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Synthesis and crystallographic characterization of multi-donor *N*-heterocyclic carbene chelating ligands and their silver complexes: Potential use in pharmaceuticals

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Abstract

The potential for *N*-heterocyclic carbenes (NHCs) to be used as novel chelating ligands for bio-inorganic pharmaceuticals is discussed. In this paper, we design, synthesize and characterize two NHC precursors, **6** and **7**, that we believe have potential for use as metal chelators for pharmaceuticals. The NHC precursors are composed of imidazolium and pyridine rings that would form mixed donor NHCs upon metallation with medicinally relevant metals. The exploration of the silver chemistry of **6** yielded the dimeric silver NHC complex **8**[BPh_4]$_2$. The study of the silver chemistry of **7** gave **9**[1/3(Ag_4Br_7)] and **10**[NO_3]$_3$. Complex **9**[1/3(Ag_4Br_7)] appears to be a silver biscarbene charge balanced by a silver bromide anionic cluster. Complex **10**[NO_3]$_3$ is a trinuclear silver cluster that is stabilized by NHCs and pyridine rings. Silver NHCs have shown themselves to be excellent transmetallation agents for access to other metal NHC systems. It is envisioned that the silver NHCs **8**[BPh_4]$_2$, **9**[1/3(Ag_4Br_7)] and **10**[NO_3]$_3$ will readily transfer to medicinally relevant metals, such ^{105}Rh.

Keywords: Silver *N*-heterocyclic carbenes; Pharmaceuticals; Imidazolium salts; Mixed donor ligands; X-ray; Trinuclear silver cluster

1. Introduction

The synthesis of metal *N*-heterocyclic carbene (NHC) complexes from imidazolium salts were first reported by Öfele and Wanzlink in 1968 [1]. Lappert and co-workers, a decade later, expanded on this work by synthesizing metal *N*-heterocyclic carbene complexes from electron rich olefins [2]. However, it was not until the isolation of the free carbene, in 1991, by Arduengo and co-workers that *N*-heterocyclic carbenes received a great deal of interest [3]. Since then, the study of *N*-heterocyclic carbenes as novel ligands for the synthesis of organometallic compounds has been an area of intense research [4]. This has been particularly true for the use of NHCs as novel ligands for catalytic functions.

The formation of silver *N*-heterocyclic carbene complexes can be accomplished by the generation of the free carbene and subsequent reaction of the free carbene with a metal reagent [5]. However, some ligand systems have been found to be sensitive to the harsh conditions required to generate the free carbene [5b,5c,6]. Also, the synthesis of metal NHCs by the free carbene method requires the use of anaerobic conditions. The reports of in situ formation of silver NHC complexes from a variety of silver reagents led to the convenient synthesis of silver NHCs in aerobic conditions [7]. However, it was not until the reported transmetallation of silver NHCs to other important metal NHC systems by Lin and colleagues that silver NHC chemistry took on an important role in the exploration of other metal NHC systems [7b]. The incorporation of other donor groups, particularly

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pyridine, into NHC systems has recently received a great deal of attention [7c,8]. The addition of donor groups to multi-dentate NHC ligands allows for the customization of the ligand to suit the needs of the specific metals.

Our group [8e,8f,9a] as well as others [9b,9c] have begun investigating *N*-heterocyclic carbenes in potential pharmaceutical applications. ^{105}Rh is being investigated in cancer therapy due to the excellent β^- emission properties of this radionuclide (0.560 MeV [70%] and 0.250 MeV [30%]) and a sufficiently long half-life, 36 h [10]. It is also an attractive radionuclide due to emission of a small amount of imagable γ-rays (306 keV [5%] and 319 keV [19%]). Currently, ^{105}Rh is only available as a series of chloro-aquo rhodium salts, including the $^{105}RhCl_3 \cdot xH_2O$ species. Recently, we have reported the transmetallation reaction of silver NHCs to a rhodium(III) NHC using $RhCl_3 \cdot 3H_2O$ [9a]. This transmetallation could have potential use in the synthesis of viable ^{105}Rh radiopharmaceuticals.

Targeted pharmaceutical are biomolecules that deliver a medicinal agent to a specific tissue in the body. A typical paradigm for a bifunctional approach for the synthesis of a targeted bioinorganic pharmaceutical is depicted in Fig. 1. The medicinally relevant metal is attached to a ligand, which is attached to the targeting group via a linker group. The targeting moiety can be a large immuno-derived antibody or smaller molecule such as a peptide or non-peptide receptor ligand. We have begun designing imidazolium ligands with functional groups that we envision could easily be attached to a targeting molecule and then undergo metallation to produce bioinorganic pharmaceuticals. Reported within is our progress toward synthesis of radiopharmaceuticals using *N*-heterocyclic carbenes as the metal chelator. We report the design and synthesis of imidazolium salts that could serve as good radiometal chelators and the investigation of their silver chemistry.

2. Results and discussion

2.1. Ligand synthesis

The first synthetic pathway we proposed is depicted in Scheme 1. In this design, the metal chelator is composed of two *N*-heterocyclic carbene rings and one pyridine ring as well as the targeting group (TG). With the advent of peptide synthesizers, the synthesis of peptides has, in general, become routine [11]. Compound **A** is envisioned to be a peptide ending with a histidine derivative. Compound **B** is an imidazolium cation with a leaving group, Y, which allows for easy displacement. The ability to adjust the solubility of a potential drug is very important in the process of designing a radiopharmaceutical [12]. If the radiopharmaceutical is too hydrophilic, the drug will not reside in the target tissue for a sufficient amount of time to accomplish its goal; on the other hand, if it is too hydrophobic, clearance and deposition of the radiopharmaceutical in the body will be a significant concern. Compound **A** and **B** have substituents R_1 and R_2, respectively. These substituents can be altered to give the desired hydrophilicity. The condensation of **A** and **B** should yield the imidazolium salt **C**. With the formation of the metal chelator and attachment of the targeting group complete, we would then begin metallation of **C** with the addition of silver oxide to form the silver NHC complex and subsequent transmetallation with $^{105}RhCl_3 \cdot xH_2O$ to give **D**. The envisioned complex **D** would be a neutral, trivalent rhodium complex. Described below is our progress in the development of NHC precursors such as **C**.

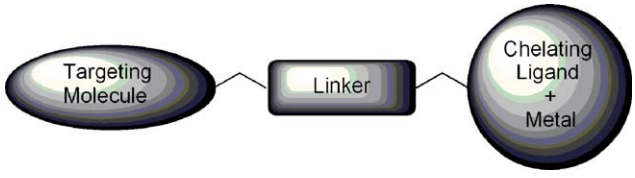
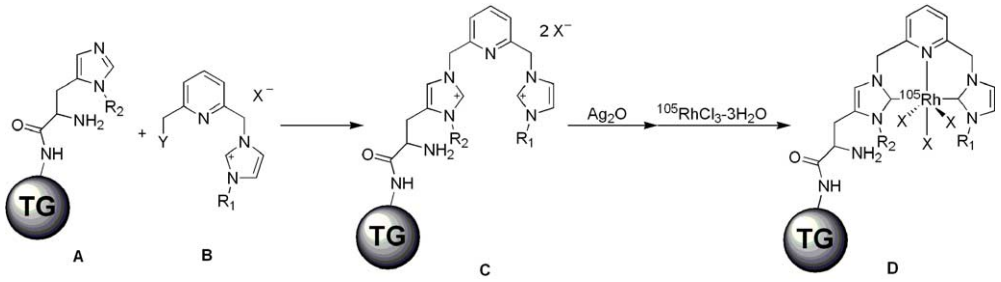


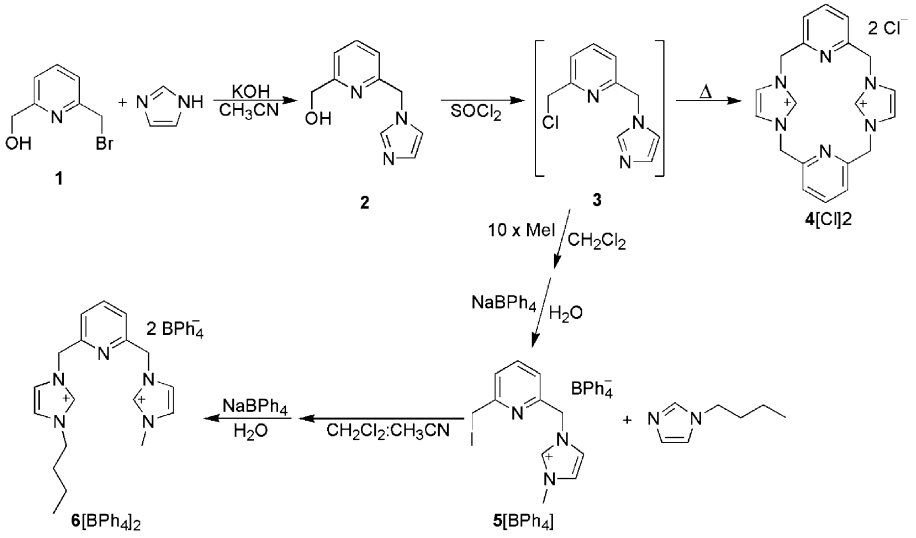
Fig. 1. Bifunctional approach for the synthesis of a radiopharmaceutical.

