Journal of Molecular Liquids 307 (2020) 112960

Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Thermal and spectroscopic investigations on three phosphonium based ionic liquids for industrial and biological applications

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ARTICLE INFO

Article history:
Received 9 July 2019
Received in revised form 18 February 2020
Accepted 20 March 2020
Available online 22 March 2020

Keywords:
Ionic liquids
Broadband dielectric spectroscopy
Thermal analysis
Anti-bacterial activity
Anti-cancer activity

ABSTRACT

We report a comprehensive result of investigations on three phosphonium based room temperature ionic liquids (ILs) of same cation, trihexyltetradecylphosphonium ($[PC_6C_6C_6C_{14}]$), with different anions *viz.* chloride $[\text{-Cl}]^-$ $[Cl]^-$, dicyanamide $[\text{-N(CN)}_2]^-$ and bis(trifluoromethylsulfonyl) imide $[\text{-NTf}_2]^-$ for catching the effect of size, symmetry, dipole moment, as well as electro-negativity of anions on glassy dynamics and charge transport of the formed ILs. The effort was made for tuning the property for getting superior conductivity, improved thermal stability, better electrode-electrolyte interaction to enable it for diverse biological and technological applications. The ILs were characterized with differential scanning calorimetry (DSC), thermogravimetry (TGA), broadband dielectric spectroscopy (BDS) along with other routine measurements like FT-IR, FT-Raman spectroscopies and computational investigations with density functional theory (DFT). The applications were evaluated by means of electrochemical and biological activities. From DSC and TGA measurements, the samples showed good thermal stability up to 573 K to project them as excellent electrolyte and better heat transfer fluid for high temperature needs in various technological fronts. Dielectric response revealed that the conductivity relaxation manifested above glass transition temperature (Tg) to be well represented by Dyre's random barrier model and it followed a Vogel–Fulcher–Tamman (VFT) behaviour against temperature. The sub-Tg relaxation reflected a Cole-Cole response with an Arrhenius T-dependence. The dielectric data revealed a slight correlation with Tg while anticorrelates with the fragility and low temperature activation energy (E_β). The DFT calculations gave the structure and other parameters in good agreement with the experimental data. The three ILs fulfilled most of the requirements needed for pharmaceuticals on evaluating pharmacokinetics, bioavailability and toxicity *via in silico* analysis. On exploring the preliminary biological studies, these ILs showed very good anti-bacterial, anti-oxidant and good anti-cancer activities highlighting their relevance and significance for pharmaceutical applications.

1. Introduction

Ionic liquids (ILs) are molten salts composed of a cation (aromatic or occasionally non-aromatic) and an anion of organic or inorganic in origin [1]. ILs received a wider acceptance and popularity in fundamental research as well as in industrial fronts owing to their novel properties like high thermal and chemical stability, low volatility, lack of inflammability as well as improved solubility vis-à-vis to many organic compounds [1–4]. Room temperature ionic liquids (RTILs) whose melting temperature is below room temperature were emerged as greener alternatives to many of the traditional volatile organic solvents with innumerable potentials and capabilities for diverse technological interests *viz.* synthetic reactions, separations and extractions, electrochemical, nanotechnological, biotechnological, and engineering processes [1–4]. Depending on the cation segment the ILs are named and categorized as ammonium, imidazolium, phosphonium, pyridinium, pyrazolium, pyrrolidinium, cholinium, sulfonium, picolinium, piperidinium,

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https://doi.org/10.1016/j.molliq.2020.112960
0167-7322/

imide $[\text{-NTf}_2]^-$ as anions to extract the effect of size, symmetry, dipole moment and electro-negativity of anions on charge transport, glassy dynamics *via* experimental and computational means. The DSC, TGA measurements pointed that the ILs to be good heat transfer fluid for electrolytic and high temperature applications with improved thermal stability up to 573 K. The dielectric measurements revealed that the conductivity relaxation follows Dyre's random barrier model arising due to the hopping of charge carriers in a random spatially varying potential landscape following a Vogel–Fulcher–Tamman (VFT) T-dependance. The sub-Tg relaxation followed a Cole-Cole response with an Arrhenius T-dependence. A cation influenced dynamics was further revealed with Tg correlates with size, while anticorrelating with the fragility and low temperature activation energy (E_β). The structure and other parameters revealed from the experimental invstigationsof FT-IR and FT-Raman are well matched with the values obtained from DFT studies. Pharmacokinetics, bioavailability and toxicity studies *via in silico* analysis revealed that the ILs fulfilled most of the requirements needed for the pharmaceutical applications. On exploring the biological applications, the ILs showed very good anti-bacterial, anti-oxidant and anti-cancer activity highlighting their significance for pharmaceutical industry.

CRediT authorship contribution statement

K.K. Thasneema: Investigation, Formal analysis, Writing – original draft. **M. Shahin Thayyil:** Supervision, Writing - review & editing. **Tancia Rosalin:** Investigation. **K.K. Elyas:** Investigation. **T. Dipin:** Formal analysis. **Pramod K. Sahu:** Formal analysis. **N.S. Krishna Kumar:** Formal analysis. **V.C. Saheer:** Formal analysis. **Mouslim Messali:** Formal analysis. **Taibi Ben Hadda:** Formal analysis.

