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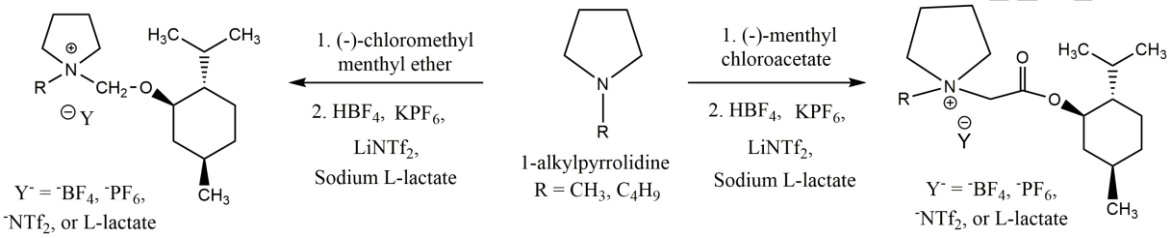

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Chiral pool based synthesis of pyrrolidinium ionic liquids

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ABSTRACT

Chiral ionic liquids show promising applications in various different fields. A series of pyrrolidinium-based chiral ionic liquids bearing a chiral cation, a chiral anion or both was prepared in good yields using an efficient, economic and simple pathway. The chirality was introduced using (L)-lactate and (L)-menthol derivatives. The resultant chiral compounds were characterized by both spectroscopy and polarimetry. We envision that these new chiral compounds can serve as effective reaction media and chiral catalysts for asymmetric reactions, which are presently being investigated in our lab.

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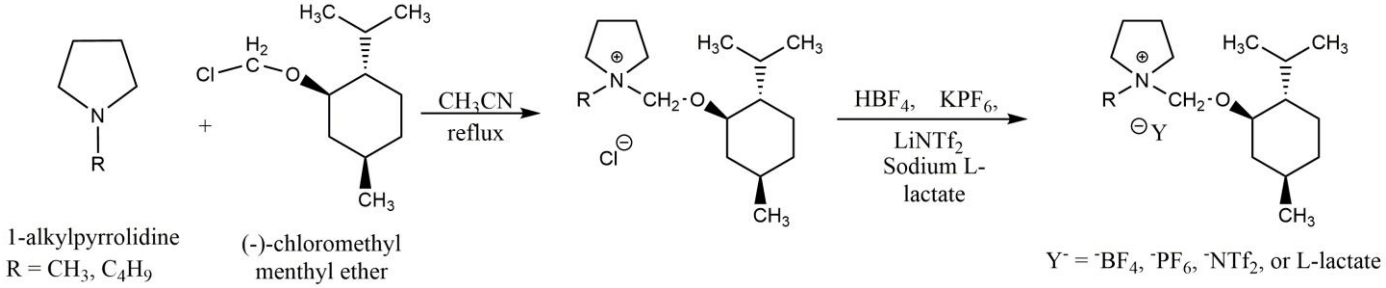
In the recent years, there has been a growing demand in the use of the room-temperature ionic liquids (RTIL) as new reaction media.[1] One of the main expected applications of ionic liquids is to replace the volatile organic solvents traditionally used in large scale in industry.[2] Ionic liquids possess a number of interesting properties over commonly used organic solvents, such as lack of significant vapor pressure, absence of flammability, tolerance for large temperature variations and ease of reuse.[3] They have been extensively used in chemical syntheses and electrosyntheses.[4]

Chiral ionic liquids (CILs) are one of the latest branches of ionic liquid research and are promising chiral solvents for many applications.[5] Chiral ionic liquids are particularly attractive due to their potential for chiral discrimination, as in asymmetric synthesis and optical resolution of racemates.[6] Because of their highly-organized nature and ionic properties, an obvious potential exists for solvent-solute interaction that may provide a mechanism for substantial improvement over conventional chiral solvents.[7] So far, chiral ionic liquids have been successfully applied in asymmetric synthesis, stereoselective polymerization, chiral stationary phases in chromatographic techniques, and chiral shift reagents in NMR spectroscopy.[8] Other advantages of using chiral ionic liquids include the following: (1) the chiral ionic liquids are easily and inexpensively prepared and can be recycled; (2) the opposite enantiomers of the chiral ionic liquids can be produced in order to enantioselectively create the desired enantiomer in excess; (3) it is possible and easy to remove the chiral ionic liquids from the final reaction mixture so that no interference is occurred. Therefore, it is important to have a range of chiral ionic liquids with different properties that can be used in various applications.

The more efficient, economic and simple way to prepare enantiomerically pure ionic liquids with central chirality is the use of precursors derived from the chiral pool either for the generation of the CIL's anion or cation or for both.[9] Chirality has been introduced to the cation using various methods and the imidazolium cation has been widely used in these preparations.[10] Under most circumstances, the imidazole-derived ionic liquids are considered to be stable and "inert" solvents, but the 2-position can be deprotonated to form a stabilized carbene which could be problematic for some applications.[11] This situation can be avoided by the use of pyrrolidinium and benzimidazolium cations. However, less attention has been given to the cations such as pyrrolidinium and benzimidazolium in the preparation of chiral ionic liquids. Additionally, recent research shows that some pyrrolidinium-based ionic liquids have excellent electrochemical and mechanical performances and are promising electrolytes for lithium batteries.[12]

