SUPRAMOLECULAR ARCHITECTURES: MACROCYCLES, CATENANES AND POLYROTAXANES

By

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in
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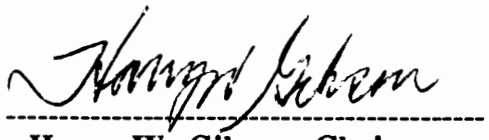

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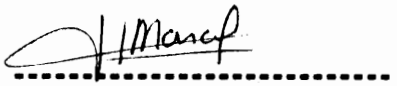

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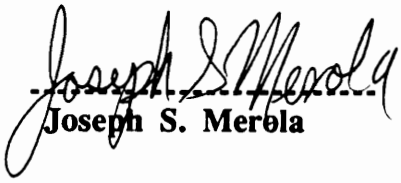
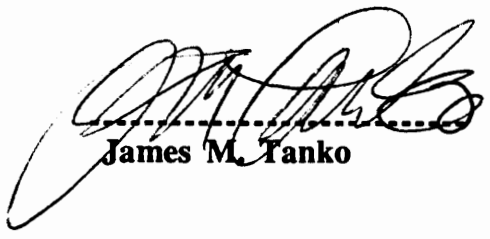


Joseph S. Merola



James M. Tanko

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SUPRAMOLECULAR ARCHITECTURES: MACROCYCLES, CATENANES AND POLYROTAXANES

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(ABSTRACT)

Polyrotaxanes are molecular composites consisting of three components: linear polymers, bulky stoppers at the ends of polymer chains and macrocycles threaded by the polymers.

A series of tetraarylmethyl derivatives as blocking groups were synthesized. Using tris(*p-tert*-butylphenyl)(4-hydroxyphenyl)methane a new blocking group/initiator (BG/init) was synthesized. The BG/init's ability of blocking/initiation in free radical polymerizations was established by polymerization of styrene.

As cyclic components, aliphatic crown ethers (30-crown-10, "42-crown-14" and "60-crown-20") were synthesized by multi-piece combination methods. The purification of the crown ethers was achieved by treatment with poly(methacryloyl chloride), column chromatography and recrystallization; by NMR in DMSO-d_6 the purity of the products was demonstrated. The 42-crown-based [2]catenane was isolated while synthesizing "42-crown-14" and characterized in terms of its physically interlocked structure. Two new hydrocarbon-based macrocycles were prepared by two-piece combination method.

Polyrotaxanes were prepared *via* free radical polymerizations of olefinic monomers (styrene, methyl acrylate, methyl methacrylate, bulky methacrylic monomers) using the

BG/init and AIBN in the presence of the aliphatic crown ethers. The control experiments, using 18-crown-6, whose cavity is too small to be threaded, showed that chain transfer was not significant. The resultant poly(styrene-rotaxa-"42-crown-14") and poly(styrene-rotaxa-"60-crown-20") formed emulsions in protic solvents such as methanol, ethanol and water. The emusification phenomenon was correlated to the threaded architecture by supporting experiments such as dispersion polymerizations of styrene in the presence of the crown ethers and a statistical mixing of polystyrene and "42-crown-14". The threading yields of poly(styrene-rotaxa-crown ether)s were 11-21 mass % of the crown ethers.

Polyrotaxanes based on acrylic and methacrylic polymers and 30-crown-10 were synthesized. Although the polymerizations were carried out in homogeneous conditions, the threading yields were lower than poly(styrene-rotaxa-crown ether)s, meaning in the statistically driven syntheses, the size of the macrocycles was an important factor in threading yield. The free radical polymerizations of two new methacrylic monomers containing bulky groups in the presence of 30-crown-10 gave side-chain polyrotaxanes with threading yields higher than the corresponding main chain analogs.

DEDICATION

to my father Geon-Joong Lee,

who is now in Heaven

with Jesus Christ

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Finally, I would like to give all thanks to Jesus Christ, my Savior and Lord, for everything He has given to me. Without His loving care and guidance, I surely would not be here now.

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CHAPTER I

INTRODUCTION: POLYMER TOPOLOGY

A *polymer* is a large molecule constructed from many smaller molecules, called *monomers*, covalently bonded together. Although as early as late 19th century many experimental observations such as solution viscosity and crystallization behavior indicated the existence of polymers or macromolecules, it was not until the early part of the 20th century that the concepts of the high molar mass molecules were generally accepted by scientists. [1] Since the pioneering works of H. Staudinger [2] the requirement of new synthetic polymers has been dramatically increasing. Indeed, our modern daily life can not be maintained without synthetic polymers from clothes and baby toys to electric devices and high performance engineering plastics.

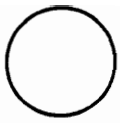
To develop new synthetic polymers structure-property relationships must be considered. The properties of polymers are ruled by chemical composition and order of connectivity of each monomer. This includes the type of monomers and covalent bonds between them and how specific atoms are connected to each other. Although the overall chemical compositions and the order of connectivity of atoms are the same, three dimensional arrangements of the molecules as a whole must also be considered.

1. POLYMER TOPOLOGY

1-1. Topologies of covalently connected polymers [3]

Cyclic polymers have no chain end. The structure with no chain ends is

A. Cyclic Polymers

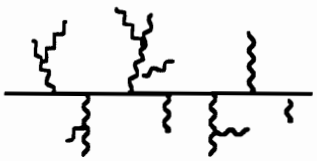


B. Linear polymers

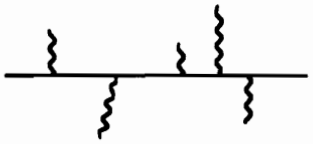
Homopolymer	A A A A A A A A A A A A A A
Statistical copolymer	A A B A B B A B A B B A A
Alternating copolymer	A B A B A B A B A B A B A
Block copolymer	A A A A A A A B B B B B B

C. Branched polymers
(Homo- or copolymers)

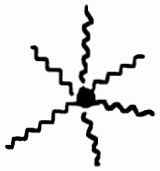
Randomly branched polymer



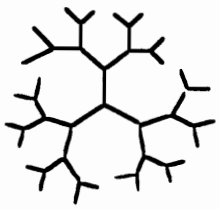
Graft polymer



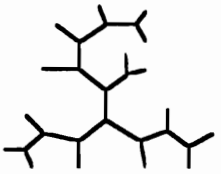
Star polymer



Dendrimer



Hyperbranched polymer



Network polymer

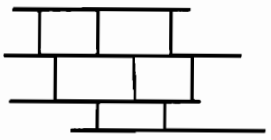


Figure 1. Topologies of covalently connected polymers.

responsible for their characteristics such as lower hydrodynamic volume and viscosity, and higher glass transition temperature than linear counterparts. [4]

Linear polymers can be defined as polymers in which each molecule has two chain ends. According to the chemical composition and order of the connection of monomers this category includes homopolymers and copolymers. A homopolymer consists of a single type of repeat unit. The properties of a homopolymer depend on the chemical composition of the monomer and the molecular weight and its distribution. [5a]

Copolymers are prepared by connection of two or more different repeat units. Statistical or random, alternating and block copolymers are in this category. In a statistical copolymer the monomers are arranged randomly along the chain while the monomers are arranged in alternating fashion in an alternating copolymer. A block copolymer is composed of two or more homopolymer segments with each end connected to the other segments. In linear copolymers, the arrangement of the monomers affects the polymer properties. As an example, although the overall monomer compositions in the polymers may be identical, an alternating copolymer usually shows the average properties of the corresponding homopolymers while in a block copolymer each corresponding homopolymer segment retains its specific behavior such as thermal transitions. This is due to the phase separation behavior of block copolymers, which is not observed in a random or an alternating copolymers. [6, 7]

Branched polymers have more than two chain ends per molecule. The simplest type of the branched polymer might be randomly branched polymers. Lower density polyethylene (or high pressure polyethylene) is such a highly branched polymer. [5b] Due to the branches on the linear backbone these polymers have lower densities than high density polyethylene (or lower pressure polyethylene) which has few or no branches.

Graft polymers are similar to randomly branched polymers, but the polymers

contain usually well-defined linear pendant units. If the branch units are long enough and of chemical units different from the backbone, the graft polymers frequently exhibit phase separation behavior in the solid state like block copolymers and are often used as compatabilizers for polymer blends. [8] Star polymers have branches of equal length radiating out from a single branch point. [5c] Due to their low radius of gyration star polymers are characterized by lower hydrodynamic volume than linear polymers with comparable molecular mass. Dendrimers and hyperbranched polymers are treelike molecules. [9] They have received substantial interest lately. The branches of the main chains on a central core are themselves branched to result in highly branched macromolecules. The well defined architecture of dendritic macromolecules draws lots of interest from many research groups due to their unique properties such as amorphous character, low intrinsic viscosity, high solubility, miscibility and high reactivity due to the presence of many chain ends.

In network polymers, each polymer chain is covalently connected to each other forming three dimensional networks which are insoluble and infusible. [5d] As crosslinking density increases the crosslinked polymer becomes more rigid and the glass transition temperature is raised. Thus, the crosslinking of a polymer results in the improvement of dimensional stability, resistance to solvents and heat stability. Thermosetting polymers such as epoxy [10] and phenolic [11] resins are commercially important examples and they are used for coatings, adhesives and matrices for composites, etc.

1-2. **Polymer blends** [12]

Polymer blends are physical mixtures of two or more polymers. Polymer blends might be the simpliest and cheapest approach to develop new polymer systems using existing polymers. The final polymer properties of a polymer blend depend on the level of mixing. If the individual polymers mix with each other at the molecular level, the resulting blends are homogeneous and shows average properties of the two components. Although several compatible systems have been reported, most of pairs of polymers are heterogeneous; in other words, most polymer blends are immiscible systems. Even many relatively compatible systems show micro/macro phase separations. If the domain size of the separated phases can be controlled, the phase separation, however, is useful in certain cases such as rubber toughened plastics. [13]

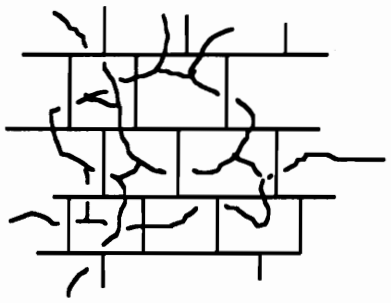
2. SUPRAMOLECULAR POLYMER ARCHITECTURE

To discuss the structure-property relationships of polymers are the above descriptions enough? We now add chemical topology beyond covalent bonds to the above list. [3, 14, 15] Although the order of connections of atoms and the type of bonds are consistent, there are topological isomers. The transition between the isomers requires the breakage of covalent bonds. Wassermann and Frisch suggested the existence of such isomers in early 1960's. [14] Catenane **1** [16], which consisits of two interlocking rings, is isomeric with the pair of non-interlocked rings **2**. Although **1** is composed of two sets of atoms and no atom of one set is chemically bound to an atom of the other, the breaking of a bond is still required to separate the sets.

1

2

Interpenetrating polymer networks (IPN) **3** [5e] may be referred to as a supramolecular architecture. In IPNs, two different polymer networks are permanently



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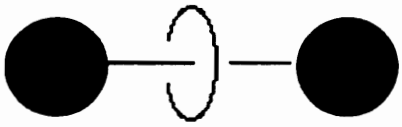
combined together by an interpenetrating structure. An IPN is obtained by polymerization of one monomer with crosslinking in the presence of the other already crosslinked polymer. Another route to prepare IPN is to carry out two polymerizations, whose polymerization mechanisms are different from each other and each of them produce crosslinked polymers, simultaneously.

3. POLYROTAXANES

The concept of a rotaxane, which is composed of a cyclic molecule threaded by a linear molecule with bulky groups at the chain ends to constrain the cyclic component, was first addressed by Frisch and Wassermann. [14] Similar to a catenane, a rotaxane **4** is a topological isomer of the physical mixture of the corresponding linear component and macrocycle **5**. The conversion of **4** to **5** requires bond breaking and reformation.



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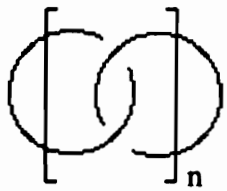
5

The above concept is expanded to polymeric systems: polyrotaxane **6** [3] and polycatenane **7** [17] and possible combinations of the two. Although there is no covalent bond between the two components, a polyrotaxane is distinct from the physical mixture

6



7

of the corresponding macrocycle and the linear macromolecule because the two components are tied together and can not be isolated from each other unless covalent bonds are broken. Furthermore, polyrotaxanes are not equivalent to graft copolymers or block copolymers with the same molecular weights. Although the cyclic moieties are

physically bound to the linear backbone, the cyclic molecules can move along the chain and circumferentially.

There are many other types of polyrotaxanes. Figure 2 shows several examples of polyrotaxanes of different architectures. In each structure, if there are no blocking groups to prevent diffusional loss of the macocycles those polyrotaxanes are referred to as *pseudo*rotaxanes. Main chain polyrotaxane **a** is the simplest of all. Several main chain polyrotaxanes, especially containing crown ethers and cyclodextrins as cyclic species, have been synthesized and reported. [3, 18] Synthesis of main chain polyrotaxane **b** can be achieved from combination of polymacrocycles [19] and linear species which can be threaded through the macrocycles of the polymer backbones. Recently, side chain polyrotaxanes **c** and **d** have been made by German chemists Ritter and Born [20] and their results demonstrated that even more complicated polyrotaxane structures could be prepared. Side chain polyrotaxane **e** is a combination of a polymer with pendant macrocyles and threaded linear species.

As mentioned above, properties of polymers can be modified by the polyrotaxane structure. In *homo*polyrotaxanes, in which linear and cyclic components have the same chemical composition, solution and melt viscosities would be changed. Melting and glass transitions can also be modified by incorporation of cyclic counterparts into the linear polymers. *Hetero*polyrotaxanes, whose cyclic and linear species are incompatible with each other, show microphase separation in the solid state because the cyclics can move along the chain and aggregate. [18a] Also it has been observed that heteropolyrotaxanes possess modified solubility [3, 8c] and viscosity [21].

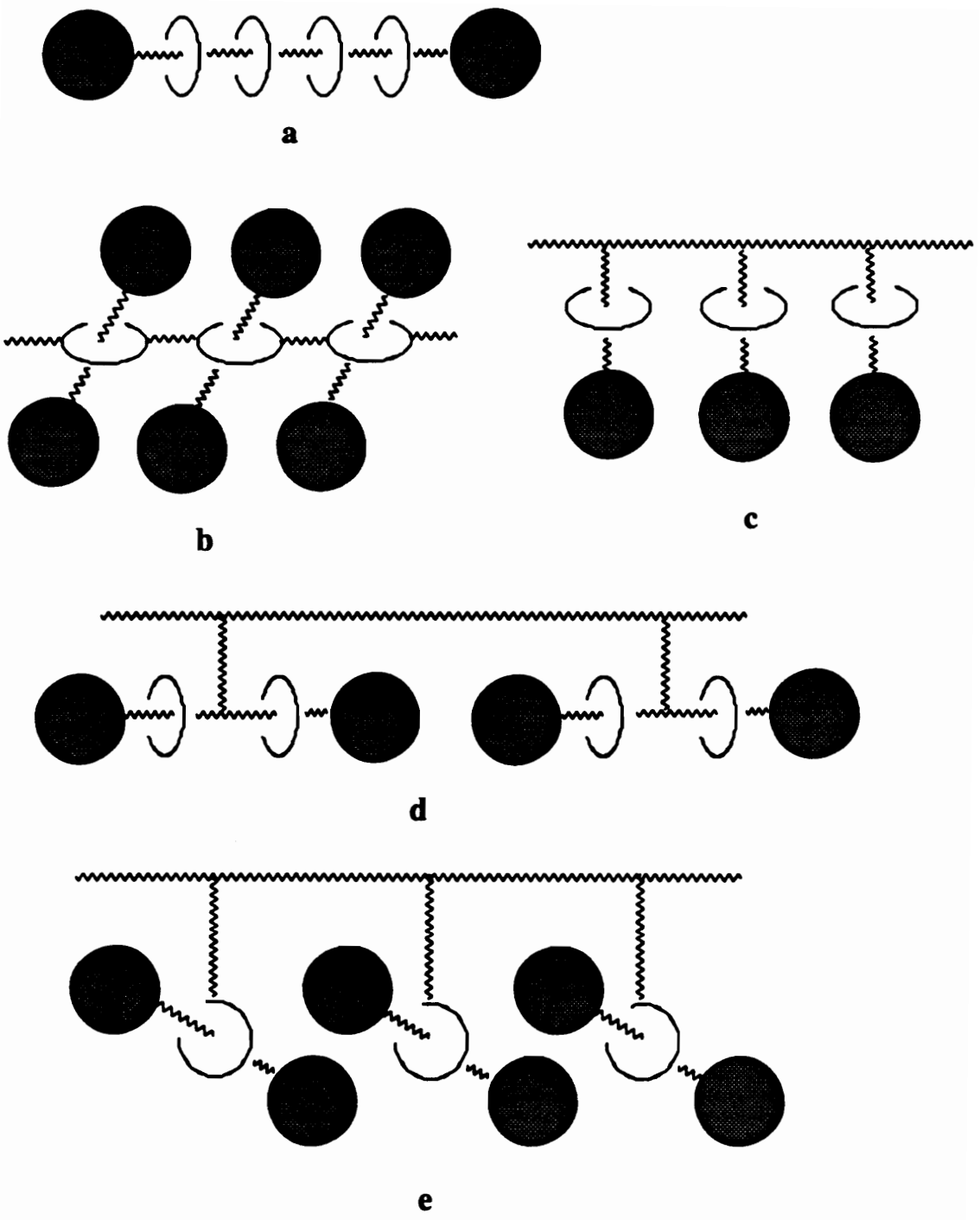


Figure 2. Polyrotaxane structures.

4. THESIS STATEMENT

The objectives of this research are syntheses of polyrotaxanes *via* free radical polymerizations and investigation of properties of the resultant polyrotaxanes in view of the supramolecular structures. To achieve the goal, research direction has been focused on the three main categories: blocking group chemistry, synthesis of cyclic components and synthesis and characterization of polyrotaxanes. To obtain stable polyrotaxanes, a blocking group/initiator was needed and thus a new blocking group was designed and prepared. Linear components are polystyrene, poly(methyl methacrylate), poly(methyl acrylate) and the polymers derived from new methacrylic monomers containing bulky stoppers.

Therefore, the thesis will discuss the followings.

1. General literature review
2. Synthesis of blocking groups, a blocking group/initiator and characterization
3. Synthesis and charaterization of cyclic components: aliphatic crown ethers, a related catenane and hydrocarbon-based macrocycles.
4. Synthesis of polyrotaxanes using the prepared blocking group/initiator and crown ethers and investigation of the properties of the polyrotaxanes.

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CHAPTER II

LITERATURE REVIEW: CATENANES, ROTAXANES AND POLYROTAXANES

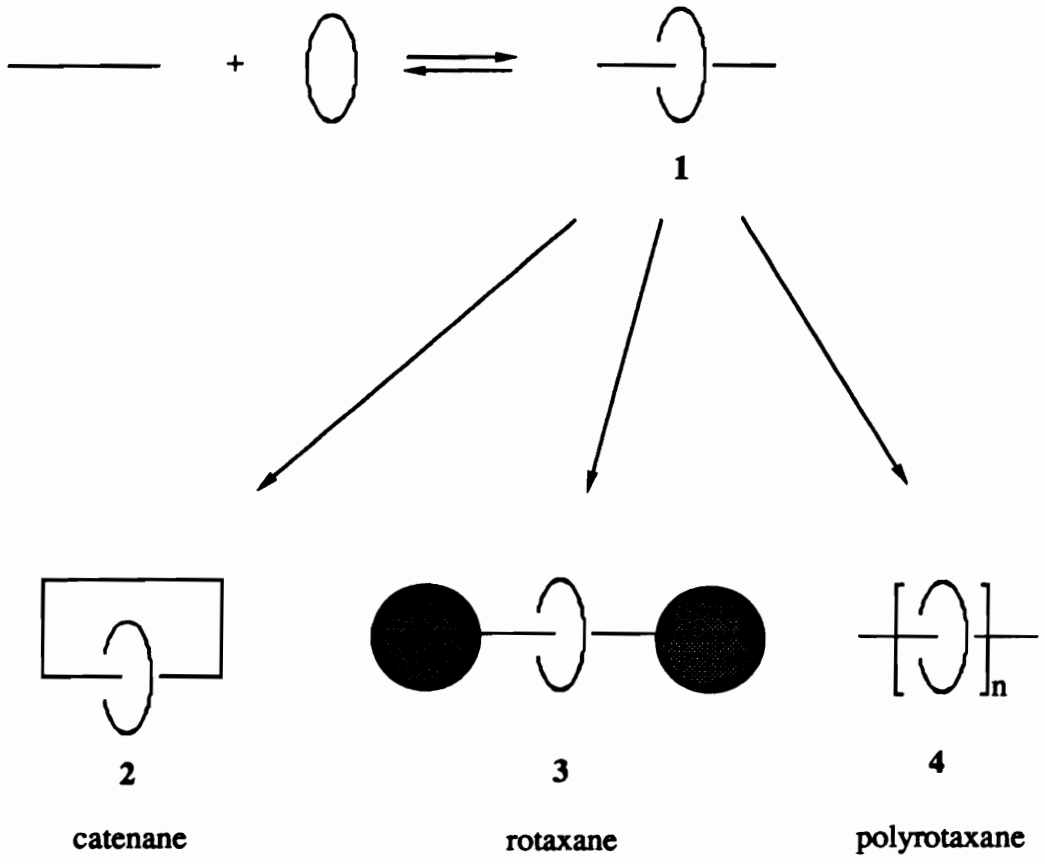
1. SYNTHETIC METHODOLOGY

The existence of interlocking rings in polysiloxanes [1] and polymeric phosphonitrile chloride [2] had been suggested by some workers, but the first experimental demonstration of the existence of catenanes was made by Wasserman in 1960. [3] Wasserman, with Frisch, also described the possibility of rotaxanes in the first published paper in 1961. [4] Three years later Schill and Lüttringhaus reported on the synthesis of catenanes by a direct chemical conversion method. [5] In 1967, Harrison and Harrison [6] and Schill and Zöllenkopf [7] reported the synthesis of rotaxanes by two different methodologies which are a modified statistical and a chemical conversion method, respectively. Since then, in the past three decades much progress has been made owing to the development of new synthetic methods and better understanding of the unique structure-properties relationships. Various types of rotaxanes and catenanes have recently been synthesized in excellent yields by utilization of attractive interactions such as metal-ligand interaction, hydrogen bonding, π-π and charge transfer interactions, and hydrophobic/hydrophilic interactions.

The preparations of rotaxanes, catenanes and polyrotaxanes are closely related to each other. In Scheme 1, a linear species threads into the cavity of a cyclic species to form a pseudorotaxane **1** which is a temporary or kinetically stable rotaxane. A catenane **2** is prepared by cyclization of the linear species of **1**. By adding bulky groups at the

chain ends a thermodynamically stable rotaxane **3** would be produced. If the linear component has proper functionalities and can be polymerized, a polypseudorotaxane **4** is obtained by polymerization of **1**.

In terms of driving forces for forming species **1** there are three methods for the synthesis of catenanes, rotaxanes, and polyrotaxanes: statistical threading, chemical conversion method and template synthesis.

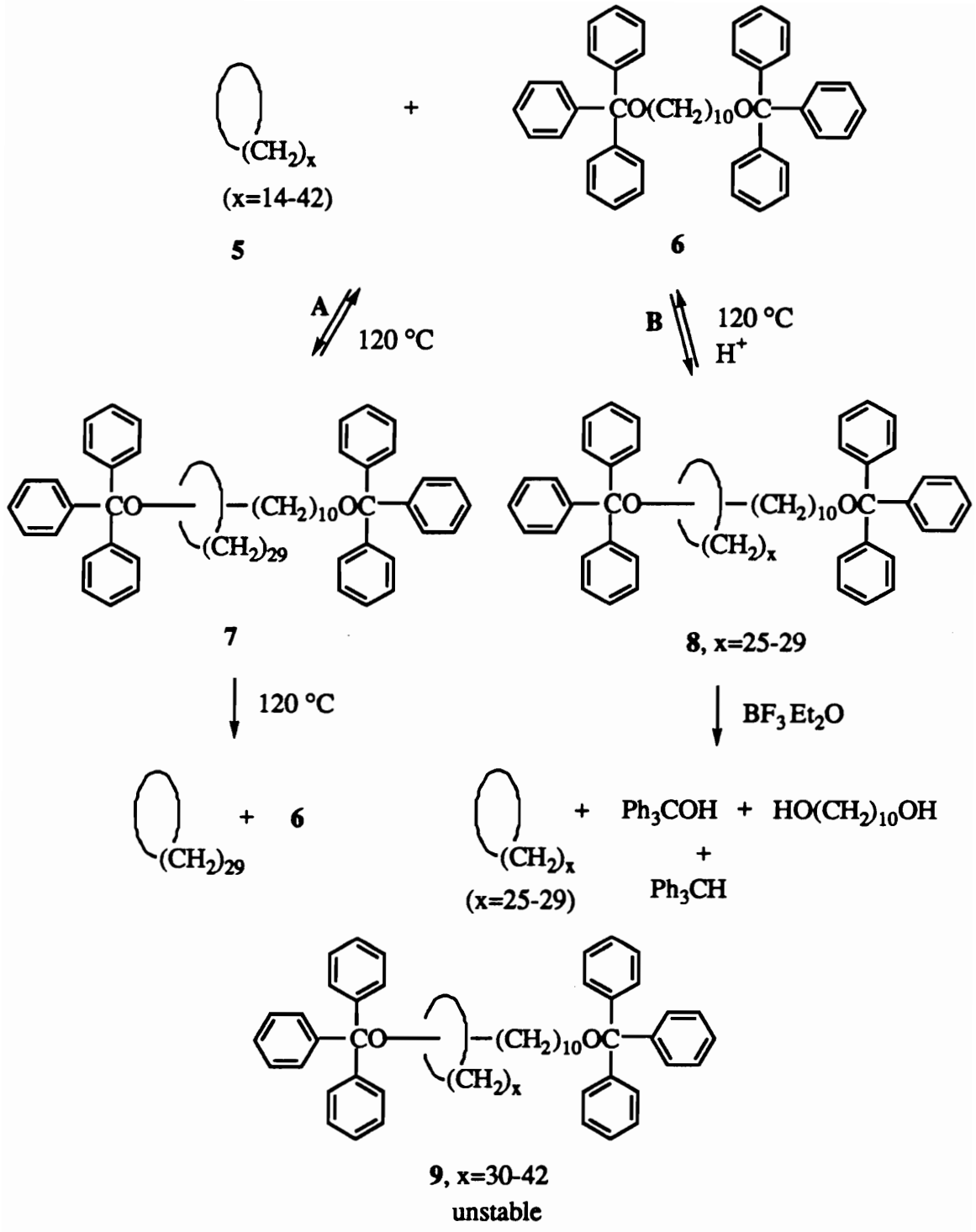


1-1. Statistical threading

In 1960, Wasserman carried out an acyloin ring closure reaction in the presence of a 34-membered cycloalkane containing 5 deuterium markers (d_5-macrocycle). [3] Through column chromatography, he was able to isolate a species which was not either d_5-macrocycle or the acyloin macrocycle. The isolated material had IR absorptions which were representative of C-D stretches of the d_5-macrocycle, and repeated chromatography demonstrated that the IR absorption was not due to contamination by unlocked d_5-macrocycle. Wasserman further proved that the compound was a catenane by oxidative cleavage of the acyloin macrocycle to recover pure d_5-macrocycle and the diacid from the acyloin macrocyle. This report is valuable in terms of the first experimental demonstration of the synthesis of a catenane; however, the yield was 1 % or even less.

Six years later Harrison and Harrison modified the Wasserman's approach to prepare a rotaxane in a better yield by using a polymeric support. [6] A Merrifield peptide resin to which the hemisuccinate ester of 2-hydroxycyclooctacosane was bound was treated with a solution of 1,10-decanediol and followed by trityl chloride. After 70 such processes, the resin was washed and hydrolyzed to give a rotaxane in 6 % yield. The chromatographic behavior and IR spectrum of the isolated material indicated that the compound was a rotaxane. The hydrolysis of the compound yielded the pure macrocycle, trityl alcohol and 1,10-decanediol, which also proved that the compound was a rotaxane.

Harrison continued the study on the formation of rotaxanes by statistical approaches: thermal vibrations (path **A**) and reversible equilibrium (path **B**), which are described in Scheme 1. [8] In the thermal vibration approach, an unspecified mixture of cyclic hydrocarbons (**5**) and 1,10-bis(triphenylmethoxy)decane (**6**) were mixed at 120 °C.



Scheme 1. Statistical threading by Harrison and Harrison.

Harrison proposed that the thermal energy made the macrocycles large enough to slip over the blocking group to afford rotaxanes; a rotaxane (**7**) which contained the 29-membered ring was indeed obtained. Smaller macrocycles were not able to go over the blocking group and rotaxanes containing macrocycles larger than 30 (**9**) were not stable because the blocking group was not big enough to constrain those cyclic hydrocarbons. This result indicated that the largest hydrocarbon macrocycle which can be retained on the linear component by the trityl group was a 30-membered one.

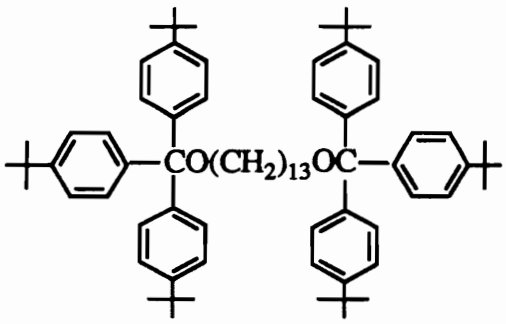
In the reversible stastistical approach (path **B**), a mixture of **5** and **6** was stirred at 120 °C for a few seconds and a catalytic amount of trichloroacetic acid was added to the mixture. While the equilibrium was established the reversible cleavage of the blocking groups of **6** yielded a mixture of rotaxanes (**8**), which, after quenching the reaction by addition of base, was isolated by chromatography. The mixture **8** was hydrolyzed and the resulting macrocycles were analyzed by gas chromatography to determine the yields of each rotaxane.

The results from this study, which was a major step in the research, revealed that the statistical threading process for the formation of rotaxanes was dependent on the sizes of the macrocycles. First, to be threaded by a methylene chain a macrocycle must be at least a 23-membered ring. Secondly, the larger macrocycles resulted in the higher threading yields; the relative yields are 1, 9, 23, 43 and 57 % for the macrocycles having 25-29 methylene units.

By similar reactions using 1,10-bis[tris(*p*-*t*-butylphenyl)methoxy]tridecane (**10**) and 1,10-decanediol bis-(dicyclohexyl)acetate (**11**) Harrison investigated the relationship between the bulkiness of blocking groups and maximum ring size of the macrocycles constrained by the bulky groups. [9] He concluded that the bis(dicyclohexyl)acetate group can squeeze through a 28-membered ring and a tris(*p*-*t*-butylphenyl)methyl group

can hold up to a 42-membered ring.

Schill et al. carried out similar studies to address blocking group effectiveness and the effect of the length of the linear species on the threading efficiency. [10] They also used thermal equilibrium and reversible threading methods with hydrocarbon macrocycles using thioethers instead of ethers as linear components. They observed similar results in this study in terms of ring size and blocking group effectiveness. In addition, they found that the yield of rotaxane increased with chain length.



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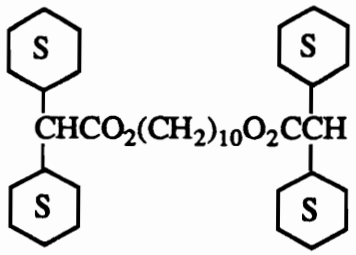
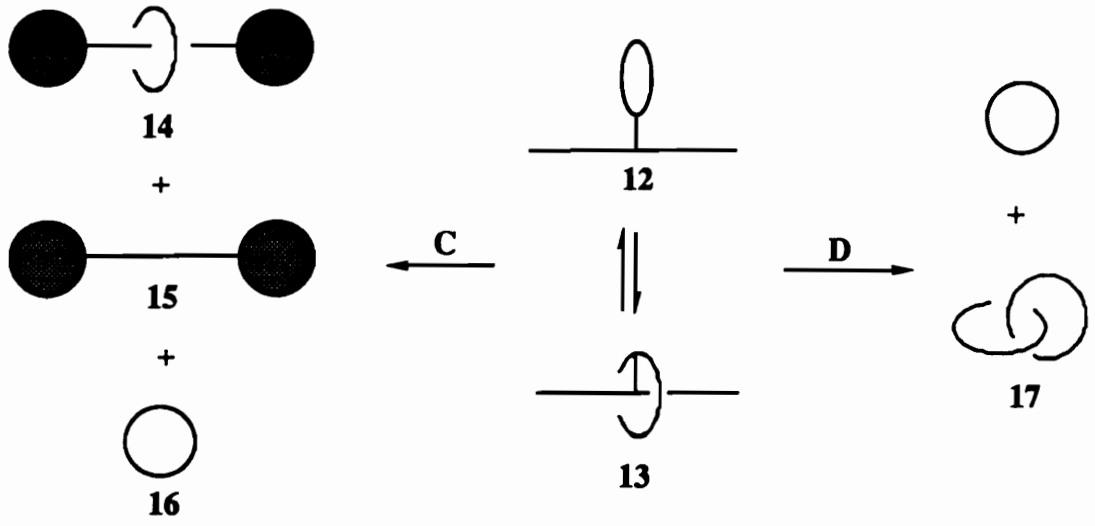


11

1-2. Chemical conversion method

Schill and Lüttringhaus introduced a direct chemical conversion approach to catenane and rotaxane syntheses. [5, 7, 11] The method involves binding the macrocycles to the linear chains to make **12**, which results in self-threaded compound **13** in equilibrium. The addition of the bulky group at the end of linear chain of **13** followed by selective cleavage of the bond between the cyclic and the linear chain affords rotaxane **14** along with the linear compound **15** and unthreaded macrocycle **16** (path **C**). If the chain ends are connected to each other, breaking of the bond between the species gives a

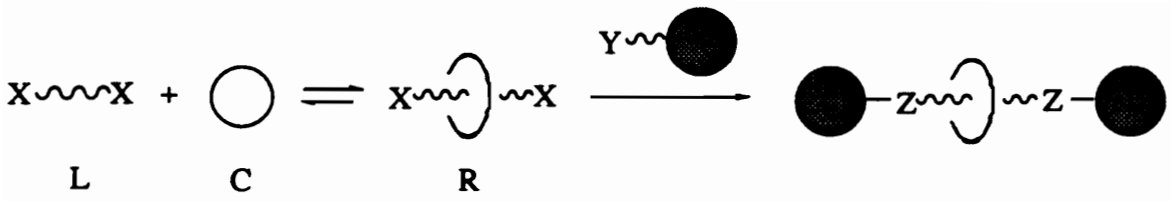
catenane (path D). While elegant, this method requires many steps to prepare the final products, and consequently the overall yields were low. The formation of **13** from **12** is statistically controlled.



1-3. Enthalphically driven or host-guest based syntheses

The enthalphically driven threading processes rely on intermolecular attractive forces between the cyclic and linear species rather than the statistical or entropic driving force. Unlike the statistical methods, those systems which provide negative ΔH's give higher yields in the preparations of rotaxanes and catenanes.

Those attractive forces include hydrogen bonding, metal-ligand complexes, $\pi-\pi$ interaction and hydrophilic-hydrophobic interactions.

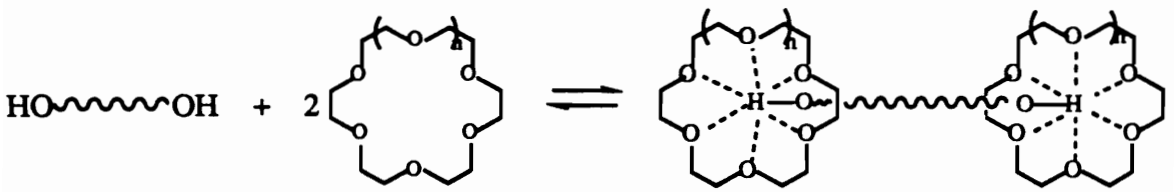


$$K = e^{-(\Delta G/RT)} = [R]/[L][C]$$

$$\ln K = -(\Delta G/RT) = -\Delta H/RT + \Delta S/R$$

1-3-1. Hydrogen bonding

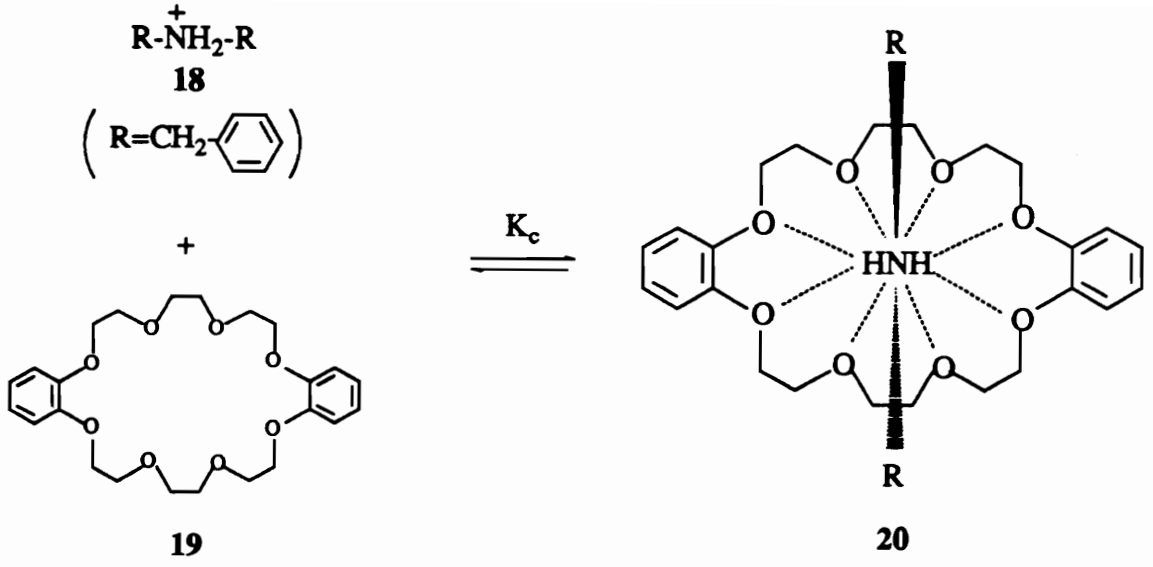
In 1976, Zilkha and coworkers published two papers concerning the formation of rotaxanes [12] and catenanes [13] from benzo-crown ethers and oligo(ethylene glycol)s. Crown ethers are known to make complexes with metal ions through ion-dipole interactions owing to the oxygen atoms which provide non-bonding electrons for the interaction. [14, 15] Furthermore, crown ethers form complexes with organic compounds, especially ammonium ions, through hydrogen bonding. [14] Although as the titles of the papers "Studies on the Formation of Topological Isomers by *Statistical* Methods" [12] and "Synthesis of a Catenane by a *Statistical* Double-Stage Method" [13] imply that the authors did not realize it, their works were probably based on hydrogen bonding between OH groups of the oligo(ethylene glycol)s and crown ethers as depicted below, which are the major driving force for the threading process.



The existence of the hydrogen bonding was supported by the experimental results. The threading yields were high, up to 63 % even when an equimolar amount of diols and crowns were used, which was considerably higher than would be expected in normal entropically driven systems. The results also indicated that the threading increased until the ratio of cyclic to linear reached two and then remained constant. Another strong evidence of the H-bonding was the fact that the extent of threading was independent of the length of the linear chain within experimental error, which means that only the OH units at the chain ends effect the threading process. The threading extent increased with the size of the crown ethers. This is probably due to the fact that the terminal OH hydrogens have more chance for H-bonding with a larger ring because of the greater number of oxygens, and/or a larger ring has a more efficient conformations for the threading than a smaller one.

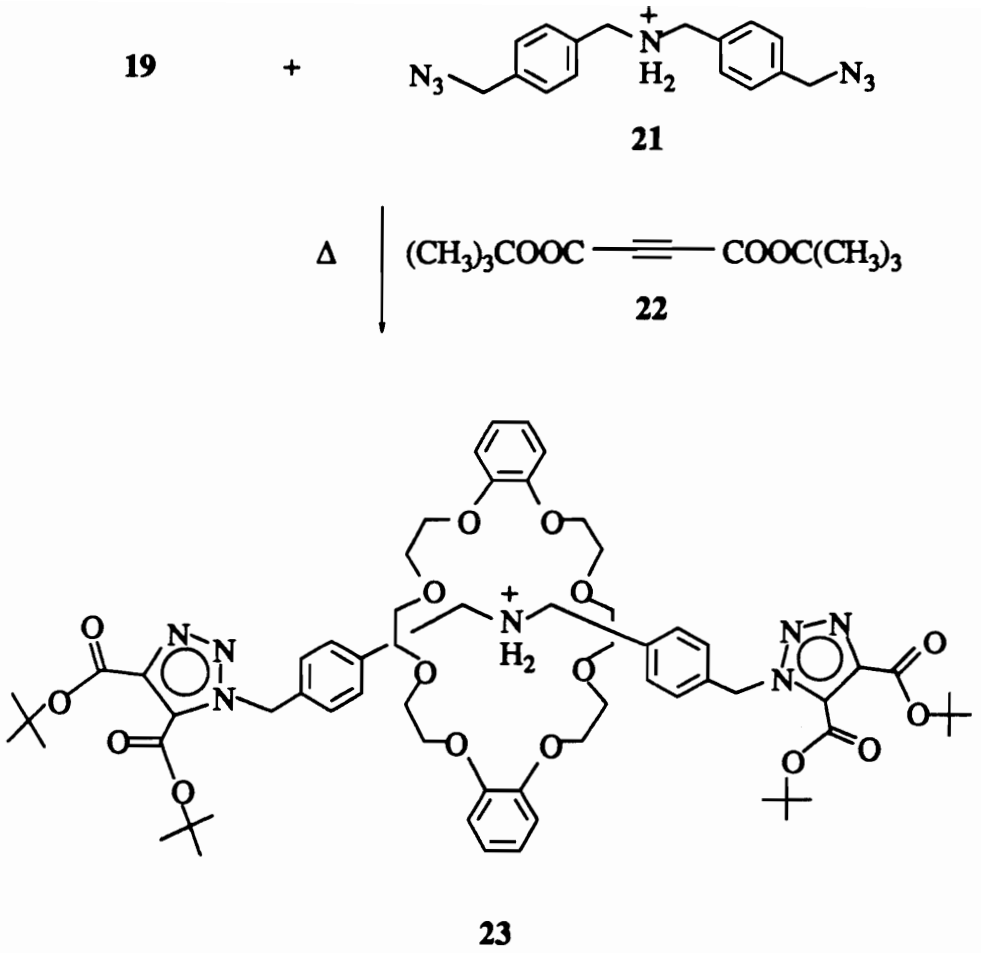
Recently, Gibson's group has synthesized polyamides [16], polyurethane [17] and polyester [18] rotaxanes containing aliphatic crown ethers. The results were similar to the Zilkha's results, indicating the importance of the H-bonding in the formation of these diol- and amine-based rotaxanes and polyrotaxanes.

Hydrogen bonding has been applied to the formation of rotaxanes by other groups. [19-22] Stoddart et al. [19, 20] and Kolchinski et al. [21] prepared pseudorotaxanes **20** based on ammonium ions **18** and dibenzo-24-crown-8 (**19**). The complexation constants (K_c) are high but dependent on solvent system, ranging from 360 in acetone-d_6 to 27,000 in $CDCl_3$ at 25 °C according to the report by Stoddart and coworkers. [19] In those cases, the hydrogen bonding takes place in the middle of the linear molecules **18** instead of at the ends; therefore, rotaxane formation is more direct and if the linear chain ends have suitable functional groups stable rotaxanes could be made efficiently.

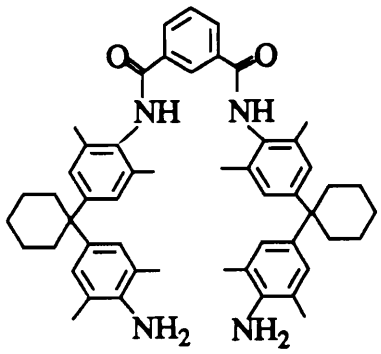


In the synthesis, ammonium compound **21** which has azido terminal groups was allowed to complex with **19** in methylene chloride followed by a cycloaddition reaction of the azide moieties with compound **22** to give stable rotaxane **23**. The yield was 31 % according to their report. [20] The X-ray crystallography of **23** provided with the ultimate structural proof.

Hydrogen bonding is also a major driving force in template syntheses of various catenanes. Hunter reported that diamine **24** reacted with isophthaloyl chloride (**25**) to produce catenane **27** which consisted of the two interlocked rings **26**, a [2]catenane, in 34 % yield. [23] The other products were single-sized macrocycle **26** (51 % yield) and the double-sized macrocyle (5 %). Detailed ^{1}H NMR study of the catenane along with the X-ray crystal data indicated that the several factors were important as well as the intermolecular H-bonding between the amide linkages: π-stacking of electron rich diamine and electron poor diacid, and the bent shape induced by the spiro linkage of diamine. [24] Leigh et al. [25] and Vögtle et al. [26] also have demonstrated the role of H-bonding for the formation of catenanes in similar systems.



Vögtle and coworkers also applied this concept to syntheses of rotaxanes which are comprised of **26** and linear molecules having isophthaloyl amide linkages in yields as high as 41 %. [22]



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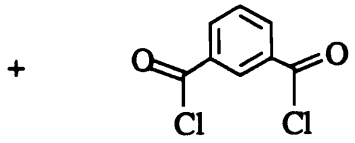
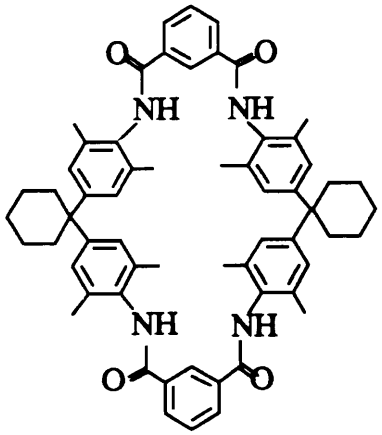
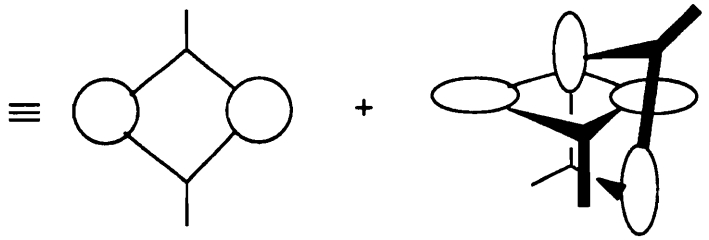


25

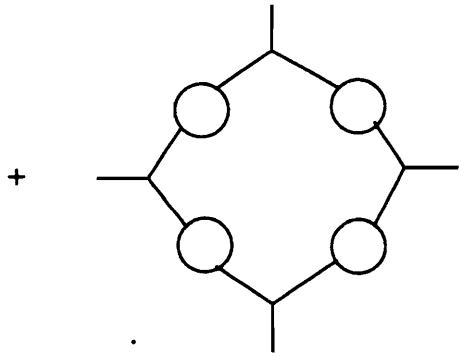
CH_2Cl_2
NEt_3



26

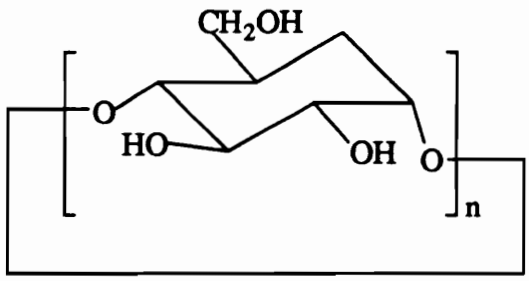


27



1-3-2. Cyclodextrin inclusion complexes

Cyclodextrins (CD) **28** are water soluble macrocyclic oligosaccharides which have hydrophobic cavities. They are known to make complexes with a variety of organic/inorganic compounds and organic salts. [27] The driving forces of the complexations are hydrophilic-hydropobic, van der Waals interactions and possibly H-bonding.



28 (n=6: α-CD, n=7: β-CD, n=8: γ-CD)

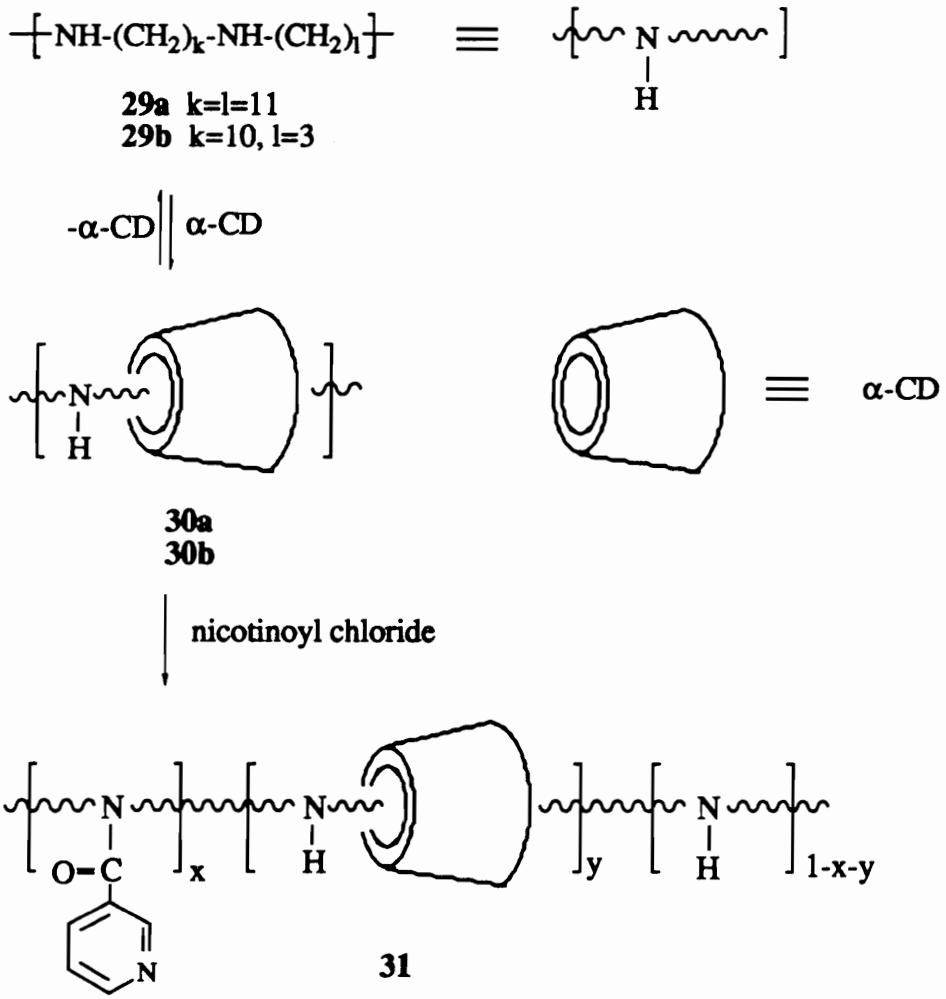
The first polyrotaxanes containing β-CD were poly(amide-rotaxa-β-CD)s synthesized by Ogata et al. in 1976. [28] Aqueous solutions of β-CD and aliphatic diamines were mixed at room temperature for a few days. The resulting white precipitates were identified as inclusion compounds of 1:1 units of β-CD and diamines. Polyrotaxanes were made by interfacial polymerizations of those inclusion diamines with acid chlorides. The structures of the final rotaxanes were determined by elemental analysis and IR after removal of possible unthreaded β-CDs. Among property changes due to the incorporation of β-CD the solubility change was remarkable. All polyamide rotaxanes dissolved easily in dimethylacetamide (DMAc), dimethylformamide (DMF), or N-methylpyrrolidone (NMP) like the polyamides; in addition, the polyrotaxanes were soluble even in hot water in some cases.

In 1979, Maciejewski reported the synthesis of poly(vinylidene chloride)-β-CD rotaxanes. [29] He obtained a complex of β-CD and vinylidene chloride in water and polymerized the complex by irradiation with γ-rays to produce a polyrotaxane. Of interest was that the polyrotaxane was lost after boiling the product in cyclohexane-water mixture or DMF at 70 °C because of dethreading of β-CD; however, when the polyrotaxane was dehydrochlorinated by NaOH in ethanol solution he got a stable polyrotaxane, probably due to enhanced interaction between CD and polymer backbone because the dehydrochlorination produced less polar backbone segments which were better guest compounds for the hydrophobic CD cavity.

Ogino et al. in 1981 prepared CD rotaxanes containing aliphatic diamines as linear molecules, using metal complexes as stoppers. [30] They found that there was a minimum chain length of eight methylene units for the linear chain to form rotaxane.

Poly(iminoundecamethylene-rotaxa-α-CD) (**30a**) and poly(iminotrimethylene-iminodecamethylene-rotaxa-α-CD) (**30b**) were synthesized by Wenz and Keller in 1992 by mixing **29a** (P_n=43±5) and **29b** (P_n=23±2) with α-CD. [31] According to their report, both ^{1}H-NMR spectroscopy and viscosity measurements revealed that, while α-CD threaded onto **29a** within a couple of hours, it took over a week for **29b** to fully thread in aqueous solution. Although equilibrium dialysis of **30a** into its separate components was over within 15 hours, dissociation of **30b** was not complete after two weeks. When **30b** was treated with nicotinoyl chloride to introduce at least two hydrophilic nicotinoyl blocking groups at arbitrary positions along the poly(iminooligomethylene) chain, polyrotaxane **31** of M_w 55,000 ±5,000 (determined by light scattering) was isolated with an average of 37 α-CD rings permanently threaded onto the chain. Wenz et al. also discovered that per(3-*O*-acyl-2,6-di-*O*-alkyl)CDs form complexes with cationic guest molecules and neutral ones as well. [32, 33] They used complexes of per(3-*O*-acyl-2,6-

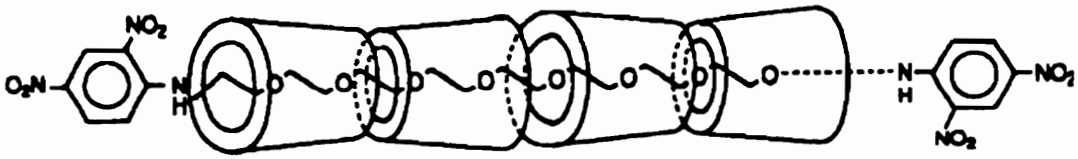
di-*O*-alkyl)CDs with 4,4'-bipyridinium cations containing extended bulky group to synthesize stable rotaxanes. According to the NMR study of the complexes they found that the modified CD had two orientations, *endo* and *exo* forms in the complexes. [33]



A series of exciting results were reported by Harada and coworkers. [34-40] They found that CD rings make complexes with oligo-poly(ethylene oxide)s [34-36], poly(propylene oxide)s [36, 37] and polyisobutylene [38]. The poly(ethylene oxide)s chains thread α-CD beads like a necklace. They have succeeded in capping the chain ends of a poly(ethylene glycol)diamine (PEG-DA, M_w=3,450) with dinitrophenyl end

blockers to prepare a stable polyrotaxane **32** [35]. The reaction was carried out in a solution of the PEG-BA in DMF saturated with α-CD and exess (46 molar equiv.) 2,4-dinitro-fluorobenzene. After an extensive purification procedure, NMR and UV analyses indicated that each linear molecule contained 20-23 α-CD rings on average.

Harada and coworkers further treated polyrotaxane **32** with 10 % NaOH and epichlorohydrin. [39] By using gel permeation chromatography they were able to show that cross-linking occured only along the polymer chain with formation of hydroxypropylene bridges. The blocking group was then cleaved with 25 % NaOH and the linear chain could be removed. The final product was molecular tube **33** which consisted of about 15 bridged α-CD units. [39]



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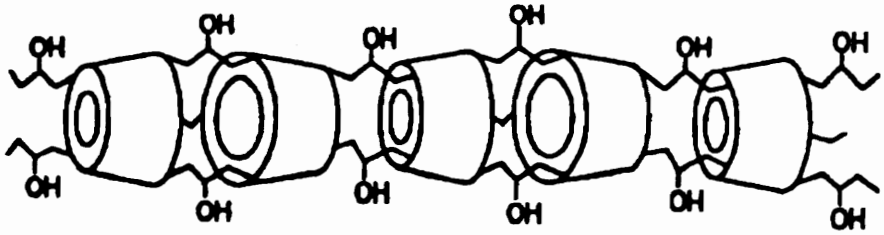
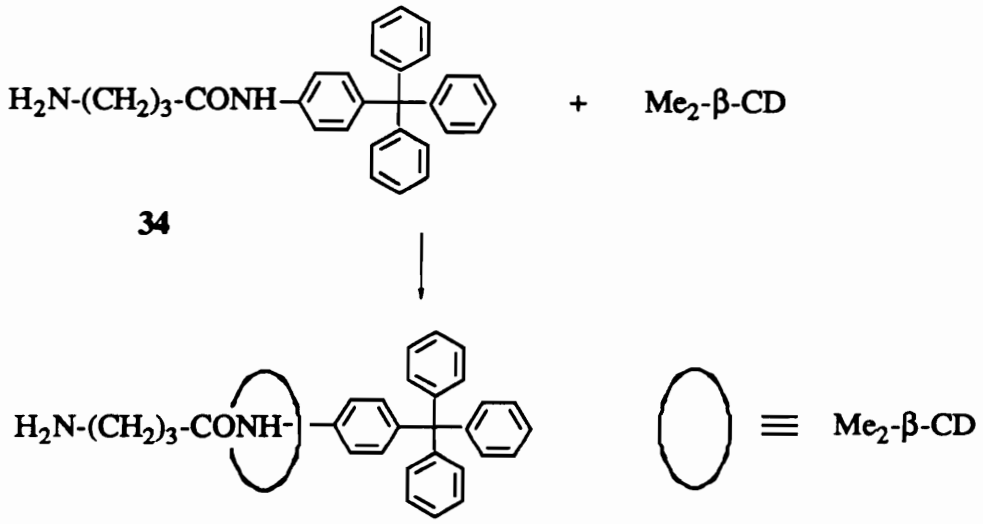


33

A major drawback of CDs as host molecules is their low solubilities in common organic solvents. Except water, only aprotic polar solvents such as dimethylsulfoxide (DMSO), DMF and NMP are good solvents for unsubstituted CDs. Thus, CDs are

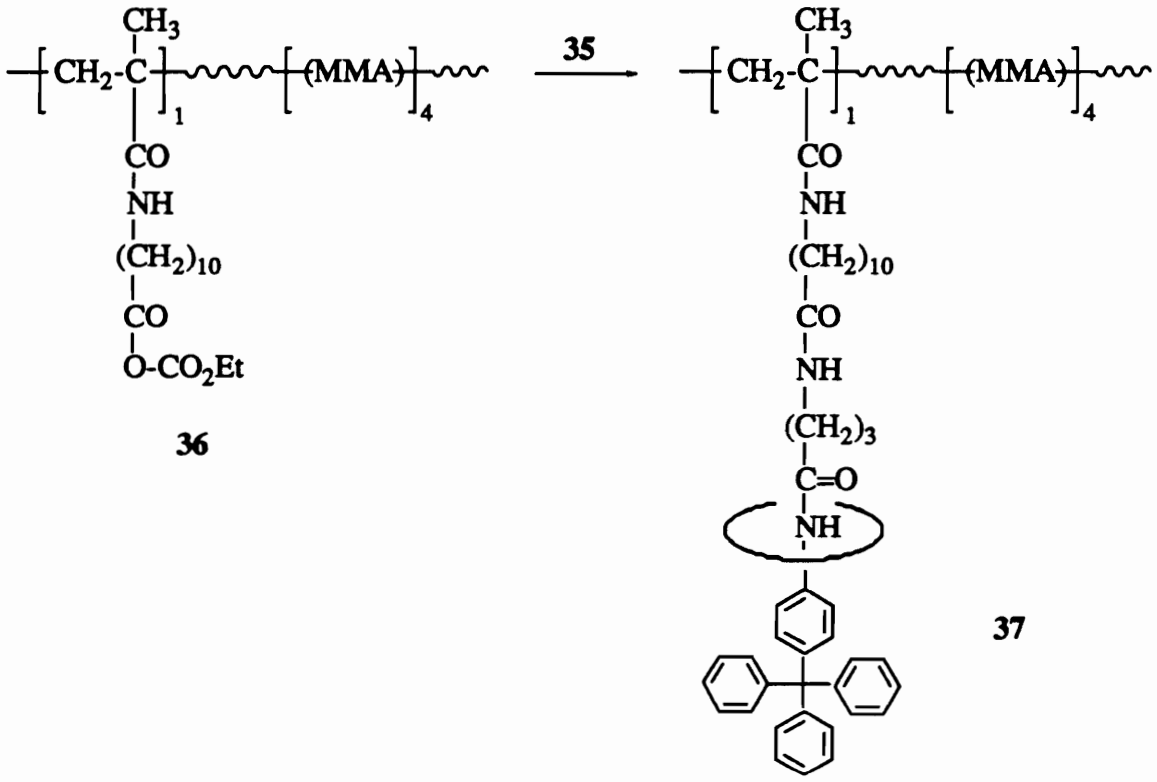
derivatized in order to vary their solubility behavior and to modify their complexation properties. Casu and Reggiani reported that 2,3,6-tri-*O*-methyl and 2,6-di-*O*-methyl derivatives of α and β-CDs form complexes with various compounds in organic solutions and association constants were higher than the unsubstituted CDs in some cases. [41] The modification of CDs, however, was not trivial and simple. The separation and purification of those sustituted CDs were difficult and costly.

Using 2,6-di-*O*-methyl β-CD Born and Ritter were able to prepare side-chain polyrotaxanes. They found that the barrier compound **34** made a complex **35** with 2,6-di-*O*-methyl β-CD (Me_2-β-CD) in water or chloroform, which was characterized by mass spectroscopy and NMR. [42]



The isolated complex was stable during grafting reactions with premade activated copolymer **36** which is based on poly(methyl methacrylate) (PMMA) to give a side-chain polyrotaxane **37** in organic solvents such as chloroform and tetrahydrofuran. They also used an activated polymer based on poly(ether-ether-ketone) and polysulfone instead of

36 to synthesize side-chain polyrotaxanes successfully. [43] By a similar reaction using **35**, Born and Ritter recently reported preparation of a new tandem polyrotaxane in which each branched polymeric side chain has a noncovalently bound Me_2-β-CD at either end. [44]



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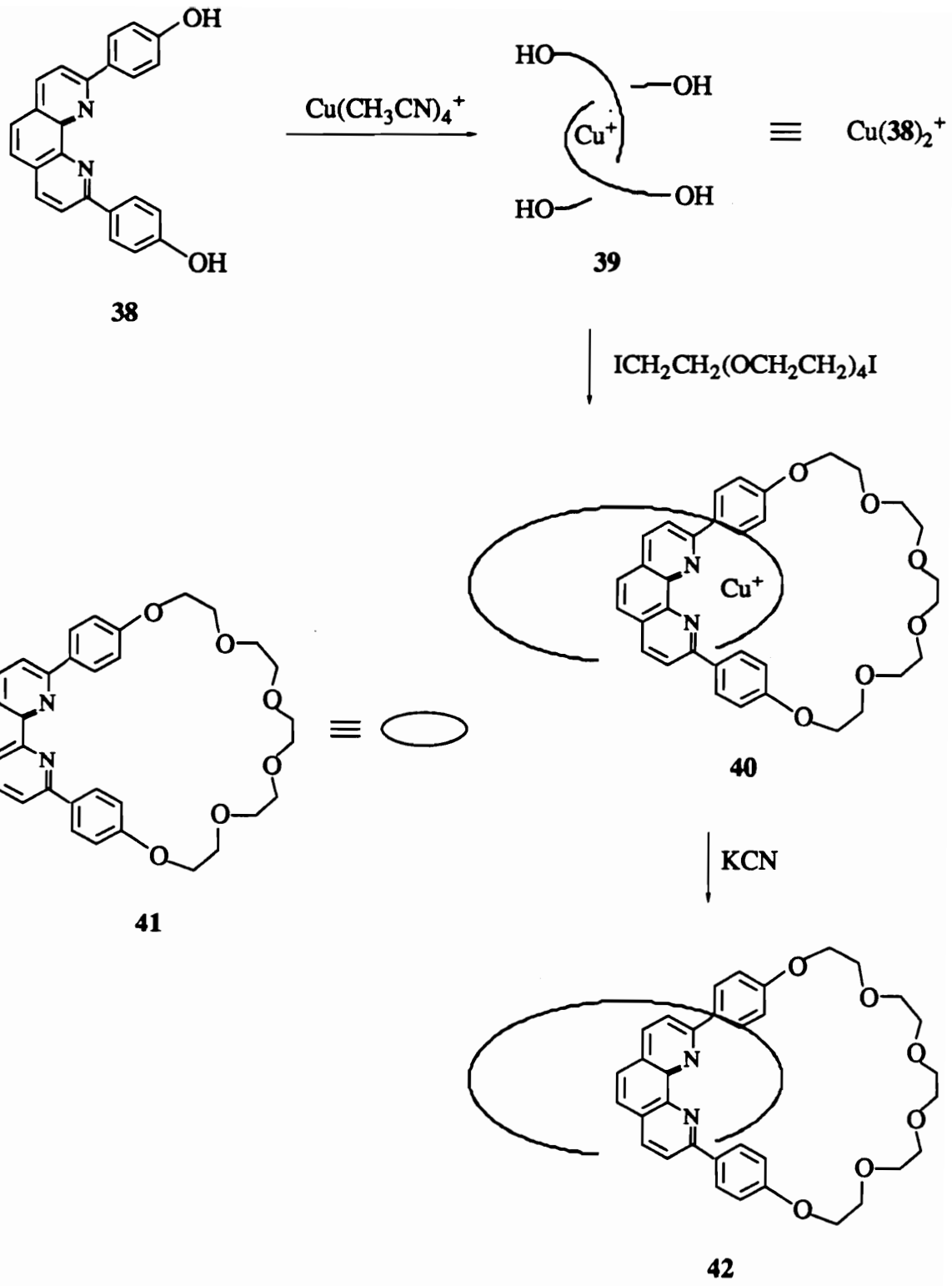
37

1-3-3. Metal-ligand template synthesis

Transition metal-organic ligand complexes were applied to syntheses of catenanes and pseudorotaxanes by Sauvage and Dietrich-Buchecker. [45-47] The linear precursor


OH
N
N
OH
38
Cu(CH3CN)4+
HO
OH
Cu+
HO
OH
39
≡
Cu(38)2+
ICH2CH2(OCH2CH2)4I
O
O
O
O
O
O
O
N
N
Cu+
40
41
≡
KCN
42

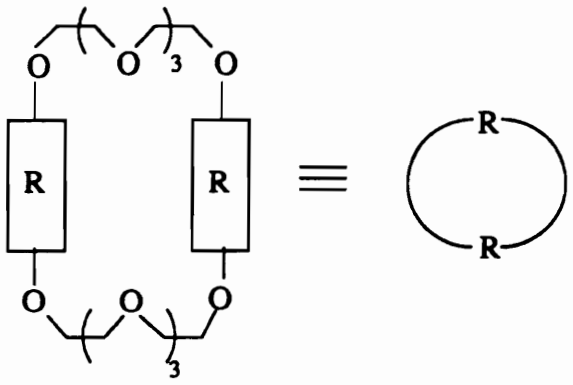
38 which ligates to Cu^+ and has a well defined, predictable tetrahedral geometry **39** produced metal complexed catenane **40** by ring formation. [45] Instead of simultaneous cyclization of complex $Cu(\mathbf{39})_2^+$ the catenane **40** can be prepared by using preformed macrocycle **41**. Thus, a complex of **41** and **38** through ligation to Cu^+ undergoes the cyclization to give **40**. [46] The cyclization step of the latter strategy affords a better yield (43 % yield) than the former one (27 % yield); however, due to the requirement of preformed macrocycle **41**, the overal yield (14 % yield) of the two-step method is lower than the one-step reaction (20 % yield). [46] The precatenane **40** bearing Cu^+ ion is able to be converted into the final metal-free catenane **42** by treatment with excess KCN to remove the metal ion.

1-3-4. Charge transfer/π–π stack complexes

In the late 1980's Stoddart et al. reported a series of results of their studies on the complexations of benzo-crown ethers (donors) with 2,2-bipyridinium and 4,4'-bipyridinium salts (acceptors) (e.g. **43/44**). [48] They found that the complexation constants were very high, in the range of $K_C=10^2$ to 10^3 L/mol. The driving forces for the complexations were charge transfer, π–π interaction, hydrogen bonding and dipole-dipole interaction. They also discovered that various linear molecules containing arylene functionalities as donors form "inverse" complexes with a macrocycle **45** which has 4,4'-bipyridinium ion units and related macrocycles. [49]

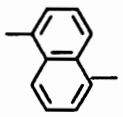
With this concept they have synthesized a variety of [*n*]catenanes (*n*=1-4) [50-52] and even a [5]catenane (so-called olympiadane) [52, 53] in good yields. Various rotaxanes have also been prepared using the charge transfer complexes. [50, 54, 55] In addition to the conventional threading and slippage methods they introduced a new

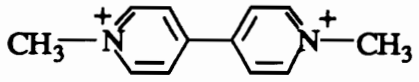
method, which is called "clipping". [55]



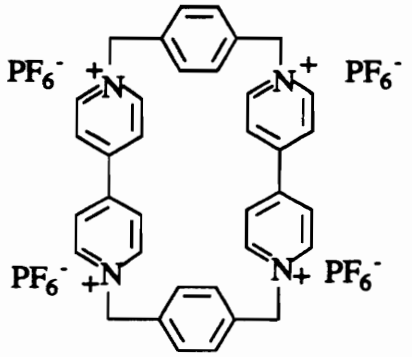
43

R=*p*-C_6H_4, *m*-C_6H_4,





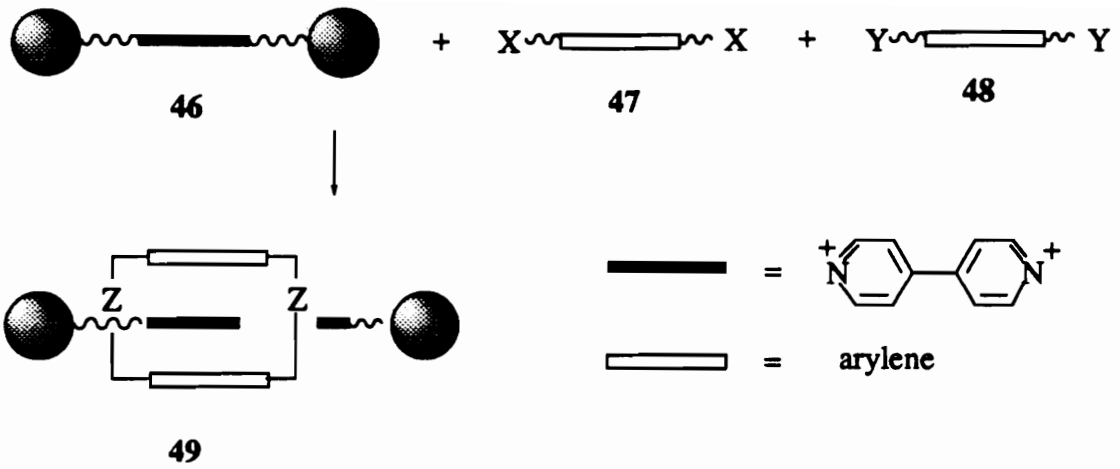
44

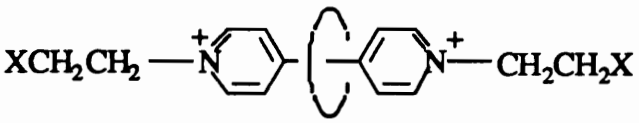


45

In the clipping method, cyclization reactions between **47** and **48**, which are functionalized 4,4'-bipyridinium ions, were carried out in the presence of blocked linear molecules **46** containing arylene units. The cyclization reaction takes place while the complexation occurs so that rotaxane **49** is obtained.

Stable rotaxane complexes **50** which have functional units at the ends of the linear species have been reported by Stoddart et al. [56] and Gibson et al. [57] Complexes **50** can be used as monomers for the syntheses of polyrotaxanes.





50, ◯ **= 43** (R=*p*-C_6H_4)

X = OH, $COOCH_3$, COOH

2. PROPERTIES OF ROTAXANES AND POLYROTAXANES

2-1. Structural proof

Catenanes and low molecular weight rotaxanes, as early researches demonstrated, can be differentiated from analogous physical mixtures of each component by chromatographies. Melting point depression, [12, 13] osmometry, [12, 13] gel permeation chromatography (GPC) [9, 12, 13] and classic mass spectroscopy [7, 11] have been used to demonstrate the rotaxane structures. Especially, mass spectroscopy is a

powerful tool to prove the structure. [19, 21, 50] Along with the total mass, the linear and cyclic fragments are the next largest fragments in most cases.

NMR spectroscopy has been used to characterize rotaxanes and catenanes. In some cases, substantial changes in the chemical shifts of protons or carbons of the cyclic and linear components are observed. [19, 32, 48, 50] These cases include cyclodextrin-based systems and bipyridinium-based rotaxanes. Nuclear Overhauser effect measurements have also been employed to support the detailed structures of catenanes and rotaxanes. [23, 32, 33] In other cases, the shifts of signals are affected very little [42, 43] or not at all [18, 22(a)] by incorporation of the rotaxane topology. Aliphatic linear/cyclic systems and oligo(ethyleneoxy)linear with crown ether systems are the examples of these cases.

For low molecular weight rotaxanes and catenanes the ultimate structural proof is X-ray crystallography. [19, 21, 24, 35, 49, 50, 57] The solid state structures also provide important clues about the intermolecular interactions that drive the threading processes. However, unfortunately, polyrotaxanes can not easily be obtained as single crystals and no such report was made so far.

An important control experiment in polyrotaxane syntheses is to perform a polymerization in the presence of a homologous macrocycle which is too small to be threaded. For example, in cases of crown ether based polyrotaxanes the stability of crown ethers and possible side reactions under the synthetic conditions could be checked by the use of 18-crown-6. [18] If no elements for the small crown ethers are found in the resulting polyrotaxanes after purification, it can be said that 1) no side reactions due to chain transfer reactions or decomposition of the crown ethers followed by incorporation into the polyrotaxanes occured and 2) unthreaded crown ethers could be removed by the purification methods.

The structural purities of polyrotaxanes are further investigated by NMR spectroscopy. During the purifications, which are usually reprecipitations or dialysis, the samples are monitored by NMR spectra and once a constant ratio of the signals for linear and cyclic components is reached the polyrotaxane is considered to be pure, in other words, free from unthreaded macrocycles. Regarding the chemical shifts changes, in many cases no changes were observed as in low molecular weight rotaxanes. [16-18] However, bipyridinium containing polyurethane rotaxanes exhibit chemical shift changes similar to those observed by Stoddart for low mass rotaxanes. [58]

GPC also provides a test of the purity of polyrotaxanes. [17, 18] The GPC trace of a simple physical mixture of a linear polymer and a cyclic component gives two distinquishable responses: one for the linear polymer and the other for the macrocycle. Thus , the absence of the signal of the macrocycle under the same experimental condition gives another evidence of the absence of the unthreaded or free cyclic species in the purified polyrotaxane.

2-2. Stability of rotaxanes and polyrotaxanes

When rotaxanes and polyrotaxanes contain stoppers of appropriate sizes to prevent diffusional loss of cyclic species, they are thermodynamically stable to dethreading. However, many rotaxanes and polyrotaxanes synthesized to date have no such blocking groups.

According to Wenz and Keller polyamine-cyclodextrin rotaxane **30a** completely dissociated in two weeks in an aqueous acidic solution. In contrast, dethreading of polyrotaxane **30b** was far from complete even after two weeks. [31] This is due to the fact that trimethylene units can not be accomodated in the hydrophobic CD cavity and the

hydrophilic ammonium ions act as barriers to motion of the CD rings along the chain.

Liu and Gibson performed a dethreading experiment using poly(butylene sebacate)-rotaxa-42c14. [59] Initially the m/n (number of macrocycles per repeating unit) was 0.18. After 11 days in refluxing THF the value decreased to 0.17, and after 35 days it fell to 0.15. This results indicate that the dethreading process of the polyrotaxane with no stoppers was very slow. The slow loss of macrocycles from high molecular weight polyrotaxanes may be explained by the following several considerations: random coiling of the polymer backbone, hydrogen bonding interactions between the terminal OH or COOH groups and crown ethers as a barrirer for dethreading, interactions between polar ester groups and crown ethers, greater motion of the chain ends than the middle sections of the chain which pushes the crowns toward the center of the backbone, and associaltion of the end groups with solvent or each other.

2-3. Solution properties

The incorporation of macrocycles into polymer backbones induces solubility changes. Poly[(alkylene sebacate)-crown ether rotaxane]s showed solubilities in methanol and water while the parent polymers are completely insoluble in those solvents. [18] Likewise Schiff base polyester rotaxanes containing crown ethers showed better solubility in DMAc than its parent polymer. [60] Related to the enhancement in solubilities, many polyrotaxanes with crown ethers showed emulsification phenomena. Polyurethane rotaxanes, [17] and polyamide rotaxanes [61] which contain crown ethers as cyclic components became soluble in water through the formation of micelles when the crown contents reached certain values.

Lipatova and coworkers reported that polystyrene-cyclic urethane rotaxanes were

insoluble in benzene or dimethylsulfoxide, which are good solvents for polystyrene and cyclic urethane, respectively. [62]

The cyclodextrin containing poly(methylmethacrylate) side chain polyrotaxane (**37**) made by Ritter et al. also displays the solubility changes. [42, 44] The polyrotaxane is soluble in ether while the parent polymer is not, apparently due to the shielding of the amide moiety by the CD ring, preventing intermolecular hydrogen bonding of the amide units.

The incorporated macrocycles induce changes in solution viscosities. For instance, Liu and Gibson found that a polyrotaxane containing about one crown per each chain which made by simple mixing of preformed poly(butylene sebacate, M_n=27.6 kg/mol) and 42-crown-14 displayed doubled intrinsic viscosity in chloroform. [63] This means that the hydrodynamic volume of the polyrotaxane was doubled and this was further confirmed by GPC and VPO measurement.

2-4. Phase transitions

When a sufficient amount of cyclic species is threaded onto linear polymers the cyclic component can crystallize independently. The polyaramide-crown ether rotaxanes prepared by Bheda and Gibson showed irreversible exothermic thermal transitions in the solid state. [16] The polyaramide-crown ether rotaxane as made showed reduced hydrogen bonding of carbonyl groups according to the IR spectrum. Also, the DSC trace indicated that the exotherm occurred at 181 °C. Interestingly, after 2 months aging at room temperature, the exotherm was detected at 251 °C. As the polymer was purified the macrocycles are isolated from one another, allowing intramolecular hydrogen bonding between crown ether and amide group. However, in the solid state as time passes, the

threaded crown ethers move aside allowing the stronger intermolecular hydrogen bonding between the amide groups.

Independent crystallization behavior is also observed in other systems such as poly[(alkylene sebacate)-crown ether rotaxane]s [18] and poly(styrene-cyclic urethane rotaxane)s [62]. Harada and coworkers found that poly[(ethylene oxide)-α-CD rotaxane]s [34] and poly(isobutylene-γ-CD rotaxane)s [38] are crystalline. According to their reports, the X-ray diffraction patterns of poly[(ethylene oxide)-α-CD rotaxane]s indicated that in the polyrotaxane α-CDs had extended a columnar structure or channel-type structure which was different from those complexes with small molecules, such as propanol and propionic acid, which have cage-type structures. [34] Likewise, in poly(isobutylene-γ-CD rotaxane)s the threaded γ-CDs have a packing structure different from that of free γ-CD. [38]

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CHAPTER III

BLOCKING GROUPS

Although "temporarily" stable or kinetically stable polyrotaxanes can be prepared without blocking groups [1, 2], introduction of blocking groups to the ends of linear chains of polyrotaxanes ensures "permanently" stable or thermodynamically stable polyrotaxanes. Design of blocking groups requires several criteria. First, the blocking groups must be larger than the size of cavities of the macrocycles to be blocked. The minimum size of a blocking group for a specific macrocyle can be calculated by computer simulations or CPK models. However, the theoretical considerations may not always match experimental results. For example, according to CPK models a 42-membered aliphatic macrocycle can slip over (*p*-hydroxyphenyl)tris(*p-tert*-butylphenyl)methane group when the bonds are manupulated forcefully. This is, however, in contrast to the experimental results of Harrison [3, 4] and Schill et al. [5] The experimental results demonstrated that tris(*p-tert*-butylphenyl)methane group can constrain up to 42-membered rings. Thus, the most probable conformations of macrocycles are also related to the blocking efficiency of a certain bulky group. Unfortunately, there are not many experimental data reported to date.

Harrison found that the triphenylmethyl (trityl) group can constrain a 30-membered aliphatic macrocycle by preparing a rotaxane from the reaction of 1,10-decanediol and trityl chloride in the presence of the macrocycle. [3] In similar reactions he found that the cyclohexylacetyl group blocked rings with less than 28 methylene units. [4] The tris(*tert*-butylphenyl)methyl unit was able to block rings with up to 42 methylene units as mentioned above. [4] However, such compounds blocked with tris(*tert*-butylphenyl)methyl chloride or trityl chloride are not stable because triaryl ether linkages

can be easily hydrolyzed. Zilkha found that a rotaxane containing trityl ether linkages decomposed upon standing for a couple of months even at room temperatuture. [6] Schill et al. avoided such instablility of the trityl group by the reaction of trityl anion and 1,10-dibromodecane in the presence of a cyclic species, preparing a stable rotaxane without the ether linkage. [5]

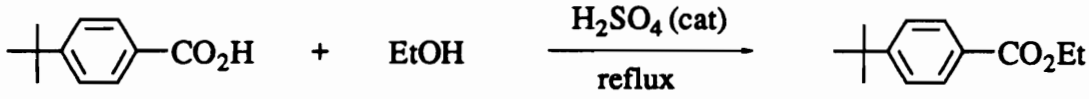
The second factor is the functionality of the blocking group. A blocking group should have a proper reactive unit in order to be attached to the chain ends. For instance, if a polyester rotaxane is synthesized by condensation of hydroxyl and acid chloride monomers a blocking group must contain such a reactive group as hydroxyl or acid chloride units.

Triarylmethyl derivatives are suitable blocking groups which are easily manipulated. [7] If they contain proper functionalities they can be used for various condensation polymerizations to produce stable polyrotaxanes. Tris(*p-tert*-butylphenyl)methyl derivatives were the major compounds which we have focused on because they are able to hold up to 42-membered macrocycles. [3, 4] Also they showed good solubilities in melts and in solutions, which is also an important factor for proper blocking groups in the polyrotaxane syntheses.

RESULTS AND DISCUSSION

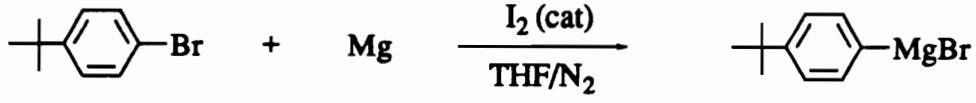
The synthesis of the basic stem of the triarymethyl derivatives was started from the reaction of ethyl *p-tert*-butylbenzoate and the Grignard reagent derived from *p*-bromo-*tert*-butylbenzene. The starting material, ethyl *p-tert*-butylbenzoate (**2**), was obtained by

refluxing *p-tert*-butylbenzoic acid (**1**) in ethanol in the presence of a catalytic amount of sulfuric acid. The reaction gave the product as a clear viscous oil in 93 % yield.

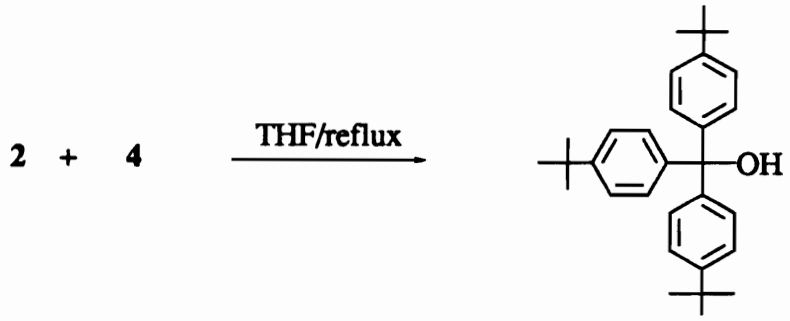


1 **2**

The Grignard reagent **4** was prepared *in situ* by the reaction of *p*-bromo-*tert*-butylbenzene (**3**) and magnesium metal. Although most preparations of Grignard reagents generate a large amount of heat, our reaction was carried out at reflux due to the low reactivity of *p*-bromo-*tert*-butylbenzene toward magnesium. There was a short wait until the reaction between **3** and Mg metal began as the general case of Grignard reactions. After work-up and a recrystallization from cyclohexane white crystals of **5** were obtained in 70 % yield; the melting point was 210-214 °C. (Lit. [8] mp=212-213 °C)



3 **4**



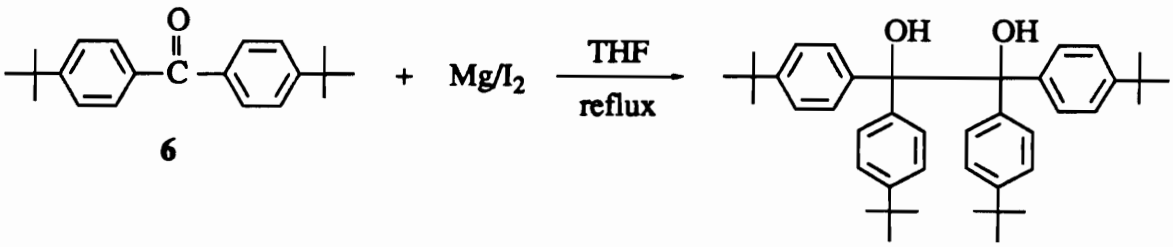
5

Although the formation of **4** might be incomplete, the use of excess Mg was avoided in this reaction because the formation of Grignard reagents is known to be almost quantitative even when equimolar bromide and Mg are used, and undesired side products such as reductive products were suspected to be produced through metallic reduction. The yield of 70 % was the highest one reported for this synthesis. Stoddart et al. reported the synthesis of **5** from the reaction of **4** and diethyl carbonate in 77 % yield without any details. [9]

The side product from the above reaction, in which excess magnesium was used, was a fluorescent compound and its melting point was 199.1-200.0 °C. Marvel and coworkers reported the synthesis of **5** in about 45 % yield, but they did not mention the side product. [8] Bheda noted that IR spectrum of the side product showed OH group(s) in it, which means that the side product came through a reductive reaction. The side product was suggested to be di(*p-tert*-butylphenyl)methanol according to the NMR, IR and elemental analysis (EA) results by Bheda. [11] However, more careful investigation of the ^{1}H NMR spectrum (Figure 1) suggests that the side product is bis(*p-tert*-butylphenylmethyl)pinacol (**7**) rather than di(*p-tert*-butylphenyl)methanol. If the byproduct were di(*p-tert*-butylphenyl)methanol the proton adjacent to the tertiary carbon (*H*-C-OH) would be shown at around 4 ppm; however, such a signal is not found in Figure 1. The peak at 2.97 ppm rather corresponds to a tertiary hydroxyl proton. The integration of the peaks in the ^{1}H NMR spectrum also indicated that the byproduct was bis(*p-tert*-butylphenylmethyl)pinacol. The formation of **7** is believed to originate from the coupling reaction of di(*p-tert*-butylphenyl)ketone (**6**) which is an intermediate of the Grignard reaction as shown in Scheme 1. Therefore, as a control reaction, a reaction of **6** with Mg/I_2 was carried out in order to check if this chemistry is responsible to the byproduct of our system. Thus, **6** was mixed with excess Mg and I_2, and it was refluxed in THF.

