QUATERNARY AMMONIUM SALTS AS CHIRAL IONIC LIQUIDS AND AS ANTIMICROBIAL SURFACES

BY

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Abstract

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MARIE F. THOMAS

Advisor: Professor Robert Engel

The focus of this research has been the preparation and characterization of a variety of new monocationic and polycationic ammonium organic salts that can be used as ionic liquids and as agents that can be used to generate antimicrobial surfaces.

Ionic liquids are anhydrous salts that have melting points below 100 ^{0}C and are usually liquid at room temperature. These materials have little vapor pressure at standard temperature and pressure, are non-flammable, and are thermally stable. The focus is on the synthesis of chiral ionic liquids. Such liquids may give selectivity in asymmetric synthesis, chiral separations and electrochemical processes. The ionic liquids that have been developed are based on the racemic and chiral forms of 3-chloro-1, 2-propane diol. Development work has been done with the racemic alkyl halide and these efforts have been extended to the more expensive chiral species. A series of racemic and chiral ionic liquids have been successfully synthesized. These

materials may be useful catalysts and/or solvents for organic reactions which exhibit enhanced reaction rates and/or selectivity in polar solvents.

In addition to making chiral ionic liquids, we have taken advantage of the antimicrobial property of quaternary ammonium salts and developed different methods for applying them to surfaces (porous and non-porous) rendering them antimicrobial. The cationic lipophilic salts used in this study were based on DABCO (diazabicyclo [2.2.2] octane). Carbohydrate-based polycationic salts were developed that can gel water and alcohols. The resulting gels exhibited significant biological activity against the Gram (+) bacterium *S. aureus*. Mannose functionalized PAMAM dendrimers and polyester fabrics were successfully modified with the DABCO salts. These materials have been shown to exhibit antibacterial activity against Gram (+) and Gram (-) bacteria. Patents are pending for some of these procedures.

Dedicated to my parents:

Seneque and Edith Thomas

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INTRODUCTION

A. Background

Quaternary ammonium salts have a wide range of interesting properties and applications. For example, they can be used as phase transfer catalysts [1], antihydrophobic agents [2], and biocides [3, 4].

The Engel laboratory has a history of synthesizing and characterizing various types of quaternary ammonium, as well as phosphonium organic salts. Past efforts on new organic salts have included the synthesis of polycationic “strings”, rings, dendrimers, cyclodextrin derivatives and ionic liquids [5]. As to be expected, the properties of these species are dependent on their structure, including the location and number of charges contained. The focus of this project has been the development of quaternary ammonium salts that can serve: a) as chiral ionic liquids, and b) antimicrobial agents that can be applied to surfaces.

Ionic liquids are defined as salts that have melting points below 100 ˚C [6]. Most desirable, for various applications, they will be liquid at room temperature and as anhydrous as possible. Most known ionic liquids are composed of, but are not limited to, an ammonium cation and an inorganic or organic anion. The most common cation types reported in the literature

include *N, N'*-dialkylimidazolium, *N*-alkylpyridinium, tetraalkylammonium and tetraalkylphosphonium (see Figure 1). Common anions include hexafluorophosphate, tetrafluoroborate, halides such as chloride and bromide and bis(trifluoromethylsulfonyl)imide (see Figure 1). Ionic liquids have often been referred to as "designer solvents", because by systematically varying the cation and/or the anion, one can design a solvent with particularly desired properties [7].

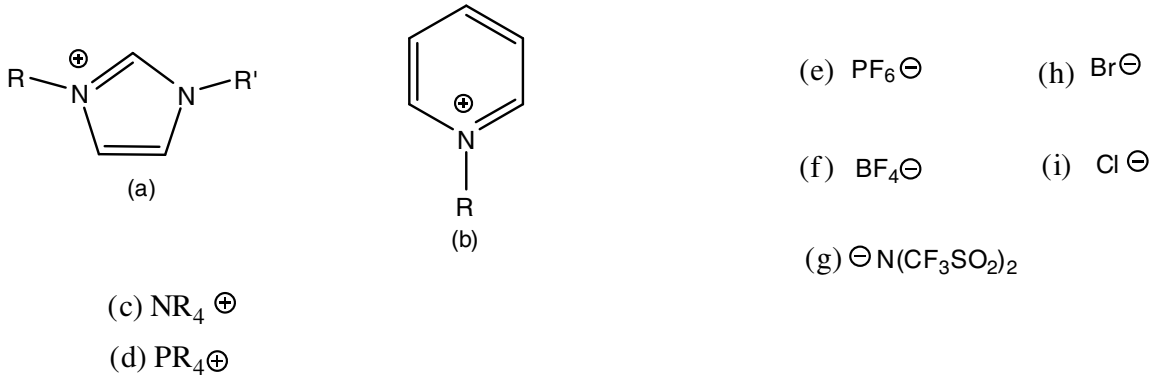


Figure 1. Common cations and anions of ionic liquids: a) *N,N'*-dialkylimidazolium b) *N*-alkylpyridimium c) tetraalkylammonium d) tetraalkylphosphonium e) hexaflurophosphate f) tetrafluoroborate g) bis(trifluoromethylsulfonyl)imide h) bromide i) chloride

Ionic liquids of these types generally are thermally stable, have a wide liquidus range, can exhibit high conductivities and are generally recyclable to some extent [8]. For some time, a defining property of ionic liquids has been that they have little to no vapor pressure. However, studies conducted by Rebelo *et al.*, and Earle *et al.*, show that commonly used aprotic ionic liquids such as the 1-alkyl-3-methyl bis(trifluoromethylsulfonyl)imide salts

can be distilled without decomposition between 200-300 ˚C at low pressure (0.1 to 7 mbar) [9, 10].

Ionic liquids have generated much interest, mostly due to their electrochemical properties, their properties with regard to radionuclides, and in some instances their presumed (by some) potential to one day replace conventional volatile organic solvents (referred to as VOCs) currently in use. In fact, much of the prior literature on ionic liquids has been concerned with their use as solvents in organic synthesis and as catalysts for a range of organic reactions [11, 12, 13, 14]. In addition to being used in synthesies, ionic liquids can be used in chemical analyses (*e.g.*, chromatography and electrophoresis), large-scale separations, and media for electrochemical processes. They can also be used as engineering fluids and performance additives [15].

Two classes of ionic liquids have been developed in the Engel laboratory, which include liquid ionic phosphates (LIPs) (which contain the phosphate anion [16]) and polyammonium ionic liquid sulfonylimides (PILS) (which contains the bis(trifluoromethylsulfonyl)imide anion [17, 18]). LIPs, which are considered hydrophilic, have the particularly desirable characteristic of being more “Green” than other types of ionic liquids. That is, the anion does not degrade to toxic materials in contact with other

solvents, and relatively little energy is consumed in their preparations. The varieties of LIPs that have been successfully prepared are shown in Figure 2. However, many of these materials are extremely viscous and/or have high melting points, making both their characterization and use in practical application difficult. This difficulty led us to synthesize the corresponding PILS, which tend to be hydrophobic. Changing the anion lowered the melting points and the viscosity of these materials while maintaining an anion that is relatively “non-degradable” to toxic products.

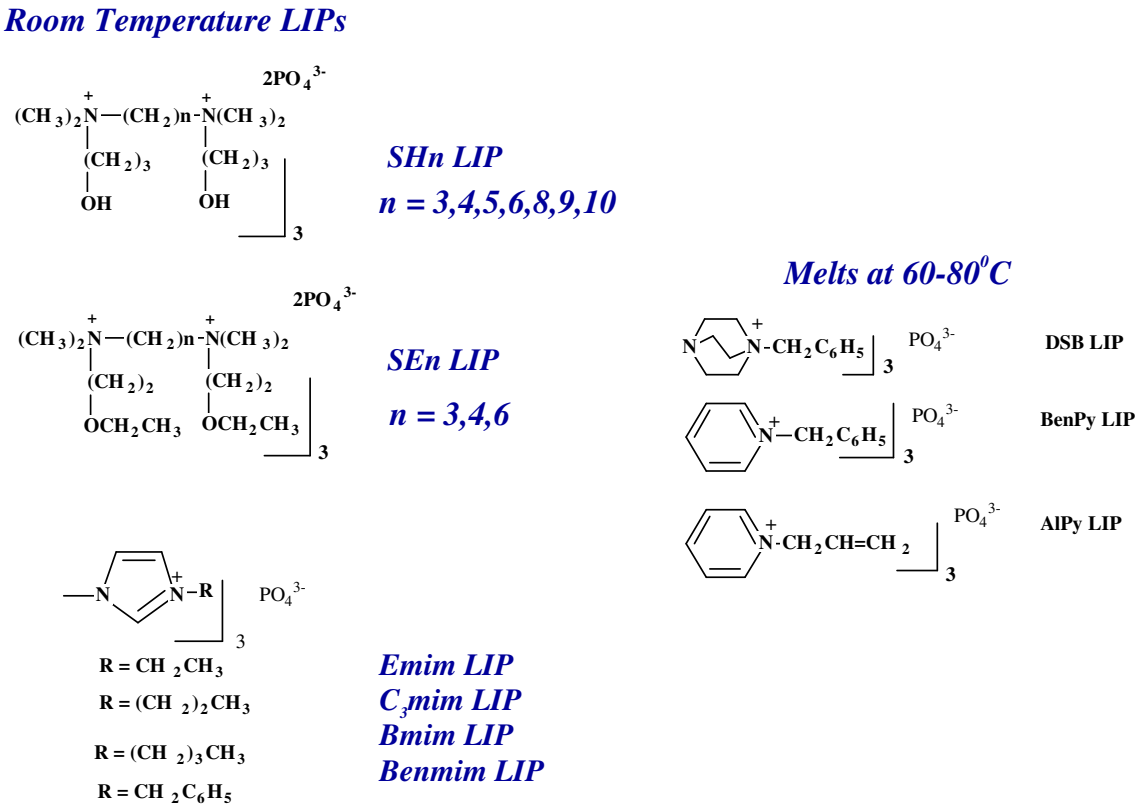


Figure 2. Various structural types of LIPs. S = string, H = hydroxyl, E = ether or ethyl, mim = methyl imidazolium, B = butyl, Ben = benzyl, D = DABCO, Py = pyridinium, Al = allyl [18].

The synthesis of ionic liquids usually starts with the generation of a halide salt. The halide salt is formed through an S_N2 reaction between a tertiary amine and an alkyl halide (see Figure 3). Then, through anion metathesis reactions with either a protic acid or a metal salt, other salts (which presumably would be liquid) are formed. For example, liquid ionic phosphates are made by using a charge equivalent of pure phosphoric acid in either methanol or ethanol [16]. The solvent is then evaporated afterwards. Polyammonium ionic liquid sulfonylimides are made by using a charge

equivalent of the metal salt lithium bis(triflouromethylsulfonyl)imide in water [19]. As stated previously, sulfonylimides tend to be hydrophobic and the salt separates from the aqueous solution. The salt is washed with water until no presence of halide is detected.

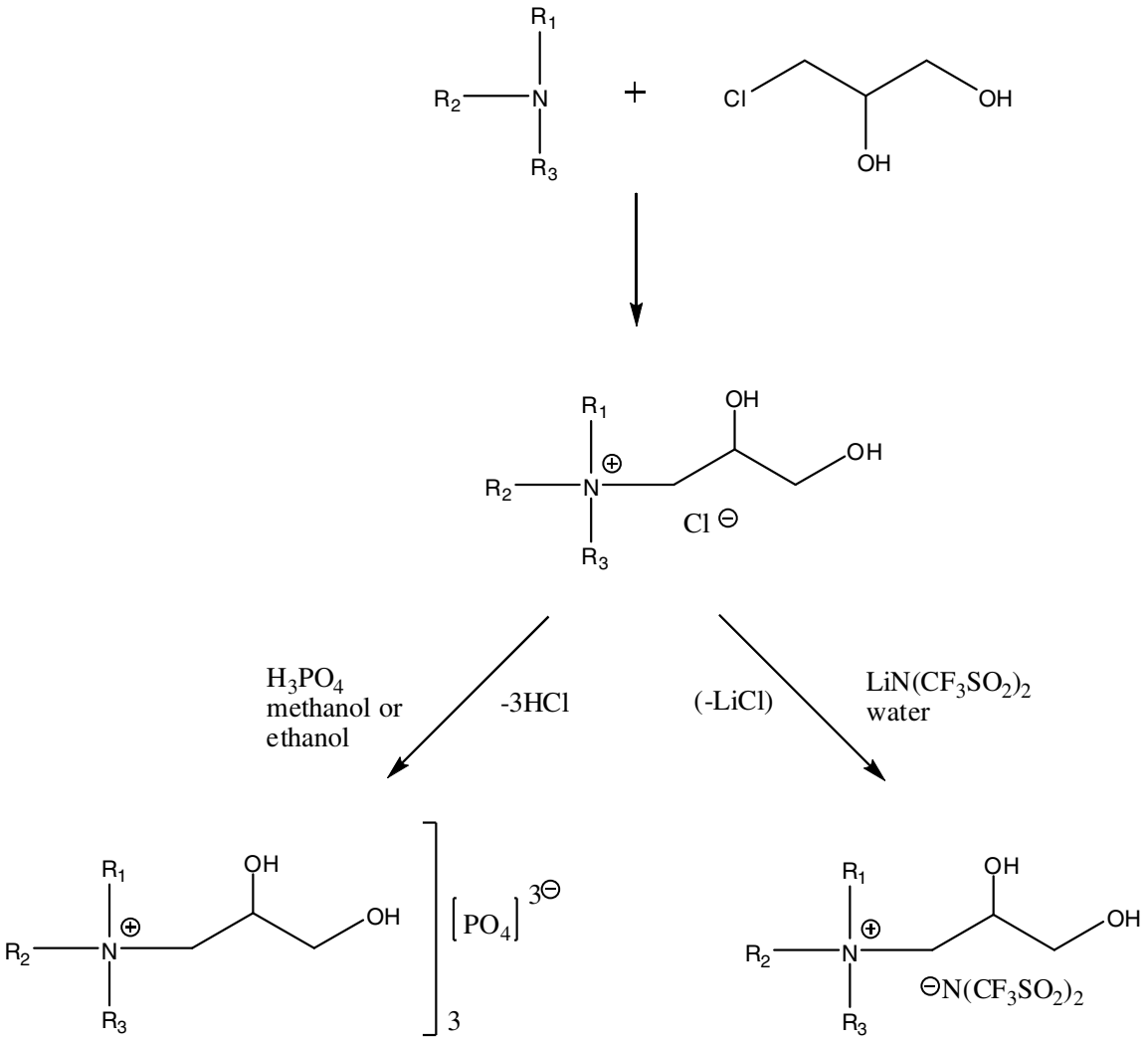


Figure 3. The synthesis of ionic liquids, in particular LIPs and PILS.

B. Chiral Ionic Liquids

We found it to be of interest to focus on the synthesis of chiral ionic liquids. Such liquids are believed to have the potential to provide selectivity in asymmetric synthesis, chiral separations, resolutions and electrochemical processes [20]. Chiral ionic liquids are usually made from precursors derived from the readily available chiral pool of chemical adjuncts. Chirality can originate with either the cation and/or the anion. Materials developed so far have found use as chiral solvents for asymmetric synthesis and stereoselective polymerization, chiral phases for gas chromatography, chiral shift reagents for NMR and chiral liquid crystals [21]. In collaboration with Prof. Ye He at John Jay Collge-CUNY, chiral ionic liquids are being studied in electrophoretic separations for forensic applications.

The ionic liquids that we have worked on are based on the chiral auxiliary 3-chloro-1,2-propane diol. This auxiliary was chosen because it was readily available and it was thought that some interesting products could be developed. We also thought that since some reactions such as the Diels-Alder could be influenced by hydrogen bonding, that these salts might be useful solvents/and or catalysts in these reactions.

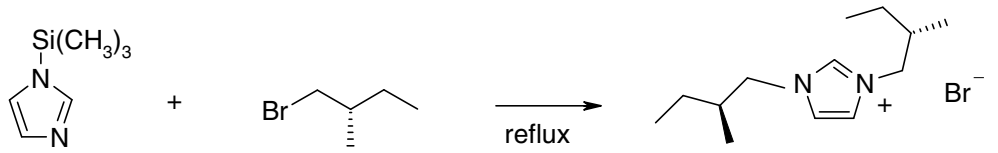
Ionic liquids are highly ordered solvents, which are capable of forming hydrogen bonding networks [22, 23, 24]. In organic synthesis, these

materials behave as polar solvents [25]. Ionic liquids can take on the role of the “innocent” or inert solvent, meaning they dissolve reagents in order so that they can react [26]. Ionic liquids act as co-catalysts or catalysts (usually Lewis acid catalysts), enhancing reaction rates. They can also play a role as ligand or ligand precursors [26].

The focus of the next few pages of this introduction will be on the synthesis of chiral ionic liquids and the use these materials as solvents and/or catalysts in asymmetric organic synthesis. An emphasis will be placed on three reactions in particular: Diels-Alder, Baylis-Hillman reaction and Michael addition. These reactions are well-known carbon-carbon bond forming reactions, which are widely used in the preparation of natural products and biologically active compounds [27, 28]. Thus, there is great interest in finding ways of enhancing the rate and selectivity of these reactions. These reactions can also be influenced by solvents and have been studied in chiral and achiral ionic liquids. We will attempt to analyze the role of these liquids in organic synthesis.

The first chiral ionic liquid was reported by Howarth *et al.,* in 1997 [29]. The salt, (S) - *N, N’*-di-(2’-methylbutane)imidazolium bromide, [MB_2IM][Br] was synthesized using TMS-imidazole **1** and (S)- (+)-1-

bromo-2-methylbutane **2** (see Figure 4). The product was obtained in 21% yield. In this material, chirality is associated with the cation.

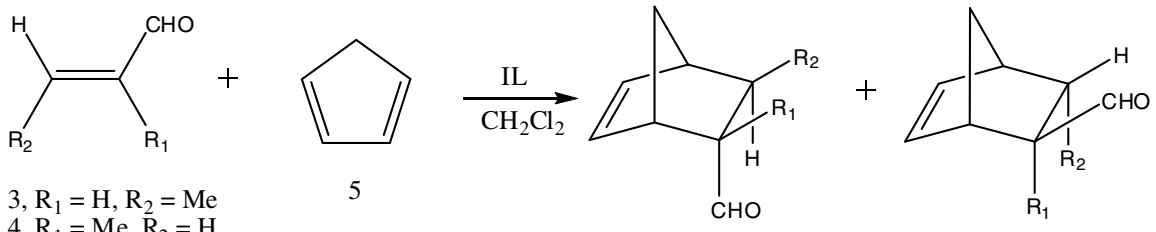


1 2 **(S)-[MB$_2$IM][Br]**

Figure 4. Synthesis of (S)-[MB$_2$IM][Br]

.

In this study, (S)-[MB$_2$IM][Br], diethylimidazolium bromide ([Et$_2$IM][Br]) and diethylimidazolium trifluoroacetate ([Et$_2$IM][CF$_3$COO]) were studied as Lewis acid catalysts in Diels-Alder reaction between cyclopentadiene with crotonaldehyde **3** or methacrolein **4** as the dienophile which formed products **6** and **7 (**see Table 1). Yields of 35 – 40 % were obtained with all the ionic liquids, with good endo/exo selectivities. However, enantiomeric excesses of less than 5% were obtained with (S)-[MB$_2$IM][Br]. When the Diels-Alder reaction was performed in dichloromethane without any catalyst under the same reaction conditions, no product formed. These results indicate that ionic liquids can act as weak Lewis acids.



3, R_1 = H, R_2 = Me
4, R_1 = Me, R_2 = H

5

endo

exo

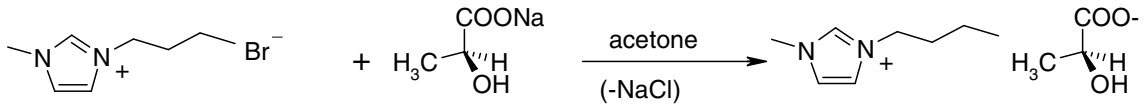
6, R_1 = H, R_2 = Me
7, R_1 = Me, R_2 = H

IL	Dienophile	% Yield	Endo/Exo Ratio
[Et_2MIM][Br]	3	35	95:5
[Et_2MIM][CF_3COO]	3	37	95:5
S-[MB_2IM][Br]	3	36	93:7
[Et_2MIM][Br]	4	40	15:85
[Et_2MIM][CF_3COO]	4	40	13:87
S-[MB_2IM][Br]	4	36	10:90

Table 1. Results of the reaction of {3} and {4} with {5} in the presence of ([Et_2IM][Br}, [Et_2IM][CF_3COO], or (S)-[MB_2IM][Br]. Reaction conditions: Temperature = -25 ˚C, Reaction time = 48 hours. 1.0 equivalent of {3} or {4}: 5.0 equivalents of {5}: 0.2 equivalents of ionic liquid.

Seddon *et al.* prepared 1-butyl-3-methylimidazolium lactate, [BMIM][lactate] shown in Figure 5 by combining 1-butyl-3-methylimidazolium bromide **8** and sodium lactate **9** in acetone. Filtration of the sodium salt, followed by evaporation of the solvent resulted in the ionic liquid [30]. This is one of the few examples where the chirality rests on the anion. This salt and a few other achiral ionic liquids were examined as recyclable alternatives to lithium perchlorate-diethyl ether mixtures for Diels-Alder reactions. It has been reported that performing reactions in

lithium perchlorate-diethyl ether mixtures (LPDE) has resulted in improved reaction rates and endo selectivities[31]. Several dienes and dienophiles were used in this study but the focus will be on the reaction between cyclopentadiene **5** and ethyl acrylate **10,** since this reaction has been performed in chiral and achiral ionic liquids, and other solvents such as water and LPDE.

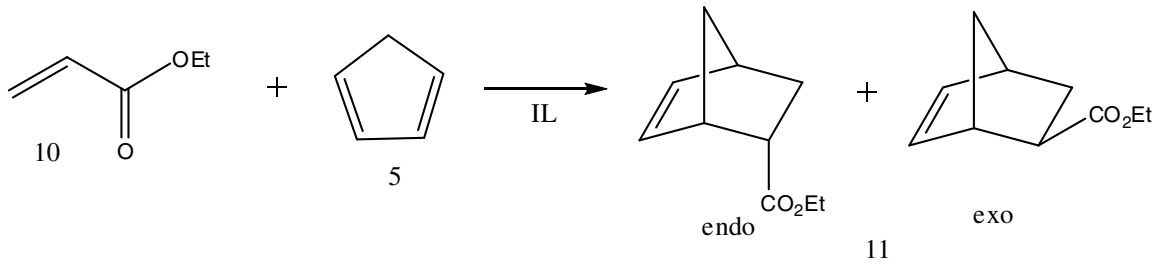


8 9 [BMIM][lactate]

Figure 5. Synthesis of [BMIM][lactate].

The reaction of **10** and **5** in [BMIM][lactate] resulted in cycloadducts that were obtained in 87 % yield with an endo selectivity of 4.4:1 after 2 hours (Table 2, entry 2). This was higher than the endo selectivity achieved in water but much lower than that achieved in LPDE. However, after twenty-four hours, the selectivity decreased to 3.7:1 (entry 3). No enantioselectivity was noted for [BMIM][lactate]. The authors indicated that the higher basicity of the lactate anion might be responsible for the lower selectivity of this ionic liquid. This group was able to achieve a similar selectivity to LPDE using the ionic liquid [BMIM][PF_6], but yields obtained in the ionic liquid were lower compared to that achieved in the ether solvent (entry 5 and 7). In comparison to non-polar organic solvents, enhanced

reaction rates and selectivity can be achieved using ionic liquids. The extent to which this occurs depends on the ionic liquid. The products were extracted using diethyl ether and the ionic liquids could be reused.



Entry	Solvent	T/˚C	Time/hr	Yield (a)	Endo/exo (a)
1	**[BMIM][OTf]**	**20**	**18**	**96**	**6.0:1**
2	**[BMIM][lactate]**	**20**	**2**	**87**	**4.4:1**
3	**[BMIM][lactate]**	**20**	**24**	**99**	**3.7:1**
4	**[BMIM][BF_4]**	**-15**	**24**	**99**	**5.0:1**
5	**[BMIM][PF_6}**	**20**	**1**	**36**	**8.0:1**
6	**Water**	**20**	**1**	**30**	**3.5:1**
7	**5M LPDE**	**20**	**1**	**61**	**8.0:1**

Table 2. Results of the reaction of {10} and {5} in a variety of BMIM (1-butyl-3-methylimidazolium) ionic liquids including [BMIM][lactate], water and 5M lithium perchlorate-dietyl ether using a 1.5:1:1 molar ratio of diene:dienophile:solvent.
a. Determined using gas chromatography (GC).

The reaction between **10** and **5** was also studied using camphor ionic liquids (S)-(+)-1-butyl-3-methylimidazolium camphorsulfonate [BMIM][CS] and (S)-(+)-1-butyl-2, 3-methylimidazolium

camphosrsulfonate [BM_2IM][CS] as the solvents [32]. The goal of this study was to analyze the effects of an anion, which is a poor hydrogen bond acceptor on stereoselectivity. The ionic liquids were obtained by converting the bromide salts to the sulfonate salts using concentrated sulfuric acid. The sulfonates were then converted to the camphorsulfonates using a strong base anion exchange resin with chiral camphor-10-sulfonic acid. Due to the viscosity of [BMIM][CS] and [BM_2IM][CS] being a solid at room temperature, the ionic liquids were mixed with [BMIM][BF_4] when used as a solvent.

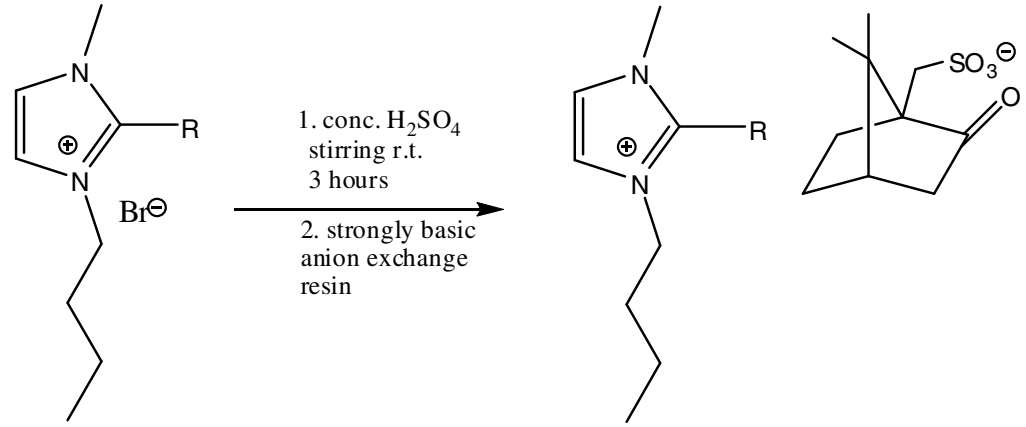


Figure 6. Synthesis of 1-butyl-3-methylimidazolium camphorsulfonates.

The results indicate that endo selectivity is increased in the presence of the [BMIM][CS] as compared to [BMIM][MS), (MS = methanesulfonate), [BMIM][OTf] (OTf = triflate), and neat [BMIM][BF_4] (see Table 3). (The reasoning behind this will be explained later in this

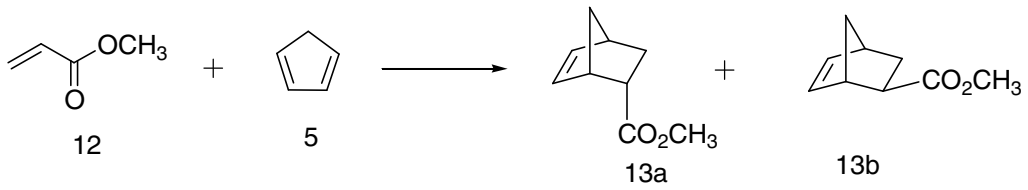
report.) The selectivity was calculated from ^{1}H NMR spectra. The selectivity decreases when [BM_2IM][CS] is used. In this case, this may be due to decreased hydrogen bonding between the imidazolium cation [BM_2IM] and the transition state (explained in more detail later). No enantioselectivity was noted for any of the chiral ionic liquids.

Added sulfonate In [BMIM][BF_4]	T/˚C	Endo/exo (a)	Isolated Yield/%
None	20	3.4	36
[BMIM][MS]	20	4.1	42
[BMIM][OTf]	20	4.0	16
[BMIM][CS]	20	6.1	29
None	-10	6.1	60
[BMIM][CS]	-10	10.3	66
[BM_2IM][CS]	20	3.0	28

Table 3. Anion effects on stereoselectivity of Diels-Alder reactions. Diene:dienophle = 2.0M:1.3M. Molar ratio of [BMIM][X]/[BMIM][BF_4] = 15/100 (X = MS, OTf, CS), Reaction time = 20 h.
a. Calculated from ^{1}H NMR spectra.

The Diels-Alder reaction is a well-known 1, 4-cycloaddition reaction. This reaction occurs between a diene and a dienophile to generate cyclic adducts. The outcome of Diels-Alder reactions can be influenced by solvent effects such as the hydrophobic effect, polarity and hydrogen-bonding [33, 34, 35]. The addition of Lewis acid catalysts are also known to enhance the rate and selectivity [36]. Welton *et al.,* studied the reaction of **5** and methyl

acrylate **12** in a series of ionic liquids and compared the results to reactions performed in conventional organic solvents to study the role of hydrogen bonding in the ionic liquids (see Table 4) [37]. It was noted that the higher the polarity of the solvent (which was measured using Reichardt's dye, E_T^N values), the greater the endo selectivity. The [BMIM] salts had selectivities, which were less than that of solvents such as methanol and ethanol. Ionic liquids such as 1-(2-hydroxyethyl)-1-methylimidazolium bis(trifluoromethylsulfonyl)imide [EtOHMIM][NTf_2], 1-(2-methoxyethyl)-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, [MOEMIM][NTf_2] and ethyl ammonium nitrate [$EtNH_3$][NO_3] had selectivities, which were comparable to those of the alcohols (Table 4, see entries 9-13).



Entry	Solvent	E_T^N	% Yield	Endo:Exo (a)
1	[BMIM][BF_4]	0.670	85	4.6
2	[BM_2IM][BF_4]	0.576	84	3.3
3	[BMIM][ClO_4]	0.680	74	4.8
4	[BMIM][PF_6]	0.660	93	4.8
5	[BMIM][OTf]	0.656	87	4.5
6	[BMIM][NTf_2]	0.645	90	4.3
7	[BMIM][CF_3COO]	0.620	89	4.0
8	[BMIM][BF_4] + [Cl] 2 M	N/A		3.7
9	[EtOHMIM][$NTf_{2]}$	0.929		6.1
10	[MOEMIM][NTf_2]	0.722		5.7
11	[$EtNH_3$][NO_3]	0.954		6.7
12	Methanol	0.762		6.7
13	Ethanol	0.654		5.2
14	Acetone	0.355		4.2
15	Diethyl ether	0.177		2.9

Table 4. Effect of polarity of ionic liquids and other solvents on yields and selectivity of Diels-Alder reactions. Reaction conditions for [BMIM] ionic liquids: 1.27 M {5}: 1.11 M {12}, Time = 72 hours, T = 25 ˚C. The values for E_T^N and endo/exo values for solvents listed in entry 9 to 12 were obtained from other sources described in reference [37]. a. Determined using gas chromatography.

Welton postulated that the endo selectivity of ionic liquids such as [BMIM][BF_4], [EtOHMIM][NTf_2], and [$EtNH_3$][NO_3] comes from the ability of the cation to hydrogen bond to the dienophile methyl methacrylate. The most acidic site on the imidazolium cation (which is considered a Lewis acid) is at the C2 carbon and the proton found at this site is believed to coordinate to the dienophile, during the transition state (see Figure 7). The ionic liquid [BMIM][BF_4] has an endo selectivity of 4.6 (Table 4, entry 1). When the proton at this site was replaced with a methyl group (Table 4, entry 2), [BM_2IM][BF_4], the endo selectivity went down to 3.3. Hydrogen bonding can still occur at the protons at C4 and C5 but the interaction is not as strong [37].

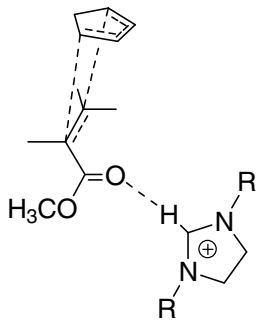


Figure 7. Interaction of the imidazolium cation with the transition state.

It was also observed that the addition of more basic anions such as chloride led to a decrease in endo selectivity. Strongly basic anions compete with the transition state for the hydrogen bond donor. Welton concluded that ionic liquids that have cations that are strong hydrogen bond donors, which

are coupled with weakly coordinating anions should strongly favor endo selectivity in Diels-Alder reactions. [EtOHMIM][NTf_2] has two locations where hydrogen bonding can occur: at the C2 on the imidazolium cation and at the hydroxyl group. Hydrogen bonding occurs at the N-H protons of [$EtNH_3$][NO_3] [37].

Dyson *et al.,* studied the reaction of **5** and **12** in a series of [BMIM] ionic liquids and in a series of bis(trifluoromethylsulfonyl)imide salts to study the solvent effects [38]. Some of these results are presented in Table 5 and Table 6. The selectivity obtained by this group for [BMIM][BF_4] and [BMIM][PF_6], (3.5 and 3.8 respectively) was lower than the values reported by Welton (4.6 and 4.8 respectively) [37]. The reactants formed a homogenous phase with [BMIM][NTf_2], [BMIM][SbF_6], and [BMIM][CF_3COO]. However, when the mole equivalent of [BMIM][BF_4] was raised to 6 (mole ratio [BMIM][BF_4]:methyl acrylate) and above, a homogenous phase was formed and the selectivity increased to an endo:exo ratio of approximately 4.8. A similar situation was also found for [BMIM][PF_6]. It appears if the reagents are able to form a homogenous mixture with the reactants, this favors endo selectivity.

Entry	Anion	Endo:Exo Ratio (a)	Yield % (a)
1	$[BF_4]$	3.5	97
2	$[PF_6]$	3.8	97
3	$[SbF_6]$	4.2	94
4	$[NTf_2]$	4.2	99
5	$[CF_3COO]$	4.4	96

Table 5. Results of reaction of {5} and [12} performed in [BMIM] ionic liquids. Millimolar ratio of diene:dienophile; 2.1:1.4 in 0.30 mL of ionic liquid at room temperature. Reaction time = 24 h. a. Determined using GC.

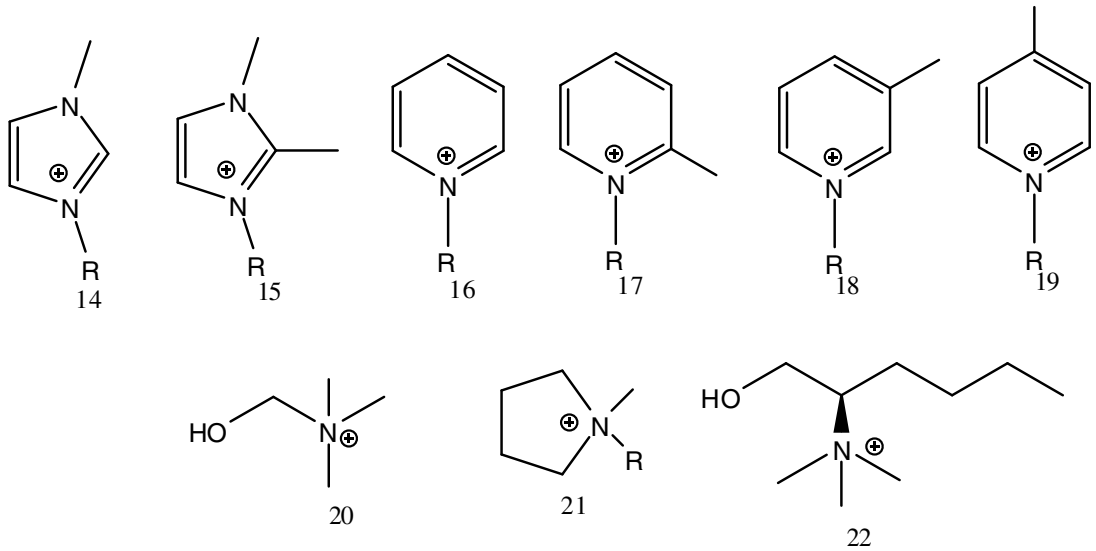
Dyson made the following conclusions based on his studies:

1) Selectivities decreased as the length of the alkyl chains increased (see Table 6, entries 2 - 6 and 12 – 15). This may be due to steric hindrance. As the alkyl chain grows it become more difficult for the cation to coordinate to the transition state.
2) Selectivities increased with the presence of functional groups such as hydroxyl, nitrile, carboxyl and benzyl.
3) The study done by Welton *et al.,* [37] showed that 1-alkyl-methylimidazolium compounds showed better selectivity than 1-alkyl-2, 3-dimethylimidazolium ones. This was said to be due to the acidic proton on the C2 carbon. One can see from Table 6 that 1-alkyl-2, 3-dimethylimidazolium compounds had better selectivity than the

1-alkyl-3-methylimidazolium compounds (see entries 10 and 11). But as stated earlier, the presence of a functional group (such as hydroxyl) that can form hydrogen bonds increased selectivity (see Table 6, entries 7, 25 – 27). Dyson concluded that selectivity does not depend solely on hydrogen bond ability of the cation and hydrogen bond donors separated from the center of charge on the cation improve selectivity.

4) The overall polarity of the ionic liquid does impact selectivity. More polar ionic liquids are better able to stabilize the more polar endo transition state.
5) A low energy LUMO promotes interaction between the transition state and the ionic liquid.
6) Strong electrostatic interactions between cations and anions lower selectivites.
7) Slight chloride impurities appear to have a negligible effect on selectivity.

No enantioselectivity was noted for the chiral ionic liquid **22** in Table 6, entry 31.



a R = CH_3
b R = C_2H_5
c R = C_4H_9
d R = C_6H_{13}
e R = C_8H_{17}
f R = $C_3H_6CO_2H$
g R = C_3H_6CN
h R = $CH_2C_6H_5$

Figure 8. Bis(trifluoromethylsulfonyl)imide ionic liquids used in the study of Dyson *et. al*,[38].

Entry	Cation	Endo:exo Ratio (b)	Yield (%) (b)	Entry	Cation	Endo:exo Ratio (b)	Yield (%)(b)
1 (a)	-	3.3	97	**17**	17b	4.2	98
2	14a	5.1	98	**18**	17c	3.9	95
3	14b	4.3	98	**19**	17h	4.3	98
4	14c	4.2	97	**20**	18c	3.9	97
5	14d	4.1	96	**21**	18e	3.8	96
6	14e	3.9	95	**22**	19b	4.7	99
7	14f	5.4	95	**23**	19c	4.2	97
8	14g	4.4	95	**24**	19h	4.8	98
9	14h	5.1	99	**25**	20b	5.5	98
10	15b	4.6	98	**26**	20c	5.1	98
11	15c	4.4	97	**27**	20d	4.7	98
12	16b	4.6	97	**28**	20h	5.2	98
13	16c	4.1	96	**29**	21c	4.8	97
14	16d	4.1	96	**30**	21h	4.8	95
15	16e	4.0	95	**31**	22	5.6	98
16	16h	4.6	97				

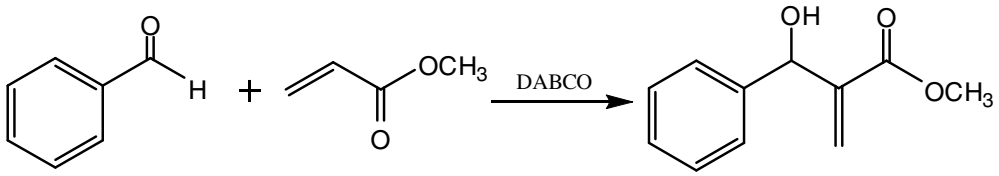
Table 6. Reaction of {5} and {12} in a series of sulfonylimide salts. Ratio of diene:dienophile; 2.1mmol:1.4 mmol in 0.30 mL of ionic liquid at room temperature. Reaction time = 24 hours. a. Neat. b. Determined from GC.

Ionic liquids can have an effect on Diels-Alder reactions, but as stated earlier, the extent of that influence depends on the cation and the anion. Ionic liquids can enhance reaction rates, usually by behaving as Lewis acids, but not necessarily as well or better than water and other polar solvents. In

fact a recent article by Kumar *et al.,* highlighted that reaction rates in water are faster than that in ionic liquids at room temperature [39]. It does appear that better selectivity can be achieved in ionic liquids than in water. Selectivity in ionic liquids is influenced by the overall polarity of the solvent, in conjuction with hydrogen bonding and the ability of the liquid to dissolve the reactants.

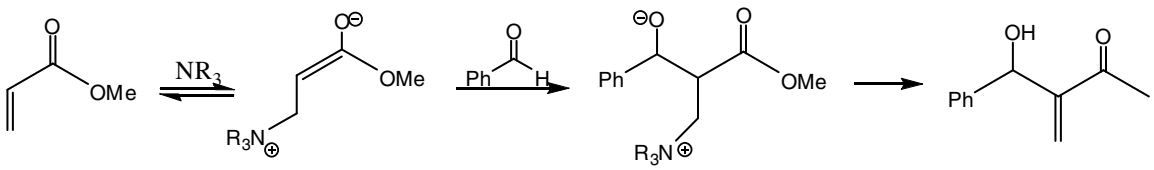
The Baylis-Hillman reaction occurs between an activated alkene and a carbon electrophile (usually an aldehyde) in the presence of a basic catalyst, which is usually a tertiary amine [28]. The reaction is selective, atom economical and produces molecules with multiple functionalities. A typical reaction between benzaldehyde **23** and methyl acrylate **12** with 1,4-diazabicylo[2.2.2]octane as the catalyst is shown in Figure 9. The mechanism involves the Michael addition of the base to the activated alkene to form a zwitterionic enolate. Attack of the electrophile by the enolate, followed by proton migration, leads to the product (see Figure 10)[28]. Baylis-Hillman reactions can be quite slow (taking several days or weeks for product formation) and the use of polar solvents such as water and methanol, have been found to enhance the rate of these reactions [40, 41]. It is believed that polar solvents are better able to solvate the zwitterionic transition state, which leads to an increase of these species. Hydrogen bonding is also

implicated as playing a major role [40, 41]. This force either stabilizes the enolate, activates the aldehyde or both. Ionic liquids are believed to effect Baylis-Hillman reactions in a similar fashion.



23 12 24

Figure 9. Baylis-Hillman reaction between benzaldehyde {23} and methyl acrylate {12} in the presence of the basic catalyst DABCO.



12 24

Figure 10. Mechanism of the Baylis-Hillman reaction.

The first report of the Baylis-Hillman reaction performed in imidazolium type ionic liquids was published by Afonso *et al.*, [42]. This group reported increased reaction rates for the coupling of benzaldehyde **23** to methyl acrylate **12** in [BMIM][BF_4] and [BMIM][PF_6] relative to reactions performed in acetonitrile. However, yields were less in the presence of the ionic liquids than when the reactions were done under neat conditions. Later Aggarwal *et al.*, published a report indicating that imidazolium based ionic liquids may not be the best reaction media for Baylis-Hillman reactions [43]. This group studied the reaction between

23 and **12** in the presence of 3-hydroxyquinuclidine in [BMIM][Cl]. They found that under mild basic conditions the imidazolium cation could be deprotonated and the resulting nucleophile can then attack the aldehyde (see Figure 11). This accounted for the low yields that this group obtained and could also account for the lower yields reported by Afonso *et al*. Later a report by Kim *et al*., showed that rate enhancement of Baylis-Hillman reactions could be achieved if catalytic amounts of imidazolium ionic liquids were used [44].

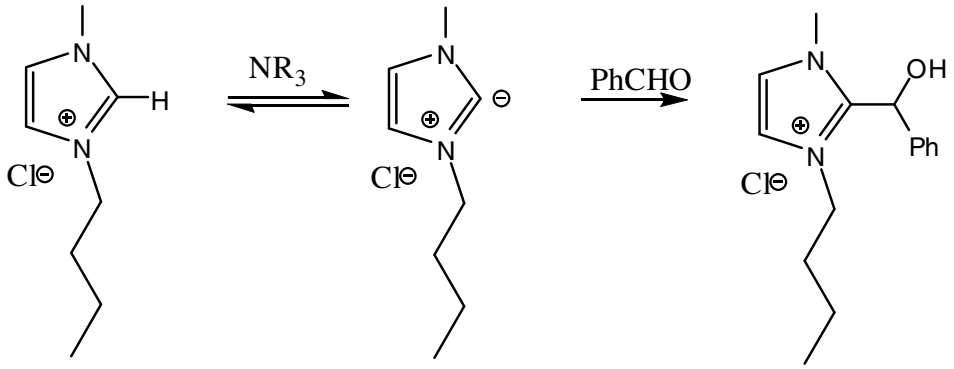
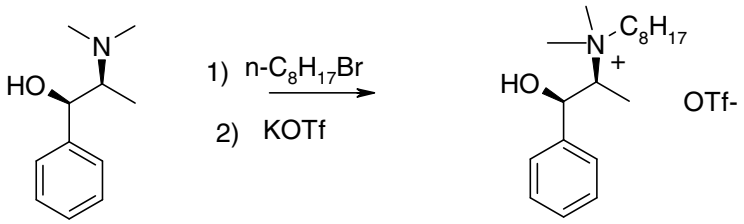


Figure 11. Deprotonation of [BMIM][Cl] under basic condition, followed by addition to the aldehyde.

The ionic liquid, (1R, 2S)-*N, N*,-dimethyl-*N*-octylephedrinium trifluoromethanesulfonate, [M_2NOEph][OTf] was used by Pegot *et al.,* as a solvent for the asymmetric Baylis-Hillman reaction (see Figure 12) [45]. The salt was synthesized in two steps with no solvent, under conditions of microwave irradiation [46]. Microwaves presumably give rise to electrostatic interactions through dipole-dipole interactions between polar

compounds and thermal effects, which ultimately results in increased reaction rates [47]. The result is reduced reaction times, improved yields and purer products [47]. Pegot and his group using conventional methods (in this case, heating with an oil bath at 95 ˚C) obtained (1R, 2S)-*N, N*-dimethyl-*N*-octylephedrinium bromide (the precursor of [M_2NOEph][OTf]) in 30 minutes with a yield of 18%. The same salt was obtained under microwave conditions at the same temperature and time with a yield of 85% [46].



25 [M_2NOEph][OTf]

Figure 12. Synthesis of (1R, 2S)-*N, N*,-Dimethyl-*N*-octylephedrinium trifluoromethanesulfonate .

Moderate to good yields were obtained with this ionic liquid, with enantioselectivities of up to 44% when the reaction of benzaldehyde **23** and methyl acrylate **12** was preformed in [M_2NOEph][OTf] (see Table 7). The authors noted the necessity of the hydroxyl group of the ionic liquid for chiral induction. When this group was replaced by an acetyl group, the enantioselectivity decreased to 6%. The origin of enantioselectivity may come from the hydrogen bond formed between the hydroxyl group and

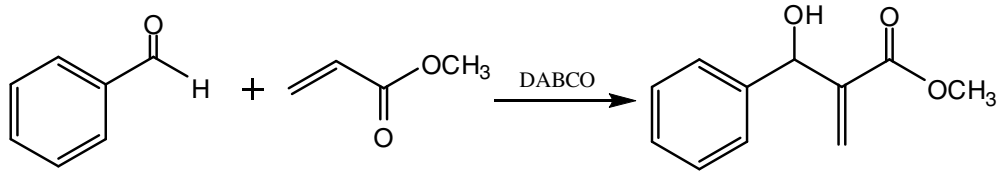
either the carbonyl group of **23** or **12** [45]. A reduction in enantioselectivity was also noted when *p*-nitrobenzaldehyde was substituted for benzaldehyde. This may be due to hydrogen bonding to the nitro group instead of to the carbonyl groups [45].

Entry	IL (equiv.)	Conversion (%)	Yield (%)	(R)-1 ee
1	0.5	86	76	20
2	1	85	78 (74)	23
3	1.5	85	73	28
4	3	65	45	32
5	1	83	67	24 (a)
6	3	75	52 (50)	32 (a)
7	3	60	30	24 (a, b)
8	3	88	60	44 (c)

Table 7. Results of asymmetric Baylis-Hillman reaction of {12} and {23} in the presence of chiral ionic liquid [M_2NOEph][OTf]. Conditions: benzaldehyde:methyl acrylate:DABCO: = 1:1:1. T = 30 ˚C. Time = 4days. Conversion and yields determined using GC. In brackets are isolated yields. Ee determined by chiral HPLC and comparison of optical rotation with literature values. a) benzaldehyde:methyl acrylate:DABCO = 1:3:0.3. b) T = 50 ˚C. c) Time = 7 days.

Baylis-Hillman reactions have been performed in a variety of ionic liquids using aliphatic, aromatic, and α, β-unsaturated aldehydes with activated alkenes such as methyl acrylate, acrylonitrile and methyl vinyl ketone. Moderate to good yields ranging from 13% to as high as 80% have been achieved. The lowest yields were obtained for α,β-unsaturated

aldehydes [48]. Our focus has been on the reaction of **12** with **23**. The results of this common reaction performed in conventional polar solvents and various ionic liquids, including the Pegot's chiral ionic liquid are presented in Table 8.



23 12 24

Entry	Base	Time	T (˚C)	Solvent	[23]: {12}: Base ratios	Yield (%)	Ref.
1	DABCO	24 h	r.t.	[BMIM][PF_6]	1:2:2	63	48
2	DABCO	24 h	r.t.	[BM_2IM][PF_6]	1:2:2	79	48
3	DABCO	11 h	25	[BPy][Cl] + 60% $AlCl_3$	1:1.2:1	75	49
4	DABCO	8 h	25	[EMIM][Cl] + 60% $AlCl_3$	1:1.2:1	80	49
5	DABCO	6 h	r.t.	[EtPy][BF_4]	3:6:1	65	50
6	HMTA	12	r.t.	[EtPy][BF_4]	3:6:1	61.5	50
7	DABCO	6 h	60	[EtPy][BF_4]	1:2:2	78	51
8	DABCO	4days	30	[M_2NOEph][OTf]	1:1:1	67	45
9	DABCO	21 h	25	Neat	1:1.2:1	65	49
10	DABCO	24 h	25	Acetonitrile	1:1.2:2	34	49
11	DABCO	24 h	r.t.	Methanol	1:1:1	78	52
12	DABCO	24 h	r.t.	Triethanol amine	1:1:1	88	52

Table 8. Results of the reaction between {23} and {12} in various ionic liquids and common solvents.

Most of the ionic liquids presented are almost as good, or better than solvents such as methanol (Table 8, entries 2,3,4,7 and 11) in terms of reaction rates and isolated yields. The rate increase in ionic liquids is attributed to the ability of these liquids to stabilize the zwitterionic

intermediate formed from the addition of the base to the activated alkene [50]. The fastest reactions rates were obtained in the chloroaluminate ionic liquids, which can be thought of as Lewis acids (Table 8, entry 3 and 4). The problem with chloroaluminates is that they are quite moisture sensitive and must be used under an inert atmosphere [53]. Hydrogen bonding can play a role as demonstrated by the use of the chiral ionic liquid [M_2NOEph][OTf]**.** This ionic liquid required the longest reaction time but as demonstrated in Table 7, reasonable yields could be achieved and moderate enantioselectivity was observed. Mi *et al.,* reported that hydroxy ionic liquid-supported catalysts showed better catalytic activity than ionic liquid-supported catalysts that did not have the hydroxy group [54]. Enhanced reaction rates could be achieved for reactions performed in ionic liquids in which the cation or anion incorporates the hydroxyl functionality.

