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Novel N-Heterocyclic Carbene Silver (I) Complexes: Synthesis, Structural Characterization, Antimicrobial, Antioxidant and Cytotoxicity Potential Studies

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Abstract

Nowadays, N-heterocyclic carbene-based silver-complexes Ag(I) have been widely used as an organometallic drug candidate in medicinal and pharmaceutical chemistry researches due to their low toxicity. Due to the success of Ag(I) complexes in biological applications, interest in the synthesis and applications of such compounds is increasing rapidly. Therefore, in this study, a series of unsymmetrical N,N-disubstituted benzimidazolium salts were synthesized as N-heterocyclic carbene (NHC) (2a-2j). The interaction of these benzimidazolium salts having their two nitrogen atoms substituted by bulky groups with Ag₂O in DMF has been carried out to afford Ag(I) complexes and characterized by ¹H NMR, ¹³C NMR, FT-IR and elemental analyses. The antimicrobial activity of Ag(I) complexes was tested against some standard culture collections of Gram-negative, Gram-positive bacterial strains and Fungal strains, which are the most frequently isolated among the society and hospital-acquired infectious microorganisms as potential metallopharmaceutical agents. The Ag-NHC complexes showed effective antimicrobial activity against microorganisms with MIC values between 0.0024 and 1.25 mg/ml. Moreover, these Ag-NHC complexes exhibited significant antioxidant activities. In addition, of benzimidazoles salts 2,4 and Ag(I) complexes 3,5 were screened for their antitumor activity. The highest antitumor activity was observed for **3e** and **3d** Complexes.

Keywords: N-heterocyclic carbene, benzimidazolium salts, silver (I)-NHC complexes, antimicrobial, antioxidant and antitumor activities

1. Introduction

N-Heterocyclic carbenes (NHCs) are nitrogen-based heterocyclic compounds containing a divalent carbon atom. Previously, many researchers tried numerous synthetic methods to isolate the stable NHCs, but they were not successful until the first stable free-carbene was isolated in 1991 as a crystal solid by Arduengo and coworkers [1]. Since then, the number of studies in carbene chemistry has

increased considerably, and has become stable in research laboratories throughout the world. Today, NHCs are one of the important classes of ligands for coordination chemistry. NHCs have strong σ -donating but, weak π -accepting properties, which show excellent support to stabilize various oxidation states of transition-metal. Also, they can provide steric and electronic properties for the optimal design of transition-metal complexes [2–8]. The modification at the nitrogen atoms of the NHCs significantly influence the reactivity and binding affinity of the ligand; thus, NHCs make the strong metal-carbon bond with different metals. Transition-metal complexes of NHCs are used as strong-, reactive- and selective-catalysts in many chemical reactions. Initially, the metal-NHC complexes were used extensively as a catalyst in organic transformations such as C-C, C-heteroatom cross-couplings, and C-H functionalization [9–12]. Also, in recent years, transition metal-NHC complexes containing Au, Pd, Cu, Ru, Pt, Ag, Rh metals have been widely used in medicine and pharmacy as the potential metallopharmaceutical agents against AMR [13–16]. Although, most of the organometallic drug research has focused on platinum- and gold-containing compounds, carbene-based silver-compounds stand out in the class of organometallic drugs owing to their low toxicity, easy synthesis, stability and limited possibility of side effects. Ag(I) complexes possess several properties, ranging from antibacterial, anticancer, anti-inflammatory and antiseptic to anti-neoplastic activity [17]. Ag(I) complexes have been recently at the focal point with increased attention due to their usually strong antimicrobial and anticancer properties, and have more effective than other transition-metal complexes, and also, they have low toxicity for humans. Ag(I) complexes also promise to be agents capable of overcoming AMR and beating antibiotic resistant bacteria, fungi and parasites [18–34]. Heterocyclic molecules are an important family of organic chemistry with a wide range of applications [35]. Although, this family is generally known for its agrochemical and veterinary applications, it is also used as a corrosion inhibitor, sanitizer, and dyestuff [36]. Many heterocyclic molecules such as favipiravir have also important pharmaceutical applications [37, 38]. For example, ribavirin is an N-heterocyclic molecule that is used in the treatment of COVID-19 [39]. The reasonable results obtained from bioactivity studies have enabled them to be a family that is frequently used in pharmaceutical chemistry [40]. NHCs, which are known for their high catalytic activity, are easily synthesized and modified [41, 42]. NHC metal complexes have become a popular research area with the frequent usage of metals in drug molecules. In our previous works, we concluded that the presence of electron-donating and bulky substituents attached to the nitrogen of the carbene ligand increases the antimicrobial activity of the silver complexes. These exciting results have led us to further investigate the antimicrobial properties of silver-NHCs. In this regard, herein, we now report the synthesis of novel NHC salts and their Ag(I) complexes and investigate their antimicrobial, antioxidant and cytotoxic activities. All salts and complex structures were characterized by elemental analysis, Fourier transforms infrared (FTIR), ^1H and ^{13}C nuclear magnetic resonance (NMR) spectroscopies.

