Synthesis and Properties of Chiral Ammonium-Based Ionic Liquids

Juliusz Pernak* and Joanna Feder-Kubis[a]

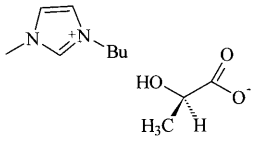
Abstract: New chiral ammonium-based ionic liquids containing the (1*R*,2*S*,5*R*)-(−)-menthyl group can be easily and efficiently prepared under ambient conditions. The preparation and characterization of trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium salts is reported. The salts have been demonstrated to be air- and moisture-stable under ambient conditions and can be readily used in a variety of standard experimental procedures. The single-crystal X-ray structure of butyldimethyl-[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chloride has been determined. The chiral, room-temperature ionic liquids have been characterized by physical properties such as specific rotation, density, viscosity, thermal degradation, and glass transition temperature. Trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chloride prototype ionic liquids have also been found to exhibit strong antimicrobial and high antielectrostatic activities.

Keywords: ammonium salts · antimicrobial activity · chirality · green chemistry · ionic liquids · menthol

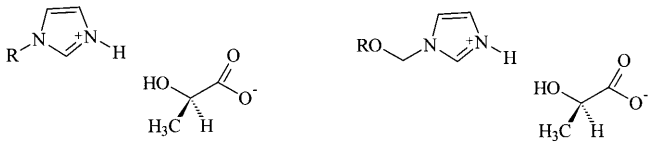
Introduction

Ionic liquids (ILs) open up a wide field for future investigations in chemistry, electrochemistry, biology, physics, material science, and medicine. The first IL was prepared almost a century ago by protonation of ethylamine with nitric acid.[1] Owing to their unique chemical and physical properties, these groups of liquids based on organic cations have been extensively studied over the past few years as neoteric and "green" solvents. ILs possess a number of interesting properties, such as their lack of vapor pressure (they cannot contribute to air pollution) and their large liquid range. They are highly solvating, yet have a noncoordinating nature and a wide accessible temperature range within which they are not flammable. They are also compatible with various organic compounds, organometallic catalysts, and even some inorganic compounds, and generally can be easily separated from reaction products. Most importantly, the ionic liquids can be recycled. A number of excellent articles are already available wherein the properties and various applications of these environmentally friendly media have been described.[2–10] In recent years, the number of possible cation and anion combinations has increased significantly and thus, due to the large number of ILs to choose from, a high potential exists to find the optimum one with satisfactory properties for a specific application.

The newest class of ILs are chiral ionic liquids (CILs). The method of synthesis of CILs and the investigation of ILs in the field of chirality have recently been reviewed.[11] Few CILs have been described and their real potential in asymmetric synthesis remains to be proven. From a structural point of view, chirality in these salts can arise from either the anion or the cation. Aprotic and protic ILs in which the chirality resides in the anion are presented in Scheme 1. Chiral salts (**I**) have been successfully used in asymmetric Diels–Alder reactions.[12] The properties and antimicrobial activities of protic imidazolium L-lactates (**II**) have recently



I



II

Scheme 1. Aprotic and protic imidazolium lactates.

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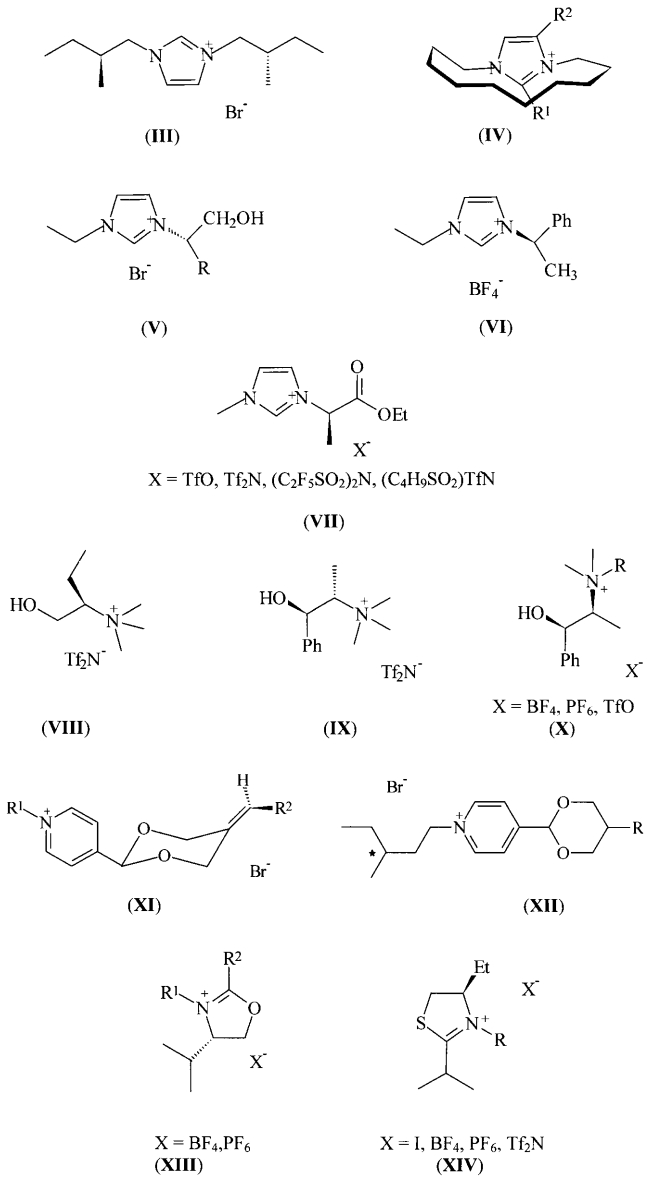
been recognized.[13] In subsequent examples, chirality in the salts has been introduced by cations such as imidazolium, ammonium, pyridinium, oxalium, and thiazolium (Scheme 2). The chiral 1,3-dialkylimidazolium bromide **III** acts as a Lewis acid in asymmetric Diels–Alder reactions.[14] Imidazolium salts with planar chirality (**IV**)[15] and chiral lateral chains (**V**, **VI**)[16] and (**VII**)[17] have also been prepared. Chiral hydroxyammonium ILs (**VIII**, **IX**) derived from chiral amino alcohols have been obtained on a kilogram scale,[18] and salts such as **X** have been produced under solvent-free conditions with the aid of microwave activation.[19] Pyridinium CILs with axial chirality (**XI**) have been synthesized through an enantioselective reaction,[11] while other pyridinium derivatives have the chirality residing in the alkyl substituent (**XII**).[20] Oxazolium salts (**XIII**)[18] have been derived from (*S*)-valine on a multigram scale and thiazolium CILs (**XIV**)[21] have been obtained from amino alcohols.

Entirely new are room-temperature ionic liquids (RTILs) from natural amino acids. A series of these has been prepared by coupling the imidazolium cation with 20 different natural amino acids.[22]

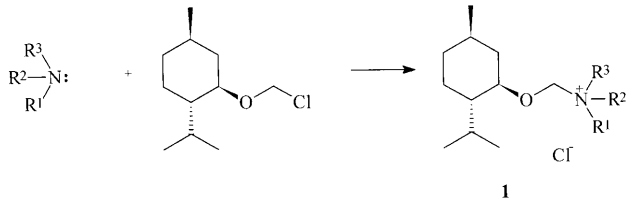
Herein, we wish to report the straightforward synthesis of a novel class of chiral ammonium-based ionic liquids, derived from the "chiral pool".



