



Synthesis and properties of new functionalized guanidinium based ionic liquids as non-toxic versatile organic materials

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ARTICLE INFO

Article history:

Received 1 July 2010

Received in revised form 4 August 2010

Accepted 13 August 2010

Available online 26 August 2010

Keywords:

Ionic liquid

Guanidinium

Organic materials

Toxicity

Interfacial properties

ABSTRACT

Functionalized guanidinium ionic liquids as a new class of versatile organic materials have been developed. Guanidinium salts containing olefinic functionalities have been prepared and completely characterized. In order to illustrate the versatility of olefinic units, they were brominated and some bromine-containing ionic liquids have been obtained. Relevant physico-chemical properties of the new synthesized salts were evaluated including their melting points, glass transition temperatures, miscibilities, densities, surface tensions and contact angles with glass and Teflon surfaces. Additionally toxicity studies were performed using the human colon carcinoma CaCo-2 cell line. Several new functionalized guanidinium based ILs showed high densities, low contact angles with Teflon, low surface tensions as well as a non-toxic behaviour.

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1. Introduction

Ionic liquids, a class of compounds, which gained relevant impact in the recent years mostly because their properties, such as almost negligible vapour pressure, low flammability, high thermal stability, large electrochemical window and capacity of dissolution of several organic molecules; properties that convert ILs as potential green alternatives to volatile organic solvents.¹ The almost infinite number of possible cation and anion combinations ($\sim 10^8$)^{2a} can be problematic in order to find an IL by trial an error with the adequate properties to a specific application. In order to facilitate the right combination of ions, some correlation studies between the structure of salts and their physico-chemical properties were recently published.² Despite these studies is already known that the majority of correct combinations between cations and anions are still to be explored. Even with the limited knowledge about this class of compounds, ILs have been used in several applications such as biocatalysis,³ synthesis,⁴ analytical chemistry⁵ (e.g., stationary phase in gas chromatography, electrolyte medium in electrophoresis, MALDI matrix), liquid membranes,⁶ design of solar cells,⁷ extractions,⁸ among other applications.

Hexaalkyl guanidinium salts, were recently described as a new generation of ionic liquids⁹ showing physico-chemical properties comparable and in some cases complementary to widely used 1,3-dialkylimidazolium based ionic liquids. Guanidinium-based ionic liquids were used as reaction media in Heck reactions,¹⁰ oxidation of benzyl alcohols,¹¹ fixation of CO₂ by epoxides,¹² Aldol reaction,¹³ Knoevenagel reaction,¹⁴ nucleophilic substitution of alkyl halides,¹⁴ Mannich reaction,¹⁴ Henry reaction,¹⁴ hydrogenation and hydroformylation,¹⁵ Sharpless asymmetric dihydroxylation.¹⁶ Differently guanidinium salts were also used as electrolyte medium in solar cells.¹⁷

In order to obtain ILs with superior performances in some applications, Task Specific Ionic Liquids (TSILs) have been developed. This class of ILs usually contains specific functionalities on cation or anion structures, which facilitate the correspondent interaction with a specific substrate or tune further physico-chemical properties. Several examples of TSILs are described in the literature such as imidazolium-based ILs containing ether and alcohol functionalities (for dissolution of inorganic salts,¹⁸ as reaction media in the benzoylation of nucleosides¹⁹ and as anti-microbial agents²⁰); fluorine-containing ILs (capacity to dissolve gases²¹ and low surface tensions²²); Carbonylic and nitrile co ILs (higher viscosity²³ and density²⁴ values); urea, thiourea and thioether-containing ILs (for extraction of Hg²⁺ and Ca²⁺ from aqueous solutions^{8a}); amine functionalized ILs (capture of CO₂ by formation of a covalent reversible bond²⁵). The ILs containing ester functionality on the cation and octylsulfate as anion are also relevant because their

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superior levels of biodegradability²⁶ and examples of the dicyanamide anion based ILs (for dissolution of carbohydrates in high concentrations²⁷). ILs containing natural chiral anions were used to induce chirality in C–H insertions and Sharpless dihydroxylations.²⁸ Finally amino acid-based ILs were applied to solubilise other amino acids²⁹ while some olefin-containing imidazolium ILs were brominated in order to obtain high density ILs.³⁰

Ruled by the structure of the IL, physico-chemical properties are essential to determine the applicability of such compounds. Density is a very important physico-chemical property that plays an essential role in extractions, in flotation fluids used in inertial instruments,³⁰ or in energetic compounds.³¹ This property is essentially ruled by the mass and volume of each atom of the compound and by the inter-molecular interactions between the components of the IL. Another property related with density is surface tension, γ :³²

$$P = \frac{M \cdot \gamma^{\frac{1}{3}}}{\rho} \quad (1)$$

where ρ is the density, M is the molar mass and P the parachor value. This property is determinant on definition of a multiphase system, to apply, for example, in homogeneous catalysis³³ and solubilisation of gases.³⁴ The relation between the structure of the IL and surface tension property was studied in the case of imidazolium,^{33–36} phosphonium,^{34,36} ammonium^{34,36} and guanidinium³⁶ based ILs.

Through Young equation surface tension γ_{LV} is linked with contact angle, θ . This angle is defined between a solid surface and the line tangent to a point, of the surface of the drop, placed at the base:

$$\gamma_{SV} = \gamma_{SL} + \gamma_{LV} \cdot \cos \theta \quad (2)$$

where γ_{SV} , γ_{SL} and γ_{LV} are the solid-vapour, solid-liquid and liquid-vapour surface tensions, respectively. Contact angle is a measure of wettability of a surface. Recently was reported that the complexity associated to ILs can be much more effective than water in order to discriminate between different solid surface compositions and profiles.³⁷ The structural variability associated to ILs can be used to tune the wettability of solid surfaces.^{38,39} Teflon type polymers are organo-fluoride compounds with high chemical inertness, physical resistance and low wettability. Differently to common organic compounds, the carbons bonded to the electronegative fluorine present positive partial charge, which can minimize possible interactions of Teflon with the most common organic compounds.⁴⁰ The design of a substance that can effectively wet Teflon can be a cumbersome task. Recently, an attempt was made to wet Teflon AF 1600 with ILs applying a potential difference but only moderate wettability was obtained.⁴¹ Herein, the development of novel guanidinium based ionic liquids, containing olefinic (allylic) functionalities are described. In order to illustrate the versatility of olefinic functionalities some ILs were then brominated. Physico-chemical properties (e.g., solubilities, melting points, glass transition and decomposition temperatures, densities and surface tensions) of the novel synthesized ILs were evaluated. Four of these ILs were selected for a detailed toxicity study using the human colon carcinoma CaCo-2 cell line. A comparative study of contact angles with Glass and Teflon PTFE surfaces were also developed using different ionic liquids and common organic solvents.

2. Results and discussion

Novel Guanidinium ILs containing allylic functional groups (olefinic positions) were synthesized (Fig. 1). These salts containing a different type of allyl groups (2 or 4) and *n*-alkyl side chains on cation unit were combined with four anions.

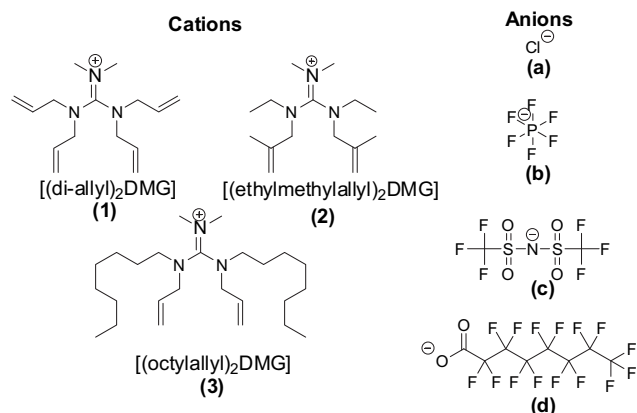
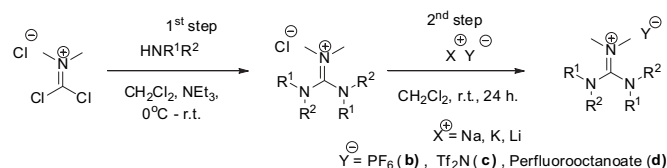


Fig. 1. Structure of functionalized guanidinium cations and anions of new synthesized ILs.

