of double-stranded DNA. A polycationic string species is one in which cationic sites (ammonium sites) are located at regular intervals along a linear covalent structure, rather than a branching one (as in a dendrimer). The question was asked, "Could such a polycationic string wind about the helix by association with the anionic sites (phosphate diester/monoanion) of the major groove?"

To answer this, a series of such polyammonium string species, each bearing two to ten cationic sites, regularly spaced along the backbone of the covalent structure, again with free-floating anions, was prepared. Such defined polycations could be generated by a reiterative two-step process involving initial generation of an ammonium ion site by alkylation of a tertiary amine using an ω-halo-1-alkanol. This is followed by conversion of the terminal hydroxyl groups to halides in order to activate the "ends" of the string. Continued alkylation would then be accomplished. A generalized approach to the synthesis of such "strings" bearing dabco units as the source of ammonium sites is shown in Scheme 4. [16]



Scheme 4

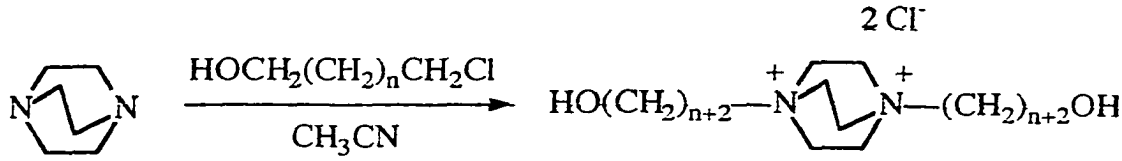
Construction of the monocationic "extension units" is accomplished by performing the reaction of dabco with one equivalent of an ω-halo-1-alkanol in ethyl acetate solution. Under these conditions the monocationic species precipitates immediately as it is formed and is readily isolated (Scheme 5).



Scheme 5

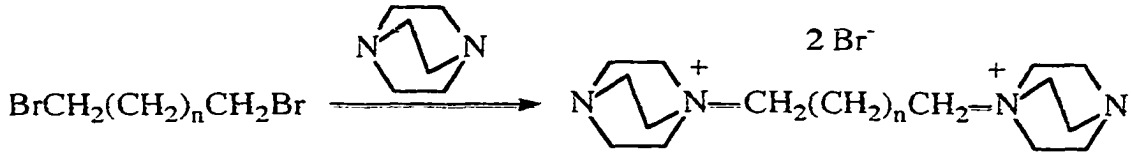
Construction of a series of dicationic strings have also been prepared by treating dabco with two equivalents of an ω-halo-1-alkanol in

acetonitrile. The solvent, acetonitrile, is used to keep the monocationic string in solution to allow quaternization of the second amine group to occur (Scheme 6).



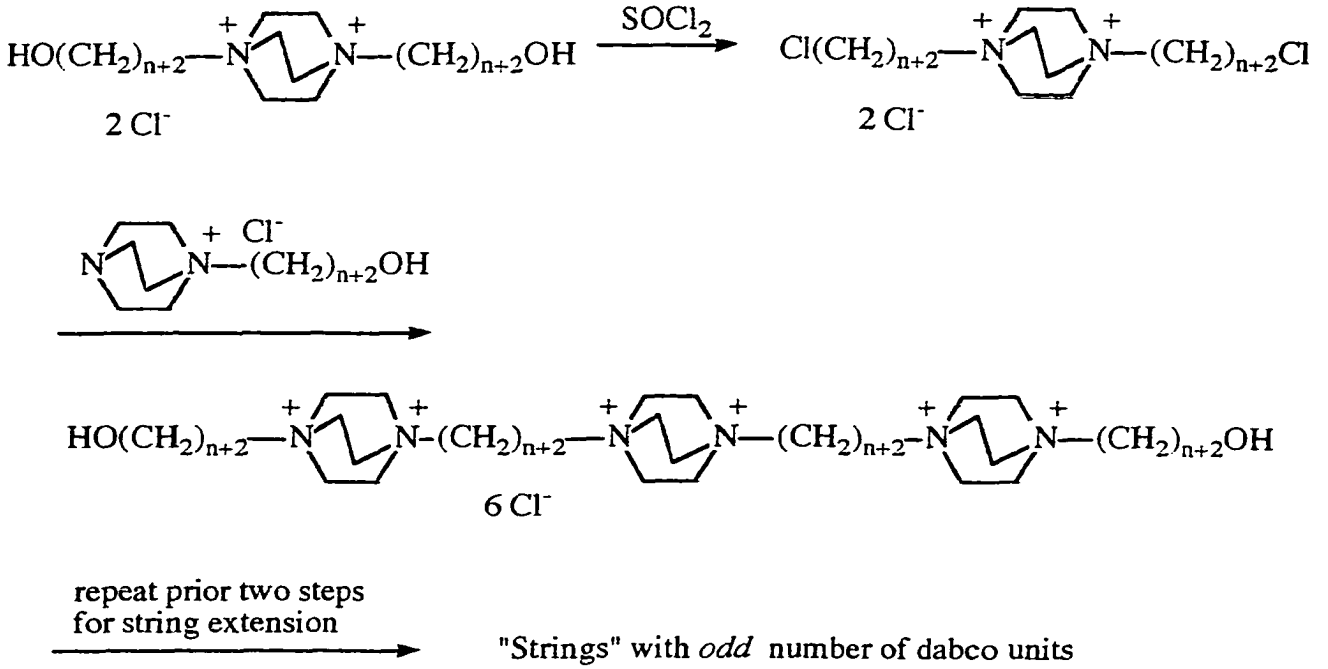
Scheme 6

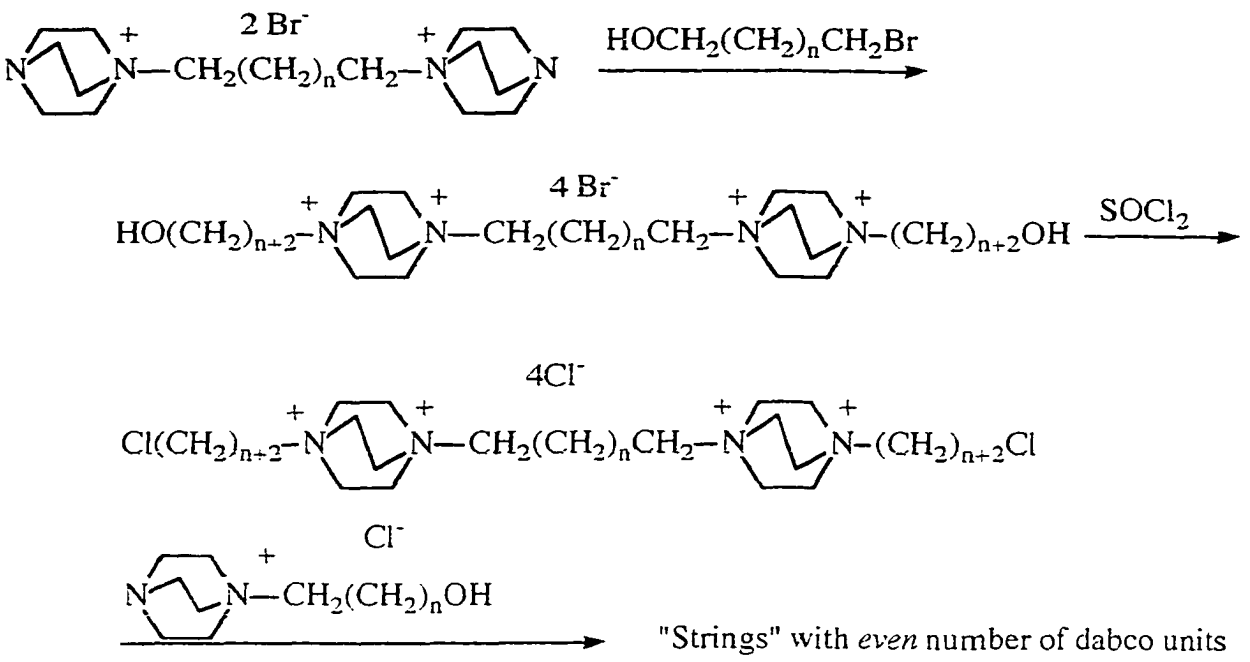
The construction of a series of dicationic strings bearing dabco units at the termini has also been prepared. These have been attained by treating an α,ω-dihaloalkane with an excess of dabco in acetonitrile (Scheme 7).



Scheme 7

The three series of cationic species allow elaboration of the string to give polycationic strings with either an odd or even number of dabco units (Scheme 8).





Scheme 8

Co-workers in this laboratory have resulted in the observation of significant antibacterial activity (*E. coli*) for several of these polycationic strings. [16-18] It is suspected that the polycationic strings increase the permeability of the outer membrane of the bacteria allowing the entrance of toxic substances and the loss of vital materials.

POLYCATIONIC COMBS

Elaboration of polycationic "strings" or dendrimeric "balloons" along an insoluble polymeric backbone provides polycationic "combs" or "comb-burst" species. Previous work in this laboratory used Merrifield's peptide resin (2% divinylbenzene/styrene crosslinked polymer which has been chloromethylated) as the backbone for the construction of the water-insoluble polycationic species which may serve as anion exchange materials. [19,20] After reaction of the parent resin with either an ω-hydroxyalkyl-substituted dabco or triethanolamine, elaboration of the string or balloon was accomplished by successive treatments with activating agent and appropriate ω-hydroxyalkyl-substituted dabco (or triethanolamine). Although complete elaboration of all reactive sites was not accomplished, very high capacities could be attained. With "balloon" type systems exchange capacities of as high as 13 meq/g could be achieved, as measured by both spectroscopic measurements of

picrylsulfonic acid exchange and ^1H NMR measurements of chloroacetate exchange. Investigation of the ion exchange capabilities of these materials indicated that the initially associated chloride ion could be exchanged readily with a variety of other monoanions (halide, nitrate, chloroacetate, tosylate), although some (conjugate bases of acids weaker than chloroacetic acid) could not be exchanged. Dianions, such as sulfate, could be taken up by the material, but not readily released. Molecular modeling of the species (Chem 3D+™) indicated that monoanions would be associated near the surface of the "balloon" but dianions could penetrate the arms of the cascade and be shielded from the water at the surface. Hydrocarbon "balloons" elaborated on the Merrifield resin, terminating in carboxylate groups provide relatively high capacity weak cation exchangers. [20] These materials rapidly exchange sodium, potassium, and silver ions.

RINGS

Another geometrically intriguing category of molecular species are rings that can surround a variety of guests. Selective recognition of guest molecules by synthetic receptors such as paracyclophanes, cyclodextrins, polyoxy- or polyamino- macrocycles and other ring structures has been extensively reported in the last few years. [21-23]

PARACYCLOPHANES

The preparation of a series of parayclophanes of the general structure (Figures 5 and 6) was first presented in 1959 by D.J. Cram and K. Dewhirst. [24]

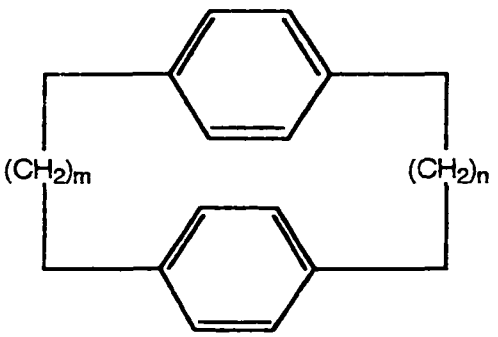


Figure 5
[m,n] paracyclophanes

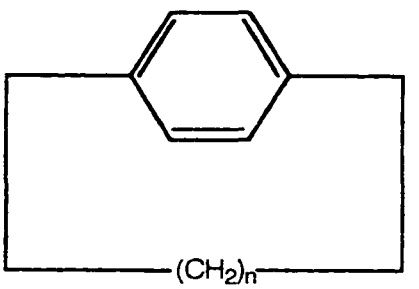


Figure 6
[n] paracyclophanes

The spectra and reactivity of compounds of structure as shown in Figure 5 vary as the distance between the two benzene rings is altered. [24,25] These effects have been interpreted in terms of transannular interaction of the p-electron clouds of the two aromatic nuclei with one another, as determined by the comparative interactions with tetracyanoethylene as shown in Figure 7. [26]

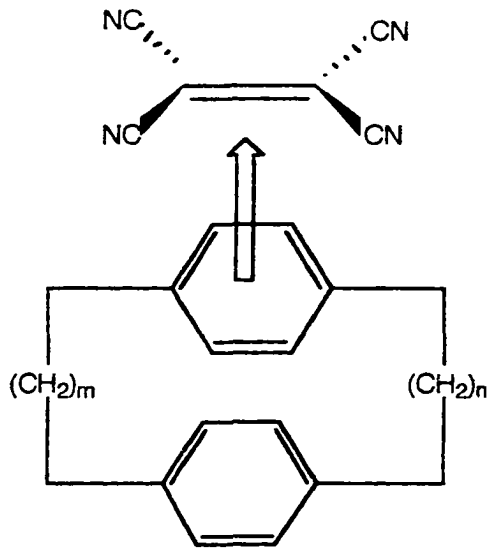


Figure 7
p-Interaction of a paracyclophane with TCNE

More than 40 years later chemists are still studying this intriguing class of host molecules. Recently, extensive experimental and theoretical studies of this category of supramolecular interaction, particularly with biological complexes (photosynthetic antennae and reaction centers), has been investigated. [27,28] These studies include the synthesis of a series of paracyclophane derivatives that hold chromophores of varying degrees of conjugation using palladium-mediated coupling reactions. [29] These molecules mimic solid-state interactions in main-chain polychromophores and conjugated emissive polymers. Their optical properties give insight into the energetics of photoexcitations localized in a discrete chromophore relative to a state containing the through-space delocalized

paracyclophane core. This optical response of chromophore aggregates provides an important tool in the studies of intermolecular interactions and bonding.

Others have investigated selective recognition of guest molecules by synthetic receptors through the formation of hydrogen bonds with the paracyclophane host. These studies have been performed mainly in lipophilic solvents because of the strong solvation of the interacting groups in polar media. [21-23]

Others have designed this class of host molecules for the selective recognition of anions, such as carboxylic acids or nucleotides, in aqueous solution. This is an important target in view of the biological relevance of studies in this solvent. [30-36] With this in mind, polyammonium macrocycles have been synthesized as they may behave as efficient receptors for polycharged anions in aqueous solution. [30-40]

Valtancoli, et al have reported on the synthesis and basicity properties of a polyamine paracyclophane macrocyle (Figure 8). [41]

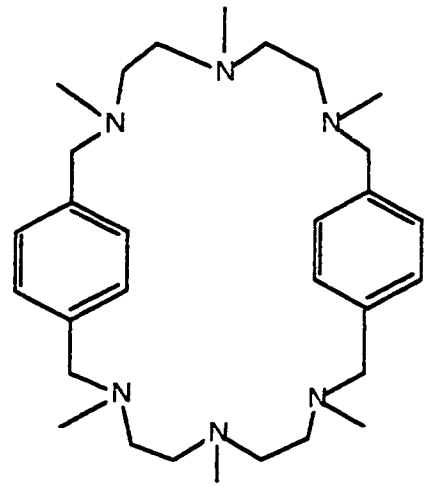


Figure 8
A polyamine paracyclophane macrocyle

Protonation of this paracyclophane occurs on the benzylic nitrogens and results in the formation of a species with a charge of 4+. This species is present in solution over a wide pH range.

The same group had also reported on the synthesis and protonation behavior of a paracyclophane containing aromatic moieties, short ethylenic chains connecting the amine groups, nitrogen methylation and piperazine rings (Figure 9). [42]

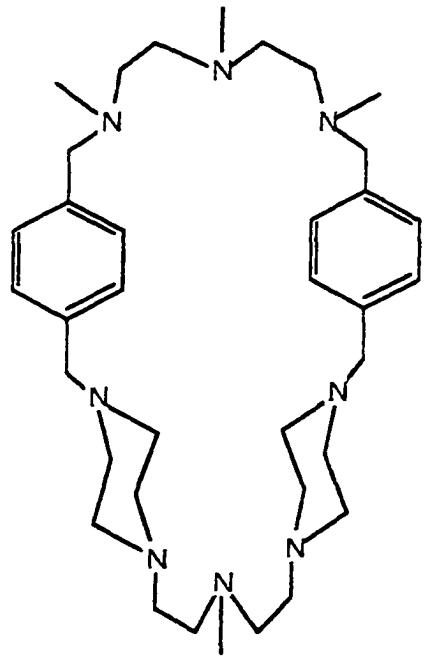


Figure 9
A paracyclophane containing piperazine moieties

The latter paracyclophane differs from the former by the presence of two piperazine rings within the macrocyclic host structure. The coordination of anionic guests can be achieved by using, as host species, polyprotonated forms of aza-paracyclophanes. [39] The binding properties of this preorganized receptor toward anionic species has been analyzed using ATP and ADP recognition. [42] The basicity properties of such a receptor are strictly related to its binding features and the study of their proton transfer behavior is a key step in the analysis of the binding characteristics toward anionic species. In this vein, potentiometric as well

as ^{1}H and ^{13}C NMR techniques have been used. [41]

With this in mind, our colleagues have been involved with the synthesis and investigations of *polycationic* paracyclophanes.

CYCLODEXTRINS

Cyclodextrins (CDs), also known as Schardinger dextrins, cycloamyloses, and cycloglucoamyloses, comprise a family of cyclic oligosaccharides obtained from starch by enzymatic degradation. They were discovered in 1891 by Villiers [43], but the first detailed description of the preparation and isolation was made in 1903 by Schardinger. [44]

There are numerous applications of CDs including their use as catalysts, as microvessels to perform chemical reactions, process aids, stabilizers of compounds, "masking effects" of a guest, a reducer of volatility of a guest, director of chemical reactions, controller of fluorescence and light absorption, an enzyme mimic, and as a drug carrier system. [45-50]

Investigation of cyclodextrin chemistry has been on the increase for several decades. The descriptions of the structure and properties of CDs and their applications have been the subject of several books [51-57], a number of review articles [58-74], more than 800 patents, and innumerable papers. This enormous effort in the study of CDs is a result

of the fact that such molecules have inherent interest, that is, their physical and chemical properties merit study.

The descriptions of the structure and properties of cyclodextrins explains why these relatively simple organic compounds exhibit complex formation with other organic molecules; acting as a *host* molecule. This is why they are excellent models of enzymes which led to their use as catalysts, both in enzymatic and nonenzymatic reactions; and they are natural products and readily available for most researchers.

Cyclodextrins are cycloamyloses, generally of 6,7, 8, or 9 carbohydrate units, respectively known as α,β, γ, or δ-CD, linked through the anomeric site (α-linkage) to the 4-position hydroxyl group. Cyclodextrins with 10-13 glucose units have also been identified by chromatographic methods. [75] CDs composed of less than six glucose units are not known to exist due to steric hindrance [76] and the 6-fold character of the starch helix. [77] As their appearance suggests in the cyclodextrin molecules, the glucose units, all in classical C1 chair conformation, are linked by α-1,4 bonds. [Figure 10]

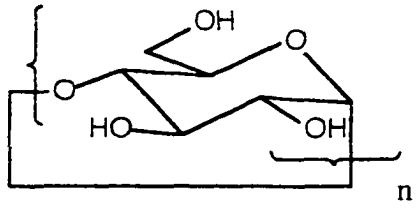


Figure 10
General structure of a cyclodextrin

This geometry gives the CD the overall shape of a truncated cone with the wider side formed by the secondary 2- and 3-hydroxyl groups and the narrower side by the primary 6-hydroxyl. [Figure 11]

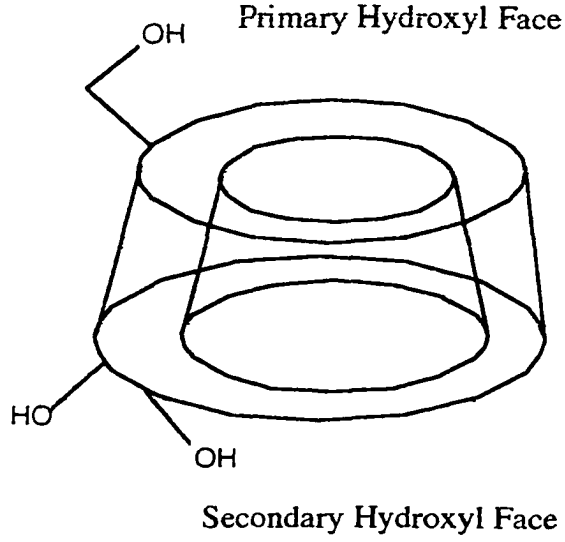


Figure 11
The cyclodextrin primary hydroxyls are located on the narrower edge of the truncated cone, while the secondary hydroxyls are located on the wider edge.

The number of glucose units determines the dimension and size of the cavity. [Figure 12]

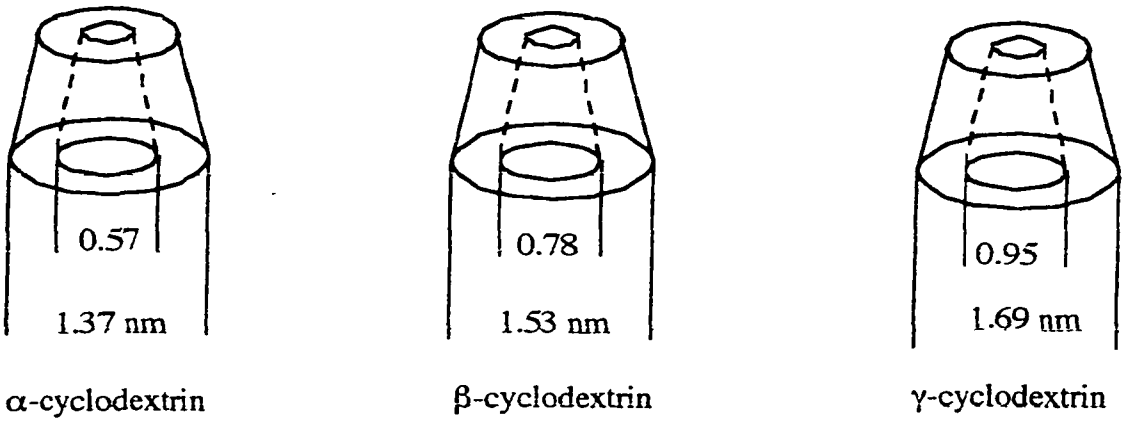


Figure 12
Dimensions and sizes of α, β,γ-CD's.

The cavity is lined by the hydrogen atoms and the glycosidic oxygen bridges. The nonbonding electron pairs of the glycosidic oxygen bridges are directed toward the inside of the cavity, producing a high electron density and lending it some Lewis base character. As a result of this special arrangement of the functional groups in the cyclodextrin molecules, the cavity is relatively hydrophobic, while the external faces are hydrophilic. In the cyclodextrin molecules a ring of hydrogen bonds is also formed intramolecularly between the 2-hydroxyl and the 3-hydroxyl groups of adjacent glucose units. This hydrogen bonding gives the CD a remarkably rigid structure.

As a consequence of these structural features, CDs have some unique physical and chemical properties. CDs are water-soluble with solubilities of 14.5, 1.85, and 23.2 g/100 mL for α–, β–, and γ-CD

respectively. Spectroscopic studies on CD in aqueous solution suggest that the conformation of CDs in solution is almost identical to their conformation in the crystalline state. CDs are stable in alkaline solutions; however, they are susceptible to acid hydrolysis. Under normal experimental conditions (pH higher than 3.5, and temperatures lower than 60°C), CDs are fairly stable. The most characteristic property of CDs is their remarkable ablity to form inclusion complexes with a wide variety of guest molecules ranging from organic or inorganic compounds of neutral or ionic nature to noble gases. An obvious requirement is that the guest molecules must fit into the cavity, even if only partially. Complex formation in solution is a dynamic equilibrium process which can be illustrated by eq 1, where CD is cyclodextrin, G is the guest molecule, and CD-G is the inclusion complex.

$$CD + G \rightleftharpoons CD\text{-}G \qquad (1)$$

The stability of the inclusion complex can be described in terms of a formation constant (K_f) or a dissociation constant (K_d) as defined in eqs 2 and 3.

$$K_f = [CD\text{-}G]/([CD][G]) \qquad (2)$$

$$K_d = 1/K_f = ([CD][G])/[CD\text{-}G] \qquad (3)$$

It has been generally accepted that the binding forces involved in the complex formation are (i) van der Waals interactions (or hydrophobic interactions) between the hydrophobic moiety of the guest molecules and the CD cavity; (ii) hydrogen bonding between the polar functional groups of the guest molecules and the hydroxyl groups of CD; (iii) release of high-energy water molecules from the cavity in the complex formation process; and (iv) release of strain energy in the ring frame system of the CD.

The geometric characteristics and the polarity of guest molecules, the medium, and temperature are the most important factors for determining the stability of the inclusion complex. Geometric rather than the chemical factors are decisive in determining the kind of guest molecules which can penetrate into the CD cavity. If the guest is too small, it will easily pass in and out of the cavity with little or no bonding at all. Complex formation with guest molecules significantly larger than the cavity may also be possible, but the complex is formed in such a way that only certain groups or side chains penetrate into the CD cavity.

The stability of an inclusion complex also depends on the polarity of the guest molecule. Only substrates that are less polar than water can form inclusion complexes with CDs. The stability of a complex is

proportional to the hydrophobic character of the guest molecule. Highly hydrophilic molecules complex very weakly or not at all.

Complexing ability can also be improved by chemically modifying the CD molecules. CDs can be modified by (i) substituting for the H atom of the primary or secondary hydroxyl groups, (ii) substituting for one or more primary and/or secondary hydroxyl groups, (iii) eliminating the hydrogen atoms of the $-CH_2OH$ groups (i.e. by conversion to -COOH), or (iv) splitting one or more C_2-C_3 bonds through a periodate oxidation.

As a result of complex formation, the characteristic properties of the guest substance, such as solubility [78,79], chemical reactivity [59,80], pK_a values [81,82], diffusion [54,83], electrochemical properties [84-87], and spectral properties [88-97] will be changed.

Cyclodextrins have served as prototypes for novel host compounds and catalysts. The use of CDs as *microvessels* to perform chemical reactions has attracted the interest of chemists since the 1960's. [98-99]

The effects of CDs on organic reactions are divided mainly into two types. The first is the effect on covalent bonds where the reaction proceeds according to Michaelis-Menten type kinetics. CD and the reactant intially form a [CD-reactant] reaction intermediate involving a covalent bond which then leads to the product. These catalytic effects have been studied and reported as the "enzyme model". The second

effect does not involve a covalent bond. The hydrophobic cavity of the CD gives the reactant access to a new reaction environment, an "extra reaction field" in which the reactivity, such as rate or selectivity, changes. The role of the CD is not always defined as catalyst. In these instances, the CD mediates the reactions. Most of our understanding of CD inclusion phenomena has been derived from studying an aqueous system in an equilibrium state. In this state, the hydrophobic forces are assumed to be responsible for driving a guest into the CD's hydrophobic interior, where a 1:1 host-guest complex usually forms and where there is no interaction with other CD molecules.

Cyclodextrins, being enantioselective, are used as drug carrier systems. The most common pharmaceutical application of CDs is to enhance the solubility, stability, and bioavailability of drug molecules. [57,100-102] However, natural cyclodextrins have relatively low solubility, both in water and organic solvents, which limits their uses in pharmaceutical formulations. Chemists have recently prepared various CD derivatives so as to extend the physicochemical properties and inclusion capacity of natural cyclodextrins as novel drug carriers. [103-105] Among the desirable properties of a drug carrier is that the carrier itself be bioadaptable. The second desirable attribute for the drug carrier is the ability to control the rate and time of drug release. Amphiphilic or

ionizable CDs can modify the rate or time of drug release and bind to the surface membrane of cells, which may be used for the enhancement of drug absorption across biological barriers. The final requirement of a drug carrier is its ablity to deliver a drug to a targeted site; conjugates of a drug with CDs partially fulfill this requirement. Thus, CDs have significant potential as drug carriers in advanced dosage forms; however, most of them are only at the beginning of safety evaluation. The future should see a growth in the number of commercial products using CD-based formulation. [45]

Cyclodextrins are extremely attractive components of artificial biocatalysts and other biomimetic materials. [46] They are readily available, they bind hydrophobic substrates into their cavities in water solution, and they have two rims of hydroxyl groups that can either react with substrates themselves or be used to attach other catalytic and functional groups. Interest in CDs as components of enzyme models was first stimulated with the publication of the book *Einschlussverbindungen* (Inclusion Compounds). [106] Since the CD is used to bind a substrate, such species can be considered to be *artificial enzymes.* These catalysts generally show substrate specificity, for molecules that can bind into the CD cavity. [47]

There are numerous industrial applications of CDs. These include

its selected use in foods such as cinnamon-flavored apples, flavored tea, peppermint-flavored chewing gum, mustard oil steak sauce, lemon and grapefruit candies, vitamin B fruit juice beverage, lemon-flavored sugar, and processed cheeses as a flavor stabilizer, flavor deliverer, its masking of bitterness and of vitamin odor, an absorbant of odor, in the removal of cholesterol, in cosmetics and personal care items such as artificial tanning lotion, powdered hair bleach, perfume, cold cream and skin cleanser in its masking of odor, prolonged release, and stability and in laundry drier sheets as a fragrance control. [107]

At this point we begin our work toward the synthesis of a variety of cyclodextrin derivatives.

RESULTS AND DISCUSSION

POLYCATIONIC STRINGS

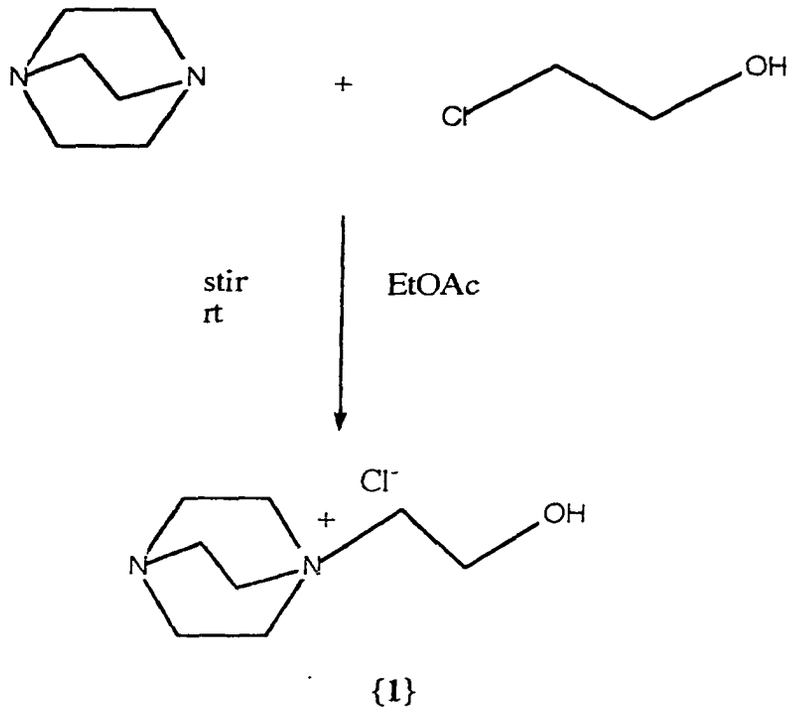
Polyammonium organic salts are an intriguing category of compounds that have been receiving particular interest in recent years. Potential applications for such highly charged, water soluble organic materials include serving as models for the investigation of biological supramolecular interactions, acting as antihydrophobic agents, and use as polyelectrolytes.

The preparation and investigation of ionene polymers has been a topic of interest for some time. [108] Ionene polymers, produced by the reaction in DMF solution of dihalides with diamines, bear quaternary ammonium ion sites at regular intervals along chains of indefinite length. Prior efforts of this laboratory have been directed toward the synthesis of non-branching (string) polycations of *defined* size and charge. [12]

Polycationic strings, salts having cationic sites located at regular intervals along a linear chain of defined length, have potential for a variety of applications. One such potential application for these highly charged organic materials is to serve as antihydrophobic agents which would increase the aqueous solubilities of otherwise relatively insoluble organic solutes. [109-113]

With this structural concept in mind, the synthesis of a series of

polycationic strings based on dabco (1,4-diazabicyclo[2.2.2]octane) units has been undertaken by our laboratory. [114] All new compounds exhibit NMR spectra in accord with their proposed structures and elemental combustion analyses in accord with hydrated forms of the proposed structures. The preparation of a *monocationic* string, 1-(2'-hydroxyethyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride {1}, previously prepared by our laboratory is shown in Scheme 9.



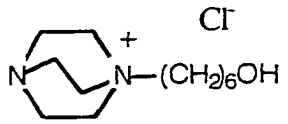
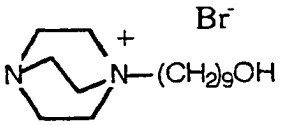
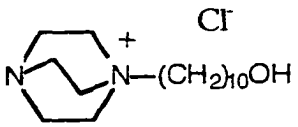
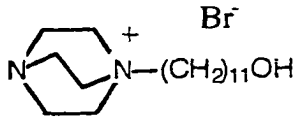
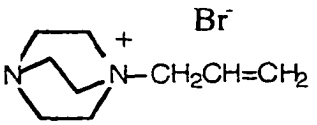
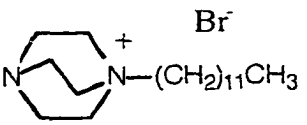
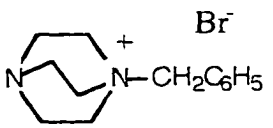
{1}

Scheme 9

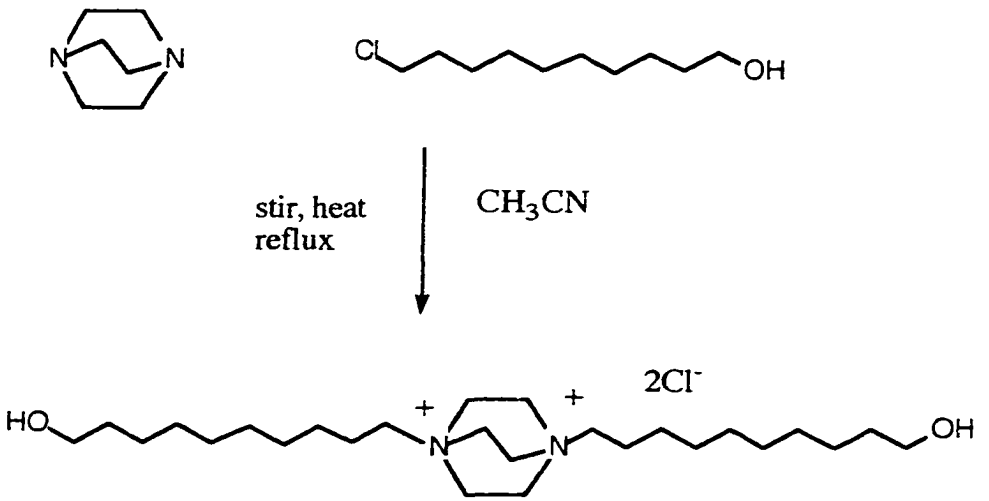
In this synthesis dabco is treated with one equivalent of 2-chloro-1-ethanol in ethyl acetate solution. The reaction mixture is stirred at room

temperature to give the monocationic salt as a precipitate. The solvent, ethyl acetate, is chosen for the synthesis of monocationic strings because precipitation occurs upon quaternization of the first tertiary amine to give the target product. Under conditions similar to these a series of *new* monocationic strings {3, 5, 6, 7, 8, 10, 11} have been synthesized, as shown in Table 1 . Previously, others in the same laboratory have prepared related monocationic strings including 1-(3-hydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride {2}, 1-(8-hydroxyoctyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride {4}, and 1-(4-butenyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide {9}.

Table 1 - New Monocationic Strings

Structure	Number	Name
	**3**	1-(6-hydroxyhexyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride
	**5**	1-(9-hydroxynonyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	**6**	1-(10-hydroxydecyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride
	**7**	1-(11-hydroxyundecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	**8**	1-(3-propenyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	**10**	1-(dodecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	**11**	1-(benzyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide

As shown in Scheme 10, a series of *dicationic dabco-based* strings have also been prepared.

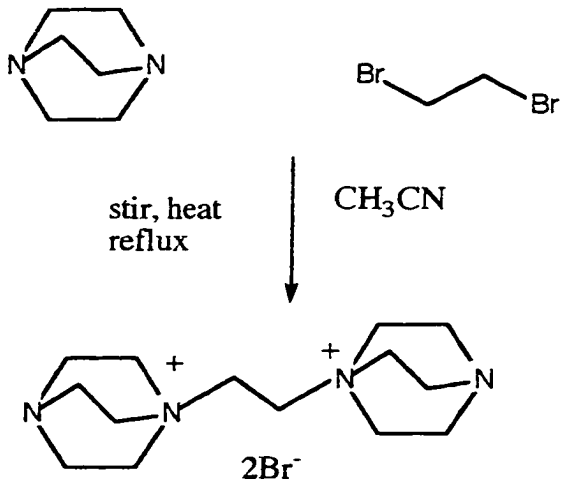


{12}

Scheme 10

The dicationic string 1,4-bis(10'-hydroxydecyl)-1,4-diazoniabicyclo[2.2.2]octane dichloride {12} is synthesized by treating one equivalent of dabco with two equivalents of 10-chloro-1-decanol in acetonitrile solution. The reaction mixture is heated and stirred at reflux. For the synthesis of the series of dabco-based dicationic strings, acetonitrile is used as the solvent to allow quaternization of the second amine to occur in solution without precipitation of the monocationic salt. [16]

Similarly, *didabco dicationic* strings have also been previously prepared by others in our laboratory as shown in Scheme 11.

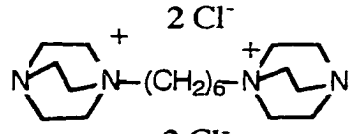
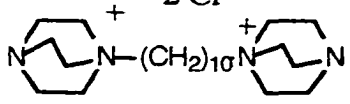
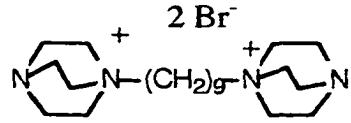
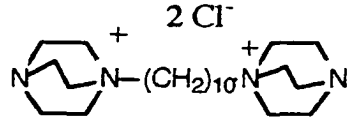
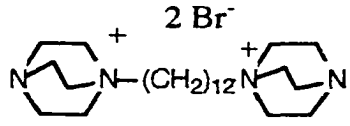
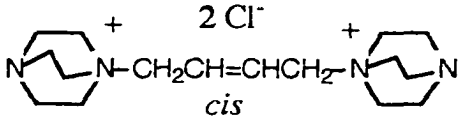
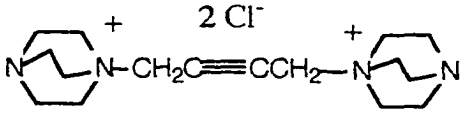


{13}

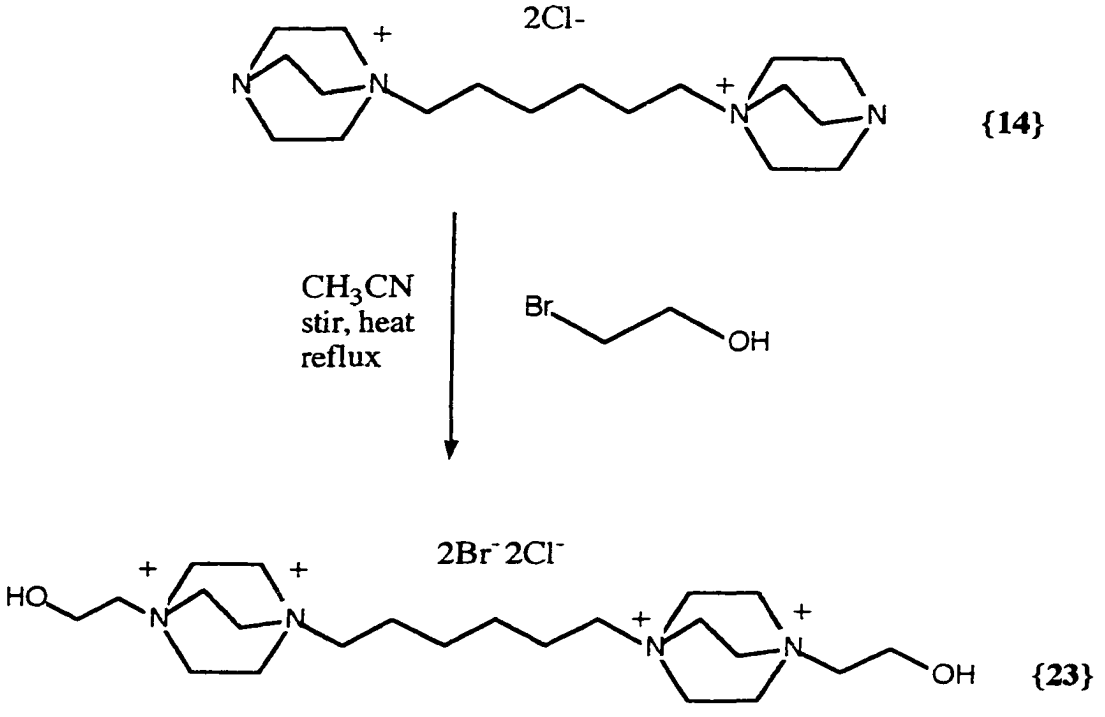
Scheme 11

The dicationic didabco string 4-(2'-{1"-azonia-4'-azabicyclo[2.2.2]octyl}-1'-ethyl)azonia-1-azabicyclo[2.2.2]octane dibromide {13} is prepared by treating four equivalents of dabco (an excess) with 1 equivalent of 1,2-dichloroethane in acetonitrile. The reaction mixture is heated and stirred at reflux and the product is isolated by filtration from the reaction medium. The remaining examples of the series of newly prepared salts {14}-{20} in this category are shown in Table 2.

Table 2 - New Dicationic Didabco Strings

Structure	Number	Name
	**14**	4-(6'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-hexyl)azonia-1-azabicyclo[2.2.2]octane dichloride
	**15**	4-(8'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-octyl)azonia-1-azabicyclo[2.2.2]octane dichloride
	**16**	4-(9'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-nonyl)azonia-1-azabicyclo[2.2.2]octane dibromide
	**17**	4-(10'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-decyl)azonia-1-azabicyclo[2.2.2]octane dichloride
	**18**	4-(12'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-dodecyl)azonia-1-azabicyclo[2.2.2]octane dibromide
	**19**	4-(10'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-decyl)azonia-1-azabicyclo[2.2.2]octane dichloride
	**20**	4-(4'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-(Z)-2'-butenyl)azonia-1-azabicyclo[2.2.2] octane dichloride

The above three series of strings (monocationic, monodabco dicationic and didabco dicationic) are used as building blocks for more elaborate string syntheses. An example of the use of the strings for further synthesis is shown in Scheme 12.



Scheme 12

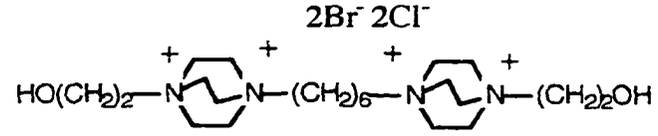
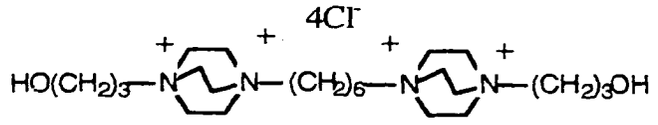
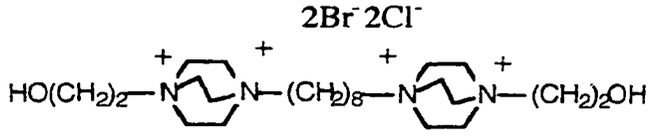
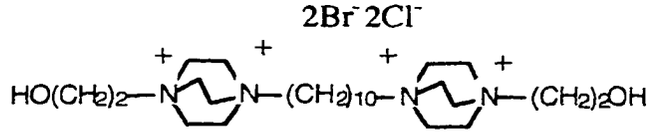
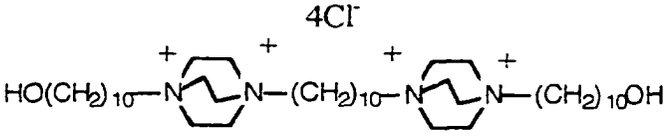
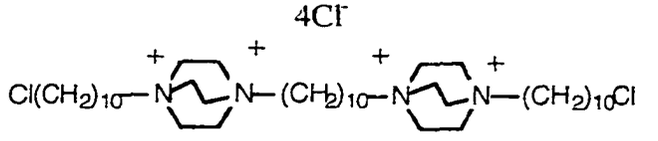
When {14} is treated with two equivalents of 2-bromo-1-ethanol in acetonitrile a *tetracationic* didabco string is generated as with 1-(β-hydroxyethyl)-4-(6'-{4"-(β-hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride {23}.

Previously, others in the laboratory have prepared two tetracationic didabco strings, 1-(β-hydroxyethyl)-4-(2'-{4"-(β-hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-ethyl)-1,4-diazoniabicyclo[2.2.2]octane tetrabromide, {21}, and 1-(β-hydroxyethyl)-4-(3'-{4"-(β-hydroxyethyl)-

1",4"-diazoniabicyclo[2.2.2]octyl}-1'-propyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride, {22}.

The series of newly prepared salts {23}-{28} in this category are shown in Table 3.

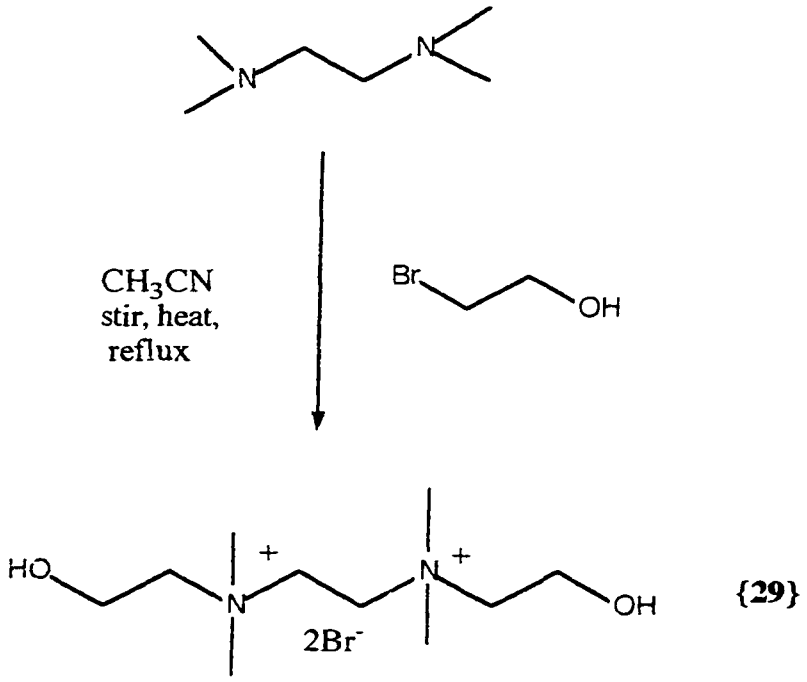
Table 3 - New tetracationic didabco strings

Structure	Number	Name
	**23**	1-(2-hydroxyethyl)-4-(6'-{4''-(2-hydroxyethyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride
	**24**	1-(3-hydroxypropyl)-4-(6'-{4''-(3-hydroxypropyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride
	**25**	1-(2-hydroxyethyl)-4-(8'-{4''-(2-hydroxyethyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-octyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride
	**26**	1-(2-hydroxyethyl)-4-(10'-{4''-(2-hydroxyethyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-decyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride
	**27**	1-(10-hydroxydecyl)-4-(10'-{4''-(10-hydroxydecyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-decyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride
	**28**	1-(10-chlorodecyl)-4-(10'-{4''-(10-chlorodecyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-decyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride

didabco strings, 1-(β–hydroxyethyl)-4-(2'-{4"-(β–hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-ethyl)-1,4-diazoniabicyclo[2.2.2]octane tetrabromide,{21} and 1-(β–hydroxyethyl)-4-(3'-{4"-(β–hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-propyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride, {22}.

Compound {28} was synthesized by treating the corresponding alcohol {27} with thionyl chloride in chloroform. Activation of the hydroxyl group thus allows further elaboration of {28} with a nucleophile to extend the chain.

A series of new dicationic strings have also been prepared using *N,N,N',N'*-tetramethylene diamine in reaction with a variety of ω–chloro-1-alkanol units. The preparation of a representative member of this category, 4,4,7,7-tetramethyl-4,7-diazoniadecan-1,10-diol dibromide, {29}, is shown below in Scheme 13.



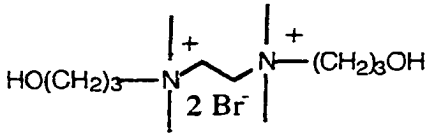
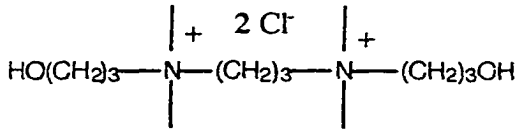
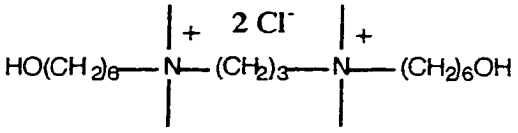
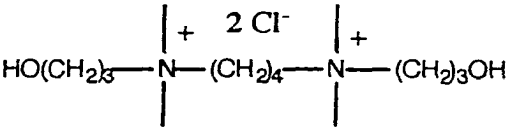
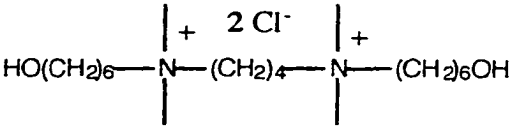
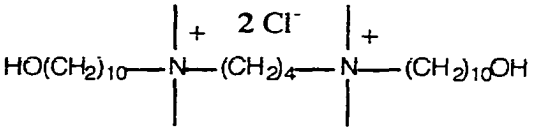
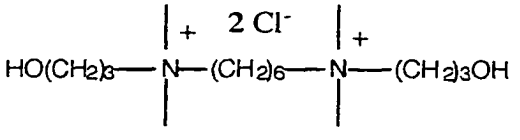
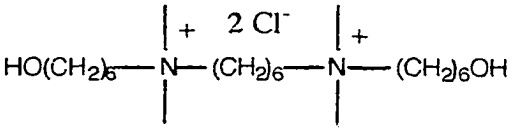
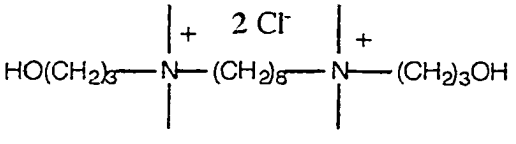
{29}

Scheme 13

A solution of *N,N,N',N'*-tetramethylethane diamine in acetonitrile is treated with two equivalents of 2-bromo-1-ethanol to give the new dicationic tetramethyl diamine string, {29}.

The series of newly prepared salts {29}-{37} in this category are shown in Table 4.

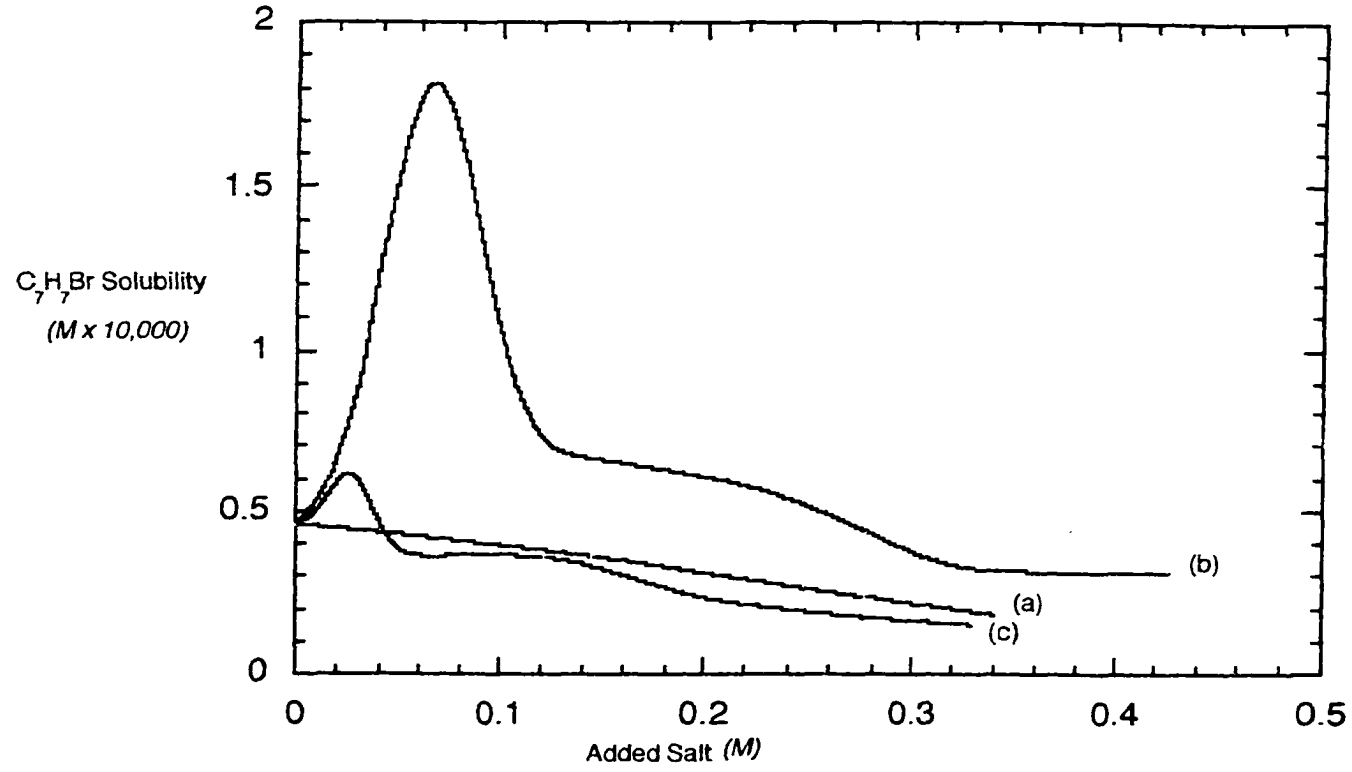
Table 4 - New dicationic tetramethyl diamine strings

Structure	Number	Name
	29	4,4,7,7-tetramethyl-4,7-diazoniadecan-1,10-diol dichloride
	30	4,4,8,8-tetramethyl-4,8-diazoniaundecan-1,11-diol dichloride
	31	7,7,11,11-tetramethyl-7,11-diazoniaheptade 1,17-diol dichloride
	32	4,4,9,9-tetramethyl-4,9-diazoniadodecan-1,12-diol dichloride
	33	7,7,12,12-tetramethyl-7,12-diazoniaoctadec 1,18-diol dichloride
	34	11,11,16,16-tetramethyl-11,16-diazonia-hexaeicosan-1,26-diol dichloride
	35	4,4,11,11-tetramethyl-4,11-diazoniatetra-decan-1,14-diol dichloride
	36	7,7,14,14-tetramethyl-7,14-diazoniaeicosan-1,20-diol dichloride
	37	4,4,13,13-tetramethyl-4,13-diazoniahexadec 1,16-diol dichloride

The effects of the polycationic strings on the solubility of weakly polar non-ionic organic substances in aqueous solution have been determined

using NMR spectrometry. [114] Sodium pivaloate, used as an internal reference material, was dissolved in deuterium oxide to a defined concentration. A saturated thermally equilibrated sample of 4-bromotoluene in this reference medium was then investigated by comparative integration of the ^1H AA'BB' signal of the 4-bromotoluene relative to the upfield singlet of the pivaloate anion to determine the solubility of the 4-bromotoluene. Salts were then added to the solution in the presence of an excess of the 4-bromotoluene and the solution reequilibrated, noting the effect of these changes on the relative integrations of the AA'BB' signal and the pivaloate anion signal. For the baseline determination, weighed quantities of NaCl were added to the solution, while for investigations of the antihydrophobic effect of the polycationic strings the exact amount of salt added was determined by integration of the ^1H NMR signals of the salts.

