

Preparation And Study Biological Action of Silver(I)-N-Heterocyclic Carbene Complexes with Alkyl Halides Chain

Fatimah Sahib Abed¹, Rana Abdulilah Abbas², Malath I. Yousif³, Ihsan Alrubaie⁴, Ali Jabbar Radhi^{5,6*}

¹ University of Kerbala, College of Dentistry, Department of Basic sciences, Kerbala, Iraq

² Department of Chemical Industrial, Institute of Technology/ Baghdad, Middle Technical University, Iraq

³ Al-Furat Al-Awsat technical university, Technical Institute, Diwanya, Iraq

⁴ Faculty of Pharmacy, Jabir ibn Hayyan Medical University, Najaf, Iraq

⁵ Ministry of Education, The General Directorate of Educational in Najaf Al-Ashraf, Najaf, Iraq

⁶ University of Al-Kafeel, College of Pharmacy, Najaf, Iraq

E-mail: alijebar56@gmail.com

Abstract

N-heterocyclic carbenes derivatives (NHCs), a novel ligand, can be found in azolium salts. They can be used in a variety of ways due to their unique features. Novel di nuclear bis-benzimidazolium bromide salt and their Ag(I)-complex was prepared as well as analyzed via many spectroscopic investigations in the current study. FTIR as well as NMR spectroscopy was used to examine the produced combinations. These compound biotic potentials were evaluated for antibacterial activity against two types of bacteria [G-ve E. Coli] and [G+ve S. aureus]. The silver complex synthesized (c1-c5) showed good inhibition for S. Aureus (6.4, 5.6, 5.1, 4.9, 5.2 17 mm) and E. Coli (5.2, 3.6, 4.3, 3.7, 4.8 mm).

Keyword: N-heterocyclic carbene, Silver complexe, Antimicrobial action, Ligand, Benzimidazole

1. Introduction

First time of preparation N-heterocyclic carbene compounds via chemists Feile as well as Wanzlick [1, 2] besides the separation as stable NHC compounds by Arduengo [3]. The synthesis of novel NHC and their complexes has attracted a lot of attention. It's a fascinating study topic where a variety of novel metal NHC complexes including transition metals and main group elements have been produced and used in various applications [4–7]. In terms of how they interact with metals, NHCs are comparable to phosphine ligands. Nonetheless, these carbene compounds are more appealing to metals than phosphines moiety, possibly because of easier synthesis procedures [8, 9]. Due to their biological activity as pharmacological materials such as antiulcer, antifungal, anticancer, and antibacterial qualities, benzimidazole compound preparation and some applications have been examined more frequently in the last decade [10–12]. The benzimidazole derivatives are utilized as effective antibacterial medicines to treat a variety of fungal and bacterial illnesses [13]. Because of the wide range of biological activity applications of benzimidazole compounds, there are many researches being done to generate more effective and less hazardous N-heterocyclic molecules for biological usage [14, 15]. Transition metals (gold, silver, and copper) are amongst the transition metals

that have received a lot of attention by reason of their exclusive structural properties and wide range of uses in several fields [16, 17]. Silver metal isn't prevalent in the organism of human body at birth, whereas they have a good effective lethal effect on microorganisms while also being less hazardous to people. Some of those silver salts have antibacterial and anticancer properties in vitro. The big problem in those (Ag) metal medications is the rapid releasing of their action via given Ag (I). That constraint may be circumvented via utilizing NHC derivatives as ligands, as they strongly attached the Ag metal return to their very good weak pi-accepting and sigma donating characteristics [18, 19]. Finally, a persistent release of Ag(I) has been seen at the target site [20]. Ag-NHC complexes have develop particularly appealing in coordination chemistry because of their ease of preparation using benzimidazolium salts and Ag₂O in a single step [13, 21, 22]. Another reason for the advantage in silver-NHC derivatives are may be employed as a ligand in carbene transfer metalation processes to preparation another NHC compounds of Pt, Au, Ni, Ru, Cu, and Rh, making the synthesis of these [24, 25] metal carbene complexes easier. Chemist Youngs and co-workers. published the first research of Ag-NHCs as an antimicrobials agent in 2004. Since then, silver carbene complexes have been proven to be physiologically active as antimicrobial and anticancer medicines [26]. When bis-benzimidazolium bromide

salts are attached with silver metal to create Ag- *N*-heterocyclic carbene complexes, they have an intriguing improved anticancer potential [27]. So, in this paper, we produced a variety of alkyl chain-substituted -benzimidazolium bromide salts and its Ag(I) complexes, in addition to antimicrobials research on them.

2. Methodology

Altogether solvents as well as chemicals stayed bought from SigmaAldrich as well as Fluka, with the maximum diagnostic rank. The Fourier conversion infrared Bruker ALPHA FT-IR, college of Science, Kufa University, documented infrared spectrum. In the University of Shahid Beheshti- Iran, NMR spectrum in DMSO-*d*₆ was gained by a Bruker spectrometers (75MHz for ¹³C NMR, as well as 300MHz of ¹H NMR correspondingly). Electro-Thermal Melting Points Device made in UK was used for the measurement of melting point.

