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Synthesis of new chiral ionic liquids based on (−)-menthol and (−)-borneol

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Abstract

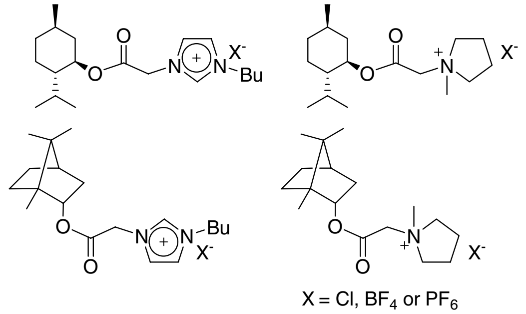
New chiral ionic liquids (CILs) based on (−)-menthol and (−)-borneol were designed and synthesized in very good yields using a simple and efficient 3-step strategy. The properties and characterization of these compounds are discussed.

Nowadays, the search for green reaction media for organic reactions has triggered the development of several alternatives to volatile and toxic organic solvents.[1] Among these, room temperature ionic liquids (RTILs) have emerged as promising candidates due to characteristics such as extremely low vapor pressure, tunability of their properties by varying the structures of the cations or anions, and recyclability, just to mention a few.[2] For these reasons, many compounds of this type have been synthesized and successfully used as solvents in organic synthesis.[1,3] In many cases, reaction yields and/or selectivities were improved when compared to the same reactions in usual organic solvents. Furthermore, being ionic in nature, they have a polar characteristic thus dissolving a wide range of organic and inorganic reagents.

More recently, chiral ionic liquids (CILs) have been designed and used as chiral environments aiming the induction of chirality in reactions involving non-chiral substrates.[4] Nevertheless, so far only a few have proved to be efficient in this task.[5] Therefore, the search for new CILs seems to be demanding. Herein, we wish to report the synthesis and characterization of several CILs based on (−)-menthol[6] and (−)-borneol[7] (Fig. 1). Although many other menthol-based CILs have been reported, most of them comprise an ether functionality.[6a,b] The introduction of an ester function, besides being an easy task, could perhaps improve some of their properties especially those related to the stabilization of polymers, which is one of our goals.

The synthesis of the ionic liquids involved a general three-step strategy, as shown in Scheme 1.[8] In the first step, chloroacetic acid was esterified with (−)-menthol and (−)-borneol, via DCC/DMAP coupling, furnishing chloroacetylmenthol and chloroacetylborneol in 81% and 96% yields, respectively.

The corresponding esters were then reacted with 1-butylimidazole or 1-methylpyrrolidine under solvent-free conditions, to form the chloride ILs (80–97% yields). In this step, a higher temperature (130 °C) had to be used in the



X = Cl, BF_4 or PF_6

Fig. 1. Synthesis of chiral ionic liquids.

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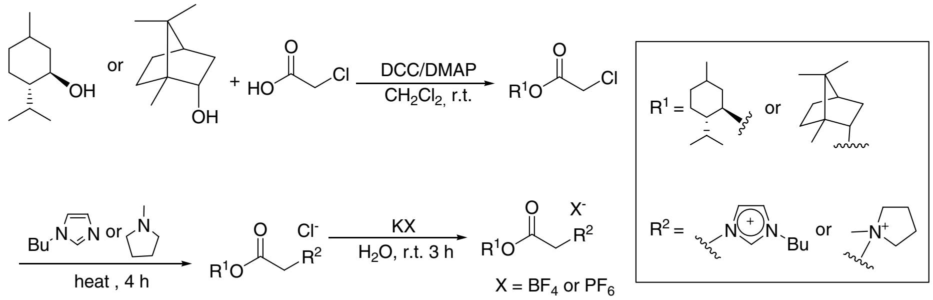
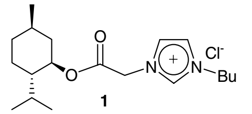
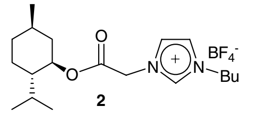
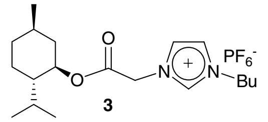
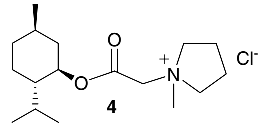
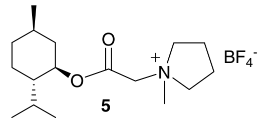
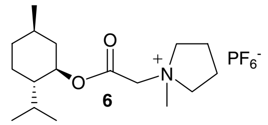
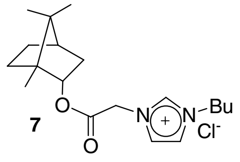
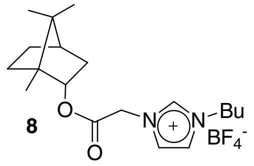
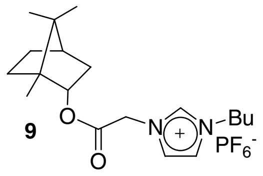


