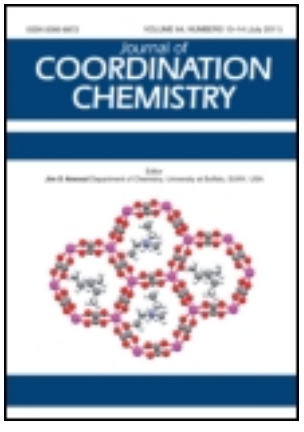

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Synthesis and antimicrobial studies of 1-methyl-2-dimethylaminoethyl-substituted benzimidazolium salts and N-heterocyclic carbene-silver complexes

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Synthesis and antimicrobial studies of 1-methyl-2-dimethylaminoethyl-substituted benzimidazolium salts and *N*-heterocyclic carbene–silver complexes

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The synthesis and antimicrobial studies of 1-methyl-2-dimethylaminoethyl-substituted carbene precursors and silver complexes are reported. The carbene precursors (**1a–d**) have been prepared from 1-methyl-2-dimethylaminoethyl-substituted benzimidazole and various alkyl halides. The silver–NHC complexes (**2a–d**) were synthesized from the benzimidazolium salts and Ag_2O in dichloromethane at room temperature. The new compounds were characterized by ^1H NMR, ^{13}C NMR, FT-IR, and elemental analyses. The new carbene precursors and Ag-complexes were tested for their *in vitro* antimicrobial activity against a variety of Gram-positive and Gram-negative bacteria, as well as for their antifungal activities against *Candida albicans* and *Candida tropicalis*.

Keywords: *N*-heterocyclic carbene; Benzimidazolium salts; Silver; Antimicrobial; Medical inorganic chemistry

1. Introduction

The coordination chemistry of *N*-heterocyclic carbenes (NHCs) has developed significantly since the isolation and first complexation studies of stable NHCs by Arduengo in the early 1990s [1–3]. NHC complexes exhibit excellent catalytic activity for many useful organic transformations, notably C–C and C–N cross-coupling reactions, C–H bond activation, and metathesis [4–19]. Silver NHC complexes have particular interest because of their wide use as ligand transfer agents to group 8–10 metals, catalysis, nanomaterials, and also biological activity as antimicrobial agents [20–37]. Ag–NHC complexes are easily prepared by three different procedures: (i) reaction of azolium salts with silver bases such as Ag_2O, Ag_2CO_3, and AgOAc; (ii) reaction of free NHC silver salts; and (iii) reaction of azolium salts with silver salts

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under basic phase transfer conditions [38–40]. Among these approaches, route (i) is more convenient and most frequently used.

We have previously reported antibacterial and antifungal properties of ruthenium(II) carbene complexes, azolium salts, and neutral 2-aryl derivatives of benzimidazole, benzothiazole, and benzoxazole [41, 42]. Herein we report the synthesis and antimicrobial activities of 1-methyl-2-dimethylaminoethyl-substituted benzimidazolium salts (**1a–d**) and their silver complexes (**2a–d**).

2. Experimental

2.1. *Materials and methods*

All preparations of 1,3-dialkylbenzimidazolium salts **1a–d** and silver–carbene complexes **2a–d** were performed under argon using standard Schlenk techniques and dry solvents. All chemicals were purchased from Aldrich Chemical Co. ^{1}H and ^{13}C NMR spectra were taken using a Bruker AC300P FT spectrometer operating at 300.13 MHz (^{1}H), 75.47 MHz (^{13}C). Chemical shifts (δ) are given in ppm relative to TMS and coupling constants (J) in Hz. FT-IR spectra were recorded on a Mattson 1000 spectrophotometer as wavenumbers in cm^{-1}. Melting points were measured in open capillary tubes with an Electrothermal-9200 melting point apparatus and are uncorrected. Elemental analyses were performed by TUBİTAK Microlab (Ankara, Turkey).