Production of *N*-Substituted Benzimidazole [28]

The circular bottom containers were filled by (0.0253 mol) benzimidazole as well as (0.3809 mol) KOH powder. 40.0 mL of organic solvent (DMSO) were added, as well as the mix was agitated for 2 hrs at 90°C. Alkyl bromide (0.0126 mol) were added cautiously dropwise by continuous stirring. Afterward full alkyl bromide adding, at 40°C, the mix was agitated for 1.5 hrs. The containers were removed. In a beaker, transfer 250 mL of iced water, spill into the reaction solution, then stir the mix quickly for 30 min. After that the mix was kept for 1 hr. before extraction by petroleum ether and D.W (3X10 mL). The petroleum ether was removed from the yields.

1-decyl-1H-benzo[d]imidazole (a1): This is produced in Pure yellow (81 % produce), FT-IR cm-1: 3050(C-Haromatic), 2920(C-Haliph), 2853(C-Haliph), 1558 (C=N),1252(C-N).¹H NMR, δ 8.25 (s, 1H, NCHN), 7.68-7.22 (m,4H, Ar-H), 4.21 (t, J = 7.0 Hz, 2H, N-CH₂), 1.76 (p, J = 6.9 Hz, 2H), 1.18-1.25 (m, 14H, 7 x CH₂), 0.83 (t, J = 6.7 Hz, 3H, CH₃), ¹³C NMR, δ 144.36(NCHN), 143.91, 134.22, 122.55, 122.14, 121.74, 119.85, 115.73, 110.70(Ar-C),44.54(N-CH₂), 31.78, 29.87, 29.44, 29.42, 29.19, 29.04, 26.60, 22.59(8-CH₂), 14.34(CH₃).

1-dodecyl-1H-benzo[d]imidazole (a2): This is produced in Pure yellow (79 %), FT-IR cm-1: 3052(C-Haromatic),2919(C-Haliph), 2852(C-Haliph), 1686 (C =N),1277 (C-N). ¹H NMR, δ 8.23 (s, 1H, NCHN), 7.73-7.21 (m, 4H, Ar-H), 4.20 (t, J = 7.0 Hz, 2H, N-CH₂), 1.76 (p, J = 6.8 Hz, 2H), 1.18-1.26 (m, 16H, 9 x CH₂), 0.83 (t, J = 6.6 Hz, 3H), ¹³C NMR, δ 144.34(NCHN), 144.04, 134.25, 122.51, 121.69, 119.90, 110.63(Ar-C),44.52(N-CH₂), 31.79, 29.89, 29.43, 29.19, 29.05, 26.62, 22.59(10-CH₂), 14.32 (CH₃).

1-tetradecyl-1H-benzo[d]imidazole (a3): This is produced in Pure yellow (86 % produce), FT-IR cm-1: 3053(C-Haromatic), 2920(C-Haliph), 2853(C-Haliph), 1617 (C=N),1252 (C-N).¹H NMR, δ 8.22 (s, 1H, NCHN), 7.66-7.13 (m, 4H, Ar-H), 4.21 (t, J = 7.1 Hz,

2H, N-CH₂), 1.76 (p, J = 7.0 Hz, 2H), 1.20-0.96 (m, 22H, 11x CH₂), 0.83 (t, J = 6.4 Hz, 3H), ¹³C NMR, δ 144.36(NCHN), 143.91, 134.21, 122.55, 121.74, 119.86, 110.68(Ar-C), 44.52(N-CH₂), 31.81, 29.86, 29.57, 29.54, 29.51, 29.44, 29.42, 29.24, 29.02, 26.59, 22.59(12-CH₂), 14.35(CH₃).

1-hexadecyl-1H-benzo[d]imidazole (a4): This is produced in Pure yellow (85 % produce), FT-IR cm-1: 3053(C-Haromatic),2921(C-Haliph), 2854(C-Haliph), 1616 (C =N),1250 (C-N).¹H NMR, δ 8.24 (s, 1H, NCHN), 7.71–7.15 (m, 4H, Ar-H), 4.25 (t, J = 7.1 Hz, 2H, N-CH₂), 3.40 (s, 2H), 2.56 (s, 1H), 1.84-1.78 (p, J = 7.0 Hz, 2H), 1.25-1.20 (m, 26H, 13x CH₂), 0.87(t, J = 6.5 Hz, 3H), ¹³C NMR, δ 144.44(NCHN), 143.93, 134.24, 122.58, 121.76, 119.88, 110.78(Ar-C), 44.51(N-CH₂), 31.79, 31.79, 29.84, 29.70, 29.53, 29.51, 29.40, 29.33, 29.21, 29.14, 28.99, 26.58, 26.57, 22.59(14-CH₂), 14.41(CH₃).

1-octadecyl-1H-benzo[d]imidazole (a5): This is produced in Pure yellow (85 % produce), FT-IR cm-1: 3053(C-Haromatic),2921(C-Haliph), 2854(C-Haliph), 1616 (C =N),1250 (C-N).¹H NMR, δ 8.24 (s, 1H, NCHN), 7.71–7.15 (m, 4H, Ar-H), 4.25 (t, J = 7.1 Hz, 2H, N-CH₂), 3.40 (s, 2H), 2.56 (s, 1H), 1.84-1.78 (p, J = 7.0 Hz, 2H), 1.25-1.20 (m, 26H, 13x CH₂), 0.87(t, J = 6.5 Hz, 3H), ¹³C NMR, δ 144.44(NCHN), 143.93, 134.24, 122.58, 121.76, 119.88, 110.78(Ar-C), 44.51(N-CH₂), 31.79, 31.79, 29.84, 29.70, 29.53, 29.51, 29.40, 29.33, 29.21, 29.14, 28.99, 26.58, 26.57, 22.59(14-CH₂), 14.41(CH₃).

