

# Synthesis, Characterization and Larvicidal Activity of Nitrile-functionalized Dinuclear Silver(I)-*N*-heterocyclic Carbene Complexes

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A series of aromatic nitrile functionalized imidazolium salts has been synthesized by the successive *N*-alkylation method. Subsequently, silver(I) complexes incorporated with *N*-heterocyclic carbene (NHC) ligands have been synthesized by the treatment of imidazolium salts with Ag<sub>2</sub>O at mild reaction conditions. Both salts and Ag(I)-NHC complexes have been characterized by <sup>1</sup>H and <sup>13</sup>C NMR, FTIR spectroscopy and elemental analysis techniques. The molecular structure of salt **2** was elucidated through single crystal -XRD analyses. The larvicidal studies against *Aedes aegypti* and *Culex quinquefasciatus*, show that complex **6** has the highest larval mortality with LC<sub>50</sub> of 27.90 and 30.27 ppm, respectively, compared to the synthesized complexes **4** and **5**. Meanwhile, all the NHC salts proved to be inactive biological activities compared with their respective complexes, indicating the utility of silver (I) ions in larvicidal applications.

**Key words:** Imidazole; Carbene; Silver; *Ae-aegypti*; *Culex quinquefasciatus*

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The chemistry of imidazole-2-ylidene is centred on the vacancy of a lone pair of electrons on a carbene carbon atom, and the reactions with electropositive metal ions possibly forming a new bond [1]. Imidazole-2-ylidene compounds have a main structural difference from their phosphine analogues, and thus their physical and chemical activities. Due to the fact that this ligand act as good *s* donors and generally weak *p* acceptors, they can produce stable metal–NHC complexes with strong metal–carbon bonds [2].

Nitrile-functionalized NHCs are possible bidentate ligands, which can give rise to carbene complexes with increased stability through ligand chelation. Their reactivity towards Ag(I) is interesting and also vital, especially on the mode of chelation [3, 4]. Further, nitrile functionalized NHC ligands displayed interesting coordination behaviour yielding NHC and nitrile coordinated Ag(I) complexes. On top of that, these nitrile-functionalized Ag complexes can be controlled by varying the metal to NHC ratio [5]. Numerous Ag(I)-NHC complexes showed spectacular supramolecular arrangements having interacted with different counter ions or solvent molecules. The field of nitrile-functionalized NHC chemistry is currently attracted significant interest and largely used in catalysis [6, 7] and medicinal organometallic

chemistry [8, 9].

The present nitrile-functionalized imidazolium salts are specifically designed to link the two metal centres. In the present paper, three different nitrile-functionalized silver(I)–NHC complexes have been prepared, methodically characterized and studied for their potential as larvicidal activities.

## EXPERIMENTAL

### 1. Measurement and Reagents

Chemicals and solvents were used as received. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at room temperature on Bruker 500 MHz Ultrashield TM. The Fourier-transform infrared spectroscopy (FT-IR) spectra of the compounds were obtained in potassium bromide disks using a Perkin Elmer 2000 system spectrometer in the range of 4000-4000 cm<sup>-1</sup>. The melting points were collected by using a Stuart Scientific SMP-1 (UK) instrument. CHN microanalysis was analysed using Perkin Elmer 2400 LS Series CHN/S analyser. Conductivity measurement was conducted with a Jenway 470 conductivity/TDS meter, with conductivity resolution of 0.01 μS–1 mS and accuracy of ±0.5% ± 2 digits.

## 2. Synthesis of N-substituted bis-imidazolium Salts (1-3)

### 2.1. Synthesis of 3,3'-(1,2-phenylenebis(methylene)) bis(1-cyclopentylimidazolium)bis(hexafluorophosphate) (1)

To a solution of 1,2-dibromomethyl benzene (0.48 g, 1.83 mmol) in 10 mL of 1,4 dioxane, 4-methylbenzo nitrile imidazole (1.00 g, 5.43 mmol) in 10 mL of 1,4 dioxane was added in a round bottom flask. The solution mixture was then stirred at reflux for 24 h. The obtained imidazolium bromide salt was filtered, washed with fresh dioxane and air dried. To a solution of obtained bromide salt in methanol, a solution of  $\text{KPF}_6$  (0.64 g, 3.5 mmol) in methanol/water of about 10 mL was added and stirred for 4h at room temperature. The white solid separated out was suction filtered and washed with distilled water to eliminate excess  $\text{KPF}_6$  and air dried to afford hexafluorophosphate salt **1** as stable white solid. Yield: 2.54 g (94.5 %); MP: 219-221 °C; Anal. Cal. of  $\text{C}_{30}\text{H}_{26}\text{N}_6\text{F}_{12}\text{P}_2$ : C, 47.25; H, 3.70; N, 11.02%. Found: C, 47.52; H, 3.57; N, 10.92%; **FT-IR** (KBr,  $\text{cm}^{-1}$ ): 3166, 3122, (C-H<sub>aliph</sub>), 2223 (C<sub>aliph</sub>≡N), 1569, 1170 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz,  $d_6$ -DMSO):  $\delta$  5.54 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.58 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>), 7.54 (16H, m, Ar H), 9.29 (2H, s, NCHN); **<sup>13</sup>C NMR** (125 MHz,  $d_6$ -DMSO): 49.1 (N<sub>imid</sub>-C-Ar), 52.03 (N<sub>imid</sub>-C-N<sub>imid</sub>), 122.1 (imid C), 118.9 (C-CN), 123.6 (C-N), 128.6, 129.6, 129.75, 130.3, 133.1, 137.5 (Ar -C), 140.4 (N<sub>imid</sub>-C-N<sub>imid</sub>).

