Synthesis and Thermochemical Properties of Stereoisomeric Dihydroxy- and Tetrahydroxyalkylammonium Salts

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Abstract: A series of stereoisomeric ammonium salts containing the 1,2-dihydroxypropyl unit were prepared. Of particular interest to us are those salts that were found to be ionic liquids, although some are solids at room temperature. The thermochemical properties of these new materials are reported.

Key words: ionic liquids, chirality, dicyanamides, bistriflimides, phosphates

Quaternary ammonium salts have a wide range of interesting properties and applications. Past studies by this laboratory include the development of ammonium salts that can be used as phase-transfer catalysts, antihydrophobic agents, and antimicrobial agents.[1–4] More recently, we have studied various structural types of quaternary ammonium salts as ionic liquids. Ionic liquids (ILs) are pure salts that have a melting point below 100 °C.[5,6] As ILs, these salts must be in a non-aqueous, liquid state and should not contain any additional neutral molecules.[5] These two requirements rule out classical molten salts and aqueous salt solutions as ILs. Although the differentiation between ILs and molten salts or salt solutions seems arbitrary, the division lies in the large number of applications that are solely for ILs. For instance, the extremely high melting point of molten salts makes them very difficult to work with and leads to incompatibilities with many reactions.[7] Salt solutions do not have the same problem as molten salts; however, their applications are much more limited compared to ILs as the solvent plays a critical role in their behavior.

Ionic liquids are typically synthesized from large organic cations and relatively small organic or inorganic anions. Common cations include *N*,*N*′-dialkylimidazolium, tetraalkylammonium, tetraalkylphosphonium, and *N*-methylpyrrolidinium, while common anions include halides, tetrafluoroborate, and bis(trifluoromethylsulfonyl)imide (see Figure 1). There are a great variety of ILs that can potentially be made, due to the limitless number of possible cation and anion combinations. Each combination results in a compound with varied physical properties, and these properties of the ionic liquid can therefore be manipulated by choosing a particular cation and anion. Because of this variability in properties based on structure, ionic liquids have been referred to as designer solvents.[8]

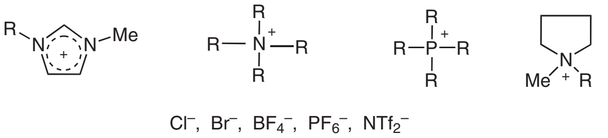

Figure 1 Common cations and anions: 1-alkyl-3-methylimidazolium, tetraalkylammonium, tetraalkylphosphonium, 1-alkyl-1-methylpyrrolidinium, chloride, bromide, tetrafluoroborate, hexafluorophosphate, and bis(trifluoromethylsulfonyl)imide

Ionic liquids in general are thermally stable, have a wide liquidus range, can exhibit high conductivities, and are usually recyclable to some extent. Most ILs also exhibit a low vapor pressure and therefore do not contribute to air pollution. Due to the ability to recycle these materials and their relative nonvolatility, ILs have received much attention as potential greener solvents. In addition, ILs have generated much interest due to their electrochemical properties and their properties with regard to radionuclides, and as possible replacements for volatile organic compounds (referred to as VOCs) currently in use. Much of the prior literature on ILs has been concerned with their use as solvents in organic synthesis and as catalysts for a range of organic reactions.[9–12] In addition to being used in synthesis, ILs can be used in chemical analyses (e.g., chromatography and electrophoresis), in large-scale separations, and as media for electrochemical processes. They can also be used as engineering fluids and performance additives.[13]

The focus of our most recent studies involving quaternary ammonium salts has been on chiral ionic liquids. Chiral ionic liquids have the potential to provide selectivity in asymmetric synthesis, chiral separations, resolutions, and electrochemical processes.[14] 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

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asymmetric synthesis and stereoselective polymerization, chiral phases for gas chromatography, chiral shift reagents for NMR spectroscopy, and chiral liquid crystals.[15]

We now report the development of a series of quaternary ammonium salts based on the potentially chiral auxiliary 3-chloropropane-1,2-diol, also known as α-chlorohydrin, with the goal of synthesizing some new ILs. This auxiliary was chosen because it is readily available and some interesting products could be developed from it. Also, since carbon–carbon bond-forming reactions such as the Diels–Alder reaction, Michael additions, or the Baylis–Hillman reaction could be influenced by hydrogen bonding, these salts might be useful solvents and/or catalysts in these types of reactions. Such reactions are widely used in the preparation of natural products and biologically active compounds. Thus, there is great interest in finding ways of enhancing rates and selectivity.

We have performed developmental work with the racemic alkyl halide 3-chloropropane-1,2-diol and have extended these efforts to the optically active species. Our goal has been to generate a series of salts, and to determine which have the best properties (low viscosity, wide liquidus range, etc.) for particular applications. Although the 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.[16] So far, they have been found to exhibit lower melting points than their racemic analogues.

Previous studies by this laboratory have involved the synthesis of two classes of ILs: liquid ionic phosphates (LIPs) which contain the phosphate anion, and polyammonium ionic liquid sulfonylimides (PILS) containing the anion bis(trifluoromethylsulfonyl)imide (also known as bistriflimide).[17,18] The synthesis of ILs usually starts with the generation of a halide salt, itself formed through an S_N2 reaction between a tertiary amine and an alkyl halide. 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, LIPs are made by using a charge equivalent amount of pure phosphoric acid in anhydrous methanol or ethanol. The solvent is then evaporated. LIPs, which are considered hydrophilic, have the particularly desirable characteristic of being more 'green' than other common types of ILs. That is, the anion does not degrade to toxic materials upon contact with other solvents, and relatively little energy is consumed in their preparation. However, many of these materials are extremely viscous and/or have high melting points, making both their characterization and use in practical applications difficult. This difficulty led to the synthesis of the corresponding PILS.