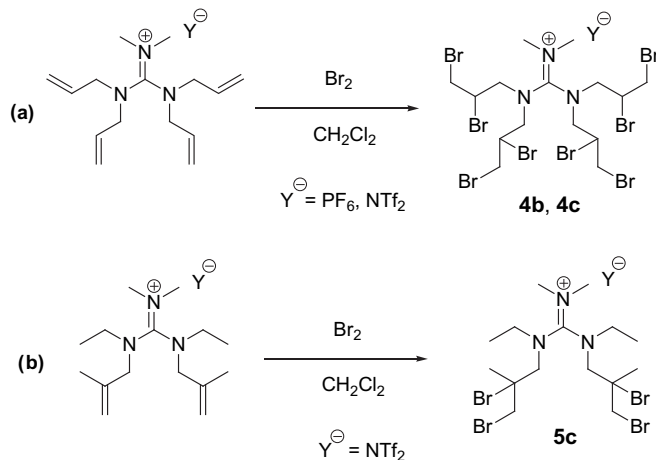
The chloride salts **1a**, **2a** and **3a** were prepared in one step according to a published method^{9a,42} starting from *N,N*-dimethylphosgeniminium chloride and a secondary amine (first step—Scheme 1). The non-chloride salts were prepared further chloride exchange (second step).



Scheme 1. Synthesis of new functionalized guanidinium ILs.

The chloride salts (**1–3**) were obtained in moderated yields (14–65%) where the other observed product was attributed to urea resulted of partial amine substitution and further hydrolysis. For the guanidinium salts (**b–d**) obtained in the second step were prepared in high yields (86–97%).

The allylic units allow the possibility of further functionalization. In order to illustrate this functional versatility, the olefin-containing ILs (**1** and **2**) were then brominated according a published procedure.³⁰ Only olefinic ILs containing non-nucleophilic anions (PF_6^- (**b**) or Tf_2N^- (**c**)) were used for bromination reactions (Scheme 2) avoiding mixtures of products. New highly brominated salts were obtained in moderate yields (14–75%). The spectral data, elemental analysis and mass spectra of the isolated compounds prove that all the olefinic positions were completely brominated.



Scheme 2. Bromination of functionalized guanidinium ILs.

2.1. Physical State, Density and Solubilities

In Table 1 is presented all the prepared guanidinium salts and some of their representative properties. Compound **3a** is the only chloride salt synthesized as a viscous liquid at room temperature; this compound presents groups of different sizes around the guanidinium core, a characteristic associated to low solid-liquid transition temperatures.^{2c} This feature is represented in Table 1, with the guanidinium cations presenting chains of different sizes (**3**, **8**, **9** and **10**) leading to room temperature ionic liquids, similarly to the case of imidazolium salts (**14**–**17**).

Table 1
Representative properties of some functionalized salts including new guanidinium ILs

Salt	Physical State	Density [g cm ⁻³]	Solubility	
			Miscible	Immiscible
1a	Solid	1.06 ^c	H ₂ O, dcm, acetone	Et ₂ O, Hex
1b	Solid	1.21 ^c	dcm, acetone	Et ₂ O, Hex, H ₂ O
1c	Liquid	1.35 ^a	H ₂ O (pm), dcm, acetone	Et ₂ O, Hex
1d	Liquid	1.37 ^b	Et ₂ O, dcm, acetone, H ₂ O (pm)	Hex
2a	Solid	1.02 ^c	dcm, acetone, H ₂ O	Et ₂ O, Hex
2c	Liquid	1.28 ^b	dcm, acetone, H ₂ O (pm)	Et ₂ O, Hex
3a	Liquid	n.d. ^d	dcm, acetone	Et ₂ O, H ₂ O
4b	Solid	1.55 ^c	dcm, acetone	Et ₂ O, Hex, H ₂ O
4c	Solid	2.15 ^c	dcm, acetone	Et ₂ O, Hex, H ₂ O
5c	Solid	1.68 ^a	dcm, acetone	Et ₂ O, Hex, H ₂ O
6a ^{9a}	Solid	—	dcm, H ₂ O	Et ₂ O, Hex
6b ^{9a}	Solid	—	dcm	Et ₂ O, H ₂ O, Hex
6c ^{9a}	Liquid	1.36	dcm	Et ₂ O, Hex, H ₂ O
7a ^{9a}	Solid	—	dcm, H ₂ O	Et ₂ O, Hex
7b ^{9a}	Solid	—	dcm	Et ₂ O, H ₂ O, Hex
8a ^{9a}	Solid	—	dcm, H ₂ O	Et ₂ O, Hex
8b ^{9a}	Liquid	—	dcm	Et ₂ O, H ₂ O, Hex
9a ^{9a}	Liquid	0.90	dcm, H ₂ O, Hex	Et ₂ O
9b ^{9a}	Liquid	—	dcm, Et ₂ O	H ₂ O, Hex
10a ^{9a}	Liquid	0.96	dcm, Et ₂ O, Hex	H ₂ O
10b ^{9a}	Liquid	0.91	dcm, Et ₂ O	H ₂ O, Hex
14a ^{18a}	Solid	1.08	—	—
14b ^{18a}	Liquid	1.31	H ₂ O	Et ₂ O
14c ⁴³	Liquid	1.44	—	H ₂ O
15a ^{18a}	Liquid	1.03	H ₂ O	—
15b ^{18a}	Liquid	1.29	—	H ₂ O ⁴³
15c ⁴³	Liquid	1.37	—	H ₂ O
16a ^{18a}	Liquid	1.00	—	—
16b ^{18a}	Liquid	1.19	—	H ₂ O, Et ₂ O
16c ⁴⁴	Liquid	1.38	—	H ₂ O, Et ₂ O, Hex
17c ⁴⁴	Liquid	1.35	—	H ₂ O, Et ₂ O, Hex
18c ⁴⁵	Liquid	—	—	—
19c ⁴⁴	Liquid	1.06	Et ₂ O	H ₂ O, Hex

^a Density of liquid compounds with volume greater than 700 μ l measured by Anton Paar DMA38 densimeter at 25 $^{\circ}$ C.

^b Density of liquid compounds with volume less than 700 μ l measured with microcycnometer at room temperature.

^c Density of solid compounds measured with indirect method at room temperature. More details about ^a, ^b and ^c methods to measure density in Experimental section.

^d Et₂O: diethyl ether; Hex: *n*-hexane; H₂O: water; dcm: dichloromethane; (pm)—partially miscible, (nd)—not determined due to low amount available. Water content μ g (H₂O)/mg (IL): **1c**=9.7, **1d**=31.0, **2c**=8.0.

Taking advantage of delocalization of negative charge and organo-fluoro units the bis(trifluoromethanesulfonyl)imide (Tf₂N) (**c**) and perfluorooctanoate (**d**) are valuable anions in order to obtain liquids at room temperature.⁴⁰ Similar to the previously reported imidazolium case (**18c**) the olefin functionalized guanidinium salts are also RTILs (**1c**, **1d** and **2d**).

The observed viscosity of these novel guanidinium based RTILs are comparable with previously reported^{9a} tetrahexylguanidinium ILs (**6**, **7** and **8**). Some complementary rheological studies are in progress.

All of brominated salts are solids at room temperature. This fact can be related with the presence of bromide, which is a volumous and polarizable element increasing the importance of the van der

Waal interactions and decreasing the conformational degrees of freedom of the cation and the entropy of fusion.

Low water content was observed for room temperature ionic liquids (Table 1) obtained by chloride exchange (**1c**, **1d**, **2c**) corresponding to 8–31 μ g H₂O.mg⁻¹ IL.

The incorporation of bromine atoms into ILs structure allowed a significant increase in the density values. Consequently, the number of bromine atoms on the cation unit is determinant for high densities (**2c**<**5c**<**4c**). The chosen anion also leads to considerably different density values (Cl⁻<PF₆⁻<bis(trifluoromethylsulfonyl)imide \approx Perfluorooctanoate) according to the synthesized examples.