Most recently, the aza-Baylis-Hillman reaction was performed in a chiral borate ionic liquid developed by Leitner *et al*. [55]. This reaction involves the coupling of activated alkenes with imines to provide highly functionalized amines. The authors wanted to incorporate a hydrogen bond donor (or Bronsted acidic center) into a chiral anion, so that a bifunctional interaction with the reaction intermediate could occur (Figure 13). Past studies by this group on the mechanism of the aza-Baylis-Hillman reaction

indicated that bifunctional stabilization of the zwitterionic intermediate is necessary in order to achieve high enantioselectivites[56].

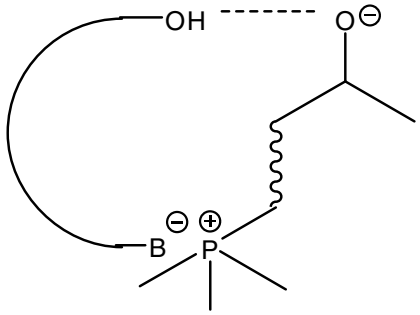


Figure 13. Proposed bifunctional interaction between the reaction intermediate and the chiral anion.

The first step in the synthesis of the borate ionic liquid was the combination of boric acid **26**, sodium hydroxide **27**, and L-(-)malic acid **28** in water to form the sodium dimalatoborate salt **29** (Figure 14) . This salt was then combined with methyltrioctylammonium chloride, $[MO_3A][Cl]$ in acetone to give methyltrioctylammonium dimalatoborate, $[MO_3A]$[dimalatoborate] (Figure 14).

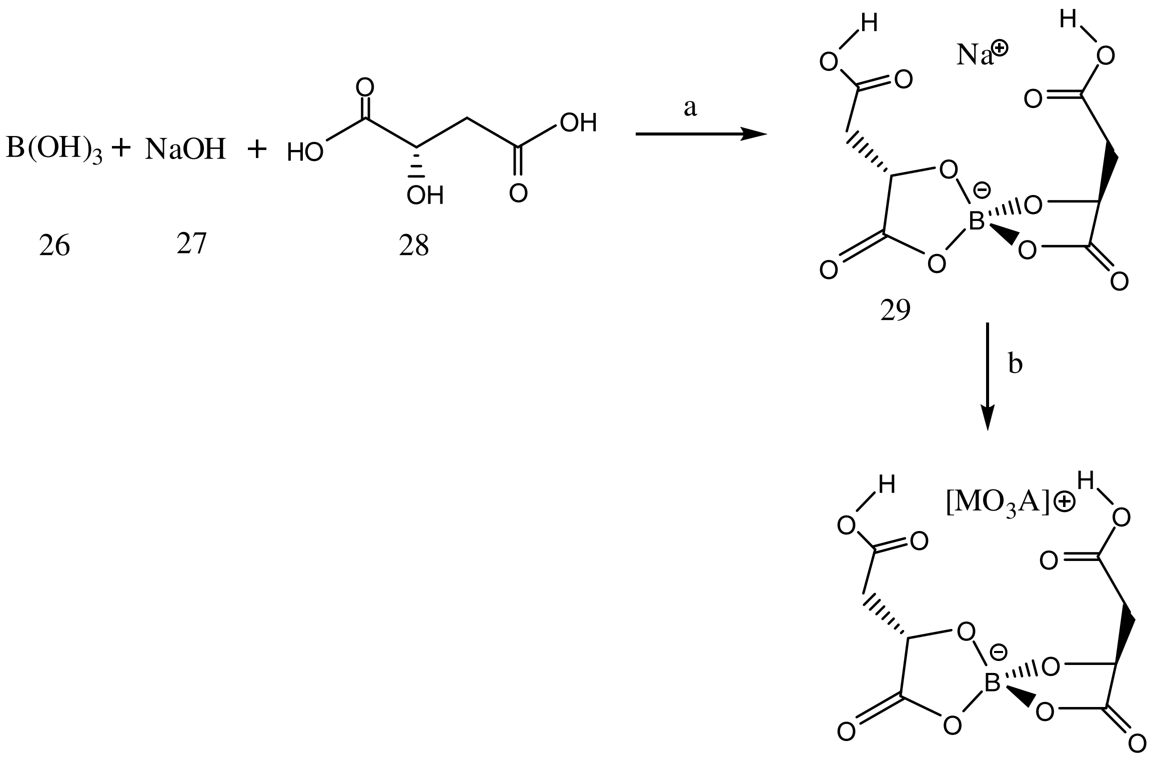


Figure 14. Synthesis of [MO$_3$A][dimalatoborate]. Reaction conditions: a. water, 100˚C, 4 hours. b. $CH_3(CH_3(CH_2)_7)_3NCl$, acetone, r.t., 14 hours.

The reaction between a series of sulfonated imines and methyl vinyl ketone using triphenyl phosphine as the nucleophilic base was done in this ionic liquid, along with two achiral derivatives. The best results were obtained in the reaction between *N*-(-4-bromobenzylidene)-4-toluenesulfonamide with methyl vinyl ketone. Yields of up to 39 % were achieved with enantioselectivities of up to 84%. This is the highest enantioselectivity reported for a chiral ionic liquid used solely as a solvent to date. The enantioselectivity observed was comparable to that observed in conventional solvents such as THF and toluene using chiral organocatalysts (83 % and 94% respectively)[57, 58]. However, the yield of product in these

solvents, were about twice as high as those obtained in the ionic liquid. This report by Leitner *et al.,* does show that it is possible to design solvents that can induce high enantioselectivities.

Michael additions occur between a carbon nucleophile (known as the Michael donor) and an α, β-unsaturated carbonyl compound (known as the Michael acceptor. The reaction is usually base-catalyzed. These 1,4 conjugate additions are reversible but polar solvents such as alcohols promote equilibrium toward the product [27].

The Michael addition of diethyl malonate to 1,3-diphenylprop-2-en-1-one was performed in the chiral ionic liquid **35**. Since the salt was a solid at room temperature, it was combined with solvents such as toluene and DMSO. The synthesis of this ionic liquid is shown in Figure 15 [59]. The product of the Michael addition was obtained with 96% yield and an enantioselectivity of up to 25% was observed with toluene as the co-solvent in ten hours. The ionic liquid was obtained in five steps from L-(-)-ethyl lactate **30**. First, the secondary hydroxyl was protected using benzyl bromide and sodium hydride. Then, reduction of the ester was accomplished with lithium aluminum hydride, followed by treatment of the resulting alcohol with tosyl chloride in pyridine. The tosylate was then converted to the bromide, using the ionic liquid 1-butyl-3-methylimidazolium bromide. The

resulting alkyl halide was then treated with 1-methylimidazole to give the ionic liquid.

The Michael addition of diethyl malonate and 1, 3-diphenylprop-2-ene-1-one was also performed in the ionic liquid [BMIM][OH]. The product was obtained with a yield of 95% in 2.5 hours [60]. This particular ionic liquid, [BMIM][OH] has attracted some attention. When the reaction between open chain 1, 3-dicarbonyl compounds and α, β-unsaturated esters or nitriles, are performed in this liquid, the bis-addition products are obtained exclusively. The reason for this is presently unknown [60, 61].

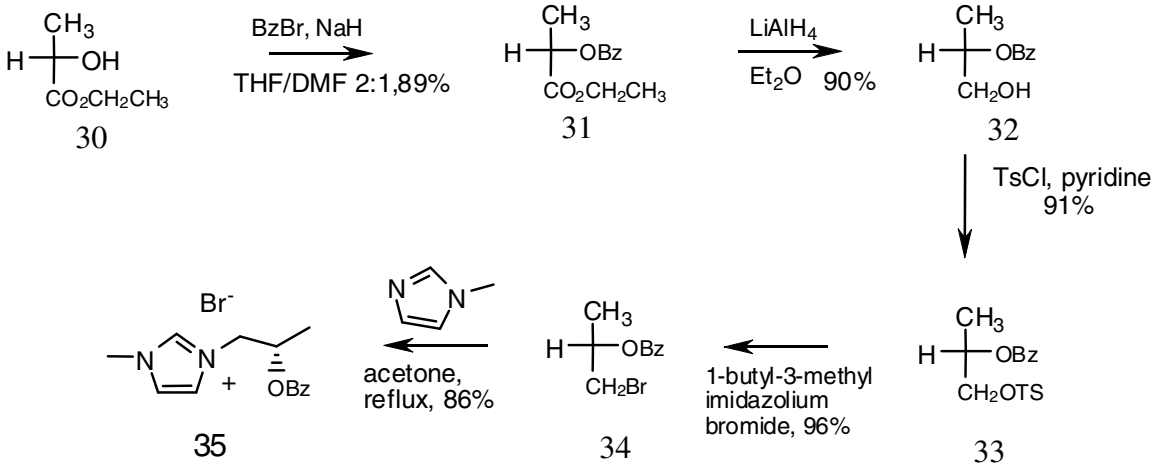
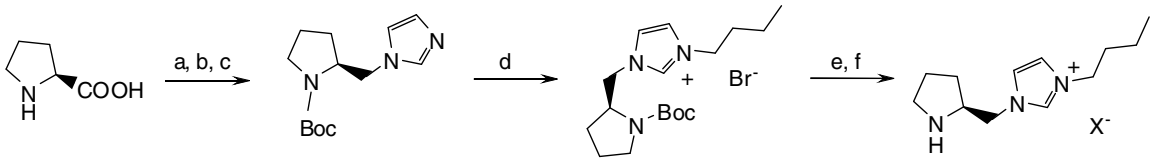


Figure 15. Synthesis of {35} derived from L-(-)-ethyl lactate.

More recently, chiral ionic liquids derived from the amino acid L-proline were used as organocatalysts for the Michael addition of ketones and aldehydes to nitroolefins [62]. The synthesis of the most effective salts **36** and **37** is shown in Figure 16. This work was inspired by the success of

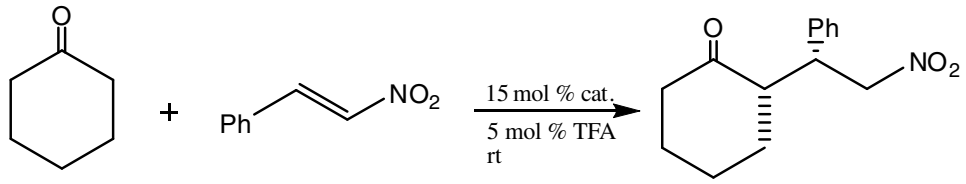
chiral pyrrolidines and imidazolines as enantioselective organocatalysts. The chiral pyrrolidine, which is covalently tethered to the ionic liquid moiety serves as the catalytic site, while the ionic liquid serves as the phase tag and chiral induction group [62]. The imidazolium cation could impart space shielding to the reaction intermediate and its proximity to the active site could create a microenvironment which would be favorable to the reaction [62].



36: X = Br, 37: X = BF_4

Figure 16. Synthesis of {36} and {37} from L-proline. a)$LiAlH_4$, THF, 75%, b) 1. Boc_2O, NaOH; 2. TosCl, pyridine, 90% for both steps; c) NaH, imidazole, 83%; d) nBuBr, toluene, 79°C, 93%; e) HCl/EtOH; then sat. $NaHCO_3$, 90%, f) NaX, acetone/acetonitrile, room temperature.

Shown in Table 9 are the results for the reaction between cyclohexanone **38** and trans-β-nitrostyrene **39** in the presence of ionic liquids **36** and **37** to give compound **40**. The products were obtained in yields of 99%, with enantioselectivities of up to 99%. The same reaction performed in DMSO with proline as the catalyst resulted in the product being obtained in 94% yield in 16 hours with enantioselectivites of 23% [63]. The ionic liquids were found to catalyze efficiently the Michael addition of a range of aldehydes and ketones to nitroolefins.



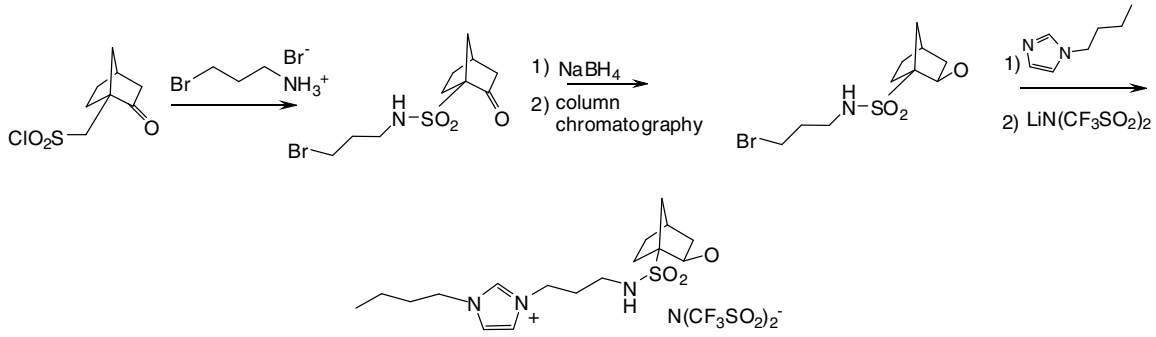
38 39 40

Entry	Catalyst	Time (h)	Yield % (a)	Syn/Anti(b)	ee %(c)
1	**36**	**10**	**99**	**99:1**	**98**
2	**37**	**20**	**99**	**99:1**	**97**
3 (d)	**37**	**8**	**100**	**99:1**	**99**

Table 9. Results of the reaction between {38} and {39} in the presence of chiral ionic liquids {36] and [37]. TFA = trifluoroacetic acid. a) Yield of isolated product. b) Determined by ^{1}H NMR spectra. c) Determined by chiral HPLC. d) 10 mol % catalyst used.

Other chiral ionic liquids that have been used as solvents in organic synthesis include those shown in Figure 17 and Figure 18. Chiral ionic liquid **41** was developed as catalyst for titanium-promoted diethylzinc addition to benzaldehyde by Gadenne *et al.,* [64]. It was obtained in five steps from D-camphor-10-sulfonyl chloride (Figure 17). The first step of the synthesis was the coupling of 3-bromopropylammonium bromide with the camphor derivative. This was followed by reduction with sodium borohydride. The resulting diastereoisomers were separated using column chromatography. The exo-product was then allowed to react with 1-butyl imidazole to generate the ammonium salt. Anion exchange was achieved using lithium bis(trifluoromethyl)sulfonylimide. This ionic liquid (and other

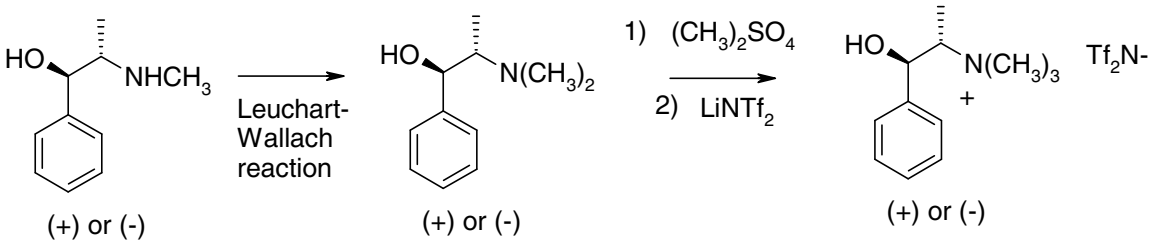
ionic derivatives) showed good catalytic ability (> 99% yield) in the titanium catalyzed alkylation of benzaldehyde and resulted in enantioselectivities of 65%.



41

Figure 17. Synthesis of the isoborneol salt, 41.

The photoisomerization of dibenzobicyclo[2.2.2.]octatrienes was performed on a series of chiral ionic liquids described by Ding, *et al.* [65]. The highest enantioselectivity (12 %) was achieved in **42**. The synthesis of this salt was initially reported by Wasserscheid, *et al.* [66]. Ephedrine was converted to *N*-methylephedrine by Leuchart-Wallach reaction. The alkylation of *N*-methylephedrine with dimethyl sulfate, followed by anion exchange resulted in the ionic liquid (see Figure 18). This ionic liquid was also used by as a stationary phase in gas chromatography. It was found effective in separating the enantiomers of alcohols, diols, sulfoxides, *N*-protected amines and epoxides [67].



42

Figure 18. Synthesis of the ephedrine salt, 42.

Other examples of chiral ionic liquids include species derived from natural amino acid [68, 69], derivatives with planar chirality [70], axial chirality [71], and natural products such as terpene and menthol [72, 73]. Comprehensive reviews of chiral ionic liquids have been written by Ding [20] and Armstrong and Gaumont, *et al.* [21].

Ionic liquids, chiral or achiral can influence organic reactions such as Diels-Alder, Baylis-Hillman, and Michael additions. The extent of that influence depends on the cation and/or anion of that liquid. The overall polarity of the solvent, the ability of the solvent to stabilize the transition state or reaction intermediate and in some cases hydrogen bonding work in tandem to influence the course of the reaction. In some respects they can be better than conventional solvents currently in use but again, this depends on the cation and anion. They can enhance reaction rates when compared to reactions done in non-polar solvents. Although this was not discussed, in all the cases presented the ionic liquids could be recycled or reused several

times after extraction of the products and excess starting materials, unlike the situation with conventional solvents. (This was normally done using diethyl ether or hexanes.) In other cases, ionic liquids may not be the best choice. In Diels-Alder reactions, chiral ionic liquids induced little to no enantioselectivity and in some cases the reaction rates decreased. Better success was achieved in the study of Baylis-Hillman reactions and Michael additions. Through careful design of the cation or anion, moderate to excellent enantioselectivies could be obtained using ionic liquids (for example, the chiral borate ionic liquid and ionic liquids derived from proline.)

As mentioned earlier the focus of our research has been on the synthesis and characterization of chiral ionic liquids made with 3-chloro-1, 2-propanediol. We were interested in using these new materials for Diels-Alder reactions. It is expected that though one could see an increase in reaction rates and endo selectivity, but little to no enantioselectivity is expected.

We have performed developmental work with the racemic alkyl halide and have extended these efforts to the more expensive chiral species. Our goal has been to generate a series of salts and find the ones with the best properties (low viscosity, wide liquidus range, *etc*.). Although physical

characteristics of racemates compared to individual enantiomers are anticipated to differ, the intent has been that synthesis of the chiral analogues of those liquids would proceed in a corresponding manner. A few of the chiral analogues have been successfully synthesized. So far they have been found to exhibit lower melting points, than their racemic analogues.

C. Antimicrobial Surfaces

There is a great concern over the rise of nosocomial or health-care associated infection [74, 75]. Most of these infections are due to drug-resistant microorganisms such as meticillin-resistant *Staphyococcus aureus* (MRSA) and *Pseudomonas aeruginosa*[74]. It is believed that the principal mode of transmission is the direct handling of patients by nursing personnel [76]. It has also been found that bacteria can survive for some time on surfaces such as fabrics and plastics [77]. Thus, it is of interest to develop new antibiotics and antimicrobial agents that can kill bacteria or inhibit their growth.

Quaternary ammonium cationic surfactants have been known for a long time to exhibit antimicrobial activity and are widely used in industry as disinfectants. These salts are understood to disrupt the cell wall and/or the cell membranes of bacterial cells. The cells lose electrolytes and nucleic

materials, which leads to cell death [78, 79]. Our efforts attempt to take advantage of this aspect of cationic surfactants to develop new salts and processes that can be applied to porous and non-porous surfaces rendering them biocidal. For the past few years the Engel lab has been involved in the modification of several types of porous surfaces, which include those that are carbohydrate-based (wood, cotton and paper), as well as those that are protein-based (silk and wool) [80, 81, 82].

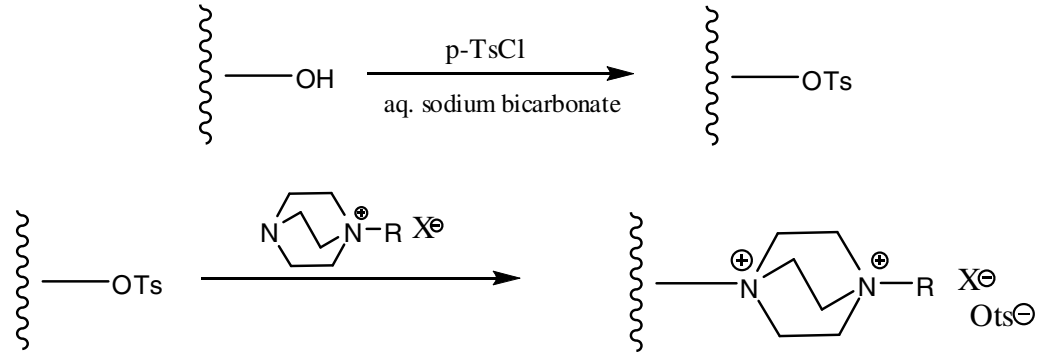


Figure 19. Modification of carbohydrate and protein based surfaces.

Modification of such surfaces involves tosylation of the primary hydroxyl groups, followed by the covalent attachment of monocationic surfactants that were synthesized using diazabicyclo[2.2.2]octane (see Figure 19). The resulting polycationic surfaces have demonstrated high antimicrobial activity against a range of Gram positive and Gram negative bacteria such as *Escherichia coli*, and *S. aureus*, as well as fungi such as *Candida albicans, Aspergillis niger* and *Saccharomyces cerevisiae*.

Antimicrobial activity is dependent on the structure of the cationic surfactant. In general, surfactants have a polar head and a long lipophilic chain. We have found that the monocationic DABCO surfactants that exhibited the most broad-spectrum antimicrobial activity were those bearing alkyl chains that were sixteen carbons or twelve carbons long [80, 81]. The structure of 1-hexadecyl-1-aza-4-azoniabicyclo[2.2.2]octane chloride (which will be referred to as DC16 in this report), one of the surfactants used in the modification of various surfaces is shown in Figure 20.

Other research groups have found the optimal chain length for a variety of water-soluble ammonium surfactants to be 10 – 14 carbons long. For example, Pernak *et al.,* studied the correlation of the structure of 1-alkoxymethylcarbamoylpyridinium salts and their antimicrobial activity (see Figure 21) [83]. This group found that salts with alkoxy chains ten to twelve carbons long were most effective against a range of bacteria and fungi. Campanac et al. studied the effect of *N*-alkylbenzyldimethyl ammonium chlorides on biofilms of *P. aeruginosa* and *S. aureus* [84]. *N*-dodecylbenzyldimethyl ammonium chloride (having an alkyl chain 12 carbons long) was most effective on *P. aeruginosa. N*-dodecylbenzyl-dimethylammonium chloride and *N*-tetradecylbenzylammonium chloride

(having an alkyl chain 14 carbons long) were most effective against *S. aureus.*

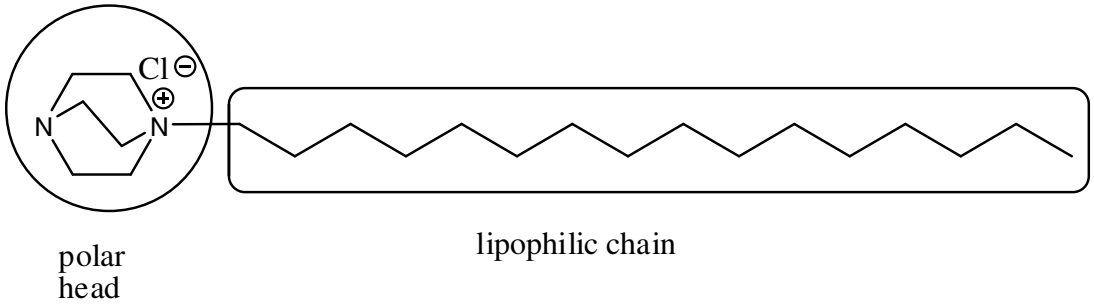


Figure 20. Structure of the cationic surfactant DC16.

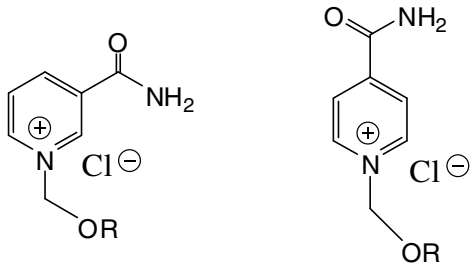


Figure 21. Pyridinium salts studied by Pernak *et al.* [83]. R = -C_2H_5, -C_3H_7, -C_4H_9, -C_5H_{11}, -C_6H_{13}, -C_7H_{15}, -C_8H_{17}, -C_9H_{19}, -$C_{10}H_{21}$, -$C_{11}H_{23}$, -$C_{12}H_{25}$.

We have recently focused our attention on modifying a variety of surfaces which include polyester fabrics, nylon and polyvinylchloride, as well as dendrimers which can be thought of as "limited surfaces". We have also developed polycationic carbohydrate derivatives that can be applied to surfaces, which provides them with antimicrobial properties. Patents have been filed for some of these procedures.

1. Polycationic Carbohydrate Surfactants

In addition to their antimicrobial properties, cationic surfactants are of interest for their ability to form supramolecular structures such as micelles, vesicles and bilayers in solution [85, 86, 87, 88]. The ability of surfactants (also known as surface active agents and amphiphiles) to form these aggregates in water can be attributed largely to the hydrophobic effect [89, 90]. Depending on the head group of the surfactant, other forces such as hydrogen bonding can also play a role. These materials tend to accumulate at interfaces such as liquid-vapor to form foams, liquid-liquid to form emulsions and liquid-solid to form suspensions [91]. Surfactants also lower interfacial tension. Because of their properties, cationic surfactants are used as antiseptic agents in cosmetics, and in the textile industry as fabric softeners, waterproofing agents, anti-static agents and dye-fixing agents. They are used for corrosion protection of pumps, pipelines and storage tanks, used for ore flotation, used in preparations of asphalt emulsions, automotive undercoating preparations, and pigment-dispersing agents in paints. Cationic surfactants are also found in hair conditioners and disinfectants [92, 93].

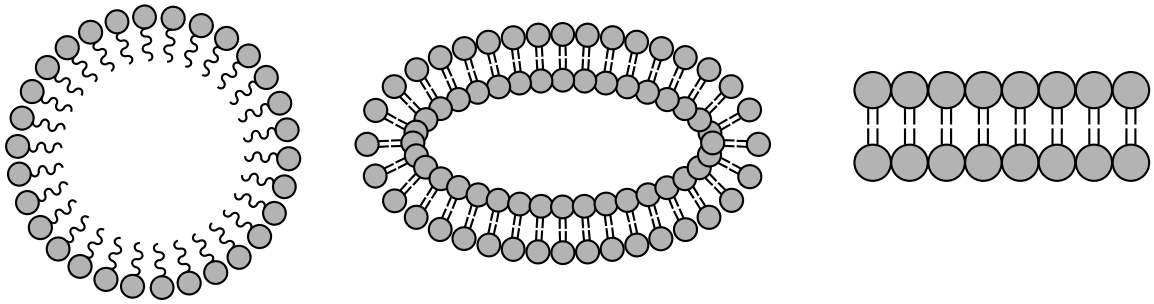


Figure 22. Structures formed by surfactants include micelles, vesicles and bilayers.

When surfactants assemble into entangled fibers which trap solvent molecules, we have the formation of a gel. A gel as defined by Flory is "a two-component, colloidal dispersion with a continuous structure with macroscopic dimensions that is permanent on the time scale of the experiment and is solidlike in its rheological behavior [94]." A simpler definition is: "If it looks like Jello, it's probably a gel [95]."

There is great interest in small molecules that can gel solvents, in particular water [96]. It has been noted that there are few small molecules that can gel water [97]. Small molecule hydrogelators may be useful in membrane and separation technology, catalysis [98], drug delivery [99], tissue engineering [100], and pollution control [96]. Gels derived from polymers, proteins and inorganic compounds are widely used in the cosmetics, food, and oil industries [100].

A series of polycationic salts based on the carbohydrate derivatives D-mannitol and α-D-methyl glucopyranosde have been developed. Some of these salts were found to gelate water and alcohols. The antimicrobial

activity of these gels was assessed and they were found to be very effective against the Gram positive bacterium *S. aureus*.

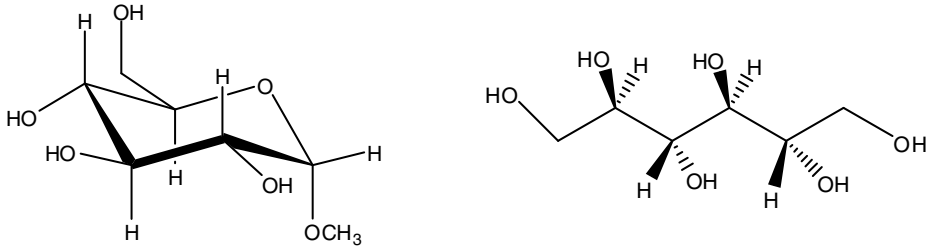


Figure 23. α-D-methyl glucopyranoside and D-mannitol.

2. Antimicrobial Dendrimers

Dendrimers are three-dimensional, globular macromolecules that incorporate four basic features: a central core, branching units that emanate from the core, extension units, and terminal functionalities (see Figure 24) [101, 102, 103].

A common approach toward their synthesis involves an iterative sequence of reaction steps, in which each iteration leads to a higher generation material [103]. Dendrimers can be synthesized divergently (starting from the core to the periphery) or convergently (starting at the periphery and ending at the core) [104, 105]. The most common types include polypropylene (PPI) and polyamidoamine (PAMAM) dendrimers, both of which are commercially available. They have attracted much attention from those involved in medicinal chemistry due to their compact

structures and the density of functional groups that can be found at the surface of these macromolecules. Further, PAMAM dendrimers of relatively low generation are degraded in the human liver. Dendrimers have been developed and studied as contrast agents for magnetic resonance imaging (MRI), agents for cancer treatment, transfection agents and as antimicrobial agents [106, 107].

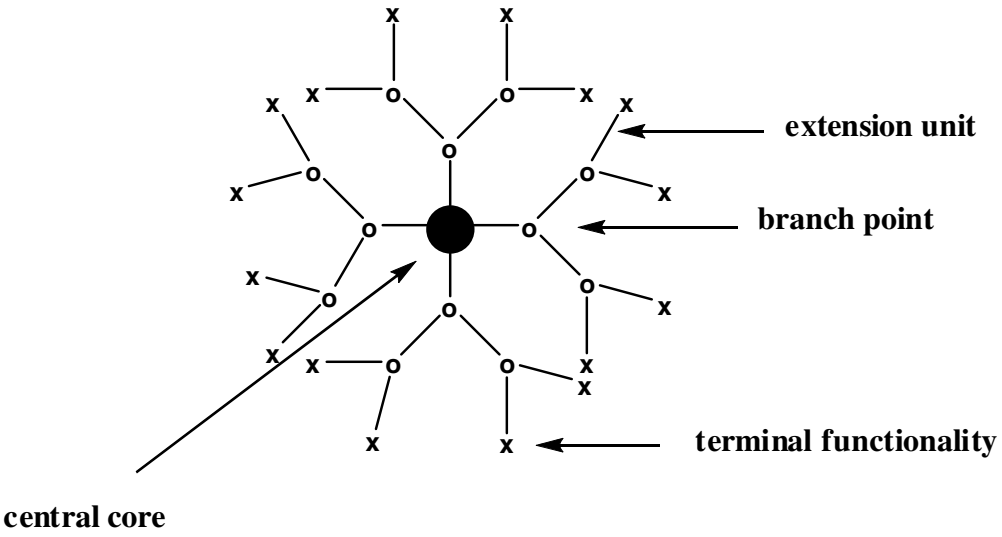


Figure 24. General structure of dendrimers

There are two main approaches to the synthesis of antimicrobial dendrimers. One can design materials with antimicrobial functionalities or design dendrimers that deliver antimicrobial agents. Balough, *et al.* prepared PAMAM dendrimer-silver complexes and nanocomposites that displayed antimicrobial activity *in vitro* [108]. The dendrimers had carboxylate terminal groups and in the presence of silver acetate in water, silver-carboxylate salts were formed at the surface, along with silver ions

that were associated within the folds of the dendrimer. The antimicrobial activity comes from the ability of the silver ions to diffuse from the dendrimer to the surface of bacteria. Zanini and Roy designed and synthesized glycodendrimers with a 3, 3'-iminobis(propylimine) core that were found to inhibit effectively the hemagglutination of human erythrocytes by influenza viruses [109]. Bacterial and viral infection may be avoided if viruses and bacteria are prevented from attaching to cells. The structure-activity relationship of a series of quaternary ammonium functionalized poly(propylene imine) dendrimers with hydrophobic chains that ranged from eight to sixteen carbons, and with generations ranging from one to five were studied by Chen, *et al.* [110]. These dendrimers (which will be discussed with more detail in Results and Discussion) were found to be effective antimicrobial agents.

We have successfully modified three generations of mannose functionalized PAMAM dendrimers developed in the laboratory of M. J. Cloninger. (This group studied the ability of these dendrimers to bind to lectin binding sites on the cell surface [111].) The first step was the tosylation of the hydroxyl group at the six position of the carbohydrate unit, followed by the addition of the monocationic surfactant DC16 or 1-(dodecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (which will be

referred to as DC12). These amphiphiles were developed by our lab and used in the modification of many of the surfaces we have developed. The result is a series of polycationic dendrimers, which have been found to be active against Gram positive and Gram negative bacteria.

3. Antimicrobial Polyester Fabrics

The development of antimicrobial textiles can be considered to have begun in 1867 with Joseph Lister, a well-known and well respected physician in Great Britain who treated wound dressings with carbolic acid (phenol) [112]. Since then various methods and antimicrobial agents have been used in the modification of textiles rendering them antibacterial and/or antifungal. Antimicrobial finishes may protect the user from microorganisms that cause odor and/or infectious disease, protect the textile from biodeterioration (caused by mold, mildew and fungi), and protect the textile from insects and other pests [113]. The most common method for modifying fabrics is by impregnating the antimicrobial agent into the fabric. The agent is slowly released over time by a controlled-release mechanism [113, 114]. Unfortunately, once all the agent has been released, the textile loses its antimicrobial function. Also, release of certain agents into the environment is a concern. Antibacterial agents can also be physically incorporated into

fabrics through covalent bonds. This allows for permanent biocidal function and is less of a risk to the environment.

Fabrics such as cotton, nylon and polyester have been modified with agents such as silver [115, 116], copper [117, 118], chitosan [119, 120], haloamines [121, 122], antibiotics [123], phosphonium surfactants [124] and quaternary ammonium surfactants. The focus here will be on cloth surfaces in which cationic surfactants have been covalently attached. An early example of this is work was reported in the 1970's by the research group of J. Isquith [125, 126]. This group was able to bind covalently organosilicon quaternary ammonium chlorides to a variety of surfaces that included siliceous surfaces (glass, sand, stone), natural fibers (cotton, wool), synthetic fibers (acrylic, polyester, spandex) and metals. These surfaces were found to exhibit antimicrobial activity against bacteria, yeast, algae and fungi. More recently a research group at MIT was able to modify textiles (cotton, wool, nylon and polyester) by immobilizing N-hexylated and methylated high molecular weight polyethyleneimine onto the surfaces [127, 128]. These materials showed strong bactericidal activity against airborne Gram positive and Gram negative bacteria and fungi.

We have focused on the modification of polyester fabrics using quaternary ammonium surfactants developed by the Engel laboratory.

Polyester fiber is commonly made from an aromatic carboxylic acid and a diol which are derived from petroleum feedstocks. The most common polyester poly(ethylene terephthalate) referred to as PET, is made from terephthalic acid and ethylene glycol. Common trademarks for polyester include Dacron, Terylene and Trevira. Polyester fibers are strong, thermally stable, and resistant to fungi and insects, chemically resistant and weatherproof [129, 130]. In our laboratory, polyester fabric has been modified in three steps. The first step is controlled reduction using sodium borohydride, which generates primary hydroxyl sites. This is followed by tosylation and the addition of the cationic surfactant DC16 or DC12. Modification of polyester in this manner has resulted in a polycationic surface which has been found to be active against Gram positive and Gram negative bacteria.

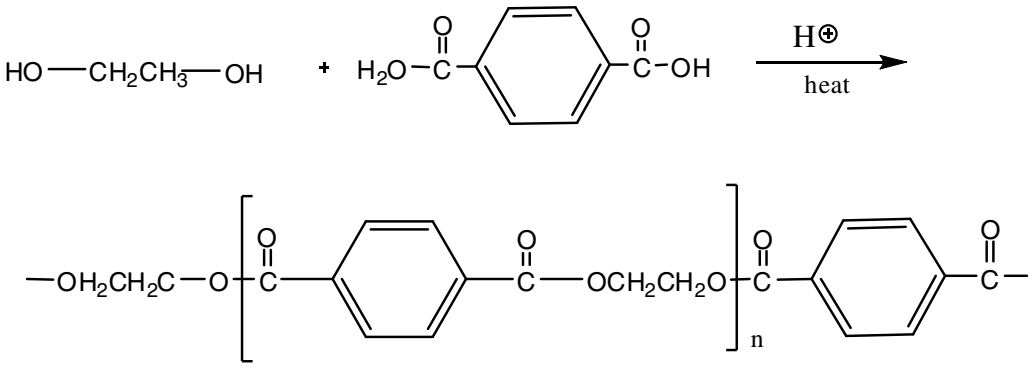


Figure 25. Synthesis of poly (ethylene terephtalate) or PET.

Chapter 2

RESULTS AND DISCUSSION

A. New Monocationic and Polycationic Ammonium Salts

The Engel research group has been involved for the past few years with the synthesis of various types of monocationic and polycationic ammonium salts which are referred to as “strings”. A polycationic “string” is a compound in which cationic sites are incorporated in the covalent structure along a linear chain with free-floating anions [5]. Monocationic strings have one positive charge and have been derived from tertiary amines such as 4-dimethyl aminopyridine (DMAP), pyridine, 1-methyl imidazole and 1, 4-diazabyclo[2.2.2]octane. The conversion of the halide salts into LIPs and PILS to generate ionic liquids started about eight years ago. Several unique categories of ionic liquids have since been developed based on previously developed strings (see Figure 1 in Chapter 1).

We continue with the synthesis of new monocationic and polycationic strings and their conversion to ionic liquids, using the chiral auxiliary 3-chloro-1, 2-propanediol. This alkyl halide can be considered as a precursor deriving from the chiral pool of organic compounds. The tertiary amines that have been used for the synthesis of these new salts include DABCO, DMAP, 1-methyl pyrrolidine, *N,N,N’,N’*-tetramethyl-1,6-hexadiamine, *N,N,N’,N’*-

tetramethyl-1,3-propanediamine and *N,N,N',N'*-tetramethyl-1,3-butanediamine. The anions of interest include chloride, phosphate, bis(trifluoromethylsulfonyl)imide, dicyanamide, and diphenyl phosphate.

Dicyanamide salts are made by reaction of the halide salt with silver dicyanamide in water [131]. The resulting silver salt is filtered and the aqueous solvent is evaporated. The diphenyl phosphate salts are made by the reaction of a charge equivalent of diphenyl phosphate and postassium hydroxide with the halide salt in ethanol. The potassium salt is filtered and the ethanol is evaporated generating the organic salt. The synthesis of the phosphates and bis(trifluoromethylsulfonyl)imides were described in the introduction.

As a general trend, if we were able to solidify the halide salts, then these salts could be simply purified by washing with an appropriate solvent. In this way, the other salts could be formed relatively pure with little need for further purification. All the new salts were dried for several days under high vacuum and their structures were verified using ^{1}H and ^{13}C NMR. Melting points were determined using a standard melting point apparatus for the solids and/or differential scanning calorimetry (DSC) for those salts that were liquid at room temperature. The thermal decomposition temperatures

for some of the ionic liquids were also determined through thermogravimetric analysis (TGA).

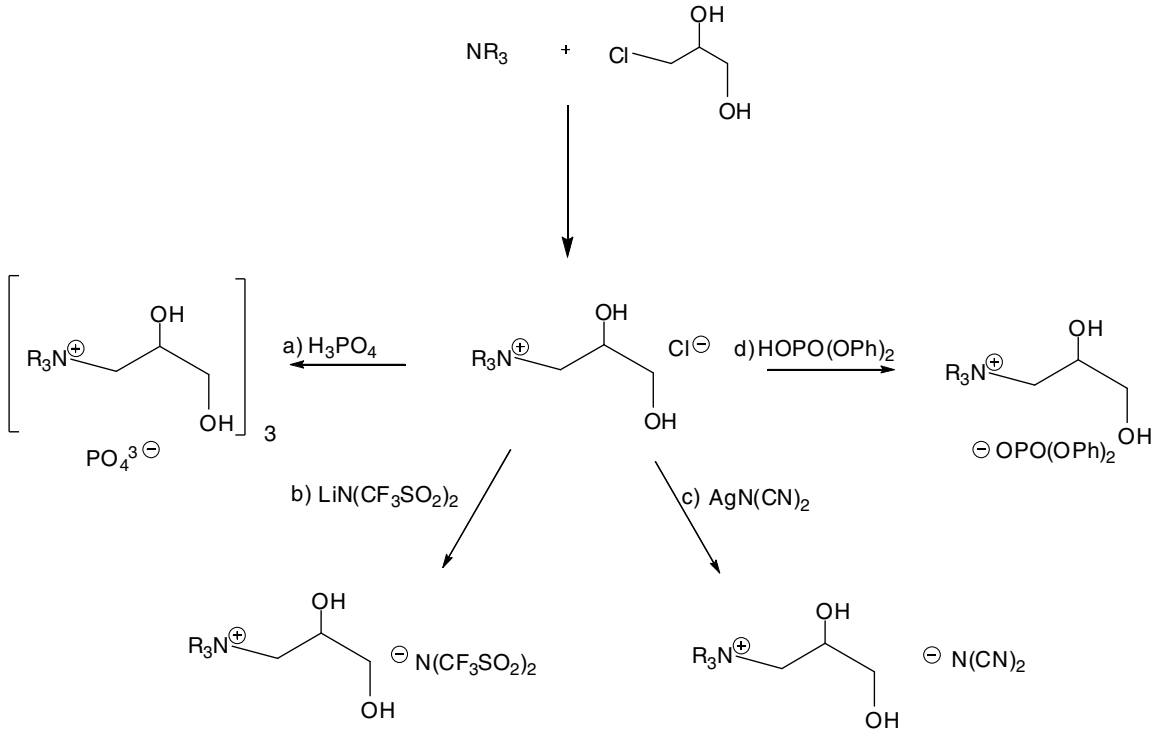


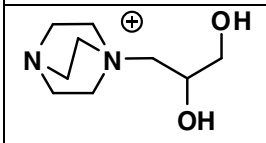
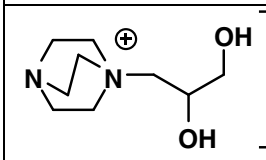
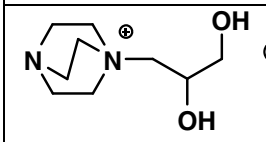
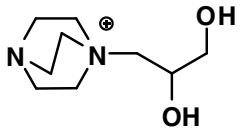
Figure 26. Synthesis of ionic liquids. NR_3 = tertiary amine. a) phosphoric acid, b)lithium bis(trifluoruosulfonyl)imide, c) silver dicyanamide d) diphenyl phosphate.

1. Monocationic DABCO salts\

The new monocationic DABCO salts are presented in Table 10 along with their melting points. The letter "D" refers to DABCO, "Cl" to chloride, "IP" to ionic phosphate, "DCA" to dicyanamide and "DPP" to diphenyl phosphate. For the salts that are considered ionic liquids, the water content at which the melting points were determined, are noted. The presence of water can influence the physical properties (such as melting points) of ionic

liquids. Almost all the DABCO salts are solids at room temperature. Only the dicyanamide salt is considered an ionic liquid with a melting point of -19 ˚C. This liquid is extremely viscous, and does not flow. This liquid begins to decompose at about 154 ˚C. An attempt was made to make the sulfonylimide salt but the product proved to be very water soluble and we were unable to eliminate the chloride impurity. In general, bis(trifluoromethylsulfonyl)imide salts are usually hydrophobic and can be separated from the aqueous layer.

Table 10. DABCO-based monocationic salts.

Structure/Code	**Melting point/ (% water)**	**Name**
 D-Cl	137 – 141 ˚C	1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride
 D-IP	125 – 130 ˚C	1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane phosphate
 D-DCA	-18.7 ˚C (0.411)	1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane dicyanamide
 D-DPP	139 – 141 ˚C	1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane diphenyl phosphate

The salt D-Cl was synthesized by adding one equivalent of 3-chloro-1, 2-propanediol to 1, 4-diazabyclo[2.2.2]octane in ethyl acetate. The reaction mixture was stirred overnight and the solvent evaporated to produce a white compound. The hydroscopic product was washed with ethyl acetate and ether and obtained in 73% yield. This salt was found to be soluable in only water, methanol and ethanol. The dicyanamide salt, D-DCA was made by the addition of a charge equivalent of silver dicyanamide in water. After filtration of silver chloride, the solvent was evaporated and the viscous liquid was obtained in 80% yield.

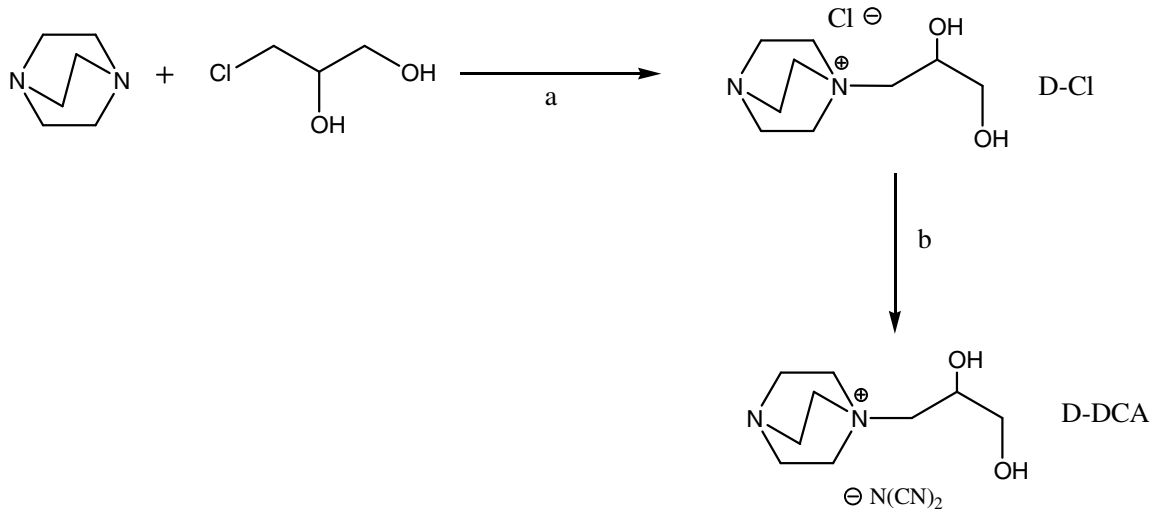


Figure 27. Synthesis of D-Cl and D-DCA. Conditions: a) ethyl acetate, RT, stir overnight, 73%; b) $AgN(CN)_2$, water, R.T, stir overnight (-AgCl), 80%.

The structure of D-Cl was verified using a variety of NMR methods. Shown in Figure 28 is the expanded ^1H NMR spectrum of D-Cl. The labeled structure of the (S) enantiomer of D-Cl is presented above the spectrum. The

triplet at 3.09 ppm (J = 7.6 Hz) corresponds to the homotopic protons H_a and $H_{a'}$ and integrates for six protons. The triplet is due to coupling with H_b and $H_{b'}$. The complex multiplet between 3.26 – 3.51 is due to the coupling between the diastereotopic protons H_y and $H_{y'}$ and H_z and $H_{z'}$ with H_x at the stereogenic center. (A doublet of doublets (dd) would be expected for each diastereotopic proton.) These peaks overlap with what should be a triplet for the protons H_b and $H_{b'}$. For H_x, eight sets of doublets should be seen. Instead there is a broad multiplet at 4.24 ppm which integrates for one proton.

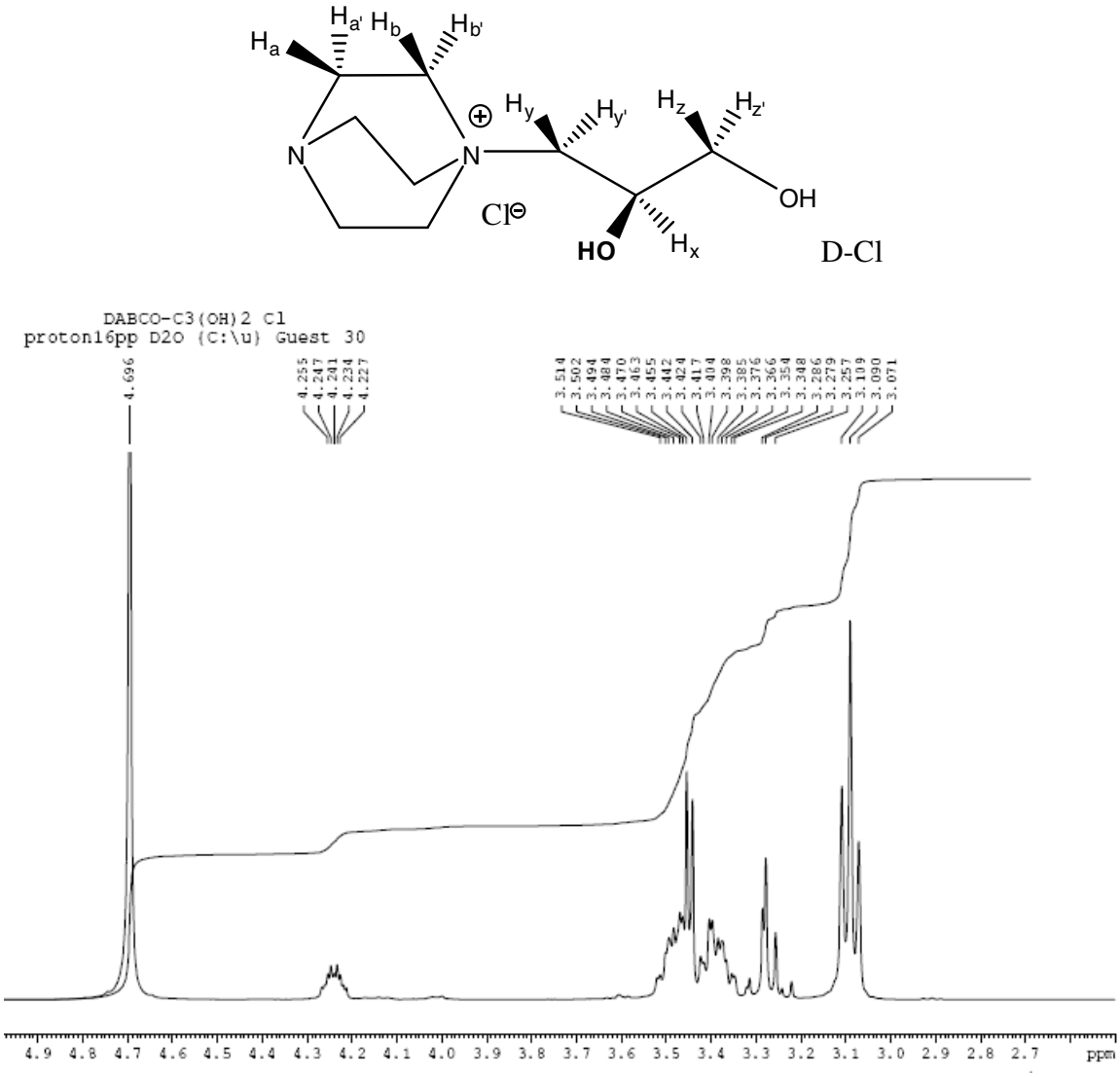


Figure 28. ^{1}H NMR spectrum of D-Cl (400 MHz, D_2O).

