Unique Trinuclear Ag(I)-*N*-Heterocyclic Carbene (NHC) Complex having Three Silver Centers: Synthesis and characterization

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Summary: The employment of carbene salts to facilitate metal-metal interactions is becoming a more pronounced zone of interest due to their efficient sigma electron donor features, facile synthesis protocols and their ability to develop strong ligand-metal interactions which may further be attributed to their flat steric factors. The research work discussed in this article was conducted to achieve this goal. Herein we report the synthesis of a novel trinuclear silver complex by a new approach. An imidazolium salt **2** was synthesized by *in situ* deprotonation and its trinuclear silver(I) complex **3** was synthesized by using initially controlled excess of precursor in order to understand the effect of excess of the selected reactant on complex formation. Both the ligand and complex were characterized by physico-chemical techniques. The results revealed the final product obtained was a trinuclear complex **3** having a core of three silver centres in a row, with the two distal silver ions bound to two carbene ligands and central one was bound by nitrogen of N-methyl imidazole. ESI-MS spectrum of compound **3** indicated that the complex chooses trinuclear structure in a solid and liquid state while in gas phase it appears as a mononuclear unit.

Key words: Trinuclear silver (I) complex, ESI-MS, *In situ* deprotonation, HSQC, Physico-chemical.

Introduction

N-Heterocyclic Carbenes (NHCs) is a class of active ligands where a carbene carbon forms bond with various types of metals [1]. Affluence of their synthesis and virtue by which they undergo transmetallation, has made the *N*-Heterocyclic carbenes (NHCs) the most attractive tool in the field of medicinal and catalytic chemistry [2-8]. Silver(I)-*N*-Heterocyclic carbene (Ag(I)-NHC) complexes have become most pronounced class of compounds having strong efficacy *in vitro* as well as *in vivo* and can be employed as strong antimicrobial and anticancer agents[9-11]. Polydendate NHC ligands produce stable metal-NHC system due to pincer or chelating effects which offer additional stabilization [9, 12, 13]. Polynuclear silver(I)-NHC systems having aliphatic or aromatic moieties as linkers and with a core encompassing more than one silver centres in a row represent a novel category of silver-based drugs on the account of their biocompatibility [14, 15]. The employment of carbene salts to facilitate metal-metal interactions is becoming more pronounced zone of interest due to their efficient sigma electron donor features, facile synthesis protocols and their ability to develop strong ligand-metal interactions which may further be attributed to their flat steric factors [16]. Recently, few noticeable examples of silver-NHC complexes have been reported where silver showed close metal-metal interactions [17-19]. In the current study, we report a unique trinuclear silver (I)-NHC complex with Ag(I)-Ag(I) interaction by adopting a different strategy. This colorless complex appears to be stable in solid and liquid state but readily dissociates into monomeric form in the gas phase. The dissociation behavior may be ascribed to weak Ag(I)-Ag(I) bonds. In the next study, we will synthesize a few more complexes of the same category and then we will evaluate bilogical applications of such unique complexes.

Experimental

Materials and Methods

Solvents were obtained from commercial sources and used without further purification. 1-Methyl imidazole (**1**), 1-chlorobutane and Ag_2O were purchased from Sigma Aldrich. The melting points were measured by using a Stuart Scientific SMP-1 (UK) instrument. EYELA 1L Rotary Evaporator N-1001V-WD was used for evaporation of solvent. The FTIR spectra of the compounds were recorded in ALPHA-P, compact FTIR spectrometer endowed with attenuated total reflectance (ATR) accessory to get electromagnetic spectrum in range of 4000−250 cm^{-1} region. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded on Bruker Avance-300 and Avance-400 or on a Varian Inova-300 spectrometer in $CDCl_3$ and DMSO-d_6 as solvents. Chemical shifts are reported in parts per million relative to tetramethylsilane, and coupling constants (J) are given in Hertz. The ^{1}H and ^{13}C spectra were referenced using the residual solvent signal as internal standard, while ^{19}F and ^{31}P spectra were referenced to $CFCl_3$ and H_3PO_4 (85%), respectively. Spectral assignments were achieved by ^{1}H–^{13}C heteronuclear single quantum correlation (HSQC) experiments. The alkylation reaction was

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monitored by Agilent Technologie, 7890A GC/MS. Elemental study of the complex for C, H, and N analysis was carried out using EA1108 (CHNS), Fisons instrument. ESI mass spectrum was recorded using ESI-POS-DI-TOF 6224 spectrometer. Samples were introduced on a continuous flow of 0.2 mL/min. Nitrogen served both as the nebulizer and dry gas.

Synthesis of 3-butyl-1-methyl-1H-imidazol-3-ium chloride **(2)**

Refluxed a mixture of *N*-methyl imidazole **1** (3.4 ml, 45 mmoles) and 1-chlorobutane (3.1 ml, 30 mmoles) without using a solvent at 80 °C for extended period of time. After 48 hours, the reaction mixture appeared as thick paste stuck to the bottom of the flask. Washed the product with ether and collected the pure oily product in yield 1.5g (60%). Slow evaporation of a saturated solution of the complex in acetonitrile at room temperature yielded colourless block like single crystals. FTIR (ATR, ν, cm^{-1}): 3384 (C_{aliph}–N_{imid} str), 2957, 2872 (C_{aliph}-H str), 1558, 1517, 1458 (C=N_{imid} str), 1169 (C_{arom}-N_{imid} str), 907, 853, 753, 665, 619 (C-H_{oop} ben). ^{1}H NMR (400MHz, $CDCl_3$, δ ppm) 0.57 (3H, t, CH_3, *J*=7.59 Hz), 0.98 (2H, m, CH_2), 1.53 (2H, m, CH_2), 3.34 (1.5H, CH_3-N_{imid}), 3.75 (3H, s, CH_3-N_{imid}), 3.97 (2H, t, R-CH_2, *J*=7.23 Hz), 6.64 (1H, d, H_{imid}, *J*=22.5 Hz), 7.12 (0.5H, s, H_{imid}),7.32 (1H, s, H_{imid}), 7.45 (1H, s, H_{imid}), 10.12 (1H, s, N-CH-N_{imid}). ^{13}C NMR (125.72 MHz, $CDCl_3$, δ ppm) 12.7 (CH_3), 18.6 (R-CH_2), 31.4 (R-CH_2), 35.7 (CH_3-N_{imid}), 48.9 (N-CH_2-R), 121.6, 123.2 (N-CH-C_{imid}), 136.7 (N_{imid}=C=N_{imid}). Anal. Calcd. for $C_8H_{15}ClN_2$: C 55.0, H 8.6, N 16.0. Found: C 55.1, H 8.5, N 15.9.