The nature of the anion might rule the influence of certain features of the cation on the density of the compounds. When the anion is bis(trifluoromethylsulfonyl)imide the olefin functionality on the cation is not so significant to rule density because **6c** and **1c** (that possess the same number of carbon atoms on the cation but **1c** has two olefin functionalities), present similar densities (1.36 and 1.35 g/cm³, respectively). With this anion, the presence of ramifications on the cation might be more significant to rule density (**1c**>**2c**). Differently when the anion is chloride, the new olefin functionalized guanidinium salts (**1a** and **2a**) possess generally higher densities than reference non-functionalized guanidinium salts (**9a** and **10a**).

A curious observation is that in the case of guanidinium salts the enhance of the number of carbon atoms leads to an increase of density (**9a**<**10a**) while the opposite trend is followed by 1,3-disubstituted imidazolium salts (**14a**>**15a**>**16a**). The reason for this behaviour may lay on the trigonal geometry of guanidinium core (corresponding to higher angles, 120 $^{\circ}$, than tetrahedron geometry) that may lead to higher distances between atoms and consequently lower density (Fig. 2).

Solubility studies of all the synthesized salts show a complete dissolution in dichloromethane and acetone and insolubility in *n*-hexane. The brominated compounds **4b**, **4c** and **5c** show the same behaviour independently of the selected anion (PF₆⁻ or bis(trifluoromethylsulfonyl)imide) being diethyl ether and water insoluble. Differently, non-brominated salts are substantially influenced by the nature of the anion. Comparing our new olefin compounds with previous guanidinium salts, the solubility behaviour is similar; the only difference is that when long chains are present allow miscibility in *n*-hexane and diethyl ether (**9a** and **10a**).

Like expect, the chloride salts prepared are water soluble, while PF₆⁻, bis(trifluoromethylsulfonyl)imide and perfluorooctanoate salts are non-soluble or partially water soluble. Curiously the perfluorooctanoate salt **1d** is the only synthesized salt soluble in diethyl ether.

2.2. Thermal properties

The DSC analysis of the prepared salts is presented in Table 2. All the bromine-containing salts are solids at room temperature as mentioned before, but is particularly relevant that compound **5c**, which contains lower number of bromine atoms in the cation, present lower melting point (74.3 $^{\circ}$ C), being considered a high density ionic liquid. The other brominated compounds didn't present transition to liquid state before decomposition. Considering the olefinic salts, all the bis(trifluoromethylsulfonyl)imide based compounds are liquid at room temperature (**1c** and **2c**) presenting low *T*_g values (similarly to the previously reported olefin functionalized imidazolium salt **18c**) and the highest decomposition temperatures (>300 $^{\circ}$ C) as observed for some previous guanidinium and imidazolium salts (**9c**, **16c**, **17c** and **19c**). Regarding the new compounds, the chloride salts are solids at room temperature with the compound containing higher degree of ramification on the cation unit (**2a**) showed a considerable higher

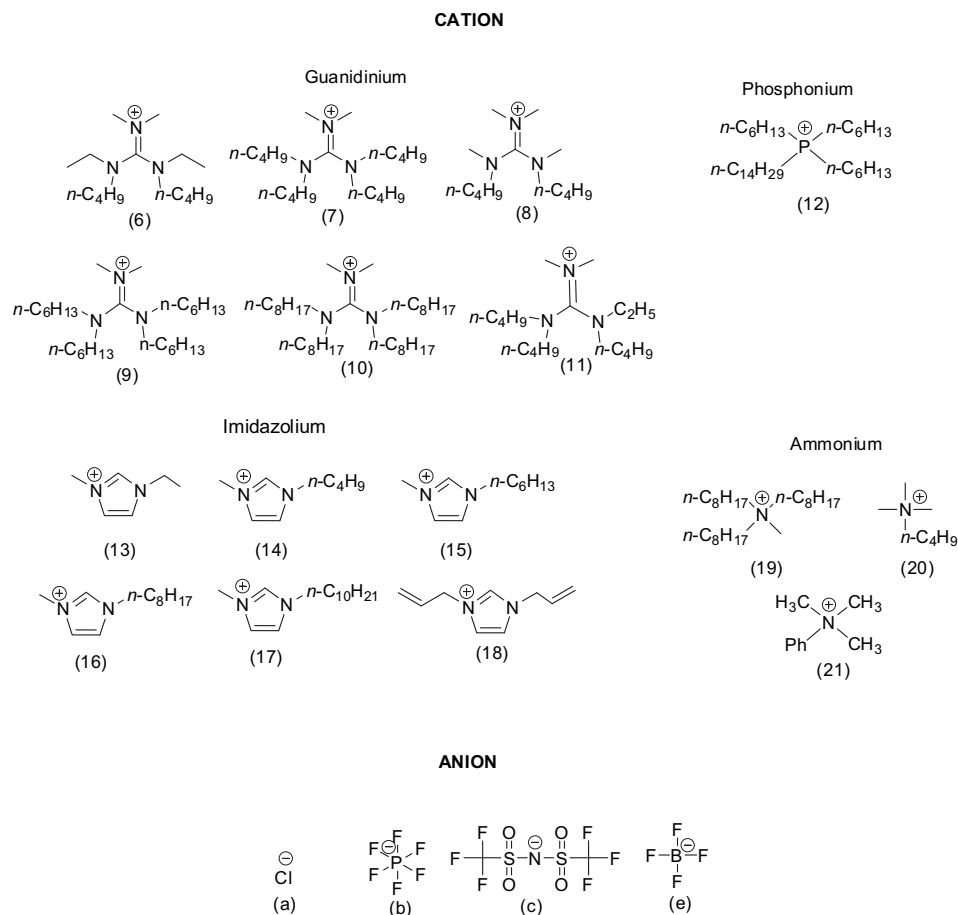


Fig. 2. Structures of non-functionalized cations and anions of previously published ionic liquids used as references.

melting point than the previously^{2c} prepared compound (**1a**) with no ramifications. Differently, the new chloride salt liquid at room temperature, with the substituents around guanidinium unit being dramatically different considering the size, leading to a low T_g value (-53.3°C). The same trend was observed in previously prepared non-functionalized guanidinium salts^{9a} (**9a**, **10a**), similarly to the medium chain imidazolium salts **15a** and **16a** and differently from long and short chain chloride based imidazolium salts **14a** and **17a**. The most interesting result was obtained with perfluorooctanoate anion (**1d**), an RTIL containing an unexplored anion.

In general, the compounds containing brominated cations present much lower decomposition temperatures than olefinic equivalents. According the results presented in Table 2 the guanidinium based salts (**1a**, **2a** and **3a**) show a similar thermal stability (or even superior) when compared to reference imidazolium salts of the same anion (**14a** and **17a**).

Considering the anion the observed order of T_d is bis(trifluoromethylsulfonyl)imide $> \text{Cl}^- > \text{PF}_6^- > \text{perfluorooctanoate}$.

Another feature observed by the majority of the synthesized salts is related with their strong jump in the molar heat capacity associated with glass transition. These high values of ΔC_{pm} indicate that many degrees of freedom are released on heating above T_g . High values of ΔC_{pm} at the glass transition appear as a specific feature of ILs.⁴⁴ The brominated salts present some of the lowest ΔC_{pm} 's as bromine's volume might preclude the release of too many degrees of freedom (**1c** vs **4c**) above T_g value. The salts **1b** and **5c** present both a T_g followed by a melting point (mp) transition and also the lowest ΔC_{pm} 's values.

2.3. Interfacial properties

The interfacial properties of the new olefin functionalized guanidinium salts as RTILs (**1c**, **1d** and **2c**) were measured (Table 3) and compared with some previously reported RTILs.