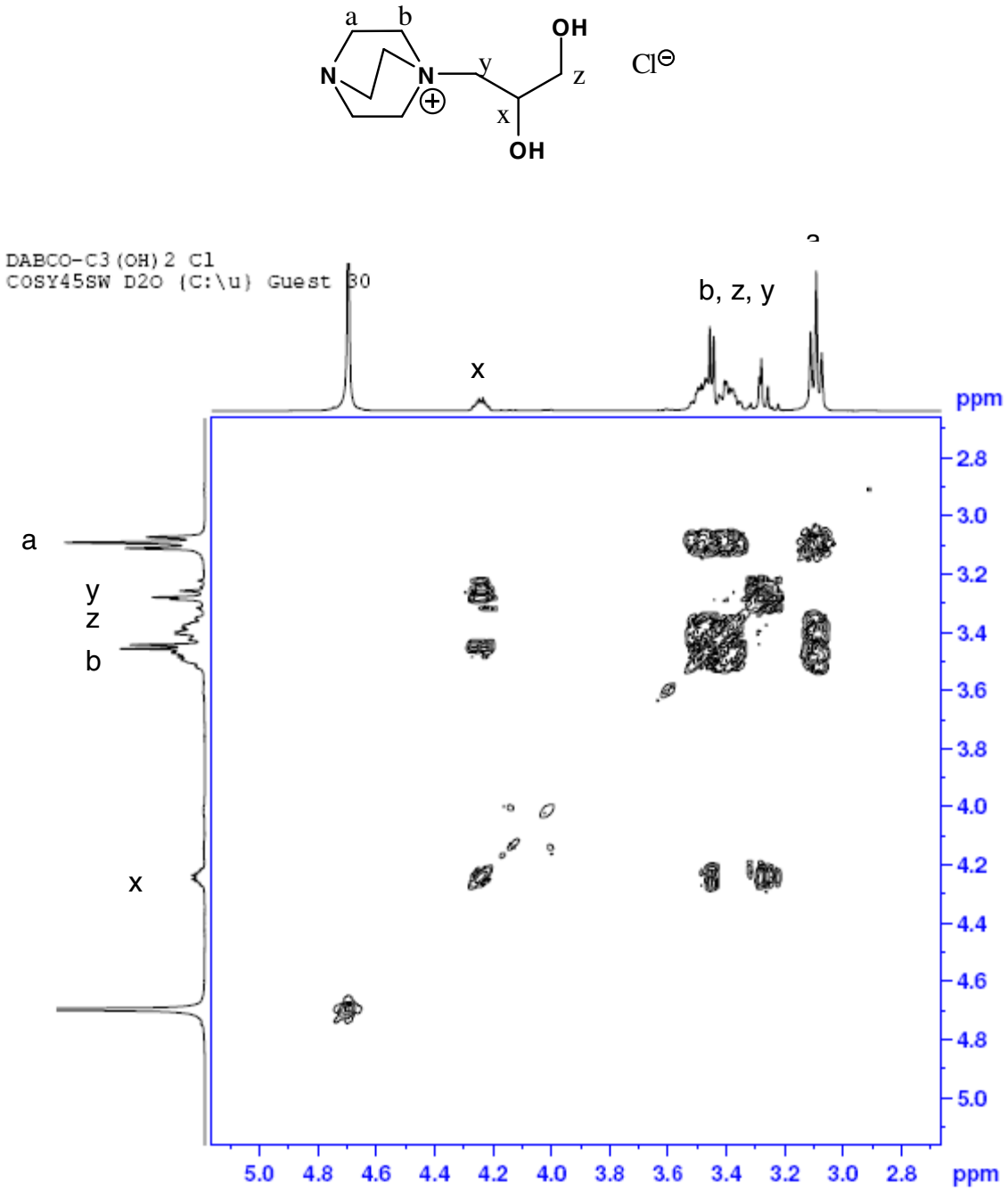
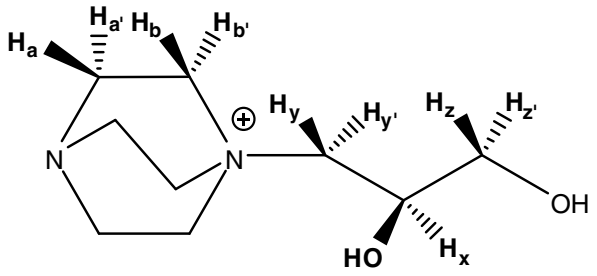


Figure 29. ^{1}H-^{1}H COSY NMR Spectrum of D-Cl (400 MHz, D_2O).

The COSY spectrum for D-Cl shows coupling between H_a and H_b. There is coupling between H_x and H_y and $H_{y'}$. Coupling is also seen between H_x and H_z and $H_{z'}$. The peak under 'y' in the COSY spectra

integrates for one proton, is assigned as H_y. H_y is in a "cis" position in regards to the secondary hydroxyl, which makes it more shielded than $H_{y'}$. It is expected that the chemical shift for H_y would be higher upfield than the shift for $H_{y'}$. Based on the ^1H NMR and ^1H-^1H COSY spectra the detailed proton assignments along with coupling constants are shown in Table 11.



Proton	Chemical shift (ppm)	J (Hz)
H_a (6 H)	3.09 (t)	7.6
H_b (6 H)	3.44 (m)	7.2
H_y (1H)	3.26-3.29 (m)	-
$H_{y'}$, H_z, $H_{z'}$	3.35-3.51 (m)	-
H_x	4.24 (m)	2.4-3.2

Table 11. ^1H shift assignments and coupling constants of D-Cl.

Five peaks are expected in the ^{13}C NMR spectra for D-Cl and this is seen in the spectra shown in Figure 30. The ^{13}C DEPT-135 experiment is

shown in Figure 31. Based on these spectra the peak assignments for the carbons found in D-Cl are presented in Table 12.

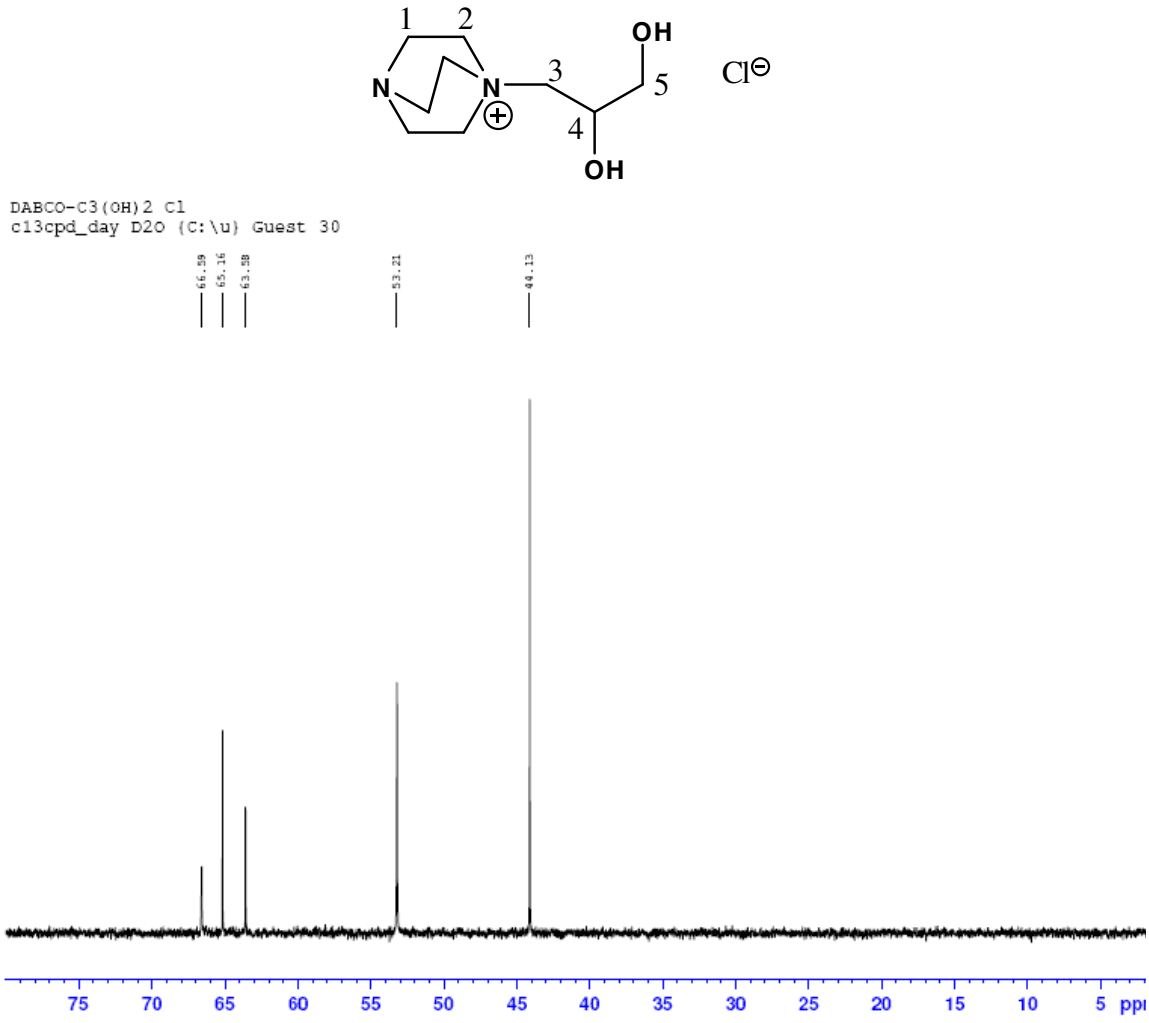


Figure 30. ^{13}C NMR spectrum of D-Cl (100 MHz, D_2O).

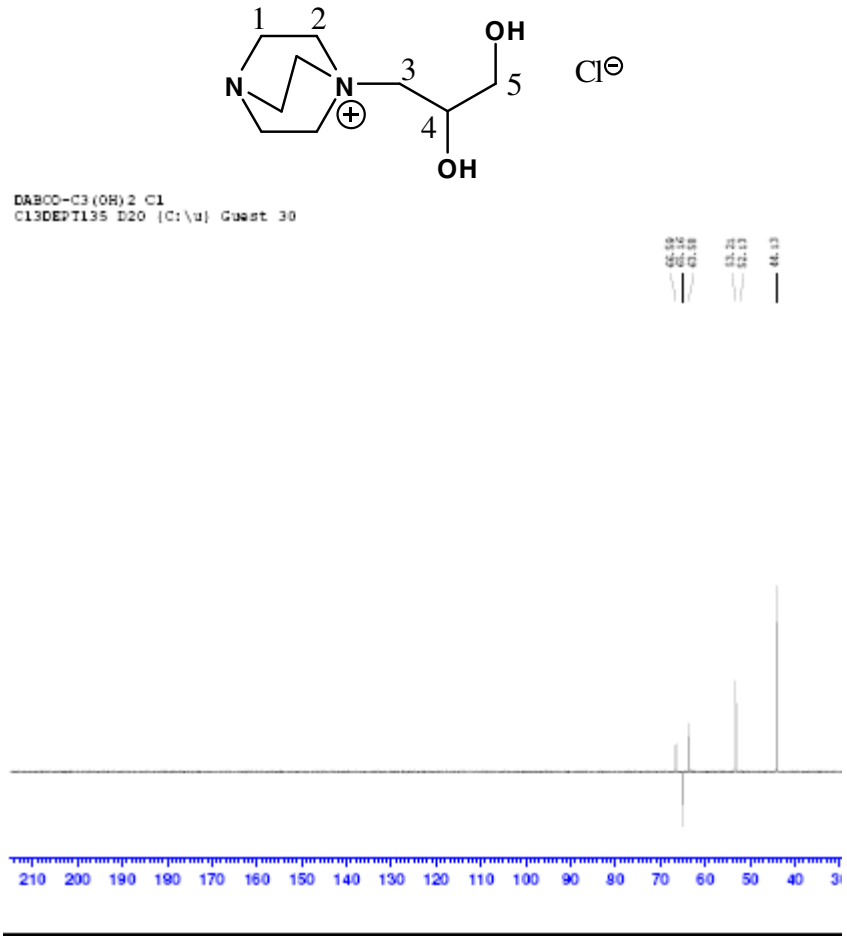


Figure 31. ^{13}C NMR DEPT experiment of D-Cl (100 MHz, D_2O).

Chemical Shift	Carbon Type	Carbon
44.1	CH_2	1
52.2	CH_2	2
63.6	CH_2	3
65.2	CH_2	5
66.6	CH	4

Table 12. Carbon assignments for D-Cl.

The chemical shifts for carbons 1, 2, and 3 show up as positive signals in the DEPT spectra, instead of as negative signals. This indicates that the coupling

constant J_{CH} for these peaks, which are indicative of carbons closest to the nitrogen atoms, may be l80 Hz or larger.

The ^{1}H NMR spectra for D-DCA is very similar to that of D-Cl (see Figure 32). In the ^{13}C NMR trace (Figure 33) a signal appears at 120 ppm. This is indicative of the carbons found in the dicyanamide anion. (It is small due to long relaxation time (T_1).

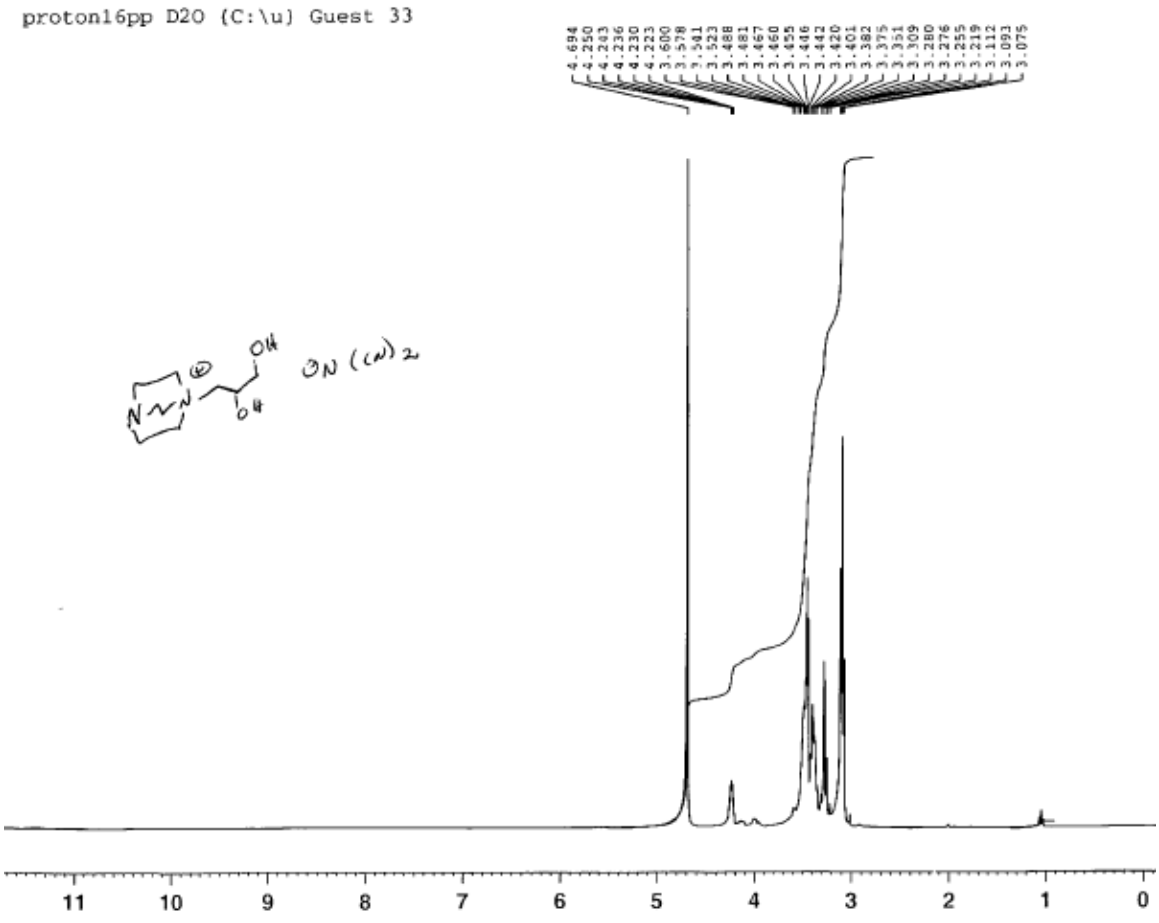


Figure 32. ^{1}H NMR spectrum of D-DCA (400 MHz, D_2O).

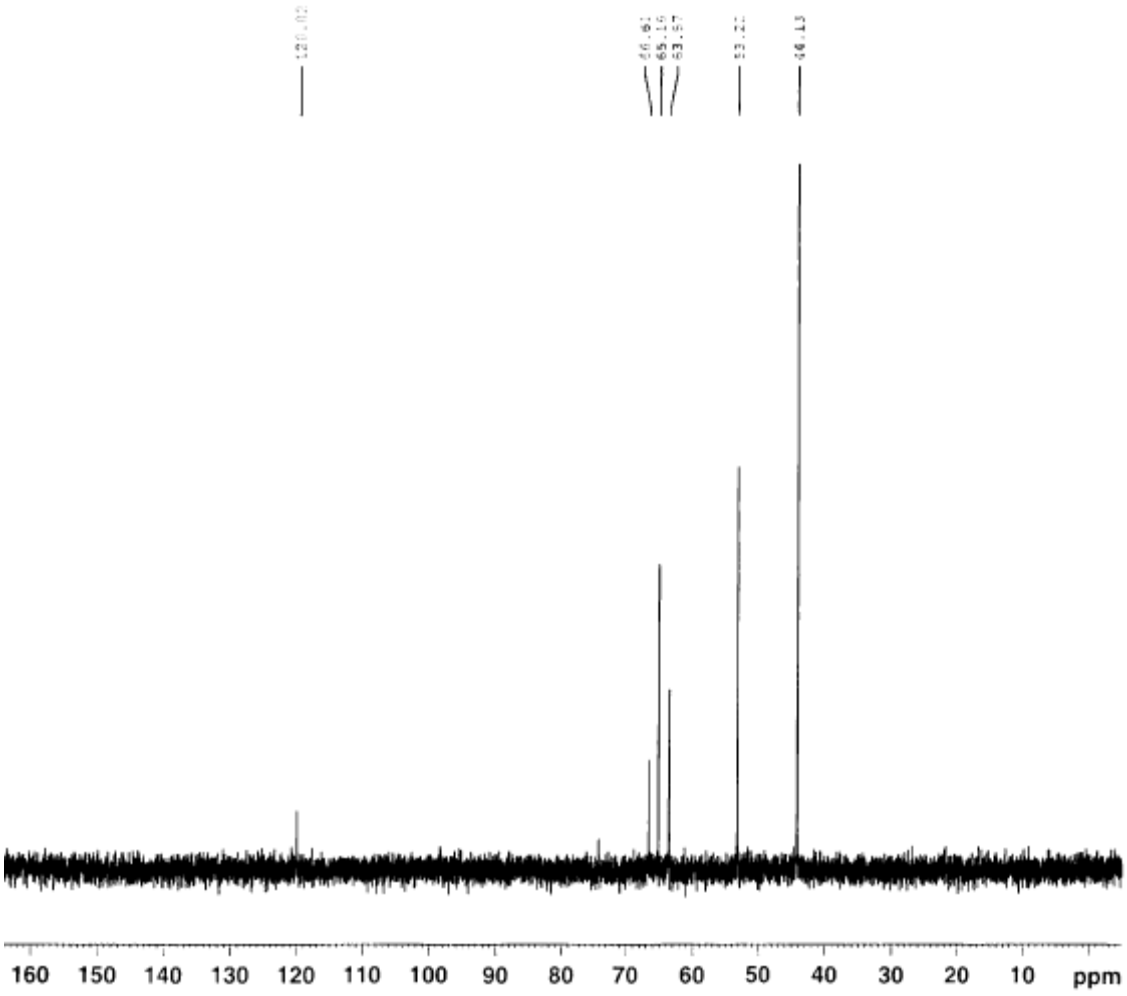


Figure 33. ^{13}C NMR Spectra of D-DCA (100 MHz, D_2O).

2. Monocationic DMAP Salts

New DMAP salts are shown in Table 14. "DMAP" refers to 4-dimethylamino pyridine and "NTf_2" to bis(trifluoromethylsulfonyl)imide. All salts are solid at room temperature. The salts DMAP-NTf_2 and DMAP-DPP can be considered ionic liquids since they have melting points that are less than 100 ˚C (49 °C and 93 °C respectively). DMAP-NTf_2 has a viscosity of 96.65 cP at 65˚C (see Entry 1, Table 13) [132]. By comparison, the

viscosity of water is 0.86 cP at room temperature. This ionic liquid is also more viscous than similar DMAP analogues and the popular [BMIM][NTf_2] (see Figure 34 and Table 13) [132]. As a general trend, an increase in the number of functional groups leads to an increase in viscosity. DMAP-NTf_2 exhibited very good conductivity (which was determined at 1.18 mS/cm at 52 ˚C) when compared to other bis(trifluoromethylsulfonyl)imide salts but only at elevated temperatures. The conductivity of 0.02M KCl solution, a common conductivity reference solution has a conductivity of 2.7 mS/cm at 25 ˚C.

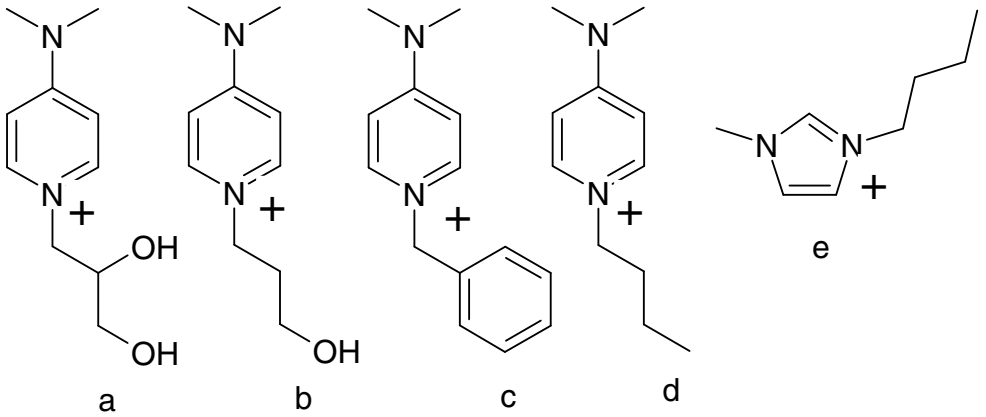


Figure 34. Cations referred to in Table 13. a) $DMAPC_3(OH)_2$ aka DMAP-NTf_2. b) $DMAPC_3OH$. c) DMAPBz. d) DMAPB e)BMIM.

Entry	Cation/Liquid	Conductivity (mS/cm)	Viscosity (cP at 65˚C)	T_m (˚C)	G.T (˚C)	Ref.
1	$DMAPC_3(OH)_2$	1.18 @ 52 ˚C	96.7	49	-33	132
2	$DMAPC_3(OH)$	0.803 @ 25 ˚C	29.1 (109 @ 35 ˚C)	-59	-	132
3	DMAPB	2.22 @ 26 ˚C	16.9 (81 @ 25˚C)	28	-70	132
4	DMAPBz	2.12 @ 63 ˚C	59.3	58	-25	132
5	BMIM	3.9 @ 20 ˚C	(52 @ 20 ˚C)	-4	-	19
6	Water	-	(0.86 @ 25 ˚C)	-	-	
7	0.02M aq. KCl	2.7 @ 25 ˚C	-	-	-	

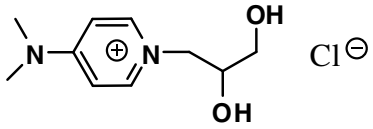
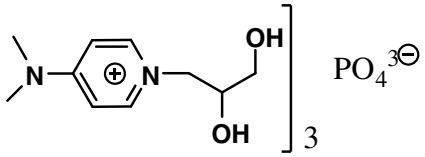
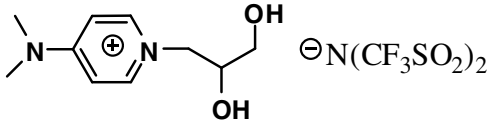
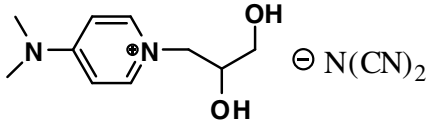
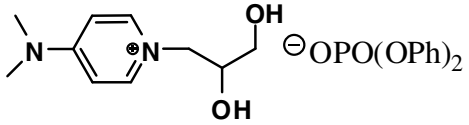
Table 13. Comparison of some of the properties of bis(trifluoromethylsulfonyl)imide salts with water and potassium chloride solution. T_m = melting point. G.T. = glass transition temperature [132].

The synthesis of DMAP-Cl was done through the addition of one equivalent 3-chloro-1,2-propanediol to 4-dimethylaminopyridine in acetonitrile. The reaction mixture was refluxed overnight. The white solid which precipitated out of solution, was filtered by vacuum and washed with ethyl acetate and ether. The solid which was obtained in 97% yield was dried under high vacuum (see Figure 35).

The salt DMAP-NTf_2 was obtained by adding a charge equivalent of lithium bis(triflouromethylsulfonyl)imide to DMAP-Cl in water. The reaction mixture was stirred overnight and the aqueous layer was carefully decanted. The ionic liquid was washed with water, until no presence of halide was detected in the wash (tested using aqueous silver nitrate). The

liquid was then dried in a vacuum oven at 70˚C for three days. The product which is a white solid was obtained with a yield of 30%. This material displayed an amphiphilic nature, so much of the material was lost during purification (see Figure 35).

Table 14. DMAP-based monocationic salts

Structure/Code	**Melting point**	**Name**
 DMAP-Cl	204 – 207 ˚C	N-(2,3-dihydroxypropyl)-4-(dimethylamino) pyridinium chloride
 DMAP-IP	116-118˚C	N-(2,3-dihydroxypropyl)-4-(dimethylamino) pyridinium phosphate
 DMAP-NTf_2	49.1 ˚C (404 ppm)	N-(2,3-dihydroxypropyl)-4-(dimethylamino) pyridinium bis(triflouromethylsulfonyl)imide
 DMAP-DCA	105-106 ˚C	N-(2,3-dihydroxypropyl)-4-(dimethylamino) pyridinium dicyanamide
 DMAP-DPP	92.9 ˚C	N-(2,3-dihydroxypropyl)-4-(dimethylamino) pyridinium diphenyl phosphate

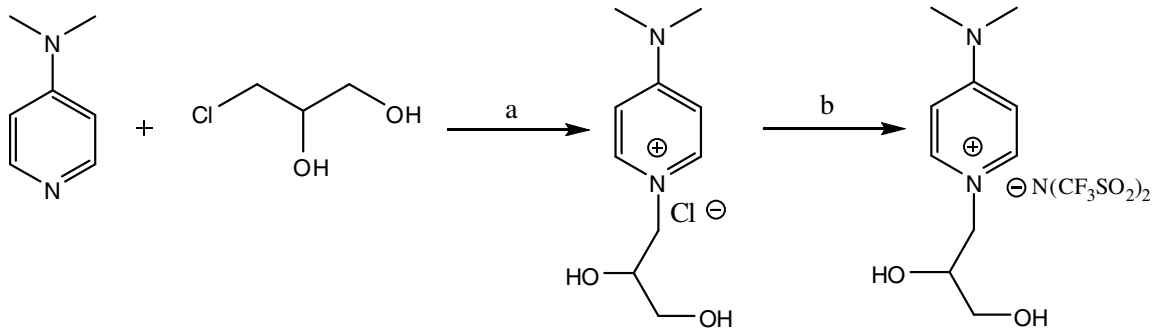


Figure 35. Synthesis of DMAP-Cl and DMAP-NTf. a) acetonitrile, overnight, T = 65˚C. b) $LiN(CF_3SO_2)_2$, water, (-LiCl) stirred overnight, r.t.

Shown in Figure 36 is the ^1H NMR spectrum of DMAP-Cl, with the labeled (S) enantiomer illustrated above. Two enantiomers are actually present. The singlet at 3.06 ppm correlates to the six methyl protons found on the nitrogen atom. The multiplet at 3.49 ppm integrates for two protons and most likely are indicative of H_y and $H_{y'}$. The multiplet at 3.91 ppm also integrates for 2 protons and are indicative of H_z and $H_{z'}$. The multiplet at 4.17 integrates for one proton, H_x. The doublet at 6.73 ppm (J = 8 Hz) integrates for for protons H_b and $H_{b'}$ found on the pyridine ring. The doublet at 7.84 ppm (J = 7.6 Hz) intergrates for protons H_c and $H_{c'}$, also on the pyridine ring.

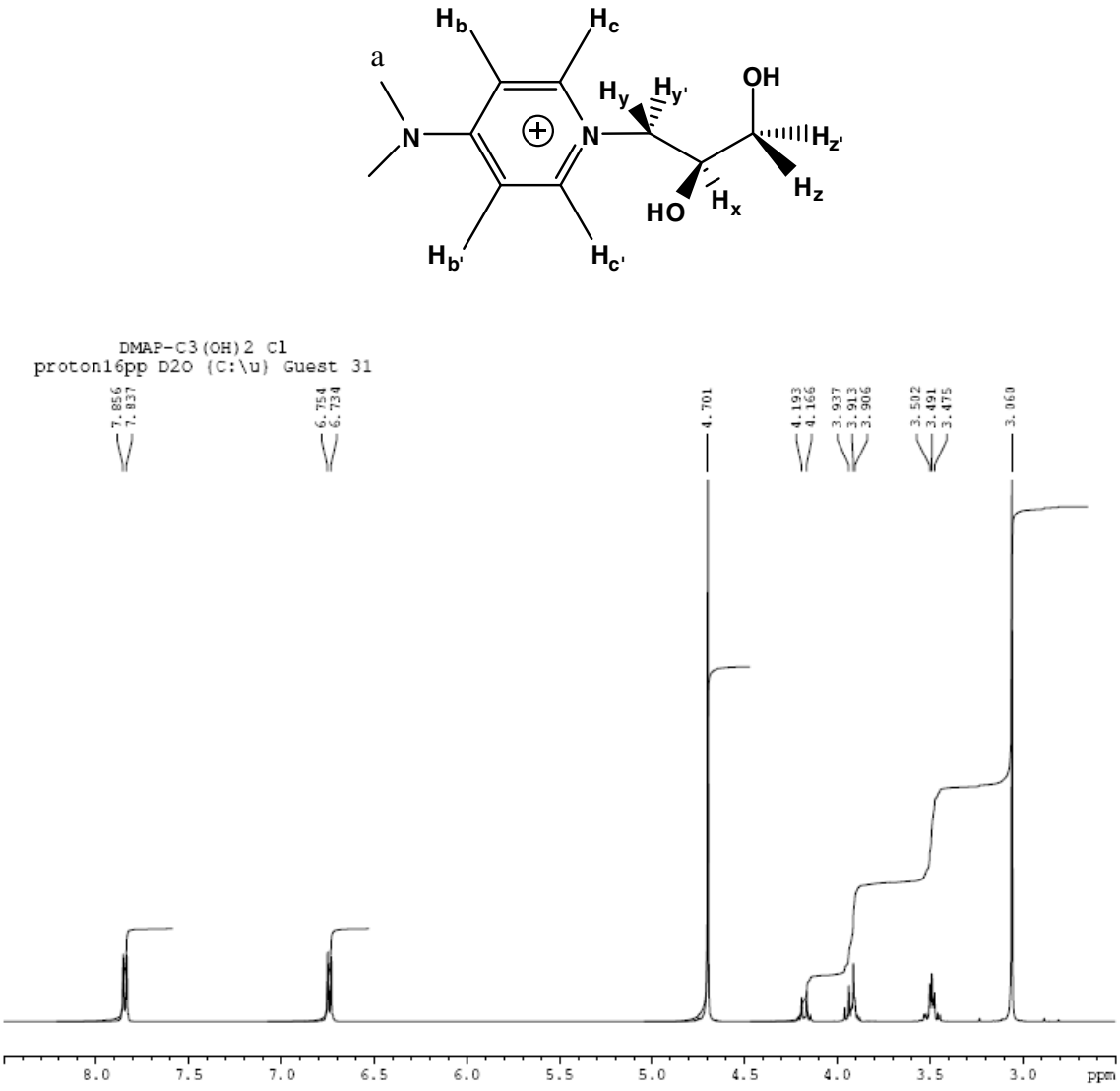


Figure 36. ^{1}H NMR spectrum of DMAP-Cl (400 MHz, D_2O).

The ^{1}H NMR spectra of DMAP-Cl was expanded between 3.0 ppm and 4.5 ppm (Figure 37). The pattern at 3.44 ppm to 3.54 ppm (J values range from 2.8 Hz to 4.4 Hz) appears characteristic of a non-first order A_2B system. This comes from geminal coulpling between H_y and $H_{y'}$ and vicinal coupling of both of these protons with H_x. The pattern between 3.87 ppm to 3.97 ppm (J values range from 2 Hz to 8.8 Hz) is also characteristic of an

A_2B system. This arises from coupling between H_z and $H_{z'}$ and coupling of both these protons to H_x. The multiplet between 4.13 and 4.22 ppm appears as a quartet and is assigned to H_x.

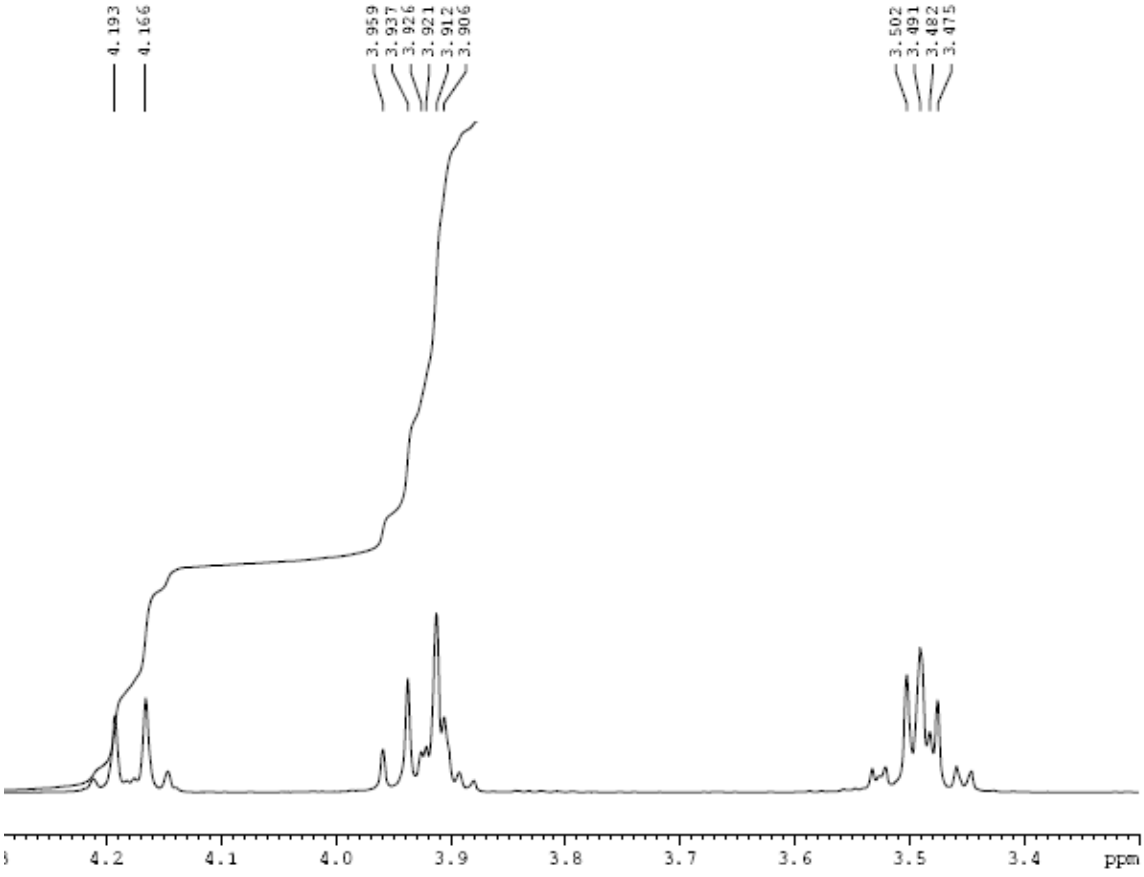
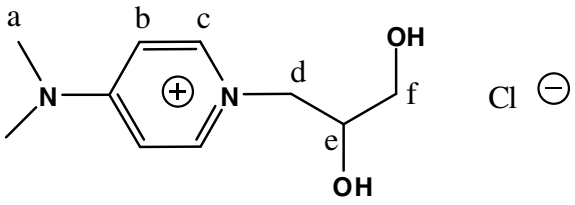


Figure 37. Expanded ^{1}H NMR spectrum of DMAP-Cl (400 MHz, D_2O).

As expected the ^{1}H COSY NMR spectrum (Figure 38) shows coupling between H_x and H_y, $H_{y'}$ and coupling between H_x with H_z, $H_{z'}$. There is also coupling between H_b and H_c.



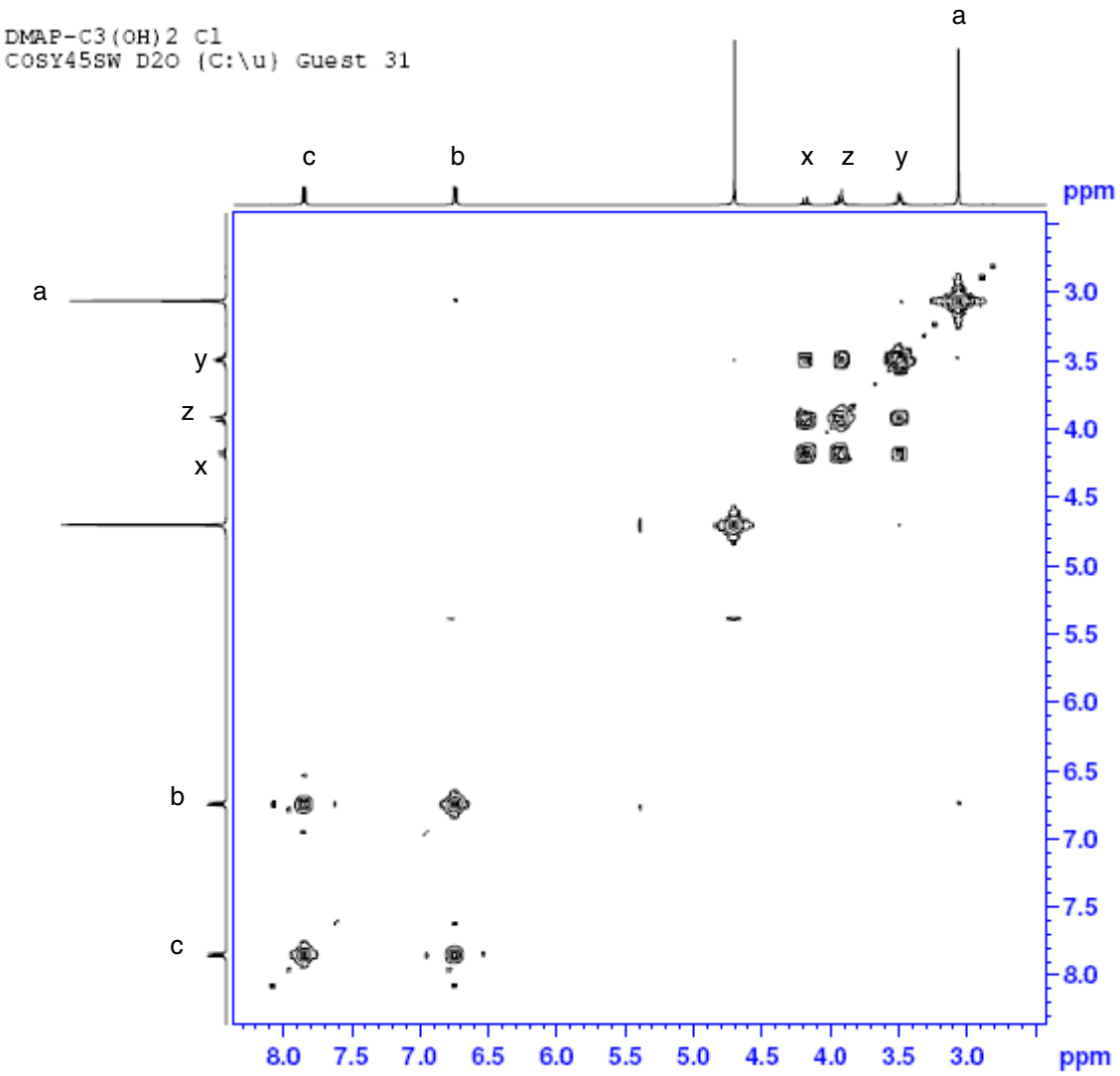
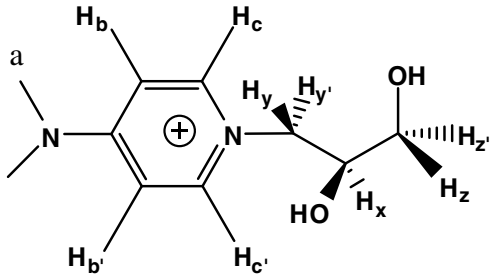


Figure 38.^{1}H-^{1}H COSY NMR spectrum of DMAP-Cl (400 MHz, D_2O).



Proton	Chemical Shift (ppm)	J (Hz)
H_a (6 H)	3.06 (s)	-
H_y, $H_{y'}$	3.44 -3.54 (m)	2.8 – 4.4
H_z, $H_{z'}$	3.87-3.97 (m)	2.0-8.8
H_x	4.13-4.22 (m)	-
H_b, $H_{b'}$	6.73 (d)	8
H_c, $H_{c'}$	7.84 (d)	7.6

Table 15. ^{1}H shift assignments and coupling constants for DMAP-Cl

Seven signals appear in the ^{13}C NMR spectra and six appear in the ^{13}C NMR DEPT spectrum (Figures 39 and 40). The CH_3- and CH- groups appear as positive peaks. The methylene carbons (CH_2) appear as negative peaks and quaternary carbons are null. Based on these spectra, the carbon peak assignments are made in Table 16.

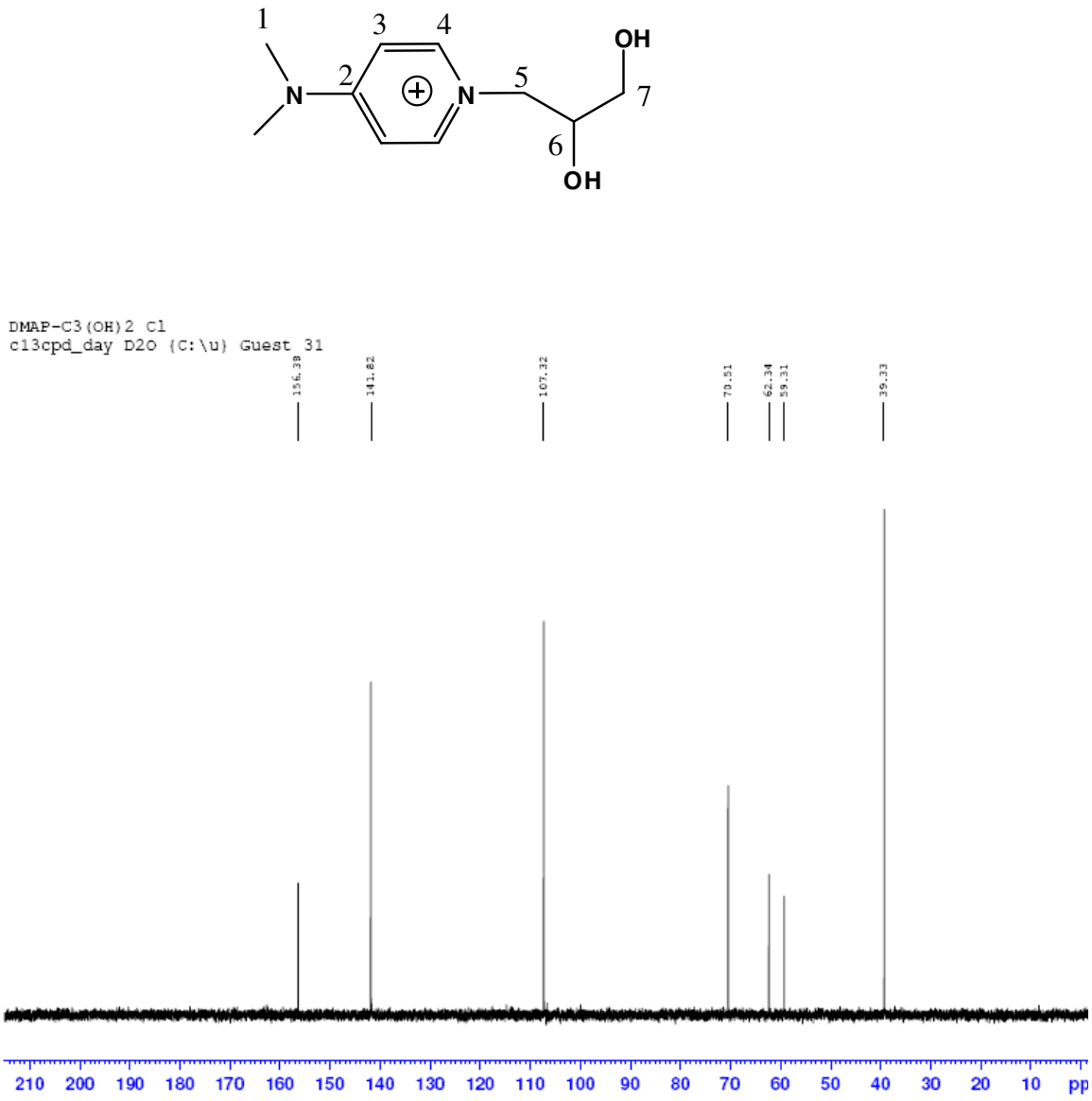
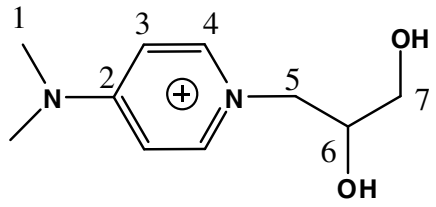


Figure 39. ^{13}C NMR spectrum of DMAP-Cl (100 MHz, D_2O).



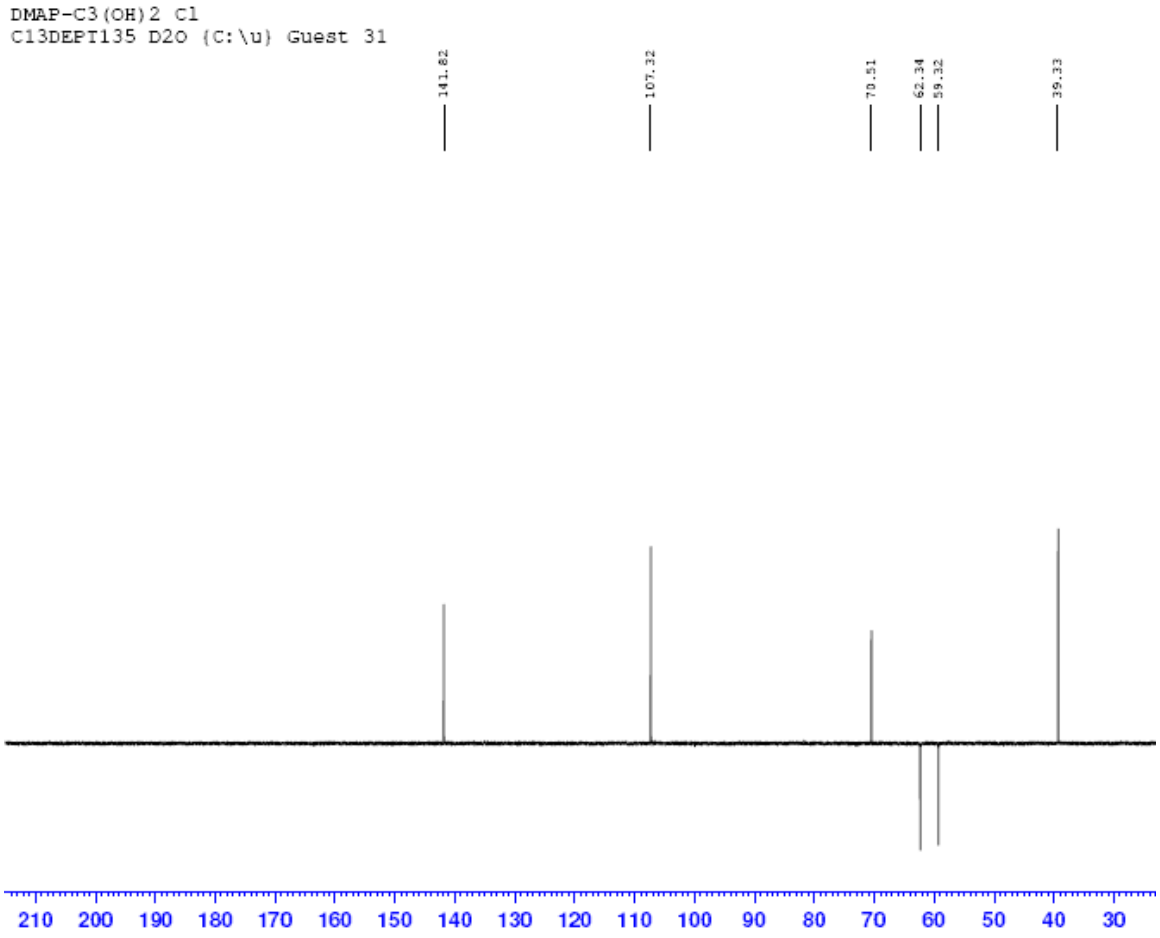
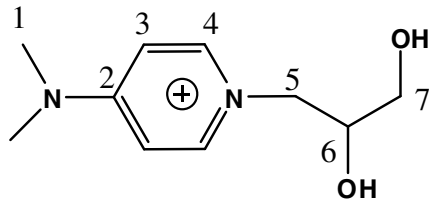


Figure 40. ^{13}C DEPT NMR spectrum of DMAP-Cl (100 MHz, D_2O).



Chemical Shift (ppm)	Carbon Type	Carbon
39.3	CH_3	1
59.3	CH_2	5
62.3	CH_2	7
70.5	CH	6
107.3	CH	3
141.8	CH	4
156.4	C	2

Table 16. Carbon assignments for DMAP-Cl.

The ^{1}H and ^{13}C NMR spectra of DMAP-NTf_2 are shown in Figure 41 and 42. The quartet in the ^{13}C NMR spectrum, 114.4 ppm, 117.6ppm, 120.8 ppm, and 124.0 ppm correlate with the carbons found on the bis(trifluoromethylsulfonyl)imide anion. (The quartet is due to coupling between the carbon and the three fluorine atoms.)