Synthesis of bis(3-butyl-1-methyl-1H-imidazol-3-ium-2-yl)silver) hexafluorophosphate **(3)**

Stirred a mixture of salt **2** (1 g, 5.7 mmoles) and silver oxide (2.6 g, 11.4 mmoles) in methanol (40 mL) for 48 hours at room temperature and covered the flask with aluminium foil to stop interaction of light. To the resulting mixture, an aqueous solution of KPF_6 (2 equivalents) was added in order to replace halide counter anion with hexafluorophosphate counterpart by metathesis by stirring for 4 h and filtered. The beige coloured precipitates were collected and washed with distilled water, then left to dry at ambient temperature. Yield 3.5g (48%); M.P 240 °C. ESI^{+}, m/z, %): ([$C_{16}H_{28}AgN_4$]$^{+}$, 383.1374, 100). FTIR (ATR, ν, cm^{-1}): 3142 (C_{aliph}–N_{imid} str), 2933, 2875 (C_{aliph}-H str), 1562, 1466 (C=N_{imid} str), 1233(C_{arom}-N_{imid} str), 825, 751, 621 (C-H_{oop} ben). ^{1}H NMR (400MHz, DMSO-d_6, δ ppm) 0.97 (12H, t, CH_3 *J*=7.53 Hz), 1.29 (8H, q, 4×CH_2), 1.77 (8H, q, CH_2), 3.76 (3H, s, CH_3-N_{imid}), 3.83 (12H, s, CH_3-N_{imid}), 4.1 (8H, t, 4×CH_2, *J*=7.01 Hz), 7.16 (1H, t, Ar-H, *J*=1.19 Hz), 7.4 (1H, t, Ar-H, *J*= 1.29 Hz), 7.45 (4H, d, H_{imid}, *J*= 1.76 Hz), 7.5 (4H, d, H_{imid}, *J*= 1.76 Hz), 8.01 (1H, s, N_{imid}-H). ^{13}C NMR (125.72 MHz, DMSO-d_6, δ ppm) 13.5 (CH_3), 19.6 (CH_2), 33.5 (R-CH_2), 38.6 (CH_3-N_{imid}) 51.63 (N-CH_2-R), 122.8, 128.9 (N-C_{imid}), 179.1 (d, C-Ag-C, *J*=195 Hz). ^{19}F (470.4 MHz, DMSO-d$_6$, δ ppm) -71.2 (d, 6F). ^{31}P (202.4 MHz, DMSO-d_6, δ ppm) -143.5 (h, 1P). Anal. Calcd. for $C_{37}H_{64}Ag_3ClF_{12}N_{10}P_2$: C 34.2, H 5.1, Cl 2.73, F 17.56, N 10.79, P 4.77. Found: C 34.22, H 5.18, N 10.79.

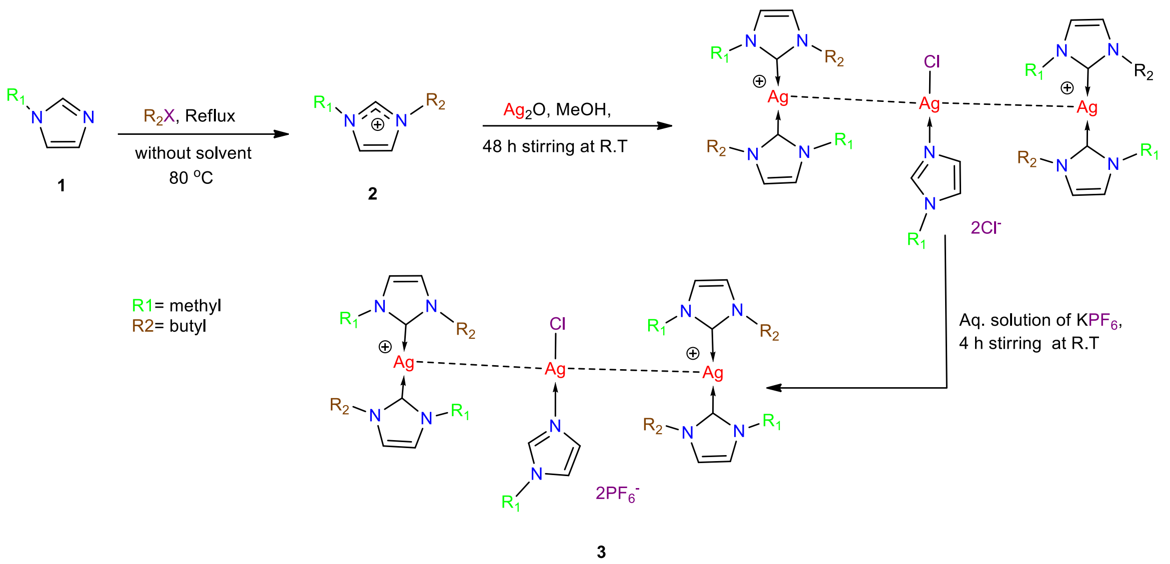
Results and Discussion

The azolium salt **2** was synthesized by following a reported method with modified protocol [20, 21] while trinuclear complex **3** was synthesized by adopting a new protocol. According to this protocol, during the synthesis of imidazolium salt **2**, an excess amount (1.5 equivalent) of N-methylimidazole was added to keep its 0.5 equivalents freely available for bonding with the metal during complexation. We also tried to get complex **3** by an alternative approach which involved isolation of pure salt **2** at first step and during complexation, we added half equivalent N-methylimidazole. Both of the adopted routes generated complex **3**. For easy handling of the end product, counter anion (halide) was replaced by hexafluorophospahte by metathesis in both methods because Ag(I)-NHC complexes having halide counter anions usually appear as a thick yellowish fluid which is difficult to handle. Scheme **1** shows the simple steps of syntheses, starting from *N*-alkylated imidazole to the trinuclear silver complex **3** having PF_6^- as a counter ion.