Production of 1,3-disubstituted benzimidazolium salt

In a round bottom flask, (0.002 mol) of *N*-alkylated was placed, and adding 30.0 mL of organic solvent 1,4-dioxane. and dissolved all reactants after a half-hour of heating and continual stirring. Then, with steady stirring, 0.01 mol of 1,4-dibromobutane was added carefully, dropwise to the solution. At 90°C, the reaction mixture was refluxed for 24 hours. This container is then withdrawn, adding 15 mL of organic solvent *n*-hexane to this mixture, then the flask was quietly shaken. After allowing combination to sit for one hour, the result was filtered. End products were washed twice by *n*-hexane then dehydrated in oven [28].

Ligand (b1): This was produced as a powder (71 % produce) (m.p=138-140 °C). FT-IR cm-1: 3081(C-Haromatic), 2921(C-Haliph), 2845(C-Haliph), 1241(C-N); ¹H NMR, δ 8.94 (s, 1H, NCHN), 7.57–7.21 (m, 8H, Ar-H), 4.56 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.25 (t, J = 7.1 Hz, 4H, N-CH₂), 1.84-1.78 (m, 8H, N-CH₂-CH₂-), 1.25-1.20 (m, 28H, 14x CH₂), 0.85(t, J = 6.5 Hz, 3H), ¹³C NMR, δ 144.87(NCHN), 143.78, 134.82, 122.47, 121.78, 120.18, 110.57(Ar-C), 48.74 (N-CH₂-butyl), 44.74(N-CH₂), 31.84, 31.76, 29.90, 29.75, 29.62, 29.47, 29.38, 29.31, 29.22, 29.03, 28.86, 28.26, 26.27, 26.04, 22.74(10-CH₂), 14.38(CH₃).

Ligand (b2): This was produced as a powder (77 % produce) (m.p=157-159 °C). FT-IR cm-1: 3085(C-Haromatic), 2928(C-Haliph), 2840(C-Haliph), 1247(C-N); ¹H NMR, δ 8.89 (s, 1H, NCHN), 7.65–7.23 (m, 8H,

Ar-H), 4.53 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.28 (t, J = 7.1 Hz, 4H, N-CH₂), 1.87-1.77 (m, 8H, N-CH₂-CH₂-), 1.29-1.21 (m, 32H, 16x CH₂), 0.86 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 145.17(NCHN), 144.24, 134.65, 122.18, 120.74, 120.07, 111.55(Ar-C), 48.28 (N-CH₂-butyl), 44.85(N-CH₂), 31.89, 31.35, 29.95, 29.79, 29.63, 29.50, 29.41, 29.30, 29.22, 29.11, 28.79, 28.12, 26.47, 26.28, 22.29(12-CH₂), 14.38(CH₃).

Ligand (b3): This was produced as a powder (69 % produce) (m.p=168-170 °C). FT-IR cm⁻¹: 3078(C-Haromatic), 2935(C-Haliph), 2841(C-Haliph), 1242(C-N); ¹H NMR, δ 8.93(s, 1H, NCHN), 7.61–7.22 (m, 8H, Ar-H), 4.54 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.29 (t, J = 7.1 Hz, 4H, N-CH₂), 1.86-1.73 (m, 8H, N-CH₂-CH₂-), 1.31-1.22 (m, 36H, 18x CH₂), 0.88 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 145.38 (NCHN), 144.78, 133.48, 122.78, 121.47, 120.09, 112.87(Ar-C), 48.37 (N-CH₂-butyl), 44.64(N-CH₂), 32.01, 31.87, 30.12, 29.96, 29.77, 29.60, 29.52, 29.43, 29.31, 29.21, 29.13, 28.89, 28.25, 27.34, 26.67, 26.18, 22.41(14-CH₂), 14.29(CH₃).

Ligand (b4): This was produced as a powder (69 % produce) (m.p=184-186 °C). FT-IR cm⁻¹: 3075 (C-Haromatic), 2932(C-Haliph), 2831(C-Haliph), 1238(C-N); ¹H NMR, δ 8.91(s, 1H, NCHN), 7.64–7.23 (m, 8H, Ar-H), 4.55 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.28 (t, J = 7.1 Hz, 4H, N-CH₂), 1.88-1.70 (m, 8H, N-CH₂-CH₂-), 1.33-1.23 (m, 40H, 20x CH₂), 0.84 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 145.87 (NCHN), 144.88, 135.05, 122.87, 121.74, 120.19, 112.04(Ar-C), 47.87 (N-CH₂-butyl), 43.98(N-CH₂), 31.98, 31.71, 30.21, 29.97, 29.84, 29.79, 29.62, 29.548, 29.40, 29.29, 29.19, 29.12, 28.80, 28.63, 28.38, 27.26, 26.42, 26.24, 22.46(16-CH₂), 14.18(CH₃).

