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Bis-imidazolium and benzimidazolium based gemini-type ionic liquids structure: synthesis and antibacterial evaluation

Nassir N. Al-Mohammed*, Yatimah Alias* and Zanariah Abdullah

Chemistry Department, Faculty of Science, University of Malaya, Lembah Pantai, Kuala Lumpur 50603, Malaysia

Corresponding authors:

Nassir N. Al-Mohammed, Email: nassir@siswa.um.edu.my and nassirnn@gmail.com

Yatimah Alias, Email: yatimah70@um.edu.my

Fax: +603-79677188

Abstract: Based on bis-imidazolium and benzimidazolium, new sets of geminal dicationic ionic liquids containing sulphonamide moiety were successfully synthesized with good yields. Their structures were confirmed by ^{1}H-NMR, ^{13}C-NMR, FT-IR, and mass spectroscopy. Selected physicochemical properties of these ILs including; thermal stability by TGA and miscibility in some common organic solvents and water were also determined. Most of the prepared dicationic ILs displayed significant level of antibacterial activities against ten selected bacterial strains of Gram-positive and Gram-negative using micro-broth dilution assay.

1. Introduction

Ionic liquids (ILs) are salts typically consist of large organic cations containing various substituents[1,2] associated with an organic or inorganic anions.[3,4] They are exhibiting several unique chemical and physical properties, such as extremely low vapour pressure, low melting point, non-flammability, wide electrochemical window, excellent solvation and high thermal stability. Further, through the modification of cation and anion, ILs can be tuned to be miscible with either low polarity organic solvents including: hexanes, toluene, ether, super critical CO_2 or high polarity solvents such as water and ethanol.[5] The interest in ILs as 'greener' solvents has dramatically expanded to include a wide unexpected range of applications that have been reported in synthesis and biotechnology.

ILs with molecular structure of Gemini surfactants (Geminal ILs) are a new class of amphiphilic molecules containing two head groups (two identical or dissimilar cationic moieties) and two aliphatic chains, linked by a rigid or flexible spacer. Comparing to traditional ILs, geminal dicationic liquids have shown superior physical properties[6-9] in: thermal stability, solubility in aqueous media, high density, interface property, lower critical micelle concentration (CMC), and unusual rheological properties. Accordingly, they have multiple promising applications in life science, petro-chemistry,

medicine, etc. Further, dicationic ILs as multifunctional ions have an exclusive approach to "tune" or alter their physicochemical properties to a greater range than more traditional monocationic ILs. The "tenability" or structural variations include the effect of the cationic part symmetry (*i.e.*, identical or not), the length and type of both spacer and the side chains, as well as the type of counter-anions.

Recently, several ammonium-based dicationic phosphate salt liquids have prepared and characterized.[10-13] In the meanwhile, some dicationic ILs based-imidazolium pyridinium and ammonium with polyether linker,[14] have been synthesized by Ohno and co-workers.[15] Additionally, two studies by Anderson *et al*.,[7] and Payagala *et al*.,[9] are dealing with synthesis and physicochemical properties manipulation of symmetrical and unsymmetrical geminal dicationic ILs, respectively. They have characterized several properties including thermal stability, surface tension, density, miscibility with a polar and nonpolar solvent, and shear viscosity of imidazolium and pyrrolidium cation based ILs. Thermal stabilities of the symmetrical and unsymmetrical dicationic ILs are higher than their corresponding conventional monocationic ILs. Precisely, Imidazolium and pyridinium geminal dicationic ILs have shown an increased thermal stability, with the onset temperatures of the thermal decomposition (T_{onset}) about 150 °C above the decomposition temperature of the monocationic ILs.[7,9] Thermogravimetric analysis (TGA) at elevated temperatures is used to evaluate thermal stability of many dicationic ILs. This method of short-term stability, called ramped temperature analysis method (also called step-tangent or dynamic analysis) with most common heating rates: 10 °C min^{-1} and 20 °C min^{-1}.[16,17] Multiple factors including the great charge and intermolecular interactions, density, molecular weight and shear viscosity associated with small free volume, were used to attribute the observed high thermal stability of dicationic ILs.[18,19]

From the ILs' structure point of view, Poly-functionalized heterocyclic compounds containing imidazole and its derivatives are acquiring more importance due to their biological activity. Most ILs contain heterocyclic derivatives as cations, *e.g.* imidazolium, benzimidazolium, pyridinium, pyrrolium, pyrrolidinium and ILs with bridged structures. Drug designs based on high therapeutic properties of the imidazole and benzimidazole are considered as an advantage towards synthesize number of novel clinical agents against various types of diseases. Moreover, extensive biochemical and pharmacological studies have confirmed imidazole and benzimidazole as effective compounds in treating various strains of microorganisms.[20-24] Their antibacterial and antifungal effects are attributed to cationic interactions with negatively charged parts of bacterial membranes.[25] Furthermore, benzenesulfonamide moiety is well known for their several pharmacological activities, with (or without) among others.[26-28] Typically, sulfonamide compounds are widely studied due to their chemotherapeutic and the interesting properties related antibacterial,[29,30] anti-inflammatory,[31,32] analgesic agents,[33] antifungal[34,35] and antiviral.[36,37] Molecular Modeling and Quantitive Structure-

activity Relationship (QSAR) method[38-41] have been used to confirm their antibacterial activity for many applications in the bio-inorganic and metal-based drug chemistry.[42-45] The enhancement of antibacterial activity of di-imidazole and di-benzimidazole compounds incorporated to sulfonamide moiety has been reported by authors of the previous work.[46] However, many research works dealt with geminal di-cationic ILs synthesis when it comes to their design,[6,7,9,18,47-52] while limited studies have considered dicationic ILs with high rigid spacer.[53,54] The current work concentrates on synthesis novel geminal bis-imidazolium and benzimidazolium ILs consist of two substituents symmetric head groups (two identical cations), linked by high rigidity spacer containing benzenesulfonamide moiety in high yield and purity. To explore the structure–activity relationship (SAR) of this novel dicationic IL series that contain multi bioactive moieties, an *in vitro* antibacterial evaluation of halogen ILs against standard strains of six Gram positive and four Gram negative, are investigated. Further, the thermal stability and miscibility of the prepared ILs are indicated as well. The presence of incorporated benzenesulfonamide moiety as well as the active side substituents into di-imidazolium and benzimidazolium cations enhanced both antibacterial activity and miscibility for the synthesized ILs. The effects of anions on antibacterial activity and thermal stability are beyond the scope of this study.

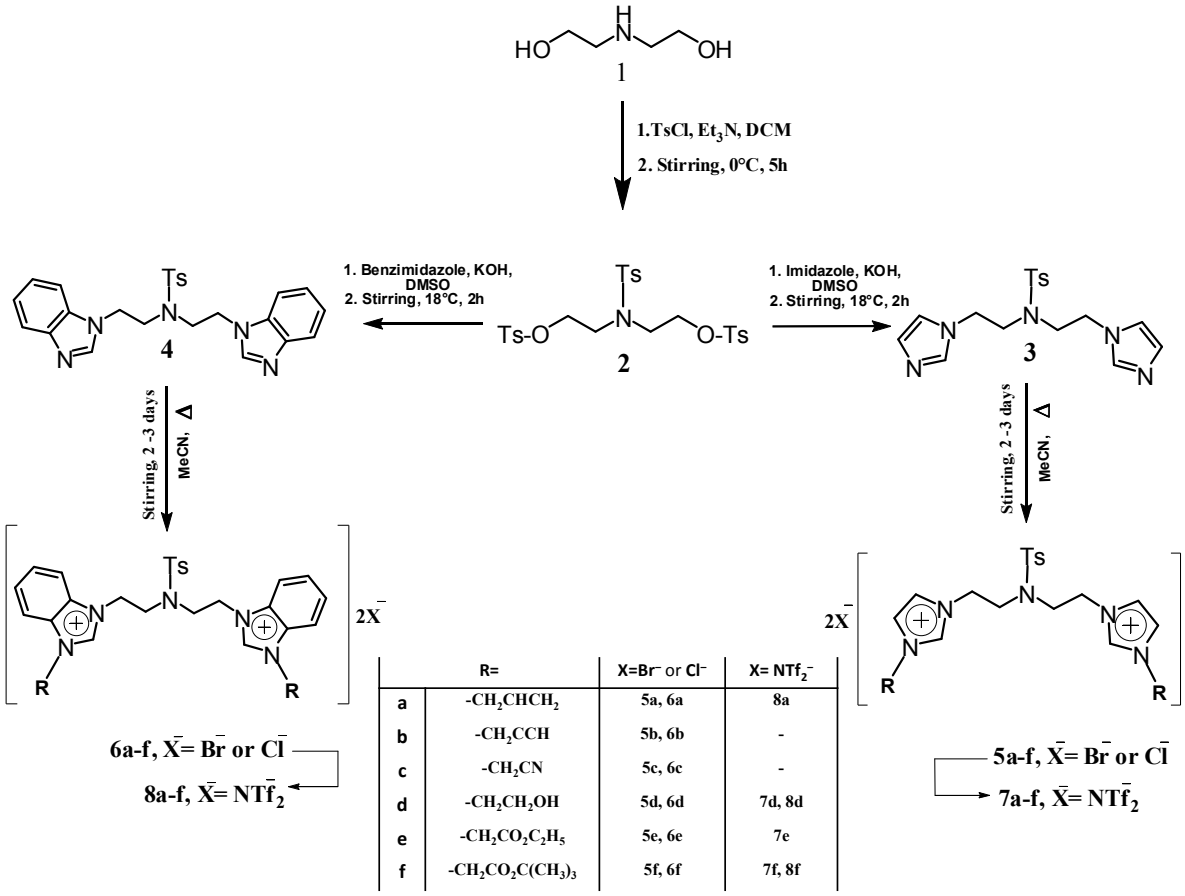
2. Results and Discussion

2.1. Synthesis

Compounds *N,N*-bis[(Imidazol-1-yl)ethyl]-4-methylbenzenesulfonamide (**3**) and *N,N*-bis [(Benzimidazol-1-yl)ethyl]-4-methylbenzenesulfonamide (**4**) were previously synthesized in sufficient purity[46] and currently used as precursors to produce bis-imidazolium and bis-benzimidazolium dicationic ILs, respectively. The highly reactive halides; allyl bromide, propargyl bromide, chloroacetonitrile, 2-bromoethanol, ethyl bromoacetate and *tert*-butyl bromoacetate were considered for alkylation reactions, thus, the high yields were not surprising according to easy substitution reaction with both imidazole and benzimidazole rings, Scheme 1.

In current work, all the synthesized halogen (chloride or bromide) ILs are semi-solid to syrup or viscous liquid at room temperature which have been considered as criteria to determine their classification as ILs.[55,56] Generally, ILs tend to be liquid at room temperature, which is attributed to the high conformational degrees of freedom. Moreover, the NTf_2 counter ion confers lower viscosity and decreased melting point compared with halogen precursors. Metathesis of halogen anion to NTf_2^- produced clear liquids at room temperature and clean samples were isolated after a simple workup. The process of counter-ions exchange involved stirring an aqueous solution of halogen ILs with $LiNTf_2$ for a few hours. A good yield of the hydrophobic ILs phase was then separated by extraction with ethyl acetate to produce the pure and clear liquid samples of ILs after organic layer evaporation

under reduced pressure. The purity of the NTf_2-ILs was confirmed by ^{13}C and ^{9}F-NMR. Table 1 summarizes the synthetic details of the prepared ILs.