Characterization

FTIR studies

FTIR spectroscopy helped to identify some specific patterns in both near and Mid-IR regions to provide an indication of synthesis of imidazolium salt and silver complex. For example, a broad signal at 3,402 cm^{-1} and sharp signals at 2850-3000 cm^{-1} in FTIR spectrum of salt **2** can be assigned to C_{aliph}–N_{imi} and C_{alip}-H stretching vibrations which appear feeble in silver complex **3** due to ligand-silver bonding [22] (Fig 1). It has been observed that bonding of silver ion with the organic molecule in complex cease most of the C_{aliph}-H vibrations [14]. An intense pattern of signals appearing at 1,350–1,500 cm^{-1} in spectrum of salt **2** can be referred to C=N stretching vibrations of imidazole rings [23] which appear in specific *four fingers* pattern in case of silver complex **3** where conjugation vanishes when silver binds to carbene carbon providing a confirmation of its synthesis [20]. Similarly, C=C stretching signals of imidazole ring can be seen in the range of 1355-1250 cm^{-1} [24]. A sharp signal at 900-675 cm^{-1} can be referred to C-H out of the plane (oop) bending vibrations of vinylic protons (Fig 1).



Scheme-1: Syntheses of N,N' dialkylated imidazolium salt **2** and its trinuclear Ag(I) complex **3**.

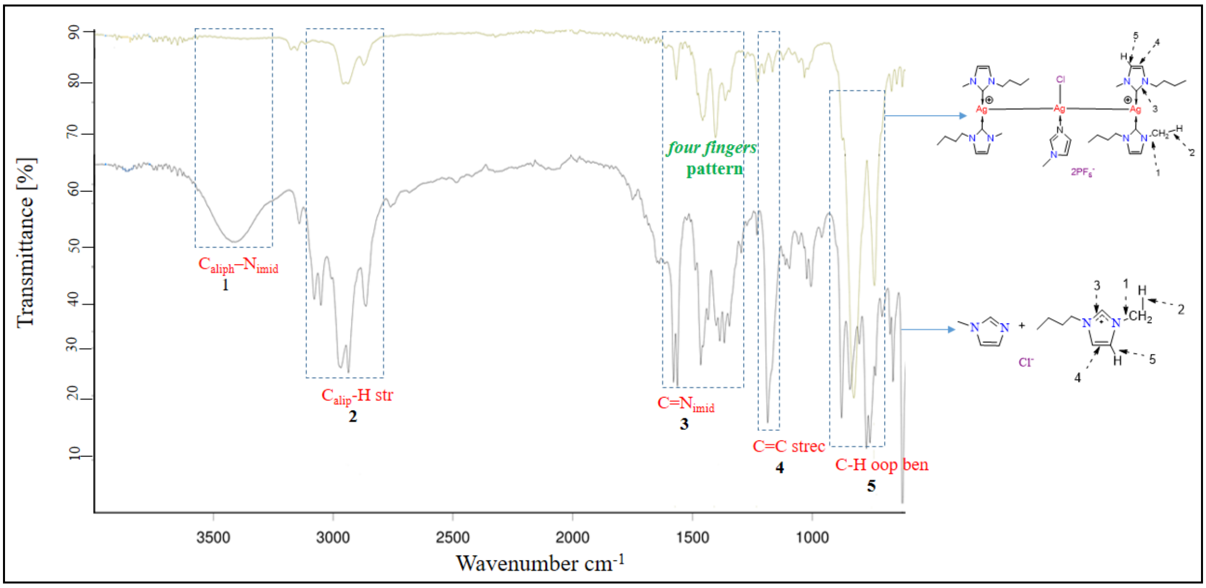


Fig. 1: FTIR spectra showing the comparison of FTIR spectral features of imidazolium salt **2** (bottom) and silver complex **3** (top). Shifts in vibrational modes and appearance of specific four fingers (*f.fs*) pattern in the spectrum of the complex is an indication of the successful synthesis of silver complexes.

NMR studies

FT-NMR spectra of ligand and complex were recorded in $CDCl_3$ and DMSO-d_6, respectively. NMR spectra of compounds **2** and **3** appeared very interesting. Appearance of signals for protons of alkyl chains at chemical shift (δ) 0.5-4 ppm and a specific signal for the most deshielded proton and carbon (N***CH***N) at 10.2 ppm in ^{1}H NMR and 138 ppm in ^{13}C NMR spectra, respectively of salt **2**is the indication of its successful synthesis [20] (Figs 2-3).