Ligand (b5): This was produced as a powder (69 % produce) (m.p=192-194 °C). FT-IR cm⁻¹: 3084 (C-Haromatic), 2941(C-Haliph), 2832(C-Haliph), 1235(C-N); ¹H NMR, δ 8.93(s, 1H, NCHN), 7.61–7.25 (m, 8H, Ar-H), 4.57 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.32 (t, J = 7.1 Hz, 4H, N-CH₂), 1.89-1.75 (m, 8H, N-CH₂-CH₂-), 1.30-1.21 (m, 44H, 22x CH₂), 0.83 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 146.07(NCHN), 143.98, 134.25, 123.05, 122.19, 120.97, 113.14(Ar-C), 46.98 (N-CH₂-butyl), 44.08(N-CH₂), 31.91, 31.58, 30.87, 30.09, 29.93, 29.81, 29.75, 29.58, 29.58, 29.44, 29.32, 29.16, 29.10, 28.82, 28.67, 28.49, 28.22, 27.20, 26.59, 26.18, 22.74(18-CH₂), 14.15(CH₃).

Syntheses of Silver(I)–NHC Complexes

The dinuclear Ag(I)-NHC compounds (c1-c5) were made by dissolving (0.006 mol) of disubstituted benzimidazolium bromide (b1-b5) in 1,4-dioxane and performing an in situ deprotonation process (25 mL). Then, with continual stirring, (2.0 equiv.) of Ag₂O was added to the mixture, completely covering the flask. The reaction mixture was stirred for 48 hours, at room temperature. To eliminate unreacted Ag₂O, the flask was removed then the solutions were filtered via layer of celite in dark place. The solvent is then removed under reduced pressure, and the resultant powder product [28].

Complex (C1): This was produced as a powder (65 %

produce) (m.p=166-168 °C). FT-IR cm⁻¹: 3075(C-Haromatic), 2945 (C-Haliph), 2862(C-Haliph), 1341(C-N); ¹H NMR, δ 7.49–7.24 (m, 8H, Ar-H), 4.53 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.28 (t, J = 7.1 Hz, 4H, N-CH₂), 1.86-1.77 (m, 8H, N-CH₂-CH₂-), 1.29-1.21 (m, 28H, 14x CH₂), 0.86 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 183.57(C-Ag), 144.25, 133.98, 123.42, 121.87, 120.29, 112.51(Ar-C), 50.70 (N-CH₂-butyl), 46.78(N-CH₂), 31.92, 31.74, 29.93, 29.72, 29.58, 29.43, 29.33, 29.27, 29.19, 29.05, 28.58, 28.31, 26.38, 26.11, 22.82(10-CH₂), 14.24 (CH₃).

Complex (C2): This was produced as a powder (68 % produce) (m.p=147-149 °C). FT-IR cm⁻¹: 3074 (C-Haromatic), 2944 (C-Haliph), 2865(C-Haliph), 1341(C-N); ¹H NMR, δ 7.57–7.25 (m, 8H, Ar-H), 4.56 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.31 (t, J = 7.1 Hz, 4H, N-CH₂), 1.88-1.76 (m, 8H, N-CH₂-CH₂-), 1.31-1.24 (m, 32H, 16x CH₂), 0.86 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 183.78(C-Ag), 144.79, 134.24, 123.28, 121.79, 120.17, 113.76(Ar-C), 49.97 (N-CH₂-butyl), 45.95(N-CH₂), 31.82, 31.47, 29.90, 29.81, 29.61, 29.48, 29.40, 29.31, 29.21, 29.12, 28.84, 28.29, 26.39, 26.21, 22.38 (12-CH₂), 14.27 (CH₃).

Complex (C3): This was produced as a powder (64 % produce) (m.p=192-194 °C). FT-IR cm⁻¹: 3075(C-Haromatic), 2956(C-Haliph), 2848(C-Haliph), 1342(C-N); ¹H NMR, δ 7.58–7.26 (m, 8H, Ar-H), 4.58 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.33 (t, J = 7.1 Hz, 4H, N-CH₂), 1.88-1.76 (m, 8H, N-CH₂-CH₂-), 1.30-1.23 (m, 36H, 18x CH₂), 0.87 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 184.14(C-Ag), 143.89, 134.87, 123.59, 121.74, 120.14, 113.82(Ar-C), 49.15 (N-CH₂-butyl), 46.13(N-CH₂), 31.94, 31.83, 30.24, 29.89, 29.74, 29.62, 29.48, 29.39, 29.30, 29.22, 29.14, 28.78, 28.21, 27.28, 26.73, 26.29, 22.75(14-CH₂), 14.18(CH₃).

Complex (C4): This was produced as a powder (71 % produce) (m.p=166-168 °C). FT-IR cm⁻¹: 3088 (C-Haromatic), 2962(C-Haliph), 2847 (C-Haliph), 1331(C-N); ¹H NMR, δ 7.59–7.27 (m, 8H, Ar-H), 4.58 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.34 (t, J = 7.1 Hz, 4H, N-CH₂), 1.86-1.74 (m, 8H, N-CH₂-CH₂-), 1.31-1.22 (m, 40H, 20x CH₂), 0.86 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 184.65 (C-Ag), 144.65, 134.37, 123.78, 122.24, 120.39, 113.17 (Ar-C), 48.82 (N-CH₂-butyl), 45.13(N-CH₂), 31.87, 31.70, 30.28, 29.84, 29.76, 29.71, 29.58, 29.51, 29.43, 29.26, 29.15, 29.07, 28.62, 28.53, 28.11, 27.41, 26.71, 26.43, 22.32(16-CH₂), 14.10(CH₃).