Upon refluxing the mixture became purple blue in color and later the color changed to brown, then, green which meant reduction was complete. After work-up, a white solid (75 % yield) was obtained whose ^1H NMR spectrum was identical to Figure 1.

Concerning this, Gomberg and Bachmann reported a series of results in 1929, which are known to be the "Gomberg-Bachmann pinacol synthesis". [12] In those articles they reported that pinacols were produced by the reaction of aromatic diketones or ketones with Mg and MgI_2 binary system.

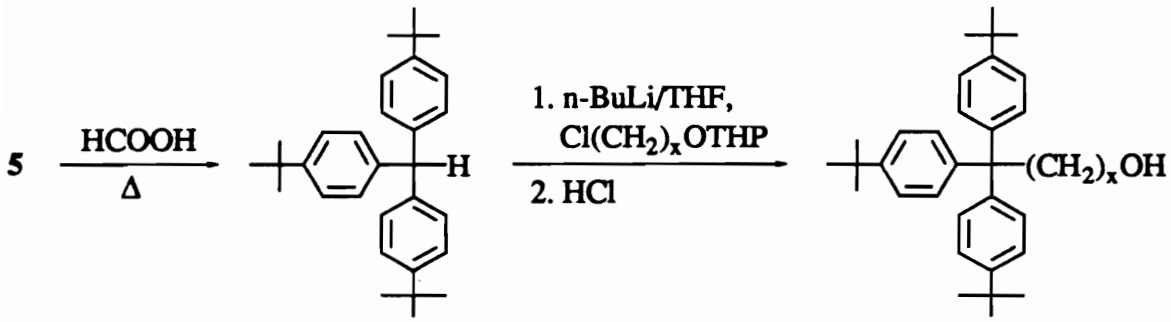


6 **7**

The mechanism for this reaction is illustrated in Scheme 2 as described by Gomberg et al. The main feature of the mechanism is a radical coupling reaction. This kind of chemistry is useful for the research of polyrotaxanes because such aromatic pinacols can be used as blocking groups as well as as monomers simultaneously to give so-called "internally blocked polyrotaxanes".

The triarylmethane **5** can not be used as a blocking group directly because the hydroxyl group is not reactive enough due to the steric hindrance, and as previously mentioned the resultant trityl ether linkage is not stable. Thus, it is necessary to modify **5** in such a way that the reactive groups are remote from the bulky triaryl group. Also, by such modifications the preparation of hydrolytically stable blocking groups can be achieved.

Compound **5** was reduced by reaction with formic acid in toluene in quantitative yield. Then, the compound **8** was converted into **9** (x=4 or 6) by the reaction of the anion of **8** and aliphatic halides. However, the conversion of **8** to **9** was quite low (5-10 %) due to the steric hindrance although an aprotic polar solvent such as HMPA was used as cosolvent. [7] Therefore, we studied carbocationic processes to incorporate spacers and functionalities, which is the synthesis of tri(*p-tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**).

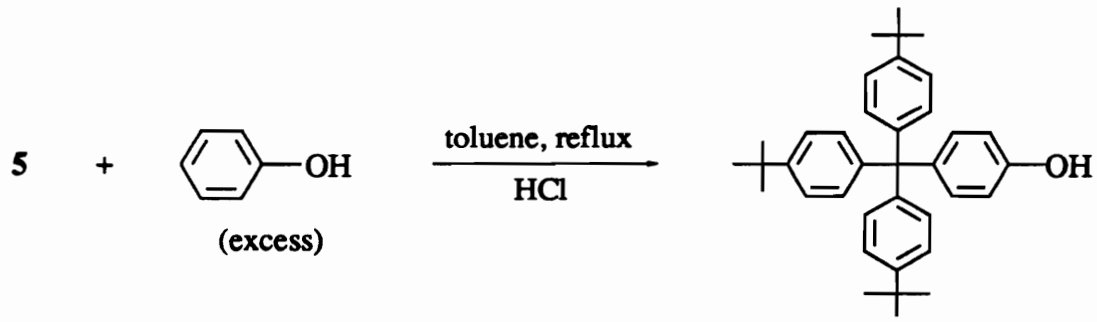


8 **9**

First, the synthesis of **11** was carried out by a reaction similar to the report by Mikroyannidis. [13] In the reaction (Scheme 3) compound **5** was converted to its tertiary chloride derivative **10** by the treatment of **5** with acetyl chloride in 94 % yield [7], and then the chloride was reacted with phenol to produce **11** *via* the Friedel-Crafts reaction. The total yield was higher than 90 %. [7] Stoddart et al. reported synthesis of **11** from the same route. They used thionyl chloride to synthesize **10** from **5** instead of acetyl chloride, but the yield (69 %) was lower. [9]

Alternatively, the reaction of **5** with phenol in the presence of catalytic amount of HCl gave **11** directly in 85 % yield. The reaction was an aromatic electrophilic substitution reaction in which carbocation **12** is formed by the acid catalyzed ionization of the

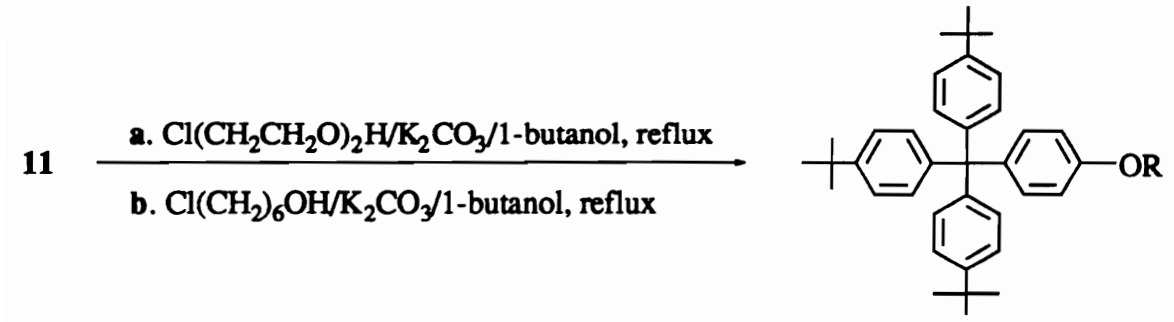
triarylmethanol (Scheme 4). The reaction can be carried out without a solvent. However, in that case the reaction mixture solidified as the reaction proceeded and it became difficult to stir the mixture. The addition of toluene made the reaction easier to handle while the reaction still proceeded rapidly under reflux. Compound **11** was easily recrystallized and it is soluble in common solvents such as $CHCl_3$, THF and toluene.



11

Compound **11** can be directly used as a blocking group for some polyrotaxanes without further modification; however, its utility is limited. For instance, **11** can not be used as a blocking group for the synthesis of polyester rotaxanes *via* transesterification reaction due to the lack of reactivity. Therefore, we modified **11** to prepare a diverse series of functional blocking groups for versatile utilizations.

The introduction of aliphatic hydroxyl units to the phenolic blocking group **11** was achieved by the reaction with α-chloro-ω-hydroxyl hydrocarbons or oligo(ethylene glycol) monochlorides. Thus, **11** was allowed to react with an excess of chloroethoxyethanol in a K_2CO_3/1-butanol system to give hydroxyl terminated blocking group **13a** in 50 % yield.



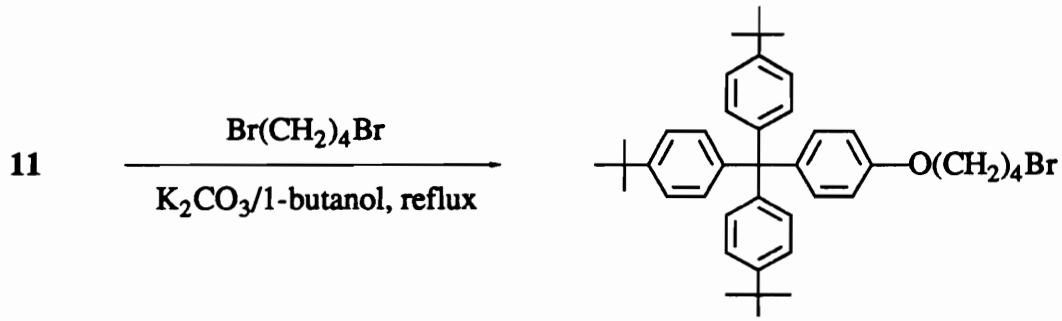
13

a. R=$(CH_2CH_2O)_2H$
b. R=$(CH_2)_6OH$

Stoddart and coworkers recently mentioned in a paper that the same reaction produced **13a** in 92 % yield without any detailed analytical data. [9] The lower yield (50 %) was probably due to the short reaction time and the loss of the product during the recrystallizations. However, a similar reaction of **11** with 6-chloro-1-hexanol gave 90 % yield, as expected. The reaction time was two days for this reaction. The melting points of **13** were 216.0-217.5 °C and 217.0-220.0 °C for **13a** and **13b**, respectively. Obviously, the introduction of flexible chains reduced the melting point of the starting material **11**, which is 301.0-301.8 °C. Thus, it is possible to adjust the melting point and solubility of hydroxyl terminated blocking groups by proper choice of chain length of the aliphatic segment. This adjustment may be necessary when the blocking group is applied to different reaction conditions.

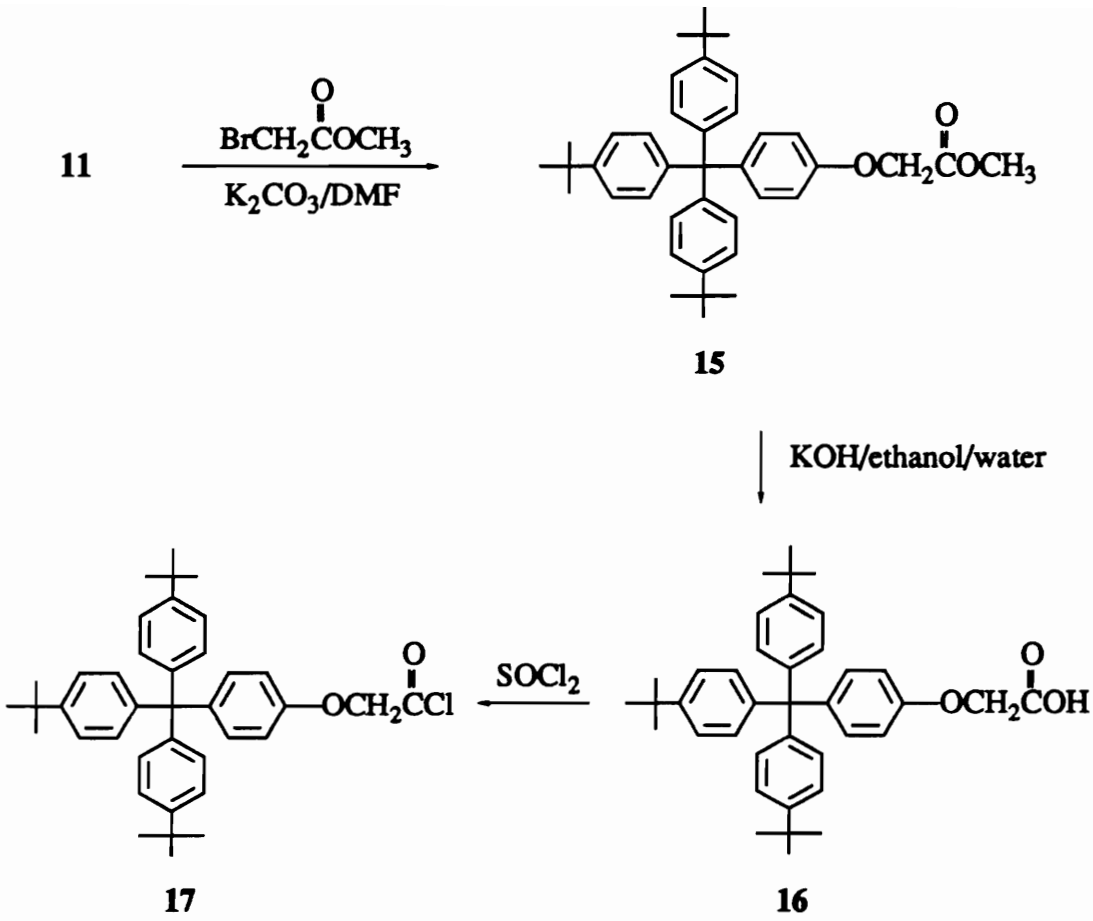
The blocking groups **13** are reactive toward electrophiles and can be used for the synthesis of polyester and polyurethane rotaxanes. For many cases blocking groups containing functional groups reactive toward nucleophiles are also needed. [11, 14] We were able to attach bromide or acid chloride terminated aliphatic chains to the blocking group **11**.

Compound **11** was allowed to react with a large excess of 1,4-dibromobutane under reflux in 1-butanol with K_2CO_3 as base to yield the aliphatic bromide terminated blocking group **14** as white crystals in 55 % yield. The melting point of **14** is 248.0-250.0 °C which is 30 °C higher than **13b**. The higher melting point is due to the shorter flexible aliphatic chain.



14

Synthesis of acid functional blocking group **16** was accomplished by the reaction of **11** with methyl bromoacetate, followed by hydrolysis. Phenolic blocking group **11** was treated with K_2CO_3 in DMF followed by the addition of methyl bromoacetate. The resultant product **15** was not isolated from the reaction mixture. Instead, after the solvent was removed ethanol and aqueous KOH were added directly to the solid residue. The mixture was initially not a solution because **15** was not soluble. However, upon stirring at room temperature the solid turned to very fine particles, which indicated that the conversion took place. Filtration of the suspension, followed by acidification gave the desired product **16** in 87 % yield. According to the ^1H NMR spectrum (Figure 2) the structure of the product was confirmed.



The acid blocking group **16** was converted into its acid chloride derivative **17** by treatment with thionyl chloride. The excess thionyl chloride was removed under dry conditions in order to prevent hydrolysis by moisture. Conversion was quantitative as shown in the ^1H NMR spectrum (Figure 3). Figure 3 showed that the reaction was complete because the peak at 4.62 ppm (CH_2) in Figure 2 disappeared; instead, a new peak appeared at 4.96 ppm. The product **17** was used without purification.

Acid chlorides are very reactive with various nucleophiles such as hydroxyl compounds. Bheda used **17** when he synthesized polyrotaxanes comprized of 30-crown-10 and an oligomeric poly(butylene oxide) and α,ω-aliphatic hydrocarbons. [11] As he noted, when an equimolar or slightly excess molar amount of **17** was used to block the

hydroxyl terminated linear molecules the resulting products were mixtures of diblocked, monoblocked and possibly unblocked products. Therefore, a series of experiments were carried out to address the blocking efficiencies of **17** for such linear compounds.

The model blocking reactions were performed in dry THF or diglyme, and pyridine was employed as acid scavenger. The linear molecules used for the study were poly(ethylene glycol)s (PEO) whose number average molecular weights were 3400, 10K and 100K. A small amount of dimethylaminopyridine (DMAP) as a catalyst was added to the reaction mixture. The reaction times were one day to five days.

$$\text{PEO} \quad + \quad \mathbf{17} \quad \xrightarrow[\text{THF, reflux}]{\text{pyridine/DMAP}} \quad \begin{matrix}\text{BG-PEO-BG +} \\ \text{BG-PEO + PEO}\end{matrix}$$

The first reaction was done using PEO (10K) and the acid chloride blocking group **17** which was used in 5.4 molar excess. After 29 hr reflux in THF, the mixture was poured into excess water in order to remove the unreacted blocking group. The product was soluble in water to leave a precipitate of the unreacted blocking group. For further purification, after evaporation of water, the solid product was dissolved in benzene and it was poured into large amount of hexane. Although hexane is a poor solvent for the blocking group and pyridine hydrochloride, which is a byproduct, due to the large excess amount, it was possible to further isolate/purify the product as a precipitate while the remaining blocking group was dissolved in hexane. The precipitate was collected by centrifugation (rpm=7000) and dried under vacuo at room temperature. The ^{1}H NMR spectrum (Figure 4) of the product indicated that the blocking yield was far from complete. The blocking yield was calculated from the peak integrations of *tert*-butyl and ethylene oxide groups in the spectrum and found to be 22 %.

Although acid chlorides are readily reactive with hydroxyl groups and the reactions are very fast even at room temperature, the above model reaction showed that a relatively high molecular weight PEO needs a large excess amount of blocking groups to achieve complete blocking. PEOs of lower molecular weight or oligo(ethylene oxide) need less blocking group to be blocked completely. This was proven by another model reaction using tetra(ethylene glycol) as the linear molecule.

$$\underset{1\ eq}{HO(CH_2CH_2O)_4H} + \underset{3\ eq}{\mathbf{17}} \xrightarrow[DME,\ reflux]{pyridine} 75\ \%\ blocking\ yield$$

The model reaction was carried out in dimethoxyethane (DME) at reflux. Small samples were taken from the reaction mixture directly to NMR tubes at certain reaction times, and the samples in the tubes were immediately placed in a vacuum desiccator and the solvent was evaporated. The samples were then analyzed by ^1H NMR. The ^{1} H NMR spectra of the samples (in $CDCl_3$) of reaction times of 0, 1, 6 and 42 hr were virtually the same (Figure 5), which means that the reaction was complete at the very initial stage. The methylene proton peak in the blocking group (-$OC\underline{H_2}COCl$) at 4.96 ppm disappeared even at 0 hr, and instead, two new peaks at 4.60 and 4.36 ppm appeared which correspond to the protons adjacent to the phenolic oxygen and the ester oxygen (Ar-$OC\underline{H_2}CO_2C\underline{H_2}CH_2$-), respectively. Thus, by integrations of the peaks (-$CO_2C\underline{H_2}CH_2O$- and -$C\underline{H_2}C\underline{H_2}O$-), it was possible to determine the blocking efficiencies. According to the ^1H NMR spectrum of the sample after 42 hr reaction, the blocking efficiency was about 75 %. This means that although a smaller amount of blocking group was used the blocking yield of this reaction was higher than the case of PEO (10K).

Therefore, a series of model reactions were carried out to investigate the relationship of molecular weight of linear molecules to be blocked and the amount of blocking group in terms of blocking efficiency. The reactions were done in DME at reflux and pyridine was used as acid scavenger as above. After evaporation of the solvent, the blocking efficiencies could be calculated by the integrations of the peaks of ethyleneoxy protons and terminal protons adjacent to the ester groups as described above. To enhance the resolution of the NMR machine the value of *np* (number of data points) was set for 128K instead of 37K which is normal for the proton nucleus. For example, Figure 6 is the ^{1}H NMR spectrum of 100 % blocked PEO (10 K) in DMSO-d_6; a small peak at 4.24 ppm corresponds to the terminal protons ($ArOCH_2COOCH_2CH_2O$-). The results of the study are summarized in Table 1.

It is clearly shown in Table 1 that higher molecular weight PEO requires a larger amount of blocking group for complete blocking. This result can be explained in terms of the dilution effect and chain entanglement. When the same molar ratios of PEO and the blocking group were used, the OH units in a higher molecular weight PEO were actually more dilute than a smaller one. Also, the hydroxyl groups in the PEO have less opportunity to encounter the blocking group molecules than a lower molecular weight PEO due to the more extensive chain entanglement which would wrap the OH units in the polymer chain segments, preventing the OH units from reacting with the blocking group molecules. The acid chloride blocking group **17** is hydrolytically unstable and it is not easy to handle and store it. In contrast, the acid blocking group **16** is more stable and readily purified by recrystallization. Therefore, to check the utilization of **16** as a blocking group two model reactions were carried out. The chemistry involved here is a coupling reaction in which N,N-dicyclohexylcarbodiimide (DCC) (**18**) is employed as coupling agent (Scheme 5). [15]

Table 1. Results of the end-capping study for PEO/17 system[a)]

M_n of PEO (g/mol)	Amount of BG (17) (molar equivalent to PEO)	Blocking efficiency (%)[b)]
$3.4x10^3$	2.9	40
	12.0	100
$1x10^4$	5.4[c)]	44
	16.0	87
	30.0	100
$1x10^5$	26.0	?[d)]

a) DME, reflux, 5 days.

b) Calculated by ^1H NMR spectra

c) THF, reflux, 29 hr.

d) could not be determined due to too small signal of the terminal CH_2 protons.

In the reaction **18** reacts with the acid **16** to form a reactive intermediate **19** which undergoes reaction with DMAP (**20**) to give another reactive intermediate **21** and a urea **22** which is a byproduct. The intermediate **21** reacts with hydroxyl group to give the final product **23**. The DCC coupling reaction is also known as a "room temperature esterification reaction" because it takes place even at room temperature

Thus, PEO (3400) was reacted with **16** in refluxing DME in the presence of DCC. A small amount of DMAP was added as catalyst. Although the reaction proceeds at room temperature, the mixture was refluxed to enhance the reaction rate. After 5 days of reflux, the urea, an insoluble solid, was filtered off and the residual solid from the filtrate after evaporation of the solvent was analyzed by ^1H NMR as described before. It was found

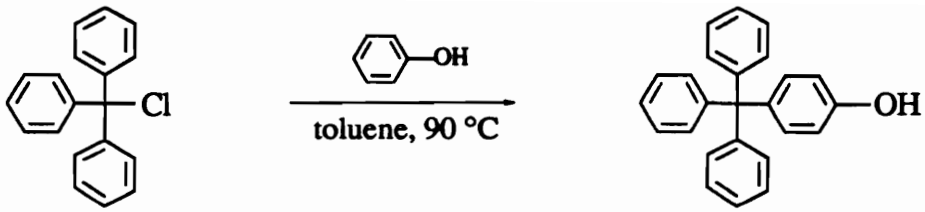
that this DCC coupling method was not so effective as the acid chloride method. As shown in Table 2, when the same amount of the blocking group was used, the blocking efficiency was lower than the acid chloride method. One of the reasons for the lower efficiency is probably a larger steric hindrance in the reaction of **16** or **19**, or **21** with PEO as compared with the case of the acid chloride method. In spite of the lower reactivity of **16** as compared with **17**, the results indicated that the acid could be used directly for the blocking reactions.

Table 2. Results of the end-capping study for PEO/acid BG system using DCC/DMAP[a)]

M_n of PEO	amount of BG (molar equivalent to PEO)	Blocking efficiency (%)
3400	4	45
	12	82

a) DME, reflux, 3 days.

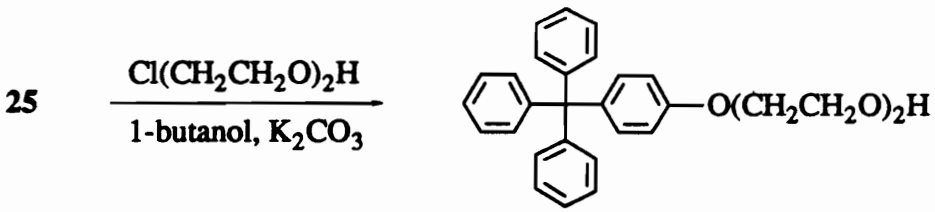
As discussed before, the trityl group can constrain up to 30-membered rings. A couple of blocking groups which contain trityl units were prepared. [3] The starting material for the synthesis is commercially available triphenylmethyl chloride (**24**). The compound **24** is reactive to nucleophiles such as hydroxyl and amino groups; however, as mentioned before the resultant polyrotaxanes are not stable due to the trityl-ether linkage. Thus, **24** was allowed to react with excess phenol in toluene solution. As the reaction proceeded, HCl gas evolved and the mixture solidified, indicating the product **25** was produced. The excess phenol was removed by pouring the mixture into a large amount of water. The crude product was filtered and it was subjected to recrystallization from a mixture of ethanol and acetone to give a 64 % yield. The yield was substantially lower than



24 **25**

expected. Although the solubility of **25** in water is very low, some crude **25** was dissolved and lost in the aqueous filtrate because a huge excess of water was used for the precipitation of the product. MacKenzie and Chuchani reported the synthesis of **25** in 92 % yield by the same procedure, but they did not report a detailed work-up process. [10] The product was nice sparkling crystals and its melting point was 287.5-291.5 °C.

Further modification of **25** by chain extension was achieved by the reaction of **25** with di(ethylene glycol) monochloride in refluxing 1-butanol with K_2CO_3 as base. The compound **26** dissolved better in 1-butanol than its analog **13a**. Also it has a lower melting point than **13a**. The better solubility and lower melting point may allow more versatile utilization in rotaxane syntheses. Therefore, if the macrocycle to be blocked is smaller than 30-membered it would be better to use **26** than **13a** in some cases.

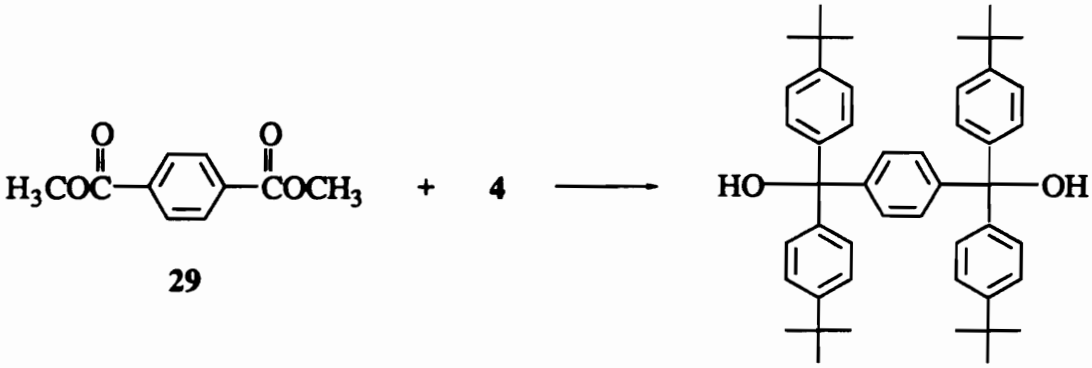


26

When triaryl derivatives are employed in the synthesis of polyrotaxanes the end capping of polymer chains is often not complete if an insufficient amount of the monofuctionalized blocking group is used. On the other hand, the use of excess blocking

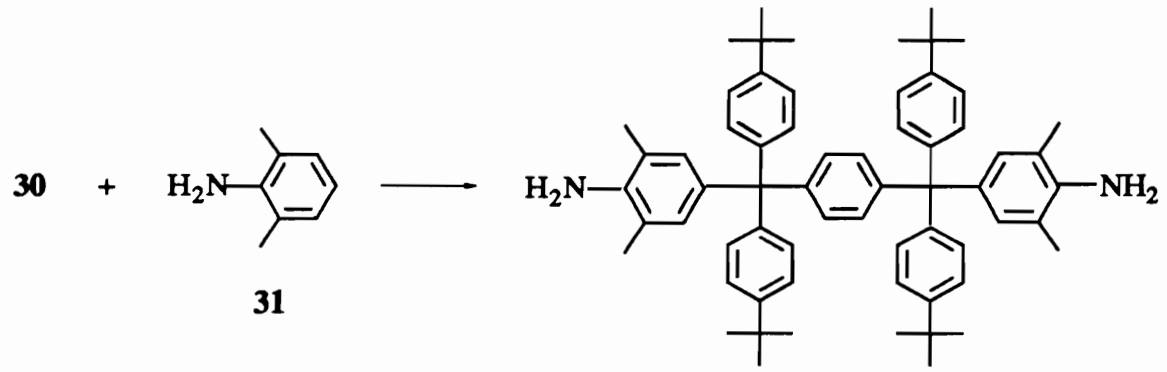
group to ensure complete blocking results in low molecular weight polymers due to the stoichiometric imbalance. However, as depicted in Scheme 6 if the blocking groups **27** can be polymerized and incorporated into the polymer backbone, we can constrain the macrocycles on the polymers and still obtain polyrotaxanes **28** with high molecular weights because there is no stoichiometric imbalance in the polymerizations. Another interesting aspect in using difunctional compounds **27** is that we are able to isolate the macrocycles from each other on the polymer backbone in this manner. The movement of macrocycles along the chains now will be limited by the incorporation of blocking groups in the polymers. By this system it is possible to investigate several phenomena related to the cyclic movement such as crystallization and phase transition behaviors of the threaded macrocycles.

Difunctional blocking group **30** was obtained by the reaction of dimethyl terephthalate (**29**) and the Grignard reagent **4**. [16] The crude product was subjected to recrystallization from toluene twice at room temperature to give crystals in 40 % yield. The ^{1}H NMR spectrum (Figure 7) confirmed the structure and it melted between 291.5-295.5 °C. Compound **30** can be further modified by introducing aliphatic chains at each side to make stable difunctional blocking groups with lower melting points as in the case of monoblocking groups.



29 **30**

30 was converted to dianiline blocking group **32** by the reaction with 2,6-dimethylaniline (**31**) in toluene solution with a catalytic amount of sulfuric acid. [16] The crude product was recystallized from toluene to give a 68 % yield and the ^1H NMR (Figure 8) supports the structure. Compound **32** did not melt up to 370 °C; it seemed to decompose above 330 °C and it turned dark in color.



CONCLUSIONS

Tri(*p-tert*-butylphenyl)methanol (**5**) was synthesized by Grignard reaction. It was found that 1,1,2,2-tetrakis(*p-tert*-butylphenyl)-1,2-dihydroxyethane (**7**), which was a byproduct, originated from the reductive coupling reaction between two molecules of the reaction intermediate di(*p-tert*-butylphenyl)ketone (**6**). The hydrolytically unstable **5** was modified by introduction of a phenolic moiety to prepare tri(*p-tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**), which is a stable blocking group. Compound **11** was further converted into a series of blocking groups: mono-*p*-[tris(*p-tert*-butylphenyl)methyl]phenyl ether of di(ethylene glycol) (**13a**), mono-*p*-[tris(*p-tert*-butylphenyl)methyl]phenyl ether of hexanediol (**13b**), 1-[*p*-{tris(*p-tert*-

butylphenyl)methyl}phenoxy]-4-bromobutane (**14**), *p*-[tris(*p*-*tert*-butylphenyl)methyl]-phenoxyacetic acid (**16**) and *p*-[tris(*p*-*tert*-butyl phenyl)methyl]phenoxyacetyl chloride (**17**). Those blocking groups were soluble in common solvents so that they can be used for the syntheses of polyrotaxanes. Using blocking groups **16** and **17** and PEOs as linear components, studies on the relationship of molecular weight *vs* blocking efficiency was carried out. The results showed that a higher moleculer weight of linear polymer requires a larger amount of blocking groups for complete blocking. *p*-Triphenylmethylphenol (**25**) was prepared and it was found to be more soluble than its analogue **11**. Compound **25** could be converted to the monotriphenylmethyl ether of di(ethylene glycol) (**26**) by introduction of a diethylene oxide unit. In a similar way, difuctional blocking groups 1,4-bis[bis(*p*-*tert*-butylphenyl)hydroxymethyl]benzene (**30**) and 1,4-bis[bis(*p*-*tert*-butylphenyl)(4'-amino-3',5'-dimethylphenyl)methyl]benzene (**32**), which can be used to prepare internally blocked polyrotaxanes, were made.

EXPERIMENTAL

Measurements. Melting points were taken in capillary tubes with a Melt-Temp II melting-point apparatus. IR spectra were obtained on Nicolet MX-1 or Perkin-Elmer 283B infrared spectrophotometers using KBr pellets unless otherwise noted. NMR spectra were obtained on a Varian Unity 400 MHz spectrometer at ambient temperature using tetramethylsilane as an internal standard. Elemental analyses were done by Atlantic Microlab of Norcross, GA. FAB mass spectra were obtained from the Mass Spectrometry Service Laboratory at the University of Nebraska, Lincoln, Nebraska using 3-nitrobenzyl alcohol (3-NBA) as matrix.

Ethyl *p-tert*-butylbenzoate (2). In a 2-L flask equipped with a condenser, a magnetic stirring bar and a heating mantle *p-tert*-butylbenzoic acid (**1**) (200.1 g, 1.12 mol), EtOH (1 L) and conc H_2SO_4 (98 %, 100 ml, 17.0 mol) were placed. The mixture was stirred at reflux for 44 hr. After most of the EtOH was evaporated 50 % NaOH aqueous solution was added until neutral to pH paper. The mixture was extracted with diethyl ether. Crude product was purified by vacuum distillation (81-85 °C/1 mm) to obtain 215 g (93 % yield) of colorless oil. (Lit: Aldrich Catalog, '96-'97 bp=122-124 °C/9 mm)
IR (KBr disc, cm^{-1}): 2945, 2885, 2700, 1706, 1598, 1450, 1397, 1355, 1264, 1173, 1100, 1007, 839, 759, 690. ^1H NMR ($CDCl_3$, ppm) : 1.33 (s, 9H, *t*-butyl), 1.38 (t, 3H, *J*=7.0 Hz, CH_3), 4.33 (q, 2H, *J*=7.0 Hz, OCH_2), 7.44 (d, *J*=11 Hz, 2H, arom.), 7.90 (d, *J*=11 Hz, 2H, arom.).

Tri(*p-tert*-butylphenyl)methanol (5). In a 500-mL flask fitted with a condenser, a magnetic stirring bar, a dropping funnel and a N_2 bubbler anhydrous THF (100 mL), Mg

turnings (11.40 g, 0.47 mol) and I_2 (catalytic amount) were placed. *p-tert*-Butylbromobenzene (**3**) (100.0 g, 0.47 mol) in THF (120 mL) was prepared. About 30 mL of this solution was added to the reaction mixture. The reaction mixture was warmed by a heating mantle and after 25 min the mixture started boiling. The remaining *p-tert*-butylbromobenzene (**3**) solution was added dropwise in such a way that the mixture kept boiling mildly. Addition of the *p-tert*-butylbromobenzene (**3**) solution was completed over 1 hr. The mixture was allowed to stir for 1 hr to make conversion complete. Ethyl *p-tert*-butylbenzoate (**2**) (47.3 g, 0.23 mol) in THF (100 mL) was added dropwise over a period of 1 hr. The mixture was stirred for 5 hr at reflux. Part of the THF was evaporated by rotary evaporation and 5 % HCl (400 mL) was added and the mixture was extracted with methylene chloride. After rotary evaporation of solvent the crude product was ground to a fine powder and washed with hot hexane. After a recrystallization from cyclohexane 64.6 g (70 % yield) of white crystals were obtained.

Mp: 210-214 °C (Lit. [8] mp=212-213 °C). IR (cm^{-1}): 3440, 2913, 2880, 2842, 1434, 1376, 1345, 1249, 1137, 1086, 983, 799, 685, 566. ^{1}H-NMR ($CDCl_3$): 1.31 (s, 27H, *t*-butyl), 7.19 (d, *J*=11 Hz, 6H, arom.), 7.33 (d, *J*=11 Hz, 6H, arom.).

1,1,2,2-Tetrakis(*p-tert*-butylphenyl)-1,2-dihydroxyethane (7). In a 50-mL flask equipped with a magnetic stirring bar, a condenser and a N_2 bubbler Mg turnings (0.13 g, 5.40 mmol), I_2 (0.12 g, 0.47 mmol) and THF (12 mL, dried over Na/benzophenone) were placed and followed by the addition of *p-tert*-butylphenyl ketone (**6**) (0.20 g, 0.68 mmol, synthesized by reaction of 4-*tert*-butylbenzoyl chloride and phenol). The color of the solution changed gradually from purple-blue to brown during the initial 20 min at room temperature. The mixture then was heated to mild reflux. The color of the mixture turned to greenish-white. During three hours stirring the solution became

gray. The reaction mixture were filtered to remove salts and THF was removed by rotary evaporation. The residual yellow solid was extracted with CH_2Cl_2 and the solution was treated with ice-water/HCl to give a clear reddish-orange solution. The organic layer was separated and CH_2Cl_2 was rotary evaporated. The yellow solid was dried under vacuum. According to the ^1H NMR spectrum in $CDCl_3$ the solid contained 75 mol % (0.15 g) of the product. The product was purified by recrystallization from methanol.

Mp: 199.6-200.4 °C (Lit [7] mp=199.6-200.4 °C). IR (cm^{-1}): 3579, 2960, 2865, 1509, 1476, 1462, 1400, 1362, 1270, 1110, 1040, 1017, 839, 828, 801, 695. ^1H NMR ($CDCl_3$): 1.26 (s, 36H, *t*-butyl), 2.97 (s, 2H, OH), 7.17 (q, *J*=6.8 Hz, 16H, arom.). Anal. Calcd for $C_{42}H_{54}O_2$: C, 85.37; H, 9.21; found: C, 85.10; H, 9.21.

Tri(*p-tert*-butylphenyl)-*p*-hydroxyphenylmethane (11). In a 250-mL round-bottomed flask equipped with a condenser and a magnetic stirring bar phenol (70.0 g, 0.74 mol), tri(*p-tert*-butylphenyl)methanol (**5**) and a few drops of conc. H_2SO_4 were placed. The reaction mixture was heated to reflux using a heating mantle. Just after it began to reflux the reaction mixture solidified and did not stir. Toluene (75 mL) was added to dilute the reaction mixture and it was allowed to stir at reflux for 5 days. Aqueous NaOH (5 wt %, 400 mL) was added to the reaction mixture and it was extracted with toluene (400 mL x 3). The combined organic phase was washed with aqueous NaOH (5 wt %, 400 mL x 3) and water (500 mL x 3). The aqueous layer was acidified by addition of conc HCl and it was extracted with toluene again. Organic layers were combined and toluene was rotary evaporated. 30 g of crude product was recystallized from toluene/hexane mixture (2/1, v/v) to give 22 g (75 % yield) of a slighly yellowish white crystals.

Mp : 293.0 °C- 294.5 °C (Lit. [9] mp=235-237 °C). IR (cm^{-1}): 3598, 3486, 2959, 2900, 2865, 1604, 1507, 1459, 1399, 1363, 1269, 1221, 1179, 1108, 1020, 847, 821, 703,

700. ^{1}H NMR ($CDCl_3$) : 1.30 (s, 27H, *t*-butyl), 4.62 (s, 1H, OH), 6.70 (d, *J*=11 Hz, 2H, arom.), 7.15 (m, 14H, arom.).

Mono-*p*-[tris(*p-tert*-butylphenyl)methyl]phenyl ether of di(ethylene glycol) (13a). In a 250-mL flask equipped with a condenser, a N_2 bubbler and a magnetic stirring bar tri(*p-tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**) (3.00 g, 5.9 mmol) and K_2CO_3 (2.46 g, 17.8 mmol) were mixed with 1-butanol (60 mL) and the mixture was refluxed for 3 hr. To the mixture di(ethylene glycol) monochloride (Aldrich, 3.00 g, 24.0 mmol) was added all at once. After refluxing for 21 hr the mixture was cooled to room temperature and CH_2Cl_2 (30 mL) was added. The salts were filtered and discarded. The solvent was rotary evaporated and the residual solid was dissolved in hot acetone (70 mL). The acetone solution was filtered to remove a small amount of insoluble material and it was placed in the refrigerator (- 20 °C). The crystals were subjected to a second recrystallization from acetone to give white powdery crystals. The yield was 1.75 g (50 %).
Mp: 216.0-217.5 °C (Lit. [7] mp=218.3-218.6 °C). IR (cm^{-1}): 3400, 2931, 2845, 1484, 1443, 1380, 1349, 1232, 1167, 1100, 1040, 1000, 803, 566. ^{1}H NMR ($CDCl_3$): 1.30 (s, 27H, *t*-butyl), 3.67 (t, *J*=5.2 Hz, 2H, $C\underline{H_2}CH_2OH$), 3.76 (t, *J*=3.6 Hz, 2H, $C\underline{H_2}OH$), 3.86 (t, *J*=3.2 Hz, 2H, $CH_2C\underline{H_2}OCH_2CH_2OH$), 4.11 (t, *J*=4.8 Hz, 2H, $ArOC\underline{H_2}$-), 6.78 (d, *J*=8.8 Hz, 2H, arom. adjacent to OCH_2-), 7.08 (m, 8H, arom.), 7.23 (d, *J*=8.8 Hz, 6H, arom.). ^{13}C NMR ($CDCl_3$): 31.37, 34.29, 61.81, 63.04, 67.20, 69.72, 72.52, 113.03, 124.03, 130.69, 132.26, 139.97, 144.07, 148.30, 156.39 (theory 15, found 15).

Mono-*p*-[tris(*p-tert*-butylphenyl)methyl]phenyl ether of 1,6-hexanediol (13b). Tri(*p-tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**) (5.0 g, 9.90 mmol) was dissolved in refluxing 1-butanol (100 mL) in a 250-mL flask equipped with a condenser, a

N_2 bubbler and a magnetic stirring bar. To the solution K_2CO_3 (4.1 g, 29 mmol) was added and the mixture was refluxed for 3 hr. 6-Chlorohexan-1-ol (6.7 g, 49 mmol) was added and the mixture was refluxed 2 days, cooled down to room temperature and the salts were filtered and discarded. After rotary evaporation of 1-butanol the residual solid was dissolved in CH_2Cl_2 (100 mL) and the solution was washed with water (100 mL x 2). The organic layer was dried over $MgSO_4$ and the solvent was rotary evaporated. The residual solid was subjected to three recrystallizations from acetone at - 20 °C. The yield was 5.3 g (90 %).

Mp: 217.0-220.0 °C. IR (cm^{-1}): 3340, 2880, 1444, 1373, 1348, 1224, 1162, 994, 555. ^1H NMR ($CDCl_3$): 1.30 (s, 27H, *t*-butyl), 1.45 (m, 4H, $OCH_2CH_2C\underline{H_2}\underline{CH_2}CH_2CH_2OH$), 1.60 (p, *J*=6.8 Hz, 2H, $OCH_2CH_2CH_2CH_2$-$C\underline{H_2}CH_2OH$), 1.78 (p, *J*=6.8 Hz, 2H, $OCH_2C\underline{H_2}CH_2CH_2CH_2CH_2OH$), 3.65 (t, *J*=6.4 Hz, 2H, $OCH_2CH_2CH_2CH_2CH_2C\underline{H_2}OH$), 3.93 (t, *J*=6.4 Hz, 1H, $OC\underline{H_2}CH_2CH_2CH_2CH_2CH_2$ -OH), 6.75 (d, *J*=8.8 Hz, 2H, arom. adjacent to OCH_2-), 7.08 (m, 8H, arom.), 7.22 (d, *J*=8.8 Hz, 6H, arom.). Anal. Calcd for $C_{43}H_{56}O_2$/ 1/3 CH_3COCH_3: C, 84.66; H, 9.37; found: C, 84.72; H, 9.30.

1-[*p*-[Tris(*p*-*tert*-butylphenyl)methyl]phenoxy]-4-bromobutane (14). In a 500-mL flask equipped with a condenser, a N_2 system and a magnetic stirring bar the phenolic blocking group **11** (8.0 g, 15.9 mmol), K_2CO_3 (6.6 g, 47 mmol) and 1-butanol (100 mL) were placed. The mixture was refluxed for 2 hr. 1,4-Dibromobutane (68.0 g, 317 mmol) was added to the mixture all at once. The mixture was refluxed for 17 hr. The mixture was cooled down and the salts were filtered and discarded. The solvent was removed by rotary evaporation. The excess 1,4-dibromobutane was recovered by vacuum distillation. The residual soild was subjected to a column chromatography (silica-gel) using

a mixture of CH_2Cl_2 and hexanes (1/10, v/v) as eluting solvent. The crude solid product was subjected to a recrystallization from a mixture of hexane and chloroform (4/1, v/v). White crystals (5.6 g, 55 % yield) were obtained.

Mp: 248.0-250.0 °C. IR (cm^{-1}): 2925, 2844, 1481, 1450, 1376, 1349, 1330, 1167, 1000, 802, 561. ^1H NMR ($CDCl_3$): 1.92 (p, *J*=6.0 Hz, 2H, $C\underline{H_2}CH_2Br$), 2.06 (p, *J*=7.6 Hz, 2H, $ArOCH_2C\underline{H_2}$-), 3.48 (t, *J*=6.6 Hz, 2H, $C\underline{H_2}Br$), 3.97 (t, *J*=6.0 Hz, 2H, $ArOC\underline{H_2}$), 6.75 (d, *J*=9.2 Hz, 2H, arom. adjacent to OCH_2), 7.08 (d, *J*=8.4 Hz, 8H, arom.), 7.23 (d, *J*=8.8 Hz, 6H, arom.). ^{13}C NMR ($CDCl_3$): 27.97, 29.53, 31.38, 33.53, 34.29, 63.04, 66.62, 112.89, 124.02, 130.71, 132.25, 139.66, 144.12, 148.30, 156.64 (theory 15, found 15). Anal. Calcd for $C_{41}H_{51}OBr$: C, 76.97; H, 8.03; found: C, 77.01; H, 8.03.

***p*-[Tris(*p-tert*-butylphenyl)methyl]phenoxyacetic acid (16).** *p*-Hydroxyphenyl-tris(*p-tert*-butylphenyl)methane (**11**) (11.60 g, 23 mmol mol) was dissolved in DMF (200 mL). To the mixture K_2CO_3 (9.02 g, 65 mmol) was added and it was stirred at 90 °C overnight. To this suspension methyl bromoacetate (25.5 g, 167 mmol) was added and the mixture was stirred at 100-110 °C for three days. It was filtered to remove salts and DMF was removed by rotary evaporation. To the residual solid ethanol (250 mL) and KOH (87 %, 4.3 g, 67 mmol) in water (50 mL) were added and the suspension was stirred at 70 °C for 20 min. Upon addition of KOH precipitation occurred and the mixture was difficult to stir. Thus water (150 mL) was added to the mixture, and it was stirred overnight. The mixture was acidfied with conc HCl down to pH 1-2 to pH paper, and it was stirred overnight. The precipitate was filtered and washed with water until the filtrate was neutral to pH paper. The fine white powder was dried under vacuo. The yield was 10.5 g (87 % yield).

Mp: 297.5-299.0 °C (Lit. [7] mp=297.5-299.0 °C) IR (cm^{-1}): 3300, 2927, 2845, 1720, 1482, 1447, 1371, 1350, 1250, 1199, 1170, 1062, 1003, 806, 566. ^1H NMR ($CDCl_3$): 1.30 (s, 27H, *t*-butyl), 4.62 (s, 2H, CH_2), 6.78 (d, *J*=8.4 Hz, 2H, arom.), 7.06 (d, *J*=8.4 Hz, 6H, arom.), 7.18 (d, *J*=8.4 Hz, 2H, arom.), 7.22 (d, *J*=8.4 Hz, 6H, arom.)

***p*-[Tris(*p-tert*-butylphenyl)methyl]phenoxyacetyl chloride (17).** *p*-[Tris(*p-tert*-butylphenyl)methyl]phenoxyacetic acid (**16**) (6.15 g, 10.9 mmol) was placed in a 250-mL flask equipped with a magnetic stirring bar, a condenser and a N_2 bubbler. To this was added 40 mL of thionyl chloride, and the mixture was refluxed for 9 hr to obtain a light yellow solution. It was cooled, and excess thionyl chloride was removed under aspirator vacuum with a drying tube connected between the aspirator and the mixture. The residual solid was further dried under vacuum 2 hr. 6.7 g (99 % yield) of light yellow solid was obtained. The product was used without purification.
Mp=270-272 °C (Lit. [7] mp=270-272 °C). IR: ^1H NMR ($CDCl_3$): 1.30 (s, 27H, *t*-butyl), 4.96 (s, 2H, CH_2), 6.75 (d, *J*=8.4 Hz, 2H, arom.), 7.06 (d, *J*=8.4 Hz, 6H, arom.), 7.13 (d, *J*=8.4 Hz, 2H, arom.), 7.23 (d, *J*=8.4 Hz, 6H, arom.)

Blocked poly(ethylene oxide) (acid chloride method, typical). In a 100-mL flask equipped with a condenser, a magnetic stirring bar and a N_2 bubbler poly(ethylene oxide) (PEO) (M_w=10K) (0.20 g, 0.04 mmol), acid chloride bocking group **17** (0.35 g, 0.6 mmol), pyridine (5 drops) and dimethoxyethane (DME) (dried and distilled over Na/benzophenone, 50 mL) were placed and the mixture was stirred for 5 days. DME was removed by rotary evaporation and the residual solid was further dried under vacuum at room temperature. The crude product was analyzed by ^1H NMR.

Blocked poly(ethylene oxide) (DCC coupling method, typical). PEO-3400 (0.30 g, 0.09 mmol), acid blocking group (**16**) (0.60 g, 1.14 mmol), dicyclohexylcarbodiimide (DCC) (0.49 g, 2.37 mmol), dimethylaminopyridine (DMAP) (15 mg, 0.12 mmol) and DME (30 mL) were stirred at reflux for 3 days. The mixture was filtered and the precipitate was washed with CH_2Cl_2. The solvent was rotary evaporated and the residual solid was further dried under vacuum. The crude product was analyzed by ^1H NMR.

***p*-Triphenylmethylphenol (25).** Phenol (20.3 g, 0.22 mol) was placed in a 250-mL flask equipped with a condenser, a N_2 system and a magnetic stirring bar. Triphenylmethyl chloride (**24**) (30.0 g, 0.11 mol) in toluene (60 mL) was added dropwise to the phenol. During the addition of **24** the mixture turned dark and HCl gas was generated. The mixture was stirred at 90 °C for 24 hr. The mixture solidified as reaction proceeded. The mixture was cooled to room temperature and THF (150 mL) was added. The suspension was poured into water (4 L) and the precipitate was filtered. Another such precipitation process was carried out. The precipitate was subjected to a recrystallization from a mixture of ethanol and acetone (2/1, v/v) at - 20 °C. 23 g (64 % yield) of crystals were obtained.

Mp: 287.5-291.5 °C (Lit. [10] mp=284-285 °C). IR (cm^{-1}): 3483, 3410, 2993, 1568, 1458, 1410, 1234, 1134, 790, 723, 670, 600, 567. ^1H NMR (DMSO-d_6): 6.65 (d, J=8.8 Hz, 2H, arom.), 6.88 (d, J=8.8 Hz, 2H, arom.), 7.10 (d, J=7.2 Hz, 6H, arom.), 7.17 (t, J=7.6 Hz, 3H, arom.), 7.26 (t, J=8.0 Hz, 6H, arom.), 9.36 (s, 1H, OH). ^{13}C NMR (DMSO-d_6): 64.16, 114.81, 126.25, 128.01, 130.90, 132.00, 137.01, 147.28, 155.69 (theory 9, found 9).

Mono-triphenylmethyl ether of di(ethylene glycol) (26). A mixture of triphenylmethane (**25**) (10.0 g, 30 mmol), 1-butanol (100 mL) and K_2CO_3 (8.2 g, 60 mmol) were refluxed in a 250-mL flask for 2 hr. Di(ethylene glycol) monochloride (Aldrich, 7.5 g, 60 mmol) was added to the mixture all at once. The mixture was refluxed for 4 days. The mixture was cooled down to room temperature and the salts was filtered and discarded. The solvent was rotary evaporated and the residual solid was recrystallized from ethanol at - 20 °C. 10.7 g (85 % yield) of powdery crystals were obtained.

Mp: 145.0-147.5 °C. IR (cm^{-1}): 3400, 2990, 2883, 2835, 1571, 1458, 1420, 1225, 1160, 1094, 1006, 794, 723, 671, 590. ^1H NMR ($CDCl_3$): 3.67 (t, *J*=4.8 Hz, 2H, $C\underline{H}_2CH_2OH$), 3.76 (t, *J*=4.8 Hz, 2H, $ArOCH_2C\underline{H}_2O$), 3.85 (t, *J*=4.8 Hz, 2H, $CH_2C\underline{H}_2OH$), 4.11 (t, *J*=4.8 Hz, 2H, $ArOC\underline{H}_2CH_2O$), 6.79 (d, *J*=8.8 Hz, 2H, arom.), 7.10 (d, *J*=8.8 Hz, 2H, arom.), 7.21 (m, 15H, arom.). ^{13}C NMR ($CDCl_3$): 61.81, 64.30, 67.24, 69.70, 72.53, 113.33, 125.85, 127.42, 131.10, 132.22, 139.36, 146.97, 156.56 (theory 13, found 13). Anal. Calcd for $C_{29}H_{28}O_3$: C, 82.05; H, 6.65; found: C, 81.91; H, 6.69.

***p*-Bis[bis(*p*-*tert*-butylphenyl)hydroxymethyl]benzene (30).** In an oven-dried 1-L 3-neck round-bottomed flask equipped with a magnetic stirring bar and a condenser, oven-dried Mg turnings (7.30 g, 0.30 mol) and dry THF (500 mL) were placed. 1-Bromo-4-*tert*-butylbenzene (**3**) (60.0 g, 0.28 mol) was added slowly to the mixture over 1.5 hours with mild heating. During the addition lots of heat was generated. The dark gray/brown mixture was refluxed for further 1.5 hours. A small portion of dimethyl terephthalate (**27**) was added to the flask, and the solution refluxed vigorously and the color of the reaction mixture turned to deep red. The remainder of the dimethyl terephthalate (**27**) (total 12.20 g, 63 mmol) in THF (30 mL) was added to the reaction

mixture dropwise. The mixture was refluxed overnight under N_2 flow. About 200 mL of THF was rotary evaporated and the residual solution was poured into 500 mL of 10 % aq HCl. Lots of heat was generated. Several pieces of ice were added to dissipate the heat. The deep reddish-brown color changed to yellow. The solution was extracted with CH_2Cl_2 (500 mL x 2) and the organic layer was washed with water (500 mL x 2). CH_2Cl_2 was rotary evaporated and the residual solid was recrystallized from toluene at room temperature overnight to give 18 g of slightly yellow crystals. A recrystallization from toluene (350 mL) at -20 °C gave 16.7 g (40 % yield) of white crystals.

Mp: 291.5-295.5 °C (Lit. [16] mp=291.5-295.5 °C). IR (cm^{-1}): 3410, 2930, 2830, 1448, 1380, 1346, 1290, 1253, 1150, 984, 800, 690, 555. ^1H NMR ($CDCl_3$): 1.30 (s, 36H, *t*-butyl), 2.75 (s, 2H, OH), 7.17 (d, *J*=8.8 Hz, 8H, arom.), 7.21 (s, 4H, arom.), 7.31 (d, *J*=8.8 Hz, 8H, arom.). ^{13}C NMR ($CDCl_3$): 31.3, 34.4, 81.5, 124.7, 127.3, 127.5, 143.9, 145.8, 149.9 (theory 9, found 9). MS (EI): 666 (M^+), 646 (M^+-OH), 533 (M^+-$C_6H_4C_4H_9$), 307, 154.

***p*-Bis[bis(*p*-*tert*-butylphenyl)(4'-amino-3',5'-dimethylphenyl)methyl]-benzene (32).** In a 100-mL 1-neck round-bottomed flask equipped with a condenser, a magnetic stirring bar and a N_2 bubbler on the top of the condenser, compound **28** (8.50 g, 12.7 mmol) and 2,6-dimethylaniline (**29**) (30.0 g, 248 mmol) were placed. Toluene (14 mL) and 6 drops of conc H_2SO_4 were added to the mixture. The mixture was allowed to reflux for two days. ^1H-NMR indicated the reaction was incomplete and further reaction was allowed at reflux for 5 days. The reaction mixture was poured into CH_2Cl_2 (400 mL) and aqueous NaOH (0.1 M, 250 mL) was added to make the solution slightly basic. The organic phase was separated and washed with water (250 mL). After CH_2Cl_2 was

removed, the crude product was recrystallized from toluene at - 20 °C to give 7.5 g (68 % yield) of white crystals.

No melting point was observed up to 370 °C (Lit. [16] no mp was observed up to 370 °C). IR (cm^{-1}): 3420, 3345, 2908, 2823, 1590, 1455, 1359, 1340, 1246, 1105, 993, 788, 549. ^{1}H NMR ($CDCl_3$) : 1.29 (s, 36H, *t*-butyl), 2.07 (s, 12H, CH_3), 3.49 (broad s, 4H, NH_2), 6.69 (s, 4H, arom.), 7.01 (s, 4H, arom.), 7.08 (d, *J*=8.4 Hz, 8H, arom.), 7.21 (d, *J*=8.4 Hz, 8H, arom.). ^{13}C NMR ($CDCl_3$): 18.0, 31.4, 34.3, 63.1, 120.2, 123.8, 130.0, 130.9, 131.2, 136.7, 140.3, 144.4, 144.7, 148.1 (theory 14, found 14). MS (EI): 872.5 (M^+), 752.5 (M^+-$C_6H_2(CH_3)_2$-NH_2), 619.4 (M^+-$C_6H_4C_4H_9$-$C_6H_2(CH_3)_2NH_2$), 460.1, 398.3, 307.1, 154.1.

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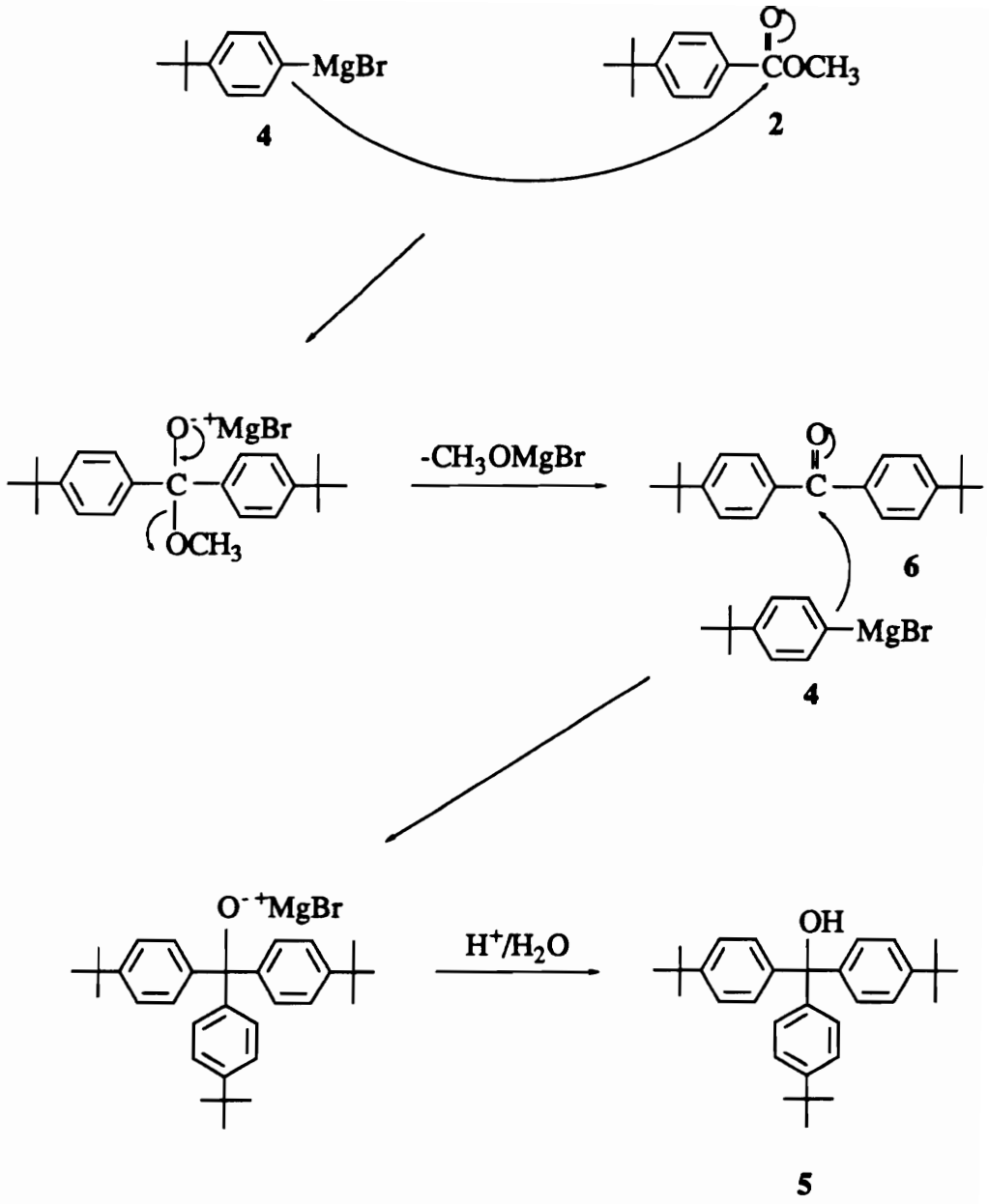
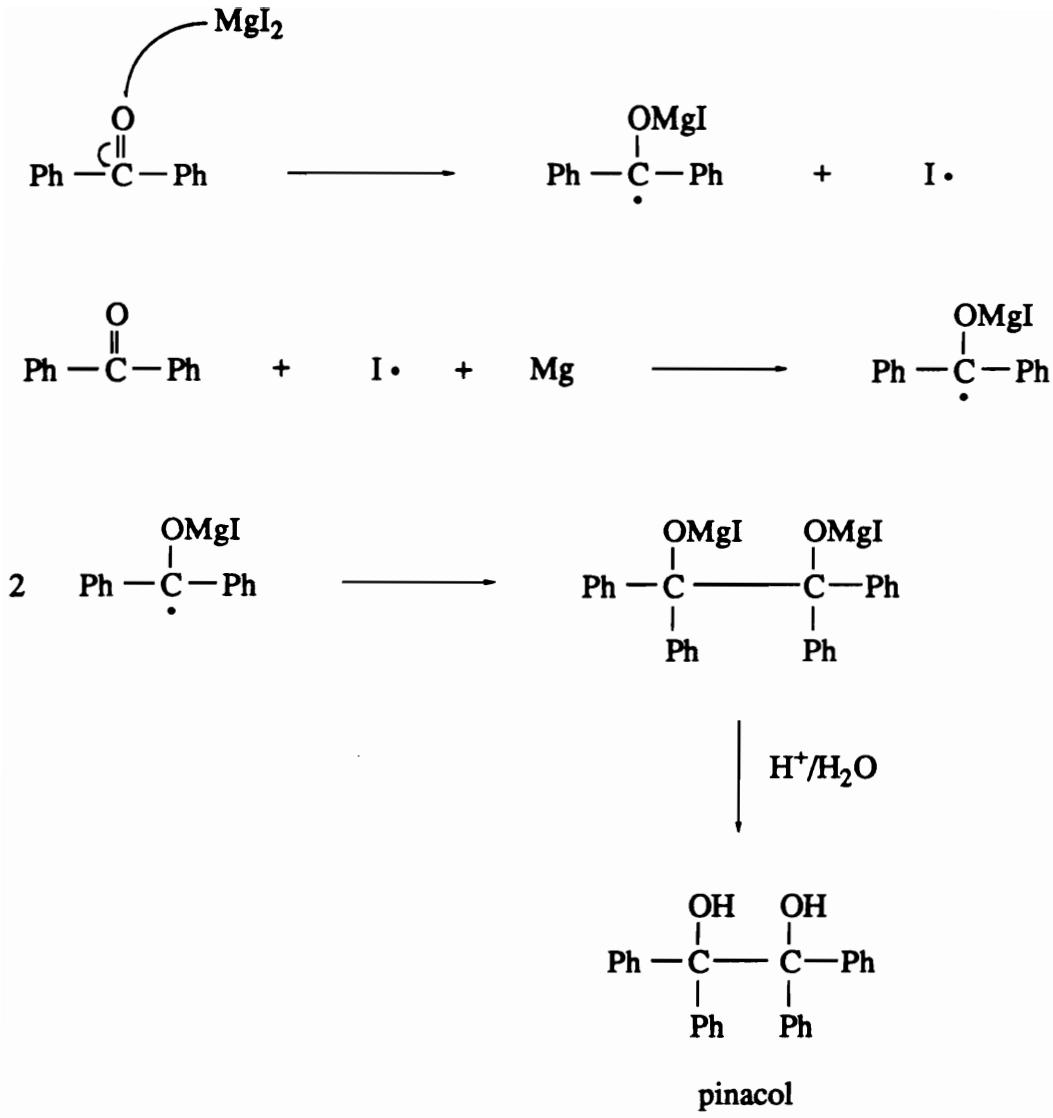
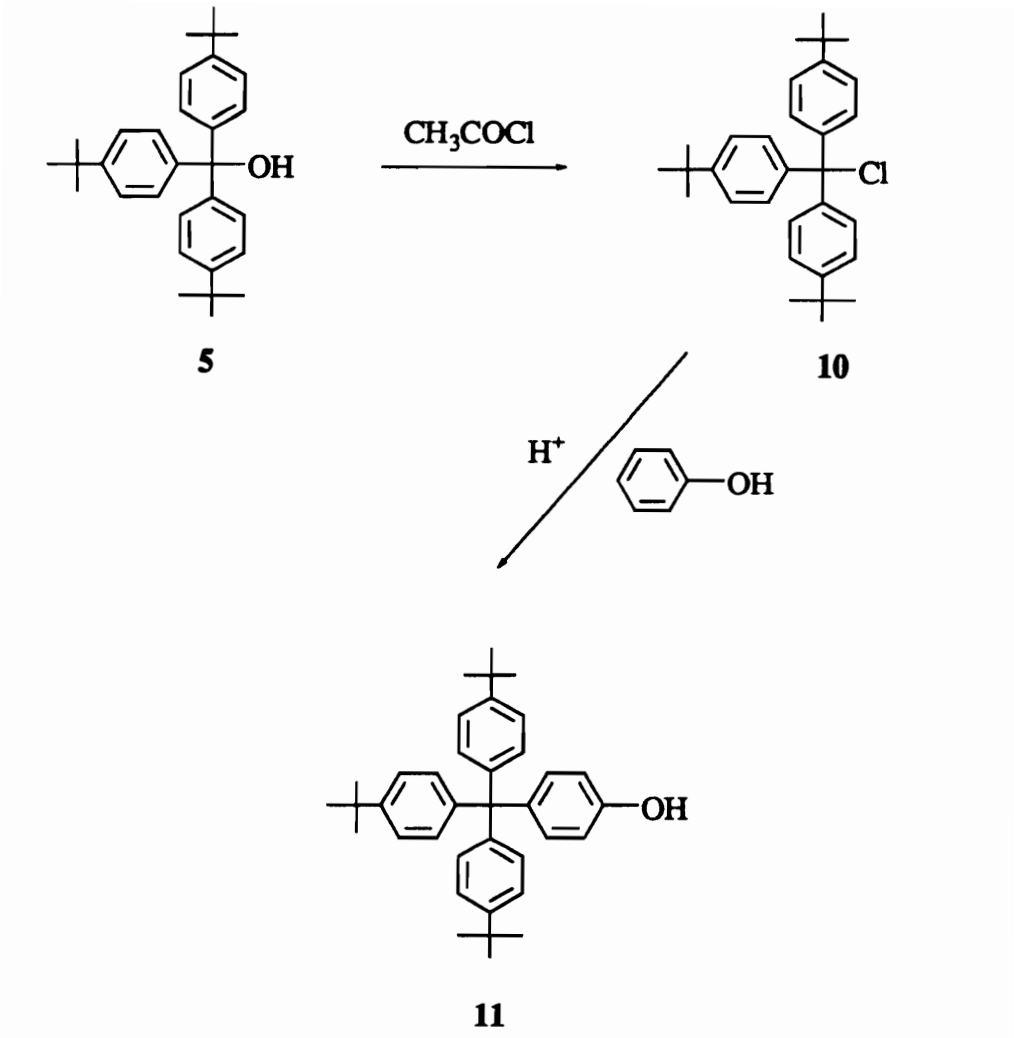


Scheme 1. Mechanism of the Grignard reaction.

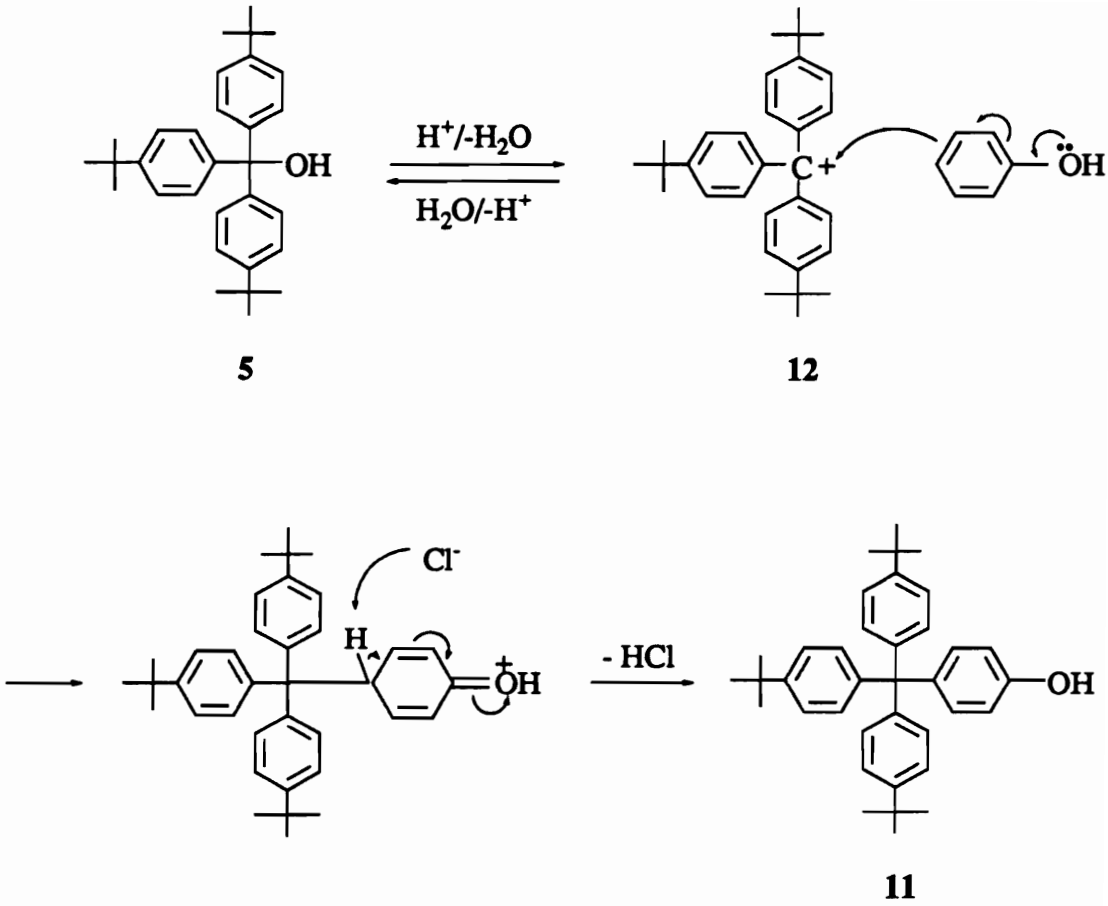


Scheme 2. Mechanism of pinacol formation.

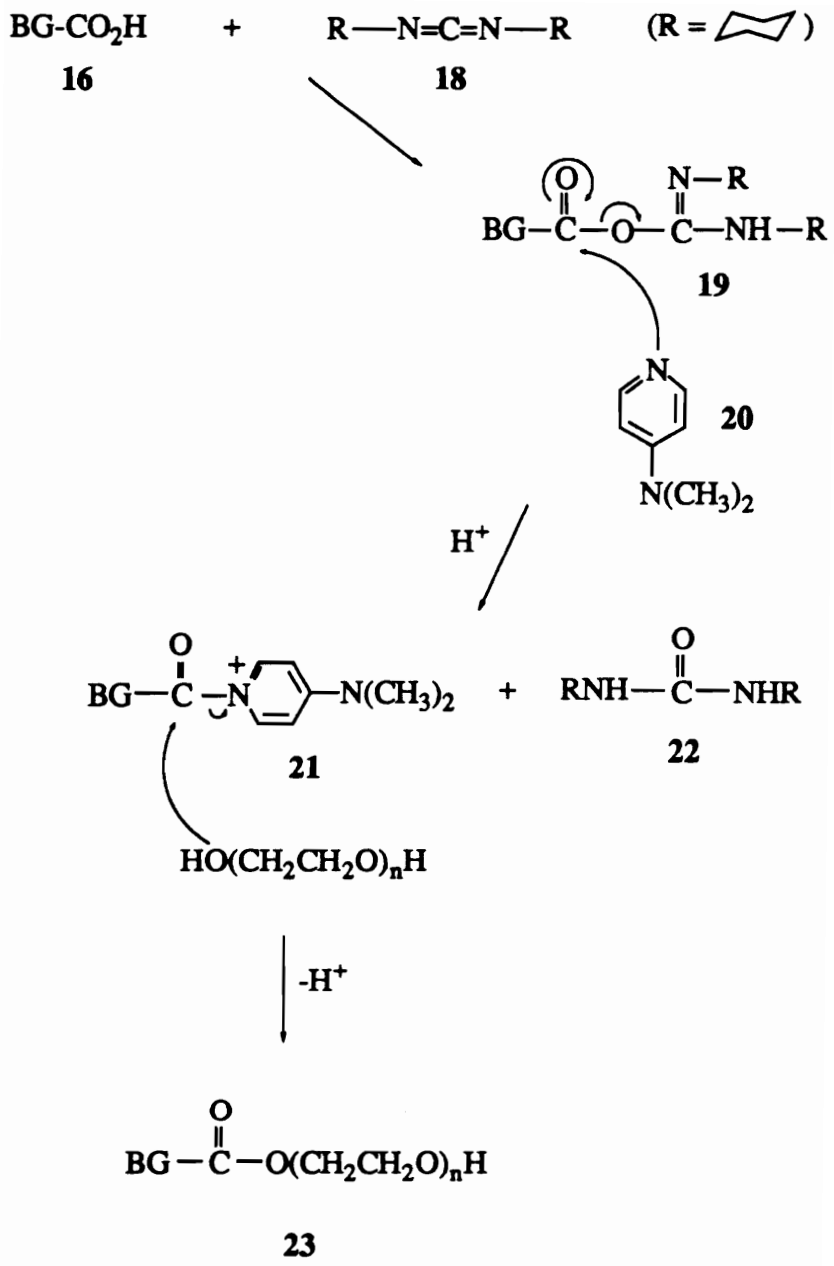


5 **10** **11**

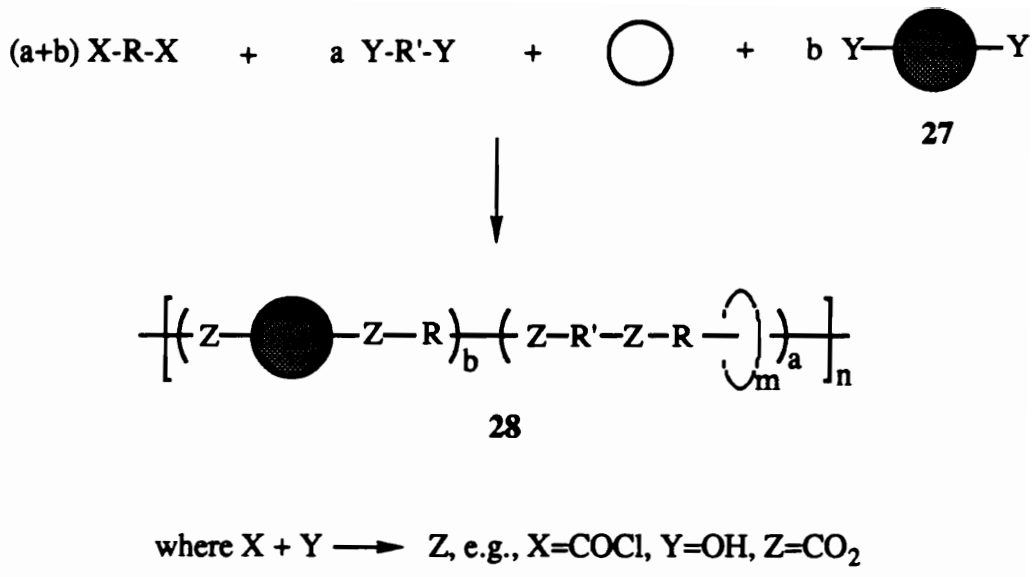
Scheme 3. Synthesis of tri(*p*-*tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**) by Fridel-Crafts reaction.



Scheme 4. Synthesis of tri(*p*-*tert*-butylphenyl)-*p*-hydroxyphenylmethane (**11**) by aromatic electrophilic substitution reaction.



Scheme 5. Mechanism of esterification by DCC coupling.



Scheme 6. Syntheses of polyrotaxanes using difunctional blocking group **27**.

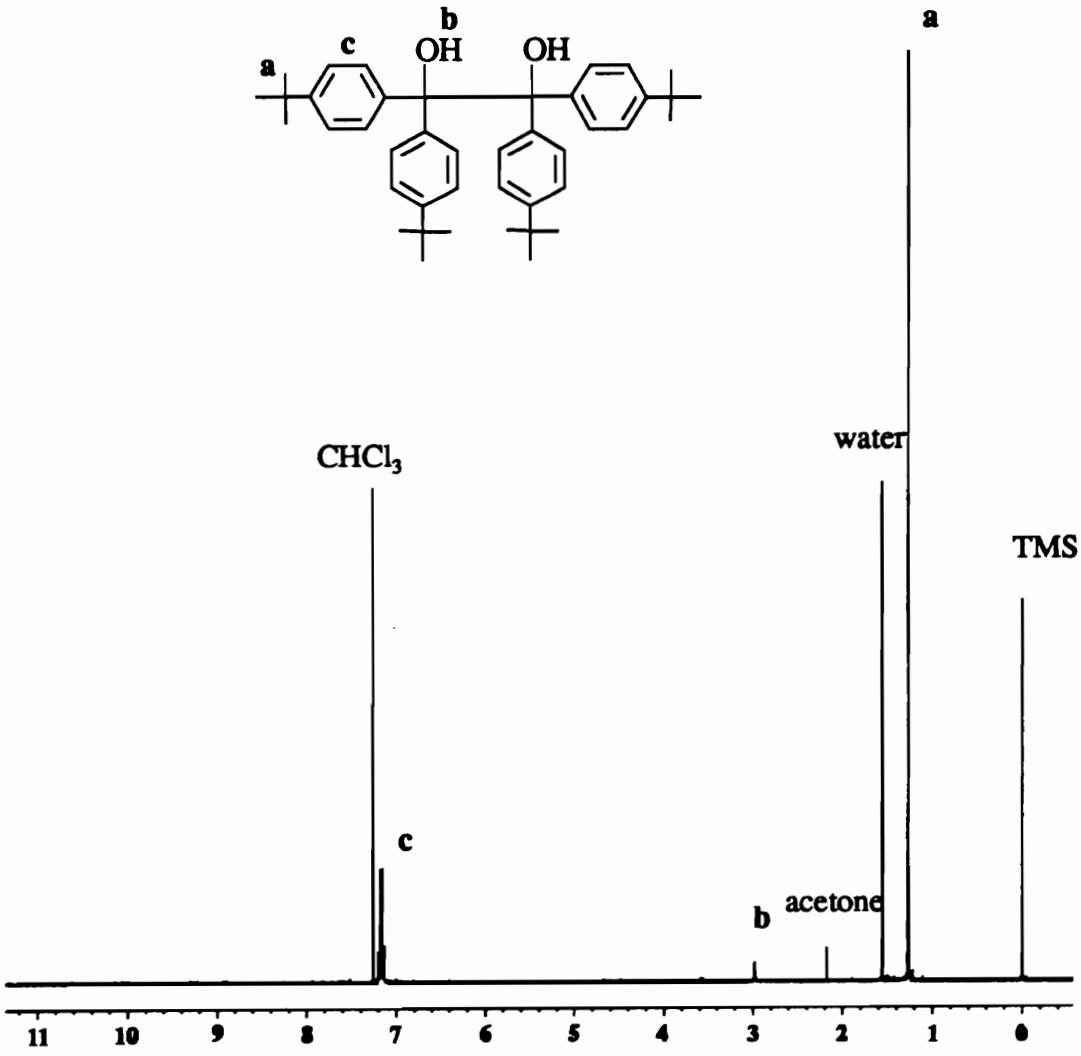


Figure 1. ^1H NMR spectrum of pinacol **7** ($CDCl_3$, 400 MHz).

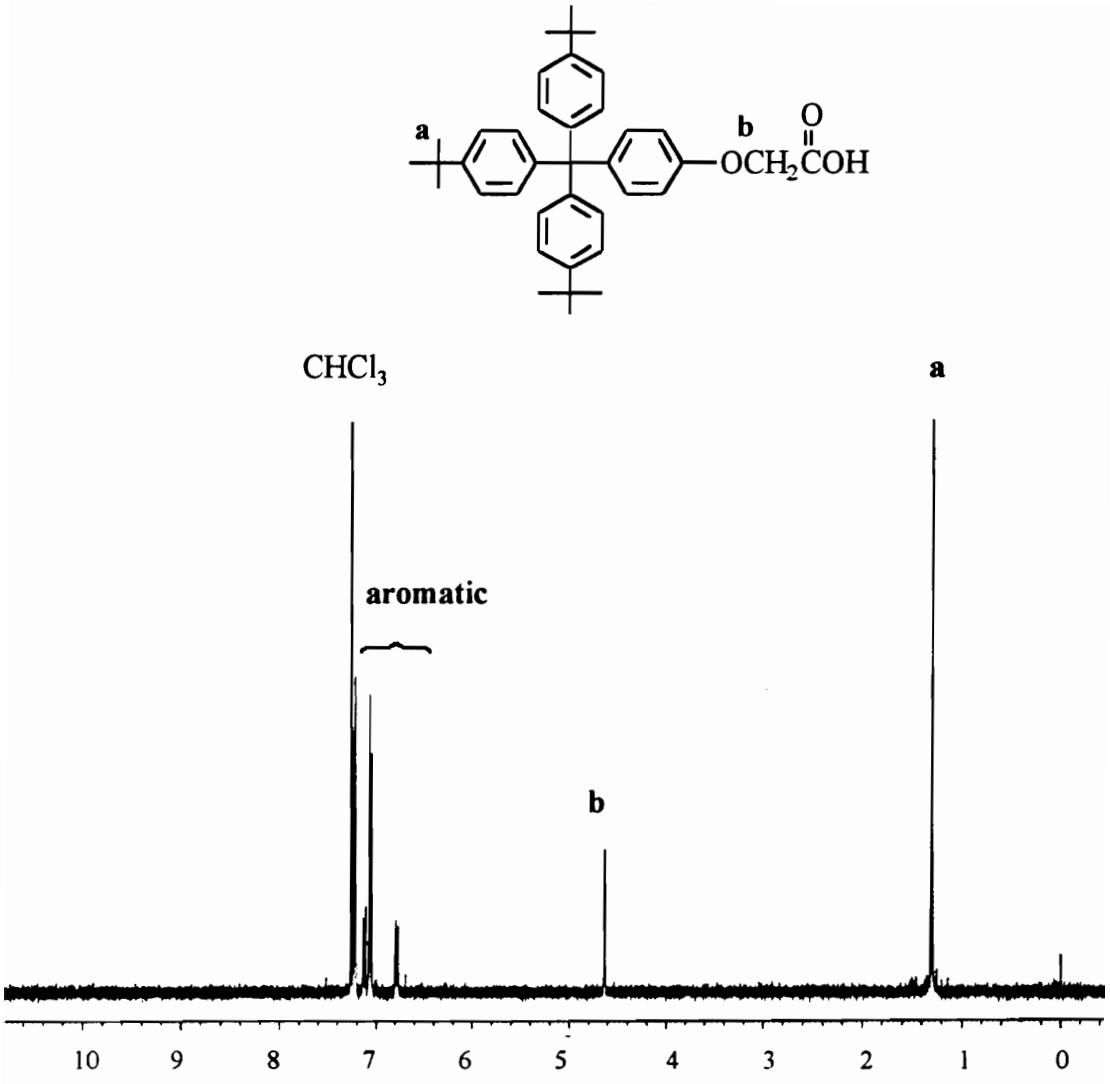


Figure 2. ^{1}H NMR spectrum of *p*-[tris(*p*-*tert*-butylphenyl)methyl]-phenoxyacetic acid (**16**) ($CDCl_3$, 400 MHz).

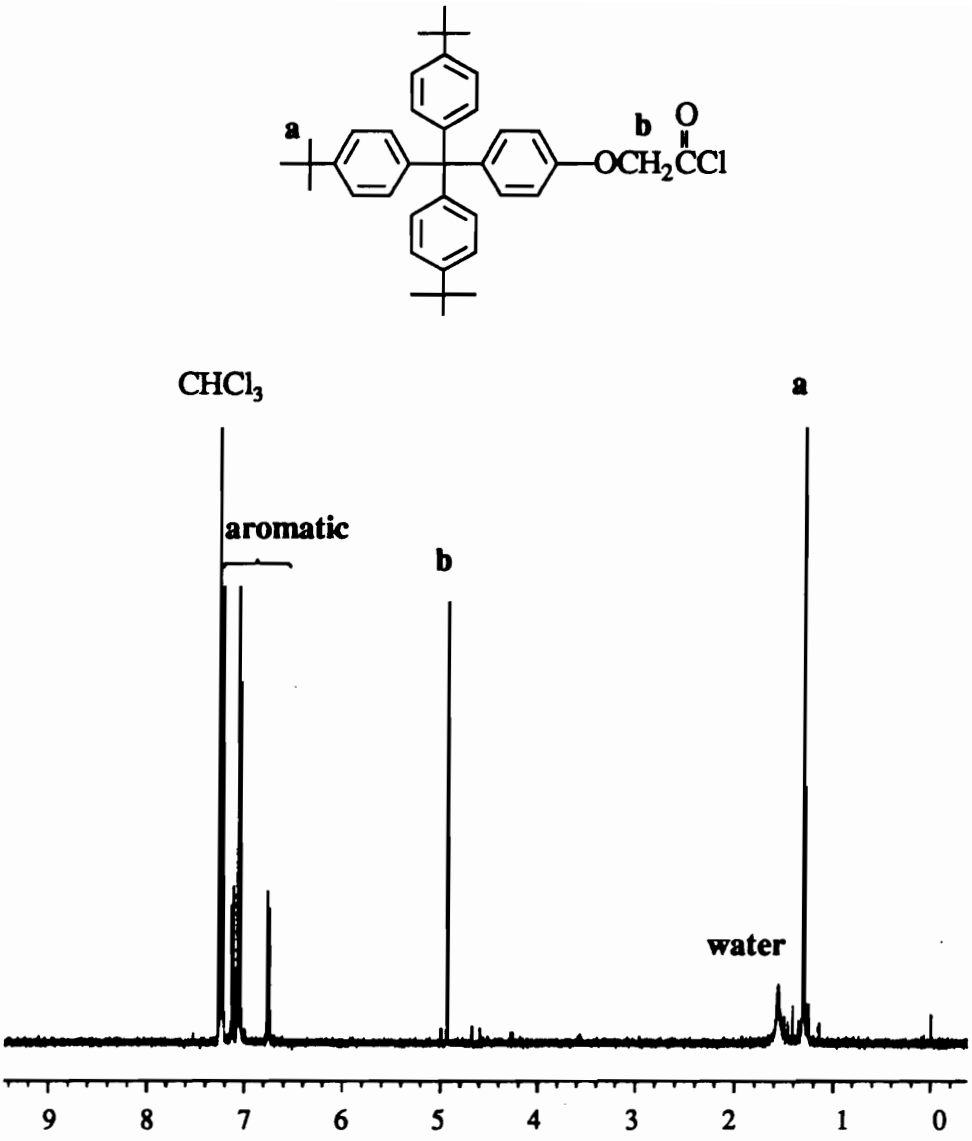
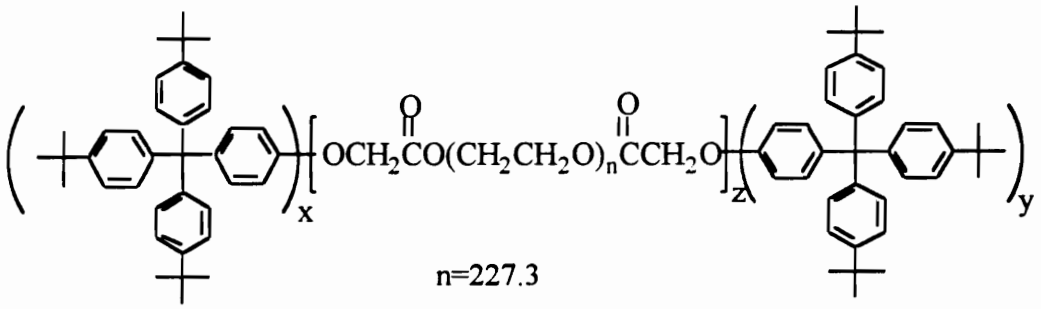


Figure 3. ^{1}H NMR spectrum of *p*-[tris(*p*-*tert*-butylphenyl)methyl]phenoxyacetyl chloride (**17**) ($CDCl_3$, 400 MHz).