Minimal inhibitory concentration for each compound was investigated against standard bacterial strains: *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 27853). These were obtained from the American Type Culture Collection (Rockville, MD, USA). The fungal strains *Candida albicans* and *Candida tropicalis* were obtained from the Department of Microbiology, Faculty of Medicine, Ege University (Turkey). Bacterial strains were subcultured on Muller Hinton Broth (HiMedia Laboratories Pvt. Ltd, Mumbai, India) and fungal strains were also on RPMI 1640 Broth (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany).

2.2. *General procedure for the preparation of the 1,3-dialkylbenzimidazolium salts (1a–d)*

Alkyl halides (1 mmol) were added slowly to a solution of 1-(1-methyl-2-dimethylaminoethyl)benzimidazole (1 mmol) in DMF (4 mL) at 25°C. The reaction mixture was stirred at room temperature for 1 h and then heated for 12 h at 60°C. Diethyl ether (10 mL) was added to obtain a white crystalline solid, which was filtered off. The solid was washed with diethyl ether (3 × 10 mL), dried under vacuum, and recrystallized from EtOH/Et_2O (1 : 2) at room temperature.

2.2.1. 1-(1-Methyl-2-dimethylaminoethyl)-3-benzylbenzimidazolium chloride (1a). Yield: 85%, m.p.: 218–219°C, IR $\nu_{(NCN)}$: 1562 cm^{-1}. Anal. Calcd for $C_{19}H_{24}N_3Cl$ (%): C, 69.18; H, 7.33; N, 12.74. Found: C, 69.19; H, 7.35; N, 12.72. ^{1}H NMR

(δ, $CDCl_3$): 1.13 (d, 3H, $J_{HH} = 6.6$ Hz, $CH(CH_3)CH_2N(CH_3)_2$), 2.31 (s, 6H, $CH(CH_3)CH_2N(CH_3)_2$), 3.28 (m, 1H, $CH(CH_3)CH_2N(CH_3)_2$), 4.50, 4.67 (m, 2H, $CH(CH_3)CH_2N(CH_3)_2$), 5.89 (s, 2H, $CH_2C_6H_5$), 7.26, 7.80 (m, 9H, Ar–*H*), 11.45 (s, 1H, NC*H*N). ^{13}C {H} NMR (δ, $CDCl_3$): 9.7, 40.3, 49.5, 51.2 ($CH(CH_3)CH_2N(CH_3)_2$), 57.9 ($CH_2C_6H_5$), 113.1, 113.6, 126.8, 126.9, 128.0, 128.1, 129.0, 129.2, 130.8, 131.6, 133.1 (Ar–*C*), 144.4 (N*C*HN).

2.2.2. 1-(1-Methyl-2-dimethylaminoethyl)-3-(2,4,6-trimethylbenzyl)benzimidazolium chloride (1b). Yield: 91%, m.p.: 208–209°C, IR $\nu_{(NCN)}$: 1563 cm^{-1}. Anal. Calcd for $C_{22}H_{30}N_3Cl$ (%): C, 71.04; H, 8.13; N, 11.30. Found: C, 71.07; H, 8.14; N, 11.32. ^{1}H NMR (δ, $CDCl_3$): 1.10 (d, 3H, $J_{HH} = 8.7$ Hz, $CH(CH_3)CH_2N(CH_3)_2$), 2.31 (s, 6H, $CH(CH_3)CH_2N(CH_3)_2$), 3.25 (m, 1H, $CH(CH_3)CH_2N(CH_3)_2$), 2.27, 2.31 (s, 9H, $CH_2C_6H_2(CH_3)_3$-2,4,6), 4.56, 4.75 (m, 2H, $CH(CH_3)CH_2N(CH_3)_2$), 5.78 (s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6), 6.91 (s, 2H, $CH_2C_6H_2(CH_3)_3$-2,4,6), 7.25, 7.84 (m, 4H, Ar–*H*), 10.88 (s, 1H, NC*H*N). ^{13}C{H} NMR (δ, $CDCl_3$): 9.5, 40.1, 47.0, 49.1 ($CH(CH_3)CH_2N(CH_3)_2$), 20.0, 21.0 ($CH_2C_6H_2(CH_3)_3$-2,4,6), 57.9 ($CH_2C_6H_2(CH_3)_3$-2,4,6), 113.1, 113.6, 125.3, 126.8, 126.9, 130.1, 131.1, 131.7, 137.9, 139.6 (Ar–*C*), 144.3 (N*C*HN).