	R=	X=Br⁻ or Cl⁻	X= NTf_2^-
a	$-CH_2CHCH_2$	5a, 6a	8a
b	$-CH_2CCH$	5b, 6b	-
c	$-CH_2CN$	5c, 6c	-
d	$-CH_2CH_2OH$	5d, 6d	7d, 8d
e	$-CH_2CO_2C_2H_5$	5e, 6e	7e
f	$-CH_2CO_2C(CH_3)_3$	5f, 6f	7f, 8f

Scheme 1: Synthesis of imidazolium and benzimidazolium geminal dicationic ILs

Table 1: Structural and synthetic details of imidazolium and benzimidazolium based dicationic ILs

IL	Cations	Incorporated side groups	Counter ions	Status[c]	M.wt.	Yield (%)
5a	Im[a]	$-CH_2CHCH_2$	Br^-	Syrup	601.40	95
5b	Im[a]	$-CH_2CCH$	Br^-	Syrup	597.37	98
5c	Im[a]	$-CH_2CN$	Cl^-	Liquid	510.44	98
5d	Im[a]	$-CH_2CH_2OH$	Br^-	Liquid	609.37	99
5e	Im[a]	$-CH_2CO_2C_2H_5$	Br^-	Semi-solid	693.45	96
5f	Im[a]	$-CH_2CO_2C(CH_3)_3$	Br^-	Semi-solid	749.55	95
6a	BIm[b]	$-CH_2CHCH_2$	Br^-	Liquid	701.51	95
6b	BIm[b]	$-CH_2CCH$	Br^-	Syrup	697.48	98
6c	BIm[b]	$-CH_2CN$	Cl^-	Syrup	610.56	94
6d	BIm[b]	$-CH_2CH_2OH$	Br^-	Liquid	709.49	98
6e	BIm[b]	$-CH_2CO_2C_2H_5$	Br^-	Syrup	793.57	98
6f	BIm[b]	$-CH_2CO_2C(CH_3)_3$	Br^-	Syrup	849.67	98
7d	Im[a]	$-CH_2CH_2OH$	NTf_2^-	liquid	1009.35	83
7e	Im[a]	$-CH_2CO_2C_2H_5$	NTf_2^-	liquid	1093.93	96
7f	Im[a]	$-CH_2CO_2C(CH_3)_3$	NTf_2^-	liquid	1150.03	95
8a	BIm[b]	$-CH_2CHCH_2$	NTf_2^-	liquid	1101.99	90
8d	BIm[b]	$-CH_2CH_2OH$	NTf_2^-	liquid	1109.98	87
8f	BIm[b]	$-CH_2CO_2C(CH_3)_3$	NTf_2^-	liquid	1250.16	97

[a] Imidazolium, [b] Benzimidazolium, [c] at room temperature

The spectral data (IR, ^1H, ^{13}C, ^{19}F-NMR and mass) are in good agreement with current proposed structures of the newly synthesized ILs. FT-IR spectra for all synthesized ILs (*i.e.* **5a**–**f**, **6a**–**f**, **7d-f** and **8a-f)** showed absorption bands at 1,329–1,364 cm^{-1} and 1,151–1,156 cm^{-1} which were assigned to the O=S=O group. These bis-imidazolium and benzimidazolium ILs showed stretching absorption bands at 3,142–3,027 cm^{-1}, 2,990–2,850 cm^{-1}, 1,644–1,590 cm^{-1}, and 1,566–1,443 cm^{-1} attributed to $(C\text{-}H)_{Aromatic}$, $(C\text{-}H)_{Aliphatic}$, (C=N), and $(C=C)_{Aromatic}$, respectively. The bands at 2,125 cm^{-1} and 2,121 cm^{-1} for compounds **5b** and **6b** were assigned to (C≡C) in propargyl substitutions, while **5c** and **6c** ILs showed characteristic stretching absorption bands at 2,238 cm^{-1} and 2,235 cm^{-1}, respectively, which were assigned to (C≡N). Incorporating ethanol groups into **5d**, **6d**, **7d**, and **8d** ILs showed (O-H) bands at 3,280–3,312 cm^{-1}. The IR spectra of compounds **5e-f**, **6e-f 7e-f** and **8f** showed sharp absorption bands at 1,739–1,748 cm^{-1} which were attributed to carbonyl stretching frequency corresponding to the ester groups. In the ^1H-NMR spectra, α-CH_2 protons appeared as singlet (compounds **5c**, **5e**, **5f**, **6c**, **6e**, **6f**, **7e**, **7f** and **8f**), doublet (**5a**, **5b**, **6a**, **6b**, **8d**) and triplet (**5d**, **6d**, **7d** and **8d**) at δ 5.16–6.13 ppm, δ 4.88–5.58 ppm, and δ 4.19–4.57, respectively. Moreover, singlet peaks appeared in the range of δ 9.72–10.31 ppm corresponding to the isolated C-H of benzimidazolium rings while these protons indicated broad triplet ~ singlet peaks in all imidazolium ILs. The chemical shifts of the imidazole and benzimidazole protons rings' in both imidazolium and benzimidazolium ILs

are consistently downfield in comparison to the analogous chemical shifts of the core di-imidazole and di-benzimidazole compounds.[46] These observations are in accord with the presence of positive charges in both ILs kinds, where the higher shifts were recorded with acetonitrile as an active side groups; compounds **5c** and **6c**. The allylic-CH in compounds **5a**, **6a** and **8a** showed characteristic multiplet peaks in the range of δ 5.98–6.15 ppm, while the allylic-CH_2 showed four individual doublet peaks with different *J* constant; 0.98, 1.22 and 1.36 Hz. Further, compounds **5b** and **6b** presented triplet peaks at δ 3.88 and 3.91 ppm, where attributed to propargyl-CH with *J* constant values of 2.72 and 2.27, respectively. The peak of O-H protons for compounds **5d, 6d, 7d** and **8d** appeared as broad singlet at δ 5.15–5.22 ppm integrating for two protons. In general, imidazolium ILs showed up-field resonance when compared to benzimidazolium ILs with both halogen and NFf_2 anions.

^{13}C-NMR was used to assign the carbon skeleton of the synthesized geminal dicationic imidazolium and benzimidazolium ILs. PENDANT experiment (Polarization enhancement nurtured during attached nucleus testing) was applied to differentiate between the methylene (CH_2) and methine (CH) carbon signals based on different H- content of carbon atoms that have environments similarity.[57] In PENDANT spectra methyl (CH_3) and methine (CH) carbons appeared as positive signals, while methylene (CH_2) and quaternary carbon (C) showed negative signals. Figure 1 demonstrated ^{13}C-NMR PENDANT spectrum of IL **6a**.

In the ^{13}C-NMR spectra of **5a**, **6a**, and **8a** ILs, the signals around δ 130 ppm and 120 ppm were assigned to allylic CH and CH_2, respectively, while the propargyl active side groups in both **5b** and **6b** ILs showed characteristic peaks in the δ 79 ppm for -C- and δ 75 ppm for CH. Additional signals were observed at 114 ppm and 113 ppm, which were assigned to the carbon atom of (CN) for compounds **5c** and **6c**, respectively. The peaks recorded at δ 165–167 ppm, were attributed to carbon atom of carbonyl groups in compounds **5e**, **5f**, **6e**, **6f**, **7e**, **7f** and **8f**. Ethanolic carbon atoms in **5d**, **6d**, **7d** and **8d** ILs were determined at 59 ppm. Carbon atoms C-F in **7d–f**, **8a, 8d and 8f** ILs, showed quartet peaks with 320 Hz constant *J* values within the range of δ 126-114 ppm. The characteristic chemical shifts for F/CF_3 were also detected in the ^{19}F-NMR spectra at –80 ppm. With the high resolution mass spectra, the identity of the bis-imidazolium and benzimidazolium ILs was confirmed as a $[M^{+2}–H]-2X^{-}$; (M= cation and X= anion) in the both kinds of IL anions.

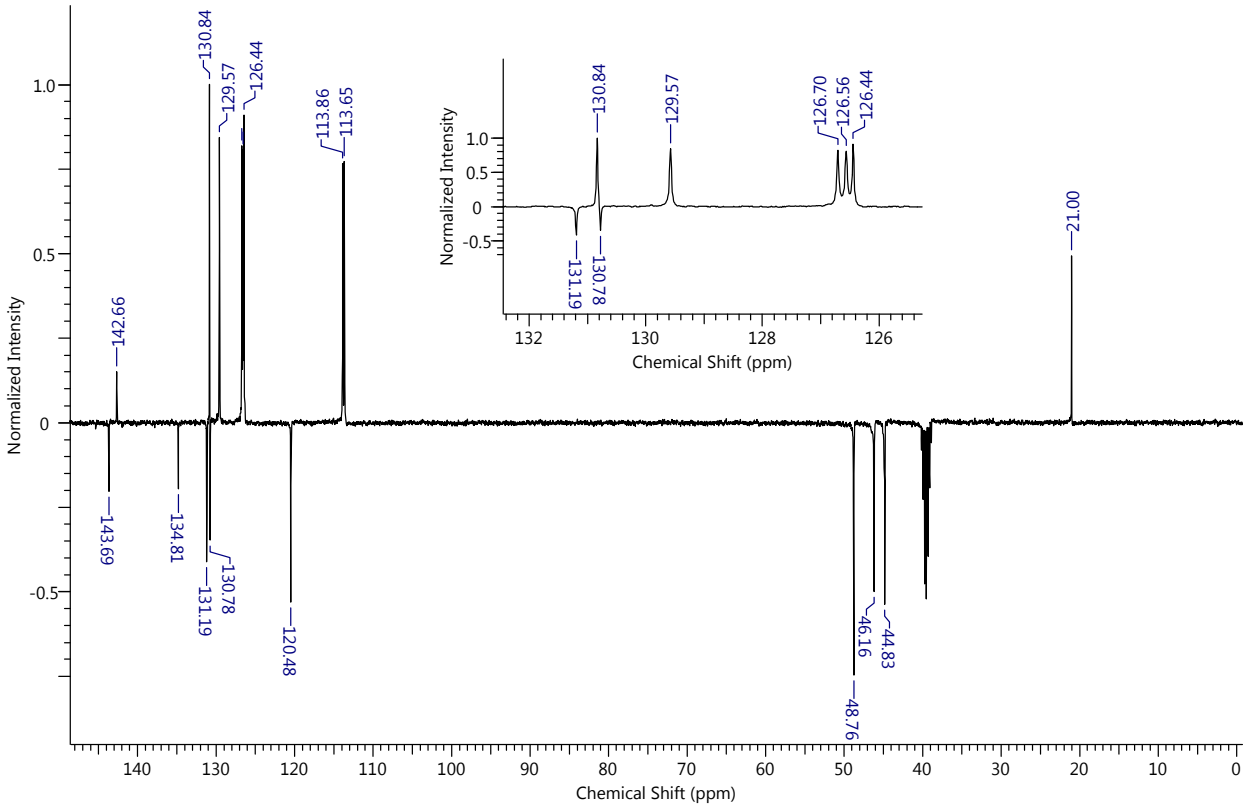


Figure 1: ^{13}C-NMR PENDANT of IL **6a**.

2.2. Solubility

Solubility behaviour of the all synthesized geminal dicationic ILs in water and common organic solvents was evaluated at room temperature. These solvents have a wide range of polarity from highly polar; water or alcohols, gradually to weakly or non-polar solvents like toluene or hexane, respectively. The observations obtained from solubility tests are summarized in Table 2.

The IL was considered miscible (if a drop of the IL dissolves in a few drops (1–5) of the solvent), partially miscible (if it dissolves in more than 10 drops of the solvent), or immiscible (if it did not dissolve in 2 ml of the solvent)[58] where termed by (+), (±) and (–), respectively. It can be observed that all halogen bis-imidazolium and benzimidazolium ILs are miscible with water while reverse miscibility was noticed for the ILs incorporated to NTf_2^- anion. All ILs studied for both kinds of anions are totally miscible with acetone, ethyl acetate, tetrahydrofuran and chloroform, while they are shown immiscible with hexane. Generally, the introduction of hydroxyl in the side active groups considerably modified the solubility behaviour of ILs **7d** and **8d** with ethanol,[59] while no significant influence have noticed for the rest of ILs when other functional groups changed neither in the introduction benzene ring into imidazolium ILs.

Table 2: Solubility of synthesized imidazolium and benzimidazolium based geminal dicationic ILs in various solvents.