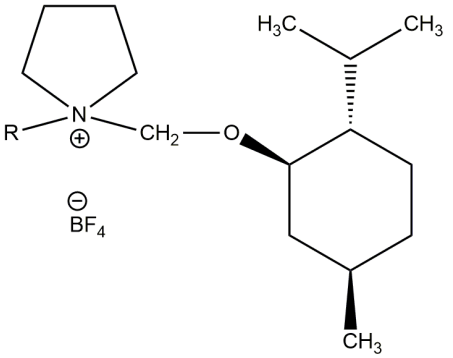
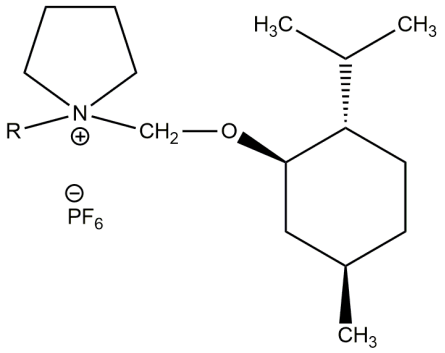
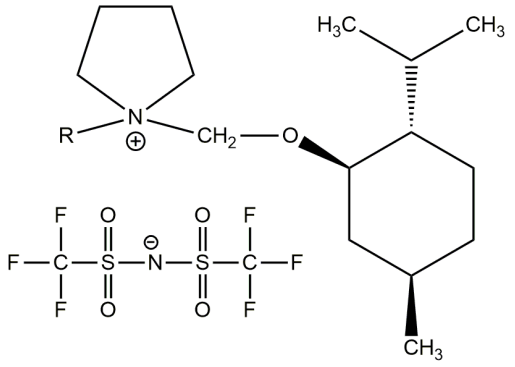
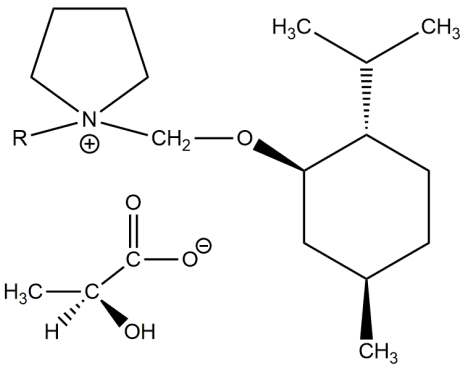
Armed with this information, we discuss the synthesis and characterization of a series of pyrrolidinium-based chiral ionic liquids. Chirality is introduced to the cation by using a menthol derivative and to the anion by sing a lactate salt. The presence of functional groups makes them potential task-specific chiral ionic liquids.[13] The concept of tailor-made task-specific chiral ionic liquids is rather new, and the synthesis of a series of new chiral ionic liquids with unique properties will benefit the collection of compounds that is currently limited in scope.

This project focused on the synthesis and characterization of pyrrolidinium-based chiral ionic liquids bearing a chiral cation, chiral anion or both using an economic, simple and efficient pathway. The enantiomerically pure ionic liquids can be prepared using chiral precursors such as aminoacids, aminoalcohols, hydroxyacids, amines, alkaloids or halogenoalkanes derived from a chiral pool for the generation of the chiral ionic liquid's anion, cation, or both.[5] In our project, the chirality for the ionic liquids was introduced using inexpensive and readily available (L)-lactate and (L)-menthol derivatives. 1-methylpyrrolidine or 1-butylpyrrolidine was heated to reflux in acetonitrile for 48h with (-)-chloromethyl menthyl ether (Scheme 1).[14] The intermediate chiral ionic salts, 1-butyl-1-menthoxymethylpyrrolidinium chloride and 1-methyl-1-menthoxymethylpyrrolidinium chloride were formed in good yields; 90% and 92% respectively. The spectroscopic analysis of intermediate ionic salts confirmed the purity of the products. The specific rotation was determined by polarimetry. The intermediate salts were then subjected to anion exchange without further purification. Ionic salts, 1-butyl-1-menthoxymethylpyrrolidinium chloride and 1-methyl-1-menthoxymethylpyrrolidinium chloride were separately reacted with tetrafluoroboric acid, potassium hexafluorophosphate and lithium bis(trifluoromethane)sulfonimide by replacing the chloride anion with tetraflouroborate, hexafluorophosphate and bis(trifluoromethane)sulfonimide respectively (Scheme 1).[14] These anion exchange reactions resulted six new ionic liquids bearing a chiral cation in good yields (Table 1; **1a-1c** and **1e-1g**). Additionally, the intermediate ionic salts were further reacted with sodium L-lactate by exchanging the chloride anion with L-lactate anion providing two chiral ionic liquids bearing both a chiral anion and a cation (Table 1; **1d** and **1h**). Both 1-butyl-1-menthoxymethylpyrrolidinium L-lactate and 1-methyl-1-menthoxymethylpyrrolidinium L-lactate were semi-solids at room temperature and obtained in good yields. The structure and the purity of final chiral ionic liquids were confirmed by ^{1}H NMR, ^{13}C NMR and IR spectroscopy.[15] The polarimetry was performed in methanol at 583 nm to determine the specific rotation for the final chiral ionic liquids (Table 1).[15]

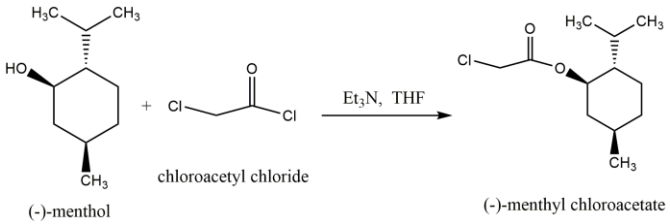


Scheme 1: Synthesis of chiral ionic liquids from the reactions of 1-alkylpyrrolidine and (-)-chloromethyl menthyl ether.