With added NaCl the anticipated "normal" decrease in solubility of a hydrophobic substance (4-bromotoluene) is observed upon increasing the ionic strength of the medium. This decrease in solubility is indicated in Figure 13 with the curve shown as curve (a).



(a) **NaCl**, (b) **{21}**, and (c) **{23}**

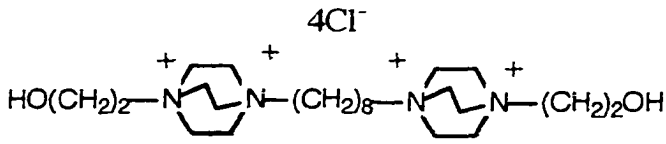
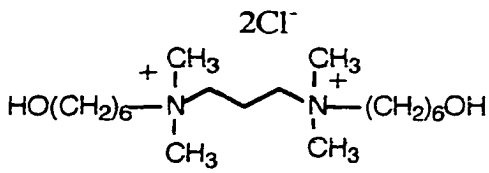
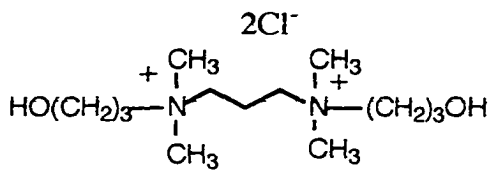
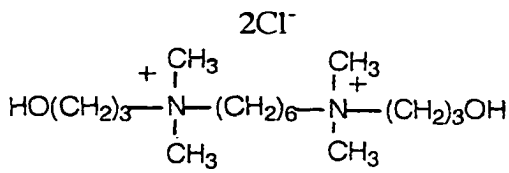
Figure 13 - Variation in 4-Bromotoluene Aqueous Solubility with Changing Salt Concentration

Such a phenomenon is the result of water-ion interactions which increase the ΔG° for cavity formation to accommodate a non-water-binding solute. [115]

For added polycationic string salts the solubility of the hydrophobic material was determined in the same manner. In general, for the range of polycationic salts investigated, an increase in aqueous solubility for the hydrophobic test substance was noted at low concentrations of added polycationic string. The increase of 4-bromotoluene aqueous solubility

upon addition of a selection of polycationic string species to particular concentrations is indicated in Table 5.

Table 5 - Aqueous Solubility of 4-Bromotoluene as a Function of Selected Added Salts

Salt	Concentration	C_7H_7Br Solubility
None	--	4.6×10^{-4} *M*
NaCl	0.342 *M*	1.8×10^{-4} *M*
	0.0036 *M*	1.3×10^{-3} *M*
	0.0275 *M*	2.0×10^{-3} *M*
	0.0071 *M*	1.0×10^{-3} *M*
	0.0096 *M*	1.1×10^{-3} *M*

The antihydrophobic effect noted (salting-in effect) is understood to be a result of a direct "bridging" interaction between the water and the hydrophobic solute. [109-113] The polycationic strings, bearing both those regions which do not have a favorable ΔG° for interaction with water (hydrophobic) and those which, being ionic, *do* have a favorable ΔG° for

interaction with water, serve to associate favorably with both solute and solvent. It would *not* appear that the antihydrophobic effect observed here is the result of aggregate formation and encapsulation of solute, as would be found with a typical detergent effect. The antihydrophobic agent involved herein is: 1) completely soluble in the aqueous medium rather than forming a bilayer or micelle, and 2) is structurally quite different from typical detergents with localized hydrophobic and hydrophilic regions, but structurally similar to dicationic "geminis" (*vide infra* p.55). The antihydrophobic effect of the polycationic strings is understood to be much closer to that of a small alcohol or polyol, serving as a "bridge" between the polar water and the non-polar hydrophobic solute.

It was observed that upon continued addition of polycationic string salt species to the aqueous medium, the solubility of the 4-bromotoluene began to decrease. (A similar decrease was noted in studies using benzene.) This variation in solubility with changing polycationic salt concentration is illustrated in Figure 13 for added {21}. The variation is shown in the curve indicated as curve (b), and as curve (c) for added salt {25}.

A large increase in ionic strength, and thereby the water-ion interactions which increase the ΔG° for cavity formation to accommodate a non-water-binding solute [115], is attendant with increasing

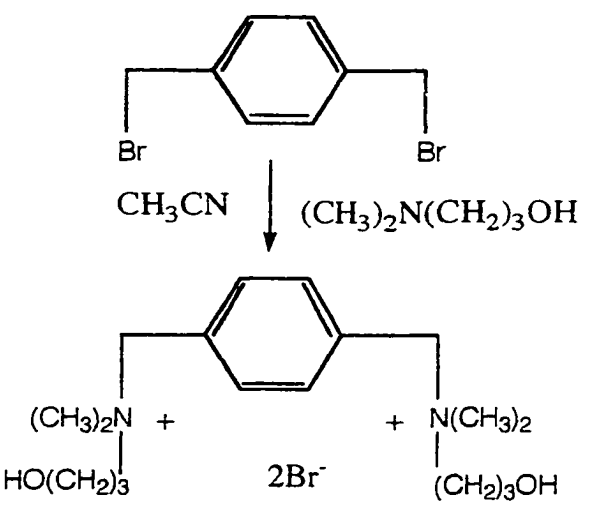
concentration of the polycationic species. At higher concentrations of the polycationic salts, the bridging antihydrophobic effect of the "organic-like" cationic species is overcome by the rapidly increasing effect of the "salting-out" process, primarily due to the (more rapidly increasing) number of associated anions.

The polycationic string species clearly exhibit a significant antihydrophobic effect, increasing the aqueous solubility of hydrophobic organic materials.

An additional intriguing system for possible interaction of the polycationic strings would be with the *polyanionic* surface of DNA duplexes. Such interactions would be anticipated to be observable through observation of the circular dichroism signals for DNA and various duplex polydeoxyribonucleotides in the UV region due to differential absorption, as well as differential scattering, as has been reported [116-121] under various solution conditions for specific condensed forms of DNA. These conditions include nonaqueous solvents, high salt concentrations, the addition of polymers, and gelation into fibers. The term psi (Ψ) has been used to characterize [117-119] these enhanced CD effects and the nucleic acid materials produced under these varying conditions are referred to as Ψ condensates. It has been proposed [119] that such condensed forms may be important in the packaging of DNA, as found in chromatin.

With this in mind, we investigated the interactions of the polycationic strings with deoxyribonucleotide duplexes using circular dichroism spectrometry. [122] Upon addition of a tetracationic string bearing two fully quaternized dabco units (4+ net charge) with carbon linkers of varying lengths, CD spectral changes were produced indicative of conformational changes. Specifically, the intensity increased by a factor greater than 100 along with small shifts in the wavelengths of the maxima and minima. This implies a high degree of specificity for the interaction between the tetracationic string and the polynucleotide chains in the Ψ condensates.

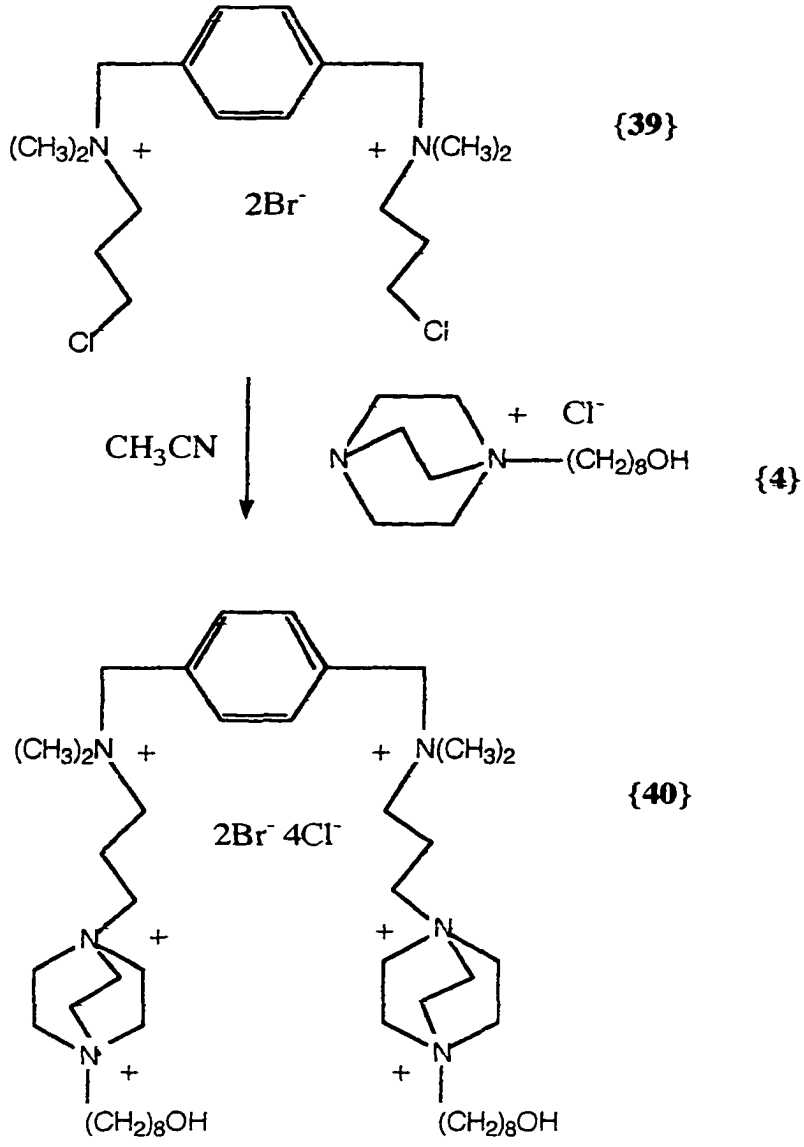
Similarly, other cationic strings have been prepared using *N,N,N',N'*-tetramethyl diamines. A representative of this series is *N,N,N',N'*-tetramethyl-*N,N'*-bis(3-hydroxypropyl)-1,4-di(azoniamethyl)benzene dibromide {38} as shown in Scheme 14.



{38}

Scheme 14

Treating α,α'-dibromo-*para*-xylene with two equivalents of 3-dimethylamino-1-propanol in acetonitrile gives the dicationic aromatic string. Upon treatment of {38} with thionyl chloride in chloroform provides the corresponding chlorinated string, *N,N,N',N'*-tetramethyl-*N,N'*-bis(3-chloropropyl)-1,4-di(azoniamethyl)benzene dichloride {39}. Once again, this activates the molecule and allows nucleophilic attack to occur and further elaborate the string as shown in the synthesis of *N,N,N',N'*-tetramethyl-*N,N'*-bis-1"-(3'-{1",4"-diazonia-4"-(8-hydroxyoctyl)bicyclo[2.2.2]octyl}-1,4-diazoniamethylbenzene) hexachloride{40} in Scheme 15.

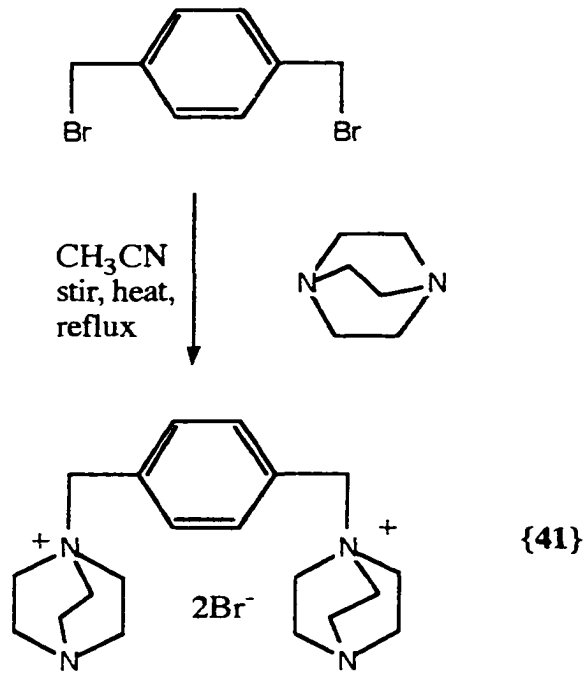


Scheme 15

Hexacationic string {40} is prepared by treating the dicationic chlorinated aromatic string {39} with two equivalents of the monocationic string {4} in acetonitrile.

Another simple type of string structure is synthesized by treating α,α'-dibromo-*para*-xylene with two equivalents of dabco in acetonitrile to

give the dicationic didabco string, 1,4-bis-(1'- azonia-4'-azabicyclo[2.2.2]octane)methyl- benzene dibromide {41} as shown in Scheme 16.



{41}

Scheme 16

POLYCATIONIC RINGS

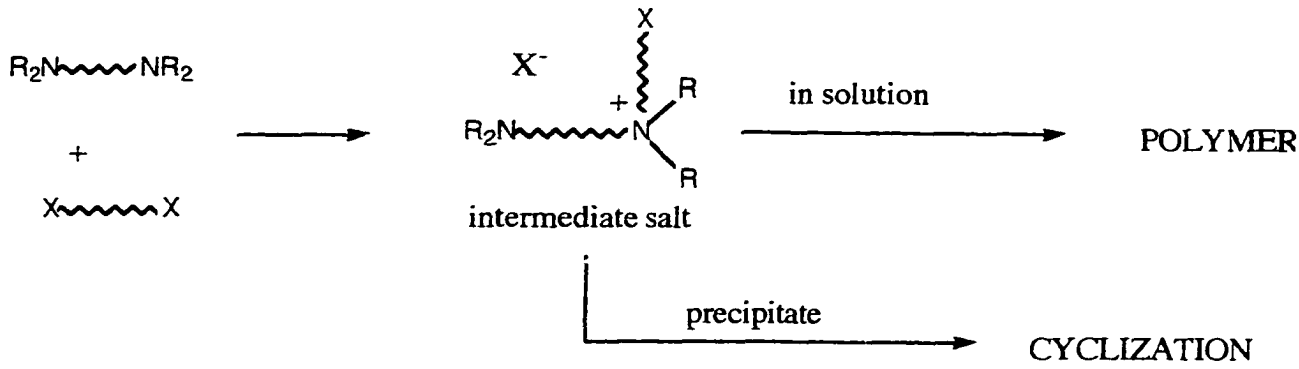
Other investigators have been concerned with the preparation and study of several types of polycationic organic species. "Ionene" polymers, relatively high molecular weight water soluble polymers containing a large number of quaternary ammonium ion sites, were earlier reported as being prepared by the reaction of α,ω-ditertiary amines in dimethylformamide solution. [123] Polymerization occurs presumably as a result of all difunctional reactants remaining in solution throughout the reaction time.

A series of studies of particular interest have also been performed on insoluble polycationic polymers, these being cross-linked polystyrene species to which are attached numerous phosphonium or ammonium sites. [124-126] These latter materials have been found to exhibit significant antibacterial activity. Dicationic salts referred to as "geminis" have also been prepared [127-129] with potential utility in skin care [129], antibacterial agents [131], separation processes [132] and solubilization processes [133]. These materials have structural similarity to certain of the "polycationic strings" previously reported from our laboratory. [134-136]

With this in mind we became concerned with the preparation of several series of cyclic polycationic organic salts. These are medium-sized ring systems (ten to twenty-six membered parent rings) wherein the quaternary ammonium ion sites are linked by saturated aliphatic chains as well as unsaturated linkages containing aromatic, olefinic, and acetylenic functionalities.

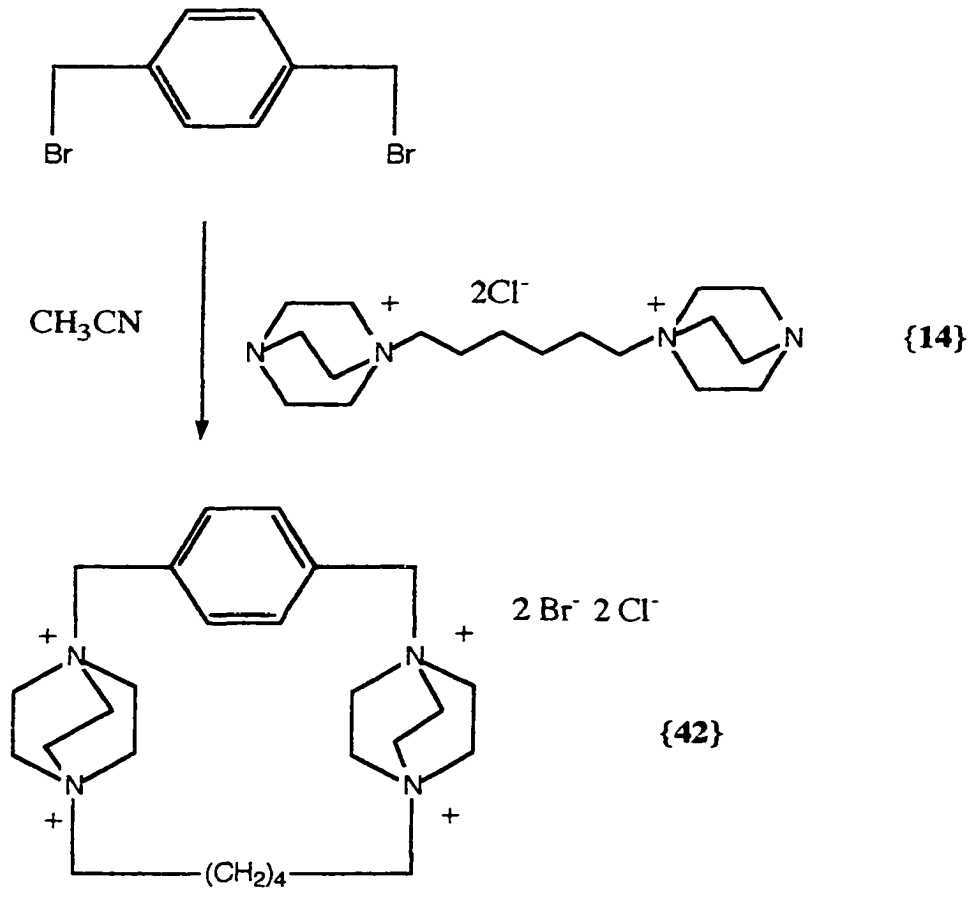
We have found that the use of a solvent system, moderately polar but only weakly favorable to dissolution of ionic species, allows cyclization of the initially formed salt species to occur when the reagents are structurally capable of ring formation. [137] We have found acetonitrile to be the solvent of particular choice for such cyclizations in that it provides only moderate solubility for quaternary

ammonium salts at room temperature, presumably denying soluble reactants ready availability to the initially formed intermediate species, thus facilitating ring formation. The stepwise formation of such cyclic salts is illustrated in Scheme 17 wherein the intermediate salt precipitates from solution and undergoes cyclization rather than remaining in solution to undergo polymerization.



Scheme 17

In this manner a variety of polycationic rings have been prepared. These include polycationic dabco systems. [137] The synthesis of a representative of this category of new ring systems is shown in Scheme 18.



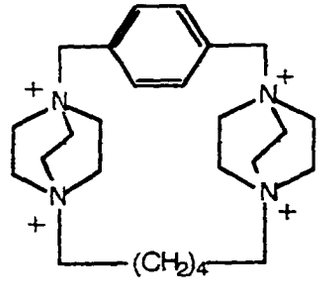
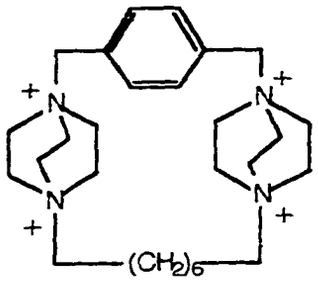
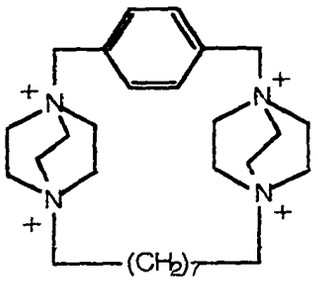
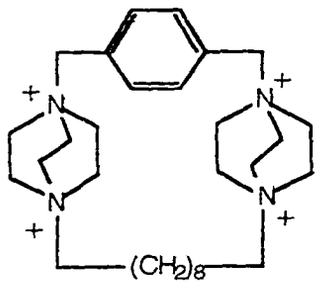
Scheme 18

Here we treat α,α'-dibromo-*para*-xylene with one equivalent of the didabco string {14} in acetonitrile solution to give the tetracationic paracyclophane, *p*-xylyl-1,4"-(4-{6'-(1",4'-diazoniabicyclo[2.2.2]octane)-1'hexyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride {42}. For this type of ring system some purification is required to remove traces of unreacted ditertiary amine reagent. This is accomplished with repeated washing of the product with hot acetonitrile, followed by ethyl acetate and anhydrous ether. The product is then dried under high vacuum to

give the pure target material.

The series of newly prepared salts {42}-{45} in this category are shown in Table 6.

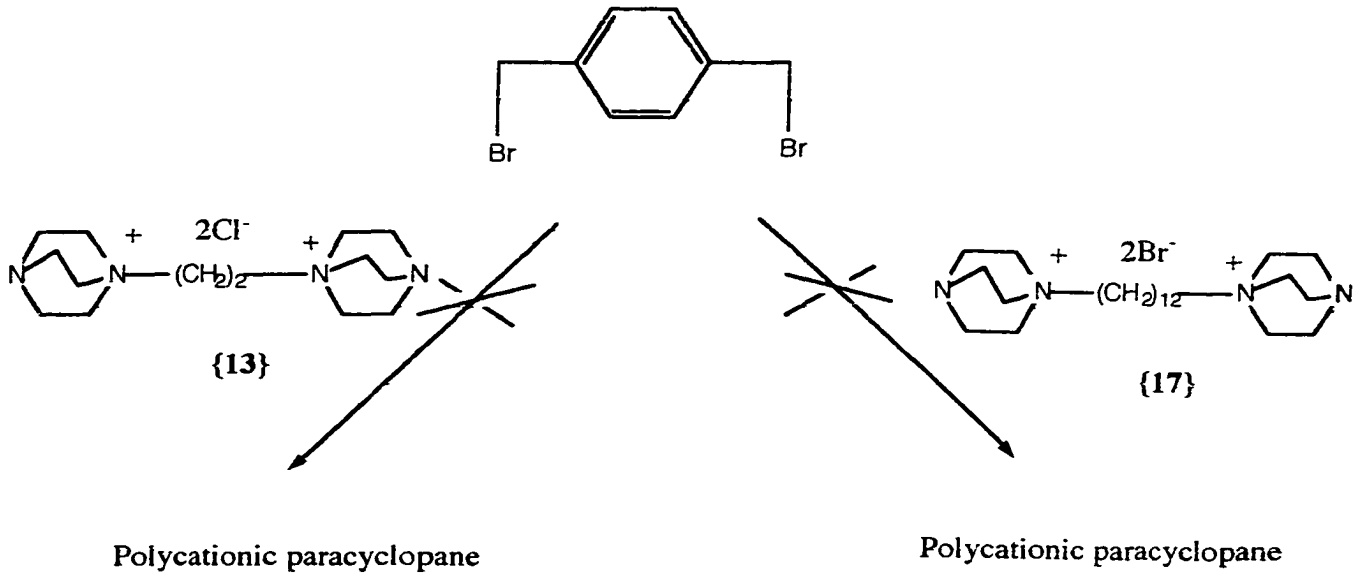
Table 6 - New paracylophane dabco rings

Structure	Number	Name
 2 Br^- 2 Cl^-	**42**	*p*-xylyl-1,4"-(4-{6'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-hexyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride
 2 Br^- 2 Cl^-	**43**	*p*-xylyl-1,4"-(4-{8'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-octyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride
 4 Br^-	**44**	*p*-xylyl-1,4"-(4-{9'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-nonyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrabromide
 2 Br^- 2 Cl^-	**45**	*p*-xylyl-1,4"-(4-{10'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-decyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride

This approach accomplishes the construction of a new category of intermediate-sized heterocyclic salts related to the intriguing

paracyclophanes. These products exhibit ^{1}H and ^{13}C NMR spectra in perfect accord with the proposed structures. The salts are mildly hydroscopic and exhibit quantitative elemental analyses in accord with simple hydrated forms of the proposed structures. (All of the polycationic salts are somewhat hydroscopic. Exposure to air results in the immediate adsorption of various amounts of water.) The ^{1}H and ^{13}C NMR spectra of the polycationic heterocyclic products are rendered relatively simple and distinct from that of starting materials, partially reacted species or polymeric species by the inherent symmetry of their structures. For example, the ^{13}C NMR spectrum of the polycationic product {42} exhibits a total of eight signals (δ, D_2O: 22.71, 26.09, 52.27, 52.54, 66.34, 69.12, 129.59, 135.52).

Both upper and lower limits are observed with regard to ring size for the facile formation of the polycationic heterocyclic salts. Attempts to generate polycationic heterocyclic salts by the general approach of addition of the α,ω-ditertiary amine in acetonitrile fail when α,α'-dibromo-*para*-xylene is treated with the dicationic didabco strings {13} and {17}, as illustrated in Scheme 19.



Scheme 19

In these instances the macrocycle forms only to a limited extent (less than 40%) with most of the starting reagents yielding ionene polymer, relative amounts being estimable from the ^{1}H NMR spectra.

It was our desire to determine if such cyclic polycationic species might be able to serve as modifiers of DNA conformation. We have previously demonstrated, through measurement of changes in the circular dichroism spectra, that polycationic "strings" can interact with double-stranded DNA. [122] Whereas polycationic "strings" might be capable of interacting with double-stranded DNA by associating helically with the phosphate-anion rich major groove of the DNA over an extensive distance along the helix, an individual unit of the polycationic heterocycles would be anticipated to be capable of interaction only at a single, relatively short

region of the helix. [137]

In spite of this, it was shown that a very significant change is observed in the CD spectra of double-stranded DNA when challenged with the polycationic heterocycles. The polycationic heterocycles clearly have a strong influence on the duplex structure of DNA. [137]

As shown in Figure 14, the addition of {42} (7.6×10^{-5}M) to a solution of poly(dGdC)-poly(dGdC) (8.2×10^{-5}M) in nucleotide phosphate produces a very notable change in the nature of the DNA CD spectrum. The less conservative CD spectrum, curve A in Figure 14, which is typical of poly(dGdC)-poly(dGdC) solutions, is changed to a more conservative CD spectrum, curve B in Figure 14, upon addition of {42}.

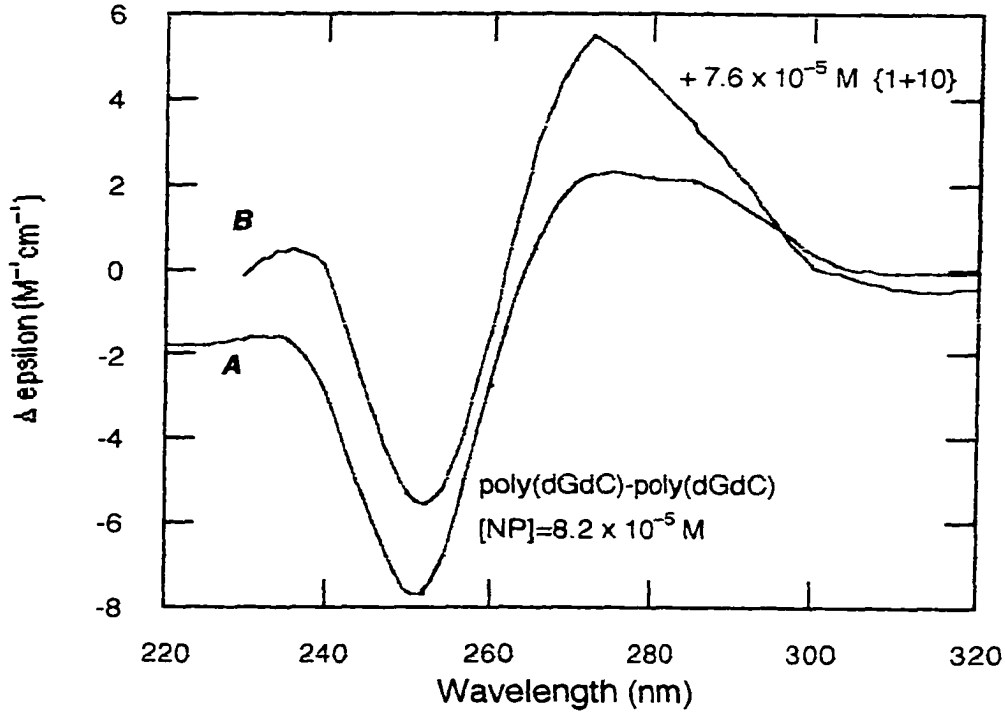


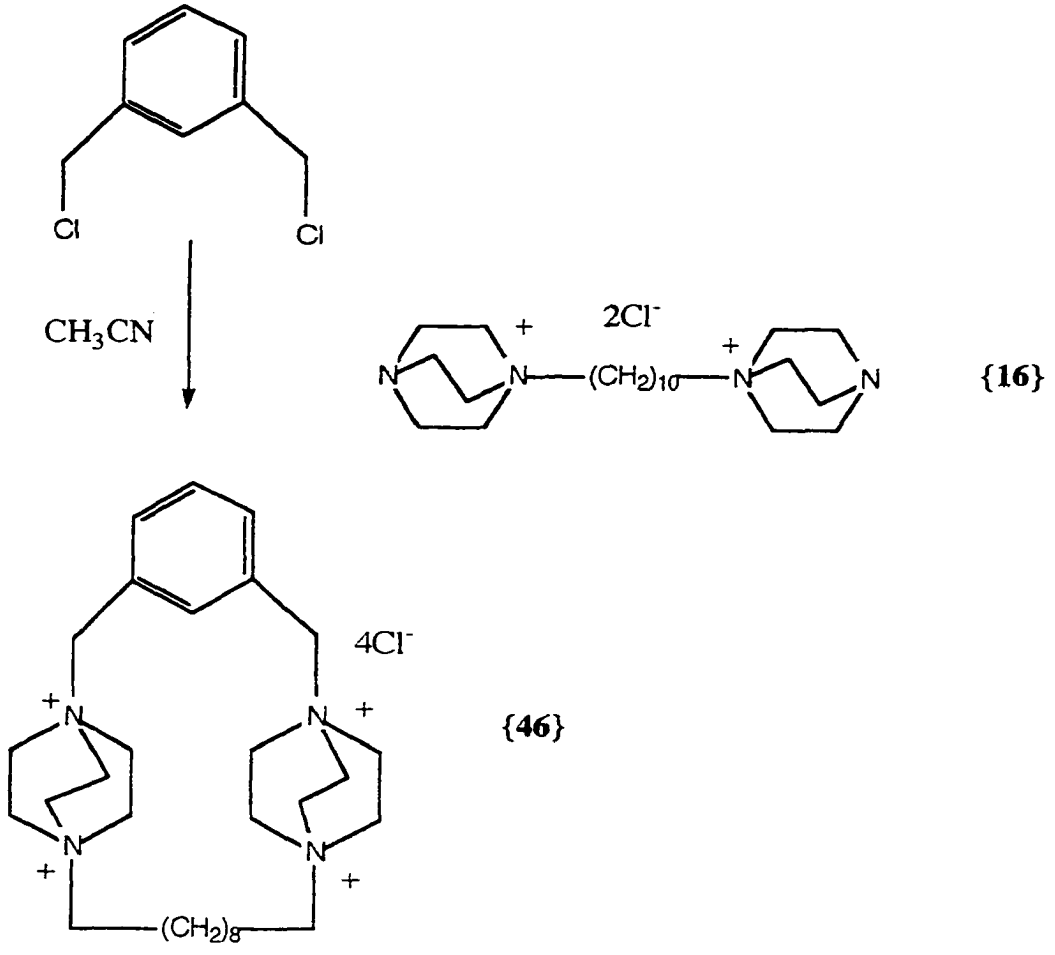
Figure 14 - Effect of {42} on the CD of poly(dGdC)-poly(dGdC).

That is, for curve B the maximum and minimum at longer and shorter wavelength about 260 nm are of approximately the same magnitude. The half-saturation point for this change occurs with an addition of {42} to an extent of 3.3×10^{-5} M, at which concentration cationic sites of the polycationic heterocycle and base pairs of the DNA are in a ratio slightly less than 1.

The conservative aspect of the CD spectra of polynucleotide

duplexes has been shown to be related to the relative displacement of the twist axis joining the paired bases from the dyad (or twofold) axis of the helix. [138] The polycationic heterocycles such as {42} clearly have a strong influence on the duplex structure of DNA as evidenced by these results.

In a similar manner, a new series of polycationic *metacylophanes* were synthesized. [139] This work was completed by Valbona Behaj, whom I mentored. An example of this series is shown in Scheme 20.



Scheme 20

Here we treat α, α'-dichloro-*meta*-xylene with one equivalent of a dicationic didabco string {16} in acetonitrile solution to give *m*-xylyl-1,4"-(4-{10'-(1",4'-diazoniabicyclo[2.2.2]octane)-1'decyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride {46}. Table 7 lists the new tetracationic *meta*cyclophanes {46]-{52}.

Table 7 - New tetracationic *meta*cyclophanes

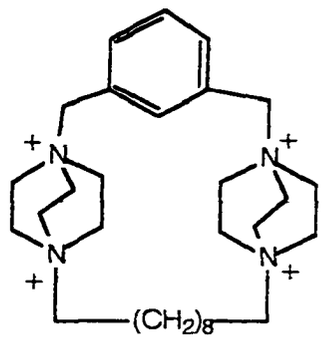
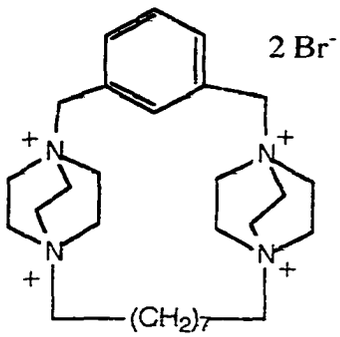
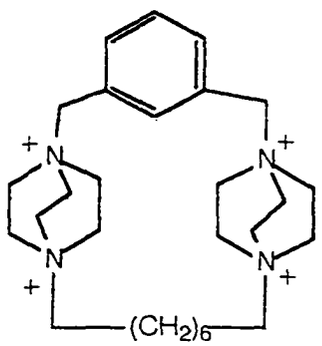
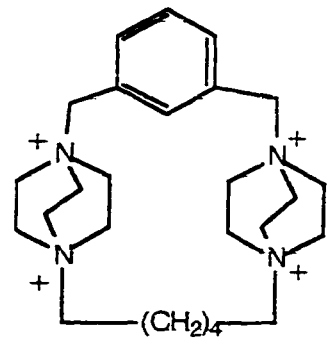
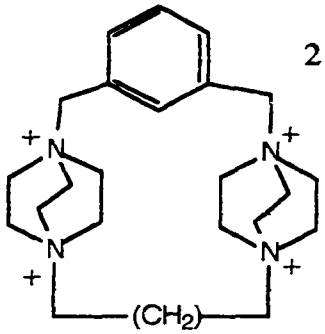
Structure	Number	Name
 4 Cl^-	**46**	*m*-xylyl-1,4"-(4-{10'-(1",4"-diazoniabicyclo-[2.2.2]octane)-1'-decyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrachloride
 2 Br^- 2 Cl^-	**47**	*m*-xylyl-1,4"-(4-{9'-(1",4"-diazoniabicyclo-[2.2.2]octane)-1'-nonyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride
 4 Cl^-	**48**	*m*-xylyl-1,4"-(4-{8'-(1",4"-diazoniabicyclo-[2.2.2]octane)-1'-octyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrachloride

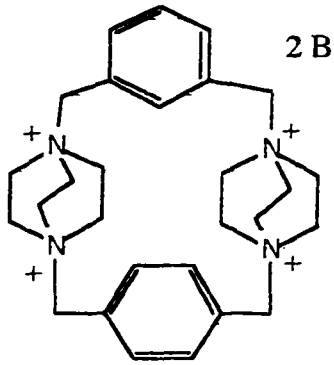
Table 7 - contd.



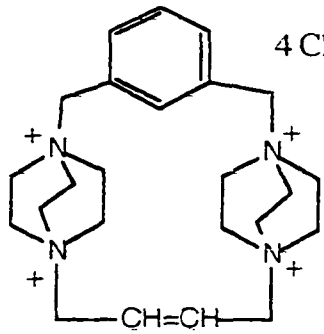
49 *m*-xylyl-1,4"-(4-{6'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-hexyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrachloride



50 *m*-xylyl-1,4"-(4-{3'-(1",4"-diazaoniabicyclo-2.2.2]octane)-1'-propyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride



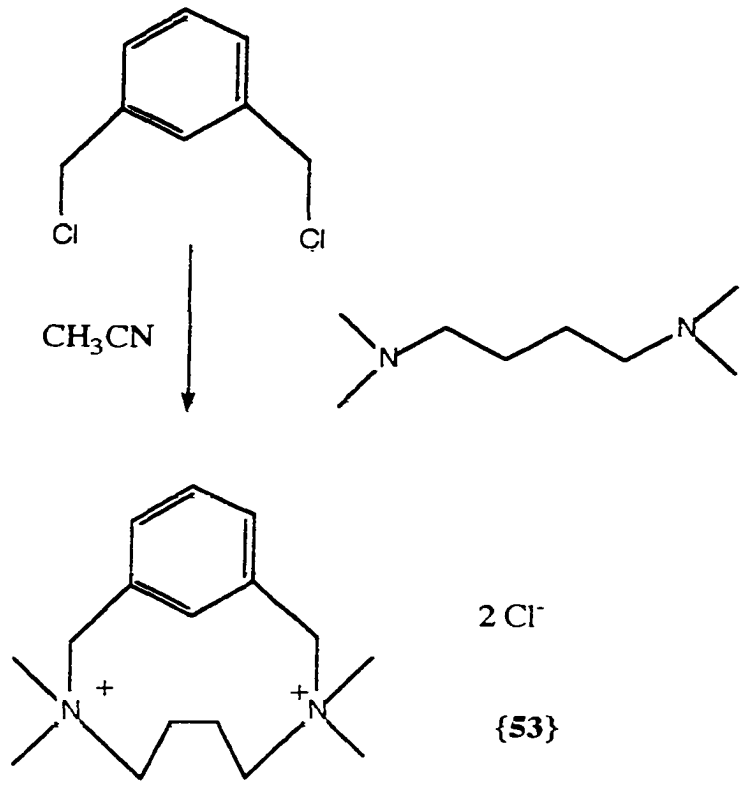
51 *m*-xylyl-1,4"-(4-{α"-(1"',4"'-diazaoniabicyclo-[2.2.2]octane)-α'-*p*-xylyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride



52 *m*-xylyl-1,4"-(4-{4'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-4-(*Z*)-2'-butenyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrachloride

A series of dicationic metacyclophanes have been prepared

similarly. This procedure involves treatment of the α,ω-dihaloaromatic ring with one equivalent of an α,ω-diaminealkyl species in acetonitrile solution. A representative member of this category is illustrated in Scheme 21.

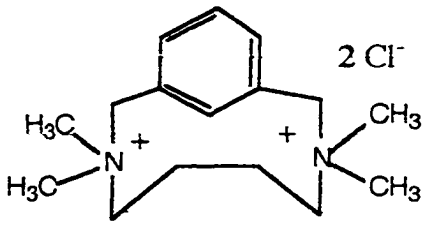
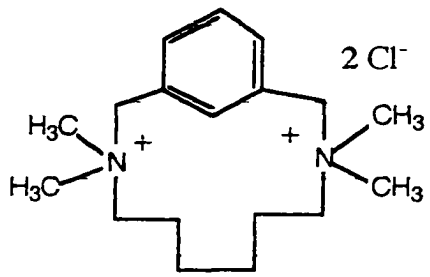


{53}

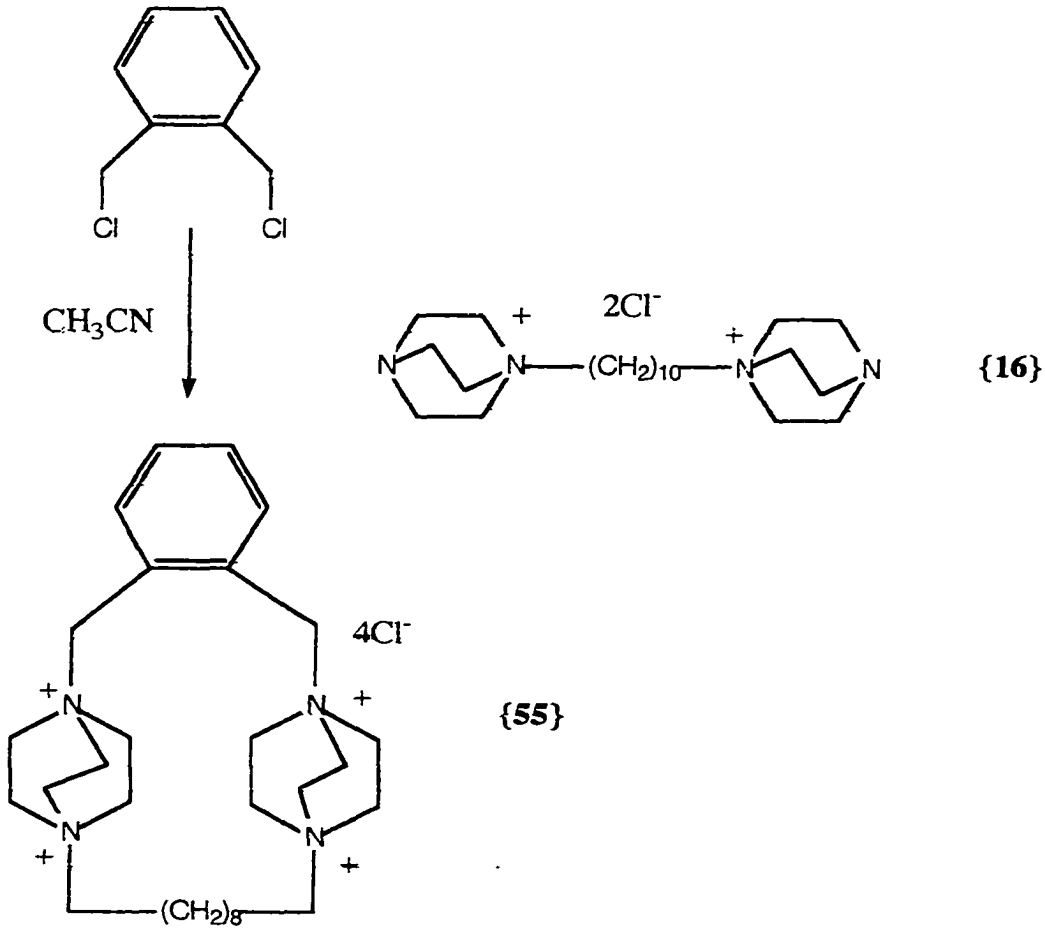
Scheme 21

Treating α,α'-dichloro-*m*-xylene with *N,N,N',N'*-tetramethylbutanediamine in acetonitrile solution gives the new dicationic metacylophane product, *m*-(2,2,7,7-tetramethyl-2,7-diazoniaoctylene benzene {53}. The new compounds {53}-{54} in this series are listed in Table 8.

Table 8 - New dicationic metacyclophane rings

Structure	Number	Name
	**53**	*m*-(2,2,7,7-tetramethyl-2,7-diazoniaoctylenyl)benzene
	**54**	*m*-(2,2-9,9-tetramethyl-2,9-diazoniadecyleneyl)benzene

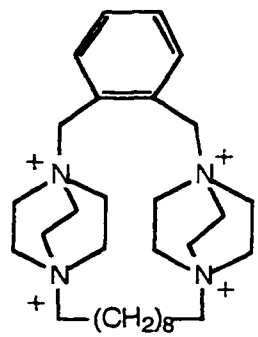
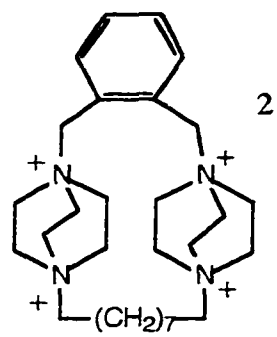
A series of tetracationic *ortho*cyclophanes have also been prepared using the same procedure as illustrated in Scheme 22. [138]



Scheme 22

In a similar manner to that noted previously, α,α'-dichloro-*ortho*-xylene was treated with a dicationic didabco string {16} in acetonitrile to give the cyclic, *o*-xylyl-1,4"-(4-{10'-(1",4'-diazoniabicyclo[2.2.2]octane)-1'decyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride {55}. Table 9 lists the compounds synthesized in this series {55}-{56}.

Table 9 - New tetracationic orthocyclophanes

Structure	Number	Name
 4 Cl^-	***55***	*o*-xylyl-1,4"-(4-{10'-(1",4"-diazaoniabicyclo-[2.2.2]octane)-1'-decyl}azonia)-1-azonia-bicyclo[2.2.2]octane tetrachloride
 2 Br^- 2 Cl^-	***56***	*o*-xylyl-1,4"-(4-{9'-(1",4"-diazaoniabicyclo-2.2.2]octane)-1'-nonyl}azonia)-1-azonia-bicyclo[2.2.2]octane dibromide dichloride

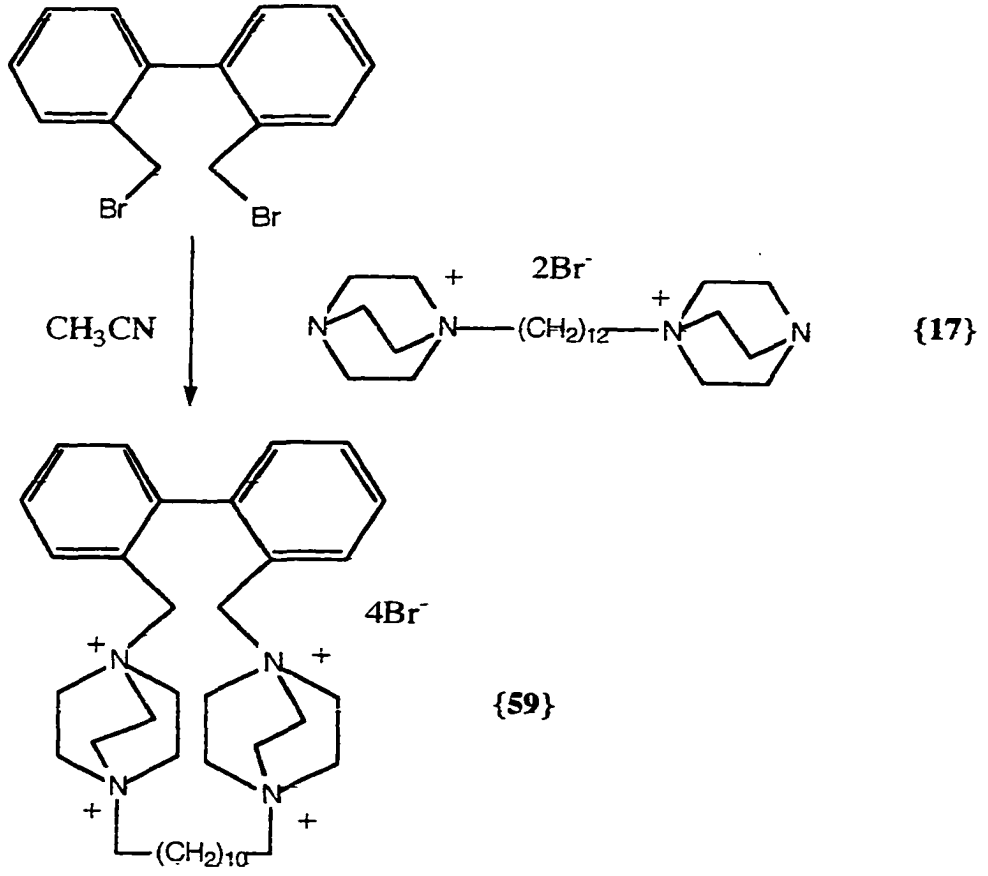
The above orthocyclophane series are *chiral.* These materials were modeled using Chem 3D+ which indicates a significant barrier to rotation, indicating the potential of these to be resolved in enantiomeric form. The general approach includes the formation of diastereoisomeric salts which should be capable of separating by ordinary means. We have used dibenzoyl tartrate for the generation of diastereoisomeric salts, as this has been accomplished with other chiral cationic species. [140]

In all instances for the rings derived from α,α'-dihalo-*para, -meta,* and -*ortho*-xylene above, product formation is rapid with precipitation of

the resultant cyclic cationic salt. Some contamination of the initially isolated product by the starting dicationic didabco string is often observed. Isolation of the pure target cyclic materials in these instances is accomplished either by repeated washings of the impure salts with warm acetonitrile, or by the use of a significant excess of the dihalide reagent.

The above three series are *mono* aromatic tetracationic ring species.

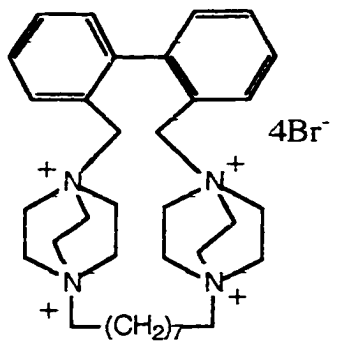
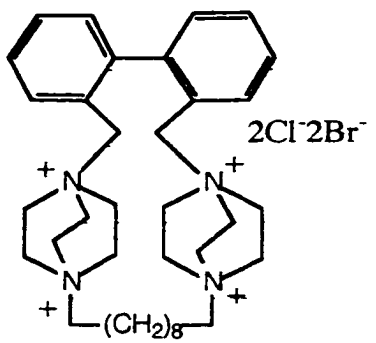
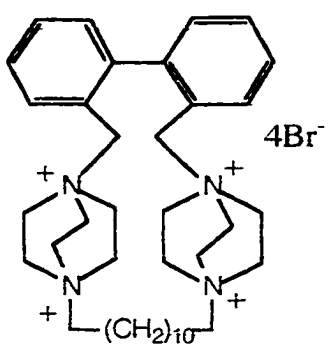
In the same manner, a series of tetracationic chiral biphenyl ring species were prepared. [139] An example of this series is shown in Scheme 23.