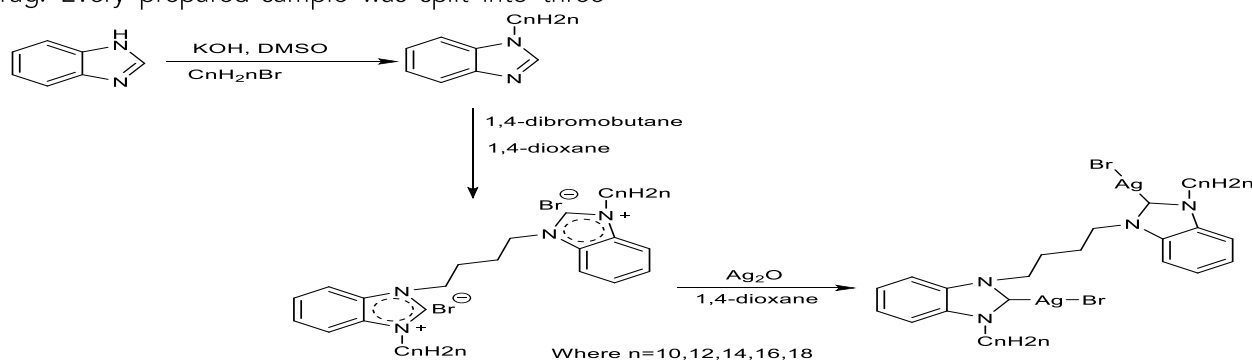
Complex (C5): This was produced as a powder (64 % produce) (m.p=171-173 °C). FT-IR cm⁻¹: 3078 (C-Haromatic), 2968(C-Haliph), 2855(C-Haliph), 1331(C-N); ¹H NMR, δ 7.54–7.22 (m, 8H, Ar-H), 4.56 (t, J = 6.4 Hz, 4H, N-CH₂-butyl), 4.35 (t, J = 7.1 Hz, 4H, N-CH₂), 1.87-1.76 (m, 8H, N-CH₂-CH₂-), 1.31-1.22 (m, 44H, 22x CH₂), 0.87 (t, J = 6.5 Hz, 3H), ¹³C NMR, δ 184.44(C-Ag), 144.24, 134.65, 123.78, 122.45, 121.17, 113.56(Ar-C), 47.24 (N-CH₂-butyl), 44.87(N-CH₂), 31.96, 31.69, 30.88, 30.14, 29.91, 29.79, 29.70, 29.54, 29.48, 29.39, 29.31, 29.17, 29.07, 28.88, 28.61, 28.32, 28.14, 27.27, 26.38, 26.21, 22.27(18-CH₂), 14.21(CH₃).

Antibacterial activity

The assessment of a new produced Ag-NHC complexes is managed by pour technique, that is adapted [29]. Gram+ve (*S. aureus*) and Gram+ve (*E. coli*) are studied. The clear zone without tested compound is used to study the antimicrobial ability of a new produced complex [30]. In bacterial growing, nutrient agar was used. All the solutions of final compounds were prepared by the organic solvents DMSO in stable concentrations (10 mg/ml). The positive control is ciprofloxacin, while the negative control is DMSO. 80 L from every tester are put in wells then incubation in 37 °C, 24 hours. Inhibiting zone is measured of mm via a Vernier caliper.

Minimum inhibitory Concentrations (MIC)

The biological activity was determined by measured zone inhibition [31], as stated in the literature. Through dissolving the end products in DMSO solvent in the 50–0.1 L range, a number of dilutions of the prepared samples were formed. In triplicate, 100 liters of each sample dilution were transferred into well dishes. The prepared target samples were filled into the wells. A 50-liter Mueller Hinton broth was poured into the remaining wells. The resazurin solution is produced via mixed a (3.7 g) resazurin capsule in 40 ml D.W. A 10 liter resazurin reagent mixture solution is placed into the same well as the sample too. In the same wells, another 10 L of bacterial suspension was introduced. In each well of the plate, pour 30 liters of Mueller Hinton. In addition, every dish was wrapped tightly in cling film to prevent microorganisms from becoming dehydrated. There were two control sets on each plate: a negative control and (ciprofloxacin) a positive drug. Every prepared sample was split into three



Scheme 1: Synthesis of Ag-NHC complexes

FT-IR Spectral

Examination via changing the distinct peak for salt as well as complex, spectral features for produced newly benzimidazolium bromide salt as well as Ag-NHC complex may describe the active production of materials [37]. For validation of the active production, FTIR spectra of synthesized salt as well as Ag(I)-NHC complexes is examined as well as changed. The distinct peak shape of produced N-alkylated salts was powerful between (1500 – 800) cm⁻¹, though it was reduced in bis-benzimidazolium salt. Because of twisting

parts and incubated for 24 hours at 37°C.

3. Result and Discussion

Synthesis

Bis-benzimidazolium salts (b1-b5) are produced in 2 step by procedures defined in literature [32–34]. N-alkylated benzimidazole derivative is primarily prepared via reaction starting material benzimidazole by alkyl bromide in the existence robust alkaline (KOH) firstly. The organic solvent utilized in the method is DMSO. It is probably to gain white oily constituent. Removing of acidic H⁺ in N² was following with a nucleophile center bind in alkyl halide, that causes bromide ion removal. Next step include dissolve two equals from produced N-alkylated imidazole rings of benzimidazole in 1,4-dioxane solvents then refluxation it by 1 equal from 1,4-dibromobutane. Free pairs electrons from N² in benzimidazole attacked electrophilic center in alkyl bromide then linked by it in 90 °C, producing benzimidazolium salt (b1-b5). The melting points for prepared salt was defined, in addition to their broad spectrum description. The reported procedures [35,36] were used to make binuclear silver NHC complexes. The compounds were created by removing acidic hydrogen from carbene carbon in vitro and treating it by Ag₂O in room temperature. Ag-NHC compound with counter ion (Br⁻) analysed in light sources, therefore, synthesis had to be done in the dark. The prepared bis-benzimidazolium bromide salts mixed with 1,4-dioxane were agitated with Ag₂O at room temperature in the dark. All of the complexes were made from solid white material. Prior to their biological use, all complexes had their melting points and spectral analysis completed.