Different surface tension (γ_{lv}) values were obtained for the new synthesized guanidinium salts; particularly relevant the lowest value in the case of perfluorooctanoate anion (**1d**) when compared with bis(trifluoromethylsulfonyl)imide based ILs (**1c** and **2c**) and previously reported ionic liquids as described in Table 3. The low interaction between the cation and the perfluorinated anion can explain this observation. Ionic liquids generally present surface tensions lower than water and higher than the traditional volatile organic solvents.³⁵ The surface tension of **1c** and **2c** was slightly higher than the previously synthesized guanidinium IL **9c** because their smaller chain substituent sizes. The same trend was previously found in the case of imidazolium (**14a**, **15a** and **16a**) and ammonium (**19c** vs **20c**) based ILs. In opposite direction, the surface tension of n -alkanes increases with the size of the molecule (Table 3). This trend in ILs is related with the decreasing of strong Coulombic interactions while the weaker van der Waals interactions increase.

Considering contact angle studies, two different solid surfaces were tested comprising different polarity profiles, soda-lime glass (microscope slide) and Teflon[®] PTFE disk.⁴⁶ The three new guanidinium ILs (**1c**, **1d** and **2c**) presented similar contact angles values with glass (Table 3) independently of the differences on cation or anion structures. The considerably smaller contact angle of tetrahexylguanidinium IL (**9c**) can be attributed as result of dispersive interactions with glass, which play an important role⁴⁷ in the

Table 2
Thermal properties of the synthesized guanidinium salts and ionic liquids

Salt	DSC Analysis				
	Mp ^a [°C]	T _g ^b [°C]	T _d ^c [°C]	ΔC _p ^d [J g ⁻¹ K ⁻¹]	ΔC _{pm} ^e [J mol ⁻¹ K ⁻¹]
1a	79.2	—	261.9	—	—
1b	56.0	–55.5	232.4	0.289	113.68
1c	—	–57.9	>300	0.488	257.92
1d	—	–49.4	159.9	0.356	235.48
2a	146.5	—	213.6	—	—
2c	—	–56.4	>300	0.337	178.11
3a	—	–53.3	195.4	0.504	215.78
4b	—	—	137.5	—	—
4c	—	10.6	143.2	0.129	150.64
5c	74.3	–10.3	161.0	0.074	63.06
6a ^{9a}	—	–79.0	—	—	—
6b ^{9a}	—	–67.8	—	—	—
7a ^{9a}	—	–55.3	—	—	—
9a ^{9a}	—	–63.0	—	—	—
9b ^{9a}	—	–60.5	—	—	—
9c ⁴⁴	—	–72.1	>300	0.3811	269
10a ^{9a}	—	–76.0	—	—	—
10b ^{9a}	—	–78.0	—	—	—
14a ⁴³	73.0	—	210.0	—	—
14b ^{18a,43}	10.0	–80.0	>300	—	—
15a ^{18a}	—	–75.0	—	—	—
15b ^{18a}	–61.0	–78.0	>300	—	—
15c ⁴³	–9.0	—	275.0	—	—
16a ^{18a}	—	–87.0	—	—	—
16b ^{18a}	—	–82.0	—	—	—
16c ⁴⁴	—	–86.5	>300	0.4229	210
17a ⁴³	31.0	—	195.0	—	—
17c ⁴⁴	—	—	>300	—	—
18c ⁴⁵	—	–91.6	—	—	—
19c ⁴⁴	—	–81.4	>300	0.3131	—

^a mp—melting point.

^b T_g—glass transition temperature.

^c T_d—onset of decomposition temperature.

^d ΔC_p—Heat Capacity Jump.

^e ΔC_{pm}—Molar Heat Capacity Jump.

definition of the contact angle. The nature of the anion (**14c** vs **14e**) can also play an important role in the interfacial behaviour of the ILs with glass. In general, the tested ionic liquids showed higher contact angles than *n*-heptane, water or even dichloromethane (Table 3), considering the glass surface. These three examples illustrate the importance of both the polar and dispersive components of the glass surface interactions.⁴⁷

Differently, the new guanidinium ILs presented dramatic differences in terms of contact angle in Teflon surface, with the perfluorooctanoate anion (**1d**) leading to a substantially lower contact angle than bis(trifluoromethanesulfonyl)imide anion (**1c** and **2c**). The long organo-fluoride chain of perfluorooctanoate might play an important role in the depression of the contact angle as Teflon is an organo-fluoride polymer. As our knowledge, **1d** is an example in terms of ILs with the lowest contact angle on Teflon surface, even lower than perfluorinated ILs previously tested in electrowetting studies.⁴¹

In this comparison it is important to note that the composition of the AF 1600 Teflon polymer in Millefiorini study⁴¹ is different from the composition of PTFE Teflon used in our work. Considering different cationic structures, the size of the alkyl substituents (**9c** vs **7c**) and the nature of the anion (**1c** vs **1d** and **14c** vs **14e**) might play an important role at the surface of Teflon, a surface where the dispersive interactions are dominant.⁴⁶

The new ILs synthesized showed lower contact angles with Teflon than water or ethyleneglycol. The compounds **1c** and **2c** presented higher contact angles than *n*-alkanes and comparable values when compared with pyridine and DMF. In the case of perfluorooctanoate anion (**1d**) the values of contact angles are also comparable relative to *n*-alkanes (between *n*-nonane and *n*-decane).

Table 3

Interfacial properties (surface tension and contact angle with Teflon[®] PTFE disk and soda-lime glass microscope slide) of the different tested ionic liquids and some representative non-ionic organic compounds

Compound	γ _{lv} ^a [mN/m]	θ ^b Teflon [®] PTFE disk	θ ^b Soda-lime glass (microscope slide)
1c	37.5	52.2	24.3
1d	25.3	27.6	22.6
2c	36.4	49.0	23.6
9c	32.8	58.1	10.6
11a	48.2 ^{48a}	—	—
11b	47.5 ^{48a}	—	—
11c	38.4 (37.5) ^{48b}	68.8	17.5
11e	48.8 (46.6) ^{48b}	81.3	34.5
12a	41.8 ^{48a}	—	—
12b	43.4 ^{48a}	—	—
13a	31.9 ^{48a}	—	—
18c	27.9 ^{48c}	—	—
19c	35.7 ^{48c}	—	—
20c	32.5 ^{48c}	—	—
1-Octanol	27.5 ^{48d}	n.a.	n.a.
Water	71.9 ^{48f}	122(adv) ⁴⁶ 94 (rec) ⁴⁶	<10 ⁴⁷
EG	n.a.	93 (adv) ⁴⁶ 64 (rec) ⁴⁶	n.a.
DMF	n.a.	79 (adv) ⁴⁶ 48 (rec) ⁴⁶	n.a.
Pyr	n.a.	72 (adv) ⁴⁶ 54 (rec) ⁴⁶	n.a.
DCM	27.8 ^{48d}	n.a.	14.4 ⁴⁷
<i>n</i> -Heptane	19.7 ^{48d}	10.3 ^{48e}	<10 ⁴⁷
<i>n</i> -Octane	21.6 ^{48d}	21.1 ^{48e}	n.a.
<i>n</i> -Nonane	n.a.	28.3 ^{48e}	n.a.
<i>n</i> -Decane	23.9 ^{48d}	32.7 ^{48e}	n.a.

^a γ_{lv}—Surface Tension measured at 25 °C.

^b θ Contact Angle. rec—receding contact angle, adv—advanced contact angle. EG—ethyleneglycol, DMF—dimethylformamide, Pyr—pyridine, DCM—dichloromethane.

Relevant is the result obtained in the case of **7e** ([bmim][BF₄]), which was the highest contact angle value observed with Teflon (as well as in glass) among the ILs here studied.

In Fig. 3 is presented the variation of the contact angle on Teflon with the structure of the IL, where is possible to observe that the new olefin functionalized guanidinium ILs (**1c** and **2c**) showed lower contact angles than reference ILs (**9c** and **14c**). In this comparison is relevant to note that the presence of olefin units instead *n*-alkyl functionalized cations allowed an increase of electron density around olefin functionality and consequently a considerable depressing of contact angle with Teflon. Considering the effect of the anion is possible to observe a dramatic decrease in the contact angle when the anion is changed from bis(trifluoromethanesulfonyl)imide to perfluorooctanoate (**1d**<**1c**).

2.4. Toxicities studies

Cations **1** and **2** were evaluated toxicologically using the human colon carcinoma CaCo-2 cell line.⁴⁹ Both cations produced similar results. They were both negligible toxic when combined with chloride (Fig. 4).