The progress of the metallation reaction of salt **2** to form silver complex **3** can be understood by observing changes in resonances of proton and carbon (of the imidazolium salt) in ^{1}H and ^{13}C NMR spectra, respectively [25]. It can be seen in **Fig. 2**, that the singlet of acidic proton in ^{1}H NMR spectrum of imidazolium salt **2** has disappeared in ^{1}H NMR spectrum of silver complex **3** which is an indication of silver-ligand bonding. Appearance of some additional signals at a 3.34, 6.64 and 7.1 ppm assigned to $\mathbf{H_d}$, $\mathbf{H_g}$ and vinylic protons in ^{1}H NMR spectrum of salt **2** (Fig 2) indicate the presence of unreacted methyl imidazole in stoichiometric ratio 1:0.5 (due to its controlled initial excess concentration used) which resulted in the formation of trinuclear silver complex during *in situ* deprotonation in the presence of silver oxide. The trinuclear structure of the complex is evident from ^{1}H NMR of compound **3** (Fig 2) where the signals appeared at 3.7, 7.1 and 7.4 ppm can be assigned to $\mathbf{H_d}$, vinylic protons and $\mathbf{H_g}$, respectively of central methyl imidazole moiety. It can be observed that these chemical shifts are displaced from their original position as appeared in ^{1}H NMR spectrum of azolium salt which indicates the coordination of N-methylimidazole with the silver. Further confirmation of trinuclear nature was achieved by ^{13}C NMR spectrum which revealed more absolute information about the nature of silver-NHC bonding. As can be seen from **Fig. 3**, the signals appeared at 33.2, 121.6, 121.9 and 140 ppm in ^{13}C NMR spectrum of **3** can be assigned to carbons of central methyl imidazole moiety. $C_{carbene}$-Ag-$C_{carbene}$ resonance of silver-NHC complex appeared as singlet at 179 ppm in ^{13}C NMR spectrum of compound **3**. Two dimensional (HSQC) ^{1}H-^{13}C correlation NMR spectrum helped to assign the signals of ^{1}H and ^{13}C NMR spectra (**Fig. 4**). Furthermore, the presence of phosphorus and fluorine in complex having PF_6^- counter ions was also confirmed by observing heptet and doublet at -141.2 ppm and -71.3 ppm in ^{31}P and ^{19}F NMR spectra, respectively (**Fig. 5 and 6**).

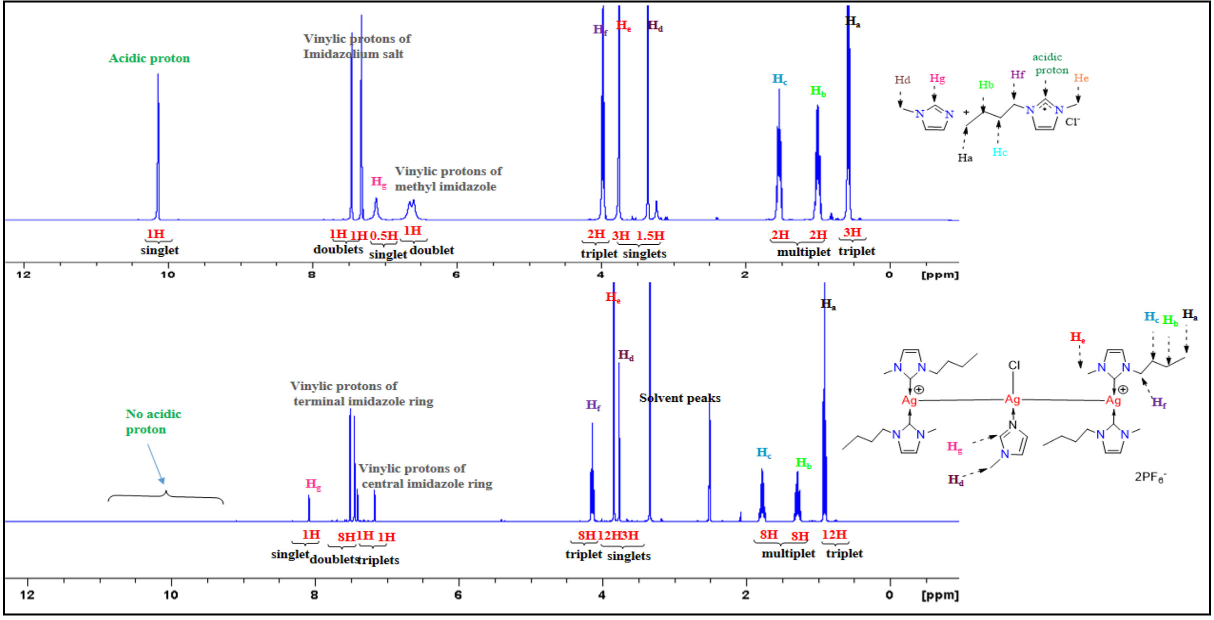


Fig. 2: ^{1}H NMR spectrum of compound 2 and 3. The appearance of peaks at 3.34, 6.64 and 7.1 ppm assigned to H_d, H_g and vinylic protons in ^{1}H NMR spectrum of 2 and at 3.7, 7.16 and 7.4 ppm assigned to H_d, vinylic protons and H_g in ^{1}H NMR spectrum of 3 are indications of trinuclear complex formation.