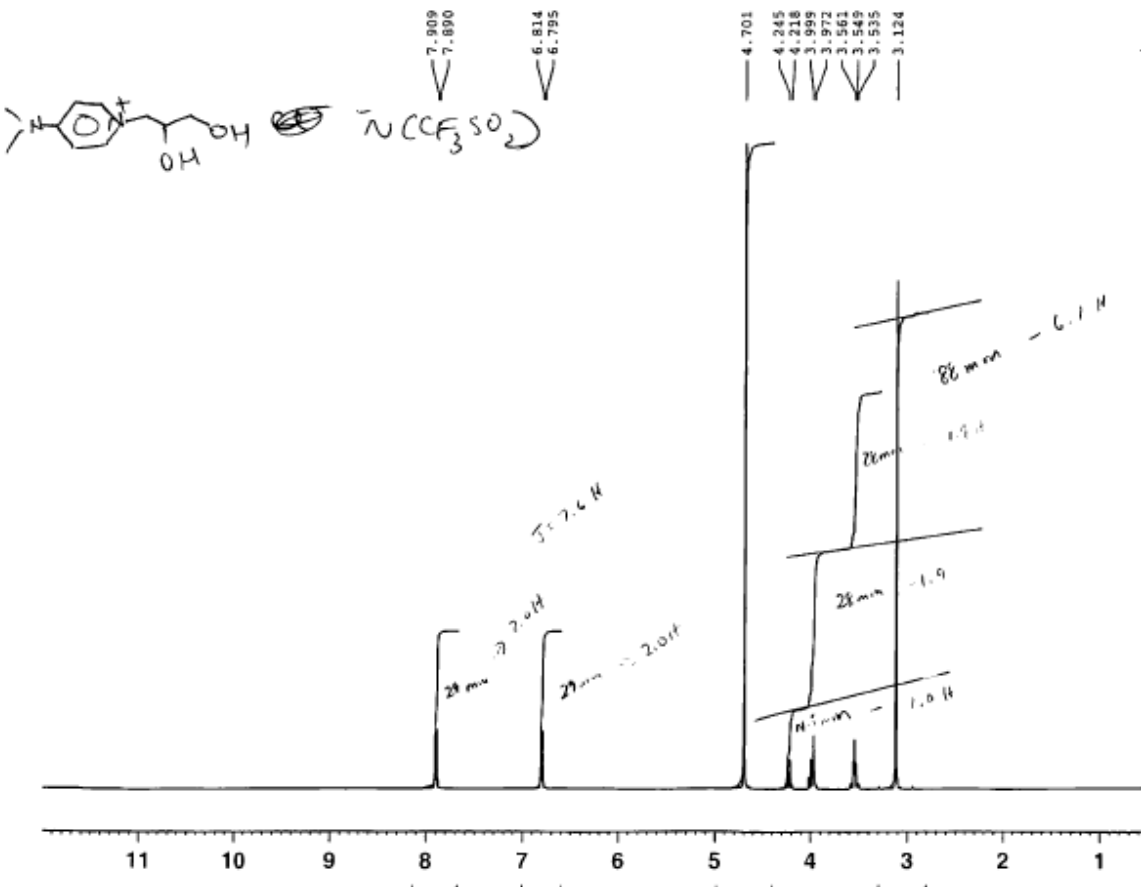


Figure 41. ^{1}H NMR spectrum of DMAP-NTf$_2$ (400 MHz, D$_2$O).

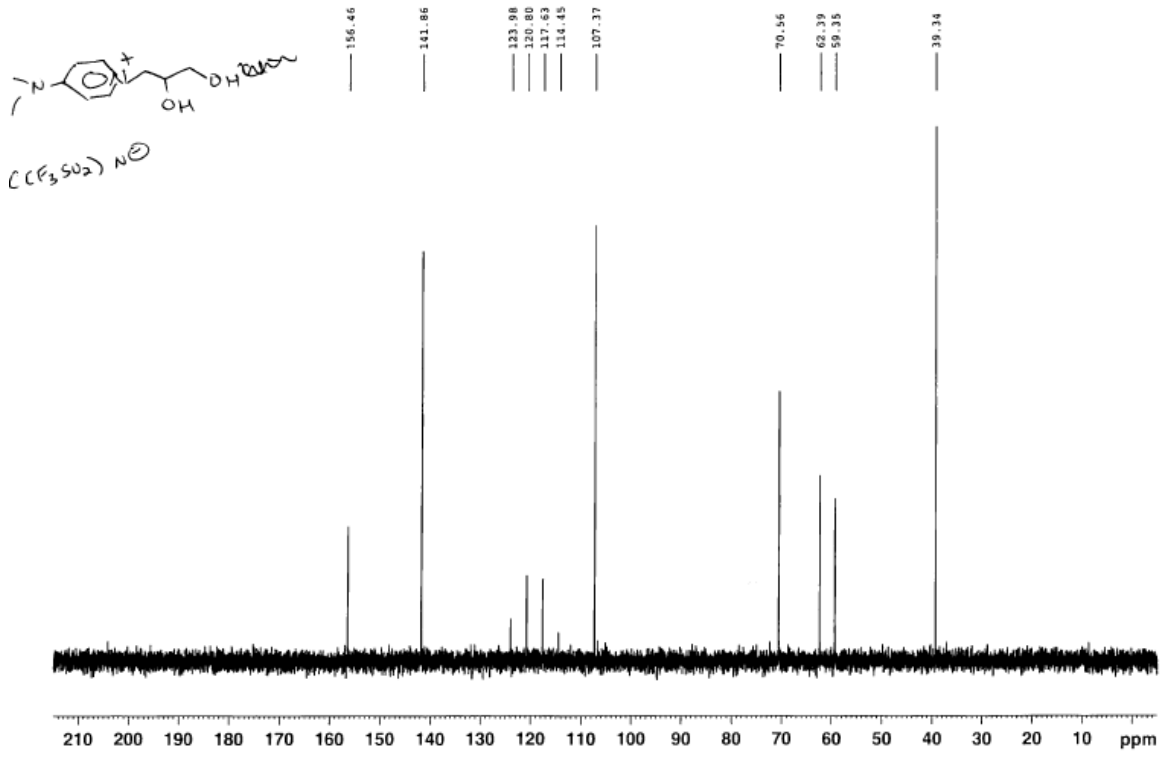


Figure 42. ^{13}C NMR spectrum of DMAP-NTf_2 (100 MHz, D_2O).

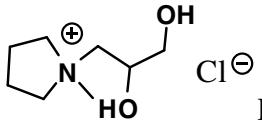
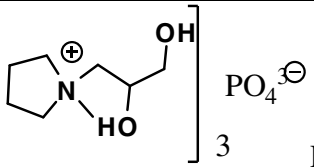
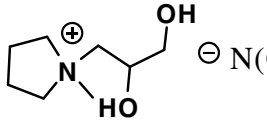
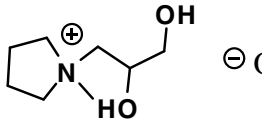
3. Monocationic Pyrrolidinium Salts

New pyrrolidinium salts are shown in Table 17. "P" refers to the pyrrolidinium cation. P-IP, P-DCA, and P-DPP can be considered ionic liquids. We noticed that a crystal grew out of P-DCA. At first we thought it may have been a form of the dicyanamide salt coming out of solution. An X-ray crystallography study revealed that the crystals were actually the chloride salt.

P-DPP is the first of a new class of ionic liquids that potentially could be developed by this laboratory. It displays an amphiphilic nature in water and is thermally stable up to 204 ˚C. An attempt was made to make the

pyrrolidinium bis(trifluoromethylsulfonyl)imide salt, but like the DABCO analogue, the salt was water soluable and we were unable to remove the chloride impurity.

Table 17. Pyrrolidinum monocationic salts.

Structure/Code	**Melting point (% water)**	**Name**
 P-Cl	105.2 ˚C	N-(2,3-dihydroxypropyl)-N-methyl pyrrolidinium chloride
 P-IP	90.4 ˚C	N-(2,3-dihydroxypropyl)-N-methyl pyrrolidinium phosphate
 P-DCA	-64.2 ˚C (206 ppm)	N-(2,3-dihydroxypropyl)-N-methyl pyrrolidinium dicyanamide
 P-DPP	-23.1 ˚C (0.175%)	N-(2,3-dihydroxypropyl)-N-methyl pyrrolidinium diphenyl phosphate

The pyrrolidinium chloride salt (P-Cl) and P-DPP will be discussed in more detail. P-Cl was synthesized by adding one equivalent of 3-chloro-1,2-propanediol to 1-methylpyrrolidine in acetonitrile. The reaction mixture was refluxed overnight and the solvent evaporated. The resulting viscous liquid was dried under high vacuum and the resulting brown solid was washed with acetonitrile until it became white. The solid was again dried and obtained in

64% yield. P-DPP was made by adding a charge equivalent of diphenyl phosphate and a charge equivalent of potassium hydroxide in absolute ethanol. After filtration of the halide salt, the solvent is evaporated under reduced pressure and the resulting viscous liquid was obtained in 47% yield after purification (Figure 43).

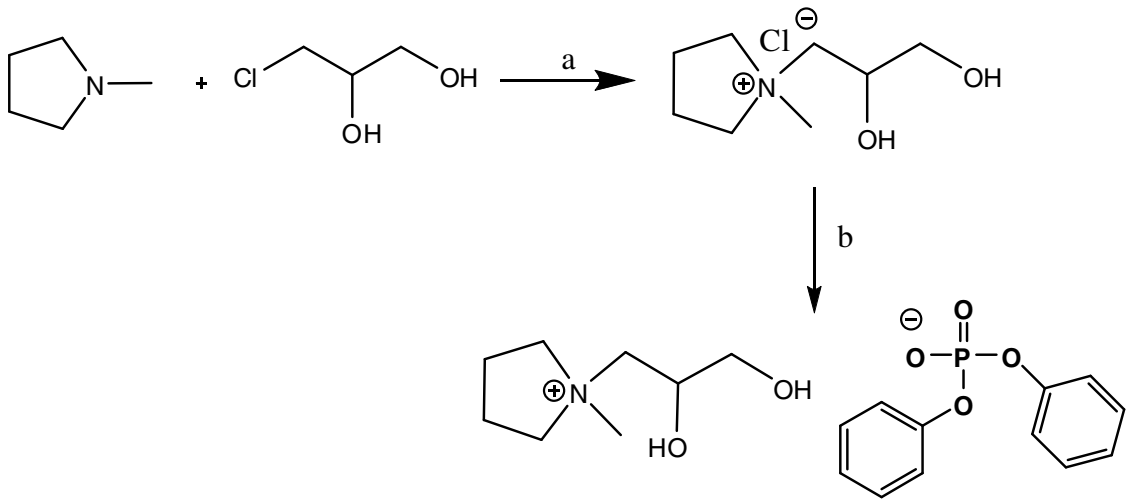
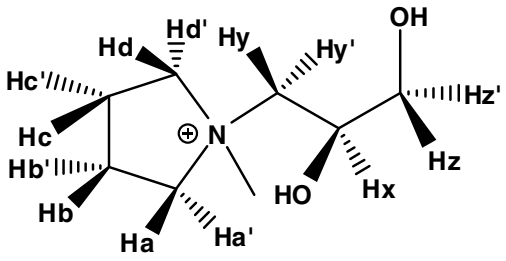


Figure 43. Synthesis of pyrrolidinium salts P-Cl and P-DPP. a)acetonitrile, reflux overnight, T = 65˚C. b) 1 equivalent of diphenyl phosphate, 1 equivalent of potassium hydroxide, absolute ethanol, (-KCl) stir overnight, r.t.

The structures of these salts were verified using ^{1}H, ^{13}C, and in the case of the diphenyl phosphate ^{31}P NMR. The expanded ^{1}H NMR spectrum of P-Cl is shown in Figure 44. The broad peak at 2.10 ppm integrates for four protons and represents the four protons H_b, $H_{b'}$, H_c, and $H_{c'}$. The singlet at 3.02 integrates for three protons, which are indicative of the methyl protons (H_e) on the nitrogen atom. The multiplet between 3.25 – 3.31 ppm integrates for one proton, most likely H_y (similar to H_y in D-Cl). The broad

multiplet between 3.25-3.55 integrates for 7 protons and encompasses overlapping peaks for H_a, $H_{a'}$, H_d, $H_{d'}$, H_z, $H_{z'}$ and $H_{y'}$. The multiplet between 4.13-4.18 integrates for 1 proton and is indicative of H_x.



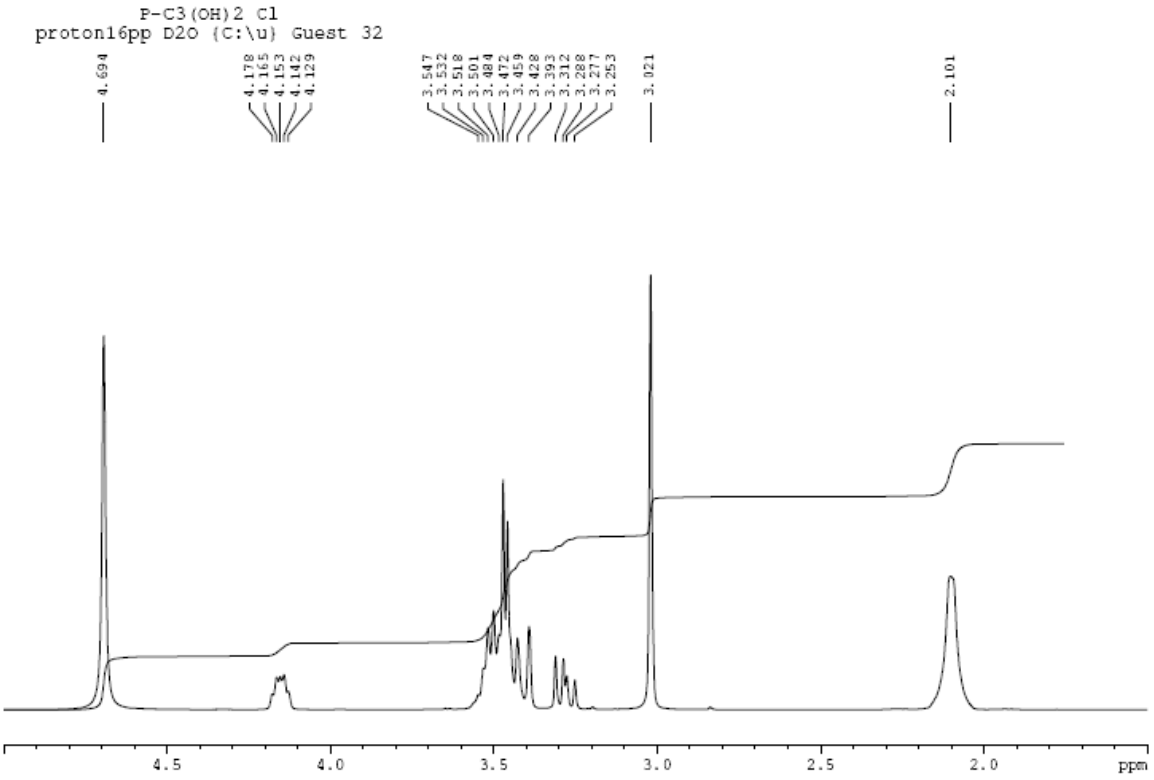


Figure 44. ^{1}H NMR spectrum of P-Cl (400 MHz, D_2O).

In the ^{1}H COSY NMR experiment (Figure 45), one sees what is probably vicinal coupling between H_c,$H_{c'}$, H_b, $H_{b'}$ and H_a, $H_{a'}$, H_d, $H_{d'}$. There

is coupling between H_x with H_y and $H_{y'}$, and coupling of H_x with H_z and $H_{z'}$. The proton assignments are shown in Table 18.

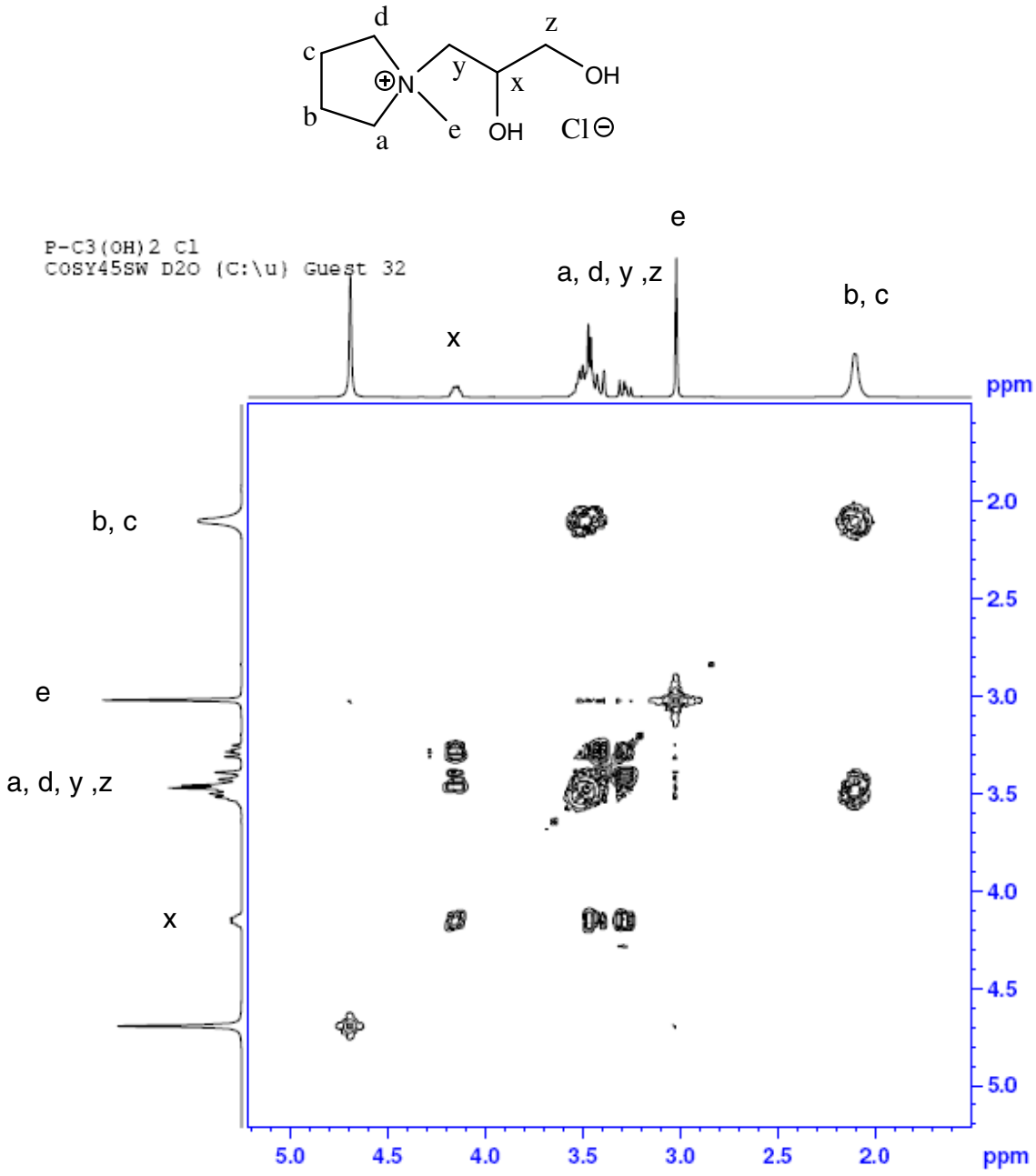
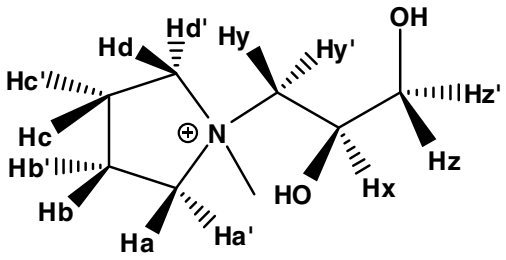


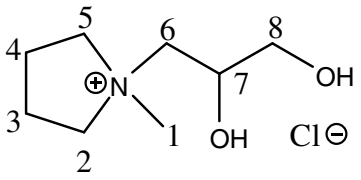
Figure 45. ^{1}H-^{1}H COSY NMR experiment for P-Cl (400 Mz, D_2O).



Proton	Chemical Shift (ppm)	J (Hz)
H_b, $H_{b'}$, H_c, $H_{c'}$	2.10 (br)	-
H_e (3 H)	3.02 (s)	-
$H_{y'}$	3.25-3.12	4.4 – 9.6
H_a, $H_{a'}$, H_d, $H_{d'}$, H_y, H_z, $H_{z'}$	3.39-3.55	-
H_x	4.13-4.18	4.4-5.2

Table 18. ^{1}H shift assignments and coupling constants for P-Cl.

There are seven signals in the ^{13}C spectrum of P-Cl (Figure 46). Ideally there should be eight. Based on this spectrum and the ^{13}C COSY spectrum (Figure 47), the carbon assignments are listed in Table 19. Based on the assignments made, a signal appears to missing for either C2 or C5. This may be a case of accidental isochrony. The signal for C2 and C5 share the same chemical shift.



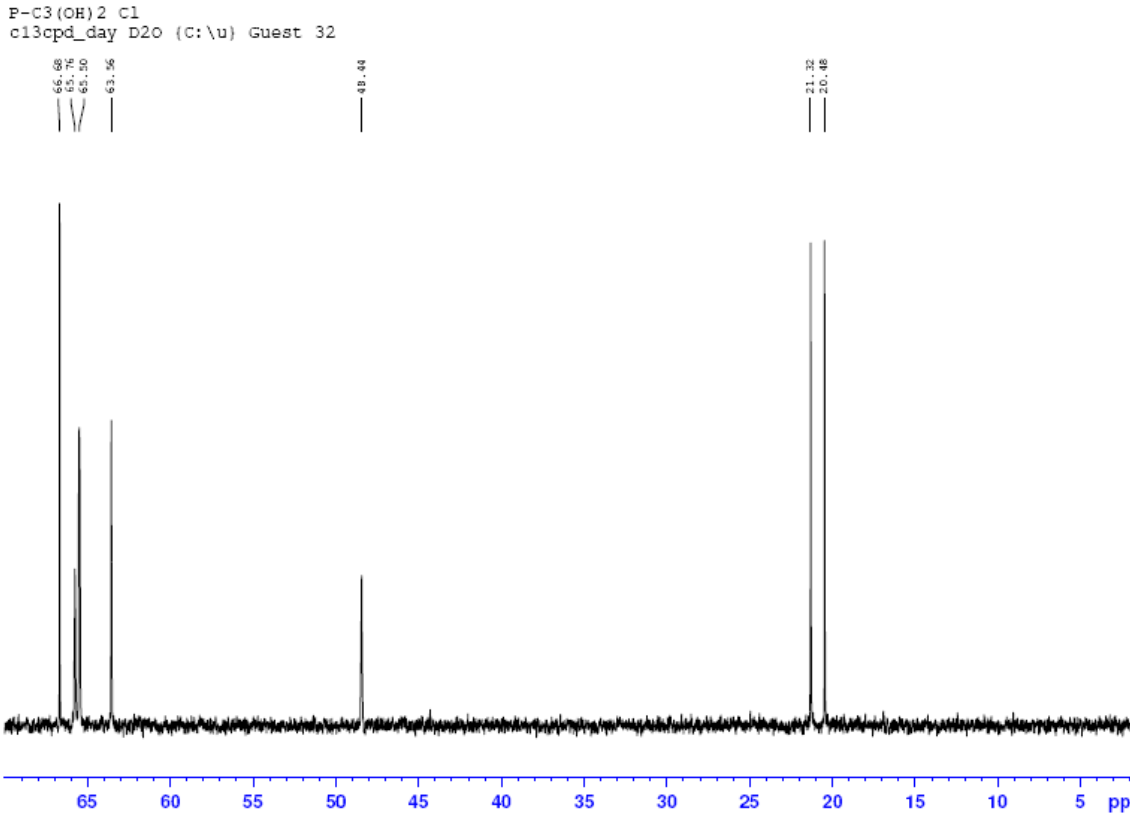


Figure 46. ^{13}C NMR spectrum for P-Cl (100 MHz, D_2O).

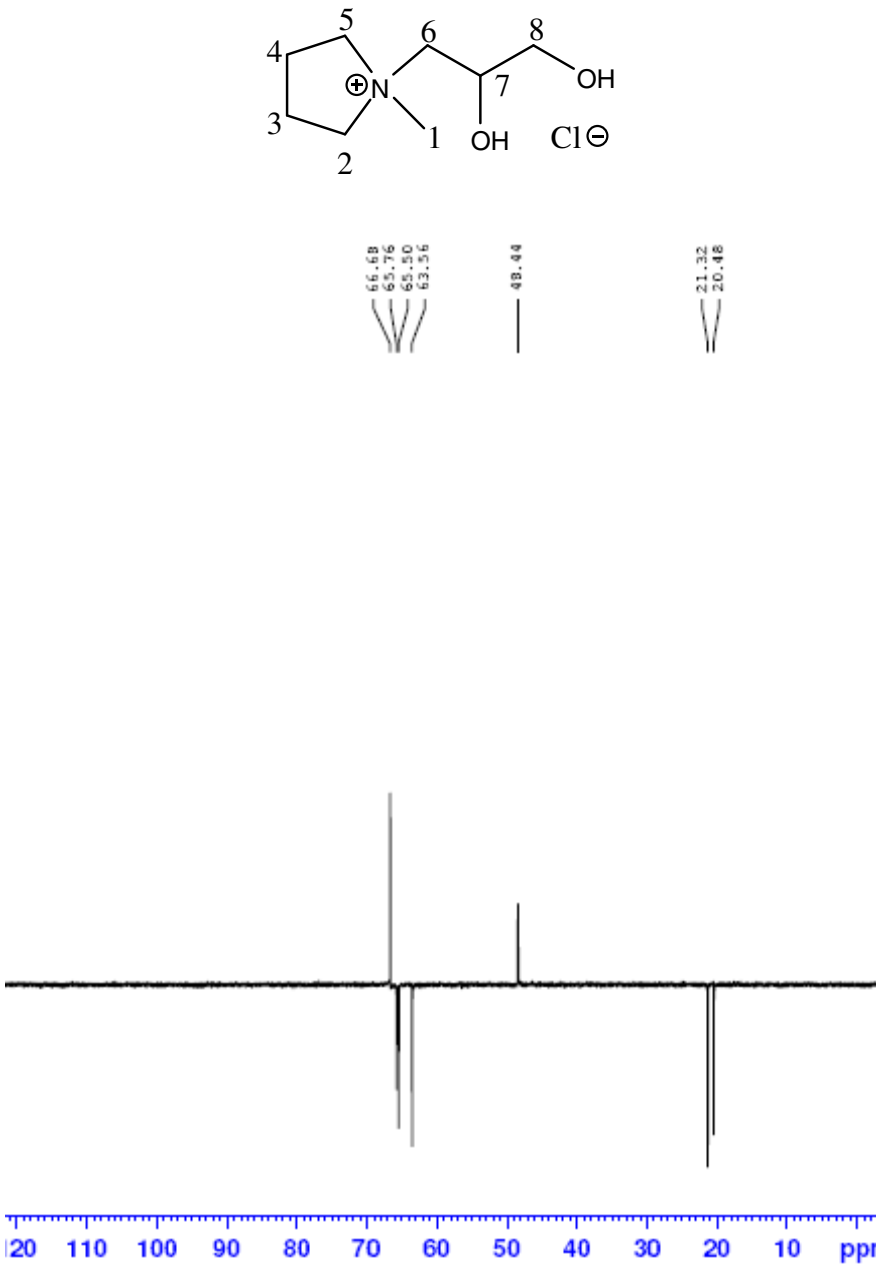


Figure 47. ^{13}C NMR DEPT experiment of P-Cl (100 MHz, D_2O).

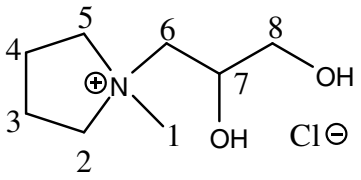


Table 19. Carbon assignments for P-Cl.

Chemical Shift (ppm)	Carbon Type	Carbon
20.5	CH_2	3 or 4
21.3	CH_2	3 or 4
48.4	CH_3	1
63.6	CH_2	2, 5
65.5	CH_2	6
65.8	CH_2	8
66.7	CH	7

The x-ray crystal structure of P-Cl is shown in Figures 48 and 49. Crystal data and structure refinement information is listed in Table 20 and selected bond lengths in Table 21. The bond lengths for the atoms of the pyrrolidinium ring are: N(1)-C(2) 1.504 A, C(2)-C(3) 1.507 A, C(3)-C(4) 1.505 A, C(4)-C(5) 1.517 A and C(5)-N(1) 1.518 A. Bond angles around the ring are: N(1)-C(2)-C(3) 105.4˚, C(2)-C(3)-C(4) 106.5˚, C(3)-C(4)-C(5) 106.0˚, C(4)-C(5)-N(1) 103.6˚, C(2)-N(1)-C(5) 102.4˚. The ring is not symmetrical and is in a distorted “envelope” conformation. Figure 48 shows hydrogen bonding between the cationic racemates and the chloride atoms.

The hydrogen bond lengths are as follows: O(8)-H(8)---Cl(11) 1.96 A and O(1)-H(1)---Cl(11) 2.21 A. Fairly strong hydrogen bonds are formed.

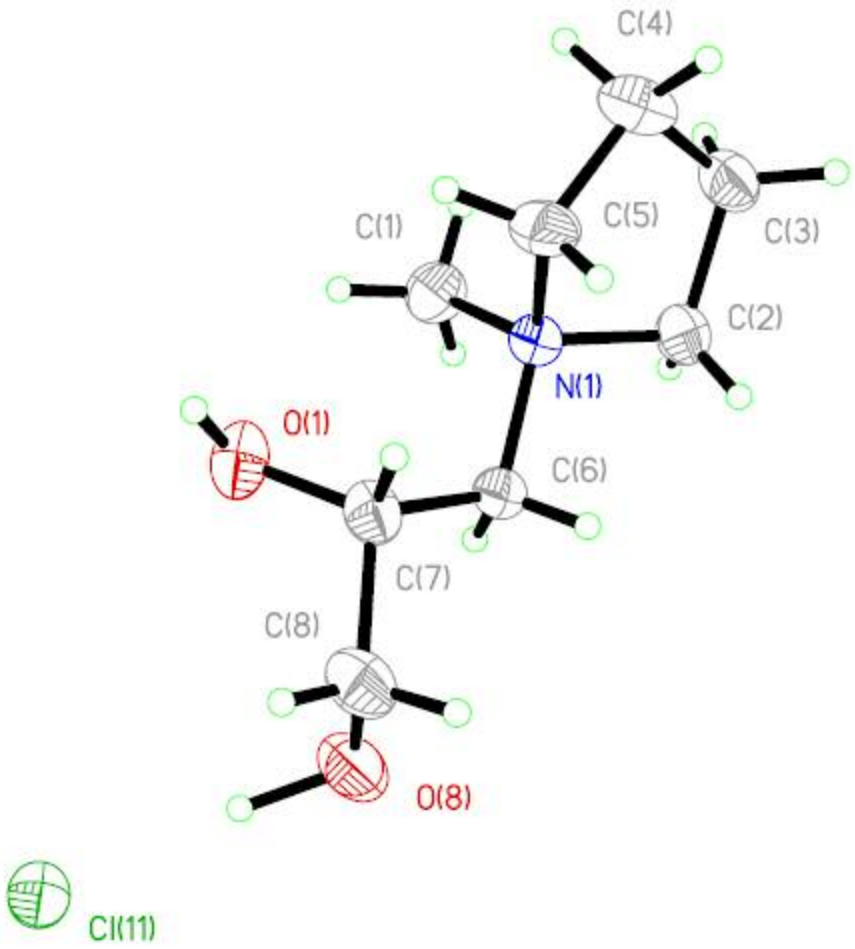


Figure 48. ORTEP representation of P-Cl.

Table 20. Crystal data and structure refinement for P-Cl

Empirical formula	C5 H9 Cl N2 O
Formula weight	148.59
Temperature	293(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 8.2530(10) A alpha = 90 deg. b = 11.733(2) A beta = 102.330(10) deg. c = 10.788(2) A gamma = 90 deg.
Volume	1020.5(3) A^3
Z, Calculated density	4, 0.967 Mg/m^3
Absorption coefficient	2.879 mm^-1
F(000)	312
Crystal size	0.45 x 0.35 x 0.25 mm
Theta range for data collection	5.64 to 72.36 deg.
Limiting indices	-10<=h<=9, 0<=k<=14, 0<=l<=13
Reflections collected / unique	2006 / 2006 [R(int) = 0.0000]
Completeness to theta = 72.36	99.4 %
Absorption correction	Empirical
Max. and min. transmission	2.109 and .150
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2006 / 0 / 181
Goodness-of-fit on F^2	1.030
Final R indices [I>2sigma(I)]	R1 = 0.0548, wR2 = 0.1200
R indices (all data)	R1 = 0.1053, wR2 = 0.1499
Largest diff. peak and hole	0.416 and -0.260 e.A^-3

Table 21. Selected bond lengths [A] and angles [deg] for P-Cl.

C(1)-N(1)	1.498(4)
N(1)-C(2)	1.504(4)
N(1)-C(6)	1.508(4)
N(1)-C(5)	1.518(4)
C(2)-C(3)	1.507(5)
C(3)-C(4)	1.505(6)
C(4)-C(5)	1.517(5)
C(6)-C(7)	1.511(4)
C(7)-O(1)	1.415(4)
C(7)-C(8)	1.526(5)
C(8)-O(8)	1.408(5)
C(1)-N(1)-C(2)	109.3(3)
C(1)-N(1)-C(6)	110.8(2)
C(2)-N(1)-C(6)	110.4(2)
C(1)-N(1)-C(5)	110.6(3)
C(2)-N(1)-C(5)	102.4(3)
C(6)-N(1)-C(5)	112.9(2)
N(1)-C(2)-C(3)	105.4(3)
C(4)-C(3)-C(2)	106.5(3)
C(3)-C(4)-C(5)	106.0(3)
C(4)-C(5)-N(1)	103.6(3)
N(1)-C(6)-C(7)	116.0(2)
O(1)-C(7)-C(6)	111.0(3)
O(1)-C(7)-C(8)	110.9(3)
C(6)-C(7)-C(8)	107.9(3)

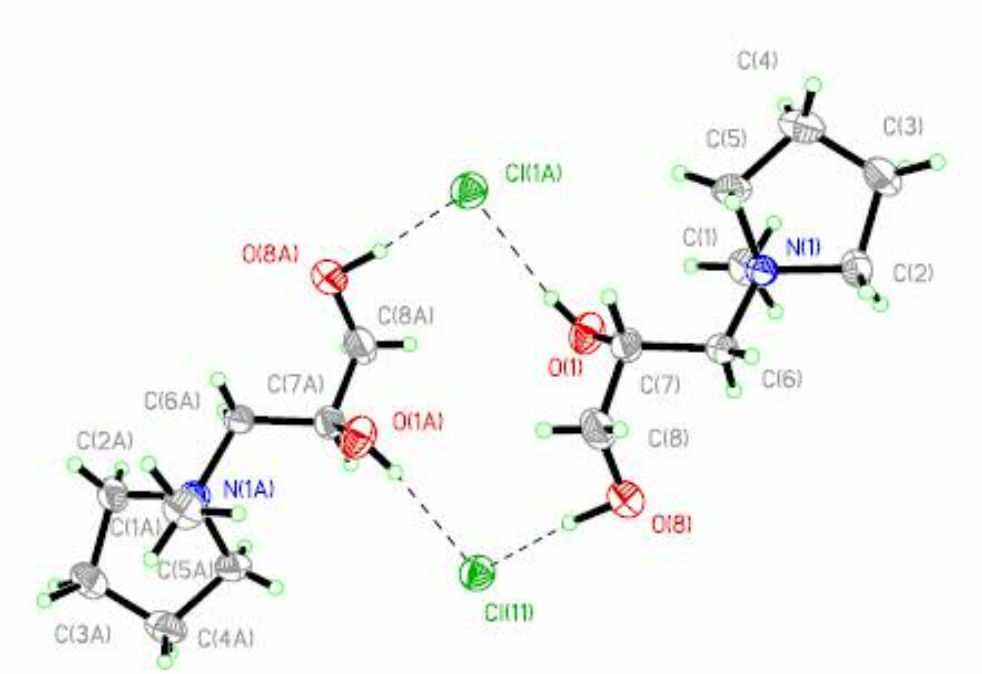


Figure 49. Hydrogen bonding between the chloride anions and the cationic racemates of P-Cl.

Shown in Figure 50, 51 and 52 are the ^{1}H, ^{13}C and ^{31}P NMR spectra for P-DPP. The presence of the anion is confirmed in the ^{13}C spectrum by the signals found at 120.20, 120.24, 120.28, 124.5, 129.9, 151.7 and 151.8 ppm. These shifts correlate to the carbons found on the phenyl rings. There is a single peak with a chemical shift of -8.8 ppm in the ^{31}P NMR spectrum. This also confirms the presence of the anion.

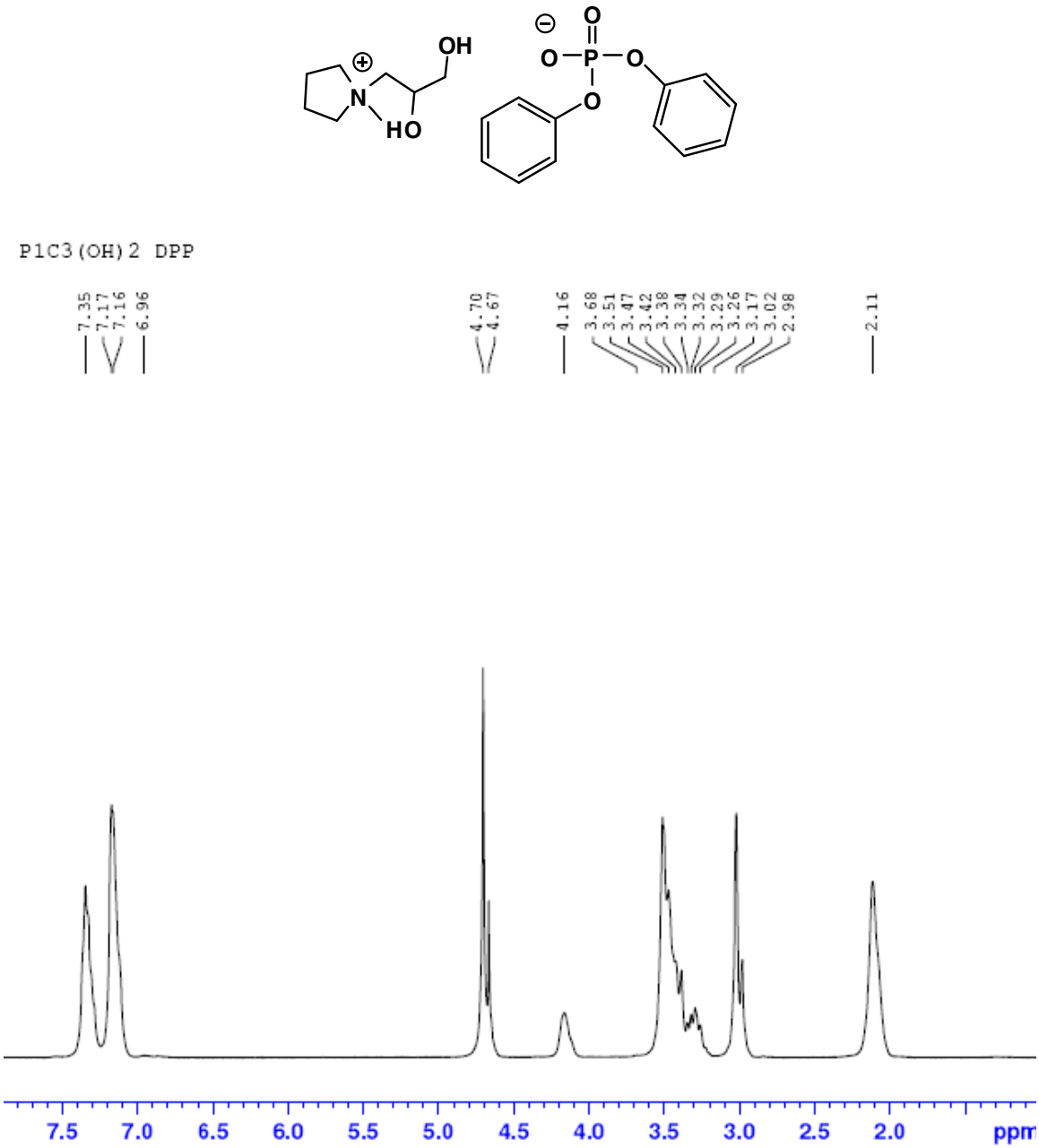


Figure 50. ^{1}H NMR spectrum of P-DPP (400 MHz, D_2O).

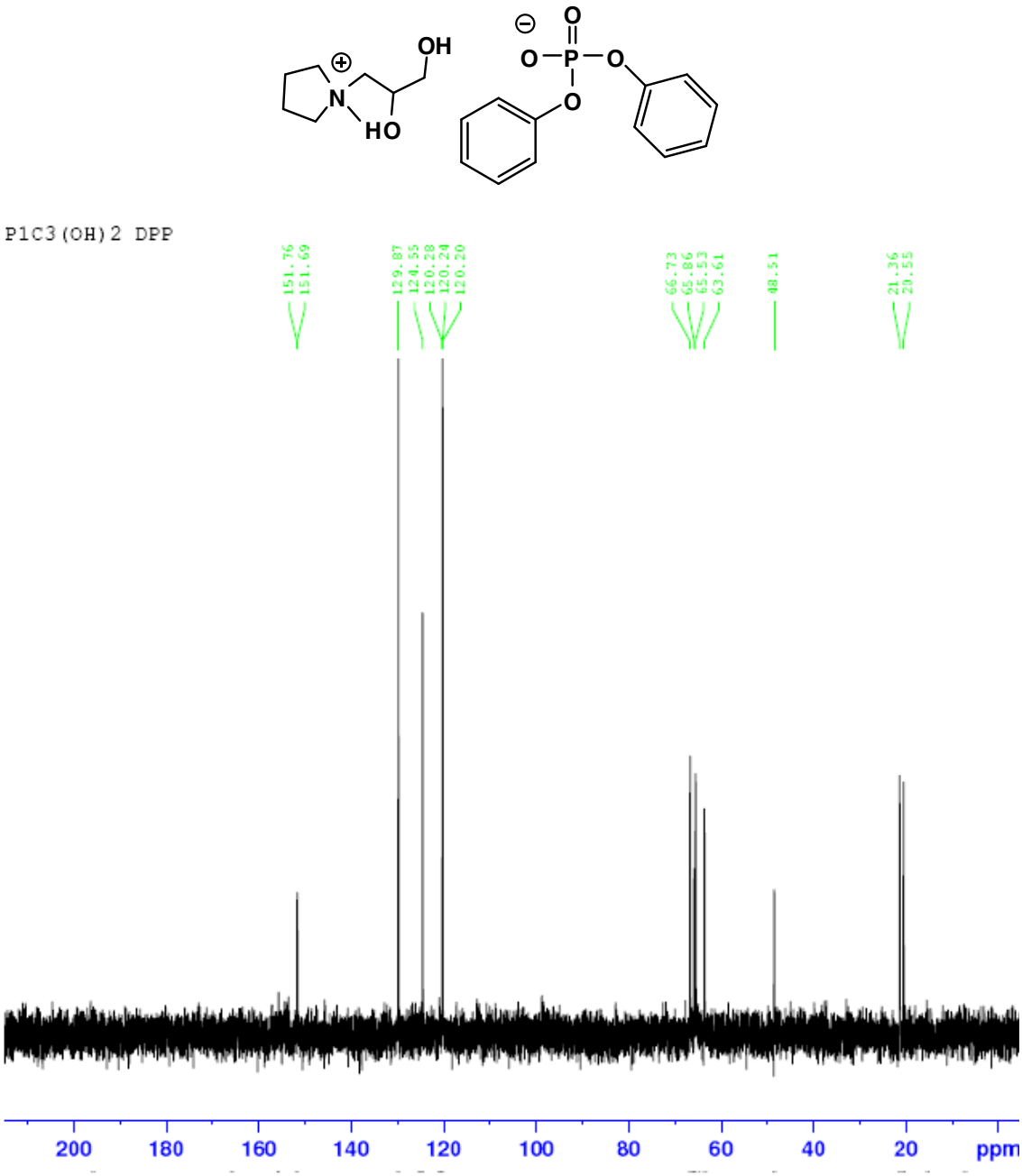


Figure 51. ^{13}C NMR spectrum of P-DPP (100 MHz, D_2O).

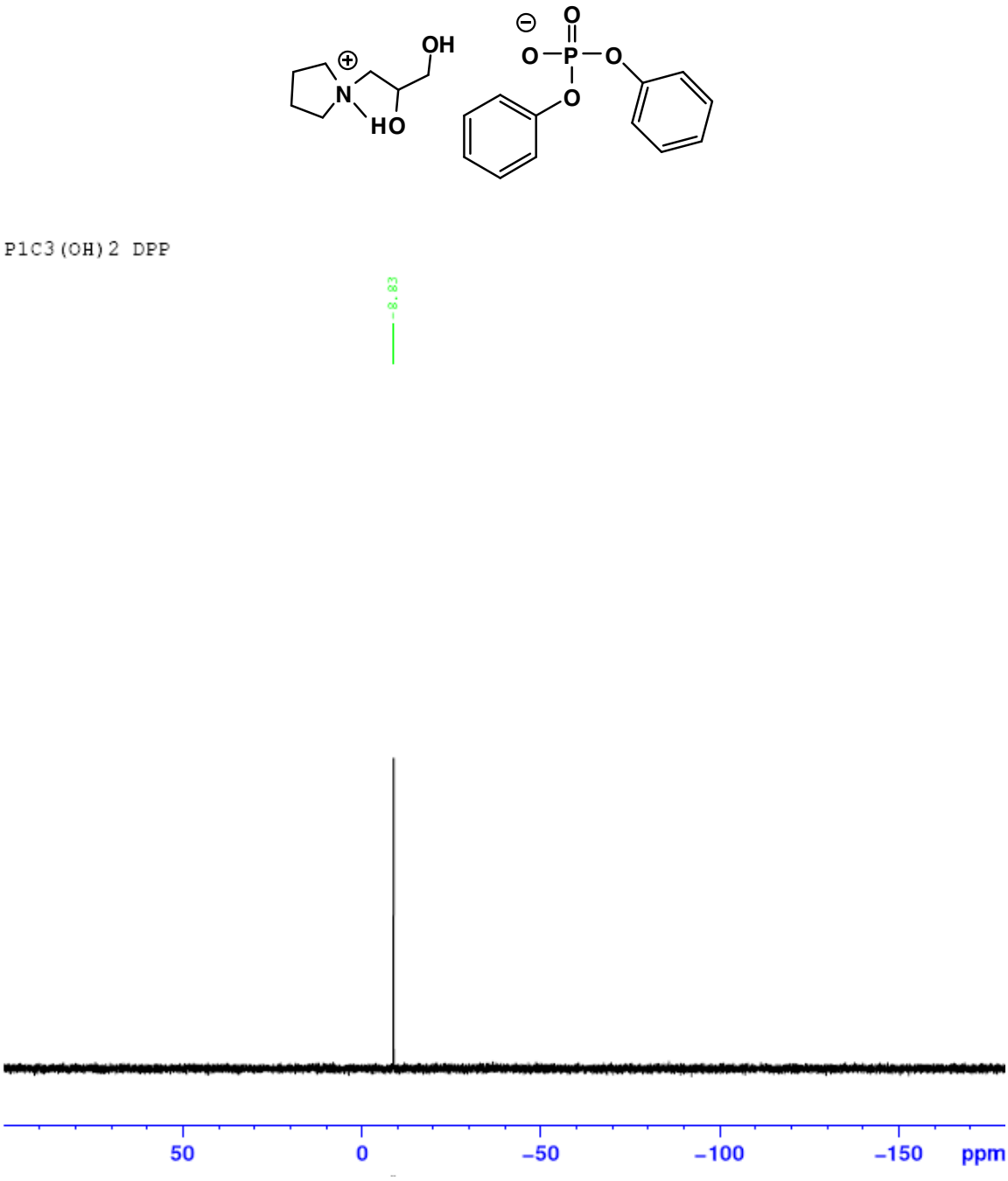


Figure 52. ^{31}P NMR spectrum of P-DPP.

4. Dicationic hexanediamine salts

New hexanediamine salts are shown in Table 22. “S6” refers to the **string** compound with six methylene groups between the nitrogen atoms. Two salts, S6-NTf_2 and S6-DCA, are viscous liquids at room temperature. S6-DCA was thermally stable up to 275 ◦C. The salts S6-Cl and S6-IP will be discussed in more detail.

S6-Cl was synthesized by adding two equivalents of 3-chloro-1,2-propanediol to *N,N,N;N’*-tetramethyl-1,6-hexanediamine in ethanol. The reaction mixture was refluxed overnight and the solvent was evaporated. The resulting white solid was washed with hexanes and obtained in 47% yield. To form S6-IP, S6-Cl was dissolved in methanol and a charge equivalent of phosphoric acid was added. The mixture was stirred overnight and the solvent evaporated. A white solid was obtained in 50% yield after recrystallization from ethanol (Figure 53).

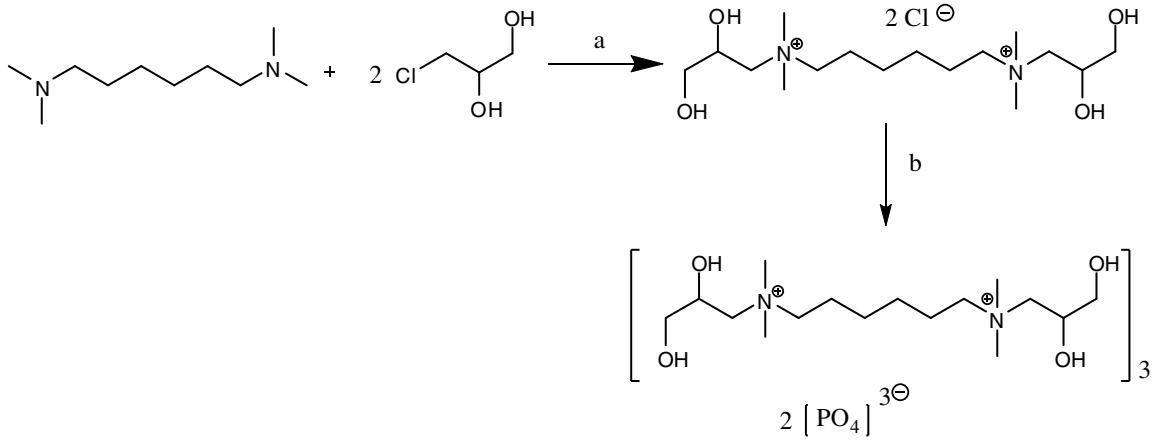
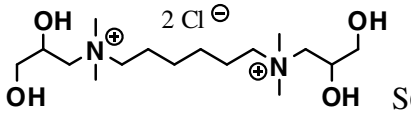
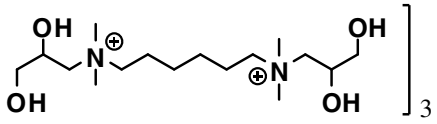
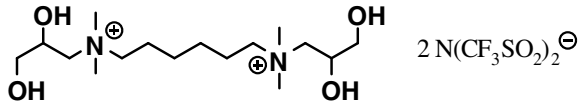
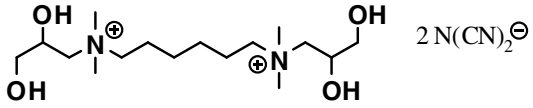
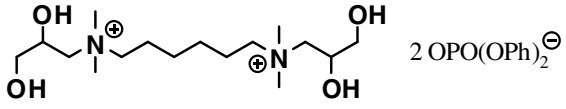


Figure 53. Synthesis of S6-Cl and S6-IP. a)95% ethanol, reflux overnight, T = 60 ˚C. b)H_3PO_4, methanol, stir overnight, (-HCl) r.t.

Table 22. Dicationic salts based on *N,N,N',N'*-tetramethyl-1,6-hexanediamine.

Structure/Code	Melting point	Name
 S6-Cl	161 – 163 ˚C	4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol chloride
 S6-IP	170 ˚C	4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol phosphate
 S6-NTf_2	-30.0 ˚C (443 ppm)	4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol bis(triflouro-methylsulfonyl)imide
 S6-DCA	-45.5 (0.220 %)	4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol dicyanamide
 S6-DPP	-5.1 (Glass Transition)	4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol diphenyl phosphate

The ^{1}H NMR and ^{1}H COSY NMR spectra are shown in Figure 54, Figure 55, and Figure 56. The broad signal at 1.32 ppm integrates for 4 protons and correspond to the methylene protons found on carbons a and a'. The broad multiplet between 1.67 ppm and 1.74 ppm integrates for four methylene protons found on carbons b and b'. The singlets at 3.05 and 3.06, each integrates for six protons respectively, which correspond to the methyl protons H_d and $H_{d'}$ or H_e and $H_{e'}$. The multiplet between 3.26 ppm – 3.36 ppm integrates for eight protons, which are indicative of the methylene protons found on carbons c and c', two H_y and two $H_{y'}$. The two sets of

doublets of doublets (dd) between 3.44 ppm – 3.50 ppm integrates for four protons, H_z and $H_{z'}$. Finally, the broad multiplet between 4.13 ppm – 4.17 ppm integrates for two protons, H_x.