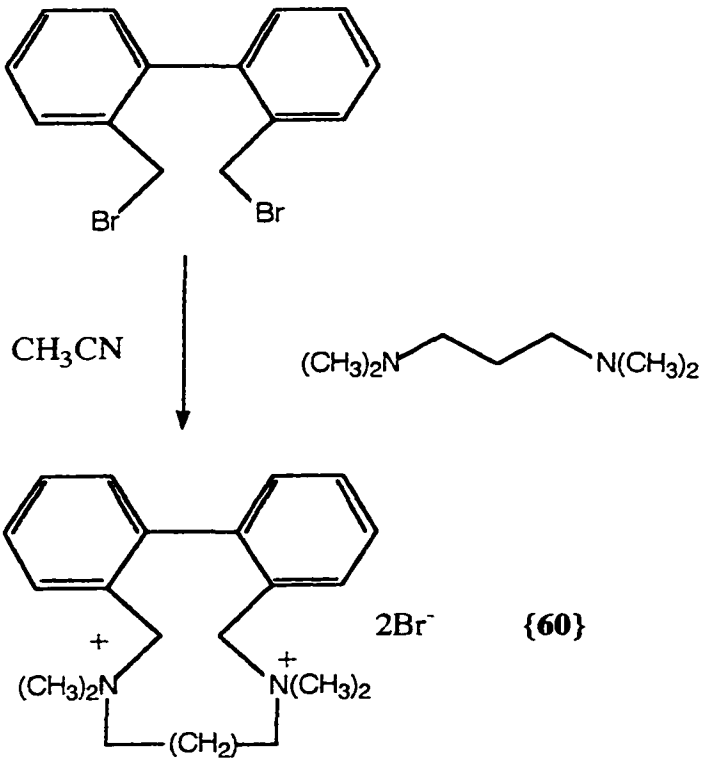
Scheme 23

These materials are synthesized by treating 2,2'-bis(bromomethyl)-1,1'-biphenyl with a dicationic didabco string species in acetonitrile solution to give the tetracationic biphenyl ring, 1,1'-biphenylylmethylene-1",4""-(4"-{12"'-(1"",4""-diazoniabicyclo[2.2.2]octane-1'"-dodecyl}azonia)-1"-azoniabicyclo[2.2.2]octane tetrabromide {59}. Table 10 lists the compounds prepared in this series {57}-{59}. [138]

Table 10 - New tetracationic chiral *biphenyl* rings

Structure	Number	Name
	**57**	1,1'-biphenylylmethylene-1",4""-(4"-{9'''-(1"",4""-diazoniabicyclo[2.2.2]octane-1'''-nonyl}azonia)1-azoniabicyclo[2.2.2]octane tetrabromide
	**58**	1,1'-biphenylylmethylene-1",4""-(4"-{10'''-(1"",4""-diazoniabicyclo[2.2.2]octane-1'''-decyl}azonia)1-azoniabicyclo[2.2.2]octane dibromide dichloride
	**59**	1,1'-biphenylylmethylene-1",4""-(4"-{12'''-(1"",4""-diazoniabicyclo[2.2.2]octane-1'''-dodecyl}azonia)1-azoniabicyclo[2.2.2]octane tetrabromide

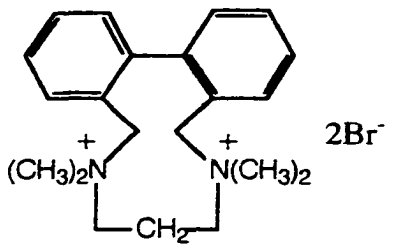
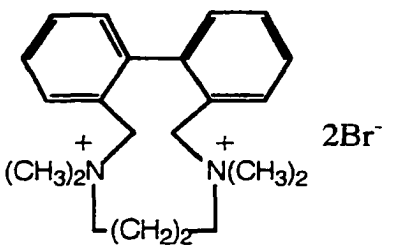
A series of dicationic *chiral* biphenyl rings were prepared under similar conditions. A representative member of this category is illustrated in Scheme 24.



Scheme 24

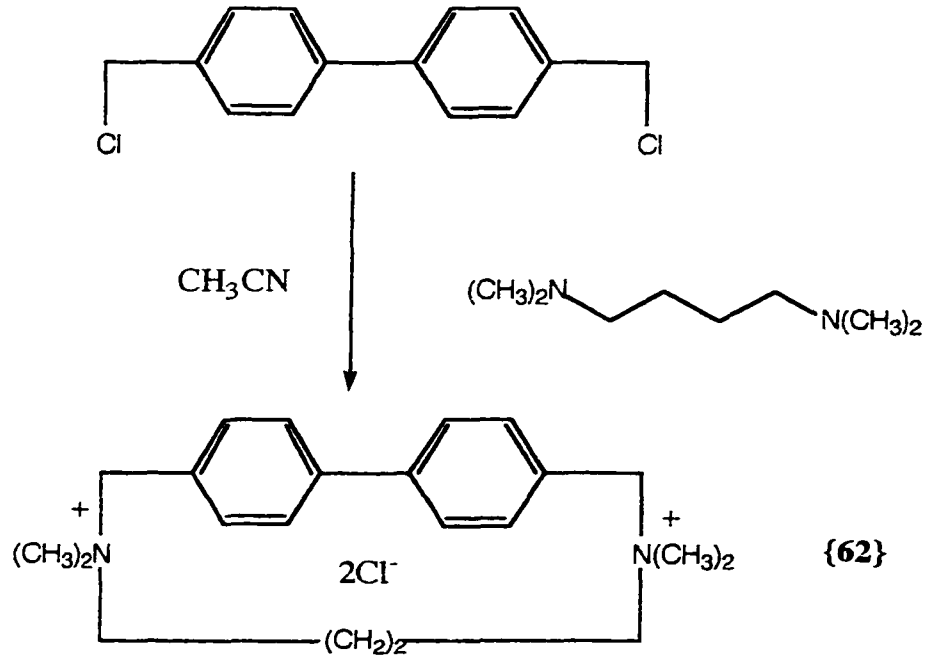
Treatment of 2,2'-bis(bromomethyl)-1,1'-biphenyl with *N,N,N',N'*-tetramethylpropane diamine in acetonitrile solution results in the cyclic product, 2,2'-(2",2",6",6"-tetramethyl-2",6"-diazoniaheptylenyl)-1,1'-biphenyl dibromide {60}. Table 11 lists the newly synthesized materials in this category {60}-{61}. [138]

Table 11 - New dicationic chiral biphenyl rings

Structure	Number	Name
	**60**	2,2'-(2",2",6",6"-tetramethyl-2",6"-diazonia-heptylenyl)-1,1'-biphenyl dibromide
	**61**	2,2'-(2",2",7",7"-tetramethyl-2",7"-diazonia-octylenyl)-1,1'-biphenyl dibromide

The resolution of the enantiomers is presently under investigation in our laboratory.

A series of dicationic non-chiral biphenyl rings have been prepared in a similar manner. A representative member is illustrated in Scheme 25.

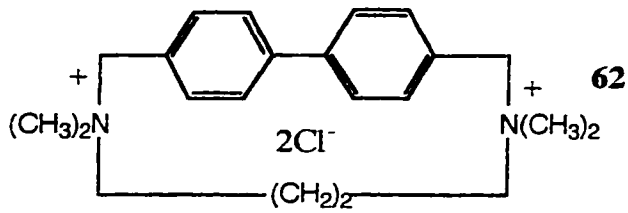
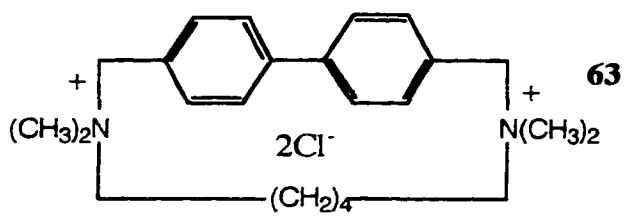


{62}

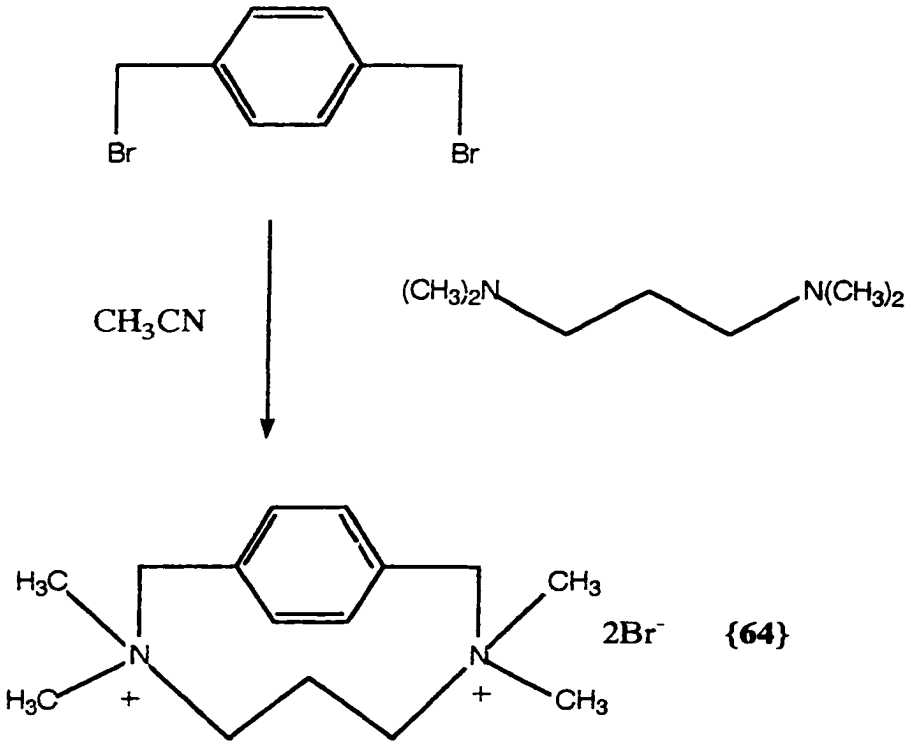
Scheme 25

This is accomplished by treating 4,4'-bis-(chloromethyl)-1,1'-biphenyl with *N,N,N',N'*-tetramethylbutane diamine in acetonitrile solution to generate 4,4'-(2",2",7",7"-tetramethyl-2",7"-diazoniaoctylenyl)-1,1'-biphenyl dichloride {62}. Table 12 lists the compounds in this category {62}-{63}. [138]

Table 12 - Dicationic nonchiral biphenyl rings

Structure	Number	Name
	**62**	4,4'-(2",2",7",7"-tetramethyl-2",7"-diazoniaoctylenyl)-1,1'-biphenyl dichloride
	**63**	4,4'-(2",2",9",9"-tetramethyl-2",9"-diazoniadecylenyl)-1,1'-biphenyl dichloride

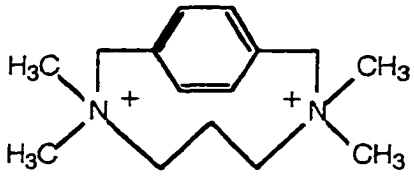
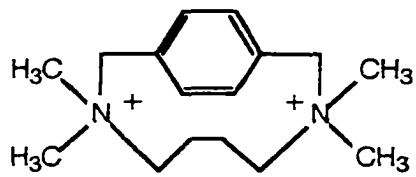
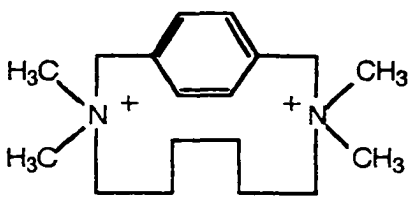
Another series of structurally simple paracyclophanes has also been prepared. This is accomplished by treating α, α'-dibromo-*para*-xylene with one equivalent of an *N,N,N',N'*-tetramethylalkyldiamine species in acetonitrile to give the new polycationic paracyclophane, *p*-(2,2,6,6-tetramethyl-2,6-diazoniaheptylenylbenzene dibromide {64} as shown in Scheme 26.



Scheme 26

The series of newly prepared salts {64}-{66} in this category are shown in Table 13. [138]

Table 13 - Dicationic paracyclophane rings

Structure	Number	Name
	64	*p*-(2,2,6,6-tetramethyl-2,6-diazonia-heptylenylbenzene dibromide
	65	*p*-(2,2,7,7-tetramethyl-2,7-diazonia-octylenylbenzene dibromide
	66	*p*-(2,2,9,9-tetramethyl-2,9-diazonia-decylenylbenzene dibromide

These new ring systems have exhibited an interaction with double-stranded DNA resulting in a change in the conformation of the DNA as evidenced through the circular dichroism (CD) spectrum. [137] The ^{1}H and ^{13}C NMR spectra of these heterocyclic products are rendered relatively simple and distinct from that of the starting materials, partially reacted species, or polymeric species by the inherent symmetry of their structures. For example, the ^{13}C NMR spectrum of the polycationic heterocyclic product {66} exhibits a total of seven signals, assignable as

shown in Figure 15a. Molecular modeling (Chem 3D+ of {66} indicates that the hydrogen atoms attached to the central carbon atoms between the ammonium sites are located between 4.7 and 5.7 Å directly above the aromatic ring, a position in which a diamagnetic anisotropic shift of their NMR signals should be observable. (For other species, e.g., {64} the bridging hydrogens are closer to the aromatic ring, but lie more toward the side of the aromatic ring rather than directly above the aromatic ring, in a zero-effect region with regard to a diamagnetic anisotropic effect; with yet other salts the bridging hydrogens are significantly more distant from the aromatic ring, albeit above it.) In fact, an upfield shift of 0.21 δ is observed (Figure 15c) for the bridging β hydrogens of the cyclic system {66} as compared with the β hydrogens of an open-chain analog {38}.

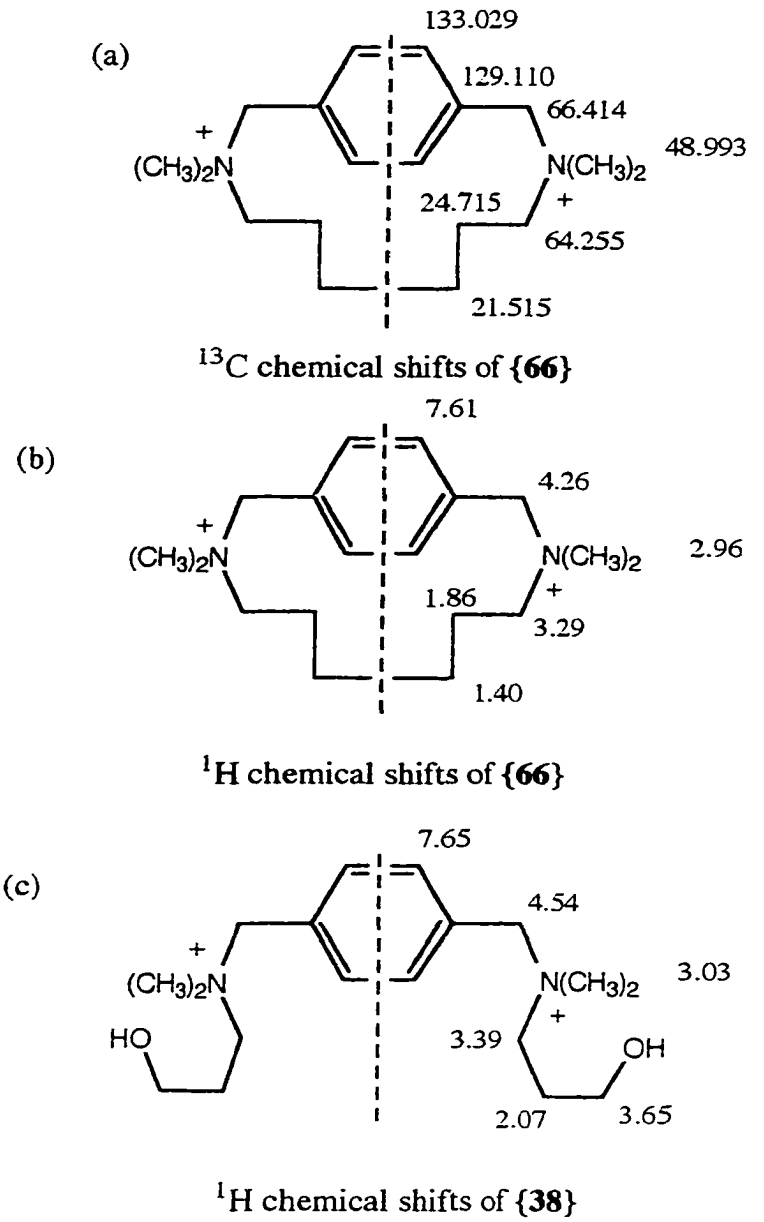
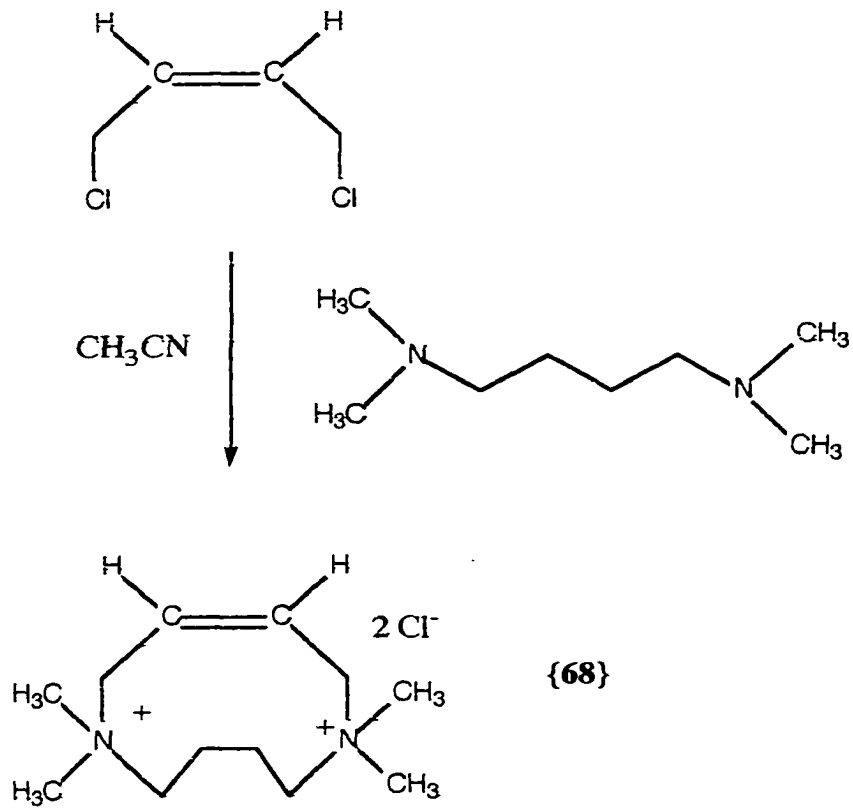


Figure 15 (a) ^{13}C chemical shifts of {66}. (b) ^{1}H chemical shifts of {66}. (c) ^{1}H chemical shifts of {38}.

A new series of dicationic rings containing olefinic linkages have also been prepared in a similar manner. The synthesis of a representative

member of this category is shown in Scheme 27.

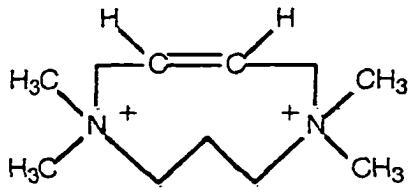
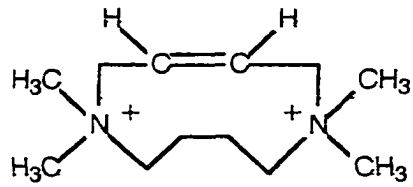
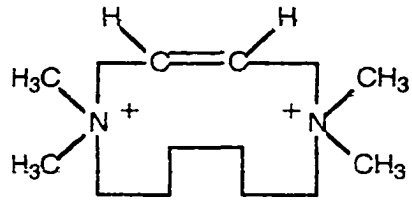


{68}

Scheme 27

Treatment of *cis*-1,4-dichloro-2-butene with one equivalent of *N,N,N',N'*-tetramethylbutanediamine in acetonitrile solution gives the new cyclic species, 4,4,9,9-tetramethyl-4,9-diazoniacyclodecene dichloride {68}. Table 14 lists the new materials in this series {67}-{69}. [138]

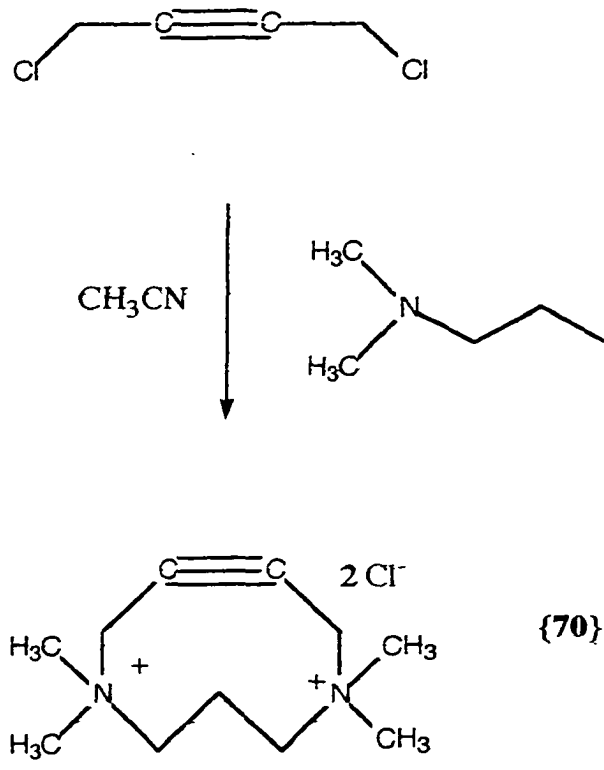
Table 14 - New dicationic olefinic rings

Structure	Number	Name
 2 Cl^-	**67**	4,4,8,8-tetramethyl-4,8-diazoniacyclo-nonene dichloride
 2 Cl^-	**68**	4,4,9,9-tetramethyl-4,9-diazoniacyclo-decene dichloride
 2 Cl^-	**69**	4,4,11,11-tetramethyl-4,11-diazoniacyclo-dodecene dichloride

These ring systems also exhibited an effect on double-stranded DNA. [137]

It is worthy of note that the cyclic salts are more soluble in acetonitrile than are the open-chain salts.

Similarly, a series of dicationic rings containing acetylenic linkages were prepared. This is illustrated in Scheme 28. [141]

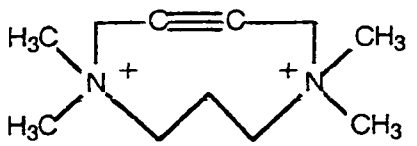
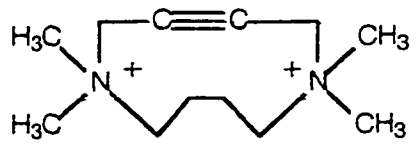
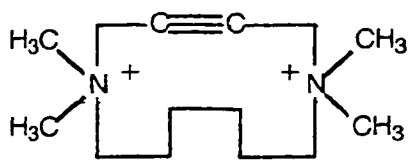


{70}

Scheme 28

Treating 1,4-dichloro-2-butyne with one equivalent of *N,N,N',N'*-tetramethylpropanediamine in acetonitrile solution generates the new dicationic ring containing an acetylenic linkage, 4,4,8,8-tetramethyl-4,8-diazoniacyclononyne dichloride {70}. Table 15 lists the prepared compounds in this series {70}-{72}. [141]

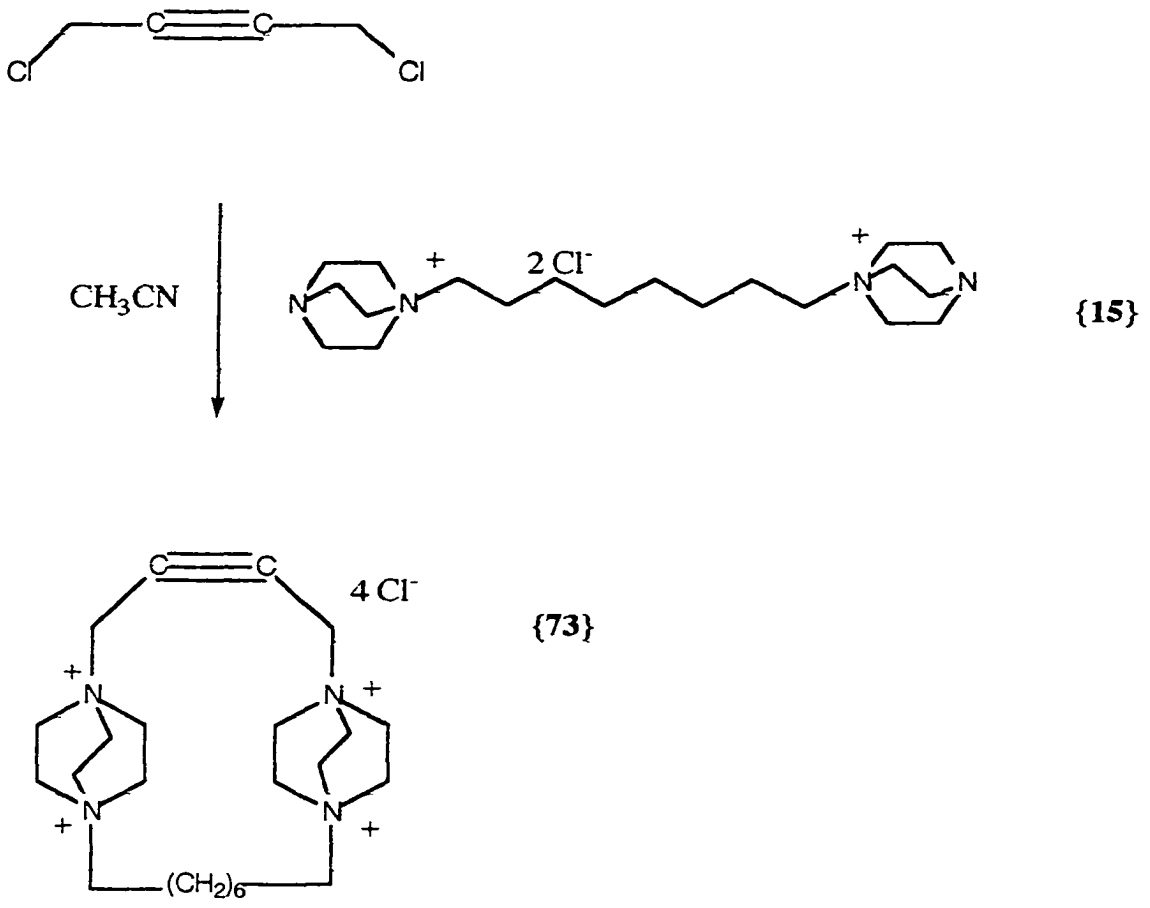
Table 15 - New dicationic acetylenic rings

Structure	Number	Name
 2 Cl^-	**70**	4,4,8,8-tetramethyl-4,8-diazoniacyclo-nonyne dichloride
 2 Cl^-	**71**	4,4,9,9-tetramethyl-4,9-diazoniacyclo-decyne dichloride
 2 Cl^-	**72**	4,4,11,11-tetramethyl-4,11-diazoniacyclo-dodecyne dichloride

The α,ω-dihaloalkanes readily undergo reaction with tertiary amines to generate quaternary ammonium salts as previously reported. [137, 139] Isolation of the salts from this series is quite facile. The precipitated salt is recovered in excellent yield by suction filtration, washing with ethyl acetate and diethyl ether, and drying under high vacuum. No further purification is required.

The construction of such polycationic heterocycles containing intermediate sized rings are of particular interest as they bear potential for selective interactions with a variety of anionic species, in addition to DNA. [137]

Similarly, a new series of tetracationic rings containing alkyne linkages have been prepared. A representative member of this category is illustrated in Scheme 29.



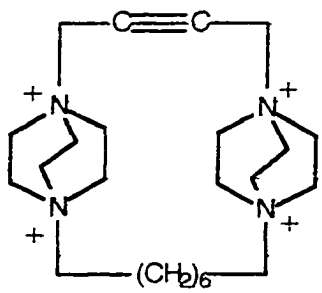
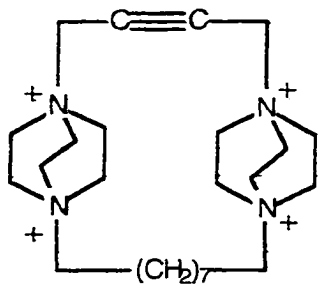
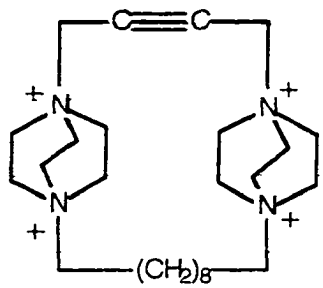
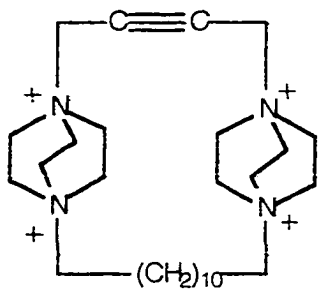
Scheme 29

Treating 1,4-dichloro-2-butyne with one equivalent of the dicationic string {15} in acetonitrile solution gives the new tetracationic alkyne ring, 1,4-but-2-yneylyl-1'-4'"(4'-{8"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-octyl}azonia-1'-azoniabicyclo-[2.2.2]octane tetrachloride {73}. Using dabco derived diamines, the reactant itself is a salt with limited solubility

in acetonitrile. Heating is required to effect solubilization of these diamines, a portion of which co-precipitates with the target tetracationic heterocyclic alkynes. Purification of the product salt requires repeated washing with hot acetonitrile to effect preferential solubilization of the starting material and leave the pure target salt.

It is notable that the α,ω-bis-(1-azonia-4-azobicyclo[2.2.2]octyl)-alkane dihalides in which the chain connecting the two dabco derived rings holds fewer than eight carbons, do not give cyclic product via this reaction. Polymeric polycationic materials are the primary products under such circumstances. Modeling (Chem 3D+) of the target cyclic species to be derived from such diamines indicates that significant strain would be present in the ring, leading to a conclusion that the diamine is incapable of reaching the required distance in a sufficiently facile manner to close such a ring. The new tetracationic alkyne rings {73}-{76} are listed in Table 16.

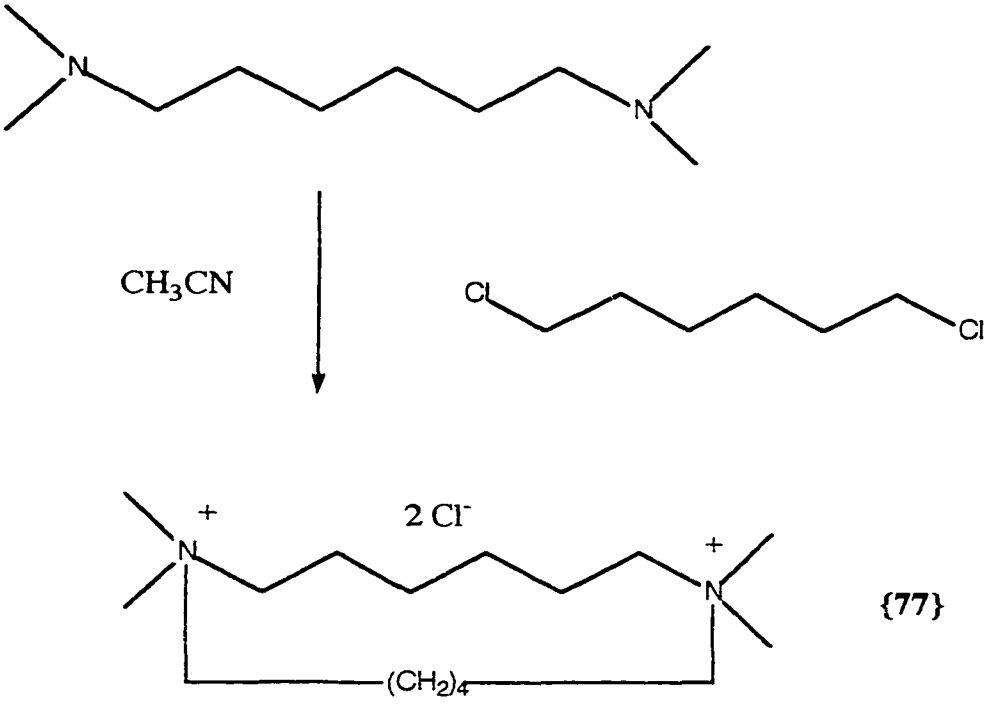
Table 16 - New tetracationic alkyne rings

Structure	Number	Name
	4 Cl^- **73**	1,4-but-2-yneylyl-1',4'"-(4'{8"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-octyl}azonia-1'-azoniabicyclo[2.2.2]octane tetrachloride
	2 Br^- 2 Cl^- **74**	1,4-but-2-yneylyl-1',4'"-(4'{9"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-nonyl}azonia-1'-azoniabicyclo[2.2.2]octane dibromide dichloride
	4 Cl^- **75**	1,4-but-2-yneylyl-1',4'"-(4'{10"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-decyl}azonia-1'-azoniabicyclo[2.2.2]octane tetrachloride
	2 Br^- 2 Cl^- **76**	1,4-but-2-yneylyl-1',4'"-(4'{12"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-dodecyl}azonia-1'-azoniabicyclo[2.2.2]octane dibromide dichloride

The polycationic heterocyclic alkynes thus synthesized exhibit intriguing characteristics in biologically related systems, including modificaton of

the conformation of double-stranded DNA [137] and the extraction of cholesterol from artificial membranes [141].

All of the above forementioned ring systems bear *unsaturated* linkages. A new series of dicationic rings bearing *saturated* linkages have been prepared. The synthesis of a representative member in this category is illustrated in Scheme 30.



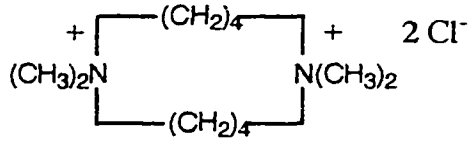
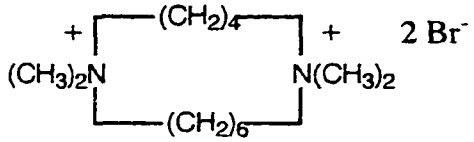
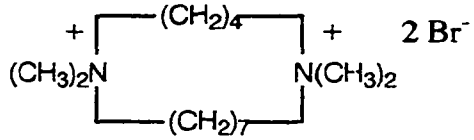
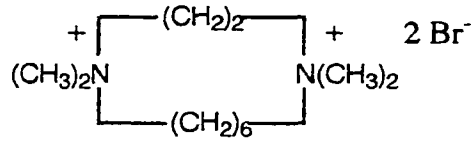
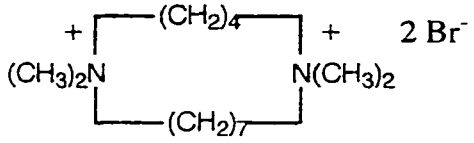
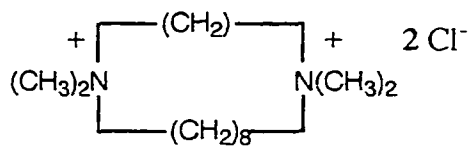
{77}

Scheme 30

Treating *N,N,N',N'*-tetramethyl-1,6-hexane diamine with 1,6-dichlorohexane in acetonitrile solution generates the new dicationic saturated ring, 1,1,8,8-tetramethyl-1,8-diazoniacyclotetradecane dichloride {77}. Table 17 lists the compounds in this category {77}-

{82}.

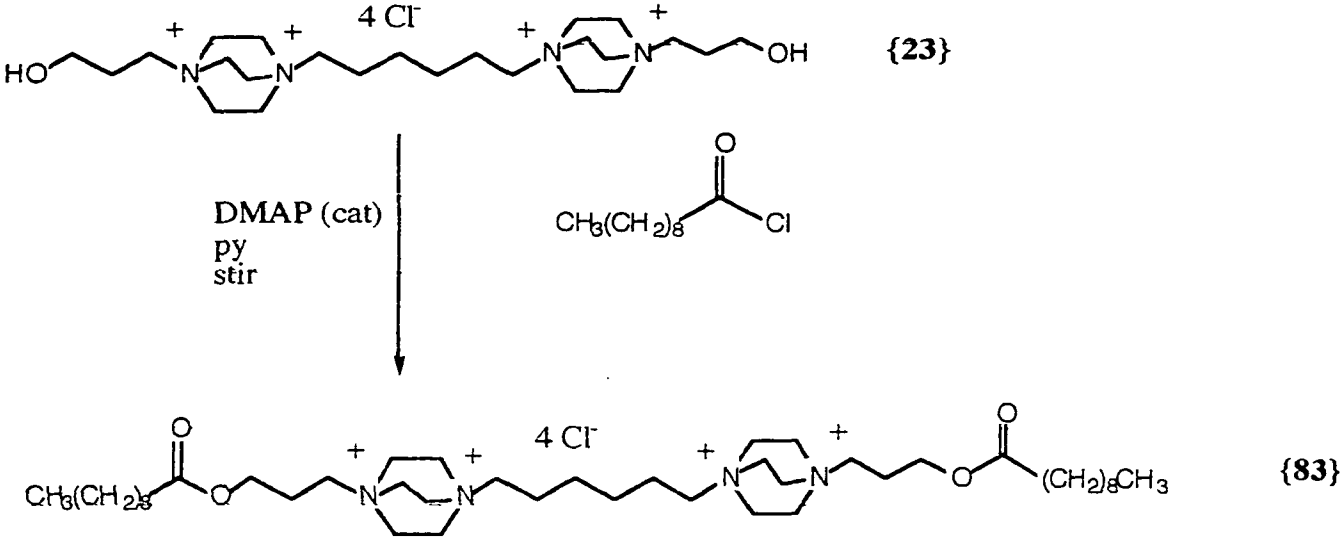
Table 17 - New dicationic saturated rings

Structure	Number	Name
	**77**	1,1,8,8-tetramethyl-1,8-diazoniacyclo-tetradecane dichloride
	**78**	1,1,8,8-tetramethyl-1,8-diazoniacyclo-hexadecane dibromide
	**79**	1,1,8,8-tetramethyl-1,8-diazoniacyclo-heptadecane dibromide
	**80**	1,1,6,6-tetramethyl-1,6-diazoniacyclo-tetradecane dibromide
	**81**	1,1,8,8-tetramethyl-1,8-diazoniacyclo-heptadecane dibromide
	**82**	1,1,5,5-tetramethyl-1,5-diazoniacyclo-pentadecane dichloride

POLYCATIONIC TRANSFECTINS

Introducing DNA into cells with cationic lipids can be a powerful tool for examining the roles of genes in biological systems. For example, antisense oligonucleotides, delivered into cells with cationic lipids, have become standard tools for the elucidation of gene funtion. [142,143] Cytofectins have been prepared that deliver DNA efficiently to a broad spectrum of cell lines in the presence of serum containing growth media. [144] It is of interest to synthesize cytofectins that can deliver plasmids as well as oligonucleotides into cell nuclei.

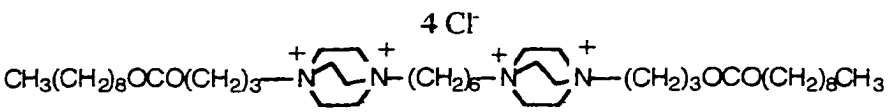
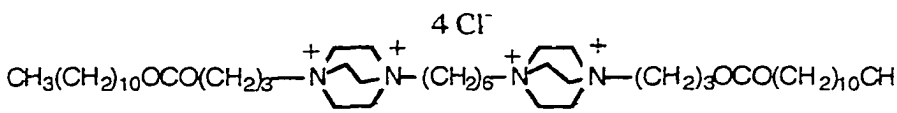
To this end a series of polyammonium salts with potential use as transfectins was prepared. The synthesis of a representative member in this category is shown in Scheme 31.



Scheme 31

This was accomplished by treating the tetracationic didabco string {23} with 4 equivalents of decanoyl chloride in pyridine with a catalytic amount of 4-dimethylamino-1-pyridine while stirring. The pyridine was evaporated under reduced pressure and the remaining crude material was dissolved in water, then allowed to react with sodium bicarbonate for neutralization of any remaining acyl chloride. Volatiles were again evaporated under reduced pressure to give the new transfectin, 1,4"-bis-(1-nonyl 4-butanoyl)-4-(6'-{1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride {83}. Table 18 lists the compounds prepared in this category {83} - {84}.

Table 18 - New Transfectins

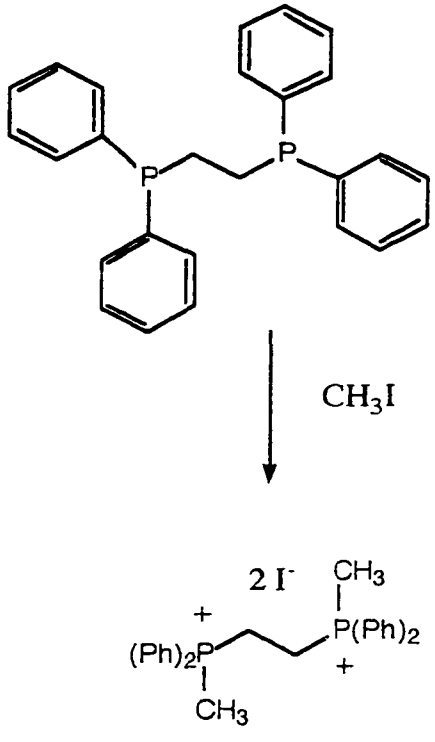
Structure & Number	Name
 **83**	1,4"-bis-(1-nonyl 4-butanoyl)-4-(6'-{1",4"-diazoniabicyclo-[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride
 **84**	1,4"-bis-(1-undecyl 4-butanoyl 4-(6'-{1",4"-diazoniabicyclo-[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride

These newly prepared materials contain both a lipid-like component so they may be able to get through cell membranes, as well as possess ionic sites that can interact with highly polar materials including enzymes to assist in performing gene splicing applications.

POLYPHOSPHONIUM STRINGS

A series of polyphosphonium strings has been prepared. Others have reported on polymeric polyphosphonium salts that demonstrated antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, leading us to new syntheses. [124-126]

With this in mind, a series of new polycationic phosphonium strings were synthesized. The synthesis of a representative member in this category is illustrated in Scheme 32.



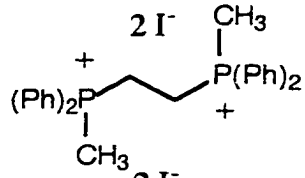
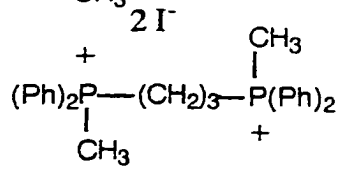
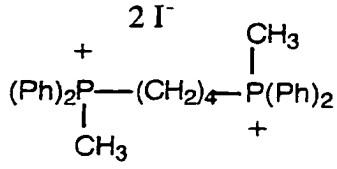
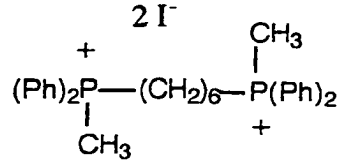
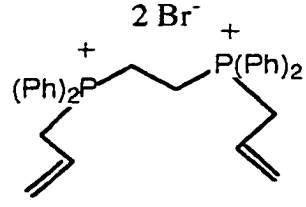
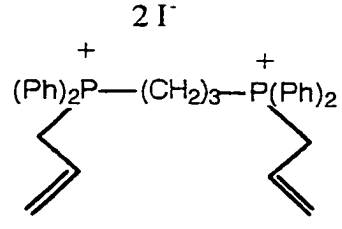
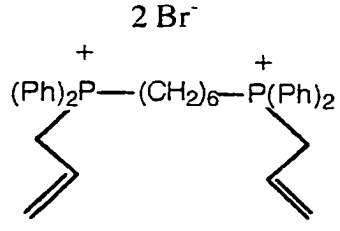
{85}

Scheme 32

Treatment of 1,2-bis(diphenylphosphino)ethane with two equivalents of

iodomethane in acetonitrile solution while heating gave the new dicationic phosphonium string, 1,2-bis(*P*-methyl-*P*,*P*-diphenyl)phosphonioethyl diiodide, {85}. Table 19 lists all of the newly prepared compounds in this category {85} - {91}.

Table 19 - New dicationic polyphosphonium strings

Structure	Number	Name
	**85**	1,2-bis(*P*-methyl-*P*,*P*-diphenyl)phosphonio-ethyl diiodide
	**86**	1,3-bis(*P*-methyl-*P*,*P*-diphenyl)phosphonio-propyl diiodide
	**87**	1,4-bis(*P*-methyl-*P*,*P*-diphenyl)phosphonio-butyl diiodide
	**88**	1,6-bis(*P*-methyl-*P*,*P*-diphenyl)phosphonio-hexyl diiodide
	**89**	1,2-bis(*P*-allyl-*P*,*P*-diphenyl)phosphonio-ethyl dibromide
	**90**	1,3-bis(*P*-allyl-*P*,*P*-diphenyl)phosphonio-ethyl diiodide
	**91**	1,6-bis(*P*-allyl-*P*,*P*-diphenyl)phosphonio-hexyl dibromide

NEW ALCOHOL PROTECTING GROUP

The development of new approaches for the protection of hydroxyl functionalities, particularly *primary* hydroxyl functionalities, is a topic of continuing interest. In the course of our efforts toward the synthesis and evaluation of characteristics of polycationic organic salts, we prepared several esters in the general category of alkyl α-azoniacarboxylates, carboxylic esters bearing a quaternary ammonium site at the α-position as shown in Figure 16.

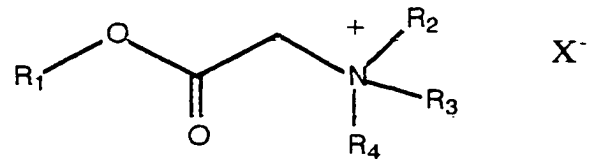
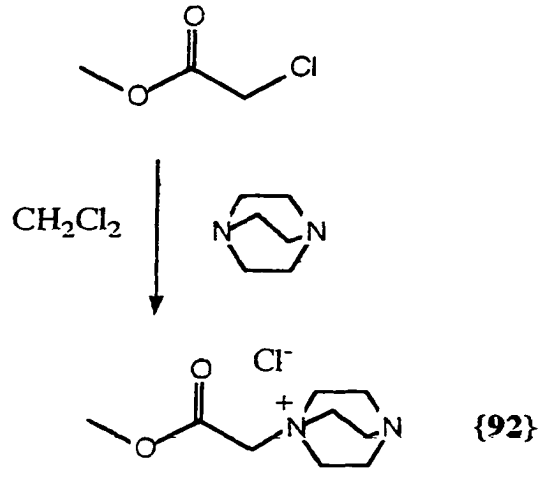


Figure 16 - A carboxylic ester bearing a quaternary ammonium site at the α-position

These materials have demonstrated stability at pH=7 but reactivity for cleavage under slightly more acidic conditions provide intriguing possibilities for serving as protecting functions. Specifically: a) given the bulk of the substituent at the α-carbon site, significant selectivity for primary as opposed to secondary hydroxyl groups is anticipated; b) the incorporation of the cationic site into the protected alcohol increases dramatically the aqueous solubility of the organic material allowing it to be operated upon efficiently by reagents in neutral aqueous solution; and

c) slight modification of the pH of the medium allows rapid cleavage of the protecting function and regeneration of the alcohol functionality.

To this end, a series of these new materials has been prepared. The synthesis of a representative member of this category is shown in Scheme 33.

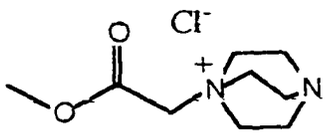
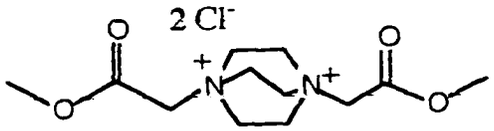
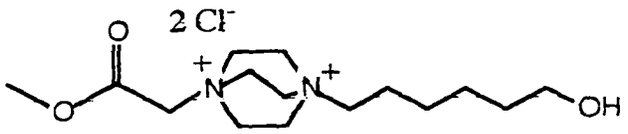
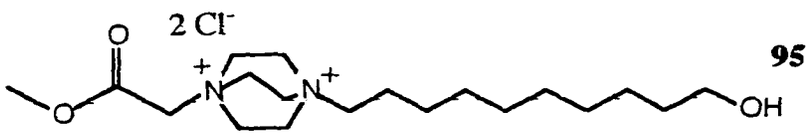


{92}

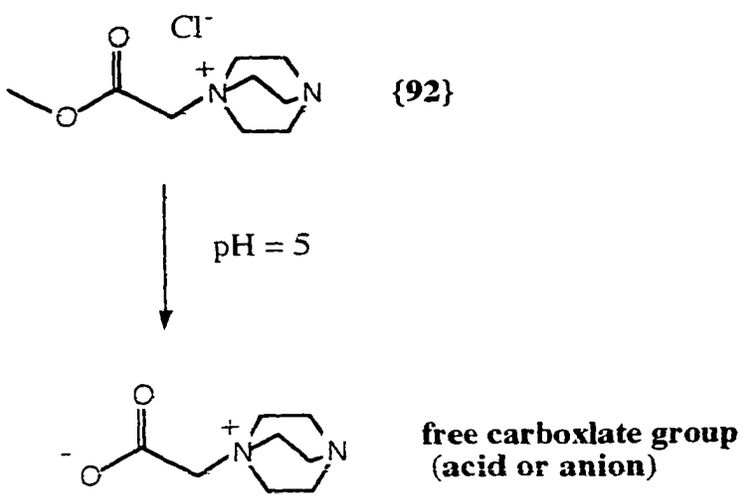
Scheme 33

Treatment of a solution of methyl chloroacetate in methylene chloride with a solution of dabco in methylene chloride with heating and stirring gives {92} with the hydroxyl protecting group attached. Table 20 lists all of the materials in this category {92} - {95}.

Table 20 - New alcohol protecting groups

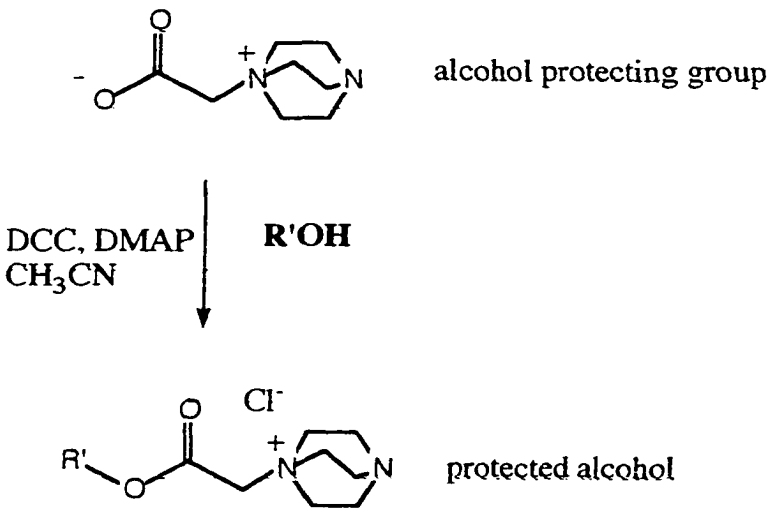
Structure	Number
	**92**
	**93**
	**94**
	**95**

The above materials are then treated with water at pH=5 to generate the free carboxylate group (acid or anion) as shown in Scheme 34.



Scheme 34

It is anticipated that these new compounds, when allowed to react with a primary alcohol will generate an ester (a masked alcohol) as illustrated in Scheme 35.



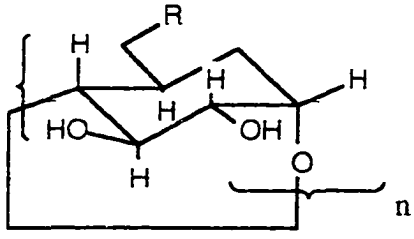
Scheme 35

An appropriate solvent must be used in order to combine both the zwitterionic salts and ordinary organic materials. However, with our experience of solubilities of salts it is expected that either pyridine or acetonitrile should allow facile ester formation. It is anticipated that facile synthesis without the use of unreasonable excesses of either the alcohol or the α-azoniacarboxylic acid species will occur.

POLYCATIONIC CYCLODEXTRIN DERIVATIVES

The functionalization of CDs for specific introduction of substituents has been thoroughly established. [145-150] A series of

polycationic derivatives of cyclodextrins (CDs) has been prepared as illustrated in Figure 17. [150]

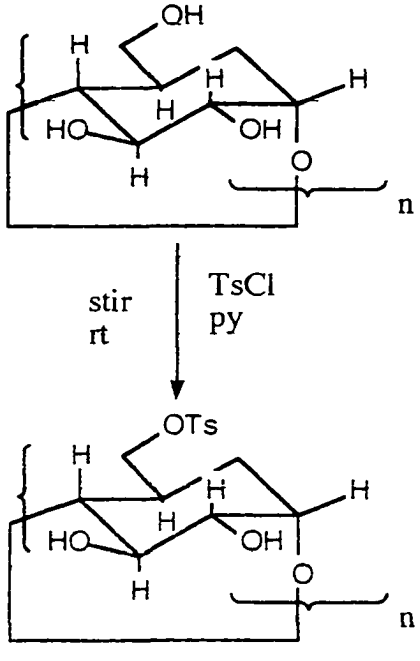


n = 6 (α), 7 (β), 8 (γ)

R = cationic substituent

Figure 17 - Polycationic derivatives of cyclodextrins

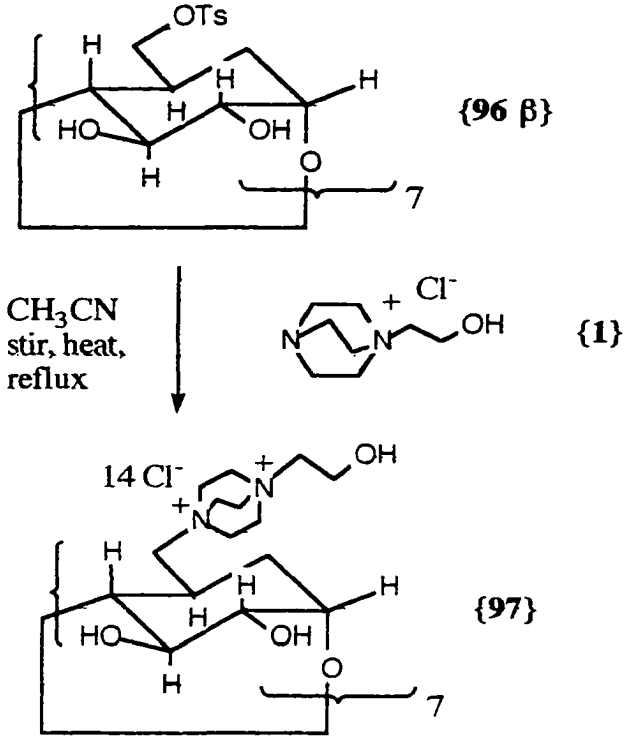
The general approach to the preparation of such materials is illustrated in Scheme 36.



{96 α : n=6}
{96 β : n=7}
{96 γ : n=8}

Scheme 36

Treatment of the parent CD with an excess of *p*-toluenesulfonylchloride in pyridine, followed by evaporation of volatiles generates a *per*-tosylated CD at the 6-position hydroxyl groups. [145] This per-tosylated CD is subsequently treated with a monocationic string as shown in Scheme 37.