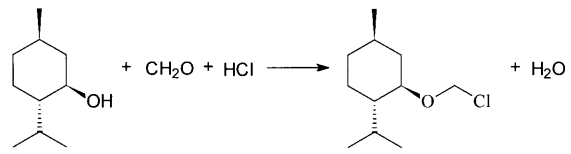
Scheme 2. Chiral imidazolium, ammonium, pyridinium, oxazolium, and thiazolium ILs.

Results and Discussion

The trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chlorides, which are prototypes of ionic liquids, were prepared by Menschutkin quaternization (Scheme 3). Chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether was obtained by chloromethylation of (1*R*,2*S*,5*R*)-(−)-menthol (Scheme 4). The (−)-isomer, a well-known compound, has previously



Scheme 3. Preparation of the trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]-ammonium chlorides by Menschutkin quaternization.



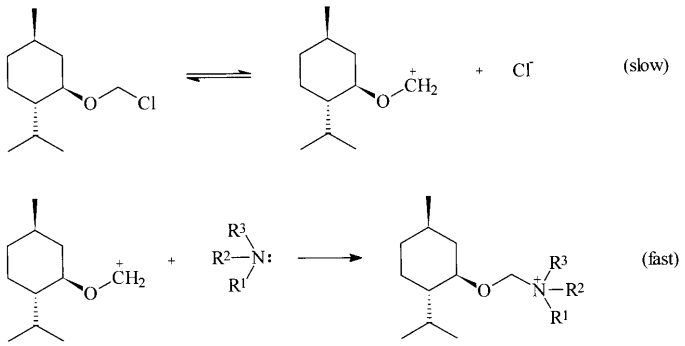
Scheme 4. Chloromethylation of (1*R*,2*S*,5*R*)-(−)-menthol.

been prepared in 55% yield[23] by bubbling anhydrous HCl through a solution of (−)-menthol and 1,3,5-trioxane in CH_2Cl_2 or in 90% yield by carrying out the same reaction in pentane solution.[24] We have now developed an effective way to synthesize this ether in up to 90% yield by using paraformaldehyde with toluene as the solvent.

In the past, chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether has been used for the synthesis of diastereomeric formaldehyde acetals[23,25,26] and for the protection of a range of chiral alcohols.[27]

Chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether is an excellent reagent for quaternization, but it is readily hydrolyzed to HCl, CH_2O, and menthol. In view of this situation, quaternization should be conducted under strictly anhydrous conditions. This permits a specific type of Menschutkin reac-

tion involving an S_N1 mechanism, giving a very high yield of 96–99%. The initial rate-determining step has been identified as being the formation of the cation (Scheme 5).



Scheme 5. Menschutkin reaction type 1.

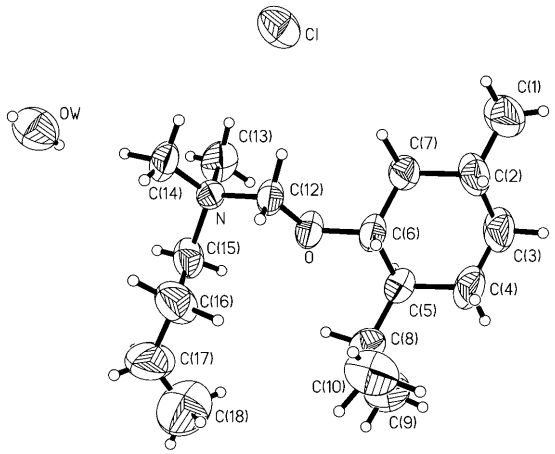


Figure 1. The molecular components of chloride **1e** showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as spheres of arbitrary radii.

Table 1 lists the chiral ammonium chlorides **1** that have been prepared by this procedure. They are very hygroscopic, but are stable in aqueous solution. Some crystalline chlorides such as **1b**, **1g**, and **1i**–**1l** are very deliquescent, which has made it difficult to determine their true melting points. The remaining chlorides are snow-white crystals. In aqueous solution, they can be assayed by a direct two-phase back titration according to the EN ISO 2871-1 (2000) norm. The assays of each product are given in Table 1. Water makes up the remainder. Specific rotations for all the chlorides are also presented in Table 1. All these precursors of ILs are soluble at room temperature in acetone, chloroform, DMF, THF, methanol, ethanol, 1-propanol, 2-propanol, and water. Aqueous solutions of chlorides **1f**–**1l** have been observed to foam during the dissolution process. At elevated temperatures, the chlorides **1** have been found to dissolve in ethyl acetate but not in hexane or diethyl ether.

Crystals of chloride **1e** suitable for single-crystal X-ray structural analysis were collected by filtration, washed with hexane, and air-dried. Figure 1 shows the asymmetric unit and the numbering scheme of **1e**. It is interesting to note that, to the best of our knowledge, this is the first example of a structurally characterized trialkyl(alkoxymethyl)ammonium cation of this type. The bond lengths and angles have typical values. The apparent shortening of the terminal C–C single bond in the *n*-butyl chain is probably an artifact of the large thermal parameters of the atoms involved. The conformation of the *n*-butyl chain can be described by N-C-C-C and C-C-C-C torsion angles along the chain of 174.7(5)° and 106.7(10)°, respectively. The crystal structures of the ionic liquids characterized to date, for example imidazolium derivatives, have been found to be mainly determined by the presence of π stacking, weak hydrogen bonds, or in some cases mainly by the presence of electrostatic anion–cation interactions (e.g., 1-ethyl-2-methyl-3-benzylimidazolium bis(trifluoromethylsulfonyl)amide).[28] The structure of the salt **1e** is different because there is no π-electron system that can interact with other π electrons or even with CH groups.[29,30] In the crystal structure, the ammonium cations are seen to create channels parallel to the two-fold screw axis along the [010] direction, and these channels are filled by chains made up of chloride anions and water molecules. The chain structure is maintained by relatively strong and directional O–H···Cl^- hydrogen bonds (see Table 2, Figures 2 and 3). Anion–water chains are connected to the cation scaffold through electrostatic interactions and weak C–H···O and C–H···Cl^- hydrogen bonds (Table 2, Figure 2). Similar water–fluoride anion chains were found in the structure of 1-butyl-3-methylimidazolium fluoride.[31]

Table 1. Trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chlorides (**1**).

	R^1	R^2	R^3	Yield [%]	M.p. [°C]	Surfactant content [%]	Specific rotation[f] $[\alpha]_D^{20}$
1a	C_2H_5	C_2H_5	C_2H_5	98.0	31–33[a]	96.5	−57.4 (c=1.1)
1b	C_2H_5	C_2H_5	CH_3	97.5	hygroscopic	96.7	−59.5 (c=0.7)
1c	C_2H_5	CH_3	CH_3	99.0	87.5–90[a]	97.0	−68.7 (c=0.9)
1d	*i*-C_3H_7	CH_3	CH_3	98.5	158–161[b]	97.9	−71.3 (c=0.6)
1e	C_4H_9	CH_3	CH_3	96.0	130–132[c]	96.5	−64.8 (c=1.1)
1f	C_6H_{13}	CH_3	CH_3	97.0	113–116[a]	97.6	−55.7 (c=0.7)
1g	C_7H_{15}	CH_3	CH_3	97.0	hygroscopic	97.9	−54.1 (c=0.7)
1h	C_8H_{17}	CH_3	CH_3	98.5	74–76[d]	99.9	−54.1 (c=1.0)
1i	C_9H_{19}	CH_3	CH_3	97.0	hygroscopic	99.1	−50.3 (c=0.5)
1j	$C_{10}H_{21}$	CH_3	CH_3	97.0	hygroscopic	99.8	−51.5 (c=1.4)
1k	$C_{11}H_{23}$	CH_3	CH_3	97.0	hygroscopic	99.9	−48.8 (c=0.8)
1l	$C_{12}H_{25}$	CH_3	CH_3	97.5	hygroscopic	99.8	−48.3 (c=1.5)
1m	CH_2Ph	CH_3	CH_3	99.0	126–129[e]	99.0	−63.5 (c=1.1)

[a] From ethyl acetate; plates. [b] From ethyl acetate/ethanol; plates. [c] From ethyl acetate/acetone; large needles. [d] From ethyl acetate; needles. [e] From ethyl acetate/chloroform; plates. [f] c in ethanol.

