Room-Temperature Zwitterionic Ionic Liquids

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A novel series of zwitterionic ionic liquids based on (*E*) or (*Z*) isomer of an urocanic moiety containing a carboxylate group have been prepared. All synthesized compounds present melting points below 100°C. This value can be easily tuned by changing the length of alkyl chain grafted on the imidazolium moiety and the stereochemistry of isomer. Hence, melting temperature as low as -20°C was obtained for *Z* isomer with a N1, N3-methyloctyl imidazolium moiety.

Introduction

Room Temperature Ionic Liquids (ILs) are tuneable and generally environmentally benign solvents that enable to tackle scientific challenges for the industrial implementation of green innovations [1]. Various IL structures were designed to adjust their physicochemical properties to specific needs in many applications [2,3]. Nevertheless, the presence of free ions can be an issue in some cases, e.g. for the study of nucleophilic reactions or in electrochemical applications where migration of IL component ions is prejudicial. Accordingly, a class of ionic liquids in which both cation and anion units tethered covalently, called Zwitterionic Ionic Liquids (ZILs) was developed. The most common zwitterionic-type ionic liquids are nitrogene heterocycles with sulfonate moiety whose examples of structures are given in Figure 1. These ZILs have been intensively studied as designable electrolyte materials for lithium batteries [4] and fuel cells [5].

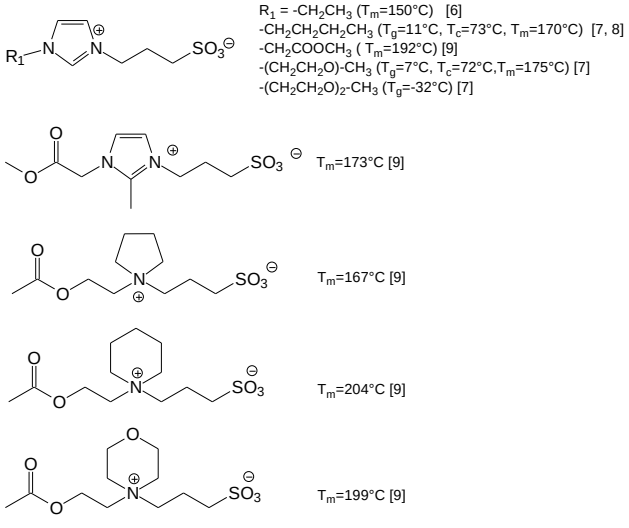


Figure 1. Some examples of zwitterionic-type molten salts containing a sulfonate group with corresponding melting temperature (T_m), glass transition temperature (T_g), and crystallization temperature (T_c).

Less explored ZILs are structures based on imidazoliums with carboxylate functions (Figure 2). They have been used as Bronsted acidic catalysts [10], for desulfurization of fuels [11], for metal oxides solubilization [12] or as liquid crystals [13].

The melting points of ZILs are generally higher than the ones of classical ILs because of a decrease in the motional freedom of each ion and strong intermolecular interactions (Figures 1-2).

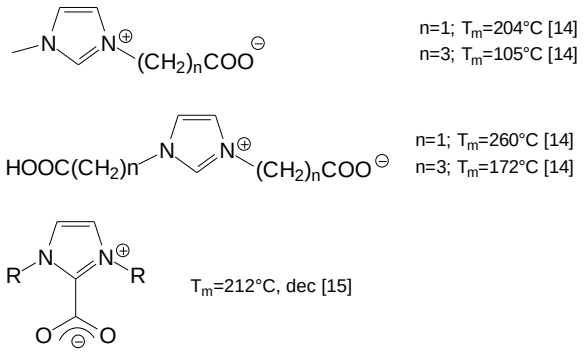
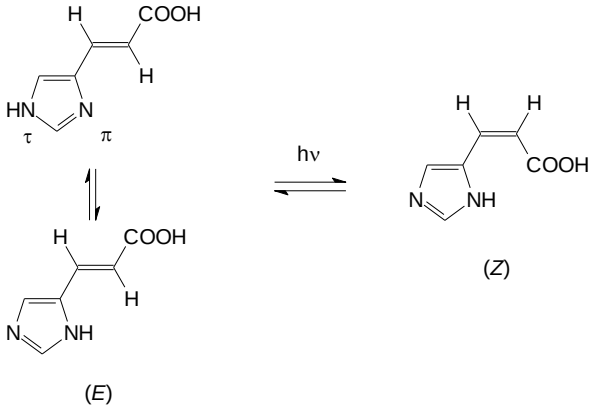


Figure 2. Some examples of zwitterionic-type molten salts containing a carboxylate group with corresponding melting temperature (T_m).