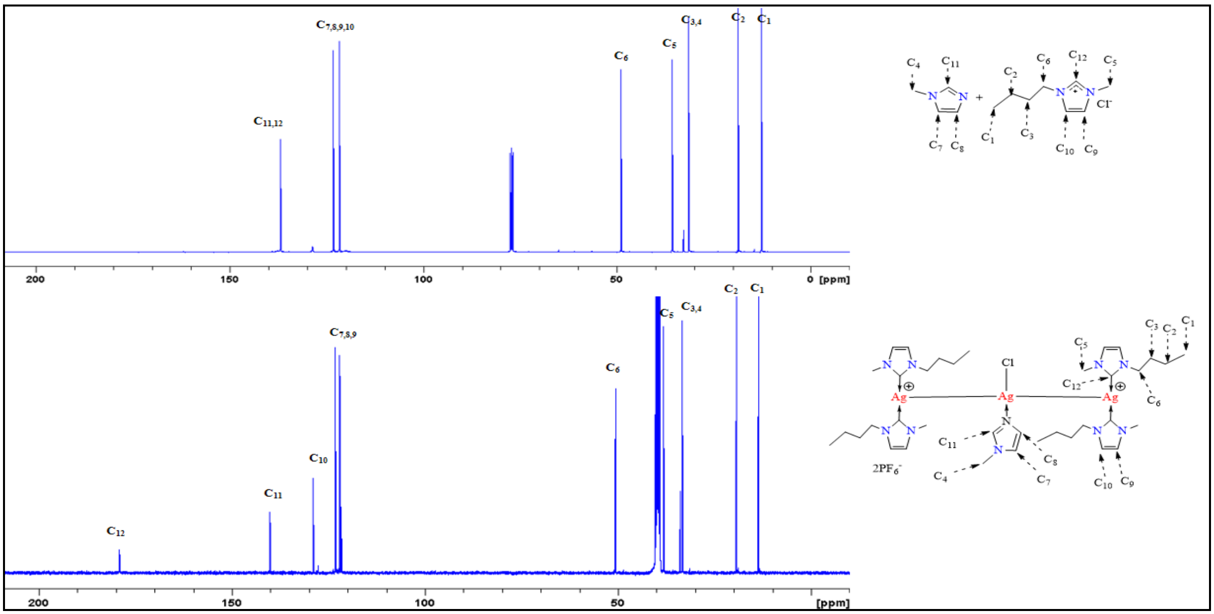


Fig 3: ^{13}C NMR of compound **2** and **3**. Signals at 33.2, 121.6, 121.9, 140 ppm can be assigned to carbons of central methyl imidazole moiety of **3** providing confirmation of its trinuclear nature.

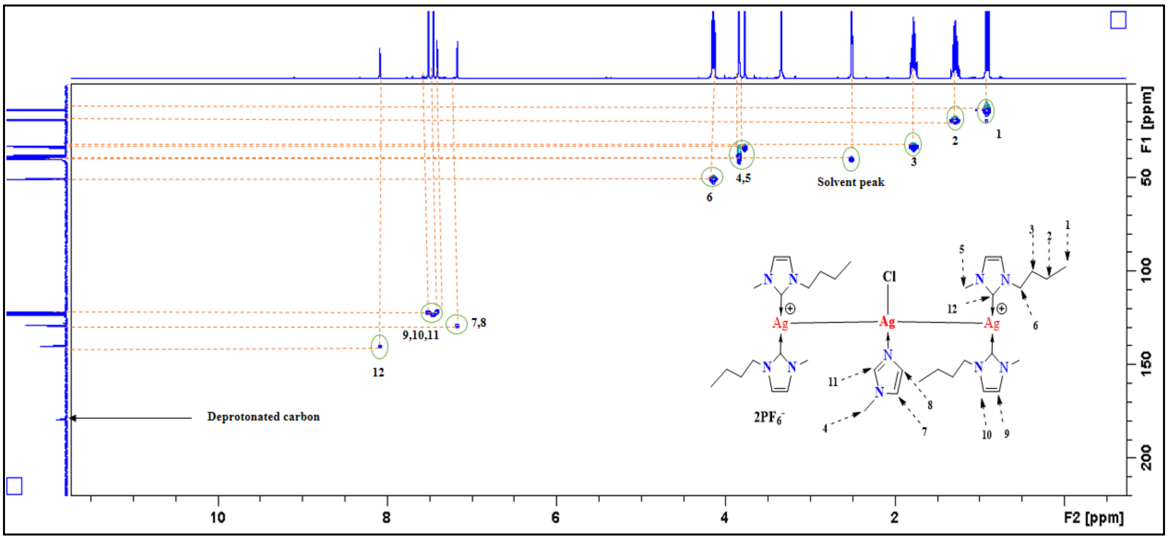


Fig 4**:** HSQC spectrum of compound **3**.

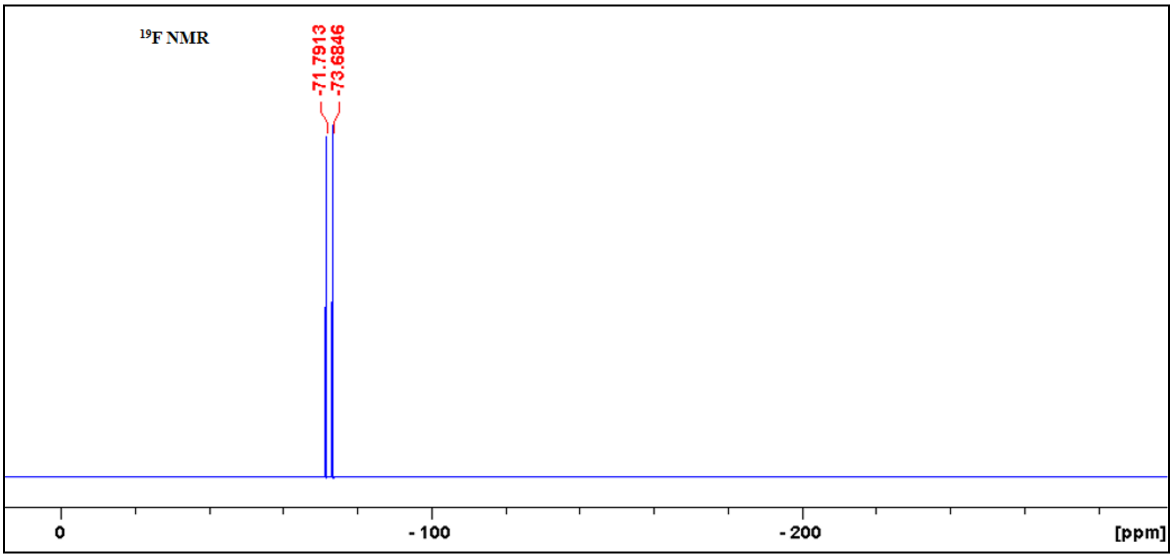


Fig 5: ^{19}F NMR spectrum of compound **3** showing the presence of hexafluorophosphate counter ion.