2. Results and discussion

2.1 Preparation of benzimidazolium salts

Nitrogen-containing heterocyclic compounds received great attention because of their wide range of catalytic and pharmacological properties in organometallic chemistry. In this study, benzimidazoles salts (**2a-j**) prepared by the reaction of N-(isobutyl)-benzimidazole (**1**) with various aryl chloride in DMF at 80°C for 24 h. The reaction pathway is shown in **Figure 1**.

Figure 1.
Synthesis of the benzimidazolium salts (2a-j).

The NMR spectra of all compounds were run in δ -CDCl₃. The acidic protons (NCHN) of the benzimidazolium salts (2a-j) were detected in the ¹H NMR spectra at 12.07, 11.81, 11.44, 11.08, 11.29, 10.48, 12.05, 11.34, 11.52, and 11.95 ppm, respectively, as a typical singlet. These are in agreement with values in the associated literature [43–49]. The methyl protons of the isopropyl group on the benzimidazolium salts (2a-j) were observed between 0.98 and 1.06 in the form of doublets, whereas the methyl protons of the benzimidazolium salts (2a-j) were signaled at 2.24–2.44 ppm as singlets. The isopropyl group H_{2'} protons on all the benzimidazolium salts were visualized as septets in the interval 2.34–2.44 ppm. Also, in the ¹H NMR spectra of (2a-j), the H_{1'} protons appeared between 4.32–4.51 ppm while the H_{1''} protons were detected as typical singlet between 5.80–6.90 ppm. The signals detected in the range of 6.94–8.64 ppm are assigned to the aromatic protons of benzimidazolium salts (2a-j). In ¹³C NMR spectra, the N-HCN (C₂) carbene peak of benzimidazole salts (2a-j) was assigned between 141.91–144.02 ppm.

Ag₂O and Benzimidazolium salts (2a-j) were reacted in dichloromethane at room temperature under dark and Ag(I)-NHC complex (3a-j) was obtained in very good yields. The Ag(I) complexes (3a-j) have good solubility in polar solvents and are stable in the air and towards the moisture. The synthetic route for the synthesis of Ag(I)-NHC complex (3a-j) is shown in **Figure 2**. In the ¹H NMR spectra, the acidic imino proton of benzimidazolium salts (NCHN) were not observed between δ 10.48–12.07 ppm. Similarly, in the ¹³C NMR spectra, imino carbon of benzimidazolium salts (NCHN) was not observed between δ 141–144 ppm.

Figure 2.
Synthesis of silver(I) complexes **3a-j**.

At the same time, the formation of the Ag(I) complexes (**3a-j**) was proven by IR spectra, which showed CN bond vibrations in the range of $1400\text{--}1591\text{ cm}^{-1}$. The antibacterial and antioxidant activities of all the synthesized benzimidazolium salts (**2a-j**) and their corresponding Ag(I) complexes (**3a-j**) were evaluated as per details given in the following text.

3. Biological activities

It is known that the number of silver centers plays an important role in biological activity. The competence of the biological potential of silver (I) complexes is essentially influenced by the type of ligands bound to the metal centre. The presence of lipophilic groups such as alkyl chains on the NHC ligand enhances the lipophilic nature of the silver complex, which helps it penetrate the cell wall easily. The complexes have shown antibacterial activity to different extents, according to the type of ligand.