vibration in =C-H groups, a strong type of band in fingerprint area for infrared spectrum, (757 - 655 cm⁻¹), is detected in infrared spectrum in all the produced benzimidazolium bromide salts ligands as well as Ag(I)-NHC complexes for ligands (b1-b5) [33]. The presence of visible band in all spectra for produced bis-benzimidazolium bromide salt in 2950-2800 cm⁻¹. The 4-finger shape [13, 36] of prepared Ag(I)-NHC complexes as well as recognized band for C=N stretching vibrating for N-alkylated imidazole rings of benzimidazolium bromide salt of chose area

1605-1310 cm^{-1} which found in produced Ag(I)-NHC complexes (c1-c5) provide a powerful sign of silver complex production [38].

NMR Spectroscopy

In case of DMSO as a solvent, ^1H as well as ^{13}C NMR spectra of produced ligands (b1-b5) as well as their Ag(I)-NHC complexes (c1-c5) are documented. In the 8.22-8.25 ppm average, salt/ligands (b1-b5) comprise clear peak for acidic proton which attach NCHN. This acidic proton in salt/ligand (b1-b5) was substituted with Ag ions in the produced complexes of Ag(I)-NHC (c1-c5) [39]. That was a highly strong reagent for a effective Ag complex production. ^{13}C NMR spectrum of produced salt (b1-b5) showed the significance peak because of carbon which binding acidic proton in average 144.87-146.07 ppm while the rate of NCHN in silver complexes(c1-c5) shifting to down field at 183.57-184.65 ppm [40,41]. This material demonstrates that Ag(I)-NHC complexes and their salts were successfully synthesized.

MIC Value

All of the complexes (c1-c5) were screened against two types of microorganism G-ve E. coli and G+ve S. aureus. All complex solution is produced in organic solvents (DMSO) which prepared at a stable concentration in 10 mg/mL. All gram-positive bacterial Staphylococcus aureus and gram-negative bacterial Escherichia coli strain has been found to be inactive against DMSO [42,43]. Ciprofloxacin was managed in similar concentration as a classic medicine against bacteria. Altogether the composites are established to be effective against assessed strain, and the value of inhibition zone are assumed in millimeter. The biological uses of Ag-NHC complexes have already been extensively studied [43]. Ciprofloxacin, a prevalent antibiotic, displayed 10.2 mm to S. aureus in addition to 10.4 mm to E. Coli strains. Conversely, silver complexes (c1-c5) showed good inhibition zone (6.4, 5.6, 5.1, 4.9, 5.2 17) mm in S. aureus besides (5.2, 3.6, 4.3, 3.7, 4.8) mm in E. Coli strains, so Ag core shared considerably to bacterial growing inhibition. The goal for the current study is to determine if silver NHC complexes (c1-c5) have considerable antibacterial persistence in terms of MIC. Figure-1 displays the consequence of antibacterial action.

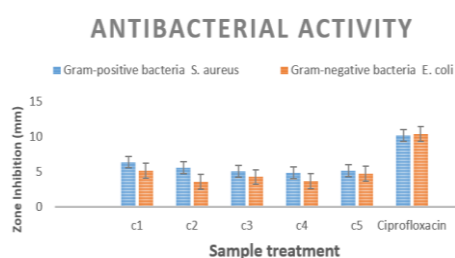


Figure 1 Antimicrobial activity of produced complexes (c1-c5) in concentrations

4. Conclusions

Primary researchers are used to prepare and describe the binuclear complex for Ag(I)-NHC (c1-c5). FTIR and NMR spectroscopy examinations showed the chemical are effectively produced. The antibacterial action for all prepared Ag(I)-NHC complexes (c1-c5) are assessed against gram+ve S. aureus as well as gram-ve E. Coli strain, in addition the complex are showed to be bacteriostatically constant. By higher concentrations, s Ag(I)-NHC complex presented a high scavenging tendency.