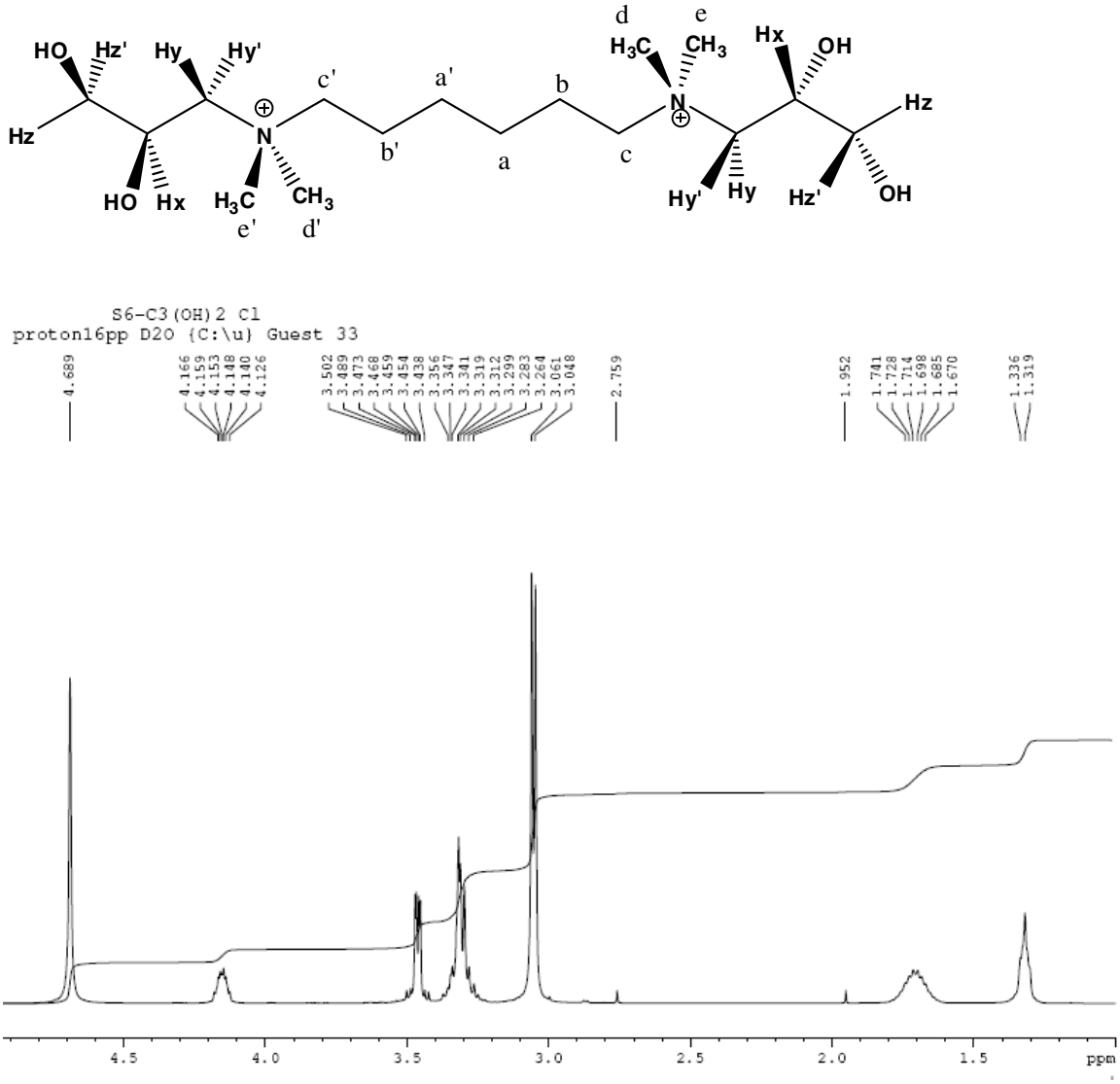


Figure 54. ^{1}H NMR spectrum of S6-Cl (400 MHz, D_2O).

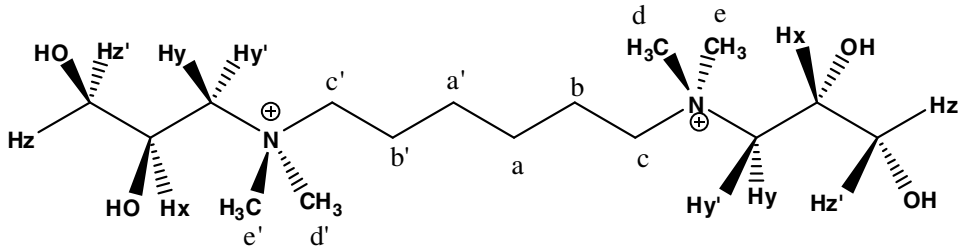
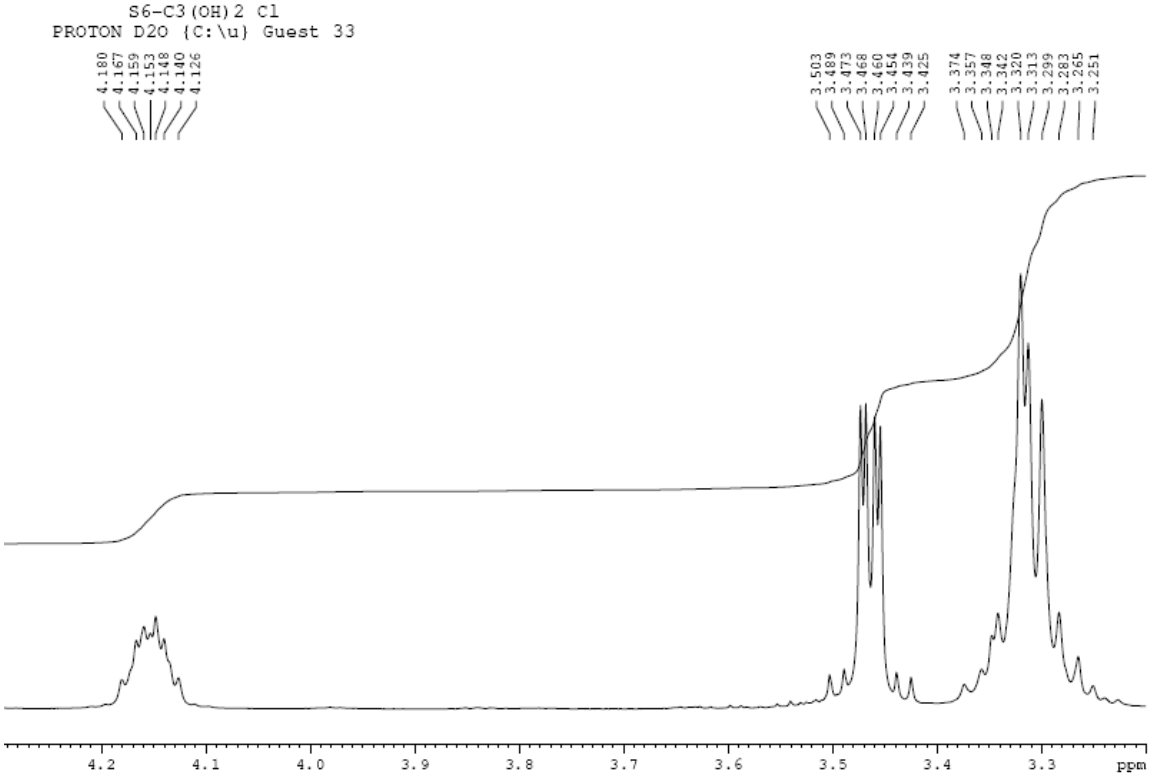


Figure 55. Expanded ^{1}H NMR spectrum of S6-Cl (400 MHz, D_2O)



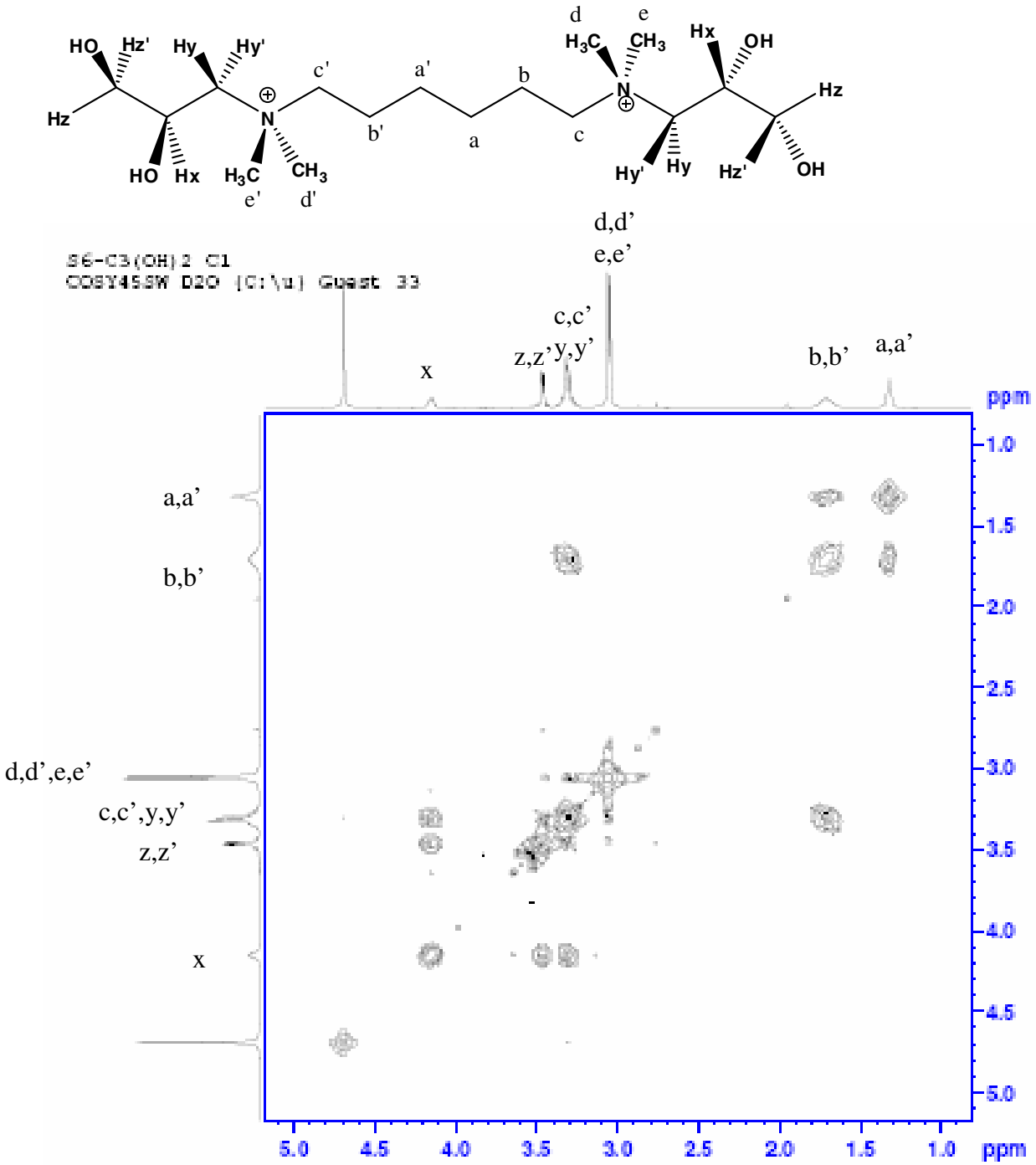
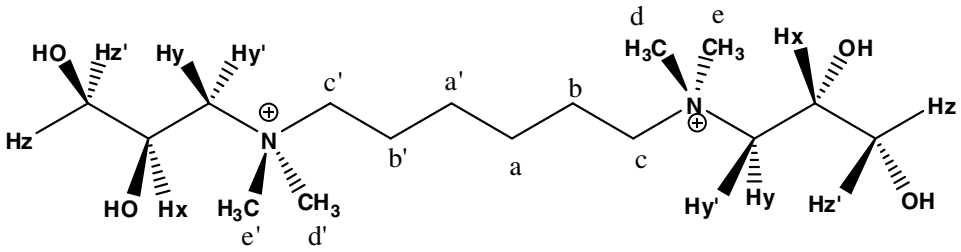


Figure 56. ^{1}H-^{1}H COSY NMR spectrum of S6-Cl (400 MHz, D_2O).

The ^{1}H COSY spectrum shows coupling between H_a, $H_{a'}$ and H_b, $H_{b'}$. There is also coupling between H_b, $H_{b'}$ and H_c, $H_{c'}$. Coupling occurs

between H_x with H_y and $H_{y'}$ and H_x with H_z and $H_{z'}$. Proton assignments are shown in Table 23.



Proton	Chemical Shift (ppm)	J (Hz)
H_a, $H_{a'}$ (4 H)	1.39-1.34 (br m)	
H_b, $H_{b'}$ (4 H)	1.67-1.74 (br m)	5.2-6.0
H_d, $H_{d'}$ (6 H)	3.05 (s)	-
H_e, $H_{e'}$ (6 H)	3.06 (s)	-
H_c, $H_{c'}$, H_y, $H_{y'}$ (8 H)	3.20-3.38 (m)	-
H_z, $H_{z'}$ (4 H)	3.40-3.50 (2 sets of dd)	2.0-5.6
H_x (2 H)	4.13-4.17 (br m)	2.0-5.6

Table 23. ^{1}H shift assignments and coupling constants of S6-Cl.

There are eight signals in the ^{13}C NMR spectrum of S6-Cl (Figure 57), and the ^{13}C DEPT experiment is shown in Figure 58. The peak assignments for the carbons based on these spectra, is presented in Table 24.

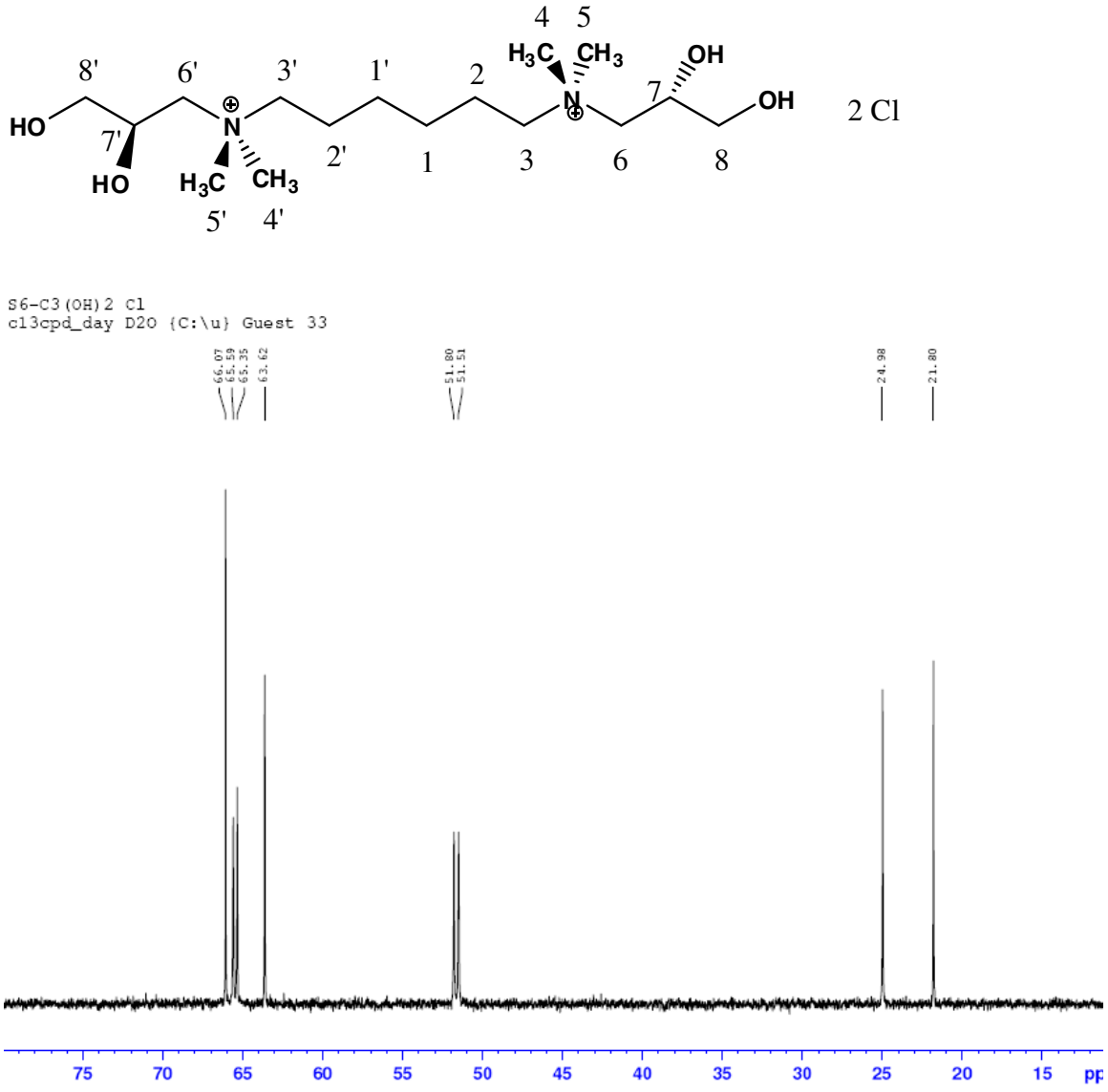


Figure 57. ^{13}C NMR spetrum for S6-Cl (100 MHz, D_2O).

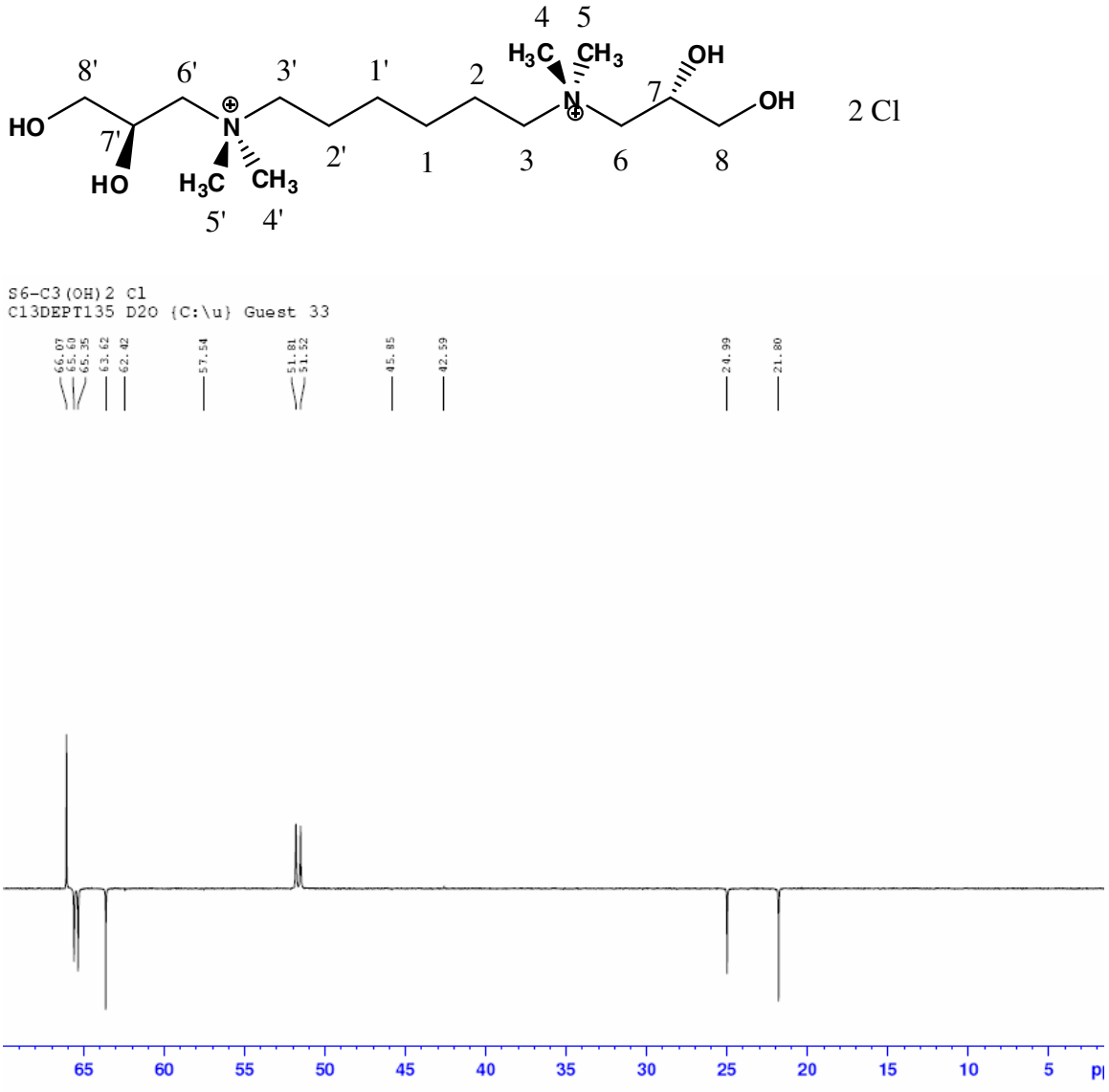
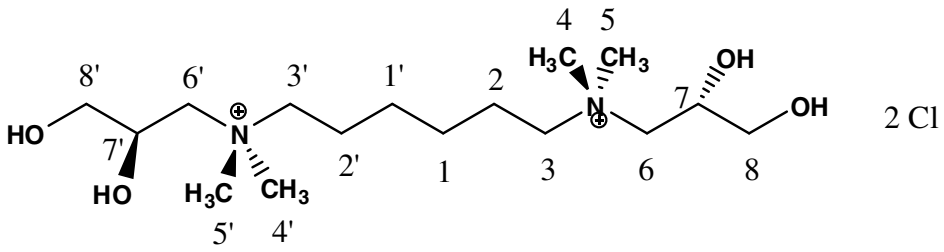


Figure 58. ^{13}C NMR DEPT spectrum of S6-Cl (100 MHz, D_2O).



Chemical Shift	Carbon Type	Carbon
21.8	CH_2	1,1’
25.0	CH_2	2, 2’
51.5	CH_3	4 or 5
51.8	CH_3	4 or 5
63.6	CH_2	3, 3’
65.3	CH_2	6, 6’
65.6	CH_2	8,8’
66.1	CH	7.7’

Table 24. Carbon assignments for S6-Cl.

The ^{1}H, ^{13}C and ^{31}P NMR spectra for S6-IP are shown in Figures 59, 60, and 61. The presence of the phosphate anion is confirmed by the singlet at 0.07 ppm in the ^{31}P NMR spectrum.

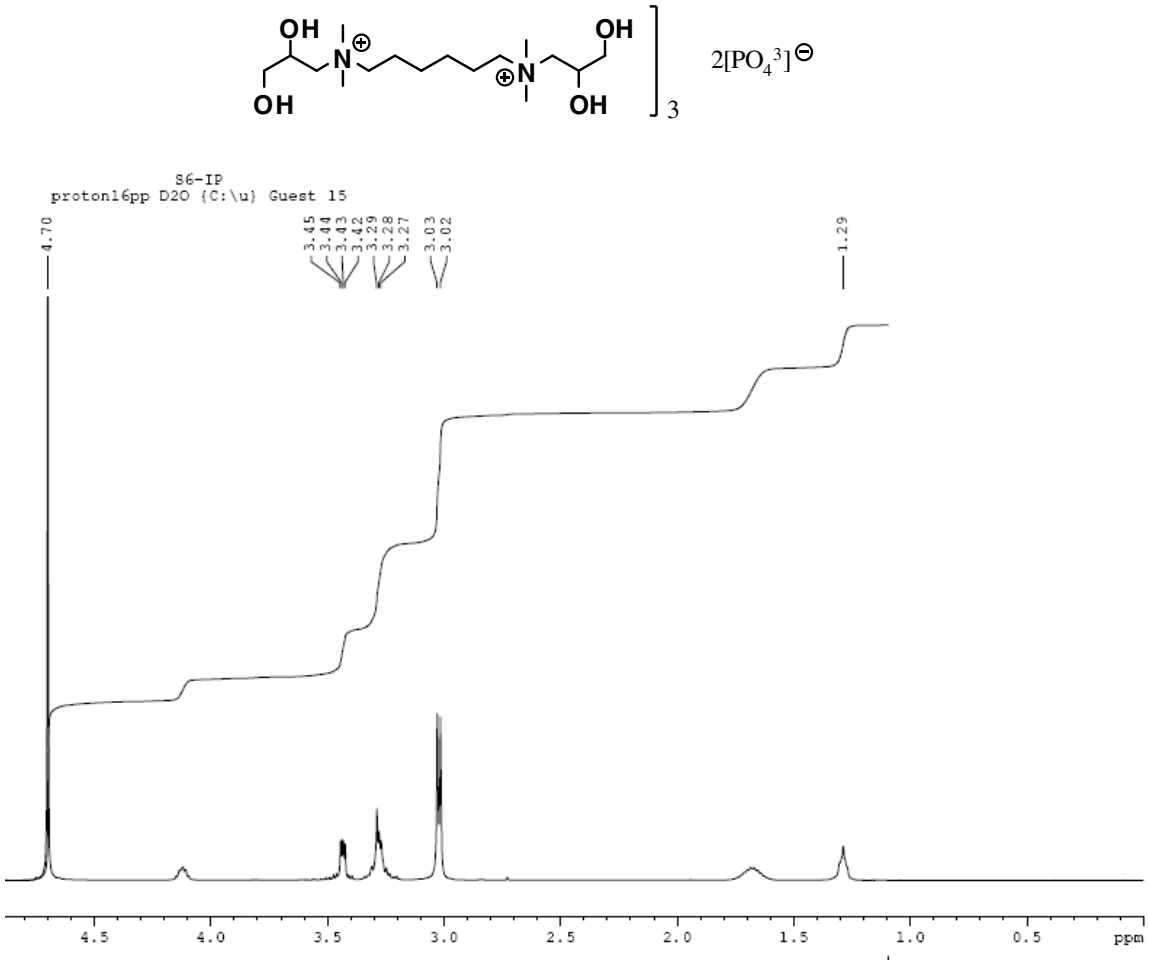


Figure 59. ^{1}H NMR spectrum of S6-IP (400 MHz, D_2O).

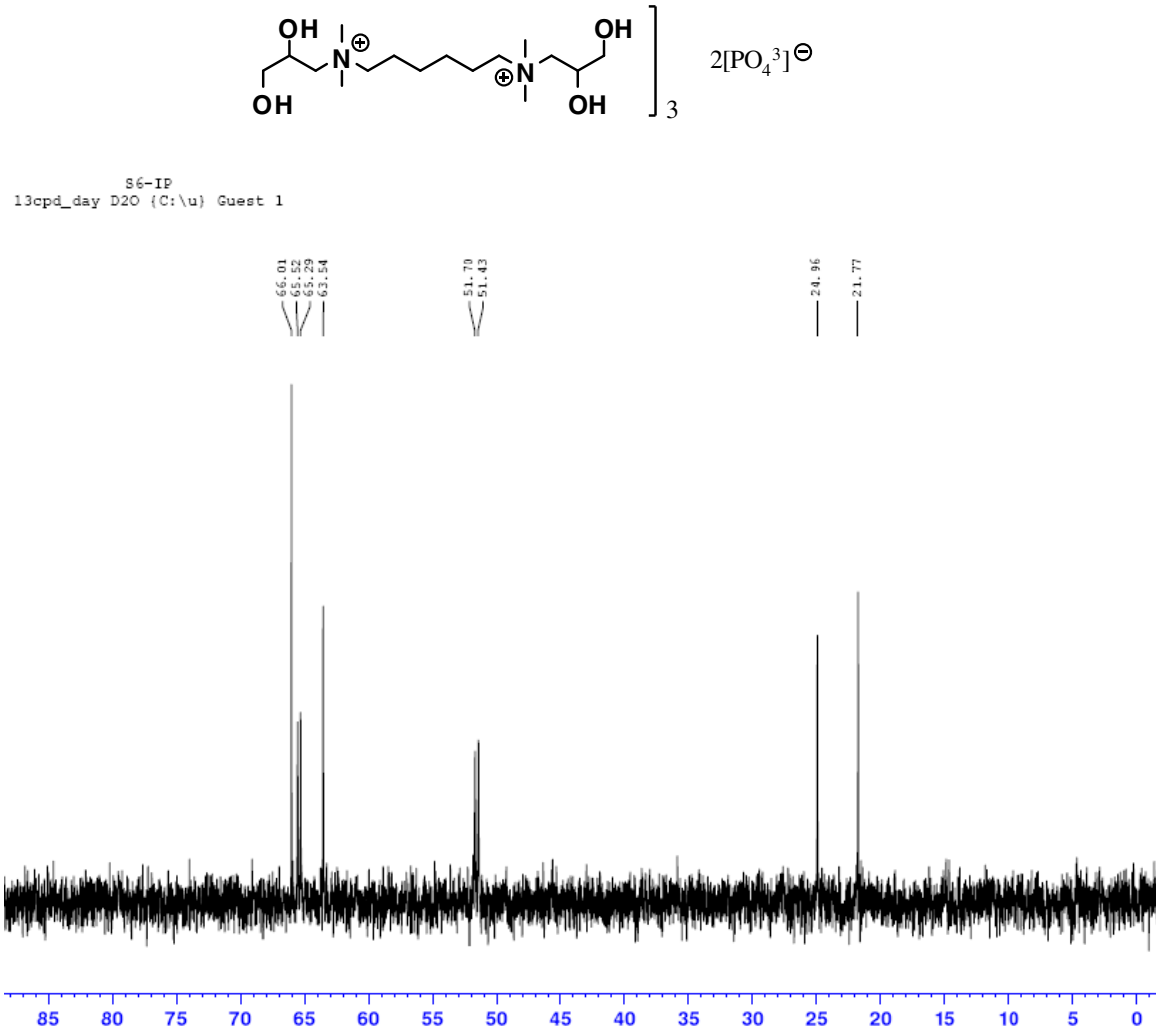
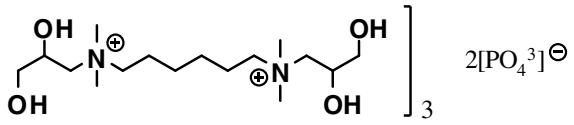


Figure 60. ^{13}C NMR spectrum of S6-IP (100 MHz, D_2O).



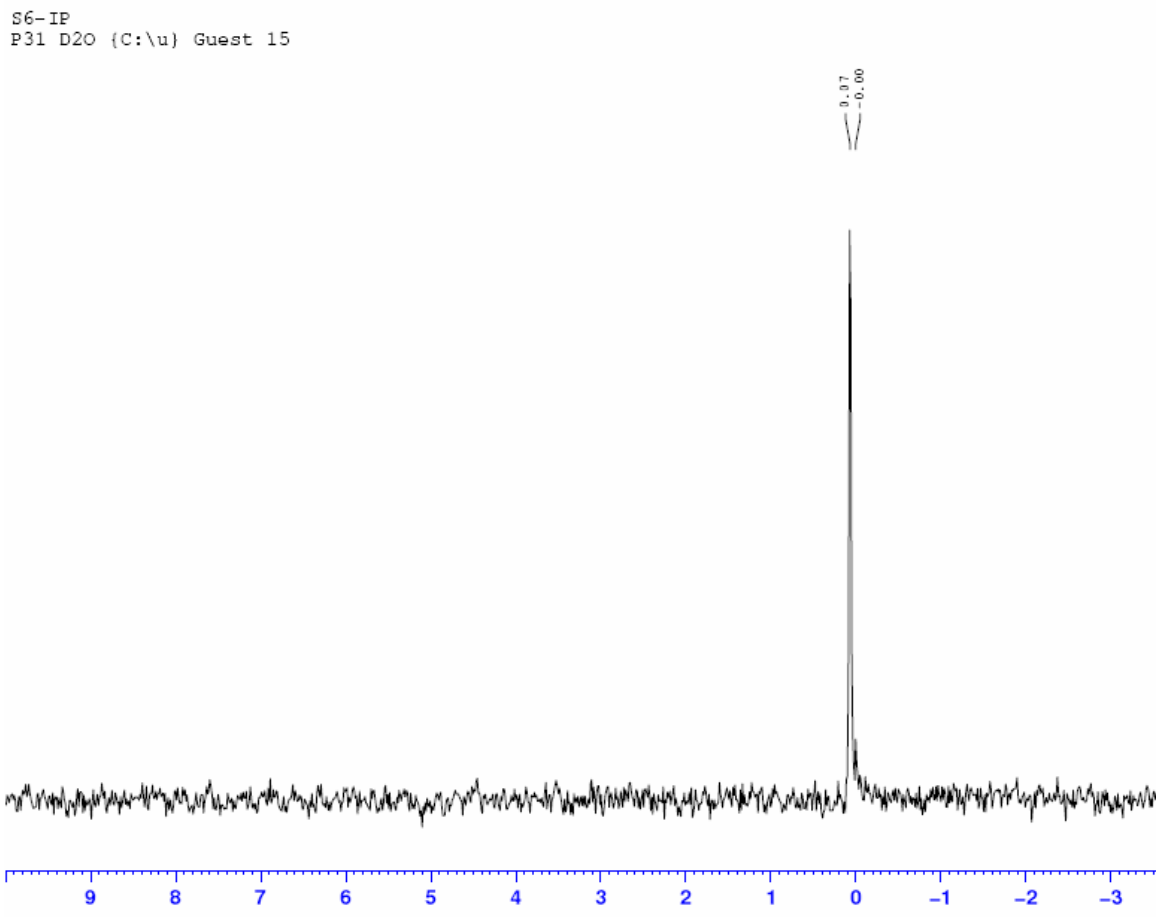
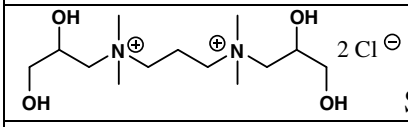
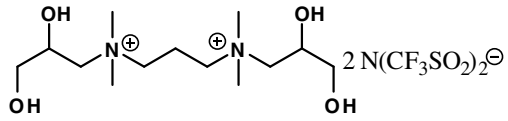
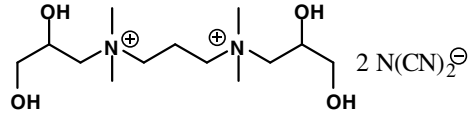
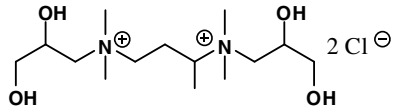
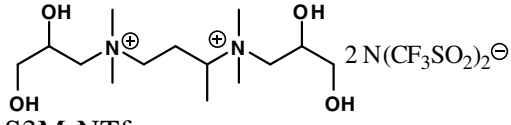


Figure 61. ^{31}P NMR spectrum of S6-IP.

Other new dicationic salts based on *N,N,N',N'*-tetramethyl-1,3-propanediamine and *N, N,N',N'*-tetramethyl-1,3-butanediamine are shown in Table 25. "S3" refers to the **string** compound with three methylene groups between the nitrogen atoms. "S3M" refers to the **string** compound with three methylene groups between the nitrogen atoms, with a **methyl** group on carbon three.

Table 25. Dicationic salts based on other α,ω-diamines.

Structure/Code	Melting point (˚C)	Name
 S3-Cl	112-115	4,4,8,8-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol chloride
 $S3\text{-}NTf_2$	-23.9	4,4,8,8-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol bis(trifluorosulfonyl)imide
 S3-DCA	-	4,4,8,8-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol dicyanamide
 S3M-Cl	-	4,4,7,8,8-pentamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol chloride
 $S3M\text{-}NTf_2$	-16.3 (Glass Transition)	4,4,8,8-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol bis(trifluorosulfonyl)imide

The chloride salts S3-Cl and S3M-Cl were obtained as a mixture of product and 3-chloro-1, 2-propanediol. We were able to obtain S3-Cl by using a protecting group (see Figure 62). The mixture was treated with 2, 2-

dimethoxypropane and p-touluenesulfonic acid in acetone. This resulted in the conversion of 3-chloro-1, 2-propanediol to the acetonide which remained in solution, while the salt remained unprotected. The salt was isolated as a white solid. The inability of the protecting group to add to the salt may be due to steric hindrance. However, we later found that by dissolving the mixture in ethanol, adding ether to precipitate the product and drying the resulting viscous liquid on the pump, we were able to get this salt to solidify. Washing with ethyl acetate yielded the product. The ^{13}C NMR spectrum of this compound showed no trace of 3-chloro-1, 2-propanediol. Figure 63 and 64 show the ^{13}C spectra of S3-Cl with and without the starting material.

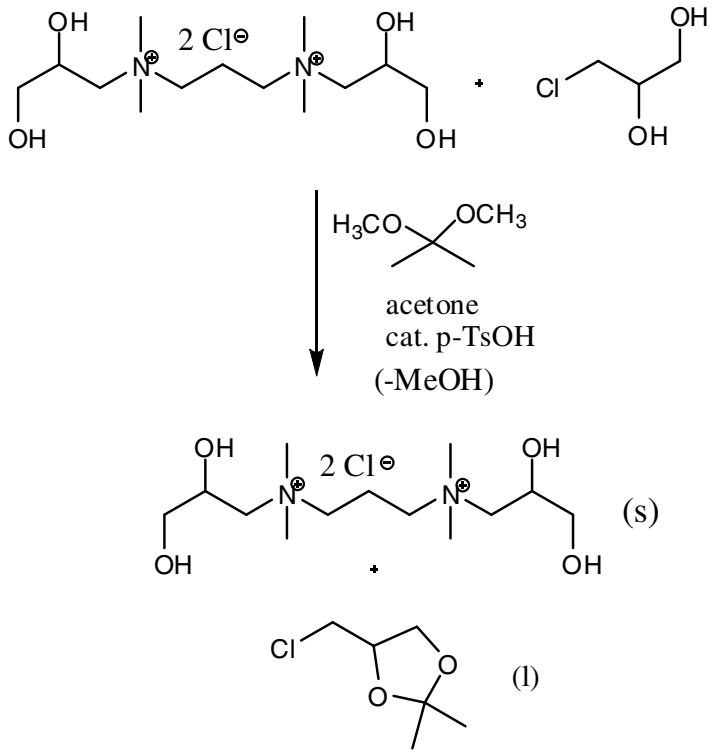


Figure 62. Isolation of S3-Cl.

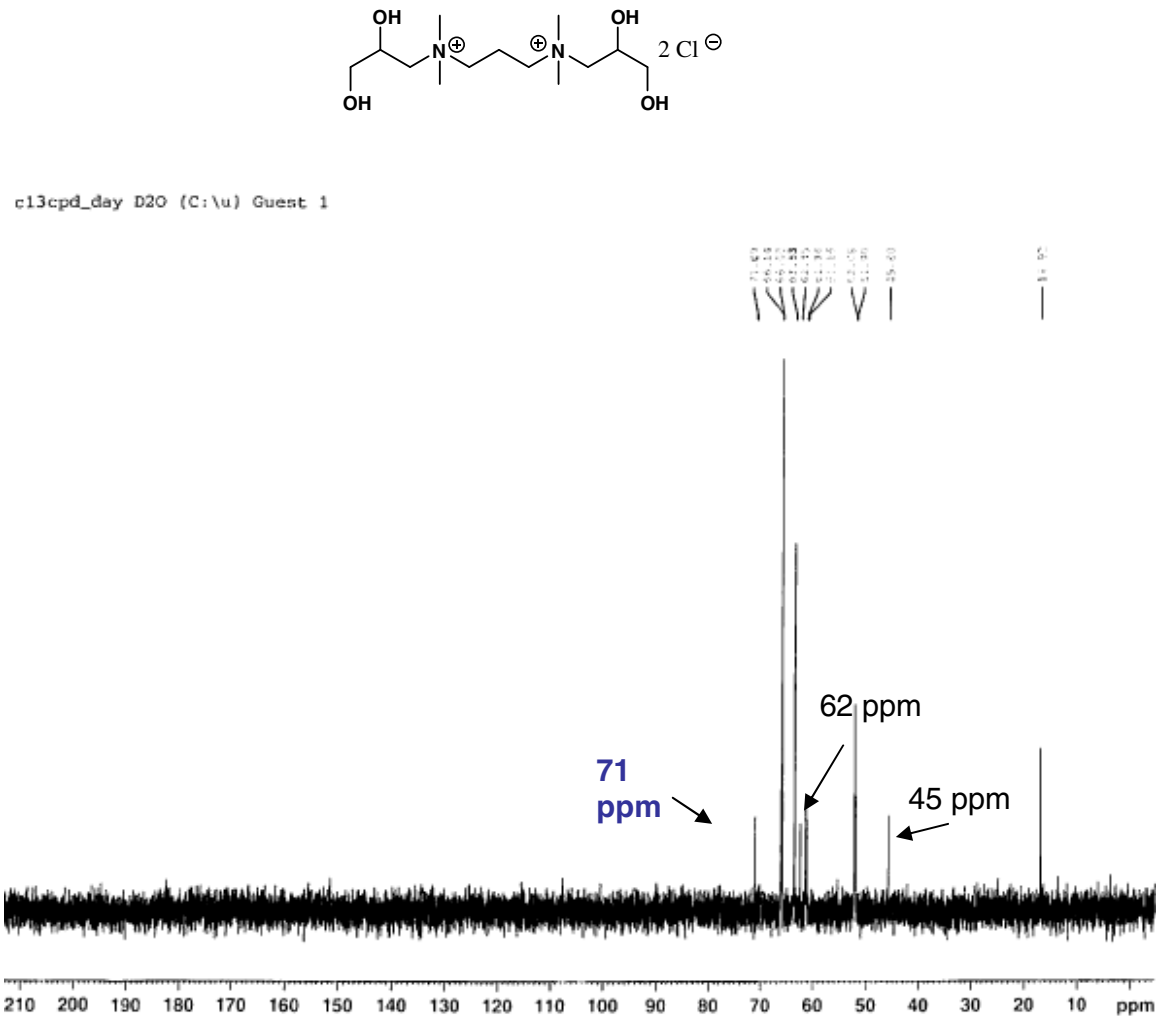


Figure 63. ^{13}C NMR of S3-Cl with excess starting material 3-chloro-1, 2-propanediol. Signals at 71, 62, and 45 ppm indicate the presence of the starting material.

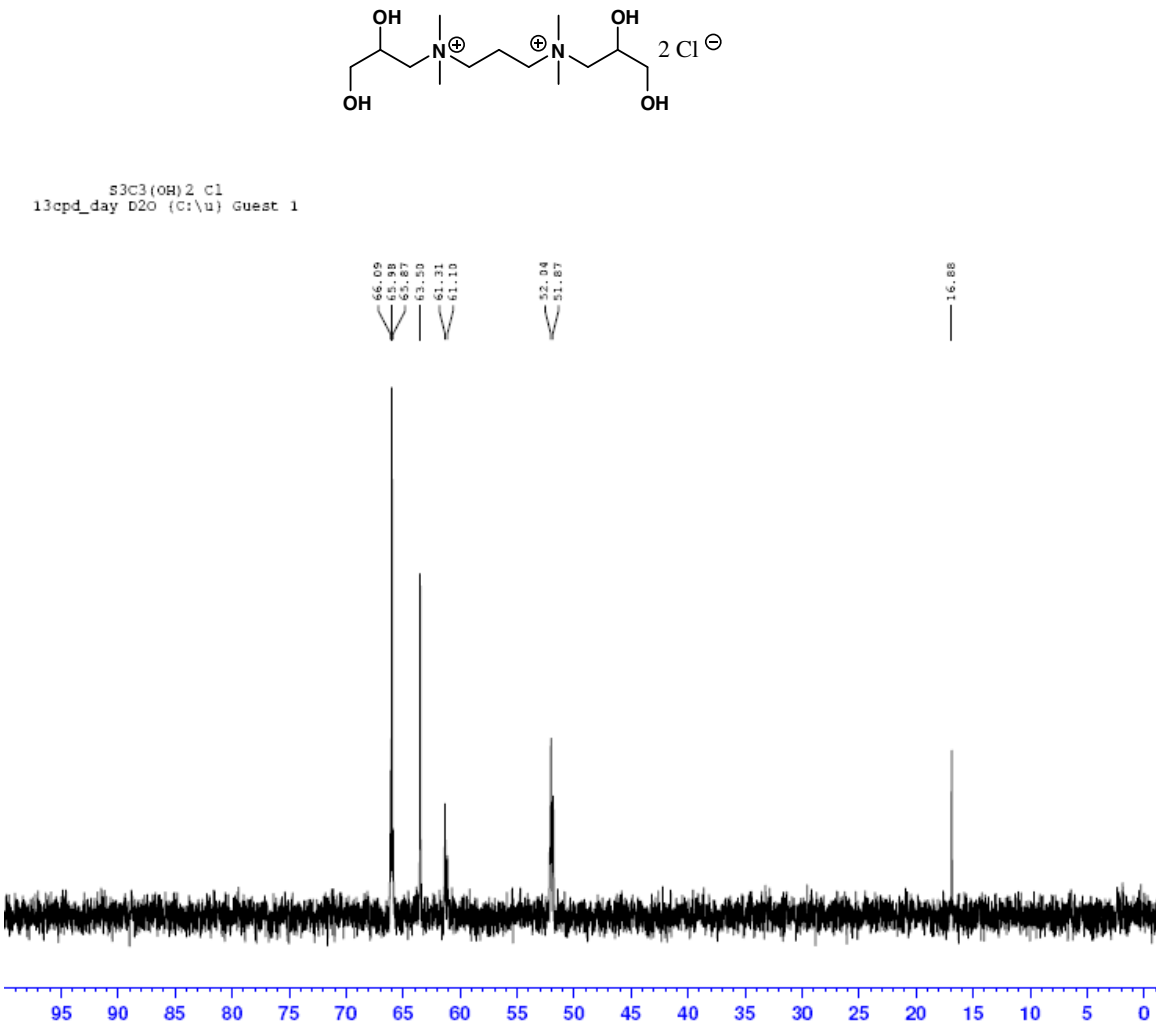


Figure 64. ^{13}C spectrum of S3-Cl (100 MHz, D_2O).

We also discovered that we can get rid of the excess starting materials by converting the dicationic salts to the sulfonylimide salts. It may be the situation that purification should be delayed to the final product, rather than complete it at intermediate stages. The dicationic salts displayed a somewhat amphiphilic nature. As a result, significant quantities of the salts were lost upon washing with water (to remove the halide impurity and the excess starting materials.)

Additional information such as glass transition points and the thermal stability of the ionic liquids are presented in Table 26. Many of the ionic liquids had glass transition points that were close to their melting points as determined by differential scanning calorimety (DSC). The glass transition point is often defined as the point in which a material becomes a glass. The DSC trace of DMAP-NTf_2 is shown in Figure 65. During the first heating cycle the trace displays an endotherm characteristic of melting. During the second cycle the endotherm displayed shows a glass transition. This indicates that DMAP-NTf_2 is slow to crystallize.

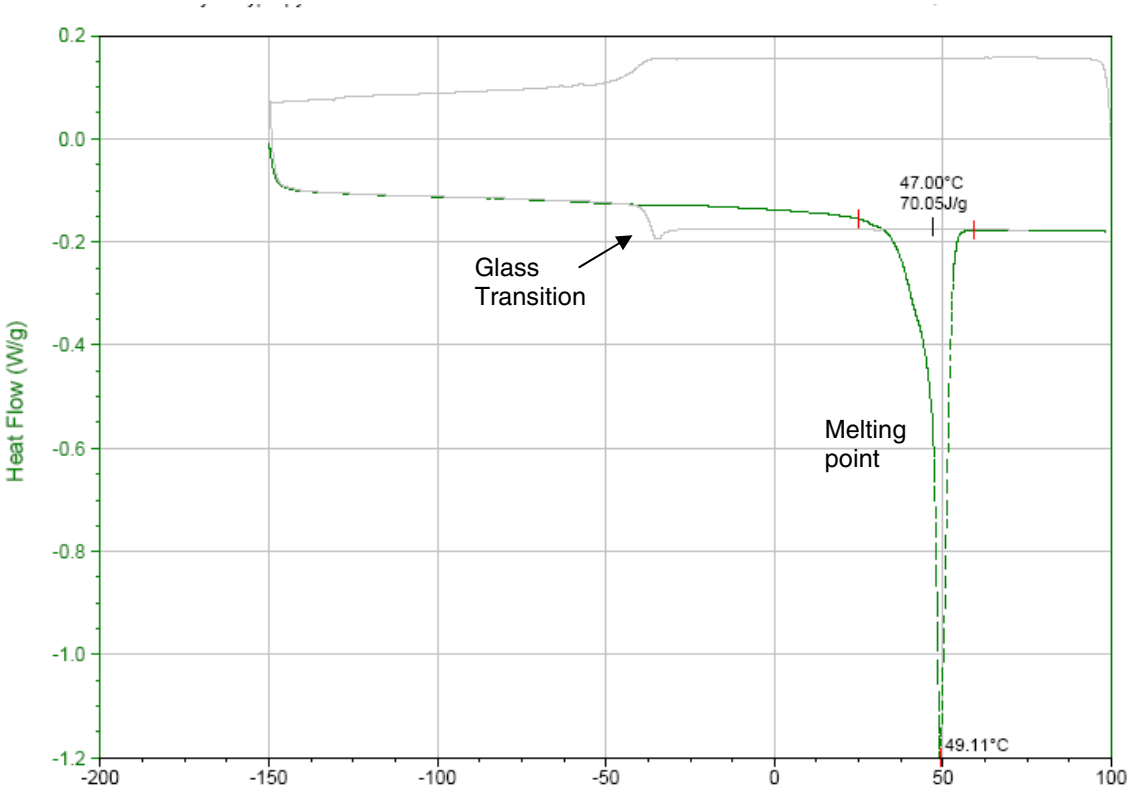


Figure 65. DSC Trace of DMAP NTf_2.

The fact that ionic liquids such as D-DCA, P-DCA, P-DPP, S6-NTf_2 and S6-DCA display melting points and glass transitions of that are close, may indicate that these materials do not crystallize. Upon cooling these materials form a glass, which melt with a small increase in temperature. The endotherms for these salts are closer to what one would see for the glass transition.

Table 26. Melting points (M.P.), glass transitions and thermal degradation temperatures (T_g) of ionic liquids.

Ionic Liquid	T_g (˚C)	M.P. (˚C)	Glass Transition (˚C)
D-DCA	154.3	-18.7	-25.7
DMAP-NTf_2	279.9	49.1	-33
P-DCA		-64.2	-68.6
P-DPP	203.9	-23.1	-27.9
S6-NTf_2		-30.0	-33.9
S6-DCA	275.0	-45.5	-50.2

A few of the chiral salts, mainly the chloride salts have been successfully synthesized. (R)- (-) DMAP-Cl was converted to the sulfonylimide salt, which just displayed a glass transition. The DMAP salts are presented in Table 27 with specific rotation data and melting points. The racemic analogues are included for comparison. The chiral DMAP salts displayed significantly lower melting points (about 40 °C less than the

melting point of the racemic salt). The chiral analogues of the other racemic salts most likely will also have lower melting points.

Table 27. Melting points and specific rotation data of chiral DMAP derivatives. G.T. = glass transition.

Ionic Liquid	Melting Point (˚C)	$[\alpha]^{25}$
DMAP-Cl	204-207	-
(R)-(-) DMAP-Cl	164.7	-100
(S)-(+) DMAP-Cl	167.2	112.5
DMAP-NTf_2	49.1 (-33, G.T)	-
(R)-(-) DMAP NTf_2	-32.9 (G.T.)	-22.4

A series of new salts have been developed using the racemic form and chiral form of 3-chloro-1, 2-propanediol, some of which have been found to be ionic liquids with very low melting points and/or glass transitions. The structures were verified using ^{1}H, ^{13}C and where applicable ^{31}P NMR analysis, elemental analysis and/or mass spectroscopy (discussed later in more detail). The elemental analysis data for the proposed species were reasonably close to the calculated values.