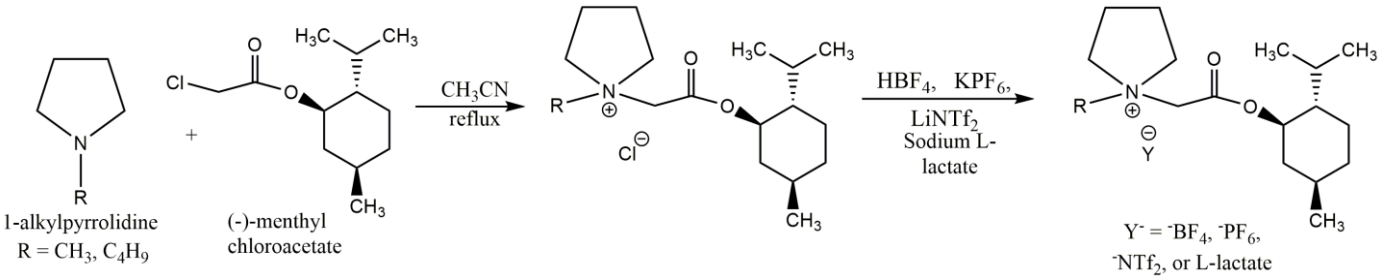
Table 1: 1-alkyl-1-menthoxymethylpyrralodinium chiral ionic liquids synthesized in the lab

Ionic liquid (Yield %)	Ionic liquid (Yield %)
 [**1a**] - R = C_4H_9, (-)-1-butyl-1-menthoxymethyl-pyrrolidinium tetrafluoroborate (84.5%) [**1e**] - R = CH_3, (-)-1-methyl-1-menthoxymethyl-pyrrolidinium tetrafluoroborate (82.3%)	 [**1b**] - R = C_4H_9, (-)-1-butyl-1-menthoxymethyl-pyrrolidinium hexafluorophosphate (81.8%) [**1f**] - R = CH_3, (-)-1-methyl-1-menthoxymethyl-pyrrolidinium hexafluorophosphate (81.0%)
 [**1c**] - R = C_4H_9, (-)-1-butyl-1-menthoxymethyl-pyrrolidinium bis(trifluoromethane)sulfonimide (89.4%) [**1g**] - R = CH_3, (-)-1-methyl-1-menthoxymethyl-pyrrolidinium bis(trifluoromethane)sulfonimide (84.4%)	 [**1d**] - R = C_4H_9, (-)-1-butyl-1-menthoxymethyl-pyrrolidinium lactate (89.5%) [**1h**] - R = CH_3, (-)-1-methyl-1-menthoxymethyl-pyrrolidinium lactate (86.4%)

Next we focused on the synthesis of functionalized chiral ionic liquids that have the potential of using as task specific chiral ionic liquids. The synthesis was started by preparing (-)-menthyl chloroacetate by the reaction of (-)-menthol, chloroacetyl chloride and triethyl amine in THF (Scheme 2).[16] The resultant (-)-menthyl chloroacetate was purified by column chromatography and analyzed by spectroscopy. It was then used to introduce the chirality for the cation. The ionic salts; 1-butyl-1-menthoxyacetylpyrrolidinium chloride and 1-methyl-1-menthoxyacetylpyrrolidinium chloride were prepared in good yields (87% and 91% respectively) by reacting (-)-menthyl chloroacetate with 1-butylpyrrolidine or 1-methylpyrrolidine respectively (Scheme 3).[17] After confirming the structure and the purity using spectroscopic methods, these intermediate ionic salts were then used in anion exchange reactions with tetrafluoroboric acid, potassium hexafluorophosphate and lithium bis(trifluoromethane)sulfonimide without further purification (Scheme 3). The new ionic liquids bearing a chiral cation were obtained in good yields and their physical properties varied from liquids to semisolids to low melting solids (Table 2; **2a-2c** and **2e-2g**). The reaction of ionic salts, 1-butyl-1-menthoxyacetylpyrrolidinium chloride and 1-methyl-1-menthoxyacetylpyrrolidinium chloride with sodium L-lactate resulted two chiral ionic liquids bearing both a chiral cation and a chiral anion, by exchanging the chloride anion with L-lactate anion (Scheme 3).[17] Both 1-butyl-1-menthoxyacetylpyrrolidinium L-lactate and 1-methyl-1-menthoxyacetylpyrrolidinium L-lactate were low melting solids at room temperature and obtained in excellent yields (Table 2; **2d** and **2h**). The structure and the purity of final chiral ionic liquids were confirmed by NMR and IR spectroscopic methods and the polarimetry was used in methanol at 583 nm to determine the specific rotation.[18]