Polyammonium ionic liquid sulfonylimides are made from the corresponding halide salts by using a charge equivalent amount of lithium bis(trifluoromethylsulfonyl)imide in water. Bistriflimides tend to be hydrophobic and the salt separates from the aqueous solution.[19] The salt is washed with water until there is no presence of halide detected. In many cases this change in the anion did result in lower melting points and lower viscosities of these materials, while maintaining an anion that is relatively 'non-degradable' to toxic products.

Racemic phosphate and bistriflimide salts were synthesized and, in addition, we have also developed dicyanamide and diphenyl phosphate salts. Dicyanamide salts are prepared by reaction of the halide salt with silver dicyanamide in water. The resulting silver salt is removed by filtration and the aqueous solvent is evaporated.[20] The diphenyl phosphate salts are generally made by the reaction of a charge equivalent amount of diphenyl phosphate and potassium hydroxide with the halide salt in ethanol. The potassium salt is removed by filtration and the ethanol is evaporated, leaving the diphenyl phosphate salt.

3-Chloropropane-1,2-diol was combined with a variety of tertiary amines, such as 1,4-diazabicyclo[2.2.2]octane (DABCO), 4-(dimethylamino)pyridine (DMAP), 1-methylpyrrolidine, *N*,*N*,*N*′,*N*′-tetramethylhexane-1,6-diamine, *N*,*N*,*N*′,*N*′-tetramethylpropane-1,3-diamine, and *N*,*N*,*N*′,*N*′-tetramethylbutane-1,3-diamine, to form the halide salts. As a general trend, the halide salts could be purified simply by washing with an appropriate solvent. In this way, the other salts, such as the phosphates, bistriflimides, and dicyanamides, could be formed relatively pure with little need for further purification. All new salts were dried for several days under high vacuum and their structures were verified using ^{1}H, ^{13}C, and, where appropriate, ^{31}P NMR spectroscopy. Spectroscopic data and elemental analysis for the various salts are presented in Tables 1– 4. The structures of the various cations with the stereogenic centers labeled are presented in Figure 2. The anions are shown in Figure 3. Each cation has been assigned a letter and each anion has been assigned a number, by which the salts are designated.

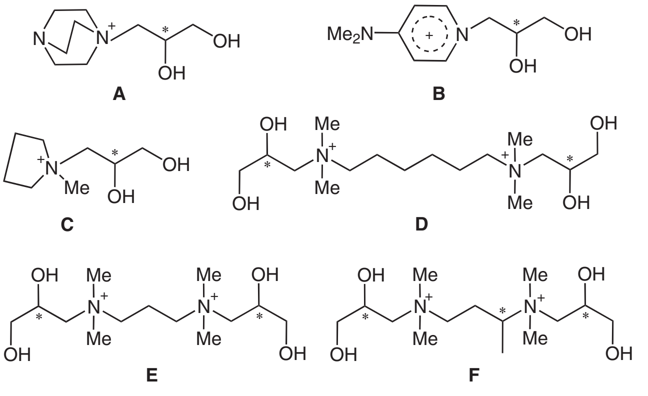

Figure 2 Cations examined in this study: 1-(2,3-dihydroxypropyl)-4-aza-1-azoniabicyclo[2.2.2]octane (**A**); 1-(2,3-dihydroxypropyl)-4-(dimethylamino)pyridinium (**B**); 1-(2,3-dihydroxypropyl)-1-methylpyrrolidinium (**C**); 4,4,11,11-tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol (**D**); 4,4,8,8-tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol (**E**); 4,4,5,8,8-pentamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol (**F**); the stereogenic sites are labeled with a star.

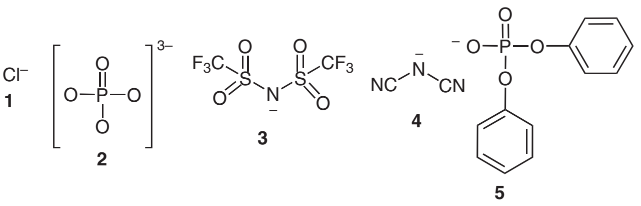

Figure 3 Anions examined in this study: chloride (**1**); phosphate (**2**); bis(trifluoromethylsulfonyl)imide (**3**); dicyanamide (**4**); diphenyl phosphate (**5**)

As demonstrated by their melting points (see Table 5), most of the salts are solid at room temperature. Melting points were determined using a capillary melting point apparatus for the solids and/or differential scanning calorimetry (DSC) for those salts that are liquid at room temperature. All of the halide salts are high-melting solids (**A1**, **B1**, **C1**, **D1**, and **E1**). The salt **F1** was prepared, but this glassy material contained the starting alkyl halide, α-chlorohydrin, which could not be readily separated. The pyridinium salt **B1** has the highest melting point range (204–207 °C). The halide salt with the lowest melting point (105 °C) is the pyrrolidinium compound **C1**. The halide salts are only soluble in water and alcohols, such as methanol and ethanol.