All known examples of imidazolium salts bearing carboxylic acid groups have high melting points and therefore have had no application as reaction media.

We describe here the synthesis and characterization of a series of ionic liquids based on imidazolium moiety with a carboxylate function, with low melting points using a natural product as starting material (*E*)-3-(1H-imidazol-4-yl)-2-propionic acid or (*E*)-urocanic acid. This compound is a major metabolite of *L*-histidine found in the skin and excreted in sweat [16,17]. It is one of the major UV light absorbers in the epidermis where it acts as a natural photoprotecting agent [18]. Under irradiation, this compound undergoes photoisomerization to give a mixture of the (*E*) and (*Z*) isomers (**Scheme 1**). The (*Z*) isomer has been found to have immunosuppressive activity. This compound presents an imidazole moiety which can be quaternized and a carboxylic function useful to prepare ZILs. Here, we describe the synthetic route for the preparation of ZILs based on urocanic moiety *E* or *Z*.



Scheme 1. Structure of the two tautomeric forms of (*E*)-urocanic acid and *E* /*Z* photoisomerization

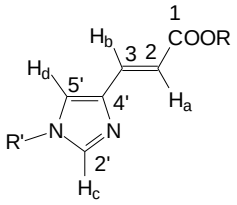
Experimental part

Material and methods.

All the solvents were purchased from Prolabo or Carlo Erba and were used without further purification. Reagents were purchased from Aldrich or Acros (>98 % purity). ^{1}H and ^{13}C RMN spectra were recorded on Brucker AC 250 and AC 400 spectrometers. The DCI/NH_3 or CH_4 mass spectra were recorded on a Nermag R10-10 apparatus and the FAB mass spectra on

a ZAB-MS apparatus (WG-ANALYTICAL, Manchester UK). The thermal properties of the ZILs were determined by Differential Scanning Calorimetry (DSC) using a Perkin Elmer Pyris 1 calorimeter. Transition temperatures were taken at the onset of the DSC peaks as the temperature increase at different heating rates, 1, 2 and 5°C/min, and finally extrapolated to 0°C/min. The microanalyses were carried out at the LCC (Toulouse, France) on Perkin Elmer analyser 2400 series 2. Irradiation was carried out in a Rayonnet type RPP 100 apparatus equipped with a turntable.

Synthesis (see scheme 2 for notations)



(*E*)-*urocanic methyl ester.* At room temperature, a suspension of (*E*)-urocanic acid (7.5 g, 54.3 mmol) in dry methanol (250 mL) was saturated with HCl gas. The solution obtained was refluxed through a Soxlet thimble containing activated 3Å sieves for 3h. The solvent was removed under reduced pressure giving the ester hydrochloride. The residue was neutralized by a saturated aqueous $NaHCO_3$ solution, extracted with ethyl acetate (3 x 25 mL) and dried over sodium sulfate. Evaporation of ethyl acetate gives (*E*)-urocanic methyl ester as a white solid in a 76% yield (6.27g).

RMN ^1H ($CDCl_3$) δ (ppm): 3.72 (s, OCH_3, 3H); 6.44 (AB, J_{AB} = 15.85 Hz, 1H, H_a); 7.20 (s, 1H, H_d); 7.55 (AB, J_{AB} = 15.85 Hz, 1H, H_b); 7.65 (s, 1H, H_c). *RMN* ^{13}C (CD_3COCD_3) δ (ppm): 50.56 (CH_3O); 114.26 (C_2); 122.10 ($C_{5'}$); 135.72 ($C_{4'}$); 136.11 (C_3); 137.36 (C_2); 167.21 (C_1). *MS* (DCI, NH_3): m/z=153, MH^+ (100%). Anal calc (%) for $C_7H_8N_2O_2$, $0.5H_2O$: C 52.17; H 5.62; N 17.38; % Found C 52.15; H 5.63; N 17.25. *DSC:* T_m = 92 °C.

*Nτ-alkyl urocanic methyl ester (**1a**, **1b**, **1c, 1d**)*

General procedure for Nτ-alkylation. At room temperature and under argon, 28 mmol of 1-bromoalkane were added dropwise to a mixture of *(E)*-urocanic methyl ester (14 mmol), K_2CO_3 (14 mmol) and 18-crown-6 (1.4 mmol) in 100 mL of anhydrous THF. The mixture was stirred 24h at 60°C. After filtration of the remaining K_2CO_3, THF was evaporated under reduced pressure. Purification by flash chromatography (silica gel, AcOEt/Et_2O 50/50, V/V) afford to obtain Nτ-alkyl urocanic methyl ester.