Table 2. Selected hydrogen bonds in the crystal structure of chloride **1e**.

Donor–H···Acceptor	D–H [Å]	H···A [Å]	D···A [Å]	D–H···A [°]
O2–H21···Cl[a]	0.96	2.27	3.190(4)	160
O2–H22···Cl[b]	0.88	2.41	3.217(4)	152
C12–H12A···Cl	0.97	2.75	3.655(4)	156
C12–H12B···O2[c]	0.97	2.53	3.455(6)	159
C13–H13A···O2[d]	0.97	2.60	3.488(7)	154
C14–H14B···O2	0.97	2.55	3.501(6)	173
C15–H15A···Cl[a]	0.97	2.76	3.693(5)	162

Symmetry codes: [a] x, $-1+y$, z; [b] $-x$, $-{}^1/_2+y$, ${}^1/_2-z$; [c] $1-x$, ${}^1/_2+y$, ${}^1/_2-z$; [d] $-x$, ${}^1/_2+y$, ${}^1/_2-z$.

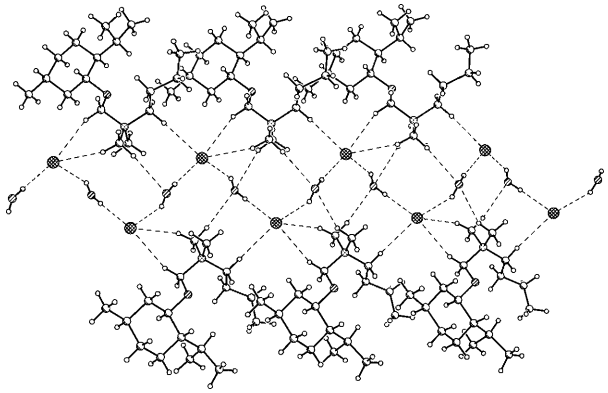


Figure 2. The packing scheme of chloride **1e** as seen approximately along the [100] direction. Hydrogen bonds are depicted as dashed lines.

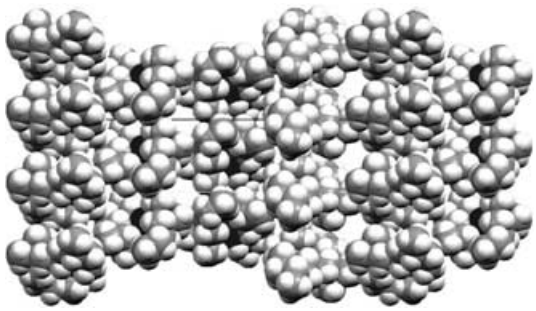


Figure 3. Space-filling model of the cationic crystal structure of **1e** as seen along the [010] direction (after removal of chloride anions and water molecules). The channels that can be filled by anion–water polymeric chains are seen along a 2_1 screw axis at (0, y, ${}^1/_4$) and (${}^1/_2$, y, ${}^3/_4$). The nine black spheres represent oxygen.

The final step of the synthesis involved metathesis of the chlorides with an appropriate inorganic salt in a water/methanol solution. The ion-exchange reaction proceeded smoothly, with the efficiency usually exceeding 90%. All of the $[BF_4]$ (**2**), $[ClO_4]$ (**3**), [I] (**4**), $[PF_6]$ (**5**), and $[CF_3COO]$ (**6**) salts with **1** were obtained as solids and could be easily crystallized from ethanol/water solution to form white plates with sharp melting points. Salts **2**–**5** were found to be insoluble in water. Thus, by changing the counteranion, hydrophilic chlorides are transformed to hydrophobic salts. We also obtained acesulfamates (**7**) in the form of oils, which proved to be fully water-miscible at room temperature. Of the 18 salts prepared, 12 would qualify as ILs (salts that melt at $<100\,^\circ C$). Table 3 contains the melting points, estimated assays in methanol/chloroform solutions, and specific rotations of **2**–**7**. These salts are insoluble in hexane or diethyl ether, but are soluble in acetone, chloroform, DMF, THF, ethyl acetate, toluene, and low-molecular-weight alcohols.

On the other hand, RTILs can be obtained by changing the chloride anion to $[Tf_2N]$. Table 4 lists 13 $[Tf_2N]$ (**8**) salts, including 10 which represent RTILs. All of the RTILs are colorless liquids, and are nonvolatile, nonflammable, and miscible with acetone, chloroform, ethyl acetate, DMF, THF, toluene, and low-molecular-weight alcohols. They are insoluble in hexane and diethyl ether, and are miscible with water. They are stable in air, in contact with water, and in commonly used organic solvents.

The salts were characterized by ^1H and ^{13}C NMR analyses and by elemental analysis. Comparison of the ^1H NMR spectra of the chlorides **1** with those of the salts **2**–**8** indicated differences in the proton chemical shifts, as listed in Table 5. These shift differences were observed most prominently in four functional groups: N^+CH_2O, OCH(menthyl-C6), $N^+CH_2R^1$, and $N^+(CH_3)_2$. The substitution of the small [Cl] anion with the larger $[Tf_2N]$ or $[PF_6]$ resulted in proton-shift differences of as much as 0.43 ppm. The ^{13}C NMR spectra of salts **1**–**8** indicated no significant variations in the carbon-signal shifts.

The RTILs can be made anhydrous by heating them at 80°C in vacuo and storing them over P_4O_{10}. The water content was determined to be less than 500 ppm by coulometric Karl–Fischer titration. After 30 days, these anhydrous liquids were found to have absorbed water from the atmosphere to a level of 1.4%. From this observation, we assume that the solubility of water in these ILs does not exceed 1.5%. On the other hand, the solubility of the ILs in water was found to be low, comparable to that of [methyltributylammonium][Tf_2N], $0.7\,g\,L^{-1}$.[32] The hydrophobic character of these RTILs is imparted by the $[Tf_2N]$ anion, which is responsible for interactions between water and the IL. Water interacts strongly with the anions and the strength of the interactions is dependent on the nature of the anions.[33] The low water content measured is of importance for future applications. Removal of chloride ions from the hydrophobic ILs has been demonstrated by rinsing them with distilled water. The specific rotations, densities, viscosities, thermal degradation temperatures, and glass transition temperatures for anhydrous and chloride-free RTILs have been measured. The results are presented in Table 4. The CILs are more dense than water (1.25 to $1.14\,g\,mL^{-1}$). As a general conclusion, it can be stated that elongation of the alkyl substituent leads to a concomitant linear decrease in density. The densities of the ILs are temperature dependent. As the temperature is varied from 30 to 40°C, the density decreases by about 3%. ILs are inherently much more viscous than common organic solvents and the viscosities vary in the range from 10 to 1000 mPa s at room temperature.[10]

Table 3. Trialkyl[(1*R*,2*S*,5*S*)-(−)-menthoxymethyl]ammonium salts (**2–7**).