### 2.2. Synthesis of 3,3'-(1,3-phenylenebis(methylene)) bis(1-cyclopentylimidazolium)bis-hexafluorophosphate (2)

Compound **2** was prepared in a manner analogous to that resulting **1**, but using 1,3-dibromomethyl benzene (0.72 g, 2.72 mmol) instead of 1,2-dibromomethyl benzene. Salt **2** was collected as white powder. Colourless crystals of **2** were obtained by re-crystallization from acetonitrile. Yield: 2.24 g (90.4 %); MP: 178-180 °C; Anal. Cal. of  $\text{C}_{30}\text{H}_{26}\text{N}_6\text{F}_{12}\text{P}_2 \cdot 6\text{H}_2\text{O}$ : C, 41.35; H, 4.36; N, 9.65%. Found: C, 41.48; H, 4.57; N, 9.35%; **FT-IR** (KBr,  $\text{cm}^{-1}$ ): 3147, 3085, (C-H<sub>aliph</sub>), 2236 (C<sub>aliph</sub>≡N), 1565, 1163 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz,  $d_6$ -DMSO):  $\delta$  5.45 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.55 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>), 7.60 (16H, m, Ar H), 9.36 (2H, s, NCHN); **<sup>13</sup>C NMR** (125 MHz,  $d_6$ -DMSO): 51.5, 51.7 (N<sub>imid</sub>-C-Ar), 51.9 (N<sub>imid</sub>-C-N<sub>imid</sub>), 111.6 (imid C), 118.4 (C-CN), 123.0 (C-N), 128.1, 128.5, 128.7, 129.0, 129.9, 132.9, 135.2, 136.7 (Ar -C), 139.9 (N<sub>imid</sub>-C-N<sub>imid</sub>).

### 2.3. Synthesis of 3,3'-(1,4-phenylenebis(methylene)) bis(1-cyclopentylimidazolium)bis-hexafluorophosphate (3)

Compound **3** was prepared in a manner analogous to

that resulting **1**, but using 1,4-dibromomethyl benzene (0.72 g, 2.72 mmol) instead of 1,2-dibromomethyl benzene. Yield: 2.34 g (93.4 %); MP: 176-179 °C; Anal. Cal. of  $\text{C}_{30}\text{H}_{26}\text{N}_6\text{F}_{12}\text{P}_2$ : C, 47.25; H, 3.70; N, 11.02%. Found: C, 46.96; H, 3.65; N, 11.17%; **FT-IR** (KBr,  $\text{cm}^{-1}$ ): 3173, 3121, (C-H<sub>aliph</sub>), 2236 (C<sub>aliph</sub>≡N), 1569, 1165 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz,  $d_6$ -DMSO):  $\delta$  5.45 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.55 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>), 7.82 (16H, m, Ar H), 9.39 (2H, s, NCHN); **<sup>13</sup>C NMR** (125 MHz,  $d_6$ -DMSO): 51.5 (N<sub>imid</sub>-C-Ar), 51.7 (N<sub>imid</sub>-C-N<sub>imid</sub>), 111.6 (imid C), 118.4 (C-CN), 123.0 (C-N), 127.6, 128.1, 128.8, 129.1, 132.7, 135.2, 136.7 (Ar -C), 139.9 (N<sub>imid</sub>-C-N<sub>imid</sub>).

## 3. Synthesis of Silver Complexes (4-6)

### 3.1. Synthesis of 3,3'-(1,2-phenylenebis(methylene)) bis(1-cyclopentylimidazolium) disilver (I) bis (hexafluorophosphate) (4)

To a solution of imidazolium bromide salt (0.50 g, 0.79 mmol) in 10 mL methanol, silver(I) oxide (0.36 g, 1.58 mmol) was added, and the mixture was stirred in dark for 2 days. Then, the reaction mixture was filtered through a Celite bed to remove unreacted silver oxide and the filtrate was collected. The filtrate was stirred with  $\text{KPF}_6$  (0.29 g, 1.58 mmol) in methanol (20 mL), which facilitate the formation of **4** as white powder. The product was filtered, washed with distilled water and dried under vacuum. Yield: 0.67 g (63.5%); MP: 178-181 °C; Anal. Cal. of  $\text{C}_{60}\text{H}_{52}\text{Ag}_2\text{F}_{12}\text{N}_{12}\text{P}_2$ : C, 49.81; H, 3.62; N, 11.62%. Found: C, 49.88; H, 3.39; N, 11.39%; **FT-IR** (KBr,  $\text{cm}^{-1}$ ): 3182, 3156, (C-H<sub>aliph</sub>), 2225 (C<sub>aliph</sub>≡N), 1598, 1170 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz,  $d_3$ -CH<sub>3</sub>CN):  $\delta$  5.21 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.61 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-N<sub>imid</sub>), 7.63 (16H, m, Ar H); **<sup>13</sup>C NMR** (125 MHz,  $d_3$ -CH<sub>3</sub>CN): 52.2 (CH<sub>2</sub>-methylbenzyl), 64.2 (CH<sub>2</sub>-benzonitrile), 118.0 (nitrile-C≡N), 118.6, 122.4 (imid C), 128.9, 129.1, 134.4 (Ar C), 179.4, 179.5, 180.5, 181.1 (NCAgN).