B. Dicationic Strings as Potential Anion Receptors

In addition to ^{1}H and ^{13}C NMR, it was of interest to use electrospray mass spectrometry to gather structure data regarding some of our new compounds. The spectra of S6-Cl exhibited a significant peak at m/z {357/359}. This was an indication that the dicationic salt may be complexing a chloride anion. This trait was noticed for other polycationic species that were previously developed by this laboratory [133].

S6-Cl was converted by anion metathesis to other salts such as S6-LIP, S6-NTf_2, and S6-DCA. S6-NTf_2 and S6-DCA were found to be room temperature ionic liquids. Samples of these salts were submitted for ESIMS and the spectra showed m/z at {161} (see Table 28). There was no indication that the other anions such as phosphate, bis(trifluorosulfonyl)imide or dicyanamide was bound by the cation. The S6 cation (and possible other polycationic strings developed by this lab) may serve as an anion receptor. The mass spectroscopy data is presented in Figures 66, 67, 68, and 69.

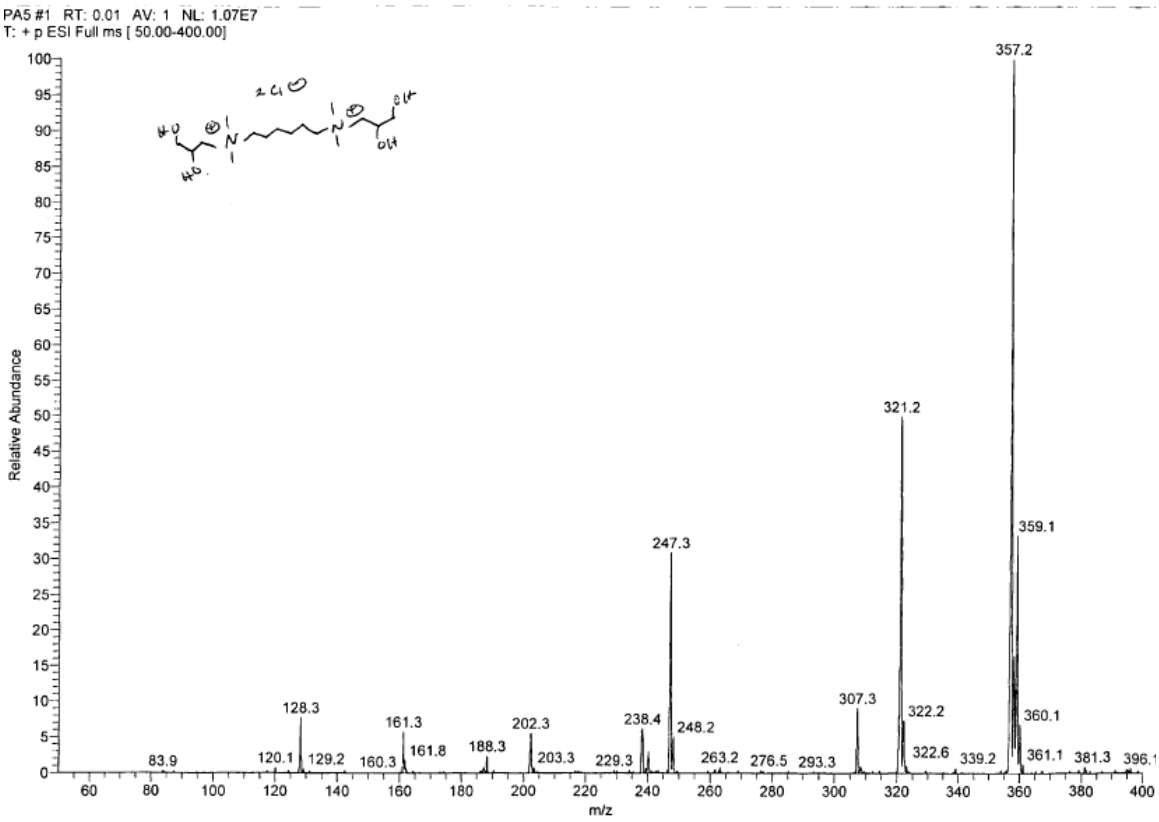


Figure 66. Mass spectrum of S6-Cl.

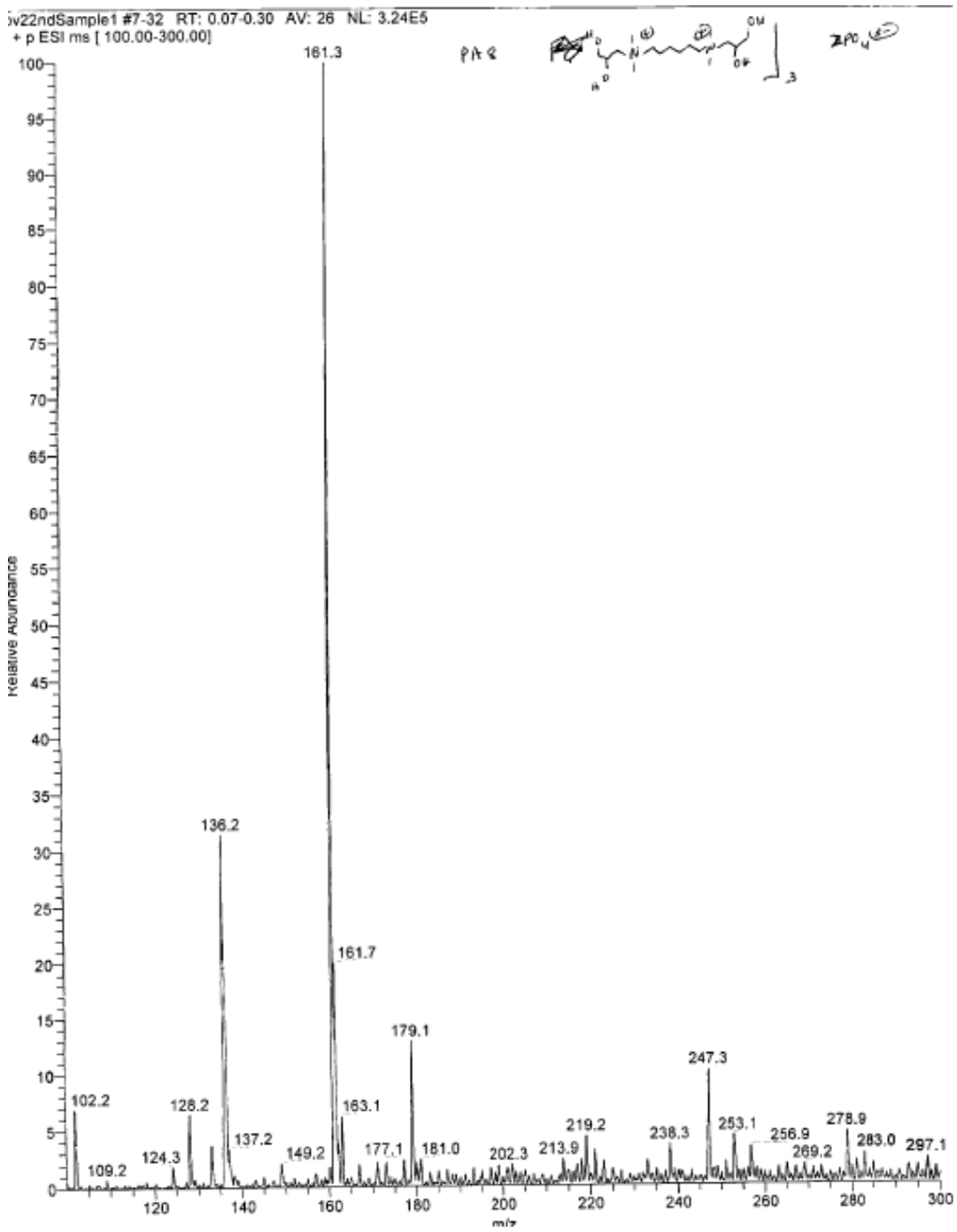


Figure 67. Mass spectrum of S6-IP.

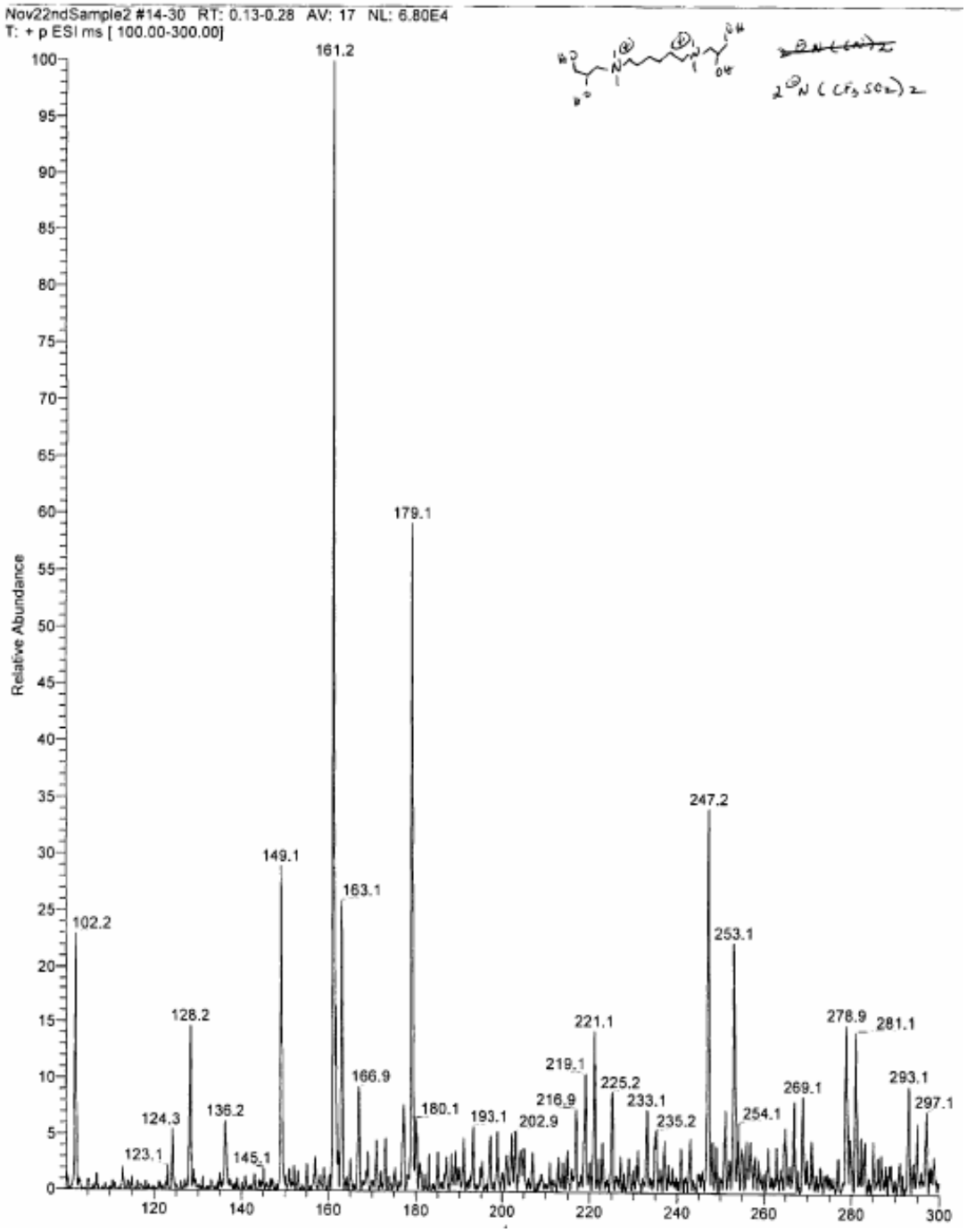


Figure 68. Mass spectrum e of S6-NTf_2

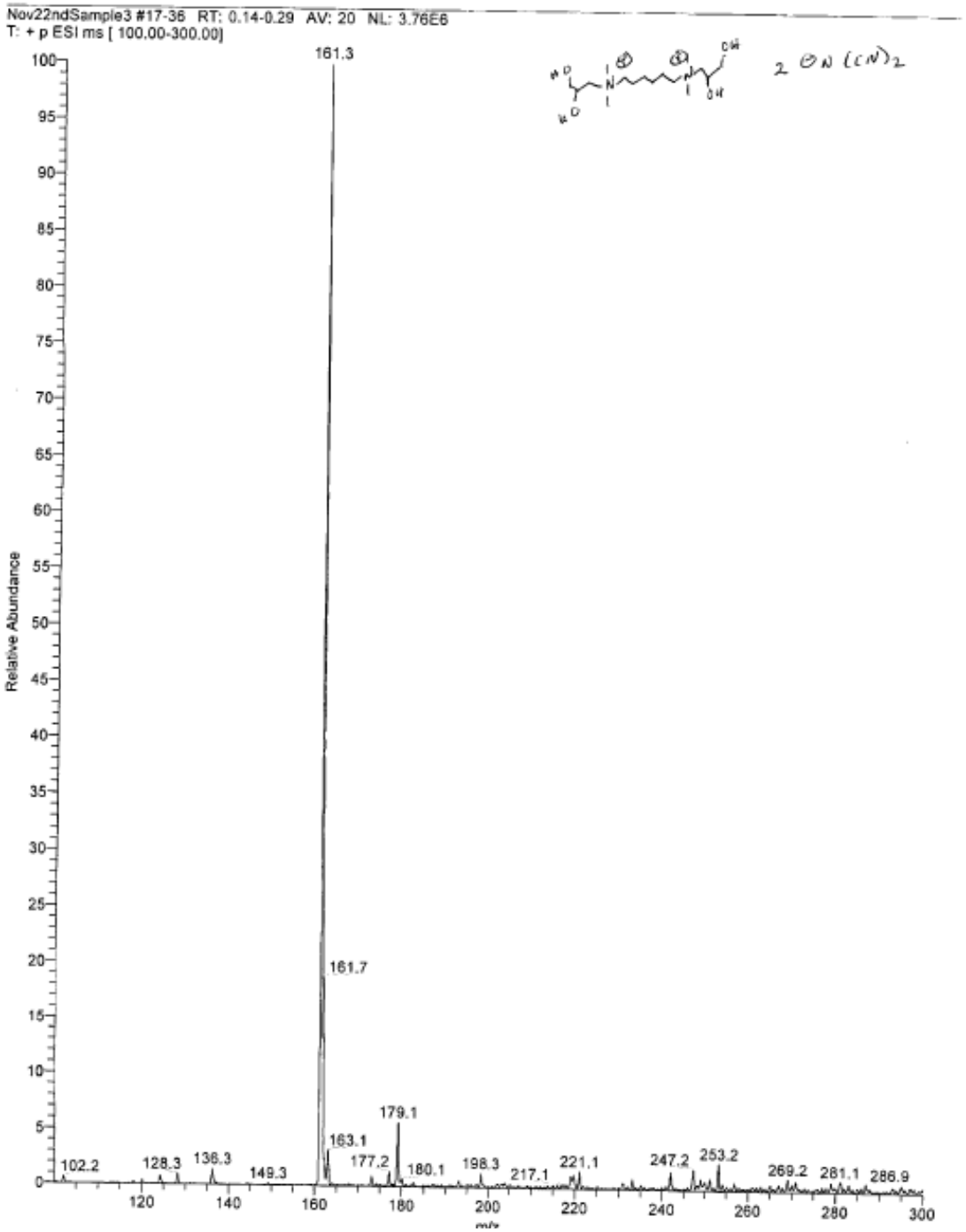


Figure 69. Mass spectrum of S6-DCA.

Table 28. Major processes in the positive electrospray mass spectrum of bis-diammonium strings

Compound	Process [m/z]	Process [m/z]
S6-Cl	$(M\text{-}Cl)^{+}$ [357/359]	$(M\text{-}2Cl)^{2+}$ [161]
S6-IP		$(M\text{-}2IP)^{2+}$ [161]
S6-NTf_2		$(M\text{-}2NTf_2)^{2+}$ [161]
S6-DCA		$(M\text{-}2DCA)^{2+}$ [161]

The design and synthesis of organic compounds that are able to act as anion binding hosts is a growing field in coordination chemistry [134]. The bicyclic katapinates were the first to be reported [135]. They were found to encapsulate a chloride anion within the interior of the bicyclic compounds. Since then many polyammonium compounds (most of which are cyclic in nature) have been synthesized that are able to complex anions. Examples are shown in Figure 70 [136, 137].

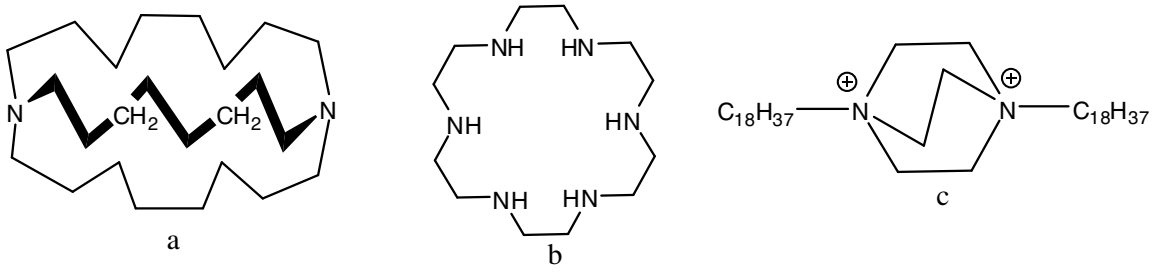


Figure 70. Various anion receptors. a)Representative structure of kaptinates developed by Park and Simmons . b) 18-azacrown-6. c) DABCO salt developed by Tabushi et al.

The ability of organic materials to complex anions can depend on size (of the anion binding host), pH, solvent, electrostatic interactions, and/or hydrogen bonding [138]. Past research of this laboratory has included the synthesis of polycationic beta-cyclodextrin derivatives that bore 14 positive charges, which were investigated for an ability to bind various types of biological anions [139]. The ability of these materials to complex anions derives from largely from electrostatic interactions. In the case of the dicationic string, in addition to electrostatic interactions, we believe that hydrogen bonding also plays a role in binding the chloride anion.

Anion receptors can be used in catalysis, separations, as ion-selective electrodes, in waste management and anion-templated reactions [134, 138].

C. New Monocationic DABCO Strings

We have prepared a series of monocationic salts that were used for the preparation of carbohydrate derivatives, the preparation of polycationic dendrimers and the modification of polyester fabrics. The salts were prepared by allowing one equivalent of an alkyl halide to react with DABCO in ethyl acetate (Figure 71). The monocationic salt precipitates out of solution and is recovered by filtration and washed with ethyl acetate and ether. The syntheses of many of the salts presented in Table 1 have been published [80, 139]. Only the synthesis of the new salts DIsp and DMPr will

be described in detail in the Experimental. DC16 and DC12 were found to exhibit the highest antimicrobial activity when bound to surfaces and are used in the modification of dendrimers and fabrics [80, 81]. Most of the salts were obtained as white powders with yields up to 99%. All structures were confirmed with ^{1}H and ^{13}C NMR and elemental analysis.

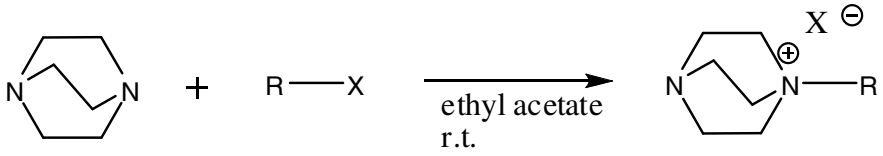
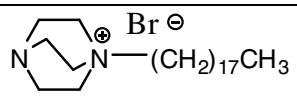
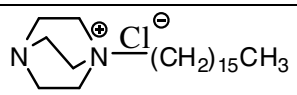
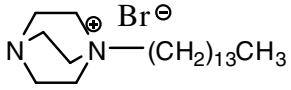
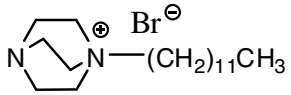
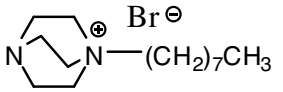
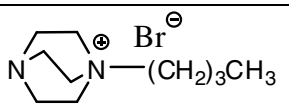
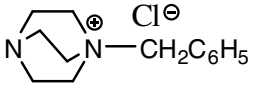
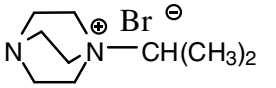
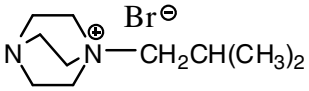


Figure 71. Synthesis of DABCO strings. R = -$C_{18}H_{37}$, -$C_{16}H_{33}$, -$C_{14}H_{29}$, -$C_{12}H_{25}$, -C_8H_{17}, -C_4H_9, -$CH_2C_6H_5$, -$CH(CH_3)_2$ and -$CH_2CH(CH_3)_2$, X = Cl or Br.

Table 29. Monocationic DABCO Strings

String	Code	Name
	DC18	1-(octadecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DC16	1-(hexadecyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride
	DC14	1-(tetradecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DC12	1-(dodecyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DC8	1-(octyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DC4	1-(butyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DBz	1-(benzyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DIsp	1-(isopropyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide
	DMPr	1-(2-methylpropyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide

D. Polycationic Carbohydrate Derivatives

It became of interest to synthesize chiral salts with the intent that they be convertible to ionic liquids. It was also desired that such chiral salts would be prepared from biorenewable sources such as carbohydrates. Such materials should be environmentally friendlier and the starting materials relatively inexpensive. With this in mind, salts were prepared using the carbohydrate derivatives D-mannitol and α-methyl-D-glucopyranoside. However, many of the derivatives of interest exhibited high melting points and were very hygroscopic. On the positive side, however, some of these derivatives, in particular those with long aliphatic chains, have been found to gelate water, making them small-molecule gelators or hydrogelators.

The new salts made from D-mannitol are shown in Table 30. Each compound is assigned a code. “Mn” refers to D-mannitol, “MIM” to 1-methylimidazole, “Bz” to benzyl, “C” to carbon and the number after “C” represents the length of the aliphatic chain. The salts were synthesized by treating the carbohydrate derivative with two equivalents of *p*-toluenesulfonyl chloride and two equivalents of sodium bicarbonate in distilled water (see Figure 72). Tosylation using aqueous sodium bicarbonate is a modification of the Schotten-Bauman method and was developed by the

Engel laboratory. This was followed by addition of two equivalents of a tertiary amine or a monocationic DABCO string.

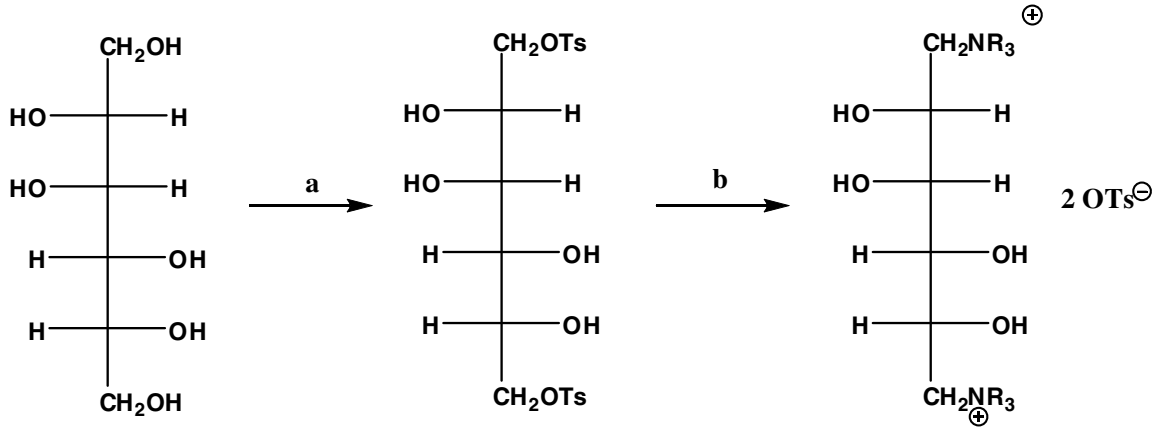
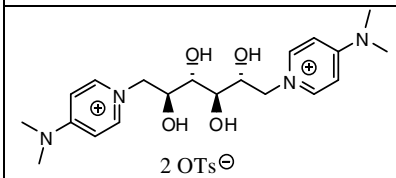
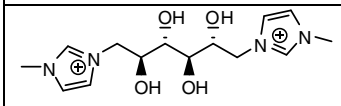
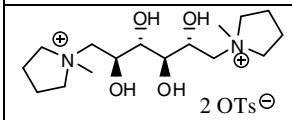
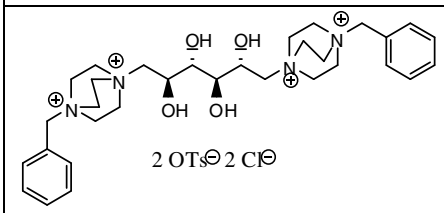
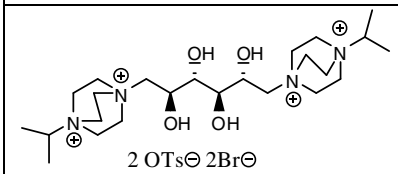
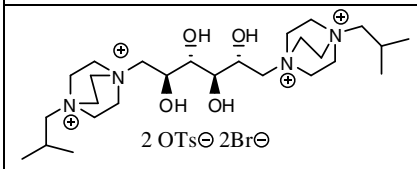
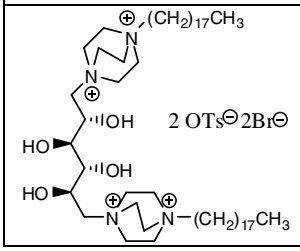
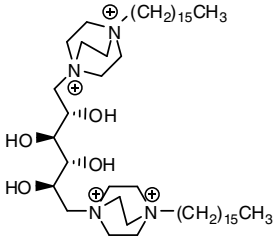
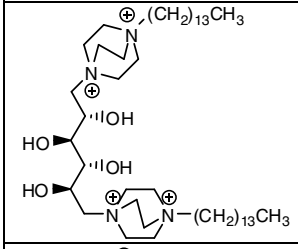
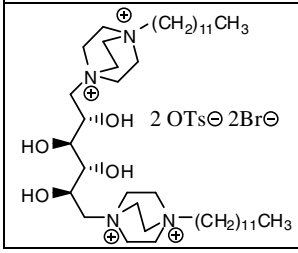


Figure 72. Synthesis of D-Mannitol Derivatives a. $NaHCO_3$, p-TsCl, water b. NR_3 = DMAP, 1-methyl imidazole, 1-methyl pyrrolidine or DABCO strings, reflux overnight.

Melting points and specific rotations for the mannitol derivatives are listed in Table 31. These compounds are hygroscopic, which made obtaining the melting points a challenge. As expected, generally as the size of the cation increased the melting point also increased.

Table 30. D-Mannitol Salts

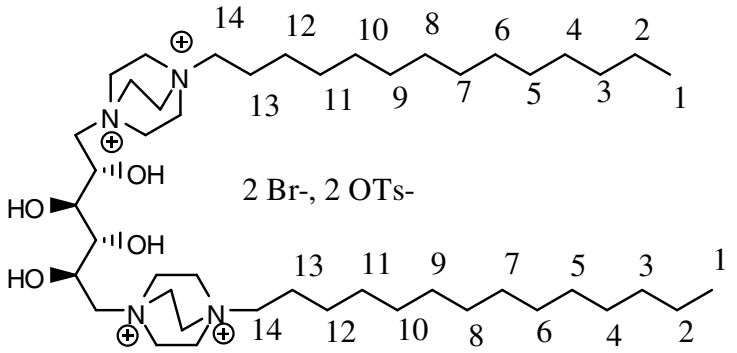
Structure	Code	Name
	MnDMAP	1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-4-(dimethyl amino) pyridinium-1,6-bis[4-dimethylamino) pyridium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate
	MnMIM	1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-3-(methyl) imidazolium)-1,6-bis[3-methyl imidazolium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate
	MnP	1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-N-(methyl) pyrrolidinium-1,6-bis[N-methyl pyrrolidinium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate
	MnDBz	1-(benzyl)-4-(6'-(4"(benzyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dichloride ditosylate
	MnDIsp	1-(isopropyl)-4-(6'-(4"(isopropyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate
	MnDMPr	1-(2-methylpropyll)-4-(6'-(4"(2-methylpropyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate
	MnDC18	1-(octyldecyl)-4-(6'-(4"(octadecyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-2,3,4,5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate (MDC18):

	MnDC16	1-(hexadecyl)-4-(6'-(4"(hexadecyl)'1",4"-diazoniabicyclo[2.2.2]octyl}-1'-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexyl)1,4-diazonia-bicyclo[2.2.2]octane dichloride ditosylate
	MnDC14	1-(tetradecyl)-4-(6"-(4"(tetradecyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-(R)-2,(R)-3,(R)-4,(R)-5,-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate
	MnDC12	1-(dodecyl)-4-(6"-(4"(dodecyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate

Compound	Melting Point (˚C)	$[\alpha]^{25}$
MnDMAP	106-116	-4.81
MnMIM	Hygroscopic	-3.08
MnP	56-66	-97.4
MnDBz	132-136	-4.56
MnDIsPr	100-108	1.49
MnDMPr	109-112	-20.3
MnDC18	224-230	-2.20
MnDC16	158-168	1.44
MnDC14	135-142	-7.89
MnDC12	154-157	-1.18

Table 31. Melting points and specific rotation of mannitol derivatives.

The structures of these salts were verified using ^{1}H and ^{13} C NMR analysis. The elemental analysis values obtained were in accord with the calculated values of the hydrated species. Because of the limited solubility of the surfactant salts in deuterated solvents such as chloroform-D, D_2O and DMSO-D_6, getting good NMR spectra on these compounds was challenging. Shown in Figures 73 and 74 is the ^{1}H and ^{13}C NMR spectra of MnDC14. The singlet found at 2.17 represents the methyl groups found on the tosylate anions. The doublets between 6.9-7.1 ppm and 7.5-7.7 ppm represent the protons ortho and meta to the methyl group respectively, on the tosylate anion. The triplet between 0.8-1.0 ppm, correspond to the six methyl protons found at the end of the alkyl chains (C1). The broad multiplet between 1.2 – 1.4 ppm correspond to forty protons found on the alkyl chain (on carbons 2 – 12). The broad signal found between 2.9 – 3.1 represent four carbons on the alkyl chains (C13). There are overlapping signals for the protons found on DABCO, the mannitol center and on carbon 14, between 3.5 – 3.8 ppm. There should be nineteen signals in the 13C NMR spectrum. Fourteen are seen. There may be some over lap among the signals for the carbons found in the alkyl chains in the region between 20 – 35 ppm. There are also two signals missing for the mannitol center (which should show between about 60 – 65 ppm). They might be hidden within baseline.



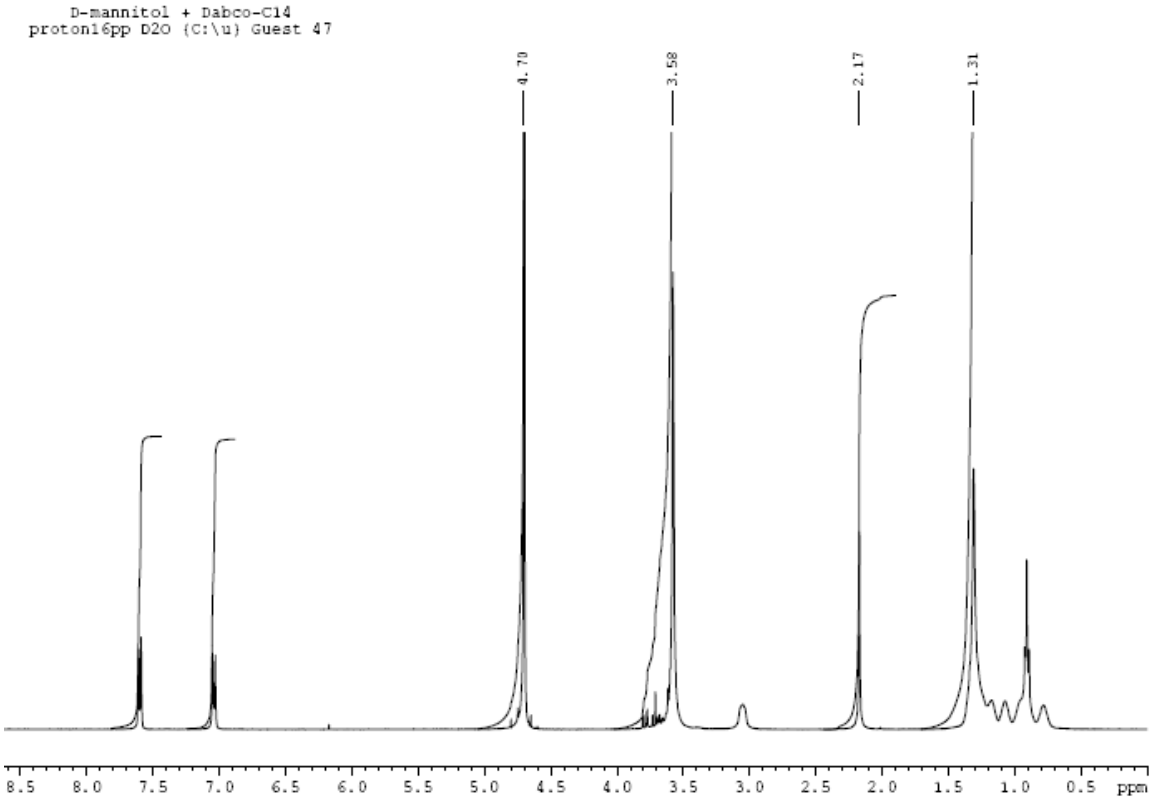


Figure 73. ^{1}H NMR spectrum of MnDC14 (400 MHz, D_2O).

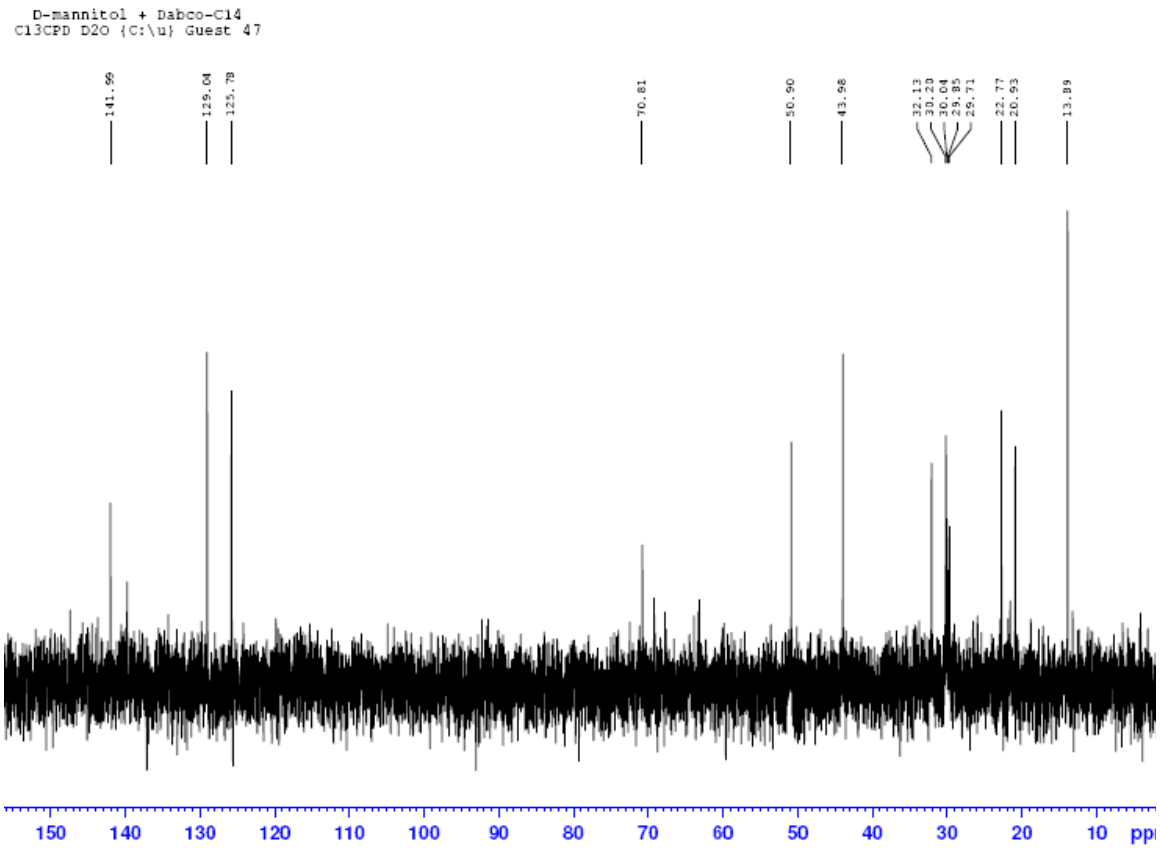


Figure 74. ^{13}C NMR spectrum of MnDC14 (D_2O, 100 MHz).

The mannitol derivatives MnDC18, MnDC16, MnDC14, MnDC12 were found to be insoluble in acetone, methylene chloride, ether, ethyl acetate, hexanes, acetonitrile and toluene. MnDC18, MnDC16 and MnDC14 gelate water. MnDC18 forms a clear gel with a w/v of 5.3%. The surfactant also forms a clear gel with ethanol (6.7 % w/v). Both gels were stable for up to two weeks. MnDC16 forms a white opaque gel with a w/v of 10% with water. This gel was found to be stable for at least twenty-two months. MnDC16 also geled ethanol (4% w/v) and n-butanol (3.3 % w/v). MnDC14 formed an unstable gel with water (30 % w/v) but a very stable gel with

ethanol (3.3%) with some precipitate. These gels are of particular interest in applications for medical adjuncts (antibacterials).

Table 32. Results of gelation tests for D-mannitol derivatives: G (gel), S (soluble), I (insoluble), and X (not tested).

Code	Water	Ethanol	N-Butanol
MnDC18	G	G	I
MnDC16	G	G	G
MnDC14	G	G	X
MnDC12	S	I	X
MnDCIsp	S	I	I
MnDCBz	S	I	I

New salts made from α-methyl-D-glucopyranoside are shown in Table 33. The synthesies of these compounds are similar to that of the D-mannitol derivatives. The sugar derivative was treated with one equivalent of *p*-toluenesulfonyl chloride and one equivalent of sodium bicarbonate in water (Figure 75). This was followed by addition of one equivalent of a tertiary amine or DABCO string. The structures of all new salts were verified with ^{1}H and ^{13}C NMR and through the elemental analysis of the hydrated forms.

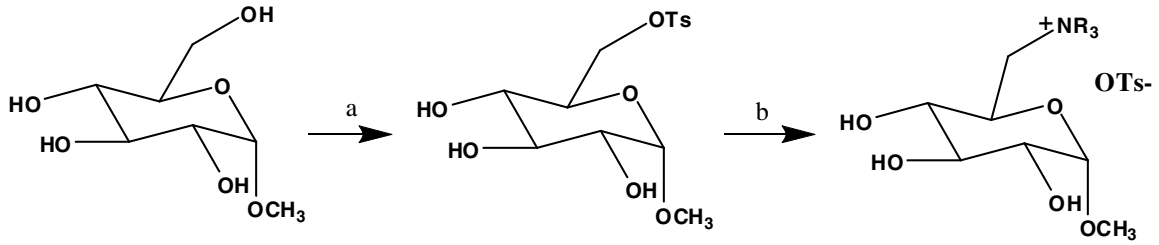


Figure 75.Synthesis of α-D-methyl glucopyranoside derivatives
a. $NaHCO_3$, p-TsCl, water
b. NR_3=DMAP, 1-methyl imidazole, 1-methyl pyrrolidine, or DABCO string

Melting points and the specific rotation data of these salts are shown in Table 34. We were able to get better melting point data for these salts since many of them were less hygroscopic than the mannitol derivatives. As expected, the surfactants such as GDC12, GDC14, GDC16, and GDC18 have lower melting points than their mannitol counterparts. The melting points of the smaller salts show some variability when compared to their mannitol counterparts. For example, GDBz has a melting point range of 133-135 ˚C, which is almost similar to that of MnDBz which has a range of 132-136 ˚C. GP has a large melting point range of 60-69 ˚C, while MnP has a lower melting point range of 56-66 ˚C. The melting point range determined for GDMPr is 127-131˚C which larger than the melting point range for MnDMPr which is 108-112 ˚C.

Table 33. Glucopyranoside Derivatives

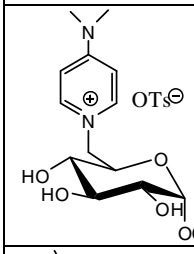
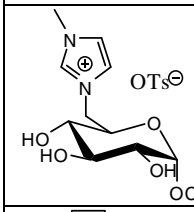
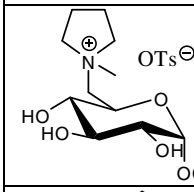
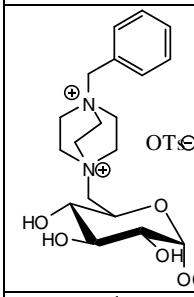
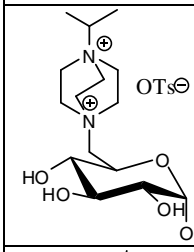
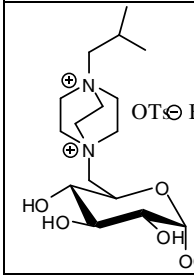
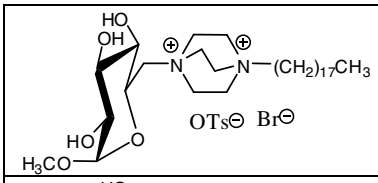
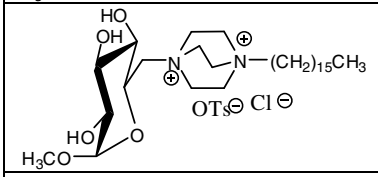
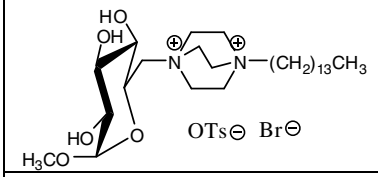
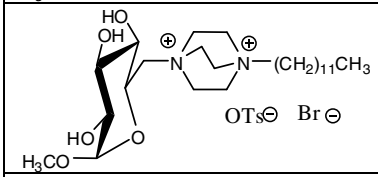
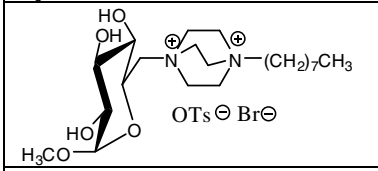
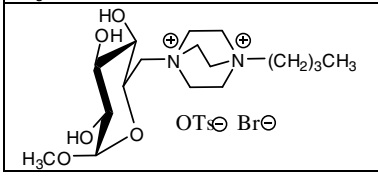
Structure	Code	Name
	GDMAP	methyl-α-D-glucopyranosyl-6-deoxy-6[4-dimethyl amino pyridinium] glucopyranoside monotosylate
	GMIM	methyl-α-D-glucopyranosyl-6-deoxy-6[3-methyl imidazolium] glucopyranoside monotosylate
	GP	methyl-α-D-glucoyranosyl-6-deoxy-6-[N-mentyl pyrrolidinium] glucopyranoside monotosylate
	GDBz	1-(benzyl)-4-(methyl-α-D-glucopyranosyl-6-deoxy-6)-1,4-diazoniabyclo[2.2.2]octane monochloride monotosylate
	GDIsp	1-(isopropyl)-4-(methyl-α-D-glucopyranosyl-6-deoxy-6)-1,4-diazoniabyclo[2.2.2]octane monobromide monotoyslate
	GDMPr	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(2-methylpropyl)-1,4-diazonia-bicyclo[2.2.2] octante monobromide monotosylate

Table 33 continued

	GDC18	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(octadecyl)-1,4-diazoniabycylo[2.2.2]octane monobromide monotoyslate
	GDC16	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(hexadecyl)-1,4-diazabicyclo[2.2.2]octane monochloride monotosylate
	GDC14	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(tetradecyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate
	GDC12	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(dodecyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC12):
	GDC8	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(octyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC8):
	GDC4	1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(butyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate

Compound	Melting Point (˚C)	$[\alpha]^{25}$
GDMAP	108-110	+63.0
GMIM	Hygroscopic	+63.5
GP	60-69	+69.8
GDBz	133-135	+39.2
GDIsp	135-138	+46.6
GDMPr	127-131	+44.0
GDC18	174-176	+25.3
GDC16	124-128	+42.9
GDC14	128-130	+33.9
GDC12	130-132	+29.3
GDC8	164-166	+42.8
GDC4	102-107	+22.5

Table 34. Melting points and specific rotations of glucopyranoside derivatives.

The structures of the salts were confirmed using ^{1}H and ^{13} NMR analysis and elemental analysis. The elemental analysis data obtained were in accord with the calculated values of the hydrated species. Presented in Figures 76 and 77 is the ^{1}H and ^{13}C NMR spectra of GDC8. In the ^{1}H spectrum a triplet between 0.74 ppm – 0.77 ppm (J = 6.4 Hz, 6.8 Hz) integrates for three protons and corresponds to the methyl protons on C1 at the end of the alkyl chain. The broad multiplet found between 1.73-1.24 ppm integrates for ten protons and are indicative on the protons found on the alkyl chain found on C2 to C6. The broad signal at 1.62-1.72 ppm integrates for two protons, and are indicative of those found on C7. The singlet found

at 2.29 ppm integrates for three protons and represents the methyl group found on the tosylate anion. The signals for the protons on DABCO, the glucopyranoside ring and on C8 overlap in the region between 3.30 – 3.79. Twenty four proton are represented by the signals in this region. The doublet found between 7.26 and 7.28 ppm (J = 8 Hz) represent the two protons ortho to the methyl group on the tosylate anion. The doublet between 7.58 – 7.60 ppm (J = 8 Hz) represent the protons meta to the methyl group on the tosylate anion. As expected, twenty-two signals appear in the ^{13}C NMR spectrum.

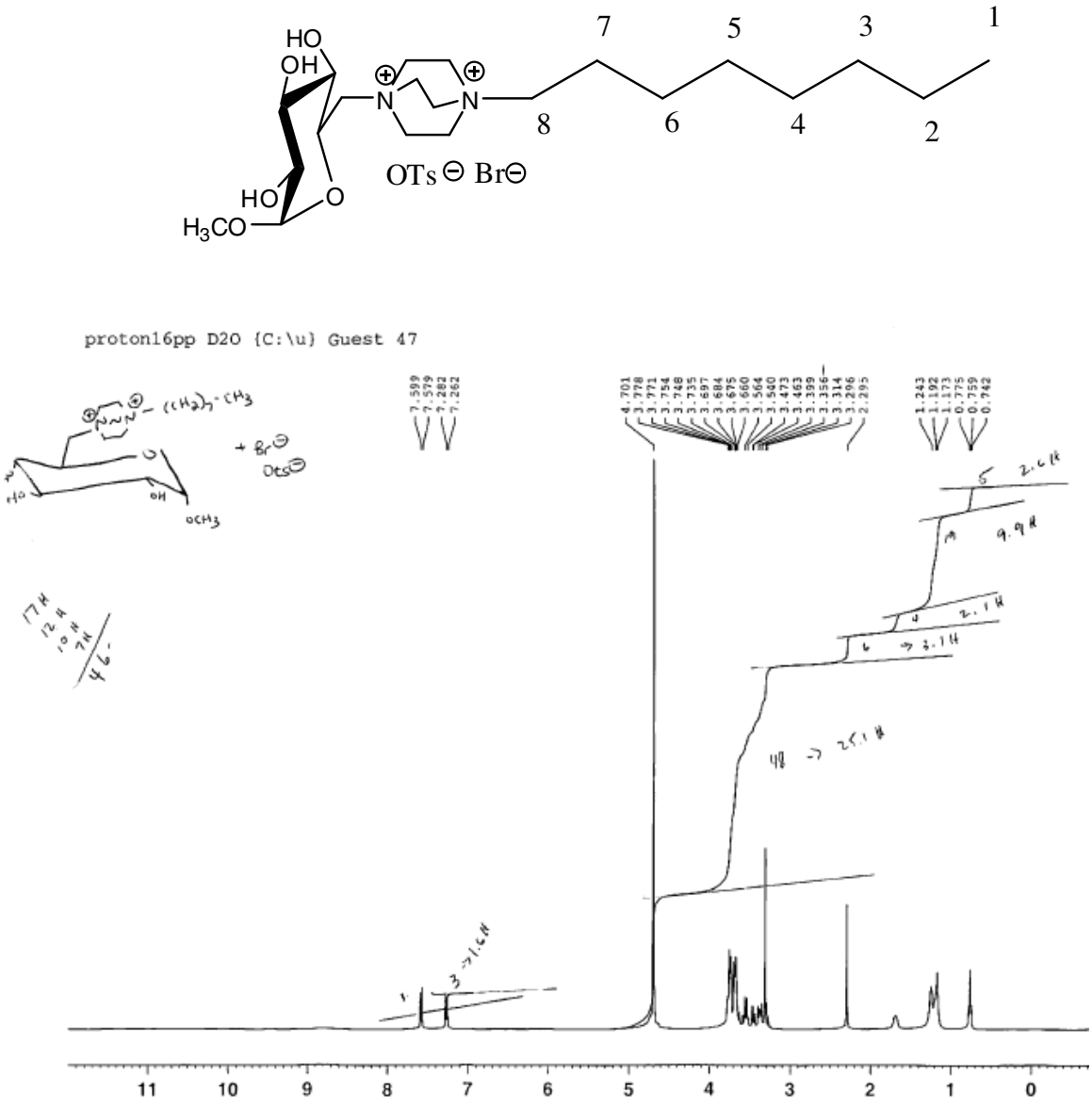


Figure 76. ^{1}H NMR spectrum of GDC8 (400 MHz, D_2O).

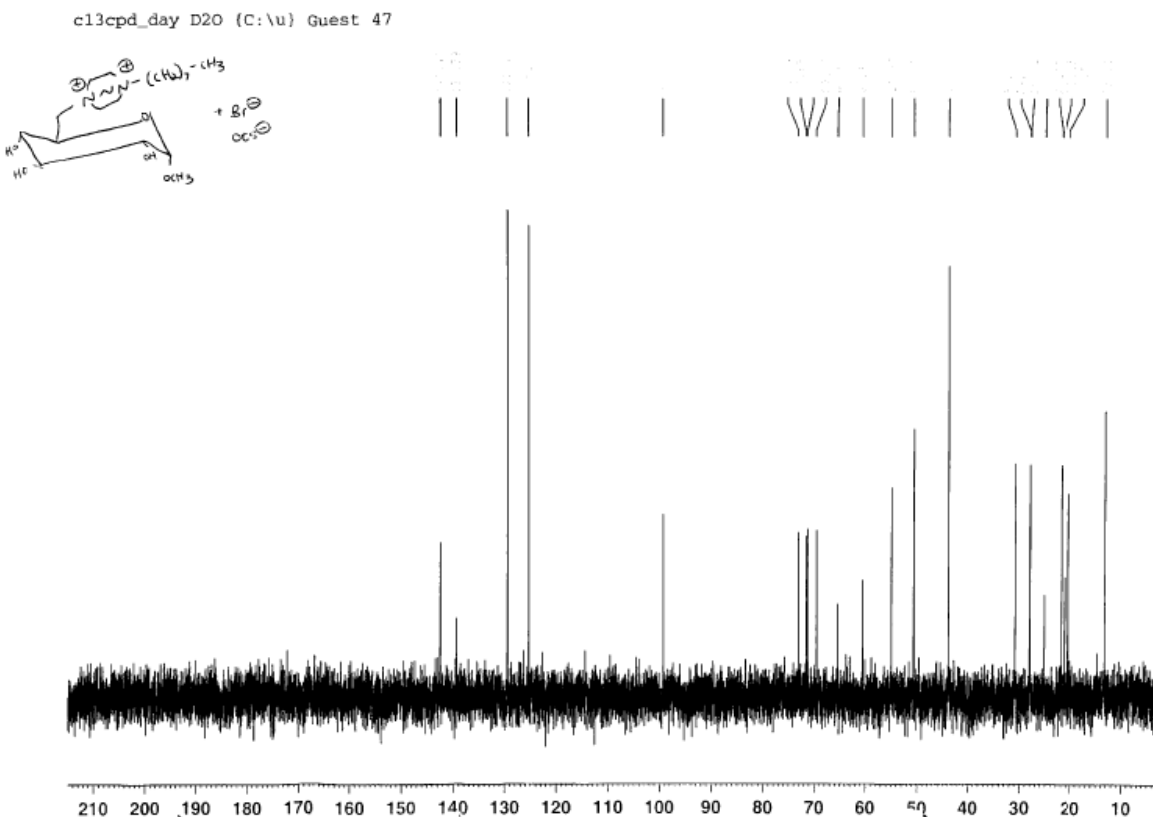


Figure 77. ^{13}C NMR spectrum of GDC8 (100 MHz, D_2O).