IL	Water	Ethanol	Acetone	Ethyl acetate	tetrahydrofuran	Chloroform	Toluene	Hexane
5a	+	+	+	+	+	+	+	–
5b	+	+	+	+	+	+	+	–
5c	+	+	+	+	+	+	±	–
5d	+	+	+	+	+	+	±	–
5e	+	+	+	+	+	+	+	–
5f	+	+	+	+	+	+	+	–
6a	+	+	+	+	+	+	+	–
6b	+	+	+	+	+	+	+	–
6c	+	+	+	+	+	+	+	–
6d	+	+	+	+	+	+	+	–
6e	+	+	+	+	+	+	+	–
6f	+	+	+	+	+	+	+	–
7d	–	±	+	+	+	+	±	–
7e	–	–	+	+	+	+	+	–
7f	–	–	+	+	+	+	+	–
8a	–	–	+	+	+	+	+	–
8d	–	±	+	+	+	+	+	–
8f	–	–	+	+	+	+	+	–

(+) miscible - a drop of the compound dissolves in a few drops (1–5) solvent
(±) moderately miscible - dissolves in more than 10 drops solvent
(–) immiscible - did not dissolve in 1-2 ml solvent

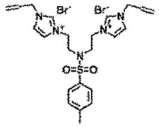
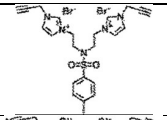
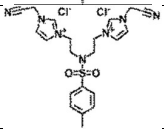
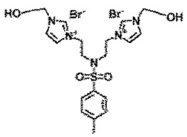
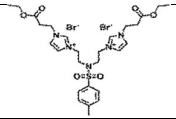
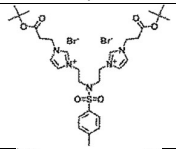
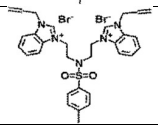
The solubility behaviour of the geminal dicationic ILs in water and all common organic solvent was significantly similar to mono-cationic ILs,[60-62] whereas the halogen and NTf_2^- dicationic ILs were noticed as miscible and immiscible with water, respectively. Obviously, the presence of hydrophobic anion (NTf_2^-) exceeds the coordinating nature of the bromide (or chloride) anion to produce immiscible ILs with water. Thus, the individual cations and anions can be tuneable to produce ILs with the desired properties and characteristics.

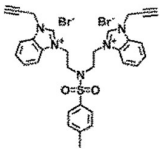
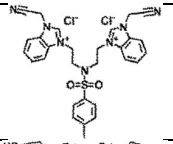
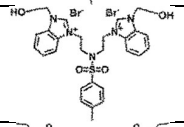
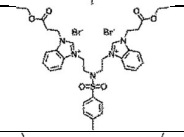
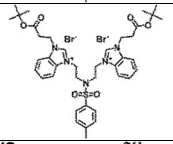
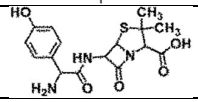
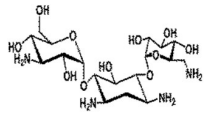
2.3. Antibacterial Activities

Microbroth dilution bioassay was used to evaluate the antibacterial activities of the synthesized halogen imidazolium and benzimidazolium geminal dicationic ILs against representative standard strains of Gram-positive and Gram-negative bacteria. Minimum inhibitory concentrations MIC (mg/mL) of the studied dicationic ILs were determined, and the results are listed in Table 3. The majority of these ILs showed significant antibacterial activity towards most of the selected microorganisms as shown in Figure 2. According to the studies of structure-activity relationship

(SAR), the incorporation of two different pharmacophores within the same molecule would enhance the resulting compounds' biological activities.[37,63,64] Therefore, the presence of incorporated benzenesulfonamide moiety adjacent to the imidazolium and benzimidazolium core ILs, successfully promoted the antibacterial activity of the produced geminal dicationic ILs. Based on antimicrobial activity studies of imidazolium ILs, the halogen anions showed the least toxicity,[21,65-68] while ILs bioactivity is largely driven by hydrophobicity and active side substitutions (or alkyl chain branching) of the cations.[69-73] Due to the similarity of ILs structure to detergents, pesticides and antibiotics, the proposed mechanism of ILs toxicity is through membrane disruption where the toxic effect may be related to a common cellular structure or process.[21,74] Further, ILs as a cationic surfactant may cause disruption in membrane-bound protein due to their interfacial properties, and the induced polar narcosis effect.[75] The current ILs substance attacked the lipid structure of membrane (lipo-polysaccharide layer), where the sulfonyl group of sulfonamide moiety interfered with cell metabolism. Thus, comparing to the previously prepared core compounds[46] (**3** and **4**), the cationic substitutions of the geminal dicationic ILs, have successfully enhanced the biological activities of both imidazolium and benzimidazolium ILs. Furthermore, imidazolium ILs showed the highest activities which could be attributed to their higher solubility in water (Table 2). The highest antibacterial toxicity was found for ILs with acetonitrile substituent (**5c** and **6c**), while the ILs of *tert*-butyl-ester (**5f** and **6f**) did not display dramatic acute biological activities at the selected concentration range. Against *β*-lactam resistant Gram-negative bacterium (*Pseudomonas aeruginosa*), all IL compounds except **5b** showed significant activities in MIC ranging values of 0.1– 0.5 mg/mL when compared to the antibiotic amoxicillin. Moreover, **5c** and **6c** ILs showed considerable antibacterial activities of 0.05 mg/mL MIC value against *Bacillus subtilis*, which required a high dose of amoxicillin[76] (0.25 mg/mL). The antibacterial results of the most tested geminal dicationic ILs demonstrated interesting inhibitory values against *Staphylococcus epidermidis*. The range of MIC values for tested compounds were between 0.05 and 0.5 mg/mL, for **6c** and **5e** sequentially, while *β*-lactam antibiotic amoxicillin displayed no activity against this strain of Gram-positive bacteria. Against *Acinetobacter calcoaceticus* Gram-negative bacteria, IL **5c** exhibited a significant antibacterial inhibitory effect at 0.05 mg/mL, while both commercial antibiotics amoxicillin and kanamycin exhibited MIC values (0.15 mg/mL and >0.5 mg/mL, respectively). Moreover, *Enterococcus faecalis* showed no effect by antibiotic kanamycin at the concentration range of the current study (0.05–0.5 mg/mL), while the dicationic IL compounds **5d**, **5e**, and **6e** demonstrated inhibitory effect with values of 0.25, 0.25 and 0.3 mg/mL, respectively against this Gram-positive bacterium. Based on bioactive compounds results, different compounds reacted variously against bacteria. In these dicationic ILs, strains of Gram-positive bacteria seem to be more sensitive than Gram negative micro-organisms.

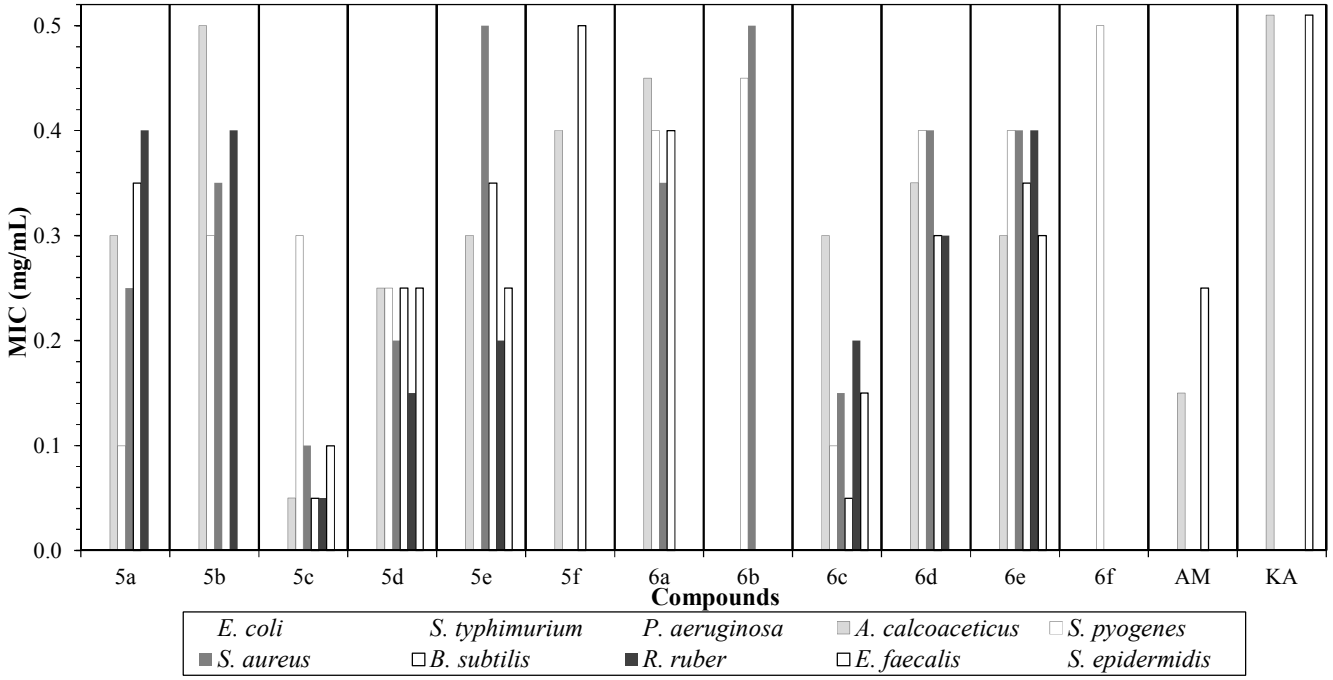
Table 3: Antibacterial activities of synthesized halogen bis-imidazolium and benzimidazolium ILs.

No.	Structure of samples	Bacteria/MICs (mg/mL)									
		Gram-negative bacteria				*Gram-positive bacteria*					
		Escherichia coli	*Salmonella typhimurium*	*Pseudomonas aeruginosa*	*Acinetobacter calcoaceticus*	*Streptococcus pyogenes*	*Staphylococcus aureus*	*Bacillus subtilis*	*Rodococcus ruber*	*Enterococcus faecalis*	*Staphylococcus epidermidis*
5a		**0.25**	**0.40**	**0.30**	**0.30**	**0.10**	**0.25**	**0.35**	**0.40**	**>0.50**	**0.30**
5b		**0.50**	**>0.50**	**>0.50**	**0.50**	**0.30**	**0.35**	**>0.50**	**0.40**	**>0.50**	**>0.50**
5c		**0.05**	**0.05**	**0.10**	**0.05**	**0.30**	**0.10**	**0.05**	**0.05**	**0.10**	**0.15**
5d		**0.15**	**0.20**	**0.15**	**0.25**	**0.25**	**0.20**	**0.25**	**0.15**	**0.25**	**0.20**
5e		**0.40**	**0.35**	**0.30**	**0.30**	**>0.50**	**0.50**	**0.35**	**0.20**	**0.25**	**0.50**
5f		**0.50**	**0.40**	**0.30**	**0.40**	**>0.50**	**>0.50**	**0.50**	**>0.5**	**>0.5**	**>0.5**
6a		**0.40**	**>0.50**	**0.50**	**0.45**	**0.40**	**0.35**	**0.40**	**>0.50**	**>0.50**	**0.40**

6b		**>0.50**	**>0.50**	**0.50**	**>0.50**	**0.45**	**0.50**	**>0.50**	**>0.50**	**>0.50**	**>0.50**
6c		**0.25**	**0.05**	**0.25**	**0.30**	**0.10**	**0.15**	**0.05**	**0.20**	**0.15**	**0.05**
6d		**0.35**	**0.20**	**0.40**	**0.35**	**0.40**	**0.40**	**0.30**	**0.30**	**>0.50**	**0.40**
6e		**0.30**	**0.35**	**0.45**	**0.30**	**0.40**	**0.40**	**0.35**	**0.40**	**0.30**	**0.30**
6f		**>0.5**	**>0.5**	**0.4**	**>0.5**	**0.5**	**>0.5**	**>0.5**	**>0.5**	**>0.5**	**>0.5**
AM		**<0.05**	**<0.05**	**nd**	**0.15**	**0.05**	**<0.05**	**0.25**	**<0.05**	**<0.05**	**nd**
KA		**<0.05**	**<0.05**	**<0.05**	**>0.5**	**<0.05**	**<0.05**	**<0.05**	**<0.05**	**>0.5**	**<0.05**

MIC: Minimum inhibitory concentration, AM: Amoxicillin, KA: Kanamycin, nd: not detected.

Figure 2: MIC's Histogram for synthesized ILs (0.05–0.50 mg/mL concentration) versus ten strains of bacteria



2.4. Thermal stability

Ramped temperature TGA method[16,17,77] (at heating rate of 10 °C min^{-1}), was used to measure the decomposition temperatures of the synthesized halogen imidazolium and benzimidazolium geminal dicationic ILs (*i.e.* **5a-f** and **6a-f**). Ramped temperature experiment (also called step-tangent or dynamic analysis)[7,78] gives rise to a point of thermal degradation, which is termed T_{onset} onset points of decomposition and defined as the value of the intercept of two linear functions: the baseline of zero weight loss and the tangent of weight *vs*. temperature upon decomposition and calculated using the thermal analysis software.[79] The actual degradation already starts at a lower temperature (T_{start}) than the T_{onset}.[80] Typically, the ramped temperature method is also characterized by a temperature of maximum degradation (T_{peak}) in between 10 to 100 °C higher than T_{onset}.[16] Moreover $T_{10\%}$ or $T_{50\%}$, which reveals the temperature at a weight loss of 10% and 50%, respectively, were reported and several research works have followed similar technique.[81,82] The decomposition temperatures ($T_{10\%}$), ($T_{50\%}$), (T_{start}), (T_{onset}) as well as the differential peak temperature (T_{peak}), for all samples were listed in Table 4.