*Compound **1a**:* Yield: 89 %. *RMN* ^1H ($CDCl_3$) δ (ppm) : 0.95 (t, ^3J = 7.3 Hz, $C\underline{H_3}(CH_2)_3N$, 3H); 1.31 (m, $CH_3C\underline{H_2}(CH_2)_2N$, 2H); 1.75 (m, $CH_3CH_2C\underline{H_2}CH_2N$, 2H); 3.77 (s, OCH_3, 3H); 3.92 (t, ^3J = 7.3 Hz, $CH_3(CH_2)_2C\underline{H_2}N$, 2H); 6.63 (AB, J_{AB} = 15.90 Hz, 1H, H_a); 7.26 (s, 1H, H_d); 7.35 (AB, J_{AB} = 15.90 Hz, 1H, H_b); 8.27 (s, 1H, H_c). *RMN* ^{13}C (CD_3COCD_3) δ (ppm): 13.41 ($\underline{C}H_3(CH_2)_3N$); 1.63 ($CH_3\underline{C}H_2(CH_2)_2N$); 32.86

($CH_3CH_2\underline{C}H_2CH_2N$); 47.02 ($CH_3(CH_2)_2\ \underline{C}H_2N$); 51.39 ($CH_3O$); 115.29 ($C_2$); 121.50 ($C_{5'}$); 136,39 ($C_3$); 138,45 ($C_{2'}$); 138,22 ($C_{4'}$); 168.08 ($C_1$). MS : DCI ($NH_3$) m/z = 209, MH^+ (100%). Anal calc (%) for $C_{11}H_{16}N_2O_2$: C 63.44; H 7.74; N 13.45; % Found C 64.35; H 7.73; N 13.43. DSC: T_m = 38 °C.

*Compound **1b:*** Yield: 90 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.86 (t, ^3J = 6.7 Hz, $C\underline{H}_3(CH_2)_5N$, 3H); 1.25 (m, $CH_3C\underline{H}_2C\underline{H}_2C\underline{H}_2\ C\underline{H}_2CH_2N$, 8H); 1.75 (m, $CH_3(CH_2)_3C\underline{H}_2CH_2N$, 2H); 3,75 (s, OCH_3, 3H) ; 3.90 (t, ^3J = 7.3 Hz, $CH_3(CH_2)_4C\underline{H}_2N$, 2H); 6.52 (AB, J_{AB} = 15,85 Hz, 1H, H_a); 707 (s, 1H, H_d); 7.45 (s, 1H, H_c); 7.53 (AB, J_{AB} = 15,85 Hz, 1H, H_b). MS: DCI (NH_3) m/z = 237, MH^+ (100%). Anal calc (%) for $C_{13}H_{20}N_2O_2$: C 66.07; H 8.53; N 11.85; % Found C 66.09; H 8.63; N 11.95. DSC: T_m=70°C.

*Compound **1c**:* Yield: 88 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.86 (t, ^3J = 6.4 Hz, $C\underline{H}_3(CH_2)_7N$, 3H); 1.26 (m, $CH_3(C\underline{H}_2)_5CH_2CH_2N$, 10H); 1.76 (m, $CH_3(CH_2)_5C\underline{H}_2CH_2N$, 2H); 3.76 (s, OCH_3, 3H,); 3.90 (t, ^3J = 7,0 Hz, $CH_3(CH_2)_6C\underline{H}_2N$, 2H); 6.53 (AB, J_{AB} = 15.85 Hz, 1H, H_a); 7.07 (s, 1H, H_d); 7.26 (s, 1H, H_c); 7.54 (AB, J_{AB} = 15,85 Hz, 1H, H_b). MS: DCI (NH_3) m/z = 256, MH^+ (100%). Anal calc (%) for $C_{15}H_{24}N_2O_2$: C 68.15; H 9.15; N 10.60; % Found C 68.09; H 9.10; N 10.65. DSC: T_m=85°C.

