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Design, synthesis and biological study of *N*-heterocyclic compounds derived from imidazole complexes

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ABSTRACT

A homologous series of new dinuclear silver(I)-NHC compounds with long-chain alkyl substituents was designed and synthesized to examine how alkyl-chain length affects their structures and antibacterial properties. Their preparation followed a three-step route. Imidazole was first *N*-alkylated with decyl, dodecyl, tetradecyl, hexadecyl, and octadecyl bromides; the resulting products were then quaternized with 1,4-dibromobutane to produce the corresponding disubstituted imidazolium salts. Finally, in situ carbene formation mediated by Ag₂O gave the dinuclear Ag(I)-NHC complexes (1s-5s). FT-IR, and NMR, spectroscopy was used to identify the chemical structure of the synthesized compounds. Together, the spectra showed the stepwise conversion of the *N*-substituted imidazoles into imidazolium salts and, ultimately, Ag(I)-NHC compounds. In particular, the imidazolium C-2 proton disappeared, while a characteristic Ag-C(NHC) resonance appeared at δ 181.47–182.78 ppm. The complexes were tested against the selected bacteria strain using MIC and IC₅₀ assays. A clear and distinct relationship was observed between chemical structure and biological activity: antibacterial activity generally increased as the number of carbon atoms in the alkyl chain increased from C₁₀ to C₁₈. With its C₁₈ chain, complex 5s showed the strongest overall activity, especially against the Gram-positive bacteria. Thus, systematically adjusting hydrophobic alkyl-chain length can significantly affect the antibacterial performance of end products dinuclear Ag(I)-NHC compounds and supports their potential as silver-based antibacterial agents.

Keywords: *N*-heterocyclic carbene, Silver(I)-NHC complexes, Imidazolium salts, Antibacterial activity, Biological Activity, Structure activity relationship, Long-chain alkyl groups

Introduction

Metal ions are involved in numerous biological processes, often by binding to particular biological components in therapeutic contexts (Warra, 2011; Thompson *et al.*, 2003) [1, 2]. Their value has been shown in diagnostic as well as therapeutic applications. Medicinal inorganic chemistry is considered one of the most important relatively modern scientific fields; however, metals have been used in medicine since ancient times (Magner, 2005) [3]. The vast diversity of potential interaction patterns and the multiple preparation methods for these metals have prompted researchers to synthesize and study a wide range of metallodrugs. In a relatively recent survey conducted by the CO-ADD (Community for Open Antimicrobial Drug Discovery) initiative—which examined 906 known and validated metal-based compounds researchers led by Frei found that these compounds achieved a higher success rate compared to their organic counterparts: 9.9% versus 0.87%, respectively. This is a significant difference that warrants further investigation and study (Frei *et al.*, 2020) [4]. The result presented above highlights the significant and distinctive potential of metal-based drugs in addressing the widespread problem of antimicrobial resistance one of the most critical challenges of our time. These changes encompass chemical reactivity, properties such as solubility and lipophilicity, oxidation states, and biological activity all of which can influence the stability of the complex. Metal centers comprising metal ions and organic ligands within organometallic coordination complexes can significantly influence the potential toxicity, dynamic properties, and biological activity (such as antibacterial effects) of metal-based drugs (Frei *et al.*, 2020) [4]. Silver has been a scientifically proven and effective antimicrobial agent since the 17th century; early antimicrobial applications including antibacterial uses relied on silver and its complexes and compounds, such as silver nitrate (Klasen, 2000) [5]. From the mid-17th century through the early 19th century, the use of silver nitrate increased markedly, and it gained widespread popularity across Europe as a treatment for ulcers and for minor to moderate acute burns (Silver *et al.*, 2006; Rust, 1834) [6, 7]. It has also frequently been used as an alternative to a cautery tool to treat and limit emerging or developed bony projections and deformities (styloid processes). After World War 2, research into silver-based antimicrobials stopped with the emergence of Penicillin (Klasen, 2000) [5]. In light of the foregoing, the emergence of drug-resistant bacterial strains specifically in 1965 renewed interest in this chemical compound (silver nitrate) (Moyer *et al.*, 1965) [8]. After three years of research, Fox and his colleagues reported that silver sulfa