Benzimidazolium salts (**2a-j**) and Ag(I) complexes (**3a-j**) were tested against bacterial strains both Gram-positive and negative bacterial. As it was reported in the literatures [50–52], the DMSO did not exhibit any antimicrobial activity. The results are reported [27–31] in **Table 1**. Generally, all the Ag(I) complexes exhibited antibacterial activity against all bacterial strains except, the two compounds **3a** and **3i** were not active against *Listeria monocytogenes*. While all the benzimidazolium salts (**2a-j**) performed a good antibacterial potential against the test Gram-negative and positive strains and showed bacterial inhibition in the range $14 \pm 0.5\text{--}36 \pm 0.2\text{ mm}$. There was rarely a difference in the antibacterial activity of benzimidazolium salts (**2a-j**) and Ag(I) complexes (**3a-j**) between all bacterial strains, except that with *Micrococcus luteus* strains, the tested compounds showed better antibacterial potential than others. The observed antibacterial activity of tested complexes is

Microorganisms Compounds	Micrococcus luteus LB 14110	Listeria monocytogenes ATCC 19117	Salmonella Typhimurium ATCC 14028	Staphylococcus aureus ATCC 6538	Pseudomonas aeruginosa
2a	20 ± 0.6	14 ± 0.5	18 ± 0.54	16 ± 0.25	16 ± 0.13
2b	22 ± 0.6	15 ± 0.6	18 ± 0.5	17 ± 0.3	17 ± 0.14
2c	35 ± 0.5	16 ± 0.2	18 ± 0.5	18 ± 0.5	22 ± 0.2
2d	30 ± 0.5	14 ± 0.5	16 ± 0.10	18 ± 0.11	16 ± 0.19
2e	25 ± 0.33	22 ± 0.5	18 ± 0.5	18 ± 0.18	20 ± 0.45
2f	36 ± 0.2	16 ± 0.3	18 ± 0.05	20 ± 0.1	20 ± 0.4
2g	28 ± 0.32	16 ± 0.5	22 ± 0.44	18 ± 0.15	22 ± 0.5
2h	30 ± 0.4	16 ± 0.2	16 ± 0.2	20 ± 0.2	18 ± 0.2
2i	30 ± 0.2	22 ± 0.2	22 ± 0.3	22 ± 0.2	20 ± 0.4
2j	34 ± 0.44	22 ± 0.5	22 ± 0.15	22 ± 0.3	20 ± 0.25
3a	20 ± 0.22	—	22 ± 0.22	18 ± 0.05	18 ± 0.22
3b	18 ± 0.2	20 ± 0.2	16 ± 0.3	20 ± 0.2	18 ± 0.2
3c	16 ± 0.2	18 ± 0.3	18 ± 0.22	16 ± 0.0	16 ± 0.5
3d	22 ± 0.2	16 ± 0.2	14 ± 0.2	20 ± 0.2	16 ± 0.2
3e	18 ± 0.2	18 ± 0.22	18 ± 0.33	18 ± 0.23	18 ± 0.22
3f	30 ± 0.4	22 ± 0.7	30 ± 0.4	25 ± 0.2	19 ± 0.17
3g	22 ± 0.3	16 ± 0.4	22 ± 0.4	18 ± 0.2	18 ± 0.2
3h	10 ± 0.4	14 ± 0.5	12 ± 0.10	14 ± 0.15	16 ± 0.10
3i	32 ± 0.32	—	16 ± 0.15	18 ± 0.1	18 ± 0.15
3j	20 ± 0.4	18 ± 0.5	18 ± 0.24	18 ± 0.5	18 ± 0.16

Table 1.
Zone of bacterial inhibition measured in mm of the synthesized salts and silver complexes [27–31].

Microorganism indicator	Compounds	MIC (mg/ml)
<i>Listeria monocytogenes</i> ATCC 19117	2h	1.25
	2j	0.625
	3f	0.0048
	Ampicillin	0.039
<i>Salmonella Typhimurium</i> ATCC 14028	2h	1.25
	2j	0.039
	3f	0.0024
	Ampicillin	0.625
<i>Micrococcus luteus</i>	2h	0.3125
	2j	0.3125
	3f	0.0024
	Ampicillin	0.0195

Table 2.
Minimal bacterial inhibitory concentration measured in mg/mL of benzimidazoles salts and Ag(I) complexes [27–31].

comparable to that of our previous silver complexes [53–55]. The MIC values of tested Ag(I) complexes and their starting material against *L. monocytogenes* ATCC 19117, *Salmonella Typhimurium* ATCC 14,028 and *M. luteus* are presented in **Table 2**.