*Compound **1d**:* Yield: 86 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.87 (t, 3H, CH_3); 1.24 (s, 20H, CH_2); 1.70 (m, 2H, $CH_{2\beta N}$); 3.76 (s, 3H, CH_3O); 3.90 (t, 2H, $CH_{2\alpha N}$); 6.52 (AB, 1H, J=15Hz, H_a); 7.07 (s, 1H, H_d); 7.45 (s, 1H, H_c); 7.55 (AB, 1H, J=15Hz, H_b). *RMN ^{13}C* ($CDCl_3$) δ (ppm): 168.14 (C_1); 138.47 (C2'); 138.35 (C4'); 136.44 (C_3); 121.48 ($C_{5'}$); 115.38 (C_2); 51.45 (CH_3O), 47.37 ($CH_{2\alpha N}$); 31.91 ($CH_{2\beta N}$); 30.95-22.69 (CH_2). MS (DCI, NH_3): m/z=321, MH^+ (100%). Anal calc (%) for $C_{19}H_{32}N_2O_2$, C 71.21; H 10.06; N 8.74 ; Found C 71.47; H 10.29; N 8,65. DSC: T_m=74.5°C.

*Compound **1e** (Nτ-octyl (Z)-urocanic methyl ester)*

Compound **1c** (150 mg, 10^{-3} mol.L^{-1}) was irradiated at 254 nm in ethanol for 6h giving a mixture of the two isomers [70% (*Z*) and 30% (*E*)]. After evaporation of the solvent, the two isomers were separated by flash chromatography (AcOEt / Et_2O: 50/50 v:v) and 100 mg (3.8 10^{-4} mol) of *Z* product was obtained with a yield of 66%.

*Nτ-alkyl, Nπ-methyl (E)-urocanic methyl ester (compounds **2a**, **2b**, **2c, 2d**, **2e**)*

General procedure. At low temperature, three equivalents of methyl iodide were added to a solution of compound **1** in 50 mL of dry acetonitrile. The balloon was closed then the mixture was stirred for 7 days at 30°C. Once the reaction is complete, the excess MeI was taken off under an argon flow and trapped into an aqueous sodium hydroxide solution. The residue, obtained after evaporation of the solvent, was solubilized in a mimimun of CH_2Cl_2 and precipitated by adding diethyl ether

(~300 mL). Compounds **2** were recovered by filtration.

*Compound **2a***: Yield: 92 %. *RMN ^1H* ($CDCl_3$) δ (ppm) : 0.91 (t, ^3J = 7.3 Hz, $C\underline{H_3}CH_2CH_2CH_2N$, 3H); 1.36 (m, $CH_3C\underline{H_2}CH_2CH_2N$, 2H); 1.90 (m, $CH_3CH_2C\underline{H_2}CH_2N$, 2H); 3,77 (s, 3H, OCH_3); 4.04 (s, 3H, N^+CH_3); 4.34 (t, ^3J = 7.0 Hz, $CH_3CH_2CH_2C\underline{H_2}N$, 2H); 6.54 (AB, J_{AB} = 15.85 Hz, 1H, H_a); 7.26 (s, 1H, H_d); 7.55 (AB, J_{AB} = 15.85 Hz, 1H, H_b); 7.58 (s, 1H, H_c). *RMN ^{13}C* (CD_3COCD_3, 300 MHz) δ (ppm): 13.53 ($\underline{C}H_3(CH_2)_3N$); 19.45 ($CH_3\underline{C}H_2(CH_2)_2N$); 31.94 ($CH_3CH_2\underline{C}H_2CH_2N$); 34.93 ($N^+CH_3$); 50.31 ($CH_3(CH_2)_2\underline{C}H_2N$); 52.46 ($CH_3O$); 122.19 ($C_{5'}$); 124.67 ($C_2$); 125.34 ($C_3$); 130.53 ($C_{4'}$); 137.93 ($C_{2'}$); 165.53 ($C_1$). MS: Electrospray mode +, m/z = 223.15 (100%). DSC: T_m=146°C.