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diazine demonstrated exceptional efficacy in treating various types of burns as well as severe wounds (Fox, 1968) [9]; it is widely marketed under the trade name "Silvadene®" at a standard concentration of 1% (Kascatan-Nebioglu *et al.*, 2007) [10]. Subsequently, however, silver-impregnated medical dressings were introduced manufactured from materials such as polyurethane, collagen and nylon designed to provide a sustained release of silver ions (Ag^+) (Lansdown, 2004) [11]. More recently, researchers have focused on *N*-heterocyclic carbene (NHC) complexes because of their favorable properties. Since NHCs are strong electron donors, they form chemical bonds between the transition metal and the organic ligand that are relatively stable and thermodynamically strong (Crudden *et al.*, 2004) [12]. Bulky organic groups attached to the NHC moiety confer additional stability; steric hindrance resulting from these groups restricts the rotation of substituents on the nitrogen atom and inhibits dimerization into the corresponding organic alkene (Hopkinson *et al.*, 2014) [13]. This effect markedly slows the release of silver ions from the Ag–NHC complex at the target site, thereby effectively preserving its antimicrobial biological properties (Kascatan-Nebioglu *et al.*, 2007) [10]. In 2004, Melaiye and colleagues reported the first Ag(I)–NHC complex exhibiting antimicrobial activity against *S. aureus*, *P. aeruginosa* and *E. coli* (Melaiye *et al.*, 2004) [14]. Changing the *N*-substituents creates steric constraints and changes the environment around the metal centers. As a result, the chemical, physical, and electronic properties of these compounds can be tuned and predicted precisely for a wide range of applications (Choo, 2019) [15]. Since this report was published, numerous focused studies have examined the antimicrobial potential of Ag(I)–NHC complexes (O’Beirne *et al.*, 2019; Patil *et al.*, 2011; Piatek *et al.*, 2023) [16, 17, 18]. A recent study also found antiviral activity against SARS-CoV-2, a significant development in the field (Gil-Moles *et al.*, 2023) [19]. In imidazolium and benzimidazolium salts, as well as in coordination complexes containing organic NHC ligands, antimicrobial activity is clearly associated with the length of the alkyl chain attached to the nitrogen atoms in the heterocyclic ring. Dembereinyamba and colleagues were the first to report, in 2004 [20], that imidazolium salts could be used directly as antibacterial agents. The lowest Minimum Inhibitory Concentration (MIC) values came from alkyl chains containing a high number of carbon atoms, from C_{10} to C_{18} . Furthermore, significant results demonstrated that imidazolium salts bearing hydrophobic groups attached to the nitrogen atoms of the heterocyclic rings exhibited markedly lower MIC values (Dembereinyamba *et al.*, 2004) [20]. This activity has been attributed to long alkyl chains at various positions on the imidazole ring, which may destabilize bacterial cell membranes and cause the leakage of cellular contents (Wang *et al.*, 2015) [21]. However, a brief survey of the available scientific literature reveals a lack of consistently documented examples of antimicrobial activity in Ag(I)–NHC complexes bearing long alkyl chains (i.e., those with more than 10 carbon atoms), even though the influence of such chains on antimicrobial efficacy is well-established (Arcau *et al.*, 2014) [22]. Researcher Kaloglu and his colleagues reported that silver(I) complexes featuring *N*-heterocyclic carbenes specifically those substituted with relatively long alkyl chains on the heterocyclic ring, which are bulkier and more electron-donating at the nitrogen atoms exhibited significant and potent antimicrobial activity. It was also noted that hydrophobic compounds those containing non-polar groups—are capable of penetrating cell membranes and releasing silver ions, which can interact with the nitrogenous bases in DNA (Kaloğlu *et al.*, 2017) [23]. This class of dinuclear complexes based on the imidazole heterocycle and linked to NHCs offers an alternative pathway for the development and improvement of proposed therapeutic agents. Sakamoto *et al.* and Haq *et al.* investigated the antimicrobial properties of mononuclear and dinuclear silver(I)–NHC coordination complexes, although the reasons underlying the differences in activity remain not fully understood or clearly elucidated. Silver oxide is one of the metal

oxides that can serve as a reagent in the synthesis of metal–NHC complexes; this method was first demonstrated by Wang and other researchers in 1998 (Haque *et al.*, 2013) [24]. Since transmetalation from Ag_2O typically produces good yields, it has remained widely used over the years (Selvarajoo *et al.*, 2017) [25]. This work focuses on the design and synthesis of a class of monovalent silver (Ag(I)) complexes, the characterization of their chemical structures, and the evaluation of the antibacterial activity of a homologous series of dinuclear complexes based on *N*-heterocyclic carbene (NHC) ligands. These ligands originate from imidazolium salts bearing alkyl chains of different lengths— C_{10} , C_{12} , C_{14} , C_{16} , and C_{18} —at the 1- and 3-positions of the imidazole ring. The study focuses on how the chain length, specifically the number of carbon atoms, affects the structures of the silver complexes and their activity against representative Gram-positive and Gram-negative bacterial strains. To establish the chemical structures of the synthesized imidazolium compounds and Ag–NHC complexes, several techniques were used, including FT-IR, ^1H NMR, and ^{13}C NMR. The biological findings were then considered alongside molecular structure and alkyl chain length, helping clarify the potential of long-chain Ag(I)–NHC complexes as antibacterial agents.

Experimental section

The bis-benzimidazole precursor was used to synthesize the bis-imidazolium ligands. *N*-alkylation employed alkyl bromide. Reactions were conducted in 1,4-dioxane, while silver(I) oxide (Ag_2O) was used to prepare the corresponding silver(I)–NHCs. The compounds’ biological activity, specifically their antibacterial activity, was evaluated against selected microorganism strains, using amoxicillin as the reference antibacterial agent. FTIR spectra were recorded over cm^{-1} . The ^{13}C and ^1H NMR spectra were measured at 75 and 300 MHz, respectively, in $\text{DMSO}-d_6$. Chemical shifts are reported as δ (ppm) relative to the appropriate reference. Melting points were measured using a suitable melting-point apparatus and reported in $^\circ\text{C}$.

Synthesis *N*-substituted benzimidazole [26]

The reaction took place in a dry round-bottom flask charged with imidazole (0.0253 mol) and powdered potassium hydroxide (KOH) (0.3809 mol). After dimethyl sulfoxide (DMSO) (40.0 mL) was added as the organic solvent, the mixture was stirred continuously at 90°C for two hours. Subsequently, the appropriate alkyl bromide (0.0126 mol) was added gradually (dropwise) while stirring continued. Following the addition, the reaction mixture was stirred at 40°C for an additional 1.5 hour. The reaction flask was removed from the heat source, and upon completion of the reaction, the product solution was poured into 250 mL of a mixture of cold water and crushed ice while stirring rapidly and continuously for half an hour. The mixture was allowed to settle for one hour after stirring ceased. Extraction was performed using the non-polar organic solvent petroleum ether. The organic layer was washed with distilled water (3×10 mL), and the petroleum ether layer was then separated and collected to obtain the desired product.

- **1-decyl- ^1H -imidazole (1b):** 83% yield of the reaction, The spectrum displayed an aromatic C–H stretching band at 3089 cm^{-1} . Bands at 2945 and 2878 cm^{-1} were characteristic of aliphatic C–H stretching. The band at 1589 cm^{-1} was assigned to C=N stretching, while that at 1259 cm^{-1} was associated with C–N stretching. ^1H NMR, δ 7.82 (1H, NCHN, s), 7.09 (1H, H-4, imidazole ring, d, $J = 1.5$ Hz), 6.94 (1H, H-5, imidazole ring, d, $J = 1.4$ Hz), 4.16 (2H, $N\text{-CH}_2$, t, $J = 7.0$ Hz), 1.79 (2H, in position 2 of alkyl chain, p, $J = 6.9$ Hz), 1.17–1.23 (14H, 7 $\times$ CH_2 , m), 0.88 (3H, CH_3 , t, $J = 6.7$ Hz), ^{13}C NMR, δ 139.47(NCHN), 126.54, 121.58 (C_4 and C_5 carbons in imidazole ring), 44.12($N\text{-CH}_2$), 31.87, 29.81, 29.37, 29.20, 29.13, 29.01, 27.11, 22.26(8-CH_2), 14.16(CH_3).