3.1 Minimum inhibitory concentration (MIC) determination

The antimicrobial activity of compounds **2h**, **2j**, and **3f** has been reported based on MIC values, which are defined as the lowest concentration of an antimicrobial that visibly inhibits bacterial growth after overnight incubation. As shown in **Table 2**, MIC values ranged between 0.0024 and 0.3125 mg mL⁻¹ for *M.luteus* LB 14110. *Listeria monocytogenes* ATCC 19117 shows the range from 0.0048 to 1.25 mg mL⁻¹ and for *Salmonella typhimurium* ATCC 14028 the MIC values varied between 0.0024 and 1.25 mg mL⁻¹. The Ag complex **3f** showed better activity than ampicillin against *Micrococcus luteus* as well as for *Salmonella Typhimurium* with an MIC of 0.0024 mg/mL. Whereas, *L. monocytogenes* exhibited an MIC value of 0.0048 mg/mL using the same complex. The MICs of the other compounds were in the range tested.

4. Antioxidant activities

The scavenging activity of the synthesized of the NHC precursors [27–31] is in **Figure 3** and Ag(I) complexes with DPPH (1,1-diphenyl- 2-picrylhydrazyl) is represented in **Figure 4**.

Figure 3.
DPPH radicals scavenging activity of benzimidazoles salts **2a**, **2d**, **2g**.

Figure 4.
DPPH radicals scavenging activity of (Ag-NHC) complexes **3d**, **3g**.

The antioxidant activities for compounds **2a**, **2d**, **2g**, **3g**, and **3d** are summarized in **Figures 3** and **4**. The results analysis indicated that the antiradical activity profiles obtained from the tested synthetic products **3g** and **3d** had improved and demonstrated antioxidant activity compared to the other products. At a concentration used (0.0625 mg/ml), **2d** showed the lowest free radical activity when compared to both gallic acid and BHT (butylated hydroxytoluene). Similarly, compounds **2a**, **2g** and **3d**, at a concentration of 0.0625 mg/ml, had lower radical activity than gallic acid as well as BHT (butylated hydroxytoluene). **2a**, **2d**, **2g**, **3g** and **3d** revealed significant DPPH activity over synthetic antioxidants at the concentration of 1 mg/ ml.

5. Cytotoxic activities

The anticancer activities of benzimidazole salts **2a-j** and Ag(I) complexes **3a-j** were investigated against breast cancer MCF-7, MDA-MB-231 cells. The results are listed in **Table 3**. The cytotoxicity of **3i** and **3f** was significantly higher against MCF7 cells as shown in **Table 3** with IC₅₀ values of 0.68 and 0.6 mg/ml, respectively, than its activity against MDA-MB-231 cells. Additionally, compound

benzimidazoles salts 2a-j and Ag(I) complexes 3a-j	Anticancer activity LC50 in mg/ml MCF7 MDA-MB-231	
	MCF7	MDA-MB-231
3a		
3b	4.2 ± 3.6	2.5 ± 4.3
3c	3.1 ± 3.1	2.6 ± 5.9
3d	1.7 ± 3.1	16 ± 2.8
3e	4.3 ± 1.8	0.0 ± 00
3f	0.68 ± 3.2	1.93 ± 2.6
3g	1.3 ± 4.1	3.3 ± 2.9
3h	2.0 ± 3.2	2.8 ± 2.9
3i	0.61 ± 3.1	1.95 ± 2.5
3j	1.3 ± 4.1	3.4 ± 2.9
2a	2.0 ± 3.2	2.7 ± 2.8
2b	NA	NA
2c	3.1 ± 5.9	6.3 ± 3.2
2d	NA	NA
2e	0.6 ± 2.9	3.1 ± 5.9
2f	Higher than 100 mg/ml	Higher than 100 mg/ml
2g	Higher than 100 mg/ml	Higher than 100 mg/ml
2h	Higher than 100 mg/ml	Higher than 100 mg/ml
2i	Higher than 100 mg/ml	Higher than 100 mg/ml
2j	Higher than 100 mg/ml	Higher than 100 mg/ml
Tetracyclinea	NT	NT

Values are mean value ± standard deviation of three different replicates. The concentration was 30 mg, NT: not tested, NA: not active.

Table 3.
Anticancer activities of synthesized benzimidazoles salts 2a-j and Ag(I) complexes 3a-j [27–31].