*Compound **2b***. Yield: 80 %. *RMN ^1H* ($CDCl_3$) δ (ppm) : 0.86 (t, ^3J = 6.7 Hz,$C\underline{H_3}(CH_2)_5N$, 3H); 1.31 (m, $CH_3(C\underline{H_2})_3CH_2CH_2N$, 6H) ; 1.96 (m, $CH_3(CH_2)_4C\underline{H_2}CH_2N$, 2H) ; 3.78 (s, 3H, OCH_3); 4.09 (s, 3H, N^+CH_3); 4.35 (t, ^3J = 7.0 Hz, $CH_3(CH_2)_4C\underline{H_2}N$, 2H); 6.58 (AB, J_{AB} = 16,10 Hz, 1H, $\underline{H_A}$); 7.26 (s, 1H, H_d); 7.39 (AB, J_{AB} = 16.10 Hz, 1H, H_b); 7.90 (s, 1H, H_c). MS: Electrospray mode +, m/z = 251.16 (100%). DSC: T_m= 120°C

*Compound **2c***. Yield: 94 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.85 (t, ^3J = 6,1 Hz, $C\underline{H_3}(CH_2)_7N$, 3H); 1.28 (m, $CH_3(C\underline{H_2})_5CH_2CH_2N$, 10H); 1.97 (m, $CH_3(CH_2)_6C\underline{H_2}CH_2N$, 2H); 3.82 (s, 3H, OCH_3); 4.09 (s, 3H, N^+CH_3); 4.35 (t, ^3J = 7.3 Hz, $CH_3(CH_2)_6C\underline{H_2}N$, 2H); 6.56 (AB, J_{AB} = 16.10 Hz, 1H, H_a); 7.26 (s, 1H, H_d); 7.36 (AB, J_{AB} = 16.10 Hz, 1H, H_b); 7.80 (s, 1H, H_c). MS: Electrospray mode +, m/z = 292.28 (100%). DSC: T_m=136°C.

*Compound **2d***. Yield: 92 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.85 (t, ^3J = 6,1 Hz, $C\underline{H_3}(CH_2)_{11}N$, 3H); 1.29 (m, $CH_3(C\underline{H_2})_9CH_2CH_2N$, 18H); 1.96 (m, $CH_3(CH_2)_9C\underline{H_2}CH_2N$, 2H); 3.80 (s, 3H, OCH_3); 4.09 (s, 3H, N^+CH_3); 4.35 (t, ^3J = 7.3 Hz, $CH_3(CH_2)_{10}C\underline{H_2}N$, 2H); 6.57 (AB, J_{AB} = 16.10 Hz, 1H, H_a); 7.26 (s, 1H, H_d); 7.37 (AB, J_{AB} = 16.10 Hz, 1H, H_b); 7.85 (s, 1H, H_c). MS: Electrospray mode +, m/z = 248.28 (100%).

*Compound **2e***. Yield: 90 %. *RMN ^1H* ($CDCl_3$) δ (ppm): 0.85 (t, ^3J = 6,1 Hz, $C\underline{H_3}(CH_2)_7N$, 3H); 1.28 (m, $CH_3(C\underline{H_2})_5CH_2CH_2N$, 10H); 1.97 (m, $CH_3(CH_2)_6C\underline{H_2}CH_2N$, 2H); 3.82 (s, 3H, OCH_3); 4.01 (s, 3H, N^+CH_3); 4.35 (t, ^3J = 7.3 Hz, $CH_3(CH_2)_6C\underline{H_2}N$, 2H); 6.18 (AB, J_{AB} = 12.3 Hz, 1H, H_a); 8.40 (s, 1H, H_d); 6.75 (AB, J_{AB} = 12.3 Hz, 1H, H_b); 10.33 (s, 1H, H_c). MS: Electrospray mode +, m/z = 292.12 (100%).

*Zwitterionic ILs (compounds **3a**, **3b**, **3c**, **3d**, **3e**)*

General procedure. To an aqueous solution of compound **2** was added Amberlite IRA 400 resin regenerated before use (930 g of resin per mole of compound). The reaction is carried out at ambient temperature for 2h. The product was obtained after lyophilization and drying under vacuum over P_2O_5.