2.2.3. 1-(1-Methyl-2-dimethylaminoethyl)-3-(2,3,5,6-tetramethylbenzyl)benzimidazolium chloride (1c). Yield: 88%, m.p.: 247–248°C, IR $\nu_{(NCN)}$: 1558 cm^{-1}. Anal. Calcd for $C_{23}H_{32}N_3Cl$ (%): C, 71.57; H, 8.36; N, 10.89. Found: C, 71.56; H, 8.34; N, 10.90. ^{1}H NMR (δ, $CDCl_3$): 1.09 (d, 3H, $J_{HH} = 6.6$ Hz, $CH(CH_3)CH_2N(CH_3)_2$), 2.16 (s, 6H, $CH(CH_3)CH_2N(CH_3)_2$), 3.44 (m, 1H, $CH(CH_3)CH_2N(CH_3)_2$), 2.16, 2.25 (s, 12H, $CH_2C_6H(CH_3)_4$-2,3,5,6), 4.47 (m, 2H, $CH(CH_3)CH_2N(CH_3)_2$), 5.78 (s, 2H, $CH_2C_6H(CH_3)_4$-2,3,5,6), 7.15 (s, 1H, $CH_2C_6H(CH_3)_4$-2,3,5,6), 7.71, 8.22 (m, 4H, Ar–*H*), 8.94 (s, 1H, NC*H*N). ^{13}C {H} NMR (δ, $CDCl_3$): 9.2, 19.0, 46.3, 48.7 ($CH(CH_3)CH_2N(CH_3)_2$), 15.7, 20.6 ($CH_2C_6H_2(CH_3)_3$-2,3,5,6), 56.7 ($CH_2C_6H_2(CH_3)_3$-2,3,5,6), 114.3, 114.4, 126.9, 127.2, 129.1, 131.7, 131.9, 133.9, 134.8 (Ar–*C*), 142.2 (N*C*HN).

2.2.4. 1-(1-Methyl-2-dimethylaminoethyl)-3-(2,3,4,5,6-pentamethylbenzyl)benzimidazolium chloride (1d). Yield: 92%, m.p.: 258–259°C, IR $\nu_{(NCN)}$: 1561 cm^{-1}. Anal. Calcd for $C_{24}H_{34}N_3Cl$ (%): C, 72.06; H, 8.57; N, 10.51. Found: C, 72.08; H, 8.53; N, 10.56. ^{1}H NMR (δ, $CDCl_3$): 1.19 (d, 3H, $J_{HH} = 6.6$ Hz, $CH(CH_3)CH_2N(CH_3)_2$), 2.02 (s, 6H, $CH(CH_3)CH_2N(CH_3)_2$), 2.73 (m, 1H, $CH(CH_3)CH_2N(CH_3)_2$), 2.16, 2.26 (s, 15H, $CH_2C_6(CH_3)_5$-2,3,4,5,6), 4.75, 5.03 (m, 2H, $CH(CH_3)CH_2N(CH_3)_2$), 5.73 (s, 2H, $CH_2C_6(CH_3)_5$-2,3,4,5,6), 7.28, 8.36 (m, 4H, Ar–*H*), 9.26 (s, 1H, NC*H*N). ^{13}C {H} NMR (δ, $CDCl_3$): 10.3, 17.2, 46.9, 48.3 ($CH(CH_3)CH_2N(CH_3)_2$), 16.9, 17.2, 17.5 ($CH_2C_6(CH_3)_5$-2,3,4,5,6), 58.4 ($CH_2C_6(CH_3)_5$-2,3,4,5,6), 114.4, 114.5, 126.3, 127.2, 127.3, 131.9, 132.2, 133.2, 134.4, 136.7 (Ar–*C*), 142.5 (N*C*HN).