Changing from Cl to bis(trifluoromethylsulfonyl)imide anion leads to some enhancement of cellular viability for high concentrations (Fig. 4). This effect seems to be associated with the anion because the same was shown for other types of cations.⁵⁰ We consider that ionic liquids that lead to a considerable increment of cellular metabolism, when compared to the control cells, are not desirable. However, such effect was not very significant for these cases: approximately 30% increase at high doses of 4.5 mM (**1c**) and 7.5 mM (**2c**) (Fig. 4).

Ionic liquid **1a** and **2a** were compared with other cations that had been already evaluated using the same model^{50,51} (Fig. 5).

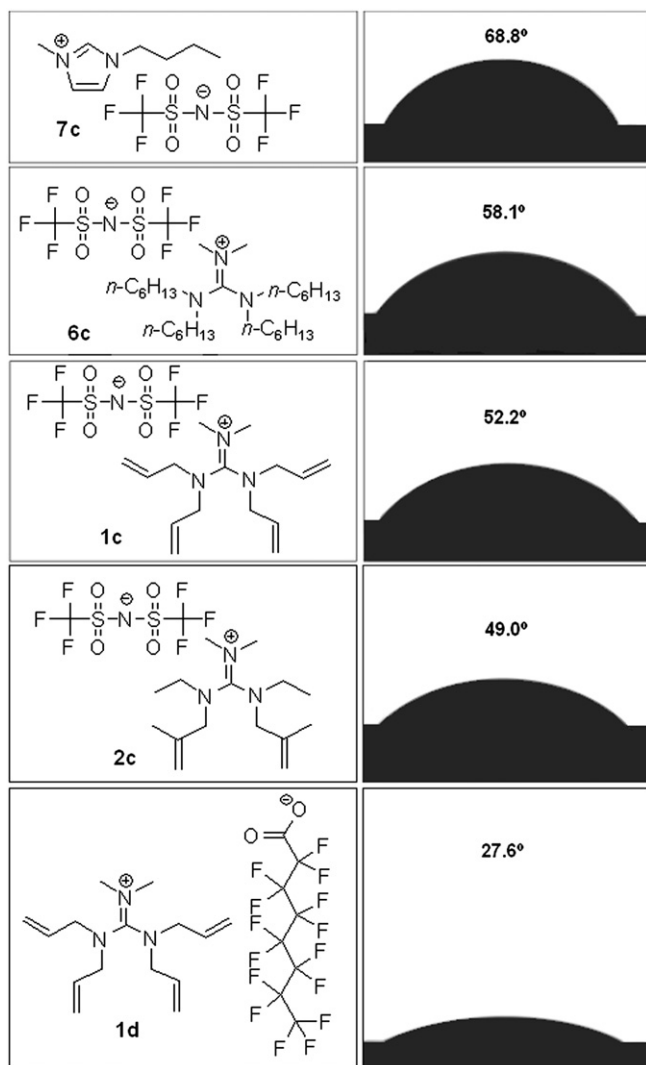


Fig. 3. Effect of both cation and anion on the contact of ILs with Teflon.

They were seen to be less toxic than dimethyl-guanidinium [(tetra-hexyl)DMG] (**9a**), [(di-butyl)(ethylbutyl)DMG] (**11a**), tri-*n*-hexyl-tetra-*n*-decylphosphonium ([P6,6,6,14]) (**12a**) and tri-*n*-octyl-methylammonium ([Aliquat]) (**19a**) (Fig. 5).

Most of this data was expected due to the longer alkyl chains of cations **9**, **12** and **19**. However, introduction of lateral groups as an

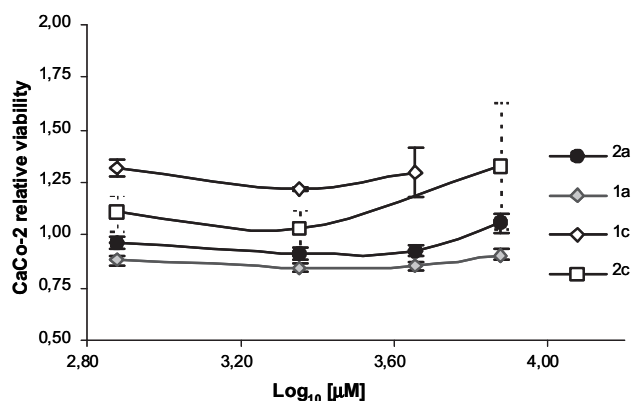


Fig. 4. Toxicological results of cations **1** and **2**, combined with chloride (**1a** and **2a**) and bis(trifluoromethanesulfonyl)imide (**1c** and **2c**) on CaCo-2 cells monolayer. Cells were exposed to the ionic liquids for 4 h and viability was assessed by the MTT reagent.

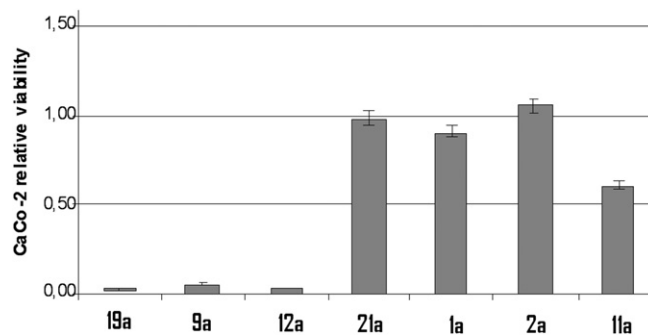


Fig. 5. Comparison of the toxic effect of different ionic liquids in CaCo-2 monolayer: cells were exposed to 7.5 mM of each ionic liquid for 4 h and viability was assessed by the MTT reagent.

attempt to reduce the number of carbons of the main alkyl chain and the presence of unsaturated bonds do not seem to contribute to toxicity.

Cation **2** had a similar effect as phenyltrimethyl-ammonium ([PhTMA]) (**21a**) in this model. We can assume that cation **1** and **2** are promising for designing of greener solvents.

3. Conclusions

In conclusion, new olefinic functionalized guanidinium ILs were synthesized and completely characterized. The olefinic positions are very versatile units, which can be easily converted in to different functionalities; this possibility was illustrated by the synthesis of high density brominated guanidinium salts. The novel cation-brominated salt **5c** and the unexplored perfluorooctanoate anion **1d** are the most promising examples of task specific ionic liquids with possible applications as high density additive (or media) and as material with relevant surface properties (lower surface tension and stronger Teflon surface interaction), respectively. Toxicity evaluation of cation **1** and **2** suggests that they are promising cations for designing of greener solvents and also the first non-toxic guanidinium ILs examples.

4. Experimental section

4.1. General

All commercial reagents were used as supplied. Solvents used during synthesis and workup phases were previously distilled from CaH₂ under an argon atmosphere before their use in the preparation of guanidinium salts. ¹H and ¹³C NMR spectra were recorded on a Bruker AMX400 spectrometer. Chemical shifts are reported downfield in parts per million from a tetramethylsilane reference. IR spectra were recorded on a Jasco FT/IR-430 spectrometer. The samples for elemental analysis were performed by Laboratório de Análises e Tecnologia (Monte de Caparica) using Thermo Finnigan-CE Instruments equipment, model Elemental Analyser 1112 series. The removal of the volatile compounds in each guanidinium salt was accomplished under high vacuum (10⁻⁶ mbar) during 5 h. The calorimetric measurements were performed with a 2920MDSC system from TA Instruments Inc. Dry high-purity helium gas with a flow rate of 30 cm³ min⁻¹ was purged through the sample. Cooling was accomplished with liquid nitrogen cooling accessory (LNCA), which provides automatic and continuous programmed sample cooling down to -150 °C. The baseline was calibrated by scanning the temperature domain of the experiments with an empty pan. The temperature calibration was performed taking the onset of the endothermic melting peak of several calibration