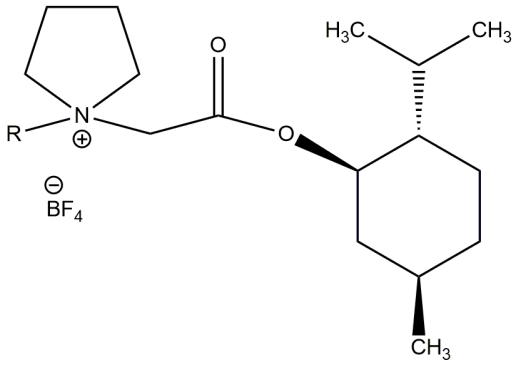
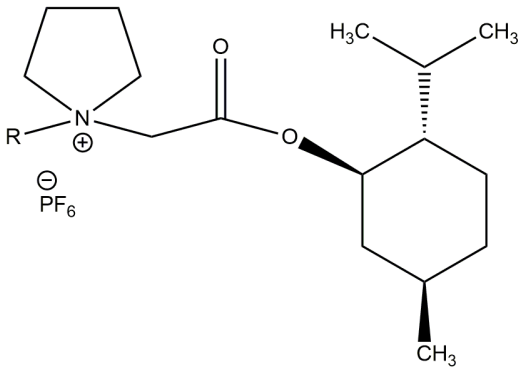
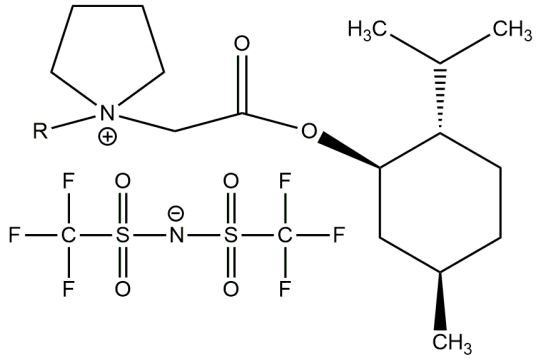
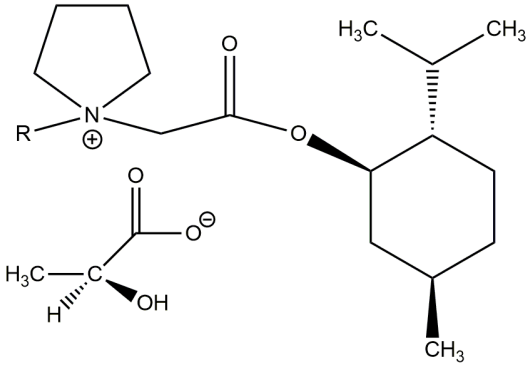


Scheme 2: Synthesis of (-)-menthyl chloroacetate.



Scheme 3: Synthesis of chiral ionic liquids from the reactions of 1-alkylpyrrolidine and (-)-menthyl chloroacetate.

Table 2: 1-alkyl-1-menthoxyacetylpyrrolodinium chiral ionic liquids synthesized in the lab

Ionic liquid (Yield %)	Ionic liquid (Yield %)
	
[**2a**] - R = C_4H_9, (-)-1-butyl-1-menthoxyacetyl-pyrrolidinium tetrafluoroborate (81.7%) [**2e**] - R = CH_3, (-)-1-methyl-1-menthoxyacetyl-pyrrolidinium tetrafluoroborate (85.1%)	[**2b**] - R = C_4H_9, (-)-1-butyl-1-menthoxyacetyl-pyrrolidinium hexafluorophosphate (87.7%) [**2f**] - R = CH_3, (-)-1-methyl-1-menthoxyacetyl-pyrrolidinium hexafluorophosphate (90.3%)
	
[**2c**] - R = C_4H_9, (-)-1-butyl-1-menthoxyacetyl-pyrrolidinium bis(trifluoromethane)sulfonimide (92.8%) [**2g**] - R = CH_3, (-)-1-methyl-1-menthoxyacetyl-pyrrolidinium bis(trifluoromethane)sulfonimide (82.6%)	[**2d**] - R = C_4H_9, (-)-1-butyl-1-menthoxyacetyl-pyrrolidinium lactate (84.4%) [**2h**] - R = CH_3, (-)-1-methyl-1-menthoxyacetyl-pyrrolidinium lactate (84.1%)

In conclusion, we have synthesized sixteen pyrrolidinium-based chiral ionic liquids of which twelve ionic liquids are bearing a chiral cation and four of them are bearing both a chiral cation and a chiral anion. These chiral ionic liquids have been prepared in good yields and characterized using spectroscopy and polarimetry. Efforts are currently underway in our lab to use these chiral compounds as effective reaction media as well as chiral catalysts in asymmetric ring opening of epoxides and the results will be reported in due course.

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14. Representative Procedure for the Synthesis of alkyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium ionic liquids (**1a – 1h**): In a round-bottomed flask, 1-alkylpyrrolidine (0.01 mol) was mixed with (1R,2S,5R)-(-)-chloromethyl menthyl ether (0.01 mol) in acetonitrile under nitrogen atmosphere. The reaction mixture was heated to reflux for 48 h. After the reaction time, the solvent was evaporated using a rotary evaporator and the resultant, alkyl [(1R,2S,5R (-)-1-menthoxymethyl]pyrrolidinium chloride, was dried in a vacuum line overnight. In the second step, chloride of the ionic liquid was replaced with tetrafluoroborate, hexafluorophosphate, bistrifluoromethane sulfonimide, or L-lactate by reacting with HBF_4, KPF_6, or bis(trifluoromethane) sulfonimide lithium salt in water or sodium L-lactate in acetone, respectively. The product was extracted into methylene chloride (2 x 10 mL) and the combined organic layers were dried with anhydrous Na_2SO_4. The solvent was evaporated using a rotary evaporator and the final ionic liquids were dried in a vacuum line prior to characterization.