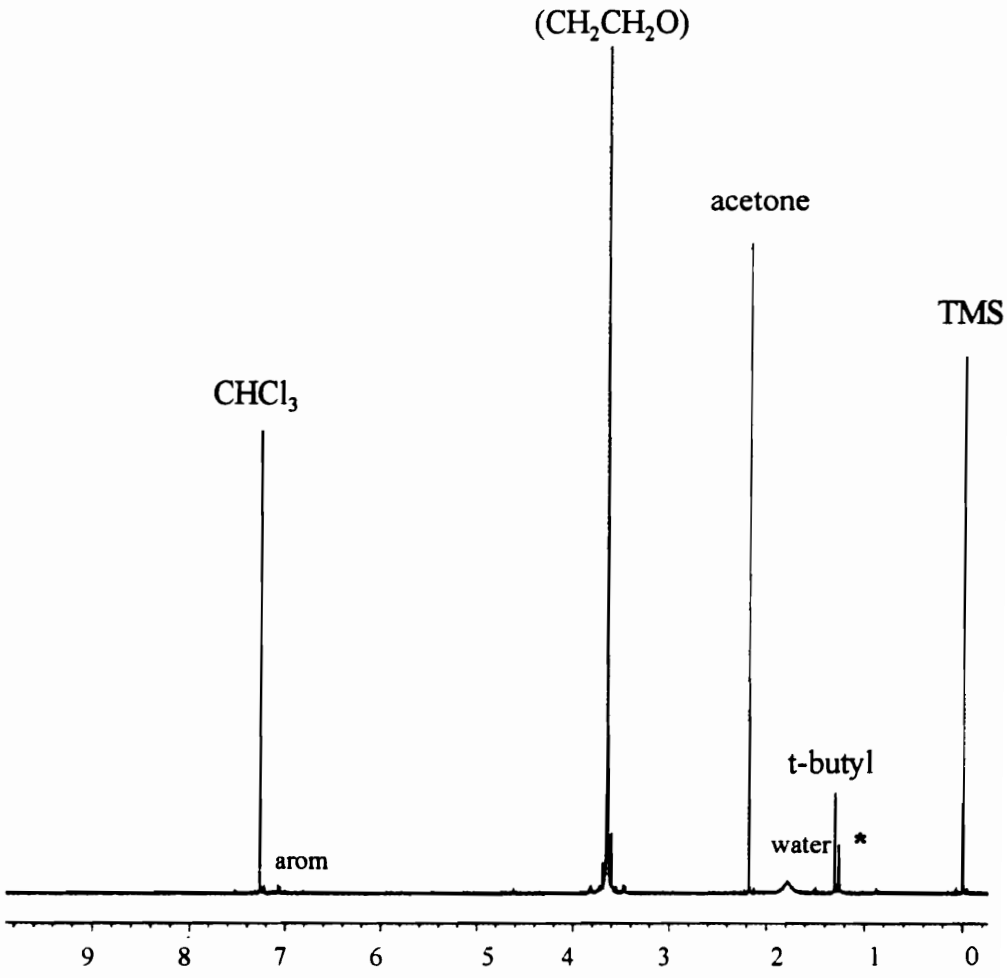


Figure 4. ^{1}H NMR spectrum of partially blocked PEO (10K), (x+y)/z = 0.44 ($CDCl_3$, 400 MHz).
* Impurity from PEO.

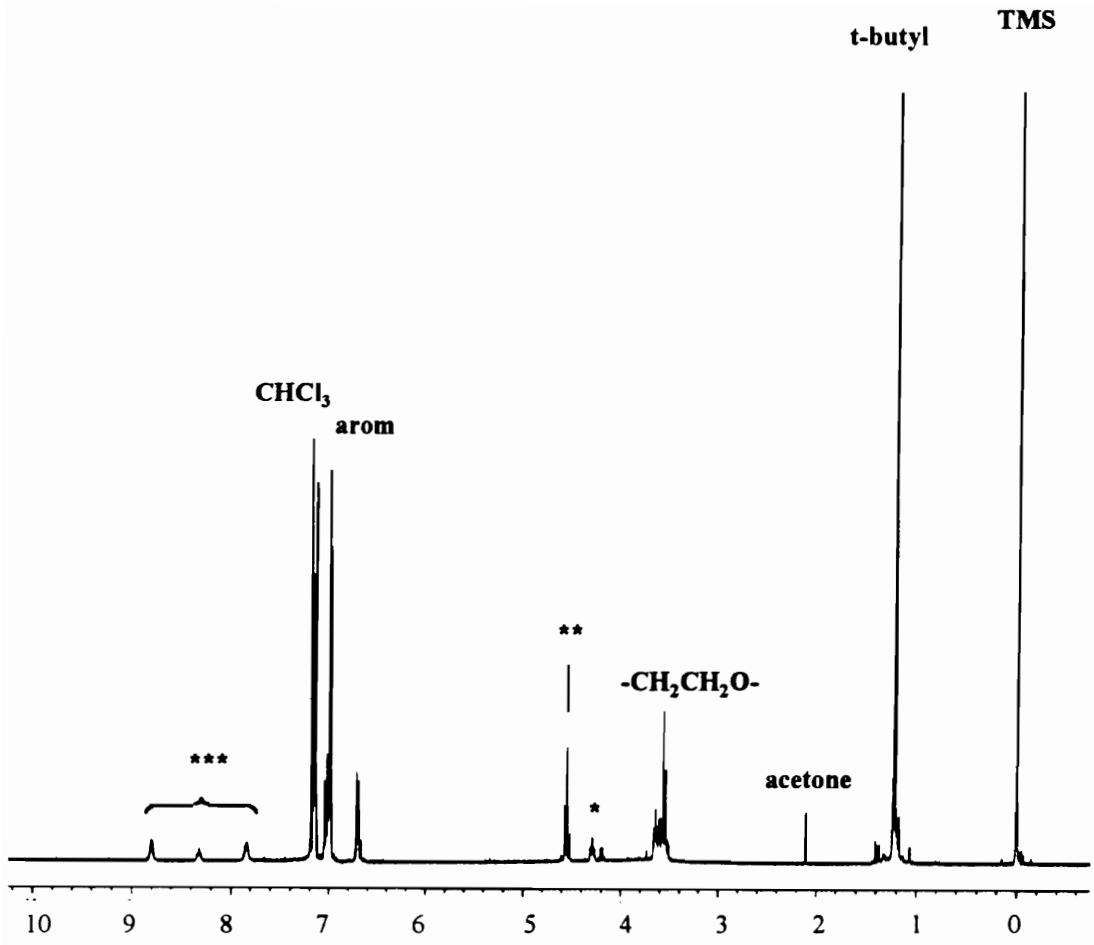


Figure 5. ^{1}H NMR spectrum of the crude product from the 42hr reaction of tetra(ethylene)glycol and **17**. ($CDCl_3$, 400 MHz)
* -$CO_2C\underline{H_2}CH_2O$- ** Ar$OC\underline{H_2}CO_2$- *** pyridine hydrochloride

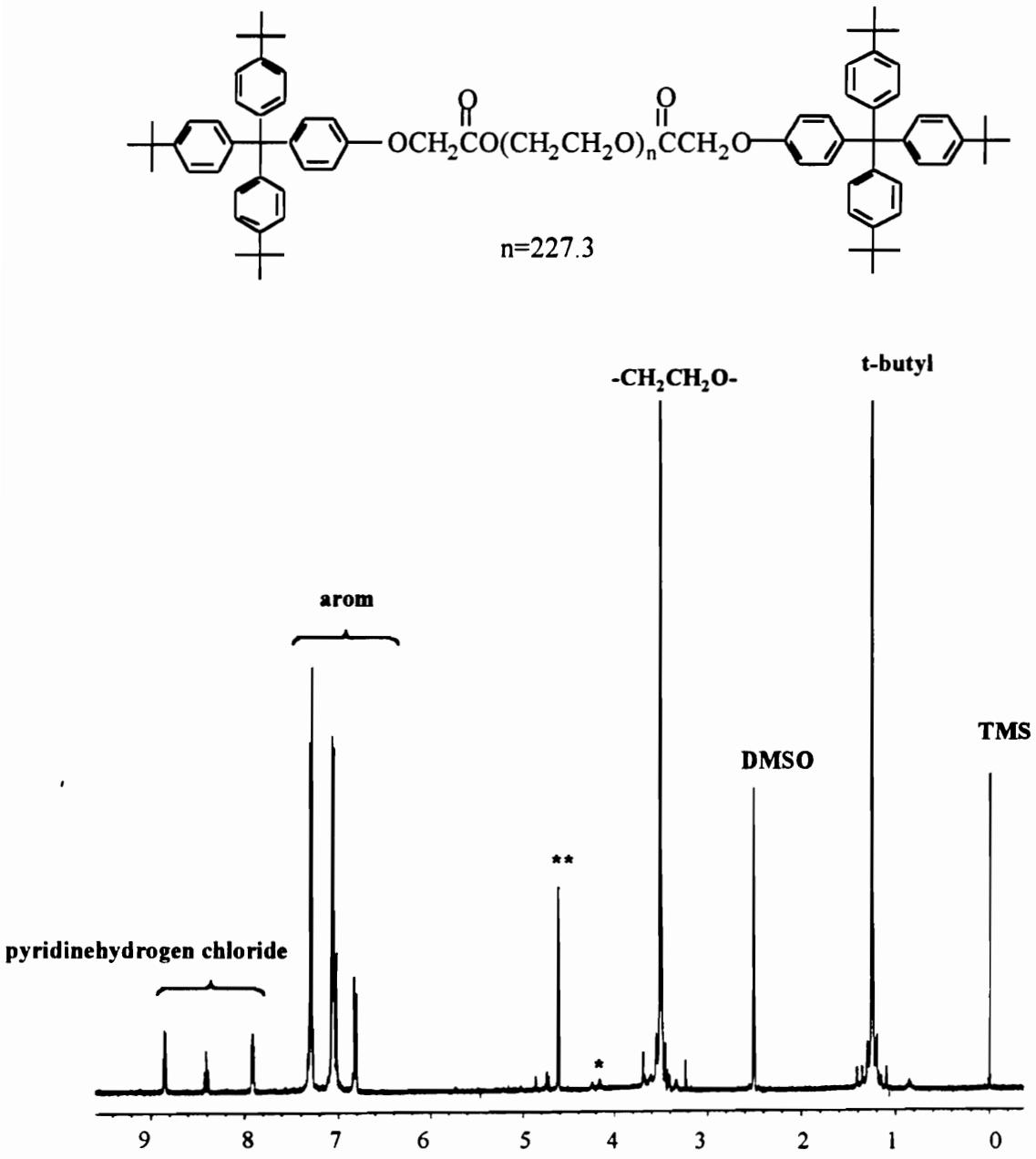


Figure 6. ^{1}H NMR spectrum of 100 % blocked PEO(10K) crude product (DMSO-d_6, 400 MHz).
* **-$CO_2C\underline{H}_2CH_2O$-** (4.24 ppm) ** **Ar$OC\underline{H}_2CO_2$-**

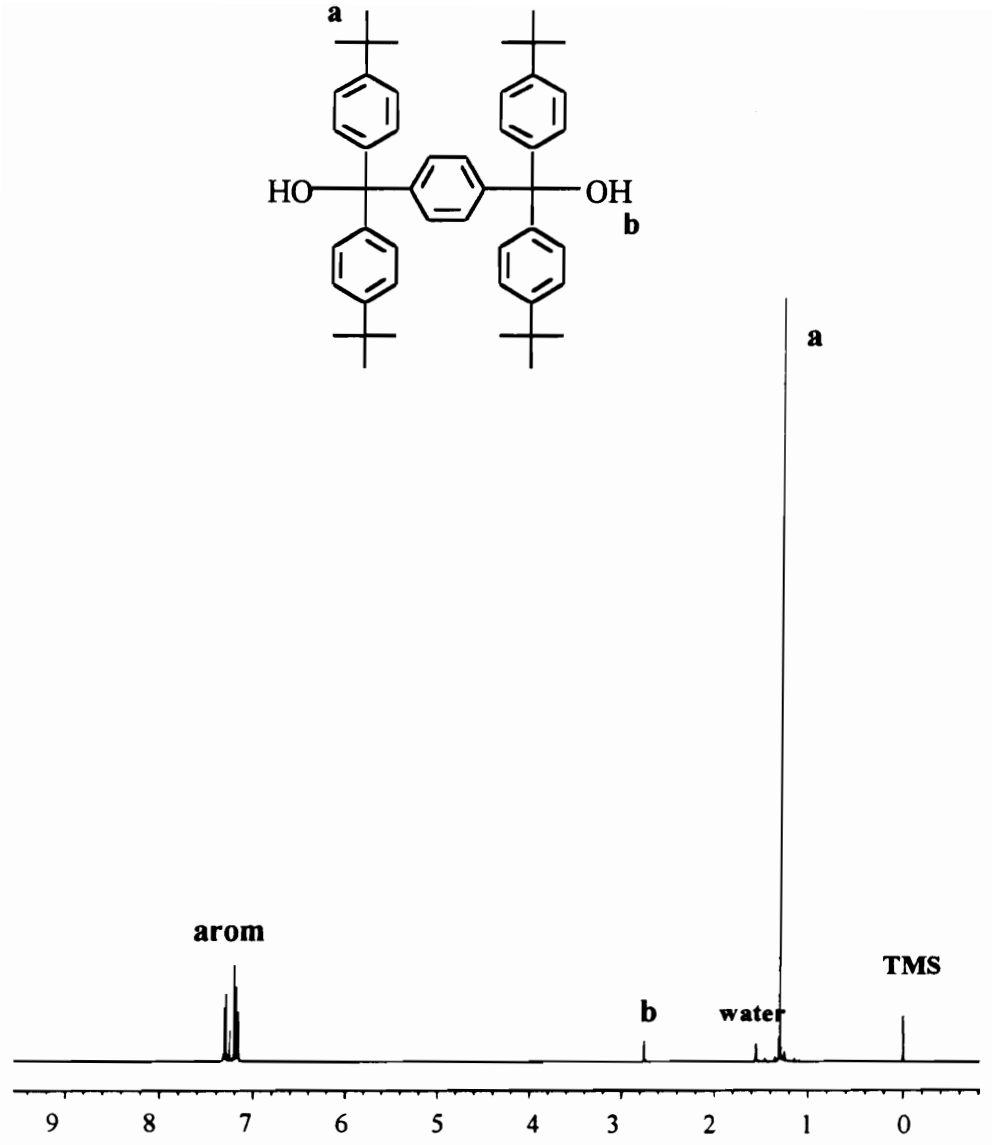


Figure 7. ^{1}H NMR spectrum of *p*-bis[bis(*p*-*tert*-butylphenylhydroxymethyl]-benzene (**30**) ($CDCl_3$, 400 MHz).

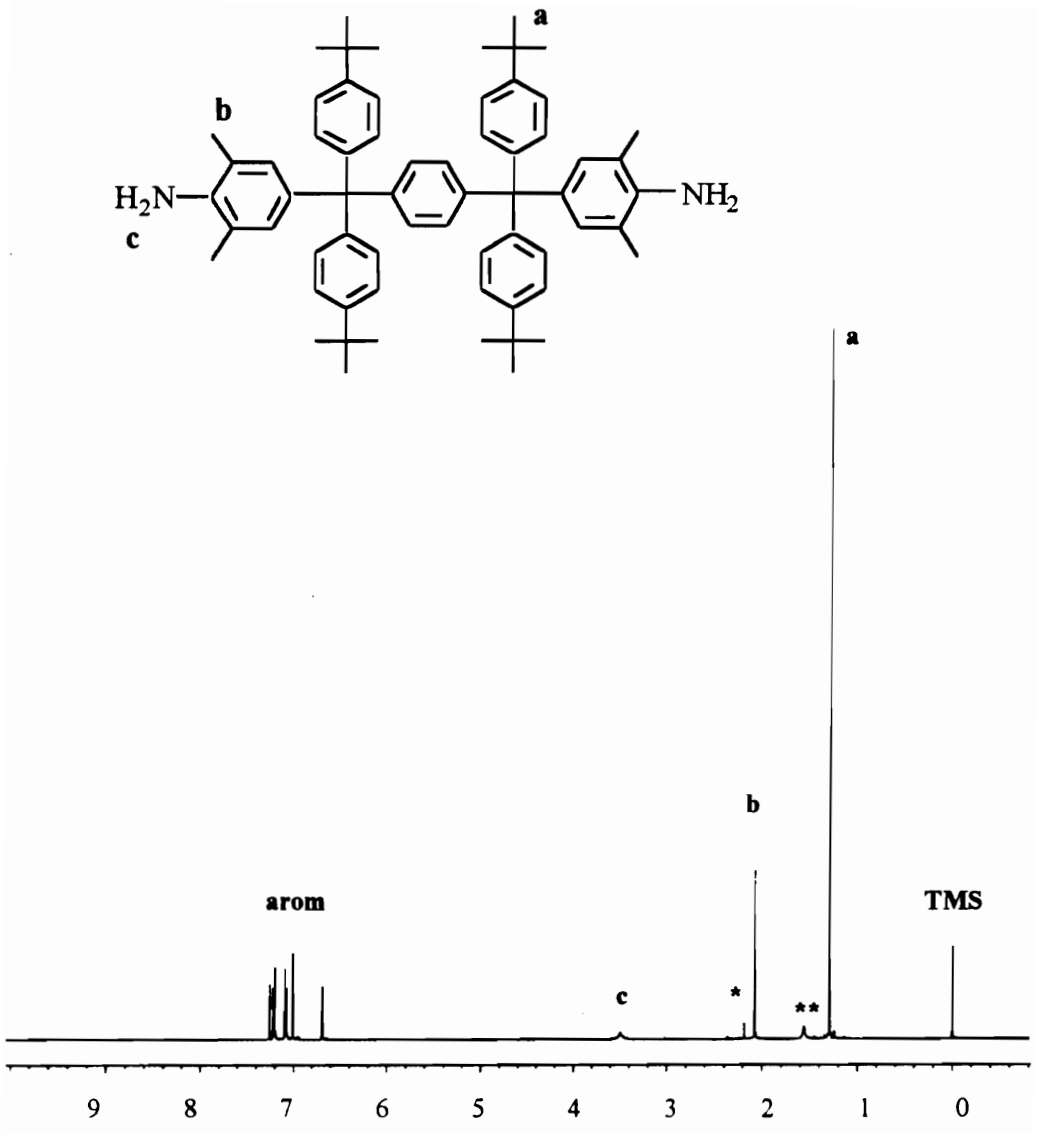


Figure 8. ^1H NMR spectrum of *p*-bis[bis(*p-tert*-butylphenyl-4'-amino-3',5'-dimethylphenyl)methyl]benzene (**32**). ($CDCl_3$, 400 MHz)
* acetone ** water

CHAPTER IV

ALIPHATIC CROWN ETHERS

The macrocycles which have been mostly used for the synthesis of rotaxanes and polyrotaxanes are crown ethers [1-6] and cyclodextrins [7-11]. The term "crown ethers" was suggested by Pedersen who reported the first detailed syntheses of macrocyclic polyethers in 1967. [12] In the large paper he showed that crown ethers form complexes with various metal ions and organic salts. Their capability as host molecules is due to the oxygen atoms in their structures which coordinate with metal ions and specific organic molecules through ion-dipole or hydrogen bonding interactions. [13, 14] The complexations are dependent on the size of cavities of crown ethers and the guest substrates. [14] Since Pedersen's discovery [12, 15, 16], there has been much research on the developement of macrocycles related to the crown ethers. [17] The modifications of crown ethers have been done by changing the structural parameters such as the aliphatic chain length, type of hetero atoms other than oxygen, cavity size and aromatic groups in the structure. [17]

The most versatile technique of polyrotaxane syntheses is polymerization of monomers in the presence of cyclic species. [1, 2, 9] Thus, in order that macrocycles be used as the cyclic species for polyrotaxanes the macrocycles should meet several requirements such as (1) they must have more than 22 methylene units to be threaded by polymer backbones, [18] (2) they should have no reactive functionalities which may interrupt the polymerization (3) they should be stable during the polymerizations, (4) their chemical nature should be different from the backbone molecule so that maximum modification of physical properties of the polymers can be achieved, (5) they may contain

polar units or donor centers capable of interacting with the monomers/polymers to enhance the threading efficiencies, (6) they may be miscible or soluble in various organic solvents, and (7) they may have low melting points so that the polymerizations can be carried out not only in the solution state but also in the melt state. (8) they should be easily prepared in multigram quantities.

The requirements 1-3 are strict; otherwise, the macrocycles can not be used as cyclic species for polyrotaxanes. The other items are not strictly required, but highly recommended for producing polyrotaxanes with good threading yields.

The natural macrocycles, cyclodextrins, have been employed as cyclic species of polyrotaxanes due to their hydrophobic cavities which can accommodate various compounds, including ionic and neutral organic substrates through complexations. [19] The complexations, however, usually occur in aqueous solutions; therefore, the utilization of cyclodextrins for the synthesis of polyrotaxanes is usually limited to the simple mixing methods in aqueous phases. Strong aprotic solvents such as DMF and DMSO, which are good solvents for cyclodextrins, may be used as solvents for the polymerizations of certain monomers in the presence of cyclodextrins. However, in such polar solvents the complexation ability of cyclodextrins are destroyed. [19] Also, in many condensation polymerizations cyclodextrins can not be employed because the hydroxyl groups of cyclodextrins interfere with the polymerizations.

On the other hand, crown ethers larger than 23 membered rings satisfy all the requirements. They do not have reactive functionality to interfere with the polymerizations and have good solubilities in a wide range of solvents from hexane to methanol. Aliphatic crown ethers have melting points lower than 60 °C, which makes it possible to prepare polyrotaxanes in melt states as well as solution states.

The complexation ability of crown ethers is of course an advantage for the synthesis of polyrotaxanes. The hydrogen bondings between terminal OH groups and oxygens on the crowns have been utilized Agam et al. [1] and Gibson et al. [2]. More recently, Stoddart and his coworkers reported complexations between dialkylammonium ions and dibenzo-24-crown-8 or bis-*p*-phenylene-34-crown-10. [3, 5] The X-ray crystallography indicated that the complexations take place through hydrogen bonding between ammonium hydrogens and oxygens in the crown ethers. [5] In addition to the complexation through ion-dipole and hydrogen bonding interactions, dibenzo-crown ethers and analogous macrocycles form 1:1 complexes with paraquat or diquat dications through charge transfer interaction. [20] This concepts have been applied to syntheses of rotaxanes by Stoddart and coworkers. [6]

RESULTS AND DISCUSSION

Part 1. Syntheses of Aliphatic Crown Ethers

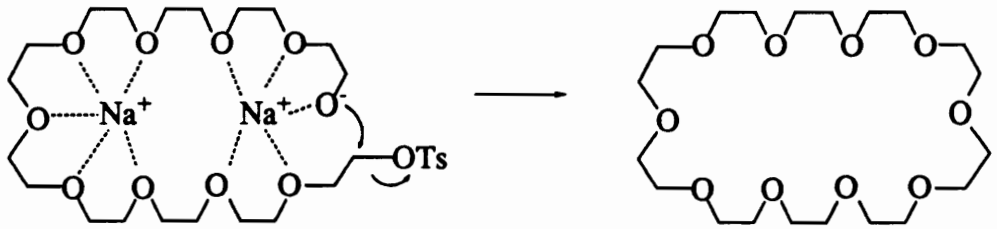
Crown ethers are usually prepared by Williamson ether synthesis, which involves S_N2 reactions. A variety of crown ethers and analogs with heteroatoms containing 27 atoms or less were synthesized and characterized. [17] However, there are relatively few examples of aliphatic crown ethers larger than 27 membered ring in the literature. [21-23]

The simplest synthetic method of aliphatic crown ethers is one-pot, one-piece cyclization. (Scheme 1). Vitali and Masci reported the synthesis of crowns of various sizes from 12-crown-4 (12c4) to 60-crown-20 (60c20) by this method. [21] Recently, Booth et al. reported the synthesis of cyclic polyethers (average M_n=1000-3000) by this method.

[22] As shown in Scheme 1 the reaction of oligo(ethylene oxide) and *p*-toluenesulfonyl chloride (tosyl chloride) in the presence of a base yields the monotosylate *in situ*, which undergoes ring closure to produce the crown ether. The cyclization reactions are usually carried out under high dilution conditions to suppress the formation of linear oligomers and polymers. [24] However, even under such high dilution conditions crown ethers larger than the crown with the same size of the precursor are produced, although the yields may be low. For example, Vitali and Masci reported that 30-crown-10 (30c10) was formed in 12 % yield from penta(ethylene glycol). [21] The one-pot method is simple and straightforward. The major drawback is, however, that the synthesis and purification of oligo(ethylene oxide)s with more than six oxyethylene units require multi-step reactions and are not trivial.

The multiple condensation method (Scheme 2) is another approach to avoid the preparation of such oligo(ethylene oxide)s. [23, 25] In Scheme 2, 1 mol of the oligo(ethylene glycol) **1** having *a* units condensed with oligo(ethylene oxide) ditosylate **2** having *b* units to yield the crown ether **3** containing *(a+b)* units of ethylene oxide. In addition to the formation of **3** the larger crowns **4** are produced by the condensation of 2 or more mols of each linear precursor. Chenevert and D'Astous synthesized aliphatic crown ethers of various sizes from 27-crown-9 (27c9) to 60c20 by the two-piece combination method. [23] Metal hydrides were used as bases and the isolation of the product was done by column chromatography. It is to be noted that the metal ions affected the yield of the crown ethers. This observation is related to the template effect. [26] The metal template effect is dependent on the size of the metal. Sodium and potassium ions have smaller sizes than the cavity of the crown ethers larger than 18-crown-6 (18c6). Thus, the authors suggested a double or multiple template effect which involves intermediates **5** of multi-ions and oligomeric precursors. [23] The multiple condensation method has an advantage

because small precursors which are readily available can be utilized. But, the yield of the crown ether of desired size may not be higher than the one-pot method, and the isolation of each crown ether is not a simple task.



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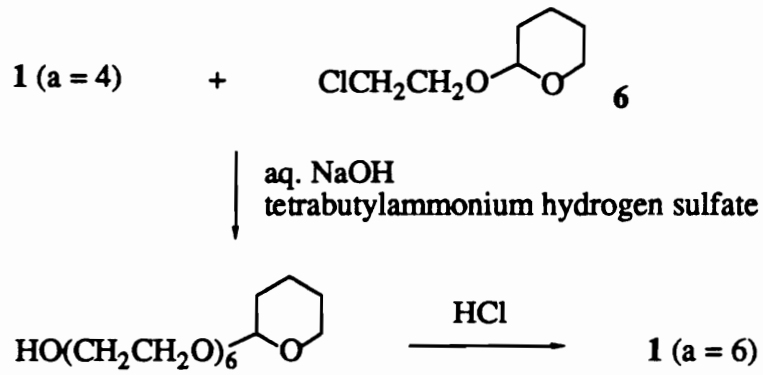
We employed the multiple condensation method to prepare 30c10 and larger aliphatic crown ethers which have cavities big enough to be threaded by linear polymers. [25] In this method the preparation and purification of relatively high molecular weight oligo(ethylene oxide)s were not neccessary; commercially available tetra- and tri(ethylene glycol) were used. However, for the synthesis of 30c10 and 60c20, which are prepared simultaneously, hexa(ethylene glycol) was synthesized in large scale.

1-1. Syntheses of hexa(ethylene glycol) and ditosylates of tri- and tetra(ethylene glycol)

Hexa(ethylene glycol) (**1**, a=6) was commercially available [27], but expensive (25 g/$ 75.55). Thus, it was synthesized in large scale by condensation of tetra(ethylene glycol) (**1**, a=4) and 2-tetrahydropyranyloxychloroethane ($ClCH_2CH_2OTHP$, **6**). Hexa(ethylene glycol) (**1**, a=6) had been prepared by the Pedersen's classical method [15] in our lab, in which tetra(ethylene glycol) (**1**, a=4) was converted to tetra(ethylene glycol) dichloride and reacted with the disodium salt of ethylene glycol to give **1** (a=6) in about 30 % yield.

A more successful preparation of hexa(ethylene glycol) (**1**, a=6) was achieved by the method reported by Bartsch and coworkers. [28] According to the report, excess $ClCH_2CH_2OTHP$ (**6**) reacted with aqueous tetra(ethylene glycol) (**1**, a=4) in a heterogeneous mixture in the presence of a phase transfer agent to give an 80 % yield of hexa(ethylene glycol) (**1**, a=6). Using this procedure, hexa(ethylene glycol) (**1**, a=6) was

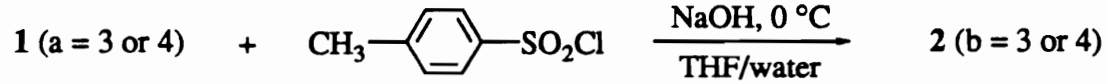


obtained in 59 % yield after deprotection and purification by two vacuum distillations (195 °C/0.2 mm). NaOH was used as base and tetrabutylammonium hydrogen sulfate was used as a phase transfer agent. The starting material **6** was easily prepared in 96 % yield by the treatment of 2-chloroethanol with 3,4-dihydro-2H-pyran in the presence of an acidic catalyst followed by vacuum distillation. [29]

Hexa(ethylene glycol) (**1**, a=6) was a colorless oil and the structure was supported by the ^1H NMR spectrum in DMSO-d_6 (Figure 1). In the spectrum the hydroxyl proton (H_d) appears as a triplet at 4.58 ppm because in DMSO the hydroxyl proton exchange is suppressed by strong solvation and consequently the alcoholic OH proton can be detected.

Other precursors, oligo(ethylene oxide) ditosylates **2**, were synthesized by the method reported by Ouchi et al. [30] In the reaction, tri(ethylene glycol) (**1**, a=3) or tetra(ethylene glycol) (**1**, a=4) was allowed to react with tosyl chloride in the presence of

NaOH as a base in an ice bath overnight. The reaction was carried out heterogeneously in a mixture of aqueous and THF solutions.



According to the report of Ouchi et al. the reaction would be fast and complete in 2 hr. However, we needed more than 10 hr to complete the reaction. After the reaction was complete 2 % aqueous HCl and CH_2Cl_2 were added and the organic layer was separated. Tri(ethylene glycol) ditosylate (**2**, b=3) was crystalline and easily purified by recrystallization of the crude product from acetone. The melting point (80.3-81.5 °C) was the same as reported [30] and the ^1H NMR spectrum (Figure 2) was clean.

It is to be noted that during the reaction keeping the temperature of the reaction mixture at 0 °C was important. When the reaction temperature was raised up to 10 °C the yield decreased significantly to 64 %. Usually the reaction gave about 90 % or higher yield when the reaction temperature was maintained at 0 °C. Interestingly, during the work-up, an oil (6 % yield) was extracted from the water layer with CH_2Cl_2. The ^1H NMR spectrum (Figure 3) suggested that the oil was a byproduct which contained relatively longer ethylene oxide units. In Figure 3, although all peaks could not be assigned, the integration of peaks at 3.58-3.75 ppm, which correspond to the middle ethylene oxide protons **a**, is approximately double the integration of peaks **b+c** in Figure 2. Thus, the oil was believed to be a mixture of ditosylates of oligo(ethylene oxide)s which are larger than tri(ethylene glycol) (**1**, a=3). The reason that the oil was slightly soluble in water is because of the longer hydrophilic ethylene oxide units. The formation of the byproduct may be explained by the dimerization or oligomerizations as depicted in Scheme 3.

While tri(ethylene glycol) ditosylate (**2**, b=3) is crystalline tetra(ethylene glycol) ditosylate (**2**, b=4) is an oil. Therefore, the crude product was washed with water and hexane to remove the salt and unreacted NaOH and tosyl chloride. Although further purifications such as column chromatography or high vacuum distillation were not carried out, the product was pure enough to use for the syntheses of crown ethers as the ^{1}H NMR (Figure 4) supported. The ^{1}H NMR spectrum (Figure 4) is similar to Figure 2 except for the integration of the middle ethylene oxide peak at 3.56 ppm.

1-2. Syntheses of aliphatic crown ethers by multi-piece combination

The syntheses of crown ethers were generally done in THF using NaH as base. High dilution conditions were employed in order to minimize the formation of linear oligomeric impurities. [24] Two synthetic procedures were employed. In procedure A, the dialkoxide (ca. 0.1 M) was prepared by the reaction of glycol **1** with excess NaH and the ditosylate **2** was added dropwise. In procedure B, glycol **1** was treated with excess NaH to form the dialkoxide in a relatively concentrated solution (ca. 0.7 M), then half an equivalent of ditosylate was added dropwise over several hours. The mixture was diluted and the other half equivalent of the ditosylate was added dropwise. In procedure C, a mixture of equimolar amounts of glycol **1** and ditosylate **2** was added dropwise into a dilute NaH suspension in THF.

The salt was filtered and discarded and THF was evaporated to give a yellow oil or solid. The oil or solid was subjected to recrystallizations from acetone or a mixture of CH_2Cl_2 and hexane (or acetone) several times. Table 1 shows the results of the syntheses of large crown ethers.

Table 1. Syntheses of crown ethers according to Scheme 2.[a]

1 a	2 b	T (°C)	3	yields (%)[b]	
				4	
				a+b	x(a+b) (x=2,3,---)
3	3	25		23[c]	
4	3	25		22[d]	27[d]
4	3	67			39
4	3	67			52[e]
4	3	101			61[e,f]
6	4	25		11[g]	11
6	4	30		17[h]	

[a] In THF using NaH as base using procedure A unless specified otherwise. [b] Three recrystallizations from acetone (-20 °C) unless specified otherwise. [c] Two recrystallizations from a mixture of acetone and CH_2Cl_2 (2/1, v/v, -20 °C). [d] [ref. 25] [e] In THF (or dioxane if so noted) using NaH as a base using procedure B: half of the ditosylate was added over 0.5 hr and stirred 16 hr, then solution was diluted ca. 9x relative to initial concentration, followed by addition of the rest of the ditosylate over 10 hr. [f] refluxing dioxane. [g] Three recrystallizations from a mixture of hexane and CH_2Cl_2 (2/1, v/v, -20 °C). [h] In THF using NaH as a base using procedure C: equivalent moles of glycol and ditosylate were dissolved in a small amount of THF and added dropwise to a dilute suspension of NaH in THF.

In Table 1, it was found that higher temperature favors the formation of larger size of crown ethers than the smaller ones. This is due to the fact that the activation energy of unimolecular cyclization, which results in the smaller ring, is smaller than the activation energy of bimolecular chain extension reaction, which ends up with the formation of larger ring. The bimolecular reaction requires energy for translational movements but the unimolecular reaction requires energy for bond rotation which is smaller than the translational energy. Thus, as temperature increases the probability of formation of larger rings increases as illustrated in Figure 5. This explanation, however, needs more experimental investigation, because the chain extention reaction does not simply mean the formation of larger crowns. At higher temperature, the rates of undesirable side reactions such as elimination (Scheme 4) and back-biting (Scheme 5) [31] which compete with S_N2 also increase, and consequently those side reactions result in increase of the amount of linear impurities.

The reaction procedure also affects the crude yields. Procedure B favors the formation of larger size crown ethers. In the first step of procedure B (Scheme 6), the formation of the smaller ring consisting of (a+b) ethylene oxide units was minimized because the reaction was done in a relatively concentrated solution. Instead, the formation of the desired linear intermediate **7** was maximized. In the second step under dilute conditions, the intermediate, $Na^+ {}^-(OCH_2CH_2)_{2a+b}O^- Na^+$, reacts with the tosylate to form the intermediate $Ts(OCH_2CH_2)O^-_{2(a+b)}Na^+$, which undergoes ring closure to give the crown ether (**4**, x=2). When the synthesis was done by procedure B in the refluxing dioxane (bp=101 °C) the crude yield after three recrystallizations from acetone was 61 %. For a two-piece combination (30c10) product, procedure C was proved to be better than procedure B. The simultaneous slow addition of the two precursors, hexa(ethylene glycol) (**1**, a=6) and tetra(ethylene glycol) ditosylate (**2**, b=4), to the highly diluted NaH

suspension in THF allowed better probability of cyclization of the intermediate [$Ts(OCH_2CH_2)_{10}O^-$ Na^+] against chain extension reaction. Therefore, using procedure C, 30c10 was synthesized in 17 % yield.

1-3. Purification of crown ethers

The preparations of aliphatic crown ethers by multi-piece combinations produced a mixture of crown ethers of several sizes. For example, when 42-crown-14 (42c14) was synthesized using tetra(ethylene glycol) (**1**, a=4) and tri(ethylene glycol) ditosylate (**2**, b=3), 21-crown-7 (**3**, a+b=7, 21c7) was produced. Then, 42c14 by four-piece combination and 63-crown-21 (63c21) by six-piece combination, etc. Scheme 7 illustrates the steps of crown ethers formation. The smallest one, 21c7 was formed by combination of one mol of **2** (b=3) and one mol of **7** followed by cyclization. If the resultant linear substrate **8** does not cyclize but reacts with **2** (b=3) and **7** the longer linear species **9** would be produced and it yields 42c14 by cyclization. In a similar way, the other bigger crowns may be prepared. The illustration of the Scheme 7 is, of course, the part of the chemistry involved in the multi-piece combination method. As mentioned before, the elimination rection (Scheme 4) is a major side reaction, and once elimination occurs, the formation of linear oligomeric impurities is inevitable.

In order to isolate 18c6, the crude product (residual oil after evaporation of the solvent) was extracted by hot hexane. 18c6 is known to form a complex with acetonitrile to give a nice crystal. [32] However, it was found that 18c6 could be recrystallized from various solvents such as hexane, CH_2Cl_2, acetone and a mixture of those solvents. Thus, after evaporation of hexane the slightly yellow oil was subjected to recrystallization from a mixture of acetone and CH_2Cl_2 (2/1, v/v) at -20 ℃ to give clear bulk crystals whose

melting point was 39.9-41.0 °C (Lit: [32] mp=36.5-38.9 °C, [33] mp=39-40 °C). In the ^{1}H NMR spectrum of 18c6 (Figure 6) in $CDCl_3$ only a singlet was found at 3.689 ppm.

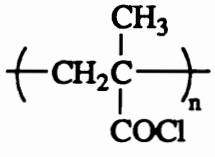
The isolation procedure for 30c10 was the same as for 18c6. The recrystallization was, however, done from a mixture of hexane and CH_2Cl_2 (2/1, v/v) at -20 °C. Like 18c6 30c10 gave nice colorless crystals and the ^{1}H NMR spectrum in $CDCl_3$ gave a singlet at 3.669 ppm. In DMSO-d_6 a singlet appeared at 3.501 ppm instead of 3.669 ppm in the ^{1}H NMR spectrum (Figure 7). The melting point of 30c10 was 38.9-40.3 °C. (Lit: [21] mp=35.5-36.8 °C, [25] mp=42.0-43.8 °C)

In contrast to 18c6 and 30c10, recrystallization of the larger crowns from acetone at -20 °C did not give nice crystals; instead, the crystals were powdery. Figure 8 shows the ^{1}H NMR spectrum (in DMSO-d_6) of crude "42c14" which was produced by the reaction of **1** (a=4) and **2** (b=3) in the refluxing THF by use of procedure B. [The quotation mark (" ") indicates that the product was not a single-sized crown ether; instead, it was a mixture of crown ethers with different sizes.] According to the ^{1}H NMR spectrum (Figure 8) it was found that "42c14" contained linear impurities whose end units were tosyl, vinyl or OH. In Figure 8, the major impurity peaks are two adjacent doublets at 6.50 ppm and two doublets of doublets at 4.18 and 3.97 ppm, which are due to the vinyl ether group. Another impurity peak is the OH proton peak as a triplet at 4.57 ppm. Also in the aromatic region two doublets are shown due to the tosyl group. The ^{1}H NMR spectrum of "60c20", which was prepared by the reaction of **1** (a=6) and **2** (b=4) and recrystallized from acetone, was virtually the same as Figure 8. Therefore, removal of those linear impurities was the main effort in the purification.

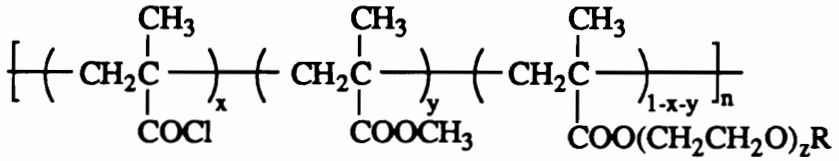
Although column chromatography could remove impurities such as remaining salts and linear oligomers with relatively high molecular weight, column chromatographic isolation of pure crown ethers was not successful. This was because the separation of the

linear oligomers from the cyclic species (crown ethers) with comparable molecular weights was virtually impossible. Also, oligo(ethylene oxide)s and all crown ethers larger than 18c6 gave long tails on TLC plates (silica gel or alumina) with most of developing solvents except methanol and ethanol. Methanol and ethanol could move the spot along the TLC plates; however, there was no separation (R_f =1). This long "tailing" is due to the strong interactions with the stationary phase (silica gel or alumina).

Therefore, after the crude products "42c14" and "60c20", were initially purified by passage through a short silica gel column with CH_2Cl_2 to remove relatively high molecular weight impurities, they were treated with poly(methacryloyl chloride) (**11**) followed by precipitation from methanol. The linear impurities which contained terminal OH groups reacted with the poly(acid chloride) in THF solution; then upon pouring the reaction mixture into excess methanol the polymer (**12**) was precipitated out while crown ethers remained in the solution.



11



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A question in this purification method is how to remove linear impurities with vinyl ether and tosyl end groups. This can be done by conversion of vinyl ether end group into OH group by HCl which was produced from the reaction of the acid chloride group with the linear impurities as illustrated in Scheme 8. The product after the polymer treatment was recrystallized from acetone at -20 ℃ to give white powdery crystals whose melting point was 53.0-55.0 °C. The ^1H NMR spectrum in DMSO-d_6 (Figure 9) of the final product,"42c14", shows the absence of linear impurities. It is to be noted that the ^1H

NMR analysis in DMSO-d_6 of PEOs [34], especially analysis of terminal OH protons, was so precise it could detect the OH proton of PEO (100K, M_n=1x10^5). For demonstration, the terminal hydroxyl proton of PEO (3.4K) appears as a clear triplet at 4.57 ppm in the ^{1}H NMR spectrum (Figure 10). Even the hydroxyl proton of PEO (100K) could be detected by ^{1}H NMR in DMSO-d_6 (Figure 11). The crude "60c20" was purified by the same method and the final powdery crystals melted between 52.5-54.5 °C.

The final yields, however, were about reduced to 60 % after the purification by treatment of "42c14" or "60c20" with poly(methacryloyl chloride) (**11**). This does not necessarily mean that the portion of the linear impurities in the crude product was about 40 %. It is believed that during the purification process, some of crown ethers were lost in the form of rotaxane through threading of the polymer chains into the crown ethers.

Part 2. HPLC Analysis of Crown Ethers

2-1. Survey of Chemical Abstracts

The item "crown compounds, ethers" in GS (*General Subject* index, 1972-1995) sections has been surveyed in order to obtain information for chromatographic analysis of crown ethers. Unfortunately, a systematic analysis of crown ethers using HPLC has not been reported yet. A few articles about GC analyses of crown ethers were found, but among them only one report was concerned about crown ethers up to 60c20. [21]

In several research articles the authors reported that they successfully used smaller crowns, especially 18c6, to modify retention behavior of the polar compounds such as amino compounds and salts in HPLC. [35] In reverse-phase HPLC, Nakagawa et al.

found that the addition of 18c6 appreciably enhanced the capacity factors of catecholamine and related compounds. [35] They explained that the effects were due to the formation of the 18c6-amino compound complexes which reduce the hydrophobicity of the compounds and consequently the amino compounds stayed longer inside the column. 18c6 has been also used in the HPLC analysis of salts. It was found that the addition of crown ethers enhanced the solubilities of the potassium sulfonates and afforded moderate retentions. [36]

Nahum and Horvath reported that they observed "irregular" retention behavior of crown ethers in reverse-phase chromatography with silica-bonded hydrocarbonaceous stationary phases. [37] They interpreted their observation by using a dual binding model. They suggested that retention was caused not only by the usual solvophobic interactions but also by "silanophilic" interactions between the eluate and the accessible silanol groups at the surface of various alkyl-silica bonded phases. In addition to the solvophobic and silanophilic interactions on retention, another factor in the case of larger crown ethers is the possible threading-dethreading process. [38] Those effects may make it harder to obtain well-separated HPLC diagrams.

Another interesting article was reported by Aoki et al. [39] According to their report they could separate crown ethers from their open-chain homologes using a silica gel-bound sulfonate type cation exchanger as a stationary phase. They reported that crown ethers were retained on the ion exchanger, while the open-chain homologes showed only a limited affinity to the column.

GC has been used for the analysis of crown ethers. According to the abstracts Egorova et al. [40] and Fedorova et al. [41] used gas chromatography to determine various organic impurities in crown ethers (18c6 and smaller ones), analyzing crude reaction mixtures. An interesting report was the recent article by Vitali and Masci. [21] They reported that using GC they carried out the analysis of crown ethers (even up to 60c20)

successfully. It is somewhat surprising that they were successful in analyzing the larger crowns, because in spite of the high injection temperature they reported (400 °C), it seems unlikely that the pure larger crowns vaporize. Furthermore, according to our results, crown ethers undergo thermal degradation at that temperature. [25] However, keeping it in mind that only a trace amount of sample and a short time are needed for GC analysis, it might be possible. As a more important point it should be pointed out that in the GC traces of their report there was overlap between crown ethers and the corresponding PEOs. Also, as the molecular weight became higher the GC traces became wider. According to our NMR analysis the major impurities in the crown ethers are PEO oligomers. Therefore, it remains as a question how they could claim their results were free from the worry of the overlap phenomenon between crown ethers and linear impurities whose molecular weights are comparable to those of the crowns.

2-2. HPLC analysis of the large crown ethers

According to the TLC results, to move crown ethers along the plate relatively polar solvents such as MeOH, EtOH, ethyl acetate, THF or acetone are needed as eluents. However, except with the alcohols crown ethers larger than 30c10 leave long tails from the spotting point on silica gel plates. CH_2Cl_2 or toluene can not make larger crowns move along the silica gel plate. When an alumina TLC plate is used, however, the extent of the "tailing" is reduced. This tailing is probably due to the interaction between OH groups bound to the silica gel and the crown ethers. Therefore, a reverse-phase column was used for the HPLC analysis. The column used was Deltabond-C_8 reverse-phase column (4.6 mm x 15 cm (I.D. x L), particle size 5 μm, pore size 300 A) supplied by Keystone Sci. Co. The temperatures of the RI detector and column were maintained at 40 °C using a

water jacket and a water circulator. The sample concentrations were 3-15 mg/mL and the injection volume was 10 μl. The flow rate was 1 mL/sec. Solvents used were MeOH, acetonitrile and the various mixtures of the two solvents.

It was found that with acetonitrile crown ethers such as 18c6 and "42c14" did not elute. Also it was found that MeOH was not able to separate crowns from each other. With MeOH the capacity factors were almost 1.0 for all samples, which meant all samples eluted without any significant retention. Therefore, it was believed that a certain mixture of MeOH and acetonitrile with a proper ratio could separate the crown ethers. In fact, as the amount of acetonitrile increased in the mixture the retention times of the samples increased. Also, as the retention time increased the peaks became broader and showed a tailing phenomenon. Therefore, it was impossible to obtain a series of well-separated peaks for all crowns without tailing and overlapping. Another problem was the open-chain homologues, which are oligomeric PEOs. It was practically impossible to separate crown ethers from their open-chain homologues.

Table 2 shows the summary of the retention times of crown ethers and PEOs using the mixtures of MeOH and acetonitrile. The retention times in Table 2 are those of the peak maxima. Figures 12 and 13 show the retention time (in sec.) *vs* molecular weight of the sample when 2:8 and 1:9 (v/v) of MeOH/acetonitrile mixtures were used as eluents, respectively.

A mixture of ratio 0.5 : 9.5 (MeOH:acetonitrile) was also used, but broader and overlapped peaks were obtained. Also isopropanol was tried, but due to the high pressure (>2000 psi) it was very difficult to obtain a stable baseline. It must be noted that as the molecular weight of the sample and the amount of the acetonitrile in the solvent increase more concentrated sample solutions were needed in order to get a peak.

Table 2. HPLC retention times of crown ethers and PEOs on a Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A).

solvent (MeOH:aceto-nitrile, v:v)	sample	retention time (sec)	remark
10 : 0	"42c14"	98.5	
	PEO(1500)	98.5	
	PEO(3400)	98.5	
	solvent	-	no peak
0 : 10	"42c14"	-	no peak
	18c6	-	no peak
7 : 3	18c6	120.0	
	"42c14"	98.0	
	PEO(3400)	92.4	
	solvent	-	no peak
5 : 5	18c6	115.2	
	30c10	103.9	
	"42c14"	99.0	
	"60c20"	101.0	
	PEO(600)	97.0	
	PEO(1500)	98.6	
	PEO(3400)	102.0	
	solvent	-	no peak
	"42c14" + 18c6	99.0, 164.4	clear separation
	PEO(600) + PEO(3400)	-	overlapped

(Table 2, continued)

2 : 8	18c6	146.6	
	30c10	135.1	
	"42c14"	127.1	
	"60c20"	126.6	
	PEO(200)	101.6	
	PEO(400)	105.6	
	PEO(600)	110.3	
	PEO(1000)	118.1	
	PEO(1500)	128.6	
	PEO(3400)	168.1	
	water	99.5	
	solvent	-	no peak
1 : 9	18c6	292.2	
	30c10	166.1	
	"42c14"	150.6	
	"60c20"	148.6	
	PEO(200)	101.6	
	PEO(400)	110.6	
	PEO(600)	119.6	
	PEO(1000)	141.6	
	PEO(1500)	171.6	
	PEO(3400)	-	no peak
	PEO(400) + 30c10	112.6, 170.1	clear separation
	30c10 + "60c20"	147.6, 174.1	overlapped

From Table 2 and Figures 12 and 13 it can be found first of all that the retention time of the crown ethers decreases as the size increases while the retention time of PEOs increases as the molecular weight increases. This result may be explained by the interaction between crown ethers and silanol groups at the surface of the stationary phase, which is the same idea as that of Nahum and Horvath. [37] Under many practical conditions in reverse-phase chromatography, retention behavior and selectivity are governed mainly by solvent effects. However at the surface of the stationary phase of C_8 reverse-phase column there are abundant silanol groups as well as hydrocarbon ligates. Therefore, when large molecules having polar functions are chromatographed the interaction between the polar functions and silanol groups can not be ignored. As well expected crown ethers are able to make stronger complexes with silanol groups than open-chain homologues. This interaction may be stronger in the case of smaller crowns because the size of the smaller crowns fits better to the size of the OH groups. In other words, larger crowns such as "60c20" can only make a loose complex like a PEO oligomer due to its large size.

Another factor to be considered is the "threading-dethreading" effect. Crown ethers larger than 30c10 are able to be threaded by hydrocarbon chains. The threading should result in the longer retention. In case of larger crowns the threaded crowns may dethread off the hydrocarbon ligates more easily than smaller ones. This threading-dethreading effect may be complicated and hard to correlate to the retention clearly. However, it was likely the threading-dethreading effect as well as silanophilic effect existed in this experiment as suggested especially from the results of the retention behaviors of the mixtures of the samples. In Table 2 when the mixture of "42c14" and 18c6 was injected using 1:1 mixture of MeOH and acetonitrile as an eluent the retention times for "42c14" and 18c6 were 99 and 164.4 sec, respectively. (Figure 14) In contrast to this, when "42c14" and 18c6 were injected individually the retention times were 99 sec and 115.2 sec,

respectively. (Figure 15) This results was not due to experimental error because repeated injections gave the same results. Although there was a possibility of the sample overloading it can be suggested that a reason for this result is the threading-dethreading process between hydrocarbons (octyl units) and "42c14"; through the threading process the octyl ligates become deactivated and the surface of the stationary phase become less hydrophobic, then consequently 18c6 feels less hydrophobic repulsion from the surface of the stationary phase and stays longer inside the column. This phenomenon was observed in another case; the mixture of 30c10 and "60c20" with the 1:9 mixture of MeOH and acetonitrile as an eluent. (Figure 16) The retentions of both of 30c10 and "60c20" became longer when the mixture was injected than those when each was injected individually. (Figure 17)

Also the retention times of crowns were different from those of open-chain homologues. For an example using 1:9 (MeOH : acetonitrile, v/v) 30c10 can be separated clearly from PEO(400) when the mixture of the two was injected. (Figure 18) Unfortunately, however, the other pairs such as "42c14"-PEO(600) and "60c20"-PEO(1000, or 600) were not clearly separated. The peaks seemed to be broad single peaks.

CONCLUSIONS

Aliphatic crown ethers (18c6, 30c10 and larger than 30c10) were prepared by muti-piece condensation of low molecular weight oligo(ethylene glycol)s and oligo(ethylene glycol) ditosylates in high dilution conditions. In this methodology, synthesis of higher molecular weight oligo(ethylene glycol)s precursors was not needed.

The smaller crown ethers, 18c6 and 30c10, were readily purified by recrystallizations from a mixture of CH_2Cl_2 and acetone or hexane. However, the larger crown ethers obtained from recrystallizations from acetone were not pure; they contained linear impurities whose ends units were hydroxyl, vinyl ether and/or tosyl groups. The removal of such linear impurities was achieved by treatment of the crude products with poly(methacyloyl chloride) followed by precipitation into methanol. The final products, "42c14" and "60c20" were proved to contain no linear impurities as demonstrated by ^1H NMR in DMSO-d_6.

The HPLC analysis of the crown ethers showed several interesting results. Using a reverse phase column (Deltabond-C_8) and a mixture of acetonitrile and methanol, it was found that the smallest crown ether had longest retention time. In contrast, linear poly(ethylene oxide)s showed the opposite phenomenon; that is, shorter chains gave shorter retention times. This was explained by silanophilic interactions between the crown ethers and the hydroxyl groups in the stationary phase. Another interesting observation was a "threading-dethreading effect". When a mixture of two crown ethers with different sizes was injected the retention time of smaller crown became longer than the retention time of the case when it was injected alone. This was rationalized by threading of the larger crown by the C_8 chain of the stationary phase, which modified the polarity of the stationary phase.

EXPERIMENTAL

Measurements. Melting points were taken in capillary tubes and corrected. NMR spectra were obtained on a Varian 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 with tetramethylsilane as an internal standard. The HPLC used was an ISCO model 2350 and the column was Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A). The temperatures of the RI detector (Waters, Differential Refractometer R401) and the column were kept at 40 °C using a water jacket. The sample (30-150 mg) was dissolved in the solvent (10 mL). The volume of the injected sample solution was 10 μl. The peak maxima were adopted as the retention times.

2-Tetrahydropyranyloxychloroethane (6). 3,4-Dihydro-2H-pyran (DHP, 211 g, 2.51 mol) was cooled in an ice bath. 2-Chloroethanol (197.5 g, 2.45 mol) was added slowly, followed by addition of a few drops of conc HCl. Immediately the mixture turned yellow and produced a lot of heat. The mixture was allowed to stir in the ice bath for 15 min and then removed from the bath and stirred for 3 hr. The product was collected by vacuum distillation at 45-50 °C/1.5 mm (Lit. [29] bp=63±2 °C/1-2 mm) as a colorless oil (387 g, 96 % yield).

^{1}H NMR (DMSO-d_6): 1.47 (m, 4H, -$CH_2C\underline{H_2}\underline{CH_2}CH_2$-), 1.66 (m, 2H, -$C\underline{H_2}$CHO), 3.64 (m, 2H, $ClCH_2$-), 3.75 (m, 2H, -$CH_2CH_2C\underline{H_2}$O-), 3.84 (m, 2H, $ClCH_2C\underline{H_2}$O-), 4.64 [t, J=3.8 Hz, 1H, -OC$\underline{H}$].

Hexa(ethylene glycol) (1, a=6). In a 5-L flask equipped with a mechnical stirrer and a condenser $ClCH_2CH_2OTHP$ (**6**) (821 g, 5.0 mol), tetra(ethylen glycol) (**1**, a=4) (242.8 g, 1.25 mol) and tetrabutylammonium hydrogen sulfate (25.0 g, 0.07 mol) were placed.

Aqueous NaOH (50 %, 1640 g) was added dropwise to the mixture at room temperature over 3 hr. Upon addition of NaOH the mixture turned yellow and salts were formed. The mixture was allowed to stir at 48 °C for 5 days. The salt was filtered, washed with CH_2Cl_2 and discarded. The oil in the filtrate was extracted with CH_2Cl_2 (300 mL x 2) and the solvent was rotary-evaporated. The unreacted **6** was recovered by vacuum distillation. To the remaining oil, a mixture of methanol and CH_2Cl_2 (1.6 L, 1:1, v/v) was added, followed by addition of 70 mL of conc HCl. The solution was stirred at room temperature for 1.5 hr to deprotect the THP group. The solution was neutralized by addition of $NaHCO_3$ and the salts were filtered and discarded. The solvents were removed by rotary evaporation and the residual oil was subjected to two vacuum distillations (195 °C/0.2 torr). (Lit. [42] bp=153-158 °C/0.07 mm) The product was colorless oil and the yield was 208 g (59 % yield)

^{1}H NMR (DMSO-d_6): 3.41 (t, J=4.8 Hz, 4H, HOC$\underline{H_2}$-), 3.48 (t, J=4.8 Hz, 4H, HOCH$_2$C$\underline{H_2}$O-), 3.51 (s, 16H, -OC$\underline{H_2}$C$\underline{H_2}$O-), 4.58 (t, J=5.6 Hz, HO-).

Tri(ethylene glycol) ditosylate (2, b=3). In a 5-L 3-neck round-bottomed flask equipped with a mechanical stirrer, NaOH (336 g, 8.4 mol) and water (600 mL) were placed. Triethylene glycol (**1**, a=3) (450 g, 3.0 mol) in THF (1.2 L) was added to the solution. The solution was cooled down to 0 °C (in ice bath) and tosyl chloride (1259 g, 6.6 mol) in THF (1.5 L) was added to the solution dropwise over 4 hr. The tosyl chloride solution was warmed by a heating gun during the addition to prevent crystallization. The mixture was allowed to stir for 16 hours. 2 % aqueous HCl (1 L) was added to the reaction mixture and the organic layer was isolated by a separatory funnel. The water phase was extracted with CH_2Cl_2 (500 mL). The combined organic phase was rotary evaporated and the residual solid was dissolved in CH_2Cl_2 (2 L) and the CH_2Cl_2 solution

was washed with water (1 Lx2). CH_2Cl_2 was rotary evaporated and the residual solid was recrystallized from acetone at room temperature overnight and in the refrigerator (-20 °C) for 2 days. The yield was 1238 g (90 % yield).

Mp=80.3-81.5 °C. (Lit. [30] mp=80.5-81.5 °C) ^{1}H NMR ($CDCl_3$): 2.44 (s, 6H, -CH_3), 3.52 (s, 4H, -O$\underline{CH_2CH_2}$O-), 3.65 (t, *J*=4.7 Hz , 4H, -OCH_2-), 4.13 (t, *J*=4.7 Hz, 4H, TsOCH_2-), 7.34 (d, *J*=8.2 Hz, arom), 7.78 (d, *J*=8.2 Hz, arom).

Tetra(ethylene glycol) ditosylate (2, b=4). Tetra(ethylene glycol) (**1**, a=4) (322 g, 1.7 mol) and NaOH (212 g, 5.30 mol) were dissolved in a mixture of water (0.9 L) and THF (0.6 L). The mixture was cooled down to 0 °C in an ice bath and tosyl chloride (690 g, 3.6 mol) in THF (0.9 L) was added dropwise over 5 hr. During the addition the heterogeneous mixture was mechanically stirred and the temperature was kept carefully at 0 °C. The total reaction time was 12 hr. The reaction mixture was poured into 10 % aqueous HCl (1.5 L) and extracted with toluene (1.5 L x 2). The organic layer was washed with water (3 L x 2), followed by with aqueous K_2CO_3 (0.5 wt %, 2 L) and then with water again (2 L). The organic layer was dried over $MgSO_4$ and toluene was removed by rotary evaporation. The residual pale yellow oil was washed with hot hexane (0.6 L x 2) to remove unreacted tosyl chloride and dried under vacuum. 805 g (94 % yield) of colorless oil was obtained.

^{1}H NMR ($CDCl_3$): 2.45 (s, 6H, -CH_3), 3.55 (m, 8H, -O$\underline{CH_2CH_2O}$$\underline{CH_2CH_2}$O-), 3.68 (t, *J*=4.7 Hz, 4H, -TsOCH_2CH_2O-), 4.15 (t, *J*=4.7 Hz, TsOCH_2-), 7.35 (d, *J*=8.2 Hz, 4H, arom), 7.80 (d, *J*=8.2 Hz, 4H, arom).

18c6 (3, a+b=6) (Procedure A). Into a 5-L 3-neck round-bottomed flask equipped with a mechanical stirrer and a N_2 bubbler, NaH (25 g, 1.05 mol, washed with n-hexane,

2x100 mL) in THF (500 mL) was placed. Tri(ethylene glycol) (**1**, a=3) (55.56 g, 0.37 mol) in THF (500 mL) was added dropwise and the mixture was stirred for 6 hr at room temperature. Tri(ethylene glycol) ditosylate (**2**, b=3) (169.7 g, 0.37 mol) in THF (1 L) was put into the mixture. The reaction mixture was diluted to 4 L and stirred for 2.5 days at room temperature. Water (10 mL) was added slowly to destroy the excess NaH. The salt was filtered and discarded. After evaporation of THF the residual brown oil was passed through a silica gel column (65 g) with $CHCl_3$ (2 L) as an eluent. After evaporation of $CHCl_3$ the remaining oil was extracted with hot hexane (3x100 mL) to obtain about 51 g of light yellow oil, which was dissolved in a mixture of acetone and CH_2Cl_2 (2/1, v/v) and the solution was placed in a refrigerator (-20 °C) overnight to give clear crystals. The crystals were subjected to a second recrystallization to give 22.5 g (23 % yield) of crystals. Mp=39.9-41.0 °C. (Lit. [32] mp=36.5-38.0 °C, [33] mp=39-40 °C) ^1H NMR ($CDCl_3$): 3.689 (s, $-CH_2O-$)

Poly(methacryloyl chloride) (11). In a round-bottomed flask (1-neck, 250-mL) equipped with a condenser, magnetic stirrer and a N_2 bubbler vacuum distilled methacryloyl chloride (30 mL, 0.31 mol), AIBN (0.5 g, $3x10^{-3}$ mol) and toluene (100 mL, distilled over Na/benzophenone) were placed. The mixture was stirred for 20 hr at 95 °C and poured into hexane (500 mL, dried over molecular sieves), and the white precipitate was filtered and dried under vacuum at room temperature. The yield was 14 g (45 %).

30c10 (3, a+b=10) and "60c20" (Procedure A) To a 5-L round-bottomed flask equipped with a mechanical stirrer and a N_2 bubbler, NaH (61.2 g, 60 % oil dispersed, 1.53 mol) was transfered. The NaH was washed with hexane (2x100 mL) and THF (2.5 L) was added. To the suspension, hexa(ethylene glycol) (**1**, a=6) (84.7 g, 0.30 mol) in

THF (500 mL) was added dropwise. The mixture was stirred 2 hr at room temperature. To the mixture tetra(ethylene glycol) ditosylate (**2**, b=4) (155.0 g, 0.308 mol) in THF (400 mL) was added dropwise over a period of 12 hr. The reaction mixture was stirred for 3 days at room temperature. Water (20 mL) was added slowly to destroy the excess NaH. The salts were filtered off and the solvents were rotary evaporated. The residual brown oil was passed through a silica gel column (3 cm dia. x 20 cm long) with CH_2Cl_2 (2 L). After rotary evaporation of CH_2Cl_2 the residual oil was extracted with hot hexane (10 x 200 mL). Hexane was removed by rotary evaporation and the residual oil was dissolved in a mixture of CH_2Cl_2/hexane (1:2, v/v) and placed in the refrigerator (-20 °C). After 2 days nice and clear crystals were found in the solution. The crystals were filtered and washed with cold CH_2Cl_2. Two such recrystallizations were done. Upon drying under vacuum, the crystals collapsed to a powder. The yield was 14.5 g (11 %).

Mp: 38.9-40.3 °C. (Lit. [25] mp=42.0-43.8 °C, [21] mp=35.5-36.8 °C) ^{1}H NMR: 3.669 ($CDCl_3$, s, -CH_2O-); 3.501 (DMSO-d_6, s, -CH_2O-).

After extracting the crude product with hexane, about 50 g of oil was left, which solidified upon cooling down to room temperature. The solid was dissolved in acetone and the solution was placed in the refrigerator (-20 °C). Off-white powdery crystals were passed through a silica-gel column (3 cm dia. x 25 cm length) with CH_2Cl_2 (1.5 L) and the CH_2Cl_2 was evaporated. The residue was dissolved in acetone and the solution was placed in the refrigerator (-20 °C). The white powdery crystals were recrystallized from acetone again (x 2). The white powdery crystals (25 g) were dissolved in a mixture of poly(methacryloyl chloride) (**11**, 25 g), pyridine (0.25 g) and THF (300 mL, refluxed over Na/benzophenone and distilled). The mixture was stirred at room temperature for 8 hr. THF (about 200 mL) was rotary evaporated and the remaining solution was poured into methanol (800 mL). The precipitate was filtered off and the solvents were rotary

evaporated. The residual oil was recrystallized from acetone at -20 °C to give 14.4 g (11 % yield) of white powdery crystals.

Mp: 52.5-54.5 °C. ^{1}H NMR ($CDCl_3$): 3.646 (s, -CH_2O-).

30c10 (3, a+b=10) (Procedure C). In a 5-L 3-neck flask equipped with a mechanical stirrer, a condenser with a N_2 bubbler, and an additional funnel, NaH (21.0 g, 0.90 mol) and THF (2.5 L) were placed. The suspension was heated to 30 °C. To the suspension a mixture of hexa(ethylene glycol) (**1**, a=6) (84.7 g, 0.30 mol) and tetra(ethylene glycol) ditosylate (**2**, b=4) (150 g, 0.30 mol) in THF (1 L) was added dropwise over a period of 21 hr. The salt was filtered off and the solvent was rotary evaporated from the filtrate. The residual brown oil was extracted with hexane (300 mL x 8). Hexane was rotary evaporated and the yellow oil was dissolved in a mixture of hexane and CH_2Cl_2 (2/1, v/v, 200 mL). The solution was placed in the refrigerator (-20 °C) overnight. The clear crystals were filtered and washed with hexane (50 mL). The crystals were recrystallized again (x 2). The crystals were dried under vacuum at 70 °C to give 22.4 g (17 % yield).

Mp: 38.5-40.5 °C. (Lit. [25] mp=42.0-43.8 °C, [21] mp=35.5-36.8 °C) ^{1}H NMR: 3.669 ($CDCl_3$, s, -CH_2O-); 3.501 (DMSO-d_6, s, -CH_2O-).

"42c14" (Procedure A) In a round-bottomed flask (3-neck, 5-L) equipped with a condenser, a N_2 bubbler and a mechanical stirrer NaH (40 g, washed with hexane 100 mL x 2, 1.33 mol) THF (fresh bottle, 1 L) were placed. To the suspension tetra(ethylene glycol) (**1**, a=4) (53. 0 g, 0.27 mol) in THF (500 mL) was added dropwise over 75 min at room temperature and for 1 hr at 60 °C. The mixture was diluted to 3 L with THF. Tri(ethylene glycol) ditosylate (**2**, b=3) (126.2 g, 0.27 mol) in THF (900 mL) was added

dropwise over 15 hr at refluxing temperature. The mixture was stirred for 3 days at refux. Water (14 g) was added to destroy the excess NaH and the salt was filtered off. After the evaporation of the solvent the yellow residue was dissolved in CH_2Cl_2 (100 mL) and the solution was passed through a short silica gel column (50 g) using CH_2Cl_2 (2 L). After evaporation of the solvent the residue was dissolved in acetone (250 mL) and recrystallized at - 20 °C. After five recrystallizations white crystals (33.2 g, 39.2 % yield) were obtained. Melting point: 53.0-55.0. ^{1}H NMR (DMSO-d_6): 3.49 (s, -CH_2O-), small impurity peaks were also found; 4.57 (t, OH), 4.18 (dd, vinyl ether), 3.97 (dd, vinyl ether), 4.09 (t, $TsOCH_2$-), 6.50 (dd, vinyl ether), 7.42 (d, arom), 7.78 (d, arom).

"42c14" (Procedure B) To a 3-necked, 1-L round-bottomed flask fitted with a condenser and a mechanical stirrer NaH (7.60 g, 80 % oil dispersed, 0.25 mol) was added and washed with n-hexane (2 x 60 mL). THF (fresh, 80 mL) was added to NaH, and tetra(ethylene glycol) (**1**, a=4) (12.14 g, 6.25×10^{-2} mol) in THF (40 mL) was added to the suspension dropwise over 30 min. The reaction mixture was allowed to stir without heating for 40 min. The reaction mixture was heated to reflux, and tri(ethylene glycol) ditosylate (**2**, b=3) (14.34 g, 3.13×10^{-2} mol) in THF (40 mL) was added dropwise over a period of 50 min with vigorous stirring. After 6 hr THF (700 mL) was added to dilute the reaction mixture and tri(ethylene glycol) ditosylate (**2**, b=3) (14.45 g, 3.15×10^{-2} mol) was added dropwise to the refluxing reaction mixture over a period of 50 min. The reaction mixture was allowed to stir for 28 hr. Water (5.5 g) was added to destroy excess NaH followed by filtration of the salts. THF was removed by rotary evaporization from the filtrate and the remaing solid was recrystallized (x 3) to give 10.02 g (52 % yield) of off-white crystals.

The crystals (2.0 g), poly(methacryloyl chloride) (**11**, 2.0 g), anhydrous pyridine (0.20 g) and THF (40 mL, distilled over Na/benzophenone) were stirred for 32 hr at room temperature. THF was removed by rotary evaporation until the volume of the mixture was about 20 mL. The mixture was poured into MeOH (250 mL) with vigorous stirring. The white precipitate that formed was filtered off and the solvent was evaporated from the filtrate. The yellow residue (1.3 g) was dissolved in CH_2Cl_2 (20 mL) and filtered through silica gel (0.50 g) using CH_2Cl_2 (100 mL). CH_2Cl_2 was rotary evaporated and the residual oil was recrystallized from acetone. White crystals (1.2 g) were obtained. The ^1H NMR in DMSO-d_6 showed no OH nor vinyl ether proton peaks.

Mp: 53.0-55.0 °C. ^1H NMR (DMSO-d_6): 3.50 (s, -CH_2O-), no other peak found.

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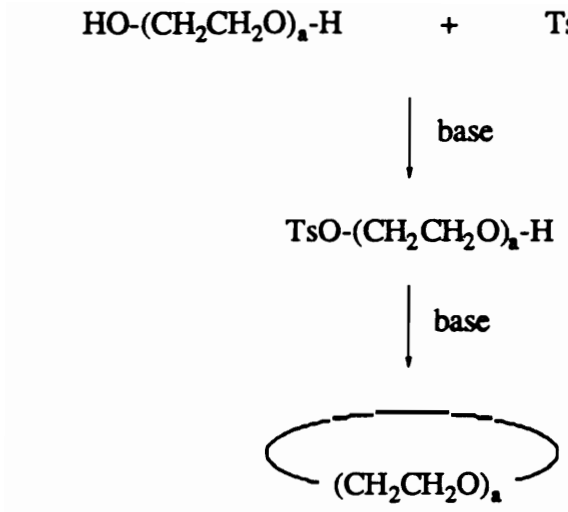
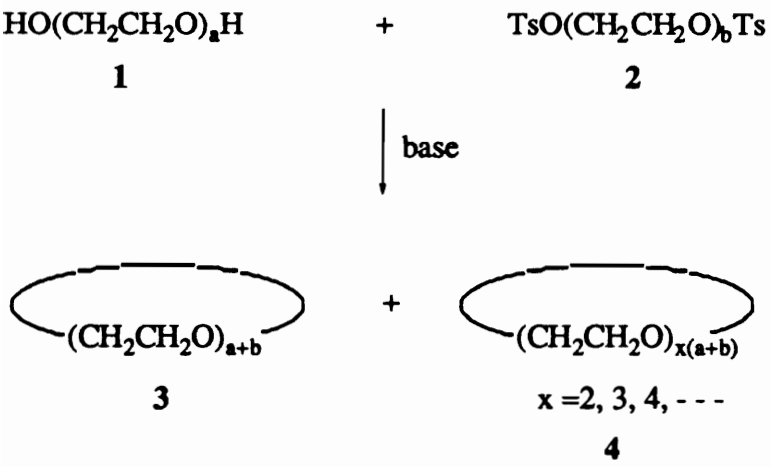
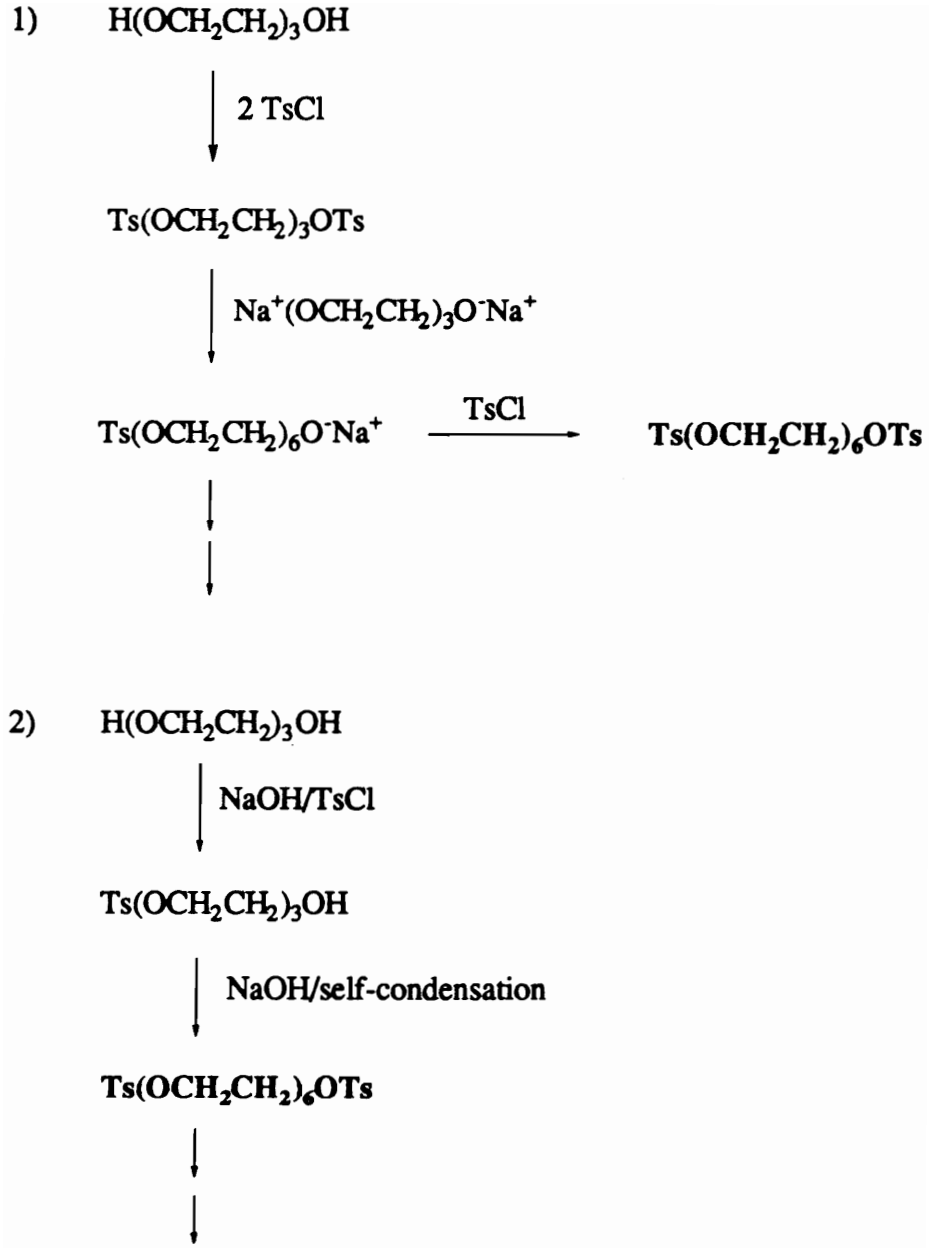


Scheme 1. One-pot method.

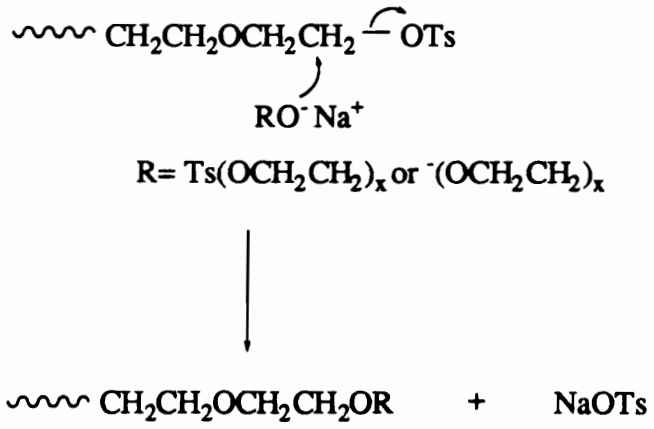


Scheme 2. Multiple condensation method.

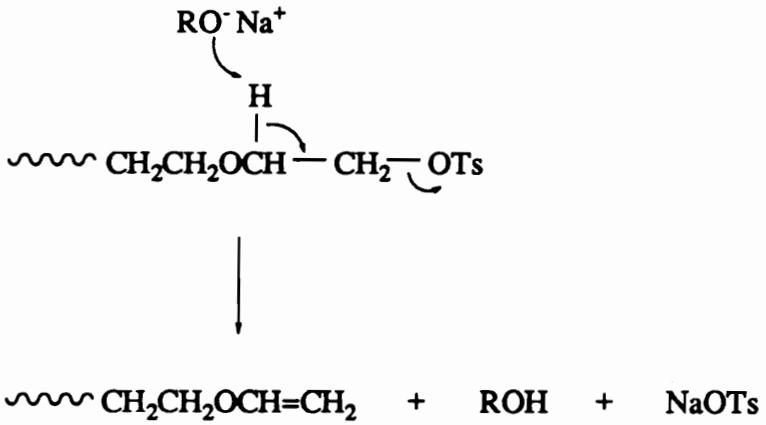


Scheme 3. Dimerization and oligomerization during tosylation.

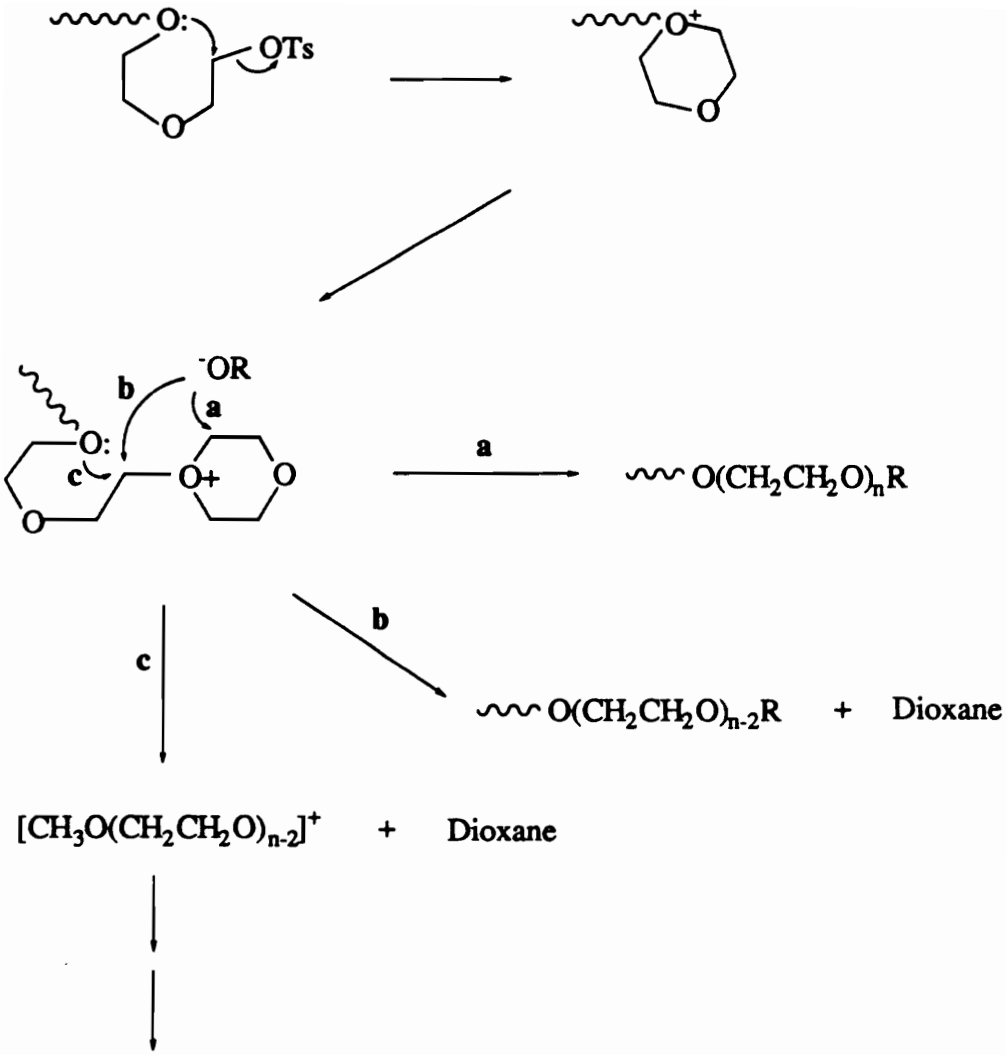
1) S_N2 mechanism



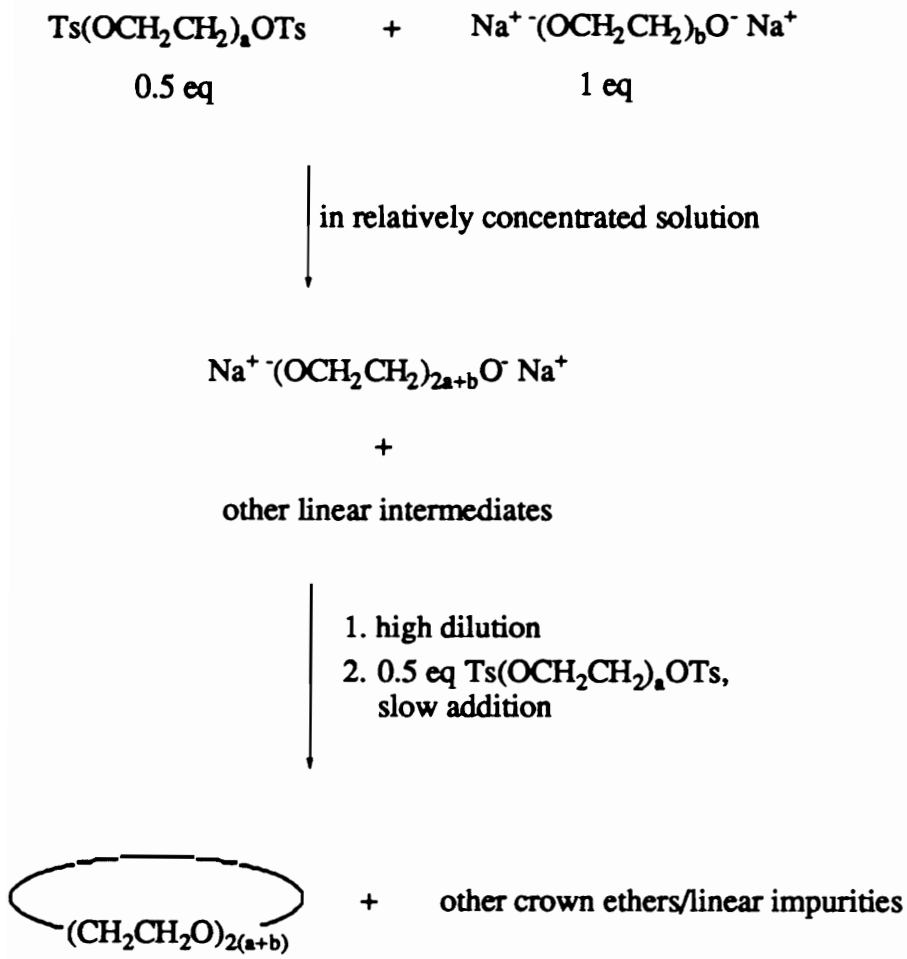
2) Elimination (E2) mechanism



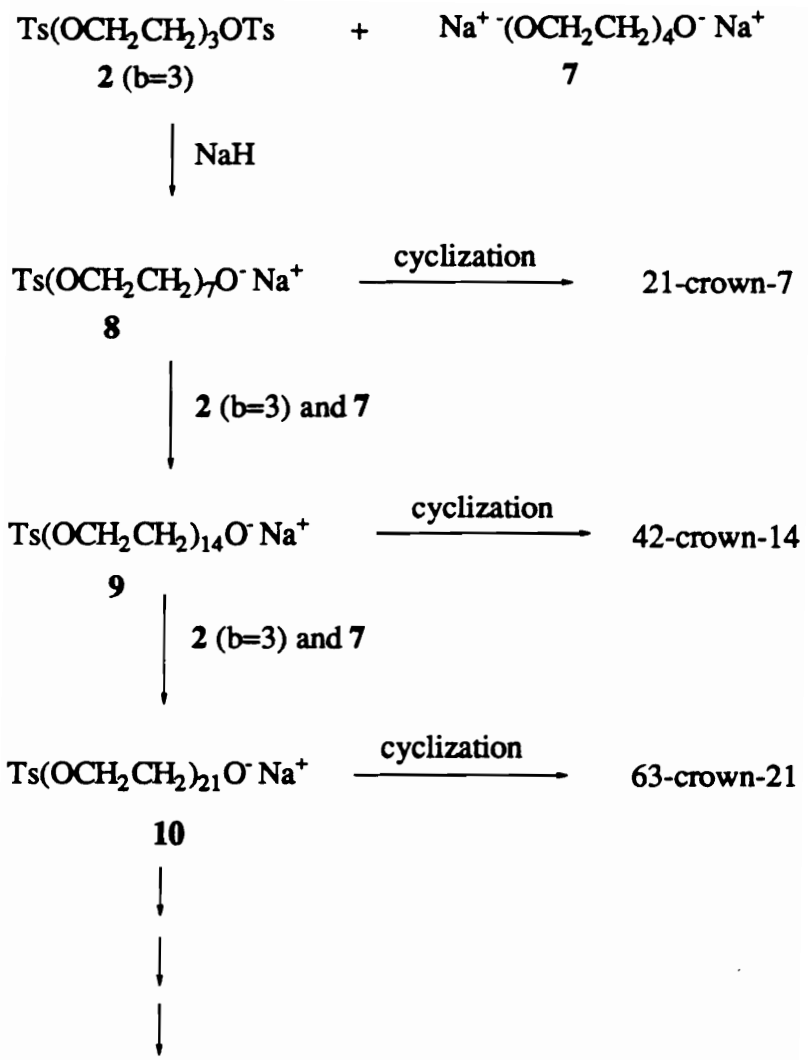
Scheme 4. Substitution reaction (S_N2) and elimination reaction (E2).