Salt	R^1	R^2	R^3	Anion	Yield [%]	M.p. [°C]	Surfactant content [%]	Specific rotation[b] $[\alpha]_D^{20}$
2a	C_2H_5	C_2H_5	C_2H_5	BF_4^-	99.5	125–126.5	99.8	−64.8 ($c=0.4$)
2b	C_2H_5	C_2H_5	CH_3	BF_4^-	99.0	150.5–152	99.5	−61.5 ($c=1.0$)
2c	C_2H_5	CH_3	CH_3	BF_4^-	99.0	161.5–164	98.9	−63.5 ($c=1.0$)
2d	*i*-C_3H_7	CH_3	CH_3	BF_4^-	99.0	203–206	98.5	−61.2 ($c=0.8$)
2e	C_4H_9	CH_3	CH_3	BF_4^-	98.5	68.5–71	97.7	−58.3 ($c=1.1$)
2f	C_6H_{13}	CH_3	CH_3	BF_4^-	99.0	42–44	99.7	−52.7 ($c=1.0$)
2g	C_7H_{15}	CH_3	CH_3	BF_4^-	99.5	69–72	99.5	−49.1 ($c=1.0$)
2h	C_8H_{17}	CH_3	CH_3	BF_4^-	99.0	87.5–88.5	98.7	−48.9 ($c=1.4$)
2i	C_9H_{19}	CH_3	CH_3	BF_4^-	99.5	69–72	99.9	−47.3 ($c=1.0$)
2j	$C_{10}H_{21}$	CH_3	CH_3	BF_4^-	99.5	55–58	98.5	−44.8 ($c=1.0$)
2k	$C_{11}H_{23}$	CH_3	CH_3	BF_4^-	99.5	43–48	99.1	−44.4 ($c=1.0$)
2l	$C_{12}H_{25}$	CH_3	CH_3	BF_4^-	99.5	42.5–43	99.9	−38.4 ($c=1.0$)
2m	CH_2Ph	CH_3	CH_3	BF_4^-	99.5	97.5–100	98.5	−58.2 ($c=1.0$)
3	C_4H_9	CH_3	CH_3	ClO_4^-	99.0	77–78.5	98.1	−56.4 ($c=0.9$)
4	C_4H_9	CH_3	CH_3	I^-	99.5	81–83	98.9	−51.3 ($c=0.9$)
5	C_4H_9	CH_3	CH_3	PF_6^-	99.0	103–105	97.75	−51.6 ($c=1.1$)
6	C_4H_9	CH_3	CH_3	CF_3COO^-	89.0	72–74	98.5	−52.8 ($c=1.1$)
7	C_4H_9	CH_3	CH_3	Ace[a]	91.5	oil	99.9	−51.2 ($c=0.4$)

[a] Acesulfamate. [b] c in ethanol.

The estimated viscosities indicate that the new ILs are highly viscous. The viscosity is strongly influenced by temperature and the presence of water or organic solvents. In the case of **8g**, increasing the temperature from 35 °C to 40, 45, 50, 55, and 60 °C was found to be accompanied by a 145, 200, 280, 380, 490, and 600 % decrease in viscosity, respectively, based on the absolute value of 130 mPa s. The dependence of viscosity upon temperature and cosolvents is dramatic, which is in line with earlier data.[34]

All RTILs show no measurable vapor pressure. The estimated thermal-degradation temperature is used to define the upper temperature limit at which the CILs can be used. Below this temperature, no alterations in liquid color have been observed. The limit of the liquid range of a given RTIL can be higher by about 40 °C if the thermogravimetric analysis (TGA) onset temperature is used as an indication. The DSC thermograms of the RTILs exhibited a single signal. This indicates that the RTILs show an abrupt increase in the molar heat capacity associated with the glass transition. They form glasses for which the glass transition temperatures are very low (approximately −50 °C). The change in heat capacity, ΔC_p, when the sample is heated from the glass state to the metastable supercooled liquid, has values between 0.38 and 0.24 J g^{-1} K^{-1}.

The antielectrostatic effect was determined according to the criteria listed in Table 6. The antielectrostatic effect of salts **1–8** reflects two quantities: the surface resistance and the half-charge decay time. The surface resistance R_S (in Ω) has been calculated from Equation (1):

$$R_S = \frac{Ul}{is} \quad (1)$$

in which U is the applied voltage ($U=100$ V), l is the length of the electrode ($l=100$ mm), i is the measured current intensity, and s is the distance between the electrodes ($s=10$ mm). The half-charge decay time (in seconds) has been calculated according to Equation (2):

$$\tau_{1/2} = \sqrt{\frac{\tau_+^2 + \tau_-^2}{2}} \quad (2)$$

in which τ_+ and τ_- are the mean half-decay times of positive and negative charges, respectively. The results are presented in Table 7. All chlorides and [Tf_2N] salts show excellent anti-

Table 4. Chiral ammonium-based ionic liquids (**8**).

CIL	R^1	R^2	R^3	Anion	Yield [%]	Specific rotation[d] $[\alpha]_D^{20}$	Density[e] [g mL^{-1}]	Viscosity[e] [mPa s]	T_g[f] [°C]	Glass transition [°C]	ΔC_p[g] [J g^{-1} K^{-1}]
8a	C_2H_5	C_2H_5	C_2H_5	Tf_2N	85.5	−38.6 ($c=1.4$)	1.25	876	179	−45.8	0.38
8b	C_2H_5	C_2H_5	CH_3	Tf_2N	94.5	−39.1 ($c=1.2$)	1.26	754	197	−48.5	0.30
8c	C_2H_5	CH_3	CH_3	Tf_2N	89.0	−40.6 ($c=1.1$)	1.27	714	199	−49.9	0.24
8d[a]	*i*-C_3H_7	CH_3	CH_3	Tf_2N	99.0	−39.5 ($c=1.1$)	–	–	–	–	–
8e	C_4H_9	CH_3	CH_3	Tf_2N	87.5	−38.2 ($c=0.9$)	1.24	745	200	−50.1	0.28
8f	C_6H_{13}	CH_3	CH_3	Tf_2N	84.5	−41.6 ($c=1.0$)	1.21	774	200	−50.2	0.29
8g	C_7H_{15}	CH_3	CH_3	Tf_2N	89.5	−34.8 ($c=1.2$)	1.19	787	202	−52.8	0.32
8h	C_8H_{17}	CH_3	CH_3	Tf_2N	93.5	−35.6 ($c=1.4$)	1.18	806	200	−53.0	0.32
8i	C_9H_{19}	CH_3	CH_3	Tf_2N	95.0	−33.2 ($c=1.4$)	1.17	829	199	−53.2	0.31
8j	$C_{10}H_{21}$	CH_3	CH_3	Tf_2N	91.0	−37.8 ($c=1.1$)	1.15	840	200	−54.4	0.30
8k	$C_{11}H_{23}$	CH_3	CH_3	Tf_2N	92.5	−32.7 ($c=1.6$)	1.14	844	206	−54.3	0.30
8l[b]	$C_{12}H_{25}$	CH_3	CH_3	Tf_2N	99.5	−31.5 ($c=1.2$)	–	–	–	–	–
8m[c]	CH_2Ph	CH_3	CH_3	Tf_2N	99.0	−39.1 ($c=1.0$)	–	–	–	–	–

[a] M.p. 40–42 °C; plates. [b] M.p. 28–30 °C; plates. [c] M.p. 46–48 °C; plates. [d] c in ethanol. [e] At 30 °C. [f] Thermal degradation temperature. [g] Heat capacity jump.