Our synthetic scheme for the synthesis of an analog of **C** is depicted in Scheme 2. The synthesis of (6-bromomethyl-pyridin-2-yl)-methanol, **1**, was prepared by known literature procedures [13]. The molecular structure of **1** is given in the supporting information. (6-imidazol-1-ylmethyl-pyridin-2-yl)-methanol, **2**, was synthesized by the generation of potassium imidazole by the combination of imidazole and potassium hydroxide in acetonitrile and subsequent addition of **1**. The reaction mixture was stirred for 16 h to give (6-imidazol-1-ylmethyl-pyridin-2-yl)-methanol in 90% yield. Single crystals of **2** suitable for X-ray diffraction studies were grown from a concentrated solution of acetonitrile. The molecular structure of **2** was revealed by X-ray crystallography (Compound **2** is depicted in the supporting information). ^{1}H and ^{13}C NMR spectra of compound **2** are consistent with the molecular structure. ES-MS of **2** (M) gave *m*/*z* peaks at 189.9 and 211.9 corresponding to the $[M + H]^+$ and $[M + Na]^+$ cations, respectively.

The hydroxyl functional group of **2** was chlorinated using thionyl chloride. ^{1}H NMR spectroscopy confirmed the transformation of the pyridylic alcohol into the pyridylic chloride. However, isolation of the 2-chloromethyl-6-imidazol-1-ylmethyl-pyridine, **3**, proved difficult due to the cyclization of **3** to form the dicationic cyclophane **4**$[Cl]_2$. The cyclization of **3** was found to proceed slowly in dilute solutions at room temperature. However, the rate of cyclization of **3** increased when the solution was concentrated and/or heated. Due to this dilute solutions of compound **3** where synthesized and quickly used in the next synthetic step. Methylation of the imidazole was carried out by the addition of a 10-fold excess of methyl iodide to a CH_2Cl_2 solution of **3**.



Scheme 1.



Scheme 2.

The solution was stirred for two days and then evaporated to dryness. The halide salt of **5** was not isolated, but was instead converted into the tetraphenylborate salt by anion exchange using sodium tetraphenylborate to give **5**[BPh_4] in 62% yield [14].

The molecular structure of **5**[BPh_4], depicted in the supporting information, revealed the formation of the desired imidazolium salt as well as an unexpected halide exchange on the pyridylic position. The pyridylic iodide bond length is typical with a bond distance, C(1)–I, of 2.147(3) Å [15]. The ^1H and ^{13}C NMR spectra are consistent with the solid state structure of **5**[BPh_4]. In the ^1H NMR, a resonance of 9.16 ppm is observed, corresponding to the C2–H, which is characteristic of the formation of an imidazolium cation. However, trace amounts of the imidazolium salt of **5**[BPh_4] with chloride on the pyridylic position where found in the NMR and ES-MS spectra of the bulk material. ES-MS of the bulk material gave *m*/*z* peaks of 313.8 and 221.9 for $[M(I)]^+$ and $[M(Cl)]^+$, respectively.

The dicationic imidazolium salt, **6**[BPh_4]$_2$, was synthesized by the combination of **5**[BPh_4] with one equivalent of butyl imidazole in a 1:1 mixture of CH_2Cl_2:CH_3CN to yield the mixed salt, **6**[BPh_4][I]. Anion exchange with sodium tetraphenylborate led to the isolation of **6**[BPh_4]$_2$ in 95% yield. The molecular structure of **6**[BPh_4]$_2$ is depicted in Fig. 2. ^1H and ^{13}C NMR spectra are consistent with the formation of the dicationic species. The two imidazolium C2–H resonances, in the ^1H NMR spectrum, are observed at 8.98 and 9.10 ppm. Analysis of **6**[BPh_4]$_2$ by ES-MS gave corresponding *m*/*z* peaks of 630.3 and 313.8 for $[M - BPh_4]^+$ and $[M - 2(BPH_4)]^{2+}$, respectively.

An alternate synthetic pathway to a plausible ^{105}Rh NHC radiopharmaceutical is depicted in Scheme 3. The proposed metal chelator would be composed of one *N*-heterocyclic carbene ring and two pyridine rings. Proposed compound **E** would be a targeting peptide that is connected to a derivative of **1** by an ether linkage. Compound **F** is a generalized depiction of **2**. It can be envisioned that the substituent R_1 group could be easily altered to give the desired hydrophilicity. Condensation of **E** and **F** should yield the imidazolium salt **G**. Metallation of **G** with silver oxide and transmetallation with $^{105}RhCl_3 \cdot xH_2O$ is expected to give complex **H**. Our progress on the synthesis of NHC precursors such as **G** is given below.

Our synthetic scheme for the synthesis of analogs of **G** is given in Scheme 4. The condensation of compounds **1** and **2** yields the imidazolium cation **7** as the bromide

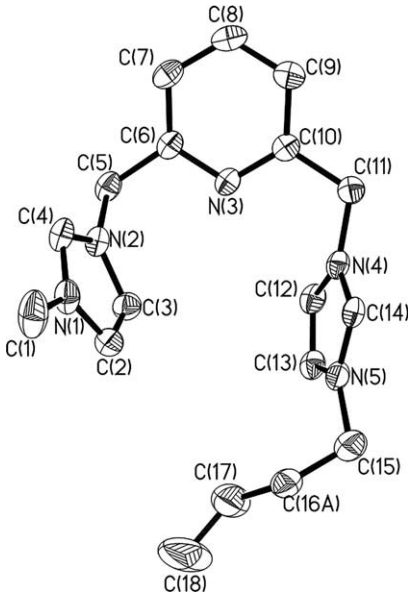


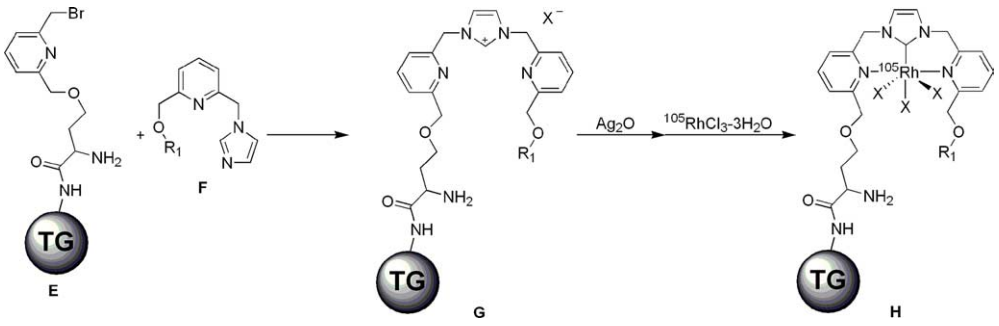
Fig. 2. Molecular structure of the cationic portion of compound **6**$[BPh_4]_2$ shown with 50% displacement ellipsoids. Selected bond lengths (Å) and angles (°): C(1)–N(1) = 1.462(3); N(1)–C(4) = 1.317(3); N(1)–C(2) = 1.365(4); C(2)–C(3) = 1.346(4); N(2)–C(3) = 1.372(3); N(2)–C(4) = 1.332(3); N(2)–C(5) = 1.467(3); C(5)–C(6) = 1.501(4); C(10)–C(11) = 1.509(3); C(11)–N(4) = 1.460(3); N(4)–C(12) = 1.380(3); N(4)–C(14) = 1.321(3); C(12)–C(13) = 1.328(4); N(5)–C(13) = 1.376(3); N(5)–C(14) = 1.329(3); N(5)–C(15) = 1.468(4); C(1)–N(1)–C(4) = 125.7(2); C(2)–N(1)–C(4) = 108.9(2); N(1)–C(4)–N(2) = 108.6(2); C(3)–N(2)–C(4) = 108.2(2); N(2)–C(5)–C(6) = 110.3(2); C(10)–C(11)–N(4) = 113.1(2); C(12)–N(4)–C(14) = 108.0(2); N(4)–C(14)–N(5) = 109.3(2); C(13)–N(5)–C(14) = 107.5(2); C(14)–N(5)–C(15) = 125.7(2).

salt. The molecular structure of **7**[Br] is depicted in Fig. 3. ^1H and ^{13}C NMR spectra in d_6-DMSO agree well with the solid state structure of **7**[Br]. The imidazolium C2–H signal was observed, in the ^1H NMR spectra, at 9.46 ppm. ES-MS analysis of **7**[Br] reveal the *m*/*z* peak 310.9 for the $[M–Br]^+$ cation. Anion exchange of **7**[Br] with sodium tetraphenylborate yielded two tetraphenylborate salts **7**$[BPh_4]$ and **7**(Na)$[BPh_4]_2$. Analysis of the bulk solid by NMR and elemental analysis revealed a 1:1 ratio of **7**$[BPh_4]$ and **7**(Na)$[BPh_4]_2$. Attempts to obtain pure **7**$[BPh_4]$ or **7**(Na)$[BPh_4]_2$ by reducing or increasing the amount of sodium tetraphenylborate, in our hands, did not yield pure products. Crystallization from the bulk material yielded both compounds as determined by X-ray crystallography. Attempts to isolate pure compounds by crystallization were not successful.