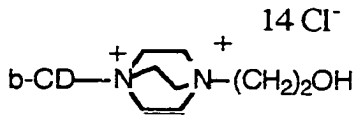
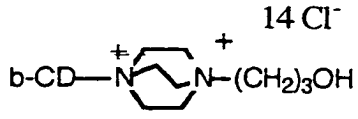
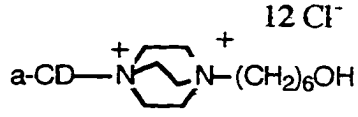
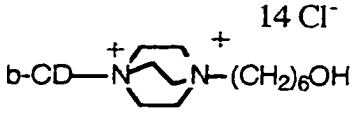
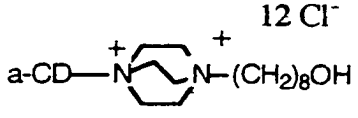
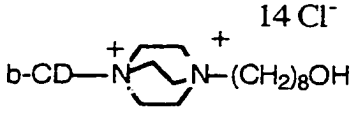
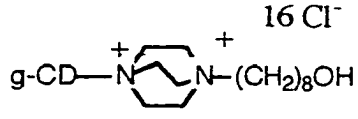


Scheme 37

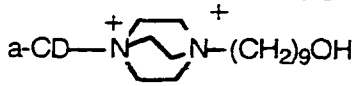
Treatment of the tosylated β-CD {96β} in acetonitrile solution with an eight equivalent solution (slight excess) of the monocationic string {1} in acetonitrile solution generates the target *per*-derivatized polycationic β-CD derivative {97}. Both solutions of tosylated CD and monocationic string must first be thoroughly heated and stirred in acetonitrile to

completely dissolve, then the two solutions can be combined. The reaction mixture is refluxed for a minimum of two days to allow full reaction to occur. The resultant precipitate is then washed with ethyl acetate and ether solutions, filtered, and the recovered solid is dried under high vacuum. Table 21 lists all of the new polycationic CD derivatives in this category {97-115}, where a-CD = α-cyclodextrin; b-CD = β-cyclodextrin; g-CD = γ-cyclodextrin. All of the materials are *per*-derivatized with a cationic substituent, as noted, at the 6-position hydroxyl groups of the cyclodextrin.

Table 21 - New polycationic CD derivatives

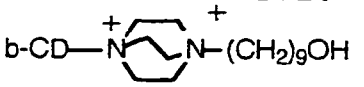
Structure	Number
	**97**
	**98**
	**99**
	**100**
	**101**
	**102**
	**103**

12 Br^-



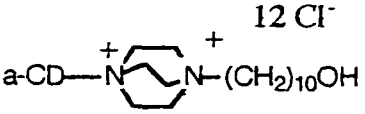
104

14 Br^-



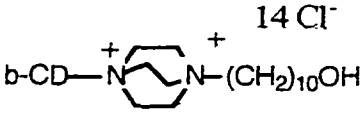
105

12 Cl^-



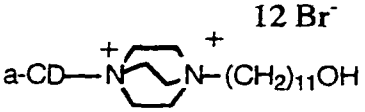
106

14 Cl^-



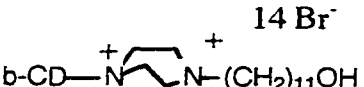
107

12 Br^-



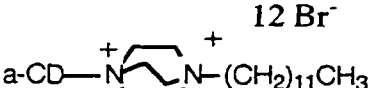
108

14 Br^-



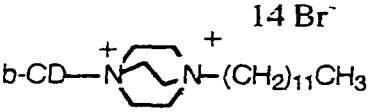
109

12 Br^-



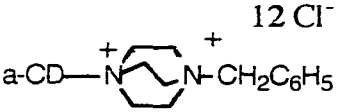
110

14 Br^-



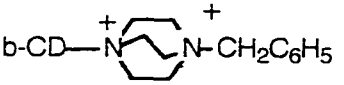
111

12 Cl^-



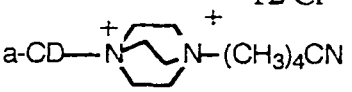
112

14 Cl^-



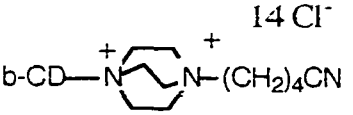
113

12 Cl^-



114

14 Cl^-

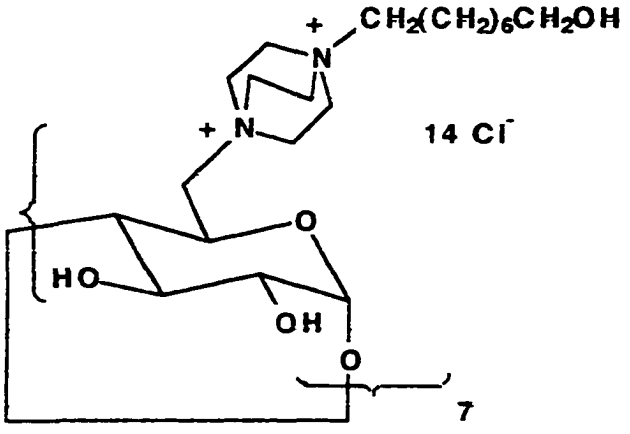


115

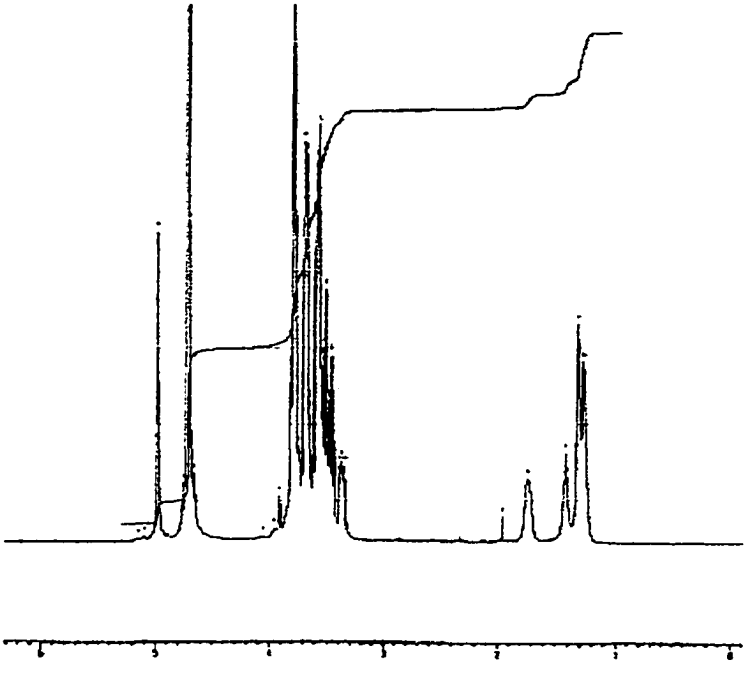
Derivatives {114} and {115} were prepared by an undergraduate, Valbona Behaj, under my direction. The starting material monocationic string was prepared by treating dabco with one equivalent of 5-chlorovaleronitrile in ethyl acetate solution to give the pure monocationic cyano salt, 5-(1'-azonia-4-azobicyclo[2.2.2]octyl)valeronitrile chloride, {116}.

A point worthy of note regarding the synthesis of these new materials concerns the *anion* of the isolated product. Performance of the reaction in acetonitrile results in the precipitation of the salts in the *halide* form rather than the tosylate form. The salt form, involving the tosylate, remains in solution in acetonitrile. Presumably, the more organic tosylate anion associates closely with the polycationic CD and maintains solubility in the organic medium, the precipitate being solely, under proper conditions, that with the halide gegenion.

All products exhibit ^{1}H and ^{13}C NMR spectra in accord with their proposed structures as demonstrated with the ^{1}H and ^{13}C NMR spectrum of {102} in Figure 18, along with satisfactory combustion analyses agreeing with their formulations. Details of the ^{1}H and ^{13}C NMR spectra are given in the experimental.



{102}



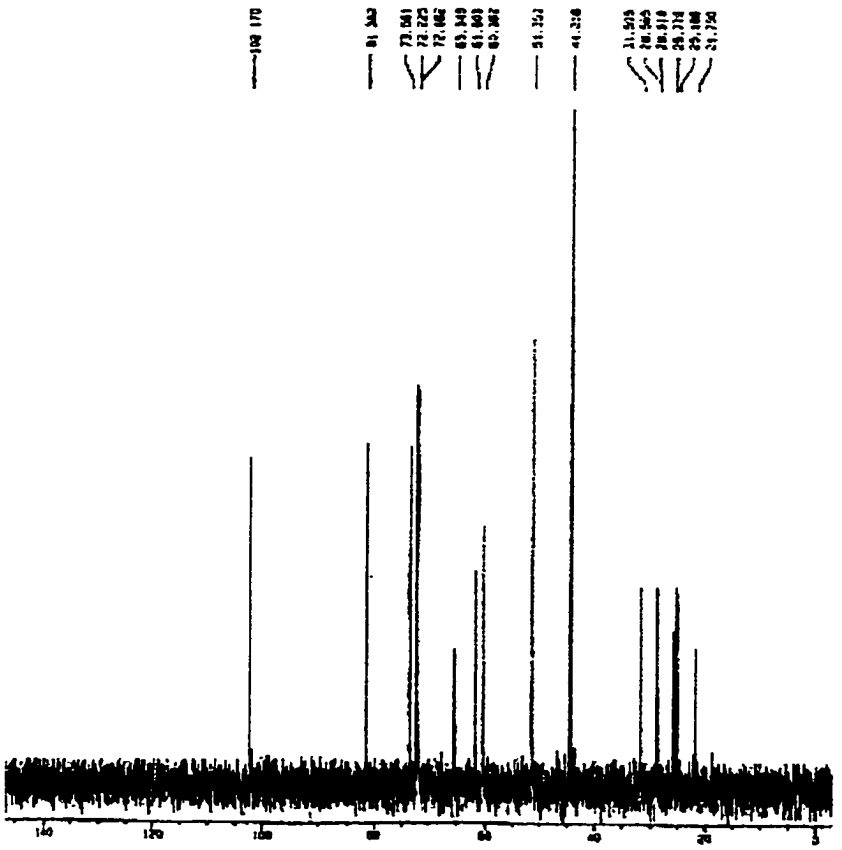


Figure 18 - Structure, ^{1}H and ^{13}C NMR spectrum of β-CD derivative {102}

All of these salts are somewhat hydroscopic, even upon short exposure to room air, so analyses are for the hydrated forms of the salts. This has been observed as well for other polycationic salts synthesized by our laboratory. [12] COSY spectra allow assignment of particular proton signals to sites within the organic structure as illustrated with the β-CD derivative {102} in Figure 19.

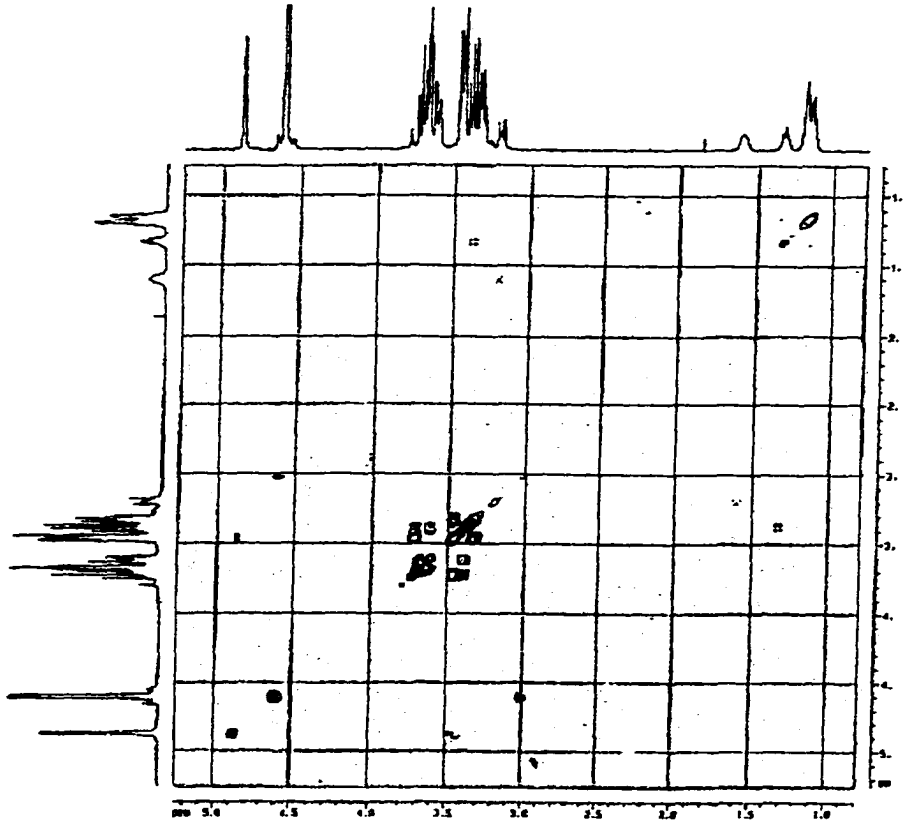


Figure 19 - COSY spectrum of β-CD derivative {102}

The yields of these new materials, as would be expected, is relatively low, based on starting material (tosylated CD or monosubstituted DABCO cation).

It was envisioned that species so substitued at the smaller rim of the conical section defined by the CD structure could exhibit particular binding characteristics toward organic anions, serving as host species for a variety of anions. These species would bear, in addition to the cylindrical cationic region, two hydrophobic regions, one within the CD

cone and the other on the opposite side, above the cationic region. The polycationic CD derivatives thus synthesized could be imagined to have a general tube shape. Each cationic region would be flanked on either side by relatively hydrophobic regions, the interior of the parent CD unit, and the so-called tails attached above as illustrated in Figure 20. The COSY spectrum shown in Figure 19 illustrates the two sets of signals for the DABCO ring at 3.4 and 3.7 ppm and the α- site at 3.7 ppm connected to the adjacent site of the chain at 1.3 ppm.

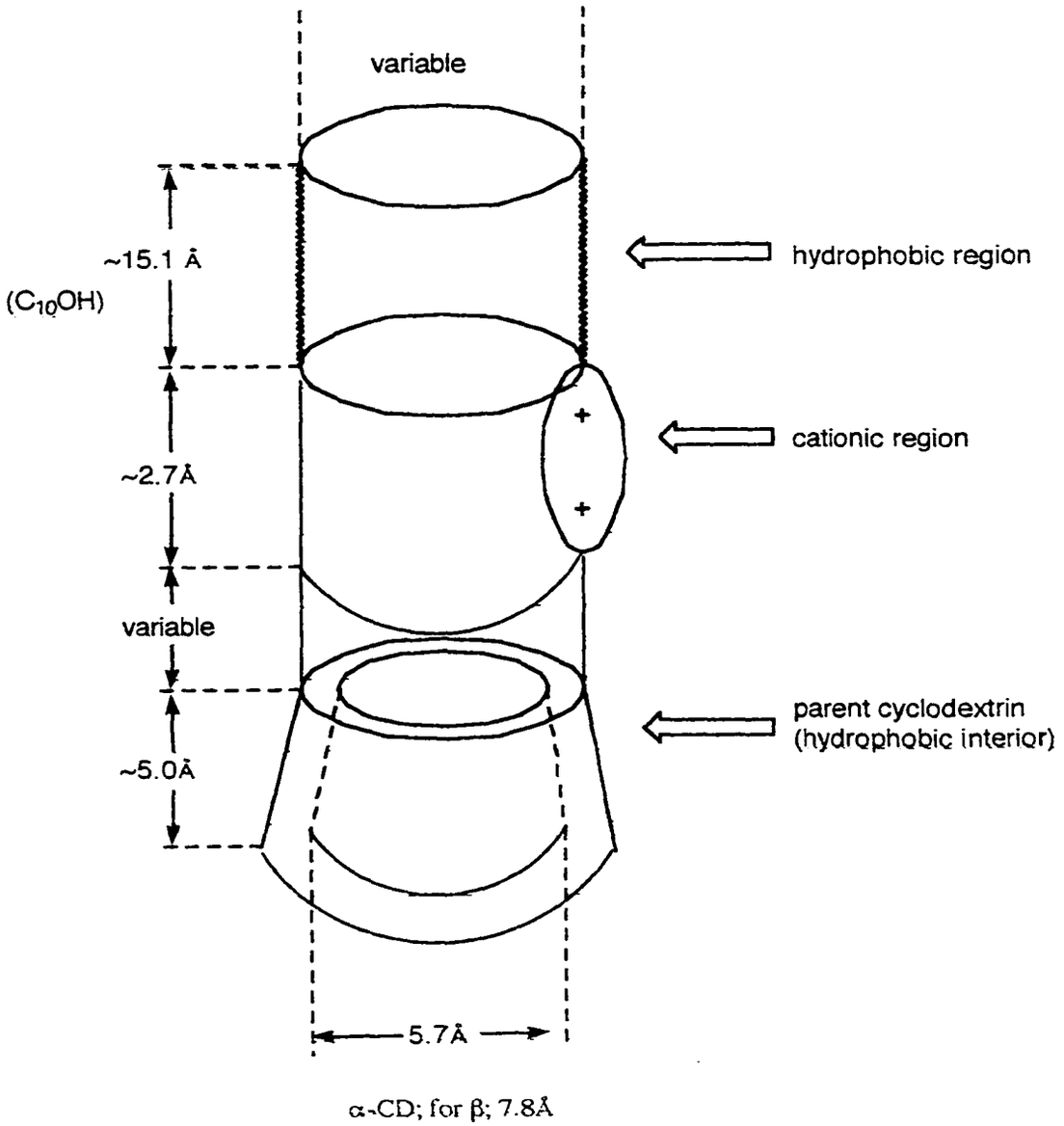


Figure 20 - "Tube shape structure" of CD derivatives showing cationic region flanked by hydrophobic regions

The tubular nature of these derivatives would be variable; while the lower portion would be rigid, the top portion may be envisioned as long flexible ropes, forming a tube when these ropes come together. The lipophilic

interaction of these ropes is assisted by hydrophobic interactions with the external water.

The inclusion of anion guests within the tube of the CD derivatives would be anticipated to modify the NMR chemical shifts of the host CD derivative in a predictable manner. Titration of the host species with added anion guest species would be expected to provide association constants for the systems, as well as indications of the orientation of host/guest interactions. The most readily observed quantitative indicator of interaction of the host and guest species is the change in the ^{1}H NMR spectrum of the host polycationic CD upon being challenged with the anionic guests. In fact, an upfield shift of the signals for hydrogens in the vicinity of the cationic sites of the polycationic CD is observed upon addition of the guest anionic species. This is in accord with an interpretation in which those hydrogens are additionally shielded from the applied magnetic field by the additional high electron density associated with the guest anionic site. Further, quite rapid exchange of guest species between the conditions of host-bound and free in solution is noted; only a single signal is observable for the polycationic CDs when challenged with the guest anionic species, rather than separate signals for associated and unassociated hosts.

Given this situation, some standard aspects commonly used in the

determination of host/guest association constants and other binding characteristics are precluded. The variation of this change in chemical shift with the changing of the relative concentrations of host and guest species can be used to determine association constants [151-153], but is not amenable to the direct determination of the stoichiometry of the association using continuous variation of mole concentration methods. [154,155] A 1:1 association of host with guest is deduced by the fit of the data with the Benesi-Hildebrand equation for such an association [151,156] and by calculations of host cavity and guest sizes using Chem 3D+.

For measurement of the association constants, to measured neutral solutions (D_2O, pD = 7) of the polycationic CD hosts were added varying amounts of measured solutions of the biologically derived oxyanion guests, volumes being adjusted for standardization.

POLYCATIONIC CYCLODEXTRIN HOST/GUEST BINDING INTERACTIONS WITH AMINO ACIDS AND TETRAPEPTIDES

The guests include a series of three phosphorus oxyanions from biological sources, six carboxylate salts of *N*-protected natural α-amino acids (and one sodium salt of a free amino acid), and two carboxylate salts of tetrapeptides. These guest species are indicated in Table 22.

Table 22 - Guest species investigated with host polycationic cyclodextrin derivatives

Phosphorus oxyanions (disodium salts)

(-)-(1R,2S)-(1,2-epoxypropyl)phosphonic acid (*i*)
2'-deoxyadenosine monophosphate (*ii*)
2'-deoxythymidine monophosphate (*iii*)

Amino acid derivatives (sodium salts)

N-acetyl-L-phenylalanine (*iv*)
N-acetyl-L-cysteine (*v*)
N-acetyl-L-tyrosine (*vi*)
N-acetyl-L-leucine (*vii*)
N-acetyl-L-glutamic acid (*viii*)
folic acid [pteroylglutamic acid] (*ix*)
L-lysine (*x*)

Peptides (sodium salts)

phenylalanylglycylglycylphenylalanine (*xi*)
prolylphenylalanylglycyllysine (*xii*)

The added guest species were sufficiently dilute that no measurable change in pH could be observed over the range of concentrations of guest used (0.1-4.5 equivalent of guest compared to host). With the exception of the highest concentration of guest, with which was measured the limiting (maximum) change of chemical shift approximating fully complexed host, calculations of association constants were made using the lower concentrations of guest relative to hosts. It is with these concentrations that the greater, and thereby more accurate for purposes of association constant calculations, changes of chemical shift with increasing concentrations could be noted.

As previously noted, interaction of the organic anion guests with the polycationic functionalized CD hosts could be noted through changes of the chemical shifts of ^{1}H-NMR signals derived from the hydrogens located near the cationic region of the host species. Specifically, upfield shifts in the signals for the hydrogens of the DABCO rings and adjacent sites of the host species were noted as a result of shielding by association with the guest anionic species. Figure 21 illustrates those particular hydrogens for the α-CD derivative {106}.

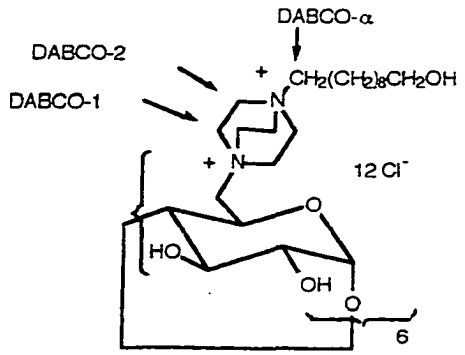


Figure 21 - Hydrogens of {106} exhibiting upfield shifts.

Representative spectra showing the changes in the chemical shifts of signals for hydrogens near the cationic sites of the host are shown in Figure 22.

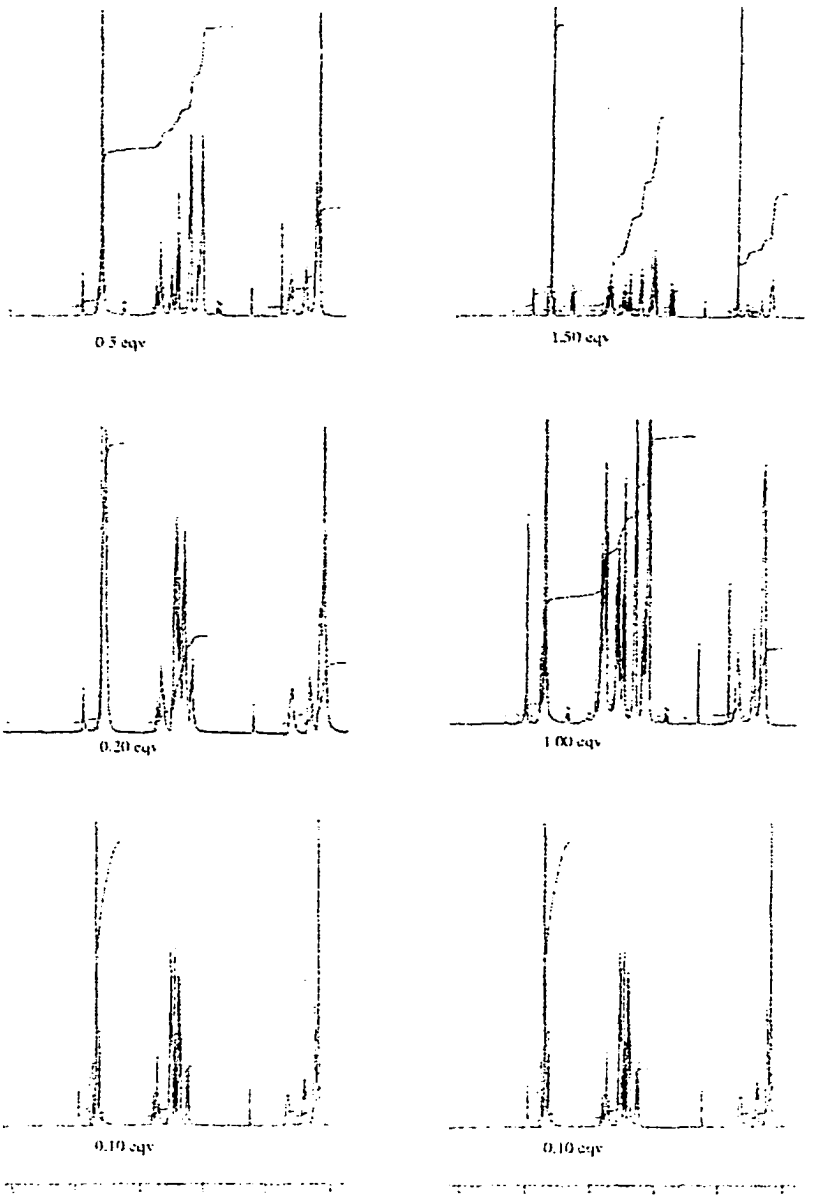


Figure 22 - Effect of guest *N*-acetyl-L-Phe (iv) on ^{1}H NMR spectrum of host polycationic CD derivatives. On left is {101}; to the right is {106}.

Specifically, representative spectra for the interactions of the polycationic α-CD derivatives {101} and {106} with *N*-acetyl-L-phenylalanine (iv) are

shown.

Assignments of the shifted signals to specific sites have been made, confirmed through the use of ^{1}H-COSY 2D NMR measurements on the parent polycationic CDs and on the complexes. Representative COSY spectra for {108} and a solution of {108} with added *N*-acetyl-L-phenylalanine (iv) are shown in Figure 23.

a)

b)

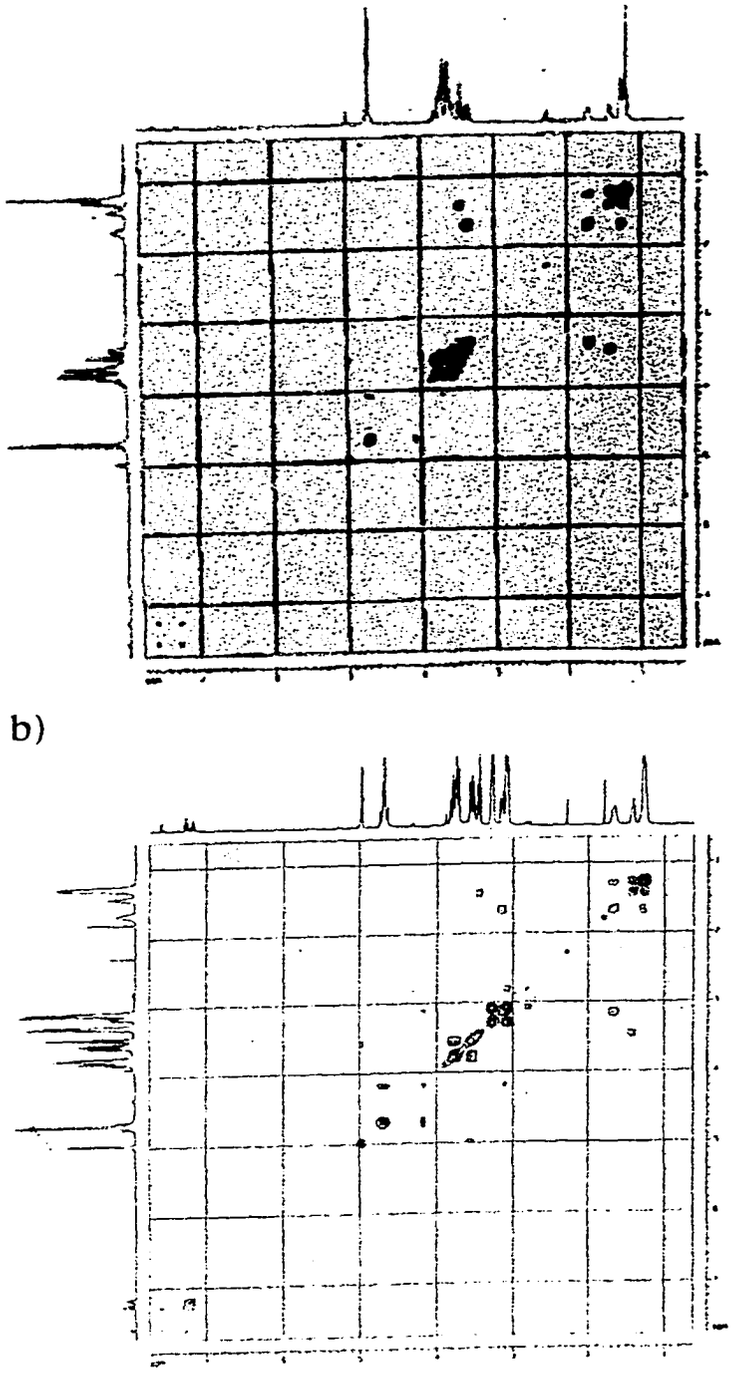


Figure 23 - (a) COSY of {106}; (b) COSY of {106} with added 0.05 equivalents of (iv).

The magnitude of chemical shift changes, even at low loading of the guest species, along with the exhibition of only a single set of NMR signals, clearly indicate several characteristics of the interactions. First, there is a rapid equilibration of "free" and "bound" guest species. Further, this association is a strong one and occurs within the "tube" of the host rather than at the external surface as illustrated in Figure 24.

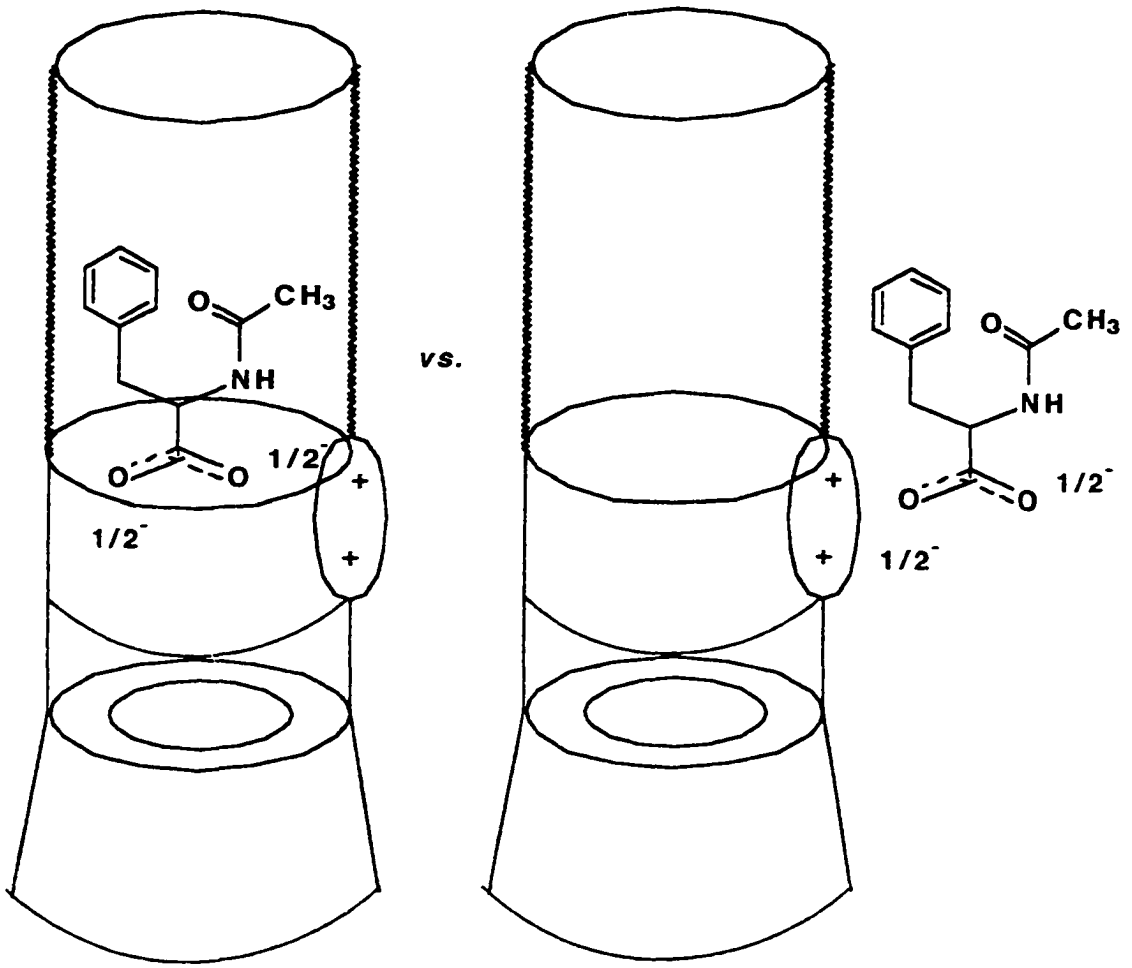


Figure 24 - Association of the guest, *N*-acetyl-phenylalanine, (iv), *inside* the "tube" of the polycationic CD host.

We understand this from the observations of only one set of signals for the affected hydrogens; the guest interacts equally with all of the charged sites of a particular chemical type. Interaction outside the tube would result in a significantly more complex NMR spectrum as all hydrogens of a particular chemical type would have different interactions with the anionic guest species.

Association constants for each guest-host interaction were determined through the measurement of the changes in chemical shift upon addition of increasing amounts of guest species using the Benesi-Hildebrand method (plot providing slope of K in Equation 1).

$$K = \frac{\left\{ \frac{(\delta_{obs} - \delta_{free})}{(\delta_{max} - \delta_{free})} [CD]_{stoic} \right\}}{\left\{ [CD]_{stoic} - \frac{(\delta_{obs} - \delta_{free})}{(\delta_{max} - \delta_{free})} [CD]_{stoic} \right\} \left\{ [guest]_{stoic} - \frac{(\delta_{obs} - \delta_{free})}{(\delta_{max} - \delta_{free})} [CD]_{stoic} \right\}}$$

Equation 1

The results are shown in Table 23.

Table 23 - Association constants (K) for binding of anions with polycationic cyclodextrin derivatives

Guest	Host									
	{101}	**{106}**	**{108}**	**{116}**	**{110}**	**{102}**	**{107}**	**{109}**	**{117}**	**{111}**
i	0.036	*	0.073	0.042	0.020	0.0048	*	0.38	0.031	*
ii	0.099	0.080	1.2	0.025	*	0.39	0.012	2.6	*	*
iii	0.086	0.049	*	*	*	0.46	0.22	*	*	*
iv	1.0	5.6	24	3.4	1.1	4.2	1.8	7.6	4.0	5.6
v	5.6	15	28	7.6	67	120	7.2	34	76	18
vi	0.16	2.2	1.1	5.3	0.24	44	0.72	2.0	1.7	1.6
vii	3.1	2.2	0.89	1.0	0.43	4.0	3.3	0.86	7.3	0.55
viii	1.4	1.9	1.0	1.0	1.1	3.9	1.3	0.45	1.4	0.71
ix	2.6	2.3	3.6	2.5	2.9	3.4	6.2	1.3	2.1	0.28
x	2.8	1.0	1.5	4.7	0.72	3.2	31	1.3	1.7	0.50
xi	1.3	0.89	1.3	1.0	0.91	23	2.7	1.7	12	0.62
xii	36	4.2	11	27	25	39	13	12	33	5.4

Calculations of K (M^1 x 10^3) in each instance were made on the basis of changes in chemical shift of the hydrogens of the DABCO ring more distant (DABCO-2) from the cyclodextrin unit (refer to Figure 21). These hydrogens in all instances exhibited the greatest maximal change in chemical shift and thereby provided the most reliable indicator of binding.

Benesi-Hildebrand type graphs of the chemical shift data for DABCO-2 hydrogens for the systems {108} and {106} with the addition of *N*-acetyl-phenylalanine (iv) are shown in Figure 25.

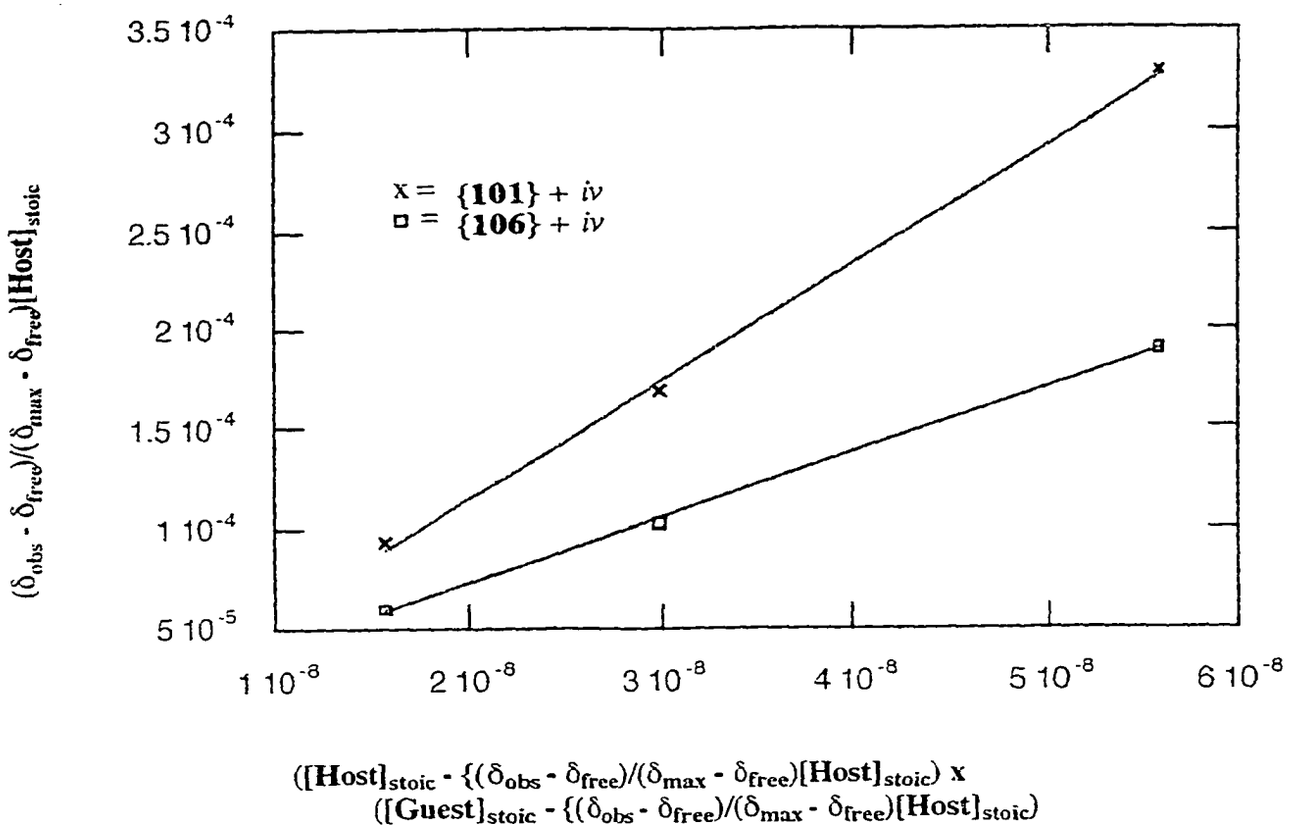


Figure 25 - Plots using Benesi-Hildebrand method for determination of *K*

The linearity of each of these plots (lines shown are least square fits of the data) is in accord only with a 1:1 association of host and guest.

There are sizable variations in the values of the association constants measured. First, the association constants noted for the phosphorus oxyanion species, while greater than unity, are generally less than 10^3 (4.8-460, with only one observed to be greater than 10^3:1,200). Significantly stronger interactions are observed with the amino acid series for which the general range is 10^3-10^4, with one instance ({102} interacting with the tetrapeptide *xii*) more than 10^5. The CD derivative most effective at serving as host for all of the amino acid series guest is {102}, that bearing the 8-hydroxyoctyl substituent on each of the DABCO rings. Significantly strong interactions are observed with each of the host CD derivatives examined. These results are promising for potential utility of the polycationic CDs as selective binding and transport agents for peptides.

While the binding of the entire series of amino acid derivatives and the tetrapeptides studied is quite strong, the orientation of binding is not the same for all of these guest species in a given host. As noted previously, the values for the association constants were determined through observation of the changes in chemical shift for the DABCO-2

hydrogens, a change that was quite similar for all of the host/guest systems. Observation of changes of all of the hydrogens within the cationic region of the CD derivatives indicates different degrees of change in chemical shift for the DABCO-α hydrogens (refer to Figure 21), depending on the specific host and guest species. Particularly with the *N*-acetyl-glutamic acid (viii) and the folic acid (ix) guest systems, with all host species, negligible change in the chemical shift of these DABCO-α hydrogens could be noted while the changes in chemical shifts for DABCO-1 and DABCO-2 hydrogens remained comparable to that for other systems studied. This was also observed for the remainder of the guests on interaction with hosts {110} and {111}, those with the dodecyl (so-called) tail lacking any functionality that could provide polar or hydrogen-bonding interaction from the tail.

These latter results suggest that approach of the guest to the host can occur in two different ways, depending on the nature of any additional polar or anionic substituent on the guest and the ability of the host to accommodate such substituents.

In the normal situation, the guest may enter the host from the "top" of the tube. The anionic portion of the guest associates with the cationic region from the top, approaching closely to the DABCO-α region. We interpret the results as demonstrating that this mode of approach occurs

with the guest species derived from Phe, Cys, Tyr, Leu, and Lys, as well as the two tetrapeptides studied.

Alternatively, approach of the guest to the host could occur from the bottom of the tube, the parent CD side. The anionic region of the guest would thereby approach first the DABCO-α hydrogens relatively unshielded. This latter approach would be favored in two types of instances: (1) with all CD derivatives, those systems for which an additional or anionic substituent is present on the guest, and (2) with all monoanionic guests interacting with a host {110} and {111} devoid of any capability of hydrogen bonding or ionic interaction involving the distal regions of the tail. The observations suggest that this approach occurs for *N*-acetyl-glutamic acid and folic acid species. Such systems involve relatively unfavorable interactions of the hydrophobic tail at the top of the host tube with any portion of the guest. Figure 26 illustrates approach of *N*-acetyl-phenylalanine (iv) to {106} versus the approach of *N*-acetyl-glutamic acid (viii) to {106}.

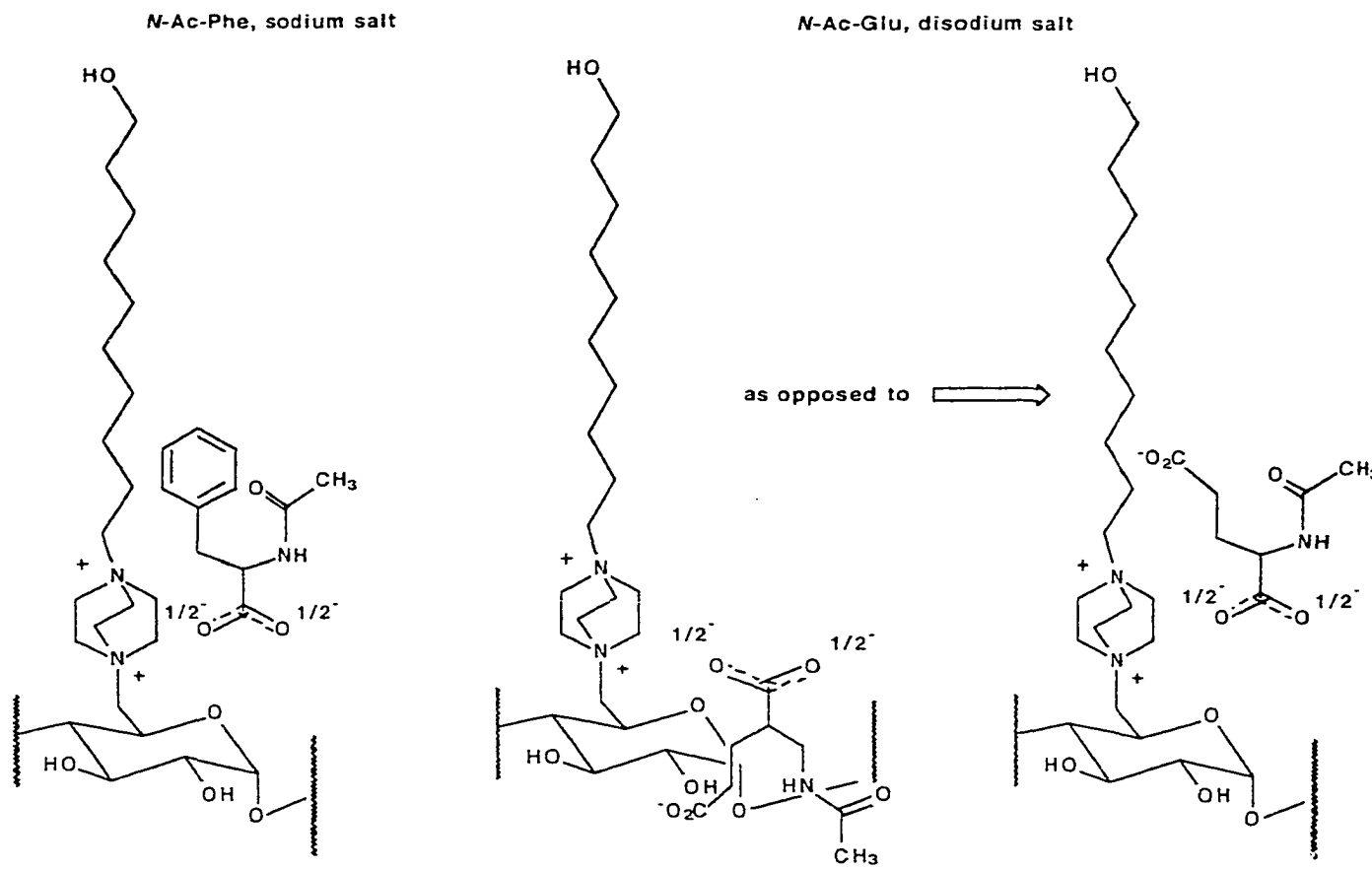


Figure 26 - Approach of *N*-acetyl-phenylalanine (iv)to to {106} versus the approach of *N*-acetyl-glutamic acid (viii)to {106}.

POLYCATIONIC CYCLODEXTRIN HOST/GUEST BINDING INTERACTIONS WITH THE CONJUGATE BASES OF PHOSPHORUS-CONTAINING AND CARBOXYLC ACIDS

The polycationic CD derivatives have also been investigated for their binding capabilities with a series of biologically significant phosphate salts and α,ω-dicarboxylic acids. These include phosphonomycin, deoxyadenosine-5'-monophosphate, deoxythymidine-5'-monophosphate, oxalate, malonate, succinate, glutarate, adipate, pimelate, subarate, azelate, sebacate, fumarate, maleate, acetylene dicarboxylate and terephthalate as illustrated in Figure 27.

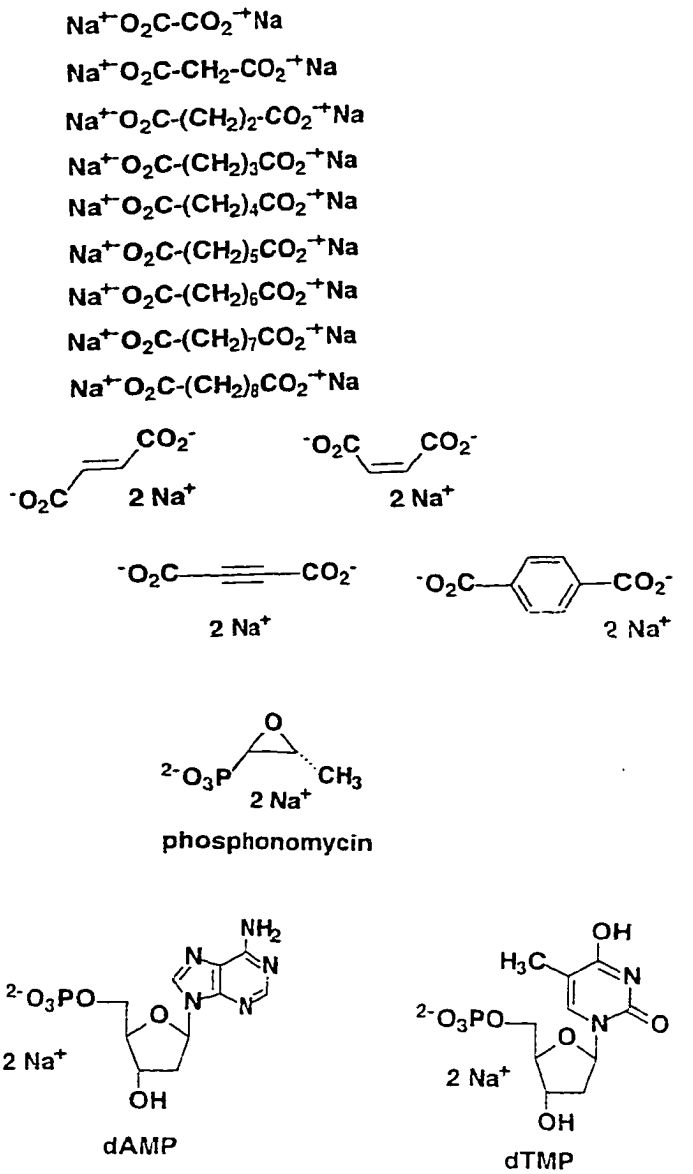


Figure 27 - Conjugate bases of phosphorus-containing and carboxylic acids investigated with polycationic CD derivatives for host/guest binding interactions

Addition of the anionic forms of the dicarboxylic acid or phosphorus acid species to aqueous (D_2O) solutions of the polycationic CD species, also results in a significant change of the ^1H NMR for those polycationic species.

As with the studies with the interaction of the modified CDs with the amino acids and peptides, the ^1H signals from the sites in the region of the positive charges are shifted *upfield* indicating those hydrogens to be shielded by the presence of the associated anions.

As previously noted, the magnitude of the shifts and the simplicity of the resulting spectra indicate that association of the guest with the host occurs inside the "tube" of the host species as illustrated in Figure 28.

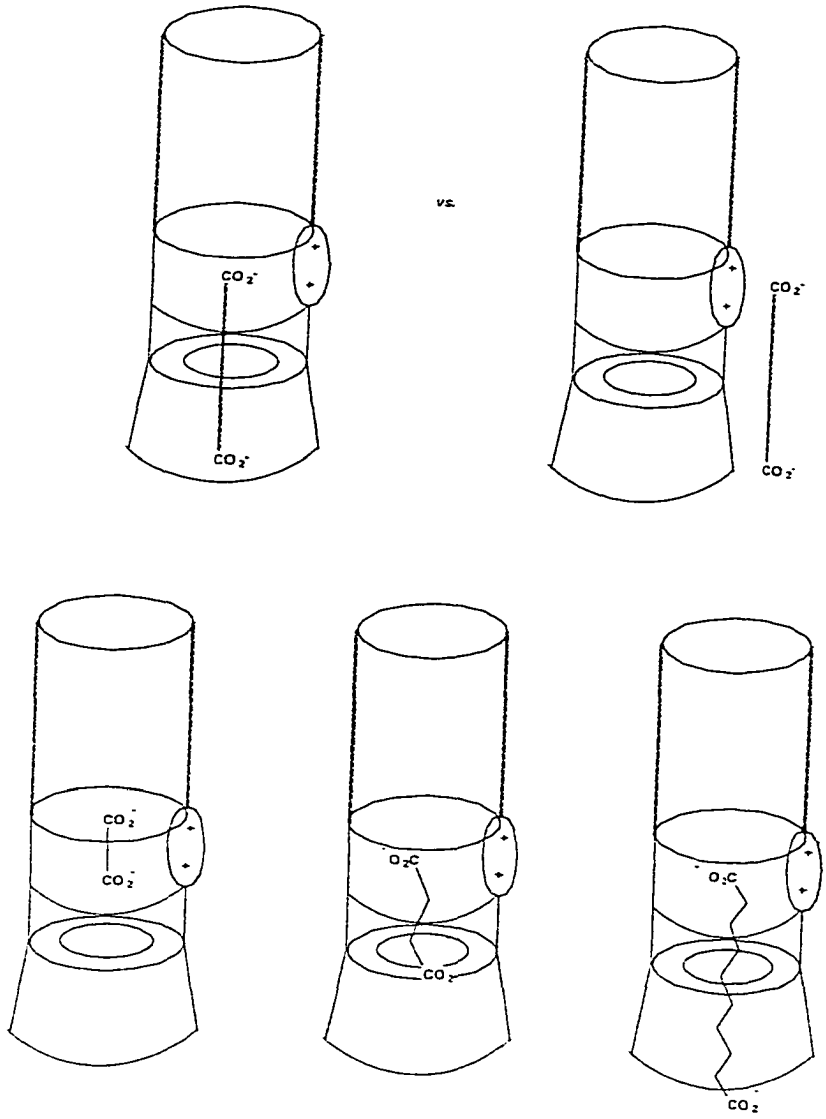


Figure 28 - Association of an α,ω-dicarboxylic acid guest *inside* the "tube" of a polycationic CD host

The variation of the change in chemical shift for the three sets of hydrogens of the α-CD derivative generated from the DABCO-substituted with the ω-hydroxydecyl group {106} (labeled DABCO-1, DABCO-2, and DABCO-α) with addition of increasing amounts of disodium sebacate is shown in Figure 29.