References

- Öfele K (1968) 1, 3-Dimethyl-4-imidazolinylden-(2)-pentacarbonylchrom ein neuer Übergangsmetall carben-komplex. J Organomet Chem 12(3):P42–P43
- Wanzlick HW, Schönherr HJ (1968) Direct synthesis of a mercury salt-carbene complex. Angewandte Chemie International Edition in English 7(2):141–142
- Arduengo III, Harlow AJRL, Kline M (1991) A stable crystalline carbene. J Am Chem Soc 113(1):361–363
- Kühl O (2007) The chemistry of functionalised N-heterocyclic carbenes. Chem Soc Rev 36(4):592–607
- van Vuuren E, Malan FP, Landman M (2021) Multidentate NHC complexes of group IX metals featuring carbon-based tethers: Synthesis and applications. Coord Chem Rev 430:213731
- Romain C, Bellemin-Lapponnaz S, Dagorne S (2020) Recent progress on NHC-stabilized early transition metal (group 3–7) complexes: Synthesis and applications. Coord Chem Rev 422:213411
- Reshi NUD, Bera JK (2020) Recent advances in annellated NHCs and their metal complexes. Coordination Chemistry Reviews, : p.213334 Page 11/16
- Herrmann WA (2002) N-heterocyclic carbenes: a new concept in organometallic catalysis. Angew Chem Int Ed 41(8):1290–1309
- Gopalakrishnan AK, Angamaly SA, Velayudhan MP (2021) An Insight into the Biological Properties of Imidazole-Based Schiff Bases: A Review. ChemistrySelect 6(40):10918–10947
- Ansari K, Lal C (2009) Synthesis and evaluation of some new benzimidazole derivatives as potential antimicrobial agents. Eur J Med Chem 44(5):2294–2299
- Shadia A Galal, Khaled H Hegab, Ahmed S Kassab, Mireya L Rodriguez, Sean M Kerwin, A Abdel-Mo'men, Hoda I El Diwani (2009) New transition metal ion complexes with benzimidazole-5-carboxylic acid hydrazides with antitumor activity. Eur J Med Chem 44(4):1500–1508
- Tacke M (2015) Benzyl-substituted carbene-metal complexes: Potential for novel antibiotics and anticancer drugs? J Organomet Chem 782:17–21
- Aqsa Habib, Muhammad AdnanIqbal, Haq Nawaz Bhatti, Amna Kamal, Shagufta Kamal (2020) Synthesis of alkyl/aryl linked binuclear silver (I)-N-Heterocyclic carbene complexes and evaluation of their antimicrobial, hemolytic and thrombolytic

potential. *Inorg Chem Commun* 111:107670

14. Yılmaz, Ü., Küçükbaş, H., Şireci, N., Akkurt, M., Günal, S., Durmaz, R., & Nawaz Tahir, M (2011) Synthesis, microwave-promoted catalytic activity in Suzuki–Miyaura cross-coupling reactions and antimicrobial properties of novel benzimidazole salts bearing trimethylsilyl group. *Appl Organomet Chem* 25(5):366–373.

15. Oehninger L, Rubbiani R, Ott I (2013) N-Heterocyclic carbene metal complexes in medicinal chemistry. *Dalton Trans* 42(10):3269–3284

16. Lin JCY et al (2009) Coinage Metal–N-Heterocyclic Carbene Complexes. *Chem Rev* 109(8):3561–3598.

17. Ielo, I., Iacopetta, D., Saturnino, C., Longo, P., Galletta, M., Drommi, D., ... & Plutino, M. R (2021) Gold Derivatives Development as Prospective Anticancer Drugs for Breast Cancer Treatment. *Applied Sciences*, 11(5): p. 2089.

18. Budagumpi, S., Haque, R. A., Endud, S., Rehman, G. U., & Salman, A. W (2013) Biologically Relevant Silver (I)–N-Heterocyclic Carbene Complexes: Synthesis, Structure, Intramolecular Interactions, and Applications. *Eur J Inorg Chem* 2013(25):4367–4388.

19. Liang, J., Sun, D., Yang, Y., Li, M., Li, H., & Chen, L (2021) Discovery of metal-based complexes as promising antimicrobial agents. *European Journal of Medicinal Chemistry*, p.113696.

20. Fatima, T., Haque, R. A., Ahmad, A., Hassan, L. E. A., Ahamed, M. B. K., Majid, A. A., & Razali, M. R (2020) Tri N-Heterocyclic Carbene Trinuclear Silver (I) complexes: Synthesis and in Vitro cytotoxicity studies. *J Mol Struct* 1222:128890

21. Syed, H. K., Iqbal, M. A., Haque, R. A., & Peh, K. K (2015) Synthesis, characterization and antibacterial activity of a curcumin–silver (I) complex. *J Coord Chem* 68(6):1088–1100

22. Haque, R. A., Iqbal, M. A., Mohamad, F., & Razali, M. R (2018) Antibacterial and DNA cleavage activity of carbonyl functionalized N-heterocyclic carbene–silver (I) and selenium compounds. *J Mol Struct* 1155:362–370

23. Iqbal, M. A., Haque, R. A., Ahamed, M. B. K., & Majid, A. M. S. A (2014) Synthesis and cytotoxicity of dinuclear silver (I)–N-heterocyclic carbene complexes. *Biochemistry and Analytical Biochemistry* 3(1):1.

24. Liu, S. T., Hsieh, T. Y., Lee, G. H., & Peng, S. M (1998) Carbene transfer between transition-metal ions. *Organometallics* 17(6):993–995 Page 12/16

25. Neetha, M., Saranya, P. V., Philip, R. M., & Anilkumar, G (2021) An Overview of Silver-Catalyzed Mannich Reactions. *ChemistrySelect* 6(40):11162–11176.

26. Youngs, W. J., Knapp, A. R., Wagers, P. O., & Tessier, C. A (2012) Nanoparticle encapsulated silver carbene complexes and their antimicrobial and anticancer properties: a perspective. *Dalton Trans* 41(2):327–336.

27. Iqbal, M. A., Haque, R. A., Nasri, S. F., Majid, A. M. S., Ahamed, M. B. K., Farsi, E., & Fatima, T. (2013). Potential of silver against human colon cancer:(synthesis, characterization and crystal

structures of xylyl (Ortho, meta, & Para) linked bis-benzimidazolium salts and Ag (I)–NHC complexes: In vitro anticancer studies). *Chemistry central journal*, 7(1), 1-17.