### 3.2. Synthesis of 3,3'-(1,3-phenylenebis(methylene)) bis(1-cyclopentylimidazolium) disilver (I) bis (hexafluorophosphate) (5)

Complex **5** was prepared in a manner analogous to that resulting **4**, but using compound **2** (0.50 g, 0.79 mmol) instead of **1**. The product of **5** was collected as thick-brownish liquid. Yield: 0.65 g (68.4 %); MP: 205-207 °C; Anal. Cal. of  $\text{C}_{60}\text{H}_{52}\text{Ag}_2\text{F}_{12}\text{N}_{12}\text{P}_2$ : C, 49.81; H, 3.62; N, 11.62%. Found: C, 49.88; H, 3.29; N, 11.79%; **FT-IR** (KBr,  $\text{cm}^{-1}$ ): 3172, 3145, (C-H<sub>aliph</sub>), 2231 (C<sub>aliph</sub>≡N), 1584, 1235 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz,  $d_3$ -CH<sub>3</sub>CN):  $\delta$  5.11 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.41 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-N<sub>imid</sub>), 7.54 (16H, m, Ar H); **<sup>13</sup>C NMR** (125 MHz,  $d_3$ -CH<sub>3</sub>CN): 52.7 (CH<sub>2</sub>-methyl benzyl), 54.1 (CH<sub>2</sub>-benzonitrile), 118.9 (nitrile-C≡N), 123.4, 126.4, 127.5, 128.4, 131.9 (Ar C), 180.9, 181.9 (NCAgN).

3.3. *Synthesis of 3,3'-[1,4-phenylenebis(methylene)] bis(1-cylopentylimidazolium) disilver (I) bis(hexafluorophosphate) (6)*

Complex **6** was prepared in a manner analogous to that resulting **4**, but using compound **3** (0.50 g, 0.79 mmol) instead of **1**. Yield: 0.80 g (68.4 %); MP: 170–173 °C; Anal. Cal. of C<sub>60</sub>H<sub>52</sub>Ag<sub>2</sub>F<sub>12</sub>N<sub>12</sub>P<sub>2</sub>: C, 49.81; H, 3.62; N, 11.62%. Found: C, 49.90; H, 3.76; N, 11.50%; **FT-IR** (KBr, cm<sup>-1</sup>): 3162, 3109, (C–H<sub>aliph</sub>), 2225 (C<sub>aliph</sub>≡N), 1632, 1125 (C<sub>arom</sub>=N<sub>imid</sub>); **<sup>1</sup>H NMR** (500 MHz, d<sub>3</sub>-CH<sub>3</sub>CN): δ 5.14 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-Ar), 5.33 (4H, s, N<sub>imid</sub>-CH<sub>2</sub>-N<sub>imid</sub>), 7.29 (16H, m, Ar H); **<sup>13</sup>C NMR** (125 MHz, d<sub>3</sub>-CH<sub>3</sub>CN): 53.9 (CH<sub>2</sub>-methyl benzyl), 54.3 (CH<sub>2</sub>-benzo nitrile), 118.9 (nitrile-C≡N), 127.6, 128.1, 128.8, 129.1, 132.7, 135.2, 136.7 (Ar–C), 180.2, 181.6 (N<sub>imid</sub>-C–N<sub>imid</sub>).

#### 4. Single Crystal Analysis

Single crystal X-ray diffraction data for **2** were collected on APEXII Duo CCD area-detector diffractometer operating at 50 kV and 30 mA using Mo K $\alpha$  radiation ( $\lambda = 0.71073$ ) at 297 K. Data collection and reduction were performed using the APEX2 and SAINT software. The SADABS software was used for absorption correction. Solution was obtained by direct methods using SHELXS 97 followed by successive refinements using full matrix least squares method against F<sup>2</sup> using SHELXL 97 [10]. The program X-Seed was used as a graphical SHELXL interface [11]. The crystal data and structure refinement details for the three compounds are shown in Table 1.

**Table 1.** Crystal data and structure refinement detail for carbene precursor **2**.

	<b>2</b>
Formula	C <sub>30</sub> H <sub>26</sub> N <sub>6</sub> F <sub>12</sub> P <sub>2</sub>
Formula weight	760.51
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	
a (Å)	9.7022(6)
b (Å)	12.2899(7)
c (Å)	16.0678(10)
$\alpha$ (o)	97.606
$\beta$ (o)	104.653(3)
$\gamma$ (o)	110.806(2)
V (Å <sup>3</sup> )	1679.60(18)
Z	2
Density (calcd) (gm/cm <sup>3</sup> )	1.504
F(000)	772
Crystal size (mm)	0.40 x 0.35 x 0.20
Temperature (K)	296
Radiation (Å)	MoKa
$\theta$ Min, max (o)	2.2-26.0
Dataset	-13: 13; -17: 17; -22: 22
Tot.; Uniq. Data (int)	66401, 9970, 0.084
R (int)	1.36
Nref, Npar	9970, 452
R, wR <sub>2</sub> , S	0.0523, 0.1747, 1.05

## 5. Larvicidal Bioassay

Larvicidal bioassay was performed based on a World Health Organization's method [12] with minor modifications, using 20 late 3<sup>rd</sup> instar larvae of *Ae-aegypti* and *Cx quinquefasciatus*. The larvae were exposed to a wide range of test concentrations and a control for 24 h to find out the activity range of the salts and complexes. After determining the mortality of larvae in this wide range of concentrations, a narrower range (5, 10, 25, 100 and 200 ppm), yielding between 0 and 100 % mortality after 24 h of exposure was selected as test concentration for the bioassay. Three replicates were set for each concentration and the control. As in the preliminary study, 20 late 3<sup>rd</sup> instar larvae were exposed to each concentration and control. The setup was maintained at (28±2) °C and 70-85 % relative humidity for 24 h and the number of dead larvae was recorded. The data were subjected to log-probit analysis for calculating LC<sub>50</sub> with 95% confidence limit using SPSS 20.0 (Statistical Package for the Social Sciences) software. Percentage mortality was calculated using Microsoft Excel 2007.