D_2O solution

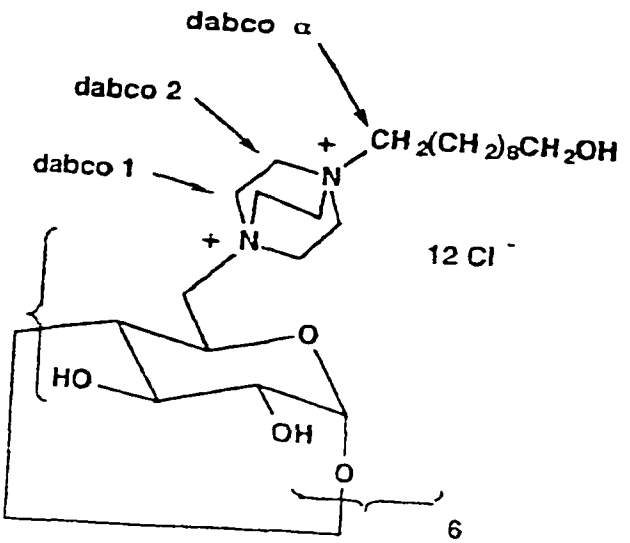
Added Guest (equivalents)	α	Upfield Shift (Hz) 1	2
0	0	0	0
0.1	17	15	19
0.2	33	30	37
0.5	72	65	80
max	220	189	245

[Host]/[Guest] (*M*)

"0.5" 0.000828/0.000413

"0.2" 0.00102/0.000203

"0.1" 0.00110/0.000110



{106}

Figure 29 - Upfield change of chemical shift upon addition of sebacate (disodium salt) to {106}

As previously noted calculation of appropriate association constants for the interactions of the dicarboxylic acids and phosphorus acid species with the modified polycationic CDs are as shown in Table 24.

Table 24 - Association constants, *K*, for the interactions of dicarboxylic acids and phosphorus acid species with the polycationic CD derivatives

Determined Values of K ($x10^3$)

Guests \ Hosts	101	102	106	107	108	109	112	113	110	111
Oxalate	*	36	13	*	57	14	*	*	12	25
Malonate	*	*	1	*	*	2	*	*	2	1.7
Succinate	*	4.5	1	*	9.9	9.9	*	*	2.8	0.5
Glutarate	*	7.6	3.1	*	1.5	4.4	*	*	2	1
Adipate	*	4	1.7	*	8.2	16	*	3.4	1.6	1.7
Pimelate	*	3.6	5.2	*	2.1	6	*	*	9.9	*
Suberate	*	26	5.5	*	13	49	*	*	*	24
Azelate	*	*	1.8	*	17	29	*	*	49	83
Sebacate	*	24	3.4	*	*	*	*	*	*	*
Fumarate	*	*	2.4	*	0.4	3.3	*	*	1.4	2.8
Maleate	*	2.4	5.6	*	3.1	4.1	*	*	7.9	7.1
Terephthalate	*	*	*	*	21	56	*	*	7.5	14
Acetylene Dicarboxylate	*	*	*	*	35	32	*	*	13	7.7
Phosphonomycin	0.036	0.005	*	*	0.073	0.38	0.042	0.031	0.020	*
dAMP	0.099	0.39	0.080	0.012	1.2	2.6	0.025	*	*	*
dTMP	0.086	0.46	0.049	0.22	*	*	*	*	*	*

Several conclusions can be made on the basis of these data. First, the association constants, in most instances, are quite significant. Second, the association constants for the phosphorus-containing anions are less than those for the dicarboxylate anions. Third, the association constants for the dicarboxylate anions are comparable with those for interaction of this type of modified CD with substituted amino acid and tetrapeptide anions. Fourth, the variation of association constant with length of the dicarboxylate chain is intriguing; the shortest chain, oxalate, measures 3.187 Å from anionic-oxygen to anionic-oxygen and exhibits a very strong equilibrium interaction. This equilibrium interaction *decreases* as the chain is lengthened as in malonate and succinate, and again *increases* with greater distance between carboxylate sites. The oxylate dianion matches best with the distance between quaternary ammonium sites on the disubstituted DABCO regions that measures 2.7 Å from anionic-oxygen to anionic-oxygen.

Several possibilities can be envisioned for the mode of association of the dicarboxylates inside the modified CD. First, we can envision one carboxylate site associating with the cationic region while the second "hangs" beneath it through the parent CD cavity. Second, there is the possibility that one carboxylate site could associate with the cationic region while the second is "elevated" above it in the hydrophobic "tube"

formed by the R' "tails". Finally, with a dicarboxylate of proper length, such as with the oxalate dianion, the two anionic sites could bridge the cationic region. The three modes of association of the dicarboxylates with the modified CDs are illustrated in Figure 30.

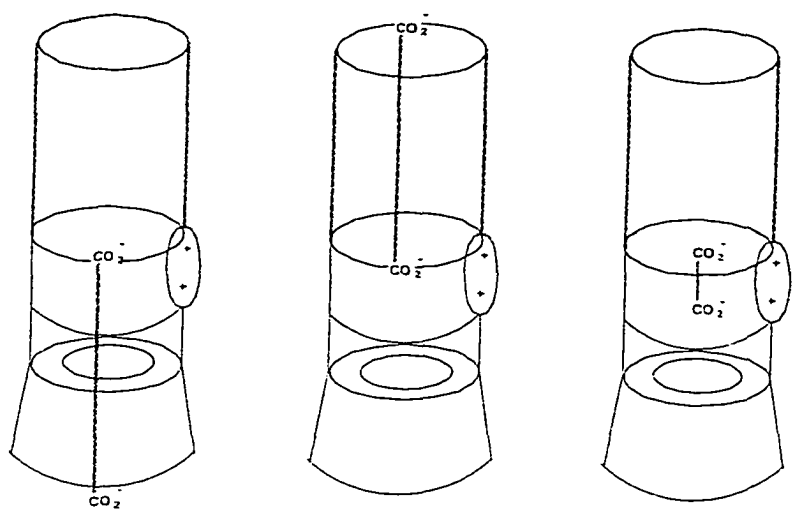


Figure 30 - Three modes of association of the dicarboxylates inside the modified CDs.

For the dicarboxylates of greater length than oxylate, a high degree of association (large value of *K*) would be expected only when the dicarboxylate was sufficiently long to allow one anionic site to associate with the cationic region while the other hangs below the hydrophobic CD cavity in the aqueous medium.

We can look at this in another way, illustrating the capability of "bridging" for the oxalate system, the loss of completely favorable interactions for the succinate system, and the ability of larger species (for example sebacate) to associate with both the cationic region of the host as well as the external aqueous medium as illustrated in Figure 31.

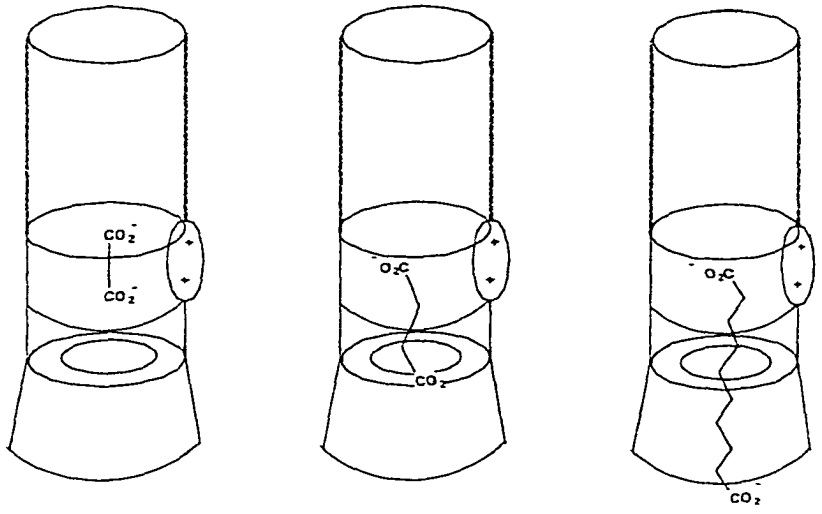
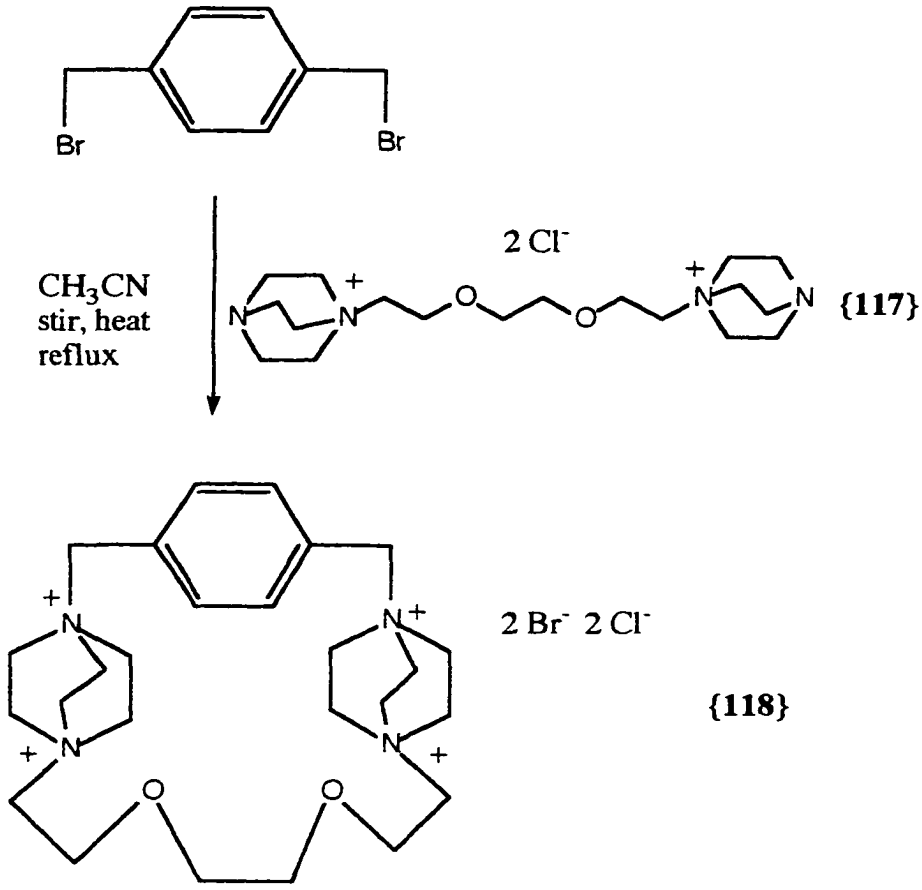


Figure 31 - Capability of "bridging" for the oxalate system, the loss of completely favorable interactions for succinate system, and the ability of sebacate to associate with both the cationic region of the host as well as the external aqueous medium.

Overall, this new class of cyclodextrin derivative provides particularly intriguing capabilities for encapsulation of anionic species in aqueous solution. We may anticipate potential utility of such host species in applications requiring selectivity, separation of anionic species, transport in biologically related systems, and analyses.

NEW CATIONIC RING SYSTEMS

A new series of polycationic rings containing ether linkages has also been prepared. The synthesis of a representative member in this category is shown in Scheme 38.

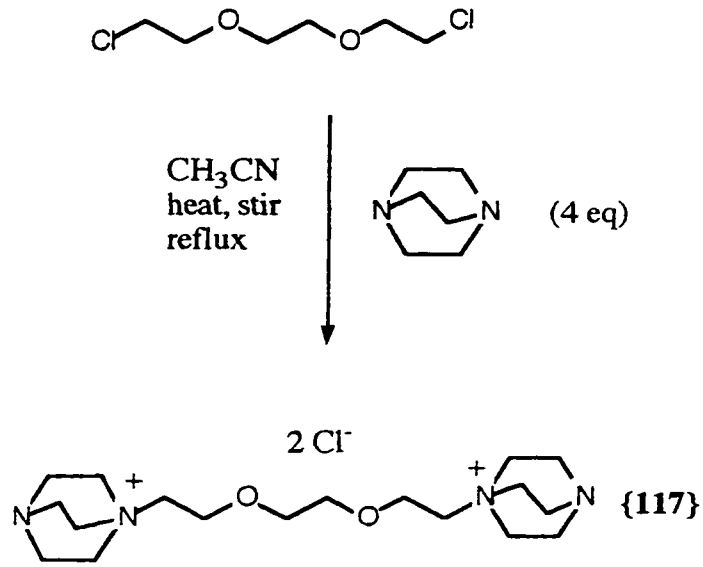


Scheme 38

Treatment of α, α'-dibromo-*p*-xylene with one equivalent of the newly prepared dicationic didabco ether linked string, 1,2-di-(2'-{1"-azonia-4"-azabicyclo[2.2.2]octyl)ethoxyethane dichloride {117} in acetonitrile solution yielded the new tetracationic heterocycle,

p-xylyl-1,4"(4-{8'-(1",4"-diazoniabicyclo[2.2.2]octane)-3',6'-dioxolo-1'-octyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride, {118}, containing ether linkages.

The preparation of the new dicationic ether linked string {117} used in the above synthesis is illustrated in Scheme 39.

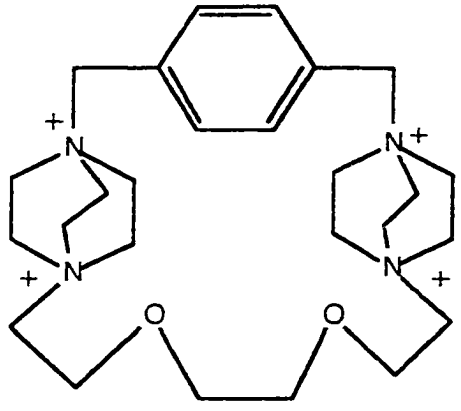
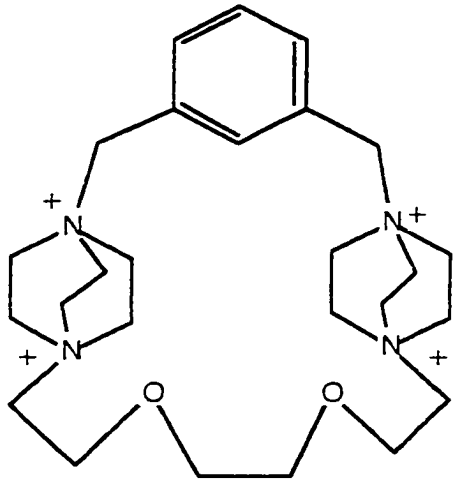


Scheme 39

Treatment of ethylene glycol bis-(2-chloroethyl) ether with an excess of dabco in acetonitrile solution generated the new dicationic didabco ether linked string, 1,2-di-(2'-{1"-azonia-4"-azobicyclo[2.2.2]octyl)ethoxyethane dichloride, {117}.

Table 25 lists the newly prepared heterocycles in this category.

Table 25 - New polycationic rings containing ether linkages

Structure		Number
	$2\,Br^-\ 2\,Cl^-$	**118**
	$4\,Cl^-$	**119**

These new materials are members of a particularly interesting category. Bearing both cationic sites and unshared pairs of electrons at heteroatoms they have the possibility of binding to small polar molecules or to metal ions with associated anions.

Molecular modeling using Chem 3D+ of the polycationic macrocycle indicates that a cavity exists of sufficient size to act as a host for a variety

of species such as highly polar small molecules. Figure 32 illustrates the new macrocycle, {118}, minimized using Chem 3D+.

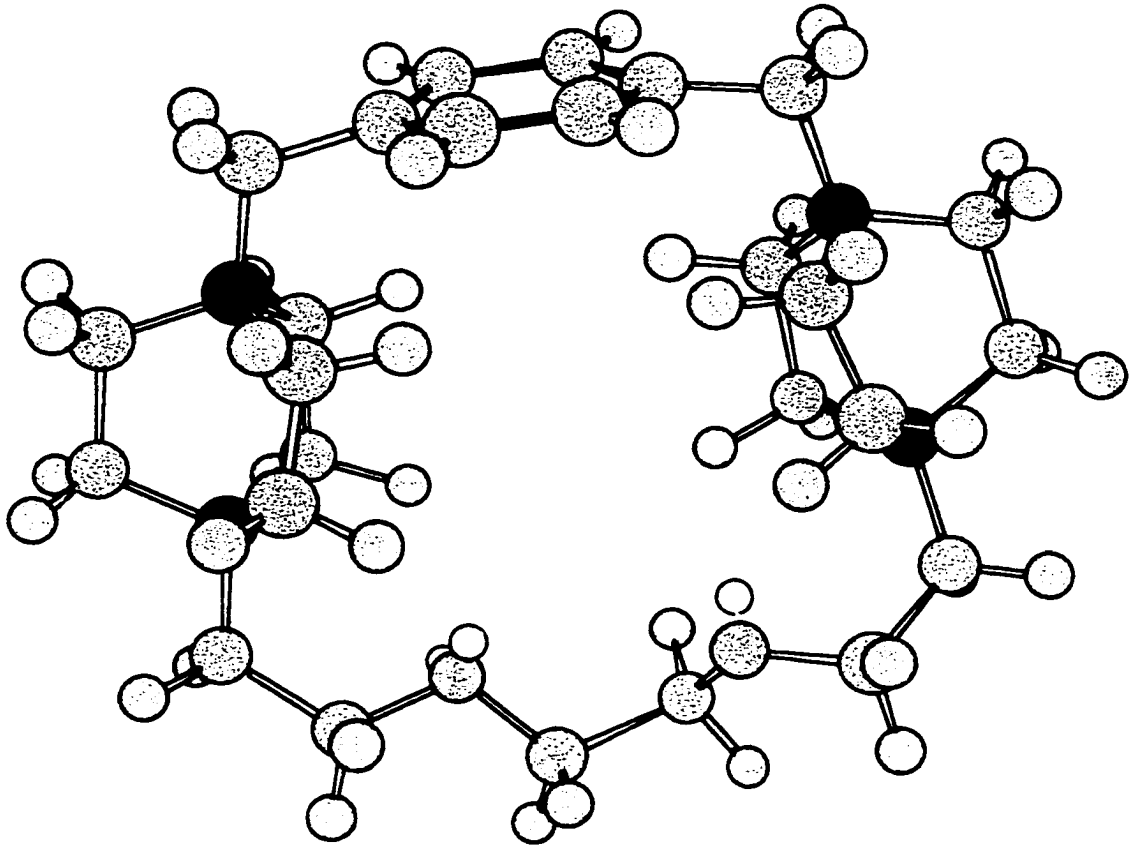
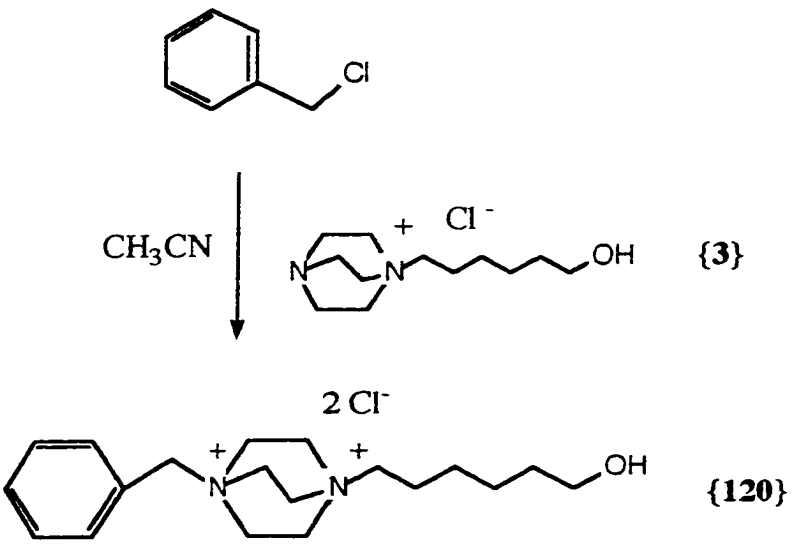


Figure 32 - Molecular modeling of {118} using Chem 3D+.

OTHER NEW POLYCATIONIC STRINGS AND RINGS

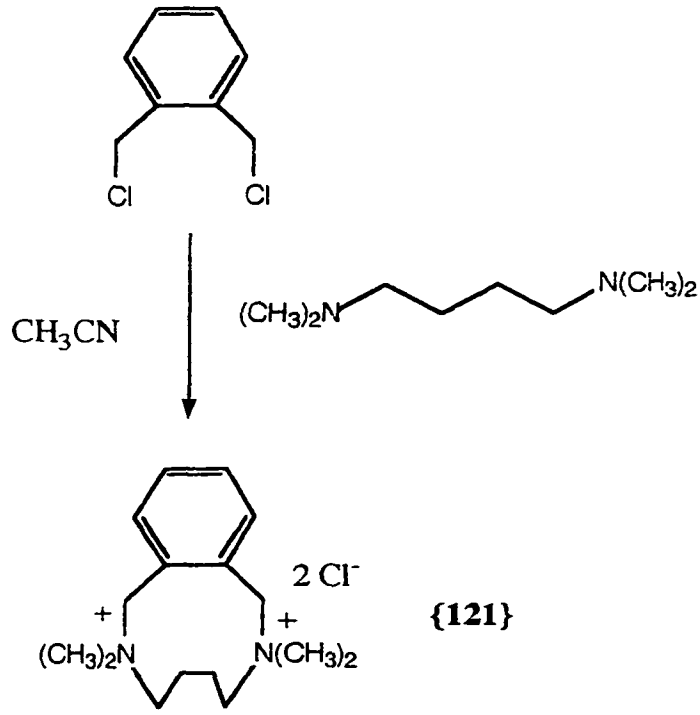
Recently, a variety of new polycationic string and ring systems have been prepared. In the string category, this includes the preparation of an unsymmetrical dicationic string as illustrated in Scheme 40.



Scheme 40

Treating α-chlorotoluene with one equivalent of monocationic string, {3}, in acetonitrile solution gives the new dicationic string, 1-benzyl-4-{6'-hydroxyhexyl}-1,4-diazoniabicyclo[2.2.2]octane dichloride, {120}.

New *ortho*-dicationic rings have also been prepared. The synthesis of a representative member of this category is illustrated in Scheme 41.

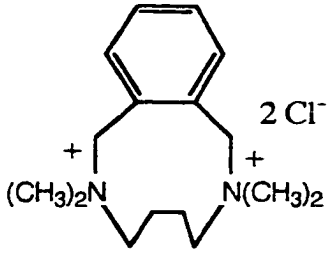
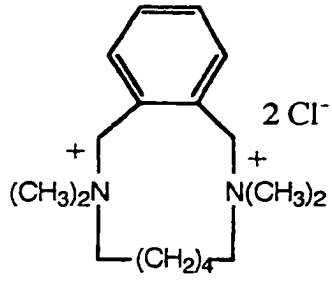


{121}

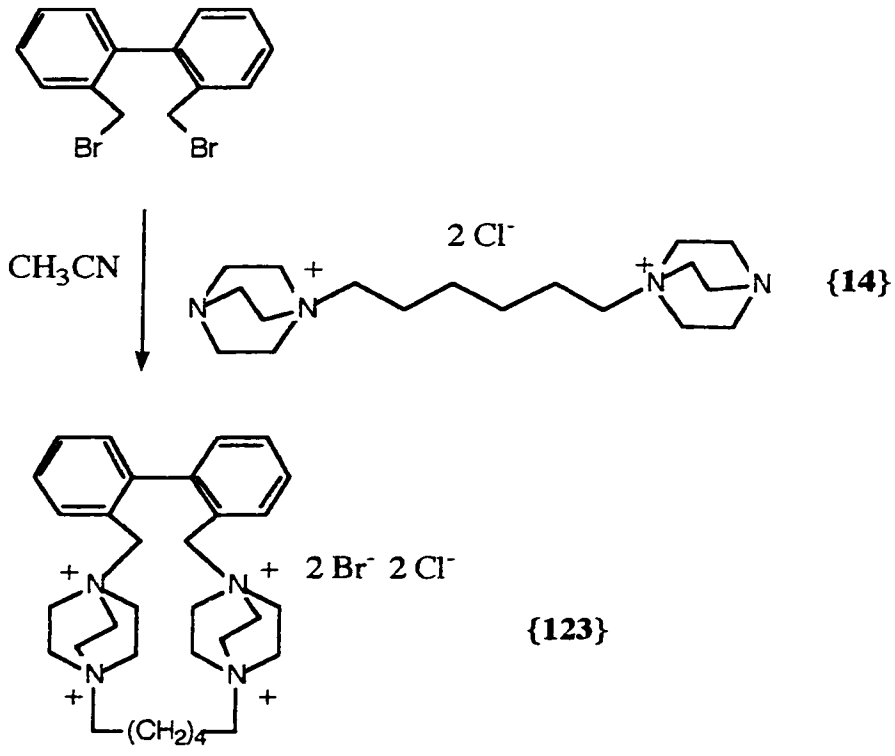
Scheme 41

Treatment of α, α'-dichloro-*o*-xylene with one equivalent of *N,N,N',N'*-tetramethylbutane diamine in acetonitrile solution gives the new dicationic *ortho* ring, 1,1,6,6-tetramethyl-1,6-diazonia[3,4]benzo-cyclodecane dichloride, {121}. Table 26 lists the compounds in this category {121,122}.

Table 26 - New dicationic ortho rings

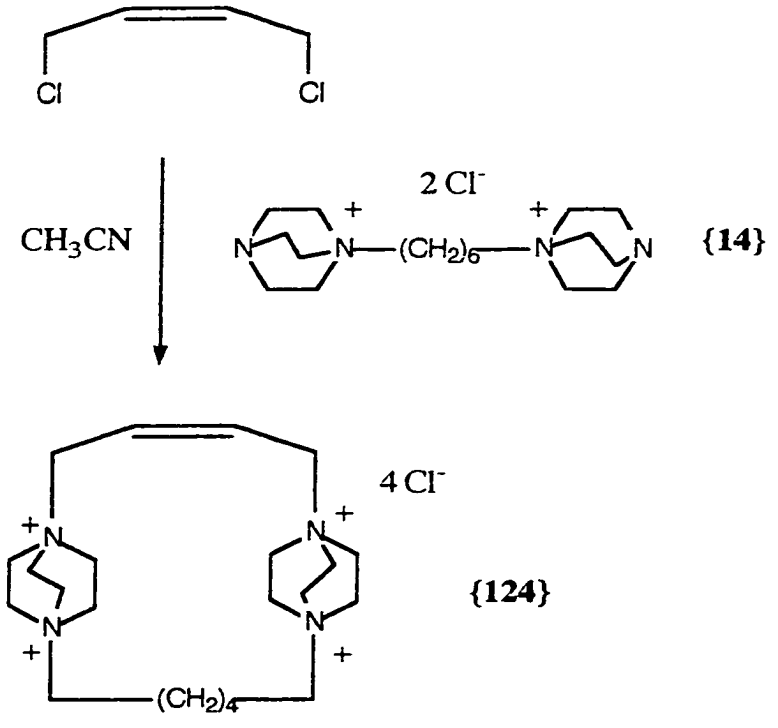
Structure	Number	Name
	121	1,1,6,6-tetramethyl-1,6-diazonia[3,4]-benzo-cyclodecane dichloride
	122	1,1,6,6-tetramethyl-1,6-diazonia[3,4]benzo-cyclododecane dichloride

A new tetracationic biphenyl ring has also been prepared in a similar manner. Scheme 42 illustrates the preparation of such by treating 2,2'-bis(bromomethyl)-1,1'-biphenyl with one equivalent of the dicationic didabco string, {14}, in acetonitrile solution to generate, 1,1'-biphenylmethylene-1",4""-(4"-{6'"-(1"",4""-diazoniabicyclo[2.2.2]octane-1'"-hexyl}azonia)1-azoniabicyclo[2.2.2]octane dibromide dichloride, {123}.



Scheme 42

Another tetracationic ring system prepared involves treatment of *cis*-1,4-dichloro-2-butene with one equivalent of the same dicationic didabco string, {14} in acetonitrile solution to give the new ring, 1,1'-biphenylylmethylene-1",4""-(4'-{12'"-(1"",4""-diazoniabicyclo[2.2.2]octane-1'"-hexyl}azonia)1-azoniabicylo[2.2.2]octane dibromide dichloride, {124} as shown in Scheme 43.



Scheme 43

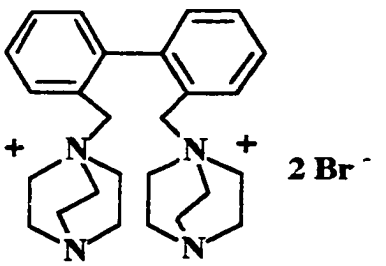
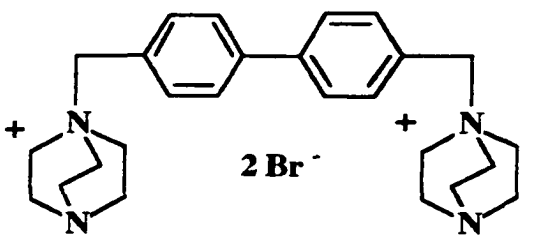
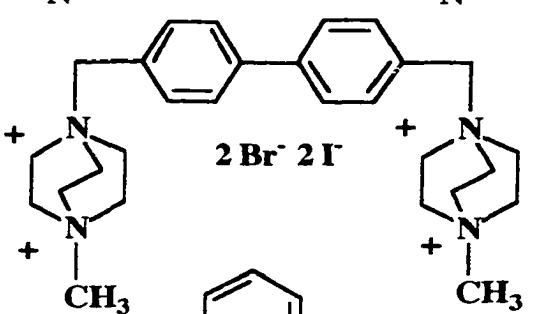
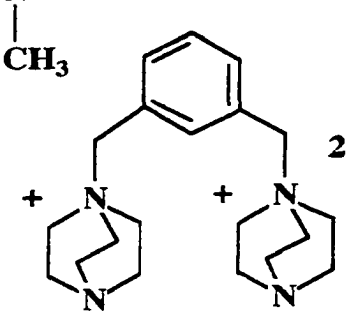
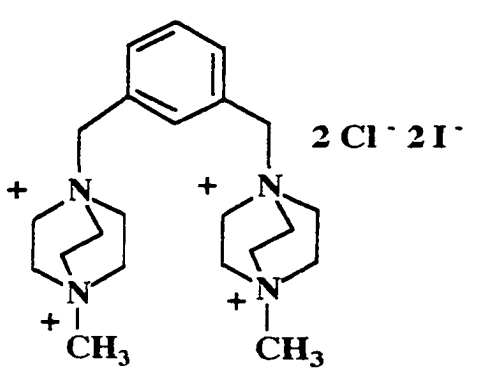
MENTORING OF UNDERGRADUATES

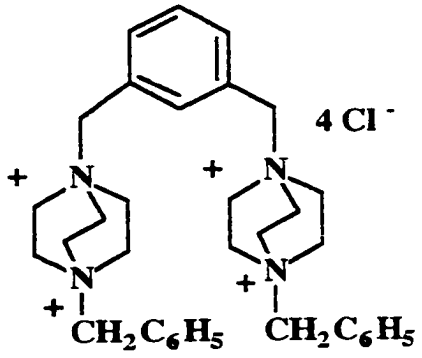
A variety of new materials including polycationic strings, rings, and CDs have been prepared by undergraduates in the laboratory under my direction.

NATALIA RIVERA, freshman undergraduate

Table 27 lists the new polycationic species synthesized by this student {125} - {138}.

Table 27 - New polycationic species prepared by N. Rivera

Structure	Number
	125
	126
	127
	128
	129



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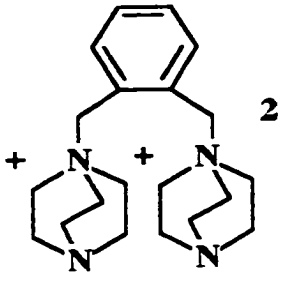
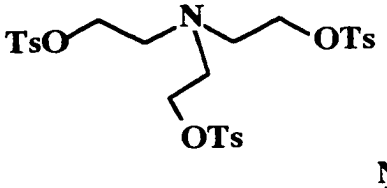
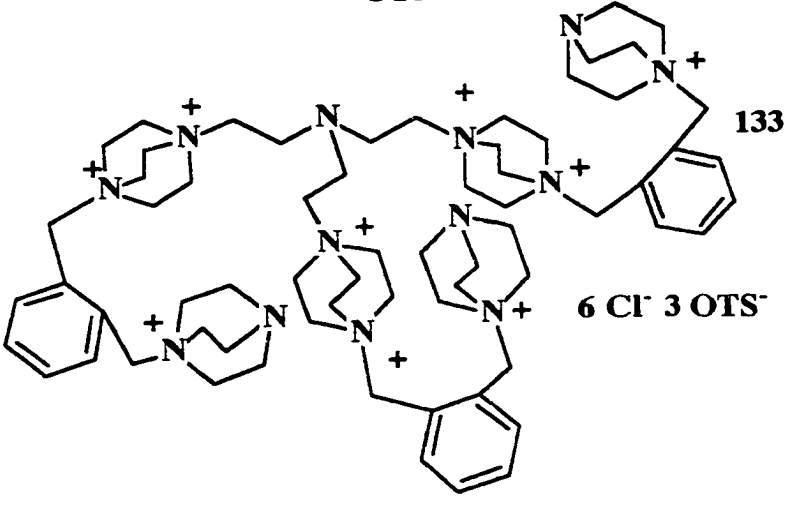


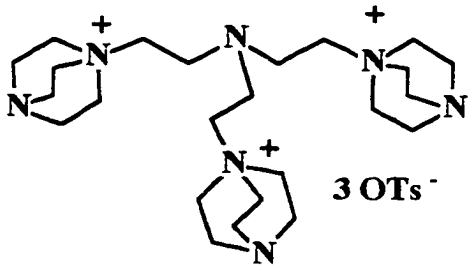
131



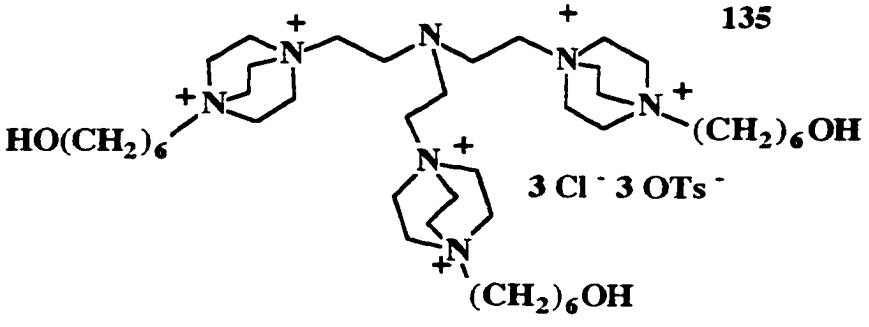
132



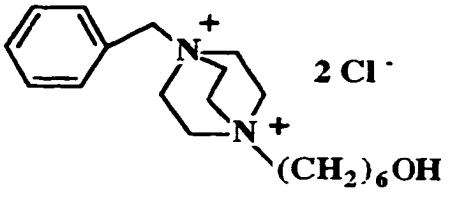
133



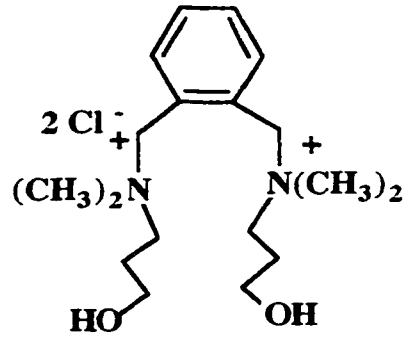
134



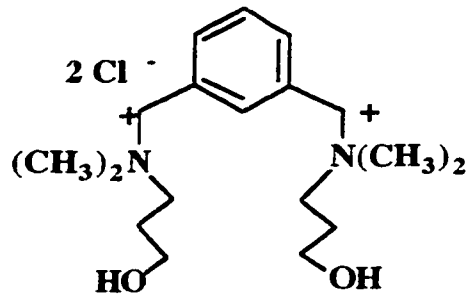
135



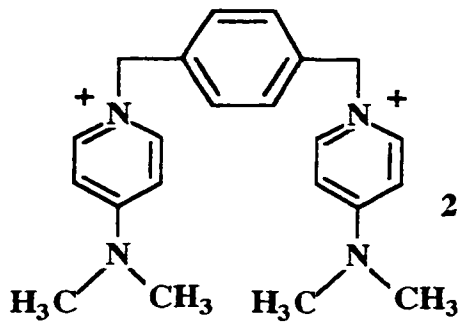
136



137



138



139

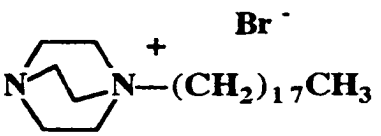
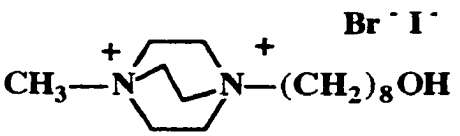
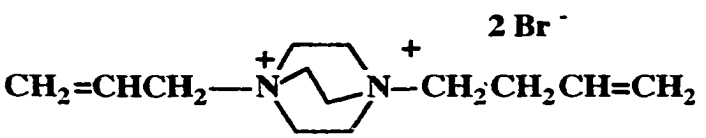
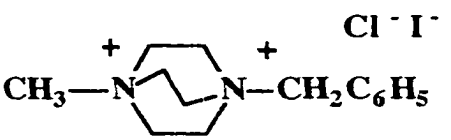
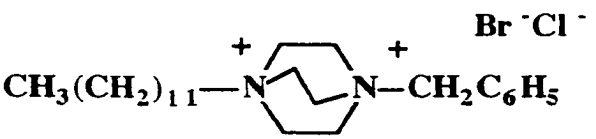
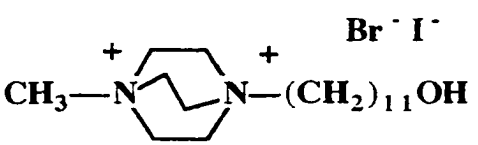
Compound {130} is prepared by treating a solution of α, α'-dichloro-*m*-xylene with two equivalents of {11} in acetonitrile with heating and stirring for a minimum of three days. Compound {132} is prepared by treating triethanolamine with five equivalents (an excess) of *p*-toluenesulfonylchloride in pyridine, and {133} is generated by treating

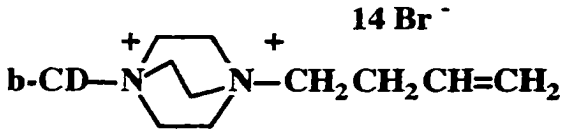
{132} with three equivalents of compound {131} in acetonitrile solution. {131} is also treated with three equivalents of DABCO (in excess) in acetonitrile solution to prepared {134}; as well as bytreating {131} with three equivalents of a monocationic string, {3} in acetonitrile to generate {135}. Monocationic string, {3}, is also treated with one equivalent of α-chlorotoluene in acetonitrile to prepare the dicationic string, {136}. Two equivalents of *N,N*-dimethylamino-1-propanol are added to an acetonitrile solution of α,α'-dichloro-*o*-xylene to give {137}. Similarly, the same starting reagent and equivalents was added to a solution of α,α'-dichloro-*m*-xylene to generate {138}. Two equivalents of DMAP in acetonitrile solution is added to an acetonitrile solution of α,α'-dibromo-*p*-xylene to prepare the new dicationic DMAP string, {139}.

MARIE THOMAS, junior undergraduate

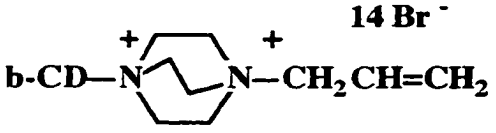
Table 28 lists all the new materials prepared by the above named student under my supervision {140} - {152}.

Table 28 - New polycationic species prepared by M. Thomas

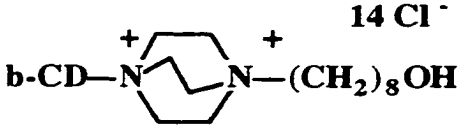
Structure	Number
	140
	141
	142
	143
	144
	145



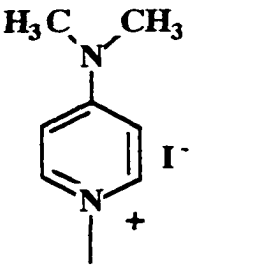
146



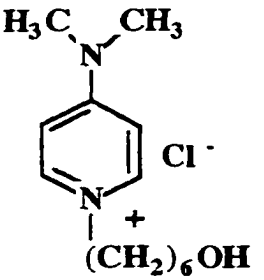
147



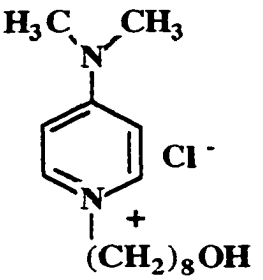
148



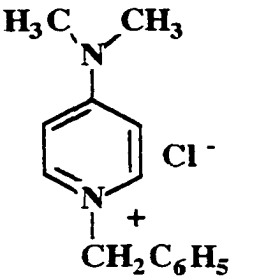
149



150



151



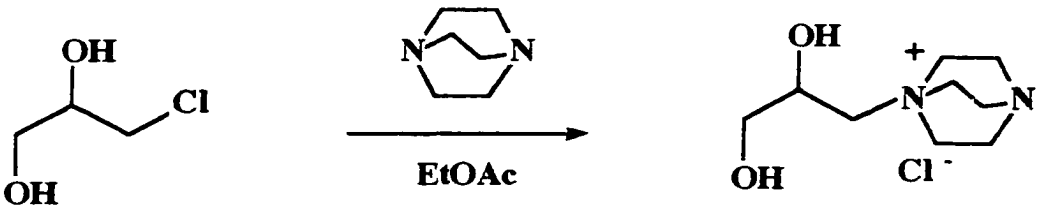
152

Shown in Table 28 is a monocationic string, {140}, which is prepared by treating one equivalent of dabco with 1-bromododecane in an ethyl acetate solution. Compound {141} is an unsymmetrical dicationic string that is prepared by treating monocationic string, {4}, with one equivalent of methyliodide in acetonitrile solution while heating

and stirring at reflux for a minimum of two days. Compound {142} is prepared by treating monocationic string, {8}, with one equivalent of 4-bromo-1-butene in acetonitrile solution. Compound {143} is generated by treating {11} with an acetonitrile solution of methyl iodide, and compound {144} is prepared by treating {11} with an equivalent of 1-bromododecane in acetonitrile solution, while {145} is prepared by treating an acetonitrile solution of {7} with iodomethane.

The β-CD polycationic derivatives, {146} - {148} are generated by treating the tosylated β-CD, {96β}, with eight equivalents of the appropriate monocationic DABCO strings. Newly prepared monocationic DMAP derivatives {149} - {152} are generated by treating DMAP with: two equivalents (an excess) of iodomethane (to generate {149}); one equivalent of the monocationic string, {3}, (to generate {150}); one equivalent of {4} (to generate {151}), and one equivalent of {11} (to generate {152}).

Another series of polycationic salts prepared by the same student is the *chiral* strings. The synthesis of a representative member in this category is illustrated in Scheme 44.

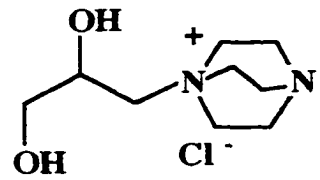
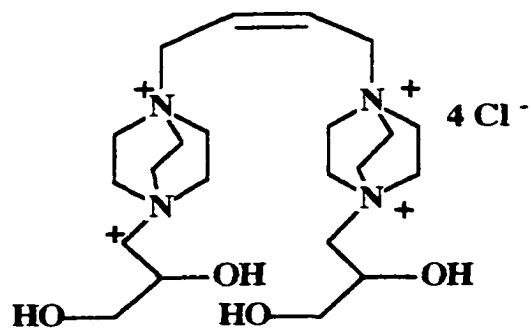
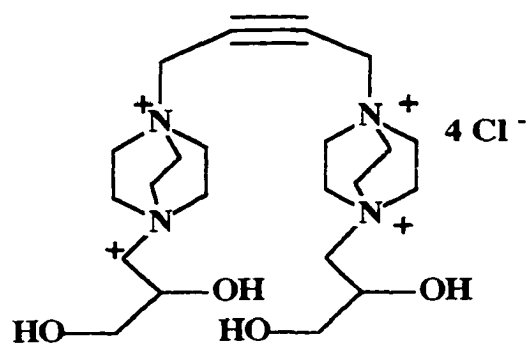
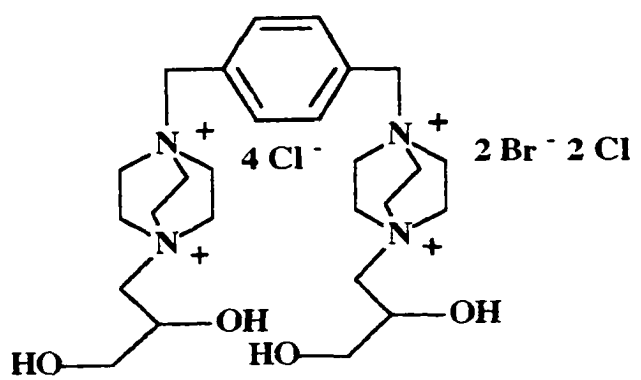


R-(-)-3-chloro-1,2-propanediol **{153}**

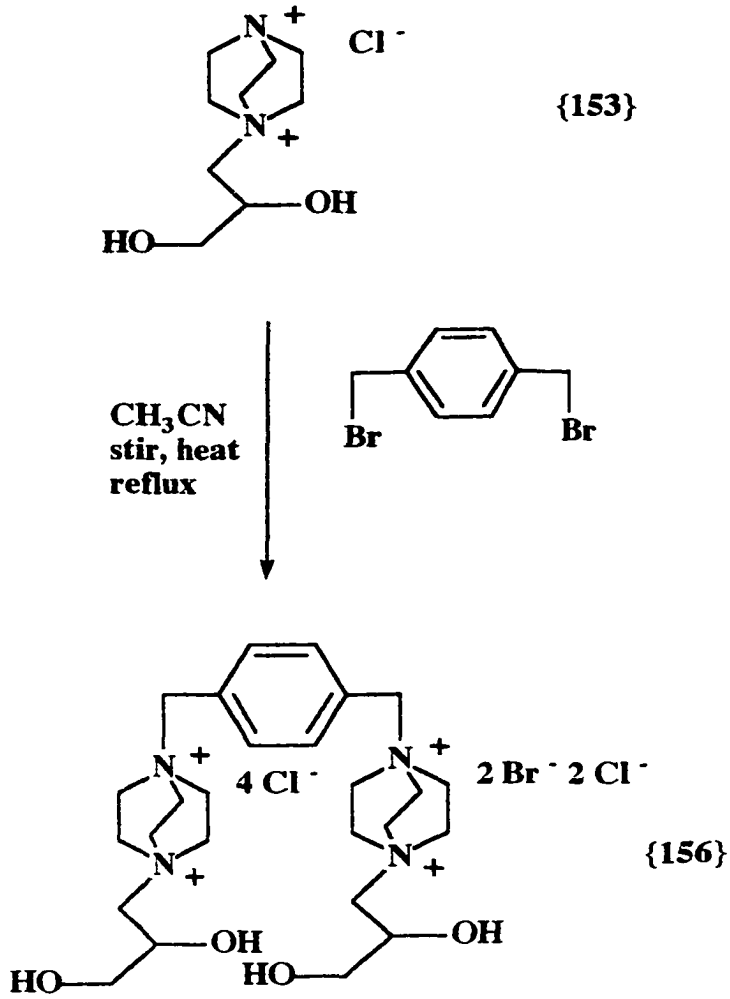
Scheme 44

Treatment of R-(-)-3-chloro-1,2-propanediol with one equivalent of dabco in an ethyl acetate solution while stirring at room temperature gives the new polycationic chiral string, {153}. Table 29 lists all of the new salts in this category {153} - {156}.

Table 29 - New polycationic *chiral* strings prepared by M. Thomas

Structure	Number	
	153	R-(-)
	154	R, R-(-)
	155	R,R-(-)
	156	R,R-(-)

Compounds {154} - {156} are prepared by treating 2 equivalents of {153} in acetonitrile solution with 1 equivalent of an α,ω-dihalo species. Scheme 45 illustrates the preparation of such materials.

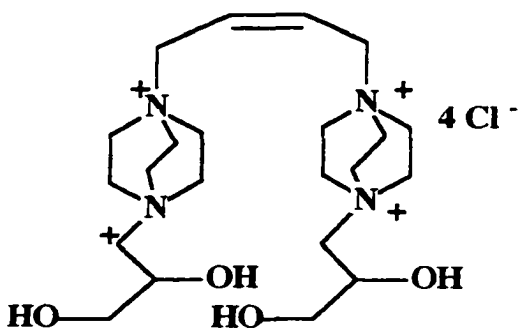
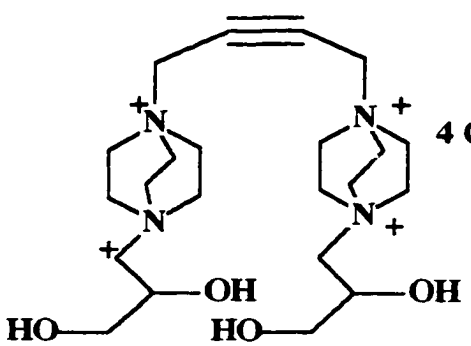
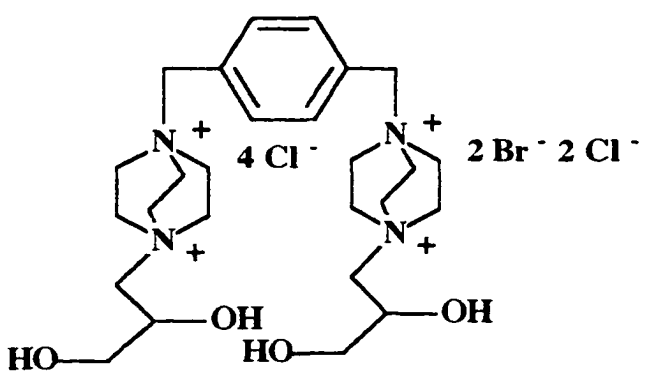


Scheme 45

Salts of the opposite stereochemistry, *i.e.* (S,S) have also been prepared using the same approach but starting with the antipode, (S)-3-chloro-1,2-propanediol. Table 30 lists the materials in this category {157}

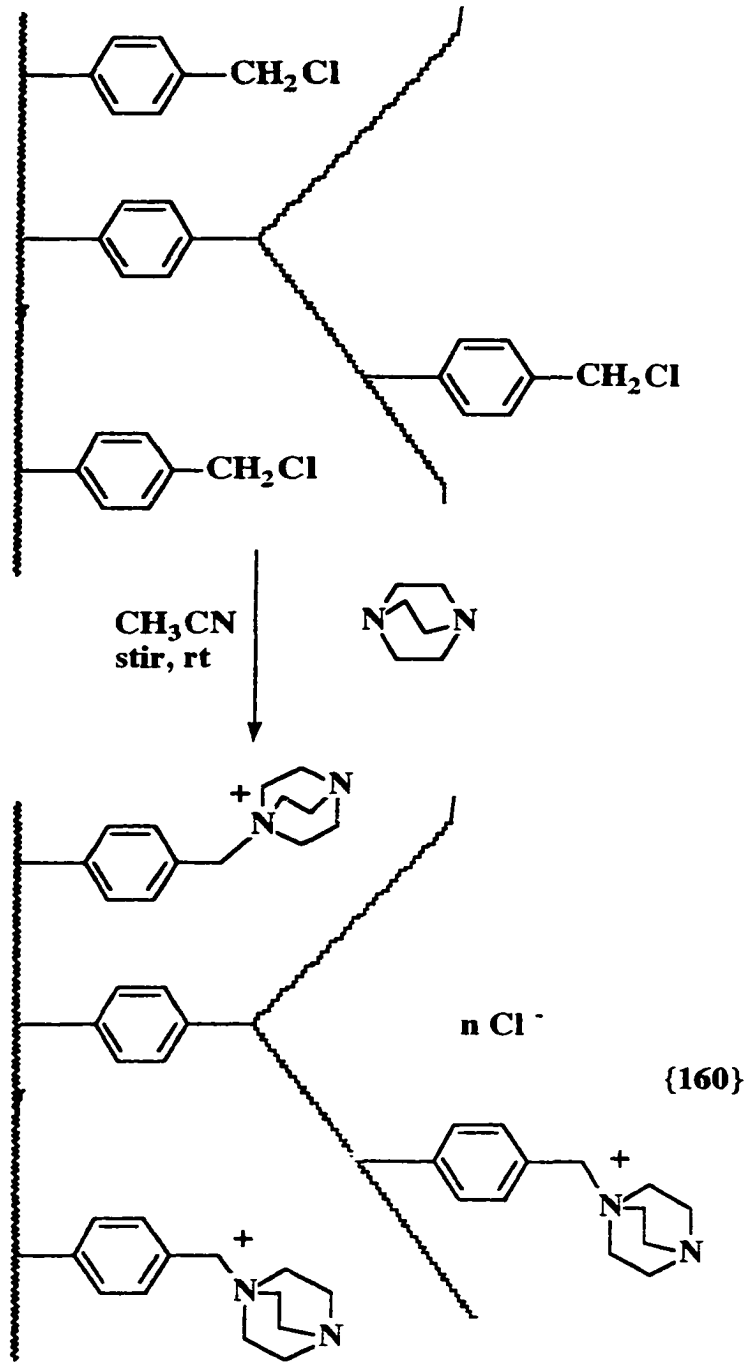
- {159}.

Table 30 - New polycationic *chiral* salts prepared by M. Thomas

Structure	Number	
	157	S, S-(-)
	158	S,S-(-)
	159	S,S-(-)

A series of polycationic resins have also been prepared by the

above-mentioned student. This is accomplished by treatment of "Merrifield's peptide resin", a chloromethylated polystyrene with 5% divinylbenzene co-polymer, with a solution of dabco or dabco derivative in acetonitrile solution. The preparation of a dabco derived string in this category is illustrated in Scheme 46.