The phosphates (**A2**, **B2**, **C2**, and **D2**) and diphenyl phosphates (**A5**, **B5**, and **D5**) are generally also high-melting salts. In general, the melting points are lower than those of the corresponding halide salts. The phosphates are quite hydrophilic, while the diphenyl phosphates appear to be less hydrophilic. All of these salts are solid at room temperature, except for **C5**. This compound is a viscous liquid at room temperature and has a glass transition of –28 °C.

The observed stereochemical characteristics of several of the salts are worthy of mention. Salts of cations **A**, **B**, and **C** are racemic mixtures, those of cation **C** thus bearing diastereotopic carbon sites within the pyrrolidinium ring system that can not become magnetically equivalent by rotation or inversion about nitrogen. In the ^{13}C NMR spectrum of halide salt **C1**, the β-carbons of the ring could be differentiated (δ 20.5 and 21.3; see Table 1), although not the α-carbons; however, in the case of the dicyanamide salt **C4**, both the diastereotopic β- and α-carbon sites of the ring could be differentiated (δ 20.6 and 21.5, along with 66.6 and 66.8; see Table 4). It would thus appear that, in the dicyanamide salts, the cation and anion have less positional variability.

In the instances of salts derived from cation **D**, two stereogenic centers are present leading to three stereoisomeric forms. These salts consist of both a racemic mixture and a *meso* structure. In the instances of the halide salt **D1**, the bistriflimide salt **D3**, and the dicyanamide salt **D4**, two signals can be observed in the ^{13}C NMR spectra for the sets of diastereotopic methyl groups attached to the two nitrogens (δ 51.5 and 51.7 for **D1** and **D4**, 51.1 and 51.2 for **D3**; see Tables 1, 3, and 4). Two signals are also observed for the two sets of methylene carbons α to the nitrogen atoms in salts **D1** and **D4** (δ 65.3 and 65.6 for **D1**, 65.6 and 66.1 for **D4**; see Tables 1 and 4); however, with the salt **D3**, only one signal is observable for these methylene carbons α to the nitrogens (δ 64.0; see Table 3). In neither salt **D3** nor **D4** was differentiation evident for the stereogenic carbon sites in the anion.

In the instances of salts derived from cation **E** (with a shorter connecting chain between the cationic sites), for the halide salt **E1** two resonances each for the methyl and internal ammonium salt carbon sites could be observed (δ 51.9, 52.1 and 61.2, 61.4, respectively; see Table 1) and for the dicyanamide salt **E4** two resonances could be observed for three separate categories of ammonium carbon atoms (δ 51.8, 52.0: the methyl carbons on the nitrogens; 61.1, 61.3: internal methylene carbons next to the nitrogen atoms; 66.0, 66.1: the carbons with the secondary hydroxy groups; see Table 4). In constrast, diastereotopic carbon sites could not be differentiated in the case of the bistriflimide salt **E3** (see Table 3). This is in keeping with the observations for the salts derived from cation **D**, in which the bistriflimide salt exhibited the greatest positional variability while the halide and dicyanamide salts were positionally less variant.

Finally, with the bistriflimide salt **F3**, wherein three stereogenic carbon sites are present, produced from two racemic reagents, rapid rotational variance is evident as diastereoisomeric differences are not observed in the ^{13}C NMR spectrum. This, again, is in keeping with the observations for the bistriflimide salts of other cations.

All the bistriflimide salts (**B3**, **D3**, **E3**, and **F3**) are viscous ILs. As previously mentioned, bistriflimides tend to be hydrophobic but the hydroxy salts presented here are amphiphilic in nature. Because of this, a sizable quantity of the salts was lost during purification. An attempt was made to synthesize **A3** and **C3**, but these salts are water soluble and the halide impurity could not be separated. The synthesis and purification of the bistriflimides were described previously. Most of the bistriflimide salts had simple DSC traces, which displayed only a glass transition. Only **B3** (a solid at room temperature) exhibited a melting point (49.1 °C) and a glass transition. The DSC trace for this ionic liquid is shown in Figure 4.

Bistriflimide salt **F3** was prepared from the **F1** mixture (salt **F1** and α-chlorohydrin). The starting material and halide impurity were removed by washing with water. It may be the situation that purification should be delayed to the final product, rather than completed at intermediate stages.

The dicyanamide salts (**A4**, **C4**, **D4**, and **E4**) are liquids at room temperature. The exception is **B4**, which has a melting point range of 105–106 °C. The ILs also had fairly simple DSC traces that showed only a glass transition. The salts are hydrophilic and only dissolve in protic polar solvents. These liquids are not as viscous as the bistriflimide salts. Since these liquids were soluble only in water and alcohols, the existence of a halide impurity can not be ruled out.