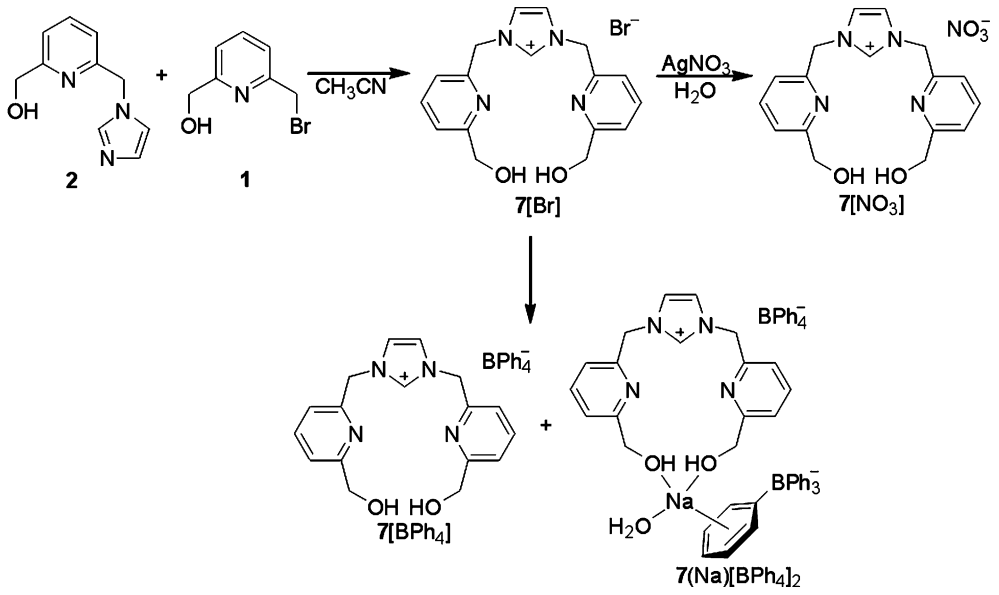
The molecular structure of the cationic portion of **7**$[BPh_4]$, as determined by X-ray diffraction studies, is identical to the cationic portion of **7**[Br] and therefore is not depicted (**7**$[BPh_4]$ is depicted in the supporting information). ^1H and ^{13}C NMR spectra were collected in d_6-DMSO of single crystals of **7**$[BPh_4]$ as determined by X-ray crystallography. The C2–H resonance of **7**$[BPh_4]$ was observed at 9.38 ppm. Unfortunately, ^1H and ^{13}C NMR spectra could not be obtained for **7**(Na)$[BPh_4]_2$ due to problems isolating a sufficient quantity of single crystals. Interestingly, the ^1H and ^{13}C NMR spectra of the bulk mixture of **7**$[BPh_4]$ and **7**(Na)$[BPh_4]_2$ give identical resonances for the cationic portion of the molecule compared to that of pure **7**$[BPh_4]$. We attribute this to either a dynamic effect in solution or the more likely explanation is that the sodium adduct, **7**(Na)$[BPh_4]_2$, does not exist in solution. In the latter case, formation of DMSO adducts of sodium tetraphenylborate is not unreasonable [16].

Compound **7**(Na)$[BPh_4]_2$, depicted in Fig. 4, is a sodium tetraphenylborate adduct of **7**$[BPh_4]$. The sodium molecule is coordinated to two oxygen atoms from the imidazolium cation, one water molecule and a π-interaction from the phenyl ring of a tetraphenylborate anion. The Na–O1 and Na–O2 bond distances are 2.284(2) and 2.328(2) Å, respectively. The sodium to phenyl-ring carbon bond distances range from 2.682(3) to 3.076(3) Å, with an average of 2.874(3) Å. The water molecule is coordinated to the sodium cation, with a Na–O3 bond distance of 2.236(2) Å, as well as hydrogen bonded to the pyridine rings. The donor–acceptor distances for N1–O3 and N4–O3 are 2.810(3) and 2.864(3) Å, respectively.

Compound **7**$[NO_3]$ was synthesized by anion exchange of **7**[Br] with one equivalent of $AgNO_3$ to



Scheme 3.



Scheme 4.

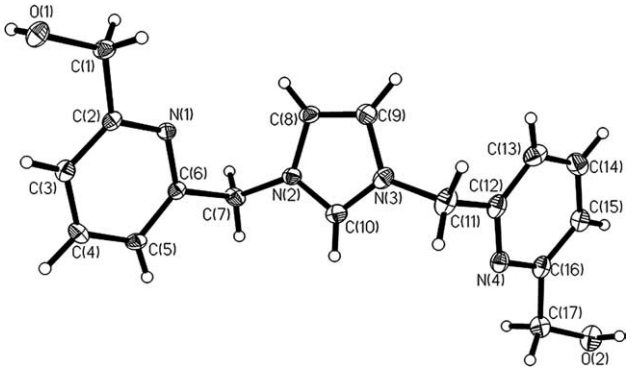


Fig. 3. Molecular structure of the cationic portion of compound **7**[Br] shown with 50% displacement ellipsoids. Selected bond lengths (Å) and angles (°): O(1)–C(1) = 1.408(3); O(2)–C(17) = 1.421(4); C(1)–C(2) = 1.507(4); C(16)–C(17) = 1.503(4); C(6)–C(7) = 1.510(4); C(11)–C(12) = 1.512(4); N(2)–C(7) = 1.462(4); N(3)–C(11) = 1.470(4); N(2)–C(8) = 1.376(3); N(3)–C(9) = 1.377(4); N(2)–C(10) = 1.325(4); N(3)–C(10) = 1.318(4); C(8)–C(9) = 1.338(4); O(1)–C(1)–C(2) = 113.3(2); O(2)–C(17)–C(16) = 114.8(3); C(6)–C(7)–N(2) = 110.2(2); N(3)–C(11)–C(12) = 111.3(2); C(7)–N(2)–C(10) = 125.4(2); C(10)–N(3)–C(11) = 126.4(3); C(8)–N(2)–C(10) = 108.2(2); C(9)–N(3)–C(10) = 108.8(2); N(2)–C(10)–N(3) = 108.8(3).

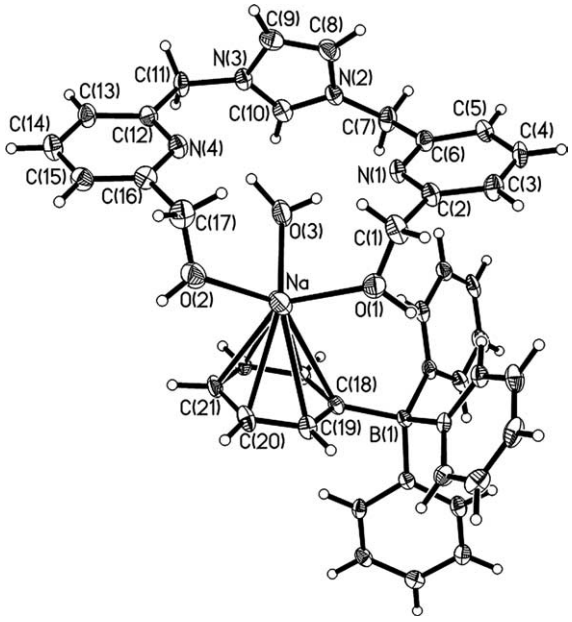


Fig. 4. Molecular structure of the cationic portion of compound **7**(Na)[BPh_4]$_2$ shown with 50% displacement ellipsoids. Selected bond lengths (Å) and angles (°): Na–O(1) = 2.284(2); Na–O(2) = 2.328(2); Na–O(3) = 2.236(2); Na–C(18) = 3.076(3); Na–C(19) = 2.882(3); Na–C(20) = 2.703(3); Na–C(21) = 2.682(3); Na–C(22) = 2.861(3); Na–C(23) = 3.039(3); O(1)–C(1) = 1.413(3); O(2)–C(17) = 1.425(4); N(2)–C(7) = 1.462(3); N(3)–C(11) = 1.461(3); N(2)–C(10) = 1.326(3); N(3)–C(10) = 1.330(3); N(2)–C(8) = 1.360(3); N(3)–C(9) = 1.378(3); C(8)–C(9) = 1.341(4); O(1)–Na–O(2) = 118.35(9); O(1)–Na–O(3) = 89.94(8); O(2)–Na–O(3) = 89.34(8); Na–O(1)–C(1) = 126.50(16); Na–O(2)–C(17) = 123.95(16); O(1)–C(1)–C(2) = 112.6(2); O(2)–C(17)–C(16) = 111.3(2); N(2)–C(7)–C(6) = 110.68(19); N(3)–C(11)–C(12) = 114.73(19); N(2)–C(10)–N(3) = 108.7(2).

produce the nitrate salt. The resulting precipitate was filtered off and the filtrate evaporated to dryness. The resulting thick oil slowly crystallized over a 12 h period to obtain **7**[NO_3] in 100% yield. Crystals of **7**[NO_3] were obtained by slow evaporation of a concentrated solution from methanol. The cationic portion is isostructural to the imidazolium salt **7**[Br] and therefore will not be discussed (the molecular structure of complex **7**[NO_3] is depicted in the supporting information). ^{1}H and ^{13}C NMR spectra of **7**[NO_3] are consistent with the molecular structure determined by X-ray crystallography. The imidazolium C2–H resonance for **7**[NO_3] appears at 9.40 ppm. Analysis by ES-MS gives a m/z peak at 310.8 corresponding to the $[M - NO_3]^+$ cation.