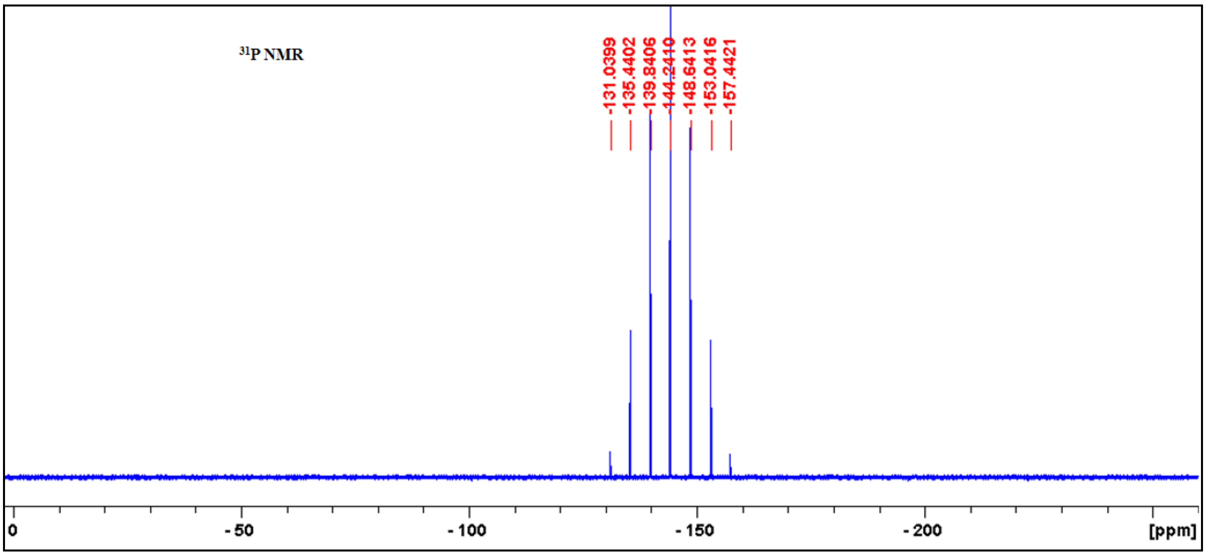


Fig 6**:** ^{31}P NMR spectrum of compound **3** showing the presence of hexafluorophosphate counter ion.

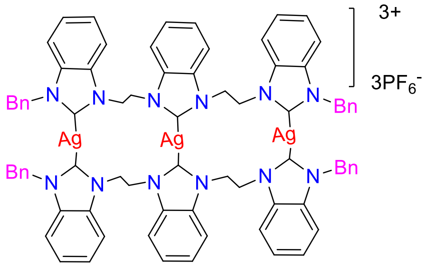


Fig. 7: Trinuclear structure of silver(I) complex without Ag(I)-Ag(I) interaction [13].

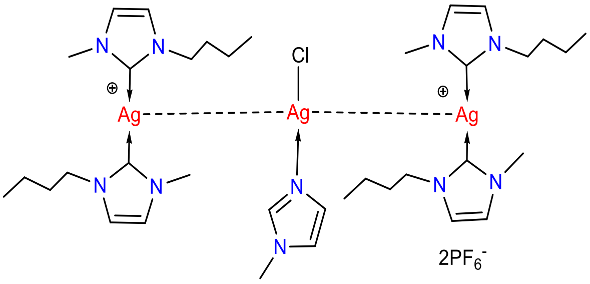


Fig. 8: Trinuclear structure of compound 3 revealed from NMR and elemental analysis.

NMR spectra of compound **3** indicated that it is a new type of trimeric compound quite different from the reported trinuclear complex [13]. Tridentate NHC ligand derived from tris azolium salt and its trinuclear silver complex having three central silver atoms linked to carbene carbons without silver-silver interactions have already been reported [13] **(Fig. 7)**while the core the compound **3** we are reporting seems to be three Ag centres in a row, with the two distal Ag atoms bound to two carbene ligands but the central one is bound by nitrogen of *N*-methyl imidazole as shown (**Fig. 8**). It arises due to controlled excess of *N*-methyl imidazole moiety during salt **2** formation in order to see its effect on the complex synthesis.

ESI-MS studies

The analysis of compound **3** by electrospray ionization (ESI$^+$) mass spectrometry displayed a peak at m/z 383.1374 (**Fig. 10**) which exactly corresponds to molecular weight of mononuclear silver complex minus hexafluorophosphate anion i.e cationic species [M]$^+$ of the compound [$C_{16}H_{28}AgN_4$]$^+$, suggesting mononuclear structure in which Ag$^+$ ion is coordinated by two carbene moieties of mono-NHC ligand [26, 27] (Fig 9). But the ^{1}H, ^{13}C, and 2D HSQC NMR spectra and elemental analysis results reveal a trinuclear structure (as discussed in NMR section).. It can be concluded that both mononuclear silver adduct and methyl imidazole bonded to silver with second nitrogen may be present in product either in free state or linked through silver core but according to our perception, the complex chooses trinuclear structure in solid and liquid state while in the gas phase it appears as mononuclear unit [23, 26-28].

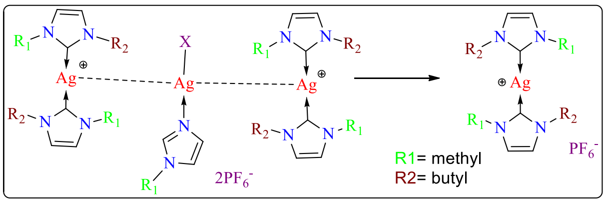


Fig. 9: Showing dissociation of trinuclear silver complex to mononuclear silver complex during vaporization to record ESI-MS spectrum.