2.3. *General method for preparation of Ag(I)–NHC complexes (2a–d)*

A solution of benzimidazolium salt (1.0 mmol), Ag_2O (0.5 mmol), and activated 4 Å molecular sieves in dichloromethane (20 mL) was stirred at room temperature for 24 h

in the dark. The reaction mixture was filtered through Celite and solvent removed under reduced pressure. The crude product was recrystallized from dichloromethane/hexane at room temperature.

2.3.1. Chloro-[1-(1-methyl-2-dimethylaminoethyl)-3-benzylbenzimidazol-2-ylidene]silver (I) (2a). Yield: 76%, m.p.: 174–175°C, IR $\nu_{(CN)}$: 1602 cm^{-1}. Anal. Calcd for $C_{19}H_{23}N_3AgCl$ (%): C, 52.25; H, 5.31; N, 9.62. Found: C, 52.23; H, 5.30; N, 9.65. ^{1}H NMR (δ, d-DMSO): 1.06 (d, 3H, $J_{HH} = 6.6$ Hz, CH(CH_3)CH$_2$N(CH$_3$)$_2$), 2.35 (s, 6H, CH(CH$_3$)CH$_2$N(CH_3)$_2$), 3.21 (heks., $J_{HH} = 6.6$ Hz, 1H, CH(CH$_3$)CH$_2$N(CH$_3$)$_2$), 4.26, 4.55 (m, 2H, CH(CH$_3$)CH_2N(CH$_3$)$_2$), 5.63 (s, 2H, CH_2C$_6$H$_5$), 7.23, 7.40 (m, 9H, Ar–H). ^{13}C {H} NMR (δ, d-DMSO): 11.4, 41.0, 52.4, 52.5 (*C*H(*C*H$_3$)*C*H$_2$N(*C*H$_3$)$_2$), 59.1 (*C*H$_2$C$_6$H$_5$), 111.6, 112.2, 124.2, 128.1, 129.1, 129.3, 133.5, 134.4, 134.9 (Ar–*C*).

2.3.2. Chloro-[1-(1-methyl-2-dimethylaminoethyl)-3-(2,4,6-trimethylbenzyl]benzimidazol-2-ylidene]silver (I) (2b). Yield: 80%, m.p.: 168–169°C, IR $\nu_{(NCN)}$: 1611 cm^{-1}. Anal. Calcd for $C_{22}H_{29}N_3AgCl$ (%): C, 55.19; H, 6.10; N, 8.78. Found: C, 55.21; H, 6.11; N, 8.80. ^{1}H NMR (δ, d-DMSO): 0.94 (d, 3H, $J_{HH} = 6.9$ Hz, CH(CH_3)CH$_2$N(CH$_3$)$_2$), 2.30 (s, 6H, CH(CH$_3$)CH$_2$N(CH_3)$_2$), 3.18 (heks., 1H, $J_{HH} = 6.9$ Hz, 1H, CH(CH$_3$)CH$_2$N(CH$_3$)$_2$), 2.24, 2.36 (s, 9H, CH$_2$C$_6$H$_2$(CH_3)$_3$-2,4,6), 4.21, 4.45 (m, 2H, CH(CH$_3$)CH_2N(CH$_3$)$_2$), 5.53 (s, 2H, CH_2C$_6$H$_2$(CH$_3$)$_3$-2,4,6), 6.98 (s, 2H, CH$_2$C$_6$$H_2$(CH$_3$)$_3$-2,4,6), 7.22, 7.41 (m, 4H, Ar–H). ^{13}C {H} NMR (δ, d-DMSO): 11.4, 41.9, 48.1, 52.7 (*C*H(*C*H$_3$)*C*H$_2$N(*C*H$_3$)$_2$), 20.4, 21.2 (CH$_2$C$_6$H$_2$(*C*H$_3$)$_3$-2,4,6), 59.1 (*C*H$_2$C$_6$H$_2$(CH$_3$)$_3$-2,4,6), 111.5, 111.8, 124.0, 124.1, 126.8, 130.1, 130.3, 134.3, 137.5, 139.4 (Ar–*C*).