- **1-dodecyl-¹H-imidazole (2b):** 74% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was observed at 3078 cm⁻¹, while the bands at 2935 and 2875 cm⁻¹ were assigned to aliphatic C–H stretching. The band at 1657 cm⁻¹ corresponded to C=N stretching, and the absorption at 1264 cm⁻¹ was attributed to C–N stretching, ¹H NMR, δ 7.93 (1H, NCHN, s), 7.07 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 6.96 (1H, H-5, imidazole, d, *J* = 1.3 Hz), 4.19 (2H, N–CH₂, t, *J* = 7.0 Hz), 1.78 (2H, CH₂ at C-2 of the alkyl chain, p, *J* = 6.8 Hz), 1.17–1.25 (16H, 9 × CH₂, m), and 0.86 (3H, CH₃, t, *J* = 6.6 Hz), ¹³C NMR, δ 139.87(NCHN), 125.97, 121.24 (C₄ and C₅ carbons in imidazole ring, 43.78(N–CH₂), 31.89, 29.98, 29.67, 29.37, 29.14, 26.87, 21.74(10–CH₂), 14.24(CH₃).
- **1-tetradecyl-¹H-imidazole (3b):** 79% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band appeared at 3074 cm⁻¹. The bands at 2947 and 2890 cm⁻¹ were attributed to aliphatic C–H stretching. The band at 1611 cm⁻¹ was assigned to C=N stretching, whereas the band at 1247 cm⁻¹ corresponded to C–N stretching, ¹H NMR, δ 7.97 (1H, NCHN, s), 7.08 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 6.96 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.23 (2H, N–CH₂, t, *J* = 7.1 Hz), 1.79 (2H, CH₂ at C-2 of the alkyl chain, p, *J* = 7.0 Hz), 1.21–1.27 (22H, 11 × CH₂, m), and 0.84 (3H, CH₃, t, *J* = 6.4 Hz), ¹³C NMR, δ 138.97(NCHN), 126.82, 121.87 (C₄ and C₅ carbons in imidazole ring, 44.92(N–CH₂), 31.93, 29.90, 29.71, 29.64, 29.53, 29.44, 29.37, 29.21, 29.09, 26.87, 23.01(12–CH₂), 14.81(CH₃).
- **1-hexadecyl-¹H-imidazole (4b):** 78% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3057 cm⁻¹. The bands at 2987 and 2852 cm⁻¹ were associated with aliphatic C–H stretching. A band at 1614 cm⁻¹ was assigned to C=N stretching, whereas the band observed at 1268 cm⁻¹ was attributed to C–N stretching, ¹H NMR, δ 7.94 (1H, NCHN, s), 7.04 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 6.93 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.29 (2H, N–CH₂, t, *J* = 7.1 Hz), 1.81–1.74 (2H, CH₂ at C-2 of the alkyl chain, p, *J* = 7.0 Hz), 1.20–1.28 (26H, 13 × CH₂, m), and 0.88 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 140.19(NCHN), 126.47, 121.98 (C₄ and C₅ carbons in imidazole ring, 44.87(N–CH₂), 31.89, 31.73, 29.97, 29.79, 29.67, 29.56, 29.41, 29.32, 29.22, 29.16, 28.97, 26.24, 26.20, 22.11(14–CH₂), 14.31(CH₃).
- **1-octadecyl-¹H-imidazole (5b):** 80% yield of the reaction, The FT-IR (cm⁻¹) FT-IR (cm⁻¹): An aromatic C–H stretching band was detected at 3107 cm⁻¹. The bands at 2987 and 2862 cm⁻¹ were associated with aliphatic C–H stretching. The band at 1621 cm⁻¹ was assigned to C=N stretching, whereas the band at 1259 cm⁻¹ was attributed to C–N stretching, ¹H NMR, δ 7.92 (1H, NCHN, s), 7.05 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 6.97 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.27 (2H, N–CH₂, t, *J* = 7.1 Hz), 1.83–1.77 (2H, CH₂ at C-2 of the alkyl chain, p, *J* = 7.0 Hz), 1.18–1.27 (30H, 15 × CH₂, m), and 0.85 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 140.14(NCHN), 127.17, 122.38 (C₄ and C₅ carbons in imidazole ring, 44.51(N–CH₂), 31.97, 31.85, 29.76, 29.68, 29.52, 29.44, 29.37, 29.30, 29.24, 29.10, 28.79, 26.79, 26.27, 22.24(14–CH₂), 13.79(CH₃).

Synthesis of 1,3-disubstituted imidazolium salts

The *N*-alkylated imidazole (0.002 mol) specifically alkylated at the N-1 position was transferred to a clean, dry round-bottom flask, and dry 1,4-dioxane (30.0 mL) was added as the organic solvent. Stirring was maintained at a constant temperature for 30 minutes to ensure the complete dissolution of the reactant; subsequently, 1,4-dibromobutane (0.01 mol) was added cautiously dropwise and at a steady rate while ensuring continuous stirring of the reaction mixture. The reaction mixture was heated at a constant temperature of 90 °C for 24 hours under continuous stirring. Upon completion of the reaction, the flask was removed from the heat source, and the organic solvent *n*-hexane

(15 mL) was added to the mixture. After the mixture was gently and continuously shaken for several minutes, it was left undisturbed for one hour to allow the formed precipitate to settle. The resulting solid product was collected by filtration, washed twice with *n*-hexane to remove impurities, and then dried in a drying oven to yield the corresponding 1,3-disubstituted imidazolium salt (Hasan *et al.*, 2026) [27].

Ligand (1m): 71% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3081 cm⁻¹. The bands at 2921 and 2845 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1241 cm⁻¹ was assigned to C–N stretching, ¹H NMR, 8.74 (1H, NCHN, s), 7.18 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.07 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.51 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.30 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.85–1.76 (8H, N–CH₂–CH₂–, m), 1.21–1.28 (28H, 14 × CH₂, m), and 0.83 (6H, 2 × CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 149.54 (NCHN), 127.24, 123.18 (C₄ and C₅ carbons in imidazole ring, 48.11 (N–CH₂–butyl), 44.24 (N–CH₂), 31.96, 31.78, 29.98, 29.79, 29.67, 29.49, 29.32, 29.27, 29.17, 29.07, 28.64, 28.04, 26.57, 25.08, 22.22 (10–CH₂), 14.31 (CH₃).