All the synthesized ILs exhibited good thermal stability with high decomposition temperatures. Generally, ILs bearing imidazolium cations exhibited higher thermal stability compared to those with benzimidazolium, Figures 3 and 4 demonstrate their thermogravimetric analysis traces, respectively. Further, the ILs containing the cyanide or ethanolic functional side groups (i.e. **5c** and **5d**) are most

stable with the highest onset decomposition temperature of 294 and 289 °C, respectively. These di-cationic ILs decompose similarly at the first stage (203–270 ^{o}C for imidazolium and 200–255 ^{o}C for benzimidazolium ILs); subsequently, they have parallel ramps in the decomposition traces, perhaps indicating a similar decomposition mechanism and products.

Generally, imidazolium and benzimidazolium geminal dicationic ILs incorporating to unsaturated side groups showed lower thermal stability than their fully saturated analogues.[7] Due to the increasing distance between alkene and nitrogen of imidazolium ring in **5a** and **6a** ILs, the increase in their thermal stability has been noticed, while the rigidity of alkyne functional groups in **5b** and **6b** ILs gave rise to decrease in the stability (propargyl *vs.* allyl).[83]

TGA thermograms of both ILs kinds reveal three main weight loss regions. The first region at a temperature range of 50 to 200 ^{o}C is due to the evaporation of physically weak and chemically strong bound water. The weight loss of the ILs in this range is about 5–8 wt.% reflecting the acceptable limit of water content. The second transition region at around 210–500 ^{o}C is due to the structural degradation of the ILs with 50–70% total weight loss within those ranges of the decomposition temperatures. The third stage weight loss occurred above 500 ^{o}C, probably due to the cleavage backbone of the ILs where the total weight loss in this stage was ~20 % at 900 ^{o}C. The decomposition of the ILs was almost completed at around 900°C and no further weight loss observed after that. Comparing to many traditional mono- and symmetric dicationic imidazolium-based ILs[6,7,9], the prepared geminal dicationic ILs showed a significant high thermal stability, *e.g.*, thermal stabilities ranging from 145, 185, 257 to 300 °C were recorded to (1-butyl-3-methylimidazolium chloride), (1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide), (1,5-bis-(3-(2-ethanolyl)-imidazol-1-iumyl)pentane bis(trifluoromethylsulfonyl)imide), and (1,5-bis-(3-methylimidazol-1-iumyl)pentane-nitrate), respectively. The thermal stability results of current synthesized ILs support the high decomposition temperatures feature for imidazolium-based dicationic ILs.

Table 4: Thermal decomposition temperatures of the synthesized bis-imidazolium and benzimidazolium ILs

IL	Incorporated side groups	Temperature (°C) corresponding to				
		T_{start} [a]	T_{10} [b]	T_{50} [c]	T_{peak} [d]	T_{onset} [e]
5a	$-CH_2CHCH_2$	270	297	299	324	285
5b	$-CH_2CCH$	260	288	310	326	285
5c	$-CH_2CN$	265	285	300	322	294
5d	$-CH_2CH_2OH$	248	262	337	330	289
5e	$-CH_2CO_2C_2H_5$	203	235	307	333	233
5f	$CH_2CO_2C(CH_3)_3$	229	279	300	347	274
6a	$-CH_2CHCH_2$	250	277	303	338	274
6b	$-CH_2CCH$	265	287	295	324	286
6c	$-CH_2CN$	213	250	265	333	252
6d	$-CH_2CH_2OH$	255	282	300	322	281
6e	$-CH_2CO_2C_2H_5$	200	232	307	331	223
6f	$CH_2CO_2C(CH_3)_3$	208	247	292	326	238

Decomposition temperatures, (°C): [a] the started decomposition, [b] at 10 % weight loss, [c] at 50 % weight loss, [d] differential peak, [e] the onset decomposition.

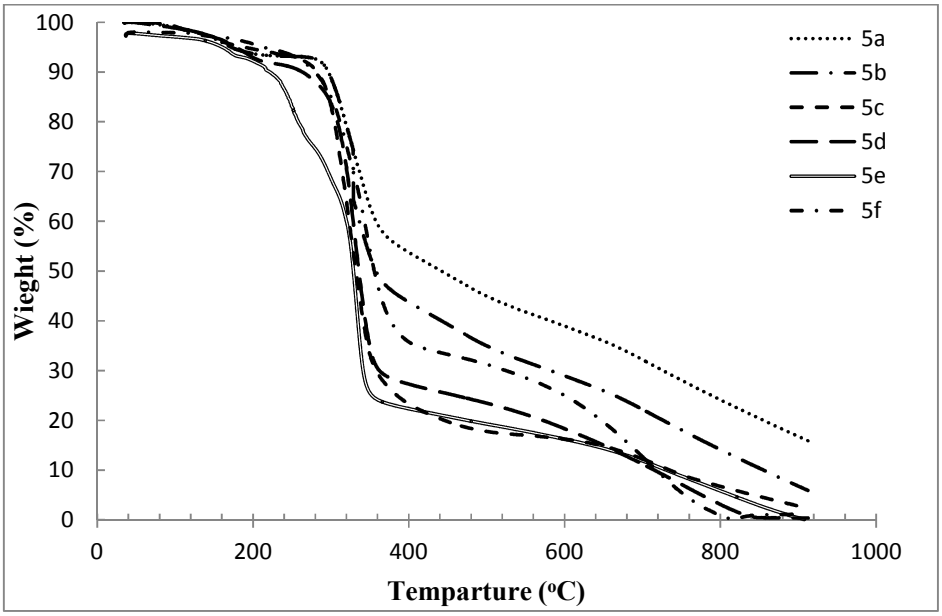


Figure 3: Ramped temperature TGA trace curves of imidazolium based geminal dicationic ILs.

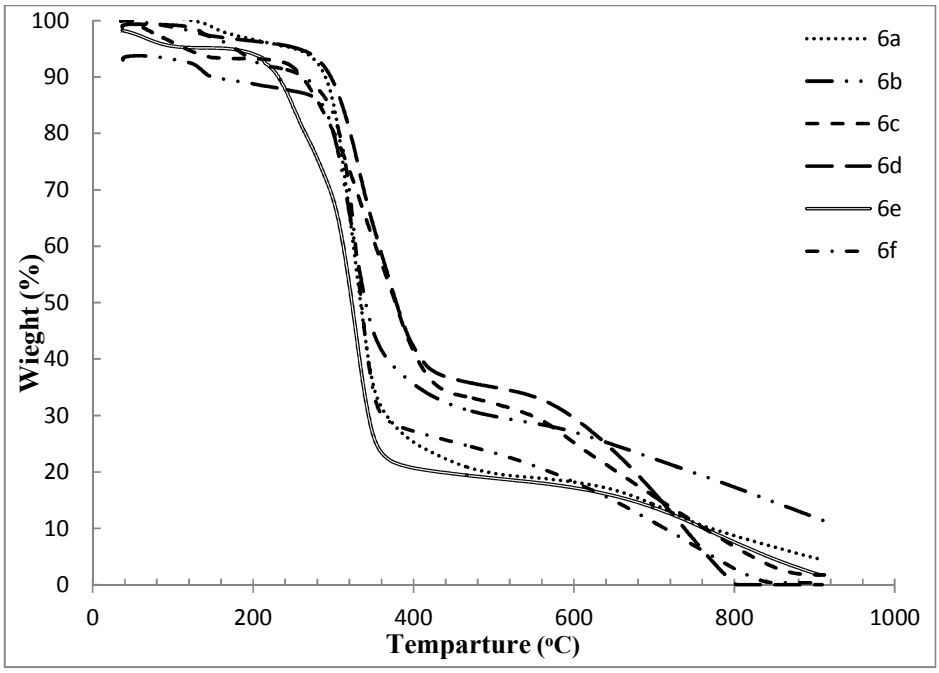


Figure 4: Ramped temperature TGA trace curves of benzimidazolium based geminal dicationic ILs.

Thermal stability of ILs does not strongly rely on the cations structure.[77,82,84] Since the prepared geminal dicationic ILs differ only in the cationic substituents of the active side groups on the imidazolium and benzimidazolium rings, minor differences are observed in the decomposition temperatures of these ILs. For example, based on TGA results, T_{onset} varies between 223°C–294°C for **6e** and **5c**, respectively, with approximate weight loss of 10–50%.

3. Experimental Section

3.1. General

Allyl bromide (99%), propargyl bromide solution (80% wt with toluene), chloroacetonitrile (99%), 2-bromoethanol (95%), ethyl bromoacetate (98%) and *tert*-butyl bromoacetate (98%) were purchased from Aldrich and used without further purification. All ILs were kept in fridge (5 °C) and freezer (–18 °C) for further evaluation of their properties. General grade solvents were purchased from commercial suppliers and used without further purification. The synthesis of compounds **2**, **3** and **4** were described and reported in previous work.[46] The IR spectra were obtained with a Perkin Elmer 400 Fourier Transform Infrared (FTIR) spectrometer. Both of ^{1}H and ^{13}C-NMR spectra were recorded on Jeol Lambda and ECA-DELTA as well as Bruker spectrometers at 400 MHz while ^{19}F-NMR was recorded using Bruker spectrometers 400 MHz. High-resolution mass spectra were recorded on Agilent Technologies 6530 Accurate Q-TOF LC–MS system, applying DMSO /MeOH eluents for ILs sample

compounds while Agilent 5975 system for EI/MS (Mass Spectra Service Centre of the National University of Singapore) for the rest of the compounds. Thermogravimetric analysis (TGA) measurements were performed using Perkin Elmer TGA4000 based on heating rate of 10 °C min^{-1} under nitrogen atmosphere. Thin layer chromatography was carried out on pre-coated silica gel plates (0.25 mm, 20 × 20 cm, 60F254, E. Merck).

3.4. Synthesis of **5a-f** *and* **6a-f**

***N*,*N*-bis[(3-allyl-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (5a)**

A solution of allyl bromide (2 g, 1.44 mL, 16.7 mmol) in acetonitrile anhydrous (5mL) was added drop-wise to a stirred solution of *N*,*N*-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) in acetonitrile anhydrous (15 mL) at room temperature under a nitrogen atmosphere. The reaction mixture was vigorously stirred for 3 h and refluxed at 50–55 °C for 2–3 days. The acetonitrile top layer was decanted and the IL was washed with diethyl ether (3 × 10 mL), then residual solvent was removed *in vacuo*. The product was dried at (40 °C, 0.01 mmHg) for 48 h to provide a viscous hygroscopic syrup in 95% yield (4.8 g). Molecular Formula: $C_{23}H_{31}Br_2N_5O_2S$; Mol. Wt.: 601.40; FTIR (cm^{-1}) 3,059 $(C\text{-}H)_{Ar}$, 2,977 $(C\text{-}H)_{Aliph}$, 1,644 $(C{=}N)_{Ar}$, 1,561, 1,493 $(C{=}C)_{Ar}$, 1,336, 1,156 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.43 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.94 (t, *J*=1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.75 (t, *J*=1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.65 (d, *J* = 8.05 Hz, 2H, $C\text{-}H_{Ar}$), 7.40 (d, *J* = 8.05 Hz, 2H, $C\text{-}H_{Ar}$), 6.08–5.98 (m, 2H, $C\text{-}H_{Allyl}$), 5.36 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(1a)Allyl}$), 5.34 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(1b)Allyl}$), 5.33 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(2a)Allyl}$), 5.29 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(2b)Allyl}$), 4.88 (d, *J*= 5.85 Hz, 4H, 2 × $(\alpha\text{-}CH_2)_{Allyl}$), 4.50 (t, *J* = 6.59 Hz, 4H, 2 × CH_2-N), 3.71 (t, *J* = 6.34 Hz, 4H, 2 × CH_2-N), 2.39 (s, 3H, $(CH_3)_{Ts}$)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.89 (C_{Ar}-S), 136.59 (2 × $CH_{Imidazole}$), 134.89 (C_{Ar}-CH_3), 131.58 (2 × $(CH)_{Allyl}$, 129.95 (2 × CH_{Ar}), 126.98 (2 × $CH_{Imidazole}$), 123.05 (2 × CH_{Ar}), 122.30 (2 × $CH_{Imidazole}$), 120.10 (2 × $(CH_2)_{Allyl}$, 50.80 (2 × $(\alpha\text{-}CH_2)_{Allyl}$), 47.90 (2 × CH_2-N), 47.12 (2 × CH_2-N_{Ar}), 20.97 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{23}H_{30}N_5O_2S^{3+}$: 440.2120, found: 440.2126.