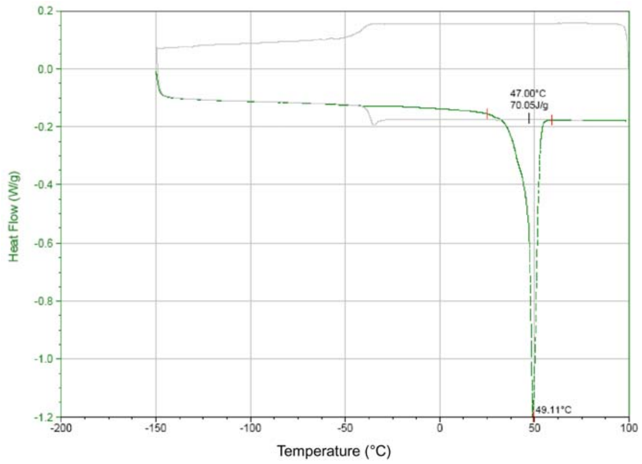

Figure 4 DSC trace for bistriflimide salt **B3**

Listed in Table 5 are the thermochemical properties of the hydroxyalkylammonium salts presented in this report, along with the water content for the ILs. The thermal decomposition onset temperatures of the ILs were determined through thermogravimetric analysis (TGA). These temperatures indicate approximately the point at which the ionic liquid begins to degrade. In general, the anion appears to have a greater influence on the thermal stability of the salts than the cation. For example, the dicyanamide anion provides the salts with the lowest degradation temperatures; thus, the degradation temperatures for **A4**, **C4**, and **D4** are 174 °C, 220 °C, and 222 °C, respectively. It should be noted that dicyanamides tend to polymerize before degrading into smaller components.[21] Evidence of this was seen during our experiments (a large amount of black solid residue remained after each experiment). Other anions such as diphenyl phosphate and bistriflimide result in salts with greater thermal stability. The diphenyl phosphate salts have degradation temperatures that range from 233 °C for **D5** to 282 °C for **B5**. The bistriflimide salts exhibit the highest thermal stability (403 °C for **B3** and 363 °C for **D3**). Rogers and co-workers noted that the onset of decomposition decreases with the increasing hydrophilicity of the anion.[22] Our findings are consistent with this observation. The TGA trace for bistriflimide salt **B3** is presented in Figure 5. The flat region between 20 °C and 100 °C indicates that very little water is present in this ionic liquid. The bistriflimide anion is known to produce ILs with high thermal stability. The cation that seems to provide the greatest thermal stability is the (dimethylamino)pyridinium cation **B**, while cations **A** and **D** result in salts with the lowest thermal stability. Most of the hydroxy ammonium salts exhibit moderate thermal stability.

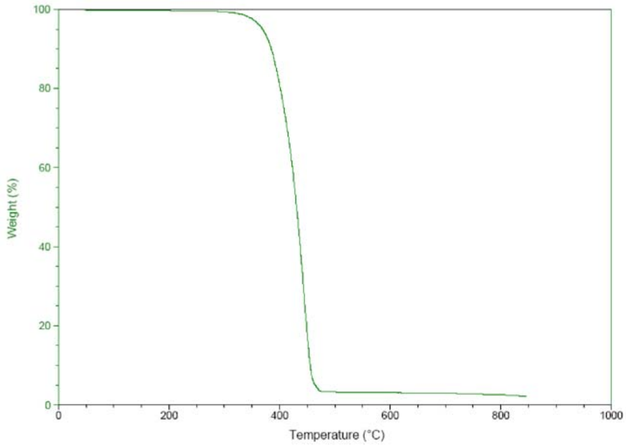

Figure 5 TGA trace for bistriflimide salt **B3**

The chiral version of the hydroxy halide salt **B1** was synthesized but we were unable to obtain the chiral pyrrolidinium halide salt **C1** in the pure form. In this case the product was complexed with unreacted starting material (α-chlorohydrin) that could not be removed. Melting points were obtained for the pure chiral salts **B1** using DSC. The melting points are about 40 degrees Celsius lower than the melting point of their racemic counterpart (see Table 6). The *S*-enantiomer of **B1** was converted into the bistriflimide salt **B3**. This chiral salt is a liquid at room temperature and the DSC trace revealed only a glass transition at 32.9 °C.

The successful synthesis of various types of stereoisomeric quaternary ammonium salts has been accomplished. Many of these salts have high melting points but some were found to be ionic liquids. These materials have the potential to be used as solvents in organic synthesis. The best potential solvent seems to be bistriflimide salt **B3**. It is easily prepared and, although a solid at room temperature, when heated to about 50 °C this ionic liquid exhibits a lower viscosity compared to the other ionic liquids developed. In addition, this liquid has a relatively high degradation temperature (403 °C).

Table 1 ^{1}H and ^{13}C NMR Spectroscopic Data and Elemental Analysis for the Halide Salts

Compound	^{1}H NMR data (400 MHz, D_2O)	^{13}C NMR data (100.6 MHz, D_2O)	Elemental analysis
A1	δ = 3.09 (t, *J* = 7.6 Hz, 6 H), 3.28 (m, 2 H), 3.40–3.52 (m, 8 H), 4.23–4.29 (br m, *J* = 2.4, 3.2 Hz, 1 H)	δ = 44.1, 53.2, 63.6, 65.2, 66.6	Calcd for $C_9H_{19}ClN_2O_2$: C, 48.54; H, 8.60. Found: C, 48.14; H, 8.36
B1	δ = 3.06 (s, 6 H), 3.44–3.54 (m, *J* = 2.8, 4.4 Hz, 2 H), 3.87–3.97 (m, *J* = 2.0, 2.4, 8.8 Hz, 2 H), 4.13–4.22 (m, 1 H), 6.73 (d, *J* = 8.0 Hz, 2 H), 7.84 (d, *J* = 7.6 Hz, 2 H)	δ = 39.4, 59.4, 62.4, 70.6, 107.4, 141.9, 156.4	Calcd for $C_{10}H_{17}ClN_2O_2\cdot H_2O$: C, 47.90; H, 7.64. Found: C, 47.83; H, 7.69