Ligand (2m): 71% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3081 cm⁻¹. The bands at 2988 and 2841 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1271 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 8.76 (1H, NCHN, s), 7.19 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.09 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.59 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.31 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.88–1.79 (8H, N–CH₂–CH₂–, m), 1.21–1.30 (32H, 16 × CH₂, m), and 0.87 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 148.10 (NCHN), 126.87, 122.38 (C₄ and C₅ carbons in imidazole ring, 47.97 (N–CH₂–butyl), 44.28 (N–CH₂), 31.96, 31.44, 29.98, 29.86, 29.71, 29.59, 29.46, 29.37, 29.29, 29.19, 28.85, 28.08, 26.78, 26.18, 22.11 (12–CH₂), 14.27 (CH₃).

Ligand (3m): 78% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3047 cm⁻¹. The bands at 2969 and 2847 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1268 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 8.75 (1H, NCHN, s), 7.23 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.08 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.48 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.33 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.87–1.77 (8H, N–CH₂–CH₂–, m), 1.23–1.32 (36H, 18 × CH₂, m), and 0.87 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 148.37 (NCHN), 126.71, 123.58 (C₄ and C₅ carbons in imidazole ring, 48.12 (N–CH₂–butyl), 44.79 (N–CH₂), 32.08, 31.90, 31.02, 29.95, 29.74, 29.63, 29.57, 29.47, 29.38, 29.28, 29.19, 28.82, 28.21, 27.49, 26.84, 26.21, 22.85 (14–CH₂), 14.14 (CH₃).

Ligand (4m): 72% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3098 cm⁻¹. The bands at 2987 and 2847 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1238 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.77 (1H, NCHN, s), 7.21 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.07 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.59 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.29 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.73–1.84 (8H, N–CH₂–CH₂–, m), 1.24–1.34 (40H, 20 × CH₂, m), and 0.89 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 149.87 (NCHN), 127.01, 122.97 (C₄ and C₅ carbons in imidazole ring, 47.74 (N–CH₂–butyl), 43.27 (N–CH₂), 31.94, 31.78, 30.48, 29.99, 29.87, 29.74, 29.60, 29.54, 29.42, 29.33, 29.18, 29.13, 28.88, 28.67, 28.41, 27.58, 26.35, 26.04, 22.78 (16–CH₂), 14.10 (CH₃).

Ligand (5m): 69% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3091 cm⁻¹. The bands at 2987 and 2862 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1252 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 8.78 (1H, NCHN, s), 7.22 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.10 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.53 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.35 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.77–1.88 (8H, N–CH₂–CH₂–, m), 1.20–1.33 (44H, 22 × CH₂, m), and 0.91 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 148.97 (NCHN), 127.91, 123.91 (C₄ and C₅ carbons in imidazole ring, 46.47 (N–CH₂–butyl), 43.14 (N–CH₂), 31.89, 31.67, 30.97, 30.59, 29.97, 29.84, 29.77, 29.68, 29.59,

29.46, 29.39, 29.26, 29.18, 28.87, 28.57, 28.39, 28.12, 27.29, 26.47, 26.09, 22.70 (18-CH₂), 14.19 (CH₃).

Syntheses of silver(I)-NHC complexes

The imidazolium salt obtained in the previous step (1.0 mmol) (1m-5m) and silver oxide (Ag₂O) (1.5 mmol) were dissolved in 15 mL of 1,4-dioxane. The reaction vessel was kept away from light, and the mixture was stirred continuously at room temperature in the dark for 48 hours. After filtration through Celite, the organic solvent was completely removed from the reaction mixture under reduced pressure (Hasan *et al.*, 2026) [27].

- **Complex (1s):** 69% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3108 cm⁻¹. The bands at 2987 and 2860 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1378 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.21 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.05 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.58 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.24 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.75–1.85 (8H, N–CH₂–CH₂–, m), 1.21–1.29 (28H, 14 × CH₂, m), and 0.88 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 181.47 (C–Ag), 127.91, 123.91 (C₄ and C₅ carbons in imidazole ring, 51.47 (N–CH₂–butyl), 47.48 (N–CH₂), 31.98, 31.84, 29.89, 29.71, 29.62, 29.48, 29.35, 29.29, 29.21, 29.09, 28.78, 28.23, 26.58, 26.09, 22.77 (10-CH₂), 14.29 (CH₃).
- **Complex (2s):** 65% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3089 cm⁻¹. The bands at 2991 and 2875 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1358 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.25 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.12 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.58 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.35 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.76–1.87 (8H, N–CH₂–CH₂–, m), 1.22–1.31 (32H, 16 × CH₂, m), and 0.89 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 181.97 (C–Ag), 126.98, 122.78 (C₄ and C₅ carbons in imidazole ring, 50.47 (N–CH₂–butyl), 45.47 (N–CH₂), 31.94, 31.68, 29.98, 29.86, 29.67, 29.49, 29.41, 29.33, 29.26, 29.15, 28.97, 28.38, 26.11, 25.79, 22.47 (12-CH₂), 14.11 (CH₃).
- **Complex (3s):** 71% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3101 cm⁻¹. The bands at 2978 and 2868 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1358 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.27 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.12 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.61 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.37 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.74–1.85 (8H, N–CH₂–CH₂–, m), 1.21–1.32 (36H, 18 × CH₂, m), and 0.91 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 182.78 (C–Ag), 127.14, 122.84 (C₄ and C₅ carbons in imidazole ring, 50.57 (N–CH₂–butyl), 46.47 (N–CH₂), 31.98, 31.85, 30.24, 29.88, 29.72, 29.60, 29.44, 29.34, 29.28, 29.19, 29.07, 28.69, 28.12, 27.08, 26.17, 25.14, 22.94 (14-CH₂), 14.10 (CH₃).
- **Complex (4s):** 71% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3122 cm⁻¹. The bands at 2995 and 2881 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1348 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.21 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.12 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.62 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.41 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.75–1.89 (8H, N–CH₂–CH₂–, m), 1.25–1.36 (40H, 20 × CH₂, m), and 0.89 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 182.60 (C–Ag), 126.21, 122.57 (C₄ and C₅ carbons in imidazole ring, 49.57 (N–CH₂–butyl), 46.47 (N–CH₂), 31.98, 31.75, 30.68, 29.97, 29.86, 29.71, 29.57, 29.50, 29.42, 29.28, 29.17, 29.01, 28.85, 28.41, 28.01, 27.32, 26.41, 25.87, 22.87 (16-CH₂), 14.28 (CH₃).