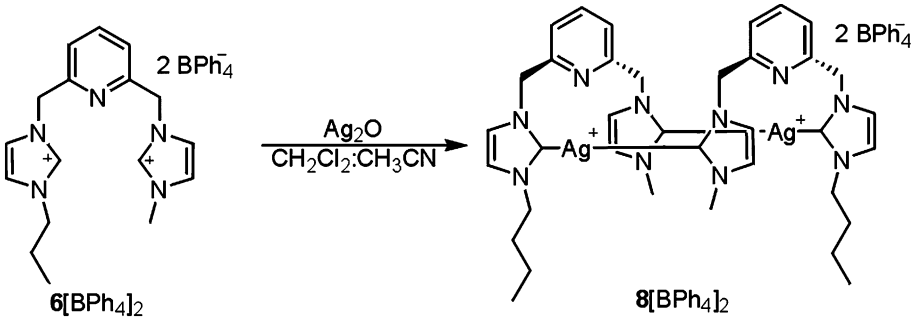
2.2. Synthesis of silver complexes

Silver complexes of the imidazolium salts were synthesized according to known literature procedures [7b–9a]. The imidazolium salt **6**[BPh_4]$_2$ was reacted with one equivalent of silver oxide to result in **8**[BPh_4]$_2$ in good yield. Unfortunately, single crystals of complex **8**[BPh_4]$_2$ could not be obtained in order to elucidate the structure of the complex with X-ray diffraction studies. However, based on the literature precedent it is very likely that complex **8**[BPh_4]$_2$ is a dimer, as depicted in Scheme 5, in the solid state [8a,8e,8f,8h]. Silver *N*-heterocyclic carbene complexes usually form silver biscarbene complexes when the counteranion is non-coordinating. The formation of a silver NHC dimer could lead to several structural isomers for **8**[BPh_4]$_2$, Fig. 5. The pyridine rings could face each other (head to head) or be opposed to each other (head to tail). Several similar silver pyridine-NHC complexes have been structurally characterized [8e,8f,8h]. All structures to date show the pyridine rings in the head to head configuration. The manner, in which, the *N*-heterocyclic carbene rings bind to the silver cations also form structural isomers. The silver cations can be bound by one *N*-butyl NHC ring and one *N*-methyl NHC ring, which is designated as "mixed" in Fig. 5, or each of the silver cations can be bound by two *N*-butyl NHC rings or two *N*-methyl NHC rings, labeled as "same". Taking into account literature precedent and steric effects, we expect that the head to head/mixed isomer to be the most stable and therefore most likely to form.

^{1}H and ^{13}C spectra of **8**[BPh_4]$_2$ are not complex and therefore suggest that the material consists of only one of the possible structural isomers. However, it has been suggested that silver carbenes are dynamic in solution [7b]. If this is indeed the case and the interconversion between the various structural isomers is faster than the NMR timescale then the resonances for the isomers would be expected to average resulting in a spectrum consistent with a single compound. The most notable spectral feature of complex **8**[BPh_4]$_2$ is the absence of the imidazolium C2–H signal in the ^{1}H NMR spectrum. Slight downfield shifts (~0.1 ppm) were noticeable for the protons on the backbone of the NHC ring. The remaining proton resonances for the cationic portion of **8**[BPh_4]$_2$ show an upfield shift that is characteristic for silver NHCs of the type [8a]. The ^{13}C NMR spectra of **8**[BPh_4]$_2$ show two broad resonances at 180.0 and 180.8 ppm that correspond to the carbenes of the *N*-butyl and *N*-methyl NHC rings.

The imidazolium salt, **7**[Br], was reacted with one equivalent of silver oxide in a 1:1 mixture of methylene chloride and acetonitrile to yield the silver complex, **9**[1/3(Ag_4Br_7)], in moderate yield (Scheme 6). We must point out that our assignment for the anion of **9** is based upon the available evidence that could be obtained. It is possible that other molecular motifs, other than the one we proposed, could be consistent with the collected data. Once complex **9**[1/3(Ag_4Br_7)] is isolated as a solid, it proved difficult to solubilize the material in any common organic solvent including the solvents, methylene chloride and acetonitrile, from which **9**[1/3(Ag_4Br_7)] was originally isolated. This could perhaps be attributed to the formation of fairly strong argentophillic interactions between the silver *N*-heterocyclic carbene complex and the anionic silver halide cluster in the solid state [7b,7c,8g,17]. Complex **9**[1/3(Ag_4Br_7)] was found to be somewhat soluble in DMF and DMSO. Unfortunately, single crystals of suitable size for X-ray diffraction studies could not be obtained from these solvents.

^{1}H and ^{13}C NMR analysis of **9**[1/3(Ag_4Br_7)] in d_6-DMSO revealed the absence of the imidazolium C2–H signal and the presence of a carbene resonance at 181.5 ppm. The carbene resonance was observed as a sharp singlet in the ^{13}C NMR. The observation of the carbene resonance as a singlet rather than a doublet of doublets are not uncommon in the literature [7,8d,8e,8j,8l,18]. Elemental analysis of **9**[1/3(Ag_4Br_7)] is consistent with the presence of an anionic silver halide cluster. Analysis of the data show that the trianionic silver halide cluster $Ag_4Br_7^{3-}$ is the likely anionic species; however, multiples of this anionic species such as $Ag_8Br_{14}^{6-}$, reported by Meyer and co-workers [17d], are



Scheme 5.

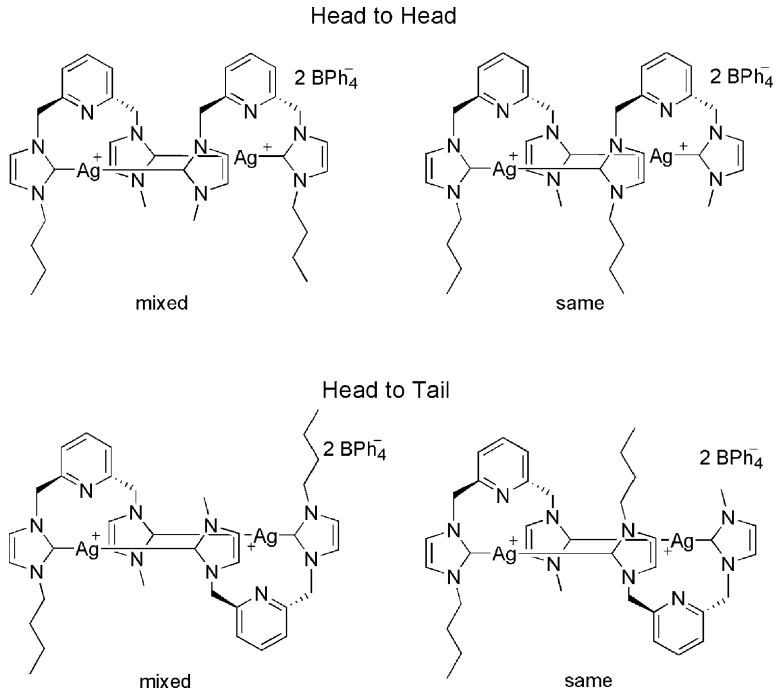
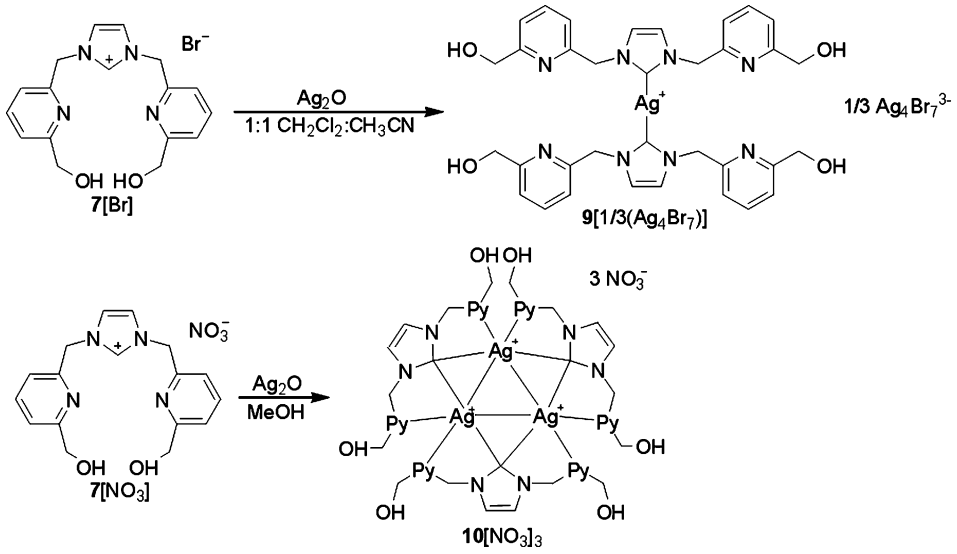


Fig. 5. Possible structural isomers of complex **8**[BPh_4]$_2$.