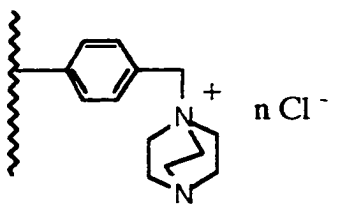
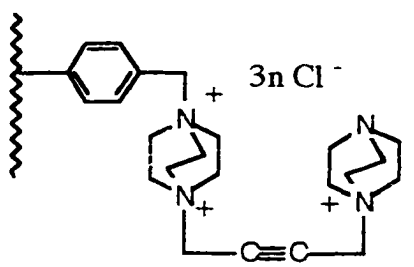
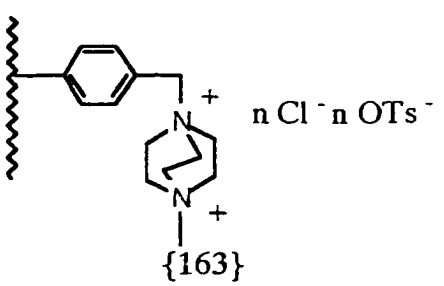


Scheme 46

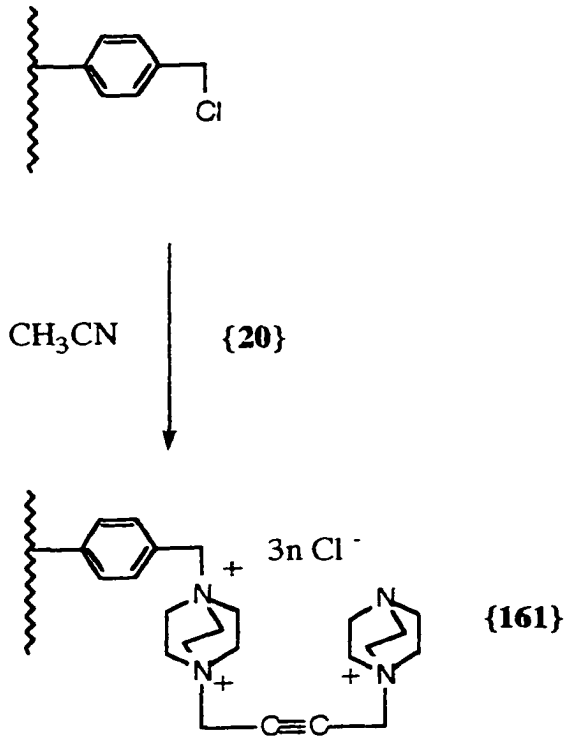
Table 31 lists the new polycationic resins prepared by M. Thomas

under my supervision {160} - {162}.

Table 31 - New polycationic resins prepared by M. Thomas

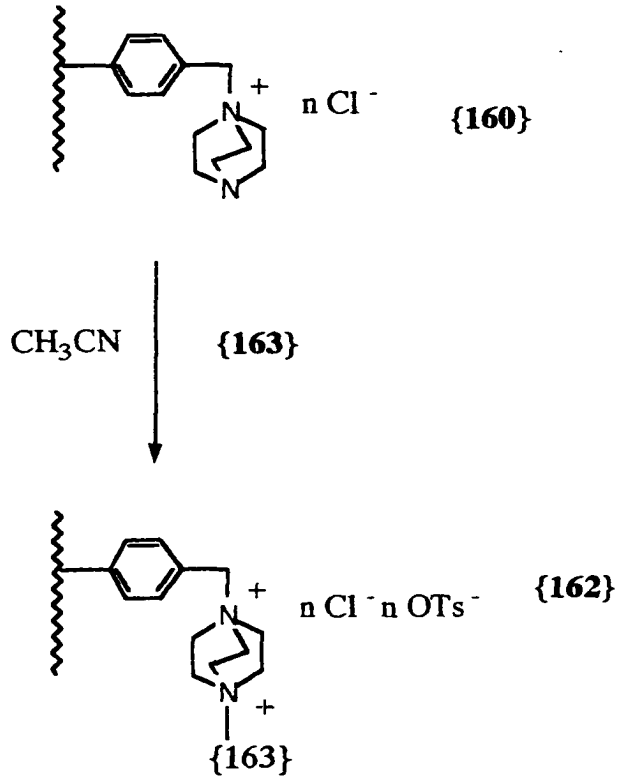
Structure	Number
	**160**
	**161**
	**162**

Polycationic resin {161} is prepared by treating the parent resin with a solution of {20} in acetonitrile as illustrated in Scheme 47.



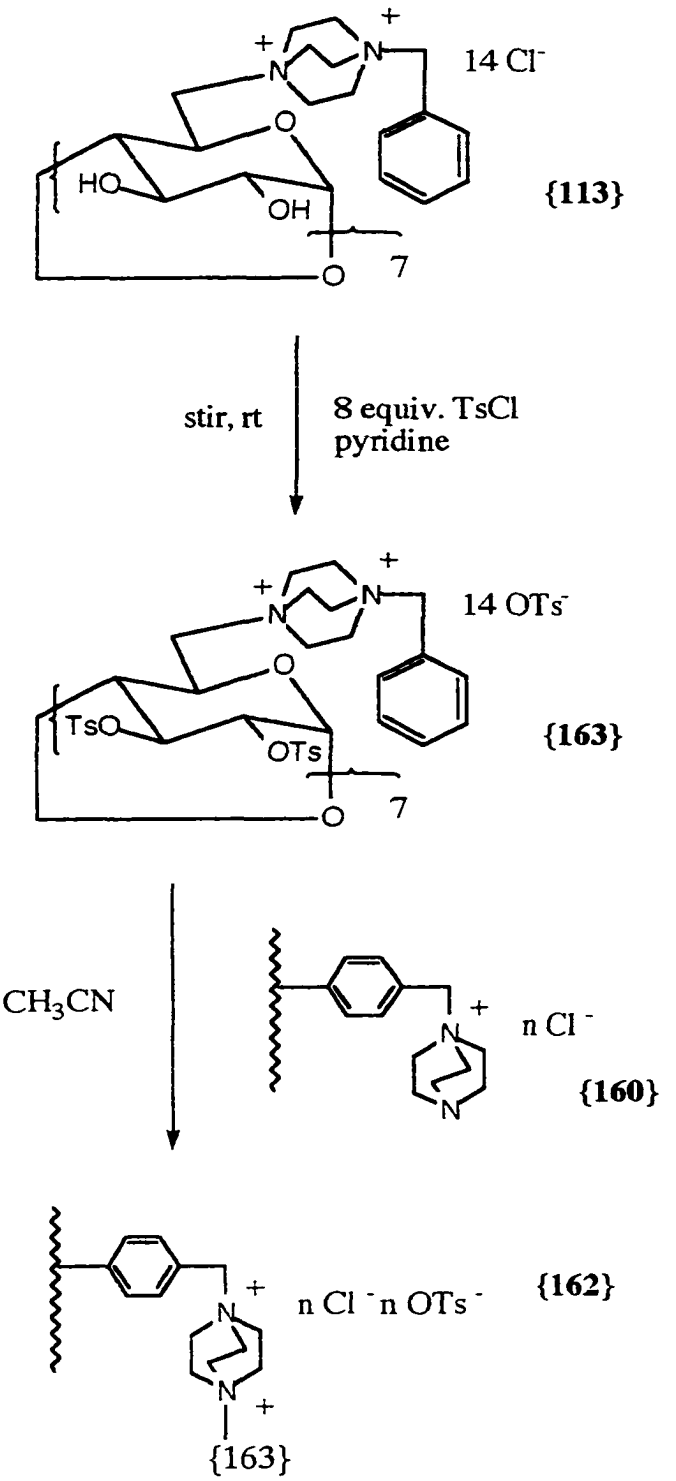
Scheme 47

Resin {162} is prepared by treating {160} with a solution of {163} in acetonitrile as shown in Scheme 48.



Scheme 48

Compound {163} is a tosylated polycationic cyclodextrin derivative that is prepared by tosylating polycationic CD derivative, {113}, at the 2 and 3 positions of the glucose ring. Further reaction of {163} allows substitution to occur with the free amine site of the dabco ring on the polycationic resin, {160}. The preparation of {163} is shown in Scheme 49.

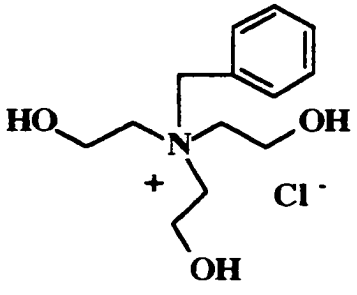
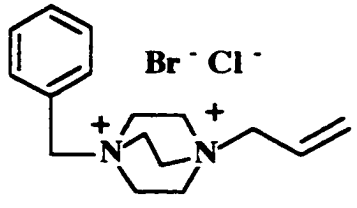
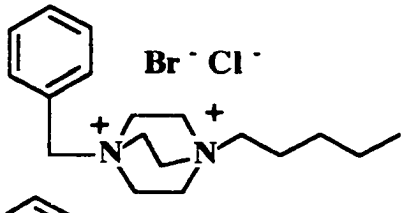
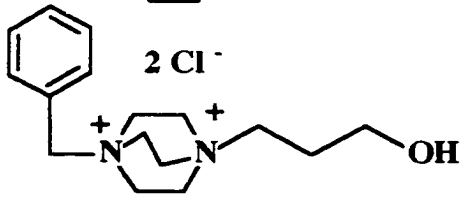
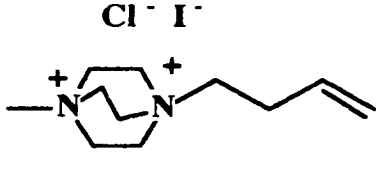


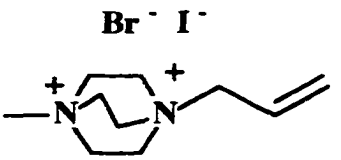
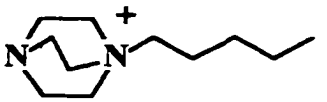
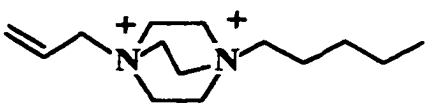
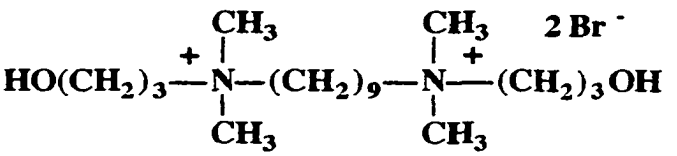
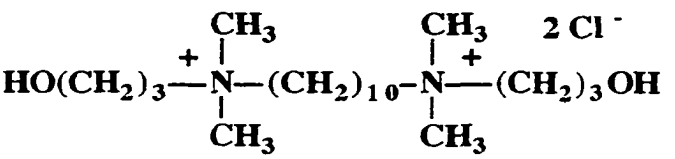
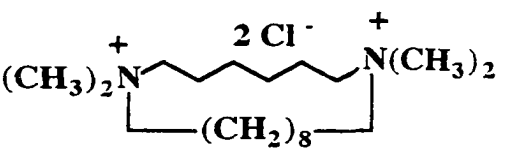
Scheme 49

AMIR RIKIN, senior undergraduate

Table 32 lists the new materials prepared by the above student under my direction {164} - {174}.

Table 32 - New polycationic species prepared by A. Rikin

Structure	Number
	164
	165
	166
	167
	168

Structure	Number
	169
	170
	171
	172
	173
	174

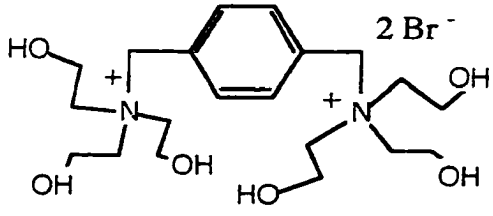
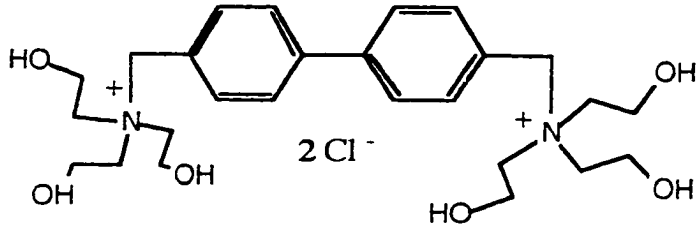
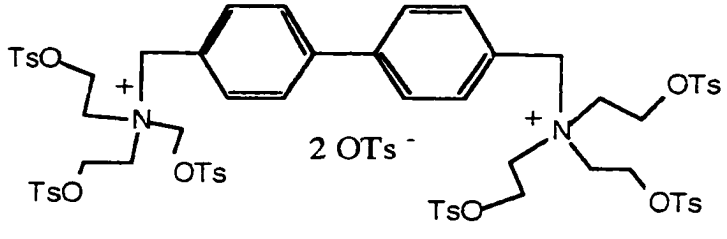
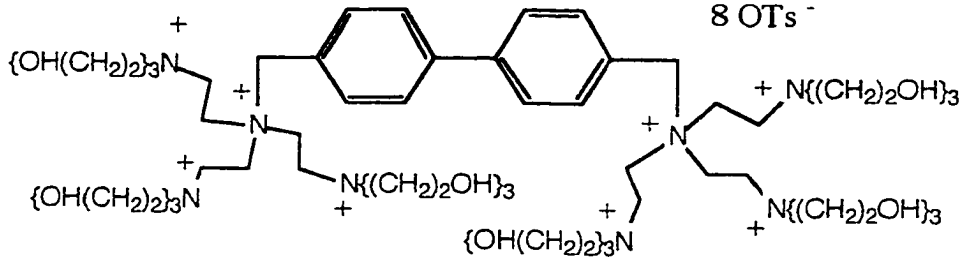
Compound {164} is prepared by treating triethanolamine with one equivalent of α-chlorotoluene in acetonitrile solution. α-Chlorotoluene is also used to prepare compounds {165} - {167} by adding one equivalent of it to an acetonitrile solution of monocationic string species, ({8} to

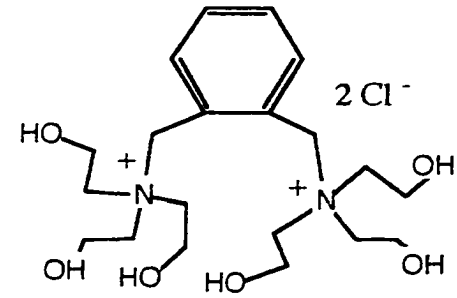
generate {165}; {170} to generate {166}; {2} to generate {167}). Compound {168} is prepared by treating DABCO with one equivalent of 4-bromo-1-butene in an ethyl acetate solution (to generate the monocationic string), followed by methylation with methyliodide in acetonitrile solution to give the dicationic unsymmetrical string. Compound {169} is prepared by treating {8} with a solution of iodomethane in acetonitrile, and compound {170} is prepared by treating DABCO with one equivalent of 1-bromopentane in an ethyl acetate solution. Compound {171} is generated by treating {170} with one equivalent of allyl bromide in acetonitrile solution. Dicationic strings {172} and {173} are prepared by treating two equivalents of dimethylamino-1-propanol with an α,ω-dihalo alkane in acetonitrile (for generation of {172} 1,9-dibromononane, and for generation of {173} 1,10-dichlorodecane) while heating and stirring at reflux for a minimum of one day. The saturated dicationic ring {174} is prepared by treating *N,N,N',N'*-tetramethylhexane diamine with one equivalent of 1,10-dichlorodecane in acetronitrile with heating and stirring.

FARRAH HOROWITZ, undergraduate

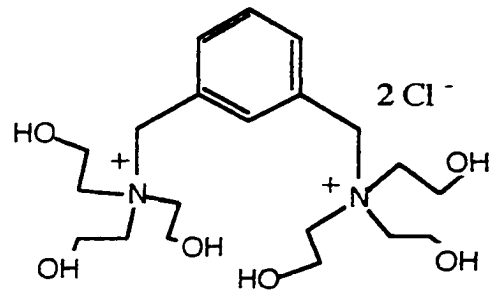
Table 33 lists all of the new materials prepared by F. Horowitz under my direct supervision {175} - {182}.

Table 33 - New materials prepared by F. Horowitz

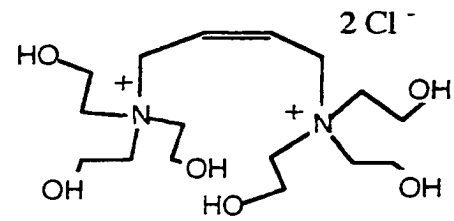
Structure	Number
	175
	176
	177
	178



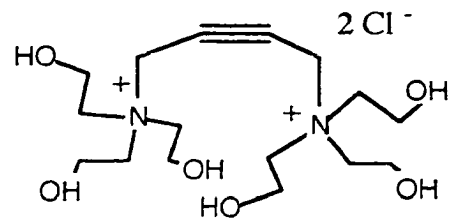
179



180



181



182

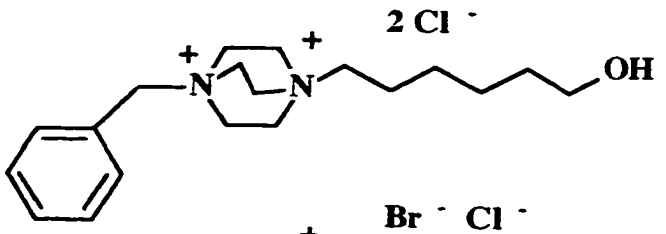
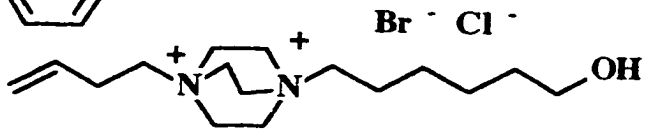
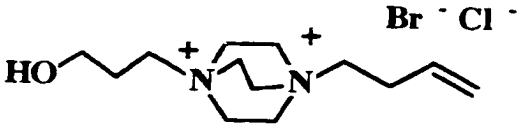
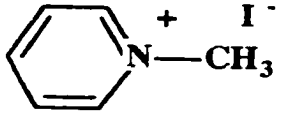
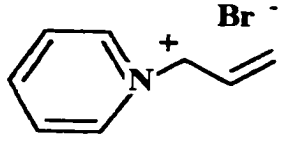
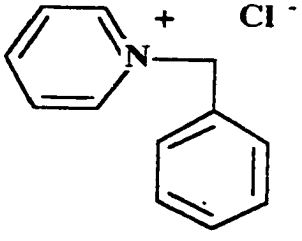
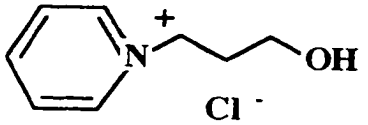
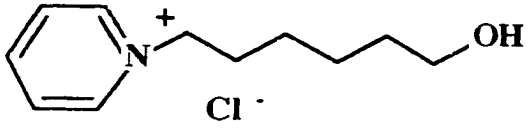
Compound {175} is prepared by treating three equivalents of triethanolamine (an excess) with α,α'-dibromo-*p*-xylene in acetonitrile solution while heating and stirring. Compound {176} is prepared similarly in that 4,4'-bis(bromomethyl)-1,1'-biphenyl is treated with an excess of triethanolamine, while {177} is generated by treating {175}

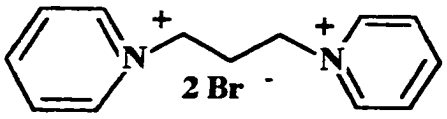
with *p*-toluenesulfonyl chloride in pyridine. The octacationic salt, {178}, is prepared by treating {176} with *p*-toluenesulfonyl chloride in pyridine solution to tosylate the hydroxyl groups, followed by reaction with eight equivalents of triethanolamine in acetonitrile. Compound {179} is synthesized by treating α,α'-dichloro-*o*-xylene with two equivalents of triethanolamine in acetonitrile solution. The *meta* analog, {180}, is generated by using α,α'-dichloro-*m*-xylene. The olefinic string, {181}, is prepared by treating two equivalents of triethanolamine with *cis*-1,4-dichloro-2-butene, and the acetylenic string, {182}, is prepared by using 1,4-dichloro-2-butyne as the dihalide. All of the salts listed in Table 33, with the exception of {177}, are heated and stirred at reflux for a minimum of two days. (Compound {177} is stirred at room temperature for one day, the volatiles are evaporated under reduced pressure, and the resultant product is then dried under high vacuum.) The products are isolated by filtration, washed with ethyl acetate and ether solutions, then dried under high vacuum.

VALBONA BEHAJ, senior undergraduate

Table 34 lists all of the prepared salts (not noted previously) prepared by V. Behaj (Shteto) under my supervision {183} - {211}.

Table 34 - Salts prepared by V. Behaj

Structure	Number
	183
	184
	185
	186
	187
	188
	189
	190



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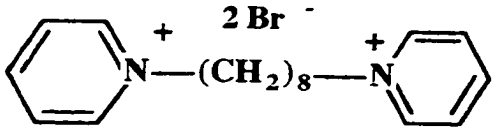

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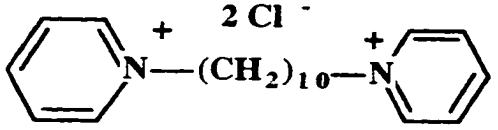

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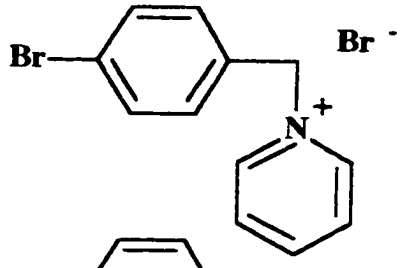

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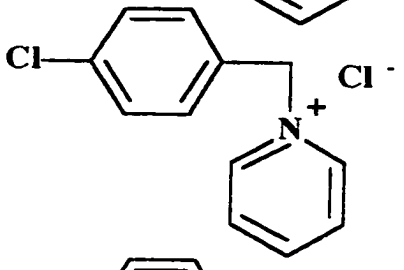

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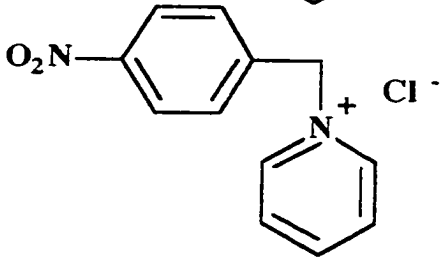

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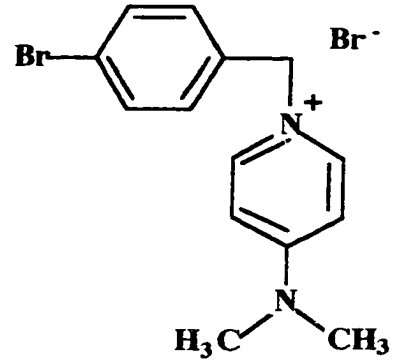

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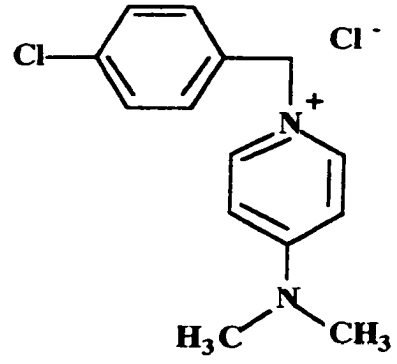

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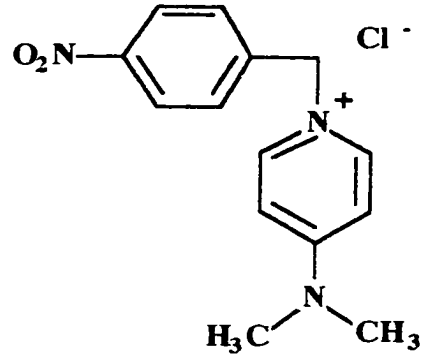

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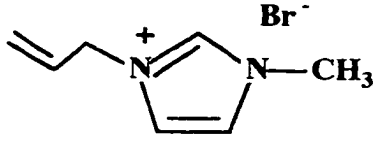

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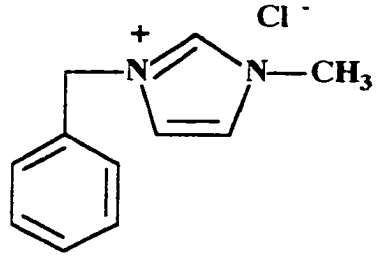

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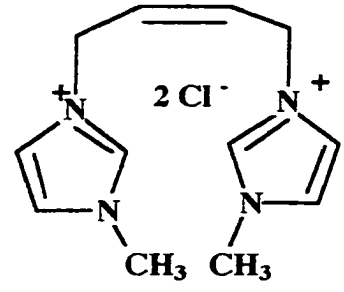

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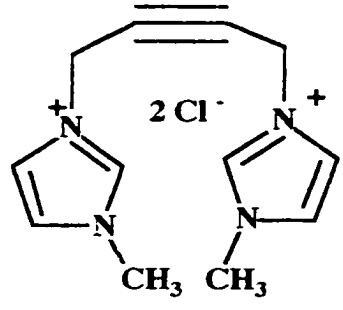

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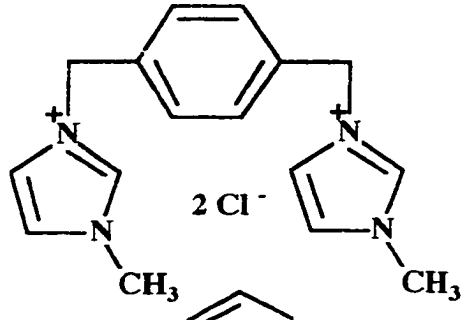

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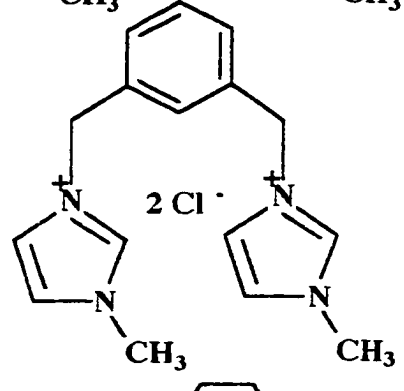

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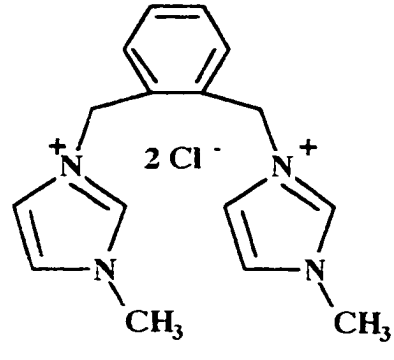

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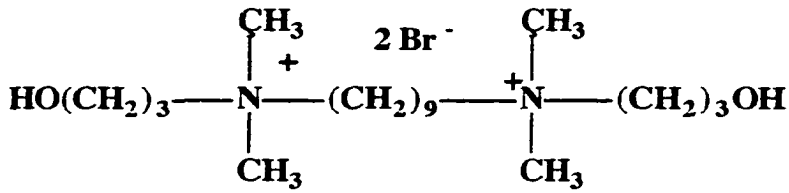

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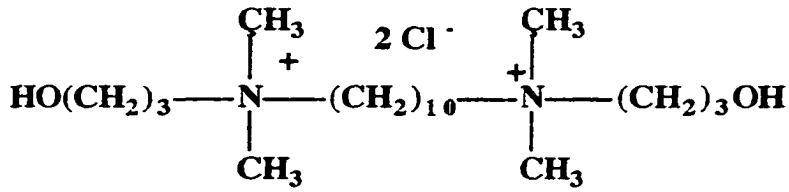

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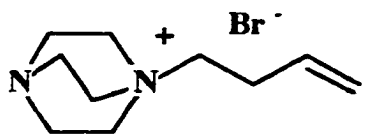

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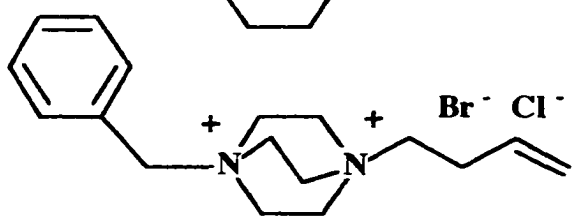

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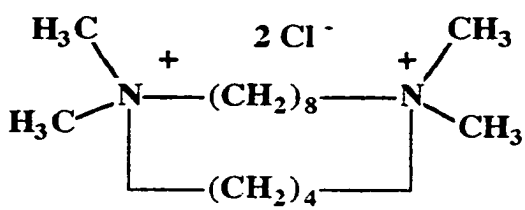


211

The dicationic unsymmetrical string, {183}, is prepared by treating a solution of monocationic string, {3}, in acetonitrile with one equivalent of α-chlorotolune. Compound {184} is similarly prepared by treating {3} with 4-bromo-1-butene, and {185} is generated by the reaction of {2} with 4-bromo-1-butene in acetonitrile. The above three reactions are

heated and stirred at reflux for a minimum of two days, precipitate collected by suction filtration, washed with solutions of ethyl acetate and ether, and dried under high vacuum. The series of monocationic pyridinium salts are prepared by treating pyridine with an α-halo species in acetonitrile. For example, {186} is prepared by treating pyridine with one equivalent of iodomethane, and {187} by treating pyridine with one equivalent of allylbromide. Similarly, {188} is prepared by treating pyridine with one equivalent of α-chlorotoluene, {189} by treating pyridine with 3-chloro-1-propanol, and {190} by treating pyridine with one equivalent of 6-chloro-1-hexanol. The products are collected by removal of volatile materials under reduced pressure, followed by drying under high vacuum. A series of dicationic, dipyridine salts have also been prepared. Treatment of an α,ω-dihaloalkane with two equivalents of pyridine in acetonitrile gives a new series of salts {191} - {193}. These products are isolated by filtration and dried under high vacuum. A series of monocationic halo-aromatic pyridine systems have also been prepared. Treating 4-bromo-α-bromotoluene with one equivalent of pyridine in acetonitrile gives {194}. Products {195} and {196} have been similarly prepared. A series of monocationic DMAP derivatives have been generated by treating an 4-halo(or nitro)-α-halo-toluene with one equivalent of DMAP in acetonitrile {197} - {199}. Another series of salts

includes imidazolium derivatives {200} - {206}. The general preparation for these materials involve treatment of 1-methyl-imidazole with an appropriate halogen species in acetonitrile. Compounds {207} and {208} were prepared by treating two equivalents of *N,N*-dimethylaminopropanol in acetonitrile solution with one equivalent of 1,9-dibromononane (to generate compound {207}) and with one equivalent of 1,10-dichlorodecane (to generate compound {208}). The monocationic string, {209} is prepared by treating dabco in ethyl acetate solution with one equivalent of 4-bromo-1-butene. Compound {209} is then dissolved in an acetonitrile solution while adding one equivalent of α-chlorotoluene to prepare the unsymmetrical dicationic string, {210}. The saturated dicationic ring, {211} is prepared by treating *N,N,N',N'*-tetramethylhexane diamine with one equivalent of 1,8-dichlorooctane in acetronitrile solution.

NEW IONIC LIQUIDS

Recently, room-temperature ionic liquids have generated much excitement among the chemistry community for their potential as green "designer solvents." They have potential for applications in batteries, as non-aqueous polar reaction media, for "green" extractive processes, and as catalysts. Some batteries contain lithium salts that is an ionic liquid, but they are not as fluid as often desired. Currently prepared materials are candidates for electrolytes in such applications. "Green" extractive processes relate to separations and isolations performed without recourse to volatile organic solvents. Thus, using an ionic liquid, which is generally non-volatile, is preferred over volatile solvents.

Ionic liquids are liquids that are comprised entirely of ion pairs. Thus, molten sodium chloride is an *ionic liquid*, whereas a solution of sodium chloride in water (a molecular solvent) is an ionic *solution*. By mixing certain organic (e.g. substituted ammonium halides) salts with an inorganic compound such as $AlCl_3$, chemists can often produce an ionic liquid at or below room temperature. In general, the anions in an ionic liquids are what provide it with its room temperature liquid characteristics. The rationale for these materials being liquid rather than solid at room temperature is that the organic cations are sufficiently big compared with the anions, much larger than cations of ordinary salts,

such as Na^+. Disparity in the size of cation and anion can be a factor in the ability to form a solid lattice. For example, with anions of high charge density and cations of low charge density the body of the cations necessarily will interact, either charges repelling and/or organic portions interacting. Thus, formation of a solid lattice could be hindered. For example, while LiF forms a very stable crystalline lattice, as does CsI, the lattice of LiI is significantly less stable. For a given cation, chemists can choose the anion that they need to make an ionic liquid. By carefully choosing the cation and anion to modify the properties, one can "tune" an ionic liquid to provide one with the precise physical and chemical properties desired.

Room-temperature ionic liquids typically consist of organic cations containing nitrogen (ammonium-type cations) and appropriate inorganic anions. In recent years a variety of mixtures of aluminum chloride with the 1-alkylpyridinium chlorides have been reported to be molten at or near room temperature. Melts of this type may be prepared easily. [151] The most common salts used to make ionic liquids are those with tetraalkylammonium, tetraalkylphosphonium, *N,N'*-dialkylimidazolium, and *N*-alkylpyridinium cations as shown in Figure 33.

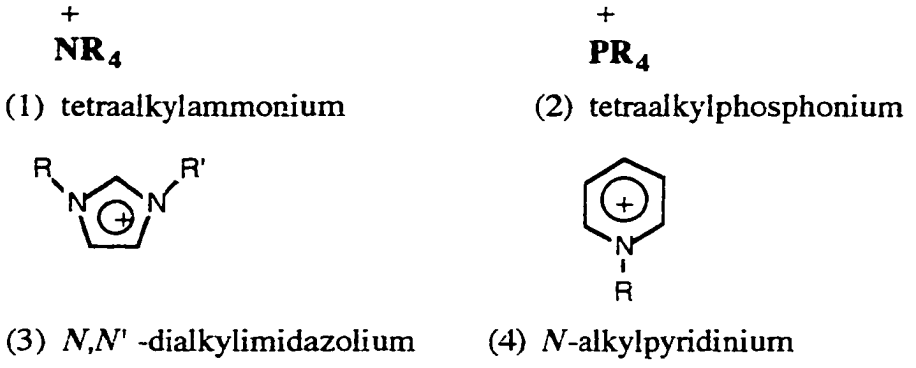
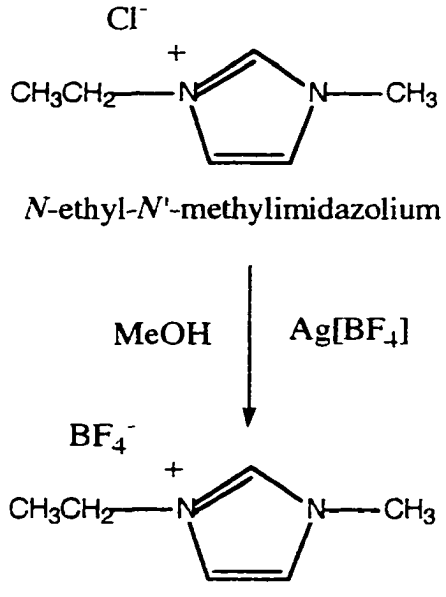


Figure 33 - (1) Tetraalkylammonium, (2) tetraalkylphosphonium, (3) *N,N'*-dialkylimidazolium, and (4) *N*-alkylpyridinium cations

The two basic approaches to the preparation of ionic salts are: 1) metathesis - adding two ionic compounds in solution so that they can swap counterions - with, for example, a silver, Group I metal or ammonium salt of the desired anion; and 2) acid-base neutralization reactions.

One of the first ionic liquids prepared that exhibited potential for use in biphasic catalysis is *N*-ethyl-*N'*-methylimidazolium tetrafluoroborate. [152] This material was prepared by metathesis of *N*-ethyl-*N'*-methylimidazolium chloride with silver tetrafluoroborate in methanol as illustrated in Scheme 50.



N-ethyl-*N*'-methylimidazolium chloride

N-ethyl-*N*'-methyl imidazolium tetrafluoroborate

Scheme 50

Ionic liquids are unconventional, yet an interesting class of aprotic solvents for studying the chemistry of inorganic, organometallic, and organic solutes. These ionic liquids are potentially useful as electrolytes in batteries, photoelectrochemical cells, and electroplating processes.

Ionic liquids may offer unique selectivity or even totally new chemical reactions compared with conventional solvents. They are nonvolatile and nonflammable, often have high thermal stability, and are relatively undemanding and inexpensive to manufacture.

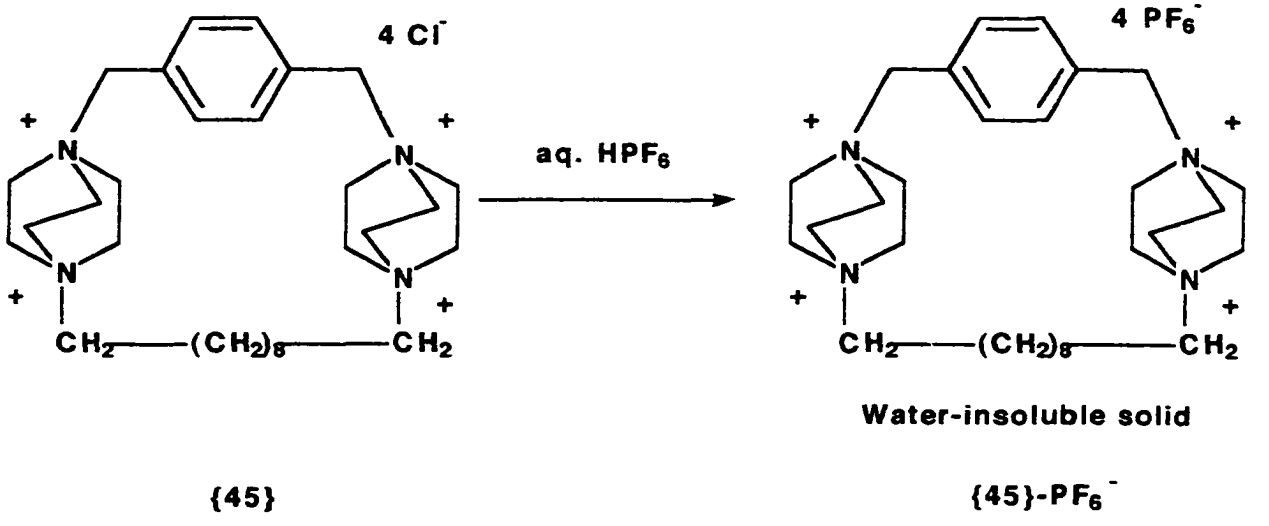
With the numerous categories of polyammonium and polyphosphonium salts synthesized in our laboratory, we began the

conversion of our new (solid) salts into a unique category of ionic liquids through exchange of the anion.

Numerous reports have been made of the conversion of monoammonium (solid) salts to non-aqueous ionic liquids by such anion exchange. The most extensively investigated series of non-aqueous ionic liquids include those in which the organic cation is either an *N*-alkylpyridinium or an *N*-alkyl-*N'*-(alkyl)'imidazolum species. [152-155] These species involve only organic *mono*cations, with the single exception of a dicationic species involving two imidazolium sites at opposite ends of a long alkyl chain. [156]

It seemed that our previously prepared *poly*cationic species, matched with appropriate anions, could produce ionic liquids with interesting properties. To this end we began the conversion of our halide salts into species with the possibility of being liquids at room temperature, and potential for industrial applications. This work was done by myself as well as undergraduates under my direction in our laboratory (Valbona Behaj, Amir Rikin, Marie Thomas and Danny Mancheno).

Initial efforts were directed toward the preparation of hexafluorophosphate salts of the polycationic species using a well-established procedure as illustrated in Scheme 51. [157]



Scheme 51

This procedure involves the treatment of the parent halide salt with an aqueous solution of hexafluorophosphoric acid (one charge equivalent). Application of this procedure to the polyammonium species {45} generated a solid that was negligibly soluble in water, with solubility characteristics corresponding to those previously reported for monocationic imidazolium and pyridinium species. This and other materials of this type could be isolated by filtration and were dried under high vacuum conditions for several days.

As these materials were isolated by recovery after precipitation from aqueous solution, their NMR spectra were measured in DMSO-d_6 solution. These materials exhibited ^{1}H and ^{13}C NMR spectra corresponding to those observed for the parent halide salts. However, the

^{31}P NMR spectra of these materials indicated that they were not the pure hexafluorophosphate species. The ^{31}P NMR spectrum shown in Figure 34 indicates the presence of the hexafluorophosphate anion with a symmetrical septet centered at approximately -144 ppm.

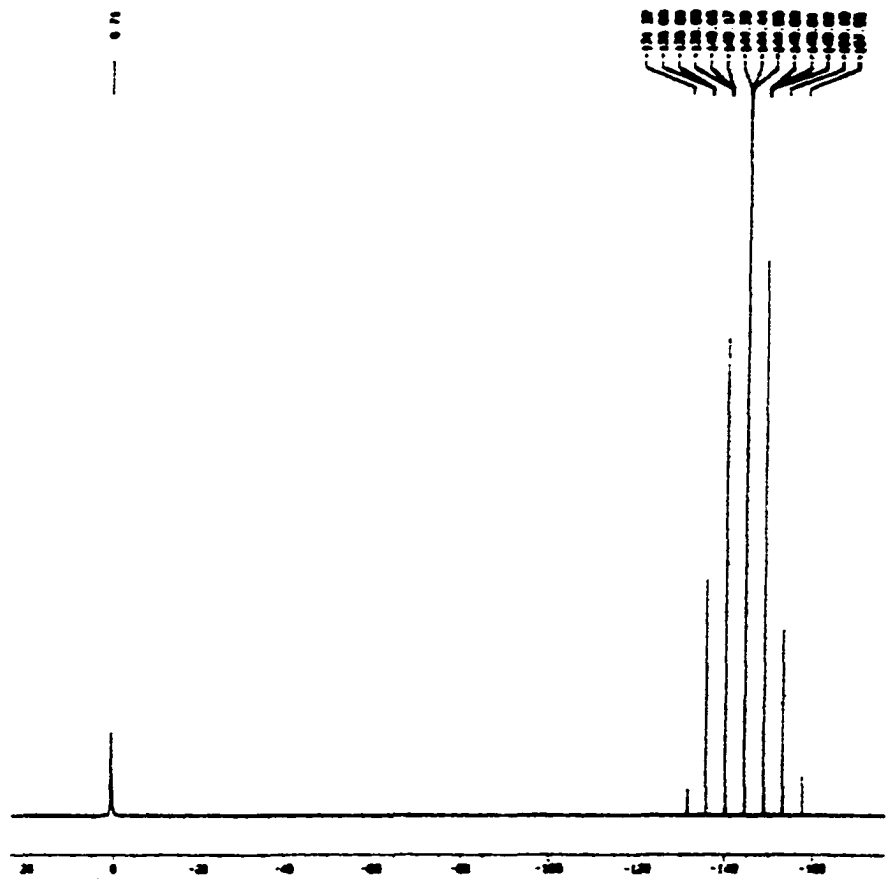
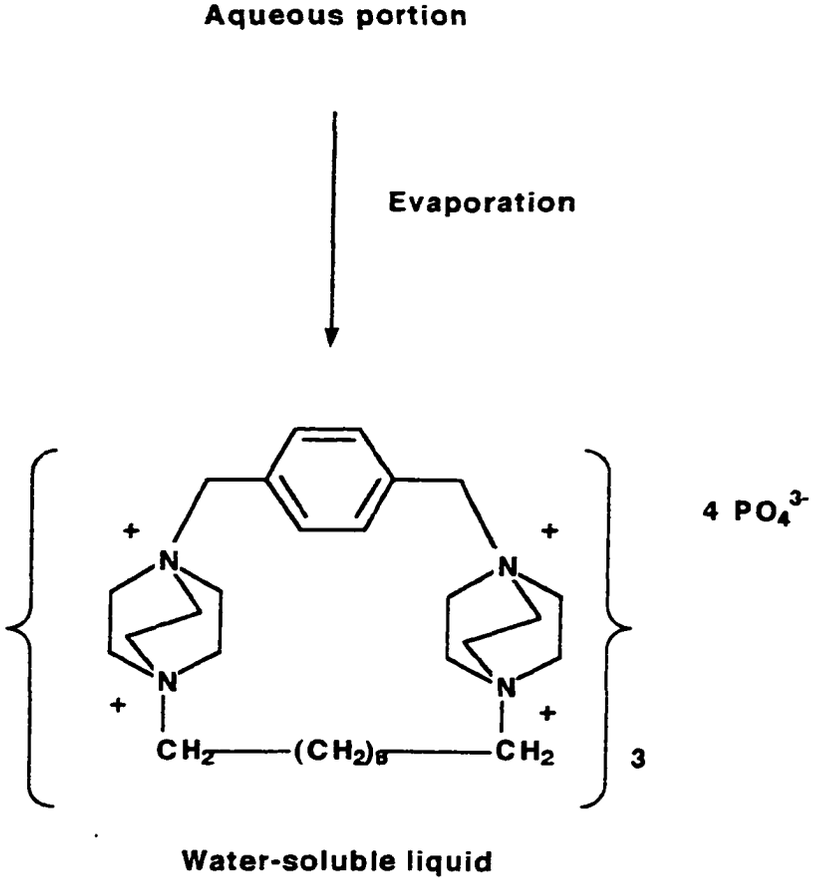


Figure 34 - ^{31}P NMR spectrum of {45}-PF_6^- from reaction of {45} with 60% hexafluorophosphoric acid

In addition, of particular note, is the presence of an additional signal in

the ^{31}P NMR spectrum near 0 ppm. In the spectrum shown above this signal is relatively small, being significantly larger in preparations with other salts. The presence of this signal, and the relatively low yields observed for the hexaflurophosphate salts (20-40%) indicated that another product could possibly be isolated from the reaction mixture, that product producing the extraneous signal in the ^{31}P NMR spectrum, but seemingly without effect on the ^{1}H and ^{13}C NMR spectra. Interestingly, work previously reported by others did not involve measuring the ^{31}P NMR spectra.

Evaporation of the remaining aqueous solution from these preparations indeed led to the isolation of a new category of ionic liquid. Removal under high vacuum conditions for a week, of the water, from the aqueous portion of the hexafluorophosphate conversion of the polyammonium halide salts gave a significant yield (30-50%) of a highly viscous liquid as illustrated in Scheme 52.



Scheme 52

Again, this liquid exhibited ^{1}H and ^{13}C NMR spectra in complete correspondence with those for the parent halide salts, but was completely soluble in D_2O, unlike the isolated solids. These water soluble liquids also exhibited clean ^{31}P NMR spectra with a single unsplit signal near 0 ppm (relative to 85% phosphoric acid) indicating the gegenion to be simple phosphate.

Hexafluorophosphate salts, which are poorly soluble in water, could be isolated and studied by repeated washings of the solid isolates with water until the ^{31}P NMR spectrum no longer exhibited the signal near 0 ppm. All of these solids, in contrast to the hexafluorophosphate salts of monocationic species, exhibited melting points well above room temperature and have thus not been the primary focus of our studies.

Testing of an aqueous solution of the new *liquids* with silver nitrate indicated chloride or bromide ion contamination to be below levels detectable by that technique. We thereby conclude that halide contamination is negligible in these products.

With the evaporation of the supernatant solution, a new series of ionic liquids, *Liquid Ionic Phosphates,* referred to as LIPs, was prepared as listed in Table 35.

Table 35 - New LIPs

{11}-LIP	{20}-LIP	{31}-LIP
{35}-LIP	{36}-LIP	{38}-LIP
{45}-LIP	{48}-LIP	{49}-LIP
{52}-LIP	{68}-LIP	{69}-LIP
{70}-LIP	{71}-LIP	{77}-LIP
{112}-LIP	{113}-LIP	{117}-LIP
{118}-LIP	{124}-LIP	{128}-LIP
{131}-LIP	{137}-LIP	{138}-LIP
{142}-LIP	{143}-LIP	{149}-LIP
{150}-LIP	{152}-LIP	{167}-LIP
{168}-LIP	{187}-LIP	{188}-LIP
{193}-LIP	{205}-LIP	{206}-LIP
{207}-LIP	{208}-LIP	{209}-LIP
{210}-LIP		

(Note, compound {209}-LIP was prepared by treating a didabco dicationic string previously prepared by others in the laboratory. The didabco dicationic string consists of three methylene groups between the dabco units. Compound {210}-LIP was prepared by treating one equivalent of ethylimidazole with iodomethane [152].)

All of these new materials exhibited ^{1}H, ^{13}C, and ^{31}P NMR spectra in accord with the proposed structures. ^{1}H NMR spectra of the LIPs, after drying under high vacuum, indicated the residual water content to be below the limit of reliable measurement by that technique. The 40 new compounds listed in Table 35 are all water soluble, viscous liquids at room temperature (approximately 25° C).

It is interesting to note that only monocationic and dicationic string LIPs have been prepared. Conversions of longer strings with a greater number of cationic sites led to phosphate salts, but those materials remained solid at room temperature, melting above 40° C.

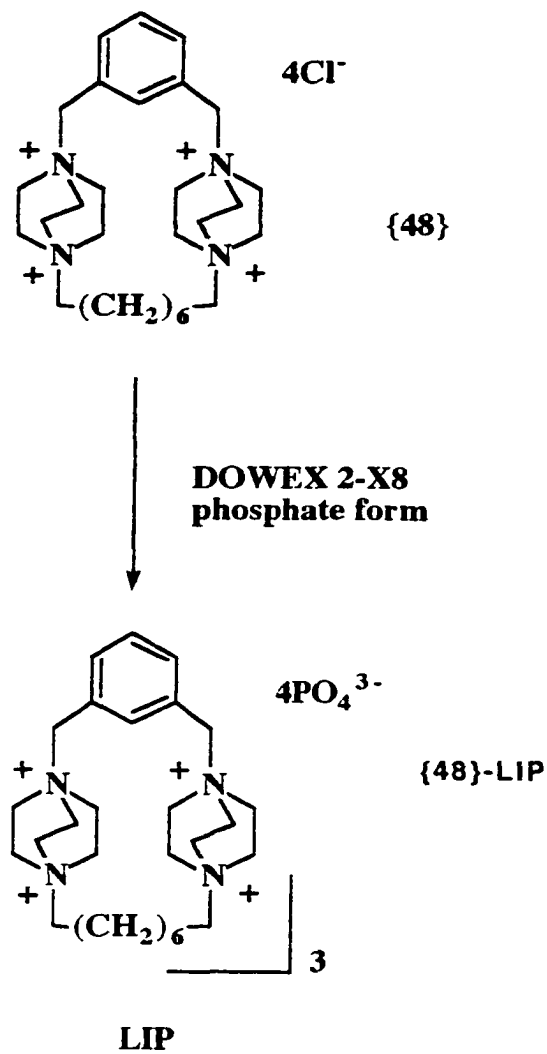
Another interesting observation is that all of the cyclic LIPs prepared bear *unsaturated* linkages. Several saturated cyclic polycations have been converted to their phosphate salts, but these remained solid at room temperature, albeit soluble in water.

A series of polycationic cyclodextrin LIPs have also been prepared. These species should be of particular interest with regard to applications owing to the host/guest binding characteristics of our polycationic cyclodextrin derivatives.

The approach to the synthesis of these LIPs proceeding through the use of hexafluorophosphoric acid has particular drawbacks. Among these are: 1) a significant portion of the yield is diverted to the hexafluorophosphate species; 2) the use of hexafluorophosphoric acid to prepare phosphates is unnecessarily expensive and hazardous for applications requiring large scale preparations; and 3) the use of fluorine is environmentally unfriendly. For these reasons, alternative approaches to the preparation of the LIPs were sought.

One approach to the preparation of LIPs involves the direct ion

exchange using classical insoluble ion exchange resins. Treatment of our halide salts with a large excess of DOWEX 2-X8 in the phosphate form in aqueous medium, followed by evaporation of the water under reduced pressure, was investigated for the preparation of large quantity of the LIPs. [158] This approach is illustrated in Scheme 53.

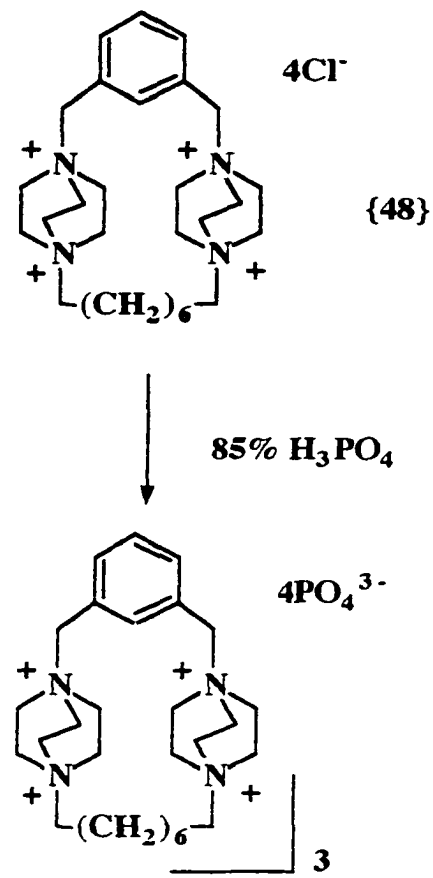


Scheme 53

In some instances this worked quite well, but in other instances was

plagued by difficulties of its own, including incomplete exchange of the halide, as noted with silver nitrate.

Yet another approach to the preparation of the LIPs was investigated, that involving treatment of the polycationic halide salts with 85% phosphoric acid (one charge equivalent) as shown in Scheme 54.



Pure LIP

Scheme 54

Removal of all volatile materials (water and hydrogen halide) under

reduced pressure, provided pure LIPs in good yield with complete conversion to the phosphate salt.

Some of the newly synthesized LIPs remain solid at room temperature, but exhibit sufficiently low melting points, in the range of 40-50° C. Table 36 lists all of the compounds in this category.

Table 36 - *Solid* LIPs melting at 40-50° C.