Table 1 ^1H and ^{13}C NMR Spectroscopic Data and Elemental Analysis for the Halide Salts (continued)

Compound	^1H NMR data (400 MHz, D_2O)	^{13}C NMR data (100.6 MHz, D_2O)	Elemental analysis
C1	δ = 2.12 (br, 4 H), 3.02 (s, 3 H), 3.12–3.25 (m, *J* = 4.4, 9.6 Hz, 1 H), 3.39–3.55 (br m, 7 H), 4.13–4.18 (m, *J* = 4.4, 4.8, 5.2 Hz, 1 H)	δ = 20.5, 21.3, 48.5, 63.6, 65.5, 65.8, 66.7	Calcd for $C_8H_{18}ClNO_2$: C, 49.10; H, 9.27. Found: C, 48.99; H, 9.41
D1	δ = 1.32 (br m, *J* = 6.4 Hz, 4 H), 1.69 (br m, *J* = 5.2, 6.4 Hz, 4 H), 3.05 (s, 6 H), 3.06 (s, 6 H), 3.28–3.34 (m, 8 H), 3.46–3.48 (m, *J* = 2.4, 2.8 Hz, 4 H), 4.15 (m, *J* = 4.6, 6.8 Hz, 2 H)	δ = 21.8, 25.0, 51.5, 51.7, 63.6, 65.3, 65.6, 66.1	Calcd for $C_{16}H_{38}Cl_2N_2O_4$: C, 48.85; H, 9.74. Found: C, 48.48; H, 9.54
E1	δ = 2.33 (m, 2 H), 3.17 (s, 6 H), 3.19 (s, 6 H), 3.44–3.54 (br m, 12 H), 4.25 (m, 2 H)	δ = 16.9, 51.9, 52.1, 61.2, 61.4, 63.6, 66.0, 66.2	–

Table 2 ^{31}P NMR Spectroscopic Data for the Phosphate and Diphenyl Phosphate Salts

Compound	^{31}P NMR data (162 MHz, D_2O)
A2	δ = 0.07 (s)
B2	δ = 0.10 (s)
C2	δ = 0.07 (s)
D2	δ = 0.10 (s)
A5	δ = –8.74 (s)
B5	δ = –8.96 (s)
C5	δ = –8.95 (s)
D5	δ = –8.88 (s)

Table 3 ^{13}C NMR Spectroscopic Data for the Bis(trifluoromethylsulfonyl)imide Salts

Compound	^{13}C NMR data (100.6 MHz, DMSO-d_6)
B3	δ = 39.3, 59.3, 62.4, 70.6, 107.4, 114.5, 117.6, 120.8, 124.0, 141.9, 156.5
D3	δ = 21.5, 25.2, 51.1, 51.2, 63.7, 64.0, 66.0, 114.6, 117.8, 121.0, 124.2
E3	δ = 16.4, 51.3, 60.7, 63.6, 65.9, 66.5, 114.6, 117.8, 121.0, 124.2
F3	δ = 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

Table 4 ^{13}C NMR Spectroscopic Data for the Dicyanamide Salts

Compound	^{13}C NMR data (100.6 MHz, D_2O)
A4	δ = 44.2, 53.3, 63.6, 65.2, 66.7, 120.0
B4	δ = 39.4, 59.4, 62.4, 70.6, 107.4, 120.0, 141.9, 156.4
C4	δ = 20.6, 21.5, 48.6, 63.7, 65.6, 65.9, 66.6, 66.8, 119.9
D4	δ = 21.9, 25.1, 51.5, 51.7, 63.6, 65.4, 65.6, 66.1, 120.0
E4	δ = 16.8, 51.8, 52.0, 61.1, 61.3, 63.5, 65.8, 66.0, 66.1, 120.0

Table 5 Thermochemical Properties of the Hydroxy Ammonium Salts[a]

Compound	Water content	Mp (°C)	T_g (°C)	T_{dcp} (°C)
A1	–	137–141	–	–
A2	–	125–130	–	–
A4	0.411%	–	–26	174
A5	–	139–141	–	252
B1	–	204–207	–	–
B2		116–118	–	–
B3	404 ppm	49.1	–33	403
B4	–	105–106	–	–
B5	–	93	–	282
C1	–	105	–	277
C2	–	90	–	–
C4	206 ppm	–	–68	220
C5	0.175%	–	–28	274
D1	–	161–163	–	–
D2	–	170	–	–
D3	443 ppm	–	–34	363
D4	0.220%	–	–50	222
D5	–	–	–5.1	233
E1	–	112–115	–	–
E3	–	–	–24	–
F3	–	–	–16	–

[a] T_g = glass transition, T_{dcp} = onset of decomposition temperature.

Table 6 Melting Points and Specific Rotations for the Chiral DMAP Derivatives

Compound	Mp (°C)	$[\alpha]_{589}^{25}$
B1	204–207	–
(*S*)-(–)-**B1**	164.7	–100
(*R*)-(+)-**B1**	164.2	+112.5
B3	49.1 (–33, glass transition)	–
(*S*)-(–)-**B3**	–32.9 (glass transition)	–22.4

All chemicals used in syntheses, purification, and comparison analyses were of commercial reagent quality and were used without further purification. All NMR measurements were performed on a Bruker 400 MHz DPX400 instrument in D_2O at r.t. Optical rotation data were measured using a Ruudolph Autopol III instrument operating at 589 nm with samples dissolved in water. These measurements were performed at Queens college, CUNY.