2.3.3. Chloro-[1-(1-methyl-2-dimethylaminoethyl)-3-(2,3,5,6-tetramethylbenzyl)-benzimidazol-2-ylidene]silver (I) (2c). Yield: 77%, m.p.: 158–159°C, IR $\nu_{(NCN)}$: 1602 cm^{-1}. Anal. Calcd for $C_{23}H_{31}N_3AgCl$ (%): C, 56.05; H, 6.34; N, 8.53. Found: C, 56.03; H, 6.35; N, 8.49. ^{1}H NMR (δ, d-DMSO): 0.97 (d, 3H, $J_{HH} = 6.6$ Hz, CH(CH_3)CH$_2$N(CH$_3$)$_2$), 2.29 (s, 6H, CH(CH$_3$)CH$_2$N(CH_3)$_2$), 3.16 (heks., 1H, $J_{HH} = 6.9$ Hz, CH(CH$_3$)CH$_2$N(CH$_3$)$_2$), 2.15, 2.16 (s, 12H, CH$_2$C$_6$H(CH_3)$_4$-2,3,5,6), 4.16, 4.41 (m, 2H, CH(CH$_3$)CH_2N(CH$_3$)$_2$), 5.51 (s, 2H, CH_2C$_6$H(CH$_3$)$_4$-2,3,5,6), 7.11, 7.75 (m, 5H, Ar–H). ^{13}C {H} NMR (δ, d-DMSO): 11.5, 40.9, 47.8, 52.9 (*C*H(*C*H$_3$)*C*H$_2$N(*C*H$_3$)$_2$), 16.2, 20.7 (CH$_2$C$_6$H(*C*H$_3$)$_4$-2,3,5,6), 59.0 (*C*H$_2$C$_6$H(CH$_3$)$_4$-2,3,5,6), 111.5, 112.9, 124.0, 124.2, 126.7, 128.8, 131.2, 133.5, 134.1, 135.0, 135.3, 143.8 (Ar–*C*).

2.3.4. Chloro-[1-(1-methyl-2-dimethylaminoethyl)-3-(2,3,4,5,6-pentamethylbenzyl)-benzimidazol-2-ylidene]silver (I) (2d). Yield: 82%, m.p.: 188–189°C, IR $\nu_{(NCN)}$: 1604 cm^{-1}. Anal. Calcd for $C_{24}H_{33}N_3AgCl$ (%): C, 56.87; H, 6.56; N, 8.29. Found: C, 56.85; H, 6.59; N, 8.30. ^{1}H NMR (δ, d-DMSO): 0.92 (d, 3H, $J_{HH} = 6.6$ Hz, CH(CH_3)CH$_2$N(CH$_3$)$_2$), 2.00 (s, 6H, CH(CH$_3$)CH$_2$N(CH_3)$_2$), 2.97 (heks., 1H, $J_{HH} = 6.8$ Hz, CH(CH$_3$)CH$_2$N(CH$_3$)$_2$), 2.18, 2.23 (s, 15H, CH$_2$C$_6$(CH_3)$_5$-2,3,4,5,6), 4.32, 4.46 (m, 2H, CH(CH$_3$)CH_2N(CH$_3$)$_2$), 5.74 (s, 2H, CH_2C$_6$(CH$_3$)$_5$-2,3,4,5,6), 7.42, 8.16

(m, 4H, Ar–*H*). ^{13}C {H} NMR (δ, d-DMSO): 11.3, 40.0, 47.3, 51.9 ($CH(CH_3)CH_2N(CH_3)_2$), 16.6, 17.4 ($CH_2C_6(CH_3)_5$-2,3,4,5,6), 57.6 ($CH_2C_6(CH_3)_5$-2,3,4,5,6), 112.6, 114.3, 124.4, 126.1, 126.9, 127.1, 131.6, 132.0, 133.4, 134.2, 135.7, 136.7, 141.8 (Ar–*C*).