Table 5. The shifts in proton signals.[a]

Salt	Anion	Functional group			
		N^+CH_2O[b]	OCH-(menthyl-C6)	$N^+CH_2R^1$	$N^+(CH_3)_2$
1e	Cl^-	4.98 (d, $J=6.9$)	3.59 (td)	3.51 (m)	3.36 (s)
		4.94 (d, $J=6.9$)			3.37 (s)
2e	BF_4^-	4.62 (d, $J=7.1$)	3.52 (td)	3.29 (m)	3.07 (s)
		4.58 (d, $J=6.9$)			
3	ClO_4^-	4.65 (t, $J=7.5$)	3.54 (td)	3.32 (m)	3.11 (s)
4	I^-	5.03 (d, $J=6.9$)	3.65 (m)	3.57 (m)	3.35 (s)
		4.93 (d, $J=6.9$)			3.36 (s)
5	PF_6^-	4.56 (d, $J=7.1$)	3.49 (td)	3.18 (m)	3.02 (s)
		4.51 (d, $J=6.9$)			
6	CF_3COO^-	4.79 (t, $J=7.7$)	3.5 (td)	3.34 (m)	3.20 (s)
					3.21 (s)
7	Ace^-[c]	4.75 (d, $J=7.4$)	3.55 (td)	3.33 (m)	3.17 (s)
		4.72 (d, $J=7.1$)			
8e	Tf_2N^-	4.57 (d, $J=6.9$)	3.49 (td)	3.24 (m)	3.01 (s)
		4.51 (d, $J=6.9$)			

[a] Shifts in ppm. [b] J in Hz. [c] Acesulfamate.

Table 6. Criteria for the estimation of the antielectrostatic effect based on the surface resistance R_S [Ω] and half-charge decay time $\tau_{1/2}$ [s].

$\log R_S$	$\tau_{1/2}$	Antielectrostatic effect
<9	<0.5	excellent
9–9.99	0.51–2	very good
10–10.99	2.1–10	good
11–11.99	10.1–100	sufficient
12–12.99	>100	insufficient
>13	>600	lack of antielectrostatic properties

Table 7. Surface resistance R_S [Ω], half-charge decay time $\tau_{1/2}$ [s], and antielectrostatic effects of the prepared salts.

Salt	$\log R_S$	$\tau_{1/2}$	Effect	Salt	$\log R_S$	$\tau_{1/2}$	Effect
1a	8.7	0.2	excellent	**2i**	11.3	88	sufficient
1b	7.5	<0.1	excellent	**2j**	11.0	45	sufficient
1c	8.3	<0.1	excellent	**2k**	11.5	25	sufficient
1d	8.0	0.3	excellent	**2l**	>13	>600	lack
1e	7.5	<0.1	excellent	**2m**	>13	>600	lack
1f	7.3	<0.1	excellent	**3**	>13	>600	lack
1g	7.6	<0.1	excellent	**4**	9.6	0.25	very good
1h	8.7	<0.1	excellent	**5**	>13	>600	lack
1i	7.7	<0.1	excellent	**8a**	8.0	0.3	excellent
1j	7.0	<0.1	excellent	**8b**	8.3	0.45	excellent
1k	7.5	<0.1	excellent	**8c**	8.5	0.3	excellent
1l	7.8	<0.1	excellent	**8d**	8.8	0.3	excellent
1m	8.3	<0.1	excellent	**8e**	8.9	0.35	excellent
2a	>13	>600	lack	**8f**	8.6	0.2	excellent
2b	>13	>600	lack	**8g**	8.9	0.25	excellent
2c	12.7	>100	insufficient	**8h**	8.0	0.25	excellent
2d	>13	>600	lack	**8i**	8.3	0.2	excellent
2e	>13	>600	lack	**8j**	8.0	0.25	excellent
2f	11.5	25	sufficient	**8k**	8.8	0.4	excellent
2g	11.0	55	sufficient	**8l**	8.7	0.2	excellent
2h	12.0	>100	insufficient	**8m**	8.5	0.2	excellent

electrostatic effects. On the other hand, the $[BF_4]$, $[ClO_4]$, and $[PF_6]$ salts show a reduced capacity to drain surface electric charge. $[Tf_2N]$ salts penetrate the polymer surface because they have unique solvation properties and are more able to disperse the electric charge. Their activity is similar to that of the known antistatic agent Catanac 609 (*N*,*N*-bis(2-hydroxyethyl)-*N*-(3′-dodecyloxy-2′-hydroxypropyl)methylammonium methanesulfate; $\log R_S=8.48$, $\tau_{1/2}=0.25$ s). Recently, imidazolium ILs have been found to represent effective antielectrostatic agents for pine and maple.[35]

Biological activities have been estimated for all of the chlorides. Minimum inhibitory concentration (MIC) values and minimum bactericidal or fungicidal concentration (MBC) values are provided in Table 8. Additionally, MIC and MBC values are presented for benzalkonium chloride (BAC, in which "alkyl" represents a mixture of alkyls ranging from C_8H_{17} to $C_{18}H_{37}$). Chlorides bearing an alkyl group containing more than five carbon atoms can be regarded as active. Relationships between mean MIC and MBC values for the studied microbes and the number of carbon atoms in the alkyl group are presented in Figure 4. The activity is seen to be related to the length of the alkyl substituent and thus to molecular mass. The curves demonstrate optimum antimicrobial efficiency. The chloride **1k**, containing an undecyl substituent, can be regarded as being the most active against cocci, rods, fungi, and bacillus, exhibiting higher efficiency than that of commercially available BAC. Chlorides **1d**, **1e**, and **1m** demonstrated low activity against some microbes. Chlorides **1a**–**1c**, on the other hand, were found to be practically inactive. Since $[Tf_2N]$ salts are insoluble in water, their MIC and MBC values could not be estimated. With reference to our earlier publication on the antimicrobial activities of ILs,[36] the $[Tf_2N]$ salts could be expected to show similar activity to that of the chlorides. If the application of ILs in biochemical processes is considered, selection of a biologically active solvent may prove fatal to organisms. It should be kept in mind that the quaternary nitrogen atom in these ammonium salts is an essential component in relation to multiple biological activities.

Conclusion

All of the prepared chiral quaternary ammonium salts are air- and moisture-stable under ambient conditions and may be handled under a variety of standard experimental conditions. Trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chlorides with more than five carbon atoms in the alkyl group exhibit a wide range of antimicrobial activities. The nature of the anion determines the consistency and hygroscopic character of the salt. Salts with the $[Tf_2N]$ anion are RTILs. The important attributes of the CILs include negligi-

Table 8. MIC and MBC values[a] of trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chlorides (**1**).