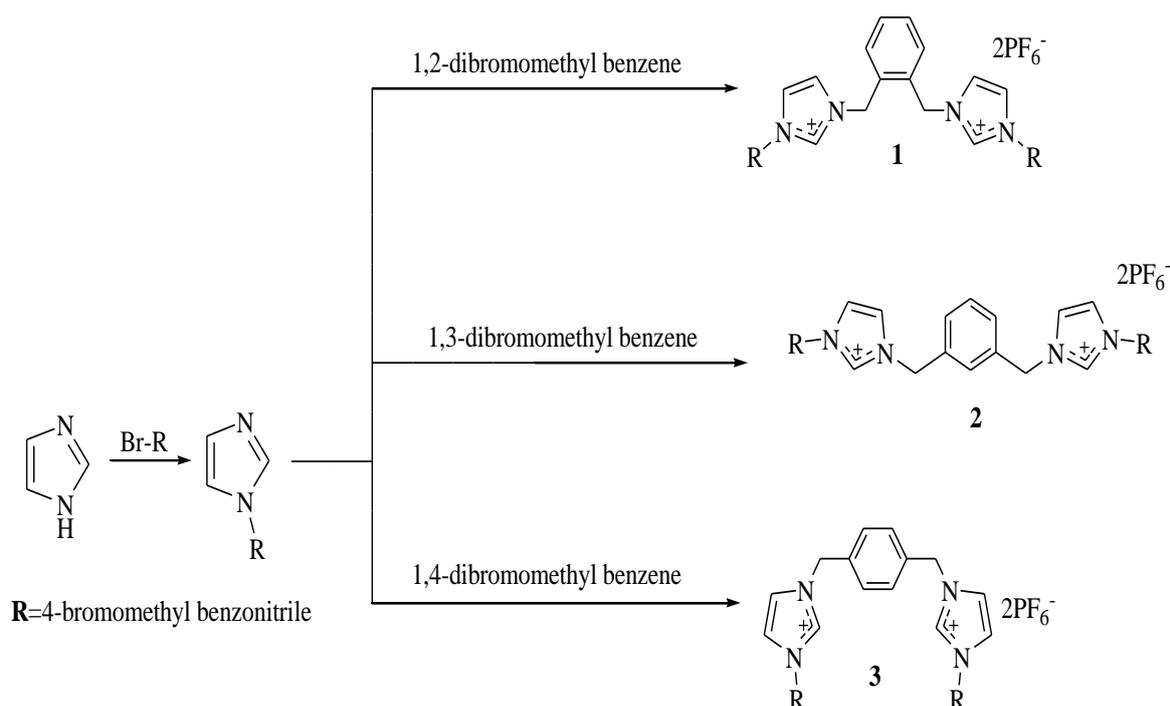
## RESULTS AND DISCUSSION

### 1. Syntheses

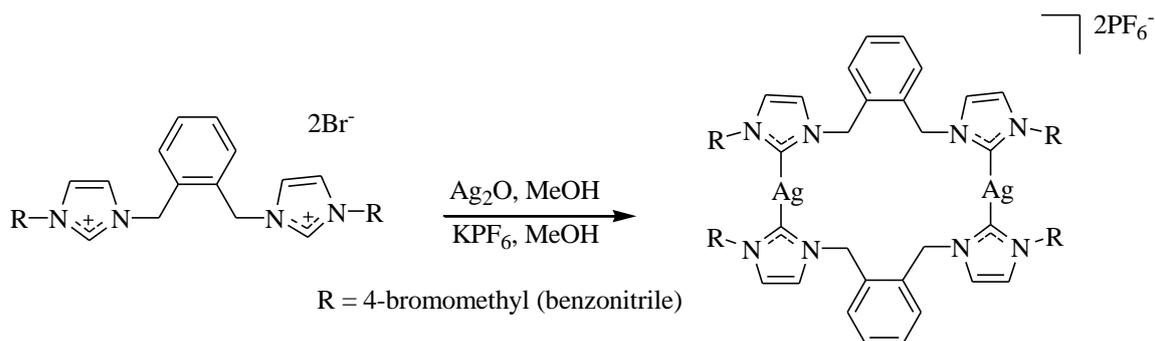
Imidazolium salts **1-3** were prepared by the similar procedures based on the method used by Dias and Jin with minor modifications [13]. The synthesis of 4-(imidazole-1-methyl)benzotrile was achieved by N-alkylation reaction of 4-bromomethyl benzotrile with 1H-benzimidazole mediated by DMSO in the presence of base potassium hydroxide (KOH) as a

proton transfer agent. The desired imidazolium bromides were obtained by the reaction of 4-(imidazole-1-methyl)benzotrile with 1,2-, 1,3-, 1,4-di(bromomethyl)benzene respectively in refluxing 1,4-dioxane for 24 h. Bromide salts were converted to potassium hexafluorophosphate in methanol to obtain nitrile-functionalized imidazolium hexafluorophosphate salts **1-3**, respectively in good yield. Reactions involved in the preparation of imidazolium salts **1-3** are shown in Scheme 1. Imidazolium salts were recrystallized from mixture of methanol/acetonitrile and diethyl ether. This method affords desired KPF<sub>6</sub> ligands in their purest form as off-white solids.