Declaration of competing interest

The authors declare that there is no conflict of interest.

Acknowledgements

The authors gratefully acknowledge A. Afsal for his supports in the dielectric measurements and Jayant Kolte for fruitful discussions. T.K.K. acknowledges the UGC, Govt. of India for financial assistance through BSR fellowship. MST acknowledges research funding from the KSCSTE, Govt. of Kerala, India (No. 005/SRSPS/2011/CSTE and No. 49/SARD/2014), and the UGC, Govt. of India (MRP F. No. 42-848/2013 (SR)). The CSIF, University of Calicut is acknowledged for providing sophisticated experimental facilities. Tancia Rosalin acknowledges UGC for MANF fellowship, Department of Biotechnology, Govt. of India and University of Calicut for the infrastructural facilities.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2020.112960.

References

[1] Jan Leys, Michael Wübbenhorst, Chirukandath Preethy Menon, Ravindran Rajesh, Jan Thoen, Christ Glorieux, Temperature dependence of the electrical conductivity of imidazolium ionic liquids, J. Chem. Phys. 128 (2008), 064509.

[2] K.K. Thasneema, P. Shabeeba, Mohamed Shahin Thayyil, Mahadevan Pillai, N.S. Krishna Kumar, G. Govindaraj, V.C. Saheer, M.P. Nighil Nath, Dielectric relaxation and electrochemical studies on trihexyl tetradecyl phosphonium chloride ionic liquid, J. Mol. Liq. 252 (2018) 488–494.

[3] Subbiah Sowmiah, Venkatesan Srinivasadesikan, Ming-Chung Tseng, Yen-Ho Chu, On the chemical stabilities of ionic liquids, Molecules 14 (2009) 3780–3813.

[4] Kyoko Fujita, Douglas R. MacFarlane, Maria Forsyth, Protein solubilising and stabilising ionic liquids, Chem. Commun. (2005) 4804–4806.

[5] Bronya Clare, Amal Sirwardana, Douglas R. MacFarlane, Synthesis, purification and characterization of ionic liquids, Top. Curr. Chem. 290 (2009)Springer-Verlag Berlin Heidelberg.

[6] Hiroyuki Tokuda, Kikuko Hayamizu, Kunikazu Ishii, Md. Abu Bin Hasan Susan, Masayoshi Watanabe, Physicochemical properties and structures of room temperature ionic liquids. 1. Variation of anionic species, J. Phys. Chem. B 108 (2004) 16593–16600.

[7] Wu Xu, Emanuel I. Cooper, C. Austen Angell, Ionic liquids: ion mobilities, glass temperatures, and fragilities, J. Phys. Chem. B 107 (2003) 6170–6178.

[8] Kazuhide Ueno, Zuofeng Zhao, Masayoshi Watanabe, C. Austen Angell, Protic ionic liquids based on decahydroisoquinoline: lost super fragility and ionicity-fragility correlation, J. Phys. Chem. B 116 (2012) 63–70.

[9] Joshua R. Sangoro, Friedrich Kremer, Charge transport and glassy dynamics in ionic liquids, Acc. Chem. Res. 45 (4) (2012) 525–532.

[10] A. Rivera, A. Brodin, A. Pugachev, E.A. Rossler, Orientational and translational dynamics in room temperature ionic liquids, J. Chem. Phys. 126 (2007), 114503.

[11] J. Leys, et al., Influence of the anion on the electrical conductivity and glass formation of 1-butyl-3-methylimidazolium ionic liquids, J. Chem. Phys. 133 (2010), 034503.

[12] Elzbieta Frackowiak, Gregorz Lota, Juliusz Pernak, Roomtemperature phosphonium ionic liquids for super capacitor applications, Appl. Phys. Lett. 86 (2005), 164104.

[13] Kris Anderson, Hector Rodriguez, Kenneth R. Seddon, Phase behavior of trihexyl (tetradecyl) phosphonium chloride, nonane and water, Green Chem. 11 (2009) 780–784.

[14] Ricardo Ferraz, V˜ania Teixeira, D 'ebora Rodrigues, R 'uben Fernandes, Cristina Prud˜encio, Jo˜ao Paulo Noronha, Zeljko Petrovski, Lu'ıs C. Branco, Antibacterial activity of ionic liquids based on ampicillin against resistant bacteria, RSC Adv. 4 (2014) 4301–4307.

[15] Ana Rita Dias, Joao Costa-Rodrigues, Maria Helena Fernandes, Ricardo Ferraz, Cristina Prudencio, The anticancer potential of ionic liquids, ChemMedChem 12 (2017) 11–18.

[16] P. Mozhiyarasi, R. Anuradha, A study on phytochemical analysis and antimicrobial activity of Hyptis suaveolens (L.) poit, J. Chem. Pharm. Res. 8 (6) (2016) 438–442.

[17] S. Chanda, R. Dave, M. Kaneria, In vitro antioxidant property of some Indian medicinal plants, J. Med. Plant Res. 5 (2) (2011) 169–179.