DSC data were collected using a Q100 Differential Scanning Calorimeter (TA Instruments). The scan rate was 5 degrees Celsius/min. Thermal degradation data were collected using a Q500 Thermogravimetric Analyzer (TGA, TA Instruments). The scan rate was 10 degrees Celsius/min. Onset decomposition temperatures were determined using the Universal Analysis 2000 Software provided by TA Instruments. Water content was determined using the TGA or a Mettler Toledo DL39 Karl Fischer Coulometer. These instruments were used at Brookhave National Laboratory, Upton, New York. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, New York.

Synthesis of the Halide Salts

1-(2,3-Dihydroxypropyl)-4-aza-1-azoniabicyclo[2.2.2]octane Chloride (A1)

DABCO (9.98 g, 0.089 mol) was dissolved in EtOAc (65 mL). To this, 3-chloropropane-1,2-diol (9.68 g, 0.088 mol) was added. The reaction mixture was stirred for 24 h. The solvent was removed by rotary evaporation under reduced pressure. The resulting solid was stirred with MeCN (50 mL) for 24 h. The solid was collected by filtration, washed with Et_2O (3 × 30 mL), and dried under high vacuum to give **A1** as a white solid; yield: 14.3 g (73%).

1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Chloride (B1)

DMAP (21.78 g, 0.18 mol) was dissolved in MeCN (150 mL). To this was added 3-chloropropane-1,2-diol (19.71 g, 0.18 mol) and the reaction mixture was stirred and refluxed at 65 °C for 24 h. This resulted in a precipitate, which was collected by gravity filtration and washed with EtOAc (3 × 30 mL) and Et_2O (3 × 30 mL). The solid was dried under high vacuum to give **B1** as a white solid; yield: 40.78 g (97%).

(*S*)-(–)-1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Chloride [(*S*)-(–)-B1]

This salt was made following the procedure described for **B1** above, using (*R*)-(–)-3-chloropropane-1,2-diol; yield: 96%.

(*R*)-(+)-1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Chloride [(*R*)-(+)-B1]

This salt was made following the procedure described for **B1** above, using (*S*)-(+)-3-chloropropane-1,2-diol; yield: 95%.

^1H NMR (400 MHz, D_2O): δ = 3.07 (s, 6 H), 3.48–3.51 (m, 2 H), 3.92–3.95 (m, 2 H), 4.17–4.20 (br m, 1 H), 6.75 (d, *J* = 8.0 Hz, 2 H), 7.84 (d, *J* = 8.0 Hz, 2 H).

1-(2,3-Dihydroxypropyl)-1-methylpyrrolidinium Chloride (C1)

1-Methylpyrrolidine (25.02 g, 0.29 mol) was dissolved in MeCN (140 mL). Then, 3-chloropropane-1,2-diol (32.5 g, 0.29 mol) was added. The reaction mixture was allowed to reflux at 65 °C for 24 h. The solvent was removed by rotary evaporation under high vacuum, and the remaining liquid was dried under high vacuum. This resulted in the formation of a brown crystalline solid, which was washed repeatedly with MeCN until it was white. The solid was dried under high vacuum; yield: 36.8 g (64%).

4,4,11,11-Tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol Dichloride (D1)

N,*N*,*N*′,*N*′-Tetramethylhexane-1,6-diamine (7.50 g, 0.044 mol) was dissolved in 95% EtOH (40 mL). To this was added 3-chloropropane-1,2-diol (10.0 g, 0.090 mol, 2 equiv). The reaction mixture was refluxed at 65 °C for 24 h. The solvent was removed by rotary evaporation leaving a white solid. The solid was washed with hexanes and dried under reduced pressure; yield: 16.56 g (94%).

4,4,8,8-Tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol Dichloride (E1)

N,*N*,*N*′,*N*′-Tetramethylpropane-1,3-diamine (5.0 g, 0.038 mol) was dissolved in a 4:1 soln of MeCN–EtOH (25 mL). To this, 3-chloropropane-1,2-diol (8.58 g, 0.078 mol) was added. The reaction mixture was refluxed at 65 °C for 24 h, and the solvent was removed by rotary evaporation under reduced pressure. The resulting viscous liquid was dissolved in EtOH (25 mL), and Et_2O (50 mL) 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 was washed with EtOAc and dried again under high vacuum; yield: 11.7 g (88%).

4,4,5,8,8-Pentamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol Dichloride (F1)

N,*N*,*N*′,*N*′-Tetramethylbutane-1,3-diamine (5.0 g, 0.035 mol) was dissolved in a 4:1 soln of MeCN–EtOH (25 mL). To this, 3-chloropropane-1,2-diol (8.48 g, 0.077 mol) was added. The reaction mixture was refluxed at 65 °C for 24 h, and the solvent was removed by rotary evaporation under reduced pressure. The resulting viscous liquid was dissolved in EtOH (25 mL), and Et_2O (50 mL) was added to precipitate the product. The solvent was decanted and the clear, yellow viscous liquid was dried under high vacuum. (The product contained excess 3-chloropropane-1,2-diol.)