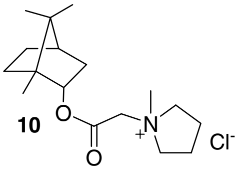
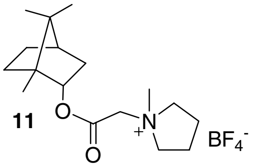
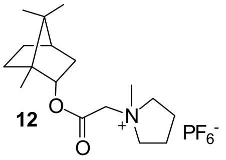
Scheme 1. General strategy for the synthesis of CILs based on (−)-menthol and (−)-borneol.

Table 1
Structures and some properties of the CILs synthesized

Entry	Name[11]	Structure	Yields (%)	$[\alpha]_D^{20}$ (c 5.0, MeOH)	Mp (°C)
1	[amebim]Cl	 **1**	96	−37.4	Liquid
2	[amebim]BF_4	 **2**	97	−28.0	Liquid
3	[amebim]PF_6	 **3**	86	−40.0	Liquid
4	[amempyr]Cl	 **4**	81	−44.2	63
5	[amempyr]BF_4	 **5**	90	−45.1	64
6	[amempyr]PF_6	 **6**	72	−53.8	66
7	[abobim]Cl	 **7**	97	−37.4	Liquid
8	[abobim]BF_4	 **8**	79	−3.2	Liquid
9	[abobim]PF_6	 **9**	86	−12.2	Liquid

(continued on next page)

Table 1 (*continued*)

Entry	Name[11]	Structure	Yields (%)	$[\alpha]_D^{20}$ (*c* 5.0, MeOH)	Mp (°C)
10	[abompyr]Cl	 **10**	80	−31.3	67
11	[abompyr]BF_4	 **11**	86	−11.1	88
12	[abompyr]PF_6	 **12**	74	−12.5	84

reactions of the borneol series as compared to the menthol series (80 °C) to get a more homogenous stirring. The last step was the anion exchange, which was easily accomplished in aqueous media using either KBF_4 or KPF_6. All imidazolium-derived ILs were obtained as viscous brownish liquids[9] (79–96% yields), whereas those derived from the *N*-methylpyrrolidine cation were low melting solids (mp <90 °C, 72–90% yields). The structures and some main characteristics of the compounds synthesized are shown in Table 1. All compounds had their structures confirmed by IR, mass spectra, ^1H NMR, and ^{13}C NMR analysis.[10] The main IR bands were the stretch of the carbonyl groups which ranged from 1740 to 1751 cm^{-1} and those of the C–O stretch in the region between 1020 and 1230 cm^{-1}.

Structural investigation using NMR spectroscopy unequivocally confirmed the structures of the CILs. The appearance of peaks of the imidazolic hydrogens (compounds **1**–**3** and **7**–**9**) and of the attached butyl group confirmed the coupling of the *N*-butylimidazole into the molecule. The diastereomeric methylenic peaks between the nitrogen and the acyl groups appear between δ 4.21 and 5.50 as singlets for the ILs of the borneol series and as two doublets ($J = 17$–18 Hz) for the menthol series (except for [amebim]PF_6 (entry 3) and [amempyr]PF_6 (entry 6), in which they appear as singlets). The CHs linked to the oxygen ester appear as triplets of doublets (menthol series, δ 4.77–4.82) or as multiplets (borneol series, δ 4.92–5.04). For the ILs based on the pyrrolidinic nucleus, the *N*-methyl group appears at δ 3.27–3.51. Interestingly, the specific rotations for all compounds in both series showed negative values[12] (Table 1).

However, the most important characteristic of the ^1H NMR spectra is the δ shift of the acidic hydrogen of the imidazolic group. A significant upfield variation was observed when the chloride anion was exchanged with the tetrafluoroborate (0.9 ppm) or hexafluorophosphate (2 ppm) anions, showing a strict relation between the IL structure and the size of the anion. The ^{13}C NMR spectra completed the analysis of the compounds, showing peaks corresponding to the imidazolic carbons (δ 120–140), to the acyl groups (δ 164–168), and to the carbinolic carbons (δ 76–84).