standards: *n*-decane ($T_m=243.75$ K), *n*-octadecane ($T_m=301.77$), hexatriacontane ($T_m=347.30$ K), indium ($T_m=430.61$ K) and tin ($T_m=506.03$ K). The organic standards were high-purity Fluka products, while the metal standards were supplied by TA Instruments Inc. The enthalpy was calibrated with indium (melting enthalpy $\Delta H_m=28.71$ J g⁻¹). The density measurements were accomplished using three different strategies according to nature and quantity of the samples: For liquid samples corresponding to volumes above 700 μ l an Anton Paar DMA38 (0–3 g cm⁻³) densimeter was used at 25 °C. Liquid samples corresponding to volumes below 700 μ l were measured using micropycnometer calibrated with paraffin. The volume of the micropycnometer is 214 μ l at 22 °C. The obtained volume was validated comparing measurements of density for polyglycol B01/240 (CH₃CH₂CH₂CH₂(OCH₂CHCH₃)_mOH with MW ca. 2300 g mol⁻¹) with Anton Paar DMA38 densimeter and micropycnometer. Finally, solid samples were measured by indirect method using pycnometer for solids. The pycnometer was calibrated with decane at 20 °C (1.085 mL) and the method validated measuring the density of sodium chloride at 20 °C in the presence of decane as the liquid used to complete de volume of the pycnometer. The measured density of NaCl was compared with the literature value (2.165 g cm⁻³ at 20 °C). The mass spectra were recorded by mass spectrometry unit at Santiago de Compostela University using Micromass equipment, Autospec model. The ionization techniques used were FAB and EI. Additionally was used Bruker equipment, model microTOF, and the ionization technique was ESI. The water content of the samples were obtained with Metrohm KF Coulometer 831 equipped with 703 TI stand and 768 KF oven. The samples were titrated in a 130 °C oven with air flux of 100 mL/min. Surface tension, interfacial tension and contact angle measurements were performed in a surface tension and contact angle meter from KSV Instruments using CAM 100 model. The pendant drop method was used to measure surface tension at 25 °C. Previously, the method to obtain surface tension was validated by measuring surface tension of 11e (BMIMBF₄) a compound with previously reported surface tension.

4.2. General procedure for the synthesis of guanidinium chlorides

All the guanidinium chlorides were prepared adapting a described procedure.^{9a}

4.2.1. (1a) [(Di-allyl)₂DMG][Cl]. Prepared following the general procedure from diallylamine (2 g, 20.6 mmol), *N,N*-dimethyl phosgeneiminium chloride (1.59 g, 9.8 mmol) and triethylamine (3.84 mL, 21.56 mmol) in dichloromethane (47 mL) during 10 h. As workup, the mixture was filtered, and the obtained solid washed with dichloromethane. The solvent of the combined organic mixture was removed under vacuum with an aqueous NaOH solution (2 M, 16 mL) added to the mixture. The aqueous phase was washed twice with diethyl ether (2 × 22 mL), and the pH adjusted to 7 by dropwise addition of hydrochloric acid (37%). The water was removed under vacuum. The guanidinium salt was obtained as a pale brown solid (1.8 g, 65%). Mp 79.2 °C, ρ 1.06 g mL⁻¹ (20 °C). IR ν_{\max} (KBr): 3082, 2978, 2920, 1643, 1589, 1539, 1419, 1338, 1277, 1234, 1146, 1061, 999, 933, 876, 671 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ : 3.06 (6H, s), 3.78–3.96 (8H, m), 5.28–5.32 (8H, m), 5.76 (4H, m); ¹³C NMR δ : 40.97, 52.64 and 52.89 (rotamers), 121.57, 131.11, 163.03. Analysis: calcd for C₁₅H₂₆ClN₃·1.7H₂O: N 13.36, C 57.29, H 9.42. Found: N 13.48, C 56.91, H 9.63.

4.2.2. (2a) [Di-ethyl(methylallyl)₂DMG][Cl]. Prepared following the general procedure from ethyl-2-methylallylamine (5 g, 50.4 mmol), *N,N*-dimethyl phosgeneiminium chloride (3.72 g, 22.92 mmol) and triethylamine (7.35 mL, 52.7 mmol) in dichloromethane (50 mL)

during 68 h. As workup, the mixture was filtered. The solvent of the organic mixture was removed under vacuum with an aqueous NaOH solution (2 M, 35 mL). The aqueous phase was washed twice with diethyl ether, and the pH adjusted to 7 by dropwise addition of hydrochloric acid (37%). Water was removed under vacuum and the residue dissolved in dichloromethane. The solution was filtered, and the solvent removed under vacuum. To the residue was added acetone, being formed a white precipitate at the bottom. The mixture was filtered and a white solid was isolated (2.94 g, 45%). Mp 146.5 °C, ρ 1.02 g mL⁻¹ (20 °C). IR ν_{\max} (KBr): 3083, 2976, 2939, 1650, 1579, 1537, 1456, 1438, 1419, 1380, 1361, 1346, 1338, 1292, 1240, 1213, 1168, 1145, 1126, 1074, 1061, 1045, 1027, 989, 918, 862, 798, 615, 580, 559, 517 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ : 1.16 (6H, ls), 1.66 (6H, s), 3.07–3.18 (10H, m), 3.81–3.91 (4H, m), 5.02–5.05 (4H, m). ¹³C NMR (100 MHz, CDCl₃) δ : 12.96 and 13.25 (rotamers), 20.32, 40.72 and 41.00 (rotamers), 44.41 and 44.72 (rotamers), 55.54 and 56.04, 117.82, 137.23, 137.65 and 163.45. Analysis: calcd for C₁₅H₃₀N₃Cl: N 14.51, C 62.19, H 10.51. Found: N 14.48, C 62.01, H 10.03. *m/z* (EI⁺) 252 (M⁺, 100), 99 (C₆H₁₂N⁺, 73), 84 (C₅H₁₀N⁺, 82). HRMS 252.244117 (C₁₅H₃₀N₃⁺ requires 252.243973).

4.2.2.1. Allyl-octylamine. Prepared by addition of sodium carbonate (2.16 g, 20.4 mmol) and chlorooctane (4 g, 26.9 mmol) to allylamine (12.28 g, 215.2 mmol). The reaction mixture was stirred during 36 h at 80 °C in a micro-reactor. As workup, the mixture was filtered and the solution was submitted to vacuum. Finally was obtained a colourless liquid (1.99 g, 44%). ¹H NMR (400 MHz, CDCl₃) δ : 0.86–0.89 (3H, t, *J*=6.8 Hz), 1.27–1.29 (10H, m), 1.48–1.53 (2H, m), 2.29 (1H, ls), 2.60–2.64 (2H, t, *J*=7.2 Hz), 3.27–3.28 (2H, d, *J*=6 Hz), 5.10–5.12 (1H, d, *J*=10.4 Hz), 5.17–5.21 (1H, d, *J*=17.2 Hz), 5.88–5.98 (1H, m). ¹³C NMR (100 MHz, CDCl₃) δ : 14.03, 22.60, 27.31, 29.21, 29.46, 29.79, 31.78, 49.23, 52.28, 116.20, 136.34.

4.2.3. (3a) [(Di-octylallyl)DMG][Cl]. Prepared following the general procedure from allyl-octylamine (1 g, 5.9 mmol), *N,N*-dimethyl phosgeneiminium chloride (0.46 g, 2.81 mmol) and triethylamine (0.9 mL) in dichloromethane (7.5 mL) during 19 h. As workup, the mixture was filtered, and the solvent was removed under vacuum. To the obtained residue was added water. After separation of the organic phase, the obtained mixture was submitted to high vacuum to obtain the residue that was dissolved in the minimum amount of dichloromethane, being added to a chromatography column where silica is the stationary phase and dichloromethane the mobile phase. The last fraction being eluted from column was presented as an orange viscous liquid (0.35 g, 14%). *T*_g –53.26 °C. ¹H NMR (400 MHz, CDCl₃) δ : 0.58–0.67 (6H, m), 0.97–1.05 (24H, m), 2.90 (6H, s), 3.01–3.03 (4H, m), 3.53–3.69 (4H, m), 5.13–5.24 (4H, m), 5.49–5.67 (2H, m). ¹³C NMR (100 MHz, CDCl₃) δ : 13.52, 22.04, 26.25, 26.46, 26.75, 27.20, 28.58, 30.63, 31.17, 40.24, 40.61, 48.84, 49.27, 49.56, 49.74, 52.18, 52.43, 52.70, 53.17, 120.80, 121.06, 130.39, 130.93, 162.85. *m/z* (EI⁺) 392 (M⁺, 78), 238 (C₁₄H₂₈N₃⁺, 38), 224 (C₁₄H₂₈N₂⁺, 58), 183 (C₁₁H₂₃N₂⁺, 57), 71 (C₄H₉N⁺, 100). HRMS 392.4005 (C₂₅H₅₀N₃⁺ require 392.3999).