Synthesis of the Phosphate Salts

1-(2,3-Dihydroxypropyl)-4-aza-1-azoniabicyclo[2.2.2]octane Phosphate (A2)

Chloride salt **A1** (7.62 g, 0.034 mol) was dissolved in MeOH (40 mL). To this, an excess of 98% H_3PO_4 (0.60 g) was added. The reaction mixture was stirred for 24 h. A white precipitate was filtered off and the solvent was evaporated. The resulting pale yellow solid was dried in a high-vacuum oven; yield: 3.92 g (41%).

1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Phosphate (B2)

Chloride salt **B1** (2.08 g, 0.009 mol) was dissolved in MeOH (35 mL). To this was added a charge equivalent amount plus 2% excess of 98% H_3PO_4 (0.38 g, 0.004 mol). The reaction mixture was stirred for 24 h. The solvent was removed by rotary evaporation under reduced pressure. The resulting white solid was recrystallized (abs EtOH) and dried under high vacuum; yield: 1.94 g (74%).

1-(2,3-Dihydroxypropyl)-1-methylpyrrolidinium Phosphate (C2)

Chloride salt **C1** (4.96 g, 0.027 mol) was dissolved in 95% EtOH (50 mL). To this was added a charge equivalent amount of 98% H_3PO_4 (1.2 g). The reaction mixture was stirred for 24 h. The solvent was removed by rotary evaporation under reduced pressure. The resulting viscous white solid was dried under high vacuum; yield: 5.0 g (96%).

Tris-(4,4,11,11-Tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol) Diphosphate (D2)

Chloride salt **D1** (7.0 g, 0.018 mol) was dissolved in MeOH (50 mL). To this, a charge equivalent amount of 85% H_3PO_4 (1.0 g) was added. The reaction mixture was stirred for 24 h. The solvent was removed by rotary evaporation under reduced pressure, leaving behind a white solid. The solid was recrystallized (EtOH) and dried under high vacuum; yield: 3.5 g (50%).

Synthesis of the Bis(trifluoromethylsulfonyl)imide Salts

1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Bis(trifluoromethylsulfonyl)imide (B3)

Chloride salt **B1** (6.0 g, 0.025 mol) was dissolved in distilled H_2O (50 mL). To this was added a charge equivalent amount of lithium bis(trifluoromethylsulfonyl)imide (7.25 g, 0.025 mol). The reaction mixture was stirred for 24 h. The solvent was carefully decanted and the remaining liquid was washed with H_2O until there was no detectable halide (50 mM aq $AgNO_3$ was used to test the wash). The resulting low-melting solid was dried under high vacuum; yield: 3.54 g (30%).

(*S*)-(–)-1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Bis(trifluoromethylsulfonyl)imide [(*S*)-(–)-B3]

This salt was prepared from chloride (*R*)-(–)-**B1** following the procedure described for **B3** above; yield: 50%.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.14 (s, 6 H), 3.25–3.30 (dd, J = 4.4, 6.4 Hz, 1 H), 3.42–3.46 (dd, J = 4.8, 5.2 Hz, 1 H), 3.70–3.80 (br m, 1 H), 4.04–4.09 (dd, J = 5.6, 8.0 Hz, 1 H), 4.30–4.34 (dd, J = 2.8, 10.8 Hz, 1 H), 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, 2 H).

4,4,11,11-Tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol Bis[bis(trifluoromethylsulfonyl)imide] (D3)

Chloride salt **D1** (10.10 g, 0.026 mol) was dissolved in distilled H_2O (50 mL). To this was added a charge equivalent amount of lithium bis(trifluoromethylsulfonyl)imide (14.93 g, 0.052 mol). The reaction mixture was stirred for 24 h. The solvent was carefully decanted and the remaining liquid was washed with H_2O until there was no detectable halide (50 mM aq $AgNO_3$ was used to test the wash). The resulting pale yellow liquid was dried under high vacuum; yield: 8.77 g (38%).

4,4,8,8-Tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol Bis[bis(trifluoromethylsulfonyl)imide] (E3)

Chloride salt **E1** (5.9 g, 0.017 mol) was dissolved in distilled H_2O (50 mL). To this was added a charge equivalent amount of lithium bis(trifluoromethylsulfonyl)imide (9.7 g, 0.034 mol). The reaction mixture was stirred for 24 h. The solvent was carefully decanted and the remaining liquid was washed with H_2O until there was no detectable halide (50 mM aq $AgNO_3$ was used to test the wash). The resulting liquid was dried under high vacuum; yield: 0.71 g (5%).

4,4,5,8,8-Pentamethyl-4,8-diazoniaundecane-1,2,10,11-tetrol Bis[bis(trifluoromethylsulfonyl)imide] (F3)

Chloride salt **F1** (a mixture of product **F1** and excess 3-chloropropane-1,2-diol starting material, 5.0 g) was dissolved in distilled H_2O (50 mL). To this was added a charge equivalent amount of lithium bis(trifluoromethylsulfonyl)imide (9.0 g, 0.031 mol). The reaction mixture was stirred for 24 h. The solvent was carefully decanted and the remaining liquid was washed with H_2O until there was no detectable halide (50 mM aq $AgNO_3$ was used to test the wash). The resulting liquid (6.0 g) was dried under high vacuum.

Synthesis of the Dicyanamide Salts

1-(2,3-Dihydroxypropyl)-4-aza-1-azoniabicyclo[2.2.2]octane Dicyanamide (A4)

Chloride salt **A1** (8.20 g, 0.037 mol) was dissolved in distilled H_2O (25 mL). To this, a charge equivalent amount of $AgN(CN)_2$ was added. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for 24 h. The resulting solid was gravity filtered and the filtrate was washed with Et_2O (3 × 30 mL), hexanes (3 × 30 mL), and EtOAc (3 × 30 mL). The water was then evaporated and the resulting viscous liquid was dried in a high-vacuum oven to give **A4** as a viscous brown liquid at r.t.; yield: 7.51 g (80%).