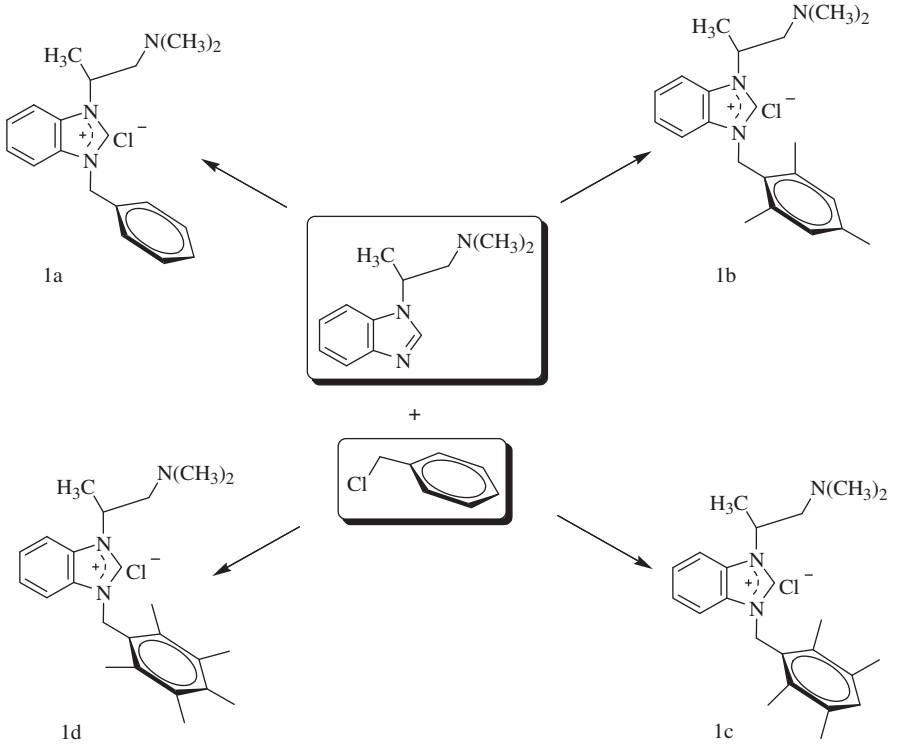
2.4. *Antimicrobial activity*

The antimicrobial activities of the Ag–NHC complexes were determined by using agar dilution procedure recommended by the Clinical and Laboratory Standards Institute [43, 44]. Minimal inhibitory concentrations for each compound were investigated against standard bacterial strains, *S. aureus*, *E. faecalis*, *E. coli*, and *P. aeruginosa* and fungal strains, *C. albicans* and *C. tropicalis*. Their turbidities matched that of a McFarland no. 0.5 Turbidity Standard. The stock solution of all compounds was prepared in DMSO. All dilutions were carried out with distilled water. The concentrations of the tested compounds were 800, 400, 200, 100, 50, 25, 12.5, and 6.25 μg mL^{-1}. Ampicillin and ciprofloxacin were used as antibacterial standard drugs, while fluconazole was used as antifungal standard drug whose minimum inhibitory concentration (MIC) values are provided. A loopful (0.01 mL) of the standardized inocula of the bacteria and yeasts (10^6 CFUs mL^{-1}) was spread over the surface of agar plates. All were inoculated after 16–20 h of incubation for bacteria and 48 h for yeasts. The lowest concentration of the compounds that prevented visible growth was considered to be the MIC.