In conclusion, 12 chiral ionic liquids based on (−)-menthol or (−)-borneol were synthesized in a straightforward 3-step strategy under very mild conditions and in very good yields. The application of these compounds as polymers stabilizers and as chiral solvents in some organic reactions is currently underway and will be published in due course.

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7. A borneol sulfonamide CIL has been reported: Gadenne, B.; Hesemann, P.; Moreau, J. J. E. *Tetrahedron Lett.* **2004**, *45*, 8157–8160.
8. General experimental procedure for the synthesis of the CILs: To a solution of 64.0 mmol of (−)-menthol (10.00 g) or (−)-borneol (9.86 g) in dry dichloromethane (50 mL) were added, under stirring and at 0 °C, 83.2 mmol of chloroacetic acid (7.82 g), 83.2 mmol of DCC (17.2 g) and 6.4 mmol of DMAP (0.78 g). Stirring was continued for 12 h at room temperature. The suspension was filtered under vacuum and washed with dry dichloromethane. The organic phase was then washed with 10% HCl (50 mL), satd $NaHCO_3$ (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered and concentrated. The residue was heated at 80 °C (130 °C for (−)-borneol) under stirring in the presence of 1.0 equiv of butylimidazole for 4 h, giving a brown oil or a solid. For the ion exchange, the residue was stirred in water (10 mL) at rt for 3 h with 1.0 equiv of either potassium tetrafluoroborate or potassium hexafluorophosphate. After water evaporation, the residue was diluted in CH_2Cl_2 (10 mL), filtered under vacuum over a pad of Celite®, dried over Na_2SO_4 and concentrated to give the corresponding chiral ionic liquids, which were further dried under vacuum at 80 °C for several hours. This procedure yielded all compounds in high purity without the need for further purification. Analytical data reported in Ref. 10 were obtained after submitting the samples to simple column chromatography eluting with hexanes/EtOAc (7:3).
9. Two structurally similar CILs based on (−)-menthol have been reported but were solids at room temperature (see Ref. 6c).
10. Selected spectroscopic data for compounds **3**–**14**: *Acetylmentholbutylimidazolium chloride, [amebim]Cl* (**3**): yield = 96%; $[\alpha]_D^{20}$ −37.4 (*c* 5.0, MeOH); IR (film): ν_{max} 3391, 1745, 1227, 1172 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 10.40 (s, 1H), 7.50 (s, 1H), 7.40 (s, 1H), 5.50 (d, $J = 18.0$ Hz, 1H), 5.40 (d, $J = 18.0$ Hz, 1H), 4.77 (td, $J = 10.7$ and 4.7 Hz, 1H), 4.40–4.25 (m, 2H), 2.22–1.30 (m, 9H), 1.10–0.80 (m, 4H), 0.97 (t, $J = 7.6$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 0.90 (d, $J = 7.4$ Hz, 3H), 0.75 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 165.6, 137.7, 123.2, 121.3, 76.7, 49.8, 49.5, 48.9, 40.1, 33.5, 31.5, 30.9, 25.6, 22.3, 21.4, 20.3, 18.8, 15.7, 13.0.

    Acetylmentholbutylimidazolium tetrafluoroborate, [amebim]BF$_4$ (**4**): yield = 97%; $[\alpha]_D^{20}$ −28.0 (*c* 5.0, MeOH); IR (film): ν_{max} 1745, 1173, 1063, 912, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 9.95 (s, 1H), 7.46 (s, 1H), 7.37 (s, 1H), 5.35 (d, $J = 18.0$ Hz, 1H), 5.26 (d, $J = 18.0$ Hz, 1H), 4.79 (td, $J = 11.2$ and 4.6 Hz, 1H), 4.29 (t, $J = 8.0$ Hz, 2H), 2.10–1.10 (m, 9H), 1.10–0.90 (m, 4H), 0.96 (t, $J = 7.5$ Hz, 3H), 0.92 (d, $J = 7.0$ Hz, 3H), 0.90 (d, $J = 7.4$ Hz, 3H), 0.75 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 165.7, 137.5, 123.4, 121.6, 77.1, 49.9, 49.6, 46.4, 40.2, 33.6, 31.7, 31.1, 25.7, 22.8, 21.6, 20.4, 19.1, 15.8, 13.2.