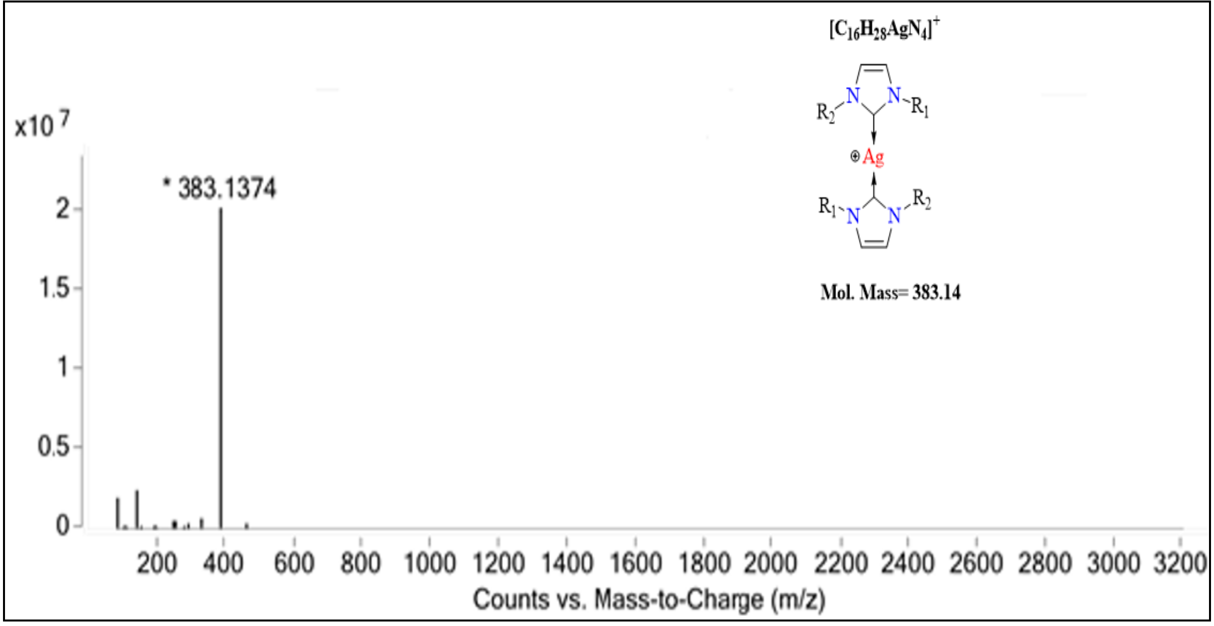


Fig. 10: ESI-MS spectrum of compound 3.

X-ray crystallography

Single crystals of complex **3** were grown by slow evaporation of its saturated solution in acetonitrile at room temperature. Preliminary calculations supported the trinuclear structure of complex as discussed previously, however, in spite of great efforts, crystal refinement data could not be collected due to poor-quality crystals, so X-ray crystallographic study could not further support our proposed structure.

Conclusion

In conclusion, adopting a different strategy of synthesis, we afforded interesting trinuclear silver complex from its imidazolium salt. It was observed that the use of the excess amount of precursor during the synthesis of imidazolium salt, results in the formation of the multinuclear complex during complexation. The same complex could be afforded by an alternative way in which initially pure salt was isolated and then during complexation, the half equivalent of precursor was added. Both of the adopted routes generated the same complex. Elemental analysis, NMR and ESI-MS results of complex indicated that the complex might choose the trinuclear structure in a solid and liquid state while in gas phase it appears as a mononuclear unit.

Conflict of Interest

The authors declare no conflicts of interest

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References

1. R.A. Haque, P.O. Asekunowo, M.R. Razali, Dinuclear silver (I)-N-heterocyclic carbene complexes of N-allyl substituted (benz) imidazol-2-ylidenes with pyridine spacers: synthesis, crystal structures, nuclease and antibacterial studies, *Transition Metal Chemistry* **39** 281 (2014).
2. A. Kamal, M.A. Iqbal, H.N. Bhatti, Therapeutic applications of selenium-derived compounds, *Reviews in Inorganic Chemistry*, **38,** 49 (2018).
3. T. Zou, C.-N. Lok, P.-K. Wan, Z.-F. Zhang, S.-K. Fung, C.-M. Che, Anticancer metal-N-heterocyclic carbene complexes of gold, platinum and palladium, *Current opinion in chemical biology*, **43** 30 (2018).
4. X. Liang, S. Luan, Z. Yin, M. He, C. He, L. Yin, Y. Zou, Z. Yuan, L. Li, X. Song, C. Lv, W. Zhang, Recent advances in the medical use of silver complex, *European Journal of Medicinal Chemistry*, **157**, 62 (2018).
5. Ş. Yaşar, T.K. Köprülü, Ş. Tekin, S. Yaşar, Synthesis, characterisation and cytotoxic properties of N-heterocyclic carbene silver(I) complexes, *Inorganica Chimica Acta*, **479** 17 (2018).
6. C. O'Beirne, H.T. Althani, O. Dada, J. Cassidy, K. Kavanagh, H. Müller-Bunz, Y. Ortin, X. Zhu, M. Tacke, Novel derivatives of the antibiotic NHC–Ag(I) drug candidate SBC3: Synthesis, biological evaluation and ^{109}Ag NMR studies, *Polyhedron* **149**, 95 (2018).
7. S. R. Mahule, M.K. Gangwar, P. Vishnoi, Neutral Binuclear Ag(I) and Au(I) N-Heterocyclic Carbene Complexes of Axially Chiral and Racemic Scaffolds: Synthesis and Characterization, *ChemistrySelect*, **3,** 4023 (2018).
8. A. Habib, M.A. Iqbal, H.N. Bhatti, M. Shahid, Effect of ring substitution on synthesis of benzimidazolium salts and their silver(I) complexes: characterization, electrochemical studies and evaluation of anticancer potential, *Transition Metal Chemistry*, **44,** 431 (2019).
9. A. Habib, M.A. Iqbal, H.N. Bhatti, Polynuclear Ag (I)-N-heterocyclic carbene complexes: synthesis, electrochemical and in vitro anticancer study against human breast cancer and colon cancer, *Journal of Coordination Chemistry* **72**, 2065 (2019).
10. A. Habib, M. Nazari, M.A. Iqbal, H.N. Bhatti, M.K. Ahmed, A.A. Majid, Unsymmetrically substituted benzimidazolium based silver (I)-N-heterocyclic carbene complexes: synthesis, characterization and in vitro anticancer study against human breast cancer and colon cancer, *Journal of Saudi Chemical Society* **23**, 795 (2019).
11. A. Habib, M.A. Iqbal, H.N. Bhatti, A. Kamal, S. Kamal, Synthesis of alkyl/aryl linked binuclear silver (I)-N-Heterocyclic carbene complexes and evaluation of their antimicrobial, hemolytic and thrombolytic potential, *Inorganic Chemistry Communications*, **111** 107670 (2020).
12. C. Segarra, G. Guisado-Barrios, F.E. Hahn, E. Peris, Hexanuclear Cylinder-Shaped Assemblies of Silver and Gold from Benzene–Hexa-N-heterocyclic Carbenes, *Organometallics* **33,** 5077- (2014).
13. T. Fatima, R.A. Haque, M.R. Razali, A new strategy towards tridentate N-heterocyclic carbene ligands derived from benzimidazolium and mixed-azolium salt, *Journal of Molecular Structure* **1141** 346 (2017).