***N*,*N*-bis[(3- propargyl-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (5b)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) and propargyl bromide solution 80% wt in toluene (4.96 g, 3.72 mL, 33.4 mmol) to provide a viscous hygroscopic syrup in 98% yield (4.9 g). Molecular Formula: $C_{23}H_{27}Br_2N_5O_2S$; Mol. Wt.: 597.37; FTIR (cm^{-1}) 3,051 $(C\text{-}H)_{Ar}$, 2,926, 2,850 $(C\text{-}H)_{Aliph}$, 2,125 (C≡C), 1,613$(C{=}N)_{Ar}$, 1,562, 1,486 $(C{=}C)_{Ar}$, 1,331, 1,154 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.40 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.89 (t, *J* = 1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.80 (t, *J* = 1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.63 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.40 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.23 (d,

J = 2.72 Hz, 4H, 2 × (α-CH_2)$_{Propargyl}$), 4.48 (t, J = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 3.88 (t, J= 2.72 Hz, 2H, (C-H)$_{Propargyl}$), 3.69 (t, J = 6.34 Hz, 4H, 2 × CH_2-N), 2.40 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 144.04 (C_{Ar}-S), 136.56 (2 × $CH_{Imidazole}$), 134.87 (C_{Ar}-CH_3), 130.01 (2 × CH_{Ar}), 127.02 (2 × $CH_{Imidazole}$), 123.33 (2 × CH_{Ar}), 122.18 (2 × $CH_{Imidazole}$), 79.21 (2 × $C_{Propargyl}$), 75.94 (2 × $CH_{Propargyl}$), 47.72 (2 × CH_2-N), 47.23 (2 × CH_2-N_{Ar}), 38.69 (2 × (α-CH_2)$_{Propargyl}$), 21.03 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{23}H_{25}N_5O_2S^{3+}$: 436.1807, found: 436.1810.

_N_,_N_-bis[(3-(cyanomethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide chloride (5c)

This compound was prepared analogously to **5a** using _N_,_N_-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) and chloroacetonitrile (1.25 g, 1.05 mL, 16.7 mmol) to provide a viscous hygroscopic liquid in 98% yield (4.2 g). Molecular Formula: $C_{21}H_{25}Cl_2N_7O_2S$; Mol. Wt.: 510.44; FTIR (cm^{-1}) 3,065 (C-H)$_{Ar}$, 2,978 (C-H)$_{Aliph}$, 2,238 (C≡N), 1,629, 1,596 (C=N)$_{Ar}$, 1,563, 1,493 (C=C)$_{Ar}$, 1,336, 1,155 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.88 (bt~s, 2H, C-$H_{Imidazole}$), 8.17 (t, J=1.83 Hz, 2H, C-$H_{Imidazole}$), 8.02 (t, J=1.83 Hz, 2H, C-$H_{Imidazole}$), 7.67 (d, J = 8.24 Hz, 2H, C-H_{Ar}), 7.39 (d, J = 8.24 Hz, 2H, C-H_{Ar}), 5.90 (s, 4H, 2 × (α-CH_2)), 4.61 (t, J = 6.10 Hz, 4H, 2 × CH_2-N_{Ar}), 3.71 (t, J= 6.10 Hz, 4H, 2 × CH_2-N), 2.38 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 144.03 (C_{Ar}-S), 137.90 (2 × $CH_{Imidazole}$), 134.56 (C_{Ar}-CH_3), 130.00 (2 × CH_{Ar}), 127.16 (2 × CH_{Ar}), 123.67 (2 × $CH_{Imidazole}$), 122.49 (2 × $CH_{Imidazole}$), 114.73 (2 × CN), 48.20 (2 × CH_2-N), 47.58 (2 × CH_2-N_{Ar}), 36.79 (2 × (α-CH_2)), 21.02 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Cl^-$ calcd. for $C_{21}H_{24}N_7O_2S^{3+}$: 438.1712, found: 438.1715.

_N_,_N_-bis[(3-(2-ethanolyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (5d)

This compound was prepared analogously to **5a** using _N_,_N_-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) and 2-bromoethanol (3.13 g, 1.77 mL, 25.1 mmol) to provide viscous hygroscopic liquid in 99% yield (5 g). Molecular Formula: $C_{21}H_{31}Br_2N_5O_4S$; Mol. Wt.: 609.37; FTIR (cm^{-1}) 3,288 (O-H), 3,139, 3,071 (C-H)$_{Ar}$, 2,954, 2,876 (C-H)$_{Aliph}$, 1,596 (C=N)$_{Ar}$, 1,562, 1,493 (C=C)$_{Ar}$, 1,335, 1,155 (O=S=O), 1,066 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.25 (bt~s, 2H, C-$H_{Imidazole}$), 7.80 (t, J=1.81 Hz, 2H, C-$H_{Imidazole}$), 7.69 (t, J=1.81 Hz, 2H, C-$H_{Imidazole}$), 7.63 (d, J = 8.15 Hz, 2H, C-H_{Ar}), 7.36 (d, J = 8.15 Hz, 2H, C-H_{Ar}), 5.16 (bs, 2H, 2 × O-H), 4.41 (t, J = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 4.19 (t, J= 4.98 Hz, 4H, 2 × (α-CH_2)), 3.69 (t, J= 4.98 Hz, 4H, 2 × C$\underline{H}_2$-OH), 3.64 (t, overlap, 4H, 2 × CH_2-N), 2.35 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 144.13 (C_{Ar}-S), 136.79 (2 × $CH_{Imidazole}$), 134.79 (C_{Ar}-CH_3), 130.11 (2 × CH_{Ar}), 127.17 (2 × CH_{Ar}), 122.75 (2 × $CH_{Imidazole}$), 122.67 (2 × $CH_{Imidazole}$), 59.37 (2 × $\underline{C}H_2$-OH), 51.76 (2 × (α-CH_2)), 48.04 (2 × CH_2-N), 47.16 (2 × CH_2-N_{Ar}), 21.11 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{21}H_{30}N_5O_4S^{3+}$: 448.2019, found: 448.2061.

***N*,*N*-bis[(3-(2-ethoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (5e)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) and ethyl bromoacetate (2.79 g, 1.86 mL, 16.7 mmol) to provide a white hygroscopic semi-solid in 96% yield (5.5 g). Molecular Formula: $C_{25}H_{35}Br_2N_5O_6S$; Mol. Wt.: 693.45; FTIR (cm^{-1}) 3,069 $(C\text{-}H)_{Ar}$, 2,982 $(C\text{-}H)_{Aliph}$, 1,742 (C=O), 1,627, 1,596 $(C{=}N)_{Ar}$, 1564 1,493, 1,449 $(C{=}C)_{Ar}$, 1,339 1,156 (O=S=O), 1,088 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.40 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.95 (t, J = 1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.80 (t, J = 1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.68 (d, J = 8.29 Hz, 2H, $C\text{-}H_{Ar}$), 7.41 (d, J = 8.05 Hz, 2H, $C\text{-}H_{Ar}$), 5.34 (s, 4H, 2 × (α-CH_2)), 4.53 (t, J = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 4.20 (q, J= 7.07 Hz, 4H, 2 × O-CH_2-), 3.67 (t, J = 6.34 Hz, 4H, 2 × CH_2-N), 2.40 (s, 3H, $(CH_3)_{Ts}$), 1.23 (t, J= 7.07 Hz, 6H, 2 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 166.69 (2 × C=O), 144.00 (C_{Ar}-S), 137.63 (2 × $CH_{Imidazole}$), 134.38 (C_{Ar}-CH_3), 129.98 (2 × CH_{Ar}), 127.16 (2 × $CH_{Imidazole}$), 123.65 (2 × CH_{Ar}), 122.55 (2 × $CH_{Imidazole}$), 61.86 (2 × $\underline{C}H_2$-O), 49.57 (2 × (α-CH_2)), 48.16 (2 × CH_2-N), 47.43 (2 × CH_2-N_{Ar}), 20.98 $(CH_3)_{Ts}$, 13.92 (2 × (CH_3)); HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{25}H_{34}N_5O_6S^{3+}$: 532.2230, found: 532.2234

***N*,*N*-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (5f)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(imidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **3**) (3 g, 8.35 mmol) and *tert*-butyl bromoacetate (3.26 g, 2.43 mL, 16.7 mmol) to provide a white hygroscopic semi-solid in 95% yield (5.9 g). Molecular Formula: $C_{29}H_{43}Br_2N_5O_6S$; Mol. Wt.: 749.55; FTIR (cm^{-1}) 3,063 $(C\text{-}H)_{Ar}$, 2,980 $(C\text{-}H)_{Aliph}$, 1,743 (C=O) 1,597 $(C{=}N)_{Ar}$, 1,566, 1,443 $(C{=}C)_{Ar}$, 1,364, 1,155 (O=S=O), 1,042 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.35 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.90 (t, J = 1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.76 (t, J = 1.71 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.68 (d, J = 8.29 Hz, 2H, $C\text{-}H_{Ar}$), 7.41 (d, J = 8.29 Hz, 2H, $C\text{-}H_{Ar}$), 5.22 (s, 4H, 2 × (α-CH_2)), 4.51 (t, J = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 3.66 (t, J = 6.34 Hz, 4H, 2 × CH_2-N), 2.40 (s, 3H, (-CH_3)$_{Ts}$), 1.45 (s, 18H, 6 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 165.71 (2 × C=O), 144.06 (C_{Ar}-S), 137.66 (2 × $CH_{Imidazole}$), 134.46 (C_{Ar}-CH_3), 130.02 (2 × CH_{Ar}), 127.18 (2 × CH_{Ar}), 123.70 (2 × $CH_{Imidazole}$), 122.49 (2 × $CH_{Imidazole}$), 83.06 (2 × C), 50.04 (2 × (α-CH_2)), 48.09 (2 × CH_2-N), 47.37 (2 × CH_2-N_{Ar}), 27.64 (6 × CH_3), 21.02 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{29}H_{42}N_5O_6S^{3+}$: 588.2856, found: 588.2913.

***N*,*N*-bis[(3-allyl-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (6a)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methyl-benzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and chloroacetonitrile 99% (2.11 g, 1.51 mL,

17.4 mmol) to provide a viscous hygroscopic liquid in 95% yield (5.8 g). Molecular Formula: $C_{31}H_{35}Br_2N_5O_2S$; Mol. Wt.: 701.51; FTIR (cm^{-1}): 3,133 3,027 $(C\text{-}H)_{Ar}$, 2,928 $(C\text{-}H)_{Aliph}$, 1,615, 1,596 $(C{=}N)_{Ar}$, 1,562, 1,485 $(C{=}C)_{Ar}$, 1,331, 1,154 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 10.09 (s, 2H, $C\text{-}H_{BImidazole}$), 8.15–8.13 (m, 2H, $C\text{-}H_{BImidazole}$), 8.00–7.96 (m, 2H, $C\text{-}H_{BImidazole}$), 7.71–7.65 (m, 4H, $CH_{BImidazole}$), 7.36 (d, *J* = 8.29 Hz, 2H, $C\text{-}H_{Ar}$), 7.11 (d, *J* = 8.29 Hz, 2H, $C\text{-}H_{Ar}$), 6.15–6.05 (m, 2H, $C\text{-}H_{Allyl}$), 5.47 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(1a)Allyl}$), 5.43 (d, *J*=1.22 Hz, 1H, $C\text{-}H_{(1b)Allyl}$), 5.40 (d, *J*=0.98 Hz, 1H, $C\text{-}H_{(2a)Allyl}$), 5.37 (d, *J*=0.98 Hz,1H, $C\text{-}H_{(2b)Allyl}$), 5.24 (d, *J*= 5.61 Hz, 4H, 2 × $(\alpha\text{-}CH_2)_{Allyl}$), 4.90 (t, *J* = 6.34 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 3.96 (t, *J* = 6.10 Hz, 4H, 2 × CH_2-N), 2.27 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.65 (C_{Ar}-S), 142.62 (2 × $CH_{BImidazole}$), 134.97 ($C_{Ar}\text{-}CH_3$), 131.16 (2 × $C_{BImidazole}$), 130.77 (2 × $(CH)_{Allyl}$, 130.75 (2 × $C_{BImidazole}$), 129.55 (2 × $CH_{BImidazole}$), 126.67 (2 × $CH_{BImidazole}$), 126.52 (2 × CH_{Ar}), 126.42 (2 × CH_{Ar}), 120.47 (2 × $(CH_2)_{Allyl}$), 113.82 (2 × $CH_{BImidazole}$), 113.60 (2 × $CH_{BImidazole}$), 48.74 (2 × $(\alpha\text{-}CH_2)_{Allyl}$), 46.19 (2 × CH_2-N), 44.82 (2 × $CH_2\text{-}N_{Ar}$), 20.95 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]–2Br^-$ calcd. for $C_{31}H_{34}N_5O_2S^{3+}$: 540.2433, found: 540.2470.