{14}-LIP	{121}-LIP	{125}-LIP
{128}-LIP	{174}-LIP	{211}-LIP
{48}-LIP		

(Note, compound {211}-LIP was prepared by a graduate student, Chris Massone, in the same laboratory. This material is a diphosphonium string that is prepared by treating α,α'-dibromo-*p*-xylene in acetonitrile solution with two equivalents of triphenylphosphine. The aforementioned student has also prepared another diphosphonium string using 4,4',-bis(bromomethyl)-1,1'-biphenyl as the α,ω-dihalo species.)
These materials have capabilities for applications as ionic liquids at relatively low temperatures.

Other newly prepared polycationic phosphates remain solid at temperatures greater that 80°C. These new materials are listed in Table 37.

Table 37 - *Solid* polycationic phosphates melting >80°C.

{10}-LIP	{42}-LIP	{43}-LIP
{70}-LIP	{74}-LIP	{105}-LIP
{111}-LIP	{126}-LIP	{165}-LIP
{168}-LIP	{170}-LIP	{191}-LIP
{209}-LIP		

Table 38 lists spectroscopic and physical characteristics for some of the newly prepared LIPs, including density and specific conductivities that were measured by a graduate student in our laboratory, Sharon Lall. [158]

Table 38 - Densities and specific conductivities of LIPs.

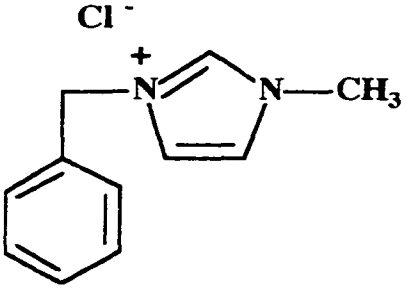
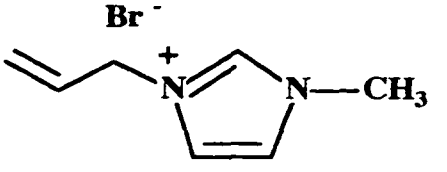
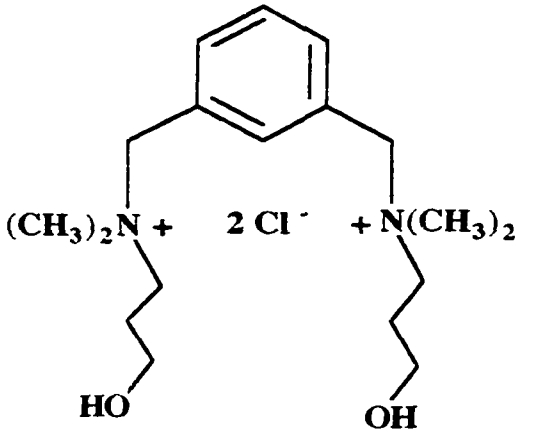
LIP	*Density (g/mL)*	*Specific Conductivity (cm-1W-1) s*			*s/KCl ref.*
		25 C	*40 C*	*60 C*	
{48}-LIP	1.78	0.057	0.063	0.061	19
{45}-LIP	1.86	0.063	0.052	0.082	21
{52}-LIP	1.82	0.063	0.060	0.071	21
{77}-LIP	1.58	0.064	0.081	0.087	21
{124}-LIP	1.82	0.038	0.052	0.050	13
{68}-LIP	1.58	0.053	0.056	0.071	18
{71}-LIP	1.96	0.026	0.027	0.042	9
{137}-LIP	1.90	0.042	0.053	0.067	14
{46}-LIP	-	0.0010	-	-	0.3
{47}-LIP	-	0.040	-	-	13

NOTE: 0.02*M* aqueous KCl reference solution, specific conductivity = 0.03 $cm^{-1}W^{-1}$ at 25 °C

Interestingly, a series of ionic liquids containing *halides* as the anion matched with either imidazolium or ammonium cations have been prepared as structurally pure materials. These new compounds are listed in Table 39.

It is intriguing that compounds {200} and {201} are liquids as the halide salts. Imidazolium salts containing only saturated substituents are solid. [152] We have isolated the *unsaturated* species {200} and {201} as liquids. Additional imidazolium halides with unsaturated linkages are being sythesized to determine if this is a general phenomenon.

Table 39 - New ionic liquids bearing *halide* anions

Structure	Number
	201
	200
	137

In comparison with previously reported room temperature non-aqueous ionic liquids, the newly prepared LIPs exhibit particular advantages. These include: 1) ease of preparation, requiring only 85% phosphoric acid rather than the use of quite reactive (and under certain

non-aqueous ionic liquids, the newly prepared LIPs exhibit particular advantages. These include: 1) ease of preparation, requiring only 85% phosphoric acid rather than the use of quite reactive (and under certain circumstances hazardous) hexafluorophosphoric acid, tetrafluoroboric acid or aluminum chloride, which require controlled atmospheric conditions; 2) the resultant salts are unreactive with water; 3) although viscous, the LIPs are liquids at room temperature, while the hexafluorophosphate salts of monocations melt above room temperature and the hexafluorophosphate salts of polycations we have prepared remain solid up to 75° C; 4) particularly high specific conductivities; and 5) the potential use as media for electrochemical processes requiring a large electrochemical window.

EXPERIMENTAL

General

All chemicals used in syntheses, purification, and comparison analyses were of commercial reagent quality and were used without purification. NMR spectra were measured using a Bruker 400 MHz DPX400 instrument. All optical rotations were measured using a Jasco DIP-140 instrument (1 dm cell, aqueous solution with a sodium vapor lamp), and all CD spectra were measured using a Jasco 500C CD/ORD instrument. All UV/Vis spectra were measured using a Hewlett-Packard model G1103A spectrophotometer. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

Preparations

Preparation of 1-(6-hydroxyhexyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride (3). 1,4-Diazabicyclo[2.2.2]octane (8.211 g, 0.0732 mol) was dissolved in ethyl acetate (40 mL). 6-Chloro-1-hexanol (10.0 g, 0.0732 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The resultant gummy precipitate was collected (16.1 g, 88.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{12}H_{25}N_2OCl \bullet 2(H_2O)$: C 57.93%, H 10.13% Found: C 58.04%, H 10.24%. NMR (δ, D_2O) - ^1H: 1.29, br, 4H; 1.45, br, 2H; 1.67, br, 2H;

3.09, br, 6H; 3.15, t (J=4 Hz), 2H, 3.29, br, 6H; 3.49, t (J=8 Hz), 2H. ^{13}C: 19.78, 23.24, 24.03, 29.63, 42.88, 50.73, 60.22, 63.22.

Preparation of 1-(6-hydroxyhexyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride (5). 1,4-Diazabicyclo[2.2.2]octane (8.00 g, 0.0713 mol) was dissolved in ethyl acetate (40 mL). 9-Bromo-1-nonanol (23.88 g, 0.0713 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The resultant brown powder precipitate was collected (19.9 g, 83.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{15}H_{31}N_2OBr \bullet 2(H_20)$: C 53.73%, H 9.32% Found: C 54.02%, H 9.53%. NMR (δ, D_2O) - ^1H: 1.06-1.41, m, 10H; 1.64, t, 2H; 1.97, br, 2H; 3.06-3.16, m, 6H; 3.27, t, 8H, 3.49, t, 2H. ^{13}C: 21.51, 25.30, 25.90, 38.40, 28.73, 28.74, 31.2, 44.52, 52.47, 66.10.

Preparation of 1-(10-hydroxydecyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride (6). 1,4-Diazabicyclo[2.2.2]octane (3.30 g, 0.0294 mol) was dissolved in ethyl acetate (40 mL). 10-Chloro-1-decanol (5.66 g, 0.0294 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for two days. The resultant white precipitate was collected (7.92 g, 88.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for

$C_{16}H_{33}N_2OCl \bullet 2(H_2O)$: C 67.00%, H 8.79% Found: C 67.11%, H 8.87%. NMR (δ, D_2O) ^1H: 1.20, br, 12H; 1.43, br, 2H; 1.64, br, 2H; 3.11, br, 6H; 3.16, br, 2H; 3.28, br, 6H; 3.49, t (J=8 Hz), 2H. ^{13}C: 21.42, 25.33, 25.85, 28.41, 28.86, 28.75, 28.81, 31.59, 44.52, 52.37, 62.21, 65.02.

Preparation of 1-(11-hydroxyundecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (7). 1,4-Diazabicyclo[2.2.2]octane (3.30 g, 0.0294 mol) was dissolved in ethyl acetate (40 mL). 11-Chloro-1-undecanol (5.50 g, 0.0294 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for three days. The resultant white precipitate was collected (7.95 g, 81.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{17}H_{35}N_2OBr \bullet (H_2O)$: C 56.19%, H 9.71% Found: C 56.24%, H 9.72%. NMR (δ, D_2O) ^1H: 1.18, br, 14H; 1.42, br, 2H; 1.63, br, 2H; 3.09, br, 6H; 3.13, br, 2H; 3.27, br, 6H; 3.46, t (J=5 Hz), 2H. ^{13}C: 23.60, 27.53, 28.04, 30.61, 30.88, 31.00, 31.11, 31.20, 33.78, 46.70, 54.54, 54.58, 64.60.

Preparation of 1-(3-propenyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (8). 1,4-Diazabicyclo[2.2.2]octane (3.0 g, 0.0267 mol) was dissolved in ethyl acetate (40 mL). Allyl bromide (3.26 g, 0.0267 mol) was slowly added with stirring. The reaction mixture was stirred at room

temperature for one day. The resultant gummy precipitate was collected (5.1 g, 82.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_9H_{17}N_2Br \bullet H_20$: C 45.08%, H 7.35% Found: C 45.16%, H 7.42%. NMR (δ, D2O) - 1H: 3.16, t, 6H; 3.38, t, 6H; 3.97, d (*J*=3 Hz), 2 H; 5.61-5.70, m, 2H; 5.90-6.00, m, 1H. 13C: 42.78, 55.57, 65.11, 122.21, 127.61.

Preparation of 1-(dodecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (10). 1,4-Diazabicyclo[2.2.2]octane (9.00 g, 0.0732 mol) was dissolved in ethyl acetate (40 mL). 1-Bromododecane (18.2g, 0.0732 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The resultant gummy precipitate was collected (23.2 g, 82.8%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{18}H_{37}N_2Br$: C 59.70%, H 10.50% Found: C 59.75%, H 10.55%. NMR (δ, D2O) - 1H: 0.73, t, 3H; 1.68-1.24, br, 18H; 1.64, br, 2H; 3.07-3.16, m, 8H; 3.27-3.30, m, 6H. 13C: 12.69, 20.34, 21.33, 24.78, 27.37, 27.67, 27.78, 27.83, 27.99, 28.02, 30.48, 43.43, 51.25, 63.90

Preparation of 1-(benzyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (11). 1,4-Diazabicyclo[2.2.2]octane (4.0 g, 0.0357 mol) was dissolved in ethyl acetate (40 mL). Benzyl bromide (9.00g, 0.0357mol) was slowly added with stirring. The reaction mixture was stirred at room temperature

for one day. The resultant brown powder precipitate was collected (7.8 g, 91.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{13}H_{19}N_2Br \bullet H_2O$: C 55.13%, H 6.76% Found: C 55.20%, H 6.82%. NMR (δ, D_2O) - ^1H: 2.95-3.12, m, 6H; 3.24-3.28, m, 6H; 4.69, s, 2H; 7.36-7.48, m, 5H. ^{13}C: 46.63, 54.44, 70.86, 127.42, 131.14, 132.33, 132.38.

Preparation of 1,4-bis(10'-hydroxydecyl)-1,4-diazoniabicyclo[2.2.2]octane dichloride (12). (6) (1.00 g, 0.00232 mol) was dissolved in acetonitrile (25 mL). 10-Chloro-1-decanol (0.45 g, 0.00232 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for five days. The resultant white precipitate was collected (0.75 g, 65.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. NMR analysis showed only 25% complete reaction; therefore, the material was dissolved in acetonitrile (50 mL) and 10-chloro-1-decanol (0.684 g, 0.00355 mol) was slowly added with stirring. Reaction was continued at reflux until the NMR of the precipitate indicated conversion was more than 99% . Calcd. for $C_{26}H_{54}N_2O_2Cl_2 \bullet 2(H_2O)$: C 58.52%, H 10.96% Found: C 58.16%, H 10.68%. NMR (δ, D_2O) - ^1H: 1.12-1.35, br, 28H; 1.35-1.48, m, 4H; 1.65-1.77, br, 4H; 3.40-3.51, m, 8H; 3.87, s, 12H. ^{13}C: 18.98, 22.89, 23.41,

25.97, 26.21, 26.30, 26.36, 29.14, 42.08, 49.93, 59.77.

Preparation of 4-(6'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-hexyl)azonia-1-azabicyclo[2.2.2]octane dichloride (14). 1,4-Diazabicyclo[2.2.2]octane (43.39 g, 0.387 mol) was dissolved in acetonitrile (75 mL). 1,6-Dichlorohexane (15.00 g, 0.0967 mol) in acetonitrile (50 mL) was added dropwise with stirring. The reaction mixture was stirred at room temperature for one day. The resultant white precipitate was collected (29.9 g, 81.7%) by suction filtration and washed with ethyl acetate (3 x 30 mL) and anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{18}H_{36}N_4Cl_2 \cdot (H_2O)$: C 54.40%, H 9.64% Found: C 54.31%, H 9.72%. NMR (δ, D_2O) - ^1H: 1.29, br, 4H; 1.66, br, 4H; 3.00 - 3.16, br, 16H; 3.26, br, 12H. ^{13}C: 27.77, 31.89, 50.85, 58.74, 70.99.

Preparation of 4-(9'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-nonyl)azonia-1-azabicyclo[2.2.2]octane dibromide (16). 1,4-Diazabicyclo[2.2.2]octane (8.50 g, 0.0758 mol) was dissolved in acetonitrile (50 mL). 1,9-Dibromononane (2.00 g, 0.00947 mol) in acetonitrile (50 mL) was added dropwise with stirring. The reaction mixture was stirred at room temperature for two days. Ethyl acetate (100 mL) was added to cause precipitation. The resultant white precipitate was collected (3.8 g, 92.2%) by suction filtration and washed with ethyl

acetate (3 x 30 mL) and anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{22}H_{44}N_4Br_2 \bullet 1.5(H_2O)$: C 56.83%, H 10.12% Found: C 56.79%, H 10.18%. NMR (δ, D_2O) - ^1H: 1.25, br, 10H; 1.63-1.65, br, 4H; 3.12-3.17, br, 16H; 3.27-3.31, br, 12H. ^{13}C: 19.30, 23.58, 26.18, 26.31, 42.35, 50.21, 62.81.

Preparation of 4-(10'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-decyl)azonia-1-azabicyclo[2.2.2]octane dichloride (17). 1,4-Diazabicyclo[2.2.2]octane (8.50 g, 0.0758 mol) was dissolved in acetonitrile (50 mL). 1,10-Dichlorodecane (2.00 g, 0.00947 mol) in acetonitrile (50 mL) was added dropwise with stirring. The reaction mixture was stirred at room temperature for two days. Ethyl acetate (100 mL) was added to to cause precipitation. The resultant white precipitate was collected (3.8 g, 92.2%) by suction filtration and washed with ethyl acetate (3 x 30 mL) and anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{22}H_{44}N_4Cl_2 \bullet 1.5(H_2O)$: C 57.13%, H 10.24% Found: C 57.22%, H 10.51%. NMR (δ, D_2O) - ^1H: 1.25, br, 12H; 1.65, br, 4H; 3.05-3.10, br, 16H; 3.25-3.31, br, 12H. ^{13}C: 22.67, 27.11, 29.68, 29.87 45.73 53.60, 66.22.

Preparation of 4-(12'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-dodecyl)azonia-1-azabicyclo[2.2.2]octane dibromide (18). 1,4-

Diazabicyclo[2.2.2]octane (20.0 g, 0.178 mol) was dissolved in acetonitrile (50 mL). 1,12-dibromododecane (14.5 g, 0.0445 mol) in acetonitrile was added dropwise with stirring. The reaction mixture was stirred at room temperature for nine days. Volatiles were evaporated under reduced pressure, then the resultant white precipitate was collected (19.2 g, 78.0%) and dried under high vacuum. NMR (δ, D_2O) - ^1H: 1.18, br, 16H; 1.65, br, 4H; 2.75, s, 4H; 3.07, t, 12H. ^{13}C: 21.46, 25.88, 28.76, 28.88, 44.52, 45.42, 52.37, 65.01. This material was used without further purification.

Preparation of 4-(10'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-(Z)-2-butenyl)azonia-1-azabicyclo[2.2.2]octane dichloride (19). 1,4-Diazabicyclo[2.2.2]octane (5.0 g, 0.0446 mol) was dissolved in acetonitrile (50 mL). *cis*-1,4-Dichloro-2-butene (2.79 g, 0.022 mol) in acetonitrile was added dropwise with stirring. The reaction mixture was stirred at room temperature for nine days. Volatiles were evaporated under reduced pressure, then the resultant white precipitate was collected (6.53 g, 85.1%) and dried under high vacuum. NMR (δ, D_2O) - ^1H: 3.14, br, 12H; 3.37, br, 12H; 4.01, d (J=14 Hz), 4H; 6.26, t, 2H. ^{13}C: 42.59, 50.66, 58.33, 124.63. This material was used without further purification.

Preparation of 4-(10'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-1'-(Z)-2-

butylyl)azonia-1-azabicyclo[2.2.2]octane dichloride (20). 1,4-Diazabicyclo[2.2.2]octane (5.0 g, 0.0445 mol) was dissolved in acetonitrile (50 mL). *cis*-1,4-Dichloro-2-butyne (2.78 g, 0.0222mol) in acetonitrile was added dropwise with stirring. The reaction mixture was stirred at room temperature for nine days. Volatiles were evaporated under reduced pressure, then the resultant white precipitate was collected (8.4 g, 86.9%) and dried under high vacuum. This material was used without further purification.

Preparation of 1-(β-hydroxyethyl)-4-(6'-{4"-(β-hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride (23). (14) (1.00 g, 0.00264 mol) was dissolved in acetonitrile (25 mL). 2-Bromo-1-ethanol (2.532 g, 0.0205 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred at reflux for one day. The resultant white precipitate was collected (0.85 g, 83.3%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{22}H_{46}N_4O_2Br_2Cl_2 \bullet 4(H_2O)$: C 37.67%, H 7.76% Found: C 37.72%, H 7.39%. NMR (δ, D_2O) - ^1H: 1.50-1.65, br, 4H; 1.85-2.04, br, 4H; 3.38-4.31, br, 36H. ^{13}C: 21.77, 25.17, 51.44, 52.35, 55.25, 65.26, 66.71.

Preparation of 1-(β-hydroxypropyl)-4-(6'-{4"-(ω-hydroxypropyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane

tetrachloride (24). (14) (10.00 g, 0.0264 mol) was dissolved in acetonitrile (75 mL). 3-Chloro-1-propanol (4.99 g, 0.0525 mol) was slowly added with stirring. The reaction mixture continue to heat and stir at reflux for one day. The resultant white precipitate was collected (14.3 g, 69.1%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. NMR analysis showed incomplete reaction; therefore, to the sample acetonitrile (75 mL) was added. 3-Chloro-1-propanol (4.99 g, 0.0525 mole) was added with stirring. Reaction mixture continue to heat and stir at reflux for one day. Residue collected by suction filtration. It was washed with ether (3 x 30 mL) and dried under high vacuum. Calcd. for $C_{42}H_{50}N_4O_2Cl_4 \bullet 4(H_2O)$: C 38.12%, H 7.54% Found: C 38.29%, H 7.60%. NMR (δ, D_2O) - ^1H: 1.51-1.64, br, 4H; 1.83-2.02, br, 4H; 2.27-2.35, br, 4H; 3.37-4.29, br, 36H. ^{13}C: 21.76, 25.15, 26.60, 51.43, 52.31, 55.21, 65.24, 66.69.

Preparation of 1-(β-hydroxyethyl)-4-(8'-{4"-(β-hydroxyethyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-octyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride (25). (15) (4.581 g, 0.01126 mol) was dissolved in acetonitrile (25 mL). 2-Bromo-1-ethanol (5.626 g, 0.0405 mol) in acetonitrile (25 mL) was slowly added with stirring. The reaction mixture continue to heat and stir at reflux for one day. The resultant white precipitate was collected (4.5 g, 61.2%) by suction filtration and washed

with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{24}H_{50}N_4O_2Br_2Cl_2 \bullet 2(H_2O)$: C 41.57%, H 7.84% Found: C 41.31%, H 7.68%. NMR (δ, D_2O) - ^1H: 1.28-1.38, br, 8H; 184-1.99, br, 4H; 3.48-4.12, br, 36H. ^{13}C: 21.83, 25.42, 28.17, 51.55, 52.41, 55.30, 65.65, 66.72.

Preparation of 1-(β-hydroxyethyl)-4-(10'-{4''-(β-hydroxyethyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-decyl)-1,4-diazoniabicyclo[2.2.2]octane dibromide dichloride (26). (17) (2.232 g, 0.00513 mol) was dissolved in acetonitrile (25 mL). 2-Bromo-1-ethanol (2.562 g, 0.0205 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred at reflux for two days. The resultant white precipitate was collected (2.1 g, 63.3%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{26}H_{54}N_4O_2Br_2Cl_2 \bullet 3(H_2O)$: C 42.22%, H 8.17% Found: C 42.52%, H 7.91%. NMR (δ, D_2O) - ^1H: 1.18-1.29, br, 12H; 1.67-1.81, br, 4H; 3.35-4.12, br, 36H. ^{13}C: 21.82, 25.54, 28.40, 28.59, 51.37, 52.36, 55.25, 65.68, 66.68.

Preparation of 1,4-bis(10'-hydroxydecyl)-1,4-diazoniabicyclo[2.2.2]octane dichloride (27). (17)(1.00 g, 0.00232 mol) was dissolved in acetonitrile (25 mL). 10-Chloro-1-decanol (0.45 g,

0.00232 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for five days. The resultant white precipitate was collected (0.75 g, 65.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. NMR analysis showed only 25% complete reaction; therefore, the material was dissolved in acetonitrile (50 mL) and 10-chloro-1-decanol (0.684 g, 0.00355 mol) was slowly added with stirring. Reaction was continued at reflux until the NMR of the precipitate indicated the reaction to have proceeded to more than 99% completion. Calcd. for $C_{42}H_{86}N_4O_2Cl_4 \bullet 2(H_2O)$: C 58.52%, H 10.96% Found: C 58.16%, H 10.68%. NMR (δ, D_2O) - ^1H: 1.18-1.29, br, 32H; 1.68-1.80, br, 8H; 2.15-2.19, m, 8H; 3.31-4.10, br, 18H; 4.11-4.15, br, 18H. ^{13}C: 18.18, 18.21, 18.26, 19.01, 19.41, 20.21, 20.78, 20.79, 21.31, 21.39, 21.65, 21.70, 21.80, 24.01, 25.49, 28.51, 28.59, 51.44, 52.49, 55.20, 65.69, 67.01.

Preparation of 1-(β-chlorodecyl)-4-(10'-{4''-(β-chlorodecyl)-1'',4''-diazoniabicyclo[2.2.2]octyl}-1'-decyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride (28). (27) (2.65g, 0.00323 mol) was dissolved in chloroform (30 mL). Thionyl chloride (8.00 g) was slowly added with stirring. After two hours, absolute ethanol was then added dropwise with stirring until reaction ceased. Volatiles were evaporated under reduced pressure then dried under high vacuum (1.7 g, 59.2%). Calcd. for

$C_{42}H_{84}N_4Cl_6 \bullet 2(H_2O)$: C 53.22%, H 9.99% Found: C 52.94%, H 10.31%. NMR (δ, D_2O) - ^1H: 1.18-1.29, br, 32H; 1.68-1.80, br, 8H; 2.15-2.19, m, 8H; 3.31-4.10, br, 18H; 4.11-4.15, br, 18H. ^{13}C: 18.18, 18.21, 18.26, 19.01, 19.41, 20.21, 20.78, 20.79, 21.31, 21.39, 21.65, 21.70, 21.80, 24.01, 25.49, 28.51, 28.59, 51.44, 52.49, 55.20, 65.69, 67.01.

Preparation of 4,4,7,7-tetramethyl-4,7-diazoniadecan-1,10-diol dichloride (29). 1,2-Dibromoethane (3.00 g, 0.0160 mol) was dissolved in absolute ethanol (75 mL). 3-Dimethylamino-1-propanol (3.295 g, 0.0319 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for six days. Volatiles were evaporated under reduced pressure and dried under high vacuum. NMR analysis showed only 35% completion of reaction; therefore, to the material 3-dimethylamino-1-propanol (excess) in absolute ethanol (50 mL) was added with stirring. Reaction continued to be heated and stirred at reflux until it was more than 99% complete reaction. The target product was isolated by filtration and dried under high vacuum (5.2 g, 82.5%). Calcd. for $C_{12}H_{30}N_2O_2Br_2 \bullet (H_2O)$: C 38.71%, H 5.98% Found: C 38.52%, H 5.87%. NMR (δ, D_2O) - ^1H: 1.88-1.91, br, 4H; 2.20-3.24, br, 4H; 3.12, s, 12H; 3.30-3.50, m, 8H; 3.59-3.75, m, 4H. ^{13}C: 19.05, 26.06, 27.34, 53.26, 60.43, 62.64, 64.81.

Preparation of 4,4,8,8-tetramethyl-4,8-diazoniaundecan-1,11-diol dichloride (30). 1,3-Dichloropropane (1.00 g, 0.00885 mol) was dissolved in absolute ethanol (75 mL). 3-Dimethylamino-1-propanol (1.826 g, 0.0177 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for two days. Volatiles were evaporated under reduced pressure and dried under high vacuum. NMR analysis showed the reaction to be only 15% complete; therefore, to the material 3-dimethylamino-1-propanol (excess) in absolute ethanol (50 mL) was added to the reaction mixture with stirring. Reaction continue to heat and stir at reflux until more than 99% complete reaction (1.6 g, 64.0%). Calcd. for $C_{13}H_{32}N_2Cl_2$: C 48.89%, H 10.10% Found: C 48.99%, H 10.39%. NMR (δ, D_2O) - ^1H: 1.90-2.01, br, 4H; 2.22-3.20, br, 2H; 3.10, s, 12H; 3.33-3.55, m, 8H; 3.60-3.79, m, 4H. ^{13}C: 19.07, 27.37, 53.23, 60.45, 62.60, 64.79.

Preparation of 7,7,11,11-tetramethyl-7,11-diazoniaheptadecan-1,17-diol dichloride (31). *N,N,N',N'*-tetramethyl-1,3-propanediamine (2.00 g, 0.01563 mol) was dissolved in acetonitrile (75 mL). 6-Chloro-1-hexanol (4.19 g, 0.03072 mol) was slowly added with stirring. The reaction mixture continue to be heated and stirred at reflux for seven days. Volatiles were evaporated under reduced pressure and dried under high vacuum to give the white powder product (4.2 g, 74.2%). Calcd. for

$C_{19}H_{44}N_2O_2Cl_2$: C 48.71%, H 10.21% Found: C 48.81%, H 10.30%. NMR (δ, D_2O) - ^1H: 1.30-1.37, br, 8H; 1.45-1.62, m, 4H; 1.68-1.78, m, 4H; 2.20-2.28, m, 2H; 3.07, s, 12H; 3.25-3.34, m, 8H, 3.51, t, 4H. ^{13}C: 14.84, 20.04, 22.75, 23.3, 29.12, 48.81, 58.14, 59.67, 62.93.

Preparation of 4,4,9,9-tetramethyl-4,9-diazoniadodecan-1,12-diol dichloride (32). *N,N,N',N'*-tetramethyl-1,4-butanediamine (2.00 g, 0.00139 mol) was dissolved in acetonitrile (75 mL). 3-Chloro-1-propanol (2.63 g, 0.0278 mol) was slowly added with stirring. The reaction mixture was continued to be heated and stirred at reflux for four days. The resultant white powder precipitate was collected by suction filtration, washed with anhydrous ether (3 x 30 mL), and dried under high vacuum. NMR analysis showed impurities present; therefore, the material was repeatedly washed until the NMR exhibited no extraneous signals beyond the limits of observable impurities. There was thus isolated the pure material (0.25 g, 54.3%). Calcd. for $C_{14}H_{34}N_2O_2Cl_2$: C 48.95%, H 10.13% Found: C 48.90%, H 10.21%. NMR (δ, D_2O) - ^1H: 1.23-1.38, m, 8H; 1.40-1.55, m, 4H; 1.61-1.80, br, 8H; 2.98, s, 12H; 3.17-3.32, br, 8H; 3.45-3.55, t, 4H. ^{13}C: 19.97, 22.63, 25.38, 26.03, 31.73, 51.30, 62.31, 63.67, 65.04.

Preparation of 7,7,12,12-tetramethyl-7,12-diazoniaoctadecan-1,18-diol

dichloride (33). *N,N,N',N'*-tetramethyl-1,4-butanediamine (2.00 g, 0.0138 mol) was dissolved in acetonitrile (75 mL). 6-Chloro-1-hexanol (3.77 g, 0.0276 mol) was slowly added with stirring. The residue was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.2 g, 73.0%). Calcd. for $C_{20}H_{46}N_2O_2Cl_2$: C 49.12%, H 10.32% Found: C 49.27%, H 10.40%. NMR (δ, D_2O) - ^1H: 1.33-1.47, br, 8H; 1.48-1.49, br, 4H; 1.61-1.64, br, 8H; 3.16, s, 12H; 3.33, m, 8H; 3.69, t, 4H. ^{13}C: 18.83, 21.48, 24.24, 24.88, 30.59, 50.15, 61.17, 62.53, 63.90.

Preparation of 11,11,16,16-tetramethyl-11,16-diazoniahexaeicosane-1,26-diol dichloride (34). *N,N,N',N'*-tetramethyl-1,4-butanediamine (2.00 g, 0.00139 mol) was dissolved in acetonitrile (75 mL). 10-Chloro-1-decanol (5.37 g, 0.0277 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred at reflux for four days. The resultant white powder precipitate was collected by suction filtration, washed with anhydrous ether (3 x 30 mL), and dried under high vacuum. NMR analysis showed impurities present; therefore, the material was repeatedly washed until the NMR exhibited no more detectable impurities. In this way the pure target material was isolated (0.50 g, 68.5%). Calcd. for $C_{28}H_{62}N_2O_2Cl_2$: C 47.72%, H 10.01% Found: C 47.69%, H 10.21%. NMR (δ, D_2O) - ^1H: 1.35-1.49, br, 12H; 1.51-1.52, br, 8H; 1.63-1.66, br, 8H;

3.19, s, 12H; 3.35, m, 8H; 3.72, t, 4H. ^{13}C: 18.21,18.52,18.83, 19.21, 19.70, 21.48, 24.27, 24.91, 30.66, 50.17, 61.20, 62.56, 63.94.

Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,14-diol dichloride (35). 1,6-dichlorohexane (1.00 g, 0.00645 mol) was dissolved in absolute ethanol (75 mL). 3-Dimethylamino-1-propanol (1.331 g, 0.0129 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for two days. Volatiles were evaporated under reduced pressure and dried under high vacuum. NMR analysis showed impurities present; therefore, it was washed with hexane (3 x 30 mL) and dried under high vacuum to give the pure material (1.8 g, 77.6%). Calcd. for $C_{16}H_{38}N_2O_2Cl_2 \bullet (H_2O)$: C 53.17%, H 10.60% Found: C 62.88%, H 10.59%. NMR (δ, D_2O) - ^1H: 1.23-1.38, m, 12H; 1.38-1.51, m, 4H; 1.60-1.75, m, 8H; 2.90-3.01, s, 12H; 3.12-3.25, m, 8H; 3.45-3.58, t, 4H. ^{13}C: 24.08, 26.83, 27.43, 27.52, 33.20, 34.08, 52.75, 63.95, 65.95, 66.22.

Preparation of 7,7,14,14-tetramethyl-7,14-diazoniaeicosan-1,20-diol dichloride (36). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (2.00 g, 0.001161 mol) was dissolved in acetonitrile (75 mL). 6-Chloro-1-hexanol (3.17 g, 0.0232 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for 6 hours. Volatiles were evaporated under reduced pressure and dried under high vacuum (0.31 g, 60.1%).

Calcd. for $C_{22}H_{50}N_2O_2Cl_2$: C 48.24%, H 10.01% Found: C 48.30%, H 10.11%. NMR (δ, D_2O) - ^1H: 1.28-1.32, m, 12H; 1.43-1.49, m, 4H; 1.66-1.67, br, 8H; 2.94, s, 12H; 3.16-3.20, m, 8H; 3.49, t, 4H. ^{13}C: 22.16, 24.68, 24.91, 25.50, 25.60, 31.31, 46.11, 62.08, 64.07, 64.32.

Preparation of 4,4,13,13-tetramethyl-4,13-diazoniahexadecan-1,16-diol dichloride (37). 1,8-Dichlorooctane (1.00 g, 0.00546 mol) was dissolved in absolute ethanol (75 mL). 3-Dimethylamino-1-propanol (1.13 g, 0.0109 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for three days. Volatiles were evaporated under reduced pressure and dried under high vacuum. NMR analysis showed 80% completion of reaction; therefore, to the material 3-dimethylamino-1-propanol (1.13g, 0.0109 mol) in absolute ethanol (25 mL) was added to the reaction mixture with stirring until reaction was more than 99% complete. In this way the pure target material was isolated (1.4 g, 61.4%). Calcd. for $C_{18}H_{44}N_2O_2Cl_2 \bullet (H_2O)$: C 48.75%, H 10.91% Found: C 49.19%, H 11.31%. NMR (δ, D_2O) - ^1H: 1.30, s, 8H; 1.65-1.75, br, 4H; 1.85-1.95, m, 4H; 2.99, s, 12H; 3.15-3.35, d (J= 4Hz), 8H; 3.61, t, 4H. ^{13}C: 20.97, 24.49, 25.02, 27.11, 49.77, 58.14, 60.58, 63.35.

Preparation of *N,N,N',N'*-tetramethyl-*N,N*-bis(3-hydroxypropyl)1,4-

di(azoniamethyl)benzene dibromide (38): α,α'-Dibromo-*p*-xylene (1.00 g, 0.00379 mol) was dissolved in ethanol (75 mL). 3-Dimethylamino-1-propanol (0.780 g, 0.00758 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for two days. Volatiles were evaporated under reduced pressure and foamy precipitate was dried under high vacuum (1.25 g, 70.2%). Calcd. for $C_{18}H_{34}N_2O_2Br_2$: C 45.97%, H 7.28% Found: C 45.73%, H 7.20%. NMR (δ, D_2O) - ^1H: 2.00, m, 4H; 2.95, s, 12H; 3.33, m, 4H; 3.57, m, 4H; 4.52, s, 4H; 7.61, s, 4H. ^{13}C: 25.72, 50.51, 58.82, 67.72, 67.82, 130.33, 134.27.

Preparation of *N,N,N',N'*-tetramethyl-*N,N'*-bis(3-chloropropyl)-1,4-di(azoniamethyl)benzene dichloride (39). (38) (1.25 g, 0.0027 mol) was dissolved in chloroform (30 mL). Thionyl chloride (excess) was slowly added with stirring. The reaction mixture was stirred at room temperature for four hours. Absolute ethanol was added with stirring until reaction ceased. Stirring was continued for one day. Volatiles were evaporated under reduced pressure, washed with ether (3 x 30 mL) and dried under high vacuum. (0.7 g, 61.9%). Calcd. for $C_{18}H_{32}N_2Cl_4 \bullet H_2O$: C 41.17%, H 6.52% Found: C 41.39%, H 6.68%. NMR (δ, CD_3CN) - ^1H: 2.01, m, 4H; 2.95, s, 12H; 3.38, m, 4H; 3.59, m, 4H; 4.56, s, 4H; 7.65, s, 4H. ^{13}C: 25.76, 50.54, 58.84, 67.75, 67.83, 130.35, 134.31.

Preparation of *N,N,N',N'*-tetramethyl-*N,N'*-bis-1"-(3'-{1",4"-diazonia-4"-(8-hydroxyoctyl)bicyclo[2.2.2]octyl}-1,4-diazoniamethylbenzene) hexachloride (40). (4) (0.89 g, 0.0021 mol) was dissolved in acetonitrile (50 mL). (39) (1.136g, 0.00420 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for three days. Volatiles were evaporated under reduced pressure and the product dried under high vacuum. (1.2 g, 53.8%). Calcd. for $C_{46}H_{90}N_6O_2Br_2Cl_4 \bullet 14(H_2O)$: C 42.08%, H 9.05% , N 6.40% Found: C 42.22%, H 9.10%, N 6.51%. NMR (δ, D_2O) - ^{13}C: 18.54, 22.85, 23.19, 26.58, 26.86, 29.87, 21.91, 45.93, 51.46, 52.75, 53.38, 53.74, 63.54, 67.15, 69.99, 131.15, 135.60.

Preparation of 4-(α'-{1"-azonia-4"-azabicyclo[2.2.2]octyl}-α-(*para*)phenyly)azonia-1-azabicyclo[2.2.2]octane dibromide (41). α,α'-Dibromo-*p*-xylene (1.00 g, 0.00379 mol) was dissolved in acetonitrile (100 mL). 1,4-Diazabicyclo[2.2.2]octane (1.70 g, 0.0152 mol) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The resultant white precipitate was collected (1.4 g, 75.7%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{20}H_{32}N_4Br_2$: C 47.44%, H 6.77% Found: C 47.13%, H 7.01%. NMR (δ, D_2O) - ^{1}H: 3.09, t, 12H; 3.39, t, 12H; 4.48, s, 4H; 7.57, s, 4H. ^{13}C: 43.35, 50.3, 66.58, 127.72, 132.93.

Preparation of *p*-xylyl-1,4"-(4-{6'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'hexyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (42). α,α'-Dibromo-*p*-xylene (2.00 g, 0.00758 mol) was dissolved in acetonitrile (75 mL). (14) (2.87 g, 0.00758 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and white powder material was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. NMR analysis revealed starting material was present; therefore, the material was washed with hot acetonitrile (3 x 30 mL) then with anhydrous ether (3 x 30 mL), then dried under high vacuum until NMR indicated to it be more than 99% pure. (4.43 g, 91.0%). Calcd. for $C_{26}H_{44}N_4Br_2Cl_2 \bullet 7(H_2O)$: C 40.58%, H 7.60% Found: C 40.25%, H 7.75%. NMR (δ, D_2O) - ^1H: 1.36, s, 4H; 1.76, s, 4H; 3.50, s, 4H; 3.75-4.15, br, 24H; 4.76-4.90, br, 4H; 7.69, s, 4H. ^{13}C: 22.71, 26.09, 52.27, 52.54, 66.34, 69.12, 129.59, 135.52.

Preparation of *p*-xylyl-1,4"-(4-{8'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'octyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromidedichloride (43). α,α'-Dibromo-*p*-xylene (1.00 g, 0.00379 mol) was dissolved in acetonitrile (75 mL). (15) (1.54 g, 0.00379 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the resultant white powder precipitate was

collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. NMR analysis revealed starting material was present; therefore, the material was washed with hot acetonitrile (3 x 30 mL) then with anhydrous ether (3 x 30 mL), then dried under high vacuum until the NMR indicated it to be more than 99% pure. (2.31 g, 90.9%). Calcd. for $C_{28}H_{48}N_4Br_2Cl_2 \bullet 3(H_2O)$: C 46.36%, H 7.50% Found: C 46.07%, H 7.82%. NMR (δ, D_2O) - ^1H: 1.28, br, 8H; 1.59-1.79, br, 4H; 3.40-3.53, m, 4H; 376-4.9, br, 24H; 4.82, s, 4H; 7.69, s, 4H. ^{13}C: 23.61, 27.22, 30.07, 53.09, 53.50, 67.50, 69.91, 130.41, 136.33.

Preparation of *p*-xylyl-1,4"-(4-{9'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'nonyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrabromide (44). α,α'-Dibromo-*p*-xylene (1.00 g, 0.00379 mol) was dissolved in acetonitrile (75 mL). (16) (1.64 g, 0.00379 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. NMR analysis revealed starting material was present; therefore, the material was washed with hot acetonitrile (3 x 30 mL) then with anhydrous ether (3 x 30 mL), then dried under high vacuum until NMR indicated more than 99% pure. (1.4 g, 47.0%). Calcd. for $C_{30}H_{52}N_4Br_4 \bullet 3(H_2O)$: C 43.82%, H 7.76% Found: C 47.65%, H 7.83%.

NMR (δ, D_2O) - ^1H: 1.27, br, 10H; 1.72, br, 4H; 3.35-3.52, br, 4H; 3.75, br, 24H; 4.82, s, 4H; 7.70, s, 4H. ^{13}C: 22.48, 26.04, 28.83, 29.08, 51.83, 52.01, 66.29, 68.61, 129.10, 135.05.

Preparation of *p*-xylyl-1,4"-(4-{10'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'decyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromidedichloride (45). α,α'-Dibromo-*p*-xylene (1.00 g, 0.00379 mol) was dissolved in acetonitrile (75 mL). (17) (1.64 g, 0.00379 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. NMR analysis revealed starting material was present; therefore, the material was washed with hot acetonitrile (3 x 30 mL) then with anhydrous ether (3 x 30 mL), then dried under high vacuum until the NMR indicated it to be more than 99% pure. (1.5 g, 57.5%). Calcd. for $C_{30}H_{52}N_4Br_2Cl_2 \bullet 3(H_2O)$: C 43.82%, H 7.76% Found: C 47.65%, H 7.83%. NMR (δ, D_2O) - ^1H: 1.11-1.36, br, 12H; 1.721, br, 4H; 3.47, br, 4H; 3.75-4.12, br, 24H; 4.82, s, 4H; 7.69, s, 4H. ^{13}C: 22.64, 26.39, 29.31, 29.52, 52.12, 52.29, 66.60, 68.94, 129.42, 135.34.

Preparation of *m*-xylyl-1,4"-(4-{10'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'decyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (46). α,α'-

Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (17) (5.22 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipiate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.3 g, 68.0%). Calcd. for $C_{30}H_{52}N_4Cl_4 \bullet 2(H_2O)$: C 45.61%, H 7.71% Found: C 47.69%, H 7.74%. NMR (δ, D_2O) - ^1H: 1.18, br, 12H; 1.48, br, 4H; 3.05, t, 4H; 4.01, br, 24H; 4.86, s, 4H; 7.79, br, 4H. ^{13}C: 21.85, 25.6, 28.49, 28.69, 51.35, 51.53, 65.87, 68.26, 127.02, 131.53, 136.49, 137.50.

Preparation of *m*-xylyl-1,4"-(4-{9'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'nonyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (47). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (16) (5.45 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (5.0 g, 57.0). Calcd. for $C_{30}H_{52}N_4Br_2Cl_2 \bullet 2(H_2O)$: C 43.71%, H 7.71% Found: C 47.64%, H 7.79%. NMR (δ, D_2O) - ^1H: 1.30, br, 10H; 1.75, br, 4H; 3.94, br, 24H; 4.88, s, 4H; 7.55-7.80, m, 4H. ^{13}C: 20.82, 24.55, 27.31, 27.54, 50.51, 64.81, 66.54, 68.94.

Preparation of *m*-xylylene-1,4"-(4-{8'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'octyl}azonia)-1-azoniabicyclo[2.2.2]octane tetradichloride (48). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (15) (4.21 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (5.2 g, 70.0%). Calcd. for $C_{28}H_{48}N_4Cl_4 \bullet (H_2O)$: C 45.31%, H 7.35% Found: C 45.20%, H 7.40%. NMR (δ, D_2O) - ^1H: 1.32, br, 8H; 1.75, br, 4H; 3.51, t, 4H; 3.94, br, 12H; 4.02, br, 12H; 4.78, s, 4H, 7.76, br, 4H. ^{13}C: 20.66, 24.29, 27.13, 50.35, 51.31, 64.40, 67.08, 125.83, 130.34, 135.30, 136.30.

Preparation of *m*-xylylene-1,4"-(4-{6'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'hexyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (49). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (14) (1.43 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (5.4 g, 83.0%). Calcd. for $C_{26}H_{44}N_4Cl_4 \bullet 2(H_2O)$: C 40.44%, H 7.62% Found: C 40.39%, H 7.69%.

NMR (δ, D_2O) - ^1H: 1.39, br, 4H; 1.79, br, 4H; 3.52, t, 4H; 3.94, br, 12H; 4.02, br, 12H; 4.86, s, 4H, 7.78, br, 4H. ^{13}C: 21.75, 25.17, 46.10, 51.58, 65.42, 68.24, 127.01, 128.71, 136.47, 137.51.

Preparation of *m*-xylylene-1,4"-(4-{3'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'propyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (50). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (13) (4.04 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate material was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.1 g, 57.0%). Calcd. for $C_{26}H_{44}N_4Br_2Cl_2 \bullet 3(H_2O)$: C 40.35%, H 7.59% Found: C 40.41%, H 7.60%. NMR (δ, D_2O) - ^1H: 2.45, br, 2H; 3.64, br, 4H; 4.05, br, 24H; 4.88, s, 4H; 7.68, br, 4H. ^{13}C: 15.61, 51.22, 52.11, 60.86, 68.34, 126.94, 131.58, 136.54, 137.23.

Preparation of *m*-xylyl-1,4"-(4-{α"'-(1"',4'"-diazoniabicyclo[2.2.2]octane)-α'-*p*-xylyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (51). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (41) (3.17 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The

solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (2.90 g, 68.0%). Calcd. for $C_{28}H_{40}N_4Br_2Cl_2 \bullet 4(H_2O)$: C 41.56%, H 7.52% Found: C 40.49%, H 7.60%. NMR (δ, D_2O) - ^1H: 4.03, br, 24H; 4.85, br, 8H; 7.63, br, 8H. ^{13}C: 44.64, 51.42, 52.48, 68.40, 126.96, 128.63, 134.12, 134.25, 134.61, 136.54.

Preparation of *m*-xylyl-1,4"-(4-{4'-(1",4"-diazoniabicyclo[2.2.2]octane)-4-(Z)-2'-butenyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (52). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (19) (1.5 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.3 g, 46.0%). Calcd. for $C_{24}H_{38}N_4Cl_4 \bullet 3(H_2O)$: C 45.58%, H 7.68% Found: C 47.62%, H 7.70%. NMR (δ, D_2O) - ^1H: 1.18, br, 12H; 1.48, br, 4H; 3.05, t, 4H; 4.01, br, 24H; 4.86, s, 4H; 7.79, br, 4H. ^{13}C: 21.85, 25.6, 28.49, 28.69, 51.35, 51.53, 65.87, 68.26, 127.02, 131.53, 136.49, 137.50.

Preparation of *m*-(2,2,7,7-tetramethyl-2,7-diazoniaoctylenyl)benzene dichloride (53). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylbutanediamine (1.73 g,

0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.1 g, 93.0%). Calcd. for $C_{16}H_{28}N_4Cl_2 \bullet (H_2O)$: C 40.35%, H 7.59% Found: C 40.41%, H 7.60%. NMR (δ, D_2O) - ^1H: 1.99, br, 4H; 3.05, s, 12H; 3.50, br, 4H; 4.60, s, 4H; 7.70, br, 4H. ^{13}C: 18.59, 48.56, 63.18, 66.75, 127.26, 129.32, 134.37, 136.38.

Preparation of *m*-(2,2,9,9-tetramethyl-2,9-diazoniadecelenyl)benzene dichloride (54). α,α'-Dibromo-*m*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylhexanediamine (2.01 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (1.1 g, 58.0%). Calcd. for $C_{18}H_{32}N_4Cl_2 \bullet (H_2O)$: C 40.41%, H 7.54% Found: C 40.45%, H 7.59%. NMR (δ, D_2O) - ^1H: 1.43, br, 4H; 1.89, br, 4H; 3.01, s, 12H; 3.34, t, 4H; 4.54, s, 4H, 7.72, br, 4H. ^{13}C: 22.43, 25.48, 49.89, 65.10, 67.68, 128.67, 130.50, 135.57, 137.54.

Preparation of *o*-xylyl-1,4"-(4-{10'-(1",4"-diazoniabicyclo[2.2.2]octane)-

1'decyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (55). α,α'-Dibromo-*o*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (17) (5.22 g, 0.012 moi) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.3 g, 69.0%). Calcd. for $C_{30}H_{52}N_4Cl_4 \bullet 2(H_2O)$: C 45.42%, H 7.65% Found: C 47.49%, H 7.70%. NMR (δ, D_2O) - ^1H: 1.22, br, 12H; 1.66, br, 4H; 3.42, br, 4H; 3.84, br, 12H; 3.98, br, 12H; 5.06 s, 4H. ^{13}C: 22.25, 26.00, 28.97, 29.08, 51.53, 51.76, 65.02, 66.22, 127.29, 133.81, 137.01.

Preparation of *o*-xylyl-1,4"-(4-{9'-(1",4"-diazoniabicyclo[2.2.2]octane)-1'-nonyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (56). α,α'-Dibromo-*o*-xylene (2.1 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (16) (5.05 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.9 g, 65.0%). Calcd. for $C_{29}H_{50}N_4Cl_4 \bullet (H_2O)$: C 45.31%, H 7.60% Found: C 47.37%, H 7.65%. NMR (δ, D_2O) - ^1H: 1.26, br, 10H; 1.69, br, 4H; 3.46, br, 4H; 3.88, br, 12H; 4.02, br, 12H; 5.10, s, 4H, 7.77, s 4H.

^{13}C: 22.06, 25.76, 28.57, 28.80, 51.39, 51.63, 65.29, 66.05, 127.12, 133.66, 136.64.

Preparation of 1,1'-biphenylylmethylene-1",4""-(4"-{9'"-(1"",4""-diazoniabicyclo[2.2.2]octane)-1'"nonyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrabromide (57). 2,2'-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (16) (6.12 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (7.8 g, 77.0%). Calcd. for $C_{35}H_{54}N_4Br_4 \bullet 3(H_2O)$: C 43.55%, H 7.41% Found: C 47.60%, H 7.46%. NMR (δ, D_2O) - ^1H: 1.19, br, 10H; 1.61, br, 4H; 3.96-3.72, br, 28H; 4.18, d (J=14 Hz), 2H; 4.84, d (J=14 Hz), 2H. ^{13}C: 21.14, 24.86, 27.65, 29.22, 43.92, 50.73, 65.06, 65.68, 122.29, 125.61, 129.77, 132.77, 134.47, 141.08.

Preparation of 1,1'-biphenylylmethylene-1",4""-(4"-{10'"-(1"",4""-diazoniabicyclo[2.2.2]octane)-1'"decyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (58). 2,2'-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (17) (5.22 g, 0.012 mol) was slowly added with

stirring. The reaction mixture was heated and stirred for three days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.37 g, 47.0%). Calcd. for $C_{36}H_{56}N_4Br_2Cl_2 \bullet 3(H_2O)$: C 43.40%, H 7.35% Found: C 47.39%, H 7.41%. NMR (δ, D_2O) - ^1H: 1.20, br, 12H; 1.62, br, 4H; 3.11-3.71, br, 28H; 4.16, d (*J*=14 Hz), 2H; 4.81, d (*J*=14 Hz), 2H, 7.55, m, 8H. ^{13}C: 23.29, 27.03, 29.88, 30.13, 46.03, 52.90, 67.26, 67.86, 124.46, 127.87, 129.77, 131.94, 134.94, 136.65, 143.25.

Preparation of 1,1'-biphenylylmethylene-1",4""-(4"-{12"'-(1"",4""-diazoniabicyclo[2.2.2]octane)-1"'dodecyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrabromide (59): 2,2'- 2,2'-bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). (18) (6.62 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (6.10 g, 57.0%). Calcd. for $C_{38}H_{60}N_4Br_4 \bullet 2(H_2O)$: C 43.76%, H 7.65% Found: C 47.81%, H 7.62%. NMR (δ, D_2O) - ^1H: 1.13, br, 16H; 1.59, br, 4H; 3.21-3.69, br, 28H; 4.14, d (*J*=14 Hz), 2H; 4.81, d (*J*=14 Hz), 2H, 7.51-7.72, m, 8H. ^{13}C: 23.06, 26.84, 29.77, 30.12, 30.20, 45.70,

52.65, 67.05, 67.71, 127.63, 131.71, 134.70, 137.25, 143.01.

Preparation of 2,2'-(2",2",6",6"-tetramethyl-2",6"diazoniaheptylenyl)-1,1'-biphenyl dibromide (60): 2,2'-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylpropanediamine (1.56 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (5.13 g, 91.0%). Calcd. for $C_{21}H_{30}N_2Br_2 \bullet (H_2O)$: C 44.16%, H 7.25% Found: C 44.25%, H 7.30%. NMR (δ, D_2O) - ^1H: 1.73, br, 2H; 2.89, br, 4H; 3.07, s, 6H; 3.19, s, 6H; 4.78, br, 4H, 6.12-7.79, m, 8H. ^{13}C: 17.57, 51.50, 56.12, 61.89, 66.02, 126.75, 129.67, 131.34, 133.58, 134.93, 141.19.

Preparation of 2,2'-(2",2",7",7"-tetramethyl-2",7"diazoniaoctylenyl)-1,1'-biphenyl dibromide (61): 2,2'-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylbutanediamine (1.73 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for three days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.64 g, 80.0%). Calcd. for $C_{22}H_{32}N_2Br_2 \bullet (H_2O)$: C 46.17%, H

7.41% Found: C 46.20%, H 7.45%. NMR (δ, D_2O) - ^1H: 2.13, br, 4H; 3.03, br, 6H; 3.13, s, 6H; 3.39, s, 4H; 3.90, br, 4H, 7.48-7.63, m, 8H. ^{13}C: 22.95, 51.79, 52.93, 65.99, 67.10, 128.68, 130.11, 130.32, 132.66, 132.97, 142.08.