- **Complex (5s):** 64% yield of the reaction, The FT-IR (cm⁻¹) An aromatic C–H stretching band was detected at 3108 cm⁻¹. The bands at 2989 and 2857 cm⁻¹ were attributed to aliphatic C–H stretching, while the band at 1351 cm⁻¹ was assigned to C–N stretching, ¹H NMR, δ 7.25 (1H, H-4, imidazole, d, *J* = 1.4 Hz), 7.14 (1H, H-5, imidazole, d, *J* = 1.4 Hz), 4.59 (4H, N–CH₂–butyl, t, *J* = 6.4 Hz), 4.39 (4H, N–CH₂, t, *J* = 7.1 Hz), 1.77–1.90 (8H, N–CH₂–CH₂–, m), 1.24–1.35 (44H, 22 × CH₂, m), and 0.85 (3H, CH₃, t, *J* = 6.5 Hz), ¹³C NMR, δ 182.76 (C–Ag), 126.99, 122.88 (C₄ and C₅ carbons in imidazole ring, 49.28 (N–CH₂–butyl), 44.78 (N–CH₂), 31.98, 31.81, 30.97, 30.74, 29.97, 29.84, 29.75, 29.50, 29.44, 29.32, 29.24, 29.14, 29.02, 28.74, 28.62, 28.48, 28.29, 27.22, 26.17, 26.01, 22.54 (18-CH₂), 14.87 (CH₃).

Bacterial strains and growth conditions

A fresh suspension of *Escherichia coli* DSM 1116 was prepared for the study by incubating a single colony overnight at 37 °C in MHB medium. MIC and EC₅₀ values were measured with standardized broth microdilution assays (Biemer, 1973) [28]. Concentrated stock solutions of the synthesized compounds were made in dimethyl sulfoxide (DMSO), then serially diluted in MHB medium to concentrations between 128 and 2.0 μM. The final DMSO concentration was kept at 1%, while the optical density at 600 nm (OD₆₀₀) was adjusted to 0.0005. For each test compound, serial dilutions were prepared in duplicate. The plates were then incubated at 37 °C for 24 hours. After incubation, each sample's absorbance was measured at 600 nm with a microplate reader. Using the resulting dose-response data, the MIC and EC₅₀ values of the previously prepared and tested compounds were determined from three independent experiments.

Antibacterial screening

The antibacterial activity of the compounds obtained in the preceding steps was assessed by the standard agar well diffusion method (Biemer, 1973) [28]. Mueller–Hinton agar plates were prepared, with each plate measuring 100 mm in diameter and containing an agar layer approximately 4 mm thick. To inoculate the plates, 100 μL of a previously prepared bacterial suspension was mixed with molten agar maintained at approximately 40 °C. The mixture was distributed uniformly and homogeneously before the agar solidified, and 8 mm diameter wells were then made in the culture medium. Each prepared compound was fully dissolved in sterile water and dispensed into the wells at 150 μL per well, producing final concentrations of 0.125, 0.25, 0.50, 1.0, and 2.0 mM. Mupirocin (5.0 μg), clindamycin (2.0 μg), and ceftazidime (30 μg) served as positive controls for monitoring and verifying the susceptibility of the bacteria under study; sterile water was used as the negative control. Afterward, the plates were incubated at 37 °C for 24 hours in a bacteriological incubator (model DH4000 B II HILAB). Antibacterial biological activity was assessed for each sample by measuring, in millimeters, the diameter of the inhibition zone around each well.

Determination of (MIC)

All synthesized compounds underwent quantitative testing for potential antibacterial activity by means of a microdilution assay in 96-well plates, according to the procedure described by (Biemer) [28]. For the bacterial inocula, the relevant microorganisms were grown in Mueller–Hinton broth for 24 hours, after which the density was adjusted to a final concentration of 10⁴ to 10⁵ CFU/mL. The compounds were dissolved in sterile water and serially diluted to final concentrations of 0.01562, 0.03125, 0.0625, 0.125, 0.25, 0.50, 1.0, and 2.0 mM. Each 96-well plate also included appropriate controls for bacterial growth and the culture medium. After the bacteria were incubated at 37 °C for 12 hours, their viability was assessed with the colorimetric MTT assay. For this, 20 μL of MTT solution (0.5 mg/mL) was added to each well, followed by incubation of the plates at 37 °C for 3 to 4 hours. During this period, metabolically active bacterial cells produced characteristic formazan crystals.

The resulting crystals were then completely dissolved in a solvent solution based on dry, pure isopropanol containing 10% Triton X-100 and 0.1 N HCl in anhydrous isopropanol—and absorbance was measured at 570 nm using a microplate reader. Each experiment was conducted in three independent replicates. The MIC represented the lowest test-compound concentration that prevented detectable bacterial growth; the IC₅₀ was the concentration required to inhibit approximately 50% of bacterial growth under the experimental conditions.

Result and discussion

Synthesis

The synthesis proceeded through three successive steps. First, imidazole was *N*-alkylated with long-chain alkyl bromides, yielding the *N*-substituted imidazole derivatives 1b–5b (Figure 1). These intermediates were then quaternized to form the corresponding 1,3-disubstituted imidazolium salts, 1m–5m. In the final step, Ag₂O mediated carbene formation and produced the dinuclear Ag(I)–NHC complexes 1s–5s. The compounds carried alkyl groups of increasing length decyl, dodecyl, tetradecyl, hexadecyl, and octadecyl so the effect of chain length on their spectroscopic properties could be examined. Structural assignments were supported by FT-IR, ¹H NMR, and ¹³C NMR spectroscopy.