***N*,*N*-bis[(3-propargyl-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (6b)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methyl-benzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and propargyl bromide solution 80% wt in toluene (5.18 g, 3.88 mL, 33.8 mmol) to provide a viscous hygroscopic syrup 98% yield (6 g). Molecular Formula: $C_{31}H_{31}Br_2N_5O_2S$; Mol. Wt.: 697.48; FTIR (cm^{-1}): 3,152 $(C\text{-}H)_{Ar}$, 2,960 $(C\text{-}H)_{Aliph}$, 2,121 (C≡C), 1,613, 1,596 $(C{=}N)_{Ar}$, 1,562, 1,486 $(C{=}C)_{Ar}$, 1,331, 1,154 (O=S=O), 1,070 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 10.02 (s, 2H, $C\text{-}H_{BImidazole}$), 8.13–8.09 (m, 2H, $C\text{-}H_{BImidazole}$), 8.05–8.00 (m, 2H, $C\text{-}H_{BImidazole}$), 7.76–7.70 (m, 4H, $CH_{BImidazole}$), 7.34 (d, *J* = 8.15 Hz, 2H,$C\text{-}H_{Ar}$), 7.10 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.58 (d, *J* = 2.72 Hz, 4H, 2 × $(\alpha\text{-}CH_2)_{Propargyl}$), 4.87 (t, *J*= 5.89 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 3.95 (t, Overlap, 4H, 2 × CH_2-N), 3.91 (t, *J*= 2.27 Hz, 2H, $(C\text{-}H)_{Propargyl}$), 2.26 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.78 (C_{Ar}-S), 142.46 (2 × $CH_{BImidazole}$), 134.70 ($C_{Ar}\text{-}CH_3$), 131.18 (2 × $C_{BImidazole}$), 130.36 (2 × $C_{BImidazole}$), 129.61 (2 × CH_{Ar}), 126.99 (2 × CH_{Ar}), 126.85 (2 × $CH_{BImidazole}$), 126.45 (2 × $CH_{BImidazole}$), 113.76 (4 × $CH_{BImidazole}$), 79.43 (2 × $C_{Propargyl}$), 75.42 (2 × $CH_{Propargyl}$), 45.99 (2 × CH_2-N), 44.90 (2 × $CH_2\text{-}N_{Ar}$), 36.77 (2 × $(\alpha\text{-}CH_2)_{Propargyl}$), 20.99 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]–2Br^-$ calcd. for $C_{31}H_{30}N_5O_2S^{3+}$: 536.2120, found: 536.2048.

***N*,*N*-bis[(3-(cyanomethyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide chloride (6c)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methyl-benzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and chloroacetonitrile (1.3 g, 1.09 mL, 17.4

mmol) to provide a viscous hygroscopic syrup in 94% yield (5 g). Molecular Formula: $C_{29}H_{29}Cl_2N_7O_2S$; Mol. Wt.: 610.56; FTIR (cm^{-1}): 3,095, 3,050 $(C\text{-}H)_{Ar}$, 2,969 $(C\text{-}H)_{Aliph}$, 2,235 (C≡N), 1,614, 1,596 $(C{=}N)_{Ar}$, 1,563, 1,487 $(C{=}C)_{Ar}$, 1,329, 1,155 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 10.31 (s, 2H, $C\text{-}H_{BImidazole}$), 8.19–8.09 (m, 4H, $C\text{-}H_{BImidazole}$), 7.81–7.71 (m, 4H, $C\text{-}H_{BImidazole}$), 7.39 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.13 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 6.13 (s, 2H, $(\alpha\text{-}CH_2)$), 4.95 (t, *J*= 6.34 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 3.89 (t, *J*= 6.34 Hz, 4H, 2 × CH_2-N), 2.26 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.92 (C_{Ar}-S), 143.83 (2 × $CH_{BImidazole}$), 134.37 ($C_{Ar}\text{-}CH_3$), 130.95 (2 × $C_{BImidazole}$), 130.27 (2 × $C_{BImidazole}$), 129.66 (2 × CH_{Ar}), 127.32 (2 × CH_{Ar}), 127.24 (2 × $CH_{BImidazole}$), 126.66 (2 × $CH_{BImidazole}$), 114.17 (2 × $CH_{BImidazole}$), 114.05 (2 × $CH_{BImidazole}$), 113.34 (2 × CN), 46.51 (2 × CH_2-N), 45.35 (2 × $CH_2\text{-}N_{Ar}$), 34.88 (2 × $(\alpha\text{-}CH_2)$), 20.96 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Cl^-$ calcd. for $C_{29}H_{28}N_7O_2S^{3+}$: 538.2025, found: 538.2077.

_N_,_N_-bis[(3-(2-ethanolyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (6d)

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methyl-benzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and 2-bromoethanol (3.26 g, 1.84 mL, 26.1 mmol) to provide a viscous hygroscopic liquid in 98% yield (6 g). Molecular Formula: $C_{29}H_{35}Br_2N_5O_4S$; Mol. Wt.: 709.49; FTIR (cm^{-1}): 3,312 (O-H), 3,137, 3,027 $(C\text{-}H)_{Ar}$, 2,982 $(C\text{-}H)_{Aliph}$, 1,614, 1,596 $(C{=}N)_{Ar}$, 1,563, 1,485 $(C{=}C)_{Ar}$, 1,330, 1,154 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.85 (s, 2H, $C\text{-}H_{BImidazole}$), 8.09–8.05 (m, 4H, $C\text{-}H_{BImidazole}$), 7.71–7.66 (m, 4H, $C\text{-}H_{BImidazole}$), 7.34 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.08 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.22 (bs, 2H, 2 × O-H), 4.84 (t, *J*= 6.34 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 4.57 (t, *J*= 4.98 Hz, 4H, 2 × $(\alpha\text{-}CH_2)$), 3.90 (t, *J* = 6.34 Hz, 4H, 2 × CH_2-N), 3.83 (bt~s, 4H, 2 × $\underline{C}H_2$-OH), 2.27 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.76 (C_{Ar}-S), 142.81 (2 × $CH_{BImidazole}$), 134.72 ($C_{Ar}\text{-}CH_3$), 131.22 (2 × $C_{BImidazole}$), 131.02 (2 × $C_{BImidazole}$), 129.69 (2 × CH_{Ar}), 129.59 (2 × CH_{Ar}), 126.65 (2 × $CH_{BImidazole}$), 126.50 (2 × $CH_{BImidazole}$), 113.99 (2 × $CH_{BImidazole}$), 113.44 (2 × $CH_{BImidazole}$), 58.68 (2 × CH_2-OH), 49.48 (2 × $(\alpha\text{-}CH_2)$), 46.08 (2 × CH_2-N), 44.68 (2 × $CH_2\text{-}N_{Ar}$), 21.05 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{29}H_{34}N_5O_4S^{3+}$: 548.2332, found: 548.2394.

_N_,_N_-bis[(3-(2-ethoxy-2-oxoethyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (6e)

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methyl-benzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and ethyl bromoacetate (2.9 g, 1.93 mL, 17.4 mmol) to provide a viscous hygroscopic syrup in 98% yield (6.8 g). Molecular Formula:

$C_{33}H_{39}Br_2N_5O_4S$; Mol. Wt.: 793.57; FTIR (cm^{-1}): 3,059 $(C\text{-}H)_{Ar}$, 2,977 $(C\text{-}H)_{Aliph}$, 1,741 (C=O), 1,614, 1,596 $(C{=}N)_{Ar}$, 1,564 1,485, $(C{=}C)_{Ar}$, 1,339 1,155 (O=S=O), 1,088 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.98 (s, 2H, $C\text{-}H_{BImidazole}$), 8.13–8.10 (m, 2H, $C\text{-}H_{BImidazole}$), 8.06–8.03 (m, 2H, $C\text{-}H_{BImidazole}$), 7.73–7.68 (m, 4H, $CH_{BImidazole}$), 7.41 (d, J = 8.54 Hz, 2H, $C\text{-}H_{Ar}$), 7.12 (d, J = 8.24 Hz, 2H, $C\text{-}H_{Ar}$), 5.69 (s, 4H, 2 × (α-CH_2)), 4.91 (t, J= 6.10 Hz, 4H, 2 × CH_2-N_{Ar}), 4.22 (q, J= 7.23 Hz, 4H, 2 × O-CH_2-), 3.89 (t, J= 6.10 Hz, 4H, 2 × CH_2-N), 2.27 (s, 3H, -$(CH_3)_{Ts}$), 1.24 (t, J= 7.32 Hz, 6H, 2 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm : 166.51 (2 × C=O), 143.89 (C_{Ar}-S), 143.53 (2 × $CH_{BImidazole}$), 134.34 (C_{Ar}-CH_3), 131.33 (2 × $C_{BImidazole}$), 130.57 (2 × $C_{BImidazole}$), 129.64 (2 × CH_{Ar}), 126.90 (2 × CH_{Ar}), 126.85 (2 × $CH_{BImidazole}$), 126.69 (2 × $CH_{BImidazole}$), 113.95 (2 × $CH_{BImidazole}$), 113.65 (2 × $CH_{BImidazole}$), 62.08 (2 × $\underline{C}H_2$-O), 47.48 (2 × CH_2-N), 46.30 (2 × (α-CH_2)), 45.19 (2 × CH_2-N_{Ar}), 20.99 $(CH_3)_{Ts}$, 13.96 (CH_3) ; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{33}H_{38}N_5O_6S^{3+}$: 632.2543, found: 632.2601.

***N*,*N*-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide (6f)**

This compound was prepared analogously to **5a** using *N*,*N*-bis[(benzimidazol-1-yl)ethyl]-4-methylbenzenesulphonamide (compound **4**) (4 g, 8.7 mmol) and *tert*-butyl bromoacetate (3.4 g, 2.54 mL, 17.4 mmol) to provide a viscous hygroscopic syrup in 98% yield (7.25 g). Molecular Formula: $C_{37}H_{47}Br_2N_5O_6S$; Mol. Wt.: 849.67; FTIR (cm^{-1}): 3,065, $(C\text{-}H)_{Ar}$, 2,979 $(C\text{-}H)_{Aliph}$, 1,739 (C=O), 1,597 $(C{=}N)_{Ar}$, 1,564, 1,488 $(C{=}C)_{Ar}$, 1,364, 1,151 (O=S=O), 1,088 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.95 (s, 2H, $C\text{-}H_{BImidazole}$), 8.12–8.08 (m, 2H, $C\text{-}H_{BImidazole}$), 8.04–8.00 (m, 2H, $C\text{-}H_{BImidazole}$), 7.73–7.68 (m, 4H, $CH_{BImidazole}$), 7.41 (d, J = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.11 (d, J = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.58 (s, 4H, 2 × (α-CH_2)), 4.90 (t, J= 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 3.88 (t, J= 6.12 Hz, 4H, 2 × CH_2-N), 2.26 (s, 3H, (-CH_3)$_{Ts}$), 1.43 (s, 18H, 6 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 166.51 (2 × C=O), 143.97 (C_{Ar}-S), 143.53 (2 × $CH_{BImidazole}$), 134.42 (C_{Ar}-CH_3), 131.39 (2 × $C_{BImidazole}$), 130.60 (2 × $C_{BImidazole}$), 129.67 (2 × CH_{Ar}), 126.96 (2 × CH_{Ar}), 126.90 (2 × $CH_{BImidazole}$), 126.79 (2 × $CH_{BImidazole}$), 113.92 (2 × $CH_{BImidazole}$), 113.64 (2 × $CH_{BImidazole}$), 83.42 (2 × C), 47.97 (2 × (α-CH_2)), 46.31 (2 × CH_2-N), 45.15 (2 × CH_2-N_{Ar}), 27.66 (6 × CH_3), 21.06 $(CH_3)_{Ts}$; HRMS: m/z, $[M^{+2}–H]-2Br^-$ calcd. for $C_{37}H_{46}N_5O_6S^{3+}$: 688.3169, found: 688.3217.