Preparation of 4,4'-(2",2",7",7"-tetramethyl-2",7"diazoniaoctylenyl)-1,1'-biphenyl dichloride (62): 4,4"-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylbutanediamine (1.73 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (4.03 g, 85.0%). Calcd. for $C_{22}H_{32}N_2Cl_2 \bullet (H_2O)$: C 46.71%, H 7.75% Found: C 46.69%, H 7.70%. NMR (δ, D_2O) - ^1H: 2.30, br, 4H; 3.05, s, 12H; 3.41, br, 4H; 4.55, s, 4H; 7.63, AA'BB', 8H. ^{13}C: 18.68, 51.28, 62.33, 69.99, 128.11, 129.44, 135.19, 143.44.

Preparation of 4,4'-(2",2",7",7"-tetramethyl-2",7"diazoniaoctylenyl)-1,1'-biphenyl dichloride (63): 4,4"-Bis-bromomethyl-1,1'-biphenyl (4.08 g, 0.012 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylhexanediamine (2.06 g, 0.012 mol) was slowly added with stirring. The reaction mixture was heated and stirred for two days. The

solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.35 g, 66.0%). Calcd. for $C_{24}H_{36}N_2Cl_2 \bullet (H_2O)$: C 47.25%, H 7.81% Found: C 47.39%, H 7.84%. NMR (δ, D_2O) - ^1H: 1.41, br, 4H; 1.86, br, 4H; 2.97, s, 12H; 3.28, br, 4H; 4.65, s, 4H, 7.67, AA'BB', 8H. ^{13}C: 22.24, 25.48, 49.72, 64.64, 67.56, 127.15, 127.86, 133.72, 141.85.

Preparation of *p*-(2,2,6,6-tetramethyl-2,6-diazoniaheptylenylbenzene dibromide (64): α,α'-Dibromo-*p*-xylene (2.64 g, 0.01 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylpropanediamine (1.3 g, 0.01 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.50 g, 89.0%). Calcd. for $C_{15}H_{26}N_2Br_2 \bullet (H_2O)$: C 47.62%, H 7.61% Found: C 47.59%, H 7.70%. NMR (δ, D_2O) - ^1H: 2.30, br, 4H; 3.05, s, 12H; 3.41, br, 4H; 4.55, s, 4H; 7.63, AA'BB', 8H. ^{13}C: 18.68, 51.28, 62.33, 69.99, 128.11, 129.44, 135.19, 143.44.

Preparation of *p*-(2,2,7,7-tetramethyl-2,7-diazoniaoctylenylbenzene dibromide (65): α,α'-Dibromo-*p*-xylene (2.64 g, 0.01 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylbutanediamine (1.44 g, 0.01

mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.47 g, 85.0%). Calcd. for $C_{16}H_{28}N_2Br_2 \bullet 3(H_2O)$: C 41.57%, H 7.41% Found: C 41.65%, H 7.25%. NMR (δ, D_2O) - ^1H: 1.87-2.15, br, 4H, 3.02, s, 12H, 3.47-3.52, br, 4H, 4.53, s, 4H, 7.65, s, 4H. ^{13}C: 18.17, 48.38, 62.45, 66.14, 128.27, 133.43.

Preparation of *p*-(2,2,9,9-tetramethyl-2,9-diazoniadecylenylbenzene dibromide (66): α,α'-Dibromo-*p*-xylene (2.64 g, 0.01 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethylhexanediamine (1.72 g, 0.01 mol) was slowly added with stirring. The reaction mixture was heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.44 g, 79.0%). Calcd. for $C_{18}H_{32}N_2Br_2 \bullet 2(H_2O)$: C 45.77%, H 7.68% Found: C 45.43%, H 7.95%. NMR (δ, D_2O) - ^1H: 1.40, br, 4H, 1.86, br, 4H, 2.96, s, 12H, 3.29, br, 4H, 4.26, s, 4H, 7.61, s, 4H. ^{13}C: 21.52, 24.72, 48.99, 64.26, 66.41, 129.11, 133.03.

Preparation of 4,4,8,8-tetramethyl-4,8-diazoniacyclononene dichloride (67). *cis*-1,4-Dichloro-2-butene (4.00 g, 0.032 mol) was dissolved in

acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,3-propanediamine (4.16 g, 0.032mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for three days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (8.5 g, 82.5%). Calcd. for $C_{11}H_{24}N_2Cl_2 \bullet 2H_2O$: C 51.24%, H 10.41% Found: C 51.17%, H 10.52%. NMR (δ, D_2O) - ^1H: 1.36, s, 4H; 1.76, s, 4H; 3.02, s, 12H; 3.21-3.35, m, 4H; 4.03 - 4.12, d(4Hz), 4H; 6.20-6.3, m, 2H. ^{13}C: 21.51, 24.70, 49.67, 59.77, 63.84, 126.33.

Preparation of 4,4,9,9-tetramethyl-4,9-diazoniacyclodecene dichloride (68). *cis*-1,4-Dichloro-2-butene (3.0 g, 0.0024 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,4-butanediamine (3.46 g, 0.0024mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for four days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (0.41 g, 63.1%). Calcd. for $C_{12}H_{26}N_2Cl_2 \bullet H_2O$: C 50.17%, H 9.82% Found: C 50.22%, H 9.74%. NMR (δ, D_2O) - ^1H: 1.85, br, 4H; 3.03, s, 12H; 3.42, br, 4H; 4.12, d, 4H; 6.21-6.34, m, 2H. ^{13}C: 21.51, 52.89, 62.80, 65.75, 129.12.

Preparation of (Z)-1,1,8,8-tetramethyl-1,8-diazoniacyclododec-3-ene dichloride (69). *cis*-1,4-Dichloro-2-butene (4.32 g, 0.0346 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (5.96 g, 0.0346mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (9.5 g, 82.5%). Calcd. for $C_{14}H_{30}N_2Cl_2 \bullet 2H_2O$: C 50.44%, H 10.28% Found: C 50.27%, H 10.41%. NMR (δ, D_2O) - ^1H: 1.36, s, 4H; 1.76, s, 4H; 3.02, s, 12H; 3.21-3.35, m, 4H; 4.03-4.12, d (*J*=4 Hz), 4H; 6.20-6.3, m, 2H. ^{13}C: 21.51, 24.70, 49.67, 59.77, 63.84, 126.33.

Preparation of 4,4,8,8-tetramethyl-4,8-diazoniacyclononye dichloride (70). *cis*-1,4-Dichloro-2-butyne (4.0 g, 0.0325 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,3-propanediamine (4.23 g, 0.0325mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (7.3 g, 89.2 %). Calcd. for $C_{11}H_{22}N_2Cl_2 \bullet 2H_2O$: C 47.33%, H 5.78% Found: C 47.51%, H 5.62%. NMR (δ, D_2O) - ^1H: 2.26, m, 2H; 3.23, s, 12H; 3.52, m,

4H; 4.65, s, 4H. ^{13}C: 16.24, 49.77, 50.39, 59.82, 79.03.

Preparation of 4,4,9,9-tetramethyl-4,9-diazoniacyclodecyne dichloride (71). *cis*-1,4-Dichloro-2-butyne (4.0 g, 0.0325 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,4-butanediamine (4.69 g, 0.0325mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (11.9 g, 90.0%). Calcd. for $C_{12}H_{24}N_2Cl_2 \bullet 3H_2O$: C 44.86%, H 9.41% Found: C 44.91%, H 9.42%. NMR (δ, D_2O) - ^1H: 1.86, br, 4H; 3.16, s, 12H; 3.49, br, 4H; 4.44, s, 4H. ^{13}C: 20.87, 51.98, 56.28, 65.41, 81.35.

Preparation of 4,4,11,11-tetramethyl-4,11-diazoniacyclododecyne dichloride (72). *cis*-1,4-Dichloro-2-butyne (4.0 g, 0.0325 mol) was dissolved in acetonitrile (75 mL). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (5.60 g, 0.0325mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (8.5 g, 89.1%). Calcd. for $C_{14}H_{28}N_2Cl_2 \bullet 2H_2O$: C 50.75%, H 9.74% Found: C 50.61%, H 9.70%. NMR (δ, D_2O) - ^1H: 1.39, br, 4H; 1.77,

br, 4H; 3.13, s, 12H; 3.39, m, 4H; 4.39, s, 4H. ^{13}C: 21.23, 24.28, 49.61, 53.4, 63.94, 78.87.

Preparation of 1,4-but-2-yneylyl-1',4'"-(4'{8"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-octyl}azonia-1'-azoniabicyclo[2.2.2]octane tetrachloride (73). *cis*-1,4-Dichloro-2-butyne (1.0 g, 0.00813 mol) was dissolved in acetonitrile (75 mL). (15) (3.31g, 0.00813 mol) was dissolved in acetonitrile (50 mL) and was slowly added with stirring. The reaction mixture continued to be heated and stirred for three days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. The material was repeatedly washed until the NMR exhibited no detectable impurities (3.8 g, 87.0%). Calcd. for $C_{24}H_{44}N_4Cl_4 \bullet H_2O$: C 52.86%, H 8.45% Found: C 52.23%, H 8.77%. NMR (δ, D_2O) - ^1H: 1.33, br, 8H; 1.78, br, 4H; 3.55, m, 4H; 4.01, m, 12H; 4.12, m, 12H; 4.79, s, 4H. ^{13}C: 20.63, 24.21, 27.06, 50.23, 50.84, 64.52, 79.29.

Preparation of 1,4-but-2-yneylyl-1',4'"-(4'{9"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-nonyl}azonia-1'-azoniabicyclo[2.2.2]octane dibromide dichloride (74): *cis*-1,4-Dichloro-2-butyne (1.0 g, 0.00813 mol) was dissolved in acetonitrile (75 mL). (16)

(4.14g, 0.00813 mol) was dissolved in acetonitrile (50 mL) and was slowly added with stirring. The reaction mixture continued to be heated and stirred for four days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. The material was repeatedly washed until NMR exhibited no detectable impurities (3.76 g, 73.0%). Calcd. for $C_{25}H_{46}N_4Br_2Cl_2 \bullet 2H_2O$: C 52.79%, H 8.83% Found: C 52.81%, H 8.87%. NMR (δ, D_2O) - ^1H: 1.30, br, 10H; 1.77, br, 4H; 3.57, br, 4H; 4.01, br, 12H; 4.12, br, 12H; 4.80, s, 4H. ^{13}C: 20.48, 24.12, 26.88, 27.04, 50.31, 50.75, 53.77, 64.39, 79.28.

Preparation of 1,4-but-2-yneylyl-1',4'"-(4'{10"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-decyl}azonia-1'-azoniabicyclo[2.2.2]octane tetrachloride (75): *cis*-1,4-Dichloro-2-butyne (1.0 g, 0.00813 mol) was dissolved in acetonitrile (75 mL). (17) (4.51g, 0.00813 mol) was dissolved in acetonitrile (50 mL) and was slowly added with stirring. The reaction mixture continued to be heated and stirred for four days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. The material was repeatedly washed until NMR exhibited no detectable impurities (3.45 g, 76.0%). Calcd. for $C_{26}H_{48}N_4Cl_4 \bullet 2H_2O$: C 52.65%, H 8.71% Found: C 52.68%, H 8.80%.

NMR (δ, D_2O) - ^1H: 1.23-1.45, br, 12H; 1.76, br, 4H; 3.51, br, 4H; 3.99, br, 12H; 4.12, br, 12H; 4.78, s, 4H. ^{13}C: 21.89, 25.61, 28.53, 28.73, 51.46, 52.09, 55.01, 65.86, 80.52.

Preparation of 1,4-but-2-yneylyl-1',4'"-(4'{12"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-dodecyl}azonia-1'-azoniabicyclo[2.2.2]octane dibromide dichloride (76): *cis*-1,4-Dichloro-2-butyne (1.0 g, 0.00813 mol) was dissolved in acetonitrile (75 mL). (18) (4.49g, 0.00813 mol) was dissolved in acetonitrile (50 mL) and was slowly added with stirring. The reaction mixture continued to be heated and stirred for five days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum. Material was repeatedly washed until NMR exhibited no detectable impurities (4.11 g, 72.0%). Calcd. for $C_{28}H_{52}N_4Br_2Cl_2 \bullet 2H_2O$: C 52.89%, H 8.66% Found: C 52.86%, H 8.71%. NMR (δ, D_2O) - ^1H: 1.08-1.28, br, 18H; 1.73, br, 4H; 3.51, br, 4H; 3.99, br, 12H; 4.08, br, 12H; 4.76, s, 4H. ^{13}C: 23.68, 27.39, 30.30, 30.63, 30.71, 53.49, 53.92, 56.88, 67.68, 82.41.

Preparation of 1,1,8,8-tetramethyl-1,8-diazoniacyclo-14-decane dichloride (77). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (1.0 g, 0.00580 mol) was dissolved in ethylacetate (75 mL). 1,6-Dichlorohexane

(0.90 g, 0.00580 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for six days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (1.63 g, 85.8%). Calcd. for $C_{16}H_{36}N_2Cl_2 \bullet 2H_2O$: C 50.14%, H 10.82% Found: C 49.89%, H 11.03%. NMR (δ, D_2O) - ^1H: 1.34, br, 10H; 1.82, br, 8H; 2.96, s, 12H; 3.23, br, 8H. ^{13}C: 23.19, 26.53, 51.54, 65.37.

Preparation of 1,1,8,8-tetramethyl-1,8-diazoniacyclohexadecane dibromide (78). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (1.0 g, 0.00580 mol) was dissolved in ethyl acetate (75 mL). 1,8-Dibromooctane (1.58 g, 0.00580 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for six days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (2.12 g, 82.5%). Calcd. for $C_{18}H_{40}N_2Br_2 \bullet 2H_2O$: C 50.14%, H 10.82% Found: C 49.89%, H 11.03%. NMR (δ, D_2O) - ^1H: 1.24-1.44, br, 12H; 1.68, br, 8H; 2.96, s, 12H; 3.20, br, 8H. ^{13}C: 20.16, 20.19, 23.50, 23.71, 26.28, 48.58, 62.26, 62.57.

Preparation of 1,1,8,8-tetramethyl-1,8-diazoniacycloheptadecane dibromide (79). *N,N,N',N'*-tetramethyl-1,6-hexanediamine (1.0 g,

0.00580 mol) was dissolved in ethyl acetate (75 mL). 1,9-Dibromononane (1.66 g, 0.00580 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (1.91 g, 73.2%). Calcd. for $C_{19}H_{34}N_2Br_2 \bullet 2H_2O$: C 50.14%, H 10.82% Found: C 49.89%, H 11.03%. NMR (δ, D_2O) - ^1H: 1.21-1.40, br, 14H; 1.68, br, 8H; 2.96, s, 12H; 3.17-3.2, br, 8H. ^{13}C: 22.39, 22.43, 25.72, 26.03, 28.67, 28.84, 50.87, 64.44, 64.81.

Preparation of 1,1,6,6-tetramethyl-1,6-diazoniacyclotetradecane dichloride (80). *N,N,N',N'*-tetramethyl-1,4-butanediamine (1.0 g, 0.00693mol) was dissolved in ethyl acetate (15 mL). 1,8-Dibromooctane (1.89 g, 0.00693 mol) was dissolved in ethylacetate (15 mL) and was slowly added with stirring to the solution. The reaction mixture continued to be heated and stirred for ten days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL) and dried under high vacuum (1.14 g, 83.2%). Calcd. for $C_{16}H_{36}N_2Br_2 \bullet 2H_2O$: C 40.86%, H 9.00% Found: C 40.51%, H 9.02%. NMR (δ, D_2O) - ^1H: 1.55, br, 8H; 1.62-1.85, br, 8H; 3.00, s, 12H; 3.16-3.38, br, 8H. ^{13}C: 19.13, 21.80, 25.25, 27.89, 50.38, 62.91, 64.35.

Preparation of 1,1,5,5-tetramethyl-1,5-diazoniacyclopentadecane dibromide (81). *N,N,N',N'*-tetramethyl-1,4-butanediamine (1.0 g, 0.0069 mol) was dissolved in ethyl acetate (75 mL). 1,9-Dibromononane (1.97 g, 0.0069 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for one day. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (2.21 g, 75.9%). Calcd. for $C_{17}H_{30}N_2Br_2 \bullet 3H_2O$: C 50.20%, H 10.89% Found: C 50.31%, H 11.05%. NMR (δ, D_2O) - ^1H: 1.30, br, 10H; 1.62-1.88, br, 8H; 3.01, s, 12H; 3.18-3.39, br, 8H. ^{13}C: 18.73, 21.42, 24.92, 27.55, 27.71, 49.99, 62.48, 63.96.

Preparation of 1,1,3,-tetramethyl-1,3-diazoniacyclo-15-decane dichloride (82). *N,N,N',N'*-tetramethyl-1,3-propanediamine (2.0 g, 0.015 mol) was dissolved in ethyl acetate (75 mL). 1,10-Dichlorodecane (3.25 g, 0.015 mol) was slowly added with stirring. The reaction mixture continued to be heated and stirred for three days. The solution was cooled and the white powder precipitate was collected by suction filtration, washed with ether (3 x 30 mL), and dried under high vacuum (3.28 g, 64.1%). Calcd. for $C_{17}H_{38}N_2Cl_2 \bullet 3H_2O$: C 54.90%, H 11.52% Found: C 54.95%, H 11.48%. NMR (δ, D_2O) - ^1H: 1.30, br, 10H; 1.62-1.88, br, 8H; 3.01, s, 12H; 3.18-

3.39, br, 8H. ^{13}C: 18.73, 21.42, 24.92, 27.55, 27.71, 49.99, 62.48, 63.96.

Preparation of 1,4"-bis-(1-nonyl 4-butanoyl)-4-(6'-{1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride (83). (23) (2.0 g, 0.003 mol) was dissolved in pyridine (50 mL). A solution of decanoyl chloride (1.03 g, 0.006 mol) in pyridine (50 mL) was slowly added with stirring. 4-Dimethylamino-1-pyridine (catalytic amount) was added to the reaction mixture. The reaction mixture continued to be stirred for three days. The volatiles were evaporated under reduced pressure and the resultant material dried under high vacuum (1.61 g, 61.4%). Calcd. for $C_{44}H_{86}N_4O_4Cl_4 \bullet H_2O$: C 55.12%, H 11.86% Found: C 55.21%, H 11.91%. NMR (δ, D_2O) - ^1H: 0.74, t (J=8 Hz), 6H; 1.19, br, 32H; 1.38-1.46, br, 8H; 1.78, br, 4H; 2.04, br, 4H; 3.51, br, 4H; 3.62, br, 4H; 3.86, br, 28H. ^{13}C: 13.86, 21.70, 22.51, 24.83, 25.14, 26.38, 29.01, 29.12, 29.23, 31.68, 38.09, 51.45, 58.07, 63.20, 65.21, 163.50, 184.46.

Preparation of 1,4"-bis-(1-undecyl 4-butanoyl)-4-(6'-{1",4"-diazoniabicyclo[2.2.2]octyl}-1'-hexyl)-1,4-diazoniabicyclo[2.2.2]octane tetrachloride (84). (23) (2.0 g, 0.003 mol) was dissolved in pyridine (75 mL). A solution dodecanoyl chloride (1.03 g, 0.003 mol) in pyridine (50 mL) was slowly added with stirring. 4-Dimethylamino-1-pyridine (catalytic

amount) was added to the reaction mixture. The reaction mixture continued to be heated and stirred for one day. The volatiles were evaporated under reduced pressure and the resultant material dried under high vacuum (1.58 g, 58.4%). Calcd. for $C_{46}H_{90}N_4O_4Cl_4 \bullet H_2O$: C 56.12%, H 11.43% Found: C 56.19%, H 11.46%. NMR (δ, D_2O) - ^1H: 0.72, t (*J*=8 Hz), 6H; 1.15, br, 32H; 1.39, br, 4H; 1.41, br, 4H; 1.75, br, 4H; 1.95, br, 4H; 2.03, t (*J*=8 Hz), 4H; 3.48, br, 4H; 3.59, br, 8H; 3.90, br, 24H. ^{13}C: 13.87, 21.71, 21.75, 22.32, 22.51, 24.81, 25.11, 26.35, 29.00, 29.10, 29.19, 31.66, 38.07, 51.45, 58.05, 63.18, 65.20, 163.50, 184.43.

Preparation of 1,2-bis(*P*-methyl-*P,P*-diphenyl)phosphonioethyl diiodide (85). 1,2-Bis-biphenylphosphinoethane (2.0 g, 0.005 mol) was dissolved in acetonitrile (75 mL). A solution of iodomethane (1.42 g, 0.01 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred for three days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (2.28 g, 67.1%). Calcd. for $C_{28}H_{30}P_2I_2 \bullet H_2O$: C 50.40%, H 10.31% Found: C 50.65%, H 10.49%. NMR (δ, D_2O) - ^1H: 2.44, m, 6H; 3.09, br, 4H; 7.64-7.80, br, 20H. ^{13}C: 65.25, 120.41, 129.21, 129.36, 131.36, 134.56. ^{31}P: 26.87.

Preparation of 1,3-bis(*P*-methyl-*P,P*-diphenyl)phosphoniopropyl diiodide (86). 1,3-Bis-biphenylphosphinopropane (2.0 g, 0.005 mol) was dissolved in acetonitrile (75 mL). A solution of iodomethane (1.41 g, 0.01 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred for four days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (2.19 g, 63.2%). Calcd. for $C_{29}H_{32}P_2I_2 \bullet H_2O$: C 50.37%, H 10.29% Found: C 50.49%, H 10.50%. NMR (δ, D_2O) - ^1H: 2.49, m, 6H; 3.12, br, 6H; 7.59-7.65, br, 20H. ^{13}C: 51.29, 65.23, 121.39, 128.06, 130.14, 130.19, 133.13. ^{31}P: 24.23.

Preparation of 1,4-bis(*P*-methyl-*P,P*-diphenyl)phosphoniobutyl diiodide (87). 1,4-Bis-biphenylphosphinobutane (2.0 g, 0.005 mol) was dissolved in acetonitrile (75 mL). A solution of iodomethane (1.39 g, 0.01 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred for four days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (2.28 g, 67.1%). Calcd. for $C_{30}H_{34}P_2I_2 \bullet H_2O$: C 50.55%, H 10.35% Found: C 50.57%, H 10.41%. NMR (δ, D_2O) - ^1H: 2.13, m, 6H; 3.31, br, 8H; 7.55-

7.72, br, 20H. ^{13}C: 49.28, 51.35, 65.19, 129.48, 129.61, 131.59, 131.69, 134.44. ^{31}P: 24.04.

Preparation of 1,6-bis(*P*-methyl-*P,P*-diphenyl)phosphoniohexyl diiodide (88). 1,6-Bis-biphenylphosphinohexane (2.0 g, 0.004 mol) was dissolved in acetonitrile (75 mL). A solution of iodomethane (1.12 g, 0.008 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred at reflux for five days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (1.75 g, 59.6%). Calcd. for $C_{32}H_{38}P_2I_2 \bullet H_2O$: C 50.65%, H 10.42% Found: C 50.70%, H 10.49%. NMR (δ, D_2O) - ^{1}H: 1.92, m, 6H; 3.25, br, 12H; 7.50-7.65, br, 20H. ^{13}C: 49.28, 50.21, 51.34, 64.99, 120.21, 130.16, 130.28, 132.38, 132.48. ^{31}P: 24.30.

Preparation of 1,2-bis(*P*-allyl-*P,P*-diphenyl)phosphonioethyl dibromide (89). 1,2-Bis-biphenylphosphinoethane (2.0 g, 0.005 mol) was dissolved in acetonitrile (75 mL). A solution of allyl bromide (1.20 g, 0.01 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred at reflux for three days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (1.96 g,

61.2%). Calcd. for $C_{32}H_{34}P_2Br_2 \bullet H_2O$: C 50.65%, H 10.42% Found: C 50.70%, H 10.49%. NMR (δ, D_2O) - ^1H: 3.01, t, 4H; 5.22, m, 4H; 5.43, d, 2H, 7.63, m, 20H; 7.83, t, 4H. ^{13}C: 50.42, 51.57, 120.55, 128.71, 128.83, 131.51, 131.56, 131.61. ^{31}P: 26.84.

Preparation of 1,3-bis(*P*-allyl-*P,P*-diphenyl)phosphonioethyl diiodide (90). 1,3-Bis-biphenylphosphinoethane (2.0 g, 0.004 mol) was dissolved in acetonitrile (75 mL). A solution of allyl bromide (0.97 g, 0.008 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred at reflux for four days. The resultant white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (1.57 g, 58.9%). Calcd. for $C_{33}H_{36}P_2Br_2 \bullet H_2O$: C 50.65%, H 10.42% Found: C 50.70%, H 10.49%. NMR (δ, D_2O) - ^1H: 1.55, m, 2H; 3.04, t, 4H; 5.19, m, 4H; 5.39, d, 2H, 7.58, m, 20H; 7.81, t, 4H. ^{13}C: 47.81, 50.39, 51.60, 65.27, 116.27, 117.11, 130.82, 133.44, 133.49, 133.54. ^{31}P: 24.66.

Preparation of 1,6-bis(*P*-allyl-*P,P*-diphenyl)phosphoniohexyl dibromide (91). 1,6-Bis-biphenylphosphinohexane (2.0 g, 0.004 mol) was dissolved in acetonitrile (75 mL). A solution of allyl bromide (0.97 g, 0.008 mol) in acetonitrile (25 mL) was added with stirring. The reaction mixture continued to be heated and stirred at reflux for five days. The resultant

white powder precipitate was collected by vacuum filtration, washed with anhydrous ether (3 x 30 mL) then dried under high vacuum (1.72 g, 62.0%). Calcd. for $C_{36}H_{42}P_2Br_2 \bullet H_2O$: C 50.65%, H 10.42% Found: C 50.70%, H 10.49%. NMR (δ, D_2O) - ^1H: 1.55, m, 2H; 3.04, t, 4H; 5.19, m, 4H; 5.39, d, 2H, 7.58, m, 20H; 7.81, t, 4H. ^{13}C: 45.55, 49.27, 50.43, 51.65, 65.31, 115,27, 118.79, 129.21, 131.83, 132.86, 133.21. ^{31}P: 23.21.

Preparation of (92). 1,4-Diazabicyclo[2.2.2]octane (5.0 g, 0.0446 mole) was dissolved in methylene chloride (50 mL). A solution of methyl chloroacetate (4.4 g, 0.0446 mol) in methylene chloride (75 mL) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The resultant white powder precipitate was collected (8.43 g, 85.7%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_9H_{17}N_2O_2Cl$: C 45.91%, H 10.70% Found: C 46.02%, H 10.85%. NMR (δ, D_2O) - ^1H: 3.13, m, 3H; 3.59, m, 12H; 3.73, s, 2H. ^{13}C: 47.77, 51.63, 52.06, 60.25, 164.01.

Preparation of (93). 1,4-Diazabicyclo[2.2.2]octane (5.0 g, 0.0446 mole) was dissolved in methylene chloride (50 mL). A solution of methyl chloroacetate (19.36 g, 0.1784 mol) in methylene chloride (75 mL) was slowly added with stirring. The reaction mixture was heated and stirred at

reflux for three days. The resultant white powder precipitate was collected (11.7 g, 79.7%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{12}H_{22}N_2O_4Cl_2$: C 45.98%, H 10.77% Found: C 46.11%, H 10.91%. NMR (δ, D_2O) - ^1H: 3.78, s, 6H; 4.30, t, 12H; 4.63, s, 4H. ^{13}C: 51.30, 52.50, 60.30, 163.20.

Preparation of (94). Methyl chloroacetate (1.30 g, 0.012 mol) was dissolved in methylene chloride (75 mL). A solution of (3) (3.0 g, 0.012 mol) in methylene chloride (75 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for three days. The resultant white powder precipitate was collected (2.95 g, 76.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{15}H_{30}N_2O_3Cl_2$: C 45.70%, H 10.87% Found: C 46.81%, H 10.99%. NMR (δ, D_2O) - ^1H: 1.23-1.45, br, 8H; 3.31, t, 4H; 3.71, s, 3H, 4.11, t, 6H; 4.20, t, 6H; 4.49, m, 2H. ^{13}C: 21.50, 25.56, 28.72, 28.79, 28.91, 32.21, 52.39, 54.01, 62.25, 65.79, 164.09.

Preparation of (95). Methyl chloroacetate (0.65 g, 0.006 mol) was dissolved in methylene chloride (75 mL). A solution of (6) (2.0 g, 0.006 mol) in methylene chloride (75 mL) was slowly added with stirring. The

reaction mixture was heated and stirred at reflux for two days. The resultant white powder precipitate was collected (1.69 g, 68.1%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{19}H_{37}N_2O_3Cl_2$: C 45.89%, H 10.89% Found: C 46.91%, H 10.97%. NMR (δ, D_2O) - ^1H: 1.20-1.41, br, 16H; 3.29, t, 4H; 3.76, s, 3H, 4.07, t, 6H; 4.16, t, 6H; 4.53, m, 2H. ^{13}C: 21.74, 25.32, 25.49, 28.37, 28.64, 28.72, 28.78, 31.57, 44.28, 51.68, 52.43, 53.98, 62.19, 65.82, 165.03.

Preparation of (96α). α-Cyclodextrin (3.0 g, 0.003 mol) was dissolved in pyridine (50 mL). A solution of *p*-toluenesulfonyl chloride (4.3 g, 0.025 mol) in pyridine (75 mL) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The volatiles were evaporated under reduced pressure and the resultant brown gum-like material was collected (4.35 g, 79.2%). Note, as these are labile materials, no analysis or NMRs of this material is listed.

Preparation of (96β). β-Cyclodextrin (3.0 g, 0.0026 mol) was dissolved in pyridine (50 mL). A solution of *p*-toluenesulfonyl chloride (4.8 g, 0.023 mol) in pyridine (75 mL) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The volatiles were evaporated under reduced pressure and the resultant brown gum-like material was collected (4.37 g, 81.7%). Note, as these are labile

materials, no analysis or NMRs of this material is listed.

Preparation of (96γ). γ-Cyclodextrin (3.0 g, 0.0026 mol) was dissolved in pyridine (50 mL). A solution of *p*-toluenesulfonyl chloride (4.9 g, 0.021 mol) in pyridine (75 mL) was slowly added with stirring. The reaction mixture was stirred at room temperature for one day. The volatiles were evaporated under reduced pressure and the resultant brown gum-like material was collected (3.78 g, 65.1%). Note, as these are labile materials, no analysis or NMRs of this material is listed.

Preparation of (97). (96β) (3.0 g, 0.0015 mol) was dissolved in acetonitrile (75 mL). A solution of (1) (4.9 g, 0.12 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The volatiles were evaporated under reduced pressure and the resultant precipitate collected (1.57 g, 40.0%). Calcd. for $C_{98}H_{182}N_{14}O_{35}Cl_{14}\bullet 3(H_2O)$: C 41.14%, H 7.02% Found: C 44.31%, H 7.11%. NMR (δ, D_2O) - ^1H: 3.48-3.55, m, 14H; 3.64, m, 28H; 3.76, m, 42H; 3.96, m, 42H; 4.04, m, 28H, 4.95, d (*J*=3 Hz), 7H. ^{13}C: 44.43, 52.21, 55.42, 60.66, 66.98, 72.33, 72.58, 73.64, 81.51, 102.36.

Preparation of (98). (96β) (3.0 g, 0.0014 mol) was dissolved in acetonitrile (75 mL). A solution of (2) (1.96 g, 0.011 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The volatiles were evaporated under

reduced pressure and the resultant precipitate collected (1.40 g, 37.0%). Calcd. for $C_{105}H_{196}N_{14}O_{35}Cl_{14}\bullet 5(H_2O)$: C 44.87%, H 7.66% Found: C 45.02%, H 7.41%. NMR (δ, D_2O) - ^1H: 2.00, m, 14H; 3.56, t (*J*=8 Hz), 14H; 3.63, t (*J*=7 Hz), 14H; 3.76-3.98, br, 126H; 4.96, d (*J*=8 Hz), 7H. ^{13}C: 23.50, 42.97, 50.28, 56.80, 59.21, 61.97, 70.84, 71.09, 72.15, 80.05, 100.88.

Preparation of (99). (96α) (3.0 g, 0.0016 mol) was dissolved in acetonitrile (75 mL). A solution of (3) (2.98 g, 0.012 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.69 g, 41.0%). Calcd. for $C_{108}H_{204}N_{12}O_{30}Cl_{12}\bullet 3(H_2O)$: C 49.32%, H 8.05% Found: C 49.20%, H 8.17%. NMR (δ, D_2O) - ^1H: 1.33, br, 24H; 1.47, m, 12H; 1.73, m, 12H; 3.41, t (*J*=8 Hz), 12H; 3.48-3.58, brm, 36H, 3.67, br, 36H; 3.73-3.81, brm, 48H; 4.96, d (*J*=3.5 Hz), 6H. ^{13}C: 23.01, 26.24, 26.79, 32.61, 45.48, 52.35, 61.75, 63.07, 66.69, 73.12, 73.52, 75.21, 82.91, 103.16.

Preparation of (100). (96β) (3.0 g, 0.0015 mol) was dissolved in acetonitrile (75 mL). A solution of (3) (2.98 g, 0.012 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated

and stirred at reflux for three days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.74 g, 39.0%). Calcd. for $C_{126}H_{238}N_{12}O_{35}Cl_{14}\bullet 2(H_2O)$: C 50.20%, H 8.10% Found: C 49.96%, H 8.37%. NMR (δ, D_2O) - ^1H: 1.33, br, 28H; 1.47, m, 14H; 1.75, m, 14H; 3.50, t (J=7.5 Hz), 14H; 3.52-3.81, brm, 20H, 4.98, d (J=4), 7H. ^{13}C: 20.78, 23.96, 24.56, 30.37, 43.89, 50.50, 59.61, 60.86, 64.52, 71.25, 71.38, 72.58, 80.52, 101.25.

Preparation of (101). (96α) (3.0 g, 0.0016 mol) was dissolved in acetonitrile (75 mL). A solution of (4) (3.31 g, 0.013 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.40 g, 32.0%). Calcd. for $C_{120}H_{228}N_{12}O_{30}Cl_{12}\bullet 4(H_2O)$: C 51.17%, H 8.44% Found: C 51.01%, H 8.62%. NMR (δ, D_2O) - ^1H: 1.34, br, 48H; 1.49, br, 12H; 1.75, br, 12H; 3.37, t (J=8.7 Hz), 12H; 3.50-3.88, brm, 120H, 5.02 d (J=3.4), 6H. ^{13}C: 22.18, 26.48, 26.92, 29.71, 29.80, 32.83, 45.65, 52.99, 61.79, 63.29, 73.46, 73.59, 73.63, 74.76, 82.71, 103.48.

Preparation of (102). (96β) (3.0 g, 0.0015 mol) was dissolved in

acetonitrile (75 mL). A solution of (4) (3.31 g, 0.012 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.97 g, 41.0%). Calcd. for $C_{140}H_{266}N_{14}O_{35}Cl_{14}\bullet 3(H_2O)$: C 51.64%, H 8.42% Found: C 51.37%, H 8.65%. NMR (δ, D_2O) ^1H: 1.35, br, 56H; 1.47, br, 14H; 1.77, br, 14H; 3.36, t (*J*=9 Hz), 14H; 3.50-3.83, brm, 140H, 5.02 d (*J*=3.5 Hz), 7H. ^{13}C: 21.79, 25.19, 25.78, 28.52, 28.56, 31.60, 44.26, 51.35, 60.36, 61.80, 65.35, 72.18, 72.22, 73.56.

Preparation of (103). (96γ) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (4) (3.59 g, 0.013 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for six days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.40 g, 29.8%). Calcd. for $C_{158}H_{300}N_{16}O_{40}Cl_{16}\bullet 4(H_2O)$: C 51.72%, H 8.51% Found: C 51.98%, H 8.76%. NMR (δ, D_2O) - ^1H: 1.35, br, 60H; 1.48, br, 16H; 1.78, br, 16H; 3.38, t (*J*=8.8 Hz), 16H; 3.51-3.85, brm, 160H, 5.04 d (*J*=4 Hz), 8H. ^{13}C: 21.79, 25.20, 25.77, 28.50, 28.59, 31.63, 44.25, 51.34, 60.39, 61.83,

65.35, 72.20, 72.25, 73.61.

Preparation of (104). (96α) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (5) (4.35 g, 0.013 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.29 g, 30.1%). Calcd. for $C_{121}H_{230}N_{12}O_{30}Br_{12}\bullet 2(H_2O)$: C 51.65%, H 8.43% Found: C 51.72%, H 8.51%. NMR (δ, D_2O) - ^1H: 1.34, br, 50H; 1.49, br, 12H; 1.76, br, 12H; 3.39, t (*J*=8 Hz), 16H; 3.49-3.83, brm, 120H, 5.03 d (*J*=3.4 Hz), 6H. ^{13}C: 21.76, 22.18, 25.19, 25.74, 28.52, 28.58, 31.61, 44.23, 51.34, 60.38, 61.80, 65.31, 72.19, 72.29, 73.64, 103.41.

Preparation of (105). (96β) (3.0 g, 0.0014 mol) was dissolved in acetonitrile (75 mL). A solution of (5) (4.35 g, 0.013 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.54 g, 32.5%). Calcd. for $C_{127}H_{239}N_{14}O_{35}Br_{14}\bullet 4(H_2O)$: C 51.72%, H 8.49% Found: C 51.68%, H 8.69%. NMR (δ, D_2O) - ^1H: 1.34, br, 58H; 1.48, br, 14H; 1.75, br, 14H;

3.37, t (J=7.5 Hz), 18H; 3.50-3.81, brm, 140H, 5.02 d (J=4 Hz), 7H. ^{13}C: 21.74, 22.17, 25.18, 25.72, 28.50, 28.56, 31.59, 44.20, 51.33, 60.37, 61.79, 65.30, 72.17, 72.28, 73.64, 103.38.

Preparation of (106). (96α) (3.0 g, 0.0014 mol) was dissolved in acetonitrile (75 mL). A solution of (6) (3.02 g, 0.011 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethylacetate and ether solutions and dried under high vacuum (1.63 g, 40.0%). Calcd. for $C_{132}H_{252}N_{12}O_{30}Cl_{12}\bullet 4(H_2O)$: C 53.11%, H 8.78% Found: C 52.90%, H 9.13%. NMR (δ, D_2O) -^1H: 1.32, br, 72H; 1.47, br, 12H; 1.76, br, 12H; 3.43, t (J=8 Hz), 12H; 3.51-3.81, brm, 120H, 5.03 d (J=3.5 Hz), 6H. ^{13}C: 20.82, 24.65, 24.86, 27.71, 28.02, 28.18, 28.21, 30.86, 43.41, 50.39, 61.27, 64.68, 71.07, 71.27, 71.48, 73.28, 81.53, 101.85.

Preparation of (107). (96β) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (6) (3.04 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.76 g, 40.0%). Calcd. for

$C_{154}H_{294}N_{14}O_{35}Cl_{14}\bullet 5(H_2O)$: C 53.05%, H 8.73% Found: C 53.12%, H 8.60%. NMR (δ, D_2O) - ^1H: 1.25, br, 84H; 1.45, br, 14H; 1.76, br, 14H; 3.35, t (*J*=9 Hz), 14H; 3.49-3.81, brm, 140H, 5.02 d (*J*=3.5 Hz), 7H. ^{13}C: 21.33, 24.06, 24.91, 25.34, 28.08, 28.17, 28.35, 31.20, 43.88, 50.90, 60.08, 61.65, 65.10, 71.57, 71.95, 73.30, 81.00, 101.93.

Preparation of (108). (96α) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (7) (3.63 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.24 g, 36.0%). Calcd. for $C_{138}H_{264}N_{12}O_{30}Br_{12}\bullet 4(H_2O)$: C 46.01%, H 7.61% Found: C 45.86%, H 7.83%. NMR (δ, D_2O) - ^1H: 1.35, br, 84H; 1.47, br, 12H; 1.78, br, 12H; 3.35, t (*J*=9 Hz), 12H; 3.51-3.88, brm, 120H, 5.04 d (*J*=3.5 Hz), 6H. ^{13}C: 23.51, 27.61, 27.68, 29.75, 30.62, 31.88, 31.97, 32.04, 33.64, 46.01, 53.01, 61.77, 63.82, 67.20, 73.68, 74.04, 75.89, 83.39, 104.05.

Preparation of (109). (96β) (3.0 g, 0.0012 mol) was dissolved in acetonitrile (75 mL). A solution of (7) (3.63 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was

collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.24 g, 44.0%). Calcd. for $C_{161}H_{308}N_{14}O_{35}Br_{14}\bullet 3(H_2O)$: C 46.34%, H 7.58% Found: C 46.31%, H 7.82%. NMR (δ, D_2O) - ^1H: 1.33, br, 98H; 1.45, br, 14H; 1.77, br, 14H; 3.36, t (*J*=9 Hz), 14H; 3.49-3.81, brm, 140H, 5.02 d (*J*=3 Hz), 7H. ^{13}C: 24.06, 27.56, 28.04, 30.79, 30.98, 31.08, 31.14, 33.91, 46.52, 53.46, 62.45, 64.26, 67.77, 74.48, 74.58, 75.94, 83.62, 104.61.

Preparation of (110). (96α) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (10) (3.61 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for six days. The brown powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.24 g, 33.0%). Calcd. for $C_{144}H_{276}N_{12}O_{24}Br_{12}\bullet 4(H_2O)$: C 48.17%, H 7.97% Found: C 48.08%, H 8.13%. NMR (δ, D_2O) - ^1H: 0.87, t (*J*=5), 18H; 1.24, br, 108H; 1.65, br, 12H; 3.32, t (*J*=9 Hz), 12H; 3.59-3.88, brm, 108H, 5.02 d (*J*=3.5 Hz), 6H. ^{13}C: 15.47, 23.37, 24.26, 24.32, 27.47, 30.46, 30.97, 31.39, 31.82, 31.90, 33.72, 45.91, 52.94, 61.58, 66.24, 72.13, 73.84, 75.77, 83.19, 103.98.

Preparation of (111). (96β) (3.0 g, 0.0012 mol) was dissolved in acetonitrile (75 mL). A solution of (10) (3.61 g, 0.010 mol) in

acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The brown powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (2.09 g, 33.0%). Calcd. for $C_{168}H_{322}N_{14}O_{28}Br_{14}\bullet 3(H_2O)$: C 48.51%, H 7.95% Found: C 48.36%, H 8.18%. NMR (δ, D_2O) - ^1H: 0.85, t (J=5), 21H; 1.16, br, 126H; 1.60, br, 14H; 3.25, t (J=9 Hz), 14H; 3.48-3.78, brm, 126H, 4.96 d (J=3.5 Hz), 7H. ^{13}C: 13.74, 21.02, 21.72, 22.34, 25.82, 28.64, 28.76, 28.87, 28.92, 29.04, 31.48, 44.20, 51.20, 51.86, 60.02, 65.25, 72.17, 73.61, 81.26, 102.38.

Preparation of (112). (96α) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (10) (2.10 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.11 g, 34.0%). Calcd. for $C_{114}H_{168}N_{12}O_{24}Cl_{12}\bullet 3(H_2O)$: C 53.28%, H 6.83% Found: C 53.16%, H 6.99%. NMR (δ, D_2O) - ^1H: 3.66, br, 12H; 3.70-3.92, brm, 108H; 4.98, br, 6H; 7.49-7.64, br, 30H. ^{13}C: 42.2, 49.3, 49.6, 59.1, 67.7, 70.3, 72.2, 80.1, 100.2, 123.6, 128.4, 130.3, 131.7.

Preparation of (113). (96β) (3.0 g, 0.0013 mol) was dissolved in

acetonitrile (75 mL). A solution of (10) (2.10 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.11 g, 31.0%). Calcd. for $C_{133}H_{196}N_{14}O_{28}Cl_{14}\bullet 4(H_2O)$: C 53.12%, H 6.84% Found: C 53.25%, H 6.62%. NMR (δ, D_2O) - ^1H: 3.49, br, 14H; 3.56-3.91, brm, 126H; 4.98, br (J=3.6 Hz), 7H; 7.47-7.59, br, 35H. ^{13}C: 44.4, 51.1, 51.2, 60.5, 72.1, 72.3, 73.4, 81.4, 102.2, 125.6, 130.0, 131.9, 133.3.

Preparation of (114). (96α) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (116) (2.30 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.22 g, 38.0%). Calcd. for $C_{102}H_{174}N_{18}O_{24}Cl_{12}\bullet 2(H_2O)$: C 49.04%, H 7.18% Found: C 49.11%, H 7.02%. NMR (δ, D_2O) - ^1H: 1.67, t (J=8 Hz), 12H; 1.88, m, 12H; 2.53, t (J=8 Hz), 12H; 3.46-3.57, brm, 24H; 3.68-3.85, brm, 96H; 4.96, d (J=4 Hz), 6H. ^{13}C: 16.44, 21.15, 21.72, 44.27, 51.29, 60.47, 64.38, 71.94, 72.30, 73.74, 81.52, 101.75.

Preparation of (115). (96β) (3.0 g, 0.0013 mol) was dissolved in acetonitrile (75 mL). A solution of (116) (2.30 g, 0.010 mol) in acetonitrile (50 mL) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for six days. The white powder precipitate was collected by filtration, washed with ethyl acetate and ether solutions and dried under high vacuum (1.46 g, 42.0%). Calcd. for $C_{119}H_{208}N_{21}O_{28}Cl_{14}\bullet 4(H_2O)$: C 48.54%, H 7.22% Found: C 48.23%, H 7.57%. NMR (δ, D_2O) - ^1H: 1.66, t (*J*=8 Hz), 14H; 1.88, m, 14H; 2.51, t (*J*=8 Hz), 14H; 3.44-3.49, brm, 28H; 3.54-3.85, brm, 112H; 4.96, d (*J*=4 Hz), 7H. ^{13}C: 18.59, 23.26, 23.82, 46.43, 53.51, 62.70, 66.50, 74.27, 74.53, 75.55, 83.55, 104.32.

Preparation of 1,2-di-(2'-{1"-azonia-4"-azobicycl[2.2.2]octyl)ethoxyethane dichloride (117). 1,4-Diazabicyclo[2.2.2]octane (5 g, 0.045 mol) was dissolved in acetonitrile (50 mL). Ethylene glycol bis-(2-chloroethyl) ether (2.06 g, 0.011 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for one day. The resultant white powder precipitate was collected (3.70 g, 82.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{18}H_{36}N_4O_2Cl_2\bullet(H_2O)$: C 41.20%, H 7.01% Found: C 41.36%, H 7.12%. NMR (δ, D_2O) -

^{1}H: 3.14, t, 12H; 3.44, m, 18H; 3.66, s, 4H; 3.93, br, 4H. ^{13}C: 46.22, 55.08, 65.30, 65.37, 71.63.

Preparation of *p*-xylyl-1,4"(4-{8'-(1",4"-diazoniabicyclo[2.2.2]octane)-3',6'-dioxolo-1'-octyl}azonia)-1-azoniabicyclo[2.2.2]octane dibromide dichloride (118). (117) (2.06 g, 0.005 mol) was dissolved in acetonitrile (50 mL). α,α'-Dibromo-*p*-xylene (1.32 g, 0.005 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for four days. The resultant white powder precipitate was collected (2.34 g, 69.5%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{26}H_{44}N_4O_2Br_2Cl_2 \bullet 2(H_2O)$: C 41.78%, H 7.01% Found: C 41.49%, H 7.35%. NMR (δ, D_2O) - ^{1}H: 3.56-3.61, br, 4H; 3.62-3.66, br, 4H; 3.97, br, 32H; 7.64, s, 4H. ^{13}C: 44.14, 51.20, 52.43, 63.74, 64.87, 68.16, 128.53, 134.53.

Preparation of *m*-xylyl-1,4"(4-{8'-(1",4"-diazoniabicyclo[2.2.2]octane)-3',6'-dioxolo-1'-octyl}azonia)-1-azoniabicyclo[2.2.2]octane tetrachloride (119). (117) (2.06 g, 0.005 mol) was dissolved in acetonitrile (50 mL). α,α'-Dichloro-*m*-xylene (0.88 g, 0.005 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The resultant white powder precipitate was collected (1.82 g,

62.3%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{26}H_{44}N_4O_2Cl_4 \bullet 2(H_2O)$: C 41.79%, H 7.03% Found: C 41.85%, H 7.12%. NMR (δ, D_2O) - ^1H: 3.54-3.59, br, 4H; 3.61-3.68, br, 4H; 4.01, br, 32H; 7.59, s, 4H. ^{13}C: 44.16, 51.24, 52.47, 63.75, 64.89, 68.20, 128.58, 134.54.

Preparation of 1-benzyl-4-(10-hydroxydecyl)-1,4-diazoniabicyclo[2.2.2]octane dichloride (120). (6) (2.00 g, 0.007 mol) was dissolved in ethyl acetate (100 mL). α-Chlorotoluene (1.01 g, 0.007 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for three days. The resultant white powder precipitate was collected (2.34 g, 78.1%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{19}H_{32}N_2OCl_2 \bullet 2(H_2O)$: C 50.31%, H 10.69% Found: C 50.42%, H 10.71%. NMR (δ, D_2O) - ^1H: 1.18-1.24, br, 18H; 1.41, br, 2H; 1.70, br, 2H; 3.46, br, 4H; 3.90-3.94, br,12H; 7.49, br, 5H. ^{13}C: 19.78, 23.24, 24.03, 29.63, 42.88, 50.73, 60.22, 63.22.

Preparation of *o*-(2,2,7,7-tetramethyl-2,7-diazoniaoctylenyl)benzene (121). α,α'-Dichloro-*o*-xylene (4.00 g, 0.023 mol) was dissolved in acetonitrile (100 mL). *N,N,N',N'*-tetramethylbutane diamine (3.31 g, 0.023 mol) was slowly added with stirring. The reaction mixture was

heated and stirred at reflux for four days. The resultant white powder precipitate was collected (4.95 g, 67.5%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{16}H_{28}N_2Cl_2 \bullet 3(H_2O)$: C 49.75%, H 9.89% Found: C 49.81%, H 10.02%. NMR (δ, D_2O) - ^1H: 1.70, br, 4H; 2.96-3.03, m, 12H; 3.68, t, 4H; 4.84, s, 4H; 7.67, br, 4H. ^{13}C: 16.92, 18.56, 48.15, 48.43, 63.28, 127.56, 130.44, 134.54.

Preparation of *o*-(2,2,9,9-tetramethyl-2,9-diazoniadecylenyl)benzene (122). α,α'-Dichloro-*o*-xylene (4.00 g, 0.023 mol) was dissolved in acetonitrile (100 mL). *N,N,N',N'*-tetramethylhexane diamine (3.30 g, 0.023 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The resultant white powder precipitate was collected (4.95 g, 62.0%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{18}H_{32}N_2Cl_2 \bullet 3(H_2O)$: C 49.79%, H 9.92% Found: C 49.85%, H 10.03%. NMR (δ, D_2O) - ^1H: 1.70, br, 8H; 2.97-3.01, m, 12H; 3.70, t, 4H; 4.85, s, 4H; 7.68, br, 4H. ^{13}C: 16.92, 17.01, 18.56, 48.15, 48.43, 63.28, 127.56, 130.44, 134.54.

Preparation of 1,1'-biphenylylmethylene-1",4""-(4"-{6'"-(1"",4""-diazoniabicyclo[2.2.2]octane)-1'"hexyl}azonia)-1-

azoniabicyclo[2.2.2]octane dibromide dichloride (123). 2,2'-Bis-bromomethyl-1,1'-biphenyl (3.00 g, 0.006 mol) was dissolved in acetonitrile (100 mL). (14) (2.27 g, 0.006 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for six days. The resultant white powder precipitate was collected (2.12 g, 49.2%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{32}H_{48}N_4Br_2Cl_2 \bullet 4(H_2O)$: C 50.61%, H 11.46% Found: C 50.72%, H 11.51%. NMR (δ, D_2O) - ^1H: 1.25, br, 4H; 1.64, br, 4H; 3.17, t, 12H; 3.21, t, 12H; 3.70, br, 4H; 4.69, s, 4H; 7.67, m, 8H. ^{13}C: 20.42, 24.01, 43.42, 50.26, 51.12, 63.70, 121.77, 121.79, 129.28, 132.29, 133.99, 140.57.

Preparation of 1,4-but-2-eneylyl-1',4'"-(4'{8"-(1'",4'"-diazoniabicyclo[2.2.2]octane)-1"-octyl}azonia-1'-azoniabicyclo[2.2.2]octane tetrachloride (124). *cis*-1,4-Dichloro-2-butene (1.0 g, 0.008 mol) was dissolved in acetonitrile (100 mL). (14) (3.00 g, 0.008 mol) was slowly added with stirring. The reaction mixture was heated and stirred at reflux for five days. The resultant white powder precipitate was collected (0.75 g, 39.1%) by suction filtration and washed with anhydrous ether (3 x 30 mL), then dried under high vacuum. Calcd. for $C_{22}H_{42}N_4Cl_4 \bullet 3(H_2O)$: C 51.32%, H 11.51% Found: C 51.40%, H 11.60%. NMR (δ, D_2O) -

^{1}H: 1.40, s, 4H; 1.80, s, 4H; 3.45-3.50, br, 4H; 3.83-4.10, br, 24H; 4.41-4.59, br, 4H; 6.39, s, 2H. ^{13}C: 22.57, 25.94, 52.22, 52.46, 61.64, 66.14, 127.78.

CONCLUSION

A series of polyammonium and polyphosphonium salts with a range of structural topologies have been synthesized. These have included those with "string" and "ring" topologies, as well as derivatives of cyclodextrins. Interactions of the polycationic salts with bacteria and DNA have been studied. With several of the "strings" inhibition of growth of bacteria has been observed, and changes in the conformation of DNA have been observed with both "strings" and "rings." Cyclodextrin derivatives have been studied as hosts for interaction with a wide range of biologically significant organic molecules.

Conversion of the polycationic salts into room temperature ionic liquids has been successful using phosphate as the counterion. These bear significant potential for a variety of applications.

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