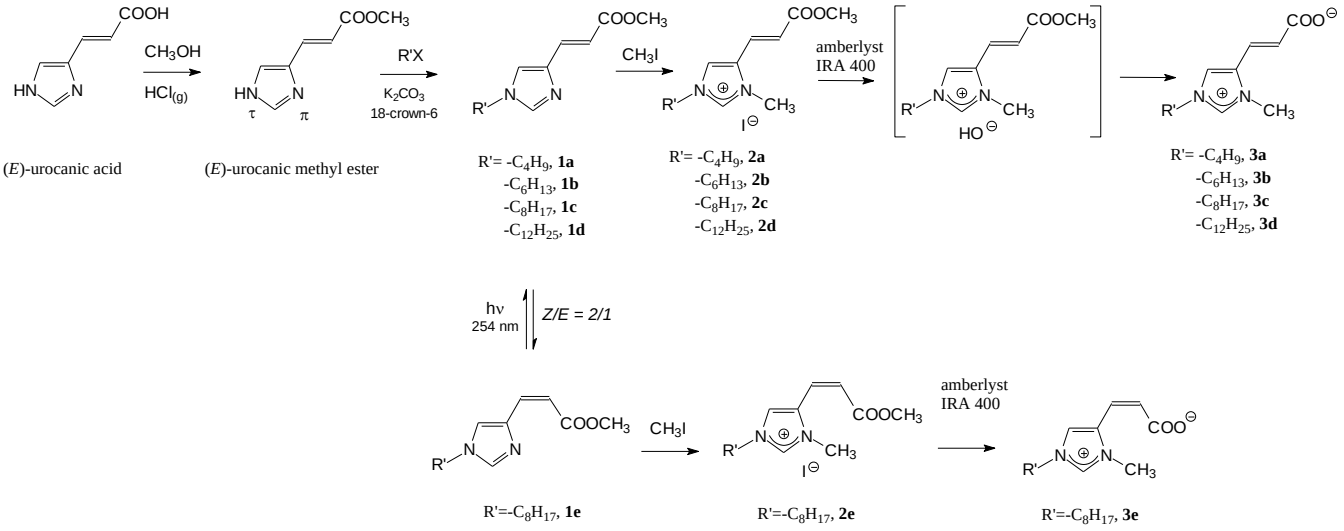
*Compound **3a**.* Yield: 95 %. *RMN ^1H* (CD_3OD, 250 MHz) δ (ppm): 1.00 (t, ^3J = 7.3 Hz, $C\underline{H}_3CH_2CH_2CH_2N$, 3H); 1.39 (m, $CH_3C\underline{H}_2CH_2CH_2N$, 2H); 1.87 (m, $CH_3CH_2C\underline{H}_2CH_2N$, 2H); 3.90 (s, 3H, N^+CH_3); 4.19 (t, ^3J = 7.4 Hz, $CH_3CH_2CH_2C\underline{H}_2N$, 2H); 6.57 (AB, J_{AB} = 15.90 Hz, 1H, H_a); 7.20 (AB, J_{AB} = 15.90 Hz, 1H, H_b); 7.99 (s, 1H, H_c). *RMN ^{13}C* (CD_3COCD_3) δ (ppm): 12.41 ($\underline{C}H_3(CH_2)_3N$); 19.08 ($CH_3\underline{C}H_2(CH_2)_2N$); 31.54 ($CH_3CH_2\underline{C}H_2CH_2N$); 33.11 ($N^+CH3$); 49.38 ($CH_3CH_2CH_2\underline{C}H_2N$); 119.56 ($C_{5'}$); 120.51 ($C_2$); 132.60 ($C_3$); 132.70 ($C_{2'}$); 171.52 ($C_1$). Anal calc (%) for $C_{11}H_{16}N_2O_2$: C 63.44; H 7.74; N 13.45; % Found C 63.05; H 8.11; N 13.23. *DSC*: T_m=81.5 °C.

*Compound **3b**. Yield*: 97 %. *RMN ^1H* (CD_3OD) δ(ppm): 0.92 (t, ^3J = 6.8 Hz, $C\underline{H}_3(CH_2)_5N$, 3H); 1.37 (m, $CH_3(C\underline{H}_2)_3CH_2CH_2N$, 6H); 1.90 (m, $CH_3(CH_2)_3C\underline{H}_2CH_2N$, 2H); 3.91 (s, 3H, N^+CH_3); 4.20 (t, ^3J = 7.4 Hz, $CH_3(CH_2)_4C\underline{H}_2N$, 2H); 6.55 (AB, J_{AB} = 16.00 Hz, 1H, H_a); 7.19 (AB, J_{AB} = 16.00 Hz, 1H, H_b); 8.00 (s, 1H, H_c). *RMN ^{13}C* (CD_3COCD_3) δ (ppm): 12.48 ($\underline{C}H_3(CH_2)_5N$); 19.48 ($CH_3\underline{C}H_2(CH_2)_3N$); 31.64 ($CH_3CH_2\underline{C}H_2CH_2N$); 33.21 ($N^+CH3$); 50.23 ($\underline{C}H_2N$); 120.58 ($C_{5'}$); 123.51 ($C_2$); 128.60 ($C_3$); 135.70 ($C_{2'}$); 168.52 ($C_1$). Anal calc (%) for $C_{13}H_{20}N_2O_2$: C 66.07; H 8.53; N 11.85; % Found C 65.65; H 8.99; N 11.73. *DSC*: T_m = 75 °C.