3.5. Synthesis of **7d-f**, **8a**, **8d** *and* **8f**

***N*,*N*-bis[(3-(2-ethanolyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bis(trifluoromethylsulphonyl)amide (7d)**

A flask was charged with *N*,*N*-bis[(3-(2-ethanolyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide **5d** (0.6 g, 1.0 mmol) and de-ionized water (10 mL). Lithium bis-(trifluoromethanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) in de-ionized water (3 mL) was added in one portion and the suspension was stirred vigorously for 7 h at room temperature. The mixture was extracted with Ethyl acetate (3×5mL) after stirring for 1h each time. The combined organic layers were evaporated on the rotary evaporator and under high vacuum for 8 h to remove the solvent and provide a clear viscous hygroscopic liquid at room temperature in 83% yield (0.83 g). Molecular Formula: $C_{25}H_{31}F_{12}N_7O_{12}S_5$; Mol. Wt.: 1,009.85; FTIR (cm^{-1}) 3,280 (O-H), 3,131, 3,068 $(C\text{-}H)_{Ar}$, 2,958, 2,875 $(C\text{-}H)_{Aliph}$, 1,585 $(C{=}N)_{Ar}$, 1,548, 1,483 $(C{=}C)_{Ar}$, 1,342, 1,218 (C-F), 1,332, 1,151 (O=S=O), 1,075 (C-O), 1,060 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 8.98 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.78 (t, *J*=1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.67 (t, *J*=1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.61 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.35 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.15 (bs, 2H, 2 × O-H), 4.41 (t, *J* = 6.34 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 4.20 (t, *J*= 4.98 Hz, 4H, 2 × (α-CH_2)), 3.68 (t, *J*= 4.98 Hz, 4H, 2 × CH_2-OH), 3.62 (t, 4H, 2 × CH_2-N), 2.33 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 144.62 (C_{Ar}-S), 136.92 (2 × $CH_{Imidazole}$), 134.87 (C_{Ar}-CH_3), 130.35 (2 × CH_{Ar}), 129.12 (2 × CH_{Ar}), 124.44, 121.22, 118.00, 114.78 (q, *J*=322 Hz, CF_3), 122.33 (2 × $CH_{Imidazole}$), 121.97 (2 × $CH_{Imidazole}$), 59.31 (2 × $\underline{C}H_2$-OH), 51.90 (2 × (α-CH_2), 48.03 (2 × CH_2-N), 47.10 (2 × $CH_2\text{-}N_{Ar}$), 21.32 $(CH_3)_{Ts}$; ^{19}F (336, MHz) δ ppm: –80.12 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{21}H_{30}N_5O_4S^{3+}$: 448.2019, found: 448.2068; m/z, $[NTF_2]^-$calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9144.

***N*,*N*-bis[(3-(2-ethoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bis(trifluoromethylsulphonyl)amide (7e)**

This compound was prepared analogously to **7d** using *N*,*N*-bis[(3-(2-ethoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide **5e** (0.7 g, 1.0 mmole) and Lithium bis-(trifluoro- -methanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) to provide a clear viscous hygroscopic liquid at room temperature in 96% yield (1.15 g). Molecular Formula: $C_{29}H_{35}F_{12}N_7O_{14}S_5$; Mol. Wt.: 1,093.93; FTIR (cm^{-1}) 3,072 $(C\text{-}H)_{Ar}$, 2,990 $(C\text{-}H)_{Aliph}$, 1,748 (C=O), 1,626, 1,590 $(C{=}N)_{Ar}$, 1,560 1,495, 1,449 $(C{=}C)_{Ar}$, 1,352 1,156 (O=S=O), 1,344, 1,218 (C-F), 1,075 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.13 (bt~s, 2H, $C\text{-}H_{Imidazole}$), 7.76 (t, *J* = 1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.72 (t, *J* = 1.81 Hz, 2H, $C\text{-}H_{Imidazole}$), 7.65 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 7.42 (d, *J* = 8.15 Hz, 2H, $C\text{-}H_{Ar}$), 5.26 (s, 4H, 2 × (α-CH_2)), 4.42 (t, *J* = 6.34 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 4.22 (q, *J*= 7.25 Hz, 4H, 2 × O-CH_2-), 3.61 (t, *J* =

6.34 Hz, 4H, 2 × CH_2-N), 2.41 (s, 3H, $(CH_3)_{Ts}$), 1.25 (t, *J*= 7.25 Hz, 6H, 2 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 166.83 (2 × C=O), 144.18 (C_{Ar}-S), 137.66 (2 × $CH_{Imidazole}$), 134.47 (C_{Ar}-CH_3), 130.04 (2 × CH_{Ar}), 127.16 (2 × $CH_{Imidazole}$), 124.34, 121.10, 117.87, 114.63 (q, *J*=322 Hz, CF_3), 123.88 (2 × CH_{Ar}), 122.61 (2 × $CH_{Imidazole}$), 61.99 (2 × $\underline{C}H_2$-O), 49.62 (2 × (α-CH_2)), 48.14 (2 × CH_2-N), 47.46 (2 × CH_2-N_{Ar}), 21.00 $(CH_3)_{Ts}$, 13.96 (2 × $(CH_3)_{BEA}$); ^{19}F (336, MHz) δ ppm: –80.00 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{25}H_{34}N_5O_6S^{3+}$: 532.2230, found: 532.2252; m/z, $[NTF_2]^-$ calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9205.

***N*,*N*-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bis(trifluoromethylsulphonyl)amide (7f)**

This compound was prepared analogously to **7d** using *N*,*N*-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-imidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide **5f** (0.75 g, 1.0 mmole) and Lithium bis-(trifluo romethanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) to provide a clear viscous hygroscopic liquid at room temperature in 95% yield (1.1 g). Molecular Formula: $C_{33}H_{43}F_{12}N_7O_{14}S_5$; Mol. Wt.: 1,150.03; FTIR (cm^{-1}) 3,072 $(C-H)_{Ar}$, 2,979, 2,880 $(C-H)_{Aliph}$, 1,743 (C=O), 1,598 $(C=N)_{Ar}$, 1,560, 1,466 $(C=C)_{Ar}$, 1,360, 1,155 (O=S=O), 1,359, 1,218 (C-F), 1,056 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.14 (bt~s, 2H, C-$H_{Imidazole}$), 7.75 (t, *J* = 1.95 Hz, 2H, C-$H_{Imidazole}$), 7.70 (t, *J* = 1.91 Hz, 2H, C-$H_{Imidazole}$), 7.65 (d, *J* = 8.29 Hz, 2H, C-H_{Ar}), 7.41 (d, *J* = 8.29 Hz, 2H, C-H_{Ar}), 5.16 (s, 4H, 2 × (α-CH_2)), 4.42 (t, *J* = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 3.61 (t, *J* = 6.34 Hz, 4H, 2 × CH_2-N), 2.41 (s, 3H, $(-CH_3)_{Ts}$), 1.46 (s, 18H, 6 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 165.85 (2 × C=O), 144.22 (C_{Ar}-S), 137.68 (2 × $CH_{Imidazole}$), 134.55 (C_{Ar}-CH_3), 130.09 (2 × CH_{Ar}), 127.16 (2 × CH_{Ar}), 124.30, 121.08, 117.86, 114.64 (q, *J*=322 Hz, CF_3), 123.92 (2 × $CH_{Imidazole}$), 122.55 (2 × $CH_{Imidazole}$), 82.97 (2 × C_{TBE}), 50.51 (2 × (α-CH_2)), 48.08 (2 × CH_2-N), 47.41 (2 × CH_2-N_{Ar}), 26.94 (6 × CH_3), 20.96 $(CH_3)_{Ts}$; ^{19}F (336, MHz) δ ppm: –80.50 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{29}H_{42}N_5O_6S^{3+}$: 588.2856, found: 588.2919; m/z, $[NTF_2]^-$ calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9145.

***N*,*N*-bis[(3-allyl-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide-bis(trifluoromethylsulphonyl)amide (8a)**

This compound was prepared analogously to **7d** using *N*,*N*-bis[(3-allyl-benzimidazol-1-iumyl) ethyl]-4-methylbenzenesulphonamide bromide **6a** (0.7 g, 1.0 mmole) and Lithium bis-(trifluoromethanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) to provide a clear viscous hygroscopic liquid at room temperature in 90% yield (1 g). Molecular Formula: $C_{35}H_{35}F_{12}N_7O_{10}S_5$; Mol. Wt.: 1,101.99; FTIR (cm^{-1}): 3,142, 3,027 $(C-H)_{Ar}$, 2,928 $(C-H)_{Aliph}$, 1,615, 1,596 $(C=N)_{Ar}$, 1,562, 1,485 $(C=C)_{Ar}$, 1,342, 1,217 (C-F), 1,331, 1,154 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.74 (s, 2H, C-

$H_{BImidazole}$), 8.08–8.05 (m, 2H, C-$H_{BImidazole}$), 7.98–7.93 (m, 2H, C-$H_{BImidazole}$), 7.73–7.66 (m, 4H, $CH_{BImidazole}$), 7.31 (d, *J* = 7.70 Hz, 2H, C-H_{Ar}), 7.08 (d, *J* = 7.70 Hz, 2H, C-H_{Ar}), 6.12–6.02 (m, 2H, C-H_{Allyl}), 5.44 (d, *J*=1.36 Hz, 1H, C-$H_{(1a)Allyl}$), 5.42 (d, *J*=1.36 Hz, 1H, C-$H_{(1b)Allyl}$), 5.40 (d, *J*=1.36 Hz, 1H, C-$H_{(2a)Allyl}$), 5.38 (d, *J*=1.36 Hz, 1H, C-$H_{(2b)Allyl}$), 5.17 (d, *J*= 5.89 Hz, 4H, 2 × (α-CH_2)$_{Allyl}$), 4.78 (t, *J* = 6.34 Hz, 4H, 2 × CH_2-N_{Ar}), 3.91 (t, *J* = 6.80 Hz, 4H, 2 × CH_2-N), 2.26 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 143.87 (C_{Ar}-S), 142.64 (2 × $CH_{BImidazole}$), 134.93 (C_{Ar}-CH_3), 131.29 (2 × $C_{BImidazole}$), 130.93 (2 × $C_{BImidazole}$), 130.74 (2 × (CH)$_{Allyl}$, 129.63 (2 × $CH_{BImidazole}$), 126.85 (2 × $CH_{BImidazole}$), 126.74 (2 × CH_{Ar}), 126.42 (2 × CH_{Ar}), 124.35, 121.15, 117.95, 114.76 (q, *J*=322 Hz, CF_3), 120.60 (2 × $(CH_2)_{Allyl}$), 113.90 (2 × $CH_{BImidazole}$), 113.54 (2 × $CH_{BImidazole}$), 48.87 (2 × (α-CH_2)$_{Allyl}$), 46.08 (2 × CH_2-N), 44.72 (2 × CH_2-N_{Ar}), 20.98 $(CH_3)_{Ts}$; ^{19}F (336, MHz) δ ppm: –80.05 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{31}H_{34}N_5O_2S^{3+}$: 540.2433, found: 540.2426; m/z, $[NTF_2]^-$calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9138.