A synthetic strategy for the preparation of desired silver(I)-complexes of nitrile-functionalized NHC ligands 4-6 were used are depicted in (Scheme 2). A combination of an imidazolium bromide salt in methanol with silver(I) oxide in a 1:2 M ratio [24] added to approximate silver(I) metalation conditions yield in each case to complete reaction of the imidazolium bromide salt and allowed formation of new bis-NHC silver(I) bromide complexes in methanol for 2 days. A solution of potassium hexafluorophosphate in methanol was dissolved to the silver(I) bromide complex solution at room temperature and allowed to stir for further 4 h resulting in the formation of the desired bis-NHC silver(I) hexafluorophosphate complexes 4-6. The cationic complexes are soluble in water, insoluble in common organic solvents such as benzene and hexane, while completely soluble in DMSO, DMF and acetonitrile. For antimicrobial and larvicidal activity, test solutions of the compounds were prepared in DMSO.



Scheme 1. Synthesis of imidazolium salts **1-3**.



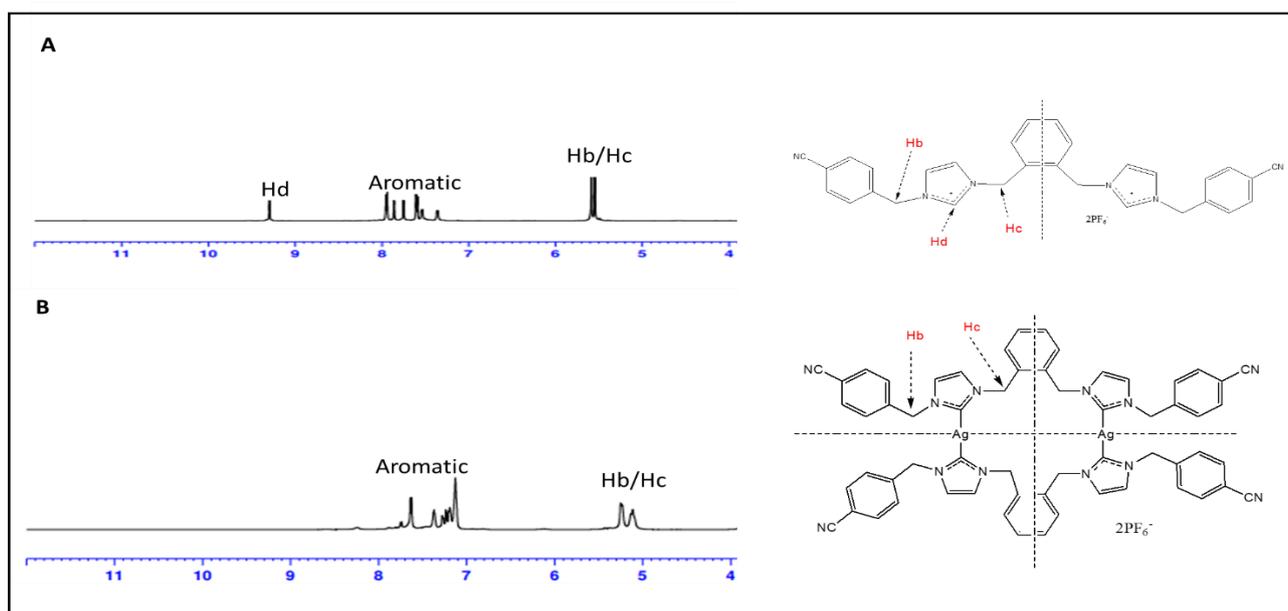
**Scheme 2:** Synthesis of Ag(I)-NHC of complex **4** from salt **1**. The syntheses of the other complexes are similar with the only difference being the bridging group that connect the two *N*-heterocyclic moieties.

## 2. NMR Spectra of the Compounds

Using NMR spectroscopic, all compounds **1-6** was analysed in  $d_3$ -CD<sub>3</sub>CN/ $d_6$ -DMSO. Analysis of the <sup>1</sup>H NMR spectra of these salts showed the presence of a characteristic Hd proton resonance in the range  $\delta$  9.29–9.39, indicating the formation of desired imidazolium salts [14, 15]. Spectra also indicated the peaks in the range  $\delta$  7.54–7.82,  $\delta$  5.55–5.58 and  $\delta$  5.45–5.54, represented to the resonance of aromatic, benzylic and benzonitrilic, protons, respectively. Also, in the case of <sup>13</sup>C NMR analysis, spectra showed the presence of a characteristic C2 carbon resonance in the downfield region in the range  $\delta$  143.0–144.3, indicating the successful formation of imidazolium salts. Lastly, a group of aromatic, nitrile and aliphatic carbon resonances were emerged in the range  $\delta$  127.6–137.5,  $\delta$  123.0–123.6 and  $\delta$  49.1–51.5, respectively.