Compounds GDC18, GDC16, GDC14, GDC12 were insoluble in ether, ethyl acetate, methylene chloride, hexanes, acetonitrile and toluene. Only GDC18 has been found to gelate water with a w/v of 5 %. This surfactant also gels ethanol (6.7% w/v).

Table 35. Results of gelation studies of glucopyranoside derivatives: G (gel), S(soluable), I(insoluable) and X (not tested).

Code	Water	Ethanol	N-Butanol
GDC18	G	G	S
GDC16	I	S	X
GDC14	S	S	X
GDC12	S	S	X
GDBz	S	I	X
GDIPr	S	I	X

The gels made with these polycationic carbohydrate surfactants and the salts themselves are expected to have antimicrobial properties. Kirk, *et al.* synthesized carbohydrate-based cationic surfactants with the goal of developing new antimicrobial agents for topical disinfection [140]. These materials, in particular the salt in shown in Figure 78, were found to exhibit antimicrobial activity against Gram positive and Gram negative bacteria and one fungal strain. The surfactants also showed good compatibility with anionic detergents. (Anionic surfactants can inhibit the action of cationic surfactants by forming insoluble complexes.)

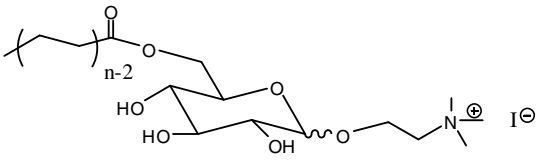


Figure 78. Carbohydrate-based antimicrobial agent developed by Kirk *et al* [40].

The research group of P. Quagliotto studied the surface and antimicrobial properties of glucopyridinium amphiphiles [141]. When compared to 1-alkyl-4-alkyl pyridinium compounds, these amphiphiles showed moderate antibacterial activity. This same group later developed glucocationic surfactants with the goal of developing materials that could be used for gene transfection [142].

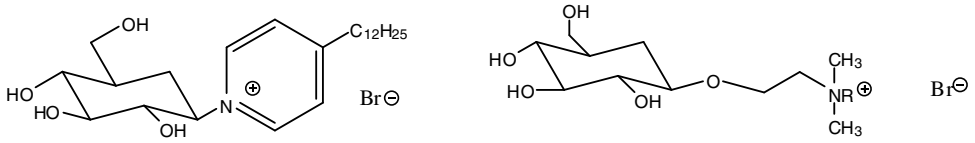


Figure 79. Glucocationic surfactants developed by Quagliotto *et. al* [141, 142].

The antimicrobial activity of the gels was evaluated against *S. aureus*. The gels were tested by adding a few microliters (25 μL) of the gel and bacteria to Luria-Bertani (LB) broth. The samples were incubated overnight and their absorbances recorded. The results of the antimicrobial activity of the gels tested are shown in Table 36. These results represent the growth of bacteria in comparison to a blank. There is almost complete kill of bacteria in the presence of these agents. The bacterial survival rates in the presence of these materials were 2% or less. Perhaps complete kill would have been

achieved if a greater concentration of the gel was used or if the samples were incubated for longer periods of time. The surfactant MnDC16 has been patented for use as an antibacterial foam. This particular surfactant formed the most stable gel, so we believe that it will form a stable foam. Also, the starting materials for MnDC16 are less expensive than those of the other gelators.

Table 36. Results of antibacterial studies of gels with *S. aureus*. These results represent the growth of bacteria in comparison to a blank.

Code	Solvent	% Survival of S. Aureus
MnDC18	Water	1%
MnDC18	Ethanol	1%
MnDC16	Water	2%
MnDC16	Ethanol	2%
MnDC16	n-Butanol	2%
GDC18	Water	1%
GDC18	Ethanol	1%

E. Polycationic Dendrimers

Polymeric drugs, in particular those made from dendrimers, can exhibit higher biological activities as compared to their monomeric counterparts. This is due to the high concentration of functional groups that can be contained at the surface of (and within) the dendrimer. In addition to increased activity, other potential benefits of polymeric drug systems include reduced toxicity, localization in specific organs, greater duration of action and improved patience compliance [99, 143].

Unlike most polymers, the size, shape, topology and surface chemistry of dendrimers can be controlled and tailored for a particular application [144]. Mannose functionalized PAMAM dendrimers were modified as shown in Figure 80 in order to incorporate quaternary ammonium salts onto the surface. The primary hydroxyl units of the mannose units were converted to tosylate and this was followed by the addition the antimicrobial precursor (DC12 or DC16) to generate the polycationic dendrimer.

As previously indicated quaternary ammonium surfactants are often used as antimicrobial agents. The mode of action that has been suggested for their activity is that the lipophilic portion of the surfactant is adsorbed into the bacterial cell surface and diffuses though the cell wall. The charged portion of the surfactant then interacts with the cytoplasmic membrane,

causing the disruption of the membrane followed by the release of potassium ions and the loss of the cell contents. The result is cell death [79].

The goal of this study was to develop materials that could be used as antimicrobials. Dendrimeric antibacterial agents can potentially deliver a lethal blow to bacteria due to the increased local concentration of active agents at the surface.

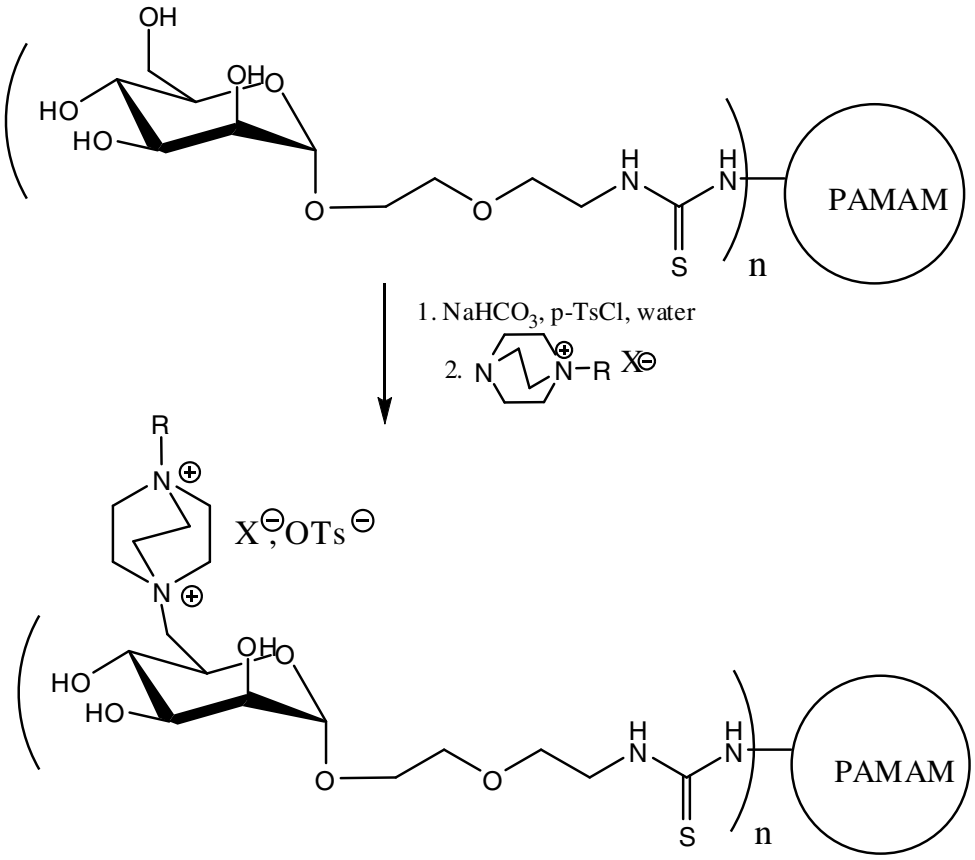


Figure 80. Modification of mannose-functionalized PAMAM dendrimers.

A series of six dendrimers were prepared (see Table 37) and were obtained as pale yellow solids. Their size and number of mannose units contained in each dendrimer are indicated. The dendrimers were

characterized using ^{1}H NMR. The smallest dendrimer Den2C12 was further characterized using FTIR. The IR spectra showed peaks that were indicative of C-H saturation, most notably C-H 2919.1. An attempt to collect MALDI TOF data on the smallest dendrimer failed. As noted with other polycationic species [145] extensive fragmentation occurs without seeing any molecular ion.

Table 37. Modified mannose functionalized PAMAM dendrimers

Dendrimer	Generation	Alkyl Chain Length	Anions	# of Sugar Sites	Theoretical MW
Den2C12	2	12	Br, OTs	15	15865
Den2C16	2	16	Cl, OTs	15	16045
Den3C12	3	12	Br, OTs	30	32230
Den3C16	3	16	Cl, OTs	30	32590
Den4C12	4	12	Br, OTs	45	53995
Den4C16	4	16	Cl, OTs	45	54535

The biological activity of the dendrimers were tested using *S. aureus*, which is a Gram positive bacterium and *E.coli* and *P. aeruginosa*, which are Gram negative bacteria. Aqueous dendrimer solutions were combined with the bacteria and added to Luria-Bertani broth. The solutions were incubated overnight and the growth of bacteria was noted by measuring the absorbance of the dendrimer/bacteria solutions at 600nm. The results of the antibacterial

tests are revealed in Table 38. The numbers represent that percentage of bacteria that survived in comparison to a blank.

Table 38. Results of antimicrobial studies of the functionalized dendrimers. Extent of Growth in Percantage of Bacteria after incubation with bacteria as compared to a blank.

Dendrimer	*E. Coli*	*P. Aeroginosa*	*S. Aureus*
Den2C12	1	>100	3
Den2C16	3	4	2
Den3C12	97	>100	1
Den3C16			
Den4C12	1	>100	1
Den4C16	2	33	1

The data in Table 38 show that all dendrimers exhibited excellent antibacterial activity against *S. aureus*. This is most likely due to the less complex membrane structure of *S. aureus*. Gram positive bacteria have a cell wall which covers its' cell membrane. Gram negeative bacteria have additional layers making up the cell wall, which then covers an inner cell membrane.

The research group of Chen, *et al.* studied the structure-activity relationships of a series of quaternary ammonium functionalized poly(propylene imine) dendrimers (Generations 1 – 5) using *E. coli* [110]. The effect of generation (overall size of the dendrimer), length of the alkyl

chain and counter ion effects were noted. A parabolic relationship was found for the effect of generation on antimicrobial activity. The biological activity was shown to be in this order,

Generation 5>Generation4>Generation1>Generation2>Generation3. Generation 5 was the most active. (All the alkyl chain lengths were the same). The most potent alkyl chain length was 10 carbons [110].

Our results with *E. coli* correlates well with Chen's studies. Our largest dendrimers Den4C12 and Den4C16 show excellent activity against *E. coli* with bacterial survival rates of 1% and 2% respectively. The large concentration of quaternary surfactants on the surface of these dendrimers may be responsible for this activity. Den2C12 and Den2C16, the smallest denderimers also show excellent biocidal activity with bacterial survival rates of 1% and 2% respectively. There is almost complete kill of *E. coli* in the presence of these dendrimers. The activity of Den3C12 against *E. coli* is poor. The bacterial survival rate in the presence of this dendrimer is 97%. It appears that the concentration of active groups at the surface is not enough to compensate for the size of this dendrimer. In this case the effect of length of the alkyl chain does not appear to play a significant role.

Alkyl chain length does appear to play a role in biological activity against *P. aeruoginosa* which happens to be most difficult bacteria to kill in

our study. Den2C12, Den3C12 and Den4C12 with alkyl chains of twelve carbons, have no effect on *Pseudomonas*. Bacteria exhibited survival rates of greater than 100% (no killing). Den2C16 shows excellent antimicrobial activity, while Den4C16 shows moderate activity (with a bacterial survival rate of 4% and 33% respectively). Both dendrimers contain alkyl chains of sixteen carbons.

F. Polycationic Polyester Surfaces

As previously indicated, this laboratory has been involved in the modification of porous surfaces such as cotton, paper, wool, and silk. These materials were successfully made antimicrobial and exhibited excellent activities against Gram negative and Gram positive bacteria. More recently, our focus has been on the modification of synthetic surfaces such as polyester, nylon and polyvinylchloride (PVC). Polyester fabric has been successfully modified in a fashion related to the manner in which previously described surfaces were. The overall process is shown in Figure 81. The key step in this process is the generation of active sites on the surface. This was accomplished through the controlled reduction of polyester with sodium borohydride in absolute ethanol. This process generates two primary hydroxyl sites; one benzylic and the other aliphatic. After quenching with aqueous ammonium chloride, the fabric was washed with distilled water and

dried. An alternative to this step would be to carefully hydrolyze the surface with a strong base such as sodium hydroxide [146]. The fabric is then treated with *p*-toluenesulfonyl chloride in aqueous sodium bicarbonate. In Figure 81, tosylation is shown only on the aliphatic site but it could also occur at the benzylic alcohol. The fabric was washed again and dried. Then the final step is treatment with DC16, which binds covalently to the fabric at the activated sites.

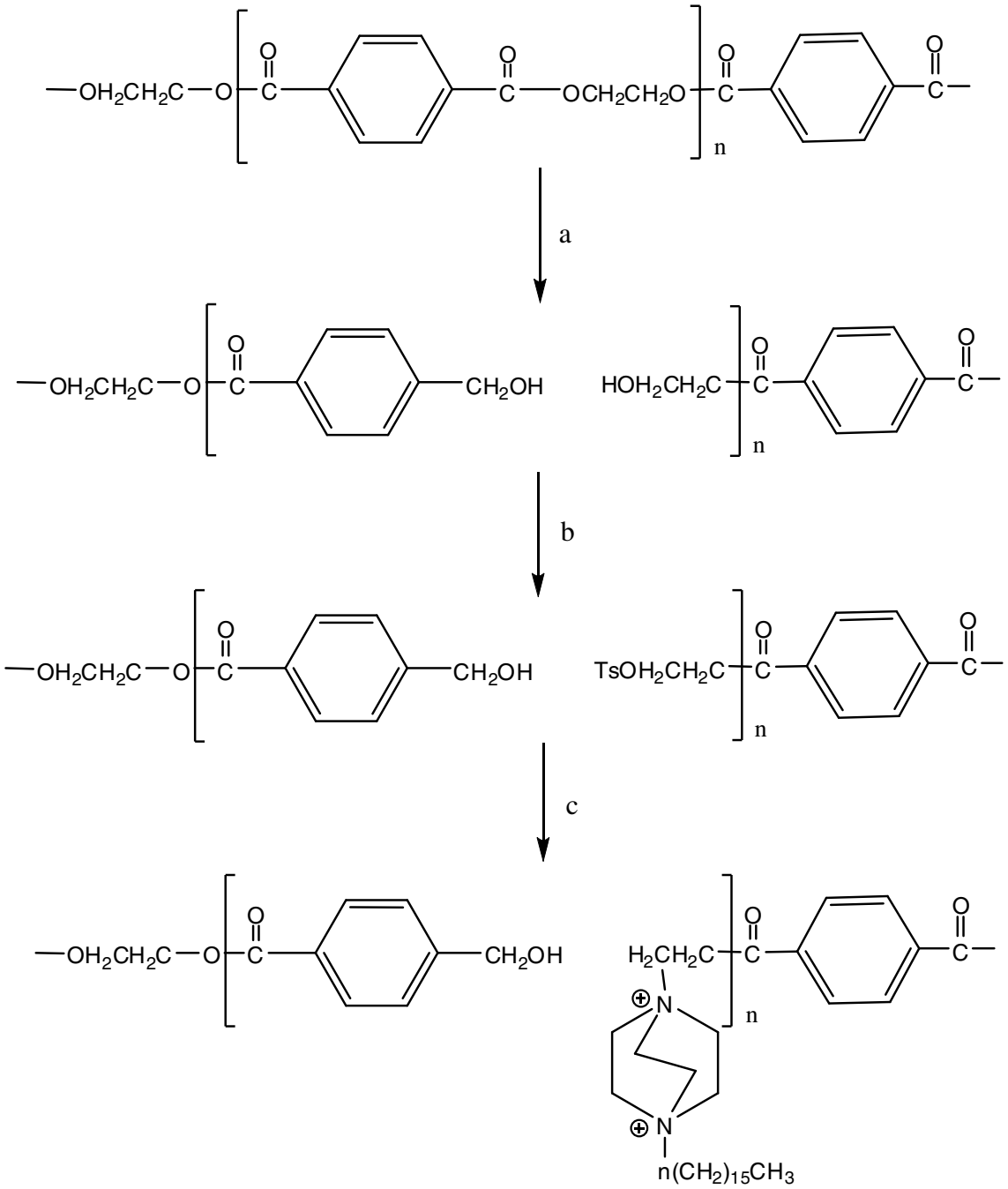


Figure 81. Modification of polyester fabric.a) $NaBH_4$, absolute ethanol. b) p-TsCl, aq. $NaHCO_3$. c) DC16, ethanol.

An attempt was made to characterize the surface using gas chromatography (GC). (Polyester fabrics, modified and unmodified, were degraded using sodium borohydride in ethanol at high temperatures. The

reaction solutions were collected and injected into the gas chromatogram.) However the results were inconclusive.

The surfaces were characterized by dipping samples of treated and untreated samples into a 1% flourescein salt solution [147]. Fluorescein dye can bind to quaternary ammonium salts [148]. The cloth samples were washed with copious amounts of distilled water, and the dye was desorbed by shaking the samples for about ten minutes in 0.25% cetyltrimethylammonium bromide solution. The absorbances of the resulting solutions were measured at 501 nm. A peak detected at this wavelength not only indicates the presence of quaternary ammonium salts bonded to the surface of the fabric but can also be used to calculate the concentration of the surfactant per area of fabric. This method was used by Klibanov, *et al*. [127, 128, 148] to determine the surface density of quaternary amino groups bound to modified surfaces. It is interesting to note that the treated cloth samples which were originally white retained a pink color even after treatment with cetyltrimethylammonium bromide solution, while the unmodified fabric samples went back to white after treatment with the same solution.

An attempt was also made to characterize the surfaces using FTIR. But there was no noticeable difference between the spectra of the modified surface and that of the unmodified surface.

The biological activity of the polyester surfaces was tested against *E. coli, S. aureus, Saccharomyces cerevisiae* (a fungus) and spores. A polyester sample (treated and untreated) was placed a Luria-Bertani agar plate. The bacteria were added on top of the fabric and the plates were incubated overnight at 37 ˚C. The fabric was removed from the plate and placed in Luria-Bertani broth and incubated overnight in a shaking water bath. The absorbance of the bacterial solution was recorded at 600 nm to determine the growth of bacteria.

The modified polyester fabrics were highly active against *S. aureus and S. cerevisiae.* With *S. aureus*, there was 100% kill and there was only 4% growth seen with *S. cerevisiae.* We did achieve 100% kill with *E. coli,* but longer treatment times and/or higher temperatures during reduction with sodium borohydride is required. The same trend was observed with spores and in the presence of the modified fabric the growth of spores was reduced to 3%.

We have shown qualitatively that the antimicrobial precursor DC16 can be bonded covalently to polyester fabrics and with enough agent bound

to the fabrics, these material can exhibit excellent antimicrobial activity against a variety of Gram positive and Gram negative bacteria and fungi.

CONCLUSION

The successful synthesis of various types of quaternary ammonium salts has been accomplished. Ammonium salts based on racemic and chiral 3-chloro-1, 2-propanediol has been developed as ionic liquids which can potentially be used as solvents in organic synthesis. In addition, some of these salts, the dicationic strings, were found to be potential selective anion receptors. These salts were made using amines such as DABCO, DMAP, 1-methylpyrrolidine and α, ω-dimethylamines and a variety of anions which included chloride, phosphate, bis(trifluoromethylsulfonyl)imide, dicyanamides and diphenyl phosphates. Most of the salts that were liquid at room temperature were of the pyrrolidinium type. The anion that gave ionic liquids with the lowest melting points was the dicyanamide. Also, a new family of ionic liquids, the dipheyl phosphates was developed. The ionic liquids usually displayed a glass transiton and a melting point. The chiral derivatives that were developed ((R) - (-)-DMAP-Cl , (S)-(+)-DMAP-Cl and (R)-(-)-DMAP-NTf_2) had significantly lower melting points than their racemic counterparts. The melting points of the salts were determined using either a melting point apparatus or by differential scanning calorimetry. The degradation temperatures of some of the salts were noted and obtained using thermogravimetric analysis. The structures of these salts were confirmed

using ^{1}H and ^{13}C NMR analysis, elemental analysis, and for the S6 salts mass spectroscopy. The crystal structure for one salt (P-Cl) was obtained.

Quaternary ammonium surfactants were also developed as antimicrobial agents and applied to surfaces, rendering those surfaces antibacterial. Ammonium surfactants based on D-mannitol and α-D-methyl glucopyranoside were developed as small molecule gelators. Gels developed were found to be active against the bacterium *S. aureus.*

Polycationic mannose-functionalized dendrimers were also developed as limited surfaces and were found active against Gram positive and Gram negative bacteria such as *S. aureus, E. coli* and *P. aeruginosa.* Attachment of the surfactant to the surface was confirmed using ^{1}H NMR analysis and to a limited extent FTIR.

Finally the modification of polyester fabric which included the covalent attachment of the ammonium surfactant DC16 to the surface, rendering it antibacterial, was achieved. This porous surface was found active against *E. coli* and *S. aureus.* A method using 1% fluorescien solution was used to confirm qualitatively that the quaternary ammonium surfactant was covalently bound to the surface.

FUTURE WORK

Chiral Ionic Liquid

While the synthesis of a series of racemic ionic liquids based on 3-chloro-1, 2-propanediol has been accomplished, the next step is the continuation of the synthesis of the chiral forms. One chiral ionic liquid (R)-(-)-DMAP-NTf_2 has been made. The salt is a viscous liquid at room temperature, where as the racemic DMAP-NTf_2 is a solid at room temperature. It was mentioned previously that these liquids might be useful solvents for organic reactions such at the Diels-Alder or Baylis-Hillman reaction that have enhanced reaction rates in polar solvents. It would be interesting to see the effects of these propanediol ionic liquids on these types of reactions. The ionic liquids that might best be suited for these reactions would be the ones that displayed an amphiphilic nature such DMAP-NTf_2, S6-NTF_2 or even P-DPP. The research group of Dyson found that ionic liquids (such as the hydrophobic sulfonylimides) that were able to form a homogenous phase with the reactants in Diels-Alder reactions resulted in higher reaction rates and selectivity for the endo product [38]. This group also found that ionic liquids that have hydrogen bond donors separated from the center of charge enhanced selectivity of the endo product. The salts that have been made by this laboratory have two hydroxyl groups both of which

can serve as hydrogen bond donors. Using the liquids that we have developed, endo selectivity should be observed and there may be enhanced reaction rates if used for Diels-Alder reactions. Based on the present literature, it would appear that chiral ionic liquids have very little effect on enantioselectivity of Diels-Alder reactions. Thus, little enantioselectivity is expected from the salts developed by this laboratory.

Better success has been achieved with chiral ionic liquids and Baylis-Hillman reactions. Though modest, enantioselectivities were achieved with Pegot's ephedrine ionic liquid [45]. This group noted the necessity of the hydroxyl group on the cation to transfer chirality. Based on this study, it is more likely that enantioselectivity would be observed using the propanediol ionic liquids that we have developed for Baylis-Hillman reactions. Baylis-Hillman reactions should be tried in the chiral ionic liquids.

Antimicrobial Surfaces

A series of quaternary ammonium surfactants has been developed using α –D-methyl glucopyranoside and D-mannitol, some of which have been found to gelate water and alcohols. Gelation is controlled by non-covalent forces such as hydrogen-bonding, Van der Waals interactions and π-π stacking. The gels that have been developed can be studied using spectroscopy techniques such NMR or IR, microscopy, and x-ray diffraction

to gain insight into what forces are driving the ability of the surfactants to aggregate. The anions of these salts are halides (chloride or bromide) and tosylates. The tosylates could be removed using an anion exchange resin and the resulting salts could be tested to see if gelation would still occur. If gelation does not occur, this may be an indication that π-π stacking is involved in the ability of the surfactants to gel solvents.

An attempt could be made to make asymmetric D-mannitol derivatives. This could be accomplished by adding a protecting group to one of the terminal hydroxyl groups. The ability of these materials to gelate solvents and depending on the length of the alkyl chains incorporated, the biological activities of these materials could be studied.

When we started with this project the goal was to make ionic liquids. I believe this is still feasible but the number of the hydroxyl groups found on the sugar derivatives should be reduced, making them less hydrophilic. (The small glucopyranoside and mannitol derivatives such as GP, MnP, GMIM and MnMIM were quite hydrophilic.) This can be accomplished through the use of protecting groups, in particular ether protecting groups. The incorporation of ethers into the cations of ionic liquids has been found to lower melting points and to reduce viscosities [18].

Polycationic Dendrimers

Mannose functionalized PAMAM dendrimers were modified using either DC16 or DC12. These dendrimers showed significant biological activity. All the dendrimers tested, (five in all) exhibited excellent activity against the Gram positive bacteria *S. aureus*. Four of the dendrimers were effective against the Gram negative bacterium *E.coli*. Only two dendrimers showed biological activity against *P. aeruginosa*, which is also a Gram negative bacterium. The dendrimers that did not do well with *E. coli* and *P. aeruginosa* all contain DC12. A combination of DC16 and DC12 (a 1:1 ratio) could be added to those dendrimers. This could result in better biological activity against Gram negative bacteria. It would also be interesting to see if the biological activity of the dendrimers that exhibited good activity against all the bacteria tested would decrease.

Antimicrobial Fabrics

Past research has included a number of attempts to modify synthetic surfaces such as PVC, nylon and polyester. Polyester fabric was successfully modified using the antimicrobial agent DC16. The surface was characterized using 1% fluorescein solution and we were able to confirm qualitatively that DC16 was covalently bonded to the surface. We also attempted to use IR and GC, but with little success. We could try performing

an IR experiment on the fluorescein treated material or UV experiments on the modified fabrics to confirm that the antimicrobial agent is covalently bonded to the surface.

Polyester could also be treated with DC12 or a combination of DC16 and DC12. The biological activity of those polyester surfaces could be compared to those surfaces treated with DC16. Using a combination of antimicrobial agents with different chain lengths could generate surfaces that could show antimicrobial activity on a broad range of bacteria, fungi and yeast.

Chapter 3

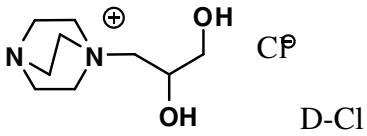
EXPERIMENTAL

A. Reagents and Instrumentation

The reagents used for synthesis and purification were of commercial quality and used without purification. NMR spectra were obtained using the Bruker 400 MHz instrument. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY. Optical rotation data on ionic liquids and carbohydrate derivatives were obtained using the Rudolph research analytical Autopol III, automatic polarimeter. Infrared spectra data on dendrimer and polyester samples were obtained using the Shimadzu FTIR 8400S spectrophotometer at Queensborough Community College. The gas chromatography data on polyester samples was obtained using the Hewlett-Packard 5890 GC/MS spectrophotometer at Pace University. UV absorbance data were obtained using the Varian Cary 5000 UV/VIS spectrometer. DSC data was collected using the DSC 100 made by TA Instruments and TGA data was collected using the TGA 500 made by TA Instruments. Both instruments were used at Brookhaven National Laboratory. The x-ray crystal structure was obtained by Dr. David Szalda, using the Enraf Nonius CAD-4 diffractometer with Cu radiation at Brookhaven National Laboratory.

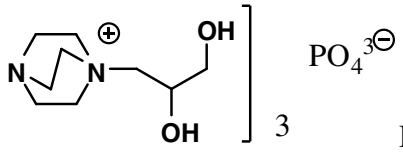
Silver dicyanamide was synthesized as needed by the reaction of one equivalent of sodium dicyanamide with silver nitrate in distilled water. The reaction mixture was stirred for five hours. The resulting white solid was filtered by gravity and washed a few times with distilled water.

B. Preparation of Ionic Liquids



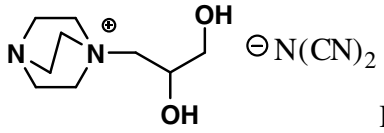
D-Cl

Preparation of 1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane chloride (D-Cl): Diazobicyclo-[2.2.2]-octane (9.98 g, 0.089 mole) was dissolved in ethyl acetate (65 mL). To this 3-chloro-1, 2-propanediol (9.68 g, 0.088 mole) was added. The reaction mixture is stirred overnight. The solvent was evaporated under reduced pressure. The resulting solid was stirred with acetonitrile (50 mL) for twenty-four hours. The solid was filtered, washed with diethyl ether (3 x 30mL) and dried under high vacuum. The product is a white solid (14.3 g, 73%). Calculated for $C_9H_{19}N_2O_2Cl$: C 48.54%, H 8.60 %, N 12.58% Found: C 48.14%, H 8.36%, N 12.40%. NMR (δ, D2O) ^{1}H: 3.09 (t, 6 H, J = 7.6), 3.28 (m, 2 H), 3.40-3.52 (m, 8 H), 4.23 – 4.29 (br m, 1 H, J = 2.4 and 3.2 Hz). ^{13}C: 44.1, 53.2, 63.6, 65.2, 66.6.



D-IP

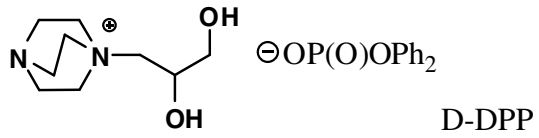
Preparation of 1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane phosphate (D-IP): D-Cl (7.62 g, 0.034 mole) was dissolved in methanol (40 mL). To this an excess of 85% phosphoric acid (.60 g) was added. The reaction mixture is stirred overnight. A white precipitate was filtered off and the solvent evaporated. The resulting pale yellow solid (3.92 g, 41%) is dried in a vacuum oven. Calculated for $C_{27}H_{57}N_6O_{10}P*3H_2O$: C 45.62%, H 8.93%, N 11.82% Found: C 45.70%, H 8.98%, N 11.62%. NMR (δ, D_2O) - ^{1}H: 3.11 (t, J = 7.2 Hz and 7.6 Hz, 6H), 3.24 – 3.52 (m, 10 H), 4.26 (q, J = 2.8 Hz, 1 H). ^{13}C: 44.1, 53.2, 63.6, 65.2, 66.6. ^{31}P: s, 0.07.



D-DCA

Preparation of 1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane dicyanamide (D-DCA): D-Cl (8.20 g, 0.037 mole) was dissolved in distilled water. To this a charge equivalent of silver dicyanamide was added. The reaction flask is covered with aluminum foil and the reaction mixture is stirred overnight. The resulting solid is filtered by gravity and the filtrate is washed with diethyl ether (3 x 30 mL), hexanes (3 x 30 mL) and ethyl

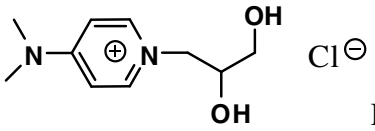
acetate (3 x 30 mL). The water is then evaporated and the resulting viscous liquid is dried in the vacuum oven. The product is a viscous brown liquid (7.51 g, 80%) at room temperature. NMR (δ, D_2O) – ^{1}H: 3.10 – 3.14 (t, J = 7.2 and 7.6 Hz, 6H), 3.23 – 3.53 (m, 10 H), 4.21 – 4.29 (br m, J = 2.4 and 2.8 Hz) 1H. ^{13}C: 44.2, 53.3, 63.6, 65.2, 66.7, 120.0.



D-DPP

Preparation of 1-(2,3-dihydroxypropyl)-1-azonia-4-azabicyclo[2.2.2]octane diphenyl phospate (D-DPP): D-Cl (2.1 g, 0.009 mole) was dissolved in absolute ethanol. To this a charge equivalent of diphenyl phosphate (2.4 g, 0.009 mole) and potassium hydroxide (0.5 g, 0.009) is added. The reaction mixture is stirred for about 3 days. The resulting solid (potassium chloride) is filtered by gravity. The solvent of the filtrate is evaporated under vacuum, leaving a viscous liquid, which later solidified. The solid was recrystallized from absolute ethanol. The white solid (1.5g, 38%) was dried under high vacuum. Calculated for $C_{21}H_{29}O_6N_2P$: C 57.87 % H 6.71% N 6.43% Found: C 57.56% H 6.84% N 6.42%. NMR (δ, D_2O) - ^{1}H: 3.04 – 3.07(t, J = 7.6 Hz) 6H), 3.21 – 3.43 (m, 10H), 4.17 – 4.25 (br m, 1H), 7.07 – 7.10 (m, J = 1.2 Hz, 3.6 Hz, and 8.4 Hz 6H), 7.25 – 7.28 (m, J = 7.6 Hz and 8 Hz, 4H). ^{13}C:

44.1, 53.2, 63.5, 65.1, 66.6, 120.1, 120.2, 124.5, 129.8, 151.5, 151.6. ^{31}P: s, -8.74.



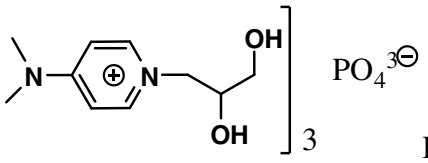
DMAP-Cl

Preparation of *N*-(2, 3-dihydroxypropyl)-4-(dimethylamino) pyridinium chloride (DMAP-Cl): 4-(dimethylamino) pyridine (21.78 g, 0.18 mole) was dissolved in acetonitrile (150 mL). To this was added 3-chloro-1, 2-propanediol (19.71 g, 0.18 mole) and the reaction mixture was stirred and refluxed overnight. This resulted in a precipitate which was filtered by gravity and washed with ethyl acetate (3 x 30 mL) and ether (3 x 30 mL). The solid was also washed with hexanes (3 x 30 mL) and dried under high vacuum. The resulting product is a white solid (40.78 g, 97%). Calculated for $C_{10}H_{17}N_2O_2Cl \bullet H_2O$: C 47.90 % H 7.64 % N 4.42 %. Found C 47.83 % H 7.69 % N 11.08 %. NMR (δ, D_2O) -^{1}H: 3.06, (s, 6 H); 3.44-3.54 (m, 2H, J = 2.8Hz and 4.4 Hz), 3.87 – 3.97 (m, 2H, J = 2.0 Hz, 2.4 Hz and 8.8 Hz), 4.13 – 4.22(m, 1H), 6.73 (d, 2 H, J = 8 Hz), 7.84 (d, 2 H, J= 7.6 Hz). ^{13}C: 39.4, 59.4, 62.4, 70.6, 107.4, 141.9, 156.4.

Preparation of (R)-(-) -*N*-(2, 3-dihydroxypropyl)-4-(dimethylamino) pyridinium chloride ((R)-(-)-DMAP-Cl): This salt was made in a similar fashion to DMAP-Cl described above. The alkyl halide (R)-(-)-3-chloro-1,2-

propanediol was used. The product was obtained with a yield of 96%. NMR (δ, D_2O) -^{1}H: 3.07(s, 6 H), 3.48 – 3.51 (m, 2 H), 3.92 – 3.95 (m, 2 H), 4.17 (br m, 1H), 6.75 (d, J = 8 Hz, 2H), 7.84 (d, J = 8 Hz, 2 H). ^{13}C:39.3, 59.3, 62.3, 70.5, 107.3, 141.8, 156.4.

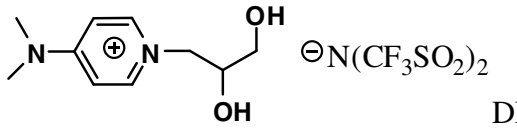
Preparation of (S)-(+)-*N*-(2, 3-dihydroxypropyl)-4-(dimethylamino) pyridinium chloride ((S)-(+)-DMAP-Cl): This salt was made in a similar fashion to DMAP-Cl described above. The alkyl halide (S)-(-)-3-chloro-1,2-propanediol was used. The product was obtained with a yield of 95%. NMR (δ, D_2O) -^{1}H: 3.07 (s, 6H), 3.48 – 3.51 (m, 2 H), 3.92 – 3.95 (m, 2 H), 4.17 – 4.20 (br m, 1H), 6.75 (d, J = 8 Hz, 2H), 7.84 (d, J = 8 Hz, 2H).



DMAP-IP

Preparation of *N*-(2,3-dihydroxypropy)-4-(dimethylamino) pyridinium phosphate (DMAP-IP): DMAP-Cl (2.08 g, 0.009 mole) was dissolved in methanol (35 mL). To this was added a charge equivalent plus excess of 98% phosphoric acid (.38 g, 0.004 mole). The reaction mixture was stirred overnight. The solvent was evaporated under high vacuum. The resulting white solid (1.94 g, 74%) was recrystallized from absolute ethanol and dried under high vacuum. Calculated for $C_{30}H_{51}O_{10}N_6P$: C 52.47% H 7.49 % N

12.24 %. Found: C 52.31 % H 7.63 % N 12.04 %. NMR (δ, D_2O) -^{1}H: 3.10 (s, 6 H), 3.52 - 3.54 (m, 2H), 3.95 – 4.00 (m, 2H), 4.20 – 4.23 (m, 1H), 6.78 (d, J = 7.2 Hz, 2 H), 7.88 (d, J = 7.2 Hz, 2 H). ^{13}C: 39.3, 59.3, 62.4, 70.5, 107.3, 141.9, 156.4. ^{31}P: s, 0.10.

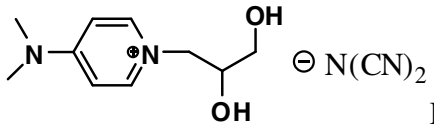


DMAP-NTf_2

Preparation of *N*-(2,3-dihydroxypropy)-4-(dimethylamino) pyridinium bis(trifluoromethane)sulfonylimide (DMAP-NTf_2): DMAP-Cl (6.0 g, 0.025 mole) was dissolved in distilled water. To this was added a charge equivalent of bis(trifluoromethane)sulfonylimide lithium salt (7.25 g, 0.025 mole). The reaction mixture was stirred overnight. The solvent was carefully decanted and the resulting liquid washed with water until there was no detectable halide. The resulting liquid (3.54 g, 30%) was dried under high vacuum. Calculated for $C_{12}H_{17}N_3O_6S_2F_6$: C 30.19%, H 3.59%, N 8.80%. Found: C 30.36%, H 3.61%, N 8.83%. NMR (δ, D_2O) -^{1}H: 3.124 (s, 6 H) 3.53-3.56 (m, 2H), 3.97-4.00 (m, 2H), 4.22 – 4.25 (m, 1H), 6.795 (d, J = 7.6 Hz, 2H), 7.890 (d, J = 7.6 Hz, 2 H). ^{13}C: 39.3, 59.3, 62.4, 70.6, 107.4, 114.5, 117.6, 120.8, 124.0, 141.9, 156.5.

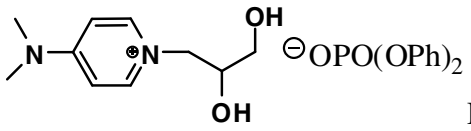
Preparation of (R)-(-)-*N*-(2,3-dihydroxypropy)-4-(dimethylamino) pyridinium bis(trifluoromethane)sulfonylimide ((R)-(-)-DMAP-NTf_2): This

salt was prepared in a fashion similar to DMAP-NTf_2. The percent yield was 50%. NMR (δ, DMSO-D_6) -^{1}H: 3.14 (s, 6H), 3.25 – 3.30 (dd, J = 4.4 Hz and 6.4 Hz), 3.42-3.46 (dd, J = 4.8 Hz, 5.2 Hz, and 6 Hz), 3.70-3.80 (br m, 1 H), 4.04-4.09 (dd, J = 5.6 Hz and 8 Hz), 4.30 – 4.34 (dd, J = 2.8 Hz and 10.8 Hz), 4.95 (br, 1 H), 5.30 (br, 1 H), 7.00 (d, J = 7.6 Hz, 2 H), 8.17 (d, J = 7.6 Hz, 2H).



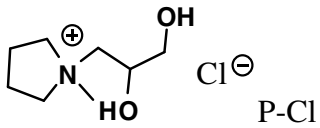
DMAP-DCA

Preparation of *N*-(2,3-dihydroxypropy)-4-(dimethylamino) pyridinium dicyanamide (DMAP-DCA): DMAP-Cl (2.14 g, 0.0092 mole) was dissolved in distilled water. To this was added a slight excess of silver dicyanamide. The reaction flask was covered with aluminum foil and the reaction mixure stirred for twenty-four hours. The resulting precipitate was filtered by gravity and the filtrate was washed with diethyl ether (3 x 30 mL) and hexanes (3 x 30 mL).The solvent evaporated under reduced pressure. The resulting pale yellow solid (1.6 g, 66%) was dried under high vacuum. Calculated for $C_{12}H_{17}N_5O_2$: C 54.74% H 6.51 % N 26.60%. Found: C 54.66 % H 6.63 % N 26.49 %. NMR (δ, D_2O) -^{1}H: 3.10 (s, 6 H), 3.52-3.54 (m, 2H), 3.95-4.00 (m, 2H) 4.21 – 4.23 (m, 1H), 6.77 (d, J = 7.2 Hz, 2 H), 7.88 (d, J = 7.2 Hz, 2 H). ^{13}C: 39.4, 59.4, 62.4, 70.6, 107.4, 141.9, 156.4.



DMAP-DPP

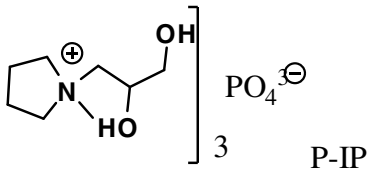
Preparation of *N*-(2,3-dihydroxypropy)-4-(dimethylamino) pyridinium diphenyl phosphate (DMAP-DPP): DMAP-Cl (2.08 g, 0.0089 mole) was dissolved in absolute ethanol (50 mL). To this was added a charge equivalent of diphenyl phosphate (2.24 g, 0.0089 mole) and potassium hydroxide (0.51 g, 0.009 mole). The reaction mixture was stirred overnight. The potassium salt was filtered by vacuum and the solvent was evaporated and the resulting white solid (3.3 g, 83%) was washed with ether (3 x 10 mL) and dried under reduced pressure. Calculated for $C_{22}H_{26}N_2O_6P \cdot H_2O$: C 57.02%, H 6.09%, N 6.04%. Found: C 57.15%, H 5.69%, N 5.90%. NMR (δ, D_2O) -^{1}H: 2.96 (s, 6H), 3.42 – 3.48 (m, 2H), 3.80 – 3.87 (m, 2H), 4.03 – 4.08 (m, 1H), 6.70 (d, J = 7.6 Hz, 2H), 7.02 – 7.04 (m, J = 0.8 Hz and 7.6 Hz, 6H), 7.20 – 7.22 (m, J = 7.6 Hz and 8.4 Hz, 4H), 7.75 (d, J = 8 Hz, 2H). ^{13}C: 39.2, 59.2, 62.3, 70.5, 107.2, 120.1, 120.1, 124.4, 129.7, 141.6, 151.5, 151.6, 156.2. ^{31}P: s, -8.96.



P-Cl

Preparation of N-2,3-dihydroxypropyl-N-methyl pyrrolidinium chloride (P-Cl): 1-methyl pyrrolidine (25.02 g, 0.29 mole) was dissolved in acetonitrile

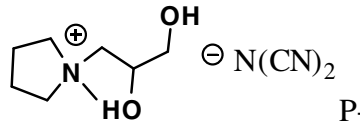
(140 mL). Then 3-chloro-1, 2-propanediol (32.5 g, 0.29 mole) was added. The reaction mixture was allowed to reflux overnight. The solvent was evaporated under high vacuum, and the remaining liquid dried under high vacuum. This resulted in the formation of a brown crystalline solid, which was washed repeatedly acetonitrile until it was white. The solid (36.8 g, 64%) was dried under high vacuum. Calculated for $C_8H_{18}NO_2Cl$: C 49.10% H 9.27% N 7.16%. Found: C 48.99% H 9.41% N 7.02%. NMR (δ, D_2O) ^1H: 2.12, (br, 4 H), 3.02 (s, 3H), 3.12 – 3.25 (m, 1H, J = 4.4 Hz and 9.6 Hz), 3.39 – 3.55 (br m, 7 H), 4.13 – 4.18 (m, 1 H, J = 4.4Hz, 4.8 Hz and 5.2 Hz). ^{13}C: 20.5, 21.3, 48.5, 63.6, 65.5, 65.8, 66.7.



P-IP

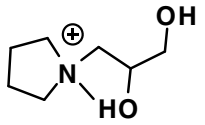
Preparation of N-2,3-dihydroxypropyl-N-methyl pyrrolidinium phosphate (P-IP) : P-Cl (4.96 g, 0.025 mole) was dissolved in 95% ethanol (50 mL). To this was added a charge equivalent of 85% phosphoric acid (1.2 g). The reaction mixture was stirred overnight. The solvent was evaporated under high vacuum. The resulting viscous white solid (5.0 g, 86%) was dried under high vacuum. Calculated for $C_{24}H_{54}N_3O_{10}P{\cdot}7\ H_2O$: C 41.07 %, H 9.76 %, N 5.98 %. Found: C 41.28 %, H 9.97%, N 6.04%. NMR (δ, D_2O) -^1H: 2.12 (br,

J = 2.8 Hz and 3.2 Hz, 4H), 3.03 (s, 3H), 3.30 – 3.53 (m, 8H), 4.18 (br m, 1H). ^{13}C: 20.5, 21.3, 48.5, 63.6, 65.5, 65.8, 66.7. ^{31}P: s, 0.07.



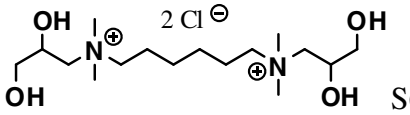
P-DCA

Preparation of N-2,3-dihydroxypropyl-N-methyl pyrrolidinium dicyanamide (P-DCA): P-Cl (5.0 g, 0.025 mole) was dissolved in distilled water. To this was added a slight excess of silver dicyanamide. The reaction flask was covered with aluminum foil and the reaction mixure stirred for twenty-four hours. The resulting silver halide salt was filtered by gravity and the filtrate was washed with diethyl ether (3 x 30 mL) and hexanes (3 x 30 mL).The solvent evaporated under reduced pressure. The yellow liquid was obtained in 80% yield (4.5 g). Calculated for $C_{10}H_{18}N_4O_2$: C 53.08% H 8.02% N 24.76%. Found: C 52.83% H 8.21% N 24.64%. NMR (δ, D_2O) – ^{1}H: 2.15 (t, J = 2.8 Hz and 3.2 Hz, 4 H), 3.07 (s, 3H), 3.31 – 3.60 (br m, 8H), 4.18 - 4.23 (m, J = 4.4 Hz and 5.2 Hz, 1H). ^{13}C: 20.6, 21.5, 48.6, 63.7, 65.6, 65.9, 66.6, 66.8, 119.9.



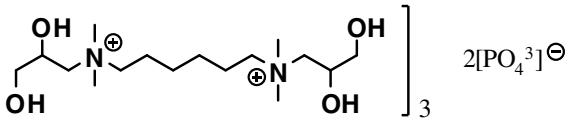
P-DPP

Preparation of N-2,3-dihydroxypropyl-N-methyl pyrrolidinium diphenyl phosphate (P-DPP): P-Cl (2.0 g, 0.01 mole) was dissolved in absolute ethanol. To this was added a charge equivalent of diphenyl phosphate (2.6 g, 0.01 mole) and potassium hydroxide (0.6 g, 0.01 mole). The reaction mixture was stirred overnight. The potassium salt was filtered by vacuum and the solvent was evaporated. The resulting yellow liquid was dissolved in methanol and a few mg of charcoal was added. The mixture was stirred overnight and the charcoal was filtered by gravity. The liquid was then passed through an alumina column. The solvent was evaporated and the resulting pale yellow liquid (1.9 g, 47%) dried under reduced pressure. Calculated for $C_{20}H_{28}NO_6P$: C 58.67% H 6.89% N 3.42%. Found: C 58.51% H 7.00% N 3.36%. NMR (δ, D_2O) - ^{1}H: 2.00 – 2.01, (t, J = 2.4 Hz and 3.6 Hz, 4 H); 2.91, (s, 3H); 3.28 – 3.42,(br m, 8H); 4.02 – 4.10,(m, 1H); 7.08 – 7.10, (m, J = 1.2 Hz and 7.2 Hz, 6 H); 7.24 – 7.28, (m, J = 7.6 Hz and 8 Hz, 4 H). ^{13}C: 20.4, 21.3, 48.8, 63.5, 65.38, 65.43, 65.7, 66.6, 120.1, 120.2, 124.5, 129.8, 129.9, 151.6, 151.67. ^{31}P: -8.95.



S6-Cl

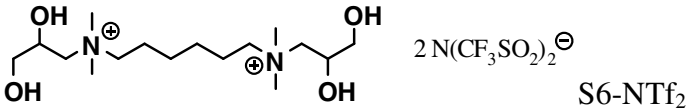
Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol chloride (S6-Cl): *N, N, N', N'*- tetramethyl-1, 6-hexanediamine (7.50 g, 0.044 mole) was dissolved in 95% ethanol (40 mL). To this were added two equivalents of 3-chloro-1, 2-propanediol (10. 0 g, 0.090 mole). The reaction mixture was refluxed overnight. The solvent was evaporated leaving a white solid. The solid (16.56 g, 47%) was washed with hexanes and dried under reduced pressure. Calculated for $C_{16}H_{38}N_2O_4Cl_2$: C 48.85%, H 9.74%, N 7.12%. Found: C 48.48%, H 9.54%, N 7.02%. NMR (δ, D_2O) - ^{1}H: 1.32 (br m, J = 6.4 Hz, 4H), 1.69 (br m, J = 5.2 Hz and 6.4 Hz, 4H), 3.05 (s, 6H), 3.06 (s, 6H), 3.28 – 3.34 (m, 8H), 3.46 – 3.48, (m, J = 2.4 and 2.8 Hz, 4 H); 4.15 (m, J = 4 Hz and 6.8 Hz, 2H). ^{13}C: 21.8, 25.0, 51.5, 51.7, 63.6, 65.3, 65.6, 66.1. MS (ESI): $(M\text{-}Cl)^+$ [357/359], $(M\text{-}2Cl)^{2+}$ [161].