3. Results and discussion

3.1. *Synthesis and characterization of benzimidazolium salts (1a–d)*

1-Methyl-2-dimethylaminoethyl-substituted benzimidazolium salts **1a–d** are conventional NHC precursors. The functionalized benzimidazolium salts **1a–d** were synthesized by consecutive alkylation of 1-(1-methyl-2-dimethylaminoethyl)benzimidazole (scheme 1). The salts (**1a–d**) were obtained in almost quantitative yield by quarternazition of 1-(1-methyl-2-dimethylaminoethyl)benzimidazole in DMF with a variety of alkyl halides. The salts are stable to air and moisture both in the solid state and in solution. The structures of **1a–d** were established by spectroscopic data and elemental analyses (see section 2). The ^{1}H NMR spectra of the benzimidazolium salts further supported the assigned structures; the resonances for C(2)–H were observed as sharp singlets at 11.45, 10.88, 8.94, and 9.26 ppm, respectively, for **1a–d**. ^{13}C NMR chemical shifts were consistent with the proposed structures; the imino carbon are typical singlets in the ^{1}H-decoupled mode at 144.4, 144.3, 142.2, and 142.5 ppm, respectively, for benzimidazolium chlorides **1a–d**. The IR data for benzimidazolium salts **1a–d** clearly indicate the presence of –C=N– with a ν(C=N) at 1562, 1563, 1558, and 1561 cm^{-1}, respectively, for **1a–d**. The NMR and IR values are similar to results of other 1,3-dialkylbenzimidazolium salts [45, 46].



Scheme 1. Synthesis of 1-(1-methyl-2-dimethylaminoethyl)-3-alkylbenzimidazolium salts.

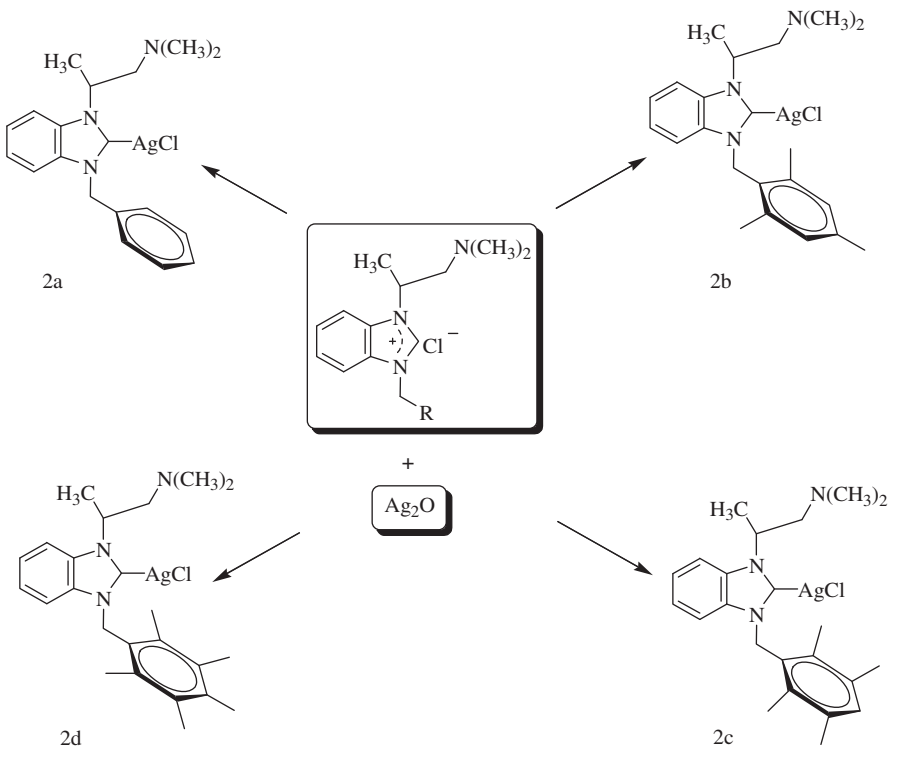
3.2. *Synthesis and characterization of silver–carbene complexes (2a–d)*

The carbene precursor 1-(1-methyl-2-dimethylaminoethyl)-3-alkylbenzimidazolium salts were prepared from 1-methyl-2-dimethylaminoethylbenzimidazole and various alkyl halides. Treatment of the benzimidazolium salts with 0.5 equivalent of Ag_2O in CH_2Cl_2 afforded quantitatively the expected carbenes **2a–d** (scheme 2) after 24 h. Ag–NHCs **2a–d** were obtained as white solids in 76–82% yield. The silver–carbene complexes (**2a–d**) were soluble in halogenated solvent and insoluble in non-polar solvents.