FT-IR spectral analysis

The FT-IR spectra initially supported the successful synthesis of the *N*-substituted imidazole derivatives, imidazolium salts, and corresponding Ag(I)–NHC complexes. Derivatives 1b–5b, bearing decyl, dodecyl, tetradecyl, hexadecyl, and octadecyl chains, respectively, showed the characteristic absorption bands of both the imidazole ring and the long aliphatic chains. In the spectrum of 1-decyl-¹H-imidazole (1b), the band at 3089 cm^{−1} was assigned to aromatic C–H

stretching, while those at 2945 and 2878 cm^{−1} corresponded to aliphatic C–H stretching vibrations. The absorption at 1589 cm^{−1} was attributed to the imidazole ring's C=N vibration; the band at 1259 cm^{−1} was assigned to C–N stretching. The other *N*-substituted imidazoles gave comparable characteristic absorptions. For compound 2b, the bands appeared at 3078, 2935, 2875, 1657, and 1264 cm^{−1}; 3b showed absorptions at 3074, 2947, 2890, 1611, and 1247 cm^{−1}. The corresponding bands for 4b were observed at 3057, 2987, 2852, 1614, and 1268 cm^{−1}, whereas 5b showed bands at 3107, 2987, 2862, 1621, and 1259 cm^{−1}. Together, the retained imidazole-ring absorptions and aliphatic C–H bands confirm both the heterocyclic ring and the progressively longer alkyl chains. After quaternization, the FT-IR spectra for the 1,3-disubstituted imidazolium salts (1m–5m) showed aromatic C–H absorptions from 3047 to 3098 cm^{−1} and aliphatic C–H stretching bands at approximately 2841–2988 cm^{−1}. C–N stretching absorptions appeared at 1238–1271 cm^{−1}. In ligand 1m, the bands occurred at 3081, 2921, 2845, and 1241 cm^{−1}; ligand 5m showed corresponding absorptions at 3091, 2987, 2862, and 1252 cm^{−1}. The FT-IR spectra for the Ag(I)–NHC complexes 1s–5s displayed aromatic C–H stretching bands from 3089 to 3122 cm^{−1}, while aliphatic C–H stretching absorptions occurred between 2857 and 2995 cm^{−1}. C–N bands were observed across 1348–1378 cm^{−1}. In complex 1s, the C–N absorption appeared at 1378 cm^{−1}; in 2s and 3s, it was found at 1358 cm^{−1}. Complexes 4s and 5s gave corresponding absorptions at 1348 and 1351 cm^{−1}, respectively. The shifts in this vibrational region are consistent with changes to the imidazole ring's electronic environment after NHC formation and coordination to Ag(I). Overall, the FT-IR results show that the characteristic functional groups of the imidazole ring and long alkyl chains remained intact throughout the synthesis. The changes observed in the C–N region accompanied the conversion of the imidazolium precursors into Ag(I)–NHC complexes.

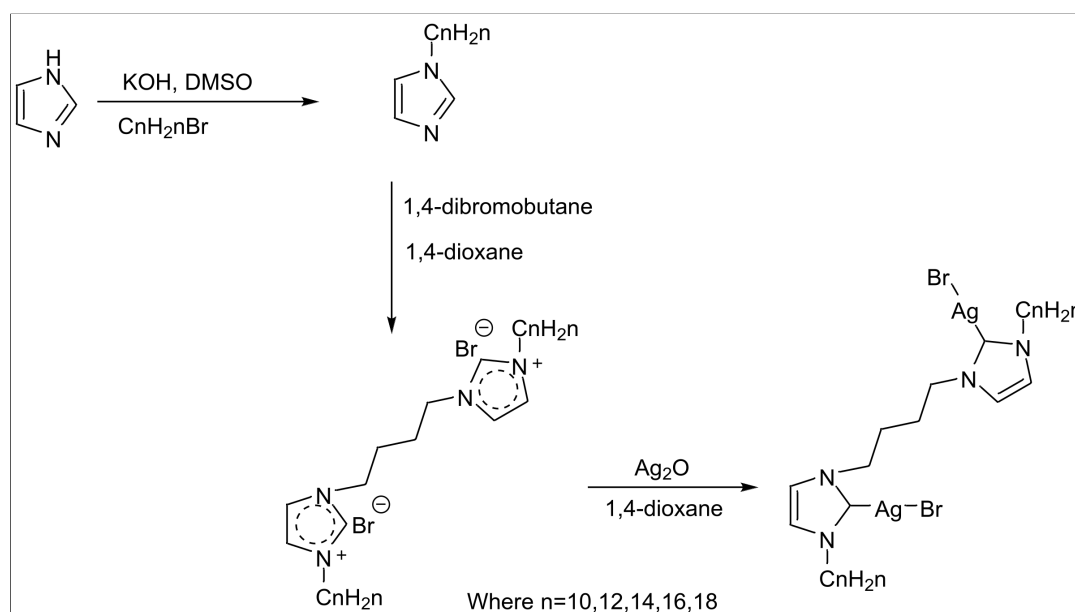


Figure 1. Synthesis of Ag-NHC complexes

¹H NMR spectral analysis

The ¹H NMR spectra provided further evidence for the successful synthesis of the *N*-substituted imidazole derivatives (1b–5b). For 1-decyl-¹H-imidazole (1b), the imidazole H-2 resonance appeared as a singlet at δ 7.82 ppm. The H-4 and H-5 resonances were doublets at δ 7.09 and 6.94 ppm, respectively. Their small coupling constants, *J* = 1.5 and 1.4 Hz, agree with the characteristic coupling between these two protons of the imidazole ring. The N–CH₂ protons gave a triplet at δ 4.16 ppm (*J* = 7.0 Hz), confirming that the decyl chain was attached to the imidazole nitrogen. Derivatives 2b–5b showed much the same pattern: the H-2 resonance occurred at δ 7.93, 7.97, 7.94, and

7.92 ppm, respectively, while H-4 and H-5 appeared within the ranges δ 7.04–7.08 and 6.93–6.97 ppm, respectively, with *J* ≈ 1.4 Hz. The N–CH₂ protons consistently appeared as triplets at δ 4.16–4.29 ppm (*J* = 7.0–7.1 Hz). Signals from the neighboring methylene groups were found at δ 1.74–1.83 ppm, while the other methylene protons formed multiplets at δ 1.17–1.34 ppm; the terminal methyl groups appeared as triplets at δ 0.84–0.88 ppm. As the alkyl chain length increased, the methylene resonances showed progressively larger integrations, supporting the successful preparation of the C₁₀–C₁₈ homologous series. By contrast, the relatively minor changes in the chemical shifts of the imidazole protons suggest that extending the alkyl chain has only a limited effect on the electronic environment of the imidazole ring.