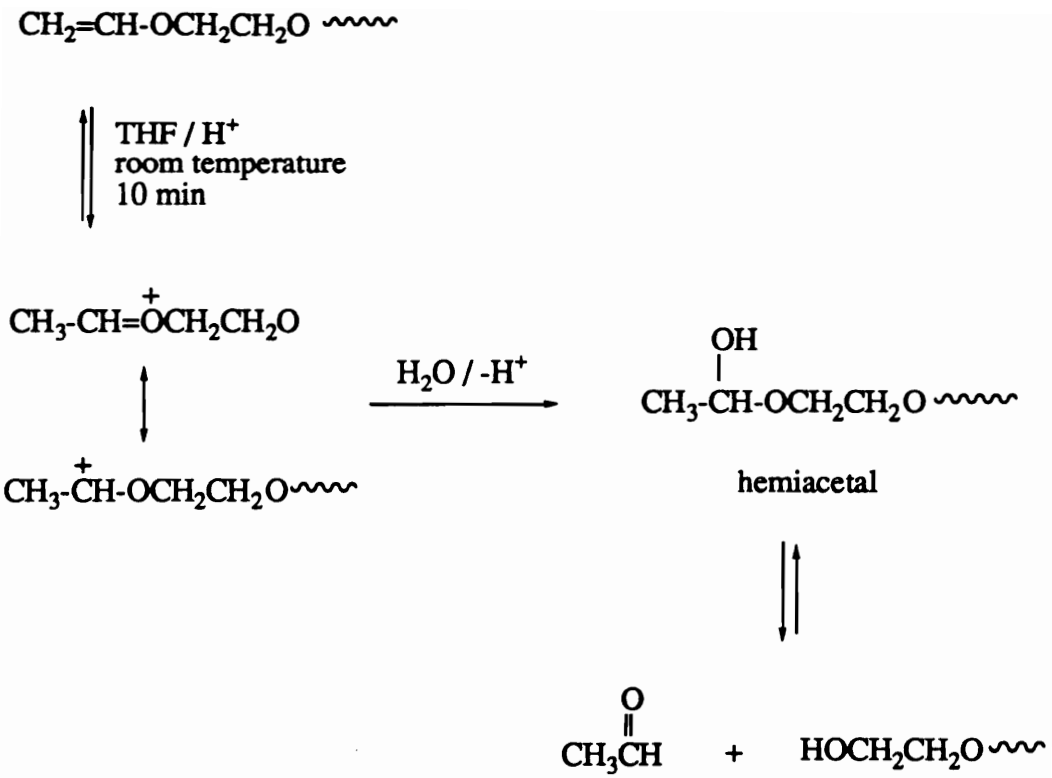
Scheme 5. Back-biting reaction.



Scheme 6. Procedure B: two-step method.



Scheme 7. Formation of crown ethers with various sizes.



Scheme 8. Conversion of vinyl ether group to OH group.

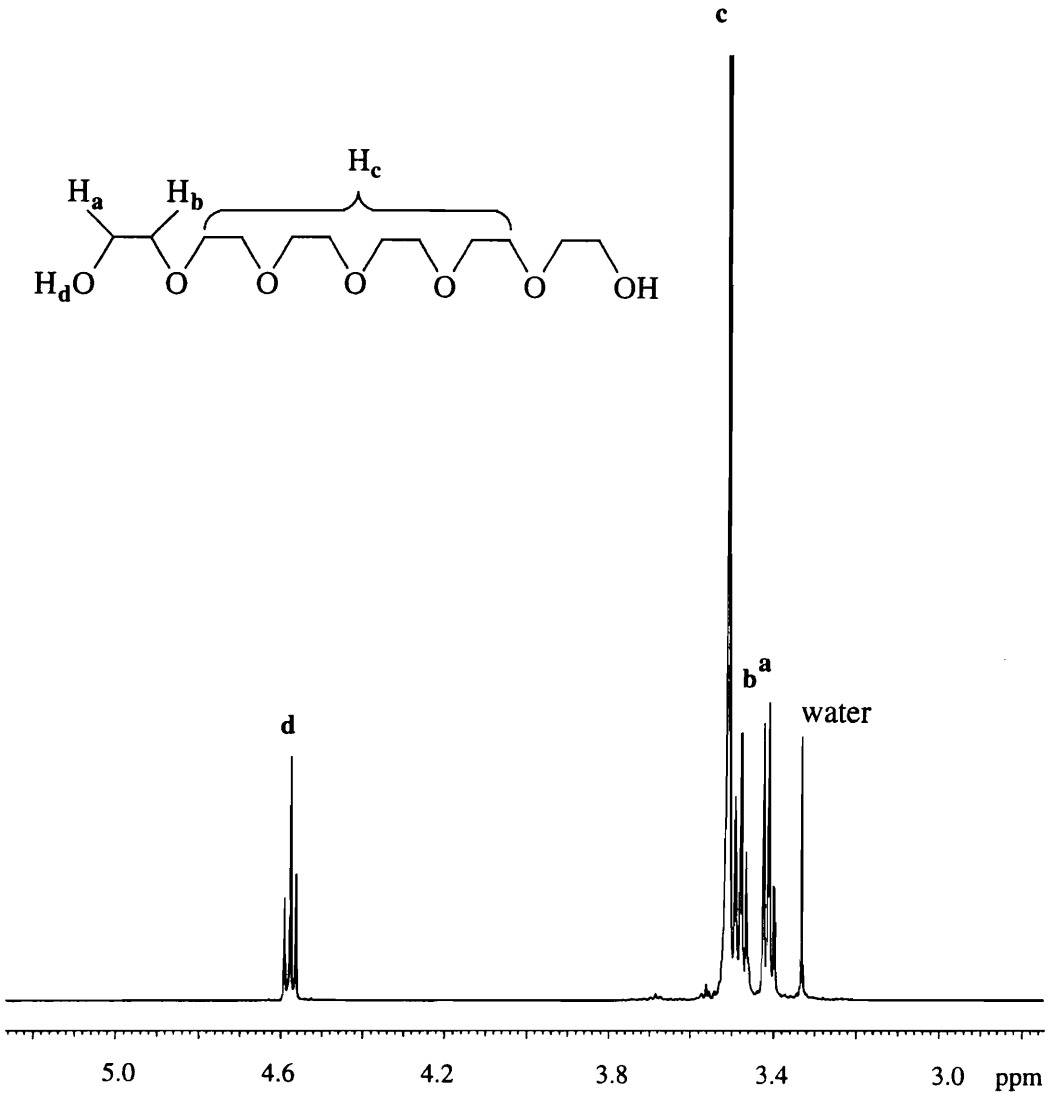


Figure 1. ^{1}H NMR spectrum of hexa(ethylene glycol) (**1**, a=6). (DMSO-d_6)

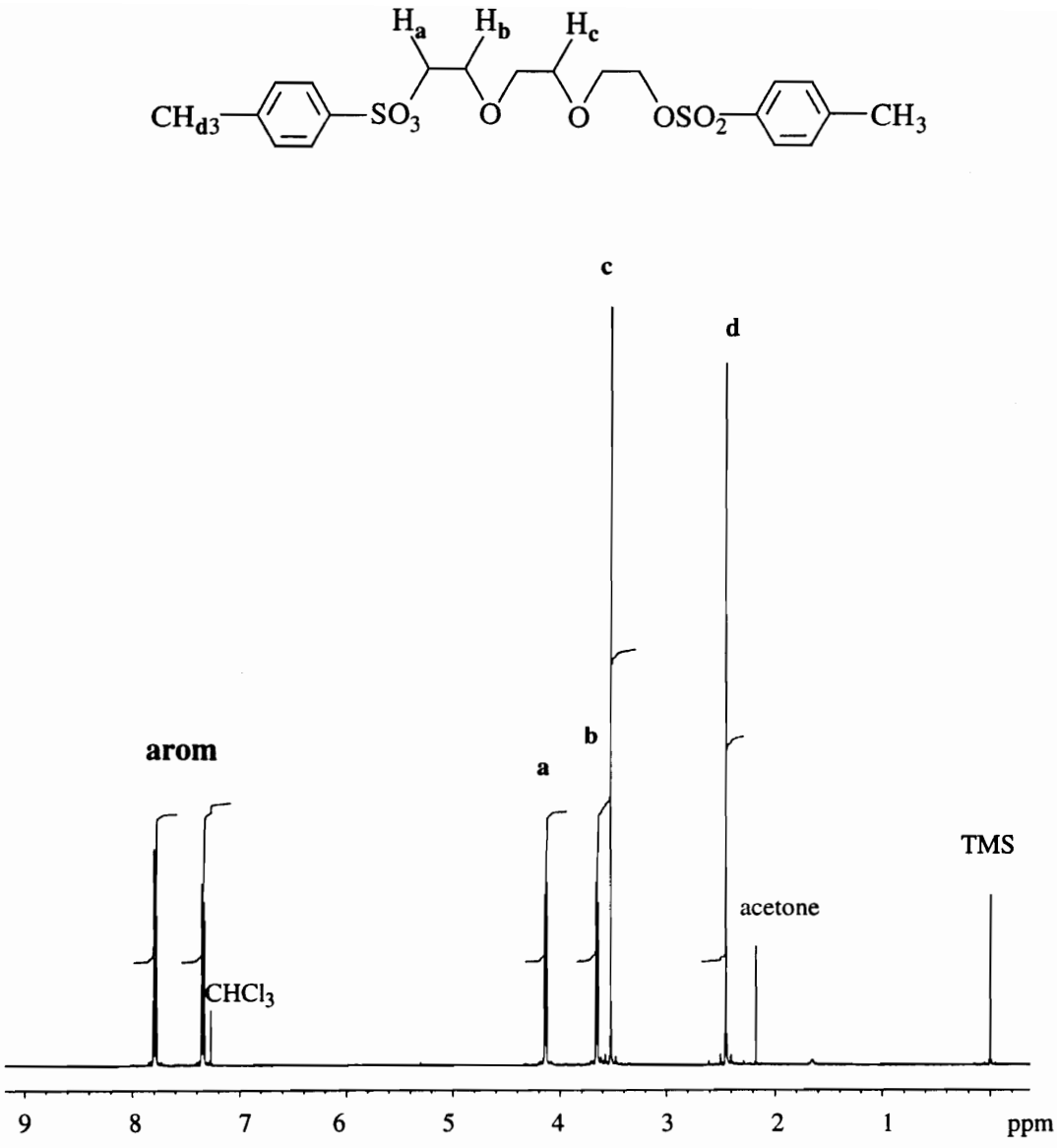
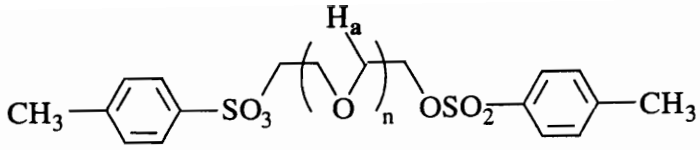


Figure 2. ^1H NMR spectrum of tri(ethylene glycol) ditosylate (**2**, b=3). ($CDCl_3$)



n=5 (average)

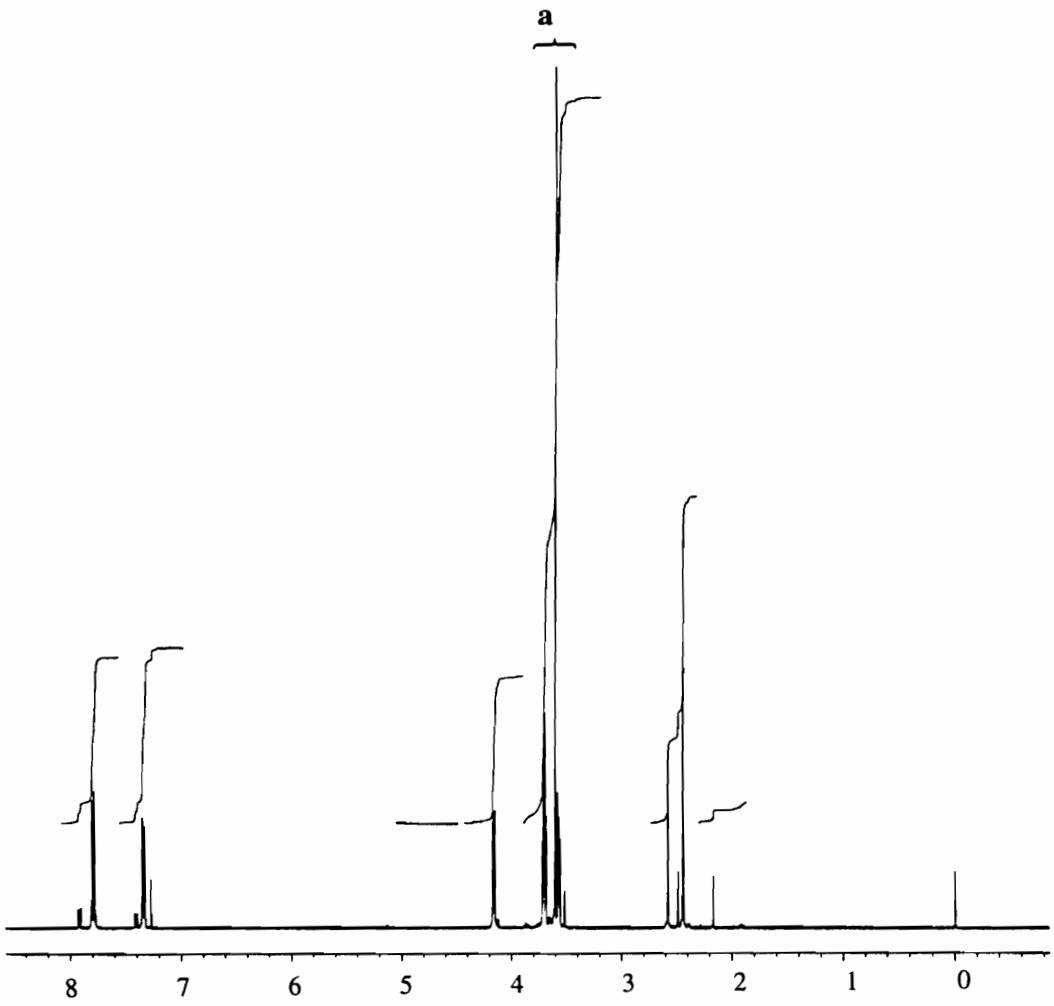


Figure 3. ^1H NMR spectrum of byproduct from aqueous layer. ($CDCl_3$)

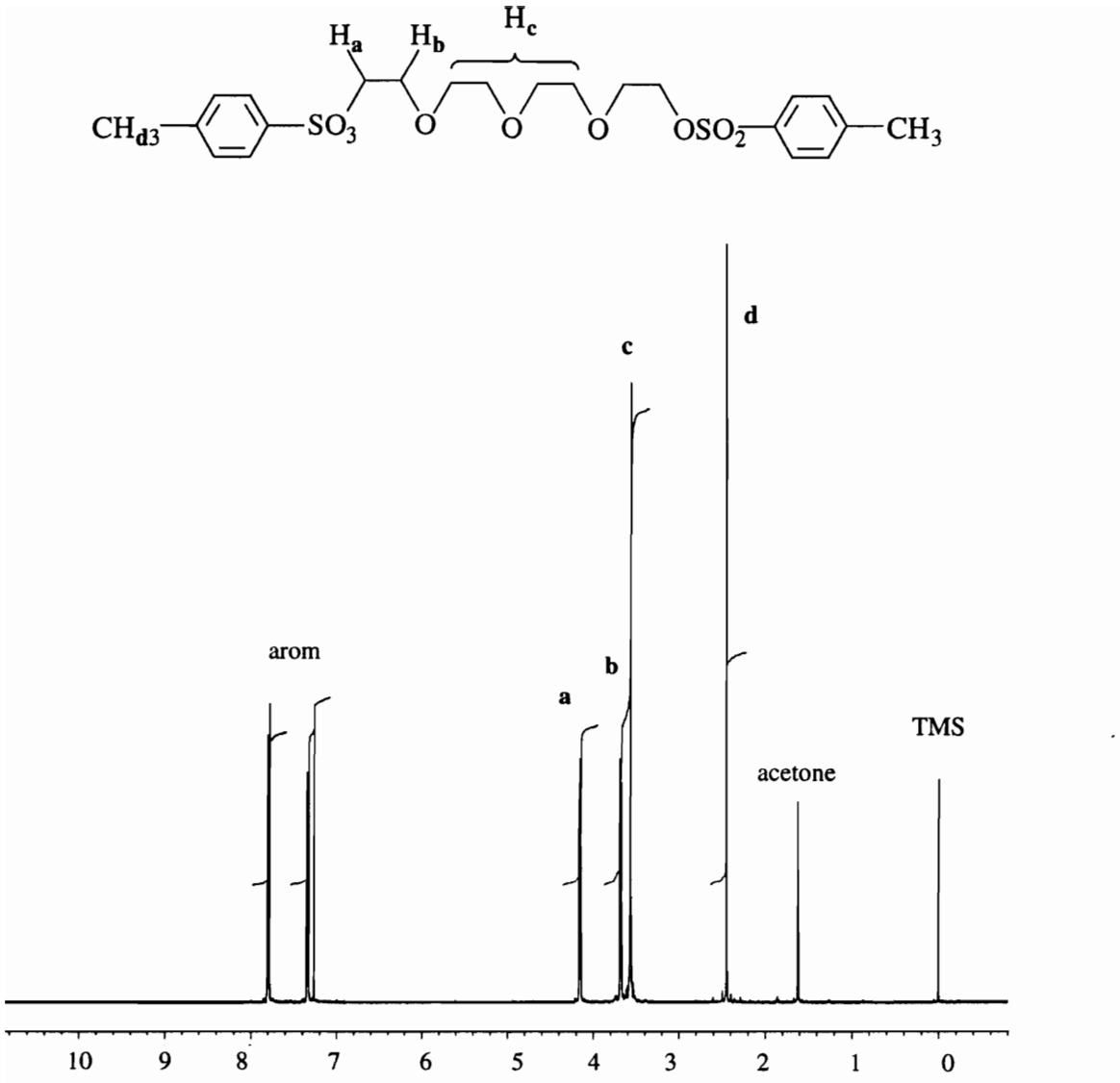
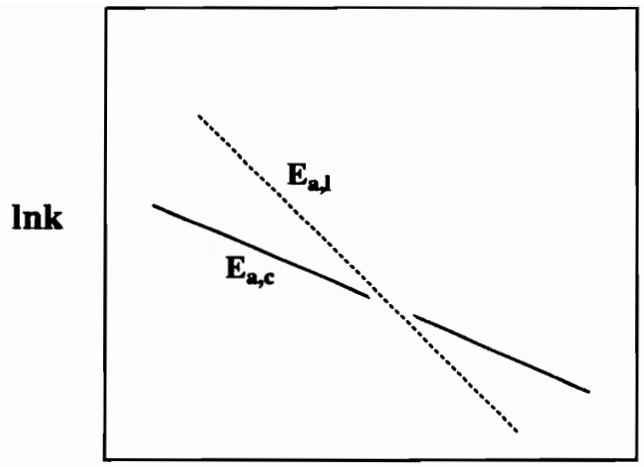


Figure 4. ^{1}H NMR spectrum of tetra(ethylene glycol) ditosylate (**2**, b=4). ($CDCl_3$)



$$\ln k = \ln A - \frac{E_a}{RT}$$

$$E_{a,l} > E_{a,c}$$

Figure 5. Temperature dependence of the reaction rates.

where T = temperature
A = constant
R = gas constant
$E_{a,l}$ = activation energy of bimolecular chain extension reaction
$E_{a,c}$ = activation energy of unimolecular cyclization reaction

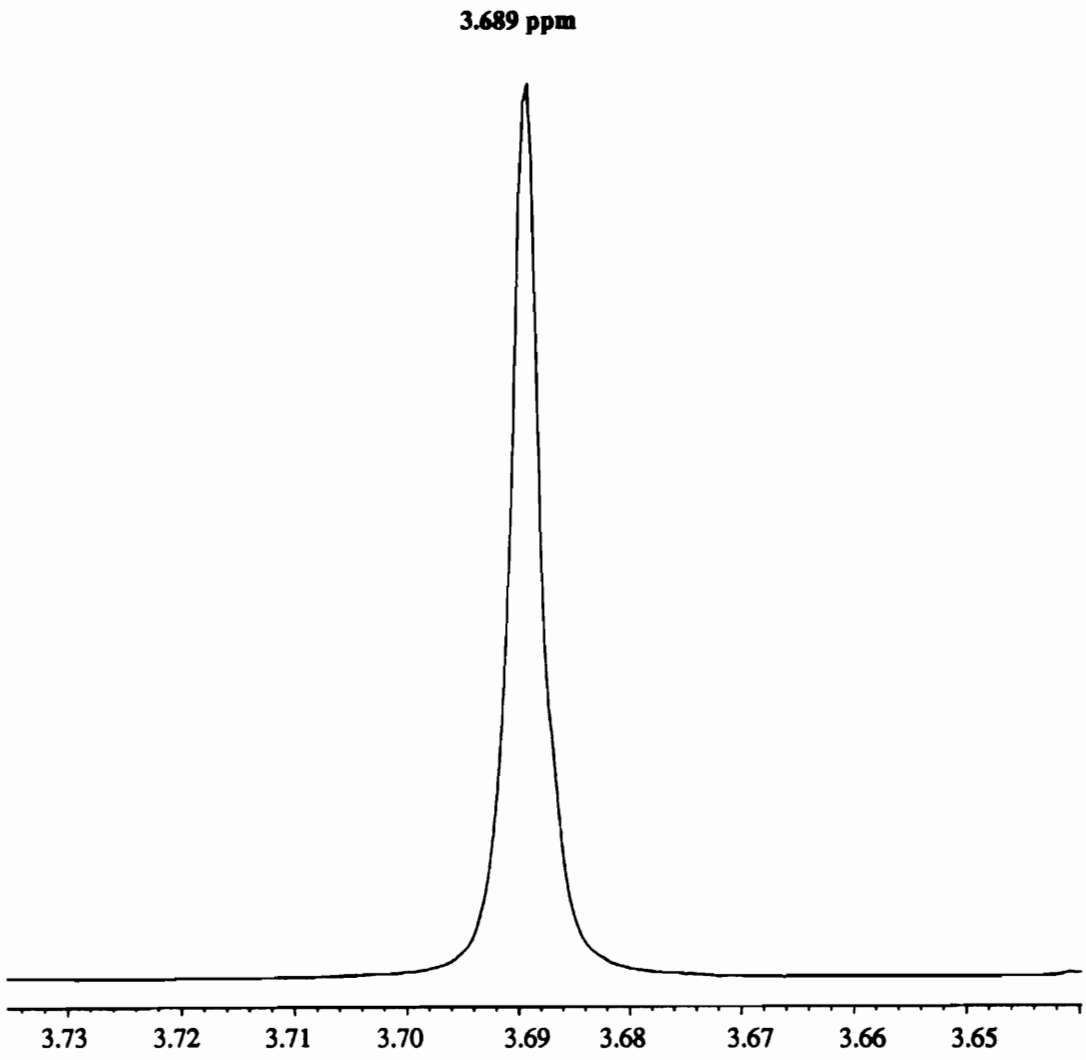


Figure 6. ^{1}H NMR spectrum of 18-crown-6. ($CDCl_3$)

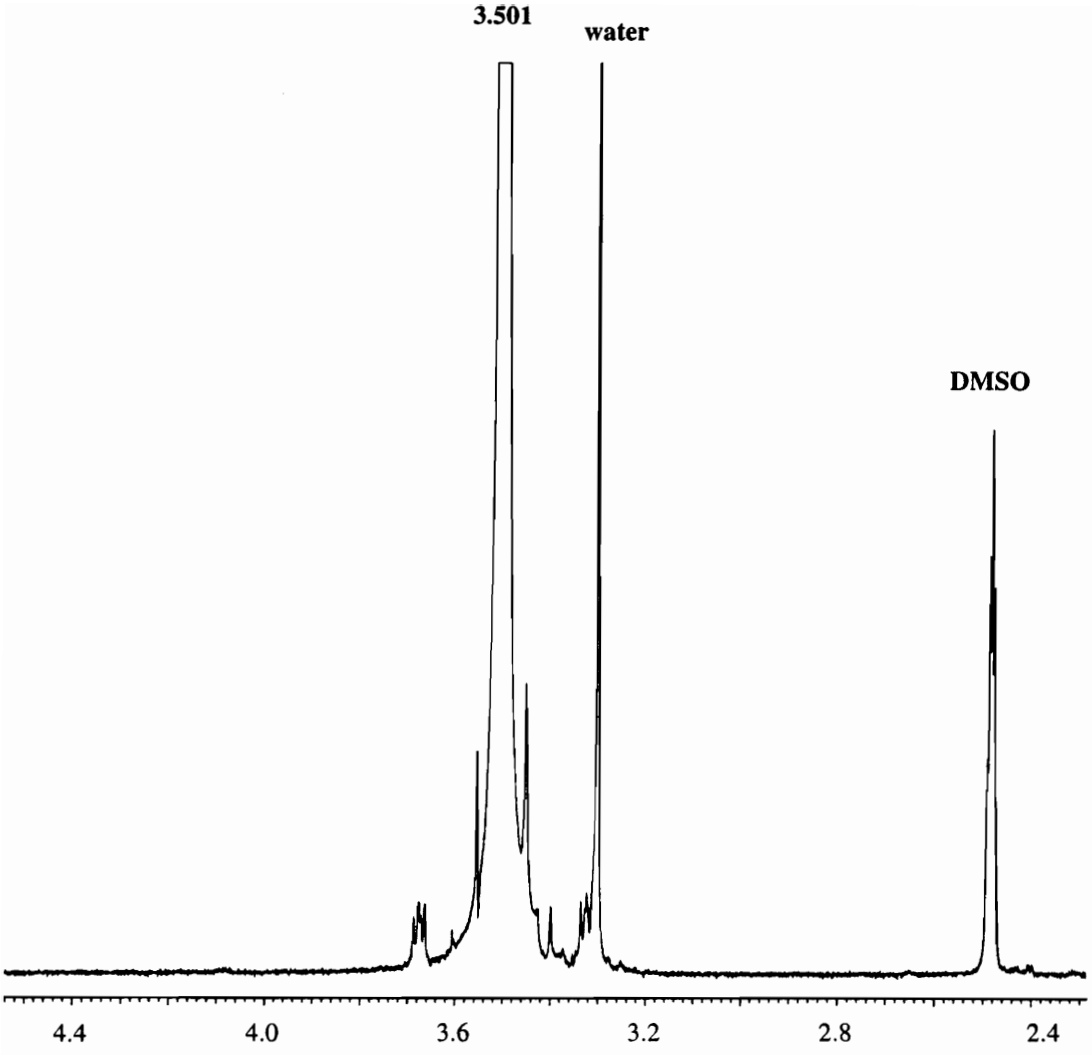


Figure 7. ^{1}H NMR spectrum 30-crown-10. (DMSO-d_6)
(Peaks at 3.32, 3.40, 3.45, 3.56, 3.60 and 3.68 ppm are side bands due to vertical expansion)

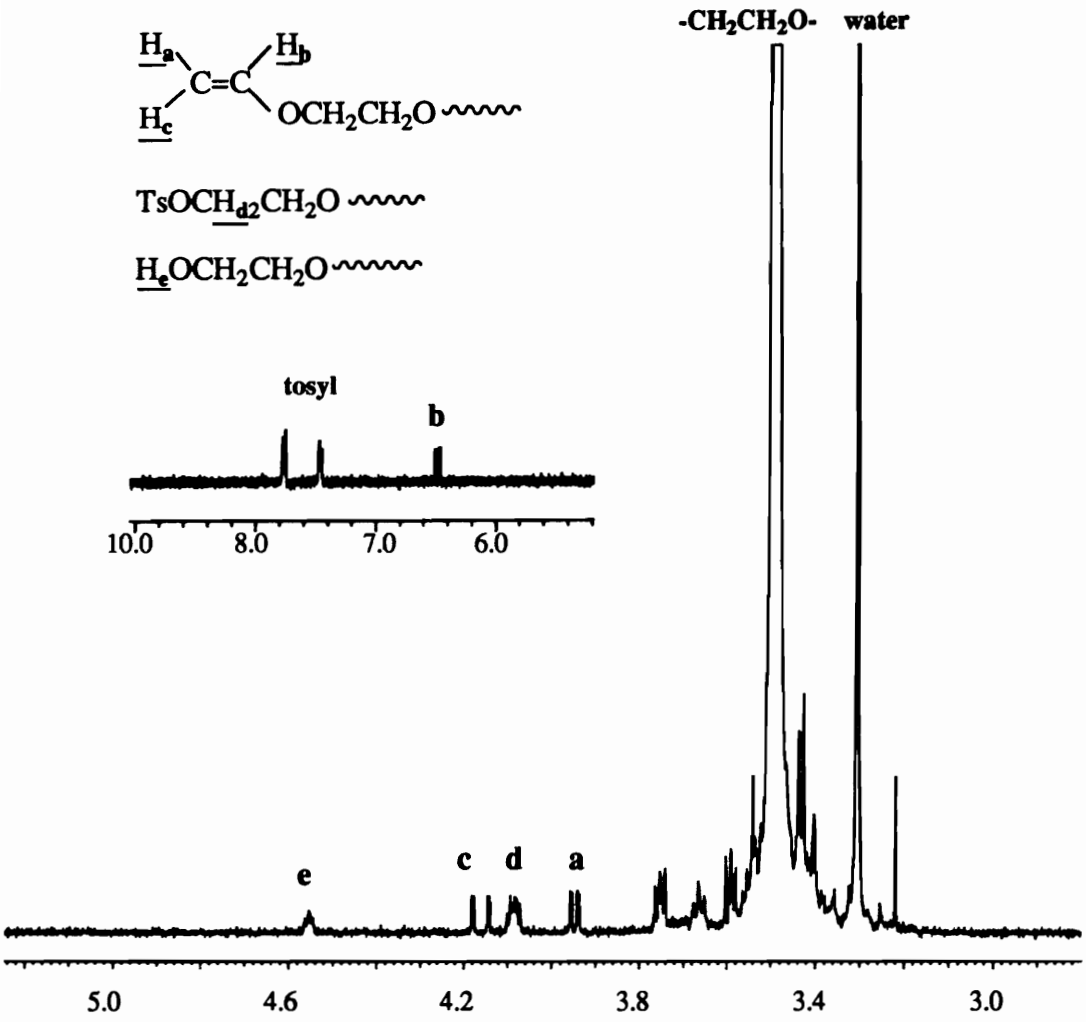


Figure 8. ^{1}H NMR spectrum of crude "42-crown-14". ($CDCl_3$)

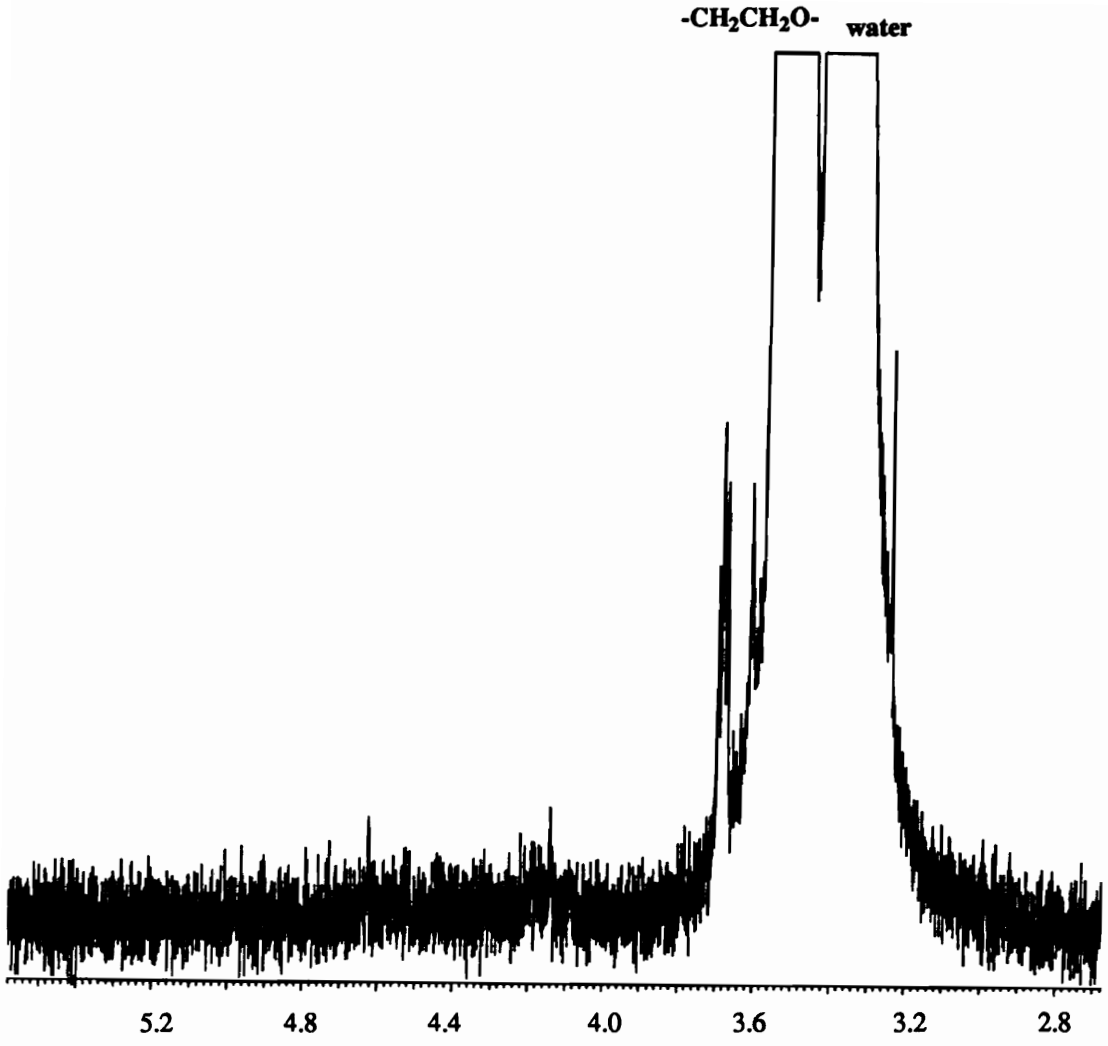


Figure 9. ^{1}H NMR spectrum of "42-crown-14" after treatment with poly(methacryloyl chloride). ($CDCl_3$)

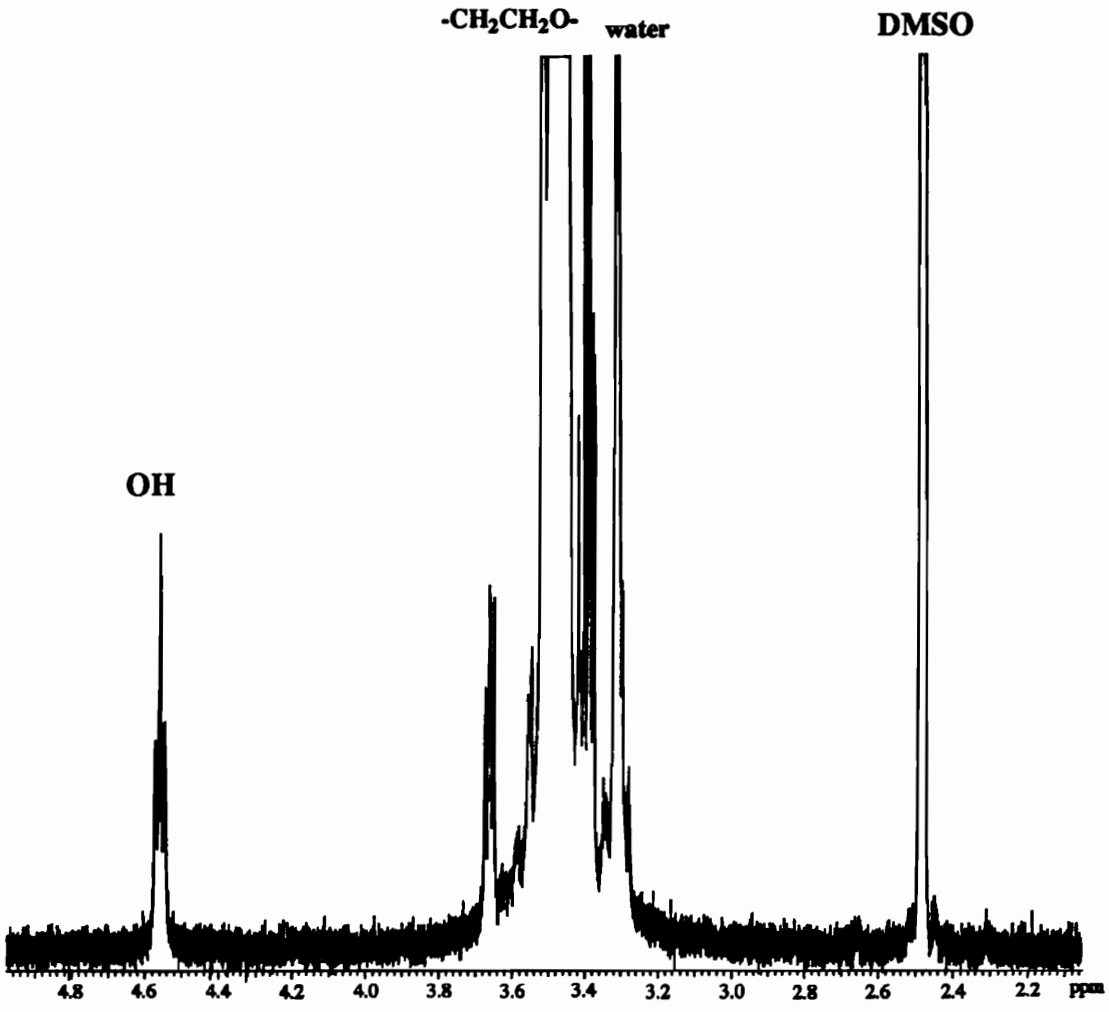


Figure 10. ^{1}H NMR spectrum of PEO (3,400) in DMSO-d_6

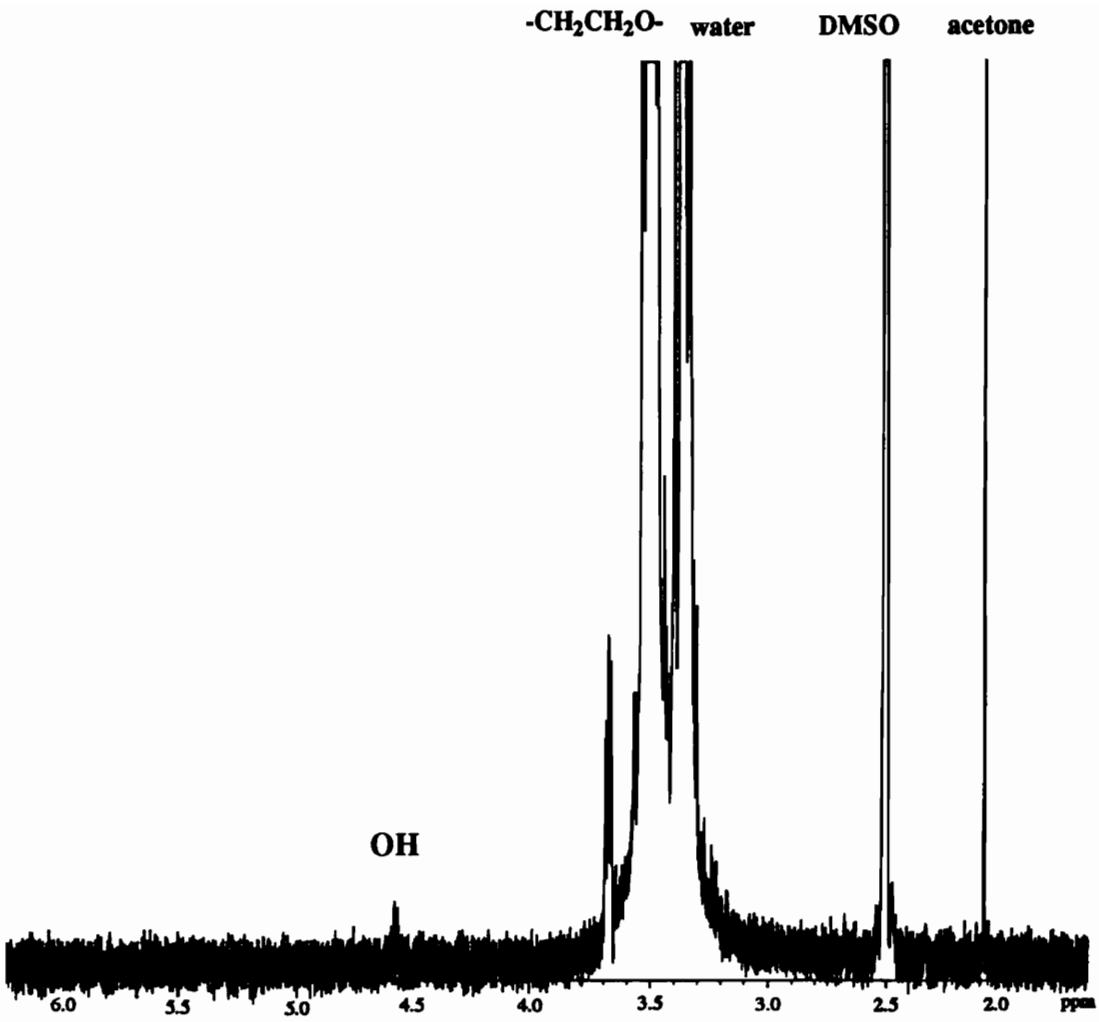


Figure 11. ^{1}H NMR spectrum of PEO (100K) in DMSO-d_6

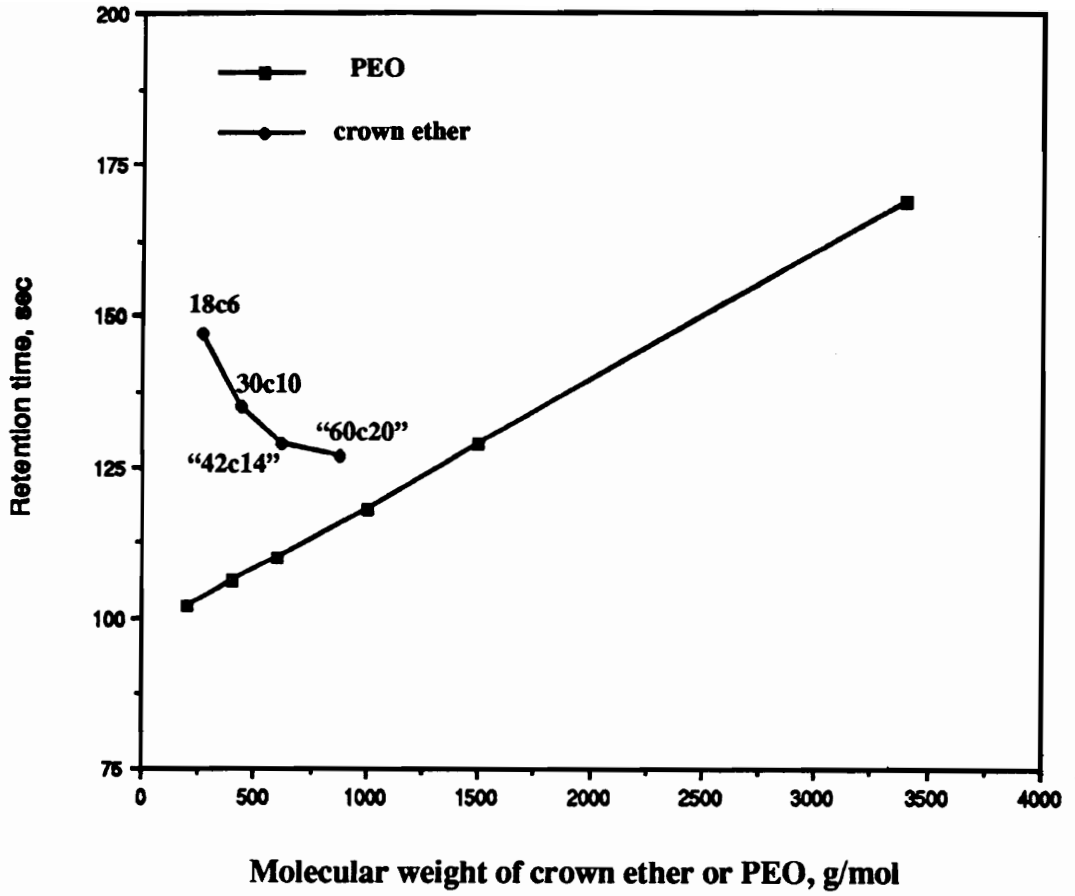


Figure 12. Retention time *vs* molecular weight of crown ethers and PEOs.
[Solvent: MeOH/acetonitrile=2/8, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

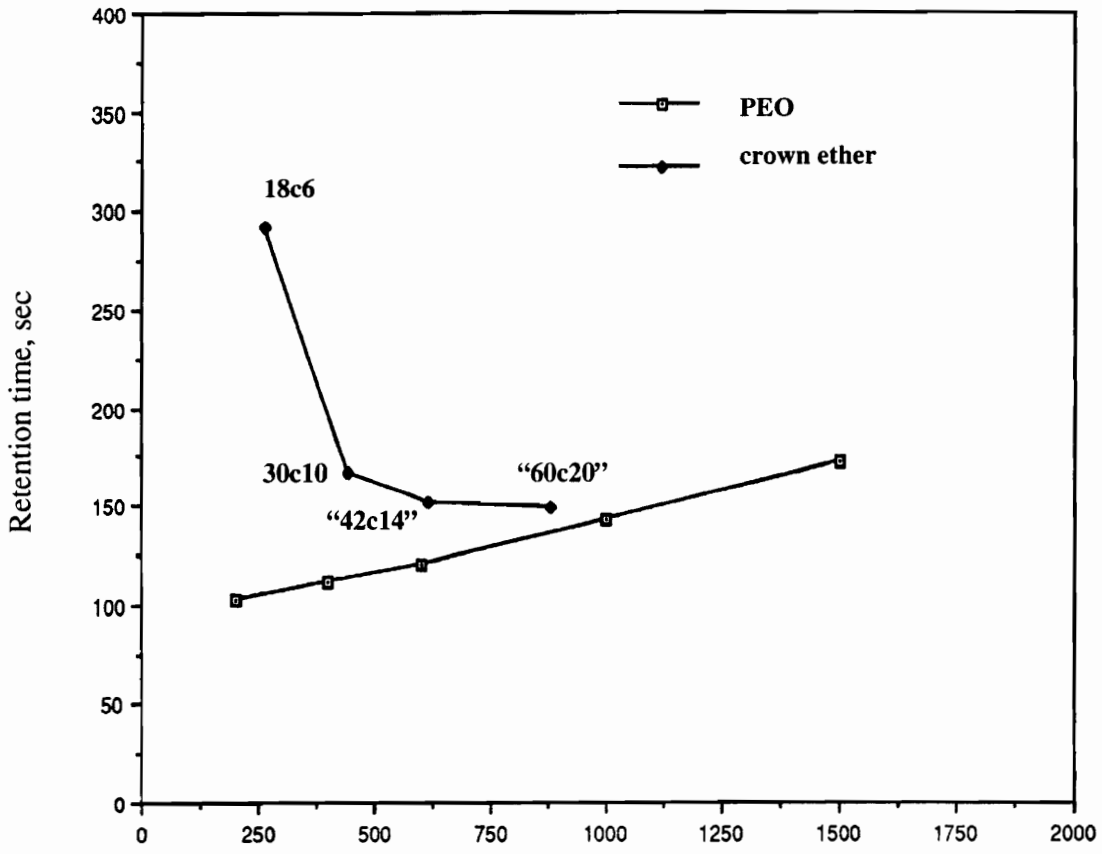


Figure 13. Retention time *vs* molecular weight of crown ethers and PEOs. [Solvent: MeOH/acetonitrile=1/9, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

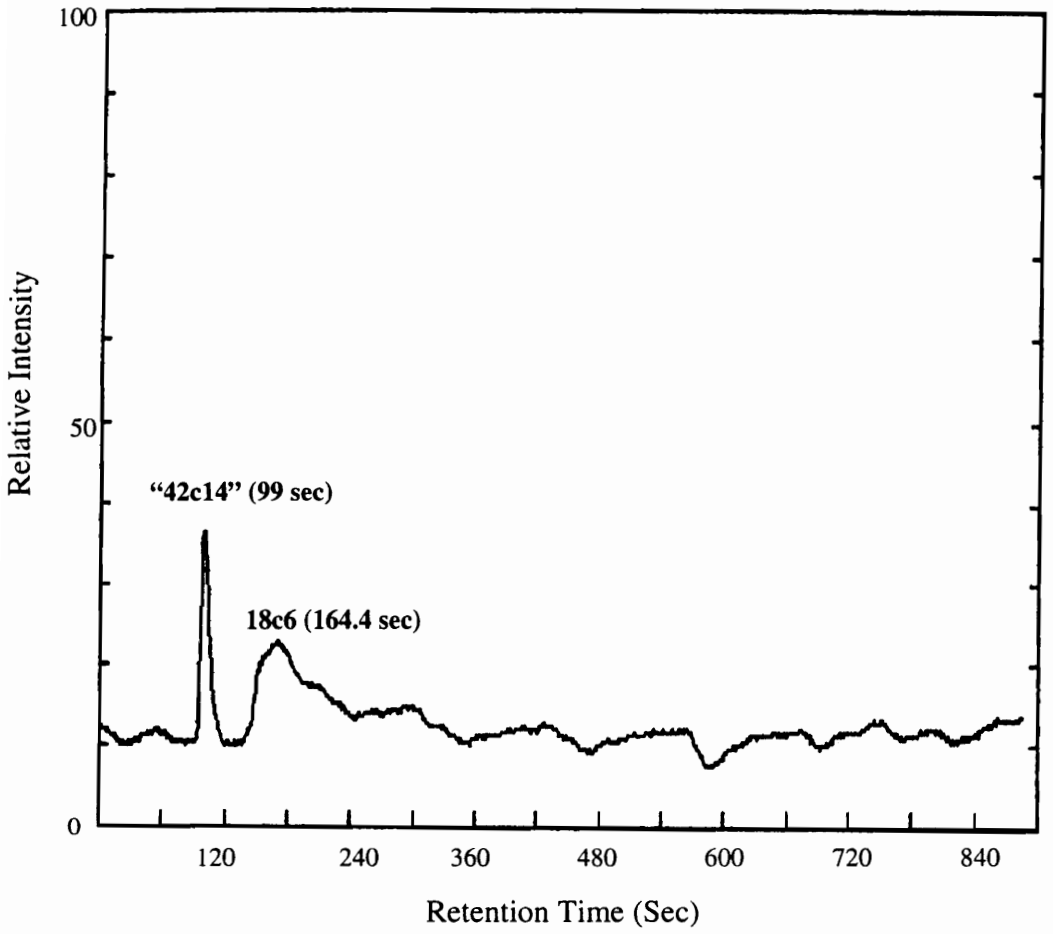


Figure 14. HPLC trace of a mixture of "42c14" and 18c6.
[Solvent: MeOH/acetonitrile=1/1, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

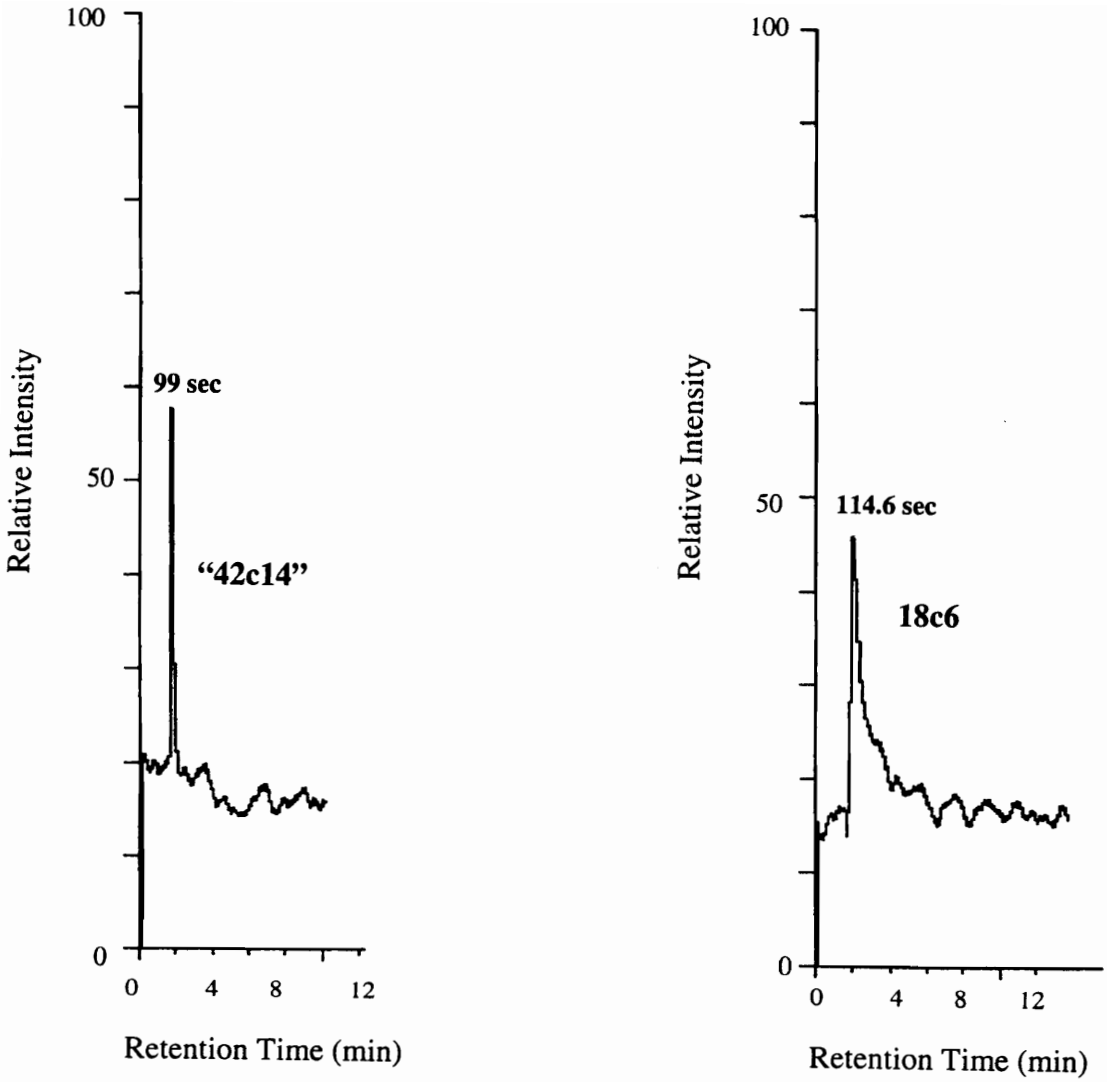


Figure 15. HPLC traces of "42c14" and 18c6.
[Solvent: MeOH/acetonitrile=1/1, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

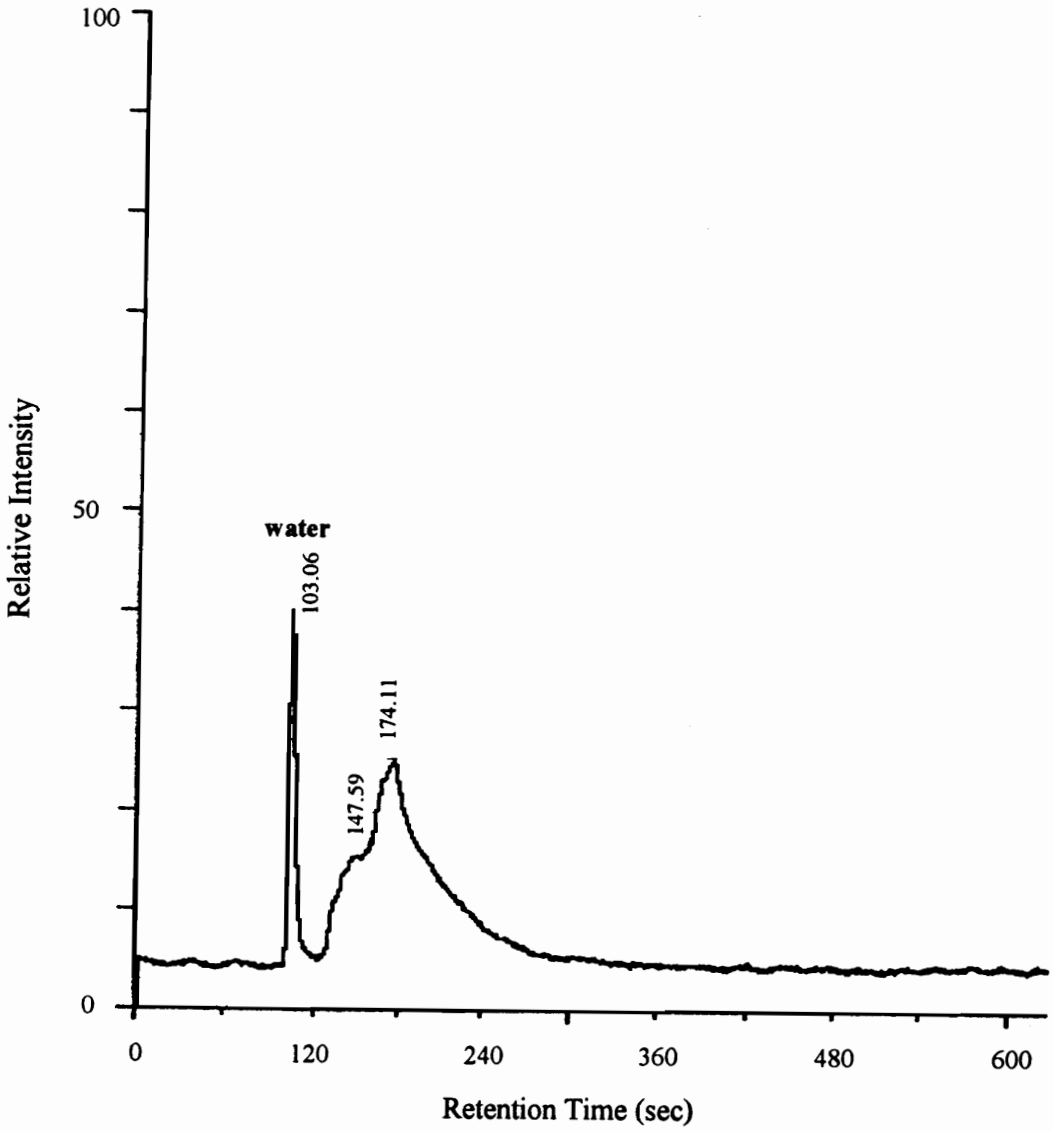


Figure 16. HPLC trace of a mixture of 30c10 and "60c20".
[Solvent: MeOH/acetonitrile=1/9, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

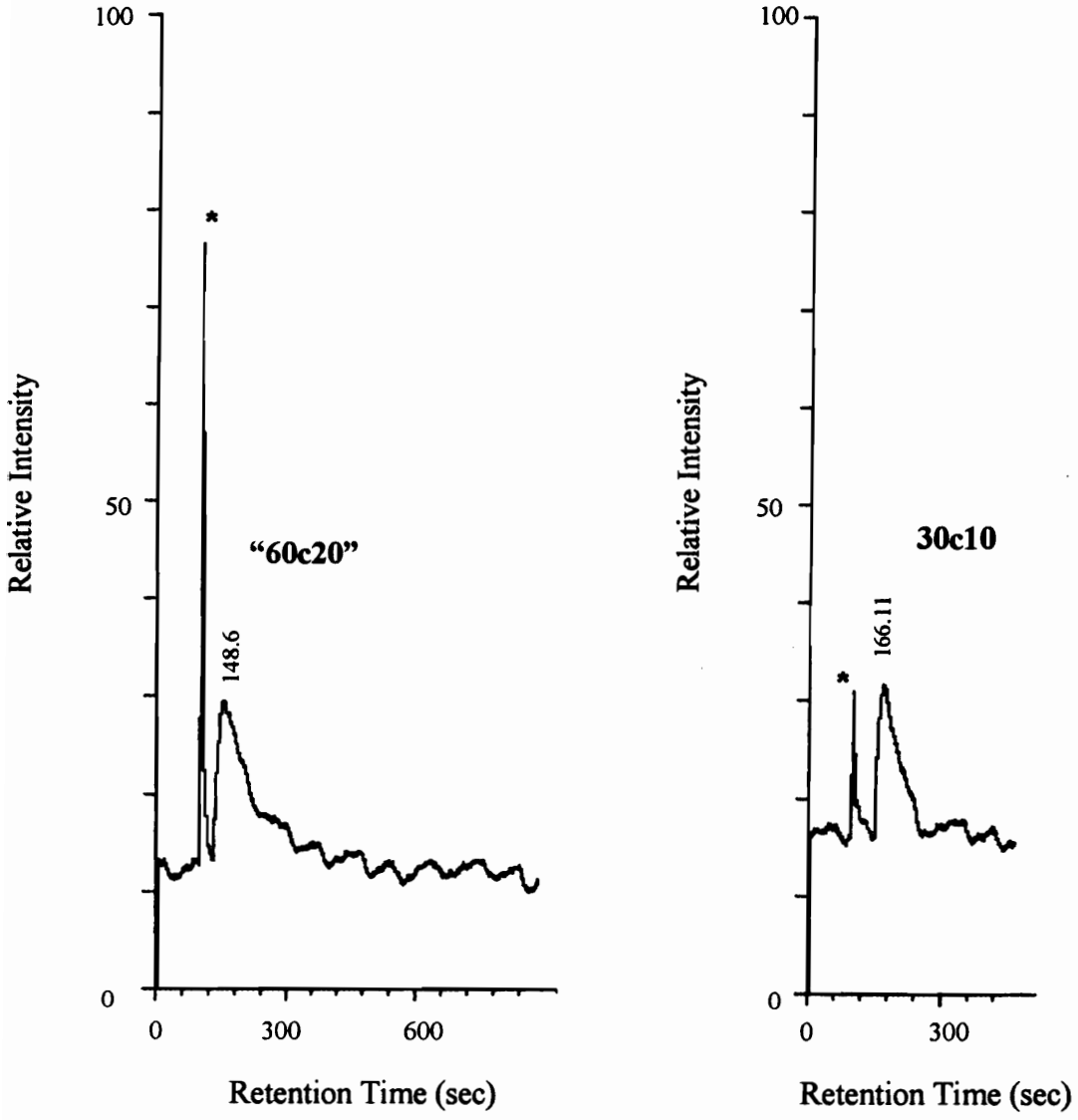


Figure 17. HPLC traces of 30c10 and "60c20".
[Solvent: MeOH/acetonitrile=1/9, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]
* water

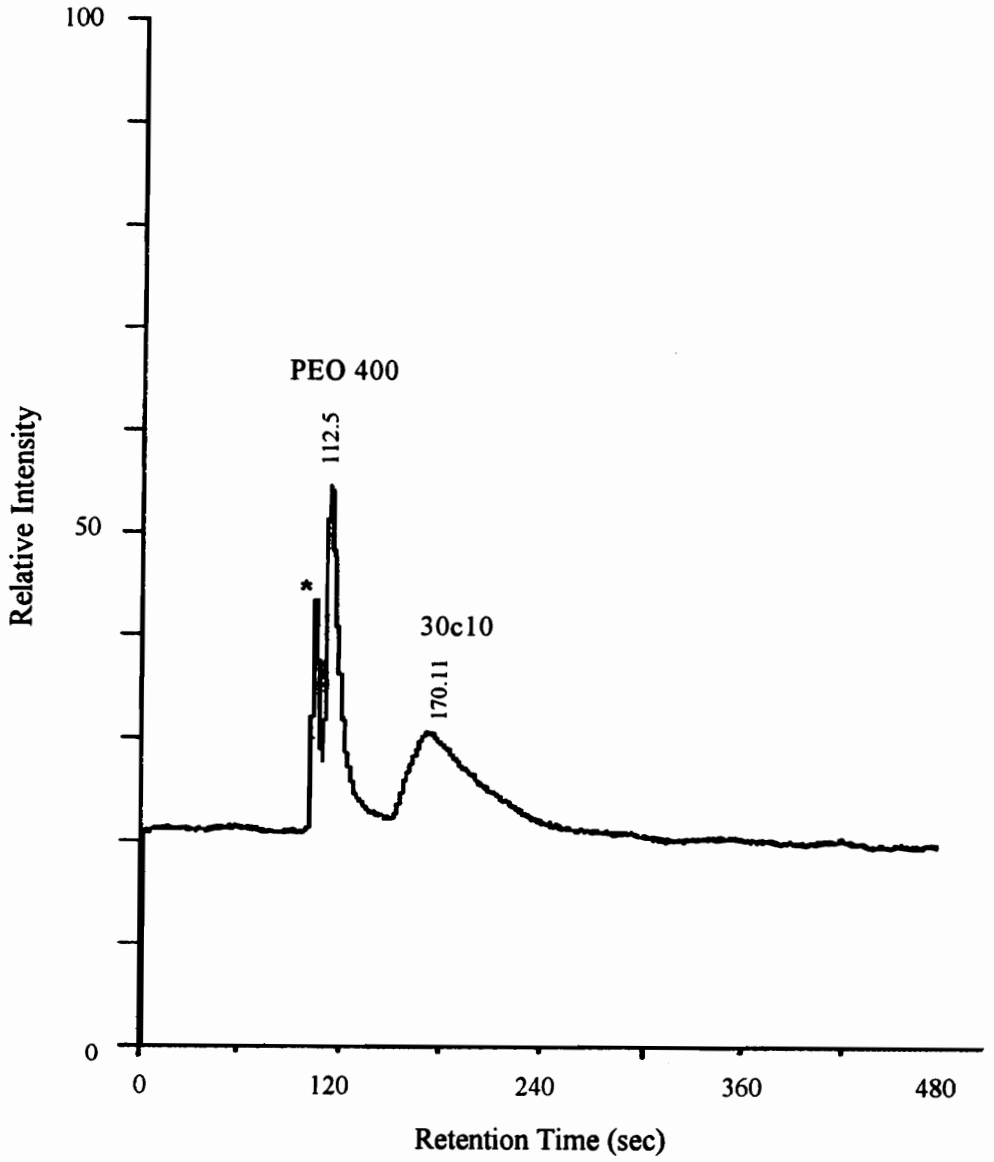


Figure 18. HPLC trace of a mixture of 30c10 and PEO (400).
[Solvent: MeOH/acetonitrile=1/9, v/v. Column: Deltabond C_8 reverse-phase column (4.6 mm x 15 cm, particle size 5 μm, pore size 300 A)]

* water

CHAPTER V

42-CROWN-14-BASED [2]CATENANE

Since Wasserman experimentally proved the existence of catenanes [1], which are physically interlocked macrocycles, in 1960, quite a few catenanes have been synthesized and their topological structures have been determined and characterized satisfactorily. [2-3] Before the concepts of the "template effect" [4] and "self assembly" [5] were successfully utilized in the syntheses of topologically complex molecules, catenanes had been prepared by statistical [1, 6-8] or central core [9] methods. Because the probability of the formation of interlocked ring structures was limited in a simply statistical method, the yields of catenanes were usually low, a few percent or less. [1, 8] Recently, however, several research groups demonstrated that certain catenanes and even more complicated topological isomers could be prepared in excellent yields by taking advantage of supramolecular interactions such as metal-ligand interactions, π–π interactions and H-bonding between the precursor molecules. [10-15] In those high yielding systems the molecules must contain certain types of chemical units which induce the attractive interactions. Thus, it is difficult to synthesize catenanes in high yields when there are no attractive interactions between the components.

Although aliphatic crown ethers are one of the oldest and simplest types of macrocycles [16-21], there has been no report on the synthesis and isolation of catenanes comprised of simple aliphatic crown ethers so far. This might be due to the difficulty in isolation as well as synthesis itself. Our group has been involved for several years in the synthesis of aliphatic crown ethers larger than 30-membered, which are capable of being threaded by linear molecules. [19] During the preparation of the 42-crown-14 (42c14) it

was found that there was a certain amount of an unknown compound in the crude product. After isolation and structural determination the unknown substance was found to be 42c14-[2]catenane. In this chapter, the first synthesis, isolation, and structural characterization of this [2]catenane are described in detail.

RESULTS AND DISCUSSION

1. Synthesis of 42-Crown-14-[2]Catenane (10)

42c14-[2]catenane was prepared during the synthesis of 42c14 in which tri(ethylene glycol) ditosylate was added slowly to a diluted suspension of the sodium dianion of tetra(ethylene glycol) in tetrahydrofuran (THF). As shown in Scheme 1, two-piece combination of the sodium dianion (**1**) of tetra(ethylene glycol) and tri(ethylene glycol) ditosylate (**2**) resulted in **3**, which either cyclized to form 21-crown-7 (21c7) (**4**) or reacted with **1** to produce dianion **5**. After the chain extension from the reaction of **5** and **2**, the resulting compound **7** afforded 42c14 (**8**) through cyclization, or reacted further with **1** and ended up with the formation of crown ethers larger than 42c14 or linear oligomers or polymers. The intermediate **3** could react with **2** to form deca(ethylene glycol) ditosylate (**6**), which produced **7** by the reaction with **1**. Once 42c14 was formed in the reaction mixture, it is believed that the "complexation" (**9**) between 42c14 and the sodium salt of **7** occurred. The cyclization of **7** in complex **9** could afford 42c14-[2]catenane (**10**). In Scheme 1, there must be side reactions such as elimination reactions and the combinations of **3** and **5** or **3** and **7** etc, which could also lead to the formation of larger crown ethers and linear polymers. Along with such side

reactions, although they could not be detected or isolated, the crude product might contain catenanes other than 42c14-[2]catenane (**10**) such as [2]catenanes comprised of 42c14 and 63-crown-21, etc.

2. Isolation of 42-Crown-14-[2]Catenane (10)

After the reaction, most of the linear polymers and large crown ethers were removed from the crude mixture by recrystallization from acetone. Therefore, 21c7 (**4**) and 42c14-[2]catenane (**10**) were enriched in the filtrate and easily detected in the ^1H NMR spectrum of the residual oil from the filtrate due to their different chemical shifts. In Figure 1, which is the ^1H NMR spectrum of the filtrate in $CDCl_3$, there are four main peaks. The signal at 3.646 ppm was the main peak in ^1H NMR spectra of poly(ethylene oxide)s (PEOs) or large crown ethers such as 42c14 and 60-crown-20. [17, 19] The peak at 3.653 and the shoulder at 3.651 ppm were found in ^1H NMR spectra of low molecular-weight PEOs. We also could assign the signal at 3.688 ppm as 21c7 (**4**). However, the peak at 3.660 ppm was not observed in ^1H NMR spectra of other crown ethers and PEOs with various molecular weights.

The isolation of the catenane from the filtrate was achieved by column chromatography. Due to strong interactions between crown ethers and the silica gel stationary phase, the chromatographic separation and isolation of the catenane was not a simple task. The residual oil from the filtrate gave a long column-like spot on silica gel TLC plates with polar solvents such as acetone and ethyl acetate, which meant that each compound had a long tailing on silica gel stationary phase. With less polar solvents such as chloroform and ethers as solvents, no development of the spot along the TLC plate was achieved. Therefore, it was necessary to fractionate the crude product into as many

fractions as possible using a polar solvent as eluent. Thus, 2.3 g of the crude mixture was separated into 200 fractions through a silica gel column with acetone as eluent. All fractions except the initial fractions (Fractions 1-15) showed "tailing" on silica-gel TLC plates. In the ^1H NMR spectra in $CDCl_3$ the initial fractions gave several peaks but consisted mainly of the 3.653 ppm signal. The main peaks of the next fractions (Fractions 16-55) appeared at 3.646 and 3.688 ppm. The peak at 3.659 ppm (or 3.660 ppm with ± 0.0005 ppm range) became a major peak of the later fractions (Fractions 56-85) as shown in Figure 2.

The last fractions (Fractions 180-200) gave only a singlet at 3.659 ppm, which was 42c14-[2]catenane (**10**). Therefore, we believe that during the chromatography oligo-PEOs eluted first, followed by 21c7 (**4**), then 42c14 (**8**) and relatively high-molecular weight oligo-PEOs, and finally 42c14-[2]catenane (**10**).

The yield of the catenane was found to be 8 % according to the peak integrations of the ^1H NMR spectrum of the residue from the filtrate (Figure 1). The pure compound isolated by the column chromatography, however, was only 20 mg (0.9 % yield).

3. Characterization

The HPLC trace and the ^1H NMR spectrum of the isolated catenane (Fractions 180-200) are shown in Figures 3 and 4, respectively. The HPLC trace (Figure 3) indicated that the isolated product was a single compound.

As shown in Figure 4, the isolated 42c14-[2]catenane (**10**) gave a sharp singlet at 3.659 ppm without any side peaks. The chemical shift 3.659 ppm rules out the possibility that the new compound was 84-crown-28 (84c28) which has the same mass as 42c14-[2]catenane. 84c28 would give a peak at 3.646 ppm in $CDCl_3$. Also, if the compound

were a *hetero*[2]catenane containing two different sizes of crown ethers the ^{1}H NMR signal would be two peaks or, at least, would not be a symmetric peak.

The chemical shift of "42c14" (mixture of **8** and larger crown ethers) was 3.646 ppm. The downfield shift of the signal of 42c14-[2]catenane (**10**) in the ^{1}H NMR spectrum by 0.013 ppm compared to "42c14" was not due to the experimental error or inconsistent instrumental conditions. It was reproducible within a range of 0.001ppm at ambient temperature. Figure 5, which is the ^{1}H NMR spectrum of a mixture of 42c14-[2]catenane and "42c14", shows the clearly separated peaks at 3.660 and 3.646 ppm. Such downfield or upfield shifts have been observed in other catenane systems. [7, 22] The shift of the ^{1}H NMR signal could be explained by solvation effects. Because in the interlocked structure the cavity of one macrocycle is occupied by segments of the other macrocycle, these segments of the macrocycles can not be solvated in the same manner as in the isolated macrocycle. Therefore, the lack of solvation results in the downfield shift of the ^{1}H NMR signal.

As well as the ^{1}H NMR spectrum, the ^{13}C NMR spectrum of the catenane **10** in $CDCl_3$ (Figure 6, $CDCl_3$ reference @ 77.992 ppm) shows a single peak at 70.635 ppm with no side peaks which appear in case of linear PEOs. Thus, possible linear oligomeric or polymeric impurities can be detected by the appearence of small side peaks due to the terminal carbons in ^{13}C NMR spectrum. [20] Compared to the "42c14" (δ=70.555 ppm) the ^{13}C NMR signal of 42c14-[2]catenane (**10**) was shifted downfield by 0.080 ppm and this observation was reproducible within a range of 0.002 ppm. Again, the ^{13}C NMR spectrum of a mixture of 42c14-[2]catenane and "42c14" (Figure 7) shows two clearly isolated peaks. Similar shifts in ^{13}C NMR spectra have been observed in hydrocarbon catenanes. [7, 22] These shifts to lower field were explained by interannular van der Waals interactions. As a good example, in the ^{13}C NMR spectrum of an aliphatic

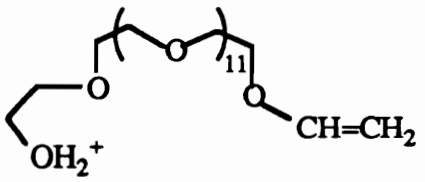
hydrocarbon catenane consisting of two rings of different sizes (46- and 28-membered) Schill et al. observed a smaller shift of the larger ring. [7] This result was rationalized by the fact that the van der Waals interactions were distributed over more carbon atoms in the larger ring via thermal motions.

The IR spectrum of catenane **10**, however, did not show any difference from those of crown ethers such as "42c14" and 30-crown-10. This might be due to the fact that the size of 42c14 (**8**) in the catenane is large enough not to cause ring strain.

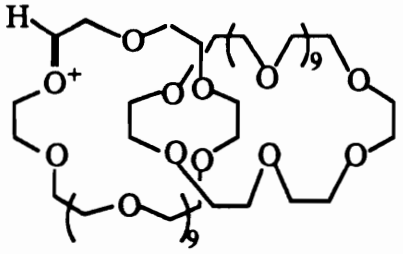
The FAB mass spectrum of the catenane from 3-nitrobenzyl alcohol matrix showed $[(M/2)+H]^+$ (m/z=617.4) and $[(M/2)+Na]^+$ (m/z=639.3) ion peaks, *i.e.* 42c14 (**8**) derived species, but no molecular ion was observed. However, in the FAB mass spectrum from glycerol/trifluoroacetic acid (1 %) (GLY/1 % TFA) matrix (Figure 8) $[M-H]^+$ (m/z=1231.5), $[M-2H+Na]^+$ (m/z=1253.3) and $[M-2H+K]^+$ (m/z=1269.2) ions were detected along with $[(M/2)+H]^+$, $[(M/2)+Na]^+$ and $[(M/2)+K]^+$ (m/z=655.3) ions.

The observation of $[M-H]^+$ ion instead of $M^{+\cdot}$ in mass spectra of crown ethers is not unusual. In many cases of EI and FAB mass spectra of crown ethers it has been emphasized that instead of $M^{+\cdot}$, $[M+H]^+$ and $[M-H]^+$ ions are detected. [23-26] In those cases, $[M+H]^+$ ions of crown ethers are likely to exist in the form of open chains instead of closed rings. [24] Therefore, there would be no or little chance to detect the $[M+H]^+$ ion peak of 42c14-[2]catenane because once a ring of the catenane breaks down to the open chain (**11**), which is $[(M/2)+H]^+$, the linear species (**11**) would dethread away from the other 42c14 macrocycle. In contrast, $[M-H]^+$ ions of crowns are likely to retain the closed ring structure,[23] so that the catenane cationic structure **12** could survive. Indeed, the $[M-H]^+$ ion (**12**) of 42c14-[2]catenane (**10**) was detected in the mass spectrum (Figure 8). An $[(M/2)-H]^+$ (m/z=615.3) peak was also detected (Figure 9), but it is much weaker than the $[(M/2)+H]^+$ (m/z=617.4). In other words, the probability of the formation of **13**

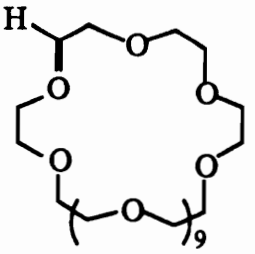
from a 42c14 ring is much lower than that of **11**.



11

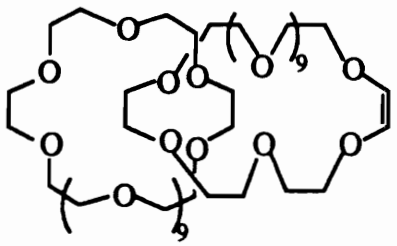


12 $[10\text{-}H]^+$

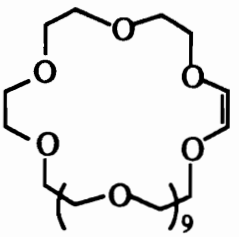


13

The observation of $[M\text{-}2H+Na]^+$ and $[M\text{-}2H+K]^+$ ions in Figure 8 suggested that the $[M\text{-}2H]^0$ catenane (**14**), formed from **12** by loss of a proton, was able to make complexes with sodium ($[\mathbf{14}+Na]^+$) or potassium ($[\mathbf{14}+K]^+$) cations better than the catenane itself. It is believed that the olefin unit allows π-electron interactions and may induce a conformational change of the ring to enhance the complexation ability.



14 $[M\text{-}2H]^0$



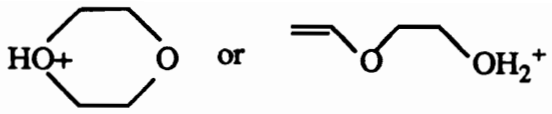
15 $[(M/2)\text{-}2H]^0$

$[(M/2)\text{-}2H+Na]^+$ (m/z=637.3, $[\mathbf{15}+Na]^+$) and $[(M/2)\text{-}2H+K]^+$ (m/z=653.3,

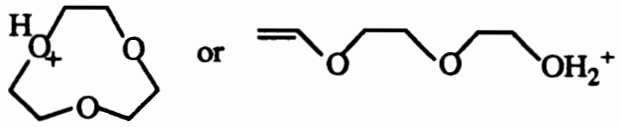
[**15**+K]$^+$) ions were also detected in the mass spectrum; however, those signals were much less intense than [(M/2)+Na]$^+$ and [(M/2)+K]$^+$, respectively. This is probably because 42c14 (**8**) is able to make a strong complex with those metal ions due to its conformational flexibility. In contrast, for the rings in the catenane structure, the conformational flexibilty is much more restricted. The peak at m/z=769.3 corresponds to the [(M/2)-2H+Na+($C_6H_{12}O_3$)]$^+$ ion. This suggests that a neutral fragment of a 42c14 of the catenane remains in the cavity of **15** until the ion reaches the detector because of template complexation by the metal ion. This phenomenon has not been observed/reported in mass spectra of normal crown ethers.

In another FAB mass spectrum of the catenane (Figure 10), which was obtained from a matrix of GLY/4 % TFA, [M-2H+Na]$^+$ ([**14**+Na]$^+$)and [M-2H+K]$^+$ ([**14**+K]$^+$) were not detected; only a strong [M-H]$^+$ ion (**12**) was observed. Interestingly, two strong signals at m/z=705.5 and 749.5 were observed in Figure 10. We believe that those peaks originated from the complex of 42c14 and fragments [$C_4H_9O_2$]$^+$ and [$C_6H_{13}O_3$]$^+$, which were clearly observed in the low m/z region of the spectrum (Figure 11). These are common fragments of crown ethers. [19, 27, 28] The peak at m/z=1005.7 in Figure 10 corresponds to [(M/2)-2H+K+($C_{16}H_{32}O_8$)]$^+$, presumably a complex of **15**, K$^+$ and neutral $C_{16}H_{32}O_8$.

In the high resolution FAB mass spectrum (Figure 12) the [M-H]$^+$ ion was detected at m/z=1231.7296, which indicated that the ion had the formulation of $C_{56}H_{111}O_{28}$ (calculated value=1231.7262) supporting the molecular formulation of 42c14-[2]catenane with 2.7 ppm error. The [M-H+1]$^+$ and [M-H+2]$^+$ isotopic peaks are present in approximately the expected abundances (62 and 29 %, respectively).



$[C_4H_9O_2]^+$ (m/z=89.06)



$[C_6H_{13}O_3]^+$ (m/z=133.08)

In the DSC thermogram (Figure 13) the catenane showed no melting endotherm or crystallization exotherm; the glass transition was observed at 13 °C. Most crown ethers are crystalline substances and the melting points are generally near or slightly higher than room temperature. [17, 19, 20] The glass transition temperatures of the crown ethers are usually detected at around -67 °C ~ -70 °C. [19] It is believed that due to the interlocked structure there would be no chance for a crystalline arrangement of the 42c14 molecules in the solid state of the catenane, which consequently is completely amorphous. As well as the difficulty for crystalline packing, the interlocking makes the rings more rigid so that the glass transition of the catenane takes place at a temperature much (>80 °) higher than for aliphatic crown ethers.

CONCLUSIONS

42c14-[2]catenane was synthesized and isolated from the reaction of tetra(ethylene glycol) with tri(ethylene glycol) ditosylate under high dilution conditions. The isolation of the catenane was achieved by column chromatography and the isolation yield was 0.9 %. The yield of the catenane, however, was 8 % according to the ^{1}H NMR although there were no specific interactions such as H-bonding or charge transfer interactions between the two rings in 42c14-[2]catenane. This yield was much higher than we expected under the dilute reaction condition. Therefore, it is believed that metal-crown ether-linear ether complexation as a "template effect" played a key role in formation of the catenane as observed in FAB mass spectra. As compared to 42c14 or PEOs the ^{1}H and ^{13}C NMR signals of the catenane showed downfield shifts because of solvation effects and interannular van der Waals interactions, respectively. In the FAB mass spectra, $[M-H]^{+}$ and $[M-2H+Na]^{+}$ ions were observed along with $[(M/2)+H]^{+}$ and $[(M/2)+Na]^{+}$ ions. In addition to those ions, a couple of ions such as $[(M/2)-2H+Na+(C_6H_{12}O_3)]^{+}$ and $[(M/2)-2H+K+(C_{16}H_{32}O_8)]^{+}$, which are complexed ions composed of (M/2) and common fragments of crown ethers, were also detected. This observation has not been reported in the cases of crown ethers. Although 42c14 and PEOs are crystalline, 42c14-[2]catenane is amorphous and shows a higher glass transition temperature than 42c14 or PEOs.