4.3. Substitution of chloride with non-nucleophilic anions: PF₆⁻, Tf₂N⁻, perfluorooctanoate

4.3.1. (1b) [(Di-allyl)₂DMG][PF₆]. Prepared from (1a) [(di-allyl)₂-DMG][Cl] (0.5 g, 1.76 mmol) and potassium hexafluorophosphate (0.407 g, 2.20 mmol) in 25 mL of dichloromethane. The reaction mixture was stirred at room temperature during 24 h. At workup the mixture was filtered and the solvent was removed under vacuum. The guanidinium salt was obtained as an orange solid (0.62 g, 89%). Mp 56.09 °C, ρ 1.21 g mL⁻¹ (25 °C). IR ν_{\max} (KBr) 3088, 3032, 2988, 2945, 2912, 1645, 1583, 1535, 1448, 1417, 1356, 1339, 1278, 1267, 1236, 1159, 1112, 1094, 1067, 1002, 956, 929, 837, 678,

648, 557 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 2.87 (6H, s), 3.68 (8H, ls), 5.25–5.29 (8H, m), 5.66 (4H, ls). ^{13}C NMR (100 MHz, CDCl_3) δ : 39.94, 52.03 and 52.49 (rotamers), 121.25 and 121.46 (rotamers), 130.63, 162.69. Analysis: calcd for $\text{C}_{15}\text{H}_{26}\text{N}_3\text{F}_6\text{P}$: N 10.68, C 45.80, H 6.66. Found: N 10.62, C 45.96, H 6.60.

4.3.2. **(1c)** [(Di-allyl)₂DMG][NTf₂]. Prepared from **(1a)** [(di-allyl)₂-DMG][Cl] (2 g, 7.06 mmol) and lithium bis(trifluoromethanesulfonyl)imide (2.53 g, 8.82 mmol) in 15 mL of acetone. The reaction mixture was stirred during 56 h at room temperature. At workup the mixture was filtered and the solvent was removed under vacuum and the residue dissolved in dichloromethane. The mixture was filtered, and the solvent removed under reduced pressure. The guanidinium salt was obtained as yellow oil (3.62 g, 97%). T_g –57.94 °C, ρ 1.342 g mL^{-1} (25 °C). IR ν_{max} (film) 3087, 2985, 2925, 1645, 1541, 1527, 1508, 1436, 1419, 1348, 1330, 1294, 1278, 1226, 1184, 1134, 1056, 993, 935, 877, 865, 788, 761, 740 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 2.93 (6H, s), 3.74 (8H, ls), 5.31–5.35 (8H, m), 5.68 (4H, ls). ^{13}C NMR (100 MHz, CDCl_3) δ : 40.27, 52.39, 52.86, 114.87, 118.06, 121.25, 121.75, 121.97, 124.44, 130.44, 162.95. Analysis: calcd for $\text{C}_{17}\text{H}_{26}\text{N}_4\text{F}_6\text{O}_4\text{S}_2 \cdot 2.9\text{H}_2\text{O}$: N 9.65, C 35.16, H 5.52. Found: N 9.87 C 34.67 H 5.00.

4.3.3. **(2c)** [Di-ethyl(methylallyl)₂DMG][NTf₂]. Prepared from **(2a)** [di-ethyl(methylallyl)₂DMG][Cl] (1.5 g, 5.2 mmol) and lithium bis(trifluoromethanesulfonyl)imide (2.46 g, 8.9 mmol) in 20 mL of acetone. The reaction mixture was stirred during 56 h at room temperature. At workup the mixture was filtered and the solvent was removed under vacuum. The residue was dissolved in dichloromethane and the resulting mixture was filtered. The solvent was removed under vacuum. The guanidinium salt was obtained as yellow oil (3.01 g, 86%). T_g –56.4 °C, ρ 1.28 g mL^{-1} (22 °C). IR ν_{max} (film) 3082, 2978, 2941, 2814, 1845, 1655, 1570, 1527, 1458, 1420, 1381, 1350, 1331, 1294, 1225, 1134, 1055, 987, 914, 870, 820, 787, 739, 652, 615, 599, 568, 513 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 1.15–1.20 (6H, m), 1.70 (6H, s), 2.94–3.03 (6H, m), 3.20–3.28 (6H, m), 3.69–3.79 (4H, m), 5.07–5.11 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ : 12.21 and 12.59 (rotamers), 19.15 and 19.65 (rotamers), 39.76, 40.01 and 40.22 (rotamers), 43.78, 44.39, 55.08, 55.66, 114.60, 117.55, 117.80, 117.99, 120.99, 124.19, 136.72, 136.99, 162.74, 163.15. Analysis: calcd for $\text{C}_{17}\text{H}_{30}\text{N}_4\text{O}_4\text{S}_2\text{F}_6$: N 10.52 C 38.34 H 5.68. Found: N 10.51 C 38.16 H 5.56.

4.3.4. **(1d)** [(Di-allyl)₂DMG][perfluorooctanoate]. Prepared from **(1a)** [(di-allyl)₂DMG][Cl] (0.5 g, 1.77 mmol) and sodium perfluorooctanoate (1.16 g, 2.65 mmol) in 25 mL of methanol. The reaction mixture was stirred during 56 h. At workup the reaction mixture was filtered and the solvent was removed under vacuum. The residue was dissolved in dichloromethane and the resulting mixture was filtered. The solvent was removed under vacuum. The guanidinium salt was obtained as yellow oil (1.02 g, 88%). T_g –49.41 °C, ρ 1.37 g mL^{-1} (21 °C). IR ν_{max} (film) 3084, 3015, 2984, 2920, 2810, 1867, 1697, 1643, 1589, 1529, 1420, 1350, 1315, 1238, 1203, 1147, 1128, 1099, 1007, 993, 929, 883, 798, 744, 734, 719, 661, 640, 559, 530 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 2.98 (6H, s), 3.75 (8H, ls), 5.27–5.31 (8H, m), 5.70 (4H, ls). ^{13}C NMR (100 MHz, CDCl_3) δ : 40.39, 52.40 and 52.80 (rotamers), 110.83, 111.14, 121.45 and 122.61, 130.87, 160.06, 160.29, 160.52, 163.06. Analysis: calcd for $\text{C}_{23}\text{H}_{26}\text{N}_3\text{O}_2\text{F}_{15}$: N 6.35, C 41.76, H 3.96. Found: N 6.49, C 41.24, H 4.16.

4.4. General procedure for the bromination of guanidinium salts

All the brominated guanidinium salts were prepared adapting a described procedure.³⁰ To a stirred mixture of guanidinium salt (1.00 mmol—the anion is non-nucleophilic) in anhydrous

dichloromethane (20 mL), under an argon atmosphere, was added bromine (Br_2 , at least 1.3 equiv per double bond present in the guanidinium salt). The stirred mixture was refluxed during several hours (specified for each case). For each case are specified the quantities and the workup procedure used.