Scheme 6.

also possible. ES-MS of **9**[1/3(Ag_4Br_7)] shows the presence of the silver biscarbene, $[L_2–^{107}Ag]^+$ and $[L_2–^{109}Ag]^+$, with *m*/*z* peaks at 727.2 and 729.2. The negative mode ES-MS spectrum of **9**[1/3(Ag_4Br_7)] did not show evidence of the trianionic silver halide cluster; however the presence of the $AgBr_2^-$ was detected.

The trinuclear silver NHC complex, **10**[NO_3]$_3$, was synthesized by reaction of the imidazolium salt **7**[NO_3] with 0.6 equivalents of silver oxide in methanol to give **10**[NO_3]$_3$ in 92% yield. Similar analogs of **10** were reported by Catalano and co-workers [8j,8l]. The molecular structure of complex **10**[NO_3]$_3$ was revealed by X-ray diffractions studies and is depicted in Fig. 6. Single crystals of complex **10**[NO_3]$_3$ were grown from a concentrated 1:1 methanol:acetonitrile solution. The trinuclear silver cluster is composed of silver-silver bonding distances that range from 2.7869(6) to 2.8070(5) Å with bonding angles that range from 59.761(13) to 60.476(13)°. The *N*-heterocyclic carbenes are symmetrically bound to the cluster with silver-carbene distance that range from 2.216(5) to 2.243(5) Å with an average of 2.229(5) Å. The trinuclear silver cluster is also stabilized by six coordinating pyridine rings. Several of the pyridine rings are disordered with two of the pyridine

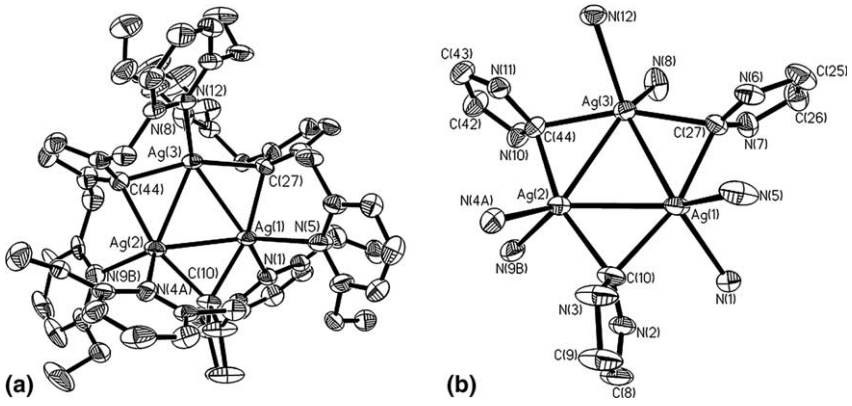


Fig. 6. Molecular structure of the cationic portion of compound **10**$[NO_3]_3$ shown with 50% displacement ellipsoids. Selected bond lengths (Å) and angles (°): Ag(1)–Ag(2) = 2.7869(6); Ag(1)–Ag(3) = 2.7870(5); Ag(2)–Ag(3) = 2.8070(5); C(10)–Ag(1) = 2.231(5); C(10)-Ag(2) = 2.219(5); C(27)–Ag(1) = 2.222(4); C(27)–Ag(3) = 2.243(5); C(44)–Ag(2) = 2.216(5); C(44)–Ag(3) = 2.241(5); N(1)–Ag(1) = 2.497(4); N(5)–Ag(1) = 2.509(5); N(8)–Ag(3) = 2.511(4); N(12)–Ag(3) = 2.504(4); N(4A)–Ag(2) = 2.656(16); N(9B)–Ag(2) = 2.38(2); Ag(1)–Ag(2)–Ag(3) = 59.764(13); Ag(1)–Ag(3)–Ag(2) = 59.761(13); Ag(2)–Ag(1)–Ag(3) = 60.476(13); Ag(1)–C(10)–Ag(2) = 77.54(14); Ag(1)–C(27)–Ag(3) = 77.24(14); Ag(2)–C(44)–Ag(3) = 78.06(16).

rings, including the nitrogen atom, being disordered over two different positions (depictions of these disorders are shown in the supporting information, the disordered pyridine rings are those rings with N4A, N4B, N9A and N9B as the nitrogen atoms). The disorders in these rings lead to pyridine–silver clusters distances with both shorter and longer than average interactions compared to the pyridine rings that were not disordered. The pyridine nitrogen–silver cluster distances range from 2.38(2) to 2.656(16) Å with an average of 2.52(1) Å.

The ^1H and ^{13}C NMR spectra of complex **10**$[NO_3]_3$ were collected in CD_3OD and d_6-DMSO and are consistent with the solid state structure. Interestingly, the NMR resonances for complex **10**$[NO_3]_3$ in d_6-DMSO are very broad. This could be due to dynamic behavior of the trinuclear complex in solution. DMSO adduct complexes with the trinuclear silver cluster, **10**$[NO_3]_3$, could result in broad resonances on the NMR timescale. The spectra of **10**$[NO_3]_3$ in CD_3OD gave sharp signals. The ^1H NMR spectra in both solvents show the absence of the imidazolium proton. Carbene resonances were not observed in the spectra collected from either CD_3OD or d_6-DMSO. Interestingly, ES-MS analysis of **10**$[NO_3]_3$ did not show the presence of the tricationic silver cluster. Analysis of the spectrum shows the existence of the cationic silver biscarbene (cationic portion of **9**$[1/3(Ag_4Br_7)]$) (L_2–Ag, where L = one NHC ligand) as well as the silver monocarbene (L–Ag).

In conclusion, we have synthesized and structurally characterized two tridentate pyridine *N*-heterocyclic carbene precursors, **6** and **7**, that we believe have potential for use as metal chelators in the synthesis of radiopharmaceuticals. These *N*-heterocyclic carbene precursors should form very strong bonds to the radionuclide and thereby reduce disassociation of the radiometal from the metal chelator and deposition of the radiometal in the body. We have also synthesized and characterized several silver complexes from these NHC precursors, **8**$[BPh_4]_2$, **9**$[1/3(Ag_4Br_7)]$ and **10**$[NO_3]_3$. As mentioned earlier, ^{105}Rh is being investigated for potential use in cancer therapy. We have previously reported that silver NHC complexes can be transferred to Rh(III) centers [9a]. Our future work will investigate the transfers of the silver NHC complexes, **8**$[BPh_4]_2$, **9**$[1/3(Ag_4Br_7)]$ and **10**$[NO_3]_3$, to $Rh(III)Cl_3 \cdot 3H_2O$ as well as other relevant radiometals. We also plan on developing the chemistry necessary for the attachment of targeting groups to these radiometal chelators.

3. Experimental section

3.1. General considerations

All reactions were carried out in aerobic conditions. Dry acetonitrile was obtained from a PureSolv™ solvent purification system. All other solvents and reagents were used as received. ^1H and ^{13}C NMR data were recorded on a Varian Gemini 300 MHz and Inova 400 MHz instruments. The spectra were referenced to the residual protons and the ^{13}C signals of the deuterated solvents. Mass spectrometry data were collected on a Bruker Daltons (Billerica, MA) Esquire-LC mass spectrometer equipped with ESI.

3.2. X-ray structure determination details

Crystals of **2**, **5**$[BPh_4]$, **6**$[BPh_4]_2$, **7**[Br], **7**$[BPh_4]$, **7**$[NO_3]$, **7**(Na)$[BPh_4]_2$ and **10**$[NO_3]_3$ were coated in paratone oil and mounted on a CryoLoop™ and placed on the goniometer head under a stream of nitrogen cooled to 100 K. The data were collected on a Bruker APEX CCD diffractometer with graphite-monochromated Mo

Kα radiation ($\lambda = 0.71073$ Å). Crystallographic and collection parameters for all structures are listed in Table 1. The unit cell was determined by using reflections from three different orientations. The data were integrated using SAINT [19]. An empirical absorption correction and other corrections were applied to the data using multi-scan SADABS [19]. Structure solution, refinement, and modeling were accomplished by using the Bruker SHELXTL package [19,20]. The structure was determined by full-matrix least-squares refinement of F^2 and the selection of the appropriate atoms from the generated difference map. Hydrogen atom positions were calculated with the exception of **7**[Br]. U_{iso}(H) values for hydrogen atoms of all structures were fixed according to a riding model.

3.2.1. Preparation of 6-imidazol-1-ylmethyl-pyridin-2-yl-methanol (2)

In a 250 mL round bottom flask was placed imidazole (0.340 g, 5 mmol) and finely ground KOH (0.335 g, 6 mmol). To the flask was then added 60 mL of dried acetonitrile. The solution was stirred for approximately 2 h over which time potassium imidazole formed. (6-bromomethyl-pyridin-2-yl)-methanol (0.202 g, 1 mmol) was added to the solution. The solution was stirred for 16 h at room temperature. The solution was filtered and **2** was obtained as a slightly yellow solid after evaporation. The material was further purified by chromatography on silica using methanol as the eluent ($R_f = 0.7$). Yield: 0.853 g, 4.51 mmol, 90%. Anal. calc. for $C_{10}H_{11}N_3O \cdot H_2O$: C, 57.94; H, 6.33; N, 20.28. Found: C, 57.91; H, 5.49; N, 20.40%. ES-MS (*m*/*z*): calc., 190.1, $[M + H]^+$ and 212.1, $[M + Na]^+$; found, 189.9 and 211.9. ^{1}H NMR (300 MHz, d_6-DMSO): δ 4.53 (s, 2H, CH_2), 5.25 (s, 2H, CH_2), 5.48, (br s, 1H, O*H*), 6.91 (s, 1H, Imid H), 6.93 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr) 7.19 (s, 1H, Imid H), 7.39 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr), 7.74 (s, 1H, Imid H) 7.77 (t, $^3J = 7.8$ Hz, 1H, *p*-Pyr). ^{13}C{^{1}H} NMR (75 MHz, d_6-DMSO): δ 51.3, 64.1 (CH_2), 119.2, 119.4, 119.9, 128.7, 137.7, 137.8, 155.8, 161.9 (aromatic).