EXPERIMENTAL

Materials. Tri(ethylene glycol), tetra(ethylene glycol), NaH, *p*-toluenesulfonyl chloride (Aldrich) and THF (Mallinckrodt) were used as received. Tri(ethylene glycol) ditosylate was synthesized by the reaction of tri(ethylene glycol) with *p*-toluenesulfonyl chloride. [19]

Synthesis and isolation of 42c14-[2]catenane (10). In a 3-neck 1-L round-bottomed flask equipped with a condenser, a mechanical stirrer and a N_2 bubbler, NaH (7.6 g, 80 % dispersed in oil, 0.25 mol) was placed. The NaH was washed with hexane (60 mL x 2) and then THF (80 mL) was added. To the suspension tetra(ethylene glycol) (12.14 g, 62.5 mmol) in THF (40 mL) was added slowly at room temperature. The mixture was heated to reflux and tri(ethylene glycol) ditosylate (14.34 g, 31.3 mmol) in THF (40 mL) was added to the mixture dropwise over a period of 50 min while the mixture was stirred vigorously. The mixture was allowed to stir for 5 hrs and diluted to 850 mL with THF. Tri(ethylene glycol) ditosylate (14.45 g, 31.4 mmol) in THF (50 mL) was added to the refluxing mixture dropwse over a period of 1 hr. The mixture was further refluxed for 28 hrs. The excess NaH was destroyed by careful addition of a minimum amount of water. The salts were filtered off and the solvent was rotary evaporated. The residual oil was dissolved in acetone (100 mL) and the acetone solution was placed in a refrigerator (- 20 °C) overnight. The crystals were filtered. After evaporation of acetone from the filtrate, a light brown oil (9 g) was obtained. 2.3 g of the oil was separated into 200 fractions through a column (silica gel, 3 cm diameter, 30 cm length) using acetone as an eluent. Each fraction was checked on TLC and analyzed by NMR, if needed.

Characterization Techniques. NMR was done on a Varian Unity 400 spectrometer at ambient temperature and tetramethylsilane and $CDCl_3$ were used as internal references for ^1H and ^{13}C NMR spectra, respectively. A Perkin Elmer 283B IR spectrometer was used. For the HPLC analysis, an ISCO model 2350 HPLC instrument was used with a Novapak-C_{18} column and the eluent was a mixture of water and acetonitrile (75:25 by vol) at a flow rate of 2 mL/min; a refractive index detector (Waters, Differential Refractometer R401) was used. Thermal analysis was done on a Perkin-Elmer DSC-4 instrument at 5 °C/min. The sample was heated to 150 °C and cooled slowly to 0 °C. The second heating was run at 5 °C/min. The FAB mass spectra were obtained from the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln and the Washington University Resource for Biomedical and Bio-organic Mass Spectrometry, St. Louis, Misouri. The experimental conditions for the FAB mass spectrometry at the Midwest Center for Mass Spectrometry were as follows: The sample was analyzed using a Fisons VG ZAB mass spectrometer operating at 8 keV in the fast atom bombardment mode. The sample was dissolved in 3-nitrobenzyl alcohol or glycerol/4 % trifluoroacetic acid as matrices. Ions were desorbed by a Cs^+ ion gun operating at 25 keV. The instrument was scanned over a mass range of 100 to 1500 u at 10 sec/decade. Data were collected and processed using a Digital VAX 3100 work station with OPUS software. The experimental conditions for the FAB mass spectrometry at the Washington University were as follows: Mass spectra were obtained on a VG ZAB SE double-focusing mass spectrometer equipped with VG OPUS data system. FAB ionization was operated at 1 mA and 8 keV using Xenon as the bombardment gas. Glycerol with 1 % trifluoroacetic acid was used as matrix.

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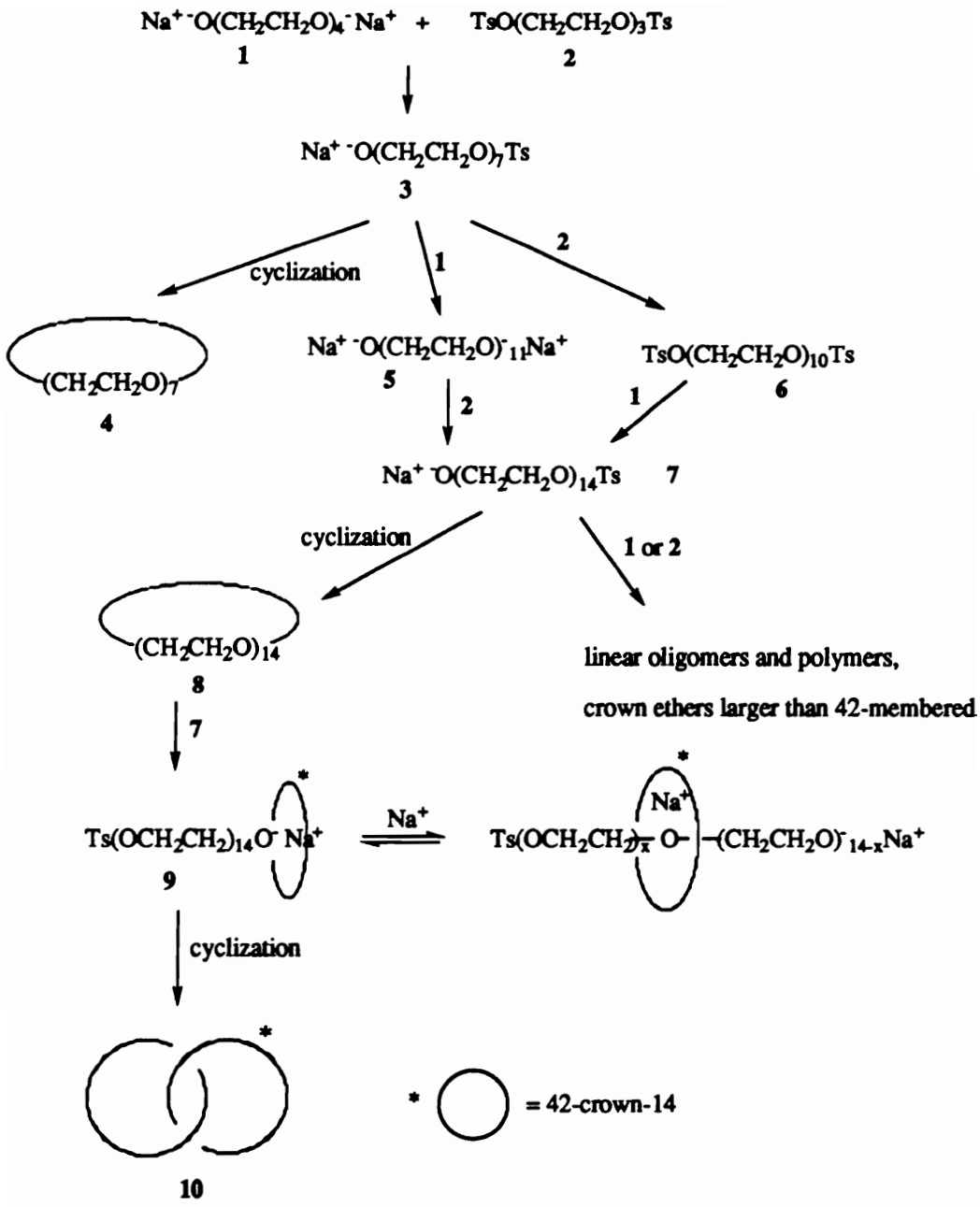


Scheme 1. The formation of 42-crown-14-[2]catenane.

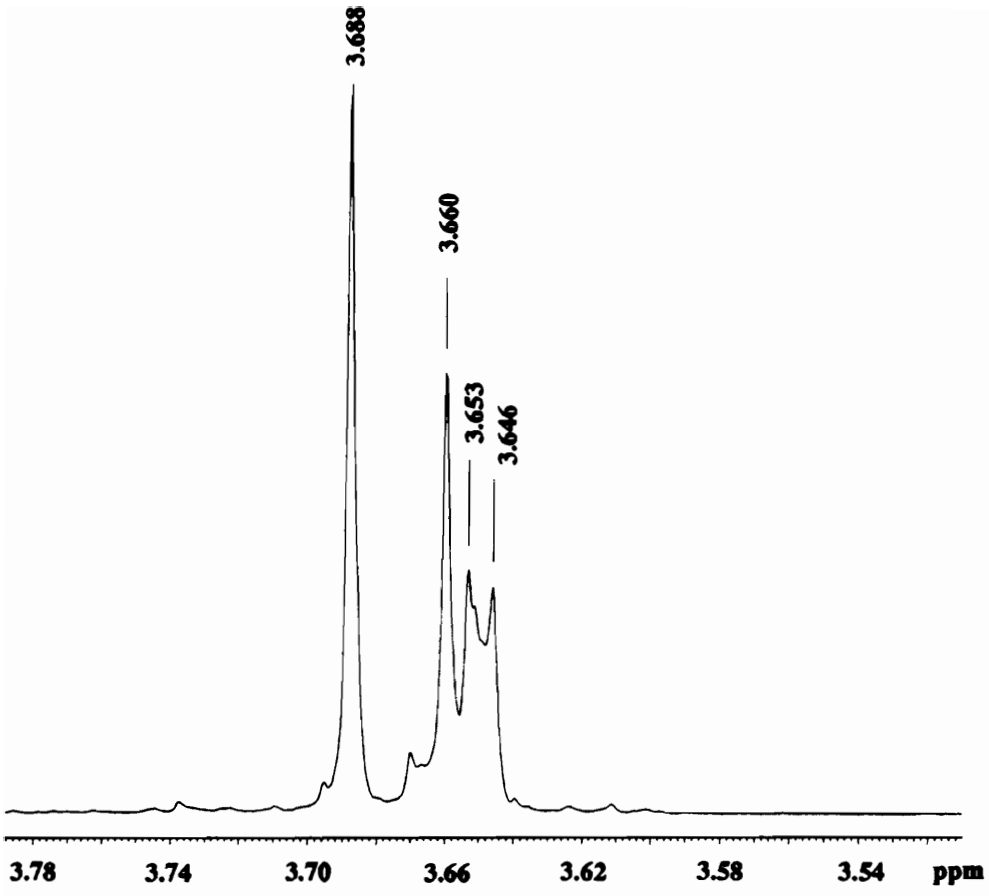


Figure 1. ^{1}H NMR spectrum of residue from the filtrate. ($CDCl_3$)

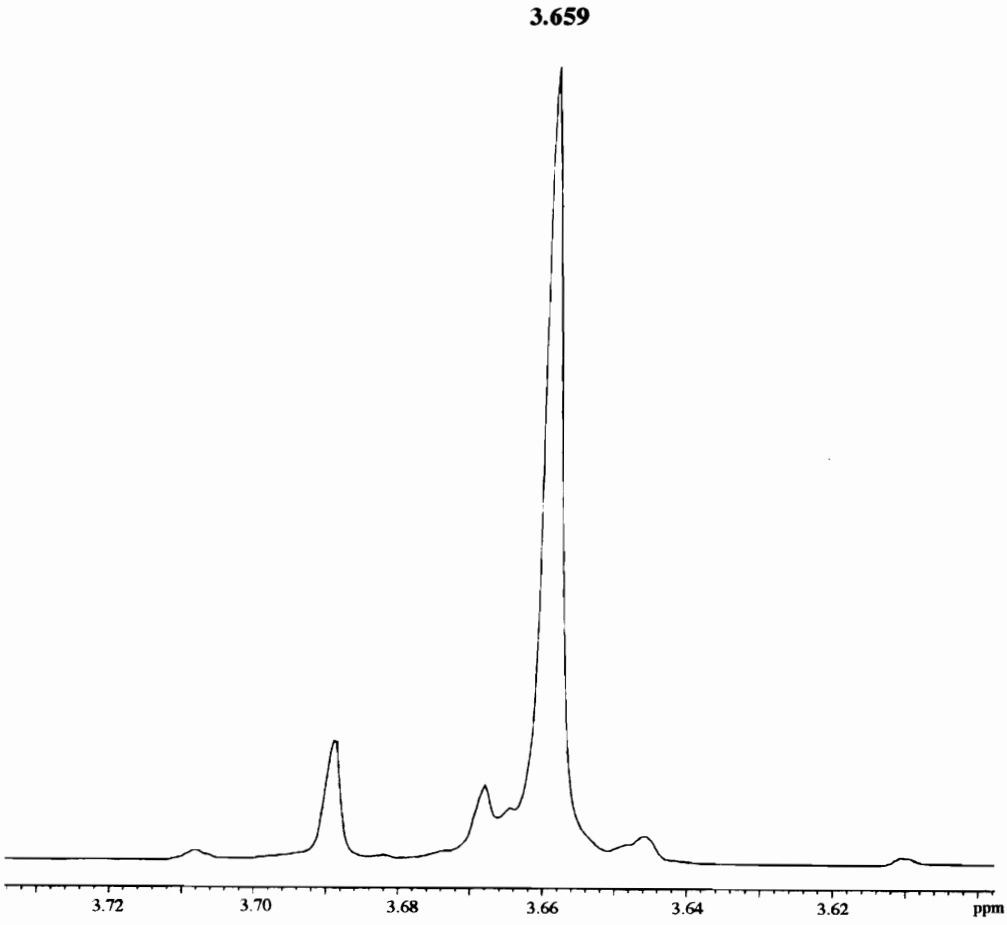


Figure 2. ^{1}H NMR spectrum of Fractions 80-85. ($CDCl_3$)

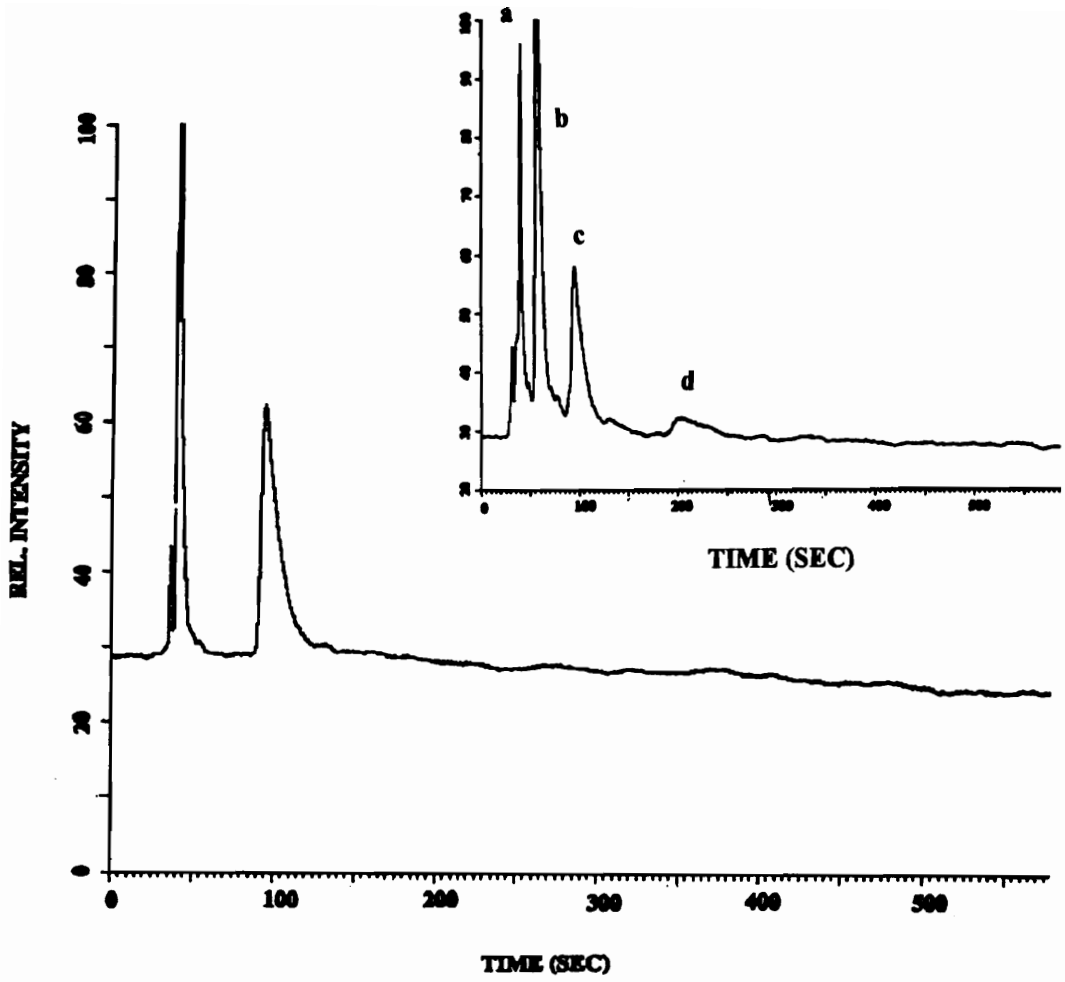


Figure 3. HPLC trace of the isolated catenane **10**. Column: Novapak-C_{18}, solvent: water/acetonitrile (75/25, v/v), flow rate: 2 mL/min, detector: RI.
* Peaks from solvents.
Inset: crude sample, a: water and oligo-PEO, b: 21c7, c: **10**, d: polymeric PEOs

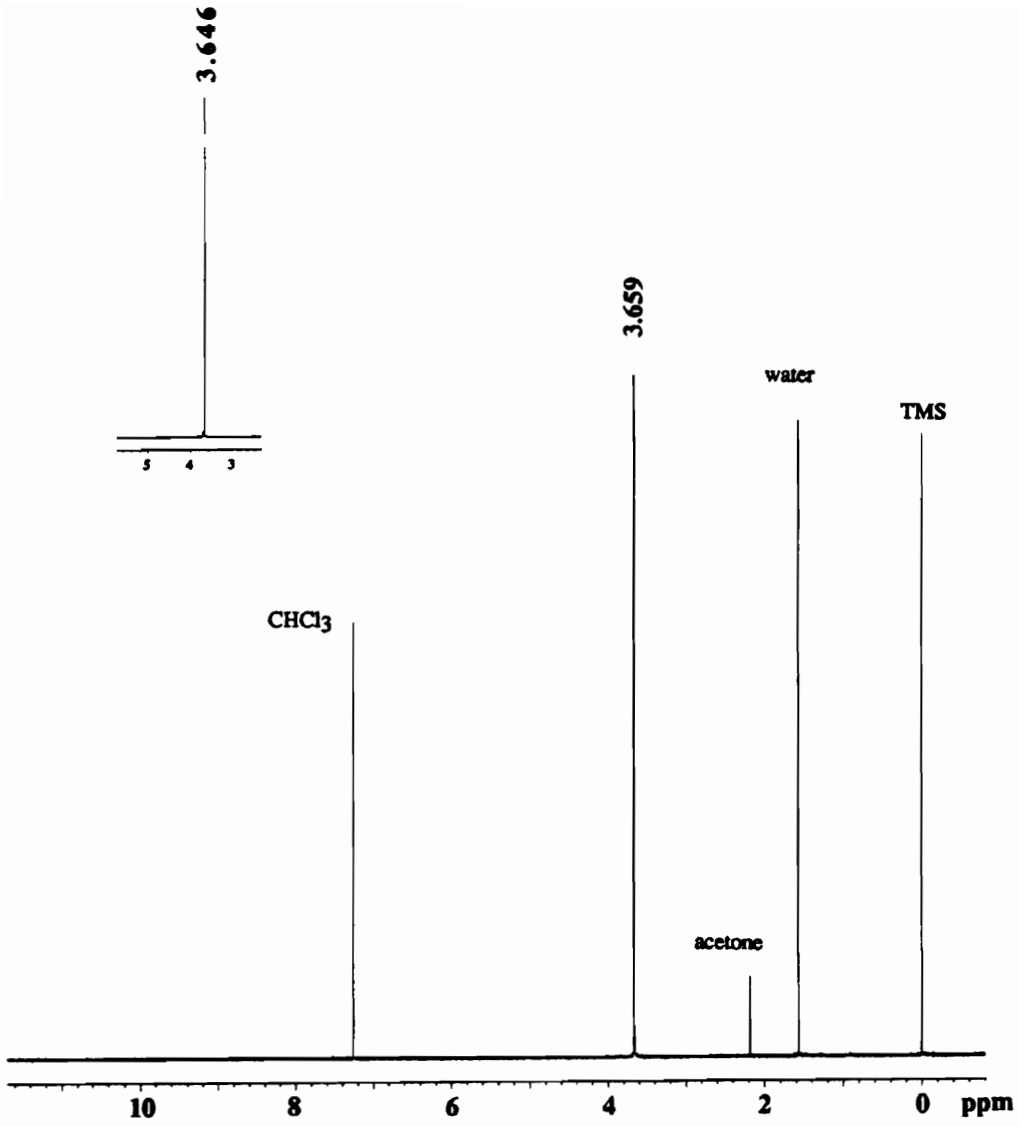


Figure 4. ^{1}H NMR spectrum of 42c14-[2]catenane (**10**). ($CDCl_3$)
Inset: ^{1}H NMR spectrum of "42c14" in $CDCl_3$.

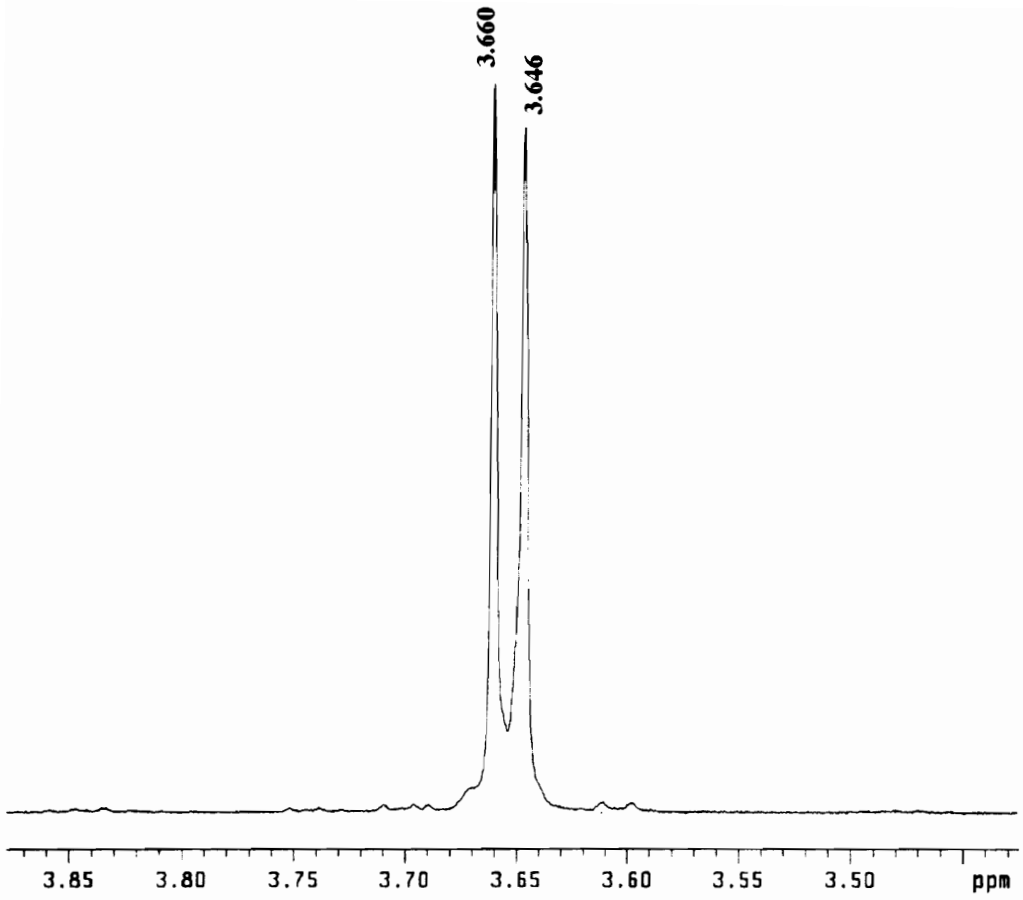


Figure 5. ^{1}H NMR spectrum of a mixture of 42c14-[2]catenane (**10**) and "42c14". ($CDCl_3$)

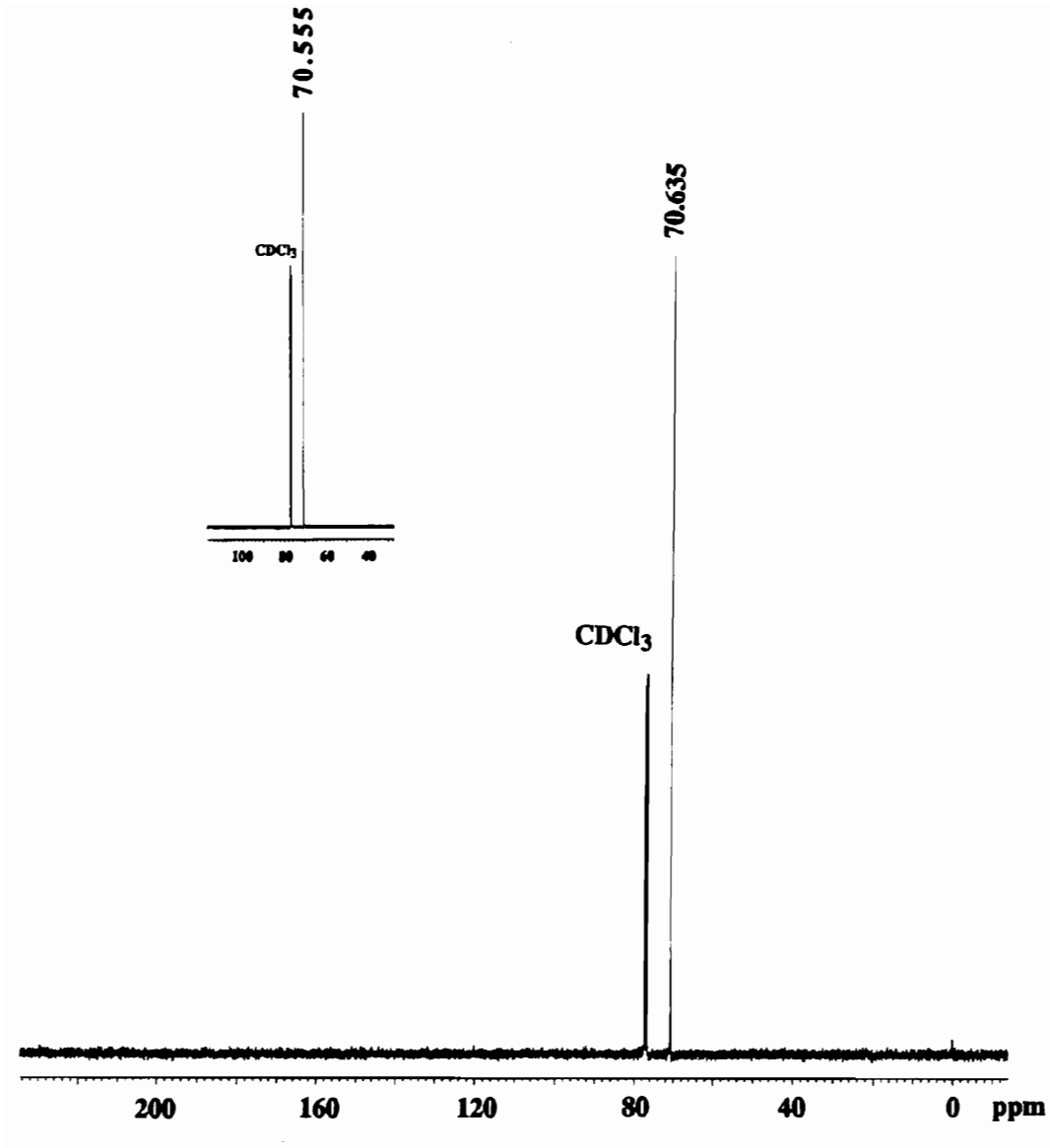


Figure 6. ^{13}C NMR spectrum of 42c14-[2]catenane (**10**). ($CDCl_3$, $CDCl_3$ reference at 77.992 ppm) Inset: ^{13}C NMR spectrum of "42c14" in $CDCl_3$.

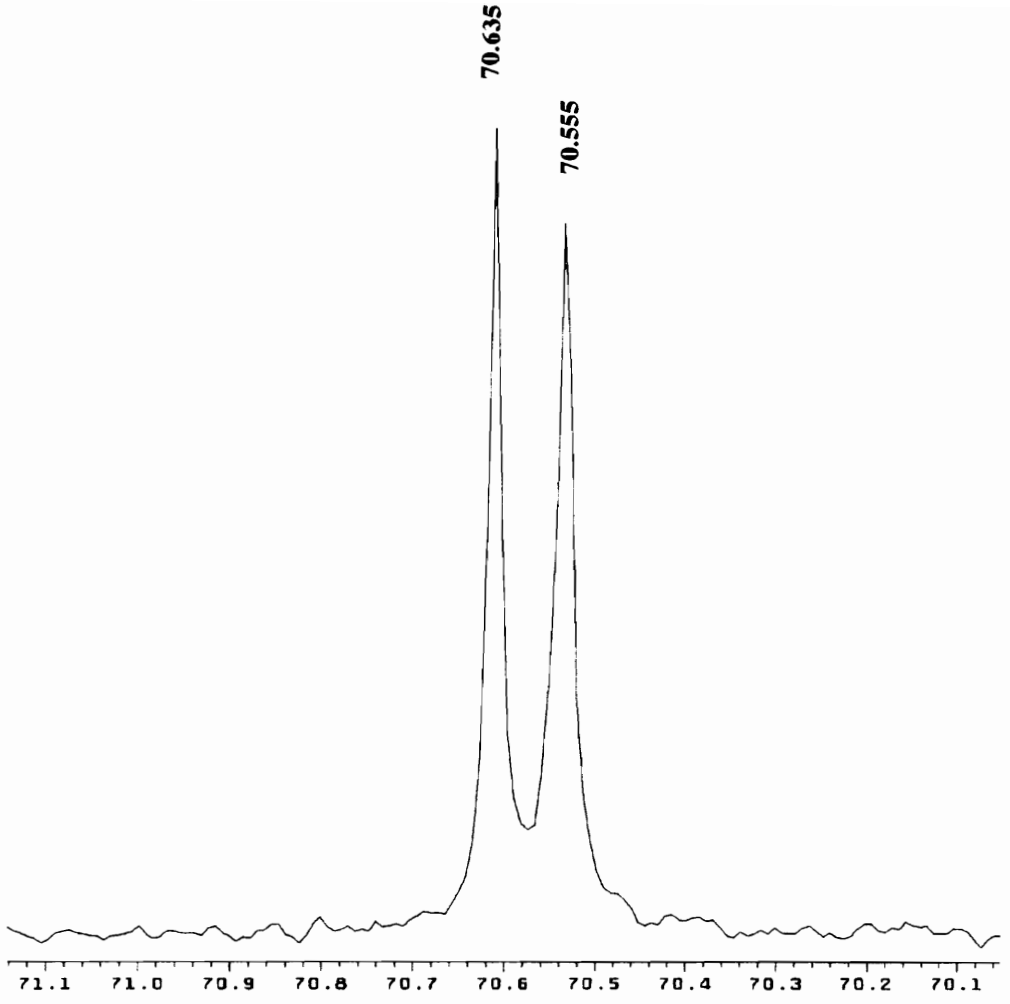


Figure 7. ^{13}C NMR spectrum of a mixture of 42c14-[2]catenane (**10**) and "42c14". ($CDCl_3$, $CDCl_3$ reference at 77.992 ppm)

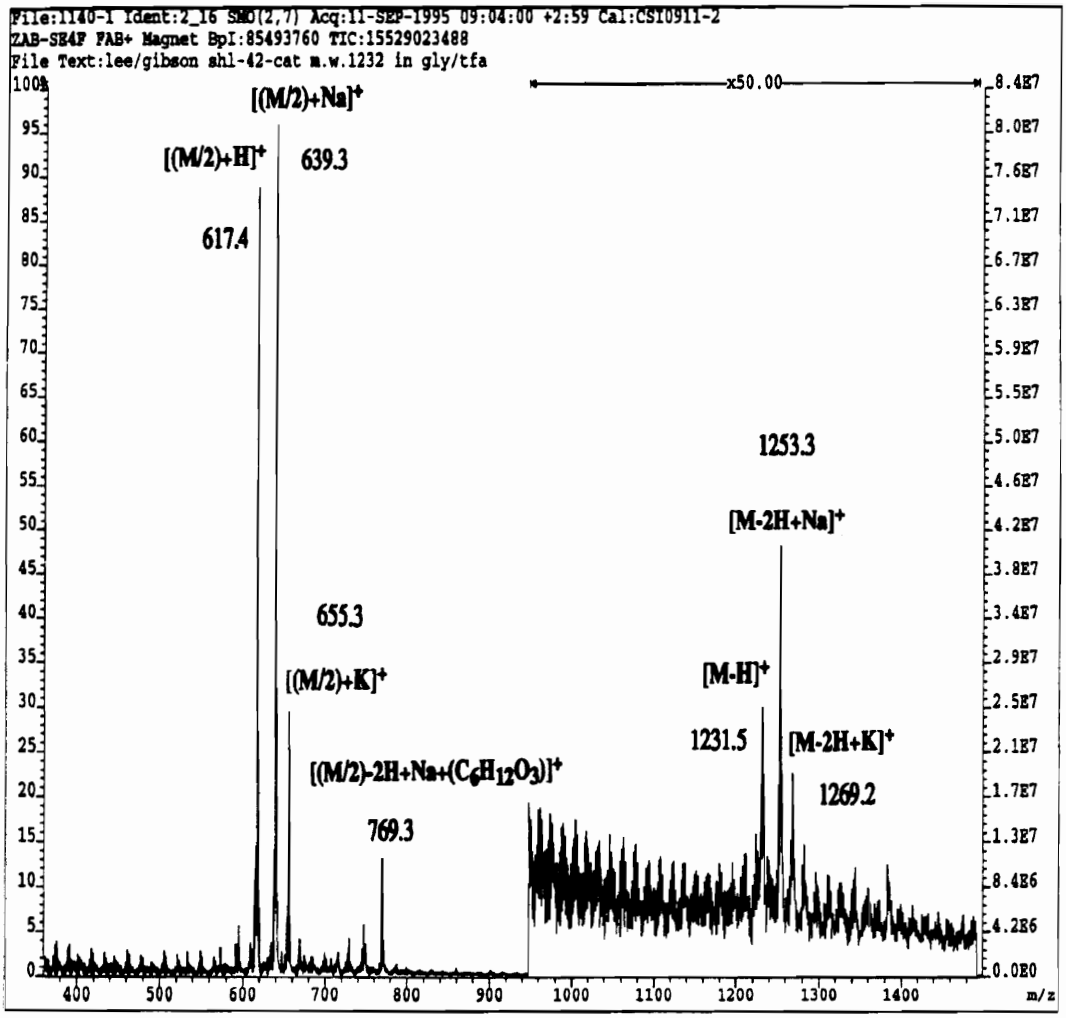


Figure 8. FAB mass spectrum of 42c14-[2]catenane (**10**). (GLY/1 % TFA matrix) (Obtained from the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry, St. Louis, Misouri)

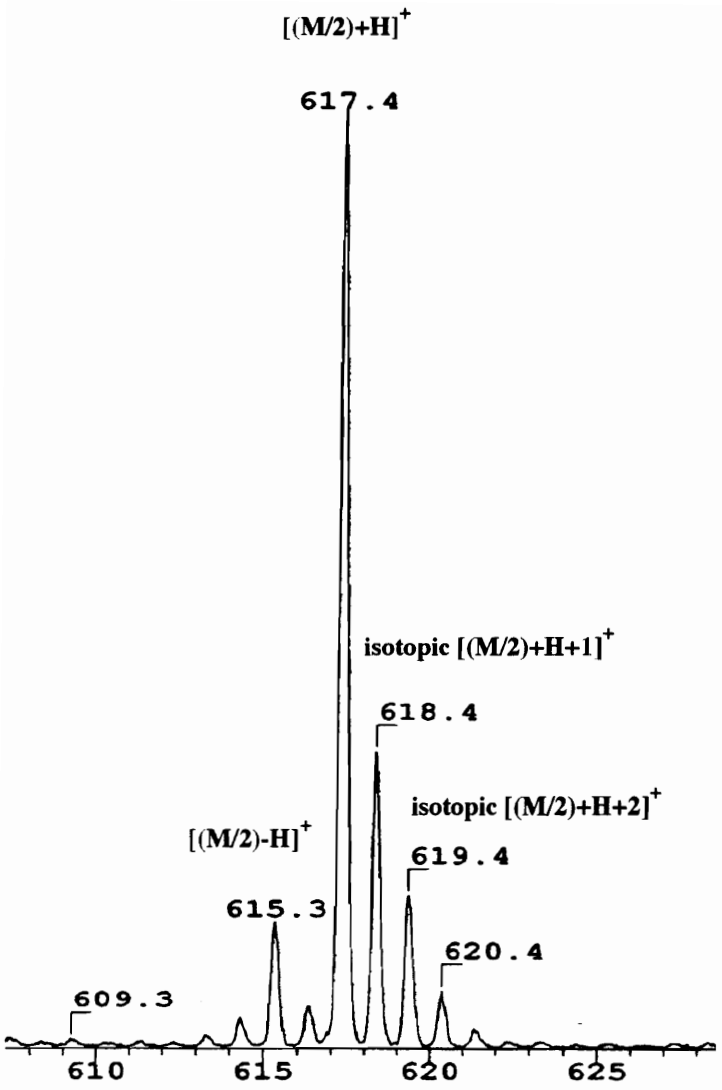


Figure 9. Expanded region around $[(M/2)+H]^+$ peak.

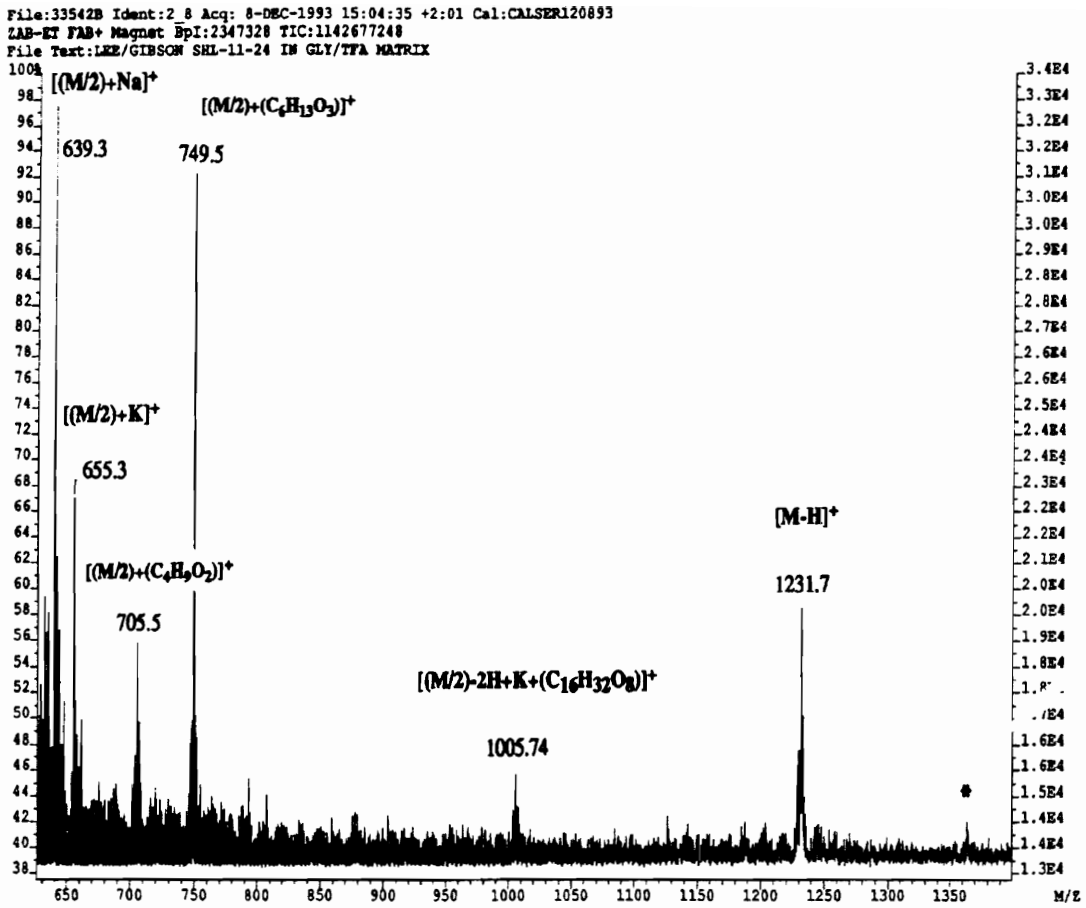


Figure 10. FAB mass spectrum of 42c14-[2]catenane (**10**). (GLY/4 % TFA matrix) (obtained from the Midwest Center for MS at the University of Nebraska-Lincoln) * $[M-H+LiI]^+$ (m/z=1366)

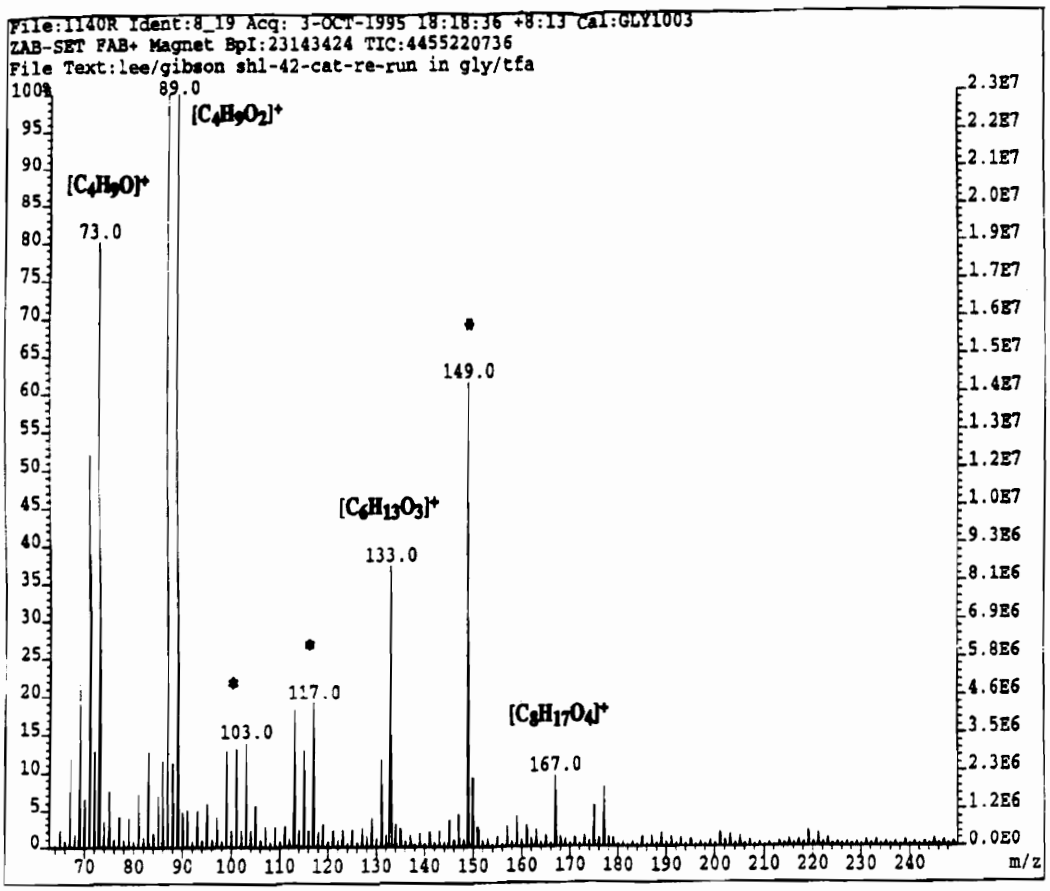


Figure 11. Low m/z region of FAB mass spectrum of 42c14-[2]catenane (**10**).
* From matrix

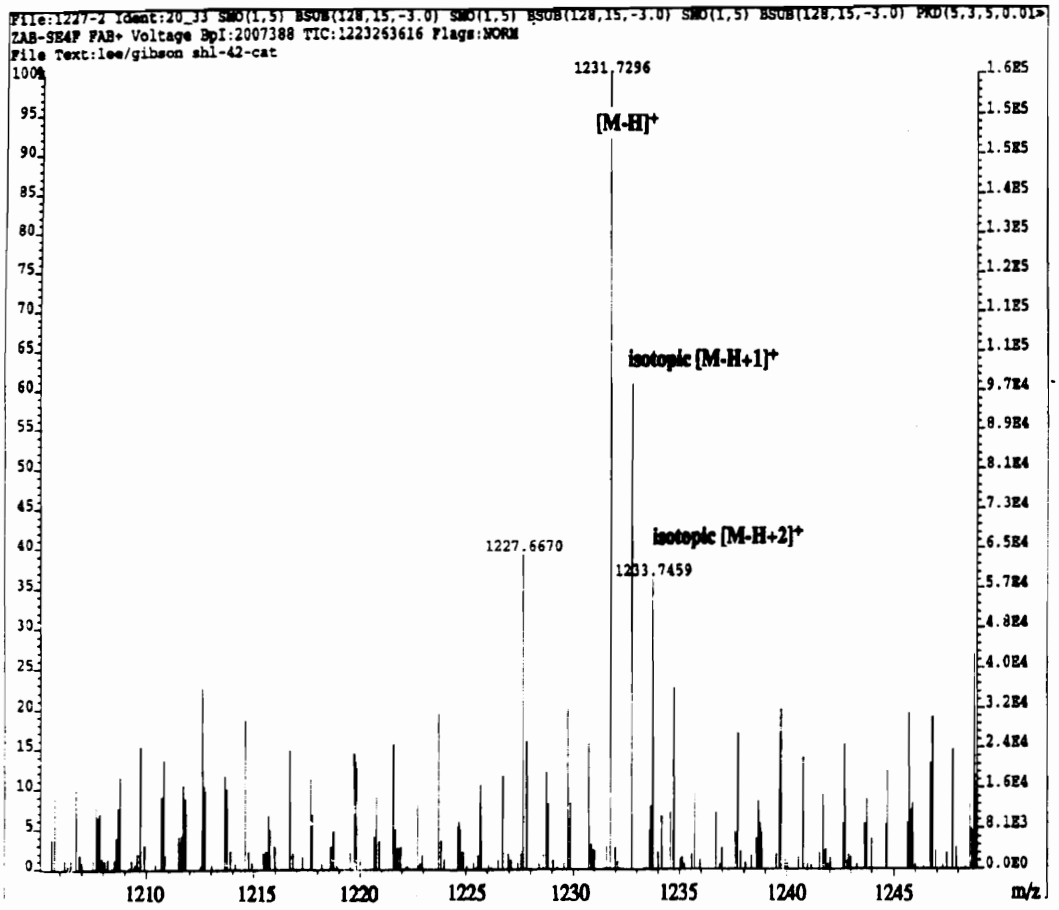


Figure 12. High resolution FAB mass spectrum of 42c14-[2]catenane (**10**).

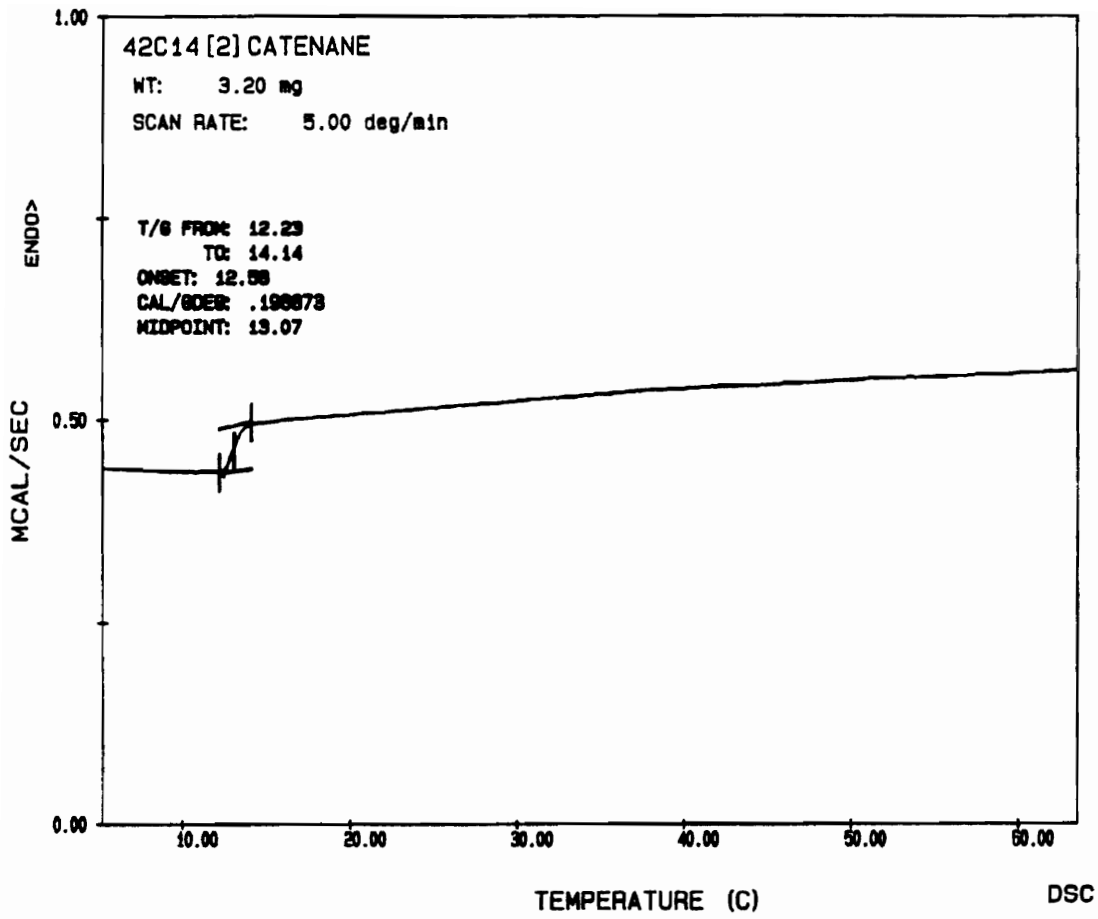


Figure 13. DSC trace of 42c14-[2]catenane (**10**). (5 °C/min, second heating)

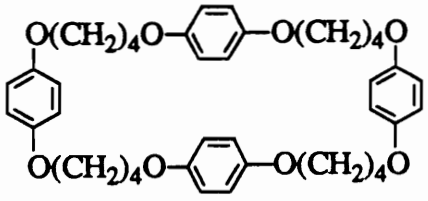
CHAPTER VI

HYDROCARBON MACROCYCLES

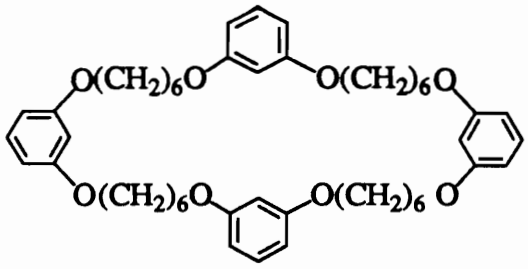
Several polyrotaxanes with crown ethers as cyclic species have been synthesized and characterized in our labs. [1] Incorporation of cyclic components into polymer backbones induces changes of properties of the polymers. For example, we demonstrated that threading with crown ethers affect the hydrodynamic volume of the polymer significantly. [2] Also, the polyrotaxanes showed dramatic changes in their solubilities in common solvents because of the incorporation of the polar crown ethers.

We designed and synthesized hydrocarbon-type macrocycles, 40- and 44-membered (**M40** and **M44**, respectively), for the ultimate syntheses of polyrotaxanes. In contrast to crown ethers, which are flexible and hydrophilic, these macrocycles would be stiffer and hydrophobic rings. Thus, polyrotaxanes containing these macrocyles are expected to show different property changes as compared to the polyrotaxanes containing crown ethers. Also, due to their symmmetic structures they were expeced to crystallize easily. These particular macrocycles are expected to have no specific attractive forces with polar monomers so that we may isolate the threading effects from other effects due to chain-cyclic interactions such as hydrogen bonding and dipole-dipole interaction.

The names for the macrocycles **M40** and **M44** are assigned arbitrarily based on the numbers of atoms in the rings.



M40



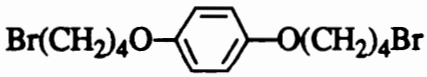
M44

RESULTS AND DISCUSSION

1. Macrocycle M40

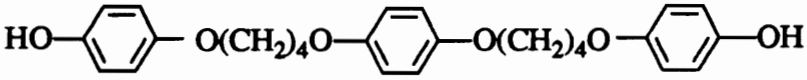
1-1. Synthesis of precursors

M40 was synthesized by combination of the two precursors, *p*-bis(4-bromobutyloxy)benzene (**1**) and *p*-bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene (**2**).



1

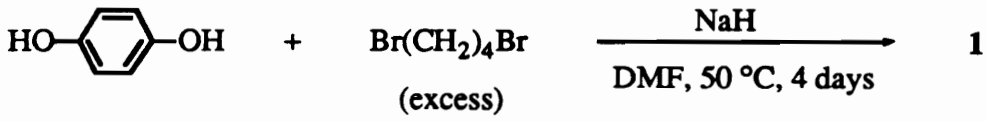
+



2

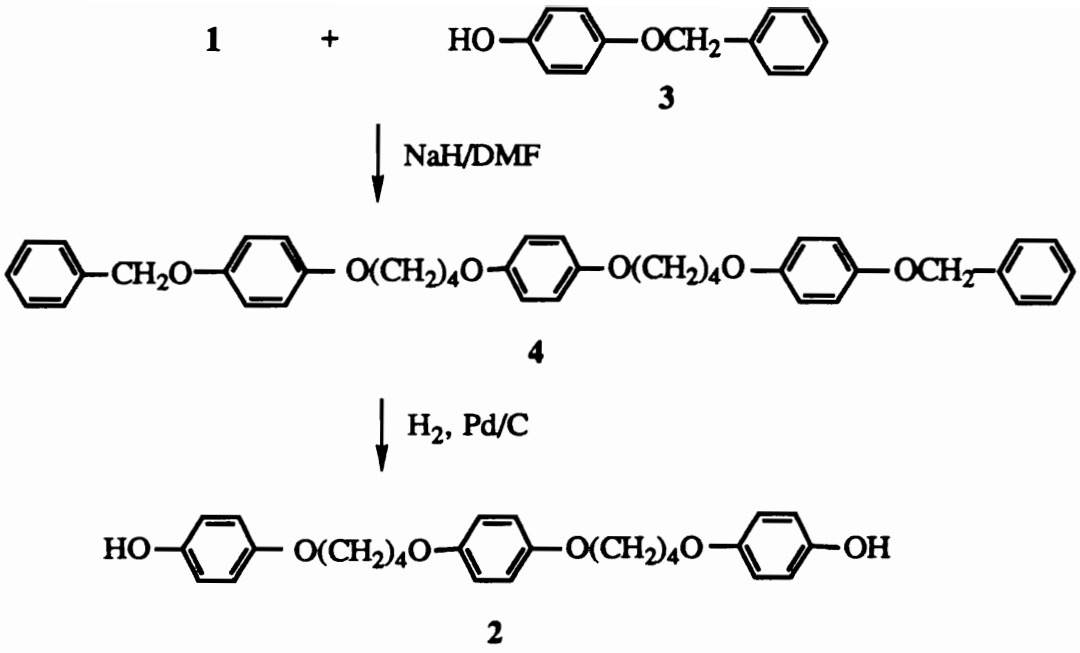
M40

p-Bis(4-bromobutyloxy)benzene (**1**) was synthesized by the reaction of hydroquinone and excess 1,4-dibromobutane in DMF with NaH as base. After the removal of the solvent and excess 1,4-dibromobutane the crude product was subjected to recrystallizations from a mixture of hexane and toluene or from ethanol. The yield was 70 % and the melting point was 88.5-90.0 °C.



Aternatively, compound **1** may be prepared using mild bases in alcoholic or mixtures of alcohols and THF or acetone solutions. According to the reports, the dibromo compounds such as *p*-bis(4-bromobutyloxy)benzene (**1**) and *p*-bis(6-bromohexyloxy)benzene were prepared by the reaction of hydroquinone and the corresponding dibromides in ethanol [3] or acetone / water mixture [4] with NaOH [3], KOH [4] or excess K_2CO_3 [4] as bases, respectively. In those reactions the conditions were much milder and the solvents and the bases used were cheaper. Moreover, excess dibromoalkane could be recovered easily. Also, the yields were reported not to be low keeping in mind that they used the dibromides in not very excess amounts. For example, according to Diana and Carabateas hydroquinone was reacted with a 6 molar excess of 1,4-dibromobutane in ethanol using NaOH as a base to give the dibromide in 44 % yield. [3]

p-Bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene (**2**), at first, was approached *via* a protected precursor **4** which was prepared by the reaction of **1** and *p*-(benzyloxy)phenol (**3**). Compound **3** is commercially available [5], but it was synthesized by the reaction of

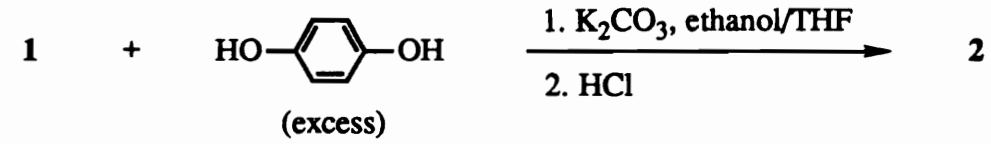


equimolar hydroquinone and benzyl bromide in ethanol solution using KOH as base. Although the reaction produced disubstituted as well as remaining unreacted hydroquinone the isolation was easy because the byproduct, *p*-bis(benzyloxy)benzene, precipitated out of the solution and thus could be removed by filtration. Therefore, the residual solid after evaporation of solvent was subjected to recrystallization from a mixture of hexane and ethyl acetate to give 26 % of desired product **3**.

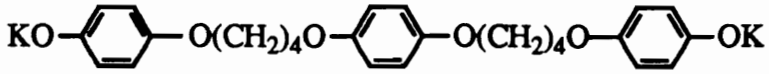
3 was allowed to react **1** in DMF solution with NaH as base to afford *p*-bis[4-{*p*-(benzyloxy)phenoxy}butyloxy]benzene (**4**). After the reaction was complete the mixture was poured into excess water to remove DMF and any unreacted NaH. The off-white precipitate was filtered and dried, and recrystallized from a large amount of ethyl acetate. The structure of the product was confirmed by NMR (Figure 1) and elemental analysis. It melted between 197.4-198.2 °C. Compound **4** had been expected to have good solubility in aromatic and common solvents such as toluene, THF, chloroform and ethyl

acetate. However, it turned out to be quite insoluble in such common solvents. It did not dissolve much in such powerful solvents as DMF and DMSO even at high temperature. This poor solubility may be explained by the highly symmetrical structure with lack of any polar unit in it. This low solubility made the next step, which was hydrogenolysis with palladium catalyst, difficult.

Since the hydrogenolysis of **4** was not available due to the solubility problem, synthesis of **2** was achieved directly from the reaction of **1** and excess hydroquinone. Thus compound **1** was allowed to react with 36 molar excess hydroquinone in K_2CO_3/ethanol/THF systems.



After the reaction was complete, unreacted hydroquinone was removed by pouring the reaction mixture into water. The white precipitate was filtered and washed with water followed by with aqueous HCl. The precipitate was soluble in hot DMSO but upon cooling it precipitated out. However, the solubility in DMSO-d_6 was good enough to take the ^{1}H NMR specrum. The ^{1}H NMR spectrum (Figure 2) showed that the precipitate was the dipotassium salt **5** of the precursor **2**. Although **5** was a disalt, it was not soluble in water. It is to be noted that because the off-white precipitate **5** was a very fine powder, and after filtration the precipitate was so cement-like dense that it could not be acidified by simply washing with aqeous HCl.



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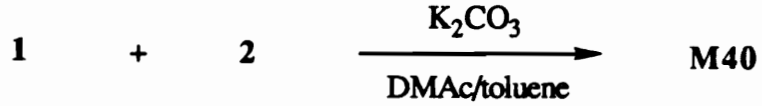
Therefore, the precipitate was dispersed in DMAc/DMF (1/1, v/v) and dilute HCl was added dropwise while stirring until the pH was about 3-4. Then it was poured into a large amount of water again and the precipitate was filtered, followed by washing with methanol to remove unreacted phenol. The precipitate was soluble in hot DMAc, DMF and DMSO, but upon cooling it precipitated out. There was a small amount of insoluble part in hot DMF and it was believed to be oligomeric impurities. Thus the insoluble part was removed by filtration of the hot solution and the residue from the filtrate was subjected to recrystallization from xylene to give white powdery crystals in 79 % yield. It was only slightly soluble in toluene, THF and chloroform even at elevated temperature. The ^{1}H NMR spectrum in DMSO-d_6 (Figure 3) showed that the precipitate was the desired product **2**. The melting point was 208-210.5 °C.

1-2. Synthesis of M40

The synthesis of macrocycle **M40** was accomplished by the reaction of precursors **1** and **2** in DMAc/toluene solution using K_2CO_3 as base.



The reaction was carried out under a high dilution condition. Using the syringe pump technique reaction mixtures can be maintained in high dilution conditions through

reaction processes. However, due to the lack of solubility of **2** syringe pump injection could not be utilized for this reaction. Thus, after removal of water from the mixture of DMAc/toluene/K_2CO_3 by reflux, an equimolar mixture of the two precursors was dissolved in hot DMAc and it was added into the reaction mixture. Such addition was done every 8 hours over two days. As the reaction proceeded salts were formed inside the reaction flask. A small amount of the salt was taken out. It dissolved in water quickly so that it was believed to be KBr. After charging all precursors and following four days reflux, a small aliquot was taken out and dried. TLC analysis indicated that in the reaction mixture there were still trace amounts of the unreacted starting materials. The reaction mixture was kept refluxing for another day. After the reaction (7 days total), about 350 mL of the reaction mixture was taken out and the solvents were rotary evaporated. When the volume of the mixture was 25 mL, it was poured into a large amount of water. The precipitate was filtered and dried. The precipitate had a limited solubility in hot DMAc. The precipitate was extracted with hot toluene (50 mL) and after toluene was evaporated a white solid was left. The ^1H NMR spectrum in DMSO-d_6 indicated that the precipitate was the desired product with some side products and the starting materals. On the other hand, the ^1H NMR spectrum in $CDCl_3$ of the soluble part of the precipitate showed almost no such impurities. This means that chloroform was a better solvent than toluene for the extraction of the desired product **M40**.

Thus, the solvents from the reaction mixture were removed by rotary evaporation and the residual solid was extracted with chloroform using a Soxhlet apparatus. Evaporation of chloroform gave about 7 g of white solid which corresponded to 60 % yield. On a silica-gel TLC plate the solid left at least 5 spots with a hexane/acetate (1:1 by vol) mixture as an eluent. Thus, with about 150 mg of the solid PTLC (preparative TLC) was carried out to separate each spot for spectroscopic analysis. However, the

PTLC experiment (silica-gel, 1:1 hexane/ethyl acetate) was not successful because almost all of the material stayed on the starting line. Only a small portion of the spot was developed along the plate. This was due to the very limited solubility of **M40** in common solvents, which was found later. Therefore, column chromatography could not be employed for isolation of the macrocycle.

However, recrystallization from ethyl acetate was found to work well in this case. Ethyl acetate was chosen because it seemed that the unreacted starting materials and the possible oligomeric impurities contained polar units in their structures while **M40** does not. The crude product (from the extraction) was dissolved in boiling ethyl acetate and the hot solution was filtered to remove a small amount of insoluble material. The solution was allowed to stand overnight at room temperature. White granular crystals were obtained and subjected to a second recrystallization from ethyl acetate to give aggregated powdery crystals.

According to the ^{1}H and ^{13}C NMR spectra in $CDCl_3$ (Figures 4 and 5, respectively) the desired product **M40** was obtained. The ^{1}H NMR sppectrum in DMSO-d_6 (Figure 6) showed no phenolic OH which would be detected at around 8.8 ppm if the sample contained some linear impurities. However, the HPLC result (Figure 7) indicated that the sample was not 100 % pure. Its purity was found to be about 92 %. In the FAB mass spectrum (Figure 8a) $[M+Na]^+$ (m/z=679.4) was observed. Although in the higher m/z region (Figure 8b) the small peak at m/z=1335.6 might be $[2M+Na]^+$, it was not confirmed that the small peak in the HPLC trace (Figure 7) was the double-sized macrocycle. According to the high resolution FAB mass spectrum the $[M+Na]^+$ ion was observed at m/z=679.3274 (deviation 3.9 ppm). The melting point of **M40** after two more recrystallizations was 160.8-162.1 °C and the yield was 25 %. The yield was somewhat lower than expected. It was probably due to an insufficient reaction time.

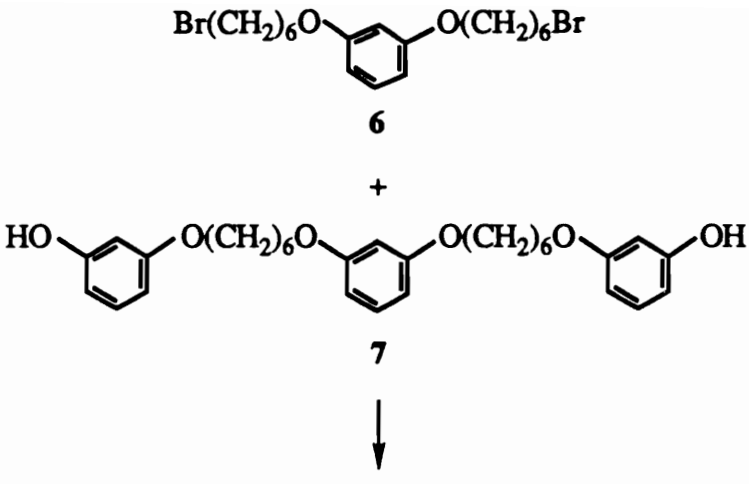
An important property of **M40** was its low solubility in aromatic hydrocarbons (toluene, benzene) or moderately polar solvents such as THF and ethyl acetate. The best solvents were chlorinated hydrocarbons such as chloroform and methylene chloride, but they are not very good solvents either. This was an unexpected result because **M40** is an aromatic and aliphatic hydrocarbon based material and so was anticiapted to have a good or very good solubility in aromatic hydrocarbons. The low solubility is probably due to the chain rigidity and the lack of polar functionality. The low solubility is a major drawback for utilization as a cyclic species of polyrotaxanes. Therefore, we decided to prepare another macrocycle **M44** which contains resorcinol units instead of hydroquinones. Also it has hexamethylene units in its structure instead of tetramethylene units. Therefore, it was expected to be a more flexible and more soluble macrocycle than **M40**.

2. Macrocycle M44

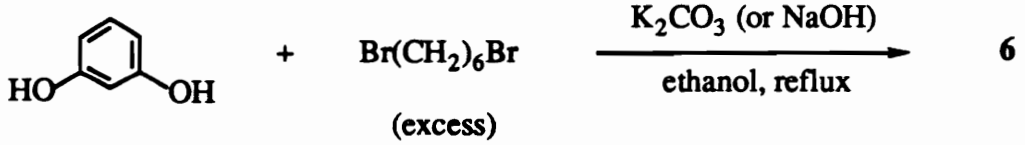
2-1. Synthesis of precursors

The desired macrocycle **M44** was synthesized by cyclization of two precursors **6** and **7.**

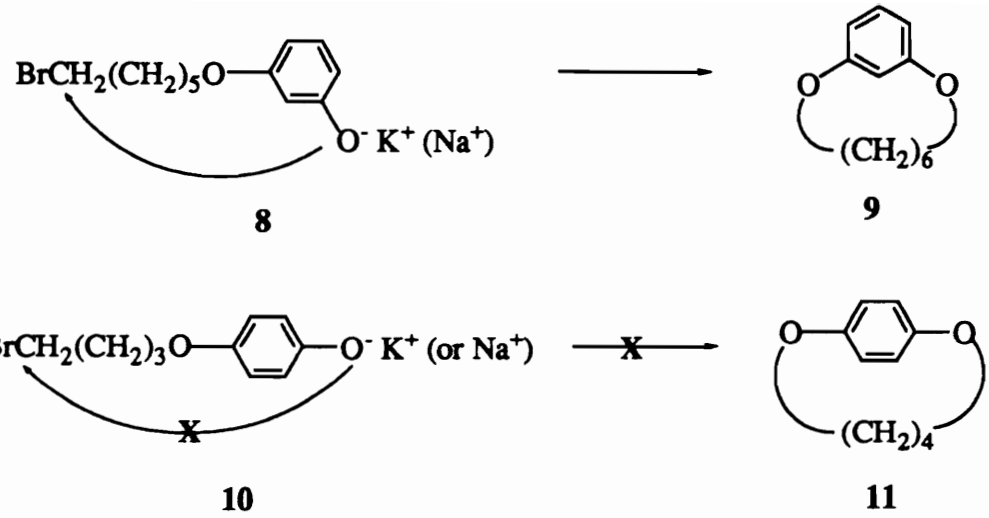
The synthesis of *m*-bis(6-bromohexyloxy)benzene (**6**) was achieved by the reaction of resorcinol with excess 1,6-dibromohexane (10 molar excess) in ethanol using NaOH as base under reflux. After the reaction was completed diethyl ether was added to the mixture, and it was washed with water to remove salt and unreacted NaOH. A brown



oil was obtained after evaporation of the diethyl ether and vacuum distillation of excess 1,6-dibromohexane. The oil did not solidify at room temperature. The product *m*-bis(6-bromohexyloxy)benzene (**6**) was a new compound. Therefore, to isolate the desired product column chromatography using silica gel was done. $CHCl_3$ was used as a eluent and the residual oil was subjected to second column chromatography using a mixture of hexane and ethyl acetate (25/1, v/v) as eluent. The isolated light yellow oil showed one spot on a silica gel TLC plate. However, the ^1H NMR spectrum showed that it contained a small amount of impurity.



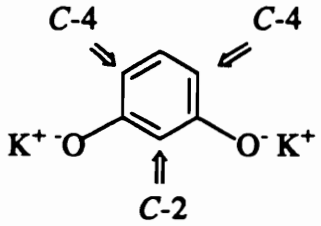
In the larger scale second synthesis of the precusor **6**, K_2CO_3 was used as base instead of NaOH because it was considered that the impurities in the first synthesis might be produced by side reactions such as elimination or substitution reactions in which excess NaOH was involved. K_2CO_3 does not get involved in such side reactions. Also, the molar ratio of resorcinol to 1,6-dibromohexane was increased to 18 molar equvalents. Like the first synthesis, a brown oil was obtained after evaporation and distillation of ethanol and 1,6-dibromohexane. Isolation of the desired product was also done by column chromatography. In the second reaction, however, the chromatography was carried out using a mixture of hexane/ethyl acetate (20/1, v/v) and followed by hexane only. With hexane, flash column chromatography was very effective to isolate the pure product while impurities were stuck to the silica-gel stationary phase. In fact, the flash column technique was a filtration process. The column chromatography with the mixture of hexane/ethyl acetate may not be necessary. By the ^1H NMR (Figure 9) and the ^{13}C NMR spectra, the structure of the isolated product was confirmed. As compared to *p*-bis(4-bromobutyloxy)benzene (**1**) the yield was lower even though the reaction conditions were similar. (46.5 % *vs* 70 %) One reason for the lower yield might be cyclization of the intermediate. The monosubstituted intermediate **8** can undergo cyclization to produce compound **9** while **10** can not yield **11** due to the para linkage and the short chain length of tetramethylene unit. The isolation of cyclic compounds **9** and **11** was not attempted.



8 **9**

10 **11**

Another reason is a great tendency of the resorcinol dianion for *C*-alkylation as compared with hydroquinone dianion because two oxy-anions are located *meta* to each other so that nucleophilic aromatic substitution reactions at *C*-2 and *C*-4 positions take place easily. [6] Thus, the extent of the *O*-alkylation reaction which yields the desired product decreases.



The second precursor, *m*-bis[6-(*m*-hydroxyphenoxy)hexyloxy]benzene (**7**), was prepared by reaction of **6** with excess resorcinol in a mixture of THF and ethanol. The use of THF/ethanol mixture instead of ethanol only was to increase the solubility of reactants **6** and product **7** and the probability of *O*-alkylation over *C*-alkylation. In protic polar solvents such as methanol and ethanol the tendency of *O*-alkylation decreases due

to strong hydrogen bonding between oxy-anion and the hydrogens of the solvent molecules. [7]

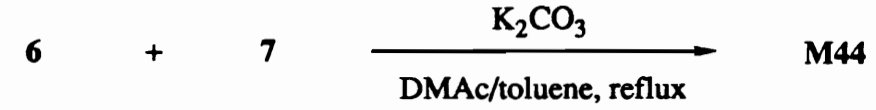
The mixture was refluxed for 28 hr. Work-up was not easy, because when the reaction mixture was poured into a large amount of water to remove excess resorcinol and salts, a solid precipitate was not formed. Instead, a gummy and sticky emulsion-like precipitate was formed and the aqueous suspension was extremely hard to filter. Centrifugation could be applicable, but the volume of the aqueous suspension was too large to treat with centrifugation. Another problem was the gummy precipitate was able to pass through filter paper. Therefore, Celite was necessary to separate the resinous precipitate by suction filtration. The resinous precipitate stuck to Celite particles; thus the filtration was possible. The filtrate was clear and reddish brown. It took several days to filter and isolate all the precipitate. The crude product was obtained by washing the Celite with ethyl acetate and acetone which were good solvents for the compound. After evaporation of the solvents a brown oil was obtained. The oil did not solidify at room temperature over several hours so the desired product was believed to be an oil initially. Therefore, the crude product was subjected to column chromatography with hexane/ethyl acetate (3/1, v/v) as eluent.

After evaporation of the solvents the residual oil, however, solidified slowly at room temperature. It was believed that the crystallization rate of the product was not as fast as usual low molecular-weight crystalline organic compounds. This is probably due to the bent structure of **7**. Also, in the crude product relatively large amounts of

impurities were believed to prevent crystallization of the product. After the column chromatography recrystallizations of the solid gave the pure product in 79 % yield. The recrystallizations were carried out using acetone first, then from ethyl acetate/hexane (2/1, v/v) at - 20 °C. The clear colorless crystals were confirmed as the desired product by the ^{1}H (Figure 10), ^{13}C NMR spectra and elemental analysis. In the ^{13}C NMR spectrum, however, only 14 lines were found although there should be 16 peaks in the spectrum theoretically. It is believed that this was because of the overlapping of the aliphatic carbon signals due to their similarity in chemical environment. The melting point was 103.4-105.9 °C and the product was a new compound.

2-2. Synthesis of **M44**

The synthesis of **M44** was carried out in DMAc/toluene at reflux under high dilution conditions.



A mixture of DMAc (2 L) and toluene (1 L) was refluxed for about 1 day to remove water from the mixture. It seemed to be necessary that before the addition of K_2CO_3 the solvents should be dried. When K_2CO_3 was added to the mixture of the solvents at the begining, it was found that the mixture became yellow to even brown and some kind of deposit was produced. The deposited solid was believed to be KOH produced from the reaction of water and K_2CO_3. In fact, once the mixture of DMAc and toluene was dried before the addition of K2CO3, the color of the mixture was kept as

colorless or very slightly yellow even after the addition of K_2CO_3 and reflux for additional several hours. The slightly yellow color was maintained through the reaction. One of the reasons for the low yield (25 %) of **M40** was the negligence of pre-drying of the solvents before the addition of K_2CO_3. In fact, at that time, the two solvents and K_2CO_3 were mixed initially and refluxed. Also, the color of the mixture was yellow before the addition of the precursors in that reaction.

The two precursors were dissolved in DMAc (70 mL). The solution was divided into six fractions and a fraction was added to the reaction mixture every 8 hr while the mixture was refluxing. A salt was formed inside the flask and it was believed to be KBr. After the last fraction was charged, the mixture was refluxed for 5 days. The salt and unreacted K_2CO_3 were filtered off and the solvents were evaporated. The filtrate was clear initially; however, after the solvents were evaporated the residual solid contained lots of salt, which meant that the salt had some solubility in DMAc. Therefore the residual solid was treated with in THF and it was filtered again to remove the salts After THF was evaporated a slightly brown solid was left. The solid was subjected to two recrystallizations from ethyl acetate at - 20 °C. The crystals were, however, still impure. Thus, column chromatography (silica gel, CH_2Cl_2 eluent) was carried out, and the residual solid from the eluting solution was subjected to a recrystallization from ethyl acetate at - 20 °C. 4.8 g (37 % yield) of white crystals were proved to be the desired macrocycle **M44** by ^1H and ^{13}C NMR spectra (Figure 11 and 12, respectively). The HPLC result (Figure 13) showed that the isolated product was pure. In the low resolution FAB mass spectrum (Figure 14) $[M+Na]^+$ (m/z=791.1) was observed and there was no double-sized macrocycle detected. High resolution FAB mass spectrum yielded the $[M+Na]^+$ peak at 791.4504 which was 0.6 ppm deviated from the caculated value. The melting point was 118.0-120.0 °C which was 42 °C lower than **M40** obviously owing to

the more flexible structure and the longer aliphatic segment. The solubility of the macrocycle was very satisfactory. It was very soluble in toluene, THF, $CHCl_3$, and showed good solubility in acetone and ethyl acetate. It was insoluble or only slightly soluble in hexane. Furthermore it was found that **M44** formed good single crystals, which means that it is capable of forming well-packed crystals. Therefore, the properties of **M44** such as low melting point, good solubility and well defined crystal structure can make the macrocycle a good candidate for a study on the properties of polyrotaxanes.

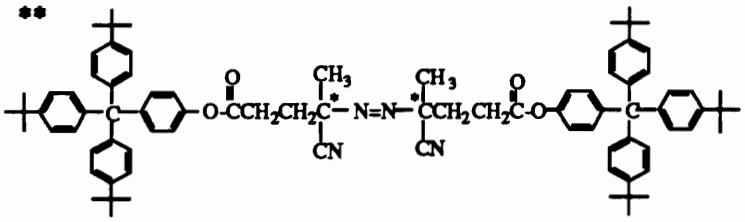
3. Attempted Synthesis of Poly(styrene-rotaxa-M44)

The attempted synthesis of poly(styrene-rotaxa-**M44**) was carried out by free radical polymerization of styrene in the presence of **M44**. The free radical initiator used was the blocking group/initiator (BG/init) (**12**) which can initiate polymerization of styrene as well as achieve blocking of the resultant polystyrene chain ends (refer to Chapter VII for detail). Toluene or ethyl acetate was used as cosolvent to maintain a homogeneous reaction mixture. The resultant polymer was isolated by Soxhlet extraction of the crude product with ethanol followed by reprecipitations (x 2) of the residual solid into hot (> 50 °C) ethanol to give 1.2 g (48 % yield) of powdery product. According to the GPC, the number average molecular weight of the polymer was 18.3 kg/mol and the polydispersity index was 2.26. The ^1H NMR spectrum of the polymer in $CDCl_3$, however, indicated that there was no **M44** in the final product. This result was supprising because due to the relatively high compatibility between **M44** and polystyrene it was anticipated that the reaction would afford a polyrotaxane. In a second trial, the polymerization was carried out in the presence of ethyl acetate instead of toluene; but the

styrene	+	**M44**	+	BG/init** **12**
0.25 g (2.4 mmol)		1.0 g (1.3 mmol)		30 mg (0.024 mmol)

toluene (1.0 g)
95 °C, 3 days

precipitations into hot ethanol



(a mixture of diastereomers:*dl*/*meso*=0.78)

result was the same. There might be a couple of reasons for the lack of threading. The cavity of **M44** molecule was probably not open in the reaction mixture; instead, the molecule collapsed on itself to result in a closed cavity which prevented the threaidng. Another reason would be the loss of the threaded macrocycles during the purification steps. Tris(*p*-*tert*-butylphenyl)methyl unit is known to constrain up to 42-membered rings [8] so that **M44** might slip over the blocking group to dethread.

CONCLUSIONS

Two new hydrocarbon-type macrocycles **M40** and **M44** were synthesized by the two piece combination method. As the precursor for **M40**, *p*-bis(4-bromobutyloxy)benzene (**1**) was prepared by reaction of excess 1,4-dibromobutane and hydroquinone in DMF with NaH as base. The reaction of **1** with excess hydroquinone in a mixture of ethanol and THF with K_2CO_3 as a base afforded *p*-bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene (**2**), which was the other precursor for **M40**. Those two precursors are crystalline and **2** was a new compound. To avoid use of large amount of hydroquinone in synthesis of **2** an alternative method in which hydrogenolysis of *p*-bis[4-{*p*-(benzyloxy)phenoxy}butyloxy]bezene (**4**) was involved was not successful due to the lack of solubility of **4** in common solvents. The cyclization of **1** and **2** in a DMAc and toluene mixture under high dilution conditions gave **M40** in 20 % yield. **M40** showed very limited solubility in common solvents including $CHCl_3$, THF, ethyl acetate, toluene and DMF due to its rigid structure and the lack of polar units.

m-Bis(6-bromohexyloxy)benzene (**6**), which was the precursor for **M44**, was obtained by reaction of resorcinol and excess 1,6-dibromohexane. The synthesis of the other precursor *m*-bis[6-(*m*-hydroxyphenoxy)hexyloxy]benzene (**7**) for **M44** was achieved by reaction of **6** with excess resorcinol. The two reactions were carried out in a mixture of ethanol and THF using K_2CO_3 as a base as the case of **1** and **2**. It is noted that the yield of **6** (46.5 %) was significantly lower than **1** (70 %) although the reaction conditions were similar. This is due to the higher tendency of *C*-alkylation of resorcinol dianion than hydroquinone dianion. Cyclization of **6** and **7** in a highly diluted DMAc/toluene mixture gave **M44** in 37 % yield. **M44** showed lower melting point (118.0-120.0 °C) than **M40** (mp=160.8-162.1 °C) owing to its bent structure and longer

methylene units. Also **M44** showed good solubility in many solvents including THF, $CHCl_3$, toluene and ethyl acetate.

The attempted synthesis of poly(styrene-rotaxa-**M44**) was carried out by free radical polymerization of styrene in the presence of **M44**. The resultant polymer, however, contained no threaded **M44** probably due to the closed cavity of the macrocycle in the reaction mixture and dethreading during the purification process.

EXPERIMENTAL

Measurements. Melting points were taken in capillary tubes with a Melt-Temp II melting point apparatus and corrected. IR spectra were obtained on Nicolet MX-1 or Perkin-Elmer 283B infrared spectrophotometers using KBr pellets unless otherwise noted and reported in cm^{-1}. NMR spectra were obtained on a Varian Unity 400 MHz spectrometer at ambient temperature using tetramethylsilane as an internal standard. GPC analyses of the polymers were performed at 20 °C in THF using a Waters system with a refractive index detector after calibration with PS standards. Elemental analyses were done by Supersun Technology Analytical Laboratory, Stony Brook, New York. High resolution FAB mass spectra were obtained from the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry, St. Louis, Misouri. For the HPLC analyses, an ISCO model 2350 HPLC instrument was used. The column used was a Novapak-C_{18} and the eluent was a mixture of tetrahydrofuran and water (65:35 by vol). The flow rate was 2 mL/min and a refractive index detector (Waters, Differential Refractometer R401) was used.

***p*-Bis(4-bromobutyloxy)benzene (1).** In a 1-L round-bottomed flask equipped with a magnetic stirring bar hydroquinone (8.25 g, 77.2 mmol) was dissolved in DMF (200 mL). NaH (7.0 g, 60 % oil dispersed, 0.18 mol) was added little by little. The solution became yellow to green to dark green upon adding NaH. The viscosity increased, and thus DMF (20 mL) was added. The mixture was stirred for 20 min at room temperature. 1,4-Dibromobutane (325 g, 1.5 mol) was added at once. The mixture was heated to 80 °C and allowed to stir for three days at that temperature. All solvents were removed by rotary evaporation and the residual solid was dissolved in methylene chloride (200 mL).

The solution was filtered to remove the salts. The filtrate was passed through a silica-gel column (3 cm dia x 30 cm lengh) with additional methylene chloride (500 mL). The residual solid after evaporation of the solvent was dissolved in hot EtOH (100 mL). The solution was placed in the refrigerator (- 20 °C) overnight. The slightly yellow crystals were filtered and dried under vacuum at room temperature. Yield : 20.0 g (70 %).

Mp: 88.5-90.0 °C (Lit. [3] mp = 89-91 °C). IR: 2907, 2842, 1433, 1377, 1252, 1201, 988, 795, 748, 707, 613. ^{1}H NMR ($CDCl_3$): 1.99 (m, 4H, -CH_2CH_2C$H_2$$CH_2$-), 3.49 (t, J=8 Hz, 2H, BrCH_2-), 3.94 (t, J=6.0 Hz, 2H, -CH_2O-), 6.81 (s, 4H, arom.). ^{13}C NMR ($CDCl_3$) : 28.0, 29.5, 33.5, 67.4, 115.4, 153.1 (theory 6, found 6).

***p*-(Benzyloxy)phenol (3).** In a 3-neck 500-mL flask equipped with a magnetic stirring bar and a condenser, hydroquinone (72 g, 650 mmol) was dissolved in ethanol (200 mL). KOH (36.4 g, 650 mmol) was added to the solution at room temperature. The mixture was viscous, so 50 mL ethanol was added. To the yellow suspension benzyl bromide (106 g, 620 mmol) was added dropwise over 3 hrs while heating the mixture (46 °C). The reaction mixture was refluxed for 22 hrs. Salts were filtered and washed with ethanol. The residual solid from the filtrate was subjected to recrystallization from ethanol. The resultant powdery crystals were recrystallized from a mixture of hexane/ethyl acetate (10/3, v/v). The resultant slightly yellow crystals were filtered and dried under vacuum at 45 °C. The yield was 32 g (26 %).

Mp: 118.0-120.5 °C. (Lit. [5] mp = 120-122 °C) IR: 3305, 3007, 2576, 2540, 1430, 1338, 1195, 1080, 786, 710, 670. ^{1}H NMR ($CDCl_3$) : 4.68 (s, 1H, OH), 5.01 (s, 2H, OCH_2), 6.75 (d, J=8.9 Hz, 2H, arom.), 6.85 (d, J=8.9 Hz, 2H, arom), 7.35 (m, 5 H, arom.). ^{13}C NMR ($CDCl_3$) : 70.78, 116.04, 116.05, 127.49, 127.90, 128.55, 137.20, 149.65, 152.96 (theory 9, found 9).

***p*-Bis[4-{*p*-(benzyloxy)phenoxy}butyloxy]benzene (4).** In a 3-neck 250-mL flask equipped with a magnetic stirring bar *p*-(benzyloxy)phenol (**3**) (2.40 g, 12 mmol) was dissolved in DMF (40 mL). NaH (0.65 g, 60 % oil dispersed, 16 mmol) was washed with hexane (30 mL) and added to the mixture slowly. Upon adding NaH the solution became yellow. The mixture contained lots of precipitate. After 5 min stirring *p*-bis(4-bromobutyloxy)benzene (**1**) (1.52 g, 4.0 mmol) was added all at once. The mixture was stirred at 85 °C for 20 hrs. The reaction mixture was poured into water (700 mL). The precipitate was filtered and washed with water (100 mL) and dried. The precipitate (2.5 g, 100 % yield) was dissolved in hot ethyl acetate (75 mL) and the solution was cooled down to room temperature. The powdery crystals were filtered and washed with ethyl acetate. Yield : 2.4 g (97 % yield).

Mp: 197.4-198.2 °C. IR: 3010, 2919, 2885, 2848, 1485, 1456, 1210, 998, 804, 713, 670. ^{1}H NMR ($CDCl_3$) : 1.96 (s, 8H, $CH_2C\underline{H_2}\underline{CH_2}CH_2$) 3.98 (s, 8H, $OC\underline{H_2}CH_2CH_2C\underline{H_2}O$), 5.01 (s, 4H, $PhCH_2$), 6.72 (s, 4H, arom), 6.76 (d, J=9.4 Hz, 4H, arom), 6.82 (d, J=9.4 Hz, 4H, arom) 7.39 (m, 10H, arom). Anal. Calcd for $C_{40}H_{42}O_6$: C, 77.64; H, 6.84; found: C, 77.34; H, 6.91.