*Compound **3c**. Yield*: 96 %. *RMN ^1H* (CD_3OD) δ (ppm): 1.17 (t, ^3J = 7.1 Hz, $C\underline{H}_3(CH_2)_7N$, 3H); 1.37 (m, $CH_3(C\underline{H}_2)_5CH_2CH_2N$, 10H); 1.90 (m, $CH_3(CH_2)_5C\underline{H}_2CH_2N$, 2H); 3.91 (s, 3H, N^+CH_3); 4.19 (t, ^3J = 7.4 Hz, $CH_3(CH_2)_6C\underline{H}_2N$, 2H); 6.57 (AB, J_{AB} = 16.0 Hz, 1H, Ha); 7.19 (AB, J_{AB} = 16.0 Hz, 1H, H_b); 8.00 (s, 1H, H_c). Anal calc (%) for $C_{15}H_{24}N_2O_2$: C 68.15; H 9.15; N 10.60; % Found C 67.35; H 9.33; N 10.23. *DSC*: T_m = 41 °C.

*Compound **3d**. Yield*: 91 %. *RMN ^1H* (CD_3OD) δ (ppm): 0.89 (t, ^3J = 7,1 Hz, $C\underline{H}_3(CH_2)_{11}N$, 3H); 1.36 (m, $CH_3(C\underline{H}_2)_9CH_2CH_2N$, 10H); 1.92 (m, $CH_3(CH_2)_9C\underline{H}_2CH_2N$, 2H); 3.90 (s, 3H, N^+CH_3); 4.18 (t, ^3J = 7.4 Hz, $CH_3(CH_2)_6C\underline{H}_2N$, 2H); 6.58 (AB, J_{AB} = 16,0 Hz, 1H, H_a); 7.19 (AB, J_{AB} = 16.0 Hz, 1H, H_b) ; 7,99 (s, 1H, H_c). Anal calc (%) for $C_{19}H_{32}N_2O_2$: C 71.21; H 10.06; N 8.74; % Found C 70.72; H 10.43; N 8.73. *DSC*: Tm = 41 °C. *DSC*: T_m = 69 °C

*Compound **3e**. Yield: 97%. RMN ^1H* ($CDCl_3$) δ (ppm): 0.81 (t, ^3J = 6.1 Hz,$C\underline{H}_3(CH_2)_7N$, 3H); 1.24 (m, $CH_3(C\underline{H}_2)_5CH_2CH_2N$, 10H); 1.74 (m, $CH_3(CH_2)_6C\underline{H}_2CH_2N$, 2H); 3.70 (s, 3H, OCH_3); 3.86 (s, 3H, N^+CH_3); 4.35 (t, ^3J = 7.3 Hz, $CH_3CH_2CH_2C\underline{H}_2N$, 2H); 5.72 (AB, J_{AB} = 16.10 Hz, 1H, Ha); 6.95 (AB, J_{AB} = 16.10 Hz, 1H, H_b); 7.40 (s, 1H, H_d); 8.36 (s, 1H, H_c). Anal calc (%) for $C_{15}H_{24}N_2O_2$, H_2O: C 63.80; H 9.28; N 9.92; % Found C 63.95; H 9.53; N 10.03. DSC: T_m = -20°C.



Scheme 2. Synthetic route for the preparation of ZILs based on urocanic moiety E or Z.

Results and discussion

The synthetic route used to obtain ZILs was described in Scheme 2. (*E*)-urocanic acid is insoluble in organic solvents, so the carboxylic function was first esterified to give (*E*)-urocanic methyl ester. As (*E*)-urocanic acid exists in two tautomeric forms, N-alkylation can occur at two sites, le N(τ) and N(π) nitrogen atoms. This question is related to the general problem concerning the N-alkylation of imidazole derivatives substituted in position 4(5). In our previous studies, we have optimized conditions which allowed to obtain the N(τ)-alkylation of the methyl urocanate, fastly, regiospecifically, with quantitative yields.[19] Hence, under solid-liquid phase transfer conditions, various bromoalkanes (n-bromobutane, n-bromohexane, n-bromooctane and n-bromododecane) were allowed to react with (*E*)-methyl urocanate in the presence of potassium carbonate, with crown ether acting as catalyst. By this regioselective Nτ-alkylation, compounds **1a-1d** were obtained in excellent yields (~ 90%).