Analysis of the complex <sup>1</sup>H NMR spectra recorded in  $d_3$ -CD<sub>3</sub>CN revealed the complete disappearance of signal corresponding to Hd proton of

the respective salt. This observation confirmed the formation of the desired bis-NHC complexes **4-6** via Hd proton abstraction (Figure 1). However, all other proton resonances corresponding to the respective salt appeared in the complex spectra with negligible differences in the peak positions. On the other hand, in the case of <sup>13</sup>C NMR spectra of complexes **4**, the resonance signals due to the silver(I) metalated carbene carbon displayed two doublets centered at 179.4, 179.5, 180.5, 181.1 bound to <sup>107</sup>Ag and <sup>109</sup>Ag with the coupling constants of 137.5 and 200 Hz in both the cases (Figure 2). The presence of carbene <sup>13</sup>C–<sup>107/109</sup>Ag coupling is feasible for silver–NHC complexes having non-coordinating counterions and has been attributed to the non-labile nature of carbene C–Ag bond. Conversely, this phenomenon is not found in the cases of **5** and **6** complexes, indicating that the corresponding C–Ag bonds are labile in nature. These observations are in line with the similar silver(I)–NHC complexes previously reported by us [16]. Apart from this major observation, spectra evidenced almost no changes in the resonance of other carbon nuclei compared to their respective salts.



**Figure 1.** <sup>1</sup>H NMR ( $d_6$ -DMSO, 500MHz) spectra for (a) salt **1** and (b) complex **4**.

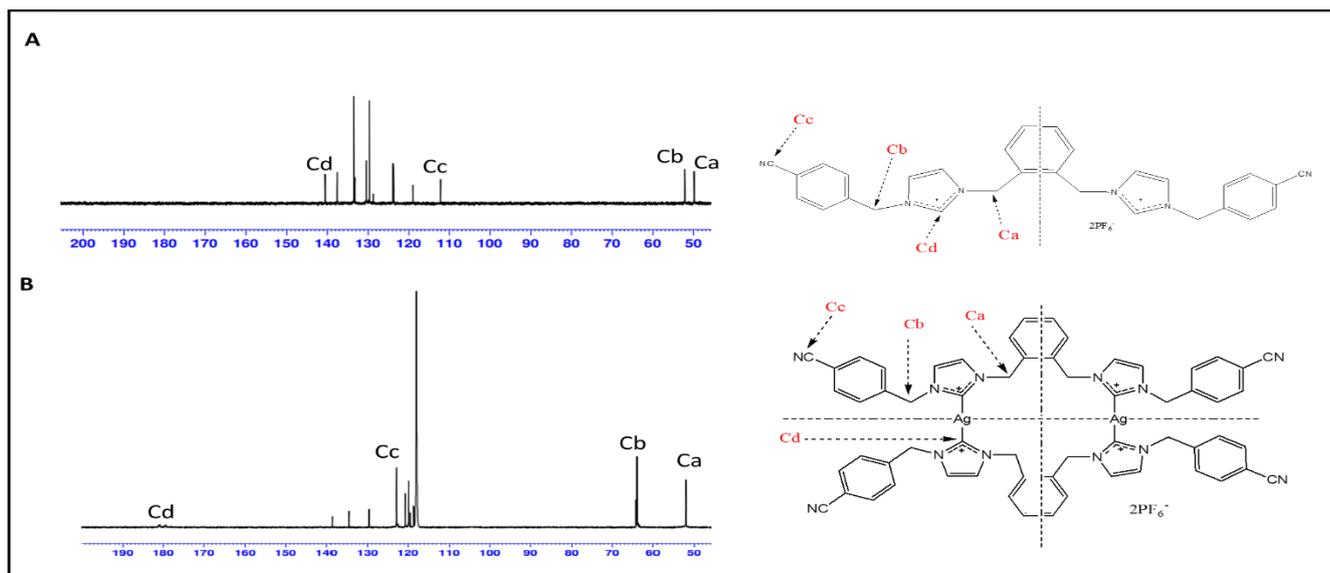


Figure 2.  $^{13}\text{C}$  NMR ( $\text{d}_3\text{-CH}_3\text{CN}$ , 125MHz) spectra for (a) salt **1** and (b) complex **4**.

### 3. FTIR Spectra of the Compounds

Due to the present research work involved the nitrile-functionalities; FTIR spectroscopic characterization was followed to discover the observations on the behaviour of nitrile group and the weak interaction with the metal centre. FTIR spectra of silver (I)-NHC complexes were compared with the imidazolium salts and calibrated using KBr disk method over  $400 - 4000 \text{ cm}^{-1}$  range. Salt spectra displayed a characteristic medium intensity band at around  $2233 - 2236 \text{ cm}^{-1}$  ascribable to the stretching vibrations of  $\text{C}\equiv\text{N}$  module [17] (Figure 3). This band remains unchanged in the complex spectra,

indicating its non-involvement in the coordination of metal centre. This is due to the stronger ligation effect by the carbene carbon than nitrile nitrogen atom. Besides, salt spectra showed the presence of medium intensity strong bands at around  $1565 \text{ cm}^{-1}$ , attributed to the stretching vibration of  $\text{C}=\text{N}$  module of heterocyclic ring system. However, the band shifted to lower energy region in the complex spectra indicating the coordination of the carbene carbon to metal centre. Finally, both the spectra evidenced the presence of aliphatic and aromatic  $\text{C-H}$  stretching vibrational bands at around  $3084$  and  $3173 \text{ cm}^{-1}$ , respectively. All these IR spectral observations are agreeable with the literature [18].