    Acetylmentholbutylimidazolium hexafluorophosphate, [amebim]PF$_6$ (**5**): yield = 86%; $[\alpha]_D^{20}$ −40.0 (*c* 5.0, MeOH); IR (film): ν_{max} 1746, 1173, 1040, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.66 (s, 1H), 7.37 (s, 1H), 7.32 (s, 1H), 4.99 (s, 2H), 4.79 (td, $J = 10.5$ and 5.0 Hz, 1H), 4.19 (t, $J = 7.0$ Hz, 2H), 2.10–1.20 (m, 9H), 1.12–0.80 (m, 4H), 0.96 (t, $J = 7.0$ Hz, 3H), 0.92 (d, $J = 7.0$ Hz, 3H), 0.90 (d, $J = 7.5$ Hz, 3H), 0.75 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 165.4, 136.4, 123.8, 121.9, 76.6, 50.0, 49.7, 46.7, 40.2, 33.9, 31.5, 31.3, 25.9, 23.0, 21.7, 20.6, 19.1, 15.9,13.1.

    Acetylmentholmethylpyrrolidine chloride, [amempyr]Cl (**6**): yield = 81%; $[\alpha]_D^{20}$ −44.2 (*c* 5.0, MeOH); mp = 63 °C; IR (KBr): ν_{max} 1740, 1181, 1098 cm^{-1}; ^{1}H NMR ($CDCl_3$): 5.11 (d, $J = 17.0$ Hz, 1H), 4.89 (d, $J = 17.0$ Hz, 1H), 4.81 (td, $J = 11.4$ and 5.4 Hz, 1H), 4.17–4.09 (m, 4H), 3.51 (s, 3H), 2.42–0.80 (m, 13H), 0.93 (d, $J = 7.5$ Hz, 3H), 0.90 (d, $J = 7.6$ Hz, 3H), 0.75 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 164.7, 77.1, 65.0, 64.9, 62.0, 48.8, 46.4, 40.3, 33.6, 31.2, 25.9, 22.8, 21.6, 21.2, 21.1, 20.6, 15.8.

    Acetylmentholmethylpyrrolidine tetrafluoroborate, [amempyr]BF$_4$ (**7**): yield = 90%; $[\alpha]_D^{20}$ −45.1 (*c* 5.0, MeOH); mp = 64 °C; IR (KBr): ν_{max} 1742, 1219, 1062 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.81 (td, $J = 11.2$ and 4.7 Hz, 1H), 4.66 (d, $J = 17.0$ Hz, 1H), 4.52 (d, $J = 17.0$ Hz, 1H), 4.08–3.85 (m, 4H), 3.40 (s, 3H), 2.40–0.80 (m, 13H), 0.92 (d, $J = 6.7$ Hz, 3H), 0.90 (d, $J = 6.9$ Hz, 3H), 0.75 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 164.5, 77.4, 65.3, 62.0, 55.1, 49.1, 46.5, 40.3, 33.7, 31.3, 26.0, 23.0, 21.7, 21.4, 21.3, 20.6, 15.9.

    Acetylmentholmethylpyrrolidine hexafluorophosphate, [amempyr]PF$_6$ (**8**): yield = 72%; $[\alpha]_D^{20}$ −53.8 (*c* 5.0, MeOH); mp = 66 °C; IR (KBr): ν_{max} 1744, 1220, 1021, 840, 558 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.82 (td, $J = 11.0$ and 5.0 Hz, 1H), 4.21 (s, 2H), 3.87–3.76 (m, 4H), 3.27 (s, 3H), 2.36–2.21 (m, 2H), 2.05–0.87 (m, 11H), 0.95 (d, $J = 6.1$ Hz, 3H), 0.92 (d, $J = 7.2$ Hz, 3H), 0.76 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 164.1, 77.8, 65.6, 62.2, 56.2, 49.5, 46.6, 40.2, 33.8, 31.4, 26.0, 23.1, 21.8, 21.5, 21.4, 20.6, 15.9.

    Acetylborneolbutylimidazole chloride, [*abobim*]*Cl* (**9**): yield = 97%; $[\alpha]_D^{20}$ −37.4 (*c* 5.0, MeOH); IR (film): ν_{max} 1744, 1168, 1085 cm^{-1};^{1}H NMR ($CDCl_3$): δ 10.51 (s, 1H); 7.51 (s, 1H), 7.35 (s, 1H), 5.58–5.42 (m, 2H), 5.03–4.93 (m, 1H), 4.30 (t, $J = 6.9$ Hz, 2H), 2.42–1.05 (m, 11H), 0.95 (t, $J = 7.1$ Hz, 3H), 0.89 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 168.0, 134.6, 120.7, 119.6, 83.7, 49.2, 49.0, 46.7, 44.9, 44.6, 38.3, 33.3, 31.8, 26.6, 19.8, 19.5, 19.0, 13.0, 11.1.