3.2.2. Preparation of 2-chloromethyl-6-imidazol-1-ylmethyl-pyridine (3)

Twenty millilitres of $SOCl_2$ was added to a flask containing (6-imidazol-1-ylmethyl-pyridin-2-yl)-methanol (1.89 g, 10 mmol). The solution was stirred for 2 h. The excess $SOCl_2$ was removed by vacuum distillation and the solid dissolved in approximately 100 mL of water. The solution was made basic using Na_2CO_3 and extracted using CH_2Cl_2 (3 × 50 mL), dried with $MgSO_4$, and filtered. Compound **3** was found to undergo self-condensation when allowed to stand at room temperature. The self-condensation reaction was accelerated upon concentration of the solution and upon mild heating. Compound **3** was typically not isolated and further reactions were carried out using dilute solutions of **3** in CH_2Cl_2. Isolation of **3** could be achieved by evaporation of the CH_2Cl_2 under reduced pressure to obtain an oily residue. NMR of the residue gives a spectrum that is fairly clean (traces of the self-condensation reaction were observed) and consistent with the desired compound. ^{1}H NMR (300 MHz, d_6-DMSO): δ 4.76 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 6.93 (s, 1H, Imid H), 7.03 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr), 7.21 (s, 1H, Imid H), 7.47 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr), 7.70 (s, 1H, Imid H), 7.83 (t, $^3J = 7.8$ Hz, 1H, *p*-Pyr).

3.2.3. Preparation of 2-iodomethyl-6-(methylimidazolium-methy)-pyridine tetraphenylborate (5[BPh4])

Iodomethane (14,1 g, 100 mmol) was added to a solution of 10 mmol of 2-chloromethyl-6-imidazol-1-ylmethyl-pyridine in CH_2Cl_2 The solution was stirred at room temperature for 4 days. The solvent was removed and approximately 200 mL of water was added to the flask. The solution was allowed to stir for 2 h. Sodium tetraphenyl borate (3.8 g, 11 mmol) was then added to the water solution. The resulting solid was filtered with a course filter and allowed to dry in the oven (40 °C). Crystals of **5**[BPh_4] were easily grown by slow evaporation of 1:1 CH_3CN:EtOH or acetone. Yield: 3.91 g, 6.17 mmol, 62%. Anal. calc. for $C_{35}H_{33}N_3IB$: C, 66.33; H, 5.25; N, 6.63. Found: C, 67.24; H, 5.28; N, 6.79%. ES-MS (*m*/*z*): calc., 314.0, $[M - BPh_4]^+$; found, 313.8. ^{1}H NMR (300 MHz, d_6-DMSO): δ 3.86 (s, 3H, N–CH_3), 4.56 (s, 2H, CH_2), 5.51 (s, 2H, CH_2), 6.81 (t, $^3J = 6.9$ Hz, 4H, B-C–CH–CH–C*H*), 6.95 (t, $^3J = 6.9$ Hz, 8H, B–C–CH–C*H*–CH), 7.21 (br s, 8H, B–C–C*H*–CH), 7.28 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr), 7.52 (d, $^3J = 7.8$ Hz, 1H, *m*-Pyr), 7.70 (s, 1H, N–C*H*–CH–N), 7.75 (s, 1H, N–CH–C*H*–N), 7.82 (t, $^3J = 7.8$ Hz, 1H, *p*-Pyr), 9.16 (s, 1H, N=C*H*–N). ^{13}C{^{1}H} NMR (75 MHz, d_6-DMSO): δ 7.3 (CH_3), 35.9, 52.9 (CH_2), 121.1, 121.5, 122.7, 122.9, 123.6, 125.3 (q, $^2J = 2.9$ Hz, B–C–*C*), 135.5, 137.2, 138.6, 153.4, 158.7 163.4 (q, $^1J = 49.0$ Hz, B–*C*).

3.2.4. Preparation of 2-(methylimidazoliummethy)-6-(butylimidazoliummethyl)-pyridine tetraphenylborate (6[BPh4]2)

2-(iodomethyl)-6-(methylimidazoliummethyl)-pyridine tetraphenylborate (0.633 g, 1 mmol), 40 mL of a 1:1 solution of CH_2Cl_2:CH_3CN and a stirring bar were placed into a flask. *N*-butylimidazole (0.124 g, 1 mmol) was then added to the solution. The solution was stirred for 2 days at room temperature. The solution was then evaporated under reduced pressure and approximately 50 mL of water was added to the flask containing the solid. To the solution was added excess sodium tetraphenylborate. The flask was heated to reflux for 4 h and allowed to cool to room temperature. The white solid was filtered and allowed to dry in air for 3 days. Yield:

Table 1
Crystallopgraphic and data collection parameters

	$C_{10}H_{11}N_3O$	$C_{35}H_{33}BIN_3$	$C_{66}H_{65}B_2N_5$	$C_{17}H_{19}BrN_4O_2$
Formula weight	189.22	633.35	949.85	391.27
Crystal dimens (mm)	$0.30 \times 0.10 \times 0.10$	$0.45 \times 0.45 \times 0.20$	$0.20 \times 0.15 \times 0.10$	$0.15 \times 0.12 \times 0.03$
Cryst. syst.	Triclinic	Orthorhombic	Triclinic	Monoclinic
Space group	$P\bar{1}$	$Pna2_1$	$P\bar{1}$	$C2/c$
a (Å)	8.0236(8)	16.844(4)	10.9398(12)	10.934(3)
b (Å)	9.4725(9)	18.250(4)	14.0711(15)	13.806(3)
c (Å)	12.7632(13)	9.560(2)	17.6512(19)	22.545(5)
α (°)	81.203(2)	90	77.495(2)	90
β (°)	78.332(2)	90	74.029(2)	96.539(5)
γ (°)	85.011(2)	90	88.866(2)	90
V (Å^3)	937.25(16)	2938.9(11)	2548.0(5)	3381.1(12)
Z	4	4	2	8
$\rho_{calc.}$ (mg m^{-3})	1.341	1.431	1.238	1.537
μ (mm^{-1})	0.091	1.119	0.071	2.449
2θ limit (°)	56.52	56.58	54.98	55.12
	$-10 \leqslant h \leqslant 10$	$-22 \leqslant h \leqslant 22$	$-14 \leqslant h \leqslant 14$	$-14 \leqslant h \leqslant 14$
	$-12 \leqslant k \leqslant 12$	$-23 \leqslant k \leqslant 23$	$-18 \leqslant k \leqslant 18$	$-17 \leqslant k \leqslant 17$
	$-16 \leqslant l \leqslant 16$	$-12 \leqslant l \leqslant 12$	$-22 \leqslant l \leqslant 22$	$-28 \leqslant l \leqslant 29$
Total data collected	8343	25,476	22,050	14,394
No. of indep. reflns.	4332	7059	11,360	3878
R_{int}	0.0164	0.0328	0.0377	0.0487
Absorp. corr.	multi-scan (SADABS)	multi-scan (SADABS)	multi-scan (SADABS)	multi-scan (SADABS)
Transmission: t_{min}/t_{max}	0.8427/0.9910	0.7140/0.8072	0.7087/0.9929	0.7136/0.9302
No. of data/restr/params	4332/0/261	7059/1/362	11,360/11/669	3878/0/276
$R_1[F_o^2 \geqslant 2(F_o^2)]$	0.0554	0.0396	0.0688	0.0477
$wR_2[F_o^2 \geqslant -3(F_o^2)]$	0.1330	0.1072	0.1790	0.1011
Goodness-of-fit	1.044	1.029	1.014	1.107
	$C_{41}H_{39}BN_4O_2$	$C_{65}H_{61}B_2N_4NaO_3$	$C_{55}H_{62}Ag_3N_{17}O_{16}$	$C_{17}H_{19}N_5O_5$
Formula weight	630.57	990.79	1540.83	373.37
Crystal dimens (mm)	$0.40 \times 0.30 \times 0.20$	$0.50 \times 0.50 \times 0.10$	$0.50 \times 0.50 \times 0.40$	0.40×0.40 0.20
Cryst. syst.	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1$	Pc	$P\bar{1}$	$C2/c$
a (Å)	9.0717(9)	12.842(5)	14.2244(11)	10.778(3)
b (Å)	16.6864(17)	11.329(5)	14.5877(11)	14.137(3)
c (Å)	10.8174(11)	18.460(8)	14.6499(11)	22.983(6)
α (°)	90	90	83.9930(10)	90
β (°)	90.398(2)	105.757(7)	85.5190(10)	94.733(4)
γ (°)	90	90	85.6060(10)	90
V (Å^3)	1637.4(3)	2584.8(18)	3006.8(4)	3490.1(15)
Z	2	2	2	8
$\rho_{calc.}$ (Mg m^{-3})	1.279	1.273	1.702	1.421
μ (mm^{-1})	0.079	0.084	1.051	0.107
2θ limit (°)	56.92	56.64	55.12	55.10
	$-12 \leqslant h \leqslant 12$	$-16 \leqslant h \leqslant 16$	$-18 \leqslant h \leqslant 18$	$-13 \leqslant h \leqslant 14$
	$-22 \leqslant k \leqslant 22$	$-14 \leqslant k \leqslant 14$	$-18 \leqslant k \leqslant 18$	$-18 \leqslant k \leqslant 18$
	$-14 \leqslant l \leqslant 14$	$-24 \leqslant l \leqslant 24$	$-18 \leqslant l \leqslant 19$	$-29 \leqslant l \leqslant 29$
Total data collected	14635	29814	37589	20880
No. of indep. reflns.	7527	11407	13560	4004
R_{int}	0.0222	0.0372	0.0296	0.0363
Absorp. corr.	multi-scan (SADABS)	multi-scan (SADABS)	multi-scan (SADABS)	multi-scan (SADABS)
Transmission: t_{min}/t_{max}	0.8552/0.9844	0.7000/0.9916	0.4607/0.6548	0.7523/0.9789
No. of data/restr/params	7527/1/435	11407/2/688	13560/0/1111	4004/0/263
$wR_2[F_o^2 \geqslant -3(F_o^2)]$ $R_1[F_o^2 \geqslant 2(F_o^2)]$	0.0441	0.0533	0.0570	0.0413
$wR_2[F_o^2 \geqslant -3(F_o^2)]$	0.1006	0.1367	0.1433	0.1087
Goodness-of-fit	1.099	1.040	1.185	1.012