14. R.A. Haque, M.A. Iqbal, S. Budagumpi, M.B. Khadeer Ahamed, A.M. Abdul Majid, N. Hasanudin, Binuclear meta‐xylyl‐linked Ag (I)‐N‐heterocyclic carbene complexes of N‐alkyl/aryl‐alkyl‐substituted bis‐benzimidazolium salts: synthesis, crystal structures and in vitro anticancer studies, *Applied Organometallic Chemistry* **27**, 214 (2013).
15. L.J. Teixeira, M. Seabra, E. Reis, M.T. Girão da Cruz, M.C. Pedroso de Lima, E. Pereira, M.A. Miranda, M.P.M. Marques, Cytotoxic activity of metal complexes of biogenic polyamines: polynuclear platinum (II) chelates, *Journal of medicinal chemistry*, **47**, 2917 (2004).
16. V.J. Catalano, M.A. Malwitz, Short Metal− Metal Separations in a Highly Luminescent Trimetallic Ag (I) Complex Stabilized by Bridging NHC Ligands, *Inorganic chemistry* **42** 5483 (2003).
17. M.A. Iqbal, R.A. Haque, S. Budagumpi, M.B. Khadeer Ahamed, A.M.S. Abdul Majid, Short metal–metal separations and in vitro anticancer studies of a new dinuclear silver(I)-N-heterocyclic carbene complex of para-xylyl-linked bis-benzimidazolium salt, *Inorganic Chemistry Communications*, **28** 64 (2013).
18. B. Jana, P. Ghosh, Structural diversities in Ag(i) complexes of xylyl platform based isomeric bis-NHC ligands: effects of pyridine wingtip substituents, *New Journal of Chemistry* **41** 2131 (2017).
19. Z. Zhou, C. He, L. Yang, Y. Wang, T. Liu, C. Duan, Alkyne Activation by a Porous Silver Coordination Polymer for Heterogeneous Catalysis of Carbon Dioxide Cycloaddition, *ACS Catalysis* **7** 2248 (2017).
20. M.A. Iqbal, R.A. Haque, M.B.K. Ahamed, A.A. Majid, S.S. Al-Rawi, Synthesis and anticancer activity of para-xylyl linked bis-benzimidazolium salts and respective Ag (I) N-heterocyclic carbene complexes, *Medicinal Chemistry Research* **22** 2455 (2013).
21. M.A. Iqbal, M.I. Umar, R.A. Haque, M.B.K. Ahamed, M.Z.B. Asmawi, A.M.S.A. Majid, Macrophage and colon tumor cells as targets for a binuclear silver (I) N-heterocyclic carbene complex, an anti-inflammatory and apoptosis mediator, *Journal of inorganic biochemistry* **146** (2015).
22. M. Asif, M.A. Iqbal, M.A. Hussein, C.E. Oon, R.A. Haque, M.B.K. Ahamed, A.S.A. Majid, A.M.S.A. Majid, Human colon cancer targeted pro-apoptotic, anti-metastatic and cytostatic effects of binuclear Silver (I)–N-Heterocyclic carbene (NHC) complexes, *European journal of medicinal chemistry* **108**, 177 (2016).
23. S. Akkoç, Y. Gök, İ. Özdemir, S. Günal, N-Heterocyclic carbene silver complexes: synthesis, characterization and in vitro antimicrobial studies, *Journal of the Chinese Advanced Materials Society* **2,** 20 (2014).
24. R. Gümüşada, M.E. Günay, N. Özdemir, B. Çetinkaya, Bicyclic N-heterocyclic carbene (NHC) ligand precursors and their palladium complexes, *Journal of Coordination Chemistry* **69,** 1463 (2016).
25. C.V. Maftei, E. Fodor, P.G. Jones, M. Freytag, M.H. Franz, G. Kelter, H.-H. Fiebig, M. Tamm, I. Neda, N-heterocyclic carbenes (NHC) with 1, 2, 4-oxadiazole-substituents related to natural products: synthesis, structure and potential antitumor activity of some corresponding gold (I) and silver (I) complexes, *European journal of medicinal chemistry*, **101**, 431 (2015).
26. L.G. Bonnet, R.E. Douthwaite, R. Hodgson, J. Houghton, B.M. Kariuki, S. Simonovic, Synthesis, structure and reactivity of palladium (II) complexes of chiral N-heterocyclic carbene–imine and–amine hybrid ligands, *Dalton Transactions*, **21,** 3528 (2004).
27. C.A. Quezada, J.C. Garrison, M.J. Panzner, C.A. Tessier, W.J. Youngs, The Potential Use of Rhodium N-Heterocyclic Carbene Complexes as Radiopharmaceuticals: The Transfer of a Carbene from Ag (I) to RhCl3⨀ 3H2O, *Organometallics* **23**, 4846 (2004).
28. J.C. Garrison, W.J. Youngs, Ag (I) N-heterocyclic carbene complexes: synthesis, structure, and application, *Chemical Reviews* **105,** 3978 (2005).