***p*-Bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene (2).** In an 1-L 3-neck flask equipped with a mechanical stirrer and a condenser hydroquinone (86.9 g, 790 mmol), K_2CO_3 (120 g, 870 mmol) and ethanol (350 mL) were placed and the mixture was refluxed for 1 hr. To the mixture THF (200 mL) was added, and *p*-bis(4-bromobutyloxy)benzene (**1**) (10.0 g, 260 mmol) in THF (80 mL) was added to the mixture dropwise over 40 min. The mixture was refluxed for 13 hr. The mixture was poured into water (8 L total). The off-white precipitate **5** was filtered and washed with water (1.5 L). **5** was dispersed in a DMAc/DMF (200 mL, 1/1, v/v) mixture and it was acidified to pH 3-4 by addition of

HCl. The suspension was poured into water (900 mL) again and the precipitate was filtered and dried. The precipitate was dissolved in hot DMF (300 mL) and filtered to remove some insoluble part. The residual solid was recrystallized from xylene to give 9.1 g (79 % yield) of off-white powdery crystals.

Mp: 208-210.5 °C. IR: 3360, 2901, 2780, 2840, 1488, 1456, 1434, 1358, 1304, 1302, 960, 798, 775, 690. ^{1}H NMR (DMSO-d_6): 1.81 (s, 8H, $CH_2CH_2CH_2CH_2$), 3.90 (t, J=5.1 Hz, 4H, OCH_2), 3.94 (t, J=5.1 Hz, 4H, OCH_2), 6.66 (d, J=8.8 Hz, 4H, arom), 6.74 (d, J=8.8 Hz, 4H, arom), 6.84 (s, 4H, arom), 8.89 (s, 2H, OH). ^{13}C NMR (DMSO-d_6): 25.45, 25.48, 67.45, 115.18, 115.26, 115.56, 150.99, 151.30, 152.48, 172.62 (theory 10, found 10). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90; found: C, 70.93; H, 7.04.

Macrocycle M40. In a 5-L flask equipped with a mechanical stirrer, a Dean-Stark trap and a condenser, a mixture of DMAc (2 L), toluene (1.1 L) and K_2CO_3 (5.0 g, 36.2 mmol) was refluxed for 3 days. After 3 days toluene (300 mL) was added to maintain the constant boiling temperature (about 140 °C). *p*-Bis(4-bromobutyloxy)benzene (**1**) (1.14 g, 3.00 mmol) and *p*-bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene (**2**) (1.315 g, 3.00 mmol) were dissolved in hot DMAc (15 mL) and the solution was poured into the reaction mixture. Every 8 hr an identical solution was added to the reaction mixture. Thus the total amount of each precursor was 18.0 mmol. The reaction mixture was refluxed further for 5 days. Solvents were evaporated and the residual solid was extracted with chloroform using a Soxhlet for 6 days. Chloroform was evaporated and the residual solid (7 g) was dissolved in boiling ethyl acetate (200 mL) and the solution was filtered to remove some insoluble parts. The solution was allowed to stand at room temperature for a couple of days. The white granular crystals were collected and subjected to another recrystallization from ethyl acetate. The crystals were dried under

vacuum at 80 °C to give 3.0 g of product (25.4 % yield).

Mp: 160.8-162.1 °C. IR: 2880, 2844, 1458, 1280, 1200, 1085, 1028, 1003, 957, 785, 762, 690. ^{1}H NMR ($CDCl_3$): 1.93 (p, J=3.6 Hz, 16H, $CH_2C\underline{H_2}\underline{CH_2}CH_2$), 3.98 (t, J=6.4 Hz, 16 H, OCH_2), 6.79 (s, 16H, arom). ^{13}C NMR ($CDCl_3$): 25.60, 67.83, 115.55, 152.95 (theory 4, found 4). High resolution FAB MS: $[M+Na]^+$; m/z=679.3274 (Calcd m/z = 679.3247, deviation 3.9 ppm).

***m*-Bis(6-bromohexyloxy)benzene (6).** In a 3-neck, 1-L round-bottomed flask equipped with a mechanical stirrer and a condenser with a N_2 bubbler on the top, resorcinol (12.5 g, 114 mmol), K_2CO_3 (40.0 g, 290 mol) and ethanol (500 mL) were placed. The mixture was refluxed for 1 hr. Upon refluxing, the mixture became green to dark green to very dark brown. 1,6-Dibromohexane (500 g, 2.05 mol) was added to the mixture all at once. The reaction mixture was refluxed for 1.5 days. The mixture was cooled down to room temperature and the salts were filtered and washed with diethyl ether (400 mL). The solvents (ethanol and ether) were removed by rotary evaporation. The unreacted 1,6-dibromohexane was recovered by vacuum distillation (55-58 °C/0.01-0.02 mmHg). A dark brown oil was obtained. The oil was dissolved in a mixture of ethyl acetate/hexane (1/20, v/v) and subjected to column chromatography (silica gel) with the same solvent system as eluent. The residual oil from the eluted solution was further purified by a flash column (silica gel) with hexane. The elution of hexane was continued until no product came out. The product was a colorless oil (24.1 g, 46.5 % yield).

IR: 2910, 2840, 1578, 1453, 1270, 1451, 1370, 1348, 1166, 1135, 1030, 815, 742, 668. ^{1}H NMR ($CDCl_3$): 1.50 (t, J=3.6 Hz, 8H, $O(CH_2)_2C\underline{H_2}\underline{CH_2}(CH_2)_2Br$), 1.79 (p, J=7.2 Hz, 4H, $O(CH_2)_4C\underline{H_2}CH_2Br$), 1.89 (p, J=6.8 Hz, 4H, $OCH_2C\underline{H_2}(CH_2)_4Br$), 3.42 (t, J=6.8 Hz, 4H, $O(CH_2)_5C\underline{H_2}Br$), 3.94 (t, J=6.4 Hz, 4H, $OC\underline{H_2}(CH_2)_5Br$), 6.47 (m, 3H,

arom), 7.15 (t, J=8.0 Hz, 1H, arom). ^{13}C NMR ($CDCl_3$): 25.32, 27.93, 29.09, 32.70, 33.80, 67.70, 101.47, 106.69, 129.81, 160.29 (theory 10, found 10). Anal. Calcd for $C_{18}H_{28}O_2Br_2$: C, 49.56; H, 6.47; found: C, 49.54; H, 6.47.

***m*-Bis[6-(*m*-hydroxyphenoxy)hexyloxy]benzene (7).** In a 3-neck, 2-L round-bottomed flask equipped with a mechanical stirrer and a condenser with a N_2 bubbler on the top, resorcinol (130 g, 1.18 mol), K_2CO_3 (163 g, 1.18 mol), and ethanol (350 mL) were placed. The mixture was refluxed for 30 min and cooled down to room temperature. *m*-Bis(6-bromohexyloxy)benzene (**6**) (15.0 g, 34 mmol) was dissolved in THF (100 mL) and the solution was added to the mixture dropwise over 50 min. After completion of the addition the mixture was heated to reflux. As the reaction proceeded the mixture became dark brown and then reddish brown. The reaction time was 28 hr. The reaction mixture was poured into excess water (8 L total). The suspension containing sticky/gummy precipitate was neutralized by addition of HCl. The precipitate was filtered and isolated by suction filtration through a glass filter with Celite. The Celite was washed with water to remove remaining resorcinol. The crude product was obtained by washing the Celite with ethyl acetate and acetone. The residue after evaporation of the solvents was subjected to column chromatography (silica gel) with ethyl acetate/hexane (1/3, v/v) as eluent. The crude product from the column chromatography was purified by recrystallizations from acetone first, and from acetone/ethyl acetate (1/2, vol) secondly. White clear crystals were obtained. The yield was 13.5 g (79 %)

Mp: 103.4-105.9 °C. IR: 3432, 3332, 2899, 2825, 1570, 1447, 1270, 1135, 1034, 998, 827, 740, 663. ^1H NMR (DMSO-d_6): 1.43 (p, J=3.6 Hz, 8H, $OCH_2CH_2C\underline{H_2}\underline{CH_2}CH_2CH_2O$), 1.68 (broad p, J=3.6 Hz, 8H, $OCH_2C\underline{H_2}CH_2CH_2C\underline{H_2}CH_2O$), 3.86 (t, J=6.4 Hz, 4H, OCH_2), 3.91 (t, J=6.4 Hz, 4H,

OCH_2), 6.3 (m, 6H, arom), 6.45 (m, 3H, arom), 7.00 (t, J=8.0 Hz, 2H, arom), 7.11 (t, J=8.0 Hz, 1H, arom), 9.31 (s, 2H, OH). ^{13}C NMR (DMSO-d_6): 25.78, 29.11, 67.54, 67.74, 101.47, 102.10, 105.54, 107.02, 108.09, 130.21, 130.29, 158.96, 160.33, 160.34 (theory 16, found 14). Anal. Calcd for $C_{30}H_{38}O_6$: C, 72.85; H, 7.74; found: C, 72.66; H, 7.84.

Macrocycle M44. In a 5-L 3-neck round-bottomed flask equipped with a mechanical stirrer and a condenser with a Dean-Stark trap and a N_2 bubbler on the top, DMAc (2 L), toluene (1 L) were placed. The mixture was refluxed until no water was condensed into the trap. More than 10 mL of water was collected. After no water came out, K_2CO_3 (6 g, 43.4 mmol) was added and the mixture was distilled for several hours further to make sure of the absence of water. The mixture was very slightly yellow. *m*-Bis(6-bromohexyloxy)benzene (**6**) (7.40 g, 17 mmol) and *m*-bis[6-(*m*-hydroxyphenoxy)hexyloxy]benzene (**7**) (8.40 mmol, 17 mmol) were dissolved in DMAc (75 mL). An aliqout (15 mL) of the solution was taken and charged to the reaction mixture. After several hours it was found that a salt (KBr) was produced and attached to the flask wall. After 8 hr another 15 mL was added. Likewise the other three aliquots were added at 8 hr intervals. Therefore, the total addition time was 32 hr. After completion of the addition of the reactants, the reaction mixture was allowed to reflux for 5 days. The reaction mixture was lightly yellow and lots of salt was found in the flask. After the salt was removed by filtration and the solvents were rotary evaporated, the crude product was subjected to two recrystallizations from ethyl acetate at - 20 °C to give 9.08 g (69.5 % yield) of white crystals. However, it was not pure according to TLC analysis. Thus, the crystals were subjected to column chromatography using silica gel with methylene chloride as an eluent. The residual solid from eluting solution was

recrystallized from ethyl acetate at - 20 °C to give 4.8 g (37 % yield) of white crystals. Mp: 118.0-120.0 °C. IR: 2898, 2827, 1567, 1436, 1366, 1270, 1244, 1154, 1120, 995, 803, 739, 662. ^{1}H NMR ($CDCl_3$): 1.53 (p, J=3.6 Hz, 16H, $OCH_2CH_2C\underline{H_2}\underline{CH_2}CH_2CH_2O$), 1.80 (p, J=6.2 Hz, 16H, $OCH_2C\underline{H_2}CH_2CH_2C\underline{H_2}CH_2O$], 3.94 (t, J=6.4 Hz, 16H, $O\underline{CH_2}CH_2CH_2CH_2CH_2\underline{CH_2}O$], 6.45 (m, 12H, arom), 7.14 (t, J=8.0 Hz, 4H, arom). ^{13}C NMR ($CDCl_3$): 25.76, 29.12, 67.71, 101.42, 106.73, 129.77, 160.30 (theory 6, found 6). High resolution FAB MS: $[M+Na]^+$; m/z=791.4504 (Calcd m/z=791.4499, deviation 0.6 ppm).

Attempted synthesis of poly(styrene-rotaxa-M44). In a 50-mL flask equipped with a Teflon valve and a magnetic stirring bar styrene (0.25 g, 2.4 mmol), **M44** (1.0 g, 1.3 mmol), BG/init (**12**) (30 mg, 0.024 mmol) and toluene (1.0 g) were placed. The mixture was treated with two cycles of freeze-pump-thaw processes. The mixture was placed in a preheated oil bath and allowed to react for 3 days at 95 °C. The mixture was Soxhlet extracted with for 2 weeks. The remaining solid was dissolved in toluene (5 mL) and poured into ethanol (100 mL). The precipitate was fine and difficult to filter. The suspension was heated to around 50-60 °C and stirred for 2 hr at that temperature. While stirring the fine particles coagulated the precipitate was filtered. Another precipitation process was done and the precipitate was dried under vacuum at room temperature. 1.2 g (48 % yield) of solid was obtained. The ^{1}H NMR spectrum showed that the product was homo-PS.

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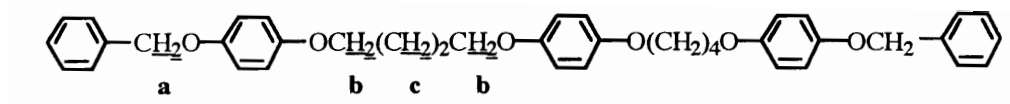


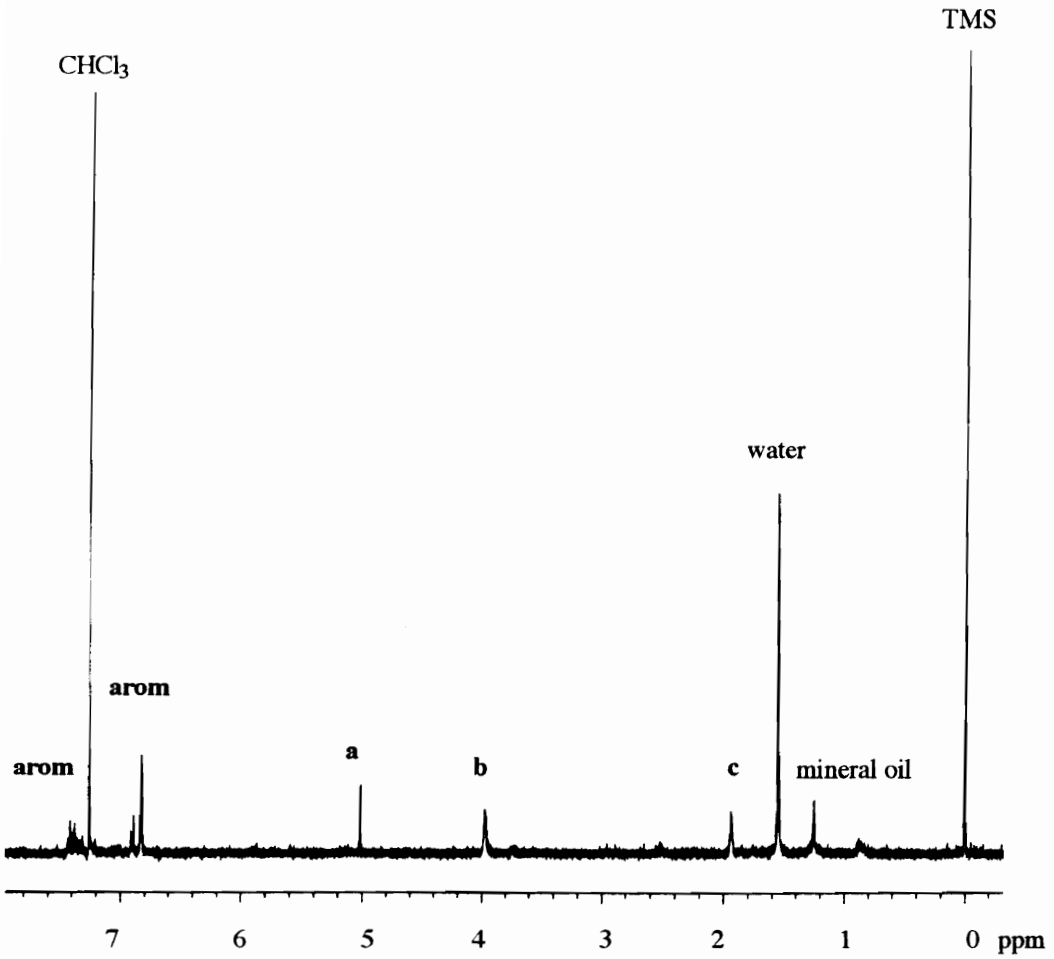


Figure 1. ^{1}H NMR spectrum of *p*-bis[4-{*p*-(benzyloxy)phenoxy}butyloxy]benzene (**4**). ($CDCl_3$)

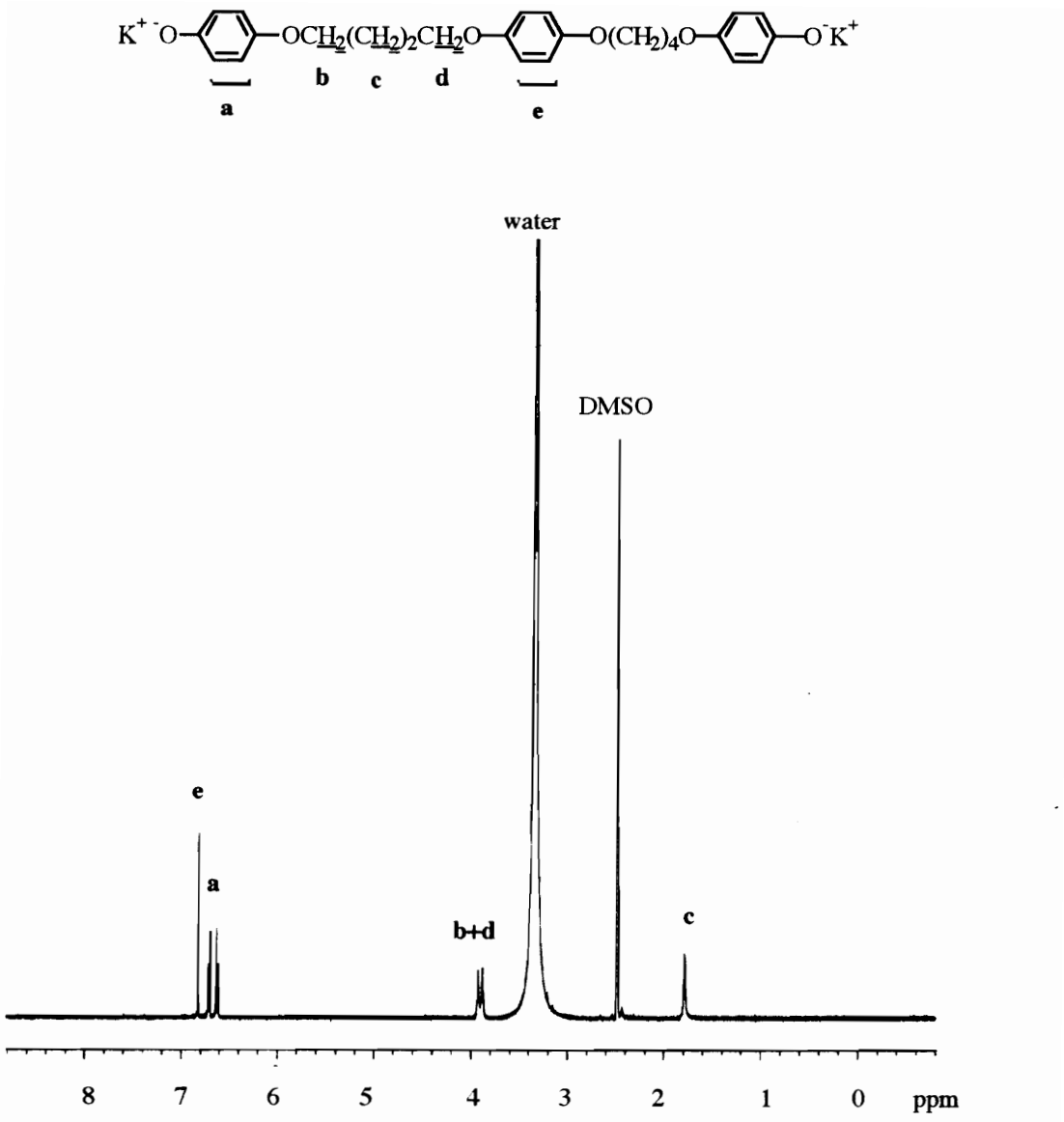


Figure 2. ^{1}H NMR spectrum of dipotassium salt of *p*-bis[4-(*p*-hydroxyphenoxy)-butyloxy]benzene. (DMSO-d_6)

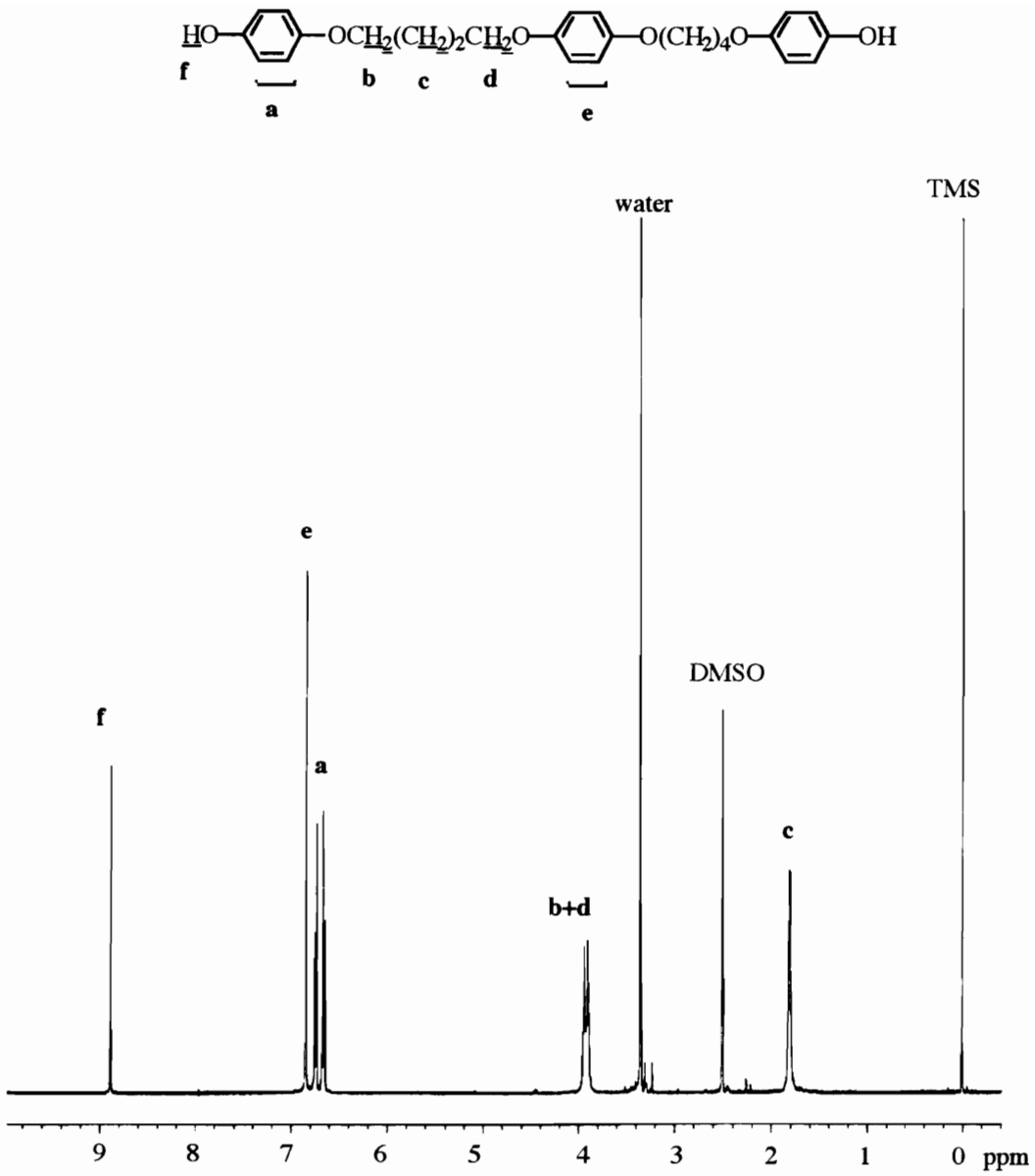


Figure 3. ^{1}H NMR spectrum of *p*-bis[4-(*p*-hydroxyphenoxy)butyloxy]benzene. (DMSO-d_6)

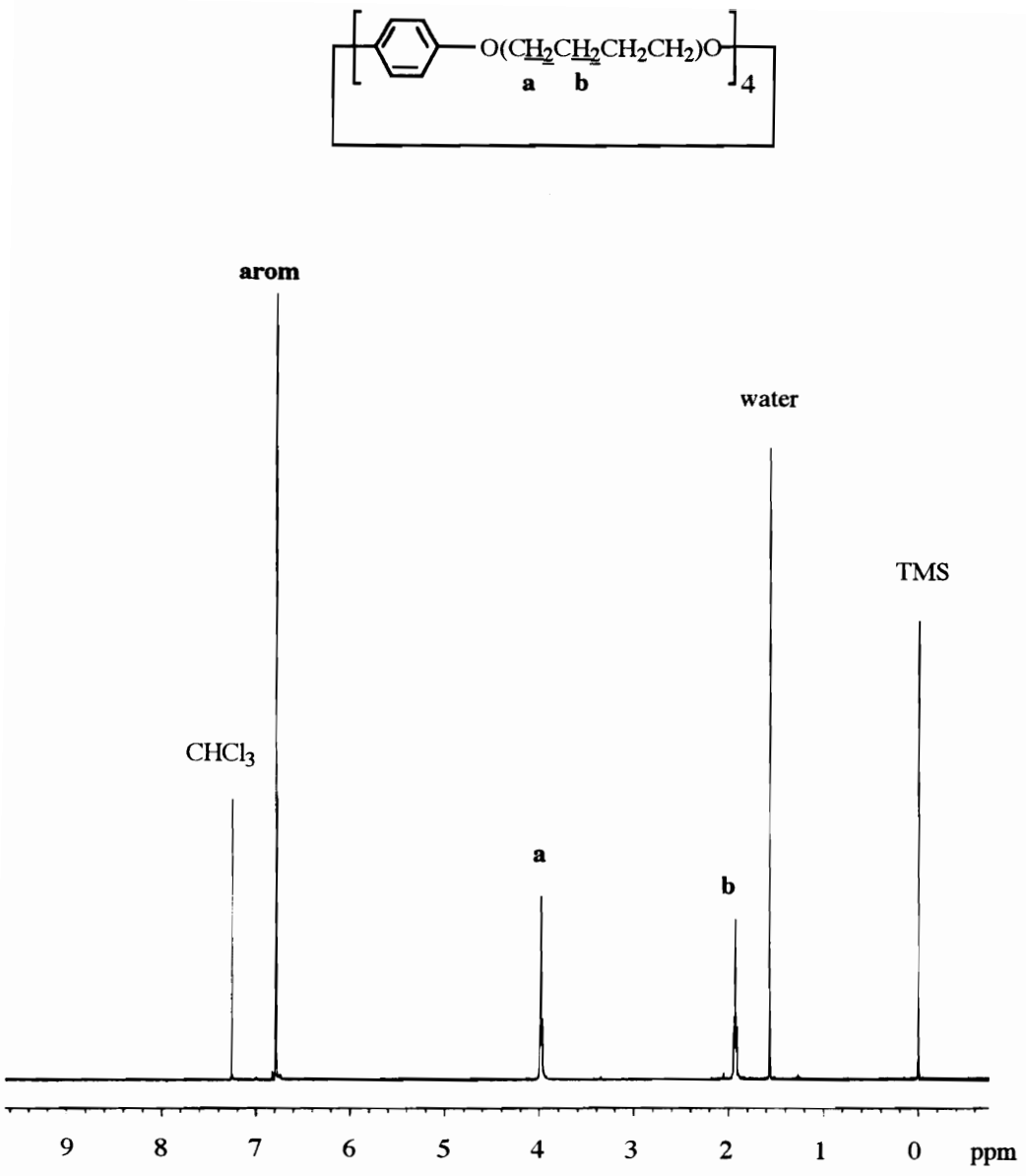


Figure 4. ^{1}H NMR spectrum of **M40**. ($CDCl_3$)

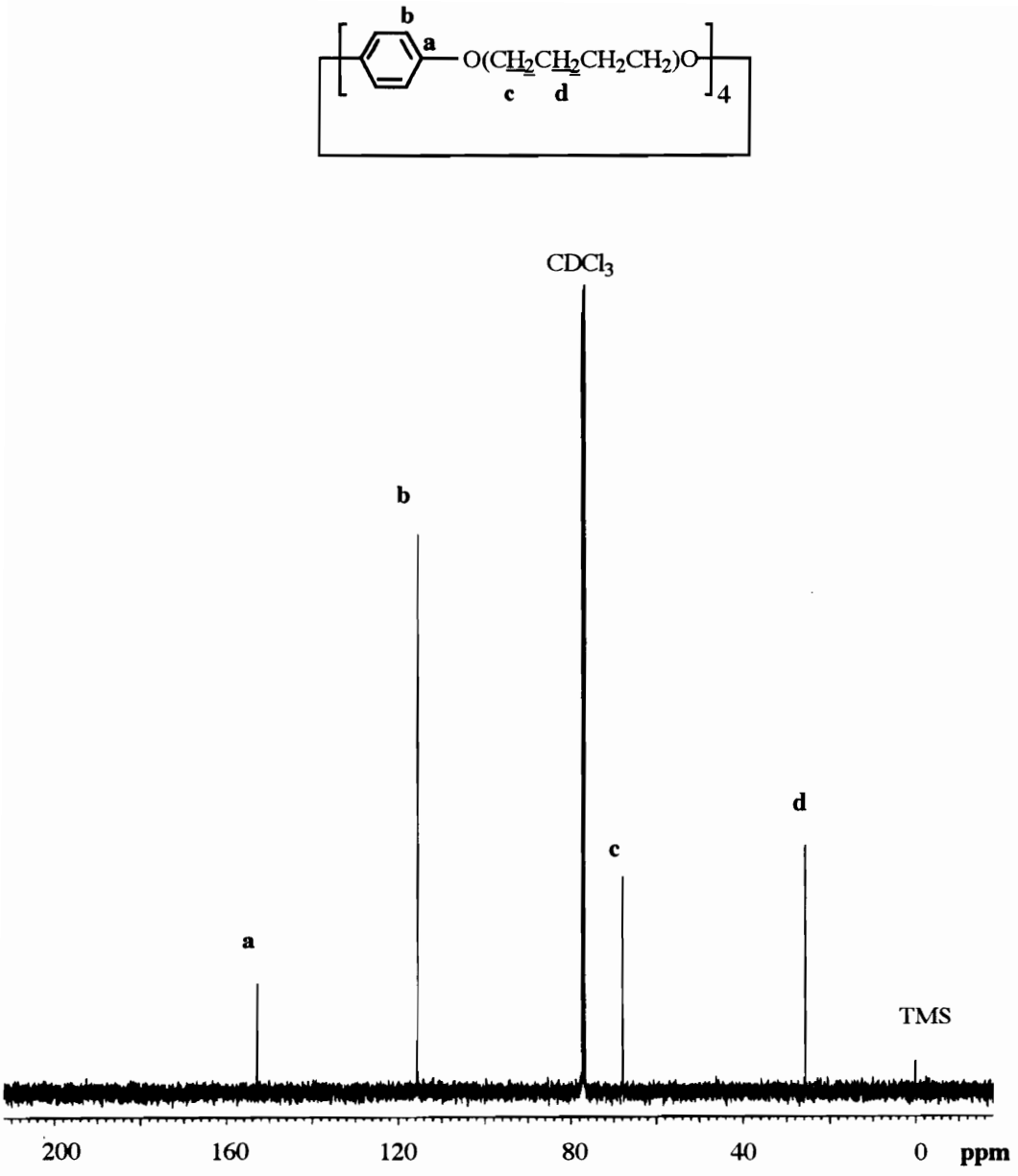


Figure 5. ^{13}C NMR spectrum of **M40**. ($CDCl_3$)

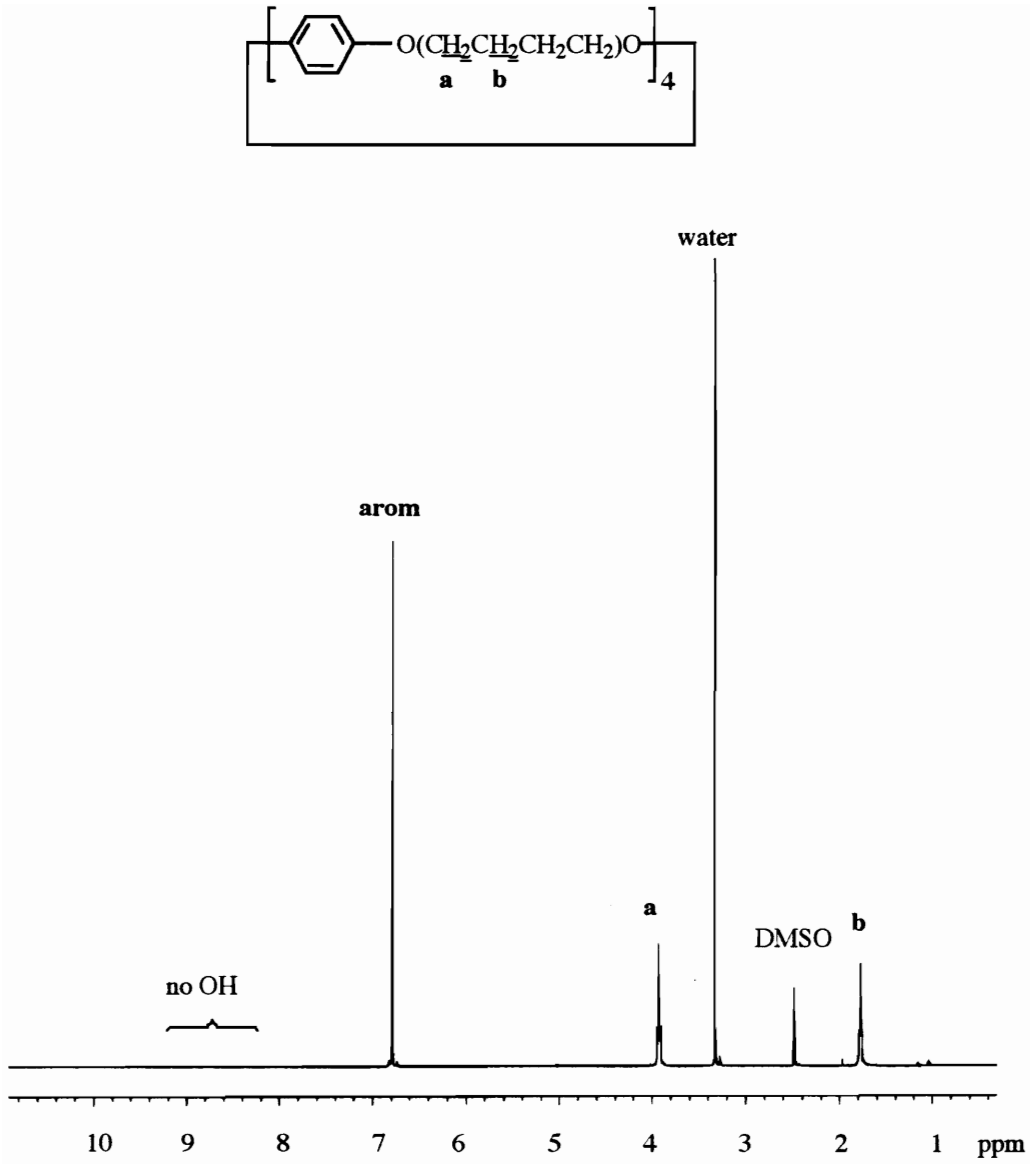


Figure 6. ^{1}H NMR spectrum of **M40**. (DMSO-d_6)

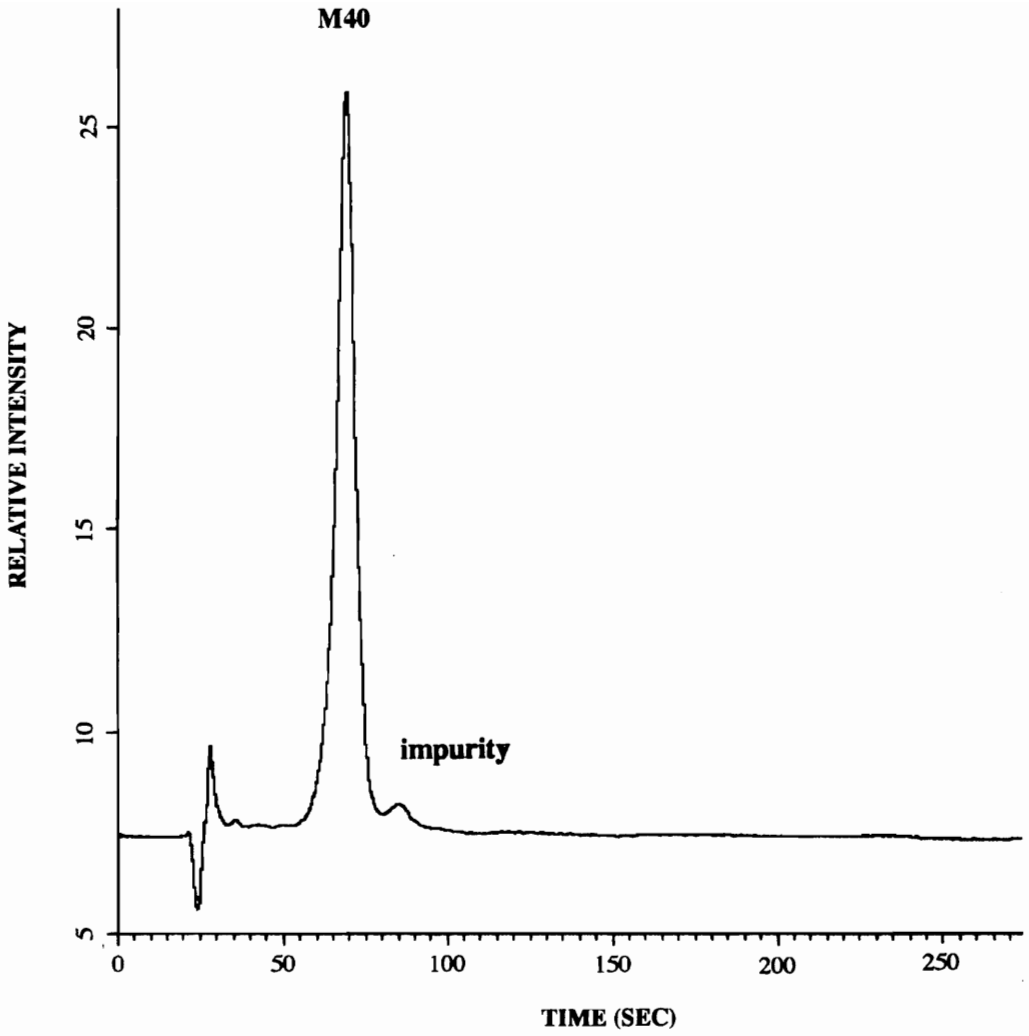


Figure 7. HPLC trace of **M40**.
(Novapak-C_{18}, THF/water=65/35 by vol, flow rate=2 mL/min, RI detector)

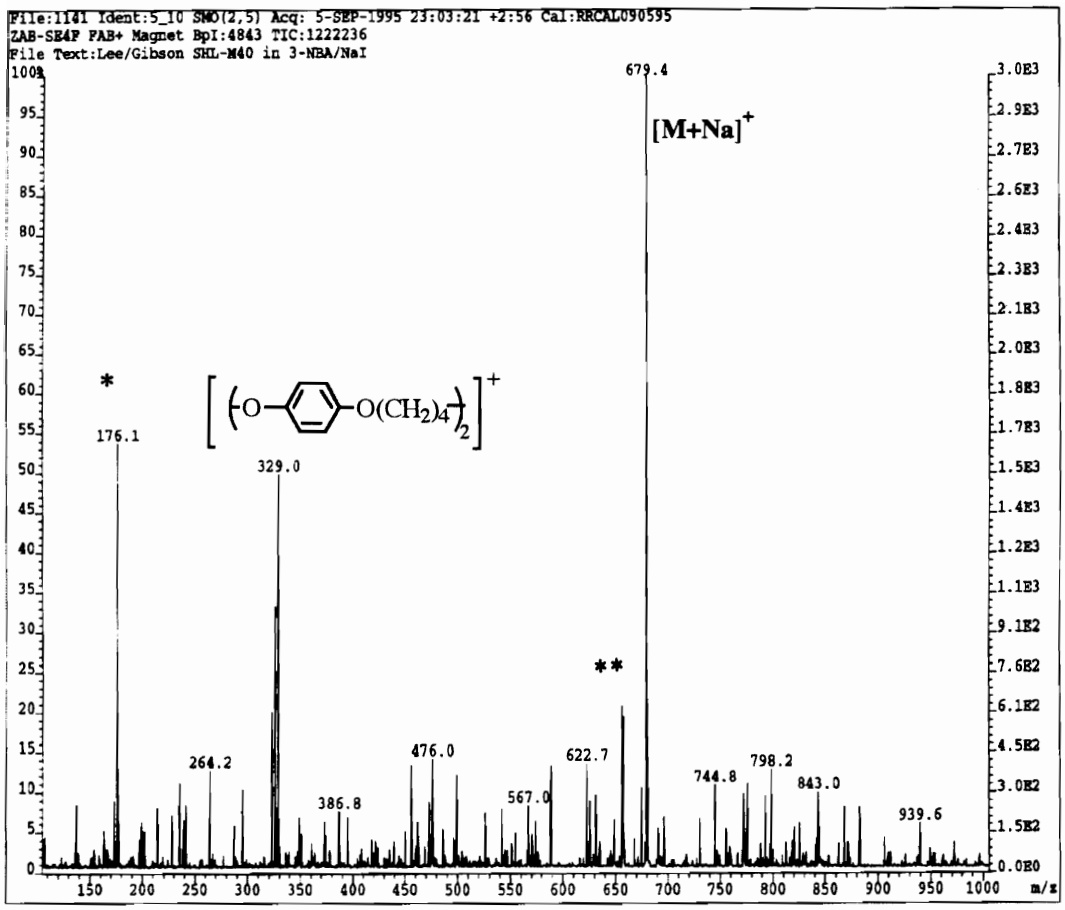


Figure 8(a). FAB mass spectrum of **M40**. (3-NBA/NaI)
* from matrix ** M^+ (m/z=656)

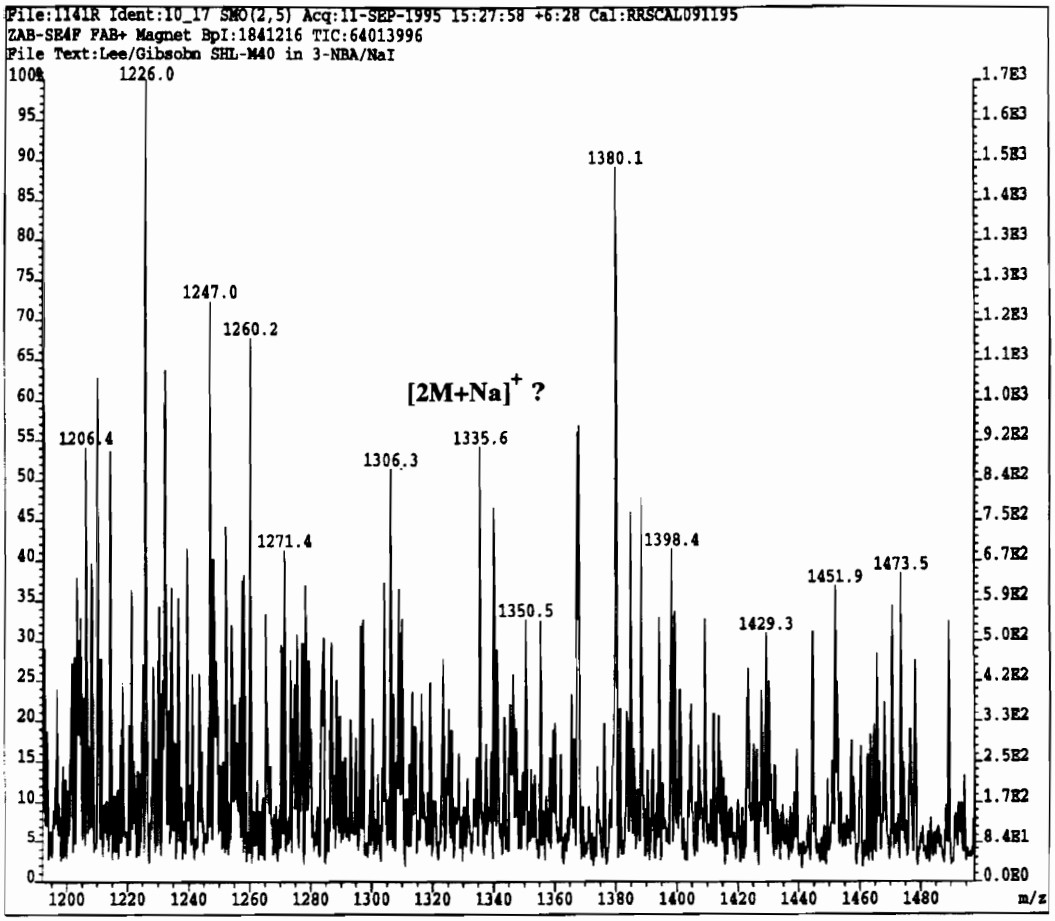


Figure 8(b). FAB mass spectrum of **M40**. (Higher m/z region) (3-NBA/NaI)

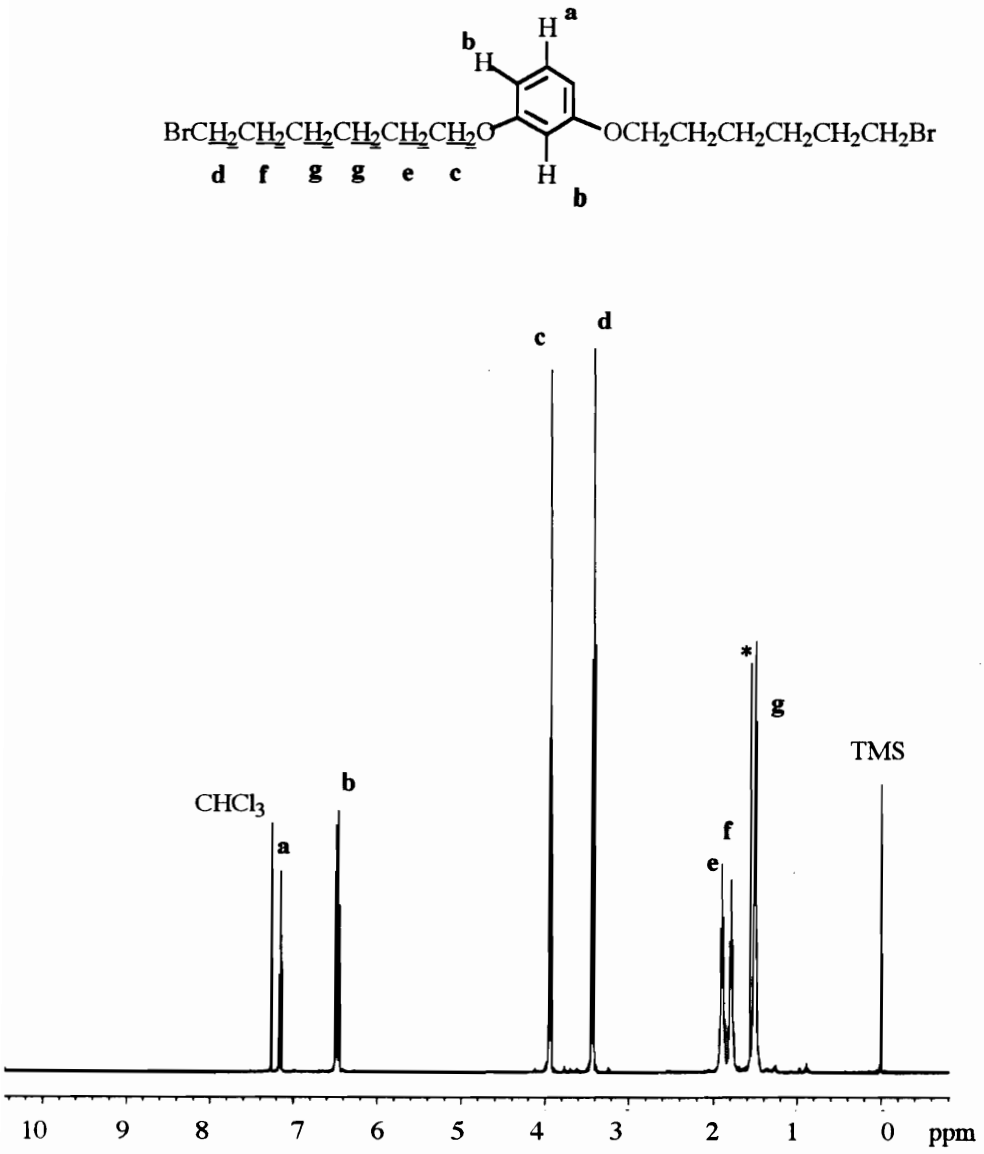


Figure 9. ^{1}H NMR spectrum of *m*-bis(6-bromohexyloxy)benzene (**6**) ($CDCl_3$) * water

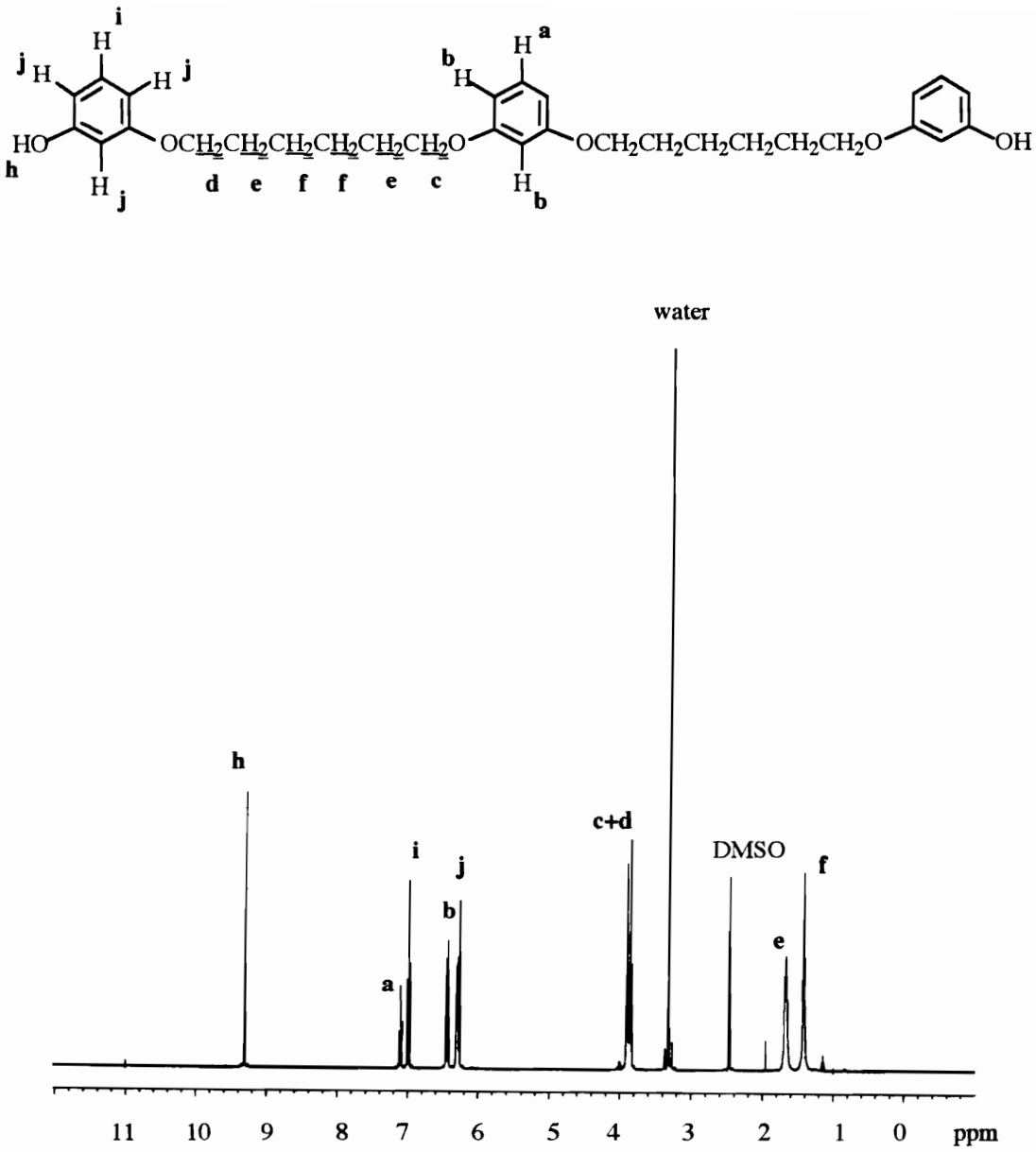


Figure 10. ^{1}H NMR spectrum of *m*-bis[6-(*m*-hydroxyphenoxy)hexyloxy]benzene (**7**) (DMSO-d_6)

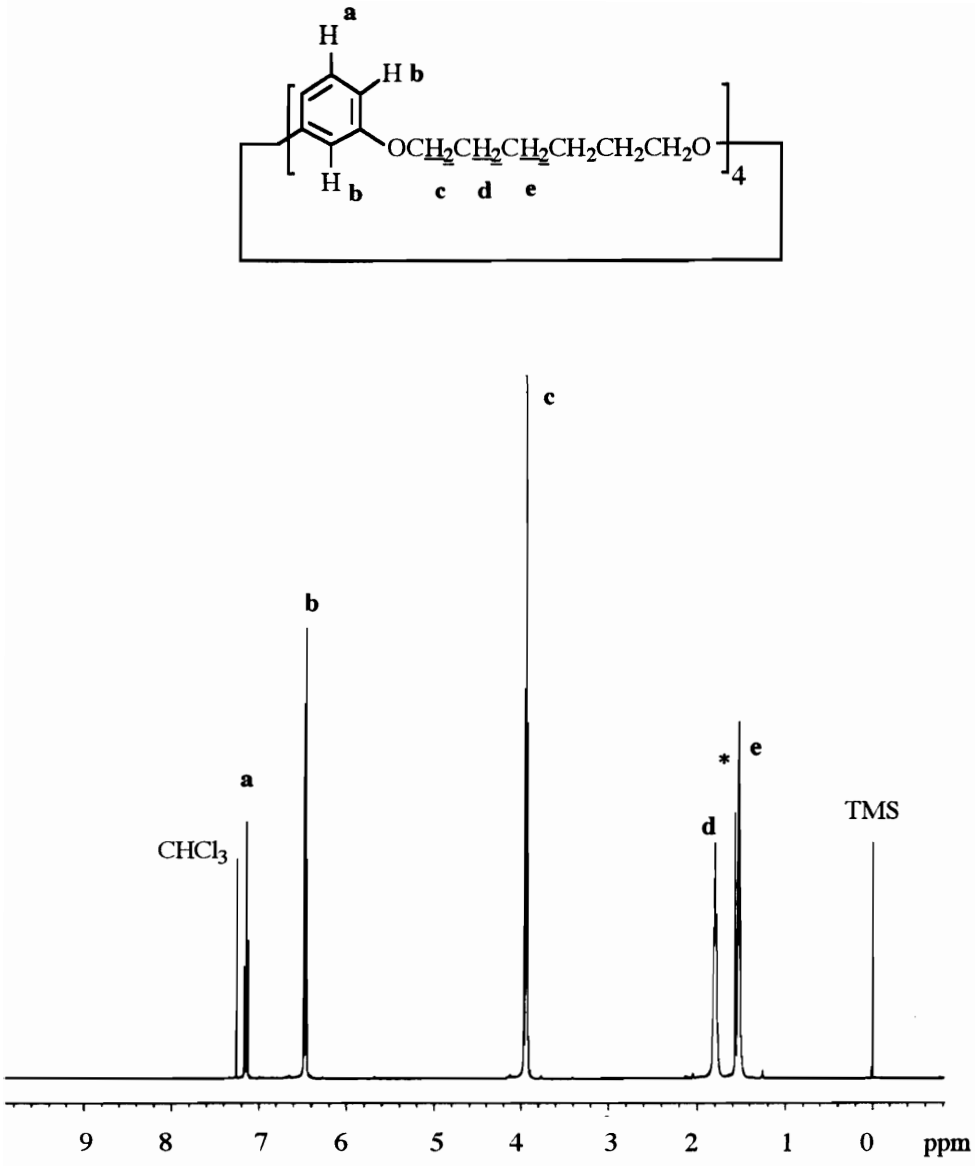


Figure 11. ^{1}H NMR spectrum **M44**. ($CDCl_3$)
* water

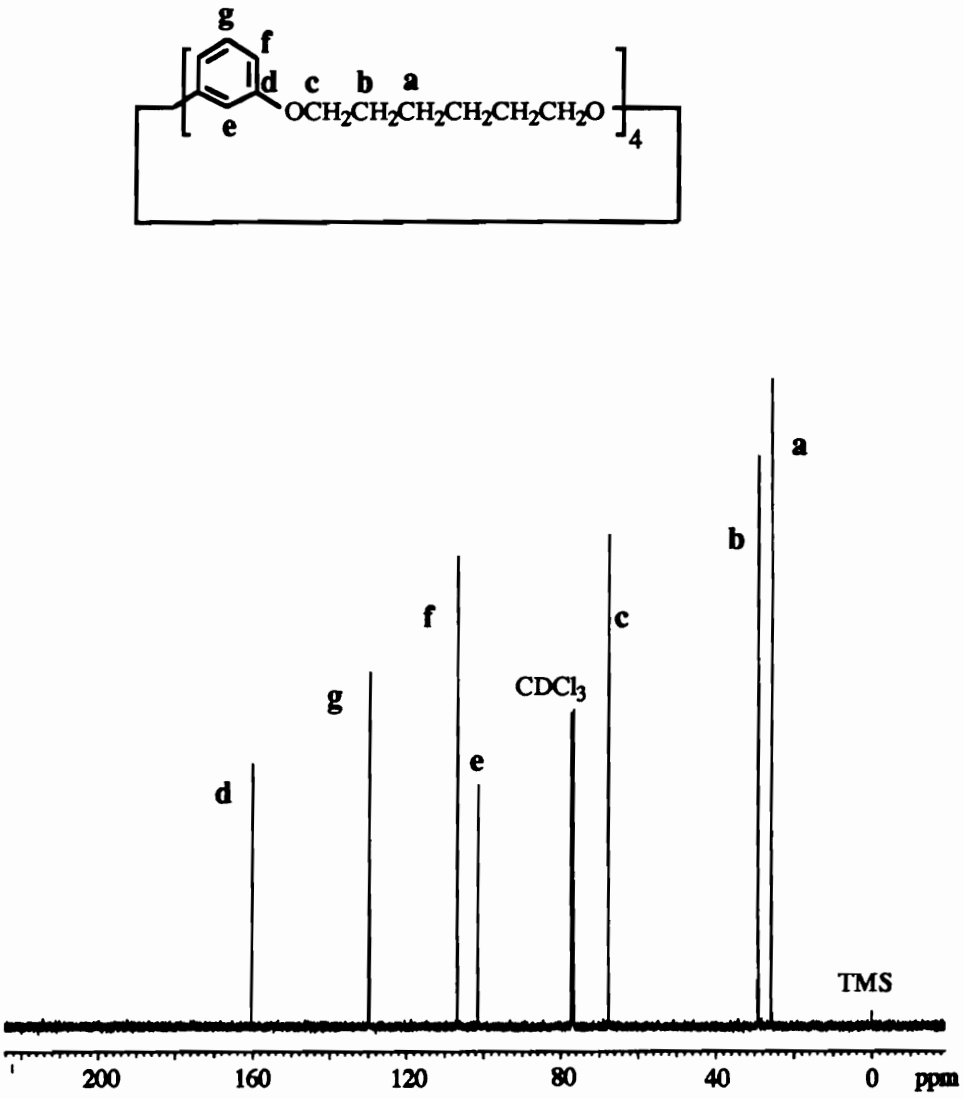


Figure 12. ^{13}C NMR spectrum of **M44**. ($CDCl_3$)

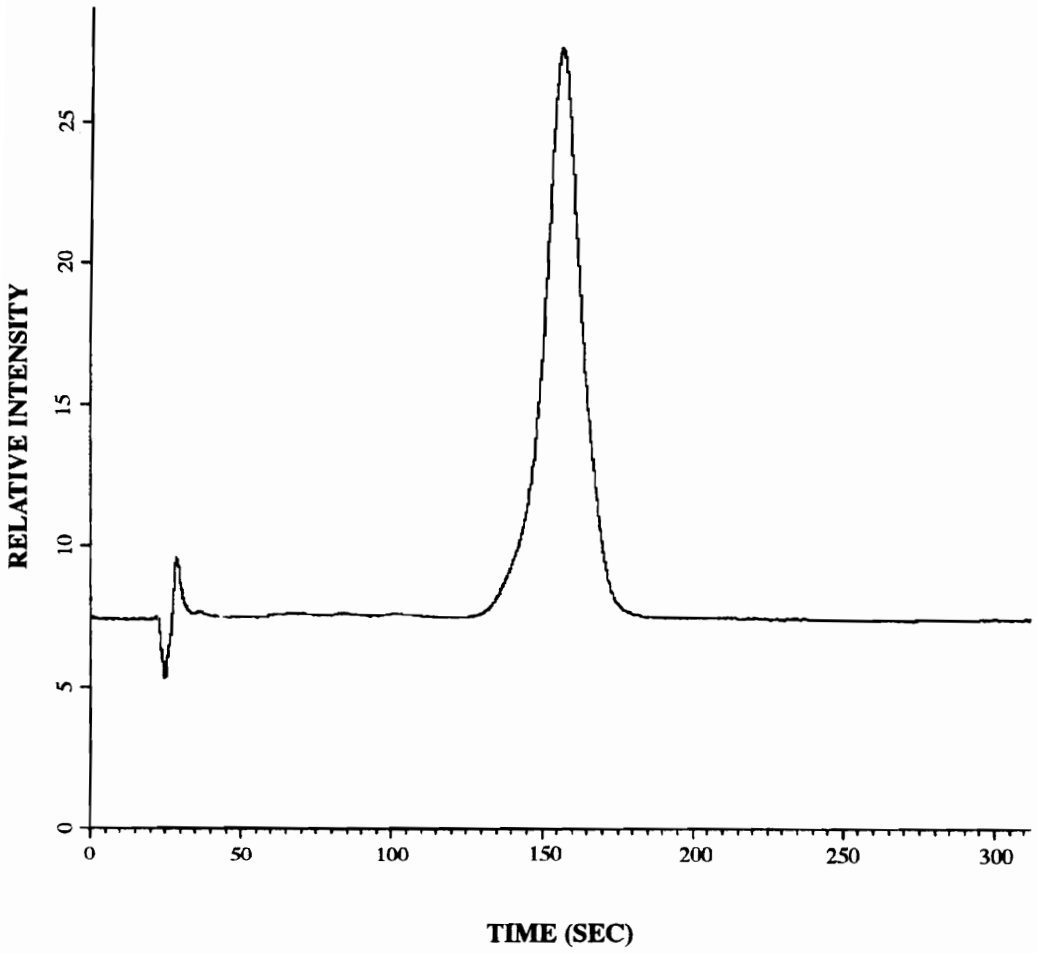


Figure 13. HPLC trace of **M44**.
(Novapak-C_{18}, THF/water=65/35 by vol, flow rate=2 mL/min, RI detector)

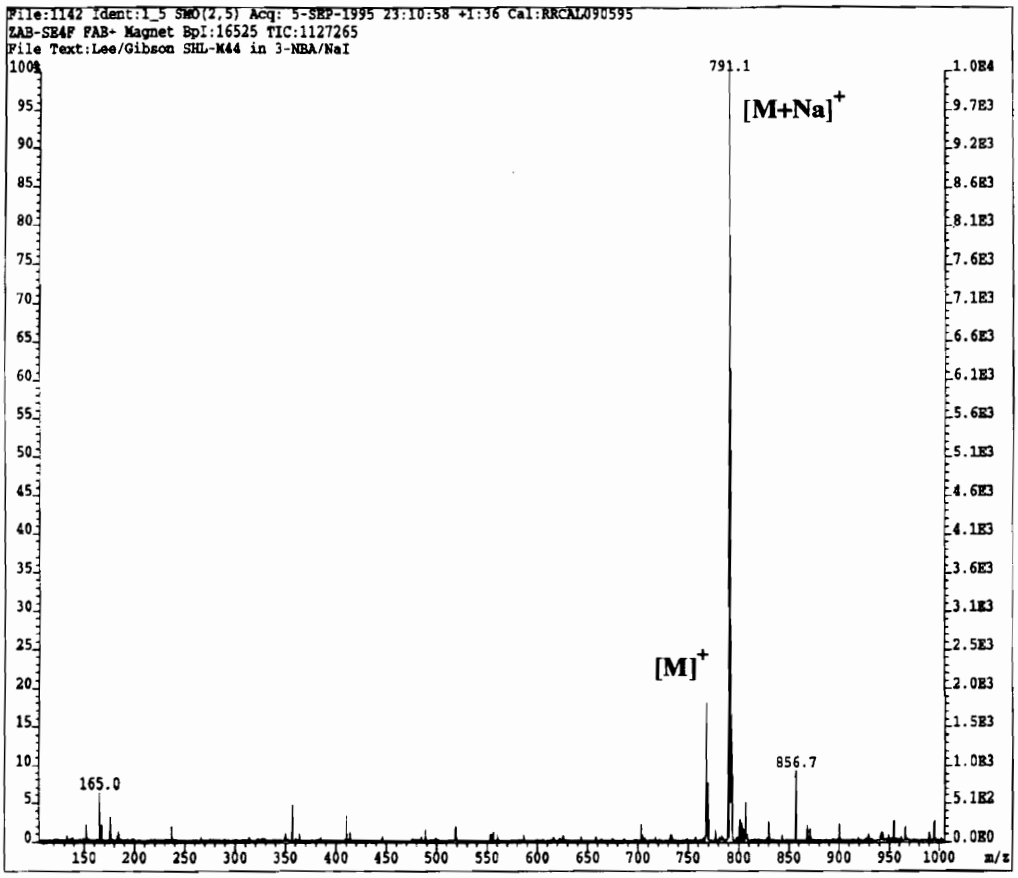


Figure 14. FAB mass spectrum of **M44**. (3-NBA/NaI)

CHAPTER VII

BLOCKING GROUP/INITIATOR

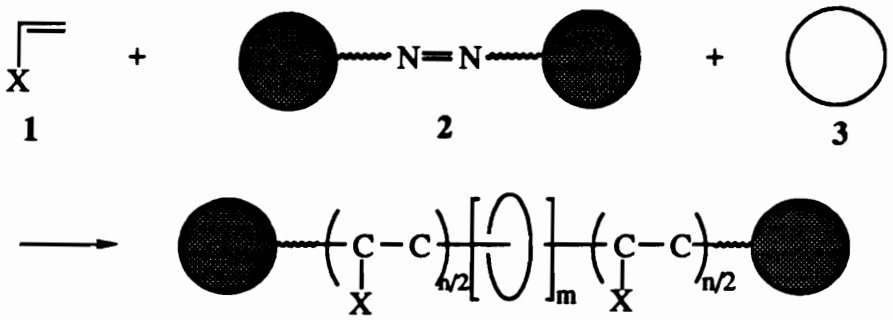
Polyrotaxanes consist of cyclic molecules threaded onto linear polymer molecules. [1] Such physically combined molecular composites have been known since 1967 [2], and recently they have been gaining more interest in view of many potential applications in material science. [1, 3-5] Polyrotaxanes are distinct from conventional polymer blends because the two components can not be separated from each other unless chemical bonds of either or both components are broken. Also, polyrotaxanes are different from traditional copolymers due to the ability for the cyclic components to move along the linear chain and circumferentially. Thus, the potential area of utilization extends from simple property changes such as modification and enhancement of solubility, thermal stability, and interfacial bonding to preparation of specialty materials such as molecular level sensors and field-response materials.

Many traditional polyrotaxanes contain synthetic backbones such as polyamides [1], polyurethanes [3], and polyesters [4], which are made from the step growth polymerizations. In those cases the syntheses of the polyrotaxanes are achieved by condensation polymerizations of the corresponding monomers in the presence of macrocycles. Bulky species or blocking groups which contain suitable functional groups are introduced at the linear chain ends during the polymerizations to prevent threaded macrocycles from dethreading. Recently, Gibson et al. reported the synthesis of various triarylmethyl derivatives suitable for end blocking for this purpose. [6]

However, if the linear species are the polymers from olefinic monomers, it would not be easy to put the blocking groups at the chain ends. For instance, when

poly(styrene-rotaxa-crown ether)s were synthesized by anionic polymerization of styrene in the presence of crown ethers by Gibson and coworkers, in order to obtain thermodynamically stable polyrotaxanes, the living polymer chains were reacted with a blocking group which contained an alkyl chloride moiety. [7] This process required lots of experimental effort such as purifications of the reagents, inert atmosphere, low reaction temperature and use of an excess amount of the blocking group to achieve complete blocking. Radical polymerizations, on the other hand, are easier to carry out than anionic polymerizations in terms of purifications of reagents and reaction conditions. In addition, many vinyl monomers such as halogenated olefins and vinyl esters do undergo free radical polymerizations while they do not polymerize anionically.

Therefore, a new azo-type radical initiator **2** was synthesized, which can afford end-blocked polyrotaxanes **4** *via* free radical polymerizations of vinyl monomers **1** in the presence of cyclic species **3**.



4 (X=Ph, CN, CO_2CH_3, etc)

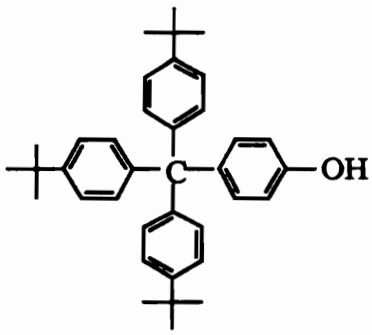
In this chapter, the synthesis and characterization of the blocking group/initiator (BG/init) are described. The results of the polymerization of styrene using the BG/init as a demonstration of the utility of the BG/init as a free radical initiator and blocking group

for the synthesis of polyrotaxanes are also discussed.

RESULTS AND DISCUSSION

1. Synthesis of Blocking Group/Initiator

The blocking group used in this work was a triarymethyl derivative, tetra(*p-tert*-butylphenyl)-4-hydroxyphenylmethane (**5**). [6]



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The introduction of the blocking group into the azo compound to synthesize BG/inits had been achieved by the acid chloride method. [8] (Scheme 1). *meso*-4,4'-Azobis-4-cyanopentanoic acid (*meso*-**6**) was initially converted to its acid chloride *meso*-**7**, which was reacted with a hydroxyl functionalized blocking group **8** [6] to give *meso*-4,4-di(*p-tert*-butylphenyl)-4-phenylbutyl 4,4'-azobis-4-cyanopentanoate (**9**).

Smith had reported the synthesis of 4,4'-azobis-4-cyanopentanoyl chloride (**7**) by treating 4,4'-azobis-4-cyanopentanoic acid (**6**) with phosphorous pentachloride. [9] However, he only reported the melting point, which was 93-95 °C. No yield or spectral

data were given. While numerous papers have reported the use of **7** or its derivatives to initiate radical polymerizations [10, 11], preparing this compound was not a trivial task according to Engen's report. [8] It was believed that this was due to the difference in reactivity between the diastereomers. In the patent of 1973 for preparing various azo compounds containing acyl functionalities, Sheppard and MacLeay reported that compound **6** could be separated into two isomers by repeated recrystallizations from ethanol and ethyl acetate. [12] The less soluble isomer, which Sheppard called the *trans* isomer, melted at 141-145 °C, and the more soluble *cis* isomer according to Sheppard melted at 125-127 °C. Also, this patent stated that before quantitative conversion of the acid **6** into the acid chloride **7** could be accomplished the two isomers had to be separated.

Following the claim [12] Engen had assigned the less soluble isomer, which melted at 141-145 °C, as the *trans* isomer, and the more soluble isomer whose melting point was 125-127 °C as the *cis* isomer. However, the structural assignment of the isomers was examined and it came to be believed that compound **6** was not a mixture of *cis* and *trans* isomers but a mixture of the racemic and *meso* compounds. The ^{1}H NMR spectrum (acetone-d_6) of **6** showed the α-CH_3 proton peaks at 1.73 and 1.79 ppm in about 1 : 1 ratio. (Figure 1) Two starred carbon atoms (*) in the structure of compound **6** are chiral; it may have the configuration of (R,R), (S,S) or *meso* diastereomers in both the *cis* and *trans* isomers.

Therefore, if compound **6** is a mixture of *trans* and *cis* isomers the α-CH_3 protons should give more than two peaks in the ^{1}H NMR spectrum, more complex peaks due to *trans-cis* isomerism as well as diastereoisomerism. The activation enthalpies for the interconversion of various azo compounds between *cis* and *trans* forms usually lie in the range of 18-40 kcal/mol or so which is not high enough to prevent the interconversion

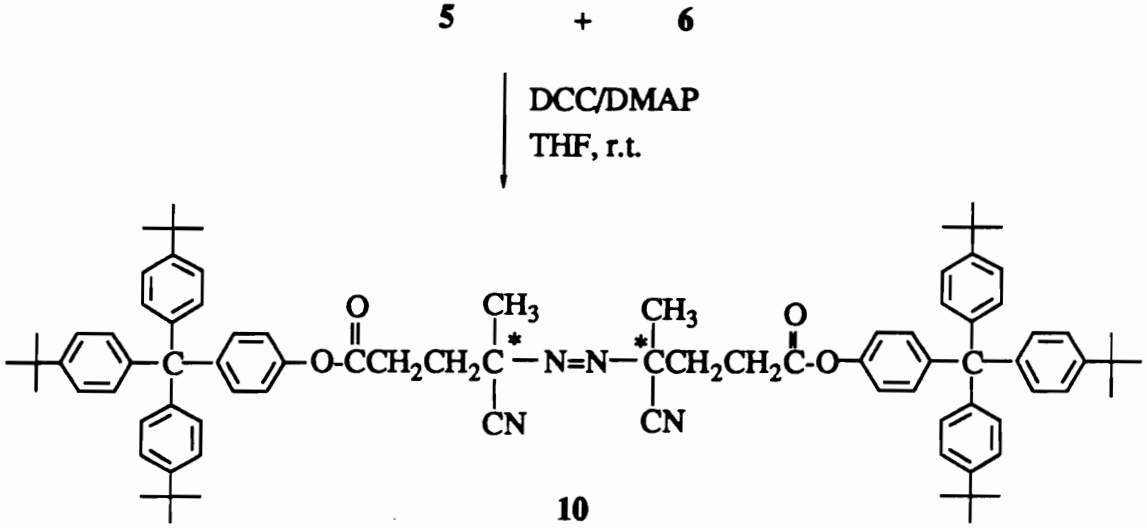
even at room temperature. [13] As a result *cis* isomers convert into the *trans* isomers even at room temperature and the azo compounds exist in the *trans* forms which are more stable than *cis* by usually 10-30 kcal/mol. [13] If the azo compound **6** is a mixture of diastereomers which are *trans* compounds, the number of the α-CH_3 proton peaks is supposed to be two, one of which comes from the *dl* compound and the other comes from the *meso* diastereomer, as observed in Figure 1. This seems true also because in the commercial syntheses of azo compounds the first step is the reaction of ketones and HCN (or H_2NNH_2), which gives the diastereomers in a ratio of about 1:1. [14]

Diastereomers have different properties such as melting point and solubility. [15] Especially, tartaric acid shows big differences in melting point and solubility. [16] *dl*-Tartaric acid has a higher melting point (206 °C) and lower solubility compared with *meso*-tartaric acid (mp=140 °C). Thus, we assigned the less soluble isomer with higher melting point (141-143 °C) as the *dl* isomer and the other (mp=125-127 °C) the *meso* isomer. In the ^1H NMR spectrum the peak at 1.79 ppm came from the *dl* isomer and the peak at 1.73 ppm is from the *meso* compound.

Using the more soluble isomer (*meso*-**6**), Engen achieved quantitative conversion of *meso*-**6** to its acid chloride (*meso*-**7**) by heating with excess thionyl chloride at 120 °C for 10 min. On the other hand, according to Engen's report [8], the *dl* isomer needed to be exposed to a larger excess of refluxing thionyl chloride for one hour at 100 °C and still there existed some of the unreacted acid.

For connecting the blocking group to the azo compound **6**, dicyclohexylcarbodiimide (DCC) coupling [17] proved to be a better way than the acid chloride method in terms of reaction simplicity. In the reaction, 4,4'-azobis-4-cyanopentanoic acid (**5**) reacted with tris(*p*-*tert*-butylphenyl)-4-hydroxyphenylmethane (**6**) at room temperature to give 4,4-[tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-

cyanopentanoate (**10**). A catalytic amount of 4-pyrrolidinopyridine or 4-dimethylaminopyridine was used to catalyze the reaction.



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The crude product was purified by column chromatography (silica gel, CH_2Cl_2) followed by recrystallization from a mixture of toluene and hexane (3/2, v/v) to give the desired product in 30 % yield. The column chromatography using CH_2Cl_2 eluent gave no separation of stereoisomers from each other. However, when a mixture of hexane and ethyl acetate (8.5/1.5, v/v) was used as developing solvent TLC analysis (silica gel) showed the product as two spots which were close to each other. (Figure 2)

In the 2-dimensional TLC experiment, the crude product was developed along the horizontal direction with CH_2Cl_2 as developing solvent first; then the resulting four spots were developed along the vertical direction with a mixture of hexane and ethyl acetate. In Figure 2, it is shown that BG/init **10** was a mixture of two different compounds.

The ^1H NMR spectrum in $CDCl_3$ (Figure 3) also demonstrated that the product 4-

[tris(*p-tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (**10**) was a mixture of the diastereomers; in Figure 3 the *tert*-butyl and α-CH_3 each show two peaks. According to the peak integrations the ratio of the two isomers was *dl/meso* = 0.78. This ratio also indicated that the reactivity of the *meso* isomer was higher than that of the *dl* isomer. Also, in the ^{13}C NMR spectrum of **10** in $CDCl_3$ 26 lines were found; only 17 would appear if there were no stereoisomerism. The BG/init **10** melted broadly between 206-217 °C as expected for the mixture of the diastereomers.

Because the BG/init **10** was a mixture of diastereomers, instead of isolation of them from each other, the relative thermal decomposition rates of the isomers were investigated in toluene at 85 °C. At the ends of 2 and 6 hr heating periods small aliquots were taken and analyzed by ^1H NMR spectroscopy. As shown in Figure 4, the rates of disappearance of peaks at 1.73 ppm (*meso*) and 1.79 ppm (*dl*) were not so different. However, the peak at 1.73 ppm (*meso*) was found to reduce slightly faster than the peak at 1.79 ppm (*dl*). This might be due to the difference in strain energy. A computer molecular simulation (Cerius ^{2}) [18] indicated that the total energy of the *meso* isomer was larger than that of *d* or *l* isomer by 3 kcal/mol, 258.74 kcal/mol *vs* 255.70 kcal/mol. Although the difference is small, the result demonstrated that the *meso* isomer would decompose faster than *dl* isomers. It is to be noted that the mechanism of thermal decomposition of symmetric azo compounds is known to be simultaneous one-step rather than two-step bond breaking. [13] Therefore, the difference in thermal decomposition rates of *dl* and *meso* **10** was not due to the racemization due to interconversion within the solvent cage. The thermal decomposition rates of *dl* and *meso* stereoisomers of a few azo compounds have been reported to be approximately the same. [13]

2. Characterization of BG/init: Polymerization of Styrene

In order to investigate the initiation of free radical polymerizations and blocking abilities of the two synthesized BG/inits, polymerizations of styrene were carried out using the BG/init **10**.

Table 1 and Figure 5 show the results of the polymerization of styrene using BG/init **10**. The polymerizations were carried out in closed flasks and in order to remove the unreacted initiator, the reaction mixtures were precipitated into excess ethanol three times.

Table 1 shows that as the amount of initiator increased the molecular weight of the polymer obtained decreased, as expected. The plot of M_n (number-average molecular weight) *vs* [M]/[initiator]$^{1/2}$ (concentration of monomer/square root of initiator concentration) (Figure 5) shows a linear relationship. For polymerization initiated by thermal homolysis of an initiator under the steady state assumption, ν (kinetic chain length), which represents the molecular weight of the resulting polymer, can be defined by the following equation.

$$\nu = \frac{k_p[M]}{2(fk_d k_t[I])^{1/2}}$$

where, [M]=concentration of monomer; [I]=concentration of initiator; k_p=rate constant for propagation; k_d=rate constant for initiator dissociation; k_t=rate constant for termination; f=initiation efficiency of initiator

Thus, the linear relationship indicates that the BG/init **10** is a well-behaved free radical

Table 1. Polymerization[a] of styrene with BG/init and AIBN.[b]

Sample	Initiator (mmol x 10^2)	Initiator (mmol)	Styrene (mmol)	Isolated yield (%)	M_n[c] (kg/mol)
1	**10**	2.5	4.9	64	18.5
2	**10**	5.0	5.0	59	15.2
3	**10**	10.0	4.9	68	9.5
4	**10**	5.0	4.9	64	13.4[d]
5	**AIBN**	3.5	4.8	95	17.2
6	**AIBN**	6.1	4.8	90	10.6
7	**AIBN**	12.0	4.8	85	6.2
8	**AIBN**	23.6	4.8	83	2.2

a. Polymerizations were done in toluene (4 mL) at 85 °C for 3 days for Samples 1-4, and in toluene (1 mL) at 100 °C for 20 hr for Samples 5-8 [8].
b. Recrystallized from ethanol before use.
c. Measured by GPC ($CHCl_3$ for Samples 1-4, THF for Samples 5-8 [8], PS standards).
d. Polymerization was done in a mixture of toluene/dimethoxyethane (2 mL/ 2 mL).

initiator. As compared to the polymerization results using AIBN [8] it is noted that the slopes of the lines are similar to each other.

The decomposition rates of azo compounds are known to primarily depend on the functional groups on the α-carbon from the azo unit. [19] The structural strain plays a role in decomposition rates too. [19-21] The carbonyl group is not likely to affect the

decomposition rates. It was reported that 4,4'-azobis-4-cyanopentanoic acid (**6**) showed a decomposition rate similar to AIBN. [22] It is, however, believed that the decomposition rate of the BG/init **10** is greater to some extent than AIBN due to the bulky groups.

Another consideration is initiation efficiency *f*. The initiation efficiency is known to depend on the viscosity of solvent and polymerization medium. The initiation efficiency decreases with viscosity because as viscosity increases the diffusion rate of the primary radicals from the solvent cage decreases. [22, 23] Therefore, the initiation efficiency of the BG/init **10** is believed to be smaller than that of AIBN because of the attached bulky blocking groups. Due to the bulkiness, the rate of diffusion of the primary radicals of the BG/init **10** from the solvent cage would be slower compared to AIBN. Therefore, it is likely that the two factors bearing on the decomposition rate, which are strain and solvent cage effects, compensated each other and resulted in the decomposition rates of the BG/init **10** similar to AIBN. The lower polymerization yields of the BG/init seem to be related to the lower initiator efficiency of the BG/init.

It is to be noted that the intercept of the line for AIBN is negative, but within experimental error this is not the case for that of the BG/init in Figure 5. This suggested that the chain transfer constants to the initiators are different. As compared to AIBN, the BG/init is believed to have smaller chain transfer constant because of steric hindrance due to the bulky blocking groups.

Along with the initiation ability, the blocking efficiency of the BG/inits is an important factor for the synthesis of polyrotaxanes. Polystyrene is known to terminate almost exclusively *via* radical coupling rather than disproportionation. [22, 24] In the synthesis of polyrotaxanes termination by coupling affords completely end blocked polyrotaxanes.

The blocking efficiencies of the BG/inits in the polymerization of styrene could be determined by comparison of the end-group analyses from the ^{1}H NMR spectra (Figure 6) and the molecular weights from the GPC of the resultant polymers. Althought the end group analysis based on the peak integrations of *tert*-butyl and aromatic protons was not easy due to peak overlap, the blocking efficiencies were found to be 100 % within an error range of ± 10 %.

CONCLUSIONS

A new BG/init, which contained an azo unit and bulky tetraarylmethyl groups at both ends, was synthesized. Thus, 4-tris(*p-tert*-butylphenyl)methylphenyl 4,4'-azobis-4-cyanopentanoate (**10**) was synthesized by the reaction of 4,4'-azobis-4-cyanopentanoic acid (**6**) with tris(*p-tert*-butylphenyl)-4-hydroxyphenylmethane (**5**) using DCC coupling.

The BG/init was found to be a mixture of diastereoisomers whose molar ratio was determined to be *dl/meso* = 0.78 by ^{1}H NMR. As compared to the ratio 1:1 (*dl/meso*) in the starting material **6** the ratio (0.78) is believed to be due to the difference in the molecular strain energies of the diastereomers. The relative thermal decomposition rates of the stereoisomers were determined using NMR analysis, and it was found that the *dl* isomer decomposed faster than the *meso* isomer. This is probably due to the difference in the molecular strain energies as demonstrated by a computer molecular modeling study.

The results of the polymerization of styrene using the BG/init demonstrated that the BG/init were a good free radical initiator, affording end-blocked polystyrenes. Thus, the two BG/init **10** can be used for the synthesis of polyrotaxanes whose linear species are made from free radical polymerizations of olefinic monomers.

EXPERIMENTAL

Measurements. Melting points were taken in capillary tubes with a Melt-Temp II melting-point apparatus. NMR spectra were obtained on a Varian Unity 400 MHz spectrometer at ambient temperature using tetramethylsilane as an internal standard. GPC analyses of the polymers were performed at 20 °C in $CHCl_3$ or THF using a Waters system with a refractive index detector after calibration with PS standards. Elemental analysis was done by Atlantic Microlab of Norcross, GA. Computer molecular energy calculations were done using Cerius ^{2}. [18]

***dl*- and *meso*-*p*-[Tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (10).** In a 100-mL 1-neck flask equipped with a condenser, a magnetic stirring bar, and a N_2 bubbler, 4,4'-azobis-4-cyanopentanoic acid (**6**) (1.00 g, 3.57 mmol), tris(*p*-*tert*-butylphenyl)-4-hydroxyphenylmethane (**5**) (5.40 g, 10.7 mmol), N,N'-dicyclohexylcarbodiimide (2.90 g, 14.1 mmol), dimethylaminopyridine (catalytic amount), and dry THF (50 mL) were stirred at room temperature for 6 hr. The mixture was filtered and the solvent was evaporated under reduced pressure. The desired product was isolated by column chromatography (silica gel, CH_2Cl_2 eluent). The white solid was recrystallized from a mixture of toluene and hexane (3:2 by vol). The yield was 1.30 g (29 %, *dl*/*meso* = 0.78).