15. All products exhibited spectral properties consistent with the assigned structures. Butyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium chloride (90.0%), $[\alpha]^{20}_D$ -59.6; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.65, 4.61 (d, *J* = 8.0 Hz, 2H), 3.72 (t, *J* = 5.9 Hz, 2H), 3.50 (t, *J* = 5.9 Hz, 2H), 3.33 (t, *J* = 6.9 Hz, 2H), 2.93 (dt, *J* = 4.0, 8.0 Hz, 1H), 2.10 (t, *J* = 6.2 Hz, 4H), 1.49–1.46 (m, 2H), 1.24-1.22 (m, 2H), 2.09-0.77 (m, 9H), 0.96 (t, *J* = 9.0 Hz, 3H), 0.89 (d, *J* = 8.0 Hz, 6H), 0.74 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 83.4, 80.7, 59.9, 59.7, 59.2, 47.9, 40.3, 33.9, 31.1, 25.8, 25.3, 22.6, 22.3, 21.9 (2C), 20.9, 19.7, 15.7, 13.6; IR (ν/cm^{-1}): 2940, 2920, 1110, 1050.
Table 1, **1a**: Butyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium tetrafluoroborate (semisolid; yield = 84.5%), $[\alpha]^{20}_D$ -52.4; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.55, 4.47 (d, *J* = 8.1 Hz, 2H), 3.61 (t, *J* = 5.8 Hz, 2H), 3.45 (t, *J* = 5.8 Hz, 2H), 3.30 (t, *J* = 5.9 Hz, 2H), 3.12 (dt, *J* = 4.0, 8.1 Hz, 1H), 2.14 (t, *J* = 6.1 Hz, 4H), 1.63-1.61 (m, 2H), 1.38-1.36 (m, 2H), 2.08-0.76 (m, 9H), 0.95 (t, *J* = 8.8 Hz, 3H), 0.88 (d, *J* = 7.9 Hz, 6H), 0.76 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 83.1, 80.9, 60.0, 59.8, 59.7, 48.1, 40.2, 34.1, 31.2, 25.9, 25.3, 22.8, 22.3, 22.1 (2C), 21.1, 19.7, 15.9, 13.6; IR (ν/cm^{-1}): 2930, 2910, 1215, 1062.
Table 1, **1b**: Butyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium hexafluorophosphate (semisolid; yield = 81.8%), $[\alpha]^{20}_D$ -47.0; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.50, 4.40 (d, *J* = 8.1 Hz, 2H), 3.58 (t, *J* = 5.9 Hz, 2H), 3.40 (t, *J* = 5.7 Hz, 2H), 3.25 (t, *J* = 5.7 Hz, 2H), 3.15 (dt, *J* = 4.0, 8.0 Hz, 1H), 2.13 (t, *J* = 5.7 Hz, 4H), 1.64-1.62 (m, 2H), 1.39-1.37 (m, 2H), 2.09-0.88 (m, 9H), 0.94 (t, *J* = 8.7 Hz, 3H), 0.89 (d, *J* = 7.8 Hz, 6H), 0.77 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 83.2, 81.0, 60.1, 59.9, 59.8, 48.0, 40.1, 34.1, 31.2, 25.9, 25.2, 22.9, 22.4, 22.3 (2C), 21.0, 19.7, 15.8, 13.5; IR (ν/cm^{-1}): 2930, 2910, 1220, 1062, 840.
Table 1, **1c**: Butyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium bis(trifluoromethane)sulfonimide (semisolid; yield = 89.4%), $[\alpha]^{20}_D$ -32.9; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.51, 4.41 (d, *J* = 8.0 Hz, 2H), 3.59 (t, *J* = 6.0 Hz, 2H), 3.40 (t, *J* = 5.7 Hz, 2H), 3.27 (t, *J* = 5.7 Hz, 2H), 3.17 (dt, *J* = 4.1, 7.9 Hz, 1H), 2.18 (t, *J* = 5.7 Hz, 4H), 1.67-1.63 (m, 2H), 1.36-1.34 (m, 2H), 2.09-0.92 (m, 9H), 0.91 (t, *J* = 8.7 Hz, 3H), 0.90 (d, *J* = 8.4 Hz, 6H), 0.77 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 121.8, 118.6, 83.0, 81.0, 60.0, 59.9 (2C), 48.0, 40.1, 34.0, 31.2, 25.9, 25.3, 22.8, 22.4, 22.3 (2C), 21.9, 19.6, 15.7, 13.4; IR (ν/cm^{-1}): 2930, 2910, 1220, 1062, 840.
Table 1, **1d**: Butyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium L-lactate (semisolid; yield = 89.5%), $[\alpha]^{20}_D$ -44.2; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.68, 4.59 (d, *J* = 7.2 Hz, 2H), 4.12 (q, *J* = 8.0 Hz, 1H), 3.58 (t, *J* = 5.8 Hz, 2H), 3.56 (t, *J* = 5.7 Hz, 2H), 3.35 (t, *J* = 5.7 Hz, 2H), 3.18 (dt, *J* = 4.0, 7.0 Hz, 1H), 3.04 (bs, 1H, OH), 2.23 (t, *J* = 5.8 Hz, 4H), 1.71- 1.70 (m, 2H), 1.38-1.36 (m, 2H), 1.33 (d, *J* = 4.0 Hz, 3H), 2.16-0.97 (m, 9H), 0.95 (t, *J* = 7.6 Hz, 3H), 0.94 (d, *J* = 7.7 Hz, 6H), 0.84 (d, *J* = 8.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 182.2, 83.5, 80.6, 68.6, 60.6, 60.3, 59.6, 48.5, 40.1, 34.5, 31.1, 25.8, 25.0, 22.3, 22.1, 22.0 (2C), 21.1, 20.3, 19.6, 15.8, 13.3; IR (ν/cm^{-1}): 3600-2500 (br), 2990, 1730, 1225, 1066.
Methyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium chloride (92.0%), $[\alpha]^{20}_D$ -59.8; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.90, 4.89 (d, *J* = 7.9 Hz, 2H), 3.79 (t, *J* = 5.9 Hz, 2H), 3.65 (t, *J* = 5.9 Hz, 2H), 3.46 (dt, *J* = 3.9, 7.8 Hz, 1H), 3.28 (s, 3H), 2.29 (t, *J* = 5.8 Hz, 4H), 2.29-0.84 (m, 9H), 0.83 (d, *J* = 7.9 Hz, 6H), 0.81 (d, *J* = 7.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 87.1, 81.5, 61.0(2C), 48.2, 47.8, 40.6, 34.0, 31.2, 25.8, 22.8, 22.2, 22.1, 21.1(2C), 16.0; IR (ν/cm^{-1}): 2980, 2920, 1050, 920.
Table 1, **1e**: Methyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium tetrafluoroborate (solid; m.p. = 134-136 ^{o}C; yield = 82.3%), $[\alpha]^{20}_D$ -61.3; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.62, 4.59 (d, *J* = 8.1 Hz, 2H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.45 (t, *J* = 5.8 Hz, 2H), 3.44 (dt, *J* = 3.8, 7.9 Hz, 1H), 3.10 (s, 3H), 2.22 (t, *J* = 5.9 Hz, 4H), 2.06-0.90 (m, 9H), 0.89 (d, *J* = 7.8 Hz, 6H), 0.78 (d, *J* = 7.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 87.3, 81.6, 61.2(2C), 48.2, 48.0, 40.3, 34.1, 31.2, 25.9, 22.8, 22.3, 22.1, 21.1(2C), 15.9; IR (ν/cm^{-1}): 2990, 2915, 1110, 940.
Table 1, **1f**: Methyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium hexafluorophosphate (solid; m.p. = 178-181 ^{o}C; yield = 81.0%), $[\alpha]^{20}_D$ -53.3; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.56, 4.52 (d, *J* = 8.0 Hz, 2H), 3.63 (t, *J* = 5.8 Hz, 2H), 3.46 (dt, *J* = 4.4, 8.0 Hz, 1H), 3.40 (t, *J* = 5.8 Hz, 2H), 3.11 (s, 3H), 2.23 (t, *J* = 5.9 Hz, 4H), 2.04-0.91 (m, 9H), 0.89 (d, *J* = 7.9 Hz, 6H), 0.78 (d, *J* = 7.8 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$, δ): 87.4, 81.7, 61.3(2C), 48.2, 48.1, 40.2, 34.1, 31.3, 25.9, 22.7, 22.4, 22.1, 21.1(2C), 15.8; IR (ν/cm^{-1}): 2995, 2920, 1200, 1050.