0.90 g, 0.95 mmol, 95%. Anal. calc. for $C_{66}H_{65}N_5B_2$: C, 83.41; H, 6.90; N, 7.37. Found: C, 82.89; H, 6.97; N, 7.54%. ES-MS (m/z): calc., 630.3, $[M - BPh_4]^+$ and 155.6, $[M - 2BPh_4]^{2+}$; found, 630.3 and 313.8. ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.89 (t, $^3J = 7.4$ Hz, 3H, CH_3), 1.24 (q, $^3J = 7.4$ Hz, 2H, CH_2), 1.74 (m, $^3J = 7.4$ Hz, 2H, CH_2), 3.81 (s, 3H, CH_3), 4.13 (t, $^3J = 7.4$ Hz, 2H, CH_2), 5.44 (s, 2H, Pyr-CH_2-Im), 5.46 (s, 2H, Pyr-CH_2-Im), 6.76 (t, $^3J = 7.2$ Hz, 8H, B–C–CH–CH–CH), 6.90 (t, $^3J = 7.2$ Hz, 16H, B–C–CH–

C*H*–CH), 7.16 (br s, 16H, B-C–C*H*–CH–CH), 7.39 (d, $^3J = 7.7$ Hz, 1H, *m*-Pyr), 7.40 (d, $^3J = 7.7$ Hz, 1H, *m*-Pyr), 7.58 (t, $^3J = 1.8$ Hz, 1H, N–C*H*-CH–N), 7.62 (t, $^3J = 1.8$ Hz, 1H, N–CH–C*H*–N), 7.63 (t, $^3J = 1.8$ Hz, 1H, N–C*H*–CH–N), 7.73 (t, $^3J = 1.8$ Hz, 1H, N–C*H*–CH–N), 7.79 (t, $^3J = 7.7$ Hz, 1H, *p*-Pyr), 8.98 (s, 1H, N–CH–N), 9.10 (s, 1H, N=CH–N). $^{13}C\{^1H\}$ NMR (100 MHz, d_6-DMSO): δ 13.2, 18.7, 31.3, 35.8, 48.7, 52.6, 52.7 (CH_2 and CH_3), 121.6, 122.2, 122.3, 123.2, 123.5, 123.6, 125.4 (q, $^2J = 2.3$ Hz, B–C–*C*), 126,7, 134.1, 135.7, 136.8, 137.3, 139.0, 153.8, 163.6 (q, $^1J = 49.6$ Hz, B–C).

3.2.5. Preparation of 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium bromide (one-pot synthesis) (7[Br])

In a 50 mL round bottom flask was placed imidazole (0.068 g, 1.0 mmol), finely powdered KOH (0.067 g, 1.2 mmol), 20 mL of dry acetonitrile and a stirring bar. The solution was allowed to stir for approximately 2 h before 2-(bromomethyl)-6-methanol-pyridine (0.202 g, 1.0 mmol) was added to the solution. The solution was stirred overnight at room temperature. The solution was filtered and an additional equivalent of the 2-(bromomethyl)-6-methanol-pyridine (0.202 g, 1.0 mmol) was added to the solution. The solution was stirred for 18 h and a white solid was obtained by filtration. Yield: 0.25 g, 0.64 mmol, 64%. Anal. calc. for $C_{17}H_{19}N_4O_2Br$: C, 52.30; H, 4.91; N, 14.36. Found: C, 51.05; H, 4.98; N, 14.03%. ES-MS (*m*/*z*): calc., 311.2, $[M - Br]^+$; found, 310.9. ^1H NMR (300 MHz, d_6-DMSO): δ 4.50 (d, $^3J = 5.7$ Hz, 4H, Pyr–CH_2–OH), 5.47 (t, $^3J = 5.7$ Hz, 2H, Pyr–CH$_2$–O*H*), 5.59 (s, 4H, Pyr–CH_2-Imid), 7.29 (d, $^3J = 7.8$ Hz, 2H, *m*-Pyr), 7.47 (d, $^3J = 7.8$ Hz, 2H, *m*-Pyr), 7.83 (s, 2H, N–C*H*–C*H*–N), 7.88 (t, $^3J = 7.8$ Hz, 2H, *p*-Pyr), 9.46 (s, 1H, N=C*H*–N). $^{13}C\{^1H\}$ NMR (75 MHz, d_6-DMSO): δ 53.1, 64.0 (CH_2), 120.0, 120.4, 123.2, 137.6, 138.1, 152.6, 162.3 (aromatic).

3.2.6. Preparation of 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium tetraphenylborate (7[BPh$_4$]) and 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium tetraphenylborate – NaBPh$_4$ adduct (7(Na)[BPh$_4$]$_2$)

1,3-di{2-(Hydroxymethyl)pyridine-6-methyl}-imidazolium bromide (0.391g, 1 mmol) was placed in a 125 mL flask and dissolved in 25 mL of water. In a separate flask was prepared a concentrated sodium tetraphenyborate solution in water. The sodium tetraphenylborate solution was slowly added to the solution containing the imidazolium salt until no additional precipitate occurred. The suspension was cooled to −20 °C overnight. The solid was allowed to warm up to room temperature and the precipitate was filtered using a course frit. The white solid was allowed to dry at room temperature overnight. Yield (based upon EA and NMR): 0.62 g, 0.77 mmol, 76%. Analysis of the bulk solid by NMR, elemental analysis and X-ray crystallography led to the conclusion that the bulk solid was composed of a 1:1 mixture of **7**[BPh_4] and **8**[BPh_4]$_2$. Anal. calc. for (1:1 $C_{41}H_{39}BN_4O_2$:$C_{65}H_{61}B_2N_4NaO_3$): C, 78.41; H, 6.23; N, 7.28. Found: C, 77.54; H, 6.14; N, 7.50%. Crystals of both of these compounds could be obtained from the slow evaporation of acetonitrile. Spectroscopic analysis of **7**[BPh_4] of these compounds were accomplished by isolation of the single crystals of each compound as determined by X-ray crystallography. *Spectral properties of* **7**[**BPh$_4$**]. ^1H NMR (300 MHz, d_6-DMSO): δ 4.50 (d, $^3J = 5.7$ Hz, 4H, Pyr–CH_2–OH), 5.45 (t, $^3J = 5.7$ Hz, 2H, Pyr–CH$_2$–O*H*), 5.55 (s, 4H, Pyr–CH_2-Imid), 6.77 (t, $^3J = 7.2$ Hz, 4H, B–C–CH–CH–C*H*), 6.91 (t, $^3J = 7.2$ Hz, 8H, B–C–CH–C*H*–CH), 7.16 (br s, 8H, B–C–C*H*–CH), 7.27 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.47 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.80 (s, 2H, N–C*H*–C*H*–N), 7.87 (t, $^3J = 7.7$ Hz, 2H, *p*-Pyr), 9.38 (s, 1H, N=C*H*–N). $^{13}C\{^1H\}$ NMR (75 MHz, d_6-DMSO): δ 53.1, 64.0 (CH_2), 120.0, 120.3, 121.5, 123.2, 125.3 (q, $^2J = 2.8$ Hz, B–C–*C*), 135.5, 137.6, 138.0, 152.5, 162.3 (q, $^1J = 49.1$ Hz, B-C).