Conversion of the *N*-substituted imidazoles to the corresponding 1,3-disubstituted imidazolium salts (1m–5m) produced a pronounced downfield shift of the H-2 resonance: from δ 7.82–7.97 ppm in the neutral imidazoles to δ 8.74–8.78 ppm in the imidazolium salts. H-2 shifted downfield, consistent with the increased electron-deficient character of the imidazolium ring following quaternization and the associated deshielding effect. In the ^1H NMR spectra of the Ag(I)–NHC complexes (1s–5s), the H-2 resonance had disappeared completely, consistent with deprotonation at C-2, formation of the *N*-heterocyclic carbene, and subsequent coordination to Ag(I). The H-4 and H-5 signals remained doublets with $J = 1.4$ Hz, appearing at approximately δ 7.21–7.27 and 7.05–7.14 ppm, respectively. Meanwhile, the N-CH_2 -butyl groups resonated at δ 4.58–4.62 ppm, and the long-chain N-CH_2 groups appeared at approximately δ 4.24–4.41 ppm (Habib *et al.*, 2019) [30]. The characteristic aliphatic resonances remain, showing that the long alkyl chains survived metalation. Meanwhile, the disappearance of H-2 from the ^1H NMR spectrum supports the successful conversion of the imidazolium precursors to the corresponding Ag(I)–NHC complexes.

^{13}C NMR spectral analysis

The ^{13}C NMR spectra followed the conversion of the *N*-substituted imidazole derivatives (1b–5b) into the corresponding imidazolium salts (1m–5m), and then into the Ag(I)–NHC complexes (1s–5s). Each spectrum for compounds 1b–5b contained three characteristic imidazole-ring carbon resonances. In compound 1b, for example, signals at δ 139.47, 126.54, and 121.58 ppm were assigned to C-2, C-4, and C-5, respectively. For compounds 2b–5b, the C-2 signals occurred at δ 139.87, 138.97, 140.19, and 140.14 ppm, respectively. The corresponding C-4 and C-5 resonances appeared in the ranges δ 125.97–127.17 and δ 121.24–122.38 ppm. N-CH_2 , the carbon directly bonded to nitrogen, resonated at approximately δ 43.78–44.92 ppm, while the remaining aliphatic carbons appeared in their expected upfield regions. After quaternization to form the imidazolium salts, the C-2 resonance moved substantially downfield, from approximately δ 139–140 ppm in the neutral imidazole derivatives to δ 148–150 ppm in the corresponding salts. For compounds 1m–5m, C-2 resonated at δ 149.54, 148.10, 148.37, 149.87, and 148.97 ppm, respectively. Its approximately 8–11 ppm shift reflects the marked alteration in the electronic environment of C-2 after the positively charged imidazolium ring formed, providing strong ^{13}C NMR evidence for quaternization. The remaining imidazolium ring carbons appeared in the δ 122–128 ppm range. Signals from the N-CH_2 carbons occurred at about δ 43–48 ppm, whereas the newly introduced N-CH_2 -butyl carbons appeared near δ 48 ppm. After the imidazolium salts were treated with Ag_2O , the ^{13}C NMR spectra of the resulting Ag(I)–NHC complexes (1s–5s) showed one particularly notable change: the characteristic imidazolium C-2 resonance had disappeared. In its place was a new, highly downfield signal assigned to the Ag-bound carbene carbon (C–Ag). For complexes 1s–5s, these C–Ag resonances occurred at δ 181.47, 181.97, 182.78, 182.60, and 182.76 ppm, respectively. The signals in the δ 181–183 ppm region are markedly different from the corresponding imidazolium C-2 resonances, which occur at approximately δ 148–150 ppm. This change is consistent with conversion of C-2 into a metal-bound *N*-heterocyclic

carbene carbon and offers strong evidence of Ag(I) coordination. By contrast, the remaining imidazole-ring carbon resonances stayed approximately within the δ 122–128 ppm range. Complex 1s, for example, showed signals at δ 127.91 and 123.91 ppm; in complexes 2s–5s, the corresponding signals fell within approximately δ 122.57–127.14 ppm. The N-CH_2 carbons of the long alkyl chains resonated at δ 45–47 ppm, while the N-CH_2 -butyl carbons appeared around δ 49–51 ppm. Overall, the ^{13}C NMR data trace a clear, systematic spectroscopic progression from *N*-substituted imidazole through the imidazolium salt to the Ag(I)–NHC complex. The C-2 resonance initially appeared at approximately δ 139–140 ppm. After the imidazolium salt formed, its signal shifted downfield to δ 148–150 ppm. Once the carbene was generated, it was replaced by the characteristic Ag–C(NHC) resonance at δ 181.47–182.78 ppm (Karataş *et al.*, 2016) [31]. The corresponding H-2 proton also disappeared from the ^1H NMR spectra. Taken together, these changes strongly support the proposed structures and confirm the successful formation of the Ag(I)–NHC complexes.

Anti-bacterial activity

The antibacterial data point to a clear structure–activity relationship (SAR) within the Ag(I)–NHC series. As the alkyl chains lengthened from 1s to 5s, MIC and IC_{50} values generally declined, corresponding to increased antibacterial potency. The pattern was most evident among the Gram-positive strains, where complexes 4s and 5s were the most active. For 5s, the lowest MIC was measured against *S. epidermidis* (24.85 μM), followed by *S. aureus* (27.45 μM) and *S. pyogenes* (30.51 μM). The IC_{50} values did not follow the same ranking: *S. pyogenes* had the lowest value (16.57 μM), whereas the values for *S. aureus* and *S. epidermidis* were 25.74 μM and 26.54 μM , respectively. By comparison, the Gram-negative bacteria generally needed higher concentrations to be inhibited, suggesting that they were less susceptible than the Gram-positive strains. Still, the increase in activity as the alkyl chain lengthened was unmistakable. For *E. coli*, the MIC fell from 1000 μM with 1s to 225 μM with 5s, and the IC_{50} dropped from 1150 to 196 μM . The shift was more pronounced in *P. aeruginosa*, where the IC_{50} declined from 1255 μM for 1s to 156 μM for 5s. A similar pattern appeared in *A. baumannii*, with the IC_{50} decreasing across the series from 1625 μM to 171 μM . Overall, 5s was the most antibacterial complex; 4s and 3s generally followed, while 1s was the least active. This stronger activity may be associated with the longer alkyl chains, which increase hydrophobicity and promote interaction with bacterial lipid membranes.