Table 1, **1g**: Methyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium bis(trifluoromethane)sulfonamide (semisolid; yield = 84.4%), $[\alpha]^{20}_D$ -36.3; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.55, 4.50 (d, *J* = 8.0 Hz, 2H), 3.56 (t, *J* = 5.9 Hz, 2H), 3.42 (dt, *J* = 4.4, 8.0 Hz, 1H), 3.38 (t, *J* = 5.9 Hz, 2H), 3.03 (s, 3H), 2.20 (t, *J* = 5.8 Hz, 4H), 2.02-0.90 (m, 9H), 0.87 (d, *J* = 7.8 Hz, 6H), 0.75 (d, *J* = 7.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 121.8, 118.9, 87.7, 81.7, 61.4(2C), 48.1, 48.0, 40.2, 34.0, 31.2, 25.9, 22.8, 22.2, 22.1, 21.9(2C), 15.7; IR (ν/cm^{-1}): 2996, 2912, 1290, 1030.

Table 1, **1h**: Methyl [(1R,2S,5R)-(-)-menthoxymethyl]pyrrolidinium L-lactate (semisolid; yield = 86.4%), $[\alpha]^{20}_D$ -67.8; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.89, 4.73 (d, *J* = 7.0 Hz, 2H), 3.94 (q, *J* = 5.4 Hz, 1H), 3.80 (t, *J* = 5.8 Hz, 2H), 3.64 (t, *J* = 5.8 Hz, 2H), 3.48 (dt, *J* = 4.4, 8.0 Hz, 1H), 3.28 (s, 3H), 2.76 (bs, 1H, OH), 2.25 (t, *J* = 5.9 Hz, 4H), 1.55 (d, *J* = 5.9 Hz, 3H), 2.14-0.92 (m, 9H), 0.87 (d, *J* = 7.8 Hz, 6H), 0.82 (d, *J* = 7.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 180.1, 87.3, 81.5, 71.4, 61.0(2C), 48.6, 48.2, 40.2, 34.0, 31.6, 25.9, 22.3, 22.2, 22.1, 21.1(2C), 21.0, 16.1; IR (ν/cm^{-1}): 3580-2525 (br), 2970, 1730, 1200, 1025.

16. Procedure for the synthesis of (1R,2S,5R)-(-)-menthyl chloroacetate: (1R,2S,5R)-(-)-menthol (0.10 mol) was reacted with chloroacetyl chloride (0.11 mol) and trimethylamine (0.11 mol) in THF, stirring overnight at room temperature. After the reaction time, the solvent was evaporated and the product was purified by silica gel flash column chromatography using a gradient mixture of hexanes/ethyl acetate as the mobile phase. (85.6%); ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.70 (dt, *J* = 6.0, 11.0 Hz, 1H), 3.97 (s, 2H), 2.14-0.91 (m, 9H), 0.86 (d, *J* = 7.9 Hz, 6H), 0.73 (d, *J* = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 166.9, 87.4, 81.7, 61.3(2C), 48.2, 48.1, 40.2, 34.1, 31.3, 25.9, 22.7, 22.4, 22.1, 21.1(2C), 15.8; IR (ν/cm^{-1}): 2995, 2920, 1200, 1050.