    Acetylborneolbutylimidazole tetrafluoroborate, [*abobim*]*BF*$_4$ (**10**): yield = 79%; $[\alpha]_D^{20}$ −3.2 (*c* 5.0, MeOH); IR (film): ν_{max} 1751, 1171, 1021, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 9.62 (s, 1H), 7.56 (s, 1H), 7.45 (s, 1H), 5.33 (s, 2H), 5.04–4.97 (m, 1H), 4.32 (t, $J = 7.3$ Hz, 2H), 2.40–1.05 (m, 11H), 1.01 (t, $J = 7.1$ Hz, 3H), 0.93 (s, 3H), 0.92 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 165.3, 136.8, 123.9, 121.9, 83.9, 48.7, 47.8, 46.8, 44.8, 44.6, 38.2, 33.4, 31.7, 26.8, 19.8, 19.5, 19.2, 13.3, 11.2.

    Acetylborneolbutylimidazole hexafluorophosphate, [*abobim*]*PF*$_6$ (**11**): yield = 86%; $[\alpha]_D^{20}$ −12.2 (*c* 5.0, MeOH); IR (film): ν_{max} 1749, 1285, 1170, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.58 (s, 1H), 7.38 (s, 1H), 7.32 (s, 1H), 5.02 (s, 2H), 4.98–4.92 (m, 1H), 4.17 (t, $J = 7.3$ Hz, 2H), 2.40–2.23 (m, 2H), 1.90–1.60 (m, 9H), 0.95 (t, $J = 7.6$ Hz, 3H), 0.88 (s, 3H), 0.87 (s, 3H), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 166.1, 136.4, 123.8, 122.9, 83.2, 48.7, 47.7, 44.9, 44.6, 38.8, 36.0, 31.8, 31.5, 26.7, 19.5, 19.1, 19.0, 18.6, 13.1.

    Acetylborneolmethylpyrrolidine chloride, [abompyr]Cl (**12**): yield = 80%; $[\alpha]_D^{20}$ −31.3 (*c* 5.0, MeOH); mp = 67 °C; IR (KBr): ν_{max} 1746, 1219, 1108, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.08 (s, 2H), 5.02–4.96 (m, 1H), 4.18–4.08 (m, 4H), 3.51 (s, 3H), 2.42–1.00 (m, 11H), 0.90 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 165.4, 82.7, 64.8, 61.9, 48.6, 47.6, 44.3, 38.6, 36.0, 27.5, 26.7, 25.6, 21.1, 19.9, 19.3, 18.4, 13.1.

    Acetylborneolmethylpyrrolidine tetrafluoroborate, [abompyr]BF$_4$ (**13**): yield = 86%; $[\alpha]_D^{20}$ −11.1 (*c* 5.0, MeOH); mp = 88 °C; IR (KBr): ν_{max} 1747, 1220, 1059 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.02–4.96 (m, 1H), 4.76 (s, 2H), 4.18–4.08 (m, 4H), 3.42 (s, 3H), 2.43–1.05 (m, 11H), 0.90 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 165.0, 82.7, 64.8, 61.8, 48.5, 47.4, 44.2, 35.8, 27.3, 26.5, 23.1, 21.1, 19.3, 19.1, 18.3, 18.2, 13.1.

    Acetylborneolmethylpyrrolidine hexafluorophosphate, [abompyr]PF$_6$ (**14**): yield = 74%; $[\alpha]_D^{20}$ −12.5 (*c* 5.0, MeOH); mp = 84 °C; IR (KBr): ν_{max} 1746, 1231, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.03–4.97 (m, 1H), 4.28 (s, 2H), 3.90–3.65 (m, 4H), 3.27 (s, 3H), 2.41–1.05 (m, 11H), 0.89 (s, 3H), 0.88 (s, 3H), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 164.9, 83.4, 65.6, 62.2, 48.8, 47.9, 44.7, 36.1, 27.6, 26.7, 25.8, 21.5, 20.1, 19.6, 18.7, 18.6, 13.2.
11. The names of the CILs synthesized herein were proposed based on their constituents and not on the IUPAC rules. In this way, reasonable abbreviations could be proposed for each one (see Ref. 10).
12. This same trend has also been observed for all other CILs based on (−)-menthol reported in Refs. 6a–c.