Membrane disruption could follow, along with improved biological availability of the Ag(I)–NHC moiety. The data also show that extending the alkyl chain can substantially strengthen the antibacterial performance of the complexes against both type of selected bacteria, though the size of the effect differs among bacterial species. The antibacterial findings from this study are compiled in Tables 1 and 2, which present the (MIC) and half-maximal inhibitory concentration (IC_{50}) values, respectively, for the tested bacterial strains. Together, the tables show the activity of the synthesized Ag(I)–NHC complexes (1s–5s) and allow their efficacy to be compared across different alkyl-chain lengths and bacterial strains.

Table 1. Biological activity of the synthesized Ag(I)–NHC complexes against selected bacterial strains, based on (MIC) values.

Bacterial strain	1s	2s	3s	4s	5s
<i>S. aureus</i>	200	120	55.65	33.52	27.45
<i>S. pyogenes</i>	120	60.5	57.5	38.25	30.51
<i>S. epidermidis</i>	175	115	52.75	32.5	24.85
<i>E. coli</i>	1000	500	500	250	225
<i>P. aeruginosa</i>	> 1500	> 1500	> 1500	1000	1000
<i>A. baumannii</i>	> 1500	1000	1000	500	500

(continued on next page)

Table 2. Quantitative evaluation and recording of the antibacterial activity of synthesized Ag(I)–NHC silver complexes based on IC₅₀ values.

Bacterial strain	1s	2s	3s	4s	5s
<i>S. aureus</i>	130	101	29.5	25.75	25.74
<i>S. pyogenes</i>	39.5	31.65	23.85	18.65	16.57
<i>S. epidermidis</i>	135	55.54	39.55	30.25	26.54
<i>E. coli</i>	1150	285	249	205	196
<i>P. aeruginosa</i>	1255	1121	875	300	156
<i>A. baumannii</i>	1625	751	354	225	171

Structure activity relationship (SAR)

The antibacterial behavior of the synthesized dinuclear Ag(I)–NHC complexes is associated mainly with the length of the terminal alkyl chains attached to the two imidazole rings. Across this series, the two imidazole-derived NHC units are joined by a 1,4-butylene linker, whereas the other nitrogen atoms bear alkyl substituents containing C₁₀, C₁₂, C₁₄, C₁₆, and C₁₈ carbon atoms in complexes 1s–5s, respectively. Keeping the Ag(I)–NHC core and the butylene linker unchanged makes it possible to assess how increasing hydrophobic chain length affects antibacterial activity. The effect was clearest among the Gram-positive strains. Complex 5s (C₁₈) produced the lowest MIC values for *S. aureus* (27.45 μM), *S. pyogenes* (30.51 μM), and *S. epidermidis* (24.85 μM). Gram-negative organisms followed the same general pattern, but were less susceptible overall. Against *E. coli*, for instance, the MIC fell from 1000 μM for 1s (C₁₀) to 225 μM for 5s (C₁₈), and the corresponding IC₅₀ dropped from 1150 to 196 μM. This greater activity with longer alkyl chains may reasonably result from the progressive increase in the hydrophobic character of the complexes, which could promote association with the lipid components of bacterial cell envelopes and strengthen their interaction with, or disruption of, bacterial membranes. The Ag(I)–NHC center could also contribute to antibacterial activity by interacting with biologically important bacterial targets, but the available MIC and IC₅₀ data do not, by themselves, identify a specific molecular mechanism. Activity did not improve in a strictly linear manner across all bacterial strains. Instead, antibacterial potency appears to reflect the combined influence of alkyl-chain length, Ag(I)–NHC coordination, molecular architecture, and the structural characteristics of the bacterial envelope. Gram-positive bacteria were generally more susceptible than bacteria, perhaps because their cell-envelope architecture differs; in particular, bacteria possess an additional outer membrane that may limit the penetration of hydrophobic and metal-containing compounds. Overall, the observed SAR suggests that lengthening the alkyl substituent from C₁₀ to C₁₈ generally improves the antibacterial activity of the Ag(I)–NHC complexes. Among the compounds examined, 5s (C₁₈) was the most active. The results indicate that adjusting alkyl-chain length can effectively tune the antibacterial properties of dinuclear Ag(I)–NHC complexes.

Conclusion

A homologous series of novel dinuclear Ag(I)–NHC complexes (1s–5s), carrying systematically varied long-chain alkyl substituents (C₁₀, C₁₂, C₁₄, C₁₆, and C₁₈), was synthesized from the corresponding disubstituted imidazolium salts. FT-IR, ¹H NMR, and ¹³C NMR spectroscopy supported the structures of the resulting compounds. In particular, the disappearance of the imidazolium H-2 signals and the appearance of the characteristic Ag–C(NHC) resonance at δ 181.47–182.78 ppm provided important evidence of NHC formation and Ag(I) coordination. When tested against tested bacterial strains, the complexes showed antibacterial activity, with the organisms generally more susceptible. Increasing the alkyl-chain length from C₁₀ to C₁₈ generally lowered the MIC and IC₅₀ values, pointing to stronger antibacterial activity and a clear structure activity relationship across the series. Among the compounds tested, complex 5s, bearing the C₁₈ alkyl chain, had the strongest overall antibacterial activity. The effect

was strongest against *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Staphylococcus epidermidis*. These findings indicate that systematic modifications to the hydrophobic alkyl chain can change the antibacterial activity of dinuclear Ag(I)–NHC complexes and support further investigation of these compounds as silver-based antibacterial agents.

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