Strain		Chlorides													
		1a	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**	**1k**	**1l**	**1m**	**BAC**[b]
M. luteus	MIC	26	106	112	55	26	6	5.8	2.8	<0.3	<0.3	<0.25	0.5	121	1.4
	MBC	52	213	450	213	52	186	89	44	21	2.6	1.2	2.4	183	11
S. aureua	MIC	818	429	1802	858	409	24	11	2.8	1.3	0.5	0.5	1.2	183	2.8
	MBC	>1637	>1715	1802	>1715	>1637	375	89	22	5.3	2.6	10	4.8	1473	23
S. epidermidis	MIC	409	213	450	429	409	12	5.8	1.4	1.3	<0.3	<0.25	0.5	47	1.4
	MBC	1637	>1715	1802	>1715	1637	93	46	5.5	2.7	2.6	2.5	4.8	183	5.6
E. faecium	MIC	818	>1715	>1802	>1715	818	48	11	5.5	1.3	0.5	<0.25	0.5	736	5.6
	MBC	>1637	>1715	>1802	>1715	1637	375	178	86	21.0	10	4.9	19	>1473	23
E. coli	MIC	818	213	450	213	818	12	5.8	2.8	1.3	1.3	2.5	0.5	47	2.8
	MBC	1637	213	450	213	1637	12	5.8	5.5	1.3	2.6	4.9	1.2	91	2.8
S. marcescens	MIC	>1637	>1715	>1802	>1715	>1637	1499	1439	691	165	159	154	299	1473	175
	MBC	>1637	>1715	>1802	>1715	>1637	>1499	1439	691	165	159	154	599	>1473	175
P. vulgaris	MIC	>1637	>1715	>1802	>1715	>1637	750	360	171	82	41	10	19	>1473	88
	MBC	>1637	>1715	>1802	>1715	>1637	1499	719	346	82	41	40	38	>1473	88
P. aeruginosa	MIC	>1637	>1715	>1802	>1715	>1637	1499	719	171	82	41	40	38	>1473	175
	MBC	>1637	>1715	>1802	>1715	>1637	1499	1439	346	165	80	77	148	>1473	175
B. subtilis	MIC	1637	213	>1802	1715	818	12	23	5.5	0.5	0.5	<0.25	1.2	183	2.8
	MBC	1637	1715	>1802	1715	818	24	23	5.5	1.3	1.3	<0.25	1.2	183	2.8
M. catarrhalis	MIC	409	213	1802	429	409	24	5.8	2.8	0.5	0.5	<0.25	0.5	47	0.6
	MBC	409	858	>1802	429	409	24	46	11	0.5	0.5	<0.25	1.2	183	1.4
C. albicans	MIC	>1637	>1715	>1802	>1715	>1637	375	178	44	11	5.1	<0.25	2.4	1473	11
	MBC	>1637	>1715	>1802	>1715	>1637	375	178	86	21	5.1	1.3	9.6	1473	88
R. rubra	MIC	>1637	>1715	>1802	>1715	>1637	375	89	22	11	2.6	2.5	2.4	736	23
	MBC	>1637	>1715	>1802	>1715	>1637	750	360	171	21	5.1	4.9	38	1473	88

[a] In μM. [b] Benzalkonium chloride.

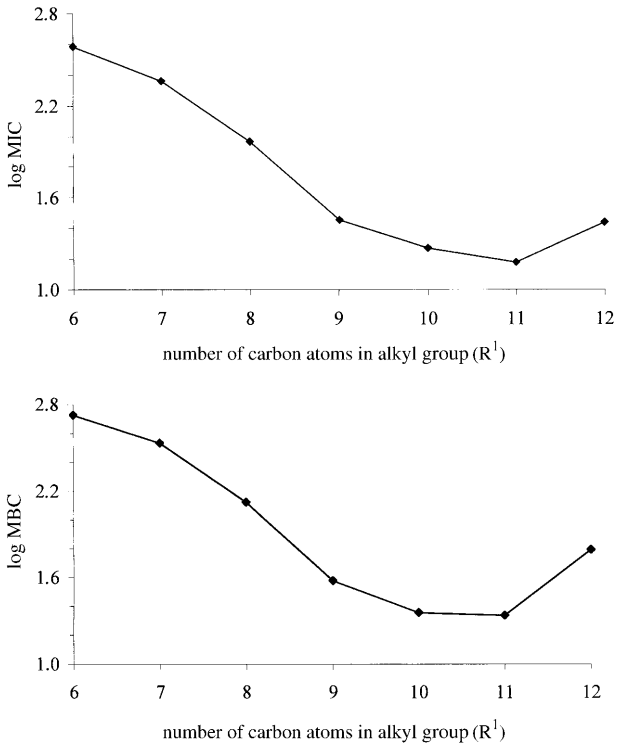


Figure 4. Mean MIC values (top) and MBC values (bottom) for microorganisms.

ble vapor pressure, compatibility with various organic compounds, ease of separation in aqueous/ionic liquid extractions, antielectrostatic activities, and their potential application in asymmetric synthesis.

Experimental Section

General: ^{1}H NMR spectra were recorded on a Mercury Gemini 300 spectrometer at 300 MHz with tetramethylsilane as the standard; ^{13}C NMR spectra were recorded on the same instrument at 75 MHz. Two-dimensional spectra were obtained using standard pulse sequences from the Bruker DRX pulse library at 600 MHz.

Elemental analyses were performed at the A. Mickiewicz University, Poznań. Melting points were determined using a model JA 9100 electrothermal digital melting-point apparatus. A Mettler Toledo DA 110 M scale was used for the mass/density measurements. A micro Ostwald viscometer was used for viscosity measurements. Thermal degradation temperatures were determined using a Büchi model B-545 automatic apparatus. Optical rotations were measured with a Perkin–Elmer 243 B polarimeter. Glass transition temperatures were determined using a Perkin–Elmer differential scanning calorimeter. The instrument temperature scale was calibrated at the crystal–crystal transition of cyclopentane (−151.16 °C) and the melting point of indium (+156.6 °C). Samples were sealed in aluminum pans and scanned at a rate of 20 K min^{-1} in a helium atmosphere.

Preparation of chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether: Gaseous hydrogen chloride was introduced into a mixture of (1*R*,2*S*,5*R*)-(−)-menthol (100 g, 0.64 mol), toluene (200 mL), and paraformaldehyde (19.5 g, 0.65 mol) with efficient mechanical stirring until the solution was saturated (5 h). The reaction was carried out under isothermal conditions at 10 °C. Water was removed and an emulsion of reaction-generated water in the organic phase was obtained, which was then dried over magnesium sulfate and concentrated under reduced pressure. Hydrogen chloride absorbed in the reaction product was stripped off with dry nitrogen.

The amount of chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether in the final product was determined by an alkalimetric method: 1 g of crude product was added to 10 mL of acetone at −20 °C. HCl absorbed on the substrate was quickly neutralized with 0.02 M KOH in MeOH. Then, hot water (5 mL) was added. HCl as a product of ether hydrolysis was neutralized with 0.2 M KOH in MeOH.

The crude product contained 92 % of chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether. This was purified by vacuum distillation to give a clear

liquid with boiling point 108 °C at 16 mmHg (lit.: 82–84 °C at 0.8 mmHg[22] or 62 °C at 0.1 mmHg[23]).