Mp: 206-217 °C. ^{1}H NMR ($CDCl_3$): 1.29 (s, 30.3H), 1.23 (s, 23.7H), 1.73 (s, 3.4H), 1.79 (s, 2.6H), 2.45-2.85 (m, 8H), 6.96 (d, J=9.2 Hz, 4H), 7.07 (dd, J=8.4 Hz, J=2 Hz, 8H), 7.18-7.26 (m, 20H). ^{13}C NMR ($CDCl_3$, ppm): 23.83, 24.11, 29.28, 29.34, 31.37, 33.04, 33.11, 43.30, 63.36, 71.82, 71.93, 117.43, 117.53, 119.83, 124.16, 130.70, 132.26, 143.64, 145.18, 145.21, 148.20, 148.22, 148.48, 148.51, 169.81, 169.88. (theory 26 for 2

diastereomers, found 26) Anal. Calcd: C, 82.39; H, 8.04; found: C, 82.00; H, 8.11.

Decomposition Study of *dl*- and *meso*-4-[tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (10). 4-[Tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (**10**) (7.6 mg) was added to toluene (5 mL, degassed with N_2 bubbling before use) in a 25-mL flask equipped with a magnetic stirring bar and a N_2 bubbler. The flask was placed in an oil bath preheated to 85 °C. Small aliquots were taken out after 2 hr and 6 hr. The samples were dried under vacuo at room temperature before ^1H NMR analysis.

Polymerization of styrene using *dl*- and *meso*-*p*-[tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (10). Styrene was washed with dilute aqueous NaOH (5 %) to remove the inhibitor (*tert*-butylcatechol) followed by water, dried over anhydrous $MgSO_4$, and vacuum distilled at room temperature with a receiver flask in a dry ice bath. Styrene (0.50 g, 4.8 mmol), *dl*-and *meso*-*p*-[tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoate (**10**) (*dl*/*meso* = 0.78) (0.060 g, 4.8 x 10^{-2} mmol) and toluene (4.0 g) were placed in a 50-mL round-bottomed flask fitted with a joint and Teflon valve. A small magnetic stirring bar was put into the reaction mixture. The reaction mixture was subjected to three cycles of freeze-pump-thaw processes on a vacuum line to remove oxygen from the reaction mixture. The flask was placed in an oil bath preheated to 85 °C. After 3 days reaction, the reaction mixture was poured into vigorously stirred ethanol (250 mL). The white precipitate was filtered and dried, then dissolved in CH_2Cl_2 (10 mL) and poured into ethanol (250 mL) again. The precipitate was filtered, and such precipitation was done once more. The final product was dried under vacuo at room temperature.

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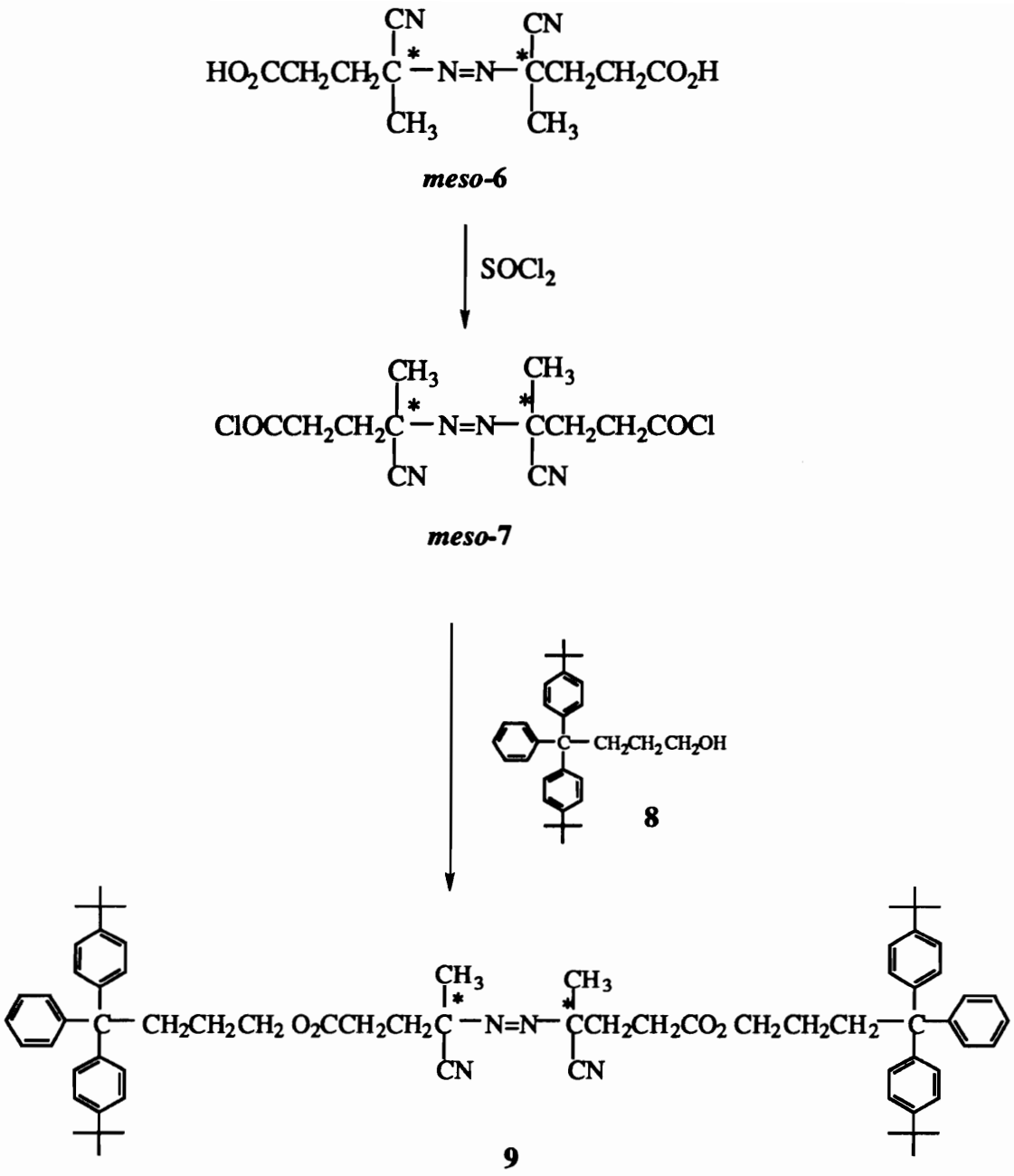


Scheme 1. Synthesis of BG/init **9** by acid chloride method.

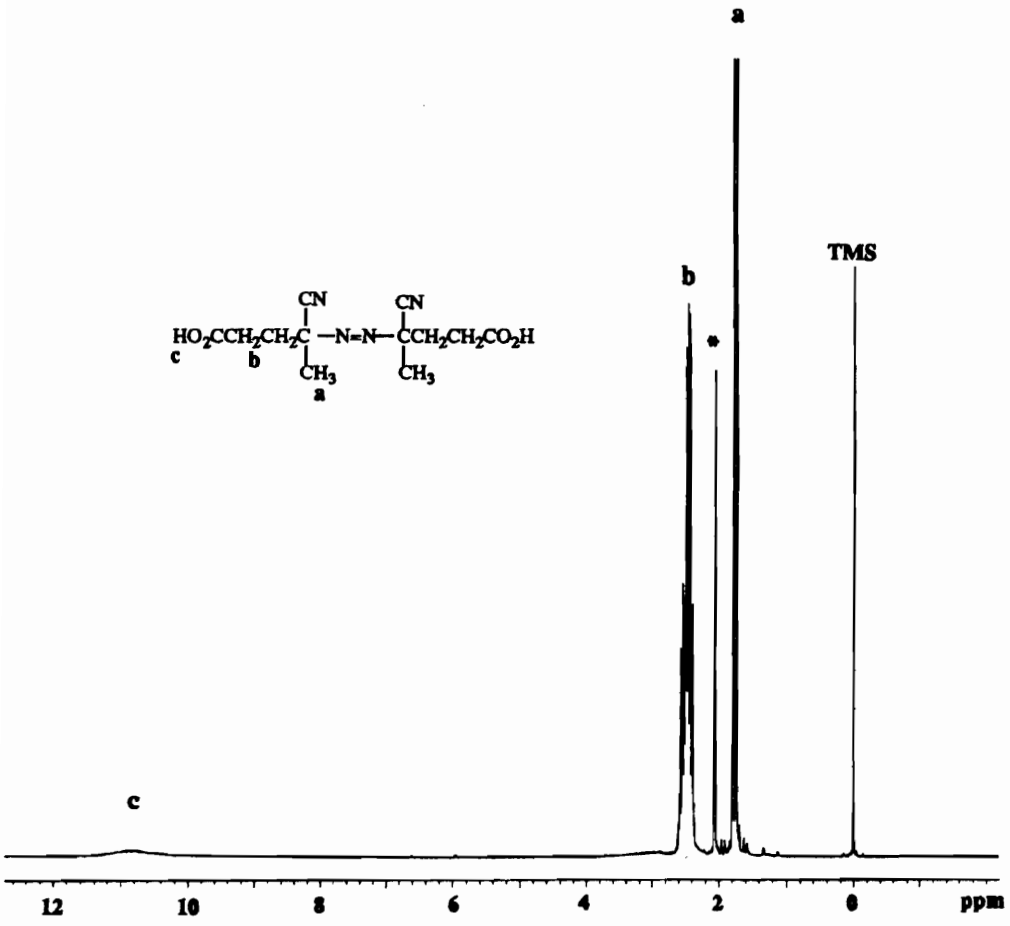


Figure 1. ^{1}H NMR spectrum of 4,4'-azobis-4-cyanopentanoic acid (**6**). (acetone-d_6) * acetone

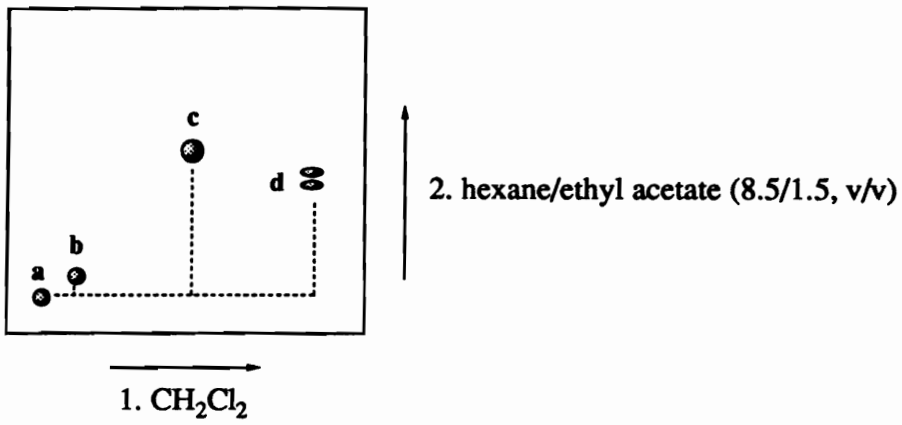


Figure 2. 2-Dimensional TLC of the crude product of BG/init **10**.
a spotting point, **b** monosubstituted product,
c unreacted blocking group **5**, **d** BG/init **10**

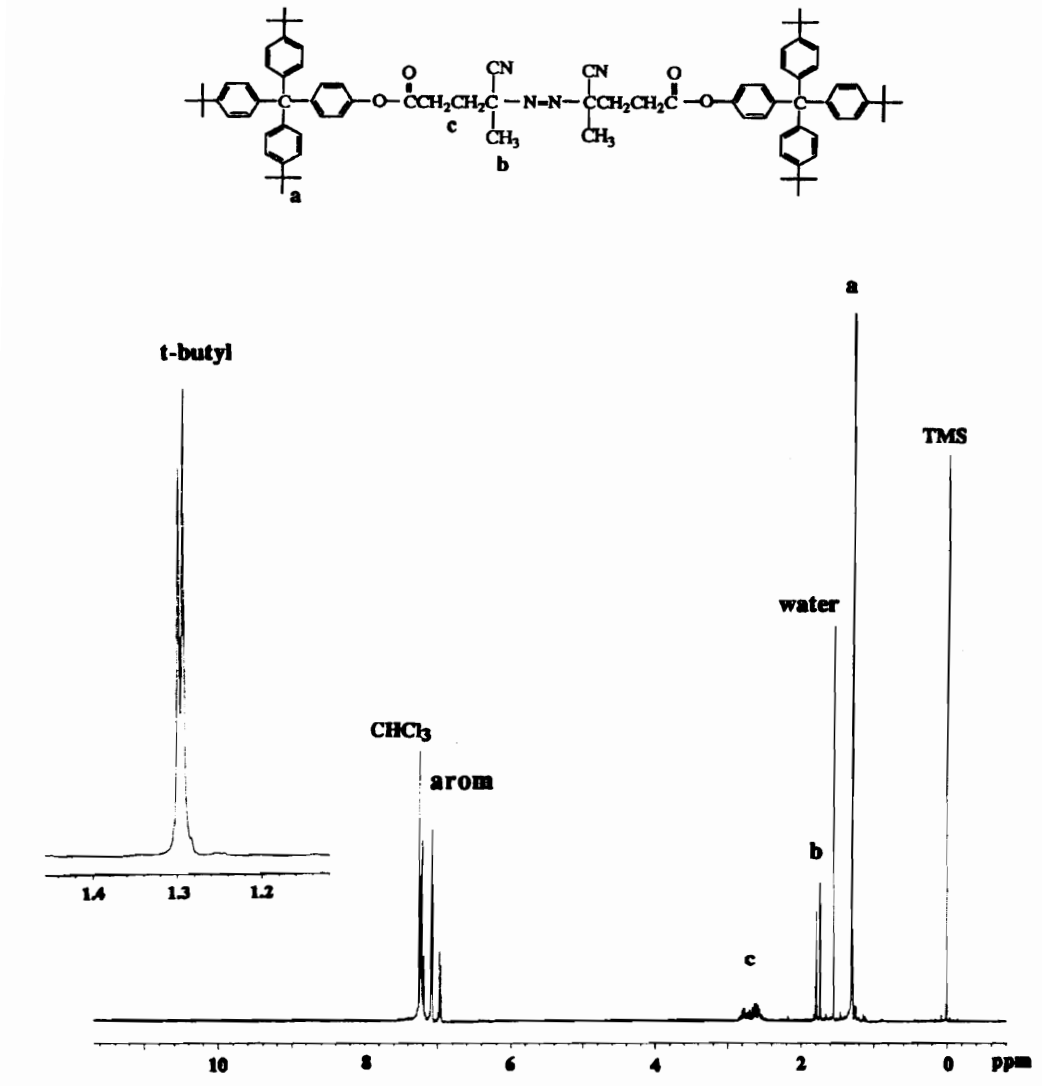


Figure 3. ^{1}H NMR spectrum of *dl*- and *meso*-4-[tris(*p*-*tert*-butylphenyl)methyl]phenyl 4,4'-azobis-4-cyanopentanoates (**10**). ($CDCl_3$)

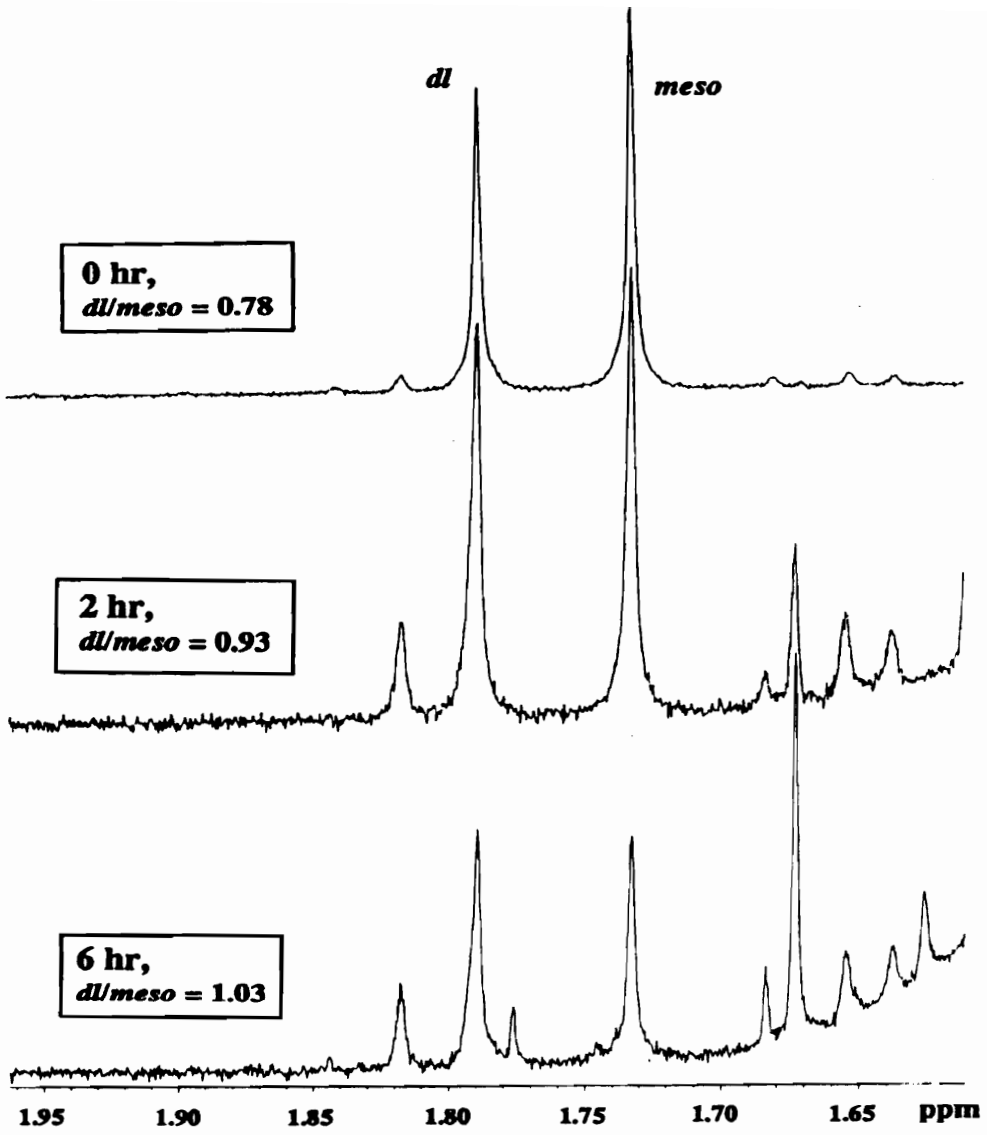


Figure 4. Relative decomposition rates of *dl*- and *meso*-4-[tris(*p*-*tert*-butylphenyl)methyl]-phenyl 4,4'-azobis-4-cyanopentanoates (**10**) in toluene at 85 °C. ($CDCl_3$)

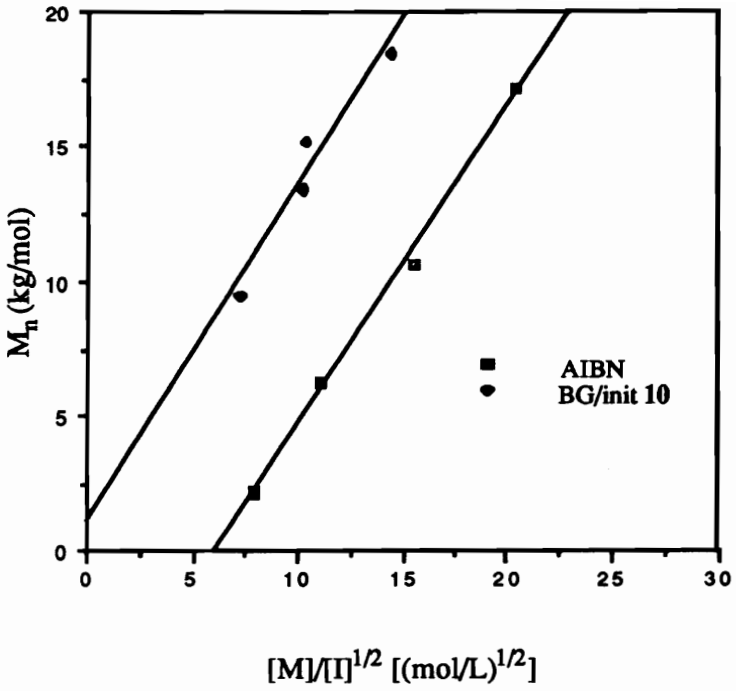


Figure 5. M_n of polystyrene *vs* $[M]/[I]^{1/2}$ using BG/init **10** and AIBN.

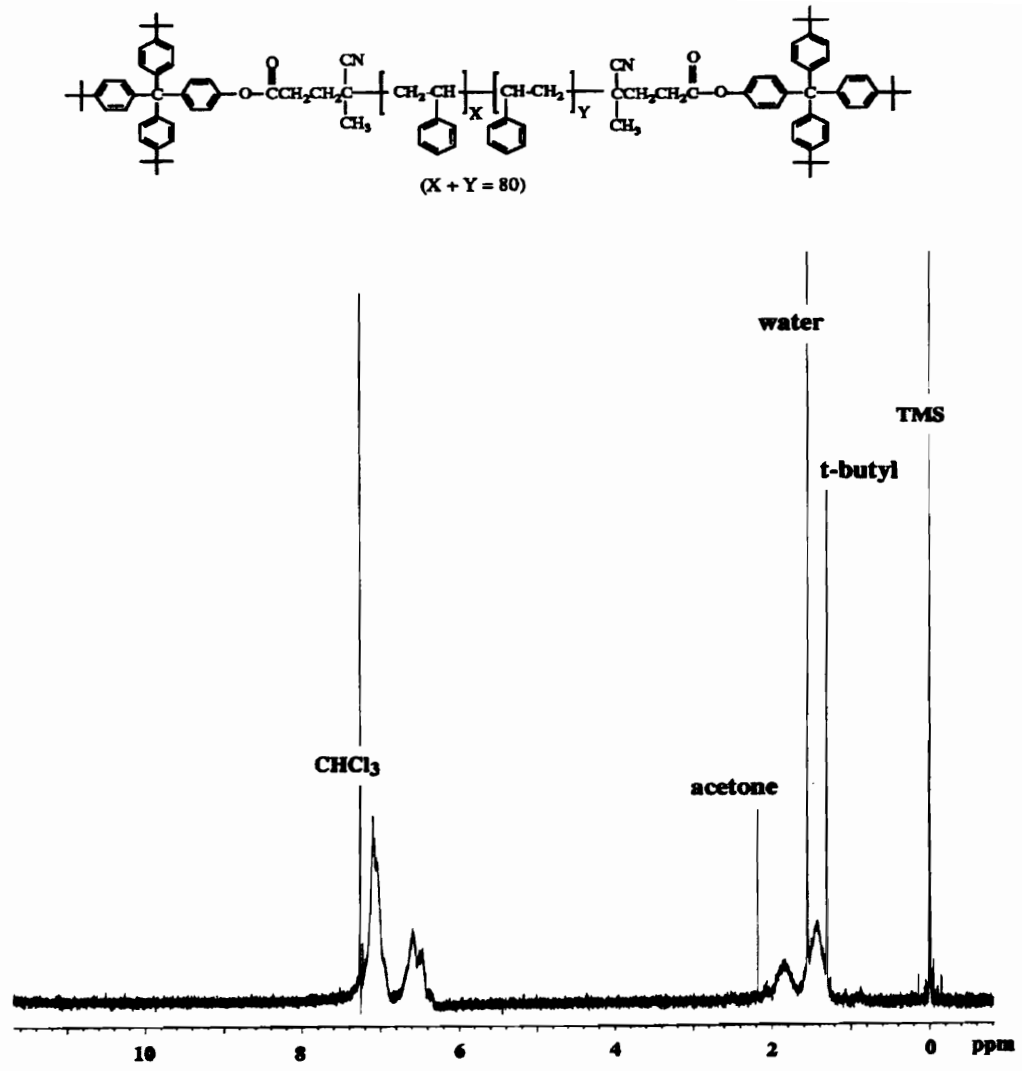


Figure 6. ^{1}H NMR spectrum of polystyrene initiated by BG/init **10**. (Sample 3) ($CDCl_3$)

CHAPTER VIII

POLYROTAXANES VIA FREE RADICAL POLYMERIZATIONS

Polyrotaxanes are molecular composites in which cyclic species are threaded by linear polymers with no covalent bonds between the two components. [1-4] Polyrotaxanes can be classified as a kind of copolymer. However, polyrotaxanes are distinct from conventional copolymers and polymer blends because of the "threaded structure" and the absence of covalent bonds between the two components. [1,2,5,6] The threaded structure prevents macroscopic phase separations permanently, but at the same time the lack of covalent bonds allows cyclic components to move along the backbone and circumferentially so that the cyclic species may get together to form microscopic domains.

Polyrotaxanes have been synthesized by direct mixing of polymers and cyclic molecules or polymerization of monomers in the presence of cyclic species. The former includes Harada's works in which poly(ethylene oxide)s [7-9], poly(propylene oxide)s [9, 10] or polybutylene [11a] were mixed with cyclodextrins (CDs) in aqueous phases to give highly threaded polyrotaxanes. The driving forces for the formation of such polyrotaxanes are mainly hydrophobic-hydrophilic interactions between the two components. [12] The more versatile methodology of polyrotaxane synthesis is polymerization of monomers in the presence of macrocycles. [2, 5, 6, 13-19] By this method, it is possible to prepare polyrotaxanes with various types of backbones and macrocycles. Gibson and coworkers have demonstrated the success of this methodology in preparation of polyrotaxanes using crown ethers as cyclic species. [2, 6, 18]

1. POLYROTAXANES PREPARED BY FREE RADICAL POLYMERIZATIONS: REVIEW

Many polyrotaxanes and rotaxanes have been prepared by condensation polymerizations [2, 6, 13, 14, 18, 19] and direct mixing methods [7-11, 20]; however, only a few polyrotaxanes have been made by free radical polymerizations in the presence of macrocycles. In 1979 Maciejewski and coworkers reported a series of results on the polymerization of vinylidene chloride in the presence of β-cyclodextrin (β-CD). [15] According to his report, the radiation polymerization of the crystalline monomeric adduct of vinylidene chloride (VDC) and β-CD gave stable polymeric products (molecular weight ca. 20 kg/mol). The products were found to contain 80 wt % β-CD linked to the VDC polymer chain (20 wt %). [15a] Considering the high stability of the product he performed the polymerizations of adducts of β-CD with other monomers [styrene and methyl methacrylate (MMA)] and analyzed the products in order to address the possibility of other side reactions such as grafting or chain transfer. He found that the products from radiation polymerizations of those adducts were unstable; the products were dissociated when purified with hot water. By this observation he suggested that the product from the polymerization of adduct of VDC and β-CD did not contain β-CD linked to the linear backbone through covalent bonds. Thus, the high threading yield was explained to be due to the stable threaded structure in the adduct of VDC and β-CD. In contrast, the absence of β-CD in the products from the polymerizations of styrene or MMA could be expained by the complexation between β-CD and the pendant units of the monomers (styrene or MMA). Thus, β-CD could easily dethread during the purification step. The lack of chemical bonding *via* chain transfer was further confirmed by the radiation copolymerization of an adduct of β-CD, VDC and allyl chloride (the monomer ratio was not given). In the

copolymerization allyl chloride competed with β-CD for the chain transfer. If the high content of β-CD was due to the chain transfer, β-CD content in the copolymerization product would be lower than 80 %. However, it was found that the final copolymerization product contained 87 % β-CD. In contrast, the copolymerizations of adducts of VDC, MMA and β-CD with various compositions gave lower contents of β-CD in the products. This result was consistent with the lack of β-CD in the product of homopolymerization of the adduct of β-CD and MMA.

Maciejewski and coworkers also carried out free radical polymerizations of various monomers such as VDC, styrene, methacrylonitrile and methyl acrylate (MA) in the presence of β-CD in concentrated dimethylformamide (DMF) solution (20 wt %) using AIBN as a initiator. [15b] The resulting polymers were purified by precipiattion into excess water, followed by boiling. Similar to the radiation polymerization results, only when VDC was used as a monomer 35-72 wt % β-CD containing polymer products were obtained depending on the reaction temperature. The products containing β-CD were soluble in DMF while poly(vinylidene chloride) (PVDC) itself was not.

In the next step, Maciejewski conducted dehydrochlorination of the PVDC containing β-CD by treatment with NaOH in boiling alcohol. [15c] The resulting polymer was purified by washing with an excess of alcohol and and fluorobenzene to give a polyrotaxane with an unsaturated backbone. Interestingly, the polyrotaxane with unsaturation was more stable than the precursor which showed dissociation of the macrocycles upon heating in hot DMF. This was due to the enhancement of the hydrophobic interaction between the β-CD cavity and the resultant unsaturated polymer chain.

Schneider and coworker also reported the synthesis of polyrotaxanes containing β-CD. [16] They studied inclusion polymerization of vinyl monomers such as 2,3-

dichlorobutadiene and 2,3-dimethyl-1,3-butadiene in canals of thiourea, perhydrotriphenylene, deoxycholic acid and β-CD. The resulting copolymers could be isolated from the matrix molecules. However, using β-CD as host, the isolation of the resulting polymers was problematic; in other words, the separation of the matrix was very incomplete. This was due to the formation of stable polyrotaxanes they surmised.

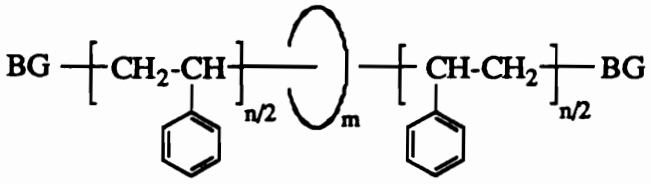
Lipatova et al. synthesized polystyrene (PS) rotaxanes containing cyclic polyurethane (CU) (34 membered). [1, 17] The synthesis was done by thermal polymerization of styrene at room temperature over 3-5 months in the presence of the macrocycle species. The cyclic species used in those syntheses was either neat CU or CU-$ZnCl_2$ complex. Interestingly, they reported that the polyrotaxane made with CU contained 20 % cyclic (by volume) while the polyrotaxane made with CU-$ZnCl_2$ complex had 40 % (by volume) of the macrocycle. Later, they also used 40 membered CU in a similar experiment and obtained 25 % and 35 % threading yields of cyclic urethane (40 membered) using CU and $ZnCl_2$-CU complexes, respectively. [5] They suggested that the higher threading yield of the latter was due to the more ordered "swarm" complexes of CU-$ZnCl_2$. Solubility changes were noted: the polyrotaxanes were insoluble in benzene or DMSO, both of which were good solvents for PS and CU.

The cyclic urethanes were crystalline and the polyrotaxanes produced an X-ray diffraction pattern which was identical to the cyclic species. [1, 5, 17] This means that the cyclic were not homogeneously distributed along the PS chain; instead, they aggregated and existed in ordered form. Similar observations have been reported by Harada et al. in the CD-containing polyrotaxanes systems in which the cyclic components were crystalline and the X-ray diffraction patterns were identical to those for low molar mass inclusion complexes.

2. POLY(STYRENE-ROTAXA-CROWN ETHER)S

2-1. Poly(styrene-rotaxa-crown ether)s: Previous work

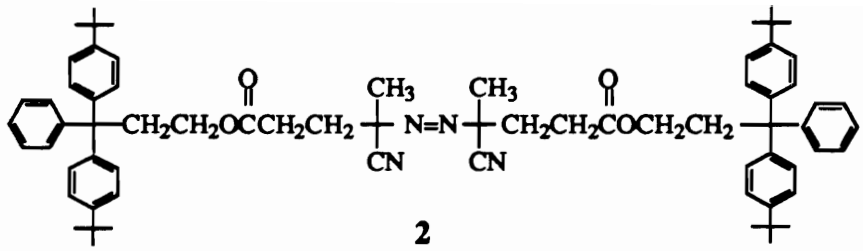
Poly(styrene-rotaxa-crown ether) (**1**), which is comprised of crown ether threaded by linear polystyrene, has been synthesised by Gibson et al. *via* free radical [21] and anionic [22, 23] polymerizations of styrene in the presence of 30c10 [24, 25], "60c20" [25] and BPP34c10. [The quotation mark (" ") on the 60c20 indicated the crown ether is not a single-sized, but rather a mixture of crown ethers with different sizes. See ref. (25)] The polyrotaxane **1** is an extreme case among polyrotaxanes prepared in Gibson's group in terms of the combination of the two components with opposite properties. PS is a hydrophobic and amorphous material while crown ethers [26] are hydrophilic and mostly crystalline.



1

BG = blocking group  = crown ether

Engen prepared **1** by free radical polymerization of styrene in the presence of 30c10, "60c20" or BPP34c10 using a blocking group/initiator (BG/init) **2**. [21]



2

The efficiency of BG/init **2** was tested in toluene for the polymerization of styrene and the results were compared with the result from AIBN. The GPC analysis of resultant polymers indicated that **2** afforded polystyrenes of controlled molecular weight comparable to AIBN. Using **2** he conducted synthesis of **1**. The polymerization was carried out at 100 ℃ for 20 hr. For the isolation of the polyrotaxanes the crude products were reprecipitated into a large amount of methanol until constant amounts of crown ethers in the precipitates were obtained. Table 1 shows the result of the synthesis of poly(styrene-rotaxa-crown ether)s.

In Table 1, first of all, low threading yields are indicated. Rings per chain are 0.26-0.67. From the Samples 1-3 it was found that use of a cosolvent was neccesary in order to obtain threading. Without toluene, which is a solvent for PS and crown ethers, practically no threading occured. Even though styrene and crown ether are miscible with each other, once the polymerization begins and the PS chain length reaches a critical point, the PS chain precipitates and the threaded rings may be dethreaded from the oligomeric PS chain resulting in no threading yield. Toluene is able to prevent the precipitation of the growing PS chain to prevent the dethreading process and because the chain could grow long enough to retain threaded rings owing to the chain entanglement, the final polymer had some permanently threaded rings. Also, the results of Samples 2 and 3 indicated that the amount of cosolvent has to be as small as possible. It is to be stressed that the result of Sample 1

Table 1. Synthesis of poly(styrene-rotaxa-crown ether)s **1** using **2**.[a]

Sample	styrene (g)	crown ether (g)	toluene (mL)	M_n[b] (kg/mol)	yield (%, polymer)	yield[c] (n/m, thread.)
1	0.45	BPP34c10 (1.0)	-	16.4	68	∞[d]
2	0.45	BPP34c10 (0.5)	0.5	9.6	54	153/1
3	0.45	BPP34c10 (0.5)	1.0	12.2	54	178/1
4	0.45	30c10 (0.5)	0.5	3.4	24	165/1
5	0.45	"60c20"+30c10 (0.5+0.5)	-	14.9	39	403/1[e]

[a] BG/init **2**: 1 mol % to styrene, polymerization: 100 °C for 20 hr.

[b] determined by GPC (THF, PS standards, RI and UV detectors).

[c] determined by ^{1}H NMR, n/m = number of crown ether/number of repeating unit.

[d] no threading.

[e] free crown ethers were found in the GPC trace.

suggested that virtually no chain transfer to BPP34c14 took place, because if there had been chain transfer during the polymerization the final product should have contained some crown ethers or crown ether derivatives permanently bonded to the polymer backbone. An interesting observation is that Sample 5 afforded threading yield while Sample 1 did not. This is probably due to the fast rotation of the benzene rings in BPP34c10 molecules which reduces the available cavity size of the crown ether so that the threading process could not take place.

It is to be noted that fractionation might occur during the reprecipitations because the threaded macrocycles may function as a surfactant. Engen reported that he used centrifugation for some cases to separate the polyrotaxanes because during the

reprecipitations he encountered an "emulsification" phenomenon. Although he did not mention it, it is likely that even centrifugation could not isolate all polyrotaxanes from the emulsions. The PS containing threaded crown ethers more than a critical amount would not precipitate from polar solvents such as MeOH and water; instead, a portion might be lost during filtration or centrifugation. Bheda, who prepared poly(styrene-rotaxa-crown ether)s *via* anionic polymerization, also reported the difficulty of purification of the product due to the emulsification. [22] In another series of experiments Engen used AIBN instead of **2** to synthesize poly(styrene-rotaxa-crown ether)s. With the amounts of the monomer, cosolvents and crown ethers varied, the results showed interestingly no trend in the threading yield. The threading yields were 10-12 wt % whatever ratio of ring to monomer and whichever crown ether and cosolvent were used. The result cannot be interpreted clearly so far. Engen explained that the result was due to the fractionation during the reprecipitations.

Taking advantage of the template effect Bheda tried to synthesize poly(styrene-rotaxa-crown ether)s with 30C10 and "60c20" by anionic polymerization. (Scheme 1) [22, 23] Table 2 shows the results. The polymerizations were done in THF or a mixture of THF and benzene (55/45, v/v) at 10 °C-room temperature for 1.5-4 hr and the initiator system was sodium naphthalide (**3**). After the polymerization was complete, both ends of the living chains were blocked by reaction with the blocking group (**4**) (1.5 equivalent) to afford polyrotaxane **5**. Like Engen, Bheda also isolated polyrotaxanes by repeated reprecipitations into methanol. He indicated that emulsification was encountered during the reprecipitations and thus the purification was very difficult. No polymer yields were reported; however, although the polymerizations were carried out under more dilute conditions than the free radical polymerization by Engen, the threading yields of the isolated polyrotaxanes were much higher than Engen's results. The result implies that there

was a template effect [27] in the anionic polymerization. The local concentration of the crown ethers at the growing chain ends was likely to be higher than the free radical polymerization case due to the ion-ion interaction between the cabanion end group and sodium cation which carried crown ethers by ion-dipole interaction.

Table 2. Syntheses of polystyrene rotaxanes **1** *via* anionic polymerization.[a]

Sample	styrene (g)	crown ether (g)	(mL)	solvent[b] (kg/mol)	M_n[c]	threading yield[d] [mass % (n/m)]
6	2.0	5.0 (30c10)		15 (M)	10	1.0 (419)
7	2.0	5.0 (30c10)		16 (M)	25	0.7 (600)
8	4.0	10.0 (30c10)		20 (T)	28	8.9 (43)
9	4.0	4.0 (30c10)		20 (T)	20	5.8 (69)
10	4.0	4.0 ("60c20")		40 (T)	16	3.9

[a] initiator: sodium naphthalide, polymerization: 10 °C - room temperature for 20 hr, blocking group: **4**.

[b] M: THF/benzene (55/45, v/v), T: THF.

[c] determined by GPC (THF, PS standards, RI and UV detectors).

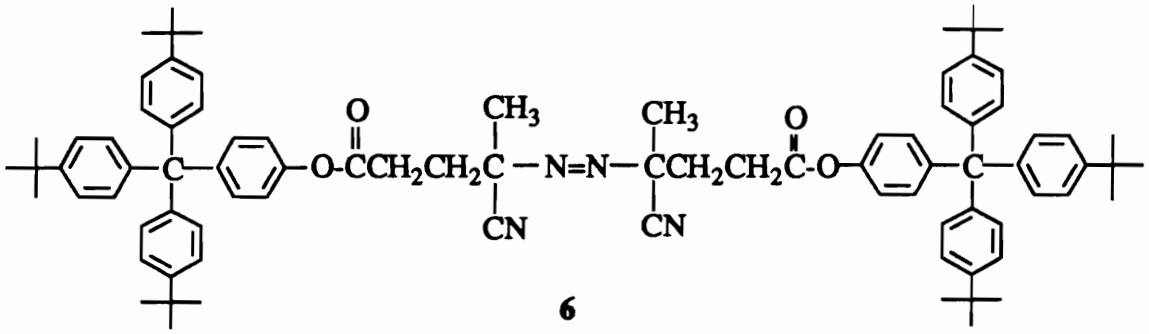
[d] n/m = number of repeating unit/crown ether, determined by ^{1}H NMR.

Another point was the solvent effect in the anionic polymerization. Obviously, the results showed that the more polar THF was better than the less polar toluene for higher threading yield. The big difference between the two was interpreted by the size of cavity of crown ethers in the reaction mixture. [22] In a more polar solvent the crown ethers might have a more open structure. It should be pointed out that there are also other factors related

to the solvent effect such as ion-pairing which affects anionic polymerization rate to a large extent. [28]

2-2. Poly(styrene-rotaxa-crown ether)s: Current work

The blocking group/initiator (BG/init) used for the synthesis was BG/init **6** which was a mixture of *dl* and *meso* isomers (*dl*/*meso*=0.78) [29] and the amount of **6** was 0.5-2.0 mol % to the monomer.



6

Toluene was used as a cosolvent due to the incompatibility between the two components, which were PS and "42c14" [25], during the polymerization so that reaction mixtures were clear and homogeneous through the reaction. [The quotation mark (" ") on the 42c14 indicated the crown ether is not a single-sized, but rather a mixture of crown ethers with different sizes. See ref. (25)] Isolation of the product was done by column chromatography (silica gel, THF). Table 3 shows the results.

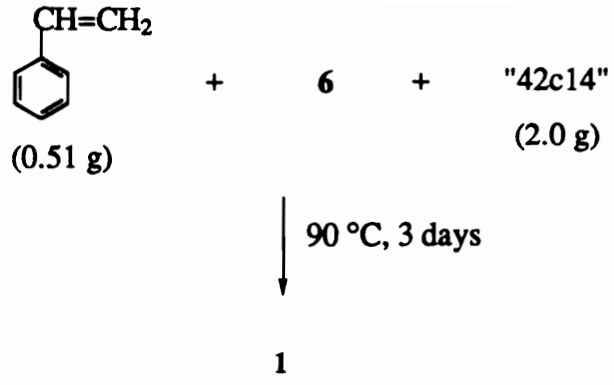


Table 3. Result of synthesis of poly(styrene-rotaxa-"42c14") **1** with purification by column chromatography (silica gel, THF).[a]

Batch	styrene (g)	**6** (mg)	toluene (g)	"42c14" (g)	yield (%, polymer)	M_n[b] (kg/mol)	thread. yield[c] (mass %)
P1	0.52	30	2.0	2.0	8	-	2
P2	0.51	60	2.0	2.0	8	18.5	13
P3	0.51	120	2.0	2.0	18	-	26

[a] polymerization: 90 °C, 3 days.

[b] M_n of substance isolated with CH_2Cl_2 and THF, determined by GPC ($CHCl_3$, PS standards, RI detector).[The quotation mark (" ") on the 60c20 indicated the crown ether is not a single-sized, but rather a mixture of crown ethers with different sizes. See ref. 25]

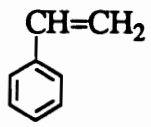
[c] determined by ^1H NMR spectrum.

The isolation/purification of polyrotaxanes from the crude mixture can also be achieved by repeated precipitations of a solution of crude product into solvents which are

good solvents for cyclic species but non-solvent for linear species. However, when the reaction mixture was poured into excess methanol with vigorous stirring in order to isolate the product no precipitation took place; instead, emulsification was encounterred as mentioned before. Because of the formation of emulsion upon pouring into excess protic solvents such as methanol, ethanol and water the purification/isolation of the products was extremely difficult. The emulsion particles are so small that they readily pass through normal filtration media such as filter paper and sintered glass filters. It was also so stable that addition of salts (KCl, NaCl or $MgSO_4$) did not induce coagulation/precipiatation and only part of the product (less than 5 wt % or so) could be isolated even after centifugation (6000-7000 rpm) for 4 hr. The precipiate obtained from centrifugation did not look like solid precipitate; it was like jelly or gel. It is believed that the threaded crown ethers in the polyrotaxane behaved as a non-ionic surfactant and stabilized the PS particles. [30] When a CH_2Cl_2 solution of a physical mixture of PS (M_n=18 kg/mol, Pd=1.2) and "42c14" (1/4, wt/wt) was poured into a large amount of methanol, the precipitation of PS readily occurred in the methanol solution. If the PS particles were stabilized by the threaded crown ethers, the crown ethers must be placed in outer layer of the particle in methanol medium as illustrated in Figure 1. When a mixture of hexane and methanol (1/1, v/v) was used to precipitate the product, some amount of precipiate was formed in the solution. This observation implies that the particle was stabilized by the crown ethers which were located in outer layer of the particles because hexane, which is a nonsolvent for "42c14", destroyed the stability of the particles to give some precipitate. The precipitation into hexane, however, could not be conducted because hexane also made free "42c14" precipitate.

An important question to answer was the occurence of chain transfe. [31] It was necessary to understand whether the stability was due to crown ethers attached to the polymer backbone *via* chain transfer or due to the threaded structure. Therefore, a control

experiment was carried out using 18c6, whose cavity is too small to be threaded by linear molecules.



(2.0 g, 4.8 mmol) + **6** + 18c6 (60 mg, 4.8×10^{-5} mol)

90 °C, 3 days

purification by precipiation into methanol

PS (M_n=14 kg/mol; contained 0.25 mass % crown ether)

The reaction mixture was poured into excess methanol (250 mL) as described above. Immediately, a white precipiate formed from the methanol solution. The precipitate was filtered and dissolved in CH_2Cl_2 (5 mL), followed by a second precipiatation into methanol. The polymer was dried and analyzed by ^1H NMR spectroscopy. In the ^1H NMR spectrum (Figure 2) in $CDCl_3$ a small broad peak at ca. 3.6 ppm was due to $C\underline{H_2}C\underline{H_2}O$ protons and according to the peak integration the amount of the crown ether species in the product was found to be 0.25 mass %. This result indicated that 1) the reprecipitation method was effective to remove free crown ethers from the crude product if precipitation readily occurs, and 2) chain transfer to crown ethers was not significant.

The effect of "threading" on the stabilization of polystyrene particles was further investigated by dispersion polymerizations of styrene in protic solvents such as methanol and water in the presence of "42c14" and linear poly(ethylene oxide)s (PEOs) with various molecular weights. The polymerization was carried out in 10 mL of the dispersion medium

(methanol or water) at reflux (methanol) or 70 ℃ (water). In all cases the amount of styrene was 1.0 g and the initiators were 4,4'-azobis-4-cyanopentanoic acid or AIBN (1.5 mol % to monomer). The reason that 4,4'-azobis-4-cyanopentanoic acid and AIBN were used as initiators instead of **6** was because **6** was not soluble in methanol or water and it was not necessary to block the ends of the produced polymer chains to retain the threaded crown ethers. Once oligomeric growng chains precipitate from the methanolic or aqueous media no dethreading can take place. Table 4 shows the results of the dispersion polymerizations.

From Batches 1 and 2 in Table 4, it was found that 4,4'-azobis-4-cyanopentanoic acid alone can not afford stable PS particles although it can produce PS whose chain ends are carboxylic acid groups which are hydrophilic. When 18c6, whose cavity is too small to be threaded, was used as additive, no formation of stable PS particles was observed. PEOs with various molecular weights also could not produce stable polymer particles. It was, however, found that PEO (M_n=100 kg/mol) could afford polymer particles to some extent. The polymer particles, however, were not stable but rapidly precipitated when the stirring was stopped. This indicated that chain transfer took place although the extent was not so significant. The formation of stable emulsions was achieved only with "42c14". This result strongly supports the importance of "threading" for the formation of the emulsions. As described in Figure 3, a small amount of styrene molecules in the dispersion media were initiated to polymerize to form oligomeric growing polymer chain **7** which was threaded by crown ethers to give an oligomeric polyrotaxane **8**. Once the length of the growing chains reaches a certain critical value, they coagulate and precipitate to form a primary particle **9** which could serve as polymerization site like in a normal surfactant-free emulsion polymerization. [32] The crown ether molecules would be located on the outer surface of the particle due to their hydrophilicity. The "threading" endows the crown

Table 4. Dispersion polymerization[a] of styrene using "42c14" as a surfactant.

Batch	Styrene (g)	Initiator[b] (1.5 mol %)	Additive (1.0 g)	Solvent (10 mL)	Emulsion[c]
1	1.5	A	-	water	no
2	1.5	A	-	MeOH	no
3	1.5	A	-	MeOH	no
4	1.5	A	18c6	MeOH	no
5	1.5	A	PEO(400)	MeOH	no
6	1.5	A	PEO(1500)	MeOH	no
7	1.5	A	PEO(3400)	MeOH	no
8	1.5	A	PEO(100K)	MeOH	no[d]
9	1.5	A	"42c14"	water	yes
10	1.5	A	"42c14"	MeOH	yes
11	1.5	B	"42c14"	water	yes

[a] reaction conditions: reflux (MeOH) or 70 °C (water), 25 hr.

[b] A: 4,4'-azobis-4-cyanopentanoic acid, B: AIBN.

[c] "no" means that the particles were unstable or coagulated upon polymerization. "yes" means that the particle was stable or not precipiated within one week.

[d] Some particles were formed, but once stirring was stoppped the particles precipitated within about 30 min.

ether molecules with "anchors" so that the crown ether can not be detached from the surface of the polymer particle and acts as a permanent surfactant molecules.

Another interesting result was obtained from the statistical mixing of polystyrene (M_n=18.0 kg/mol, Pd=1.2) (0.10 g) and "42c14" (1.0 g) in refluxing THF (6 mL). After mixing for a week the solution was poured into methanol (50 mL) with vigourous stirring. White precipitate was formed. The precipitate was, however, not a dense solid; interestingly, it was gel-like and passed through filter paper, so the suspension was subjected to centrifugation to isolate the precipiate. The precipitate was dissolved in CH_2Cl_2 (3 mL) and poured into methanol (50 mL) and centrifuged; this was repeated. Precipitation occurred the third time, but the filtrate was not clear; instead, it was an emulsion. The precipitate (0.10 g) was isolated by centrifugation and it was found to contain 0.3 mass % of crown ether by ^1H NMR. Methanol was removed from the filtrate by rotary evaporation and the residual solid was dried under vacuum at room temperature. According to the ^1H NMR spectrum the mass % of the crown ether in the residual solid (ca. 10 mg, 1 % yield) was 20 %. This result again suggested strongly the origin of the emulsification phenomenon. From the fact that the emulsification did not take place for the first two precipitations, but occured during the third precipitation implies that the threaded macrocycles indeed moved along the chain to aggregate together (in other words, microphase separation along the chain) to stabilize the PS particles. For the threaded crown ethers to move along the polymer chain needed a certain period time and it was achieved during the repeated precipitations.

Because of the difficulty of utilization of the precipitation-filtration method, the isolation of the product was attempted by column chromatography. Although "42c14" almost did not move through the silica gel column with THF, the R_f of PS was found to be nearly 1.0. Therefore, the crude product was charged into a silica gel column and it was

eluted with CH_2Cl_2 first to remove the unreacted **6** and unthreaded PS. The solid after evaporation of CH_2Cl_2 was tested by ^1H NMR to make sure of the absence of the crown ether species. The amounts of unreacted **6** and PS were 0.13 g (P1), 0.12 g (P2) and 0.20 g (P3). After no more substance was eluted with CH_2Cl_2, THF was used to elute until no substance was detected in the eluting solution. 0.04 g (P1), 0.04 g (P2) and 0.09 g (P3) of polyrotaxanes were obtained. The threading yields were determined by ^1H NMR spectra from the ratios of peak integrations. The results (Table 3) indicated that smaller amounts of initiator gave lower threading yields. This suggested that during polymerization the threaded crown ethers located at the growing chain ends underwent dethreading. With smaller amounts of initiator, there must be longer time for the threaded crown ethers to be dethreaded.

The GPC trace (Figure 4) of the product Batch P2 should be mentioned. The GPC trace of the eluted sample which was a mixture of the polyrotaxane (eluted with THF) and polystyrene (eluted with CH_2Cl_2) was found not to be unimodal but bimodal. It was demonstrated by Liu and Gibson that threaded macrocycles would change the hydrodynamic volume of the linear polymer significantly. [33] They found that a polyrotaxane containing about one crown per each chain which was made by simple mixing of preformed poly(butylene sebacate) (M_n=27.6 kg/mol) and "42c14" displayed doubled intrinsic viscosity in chloroform. This means that the hydrodynamic volume of the polyrotaxane was doubled and this was further confirmed by GPC and VPO measurements. Therefore, although the molecular weight of the linear species of the polyrotaxane is comparable to that of free PS, the apparent molecular weight of former must be larger than that of the latter in GPC measurement. Thus, it is believed that the lower elution volume corresponds to the poly(styrene-rotaxa-crown ether)s and the longer retention time trace to free PS. Also, the average molecular weight calculated from the

GPC trace was higher than the molecular weight of PS (M_n=15 kg/mol) which was prepared by polymerization of styrene under the similar condition using toluene (4.0 g) without crown ether.

The low yields in Table 3 suggested that the isolation of the products was probably incomplete. In other words, a portion of product for each batch containing a larger amount of threaded crown ether did not elute with THF. When the column was eluted with methanol, surprisingly, an emulsion was eluted. The emulsion contained polystyrene species as well as crown ether. This indicated that the product with higher threading yield still stayed inside the column and never eluted with THF. When it contacted methanol, the emulsification occurred and the resulting emulsion was eluted.

So, in a second synthesis of poly(styrene-rotaxa-crown ether)s the purification was done by a combination of filtration and centrifugation in order to isolate as much product as possible. The second synthesis was carried out under the same reaction conditions with 1 mol % initiator **6**. Table 5 shows the results of the experiments.

When the reaction mixture was poured into methanol (250 mL) with vigorous stirring, an emulsion was formed except with Batch P4 in which 30c10 was used as cyclic species. The emulsion was filtered using a glass filter with very fine pores. The filtration took a long time, as much as a whole day. To the isolated precipitate ethanol (50 mL) was added, followed by vigorous stirring. Upon stirring the precipiate turned back to an emulsion which was subjected to centrifugation for 2-3 hr.. The supernant was decanted and the precipiate was subjected to the same process. Complete isolation, however, was not achieved. The filtrate after filtation was not perfectly clear, which means that in spite of using a fine filtration medium a part of the product was lost during the process. Furthermore, the centrifugation did not afford complete isolation of the product either. The supernant was a little bit hazy, meaning that it contained some of the product. It is believed

Table 5. Results of synthesis of poly(styrene-rotaxa-crown ether)s **1** with purification by filtration and centrifugation[a]

Batch	styrene (g)	**6** (mg)	crown ether (g)	toluene (g)	yield (%, polymer)	M_n[b] (kg/mol)	thread. yield[c] (mass %)
P4	0.75	90	30c10 (3.0)	3.0	87[d]	27.4	1.4
P5	0.50	60	"42c14" (2.0)	2.0	36[e]	23.4	21
P6	0.50	60	"60c20" (2.0)	2.0	40[e]	11.0	11

[a] polymerization: 90-95 °C, 3 days.

[b] determined by GPC ($CHCl_3$, universal calibaration)

[c] determined by ^1H NMR spectrum.

[d] three precipitations into methanol.

[e] a precipiatation into methanol and filtration followed by two centrifugations.

that the low polymer yields of Batches P5 and P6 were due to the loss of products during the purification steps. Such low yields were reported by Engen when he prepared PS rotaxanes using 30c10 and "60c20" in which the filtration method was adopted to isolate the products. However, Batch P4 gave an 87 % polymer yield after three reprecipitations from methanol, which is much higher than Engen's result [21] (24 %).

Regarding the molecular weight, Batch P4 gave the highest and it may be related to the problem in the purification procedures. Batch P4 gave virtually no threading. According to CPK models 30c10 can be threaded by the PS chain, but, because the formation of poly(styrene-rotaxa-crown ether) is statistically driven, the cavity size of the cyclic species is critical. The polymer yield and molecular weight of Batch P5 were comparable to the results of Batch P2 (Table 3). The threading yield of Batch P5,

however, was higher than that of P2. This is probably because the retention behavior of the polyrotaxane in the chromatography was sensitive to the threaded crown content.

Figure 5 shows the GPC traces of (a) "42c14" (M_n=2.39 kg/mol, Pd=1.08, PS equiv.) (b) a physical blend of PS (M_n=35.5 kg/mol, Pd=2.4) and 50 mass % "42c14" and (c) poly(styrene-rotaxa-"42c14") (M_n=23.4 kg/mol, Pd=1.3). Figure 5(b) demonstrates that GPC can test the purity of the resulting product because the two components can be separated through GPC. Thus, Figure 5(c) indicates the lack of the free crown ether in final product. It is to be noted that a small shoulder in Figure 5(c) might be due to the free PS although it is not as clear as in Figure 4.

The result of Batch P6 is a puzzle. Unexpectedly, "60c20" resulted in the lowest molecular weight polymer with lower threading yield than "42c14". This result is not clearly understood at this point. It could be related to the composition of "60c20" which showed broader molecular weight distribution (M_n=1.82 kg/mol, Pd=2.10) than "42c14" with more than one peak. (Figure 6) The lower threading yield might be due to the higher portion of cyclic species, which is larger than 42-membered, in "60c20" than "42c14", because the blocking group can hold only up to 42-membered rings.

The thermal behavior of poly(styrene-rotaxa-"42c14") (P5, Table 5) was investigated by DSC. Figure 7 shows the DSC traces of (*A*) "42c14" (second heat), (*B*) PS (M_n=15.2 kg/mol) (third heat), (*C*) and (*D*) PS-rotaxa-"42c14" (M_n=23.4 kg/mol, 21 % of crown ether) (first heat and second heat, respectively). As shown in traces *C* and *D*, the polyrotaxane did not show a melting peak for the crown ether. Interestingly, in those traces two glass transitions are observed at around -10 °C and 56 °C. The higher T_g is believed to be from the PS backbone and the lower one to be from the crown ether. Thus, the T_g of PS was decreased in the polyrotaxane as compared to homo-PS and the T_g of the crown ether, which is usually -65 ~ -70 °C, was much increased. It is believed that

range of temperature. It is believed that the threading prevents the crystallization of the threaded crown ether and resulted in the T_g shifts due to the phase mixing. However, further investigations are needed to draw clear conclusions. There must be a critical value of loading of the crown ether which allow for the cyclic to cystallize along the chain. Thus, synthesis of PS-rotaxa-"42c14" with different threading yields is valuable for the future.

3. POLYROTAXANES OF ACRYLIC AND METHACRYLIC POLYMERS

The main driving force for the formation of poly(styrene-rotaxa-crown ether)s is statistical mixing; in other words, there is no specific attractive force between styrene/PS and crown ethers. The acrylic and methacrylic monomers, however, carry polar functional groups, so they are more compatible than styrene and an attractive force with crown ethers may exist although it is not strong. Therefore, methyl acrylate (MA), methyl methacrylate (MMA) and acrylonitrile (AN) were used for the syntheses of polyrotaxanes with 30c10 as a macrocycle. The polymerizations of the monomers were carried out in bulk states using AIBN as initiator. It was found that if molecular weights of linear polymers are large enough to prevent dethreading of macrocycles owing to chain entanglement, it is not necessary to block the ends of the chains. The mole ratios of monomer to 30c10 were 1 and the amounts of initiator were 1 mol % to monomers. For the control experiments, the same mass of 18c6 was used instead of 30c10.

The reaction mixtures were subjected to three cycles of freeze-pump-thaw processes and the polymerizations were done at 70-72 °C for 3 days. For the isolation of the resultant polymers the reaction mixtures were reprecipitated from a large amount of water (methanol

for Batches P9 and P12) until no free crown (3.670 ppm in $CDCl_3$) was found in the ^1H NMR spectra. Table 6 shows the results of the experiments.

Table 6. Results of synthesis of PMA-rotaxa-30c10, PMMA-roaxa-30c10 and PAN-rotaxa-30c10, and control polymerizations using 18c6.[a]

Batch	monomer (g)	crown ether (g)	M_n[b] (kg/mol)	thread. yield[c] [mass %, (n/m)]
P7	MA (0.20)	30c10 (1.0)	35.5	3.8 (123)
P8	MMA (0.23)	30c10 (1.0)	113.1	1.7 (254)
P9	AN (0.12)	30c10 (1.0)	4.7	unknown[d]
P10	MA (0.40)	18c6 (2.0)	-	0
P11	MMA (0.51)	18c6 (2.0)	-	0
P12	AN (0.25)	18c6 (2.0)	-	0

[a] polymerization condition: 70-72 °C, 3 days.

[b] determined by GPC (P7, P8: $CHCl_3$; P9: NMP; universal calibration).

[c] determined by ^1H NMR spectrum (P7, P8, P10, P11: $CDCl_3$; P9, P12: DMSO-d_6).

[d] crown ether was detected, but it was likely from chain transfer.

All reaction mixtures were initially clear and homogeneous and the mixtures for P7, P8, P10 and P11 were maintained homogeneous and transparent through the whole polymerization process, indicating the compatibilities of poly(methyl acrylate) (PMA) and poly(methyl methacrylate) (PMMA) with 30c10. The reaction mixtures for P9 and P12 (polyacrylonitrile, PAN), however, became heterogeneous and the polymers precipitated from the reaction mixtures while polymerizations proceeded. The low molecular weight of P9 was believed to be due to the precipitation.

from the reaction mixtures while polymerizations proceeded. The low molecular weight of P9 was believed to be due to the precipitation.

The threading yields were determined by peak integrations in the ^1H NMR spectra. The difficulty in determining the threading yields of PMA and PMMA was due to the overlapping of OCH_3 and crown ether peaks. Those protons have the almost same chemical shifts (free 30c10: 3.670 ppm, OCH_3: 3.665 ppm), and furthermore, threaded 30c10 might have the different chemical shift as compared to the free 30c10. Therefore, the determination of the threading yields had to be very careful. Figures 8 and 9 are the ^1H NMR spectra of the isolated PMA samples P7 and P10, respectively. The two spectra are virtually the same except for the peak integrations. According to the integrations, the relative intensity of the peak at 3.65 ppm was larger in Figure 8 than in Figure 9. The ratio of the integrations of peaks at 3.65 ppm (OCH_3) and the others (CH_2-CH) was exactly 1:1 in Figure 9. In Figure 9, an unexpected peak (marked by *) is found at 3.559 ppm. The small peak at 3.559 ppm was obviously not from the threaded crown ether because 18c6 can not be threaded. The peak at 3.559 ppm is also found in Figure 8 and it is believed that the peak was produced by chain transfer. Therfore, based on the integrations of the peaks at 3.66 and 2.6 (**a**), the threading yield was calculated to be 3.8 mass %. 3.8 mass % was much higher than the poly(styrene-rotaxa-30c10) although a smaller amount of 30c10 was used. This is probably because of the compatibility of PMA and 30c10 and the fact that the polymerization was carried out in the bulk state.

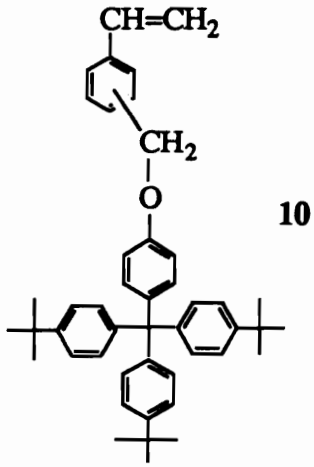
Figure 10 is the ^1H NMR spectrum of the isolated PMMA sample P8. The spectrum (Figure 11) of the product of control PMMA sample P11 was the same as Figure 10 except for the absence of a small peak at 3.746 ppm which are marked by an arrow. It is to be stressed that the small peak at 3.599 ppm in Figures 8 and 9 was not found in Figures 10 and 11. This implies that growing PMMA radical has less tendency for chain

transfer to crown ether than PMA radical probably due to the steric hindrance of the chain end. The peak at 3.746 ppm (Figure 10) was analyzed by 2D COSY and 2D NOESY NMR techniques. In neither spectrum, was there a correlation between the peak at 3.746 ppm and others. However, the origin of the peak is likely to be the threaded 30c10. The lack of correlation in the 2D COSY spectrum shows that the peak was from an isolated species, in other words, from a material which was not covalently bonded to the polymer backbone. The reason for the lack of correlation in the 2D NOESY spectrum may the weak intensity of the signal and that the through-space interactions are not strong. The threading yield was found to be 1.7 mass % under the assumption that the peak at 3.746 ppm was from the threaded 30c10. This value is much lower than MA case and it seems to be due to the larger size of MMA molecule as comapred to MA, which made it harder to sit in and to be threaded through the cavity of 30c10.

The ^{1}H NMR spectrum (Figure 12) of the PAN sample P9 in DMSO-d_6 was substantially different from the others. As shown in Figure 12, along with broad methine (3.08 ppm) and methylene (2.00 ppm) proton peaks, a sharp peak was found at 3.46 ppm. The ^{1}H NMR spectrum of the PAN from the control experiment (P12) was the same as Figure 12 with only a difference in the intensity of the peak at 3.46 ppm. The ratios of integration of the methine peak (3.08 ppm) to the 3.46 ppm peak were 1.02 and 0.44 for the products from P9 and P12, respectively. This strongly suggests that the peak at 3.46 ppm was due to the chain transfer during the polymerization. It is interesting that for P9 the integration indicates incorporation of one 30c10 per 41 PAN units, while in P12 there is one 18c6 or equivalent per 11 PAN units. The enhanced incorporation of crown ether in P12 is due to its higher (1.7x) molar concentration. Engen reported the synthesis of PAN-rotaxa-"60c20" with threading yields of up to 38 mass %. [21, 23, 34] The current result implies that parts of the crown ether in his products were produced by chain transfer.

4. SIDE-CHAIN POLYROTAXANE VIA FREE RADICAL POLYMERIZATION

Bheda and Gibson reported the synthesis of styrenic monomer (**10**) bearing a bulky blocking group and its anionic and free radical polymerizations to show a possible route to prepare side-chain polyrotaxanes or polyrotaxanes with in-chain "stoppers". [35] Born and Ritter reported preparation of side-chain polyrotaxanes containing 2,6-di-*O*-methyl β-CD (Me_2-β-CD). [36, 37] They obtained side-chain polyrotaxanes by the reactions of the precursor (**11**) [36] and the pre-formed polymers based on PMMA and poly(ether-ether-ketone) which contained reactive functional groups.



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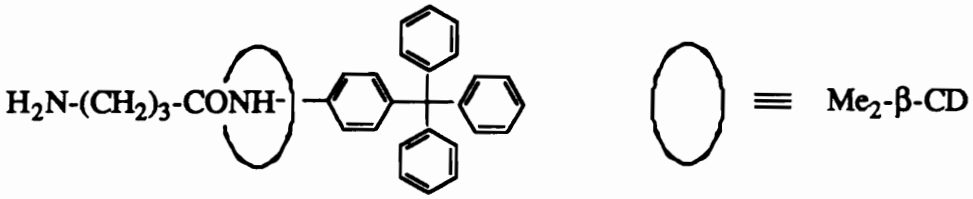

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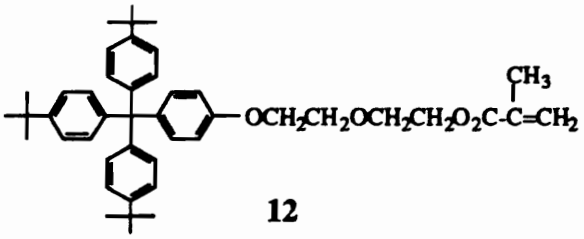
In the current work, blocking group/monomers (BG/M) **12** and **13** were initiated by AIBN and polymerized in the presence of 30c10 (mass ratio of BG/M:30c10=0.1) to give side chain polyrotaxanes **14**. (Scheme 2) The syntheses of **12** and **13** were achieved by the reaction of mono-*p*-[tris(*p*-*tert*-butylphenyl)methyl]phenyl ether [38] of di(ethylene glycol) and mono-triphenylmethyl ether of di(ethylene glycol) with methacryloyl chloride, respectively, in THF at room temperature in the presence of pyridine as an acid scavenger. The ^{1}H NMR spectra (Figure 13 and 14) of the products confirmed the structures and the melting points were 180.5-182.0 (**12**) and 95.0-97.5 °C (**13**).



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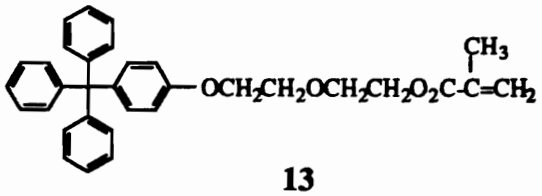

13

BG/M **12** had a limited solubility in 15 equivalents of 30c10 even at 110 °C so that a small amount of toluene had to be added to the mixture to obtain a homogeneous solution during the polymerization process. The polymerization temperature was 80 °C and the reaction time was 3 days. The final product was obtained after three reprecipitations into a large amount of methanol.

While **12** was not well soluble in 30c10, **13** completely dissolved in 11 equivalents of 30c10 when the mixture was heated. Once **13** was dissolved in 30c10, even after the mixture was cooled to room temperature, it was clear and homogeneous. Thus, the polymerization of **13** in the presence of 30c10 did not need a cosolvent, so the synthesis was carried out in the bulk state at 90 °C for 26 hr. The product was isolated in the same way, that is, reprecipitations into a large amount of methanol. The yields were 87 % and

85 % for **14** (R=*t*-butyl) and **14** (R=H), respectively. The GPC traces (Figure 15) indicate the absence of free 30c10 in the products. The molecular distributions are broad and the number average molecular weight of **14** (R=*t*-butyl) (M_n=49.7 kg/mol) is lower than **14** (R=H) (M_n=65.9) because the former was prepared in a solution while the latter in neat conditions.

Interestingly, in the ^{1}H NMR spectra [Figure 16, 17(a, b)] in $CDCl_3$ of the products **14** a small broad signal at 3.4 ppm was found. To identify the origin of the peaks a polymerization of **13** as control experiment was carried out using 18c6 (same mass as 30c10) under the same reaction conditions. The ^{1}H NMR spectrum (Figure 18) of the isolated polymer showed no such signals at 3.4 ppm. Thus, it can be concluded that the small peaks were from a source other than the polymer itself and not from a chain transfer. It is likely that the peaks were due to the threaded 30c10. The two peaks reflect probably the tacticity of the polymer. Recently, Gong and Gibson reported synthesis of a polyester/crown ether rotaxane derived from a difunctional blocking group in which the threaded 30c10 showed an upfield shift in its ^{1}H NMR spectrum as compared to free 30c10. [39] This was rationalized by the shielding effect of the aromatic π-electrons of the BG on threaded crown ether; this was supported by the 2D COSY and 2D NOESY NMR spectra. Likewise, the signal at 3.4 ppm was analyzed by these NMR techniques. As shown in Figure 19(a, b) which are the 2D COSY spectra, there is no correlation between the peak at 3.4 ppm and other aliphatic protons, meaning the peak was not due to crown ethers covalently bonded to the polymer backbone through chain transfer. Also, this result is consistent with the lack of chain transfer in the control experiment, which was a radical polymerization of MMA in the presence of 18c6. However, the 2D NOESY spectrum of **14**(R=H) did not show any interaction through space between the peak at 3.4 ppm and others. This is believed to be the weak intensity of the peak as mentioned before. The

threading yields calculated by peak integrations were found to be 1.5 mass % for **14**(R=*t*-butyl) and 1.6 mass % for **14**(R=H). These values correspond to n/m=45 for **14**(R=*t*-butyl) and n/m=56 for **14**(R=H), which are much higher than for PMMA (P8 in Table 6, n/m=254). (n/m = number of crown ether/number of repeating unit) This may be due to the use of larger amount of 30c10. The results also imply that the dethreading process took place during the synthesis of PMMA-rotaxa-30c10.

CONCLUSIONS

Poly(styrene-rotaxa-crown ether)s were synthesized by free radical polymerizations of styrene in the presence of crown ethers using blocking group/initiator **6**. The chain transfer of the growing polystyrene radical to crown ether was addressed. According to the control reaction using 18c6 whose cavity is too small to be threaded, the chain transfer indeed occurs, but the extent was found to be negligible. The purification by precipitation into methanol which is a good solvent for crown ethers but a non-solvent for polystyrene was not utilized for the current work because of the formation of emulsions. The emulsification was suggested to be due to the rotaxane structure which provides threaded crown ethers with "anchors" to the particle so that they behave as a surfactant. The dispersion polymerization of styrene in protic solvents such as water and methanol in the presence of "42c14" afforded stable emulsions. In contrast, 18c6 or poly(ethylene oxide)s of various molecular weights could not stabilize the polystyrene particles. This observation was interpreted as due to the threading of crown ether by polystyrene.

Purification by column chromatography and filtration/ultracentrifugation enable isolation of poly(styrene-rotaxa-crown ether)s whose threading yields were 10-20 mass %.

The isolated polyrotaxanes were characterized by NMR and GPC. The DSC results showed that the threaded crown ether changes thermal properties of polystyrene significantly.

Acrylic (methyl acrylate, acrylonitrile) and methacrylic (methyl methacrylate) nomomers were polymerized using AIBN in the presence of 30c10. Methyl acrylate and methyl methacrylate afforded a few mass % of threading yields, but acrylonitrile showed a strong tendency for chain transfer as supported by a control experiment in which 18c6 was used.

Two blocking groups containing methacrylate moieties were used to synthesize side-chain polyrotaxanes containing 30c10. A change in chemical shift of the threaded 30c10 is believed to have occurred. The threading yields (n/m = number of crown ether/number of repeating unit) of the side-chain polyrotaxanes were higher than those of PMMA-rotaxa-30c10 or PMA-rotaxa-30c10. This is probably related to the fact that these monomers present a long segment for threading and the blocking groups prevent once-threaded crown ethers from dethreading during the polymerization procedure.

EXPERIMENTAL

Experimental methods and measurements. Melting points were taken in capillary tubes with a Melt-Temp II melting point apparatus and have been corrected. Centrifugation speed was 6000-7000 rpm. NMR spectra were obtained on a Varian Unity 400 MHz spectrometer at ambient temperature using tetramethylsilane as an internal standard unless noted otherwise. GPC analyses of the polymers were performed at 20 °C in THF or $CHCl_3$ using a Waters system with a refractive index detector after calibration with PS standards and a Viscotek 100 differential viscometer detector using universal calibration. Thermal analysis was done on a TA Instruments DSC 2920 instrument at 10 °C/min. Elemental analyses were done by Atlantic Microlab of Norcross, GA.

Synthesis of poly(styrene-rotaxa-"42c14") with purification by column chromatography. In a 50 mL flask equipped with a Teflon valve and a magnetic stirring bar, styrene (0.51 g, 4.9 mmol), the blocking group/initiator (**6**) (60 mg, 4.8×10^{-5} mol), toluene (2.0 g) and "42c14" (2.0 g) were placed. The mixture was subjected to three cycles of freeze-pump-thaw processes on a vacuum line (1×10^{-5} mmHg) to remove oxygen. The mixture was placed in an oil bath preheated to 90 °C and stirred for 3 days at that temperature. CH_2Cl_2 (ca. 5 mL) was added to the mixture and the solution was poured into methanol (250 mL) with vigorous stirring. An emulsion was obtained. The emulsion could not be filtered with normal filtration media such as filter paper or glass filters. All solvents were rotary evaporated and the residual solid was dissolved in CH_2Cl_2 (ca. 10 mL) and the solution was charged into a silica gel column (3 cm diameter x 20 cm length) saturated with CH_2Cl_2. CH_2Cl_2 was eluted until no substance was detected on TLC plate when exposured to I_2 vapor. 120 mg of white solid was obtained. THF was

eluted until no more substance was received. 40 mg (8 % yield) of the product was obtained. Polymerization of styrene was carried out with 18c6 instead of "42c14" as a control experiment (same masses). The mixture was poured into methanol (250 mL) with vigorous stirring to give a nice precipiate which was filtered and dissolved in CH_2Cl_2 (ca. 5 mL), followed by a second precipiatation into methanol. A third such process was done, and the final product was dried under vacuum at room temperature.

Dispersion polymerization of styrene using "42c14" as a pre-surfactant. In a 25-mL flask a mixture of styrene (1.5 g, 14 mmol), 4,4'-azobis-4-cyanopentanoic acid (80 mg, 0.22 mmol), "42c14" (1.0 g) and methanol (10 mL) was placed and it was put in a pre-heated oil bath (70 °C). The mixture was stirred and after 5-10 min the mixture became hazy and after 30 min, the mixture was milky. The reaction was continued for 25 hr. The resultant emulsion was stable for at least for a week; after that the particles gradually coagulated and precipitated.

Statistical threading of preformed PS with "42c14". Polystyrene (M_n=18 kg/mol, Pd=1.2) (0.10 g) and "42c14" (1.0 g) were dissolved in THF (6 mL) and the mixture was stirred at reflux for a week. The solution was poured into methanol (50 mL) with vigourous stirring. A white precipitate formed. The filtered precipiate was dissolved in CH_2Cl_2 (3 mL) and reprecipitated into methanol (50 mL). A third reprecipitation was carried out by the same procedure. Precipitation occurred, but the filtrate was not clear; instead, it was an emulsion. The precipitate (0.10 g) was isolated by centrifugation and it was found to contain 0.3 mass % of crown ethers from its ^1H the NMR spectrum. Methanol was removed from the filtrate by rotary evaporation and the residual solid was

dried under vacuum at room temperature. According to the ^1H NMR spectrum the mass % of the crown ether of the solid (ca. 10 mg, 1 % yield) was 20.

Synthesis of poly(styrene-rotaxa-crown)s with purification by filtration and centrifugation. A mixture of styrene (0.50 g, 4.8 mmol), "42c14" (2.0 g), **6** (60 mg, 4.8×10^{-5} mol) and toluene (2.0 g) was subjected to three cycles of freeze-pump-thaw processes on a vacuum line (1×10^{-5} mmHg). The mixture was placed in a pre-heated oil bath at 90 °C and stirred by a magnetic stirrer for 3 days at 90-95 °C. To the mixture CH_2Cl_2 (ca. 5 mL) was added and the mixture was poured into methanol (250 mL) with vigorous stirring. An emulsion was formed. The emulsion was filtered by a very fine sintered glass filter. To the precipitate ethanol (50 mL) was added and the mixture was stirred using a magnetic stirrer. The precipitate turned back to an emulsion. The emulsion was subjected to centrifugation for ca 2 hr. The supernant was decanted off and ethanol (50 mL) was added to the precipitate. The same procedure (stirring, centrifugation and decantation) was repeated. The precipitate was dried under vacuum at room temperature.

Synthesis of poly(methyl acrylate-rotaxa-30c10). In a 25-mL flask fitted with a Teflon valve methyl acrylate (0.20 g, 2.3 mmol), 30c10 (1.0 g, 2.3 mmol) and AIBN (3.7 mg, 2.3×10^{-5} mol) were placed. The mixture was subjected to three cycles of freeze-pump-thaw processes on a vacuum line. The flask was placed in an oil bath pre-heated to 70 °C and the mixture allowed to stir magnetically for 3 days at 70-72 °C. The reaction mixture was poured into vigorously stirred water (200 mL). The gummy precipitate was collected and dissolved in THF (ca. 5 mL), followed by precipitation into water again. Two such precipitations were done. The final product was dried under vacuum at room tempeature.

Purifications of the products from Batches P9 and P12 were done by precipitations of DMSO solutions (ca. 5 mL) into methanol (200 mL) instead of from CH_2Cl_2 solutions into water.

Blocking group/monomer (12). In an oven-dried 50-mL flask, mono-*p*-[tris(*p*-*tert*-butylphenyl)methyl]phenyl ether of di(ethylene glycol) (1.00 g, 1.69 mmol), pyridine (0.48 g, 5.70 mmol) and THF (20 mL, distilled over Na/benzophenone) were placed. To the mixture methacryloyl chloride (0.51 g, 4.88 mmol) was added, followed by stirring for 12 hr. The mixture was poured into aqueous $NaHCO_3$ (0.5 g salt/150 mL) and it was extracted with CH_2Cl_2 (100 mLx2). The combined organic layer was dried over $MgSO_4$ and the solvents were rotary evaporated. The residual solid was passed through a short silica gel column to remove remaining salt and colored impurities. After rotary evaporation of CH_2Cl_2 the solid was recrystallized from acetone at - 20 °C to give 0.39 g (35 % yield) of white powdery crystals.

Mp: 180.5-182.0 °C. ^{1}H NMR ($CDCl_3$): 1.30 (s, 27H, *t*-butyl), 1.94 (m, 3H, CH_3), 3.82 (t, *J*=4.8 Hz, 2H, $OC\underline{H_2}CH_2OPh$), 3.86 (t, *J*=4.8 Hz, 2H, $OC\underline{H_2}CH_2O_2C$), 4.10 (t, *J*=4.8 Hz, 2H, $OCH_2C\underline{H_2}OPh$), 4.33 (t, *J*=4.8 Hz, 2H, $OCH_2C\underline{H_2}O_2C$), 5.55 (p, *J*=1.6 Hz, 1H, vinyl proton), 6.12 (dt, *J*=1.6 Hz, *J*=1.6 Hz, 1H, vinyl proton), 6.78 (d, *J*=8.8 Hz, 2H, arom), 7.01 (d, *J*=8.8 Hz, 2H, arom), 7.07 (d, *J*=8.8 Hz, 6H, arom), 7.23 (d, *J*=8.8 Hz, 6H, arom). ^{13}C NMR ($CDCl_3$, $CDCl_3$ ref. at 77.011): 18.33, 31.38, 34.30, 63.05, 63.87, 67.28, 69.31, 69.74, 113.07, 124.03, 125.81, 130.71, 132.23, 136.11, 139.85, 144.12, 148.30, 156.50, 167.39 (theory 19, found 19).

Blocking group/monomer (13). In a 50-mL flask the mono-triphenylmethyl ether of di(ethylene glycol) (1.5 g, 3.54 mmol) was dissolved in THF (20 mL, distilled over

Na/benzophenone). Methacryloyl chloride (0.74 g, 7.1 mmol) was added, followed by addition of pyridine (0.60 g, 7.1 mmol). The mixture was allowed to stir at room temperature for 9 hr. The residual solid after evaporation of the solvent was subjected to column chromatography (silica gel, $CHCl_3$) and the isolated product was further purified by recrystallization from ethanol at - 20 °C to give 1.3 g (74 % yield) of white powdery crystals.

Mp: 95.0-97.5 °C. ^1H NMR ($CDCl_3$): 1.93 (m, 3H, CH_3), 3.81 (t, J=4.8 Hz, 2H, OCH_2CH_2OPh), 3.85 (t, J=4.8 Hz, 2H, $OCH_2CH_2O_2C$), 4.10 (t, J=4.8 Hz, 2H, OCH_2CH_2OPh), 4.32 (t, J=4.8 Hz, 2H, $OCH_2CH_2O_2C$), 5.55 (p, J=1.6 Hz, 1H, vinyl proton), 6.12 (dt, J=1.6 Hz, J=1.6 Hz, 1H, vinyl proton), 6.78 (d, 8.8 Hz, 2H, arom), 7.09 (d, J=9.2 Hz, 2H, arom), 7.21 (m, 11H, arom). ^{13}C NMR ($CDCl_3$): 18.31, 63.84, 64.30, 67.30, 69.31, 69.71, 113.35, 125.79, 125.84, 127.40, 131.11, 132.18, 136.12, 139.24, 147.00, 156.66, 167.37 (theory 17, found 17). Anal. Calcd: C, 80.46; H, 6.55; found: C, 80.26; H, 6.60.

Side-chain polyrotaxane (14) (R=*t*-butyl). Compound **12** (0.23 g, 0.35 mmol) and 30c10 (2.3 g, 5.2 mmol) were mixed at 110 °C. To the mixture, toluene was added dropwise slowly until a homogeneous solution was obtained (ca 5 mL toluene added). To the mixture AIBN (ca. 2 mg, $6x10^{-6}$ mol) was added. The mixture was stirred at 80 °C for 3 days. The mixture was dissolved in $CHCl_3$ (10 mL) and the solution was poured into methanol (150 mL) with vigorous stirring. Three more precipitations were done. The product was dried under vacuum at room temperature to give 0.20 g (87 % yield) of a white solid.

Side-chain polyrotaxane (14) (R=H). In a 50 mL flask equipped with a Teflon valve and a magnetic stirring bar, a solution of **13** (0.20 g, 0.41 mmol), 30c10 (2.0 g, 4.5 mmol) and AIBN (0.6 mg, $4x10^{-6}$ mol) was subjected to three cycles of freeze-pump-thaw processes on a vacuum line ($1x10^{-5}$ mmHg). The flask was placed in an oil bath at 90 ℃ and the mixture was allowed to stir for 26 hr. The product was isolated by three reprecipitations from $CHCl_3$ solution (ca. 10 mL) into methanol (200 mL). The product was dried under vacuum at room temperature to give 0.17 g (85 % yield) of white solid.

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molecular weights and distributions, however, are unknown at this point.