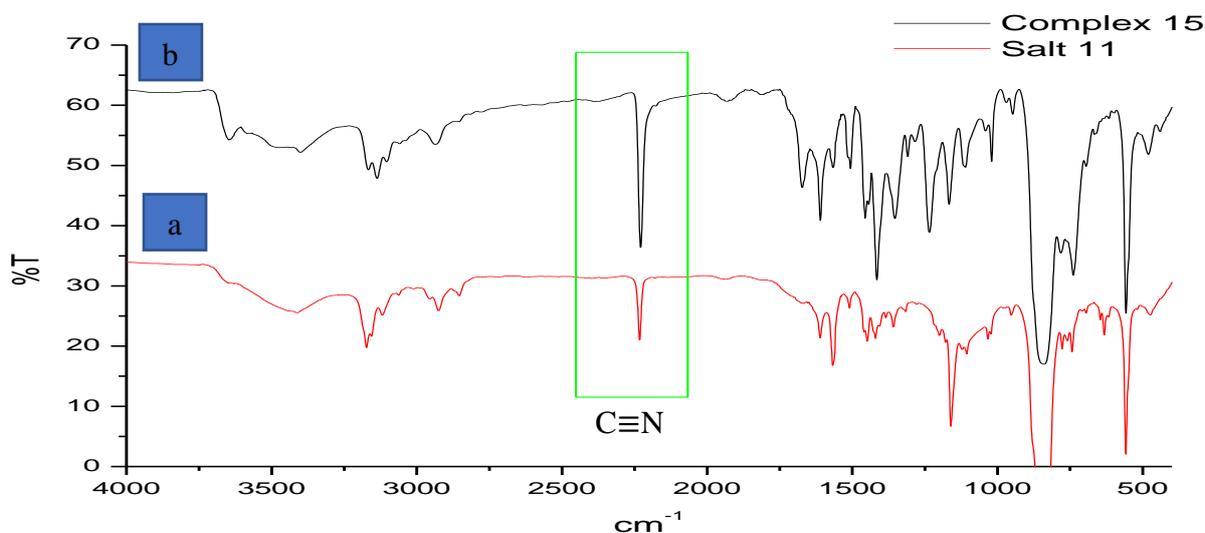


Figure 3: IR- spectra of (a) imidazolium salt **4** and respective (b) silver(I)NHC complex, **6**

#### 4. Molar Conductivity Measurements

The molar conductance values of the imidazolium salts and their bis-carbene silver(I) complexes were obtained at room temperature in DMF solution at  $10^{-3}$  M concentration. The compounds were dissolved in DMF and the molar conductivities of their solutions were measured at  $25 \pm 2$  °C. The conductivity measurements are altered by the electrostatic force of attraction between imidazolium cations and  $KPF_6$  anions. The molar conductivity values of the imidazolium salts (**1-3**) are found at range of 140.0–160.0  $S\ cm^2\ mol^{-1}$ , which is observed values reported for non-complex 1:1 electrolyte. While the values for the bis-carbene coordinated complexes (**4-6**) are found at around weak 1:1 electrolyte 45.0–67.0  $S\ cm^2\ mol^{-1}$ , which could be due to the strong interactions operating between complex cation and  $KPF_6$  anions. The expected range for electrolyte is 1:1 [19].

#### 5. Single Crystal X-ray Diffraction Studies

Structure of imidazolium salt **2** was elucidated by means of single crystal X-ray crystallography, as additional support to confirm atom connectivity, molecular structure and geometry. Suitable single crystal of **2** for X-ray diffraction studies were grown by slow diffusion of diethyl ether into a solution of the salt dissolved in acetonitrile at room temperature. In accordance with all the spectral data, single crystal X-ray analysis of compounds overall confirms the expected structure. Crystal refinement data, pertinent bond distances and angles of compound **2** given in

Tables 2. Crystals of imidazolium salt **2** are triclinic, *P*-1 space group, having occupied one imidazolium cation and one hexafluorophosphate anion in a symmetric unit. This is a well-ordered salt found no solvent or water molecules of crystallization. A thermal ellipsoid plot of salt **2** is depicted in Figure 4. Benzonitrile arms of the salt are on either sides of the imidazole ring that are inclined at an angle of 113.5 (5)° for N2-C8-C5 and 112.1 (6)° for N5-C23-C24 (Table 2) [20, 21]. The internal ring angle at C2 of imidazole (N2-C11-N3) is 109.7(8)°, which is in agreement with the reported compounds having similar architecture [22, 23]. In the crystal packing, imidazole cations related to hexafluorophosphate anions via intermolecular hydrogen bonding (1.421–1.559 Å) forming a 3-dimensional framework. While attempts to obtain crystals for single crystal X-ray diffraction study for silver(I)-NHC complexes were unsuccessful, therefore propose the structure of these complexes based on the previous reported structure [24].

#### 6. Larvicidal Activity

Mortality assessment on mosquito larvae using the salts (**1-3**) and complexes (**4-6**) exhibited contrasting responses. From the preliminary test, exposure to the test concentrations (even at 400 ppm) induced no mortality in the imidazolium salts and control treatments. Based on their efficacy against larvae during preliminary experiments, only complexes were chosen. All the complexes showed that concentration of 200 ppm caused total (100%) mortality in both mosquito species.