***N*,*N*-bis[(3-(2-ethanolyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide-bis(trifluoromethylsulphonyl)amide (8d)**

This compound was prepared analogously to **7d** using *N*,*N*-bis[(3-(2-ethanolyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide **6d** (0.71 g, 1.0 mmole) and Lithium bis-(trifluoro methanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) to provide a clear viscous hygroscopic liquid at room temperature in 87% yield (0.97 g). Molecular Formula: $C_{33}H_{35}F_{12}N_7O_{12}S_5$; Mol. Wt.: 1,109.98; FTIR (cm^{-1}): 3,312 (O-H), 3,137, 3,027 (C-H)$_{Ar}$, 2,982 (C-H)$_{Aliph}$, 1,614, 1,596 (C=N)$_{Ar}$, 1,563, 1,485 (C=C)$_{Ar}$, 1,344, 1,221 (C-F), 1,330, 1,154 (O=S=O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.72 (s, 2H, C-$H_{BImidazole}$), 8.07–8.01 (m, 4H, C-$H_{BImidazole}$), 7.73–7.67 (m, 4H, C-$H_{BImidazole}$), 7.33 (d, *J* = 8.31 Hz, 2H, C-H_{Ar}), 7.08 (d, *J* = 8.07 Hz, 2H, C-H_{Ar}), 5.20 (bs, 2H, 2 × O-H), 4.79 (t, *J*= 6.11 Hz, 4H, 2 × CH_2-N_{Ar}), 4.56 (t, *J*= 4.98 Hz, 4H, 2 × (α-CH_2)), 3.88 (t, *J* = 6.11 Hz, 4H, 2 × CH_2-N), 3.84 (t, *J*= 4.98 Hz, 4H, 2 × CH_2-OH), 2.27 (s, 3H, $(CH_3)_{Ts}$); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm : 143.82 (C_{Ar}-S), 142.83 (2 × $CH_{BImidazole}$), 134.74 (C_{Ar}-CH_3), 131.21 (2 × $C_{BImidazole}$), 131.05 (2 × $C_{BImidazole}$), 129.92 (2 × CH_{Ar}), 129.57 (2 × CH_{Ar}), 126.67 (2 × $CH_{BImidazole}$), 126.48 (2 × $CH_{BImidazole}$), 124.33, 121.13, 117.93, 114.73 (q, *J*=322 Hz, CF_3), 113.95 (2 × $CH_{BImidazole}$), 113.37 (2 × $CH_{BImidazole}$), 58.62 (2 × $\underline{C}H_2$-OH), 49.48 (2 × (α-CH_2)), 46.08 (2 × CH_2-N), 44.60 (2 × CH_2-N_{Ar}), 20.96 $(CH_3)_{Ts}$; ^{19}F (336, MHz) δ ppm: –80.20 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{29}H_{34}N_5O_4S^{3+}$: 548.2332, found: 548.2290; m/z, $[NTF_2]^-$calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9218.

_N_,_N_-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphon-amide bis(trifluoromethylsulphonyl)amide (8f)

This compound was prepared analogously to **7d** using *N*,*N*-bis[(3-(2-*tert*-butoxy-2-oxoethyl)-benzimidazol-1-iumyl)ethyl]-4-methylbenzenesulphonamide bromide **6f** (0.85 g, 1.0 mmole) and Lithium bis-(trifluoro methanesulphonyl)imide $LiNTf_2$ (0.72 g, 2.5 mmol) to provide a clear viscous hygroscopic liquid at room temperature in 97% yield (1.2 g). Molecular Formula: $C_{41}H_{47}F_{12}N_7O_{14}S_5$; Mol. Wt.: 1,250.16; FTIR (cm^{-1}): 3,065, $(C\text{-}H)_{Ar}$, 2,979 $(C\text{-}H)_{Aliph}$, 1,739 (C=O), 1,597 $(C{=}N)_{Ar}$, 1,564, 1,488 $(C{=}C)_{Ar}$, 1,364, 1,151 (O=S=O), 1,354, 1,222 (C-F), 1,088 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 9.76 (s, 2H, $C\text{-}H_{BImidazole}$), 8.05–8.00 (m, 4H, $C\text{-}H_{BImidazole}$), 7.72–7.67 (m, 4H, $C\text{-}H_{BImidazole}$), 7.39 (d, *J* = 8.07 Hz, 2H, $C\text{-}H_{Ar}$), 7.11 (d, *J* = 8.07 Hz, 2H, $C\text{-}H_{Ar}$), 5.51 (s, 4H, 2 × $(\alpha\text{-}CH_2)_{TBE}$), 4.82 (t, *J*= 6.11 Hz, 4H, 2 × $CH_2\text{-}N_{Ar}$), 3.85 (t, *J*= 6.11 Hz, 4H, 2 × CH_2-N), 2.27 (s, 3H, $(\text{-}CH_3)_{Ts}$), 1.89 (s, 18H, 6 × (-CH_3)); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm : 167.97 (2 × C=O), 144.08 (C_{Ar}-S), 143.57 (2 × $CH_{BImidazole}$), 134.41 ($C_{Ar}\text{-}CH_3$), 131.50 (2 × $C_{BImidazole}$), 130.63 (2 × $C_{BImidazole}$), 129.73 (2 × CH_{Ar}), 127.04 (2 × CH_{Ar}), 126.93 (2 × $CH_{BImidazole}$), 126.73 (2 × $CH_{BImidazole}$), 124.24, 121.18, 117.95, 114.71 (q, *J*=322, CF_3), 113.99 (2 × $CH_{BImidazole}$), 113.54 (2 × $CH_{BImidazole}$), 83.57 (2 × C), 47.58 (2 × ($\alpha\text{-}CH_2$)), 46.29 (2 × CH_2-N), 45.09 (2 × $CH_2\text{-}N_{Ar}$), 27.25 (6 × CH_3), 21.12 $(CH_3)_{Ts}$; ^{19}F (336, MHz) δ ppm: –80.09 (CF_3); HRMS: m/z, $[M^{+2}–H]–2NTF_2^-$ calcd. for $C_{37}H_{46}N_5O_6S^{3+}$: 688.3169, found: 688.3222; m/z, $[NTF_2]^-$ calcd. for $C_2F_6NO_4S_2^-$: 279.9173, found: 279.9180.

Antibacterial Evaluation

Ten standard strains of Gram positive and negative bacteria were used to evaluate the antibacterial activities of the synthesized ILs compounds; **5a**–**f** and **6a**–**f**. Based on CLSI guidelines[85], the activities were assessed in terms of minimum inhibitory concentrations (MICs) using microbroth dilution assays. The MIC's values are given in mg/mL and defined as a lowest concentration that inhibits the bacterial strains growth. Gram positive bacteria included: *Streptococcus pyogenes* ATCC19615, *Staphylococcus aureus* ATCC 29213, *Bacillus subtilis* ATCC6051, *Rodococcus Ruber* ATCC27863, *Enterococcus faecalis* ATCC 29212, *Staphylococcus epidermidis* ATCC12228, while Gram negative bacteria included*: Escherichia coli* ATCC10538, *Salmonella typhimurium* ATCC14028, *Pseudomonas aeruginosa* ATCC15442, *Acinetobacter calcoaceticus* ATCC 23055. These standards strains were obtained from the collection of Biosciences and Biotechnology School, Faculty of Science and Technology, University Kebangsaan, Malaysia.

Distilled water was used as negative control to dissolve all the tested ILs in concentrations range of 0.05– 0.5 mg/mL, while, commercial antibiotics amoxicillin and kanamycin were used as a positive control in the same range of concentrations. A loopful of bacterial cells from the nutrient agar plates of

stock cultures was inoculated into 100 mL nutrient broth of 250 mL side arm Erlenmeyer flask. They were incubated at 37 °C for 16 h with vigorous shaking. After incubation, the culture was diluted with fresh media to produce an O.D 600 nm of 0.1. Fifty µL of standardized 18 h incubated bacterial culture were introduced into test tubes containing 5 mL media, followed by adding various concentrations of the tested ILs. All assays were performed in triplicate

Thermal stability

Thermal stability in the term of decomposition temperatures of the synthesized halogen ILs was evaluated using thermogravimetric analyser (TGA Perkin Elmer TGA4000, with Pyris 9.1 software). For thermogravimetry measurements, an open alumina crucible of up to 10 mg weight samples placed on a sample pan with 20 $ml \cdot min^{-1}$ flow-rate of high pure nitrogen at ambient temperature. Consequently, the samples were heated from 35 to 900 °C, at heating rate of 10 °C min^{-1} and the weight change was recorded as a function of the heating temperature. The decomposition temperatures are stated in terms of T_{start} (the temperature at which the decomposition of the sample starts), $T_{10\%}$ and $T_{50\%}$ (the temperatures at which a mass loss of 10% and 50%, respectively, is reached), T_{peak} (the maximum temperature derivative of the weight change with respect to time), as well as T_{onset} (the intersection of the zero mass loss baseline and the tangent line through T_{peak}).

4. Conclusions

Novel sets of halogen and NTF_2 di-imidazolium and di-benzimidazolium ILs containing high rigid spacer incorporated into benzenesulfonamide moiety and various active side substituents were successfully prepared. The structures of these di-cationic ILs were confirmed by classical FTIR, NMR, and HRMS techniques. Metathesis of halogen anion to NTf_2 was tuned all ILs to clear liquids at room temperature in excellent yield and purity. Both imidazolium and benzimidazolium series of halogen anions were evaluated for thermal stability as well as *in vitro* antibacterial activities against ten strains of bacteria. The miscibility of the prepared ILs in both water and common organic solvents are indicated as well. ILs with acetonitrile substituents (*i.e.* **5c** and **6c**) on imidazolium rings displayed the highest bioactivity and the onset decomposition temperature among the studied dicationic ILs. However, most of these ILs demonstrated significant activities against both Gram-positive and Gram-negative bacteria comparing to commercial antibiotic; amoxicillin and kanamycin beside high thermal stability. Generally, ILs bearing imidazolium dications exhibited higher results of antibacterial and thermal stability as compared to those with benzimidazolium. Surface properties including critical micelle concentration CMC, surface tension γ_{cmc}, Krafft temperature and Cloud point as well as more

physical properties of the synthesized geminal dicationic ILs (*e.g.*, viscosity and fluorescence) will be reported in due course.

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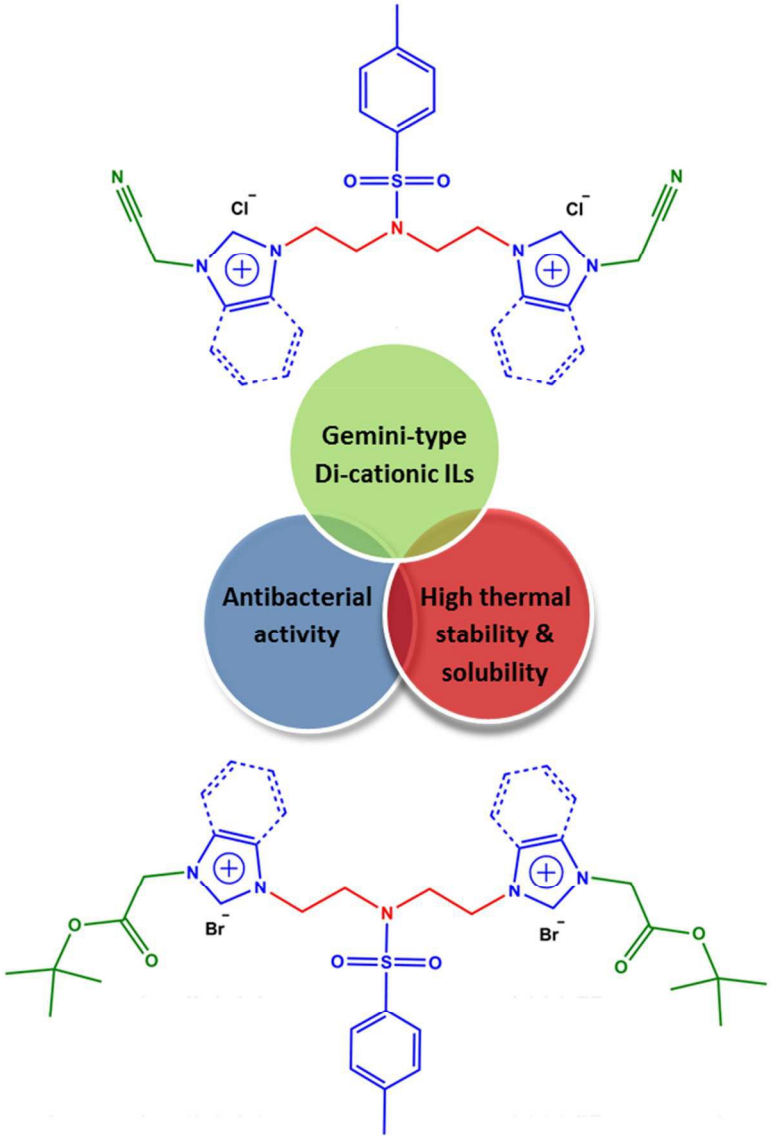
Bis-imidazolium and benzimidazolium based gemini-type ionic liquids structure: synthesis and antibacterial evaluation



The incorporated benzenesulfonamide moiety and the active side substituents into di-imidazolium and benzimidazolium cations enhanced both antibacterial activity and miscibility for the synthesized gimini type ILs.