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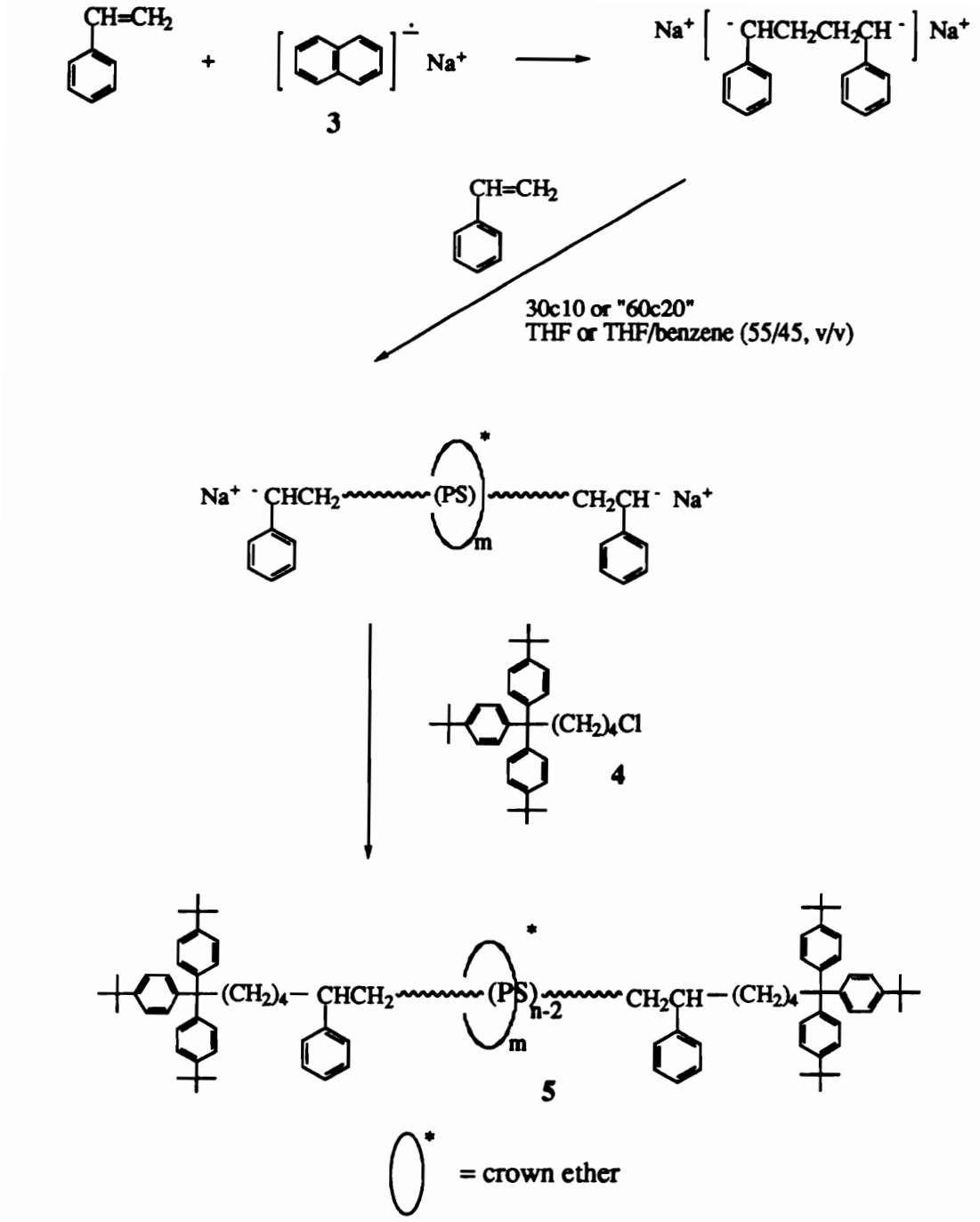
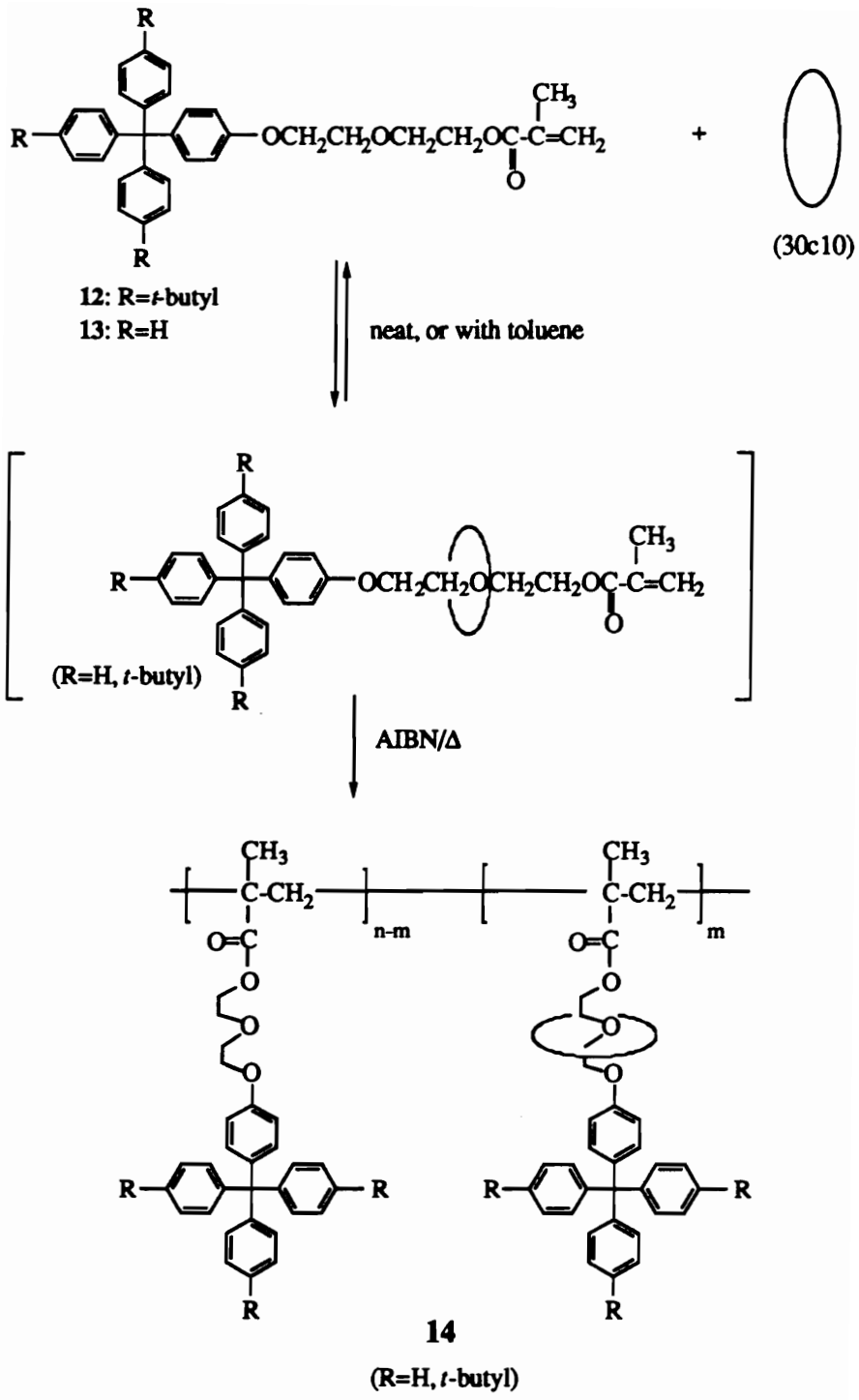


Scheme 1. Synthesis of poly(styrene-rotaxa-crown ether)s (**1**) by anionic polymerization



Scheme 2. Syntheses of side-chain polyrotaxanes.

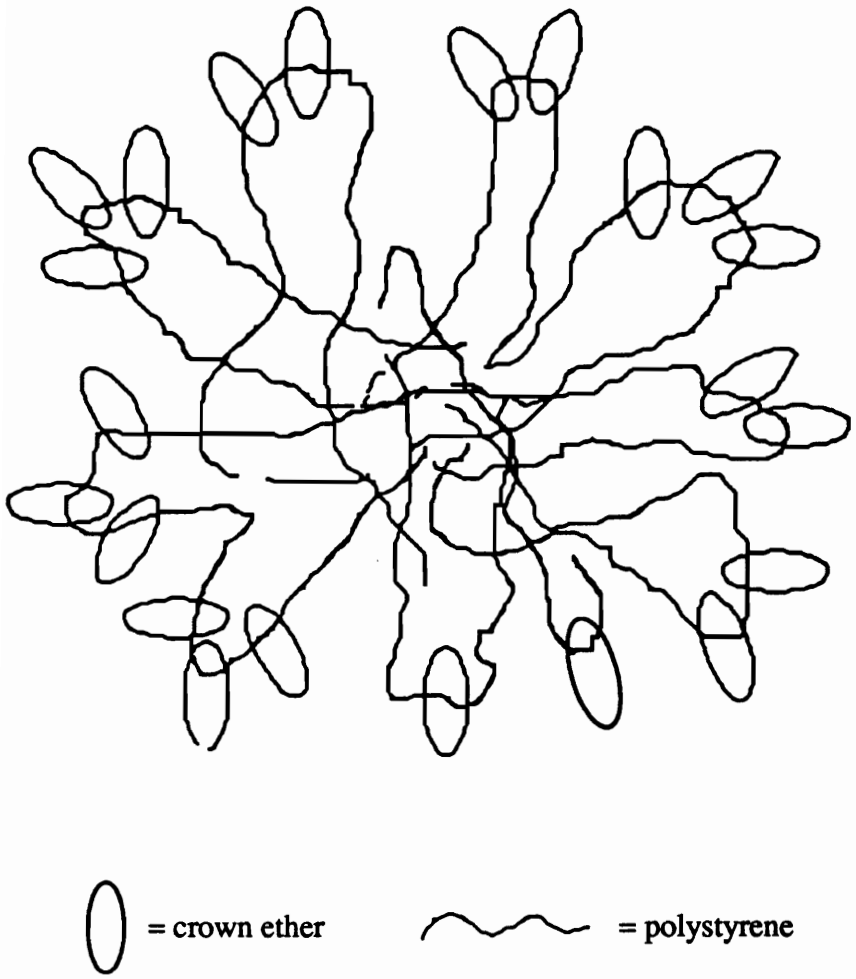


Figure 1. Polystyrene micelle stabilized by threaded crown ether.

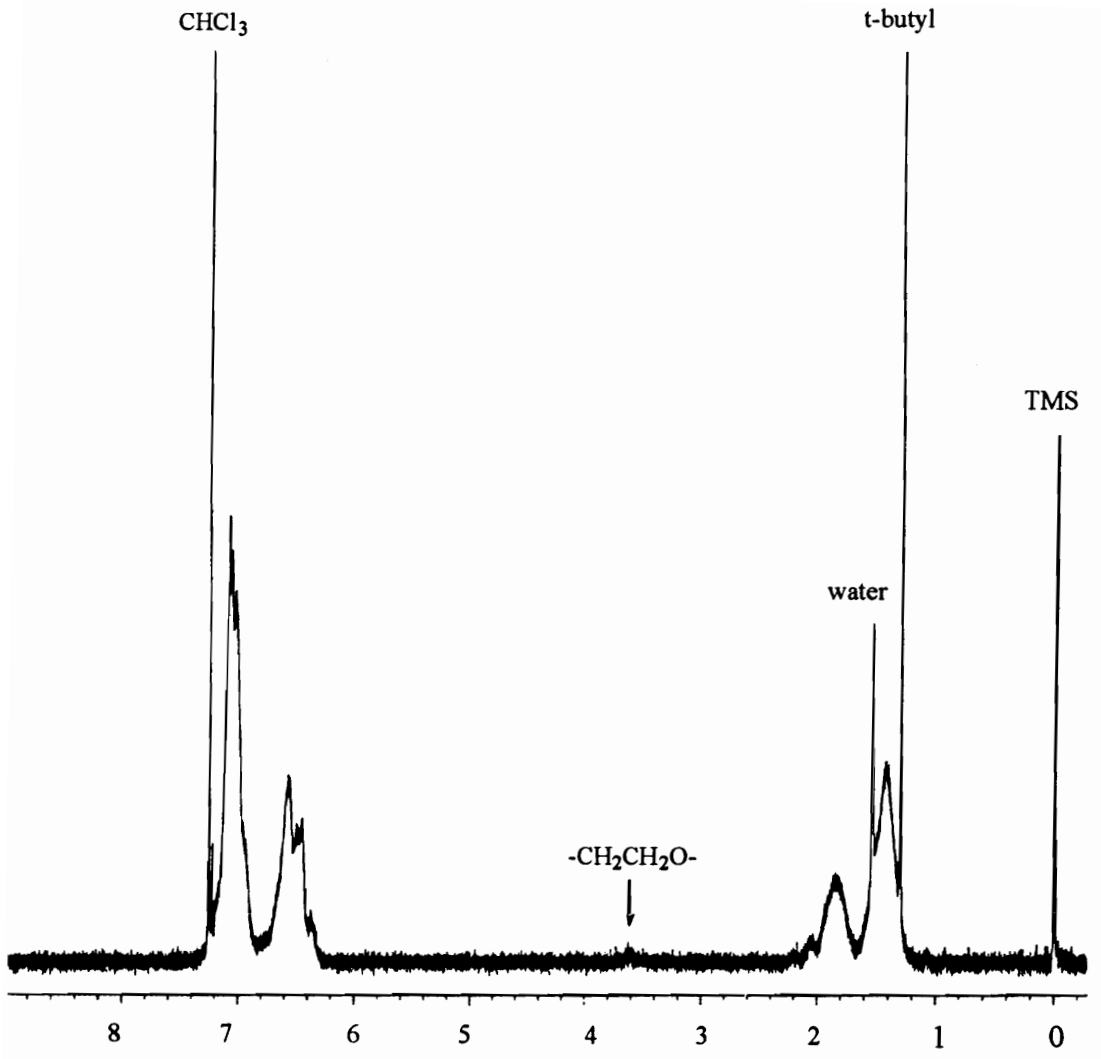


Figure 2. ^{1}H NMR spectrum of polystyrene obtained from control reaction using BG/init **6** and 18-crown-6. ($CDCl_3$)

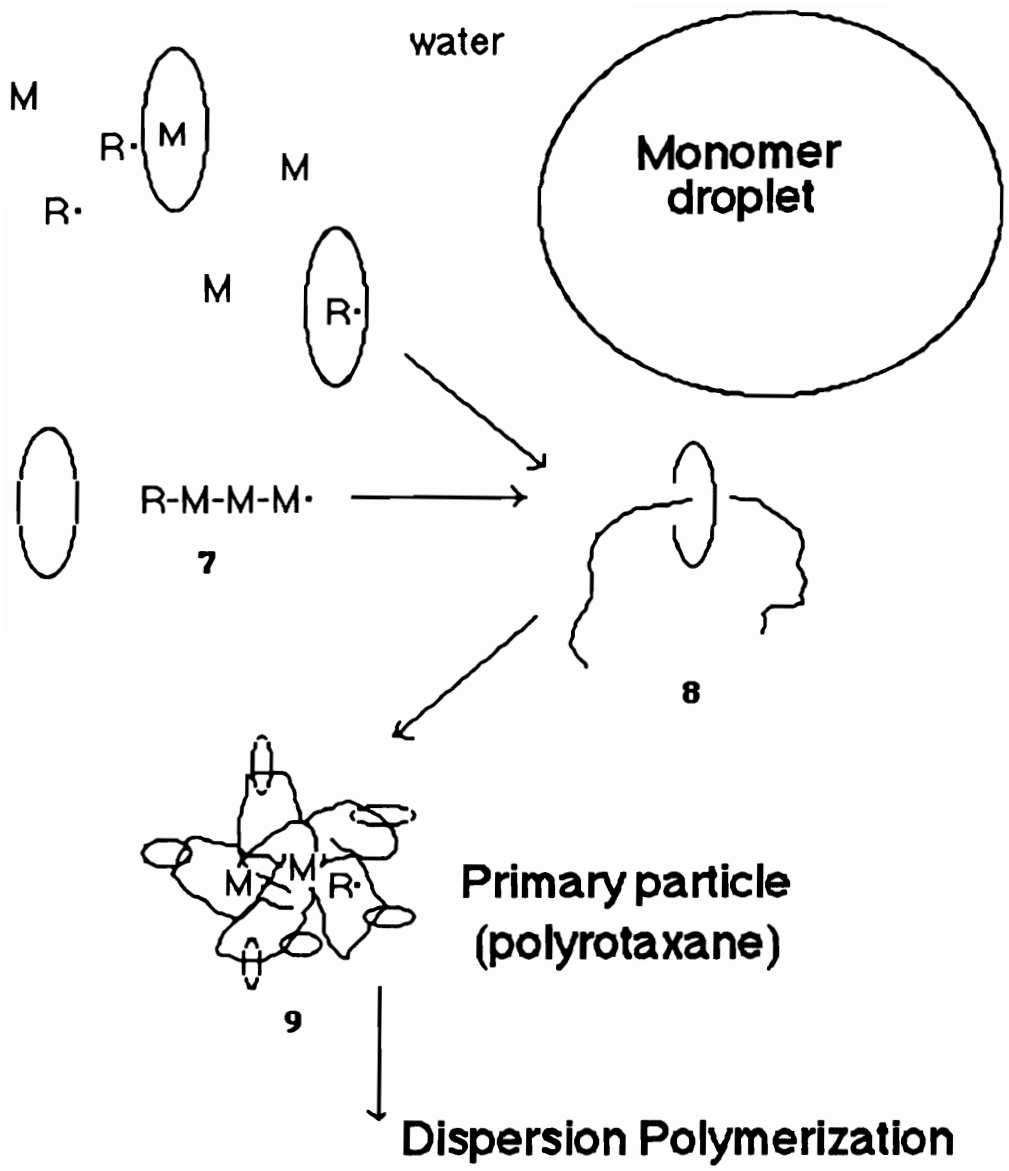


Figure 3. Mechanism of dispersion polymerization of styrene with "42c14"

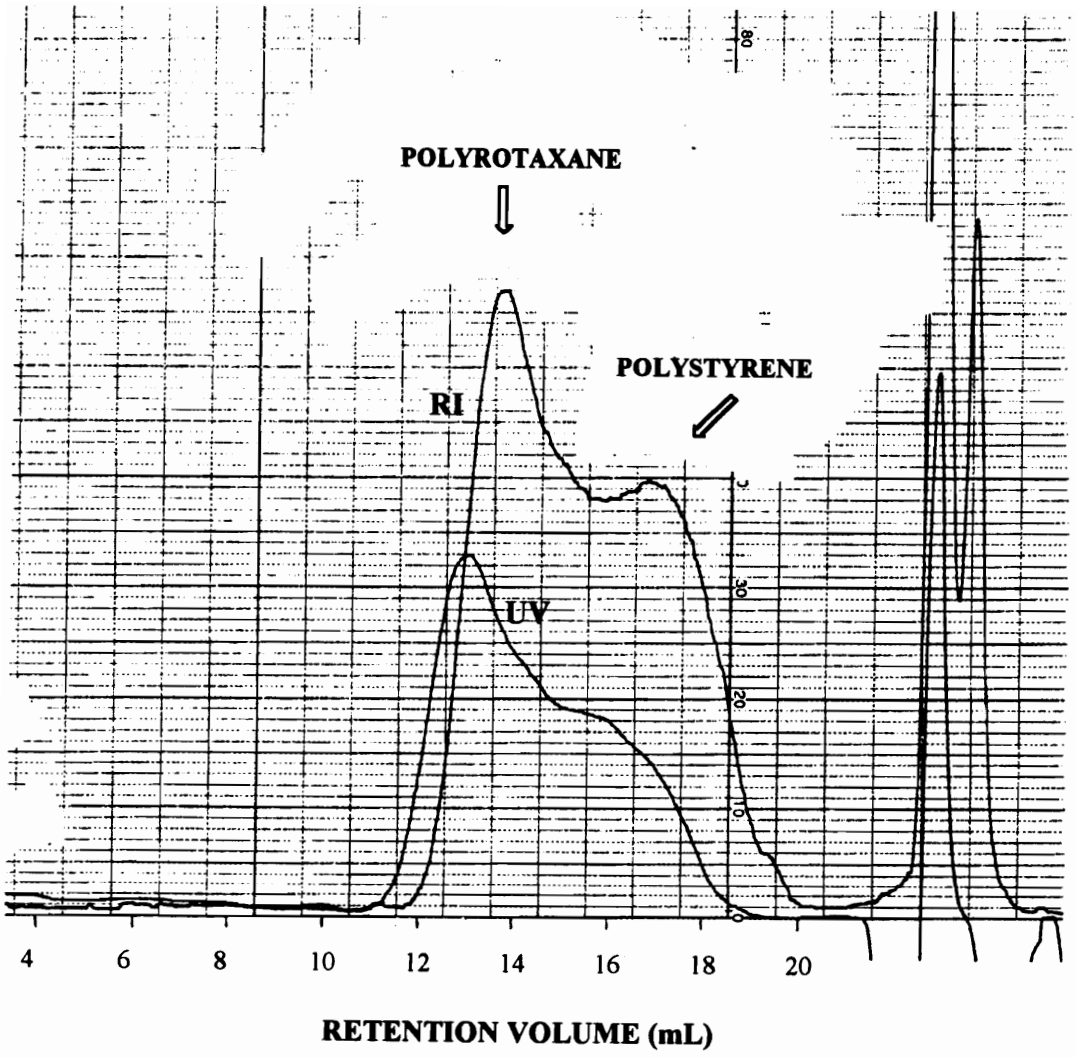


Figure 4. GPC traces of the product (Batch P2) eluted from the silica gel column with CH_2Cl_2 and THF. (THF, PS standards, RI and UV detectors)

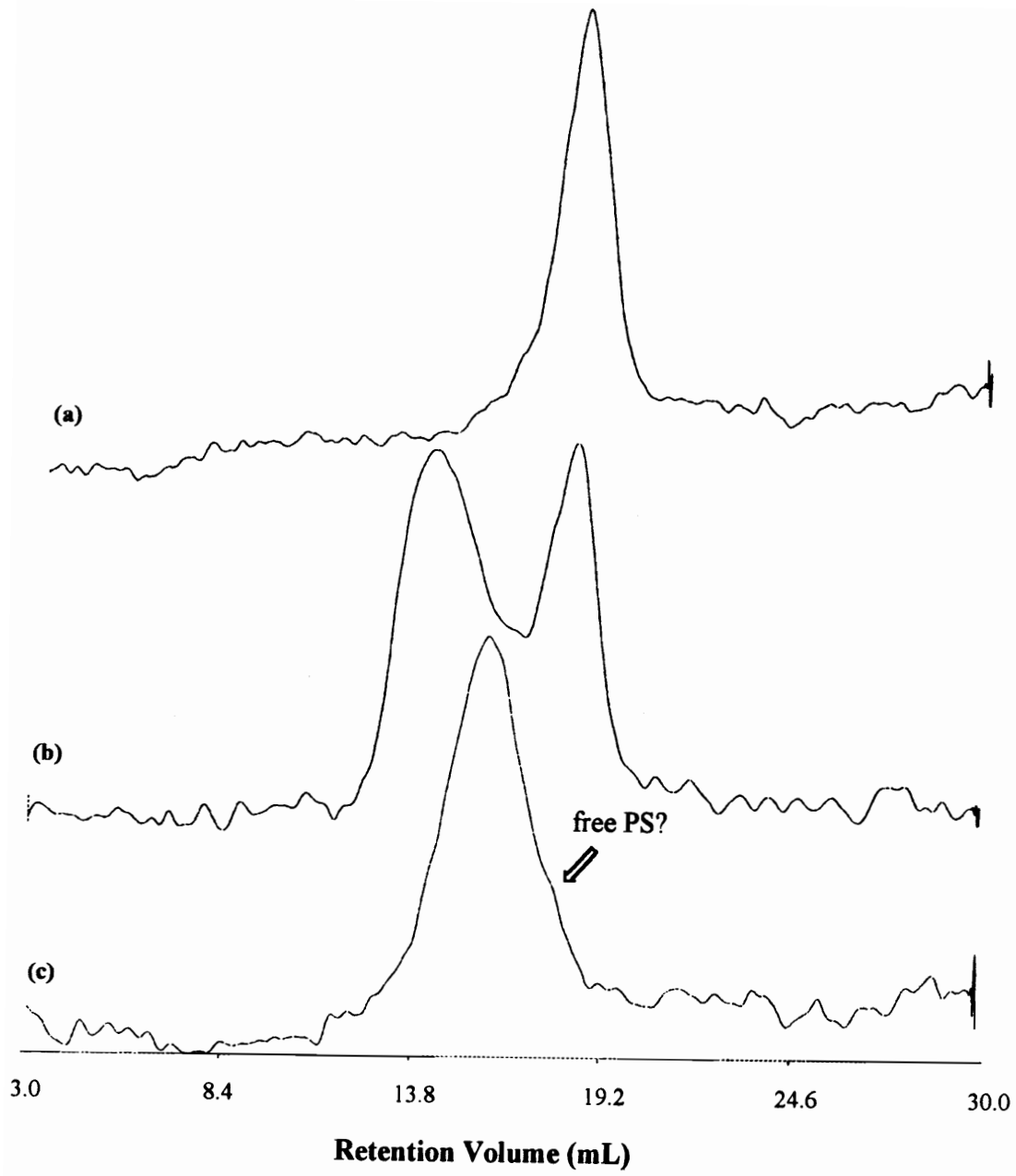


Figure 5. GPC traces of (a) "42c14" (M_n=2.4 kg/mol, Pd=1.08), (b) a blend of PS (M_n=35.5 kg/mol, Pd=2.4) and "42c14" (50 mass %), and (c) poly(styrene-rotaxa-"42c14") (P5, M_n=23.4 kg/mol, Pd=1.3): PS standards, solvent $CHCl_3$, differential viscometric detector.

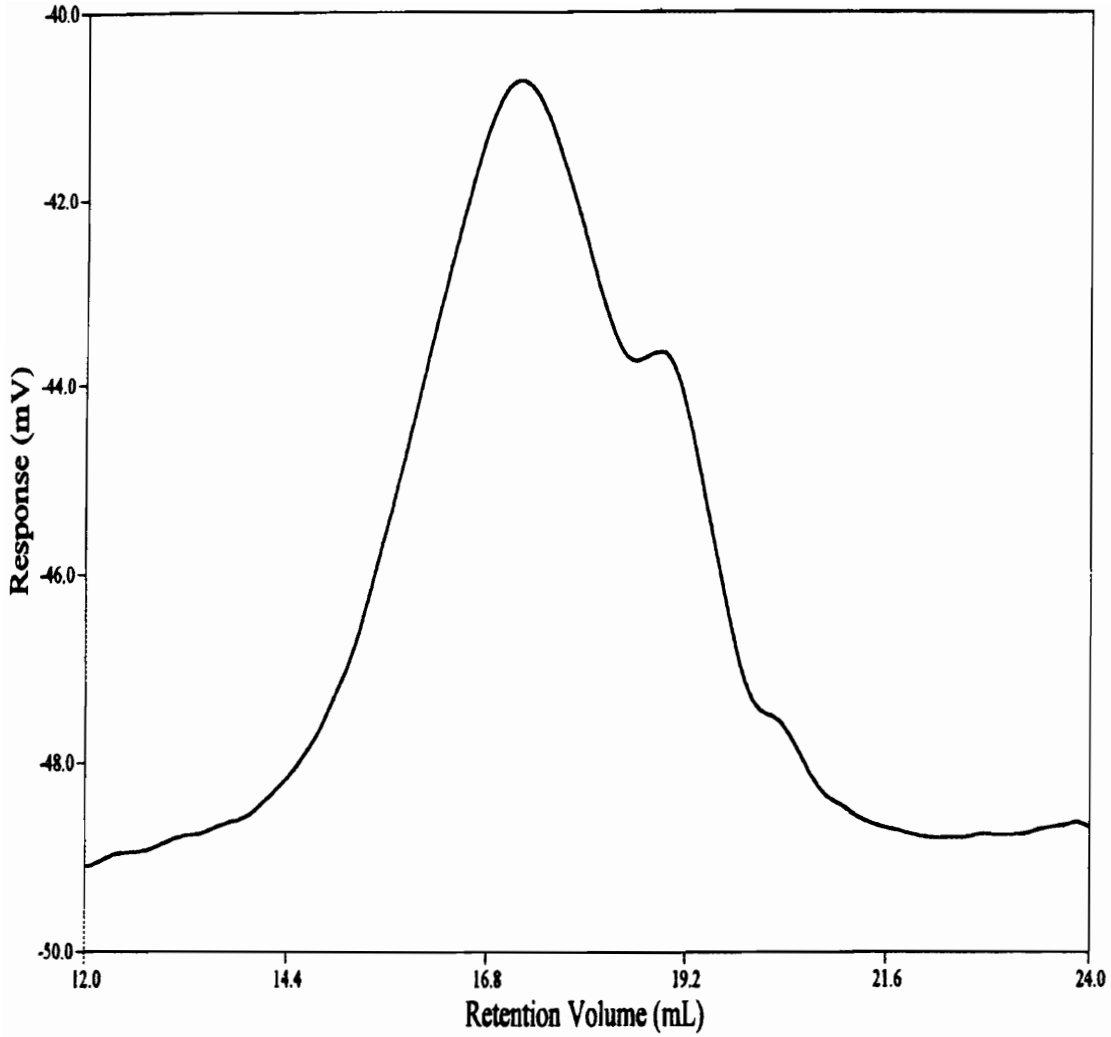


Figure 6. GPC trace of '60c20" (M_n=1.8 kg/mol, Pd=2.10) ($CHCl_3$, PS standards, differential viscometric detector)

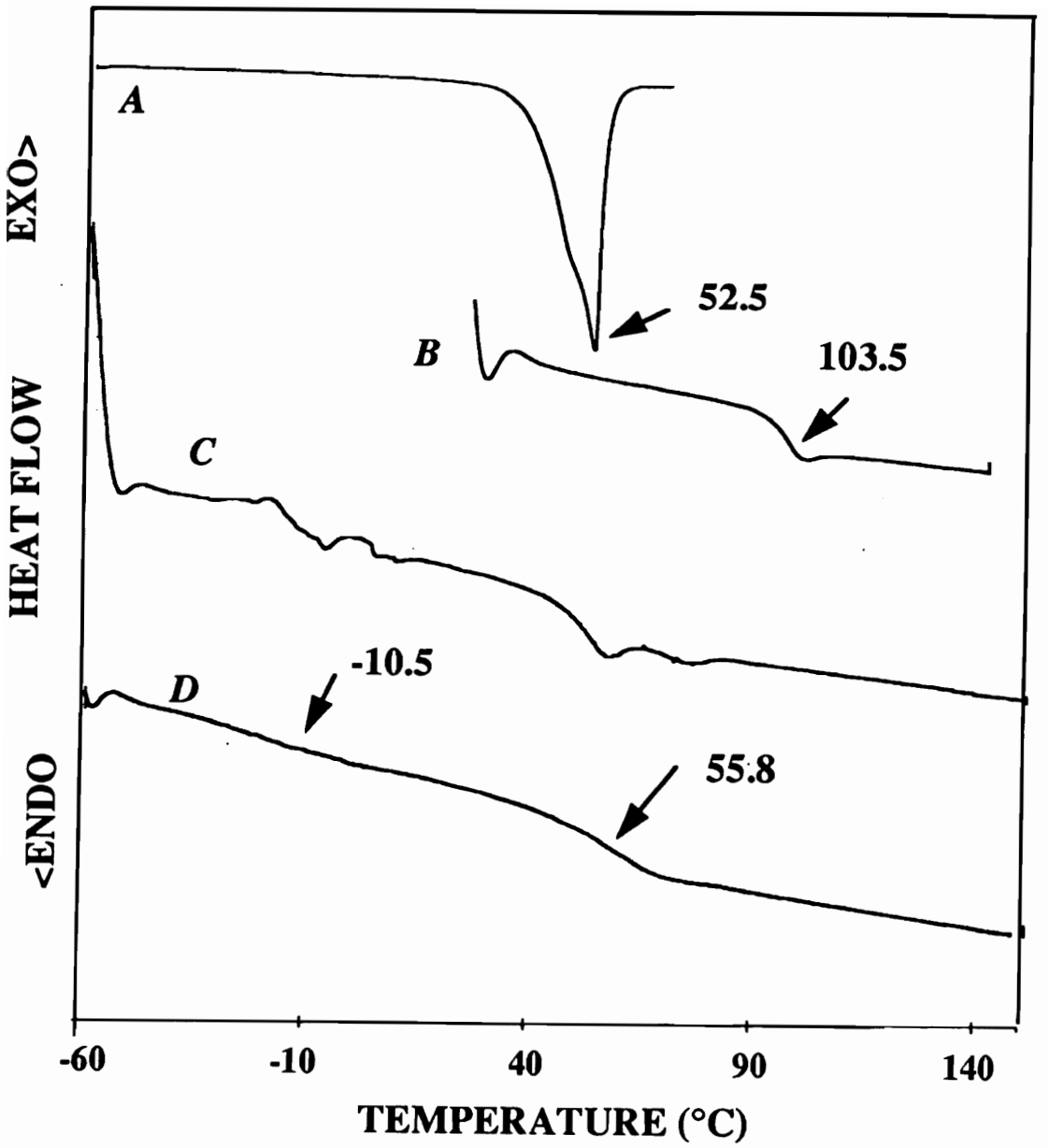


Figure 7. DSC traces of (A) "42c14" (second heat), (B) PS (M_n=15.2 kg/mol, third heat), (C) and (D) PS-rotaxa-"42c14" (M_n=23.4 kg/mol, P5 Table 5, 21 wt % threading, first and second heat, respectively). Heating rate: 10 °C/min.

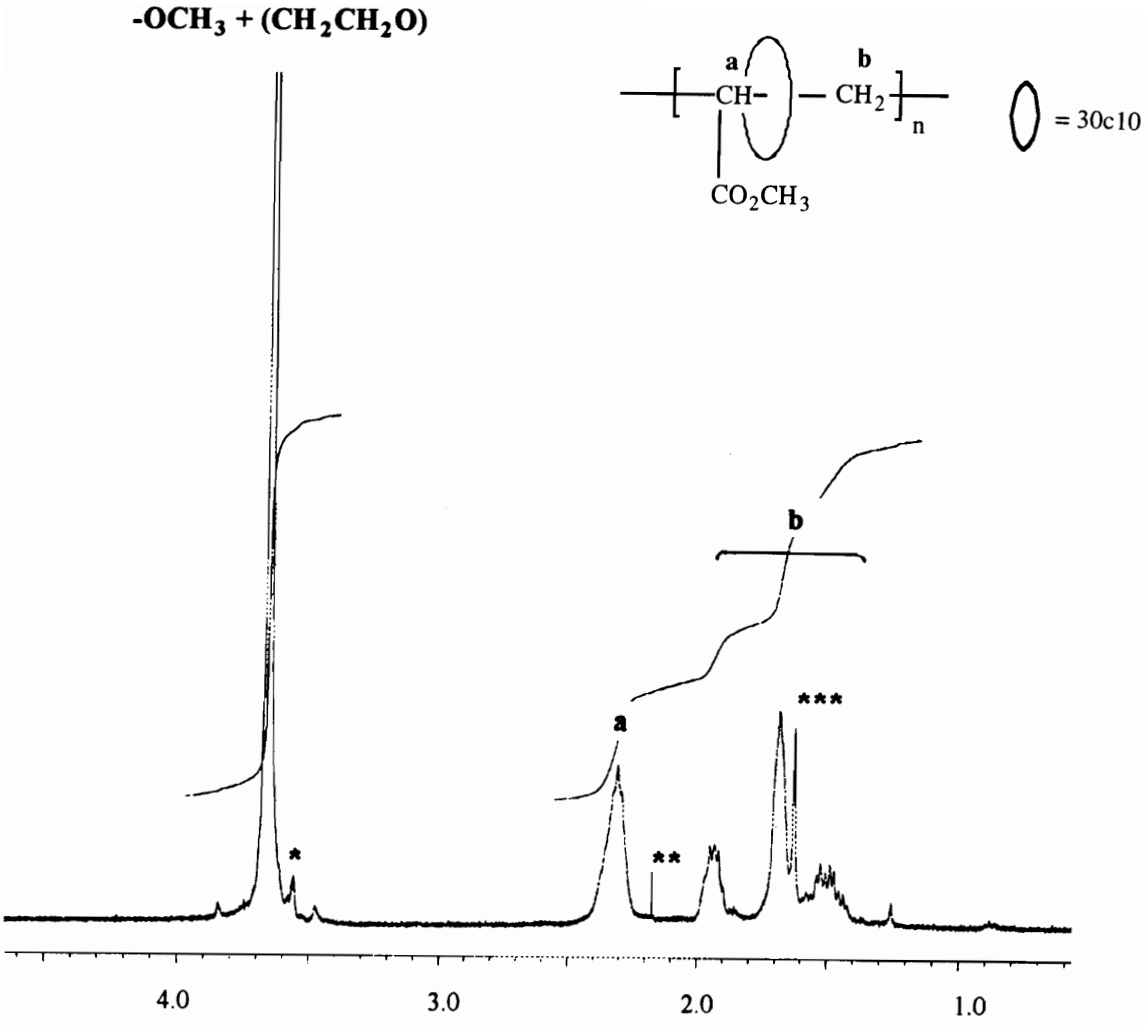


Figure 8. ^{1}H NMR spectrum of PMA-rotaxa-30c10 (Batch P7). ($CDCl_3$)

* crown ether species from chain transfer

** acetone *** water

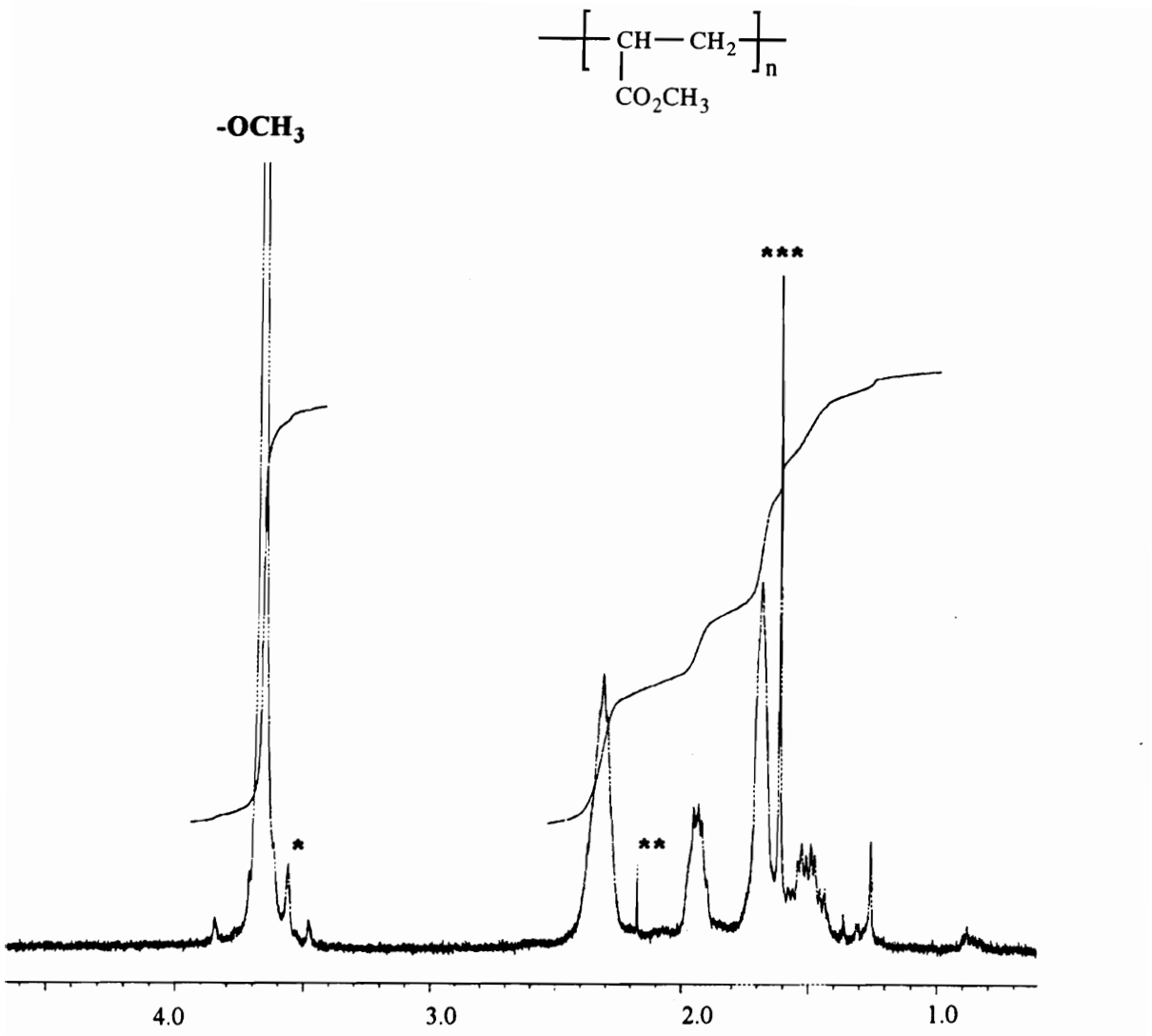


Figure 9. ^{1}H NMR spectrum of PMA from control experiment, Batch P10. ($CDCl_3$)

* crown ether species from chain transfer

** acetone *** water

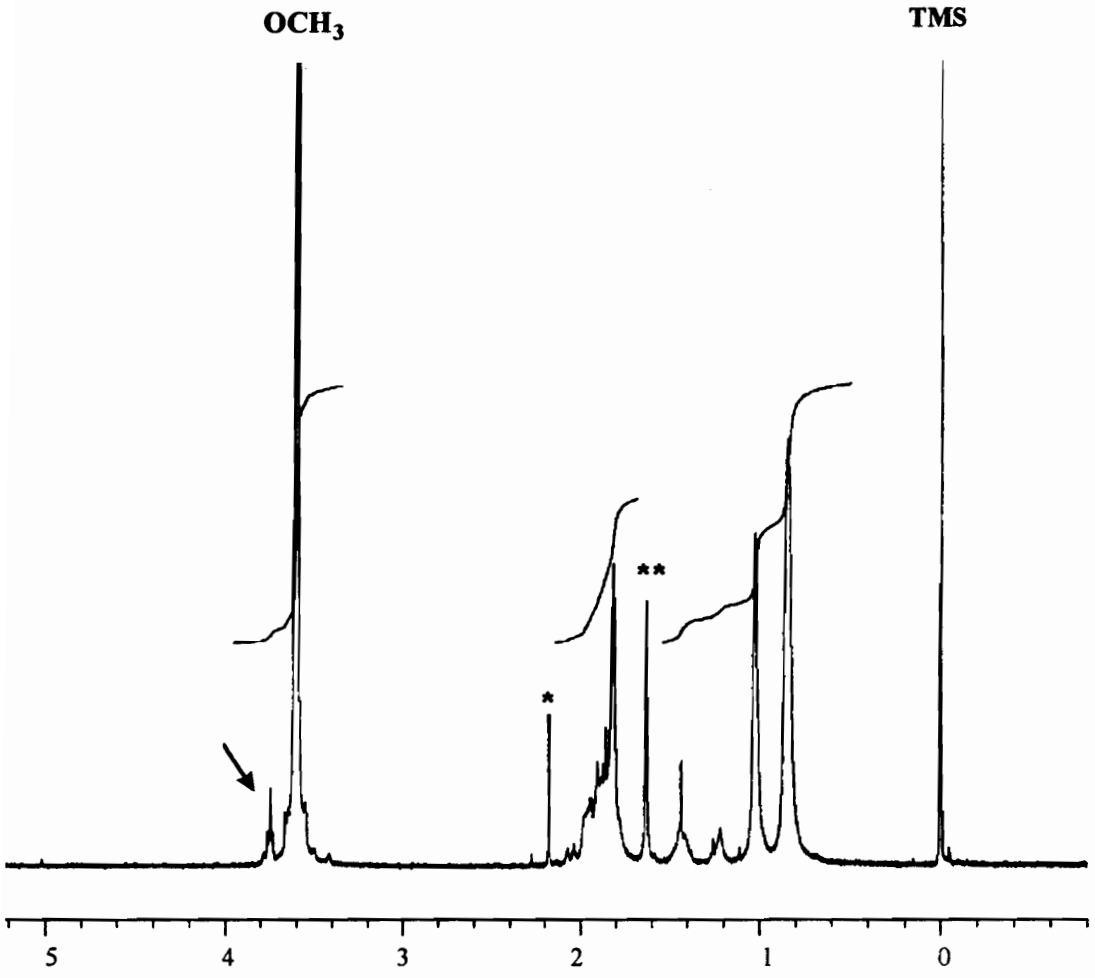


Figure 10. ^{1}H NMR spectrum of PMMA-rotaxa-30c10, Batch P8. ($CDCl_3$)
* acetone ** water

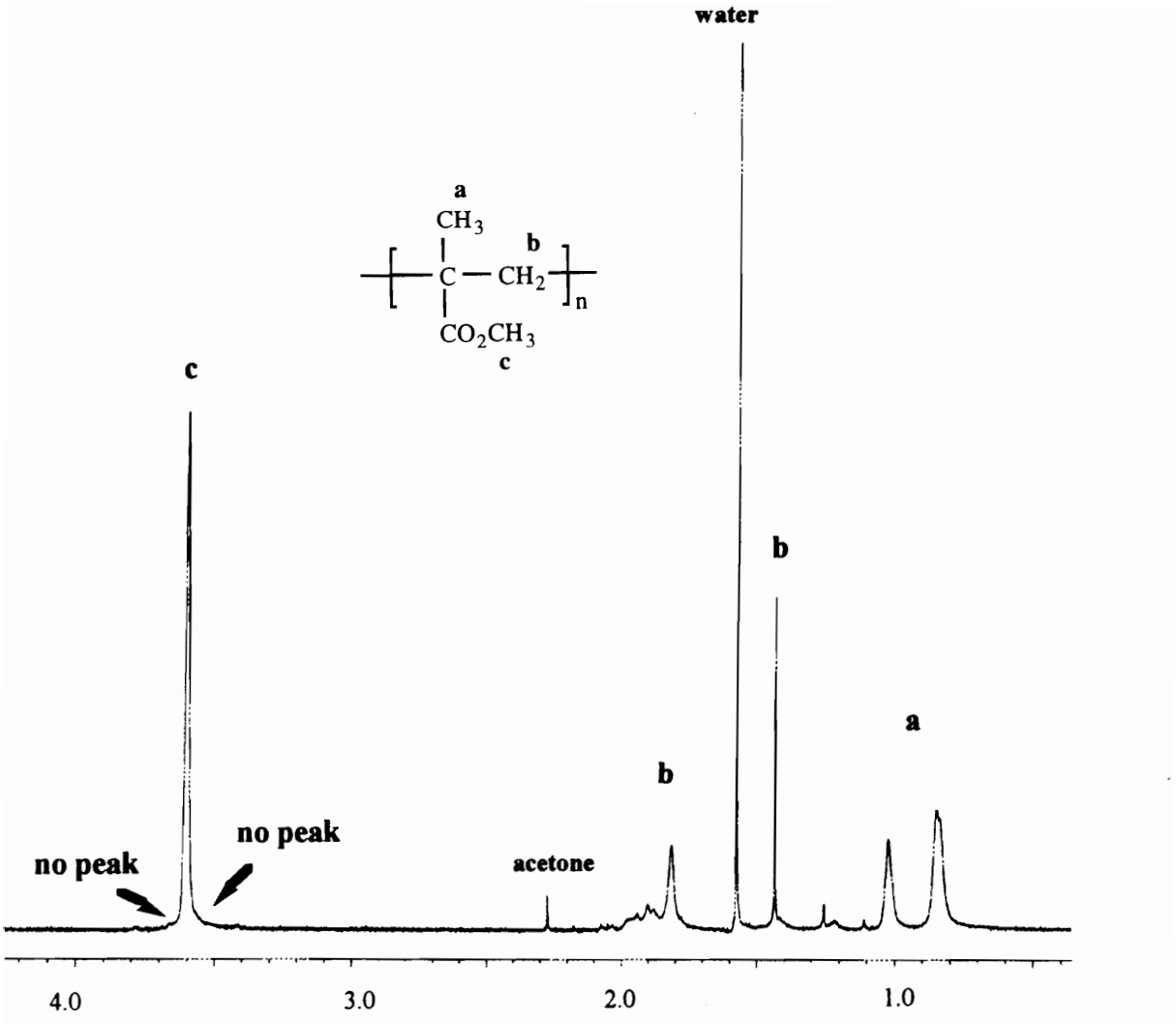


Figure 11. ^{1}H NMR spectrum of PMMA, Batch P11. ($CDCl_3$)

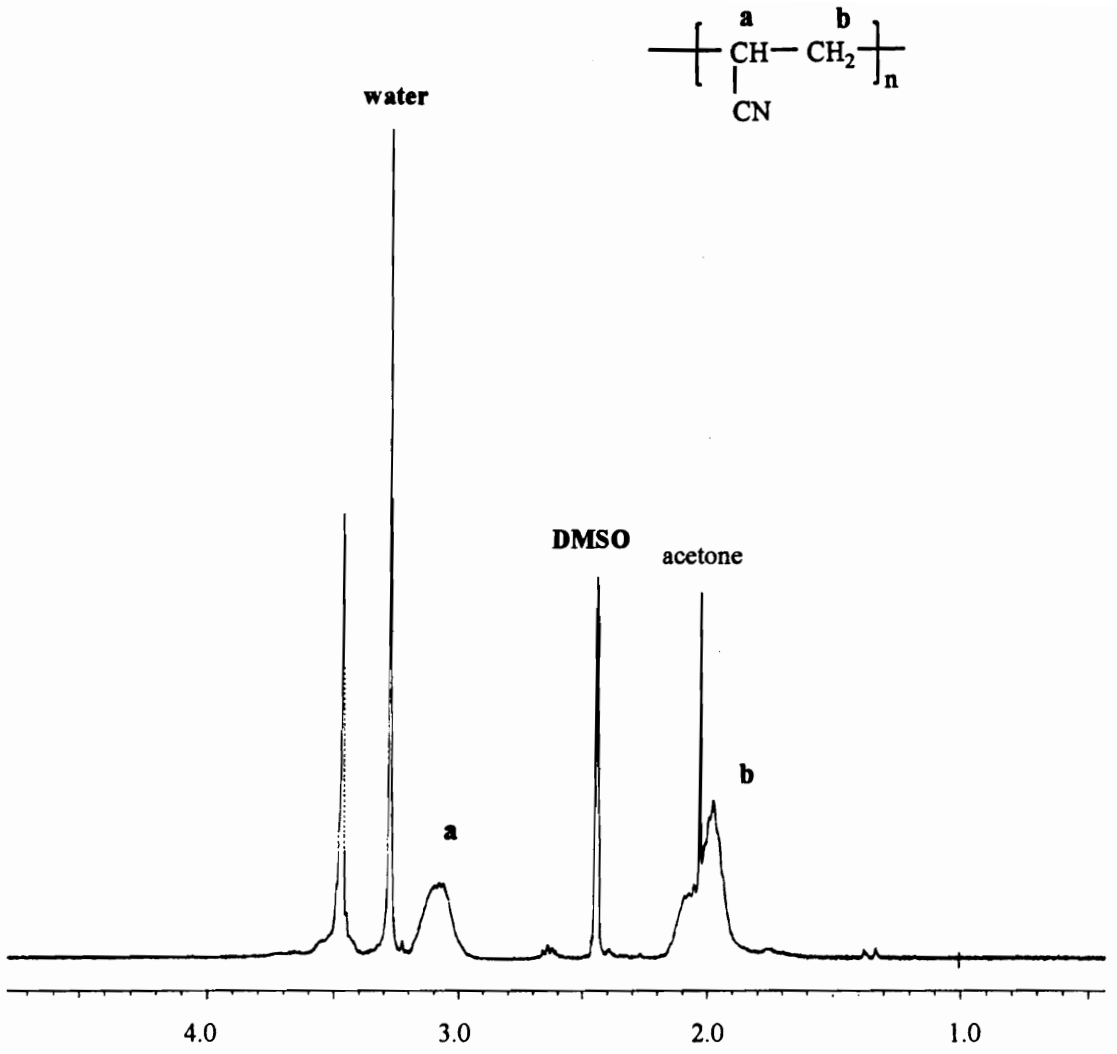


Figure 12. ^{1}H NMR spectrum of PAN, Batch P9. (DMSO-d_6)

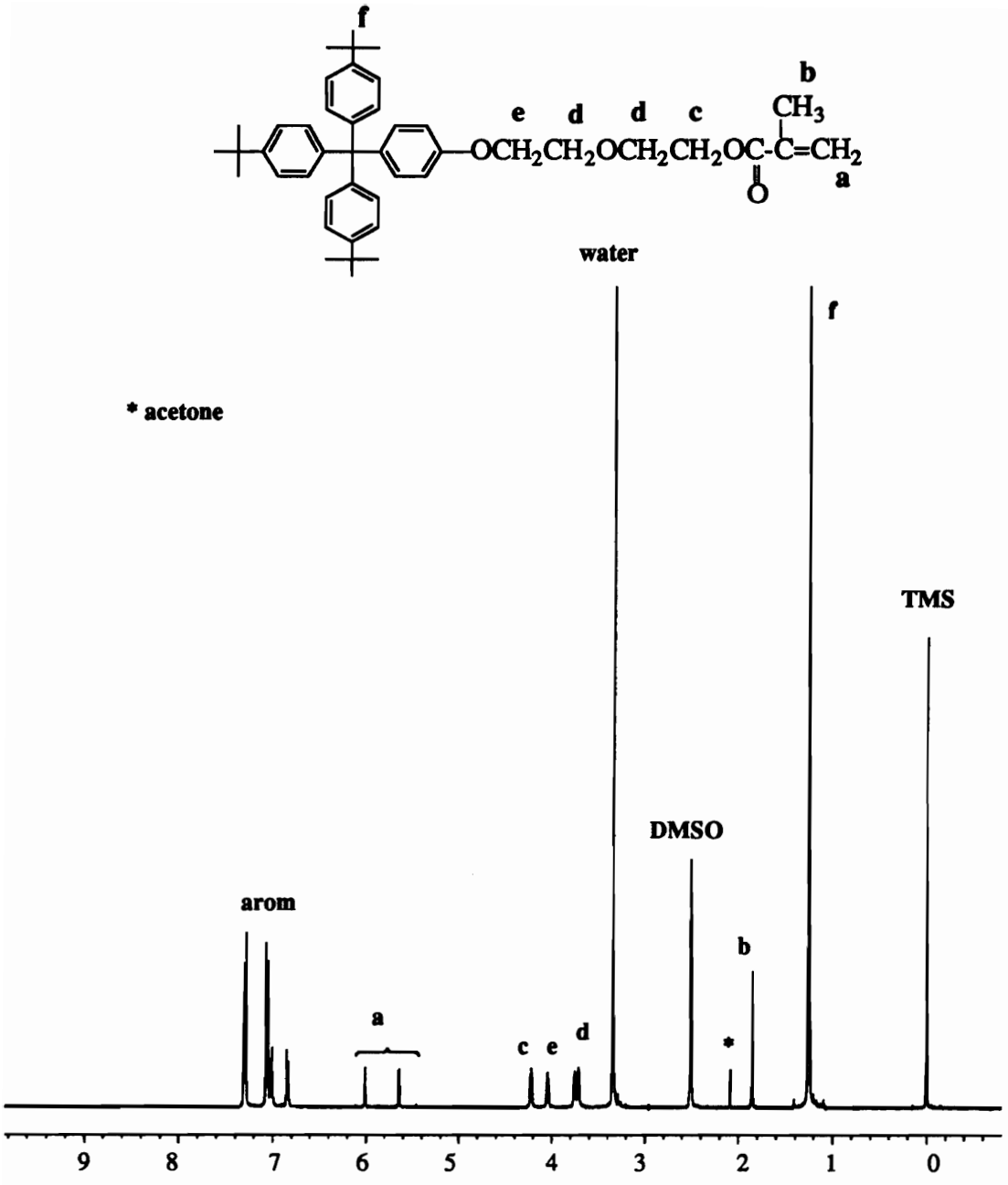


Figure 13. ^{1}H NMR spectrum of **12**. (DMSO-d_6)
* acetone

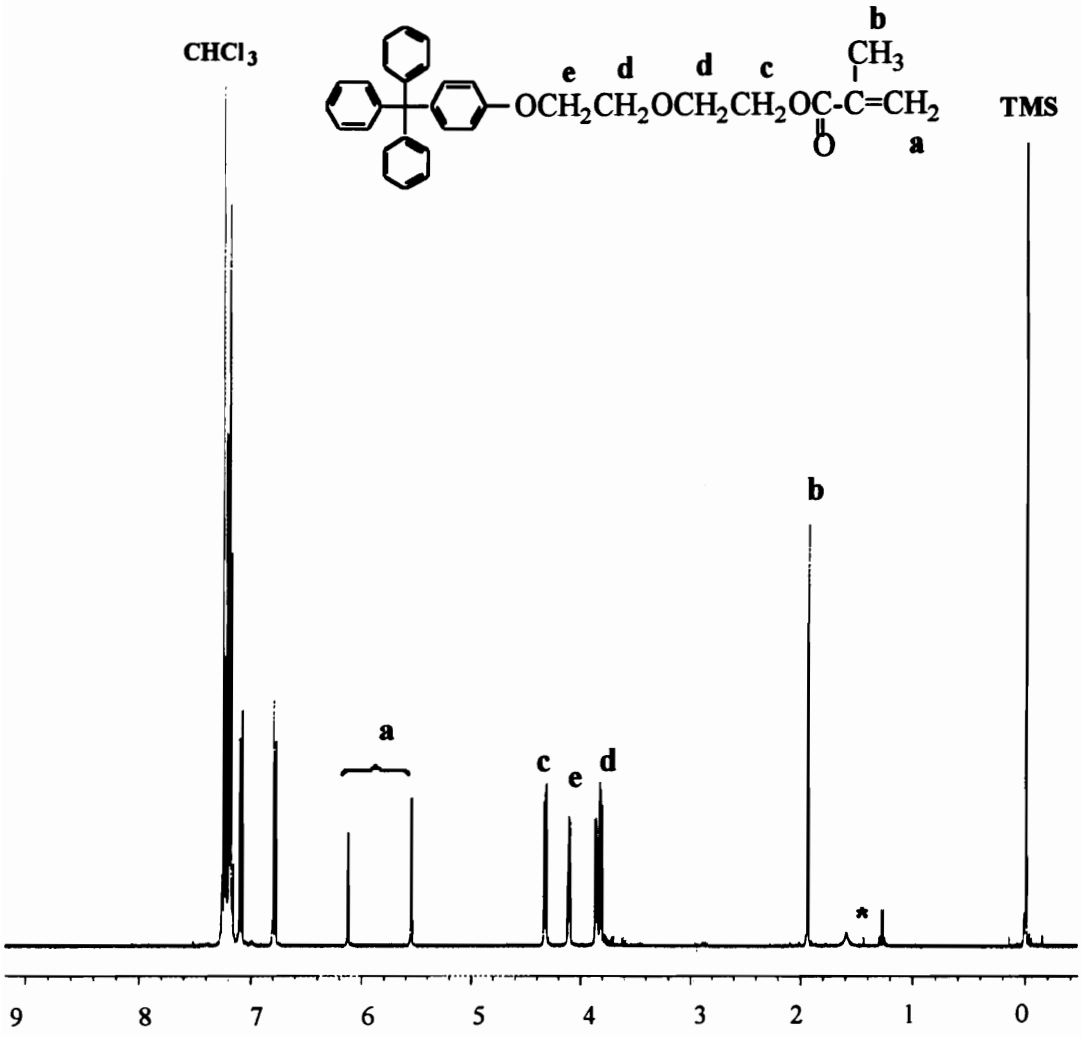


Figure 14. ^{1}H NMR spectrum of **13**. ($CDCl_3$)
* water

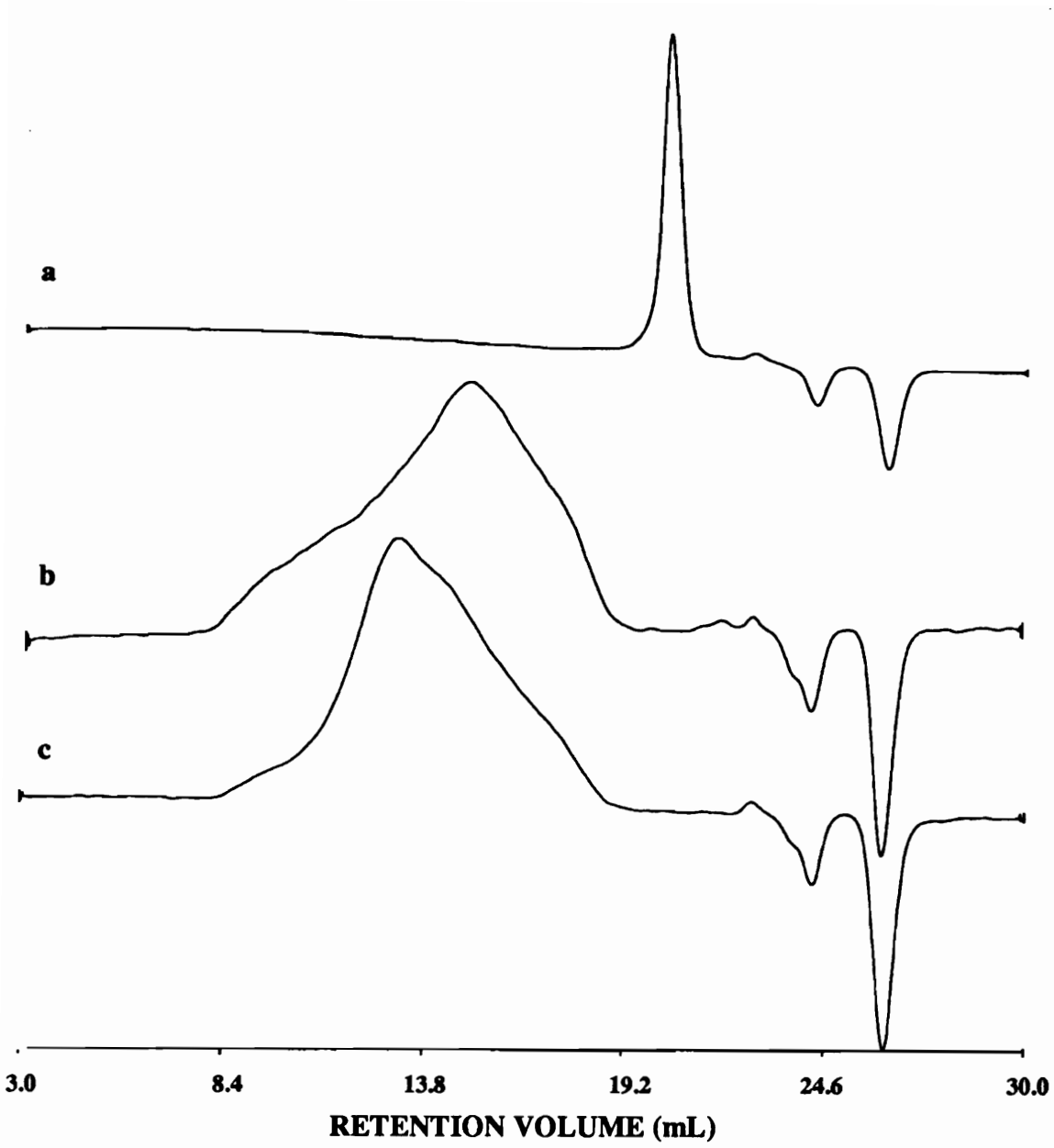


Figure 15. GPC traces of (a) 30c10 (M_n=1.3 kg/mol, Pd=1.01), (b) poly(**12**-rotaxa-30c10) (M_n=49.7 kg/mol, Pd=55.3), and (c) poly(**13**-rotaxa-30c10) (M_n=65.9 kg/mol, Pd=16.1): PS standards, solvent $CHCl_3$, RI detector.

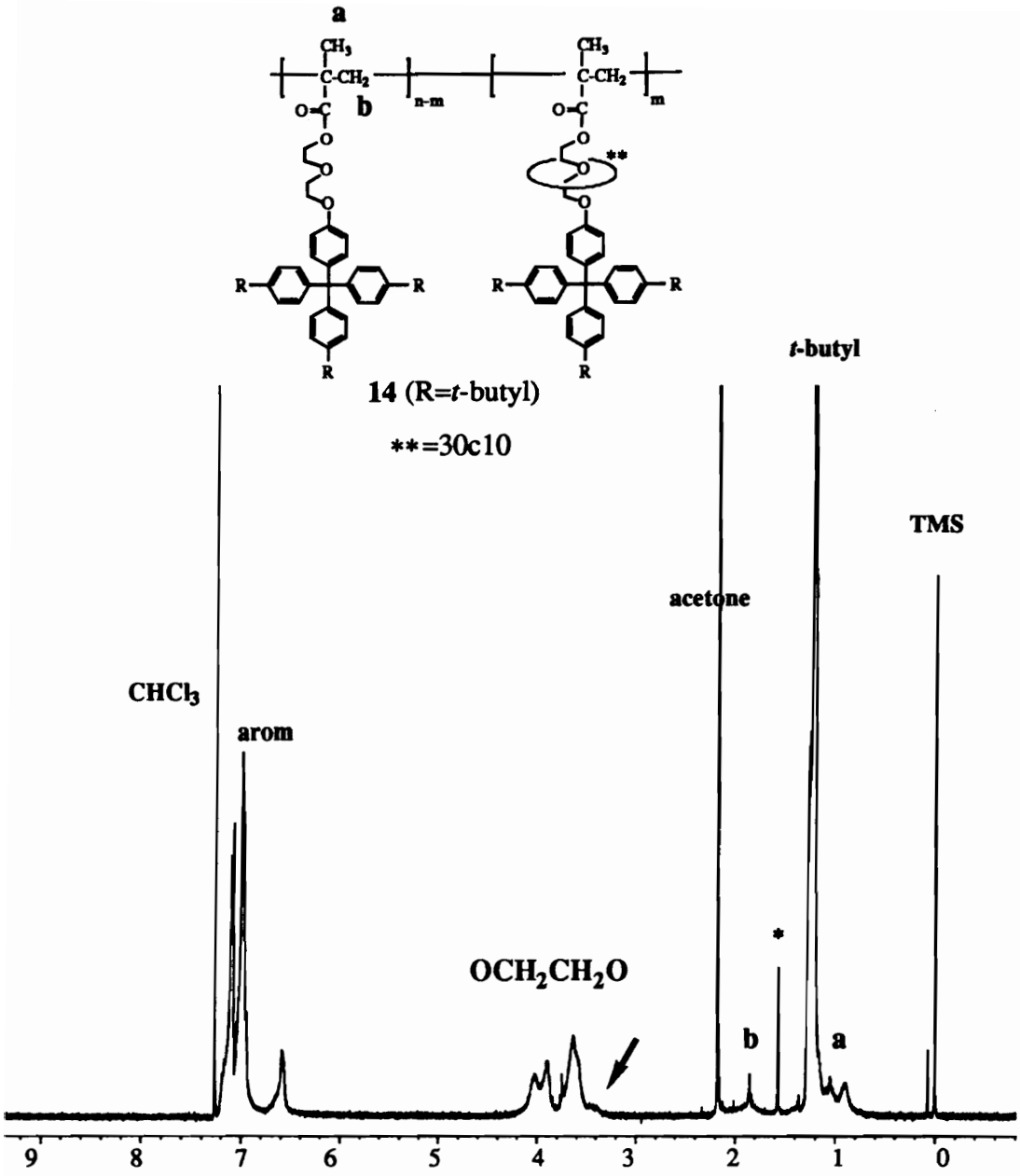


Figure 16. ^{1}H NMR spectrum of poly(**12**-rotaxa-30c10) (**14**, R=*t*-butyl). ($CDCl_3$)
* water

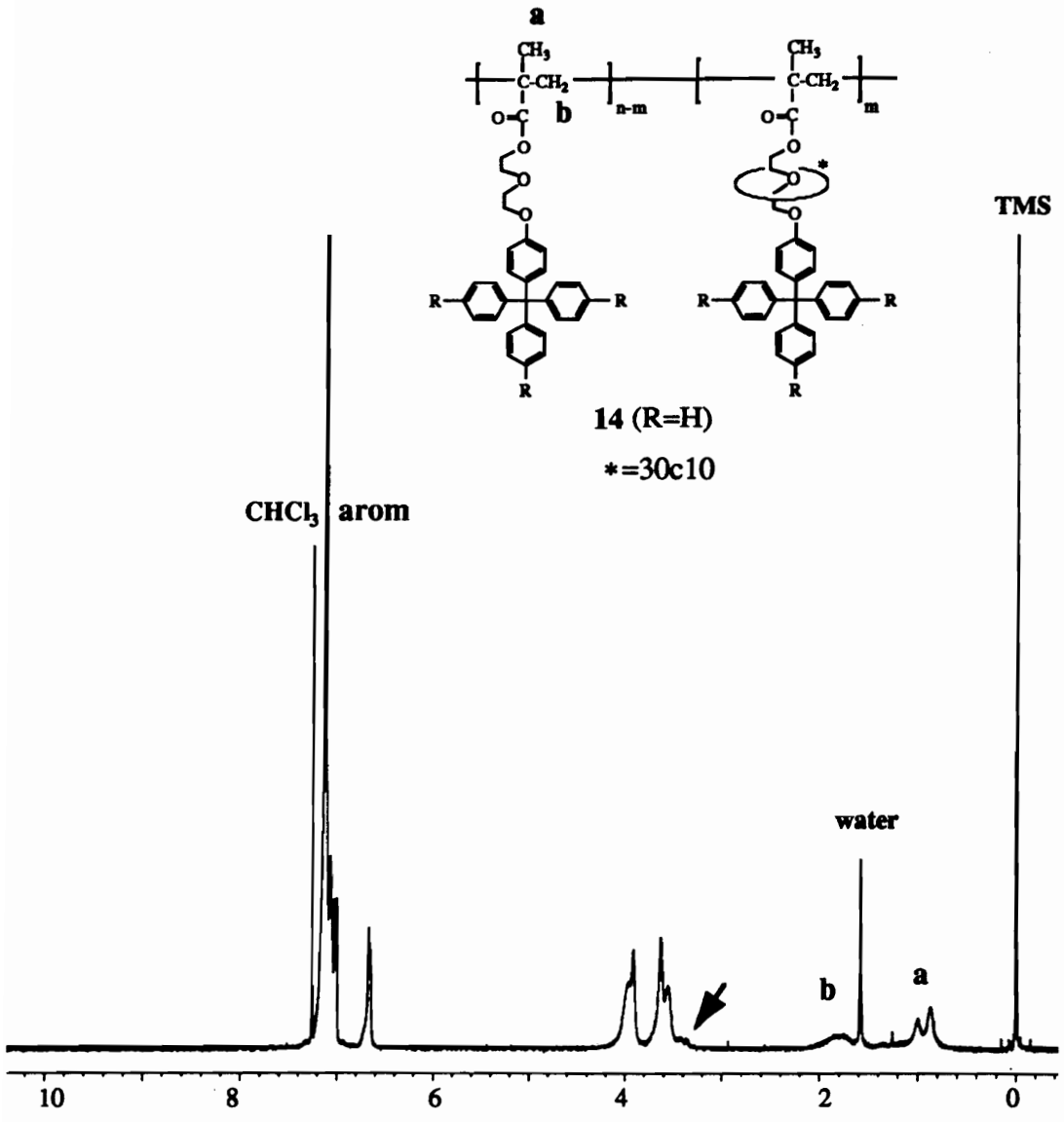


Figure 17(a). ^{1}H NMR spectrum of poly(**13**-rotaxa-30c10) (**14**, R=H). ($CDCl_3$)

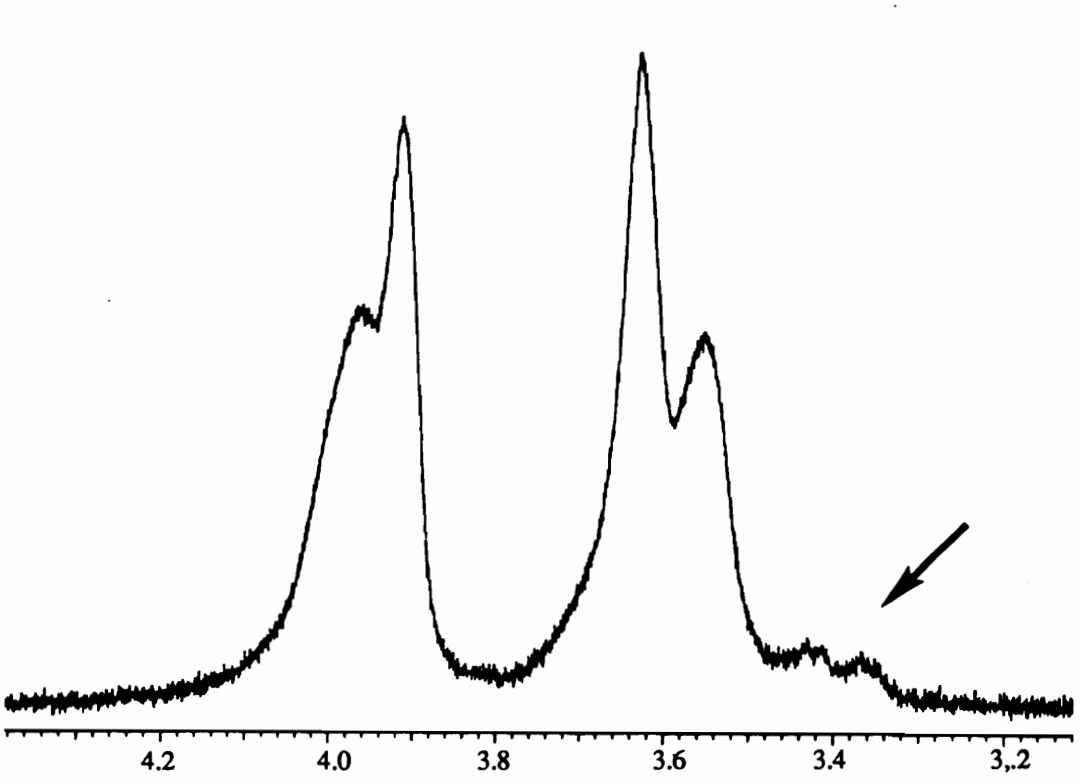


Figure 17(b). ^{1}H NMR spectrum of poly(**13**-rotaxa-30c10) (**14**, R=H). (expanded, $CDCl_3$)

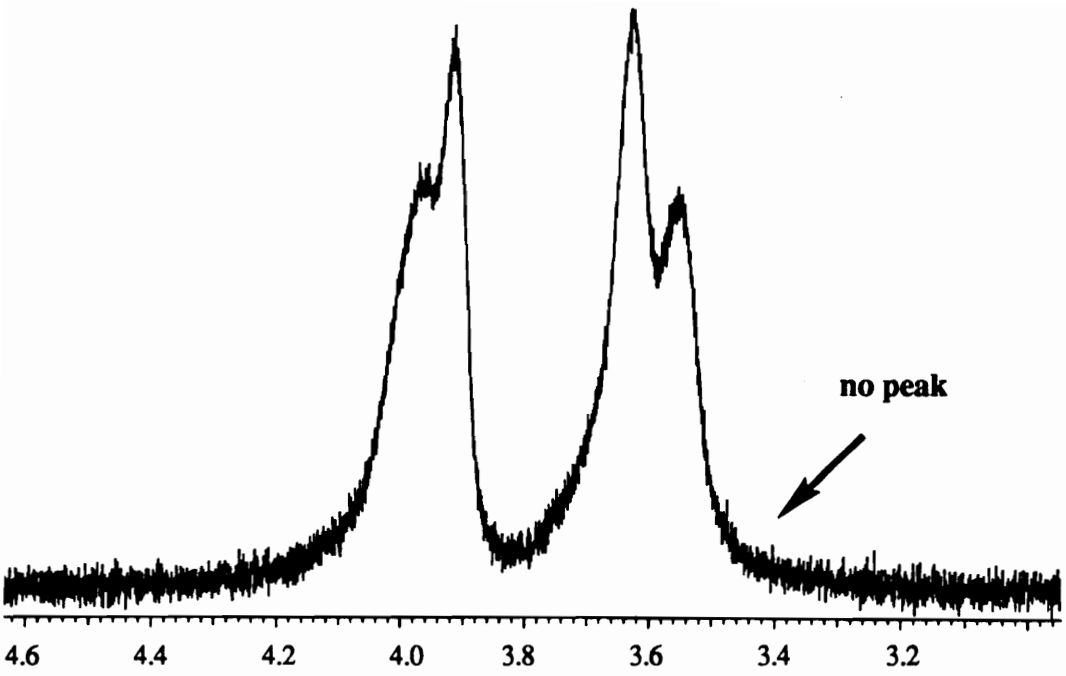


Figure 18. ^{1}H NMR spectrum of poly(**13**) (**14**, R=H, m=0) prepared in the presence of 18c6. (expanded, $CDCl_3$)

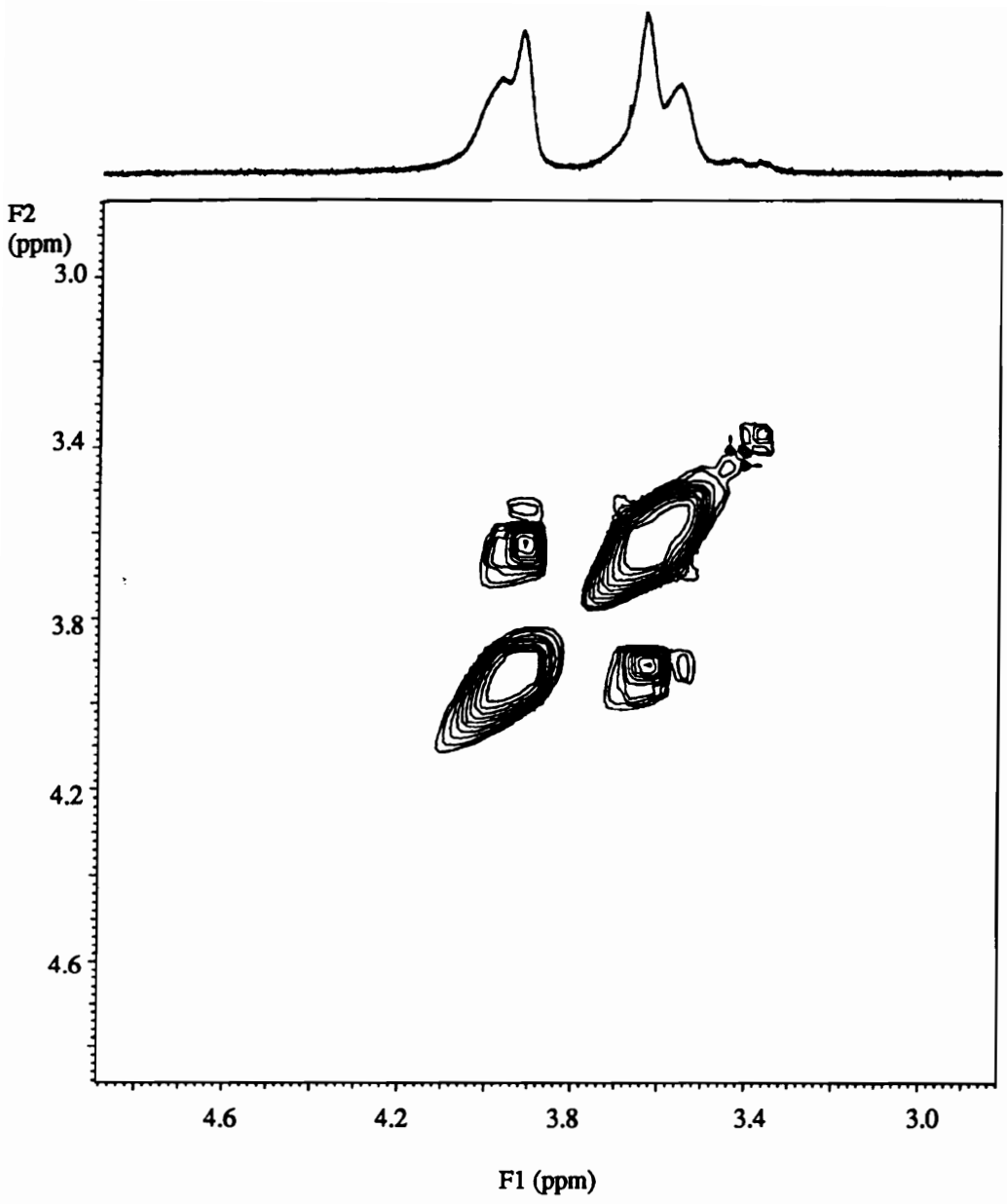


Figure 19(a). 2D COSY spectrum of poly(**13**-rotaxa-30c10) (**14**, R=H). ($CDCl_3$)

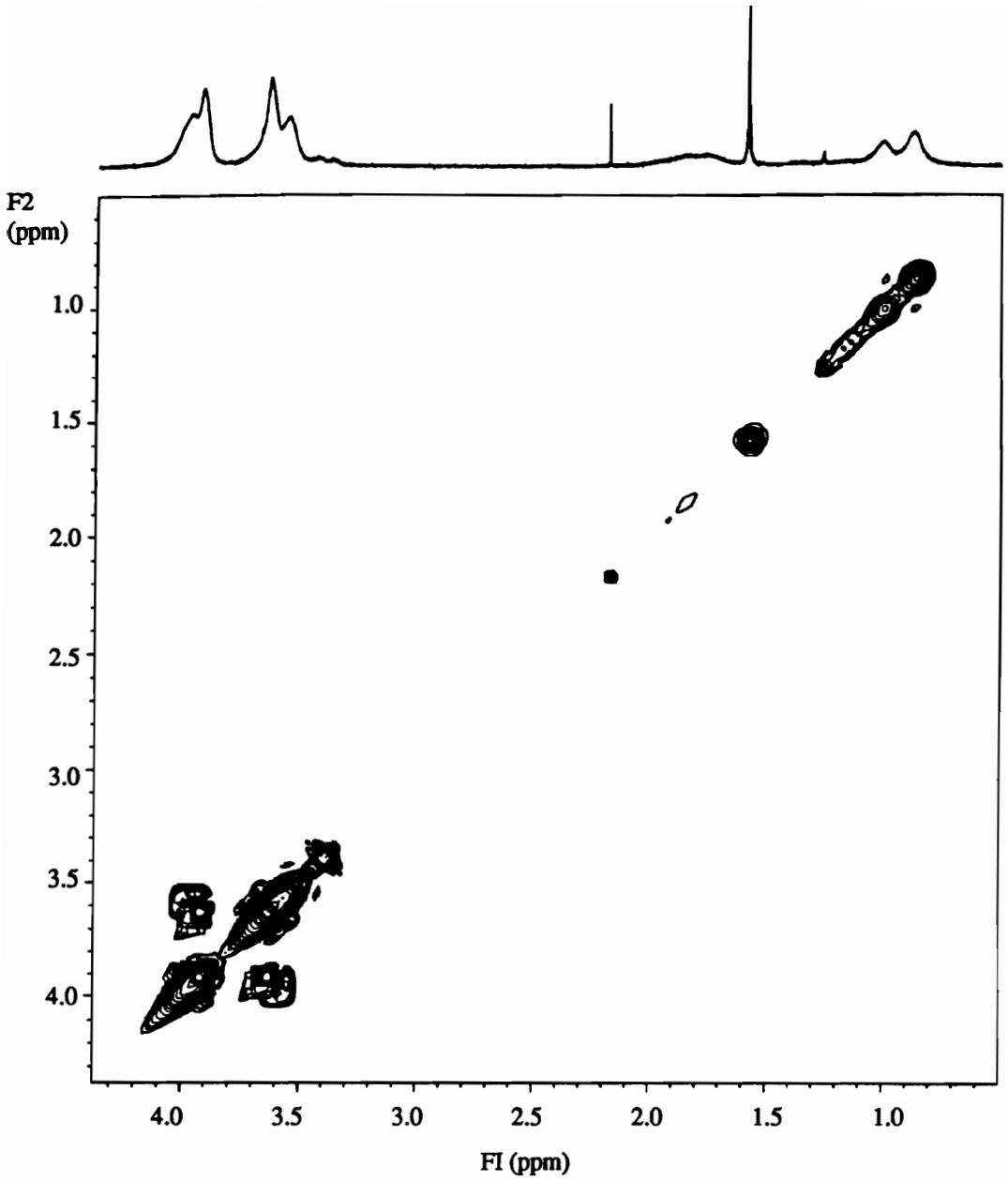


Figure 19(b). 2D COSY spectrum of poly(**13**-rotaxa-30c10) (**14**, R=H). (whole aliphatic region, $CDCl_3$)

CONCLUSIONS AND FUTURE WORK

Polyrotaxanes containing polystyrene, poly(methyl acrylate) and poly(methyl methacrylate) as linear chains have been prepared by free radical polymerization of those monomers in the presence of aliphatic crown ethers. The threading yield was dependent on the cavity size of the crown ethers and it generally was up to 21 mass %. The use of 18-crown-16 in the control reactions was proved to be a good tool to investigate the possible side reactions, here, chain transfer. A characteristic of poly(styrene-rotaxa-crown ether)s was the formation of micelles in protic solvents. The stability of the emulsions was explained due to the 'threaded' structure, which was further supported by dispersion polymerization of styrene using "42-crown-14" as a 'pre-surfactant'. Due to the incompatibility between the two components crown ethers gather to form microscopic domains along the chain. DSC study indicated that the loading of the crown ether changed thermal property of the polystyrene backbone significantly. Methyl acrylate and methyl methacrylate gave polyrotaxanes with higher threading yields than styrene, suggesting the effect of the miscibility and possible attractive interaction between those and crown ethers. Synthesis of side-chain polyrotaxanes by free radical polymerization of methacrylic monomers with bulky groups affords higher threading yields than methyl methacrylate, indicating that dethreading might occur during the polymerization of methyl methacrylate in the solution of 30-crown-10.

As general conclusion, the changes of the polymer properties such as solution behavior and thermal behavior can be achived by the loading of macrocycles onto polymers through threading. The final properties of the polyrotaxanes will be dependent on the properties of the macrocycle as well as the polymer properties.

In the future, the study on the side-chain polyrotaxane must be continued. Because dethreading can not occur during the synthesis of these polyrotaxanes, the study will give important answers to basic questions in polyrotaxane chemistry such as threading-dethreading equilibria during the polymerizations and effects of size of macrocycle, solvent, feed ratio, temperature and amount of initiator on threading yield. The 'threading-dethreading" effect on the retention behaviors of the large crown ethers can be further investigated using a C_{18} reverse-phase column. The low temperature NMR study of 42c14-[2]catenane would be interesting because at a low temperature the molecular motion of each 42c14 ring is restricted so that it would be possible to differentiate the inner protons from the outer protons. None of polyrotaxanes has been applied to industry so far although many aspects of rotaxane and polyrotaxane chemistry have been well established. Therefore, the industrial application of polyrotaxane systems must be pursued in the future. For instance, an azo compound containing two macrocycles (e.g., BMP32c10) at the ends like the blocking group/initiator can afford various oligomeric/polymeric macromolecules containing the macrocycles at the chain ends by free radical polymerizations. Another azo compound may have two paraquat units at both ends and thus free radical polymerizations of olefinic monomers will give polymers with paraquat moieties at the chain ends. The combination of the two resultant polymers will display enhanced miscibility and probably show microphase separation like block copolymers. Those materials also can be used as additives for property modification of conventional polymers.

The publications which have been already appeared on this research are listed below.

1. *New Triarylmetyl Derivatives: "Blocking Groups" for Rotaxanes and Polyrotaxanes*, Gibson, H. W.; Lee, S.-H.; Engen, P. T.; Lecavalier, P.; Sze, J.; Shen, Y. X.;

Bheda, M. C. *J. Org. Chem.* **1993**, 58, 3748.

2. *Happy Physical Marriage of Small & Large Molecules: Polyrotaxane,* Gibson, H. W.; Engen, P. T.; Lee, S.-H.; Liu, S.; Marand, H.; Bheda, M. C. *Polym. Preprints, Am. Chem. Soc. Div. Polym. Chem.* **1993**, 34(1), 64.
3. *Synthesis and Characterization of Large (30-60-Membered) Aliphatic Crown Ethers,* Gibson, H. W.; Bheda, M. C.; Engen, P. T.; Shen, Y. X.; Sze, J.; Zhang, H.; Gibson, M. D.; Delaviz, Y.; Lee, S.-H.; Liu, S.; Wang, F.; Nagvekar, D. *J. Org. Chem.* **1994**, 59, 2186.
4. *The Polyrotaxane Architecture: a New Approach to Molecular Engineering,* Gibson, H. W.; Liu, S.; Shen, Y. X.; Bheda, M. C.; Lee, S.-H.; Wang, F. *Molecular Engineering for Advanced Materials.* NATO Advanced Study Institute Series, Kluwer Pub., **1995**, 45.
5. *Knots for Molecular Strings of Beads,* Liu, S.; Lee, S.-H.; Shen, Y. X.; Gibson. H. W. *J. Org. Chem.* **1995**, 60, 3155.
6. *More Fun and Games with Rings, Strings and Rods,* Gibson, H. W.; Liu, S.; Lee, S.-H.; Marand, H.; Prasad, A.; Wang, F.; Bheda, M.; Nagvekar, D. *Makromol. Chem., Macromol. Symp.* **1995**, 98, 501.
7. *Blocking group/initiators for the Synthesis of Polyrotaxanes via Free Radical Polymerization,* Lee, S.-H.; Engen, P. T.; Gibson, H. W. (*Macromolecules,* accepted)

VITA

Sang-Hun Lee was born in May 21, 1959 in Chon-ju, a city of Republic of Korea. After graduation from Seoul National University, Seoul, Korea with B.S. in Chemical Technology in 1983, he began his graduate career at Korea Advanced Institute of Science and Technology (KAIST). Upon graduation from KAIST with an M.S. in Polymer Chemistry in 1985, he joined the Polymer Division at the Korea Research Institute of Chemical Technology (KRICT) and worked for five and half years. He came to the USA in 1990 and entered the graduate school at North Carolina State University, Raleigh, North Carolina and majored in organic chemistry. In 1992, he transfered to Virginia Polytechnic Institute and State University and joined Dr. Harry W. Gibson's research group. He is planning to further study as a postdoc in the USA seeking for a job eventually in a university in Korea, his home country.

Lee, Sang-Hun