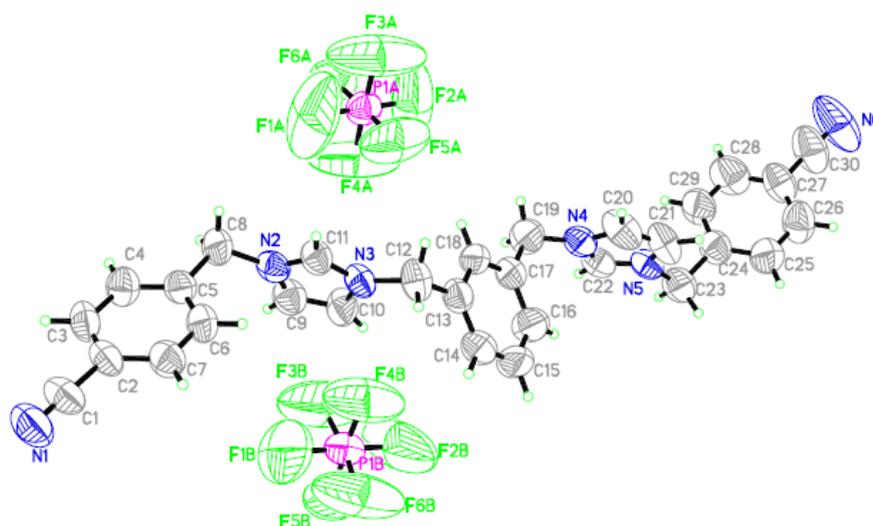


Figure 4. Structure of **2** with ellipsoids shown at 50% probability.

**Table 2.** Selected bond lengths (Å) and angles (°) of salt **3**.

<b>Bond Distance (Å)</b>			
N2-C9	1.307(8)	C4-C5	1.360(8)
N2-C11	1.319(8)	N1-C1	1.102(8)
N3-C12	1.481(8)	C1-C2	1.437(8)
C9-C10	1.322(9)	C12-C13	1.509(8)
N2-C8	1.444(7)		
<b>Bond Angles (°)</b>			
N2-C11-N3	109.7(5)	N2-C8-C5	113.5(5)
N2-C11-H11A	125.00	N2-C9-C10	109.0(6)
C11-N3-C12	123.8(5)	C3-C4-C5	121.1(6)
C8-N2-C11	124.4(5)	N2-C12-C13	110.1(5)
C9-N2-C11	108.1(5)		

Insecticide -based products for mosquito control are inadequate to achieve the desired level of ability due to the development of insecticide resistance. The strength of NHCs to form stable transition metal complexes, especially with silver(I) makes them varied pharmacophores, which depends on the nature of the carbene carbon and metal bond strength. Toxicity of the test compounds against third instar larvae of *Ae. aegypti* and *Cx. Quinquefasciatus* shows that LC<sub>50</sub> were significantly different from each other. Complex **6** showed the highest larval mortality with LC<sub>50</sub> of 27.90 and 30.27 ppm against *Ae. aegypti* and *Cx. quinquefasciatus*, respectively

(Table 3 Based on Cheng et al. [25], extracts with LC<sub>50</sub> values of 50–100 ppm were considered active, while those below 50 ppm and those above 100 ppm were deemed highly active and inactive respectively. According to this classification to the synthesized complexes in this study showed that complexes **6** highly active on *Ae. Aegypti* while **4** and **5** are active. On *Cx. Quinque-fasciatus*, complexes **5** is inactive while **4** and **6** are active and highly active, respectively. Based on the obtained results, we can clearly conclude that chemical structure of complexes played a role in the toxicity caused by different bridging group.

**Table 3.** Larvicidal activity of complexes (4-6) against larvae *Ae-aegypti* and *Cx.p. quinquefasciatus*.

Mosquito species	Complex	Regression equation	LC <sub>50</sub> (ppm)	95% fiducial limit (UCL-LCL) <sup>a</sup> ,ppm	Larvicidal activity
<i>Ae- aegypti</i>	<b>4</b>	y=0.51x+3.83	60.71	102.30-36.03)	Active
	<b>5</b>	y=0.37x+4.01	79.57	(159.57-39.75)	Active
<i>Cx.p. quinquefasciatus</i>	<b>6</b>	y=0.56x+4.36	27.90	(46.00-16.92)	Highly active
	<b>4</b>	y=0.59x+3.51	71.82	(114.99-44.85)	Active
	<b>5</b>	y=0.33x+3.90	128.15	(282.58-58.12)	Inactive
	<b>6</b>	y=0.49x+4.37	30.27	(52.21-17.55)	Highly active

<sup>a</sup>UCL, Upper confidence limit; LCL, Lower confidence limit.

## CONCLUSIONS

In conclusion, the syntheses, characterizations, biological evaluations and larvicidal activities of a series of nitrile-functionalized imidazolium salts and respective bis-NHC silver(I) complexes have been reported. Salts have been prepared by the successive N-alkylation method, while complexes from the in-situ deprotonation of azolium salts at basic reaction conditions. All reported compounds were characterized by  $^1\text{H}$  and  $^{13}\text{C}$  NMR, FTIR spectral, elemental analysis techniques and molar conductivity measurement. Additionally, molecular structure of ligand **2** was established using single crystal X-ray diffraction method. Our study on biological evaluations has showed that new class of complexes is not suitable for antimicrobial studies. Further study on larvicidal activity has furnished the highest mortality is displayed for complex **6** with the  $\text{LC}_{50}$  of 27.90 and 30.27 ppm against *Ae. aegypti* and *Cx. Quinquefasciatus*, respectively adversely affected the development of larvae into adults at the tested concentrations.

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