1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Dicyanamide (B4)

Chloride salt **B1** (2.14 g, 0.009 mol) was dissolved in distilled H_2O (25 mL). To this was added a charge equivalent amount plus 2% excess of $AgN(CN)_2$. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for 24 h. The resulting precipitate was gravity filtered and the filtrate was washed with Et_2O (3 × 30 mL) and hexanes (3 × 30 mL). The aqueous solvent was removed by rotary evaporation under reduced pressure. The resulting pale yellow solid was dried under high vacuum; yield: 1.6 g (66%).

1-(2,3-Dihydroxypropyl)-1-methylpyrrolidinium Dicyanamide (C4)

Chloride salt **C1** (5.0 g, 0.025 mol) was dissolved in distilled H_2O (25 mL). To this was added a charge equivalent amount plus 2% excess of $AgN(CN)_2$. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for 24 h. The resulting silver halide salt was gravity filtered and the filtrate was washed with Et_2O (3 × 30 mL) and hexanes (3 × 30 mL). The aqueous solvent was removed by rotary evaporation under reduced pressure to give a yellow liquid; yield: 4.5 g (80%).

4,4,11,11-Tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol Bis(dicyanamide) (D4)

Chloride salt **D1** (5.46 g, 0.014 mol) was dissolved in distilled H_2O (25 mL). To this was added a charge equivalent amount plus 2% excess of $AgN(CN)_2$. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for 24 h. The resulting silver halide salt was gravity filtered and the filtrate was washed with Et_2O (3 × 30 mL) and hexanes (3 × 30 mL). The aqueous solvent was removed by rotary evaporation under reduced pressure. The resulting yellow liquid was dried under reduced pressure; yield: 4.45 g (70%).

4,4,8,8-Tetramethyl-4,8-diazoniaundecane-1,2,10,11-tetrol Bis(dicyanamide) (E4)

Chloride salt **E1** (5.8 g, 0.017 mol) was dissolved in distilled H_2O (25 mL). To this was added a charge equivalent amount plus 2% excess of $AgN(CN)_2$. The reaction flask was covered with aluminum foil and the reaction mixture was stirred for 24 h. The resulting silver halide salt was vacuum filtered. The aqueous solvent was removed by rotary evaporation under reduced pressure. The resulting yellow liquid was dried under high vacuum; yield: 4.9 g (70%).

Synthesis of the Diphenyl Phosphate Salts

1-(2,3-Dihydroxypropyl)-4-aza-1-azoniabicyclo[2.2.2]octane Diphenyl Phosphate (A5)

Chloride salt **A1** (2.1 g, 0.009 mol) was dissolved in abs EtOH (50 mL). To this, a charge equivalent amount of diphenyl phosphate (2.4 g, 0.009 mol) and KOH (0.5 g, 0.009 mol) were added. The reaction mixture was stirred for about 3 d. The resulting solid (KCl) was removed by gravity filtration. The solvent of the filtrate was removed by rotary evaporation under reduced pressure, leaving a viscous liquid, which later solidified. The solid was recrystallized (abs EtOH), and the white solid was dried under high vacuum; yield: 1.5 g (38%).

1-(2,3-Dihydroxypropyl)-4-(dimethylamino)pyridinium Diphenyl Phosphate (B5)

Chloride salt **B1** (2.08 g, 0.009 mol) was dissolved in abs EtOH (50 mL). To this were added a charge equivalent amount of diphenyl phosphate (2.24 g, 0.009 mol) and KOH (0.51 g, 0.009 mol). The reaction mixture was stirred for 24 h. The potassium salt was removed by vacuum filtration and the solvent of the filtrate was evaporated. The resulting white solid was washed with Et_2O (3 × 10 mL) and dried under reduced pressure; yield: 3.3 g (83%).

1-(2,3-Dihydroxypropyl)-1-methylpyrrolidinium Diphenyl Phosphate (C5)

Chloride salt **C1** (2.0 g, 0.01 mol) was dissolved in abs EtOH (50 mL). To this were added a charge equivalent amount of diphenyl phosphate (2.6 g, 0.01 mol) and KOH (0.6 g, 0.01 mol). The reaction mixture was stirred for 24 h. The potassium salt was removed by vaccum filtration and the solvent of the filtrate was evaporated. The resulting yellow liquid was dissolved in MeOH (50 mL) and charcoal (5–10 mg) was added. The mixture was stirred for 24 h and the charcoal was removed by gravity filtration. The liquid was then passed through an alumina column. The solvent was evaporated and the resulting pale yellow liquid was dried under reduced pressure; yield: 1.9 g (47%).

4,4,11,11-Tetramethyl-4,11-diazoniatetradecane-1,2,13,14-tetrol Bis(diphenyl phosphate) (D5)

Chloride salt **D1** (5.0 g, 0.013 mol) was dissolved in MeOH (50 mL). To this was added a charge equivalent amount of diphenyl phosphate (6.2 g, 0.025 mol). The reaction mixture was stirred for 24 h. The solvent was evaporated and the resulting white solid was dried under reduced pressure; yield: 10.1 g (95%).

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