3j exhibited cytotoxicity towards MCF7 and MDA-MB-231 cells equal to 2.3 and 3.4 mg/ml. whereas compounds 2a and 2d were not active against MCF7 and MDA-MB-231. The compounds 2f-j had showed IC50 values higher than 100 mg/ml.

On the other hand, benzimidazolium salts (4a-4j) have been synthesized following our previous work [56, 57] (Figure 5). The ¹H NMR spectra of the benzimidazolium salts (4a-j) showed an acid proton H₂ which appeared as a typical singlet at 12.02, 11.80, 12.02, 11.77, 11.61, 11.79, 12.15, 12.27, 11.46 and 11.26 ppm, respectively.

The protons of the aromatic group on benzimidazolium salts (4a-4j) were identified in the range of 6.30–8.02 ppm. The H₂ protons of the isobutyl group were seen as heptate in the range between 2.25 and 2.44 ppm. The signals resonated between 0.98 and 1.04 are assigned to protons of isobutyl group H_{ab} on benzimidazolium salts (4a-4j). Further evidence for the formation of benzimidazolium salts (4a-4j) is provided by the peak of C2 of the carbons as typical singlets in the range 144.1–144.5 ppm. The ¹³C NMR spectra showed also aromatic carbons of benzimidazolium salts (4a-4j) in the range of 105.8–153.8 ppm. The terminal carbons C_{ab} of the isobutyl group of all benzimidazolium salts (4a-4j) showed peaks in the

Figure 5.
Synthesis of benzimidazoles salts **4a-j**.

region 19.3–19.9 ppm. While the carbons C_2' of the isobutyl group were identified between 28.6–28.9 ppm. These values are consistent with those in the corresponding literature [58].

The synthesis of Ag(I) complexes was performed in the absence of light. The reaction is carried out between benzimidazolium salt with 1 equiv. Ag_2O in dichloromethane at room temperature. The Ag(I) complex was produced as a crystalline solid (**Figure 6**). The reaction was monitored by ^1H NMR spectroscopy in $\delta\text{-CDCl}_3$ and demonstrated that the benzimidazolium salts were fully converted to silver complexes in moderate yields (72–93%).

The Ag(I) complexes are stable in air and moisture with high solubility in polar solvents. The formation of the silver carbene complexes was proved by the absence of an NCHN proton peak in their ^1H NMR spectra, which confirms the complete conversion to Ag(I) complexes (**5a-5j**).

The successful formation of the silver carbene complexes was also indicated by the presence of the characteristic carbon (NCHN) signals in the bottom region of the field in comparison with those of the corresponding benzimidazolium salts (**4a-4j**). For example, it was observed at 186.7 ppm for complex **5j**. However, the rest of the carbon signal for the rest of the complexes was not observed. These values are in agreement with reported by Asekunowo et al. [59, 60] who have reported the synthesis of a series of monocarbon silver halides $[\text{R}_2\text{NHC}]\text{-AgCl}$ and demonstrated the effect of halide ions and solvent on the structural formulas of Ag(I) complexes. In addition, the formation of the Ag(I) complexes (**5a-5j**) was verified by the IR

Figure 6.
 Synthesis of Ag-NHC **4a-j**.

spectra, which showed vibrations of the CN bond at 1567, 1583, 1450, 1467, 1433, 1437, 1450, 1433, 1600 cm^{-1} , respectively.

6. Biological, cytotoxic and antibacterial activities

All the synthesized benzimidazolium salts (**4a-4j**) and their corresponding Ag(I) complexes (**5a-5j**) were investigated for antibacterial against the gram (+)/(-) bacteria. The DMSO did not exhibit any antimicrobial activity as reported earlier [61–73].

All tested compounds exhibited antibacterial activities against all bacteria strains. Compound **5i** was found the most effective in inhibiting the growth of the *Micrococcus luteus* LB 14110. Also, for compounds **5c**, **5h** and **5f** showed excellent activities against the same bacteria strain. Moreover, NHC precursors (**4a-j**) were less active than corresponding silver complexes (**5a-5j**) against all bacteria strains. The complexes showed an increased antibacterial activity due to the synergistic effect that increases the lipophilicity of the complexes, which facilitates the penetration of the complexes through the cell's membrane.

6.1 MIC determination

The MIC values of tested silver complexes and their starting material against *Listeria monocytogenes* ATCC 19117, *Salmonella* Typhimurium ATCC 14028 and *M. luteus* are presented in **Table 4**.