3.2.7. Preparation of 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium nitrate (7[NO$_3$])

1,3-di{2-(Hydroxymethyl)pyridine-6-methyl}-imidazolium bromide (0.391 g, 1.0 mmol) and 10 mL of deionized water was added to a 25 mL Erlenmeyer flask. -Silver nitrate (0.170 g, 1 mmol) was dissolved in 5 mL of deionized water and added to the flask. Upon addition a yellowish precipitate formed and the suspension was stirred for 1 h at room temperature. The solution was filtered with a buckner funnel (using celite as a filter aid) and the solid washed with deionized water. The filtrate was then evaporated to dryness to obtain a colorless oil, which upon setting overnight solidified as a off-white solid. Yield: 0.373 g, 1.00 mmol, 100%. Anal. calc. for $C_{17}H_{19}N_5O_5$: C, 54.67; H, 5.13; N, 18.76. Found: C, 53.86; H, 4.95; N, 18.17%. ES-MS (*m*/*z*): calc., 311.2, $[M - NO_3]^+$; found, 310.8. ^1H NMR (400 MHz, d_6-DMSO): δ 4.50 (d, $^3J = 5.9$ Hz, 4H, Pyr–CH_2–OH), 5.44 (t, $^3J = 5.9$ Hz, 2H, O*H*), 5.56 (s, 4H, Imid-CH_2-Pyr), 7.28 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.47 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.80 (s, 2H, N;–C*H*;-C*H*;-N), 7.88 (t, $^3J = 7.7$ Hz, 2H, *p*-Pyr), 9.40 (s, 1H N=C*H*–N). $^{13}C\{^1H\}$ NMR (100 MHz, d_6-DMSO): δ 53.2, 64.1 (CH_2), 120.1, 120.5, 123.3 137.8, 138.2 152.7, 162.5 (aromatic).

3.2.8. Preparation of the silver complex of 2-(methylimidazoliummethy)-6-(butylimidazoliummethyl)-pyridine tetraphenylborate (8[BPh$_4$]$_2$)

2-(methylimidazoliummethy)-6-(butylimidazoliummethyl)-pyridine tetraphenylborate (0.366 g, 0.39 mmol) and Ag_2O (0.092 g, 0.40 mmol) was placed in a 50 mL

Erlenmeyer flask. 20 mL of a 1:1 CH_3CN:CH_2Cl_2 solution was added to the flask. The solution was stirred at 50 °C for 18 h. The solution was filtered and evaporated to dryness resulting in a white solid. Yield: 0.200 g, 0.135 mmol, 69%. ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.85 (t, $^3J = 7.3$ Hz, 3H, CH_3), 1.21 (m, $^3J = 7.3$ Hz, 2H, CH_2), 1.71 (m, $^3J = 7.3$ Hz, 2H, CH_2), 3.72 (s, 3H, CH_3), 4.02 (t, $^3J = 7.3$ Hz, 2H, CH_2), 5.28 (s, 2H, Pyr-CH_2-Im), 5.29 (s, 2H, Pyr-CH_2-Im), 6.78 (t, $^3J = 7.6$ Hz, 8H, B-C–CH–CH–C*H*), 6.91 (t, $^3J = 7.6$ Hz, 16H, B–C–CH–C*H*–CH), 7.10 (d, $^3J = 7.6$ Hz, 1H, *m*-Pyr), 7.15 (d, $^3J = 7.7$ Hz, 1H, *m*-Pyr), 7.18 (m, 16H, B–C–C*H*–CH–CH), 7.42 (d, $^3J = 1.8$ Hz, 1H, N–C*H*–CH–N), 7.48 (m, 2H, N–CH–C*H*–N), 7.49 (d, $^3J = 1.8$ Hz, 1H, N–C*H*–CH–N), 7.72 (t, $^3J = 7.7$ Hz, 1H, *p*-Pyr). ^{13}C{^{1}H} NMR (100 MHz, d_6-DMSO): δ 13.4, 19.0, 33.0, 38.1, 50.7, 55.3, 55.4 (CH_2 and CH_3), 121.3, 121.4, 121.7, 122.8, 122.8, 125.2 (q, $^2J = 3.1$ Hz, B–C–*C*), 135.5 (q, $^3J = 1.5$ Hz, B–C–C–*C*), 138.7, 155.8, 155.9, 163.3 (q, $^1J = 49.6$ Hz, B–C), 180.0 (br s, C–Ag), 180.8 (br s, C–Ag).

3.2.9. Preparation of silver complex of 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium bromide (**9**[1/3(Ag_4Br_7)])

1,3-di{2-(Hydroxymethyl)pyridine-6-methyl}-imidazolium bromide (0.380 g, 0.97 mmol) and Ag_2O (0.348 g, 1.5 mmol) was placed in a 125 mL Erlenmeyer flask. Sixty millilitres of a 1:1 CH_2Cl_2:CH_3CN mixture was added to the flask. The flask was stirred at room temperature for 18 h. The solution was filtered through a microfilter and the solvent removed under reduced pressure to yield a white powder. Yield: 0.35 g, 0.11 mmol, 68%. Crystals were grown from the slow evaporation of a concentrated DMF solution. Anal. calc. for $C_{102}H_{108}N_{24}O_{12}Ag_7Br_7$: C, 38.57; H, 3.43; N, 10.58. Found: C, 38.87; H, 3.36; N, 10.37%. ES-MS (*m*/*z*): calc., 727.2, $[L_2–^{107}Ag]^+$; 729.2, $[L_2–^{109}Ag]^+$; 264.7, $[^{79}Br_2–^{107}Ag]^-$; 266.7, $[^{79}Br_2–^{109}Ag]^-$, $[^{79}Br–^{107}Ag–^{81}Br]^-$; 268.7, $[^{81}Br_2–^{107}Ag]^-$, $[^{79}Br–^{109}Ag–^{81}Br]^-$; and 270.7, $[^{81}Br_2–^{109}Ag]^{-+}$; found, 727.2, 729.2, 264.8, 266.6, 268.5 and 270.5. ^{1}H NMR (300 MHz, d_6-DMSO): δ 4.53 (d, $^3J = 5.7$ Hz, 4H, Pyr-CH_2-OH), 5.37 (s, 4H, Imid-CH_2-Pyr), 5.42 (t, $^3J = 5.7$ Hz, 2H, O*H*), 7.05 (d, $^3J = 7.5$ Hz, 2H, *m*-Pyr), 7.40 (d, $^3J = 7.6$ Hz, 2H, *m*-Pyr), 7.55 (s, 2H, N–C*H*–C*H*–N), 7.77 (t, $^3J = 7.8$ Hz, 2H, *p*-Pyr). ^{13}C{^{1}H} NMR (75 MHz, d_6-DMSO): δ 55.8, 64.1 (CH_2), 119.4, 119.8, 137.8, 155.0, 162.1 (aromatic), 181.5 (C–Ag).

3.2.10. Preparation of the silver complex of 1,3-di{2-(hydroxymethyl)pyridine-6-methyl}-imidazolium nitrate (**10**[NO_3])

1,3-di{2-(Hydroxymethyl)pyridine-6-methyl}-imidazolium nitrate (0.747 g, 2.0 mmol), silver oxide (0.277 g, 1.2 mmol) and 60 mL of methanol was placed into a round bottom flask. The solution was stirred for 18 h at room temperature. The solution was then filtered, using celite as a filter aid, and evaporated to dryness under vacuum to obtain a reddish solid. Yield: 0.881 g, 0.61 mmol, 92%. Crystals were grown by slow evaporation of an 1:1 methanol:acetonitrile solution. Anal. calc. for $Ag_3C_{51}H_{54}N_{15}O_{15}$: C, 42.59; H, 3.79; N, 14.62. Found: C, 40.16; H, 3.71; N, 13.31%. ES-MS (*m*/*z*): calc., 417.0, $[L–^{107}Ag]^+$; 419.0, $[L–^{109}Ag]^+$; 727.2, $[L_2–^{107}Ag]^+$ and 729.2, $[L_2–^{109}Ag]^+$; found, 417.0, 418.9, 727.3 and 729.2. ^{1}H NMR (400 MHz, CD_3OD): δ 4.80 (s, 4H, Pyr-CH_2–OH), 5.43 (s, 4H, Imid-CH_2-Pyr), 7.56 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.60 (d, $^3J = 7.7$ Hz, 2H, *m*-Pyr), 7.78 (s, 2H, N–C*H*–C*H*–N), 7.98 (t, $^3J = 7.7$ Hz, 2H, *p*-Pyr). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 57.9, 65.6 (CH_2), 124.2, 125.0, 127.7, 141.4, 154.1, 163.6 (aromatic).

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Appendix A. Supplementary data

The thermal ellipsoids of all crystallographically characterized compounds are depicted. ES-MS spectra for **2**, **5**[BPh_4], **6**[BPh_4]$_2$, **7**[Br], **7**[NO_3], **9**[1/3(Ag_4Br_7)] and **10**[NO_3]$_3$ are also shown. Crystallographic data for compounds **1**, **2**, **5**[BPh_4], **6**[BPh_4]$_2$, **7**[Br], **7**[BPh_4], **7**[NO_3], **7**(Na)[BPh_4]$_2$ and **10**[NO_3]$_3$ have been deposited with the Cambridge Crystallographic Data Center, CCDC reference numbers 275908–275916 in CIF format. Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.jorganchem.2005.07.102.

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