28. Choon WanYeap, Rosenani A.Haque, Wan SinnYam, Mohd.R.Razali(2019) The first mesomorphic benzimidazolium-based silver(I)–N-heterocyclic dicarbene complexes: Synthesis, characterization and phase properties, *Journal of Molecular Liquids*.277, P. 341-348.

29. Ali Jabbar Radhi, Ezzat Hussein Zimam , Emad Abbas Jaffar Al-Mulla, (2021) New Barbiturate Derivatives as Potent *in vitro* α -Glucosidase Inhibitors, *Egypt. J. Chem.*, 64, (1), 117 – 123

30. Majed Jary Mohammed, Zeyad Kadhim Olewi, Muntadher Abdulabbas Hasan, Ahmed K. H. Mubarak, Ehab K.O., Ali Jabbar Radhi: Synthesis and Study Biological Activity of Gemcitabine Linked Heterocyclic Hybrids, *Research J. Pharm. and Tech.* 2020; 13(7): 3257-3261.

31. Ali Jabbar Radhi, Dhurgham Qasim Shaheed, Mohammed Hamza Heriz, Zeyad Kadhim Olewi, Preparation and Study Biological Activity of Polybarbiturate Linked Tetrazole Ring, *Research J. Pharm. and Tech.* 2021, 14(6):3377-3379.

32. Iqbal MA et al (2013) Potential of silver against human colon cancer:(synthesis, characterization and crystal structures of xylyl (Ortho, meta, & Para) linked bis-benzimidazolium salts and Ag (I)–NHC complexes: In vitro anticancer studies). *Chemistry Central Journal*, 7(1): p. 27

33. Ashraf, R., Bhatti, H. N., Iqbal, M. A., & Jamil, Y. (2020). Synthesis of aryl linked binuclear silver N-heterocyclic carbene complexes, DNA interaction study and biological potentials. *Inorganic Chemistry Communications*, 119, 108077.

34. Haque, R. A., Ghadhayeb, M. Z., Budagumpi, S., Salman, A. W., Ahamed, M. B. K., & Majid, A. M. S. A. (2013). Non-symmetrically substituted N-heterocyclic carbene–Ag (I) complexes of benzimidazol-2-ylidenes: Synthesis, crystal structures, anticancer activity and transmetallation studies. *Inorganica Chimica Acta*, 394, 519-525.

35. Haque, R. A., Choo, S. Y., Budagumpi, S., Iqbal, M. A., & Abdullah, A. A. A. (2015). Silver (I) complexes of mono- and bidentate N-heterocyclic carbene ligands: Synthesis, crystal structures, and in vitro antibacterial and anticancer studies. *European journal of medicinal chemistry*, 90, 82-92.

36. Atif, M., Bhatti, H. N., Haque, R. A., Iqbal, M. A., Ahamed Khadeer, M. B., & Majid, A. M. S. A. (2020). Synthesis, structure, and anticancer activity of symmetrical and non-symmetrical silver (I)–N-heterocyclic carbene complexes. *Applied Biochemistry and Biotechnology*, 191(3), 1171-1189.

37. Haziz, U. F., Haque, R. A., Amirul, A. A., Shaheeda, N., & Razali, M. R. (2016). Synthesis, structures and antibacterial studies of non-functionalized and nitrile-functionalized bis-benzimidazolium salts and respective dinuclear silver (I)–N-heterocyclic carbene complexes. *Polyhedron*, 117, 628-636.

38. Gümüřada, R., Guenay, M. E., Özdemir, N., & Cetinkaya, B. (2016). Bicyclic N-heterocyclic carbene (NHC) ligand precursors and their palladium complexes. *Journal of Coordination Chemistry*, 69(9), 1463-1472.
39. Kamal A, Iqbal MA, Bhatti HN (2018) Therapeutic applications of selenium-derived compounds. *Rev Inorg Chem* 38(2):49–76
40. Habib A, Iqbal MA, Bhatti HN (2019) Polynuclear Ag (I)-N-heterocyclic carbene complexes: synthesis, electrochemical and in vitro anticancer study against human breast cancer and colon cancer. *J Coord Chem* 72(12):2065–2079 Page 13/16
41. Karatař, M. O., Olgundeniz, B., Günal, S., Özdemir, İ., Alıcı, B., & Çetinkaya, E. (2016). Synthesis, characterization and antimicrobial activities of novel silver (I) complexes with coumarin substituted N-heterocyclic carbene ligands. *Bioorganic & Medicinal Chemistry*, 24(4), 643-650.
42. Streciwilk, W., Cassidy, J., Hackenberg, F., Müller-Bunz, H., Paradisi, F., & Tacke, M. (2014). Synthesis, cytotoxic and antibacterial studies of p-benzyl-substituted NHC–silver (I) acetate compounds derived from 4, 5-di-p-diisopropylphenyl-or 4, 5-di-p-chlorophenyl-1H-imidazole. *Journal of Organometallic Chemistry*, 749, 88-99.
43. řenkardeř S et al řenkardeř, S., İhsan Han, M., Gürboęa, M., Özakpınar, Ö. B., & Güniz Küçükğüzel, ř. (2022). Synthesis and anticancer activity of novel hydrazone linkage-based aryl sulfonate derivatives as apoptosis inducers. *Medicinal Chemistry Research*, 31(2), 368-379.