In the following step, the action of iodomethane on compounds **1a-1d** led to the Nτ, Nπ-disubstituted products (compounds **2a-2d**) with yields between 80 and 94%. Then the iodide counter-ion was exchanged by a hydroxide anion thanks to a basic amberlite resin (IRA 400). The basic hydrolysis occurred spontaneously leading to (*E*)-1-alkyl-3-methyl-4-propen-carboxylate imidazoliums with a butyl (**3a**), hexyl (**3b**), octyl (**3c**) or dodecyl (**3d**) chain in quantitative yields. Overall yields are 60, 53, 60, 55 % respectively.

The melting points of the compounds **3a-3d** were measured by DSC. The values obtained are reported in Table 2.

Table 2. Values of melting point of ZILs synthesized determined by DSC

compounds	T_m /°C * E isomers	compound	T_m /°C * Z isomer
3a	81.5		
3b	75.0		
3c	41.0	**3e**	-20
3d	69.0		

* onset temperature obtained from extrapolation of measured values at a 0°C/min heating rate.

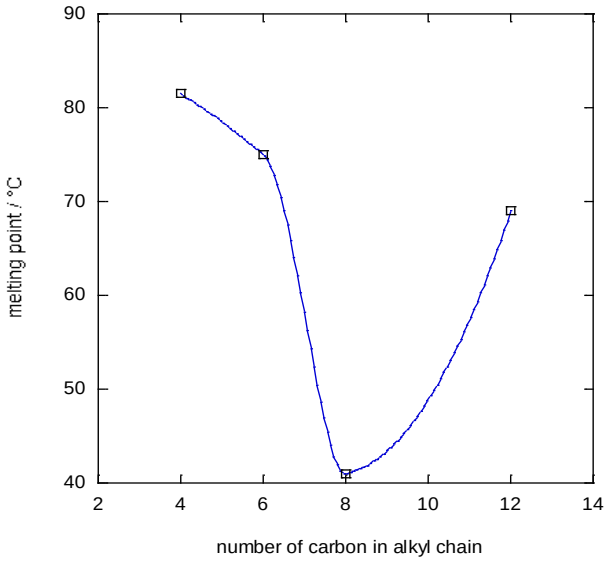


Figure 3. Melting points for (*E*)-3-(1-alkyl-3-methyl-1H-imidazol-4-ium)-2-methylpropenoate zwitterions (**3a-3d**) as a function of alkyl chain length substituted on the N(τ)-position.

Comparatively to the ZILs previously synthesized in literature (see Figure 1 and 2), the melting points obtained were found at moderate temperatures and in all cases below 100°C. In addition, these temperatures were strongly dependent on the alkyl chain length. As shown on figure 3, a minimum value equal to 41°C for R'=C_8H_{17} (**3c**) was obtained. This effect is ascribed to structural effect, indeed, the size and the symmetry of ions directly impacts upon melting point values. This trend was previously described for 1-alkyl-3-methyl imidazolium salts [2] for which a minimum melting temperature was obtained for N-hexyl and N-octyl chains.

To further decrease the melting point of these ZILs, we decided to perform photoisomerization of E isomers to form the Z. The direct photoisomerization of E isomers (**3a-3d**) did not lead to the formation of corresponding Z isomers. Therefore, we decided to perform the synthesis of (*Z*)-1-octyl-3-methylurocanate (**3e**) from compound **1c**. Under irradiation at 254 nm in ethanol, **1c** undergoes photoisomerization to give a mixture of the E and Z corresponding isomers (**1c** and **1e**), which were separated on a silica column (at photostationary equilibrium *E*/*Z*= 1:2). After separation, **1e** was obtained with a yield of 66%. The two following steps, quaternization and iodide exchange, gave the (*Z*)-3-(1-octyl-3-methyl-1H-imidazol-4-ium)-2-methylpropenoate (**3e**) which is liquid as room

temperature. The overall yield of **3e** is 38%. The melting point of **3e** determined by DSC is of -20°C.

Conclusions

A route to zwitterionic ionic liquids bearing carboxylate function using a natural product as starting material (*E*)-3-(1H-imidazol-4-yl)-2-propionic acid or (*E*)-urocanic acid has been established. For all these compounds, melting points below 100°C were observed. The lowest melting point among the *E* isomer (41°C) is sufficiently low to enable applications as a solvent. This temperature can be further decreased by using *Z* isomer down to -20°C. This opens promising opportunities to use such ZILs as reaction medium.

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