17. Representative Procedure for the Synthesis of alkyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium ionic liquids (**2a – 2h**): In a round-bottomed flask, 1-alkylpyrrolidine (0.01 mol) was mixed with (1R,2S,5R)-(-)-menthyl chloroacetate (0.01 mol) in acetonitrile under nitrogen atmosphere. The reaction mixture was heated to reflux for 48 h. After the reaction time, the solvent was evaporated using a rotary evaporator and the resultant, alkyl [(1R,2S,5R (-)-1-menthoxyacetyl]pyrrolidinium chloride, was dried in a vacuum line overnight. In the second step, chloride of the ionic liquid was replaced with tetrafluoroborate, hexafluorophosphate, bistrifluoromethane sulfonimide, or L-lactate by reacting with HBF_4, KPF_6, or bis(trifluoromethane) sulfonimide lithium salt in water or sodium L-lactate in acetone, respectively. The product was extracted into methylene chloride (2 x 10 mL) and the combined organic layers were dried with anhydrous Na_2SO_4. The solvent was evaporated using a rotary evaporator and the final ionic liquids were dried in a vacuum line prior to characterization.

18. All products exhibited spectral properties consistent with the assigned structures. Butyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium chloride (87%), $[\alpha]^{20}_D$ - 35.2; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.60 (dt, *J* = 4.2, 10.1 Hz, 1H), 4.54, 4.27 (d, *J* = 10.6 Hz, 2H), 3.98 (t, *J* = 5.8 Hz, 2H), 3.70 (t, *J* = 5.8 Hz, 2H), 3.39 (t, *J* = 5.8 Hz, 2H), 2.13 (t, *J* = 5.8 Hz, 4H), 1.50-1.47 (m, 2H), 1.20-1.18 (m, 2H), 2.05–0.90 (m, 9H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H), 0.68 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.5, 77.4, 71.0, 64.3, 64.2, 60.9, 46.5, 40.4, 33.7, 31.3, 26.2, 25.6, 22.9, 21.8, 21.6, 21.0, 20.6, 19.6, 16.1, 13.6; IR (ν/cm^{-1}): 2983, 1742, 1188, 1091.

Table 2, **2a**: Butyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium tetrafluoroborate (solid; m.p. = 52-54 °C; yield = 81.7%), $[\alpha]^{20}_D$ - 42.1; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.77 (dt, *J* = 4.0, 10.7 Hz, 1H), 4.13, 4.11 (d, *J* = 7.6 Hz, 2H), 3.79 (t, *J* = 5.8 Hz, 4H), 3.37 (t, *J* = 5.9 Hz, 2H), 2.23 (t, *J* = 5.7 Hz, 4H), 1.67-1.65 (m, 2H), 1.36-1.34 (m, 2H), 2.12–0.98 (m, 9H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.6 Hz, 3H), 0.69 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.4, 77.6, 71.5, 64.7, 64.5, 61.1, 46.7, 40.4, 34.6, 31.5, 25.9, 25.7, 23.2, 22.2, 21.9, 21.0, 20.7, 19.6, 16.0, 13.5; IR (ν/cm^{-1}): 2973, 1748, 1211, 1033.

Table 2, **2b**: Butyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium hexafluorophosphate (solid; m.p. = 38-39 °C; yield = 87.7%), $[\alpha]^{20}_D$ -40.2; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.76 (dt, *J* = 4.2, 11.0 Hz, 1H), 4.07, 4.02 (d, *J* = 7.6 Hz, 2H), 3.67 (t, *J* = 5.9 Hz, 4H), 3.37 (t, *J* = 5.4 Hz, 2H), 2.21 (t, *J* = 5.7 Hz, 4H), 1.60-1.58 (m, 2H), 1.39-1.36 (m, 2H), 2.09–0.92 (m, 9H), 0.93 (t, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H), 0.71 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.1, 77.4, 71.6, 64.8, 64.6, 61.4, 46.7, 40.3, 33.9, 31.7, 25.3, 25.0, 23.4, 21.9, 21.8, 21.6, 20.7, 19.5, 16.0, 13.4; IR (ν/cm^{-1}): 2979, 1750, 1207, 1056.

Table 2, **2c**: Butyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium bis(trifluoromethane)sulfonimide (liquid; yield = 92.8%) $[\alpha]^{20}_D$ -32.1; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.80 (dt, *J* = 4.0, 10.6 Hz, 1H), 4.10, 4.09 (d, *J* = 7.5 Hz, 2H), 3.70 (t, *J* = 5.8 Hz, 4H), 3.38 (t, *J* = 5.4 Hz, 2H), 2.24 (t, *J* = 5.7 Hz, 4H), 1.67-1.66 (m, 2H), 1.41-1.37 (m, 2H), 2.13–0.98 (m, 9H), 0.95 (t, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 6.7 Hz, 3H), 0.72 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.1, 120.9, 118.0, 77.2, 71.5, 64.7, 64.6, 61.4, 46.7, 40.3, 33.9, 31.7, 25.6, 25.2, 23.6, 21.8, 21.7, 21.0, 20.6, 19.5, 16.0, 13.3; IR (ν/cm^{-1}): 2991, 1744, 1284, 1006.