^{1}H and ^{13}C NMR spectra are consistent with the proposed formulae. In the ^{1}H NMR and ^{13}C NMR spectra in d-DMSO, loss of signals for the benzimidazolium proton (NC*H*N) at 11.45, 10.88, 8.94, 9.26 ppm and benzimidazolium carbon (N*C*HN) at 144.4, 144.3, 142.2, 142.5 ppm showed the formation of the expected silver complexes. In **2a–d**, the resonances for carbene carbon were not detected, which has also been mentioned in the literature and given as a reason for the fluxional behavior of NHC complexes [18, 47–51]. Silver–NHC complexes exhibit a characteristic ν(C=N) band at 1602, 1611, 1602, and 1604, respectively, for **2a–d**.

3.3. *Antimicrobial properties of carbene precursors and silver complexes*

The antimicrobial activities reported in terms of MIC values are defined as the lowest concentration of an antimicrobial that visibly inhibits growth of bacteria after overnight



Scheme 2. Synthesis of Ag(I)–NHC complexes.

incubation. Minimal inhibitory concentrations for each compound were investigated against bacterial strains *S. aureus* (ATCC 29213), *E. faecalis* (ATCC 29212), *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853) and fungal strains *C. albicans* and *C. tropicalis*. Antimicrobial activities of the carbene precursors and silver complexes were determined by using agar dilution procedure and tested with different concentrations of the compounds. The MIC of synthesized compounds against Gram-positive, Gram-negative, and fungi are summarized in table 1. Ampicillin, ciprofloxacin, and fluconazole were used as standard drugs for comparison.

As shown in table 1, antimicrobial activities against bacteria and fungi in the carbene precursors (**1a–d**) were 800–100 $\mu g\,mL^{-1}$ and silver complexes 100–50 $\mu g\,mL^{-1}$ concentrations. The silver complexes (**2a–d**) exhibit activity on both bacteria and fungi, but the activities are much poorer than the standards.

Benzimidazolium salt (**1a**) containing benzyl on the *N*-atom showed poor antimicrobial activity against both bacteria and fungi. However, **1b** bearing mesityl methyl group showed activity against bacteria *S. aureus* and *E. faecalis*. The salts (**1c**) and (**1d**) exhibit the same activity against all bacteria. While **1b** and **1d** showed activity (MIC 100 $\mu g\,mL^{-1}$), **1c** showed poor activity against all fungi.

Similar results were observed for the silver complexes; **2b** derived from benzimidazolium salt (**1b**) showed better antibacterial activity (MIC 50 $\mu g\,mL^{-1}$) than **2a**, **2c**, and **2d**. All of the silver–carbene complexes exhibit similar activity against all fungi.

Table 1. MIC ($\mu g\,mL^{-1}$) carbene precursors and silver–NHCs tested against bacterial and fungus.

Ag–NHC	*E. coli*	*S. aureus*	*E. faecalis*	*P. aeruginosa*	*C. albicans*	*C. tropicalis*
1a	800	400	400	800	400	400
1b	800	100	100	800	100	100
1c	800	200	400	800	200	200
1d	800	200	400	800	100	100
2a	50	100	50	50	50	50
2b	50	50	50	50	50	50
2c	50	100	50	50	50	50
2d	50	100	100	100	50	50
Ampicillin	3.12	3.12	1.56	–	–	–
Ciprofloxacin	1.56	0.39	0.78	3.12	–	–
Fluconazole	–	–	–	–	3.12	3.12

From the data obtained in this work, the position of methyl on the aromatic ring may play a crucial role in antimicrobial activity.

4. Conclusions

We have synthesized and characterized carbene precursors and their silver complexes. Antimicrobial activities of the new compounds were investigated for bacteria and fungi. The silver complexes (**2a–d**) showed better activity against all bacteria and fungi than carbene precursors (**1a–d**). Although the mechanism of antimicrobial activity is not known, it was found that substituents on nitrogen have an effect on antimicrobial activity. Detailed investigations focusing on new compound and other biomedical applications are ongoing.

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