[18] Prakash Veeru, Mishra Pankaj Kishor, Mishra Meenakshi, Screening of medicinal plant extracts for antioxidant activity, J. Med. Plant Res. 3 (8) (2009) 608–612.

[19] W. Brand-Williams, M.E. Cuvelier, C. Berset, Use of free radical method to evaluate antioxidant activity, Lebensm Wiss U Technol 28 (1995) 25–30.

[20] Nur Afiqah Ahmad, Khairulazhar Jumbri, Anita Ramli, Noraini Abd Ghani, Haslina Ahmad, Mohd Azlan Kassimd, Synthesis, characterisation and antioxidant properties of ferulate-based protic ionic liquids: experimental and modelling approaches, J. Mol. Liq. 278 (2019) 309–319.

[21] Sanjay V. Malhotra, Vineet Kumar, A profile of the in vitro anti-tumor activity of imidazolium based ionic liquids, Bioorg. Med. Chem. Lett. 20 (2010) 581–585.

[22] Vineet Kumar, Sanjay V. Malhotra, Study on the potential anti-cancer activity of phosphonium and ammonium-based ionic liquids, Bioorg. Med. Chem. Lett. 19 (2009) 4643–4646.

[23] N. Murugan,a L. Kavitha,c E. Shinyjoy,a D. Rajeswari,d K. Vimala,e S. Kannane and D. Gopi, Smart rose flower like bioceramic/metal oxide dual layer coating with enhanced anti-bacterial, anticancer, anti-corrosive and biocompatible properties for improved orthopedic applications, RSC Adv., 5, 85831–85844 (2015).

[24] Thondhi Ponraj, Manickam Paulpandi, Raju Vivek, Karuppaiya Vimala, Soundarapandian Kannan, Protein regulation and apoptotic induction in human breastcarcinoma cells (MCF-7) through lectin from G. beauts, Int. J. Biol. Macromol. 95 (2017) 1235–1245.

[25] Nadjet Rezki, Salsabeel A. Al-Sodies, Mouslim Messali, Sanaa K. Bardaweel, Pramod K. Sahu, Fawzia F. Al-blewi, Praveen K. Sahu, Mohamed R. Aouad, Identification of new pyridinium ionic liquids tagged with Schiff bases:design, synthesis, in silico ADMET predictions and biological evaluations, J. Mol. Liq. 264 (2018) 367–374.

[26] Mouslim Messali, Mohamed R. Aouad, Wael S. El-Sayed, Adeeb Al-Sheikh Ali, Taibi Ben Hadda, Belkheir Hammouti, New eco-friendly 1-alkyl-3-(4-phenoxybutyl) imidazolium-based ionic liquids derivatives: a green ultrasound-assisted synthesis, characterization, antibacterial activity and POM analyses, Molecules 19 (2014) 11741–11759.

[27] Maria Villanueva, Alberto Coronas, Josefa Garcia, Josefa Salgado, Thermal stability of ionic liquids for their application as new absorbents, Ind.Eng.Chem.Res 52 (2013) 15718–15727.

[28] Léa Chanceliera, Olivier Boyrona, Thibaut Gutelb, Catherine C. Santinia, Thermal stability of imidazolium-based ionic liquids, French-Ukrainian J. Chem. Volume 04 (Issue 01) (2016).

[29] Fathy A. Yassin, Fathy Y. El Kady, Hoda S. Ahmed, Latifa K. Mohamed, Seham A. Shaban, Ahmed K. Elfadaly, Highly effective ionic liquids for biodiesel production from waste vegetable oils, Egypt. J. Pet. 24 (2015) 103–111.

[30] C. Krause, J.R. Sangoro, C. Iacob, F. Kremer, Charge transport and dipolar relaxations in imidazolium-based ionic liquids, J. Phys. Chem. B 114 (2010) 382–386.

[31] Z. Wojnarowska, et al., Molecular dynamics studies on the water mixtures of pharmaceutically important ionic liquid lidocaine HCl, Mol. Pharm. 9 (2012) 1250–1261.

[32] K.P Safna Hussan, M. Shahin Thayyil, S.K. Deshpande, T.V Jinitha, K. Manoj, K.L. Ngai, Molecular dynamics and the translational–rotational coupling of an ionically conducting glass-former: amlodipine besylate, RSC Adv. 8 (2018) 20630–20636.

[33] F. Kremer, A. Schonhals, Broadband Dielectric Spectroscopy, ISBN 3-540-43407-0 Springer-Verlag, Berlin Heidelberg New York, 2003.

[34] K.P Safna Hussan, M. Shahin Thayyil, V.K. Rajan, Anu Antony, The interplay between charge transport and CO2 capturing mechanism in [EMIM][SCN] ionic liquid: a broadband dielectric study, J. Phys. Chem. B 123 (2019) 6618–6626.

[35] J. Sangoro, et al., Electrical conductivity and translational diffusion in the 1-butyl-3-methylimidazolium tetrafluoroborate ionic liquid, J.chem.phys 128 (2008), 214509.