Table 2, **2d**: Butyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium L-lactate (semisolid; yield = 84.4%), $[\alpha]^{20}_D$ -39.8; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.65 (dt, *J* = 4.0, 10.4 Hz, 1H), 4.62, 4.36 (d, *J* = 7.6 Hz, 2H), 4.05 (q, *J* = 5.5 Hz, 1H), 3.75 (t, *J* = 5.7 Hz, 4H), 3.42 (t, *J* = 5.9 Hz, 2H), 2.93 (bs, 1H, OH), 2.20 (t, *J* = 5.6 Hz, 4H), 1.55-1.52 (m, 2H), 1.29-1.26 (m, 2H), 1.19 (d, J = 6.0 Hz, 3H), 2.07–0.98 (m, 9H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.76 (d, *J* = 7.0 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H), 0.73 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 182.4, 164.7, 77.6, 71.1, 67.9, 64.4, 64.0, 60.2, 46.6, 40.5, 34.5, 31.6, 25.6, 25.3, 23.6, 21.8, 21.6, 21.2, 20.7, 20.3, 19.7, 16.0, 13.5; IR (ν/cm^{-1}): 2996, 1758, 1749, 1233, 1016.

Methyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium chloride (91%), $[\alpha]^{20}_D$ -54.0; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.91, 4.75 (d, *J* = 11.1 Hz, 2H), 4.71 (dt, *J* = 4.5, 11.1 Hz, 1H), 3.98 (t, *J* = 5.8 Hz, 4H), 3.37 (s, 3H), 2.20 (t, *J* = 5.8 Hz, 4H), 2.05–0.95 (m, 9H), 0.90 (d, *J* = 7.5 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 165.0, 77.6, 71.1, 65.2, 65.1, 50.1, 46.4, 40.6, 33.7, 31.5, 26.1, 23.1, 21.8, 21.4, 21.0, 20.8, 16.1; IR (ν/cm^{-1}): 2980, 1740, 1180, 1090.

Table 2, **2e**: Methyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium tetrafluoroborate (solid; m.p. =

63-64 °C; yield = 85.1%), $[\alpha]^{20}_{D}$ -49.7; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.76 (dt, *J* = 4.7, 11.2 Hz, 1H), 4.26, 4.25 (d, *J* = 7.0 Hz, 2H), 3.78 (t, *J* = 5.8 Hz, 2H), 3.68 (t, *J* = 5.8 Hz, 2H), 3.25 (s, 3H), 2.24 (t, *J* = 5.8 Hz, 4H), 2.12–0.90 (m, 9H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 7.6 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.5, 77.4, 71.6, 65.5 (2C), 50.1, 46.7, 40.2, 34.6, 31.5, 25.9, 23.3, 21.9, 21.6, 21.1, 20.7, 16.1; IR (ν/cm^{-1}): 2994, 1742, 1220, 1060.

Table 2, **2f**: Methyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium hexafluorophosphate (solid; m.p. = 64-66 °C; yield = 90.3%), $[\alpha]^{20}_{D}$ -48.6; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.78 (dt, *J* = 4.8, 11.1 Hz, 1H), 4.17, 4.12 (d, *J* = 5.9 Hz, 2H), 3.78 (t, *J* = 5.7 Hz, 2H), 3.64 (t, *J* = 5.7 Hz, 2H), 3.23 (s, 3H), 2.25 (t, *J* = 5.8 Hz, 4H), 2.14-0.91 (m, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.0 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.3, 77.9, 71.6, 65.7 (2C), 50.1, 46.7, 40.4, 34.6, 31.5, 26.1, 23.2, 21.9, 21.6, 21.1, 20.7, 16.2; IR (ν/cm^{-1}): 2990, 1745, 1217, 1053.

Table 2, **2g**: Methyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium bis(trifluoromethane)sulfonamide (liquid; yield = 82.6%), $[\alpha]^{20}_{D}$ -35.8; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.79 (dt, *J* = 4.9, 11.0 Hz, 1H), 4.21, 4.18 (d, *J* = 5.4 Hz, 2H), 3.78 (t, *J* = 5.9 Hz, 2H), 3.66 (t, *J* = 5.9 Hz, 2H), 3.24 (s, 3H), 2.26 (t, *J* = 5.8 Hz, 4H), 2.15-0.96 (m, 9H), 0.90 (d, *J* = 7.2 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 164.2, 121.9, 119.0, 78.0, 71.6, 65.8, 65.7, 50.1, 46.7, 40.4, 34.6, 31.7, 26.2, 23.2, 21.8, 21.5, 21.0, 20.6, 16.2; IR (ν/cm^{-1}): 2986, 1744, 1222, 1025.

Table 2, **2h**: Methyl [(1R,2S,5R)-(-)-menthoxyacetyl]pyrrolidinium L-lactate (semisolid; yield = 84.1%), $[\alpha]^{20}_{D}$ -48.0; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.89 (dt, *J* = 4.9, 11.0 Hz, 1H), 4.41, 4.37 (d, *J* = 5.4 Hz, 2H), 4.10 (q, *J* = 4.5 Hz, 1H), 3.78 (t, *J* = 5.4 Hz, 2H), 3.66 (t, *J* = 5.4 Hz, 2H), 3.26 (s, 3H), 2.25 (t, *J* = 5.8 Hz, 4H), 1.32 (d, *J* = 5.8 Hz, 3H), 2.03-0.90 (m, 9H), 0.91 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 182.4, 164.2, 77.8, 68.6 (2C), 66.2, 62.7, 49.9, 46.6, 40.1, 34.1, 31.5, 26.2, 23.4, 23.3, 23.4, 21.8, 20.5, 20.4, 16.0; ; IR (ν/cm^{-1}): 3555-2480 (br), 1744, 1734, 1218, 1009.

Highlights

- A series of pyrrolidinium-based chiral ionic liquids bearing a chiral cation, a chiral anion or both was prepared in good yields.
- The synthesis used an efficient, economic and simple pathway.
- The chirality was introduced using inexpensive and readily available compounds from a chiral pool.
- The new chiral ionic liquids were characterized by both spectroscopy and polarimetry.