General procedure for Menschutkin quaternization: All reactions were performed under anhydrous conditions. A solution of freshly distilled trialkylamine (0.036 mol) in hexane (30 mL) was prepared. Chloromethyl (1*R*,2*S*,5*R*)-(−)-menthyl ether (7.36 g, 0.036 mol) was slowly added and the resulting mixture was vigorously stirred for 30 min at room temperature. The white precipitate produced was removed by filtration and the filter cake was washed with hexane. The crude product was recrystallized from either ethyl acetate, ethyl acetate/ethanol, ethyl acetate/acetone, or ethyl acetate/chloroform. The product was dried under reduced pressure overnight.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chloride (1e): ^{1}H NMR (2D spectra) ($CDCl_3$, 25 °C): $\delta = 0.81$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.86 (td, $J = 12.4$, $J = 3.1$ Hz, 1H; Ha-3), 0.92 (d, $J = 6.5$ Hz, 3H; H1), 0.93 (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.95 (m, 1H; Ha-7), 0.98 (m, 1H; Ha-4), 0.99 (t, $J = 7.4$ Hz, 3H; H18), 1.32 (m, 1H; H5), 1.42 (m, 1H; H2), 1.42 (m, 2H; H17), 1.65 (m, 1H; Hb-4), 1.67 (m, 1H; Hb-3), 1.68 (m, 2H; H16), 2.07 (sept d, $J = 6.9$, $J = 2.4$ Hz, 1H; H8), 2.18 (d, $J = 11.7$ Hz, 1H; Hb-7), 3.36 (s, 3H; H13 or H14), 3.37 (s, 3H; H13 or H14), 3.51 (m, 2H; H15), 3.59 (td, $J = 10.6$, $J = 4.2$ Hz, 1H; H6), 4.98, 4.94 ppm (d, $J = 6.9$ Hz, 2H; AB system); ^{13}C NMR ($CDCl_3$): $\delta = 13.4$ (C18), 15.7 (C9 or C10), 19.4 (C17), 20.7 (C1), 21.8 (C9 or C10), 22.4 (C4), 24.0 (C16), 25.5 (C8), 30.9 (C2), 33.7 (C3), 40.3 (C7), 47.5 (C13 or C14), 47.6 (C13 or C14), 47.9 (C5), 60.7 (C15), 81.2 (C6), 87.3 ppm (C12); elemental analysis calcd (%) for $C_{17}H_{36}NClO$ (305.5): C 66.74, H 11.86, N 4.58; found: C 66.93, H 11.99, N 4.31.

Preparation of trialkyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium salts (2–8): A solution of the requisite ammonium chloride (**1**) in either water (15 mL) (with **1a**–**1e**) or methanol (20 mL) (with **1f**–**1l**) was added to a stoichiometric amount of a saturated aqueous solution of $NaBF_4$, $NaClO_4$, KI, KPF_6, CF_3COONa, Tf_2NLi, or acesulfame-K. The reaction solution was stirred at room temperature for 2 h. After separation of the phases, the aqueous phase was decanted and the salt obtained was washed with cold, distilled water until chloride ions were no longer detected using $AgNO_3$. The crude product that solidified upon cold storage was recrystallized from ethanol/water. Liquids were dried for 10 h at 80 °C in vacuo (8 mmHg).

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium tetrafluoroborate (2e): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.79$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.92 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.38 (m, 4H; H2, H5, H17), 1.68 (m, 4H; Hb-3, Hb-4, H16), 2.07 (m, 2H; Hb-7, H8), 3.07 (s, 6H; H13, H14), 3.29 (m, 2H; H15), 3.52 (td, $J = 10.4$, $J = 4.1$ Hz, 1H; H6), 4.58, 4.62 ppm (d, $J = 6.9$, $J = 7.1$ Hz, 2H; AB system); ^{13}C NMR ($CDCl_3$): $\delta = 13.4$ (C18), 15.6 (C9 or C10), 19.5 (C17), 20.9 (C1), 21.9 (C9 or C10), 22.6 (C4), 24.0 (C16), 25.7 (C8), 31.1 (C2), 33.9 (C3), 40.2 (C7), 47.4 (C13 or C14), 47.5 (C13 or C14), 48.1 (C5), 61.1 (C15), 81.6 (C6), 87.7 ppm (C12); elemental analysis calcd (%) for $C_{17}H_{36}NOBF_4$ (357.3): C 57.10, H 10.15, N 3.92; found: C 56.92, H 9.83, N 3.88.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium perchlorate (3): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.80$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.96 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.38 (m, 4H; H2, H5, H17), 1.69 (m, 4H; Hb-3, Hb-4, H16), 2.09 (m, 2H; Hb-7, H8), 3.11 (s, 6H; H13, H14), 3.32 (m, 2H; H15), 3.54 (td, $J = 10.7$, $J = 4.2$ Hz, 1H; H6), 4.65 ppm (t, $J = 7.5$ Hz, 2H; H12); ^{13}C NMR ($CDCl_3$): $\delta = 13.6$ (C18), 15.9 (C9 or C10), 19.7 (C17), 21.1 (C1), 22.1 (C9 or C10), 22.8 (C4), 24.3 (C16), 25.9 (C8), 31.2 (C2), 34.0 (C3), 40.4 (C7), 47.8 (C13 and C14), 48.1 (C5), 61.3 (C15), 81.8 (C6), 88.0 ppm (C12); elemental analysis calcd (%) for $C_{17}H_{36}NOClO_4$ (369.9): C 55.20, H 9.81, N 3.79; found: C 55.49, H 10.01, N 3.71.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium iodide (4): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.82$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.97 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.40 (m, 4H; H2, H5, H17), 1.70 (m, 4H; Hb-3, Hb-4, H16), 2.07 (m, 1H; H8), 2.22 (d, $J = 11.5$ Hz, 1H; Hb-7), 3.55 (s, 3H; H13 or H14), 3.36 (s, 3H; H13 or H14), 3.57 (m, 2H; H15), 3.65 (m, 1H; H6), 4.93, 5.03 ppm (d, $J = 6.87$ Hz, 2H; AB system); ^{13}C NMR ($CDCl_3$): $\delta = 13.4$ (C18), 15.9 (C9 or C10), 19.4 (C17), 20.8 (C1), 21.8 (C9 or C10), 22.5 (C4), 24.2 (C16), 25.6 (C8), 30.9 (C2), 33.7 (C3), 40.4 (C7), 47.9 (C5, C13 or C14), 61.1 (C15), 81.4 (C6), 87.6 ppm (C12); elemental analysis calcd (%) for $C_{17}H_{36}NOI$ (397.4): C 51.38, H 9.13, N 3.52; found: C 51.73, H 9.01, N 3.73.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium hexafluorophosphate (5): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.79$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.94 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.37 (m, 4H; H2, H5, H17), 1.67 (m, 4H; Hb-3, Hb-4, H16), 2.47 (m, 2H; Hb-7, H8), 3.02 (s, 6H; H13, H14), 3.18 (m, 2H; H15), 3.49 (td, $J = 10.7$, $J = 4.4$ Hz, 1H; H6), 4.51, 4.56 ppm (d, $J = 6.9$, $J = 7.1$ Hz, 2H; AB system); ^{13}C NMR ($CDCl_3$): $\delta = 13.5$ (C18), 15.8 (C9 or C10), 19.6 (C17), 21.1 (C1), 22.0 (C9 or C10), 22.8 (C4), 24.1 (C16), 25.9 (C8), 31.2 (C2), 34.0 (C3), 40.2 (C7), 47.6 (C13 or C14), 47.7 (C13 or C14), 48.1 (C5), 61.3 (C15), 81.8 (C6), 87.8 ppm (C12); elemental analysis calcd (%) for $C_{17}H_{36}NOPF_6$ (415.4): C 49.15, H 8.73, N 3.37; found: C 48.81, H 8.93, N 3.01.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium trifluoroacetate (6): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.79$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.94 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.37 (m, 4H; H2, H5, H17), 1.67 (m, 4H; Hb-3, Hb-4, H16), 2.48 (m, 2H; Hb-7, H8), 3.20 (s, 3H; H13 or H14), 3.21 (s, 3H; H13 or H14), 3.34 (m, 2H; H15), 3.51 (td, $J = 10.7$, $J = 4.1$ Hz, 1H; H6), 4.79 ppm (t, $J = 7.8$ Hz, 2H; H12); ^{13}C NMR ($CDCl_3$): $\delta = 13.4$ (C18), 15.6 (C9 or C10), 19.5 (C17), 20.9 (C1), 21.8 (C9 or C10), 22.4 (C4), 24.1 (C16), 25.7 (C8), 31.0 (C2), 33.8 (C3), 40.3 (C7), 47.3 (C13 or C14), 47.4 (C13 or C14), 48.0 (C5), 60.9 (C15), 81.5 (C6), 87.6 ppm (C12), anion: 115.3, 119.2, 160.0, 160.4, 160.9, 161.3 ppm; elemental analysis calcd (%) for $C_{19}H_{36}F_3NO_3$ (383.5): C 59.51, H 9.46, N 3.65; found: C 59.19, H 9.23, N 3.74.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium acesulfamate (7): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.79$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.96 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.37 (m, 4H; H2, H5, H17), 1.71 (m, 4H; Hb-3, Hb-4, H16), 2.09 (m, 5H; Hb-7, H8, and anion), 3.17 (s, 6H; H13, H14), 3.33 (m, 2H; H15), 3.55 (td, $J = 10.7$, $J = 4.4$ Hz, 1H; H6), 4.72, 4.75 (d, $J = 7.1$, $J = 7.4$ Hz, 2H; AB system), 5.44 ppm (d, $J = 1.1$ Hz, 1H; anion); ^{13}C NMR ($CDCl_3$): $\delta = 13.3$ (C18), 15.6 (C9 or C10), 19.4 (anion), 19.7 (C17), 20.8 (C1), 21.8 (C9 or C10), 22.4 (C4), 24.0 (C16), 25.5 (C8), 30.9 (C2), 33.8 (C3), 40.2 (C7), 47.4 (C13 or C14), 47.5 (C13 or C14), 47.8 (C5), 60.8 (C15), 81.3 (C6), 87.5 ppm (C12), anion: 102.1, 160.5, 169.3 ppm; elemental analysis calcd (%) for $C_{21}H_{40}N_2O_5S$ (432.6): C 58.39, H 9.32, N 6.48; found: C 58.76, H 9.61, N 6.56.

Butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium bis(trifluoromethanesulfonyl)imide (8e): ^{1}H NMR ($CDCl_3$, 25 °C): $\delta = 0.78$ (d, $J = 6.9$ Hz, 3H; H9 or H10), 0.95 (m, 12H; Ha-3, H1, H9 or H10, Ha-7, Ha-4, H18), 1.37 (m, 4H; H2, H5, H17), 1.67 (m, 4H; Hb-3, Hb-4, H16), 2.47 (m, 2H; Hb-7, H8), 3.01 (s, 6H; H13, H14), 3.24 (m, 2H; H15), 3.49 (td, $J = 10.7$, $J = 4.4$ Hz, 1H; H6), 4.51, 4.57 ppm (d, $J = 6.9$, $J = 7.1$ Hz, 2H; AB system); ^{13}C NMR ($CDCl_3$): $\delta = 13.3$ (C18), 15.5 (C9 or C10), 19.4 (C17), 20.9 (C1), 21.8 (C9 or C10), 22.6 (C4), 24.0 (C16), 25.7 (C8), 31.0 (C2), 33.9 (C3), 40.1 (C7), 47.5 (C13 or C14), 47.7 (C13 or C14), 47.9 (C5), 61.3 (C15), 81.5 (C6), 87.9 ppm (C12), anion: 113.6, 117.5, 121.7, 126.0 ppm; elemental analysis calcd (%) for $C_{19}H_{36}N_2F_6O_5S_2$ (550.6): C 41.45, H 6.59, N 5.09; found: C 41.25, H 6.39, N 5.01.

Antielectrostatic properties: The antielectrostatic effect was measured on a polyethylene film, which did not contain any lubricants or antioxidants. Thin films of the studied salts were deposited on disks of diameter 0.125 m. The disks were stored for 24 h in an air-conditioned room at 20 °C with a relative humidity of 65%. The measuring apparatus and the method have recently been described elsewhere.[37] The relative error in the determination of two quantities did not exceed 5%.

X-ray crystallography: The crystal structure of butyldimethyl[(1*R*,2*S*,5*R*)-(−)-menthoxymethyl]ammonium chloride (**1e**) was determined by single-crystal X-ray diffraction at room temperature, using a Kuma KM-4 diffractometer with a single-point detector and graphite-monochromated $Cu_{K\alpha}$ radiation ($\lambda = 1.54178$ Å). The data were processed routinely and the structure was solved by direct methods (Sheldrick, 1990)[38] and refined with anisotropic thermal parameters by full-matrix least-squares techniques (Sheldrick, 1997).[39] The H atoms were placed in calculated

positions. H atoms were placed in geometrically idealized positions. Only the H atoms of water molecules were found in difference Fourier maps. *Crystal data for* ***1e***: formula $C_{17}H_{36}ON^{+}Cl^{-}\cdot H_2O$, $M_r = 295.5$, orthorhombic, space group $P2_12_12_1$, crystal size $0.5\times0.3\times0.1$ mm, $a = 7.5261(16)$, $b = 7.669(3)$, $c = 35.622(7)$ Å, $V = 2056.2(10)$ Å^3, $T = 293(2)$ K, $Z = 4$, $\mu(Cu_{K\alpha}) = 1.668$ mm^{-1}, $R_1 = 0.630$, $wR_2 = 0.1803$ ($I > 2\sigma(I)$). CCDC 259728 contains the supplementary crystallographic data for chloride **1e**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Antimicrobial activities: The following microbial strains were used as test microbes: rods: *Pseudomonas aeruginosa* NCTC 6749, *Escherichia coli* ATCC 25922, *Proteus vulgaris* NCTC 4635, *Serratia marcescens* ATCC 8100; cocci: *Staphylococcus epidermidis* ATCC 49134, *Staphylococcus aures* NCTC 4163, *Micrococcus luteus* NCTC 7743, *Enterococcus faecium* ATCC 49474, *Moraxella catarrhalis* ATCC 25238; bacillus: *Bacillus subtilis* ATCC 6633; yeast-like fungi: *Candida albicans* ATCC 10231, *Rhodotorula rubra* (Demml 1889, Lodder 1934). Standard strains were supplied by the National Collection of Type Cultures (NCTC), London, and the American Type Culture Collection (ATCC). *Rhodotorula rubra* was obtained from the Department of Pharmaceutical Bacteriology, Poznań, Poland.

Antimicrobial activity was determined by the tube dilution method. A series of ammonium chloride dilutions was prepared in Mueller–Hinton broth medium (bacteria) or Sabouraud broth medium (fungi). Bacteria strains were cultured in Mueller–Hinton broth medium for 24 h and fungi in Sabouraud broth medium for 48 h. Suspensions of microbes at a concentration of 10^6 cfu mL^{-1} were then prepared from each culture. Then, each dilution of the broth medium was inoculated with one of the above-mentioned suspensions in a 1:1 ratio. Growth (or lack thereof) of the microorganisms was determined visually after incubation for 24 h at 37 °C (bacteria) or for 48 h at 28–30 °C (fungi). The lowest concentration at which there was no visible growth (turbidity) was taken as the MIC (minimal inhibitory concentration). Then, an aliquot taken from each tube in a sample loop was cultured in an agar medium with inactivation agents (0.3 % lecithin, 3 % polysorbate 80, and 0.1 % L-cysteine) and incubated for 48 h at 37 °C (bacteria) or for 5 days at 28–30 °C (fungi). The lowest concentration of the ammonium chloride preventing colony formation was defined as the MBC (minimum bactericidal or fungicidal concentration).

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