4.4.1. **(4b)** *N,N*-Dimethyl-*N',N'',N'''*-tetrakis(2,3-dibromopropyl)-guanidinium hexafluorophosphate. Prepared from *N,N*-dimethyl-*N',N'',N'''*-tetraallyl guanidinium hexafluorophosphate (**1b**) (0.4 g, 1.02 mmol), bromine (Br_2 —0.835 g, 5.29 mmol) in 20 mL of dichloromethane. The stirred mixture was refluxed during 24 h. At workup, the mixture was filtered, and the recovered organic phase was washed with 2×10 mL of aqueous solution of sodium sulfite (10%). The resulting organic phase was washed with 3×10 mL of water. The product was isolated by crystallization being added ethyl ether to the organic phase. The guanidinium salt was obtained as a white solid (0.144 g, 14%). ρ 1.55 g mL^{-1} (25 °C). IR ν_{max} (KBr) 3001, 2935, 2362, 2345, 1585, 1517, 1419, 1383, 1313, 1284, 1242, 1151, 1124, 1084, 1063, 949, 935, 901, 840, 655, 575 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 3.30–3.38 (8H, m), 3.79–3.88 (14H, m), 4.04–4.16 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ : 33.89, 33.94, 34.48, 34.69, 35.27, 35.38, 35.58, 35.77, 42.18, 42.27, 42.32, 42.53, 42.63, 46.43, 46.62, 47.32, 47.56, 47.62, 47.95, 48.09, 48.93, 53.20, 53.35, 53.77, 54.31, 54.69, 54.78, 56.31, 57.91, 163.89, 164.89. m/z (FAB⁺) 894 (M^+ , 2), 893 (M^+ , 10), 892 (M^+ , 7), 891 (M^+ , 38), 890 (M^+ , 14), 889 (M^+ , 79), 888 (M^+ , 18), 887 (M^+ , 100), 885 (M^+ , 81), 884 (M^+ , 8), 883 (M^+ , 43), 882 (M^+ , 2), 881 (M^+ , 13)—several combinations of isotopes of bromine. 807 ($\text{C}_{15}\text{H}_{27}\text{Br}_7\text{N}_3^+$, 17)—fragment with the more abundant combination of isotopes. 727 ($\text{C}_{15}\text{H}_{27}\text{Br}_6\text{N}_3^+$, 34)—fragment with the more abundant combination of isotopes. 645 ($\text{C}_{15}\text{H}_{27}\text{Br}_5\text{N}_3^+$, 8)—fragment with the more abundant combination of isotopes, 568 ($\text{C}_{15}\text{H}_{27}\text{Br}_4\text{N}_3^+$, 8)—fragment with the more abundant combination of isotopes.

4.4.2. **(4c)** *N,N*-Dimethyl-*N',N'',N'''*-tetrakis(2,3-dibromopropyl)-guanidinium bis(trifluoromethanesulfonyl)imide. Prepared from *N,N*-dimethyl-*N',N'',N'''*-tetraallyl guanidinium bis(trifluoromethanesulfonyl)imide (**1c**) (1.51 g, 2.86 mmol), bromine (Br_2 —3.65 g, 22.87 mmol) in 20 mL of dichloromethane. The stirred mixture was refluxed during 51 h. At workup, the mixture was filtered, and the recovered organic phase was washed with 1×35 mL of aqueous solution of sodium sulfite (20%). The resulting organic phase was washed with 3×20 mL of water. The solvent was removed under vacuum. The guanidinium salt was obtained as a brown solid (1.47 g, 44%). T_g 10.60 °C, ρ 2.15 g mL^{-1} (20 °C). IR ν_{max} (KBr): 3032, 3003, 2957, 2930, 1582, 1522, 1458, 1431, 1344, 1223, 1190, 1132, 1045, 959, 937, 897, 793, 741, 652, 619, 569, 514 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 3.32–3.34 (8H, m), 3.39–3.41 (6H, m), 3.80–3.84 (8H, m), 3.99–4.05 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ : 32.95, 33.08, 33.30, 33.67, 33.84, 34.27, 53.71, 53.96, 54.29, 54.60, 57.11, 114.99, 118.19, 121.38, 124.58, 163.85, 164.64 and 165.71. Analysis: calcd for $\text{C}_{17}\text{H}_{26}\text{Br}_8\text{F}_6\text{N}_4\text{O}_4\text{S}_2$: N 4.80, C 17.48, H 2.24. Found: N 4.40, C 17.04, H 2.49.

4.4.3. **(5c)** *N,N*-Dimethyl-*N',N''*-diethyl-*N',N''*-bis(2,3-dibromo-2-methylpropyl) guanidinium bis(trifluoromethanesulfonyl)imide. Prepared from *N,N*-dimethyl-*N',N''*-diethyl-*N',N''*-bis(2-methylallyl) guanidinium bis(trifluoromethanesulfonyl)imide (**2c**) (1.76 g, 3.31 mmol), bromine (Br_2 —2.12 g, 13.2 mmol) in 25 mL of dichloromethane. The stirred mixture was refluxed during 56 h. At workup, the mixture was filtered, and the recovered organic phase was washed with 1×25 mL of aqueous solution of sodium sulfite (20%). The resulting organic phase was washed with 2×25 mL of water. The solvent was removed under vacuum. The guanidinium salt was obtained as yellow solid (2.00 g, 75%). T_g –10.41 °C, M_p 74.31 °C, ρ 1.68 g/mL^{-1} (20 °C). IR ν_{max} (KBr): 3038, 2995, 2977,

2945, 2588, 2468, 2365, 2316, 2270, 1961, 1928, 1880, 1589, 1577, 1506, 1452, 1419, 1386, 1348, 1296, 1259, 1224, 1174, 1134, 1054, 1045, 1003, 980, 933, 897, 869, 834, 764, 727, 715, 651, 635 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ: 1.33–1.43 (6H, m), 1.87–2.01 (6H, m), 2.97–2.99 (4H, m), 3.27–3.29 (6H, m), 3.66–3.71 (4H, m), 3.79–3.92 (4H, m). ¹³C NMR (100 MHz, CDCl₃) δ: 12.34, 12.70, 12.96, 13.28, 13.49, 13.94, 14.05, 29.08, 29.26, 29.31, 39.92, 40.89, 41.60, 41.82, 47.96, 48.11, 48.22, 48.59, 54.20, 54.79, 54.97, 57.02, 57.24, 65.01, 66.79, 66.99, 67.27, 115.06, 118.25, 121.45, 124.65, 166.81, 167.42. Analysis: calcd for C₁₇H₃₀N₄O₄S₂F₆Br₄: N 6.57, C 23.96, H 3.55. Found: N 6.57, C 23.93, H 3.85. *m/z* (ESI-TOF) 577 (M⁺, 2), 576 (M⁺, 21), 575 (M⁺, 12), 574 (M⁺, 83), 573 (M⁺, 20), 572 (M⁺, 100), 571 (M⁺, 14), 570 (M⁺, 82), 569 (M⁺, 2), 568 (M⁺, 24). HRMS: 571.9135 (C₁₅H₃₀Br₄N₃⁺ requires 571.9132).

4.5. Toxicological studies

Human colon carcinoma CaCo-2 (ATTC, USA) were kept in 175 cm² flasks in RPMI Medium 1640 (GIBCO), supplemented with 10% fetal bovine serum (FBS, GIBCO) and 2 mM L-glutamine (GIBCO) at 37 °C in a humidified atmosphere of 5% CO₂. For the assay, cells were cultured in 96-well-plates until reaching confluence and consequently, formation of a monolayer. Stock solutions of the ionic liquids were diluted with the cell culture medium in order to attain the desirable concentrations. Cells were incubated with the different ionic liquids for 4 h. Afterwards, medium was removed and fresh medium with 3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT, Sigma) 0.5 mg/mL was added to the cells. Plate returned to the incubator for 3–4 h. During this period, MTT was reduced by a mitochondrial enzyme in metabolic active cells. The resultant formazan product was solubilised with 150 μL DMSO/well. The purple product was measured in a plate reader spectrophotometer using the wavelength of 570 nm and 690 nm. Incubations were done in triplicate, as the controls. The ratio between the absorbance of sample treated cells and the absorbance of control cells was used to determine the cell viability and this parameter was plotted in function of the base 10 logarithm of the ionic liquid concentration (μM).

Acknowledgements

We are grateful to REQUIMTE and Fundação para a Ciência e Tecnologia (PTDC/QUI/70902/2006 project and SFRH/BD/18354/2004); Professor Anabela Raymundo and Dra Cristiana Nunes for viscosity measurements; Dr. Nuno Lourenço for water content titrations; Professor João Sottomayor for helpful discussions; Solchemar Lda and Cytec Co. for availability of some ionic liquids used in surface tension and contact angle studies.

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