S6-IP

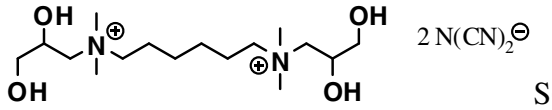
Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol phosphate (S6-IP): S6-Cl (7.0 g, 0.0178 mole) was dissolved in methanol (50 mL). To this a charge equivalent of 85% phosphoric acid (1.0 g) was added. The reaction mixture was stirred overnight. The solvent was

evaporated under reduced pressure leaving behind a white solid. The solid was recrystallized from ethanol. The solid (3.5g, 50 % yield) was dried under reduced pressure. NMR (δ, D_2O) -^{1}H: 1.31 (br, 4H), 1.73 (br, 4H) 3.04 (s, 6H), 3.06 (s, 6H), 3.30 – 3.31 (m, 8H), 3.45 – 3.47(m, J = 4 Hz, 4H), 4.15 (m, 2H). ^{13}C: 21.8, 25.0, 51.5, 51.7, 63.6, 65.3, 65.6, 66.1. ^{31}P: s, 0.10. MS (ESI): m/z $(M\text{-}2IP)^{2+}$ [161].



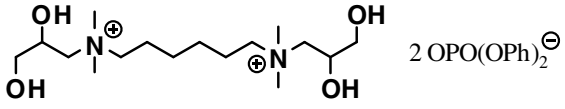
S6-NTf_2

Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol bis(trifluoromethane)sulfonylimide (S6-NTf_2): S6-Cl (10.10 g, 0.026 mole) was dissolved in distilled water. To this was added a charge equivalent of bis(trifluoromethanesulfonyl)imide lithium salt (14.93 g, 0.052 mole). The reaction mixture was stirred overnight. The solvent was carefully decanted and the resulting liquid washed with water until there was no detectable halide. The resulting pale yellow liquid (8.77 g, 38%) was dried under high vacuum. NMR (δ, DMSO) – ^{1}H: 1.31 (br, 4H), 1.70 (br, J = 6 Hz and 6.4 Hz, 4H), 3.076 (s, 6H), 3.083 (s, 6H), 3.22 – 3.46 (m, 12H), 4.00 (m, 2H) 5.02 (t, J = 5.2 Hz and 5.6 Hz, 2H), 5.37 (d, J = 5.2 Hz, 2H). ^{13}C: 21.5, 25.2, 51.1, 51.2, 63.7, 64.0, 66.0, 114.6, 117.8, 121.0, 124.2. MS (ESI); m/z $(M\text{-}NTf_2)^{2+}$ [161].



S6-DCA

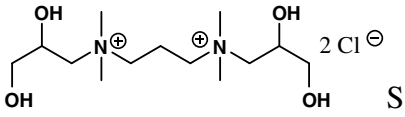
Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol dicyanamide (S6-DCA): S6-Cl (5.46 g, 0.014 mole) was dissolved in distilled water. To this was added a slight excess of silver dicyanamide. The reaction flask was covered with aluminum foil and the reaction mixture stirred for twenty-four hours. The resulting silver halide salt was filtered by gravity and the filtrate was washed with diethyl ether (3 x 30 mL) and hexanes (3 x 30 mL).The solvent evaporated under reduced pressure. The resulting yellow liquid (4.45 g, 70%) was dried under reduced pressure. NMR (δ, D_2O): ^{1}H: 1.32 (m, 4H), 1.72 – 1.73 (br m, J = 5.6 Hz, 4H), 3.061 (s, 6H), 3.073 (s, 6H), 3.29 – 3.35 (m, 8H), 3.47 – 3.50 (m, 4H), 4.15 – 4.17 (br m, J = 4.4 Hz and 5.2 Hz, 2H). ^{13}C: 21.9, 25.1, 51.5, 51.7, 63.6, 65.4, 65.6, 66.1, 120.0. MS (ESI): m/z $(M\text{-}2DCA)^{2+}$ [161].



S6-DPP

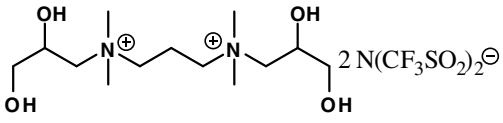
Preparation of 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14,-tetrol diphenyl phosphate (S6-DPP): S6-Cl (5.0 g, 0.013 mole) was dissolved in methanol. To this was added a charge equivalent of diphenyl phosphate (6.2 g, 0.025 mole). The reaction mixture was stirred overnight. The solvent was evaporated and the resulting white solid (10.1 g, 95% yield)

dried under reduced pressure. NMR (δ, D_2O): ^{1}H: 1.24 (m, 4H), 1.62 – 1.63 (br m, J = 5.6 Hz, 4H), 2.97(s, 6H), 2.99 (s, 6H) 3.19 – 3.25 (m, 8H), 3.41 – 3.44 (m, 4 H), 4.08 – 4.11 (br m, J = 4.8 Hz and 5.2 Hz, 2H), 7.08 – 7.10 (m, J = 8 Hz, 12H), 7.26 – 7.29 (m, J = 7.6 Hz, 8H). ^{13}C: 21.8, 25.0, 51.4, 51.7, 63.6, 65.3, 65.6, 66.0, 120.16, 120.21, 124.5, 129.8, 151.55, 151.6. ^{31}P: -8.88.



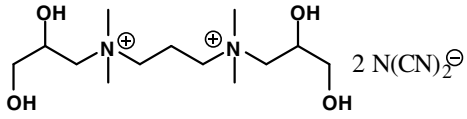
S3-Cl

Preparation of 4,4,8,8,-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol chloride (S3-Cl): *N, N, N', N'*, -tetremethyl-1,3-propanediamine (5.0 g, 0.038 mole) was dissolved in 4:1 solution of acetonitrile/ethanol (25 mL). To this 3-chloro-1,2-propanediol (8.58 g, 0.077 mole)was added. The reaction mixture was refluxed overnight and the solvent evaporated under high vacuum. The resulting viscous liquid was dissolved in ethanol and ether was added to precipitate the product. The solvent was decanted and the still viscous white liquid was dried under high vacuum. The resulting white solid (11.7 g, 88%) was washed with ethyl acetate and dried again under high vacuum. NMR (δ, D_2O): ^{1}H: 2.33 (m, 2H), 3.17 (s, 6H) 3.19 (s, 6H), 3.44 – 3.54 (br m, 12 H) 4.225 (m, 2 H). ^{13}C: 16.94, 51.93, 52.12, 61.19, 61,39, 63.57, 66.03, 66.18.



S3-NTf_2

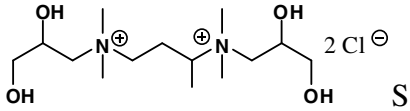
Preparation of 4,4,8,8,-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol bis(trifluoromethylsulfonyl)imide (S3-NTf_2): S3-Cl (5.9 g, 0.017 mole) was dissolved in distilled water. To this was added a charge equivalent of bis(trifluoromethanesulfonyl)imide lithium salt (9.7 g, 0.034 mole). The reaction mixture was stirred overnight. The solvent was carefully decanted and the resulting liquid washed with water until there was no detectable halide. The resulting liquid (0.71 g, 5% yield) was dried under high vacuum. NMR (δ, DMSO-D_6): ^{1}H: 2.04 – 2.23 (br m, 2H), 3.08 – 3.12 (m, 14H), 3.26-3.36 (br m, 10 H), 3.90-4.10 (br m, 2 H), 5.08 (d, J = 4.8 Hz, 2H), 5.43 (d, J = 4.8 Hz, 2 H). ^{13}C: 16.4, 51.3, 60.7, 63.6, 65.9, 66.5, 114.6, 117.8, 121.0, 124.2.



S3-DCA

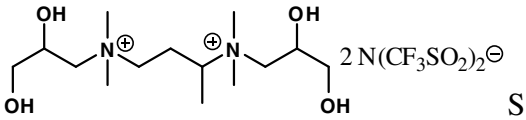
Preparation of 4,4,8,8,-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol dicyanamide (S3-DCA): S3-Cl (5.8 g, 0.017 mole) was dissolved in distilled water. To this was added a slight excess of silver dicyanamide. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for twenty-four hours. The resulting halide salt was filtered by vacuum. The

solvent evaporated under reduced pressure. The resulting yellow liquid (4.9 g, 70% yield) was dried under high vacuum. NMR (δ, D_2O): ^1H: 2.28 – 2.39 (br m, 2H), 3.08 (s, 6 H), 3.12 (s, 6 H), 3.23 – 4.17 (br m, 12 H), 4.18 (m, 2H). ^{13}C: 16.8, 51.8, 52.0, 61.1, 61.3, 63.5, 65.8, 66.0, 66.1, 120.0.



S3M-Cl

Preparation of 4,4,7,8,8,-pentaamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol chloride (S3M-Cl): *N, N, N', N',* -tetremethyl-1,3-butanediamine (5.0 g, 0.035 mole) was dissolved in 4:1 solution of acetonitrile/ethanol (25 mL). To this 3-chloro-1,2-propanediol (8.48 g, 0.077 mole)was added. The reaction mixture was refluxed overnight and the solvent evaporated under high vacuum. The resulting viscous liquid was dissolved in ethanol and ether was added to precipitate the product. The solvent was decanted and the yellow clear viscous liquid was dried under high vacuum. (The product contained excess 3-chloro-1,2-propanediol.)

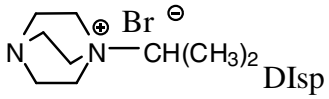


S3M-Cl

Preparation of 4,4,7,8,8,-pentamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol bis(trifluoromethylsulfonyl)imide (S3M-NTf_2): S3M-Cl (a mixture of product and excess starting material, 5.0 g) was dissolved in distilled water. To this was added a charge equivalent of bis(trifluoromethanesulfonyl)imide

lithium salt. The reaction mixture was stirred overnight. The solvent was carefully decanted and the resulting liquid washed with water until there was no detectable halide. The resulting liquid (6.0 g) was dried under high vacuum. NMR (δ, DMSO-D_6): ^{1}H: 1.34 (m, 3H), 1.3-2.0 (br m, 2H), 3.05-3.13 (m, 14 H), 3.20-3.61, (br m, 9 H), 4.00-4.10 (br m, 2H), 5.09 (m, 2H), 5.43 (m, 2H). ^{13}C: 13.2, 13.3, 13.4, 48.7, 51.4, 51.5, 61.2, 63.6, 65.2, 65.9, 66.2, 114.6, 117.8, 121.0, 124.2.

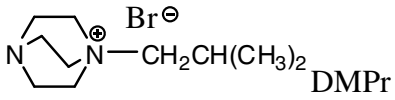
C. Synthesis of New Monocationic Strings



DIsp

Preparation of 1-isopropyl-1-azonia-4-azabicyclo[2.2.2]octane bromide (DIsp): 1,4-diazabicyco[2.2.2]octane (5.46 g, 0.049 mole) was dissolved in ethyl acetate (100 mL). To this was added one equivalent of 2-bromopropane (5.98 g, 0.049 mole). The reaction mixture was stirred for several days. The resulting white powder (5.70 g, 50%) was filtered by vacuum and washed with ethyl acetate (3 x 30 mL) and ether (3 x 30 mL). The solid was dried under reduced pressure. Calculated for $C_{10}H_{21}N_2Br•H_2O$: C 44.94%, H 8.68, N 10.48%. Found: C 45.28%, H 9.04%, N 10.50%. NMR (δ, D_2O) - ^{1}H: 1.28 – 1.30 (d, J = 6.8 Hz , 6H), 3.08

– 3.11 (t, J = 6.8 Hz and 7.6 Hz, 6H), 3.29 – 3.32 (t, J = 7.2 Hz and 7.6 Hz, 6H), 3.47 – 3.51 (m, 1H). ^{13}C: 15.29, 44.21, 49.02, 66.41.

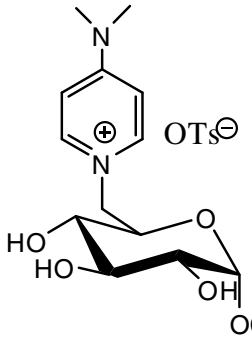


DMPr

Preparation of 1-(2-methylpropyl)-1-azonia-4-azabicyclo[2.2.2]octane bromide (DMPr): 1,4-diazabicyco[2.2.2]octane (5.20 g, 0.046 mole) was dissolved in ethyl acetate. To this was added one equivalent of 1-bromo-2-methyl propane (6.36 g, 0.046 mole). The reaction mixture was stirred for several days. The resulting white powder was filtered by vacuum and washed with ethyl acetate (3 x 30 ml) and ether (3 x 30 mL). The solid (7.46 g, 65%) was dried under reduced pressure. Calculated for $C_9H_{19}N_2Br•H_2O$: C 42.70%, H 8.36%, N 11.06%. Found: C 42.87%, H 8.71%, N 11.12%. NMR (δ, D_2O): ^{1}H: 0.99 – 1.01 (d, J = 6.8 Hz, 6H), 2.20 – 2.29 (br m, 1H), 3.09 - 3.13 (m, J = 6 Hz and 8 Hz, 8H), 3.35 – 3.38 (t, J = 6.8 Hz and 7.2 Hz, 6H). ^{13}C: 21.98, 22.36, 44.20, 52.51, 72.35.

D. Synthesis of Carbohydrate Derivatives

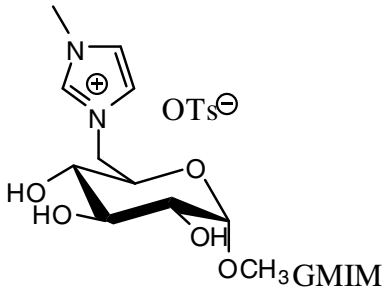
Glucopyranosides



GDMAP

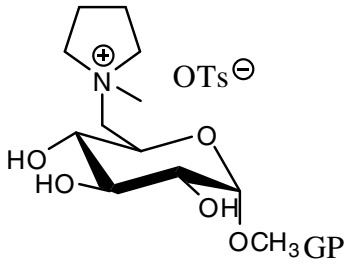
Preparation of methyl-α-D-glucopyranosyl-6-deoxy-6[4-dimethyl amino pyridinium] glucopyranoside monotosylate (GDMAP): The salt was prepared by dissolving methyl-α-D-glucopyranoside (5.0 g, 0.026 mole, Sigma, 99%) in distilled water. One equivalent of sodium bicarbonate (2.35 g, 0.028 mole, JT Baker), followed by one equivalent of p-toluenesulfonyl chloride (4.96 g, 0.026 mole, Aldrich 98%) was added. The mixture was stirred for one hour. Then one equivalent of 4-(dimethylamino)-pyridine (3.18 g, 0.026 mole, prilled, Aldrich, 99%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product was dried under high vacuum and became a yellow solid. The solid was dissolved in 95% ethanol and an insoluable solid was filtered off. The solvent was again evaporated under reduced pressure and the remaining liquid dried to yield the solid (12.32g, 92%). Calculated for $C_{21}H_{30}N_2O_8S \cdot 2.5\ H_2O$: C 48.92%, H

6.84%, N 5.43%. Found: C 48.83%, H 6.48%, N 5.06%. NMR (D2O, δ) ^{1}H: 2.26 (s, 3H), 3.03 (s, 6H), 3.30 (s, 3H), 3.26 – 3.77 (m, 7H), 6.67 (d, J = 7.6 Hz, 2H), 7.21 (d, J = 8 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H). 7.85 (d, J = 7.2 Hz, 2H). ^{13}C: 20.4, 39.1, 54.9, 60.5, 69.5, 71.2, 71.5, 73.0, 99.2, 106.7, 125.3, 129.4, 139.3, 142.4, 157.1.



Preparation of methyl-α-D-glucopyranosyl-6-deoxy-6[3-methyl imidazolium] glucopyranoside monotosylate (GMIM): The salt was prepared by dissolving methyl-α-D-glucopyranoside (5.0 g, 0.026 mole) in distilled water. One equivalent of sodium bicarbonate (2.16 g, 0.026 mole), followed by one equivalent of p-toluenesulfonyl chloride (4.94 g, 0.026ole) was added. The mixture was stirred for one hour. Then one equivalent of 1-methylimidazole (2.12 g, 0.026 mole, Aldrich, 99%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product was dried under high vacuum and became a brown solid (10.88 g, 89%). Calculated for $C_{17}H_{26}N_2O_8S\bullet 3H_2O$: C 43.21%, H 6.83%, N 5.93%. Found: C

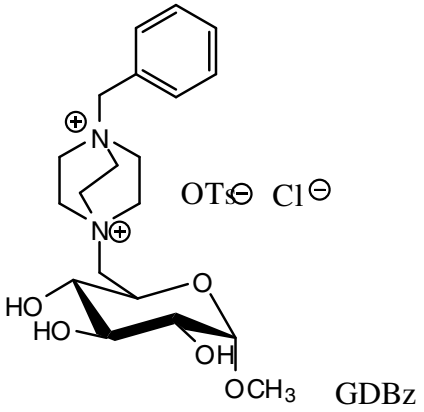
43.59%, H 6.51%, N 6.26%. NMR (D_2O, δ) ^1H: 2.27 (s, 3H), 3.32 (s, 3H), 3.78 (s, 3H), 3.27 – 3.78 (m, 7H), 7.22 – 7.27 (m, 4H), 7.55 (d, J = 8 Hz, 2H), 8.44 (s, 1H). ^{13}C: 20.46, 35.24, 55.01, 60.56, 69.57, 71.22, 71.57, 73.09, 99.26, 119.94, 122.82, 125.31, 129.39, 135.10, 139.46, 142.38.



Preparation of methyl-α-D-glucoyranosyl-6-deoxy-6-[N-methyl pyrrolidinium] glucopyranoside monotosylate (GP): The salt was prepared by dissolving methyl-α-D-glucopyranoside (6.25 g, 0.032 mole) in distilled water. One equivalent of sodium bicarbonate (2.69 g, 0.032 mole), followed by one equivalent of p-toluenesulfonyl chloride (6.1 g, 0.032 mole) was added. The mixture was stirred for one hour. Then one equivalent of 1-methylpyrrolidine (2.72 g, 0.032 mole, Aldrich, 97%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product was dried under high vacuum and became an off-white solid (13.06 g, 90.7%). Calculated for $C_{19}H_{31}NO_8$•7.5 H_2O: C 40.13%, H 8.15%, N 2.46%. Found: C 40.01%, H 8.27%, N 2.64%. NMR (D_2O, δ) ^1H: 1.92 (m, 2H), 2.08 (m, 2H), 2.34 (s, 3H), 2.84 (s, 3H), 2.97 (m, 2H), 3.30 – 3.37 (m, 5H), 3.45 -

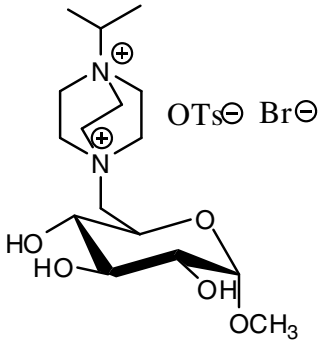
3.82 (m, 7H), 7.32 (d, J = 8 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H). ^{13}C: 20.49, 22.85, 40.60, 55.03, 55.79, 60.58, 69.59, 71.24, 71.60, 73.12, 99.29, 125.37, 129.46, 139.47, 142.48.

The syntheses of the salts listed next are similar to the previously described salts (give ref). The amines attached are monocationic strings. The strings shown in Table 2 (under R) were made by reacting DABCO with one equivalent of the appropriate alkyl halide in ethyl acetate.



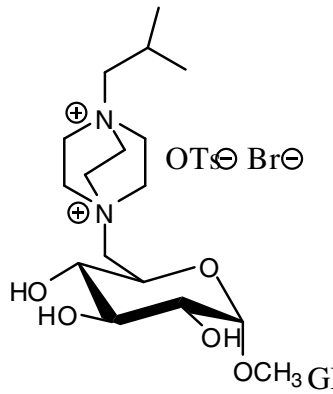
GDBz

Preparation of 1-(benzyl)-4-(methyl-α-D-glucopyranosyl-6-deoxy-6)-1,4-diazoniabyclo[2.2.2]octane monochloride monotosylate (GDBz): This product is a pale yellow solid (>99%). Calculated for $C_{27}H_{39}N_2O_8SCl•3H_2O$ C: 50.58%, H 7.07%, N 4.37%. Found: C 50.51%, H 7.00%, N 4.63%. NMR (δ, D_2O) – ^{1}H: 2.34 (s, 3 H), 3.36 (s, 3 H), 3.32 – 3.84 (m, 19 H), 4.66 (s, 2 H), 7.32 (d, J = 8 Hz, 2 H), 7.50 – 7.64 (m, J = 8 Hz, 7 H). ^{13}C: 20.49, 44.06, 50.65, 55.05, 60.60, 69.02, 69.61, 71.26, 71.62, 73.13, 99.31, 125.39, 129.48, 129.58, 131.44, 132.98, 139.49, 145.52.



GDIsp

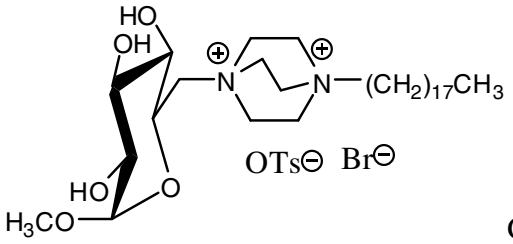
Preparation of 1-(isopropyl)-4-(methyl-α-D-glucopyranosyl-6-deoxy-6)-1,4-diazoniabyclo[2.2.2]octane monobromide monotoyslate (GDIsp): This product is a white solid (94%). Calculated for $C_{23}H_{39}N_2O_8SBr \bullet 8.5\ H_2O$: C 37.50%, H 7.66 %, N 3.80 %. Found: C 37.53%, H 7.37%, 3.78%. NMR (δ, D_2O) – ^1H: 1.36 (d, J = 6.4 Hz, 6H), 2.31 (s, 3H), 3.33 (s, 3 H), 3.28 – 3.80 (m, 19 H), 7.28 (d, J = 8 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H). ^{13}C: 15.47, 20.53, 43.98, 47.84, 55.06, 60.59, 68.32, 69.60, 71.25, 71.59, 73.12, 99.28, 125.37, 129.52, 139.51, 142.53.



GDMPr

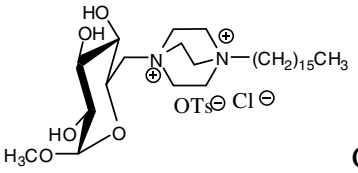
Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(2-methylpropyl)-1,4-diazonia-bicyclo[2.2.2] octante monobromide monotosylate (GDMPr): The product is a white solid (95%). Calculated for

$C_{24}H_{41}N_2O_8SBr•9\ H_2O$: C 37.94%, H 7.82 %, N 3.68 %. Found: C 38.12%, H 7.79%, 3.43%. NMR (δ, D_2O) – ^{1}H: 1.01 (d, J = 6.8 Hz, 6H), 2.21 (br m, 1H), 2.30 (s, 3H), 3.35 (s, 3H), 3.33 – 3.87 (m, 21 H), 7.27 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8 Hz, 2H). ^{13}C: 20.61, 21.86, 22.93, 43.98, 51.15, 55.10, 60.64, 69.64, 71.28, 71.61, 72.87, 73.15, 74.21, 99.29, 125.41, 129.59, 139.65, 142.52.



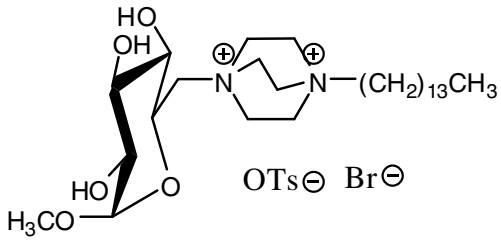
GDC18

Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(octadecyl)-1,4-diazoniabycylo[2.2.2]octane monobromide monotoyslate (GDC18): This product is a pale yellow solid (>99%). NMR (δ, DMSO-D_6) – ^{1}H: 0.86 (br t, 3H), 1.24 (br s, 30H), 1.69 (br, 2H), 2.29 (s, 3H), 3.042 (t, 2H), 3.31 (s, 3H), 3.19 – 3.60 (m, 18H), 4.51 (d, 2H), 7.11 (d, 2H), 7.47 (d, 2H). ^{13}C: 13.93, 20.75, 22.06, 28.66, 29.00, 43.46, 50.48, 54.22, 70.28, 71.92, 72.57, 99.61, 125.45, 128.04.



GDC16

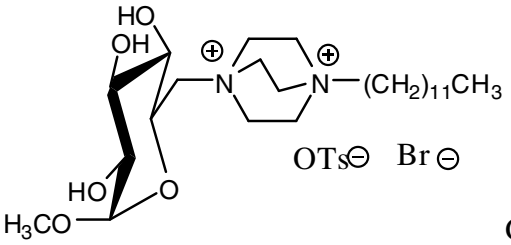
Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(hexadecyl)-1,4-diazabicyclo[2.2.2]octane monochloride monotosylate (GDC16): The product is a pale yellow solid (91%). Calculated for $C_{36}H_{65}N_2O_8SCl$•11.5 H_2O: C 46.56%, H 9.55 %, N 3.02%. Found: C 46.53%, H 9.18%, N 2.72%. NMR (δ, $CDCl_3$) – ^{1}H: 0.81 (t, 3H), 1.19 (s, 26H). 1.69 (m, 2H), 2.15 (s, 3H) 3.32 (s, 3H), 3.44 – 3.87 (m, 21H), 6.94 (d, J = 8 Hz, 2H), 7.55 (d, J = 7.2 Hz, 2H). ^{13}C: 14.11, 21.19, 22.70, 26.08, 26.90, 28.90, 29.36, 29.41, 29.47, 29.55, 29.66, 29.68, 29.73, 29.81, 29.89, 31.95, 32.67, 44.25, 45.21, 50.65, 55.32, 60.85, 69.73, 71.58, 71.71, 73.47, 99.34, 125.85, 129.11, 140.07, 141.90.



GDC14

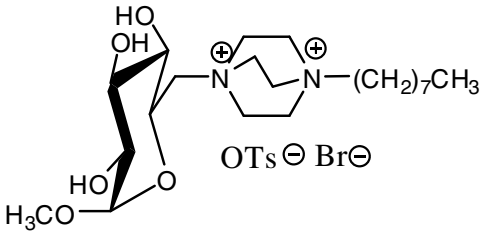
Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(tetradecyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC14): This product is a white solid (>99%). Calculated for $C_{34}H_{61}N_2O_8SBr$•2 H_2O: C 52.77% H 8.47% N 3.62%. Found: C 52.83% H 8.52% N 3.56%. NMR (δ,

D_2O) – ^1H: 0.87 (br t, J = 5.6 Hz and 6.4 Hz, 3H). 0.94 – 1.26 (br, 22 H) 2.16 (s, 3H) 3.48 (s, 3H), 3.30 – 3.76 (m, 23H), 7.04 (d, 2H), 7.58 (d, J = 7.2 Hz, 2H). ^{13}C: 13.91, 20.97, 21.72, 22.78, 25.98, 29.07, 29.72, 29.84, 30.02, 30.14, 32.15, 44.07, 50.84, 55.10, 60.64, 64.68, 69.64, 71.29, 71.64, 73.17, 99.33, 125.85, 129.13, 139.82, 142.06.



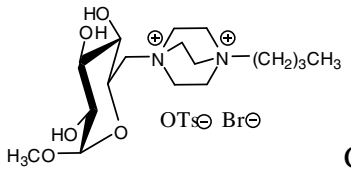
GDC12

Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(dodecyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC12): This product is a white solid (>99%). Calculated for $C_{32}H_{57}O_8N_2SBr•2\ H_2O$: C 51.53% H 8.24% N 3.76%. Found: C 51.46% H 8.31% N 3.74%. NMR (δ, D_2O) ^1H: 0.84 (br t, 3H) 0.86 – 1.01 (br m, 16H), 1.24 (br, 2H), 2.19 (s, 3H), 3.12 (br, 2H), 3.30 – 3.32 (m, 2H), 3.32 (s, 3H), 3.43 – 3.76 (m, 19H), 7.08 (d, 2H), 7.57 (d, 2H). ^{13}C: 13.71, 20.75, 22.52, 29.31, 29.42, 29.59, 31.81, 43.93, 50.86, 54.97, 60.50, 69.51, 71.17, 71.53, 73.04, 99.23, 125.62, 129.13, 141.18.



GDC8

Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(octyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC8): This product is a pale yellow solid (>99%). Calculated for $C_{28}H_{49}N_2O_8SBr•2H_20$: C 48.76% H 7.75% N 4.06% Found: C 48.77% H 7.80% N 4.17%. NMR (δ, D_2O) – ^1H: 0.76 (t, J = 6.8 Hz and 6.4 Hz, 3H), 1.17 – 1.24 (br, 10H), 1.69 (br, 2H), 2.29 (s, 3H), 3.36 (s, 3 H), 3.30 – 3.78 (br m, 22H), 7.26 (d, J = 8 Hz, 2 H), 7.58 (d, J = 8 Hz, 2H). ^{13}C: 13.34, 20.45, 21.33, 21.92, 25.24, 28.02, 28.07, 30.88, 43.90, 50.70, 54.97, 60.50, 65.33, 69.51, 71.17, 71.53, 73.04, 99.23, 125.30, 129.44, 139.38, 142.47.

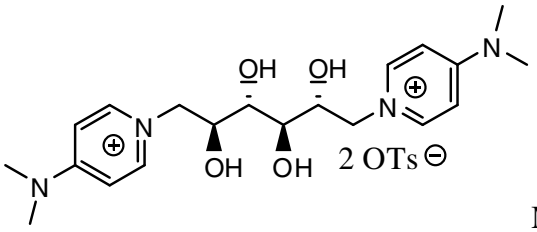


GDC4

Preparation of 1-(methyl-α-D-glucopyranosyl-6-deoxy-6)-4-(butyl)-1,4-diazabicyclo[2.2.2]octane monobromide monotosylate (GDC4): This product is a pale yellow solid (98%). Calculated for $C_{24}H_{41}N_2O_8*5H_2O$: C 41.92%, H 7.47 %, N 4.07%. Found: C 41.65%, H 7.76 %, N 3.85%. NMR (δ, D_2O) – ^1H: 0.83 (tr, J = 7.2 Hz and 7.6 Hz, 3H), 1.28 (m, 2 H), 1.64 (m, 2

H), 2.29 (s, 6 H), 3.29 – 3.56 (m, 5H), 3.69 – 3.80 (m, 16 H), 7.26 (d, J = 8Hz, 2 H), 7.58 (d, J = 8 Hz, 2H). ^{13}C: 12.7, 18.9, 20.5, 43.9, 50.7, 55.0, 60.5, 65.1, 69.5, 71.2, 71.5, 73.0, 99.2, 125.3, 129.5, 139.4, 142.5.

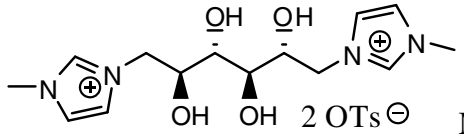
Mannitol Derivatives



MnDMAP

Preparation of 1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-4-(dimethyl amino) pyridinium-1,6-bis[4-dimethylamino) pyridium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate (MnDMAP): The salt was prepared by dissolving D-mannitol (5.02 g, 0.027 mole, Sigma, 98%) in distilled water. Two equivalents of sodium bicarbonate (4.54 g, 0.054 mole, JT Baker), followed by two equivalents of p-toluenesulfonyl chloride (10.3 g, 0.054 mole, Aldrich, 98%) were added. The mixture was stirred for one hour. Then two equivalents of 4-(dimethylamino)-pyridine (6.60 g, 0.054 mole, prilled, Aldrich, 99%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product (11.74 g, 59.17% yield) was dried under high vacuum and it became a yellow solid. Calculated for $C_{34}H_{46}N_4O_{10}S_2$: C 55.56%, H 6.31%, N 7.62%. Found: C 55.21%, H 6.63%,

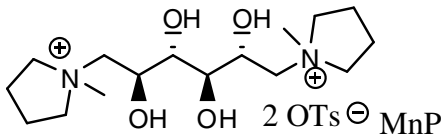
N 7.67%. NMR (δ, D_2O) – ^1H: 2.28 (s, 6H), 3.03 (s, 12 H), 3.51-3.75 (m, 8 H), 6.69 (d, J=7.6 Hz, 4H), 7.23 (d, J = 8 Hz, 4H), 7.56 (d, J = 8.2 Hz, 4H), 7.88 (d, J = 7.2 Hz, 4H). ^{13}C: 20.44, 39.06, 63.19, 69.24, 70.80, 106.75, 125.31, 129.39, 139.39, 140.12, 142.40, 157.00.



MnMIM

Preparation of 1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-3-(methyl) imidazolium)-1,6-bis[3-methyl imidazolium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate (MnMIM): The salt was prepared by dissolving D-mannitol (6.0 g, 0.033mole) in distilled water. Two equivalents of sodium bicarbonate (5.54 g. 0.066 mole), followed by two equivalents of p-toluenesulfonyl chloride (12.58 g, 0.066 mole) were added. The mixture was stirred for one hour. Then two equivalents of 1-methylimidazole (5.42 g, 0.066 mole, Aldrich, 99%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product was dried under high vacuum and it became a yellow solid. The solid was then dissolved in 95% ethanol. (There was an insoluable white solid that was filtered off.) The solvent was then evaporated under high vacuum, leaving behind a dark yellow liquid and a solid. The liquid was carefully decanted. The remaining solid was dried

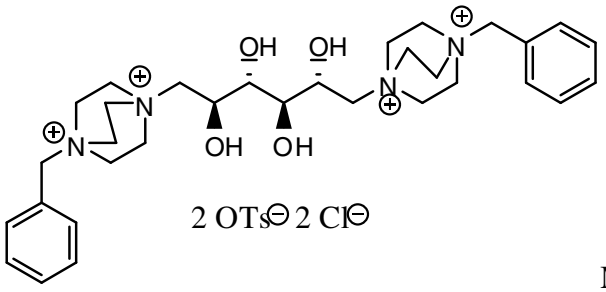
under high vacuum (20.98, 97 %). Calculated for $C_{28}H_{38}N_4O_{10}S_2$:C 51.36% H 5.85% N 8.56%. Found: C 51.08% H 6.01% N 8.47%. NMR (δ, D_2O) – ^{1}H: 2.26 (s, 6H), 3.55 – 3.78 (m, 8 H) 3.78 (s, 6H), 7.23 – 7.27 (m, J = 8 Hz, 8 H), 7.57 (d, J = 8 Hz, 4H), 8.44 (s, 2H). ^{13}C: 20.43, 35.23, 63.17, 69.18, 70.75, 119.88, 122.79, 125.27, 129.38, 135.05, 139.33, 142.40.



Preparation of 1-(N-((R)-2, (R)-3, (R)-4, (R)-5 tetrahydroxyhexyl)-N-(methyl) pyrrolidinium-1,6-bis[N-methyl pyrrolidinium-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexane ditosylate (MnP): The salt was prepared by dissolving D-mannitol (8.0 g, 0.044 mole) in distilled water. Two equivalents of sodium bicarbonate (7.39 g, 0.088 mole), followed by two equivalents of p-toluenesulfonyl chloride (16.78 g, 0.088 mole) were added. The mixture was stirred for one hour. Then two equivalents of 1-methylpyrrolidine (7.49 g, 0.088 mole, Aldrich, 97%) was added and the reaction mixture was stirred and refluxed over night. The solvent was evaporated under high vacuum leaving a viscous liquid. This product was dried under high vacuum and it became a yellow solid. The solid was washed with diethyl ether (3 x 30mL). The solid was again dried under high vacuum (30.9 g, >99%). Calculated for $C_{30}H_{48}N_2O_{10}S_2 \bullet H_20$: C 53.07%, H

7.42%, N 4.12%. Found: C, 53.22%, H 7.69%, N 4.33%. NMR (δ, D_2O) ^{1}H: 2.00 (br d, 8 H), 2.34 (s, 6H), 2.85 (s, 6H), 2.98 (br, 4 H), 3.60-3.83 (m, 14 H) 7.32 (d, J = 8 Hz, 4 H), 7.64 (d, J= 8 Hz, 4 H). ^{13}C: 20.49, 22.85, 40.60, 55.79, 63.23, 69.28, 70.86, 125.36, 129.46, 139.45, 142.49.

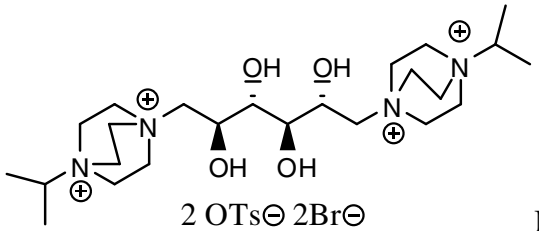
The syntheses of the salts listed next are similar to the previously described salts. The amines attached are monocationic strings. The monocationic strings are shown in Table 3 (under R).



MnDBz

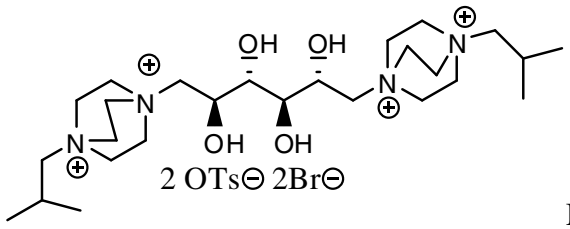
Preparation of 1-(benzyl)-4-(6'-(4"(benzyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dichloride ditosylate (MnDBz): This product is a white solid (87%). Calculated for $C_{46}H_{64}N_4O_{10}S_2Cl_2 \bullet 12.5H_20$: C 46.30%, H 7.51%, N 4.69%. Found: C, 46.30%, H 7.58%, N, 4.83%. NMR (δ, D_2O) ^{1}H: 2.28 (s, 6H), 3.67 – 3.84 (m, 32H), 4.62 (s, 4H) 7.25 (d, J = 8.2 Hz, 4H), 7.45 – 7.49 (m, 10 H), 7.58

(d, J = 8 Hz, 4H). ^{13}C: 20.51, 44.02, 50.46, 63.24, 69.03, 69.30, 70.88, 124.97, 125.35, 129.50, 129.61, 131.48, 132.96, 139.52, 142.50.



MnDIsp

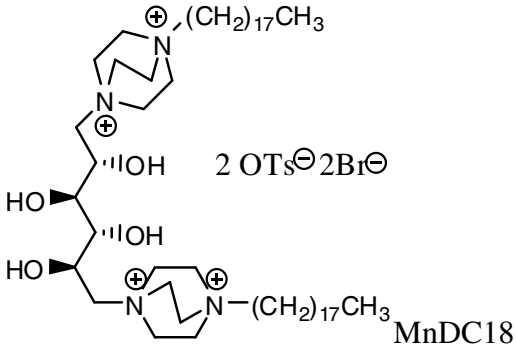
Preparation of 1-(isopropyl)-4-(6'-(4"(isopropyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate (MnDIPr): The product is a pale yellow solid (>99%). Calculated for $C_{38}H_{64}N_4O_{10}S_2Br_2 \bullet 14.5\ H_20$: C 37.35%, H 7.67%, N 4.58%. Found: C, 37.26%, H 7.69%, N 4.45%. NMR (δ, D_2O) ^{1}H: 1.36 (d, J = 6.8 Hz, 12H), 2.31 (s, 6H), 3.55 – 3.78 (m, 34 H) 7.30 (d, 4H), 7.60 (d, J = 8.4 Hz, 4H). ^{13}C: 15.54, 20.58, 44.01, 47.85, 63.26, 68.38, 69.31, 70.90, 125.39, 129.58, 139.58, 142.56.



MnDMPr

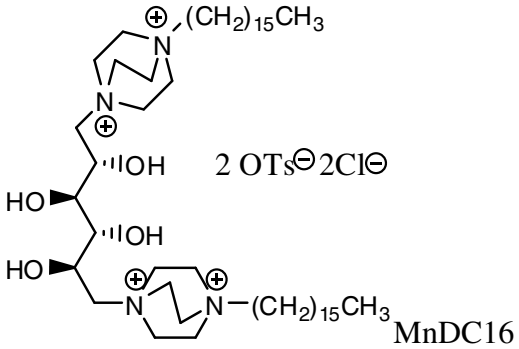
Preparation of 1-(2-methylpropyll)-4-(6'-(4"(2-methylpropyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1"-((R)-2, (R)-3. (R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate

(MnDMPr): This white solid was obtained in 82% yield. Calculated for $C_{40}H_{68}O_{10}N_4S_2Br_2$•10 H2O: C 41.09%, H 7.58 %, N 4.79%. Found: C 40.85%, H 7.30%. N 5.16%. NMR (δ, D_2O) ^{1}H: 1.01 (d, J = 6.8 Hz,12H), 2.24 (br 2H), 2.31 (s, 6H), 3.32 (d, 4H), 3.58 – 3.86 (m, 32H), 7.27 (d, 4H), 7.62 (d, 4H). ^{13}C: 20.51, 21.80, 22.83, 43.97, 51.29, 63.24, 69.29, 70.86, 72.81, 125.37, 129.37, 139.50, 142.53.



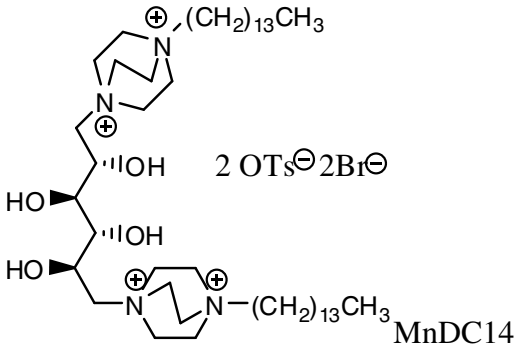
MnDC18

Preparation of 1-(octyldecyl)-4-(6'-(4"(octadecyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-2,3,4,5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate (MnDC18): The product is a white solid (97% yield). Calculated for $C_{68}H_{124}N_4O_{10}S_2Br_2 \cdot 9H_2O$: C 52.90%, H 9.27%, N 3.63%. Found: C 53.10%, H 9.14%, N 3.69%. NMR (δ, DMSO-D_6) ^{1}H: 0.86 (br t, 6H), 1.24 (br, 60H), 1.68 (br, 4H), 2.29 (s, 6H), 3.28 – 3.66 (br m, 36H), 7.14 (d, 4H) 7.48 (d, 4H). ^{13}C: 13.93, 20.74, 22.06, 29.00, 31.25, 43.67, 63.81, 69.62, 71.26, 125.45, 128.03.



MnDC16

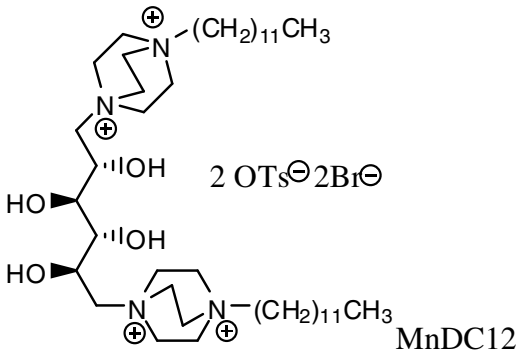
Preparation of 1-(hexadecyl)-4-(6'-(4"(hexadecyl)'1",4"-diazoniabicyclo[2.2.2]octyl}-1'-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexyl)1,4-diazonia-bicyclo[2.2.2]octane dichloride ditosylate (MnDC16): The product is a white solid (80 %). NMR (δ, DMSO-D_6) ^{1}H: 0.86 (t, J = 6.8 Hz and 6.4 Hz, 6H), 1.24 (br, 52H), 2.29 (s, 6H), 3.36 – 3.68 (m, 36H), 7.11 (d, J = 8 Hz, 4H), 7.48 (d, J = 8 Hz, 4H). ^{13}C: 13.9, 20.8, 22.2, 29.01, 50.6, 63.9, 69.8, 71.4, 125.47, 128.04.



MnDC14

Preparation of 1-(tetradecyl)-4-(6"-(4"(tetradecyl)-1",4"-diazoniabicyclo[2.2.2]octyl}-1'-(R)-2,(R)-3,(R)-4,(R)-5,-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate (MnDC14): This product is obtained as a white solid (>99%). Calculated for

$C_{60}H_{108}N_4O_{10}S_2Br_2 \bullet 3H_2O$: C 54.45% H 8.68% N 4.23%. Found: C 54.37% H 8.72% N 4.11%. NMR (δ, D_2O) ^1H: 0.78 (br t, 6H), 1.15 – 1.19 (br, 44H), 2.26 (s, 6H), 3.20 (br, 4H), 3.45 – 3.69(br m, 32H), 7.19 (d, 4H). 7.58 (d, 4H). ^{13}C: 13.50, 22.20, 29.04, 31.40, 43.98, 125.43, 129.29.



MnDC12

Preparation of 1-(dodecyl)-4-(6”-(4”(dodecyl)-1”,4”-diazoniabicyclo[2.2.2]octyl}-1’-(R)-2,(R)-3,(R)-4,(R)-5-tetrahydroxyhexyl)-1,4-diazonia-bicyclo[2.2.2]octane dibromide ditosylate (MnDC12): The product is obtained as a white solid (96%). Calculated for $C_{56}H_{100}N_4O_{10}S_2Br \bullet 3H_2O$: C 53.07 % H 8.43 % N 4.42 %. Found: C 52.96 %, H 8.48 % N 4.37 %. NMR (δ, D_2O): ^1H: 0.51 (br t, 6H), 1.10 – 1.20 (br, 36H), 1.58 (br, 4H), 2.25 (s, 6H), 3.20 (br, 4H), 3.48 – 3.69 (m, 32H), 7.18 (d, 4H), 7.57 (d, 4H). ^{13}C: 13.55, 29.17, 43.96, 51.05, 63.16, 69.19, 70.75, 125.45, 129.27.

E. Preparation of Gels

The gels were prepared by adding approximately 100 mg of the carbohydrate derivative to a clean vial. Then using an Eppendorf pipette, 1.0 mL of distilled water is added. The vials are sealed and the mixture is heated to about 70 ˚C to allow the solid dissolve and then the solution is cooled to room temperature. The vial is then inverted to see if gelation has occurred. If there is no flow, we have a gel. If gelation occurs, more solvent is added and the steps above are repeated to see if gelation continues. If gelation does not occur, more of the solid is added.

F. Testing of Gels for Antimicrobial Activity

Twenty-five microliters of the gel and five microliters of a stock solution of bacteria (~5 x 10^4, *S. aureus)* were added to two mL of Luria-Bertani (LB) broth. The growth medium was incubated overnight at 37 ˚C in a shaking water bath. The absorbance (abs) at 600nm was recorded. The results are reported as % growth = (abs of sample/abs of blank) x 100.

G. Modification of Mannose-functionalized Dendrimers

Preparation of Den2C12: The mannose functionalized, generation 2 dendrimer (15 mannose units, 111.6mg, 0.014 mmol) was dissolved in

distilled water (10 mL). To this were added sixteen equivalents of sodium bicarbonate (21.4 mg, 0.25 mmol) and sixteen equivalents of p-toluenesulfonyl chloride (44.2 mg, 0.23 mmol). The reaction mixture was stirred for one hour. Then 1-dodecyl-1-aza-4-azoniabicyclo[2.2.2]octane bromide (85 mg, 0.23 mmol) and ethanol (10 mL) were added and reaction mixture stirred overnight. The solvent was evaporated and the resulting solid was dried under high vacuum. NMR (δ, D_2O) ^1H: 0.83, t, (-$(CH_2)_{11}$-C***H***$_3$); 1.02 – 1.33, br m, (-(C***H***$_2)_9$-CH_3); 1.46 br m, (-C***H***$_2$-$(CH_2)_9$-CH_3); 2.25, s, (C***H***$_3C_6H_4SO_3$); 2.67 – 2.83, br m, (C***H***$_2$N-); 3.12 – 3.27, m, (-N(C***H***$_2$C***H***$_2)_3$N-); 3.34, br m, (-N$(CH_2CH_2)_3$N-C***H***$_2(CH_2)_{11}$-)); 3.42, br m, (-CH_2-N$(CH_2CH_2)_3$N-); 3.56-3.90m, C_6H_6-mannose); 4.79, s, (anomeric C-H); 7.21, d, (tosylate 2H); 7.60, d, (tosylate 2H).

Preparation of Den2C16: The mannose functionalized, generation 2 dendrimer (15 mannose units, 105 mg, 0.013 mmol) was dissolved in distilled water (10 mL). To this were added sixteen equivalents of sodium bicarbonate (20.3 mg, 0.24 mmol) and sixteen equivalents of p-toluenesulfonyl chloride (41.3 mg, 0.22 mmol). The reaction mixture was stirred for one hour. Then 1-hexadecyl-1-aza-4-azoniabicyclo[2.2.2]octane chloride (83 mg, 0.22 mmol) and ethanol (10 mL) were added and reaction

mixture stirred overnight. The solvent was evaporated and the resulting solid was dried under high vacuum. NMR (δ, D_2O) ^1H: 0.88, t, (-$(CH_2)_{16}$-C***H***$_3$); 1.10 – 1.30, br m, (-(C***H***$_2)_{13}$-CH_3); 1.71 br m, (-C***H***$_2$-$(CH_2)_{13}$-CH_3); 2.20, s, (C***H***$_3C_6H_4SO_3$); 2.58 – 2.78, br m, (C***H***$_2$N-); 3.06 – 3.16, m, (-N(C***H***$_2$C***H***$_2)_3$N-); 3.33 – 3.44, br m, (-C***H***$_2$-$N(CH_2CH_2)_3$N-C***H***$_2(CH_2)_{15}$-); 3.58 – 3.89 m, C_6H_6-mannose); 4.82, s, (anomeric C-H); 7.09, d, (tosylate 2H); 7.58, d, (tosylate 2H).

The other dendrimers were prepared in a similar fashion.

H. Testing of Dendrimers for Antimicrobial Activity

The dendrimer solution (5 μL) and a stock solution of bacteria (5 μL, ~5 x 10^4, *S. aureus*, *E. coli*, or *P. aeruginosa*) were added to 4 mL of LB broth. The growth medium was incubated overnight at 37 ˚C and absorbances recorded at 600nm.

I. Modification of Polyester Surfaces

Sodium borohydride was added to absolute ethanol (100 mL). The mixture was stirred and heated to 80 ˚C. Then polyester strips were added and the fabric is left in the reaction mixture for 30 minutes. The reaction mixture is cooled for about five minutes and aqueous ammonium chloride is added.

The polyester fabric is then washed with distilled water and dried. The fabric is then placed in a mixture of concentrated sodium bicarbonate solution along with p-toluenesulfonyl chloride. The mixture is stirred overnight. The fabric is washed with distilled water and dried. Then the fabric is placed in a solution of ethanol containing dabco-C16. The mixture is stirred overnight. The fabric is washed again with distilled water and dried.

J. Testing of Polyester Surfaces for Antimicrobial Activity

A 1cm x 1cm piece of polyester (treated and untreated) was placed in a LB agar plate. Then a stock solution of bacteria (5 μL, ~5 x 10^4, *S. aureus*, *E. coli*, or *P. aeruginosa*) was added on top of each piece of fabric. The plates were incubated at 37 ˚C overnight (12 – 24 hours). The cloth was removed from the plate and placed in mL of LB broth and incubated overnight at 37 ˚C in a shaking water bath. The absorbance of of the medium was recorded at 600 nm.

K. Characterization of Polyester Surfaces-Gas Chromatograpy

A 2 cm x 3 cm sample of polyester fabric (modified and unmodified) was placed in absolute ethanol which contained dissolved sodium borohydride. The mixture was heated to at least 130 ˚C and stirred till it appeared that the

polyester had degraded. The reaction was quenched with aqueous ammonium chloride and the reaction solvent was carefully decanted. The solvent was injected into the gas chromatogram.

L. Characterization of Polyester Surfaces with Fluorescein

A 2 cm x 3 cm sample of polyester fabric (modified and unmodified) was place in 5 mL of 1% fluorescein salt solution. (The fluorescein salt was made using fluorescein and sodium hydroxide.) The solution and fabric were in a capped vial which was inverted several times. After being immersed in the solution for about five minutes, the fabric was removed and washed with copious amounts of water. The fabric was then place in a vial containing 10 mL of 0.25 % cetyltrimethylammonium bromide solution for about 10 minutes. The vial was shaken several times. The fabric was then removed and 1 mL of saline-phosphate buffer, pH 8 was added. The absorbance of the resulting solution was recorded at 501 nm.

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