The antimicrobial activity of compounds **4h**, **4i** and **5f** was also reported in terms of the MIC values, defined as the lowest concentration of an antimicrobial that visibly inhibits the growth of the bacteria after overnight incubation.

Microorganism indicator	Compounds	MIC (mg/ml)
<i>Listeria monocytogenes</i> ATCC 19117	4h	1.25
	4j	0.635
	5f	0.0058
	Ampicillin	0.049
<i>Salmonella Typhimurium</i> ATCC 14028	4h	1.26
	4j	0.041
	5f	0.0034
	Ampicillin	0.635
<i>Micrococcus luteus</i>	4h	0.3225
	4j	0.3125
	5f	0.0034
	Ampicillin	0.0195

Table 4.
Minimal bacterial inhibitory concentration (MIC) of benzimidazoles salts and Ag(I) complexes [27–31].

As shown in **Table 4**, Silver complex **5f** showed better activity than ampicillin against *L. monocytogenes*, *Salmonella Typhimurium* and *M. luteus* with an MIC of 0.0058, 0.0034, and 0.0034 mg mL^{−1}, respectively. The NHC precursor **4i** gave a good result with an MIC of 0.041 mgmL^{−1} against *Salmonella Typhimurium*. The other compound performed poorly.

7. Cytotoxic activities

Salts (**4a-j**) and Ag(I) complexes (**5a-j**) were screened for their in vitro anticancer activities on human cancer cell lines MCF7 and MDA-MB-231 using the MTT test. The results are given in **Table 5**.

Compounds	Anticancer activity IC50 / (µg mL ^{−1})	
	MCF7	MDA-MB-231
5a	4.2 ± 3.5	4.3 ± 3.3
5b	4.1 ± 3.6	2.6 ± 4.3
5c	3.2 ± 3.1	2.7 ± 5.9
5d	1.8 ± 3.1	15 ± 2.8
5e	4.2 ± 1.8	0.0 ± 00
5f	0.69 ± 3.2	1.94 ± 2.6
5g	1.4 ± 4.1	3.4 ± 2.9
5h	2.1 ± 3.2	2.7 ± 2.9
5i	0.63 ± 3.1	1.96 ± 2.5
5j	1.4 ± 4.1	3.5 ± 2.9
4a	2.1 ± 3.2	2.8 ± 2.8
4b	NA	NA

Compounds	Anticancer activity IC50 / (µg mL ⁻¹)	
	MCF7	MDA-MB-231
4c	3.2 ± 5.9	6.2 ± 3.2
4d	NA	5.2 ± 3.1
4e	0.6 ± 2.9	3.1 ± 5.9
4f	> 100	> 100
4g	> 100	> 100
4h	> 100	> 100
4i	> 100	> 100
4j	> 100	> 100
Tetracyclina	NT	NT

The concentration was 30 µg. NA: not active; IC₅₀: half maximal inhibitory concentration; MCF7 and MDA-MB-231: human cancer cell lines; NT: not tested. Values are mean value ± standard deviation of three different replicates.

Table 5.
Anticancer activity of synthesized of benzimidazoles salts [27–31] **4a-4j** and Ag(I) complexes **5a-5j**.

The cytotoxicity of **5i** and **5f** was higher in MCF7 with half-maximal inhibitory concentration (IC₅₀) values of 0.63 and 0.69 µg mL⁻¹, respectively, as compared to their activity on MDA-MB-231 cells. Complexes **5j** and **4a** were also determined to be toxic towards MCF7 and MDA-MB-231 with values of (IC₅₀) 2.1 and 2.8 µg mL⁻¹ respectively. While, the compound 4d was inactive against MCF7.

8. Conclusions

In summary, a series of Ag(I) complexes were synthesized and characterized using different spectroscopic and analytical techniques. Antimicrobial properties of all Ag(I) complexes were evaluated against four Gram-negative, three Gram-positive bacterial strains and two fungal strains. New silver complexes showed high antibacterial activity compared with the precursors against gram (+)/(-) bacteria and fungi strains. Various substituents on nitrogen atoms have a different effect on antimicrobial activity. In addition, the Ag(I) complexes **5i** and **5f** showed good antitumor activity against MDA-MB-231, and MCF-7 cell lines. Moreover, further studies focused on the synthesis of (benz)imidazol-2-ylidene-based silver-complexes and their medical applications as potential metallopharmaceutical agents are currently underway by our research group.

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